Cobalt(III)- and Manganese(I)-Catalyzed C–H and C–C Activations

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Hui Wang

From Anhui (China)

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Thesis Committee

Prof. Dr. Lutz Ackermann, Institute of Organic and Biomolecular Chemistry

Dr. Alexander Breder, Institute of Organic and Biomolecular Chemistry

Members of the Examination Board

Reviewer: Prof. Dr. Lutz Ackermann, Institute of Organic and Biomolecular Chemistry

Second Reviewer: Dr. Alexander Breder, Institute of Organic and Biomolecular Chemistry

Further members of the Examination Board

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Dr. Shoubhik Das, Institute of Organic and Biomolecular Chemistry

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List of Abbreviations

Ac	acetyl
acac	acetyl acetonate
Alk	alkyl
AMLA	ambiphilic metal-ligand activation
aq.	aqueous
Ar	aryl
atm	atmospheric pressure
BHT	2,6-*di*-*tert*-butyl-4-methylphenol
BIES	base-assisted internal electrophilic substitution
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Bu	butyl
Bz	benzoyl
calc.	calculated
cat.	catalytic
CMD	concerted-metalation-deprotonation
conv.	conversion
Cp*	cyclopentadienyl
Cy	cyclohexyl
δ	chemical shift
d	doublet
DCE	1,2-dichloroethane
dd	doublet of doublet
DFT	density functional theory
DG	directing group
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide

DMSO	dimethyl sulfoxide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
dt	doublet of triplet
EI	electron ionization
equiv	equivalent
ES	electrophilic substitution
ESI	electronspray ionization
Et	ethyl
FG	functional group
g	gram
GC	gas chromatography
h	hour
Hal	halogen
Het	hetero atom
Hept	heptyl
Hex	hexyl
HPLC	high performance liquid chromatography
HR-MS	high resolution mass spectrometry
Hz	Hertz
i	*iso*
IR	infrared spectroscopy
IES	internal electrophilic substitution
J	coupling constant
KIE	kinetic isotope effect
L	ligand
m	*meta*
m	multiplet
M	molar
$[M]^+$	molecular ion peak

Me	methyl
Mes	mesityl
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mmol	millimol
M. p.	melting point
MS	mass spectrometry
m/z	mass-to-charge ratio
NCTS	*N*-cyano-4-methyl-*N*-phenyl benzenesulfonamide
NMTS	*N*-cyano-*N*-(4-methoxy)phenyl-*p*-toluenesulfonamide
NMP	*N-methylpyrrolidinone*
NMR	nuclear magnetic resonance
o	*ortho*
OA	oxidative addition
OPV	oil pump vacuum
p	*para*
Ph	phenyl
PMP	*para*-methoxyphenyl
Piv	pivaloyl
ppm	parts per million
Pr	propyl
PTSA	*p*-Toluenesulfonic acid
py	pyridyl
pym	pyrimidine
pyr	pyrazol
q	quartet
RT	room temperature

s	singlet
sat.	saturated
SPS	solvent purification system
t	*tert*
t	triplet
T	temperature
THF	tetrahydrofuran
TLC	thin layer chromatography
TM	transition metal
TMP	2,2,6,6-tetramethylpiperidine
TMS	trimethylsilyl
Ts	*para*-toluenesulfonyl
TS	transition state
wt%	weight by volume

1. Introduction

Life is based on the properties of carbon, which leads to the importance of organic molecules for the various species of living organisms as well as individuals.[1] Most organic molecules have a carbon backbone, whose versatility provides the key skeleton to biomolecule structures. Understanding the chemical structures of organic molecules allows us to understand better the action of life and modification of them. The range of applications of organic molecules is enormous, which are widely found in pharmaceuticals, agrochemicals, materials, fuels and a vast number of other areas.[2] As a consequence, methods to synthesize these complex molecules are highly desired not only in fundamental research but also in pharmaceutical and fine chemical industries. In modern synthetic chemistry, the main challenges are how to seek efficient, green and economic ways to construct chemical bonds from simple precursors.

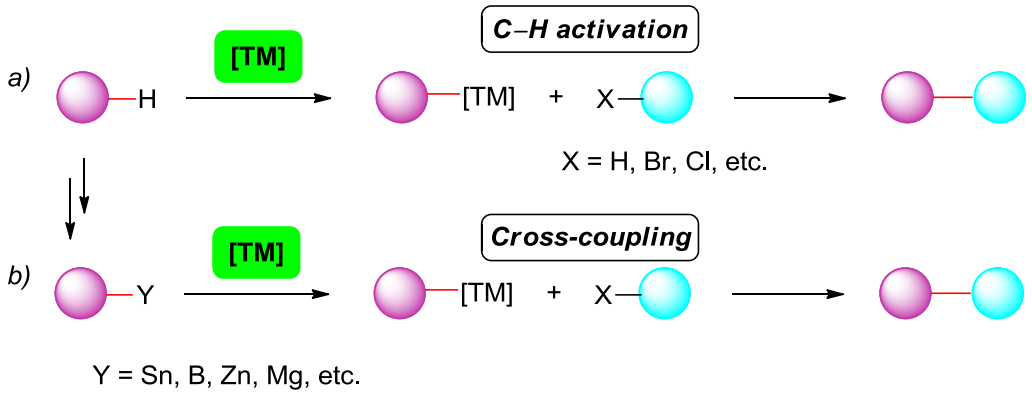
Hydrocarbons are organic compounds consisting of hydrogen and carbon, which could be found in crude oil and natural gas. The efficiency of the transformation process of hydrocarbons into other more useful and high value organic molecules, such as alcohols, ketones and acids, is of high importance in chemical industies.[3] C–H bonds are ubiquitous in organic molecules. Thus, from an atom- and step-economic point of view, the direct functionalization of C–H bonds to C–C and C–Het (Het = N, O, P, S, Si, etc.) bonds has emerged as one of the most straightforward and valuable approaches in organic synthesis.

Catalysis is one of the foundations of the chemical industry. Significant successes in this field of chemistry have already been achieved on solving numerous economic, environmental and technological problems during the last century.[4] Furthermore, catalysis is also one of the twelve principles of green chemistry, as defined by Warner and Anastas in 1998.[5] Therefore, the combination of direct C–H activation and catalysis could provide a more effective, atom- and step-economic platform for developing novel products in synthetic chemistry.

1.1 Transition Metal-Catalyzed C–H Functionalizations

1.1.1 The Advantages of Transition Metal-Catalyzed C–H Activation

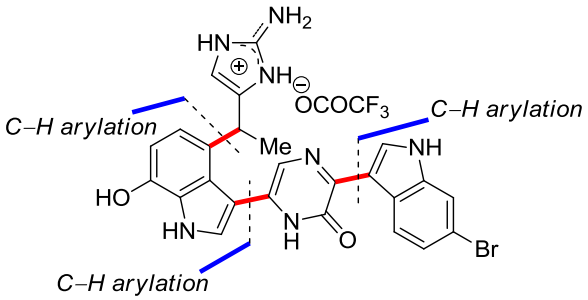
The direct catalyzed C–H functionalization is a highly important method, as it allows the conversion of C–H bonds into valuable C–C and C–Het bonds. However, the main question is how to directly activate the C–H bond. It is well known that the dissociation energy of C–H bond is generally very high (≈ 110 kcal mol^{-1} for C(aryl)–H and ≈ 105 kcal mol^{-1} for alkanes).[6] In early studies the cleavage of C–H bonds often required harsh reaction condition.[7] Therefore, a strategy in which the transition metal catalyst directly reacts with a C–H bond to generate a C–TM bond under mild reaction conditions is an ideal option to achieve C–H functionalization (Scheme 1.1.1a). The resulting C–TM bonds are more reactive than the C–H bonds, and can thus be easily converted to other valuable functional groups. Indeed, the last few decades have witnessed explosive progress in the field of transition metal-catalyzed C–H functionalization.[8]



Scheme 1.1.1 Transition metal-catalyzed C–H functionalization.

It is well known that traditional cross-coupling reactions have been one of the most useful synthetic methods for the formation of carbon-carbon bonds, such as Suzuki-Miyaura, Negishi and Heck reactions, which led to the 2010 Nobel Prize in chemistry.[9] In these transformations, one of the key steps is the generation of the organometallic C–TM species (Scheme 1.1.1b). However, cross coupling reactions heavily rely on the transformations of various functional groups, thus requiring the pre-functionalized substrates, such as organic halides and organometallic compounds, such as highly reactive Grignard reagents. Moreover, some of the reagents are difficult to handle and store,

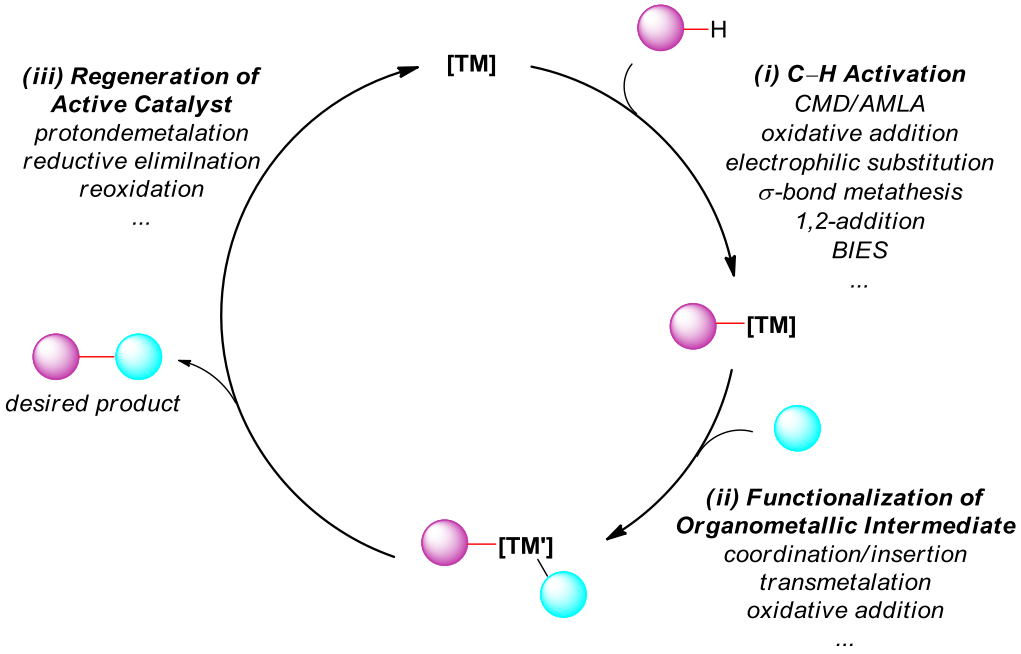
and the generation of stoichiometric amounts of salt wastes, significantly decreases the atom- and step-economy. In sharp contrast, the direct transition metal-catalyzed C–H activation could reduce the steps of those procedures, thus making the reaction cost-effective and environmentally-friendly. As a result, over the last 20 years creative applications of metal-catalyzed C–H functionalizations have been made in the synthesis of natural products, pharmaceuticals, and functional materials, among others.[8] For example, Stoltz and co-workers in 2002 completed the synthesis of dragmacidin D (**1**) in 25 steps,[10] while Yamaguchi and Itami in 2011 achieved it in only 15 steps based on three-fold C–H arylation (Scheme 1.1.2).[11] Therefore, the traditional synthetic methods could be revised by using C–H functionalizations.



Scheme 1.1.2 Example of C–H functionalizations in the total synthesis of natural product.

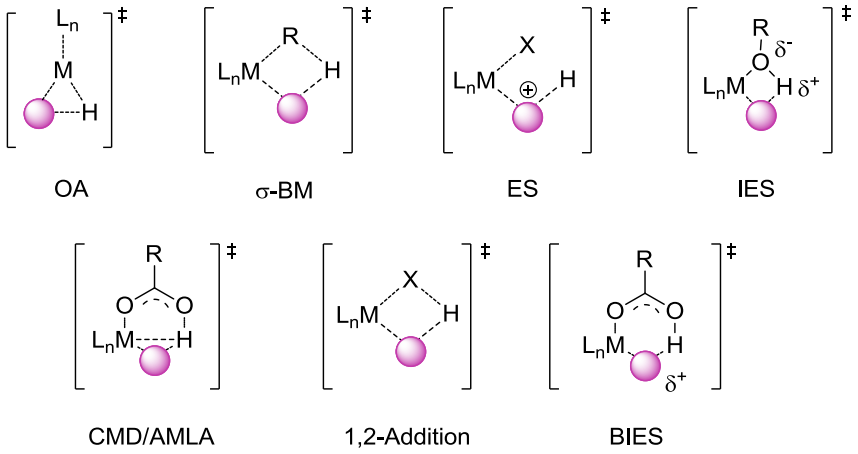
Meanwhile, experimental and computational mechanistic studies for transition metal-catalyzed C–H functionalization have also provided detailed insights into those reactions.[12] In many cases, the great achievements of C–H activation have resulted from the good understanding of the reaction mechanism. Even though the details of reaction mechanism may change from in select cases, the catalytic cycle can be often devided into three main steps (Scheme 1.1.3): (*i*) the C–H activation; (*ii*) functionalization of the organometallic intermediate; and finally, (*iii*) regeneration of the active catalyst, in some cases, if required, an oxidant is needed.

1.1.2 Mechanistic Manifolds



Scheme 1.1.3 General catalytic cycle for transition metal-catalyzed C–H activation reactions.

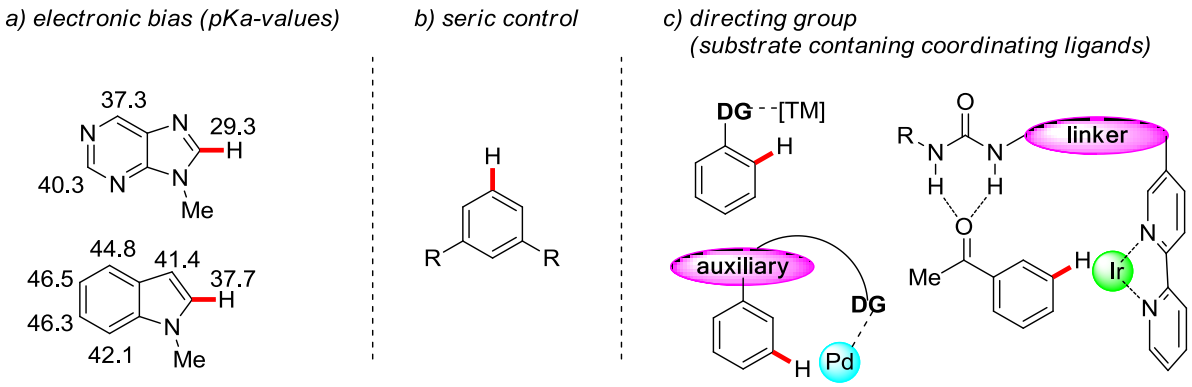
In general terms, the C–H cleavage event is a key step of the mechanism. It is very important to understand how the C–H bond can be cleaved by transition metals. Recent mechanistic studies indicated that several distinct transition states could be involved in the C–H metalation step (Scheme 1.1.4).[13] The possible mechanistic modes of action include: oxidative addition (OA);[14] σ-bond metathesis (σ-BM);[15] electrophilic substitution (ES);[16] 1,2-addition;[17] concerted metalation-deprotonation (CMD),[18] also called ambiphilic metal ligand activation (AMLA);[19] internal electrophilic substitution (IES) based on a four-membered transition state;[20] and base-assisted internal electrophilic substitution (BIES) *via* a six-membered transition state.[21] For example, a cobalt(III)-catalyzed C–H alkylation provided the branched products based on a BIES-type addition, which has been studied by Ackermann and co-workers using detailed experimental and computational methods.[22]



Scheme 1.1.4 Possible transition states for C–H metalation.

1.1.3 Selectivity Control in Transition Metal-Catalyzed C–H Functionalizations

Although the strategy of direct C–H functionalization has enormous potential in synthetic chemistry, there are still some fundamental challenges which have to be addressed. The C–H bonds are ubiquitous in organic molecules and often exhibit similar dissociation energies. Therefore, selective and efficient functionalization of one specific C–H bond is highly challenging. This goal has been identified as the "Holy Grail" of organic synthesis,[23] and several different strategies have been employed to address this issue (Scheme 1.1.5).



Scheme 1.1.5 Strategies to achieve site-selectivity in C–H activation.

The site-selectivity can be controlled by (a) enhancing the acidity of specific C–H bonds,[24] (b) using sterically hindered substrates in combination with catalyst,[25] and (c) using coordinating directing

groups.[26] However, due to the dependency on the substrate substitution patten, the first two strategies are difficult to be widely used in this field. In contrast, a variety of catalytic transformations have been achieved by using directing groups to control the site-selectivities. The directing group can be the part of various different substrates, and in many cases it also can be easily removed after the transformation.[27] Generally, Lewis basic directing atom can coordinate to the metal center and bring the catalyst to a proximal C–H bond. Then, the transition metal can directly activate this C–H bond. Many different transition metals, such as palladium, rhodium, ruthenium and iridium, can undergo this cyclometalation step.[28]

In contrast, the rise of green chemistry has increased the emphasis on low-waste transformations.[29] The same strategy generally could reduce the cost and toxicity of the reaction by employing 3d metals, such as cobalt and manganese.

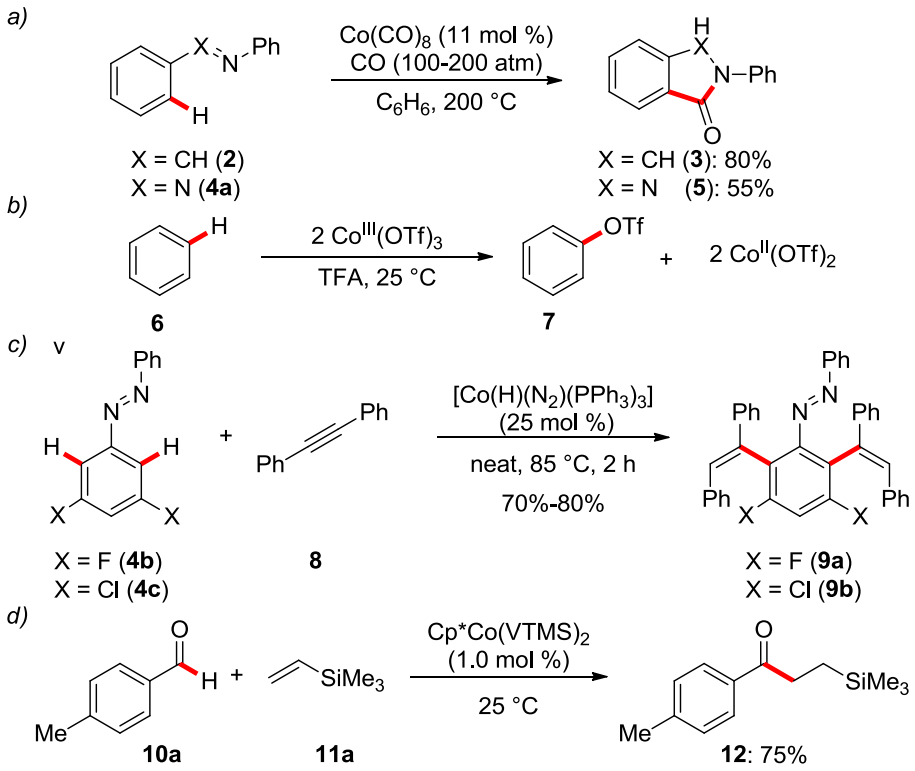
1.2 Cobalt(III)-Catalyzed C–H Activation

Although transition metal-catalyzed C–H functionalization has been considered as one of the most powerful and reliable tools for constructing C–C and C–Het bonds over the last decades, precious metals, such as palladium,[30] rhodium,[31] platinum,[32] ruthenium[33] and iridium[34] have been thus far dominant in this field. However, there are some problems associated with their continuous use in catalytic processes, such as their low natural abundance,[35] high cost and toxicity.[36] In contrast, the inexpensive, Earth-abundant, and low toxic base metals could serve as a suitable alternative to precious metals for C–H activation. As a result, various inexpensive early transition metals have recently attracted much attention in the area of C–H activations. In this regard, cobalt is an attractive candidate because of its unique properties.[37] Compared with 4d transition metals, for example rhodium, cobalt exhibits a lower electronegativity leading to the formation of more nucleophilic intermediates, which could set the stage for unexpected reaction outcomes.

1.2.1 Early Examples of Cobalt-Catalyzed C–H Activations

In 1955, the first example of chelation-assisted cobalt-catalyzed C–H functionalization was disclosed by Murahashi, providing access to phthalimidine **3** or indazolone **5** through the carbonylation/cyclization of Schiff base with $Co_2(CO)_8$ as the catalyst (Scheme 1.2.1a).[38] However,

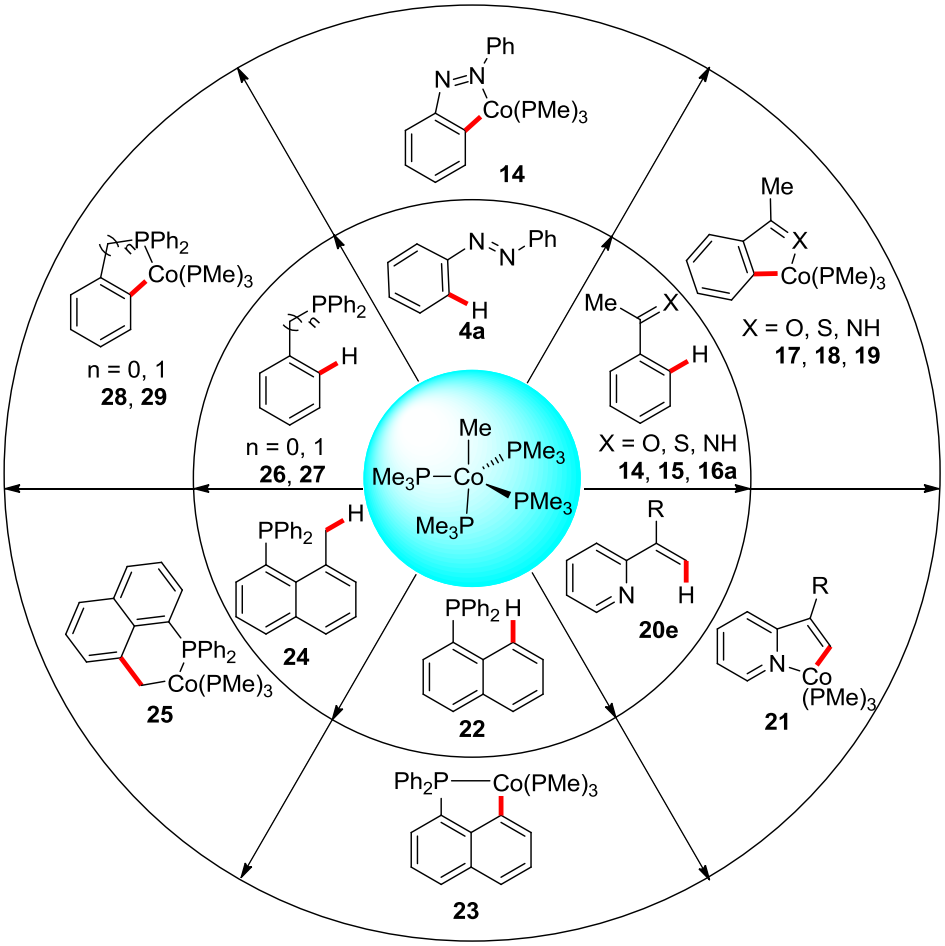
further applications were limited because of the harsh reaction conditions. Until recent years, only few examples have been sporadically reported for cobalt-catalyzed C–H activation. For example, in 1973, Kochi and co-workers reported the first example of high-valent cobalt(III)-mediated trifluoroacetylation of aromatic compounds operating *via* a proposed SET mechanism (Scheme 1.2.1b).[39] And in 1994, Kisch and coworkers developed the alkenylation of alkynes by well-defined cobalt(I) catalysts $[Co(H)(N_2)(PPh_3)_3]$ or $[CoH_3(PPh_3)_3]$ (Scheme 1.2.1c).[40] Subsequently, Brookhart and coworkers developed various Cp*Co(I)-catalyzed C–H functionalizations (Scheme 1.2.1d), including C–H hydroacylation of olefins,[41] synthesis of enamines by C(sp^3)–H bond activation,[42] and C–H activation of simple benzene.[43]



Scheme 1.2.1 Early examples of cobalt-catalyzed/mediated C–H activation.

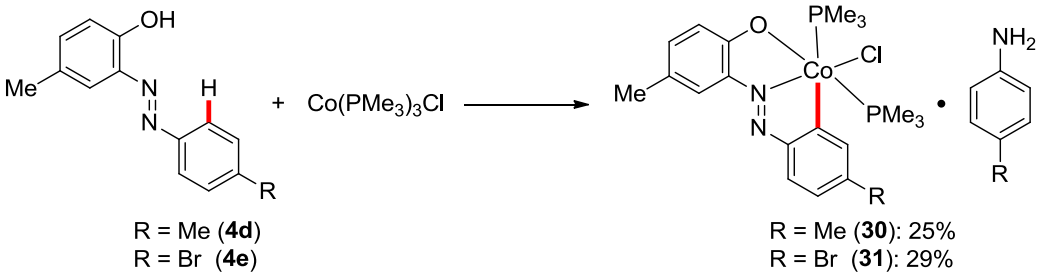
It is noteworthy that a cyclometalated cobalt complex is often the key intermediate in C–H activation catalytic cycles. Thus, the isolation and characterization of such cyclocobaltated complexes are essential to understand the mechanism of these reactions. In 1993, Klein and co-workers isolated the cyclometalated cobalt complex of azobenzene (**4a**) and phenyl phosphites (**14**) with stoichiometric $[Co(CH_3)(PMe_3)_4]$.[44] Later, the cyclometalation could be achieved with various substrates bearing different donor groups, featuring oxygen,[45] nitrogen,[46] sulfur,[47] and

phosphorus[48] (Scheme 1.2.2).



Scheme 1.2.2 Cyclocobaltated complexes prepared by C–H activation using stoichiometric $[Co(CH_3)(PMe_3)_4]$.

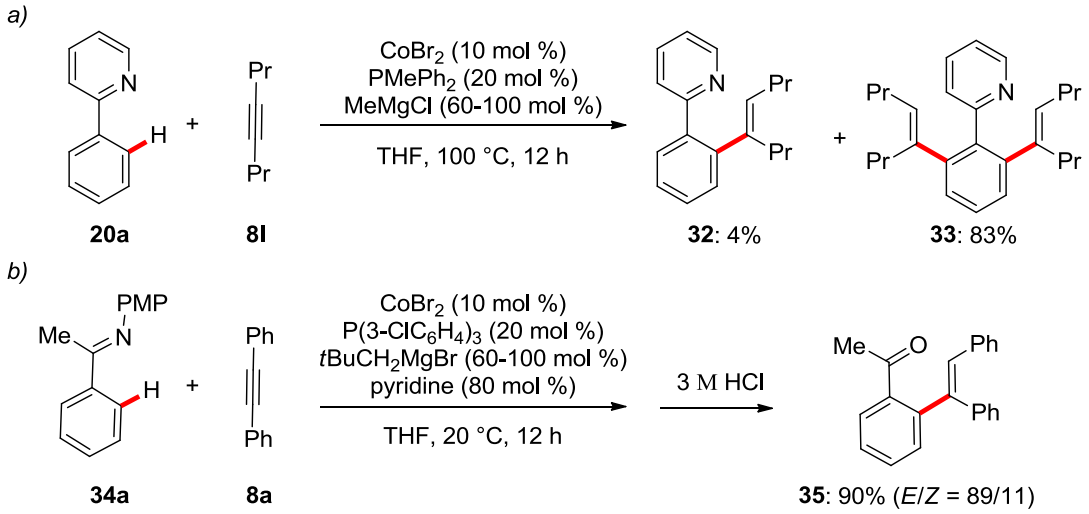
In 2008, Li and Wang also reported a cyclocobaltated complex of azobenzene (**4**) with hydroxyl as an additional donor group using stoichiometric $Co(PMe_3)_3Cl$, along with the complete cleavage of the N=N bond (Scheme 1.2.3).[49]



Scheme 1.2.3 Reaction of $Co(PMe_3)_3Cl$ with 2-(arylazo)phenols for C–H activation.

Based on the Kisch's work, significant contribution was achieved by Yoshikai and coworkers on the

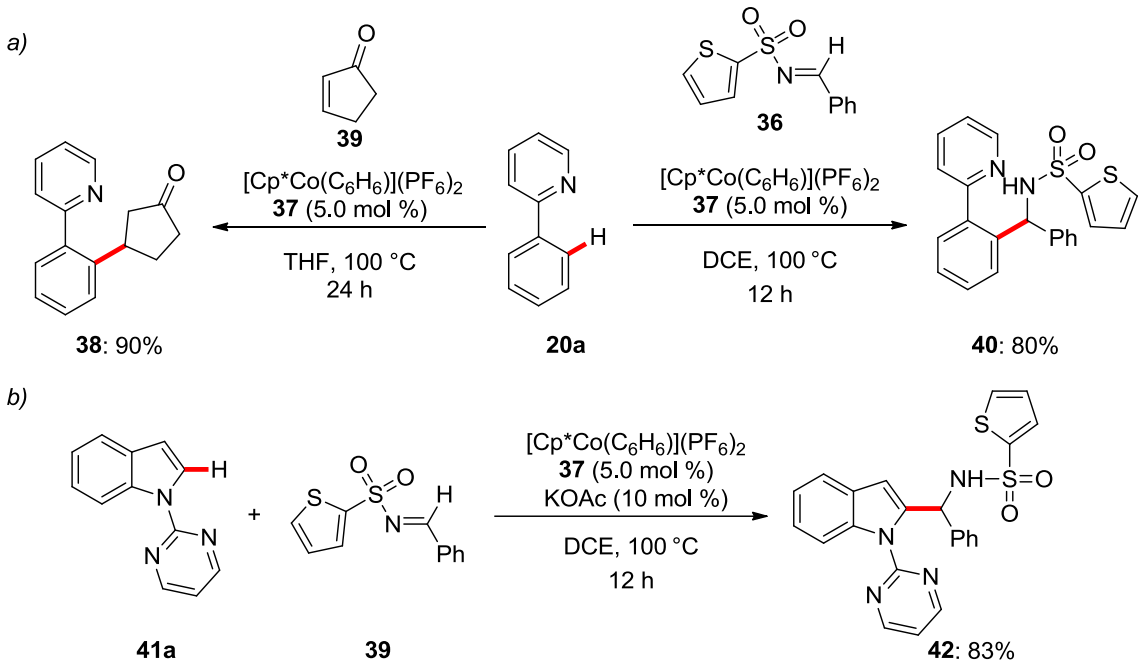
low-valent cobalt-catalyzed hydroarylation of internal alkynes **8** in 2010.[50] The electron-rich cobalt species could be generated *in situ* from the simple cobalt(II) salts, phosphine ligands and Grignard reagents. The role of the Grignard reagent was proposed to serve as a base and a reductant in the reaction (Scheme 1.2.4). Thereafter, the low-valent cobalt-catalyzed C–H functionalizations have been rapidly developed by the groups of Yoshikai,[8a, 51] Nakamura,[52] Ackermann,[53] among others[54] over the last 10 years. However, a disadvantage of this manifold is the requirement of large amount of Grignard reagents, which could make undesired coupling reactions, generate lots of metal wastes, and limit the functional group tolerance. Therefore, the development of new cobalt-catalyzed C–H functionalizations without Grignard reagents under mild reaction conditions was in high demand.



Scheme 1.2.4 Low-valent cobalt-catalyzed hydroarylation of internal alkynes.

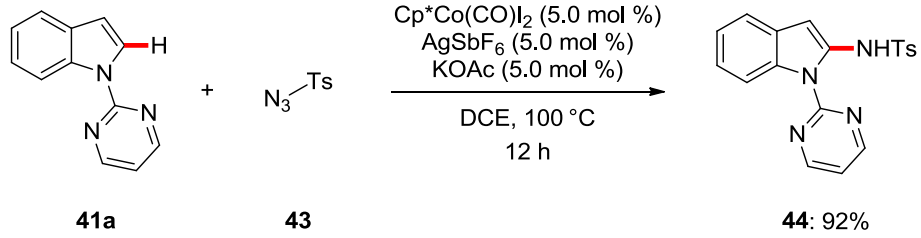
1.2.2 High-Valent Cobalt(III)-Catalyzed C–H Activations

Based on the earlier work of Brookhart,[55] in 2013, a significant advance in high-valent cobalt(III)-catalyzed C–H activation was made by Matsunaga/Kanai and coworkers, which employed a Cp*Co(III)-type complexes as catalysts (Scheme 1.2.5a).[56] This work showed the high catalytic activity of $[Cp^*Co(C_6H_6)](PF_6)_2$ (**37**) in addition reactions of 2-phenylpyridine (**20a**) to sulfonyl imines (**36**) and α,β-unsaturated ketones (**39**). Afterwards, the same auther successfully extended this approach with catalytic amounts of cobalt complex **37** and KOAc to the *N*-(2-pyrimidyl)-indole (**41a**)[57] substrates (Scheme 1.2.5b).[58]



Scheme 1.2.5 Cobalt(III)-catalyzed hydroarylation of electrophiles *via* C–H activation.

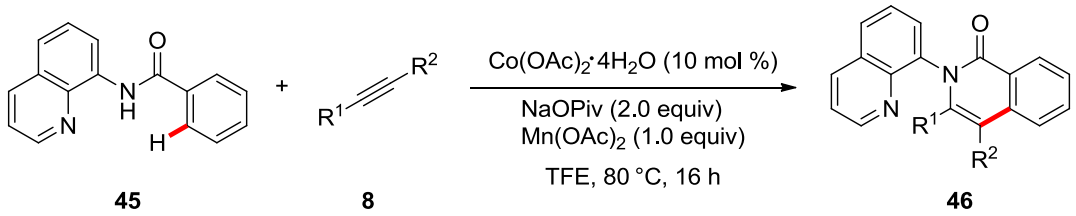
The following year, the same group further developed a more general catalytic system using $Cp^*Co(CO)I_2$ in combination with a silver salt, which displayed a superior activity for C-2 selective C–H amidation of indoles **41a** with sulfonyl azides (**43**) (Scheme 1.2.6).[59] They also disclosed a procedure for preparing the catalyst of $Cp^*Co(CO)I_2$ with slight modification of reported methods.[60]



Scheme 1.2.6 Cobalt(III)-catalyzed C–H amidation.

In 2014, Daugulis and coworkers also developed a new method for the Co(III)-catalyzed C–H alkenylation with alkynes with the aid of aminoquinolines **45** as the directing groups (Scheme 1.2.7).[61] This reaction employed $Co(OAc)_2{\cdot}4H_2O$ as the precatalyst, which then was oxidized *in situ* to the activated Co^{III} species by adding an external chemical oxidant of $Mn(OAc)_2$. This reaction showed high functional group tolerance, and both internal and terminal alkynes were compatible

with the coupling.

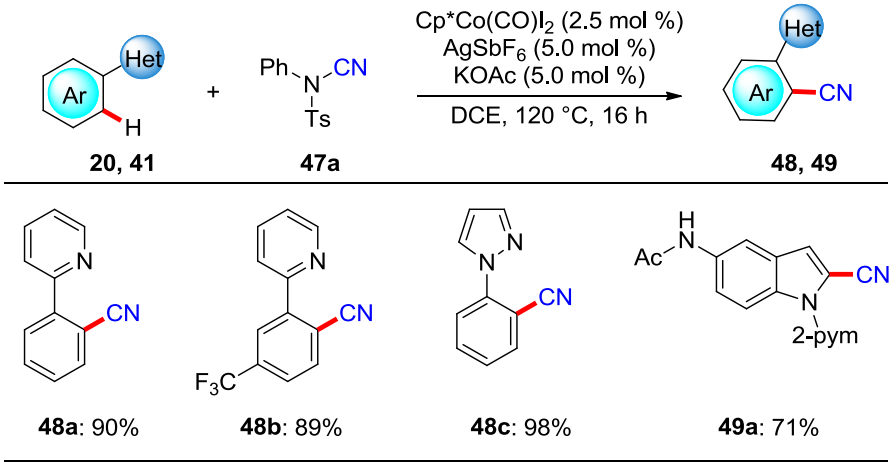


Scheme 1.2.7 Cobalt(III)-catalyzed, aminoquinoline-directed C–H bond alkenylation with alkynes.

Since then, the recent years witnessed a rapid growth in high-valent cobalt(III)-catalyzed C–H functionalizations. The next chapter will discuss some typical examples of the high-valent Cp*Co(III)-catalyzed C–H activation reactions.

1.2.2.1 Cp*Co(III)-Catalyzed Cyanation and Halogenation

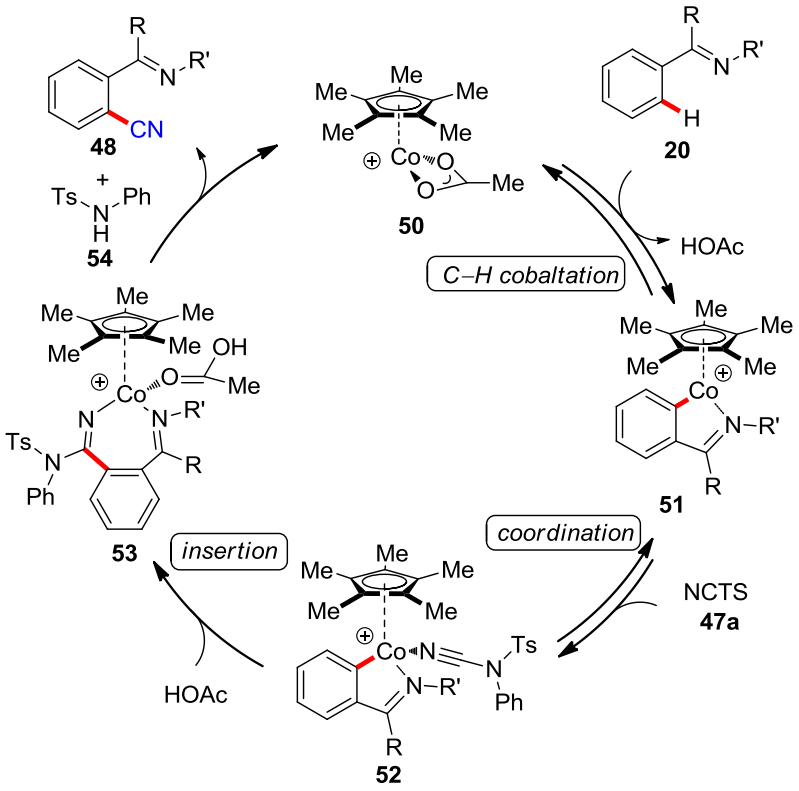
In 2015, Ackermann and coworkers developed the first example of Cp*Co(III)-catalyzed C–H cyanation of 2-phenylpyridines (**20**) and (hetero)arenes with *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS) (**47a**) as the cyanating reagent (Scheme 1.2.8)[62]. This reaction showed high functional group tolerance, as well as high site-selectivity and ample scope. The pyrimidyl group could be easily removed in a traceless fashion.



Scheme 1.2.8 Cobalt(III)-catalyzed C–H cyanation.

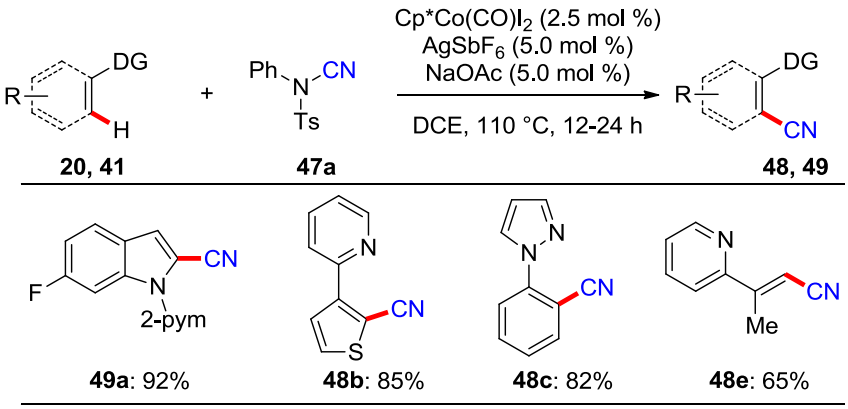
A plausible catalytic cycle was proposed for this cobalt(III)-catalyzed cyanation protocol. After reversible C–H bond cobaltation of substrate **20** resulting from the active cationic cobalt species **50,**

thus generated the cobalt intermediate **51** undergoes coordination and insertion with NCTS (**47a**), and then affords the complex **53**. The desired cyanation product **48** is obtained by β-elimination and the active cobalt(III) catalyst **50** is regenerated by proto-demetalation (Scheme 1.2.9).



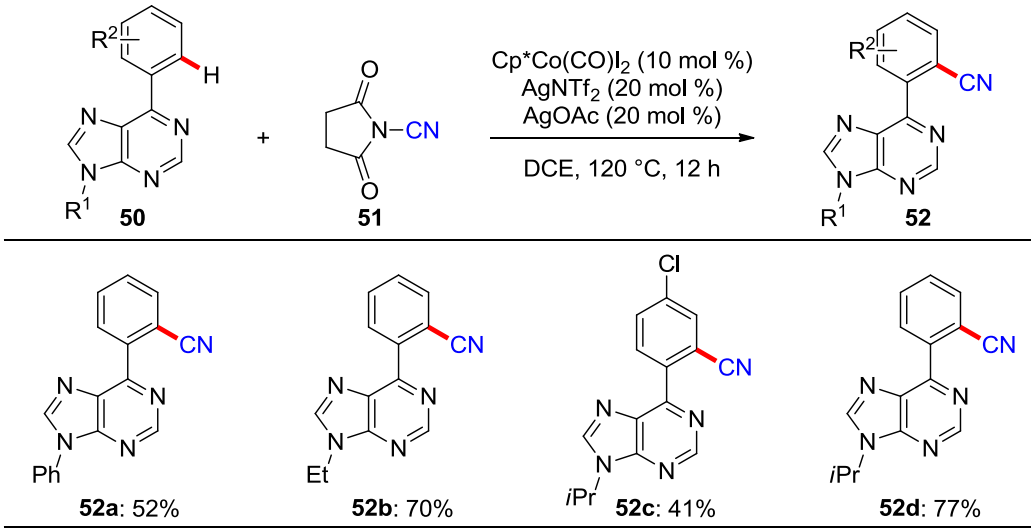
Scheme 1.2.9 Plausible catalytic cycle for cobalt(III)-catalyzed C–H cyanation.

Thereafter, Glorius and coworkers reported a similar work on cobalt(III)-catalyzed C–H cyanation using NaOAc as the base (Scheme 1.2.10).[63] At the same time, a selective C–H halogenation in the presence of Cp*Co(CO)I_2, $AgSbF_6$, and PivOH was also developed.



Scheme 1.2.10 Cobalt(III)-catalyzed C–H cyanation and halogenation.

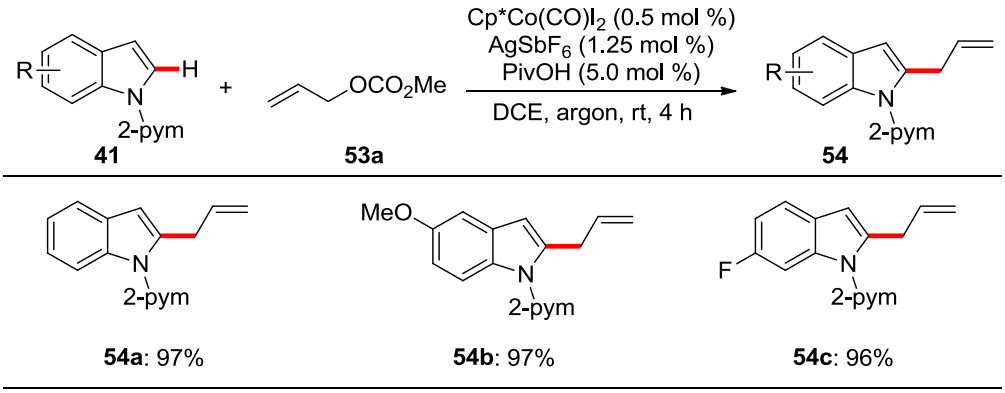
Moreover, a similar approach of C–H cyanation was developed by Chang and coworkers using *N*-cyanosuccinimide (**51**) as a more efficient cyanating reagent (Scheme 1.2.11).[64]. 6-Arylpurines **50** were found to be suitable substrates and furnished the desired products **52** in moderate to good yields



Scheme 1.2.11 Cobalt(III)-catalyzed C–H cyanation of arylpurines.

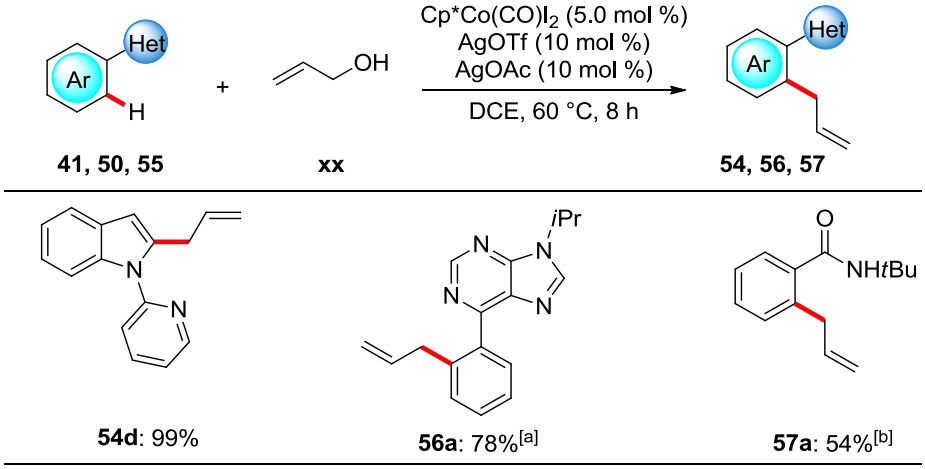
1.2.2.2 Cp*Co(III)-Catalyzed Allylations

The allyl group can be easily manipulated to access a wide variety of functionalized building blocks,[65] making allylation reactions very important in organic synthesis. However, metal-catalyzed C–H allylation reactions have been dominated by precious metals over the last decade.[66] Recently, efforts toward cobalt(III)-catalyzed C–H allylation have been made by Glorius,[63] Ackermann,[67] Matsunaga/Kanai,[68] and Li.[69] Glorius and coworkers developed the cobalt(III)-catalyzed C–H allylation reactions of *N*-pyrimidylindoles **41** with allyl carbonates (**53a**) in the presence of Cp*Co(CO)I_2, $AgSbF_6$ and PivOH (Scheme 1.2.12).[63] A remarkable feature of this reaction was that when even lowering the Cp*Co(CO)I_2 catalyst loading to 0.5 mol %, the desired C-2 allylated indole products **54** could still be obtained over 90% yield at ambient temperature with a 2200 TON.

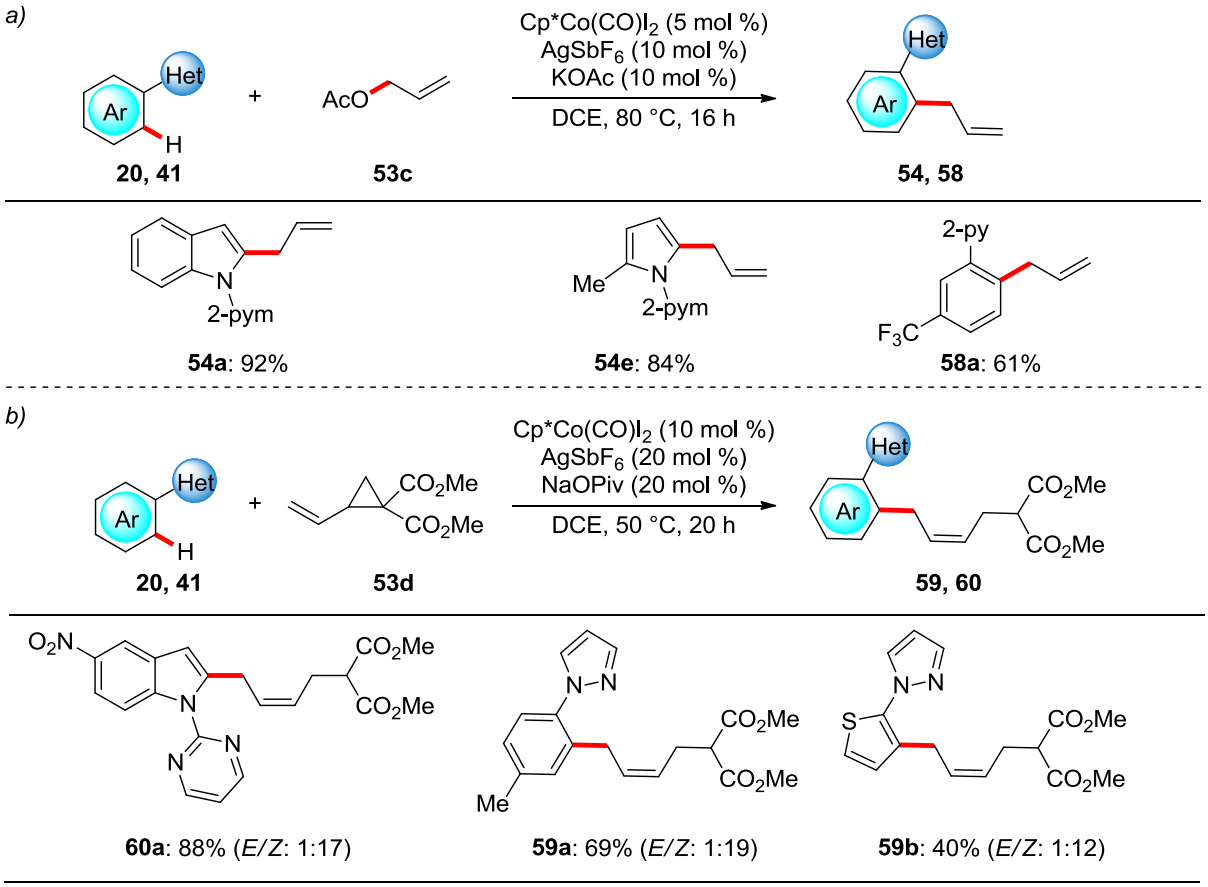


Scheme 1.2.12 Cp*Co(III)-catalyzed C–H allylation with allyl methyl carbonate **53a**.

Matsunaga and Kanai developed the dehydrative allylation of indoles **41** with allylic alcohols (Scheme 1.2.13).[68a] The desired products could be more efficiently obtained with Cp*Co(CO)I_2 compared with the analogous [Cp*$RhCl_2$]$_2$ catalyst. Various functional groups were tolerated under the optimized conditions. The Cp*Co(III) catalysis was successfully applied to 6-arylpurines **50**, benzamides **55**, and aromatic Weinreb amide substrates.[68b]

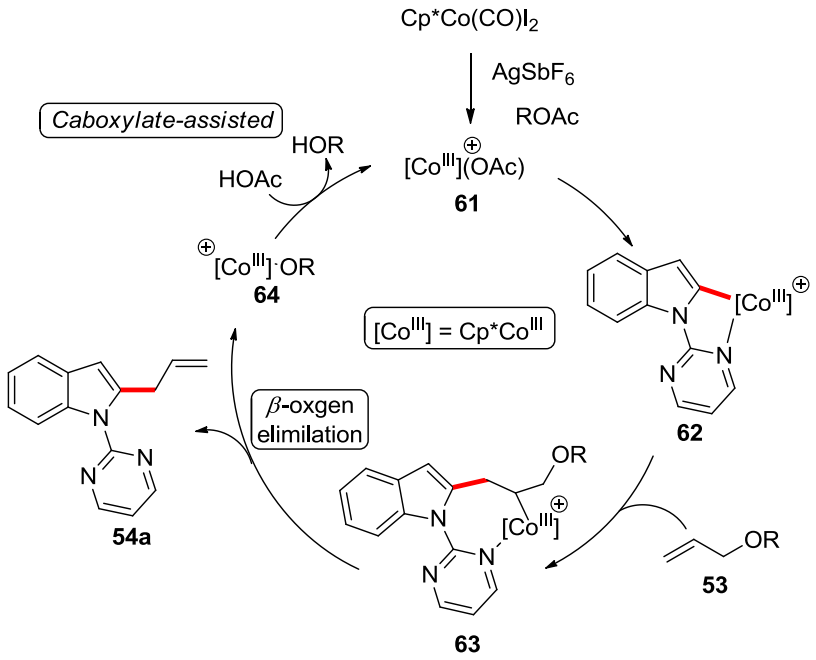


Scheme 1.2.13 Cp*Co(III)-catalyzed C–H allylation with prop-2-en-1-ol. [a] TFE as the solvent. [b] 20 mol % $AgNTf_2$ instead of AgOTf, HFIP as the solvent, 80 °C, 24 h.



Scheme 1.2.14 Cp*Co(III)-catalyzed C–H allylation *via* C–H/C–C activation.

In 2015, Ackermann and coworkers disclosed a versatile cobalt(III)-catalyzed C–H allylation reaction on arenes **20**, indoles **41**, and pyrroles **20e** with allyl acetates **53c** (Scheme 1.2.14a).[67] The following year, the same group also reported the *Z*-selective allylation *via* C–H/C–C activation by cobalt(III) catalysis under mild conditions (Scheme 1.2.14b).[70] Remarkably, this reaction showed a broad reaction scope and delivered the thermodynamically less stable (*Z*)-alkenes with excellent diastereoselectivity. Thereafter, Li developed a C–H/C–O allylation reaction of *N*-pyrimidinylindoles with strained rings such as 7-oxabenzonorbornadienes and 2-vinyloxirane under mild conditions.[69] A plausible catalytic cycle of these cobalt(III)-catalyzed allylations is proposed to be initiated by the formation of an active cobalt species **61** from the precatalyst Cp*Co(CO)I_2 and silver salts (Scheme 1.2.15). The following C–H metalation resulting in the formation of complex **62** involves a BIES pathway. Subsequent coordination and olefin insertion give the intermediate **63**, which then undergoes β-oxygen elimination to afford the desired product **54a**. The active cobalt catalyst **61** is then regenerated with the assistance of acid.

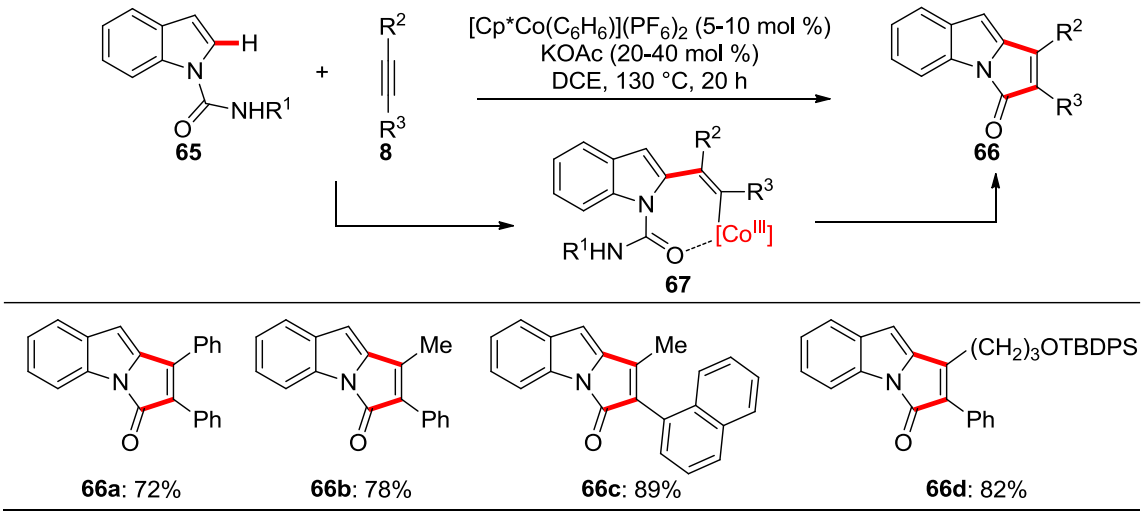


Scheme 1.2.15 Plausible catalytic cycle for cobalt(III)-catalyzed C–H allylation.

1.2.2.3 Cp*Co(III)-Catalyzed Annulation

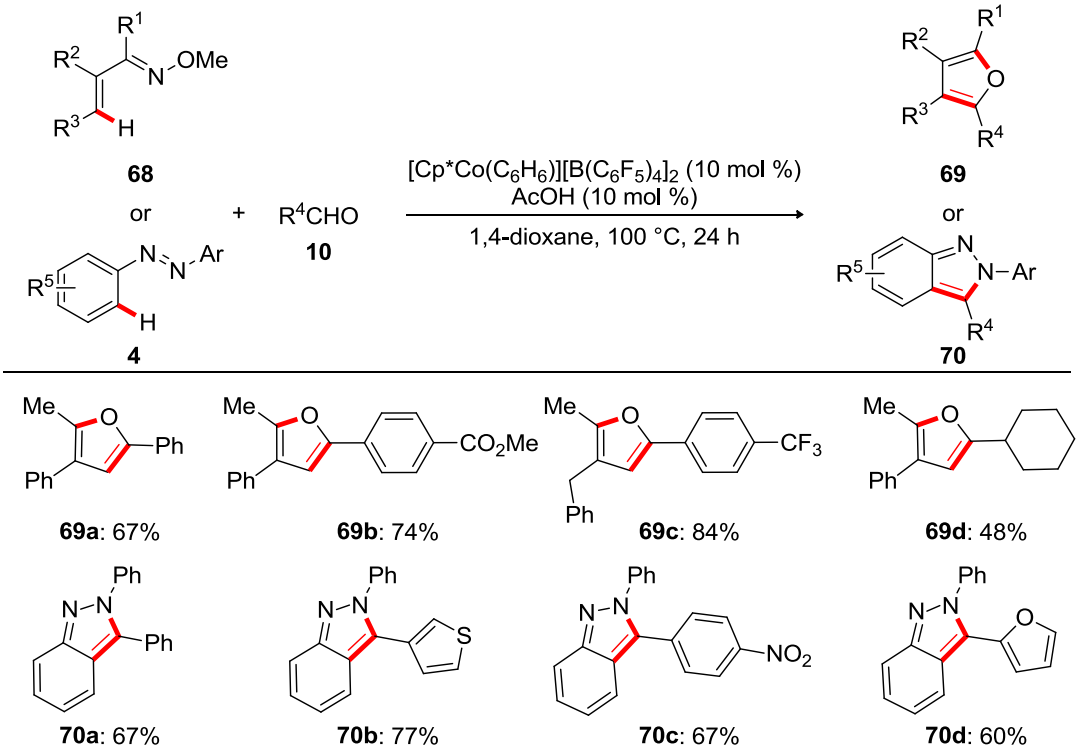
Annulation reactions are among the most fundamental and useful transformation in organic synthesis.[71] They provide a straightforward and step-economical method for the synthesis of heterocycles, which are important motifs in pharmaceuticals, natural products and agrochemicals.[72] During the last years, a broad range of examples using Cp*Co(III)-type catalysts for annulation reactions have been developed.[37a, 37b, 73] Here, only selected examples of cobalt(III)-catalyzed annulation reactions will be discussed in this context.

Matsunaga and Kanai developed a Cp*Co(III)-catalyzed redox-neutral C-2 selective C–H alkenylation/annulation of *N*-carbamoyl indoles **65** with internal alkynes **8** (Scheme 1.2.16).[74] The intramolecular addition of an alkenyl-Cp*Co species **67** to a carbamoyl moiety provided pyrroloindolones **66** in moderate to good yields. A variety of unsymmetrical alkynes underwent this reaction smoothly and afforded the desired products in high yields and regioselectivities. In addition, when the reaction temperature was decreased to 80 °C, only simple C–H alkenylated products were obtained. In contrast, the analogous Cp*Rh(III) catalysis failed to achieve the intramolecular additions, highlighting the unique nucleophilicity of the organocobalt species.



Scheme 1.2.16 Pyrroloindolone **66** synthesis *via* Cp*Co(III)-catalyzed C–H alkenylation/annulation.

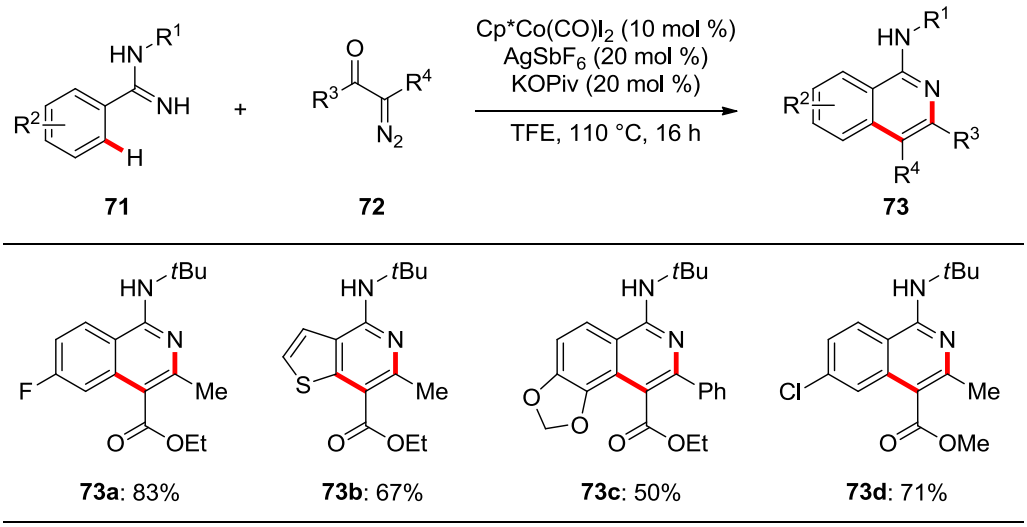
Ellman and Hummel disclosed a cobalt(III)-catalyzed C–H addition reaction to aldehydes (Scheme 1.2.17).[75] The air-stable cationic cobalt catalyst $[Cp^*Co(C_6H_6)][B(C_6H_5)_4]_2$ was developed to achieve the cyclization and aromatization with a catalytic amount of AcOH, affording *N*-aryl-2*H*-indazoles **70** and furans **69** in good yield. A wide range of aryl, heteroaryl, and alkyl aldehydes were found to be suitable substrates, efficiently delivering the desired substituted heterocycles.



Scheme 1.2.17 Cp*Co(III)-catalyzed C–H hydroarylation/annulation of azos **4** and oximes **68** with

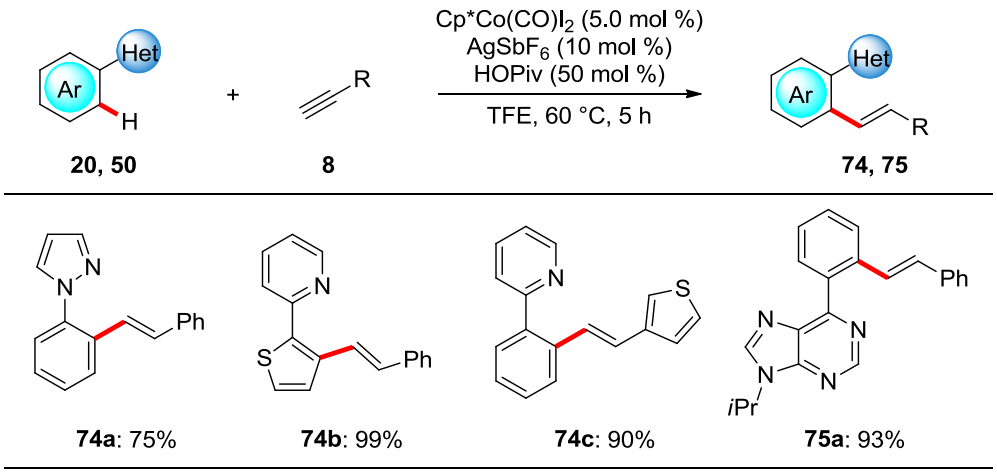
aldehydes.

Recently, Ackermann and coworkers reported a C–H/N–H bond functionalization for the synthesis of 1-aminoisoquinolines **73** from aryl benzimidamide **71** and diazo compounds **72** under mild conditions by cobalt(III) catalysis (Scheme 1.2.18).[76] This reaction showed a broad substrate scope and functional groups tolerance. Moreover, H_2O and N_2 were the sole byproducts of the transformation, making the process environmentally-benign.



Scheme 1.2.18 Cobalt(III)-catalyzed C–H/N–H functionalization for the synthesis of isoquinolines **73**.

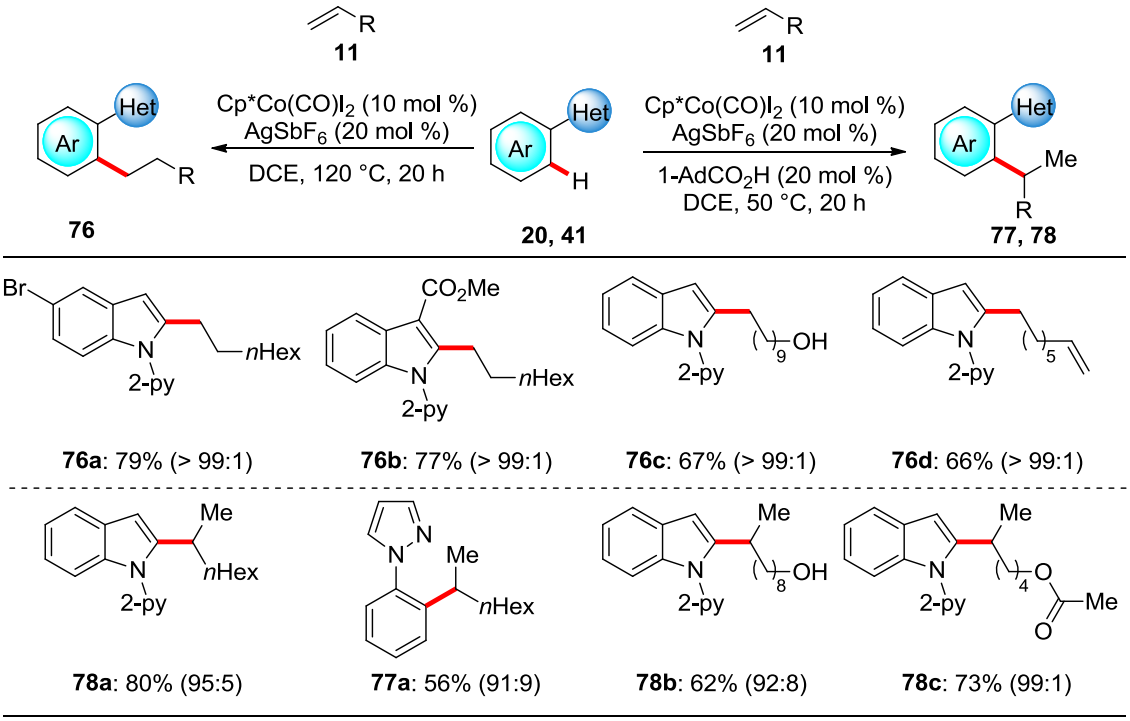
1.2.2.4 Cp*Co(III)-Catalyzed Hydroarylation



Scheme 1.2.19 Cp*Co(III)-catalyzed hydroarylation of alkynes.

The Cp*Co(III)-catalyzed direct addition of unactivated arenes and 6-arylpurines to terminal alkynes under mild conditions was described by Yu and Chen in 2016 (Scheme 1.2.19).[77] This process selectively provided only the (*E*)-stereoisomer in very high yield and also showed high functional group compatibility.

Recently, Ackermann and coworkers reported a cobalt(III)-catalyzed C–H alkylations with unactivated alkenes, in which the excellent regio-selectivities (linear- and branched-products) could be controlled by tunning the reaction conditions (Scheme 1.2.20).[22] A combination of Cp*Co(CO)I_2 and $AgSbF_6$ was employed (under additive free conditions) to provide the linear *anti*-Markovnikov products **76**. In contrast, when using sterically hindered 1-AdCO_2H as the additive and decreasing the reaction temperature to 50 °C, the unexpected branched-selective C–H alkylation products **77** and **78** were obtained. Detailed mechanistic studies showed that the selectivity was obtained by a change of mechanism from a linear-selective ligand-to-ligand hydrogen transfer (LLHT) to a branched-selective base-assisted internal electrophilic-type substitution (BIES).

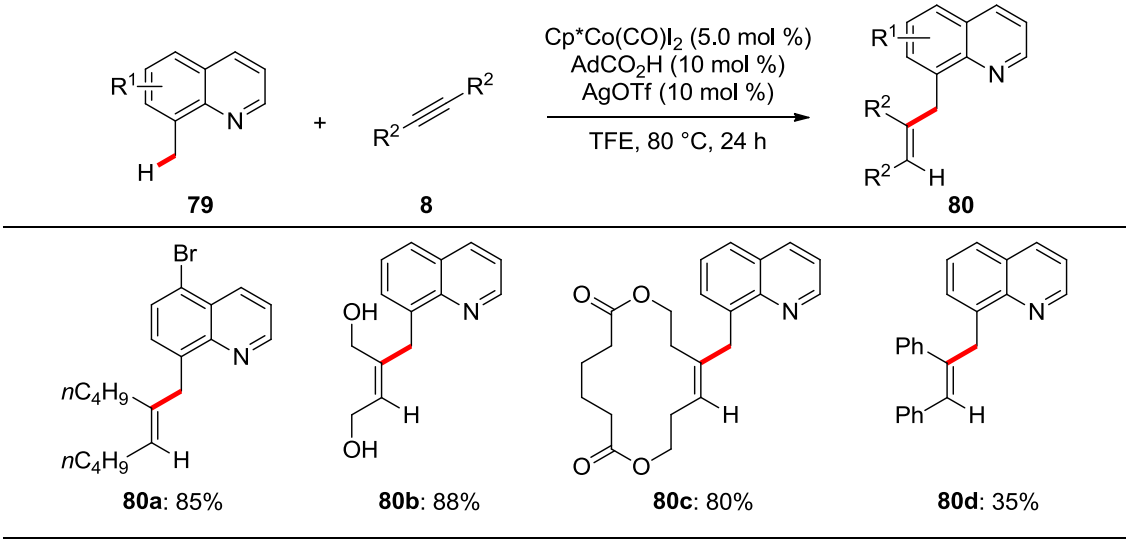


Scheme 1.2.20 Full selectivity control in cobalt(III)-catalyzed C–H alkylations.

1.2.2.5 Cp*Co(III)-Catalyzed C(sp^3)–H activation

Although great achievements in Cp*Co(III)-catalyzed C(sp^2)–H bond functionalizations have been

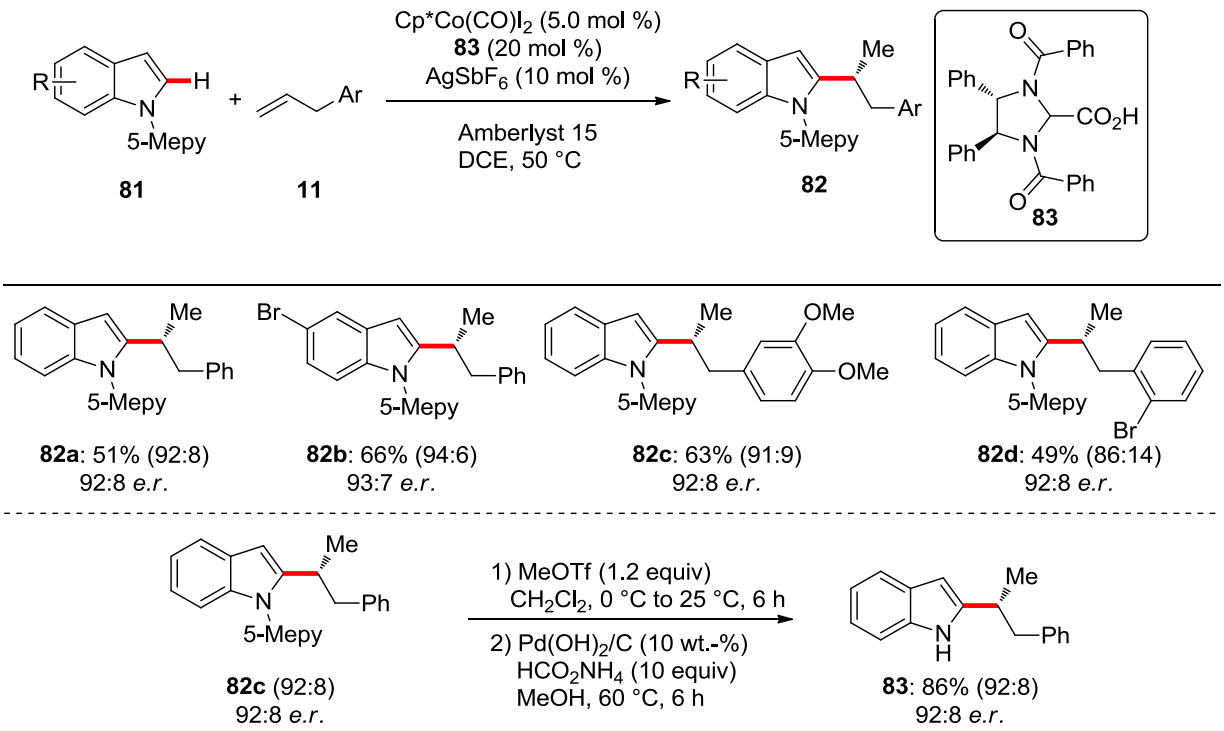
reported in recent years, significantly less efforts have been devoted to C(sp^3)–H bond activation in this field. Thus, Sundararaju and coworkers reported the C(sp^3)–H alkenylation of 8-methylquinolines **79** in the presence of catalytic amounts of Cp*Co(CO)I_2, $AdCO_2H$, and AgOTf (Scheme 1.2.21).[78] Compared to Cp*Rh(III) catalysis, stoichiometric amount of copper salts were not necessary in this Cp*Co(III) catalysis. However, a low reactivity of aryl alkynes under the optimized conditions was observed. A Cp*Co(III)-catalyzed C(sp^3)–H amidation of 8-methylquinoline with dioxazolones was also developed.[79]



Scheme 1.2.21 Cp*Co(III)-catalyzed C(sp^3)–H alkenylation and amidation.

1.2.2.6 Asymmetric Cp*Co(III)-Catalyzed C–H Functionalization

Ackermann and coworkers disclosed the first enantioselective Cp*Co(III)-catalyzed C–H alkylation of indoles **81** with alkenes **11** using a novel chiral acid as ligand **83** (Scheme 1.2.22).[80] A variety of substituted indoles and alkenes were successfully converted, yielding the corresponding products in moderate to good yields with high regio- and enantio-selectivities. A combination of experimental and computational studies in a chiral setting demonstrated that the C–H activation step is reversible and the formation of the (*R*)-enantiomer could be rationalized by DFT studies. Moreover, the 5-methylpyridine could be easily removed, yielding the free indole **83** in 86% yield without loss in the enantiomeric excess.



Scheme 1.2.22 First example of Cp*Co(III)-catalyzed asymmetric reaction by C–H activation.

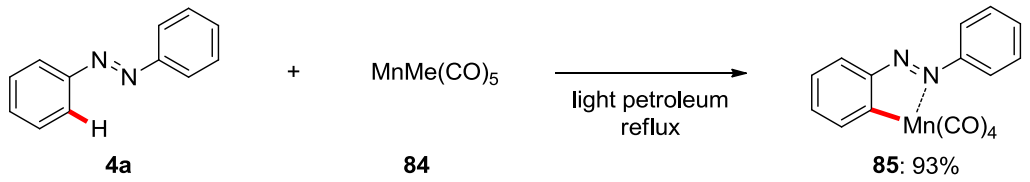
1.3 Manganese(I)-Catalyzed C–H Activation

Although transition metal catalysis has revolutionized the hydrocarbon chemistry compared to traditional synthetic strategies, the field of C–H functionalization to date was still dominated by precious metals.[81] Recent developments have changed the potential of catalytic reactions using Earth-abundant 3d metals, such as iron, cobalt, and manganese.[35b] In this regard, manganese is an attractive alternative for the C–H activation catalysis due to its natural abundancy, low toxicity, and unique reactivity. The low toxicity is reflected by its key importance as an essential trace element for several organisms on Earth.[82] The range of oxidation states of manganese is from -3 to +7, which bears great potential of exhibiting extraordinary activity. The recent years have witnessed many advances in manganese-catalyzed C–H functionalizations.[83]

Only representative examples of manganese(I)-catalyzed C–H functionalizations developed in recent years are summarized herein. The high-valent manganese species catalyzed C–H oxygenations,[84] halogenations,[85] and nitrogenations[86] *via* outer-sphere radical mechanisms are not discussed here.

1.3.1 Early Examples of Manganese-Catalyzed C–H Functionalizations

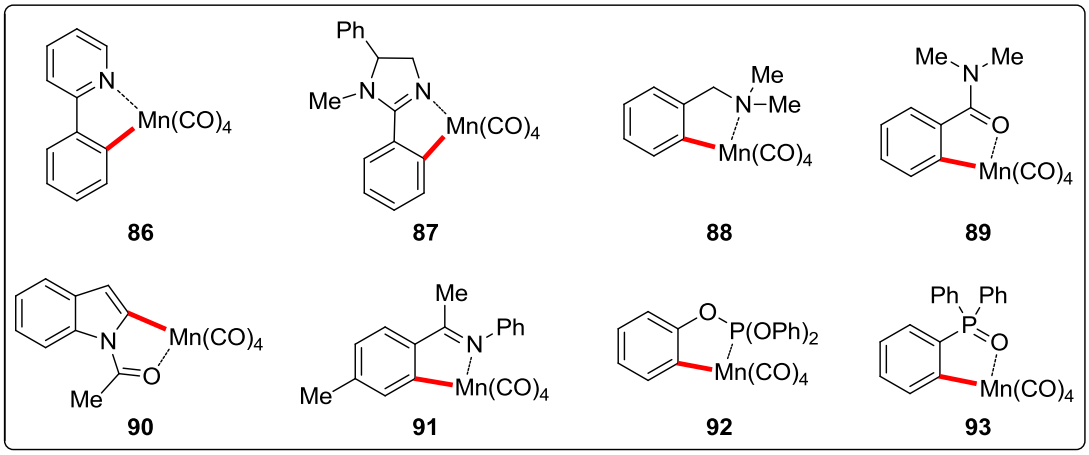
An early example of stoichiometric manganese-mediated C–H activation of azobenzene (**4a**) was reported by Stone/Bruce and coworkers in 1970 (Scheme 1.3.1).[87] The cyclometalated manganese complex **85** could be isolated in 93% yield from the $MnMe(CO)_5$ precursor under thermal conditions.



4a **84** **85**: 93%

Scheme 1.3.1 The first synthesis of five-membered manganaycle **85** *via* C–H activation.

Based on the pioneering work of Stone and Bruce, a wide range of well-defined manganacycles were successfully prepared according to a similar strategy using stoichiometric amounts of $MnR(CO)_5$ (with R= Me, Bn, or Ph). Notably, the directing groups were necessary for manganese to achieve the C–H metalation. Representative directing groups include imidazole,[88] azo,[89] imino,[90] amido,[91] keton,[92] and formyl,[93] among others.[94] The directing atom can bind to the manganese center of $MnR(CO)_5$ and bring it to the proximal C–H bond, which is followed by C–H activation along with the release of CO and RH.



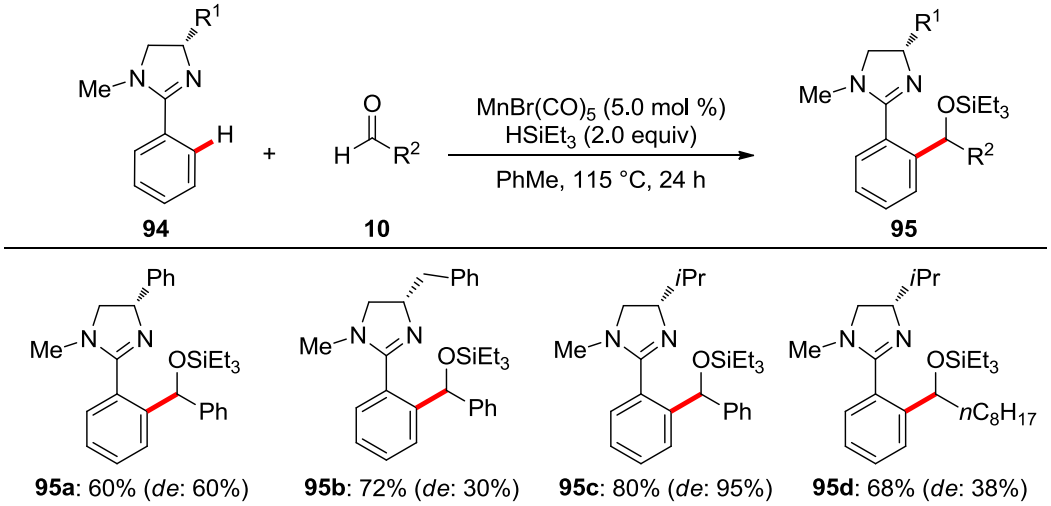
86 **87** **88** **89**

90 **91** **92** **93**

Scheme 1.3.2 Selected manganese complexes synthesized by C–H activation from $MnR(CO)_5$.

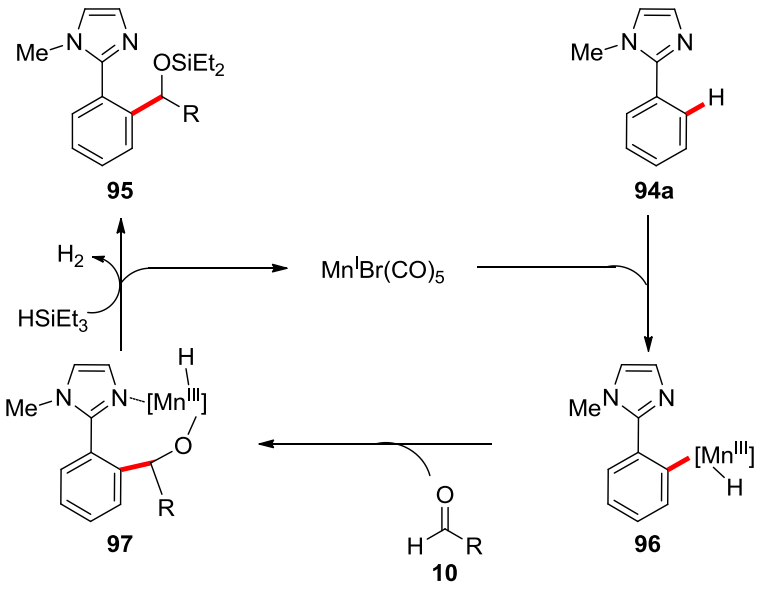
Although many years of research have passed since the initial synthesis of manganaycle complexes

via C–H activation, no directed manganese-catalyzed C–H activation was developed until a reported by Kuninobu/Takai and coworkers in 2007.[95] Here, the authors described the manganese(I)-catalyzed C–H addition to aldehydes using imidazole as the directing group. In the course of their optimization studies, the stoichiometric reaction of 2-phenylimidazoles with $MnBr(CO)_5$ was accomplished, followed by the addition to the C=O bond of the aldehyde leading to the formation of alcohol. It was found that the catalytic reaction could only be achieved with the assistance of Et_3SiH. Remarkably, the authors demonstrated that stereoselective reactions of chiral imidazolines **94** with aldehydes **10** gave the desired products **95** in moderate to good yields with varying diastereomeric excesses of *de*: 30-95% (Scheme 1.3.3).



Scheme 1.3.3 Manganese(I)-catalyzed hydroarylation of aldehydes by Kuninobu and Takai *et al*.

Moreover, a plausible mechanism was proposed by Kuninobu and Takai. First, the $MnBr(CO)_5$ undergoes C–H activation by oxidative addition, furnishing the Mn(III)-hydride species **96**. Then, a migratory insertion of the aldehyde into the manganese-carbon bond forms the intermediate **97**. Finally, the desired product **95** is released along with H_2 by treatment with Et_3SiH (Scheme 1.3.4).



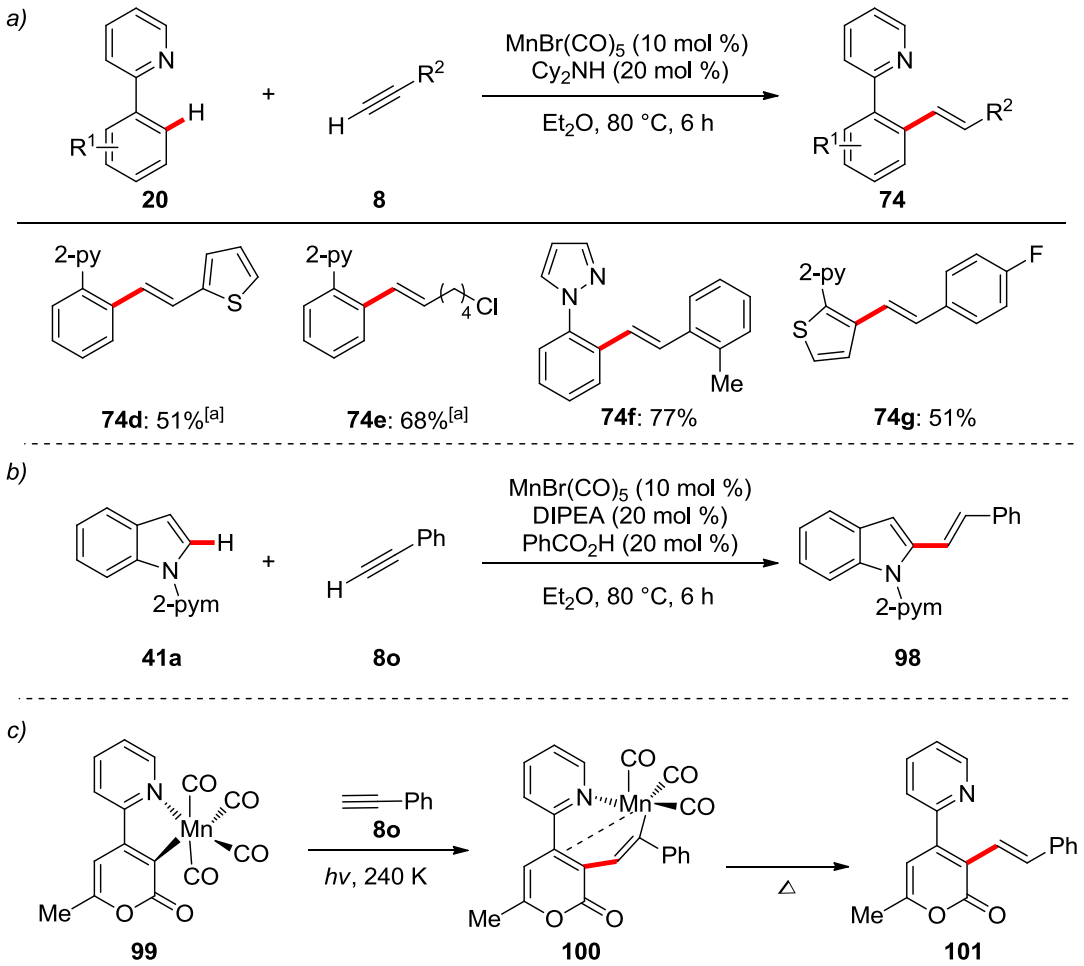
Scheme 1.3.4 Proposed mechanism for the hydroarylation of aldehydes.

1.3.2 Examples of Manganese(I)-Catalyzed C–H Functionalizations

1.3.2.1 Manganese(I)-Catalyzed C–H Hydroarylations

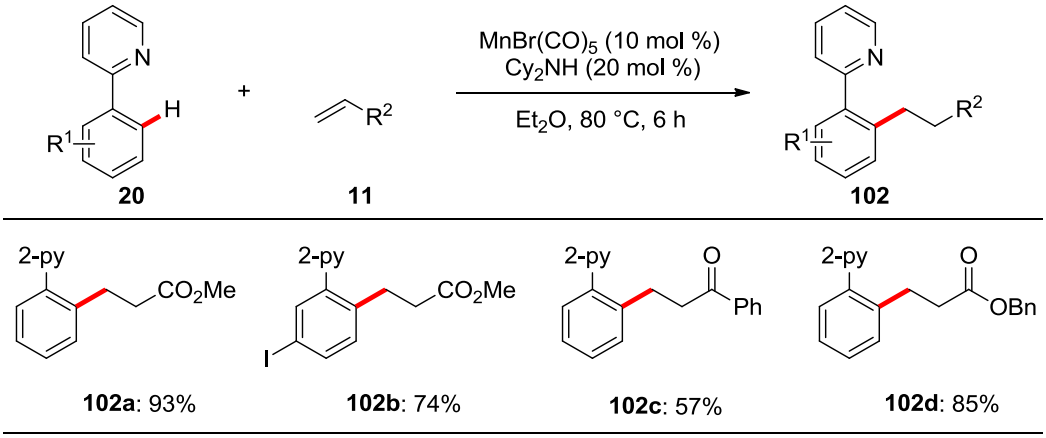
In 2013, Wang and coworkers reported the manganese-catalyzed C–H alkenylation of 2-phenylpyridines **20** with terminal alkynes **8** in the presence of Cy_2NH as the base (Scheme 1.3.5a).[96] From the optimized conditions, weak organic bases showed better performance than strong bases. Moreover, this hydroarylation process exhibited high (*E*)-diastereo, regio-, and mono-selectivities. Various functional groups, such as fluoro, chloro, bromo, iodo, ester, and nitro groups were well tolerated under the optimized conditions.

Furthermore, Li and coworkers also reported in 2015 a similar manganese-catalyzed C–H alkenylation reaction of indoles **41a** using benzoic acid as the additive instead of the Cy_2NH base.[97] The authors proposed that the benzoic acid serves as the selectivity controlling element *via* a *H*-transfer process (Scheme 1.3.5b). Very recently, Fairlamb/Lynam and coworkers described a highly reactive seven-membered Mn(I) intermediate **100**, which was shown to be effective for *H*-transfer to provide alkenylated products **101** (Scheme 1.3.5c).[98] The detailed computational studies provided novel insights into the mechanism for manganese-catalyzed C–H activation.



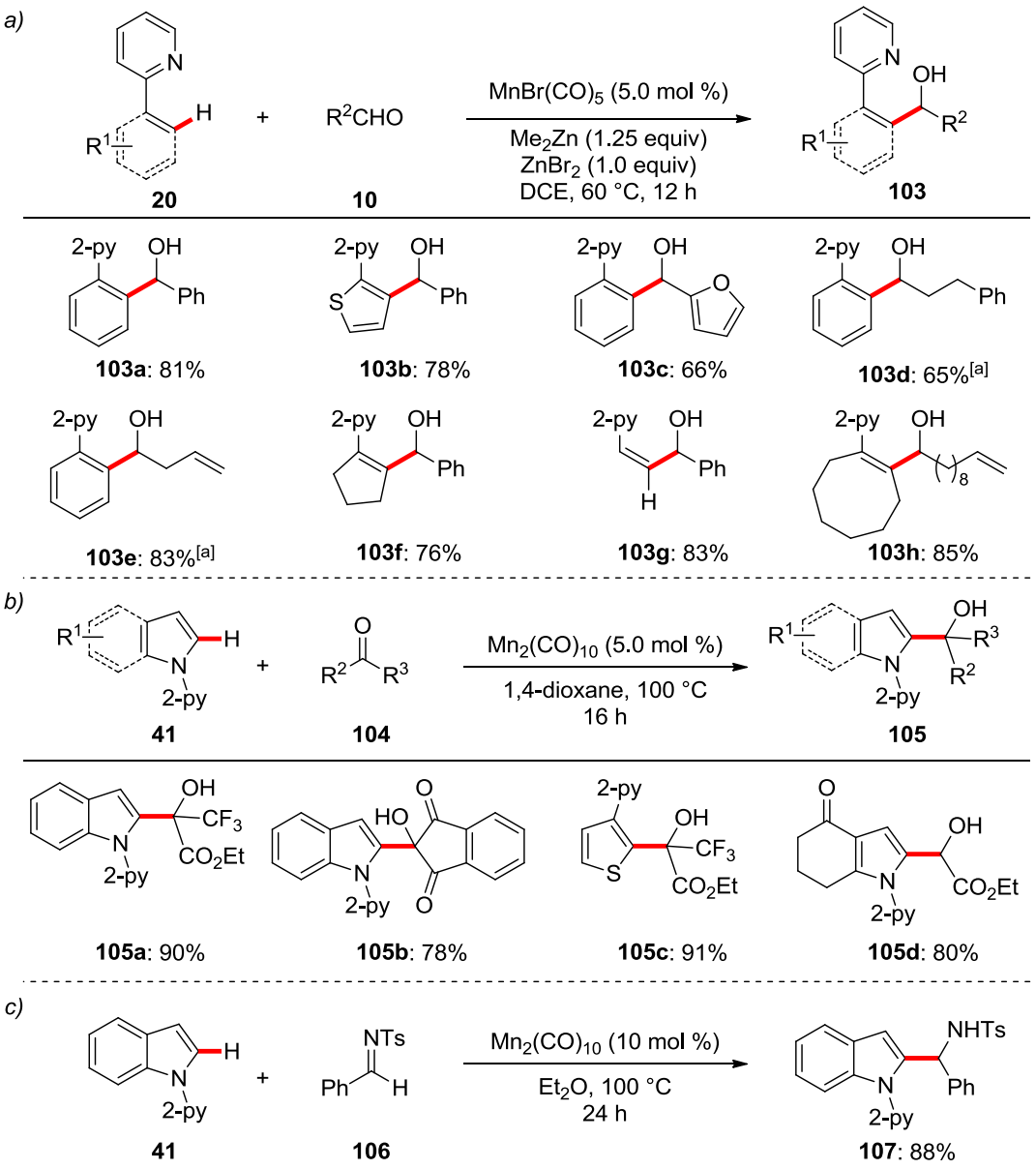
Scheme 1.3.5 Manganese(I)-catalyzed C–H hydroarylations with alkynes. [a]100 °C.

The manganese-catalyzed hydroarylation-type C–H activation strategy was further extended to the C=C double bond. In 2014, Wang and coworkers developed the manganese-catalyzed direct aromatic C–H addition reaction to α,β-unsaturated carbonyls **11** as well (Scheme 1.3.6).[99] This reaction featured a simple catalyst system, high chemo- and mono-selectivity, and a broad compatibility of functional groups.



Scheme 1.3.6 Manganese(I)-catalyzed C–H alkylation with alkenes.

Furthermore, the manganese-catalyzed C–H hydroarylation was not limited to carbon-carbon multiple bonds, but electrophilic C–Het multiple bonds, such as C=O, and C=N bonds, also proved to be viable. Wang and coworkers reported the manganese-catalyzed Grignard-type nucleophilic addition to aldehydes **10**, affording various alcohol products **103**. The reaction showed a broad substrate scope. Various aliphatic aldehydes, including primary, secondary, and tertiary ones and olefinic C–H bonds all underwent the reaction smoothly, delivering the desired alcohols in good yields (Scheme 1.3.7a).[100] In 2016, Ackermann and coworkers reported an unprecedented hydroarylation of C=O double bonds by manganese catalysis under additive-free conditions (Scheme 1.3.7b).[101] Challenging aldehydes and ketones were also successfully employed, delivering the corresponding products in good yields with high C-2 selectivities. Moreover, it is noteworthy that the first manganese-catalyzed C–H hydroarylation with imines **106** was achieved (Scheme 1.3.7c). Thereafter, the similar works of manganese(I)-catalyzed C–H hydroarylation of imines were reported by the same group[102] and Wang,[103] respectively.

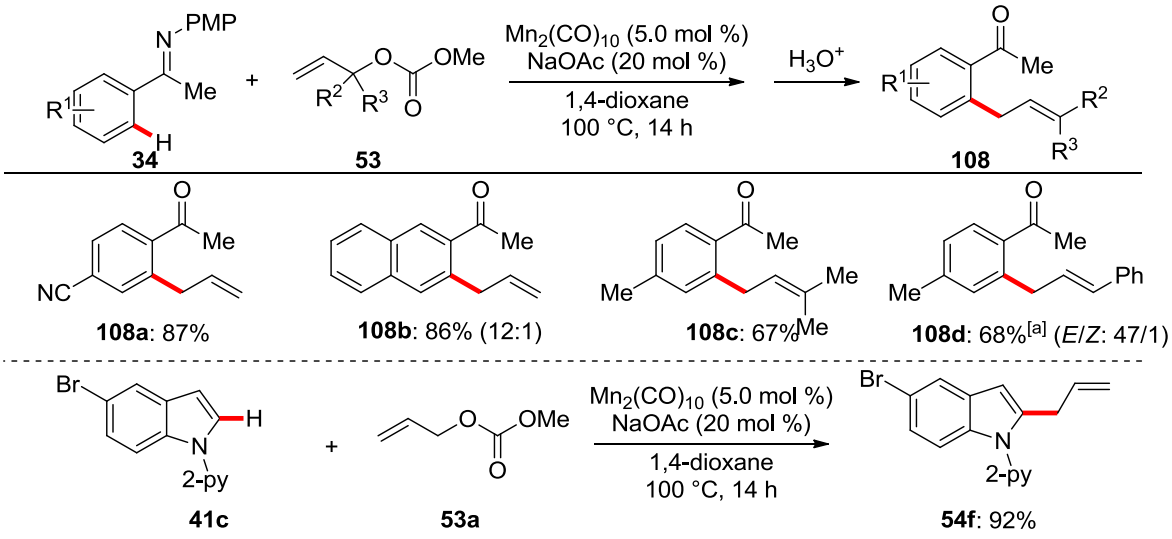


Scheme 1.3.7 Manganese(I)-catalyzed C–H addition onto C=Het double bonds. [a] 80 °C.

1.3.2.2 Manganese(I)-Catalyzed C–H Allylation

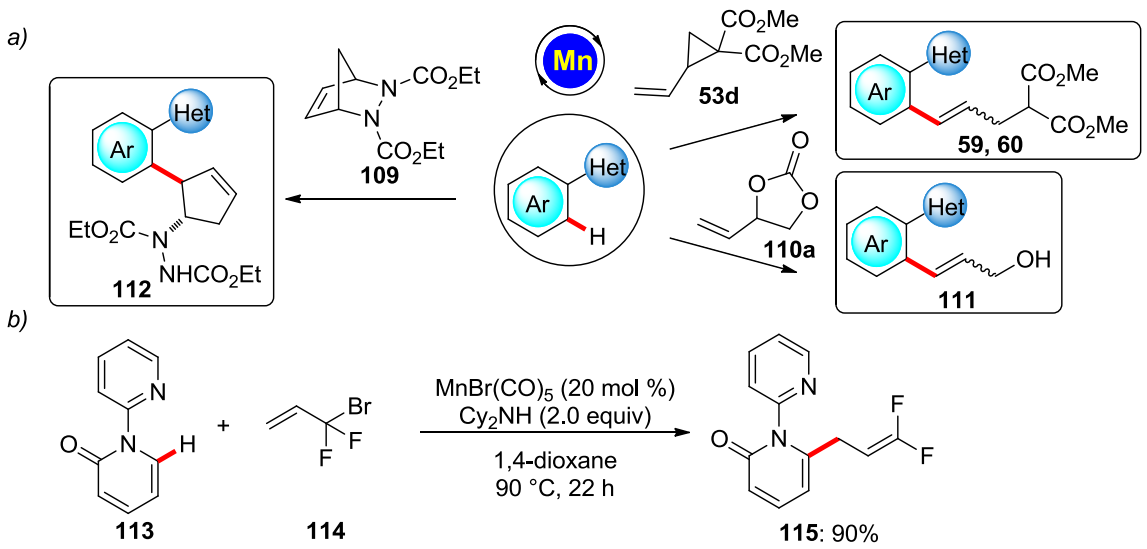
In 2016, Ackermann and coworkers reported the first example of manganese(I)-catalyzed C–H allylations of arenes **34** with allyl carbonates **53** (Scheme 1.3.8).[104] Both electron-rich and electron-withdrawing heterocycles, including various functional groups such as fluoro, chloro, bromide, iodo, cyano, aldehyde, and amine, could be employed in the reaction. The α-substituted allyl carbonates **53c** were also found to be suitable substrates and provided linear allylation products **108c** with good yields. Mechanistic studies showed that electron-rich ketimines exhibited

higher reactivity, and a significant H/D-scrambling in C-2 position of ketimines was observed as well. Both observations were in accordance with a base-assisted intramolecular electrophilic-type substitution (BIES) for manganese-catalyzed C–H activation.



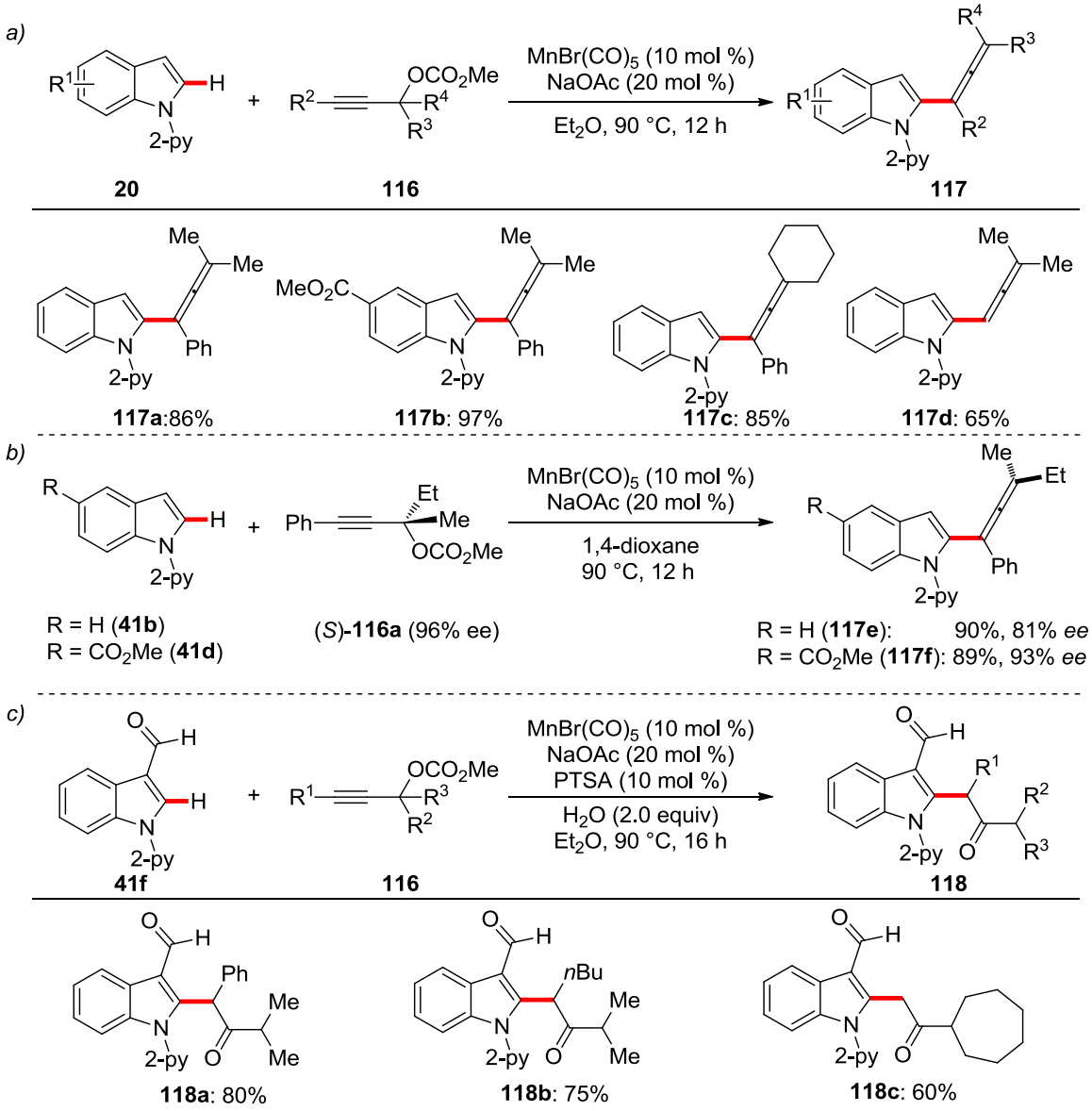
Scheme 1.3.8 Manganese(I)-catalyzed C–H allylation. [a]120 °C.

Afterwards, Glorius and coworkers also developed a similar manganese(I)-catalyzed C–H allylation reaction (Scheme 1.3.9a).[105] New types of allyl coupling partners were employed in this reaction, affording allylic alcohols **111**, allylated arenes **59** and functionalized cyclopentenes **112** in moderate to good yields and acceptable *E*/*Z* ratios. In the same year, Zhang and coworkers also reported a manganese(I)-catalyzed C–H 3,3-difluoroallylation using 3-bromo-3,3-difluoroprop-1-ene (**114**) as the allylating reagent (Scheme 1.3.9b).[106] The reaction featured a broad substrate scope, and high functional group compatibility. Nevertheless the industrial applicability of such reaction was compromised by the high catalyst loading of 20 mol %.



Scheme 1.3.9 Manganese(I)-catalyzed C–H allylation with different coupling partners.

Moreover, Glorius and coworkers also reported manganese(I)-catalyzed allylation-type C–H activation providing a direct access to 2-allenylindoles **117** (Scheme 1.3.10).[107] The protocol provided an alternative method for the synthesis of fully substituted allenes **117** with high enantioselecties *via* chirality transfer (Scheme 1.3.10a and b). It is noteworthy that the ketone products **118** could be obtained in good yields when indole substrates bearing a 3-formyl group were employed in this C–H activation in the presence of the PTSA and H_2O as additives (Scheme 1.3.10c).

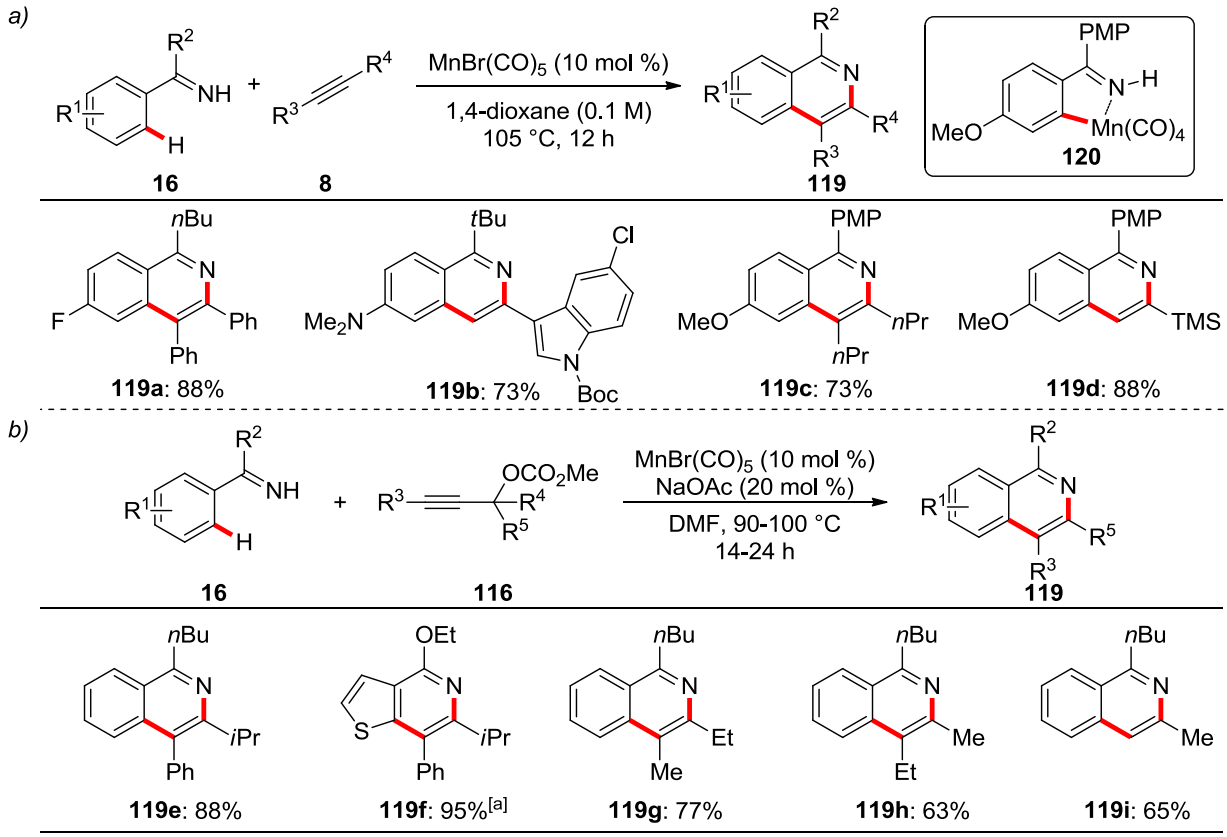


Scheme 1.3.10 Manganese(I)-catalyzed C–H allylation for the synthesis of 2-allenylindoles.

1.3.2.3 Manganese(I)-Catalyzed C–H Annulations

Isoquinolines are among the most abundant and important classes of heterocycles found in natural products, agrochemicals, and pharmaceuticals.[108] Many routes for the assembly of this heterocyclic skeleton have been developed during the last century.[109] Recent advances in C–H activation/annulation to access certain substituted isoquinolines have been developed by manganese(I) catalysis in this context. In 2014, Wang and coworkers disclosed a manganese(I)-catalyzed dehydrogenative [4+2] annulation of *N*–H imines **16** and alkynes **8**, which provided an expedient access to isoquinoline derivatives **119**.[110] Compared with other well known

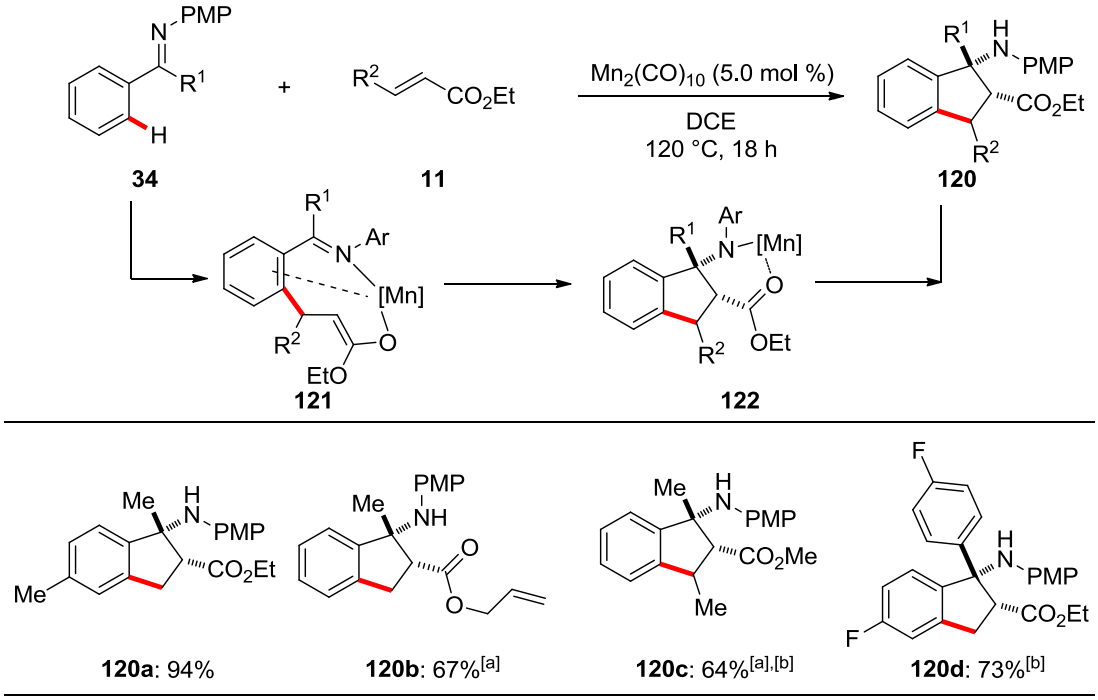
isoquinoline synthesis processes,[111] this manganese-catalyzed C–H annulation does not require any oxidants, external ligands, and additives, highlighting a unique and robust manganese catalyst. Detailed mechanistic studies suggested that the isolated five-membered manganacycle **120** is a key reaction intermediate in the catalytic cycle (Scheme 1.3.11a). Moreover, Glorius and coworkers also reported a manganese(I)-catalyzed C–H annulation to the synthesis of isoquinolines using alkyne coupling partners with a traceless directing group very recently (Scheme 1.3.11b).[112] Indeed, aliphatic, terminal, dialkyl- and monoalkyl-substitued alkynes were all compatible in this C–H annulation and delivered the desired products **119**.



Scheme 1.3.11 Manganese(I)-catalyzed C–H annulations with alkynes. [a]BPh_3 (10 mol %) and 1,2-dimethoxyethane (DME) were employed.

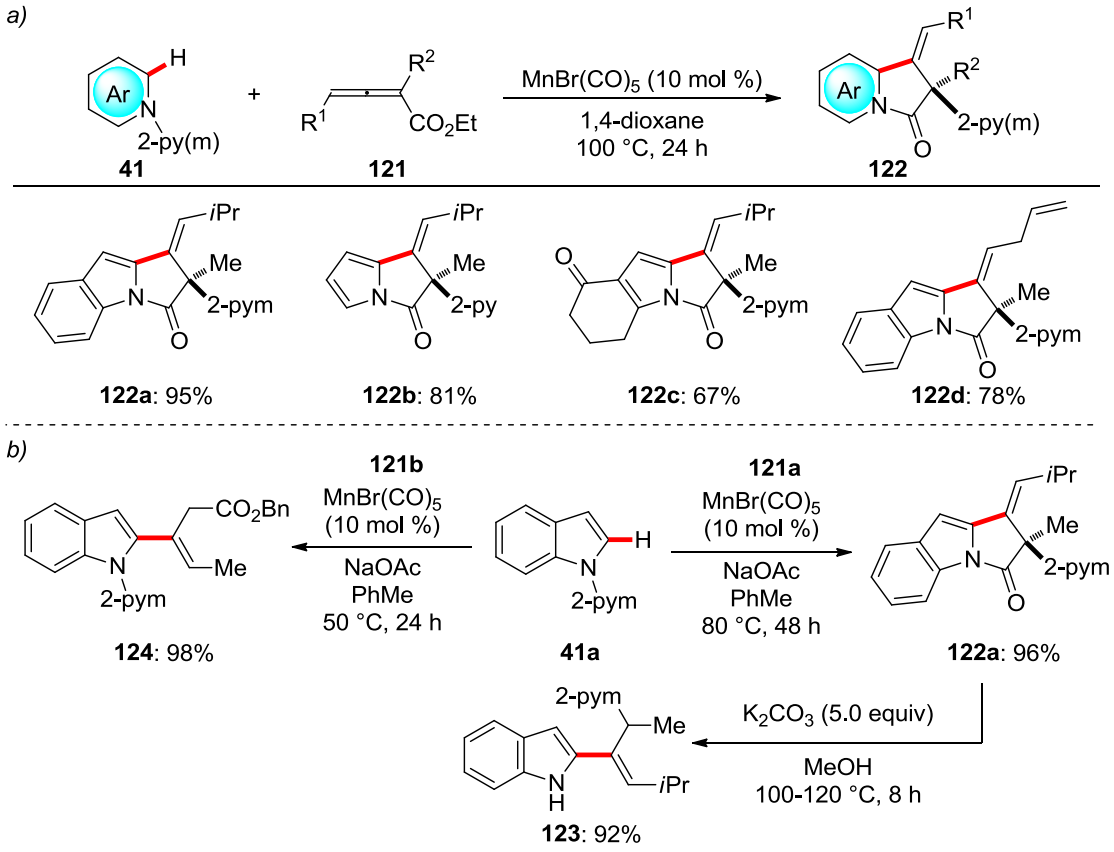
Manganese exhibits a lower electronegativity in comparison to 4d transition metals such as rhodium, ruthenium, and iridium, which could form more nucleophilic intermediates leading to more significant reactions. Indeed, in 2015, Ackermann and coworkers developed the first manganese-catalyzed C–H annulation of ketimines **34** with acrylates **11**, providing expedient access to valuable β-amino acid esters (Scheme 1.3.12).[113] The features of the reaction included high

catalytic efficacy, good functional group tolerance, and an unusual *cis* stereo-selectivity. The catalytic cycle include a manganese nucleophilic intermediate which undergoes the intramolecular nucleophilic addition to the carbon atom of the imine moiety and then delivers the desired product **120**.



Scheme 1.3.12 Manganese(I)-catalyzed synthesis of *cis*-β-amino acid esters *via* C–H activation. [a] In PhMe. [b] With $Mn_2(CO)_{10}$ (10 mol %).

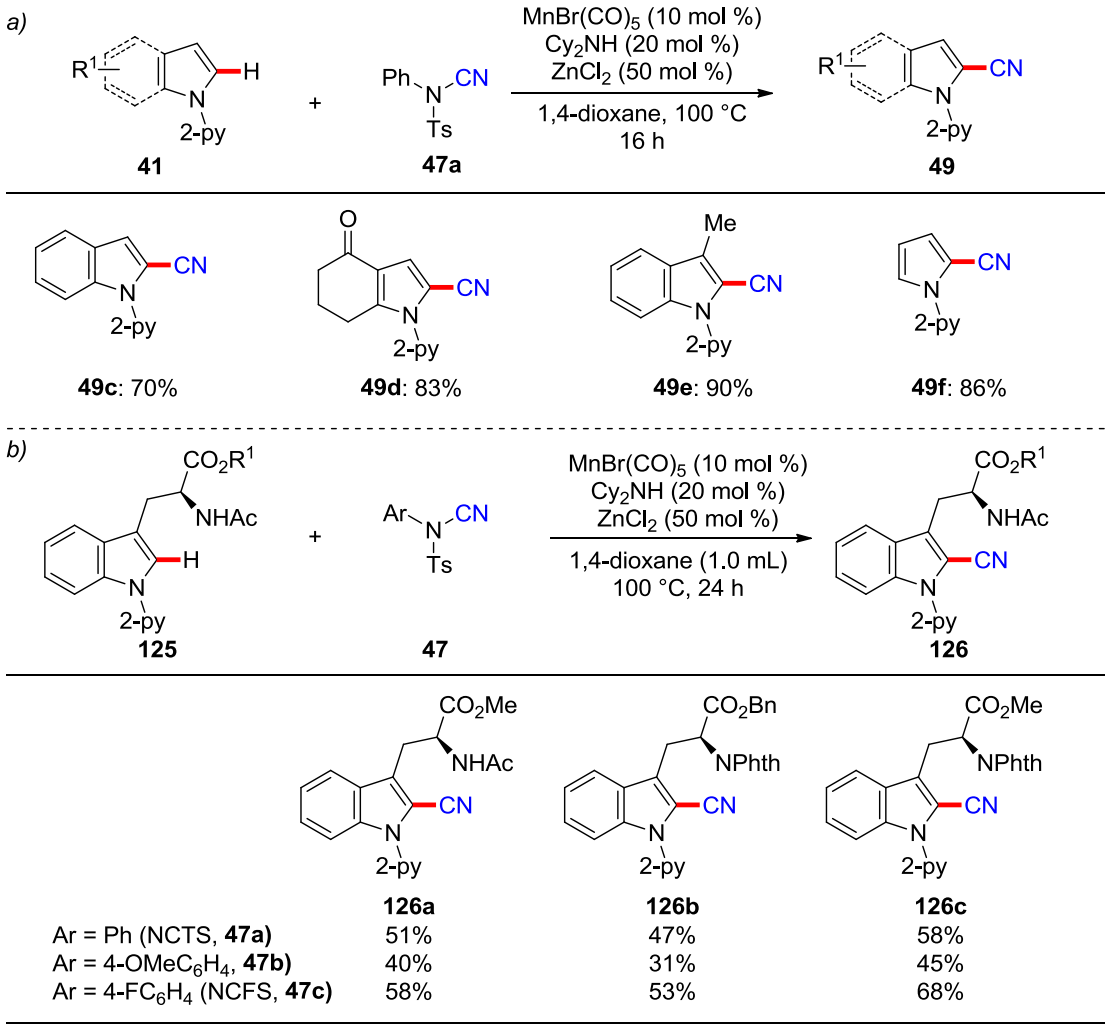
Thereafter, Rueping[114] and Wang/Li[115] independently developed the unprecedented C–H/C–N functionalization of pyrimidinyl-indoles **41** with allenes **121**. The optimized reactions showed that a high yield could be obtained when NaOAc was used as the additive. The use of disubstituted allenes **121b** resulted in the selectively alkenylated C-2 indoles **124** under mild reaction conditions. However, when trisubstituted allenes were employed under similar reaction conditions, the unexpected annulation products **122** were obtained (Scheme 1.3.13a). In Wang/Li's system, the reaction proceeded under simple reaction conditions with no additives or even solvent-free conditions, but a high reaction temperature of 100 °C was necessary, providing the hydroarylation/cyclization products **122** in moderate to good yields with high stereo- and regio-selectivity. The decarboxylative ring-opening of the products **122** offered a series of vicinal biheteroaryl **123** by treatment with K_2CO_3 in methanol (Scheme 1.3.13b).



Scheme 1.3.13 Manganese(I)-catalyzed C–H/C–N functionalization.

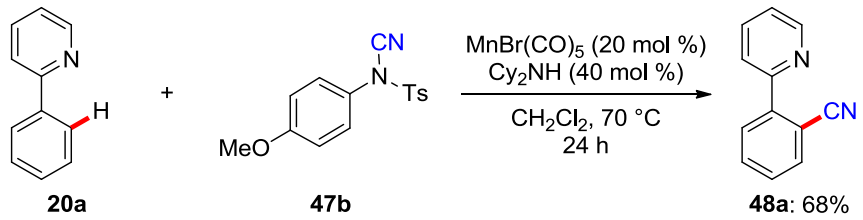
1.3.2.4 Manganese(I)-Catalyzed C–H Cyanations

In 2016, Ackermann and coworkers reported a manganese-catalyzed C–H cyanation of heteroarenes with NTCS (**47a**) as the cyanating reagent.[116] A combination of $MnBr(CO)_5$ and Cy_2NH gave the highest efficiency to provide cyanated products **49** with the assistance of $ZnCl_2$. The intermolecular competition experiments showed that electron-rich substrates reacted preferentially. Moreover, this catalyst enabled C–H cyanations on heterocycles, including pyrroles and thiophenes, with high mono- and C-2 selectivities (Scheme 1.3.14a). It is noteworthy that this cyanation strategy could be applied to tryptophan derivatives **125** and the authors showed that electron-deficient cyanating reagents could provide the desired products **126** in higher yields, presumably due to their enhanced electrophilic character (Scheme 1.3.14b).



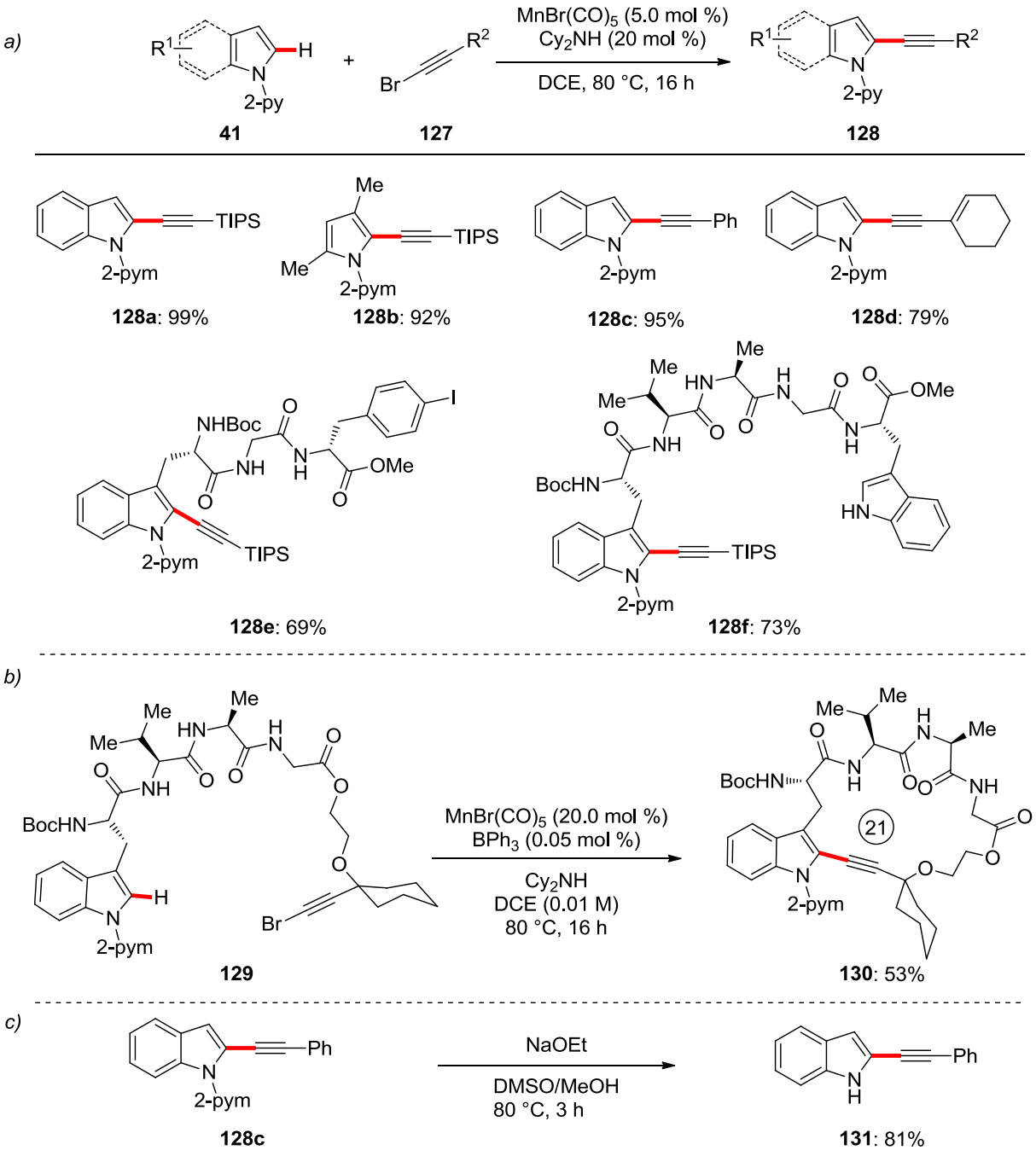
Scheme 1.3.14 Manganese(I)-catalyzed C–H cyanation.

Very recently, Bao and coworkers also described a manganese-catalyzed C–H cyanation reaction of arenes by using *N*-cyano-*N*-(4-methoxy)phenyl-*p*-toluenesulfonamide (NMTS) (**47b**) as the cyanating reagent.[117] The aromatic nitriles were obtained in 27-79% yields in the presence of 20 mol % of $MnBr(CO)_5$ catalyst (Scheme 1.3.15).



Scheme 1.3.15 Manganese(I)-catalyzed C–H cyanation by using NMTS as the cyanating reagent.

1.3.2.5 Manganese(I)-Catalyzed C–H Alkynylation

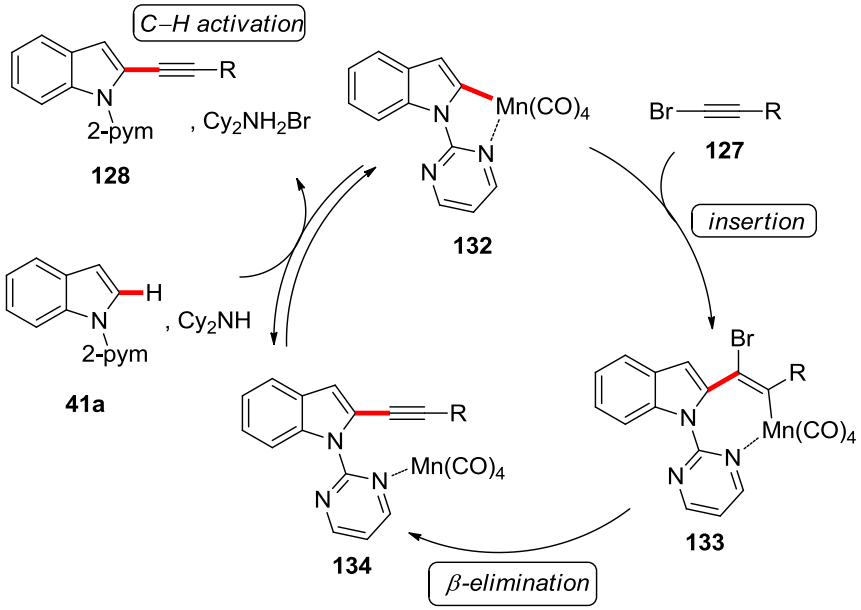


Scheme 1.3.16 Manganese(I)-catalyzed C–H alkynylation.

In 2017, Ackermann and coworkers described the first manganese(I)-catalyzed substitutive alkynylation with bromoalkynes **127** (Scheme 1.3.16).[118] The unique robustness of manganese catalyst was reflected by the unparalleled substrate scope, and valuable electrophilic functional group tolerance, including ester, cyano, halo, and nitro. Moreover, the substrate scope could be

further extended to aryl, alkenyl, and alkyl alkynes using a combination of $MnBr(CO)_5$ and triphenylborane as the key cocatalytic additive. It is worth noting that high efficiency was achieved, even with cocatalyst loadings as low as 0.05 mol %. More important, various acyclic peptides could also be employed as suitable substrates in this remarkable C–H alkynylation approach, delivering the corresponding products **128** in 53-82% yields without any racemization (Scheme 1.3.16a). In addition, a highly challenging macrocyclization was accomplished to provide the 21-membered cyclic peptide **130** under high-dilution conditions (Scheme 1.3.16b). At last, the pyridine group could also be removed in a traceless fashion under mild conditions.

The detailed mechanistic studies, including H/D exchange, KIE, and kinetic experiments revealed a fast and reversible C–Mn bond formation. Thereafter, a plausible catalytic cycle was proposed to be initiated by a facile organometallic C–H activation. Subsequently, the alkyne migratory insertion gives the seven-membered intermediate **133**. The final alkynylation product **128** was most likely generated through β-elimination, although a mechanism involving oxidative addition and reductive elimination could not be ruled out (Scheme 1.3.17).

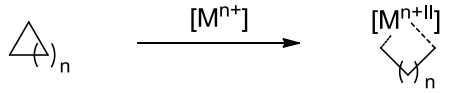


Scheme 1.3.17 Proposed catalytic cycle for manganese(I)-catalyzed C–H alkynylation.

1.4 Transition Metal-Catalyzed C–C Functionalizations

Selective transition metal-catalyzed carbon−carbon single bond functionalizations have recently been shown to be increasingly versatile tools for organic synthesis. Although numerous examples in this field have been disclosed in the past decade,[119] the reported examples are still much fewer than the reports of transition metal-catalyzed C–H functionalizations due to the intrinsic difficulties in activating C–C bonds *versus* C–H bonds in terms of thermodynamics and kinetics. The dissociation energy of C–C bond is rather high of up to 375 kcal mol^{-1},[120] which results in a higher inertness of C–C bond. Moreover, C–C σ-bond has a less favorable orbital directionality than C–H bond, which makes the orbital interaction with transition metals more difficult.[121] Therefore, selective C–C activations often needed harsh reaction conditions. However, applying more forcing conditions may end up the reactions in side products. To date, many different strategies have been developed to solve these problems in order to achieve the C–C bond cleaving transformations. The currently main methods for C–C bond activation are restricted to the highly strained systems such as three- and four-membered rings, or more polarized C–C bonds, for example, towards C–CN bond activation (Scheme 1.4.1). The strain-release energy (cyclopropane is 29.0 kcal mol^{-1})[122] facilitates the transition metal insertion leading to the formation of organometallic intermediate, which provides access to other organic molecules.[123] In addition, the strong electron-withdrawing cyano group could weaken the C–CN bond and coordinate to the transition metals that achieve the C–C bond activation.[124]

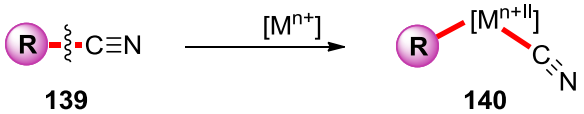
a) strain-release substrates



135, **136**
n = 1, 2

137, **138**
n = 1, 2

b) strong M–C(sp) bond

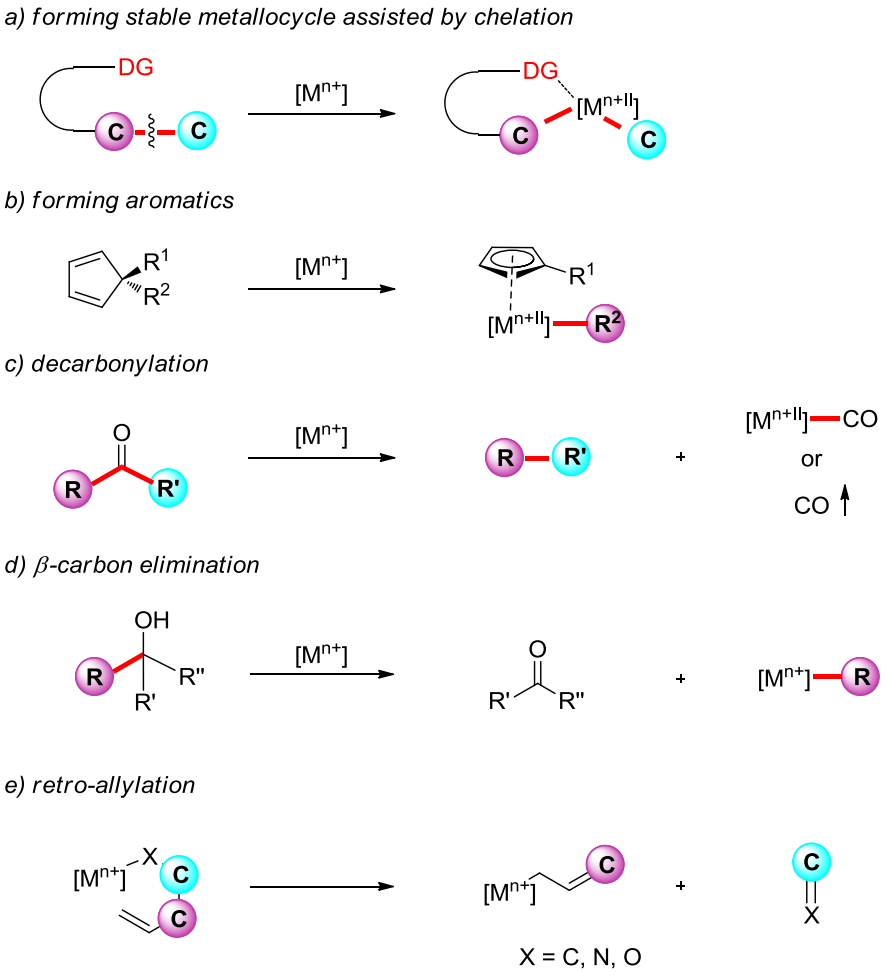


139

140

Scheme 1.4.1 C–C bond activations of strained and polarized substrates.

Besides these two transformations, other strategies have also been devised to enforce C–C cleavages (Scheme 1.4.2), including: a) forming stable metallacycles *via* a chelation-assisted oxidative addition step;[125] b) forming metallic aromatics;[126] c) decarbonylation of unstrained ketones;[127] d) forming the stable metal–carbon bond *via* a β-carbon elimination step;[128] e) retro-allylation base on a 6-membered transition state.[119a, 129]



Scheme 1.4.2 Other promising strategies for C–C bond activations.

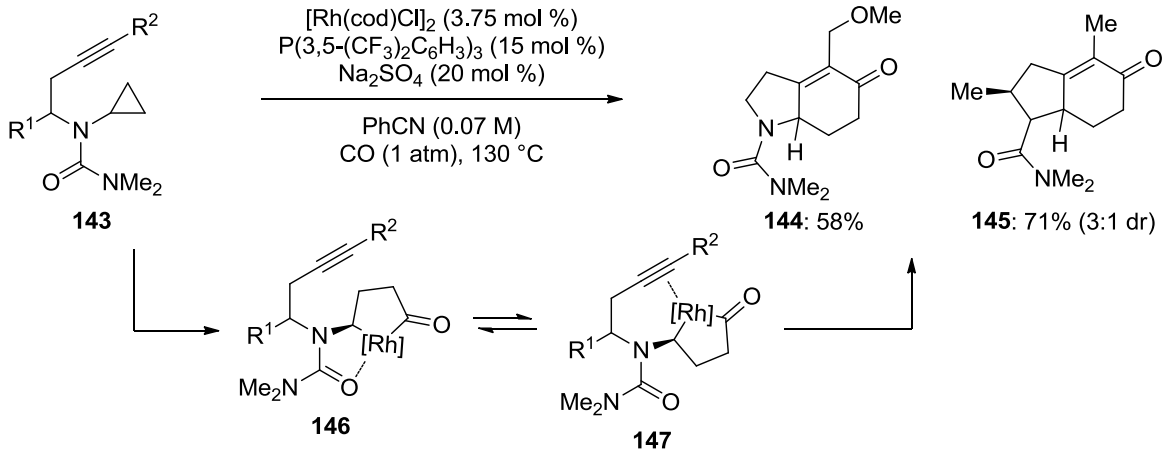
1.4.1 Transition Metal-Catalyzed C–C Functionalizations

The fist example of C–C activation by transition metal insertion was reported by Tipper in 1955 (Scheme 1.4.3).[130] The C–C bond of cyclopropane (**135**) was activated by $[H_2PtCl_6]$ generating a platinacyclobutane intermediate **141** (structure was corrected by Chatt in 1961, Tipper thought it reacted with"$PtCl_2$")[131] *via* an oxidative addition step.

135 **141** **142**

Scheme 1.4.3 Stoichiometric C–C cleavage cyclopropane *via* oxidative addition.

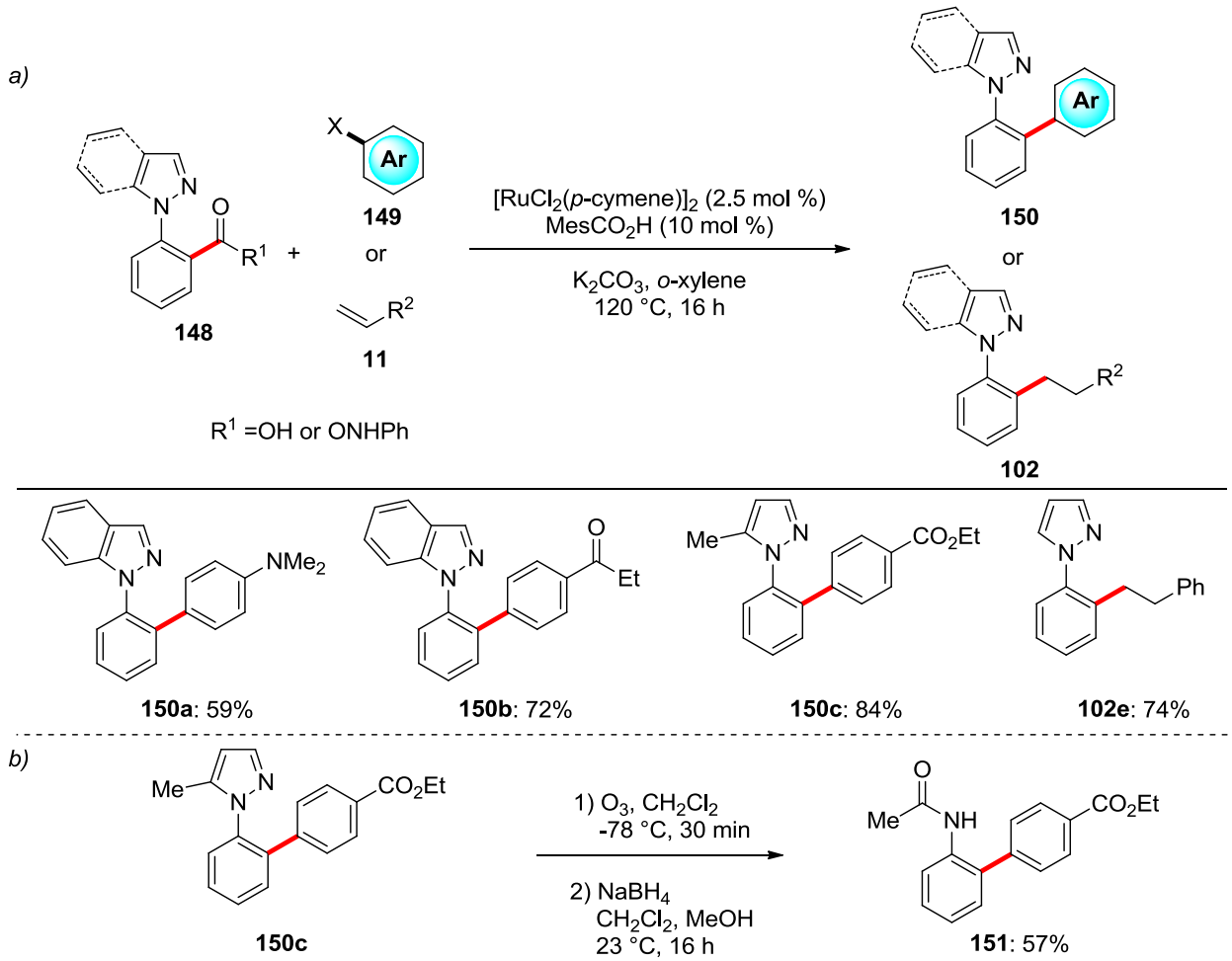
Inspired by the pioneering work of Tipper and Chatt, strained ring systems have thus emerged as role models for a number of C–C cleaving transformations.[123] For example, in 2013, Bower and coworkers developed rhodium-catalyzed multicomponent synthesis of *N*-heterobicyclic enones **144** and **145** by carbonylative C–C bond activation of aminocyclopropanes **143** (Scheme 1.4.4).[132] A plausible pathway was postulated. Firstly, the rhodium catalyst activates the proximal C–C bond of cyclopropane with the aid of *N*-protecting group, and then undergoes CO insertion generating the rhodacyclopentanone intermediate **146.** Finally, the desired product was obtained by the alkyne insertion and C–C bond reductive elimination.



Scheme 1.4.4 Rhodium-catalyzed carbonylative C–C activation of aminocyclopropanes.

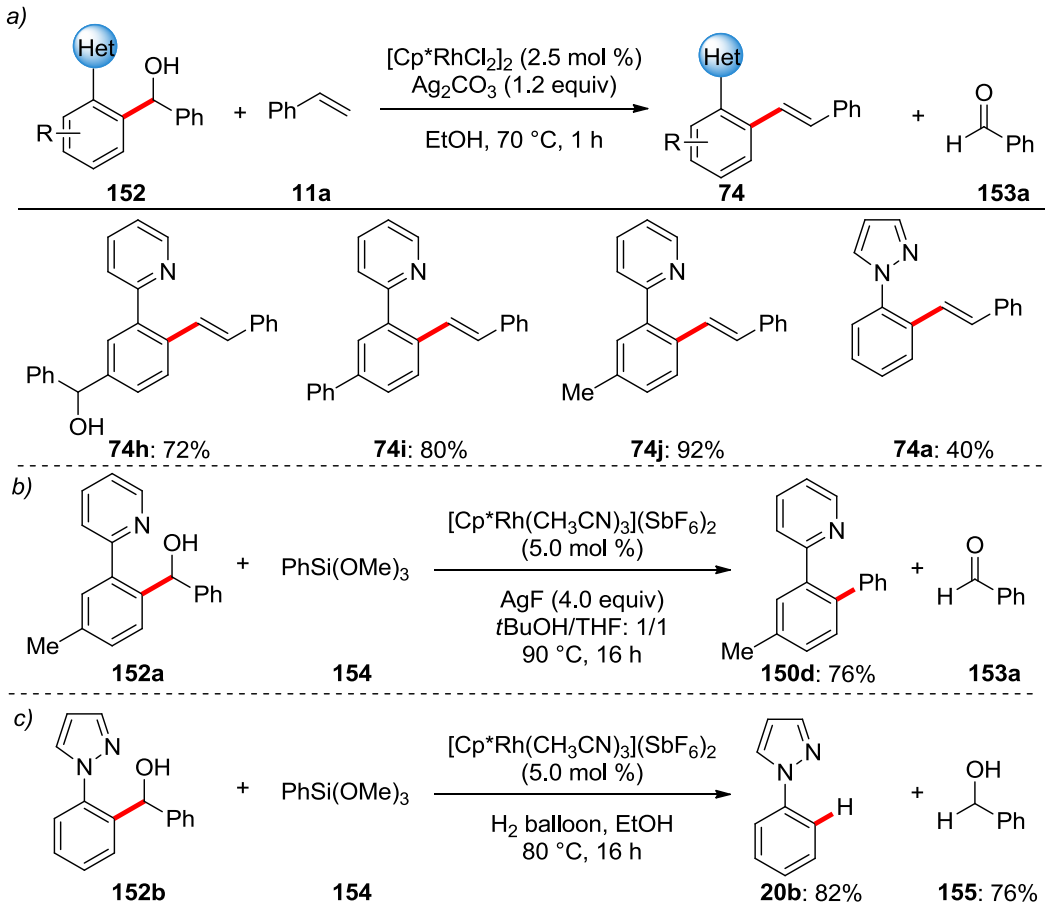
Meanwhile, other unstained substrates were also successfully employed for C–C activations, such as C–C bond cleavage assisted by chelation. Recently, Ackermann and coworkers reported an unprecedented ruthenium-catalyzed C–C arylations as well as C–C alkylations on decorated pyrazoles **148**.[133] The robust and unique ruthenium catalyst was reflected by fully tolerating valuable functional groups, including nitriles, cyano, free NH_2, halides, alkenes, esters, and ketones. The leaving group for C–C bond cleavage is not limited to the amide. Indeed, the decarboxylative C–C arylations and C–C alkylations were also successfully achieved under the optimal conditions.

Detailed mechanistic studies indicated a facile and reversible C–C metalation step (Scheme 1.4.5a). Moreover, the pyrazole group could be easily removed by ozonolysis,[134] providing the arylated anilides **151** in moderate yields (Scheme 1.4.5b).



Scheme 1.4.5 Ruthenium(II)-catalyzed C–C functionalizations by Ackermann and coworkers.

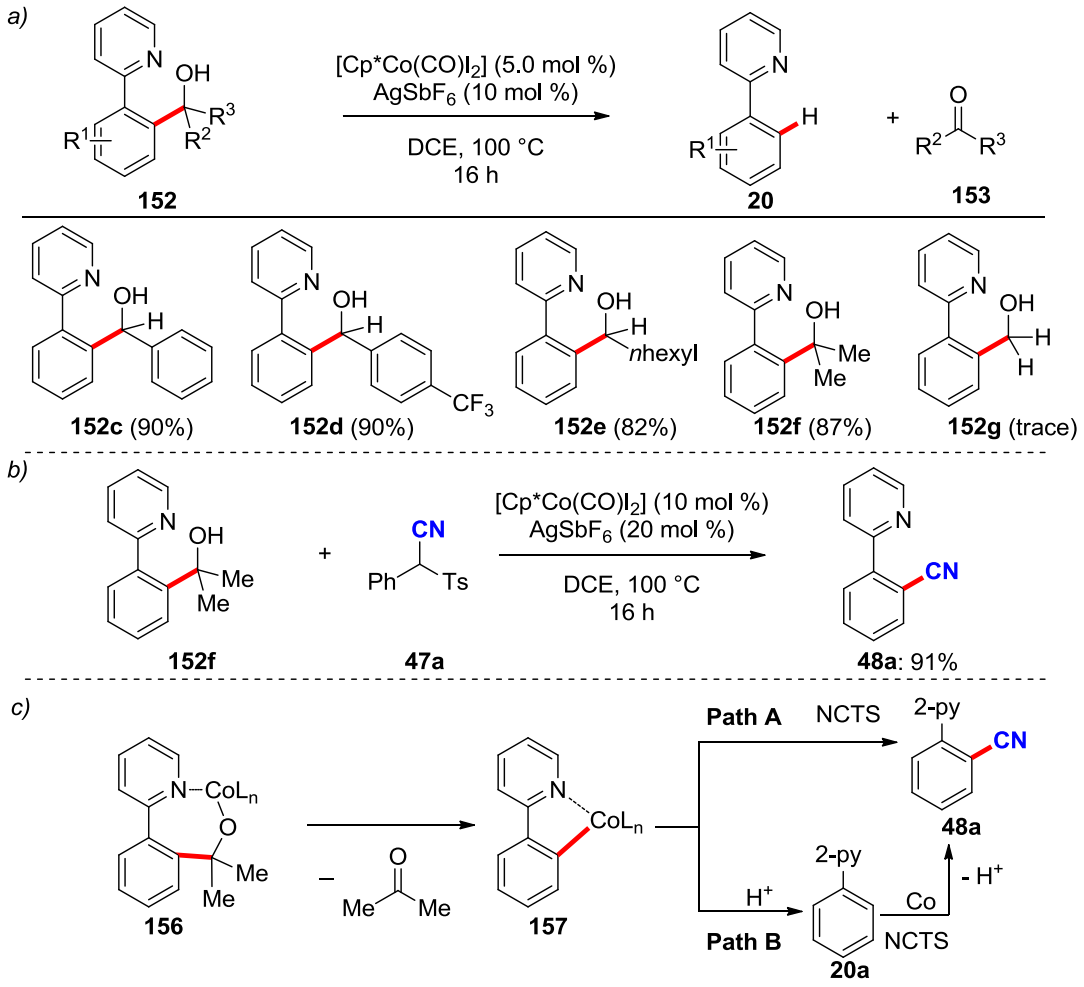
In 2011, Shi and coworkers developed a rhodium-catalyzed selective C–C bond activation of secondary alcohols **152** with the aid of a pyridinyl group *via* β-carbon elimination.[135] This C–C alkenylation features a broad reaction scope and highly functional group tolerance. Inter- and intra-molecular competition experiments both supported that C–C bond activation was much faster than the direct C–H activation under the optimal conditions. This strategy offered a mild and efficient process for C–C cleavage (Scheme 1.4.6a). Thereafter, the same group also reported the rhodium-catalyzed C–C arylation under an oxidative condition, and reductive cleavage of the C(sp^2)-C(sp^3) bond in the presence of H_2 as the reducing agent, respectively (Scheme 1.4.6b and c).[136]



Scheme 1.4.6 C–C bond activation *via* β-carbon elimination.

Compared to the noble metals, such as rhodium, cobalt is an alternative candidate for C–C bond activation due to its benefits of Earth-abundant, nontoxic. In 2015, Morandi and coworkers developed the C–C cleavage by using inexpensive cobalt as catalyst through a β-carbon elimination step.[137] The electronic and steric effects of the substrates both had little influence on the transformation of C–C cleavage. The secondary and tertiary alcohols underwent the reaction smoothly, but the primary alcohol could not achieve the C–C bond activation (Scheme 1.4.7a). Moreover, when the cyanating reagent NCTS (**47a**) was selected as the reaction partner, the desired product was obtained in 91% yield (Scheme 1.4.7b). Two possible pathways were proposed for the cobalt(III)-catalyzed C–C cyanation reaction. The cobalt intermediate **157** was firstly generated by the initial β-carbon elimination, and then underwent the cyanation directly, delivering the final product (Path A, direct C–C activation). Alternatively, the intermediate **157** could be trapped by proton providing the phenylpyridine firstly, then underwent the C–H functionalization and gave the desired product (Path B, C–C activation and then C–H functionalization) (Scheme

1.4.7c).

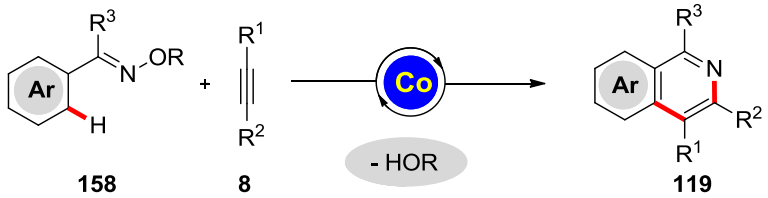


Scheme 1.4.7 Cobalt(III)-catalyzed C–C bond activation by Morandi and coworkers.

2 Objectives

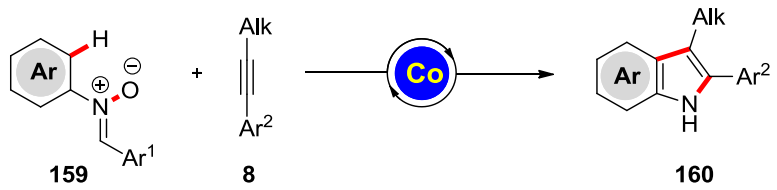
Transition metal-catalyzed C–H functionalizations have emerged as increasingly powerful tools for sustainable organic syntheses.[81b, 138] Remarkable advances in this area have been achieved by *Prof. Dr. Lutz Ackermann* and coworkers, which is mainly focused on the development of chemo- and site-selective syntheses of valuable organic molecules, with applications to pharmaceutical chemistry, materials sciences and peptide assembly.[80, 139] Within this context, major efforts were made to develop novel C–H or C–C activation reactions by environmentally-benign, less expensive and Earth-abundant versatile cobalt(III)/manganese(I) catalysts.

In the past few years, alkyne annulations by C–H/N–O functionalizations have proven to be instrumental for the step-economical assembly of various heterocycles with activities of relevance to medicinal chemistry and biology.[109c, 140] In addition, in light of the beneficial features of naturally abundant 3d transition metals, focus has shifted in recent years to the use of environmentally-benign, less expensive base metal catalysts for the C–H activation processes, such as cobalt catalyst. Therefore, it was of great interest to establish a novel approach for cobalt(III)-catalyzed C–H/N–O functionalization for the redox-neutral preparation of isoquinolines (Scheme 2.1).[141]



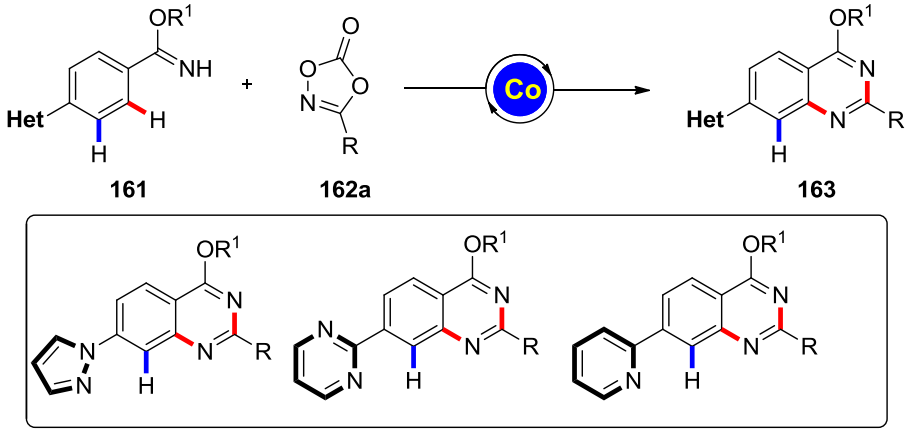
Scheme 2.1 Cobalt(III)-catalyzed C–H/N–O functionalization of *O*-acyl oximes **158**.

Substituted indoles are important structural motifs widely found in compounds of relevance to medicinal chemistry, crop protection, and drug discovery, among others.[142] Although the recent years have witnessed the emergence of C–H functionalization as increasingly powerful tools for the direct synthesis of indoles, these protocols largely required precious 4d and 5d transition metals.[143] In this regard, an Earth-abundant and environmentally-benign cobalt catalyst would be desired to be used for the synthesis of unprotected indoles by site-selective C–H activation (Scheme 2.2).[144]



Scheme 2.2 Selective synthesis of indoles by cobalt(III)-catalyzed C–H/N–O functionalization with nitrones **159**.

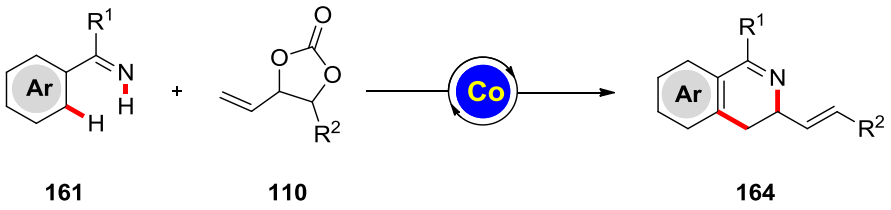
Biologically relevant *N*-heterocycles, such as pyrazoles, oxazolines, pyrimidines, or pyridines, can strongly coordinate to the active transition metals, in some cases, resulting in C–H activation at undesired position or catalyst poisoning,[145] which severely limits the application of these reactions in material sciences or drug discovery. In 2014, Yu reported the palladium-catalyzed position-selective C–H functionalizations of the substrates containing two different directing groups, which the *N*-heterocycles, such as pyridine, quinolone, pyrazine, pyrimidine, pyrazole, thiazole, and oxazoline, are fully tolerant.[146] Although major advances in cobalt(III)-catalyzed C–H functionalizations have been accomplished in recent years, no example was reported for cobalt(III)-catalyzed C–H activation fully tolerating strongly coordinating *N*-heterocycles. Herein, we would plan to establish cobalt(III)-catalyzed C–H amidation by the assistance of imidate that tolerated strongly coordinating *N*-heterocycles (Scheme 2.3).[147]



Scheme 2.3 Strongly coordinating *N*-heterocycles were fully tolerated in cobalt-catalyzed C–H amidations.

Despite significant progress of Cp*Co(III)-catalyzed C–H activation has been accomplished recently, large transformations still largely continue to simply mirror the activities and selectivities observed

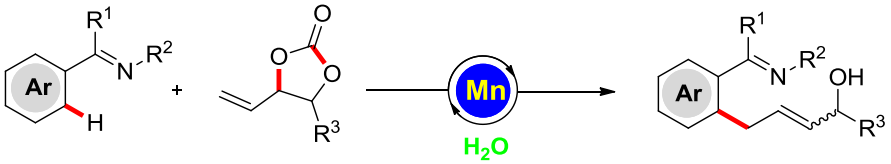
from their analogous Cp*Rh(III) counterparts. Herein, a first cobalt(III)-catalyzed domino reaction comprising C–H/N–H allylation for the direct synthesis of isoquinolines has been developed, which notably could not be achieved by Rh(III) catalysis (Scheme 2.4).[148]



161 **110** **164**

Scheme 2.4 Cobalt-catalyzed domino C–H/N–H allylations of imidates **161**.

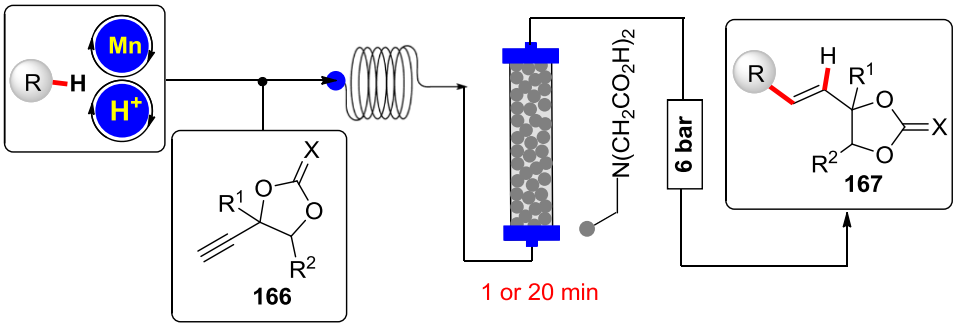
In 2016, Ackermann and coworkers reported an unprecedented manganese(I)-catalyzed substitutive C–H allylation with allyl carbontates **53**.[104] Based on this work, further expansion for manganese-catalyzed C–H allylation in water using dioxolanones **110** as the allyl source was investigated (Scheme 2.5).[149]



34, 41 **110** **111, 165**

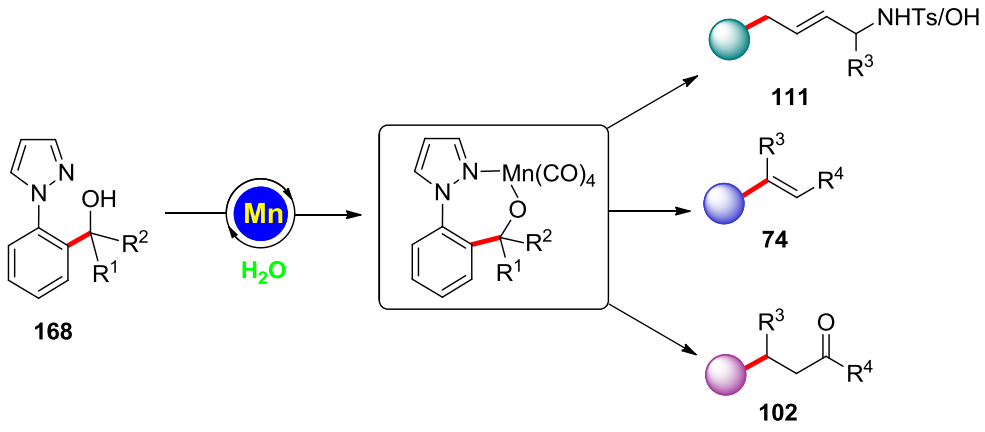
Scheme 2.5 Manganese(I)-catalyzed C–H activation for decarboxylative C–H/C–O cleavages.

Flow chemistry bears huge potential to address the needs of sustainable synthesis, facilitating challenging synthetic transformations and providing additional advantages, such as safer and faster reactions, clean products, and easy scale-up.[150] In addition, remarkable advances have been achieved with the aid of less toxic manganese catalysis over the last decade.[83] Nevertheless, all manganese(I)-catalyzed functionalization of substrates, bearing leaving groups in proximity to the C–C multiple bond, thus far resulted in β-heteroatom eliminations.[104-107, 151] Therefore, it is of great significance to develop a new versatile protocol, combining with continuous flow for manganese(I)-catalyzed C–H alkenylations without concurrent β-O elimination (Scheme 2.6).[152]



Scheme 2.6 Manganese(I)-catalyzed synergistic C–H activation for chemoselective hydroarylation in flow.

Recent years have witnessed great sucssess in transition-metal-catalyzed C–C bond activations, offering new opportunities to the synthesis of valuable and novel organic moleculars.[119] However, precious metals, such as rhodium, ruthenium and palladium, have always played a predominant role in this field, which limites their further application in synthetic chemistry due to the high cost and toxicity of these metals. In this regard, catalysts based on Earth-abundant metals, for example manganese, are highly desirable for C–C bond functionalization. In addition, organic synthesis reactions catalyzed in water is consistent with the requirements of green chemistry.[29] However, to date, transition-metal-catalyzed C–C functionalizations in water have proven elusive. Within our program on sustainable C–C functionalizations,[153] herein, we disclosed the first versatile C–C activation by inexpensive and less toxic manganese catalyst in water (Scheme 2.7).[154]



Scheme 2.7 Chelation-assisted manganese-catalyzed C–C activations in H_2O.

3 Results and Discussion

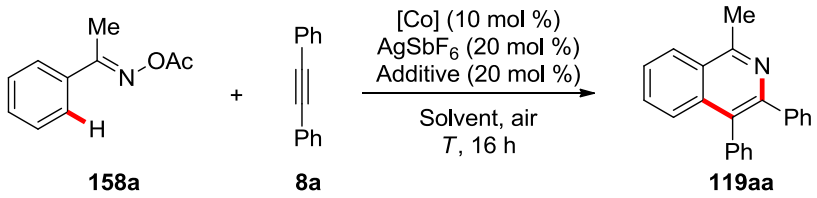
3.1 Cobalt(III)-Catalyzed C–H/N–O Functionalizations: Isohypsic Access to Isoquinolines

Isoquinolines are versatile heterocycles that are widely used as a key structural moiety present in integrate molecules with medicinal benefits, natural products and diverse bioactivities.[108] As a consequence, the development of efficient methods for the synthesis of isoquinolines continues to be of great interest. Over the past years, with advances in transition metal-catalyzed C–H bond functionalizations, many effective methods have been developed to synthesize isoquinolines mainly using second- and third-row transition metals.[109c, 140b-d, 155] Since the pioneering work of Matsunaga and Kanai,[56] Cp*Co(III) catalysts have been shown as an inexpensive alternative to Cp*Rh(III) catalysts for directed C–H activation. Within our research program on cobalt(III)-catalyzed C–H activation,[156] we developed a novel cobalt(III)-catalyzed C–H/N–O functionalizations for the redox-neutral preparation of isoquinolines.

3.1.1 Optimization Studies for the Synthesis of Isoquinoline

The cobalt(III)-catalyzed C–H annulation was initiated using (*E*)-acetophenone *O*-acetyl oxime (**158a**) and 1,2-diphenylethyne (**8a**) in the presence of Cp*Co(CO)I_2 as the catalyst (Table 3.1.1). Preliminary experiments indicated DCE to be the solvent of choice, while low yields of the product **119aa** were obtained in MeOH, H_2O, 1,4-dioxane, and toluene (entries 1-5). Attempts to decrease the catalyst loading or reaction temperature of this annulation reaction resulted in a significant decrease in the product yields (entries 6-7). The desired product was isolated in only 48% yield when HOPiv was introduced as the additive (entry 8). It is worth noting that the cobalt(III)-catalyzed alkyne annulation proceeded efficiently under an atmosphere of air (entry 9). A significant decrease in reaction efficacy was observed when the [Cp*Co(C_6H_6)](PF_6)$_2$ catalyst was employed for this reaction (entry 10). As anticipated, other cobalt catalysts did not afford the desired product **119aa** under the otherwise identical conditions (entries 11-13).

Table 3.1.1 Optimization studies for the synthesis of isoquinoline 119aa[a]



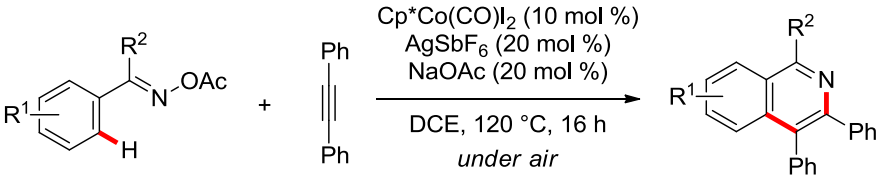
Entry	[Co]	Additive	Solvent	Yield
1	$Cp^*Co(CO)I_2$	NaOAc	MeOH	trace[b]
2	$Cp^*Co(CO)I_2$	NaOAc	H_2O	trace[b]
3	$Cp^*Co(CO)I_2$	NaOAc	1,4-dioxane	18%[b]
4	$Cp^*Co(CO)I_2$	NaOAc	toluene	11%[b]
5	$Cp^*Co(CO)I_2$	NaOAc	DCE	86%[b]
6	$Cp^*Co(CO)I_2$	NaOAc	DCE	63%[c]
7	$Cp^*Co(CO)I_2$	NaOAc	DCE	60%[d]
8	$Cp^*Co(CO)I_2$	HOPiv	DCE	48%
9	**$Cp^*Co(CO)I_2$**	**NaOAc**	**DCE**	**87%**
10	$[Cp^*Co(C_6H_6)](PF_6)_2$	NaOAc	DCE	45%[e]
11	$CoCl_2$	NaOAc	DCE	---
12	$Co(OAc)_2$	NaOAc	DCE	---
13	$Co(acac)_2$	NaOAc	DCE	---

[a] Reaction conditions: **158a** (0.50 mmol), **8a** (0.75 mmol), [Co] (10 mol %), $AgSbF_6$ (20 mol %), additive (20 mol %), solvent (2.0 mL), under air, 120 °C, 16 h, isolated yield. [b] Under N_2. [c] $Cp^*Co(CO)I_2$ (5.0 mol %) was used. [d] *T* = 100 °C. [e] **158a** (0.25 mmol) was used.

3.1.2 Scope of Cobalt(III)-Catalyzed C–H/N–O Functionalization

3.1.2.1 Cobalt(III)-Catalyzed C–H/N–O Functionalization with Substituted Arenes 158

With the optimized catalytic conditions in hand (Table 3.1.1, entry 9), we evaluated the reaction versatility by utilizing various substituted arenes **158** (Scheme 3.1.1).



R = H (**119aa**): 81% (1.2 g scale)
R = Me (**119ba**): 61%[a]
R = OMe (**119ca**): 87%
R = Ph (**119da**): 83%[a]
R = CF_3 (**119ea**): 95%[a]
R = F (**119fa**): 94%[a]
R = Cl (**119ga**): 94%[a]
R = Br (**119ha**): 82%[a]
R = NO_2 (**119ia**): 47%
R = CN (**119ja**): 90%[a]

119ka: 64%

R = Me (**119la**): 53%[a]
R = Cl (**119ma**): 70%
R = Br (**119na**): 76%

119oa: 45%

119pa: 83%

119qa: 85%[a]

R = Et (**119ra**): 88%[a]
R = *i*Pr (**119sa**): 83%

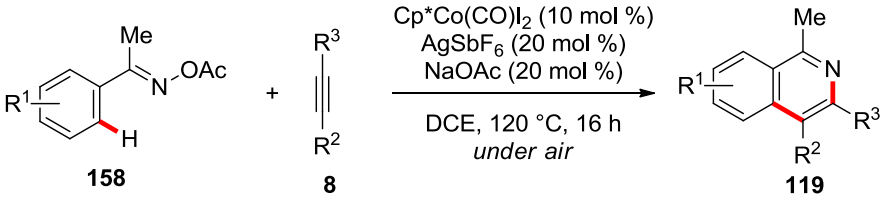
119ta: 85%[b]

Scheme 3.1.1 Scope of cobalt(III)-catalyzed C–H/N–O functionalization with substituted arenes **158**. [a] 15 min reaction time. [b] In HFIP.

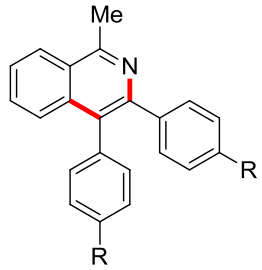
Both electron-donating and -withdrawing groups at the *para*-position, such as alky, methoxy, fluoro, trifluoromethyl, chloro, bromo, nitro, and cyano, were all well tolerated and afforded the desired products **119** in moderate to excellent yields. When *O*-acetyl oximes **158l-158m** bearing methyl, chloro and bromo groups at the *meta*-positions were chosen as the substrates, the C–H activation occurred at the least hindered site and afforded the desired product in good yields with excellent

selectivities, due to the small size of the cobalt. However, while the secondary interactions dominated in oxime derivatives, the totally opposite positions were selectively functionalized (**119oa** and **119pa**). The C–H/N–O annulation with substituted arene **158q** set the stage for the assembly of the tricyclic product **119qa**. In addition, the heterocyclic product **119ta** was obtained in 85% yield with good regioselectivity when HFIP was employed as the reaction solvent. It is noteworthy that high catalytic activity of this cobalt(III) catalyst was showcased by obtaining the annulation products in high yields within only 15 min.

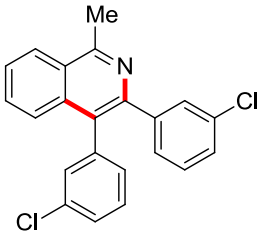
3.1.2.2 Isohypsic Annulation of Alkynes 8



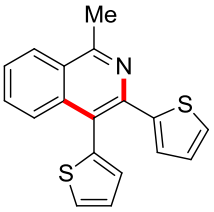
(i) aryl alkynes



R = Me (**119ab**): 89%[a]
R = CF_3 (**119ae**): 65%
R = F (**119af**): 67%
R = Cl (**119ag**): 66%
R = Br (**119ah**): 71%

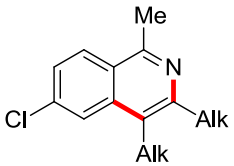


119ai: 52%



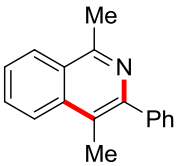
119aj: 84%

(ii) alkyl alkynes

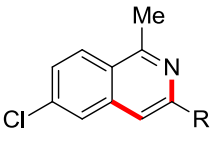


R = Et (**119gk**): 75%[a]
R = *n*Pr (**119gl**): 61%
R = *n*Bu (**119gm**): 85%

(iii) unsymmetrical alkynes



119an: 68%



R = Ph (**119go**): 65%
R = *p*Tol (**119gp**): 61%

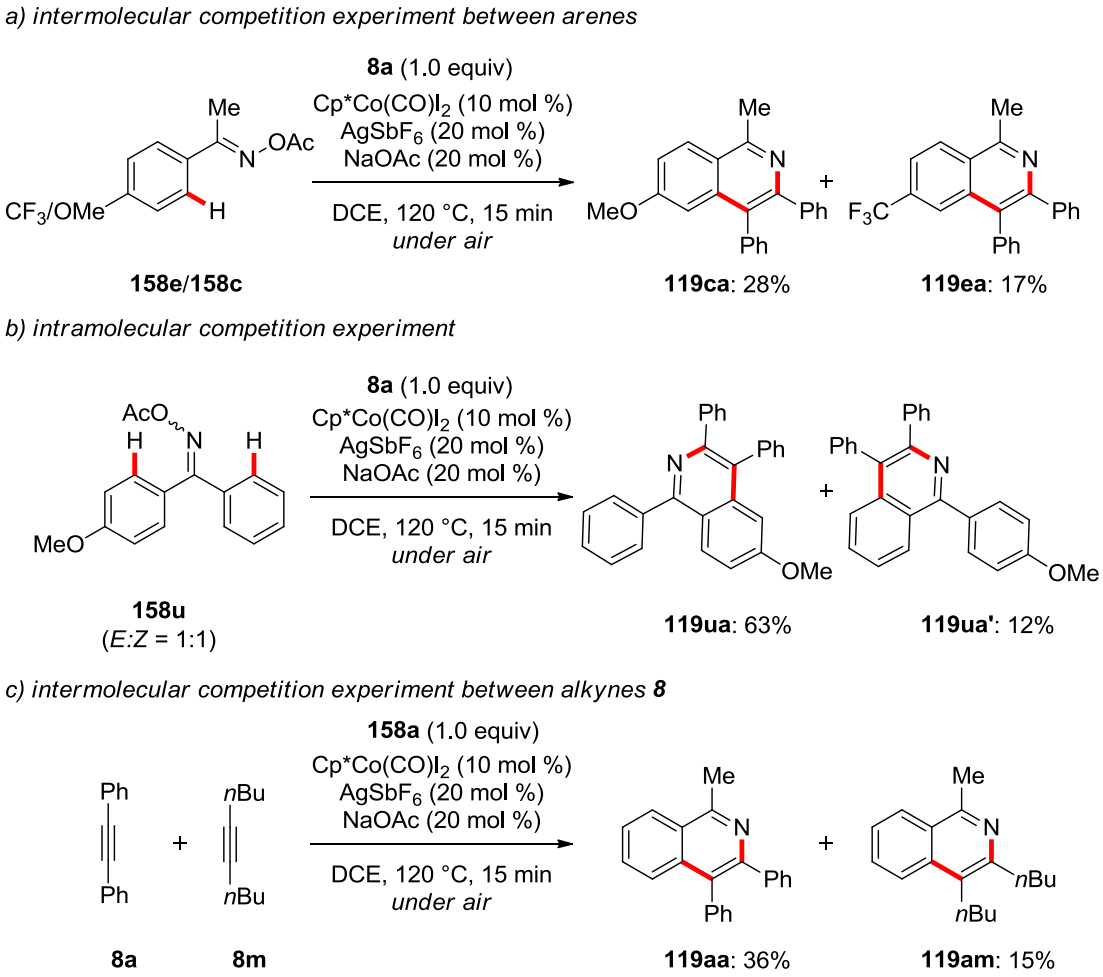
Scheme 3.1.2 Isohypsic annulation of alkynes **8**. [a] 15 min reaction time.

Subsequently, we further explored the scope of this cobalt(III)-catalyzed C–H/N–O functionalization

by testing different alkynes **8** (Scheme 3.1.2). Various aryl- and alkyl-substituted alkynes were viable substrates, delivering the desired products in moderate to good yields (**8b**-**8m**). Unsymmetrical alkyne **8n** underwent the reaction smoothly and provided the single products **119an** with the phenyl substituent next to nitrogen in 68% yield. Terminal alkynes were also successfully applied for this annulation reaction, generating the desired products in good yields with excellent regio-selctivity (**119go**-**119gp**).

3.1.3 Mechanistic Studies

3.1.3.1 Competition Experiments



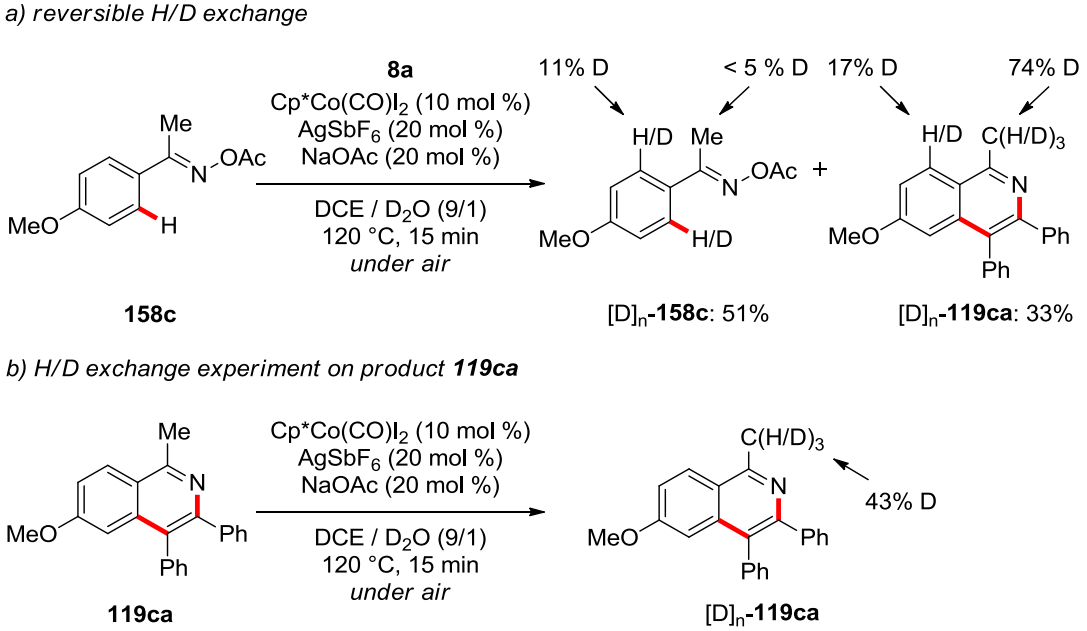
Scheme 3.1.3 Intermolecular and intramolecular competition experiments.

Furthermore, intermolecular and intramolecular competition experiments between electron-rich **158c** and electron-deficient arenes **158e** under the optimized conditions were carried out (Scheme

3.1.3a and b). As a result, the electron-rich arenes react preferentially, which possibly supports a base-assisted internal electrophilic-type substitution (BIES) C–H activation by the cationic cobalt catalyst. It is noteworthy that the diastereomeric mixture of substrate **158u** afforded the annulation product in high yield (63% + 12%). This result indicated that a *Z*-configuration of the *O*-acetyl oximes is not a prerequisite for this alkyne annulation reaction.[157] Further, a competition experiment between different alkynes showed that aromatic substituents increased the inherent reaction rate (Scheme 3.1.3c).

3.1.3.2 H/D-Exchange Experiments

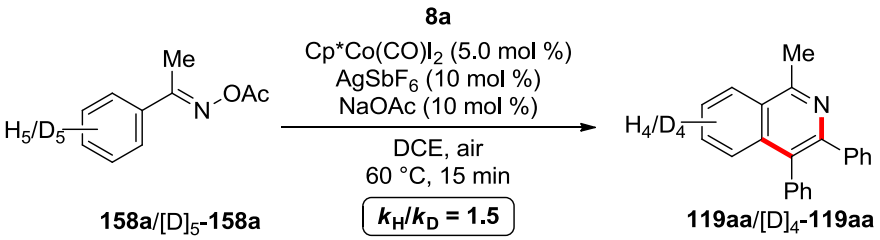
Moreover, in order to understand the mechanism of this C–H activation reaction, the H/D-exchange experiment using substrate (*E*)-1-(4-methoxyphenyl)ethanone *O*-acetyl oxime (**158c**) with D_2O as the co-solvent was conducted. Here, significant deuterium incorporation was observed in the *ortho*-position of reisolated substrate $[D]_n$-**158c** as well as the product $[D]_n$-**119ca** (Scheme 3.1.4a), revealing the C–H cobaltation process is reversible. Moreover, a 74% D incorporation was observed at the C(sp^3)–H bond of the product $[D]_n$-**119ca**, suggesting that the cationic cobalt catalyst could enolize the product (Scheme 3.1.4b).

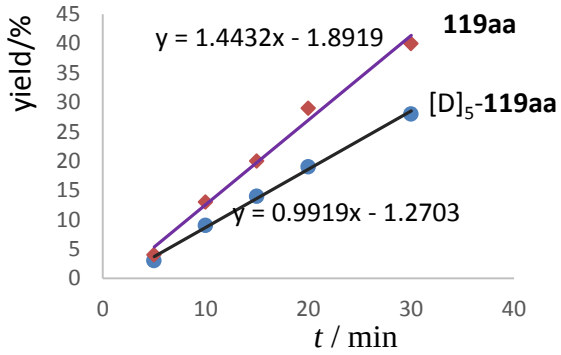


Scheme 3.1.4 H/D exchange experiments.

3.1.3.3 Kinetic Isotope Effect

The kinetic isotope effect (KIE) of the cobalt(III)-catalyzed C–H activation was determined by independent experiments of substrates **158a** and [D]$_5$-**158a** to be $k_H/k_D \approx 1.5$ (Scheme 3.1.5). The result suggested that the reversible C–H metalation is not the rate-determining step.

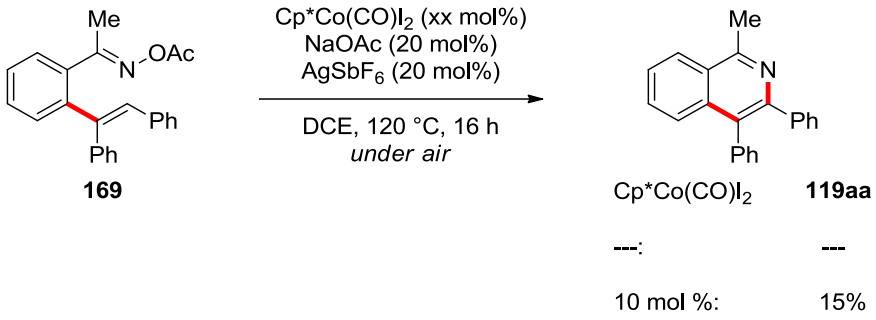




Scheme 3.1.5 Kinetic isotope effect experiment.

3.1.3.4 Attempted Cyclization of *ortho*-Alkenylated Arene 169

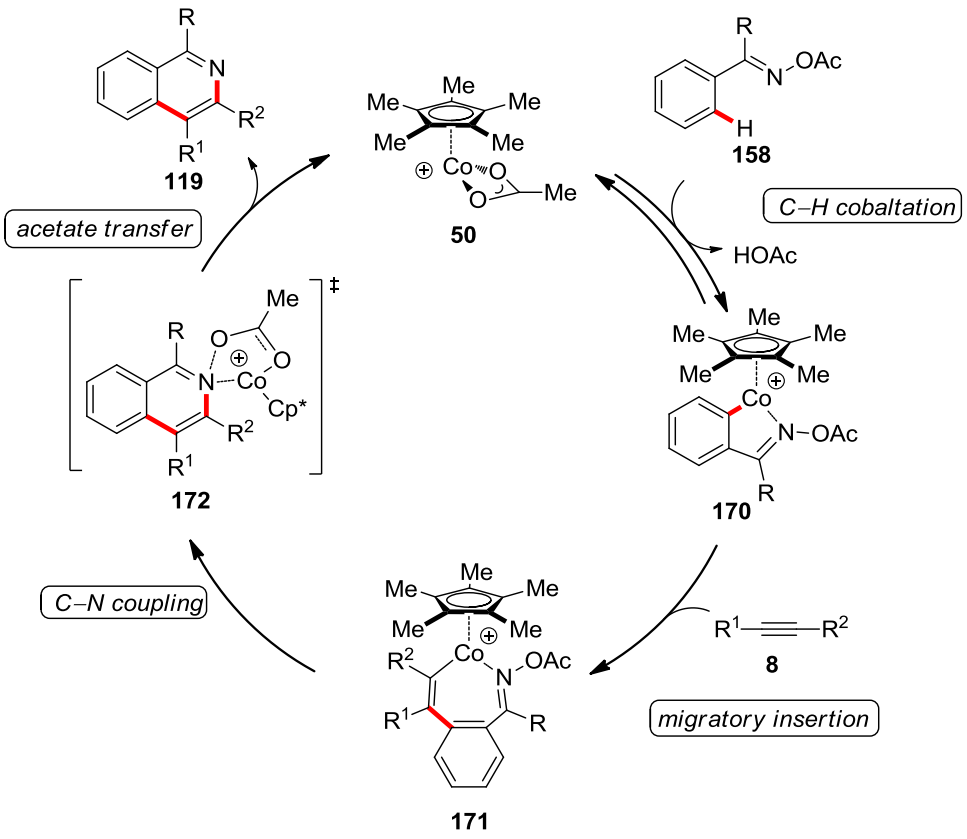
Additionally, the *ortho*-alkenylated intermediate **169** was separately prepared and subjected to the reaction conditions (Scheme 3.1.6). Notably, the cyclic product **119aa** as not observed when the reaction was performed without Cp*Co(III) catalyst. Likewise, the attempted transformation of substrate **169** in the presence of Cp*Co(III) catalyst gave the isohypsic alkyne annulation product in only 15% yield, suggesting a hydroarylation/electrocyclization sequence unlikely to be operative.



Scheme 3.1.6 Attempted cyclization of *ortho*-alkenylated arene **169**.

3.1.4 Proposed Catalytic Cycle

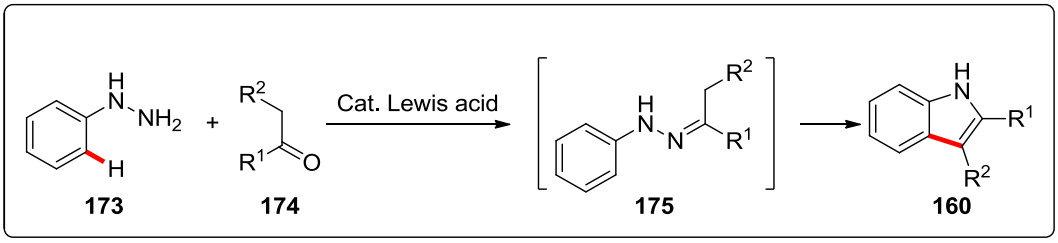
In summary, based on the mechanistic findings, a catalytic cycle was proposed for the cobalt(III)-catalyzed C–H/N–O functionalization (Scheme 3.1.7). The catalytically active species might be a cationic cobalt(III)-acetate complex **50** formed by reaction of cobalt(III) precursor and $AgSbF_6$. The reaction is initiated by reversible C–H cobaltation of *O*-acetyl oxime **158**, assisted by the acetate additive and presumably proceeds *via* a BIES-type pathway to furnish the intermediate **170**. Then the key alkenyl intermediate **171** is generated by the alkyne migratory insertion, which subsequently undergoes the intramolecular cyclization by a C–N bond formation. Finally, the desired product **119** was obtained along with the regeneration of the catalytic cobalt(III) complex **50** by a concerted acetate transfer process.



Scheme 3.1.7 Proposed catalytic cycle.

3.2 Selective Synthesis of Indoles by Cobalt(III)-Catalyzed C–H/N–O Functionalization with Nitrones

Substituted indoles are important building blocks abundantly found in natural products and pharmaceutically active compounds.[142b] Since Fischer and coworkers developed the new method for the synthesis of indole in 1883 from an arylhydrazine with a ketone or an aldehyde *via* the acid-mediated arylhydrazone formation, following by [3,3]-sigmatropic rearrangement (Scheme 3.2.1),[158] indole synthese have become one of the most important topics in modern synthetic chemistry. Among those methods, C–H activation has recently rapidly emerged as a robust tool for the synthesis of indole derivatives, avoiding the use of pre-functionalized substrates.[8, 13b] In the past few years, significant progress has been achieved in C–H activation using Earth-abundant and inexpensive first-row transition metals.[35b] While many routes for the synthesis of indoles have been reported, developing mild, environmentally-benign and atom-economical methods remains an important area. Herein, we became attracted to devise a protocol for cobalt(III)-catalyzed indole synthesis.



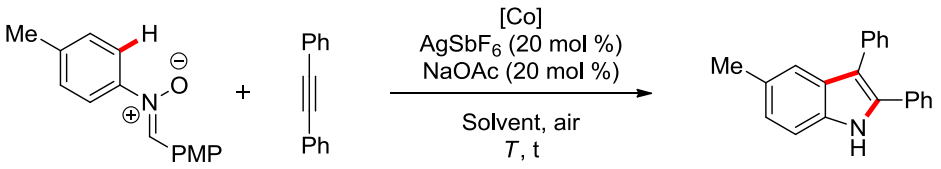
Scheme 3.2.1 Fischer indole synthesis.

3.2.1 Optimization of Cobalt(III)-Catalyzed C–H/N–O Alkyne Annulation

We initiated our studies by testing the feasibility of the envisioned cobalt(III)-catalyzed C–H/N–O functionalization with nitrone **159a** and 1,2-diphenylethyne (**8a**) (Table 3.2.1). Preliminary experiments highlighted Cp*Co(CO)I_2 to be the catalyst of choice and indicated that TFE and HFIP were most suitable solvents (entries 1-7). A significant decrease in the product yields was observed when lower catalyst loadings or shorter reaction time were tested (entries 8-11). The isohypsic alkyne annulation proceeded at lower reaction temperatures, yet the best yield of the indole product **160aa** was accomplished at 100 °C (entries 12-15). Moreover, the desired product was

formed in 92% yield by a cationic single-component catalyst, thus avoiding the use of any silver salts (entry 16). It is noteworthy that only 13% yield of the annulation product **160aa** was observed in the presence of $[Cp^*RhCl_2]_2$ as the catalyst (entry 17).

Table 3.2.1 Optimization of alkyne annulation[a]

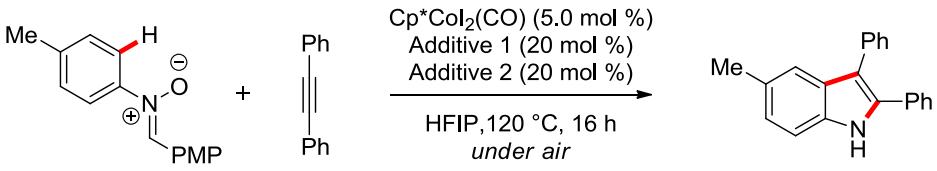


159a **8a** **160aa**

Entry	[Co] / mol %	Solvent	*T* / °C	Yield[b]
1	$Cp^*CoI_2(CO)$ / 10	TFE	120	88%
2	$Cp^*CoI_2(CO)$ / 10	TFE	120	75%
3	$Cp^*CoI_2(CO)$ / 10	DCE	120	21%
4	$Cp^*CoI_2(CO)$ / 10	1,4-dioxane	120	trace
5	$Cp^*CoI_2(CO)$ / 10	MeOH	120	--
6	$Cp^*CoI_2(CO)$ / 10	HFIP	120	6% [c]
7	$Cp^*CoI_2(CO)$ / 5.0	HFIP	120	90%
8	$Cp^*CoI_2(CO)$ / 2.5	HFIP	120	64%
9	$Cp^*CoI_2(CO)$ / 1.0	HFIP	120	5%
10	$Cp^*CoI_2(CO)$ / 5.0	HFIP	120	49% [d]
11	$Cp^*CoI_2(CO)$ / 5.0	HFIP	120	67% [e]
12	**$Cp^*CoI_2(CO)$ / 5.0**	**HFIP**	**100**	**92%**
13	$Cp^*CoI_2(CO)$ / 5.0	HFIP	80	77%
14	$Cp^*CoI_2(CO)$ / 5.0	HFIP	50	46%
15	$Cp^*CoI_2(CO)$ / 5.0	HFIP	23	9%
16	**$[Cp^*Co(CH_3CN)_3](SbF_6)_2$ / 5.0**	**HFIP**	**120**	**92%** [f]
17	$[Cp^*RhCl_2]_2$ / 2.5	HFIP	120	13%

[a] Reaction conditions: **159a** (0.50 mmol), **8a** (0.75 mmol), $AgSbF_6$ (20 mol %), NaOAc (20 mol %), solvent (2.0 mL), under air, 100 °C, 16h. [b] Yield of isolated product. [c] $Cu(OAc)_2$ (1.0 equiv) was used. [d] 1 h. [e] 3 h. [f] Without Ag salts.

Table 3.2.2 Effect of additives[a]



159a **8a** **160aa**

Entry	Additive 1	Additive 2	Yield[b]
1	**$AgSbF_6$**	**NaOAc**	**92%**
2	$AgPF_6$	NaOAc	82%
3	$AgBF_4$	NaOAc	80%
4	AgOTs	NaOAc	82%
5	AgOTf	NaOAc	86%
6	--	K_2CO_3	10%
7	$AgSbF_6$	KOAc	86%
8	$AgSbF_6$	CsOAc	88%
9	$AgSbF_6$	--	7%
10	$AgSbF_6$	NaOAc	--[c]

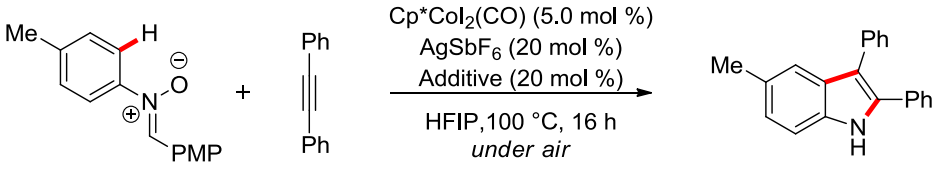
[a] Reaction conditions: **159a** (0.50 mmol), **8a** (0.75 mmol), $Cp^*CoI_2(CO)$ (5.0 mol %), additive 1 (20 mol %), additive 2 (20 mol %), HFIP (2.0 mL), under air, 120 °C, 16h. [b] Yield of isolated product. [c] Without $Cp^*CoI_2(CO)$.

Furthermore, various additives were tested for the cobalt(III)-catalyzed C–H/N–O functionalization (Table 3.2.2). Different silver salts were firstly employed for the reaction, delivering the desired product **160aa** in satisfactory yields. $AgSbF_6$ was optimal, presumably because hexafluoroantimonate is a weakly-coordinating and non-nucleophilic anion which stabilizes the cationic cobalt species (entries 1-5). Subsequently, the reactions with different bases or without base were examined, and these results suggested that NaOAc is the most effective (entries 6-9). A control experiment showed that there was no reaction in the absence of the cobalt(III) catalyst (entry 10).

The last few years have witnessed the significant progress of *N*-acyl amino acids as powerful ligands in transition metal-catalyzed C–H activation, as reported by Yu[159] and Ackermann group.[160]

Therefore, with the previous optimization results in hand, we tested a series of amino acid ligands instead of NaOAc for the cobalt(III)-catalyzed C–H/N–O functionalization with nitrone **159a** (Table 3.2.3). Notably, Piv-Leu-OH proved to be a powerful ligand, delivering the desired indole **160aa** in 88% yield (entry 4).

Table 3.2.3 Effect of different amino acid ligands[a]



159a **8a** **160aa**

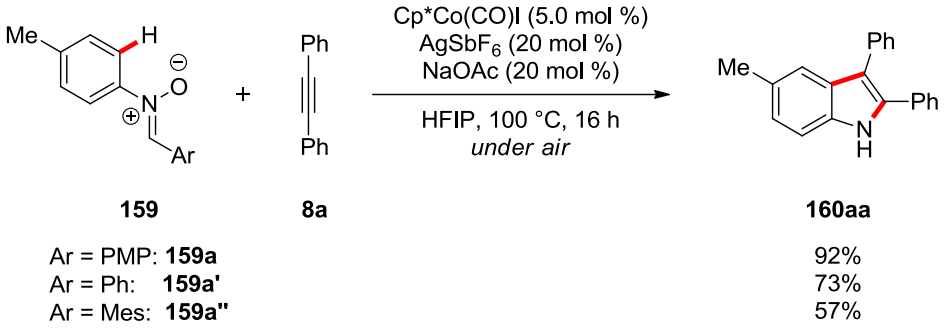
Entry	Additive	Yield[b]
1	Piv-Ile-COONa	73%
2	Ac-Ile-COONa	83%
3	Piv-Phe-OH	71%
4	**Piv-Leu-OH**	**88%**
5	Piv-Ile-OH	78%
6	$MeCO_2$-Ile-OH	74%
7	Piv-Pro-OH	74%
8	Fmoc-Met-OH	6%
9	Ac-Tyr-OH	68%
10	Piv-Ala-OH	72%
11	Ac-Ile-OH	77%
12	Piv-Asn-OH	73%
13	Ac-Leu-COONa	87%

Reaction conditions: **159a** (0.50 mmol), **8a** (0.75 mmol), $Cp^*CoI_2(CO)$ (5.0 mol %), $AgSbF_6$ (20 mol %), additive (20 mol %), HFIP (2.0 mL), under air, 100 °C, 16h. [b] Yield of isolated product.

3.2.2 Influence of the *C*–Substitution Pattern

Moreover, we also tested the dependence of the catalytic efficacy on the *C*–substitution pattern of the nitrones **159** (Scheme 3.2.2). These test reactions under the optimized reaction conditions

verified the importance of the *C*–substitution pattern. Notably, the electron-donating PMP substituent afforded the desired product **160aa** in the highest yield of 92%, presumably due to the fine tunning of electronic and steric factors.

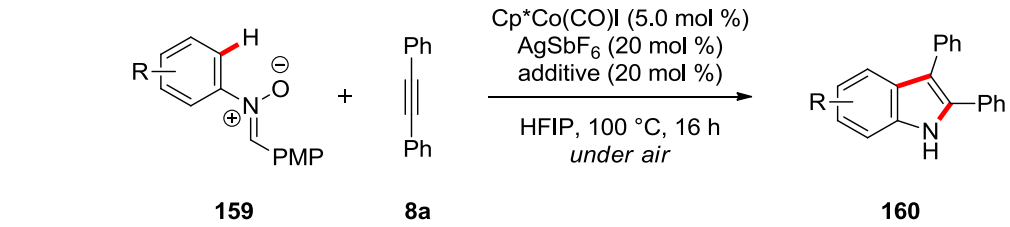


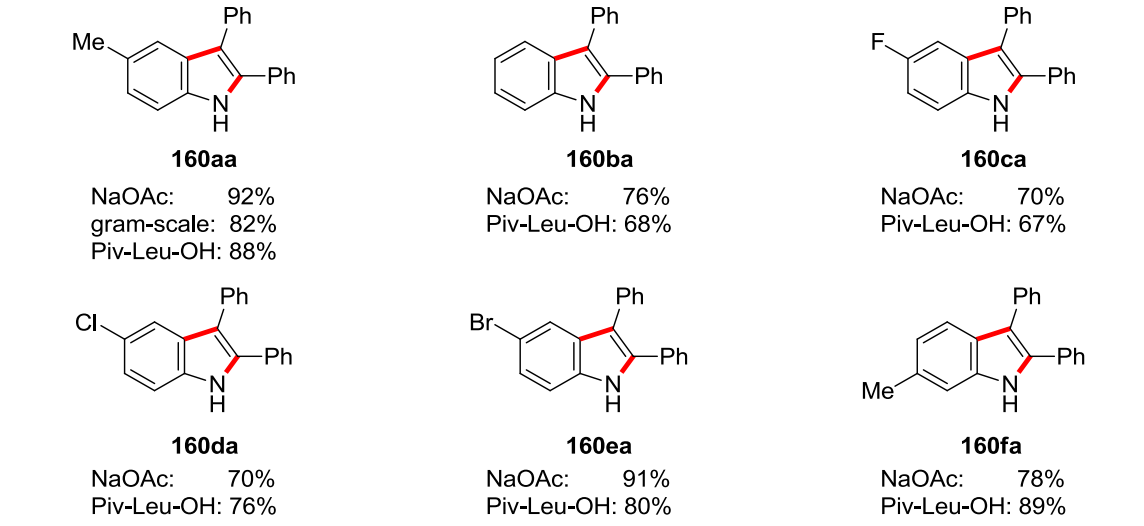
Scheme 3.2.2 Influence of the *C*–substitution pattern on nitrones.

3.2.3 Scope of Cobat-Catalyzed C–H/N–O Functionalization

3.2.3.1 C–H/N–O Functionalization with Nitrones 159

With the optimized catalytst in hand (Table 3.2.1, entry 12 and Table 3.2.3, entry 4), the scope of the cobalt(III)-catalyzed C–H/N-O annulation with various substituted nitrones **159** was examined (Scheme 3.2.3). A variation of substituents in *para*-position of the nitrones led to overall good to excellent yields. Moreover, valuable functional groups, such as fluoro, chloro, and bromo, were well tolerated under the optimal reaction conditions (**160ca**-**160ea**). The intramolecular competition experiment with *meta*-substituted nitrone **159f** bearing two different *ortho*-C–H bonds delivered site-selectively indole **160fa** as the sole product. Moreover, there are no significant differences in the product yields between Piv-Leu-OH and NaOAc as the additives.

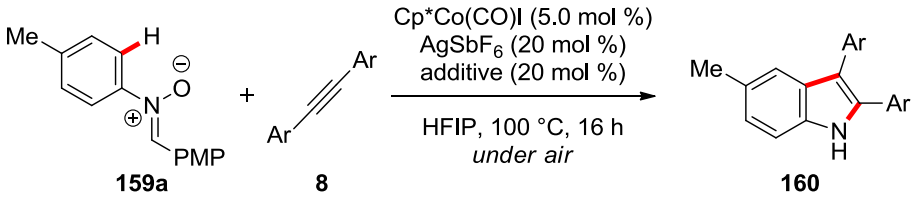


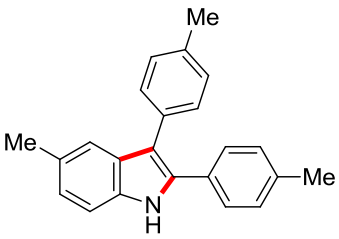


Scheme 3.2.3 C–H/N–O functionalization with nitrones **159**.

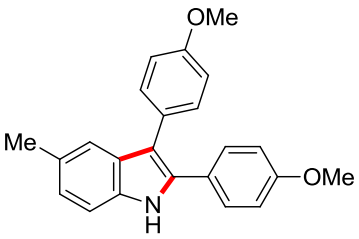
3.2.3.2 Cobalt(III)-Catalyzed Annulation of Tolanes

Furthermore, the reaction was explored with differently substituted tolane derivatives **8**, which also proved to be viable for the C–H annulation reaction and afforded the 2,3-diaryl indoles **160** in moderate to good yields (Scheme 3.2.4). Notably, this cobalt(III)-catalyzed annulation reaction was shown tolerant for both electron-donating and electron-withdrawing groups, including Me (**8b**), OMe (**8c**), Cl (**8g, 8h**) and CF_3 (**8e**).

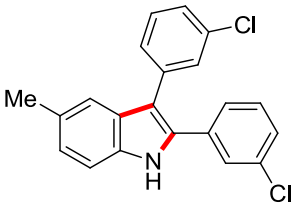




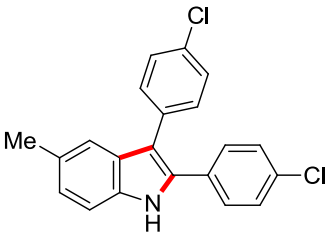
160ab
NaOAc: 57%
Piv-Leu-OH: 74%



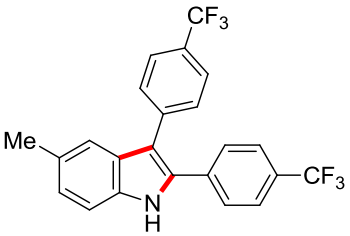
160ac
NaOAc: 76%
Piv-Leu-OH: 71%



160ah
NaOAc: 83%
Piv-Leu-OH: 78%



160ag
NaOAc: 53%
Piv-Leu-OH: 56%

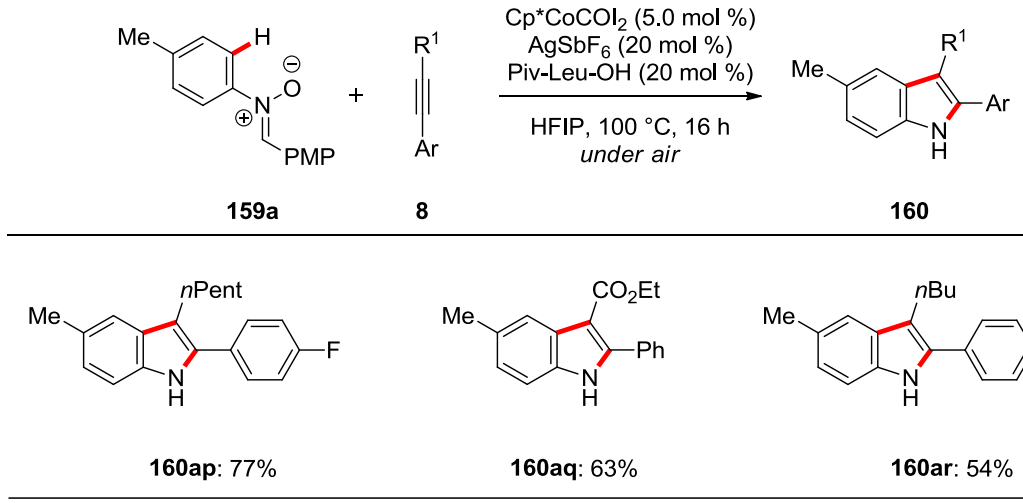


160ae
NaOAc: 68%
Piv-Leu-OH: 73%

Scheme 3.2.4 Cobalt(III)-catalyzed annulation of tolanes **8**.

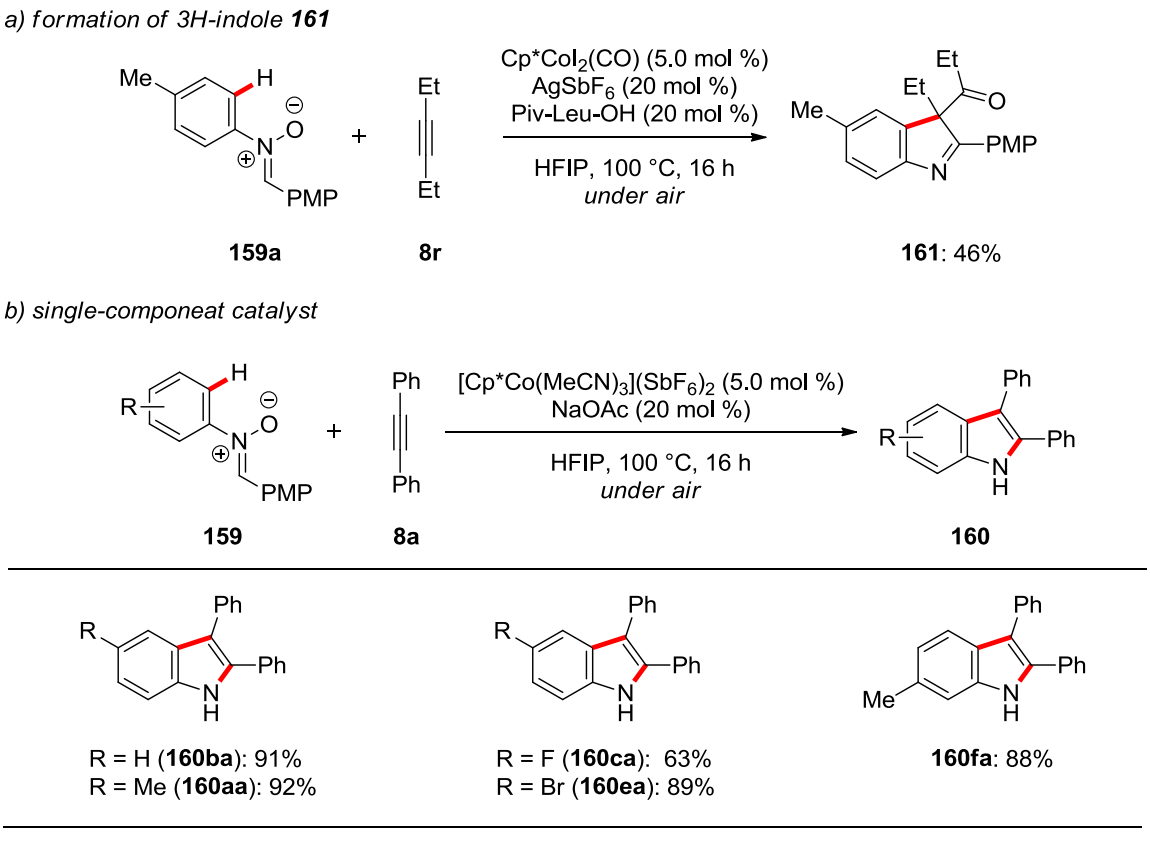
3.2.3.3 Cobalt(III)-Catalyzed Annulation of Unsymmetrical Alkynes

Particularly, when unsymmetrically substituted alkynes **8** were applied to this reaction using Piv-Leu-OH as the additive, the corresponding products **160ap-160ar** was obtained in good yields and excellent regio-selectivities (Scheme 3.2.5). By comparison with a related rhodium(III)-catalyzed indole synthesis,[161] higher regio-selectivities (*E*/*Z* >15) were obtained, highlighting a more effective cobalt catalysis for this annulation reaction.



Scheme 3.2.5 Cobalt(III)-catalyzed annulation of unsymmetrical alkynes **8.**

3.2.4 Formation of 3*H*-Indole and Cationic Cobalt(III) as the Catalyst



Scheme 3.2.6 Formation of 3*H*-indole **161** and cationic cobalt(III) as the catalyst.

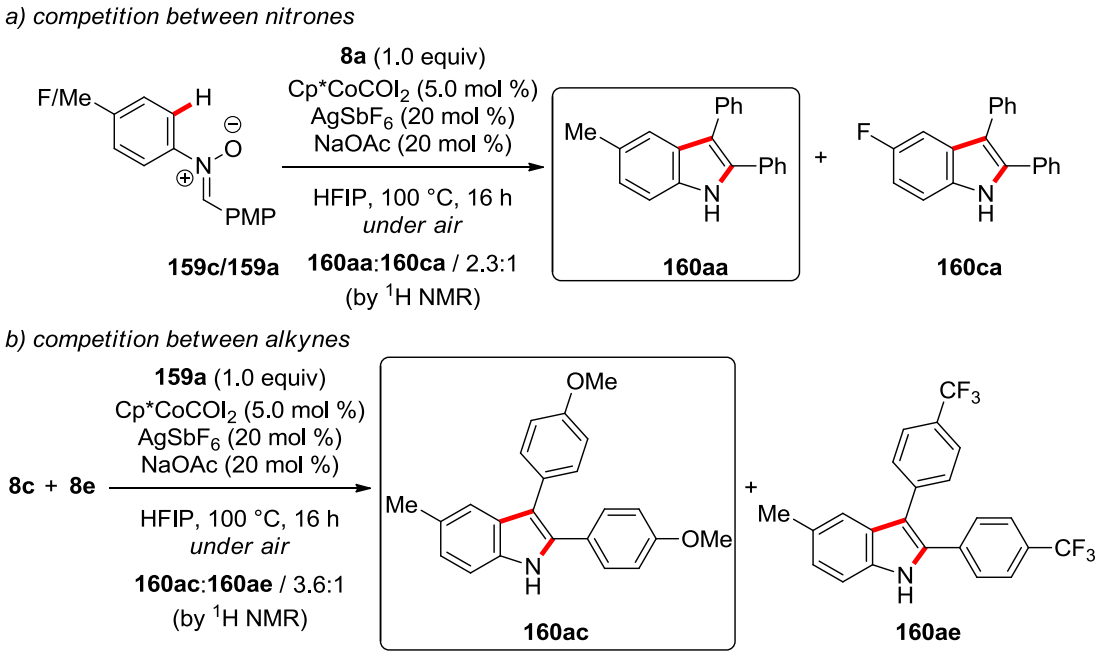
Interestingly, when the dialkyl-substituted alkyne **8** was employed under the optimal reaction conditions, the unexpected 3,3-disubstituted 3*H*-indole **161** was obtained, which was in agreement

with Chang's work[162] reported on rhodium(III)-catalyzed C–H activation for the synthesis of indolines (Scheme 3.2.6a) Moreover, the user-friendly nature of this C–H activation strategy was reflected by using a cationic single-component cobalt catalyst, thus avoiding the use of additional silver salts (Scheme 3.2.6b).

3.2.5 Mechanistic Studies

3.2.5.1 Competition Experiments

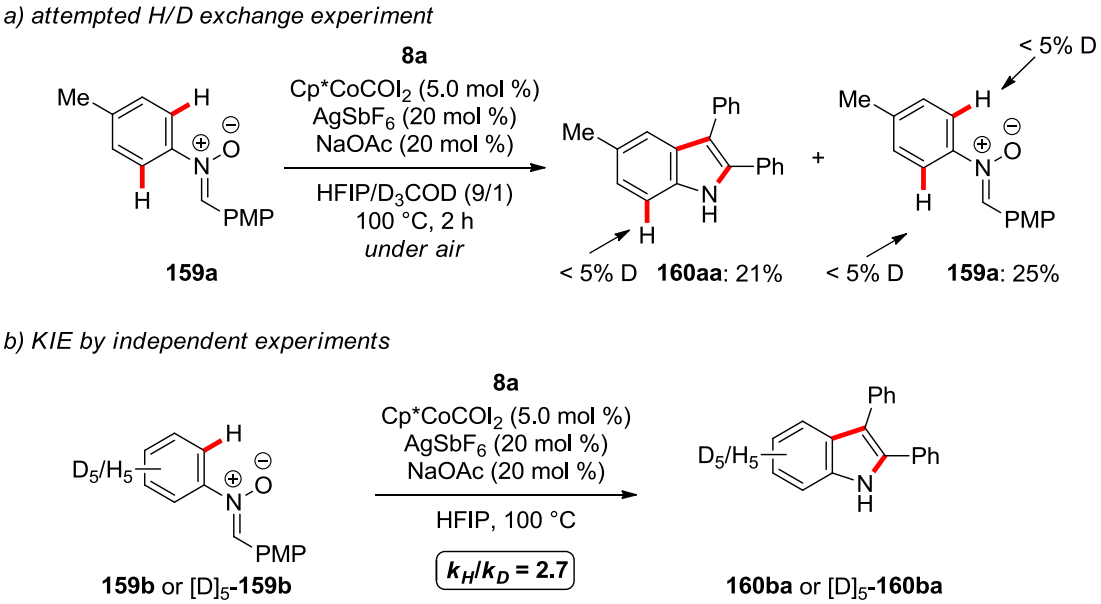
Subsequently, an intermolecular competition experiment between electron-rich and electron-deficient *para*-substituted nitrones under the optimized conditions was carried out (Scheme 3.2.7a). As a result, the electron-rich nitrones **159a** reacted preferentially, which supports a base (acetate)-assisted electrophilic-type (BIES) C–H activation. Further competition experiments between electronically distinct alkynes **8c** and **8e** showed that electron-rich alkynes were found to be preferentially converted (Scheme 3.2.7b).



Scheme 3.2.7 Competition experiments.

3.2.5.2 H/D Exchange and Kinetic Isotope Effect Study

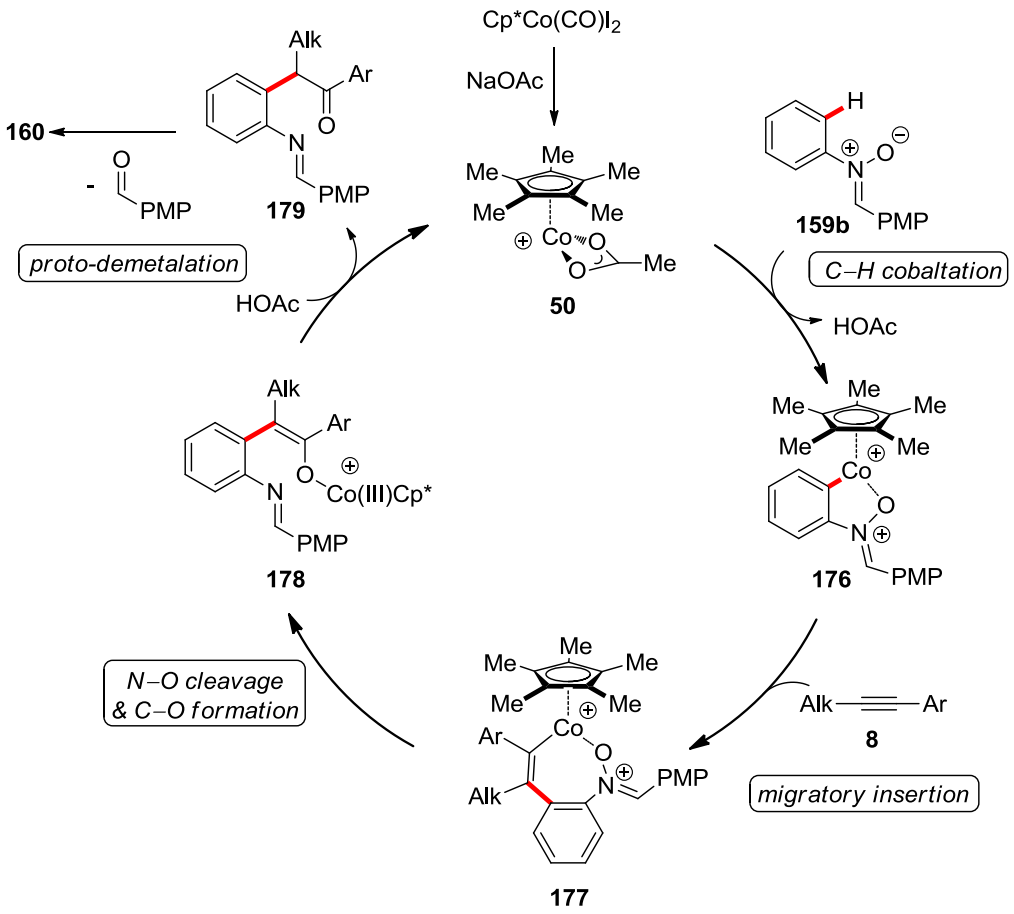
When the reaction was performed in the presence of isotopically labelled CD_3OD as co-solvent, we did not observe any H/D scrambling on both the reisolated starting material **159a** and the desired product **160aa** (Scheme 3.2.8a). Moreover, the KIE of the cobalt(III)-catalyzed C–H/N–O annulation was determined by comparison of independent reaction rates of substrates **159b** and $[D]_5$-**159b**, resulting in a value of $k_H/k_D \approx 2.7$ (Scheme 3.2.8b). These results suggested that the C–H metalation is the rate-determining step.



Scheme 3.2.8 H/D exchange and kinetic isotope effect study.

3.2.6 Plausible Catalytic Cycle

At last, a catalytic cycle for this cobalt(III)-catalyzed C–H functionalization is proposed based on our mechanistic findings (Scheme 3.2.9). The BIES C–H activation is likely assisted by the carboxylate, which *in situ* forms the cationic cobalt(III)-carboxylate complex **50**. After the metallacyle **176** is generated, coordination and insertion of alkyne **8** furnishes the key intermediate **177**, then the following N–O bond cleavage and C–O bond formation generates the intermediate **178**. Afterwards, the active cationic catalyst **50** is regenerated by a proto-demetalation, while the protected *ortho*-amino ketone **179** is also formed, which upon hydrolysis and subsequent intramolecular condensation provides the desired product **160**.



Scheme 3.2.9 Plausible catalytic cycle.

3.3 Overcoming the Limitations of C–H Activation with Strongly Coordinating *N*-Heterocycles by Cobalt Catalysis

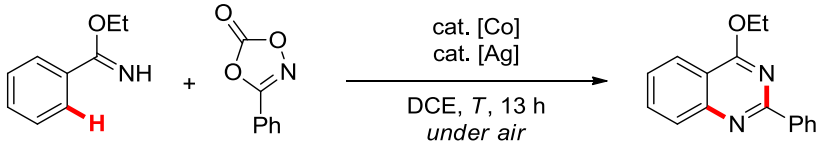
The synthesis of heterocycles has always attracted great attention in organic chemistry, because they widely exist in various pharmaceutical molecules and natural products.[163] Over the past few decades, transition metal-catalyzed C–H functionalization has emerged as one of the most powerful approaches for the synthesis and diversification of novel heterocycles.[164] However, in direct C–H activation, all nitrogen atoms present in heterocyclic substrates will strongly coordinate with metal catalysts, which in some cases could either activate an undesired C–H bond or poison the catalyst. Thus, the solution to achieving the control of positional selectivity in C–H activation will be a very meaningful topic in organic synthesis. But only one example was reported in 2014 by Yu and coworkers to achieve the position-selective C–H activation on heterocycles with different *N*-atoms.[146] Despite great success in cobalt(III)-catalyzed C–H functionalizations in recent years,[37a-c, 37e, 37f] there is no example for cobalt catalysis which achieves the control of positional selectivity on substrates with strongly coordinating *N*-atoms. Therefore, the demand for a robust C–H activation achieving the positional selectivity on heterocycles by cobalt catalysis is highly desirable.

3.3.1 Optimization of the Cobalt(III)-Catalyzed C–H Amidation of Imidates

We initiated our studies by testing a variety of reaction conditions for cobalt(III)-catalyzed C–H amidation of ethyl benzimidate (**161a**) with 3-phenyl-1,4,2-dioxazol-5-one (**162a**) (Table 3.3.1). Firstly, the desired amidation product **163aa** could be obtained in good yields with $Cu(OAc)_2$ and NaOAc as the additives (entries 1, 2). However, a quantitative yield of the product could be obtained without any additives (entry 3). The catalyst loading and reaction temperature could be significantly decreased, which still furnished the desired product **163aa** in excellent yields (entries 3-6). Among a set of representative silver salts, $AgSbF_6$ and $AgBF_4$ provided the optimal results (entries 7-12). Moreover, the C–H amidation was achieved with $Cp^*Co(CO)I_2$ as the sole component catalyst in the absence of silver salts, albeit delivering the desired product **163aa** in a lower yield (entry 13). Notably, no reactivity was observed using other typical cobalt catalysts or omitting the $Cp^*Co(Co)I_2$ catalyst (entries 14-16). It is noteworthy that the well-defined complex

[Cp*Co(CH_3CN)$_3$](SbF_6)$_2$ (**180**) was identified as a user-friendly single component catalyst, which also provided the desired product **163aa** with high efficiency (entries 17 and 18).

Table 3.3.1 Optimization of the Cobalt(III)-Catalyzed C–H Amidation of Imidate



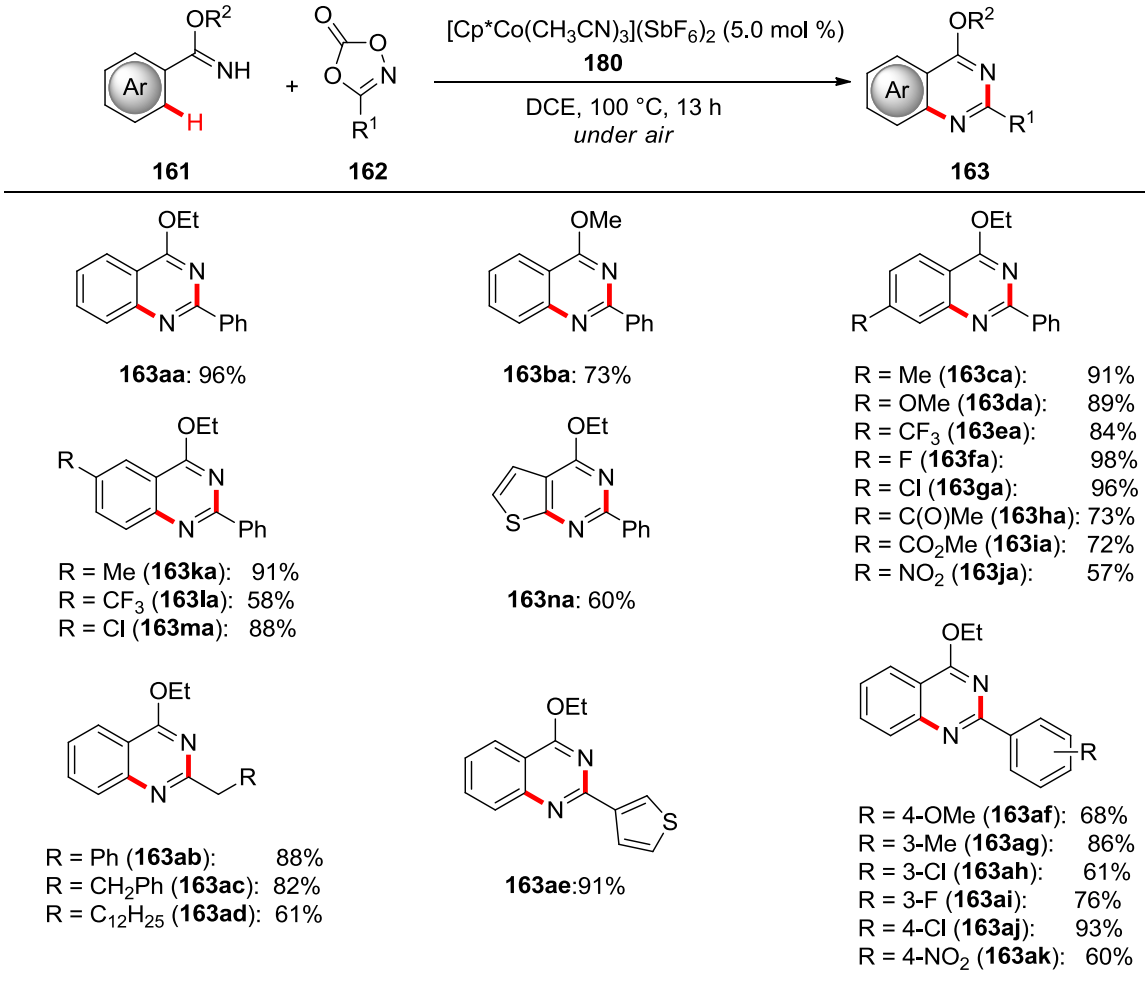
161a **162a** **163aa**

Entry	[Co] / mol %	Ag salt / mol %	*T* / °C	Yield[a]
1	Cp*CoI_2(CO) / 10	$AgSbF_6$ / 20	120	81% [b, c, d]
2	Cp*CoI_2(CO) / 10	$AgSbF_6$ / 20	120	85% [c, d]
3	Cp*CoI_2(CO) / 10	$AgSbF_6$ / 20	120	99% [d]
4	Cp*CoI_2(CO) / 5	$AgSbF_6$ / 10	120	99% [d]
5	Cp*CoI_2(CO) / 5	$AgSbF_6$ / 10	100	99% [d]
6	Cp*CoI_2(CO) / 5	$AgSbF_6$ / 10	80	83% [d]
7	**Cp*CoI_2(CO) / 5**	**$AgSbF_6$** / 10	**100**	**99%**
8	Cp*CoI_2(CO) / 5	$AgBF_4$ / 10	100	96%
9	Cp*CoI_2(CO) / 5	$AgPF_6$ / 10	100	99%
10	Cp*CoI_2(CO) / 5	AgOTf / 10	100	80%
11	Cp*CoI_2(CO) / 5	$AgN(OTf)_2$ (10)	100	88%
12	Cp*CoI_2(CO) / 5	AgOTs / 10	100	19%
13	Cp*CoI_2(CO) / 5	--	100	56%
14	$Co(OAc)_2$ / 5	$AgSbF_6$ / 10	100	--
15	$Co(acac)_3$ / 5	$AgSbF_6$ / 10	100	--
16	--	$AgSbF_6$ / 10	120	--
17	[Cp*$Co(CH_3CN)_3$] (SbF_6)$_2$ / 5	--	100	94% [e]
18	**[Cp*$Co(CH_3CN)_3$] (SbF_6)$_2$ / 5**	**--**	**100**	**96%**

[a] Reaction conditions: **161a** (0.25 mmol), **162a** (0.375 mmol), DCE (1.0 mL), *T*, 13 h, yields of isolated products are given. [b] $Cu(OAc)_2$ (2.0 equiv). [c] NaOAc (20 mol %). [d] **180** (2.0 equiv). [e]

Under N_2.

3.3.2 Cobalt-Catalyzed C–H Amidation of Imidates



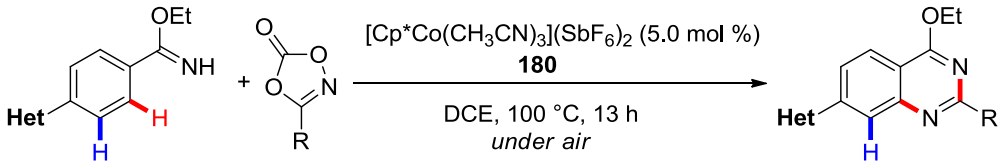
Scheme 3.3.1 Cobalt-catalyzed C–H amidation of imidates **161**.

The scope of substrates was surveyed using the single component catalyst **180** (Scheme 3.3.1). A variety of substituents on the aryl ring of benzimidates **161** could directly couple with **162** in moderate to good yields. Various valuable functional groups, such as trifluoromethyl, fluoro, chloro, ester, ketone, and nitro, were also well tolerated under the optimized conditions (**163ea**-**163ja**). The *meta*-substituted benzimidates delivered the corresponding products at the less hindered C–H bond (**163ka**-**163ma**). It is worth mentioning that thiophene imidate **161n** was also shown to be a suitable substrate and the desired product was obtained in 60% yield with high regioselectivity (**163na**). Next, we explored the generality of this cobalt(III)-catalyzed C–H amidation reaction with respect to dioxazolones **162**. High yields were obtained with different alkyl- as well as heteroaryl-substituted

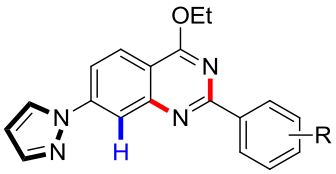
dioxazolones (**162c**-**162e**). Likewise, both electron-donating and electron-withdrawing groups, such as methoxy, methyl, chloro, fluoro, and nitro, were all compatible to react with benzimidate **161a**, delivering the desired products in good to excellent yields (**163af**-**163ak**).

3.3.3 Overriding the Conventional Selectivity Dictated by Strongly Coordinating Heterocycles

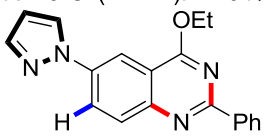
Encouraged by the success of above results, more challenging benzimidate substrates **161** containing strongly coordinating *N*-heterocyclic directing groups, were further investigated (Scheme 3.3.2). To our delight, various strongly coordinating heterocycles, such as pyrazole, pyrimidine, pyrazine, and even pyridine, were fully tolerated for the cobalt(III)-catalyzed C–H amidation by imidate assistance, delivering the quinazolines **163** as the sole products. Moderate to good yields of the desired C–H annulation products were obtained with excellent positional and regioselectivity when *meta*- and *para*-pyrazole substituted benzimidates were applied to react with different dioxazolones. Benzimidate bearing a *meta*-pyrazole group showed good reactivity towards the less sterically hindered C–H bond (**163la**). Furthermore, we subsequently replaced the pyrazole by other groups, including the heterocylics adjacent to an *O*-atom, amide and pyridines, and moderate to good yields of the desired products were obtained with excellent positional selectivity (**163na**-**163te**). Remarkably, the competition experiments were performed by *Dr. M. M. Lorion* with various directing groups for this cobalt(III)-catalyzed C–H functionalization. The relative directing capabilities of *N*-heterocycles were found to decrease in the order: imidate ≥ pyridine ≈ pyrazole > oxazoline > pyrimidine.



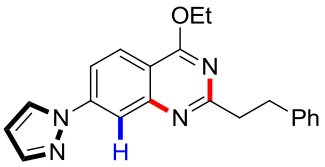
161 **162** **163**



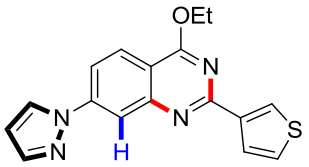
R = H (**163ka**): 70%
R = 4-OMe (**163kf**): 59%
R = 3-Me (**163kg**): 63%
R = 3-F (**163ki**): 59%
R = 3-Cl (**163kh**): 64%



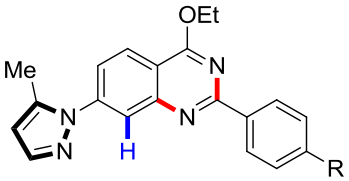
163la: 62%



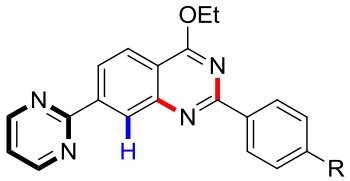
163kc: 55%



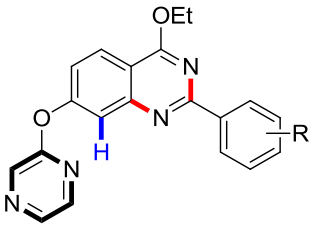
163ke: 81%



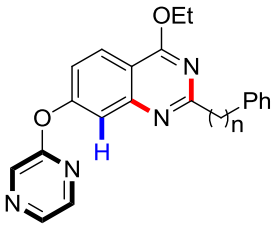
R = Br (**163ml**): 64%
R = NO_2 (**163mk**): 58%



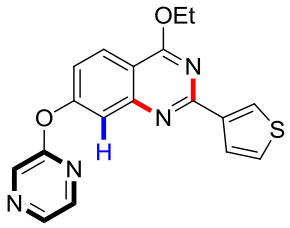
R = H (**163na**): 73%
R = Cl (**163nj**): 71%
R = Br (**163nl**): 85%



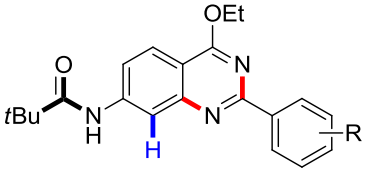
R = H (**163oa**): 89%
R = 4-Me (**163om**): 75%
R = 3-Me (**163og**): 84%
R = 4-Cl (**163oj**): 87%
R = 4-NO_2 (**163ok**): 71%



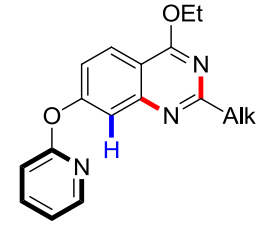
n = 1 (**163ob**): 78%
n = 2 (**163oc**): 87%



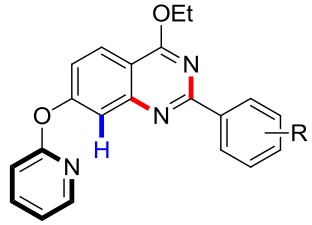
163oe: 86%



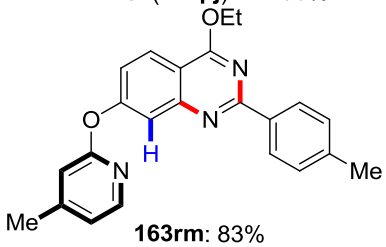
R = 3-Me (**163pg**): 85%
R = 4-OMe (**163pf**): 85%
R = 4-Cl (**163pj**): 90%



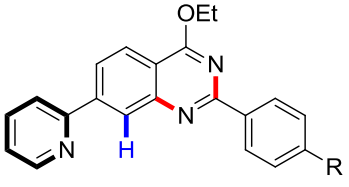
Alk = $(CH_2)_2Ph$ (**163qc**): 81%
Alk = $nC_{13}H_{27}$ (**163qd**): 86%



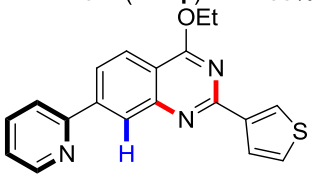
R = H (**163qa**): 80%
R = 4-OMe (**163qf**): 73%
R = 3-F (**163qi**): 88%



163rm: 83%



R = H (**163sa**): 54%
R = Cl (**163sj**): 62%



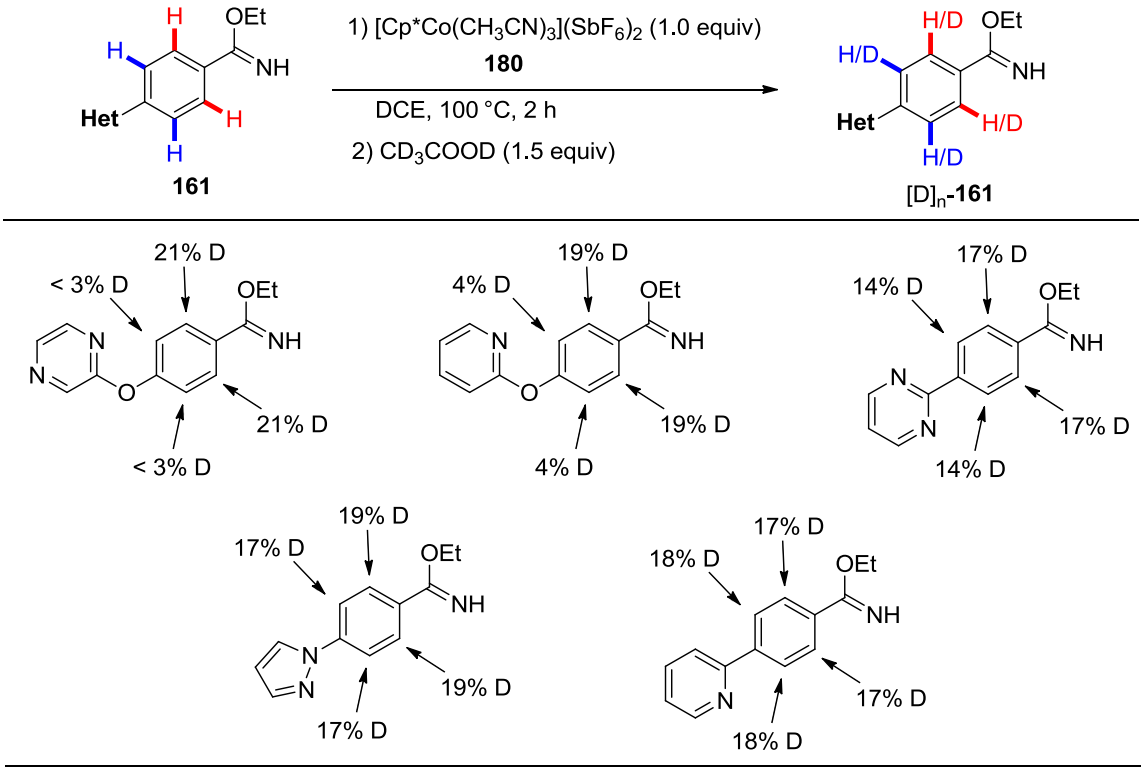
163te: 51%

Scheme 3.3.2 Overriding the conventional selectivity dictated by strongly coordinating heterocycles.

3.3.4 Mechanistic Studies

3.3.4.1 Positional Selectivity in Stoichiometric C–H Cobaltation

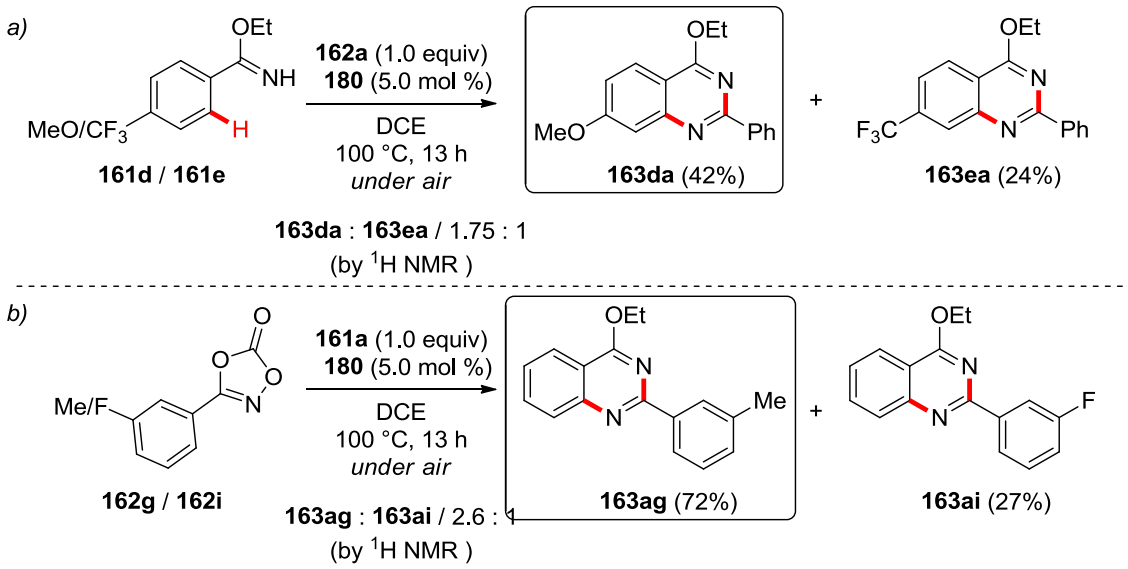
Subsequently, the H/D exchange studies as to the positional selectivity of the key C–H activation step were carried out using the stoichiometric single-component catalyst **180** and then quenched with CD_3CO_2D (Scheme 3.3.3). Similar amounts of deuterium incorporation at *ortho*-position of both directing groups were detected after the treatment with CD_3CO_2D, when *para*-pyrazole, pyrimidine or pyridine substituted benzimidates were employed. These findings indicate that the positional selectivity is not determined in the C–H metalation, but the C–N bond-forming step is.



Scheme 3.3.3 Positional selectivity in stoichiometric C–H cobaltation.

3.3.4.2 Intermolecular Competition Experiments

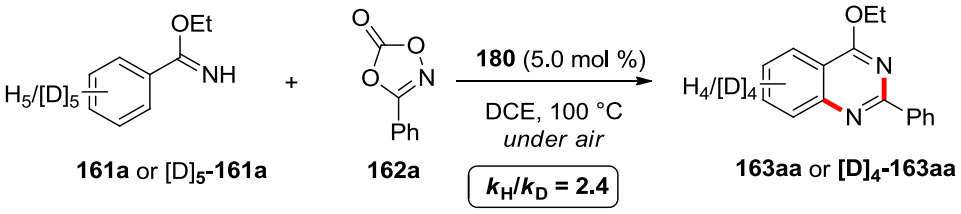
Additionally, intermolecular competition experiments showed that the electron-rich imidate **161d** and dioxazolone **162g** both were preferred for this cobalt(III)-catalyzed C–H amidation (Scheme 3.3.4).



Scheme 3.3.4 Intermolecular competition experiments.

3.3.4.3 Kinetic Isotope Effect

To gain deeper insight into the C–H activation mechanism, a KIE study by comparison of initial rates of independent reactions with substrates **161a** and [D]$_5$-**161a** was carried out (Scheme 3.3.5). A KIE of $k_H/k_D \approx 2.4$ suggested a rate-limiting step of the C–H metalation likely to be operative.

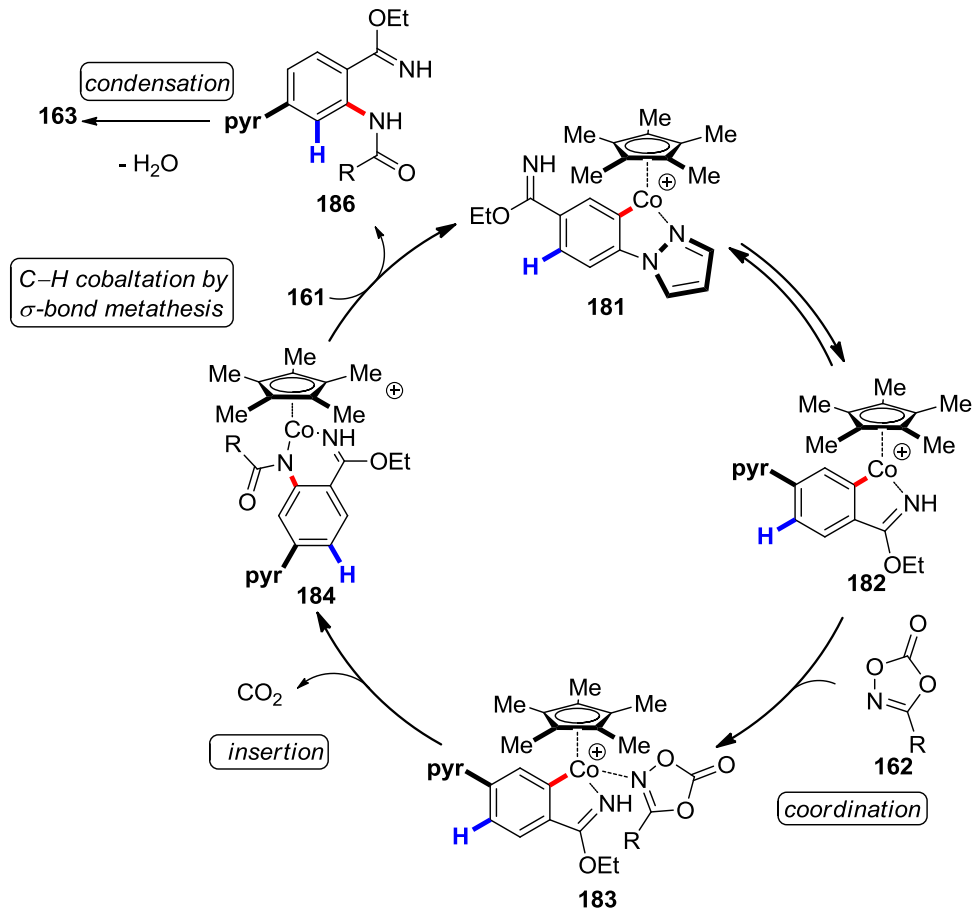


Scheme 3.3.5 Kinetic isotope effect.

3.3.5 Proposed Catalytic Cycle

Based on our mechanistic findings and literature precedestes on cobalt(III)-catalyzed C–H activation,[37b] a catalytic cycle of this reaction is proposed (Scheme 3.3.6). Presumably, the reaction involves a reversible and feasible C–H activation step which is indicated by the significant H/D exchange studies of positional selectivity. The elementary step of C–H activation possibly proceeds by BIES mechanism based on the competition experiment, showing a preference for electron-rich substrates. Subsequently, the intermediate **182** is generated by the coordination and migratory

insertion with dioxazolones **162**, resulting in the C–N bond formation and CO_2 extrusion. Finally, the desired product **163** is obtained through the intramolecular condensation following the amination product generation, along with the regeneration of the active cobalt(III) complex **181**.



Scheme 3.3.6 Proposed catalytic cycle.

3.4 Domino C–H/N–H Allylation of Imidates by Cobalt Catalysis

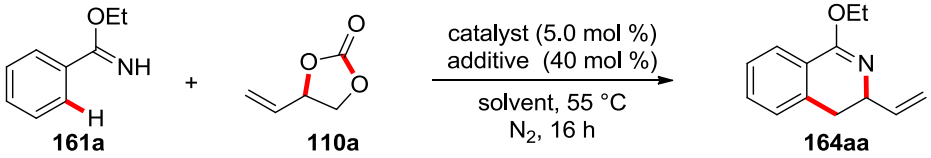
In modern synthetic chemistry, a green reaction is an increasingly attractive option to all chemists, which aims to provide the products with efficiency, while minimizing the generation of waste and avoiding the use of toxic reagents or solvents.[165] During the last few decades, the transition metal-catalyzed C–H functionalization has made great success in such transformations, because of its practicality and high atom economy.[8b, 166] With the increasing attention to environmental issues, we have to face the question of how to synthesize the desired products in a green manner. In this regard, domino reactions have the potential to simplify reactions by forming several bonds in a one-pot fashion, which allows for minimization of waste compared to the stepwise reactions.[167] Recent advances indicated that the direct C–H activation in combination with domino reactions showed great promises in sustainable chemistry.[168] However, precious metals such as palladium, rhodium, and iridium, have overwhelmingly dominated this field, which was inconsistent with the principles of green chemistry. With the advantages of Earth abundant metals, for example low price and low toxicity, we became interested in developing direct C–H domino reactions with 3d transition metals. Moreover, we had great success in cobalt(III)-catalyzed C–H annulation reactions recently.[37e] Therefore, we started to explore the possibility of developing direct cobalt(III)-catalyzed C–H domino reactions.

3.4.1 Optimization of the Domino C–H/N–H Allylation of Imidate

The optimization studies for the direct domino C–H/N–H allylation reaction were initiated by testing various solvents, which delivered the desired vinyl-substituted heteroarene **164aa**. Initially, no reactivity or unsatisfactory yields of the desired product **164aa** were observed (Table 3.4.1, entries 1-5). In contrast, HFIP turned out to be the solvent of choice, resulting in the formation of the desired product in moderate yield (entry 6). Control experiments revealed that the C–H functionalization did not occur without the cationic cobalt(III)-catalyst or with other typical cobalt complexes (entries 7-9). Only trace amounts of the desired product were obtained in the absence of NaOAc (entry 10). By investigating different additives, we found that NaOAc was the optimal additive for this domino C–H/N–H allylation (entries 6, 10-16). To our delight, the reaction efficacy

could be improved by adding cocatalytic amounts of the Lewis acid BPh_3 (entries 17, 18). Subsequently, several different cobalt(III) catalysts were tested for this domino reaction (entries 19-22), and it turned out that the new single-component complex $[Cp^*Co(CH_3CN)_3](PF_6)_2$ provided the highest catalytic efficacy. The complex $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ failed in this domino C–H/N–H allylation reaction (entries 23, 24).

Table 3.4.1 Optimization of the Domino C–H/N–H Allylation of Imidate 161a[a]



Entry	Catalyst	Additive	Solvent	Yield[b]
1	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	MeOH	--
2	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	GVL	--
3	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	TFE	13%
4	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	PhCl	16%
5	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	DCE	34%
6	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	HFIP	50%
7	--	NaOAc	HFIP	--
8	$Co(OAc)_2$	NaOAc	HFIP	--
9	CoC_2O_4	NaOAc	HFIP	--
10	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	--	HFIP	< 2%
11	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOPiv	HFIP	34%[c]
12	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaO_2CAd	HFIP	30%
13	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	CsOAc	HFIP	trace
14	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	$Cu(OAc)_2$	HFIP	26%
15	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	HOPiv	HFIP	22%

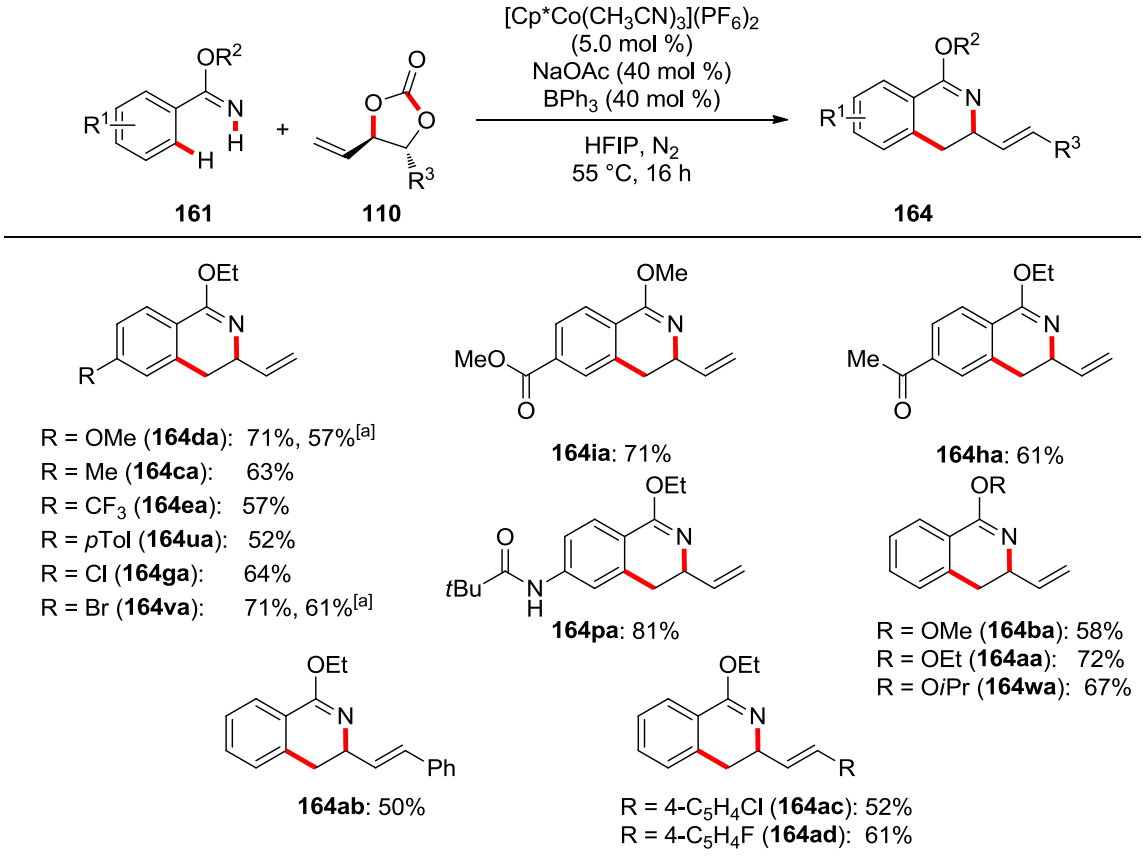
16	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	HO_2CAd	HFIP	43%
17	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	HFIP	36%[c]
18	$[Cp^*Co(CH_3CN)_3](SbF_6)_2$	NaOAc	HFIP	62%[d]
19	$Cp^*Co(CO)I_2$	NaOAc	HFIP	< 2%[d,e]
20	$[Cp^*Co(CH_3CN)_3](BF_4)_2$	NaOAc	HFIP	50%[d]
21	$[Cp^*Co(CH_3CN)_3](PF_6)_2$	NaOAc	HFIP	64%
22	**$[Cp^*Co(CH_3CN)_3](PF_6)_2$**	**NaOAc**	**HFIP**	**72%[d]**
23	$[Cp^*Rh(CH_3CN)_3](SbF_6)_2$	NaOAc	DCE	< 2%
24	$[Cp^*Rh(CH_3CN)_3](SbF_6)_2$	NaOAc	HFIP	< 2%[d]

[a] Reaction conditions: **161a** (0.25 mmol), **110a** (0.75 mmol), catalyst (5.0 mol %), additive (40 mol %), solvent (1.0 mL), 55 °C, 16 h. [b] Yields of isolated products. [c] $In(OTf)_3$ (40 mol %). [d] BPh_3 (40 mol %). [e] $AgSbF_6$ (15 mol %).

3.4.2 Scope of Cobalt(III)-Catalyzed Domino C–H/N–H Allylation

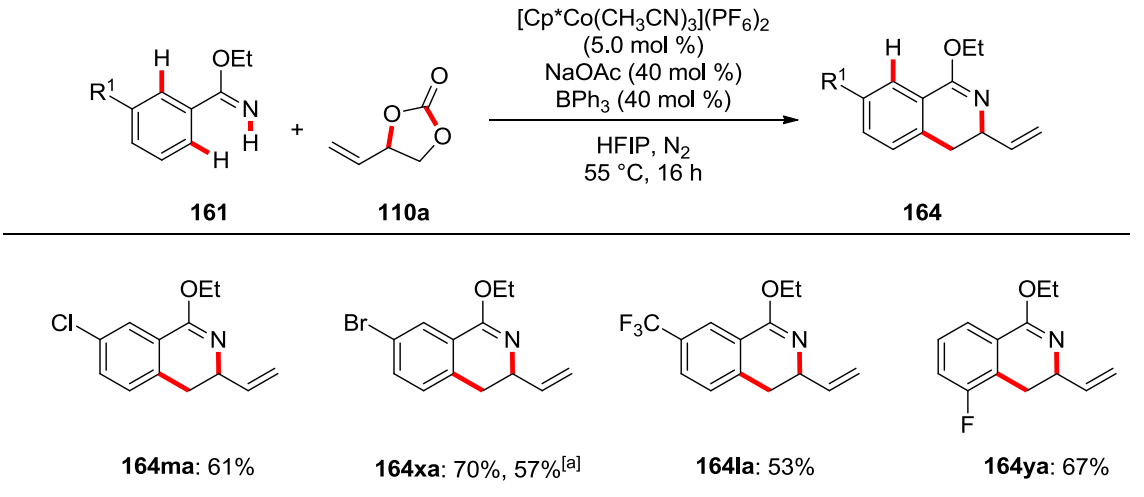
3.4.2.1 Scope of Cobalt(III)-Catalyzed C–H Allylation

With the optimized catalytic reaction conditions being identified, we tested the versatility of the cationic Cp*Co(III)-catalyzed C–H allylation towards the synthesis of vinyl-substituted 3,4-dihydroisoquinolines **164** with various imidates **161** (Scheme 3.4.1). Thus, aryl-substituted imidates bearing various electron-donating and electron-withdrawing groups at different positions reacted smoothly with **110a**, affording the corresponding products in moderate to good yields. Moreover, the catalytic system also tolerated various functional groups on the arene part such as halides, ester, ketone and amide substituents, which can be easily transformed into other functionalities. Notably, an increased level of catalytic efficacy was achieved with the Lewis acid BPh_3. The alkoxy-substituted benzimidates **110b** and **110w** were also well tolerated under the optimized conditions, delivering the allylation products in good yields. Likewise, the reaction system displayed a good reactivity when different substituted dioxolanones were examined (**164ab**-**164ad**).



Scheme 3.4.1 Scope of the domino C–H/N–H allylation. [a] Without BPh_3.

3.4.2.2 Scope of Cobalt(III)-Catalyzed C–H Allylation with *meta*-Substituted Imidates



Scheme 3.4.2 Scope of cobalt(III)-catalyzed C–H allylation with *meta*-substituted imidates. [a] Without BPh_3.

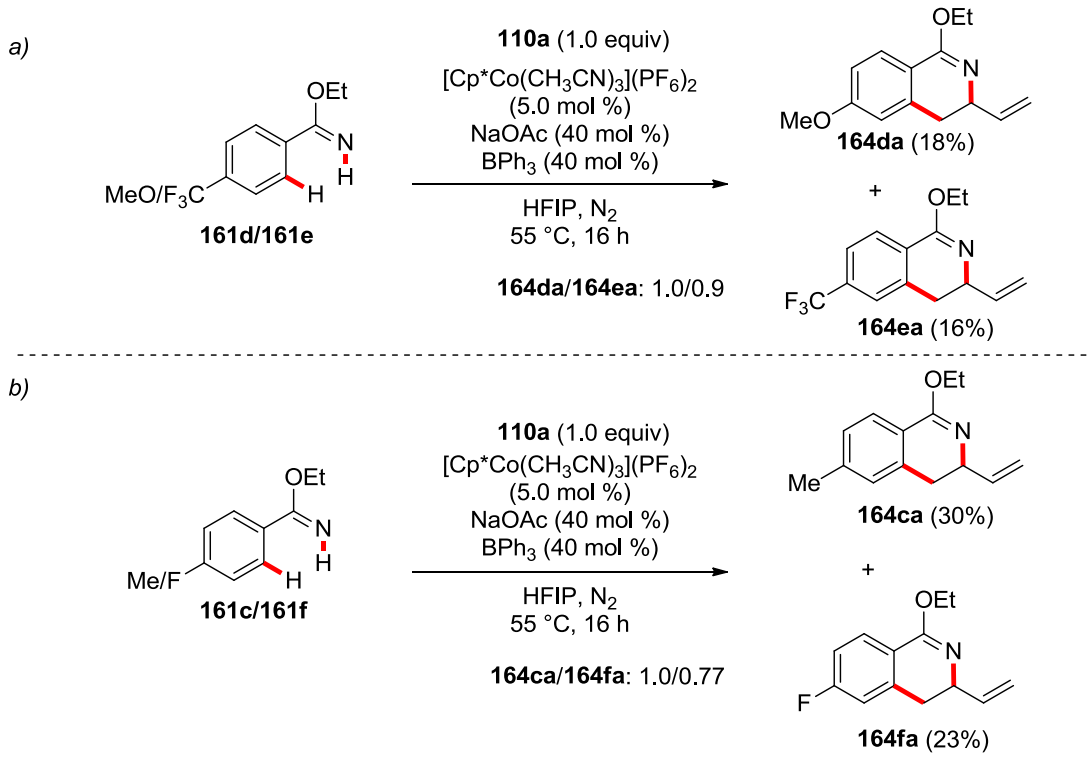
The intramolecular competition experiments with *meta*-substituted arylimidates **161m**, **161x** and

161l bearing two different *ortho*-C–H bonds showed excellent selectivity for the sterically less hindered position and delivered the products **164ma**, **164xa** and **164la** in moderate yields. In contrast, the *meta*-fluoro substituted imidate **161y** reacted preferentially at the more sterically hindered position, providing compound **164ya** as the sole product in 67% yield (Scheme 3.4.2).

3.4.3 Key Mechanistic Findings

3.4.3.1 Intermolecular Competition Experiments

Intermolecular competition experiments were performed between electron-rich and electron-deficient benzimidates under the optimal conditions (Scheme 3.4.3). As a result, the electron-rich substrates **161d** and **161c** reacted preferrentally in this C–H/N–H allylation reaction, which is in good agreement with a BIES-type C–H activation.

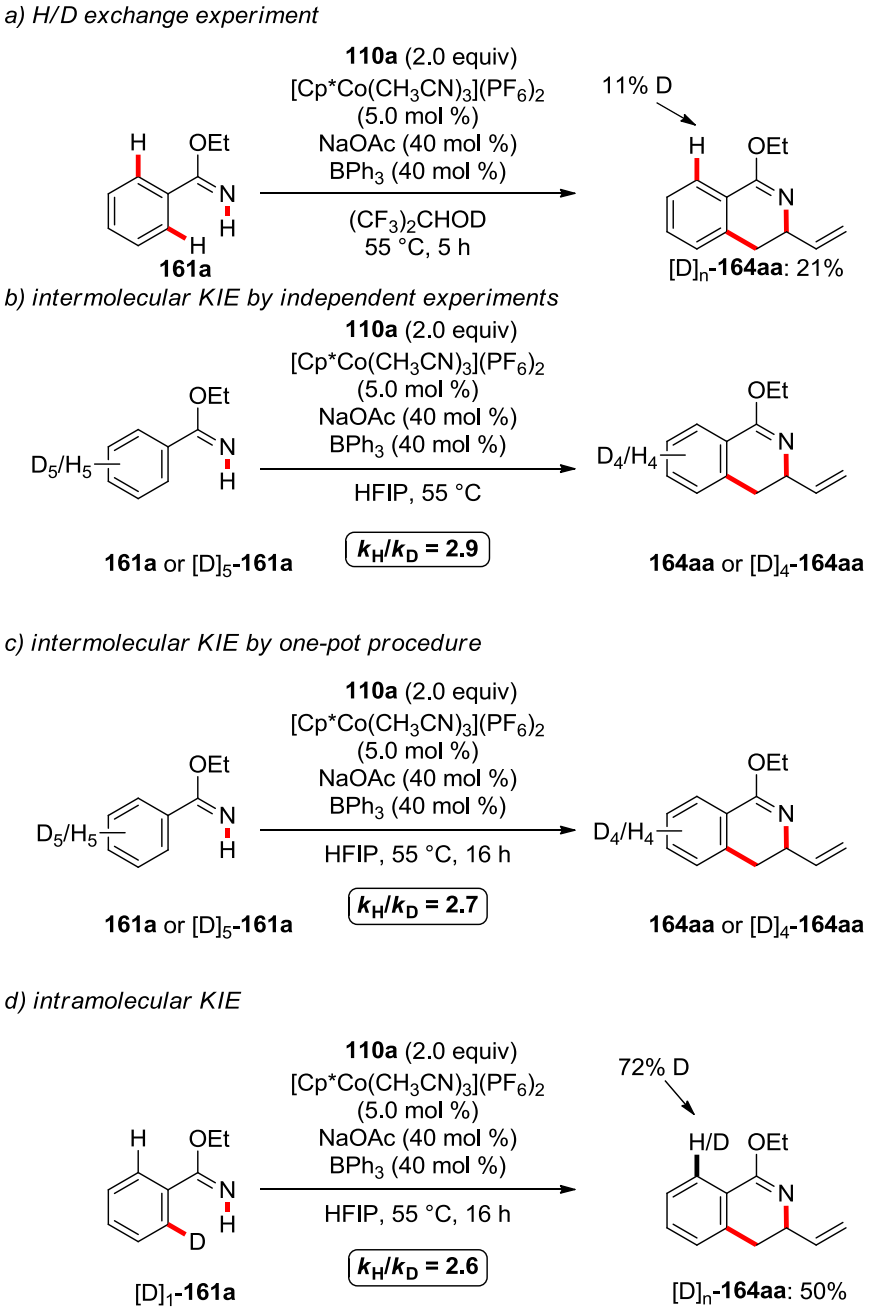


Scheme 3.4.3 Intermolecular competition experiments.

3.4.3.2 H/D Exchange and KIE Studies

In order to further investigate the reaction mechanism of the C–H activation step, a series of important test reactions was thereafter conducted, including H/D exchange, inter- and

intra-molecular KIE experiments (Scheme 3.4.4).



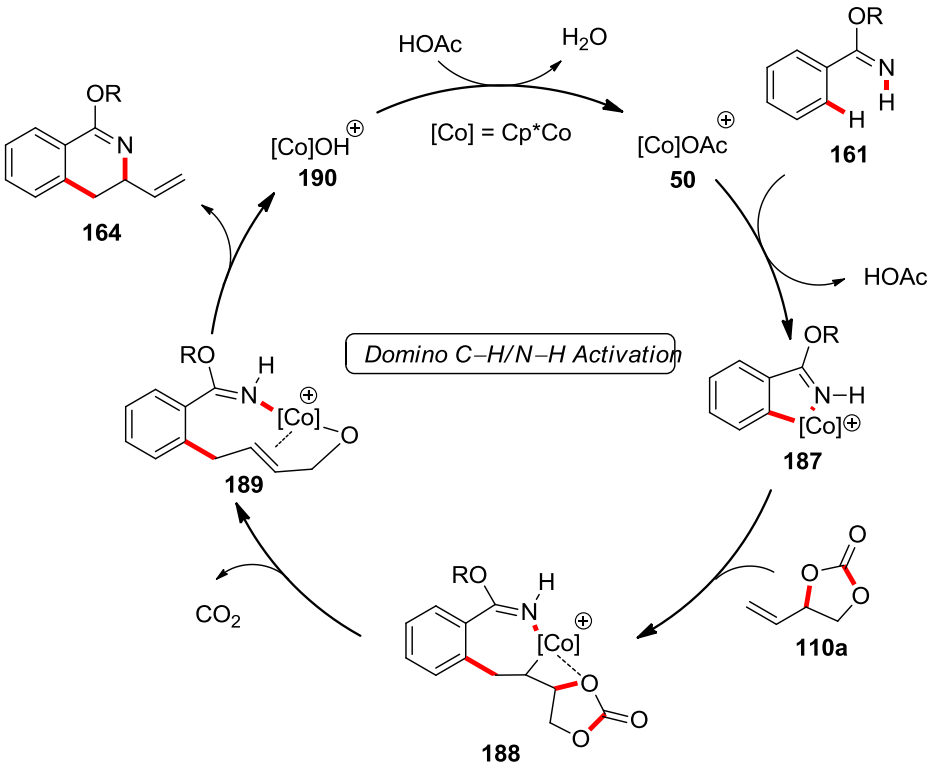
Scheme 3.4.4 H/D exchange and KIE studies.

The H/D exchange experiment was performed in CF_3CHOD as the reaction solvent under the optimal conditions. As a result, a minor H/D exchange in *ortho*-position of product **164aa** was observed (a). The kinetic isotope effect of the cobalt(III)-catalyzed C–H/N–H annulation was studied with labeled substrate $[D]_5$-**161a** by independent experiment, resulting in a value of $k_H/k_D \approx 2.9$ (b). In addition, a one-pot intermolecular KIE experiment showed a similar result of $k_H/k_D \approx 2.7$ (c).

Furthermore, an intramolecular KIE of $k_H/k_D \approx 2.6$ was observed, which is in good agreement with the above mentioned results of the intermolecular KIE experiments (d). The mechanistic studies indicated that the C–H activation step is the rate-limiting step of the catalytic cycle.

3.4.4 Proposed Catalytic Cycle

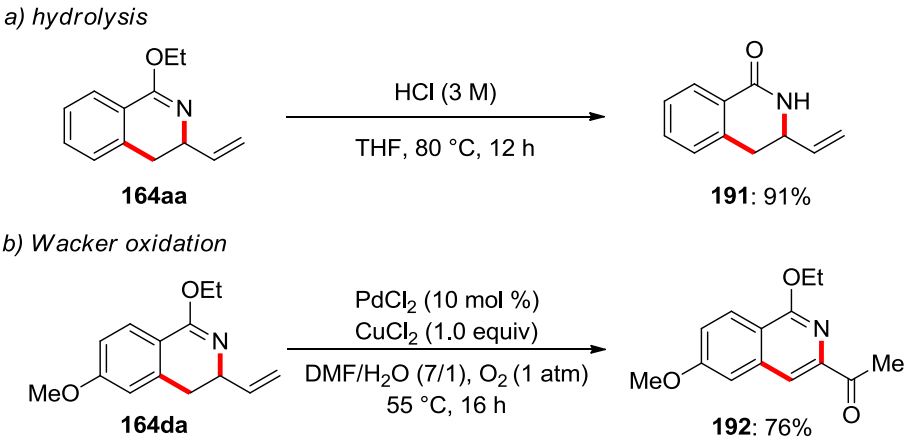
Based on the mechanistic observations, a plausible mechanism was proposed for the cobalt(III)-catalyzed C–H functionalization (Scheme 3.4.5). Initially, benzimdate **161** undergoes the C–H metalation with single-component cationic cobalt(III) catalyst, forming intermediate **187**. Then, coordination of 4-vinyl-1,3-dioxolan-2-one **110a** and migratory insertion into the cobalt–carbon bond generates complex **188**, which undergoes extrusion of CO_2 to form intermediate **189**. Subsequently, the desired product **164** is obtained through an intramolecular cyclization by nucleophilic attack of the *N*-atom with the help of cobalt(III) catalyst and BPh_3. Finally, the active cationic cobalt(III) catalyst is regenerated by the reaction with acetic acid, which was formed in the initial C–H metalation step.



Scheme 3.4.5 Proposed catalytic cycle.

3.4.5 Diversification of Vinylated Heteroarenes

Finally, the utility of the obtained vinyl-substituted heteroarenes **164** was investigated (Scheme 3.4.6). Hydrolysis of product **164aa** provided access to vinyl-substituted dihydroisoquinolone derivatives **191**. Furthemore, acetylated isoquinoline **192** was obtained in 76% yield through Wacker oxidation conditions.[169]



Scheme 3.4.6 Diversification of vinylated heteroarenes **164**.

3.5 Air-Stable Manganese(I)-Catalyzed C–H Activation for Decarboxylative C–H/C–O Cleavages in Water

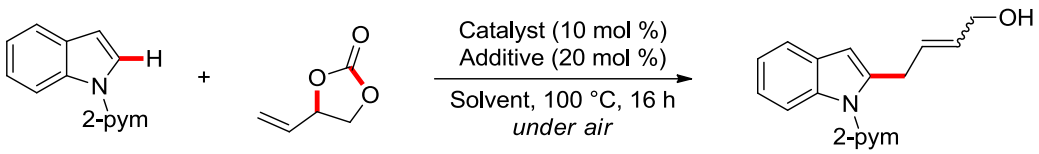
The allyl structural unit has proven to be a very useful building block in organic synthesis, which is widely found in natural products, pharmaceuticals and agrochemicals.[65] Recent developments in transition metal-catalyzed C–H allylation provided attractive approaches that streamlined the synthesis of allylic compounds without the need for pre-functionalizations.[170] However, in most of these methods, expensive and rare 4d or 5d transition metals, such as rhodium, palladium, iridium, and ruthenium, are necessary. In contrast, 3d metals, such as cobalt, manganese, nickel, and iron are typically cheap and Earth-abundant.[35b] In this regard, developing an alternative allylation reaction by replacing these noble metal catalysts by inexpensive ones is highly desirable. With the emergence of the concept of green chemistry, a mild and environmentally-benign reaction is considerably attractive.[29] Consequently, a reaction explored in water, under air, and by using 3d metal would be an ideal option. Based on our great achievement in manganese-catalyzed substitutive C–H allylation of arenes,[83] we now are interested in exploring the possibility of air-stable manganese-catalyzed decarboxylative C–H/C–O cleavages in water.

3.5.1 Optimization of Decarboxylative C–H/C–O Activation

We initiated our studies with 1-(pyridin-2-yl)-1*H*-indole (**41a**) and 4-vinyl-1,3-dioxolan-2-one (**110a**) as model substrates and optimized the reaction conditions (Table 3.5.1). Initially, we probed various solvents for the envisioned manganese(I)-catalyzed C–H activation. We found that the solvent plays a significant role in promoting the reaction efficiency. As a result, the polar solvents TFE and H_2O displayed highest reactivities with good diastereoselectivities (entries 1-9). No reaction was observed in the absence of the manganese catalyst (entry 10). Moreover, other manganese sources, such as $MnCl_2$, $MnBr_2$, and $Mn_2(CO)_{10}$, were also not applicable to this C–H/C–O allylation reaction (entries 10-13). It should be noted that this manganese(I)-catalyzed C–H activation was not only tolerant towards water, but also delivered good results under an atmosphere of air (entry 14). Next, the effect of different bases was explored for the reaction. Trace amounts of the product **111aa** were observed when the strong base K_2CO_3 was used (entry 15). Organic bases like Cy_2NH or

monoprotected amino acid only provided the desired product in low yields (entries 16, 17). A lower catalyst loading (2.5 mol %) was tested for this reaction, affording the allylated product **111aa** in 79% yield (entry 18). Importantly, a slight decrease of the catalytic activity was observed when the reaction temperature was decreased to 80 °C. Even at 60 °C, we could still obtain the desired product in 80% yield, reflecting the robustness of the manganese(I) catalysis system for this C–H transformation (entries 19, 20).

Table 3.5.1 Optimization of decarboxylative C–H/C–O activation.



41a **110a** **111aa**

Entry	Catalyst	Additive	Solvent	Yield[a]	*E*/*Z*
1	$MnBr(CO)_5$	NaOAc	Et_2O	92%[b]	5.5
2	$MnBr(CO)_5$	NaOAc	nBu_2O	85%[b]	1.8
3	$MnBr(CO)_5$	---	nBu_2O	21%[b]	3.5
4	$MnBr(CO)_5$	NaOAc	MeCN	21%[b]	1.9
5	$MnBr(CO)_5$	NaOAc	CH_2Cl_2	77%[b]	2.4
6	$MnBr(CO)_5$	NaOAc	1,4-dioxane	90%[b]	1.4
7	$MnBr(CO)_5$	NaOAc	TFE	92%[b]	5.1
8	$MnBr(CO)_5$	NaOAc	DCE	84%[b]	2.8
9	$MnBr(CO)_5$	NaOAc	H_2O	93%[b]	6.4
10	--	NaOAc	H_2O	--[b]	--
11	$MnCl_2$	NaOAc	H_2O	--[b]	--
12	$MnBr_2$	NaOAc	H_2O	--[b]	--
13	$Mn_2(CO)_{10}$	NaOAc	H_2O	<5%[b,c,d]	--
14	**$MnBr(CO)_5$**	**NaOAc**	**H_2O**	**94%**	**5.9**
15	$MnBr(CO)_5$	K_2CO_3	H_2O	<10%[d]	--
16	$MnBr(CO)_5$	Cy_2NH	H_2O	24%	6.4
17	$MnBr(CO)_5$	Piv-Val-OH	H_2O	46%	5.7

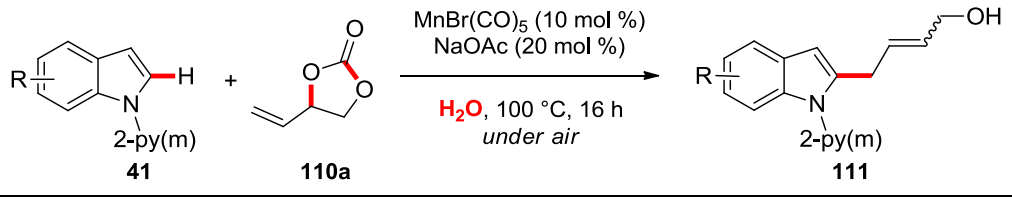
18	$MnBr(CO)_5$	NaOAc	H_2O	79%[c,e]	5.7
19	$MnBr(CO)_5$	NaOAc	H_2O	84%[f]	5.9
20	$MnBr(CO)_5$	NaOAc	H_2O	80%[g]	5.9

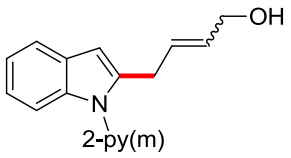
[a] Reaction conditions: **41a** (0.25 mmol), **110a** (0.75 mmol), catalyst (10 mol %), additive (20 mol %), solvent (1.0 mL), under air, 100 °C, 16 h, isolated yield. [b] Under N_2. [c] NaOAc (10 mol %). [d] GC conversation. [e] $MnBr(CO)_5$ (5 mol %). [f] 80 °C. [g] 60 °C.

3.5.2 Scope of Manganese(I)-Catalyzed C–H/C–O Activation

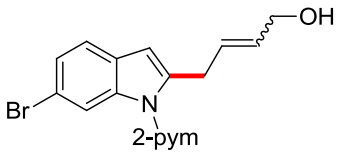
3.5.2.1 Scope of Manganese(I)-Catalyzed Allylation of Indoles

With the optimized reaction conditions in hand, we explored the scope of the manganese(I)-catalyzed C–H/C–O activation on differently substituted indoles **41** in H_2O or TFE (Scheme 3.5.1). Notably, various functional groups, such as halogens, hydroxyl, ester and ketone, were fully tolerated in the reaction conditions. Aryl-substituted indoles bearing electron-donating and electron-withdrawing groups at different positions all reacted smoothly with 4-vinyl-1,3-dioxolan-2-one **110a**, delivering the allylated products in moderate to good yields with good *E*/*Z* ratio. Moreover, sterically demanding substituents in C-3 position were investigated. When TFE was chosen as the reaction solvent, the desired products were obtained in good yields (**111la**-**111na, 111pa**). However, the allylation of 3-methyl-substituted indole **41m** gave a lower yield of the desired product **111ma** in H_2O, probably due to the low solubility of the substrate **41m** in H_2O. In addition, 2-phenylpyridine was also shown to be a viable substrate and the desired product **111qa** was obtained in 64% yield.

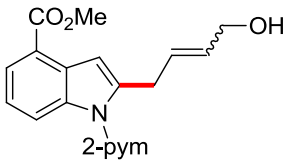




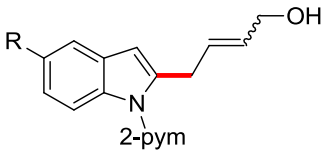
2-pym (**111aa**): 93% (5.9), 95% (5.1)[a]
2-py (**111ba**): 98% (5.2) , 73% (5.3)[a]



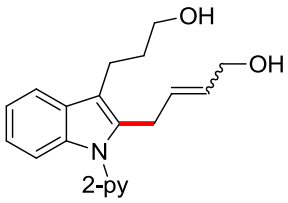
111ea: 92% (5.3)[a]



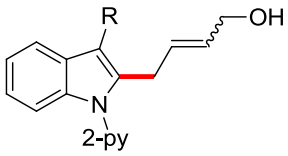
111fa: 96% (4.7)[a]



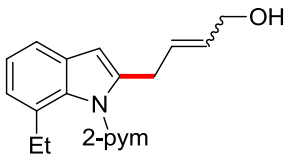
R = Me (**111ga**): 94% (5.2), 92% (5.3)[a]
R = OMe (**111ha**): 65% (6.7), 79% (5.5)[a]
R = F (**111ia**): 82% (5.4), 93% (5.9)[a]
R = Cl (**111ja**): 76% (5.5)[a]
R = Br (**111ca**): 93% (4.4)[a]
R = I (**111ka**): 88% (5.5)[a]



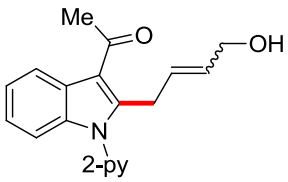
111la: 74% (5.3)[a]



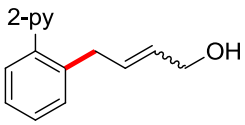
R = Me (**111ma**): 55% (4.2), 90% (4.1)[a]
R = Br (**111na**): 75% (4.3), 77% (4.6)[a]



111oa: 63% (5.6), 61% (5.7)[a]



111pa: 88% (5.5)[a]

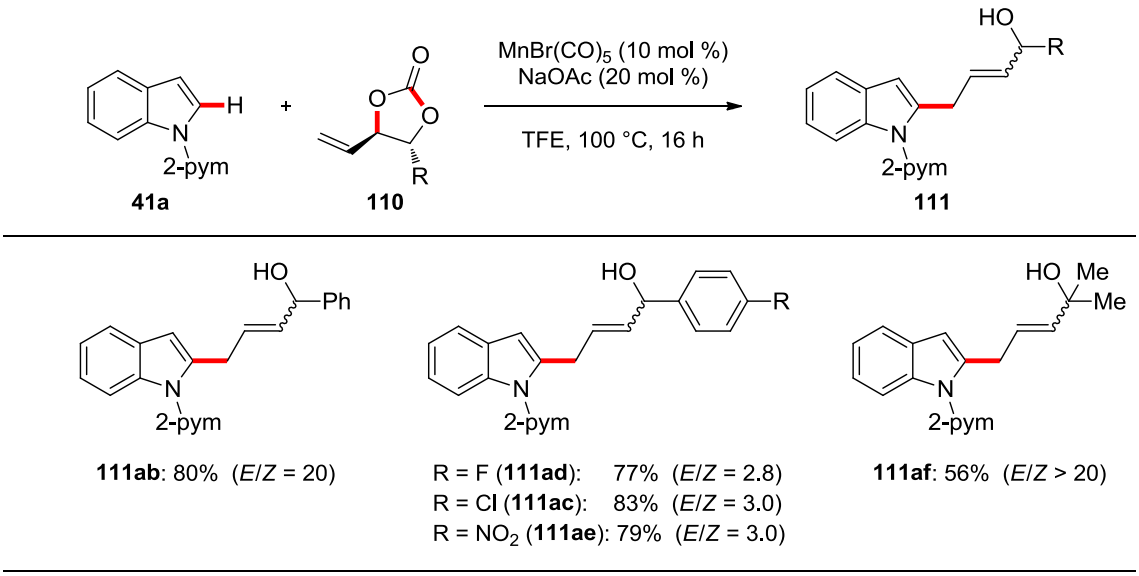


111qa: 64% (7.3)[a]

Scheme 3.5.1 Scope of manganese(I)-catalyzed allylation of indoles. *E*/*Z* ratio in parentheses. [a] TFE as the solvent.

3.5.2.2 Scope of Manganese(I)-Catalyzed Allylation with Dioxolanones 110

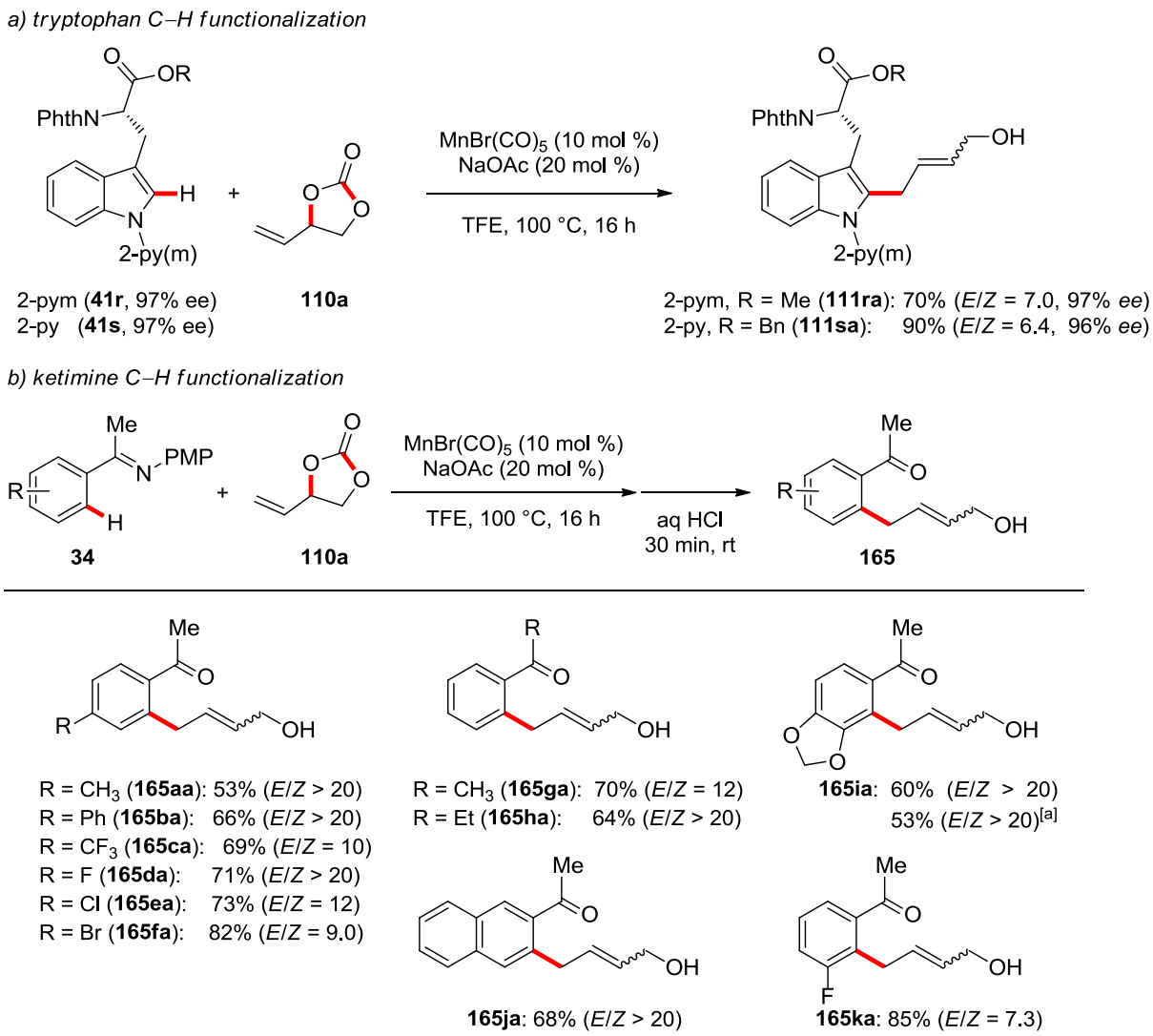
Subsequently, we also examined the applicability towards a representative set of vinylated dioxolanones **110** (Scheme 3.5.2). Notably, our method was compatible with different substitution pattern on dioxolanones and provided secondary and tertiary allylic alcohol products **111** in good yields with high diastereoselectivities. A variety of functional groups was also well tolerated, such as halogens, and even in case of the challenging nitro-substituent, a 79% yield of the desired product **111ae** was obtained.



Scheme 3.5.2 Scope of manganese(I)-catalyzed C–H/C–O allylation with dioxolanones **110**.

3.5.3 Manganese(I)-Catalyzed C–H/C–O Functionalization of Tryptophan and Ketimines

Furthermore, the synthetic utility of the manganese(I)-catalyzed C–H activation strategy was reflected by the direct modification of tryptophan **41r** and **41s**, delivering the desired products **111ra** and **111sa** in good yields without racemization (Scheme 3.5.3a). Motivated by the range of tolerated indoles and tryptophan derivatives, the applicability was further investigated by testing a variety of synthetically useful ketimines **34** (Scheme 3.5.3b). Remarkably, electron-rich as well as electron-deficient ketimines reacted smoothly and furnished the ketone products **165** in good yields with excellent diastereoselectivities. The position-selectivity of *meta*-substituted ketimines **34i** and **34k** was controlled by steric interactions, delivering the ketones **165ia** and **165ka** as sole products in 60%, and 85% yields, respectively. These results highlighted a broad applicability and excellent functional group tolerance of this manganese(I) catalytic system.

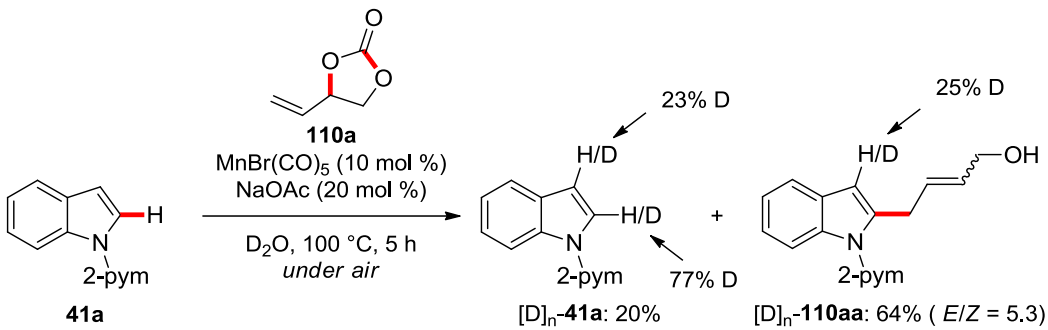


Scheme 3.5.3 Manganese(I)-catalyzed C–H/C–O functionalization of tryptophan **41** and ketimines **34**. [a] In H_2O.

3.5.4 Key Mechanistic Findings

3.5.4.1 H/D Exchange Experiment

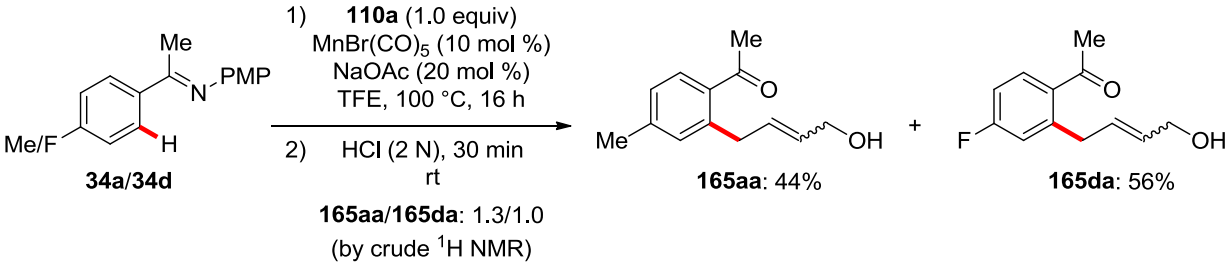
In order to delineate the manganese catalyst's mode of action, a series of mechanistic studies was performed. Firstly, a H/D exchange experiment in the presence of isotopically labeled D_2O was conducted (Scheme 3.5.4). A significant H/D exchange was observed in C-2 position of the re-isolated starting material $[D]_n$-**41a**, indicating a reversible C–H activation elementary step to be operative.



Scheme 3.5.4 H/D exchange experiment.

3.5.4.2 Intermolecular Competition Experiment

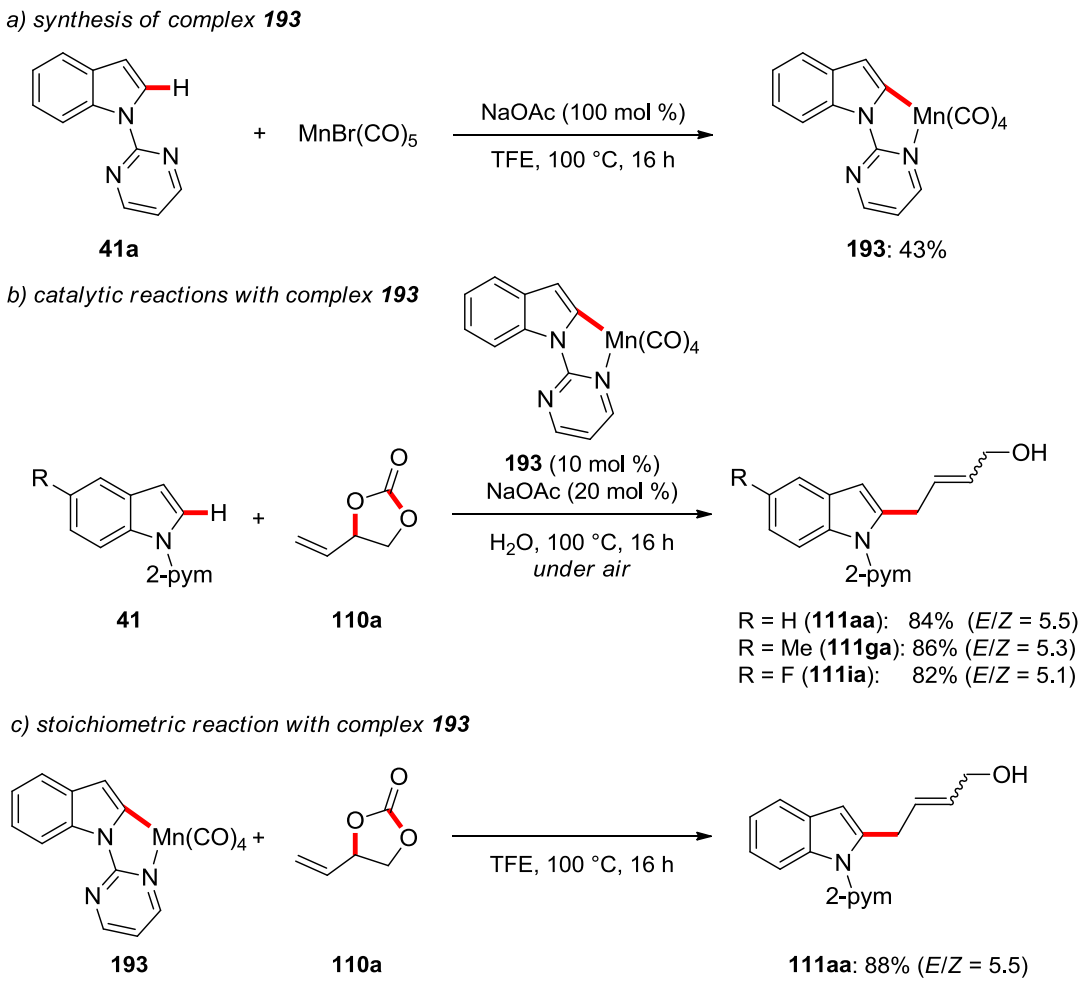
Then, an intermolecular competition experiment was carried out by comparing the reaction rates between electronically differentiated ketimines **34a** and **34d** (Scheme 3.5.5). This result showed a minor preference for the electron-deficient substrate under the optimized conditions.



Scheme 3.5.5 Intermolecular competition experiment.

3.5.4.3 Decarboxylative C–H/C–O Activation with Cyclometalated Complex 193

The organometallic complex **193** was independently prepared by the C–H activation of stoichiometric amounts of $MnBr(CO)_5$ with substrate **41a**. Remarkably, complex **193** showed a high reaction efficiency to afford the allylic alcohol products **111** not only in a catalytic reaction, but also in a stoichiometric experiment (Scheme 3.5.6). Overall, these results showed that this manganese cyclometalated complex probably is a key intermedate in the catalytic cycle.



Scheme 3.5.6 Decarboxylative C–H/C–O activation with cyclometalated complex **193**.

3.6 Synergistic Manganese(I) C–H Activation Catalysis in Continuous Flow: Chemoselective Hydroarylation

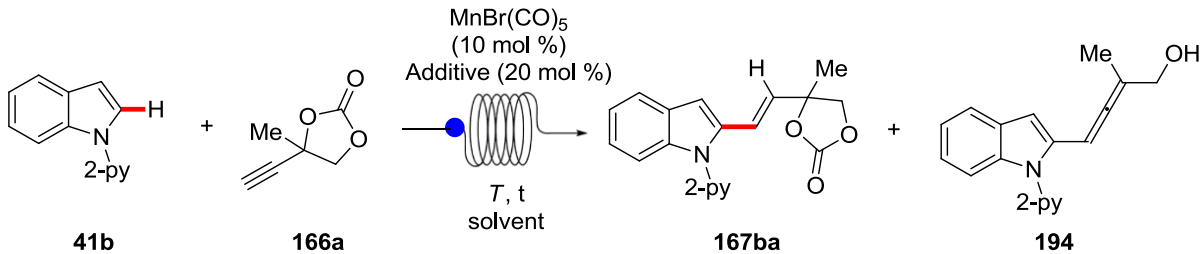
In recent years, the number and types of reactions performed in continuous flow have grown substantially, which were already widely applied to many fields, such as catalytic reactions, green chemistry, pharmaceutical and fine chemical industries due to the number of benefits, including: 1) improved process safety, 2) increased product quality and yield, 3) decreased reaction time, and 4) easy scale-up of chemical reactions.[150] In addition, significant processes in transition metal-catalyzed C–H activation also have been achieved during last few decades.[8, 13b] However, metal-catalyzed C–H activation in combination with continuous flow technology thus far has proven elusive. Only a few examples in this field have been very recently reported by Ackermann[171] and Noël[172]. In addition, from a sustainable perspective, Earth abundant 3d metals as the catalyst for C–H activation would be highly desirable. Based on our previous studies on C–H functionalizations,[160, 173] we hence became interested in developing a chemoselective manganese(I)-catalyzed C–H hydroarylation in continuous flow.

3.6.1 Optimization of Synergistic Hydroarylation in Flow

The optimization studies were commenced by probing the feasibility of the manganese(I)-catalyzed C–H hydroarylation of substrate **41b** with 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**) in continuous flow. Efforts towards the chemo-selective hydroarylation product **167ba**, being fully tolerant of β-O leaving groups, were optimized (Table 3.6.1). No reaction took place at 60 °C in the presence of NaOAc (entry 1). However, when we increased the reaction temperature to 100 °C, 56% of the allene product was obtained (entry 2). Similar results were observed with Cy_2NH as organic base or without additives (entries 3-4). When we chose $(n\text{Bu})_4\text{NOAc}$ as the additive, the desired product **167ba** was obtained in 26% yield (entry 5). A significant breakthrough was made by using acidic conditions. The use of pivalic acid furnished the desired hydroarylation product in good yield without formation of the allene product (**194**) (entry 6). Subsequently, we tried to optimize the flow rate with HOPiv as the additive. As a result, a longer residence time of the reaction in flow resulted in a slightly higher performance (entries 7-10). Notably, the reaction temperature played a major

role in the reaction (entry 11). Moreover, the high yields of the hydroarylation product were obtained with HOAc as the additive (entries 12-15). Switching to toluene or DCE as the reaction solvent, reducing the catalyst loading or decreasing the reaction temperature resulted in a significant decrease in the yield of the desired product **167ba** (entries 16-19). At last, the product was not observed in the absence of the manganese catalyst (entry 20).

Table 3.6.1 Optimization of synergistic hydroarylation of 41b in flow



41b **166a** **167ba** **194**

Entry	Additive	Solvent	Rate / (μL/min)	*T* / °C	Yield[a]	
					167ba	**194**
1	NaOAc	1,4-dioxane	100	60	--	--
2	NaOAc	1,4-dioxane	500	100	trace	56%
3	Cy_2NH	1,4-dioxane	500	100	--	32%
4	--	1,4-dioxane	500	100	--	63%
5	$(n\text{Bu})_4NOAc$	1,4-dioxane	500	100	26%	40%
6	HOPiv	1,4-dioxane	500	100	71%	--
7	HOPiv	1,4-dioxane	150	100	85%	--
8	HOPiv	1,4-dioxane	200	100	87%	--
9	HOPiv	1,4-dioxane	250	100	80%	--
10	HOPiv	1,4-dioxane	300	100	75%	--
11	HOPiv	1,4-dioxane	500	80	trace	--
12	HOAc	1,4-dioxane	200	100	93%	-

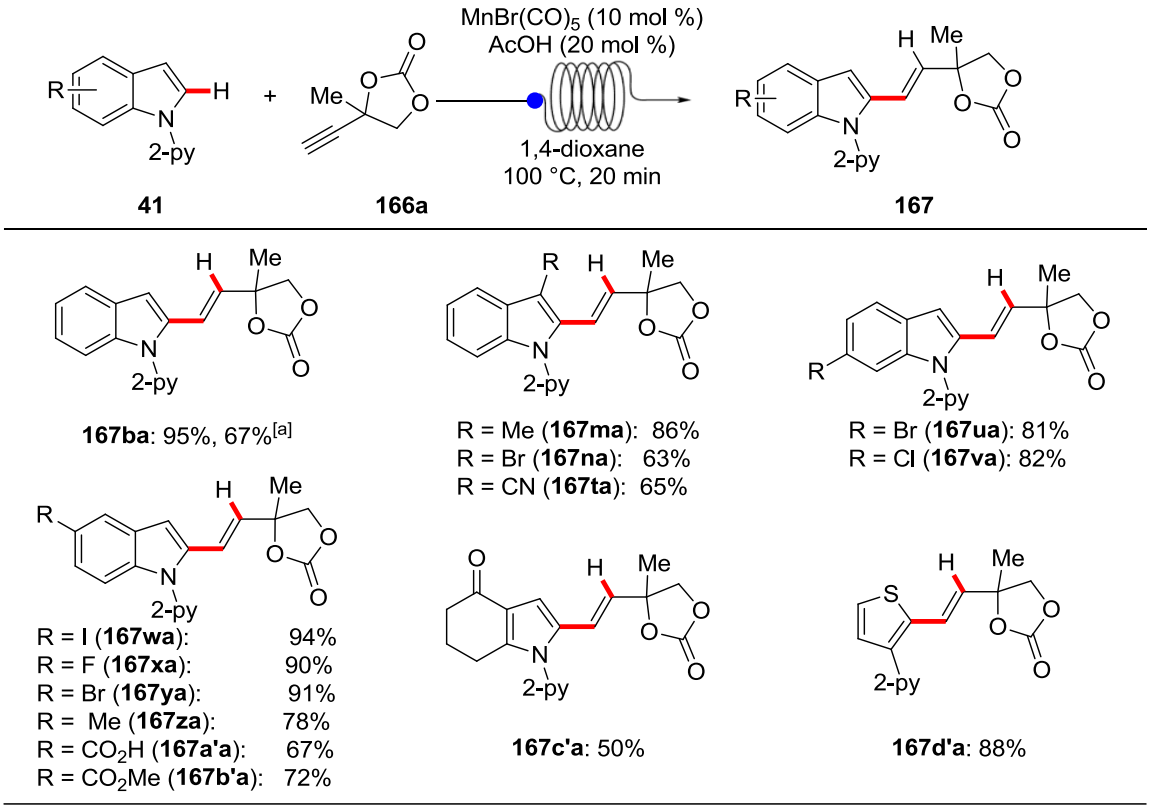
13	HOAc	1,4-dioxane	300	100	92%	--
14	**HOAc**	**1,4-dioxane**	**500**	**100**	**95%**	**--**
15	HOAc	1,4-dioxane	1000	100	82%	--
16	HOAc	toluene	500	100	25%	--
17	HOAc	DCE	500	100	24%	--
18	HOAc	1,4-dioxane	500	80	57%	--
19[b]	HOAc	1,4-dioxane	500	100	61%	--
20[c]	HOAc	1,4-dioxane	500	100	--	--

[a] Reaction conditions: **41b** (0.25 mmol), **166a** (0.50 mmol), $MnBr(CO)_5$ (10.0 mol %), additive (20.0 mol %), solvent (1.0 mL), under air, *T*, isolated yield. [b] $MnBr(CO)_5$ (5.0 mol %) was used. [c] Without $MnBr(CO)_5$.

3.6.2 Scope of Synergistic C–H Activation in Flow

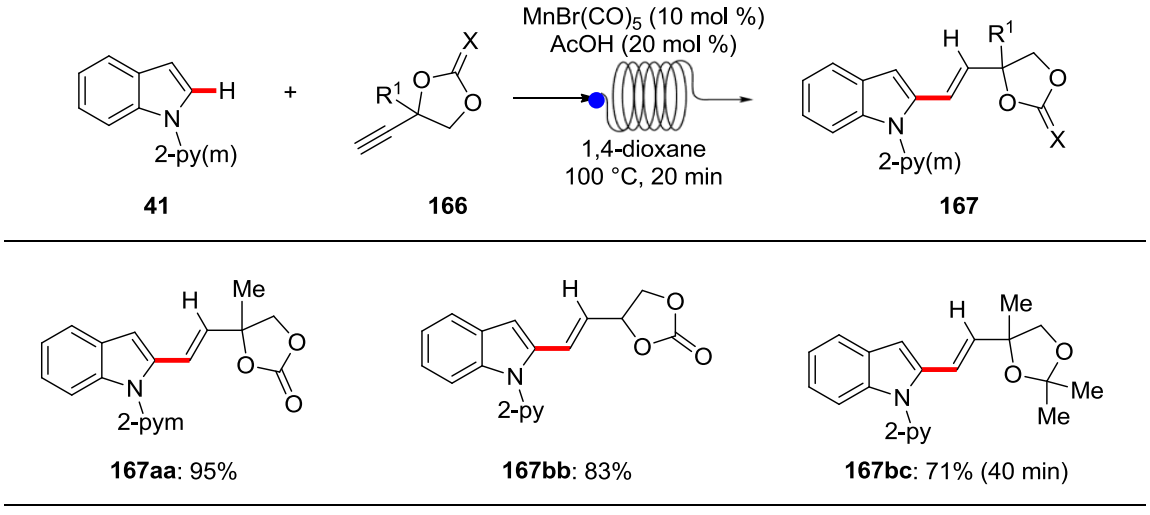
3.6.2.1 Scope of C–H Activation of the Heteroarenes 41 in Flow

Having established the optimized catalytic system, we explored the generality and scope of various indoles **41** for the manganese(I)-catalyzed C–H hydroarylation in continuous flow (Scheme 3.6.1). Notably, these results showed a broad substrate applicability and excellent tolerance towards various functional groups, such as halogens, cyano, ester and carboxylic acid, which delivered the corresponding products in moderate to good yields. It should be noted that the C-3 substituted sterically hindered substrates **41m, 41n,** and **41t** were found to be suitable for this flow C–H alkenylation and furnished the desired products **167ma, 167na,** and **167ta** in good yields. Moreover, the heterocyclic substrate **41d'** also underwent this process smoothly, affording the desired product **167d'a** in good yield with high chemo- and regio-selectivity. Remarkably, this flow C–H hydroarylation reaction could be conducted within only one minute at 150 °C, which demonstrated the major advantage of flow chemistry, avoiding the use of high-pressure sealed-tube equipment.



Scheme 3.6.1 Synergistic C–H activation of the heteroarenes **41** in flow. [a] 150 °C, 1 min.

3.6.2.2 Scope of C–H Hydroarylation with Propargylic Alkynes 166 in Flow



Scheme 3.6.2 C–H activation/hydroarylation with the propargylic alkynes **166** in flow.

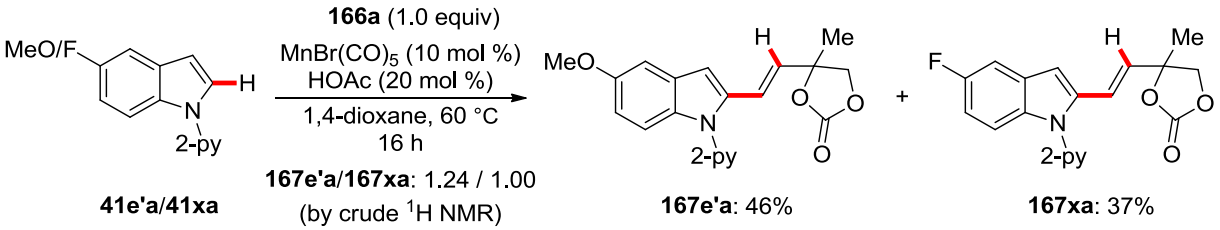
Motivated by the success in the synergistic C–H activation with a wide range of heteroarenes **41**, we

next tested the effect of propargylic alkynes **166** on the reaction process (Scheme 3.6.2). As expected, substituted propargylic alkynes **166** were also viable in this flow reaction, delivering the desired products in good yields with excellent levels of chemo-selectivity. Additional dioxolanone alkynes were tested by *Dr. Pesciaioli*.[152]

3.6.3 Key Mechanistic Findings

3.6.3.1 Intermolecular Competition Experiment

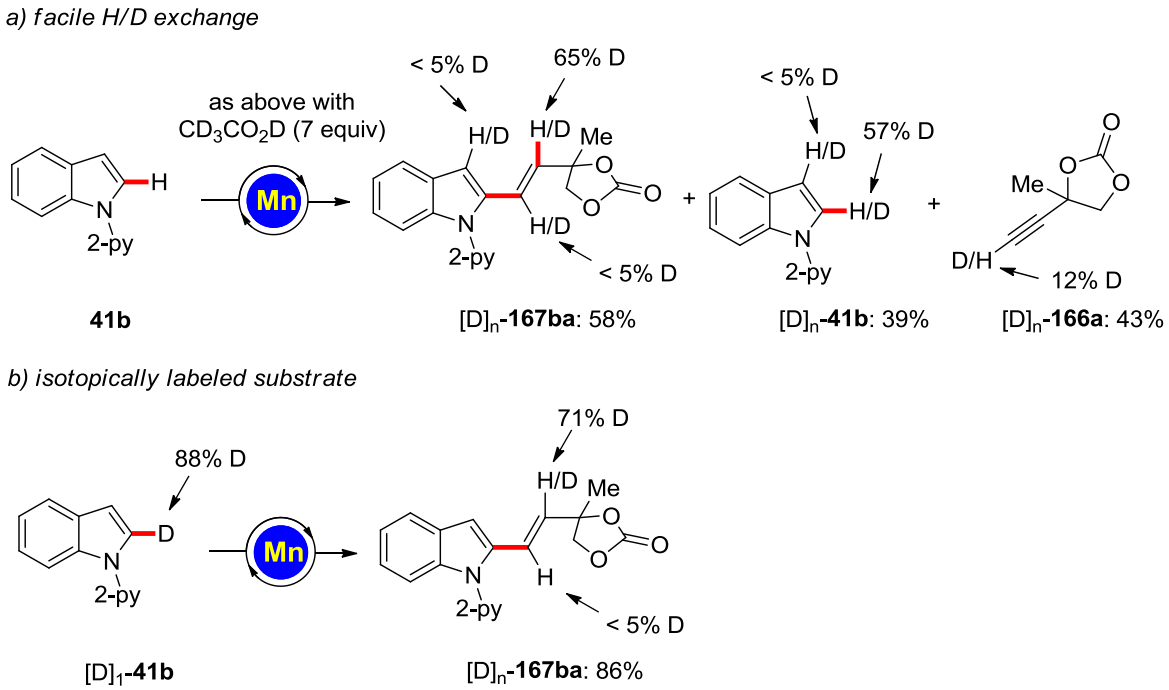
To further understand the mechanism of this unique manganese(I)-catalyzed C–H hydroarylation, a set of experiments was carried out to delineate its mode of action. Firstly, an intermolecular competition experiment between electronically distinct substrates **41e'a** and **41xa** was performed (Scheme 3.6.3). The result showed that the electron-rich substrate **41e'a** reacted preferentially under the reaction conditions (Scheme 3.6.3).



Scheme 3.6.3 Intermolecular competition experiment.

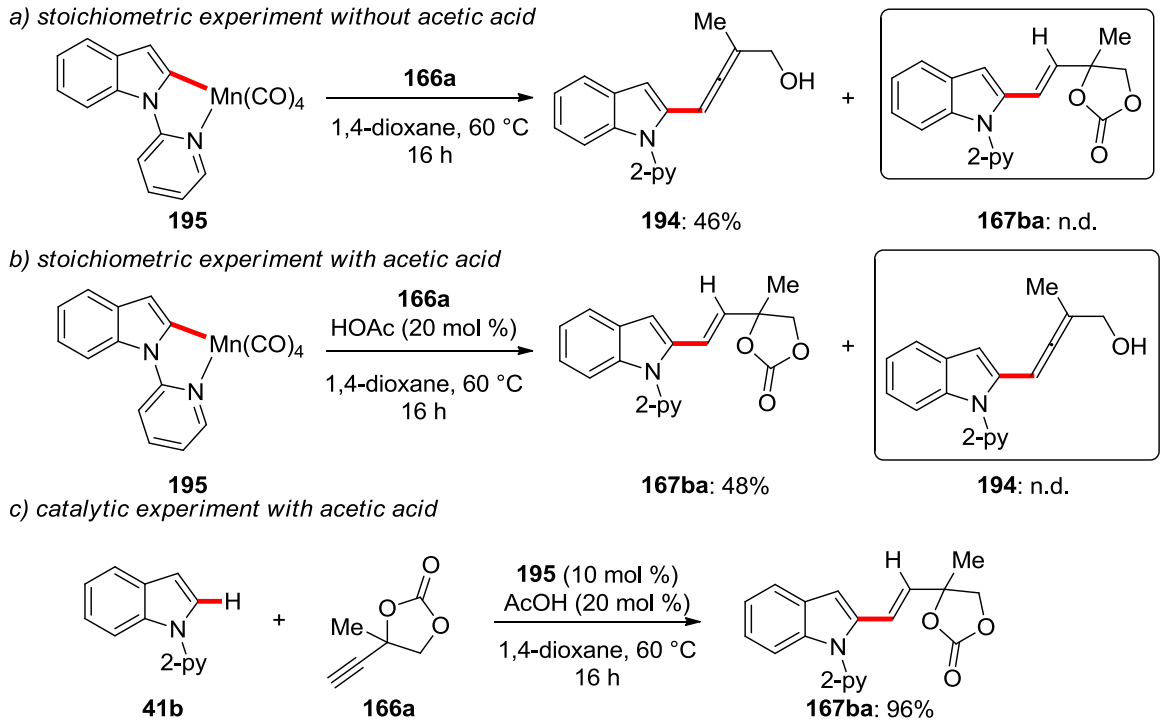
3.6.3.2 H/D Exchange Experiments

Furthermore, H/D exchange studies were conducted in the presence of isotopically labeled acetic acid as the additive. A notable H/D scrambling in C-2 position of the re-isolated starting material **41b** was observed, indicating a reversible C–H metalation to be operative. Importantly, a deuterium incorporation of 65% in the β-position of the product $[D]_n$-**167ba** was also observed. In contrast, no H/D exchange in the C-3 position of the product **167ba** as well as the re-isolated starting material was detected (Scheme 3.6.4a). The catalytic reaction of deuterated substrate $[D]_1$-**41b** further supported that the β-proton source of the product **167ba** is from the C-2 position of indole substrate **41b**, when catalytic amount of acetic acid was used (Scheme 3.6.4b).



Scheme 3.6.4 H/D exchange experiments.

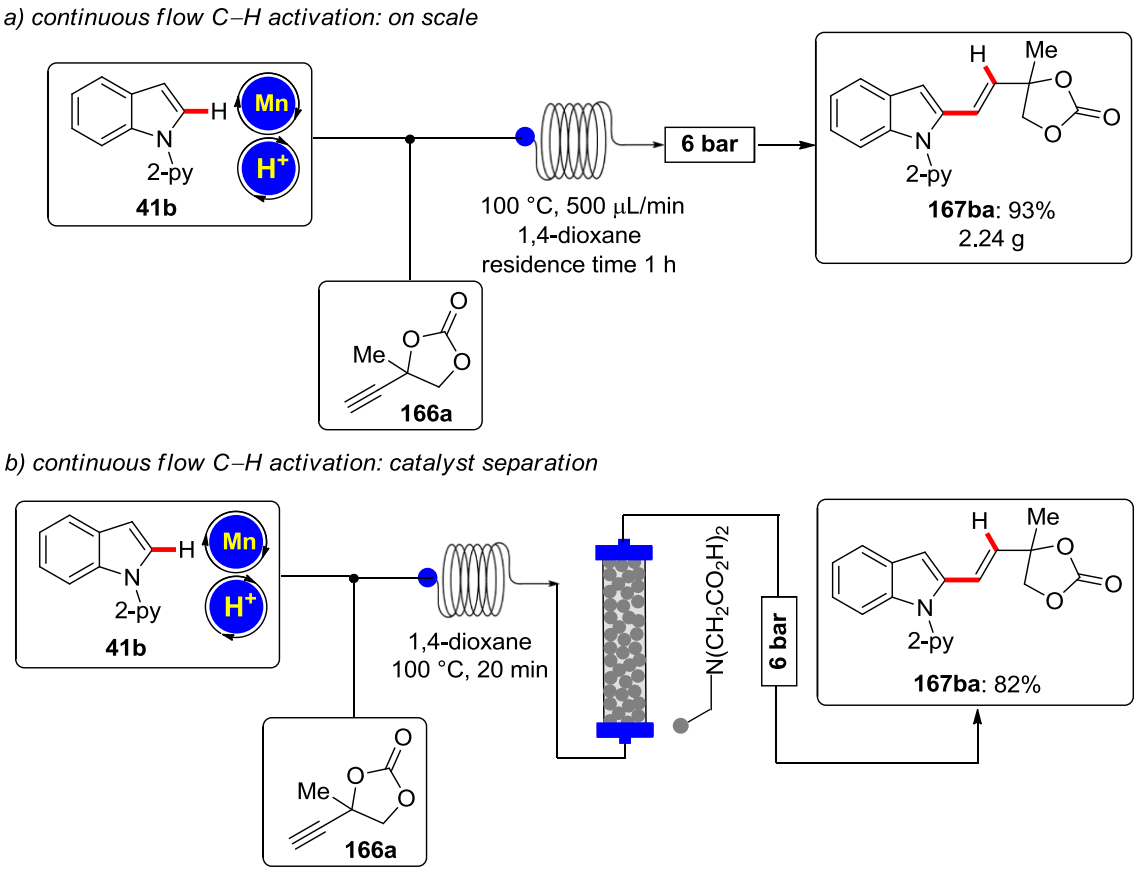
3.6.3.3 C–H Activation/Hydroarylation with Complex 195



Scheme 3.6.5 C–H activation/hydroarylation with complex **195**. n.d. = no reaction.

At last, in order to elucidate the nature of the active manganese catalyst, the performance of cyclometalated complex **195** was investigated in stoichiometric and catalytic reactions (Scheme 3.6.5). Interestingly, the stoichiometric reaction was conducted in absence of acetic acid, delivering only allene **194** in 46% yield by β-O elimination without any hydroarylation product being observed (Scheme 3.6.5a). In contrast, under acidic conditions, the cyclometalated complex **195** only afforded the hydroarylation product **167ba** in 48% yield (Scheme 3.6.5b). Moreover, complex **195** showed a very high activity in the catalytic reaction in the presence of a catalytic amount of acetic acid and the desired product in almost quantitative yield (Scheme 3.6.5c). These results showed that this complex **195** could play a very important role in the manganese catalytic cycle.

3.6.4 Continuous Flow Manganese-Catalyzed C–H Activation on Scale and Catalyst Separation



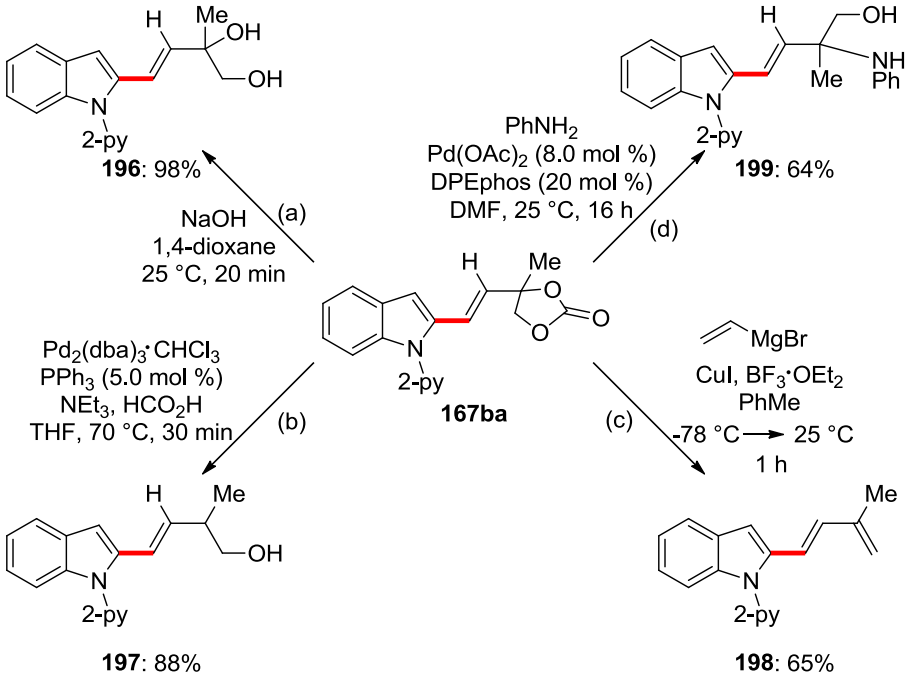
Scheme 3.6.6 Continuous flow manganese-catalyzed C–H activation on scale and catalyst separation.

In addition, the continuous flow C–H activation was conducted on a gram scale, and the desired

product **167ba** could be obtained in excellent yield with high chemo-selectivity, reflecting the robust and efficient manganese catalysis (Scheme 3.6.6a). Furthermore, we developed a convenient separation strategy for removing the manganese catalyst by using different types of resins (Scheme 3.6.6b). Further applications of this new technology in organic synthesis are still under investigation.

3.6.5 Late-Stage Modifications of Product 167

Finally, in order to demonstrate the unique synthetic utility of the obtained allylic carbonates **167**, a large number of diversification reactions were carried out (Scheme 3.6.7). Notably, the hydroarylation product could be easily transformed into other useful compounds. Firsty, compound **167ba** was hydrolyzed by treatment with sodium hydroxide in 1,4-dioxane to afford the 1,2-diol product **196** in near to quantitative yield (a). Additionally, decarboxylation of **167ba** provided the product **197** in 88% yield with palladium as catalyst (b).[174] Interestingly, when **167ba** was reacted with Grignard reagent under copper catalysis, 1,3-diene product **198** was obtained (c).[175] Finally, nucleophilic substitution of compound **167ba** by aniline catalyzed by palladium with DPEphos as the ligand smoothly provided product **199** in good yield (d),[176] which was performed by *Dr. Pesciaioli*.



Scheme 3.6.7 Late-stage modifications of product **167ba**.

3.7 Versatile and Robust C–C Activation by Chelation-Assisted Manganese-Catalysis

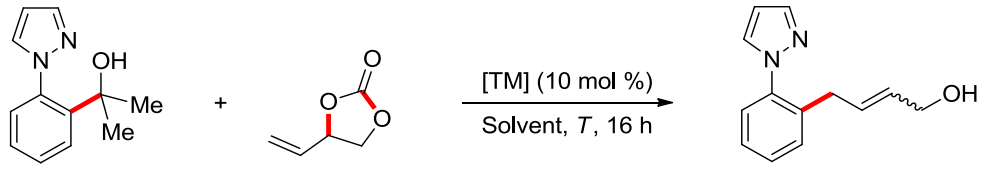
Transition metal catalysis has emerged as an important and straightforward method for the syntheses of complex molecules, which are very useful in pharmaceutical and fine chemical industries.[119d, 177] Direct C–C bond cleavage by transition metal complexes has recently attracted considerable attention, in consequence of the potential applications to organic synthesis.[119b-d] An ideal reaction should be performed with high atom economy at low reaction temperature and pressure, minimizing the waste, and using Earth-abundant elements, such as water as the solvent and 3d metal as the catalyst. Although great breakthroughs in direct C–C functionalization have been achieved, there are still many challanges in this field, including 1) requirement of harsh conditions; 2) relying on the strained or polarized C–C bonds;[178] 3) using noble metals as the catalysts, especially rhodium,[179] ruthenium,[153] and palladium;[180] 4) often the mechanism is not fully understood; and 5) limited substrate scopes. In this context, here we will focus on a distinct approach, which would carry out the C–C functionalization in water with Earth-abundant manganese as the catalyst relying on a β-carbon elimination step.[135-136]

3.7.1 Optimization of Manganese-Catalyzed C–C Cleavage

Initially, we examined the reaction of 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) with 4-vinyl-1,3-dioxolan-2-one (**110a**) at 120 °C in the presence of $MnBr(CO)_5$ as the catalyst by screening various solvents (Table 3.7.1, entries 1-6). Remarkably, nontoxic and nonflammable water turned out to be the optimal solvent for this manganese(I)-catalyzed C–C activation (entry 6). In contrast, other polar solvents, such as *n*BuOH and GVL, shut down the reaction completely (entries 4 and 5). It was further shown that the addition of acid or base was not required for the reaction (entries 7 and 8). A decreased yield of the desired product was observed when lower or higher reaction temperature was employed (entries 9-11). It was found that attempts to lower the catalyst loading, led to a significant decrease in reactivity (entry 12). No reaction was observed without $MnBr(CO)_5$ catalyst or with other manganese sources (entries 13-16). Furthermore, control experiments clearly showed that the manganese catalyst is unique and robust for this C–C functionalization, while other metals, such as palladium, rhodium, ruthenium, copper, and iron

complexes, failed to deliver the desired product **111aa** (entries 17-23).

Table 3.7.1 Optimization of manganese-catalyzed C–C cleavage



168a **110a** **111aa**

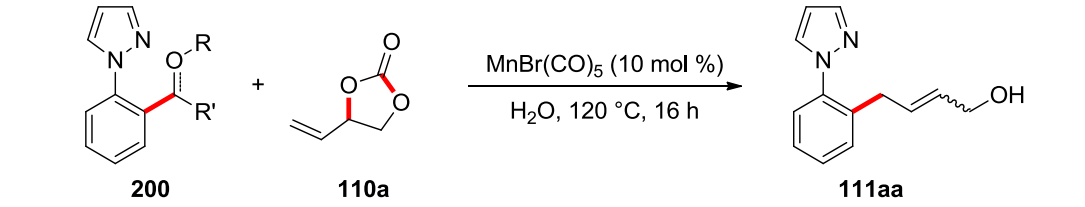
Entry	TM	*T* / °C	Solvent	Yield[a]	*E*/*Z*
1	$MnBr(CO)_5$	120	1,4-dioxane	65%	2.6
2	$MnBr(CO)_5$	120	toluene	63%	2.1
3	$MnBr(CO)_5$	120	DCE	71%	3.5
4	$MnBr(CO)_5$	120	*n*BuOH	---	---
5	$MnBr(CO)_5$	120	GVL	---	---
6	**$MnBr(CO)_5$**	**120**	**H_2O**	**75%**	**4.9**
7	$MnBr(CO)_5$	120	H_2O	17%[b]	4.3
8	$MnBr(CO)_5$	120	H_2O	---[c]	---
9	$MnBr(CO)_5$	100	H_2O	62%	4.5
10	$MnBr(CO)_5$	140	H_2O	65%	5.1
11	$MnBr(CO)_5$	80	H_2O	45%	4.6
12	$MnBr(CO)_5$	120	H_2O	59%[d]	4.1
13	---	120	H_2O	---	---
14	$MnCl_2$	120	H_2O	---	---
15	$Mn(OTf)_2$	120	H_2O	---	---
16	$Mn_2(CO)_{10}$	120	H_2O	---	---
17	$Pd(OAc)_2$	120	H_2O	---	---
18	$[Rh(COD)Cl]_2$	120	H_2O	---	---
19	$[RuCl_2(p\text{-cymene})]_2$	120	H_2O	trace	---
20	Cu(IPr)Cl	120	H_2O	--	--
21	$CpFe(CO)_2I$	120	H_2O	--	--
22	$[Cp^*RhCl_2]_2$	120	H_2O	--[e]	--
23	$[Cp^*RhCl_2]_2$	120	1,4-dioxane	--[e]	--

[a] Reaction conditions: **168a** (0.25 mmol), **110a** (0.50 mmol), [TM] (10 mol %), additive (20 mol %), solvent (1.0 mL), under N_2, 16 h, isolated yield. [b] NaOAc (20 mol %). [c] HOPiv (20 mol %). [d]

$MnBr(CO)_5$ (5.0 mol %). [e] $[Cp^*RhCl_2]_2$ (5.0 mol %). TM = transition metal.

3.7.2 Effect of Different Leaving Groups

Subsequently, the effect of the leaving group at the substrate moiety under the optimized conditions was investigated (Scheme 3.7.1). As a result, the substrates **200** with arene groups reacted smoothly, delivering the desired products **111aa** in moderate yields, while other secondary alcohols **200e**-**200g** failed to achieve the C–C functionalization. It proves that the arene group of the secondary alcohol substrates is essential for the manganese-catalyzed C–C activation. It is noteworthy that ether **200h**, ketone **200i**, and acid **200j** were not suitable leaving groups for the C–C activation reaction.



R = H (**200a**): 70% (4.8)
R = Me (**200b**): 65% (5.2)
R = CF_3 (**200c**): 43% (4.9)
R = F (**200d**): 54% (5.1)

R = H (**200e**): 0%
R = Me (**200f**): 0%
R = *n*Pr (**200g**): 0%

200h: ---

200i: ---

200j: ---

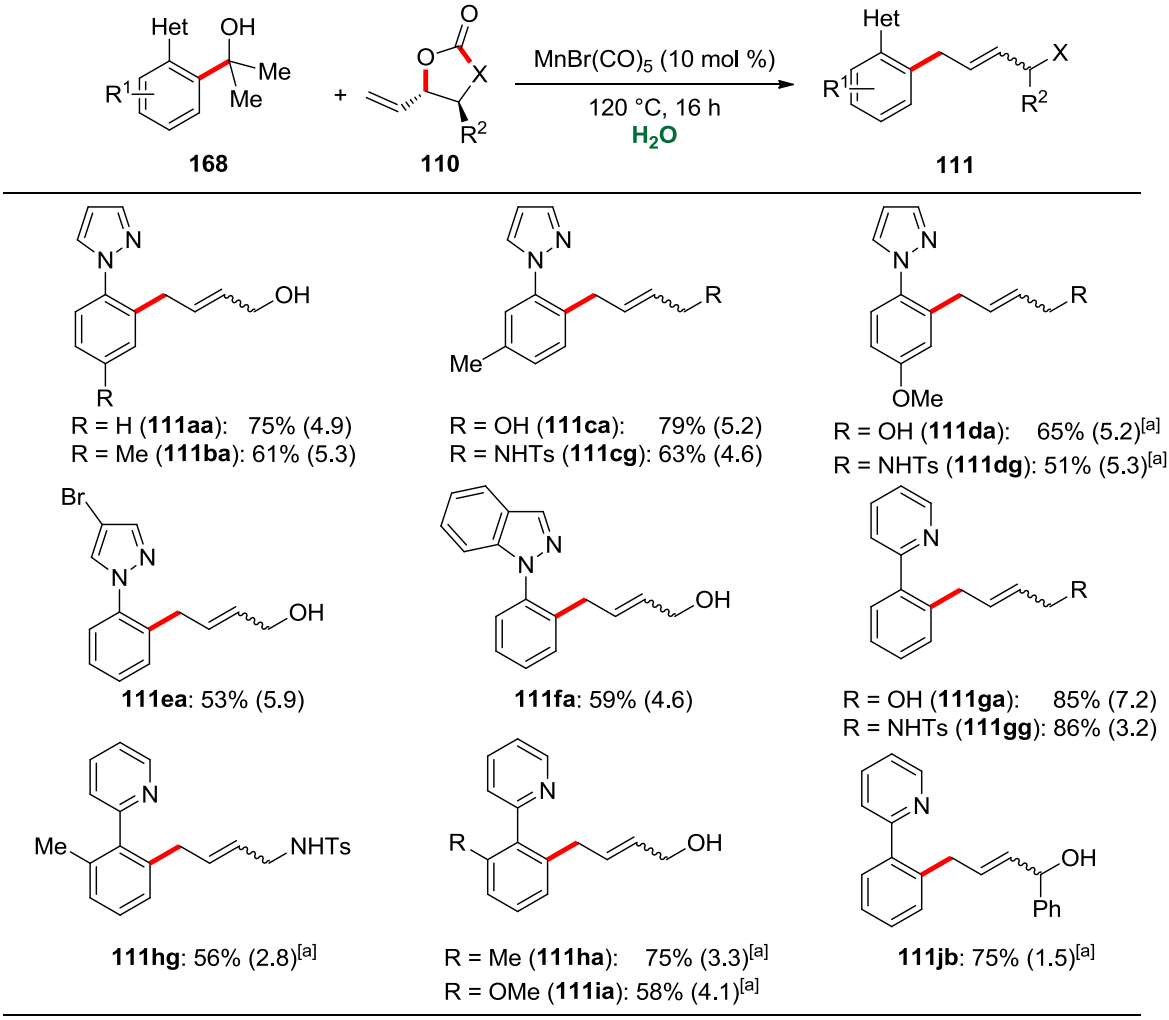
Scheme 3.7.1 Effect of leaving groups. *E*/*Z* ratio in parentheses.

3.7.3 Substrate Scope of C–C Functionalization in Water

3.7.3.1 Scope of Manganese(I)-Catalyzed C–C Allylation in Water

With the optimized catalytic system in hand, we evaluated the scope of the manganese(I)-catalyzed C–C functionalization with diversely decorated arenes **168** (Scheme 3.7.2). Notably, different directing groups, such as pyrazoles, pyridines and indazoles, could be smoothly converted in water. In addition, various valuable functional groups, such as bromo, amido and hydroxo, were well tolerated in this manganese catalytic system. Moreover, the manganese-catalyzed C–C activation protocol was not limited to the allylic alcoholic products **111ca**. Indeed, allylic amides could be also

obtained in good yields (**111cg**, **111dg**, **111gg** and **111hg**). The substituted propargylic alkene **110b** was also shown to be efficient for this C–C activation, delivering the desired product in 75% yield (**111jb**).

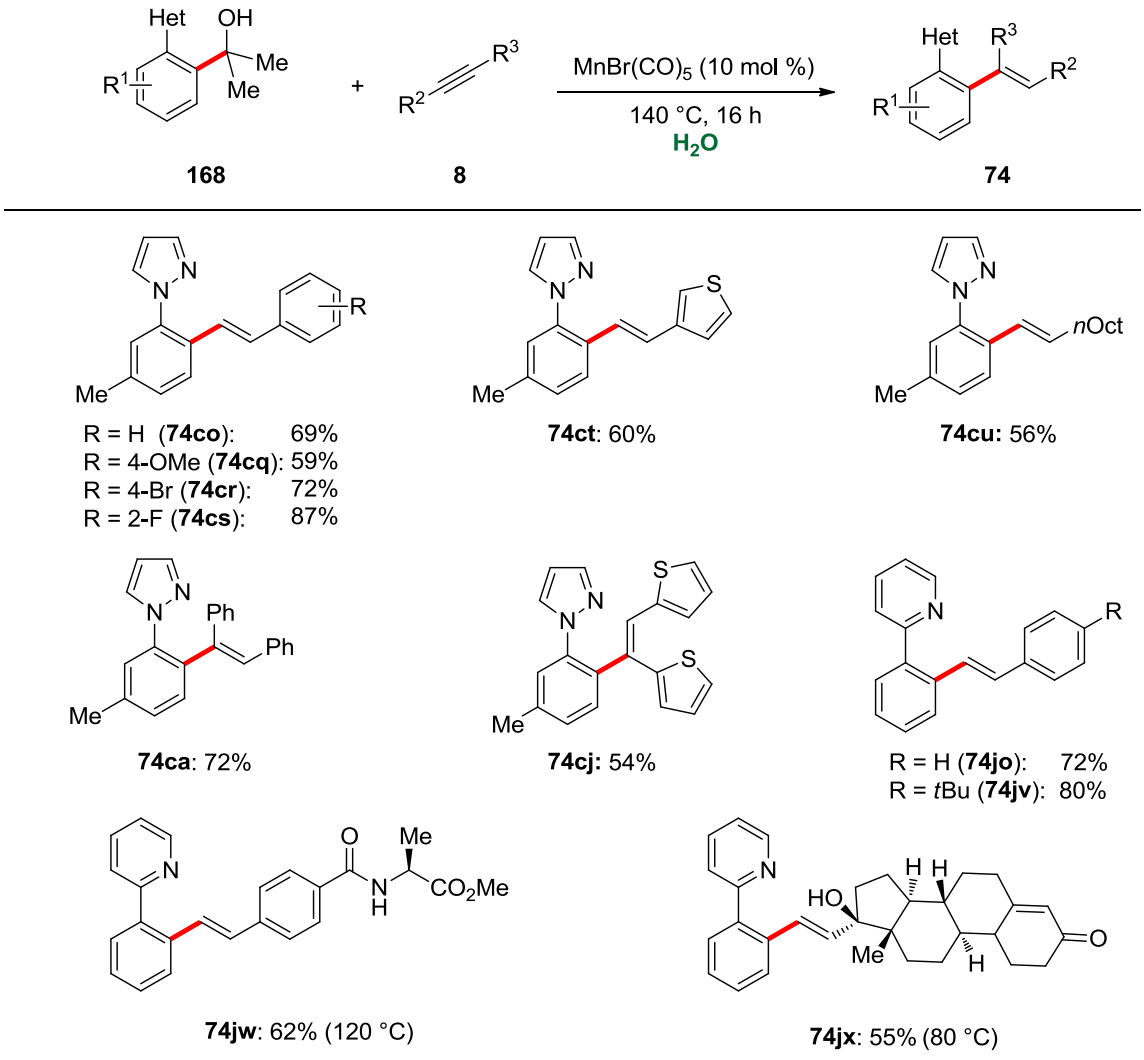


Scheme 3.7.2 Manganese(I)-catalyzed C–C allylation by chelation assistance. *E*/*Z* ratio in parenthesis. [a] PhCHO as leaving group.

3.7.3.2 Manganese(I)-Catalyzed C–C Activation for Additions of Alkynes in Water

Likewise, the versatile C–C activation was accomplished with various alkynes **8** under otherwise identical reaction conditions (Scheme 3.7.3). At first, *ortho*- and *para*-substituted phenylacetylenes (**8**), including electron-donating and electron-withdrawing groups, were efficiently converted into the alkenylation products **74** with excellent diastereoselectivity. Importantly, the 3-ethynylthiophene (**8t**) and dec-1-yne (**8u**) underwent this catalytic process with good catalytic

efficacy as well. It should be noted that the C–C activation was not limited to the internal alkynes, but terminal alkynes were also shown to be viable substrates and furnished the thermodynamically more stable isomer in good yields (**74ca**-**74cj**). The reaction of 2-[2-(pyridin-2-yl)phenyl]propan-2-ol (**168j**) also gave the corresponding products **74jo** and **74jv** in good yields with high diastereoselectivities. Finally, the manganese(I)-catalyzed C–C activation was also applied to amino acid (**8w**) and steroid (**8x**), affording the desired products in good yields without any racemization (**74jw** and **74jx**).

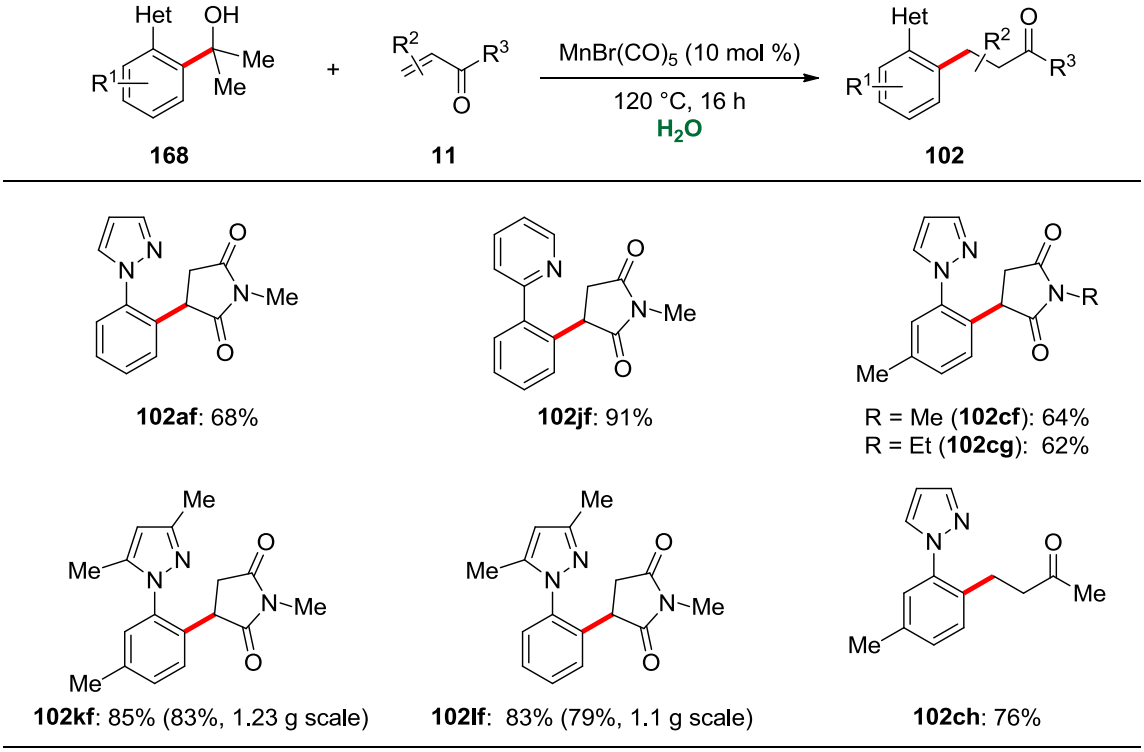


Scheme 3.7.3 Manganese(I)-catalyzed C–C activation for additions of alkynes **8** in water.

3.7.3.3 Manganese(I)-Catalyzed C–C Activation with Alkenes in Water

To our delight, the C–C hydroarylation manifold was not restricted to the alkynes **8**, but the alkenes

11 were also identified as competent substrates, again featuring water as the ideal solvent. The manganese catalyst turned out to be efficient and widely applicable for this C–C hydroarylation reaction, furnishing the corresponding products in good to excellent yields (Scheme 3.7.4). The reaction of substrates **168k** and **168l** could be performed on 5.0 mmol scale as well and provided the alkylated products in comparable yields (**102kf** and **102lf**). Moreover, the reaction with α,β-unsaturated ketone **11h** also proceeded to give the desired product **102ch** in 76% yield.

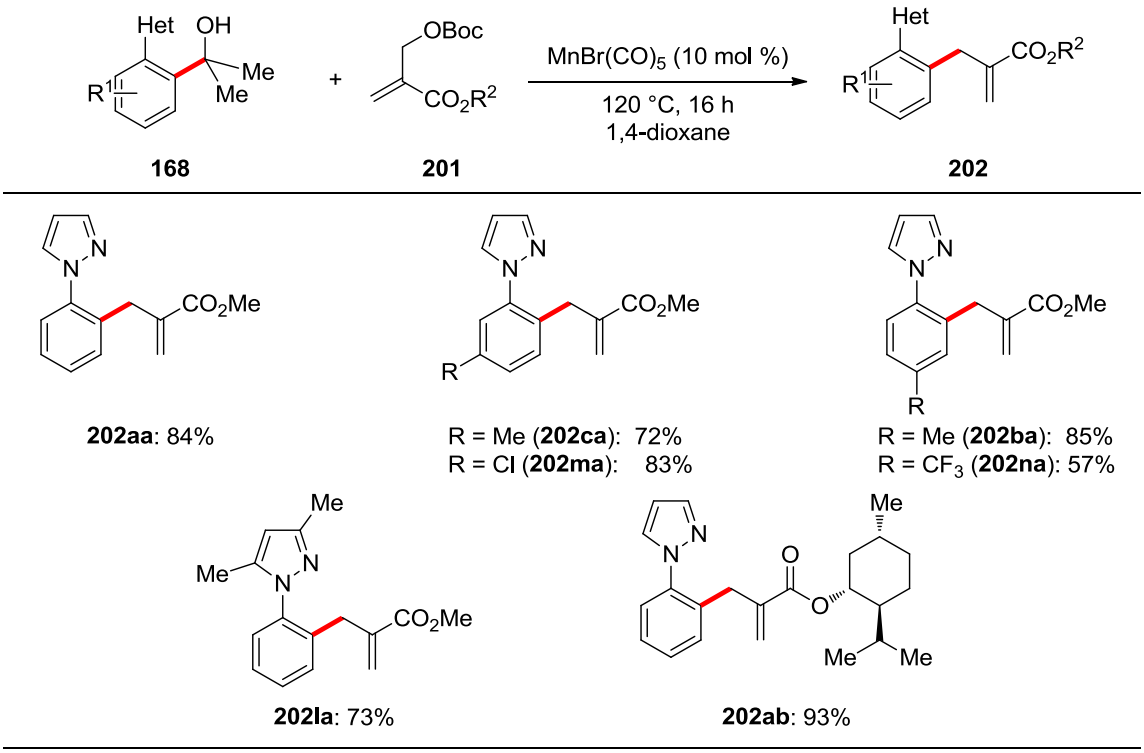


Scheme 3.7.4 Manganese(I)-catalyzed C–C activation with alkenes **11** in water.

3.7.3.4 Scope of Manganese(I)-Catalyzed C–C Allylation to Synthesize α,β-Unsaturated Esters

Furthmore, we also developed a new allylation reaction using various allylic reagents that provided expedient access to useful α,β-unsaturated esters **201** (Scheme 3.7.5). Notably, this transformation showed a good functional group tolerance and high regio-selectivity. It was demonstrated that the electron-withdrawing substrates **168m** and **168n** could react smoothly to provide the allylation products in good yields (**202ma** and **202na**). The challenging substrate **201b** was also found to be reactive under the newly developed conditions (**202ab**). This remarkable C–C functionalization could be achieved by reacting with various alkenes **11**, **201** and alkynes **8** in moderate to good yields

with good diastereoselectivies.

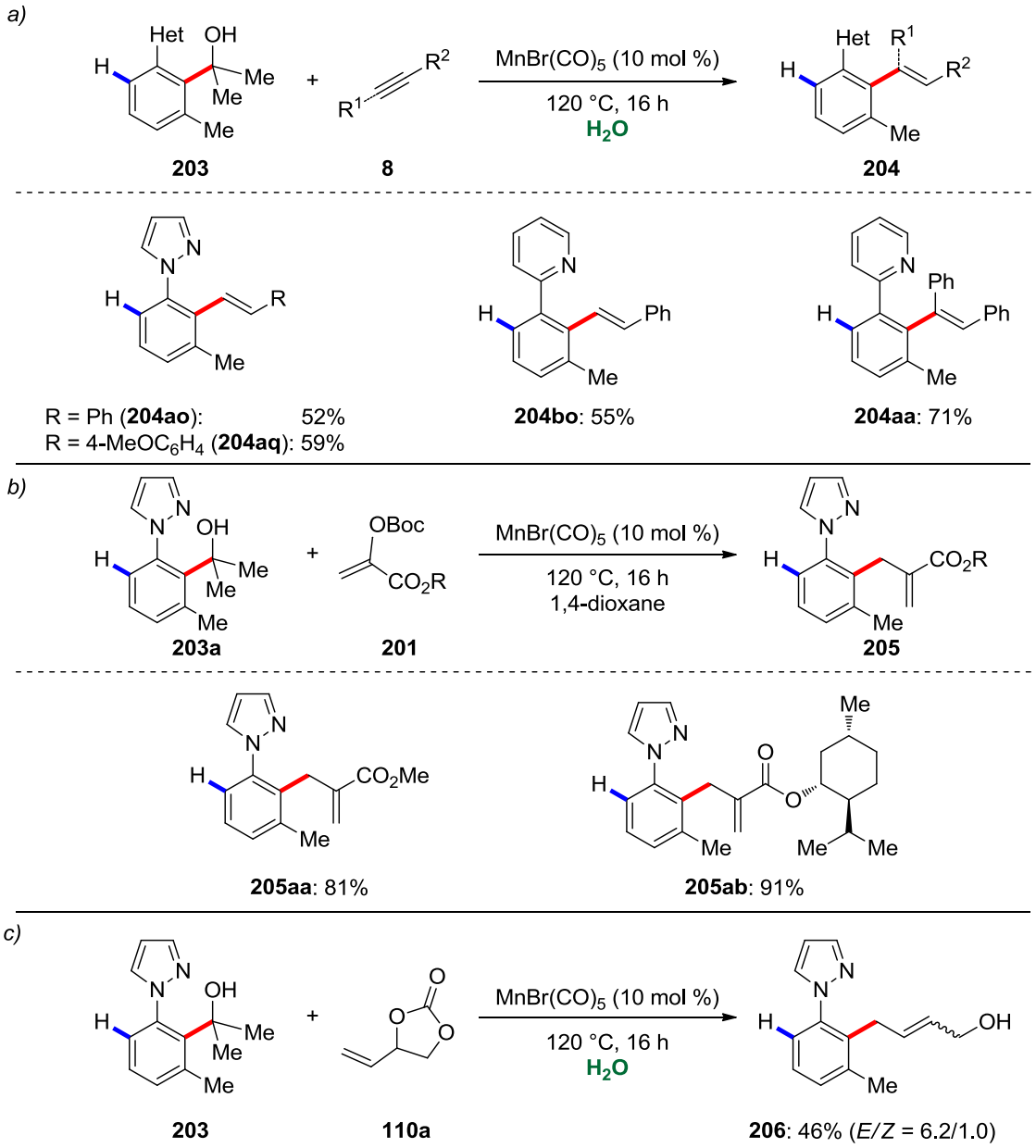


Scheme 3.7.5 Manganese(I)-catalyzed C–C allylation.

3.7.4 Position-Selective Manganese(I)-Catalyzed C–C Activation Highlighting Unique Benefits over C–H Activation

3.7.4.1 Position-Selective Manganese(I)-Catalyzed C–C Activation

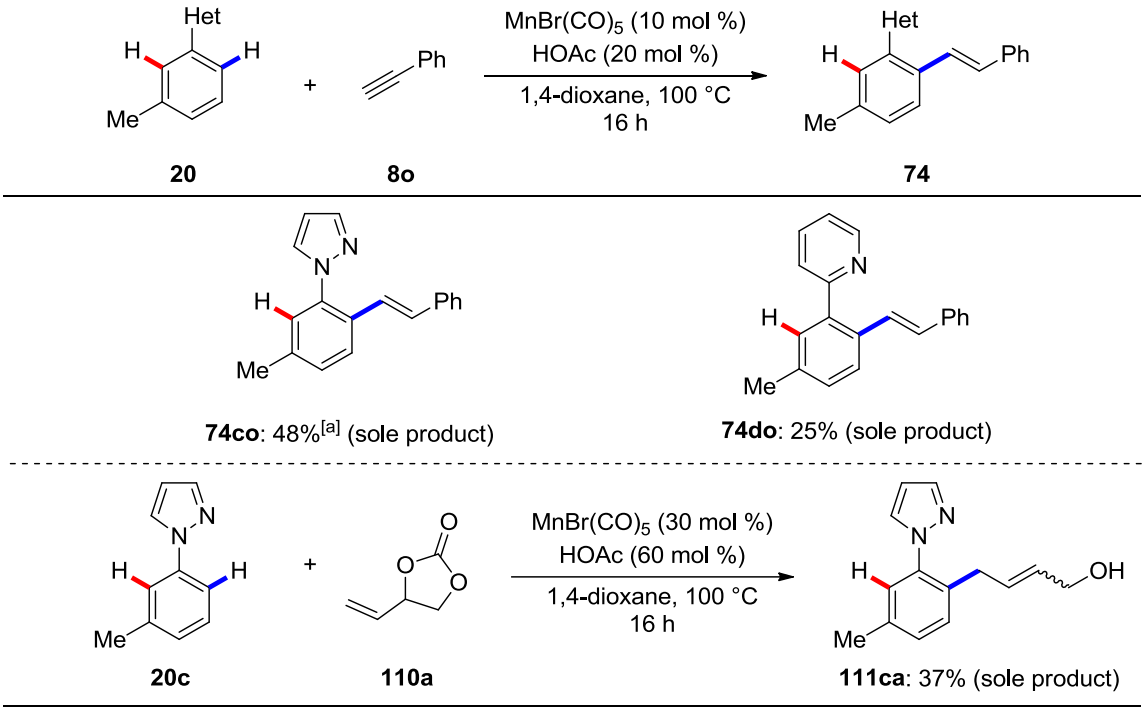
In order to overcome the limitations in the synthetic utility of the reaction, we here highlighted the unique C–C activation strategy by achieving the position-selectivity for the synthesis of 1,2,3-tri-substituted arenes **204**, **205** and **206** (Scheme 3.7.6). As we expected, these products could not be obtained by a C–H activation process, instead the 1,2,5-tri-substituted isomers were formed by steric control in very low yields (Scheme 3.7.7). Both terminal and internal alkynes **8** afforded the 1,2,3-tri-substituted products in moderate to good yields (a). High yields of the position-selective allylic products **205aa** and **205ab** were obtained from the reaction with substrates **201a** and **201b** (b). The desired allylic alcohol product **206** also could be obtained in 46% yield with good diastereoselectivity (c).



Scheme3.7.6 Position-selective manganese(I)-catalyzed C–C activation.

3.7.4.2 Manganese(I)-Catalyzed C–H Activation

In contrast, the C–H bond activation, which was performed in the presence of acetic acid, with phenylacetylene (**8o**) and 4-vinyl-1,3-dioxolan-2-one (**110a**) furnished 1,2,5-tri-substituted products **74co**, **74do,** and **111ca** in low yields without any observation of 1,2,3-tri-substituted products (Scheme 3.7.7). These results reflected the unique benefits of the C–C activation strategy over the C–H process.

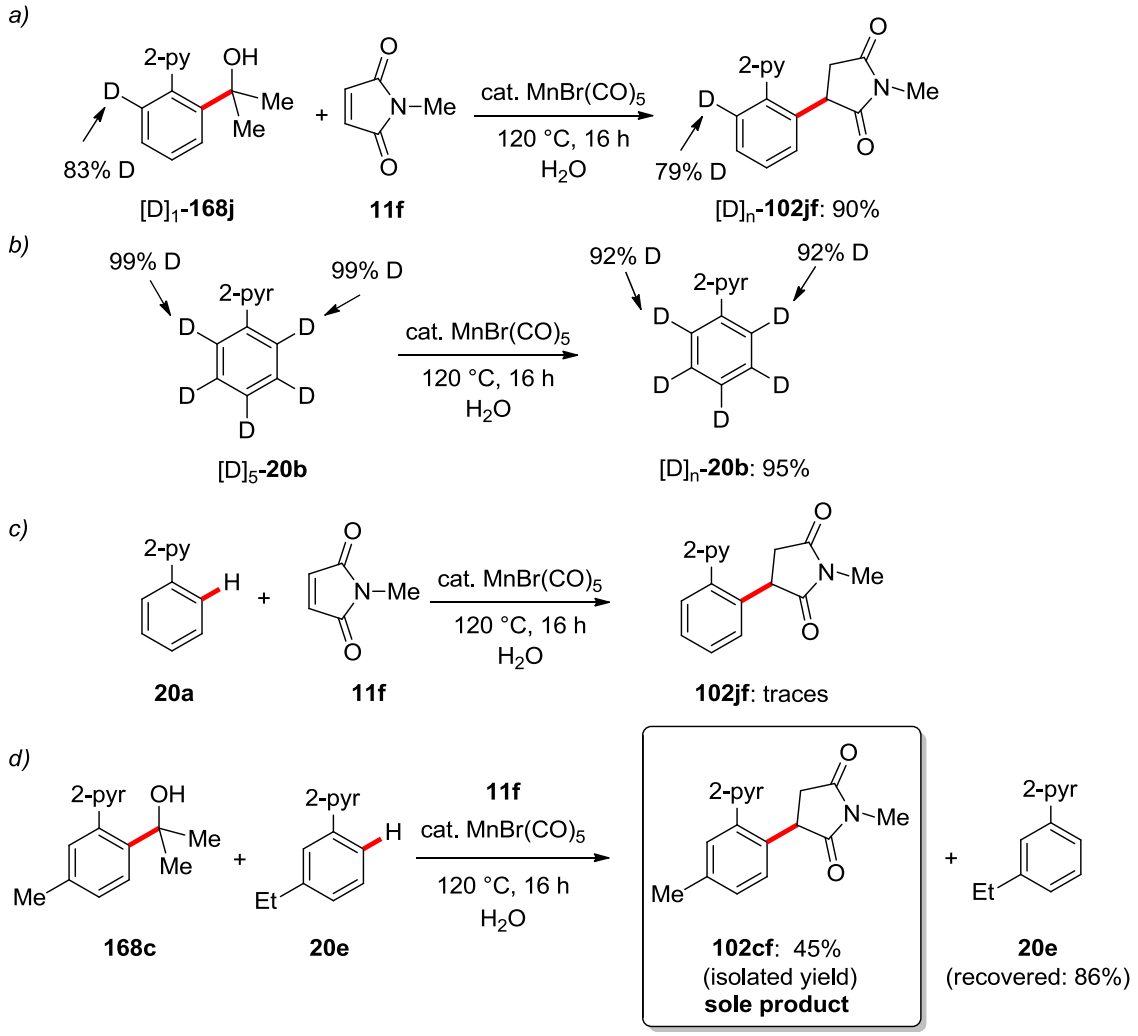


Scheme 3.7.7 Manganese(I)-catalyzed C–H activation. [a] 20 mol % [$MnBr(CO)_5$] was used.

3.7.5 Key Mechanistic Findings

3.7.5.1 C–C *versus* C–H Activation Experiments

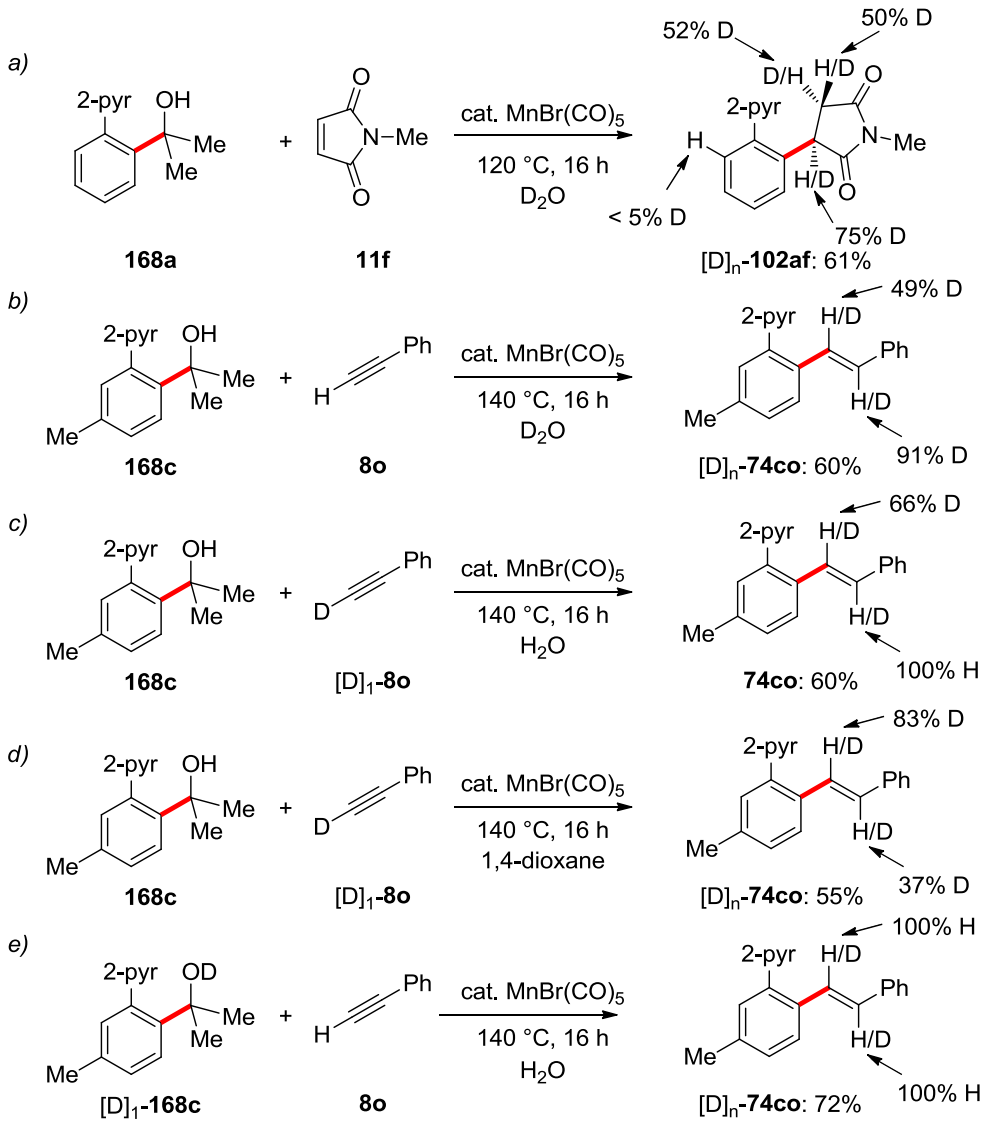
In order to showcase the benefits of the position-selective manganese(I)-catalyzed C–C activation, a set of mechanistic study experiments was conducted (Scheme 3.7.8). Firstly, C–C hydroarylation with the labelled substrate $[D]_1$-**168j** did not lead to D/H scrambling, making a C–H activation unlikely (a). When the labelled compound $[D]_5$-**20b** was tested in the absence of substrate **11f** under the optimized conditions, we could still get 92% D incorporation at *ortho*-C–H position (b). When substrate **20a** was reacted under the C–C activation conditions, it failed to furnish the C–H activation product **102jf** (c). Lastly, an intermolecular competition experiment between substrate **168c** and arene **20e** was investigated. The desired product **102cf** was obtained as the sole product without any C–H product formation (d), further demonstrating the unique manganese(I)-catalyzed C–C activation process.



Scheme 3.7.8 C–C *versus* C–H activation experiments.

3.7.5.2 H/D Exchange Experiments

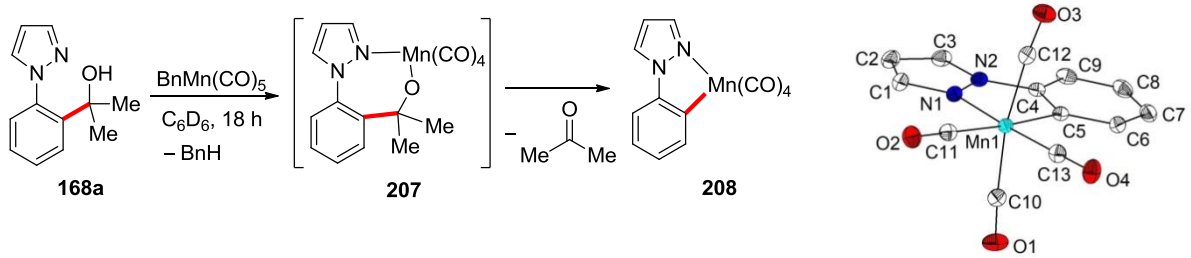
H/D exchange experiments were also carried out to elucidate the mechanism of this C–C activation (Scheme 3.7.9). Firstly, the reactions were conducted with substrate **168a** and phenylacetylene **80** in the presence of isotopically labelled D_2O. A large amount of deuterium incorporation at both β-positions of the products $[D]_n$-**102af** and $[D]_n$-**74co** was observed (a and b). Moreover, the reactions of substrate $[D]_1$-**8o** were conducted in different solvents and no H/D scrambling at β-position was observed in water, but a deuterium incorporation of 37% in 1,4-dioxane was determined (c and d). Importantly, when substrate $[D]_1$-**168c** reacted with phenylacetylene (**8o**) under the optimized conditions, no deuterium was detected in product **74co** (e). These findings clearly showed that the proto-demetalated step is caused by the vast excess of water.

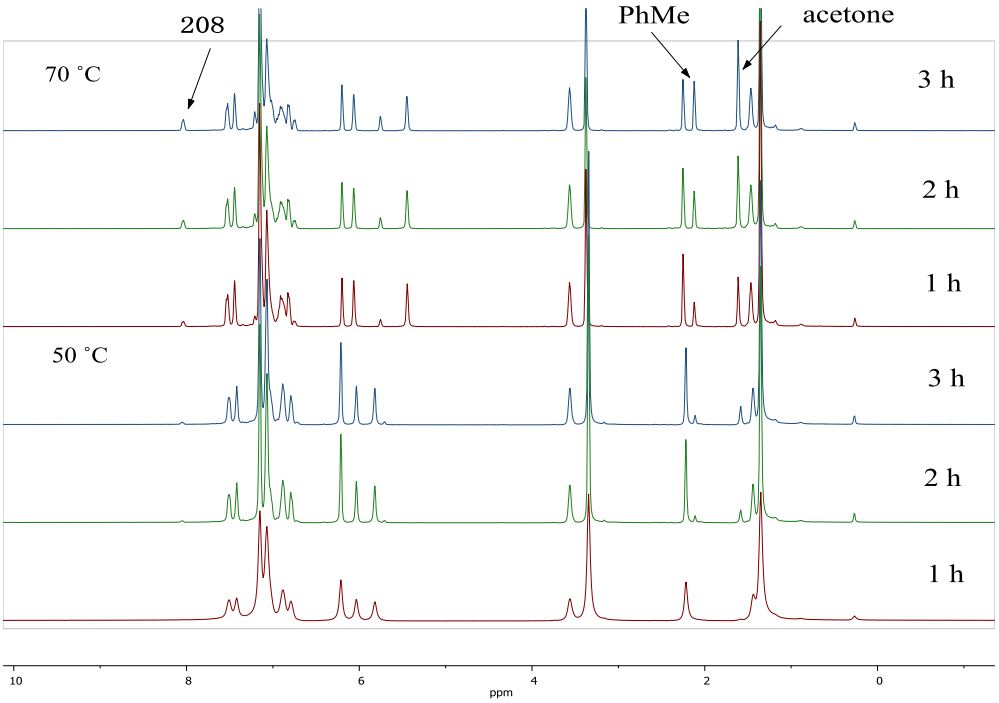


Scheme 3.7.9 H/D exchange experiments.

3.7.5.3 Stoichiometric C–C Cleavage by X-ray and NMR Spectroscopy

Thus, the stoichiometric C–C activation of compound **168a** by $BnMn(CO)_5$ provided the intermediate **208**, which was characterized by X-ray diffraction analysis. Further ^1H NMR experiments of the stoichiometric reaction provided strong evidence for the generation of complex **208** by the formation of equimolar amounts of toluene and acetone (Scheme 3.7.10).

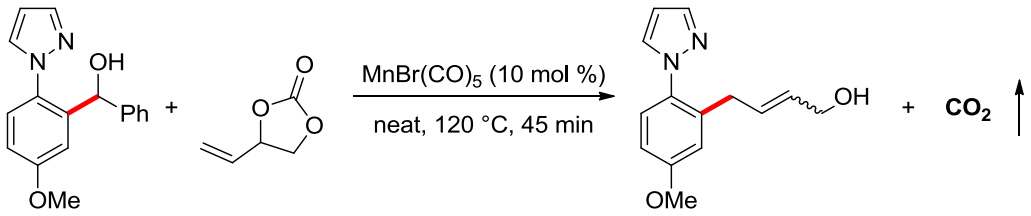




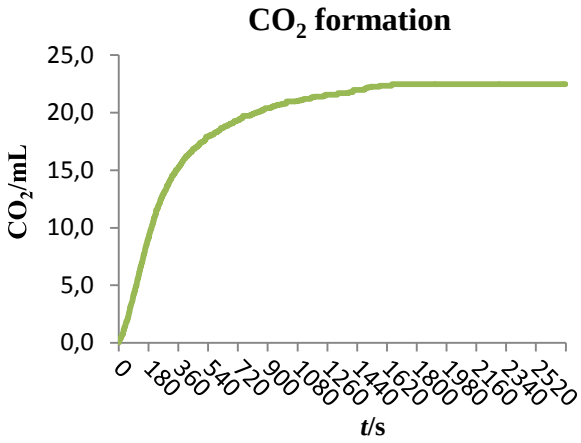
Scheme 3.7.10 Stoichiometric C–C cleavage detected by X-ray and ^{1}H NMR spectroscopy.

3.7.5.4 Detection and Quantification of CO_2

Furthermore, in order to detect and quantify the generation of CO_2. A volumetric analysis was perfomed (Scheme 3.7.11). The observed formation of CO_2 is in good agreement with the results obtained from the C–C allylation reaction.



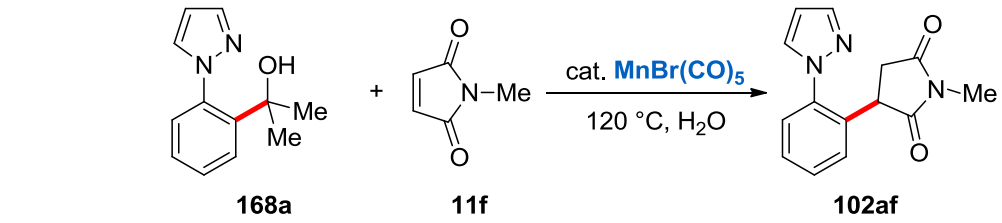
168d' **110a** **111da**: 66%



Scheme 3.7.11 Detection and quantification of CO_2.

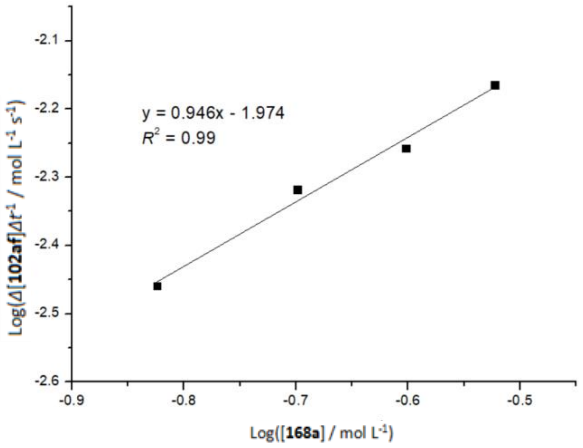
3.7.5.5 Kinetic Reaction Orders

The kinetic order of the reaction with respect to the concentration of 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) as well as the manganese catalyst showed a first order dependence, indicating that the substrate **168a** and the catalyst $MnBr(CO)_5$ both are part of the turnover-limiting step of the catalytic cycle (Scheme 3.7.12a and b). In sharp contrast, a zero order dependence on the concentration of the substrate **11f** was observed, providing strong support for a rate-determining C–C metalation (c). These results are also in good agreement with detailed DFT calculations performed by *M.Sc. Rogge*.[154]

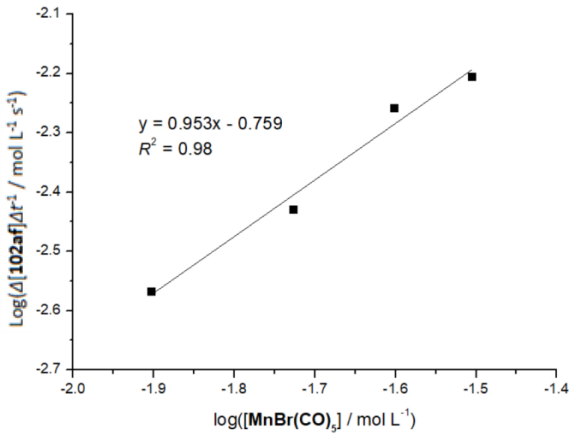


168a **11f** **102af**

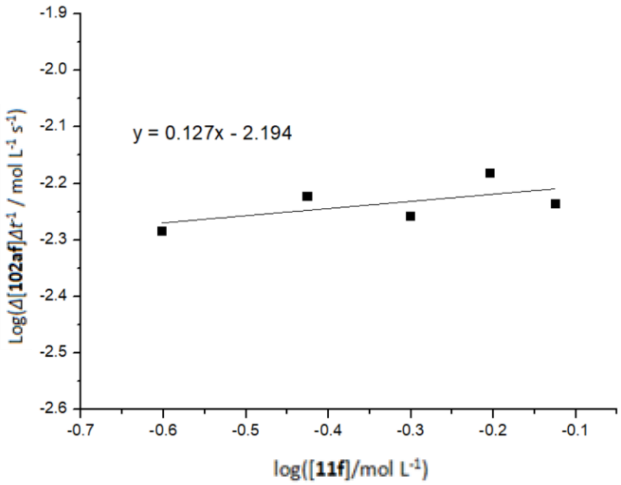
*(a) order in **168a***



*(b) order in **MnBr(CO)5***



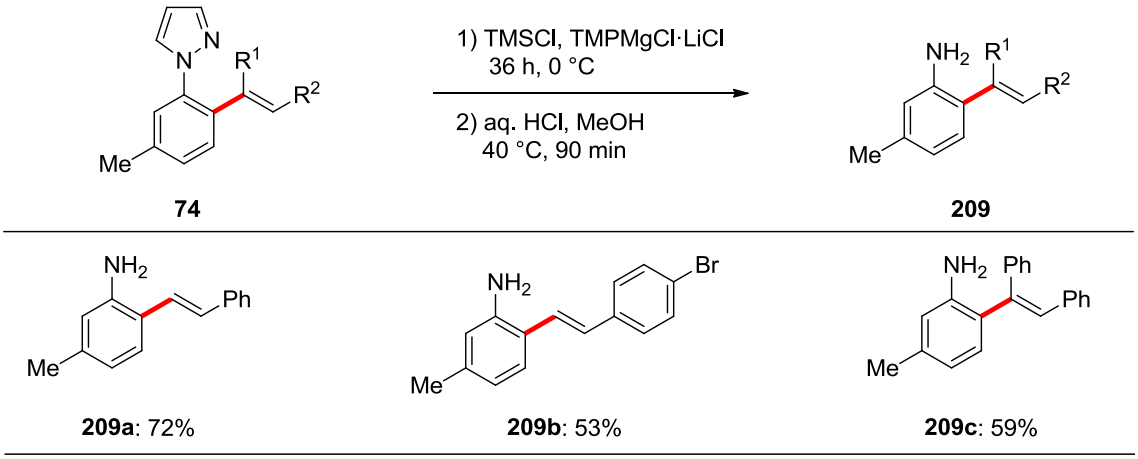
*(c) order in **11f***



Scheme 3.7.12 Kinetic order of coumpounds **168a**, **11f** and manganese catalyst.

3.7.6 Traceless Removal of the Pyrazole Group

Finally, the synthetic utility of this C–C activation strategy was investigated by the traceless removal of the pyrazole group, delivering the corresponding anilines **209** in moderate to good yields, which could be easily transformed into other useful compounds (Scheme 3.7.13).

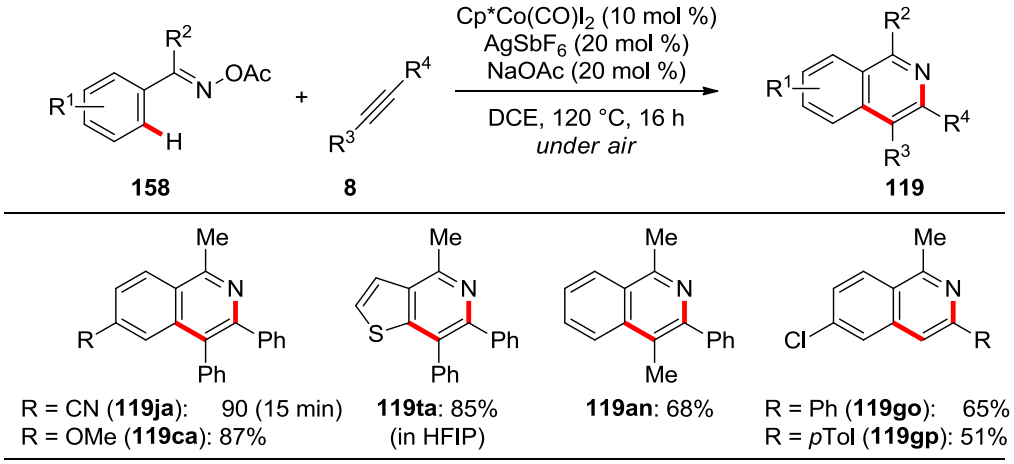


Scheme 3.7.13 Traceless removal of the pyrazole group.

4 Summary and Outlook

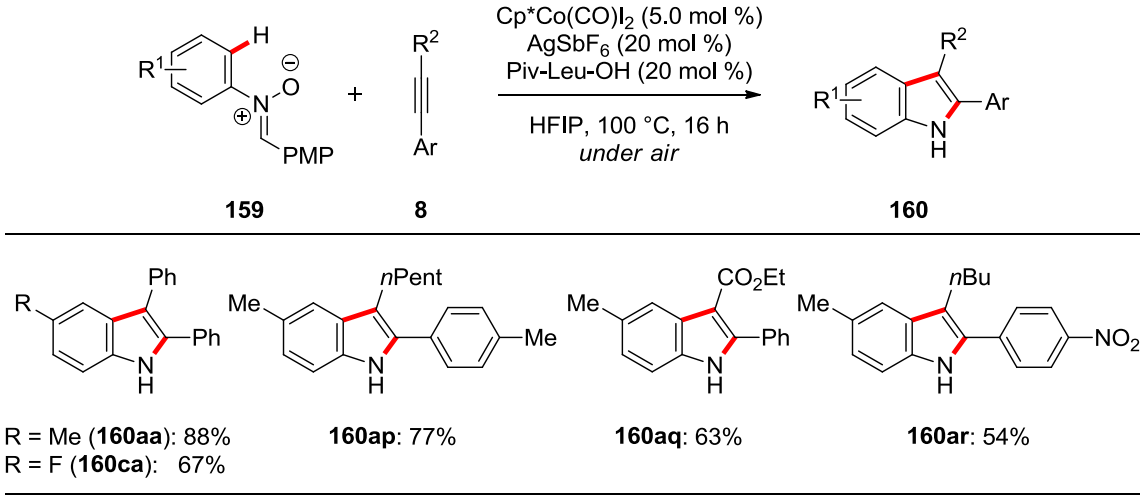
Metal-catalyzed C–H and C–C functionalizations have become an increasingly viable approach, which allows the direct formation of C–C and C–heteroatom bonds in an atom- and step-economical manner. However, the significant accomplishments in this field have heavily relied on the use of precious transition metals, such as rhodium, palladium, ruthenium, and iridium, over the last few decades. The high cost and potential toxicity of these metals limit the applications in pharmaceutical and fine chemical industries. Therefore, developing efficient and economic C–H and C–C functionalization by inexpensive and Earth-abundant metals is highly desirable. In this thesis, we summarize our recent achievements in direct C–H and C–C bond transformations by cobalt(III)- and manganese(I)-catalysis.

In the first project, a cobalt(III)-catalyzed C–H/N–O functionalization was achieved for the synthesis of substituted isoquinolines derivatives (Scheme 3.8.1). Notable features of this developed annulation reaction were a wide substrate scope applicable and tolerance of various functional groups. The N–O bond of the oxime was successfully utilized as the internal oxidant in this process. Importantly, the reaction was not limited to the symmetrical alkynes, but also unsymmetrical and terminal alkynes could be employed in the reaction to afford the isoquinolines in good yields with high regio-selectivities. In many cases, the annulation products were obtained high yields within only 15 min. The mechanistic findings, including H/D exchange, competition experiments and KIE studies, revealed a reversible and facile BIES-type C–H metalation pathway was involved.



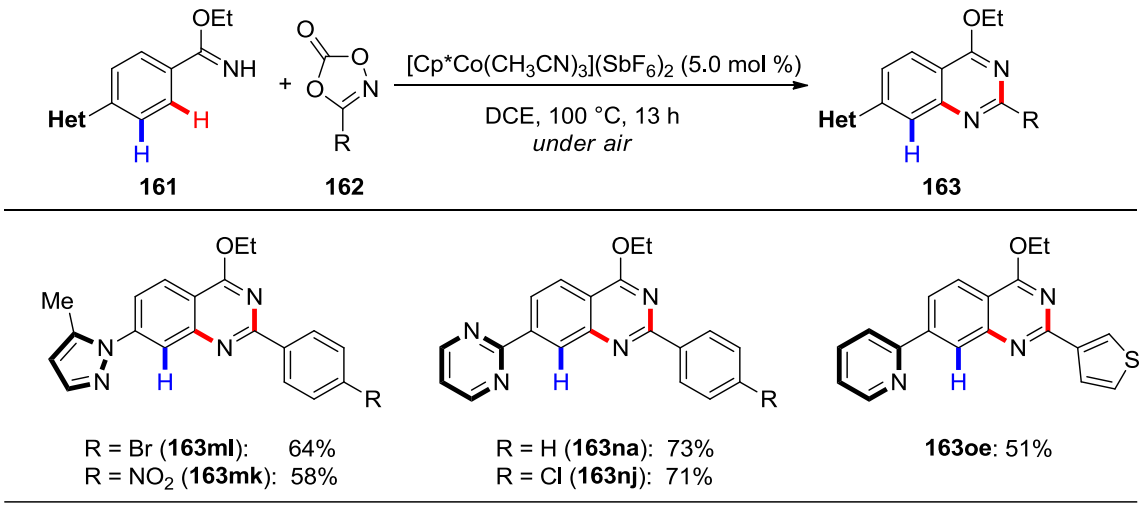
Scheme 3.8.1 Cobalt(III)-catalyzed C–H/N–O functionalization for the synthesis of isoquinolines.

In the second project, a good site- and regio-selective cobalt(III)-catalyzed C–H annulation of various nitrones approached the novel and useful indole synthesis (Scheme 3.8.2). The versatile cobalt(III) catalyst proved to be particularly effective for challenging unsymmetrically substituted alkynes, when employing a catalytic amounts of Piv-Leu-OH as ligand, delivering unprotected indoles in good yields with excellent levels of regioselectivity. Detailed mechanistic studies, such as H/D exchange and KIE experiments, provided strong support for a rate-determining C–H metalation step.



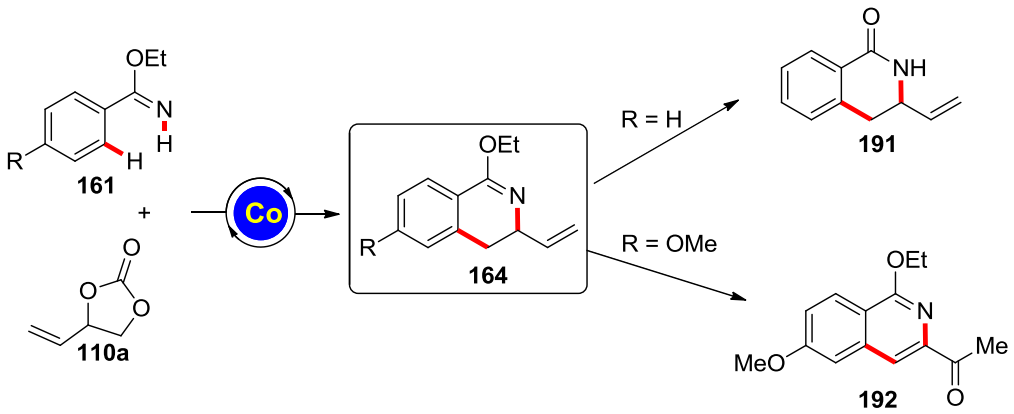
Scheme 3.8.2 Cobalt(III)-catalyzed C–H/N–O functionalization for the synthesis of indoles.

In the third project, we developed the first cobalt(III)-catalyzed position-selective C–H functionalization, which fully tolerated strongly coordinating heterocycles, such as pyridines, pyrimidines, and pyrazoles (Scheme 3.8.3). This reaction was showed a wide substrate scope with various functional groups tolerance, such as chloro, fluoro, ester, ketone, nitro, and thiophene. The preliminary mechanistic studies, especially the H/D exchange experiments, indicated that the positional selectivity of this C–H amination is determined in the C–N bond forming step.



Scheme 3.8.3 Cobalt(III)-catalyzed position-selective C–H functionalization.

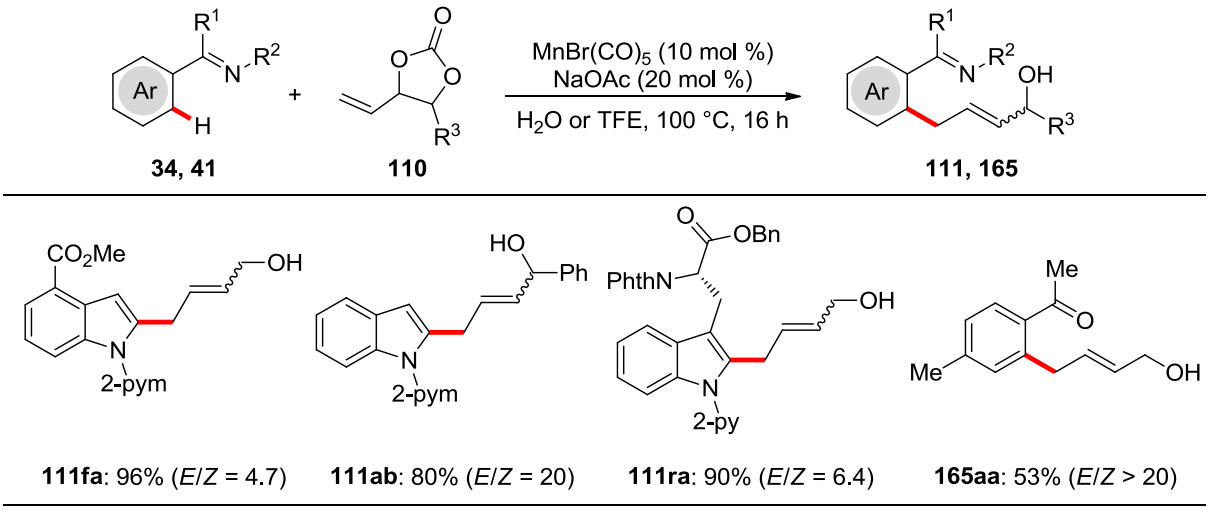
In the fourth project, a cobalt(III)-catalyzed domino C–H/N–H allylation reaction of aryl imidates with dioxolanones was accomplished (Scheme 3.8.4). The reaction was performed under mild reaction conditions with water and generated CO_2 as the only byproducts. This step-economic method using an earth-abundant cobalt catalyst provided expedient access to decorated vinyl 3,4-dihydroisoquinolines, which could not be obtained using a rhodium catalysis.[181] Aryl-substituted imidates bearing various electron-donating and electron-withdrawing groups are compatible with the reaction conditions, delivering the cyclization products **164** in good yields with high levels of regio-selectivity. Furthermore, the obtained product **164** could be easily transformed to dihydroisoquinolone **191** and acetylated isoquinoline **192**.



Scheme 3.8.4 Cobalt(III)-catalyzed domino C–H/N–H allylation.

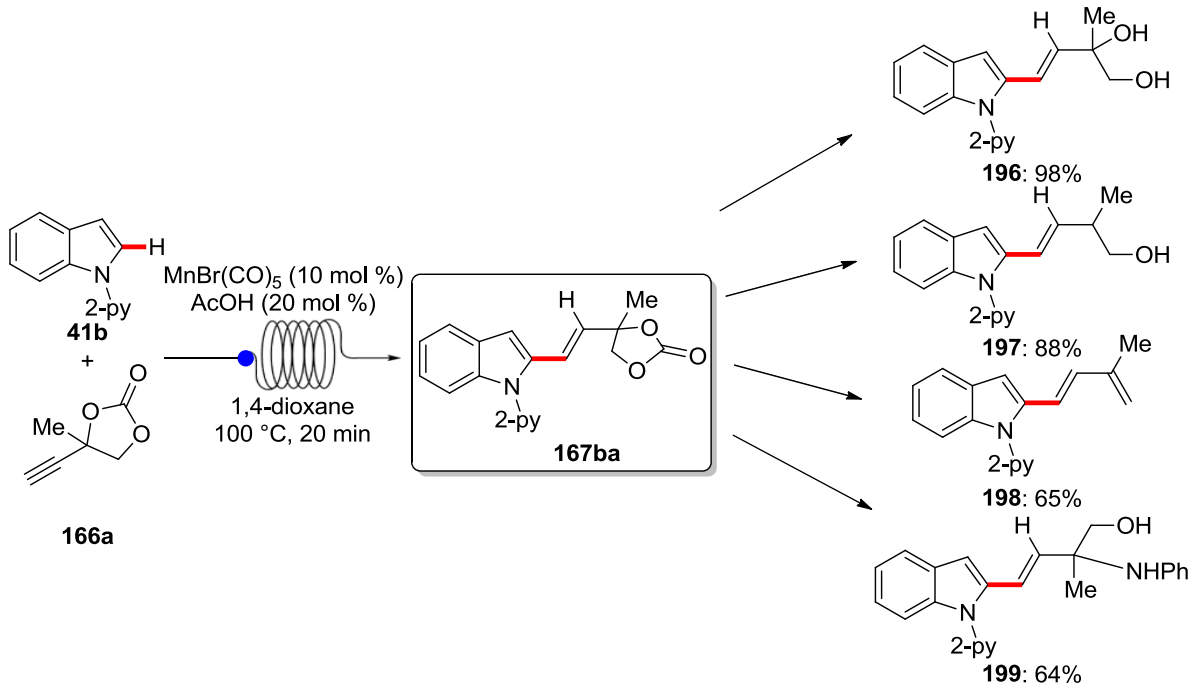
In the fifth project, a manganese(I)-catalyzed decarboxylative C–H/N–O allylation in water was

developed (Scheme 3.8.5). When indole substrates were employed, the reaction features a broad substrate scope and good functional group tolerance. This organometallic C–H activation was also tolerant to air and water. The organomanganese intermediate **193** could be isolated and showed high catalytic efficiency in both catalytic and stoichiometric experiments. The detailed mechanistic findings including competition experiments, H/D exchange and KIE studies strongly support a facile and reversible C–H metalation step. At last, this versatile C–H allylation was also successfully applied to the amino acids and aryl ketimines, delivering the allylation products in good yields with high levels of chemo- and regio-selectivities.



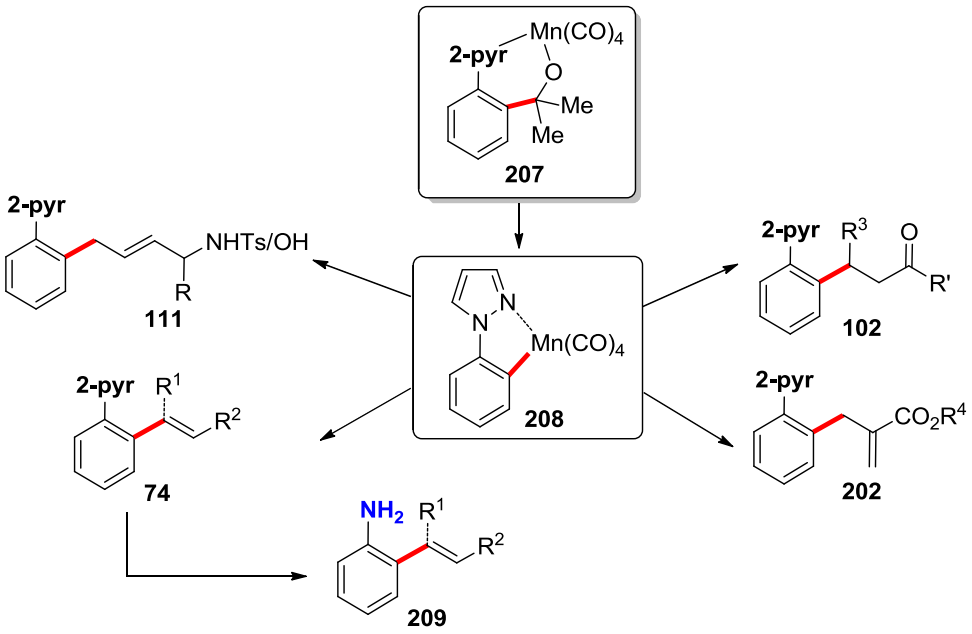
Scheme 3.8.5 Manganese(I)-catalyzed decarboxylative C–H/N–O functionalization.

In the sixth project, a synergistic Brønsted acid/manganese(I)-catalyzed C–H hydroarylation with high chemo- and regio-selectivities in continuous flow was accomplished (Scheme 3.8.6). With the assistance of carboxylic acid, the undesired β-O elimination could be avoided and provided a robust access to allylic carbonates in high yields with excellent chemo- and regio-selectivities. Moreover, this catalytic system tolerated a variety of valuable functional groups, including chloro, bromo, iodo, ether, carboxylic acid, and ester. The first manganese(I)-catalyzed C–H activation in continuous flow could be conducted within only 20 minutes under an atmosphere of air. Mechanistic findings indicated that a fast organometallic C–H metalation step, as well as an intramolecular proton transfer were involved.[152] Furthermore, late-stage diversification of the allylic carbonates **167ba** could be achieved, giving rise to a plethora of valuable building blocks.



Scheme 3.8.6 Synergistic manganese(I)-catalyzed C–H hydroarylation in continuous flow.

In the last project, we have developed versatile C–C activations in water by inexpensive and Earth-abundant manganese catalysis (Scheme 3.8.7). The organometallic C–C functionalizations, including C–C allylations, C–C alkenylations, and C–C alkylations, occurred efficiently in environmentally-benign solvent with excellent levels of chemo-, regio-, and position-selectivities. The unique manganese(I)-catalyzed C–C activation was characterized by a broad substrate scopes, functional group tolerance and position-selective synthesis. Competition and H/D exchange experiments clearly showed that the C–C cleavage is much faster than the C–H activation under the optimal condition. This result was showcased by the synthesis of 1,2,3-*tri*-substituted arenes, which could not be achieved by C–H activation. Importantly, the pyrazole group could be easily removed, furnishing the synthetically useful anilines **209**.



Scheme 3.8.7 Manganese(I)-catalyzed C–C functionalizations in water.

5 Experimental Section

5.1 General Remarks

The catalysis in water or under an atmosphere of air use the sealed tubes or Schlenk tubes. Unless otherwise noted, other reactions were performed under N_2 atmosphere using pre-dried glassware and standard Schlenk techniques.

If not otherwise noted, yields refer to isolated compounds, estimated to be >95% pure as determined by ^{1}H-NMR.

Vacuum

The following pressures were measured on the used vacuum pump and were not corrected: membrane pump vacuum (MPV): 0.5 mbar, oil pump vacuum (OPV): 0.1 mbar.

Melting Points (M.p.)

Melting points were measured using a *Stuart®* Melting Point Apparatus *SMP3* from BARLOWORLD SCIENTIFIC. The reported values are uncorrected.

CO_2

The CO_2 was detected and quantified by a GM5-KONT instrument from MesSen Nord.

Chromatography

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60F-plates (MACHEREY-NAGEL) with 254 nm fluorescent indicator from MERCK. Plates were visualized under UV-light or developed by treatment with a $KMnO_4$ solution followed by careful applying a heat gun. Chromatographic purification of products was accomplished by flash column chromatography on MERCK silica gel, grade 60 (0.040–0.063 mm and 0.063–0.200 mm).

Gas Chromatograpgy (GC)

The conversion of the reactions was monitored applying coupled gas chromatography/mass spectrometry using G1760C GCDplus with mass detector *HP 5971*, *5890 Series II* with mass detector *HP 5972* from HEWLETT-PACKARD and 7890A *GC-System* with mass detector *5975C (Triplex-Axis-Detector)* from AGILENT TECHNOLOGIES equipped with *HP-5MS* columns (30 m × 0.25 mm × 0.25 m) were used.

Gel permeation chromatography (GPC)

GPC purifications were performed on a JAI system (JAI-*LC-9260 II NEXT*) equipped with two sequential columns (*JAIGEL-2HR*, gradient rate: 5.000; *JAIGEL-2.5HR*, gradient rate: 20.000; internal diameter = 20 mm; length = 600 mm; Flush rate = 10.0 mL/min and chloroform (HPLC-quality with 0.6% ethanol as stabilizer) was used as the eluent.

Infrared Spectroscopy

Infrared spectra were recorded at a BRUKER *Alpha-P ATR FT-IR* spectrometer. Liquid samples were measured as a film, solid samples neat. The analysis of the spectra was carried out using the software from BRUKER *OPUS 6*. The absorption is given in wave numbers (cm^{-1}) and the spectra were recorded in the range of 4000–400 cm^{-1}. *In situ*-IR studies were performed on METTLER TOLEDO *ReactIR™ 15* with an *iC IR 4.3* software.

Mass Spectrometry

Electron ionization (EI) and EI high resolution mass spectra (HR-MS) were measured on a *time-of-flight* mass spectrometer *AccuTOF* from JOEL. Electrospray ionization (ESI) mass spectra were recorded on an *Ion-Trap* mass spectrometer *LCQ* from FINNIGAN, a *quadrupole time-of-flight maXis* from BRUKER DALTONIC or on a *time-of-flight mass* spectrometer microTOF from BRUKER DALTONIC. ESI-HRMS spectra were recorded on a BRUKER *Apex IV* or a BRUKER *Daltonic 7T*, fourier transform ion cyclotron resonance (FTICR) mass spectrometer. The ratios of mass to charge (*m*/*z*) are indicated and intensities relative to the base peak (*I* = 100) are written in parentheses.

Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance (NMR) spectra were recorded on VARIAN *Inova 500*, *600*, VARIAN *Mercury 300*, *VX 300*, VARIAN *Avance 300*, VARIAN *VNMRS 300* and BRUKER *Avance III 300*, *400* and *HD 500* spectrometers. All chemical shifts are given as *δ*-values in ppm relative to the residual proton peak of the deuterated solvent or its carbon atom, respectively. ^{1}H and ^{13}C NMR spectra were referenced using the residual proton or solvent carbon peak (see table), respectively. ^{13}C and ^{19}F NMR were measured as proton-decoupled spectra.

	^{1}H-NMR	^{13}C-NMR
$CDCl_3$	7.26	77.16
$[D]_6$-DMSO	2.50	39.52

The observed resonance-multiplicities were described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), hept (heptet), m (multiplet) or analogous representations. The coupling constants *J* are reported in Hertz (Hz). Analysis of the recorded spectra was carried out with *MestReNova 10* software.

Solvents

All solvents for reactions involving moisture-sensitive reagents were dried, distilled and stored under an inert atmosphere (Ar or N_2) according to the following standard procedures.

1,2-Dichloroethane (**DCE**), ***N*,*N*-dimethylformamide** (**DMF**) and ***γ*-Valerolactone** (**GVL**) were dried over CaH_2 for 8 h, degassed and distilled under reduced pressure.

1,1,1,3,3,3-Hexafluoropropan-2-ol (**HFIP**) and **Chlorobenzene** (**PhCl**) were distilled from 3 Å molecular sieves.

Methanol (**MeOH**) was stirred over magnesium turnings at 65 °C for 3 h prior to distillation from $Mg(OMe)_2$.

Toluene (**PhMe**), **Tetrahydrofuran** (**THF**), **Dichloromethane** (**DCM**) and **ethyl ether** (**Et_2O**) were purified using a solvent purification system (*SPS-800*) from M. BRAUN.

Acetonitrile (**MeCN**) was dried over P_2O_5 for 24 h degassed and distilled under reduced pressure.

2,2,2-Trifluoroethanol (**TFE**) was stirred over $CaSO_4$ and distilled under reduced pressure.

Water (**H_2O**) was degassed by repeated *Freeze-Pump-Thaw* degassing procedure.

1,4-Dioxane and **Di-(*n*-butyl)-ether** (***n*Bu$_2$O**) were distilled from sodium benzophenone ketyl.

Reagents

Chemicals obtained from commercial sources with purity above 95% were used without further purification. The following compounds are known and were synthesized according to previously described methods:

Cp*CoI$_2$(CO),[56] *O*-acyloximes **158a-158n**,[182] [D]$_1$-**158a**,[113] [D]$_5$-**158a**, alkynes **8b**-**8j,**[183] (*E*)-1-{2-[(*E*)-1,2-diphenylvinyl]phenyl}ethanone *O*-acetyl oxime **158u**.[184] , nitrones **159**,[185] aryl alkyl alkynes **8p-8r**.[186] [Cp*Co(CH$_3$CN)$_3$](PF$_6$)$_2$, [Cp*Co(CH$_3$CN)$_3$](BF$_4$)$_2$, and [Cp*Co(MeCN)$_3$][SbF$_6$]$_2$,[136a] Benzimidates **161a-161n**,[187] dioxazolones **162a-162k**,[188] substrates **41a**,[57, 189] **41b**-**41e**,[190] **20a**,[191] **110b**-**110f**,[192] **168a**-**168g**,[135] **110g**,[137] and complex **193.**[193]

The following compounds were obtained by the generous courtesy of the following persons:

M. Sc. Julian Koeller: (*E*)-1-(2-[(*E*)-1,2-diphenylvinyl)phenyl]ethanone *O*-acetyl oxime **158u**.

Dr. Mélanie M. Lorion: 3-tosyl-5-vinyloxazolidin-2-one **110g**.

Dr. Weiping Liu: (*E*)-*N*-[1-(4-fluorophenyl) ethylidene]-4-methoxyaniline **34d**, (*E*)-*N*-{1-[(1,1'-biphenyl)-4-yl]ethylidene}-4- methoxyaniline **34b**.

M. Sc. Issac Choi: [2-(1*H*-pyrazol-1-yl)phenyl)(phenyl)methanol **200a**.

M. Sc. Nikolaos Kaplaneris: methyl 2-{[(tert-butoxycarbonyl)oxy]methyl}acrylate **201**.

5.2 General Procedures

General Procedure A: Cobalt(III)–Catalyzed C–H/N–O Functionalization for the Synthesis of Isoquinolines 119

A suspension of *O*-acetyl oxime **158** (0.50 mmol, 1.0 equiv), alkynes **8** (0.75 mmol, 1.5 equiv), Cp*CoI_2(CO) (24.0 mg, 10.0 mol %), $AgSbF_6$ (34.4 mg, 20.0 mol %) and NaOAc (8.2 mg, 20.0 mol %) in DCE (2.0 mL) was stirred at 120 °C for 15 min or 16 h under air. After cooling to ambient temperature, the solvent was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel to afford the desired products **119**.

General Procedure B: Cobalt(III)–Catalyzed C–H/N–O Functionalization for the Synthesis of Indoles 160

A suspension of nitrone **159** (0.50 mmol, 1.0 equiv), alkyne **8** (0.75 mmol, 1.5 equiv), Cp*CoI_2(CO) (12.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20.0 mol %), NaOAc (8.2 mg, 20.0 mol %) or Piv-Leu-OH (22.1 mg, 20.0 mol %) was stirred at 100 °C for 16 h under air. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel and optionally by GPC afforded the desired products **160**.

General Procedure C: Cobalt(III)–Catalyzed C–H Functionalization for the Synthesis of Quinazolines 163

A suspension of benzimidates **161** (0.25 mmol, 1.0 equiv), dioxazolones **162** (0.30 mmol, 1.2 equiv), [Cp*Co(CH_3CN)$_3$](SbF_6)$_2$ (**180**) (6.9 mg, 5.0 mol %) in DCE (1.0 mL) was stirred at 100 ˚C for 13 h under air. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel afforded the desired products **163**.

General Procedure D: Cobalt-Catalyzed C–H/N–H Activation for the Synthesis of Vinyl-Substituted Dihydroisoquinolines 164

A suspension of benzimidates **161** (0.25 mmol, 1.0 equiv), dioxolanone **110** (0.75 mmol, 3.0 equiv), NaOAc (8.2 mg, 40.0 mol %), BPh_3 (24.2 mg, 40.0 mol %), $[Cp^*Co(CH_3CN)_3](PF_6)_2$ (7.6 mg, 5.0 mol %) in HFIP (1.0 mL) was stirred at 55 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel afforded the desired products **164**.

General Procedure E: Manganese(I)-Catalyzed C–H/C–O Activation with Heteroarenes

A suspension of heteroarenes **41** (0.25 mmol, 1.0 equiv), dioxolanones **110** (0.75 mmol, 3.0 equiv), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) and NaOAc (4.1 mg, 20.0 mol %) in H_2O or TFE (1.0 mL) was stirred at 100 °C for 16 h under air (or under N_2 when specified). After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel afforded the desired products **111**.

General Procedure F: Manganese(I)-Catalyzed C–H/C–O Activation with Ketimines 34

A suspension of ketimines **34** (0.25 mmol, 1.0 equiv), dioxolanones **110** (0.75 mmol, 3.0 equiv), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) and NaOAc (4.1 mg, 20.0 mol %) in TFE (1.0 mL) was stirred at 100 °C for 16 h under N_2. After cooling to ambient temperature, HCl (2 N, 3.0 mL) was added. The resulting mixture was stirred for 30 min at 25 °C and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded the desired products **165**.

General procedure G: Manganese(I)-Catalyzed C–H Hydroarylation in Flow

A 10 mL oven-dried volumetric flask was charged with heteroarenes **41** (0.25 mmol, 1.0 equiv), propargylic alkynes **166** (0.50 mmol, 2.0 equiv), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %), HOAc (2.8 µL, 20.0 mol %) and 1,4-dioxane (1.0 mL) under air. Subsequently, the solution was connected to the inlet of the 10 mL standard heated reactor by a syringe pump (Vapourtec V-3). The syringe pump was operated at a flow rate of 500 µL / min (20 min residence time). The back pressure was set up around 8.0 bar and the temperature of the standard heated reactor was set at 100 °C. Using the Flow Wizard system, the solution was collected automatically. Next, the mixture was concentrated

in *vacuo*. Purification by column chromatography on silica gel afforded the desired products **167**.

General Procedure H: Manganese(I)-Catalyzed C–C Allylation with Dioxolanones 110

A suspension of heteroarenes **168** (0.25 mmol, 1.0 equiv), dioxolanones **110** (0.50 mmol, 2.0 equiv), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded the desired products **111**.

General Procedure I: Manganese(I)-Catalyzed C–C Alkenylation with Alkynes 8

A suspension of heteroarenes **168** (0.25 mmol, 1.0 equiv), alkynes **8** (0.50 mmol, 2.0 equiv), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 140 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded the desired products **74**.

General procedure J: Manganese(I)-Catalyzed C–C Alkylation with Alkenes 11

A suspension of heteroarenes **168** (0.25 mmol, 1.0 equiv), alkenes **11** (0.50 mmol, 2.0 equiv), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded the desired products **102**.

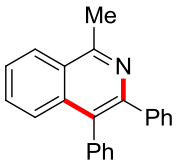
General procedure K: Manganese(I)-Catalyzed C–C Allylation with Morita-Baylis-Hillman Adducts 201

A suspension of heteroarenes **168** (0.25 mmol, 1.0 equiv), Morita-Baylis-Hillman adducts **201** (0.50 mmol, 2.0 equiv), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel afforded the desired products **202**.

5.3 Experimental and Analytical Data

5.3.1 Data for Cobalt(III)-Catalyzed C–H/N–O Functionalizations: Isohypsic Access to Isoquinolines

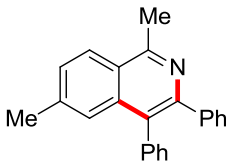
Characterization Data



1-Methyl-3,4-diphenylisoquinoline (119aa): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 25/1 → 20/1) yielded **119aa** (129 mg, 87%) as a pale yellow solid.

M.p. = 153−155 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.23–8.19 (m, 1H), 7.71–7.67 (m, 1H), 7.62–7.57 (m, 2H), 7.42–7.31 (m, 5H), 7.27–7.16 (m, 5H), 3.10 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.7 (C_q), 149.4 (C_q), 141.0 (C_q), 137.6 (C_q), 136.0 (C_q), 131.4 (CH), 130.2 (CH), 130.0 (CH), 129.1 (C_q), 128.2 (CH), 127.6 (CH), 127.1 (CH), 126.9 (CH), 126.5 (CH), 126.2 (CH), 126.1 (C_q), 125.5 (CH), 22.7 (CH_3). **IR** (ATR) ν = 1567, 1389, 1334, 1072, 1026, 765, 695, 612, 563, 496 cm^{-1}. **MS** (ESI) m/z (relative intensity): 296 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{18}N$ $[M+H]^+$: 296.1434, found: 296.1434.

The analytical data were in accordance with those reported in the literature.[109c]

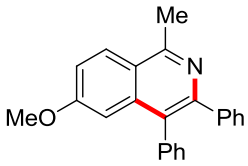


1,6-Dimethyl-3,4-diphenylisoquinoline (119ba): The general procedure **A** was followed using (*E*)-1-(*p*-tolyl)ethanone *O*-acetyl oxime (**158b**) (96 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ba** (94 mg, 61%) as a white solid.

M.p. = 168−169 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.9 Hz, 1H), 7.43–7.39 (m, 2H), 7.37–7.30 (m, 5H), 7.23–7.14 (m, 5H), 3.04 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.3 (C_q), 149.6 (C_q), 141.2 (C_q), 140.1 (C_q), 137.7 (C_q), 136.2 (C_q), 131.4 (CH), 130.2 (CH), 128.7 (C_q), 128.6 (CH),

128.1 (CH), 127.5 (CH), 127.0 (CH), 126.8 (CH), 125.4 (CH), 125.0 (CH), 124.5 (C_q), 22.6 (CH_3), 22.1 (CH_3). **IR** (ATR) *v* = 3061, 2917, 1621, 1566, 1493, 1384, 1335, 1070, 1028, 796, 696, 612 cm^{-1}. **MS** (ESI) m/z (relative intensity): 310 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{20}N$ $[M+H]^+$: 310.1590, found: 310.1593.

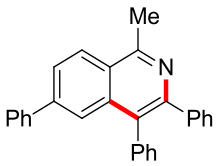
The analytical data were in accordance with those reported in the literature.[109c]



6-Methoxy-1-methyl-3,4-diphenylisoquinoline (119ca): The general procedure **A** was followed using (*E*)-1-(4-methoxyphenyl)ethanone *O*-acetyl oxime (**158c**) (104 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1 → 10/1) yielded **119ca** (141 mg, 87%) as a pale yellow solid.

M.p. = 180−182 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.11 (dd, *J* = 9.2, 0.5 Hz, 1H), 7.37–7.27 (m, 5H), 7.25–7.12 (m, 6H), 6.92 (d, *J* = 2.5 Hz, 1H), 3.73 (s, 3H), 3.02 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 160.7 (C_q), 157.1 (C_q), 150.3 (C_q), 141.4 (C_q), 138.2 (C_q), 138.1 (C_q), 131.5 (CH), 130.4 (CH), 128.7 (C_q), 128.4 (CH), 127.7 (CH), 127.6 (CH), 127.2 (CH), 127.0 (CH), 122.0 (C_q), 118.8 (CH), 104.7 (CH), 55.4 (CH_3), 22.8 (CH_3). **IR** (ATR) *v* = 3059, 1500, 1410, 1273, 1229, 1205, 1070, 1024, 853, 696 cm^{-1}. **MS** (ESI) m/z (relative intensity): 326 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{20}NO$ $[M+H]^+$: 326.1539, found: 326.1538.

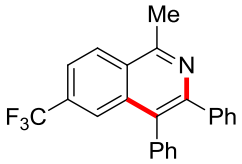
The analytical data were in accordance with those reported in the literature.[194]



1-Methyl-3,4,6-triphenylisoquinoline (119da): The general procedure **A** was followed using (*E*)-1-[(1,1'-biphenyl)-4-yl]ethanone *O*-acetyl oxime (**158d**) (127 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119da** (154 mg, 83%) as a pale yellow solid.

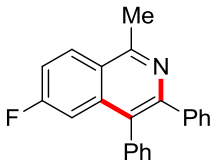
M.p. = 178−179 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.27 (dd, *J* = 8.7, 0.7 Hz, 1H), 7.89 (dd, *J* = 1.8, 0.7

Hz, 1H), 7.85 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.59–7.55 (m, 2H), 7.46–7.39 (m, 4H), 7.39–7.32 (m, 4H), 7.31–7.27 (m, 2H), 7.25–7.18 (m, 3H), 3.11 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.5 (C_q), 149.9 (C_q), 142.4 (C_q), 141.0 (C_q), 140.4 (C_q), 137.5 (C_q), 136.3 (C_q), 131.4 (CH), 130.2 (CH), 129.3 (C_q), 128.8 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 127.4 (CH), 127.1 (CH), 127.0 (CH), 126.9 (CH), 126.1 (CH), 125.1 (C_q), 123.9 (CH), 22.7 (CH_3). **IR** (ATR) *v* = 3058, 3025, 1611, 1567, 1434, 1340, 1158, 1073, 1029, 955, 894, 760, 751, 691, 611 cm^{-1}. **MS** (ESI) m/z (relative intensity): 372 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{28}H_{22}N$ $[M+H]^+$: 372.1747, found: 372.1751.



6-(Trifluoromethyl)-1-methyl-3,4-diphenylisoquinoline (119ea): The general procedure **A** was followed using (*E*)-1-(4-(trifluoromethyl)phenyl)ethanone *O*-acetyl oxime (**158e**) (123 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 30:1 → 20:1 → 15:1) yielded **119ea** (173 mg, 95%) as a pale yellow solid. **M.p.** = 112−113 °C. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ = 8.33 (dt, *J* = 8.7, 0.8 Hz, 1H), 7.98–7.97 (m, 1H), 7.76 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.41–7.34 (m, 5H), 7.25–7.18 (m, 5H), 3.12 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.0 (C_q), 151.1 (C_q), 140.6 (C_q), 136.6 (C_q), 135.6 (C_q), 131.5 (q, $^{2}J_{C-F}$ = 32 Hz, C_q), 131.4 (CH), 130.4 (CH), 129.9 (C_q), 128.7 (CH), 127.9 (CH), 127.8 (CH), 127.5 (CH), 127.1 (C_q), 127.0 (CH), 124.0 (q, $^{3}J_{C-F}$ = 5 Hz, CH), 123.8 (q, $^{1}J_{C-F}$ = 273 Hz, C_q), 122.2 (q, $^{4}J_{C-F}$ = 3 Hz, CH), 23.0 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = −63.3 (s). **IR** (ATR) *v* = 2958, 1555, 1336, 1305, 1177, 1156, 1135, 1082, 909, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{16}F_3N$ $[M+H]^+$: 364.1308, found: 364.1315.

The analytical data were in accordance with those reported in the literature.[109c]

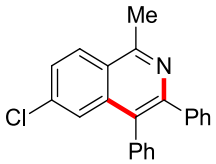


6-Fluoro-1-methyl-3,4-diphenylisoquinoline (119fa): The general procedure **A** was followed using 6-fluoro-1-methyl-3,4-diphenylisoquinoline (**158f**) (98 mg, 0.50 mmol) and diphenylacetylene (**8a**)

(134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30:1 → 20:1) yielded **119fa** (147 mg, 94%) as a pale yellow solid.

M.p. = 139−140 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.22 (ddd, *J* = 9.2, 5.7, 0.5 Hz, 1H), 7.39–7.31 (m, 6H), 7.28–7.25 (m, 1H), 7.23–7.15 (m, 5H), 3.06 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 163.3 (d, $^{1}J_{C-F}$ = 251 Hz, C_q), 157.7 (C_q), 150.6 (C_q), 140.8 (C_q), 138.2 (d, $^{3}J_{C-F}$ = 10 Hz, C_q), 137.3 (C_q), 131.4 (CH), 130.4 (CH), 129.1 (d, $^{4}J_{C-F}$ = 5.2 Hz, C_q), 128.8 (d, $^{3}J_{C-F}$ = 10 Hz, CH), 128.6 (CH), 127.8 (CH), 127.5 (CH), 127.3 (CH), 123.6 (C_q), 116.8 (d, $^{2}J_{C-F}$ = 25.2 Hz, CH), 110.0 (d, $^{2}J_{C-F}$ = 22.2 Hz, CH), 23.0 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = −108.0 (ddd, *J* = 10.9, 8.0, 5.6 Hz). **IR** (ATR) *v* = 1623, 1571, 1504, 1398, 1260, 1183, 874, 830, 704 cm^{-1}. **MS** (ESI) m/z (relative intensity): 314 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{17}N_{19}F$ $[M+H]^+$: 314.1340, found: 314.1339.

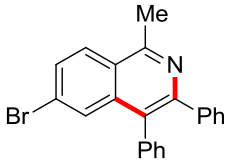
The analytical data were in accordance with those reported in the literature.[195]



6-Chloro-1-methyl-3,4-diphenylisoquinoline (119ga): The general procedure **A** was followed using (*E*)-1-(4-chlorophenyl)ethanone *O*-acetyl oxime (**158g**) (106 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ga** (156 mg, 94%) as a pale yellow solid.

M.p. = 177−178 °C. **^{1}H-NMR** (500 MHz, $CDCl_3$): δ = 8.11 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.64 (dd, *J* = 2.2, 0.5 Hz, 1H), 7.51 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.39–7.32 (m, 5H), 7.22–7.17 (m, 5H), 3.04 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.6 (C_q), 150.5 (C_q), 140.6 (C_q), 137.0 (C_q), 136.8 (C_q), 136.3 (C_q), 131.2 (CH), 130.1 (CH), 128.4 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 127.3 (CH), 127.1 (CH), 125.0 (CH), 124.3 (C_q), 22.7 (CH_3). **IR** (ATR) *v* = 3064, 3026, 1602, 1548, 1493, 1446, 1386, 1329, 1098, 957, 752, 698, 626 cm^{-1}. **MS** (ESI) m/z (relative intensity): 330 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{17}ClN$ $[M+H]^+$: 330.1044, found: 330.1043.

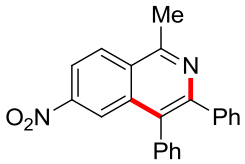
The analytical data were in accordance with those reported in the literature.[195]



6-Bromo-1-methyl-3,4-diphenylisoquinoline (119ha): The general procedure **A** was followed using (*E*)-1-(4-bromophenyl)ethanone *O*-acetyl oxime (**158h**) (128 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 20/1 → 10/1) yielded **119ha** (154 mg, 82%) as a slightly yellow solid.

M.p. = 193−195 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.06 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.81 (d, *J* = 2.0 Hz, 1H), 7.67 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.39–7.32 (m, 5H), 7.22–7.15 (m, 5H), 3.05 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.6 (C_q), 150.5 (C_q), 140.6 (C_q), 137.4 (C_q), 136.8 (C_q), 131.2 (CH), 130.3 (CH), 130.1 (CH), 128.4 (CH), 128.4 (CH) 128.3 (C_q), 127.6 (CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 125.0 (C_q), 124.3 (C_q), 22.7 (CH_3). **IR** (ATR) *v* = 3064, 1597, 1561, 1481, 1445, 1386, 1329, 1071, 1029, 697 cm^{-1}. **MS** (ESI) m/z (relative intensity): 374 (100) $[M+H]^+$, 296 (55). **HR-MS** (ESI) m/z calcd for $C_{22}H_{17}BrN$ $[M+H]^+$: 374.0539, found: 374.0539.

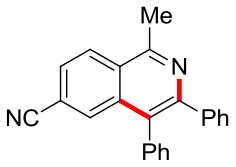
The analytical data were in accordance with those reported in the literature.[109c]



1-Methyl-6-nitro-3,4-diphenylisoquinoline (119ia): The general procedure **A** was followed using (*E*)-1-(4-nitrophenyl)ethanone *O*-acetyl oxime (**158i**) (111 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 10:1→ 8:1 → 5:1) yielded **119ia** (80 mg, 47%) as a yellow solid.

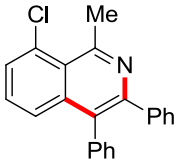
M.p. = 170−173 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.59 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.35 (d, *J* = 0.8 Hz, 1H), 8.33 (d, *J* = 2.1 Hz, 1H), 7.50–7.29 (m, 5H), 7.26–7.18 (m, 5H), 3.14 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.2 (C_q), 151.8 (C_q), 148.4 (C_q), 140.1 (C_q), 136.1 (C_q), 136.0 (C_q), 131.3 (CH), 130.6 (C_q), 130.3 (CH), 128.9 (CH), 128.2 (CH), 127.9 (C_q), 127.9 (CH), 127.8 (CH), 127.7 (CH), 122.9 (CH), 120.0 (CH), 23.1 (CH_3). **IR** (ATR) *v* = 1531, 1343, 1326, 1312, 902, 832, 767, 738, 698, 623 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 341 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_2O_2$ $[M+H]^+$: 341.1285, found: 341.1285.

The analytical data were in accordance with those reported in the literature.[194]



1-Methyl-3,4-diphenylisoquinoline-6-carbonitrile (119ja): The general procedure **A** was followed using (*E*)-4-(1-(acetoxyimino)ethyl)benzonitrile (**158j**) (101 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 10/1) yielded **119ja** (144 mg, 90%) as a pale yellow solid.

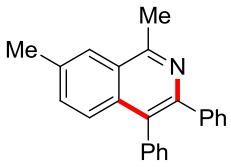
M.p. = 171–172 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.27 (dd, *J* = 8.6, 0.7 Hz, 1H), 8.03 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.71 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.41–7.32 (m, 5H), 7.22–7.15 (m, 5H), 3.08 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.0 (C_q), 151.3 (C_q), 140.1 (C_q), 136.1 (C_q), 135.5 (C_q), 132.5 (CH), 131.2 (CH), 130.2 (CH), 129.0 (C_q), 128.6 (CH), 127.9 (CH), 127.8 (CH), 127.5 (CH), 127.1 (CH), 126.9 (CH), 126.7 (C_q), 118.5 (C_q), 113.5 (C_q), 22.7 (CH_3). **IR** (ATR) *v* = 3067, 2229, 1612, 1564, 1493, 1441, 1385, 1330, 900, 823, 799, 696, 608 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 321 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{17}N_2$ $[M+H]^+$: 321.1392, found: 321.1386.



8-Chloro-1-methyl-3,4-diphenylisoquinoline (119ka): The general procedure **A** was followed using (*E*)-1-(2-chlorophenyl)ethanone *O*-acetyl oxime (**158k**) (106 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 60/1 → 30/1) yielded **119ka** (106 mg, 64%) as a pale green solid.

M.p. = 139–141 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.56 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.39–7.31 (m, 6H), 7.22–7.15 (m, 5H), 3.39 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 157.1 (C_q), 149.3 (C_q), 140.2 (C_q), 139.2 (C_q), 137.5 (C_q), 132.2 (C_q), 131.3 (CH), 130.1 (CH), 129.5 (CH), 129.2 (CH), 129.0 (C_q), 128.3 (CH), 127.6 (CH), 127.3 (CH), 127.2 (CH), 125.8 (CH), 124.5 (C_q), 29.9 (CH_3). **IR** (ATR) *v* = 3022, 1601, 1432, 1382, 1260, 1087, 1027, 819, 787, 762, 695, 572 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 330 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}ClN$ $[M+H]^+$: 330.1050, found:

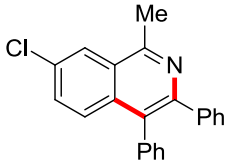
330.1044.



1,7-Dimethyl-3,4-diphenylisoquinoline (119la): The general procedure **A** was followed using (*E*)-1-(m-tolyl)ethanone *O*-acetyl oxime (**158l**) (96 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1→ 20:1) yielded **119la** (82 mg, 53%) as a pale yellow solid.

M.p. = 132−134 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.95 (t, *J* = 2.0 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.41 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.38–7.26 (m, 5H), 7.24–7.10 (m, 5H), 3.05 (s, 3H), 2.57 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 157.0 (C_q), 148.6 (C_q), 141.1 (C_q), 137.7 (C_q), 136.3 (C_q), 134.1 (C_q), 132.0 (CH), 131.4 (CH), 130.2 (CH), 129.0 (C_q), 128.1 (CH), 127.5 (CH), 127.0 (CH), 126.7 (CH), 126.3 (C_q), 126.1 (CH), 124.5 (CH), 22.7 (CH_3), 21.8 (CH_3). **IR** (ATR) *v* = 3055, 3023, 2916, 1553, 1505, 1443, 1387, 1322, 1073, 1028, 905, 831, 767, 699 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 310 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N$ $[M+H]^+$: 310.1590, found: 310.1588.

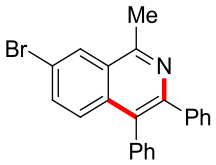
The analytical data were in accordance with those reported in the literature.[109c]



7-Chloro-1-methyl-3,4-diphenylisoquinoline (119ma): The general procedure **A** was followed using (*E*)-1-(3-chlorophenyl)ethanone *O*-acetyl oxime (**158m**) (106 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1 → 15/1) yielded **119ma** (115 mg, 70%) as an off-white solid.

M.p. = 145−147 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 2.2, 0.6 Hz, 1H), 7.61 (dd, *J* = 9.0, 0.6 Hz, 1H), 7.51 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.38–7.31 (m, 5H), 7.23–7.15 (m, 5H), 3.04 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.0 (C_q), 150.0 (C_q), 140.8 (C_q), 137.2 (C_q), 134.6 (C_q), 132.4 (C_q), 131.4 (CH), 130.8 (CH), 130.4 (CH), 129.2 (C_q), 128.5 (CH), 128.3 (CH), 127.8 (CH), 127.5 (CH), 127.3 (CH), 127.0 (C_q), 124.7 (CH), 22.9 (CH_3). **IR** (ATR) *v* = 2956, 1544, 1498, 1444, 1409, 880, 868, 794, 701, 568 cm^{-1}.

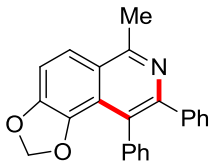
MS (ESI) *m/z* (relative intensity): 330 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}ClN$ $[M+H]^+$: 330.1044, found: 330.1048.



7-Bromo-1-methyl-3,4-diphenylisoquinoline (119na): The general procedure **A** was followed using (*E*)-1-(3-bromophenyl)ethanone *O*-acetyl oxime (**158n**) (128 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **119na** (142 mg, 76%) as a yellow solid.

M.p. = 133−135 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 2.0 Hz, 1H), 7.64 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.54 (d, *J* = 9.0 Hz, 1H), 7.39–7.31 (m, 5H), 7.24–7.16 (m, 5H), 3.04 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 156.9 (C_q), 150.0 (C_q), 140.7 (C_q), 137.1 (C_q), 134.8 (C_q), 133.4 (CH), 131.4 (CH), 130.3 (CH), 129.2 (C_q), 128.5 (CH), 128.4 (CH), 128.0 (CH), 127.8 (CH), 127.5 (CH), 127.4 (C_q), 127.3 (CH), 120.7 (C_q), 22.8 (CH_3). **IR** (ATR) *v* = 3052, 3023, 1544, 1496, 1434, 1407, 1380, 868, 766, 700 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 374 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}BrN$ $[M+H]^+$: 374.0539, found: 374.0541.

The analytical data were in accordance with those reported in the literature.[182]

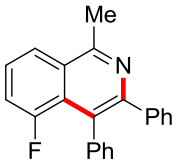


5,6-(Methylenedioxy)-1-methyl-3,4-diphenylisoquinoline (119oa): The general procedure **A** was followed using (*E*)-1-(benzo[d][1,3]dioxol-5-yl)ethanone *O*-acetyl oxime (**158o**) (111 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1 → 8/1 → 5/1) yielded **119oa** (76 mg, 45%) as a white solid.

M.p. = 250−253 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.8 Hz, 1H), 7.29–7.26 (m, 2H), 7.25–7.10 (m, 9H), 5.83 (s, 2H), 2.99 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.9 (C_q), 150.3 (C_q), 147.8 (C_q) 141.8 (C_q), 141.0 (C_q), 138.6 (C_q), 131.3 (CH), 130.3 (CH), 127.6 (CH), 127.2 (CH), 127.0 (CH), 126.9 (CH), 124.9 (C_q), 123.4 (C_q), 122.7 (C_q), 121.1 (CH), 111.0 (CH), 101.6 (CH_2), 23.6 (CH_3). **IR** (ATR)

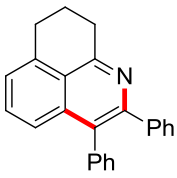
v = 1431, 1384, 1353, 1279, 1049, 1031, 794, 767, 698, 644 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 340 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{18}NO_2$ $[M+H]^+$: 340.1332, found: 340.1335.

The analytical data were in accordance with those reported in the literature.[109c]



5-Fluoro-1-methyl-3,4-diphenylisoquinoline (119pa): The general procedure **A** was followed using (*E*)-1-(3-fluorophenyl)ethanone *O*-acetyl oxime (**158p**) (98 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1→ 15:1) yielded **119pa** (130 mg, 83%) as a pale yellow solid.

M.p. = 123−125 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.01 (ddd, *J* = 8.4, 1.2, 0.5 Hz, 1H), 7.53 (ddd, *J* = 8.4, 7.7, 4.6 Hz, 1H), 7.32–7.12 (m, 11H), 3.08 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 159.0 (d, $^1J_{C-F}$ = 258 Hz, C_q), 157.4 (d, $^4J_{C-F}$ = 2 Hz, Cq), 151.4 (Cq), 140.71 (Cq), 139.3 (d, $^3J_{C-F}$ = 4 Hz, Cq), 130.4 (d, $^4J_{C-F}$ = 3 Hz, CH), 130.1 (CH), 128.0 (d, $^4J_{C-F}$ = 3 Hz, Cq), 127.3 (d, $^2J_{C-F}$ = 22 Hz, CH), 126.83 (CH), 126.76 (CH), 126.66 (CH), 125.9 (d, $^3J_{C-F}$ = 9 Hz, Cq), 125.6 (d, $^4J_{C-F}$ = 3 Hz, Cq), 121.8 (d, $^3J_{C-F}$ = 5 Hz, CH), 115.5 (d, $^2J_{C-F}$ = 22.1 Hz, CH), 23.21 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -105.64 (dd, *J* = 12.7, 4.5 Hz). **IR** (ATR) *v* = 3087, 3056, 1552, 1502, 1430, 1391, 1326, 1245, 1028, 904, 769 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 314.1 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}FN$ $[M+H]^+$: 314.1340, found: 314.1342.

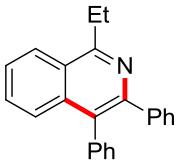


2,3-Diphenyl-8,9-dihydro-7*H*-benzo[*de*]quinolone (119qa): The general procedure **A** was followed using (*E*)-3,4-dihydronaphthalen-1(*2H*)-one *O*-acetyl oxime (**158q**) (102 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 20/1 → 15/1) yielded **119qa** (144 mg, 85%) as a light brown solid.

M.p. = 148−150 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.52–7.45 (m, 2H), 7.38–7.28 (m, 6H), 7.24–7.14 (m, 5H), 3.39 (t, *J* = 6.4 Hz, 2H), 3.21 (t, *J* = 6.2 Hz, 2H), 2.32–2.25 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$):

δ = 159.4 (C_q), 149.6 (C_q), 141.3 (C_q), 138.6 (C_q), 138.0 (C_q), 136.4 (C_q), 131.5 (CH), 130.4 (CH), 130.1 (CH), 129.2 (C_q), 128.3 (CH), 127.7 (CH), 127.2 (CH), 127.0 (CH) 124.9 (CH), 124.0 (C_q), 123.7 (CH), 35.0 (CH_2), 31.0 (CH_2), 23.6 (CH_2). **IR** (ATR) *v* = 2934, 1577, 1551, 1496, 1444, 1387, 1372, 765, 695, 625 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 322 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{20}N$ $[M+H]^+$: 322.1590, found: 322.1588.

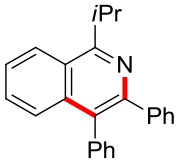
The analytical data were in accordance with those reported in the literature.[182]



1-Ethyl-3,4-diphenylisoquinoline (119ra): The general procedure **A** was followed using (*E*)-propiophenone *O*-acetyl oxime (**158r**) (96 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 20/1) yielded **119ra** (136 mg, 88%) as a colorless solid.

M.p. = 114−116 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.28–8.24 (m, 1H), 7.70–7.65 (m, 1H), 7.61–7.55 (m, 2H), 7.42–7.31 (m, 5H), 7.26–7.15 (m, 5H), 3.46 (q, *J* = 7.6 Hz, 2H), 1.55 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 162.4 (C_q), 149.4 (C_q), 141.3 (C_q), 137.9 (C_q), 136.5 (C_q), 131.5 (CH), 130.5 (CH), 129.8 (CH), 129.1 (C_q), 128.4 (CH), 127.7 (CH), 127.3 (CH), 127.0 (CH), 126.6 (CH), 125.4 (C_q), 125.3 (CH), 29.0 (CH_2), 14.1 (CH_3). **IR** (ATR) *v* = 3025, 2981, 2937, 1553, 1504, 1422, 1316, 762, 704, 597 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 310 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N$ $[M+H]^+$: 310.1590, found: 310.1597.

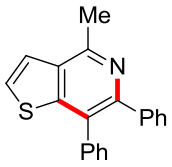
The analytical data were in accordance with those reported in the literature.[109c]



1-Isopropyl-3,4-diphenylisoquinoline (119sa): The general procedure **A** was followed using acetophenone *O*-acetyl oxime (**158s**) (103 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 20/1) yielded **119sa** (135 mg, 83%) as a colorless solid.

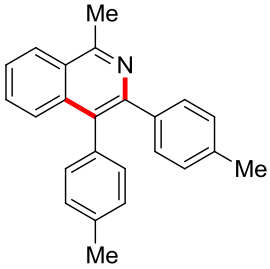
M.p. = 142−144 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.33–8.29 (m, 1H), 7.70–7.65 (m, 1H), 7.61–7.53 (m, 2H), 7.49–7.44 (m, 2H), 7.42–7.33 (m, 3H), 7.29–7.24 (m, 2H), 7.24–7.16 (m, 3H), 4.05 (sept, *J* = 6.8 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 165.1 (C_q), 148.7 (C_q), 141.4 (C_q), 138.3 (C_q), 136.7 (C_q), 131.6 (CH), 130.7 (CH), 129.5 (CH), 128.5 (C_q), 128.4 (CH), 127.5 (CH), 127.2 (CH), 127.0 (CH), 126.6 (CH), 126.4 (CH), 124.9 (C_q), 124.7 (CH), 31.5 (CH), 22.4 (CH_3). **IR** (ATR) *v* = 2969, 1551, 1381, 1032, 761, 703, 678, 633, 596, 569 cm^{-1}. **MS** (ESI) *m/z* (re:lative intensity): 324 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N$ $[M+H]^+$: 324.1747, found: 324.1748.

The analytical data were in accordance with those reported in the literature.[194]



4-Methyl-6,7-diphenylthieno[3,2-*c*]pyridine (119ta): The general procedure **A** was followed using (*E*)-1-(thiophen-3-yl)ethanone *O*-acetyl oxime (**158t**) (92 mg, 0.50 mmol) and diphenylacetylene (**8a**) (134 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 20/1) yielded **119ta** (127 mg, 72%) as a pale solid.

M.p. = 147–149 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 5.5 Hz, 1H), 7.45 (d, *J* = 5.5 Hz, 1H), 7.41–7.36 (m, 2H), 7.34–7.29 (m, 5H), 7.23–7.17 (m, 3H), 2.93 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 152.5 (C_q), 149.9 (C_q), 149.6 (C_q), 140.2 (C_q), 138.5 (C_q), 133.8 (C_q), 130.3 (CH), 129.7 (CH), 128.6 (CH), 127.71 (CH), 127.68 (CH), 127.64 (C_q), 127.60 (CH), 127.2 (CH), 122.5 (CH), 22.8 (CH_3). **IR** (ATR) *v* = 3060, 1544, 1414, 1387, 1073, 1028, 898, 754, 728, 696, 619 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 302 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{16}NS$ $[M+H]^+$: 302.1003, found: 302.0998.

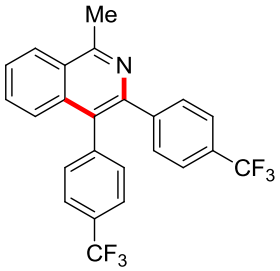


Methyl-3,4-di-p-tolylisoquinoline (119ab): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 1,2-di-p-tolylethyne (**8b**) (155 mg,

0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ab** (145 mg, 89%) as a pale yellow solid.

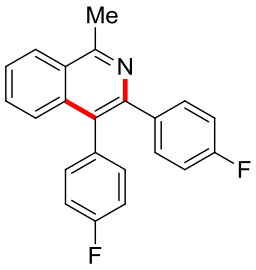
M.p. = 151−153 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.20–8.14 (m, 1H), 7.70–7.64 (m, 1H), 7.59–7.53 (m, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 3.07 (s, 3H), 2.40 (s, 3H), 2.29 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 157.3 (C_q), 149.3 (C_q), 138.2 (C_q), 136.5 (C_q), 136.4 (C_q), 136.2 (C_q), 134.6 (C_q), 131.1 (CH), 130.1 (CH), 129.6 (CH), 128.9 (CH), 128.8 (C_q), 128.3 (CH), 126.2 (CH), 126.0 (C_q), 125.4 (CH), 22.7 (CH_3), 21.2 (CH_3), 21.1 (CH_3). **IR** (ATR) *v* = 3024, 3000, 2918, 1607, 1569, 1546, 1510, 1430, 1389, 1370, 1329, 1261, 1182, 1106, 1022, 817, 756, 728, 595, 564 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 324 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N$ $[M+H]^+$: 324.1747, found: 324.1751.

The analytical data were in accordance with those reported in the literature.[195]



1-Methyl-3,4-bis(4-(trifluoromethyl)phenyl)isoquinoline (119ae): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 1,2-bis(4-(trifluoromethyl)phenyl)ethyne (**8e**) (236 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ae** (140 mg, 65%) as a pale yellow solid.

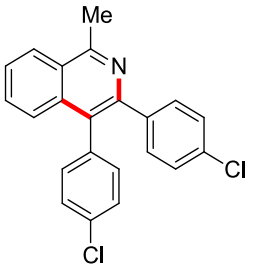
M.p. = 151–152 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.26–8.21 (m, 1H), 7.68–7.61 (m, 4H), 7.58–7.54 (m, 1H), 7.46 (m, 4H), 7.36 (d, *J* = 7.8 Hz, 2H), 3.08 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.9 (C_q), 148.0 (C_q), 144.1 (C_q), 141.1 (C_q), 135.4 (C_q), 131.7 (CH), 130.6 (CH), 130.5 (CH), 129.8 (q, $^{2}J_{C\text{-}F}$ = 32 Hz, C_q), 129.3 (q, $^{2}J_{C\text{-}F}$ = 32 Hz, C_q), 128.3 (C_q), 127.3 (CH), 126.4 (C_q), 125.8 (C_q), 125.4 (q, $^{3}J_{C\text{-}F}$ = 4 Hz, CH), 124.8 (q, $^{3}J_{C\text{-}F}$ = 4 Hz, CH), 124.0 (d, $^{1}J_{C\text{-}F}$ = 272 Hz, C_q), 124.0 (d, $^{1}J_{C\text{-}F}$ = 272 Hz, C_q), 22.74 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = 62.5, 62.6. **IR** (ATR) *v* = 3063, 2985, 1618, 1556, 1411, 1394, 1320, 1160, 1104, 1064, 1017, 951, 848, 834, cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 432 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{16}F_6N$ $[M+H]^+$: 432.1181, found: 432.1182.



3,4-Bis(4-fluorophenyl)-1-methylisoquinoline (119af): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 1,2-bis(4-fluorophenyl)ethyne (**8f**) (161 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119af** (111 mg, 67%) as a pale yellow solid.

M.p. = 138−140 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.23–8.14 (m, 1H), 7.65–7.55 (m, 3H), 7.37–7.28 (m, 2H), 7.21–7.13 (m, 2H), 7.11–7.01 (m, 2H), 6.95–6.86 (m, 2H), 3.05 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 162.0 (d, $^{1}J_{C-F}$ = 248 Hz, C_q), 162.0 (d, $^{1}J_{C-F}$ = 247 Hz, C_q), 158.0 (C_q), 148.6 (C_q), 136.9 (d, $^{4}J_{C-F}$ = 4 Hz, C_q), 135.9 (C_q), 133.3 (d, $^{4}J_{C-F}$ = 4 Hz, C_q), 132.9 (d, $^{3}J_{C-F}$ = 8 Hz, CH), 131.9 (d, $^{3}J_{C-F}$ = 8 Hz, CH), 130.1 (CH), 128.0 (C_q), 126.7 (CH), 126.2 (C_q), 125.9 (CH), 125.6 (CH), 115.4 (d, $^{2}J_{C-F}$ = 21 Hz, CH), 114.6 (d, $^{2}J_{C-F}$ = 21 Hz, CH), 22.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = 114.6 (tt, *J* = 8.8, 5.6 Hz), −115.2 (tt, *J* = 8.7, 5.5 Hz). **IR** (ATR) *v* = 3071, 3035, 1603, 1572, 1507, 1437, 1391, 1222, 1093, 837, 759, 728 cm^{-1}. **MS** (ESI) m/z (relative intensity): 332 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{16}F_2N$ $[M+H]^+$: 332.1245, found: 332.1246.

The analytical data were in accordance with those reported in the literature.[109c]

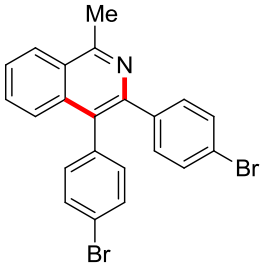


3,4-Bis(4-chlorophenyl)-1-methylisoquinoline (119ag): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 1,2-bis(4-chlorophenyl)ethyne (**8g**) (185 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ag** (120 mg, 66%) as a pale yellow solid.

M.p. = 149−151 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.22–8.16 (m, 1H), 7.62–7.57 (m, 3H), 7.37–7.33

(m, 2H), 7.31–7.27 (m, 2H), 7.21–7.17 (m, 2H), 7.16–7.12 (m, 2H), 3.06 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 158.3 (C_q), 148.1 (C_q), 139.2 (C_q), 135.8 (C_q), 135.7 (C_q), 133.4 (C_q), 133.2 (C_q), 132.6 (CH), 131.5 (CH), 130.2 (CH), 128.7 (CH), 128.0 (C_q), 127.9 (CH), 126.9 (CH), 126.2 (C_q), 125.8 (CH), 125.6 (CH), 22.6 (CH_3). **IR** (ATR) ν = 3070, 1568, 1552, 1488, 1431, 1333, 1084, 1013, 796, 460 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{16}Cl_2N$ $[M+H]^+$: 364.0654, found: 364.0652.

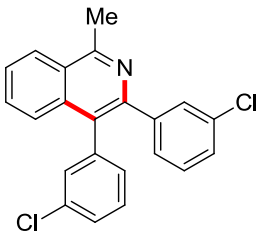
The analytical data were in accordance with those reported in the literature.[195]



3,4-Bis(4-bromophenyl)-1-methylisoquinoline (119ah): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 1,2-bis(4-bromophenyl)ethyne (**8h**) (252 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ah** (161 mg, 71%) as a pale yellow solid.

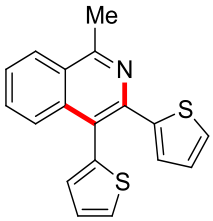
M.p. = 176–178 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.22–8.13 (m, 1H), 7.65–7.55 (m, 3H), 7.54–7.46 (m, 2H), 7.36–7.32 (m, 2H), 7.24–7.20 (m, 2H), 7.10–7.06 (m, 2H), 3.04 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.4 (C_q), 148.1 (C_q), 139.6 (C_q), 136.2 (C_q), 135.6 (C_q), 132.9 (CH), 131.9 (CH), 131.7 (CH), 130.9 (CH), 130.3 (CH), 127.9 (C_q), 126.9 (CH), 126.2 (C_q), 125.8 (CH), 125.7 (CH), 121.6 (C_q), 121.5 (C_q), 22.7 (CH_3). **IR** (ATR) ν = 3060, 1544, 1414, 1387, 1073, 1028, 898, 754, 728, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 454 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{16}Br_2N$ $[M+H]^+$: 451.9649, found: 451.9643.

The analytical data were in accordance with those reported in the literature.[195]



3,4-Bis(3-chlorophenyl)-1-methylisoquinoline (119ai): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 1,2-bis(3-chlorophenyl)ethyne (**8i**) (185 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119ai** (95 mg, 52%) as a pale yellow solid.

M.p. = 107–109 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.23–8.17 (m, 1H), 7.66–7.57 (m, 3H), 7.47–7.46 (m, 1H), 7.36–7.23 (m, 3H), 7.19–7.14 (m, 1H), 7.14–7.06 (m, 3H), 3.06 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.5 (C_q), 147.9 (C_q), 142.4 (C_q), 139.1 (C_q), 135.6 (C_q), 134.3 (C_q), 133.8 (C_q), 131.2 (CH), 130.4 (CH), 130.3 (CH), 129.7 (CH), 129.6 (CH), 128.8 (CH), 128.3 (CH), 128.1 (C_q), 127.7 (CH), 127.4 (CH), 127.0 (CH), 126.3 (C_q), 125.9 (CH), 125.7 (CH), 22.7 (CH_3). **IR** (ATR) ν = 3065, 1593, 1565, 1434, 1390, 1330, 1078, 783, 760, 703, 631 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{16}Cl_2N$ $[M+H]^+$: 364.0654, found: 364.0656.

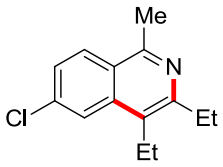


1-Methyl-3,4-di(thiophen-3-yl)isoquinoline (119aj): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and 2-(thiophen-3-ylethynyl)thiophene (**8j**) (143 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 60/1 → 30/1) yielded **119aj** (129 mg, 84%) as a pale yellow solid.

M.p. = 120–122 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.09 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.63–7.55 (m, 3H), 7.52 (ddd, *J* = 8.1, 6.5, 1.5 Hz, 1H), 7.30 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.26 (dd, *J* = 5.2, 3.4 Hz, 1H), 7.09 (dd, *J* = 3.4, 1.1 Hz, 1H), 6.91 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.75 (dd, *J* = 3.8, 1.1 Hz, 1H), 3.03 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 158.7 (C_q), 144.9 (C_q), 144.2 (C_q), 137.9 (C_q), 137.7 (C_q), 130.3 (CH), 129.1 (CH), 127.8 (CH), 127.6 (CH), 127.4 (CH), 127.2 (CH), 126.4 (CH), 125.9 (CH), 125.7 (C_q), 125.3

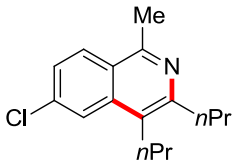
(CH), 118.7 (C_q), 22.6 (CH_3). **IR** (ATR) *v* = 3097, 3066, 1609, 1558, 1530, 1433, 1382, 1233, 1063, 904, 843, 816, 756, 702, 611, 541 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 308 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{14}NS_2$ $[M+H]^+$: 308.0562, found: 308.0565.

The analytical data were in accordance with those reported in the literature.[140a]



6-Chloro-3,4-diethyl-1-methylisoquinoline (119gk): The general procedure **A** was followed using (*E*)-1-(4-chlorophenyl)ethanone *O*-acetyl oxime (**158g**) (106 mg, 0.50 mmol) and hex-3-yne (**8k**) (66 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 15/1) yielded **119gk** (88 mg, 75%) as a pale yellow solid.

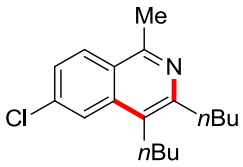
M.p. = 34–36 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.90 (dd, *J* = 2.1, 0.5 Hz, 1H), 7.39 (dd, *J* = 8.9, 2.1 Hz, 1H), 2.94 (q, *J* = 7.6 Hz, 4H), 2.86 (s, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.25 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 155.7 (C_q), 153.9 (C_q), 136.2 (C_q), 135.8 (C_q), 127.9 (CH), 126.5 (C_q), 126.1 (CH), 124.3 (C_q), 122.5 (CH), 28.5 (CH_2), 22.3 (CH_3), 20.6 (CH_2), 15.1 (CH_3), 14.7 (CH_3). **IR** (ATR) *v* = 2963, 2931, 2870, 1606, 1565, 1448, 1387, 1308, 1164, 1097, 1001, 875, 817, 805 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 234 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{17}ClN$ $[M+H]^+$: 234.1044, found: 234.1049.



6-Chloro-1-methyl-3,4-dipropylisoquinoline (119gl): The general procedure **A** was followed using (*E*)-1-(4-chlorophenyl)ethanone *O*-acetyl oxime (**158g**) (106 mg, 0.50 mmol) and oct-4-yne (**8l**) (83 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 15/1) yielded **119gl** (80 mg, 61%) as a pale yellow oil.

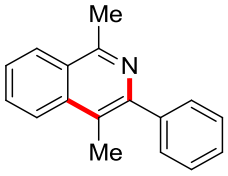
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.87 (dd, *J* = 2.1, 0.5 Hz, 1H), 7.39 (dd, *J* = 8.9, 2.0 Hz, 1H), 2.93–2.83 (m, 7H), 1.82–1.69 (m, 2H), 1.68–1.56 (m, 2H), 1.07 (t, *J* = 7.4 Hz, 3H), 1.01 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 155.5 (C_q), 153.0 (C_q), 136.4 (C_q), 135.7 (C_q),

127.8 (CH), 126.1 (CH), 125.5 (C_q), 124.2 (C_q), 122.7 (CH), 37.4 (CH_2), 29.7 (CH_2), 24.1 (CH_2), 23.6 (CH_2), 22.3 (CH_3), 14.5 (CH_3), 14.3 (CH_3). **IR** (ATR) *v* = 2958, 2870, 1606, 1567, 1455, 1393, 1329, 1102, 991, 870, 812, 625 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 262 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{21}ClN$ $[M+H]^+$: 262.1357, found: 262.1358.



3,4-Dibutyl-6-chloro-1-methylisoquinoline (119gm): The general procedure **A** was followed using (*E*)-1-(4-chlorophenyl)ethanone *O*-acetyl oxime (**158g**) (106 mg, 0.50 mmol) and dec-5-yne (**8m**) (104 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119gm** (123 mg, 85%) as a pale yellow solid.

M.p. = 41–42 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.88 (dd, *J* = 2.1, 0.5 Hz, 1H), 7.39 (dd, *J* = 8.9, 2.0 Hz, 1H), 2.93–2.86 (m, 4H), 2.85 (s, 3H), 1.76–1.66 (m, 2H), 1.62–1.38 (m, 6H), 0.99 (t, *J* = 7.6 Hz, 3H), 0.95 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 155.5 (C_q), 153.2 (C_q), 136.4 (C_q), 135.7 (C_q), 127.8 (CH), 126.0 (CH), 125.5 (C_q), 124.2 (C_q), 122.6 (CH), 35.3 (CH_2), 33.0 (CH_2), 32.7 (CH_2), 27.4 (CH_2), 23.1 (CH_2), 23.0 (CH_2), 22.3 (CH_3), 14.1 (CH_3), 13.9 (CH_3). **IR** (ATR) *v* = 2951, 2926, 2870, 1605, 1565, 1490, 1392, 1332, 1101, 991, 896, 877, 810, 773, 616 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 290 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{25}ClN$ $[M+H]^+$: 290.1670, found: 290.1677.

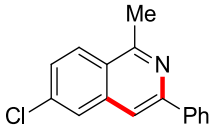


1,4-Dimethyl-3-phenylisoquinoline (119an): The general procedure **A** was followed using (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.50 mmol) and prop-1-yn-1-ylbenzene (**8n**) (88 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 40/1 → 20/1) yielded **119an** (79 mg, 68%) as a pale yellow solid.

M.p. = 95–97 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.17–8.13 (m, 1H), 8.04 (ddd, *J* = 7.5, 4.2, 3.4 Hz, 1H), 7.73 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.62–7.54 (m, 3H), 7.48–7.43 (m, 2H), 7.40–7.34 (m, 1H),

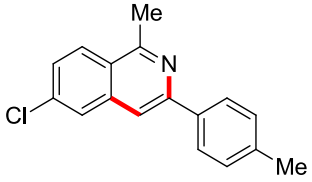
2.98 (d, *J* = 0.4 Hz, 3H), 2.59 (d, *J* = 0.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* = 155.8 (C_q), 150.6 (C_q), 141.6 (C_q), 136.2 (C_q), 129.8 (CH), 129.8 (CH), 128.1 (CH), 127.4 (CH), 126.2 (CH), 126.1 (C_q), 126.0 (CH), 124.1 (CH), 122.1 (Cq), 22.5 (CH_3), 15.4 (CH_3). **IR** (ATR) *v* = 2948, 1568, 1501, 1431, 1333, 1084, 1013, 837, 757, 561 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 234 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{16}N$ $[M+H]^+$: 234.1277, found: 234.1281.

The analytical data were in accordance with those reported in the literature.[194]



6-Chloro-1-methyl-3-phenylisoquinoline (119go): The general procedure **A** was followed using (*E*)-1-(4-chlorophenyl)ethanone *O*-acetyl oxime (**158g**) (106 mg, 0.50 mmol) and ethynylbenzene (**8o**) (77 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 60/1 → 30/1) yielded **119go** (82 mg, 65%) as a pale yellow solid.

M.p. = 90–92 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* = 8.12–8.07 (m, 2H), 8.01 (d, *J* = 10 Hz, 1H), 7.78 (t, *J* = 5 Hz, 2H), 7.51–7.44 (m, 3H), 7.40 (t, *J* = 10 Hz, 1H), 2.98 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): *δ* = 158.5 (C_q), 151.1 (C_q), 139.3 (C_q), 137.6 (C_q), 136.1 (C_q), 128.7 (CH), 128.6 (CH), 127.6 (CH), 127.3 (CH), 127.0 (CH), 126.2 (CH), 124.7 (C_q), 114.2 (CH), 22.6 (CH_3). **IR** (ATR) *v* = 3068, 3032, 2922, 1615, 1566, 1489, 1385, 1361, 1086, 912, 886, 814, 772, 688 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 254 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{13}ClN$ $[M+H]^+$: 254.0731, found: 254.0736.

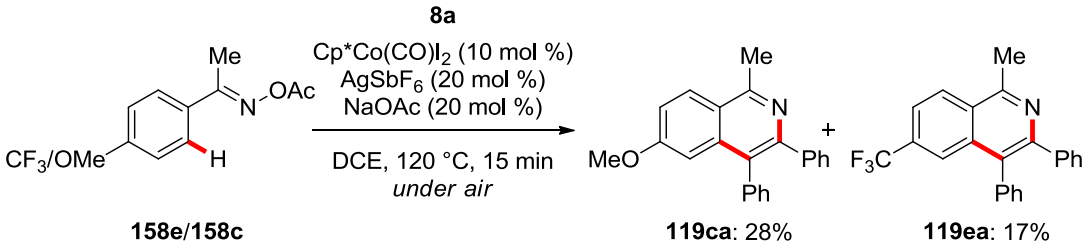


6-Chloro-1-methyl-3-(*p*-tolyl)isoquinoline (119gp): The general procedure **A** was followed using (*E*)-1-(4-chlorophenyl)ethanone *O*-acetyl oxime (**158g**) (106 mg, 0.50 mmol) and 1-ethynyl-4-methylbenzene (**8p**) (87 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 60/1 → 30/1) yielded **119gp** (68 mg, 51%) as a pale yellow solid.

M.p. = 92–93 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* = 8.04–7.97 (m, 3H), 7.78 (d, *J* = 2.1 Hz, 1H), 7.76 (s, 1H), 7.44 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.29–7.27 (m, 2H), 2.98 (d, *J* = 0.4 Hz, 3H), 2.41 (s, 3H). **^{13}C NMR**

(100 MHz, $CDCl_3$): δ = 158.4 (C_q), 151.1 (C_q), 138.6 (C_q), 137.7 (C_q), 136.5 (C_q), 136.0 (C_q), 129.5 (CH), 127.4 (CH), 126.8 (CH), 126.2 (CH), 124.6 (C_q), 113.6 (CH), 22.6 (CH_3), 21.3 (CH_3). **IR** (ATR) ν = 3063, 2918, 1613, 1568, 1439, 1178, 1085, 914, 881, 818 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 268 $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{15}ClN$ $[M+H]^+$: 268.0888, found: 268.0888.

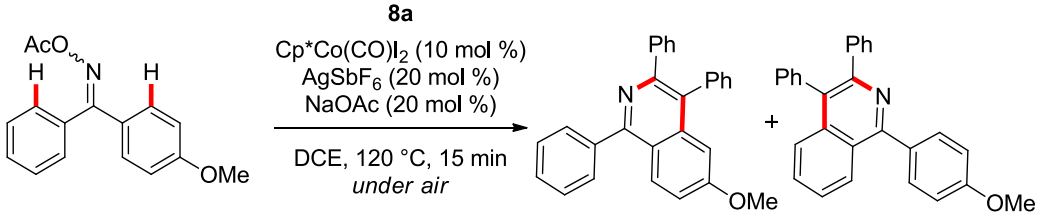
Intermolecular Competition Experiment



158e/158c **119ca**: 28% **119ea**: 17%

A suspension of (*E*)-1-(4-methoxyphenyl)ethanone *O*-acetyl oxime (**158c**) (104 mg, 0.5 mmol), (*E*)-1-[4-(trifluoromethyl)phenyl]ethanone *O*-acetyl oxime (**158e**) (123 mg, 0.5 mmol), diphenylacetylene (**8a**) (89 mg, 0.5 mmol), $Cp^*Co(CO)I_2$ (24 mg, 10 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and NaOAc (8.2 mg, 20 mol %) in DCE (2.0 mL) was stirred at 120 °C for 15 min under air. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with DCM (20 mL) and concentrated under reduced pressure, purified by flash column chromatography on silica gel (*n*-hexane/EtOAc: 30/1 → 20/1 → 10/1) yielded the products **119ca** (45 mg, 28%) and **119ea** (31 mg, 17%).

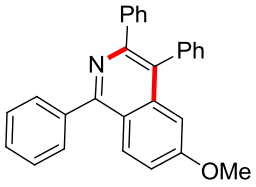
Intramolecular Competition Experiment



158u (*E*:*Z* = 1:1) **119ua**: 63% **119ua'**: 12%

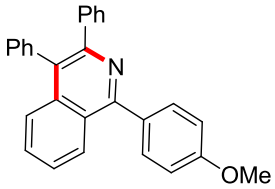
A suspension of (4-methoxyphenyl)(phenyl)methanone *O*-acetyl oxime (**158u**) (135mg, 0.5 mmol), diphenylacetylene (**8a**) (89 mg, 0.5 mmol), $Cp^*Co(CO)I_2$ (24 mg, 10 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and NaOAc (8.2 mg, 20 mol %) in DCE (2.0 mL) was stirred at 120 °C for 15 min under air. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with

DCM (20 mL) and concentrated under reduced pressure, purified by flash column chromatography on silica gel (*n*-hexane/EtOAc: 60/1→40/1) to afford the product **119ua** (122 mg, 63%) and **119ua'** (23mg, 12%).



6-Methoxy-1,3,4-triphenylisoquinoline (119ua): A white solid.

M.p. = 183–185 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 9.2 Hz, 1H), 7.86–7.73 (m, 2H), 7.58–7.47 (m, 3H), 7.45–7.28 (m, 7H), 7.22–7.10 (m, 4H), 6.98 (d, *J* = 2.6 Hz, 1H), 3.73 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 160.5 (C_q), 159.1 (C_q), 150.3 (C_q), 141.1 (C_q), 139.9 (C_q), 139.0 (C_q), 137.8 (C_q), 131.2 (CH), 130.4 (CH), 130.1 (CH), 129.4 (CH), 129.0 (C_q), 128.4 (CH), 128.4 (CH), 128.2 (CH), 127.4 (CH), 127.2 (CH), 126.9 (CH), 121.2 (C_q), 118.8 (CH), 104.2 (CH), 55.2 (CH_3). **IR** (ATR) *v* = 1407, 1374, 1220, 1029, 833, 775, 752, 702, 694, 666 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 388 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{22}NO$ $[M+H]^+$: 388.1696, found: 388.1699.

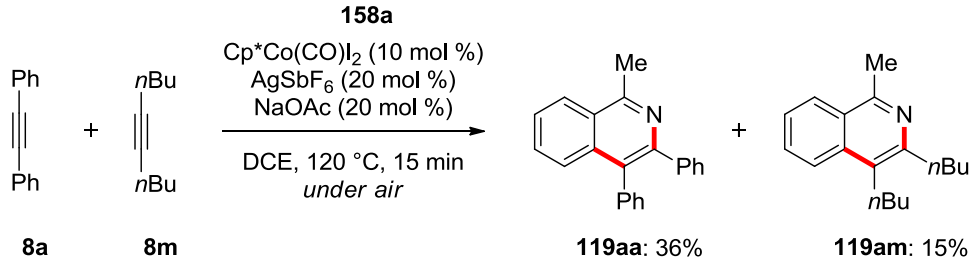


1-(4-Methoxyphenyl)-3,4-diphenylisoquinoline (119ua'): A white solid.

M.p. = 155–157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.22 (ddd, *J* = 8.3, 1.4, 0.7 Hz, 1 H), 7.84–7.75 (m, 2 H), 7.70 (ddd, *J* = 8.5, 1.3, 0.7 Hz, 1 H), 7.57 (ddd, *J* = 8.4, 6.7, 1.4 Hz, 1 H), 7.51 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1 H), 7.45–7.32 (m, 5 H), 7.31–7.27 (m, 2 H), 7.21–7.14 (m, 3 H), 7.08 (d, *J* = 8.7 Hz, 2 H), 3.90 (s, 3 H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 160.0 (C_q), 159.4 (C_q), 149.6 (C_q), 141.0 (C_q), 137.6 (C_q), 137.0 (C_q), 132.4 (C_q), 131.6 (CH), 131.4 (CH), 130.4 (CH), 129.8 (CH), 129.3 (C_q), 128.3 (CH), 127.5 (CH), 127.5 (CH), 127.2 (CH), 126.9 (CH), 126.4 (CH), 126.0 (C_q), 125.4 (CH), 113.8 (CH), 55.4 (CH_3). **IR** (ATR) *v* = 3055, 2928, 1736, 1606, 1540, 1501, 1384, 1245, 1170, 1028, 980, 841, 768, 700 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 388 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{22}NO$ $[M+H]^+$: 388.1696, found: 388.1699.

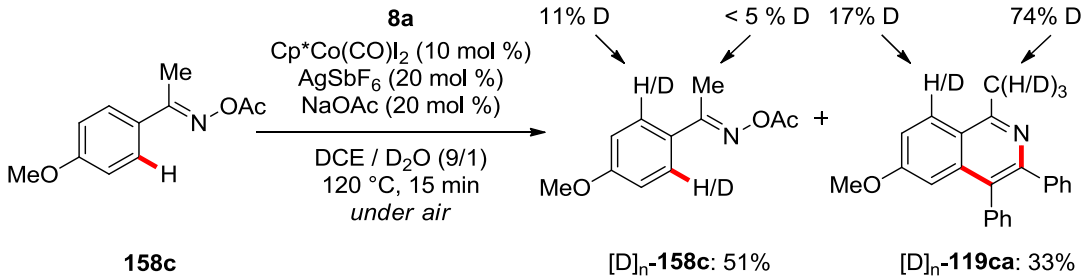
The analytical data were in accordance with those reported in the literature.[196]

Intermolecular Competition Experiment between Alkynes

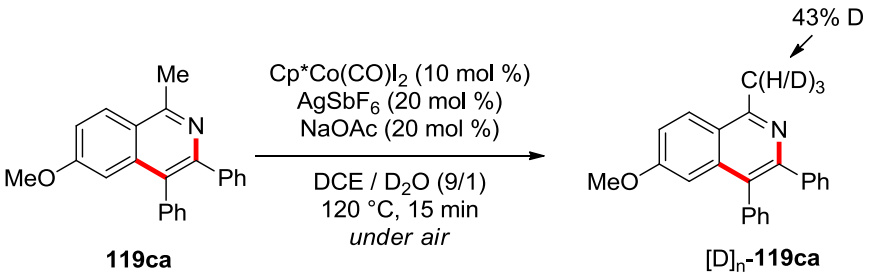


To a solution of (*E*)-acetophenone *O*-acetyl oxime (**158a**) (89 mg, 0.5 mmol), diphenylacetylene (**8a**) (89 mg, 0.5 mmol), dec-5-yne (**8m**) (69 mg, 0.5 mmol), Cp*Co(CO)I_2 (24 mg, 10 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and NaOAc (8.2 mg, 20 mol %) in DCE (2.0 mL) was stirred at 120 °C for 15 min under air. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with DCM (20 mL) and concentrated under reduced pressure, purified by flash column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) to afford the products (**119aa** + **119am**: 73 mg) and the yields were determined by ^{1}H NMR spectroscopy.

H/D Exchange Experiment

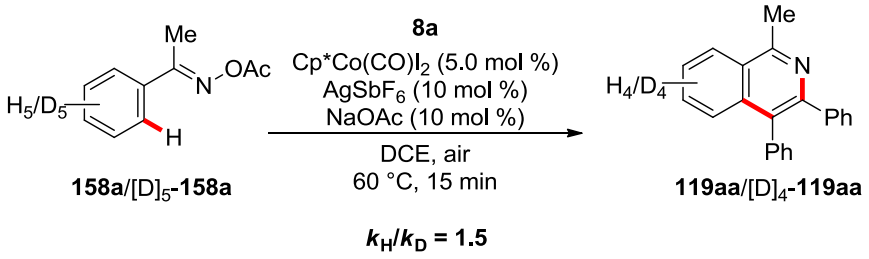


(*E*)-1-(4-Methoxyphenyl)ethanone *O*-acetyl oxime (**158c**) (104 mg, 0.5 mmol), diphenylacetylene (**8a**) (89 mg, 0.50 mmol), Cp*Co(CO)I_2 (24 mg, 10 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), NaOAc (8.2 mg, 20 mol %), DCE (1.8 mL) and D_2O (0.2 ml) were placed in a 25 mL Schlenk tube under air and then were stirred at 120 °C for 15 min. At ambient temperature, the reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc: 40/1→15/1) yielded $[D]_n$-**158c** (53 mg, 51%) and $[D]_n$-**119ca** (54 mg, 33%). The H/D exchange results of this reaction were determined by ^{1}H NMR spectroscopy.



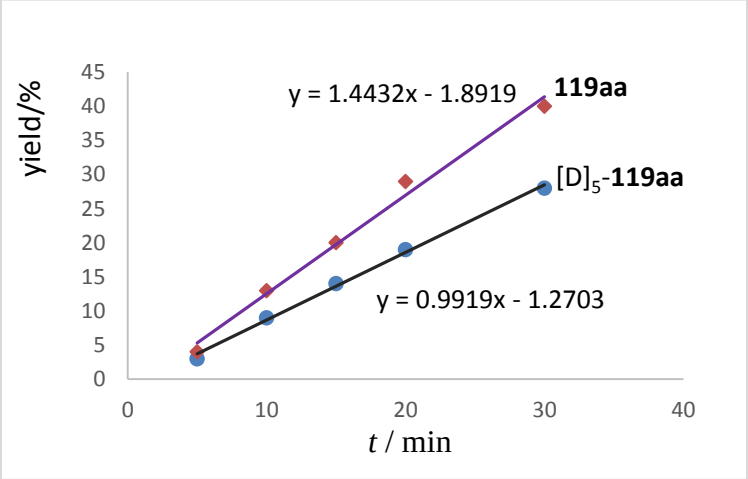
6-Methoxy-1-methyl-3,4-diphenylisoquinoline (**119ca**) (163mg, 0.5 mmol), Cp*Co(CO)I_2 (24 mg, 10 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), NaOAc (8.2 mg, 20 mol %), DCE (1.8 mL) and D_2O (0.2 ml) were placed in a 25 mL Schlenk tube under air and were then stirred at 120 °C for 15 min. At ambient temperature, the reaction mixture was filtered over a short plug of silica and the result of *H*/*D* exchange experiment was determined by crude ^{1}H NMR. Then the reaction mixture was transferred into a round bottom flask with DCM (20 mL) and concentrated under reduced pressure, purified by flash column chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded [D]$_n$-**119ca** (155 mg, 95%).

Kinetic Isotope Effect Experiment

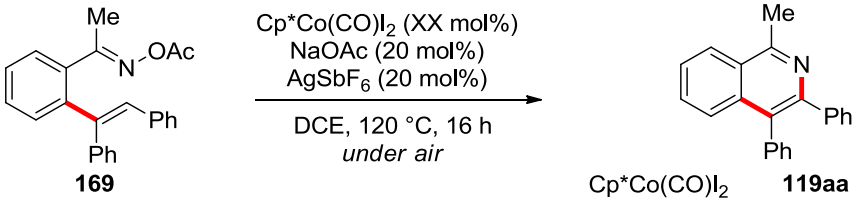


Two parallel reactions of **8a** with **158a** and [D]$_5$-**158a** respectively were performed to determine the corresponding KIE value: **158a** (89 mg, 0.5 mmol) or [D]$_5$-**158a** (93 mg, 0.5 mmol), diphenylacetylene (**8a**) (134 mg, 0.75 mmol), Cp*Co(CO)I_2 (12 mg, 5 mol %), $AgSbF_6$ (17.2 mg, 10 mol %), NaOAc (4 mg, 20 mol %), 1,3,5-trimethoxybenzene (28 mg, 0.5/3 mmol) and DCE (2.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 60 °C, a periodic aliquot (0.05 mL) was taking out by syringe and analyzed by GC to provide the following conversions:

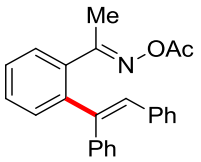
t / min yield / %	5	10	15	20	30
119aa	4	13	20	29	40
[D]$_5$-**119aa**	3	9	14	19	28



Attempted Cyclization of ortho-Alkenylated Arene 119aa



(*E*)-1-{2-[(*E*)-1,2-diphenylvinyl]phenyl}ethanone *O*-acetyl oxime (**169**) (25mg, 70 umol), Cp*Co(CO)I_2 (3.4 mg, 10 mol %), $AgSbF_6$ (5 mg, 20 mol %), NaOAc (2 mg, 20 mol %), DCE (0.3 mL) were placed in a 25 mL Schlenk tube under air and were then stirred at 120 °C for 16 h. After cooling to ambient temperature, the reaction mixture was transferred into a round bottom flask with DCM (10 mL) and concentrated under reduced pressure, purified by flash column chromatography on silica gel (*n*-hexane/EtOAc: 25/1) yielded **119aa** (15%). In the absence of the Co-catalyst no reaction was observed and only starting material was recovered.



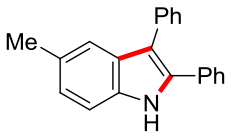
(*E*)-1-{2-[(*E*)-1,2-Diphenylvinyl]phenyl}ethanone *O*-acetyl oxime (169): A white solid.

M.p. = 110−114 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.46–7.38 (m, 3H), 7.35–7.23 (m, 5H), 7.19–7.09 (m, 3H), 7.04–6.99 (m, 3H), 2.01 (s, 3H), 1.89 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 170.8 (C_q), 163.5 (C_q), 142.7 (C_q), 141.2 (C_q), 139.4 (C_q), 137.1 (C_q), 136.4 (C_q), 132.0 (CH), 130.0 (CH), 129.5 (CH), 129.4 (CH), 129.1 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 127.8 (CH), 127.5 (CH), 127.2 (CH), 20.1 (CH_3), 16.6 (CH_3). **IR** (ATR) ν = 1772, 1317, 1210, 924, 762, 750, 697, 644 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 378 (100) $[M+Na]^+$, 296 (70) $[M-OAc]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{21}N_2NaO$ $[M+Na]^+$: 378.1465, found: 378.1466.

The analytical data were in accordance with those reported in the literature.[182]

5.3.2 Data for the Products of Indoles by Cobalt(III)-Catalyzed C–H/N–O Functionalizations with Nitrones

Characterization Data

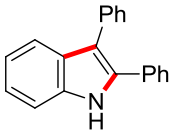


5-Methyl-2,3-diphenyl-1*H*-indole (160aa): The general procedure **B** was followed using *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.50 mmol) and 1,2-diphenylethyne (**8a**) (134 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160aa** (130 mg, 92%) as a white solid.

M. p. = 143−145 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.58–7.37 (m, 7H), 7.36–7.19 (m, 5H), 7.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 135.2 (C_q), 134.2 (C_q), 134.2 (C_q), 132.8 (C_q), 130.2 (CH), 129.7 (C_q), 129.0 (C_q), 128.6 (CH), 128.5 (CH), 128.1 (CH), 127.5 (CH), 126.1 (CH), 124.3 (CH), 119.2 (CH), 114.6 (C_q), 110.5 (CH), 21.5 (CH_3). **IR** (ATR) ν = 3368, 3056, 1600, 1448, 1316, 1030, 780, 760, 696 cm^{-1}. **MS** (ESI) m/z (relative intensity): 282 (100) $[M-H]^-$.

HR-MS (ESI) m/z calcd for $C_{21}H_{17}N$ $[M-H]^-$: 282.1288, found: 282.1292.

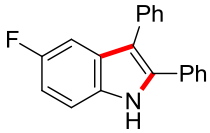
The analytical data were in accordance with those reported in the literature.[161]



2,3-Diphenyl-1*H*-indole (160ba): The general procedure **B** was followed using *N*-(4-methoxybenzylidene)aniline oxide (**159b**) (113.6 mg, 0.50 mmol) and 1,2-diphenylethyne (**8a**) (134 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160ba** (102.3 mg, 76%) as a white solid.

M. p. = 98−100 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.18 (s, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.55–7.38 (m, 7H), 7.38–7.22 (m, 5H), 7.17 (t, J = 7.5 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 135.8 (C_q), 135.0 (C_q), 134.0 (C_q), 132.6 (C_q), 130.1 (CH), 128.7 (C_q), 128.6 (CH), 128.5 (CH), 128.1 (CH), 127.7 (CH), 126.2 (CH), 122.7 (CH), 120.4 (CH), 119.7 (CH), 115.0 (C_q), 110.7 (CH). **IR** (ATR) ν = 3389, 3039, 1601, 1455, 1151, 1008, 748, 694, 606, 515 cm^{-1}. **MS** (ESI) m/z (relative intensity): 269 (100), 296 (85), 381 (20) $[M]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{15}N$ $[M]^+$: 269.1199, found: 269.1197.

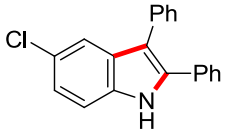
The analytical data were in accordance with those reported in the literature.[161]



5-Fluoro-2,3-diphenyl-1*H*-indole (160ca): The general procedure **B** was followed using 4-fluoro-*N*-(4-methoxybenzylidene)aniline oxide (**159c**) (122.6 mg, 0.50 mmol) and 1,2-diphenylethyne (**8a**) (134 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160ca** (101 mg, 70%) as a white solid.

M. p. = 124−126 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.13 (s, 1H), 7.50–7.37 (m, 7H), 7.36–7.26 (m, 5H), 7.01 (td, J = 9.0, 2.5 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 158.4 (d, $^1J_{C\text{-}F}$ = 235.3 Hz, C_q), 135.8 (C_q), 134.6 (C_q), 132.3 (C_q), 132.3 (C_q), 129.9 (CH), 129.2 (d, $^3J_{C\text{-}F}$ = 10.1 Hz, C_q), 128.7 (CH), 128.6 (CH), 128.1 (CH), 127.9 (CH), 126.4 (CH), 115.2 (d, $^4J_{C\text{-}F}$ = 4.7 Hz, C_q), 111.6 (d, $^3J_{C\text{-}F}$ = 9.8 Hz, CH), 111.0 (d, $^2J_{C\text{-}F}$ = 26.5 Hz, CH), 104.6 (d, $^2J_{C\text{-}F}$ = 24.1 Hz, CH). **^{19}F NMR** (283 MHz, $CDCl_3$): δ = -123.44 (td, J = 9.5,

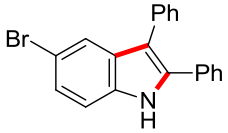
4.4 Hz). **IR** (ATR) *v* = 3423, 1600, 1474, 1069, 951, 859, 754, 692 cm^{-1}. **MS** (ESI) m/z (relative intensity): 286 (100) $[M-H]^-$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{14}NF$ $[M-H]^-$: 286.1038, found: 286.1040. The analytical data were in accordance with those reported in the literature.[161]



5-Chloro-2,3-diphenyl-1*H*-indole (160da): The general procedure **B** was followed using 4-chloro-*N*-(4-methoxybenzylidene)aniline oxide (**159d**) (131 mg, 0.50 mmol) and 1,2-diphenylethyne (**8a**) (134 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160da** (115 mg, 76%) as a pale yellow solid.

M. p. = 110−112 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8. 20 (s, 1H), 7.63 (d, *J* = 2.0 Hz, 1H), 7.50–7.34 (m, 6H), 7.34–7.25 (m, 5H), 7.18 (dd, *J* = 8.6, 2.0 Hz, 1H). **^{13}C NMR** (76 MHz, $CDCl_3$): δ = 135.4 (C_q), 134.3 (C_q), 134.2 (C_q), 132.1 (C_q), 130.0 (CH), 129.9 (C_q), 128.7 (CH), 128.6 (CH), 128.1 (CH), 128.0 (CH), 126.5 (CH), 126.1 (C_q), 122.9 (CH), 119.1 (CH), 114.7 (C_q), 111.9 (CH). **IR** (ATR) *v* = 3438, 3420, 1506, 1458, 762, 694, 607 cm^{-1}. **MS** (ESI) m/z (relative intensity): 302 (100), 304 (30) $[M-H]^-$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{14}NCl$ $[M-H]^-$: 302.0742, found: 302.0743.

The analytical data were in accordance with those reported in the literature.[161]

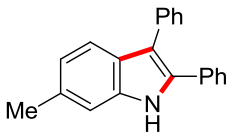


5-Bromo-2,3-diphenyl-1*H*-indole (160ea): The general procedure **B** was followed using 4-bromo-*N*-(4-methoxybenzylidene)aniline oxide (**159e**) (153 mg, 0.50 mmol) and 1,2-diphenylethyne (**8a**) (134 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160ea** (158 mg, 91%) as a pale yellow solid.

M. p. = 133−135 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.19 (s, 1H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.49–7.36 (m, 6H), 7.35–7.21 (m, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 135.2 (C_q), 134.4 (C_q), 134.3 (C_q), 132.0 (C_q), 130.5 (C_q), 130.0 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 128.0 (CH), 126.5 (CH), 125.4 (CH), 122.1 (CH), 114.6 (C_q), 113.7 (C_q), 112.3 (CH). **IR** (ATR) *v* = 3451, 1449, 1306, 1286, 760, 696, 648, 586, 508,

445 cm^{-1}. **MS** (ESI) m/z (relative intensity): 346 (100) $[M-H]^-$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{14}NBr$ $[M-H]^-$: 346.0237, found: 346.0231.

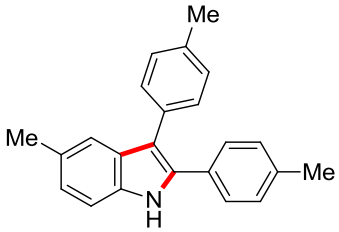
The analytical data were in accordance with those reported in the literature.[161]



6-Methyl-2,3-diphenyl-1*H*-indole (160fa): The general procedure **B** was followed using *N*-(4-methoxybenzylidene)-3-methylaniline oxide (**159f**) (121 mg, 0.50 mmol) and 1,2-diphenylethyne (**8a**) (134 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160fa** (126 mg, 89%) as a white solid.

M. p. = 95–97 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.07 (s, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.48–7.36 (m, 5H), 7.35–7.24 (m, 5H), 7.22–7.19 (m, 1H), 6.99 (dd, *J* = 8.2, 0.9 Hz, 1H), 2.49 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 136.3 (C_q), 135.2 (C_q), 133.3 (C_q), 132.8 (C_q), 132.6 (C_q), 130.1 (CH), 128.6 (CH), 128.5 (CH), 128.0 (CH), 127.5 (CH), 126.6 (C_q), 126.1 (CH), 122.2 (CH), 119.3 (CH), 114.9 (C_q), 110.8 (CH), 21.7 (CH_3). **IR** (ATR) *v* = 3406, 1601, 1502, 1449, 1439, 1250, 914, 804, 763, 697 cm^{-1}. **MS** (ESI) m/z (relative intensity): 282 (100) $[M-H]^-$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{17}N$ $[M-H]^-$: 282.1288, found: 282.1289.

The analytical data were in accordance with those reported in the literature.[161]

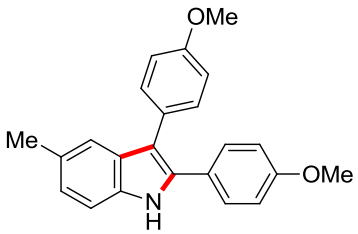


5-Methyl-2,3-di-*p*-tolyl-1*H*-indole (160ab): The general procedure **B** was followed using *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.50 mmol) and 1,2-di-p-tolylethyne (**8b**) (155 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-pentane/EtOAc: 30/1) yielded **160ab** (115.2 mg, 74%) as a white solid.

M. p. = 157–160 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.05 (s, 1H), 7.44 (s, 1H), 7.35–7.28 (m, 5H), 7.23–7.17 (m, 2H), 7.16–7.09 (m, 2H), 7.05 (dd, *J* = 8.4, 1.6 Hz, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 2.35 (s,

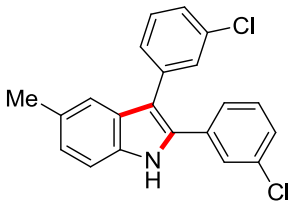
3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 137.2 (C_q), 135.5 (C_q), 134.0 (C_q), 132.2 (C_q), 130.0 (C_q), 129.9 (CH), 129.9 (C_q) 129.4 (C_q), 129.2 (CH), 129.1 (CH), 129.1 (C_q), 127.8 (CH), 123.9 (CH), 119.1 (CH), 114.1 (C_q), 110.4 (CH), 21.6 (CH_3), 21.3 (CH_3), 21.3 (CH_3). **IR** (ATR) *v* = 3379, 2917, 1510, 1439, 821, 798, 723, 517 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 327 (17), 311 (100) $[M]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{21}N$ $[M]^+$: 311.1674, found: 311.1665.

The analytical data were in accordance with those reported in the literature.[197]



2,3-Bis(4-methoxyphenyl)-5-methyl-1*H*-indole (160ac): The general procedure **B** was followed using *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.50 mmol) and 1,2-bis(4-methoxyphenyl)ethyne (**8c**) (178 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-pentane/EtOAc: 10/1) yielded **160ac** (122 mg, 71%) as a yellow solid.

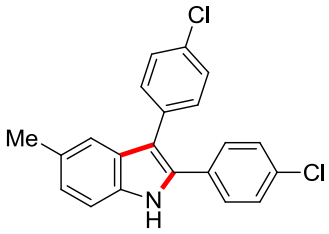
M. p. = 147–150 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.40 (s, 1H), 7.37–7.30 (m, 4H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.03 (s, 1H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 3.85 (s, 3H), 3.80 (s, 3H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 159.0 (C_q), 157.9 (C_q), 134.0 (C_q), 133.8 (C_q), 131.1 (CH), 129.4 (C_q), 129.2 (CH), 127.7 (C_q), 125.4 (C_q), 123.8 (CH), 119.0 (CH), 114.3 (C_q), 114.1 (CH), 114.0 (CH), 113.3 (C_q) 110.4 (CH), 55.2 (CH_3), 55.2 (CH_3), 21.5 (CH_3). **IR** (ATR) *v* = 3362, 2928, 2835, 1510, 1455, 1231, 1172, 1023, 829, 791 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 343 (100) $[M]^+$, 328 (50). **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{21}NO_2$ $[M]^+$: 343.1572, found: 343.1572.



2,3-Bis(3-chlorophenyl)-5-methyl-1*H*-indole (160ah): The general procedure **B** was followed using *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.50 mmol) and

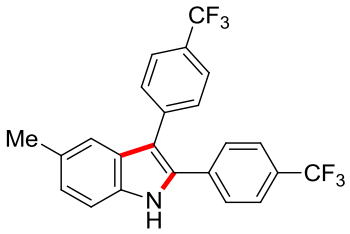
1,2-bis(3-chlorophenyl)ethyne (**8h**) (185 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160ah** (146 mg, 83%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.46–7.39 (m, 3H), 7.34–7.28 (m, 3H), 7.28–7.18 (m, 4H), 7.10 (dd, *J* = 8.5, 1.4 Hz, 1H), 2.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 136.7 (C_q), 134.6 (C_q), 134.3 (C_q), 134.2 (C_q), 134.1 (C_q) 132.9 (C_q), 130.3 (C_q), 129.9 (CH), 129.8 (CH), 129.8 (CH), 128.5 (C_q), 128.3 (CH), 127.8 (CH), 127.7 (CH), 126.5 (CH), 126.4 (CH), 125.0 (CH), 119.0 (CH), 114.1 (C_q), 110.7 (CH), 21.5 (CH_3). **IR** (ATR) *v* = 3399, 2917, 1594, 1562, 1485, 1458, 1077, 883, 784, 733 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 351 (100), 315 (11), 381 (10), 178 (7). **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{21}NO_2$ $[M]^+$: 351.0582, found: 351.0588.



2,3-Bis(4-chlorophenyl)-5-methyl-1*H*-indole (160ag): The general procedure **B** was followed using nitrone (**159a**) (121 mg, 0.50 mmol) and 1,2-bis(4-chlorophenyl)ethyne (**8g**) (185 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160ag** (99 mg, 56%) as a pale yellow solid.

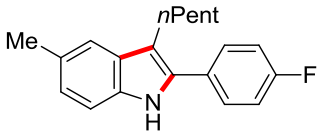
M. p. = 131–132 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.08 (s, 1H), 7.40 (s, 1H), 7.39–7.31 (m, 9H), 7.08 (d, *J* = 9.4 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 134.2 (C_q), 133.6 (C_q), 133.3 (C_q), 133.1 (C_q), 132.1 (C_q), 131.2 (CH), 130.9 (C_q), 130.1 (C_q), 129.2 (CH), 128.9 (CH), 128.8 (CH), 128.6 (C_q), 124.7 (CH), 118.9 (CH), 113.8 (C_q), 110.6 (CH), 21.6 (CH_3). **IR** (ATR) *v* = 3452, 3390, 1498, 1471, 1086, 1013, 833, 784 cm^{-1}. **MS** (ESI) m/z (relative intensity): 350 (100), 351 (20), 352 (60) $[M-H]^-$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{15}NCl_2$ $[M-H]^-$: 350.0509, found: 350.0508.



5-Methyl-2,3-bis[4-(trifluoromethyl)phenyl]-1*H*-indole (160ae): The general procedure **B** was

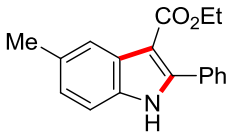
followed using *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.50 mmol) and 1,2-bis[4-(trifluoromethyl)phenyl]ethyne (**8e**) (236 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded **160ae** (153 mg, 73%) as a yellow solid.

M. p. = 149–150 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.21 (s, 1H), 7.68–7.54 (m, 4H), 7.49 (t, *J* = 8.7 Hz, 4H), 7.42 (s, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 2.45 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 138.7 (C_q), 135.8 (C_q), 134.6 (C_q), 133.1 (C_q), 130.7 (C_q), 129.8 (q, $^2J_{C\text{-}F}$ = 33.1 Hz, C_q), 130.3 (CH), 128.5 (q, $^2J_{C\text{-}F}$ = 31.9 Hz, C_q), 128.5 (C_q), 128.3 (CH), 125.9 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, CH), 125.6 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, CH), 125.4 (CH), 124.3 (q, $^1J_{C\text{-}F}$ = 272.0 Hz, C_q), 124.0 (q, $^1J_{C\text{-}F}$ =273.0 Hz, C_q), 119.1 (CH), 114.7 (C_q), 111.0 (CH), 21.5 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -62.34, -62.67. **IR** (ATR) *v* = 3474, 2922, 1617, 1319, 1154, 1090, 1060, 840, 793 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 343 (100), 328 (50), 268 (9) 171 (5). **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{15}F_6N$ $[M]^+$: 419.1109, found: 419.1120.



2-(4-Fluorophenyl)-5-methyl-3-pentyl-1*H*-indole (160as): The general procedure **B** was followed using nitrone (**159a**) (121 mg, 0.50 mmol, 1.0 equiv) and 1-fluoro-4-(hept-1-yn-1-yl)benzene (**8s**) (143 mg, 0.75 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 10/1) and GPC yielded **160as** (114 mg, 77%) as a pale yellow solid.

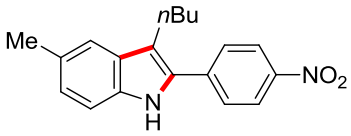
M. p. = 118–120 °C. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 10.98 (s, 1H), 7.65-7.58 (m, 2H), 7.35 (d, *J* = 8.9 Hz, 2H), 7.31 (d, *J* = 1.8 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 6.92 (dd, *J* = 8.2, 1.6 Hz, 1H), 2.78 (t, *J* = 7.8 Hz, 2H), 2.39 (s, 3H), 1.62 (p, *J* = 7.2 Hz, 2H), 1,35-1.25 (m, 4H), 0.83 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 161.3 (d, $^1J_{C\text{-}F}$ = 245 Hz, C_q), 134.3 (C_q), 132.9 (C_q), 129.5 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, CH), 128.9 (C_q), 127.0 (C_q), 123.0 (CH), 119.9 (C_q), 118.1 (CH), 115.6 (d, $^2J_{C\text{-}F}$ = 21.5 Hz, CH), 111.7 (C_q), 110.8 (CH), 31.4 (CH_3), 30.3 (CH_2), 24.0 (CH_2), 22.0 (CH_3), 21.3 (CH_2), 13.9 (CH_2). **^{19}F NMR** (282 MHz, DMSO-d_6): δ = 115.01. **IR** (ATR) *v* = 3381, 2923, 2857, 1506, 1441, 1225, 838, 797, 516, 477 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 295 (6) $[M]^+$, 312 (100), 334 (34), 350 (24). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{22}FN$ $[M]^+$: 295.1736, found: 295.1727.



Ethyl 5-methyl-2-phenyl-1*H*-indole-3-carboxylate (160at): The general procedure **B** was followed using nitrone (**159a**) (121 mg, 0.50 mmol, 1.0 equiv) and ethyl 3-phenylpropiolate (**8t**) (131 mg, 0.75 mmol, 1.5 equiv). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 10/1) and GPC yielded **160at** (86.6 mg, 63%) as a colorless solid.

M. p. = 145–147 °C. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 11.97 (s, 1H), 7.86 (d, J = 1.0 Hz, 1H), 7.68–7.65 (m, 2H), 7.52–7.45 (m, 3H), 7.33 (d, J = 8.2 Hz, 1H), 7.44 (dd, J = 8.2, 1.1 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 2.43 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, DMSO-d_6): δ = 164.5 (C_q), 144.3 (C_q), 133.9 (C_q), 132.0 (C_q), 129.9 (C_q), 129.8 (CH), 128.6 (CH), 127.7 (CH), 127.5 (C_q), 124.0 (CH), 120.8 (CH), 111.4 (CH), 102.4 (C_q), 58.8 (CH_2), 21.4 (CH_3), 14.1 (CH_3). **IR** (ATR) ν = 3232, 1652, 1476, 1451, 1268, 1218, 1145, 1049, 777, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 280 (6) $[M+H]^+$, 302 (100) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{17}NNaO_2$ $[M+Na]^+$: 302.1157, found: 302.1159.

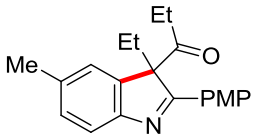
The analytical data were in accordance with those reported in the literature.[198]



3-Butyl-5-methyl-2-(4-nitrophenyl)-1*H*-indole (160au): The general procedure **B** was followed using nitrone (**159a**) (121 mg, 0.50 mmol, 1.0 equiv) and 1-(hex-1-yn-1-yl)-4-nitrobenzene (**8u**) (152 mg, 0.75 mmol, 1.5 equiv). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 30/1) and GPC yielded **160au** (84 mg, 54%) as a yellow solid.

M. p. = 126–128 °C. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 11.23 (s, 1H), 8.34 (d, J = 8.9 Hz, 2H), 7.87 (d, J = 8.9 Hz, 2H), 7.37 (d, J = 1.6 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.00 (dd, J = 8.4, 1.5 Hz, 1H), 2.89 (dd, J = 8.7, 6.8 Hz, 2H), 2.40 (s, 3H), 1.62 (tt, J = 8.0, 6.2 Hz, 2H), 1.39 (tt, J = 7.3, 7.3 Hz, 2H), 0.90 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (75 MHz, DSMO-d_6): δ = 145.5 (C_q), 139.7 (C_q), 135.1 (C_q), 131.3 (C_q), 128.3 (C_q), 127.7 (CH), 127.5 (C_q), 124.5 (CH), 123.9 (CH), 118.5 (CH), 115.2 (C_q), 111.1 (CH), 32.6 (CH_2), 23.9 (CH_2), 22.0 (CH_2), 21.2 (CH_3), 13.7 (CH_3). **IR** (ATR) ν = 3313, 1684, 1306, 1234, 1106, 755, 693, 654, 608, 590 cm^{-1}. **MS** (ESI) m/z (relative intensity): 331.2 (100) $[M+Na]^+$, 356.2 (25). **HR-MS** (ESI) m/z

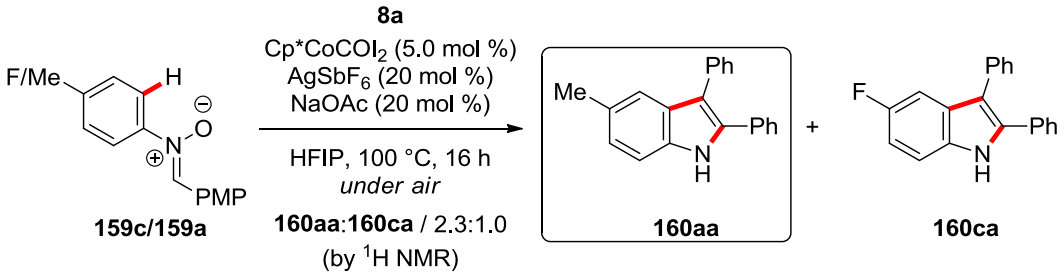
calcd for $C_{19}H_{20}N_2O_2Na$ $[M+Na]^+$: 331.1422, found: 331.1410.



1-[3-Ethyl-2-(4-methoxyphenyl)-5-methyl-3*H*-indol-3-yl]propan-1-one (161): The general procedure **B** was followed using nitrone (**159a**) (121 mg, 0.50 mmol, 1.0 equiv) and 3-hexyne (**8r**) (61.6 mg, 0.75 mmol, 1.5 equiv). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 10/1) and GPC yielded **161** (74 mg, 46%) as a colorless solid.

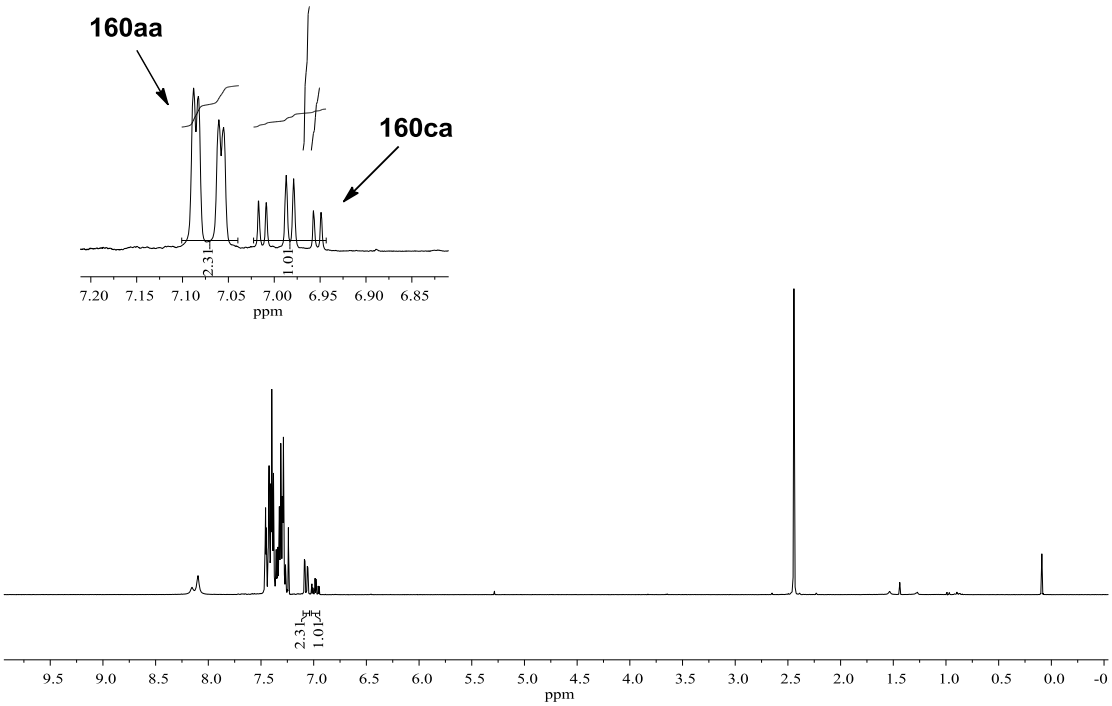
M. p. = 96–98 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.9 Hz, 2H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.24 (ddd, *J* = 8.0, 1.7, 0.8 Hz, 1H), 6.99 (d, *J* = 0.8 Hz, 1H), 6.96 (d, *J* = 9.0 Hz, 2H), 3.86 (s, 3H), 2.53–2.27 (m, 2H), 2.40 (s, 3H), 2.03-1.75 (m, 2H), 0.8 (t, *J* = 7.2 Hz, 3H), 0.24 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 207.3 (C_q), 175.8 (C_q), 162.2 (C_q), 155.0 (C_q), 139.1 (C_q), 136.3 (C_q), 129.9 (CH), 129.7 (CH), 125.7 (C_q), 122.7 (CH), 120.4 (CH), 114.6 (CH), 75.4 (C_q), 55.6 (CH_3), 31.3 (CH_3), 26.6 (CH_2), 21.7 (CH_2), 8.3 (CH_3), 7.3 (CH_3). **IR** (ATR) *v* = 2967, 3935, 1706, 1603, 1505, 1459, 1254, 1174, 1033, 836 cm^{-1}. **MS** (ESI) m/z (relative intensity): 306.2 (70) $[M-Me]^+$, 322.2 (41) $[M+H]^+$, 344.2 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{23}NO_2Na$ $[M+Na]^+$: 344.1626, found: 344.1624.

Intermolecular Competition Experiment

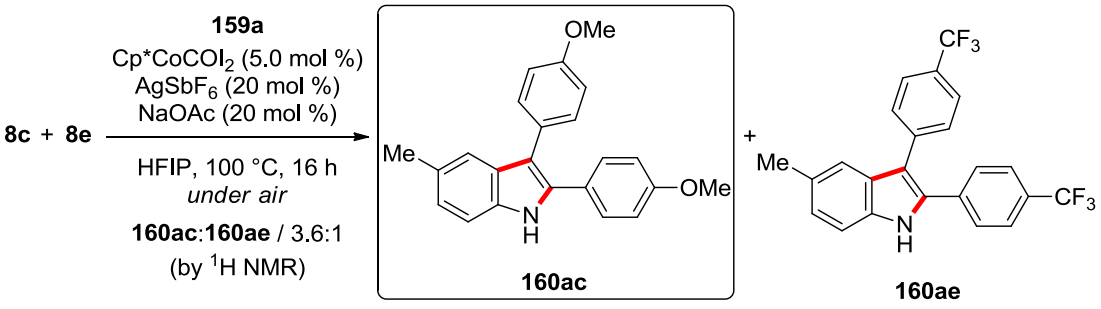


A suspension of *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.5 mmol), 4-fluoro-*N*-(4-methoxybenzylidene)aniline oxide (**159c**) (123 mg, 0.5 mmol), diphenylacetylene (**8a**) (89 mg, 0.5 mmol), $Cp^*CoI_2(CO)$ (12 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and NaOAc (8.2 mg, 20 mol %) in HFIP (2.0 mL) was stirred under air at 100 °C for 16 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and

concentrated in *vacuo*. Purification by flash column chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded the products **160aa** and **160ca** (120 mg) and the conversions were determined by ^{1}H NMR spectroscopy.

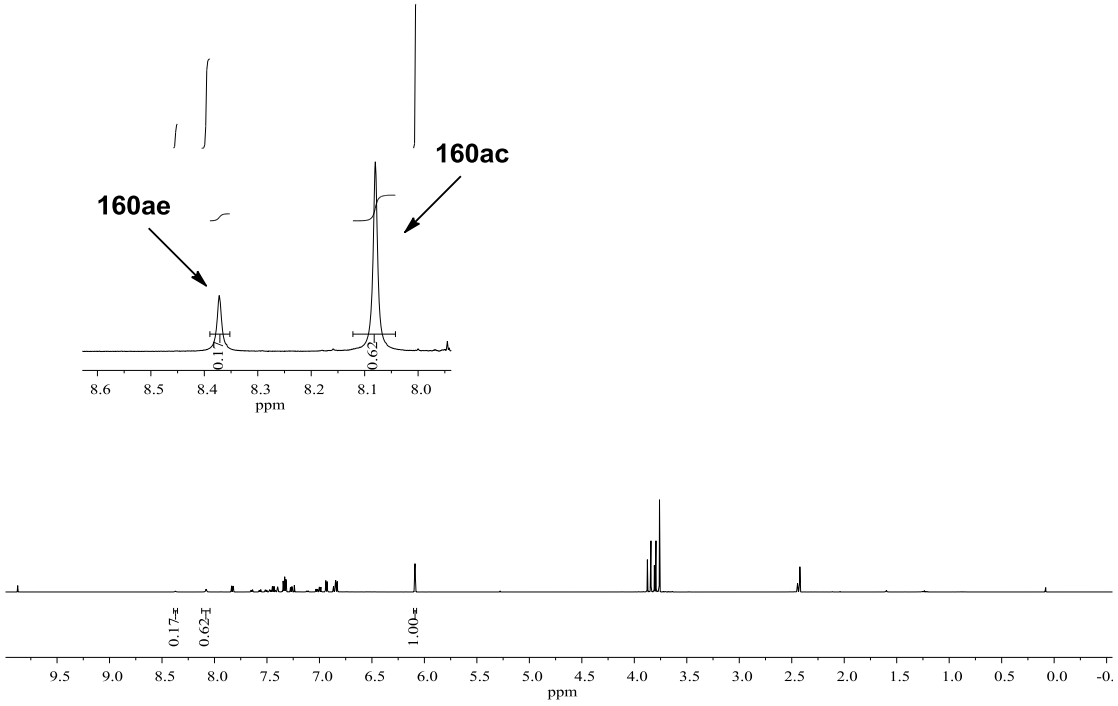


Competition Experiment between Alkynes 8

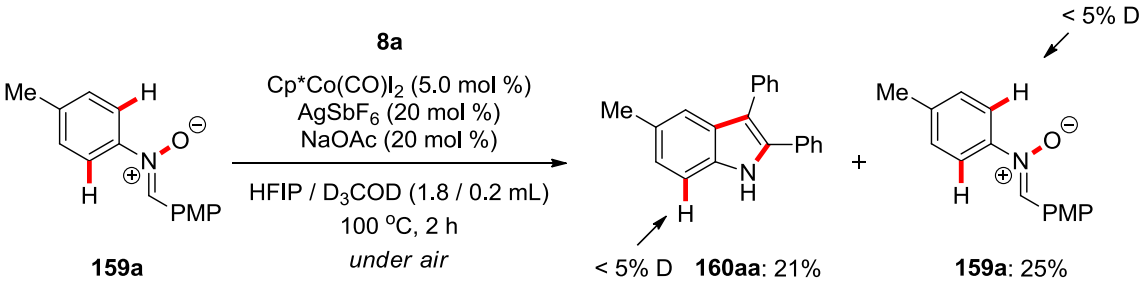


A suspension of 1,2-bis(4-methoxyphenyl)ethyne (**8a**) (119 mg, 0.5 mmol), 1,2-bis[4-(trifluoromethyl)phenyl]ethyne (**8e**) (157 mg, 0.5 mmol), *N*-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.5 mmol), Cp*CoI_2(CO) (12 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and NaOAc (8.2 mg, 20 mol %) in HFIP (2.0 mL) was stirred at 100 °C for 16 h under air. After cooling to ambient temperature, the mixture was filtered through a short pad of celite, rinsed with CH_2Cl_2 (20 mL) and concentrated in *vacuo.* The crude ^{1}H NMR was

measured to determine the conversions to the products **160ac** (62%) and **160ae** (17%) using the 1,3,5-trimethoxybenzene as the internal standard.



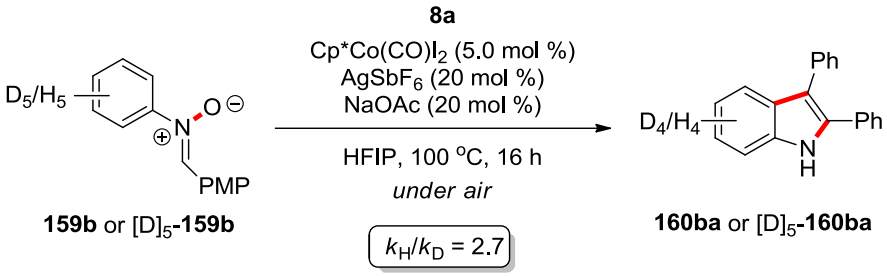
H/D Exchange Experiments



N-(4-methoxybenzylidene)-4-methylaniline oxide (**159a**) (121 mg, 0.5 mmol), diphenylacetylene (**8a**) (89 mg, 0.5 mmol), $Cp^*CoI_2(CO)$ (12 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and NaOAc (8.2 mg, 20 mol %), HFIP (1.8 mL) and D_3COD (0.2 ml) were placed in a 25 mL Schlenk tube under air and the mixture was stirred at 100 °C for 2 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by flash column chromatography on silica gel (*n*-hexane/CH_2Cl_2: 3/1) yielded the product **160aa** (80 mg,

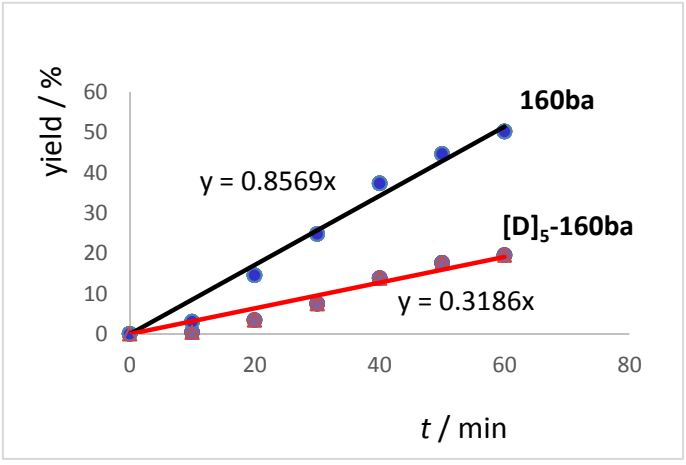
21%) and **159a** (31 mg, 25%) (*n*-hexane/EtOAc: 3/1).

Kinetic Isotope Effect Experiment



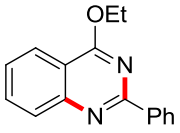
Two parallel reactions of **8a** with **159a** or [D]$_5$-**159a** were performed to determine the corresponding KIE value. **159a** (113.6 mg, 0.5 mmol) or [D]$_5$-**159a** (116.2 mg, 0.5 mmol), diphenylacetylene (**8a**) (134 mg, 0.75 mmol), Cp*CoI$_2$(CO) (12 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), NaOAc (8.2 mg, 20 mol %), 1,3,5-trimethoxybenzene (28 mg, 0.17 mmol) as internal standard and HFIP (2.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 100 °C, a periodic aliquot (0.05 mL) was removed by syringe and analyzed by GC to determine the following conversions:

t / min yield / %	10	20	30	40	50	60
160ba	3	14.5	24.8	37.3	44.6	50.2
[D]$_5$-160ba	0.4	3.4	7.5	13.8	44.6	50.2



5.3.3 Data for the Products of Quinazolines by Cobalt(III)-Catalyzed C–H/N–O Functionalizations with Benzimidates

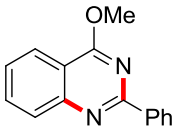
Characterization Data



4-Ethoxy-2-phenylquinazoline (163aa): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 30/1) yielded **163aa** (60 mg, 96%) as a white solid.

M. p. = 64–65 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.58 (dd, *J* = 7.3, 2.3 Hz, 2H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.58–7.40 (m, 4H), 4.76 (q, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 160.0 (C_q), 151.8 (C_q), 138.2 (C_q), 133.3 (CH), 130.4 (CH), 128.4 (CH), 128.3 (CH), 127.9 (CH), 126.2 (CH), 123.5 (CH), 115.3 (C_q), 62.8 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 3056, 2973, 1575, 1557, 1422, 1324, 1045, 1020, 763, 693 cm^{-1}. **MS** (ESI) m/z (relative intensity): 224 (40), 251 (100) $[M+H]^+$, 273 (10) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$: 251.1179, found: 251.1183.

The analytical data were in accordance with those reported in the literature.[199]

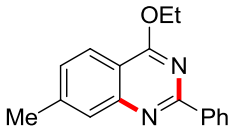


4-Methoxy-2-phenylquinazoline (163ba): The general procedure **C** was followed using methyl benzimidate (**161b**) (33.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ba** (43.0 mg, 73%) as a white solid.

M. p. = 49–50 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.63–8.60 (m, 2H), 8.16 (ddd, *J* = 8.2, 1.5, 0.7 Hz, 1H), 8.00 (ddd, *J* = 8.4, 1.2, 0.7 Hz, 1H), 7.81 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.55–7.48 (m, 4H), 4.29 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 167.2 (C_q), 160.2 (C_q), 152.0 (C_q), 138.3 (C_q), 133.6 (CH), 130.6

(CH), 128.6 (CH), 128.5 (CH), 128.1 (CH), 126.5 (CH), 123.6 (CH), 115.4 (C_q), 54.2 (CH_3). **IR** (ATR) *v* = 3058, 1620, 1557, 1501, 1444, 1375, 1103, 911, 759, 672 cm^{-1}. **MS** (ESI) m/z (relative intensity): 237 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{15}H_{13}N_2O$ $[M+H]^+$: 237.1022, found: 237.1026.

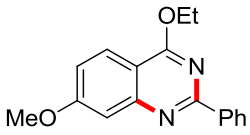
The analytical data were in accordance with those reported in the literature.[199]



4-Ethoxy-7-methyl-2-phenylquinazoline (163ca): The general procedure **C** was followed using ethyl 4-methylbenzimidate (**161c**) (40.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ca** (60.0 mg, 91%) as a white solid.

M. p. = 92–93 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.56 (dd, *J* = 7.5, 2.3 Hz, 2H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.76 (s, 1H), 7.58–7.40 (m, 3H), 7.30 (dd, *J* = 8.3, 1.6 Hz, 1H), 4.74 (q, *J* = 7.1 Hz, 2H), 2.53 (s, 3H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.5 (C_q), 160.1 (C_q), 152.1 (C_q), 144.1 (C_q), 138.4 (C_q), 130.3 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.1 (CH), 123.2 (CH), 113.2 (C_q), 62.6 (CH_2), 22.1 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2958, 1622, 1553, 148.95, 1414, 1326, 1018, 927, 799, 679 cm^{-1}. **MS** (ESI) m/z (relative intensity): 237 (25), 265 (100) $[M+H]^+$, 287 (10) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1335, found: 265.1339.

The analytical data were in accordance with those reported in the literature.[199]

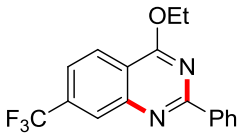


4-Ethoxy-7-methoxy-2-phenylquinazoline (163da): The general procedure **C** was followed using ethyl 4-methoxybenzimidate (**161d**) (44.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163da** (62.2 mg, 89%) as a white solid.

M. p. = 131–132 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.55 (dd, *J* = 7.8, 1.9 Hz, 2H), 8.02 (d, *J* = 9.3 Hz, 1H), 7.63–7.41 (m, 3H), 7.29 (d, *J* = 2.5 Hz, 1H), 7.08 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.72 (q, *J* = 7.1 Hz, 2H),

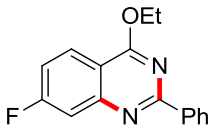
3.94 (s, 3H), 1.53 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.3 (C_q), 163.7 (C_q), 160.7 (C_q), 154.2 (C_q), 138.3 (C_q), 130.3 (CH), 128.4 (CH), 128.3 (CH), 124.8 (CH), 118.5 (CH), 109.7 (C_q), 106.5 (CH), 62.5 (CH_2), 55.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2982, 1622, 1584, 1438, 1348, 1210, 1158, 1019, 768, 703 cm^{-1}. **MS** (ESI) m/z (relative intensity): 253 (25), 281 (100) $[M+H]^+$, 203 (10) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$: 281.1285, found: 282.1281.

The analytical data were in accordance with those reported in the literature.[199]



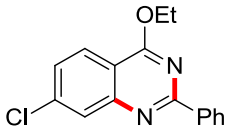
4-Ethoxy-2-phenyl-7-(trifluoromethyl)quinazoline (163ea): The general procedure **C** was followed using ethyl 4-(trifluoromethyl)benzimidate (**161e**) (54.3 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ea** (66.9 mg, 84%) as a white solid.

M. p. = 101–103 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.56 (dd, *J* = 6.5, 3.3 Hz, 2H), 8.23 (d, *J* = 7.9 Hz, 2H), 7.64 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.57–7.44 (m, 3H), 4.76 (q, *J* = 7.1 Hz, 2H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.5 (C_q), 161.3 (C_q), 151.3 (C_q), 137.5 (C_q), 134.9 (q, $^2J_{C-F}$ = 32.9 Hz, C_q), 130.9 (CH), 128.5 (CH), 128.4 (CH), 125.6 (q, $^3J_{C-F}$ = 4.1 Hz, CH), 124.9 (CH), 121.9 (q, $^3J_{C-F}$ = 3.2 Hz, CH), 123.6 (q, $^1J_{C-F}$ = 273.3 Hz, C_q), 117.0 (C_q), 63.3 (CH_2), 14.3 (CH_3). **^{19}F NMR** (283 MHz, $CDCl_3$) δ = -63.20. **IR** (ATR) *v* = 2995, 1581, 1557, 1450, 1327, 1176, 1119, 895, 715 cm^{-1}. **MS** (ESI) m/z (relative intensity): 319 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{14}N_2OF_3$ $[M+H]^+$: 319.1053, found: 319.1055.



4-Ethoxy-7-fluoro-2-phenylquinazoline (163fa): The general procedure **C** was followed using ethyl 4-fluorobenzimidate (**161f**) (41.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163fa** (66.9 mg, 98%) as a white solid.

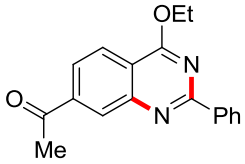
M. p. = 93–94 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.55 (dd, *J* = 6.6, 3.2 Hz, 2H), 8.13 (dd, *J* = 9.0, 6.2 Hz, 1H), 7.57 (dd, *J* = 10.1, 2.5 Hz, 1H), 7.52–7.47 (m, 3H), 7.21 (td, *J* = 8.7, 2.5 Hz, 1H), 4.73 (q, *J* = 7.1 Hz, 2H), 1.54 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.4 (C_q), 165.7 (d, $^{1}J_{C\text{-}F}$ = 253.1 Hz, C_q), 161.2 (C_q), 153.7 (d, $^{3}J_{C\text{-}F}$ = 13.9 Hz, C_q), 137.8 (C_q), 130.7 (CH), 128.5 (CH), 128.4 (CH), 126.2 (d, $^{3}J_{C\text{-}F}$ = 11.1 Hz, CH), 116.0 (d, $^{2}J_{C\text{-}F}$ = 24.9 Hz, CH), 112.2 (d, $^{4}J_{C\text{-}F}$ = 3.7 Hz, C_q), 112.0 (d, $^{2}J_{C\text{-}F}$ = 20.4 Hz, CH), 62.9 (CH_2), 14.3 (CH_3). **^{19}F NMR** (283 MHz, $CDCl_3$) δ = -104.33 (ddd, *J* = 10.1, 8.4, 6.2 Hz). **IR** (ATR) *v* = 2975, 1626, 1562, 1416, 1340, 1156, 1018, 861, 770, 676 cm^{-1}. **MS** (ESI) m/z (relative intensity): 241 (30), 269 (100) $[M+H]^+$, 291 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}N_2OF$ $[M+H]^+$: 269.1085, found: 269.1086.



7-Chloro-4-ethoxy-2-phenylquinazoline (163ga): The general procedure **C** was followed using ethyl 4-chlorobenzimidate (**161g**) (45.9 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ga** (68.0 mg, 96%) as a white solid.

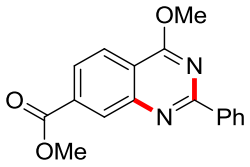
M. p. = 104–105 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.56–8.52 (m, 2H), 8.05 (dd, *J* = 8.7, 0.5 Hz, 1H), 7.94 (dd, *J* = 2.0, 0.5 Hz, 1H), 7.63–7.44 (m, 3H), 7.41 (dd, *J* = 8.7, 2.0 Hz, 1H), 4.73 (q, *J* = 7.1 Hz, 2H), 1.54 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.5 (C_q), 161.1 (C_q), 152.6 (C_q), 139.4 (C_q), 137.8 (C_q), 130.7 (CH), 128.5 (CH), 128.4 (CH), 127.1 (CH), 127.1 (CH), 124.9 (CH), 113.7 (C_q), 63.0 (CH_2), 14.3 (CH_3). **IR** (ATR) *v* = 2975, 1615, 1556, 1431, 1340, 1317, 1018, 871, 772, 704 cm^{-1}. **MS** (ESI) m/z (relative intensity): 257 (30), 285 (100) $[M+H]^+$, 307 (20) $[M+N_a]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}N_2OCl$ $[M+H]^+$: 285.0789, found: 285.0792.

The analytical data were in accordance with those reported in the literature.[199]



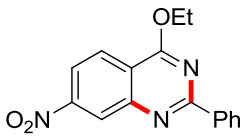
1-(4-Ethoxy-2-phenylquinazolin-7-yl)ethanone (163ha): The general procedure **C** was followed using ethyl 4-acetylbenzimidate (**161h**) (47.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ha** (53.4 mg, 73%) as a pale yellow solid.

M. p. = 139–140 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.56 (dd, *J* = 6.7, 3.2 Hz, 2H), 8.49 (d, *J* = 1.6 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 8.03 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.59–7.42 (m, 3H), 4.77 (q, *J* = 7.1 Hz, 2H), 2.74 (s, 3H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 197.8 (C_q), 166.6 (C_q), 161.0 (C_q), 151.8 (C_q), 140.8 (C_q), 137.7 (C_q), 130.8 (CH), 129.3 (CH), 128.5 (CH), 128.5 (CH), 124.2 (CH), 124.1 (CH), 117.8 (C_q), 63.3 (CH_2), 26.9 (CH_3), 14.3 (CH_3). **IR** (ATR) *v* = 2974, 1686, 1551, 1384, 1318, 1221, 1019, 777, 714, 676 cm^{-1}. **MS** (ESI) m/z (relative intensity): 293 (95) $[M+H]^+$, 315 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{17}N_2O_2$ $[M+H]^+$: 293.1285, found: 293.1280.



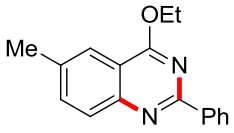
Methyl 4-methoxy-2-phenylquinazoline-7-carboxylate (163ia): The general procedure **C** was followed using methyl 4-[imino(methoxy)methyl]benzoate (**161i**) (48.3 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **163ia** (48.0 mg, 72%) as a white solid.

M. p. = 124–125 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.62 (d, *J* = 2.1 Hz, 1H), 8.60–8.54 (m, 2H), 8.14 (dd, *J* =8.5, 0.7 Hz, 1H), 8.07–8.03 (m, 1H), 7.55–7.45 (m, 3H), 4.26 (s, 3H), 3.97 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.9 (C_q), 166.3 (C_q), 160.7 (C_q), 151.4 (C_q), 137.7 (C_q), 134.5 (C_q), 130.7 (CH), 130.1 (CH), 128.5 (CH), 128.4 (CH), 125.9 (CH), 123.7 (CH), 117.6 (C_q), 54.3 (CH_3), 52.5 (CH_3). **IR** (ATR) *v* = 2945, 1718, 1556, 148.99, 1373, 1267, 909, 753, 713 cm^{-1}. **MS** (ESI) m/z (relative intensity): 295 (100) $[M+H]^+$, 317 (95) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{15}N_2O_3$ $[M+H]^+$: 295.1077, found: 295.1080.



4-Ethoxy-7-nitro-2-phenylquinazoline (163ja): The general procedure **C** was followed using ethyl 4-nitrobenzimidate (**161j**) (48.9 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ja** (42.0 mg, 57%) as a white solid.

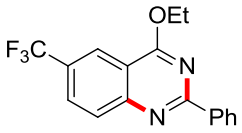
M. p. = 151–153 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.74 (dd, *J* = 2.2, 0.6 Hz, 1H), 8.62–8.48 (m, 2H), 8.24 (dd, *J* = 8.9, 0.6 Hz, 1H), 8.17 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.41–6.70 (m, 3H), 4.76 (q, *J* = 7.1 Hz, 2H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.4 (C_q), 162.0 (C_q), 151.7 (C_q), 150. 9 (C_q), 137.1 (C_q), 131.2 (CH), 128.6 (CH), 128.5 (CH), 125.5 (CH), 123.7 (CH), 119.5 (CH), 118.5 (C_q), 63.7 (CH_2), 14.2 (CH_3). **IR** (ATR) *v* = 2982, 1565, 1531, 1337, 1068, 1012, 892, 821, 739, 670 cm^{-1}. **MS** (ESI) m/z (relative intensity): 296 (95) $[M+H]^+$, 318 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{13}N_3O_3$ $[M+H]^+$: 296.1030, found: 296.1027.



4-Ethoxy-6-methyl-2-phenylquinazoline (163ka): The general procedure **C** was followed using ethyl 3-methylbenzimidate (**161k**) (41.0 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ka** (60.0 mg, 91%) as a white solid.

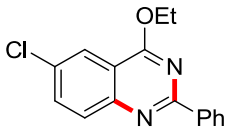
M. p. = 89–91 ˚C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.56 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.92 (s, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.54–7.40 (m, 3H), 4.75 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.2 (C_q), 159.2 (C_q), 150.2 (C_q), 138.3 (C_q), 136.3 (C_q), 135.3 (CH), 130.2 (CH), 128.3 (CH), 128.3 (CH), 127.6 (CH), 122.4 (CH), 115.1 (C_q), 62.6 (CH_2), 21.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2976, 1562, 1383, 1312, 1108, 1023, 780, 707 cm^{-1}. **MS** (ESI) m/z (relative intensity): 265 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1335, found: 265.1338.

The analytical data were in accordance with those reported in the literature.[199]



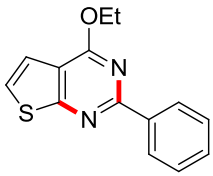
4-Ethoxy-2-phenyl-6-(trifluoromethyl)quinazoline (163la): The general procedure **C** was followed using ethyl 3-(trifluoromethyl)benzimidate (**161l**) (54.3 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163la** (46.0 mg, 58%) as a white solid.

M. p. = 129–130 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.62–8.52 (m, 2H), 8.45 (t, *J* = 0.9 Hz, 1H), 8.05 (d, *J* = 8.8 Hz, 1H), 7.95 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.57–7.46 (m, 3H), 4.80 (q, *J* = 7.1 Hz, 2H), 1.58 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 167.0 (C_q), 162.0 (C_q), 153.3 (C_q), 137. 6 (C_q), 131.1 (CH), 129.2 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz, CH), 128.9 (CH), 128.7 (CH), 128.5 (CH), 127.9 (q, $^{2}J_{C\text{-}F}$ = 33.0 Hz, C_q) 123.8 (q, $^{1}J_{C\text{-}F}$ = 271.9 Hz, C_q), 121.8 (q, $^{3}J_{C\text{-}F}$ = 4.5 Hz, CH), 114.7 (C_q), 63.4 (CH_2), 14.3 (CH_3). **^{19}F NMR** (283 MHz, $CDCl_3$) δ = -62.27. **IR** (ATR) *v* = 2992, 1634, 1575, 1443, 1320, 1107, 873, 686 cm^{-1}. **MS** (ESI) m/z (relative intensity): 295 (90), 319 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{14}N_2OF_3$ $[M+H]^+$: 319.1053, found: 319.1049.



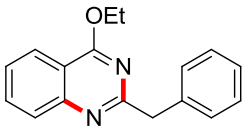
6-Chloro-4-ethoxy-2-phenylquinazoline (163ma): The general procedure **C** was followed using ethyl 3-chlorobenzimidate (**161m**) (46 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ma** (62.3 mg, 88%) as a white solid.

M. p. = 132–133 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.53 (dd, *J* = 6.7, 3.2 Hz, 2H), 8.09 (d, *J* = 2.4 Hz, 1H), 7.87 (d, *J* = 8.9 Hz, 1H), 7.69 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.53–7.43 (m, 3H), 4.73 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 165.8 (C_q), 160.2 (C_q), 150.3 (C_q), 137.8 (C_q), 134.1 (CH), 131.7 (C_q), 130.6 (CH), 129.5 (CH), 128.4 (CH), 128.4 (CH), 122.7 (CH), 115.9 (C_q), 63.1 (CH_2), 14.3 (CH_3). **IR** (ATR) *v* = 2975, 1555, 1488, 1412, 1306, 1022, 834, 670, 547 cm^{-1}. **MS** (ESI) m/z (relative intensity): 285 (100) $[M+H]^+$, 287 (30). **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}N_2OCl$ $[M+H]^+$: 285.0789, found: 285.0789.



4-Ethoxy-2-phenylthieno[2,3-d]pyrimidine (163na): The general procedure **C** was followed using ethyl thiophene-3-carbimidate (**161n**) (39 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded **163na** (38.0 mg, 60%) as a white solid.

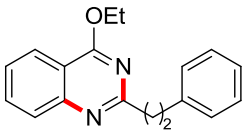
M. p. = 51–53 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.54–8.51 (m, 2H), 7.53–7.46 (m, 3H), 7.38 (d, *J* = 5.9 Hz, 1H), 7.33 (d, *J* = 5.9 Hz, 1H), 4.75 (q, *J* = 7.1 Hz, 2H), 1.54 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 169.7 (C_q), 163.8 (C_q), 159.9 (C_q), 137.8 (C_q), 130.5 (CH), 128.6 (CH), 128.5 (CH), 124.1 (CH), 118.8 (CH), 117.5 (C_q), 62.7 (CH_2), 14.7 (CH_3). **IR** (ATR) *v* = 2982, 1618, 1567, 1535, 1468, 1381, 1319, 1038, 889, 686, 664 cm^{-1}. **MS** (ESI) m/z (relative intensity): 257 (100) $[M+H]^+$, 279 (23) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{14}H_{13}N_2OS$ $[M+H]^+$: 257.0749, found: 257.0745.



2-Benzyl-4-ethoxyquinazoline (163ab): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-benzyloxazol-2(5*H*)-one (**162b**) (52.6 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded **163ab** (56.9 mg, 88%) as a yellow oil.

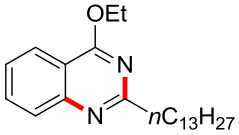
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.11 (ddd, *J* = 8.2, 1.5, 0.7 Hz, 1H), 7.88 (ddd, *J* = 8.4, 1.2, 0.6 Hz, 1H), 7.77 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.50–7.44 (m, 3H), 7.32–7.27 (m, 2H), 7.23–7.17 (m, 1H), 4.59 (q, *J* = 7.1 Hz, 2H), 4.26 (s, 2H), 1.45 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.8 (C_q), 165.3 (C_q), 151.1 (C_q), 138.9 (C_q), 133.3 (CH), 129.5 (CH), 128.3 (CH), 127.4 (CH), 126.4 (CH), 126.2 (CH), 123.5 (CH), 115.1 (C_q), 63.0 (CH_2), 46.5 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2926, 1619, 1573, 148.97, 1457, 1420, 1325, 1105, 770, 696 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 265 (100) $[M+H]^+$, 237 (29), 287 (15) $[M+Na]^+$. **HRMS** (ESI) calcd for $C_{17}H_{17}N_2O$ ($[M+H]^+$): 265.1335; found 265.1337.

The analytical data were in accordance with those reported in the literature.[199]



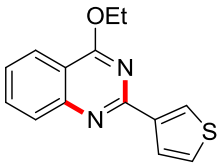
4-Ethoxy-2-phenethylquinazoline (163ac): The general procedure **C** was followed using ethyl benzimidate (**161c**) (37.3 mg, 0.25 mmol) and 5-phenethyloxazol-2(5*H*)-one (**162a**) (56.8 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **163ac** (56.9 mg, 82%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 (ddd, *J* = 8.2, 1.6, 0.7 Hz, 1H), 7.86 (ddd, *J* = 8.4, 1.3, 0.7 Hz, 1H), 7.76 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.47 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.32–7.24 (m, 4H), 7.20–7.14 (m, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 3.31–3.29 (m, 4H), 1.50 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.6 (C_q), 166.1 (C_q), 151.4 (C_q), 141.9 (C_q), 133.3 (CH), 128.5 (CH), 128.4 (CH), 127.2 (CH), 126.0 (CH), 125.9 (CH), 123.5 (CH), 115.0 (C_q), 62.9 (CH_2), 41.5 (CH_2), 35.0 (CH_2), 14.6 (CH_3). **MS** (ESI) m/z (relative intensity): 279 (100) $[M+H]^+$. **IR** (ATR) *v* = 2979, 1620, 1572, 1496, 1419, 1322, 1103, 769, 683 cm^{-1}. **HR-MS** (ESI) m/z calcd for $C_{18}H_{18}N_2O$ $[M+H]^+$: 279.1492, found: 279.1497.



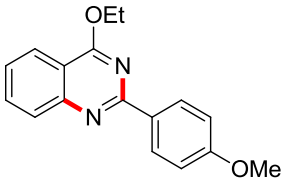
4-Ethoxy-2-tridecylquinazoline (163ad): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-tridecyloxazol-2(5*H*)-one (**162d**) (80.8 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 30/1) yielded **163ad** (54.0 mg, 61%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.75 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.46 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 2.94–2.89 (m, 2H), 1.91–1.81 (m, 2H), 1.50 (t, *J* = 7.1 Hz, 3H), 1.42–1.14 (m, 20H), 0.89–0.85 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 167.5 (C_q), 166.6 (C_q), 151.5 (C_q), 133.3 (CH), 127.2 (CH), 125.9 (CH), 125.5 (CH), 115.0 (C_q), 62.8 (CH_2), 40.1 (CH_2), 32.1 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 28.8 (CH_2), 22.8 (CH_2), 14.5 (CH_3), 14.3 (CH_3). **IR** (ATR) *v* = 2922, 2852, 1621, 1571, 1496, 1419, 1325, 1102, 768 cm^{-1}. **MS** (ESI) m/z (relative intensity): 357 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{36}N_2O$ $[M+H]^+$: 357.2900, found: 357.2905.



4-Ethoxy-2-(thiophen-3-yl)quinazoline (163ae): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-(thiophen-3-yl)oxazol-2(5*H*)-one (**162e**) (50.7 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ae** (58.1 mg, 91%) as a colorless oil.

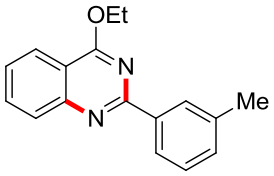
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.08 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.77 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.48–7.43 (m, 2H), 7.16 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.73 (q, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 157.0 (C_q), 151.2 (C_q), 144.4 (C_q), 133.6 (CH), 129.6 (CH), 128.9 (CH), 128.2 (CH), 127.6 (CH), 126.1 (CH), 123.7 (CH), 115.4 (C_q), 63.1 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2980, 1618, 1560, 1494, 1417, 1339, 1104, 845, 767 cm^{-1}. **MS** (ESI) m/z (relative intensity): 229 (40), 257 (100) $[M+H]^+$, 279 (20) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{14}H_{12}N_2OS$ $[M+H]^+$: 257.0743, found: 257.0744.



4-Ethoxy-2-(4-methoxyphenyl)quinazoline (163af): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-(4-methoxyphenyl)oxazol-2(5*H*)-one (**162f**) (57.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **163af** (46.9 mg, 68%) as a white solid.

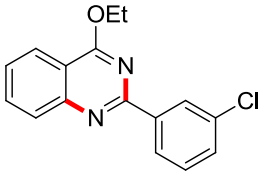
M. p. = 70–71 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.54 (d, *J* = 9.0 Hz, 2H), 8.14 (ddd, *J* = 8.2, 1.5, 0.7 Hz, 1H), 7.94 (ddd, *J* = 8.5, 1.2, 0.7 Hz, 1H), 7.78 (ddd, *J* = 8.5, 1.2, 1.6 Hz, 1H), 7.46 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.02 (d, *J* = 9.0 Hz, 2H), 4.76 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 165.5 (C_q), 161.7 (C_q), 159.9 (C_q), 152.0 (C_q), 133.3 (CH), 131.1 (C_q), 130.1 (CH), 127.7 (CH), 125.8 (CH), 123.5 (CH), 115.2 (C_q), 113.8 (CH), 62.8 (CH_2), 55.5 (CH_3), 14.7 (CH_3). **IR** (ATR) *v* = 3047, 1603, 1574, 1497, 1328, 1249, 1151, 765, 680, 542 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 281 (100) $[M+H]^+$. **HRMS** (ESI) *m/z* calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$: 281.1290 found 281.1285.

The analytical data were in accordance with those reported in the literature.[200]



4-Ethoxy-2-(*m*-tolyl)quinazoline (163ag): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-(*m*-tolyl)oxazol-2(5*H*)-one (**162g**) (53.2 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ag** (56.9 mg, 86%) as a white solid.

M. p. = 72–74 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.42–8.34 (m, 2H), 8.15 (ddd, *J* = 8.2, 1.5, 0.6 Hz, 1H), 7.97 (ddd, *J* = 8.4, 0.7 Hz, 1H), 7.78 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.48 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 4.77 (q, *J* = 7.1 Hz, 2H), 2.48 (s, 3H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.6 (C_q), 160.2 (C_q), 151.8 (C_q), 138.2 (C_q), 137.9 (C_q), 133.3 (CH), 131.2 (CH), 128.9 (CH), 128.3 (CH), 127.8 (CH), 126.1 (CH), 125.7 (CH), 123.5 (CH), 115.3 (C_q), 62.8 (CH_2), 21.5 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2982, 1620, 1561, 1498, 1418, 1323, 1161, 1104, 1018, 765 cm^{-1}. **MS** (ESI) m/z (relative intensity): 265 (100) $[M+H]^+$, 287 $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1335, found: 265.1332.

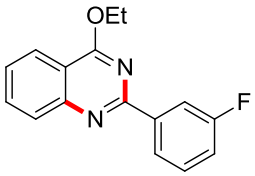


2-(3-Chlorophenyl)-4-ethoxyquinazoline (163ah): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-(3-chlorophenyl)oxazol-2(5*H*)-one (**162h**) (59.3 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ah** (43.4 mg, 61%) as a white solid.

M. p. = 85–87 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.54 (td, *J* = 1.7, 0.7 Hz, 1H), 8.48.9–8.38 (m, 1H), 8.15 (ddd, *J* = 8.2, 1.5, 0.7 Hz, 1H), 7.95 (ddd, *J* = 8.4, 1.1, 0.7 Hz, 1H), 7.79 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.50 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.45–7.36 (m, 2H), 4.74 (q, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.8 (C_q), 158.6 (C_q), 151.7 (C_q), 140.1 (C_q), 134.5 (C_q), 133.5

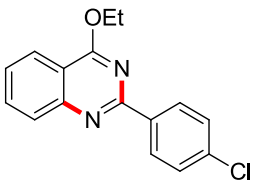
(CH), 130.3 (CH), 129.6 (CH), 128.5 (CH), 127.9 (CH), 126.6 (CH), 126.5 (CH), 123.5 (CH), 115.5 (C_q), 63.0 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2975, 1620, 1575, 1499, 1418, 1325, 1171, 1015, 764, 672 cm^{-1}. **MS** (ESI) m/z (relative intensity): 285 (100) $[M+H]^+$, 307 (30) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}N_2OCl$ $[M+H]^+$: 285.0789, found: 285.0788.

The analytical data were in accordance with those reported in the literature.[199]



4-Ethoxy-2-(3-fluorophenyl)quinazoline (163ai): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 3-(3-fluorophenyl)-1,4,2-dioxazol-5*H*-one (**162i**) (54.3 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 40/1) yielded **163ai** (51.3 mg, 76%) as a white solid.

M. p. = 84–86 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.36 (ddd, *J* = 7.8, 1.5, 1.0 Hz, 1H), 8.26 (ddd, *J* = 10.5, 2.5, 1.4 Hz, 1H), 8.14 (ddd, *J* = 8.2, 1.5, 0.7 Hz, 1H), 7.95 (ddd, *J* = 8.4, 1.1, 0.7 Hz, 1H), 7.79 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.58–7.37 (m, 2H), 7.16 (ddd, *J* = 8.3, 2.7, 1.0 Hz, 1H), 4.74 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.7 (C_q), 163.1 (d, ^1J = 246.3 Hz, C_q), 168.8 (d, ^4J = 3.8 Hz, C_q), 151.7 (C_q), 140.7 (d, ^3J = 7.8 Hz, C_q), 133.5 (CH), 130.0 (d, ^3J = 7.8 Hz, CH), 127.9 (CH), 126.5 (CH), 124.0 (d, ^4J = 2.9 Hz, CH), 123.5 (CH), 117.2 (d, ^2J = 21.4 Hz, CH), 115.5 (C_q), 115.3 (d, ^2J = 22.2 Hz, CH), 62.9 (CH_2), 14.4 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -113.58 (ddd, *J* = 10.3, 8.4, 5.9 Hz). **IR** (ATR) *v* = 2984, 1622, 1575, 1499, 1424, 1325, 1167, 1018, 902, 770 cm^{-1}. **MS** (ESI) m/z (relative intensity): 265 (100) $[M+H]^+$, 287 $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}FN_2O$ $[M+H]^+$: 269.1085, found: 269.1086.

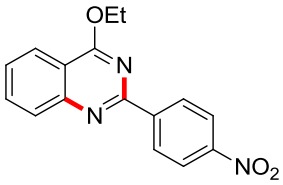


2-(4-Chlorophenyl)-4-ethoxyquinazoline (163aj): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-(4-chlorophenyl)oxazol-2(5*H*)-one (**162j**) (59.3 mg,

0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 30/1) yielded **163aj** (66.0 mg, 93%) as a white solid.

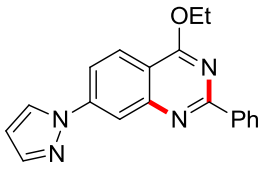
M. p. = 119–120 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.57 (d, *J* = 8.6 Hz, 2H), 8.15 (d, *J* = 7.1 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.79 (ddd, *J* = 8.5, 6.9, 1.6 Hz, 1H), 7.53–7.49 (m, 1H), 7.46 (d, *J* = 8.6 Hz, 2H), 4.73 (q, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.8 (C_q), 159.1 (C_q), 151.8 (C_q), 138.8 (C_q), 136.6 (C_q), 133.6 (CH), 129.9 (CH), 128.7 (CH), 128.0 (CH), 126.6 (CH), 123.6 (CH), 115.5 (C_q), 63.0 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2979, 1620, 1575, 1501, 1325, 1088, 937, 837, 763, 539 cm^{-1}. **MS** (ESI) m/z (relative intensity): 285 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}N_2OCl$ $[M+H]^+$: 285.0789, found: 285.0789.

The analytical data were in accordance with those reported in the literature.[199]



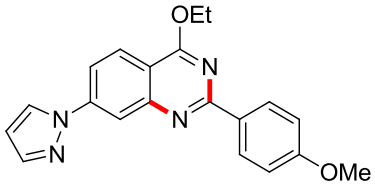
4-Ethoxy-2-(4-nitrophenyl)quinazoline (163ak): The general procedure **C** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 5-(4-nitrophenyl)oxazol-2(5*H*)-one (**162k**) (62.4 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **163ak** (44.8 mg, 60%) as a pale yellow solid.

M. p. = 154–155 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 9.0 Hz, 2H), 8.33 (d, *J* = 9.0 Hz, 2H), 8.21 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.86 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.58 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 4.79 (q, *J* = 7.1 Hz, 2H), 1.60 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 167.1 (C_q), 157.9 (C_q), 151.7 (C_q), 148.9 (C_q), 144.3 (C_q), 134.0 (CH), 129.3 (CH), 128.3 (CH), 127.5 (CH), 123.8 (CH), 123.7 (CH), 115.7 (C_q), 63.3 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2987, 1622, 1576, 1501, 1343, 1331, 1081, 765, 715, 670 cm^{-1}. **MS** (EI) *m/z* (relative intensity): 268 (15), 296 (100) $[M+H]^+$, 318 (60) $[M+Na]^+$. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}N_3O_3$ $[M+H]^+$: 296.1030, found 296.1030.



4-Ethoxy-2-phenyl-7-(1*H*-pyrazol-1-yl)quinazoline (163ka): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 25/1) yielded **163ka** (55.4 mg, 70%) as a white solid.

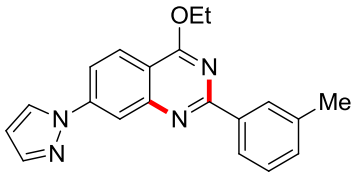
M. p. = 129–130 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.62–8.50 (m, 2H), 8.21 (dd, *J* = 8.9, 0.5 Hz, 1H), 8.12 (dd, *J* = 2.6, 0.6 Hz, 1H), 8.10 (dd, *J* = 2.2, 0.4 Hz, 1H), 8.04 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.79 (dd, *J* = 1.7, 0.6 Hz, 1H), 7.55–7.45 (m, 3H), 6.53 (dd, *J* = 2.6, 1.7 Hz, 1H), 4.75 (q, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.5 (C_q), 161.2 (C_q), 152.8 (C_q), 143.7 (C_q), 142.0 (CH), 138.0 (C_q), 130.6 (CH), 128.5 (CH), 128.4 (CH), 127.1 (CH), 125.3 (CH), 118.4 (CH), 115.1 (CH), 113.3 (C_q), 108.6 (CH), 63.0 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2974, 1713, 1626, 1565, 1472, 1394, 1333, 1025, 740, 698 cm^{-1}. **MS** (ESI) m/z (relative intensity): 317 (100) $[M+H]^+$, 339 (75) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{17}N_4O$ $[M+H]^+$: 317.1397, found: 317.1400.



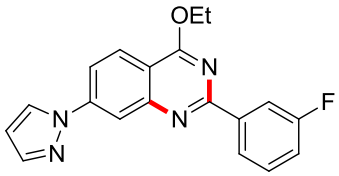
4-Ethoxy-2-(4-methoxyphenyl)-7-(1*H*-pyrazol-1-yl)quinazoline (163kf): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 3-(4-methoxyphenyl)-1,4,2-dioxazol-5-one (**162f**) (58.0 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163kf** (51.0 mg, 59%) as a white solid.

M. p. = 138–140 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 9.0 Hz, 2H), 8.19 (dd, *J* = 8.9, 0.6 Hz, 1H), 8.11 (d, *J* = 3.0 Hz, 1H), 8.06 (d, *J* = 1.8 Hz, 1H), 8.00 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.78 (d, *J* = 1.4 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 2H), 6.52 (dd, *J* = 2.5, 1.7 Hz, 1H), 4.73 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.3 (C_q), 161.8 (C_q), 161.0 (C_q), 152.9 (C_q), 143.7 (C_q), 141.9 (CH), 130.7 (C_q), 130.1 (CH), 127.1 (CH), 125.3 (CH), 117.9 (CH), 114.8 (CH), 113.7 (CH), 113.1 (C_q), 108.5 (CH), 62.8 (CH_2), 55.4 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2983, 2834, 1626, 1579, 1512,

1422, 1331, 1159, 1018, 749 cm^{-1}. **MS** (ESI) m/z (relative intensity): 236 (20), 347 (100) $[M+H]^+$, 369 (20) $[M+Na]^+$, 715 (10) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{19}N_4O_2$ $[M+H]^+$: 347.1503, found: 347.1504.

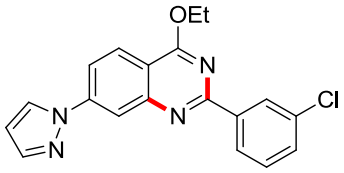


4-Ethoxy-7-(1*H*-pyrazol-1-yl)-2-(*m*-tolyl)quinazoline (163kg): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 3-(*m*-tolyl)-1,4,2-dioxazol-5-one (**162g**) (53.2 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **163kg** (51.8 mg, 63%) as a white solid. **M. p.** = 149–151 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.38–8.33 (m, 2H), 8.23 (dd, *J* = 8.9, 0.6 Hz, 1H), 8.13 (dd, *J* = 2.6, 0.6 Hz, 1H), 8.11 (dd, *J* = 2.2, 0.6 Hz, 1H), 8.05 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.79 (dd, *J* = 1.7, 0.6 Hz, 1H), 7.39 (td, *J* = 7.5, 0.8 Hz, 1H), 7.32–7.28 (m, 1H), 6.53 (dd, *J* = 2.6, 1.7 Hz, 1H), 4.76 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.5 (C_q), 161.4 (C_q), 152.8 (C_q), 143.7 (C_q), 142.0 (CH), 138.0 (C_q), 137.9 (C_q), 131.5 (CH), 129.0 (CH), 128.3 (CH), 127.1 (CH), 125.7 (CH), 125.4 (CH), 118.4 (CH), 115.0 (CH), 113.3 (C_q), 108.6 (CH), 63.0 (CH_2), 21.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 3127, 2977, 1625, 1579, 1435, 1333, 1017, 870, 767, 600 cm^{-1}. **MS** (ESI) m/z (relative intensity): 331 (100) $[M+H]^+$, 353 (20) $[M+Na]^+$, 683 (20) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{19}N_4O$ $[M+H]^+$: 331.1553, found: 331.1557.

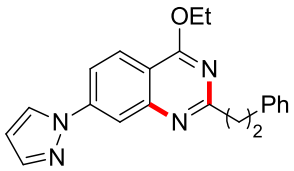


4-Ethoxy-2-(3-fluorophenyl)-7-(1*H*-pyrazol-1-yl)quinazoline (163ki): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 3-(3-fluorophenyl)-1,4,2-dioxazol-5-one (**162i**) (54.4 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded **163ki** (49.1 mg, 59%) as a white solid. **M. p.** = 154–155 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.39 (dt, *J* = 7.8, 1.1 Hz, 1H), 8.34–8.23 (m, 2H),

8.16 (dd, *J* = 2.6, 0.4 Hz, 1H), 8.15–8.07 (m, 2H), 7.83 (d, *J* = 1.6 Hz, 1H), 7.49 (td, *J* = 8.0, 5.8 Hz, 1H), 7.21 (tdd, *J* = 8.3, 2.7, 1.0 Hz, 1H), 6.58 (dd, *J* = 2.6, 1.6 Hz, 1H), 4.79 (q, *J* = 7.1 Hz, 2H), 1.60 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.5 (C_q), 163.1 (d, ^1J = 244.4 Hz, C_q), 160.0 (d, ^4J = 3.4 Hz, C_q), 152.6 (C_q), 143.8 (C_q), 142.1 (CH), 140.4 (d, ^3J = 7.8 Hz, C_q), 129.8 (d, ^3J = 7.8 Hz, CH), 127.1 (CH), 125.4 (CH), 124.1 (d, ^4J = 2.8 Hz, CH), 118.7 (CH), 117.4 (d, ^2J = 21.5 Hz, CH), 115.3 (d, ^2J = 23.2 Hz, CH), 115.0 (CH), 113.4 (C_q), 108.7 (CH), 63.1 (CH_2), 14.4 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -113.44 (ddd, *J* = 10.5, 8.5, 5.9 Hz). **IR** (ATR) *v* = 3129, 2979, 1624, 1578, 1564, 1333, 956, 875, 778, 676 cm^{-1}. **MS** (ESI) m/z (relative intensity): 335 (100) $[M+H]^+$, 357 (80), 691 $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}FN_4O$ $[M+H]^+$: 335.1303, found: 335.1305.

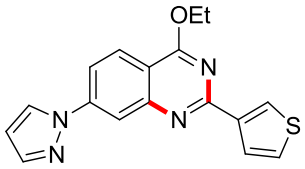


2-(3-Chlorophenyl)-4-ethoxy-7-(1*H*-pyrazol-1-yl)quinazoline (163kh): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 3-(3-chlorophenyl)-1,4,2-dioxazol-5-one (**162h**) (59.3 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **163kh** (56.3 mg, 64%) as a white solid. **M. p.** = 168–170 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 1.8 Hz, 1H), 8.46 (dt, *J* = 6.8, 1.8 Hz, 1H), 8.24 (dd, *J* = 8.7, 0.6 Hz, 1H), 8.15 (d, *J* = 2.6 Hz, 1H), 8.12–8.00 (m, 2H), 7.82 (d, *J* = 1.5 Hz, 1H), 7.56–7.37 (m, 2H), 6.57 (dd, *J* = 2.5, 1.8 Hz, 1H), 4.77 (q, *J* = 7.1 Hz, 2H), 1.59 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 159.8 (C_q), 152.6 (C_q), 143.8 (C_q), 142.1 (CH), 139.9 (C_q), 134.5 (C_q), 130.5 (CH), 129.6 (CH), 128.5 (CH), 127.1 (CH), 126.6 (CH), 125.4 (CH), 118.7 (CH), 115.0 (CH), 113.4 (C_q), 108.7 (CH), 63.2 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2979, 1626, 1578, 1381, 1333, 875, 745, 676, 603 cm^{-1}. **MS** (ESI) m/z (relative intensity): 351 (100) $[M+H]^+$, 732 (60) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}ClN_4O$ $[M+H]^+$: 351.1007, found: 351.1007.



4-Ethoxy-2-phenethyl-7-(1*H*-pyrazol-1-yl)quinazoline (163kc): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 3-phenethyl-1,4,2-dioxazol-5-one (**162c**) (57.4 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163kc** (47.2 mg, 55%) as a white solid.

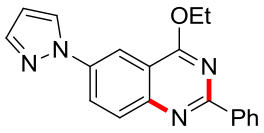
M. p. = 92–93 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.20 (dd, *J* = 8.9, 0.6 Hz, 1H), 8.09 (dd, *J* = 2.6, 0.6 Hz, 1H), 8.05 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.99 (dd, *J* = 2.2, 0.5 Hz, 1H), 7.78 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.31–7.24 (m, 4H), 7.20–7.13 (m, 1H), 6.52 (dd, *J* = 2.6, 1.7 Hz, 1H), 4.62 (q, *J* = 7.1 Hz, 2H), 3.31–3.17 (m, 4H), 1.50 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 167.4 (C_q), 166.4 (C_q), 152.3 (C_q), 143.6 (C_q), 142.0 (CH), 141.7 (C_q), 128.5 (CH), 128.3 (CH), 127.0 (CH), 125.9 (CH), 125.3 (CH), 118.2 (CH), 114.3 (CH), 112.9 (C_q), 108.7 (CH), 62.9 (CH_2), 41.3 (CH_2), 34.3 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 3118, 3027, 2932, 1622, 1573, 1474, 1338, 1107, 863, 695 cm^{-1}. **MS** (ESI) m/z (relative intensity): 117 (40), 345 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{21}N_4O$ $[M+H]^+$: 345.1710, found: 345.1713.



4-Ethoxy-7-(1*H*-pyrazol-1-yl)-2-(thiophen-3-yl)quinazoline (163ke): The general procedure **C** was followed using ethyl 4-(1*H*-pyrazol-1-yl)benzimidate (**161k**) (53.8 mg, 0.25 mmol) and 3-(thiophen-3-yl)-1,4,2-dioxazol-5-one (**162e**) (51.8 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163ke** (65.0 mg, 81%) as a white solid.

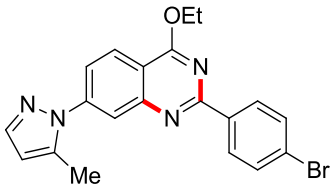
M. p. = 167–169 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.20–8.11 (m, 1H), 8.09 (d, *J* = 2.6 Hz, 1H), 8.04 (dd, *J* = 3.7, 1.2 Hz, 1H), 8.02–7.96 (m, 2H), 7.77 (d, *J* = 1.4 Hz, 1H), 7.46 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.13 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.50 (dd, *J* = 2.6, 1.8 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 1.53 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.2 (C_q), 157.8 (C_q), 152.6 (C_q), 144.0 (C_q), 143.7 (C_q), 141.9 (CH), 129.8 (CH), 129.1 (CH), 128.0 (CH), 127.0 (CH), 125.3 (CH), 118.0 (CH), 114.5 (CH), 113.1 (C_q), 108.6

(CH), 63.1 (CH_2), 14.3 (CH_3). **IR** (ATR) *v* = 3115, 2979, 1624, 1565, 1414, 1330, 1167, 875, 779, 704 cm^{-1}. **MS** (ESI) m/z (relative intensity): 323 (100) $[M+H]^+$, 345 (55) $[M+Na]^+$, 667 (45) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{15}N_4OS$ $[M+H]^+$: 323.0961, found: 323.0960.



4-Ethoxy-2-phenyl-6-(1*H*-pyrazol-1-yl)quinazoline (163la): The general procedure **C** was followed using ethyl 3-(1*H*-pyrazol-1-yl)benzimidate (**161l**) (53.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 10/1 to 6/1) yielded **163la** (48.9 mg, 62%) as a white solid.

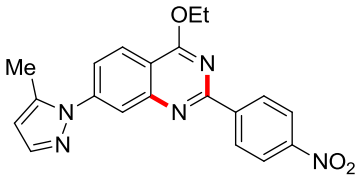
M. p. = 130–131 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.61–8.50 (m, 2H), 8.35 (d, *J* = 2.5 Hz, 1H), 8.19 (dd, *J* = 9.1, 2.6 Hz, 1H), 8.07–7.95 (m, 2H), 7.77 (d, *J* = 1.7 Hz, 1H), 7.53–7.44 (m, 3H), 6.51 (dd, *J* = 2.5, 1.8 Hz, 1H), 4.76 (d, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.5 (C_q), 159.9 (C_q), 150.2 (C_q), 141.6 (CH), 137.9 (C_q), 137.7 (C_q), 130.5 (CH), 129.5 (CH), 128.7 (CH), 128.3 (CH), 126.9 (CH), 125.4 (CH), 115.6 (C_q), 112.0 (CH), 108.1 (CH), 63.1 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2983, 1579, 1507, 1391, 1312, 1019, 774, 701, 560 cm^{-1}. **MS** (ESI) m/z (relative intensity): 345 (100) $[M+H]^+$, 367 (20) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{17}N_4O_2$ $[M+H]^+$: 345.1346, found: 345.1347.



2-(4-Bromophenyl)-4-ethoxy-7-(5-methyl-1*H*-pyrazol-1-yl)quinazoline (163ml): The general procedure **C** was followed using ethyl 4-(5-methyl-1*H*-pyrazol-1-yl)benzimidate (**161m**) (57.3 mg, 0.25 mmol) and 3-(4-bromophenyl)-1,4,2-dioxazol-5-one (**162l**) (72.6 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded **163ml** (63.1 mg, 64%) as a white solid.

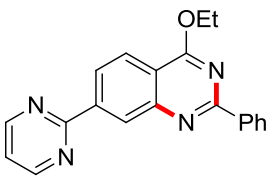
M. p. = 184–186 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.39 (d, *J* = 8.6 Hz, 2H), 8.15 (d, *J* = 9.7 Hz, 1H), 8.05–7.94 (m, 3H), 7.59 (d, *J* = 8.5 Hz, 2H), 6.30 (d, *J* = 2.5 Hz, 1H), 4.70 (q, *J* = 7.1 Hz, 2H), 2.39 (s,

3H), 1.54 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.5 (C_q), 160.0 (C_q), 152.7 (C_q), 151.6 (C_q), 143.8 (C_q), 137.0 (C_q), 131.5 (CH), 130.0 (CH), 127.6 (CH), 125.3 (C_q), 125.2 (CH), 118.2 (CH), 114.1 (CH), 112.9 (C_q), 108.8 (CH), 63.0 (CH_2), 14.4 (CH_3), 13.8 (CH_3). **IR** (ATR) *v* = 2974, 1628, 1579, 1536, 1426, 1337, 1010, 935, 754 cm^{-1}. **MS** (ESI) m/z (relative intensity): 372 (15), 409 (100) $[M+H]^+$, 411 (100), 431 (15) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{18}N_4OBr$ $[M+H]^+$: 409.0659, found: 409.0649.



4-Ethoxy-7-(5-methyl-1*H*-pyrazol-1-yl)-2-(4-nitrophenyl)quinazoline (163mk): The general procedure **C** was followed using ethyl 4-(5-methyl-1*H*-pyrazol-1-yl)benzimidate (**161m**) (57.3 mg, 0.25 mmol) and 5-(4-nitrophenyl)oxazol-2(5*H*)-one (**162k**) (62.4 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1 to 4/1) yielded **163mk** (54.4 mg, 58%) as a yellow solid.

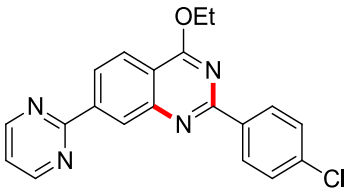
M. p. = 182–184 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 8.9 Hz, 2H), 8.31 (d, *J* =8.9 Hz, 2H), 8.21 (dd, *J* = 8.3, 1.2 Hz, 1H), 8.06-8.03 (m, 2H), 8.01 (d, *J* = 2.5 Hz, 1H), 6.34 (d, *J* = 2.5 Hz, 1H), 4.75 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.59 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.8 (C_q), 158.9 (C_q), 152.7 (C_q), 152.0 (C_q), 149.3 (C_q), 144.1 (C_q), 144.0 (C_q), 129.4 (CH), 127.8 (CH), 125.5 (CH), 123.7 (CH), 119.7 (CH), 114.5 (CH), 113.2 (C_q), 109.2 (CH), 63.4 (CH_2), 14.5 (CH_3), 14.0 (CH_3). **IR** (ATR) *v* = 2985, 1622, 1577, 1539, 1512, 1427, 1340, 1319, 1038, 867 cm^{-1}. **MS** (ESI) m/z (relative intensity): 376 (100) $[M+H]^+$, 398 (58) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{18}N_5O_3$ $[M+H]^+$: 376,1410, found: 376.1404.



4-Ethoxy-2-phenyl-7-(pyrimidin-2-yl)quinazoline (163na): The general procedure **C** was followed using ethyl 4-(pyrimidin-2-yl)benzimidate (**161n**) (56.9 mg, 0.25 mmol) and

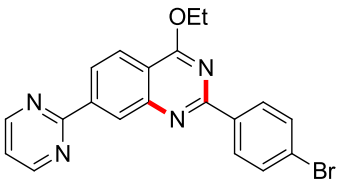
5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 5/1) yielded **163na** (60 mg, 73%) as a white solid.

M. p. = 145–146 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 9.08 (d, *J* = 1.1 Hz, 1H), 8.86 (d, *J* = 4.8 Hz, 2H), 8.67–8.57 (m, 2H), 8.54 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.23 (dd, *J* = 8.6, 0.6 Hz, 1H), 7.70–7.41 (m, 3H), 7.24 (t, *J* = 4.8 Hz, 1H), 4.77 (q, *J* = 7.1 Hz, 2H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.5 (C_q), 163.8 (C_q), 160.2 (C_q), 157.2 (CH), 152.1 (C_q), 142.1 (C_q), 138.1 (C_q), 130.3 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 125.4 (CH), 123.7 (CH), 119.7 (CH), 116.5 (C_q), 62.9 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2974, 1623, 1562, 1431, 1324, 1163, 1025, 756, 708 cm^{-1}. **MS** (ESI) m/z (relative intensity): 329 (100) $[M+H]^+$, 351 (40) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{17}N_4O$ $[M+H]^+$: 329.1397, found: 329.1397.



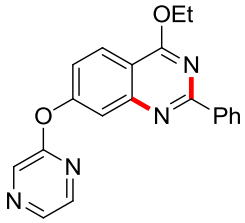
2-(4-Chlorophenyl)-4-ethoxy-7-(pyrimidin-2-yl)quinazoline (163nj): The general procedure **C** was followed using ethyl 4-(pyrimidin-2-yl)benzimidate (**161n**) (56.8 mg, 0.25 mmol) and 3-(4-chlorophenyl)-1,4,2-dioxazol-5-one (**162j**) (59.3 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163nj** (64.4 mg, 71%) as a yellow solid.

M. p. = 198–190 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 9.02 (d, *J* = 1.2 Hz, 1H), 8.85 (d, *J* = 4.8 Hz, 2H), 8.56–8.46 (m, 3H), 8.18 (d, *J* = 8.6 Hz, 1H), 7.49–7.39 (m, 2H), 7.27–7.18 (m, 1H), 4.71 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 163.7 (C_q), 159.2 (C_q), 157.3 (CH), 152.0 (C_q), 142.2 (C_q), 136.6 (C_q), 136.5 (C_q), 129.7 (CH), 128.5 (CH), 128.0 (CH), 125.6 (CH), 123.7 (CH), 119.8 (CH), 116.5 (C_q), 63.0 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2982, 1623, 1560, 1494, 1415, 1325, 1012, 840, 787 cm^{-1}. **MS** (ESI) m/z (relative intensity): 363 (100) $[M+H]^+$, 364 (20), 365 (30), 385 (10) $[M+Na]^+$, 747 (10) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{16}ClN_4O$ $[M+H]^+$: 363.1007, found: 363.1010.



2-(4-Bromophenyl)-4-ethoxy-7-(pyrimidin-2-yl)quinazoline (163nl): The general procedure **C** was followed using ethyl 4-(pyrimidin-2-yl)benzimidate (**161n**) (56.8 mg, 0.25 mmol) and 3-(4-bromophenyl)-1,4,2-dioxazol-5-one (**162l**) (72.6 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 5/1) yielded **163nl** (87.0 mg, 85%) as a white solid.

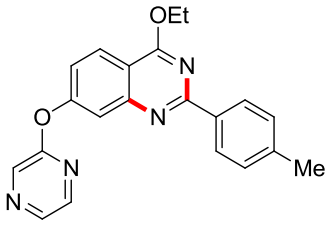
M. p. = 191–193 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 9.03 (d, *J* = 1.3 Hz, 1H), 8.85 (d, *J* = 4.8 Hz, 2H), 8.53 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.43 (d, *J* = 8.6 Hz, 2H), 8.20 (d, *J* = 8.6 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.24 (t, *J* = 4.8 Hz, 1H), 4.72 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.7 (C_q), 163.7 (C_q), 159.3 (C_q), 157.4 (CH), 152.0 (C_q), 142.3 (C_q), 137.1 (C_q), 131.5 (CH), 130.0 (CH), 128.0 (CH), 125.7 (CH), 125.1 (C_q), 123.7 (CH), 119.8 (CH), 116.5 (C_q), 63.0 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2976, 1625, 1560, 1414, 1325, 1160, 1011, 837, 785, 738 cm^{-1}. **MS** (ESI) m/z (relative intensity): 301 (10), 360 (10), 407 (100) $[M+H]^+$, 409 (100). **HR-MS** (ESI) m/z calcd for $C_{20}H_{16}N_4OBr$ $[M+H]^+$: 407.0502, found: 407.0499.



4-Ethoxy-2-phenyl-7-(pyrazin-2-yloxy)quinazoline (163oa): The general procedure **C** was followed using ethyl 4-(pyrazin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **163oa** (76.9 mg, 89%) as a white solid.

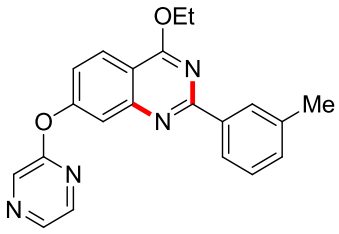
M. p. = 129–130 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.60–8.45 (m, 3H), 8.33 (d, *J* = 2.7 Hz, 1H), 8.20 (dd, *J* = 8.9, 0.4 Hz, 1H), 8.13 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.70 (dd, *J* = 2.3, 0.4 Hz, 1H), 7.53–7.42 (m, 3H), 7.29 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.76 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.3 (C_q), 160.8 (C_q), 159.3 (C_q), 157.2 (C_q), 153.3 (C_q), 141.1 (CH), 139.3 (CH), 137.9 (C_q), 136.3 (CH), 130.5 (CH), 128.4 (CH), 128.3 (CH), 125.4 (CH), 120.6 (CH), 117.6 (CH), 112.7 (C_q), 62.9

(CH_2), 14.5 (CH_3). **IR** (ATR) ν = 2975, 1623, 1579, 1405, 1343, 1285, 1150, 1107, 848, 706 cm^{-1}. **MS** (ESI) m/z (relative intensity): 317 (100) $[M+H]^+$, 339 (40) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{17}N_4O$ $[M+H]^+$: 317.1397, found: 317.1397.



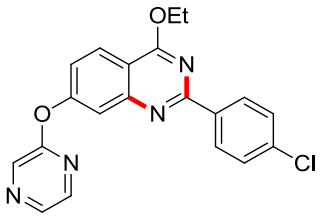
4-Ethoxy-7-(pyrazin-2-yloxy)-2-(*p*-tolyl)quinazoline (163om): The general procedure **C** was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 3-(*p*-tolyl)-1,4,2-dioxazol-5-one (**162m**) (53.1 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **163om** (67.2 mg, 75%) as a white solid.

M. p. = 151–153 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.54 (d, J = 1.4 Hz, 1H), 8.45 (d, J = 8.2 Hz, 2H), 8.35 (d, J = 2.7 Hz, 1H), 8.22 (d, J = 8.9 Hz, 1H), 8.16 (dd, J = 2.7, 1.4 Hz, 1H), 7.70 (d, J = 2.3 Hz, 1H), 7.35–7.24 (m, 3H), (dd, J = 8.8, 2.3 Hz, 1H), 4.78 (q, J = 7.1 Hz, 2H), 2.43 (s, 3H), 1.57 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 161.3 (C_q), 159.7 (C_q), 157.5 (C_q), 153.7 (C_q), 141.4 (CH), 141.0 (C_q), 139.6 (CH), 136.5 (CH), 135.5 (C_q), 129.3 (CH), 128.7 (CH), 125.7 (CH), 120.6 (CH), 117.8 (CH), 112.9 (C_q), 63.0 (CH_2), 21.7 (CH_3), 14.6 (CH_3). **IR** (ATR) ν = 2981, 1623, 1575, 1558, 1419, 1399, 1381, 1275, 1177, 1160 cm^{-1}. **MS** (ESI) m/z (relative intensity): 359 (100) $[M+H]^+$, 376 (4) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{19}N_4O_2$ $[M+H]^+$: 359.1508, found: 359.1503.



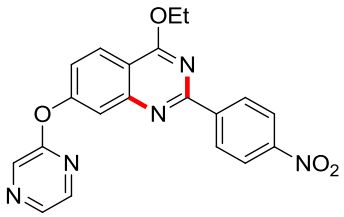
4-Ethoxy-7-(pyrazin-2-yloxy)-2-(thiophen-3-yl)quinazoline (163og): The general procedure **C** was followed using ethyl 4-(pyrazin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 5-(*m*-tolyl)oxazol-2(5*H*)-one (**162g**) (53.1 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **163og** (75.3 mg, 84%) as a white solid.

M. p. = 114–116 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.55 (s, 1H), 8.37-8.34 (m, 3H), 8.23 (dd, *J* = 8.8, 0.5 Hz, 1H), 8.16 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.72 (d, *J* = 2.3 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.34–7.29 (m, 2H), 4.79 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.7 (C_q), 166.6 (C_q), 161.4 (C_q), 159.7 (C_q), 157.5 (C_q), 153.6 (C_q), 141.4 (CH), 139.6 (CH), 138.2 (C_q), 136.6 (CH), 131.5 (CH), 129.2 (CH), 128.4 (CH), 125.9 (CH), 125.7 (CH), 120.8 (CH), 117.8 (CH), 112.9 (C_q), 63.1 (CH_2), 21.7 (CH_3), 14.6 (CH_3). **IR** (ATR) *v* = 2923, 1623, 1576, 1497, 1419, 1325, 1106 cm^{-1}. **MS** (ESI) m/z (relative intensity): 359 (100) $[M+H]^+$, 739 (11) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{19}N_4O_2$ $[M+H]^+$: 359.1508, found: 359.1505.



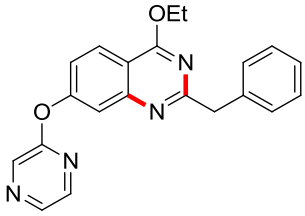
2-(4-Chlorophenyl)-4-ethoxy-7-(pyrazin-2-yloxy)quinazoline (163oj): The general procedure **C** was followed using ethyl 4-(pyrazin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 5-(4-chlorophenyl)oxazol-2(5*H*)-one (**162j**) (59.3 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **163oj** (82.3 mg, 87%) as a white solid.

M. p. = 167–169 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.54 (dd, *J* = 1.4, 0.5 Hz, 1H), 8.53–8.47 (m, 2H), 8.36 (dd, *J* = 2.7, 0.5 Hz, 1H), 8.23 (dd, *J* = 8.9, 0.5 Hz, 1H), 8.16 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.70 (dd, *J* = 2.3, 0.5 Hz, 1H), 7.56–7.40 (m, 2H), 7.33 (dd, *J* = 8.9, 2.4 Hz, 1H), 4.77 (q, *J* = 7.1 Hz, 2H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.7 (C_q), 160.1 (C_q), 159.5 (C_q), 157.6 (C_q), 153.5 (C_q), 141.3 (CH), 139.6 (CH), 136.9 (C_q), 136.6 (C_q), 136.5 (CH), 130.0 (CH), 128.7 (CH), 125.7 (CH), 121.0 (CH), 117.8 (CH), 112.9 (C_q), 63.1 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2984, 1623, 1576, 1499, 1444, 1403, 1285, 1108, 937 cm^{-1}. **MS** (ESI) m/z (relative intensity): 379 (100) $[M+H]^+$, 779 (19) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{16}ClN_4O_2$ $[M+H]^+$: 379.0962, found: 379.0957.



4-Ethoxy-2-(4-nitrophenyl)-7-(pyrazin-2-yloxy)quinazoline (163ok): The general procedure **C** was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 5-(4-nitrophenyl)oxazol-2(5*H*)-one (**162k**) (62.4 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1 to 4/1) yielded **163ok** (69.1 mg, 71%) as a yellow solid.

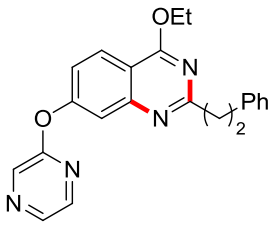
M. p. = 188–190 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 9.1 Hz, 2H), 8.57 (dd, *J* = 1.4, 0.5 Hz, 1H), 8.38 (dd, *J* = 2.7, 0.5 Hz, 1H), 8.33 (d, *J* = 9.1 Hz, 2H), 8.27 (dd, *J* = 8.9, 0.5 Hz, 1H), 8.17 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.76 (dd, *J* = 2.3, 0.5 Hz, 1H), 7.40 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.80 (q, *J* = 7.1 Hz, 2H), 1.59 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.9 (C_q), 159.5 (C_q), 158.9 (C_q), 157.8 (C_q), 153.3 (C_q), 149.3 (C_q), 144.0 (C_q), 141.3 (CH), 139.8 (CH), 136.6 (CH), 129.5 (CH), 125.8 (CH), 123.7 (CH), 121.9 (CH), 118.0 (CH), 113.1 (C_q), 63.5 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2987, 1621, 1576, 1520, 1401, 1345, 1280, 1167, 1082 cm^{-1}. **MS** (ESI) m/z (relative intensity): 412 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{15}N_5O_4Na$ $[M+Na]^+$: 412.1022, found: 412.1016.



2-Benzyl-4-ethoxy-7-(pyrazin-2-yloxy)quinazoline (163ob): The general procedure **C** was followed using ethyl 4-(pyrazin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 5-benzyloxazol-2(5*H*)-one (**162b**) (53.1 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **163ob** (69.9 mg, 78%) as a white solid.

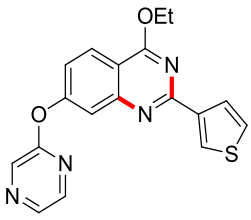
M. p. = 122–124 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.54 (d, *J* = 1.4 Hz, 1H), 8.36 (d, *J* = 2.7 Hz, 1H), 8.18 (d, *J* = 8.9 Hz, 1H), 8.16 (dd, *J* = 2.8, 1.4 Hz, 1H), 7.64 (dd, *J* = 2.4, 0.5 Hz, 1H), 7.48–7.45 (m, 2H), 7.33–7.28 (m, 3H), 7.25–7.19 (m, 1H), 4.62 (q, *J* = 7.1 Hz, 2H), 4.25 (s, 2H), 1.46 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 166.5 (C_q), 159.5 (C_q), 157.4 (C_q), 153.2 (C_q), 141.4 (CH), 139.6

(CH), 138.7 (C_q), 136.6 (CH), 129.4 (CH), 128.4 (CH), 126.5 (CH), 125.5 (CH), 120.7 (CH), 117.2 (CH), 112.4 (C_q), 63.1 (CH_2), 46.5 (CH_2), 14.4 (CH_3). **IR** (ATR) ν = 2981, 1623, 1575, 1421, 1344, 1278, 1136 cm^{-1}. **MS** (ESI) m/z (relative intensity): 359 (100) $[M+H]^+$, 381 (5) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{19}N_4O_2$ $[M+H]^+$: 359.1508, found: 359.1503.



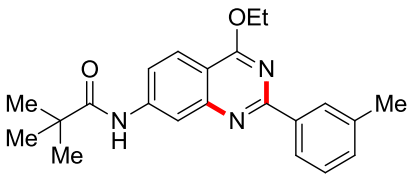
4-Ethoxy-2-phenethyl-7-(pyrazin-2-yloxy)quinazoline (163oc): The general procedure **C** was followed using ethyl 4-(pyrazin-2-yloxy)benzimidate (**161o**) (60.6 mg, 0.25 mmol) and 5-phenethyloxazol-2(5*H*)-one (**162c**) (57.3 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **163oc** (81.0 mg, 87%) as a white solid.

M. p. = 94–96 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.52 (d, J = 1.4 Hz, 1H), 8.35 (d, J = 2.6 Hz, 1H), 8.20 (d, J = 8.9 Hz, 1H), 8.14 (dd, J = 2.6, 1.4 Hz, 1H), 7.60 (d, J = 2.3 Hz, 1H), 7.32–7.24 (m, 5H), 7.22–7.15 (m, 1H), 4.64 (q, J = 7.1 Hz, 2H), 3.28–3.19 (m, 4H), 1.50 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 167.4 (C_q), 166.5 (C_q), 159.5 (C_q), 157.4 (C_q), 153.1 (C_q), 141.9 (C_q), 141.4 (CH), 139.6 (CH), 136.6 (CH), 128.6 (CH), 128.5 (CH), 126.0 (CH), 125.6 (CH), 120.5 (CH), 117.0 (CH), 112.5 (C_q), 63.6 (CH_2), 41.4 (CH_2), 34.5 (CH_2), 14.5 (CH_3). **IR** (ATR) ν = 2980, 1623, 1574, 1495, 1420, 1278, 1136 cm^{-1}. **MS** (ESI) m/z (relative intensity): 373 (100) $[M+H]^+$, 395 (10) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{21}N_4O_2$ $[M+H]^+$: 373.1665, found: 373.1659.



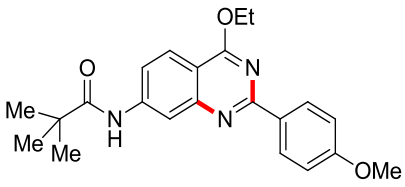
4-Ethoxy-7-(pyrazin-2-yloxy)-2-(thiophen-3-yl)quinazoline (163oe): The general procedure **C** was followed using ethyl 4-(pyrazin-2-yloxy)benzimidate (**161o**) (60.8 mg, 0.25 mmol) and 5-(thiophen-3-yl)oxazol-2(5*H*)-one (**162e**) (50.7 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **163oe** (75.3 mg, 86%) as a white solid.

M. p. = 145–147 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.53 (dd, *J* = 1.4, 0.4 Hz, 1H), 8.36 (dd, *J* = 2.7, 0.4 Hz, 1H), 8.19 (dd, *J* = 8.9, 0.5 Hz, 1H), 8.16 (dd, *J* = 2.7, 1.4 Hz, 1H), 8.07 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.64 (dd, *J* = 2.3, 0.5 Hz, 1H), 7.48 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.28 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.15 (d, *J* = 5.0, 3.7 Hz, 1H), 4.74 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.5 (C_q), 159.6 (C_q), 157.9 (C_q), 157.7 (C_q), 153.5 (C_q), 144.2 (C_q), 141.4 (CH), 139.6 (CH), 136.6 (CH), 129.9 (CH), 129.3 (CH), 128.2 (CH), 125.7 (CH), 120.5 (CH), 117.4 (CH), 112.8 (C_q), 63.3 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2981, 1621, 1575, 1496, 1452, 1400, 1343, 1318, 1150 cm^{-1}. **MS** (ESI) m/z (relative intensity): 351 (100) $[M+H]^+$, 723 (11) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{15}N_4O_2S$ $[M+H]^+$: 351.0916, found: 351.0914.



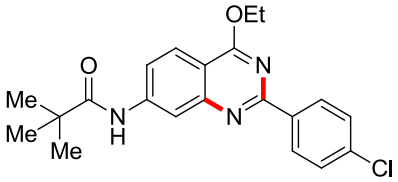
***N*-[4-Ethoxy-2-(*m*-tolyl)quinazolin-7-yl]pivalamide (163pg)**: The general procedure **C** was followed using ethyl 4-pivalamidobenzimidate (**161p**) (62.1 mg, 0.25 mmol) and 3-(*m*-tolyl)-1,4,2-dioxazol-5-one (**162g**) (53.2 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163pg** (77.0 mg, 85%) as a white solid.

M. p. = 199–201 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.39 (s, 1H), 8.36 (s, 1H), 8.08 (d, *J* = 8.9 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 7.83 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.65 (s, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.4 Hz, 1H), 4.75 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 3H), 1.57 (t, *J* = 7.1 Hz, 3H), 1.38 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 176.8 (C_q), 166.2 (C_q), 160.7 (C_q), 152.8 (C_q), 142.6 (C_q), 138.2 (C_q), 137.9 (C_q), 131.2 (CH), 129.0 (CH), 128.2 (CH), 125.7 (CH), 124.5 (CH), 119.5 (CH), 116.0 (CH), 111.8 (C_q), 62.7 (CH_2), 39.9 (C_q), 27.6 (CH_3), 21.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 3333, 2958, 1665, 1572, 1436, 1326, 1028, 1169, 1110, 788 cm^{-1}. **MS** (ESI) m/z (relative intensity): 364 (100) $[M+H]^+$, 386 (10) $[M+Na]^+$, 727 (10) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{26}N_3O_2$ $[M+H]^+$: 364.2020, found: 364.2025.



***N*-[4-Ethoxy-2-(4-methoxyphenyl)quinazolin-7-yl]pivalamide (163pf)**: The general procedure **C** was followed using ethyl 4-pivalamidobenzimidate (**161p**) (62.1 mg, 0.25 mmol) and 3-(4-methoxyphenyl)-1,4,2-dioxazol-5-one (**162f**) (57.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163pf** (81.0 mg, 85%) as a white solid.

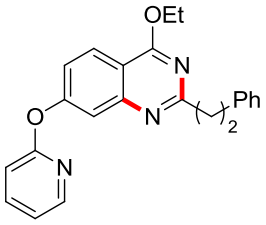
M. p. = 211–213 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.48 (d, *J* = 9.0 Hz, 2H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.95 (d, *J* = 2.1 Hz, 1H), 7.73 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.61 (s, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 4.68 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H), 1.33 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 176.8 (C_q), 166.0 (C_q), 161.6 (C_q), 160.3 (C_q), 152.9 (C_q), 142.4 (C_q), 130.9 (C_q), 130.0 (CH), 124.4 (CH), 119.1 (CH), 115.8 (C_q), 113.6 (CH), 111.5 (CH), 62.5 (CH_2), 55.3 (CH_3), 39.8 (C_q), 27.5 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 3351, 2969, 1662, 1579, 1442, 1326, 1251, 1164, 1027, 845, 791 cm^{-1}. **MS** (ESI) m/z (relative intensity): 380 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{26}N_3O_3$ $[M+H]^+$: 380.1969, found: 380.1970.



***N*-[2-(4-Chlorophenyl)-4-ethoxyquinazolin-7-yl]pivalamide (163pj)**: The general procedure **C** was followed using ethyl 4-pivalamidobenzimidate (**161p**) (62.1 mg, 0.25 mmol) and 3-(4-chlorophenyl)-1,4,2-dioxazol-5-one (**162j**) (59.3 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163pj** (86.0 mg, 90%) as a white solid.

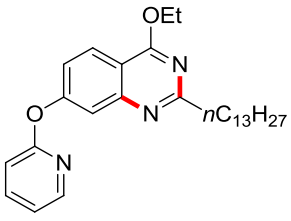
M. p. = 228–230 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.48 (d, *J* = 8.6 Hz, 2H), 8.06 (d, *J* = 8.9 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 7.79 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.66 (s, 1H), 7.45 (d, *J* = 8.6 Hz, 2H), 4.70 (q, *J* = 7.1 Hz, 2H), 1.55 (t, *J* = 7.1 Hz, 3H), 1.39 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 176.8 (C_q), 166.3 (C_q), 159.5 (C_q), 152.8 (C_q), 142.7 (C_q), 136.8 (C_q), 136.5 (C_q), 129.8 (CH), 128.5 (CH), 124.5 (C_q), 119.7 (CH), 115.9 (CH), 111.8 (CH), 62.8 (CH_2), 39.9 (C_q), 27.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 3323, 2984, 1659,

1579, 1437, 1324, 1205, 1089, 1014, 789 cm^{-1}. **MS** (ESI) m/z (relative intensity): 384 (100) $[M+H]^+$, 406 (10) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 384.1473, found: 384.1476.



4-Ethoxy-2-phenethyl-7-(pyridin-2-yloxy)quinazoline (163qc): The general procedure **C** was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161q**) (60.8 mg, 0.25 mmol) and 5-phenethyloxazol-2(5*H*)-one (**162c**) (57.3 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **163qc** (75.2 mg, 81%) as a colorless oil.

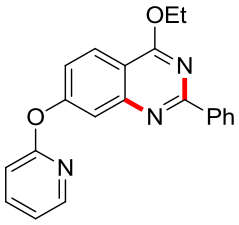
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.25 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 8.15 (dd, *J* = 8.9, 0.4 Hz, 1H), 7.78–7.72 (m, 1H), 7.51 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.34–7.24 (m, 5H), 7.22–7.15 (m, 1H), 7.08 (dd, *J* = 7.3, 5.0 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 3.28–3.18 (m, 4H), 1.49 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 167.0 (C_q), 166.5 (C_q), 162.8 (C_q), 158.9 (C_q), 153.2 (C_q), 148.1 (CH), 141.9 (C_q), 139.9 (CH), 128.6 (CH), 128.4 (CH), 125.9 (CH), 125.3 (CH), 120.6 (CH), 119.7 (CH), 115.9 (CH), 112.9 (CH), 111.8 (C_q), 62.8 (CH_2), 41.4 (CH_2), 34.5 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 2979, 1622, 1569, 1416, 1340, 1238, 1135, 1104 cm^{-1}. **MS** (ESI) m/z (relative intensity): 372 (100) $[M+H]^+$, 394 (10) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{22}N_3O_2$ $[M+H]^+$: 372.1712, found: 372.1707.



4-Ethoxy-7-(pyridin-2-yloxy)-2-*n*-tridecylquinazoline (163qd): The general procedure **C** was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161q**) (60.6 mg, 0.25 mmol), 5-tridecyloxazol-2(5*H*)-one (**162d**) (80.8 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **163qd** (96.7 mg, 86%) as a colorless oil.

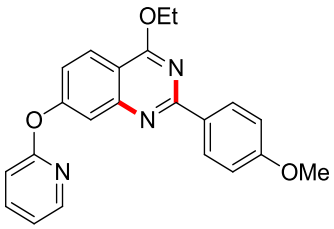
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.23 (ddd, *J* = 4.9, 2.0, 0.6 Hz, 1H), 8.14 (d, *J* = 8.9 Hz, 1H), 7.77–7.71 (m, 1H), 7.53 (s, 1H), 7.28 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.06 (dd, *J* = 7.4, 4.9, 0.6 Hz, 1H), 7.02 (d, *J* = 8.2

Hz, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 2.90 (t, *J* = 7.7 Hz, 2H), 1.84 (q, *J* = 7.6 Hz, 2H), 1.48 (t, *J* = 7.1 Hz, 3H), 1.41–1.24 (m, 20H), 0.89–0.84 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 168.3 (C_q), 166.6 (C_q), 162.7 (C_q), 159.1 (C_q), 148.1 (CH), 139.9 (CH), 125.3 (CH), 120.6 (CH), 119.7 (CH), 115.7 (C_q), 115.6 (CH), 112.9 (CH), 111.6 (C_q), 62.9 (CH_2), 39.8 (CH_2), 32.0 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 28.7 (CH_2), 22.8 (CH_2), 14.5 (CH_3), 14.2 (CH_3). **IR** (ATR) *v* = 2922, 2852, 1623, 1571, 1464, 1341, 1241, 1137, 779 cm^{-1}. **MS** (ESI) m/z (relative intensity): 450 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{28}H_{39}N_3O_2Na$ $[M+Na]^+$: 472.2940, found: 472.2934.



4-Ethoxy-2-phenyl-7-(pyridin-2-yloxy)quinazoline (163qa): The general procedure **C** was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161q**) (60.6 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded **163qa** (69.1 mg, 80%) as a colorless oil.

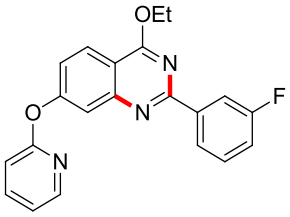
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.63–8.46 (m, 2H), 8.24 (dd, *J* = 4.9, 1.9 Hz, 1H), 8.18 (d, *J* = 8.9 Hz, 1H), 7.73 (ddd, *J* = 8.3, 7.4, 1.9 Hz, 1H), 7.63 (d, *J* = 2.3 Hz, 1H), 7.54–7.43 (m, 3H), 7.30 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.11–6.97 (m, 2H), 4.76 (q, *J* = 7.1 Hz, 2H), 1.54 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.4 (C_q), 162.7 (C_q), 160.7 (C_q), 158.8 (C_q), 153.5 (C_q), 147.9 (CH), 139.7 (CH), 138.1 (C_q), 130.4 (CH), 128.4 (CH), 128.3 (CH), 125.2 (CH), 120.8 (CH), 119.5 (CH), 116.7 (CH), 112.6 (CH), 112.1 (C_q), 62.7 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2980, 1620, 1573, 148.95, 1417, 1343, 1242, 969, 774, 710 cm^{-1}. **MS** (ESI) m/z (relative intensity): 344 (100) $[M+H]^+$, 366 (45) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{18}N_3O_2$ $[M+H]^+$: 344.1394, found: 344.1396.



4-Ethoxy-2-(4-methoxyphenyl)-7-(pyridin-2-yloxy)quinazoline (163qf): The general procedure **C**

was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161q**) (60.6 mg, 0.25 mmol) and 5-(4-methoxyphenyl)oxazol-2(5*H*)-one (**162f**) (57.9 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 8/2) yielded **163qf** (68.1 mg, 73%) as a white solid.

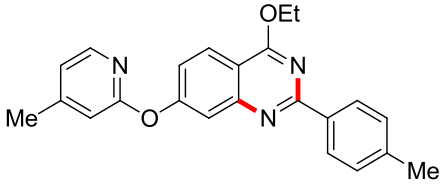
M. p. = 118–119 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 9.0 Hz, 2H), 8.26 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 8.17 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.76 (ddd, *J* = 8.2, 7.3, 2.0 Hz, 1H), 7.59 (d, *J* = 2.3 Hz, 1H), 7.28 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.08 (ddd, *J* = 7.3, 5.0, 0.9 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.99 (d, *J* = 9.0 Hz, 2H), 4.76 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.5 (C_q), 162.9 (C_q), 161.8 (C_q), 160.7 (C_q), 158.9 (C_q), 153.8 (C_q), 148.2 (CH), 139.7 (CH), 131.0 (C_q), 130.3 (CH), 125.4 (CH), 120.5 (CH), 119.7 (CH), 116.7 (CH), 113.8 (CH), 112.8 (CH), 112.1 (C_q), 62.8 (CH_2), 55.5 (CH_3), 14.6 (CH_3). **IR** (ATR) *v* = 2977, 1624, 1577, 1497, 1445, 1344, 1250, 1106 cm^{-1}. **MS** (ESI) m/z (relative intensity): 374 (100) $[M+H]^+$, 396 (7) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{19}N_3NaO_3$ $[M+Na]^+$: 396.1324, found: 396.1321.



4-Ethoxy-2-(3-fluorophenyl)-7-(pyridin-2-yloxy)quinazoline (163qi): The general procedure **C** was followed using ethyl 4-(pyridin-2-yloxy)benzimidate (**161q**) (60.6 mg, 0.25 mmol) and 3-(3-fluorophenyl)-1,4,2-dioxazol-5*H*-one (**162i**) (54.3 mg, 0.30 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **163qi** (79.5 mg, 88%) as a white solid.

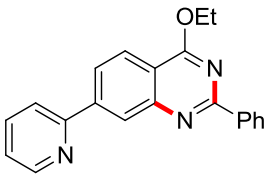
M. p. = 101–104 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.34 (dt, *J* = 7.9, 1.2 Hz, 1H), 8.27–8.26 (m, 2H), 8.20 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.78 (ddd, *J* = 8.2, 7.3, 2.0 Hz, 1H), 7.63 (d, *J* = 2.3 Hz, 1H), 7.44 (td, *J* = 8.0, 5.8 Hz, 1H), 7.34 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.16 (tdd, *J* = 8.3, 2.7, 1.0 Hz, 1H), 7.10 (ddd, *J* = 7.4, 5.0, 1.0 Hz, 1H), 7.06 (dt, *J* = 8.3, 0.9 Hz, 1H) 4.77 (q, *J* = 7.1 Hz, 2H), 1.57 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.6 (C_q), 163.1 (d, ^{1}J = 243.9 Hz, C_q), 162.7 (C_q), 160.0 (d, ^{4}J = 3.3 Hz, C_q) 159.0 (C_q), 153.5 (C_q), 148.0 (CH), 140.7 (d, ^{3}J = 7.8 Hz, C_q), 139.9 (CH), 129.8 (d, ^{3}J = 7.8 Hz, CH), 125.3 (CH), 124.1 (d, ^{4}J = 2.8 Hz, CH), 121.3 (CH), 119.7 (CH), 117.3 (d, ^{2}J = 21.4 Hz, CH), 116.9 (CH), 115.4 (d, ^{2}J = 23.0 Hz, CH), 112.8 (CH), 112.4 (C_q), 63.1 (CH_2), 14.7 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -113.58 (ddd, *J* = 10.5, 8.4, 5.8 Hz). **IR** (ATR) *v* = 2981, 1622, 1592, 1577, 1427, 1325, 1245, 1141

cm^{-1}. **MS** (ESI) m/z (relative intensity): 362 (100) $[M+H]^+$, 745 (10) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{17}FN_3O_2$ $[M+H]^+$: 362.1305, found: 362.1299.



4-Ethoxy-7-[(4-methylpyridin-2-yl)oxy]-2-(*p*-tolyl)quinazoline (163rm): The general procedure **C** was followed using ethyl 4-[(4-methylpyridin-2-yl)oxy]benzimidate (**161r**) (64.1 mg, 0.25 mmol) and 3-(*p*-tolyl)-1,4,2-dioxazol-5-one (**162m**) (53.2 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **163rm** (77.2 mg, 83%) as a white solid.

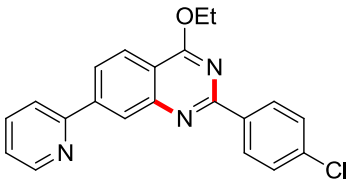
M. p. = 102–104 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.42 (d, *J* = 8.2 Hz, 2H), 8.14 (d, *J* = 8.9 Hz, 1H), 8.07 (d, *J* = 2.4 Hz, 1H), 7.59–7.50 (m, 2H), 7.30–7.20 (m, 3H), 6.93 (d, *J* = 8.3 Hz, 1H), 4.74 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 2.31 (s, 3H), 1.54 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.3 (C_q), 160.8 (C_q), 160.7 (C_q), 159.5 (C_q), 153.5 (C_q), 147.8 (CH), 140.6 (C_q), 140.5 (CH), 135.4 (C_q), 129.1 (C_q), 129.1 (CH), 128.4 (CH), 125.2 (CH), 120.2 (CH), 115.7 (CH), 112.4 (CH), 111.8 (C_q), 62.7 (CH_2), 21.5 (CH_3), 17.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2976, 2921, 1603, 1568, 1470, 1341, 1279, 1156, 890, 788 cm^{-1}. **MS** (ESI) m/z (relative intensity): 372 (100) $[M+H]^+$, 394 (5) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{22}N_3O_2$ $[M+H]^+$: 372.1707, found: 372.1706.



4-Ethoxy-2-phenyl-7-(pyridin-2-yl)quinazoline (163sa): The general procedure **C** was followed using ethyl 4-(pyridin-2-yl)benzimidate (**161s**) (56.9 mg, 0.25 mmol) and 5-phenyloxazol-2(5*H*)-one (**162a**) (48.9 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 15/1) yielded **163sa** (44.2 mg, 54%) as a white solid.

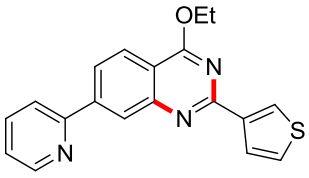
M. p. = 130–131 ˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.76 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.64–8.55 (m, 2H), 8.50 (dd, *J* = 1.5, 0.7 Hz, 1H), 8.30–8.20 (m, 2H), 7.93 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.85–7.73 (m, 1H), 7.57–7.42 (m, 3H), 7.29 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 4.78 (q, *J* = 7.1 Hz, 2H), 1.58 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.7 (C_q), 160.5 (C_q), 156.3 (C_q), 152.3 (C_q), 148.9 (CH), 144.1 (C_q), 138.3 (C_q), 136.9 (CH), 130.4 (CH), 128.5 (CH), 128.4 (CH), 125.8 (CH), 125.2 (CH), 124.0 (CH), 122.9 (CH), 121.3 (CH), 115.4 (C_q), 62.9 (CH_2), 14.4 (CH_3). **IR** (ATR) ν = 2968, 1703, 1621, 1553, 1431, 1321, 1261, 1106, 1016, 769 cm^{-1}. **MS** (ESI) m/z (relative intensity): 328 (100) $[M+H]^+$, 350 (30) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{17}N_3O$ $[M+H]^+$: 328.1444, found: 328.1446.



2-(4-Chlorophenyl)-4-ethoxy-7-(pyridin-2-yl)quinazoline (163sj): The general procedure **C** was followed using ethyl 4-(pyridin-2-yl)benzimidate (**161s**) (56.6 mg, 0.25 mmol) and 3-(4-chlorophenyl)-1,4,2-dioxazol-5-one (**162j**) (59.3 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 5/1) yielded **163sj** (56.0 mg, 62%) as a white solid.

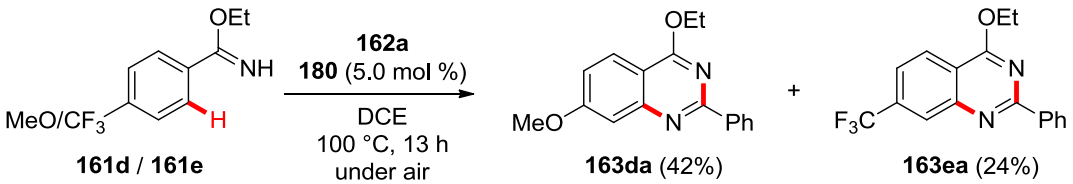
M. p. = 192–194 ˚C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.78 (d, *J* = 4.8 Hz, 1H), 8.53 (d, *J* = 8.7 Hz, 2H), 8.48 (s, 1H), 8.32–8.19 (m, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.82 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.38–7.25 (m, 1H), 4.76 (q, *J* = 7.1 Hz, 2H), 1.59 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.7 (C_q), 159.4 (C_q), 156.1 (C_q), 152.1 (C_q), 149.9 (CH), 144.2 (C_q), 136.9 (CH), 136.7 (C_q), 136.6 (C_q), 129.8 (CH), 128.6 (CH), 125.7 (CH), 125.4 (CH), 124.0 (CH), 123.0 (CH), 121.2 (CH), 115.4 (C_q), 63.0 (CH_2), 14.4 (CH_3). **IR** (ATR) ν = 2978, 1624, 1566, 1379, 1327, 1089, 1013, 990, 770, 738 cm^{-1}. **MS** (ESI) m/z (relative intensity): 362 (100) $[M+H]^+$, 384 (10) $[M+Na]^+$, 745 (10) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{17}ClN_3O$ $[M+H]^+$: 362.1055, found: 362.1056.



4-Ethoxy-7-(pyridin-2-yl)-2-(thiophen-3-yl)quinazoline (163te): The general procedure **C** was followed using ethyl 4-(pyridin-2-yl)benzimidate (**161t**) (56.6 mg, 0.25 mmol) and 3-(thiophen-3-yl)-1,4,2-dioxazol-5-one (**162e**) (50.7 mg, 0.30 mmol). Purification by coloumn chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **163te** (43.2 mg, 51%) as a white solid.

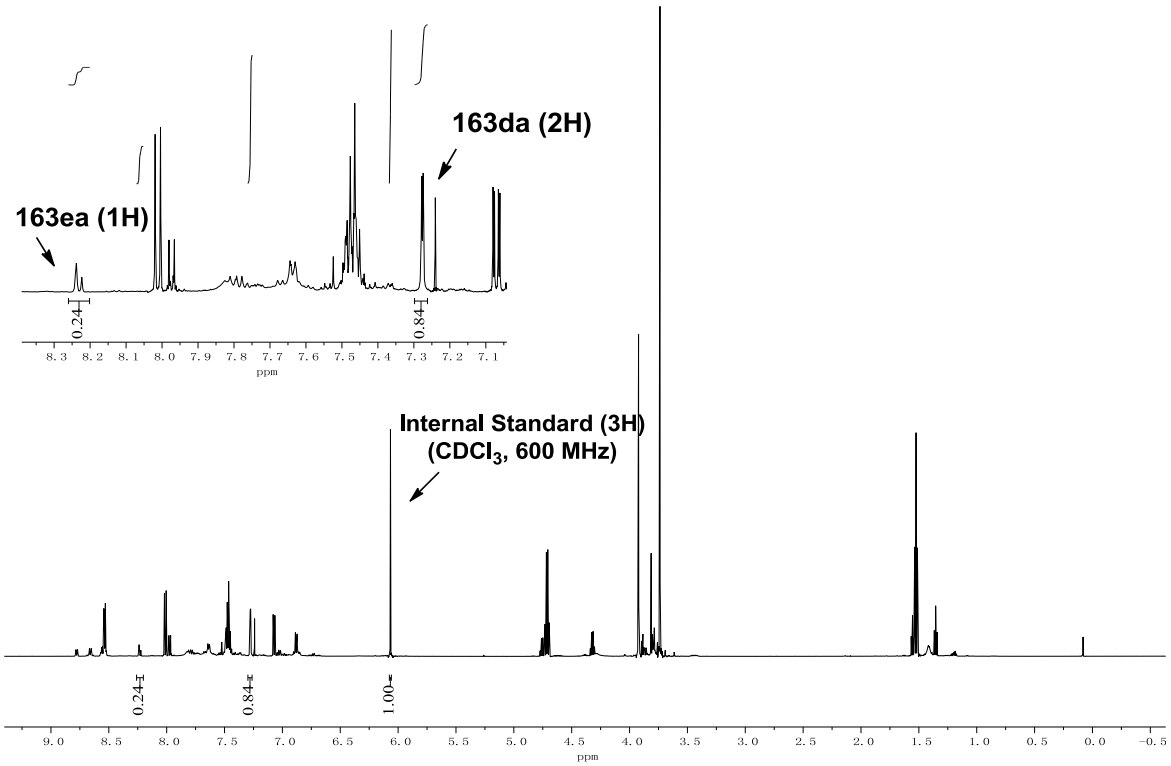
M. p. = 109–111 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.75 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 8.41 (dd, *J* = 1.6, 0.7 Hz, 1H), 8.30–8.15 (m, 2H), 8.07 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.92 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.80 (ddd, *J* = 8.0, 7.5, 1.8 Hz, 1H), 7.46 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.29 (ddd, *J* = 7.4, 4.8, 1.2 Hz, 1H), 7.15 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.73 (q, *J* = 7.1 Hz, 2H), 1.56 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.4 (C_q), 157.1 (C_q), 156.1 (C_q), 152.0 (C_q), 149.7 (CH), 144.2 (C_q), 144.1 (C_q), 136.8 (CH), 129.5 (CH), 128.8 (CH), 128.0 (CH), 125.3 (CH), 124.9 (CH), 124.0 (CH), 122.9 (CH), 121.2 (CH), 115.2 (C_q), 63.1 (CH_2), 14.5 (CH_3). **IR** (ATR) *v* = 3069, 2977, 1623, 1555, 1416, 1319, 1110, 846, 774, 703 cm^{-1}. **MS** (ESI) m/z (relative intensity): 306 (10), 334 (100) $[M+H]^+$, 356 (10) $[M+Na]^+$, 689 (10) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}N_3OS$ $[M+H]^+$: 334.1009, found: 334.1013.

Intermolecular competition experiments between different benzimidates 161

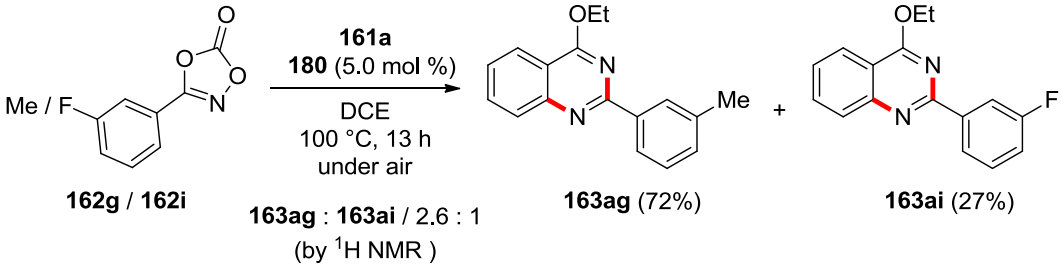


163da : **163ea** / 1.75 : 1
(by ^{1}H NMR)

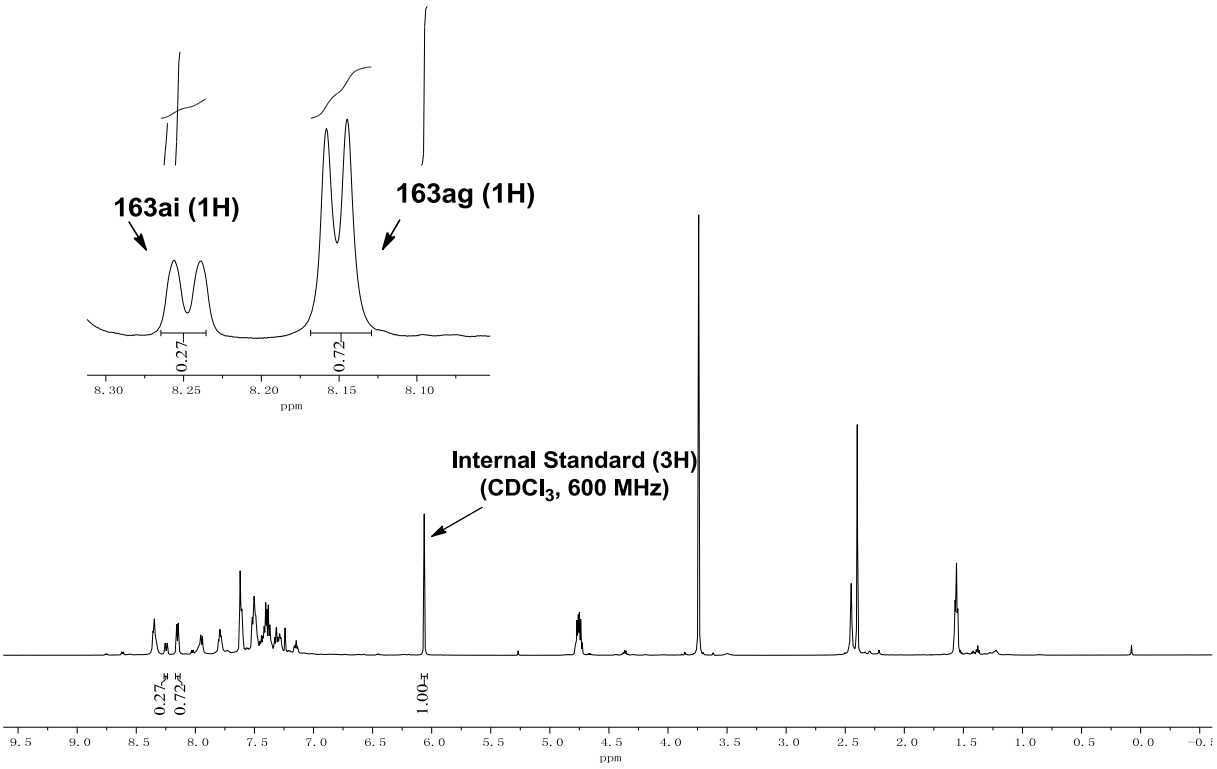
A suspension of ethyl 4-methoxybenzimidate (**161d**) (53.8 mg, 0.3 mmol), ethyl 4-(trifluoromethyl)benzimidate (**161e**) (65.2 mg, 0.3 mmol), 5-phenyloxazol-2(5*H*)-one (**162a**) (40.8 mg, 0.25 mmol) and $[Cp^*Co(CH_3CN)_3](SbF_6)_2$ (**180**) (6.9 mg, 5.0 mol %) in DCE (1.0 mL) was stirred under air at 100 °C for 13 h. After cooling to ambient temperature, the mixture was filtered through a short pad of celite, rinsed with CH_2Cl_2 (20 mL) and concentrated in *vacuo.* The crude ^{1}H NMR was measured to determine the conversions to the products **163da** (42%) and **163ea** (24%) using 1,3,5-trimethoxybenzene (13.9 mg, 0.083 mmol) as the internal standard.



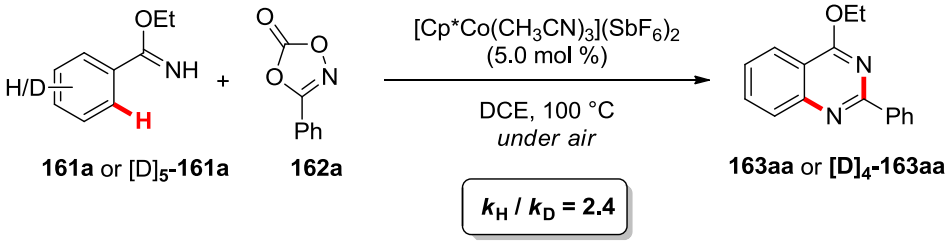
Intermolecular competition experiment between different dioxazolones 162



A suspension of ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol), 3-(*m*-tolyl)-1,4,2-dioxazol-5*H*-one (**162g**) (53.2 mg, 0.3 mmol), 3-(3-fluorophenyl)-1,4,2-dioxazol-5*H*-one (**162i**) (54.4 mg, 0.3 mmol) and $[Cp^*Co(CH_3CN)_3](SbF_6)_2$ (**180**) (6.9 mg, 5.0 mol %) in DCE (1.0 mL) was stirred under air at 100 °C for 13 h. After cooling to ambient temperature, the mixture was filtered through a short pad of celite, rinsed with CH_2Cl_2 (20 mL) and concentrated in *vacuo.* The crude ^1H NMR was measured to determine the conversions to the products **163ag** (72%) and **163ai** (27%) using 1,3,5-trimethoxybenzene (13.9 mg, 0.083 mmol) as the internal standard.

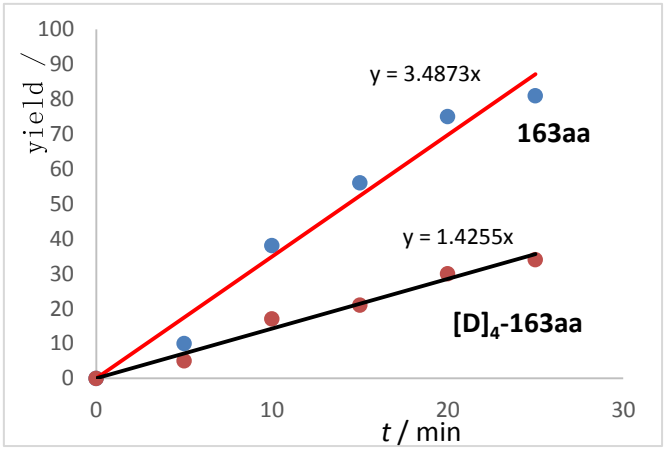


Kinetic Isotope Effect Experiment



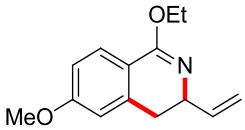
Two parallel reactions of **162a** with **161a** or [D]$_5$-**161a** were performed to determine the corresponding KIE value. **161a** (37.3 mg, 0.25 mmol) or [D]$_5$-**161a** (38.6 mg, 0.25 mmol), 3-phenyl-1,4,2-dioxazol-5*H*-one (**162a**) (48.9 mg, 0.30 mmol), [Cp*Co(CH$_3$CN)$_3$](SbF$_6$)$_2$ (**180**) (6.9 mg, 5.0 mol %) and 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol) as internal standard and DCE (1.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 100 °C, a periodic aliquot (0.05 mL) was removed by syringe and analyzed by GC to determine the following conversions:

t/ min / yield / %	5	10	15	20	25
163aa	10	38	56	75	81
[D]$_4$-**163aa**	5	17	21	30	34



5.3.4 Data for Cobalt(III)-Catalyzed Domino C–H/N–H Allylations of Imidates

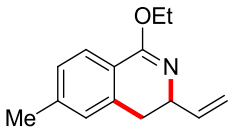
Characterization Data



1-Ethoxy-6-methoxy-3-vinyl-3,4-dihydroisoquinoline (164da): The general procedure **D** was followed using ethyl 4-methoxybenzimidate (**161d**) (44.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164da** (41 mg, 71%) as a colorless oil.

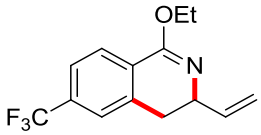
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 8.5 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.68 (d, *J* = 2.5 Hz, 1H), 5.95 (ddd, *J* = 17.1, 10.3, 5.9 Hz, 1H), 5.26 (dt, *J* = 17.1, 1.7 Hz, 1H), 5.07 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.35–4.14 (m, 3H), 3.80 (s, 3H), 2.87 (dd, *J* = 15.6, 5.5 Hz, 1H), 2.62 (dd, *J* = 15.6, 9.5 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 161.5 (C_q), 159.6 (C_q), 140.3 (CH), 140.2 (C_q), 126.4 (CH), 118.8 (C_q), 114.4 (CH_2), 112.6 (CH), 111.9 (CH), 60.8 (CH_2), 57.0 (CH), 55.3 (CH_3), 33.1 (CH_2), 14.4 (CH_3). **IR** (ATR) ν = 2977, 2936, 1636, 1606, 1298, 1254, 1150, 1034, 918, 675 cm^{-1}. **MS** (ESI) m/z

(relative intensity): 232 (100) $[M+H]^+$, 204 (40). HR-MS (ESI) m/z calcd for $C_{14}H_{18}NO_2$ $[M+H]^+$: 232.1332, found: 232.1339.



1-Ethoxy-6-methyl-3-vinyl-3,4-dihydroisoquinoline (164ca): The general procedure **D** was followed using ethyl 4-methylbenzimidate (**164c**) (40.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ca** (34 mg, 63%) as a colorless oil.

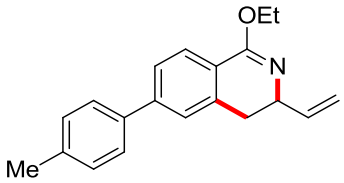
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 7.8 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.97 (s, 1H), 5.95 (ddd, *J* = 17.0, 10.3, 5.8 Hz, 1H), 5.26 (dt, *J* = 17.1, 1.7 Hz, 1H), 5.07 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.42–4.10 (m, 3H), 2.86 (dd, *J* = 15.6, 5.5 Hz, 1H), 2.61 (dd, *J* = 15.6, 9.6 Hz, 1H), 2.34 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 159.8 (C_q), 141.1 (C_q), 140.3 (CH), 138.1 (C_q), 128.0 (CH), 127.4 (CH), 124.6 (CH), 123.1 (C_q), 114.4 (CH_2), 60.8 (CH_2), 57.1 (CH), 32.7 (CH_2), 21.5 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 2977, 1648, 1637, 1575, 1298, 1168, 1099, 918, 827, 674 cm^{-1}. **MS** (ESI) m/z (relative intensity): 216 (100) $[M+H]^+$, 188 (40). **HR-MS** (ESI) m/z calcd for $C_{14}H_{18}NO$ $[M+H]^+$: 216.1383, found: 216.1387.



1-Ethoxy-6-(trifluoromethyl)-3-vinyl-3,4-dihydroisoquinoline (164ea): The general procedure **D** was followed using ethyl 4-(trifluoromethyl)benzimidate (**161e**) (54.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ea** (38 mg, 57%) as a colorless oil.

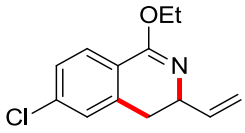
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.42 (s, 1H), 5.93 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.27 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.10 (dt, *J* = 10.3, 1.5 Hz, 1H), 4.48–4.10 (m, 3H), 2.96 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.70 (dd, *J* = 15.8, 9.6 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.4 (C_q), 139.5 (CH), 138.8 (C_q), 132.5 (q, ^2J = 32.1 Hz, C_q), 128.5 (C_q), 125.1 (CH), 124.2 (q, ^3J = 3.7 Hz, CH), 123.8 (q, ^1J = 273.3 Hz, C_q), 123.7 (q, ^3J = 4.0 Hz, CH), 115.0 (CH_2),

61.3 (CH_2), 56.7 (CH), 32.5 (CH_2), 14.3 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -62.90. **IR** (ATR) ν = 2981, 1651, 1297, 1167, 1125, 1101, 1070, 920, 844, 679 cm^{-1}. **MS** (ESI) m/z (relative intensity): 270 (100) $[M+H]^+$, 242 (40). **HR-MS** (ESI) m/z calcd for $C_{14}H_{15}F_3NO$ $[M+H]^+$: 270.1100, found: 270.1110.



1-Ethoxy-6-(*p*-tolyl)-3-vinyl-3,4-dihydroisoquinoline (164ua): The general procedure **D** was followed using ethyl 4'-methyl-(1,1'-biphenyl)-4-carbimidate (**161u**) (59.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ua** (37.9 mg, 52%) as a white solid.

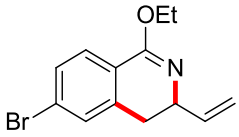
M.p. = 64–66 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.73 (d, J = 8.0 Hz, 1H), 7.55–7.44 (m, 3H), 7.38 (s, 1H), 7.24 (d, J = 7.9 Hz, 2H), 5.99 (ddd, J = 17.0, 10.3, 5.9 Hz, 1H), 5.30 (dt, J = 17.0, 1.6 Hz, 1H), 5.10 (dt, J = 10.3, 1.6 Hz, 1H), 4.65–4.12 (m, 3H), 2.97 (dd, J = 15.7, 5.6 Hz, 1H), 2.72 (dd, J = 15.7, 9.6 Hz, 1H), 2.39 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 159.7 (C_q), 143.7 (C_q), 140.1 (CH), 138.6 (C_q), 137.7 (C_q), 137.4 (C_q), 129.5 (CH), 127.0 (CH), 125.8 (CH), 125.3 (CH), 125.2 (CH), 124.2 (C_q), 114.7 (CH_2), 61.2 (CH_2), 57.0 (CH), 32.9 (CH_2), 21.1 (CH_3), 14.4 (CH_3). **IR** (ATR) ν = 2977, 1634, 1314, 1291, 1100, 919, 814, 674 cm^{-1}. **MS** (ESI) m/z (relative intensity): 292 (100) $[M+H]^+$, 264 (20). **HR-MS** (ESI) m/z calcd for $C_{20}H_{22}NO$ $[M+H]^+$: 292.1696, found: 292.1697.



6-Chloro-1-ethoxy-3-vinyl-3,4-dihydroisoquinoline (164ga): The general procedure **D** was followed using ethyl 4-chlorobenzimidate (**161g**) (45.9 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 30/1) yielded **164ga** (38 mg, 64%) as a colorless oil.

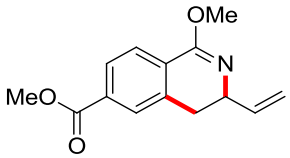
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 (d, J = 8.2 Hz, 1H), 7.22 (dt, J = 8.2, 2.1 Hz, 1H), 7.15 (d, J = 2.1 Hz, 1H), 5.92 (ddd, J = 17.1, 10.3, 5.8 Hz, 1H), 5.25 (dt, J = 17.1, 1.6 Hz, 1H), 5.08 (dt, J = 10.3, 1.6 Hz, 1H), 4.49–4.06 (m, 3H), 2.87 (dd, J = 15.8, 5.6 Hz, 1H), 2.62 (dd, J = 15.8, 9.6 Hz, 1H), 1.36 (t, J = 7.1 Hz,

3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.8 (C_q), 140.0 (C_q), 139.7 (CH), 136.6 (C_q), 127.4 (CH), 126.9 (CH), 126.1 (CH), 124.1 (C_q), 114.8 (CH_2), 61.1 (CH_2), 56.8 (CH), 32.5 (CH_2), 14.3 (CH_3). **IR** (ATR) ν = 2978, 1638, 1595, 1294, 1103, 920, 830, 665 cm^{-1}. **MS** (ESI) m/z (relative intensity): 236 (100) $[M+H]^+$, 208 (60). **HR-MS** (ESI) m/z calcd for $C_{13}H_{15}NOCl$ $[M+H]^+$: 236.0837, found: 236.0840.



6-Bromo-1-ethoxy-3-vinyl-3,4-dihydroisoquinoline (164va): The general procedure **D** was followed using ethyl 4-bromobenzimidate (**161v**) (57.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164va** (50 mg, 71%) as a colorless oil.

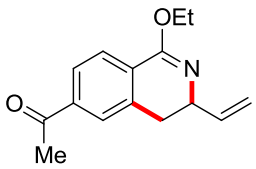
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.52 (d, *J* = 8.2 Hz, 1H), 7.38 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.31 (d, *J* = 2.0 Hz, 1H), 5.92 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.25 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.08 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.46–4.12 (m, 3H), 2.87 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.62 (dd, *J* = 15.8, 9.5 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 158.9 (C_q), 140.1 (C_q), 139.7 (CH), 130.3 (CH), 129.9 (CH), 126.3 (CH), 125.0 (C_q), 124.5 (C_q), 114.8 (CH_2), 61.1 (CH_2), 56.8 (CH), 32.3 (CH_2), 14.3 (CH_3). **IR** (ATR) ν = 2938, 2898, 1638, 1588, 1366, 1273, 1101, 918, 828, 665 cm^{-1}. **MS** (ESI) m/z (relative intensity): 282 (98) $[M+H]^+$ (^{81}Br), 280 (100) $[M+H]^+$ (^{79}Br), 254 (48) (^{81}Br), 252 (50) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{13}H_{15}NO^{79}Br$ $[M+H]^+$: 280.0332, found: 280.0333, $C_{13}H_{15}NO^{81}Br$ $[M+H]^+$: 282.0311, found: 282.0313.



Methyl 1-methoxy-3-vinyl-3,4-dihydroisoquinoline-6-carboxylate (164ia): The general procedure **D** was followed using methyl 4-[imino(methoxy)methyl]benzoate (**161i**) (48.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ia** (38 mg, 71%) as a white solid.

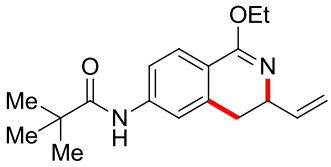
M.p. = 56–58 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.92 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.84 (s, 1H), 7.70 (d, *J* =

8.0 Hz, 1H), 5.94 (ddd, *J* = 17.1, 10.3, 5.7 Hz, 1H), 5.27 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.09 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.25 (ddd, *J* = 9.5, 5.7, 1.5 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 2.96 (dd, *J* = 15.8, 5.7 Hz, 1H), 2.69 (dd, *J* = 15.7, 9.7 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.5 (C_q), 159.3 (C_q), 139.6 (CH), 138.2 (C_q), 132.0 (C_q), 129.0 (C_q), 128.4 (CH), 128.1 (CH), 124.6 (CH), 114.9 (CH_2), 56.8 (CH), 52.9 (CH_3), 52.3 (CH_3), 32.5 (CH_2). **IR** (ATR) *v* = 2947, 1724, 1651, 1433, 1289, 1266, 1197, 1114, 906, 736 cm^{-1}. **MS** (ESI) m/z (relative intensity): 246 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{14}H_{16}NO_3$ $[M+H]^+$: 246.1125, found: 246.1125.



1-(1-Ethoxy-3-vinyl-3,4-dihydroisoquinolin-6-yl)ethanone (164ha): The general procedure **D** was followed using ethyl 4-acetylbenzimidate (**161h**) (47.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1→10/1) yielded **164ha** (37 mg, 61%) as a colorless oil.

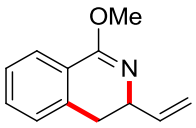
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.77–7.68 (m, 2H), 5.92 (ddd, *J* = 17.1, 10.3, 5.7 Hz, 1H), 5.25 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.08 (dt, *J* = 10.3, 1.5 Hz, 1H), 4.50–4.10 (m, 3H), 2.96 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.69 (dd, *J* = 15.7, 9.5 Hz, 1H), 2.58 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 197.6 (C_q), 158.7 (C_q), 139.6 (CH), 138.6 (C_q), 138.4 (C_q), 129.2 (C_q), 127.0 (CH), 126.9 (CH), 124.8 (CH), 114.8 (CH_2), 61.2 (CH_2), 56.8 (CH), 32.5 (CH_2), 26.7 (CH_3), 14.3 (CH_3). **IR** (ATR) *v* = 2978, 1685, 1637, 1421, 1359, 1300, 1280, 1105, 918, 671 cm^{-1}. **MS** (ESI) m/z (relative intensity): 266 (60) $[M+Na]^+$, 244 (100) $[M+H]^+$, 216 (50). **HR-MS** (ESI) m/z calcd for $C_{15}H_{18}NO_2$ $[M+H]^+$: 244.1332, found: 244.1334.



***N*-(1-Ethoxy-3-vinyl-3,4-dihydroisoquinolin-6-yl)pivalamide (164pa)**: The general procedure **D** was followed using ethyl 4-pivalamidobenzimidate (**161p**) (62.1 mg, 0.25 mmol) and

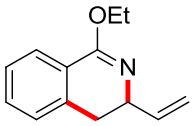
4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 4/1) yielded **164pa** (61 mg, 81%) as a white solid.

M.p. = 54–56 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 2.3 Hz, 1H), 7.37 (brs, 1H), 7.25 (dd, *J* = 8.4, 2.3 Hz, 1H), 5.91 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.23 (dt, *J* = 17.1, 1.7 Hz, 1H), 5.05 (dt, *J* = 10.3, 1.7 Hz, 1H), 4.43–4.08 (m, 3H), 2.88 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.62 (dd, *J* = 15.7, 9.2 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.29 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 176.7 (C_q), 159.3 (C_q), 140.2 (C_q), 140.0 (CH), 139.5 (C_q), 125.6 (CH), 121.6 (C_q), 118.2 (CH), 117.4 (CH), 114.6 (CH_2), 60.9 (CH_2), 56.9 (CH), 39.7 (C_q), 32.9 (CH_2), 27.6 (CH_3), 14.4 (CH_3). **IR** (ATR) *v* = 3331, 2973, 1650, 1636, 1585, 1520, 1302, 1166, 917, 732 cm^{-1}. **MS** (ESI) m/z (relative intensity): 323 (25) $[M+Na]^+$, 301 (100) $[M+H]^+$, 273 (10). **HR-MS** (ESI) m/z calcd for $C_{18}H_{25}N_2O_2$ $[M+H]^+$: 301.1911, found: 301.1914.



1-Methoxy-3-vinyl-3,4-dihydroisoquinoline (164ba): The general procedure **D** was followed using methyl benzimidate (**161b**) (33.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ba** (27 mg, 58%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.65 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.35 (td, *J* = 7.4, 1.5 Hz, 1H), 7.29–7.21 (m, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 5.97 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.29 (dt, *J* = 17.1, 1.7 Hz, 1H), 5.09 (dt, *J* = 10.3, 1.7 Hz, 1H), 4.22 (ddd, *J* = 9.9, 5.7, 1.5 Hz, 1H), 3.88 (s, 3H), 2.91 (dd, *J* = 15.7, 5.7 Hz, 1H), 2.66 (dd, *J* = 15.7, 9.9 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 160.0 (C_q), 140.1 (CH), 138.1 (C_q), 130.9 (CH), 127.3 (CH), 126.7 (CH), 125.5 (C_q), 124.6 (CH), 114.6 (CH_2), 57.0 (CH), 52.7 (CH_3), 32.7 (CH_2). **IR** (ATR) *v* = 2942, 1650, 1638, 1436, 1310, 1901, 919, 738, 671 cm^{-1}. **MS** (ESI) m/z (relative intensity): 188 (100) $[M+H]^+$. HR-MS (ESI) m/z calcd for $C_{12}H_{14}NO$ $[M+H]^+$: 188.1070, found: 188.1071.

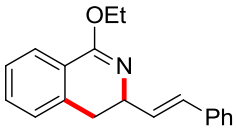


1-Ethoxy-3-vinyl-3,4-dihydroisoquinoline (164aa): The general procedure **D** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164aa** (36 mg, 72%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.34 (td, *J* = 7.5, 1.4 Hz, 1H), 7.25 (d, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 5.96 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.28 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.08 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.45–4.07 (m, 3H), 2.90 (dd, *J* = 15.6, 5.5 Hz, 1H), 2.65 (dd, *J* = 15.6, 9.8 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 159.5 (C_q), 140.2 (CH), 138.1 (C_q), 130.8 (CH), 127.2 (CH), 126.7 (CH), 125.7 (C_q), 124.6 (CH), 114.5 (CH_2), 60.9 (CH_2), 57.0 (CH), 32.7 (CH_2), 14.4 (CH_3). **IR** (ATR) *v* = 2978, 1649, 1638, 1366, 1300, 1093, 917, 738, 680 cm^{-1}. **MS** (ESI) m/z (relative intensity): 202 (100) $[M+H]^+$, 174 (75). **HR-MS** (ESI) m/z calcd for $C_{13}H_{16}NO$ $[M+H]^+$: 202.1226, found: 202.1230.

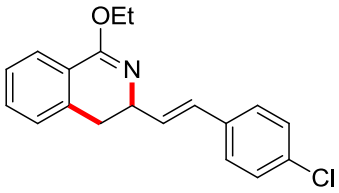
1-Isopropoxy-3-vinyl-3,4-dihydroisoquinoline (164wa): The general procedure **D** was followed using isopropyl benzimidate (**161w**) (40.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164wa** (36 mg, 67%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.67 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.33 (ddd, *J* = 7.7, 7.5, 1.5 Hz, 1H), 7.25 (ddd, *J* = 7.7, 7.5, 1.5 Hz, 1H), 7.15 (d, *J* = 7.3 Hz, 1H), 5.96 (ddd, *J* = 17.2, 10.3, 5.7 Hz, 1H), 5.42–5.20 (m, 2H), 5.07 (dt, *J* = 10.3, 1.7 Hz, 1H), 4.27–4.16 (m, 1H), 2.90 (dd, *J* = 15.6, 5.5 Hz, 1H), 2.64 (dd, *J* = 15.6, 9.7 Hz, 1H), 1.34 (d, *J* = 6.2 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 158.7 (C_q), 140.4 (CH), 138.2 (C_q), 130.7 (CH), 127.2 (CH), 126.6 (CH), 126.1 (C_q), 124.7 (CH), 114.4 (CH_2), 67.0 (CH), 56.9 (CH), 32.7 (CH_2), 22.0 (CH_3), 21.8 (CH_3). **IR** (ATR) *v* = 2975, 1637, 1359, 1298, 1114, 1089, 918, 778, 739, 682 cm^{-1}. **MS** (ESI) m/z (relative intensity): 238 (10) $[M+Na]^+$, 216 (10) $[M+H]^+$, 196 (20), 174 (100). HR-MS (ESI) m/z calcd for $C_{14}H_{18}NO$ $[M+H]^+$: 216.1383, found: 216.1385.



(*E*)-1-Ethoxy-3-styryl-3,4-dihydroisoquinoline (164ab): The general procedure **D** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and (*trans*)-4-phenyl-5-vinyl-1,3-dioxolan-2-one (**110b**) (142.7 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ab** (34.7 mg, 50%) as a colorless oil.

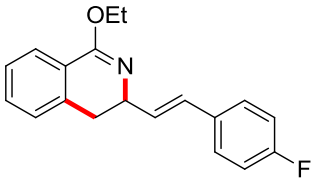
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.71 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.43–7.32 (m, 3H), 7.31–7.23 (m, 3H), 7.22–7.12 (m, 2H), 6.66 (dd, *J* = 15.8, 1.4 Hz, 1H), 6.31 (dd, *J* = 15.8, 6.3 Hz, 1H), 4.50–4.25 (m, 3H), 2.98 (dd, *J* = 15.7, 5.4 Hz, 1H), 2.74 (dd, *J* = 15.7, 9.8 Hz, 1H), 1.41 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 159.6 (C_q), 138.1 (C_q), 137.3 (C_q), 131.9 (CH), 130.8 (CH), 129.8 (CH), 128.3 (CH), 127.2 (CH), 127.1 (CH), 126.7 (CH), 126.3 (CH), 125.7 (C_q), 124.7 (CH), 61.1 (CH_2), 56.9 (CH), 33.3 (CH_2), 14.5 (CH_3). **IR** (ATR) ν = 2977, 1639, 1493, 1367, 1298, 1095, 964, 731, 691 cm^{-1}. **MS** (ESI) m/z (relative intensity): 278 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{20}NO$ $[M+H]^+$: 278.1539, found: 278.1542.



(*E*)-3-(4-Chlorostyryl)-1-ethoxy-3,4-dihydroisoquinoline (164ac): The general procedure **D** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and (*trans*)-4-(4-chlorophenyl)-5-vinyl-1,3-dioxolan-2-one (**110c**) (168.5 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **164ac** (41.2 mg, 53%) as a white solid.

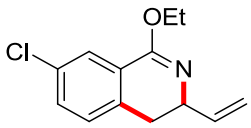
M.p. = 120–123 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.70 (d, *J* = 7.7 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.29–7.17 (m, 6H), 6.62 (dd, *J* = 15.8, 1.4 Hz, 1H), 6.29 (dd, *J* = 15.8, 10.3 Hz, 1H), 4.38–4.28 (m, 3H), 2.96 (dd, *J* = 15.6, 5.4 Hz, 1H), 2.72 (dd, *J* = 15.6, 10.3 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 160.0 (C_q), 138.2 (C_q), 136.0 (C_q), 132.9 (C_q), 132.8 (CH), 131.2 (CH), 128.9 (CH), 128.7 (CH), 127.8 (CH), 127.5 (CH), 127.0 (CH), 125.8 (C_q), 125.0 (CH), 61.4 (CH_2), 56.9 (CH), 33.2 (CH_2), 14.5 (CH_3). **IR** (ATR) ν = 2972, 1640, 1488, 1366, 1217, 1160, 1011, 779, 504 cm^{-1}. **MS** (ESI)

m/z (relative intensity): 312 (100) $[M+H]^+$, 240 (20). **HR-MS** (ESI) m/z calcd for $C_{19}H_{19}ClNO$ $[M+H]^+$: 312.1150, found: 312.1153.



(*E*)-1-Ethoxy-3-(4-fluorostyryl)-3,4-dihydroisoquinoline (164ad): The general procedure **D** was followed using ethyl benzimidate (**161a**) (37.3 mg, 0.25 mmol) and (*trans*)-4-(4-fluorophenyl)-5-vinyl-1,3-dioxolan-2-one (**110d**) (156.2 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ad** (45.0 mg, 61%) as a white solid.

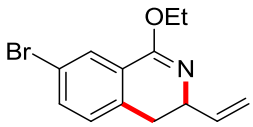
M.p. = 89–90 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.71 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.42–7.25 (m, 4H), 7.19 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.05–6.88 (m, 2H), 6.63 (dd, *J* = 15.8, 1.4 Hz, 1H), 6.23 (dd, *J* = 15.8, 6.4 Hz, 1H), 4.50–4.22 (m, 3H), 2.97 (dd, *J* = 15.7, 5.4 Hz, 1H), 2.73 (dd, *J* = 15.7, 10.0 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 162.0 (d, $^1J_{C-F}$ = 247.0 Hz, C_q), 159.6 (C_q), 138.0 (C_q), 133.4 (d, $^4J_{C-F}$ = 3.2 Hz, C_q), 131.7 (CH), 130.9 (CH), 128.6 (CH), 127.8 (d, $^3J_{C-F}$ = 8.0 Hz, CH), 127.2 (CH), 126.7 (CH), 125.6 (C_q), 124.7 (CH), 115.3 (d, $^2J_{C-F}$ = 21.6 Hz, CH), 61.1 (CH_2), 56.9 (CH), 33.3 (CH_2), 14.5 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -115.23 (ddd, *J* = 14.0, 8.7, 5.4 Hz). **IR** (ATR) *v* = 1638, 1508, 1365, 1296, 1224, 1160, 1097, 730, 677 cm^{-1}. **MS** (ESI) m/z (relative intensity): 296 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{19}FNO$ $[M+H]^+$: 296.1445, found: 296.1450.



7-Chloro-1-ethoxy-3-vinyl-3,4-dihydroisoquinoline (164ma): The general procedure **D** was followed using ethyl 3-chlorobenzimidate (**161m**) (45.9 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164mq** (36 mg, 61%) as a colorless oil.

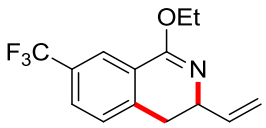
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.65 (d, *J* = 2.2 Hz, 1H), 7.31 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 5.92 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.25 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.08 (dt, *J* = 10.3, 1.5 Hz, 1H),

4.53–3.99 (m, 3H), 2.87 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.61 (dd, *J* = 15.7, 9.6 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.5 (C_q), 139.8 (CH), 136.4 (C_q), 132.4 (C_q), 130.7 (CH), 128.6 (CH), 127.0 (C_q) 124.9 (CH), 114.8 (CH_2), 61.2 (CH_2), 56.9 (CH), 32.0 (CH_2), 14.3 (CH_3). **IR** (ATR) *v* = 2977, 1650, 1482, 1302, 1258, 1106, 1019, 792, 512 cm^{-1}. **MS** (ESI) m/z (relative intensity): 236 (100) $[M+H]^+$, 208 (60). **HR-MS** (ESI) m/z calcd for $C_{13}H_{15}ClNO$ $[M+H]^+$: 236.0837, found: 236.0838.



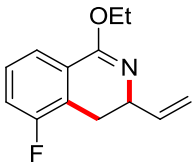
7-Bromo-1-ethoxy-3-vinyl-3,4-dihydroisoquinoline (164xa): The general procedure **D** was followed using ethyl 3-bromobenzimidate (**161x**) (57.0 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164xa** (49 mg, 70%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.81 (d, *J* = 2.0 Hz, 1H), 7.46 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 5.91 (ddd, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.25 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.08 (dt, *J* = 10.3, 1.5 Hz, 1H), 4.61–4.06 (m, 3H), 2.86 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.59 (dd, *J* = 15.8, 9.5 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 158.4 (C_q), 139.5 (CH), 136.9 (C_q), 133.8 (CH), 128.9 (CH), 127.8 (CH), 127.1 (C_q), 120.3 (C_q), 114.9 (CH_2), 61.5 (CH_2), 56.7 (CH), 32.0 (CH_2), 14.3 (CH_3). **IR** (ATR) *v* = 2977, 1650, 1567, 1479, 1303, 1258, 1101, 919, 815 cm^{-1}. **MS** (ESI) m/z (relative intensity): 282 (98) (^{81}Br), 280 (100) $[M+H]^+$ (^{79}Br), 254 (50) (^{81}Br), 252 (48) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{13}H_{15}NO^{79}Br$ $[M+H]^+$: 280.0332, found: 280.0334, $C_{13}H_{15}NO^{81}Br$ $[M+H]^+$: 282.0311, found: 282.0314.



1-Ethoxy-7-(trifluoromethyl)-3-vinyl-3,4-dihydroisoquinoline (164la): The general procedure **D** was followed using ethyl 3-(trifluoromethyl)benzimidate (**161l**) (54.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164la** (36 mg, 53%) as a colorless oil.

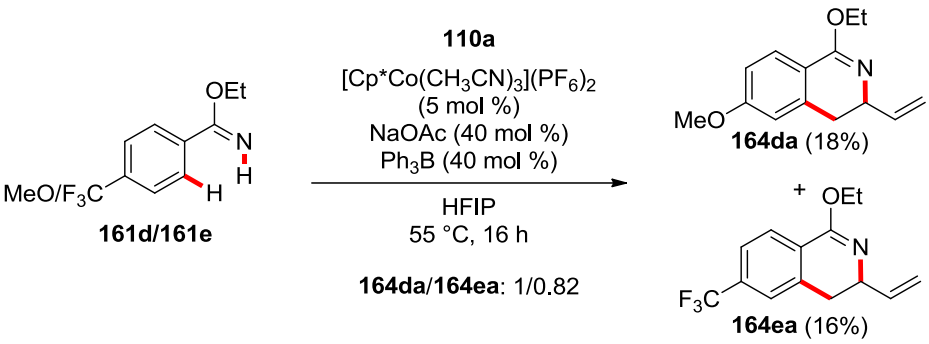
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (s, 1H), 7.59 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 5.93 (ddd, *J* = 17.1, 10.3, 5.7 Hz, 1H), 5.27 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.10 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.46–4.16 (m, 3H), 2.96 (dd, *J* = 15.9, 5.6 Hz, 1H), 2.70 (dd, *J* = 15.9, 9.6 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.3 (C_q), 142.0 (C_q), 139.6 (CH), 129.3 (q, $^{2}J_{C\text{-}F}$ = 32.4 Hz, C_q), 127.8 (CH), 127.3 (q, $^{3}J_{C\text{-}F}$ = 3.7 Hz, CH), 126.2 (C_q), 123.9 (q, $^{1}J_{C\text{-}F}$ = 272.8 Hz, C_q), 121.7 (q, $^{3}J_{C\text{-}F}$ = 3.9 Hz, CH), 114.9 (CH_2), 61.3 (CH_2), 56.6 (CH), 32.5 (CH_2), 14.3 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -62.50. **IR** (ATR) *v* = 2981, 1653, 1336, 1301, 1259, 1167, 1124, 1101, 917 cm^{-1}. **MS** (ESI) m/z (relative intensity): 270 (100) $[M+H]^+$, 242 (50). **HR-MS** (ESI) m/z calcd for $C_{14}H_{15}NOF_3$ $[M+H]^+$: 270.1100, found: 2270.1101.



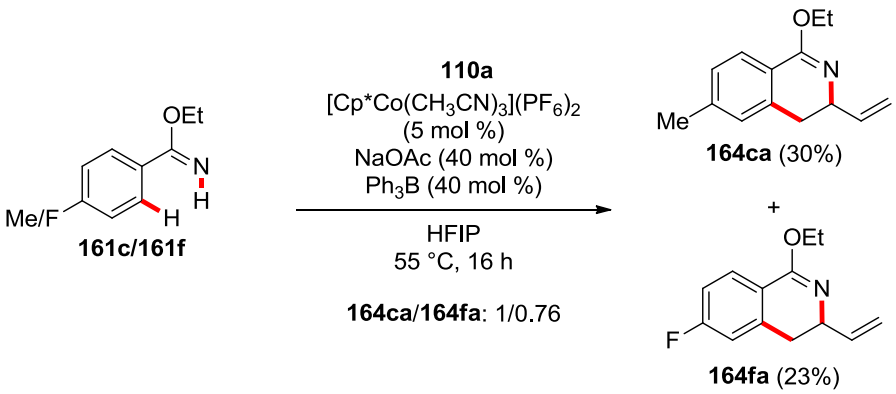
1-Ethoxy-5-fluoro-3-vinyl-3,4-dihydroisoquinoline (164ya): The general procedure **D** was followed using ethyl 3-fluorobenzimidate (**161y**) (41.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) yielded **164ya** (37 mg, 67%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.48 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.31–7.16 (m, 1H), 7.09 (dd, *J* = 8.6, 1.2 Hz, 1H), 5.96 (ddd, *J* = 17.1, 10.3, 5.7 Hz, 1H), 5.28 (dt, *J* = 17.1, 1.6 Hz, 1H), 5.10 (dt, *J* = 10.3, 1.6 Hz, 1H), 4.50–4.10 (m, 3H), 2.98 (dd, *J* = 16.1, 5.7 Hz, 1H), 2.60 (dd, *J* = 16.2, 9.7 Hz, 1H), 1.37 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 159.1 (d, $^{1}J_{C\text{-}F}$ = 243.9 Hz, C_q), 158.5 (d, $^{4}J_{C\text{-}F}$ = 4.3 Hz, C_q), 139.8 (CH), 127.3 (d, $^{3}J_{C\text{-}F}$ = 6.1 Hz, C_q), 127.2 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz, CH), 124.8 (d, $^{2}J_{C\text{-}F}$ = 19.4 Hz, C_q), 120.4 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz, CH), 117.5 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz, CH), 114.6 (CH_2), 61.1 (CH_2), 56.3 (CH), 24.9 (d, $^{3}J_{C\text{-}F}$ = 1.4 Hz, CH_2), 14.4 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -120.72 (dd, *J* = 8.9, 5.5 Hz). **IR** (ATR) *v* = 2979, 1651, 1583, 1467, 1293, 1040, 920, 798, 732 cm^{-1}. **MS** (ESI) m/z (relative intensity): 220 (100) $[M+H]^+$, 192 (80). **HR-MS** (ESI) m/z calcd for $C_{13}H_{15}NOF$ $[M+H]^+$: 220.1132, found: 220.1134.

Intermolecular Competition Experiments

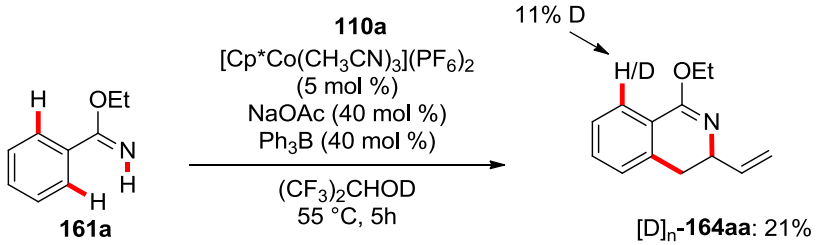


A suspension of ethyl 4-methoxybenzimidate (**161d**) (44.8 mg, 0.25 mmol), ethyl 4-(trifluoromethyl)benzimidate (**161e**) (54.3 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (28.6 mg, 0.25 mmol), NaOAc (8.2 mg, 40 mol %), Ph_3B (24.2 mg, 40 mol %) and $[Cp^*Co(CH_3CN)_3](PF_6)_2$ (**180**) (7.6 mg, 5.0 mol %) in HFIP (1.0 mL) was stirred under N_2 at 55 °C for 5 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1→10/1) afforded product **164da** (10 mg, 18%) and **164ea** (11 mg, 16%).

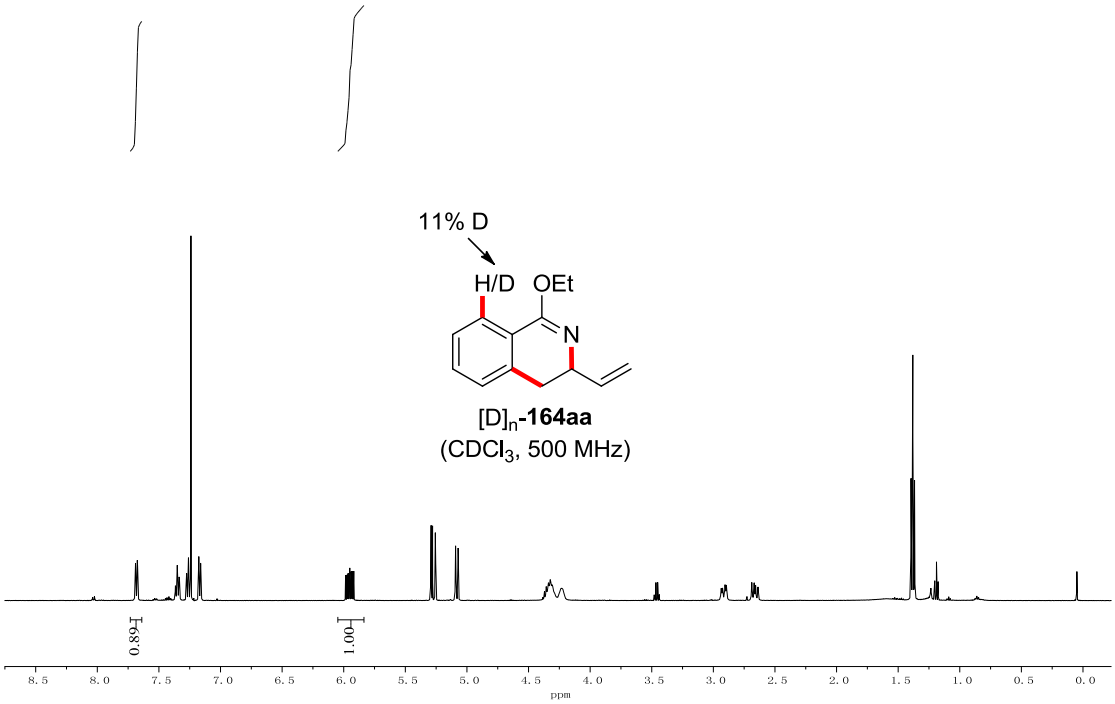


A suspension of ethyl 4-methylbenzimidate (**161c**) (40.8 mg, 0.25 mmol), ethyl 4-fluorobenzimidate (**161f**) (41.8 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (28.6 mg, 0.25 mmol), NaOAc (8.2 mg, 40 mol %), Ph_3B (24.2 mg, 40 mol %) and $[Cp^*Co(CH_3CN)_3](PF_6)_2$ (**180**) (7.6 mg, 5.0 mol %) in HFIP (1.0 mL) was stirred under N_2 at 55 °C for 5 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1→10/1) afforded product **164ca** (16.2 mg, 30%) and **164fa** (12.3 mg, 23%).

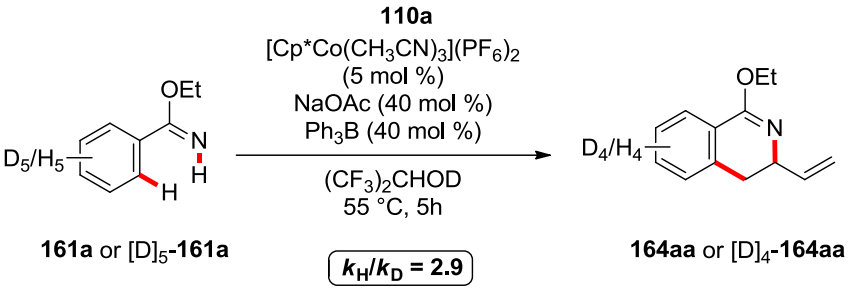
H/D Exchange Experiment



A suspension of benzimidate (**161a**) (37.3 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (8.2 mg, 40 mol %), Ph_3B (24.2 mg, 40 mol %) and $[Cp^*Co(CH_3CN)_3](PF_6)_2$ (**180**) (7.6 mg, 5.0 mol %) in $(CF_3)_2CHOD$ (1.0 mL) was stirred under N_2 at 55 °C for 5 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-pentane/Et_2O: 20/1) afforded product $[D]_n$-**164aa** (11 mg, 21%). The H/D exchange result was determined by ^1H NMR spectroscopy.

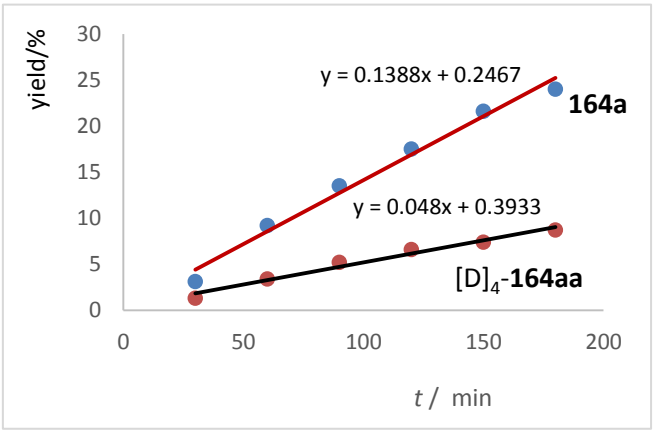


Intermolecular KIE Experiment

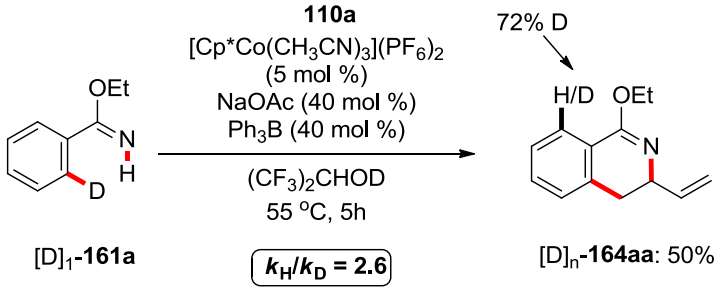


Two parallel reactions of **110a** with **161a** or [D]$_5$-**161a** were performed to determine the corresponding KIE value. **164aa** (37.3 mg, 0.25 mmol) or [D]$_5$-**164aa** (38.6 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (8.2 mg, 40 mol %), Ph_3B (24.2 mg, 40 mol %), and $[Cp^*Co(CH_3CN)_3](PF_6)_2$ (7.6 mg, 5.0 mol %), 1,3,5-trimethoxybenzene (42.0 mg, 0.25 mmol) as internal standard and HFIP (1.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 55 °C, and a periodic aliquot (0.05 mL) was removed by syringe and analyzed by GC to determine the following conversions:

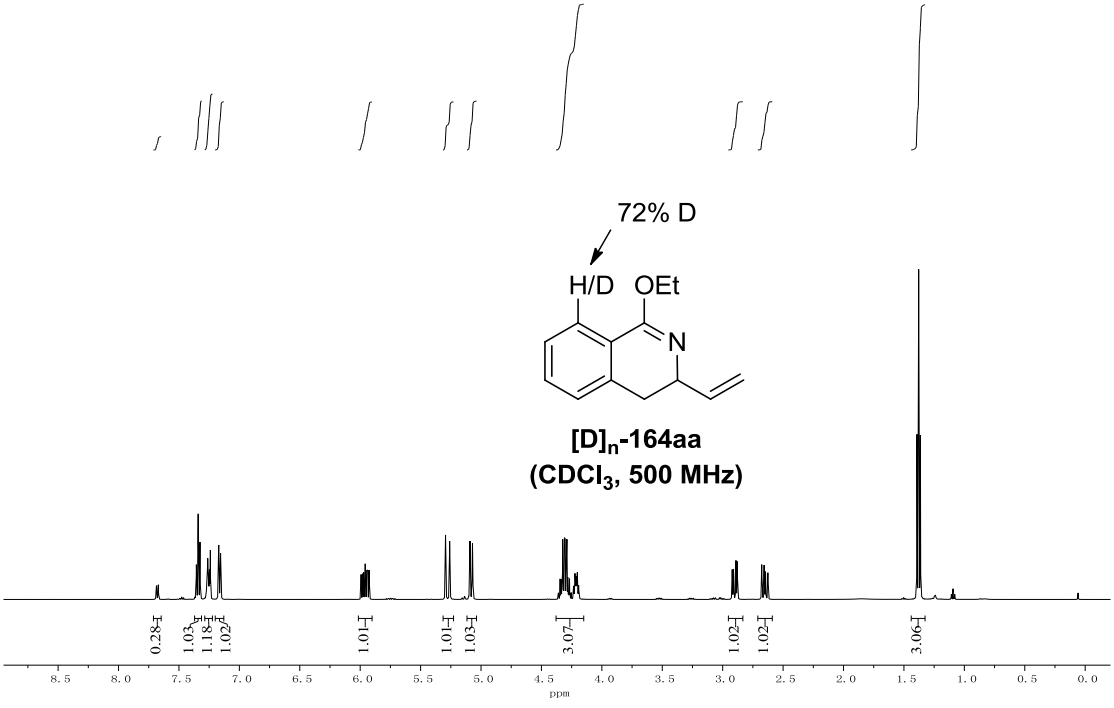
t / min yield / %	30	60	90	120	150	180
164aa	3.1	9.2	13.5	17.5	21.6	24.0
[D]$_4$-**164aa**	1.3	3.4	5.2	6.6	7.4	8.7



Intramolecular KIE Experiment

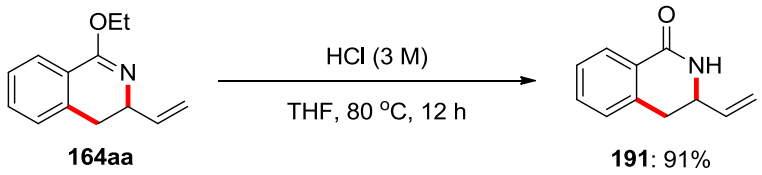


A suspension of $[D]_1$-**161a** (37.6 mg 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (8.2 mg, 40 mol %), Ph_3B (24.2 mg, 40 mol %), and $[Cp^*Co(CH_3CN)_3](PF_6)_2$ (**180**) (7.6 mg, 5.0 mol %) in HFIP (1.0 mL) was stirred for 16 h at 55 °C. After cooling to ambient temperature, the reaction mixture was transferred into a round flask with CH_2Cl_2 (20 mL) and concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) to afford $[D]_n$-**164aa** (25.3 mg, 50%). The kinetic isotope effect of this reaction was determined to be k_H/k_D = 2.6 as estimated by ^{1}H NMR spectroscopy.



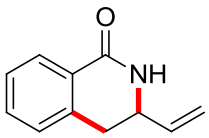
Diversification of Vinylated Heteroarenes 164

a) Synthesis of Dihydroisoquinolone 191



164aa **191**: 91%

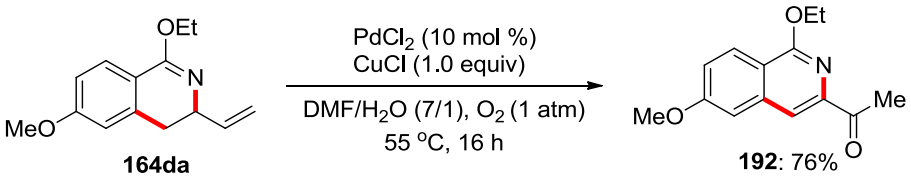
To a solution of **164aa** (50.4 mg 0.25 mmol) in THF (2.0 mL) was added aqueous HCl (3 M, 2.0 mL), and the mixture was stirred at 80 °C for 12 h. After cooling to ambient temperature, the solution was neutralized with a saturated $NaHCO_3$ solution and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (40 mL), dried over Na_2SO_4, and evaporated *in vacuo*. Purification by column chromatography (EtOAc/*n*-hexane: 4/1) afforded product **191** (39.4 mg, 91%) as a white solid.



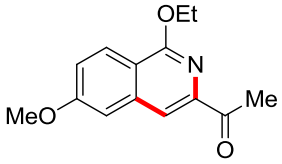
3-Vinyl-3,4-dihydroisoquinolin-1(2*H*)-one (191)

M.p.: 90–92 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.04 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.42 (td, *J* = 7.5, 1.5 Hz, 1H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 6.34 (brs, 1H), 5.88 (ddd, *J* = 17.0, 10.2, 6.6 Hz, 1H), 5.29 (dd, *J* = 17.0, 1.5 Hz, 1H), 5.18 (dd, *J* = 10.3, 1.5 Hz, 1H), 4.31–4.17 (m, 1H), 3.05 (dd, *J* = 15.6, 5.0 Hz, 1H), 2.91 (dd, *J* = 15.6, 9.3 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 166.0 (C_q), 137.3 (CH), 132.3 (CH), 128.4 (C_q), 127.9 (CH), 127.4 (CH), 127.1 (CH), 117.2 (C_q), 117.1 (CH_2), 53.9 (CH), 34.4 (CH_2). **IR** (ATR) ν = 3188, 3039, 2925, 1659, 1470, 1406, 1346, 915, 740, 535 cm^{-1}. **MS** (ESI) m/z (relative intensity) 296 (60) $[M+Na]^+$, 174 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{11}H_{12}NO$ $[M+H]^+$: 174.0913, found: 174.0916.

b) Synthesis of Acetylated Isoquinoline 192 by Wacker-Type Oxidation



To a stirred solution of $PdCl_2$ (4.4 mg, 0.025 mmol) and CuCl (24.8 mg, 0.25 mmol) in DMF and H_2O (7:1, 2 mL) was added **164da** (57.8 mg, 0.25 mmol) under ambient O_2 atmosphere. The reaction mixture was stirred at ambient temperature for 12 h and extracted with Et_2O. The organic layer was dried over Na_2SO_4 and evaporated *in vacuo*. The crude product was separated by column chromatography (EtOAc/*n*-hexane: 10/1) to afford product **192** (46.6 mg, 76%) as a white solid.

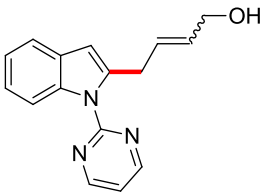


1-(1-Ethoxy-6-methoxyisoquinolin-3-yl)ethanone (192)

M.p. = 127–129 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.16 (d, *J* = 9.1 Hz, 1H), 7.91 (s, 1H), 7.21 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 4.60 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 2.71 (s, 3H), 1.50 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 200.5 (C_q), 161.2 (C_q), 159.7 (C_q), 145.4 (C_q), 139.4 (C_q), 125.9 (CH), 120.5 (CH), 116.4 (C_q), 113.8 (CH), 106.7 (CH), 62.1 (CH_2), 55.5 (CH_3), 26.5 (CH_3), 14.6 (CH_3). **IR** (ATR) *v* = 3076, 2937, 1685, 1574, 1412, 1327, 1236, 1160, 910, 630 cm^{-1}. **MS** (ESI) m/z (relative intensity) 268 (100) $[M+Na]^+$, 246 (95) $[M+H]^+$, 218 (60). **HR-MS** (ESI) m/z calcd for $C_{14}H_{16}NO_3$ $[M+H]^+$: 246.1125, found: 246.1127.

5.3.5 Data for Maganese(I)-Catalyzed C–H Activation for Decarboxylative C–H/C–O Functionalization in Water

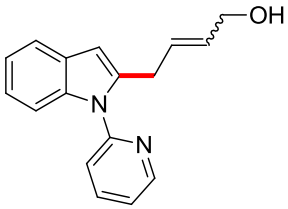
Characterization Data



(*E*/*Z*)-4-[1-(Pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111aa): The general procedure **E** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111aa** (61.7 mg, 93%, *E*/*Z* = 5.9/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 2H), 8.22 (d, *J* = 7.7 Hz, 1H), 7.52 (dd, *J* = 6.5, 1.5 Hz, 1H), 7.31–7.07 (m, 2H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.46 (s, 1H), 6.00–5.52 (m, 2H), 4.22 (d, *J* = 5.3 Hz, 0.35H), 4.00 (dd, *J* = 5.8, 1.2 Hz, 1.65H), 3.98–3.85 (m, 2H), 1.54 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major isomer*: δ = 158.1 (CH), 158.1 (C_q), 139.6 (C_q), 137.0 (C_q), 131.0 (CH), 129.4 (CH), 129.1 (C_q), 122.7 (CH), 121.8 (CH), 119.8 (CH), 117.1 (CH), 113.7 (CH), 106.4 (CH), 63.3 (CH_2), 32.4 (CH_2). *Minor isomer*: δ = 139.6 (C_q), 130.1 (CH), 129.0 (CH), 122.7 (CH), 121.9 (CH), 113.8 (CH), 106.2 (CH), 58.5 (CH_2), 28.1 (CH_2). (Due to overlap, five peaks are missing). **IR** (ATR) *v* = 3376, 2862, 1562, 1454, 1425, 1348, 1207, 973, 802, 746 cm^{-1}. **MS** (ESI) m/z (relative intensity): 288 (100) $[M+Na]^+$, 266 (20) $[M+H]^+$, 248 (40). **HR-MS** (ESI) m/z calcd for $C_{16}H_{16}N_3O$ $[M+H]^+$: 266.1288, found: 266.1288.

The analytical data were in accordance with those reported in the literature.[69]

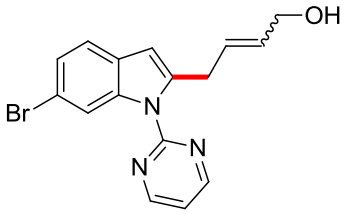


(*E*/*Z*)-4-[1-(Pyridin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ba): The general procedure **E** was followed using methyl 1-(pyridin-2-yl)-1*H*-indole (**41b**) (48.6 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one

(**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ba** (64.8 mg, 98%, *E*/*Z* = 5.2/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.62 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.89–7.81 (m, 1H), 7.58–7.50 (m, 1H), 7.43 (d, *J* = 8.0 Hz, 0.17H), 7.40 (d, *J* = 8.0 Hz, 0.83H), 7.34–7.27 (m, 2H), 7.17–7.08 (m, 2H), 6.43 (s, 1H), 5.73–5.38 (m, 2H), 4.06 (d, *J* = 4.7 Hz, 0.32H), 3.93 (d, *J* = 6.5 Hz, 1.68H), 3.63 (d, *J* = 5.3 Hz, 0.32H), 3.60 (d, *J* = 6.6 Hz, 1.68H), 1.77 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major isomer*: δ = 151.2 (C_q), 149.5 (CH), 138.9 (C_q), 138.3 (CH), 137.3 (C_q), 131.1 (CH), 128.5 (CH), 128.4 (C_q), 122.1 (CH), 121.8 (CH), 121.1 (CH), 120.7 (CH), 120.0 (CH), 110.0 (CH), 103.1 (CH), 63.1 (CH_2), 30.6 (CH_2). *Minor isomer*: δ = 151.2 (C_q), 149.5 (CH), 139.2 (C_q), 138.4 (CH), 130.3 (CH), 128.2 (CH), 120.7 (CH), 110.0 (CH), 102.9 (CH), 58.2 (CH_2), 26.1 (CH_2). (Due to overlap, six peaks are missing). **IR** (ATR) *v* = 3355, 2862, 1587, 1469, 1456, 1437, 1348, 1212, 972, 782, 754 cm^{-1}. **MS** (ESI) m/z (relative intensity): 287 (60) $[M+Na]^+$, 265 (80) $[M+H]^+$, 247 (100). **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1335, found: 265.1337.

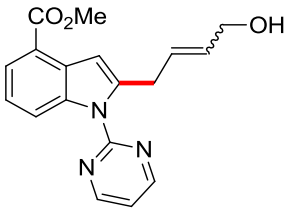
The analytical data were in accordance with those reported in the literature.[66c]



(*E*/*Z*)-1-[2-(4-Hydroxybut-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indol-3-yl]ethanone (111ea): The general procedure **E** was followed using 6-bromo-1-(pyrimidin-2-yl)-1*H*-indole (**41e**) (68.5 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ea** (79.2 mg, 92%, *E*/*Z* = 5.3/1.0 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 2H), 8.48–8.44 (m, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.28 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 6.43 (s, 1H), 5.87–5.59 (m, 2H), 4.23 (d, *J* = 4.9 Hz, 0.26H), 4.02 (dd, *J* = 5.7, 1.2 Hz, 1.74H), 3.95–3.89 (m, 2H), 1.67 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major Isomer*: δ = 158.1 (CH), 157.7 (C_q), 140.4 (C_q), 137.6 (C_q), 131.2 (CH), 128.9 (CH), 127.9 (C_q), 124.9 (CH), 120.8 (CH), 117.4 (CH), 116.9 (CH), 116.2 (C_q), 106.2 (CH), 63.2 (CH_2), 32.5 (CH_2). *Minor Isomer*: δ = 137.6 (C_q), 130.4 (CH), 128.6 (CH), 125.0 (CH), 117.4 (CH), 117.0 (CH), 116.3 (C_q),

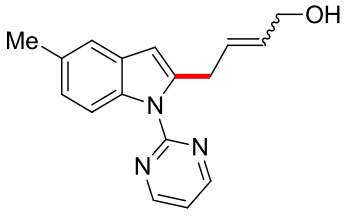
106.0 (CH), 58.5 (CH_2), 28.1 (CH_2). (Due to overlap, five peaks are missing). **IR** (ATR) *v* = 3347, 2917, 1575, 1422, 1343, 973, 815, 736 cm^{-1}. **MS** (ESI) m/z (relative intensity): 368 (100) $[M+Na]^+$ (^{81}Br), 366 (98) $[M+Na]^+$ (^{79}Br), 346 (50) $[M+H]^+$ (^{81}Br), 344 (50) $[M+H]^+$ (^{79}Br), 328 (45) (^{81}Br), 326 (45) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{16}H_{14}BrN_3ONa$ $[M+Na]^+$: 366.0212, found: 366.0223.



(*E*/*Z*)-Methyl 2-(4-hydroxybut-2-en-1-yl)-1-(pyrimidin-2-yl)-1*H*-indole-4-carboxylate (111fa): The general procedure **E** was followed using methyl 1-(pyrimidin-2-yl)-1*H*-indole-4-carboxylate (**41f**) (63.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111fa** (77.6 mg, 96%, *E*/*Z* = 4.7/1.0 by ^1H NMR) as a colorless oil.

^1H NMR (300 MHz, $CDCl_3$) δ = 8.77 (d, *J* = 4.8 Hz, 2H), 8.38 (d, *J* = 8.3 Hz, 1H), 7.91 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.37–7.00 (m, 3H), 5.96–5.50 (m, 2H), 4.24 (d, *J* = 5.2 Hz, 0.34H), 4.06–3.85 (m, 6.66H), 1.63 (s, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major isomer*: δ = 167.8 (C_q), 158.2 (CH), 157.7 (C_q), 142.0 (C_q), 137.7 (C_q), 131.4 (CH), 129.1 (C_q), 128.9 (CH), 124.8 (CH), 121.9 (CH), 120.5 (C_q), 118.2 (CH), 117.6 (CH), 106.9 (CH), 63.3 (CH_2), 51.7 (CH_3), 32.4 (CH_2). *Minor isomer*: δ = 142.0 (C_q), 130.4 (CH), 128.5 (CH), 124.8 (CH), 118.3 (CH), 106.8 (CH), 58.5 (CH_2), 28.1 (CH_2). (Due to overlap, nine peaks are missing). **IR** (ATR) *v* = 3439, 2950, 1708, 1566, 1420, 1258, 1137, 973, 804, 753 cm^{-1}. **MS** (ESI) m/z (relative intensity): 346 (100) $[M+Na]^+$, 324 (40) $[M+H]^+$, 306 (60). **HR-MS** (ESI) m/z calcd for $C_{18}H_{18}N_3O_3$ $[M+H]^+$: 324.1343, found: 324.1353.

The analytical data were in accordance with those reported in the literature.[69]

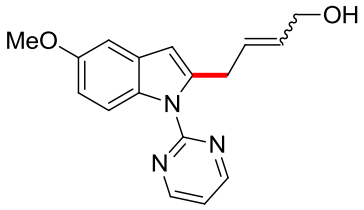


(*E*/*Z*)-4-[5-Methyl-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ga): The general procedure **E**

was followed using 5-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**41g**) (52.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ga** (65.4 mg, 94%, *E*/*Z* = 5.2/1.0 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 2H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.31 (s, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 7.04 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.40 (s, 1H), 5.92–5.62 (m, 2H), 4.27 (d, *J* = 5.5 Hz, 0.32 H), 4.05 (d, *J* = 5.7 Hz, 1.68 H), 4.00–3.94 (m, 2H), 2.44 (s, 3H), 1.60 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major Isomer*: δ = 158.2 (C_q), 158.1 (CH), 139.7 (C_q), 135.3 (C_q), 131.2 (C_q), 130.9 (CH), 129.6 (CH), 129.4 (C_q), 124.1 (CH), 119.8 (CH), 116.9 (CH), 113.6 (CH), 106.3 (CH), 66.4 (CH_2), 32.7 (CH_2), 21.4 (CH_3). *Minor Isomer*: δ = 158.2 (CH), 139.8 (C_q), 135.4 (C_q), 131.3 (C_q), 130.2 (CH), 129.6 (CH), 129.4 (C_q), 129.1 (CH), 124.2 (CH), 116.9 (CH), 113.8 (CH), 106.2 (CH), 58.6 (CH_2), 28.3 (CH_2). (Due to overlap, two peaks are missing). **IR** (ATR) *v* = 3315, 2924, 1646, 1429, 1137, 1027, 924, 661 cm^{-1}. **MS** (ESI) m/z (relative intensity): 302 (100) $[M+Na]^+$, 280 (43) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_3ONa$ $[M+Na]^+$: 302.1264, found: 302.1265.

The analytical data were in accordance with those reported in the literature.[69]

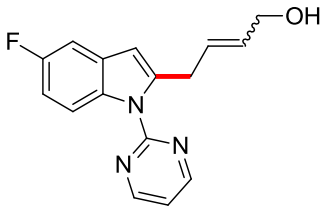


(*E*/*Z*)-4-[5-Methoxy-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ha): The general procedure **E** was followed using 5-methoxy-1-(pyrimidin-2-yl)-1*H*-indole (**41h**) (56.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ha** (48.0 mg, 65%, *E*/*Z* = 6.7/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 4.8 Hz, 2H), 8.18 (d, *J* = 9.1 Hz, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.98 (d, *J* = 2.5 Hz, 1H), 6.84 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.38 (d, *J* = 0.9 Hz, 1H), 5.93–5.57 (m, 2H), 4.22 (d, *J* = 5.5 Hz, 0.31H), 4.00 (dd, *J* = 5.8, 1.1 Hz, 1.69H), 3.98–3.88 (m, 2H), 3.83 (s, 3H), 1.68 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer*: δ = 158.0 (C_q), 157.9 (CH), 155.3 (C_q), 140.3 (C_q), 131.9 (C_q), 130.9 (CH), 129.9 (C_q), 129.5 (CH), 116.7 (CH), 114.9 (CH), 111.5 (CH), 106.4 (CH), 102.3 (CH), 63.3

(CH_2), 55.6 (CH_3), 32.7 (CH_2). *Minor isomer*: δ = 155.3 (C_q), 130.1 (CH), 129.0 (CH), 116.7 (CH), 115.1 (CH), 111.6 (CH), 106.3 (CH), 58.5 (CH_2), 28.4 (CH_2). (Due to overlap, seven peaks are missing). **IR** (ATR) *v* = 3389, 2995, 2832, 1613, 1561, 1422, 1204, 801 cm^{-1}. **MS** (ESI) m/z (relative intensity): 318 (100) $[M+Na]^+$, 296 (56) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{18}N_3O_2$ $[M+H]^+$: 296.1394, found: 296.1405.

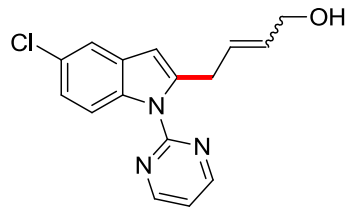
The analytical data were in accordance with those reported in the literature.[69]



(*E*/*Z*)-4-[5-Fluoro-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ia): The general procedure **E** was followed using 5-fluoro-1-(pyrimidin-2-yl)-1*H*-indole (**41i**) (53.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ia** (58.7 mg, 82%, *E*/*Z* = 5.4/1 by ^{1}H NMR) as a white solid.

M.p. = 93–96 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 2H), 8.25–8.16 (m, 1H), 7.18–7.05 (m, 2H), 6.92 (td, *J* = 9.2, 2.6 Hz, 1H), 6.41 (d, *J* = 0.9 Hz, 1H), 5.97–5.53 (m, 2H), 4.23 (d, *J* = 5.4 Hz, 0.29H), 4.02 (dd, *J* = 5.8, 1.2 Hz, 1.71H), 3.98–3.85 (m, 2H), 1.46 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer*: δ = 158.9 (d, $^1J_{C\text{-}F}$ = 237.9 Hz, C_q), 158.1 (CH), 157.9 (C_q), 141.4 (C_q), 133.4 (C_q), 131.2 (CH), 129.9 (d, $^3J_{C\text{-}F}$ = 9.6 Hz, C_q), 129.1 (CH), 117.2 (CH), 114.9 (d, $^3J_{C\text{-}F}$ = 8.9 Hz, CH), 110.3 (d, $^2J_{C\text{-}F}$ = 25.3 Hz, CH), 106.3 (d, $^4J_{C\text{-}F}$ = 3.4 Hz, CH), 105.0 (d, $^2J_{C\text{-}F}$ = 23.5 Hz, CH), 63.3 (CH_2), 32.7 (CH_2). *Minor isomer*: δ = 130.3 (CH), 128.8 (CH), 117.2 (CH), 115.0 (d, $^3J_{C\text{-}F}$ = 8.9 Hz, CH), 110.3 (d, $^2J_{C\text{-}F}$ = 25.3 Hz, CH), 106.1 (d, $^4J_{C\text{-}F}$ = 3.4 Hz, CH), 58.5 (CH_2), 28.3 (CH_2). (Due to overlap, seven peaks are missing). **^{19}F NMR** (376 MHz, $CDCl_3$) *Major isomer*: δ = -122.33 (td, *J* = 9.2, 4.7 Hz). *Minor isomer*: -122.42 (td, *J* = 9.1, 4.7 Hz). **IR** (ATR) *v* = 3272, 1562, 1431, 1174, 1109, 978, 782, 592 cm^{-1}. **MS** (ESI) m/z (relative intensity): 306 (100) $[M+Na]^+$, 284 (40) $[M+H]^+$, 266 (90). **HR-MS** (ESI) m/z calcd for $C_{16}H_{15}FN_3O$ $[M+H]^+$: 284.1194, found: 284.1195.

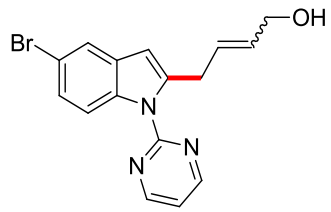
The analytical data were in accordance with those reported in the literature.[69]



(*E*/*Z*)-4-[5-Chloro-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ja): The general procedure **E** was followed using 5-chloro-1-(pyrimidin-2-yl)-1*H*-indole (**41j**) (57.4 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ja** (57.0 mg, 76%, *E*/*Z* = 5.5/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 2H), 8.16 (d, *J* = 8.9 Hz, 1H), 7.45 (d, *J* = 2.2 Hz, 1H), 7.19–7.01 (m, 2H), 6.39 (s, 1H), 5.99–5.48 (m, 2H), 4.23 (dd, *J* = 4.6, 0.7 Hz, 0.23H), 4.02 (dd, *J* = 5.7, 1.2 Hz, 1.77H), 3.97–3.88 (m, 2H), 1.50 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer*: δ = 158.1 (CH), 157.8 (C_q), 141.2 (C_q), 135.3 (C_q), 131.3 (CH), 130.3 (C_q), 129.0 (CH), 127.3 (C_q), 122.7 (CH), 119.3 (CH), 117.3 (CH), 115.0 (CH), 105.8 (CH), 63.3 (CH_2), 32.6 (CH_2). *Minor isomer*: δ = 130.4 (CH), 128.7 (CH), 127.3 (C_q), 122.8 (CH), 119.2 (CH), 117.3 (CH), 115.2 (CH), 105.6 (CH), 58.5 (CH_2), 28.2 (CH_2). (Due to overlap, five peaks are missing). **IR** (ATR) *v* = 3357, 2918, 1574, 1561, 1242, 1200, 1069, 974, 802 cm^{-1}. **MS** (ESI) m/z (relative intensity): 322 (100) $[M+Na]^+$, 300 (40) $[M+H]^+$, 282 (85). **HR-MS** (ESI) m/z calcd for $C_{16}H_{15}ClN_3O$ $[M+H]^+$: 300.0898, found: 300.0890.

The analytical data were in accordance with those reported in the literature.[69]

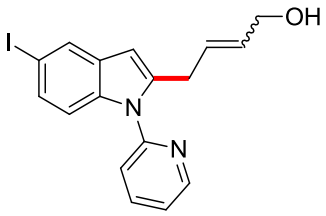


(*E*/*Z*)-4-[5-Bromo-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ca): The general procedure **E** was followed using 5-bromo-1-(pyrimidin-2-yl)-1*H*-indole (**41c**) (68.5 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ca** (80 mg, 93%, *E*/*Z* = 4.4/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 1H), 7.61 (d, *J* = 2.0 Hz, 1H),

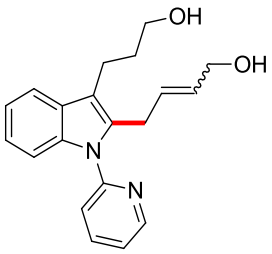
7.32–7.21 (m, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 6.38 (s, 1H), 5.89–5.75 (m, 1H), 5.74–5.52 (m, 1H), 4.23 (d, *J* = 4.8 Hz, 0.35H), 4.02 (d, *J* = 5.6 Hz, 1.65H), 3.98–5.85 (m, 2H), 1.41 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major isomer*: *δ* = 158.1 (CH), 157.8 (C_q), 141.0 (C_q), 135.7 (C_q), 131.3 (CH), 130.9 (C_q), 129.0 (CH), 125.3 (CH), 122.3 (CH), 117.4 (CH), 115.4 (CH), 115.0 (C_q), 105.7 (CH), 63.3 (CH_2), 32.5 (CH_2). *Minor isomer*: *δ* = 130.4 (CH), 128.7 (CH), 125.4 (CH), 115.6 (CH), 115.0 (C_q), 58.5 (CH_2), 28.2 (CH_2). (Due to overlap, seven peaks are missing). **IR** (ATR) *ν* = 3357, 2863, 1560, 1420, 1198, 973, 799 cm^{-1}. **MS** (ESI) m/z (relative intensity): 368 (98) $[M+Na]^+$ (^{81}Br), 366 (98) $[M+Na]^+$ (^{79}Br), 356 (95) $[M+H]^+$ (^{81}Br), 344 (95) $[M+H]^+$ (^{79}Br), 328 (100) (^{81}Br), 326 (100) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{16}H_{15}BrN_3O$ $[M+H]^+$: 344.0393, found: 344.0394.

The analytical data were in accordance with those reported in the literature.[201]



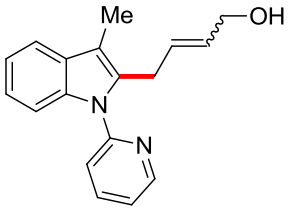
(*E*/*Z*)-4-[5-Iodo-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ka): The general procedure **E** was followed using 5-iodo-1-(pyridin-2-yl)-1*H*-indole (**41k**) (80.0 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ka** (85.8 mg, 88%, *E*/*Z* = 5.5/1.0 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) *δ* = 8.62 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.89–7.84 (m, 2H), 7.39–7.30 (m, 3H), 7.07 (dt, *J* = 8.6, 0.7 Hz, 1H), 6.34 (d, *J* = 0.9 Hz, 1H), 5.72–5.42 (m, 2H), 4.07 (d, *J* = 5.6 Hz, 0.31 H), 3.95 (dd, *J* = 5.7, 1.2 Hz, 1.69H), 3.62–3.55 (m, 2H), 1.71 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major Isomer*: *δ* = 150.8 (C_q), 149.5 (CH), 139.8 (C_q), 138.3 (CH), 136.4 (C_q), 131.4 (CH), 130.8 (C_q), 130.0 (CH), 128.7 (CH), 128.0 (CH), 122.3 (CH), 120.9 (CH), 112.0 (CH), 102.2 (CH), 84.1 (C_q), 63.1 (CH_2), 30.5 (CH_2). *Minor Isomer*: *δ* = 150.7 (C_q), 149.6 (CH), 140.1 (C_q), 138.4 (CH), 130.4 (CH), 130.1 (CH), 128.8 (CH), 127.8 (CH), 122.4 (CH), 120.9 (CH), 111.9 (CH), 102.0 (CH), 84.2 (C_q), 58.3 (CH_2), 26.1 (CH_2). (Due to overlap, two peaks are missing). **IR** (ATR) *ν* = 3321, 2913, 2860, 1586, 1470, 1439, 1274, 782, 580 cm^{-1}. **MS** (ESI) m/z (relative intensity): 391 (100) $[M+H]^+$, 413 (67) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{16}N_2OI$ $[M+H]^+$: 391.0302, found: 391.0315.



(*E*/*Z*)-4-[3-(3-Hydroxypropyl)-1-(pyridin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111la): The general procedure **E** was followed using 3-[1-(pyridin-2-yl)-1*H*-indol-3-yl]propan-1-ol (**41l**) (63.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111la** (59.6 mg, 74%, *E*/*Z* = 5.3/1.0 by ^{1}H NMR) as a yellow oil.

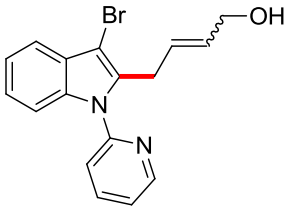
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 4.9 Hz, 1H), 7.74 (td, *J* = 7.7, 2.0 Hz, 1H), 7.48–7.44 (m, 1H), 7.32–7.26 (m, 1H), 7.21–7.15 (m, 2H), 7.06–7.01 (m, 2H), 5.51–5.18 (m, 2H), 3.92 (d, *J* = 6.1 Hz, 0.32 Hz), 3.72 (d, *J* = 5.9 Hz, 1.68H), 3.57–3.48 (m, 4H), 2.97 (brs, 2H), 2.74–2.69 (m, 2H), 1.86–1.68 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major Isomer*: δ = 151.4 (C_q), 149.5 (CH), 138.3 (CH), 136.7 (C_q), 133.9 (C_q), 130.2 (CH), 128.9 (CH), 128.7 (CH), 128.5 (C_q), 121.9 (CH), 121.3 (CH), 120.2 (CH), 118.4 (CH), 114.8 (C_q), 110.0 (CH), 62.8 (CH_2), 61.9 (CH_2), 33.0 (CH_2), 27.8 (CH_2), 20.4 (CH_2). *Minor Isomer*: δ = 151.3 (C_q), 149.3 (CH), 138.3 (CH), 136.6 (C_q), 134.7 (C_q), 129.0 (CH), 128.7 (CH), 128.5 (C_q), 121.9 (CH), 121.2 (CH), 120.3 (CH), 118.3 (CH), 114.6 (C_q), 109.9 (CH), 61.7 (CH_2), 57.6 (CH_2), 32.8 (CH_2), 23.5 (CH_2), 20.3 (CH_2). (Due to overlap, one peak is missing). **IR** (ATR) *v* = 3315, 2928, 2857, 1588, 1471, 1458, 1437, 1060, 742 cm^{-1}. **MS** (ESI) m/z (relative intensity): 345 (87) $[M+Na]^+$, 323 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{22}N_2O_2Na$ $[M+H]^+$: 345.1573, found: 345.1586.



(*E*/*Z*)-4-[3-Methyl-1-(pyridin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ma): The general procedure **E** was followed using 3-methyl-1-(pyridin-2-yl)-1*H*-indole (**41m**) (52.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ma** (38.2 mg, 55%, *E*/*Z* = 4.2/1.0 by ^{1}H NMR) as a yellow

oil.

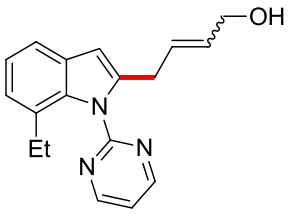
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.61 (d, *J* = 4.0 Hz, 1H), 7.87–7.81 (m, 1H), 7.55–7.53 (m, 1H), 7.41–7.37 (m, 1H), 7.33–7.24 (m, 2H), 7.15–7.12 (m, 2H), 5.61–5.28 (m, 2H), 3.97 (d, *J* = 6.1 Hz, 0.39H), 3.87 (d, *J* = 5.9 Hz, 1.61H), 3.68 (d, *J* = 6.1 Hz, 0.39H), 3.63 (d, *J* = 6.2 Hz, 1.61H), 2.32 (s, 0.59H), 2.30 (s, 2.41H), 1.59 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major Isomer*: δ = 151.6 (C_q), 149.4 (CH), 138.1 (CH), 136.5 (C_q), 133.7 (C_q), 130.1 (CH), 129.3 (C_q), 129.0 (CH), 122.0 (CH), 121.7 (CH), 121.0 (CH), 120.2 (CH), 118.3 (CH), 110.7 (C_q), 109.9 (CH), 63.2 (CH_2), 27.8 (CH_2), 8.7 (CH_3). *Minor Isomer*: δ = 151.6 (C_q), 149.9 (CH), 139.3 (CH), 134.4, 129.4 (C_q), 122.1 (CH), 121.7 (CH), 121.1 (CH), 120.3 (CH), 118.3 (CH), 110.3 (C_q), 109.8 (CH), 58.1 (CH_2), 23.8 (CH_2), 8.8 (CH_3). (Due to overlap, four peaks are missing). **IR** (ATR) *v* = 3349, 3054, 2916, 1587, 1471, 1457, 1381, 1315, 1087, 740 cm^{-1}. **MS** (ESI) m/z (relative intensity): 301 (85) $[M+Na]^+$, 279 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{19}N_2O$ $[M+H]^+$: 279.1497, found: 279.1492.



(*E*/*Z*)-4-[3-Bromo-1-(pyridin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111na): The general procedure **E** was followed using 3-bromo-1-(pyridin-2-yl)-1*H*-indole (**41n**) (68.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111na** (64.4 mg, 75%, *E*/*Z* = 4.3/1 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.61 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.85 (ddd, *J* = 7.9, 7.4, 2.0 Hz, 1H), 7.57–7.53 (m, 1H), 7.40–7.14 (m, 5H), 5.58–5.27 (m, 2H), 3.99 (d, *J* = 6.2 Hz, 0.36H), 3.83 (dd, *J* = 5.7, 1.3 Hz, 1.64H), 3.72 (d, *J* = 6.2 Hz, 0.36H), 3.68 (dd, *J* = 6.2, 1.3 Hz, 1.64H), 2.03 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major Isomer*: δ = 150.6 (C_q), 149.5 (CH), 138.3 (CH), 136.1 (C_q), 135.7 (C_q), 131.0 (CH), 127.3 (C_q), 127.0 (CH), 123.1 (CH), 122.5 (CH), 121.3 (CH), 121.1 (CH), 118.8 (CH), 110.3 (CH), 94.2 (C_q), 62.9 (CH_2), 28.6 (CH_2). *Minor Isomer*: δ = 150.6 (C_q), 149.6 (CH), 138.5 (CH), 136.0 (C_q), 135.7 (C_q), 135.2 (C_q), 129.8 (CH), 127.3 (C_q), 123.2 (CH), 122.5 (CH), 121.4 (CH), 110.2 (CH), 93.9 (C_q), 58.2 (CH_2), 24.7 (CH_2). (Due to overlap, two peaks are missing). **IR** (ATR) *v* = 3355, 3053, 2918,

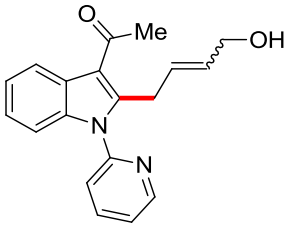
1588, 1452, 1436, 1213, 994, 741 cm^{-1}. **MS** (ESI) m/z (relative intensity): 367 (98) $[M+Na]^+$ (^{81}Br), 365 (100) $[M+Na]^+$ (^{79}Br), 345 (88) $[M+H]^+$ (^{81}Br), 343 (90) $[M+H]^+$ (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{17}H_{16}N_2OBr$ $[M+H]^+$: 343.0446, found: 343.0441.



(*E*/*Z*)-4-[7-Ethyl-1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111oa): The general procedure **E** was followed using 7-ethyl-1-(pyrimidin-2-yl)-1*H*-indole (**41o**) (55.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111oa** (46.2 mg, 63%, *E*/*Z* = 5.6/1.0 by ^1H NMR) as a yellow oil.

^1H NMR (300 MHz, $CDCl_3$) δ = 8.85 (d, *J* = 4.8, 2H), 7.43 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.32 (t, *J* = 4.8 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.3Hz, 1H), 6.44 (s, 1H), 5.72–5.38 (m, 2H), 4.11 (d, *J* = 5.4 Hz, 0.30H), 3.94 (d, *J* = 5.6 Hz, 1.70H), 3.51 (d, *J* =6.4 Hz, 2H), 2.31 (q, *J* = 7.4 Hz, 2H), 1.60 (brs, 1H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major Isomer*: δ = 159.1 (C_q), 158.2 (CH), 139.5 (C_q), 135.8 (C_q), 130.8 (CH), 129.6 (C_q), 128.6 (CH), 127.9 (C_q), 122.9 (CH), 121.4 (CH), 119.2 (CH), 118.0 (CH), 104.2 (CH), 63.2 (CH_2), 30.8 (CH_2), 25.8 (CH_2), 14.0 (CH_3). *Minor Isomer*: δ = 159.1 (C_q), 158.3 (CH), 139.8 (C_q), 136.0 (C_q), 130.2 (CH), 127.9 (C_q), 121.4 (CH), 119.2 (CH), 104.0 (CH), 58.3 (CH_2), 26.3 (CH_2), 25.8 (CH_2). (Due to overlap, four peaks are missing). **IR** (ATR) *v* = 3312, 2966, 1561, 1416, 1265, 1092, 743 cm^{-1}. **MS** (ESI) m/z (relative intensity): 316 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{19}N_3ONa$ $[M+Na]^+$: 316.1420, found: 316.1432.

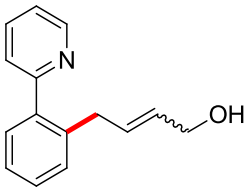
The analytical data were in accordance with those reported in the literature.[69]



(*E*/*Z*)-1-[2-(4-Hydroxybut-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indol-3-yl]ethanone (111pa): The general

procedure **E** was followed using 1-[1-(pyridin-2-yl)-1*H*-indol-3-yl]ethanone (**41p**) (59.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111pa** (67.4 mg, 88%, *E*/*Z* = 5.7/1 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.65 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.96 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.88 (td, *J* = 7.8, 1.9 Hz, 1H), 7.42–7.34 (m, 2H), 7.26–7.20 (m, 1H), 7.16–7.05 (m, 2H), 5.69–5.22 (m, 2H), 3.99 (d, *J* = 7.3 Hz, 0.3H), 3.89–3.85 (m, 3.7H), 2.69 (s, 0.45H), 2.67 (s, 2.55H), 1.60 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major Isomer*: δ = 194.8 (C_q), 150.1 (CH), 149.8 (C_q), 145.4 (C_q), 138.7 (CH), 137.2 (C_q), 131.0 (CH), 127.8 (CH), 126.2 (C_q), 123.8 (CH), 123.0 (CH), 122.7 (CH), 122.5 (CH), 120.9 (CH), 115.6 (C_q), 110.9 (CH), 63.2 (CH_2), 31.8 (CH_3), 29.2 (CH_2). *Minor Isomer*: δ = 195.3 (C_q), 150.3 (CH), 149.9 (C_q), 146.5 (CH), 138.9 (CH), 137.1 (C_q), 129.9 (CH), 127.2 (CH), 126.1 (C_q), 124.0 (CH), 122.8 (CH), 122.7 (CH), 120.7 (CH), 111.0 (CH), 57.8 (CH_2), 31.9 (CH_3), 25.3 (CH_2). (Due to overlap, two peaks are missing). **IR** (ATR) *v* = 3377, 3032, 2922, 1640, 1588, 1509, 1393, 1192, 743 cm^{-1}. **MS** (ESI) m/z (relative intensity): 329 (100) $[M+Na]^+$, 307 (26) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{18}N_2O_2Na$ $[M+Na]^+$: 329.1260, found: 329.1262.

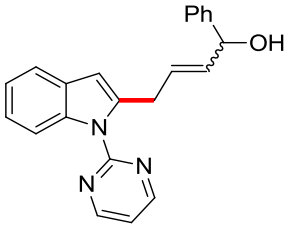


(*E*/*Z*)-4-[2-(Pyridin-2-yl)phenyl]but-2-en-1-ol (111qa): The general procedure **E** was followed using 2-phenylpyridine (**20a**) (38.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1 to 1/1) yielded **111qa** (36.0 mg, 64%, *E*/*Z* = 7.3/1.0 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.69 (brs, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.41–7.24 (m, 6H), 5.74–5.42 (m, 2H), 4.03 (d, *J* = 5.1 Hz, 0.25 Hz), 3.99 (d, *J* = 5.4 Hz, 1.75H), 3.54 (d, *J* = 5.4 Hz, 0.25 Hz), 3.49 (d, *J* = 6.4 Hz, 1.75H), 1.67 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major Isomer*: δ = 159.9 (C_q), 149.1 (CH), 140.3 (C_q), 137.8 (C_q), 136.3 (CH), 131.3 (CH), 130.2 (CH), 130.0 (CH), 129.9 (CH), 128.5 (CH), 126.4 (CH), 124.2 (CH), 121.9 (CH), 63.4 (CH_2), 36.0 (CH_2). *Minor Isomer*: δ = 138.3 (C_q), 136.6 (CH), 131.2 (CH), 130.0 (CH), 129.8 (CH), 129.1 (CH), 128.6 (CH), 128.4 (CH), 126.3 (CH), 126.4 (CH), 124.4 (CH),

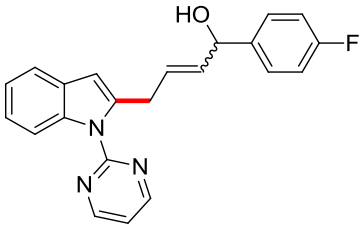
58.1 (CH_2), 31.1 (CH_2). (Due to overlap, two peaks are missing). **IR** (ATR) ν = 3308, 2853, 1586, 1468, 1425, 1023, 995, 795, 751 cm^{-1}. **MS** (ESI) m/z (relative intensity): 248 (13) $[M+Na]^+$, 226 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{15}H_{16}NO$ $[M+H]^+$: 226.1226, found: 226.1226.

The analytical data were in accordance with those reported in the literature.[69]



(*E*/*Z*)-1-Phenyl-4-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ab): The general procedure **E** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and (*trans*)-4-phenyl-5-vinyl-1,3-dioxolan-2-one (**110b**) (142.6 mg, 0.75 mmol). Purification by column chromatography on silica gel (CH_2Cl_2/Et_2O: 20/1) yielded **111ab** (68.3 mg, 80%, *E*/*Z* > 20/1 by ^1H NMR) as a colorless oil.

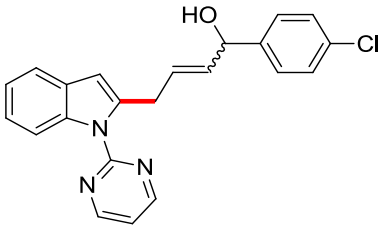
^1H NMR (500 MHz, $CDCl_3$) δ = 8.68 (d, *J* = 4.8 Hz, 2H), 8.20 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.52 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.39–7.09 (m, 7H), 7.01 (t, *J* = 4.8 Hz, 1H), 6.46 (s, 1H), 5.87 (ddt, *J* = 15.3, 6.5, 1.1 Hz, 1H), 5.63 (ddt, *J* = 15.3, 6.9, 1.5 Hz, 1H), 5.08 (dd, *J* = 7.0, 3.0 Hz, 1H), 3.97 (d, *J* = 6.6 Hz, 2H), 1.81 (d, *J* = 3.5 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 158.0 (C_q), 157.9 (CH), 142.9 (C_q), 139.3 (C_q), 137.0 (C_q), 134.2 (CH), 129.1 (C_q), 129.0 (CH), 128.4 (CH), 127.4 (CH), 126.0 (CH), 122.7 (CH), 121.8 (CH), 119.8 (CH), 117.1 (CH), 113.6 (CH), 106.5 (CH), 74.8 (CH), 32.4 (CH_2). **IR** (ATR) ν = 3385, 1561, 1453, 1424, 1348, 1205, 971, 908, 802, 744, 699 cm^{-1}. **MS** (ESI) m/z (relative intensity): 364 (40) $[M+Na]^+$, 342 (10) $[M+H]^+$, 324 (100). **HR-MS** (ESI) m/z calcd for $C_{22}H_{20}N_3O$ $[M+H]^+$: 342.1601, found: 342.1598.



(*E*/*Z*)-1-(4-Fluorophenyl)-4-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ad): The general procedure **E** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and (*trans*)-4-(4-fluorophenyl)-5-vinyl-1,3-dioxolan-2-one (**110d**) (156.2 mg, 0.75 mmol). Purification by

column chromatography on silica gel (CH_2Cl_2/Et_2O: 20/1) yielded **111ad** (69.2 mg, 77%, *E*/*Z* = 2.8/1.0 by ^{1}H NMR) as a yellow oil.

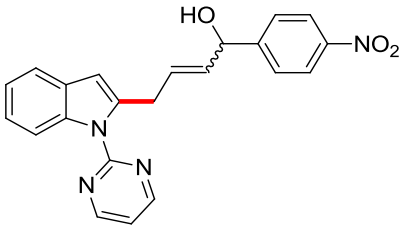
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 0.44H), 8.68 (d, *J* = 4.8 Hz, 1.56H), 8.35–8.24 (m, 0.28H), 8.20 (dd, *J* = 8.2, 1.4 Hz, 0.72H), 7.54–7.48 (m, 1H), 7.37–7.09 (m, 4H), 7.08–6.90 (m, 3H), 6.45 (d, *J* = 0.9 Hz, 1H), 5.93–5.53 (m, 2H), 5.04 (d, *J* = 6.9 Hz, 1H), 4.24–3.90 (m, 2H), 2.05 (brs, 0.22H), 1.90 (brs, 0.78H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer*: δ = 162.2 (d, $^1J_{C\text{-}F}$ = 245.3 Hz, C_q), 158.0 (C_q), 158.0 (CH), 139.2 (C_q), 138.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz, C_q), 137.0 (C_q), 134.0 (CH), 129.1 (C_q), 129.2 (CH), 127.7 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, CH), 122.8 (CH), 121.9 (CH), 119.8 (CH), 117.0 (CH), 115.2 (d, $^2J_{C\text{-}F}$ = 21.4 Hz, CH), 113.7 (CH), 106.6 (CH), 74.1 (CH), 32.4 (CH_2). *Minor isomer*: δ = 162.2 (d, $^1J_{C\text{-}F}$ = 245.3 Hz, C_q), 158.1 (CH), 158.0 (C_q), 139.3 (C_q), 138.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz, C_q), 137.0 (C_q), 133.4.0 (CH), 129.1 (C_q), 128.6 (CH), 127.7 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, CH), 122.9 (CH), 122.0 (CH), 119.9 (CH), 117.1 (CH), 115.3 (d, $^2J_{C\text{-}F}$ = 21.4 Hz, CH), 114.0 (CH), 106.6 (CH), 69.0 (CH), 28.4 (CH_2). **^{19}F NMR** (376 MHz, $CDCl_3$) *Major isomer*: δ = -115.2 (tt, *J* = 8.7, 5.4 Hz). *Minor isomer*: δ = -115.1 (tt, *J* = 8.8, 5.4 Hz). **IR** (ATR) *v* = 3373, 3047, 1562, 1507, 1454, 1425, 1349, 1218, 972, 803, 745 cm^{-1}. **MS** (ESI) m/z (relative intensity): 382 (30) $[M+Na]^+$, 360 (5) $[M+H]^+$, 342 (100). **HR-MS** (ESI) m/z calcd for $C_{22}H_{19}FN_3O_3$ $[M+H]^+$: 360.1507, found: 360.1508.



(*E*/*Z*)-1-(4-Chlorophenyl)-4-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ac): The general procedure **E** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and (*trans*)-4-(4-chlorophenyl)-5-vinyl-1,3-dioxolan-2-one (**110c**) (168.5 mg, 0.75 mmol). Purification by column chromatography on silica gel (CH_2Cl_2/Et_2O: 20/1) yielded **111ac** (78.1 mg, 83%, *E*/*Z* = 3.0/1.0 by ^{1}H NMR) as a colorless oil.

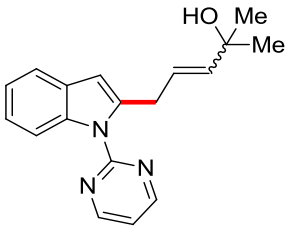
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.71 (d, *J* = 4.8 Hz, 0.44H), 8.63 (d, *J* = 4.8 Hz, 1.56H), 8.30–8.23 (m, 0.22H), 8.19–8.11 (m, 0.78H), 7.58–7.40 (m, 1H), 7.24–7.11 (m, 4H), 7.11–7.04 (m, 2H), 6.97 (t, *J* = 4.8 Hz, 1H), 6.42 (s, 1H), 5.87–5.40 (m, 2H), 4.96 (d, *J* = 6.9 Hz, 1H), 4.16–3.81 (m, 2H), 2.23 (brs, 0.22H), 2.11 (brs, 0.78H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer*: δ = 158.0 (C_q), 157.8 (CH), 141.3

(C_q), 139.0 (C_q), 137.0 (C_q), 133.7 (CH), 132.9 (C_q), 129.3 (CH), 128.9 (C_q), 128.4 (CH), 127.3 (CH), 122.8 (CH), 121.8 (CH), 119.8 (CH), 117.0 (CH), 113.6 (CH), 106.6 (CH), 74.1 (CH), 32.4 (CH_2). *Minor isomer*: δ = 158.0 (CH), 141.7 (C_q), 139.1 (C_q), 136.9 (C_q), 133.1 (CH), 133.0 (C_q), 129.0 (C_q), 128.7 (CH), 128.4 (CH), 127.2 (CH), 122.7 (CH), 121.9 (CH), 119.8 (CH), 117.0 (CH), 113.9 (CH), 106.5 (CH), 68.9 (CH), 28.4 (CH_2). (Due to overlap, one peak is missing). **IR** (ATR) ν = 3375, 3046, 1562, 1454, 1424, 1348, 1088, 1013, 907, 802, 730 cm^{-1}. **MS** (ESI) m/z (relative intensity): 398 (30) $[M+Na]^+$, 376 (10) $[M+H]^+$, 358 (100). **HR-MS** (ESI) m/z calcd for $C_{22}H_{19}ClN_3O$ $[M+H]^+$: 376.1211, found: 376.1211.



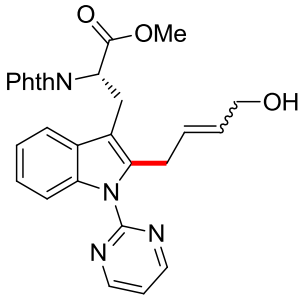
(*E*/*Z*)-1-(4-Nitrophenyl)-4-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]but-2-en-1-ol (111ae): The general procedure **E** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and (*trans*)-4-(4-nitrophenyl)-5-vinyl-1,3-dioxolan-2-one (**110e**) (176.4 mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111ae** (76.4 mg, 79%, *E*/*Z* = 3.0/1 by ^{1}H NMR) as a yellow solid.

M.p. = 128–130 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.77 (d, *J* = 4.7 Hz, 0.66H), 8.67 (d, *J* = 4.8 Hz, 1.34H), 8.27 (d, *J* = 8.0 Hz, 0.29H), 8.19 (d, *J* = 7.4 Hz, 0.71H), 8.16–8.03 (m, 2H), 7.58–7.42 (m, 2H), 7.33 (d, *J* = 8.9 Hz, 1H), 7.29–7.09 (m, 2H), 7.03 (t, *J* = 4.8 Hz, 1H), 6.45 (d, *J* = 5.9 Hz, 1H), 6.02–5.79 (m, 1H), 5.70–5.43 (m, 1H), 5.11 (d, *J* = 7.2 Hz, 1H), 4.27–3.84 (m, 2H), 2.26 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *Major isomer*: δ = 158.0 (C_q), 158.0 (CH), 150.0 (C_q), 147.0 (C_q), 138.7 (C_q), 137.0 (C_q), 132.9 (CH), 130.8 (CH), 129.0 (C_q), 126.6 (CH), 123.5 (CH), 122.9 (CH), 122.0 (CH), 119.9 (CH), 117.1 (CH), 113.8 (CH), 106.8 (CH), 73.9 (CH), 32.3 (CH_2). *Minor isomer*: δ = 158.2 (CH), 150.3 (C_q), 147.1 (C_q), 138.8 (C_q), 137.0 (C_q), 132.4 (CH), 129.8 (CH), 129.0 (C_q), 126.6 (CH), 123.6 (CH), 123.0 (CH), 122.1 (CH), 119.9 (CH), 117.2 (CH), 114.0 (CH), 106.6 (CH), 68.6 (CH), 28.4 (CH_2). (Due to overlap, one peak is missing). **IR** (ATR) ν = 3377, 2917, 1562, 1515, 1474, 1422, 1342, 1208, 972, 804, 745 cm^{-1}. **MS** (ESI) m/z (relative intensity): 409 (40) $[M+Na]^+$, 387 (35) $[M+H]^+$, 369 (100). **HR-MS** (ESI) m/z calcd for $C_{22}H_{19}N_4O_3$ $[M+H]^+$: 387.1452, found: 387.1458.



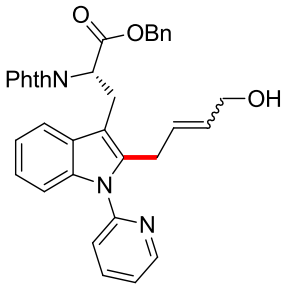
(*E*/*Z*)-2-Methyl-5-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]pent-3-en-2-ol (111af): The general procedure **E** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and 4,4-dimethyl-5-vinyl-1,3-dioxolan-2-one (**110f**) (106.6. mg, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111af** (41.1 mg, 56%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 2H), 8.25–8.16 (m, 1H), 7.56–7.48 (m, 1H), 7.23–7.07 (m, 3H), 6.45 (q, *J* = 0.9 Hz, 1H), 5.74 (dt, *J* = 15.6, 6.4 Hz, 1H), 5.56 (dt, *J* = 15.6, 1.3 Hz, 1H), 3.92 (dt, *J* = 6.3, 1.2 Hz, 2H), 1.31 (bs, 1H), 1.18 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 158.1 (C_q), 158.0 (CH), 139.8 (C_q), 139.8 (CH), 137.0 (C_q), 129.1 (C_q), 123.9 (CH), 122.6 (CH), 121.7 (CH), 119.7 (CH), 117.0 (CH), 113.5 (CH), 106.4 (CH), 70.6 (C_q), 32.4 (CH_2), 29.7 (CH_3). **IR** (ATR) *v* = 3426, 2971, 1562, 1454, 1424, 1349, 1151, 974, 802, 745 cm^{-1}. **MS** (ESI) m/z (relative intensity): 316 (40) $[M+Na]^+$, 294 (15) $[M+H]^+$, 276 (100). **HR-MS** (ESI) m/z calcd for $C_{18}H_{20}N_3O$ $[M+H]^+$: 294.1601, found: 294.1608.



(*S*,*E*)-Methyl 2-(1,3-dioxoisoindolin-2-yl)-3-[2-(4-hydroxybut-2-en-1-yl)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (111ra): The general procedure **E** was followed using (*S*)-methyl 2-(1,3-dioxoisoindolin-2-yl)-3-[1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (**41r**) (42.6 mg, 0.1 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a)** (34.2 mg, 0.3 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/2) yielded **111ra** (34.8 mg, 70%, *E*/*Z* = 7.0/1.0 by ^{1}H NMR) as a pale yellow solid.

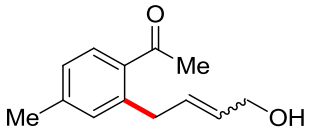
[α]$_D$ = + 38.8 °. **M. p.** = 71–73 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 2H), 8.06 (ddd, *J* = 8.3, 1.3, 0.7 Hz, 1H), 7.77–7.71 (m, 2H), 7.67–7.63 (m, 2H), 7.53–7.49 (m, 1H), 7.16–7.03 (m, 3H), 5.70–5.27 (m, 3H), 4.09–3.89 (m, 2H), 3.80 (s, 3H), 3.73 (dd, *J* = 5.9, 1.1 Hz, 2H), 3.76–3.71 (m, 2H), 1.53 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 169.6 (C_q), 167.8 (C_q), 158.3 (CH), 158.0 (C_q), 136.3 (C_q), 136.1 (C_q), 134.2 (CH), 131.9 (C_q), 130.3 (CH), 130.2 (CH), 129.3 (C_q), 123.6 (CH), 123.2 (CH), 121.9 (CH), 118.1 (CH), 117.4 (CH), 113.3 (CH), 113.1 (C_q), 63.4 (CH_2), 53.1 (CH), 52.7 (CH_3), 28.9 (CH_2), 24.2 (CH_2). **IR** (ATR) *v* = 3349, 2926, 2854, 1744, 1714, 1427, 1104, 721 cm^{-1}. **MS** (ESI) m/z (relative intensity): 519 (100) $[M+Na]^+$, 497 (28) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{28}H_{24}N_4O_5Na$ $[M+Na]^+$: 519.1639, found: 519.1639.



(*S*,*E*)-Benzyl 2-(1,3-dioxoisoindolin-2-yl)-3-[2-(4-hydroxybut-2-en-1-yl)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (111sa): The general procedure **E** was followed using (*S*)-benzyl 2-(1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)-3-[1-(pyridin-2-yl)-1*H*-indol-3-yl]propanoate (**41s**) (50.2 mg, 0.1 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (34.2 mg, 0.3 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/1) yielded **111sa** (51.4 mg, 90%, *E*/*Z* = 6.4/1 by ^{1}H NMR) as a yellow solid.

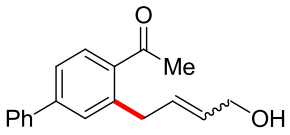
M. p. = 59–61 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.58 (d, *J* = 4.8 Hz, 1H), 7.82 (td, *J* = 7.7, 1.9 Hz, 1H), 7.77–7.72 (m, 2H), 7.67–7.64 (m, 2H), 7.59–7.63 (m, 1H), 7.34–7.25 (m, 7H), 7.23–7.20 (m, 1H), 7.08–6.99 (m, 2H), 5.51–5.21 (m, 5H), 3.88–3.80 (m, 2H), 3.68 (dd, *J* = 14.0, 5.7 Hz, 4H), 1.55 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major Isomer:* δ = 169.1 (C_q), 167.9 (C_q), 151.4 (C_q), 149.6 (CH), 138.3 (CH), 136.7 (C_q), 135.8 (C_q), 135.4 (C_q), 134.2 (CH), 131.9 (C_q), 130.7 (CH), 129.1 (CH), 128.7 (CH), 128.4 (C_q), 128.3 (CH), 128.2 (CH), 123.6 (CH), 122.2 (CH), 122.1 (CH), 121.4 (CH), 120.7 (CH), 118.3 (CH), 110.2 (C_q), 110.1 (CH), 67.7 (CH_2), 63.2 (CH_2), 53.1 (CH), 27.9 (CH_2), 24.4 (CH_2). *Minor Isomer*: δ = 169.2 (C_q), 167.6 (C_q), 151.4 (C_q), 149.7 (CH), 138.5 (CH), 136.8 (C_q), 136.7 (C_q), 135.3 (C_q), 134.4 (CH), 131.9 (C_q), 129.6 (CH), 128.5 (CH), 128.4 (CH), 118.3 (C_q), 123.7 (CH), 122.4 (CH), 121.5

(CH), 120.8 (CH), 118.1 (CH), 109.8 (C_q), 67.8 (CH_2), 58.3 (CH_2), 52.7 (CH), 29.8 (CH_2), 24.6 (CH_2). (Due to overlap, four peaks are missing). **IR** (ATR) ν = 3318, 2926, 1775, 1743, 1588, 1470, 1438, 1388, 906, 722 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1143 (5) $[2M+H]^+$, 572 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{35}H_{30}N_3O_5$ $[M+H]^+$: 572.2180, found: 572. 2186.



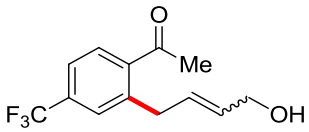
(*E*/*Z*)-1-[2-(4-hydroxybut-2-en-1-yl)-4-methylphenyl]ethanone (165aa): The general procedure **F** was followed using (*E*)-4-methoxy-*N*-[1-(*p*-tolyl)ethylidene]aniline (**34a**) (59.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165aa** (27.0 mg, 53%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59 (d, *J* = 7.9 Hz, 1H), 7.15–6.99 (m, 2H), 5.85 (dtt, *J* = 15.7, 6.5, 1.4 Hz, 1H), 5.62 (dtt, *J* = 15.3, 5.9, 1.5 Hz, 1H), 4.07 (dd, *J* = 5.9, 1.2 Hz, 2H), 3.62 (dd, *J* = 6.5, 1.4 Hz, 2H), 2.53 (s, 3H), 2.34 (s, 3H), 1.53 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 201.2 (C_q), 142.4 (C_q), 140.4 (C_q), 134.6 (C_q), 132.1 (CH), 131.8 (CH), 129.9 (CH), 129.9 (CH), 126.8 (CH), 63.6 (CH_2), 36.8 (CH_2), 29.5 (CH_3), 21.4 (CH_3). **IR** (ATR) ν = 3406, 2920, 1678, 1608, 1431, 1356, 1259, 971, 817 cm^{-1}. **MS** (ESI) m/z (relative intensity): 227 (100) $[M+Na]^+$, 187 (80). **HR-MS** (ESI) m/z calcd for $C_{13}H_{16}O_2Na$ $[M+Na]^+$: 227.1043, found: 227.1044.



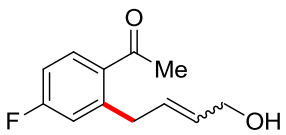
(*E*/*Z*)-1-{3-(4-Hydroxybut-2-en-1-yl)-[1,1'-biphenyl]-4-yl}ethanone (165ba): The general procedure **F** was followed using (*E*)-*N*-{1-[(1,1'-biphenyl)-4-yl]ethylidene}-4-methoxyaniline (**34b**) (75.4 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ba** (44.0 mg, 66%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.68–7.55 (m, 2H), 7.52–7.31 (m, 5H), 5.90 (dtt, *J* = 15.5, 6.4, 1.3 Hz, 1H), 5.66 (dtt, *J* = 15.4, 5.8, 1.4 Hz, 1H), 4.08 (dd, *J* = 5.8, 1.2 Hz, 2H), 3.72 (dd, *J* = 6.5, 1.4 Hz, 2H), 2.59 (s, 3H), 1.68 (bs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 201.1 (C_q), 144.3 (C_q), 140.7 (C_q), 139.7 (C_q), 136.0 (C_q), 131.4 (CH), 130.2 (CH), 130.0 (CH), 30.0 (CH), 128.8 (CH), 128.0 (CH), 127.1 (CH), 124.7 (CH), 63.5 (CH_2), 36.9 (CH_2), 29.7 (CH_3). **IR** (ATR) *v* = 3384, 2918, 2860, 1677, 1605, 1430, 1250, 971, 764, 697 cm^{-1}. **MS** (ESI) m/z (relative intensity): 289 (100) $[M+Na]^+$, 249 (95). **HR-MS** (ESI) m/z calcd for $C_{18}H_{19}O_2$ $[M+H]^+$: 267.1380, found: 267.1376.



(*E*/*Z*)-1-[2-(4-Hydroxybut-2-en-1-yl)-4-(trifluoromethyl)phenyl]ethanone (165ca): The general procedure **F** was followed using (*E*)-4-methoxy-*N*-{1-[4-(trifluoromethyl)phenyl]ethylidene}aniline (**34c**) (73.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ca** (44.5 mg, 69%, *E*/*Z* = 10/1 by ^{1}H NMR) as a colorless oil.

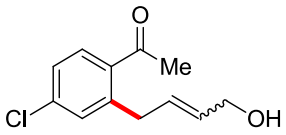
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 (d, *J* = 8.0 Hz, 1H), 7.59–7.44 (m, 2H), 5.81 (dtt, *J* = 15.5, 6.4, 1.4 Hz, 1H), 5.62 (dtt, *J* = 15.4, 5.7, 1.4 Hz, 1H), 4.25 (dd, *J* = 11.5, 3.2 Hz, 0.18H), 4.08 (d, *J* = 5.6 Hz, 1.82H), 3.76 (d, *J* = 3.0 Hz, 0.19H), 3.62 (d, *J* = 7.0 Hz, 1.81), 2.56 (s, 3H), 1.53 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 201.5 (C_q), 141.2 (C_q), 140.3 (C_q), 133.0 (q, ^2J = 32.0 Hz, C_q), 132.2 (CH), 130.0 (CH), 128.9 (CH), 127.9 (q, ^3J = 3.6 Hz, CH), 123.5 (q, ^1J = 273.6 Hz, C_q), 123.2 (d, ^3J = 4.0 Hz, CH), 63.3 (CH_2), 36.2 (CH_2), 30.0 (CH_3). **^{19}F NMR** (283 MHz, $CDCl_3$) δ = -63.07. **IR** (ATR) *v* = 3373, 2918, 1691, 1359, 1164, 1122, 1088, 970, 831 cm^{-1}. **MS** (ESI) m/z (relative intensity): 281 (100) $[M+Na]^+$, 241 (90). **HR-MS** (ESI) m/z calcd for $C_{13}H_{13}F_3O_2Na$ $[M+Na]^+$: 281.0760, found: 281.0764.



(*E*/*Z*)-1-[4-Fluoro-2-(4-hydroxybut-2-en-1-yl)phenyl]ethanone (165da): The general procedure **F** was followed using (*E*)-*N*-[1-(4-fluorophenyl)ethylidene]-4-methoxyaniline (**34d**) (60.8 mg, 0.25

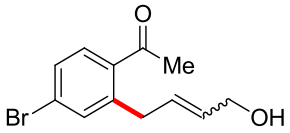
mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165da** (37.0 mg, 71%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75–7.64 (m, 1H), 7.01–6.87 (m, 2H), 5.94–5.74 (m, 1H), 5.72–5.55 (m, 1H), 4.08 (d, *J* = 5.6 Hz, 2H), 3.64 (d, *J* = 5.3 Hz, 2H), 2.54 (s, 3H), 1.58 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 200.1 (C_q), 164.2 (d, ^{1}J = 254.1 Hz, C_q) 144.1 (d, ^{3}J = 7.9 Hz, C_q), 133.6 (d, ^{4}J = 3.2 Hz, C_q), 132.0 (d, ^{3}J = 9.2 Hz, CH), 130.9 (CH), 130.4 (CH), 118.1 (d, ^{2}J = 21.5 Hz, CH), 113.1 (d, ^{2}J = 21.5 Hz, CH), 63.4 (CH_2), 36.6 (CH_2), 29.6 (CH_3). **^{19}F NMR** (283 MHz, $CDCl_3$) δ = -107.21 (ddd, *J* = 9.6, 7.9, 5.7 Hz). **IR** (ATR) *v* = 3393, 2861, 1680, 1581, 1356, 1233, 972, 817, 578 cm^{-1}. **MS** (ESI) m/z (relative intensity): 231 (90) $[M+Na]^+$, 191 (100). **HR-MS** (ESI) m/z calcd for $C_{12}H_{14}FO_2$ $[M+H]^+$: 209.0972, found: 209.0966.



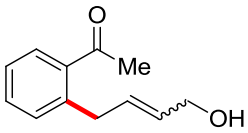
(*E*/*Z*)-1-[4-Chloro-2-(4-hydroxybut-2-en-1-yl)phenyl]ethanone (165ea): The general procedure **F** was followed using (*E*)-*N*-[1-(4-chlorophenyl)ethylidene]-4-methoxyaniline (**34e**) (64.9 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ea** (41.0 mg, 73%, *E*/*Z* = 11.5/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.59 (d, *J* = 9.0 Hz, 1H), 7.34–7.12 (m, 2H), 5.81 (dtt, *J* = 15.5, 6.3, 1.3 Hz, 1H), 5.63 (dtt, *J* = 15.4, 5.7, 1.4 Hz, 1H), 4.08 (dd, *J* = 5.6, 1.2 Hz, 2H), 3.60 (dd, *J* = 6.4, 1.3 Hz, 2H), 2.53 (s, 3H), 1.52 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 200.4 (C_q), 142.2 (C_q), 137.6 (C_q), 135.8 (C_q), 131.2 (CH), 130.9 (CH), 130.6 (CH), 130.3 (CH), 126.3 (CH), 63.4 (CH_2), 36.4 (CH_2), 29.7 (CH_3). **IR** (ATR) *v* = 3378, 2860, 1681, 1590, 1557, 1356, 1248, 1102, 970, 816 cm^{-1}. **MS** (ESI) m/z (relative intensity): 247 (100) $[M+Na]^+$, 207 (95). **HR-MS** (ESI) m/z calcd for $C_{12}H_{14}ClO_2$ $[M+H]^+$: 225.0677, found: 225.0690.



(*E*/*Z*)-1-[4-Bromo-2-(4-hydroxybut-2-en-1-yl)phenyl]ethanone (165fa): The general procedure **F** was followed using (*E*)-*N*-[1-(4-bromophenyl)ethylidene]-4-methoxyaniline (**34f**) (76.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165fa** (55.2 mg, 82%, *E*/*Z* = 9.0/1.0 by ^{1}H NMR) as a colorless oil.

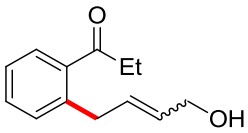
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.51 (d, *J* = 8.8 Hz, 1H), 7.46–7.33 (m, 2H), 5.81 (dtt, *J* = 15.5, 6.4, 1.3 Hz, 1H), 5.62 (dtt, *J* = 15.4, 5.7, 1.3 Hz, 1H), 4.08 (dd, *J* = 5.7, 1.2 Hz, 2H), 3.59 (dd, *J* = 6.4, 1.3 Hz, 2H), 2.53 (s, 3H), 1.51 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 200.6 (C_q), 142.2 (C_q), 136.2 (C_q), 134.1 (CH), 130.9 (CH), 130.6 (CH), 130.3 (CH), 129.3 (CH), 126.1 (C_q), 63.4 (CH_2), 36.4 (CH_2), 29.7 (CH_3). **IR** (ATR) *v* = 3379, 2861, 1681, 1584, 1554, 1355, 1250, 1092, 971, 814 cm^{-1}. **MS** (ESI) m/z (relative intensity): 293 (100) $[M+Na]^+$ (^{81}Br), 291 (100) $[M+Na]^+$ (^{79}Br), 253 (90) (^{81}Br), 251 (90) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{12}H_{13}BrO_2Na$ $[M+Na]^+$: 290.9991, found: 290.9999.



(*E*/*Z*)-1-[2-(4-Hydroxybut-2-en-1-yl)phenyl]ethanone (165ga): The general procedure **F** was followed using (*E*)-4-methoxy-*N*-(1-phenylethylidene)aniline (**34g**) (63.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ga** (33.3 mg, 70%, *E*/*Z* = 12/1.0 by ^{1}H NMR) as a colorless oil.

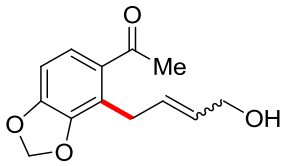
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.39 (td, *J* = 7.5, 1.4 Hz, 1H), 7.34–7.19 (m, 2H), 5.85 (dtt, *J* = 15.4, 6.5, 1.4 Hz, 1H), 5.61 (dtt, *J* = 15.3, 5.9, 1.5 Hz, 1H), 4.24 (dd, *J* = 7.1, 1.1 Hz, 0.16H), 4.06 (dd, *J* = 5.8, 1.3 Hz, 0.84H), 3.62 (dd, *J* = 6.5, 1.3 Hz, 2H), 2.55 (s, 3H), 1.56 (brs, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 202.0 (C_q), 139.8 (C_q), 137.7 (C_q), 131.6 (CH), 131.5 (CH), 131.3 (CH), 130.2 (CH), 129.1 (CH), 126.2 (CH), 63.5 (CH_2), 36.5 (CH_2), 29.7 (CH_3). **IR** (ATR) *v* = 3381, 2860, 1680,

1429, 1356, 1252, 1089, 972, 759, 601 cm^{-1}. **MS** (ESI) m/z (relative intensity): 213 (100) $[M+Na]^+$, 210 (40), 173 (80). **HR-MS** (ESI) m/z calcd for $C_{12}H_{14}O_2Na$ $[M+Na]^+$: 213.0886, found: 213.0891.



(*E*/*Z*)-1-[2-(4-Hydroxybut-2-en-1-yl)phenyl]propan-1-one (165ga): The general procedure **F** was followed using (*E*)-4-methoxy-*N*-(1-phenylpropylidene)aniline (**34h**) (59.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ga** (32.7 mg, 64%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a colorless oil.

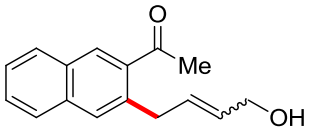
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 (dd, *J* = 7.2, 1.7 Hz, 1H), 7.42–7.35 (m, 1H), 7.33–7.19 (m, 2H), 5.84 (dtt, *J* = 15.7, 6.5, 1.4 Hz, 1H), 5.60 (dtt, *J* = 15.4, 5.9, 1.5 Hz, 1H), 4.06 (dd, *J* = 5.9, 1.2 Hz, 2H), 3.56 (dd, *J* = 6.6, 1.4 Hz, 2H), 2.88 (q, *J* = 7.3 Hz, 2H), 1.49 (brs, 3H), 1.16 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 205.4 (C_q), 139.3 (C_q), 138.4 (C_q), 131.6 (CH), 131.1 (CH), 131.1 (CH), 130.2 (CH), 128.1 (CH), 126.2 (CH), 63.5 (CH_2), 36.4 (CH_2), 35.0 (CH_2), 8.3 (CH_3). **IR** (ATR) *v* = 3407, 2937, 1685, 1445, 1220, 1089, 973, 755 cm^{-1}. **MS** (ESI) m/z (relative intensity): 227 (100) $[M+Na]^+$, 187 (80). **HR-MS** (ESI) m/z calcd for $C_{13}H_{16}O_2Na$ $[M+Na]^+$: 227.1043, found: 227.1043.



(*E*/*Z*)-1-{4-(4-Hydroxybut-2-en-1-yl)benzo[d][1,3]dioxol-5-yl}ethanone (165ia): The general procedure **F** was followed using (*E*)-*N*-{1-(benzo[d][1,3]dioxol-5-yl)ethylidene}-4-methoxyaniline (**34i**) (67.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ia** (35.2 mg, 60%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a white solid.

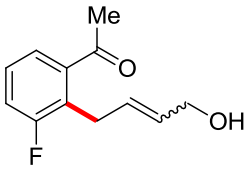
M.p. = 78–80 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.36 (d, *J* = 8.2 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.00 (s, 2H), 5.85 (dtt, *J* = 15.4, 6.3, 1.3 Hz, 1H), 5.64 (dtt, *J* = 15.4, 5.9, 1.4 Hz, 1H), 4.03 (dq, *J* = 5.9, 1.2 Hz, 2H), 3.63 (dd, *J* = 6.3, 1.3 Hz, 2H), 2.50 (s, 3H), 1.56 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =

199.2 (C_q), 149.9 (C_q), 147.3 (C_q), 131.3 (C_q), 130.0 (CH), 129.9 (CH), 126.1 (CH), 122.4 (C_q), 105.6 (CH), 101.5 (CH_2), 63.6 (CH_2), 29.4 (CH_2), 29.2 (CH_3). **IR** (ATR) ν = 3408, 2906, 1671, 1596, 1448, 1263, 1050, 982, 807. **MS** (ESI) m/z (relative intensity): 257 (70) $[M+Na]^+$, 217 (100). **HR-MS** (ESI) m/z calcd for $C_{13}H_{14}O_4Na$ $[M+H]^+$: 257.0784, found: 257.0784.



(*E*/*Z*)-1-[3-(4-Hydroxybut-2-en-1-yl)naphthalen-2-yl]ethanone (165ja): The general procedure **F** was followed using (*E*)-4-methoxy-*N*-(1-(naphthalen-2-yl)ethylidene)aniline (**34j**) (68.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **165ja** (41.0 mg, 68%, *E*/*Z* > 20/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.18 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.65 (s, 1H), 7.59–7.40 (m, 2H), 5.92 (dtt, *J* = 15.6, 6.5, 1.4 Hz, 1H), 5.63 (dtt, *J* = 15.3, 5.9, 1.5 Hz, 1H), 4.08 (dd, *J* = 5.9, 1.3 Hz, 2H), 3.79 (d, *J* = 6.5 Hz, 2H), 2.67 (s, 3H), 1.55 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 201.7 (C_q), 136.3 (C_q), 136.2 (C_q), 134.7 (C_q), 131.8 (CH), 131.1 (C_q), 130.5 (CH), 130.3 (CH), 129.6 (CH), 128.4 (CH), 128.2 (CH), 127.2 (CH), 126.3 (CH), 63.6 (CH_2), 36.7 (CH_2), 29.6 (CH_3). **IR** (ATR) ν = 3401, 2862, 1678, 1460, 1356, 1271, 1200, 974, 750 cm^{-1}. **MS** (ESI) m/z (relative intensity): 263 (95) $[M+Na]^+$, 223 (100). **HR-MS** (ESI) m/z calcd for $C_{16}H_{16}O_2Na$ $[M+H]^+$: 263.1043, found: 263.1046.

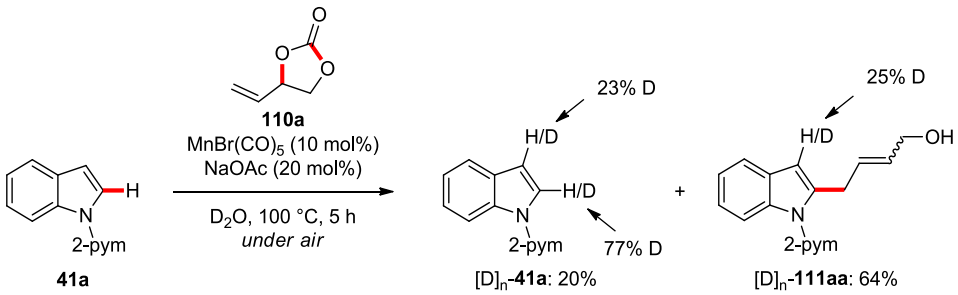


(*E*/*Z*)-1-[3-Fluoro-2-(4-hydroxybut-2-en-1-yl)phenyl]ethanone (165ka): The general procedure **F** was followed using (*E*)-*N*-[1-(3-fluorophenyl)ethylidene]-4-methoxyaniline (**34k**) (60.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **165ka** (44.2 mg, 85%, *E*/*Z* = 7.3/1 by ^{1}H NMR) as a brown oil.

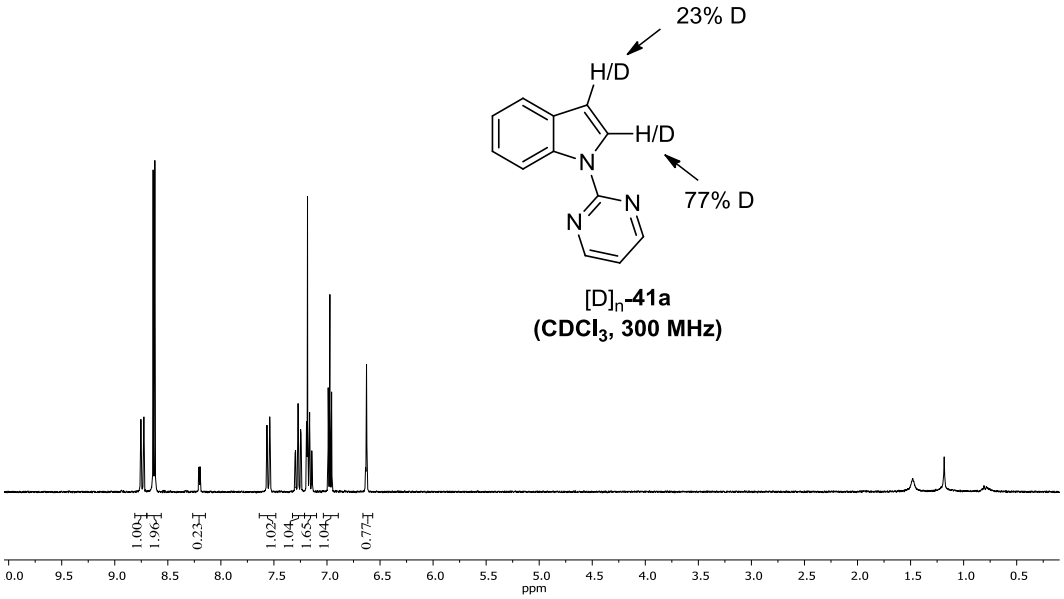
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.42 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.29–7.22 (m, 1H), 7.15 (ddd, *J* = 9.6, 8.2,

1.4 Hz, 1H), 5.87–5.57 (m, 2H), 4.27 (d, *J* = 7.1 Hz, 0.17H), 4.04 (dd, *J* = 5.8, 1.3 Hz, 1.83H), 3.62–3.58 (m, 2H), 2.55 (s, 3H), 1.83 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer*: δ = 201.4 (d, $^4J_{C\text{-}F}$= 2.6 Hz, C_q), 161.7 (d, ^1J = 246.7 Hz, C_q), 140.1 (d, $^3J_{C\text{-}F}$ = 4.1 Hz, C_q), 130.4 (CH), 129.9 (CH), 127.6 (d, $^3J_{C\text{-}F}$ = 8.7 Hz, CH), 126.8 (d, $^2J_{C\text{-}F}$ = 16.8 Hz, C_q), 124.6 (d, $^4J_{C\text{-}F}$ = 3.4 Hz, CH), 118.6 (d, $^2J_{C\text{-}F}$ = 23.8 Hz, CH), 63.5 (CH_2), 30.1 (CH_3), 28.1 (d, $^3J_{C\text{-}F}$ = 3.9, CH_2). *Minor isomer*: δ = 201.9 (d, ^4J = 2.4 Hz, C_q), 161.6 (d, $^1J_{C\text{-}F}$ = 240.1 Hz, C_q), 139.9 (d, $^3J_{C\text{-}F}$ = 4.0 Hz, C_q), 130.6 (CH), 130.2 (CH), 127.6 (d, $^3J_{C\text{-}F}$ = 9.0 Hz, CH), 127.4 (d, $^2J_{C\text{-}F}$ = 16.3 Hz, C_q), 125.0 (d, $^4J_{C\text{-}F}$ = 3.3 Hz, CH), 118.8 (d, $^2J_{C\text{-}F}$ = 23.9 Hz, CH), 58.2 (CH_2), 29.7 (CH_3), 23.9 (d, ^3J = 4.0 Hz, CH_2). **^{19}F NMR** (376 MHz, $CDCl_3$) *Major isomer*: δ = -115.82 (t, *J* = 6.8 Hz). *Minor isomer*: δ = -115.95 (dd, *J* = 9.3, 6.0 Hz). **IR** (ATR) *v* = 3419, 2925, 1687, 1576, 1452, 1259, 792 cm^{-1}. **MS** (ESI) m/z (relative intensity): 231 (100) $[M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{12}H_{13}O_2FNa$ $[M+Na]^+$: 231.0792, found: 231.0792.

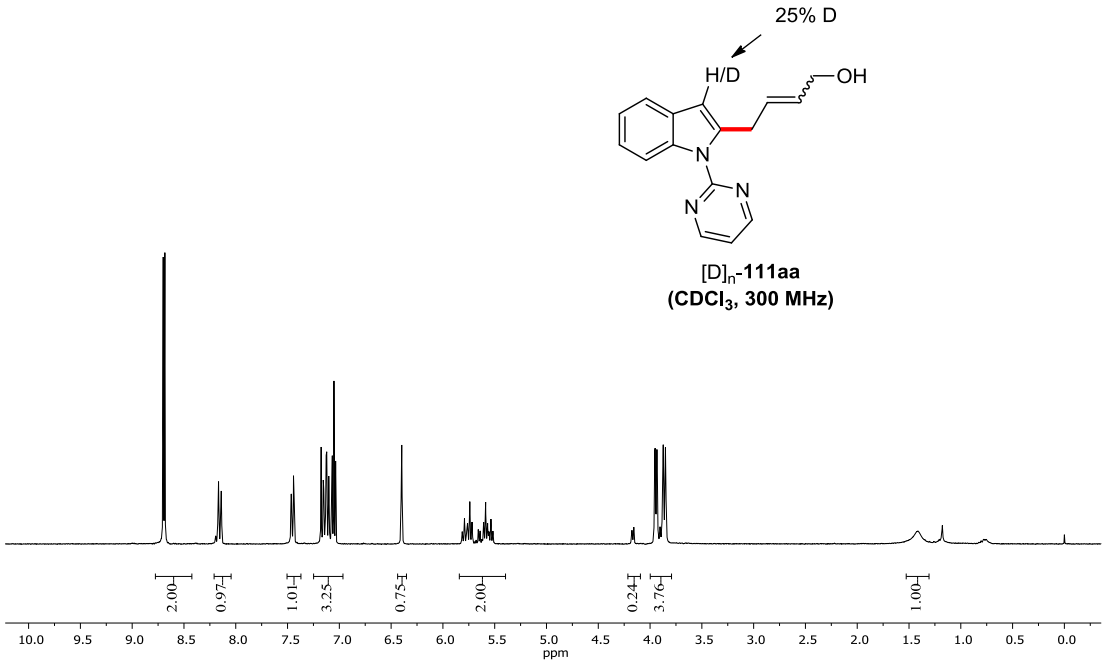
H/D Exchange Experiment



Substrates **41a** (48.8 mg, 0.25 mmol), **110a** (85.5 mg, 0.75 mmol), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %), NaOAc (4.1 mg, 20.0 mol%) and D_2O (1.0 mL) were placed in a 25 mL Schlenk tube under ambient air and stirred at 100 °C for 5 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1 to 1/1) yielded $[D]_n$-**41a** (9.8 mg, 20%) and $[D]_n$-**111aa** (42.4 mg, 64%). The D incorporation was determined by ^{1}H-NMR spectroscopy.

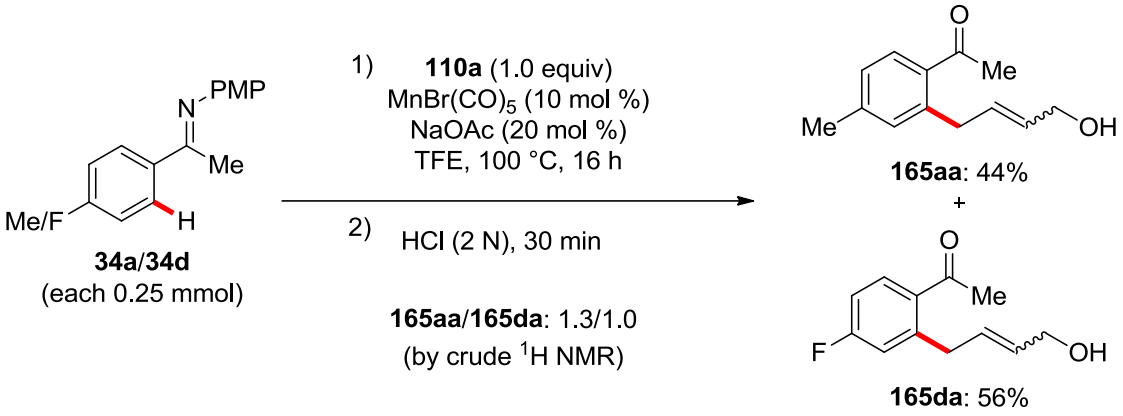


[D]$_n$-41a
(CDCl$_3$, 300 MHz)

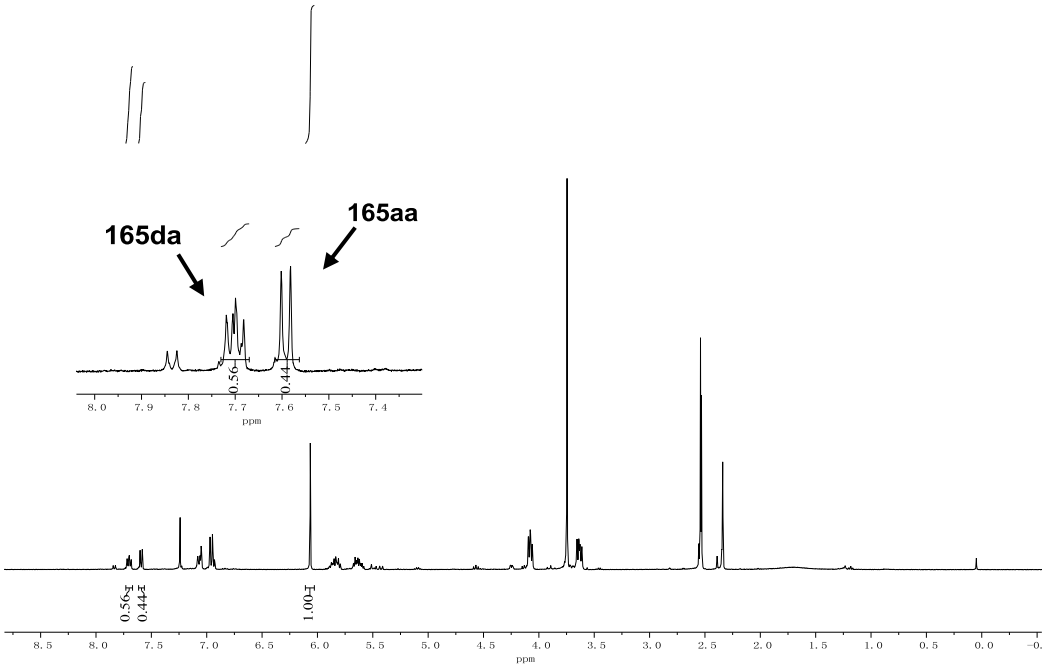


[D]$_n$-111aa
(CDCl$_3$, 300 MHz)

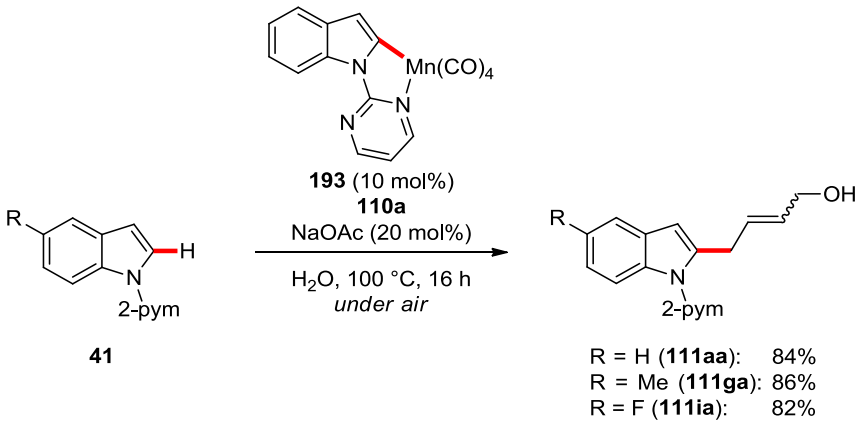
Intermolecular Competition Experiment



A suspension of (*E*)-4-methoxy-*N*-[1-(p-tolyl)ethylidene]aniline (**34a**) (59.8 mg, 0.25 mmol), (*E*)-*N*-[1-(4-fluorophenyl)ethylidene]-4-methoxyaniline (**34d**) (60.8 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (4.1 mg, 20.0 mol %) and [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in TFE (1.0 mL) was stirred at 100 °C for 16 h under N_2. After cooling to ambient temperature, HCl (2 N, 3.0 mL) was added. The resulting mixture was stirred for 30 min at 25 °C and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude ^1H NMR was measured to determine the conversions to the products **165aa** (44%) and **165da** (56%) using 1,3,5-trimethoxybenzene as the internal standard.



Decarboxylative C–H/C–O Activation with Cyclometalated Complex 4 in catalytic reactions

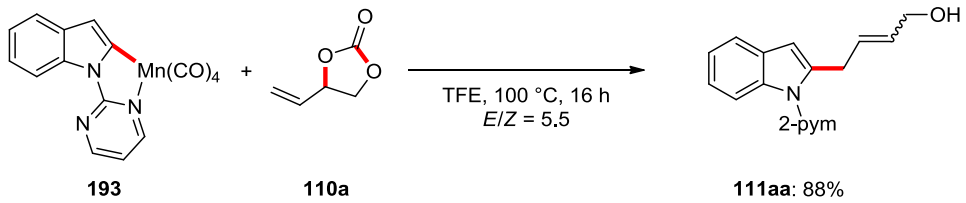


The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (4.1 mg, 20.0 mol %) and complex **193** (9.0 mg, 10.0 mol %). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111aa** (61.3 mg, 84% based on 0.275 mmol)

The general procedure **F** was followed using 5-methyl-1-(pyrimidin-2-yl)-1*H*-indole (**41g**) (52.3 mg, 0.25 mmol) 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (4.1 mg, 20.0 mol %) and complex **193** (9.0 mg, 10.0 mol %). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) afforded 64.1 mg of a 9.4/1 mixture of **111ga** (0.215 mmol, 86%) and **111ga'** (0.014 mmol, 56%)

The general procedure **F** was followed using 5-fluoro-1-(pyrimidin-2-yl)-1*H*-indole (**41i**) (53.3 mg, 0.25 mmol) 4-vinyl-1,3-dioxolan-2-one (**110a**) (72.0 µL, 0.75 mmol), NaOAc (4.1 mg, 20.0 mol %) and complex **193** (9.0 mg, 10.0 mol %). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) afforded 62.5 mg of a 9.2/1 mixture of **111ia** (0.205 mmol, 82%) and **111ia'** (0.016 mmol, 64%).

Decarboxylative C–H/C–O Activation with Cyclometalated Complex 193 in stoichiometric reaction

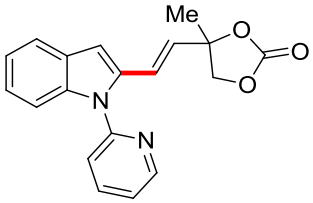


193 **110a** **111aa**: 88%

Complex **193** (54.2 mg, 0.15 mmol), dioxolanone **110a** (51.3 mg, 0.45 mmol) and TFE (1.0 mL) were placed in a 25 mL Schlenk tube under ambient air and stirred at 100 °C for 16 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111aa** (35.0 mg, 88%, *E*/*Z* = 5.5/1 by ^{1}H NMR).

5.3.6 Data for Synergistic Manganese(I)-Catalyzed Chem-Selective C–H Hydroarylation in Continous Flow

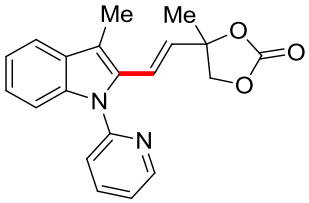
Characterization Data



(*E*)-4-Methyl-4-{2-[1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-1,3-dioxolan-2-one (167ba): The general procedure **G** was followed using 1-(pyridin-2-yl)-1*H*-indole (**41b**) (48.6 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ba** (76.1 mg, 95%) as colorless oil.

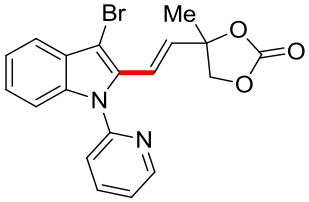
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.89 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), 7.67–7.57 (m, 1H), 7.49–7.41 (m, 1H), 7.37 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.34 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 7.22–7.12 (m, 2H), 6.87 (s, 1H), 6.77 (d, *J* = 16.0 Hz, 1H), 6.17 (d, *J* = 16.0 Hz, 1H), 4.29 (d, *J* = 8.4 Hz, 1H), 4.19 (d, *J* = 8.4 Hz, 1H), 1.62 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 154.2 (C_q), 150.7 (C_q), 149.7

(CH), 138.5 (CH), 137.7 (C_q), 135.5 (C_q), 128.7 (CH), 128.2 (C_q), 123.4 (CH), 122.3 (CH), 121.9 (CH), 121.5 (CH), 121.1 (CH), 120.8 (CH), 110.8 (CH), 103.6 (CH), 82.6 (C_q), 74.6 (CH_2), 24.4 (CH_3). **IR** (ATR) *v* = 2922, 1779, 1586, 1468, 1340, 1213, 1044, 969, 793, 754 cm^{-1}. **MS** (ESI) m/z (relative intensity): 369 (20), 337 (100) $[M+Na]^+$, 321 (80) $[M+H]^+$, 299 (20), 277 (20). **HR-MS** (ESI) m/z calcd for $C_{19}H_{17}N_2O_3$ $[M+H]^+$: 321.1234, found: 321.1233.



(*E*)-4-Methyl-4-{2-[3-methyl-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-1,3-dioxolan-2-one (167ma): The general procedure **G** was followed using 3-methyl-1-(pyridin-2-yl)-1*H*-indole (**41m**) (52.1 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ma** (72.0 mg, 86%) as colorless oil.

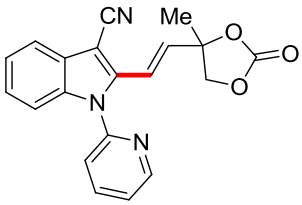
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.63 (ddd, *J* = 4.8, 2.0, 1.0 Hz, 1H), 7.85 (ddd, *J* = 8.0, 7.4, 2.0 Hz, 1H), 7.59 (dd, *J* = 6.5, 1.2 Hz, 1H), 7.45 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.36–7.25 (m, 2H), 7.24–7.14 (m, 2H), 6.79 (d, *J* = 16.3 Hz, 1H), 5.69 (d, *J* = 16.3 Hz, 1H), 4.22 (d, *J* = 8.4 Hz, 1H), 4.17 (d, *J* = 8.4 Hz, 1H), 2.43 (s, 3H), 1.60 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 154.2 (C_q), 151.6 (C_q), 149.5 (CH), 138.3 (CH), 137.4 (C_q), 130.9 (C_q), 130.0 (CH), 129.3 (C_q), 124.0 (CH), 122.0 (CH), 121.3 (CH), 121.2 (CH), 120.9 (CH), 119.2 (CH), 115.0 (C_q), 110.7 (CH), 82.8 (C_q), 74.7 (CH_2), 24.3 (CH_3), 10.0 (CH_3). **IR** (ATR) *v* = 2978, 1801, 1588, 1470, 1455, 1227, 1056, 743 cm^{-1}. **MS** (ESI) m/z (relative intensity): 691 (70) $[2M+Na]^+$, 357 (100) $[M+Na]^+$, 335 (40) $[M+H]^+$, 313 (35), 291 (30). **HR-MS** (ESI) m/z calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$: 335.1390, found: 335.1387.



(*E*)-4-{2-[3-Bromo-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-4-methyl-1,3-dioxolan-2-one (167na): The general procedure **G** was followed using 3-bromo-1-(pyridin-2-yl)-1*H*-indole (**41n**) (68.3 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by

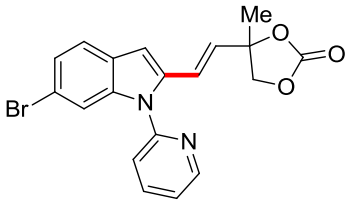
column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **167na** (62.9 mg, 63%) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.67 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.91 (ddd, *J* = 7.9, 7.5, 2.0 Hz, 1H), 7.67–7.56 (m, 1H), 7.48–7.31 (m, 3H), 7.31–7.21 (m, 2H), 6.71 (d, *J* = 16.4 Hz, 1H), 6.30 (d, *J* = 16.4 Hz, 1H), 4.27 (d, *J* = 8.4 Hz, 1H), 4.20 (d, *J* = 8.4 Hz, 1H), 1.63 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 154.0 (C_q), 150.5 (C_q), 149.7 (CH), 138.5 (CH), 136.8 (C_q), 132.3 (CH), 130.9 (C_q), 127.8 (C_q), 124.8 (CH), 122.8 (CH), 122.0 (CH), 121.5 (CH), 119.7 (CH), 119.5 (CH), 110.9 (CH), 96.3 (C_q), 82.5 (C_q), 74.6 (CH_2), 24.4 (CH_3). **IR** (ATR) *v* = 2981, 1796, 1587, 1466, 1435, 1343, 1214, 1054, 739 cm^{-1}. **MS** (ESI) m/z (relative intensity): 423 (10) (^{81}Br) $[M+H]^+$, 421 (10) (^{79}Br) $[M+H]^+$, 401 (100) (^{81}Br) $[M+H]^+$, 399 (100) (^{79}Br) $[M+H]^+$, 342 (10). **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}N_2O_3{}^{81}Br$ $[M+H]^+$: 401.0319, found: 401.0322, $C_{19}H_{16}N_2O_3{}^{79}Br$ $[M+H]^+$: 399.0339, found: 399.0341.



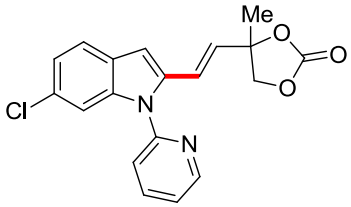
(*E*)-2-[2-(4-Methyl-2-oxo-1,3-dioxolan-4-yl)vinyl]-1-(pyridin-2-yl)-1*H*-indole-3-carbonitrile (167ta): The general procedure **G** was followed using 1-(pyridin-2-yl)-1*H*-indole-3-carbonitrile (**41t**) (54.8 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ta** (56.1 mg, 65%) as white solid.

M.p. = 151–153 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.70 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.97 (td, *J* = 7.7, 1.9 Hz, 1H), 7.85–7.68 (m, 1H), 7.46 (ddd, *J* = 7.6, 4.9, 1.0 Hz, 1H), 7.43–7.36 (m, 2H), 7.35–7.26 (m, 2H), 6.84 (d, *J* = 16.2 Hz, 1H), 6.70 (d, *J* = 16.2 Hz, 1H), 4.37 (d, *J* = 8.5 Hz, 1H), 4.25 (d, *J* = 8.5 Hz, 1H), 1.67 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 153.8 (C_q), 150.2 (CH), 148.9 (C_q), 141.2 (C_q), 139.1 (CH), 136.2 (C_q), 135.4 (CH), 127.5 (C_q), 125.3 (CH), 124.0 (CH), 123.5 (CH), 121.5 (CH), 119.6 (CH), 118.0 (CH), 116.3 (C_q), 111.6 (CH), 86.6 (C_q), 82.2 (C_q), 74.5 (CH_2), 24.7 (CH_3). **IR** (ATR) *v* = 2923, 2215, 1788, 1612, 1467, 1392, 1220, 1144, 1065, 760 cm^{-1}. **MS** (ESI) m/z (relative intensity): 713 (30) $[2M+Na]^+$, 368 (60) $[M+Na]^+$, 346 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{16}N_3O_3$ $[M+H]^+$: 346.1186, found: 346.1188.



(*E*)-4-{2-[6-Bromo-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-4-methyl-1,3-dioxolan-2-one (167ua): The general procedure **G** was followed using 6-bromo-1-(pyridin-2-yl)-1*H*-indole (**41u**) (68.3 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ua** (80.8 mg, 81%) as colorless oil.

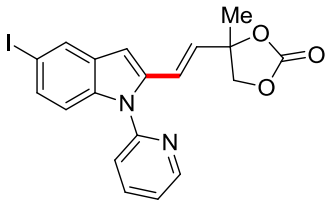
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.91 (td, *J* = 7.7, 2.0 Hz, 1H), 7.59 (d, *J* = 1.9 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.36 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 7.32 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.28–7.22 (m, 1H), 6.81 (s, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.17 (d, *J* = 16.0 Hz, 1H), 4.27 (d, *J* = 8.4 Hz, 1H), 4.18 (d, *J* = 8.4 Hz, 1H), 1.61 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 154.1 (C_q), 150.2 (C_q), 149.8 (CH), 138.7 (CH), 138.4 (C_q), 136.1 (C_q), 129.5 (CH), 126.9 (C_q), 124.8 (CH), 122.7 (CH), 122.0 (CH), 121.3 (CH), 121.1 (CH), 117.0 (C_q), 113.9 (CH), 103.4 (CH), 82.5 (C_q), 74.5 (CH_2), 24.3 (CH_3). **IR** (ATR) *v* = 2981, 1798, 1587, 1470, 1441, 1340, 1229, 1057, 948 cm^{-1}. **MS** (ESI) m/z (relative intensity): 423 (95) (^{81}Br) $[M+H]^+$, 421 (100) (^{79}Br) $[M+H]^+$, 401 (30) (^{81}Br) $[M+H]^+$, 399 (30) (^{79}Br) $[M+H]^+$, 357 (30) (^{81}Br), 355 (30) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}N_2O_3{}^{81}Br$ $[M+H]^+$: 401.0321, found: 401.0314, $C_{19}H_{16}N_2O_3{}^{79}Br$ $[M+H]^+$: 399.0339, found: 399.0335.



(*E*)-4-{2-[6-Chloro-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-4-methyl-1,3-dioxolan-2-one (167va): The general procedure **G** was followed using 6-chloro-1-(pyridin-2-yl)-1*H*-indole (**41v**) (57.2 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167va** (73.0 mg, 82%) as colorless oil.

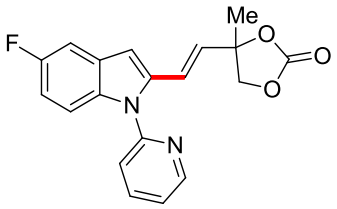
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.91 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), 7.49

(d, *J* = 8.5 Hz, 1H), 7.44 (dt, *J* = 1.9, 0.7 Hz, 1H), 7.36 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 7.32 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.11 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.81 (s, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.16 (d, *J* = 16.0 Hz, 1H), 4.27 (d, *J* = 8.4 Hz, 1H), 4.18 (d, *J* = 8.4 Hz, 1H), 1.61 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 154.1 (C_q), 150.2 (C_q), 149.8 (CH), 138.7 (CH), 138.0 (C_q), 136.2 (C_q), 129.3 (C_q), 129.3 (CH), 126.6 (C_q), 122.7 (CH), 122.2 (CH), 121.6 (CH), 121.4 (CH), 121.0 (CH), 111.0 (CH), 103.4 (CH), 82.5 (C_q), 74.6 (CH_2), 24.3 (CH_3). **IR** (ATR) *v* = 2982, 1799, 1587, 1471, 1442, 1342, 1230, 1057, 956 cm^{-1}. **MS** (ESI) m/z (relative intensity): 377 (100) $[M+Na]^+$, 355 (30) $[M+H]^+$, 333 (25), 311 (30). **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}ClN_2O_3$ $[M+H]^+$: 355.0844, found: 355.0845.



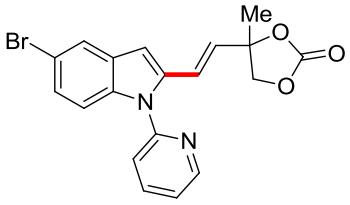
(*E*)-4-{2-[5-Iodo-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-4-methyl-1,3-dioxolan-2-one (167wa): The general procedure **G** was followed using 5-iodo-1-(pyridin-2-yl)-1*H*-indole (**41w**) (80.1 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167wa** (104.9 mg, 94%) as white solid.

M.p. = 49–51 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.99–7.83 (m, 2H), 7.41 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.36 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 1H), 6.76 (s, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.19 (d, *J* = 16.0 Hz, 1H), 4.29 (d, *J* = 8.4 Hz, 1H), 4.19 (d, *J* = 8.4 Hz, 1H), 1.62 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 154.1 (C_q), 150.2 (C_q), 149.8 (CH), 138.6 (CH), 136.8 (C_q), 136.2 (C_q), 131.7 (CH), 130.6 (C_q), 129.7 (CH), 129.5 (CH), 122.7 (CH), 121.3 (CH), 121.1 (CH), 112.9 (CH), 102.3 (CH), 85.0 (C_q), 82.5 (C_q), 74.6 (CH_2), 24.4 (CH_3). **IR** (ATR) *v* = 2978, 1791, 1586, 1469, 1439, 1373, 1209, 1051, 956, 786 cm^{-1}. **MS** (ESI) m/z (relative intensity): 915 (40) $[2M+Na]^+$, 469 (35) $[M+Na]^+$, 447 (100) $[M+H]^+$, 425 (30), 314 (25). **HR-MS** (ESI) m/z calcd for $C_{19}H_{15}IN_2O_3$ $[M+H]^+$: 447.0200, found: 447.0195.



(*E*)-4-{2-[5-Fluoro-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-4-methyl-1,3-dioxolan-2-one (167xa): The general procedure **G** was followed using 5-fluoro-1-(pyridin-2-yl)-1*H*-indole (**41x**) (53.1 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167xa** (76.0 mg, 90%) as colorless oil.

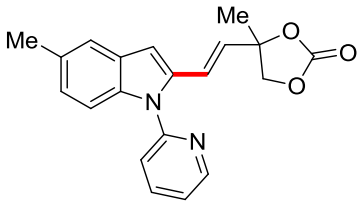
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.90 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), 7.46–7.30 (m, 3H), 7.23 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.92 (td, *J* = 9.1, 2.5 Hz, 1H), 6.81 (s, 1H), 6.73 (d, *J* = 16.0 Hz, 1H), 6.19 (d, *J* = 16.0 Hz, 1H), 4.29 (d, *J* = 8.4 Hz, 1H), 4.20 (d, *J* = 8.4 Hz, 1H), 1.62 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 158.6 (d, $^{1}J_{C\text{-}F}$ = 237.6 Hz, C_q), 154.0 (C_q), 150.4 (C_q), 149.6 (CH), 138.5 (CH), 136.8 (C_q), 134.2 (C_q), 129.4 (CH), 128.6 (d, $^{3}J_{C\text{-}F}$ = 9.9 Hz, C_q), 122.5 (CH), 121.5 (CH), 121.0 (CH), 111.8 (d, $^{3}J_{C\text{-}F}$ = 9.2 Hz, CH), 111.7 (d, $^{2}J_{C\text{-}F}$ = 26.3 Hz, CH), 105.5 (d, $^{2}J_{C\text{-}F}$ = 24.0 Hz, CH), 103.3 (d, $^{4}J_{C\text{-}F}$ = 4.5 Hz, CH), 82.5 (C_q), 74.6 (CH_2), 24.5 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -122.51 (td, *J* = 9.2, 4.4 Hz). **IR** (ATR) *v* = 2982, 1796, 1586, 1467, 1386, 1236, 1185, 1054, 958, 782 cm^{-1}. **MS** (ESI) m/z (relative intensity): 699 (20) $[2M+Na]^+$, 361 (20) $[M+Na]^+$, 339 (100) $[M+H]^+$, 317 (30). **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}N_2O_3F$ $[M+H]^+$: 339.1139, found: 339.1140.



(*E*)-4-{2-[5-Bromo-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-4-methyl-1,3-dioxolan-2-one (167ya): The general procedure **G** was followed using 5-bromo-1-(pyridin-2-yl)-1*H*-indole (**41y**) (68.3 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ya** (91.2 mg, 91%) as pale yellow solid.

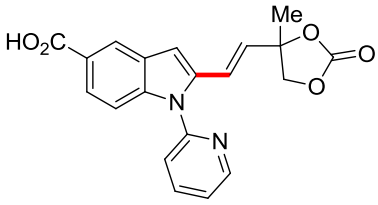
M.p. = 45–47 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.65 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.90 (ddd, *J* = 7.9, 7.5,

1.9 Hz, 1H), 7.71 (d, *J* = 1.9 Hz, 1H), 7.47–7.16 (m, 4H), 6.77 (s, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.19 (d, *J* = 16.0 Hz, 1H), 4.28 (d, *J* = 8.4 Hz, 1H), 4.19 (d, *J* = 8.4 Hz, 1H), 1.62 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 154.0 (C_q), 150.2 (C_q), 149.7 (CH), 138.5 (CH), 136.5 (C_q), 136.3 (C_q), 129.7 (C_q), 129.7 (CH), 126.1 (CH), 123.1 (CH), 122.6 (CH), 121.3 (CH), 121.0 (CH), 114.5 (C_q), 112.4 (CH), 102.6 (CH), 82.4 (C_q), 74.6 (CH_2), 24.5 (CH_3). **IR** (ATR) *v* = 2981, 1791, 1586, 1440, 1382, 1228, 1209, 1050, 957, 786 cm^{-1}. **MS** (ESI) m/z (relative intensity): 401 (100) (^{81}Br) $[M+H]^+$, 399 (100) (^{79}Br) $[M+H]^+$, 357 (15) (^{81}Br), 355 (15) (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}N_2O_3{}^{81}Br$ $[M+H]^+$: 401.0319, found: 401.0315, $C_{19}H_{16}N_2O_3{}^{79}Br$ $[M+H]^+$: 399.0339, found: 399.0334.



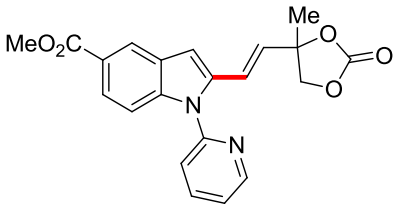
(*E*)-4-Methyl-4-{2-[5-methyl-1-(pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-1,3-dioxolan-2-one (167za): The general procedure **G** was followed using 5-methyl-1-(pyridin-2-yl)-1*H*-indole (**41z**) (52.1 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167za** (65.2 mg, 78%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (dd, *J* = 5.1, 2.1 Hz, 1H), 7.88 (ddd, *J* = 8.0, 7.4, 2.0, Hz, 1H), 7.42–7.28 (m, 4H), 7.01 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.79 (s, 1H), 6.77 (d, *J* = 16.1 Hz, 1H), 6.15 (d, *J* = 16.1 Hz, 1H), 4.29 (d, *J* = 8.4 Hz, 1H), 4.19 (dd, *J* = 8.4 Hz, 1H), 2.42 (s, 3H), 1.62 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 154.3 (C_q), 150.9 (C_q), 149.6 (CH), 138.5 (CH), 136.2 (C_q), 135.5 (C_q), 130.9 (C_q), 128.5 (C_q), 128.4 (CH), 125.2 (CH), 122.2 (CH), 122.1 (CH), 121.0 (CH), 120.5 (CH), 110.6 (CH), 103.4 (CH), 82.7 (C_q), 74.7 (CH_2), 24.4 (CH_3), 21.4 (CH_3). **IR** (ATR) *v* = 2924, 1800, 1588, 1470, 1437, 1384, 1301, 1187, 1057 cm^{-1}. **MS** (ESI) m/z (relative intensity): 335 (100) $[M+H]^+$, 313 (40), 271 (40). **HR-MS** (EI) m/z calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$: 335.1390, found: 335.1393.



(*E*)-2-[2-(4-Methyl-2-oxo-1,3-dioxolan-4-yl)vinyl]-1-(pyridin-2-yl)-1*H*-indole-5-carboxylic acid (167a'a): The general procedure **G** was followed using 1-(pyridin-2-yl)-1*H*-indole-5-carboxylic acid (**41a'**) (59.6 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (EtOAc/MeOH: 20/1) yielded **167a'a** (61.1 mg, 67%) as white solid.

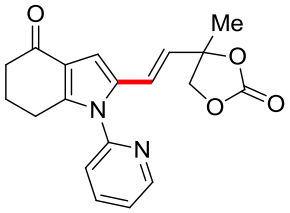
M.p. = 135–137 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.70 (dd, *J* = 4.9, 2.0 Hz, 1H), 8.45 (s, 1H), 8.11–7.84 (m, 2H), 7.53–7.37 (m, 3H), 6.96 (s, 1H), 6.74 (dd, *J* = 16.0 Hz, 1H), 6.23 (d, *J* = 16.0 Hz, 1H), 4.31 (d, *J* = 8.4 Hz, 1H), 4.21 (d, *J* = 8.4 Hz, 1H), 1.64 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 171.8 (C_q), 154.0 (C_q), 150.9 (C_q), 149.8 (CH), 140.5 (C_q), 138.7 (CH), 137.1 (C_q), 130.0 (CH), 127.7 (C_q), 125.1 (CH), 124.5 (CH), 123.0 (CH), 122.5 (C_q), 121.3 (CH), 121.1 (CH), 110.7 (CH), 104.3 (CH), 82.4 (C_q), 74.6 (CH_2), 24.6 (CH_3). **IR** (ATR) *v* = 2924, 1796, 1678, 1470, 1228, 1053, 905, 767, 726 cm^{-1}. **MS** (ESI) m/z (relative intensity): 751 (50) $[2M+Na]^+$, 387 (70) $[M+Na]^+$, 365 (100) $[M+H]^+$, 343 (55). **HR-MS** (ESI) m/z calcd for $C_{20}H_{17}N_2O_5$ $[M+H]^+$: 365.1132, found: 365.1124.



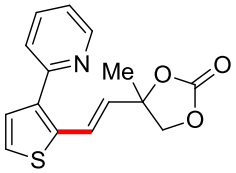
(*E*)-Methyl 2-[2-(4-methyl-2-oxo-1,3-dioxolan-4-yl)vinyl]-1-(pyridin-2-yl)-1*H*-indole-5-carboxylate (167b'a): The general procedure **G** was followed using methyl 1-(pyridin-2-yl)-1*H*-indole-5-carboxylate (**41b'**) (63.1 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167b'a** (68.1 mg, 72%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 (dd, *J* = 4.9, 1.9 Hz, 1H), 8.34 (d, *J* = 1.7 Hz, 1H), 7.92 (ddd, *J* = 8.0, 7.5, 1.9 Hz, 1H), 7.86 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.42 (dt, *J* = 8.7, 0.8 Hz, 1H), 7.40–7.31 (m, 2H), 6.92 (s, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.21 (d, *J* = 16.0 Hz, 1H), 4.29 (d, *J* = 8.4 Hz, 1H), 4.19 (d, *J* = 8.4 Hz, 1H), 3.91 (s, 3H), 1.61 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 167.6 (C_q), 154.1 (C_q), 150.2 (C_q), 149.8 (CH), 140.0 (C_q), 138.7 (CH), 137.0 (C_q), 129.9 (CH), 127.7 (C_q), 124.6 (CH), 123.7 (CH), 123.5 (C_q), 122.9 (CH), 121.2 (CH), 121.2 (CH), 110.6 (CH), 104.2 (CH), 82.4 (C_q), 74.6 (CH_2), 51.9 (CH_3), 24.4 (CH_3). **IR** (ATR) *v* = 2951, 1795, 1706, 1588, 1469, 1434, 1309, 1253, 1089, 1053 cm^{-1}. **MS** (ESI) m/z (relative

intensity): 779 (30) $[2M+Na]^+$, 757 (30) $[2M+H]^+$, 401 (10) $[M+Na]^+$, 379 (100) $[M+H]^+$, 357 (30), 335 (35). **HR-MS** (ESI) m/z calcd for $C_{21}H_{19}N_2O_3$ $[M+H]^+$: 379.1288, found: 379.1289.

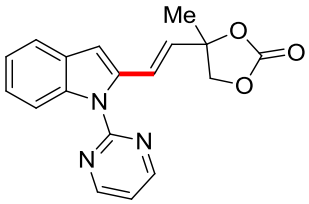


(*E*)-2-[2-(4-Methyl-2-oxo-1,3-dioxolan-4-yl)vinyl]-1-(pyridin-2-yl)-6,7-dihydro-1*H*-indol-4(5*H*)-one (167c'a): The general procedure **G** was followed using 1-(pyridin-2-yl)-6,7-dihydro-1*H*-indol-4(5*H*)-one (**41c'**) (53.1 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/3) yielded **167c'a** (42.3 mg, 50%) as a white solid. **M.p.** = 149–151 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.59 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.87 (td, *J* = 7.7, 1.9 Hz, 1H), 7.38 (ddd, *J* = 7.6, 4.9, 1.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 6.79 (s, 1H), 6.31 (d, *J* = 16.0 Hz, 1H), 5.89 (d, *J* = 16.0 Hz, 1H), 4.17 (d, *J* = 8.4 Hz, 1H), 4.11 (d, *J* = 8.4 Hz, 1H), 2.66 (td, *J* = 6.1, 2.7 Hz, 2H), 2.49–2.37 (m, 2H), 2.14–1.97 (m, 2H), 1.51 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 194.1 (C_q), 154.0 (C_q), 149.7 (CH), 149.4 (C_q), 145.5 (C_q), 138.6 (CH), 131.2 (C_q), 126.8 (CH), 123.7 (CH), 121.6 (CH), 121.4 (C_q), 120.1 (CH), 105.0 (CH), 82.5 (C_q), 74.7 (CH_2), 37.9 (CH_2), 24.5 (CH_3), 23.6 (CH_2), 23.0 (CH_2). **IR** (ATR) *v* = 2930, 1796, 1656, 1460, 1438, 1220, 1134, 1093, 1054, 733 cm^{-1}. **MS** (ESI) m/z (relative intensity): 699 (70) $[2M+Na]^+$, 361 (40) $[M+Na]^+$, 339 (100) $[M+H]^+$, 317 (80). **HR-MS** (ESI) m/z calcd for $C_{19}H_{19}N_2O_4$ $[M+H]^+$: 339.1339, found: 339.1340.



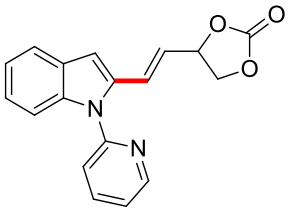
(*E*)-4-Methyl-4-{2-[3-(pyridin-2-yl)thiophen-2-yl]vinyl}-1,3-dioxolan-2-one (167d'a): The general procedure **G** was followed using 2-(thiophen-3-yl)pyridine (**41d'**) (40.3 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/1) yielded **167d'a** (63.2 mg, 88%) as colorless oil.

^{1}H NMR (300 MHz, C_6D_6) δ = 8.62 (dt, *J* = 4.8, 1.5 Hz, 1H), 7.89 (d, *J* = 16.1 Hz, 1H), 7.32–7.08 (m, 3H), 6.88 (d, *J* = 5.3 Hz, 1H), 6.72 (ddd, *J* = 5.7, 4.8, 2.9 Hz, 1H), 5.93 (d, *J* = 16.1 Hz, 1H), 3.54 (d, *J* = 8.4 Hz, 1H), 3.34 (d, *J* = 8.4 Hz, 1H), 1.06 (s, 3H). **^{13}C NMR** (75 MHz, C_6D_6) δ = 154.5 (C_q), 154.0 (C_q), 149.7 (CH), 139.9 (C_q), 138.1 (C_q), 136.2 (CH), 129.5 (CH), 128.5 (CH), 125.4 (CH), 124.1 (CH), 122.9 (CH), 121.7 (CH), 81.8 (C_q), 73.8 (CH_2), 23.4 (CH_3). **IR** (ATR) *v* = 1800, 1585, 1474, 1439, 1265, 1230, 1095, 1057, 958, 772 cm^{-1}. **MS** (ESI) m/z (relative intensity): 266 (70), 288 (100) $[M+H]^+$, 310 (80) $[M+Na]^+$, 597 (40) $[2M+Na]^+$. **HR-MS** (ESI) m/z calcd for $C_{15}H_{13}NO_3S$ $[M+H]^+$: 288.0689, found: 288.0691.



(*E*)-4-Methyl-4-{2-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]vinyl}-1,3-dioxolan-2-one (167aa): The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41a**) (48.8 mg, 0.25 mmol) and 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**110a**) (58.0 µL, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167aa** (57.8 mg, 72%) as colorless oil.

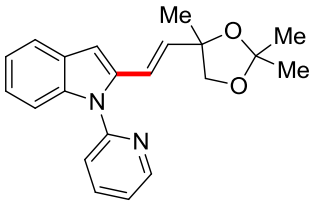
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.78 (d, *J* = 4.7 Hz, 2H), 8.35 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.36 (d, *J* = 15.9 Hz, 1H), 7.32–7.04 (m, 3H), 6.85 (s, 1H), 6.19 (d, *J* = 15.9 Hz, 1H), 4.39 (d, *J* = 8.2 Hz, 1H), 4.24 (d, *J* = 8.2 Hz, 1H), 1.70 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.2 (CH), 157.8 (C_q), 154.5 (C_q), 137.2 (C_q), 136.4 (C_q), 128.9 (C_q), 127.6 (CH), 124.6 (CH), 124.1 (CH), 122.4 (CH), 120.6 (CH), 117.3 (CH), 114.5 (CH), 106.5 (CH), 82.8 (C_q), 74.8 (CH_2), 24.5 (CH_3). **IR** (ATR) *v* = 2981, 1791, 1562, 1419, 1344, 1233, 1210, 1091, 947, 746 cm^{-1}. **MS** (ESI) m/z (relative intensity): 665 (70) $[2M+Na]^+$, 344 (10) $[M+Na]^+$, 322 (100) $[M+H]^+$, 300 (20), 278 (60), 260 (20). **HR-MS** (ESI) m/z calcd for $C_{18}H_{16}N_3O_3$ $[M+H]^+$: 322.1186, found: 322.1195.



(*E*)-4-{2-[1-(Pyridin-2-yl)-1*H*-indol-2-yl]vinyl}-1,3-dioxolan-2-one (167bb): The general procedure **G**

was followed using 1-(pyridin-2-yl)-1*H*-indole (**41b**) (48.6 mg, 0.25 mmol) and 4-ethynyl-1,3-dioxolan-2-one (**110b**) (56.1 mg, 0.5 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167bb** (63.6 mg, 83%) as colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.91 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), 7.70–7.59 (m, 1H), 7.48–7.31 (m, 3H), 7.23–7.06 (m, 2H), 6.94 (s, 1H), 6.83 (d, *J* = 15.8 Hz, 1H), 6.10 (dd, *J* = 15.8, 7.9 Hz, 1H), 5.19 (qd, *J* = 7.9, 0.9 Hz, 1H), 4.57 (ddd, *J* = 8.7, 8.0, 0.9 Hz, 1H), 4.17 (ddd, *J* = 8.7, 8.0, 0.9 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 154.5 (C_q), 150.6 (C_q), 149.6 (CH), 138.5 (CH), 137.8 (C_q), 135.0 (C_q), 128.0 (C_q), 126.7 (CH), 123.7 (CH), 123.2 (CH), 122.4 (CH), 121.5 (CH), 121.2 (CH), 121.0 (CH), 110.7 (CH), 104.4 (CH), 77.7 (CH), 69.2 (CH_2). **IR** (ATR) *v* = 3055, 1794, 1586, 1467, 1436, 1160, 1149, 1047, 933, 743 cm^{-1}. **MS** (ESI) m/z (relative intensity): 329 (10) $[M+Na]^+$, 307 (100) $[M+H]^+$, 285 (15), 245 (10). **HR-MS** (ESI) m/z calcd for $C_{18}H_{15}N_2O_3$ $[M+H]^+$: 307.1077, found: 307.1075.

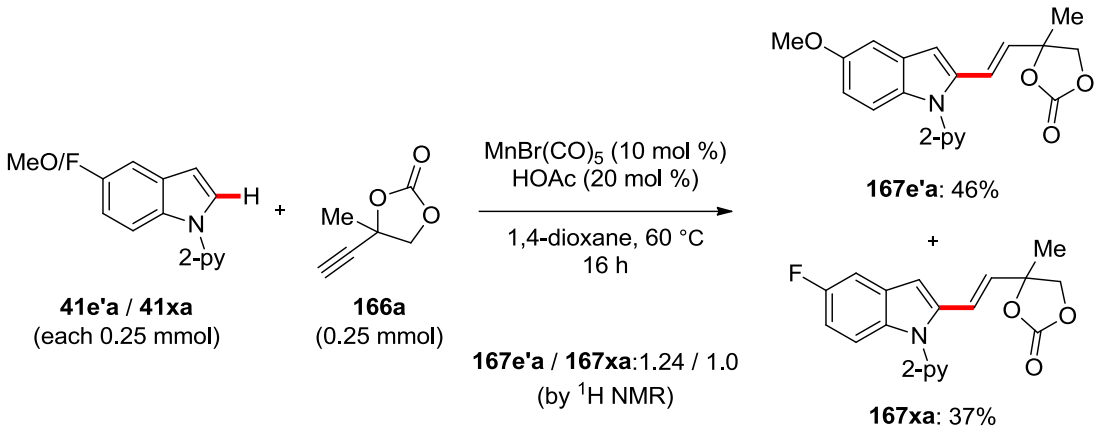


(*E*)-1-(Pyridin-2-yl)-2-[2-(2,2,4-trimethyl-1,3-dioxolan-4-yl)vinyl]-1*H*-indole (167bc): The general procedure **G** was followed using 1-(pyridin-2-yl)-1*H*-indole (**41b**) (48.6 mg, 0.25 mmol) and 4-ethynyl-2,2,4-trimethyl-1,3-dioxolane (**110c**) (70.1 mg, 0.5 mmol) for 40 min. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **167bc** (59.4 mg, 71%) as colorless oil.

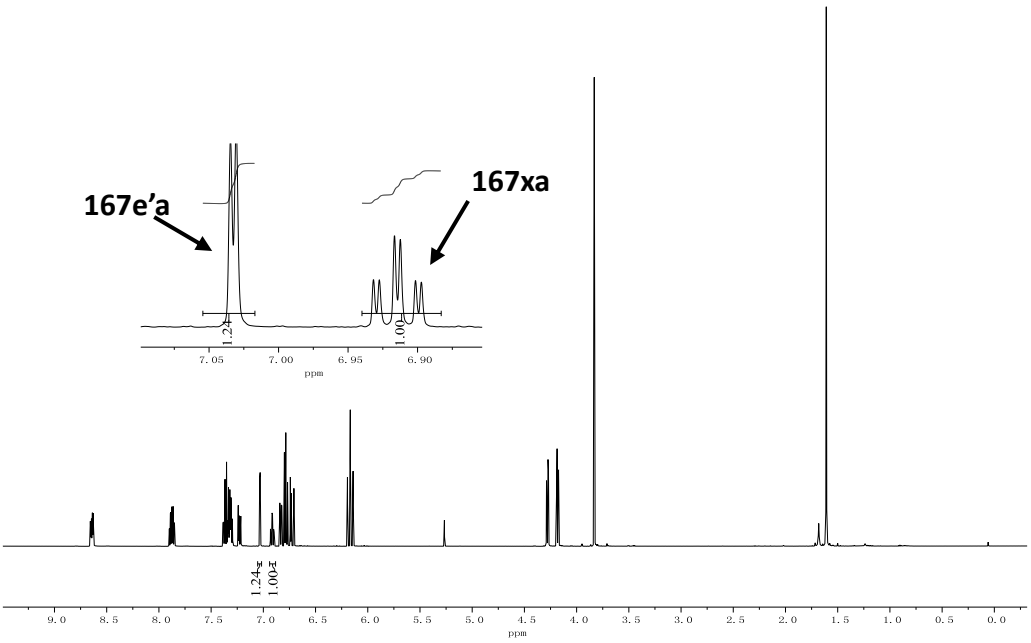
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.84 (ddd, *J* = 8.0, 7.4, 2.0 Hz, 1H), 7.62–7.55 (m, 1H), 7.52–7.42 (m, 1H), 7.34 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.30 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 7.22–7.07 (m, 2H), 6.81 (s, 1H), 6.66 (d, *J* = 15.9 Hz, 1H), 6.25 (d, *J* = 15.9 Hz, 1H), 3.91 (d, *J* = 8.4 Hz, 1H), 3.82 (d, *J* = 8.4 Hz, 1H), 1.42 (d, *J* = 0.7 Hz, 3H), 1.39 (s, 3H), 1.36 (d, *J* = 0.7 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 151.2 (C_q), 149.5 (CH), 138.1 (CH), 137.6 (C_q), 137.2 (C_q), 135.3 (CH), 128.5 (C_q), 122.7 (CH), 121.9 (CH), 121.4 (CH), 121.2 (CH), 120.4 (CH), 118.8 (CH), 110.8 (CH), 109.9 (C_q), 102.3 (CH), 80.7 (C_q), 74.6 (CH_2), 27.1 (CH_3), 26.5 (CH_3), 25.4 (CH_3). **IR** (ATR) *v* = 2982, 1386, 1468, 1452, 1212, 1103, 1057, 972, 745 cm^{-1}. **MS** (ESI) m/z (relative intensity): 357 (100) $[M+Na]^+$, 335 (50)

$[M+H]^+$, 277 (20). **HR-MS** (ESI) m/z calcd for $C_{21}H_{23}N_2O_2$ $[M+H]^+$: 335.1754, found: 335.1749.

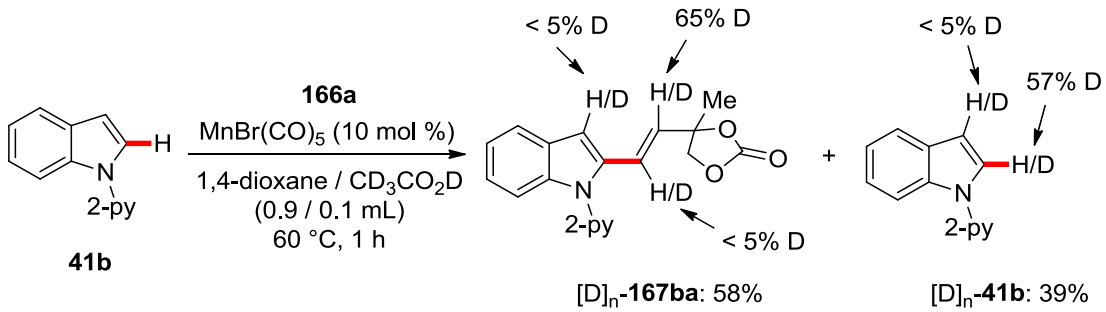
Intermolecular Competition Experiment



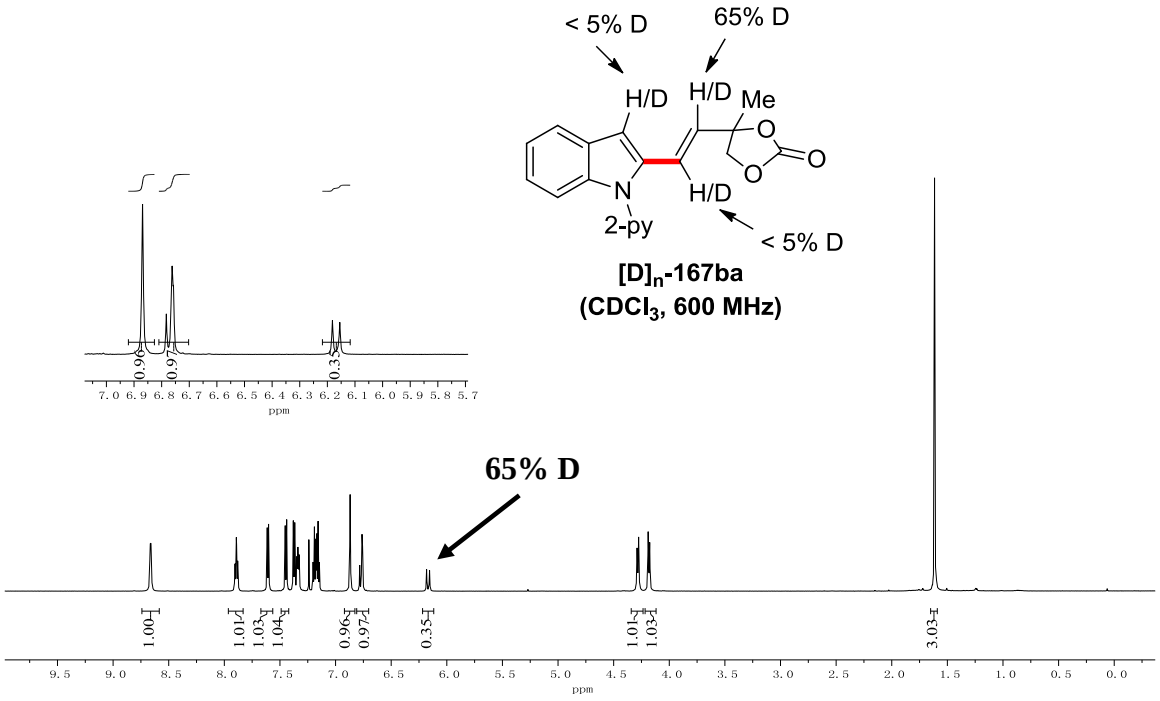
A suspension of 5-methoxy-1-(pyridin-2-yl)-1*H*-indole (**41e'a**) (56.1 mg, 0.25 mmol), 5-fluoro-1-(pyridin-2-yl)-1*H*-indole (**41xa**) (60.8 mg, 0.25 mmol), 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**) (58.0 µL, 0.5 mmol), HOAc (2.8 µL, 20.0 mol %) and $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 60 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel afforded the products (**167e'a** + **167xa**: 71.6 mg) and the ratio were determined by ^{1}H NMR spectroscopy.



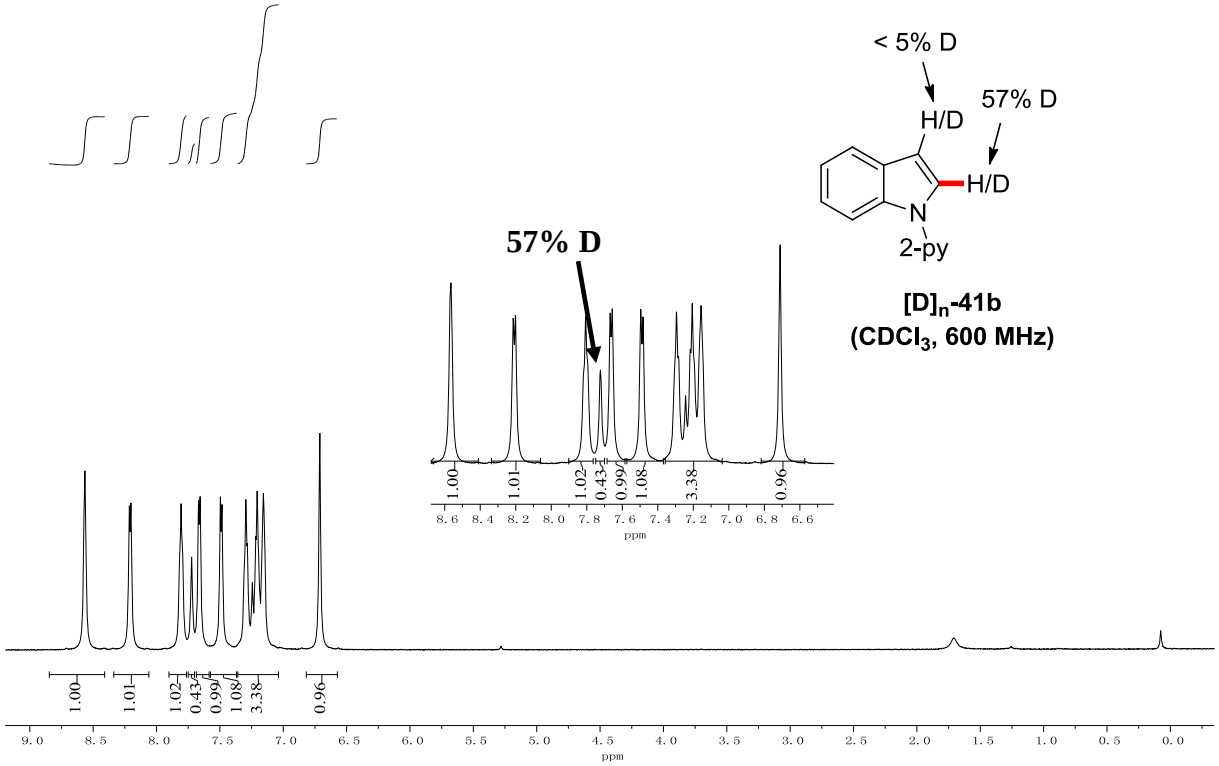
H/D Exchange Experiments



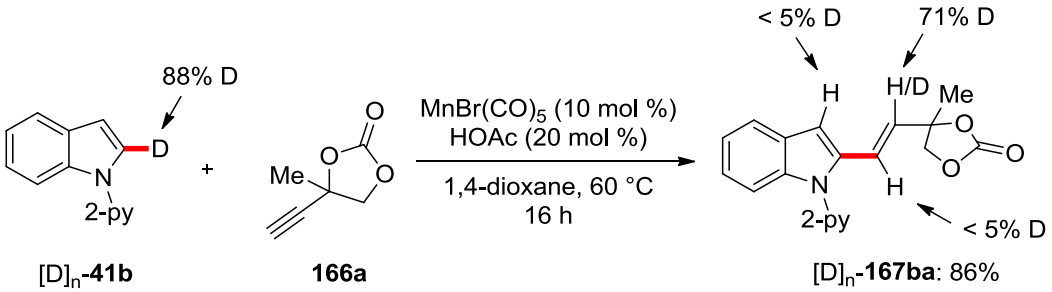
Substrates **41b** (48.6 mg, 0.25 mmol), **166a** (58 µL, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %), 1,4-dioxane (0.9 mL) and CD_3CO_2D (0.1 mL, 7.0 equiv) were placed in a 25 mL Schlenk tube under N_2 and stirred at 60 °C for 1 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1 to 3/2) yielded $[D]_n$-**167ba** (46.5 mg, 58%), $[D]_n$-**41b** (18.9 mg, 39%) and $[D]_n$-**166a** (27.0 mg, 43%). The D incorporation was determined by ^1H NMR spectroscopy.



$[D]_n$-167ba
($CDCl_3$, 600 MHz)

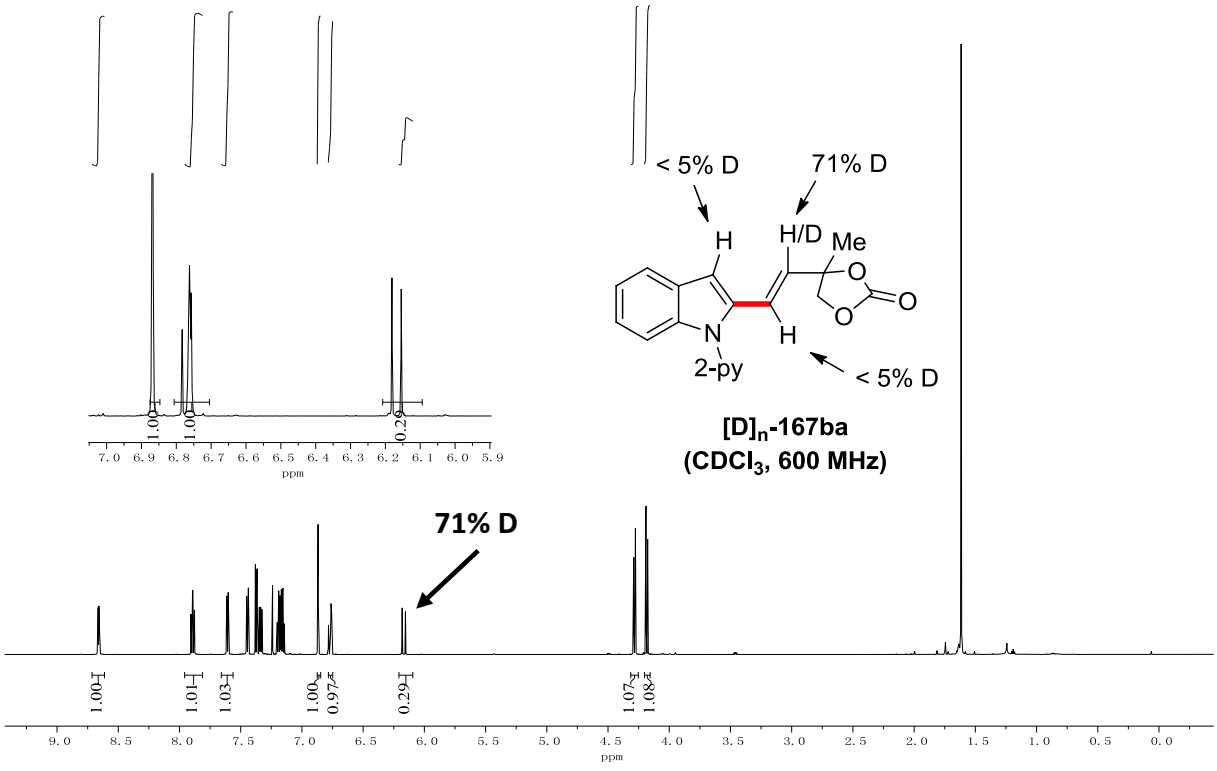


$[D]_n$-41b
($CDCl_3$, 600 MHz)



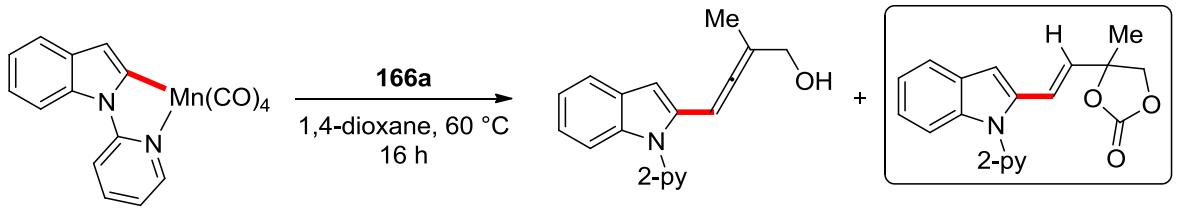
[D]$_n$-**41b** **166a** [D]$_n$-**167ba**: 86%

Substrates [D]$_1$-**41b** (48.8 mg, 0.25 mmol), **166a** (58 µL, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %), HOAc (2.8 µL, 20.0 mol%) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2 and stirred at 60 °C for 16 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded [D]$_n$-**167ba** (68.9 mg, 86%). The D incorporation was determined by ^{1}H-NMR spectroscopy.



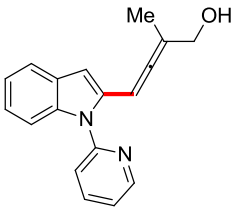
Synergistic hydroarylation with cyclometalated complex 195

a) Stoichiometric reaction without HOAc



195 **194**: 46% **167ba**: --

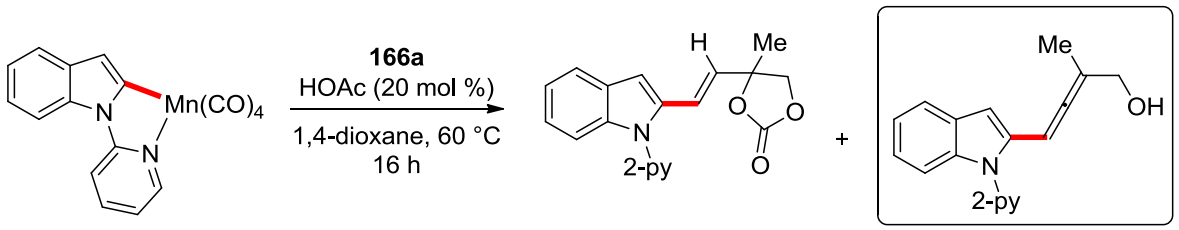
Complex **195** (36.0 mg, 0.10 mmol), 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**) (25.3 mg, 0.2 mmol) and 1,4-dioxane (0.5 mL) were placed in a 10 mL Schlenk tube under N_2 and stirred at 60 °C for 16 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **194** (32.0 mg, 46%) as colorless oil, the desired compound **167ba** was not detected by coupled gas chromatography-mass spectrometry.



2-Methyl-4-[1-(pyridin-2-yl)-1*H*-indol-2-yl]buta-2,3-dien-1-ol (194)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 4.1 Hz, 1H), 7.86 (td, *J* = 7.7, 1.5 Hz, 1H), 7.59–7.50 (m, 1H), 7.39 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.31 (ddd, *J* = 7.6, 4.8, 1.0 Hz, 1H), 7.24–7.16 (m, 1H), 7.15–7.02 (m, 2H), 6.63 (s, 1H), 6.42 (q, *J* = 3.1 Hz, 1H), 3.84 (s, 2H), 2.08 (brs, 1H), 1.51 (d, *J* = 3.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 201.4 (C_q), 151.5 (C_q), 149.6 (CH), 138.7 (C_q), 138.3 (CH), 133.2 (C_q), 128.4 (C_q), 122.6 (CH), 122.5 (CH), 122.1 (CH), 121.0 (CH), 120.2 (CH), 110.2 (CH), 104.4 (CH), 104.3 (C_q), 88.2 (CH), 63.6 (CH_2), 15.2 (CH_3). **IR** (ATR) ν = 3346, 2857, 1587, 1470, 1437, 1345, 1023, 780, 744 cm^{-1}. **MS** (ESI) m/z (relative intensity): 575 (100) $[2M+Na]^+$, 431 (10), 299 (60) $[M+Na]^+$, 276 (55) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{17}N_2O$ $[M+H]^+$: 277.1335, found: 277.1334.

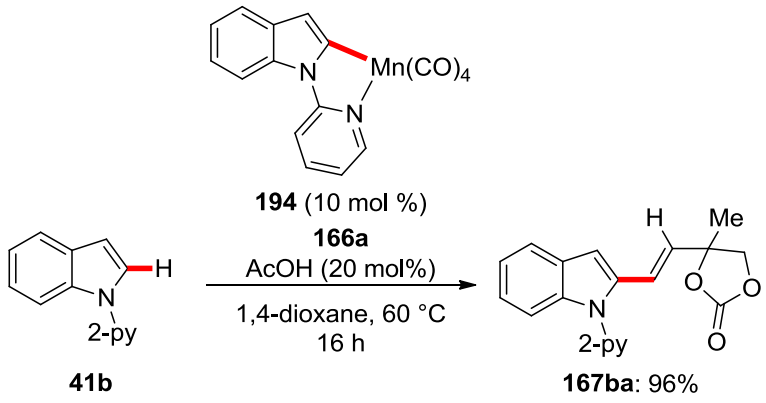
b) Stoichiometric reaction with HOAc



195 **167ba**: 48% **194**: --

Complex **195** (36.0 mg, 0.10 mmol), 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**) (25.3 mg, 0.2 mmol), HOAc (1.2 µL, 20.0 mol %) and 1,4-dioxane (0.5 mL) were placed in a 10 mL Schlenk tube under N_2 and stirred at 60 °C for 16 h. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ba** (38.5 mg, 48%), the allene **194** was not detected coupled gas chromatography-mass spectrometry.

c) Complex 195 as catalyst

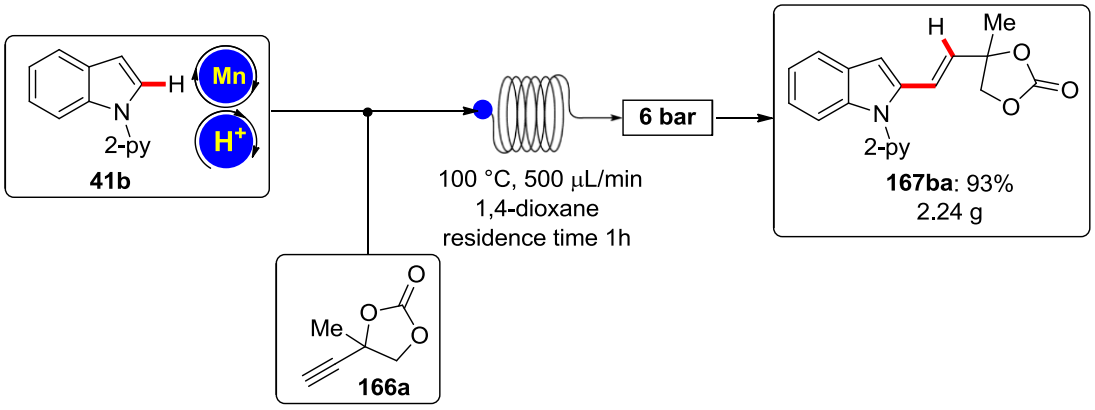


41b **167ba**: 96%

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**41b**) (46.6 mg, 0.24 mmol), 4-ethynyl-4-methyl-1,3-dioxolan-2-one (**166a**) (58.0 µL, 0.5 mmol), HOAc (2.8 µL, 20.0 mol %) and complex **195** (9.0 mg, 10.0 mol %). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **167ba** (76.9 mg, 96%) as colorless oil.

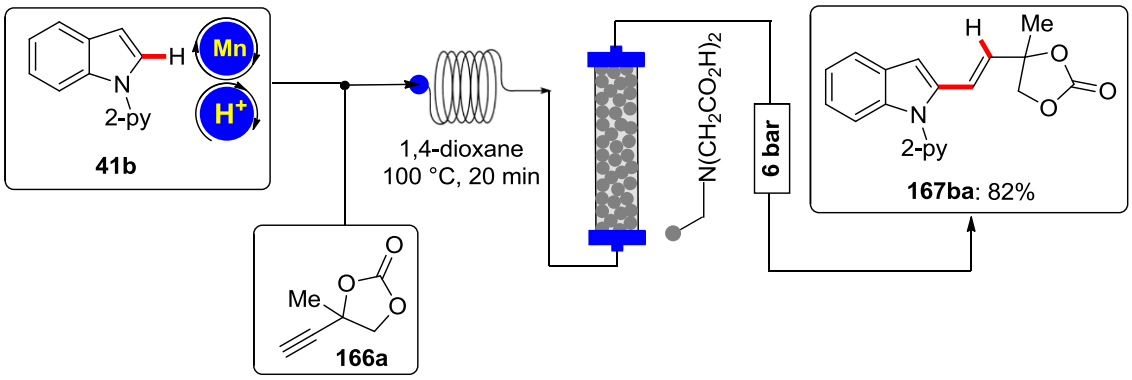
Evaluation of the Mxing Effect

a) Continuous Flow C–H Activation: On Scale



A solution of **41b** (7.5 mmol, 1.0 equiv), [$MnBr(CO)_5$] (206 mg, 10.0 mol %) and HOAc (85 µL, 20.0 mol %) in 1,4-dioxane was prepared in vial 1 and brought to a volume of 15 mL. A solution of **166a** (1.75 mL, 15 mmol) in dioxane was prepared in vial 2 and brought to a final volume of 15 mL. The solutions were taken into separate syringes and operated at a flow rate of 250 µL / min. The two solutions were mixed at a T-joint connection and subsequently reacted in a 10 mL reactor for 1 h residence time. Using the Flow Wizard system, the solution was collected automatically. Next, the mixture was concentrated in *vacuo*. Purification by column chromatography on silica gel yielded the desired product **167ba** (2.24 g mg, 93%).

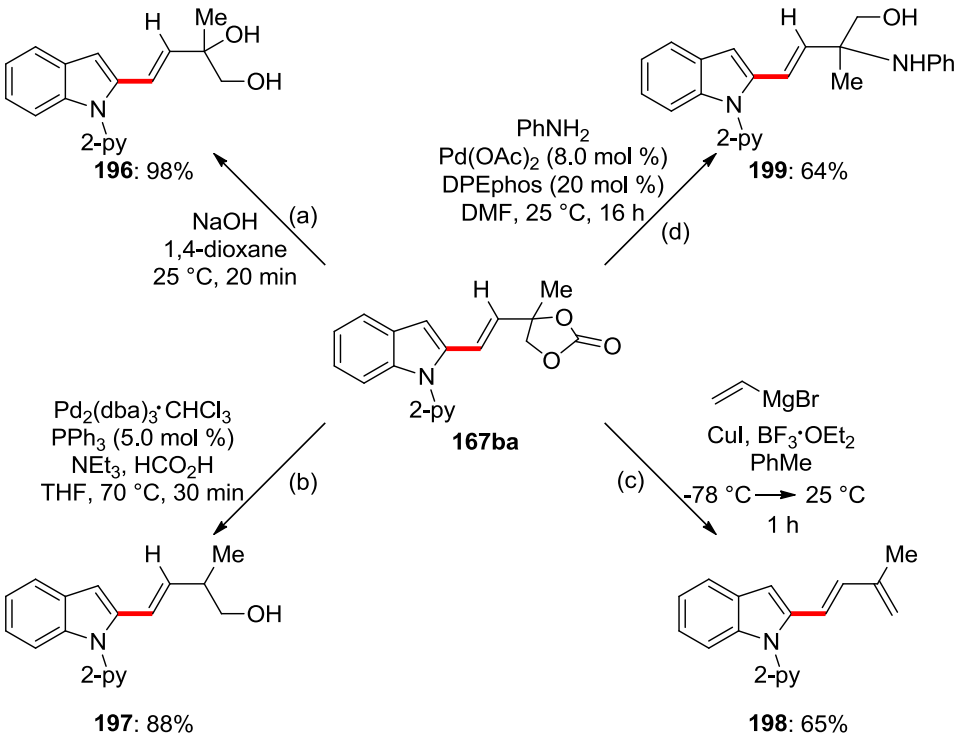
b) Continuous Flow C–H Activation: Catalyst Separation



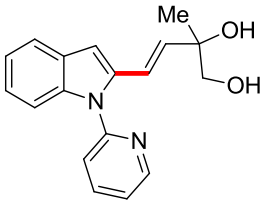
A solution of **41b** (0.50 mmol, 1.0 equiv), [$MnBr(CO)_5$] (13.8 mg, 10.0 mol %) and HOAc (5.6 µL, 20.0 mol %) in 1,4-dioxane was prepared in vial 1 and brought to a volume of 1.0 mL. A solution of **166a**

(116.0 µL, 1.0 mmol) in dioxane was prepared in vial 2 and brought to a final volume of 1.0 mL. The solutions were taken into separate syringes and operated at a flow rate of 250 µL / min and the two solutions were mixed at a T-joint connection. Subsequently, the reaction media was connected to the inlet of 10 mL standard heated reactor coupled with a column reactor (Ø = 8 mm) packed with 500 mg of QuadraPure® IDA (V = 2.5 mL). Using the Flow Wizard system, the solution was collected automatically. Next, the mixture was concentrated in *vacuo*. Purification by column chromatography on silica gel yielded the desired product **167ba** (132.0 mg, 82%).

Diversification of 167ba



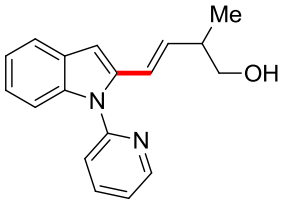
Reaction (a): The product **167ba** (64.1 mg, 0.20 mmol) was dissolved in 1,4-dioxane (2.0 mL), followed by NaOH (1 N, 2.0 mL). The resulting solution was allowed to stir for 30 min at 25 °C. The mixture was transferred into a round bottom flask with CH_2Cl_2 (20.0 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (EtOAc: 100%) afforded the desired products **196** (57.7 mg, 98%) as colorless oil.



(*E*)-2-Methyl-4-(1-(pyridin-2-yl)-1*H*-indol-2-yl)but-3-ene-1,2-diol (196)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.62 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.86 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), 7.66–7.52 (m, 1H), 7.45–7.37 (m, 2H), 7.30 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 7.19–7.10 (m, 2H), 6.76 (s, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 6.14 (d, *J* = 16.0 Hz, 1H), 3.50 (d, *J* = 11.1 Hz, 1H), 3.40 (d, *J* = 11.1 Hz, 1H), 2.58 (brs, 2H), 1.25 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 151.0 (C_q), 149.5 (CH), 138.4 (CH), 137.5 (C_q), 137.2 (C_q), 135.7 (CH), 128.5 (C_q), 122.8 (CH), 122.1 (CH), 121.4 (CH), 121.3 (CH), 120.5 (CH), 119.9 (CH), 110.6 (CH), 102.3 (CH), 73.5 (C_q), 69.8 (CH_2), 24.1 (CH_3). **IR** (ATR) *v* = 3352, 2929, 1587, 1451, 1436, 1347, 1347, 1044, 907, 780, 730 cm^{-1}. **MS** (ESI) m/z (relative intensity): 311 (100) $[M+Na]^+$, 295 (80) $[M+H]^+$, 277 (70). **HR-MS** (ESI) m/z calcd for $C_{18}H_{19}N_2O_2$ $[M+H]^+$: 295.1441, found: 295.1440.

Reaction (b): To **167ba** (64.1 mg, 0.20 mmol) in THF (10 mL) was added $Pd_2(dba)_3{\cdot}CHCl_3$ (10.2 mg, 5.0 mol %), PPh_3 (2.6 mg, 5.0 mol %), Et_3N (101.2 mg, 5.0 equiv) and HCO_2H (38.0 µL, 5.0 equiv). The reaction was stirred at 70 °C for 30 min. The reaction was then allowed to cool to 25 °C, diluted with Et_2O (10.0 mL) and filtered through a plug of silica gel. After concentration in *vacuo* the crude mixture was purified by silica gel column chromatography (*n*-hexane/EtOAc: 3/2) to yield **197** (49.0 mg, 88%) as colorless oil.

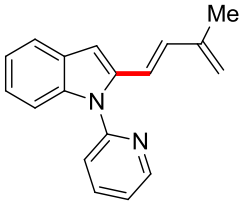


(*E*)-2-Methyl-4-[1-(pyridin-2-yl)-1*H*-indol-2-yl]but-3-en-1-ol (197)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.64 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.86 (ddd, *J* = 8.1, 7.5, 2.0 Hz, 1H), 7.65–7.53 (m, 1H), 7.48–7.37 (m, 2H), 7.30 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.17–7.10 (m, 2H), 6.76 (s, 1H), 6.41 (dt, *J* = 15.9, 1.0 Hz, 1H), 6.03 (dd, *J* = 15.9, 8.0 Hz, 1H), 3.51 (dd, *J* = 10.7, 5.5 Hz, 1H), 3.42 (dd, *J* = 10.7, 8.0 Hz, 1H), 2.44 (qdd, *J* = 8.0, 6.8, 5.5 Hz, 1H), 2.08 (brs, 1H), 1.02 (d, *J* = 6.8 Hz, 3H). **^{13}C**

NMR (100 MHz, $CDCl_3$) δ = 151.1 (C_q), 149.4 (CH), 138.3 (CH), 137.8 (C_q), 137.3 (C_q), 135.3 (CH), 128.6 (C_q), 122.5 (CH), 122.0 (CH), 121.3 (CH), 121.2 (CH), 121.2 (CH), 120.4 (CH), 110.5 (CH), 101.7 (CH), 67.1 (CH_2), 40.2 (CH), 16.1 (CH_3). **IR** (ATR) ν = 3364, 2868, 1586, 1468, 1451, 1344, 1026, 783, 744 cm^{-1}. **MS** (ESI) m/z (relative intensity): 301 (20) $[M+Na]^+$, 279 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{19}N_2O$ $[M+H]^+$: 279.1492, found: 279.1492.

Reaction (c): To a stirred solution of CuI (57.1 mg, 3.0 equiv) in dry THF (1 mL) at -78 °C under N_2 was added vinylmagnesium bromide (1.0 M in THF, 1.2 mL, 6.0 equiv) and $BF_3{\cdot}OEt_2$ (0.3 mL, 1.2 equiv). Then, **167ba** (64.1 mg, 0.20 mmol) in dry THF (0.5 mL) was added and the mixture was allowed to warm to 25 °C for 1 h. To the reaction mixture was added a saturated aqueous NH_4Cl solution (2.0 mL) and extracted with Et_2O (20.0 mL x 3). The organic layer was dried over Na_2SO_4 and evaporated in *vacuo*. Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **198** (34.0 mg, 65%) as colorless oil.

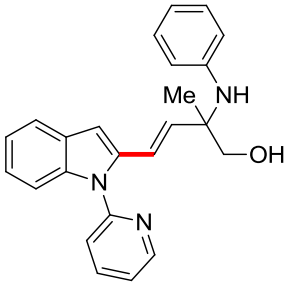


(*E*)-2-(3-Methylbuta-1,3-dien-1-yl)-1-(pyridin-2-yl)-1*H*-indole (198)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.69 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.86 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), 7.63–7.57 (m, 1H), 7.52–7.44 (m, 1H), 7.37 (dt, *J* = 8.0, 0.9 Hz, 1H), 7.32 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H), 7.19–7.10 (m, 2H), 6.88 (s, 1H), 6.87 (d, *J* = 16.1 Hz, 1H), 6.50 (d, *J* = 16.1 Hz, 1H), 5.08 (d, *J* = 2.1 Hz, 1H), 5.04 (d, *J* = 2.1 Hz, 1H), 1.83 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 151.3 (C_q), 149.5 (CH), 141.9 (C_q), 138.1 (CH), 138.0 (C_q), 137.8 (C_q), 133.6 (CH), 128.7 (C_q), 122.7 (CH), 122.0 (CH), 121.4 (CH), 121.2 (CH), 120.4 (CH), 118.4 (CH), 117.7 (CH_2), 110.8 (CH), 102.1 (CH), 18.3 (CH_3). **IR** (ATR) ν = 3051, 1585, 1467, 1450, 1435, 1335, 1213, 956, 784, 744 cm^{-1}. **MS** (ESI) m/z (relative intensity): 261 (100) $[M+H]^+$, 207 (30). **HR-MS** (ESI) m/z calcd for $C_{18}H_{17}N_2$ $[M+H]^+$: 261.1386, found: 261.1387.

Reaction (d): An oven-dired Schlenk tube, equipped with a stirring bar and a septum, was charged with **167ba** (64 mg, 0.2 mmol), $Pd(OAc)_2{\cdot}CHCl_3$ (3.6 mg, 8.0 mol%) and DPEPhos (21.5 mg, 40.0

mol %). Then, DMF (0.4 mL) and aniline (27.5 mg, 0.3 mmol) were added. The reaction mixture was stirred at 25 °C for 16 h. Then the mixture was transferred into a round bottom flask with CH_2Cl_2 (20.0 mL) and concentrated in vacuo. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **199** (47.8 mg, 64%) as colorless oil.

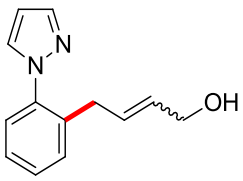


(*E*)-2-Methyl-2-(phenylamino)-4-[1-(pyridin-2-yl)-1*H*-indol-2-yl]but-3-en-1-ol (199)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.51 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.68–7.55 (m, 2H), 7.50–7.42 (m, 1H), 7.23–7.04 (m, 6H), 6.79 (s, 1H), 6.74–6.61 (m, 3H), 6.49 (d, *J* = 16.1 Hz, 1H), 6.19 (d, *J* = 16.1 Hz, 1H), 3.60 (d, *J* = 11.0 Hz, 1H), 3.50 (d, *J* = 11.0 Hz, 1H), 2.79 (brs, 1H), 1.40 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 150.9 (C_q), 149.3 (CH), 145.6 (C_q), 138.8 (C_q), 138.3 (CH), 137.3 (C_q), 134.3 (CH), 128.8 (CH), 128.6 (C_q), 122.8 (CH), 122.1 (CH), 121.8 (CH), 121.3 (CH), 121.1 (CH), 120.5 (CH), 117.7 (CH), 116.1 (CH), 110.9 (CH), 102.3 (CH), 69.5 (CH_2), 58.4 (C_q), 22.1 (CH_3). **IR** (ATR) *v* = 3500, 3052, 2928, 1600, 1468, 1452, 1348, 1051, 783, 747 cm^{-1}. **MS** (ESI) m/z (relative intensity): 383 (20) $[M+Na]^+$, 381 (100). **HR-MS** (ESI) m/z calcd for $C_{24}H_{23}N_3O$ $[M]^+$: 369.1836, found: 369.1828.

5.3.7 Data for the Products of Quinazolines by Cobalt(III)-Catalyzed C–H/N–O Functionalizations with Benzimidates

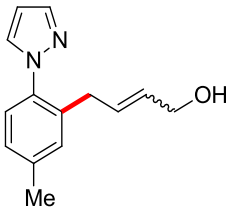
Characterization Data



4-[2-(1*H*-Pyrazol-1-yl)phenyl]but-2-en-1-ol (111aa): The general procedure **H** was followed using

2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111aa** (45.3 mg, 75%, *E*/*Z* = 4.9/1.0 by ^{1}H NMR) as a colorless oil.

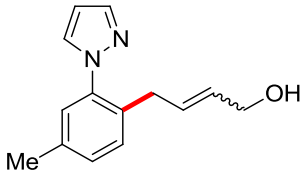
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 1.9, 0.7 Hz, 0.17H), 7.66 (dd, *J* = 1.9, 0.7 Hz, 0.83H), 7.57–7.49 (m, 1H), 7.40–7.16 (m, 4H), 6.40 (dd, *J* = 2.4, 1.9 Hz, 0.17H), 6.38 (dd, *J* = 2.4, 1.9 Hz, 0.83H), 5.58 (dtt, *J* = 15.4, 6.4, 1.4 Hz, 1H), 5.40 (dtt, *J* = 15.4, 5.6, 1.4 Hz, 1H), 3.97 (d, *J* = 5.8 Hz, 0.33H), 3.91 (d, *J* = 5.8 Hz, 1.67H), 3.30 (d, *J* = 5.8 Hz, 0.33H), 3.25 (d, *J* = 5.8 Hz, 1.67H), 2.68 (s, 0.17H), 2.57 (s, 0.83H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 140.2 (CH), 139.5 (C_q), 136.0 (C_q), 130.9 (CH), 130.9 (CH), 130.6 (CH), 129.7 (CH), 128.7 (CH), 127.0 (CH), 126.6 (CH), 106.2 (CH), 63.0 (CH_2), 34.3 (CH_2). *Minor isomer:* δ = 140.4 (CH), 139.3 (C_q), 136.5 (C_q), 130.9 (CH), 130.3 (CH), 130.0 (CH), 129.5 (CH), 128.9 (CH), 126.9 (CH), 126.6 (CH), 106.4 (CH), 58.0 (CH_2), 29.5 (CH_2). **IR** (ATR) *v* = 3347, 2855, 1517, 1395, 1328, 1100, 972, 916, 755, 597 cm^{-1}. **MS** (ESI) m/z (relative intensity): 237 (50) $[M+Na]^+$, 215 (30) $[M+H]^+$, 197 (100). **HR-MS** (ESI) m/z calcd for $C_{13}H_{15}N_2O$ $[M+H]^+$: 215.1179, found: 215.1181.



4-[5-Methyl-2-(1*H*-pyrazol-1-yl)phenyl]but-2-en-1-ol (111ba): The general procedure **H** was followed using 2-[5-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168b**) (54.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **111ba** (35.0 mg, 61%, *E*/*Z* = 5.3/1.0 by ^{1}H NMR) as a colorless oil.

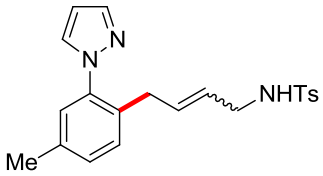
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 (d, *J* = 1.9 Hz, 0.16H), 7.66 (d, *J* = 1.9 Hz, 0.84H), 7.55–7.50 (m, 1H), 7.21–7.05 (m, 3H), 6.40 (t, *J* = 2.1 Hz, 0.16H), 6.38 (t, *J* = 2.1 Hz, 0.84H), 5.61 (dtt, *J* = 15.4, 6.5, 1.2 Hz, 1H), 5.45 (dtt, *J* = 15.4, 5.8, 1.4 Hz, 1H), 4.01 (d, *J* = 6.0 Hz, 0.31H), 3.97 (d, *J* = 6.0 Hz, 1.69H), 3.30 (dd, *J* = 6.8, 1.4 Hz, 0.31H), 3.25 (dd, *J* = 6.8, 1.4 Hz, 1.69H), 2.36 (s, 3H), 1.79 (brs, 0.16H), 1.71 (brs, 0.84H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 140.1 (CH), 138.7 (C_q), 137.2 (C_q), 135.7 (C_q), 131.1 (CH), 130.8 (CH), 130.5 (CH), 130.3 (CH), 127.7 (CH), 126.4 (CH), 106.0 (CH), 63.3 (CH_2),

34.3 (CH_2), 21.1 (CH_3). *Minor isomer:* δ = 140.3 (CH), 138.9 (C_q), 137.0 (C_q), 136.2 (C_q), 131.0 (CH), 130.9 (CH), 130.1 (CH), 129.5 (CH), 127.6 (CH), 126.5 (CH), 106.2 (CH), 58.0 (CH_2), 29.3 (CH_2), 21.1 (CH_3). **IR** (ATR) ν = 3352, 2918, 1518, 1395, 1101, 972, 945, 820, 753, 626 cm^{-1}. **MS** (ESI) m/z (relative intensity): 479 (100) $[2M+Na]^+$, 263 (40), 251 (100) $[M+Na]^+$, 229 (30) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{14}H_{18}N_2O$ $[M+H]^+$: 229.1335, found: 229.1334.



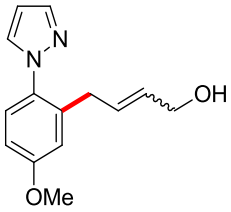
4-[4-Methyl-2-(1*H*-pyrazol-1-yl)phenyl]but-2-en-1-ol (111ca): The general procedure **H** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **111ca** (45.1 mg, 79%, *E*/*Z* = 5.2/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 (d, *J* = 1.9 Hz, 0.16H), 7.66 (d, *J* = 1.9 Hz, 0.84H), 7.55 (dd, *J* = 2.3, 0.6 Hz, 0.16H), 7.54 (dd, *J* = 2.3, 0.6 Hz, 0.84H), 7.21–7.07 (m, 3H), 6.41 (t, *J* = 1.9 Hz, 0.16H), 6.38 (t, *J* = 1.9 Hz, 0.84H), 5.59 (dtt, *J* = 15.3, 6.4, 1.4 Hz, 1H), 5.58 (dtt, *J* = 15.3, 5.7, 1.6 Hz, 1H), 4.00 (d, *J* = 6.8 Hz, 0.32H), 3.95 (dd, *J* = 6.8 Hz, 1.68H), 3.29 (d, *J* = 6.4 Hz, 0.32H), 3.25 (d, *J* = 6.4 Hz, 1.68H), 2.33 (s, 3H), 2.11 (brs, 0.16H), 1.85 (brs, 0.84H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 140.2 (CH), 139.4 (C_q), 137.0 (C_q), 132.6 (C_q), 130.7 (CH), 130.5 (CH), 130.4 (CH), 130.4 (CH), 129.4 (CH), 127.1 (CH), 106.1 (CH), 63.2 (CH_2), 33.9 (CH_2), 20.7 (CH_3). *Minor isomer:* δ = 140.3 (CH), 139.2 (C_q), 136.9 (C_q), 133.2 (C_q), 130.9 (CH), 130.2 (CH), 130.1 (CH), 129.6 (CH), 129.5 (CH), 127.2 (CH), 106.2 (CH), 57.9 (CH_2), 29.0 (CH_2), 20.7 (CH_3). **IR** (ATR) ν = 3356, 1516, 1392, 1327, 1191, 1100, 1041, 970, 752 cm^{-1}. **MS** (ESI) m/z (relative intensity): 479 (100) $[2M+Na]^+$, 251 (50) $[M+Na]^+$, 229 (30) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{14}H_{17}N_2O$ $[M+H]^+$: 229.1335, found: 229.1332.



4-Methyl-*N*-{4-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]but-2-en-1-yl}benzenesulfonamide (111cg): The general procedure **H** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 3-tosyl-5-vinyloxazolidin-2-one (**110g**) (133.7 mg, 0.50 mmol). Purification by column chromatography on silica gel (DCM: 100% → *n*-hexane/EtOAc: 2/1) yielded **111cg** (60.1 mg, 63%, *E*/*Z* = 4.6/1.0 by ^{1}H NMR) as a colorless oil.

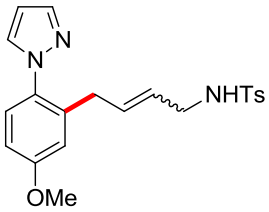
^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.74–7.58 (m, 3H), 7.49 (d, *J* = 2.4 Hz, 0.18H), 7.48 (d, *J* = 2.4 Hz, 0.82H), 7.29–7.22 (m, 2H), 7.13–7.03 (m, 3H), 6.37 (t, *J* = 2.1 Hz, 1H), 5.47 (dtt, *J* = 15.6, 6.3, 1.3 Hz, 0.82H), 5.40 (dtt, *J* = 10.7, 7.3, 1.2 Hz, 0.18H), 5.24 (dtt, *J* = 10.7, 6.9, 1.8 Hz, 0.18H), 5.13 (dtt, *J* = 15.6, 6.3, 1.6 Hz, 0.82H), 4.76 (t, *J* = 6.3 Hz, 0.18H), 4.56 (t, *J* = 6.3 Hz, 0.82H), 3.44 (t, *J* = 6.9 Hz, 0.34H), 3.39 (t, *J* = 6.6 Hz, 1.66H), 3.19 (d, *J* = 6.6 Hz, 0.34H), 3.16 (d, *J* = 6.6 Hz, 1.66H), 2.40 (s, 0.51H), 2.38 (s, 2.49H), 2.32 (s, 2.49H), 2.31 (s, 0.51H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 143.2 (C_q), 140.1 (CH), 139.3 (C_q), 137.1 (C_q), 136.9 (C_q), 132.3 (CH), 132.0 (C_q), 130.5 (CH), 130.3 (CH), 129.5 (CH), 129.3 (CH), 127.0 (CH), 127.0 (CH), 125.7 (CH), 106.1 (CH), 45.0 (CH_2), 34.0 (CH_2), 21.5 (CH_3), 20.8 (CH_3). *Minor isomer:* δ = 143.2 (C_q), 140.2 (CH), 139.1 (C_q), 137.0 (C_q), 137.0 (C_q), 132.5 (C_q), 131.8 (CH), 130.6 (CH), 130.0 (CH), 129.5 (CH), 129.5 (CH), 127.1 (CH), 127.0 (CH), 124.9 (CH), 106.2 (CH), 39.8 (CH_2), 29.1 (CH_2), 21.5 (CH_3), 20.8 (CH_3). **IR** (ATR) *v* = 3278, 1516, 1405, 1326, 1157, 1094, 1043, 911, 732, 663 cm^{-1}. **MS** (ESI) m/z (relative intensity): 785 (40) $[2M+Na]^+$, 404 (70) $[M+Na]^+$, 382 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{24}N_3O_2S$ $[M+H]^+$: 382.1584, found: 382.1582.



4-[5-Methoxy-2-(1*H*-pyrazol-1-yl)phenyl)but-2-en-1-ol (111da): The general procedure **H** was followed using 2-[5-methoxy-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168d**) (58.1 mg, 0.25 mmol)

and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **111da** (40.0 mg, 65%, *E*/*Z* = 3.8/1.0 by ^{1}H NMR) as a colorless oil.

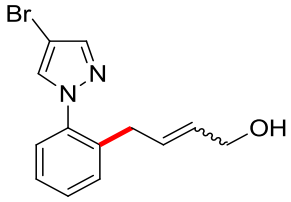
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.67 (dd, *J* = 1.9, 0.7 Hz, 0.21H), 7.65 (dd, *J* = 1.9, 0.7 Hz, 0.79H), 7.53–7.45 (m, 1H), 7.23–7.14 (m, 1H), 6.86–6.72 (m, 2H), 6.39 (dd, *J* = 2.3, 1.9 Hz, 0.21H), 6.37 (dd, *J* = 2.3, 1.9 Hz, 0.79H), 5.60 (dtt, *J* = 15.3, 6.5, 1.1 Hz, 1H), 5.45 (dtt, *J* = 15.3, 5.7, 1.3 Hz, 1H), 4.08–3.93 (m, 2H), 3.81 (s, 3H), 3.25 (dd, *J* = 6.8, 1.4 Hz, 0.42H), 3.20 (dd, *J* = 6.8, 1.4 Hz, 1.58H), 2.14 (s, 0.21H), 1.90 (s, 0.79H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 159.6 (C_q), 140.0 (CH), 137.8 (C_q), 132.9 (C_q), 131.1 (CH), 130.9 (CH), 129.7 (CH), 127.9 (CH), 115.7 (CH), 111.8 (CH), 105.9 (CH), 63.1 (CH_2), 55.5 (CH_3), 34.3 (CH_2). *Minor isomer:* δ = 159.7 (C_q), 140.2 (CH), 138.2 (C_q), 132.7 (C_q), 131.2 (CH), 130.0 (CH), 129.5 (CH), 127.9 (CH), 115.4 (CH), 111.8 (CH), 106.1 (CH), 57.8 (CH_2), 55.5 (CH_3), 29.4 (CH_2). **IR** (ATR) *v* = 3370, 2839, 1608, 1500, 1241, 1043, 756, 624 cm^{-1}. **MS** (ESI) m/z (relative intensity): 511 (100) $[2M+Na]^+$, 267 (60) $[M+Na]^+$, 245 (70) $[M+H]^+$, 227 (20). **HR-MS** (ESI) m/z calcd for $C_{14}H_{17}N_2O_2$ $[M+H]^+$: 245.1285, found: 245.1282.



***N*-{4-[5-Methoxy-2-(1*H*-pyrazol-1-yl)phenyl]but-2-en-1-yl}-4-methylbenzenesulfonamide (111dg)**: The general procedure **H** was followed using 2-[5-methoxy-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168d**) (58.1 mg, 0.25 mmol) and 3-tosyl-5-vinyloxazolidin-2-one (**110g**) (133.7 mg, 0.50 mmol). Purification by column chromatography on silica gel (Hexane/EtOAc/Et_3N: 3/1/0.3 → *n*-hexane/EtOAc: 1/1) yielded **111dg** (51.0 mg, 51%, *E*/*Z* = 5.3/1.0 by ^{1}H NMR) as a colorless oil.

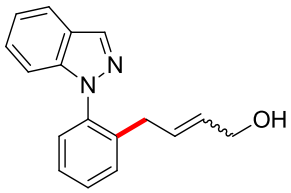
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.75–7.65 (m, 2H), 7.63 (d, *J* = 1.9 Hz, 0.84H), 7.59 (d, *J* = 1.9 Hz, 0.16H), 7.47–7.41 (m, 1H), 7.32–7.22 (m, 2H), 7.17 (d, *J* = 8.6 Hz, 0.84H), 7.13 (d, *J* = 8.6 Hz, 0.16H), 6.84–6.73 (m, 1.16H), 6.71 (d, *J* = 2.9 Hz, 0.84H), 6.36 (dd, *J* = 2.3, 1.8 Hz, 1H), 5.47 (dtt, *J* = 15.3, 6.6, 1.4 Hz, 1H), 5.27 (dtt, *J* = 10.5, 7.1, 1.7 Hz, 0.16H), 5.15 (dtt, *J* = 15.3, 6.3, 1.5 Hz, 0.84H), 4.72 (t, *J* = 6.0 Hz, 0.16H), 4.51 (t, *J* = 6.0 Hz, 0.84H), 3.80 (s, 3H), 3.45–3.37 (m, 2H), 3.19–3.08 (m, 2H), 2.40 (s, 0.52H), 2.38 (s, 2.48H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 159.6 (C_q), 143.3 (C_q), 140.1

(CH), 137.2 (C_q), 136.9 (C_q), 132.9 (C_q), 131.9 (CH), 131.0 (CH), 129.6 (CH), 127.9 (CH), 127.1 (CH), 126.2 (CH), 115.7 (CH), 111.9 (CH), 106.0 (CH), 55.5 (CH_3), 45.0 (CH_2), 34.4 (CH_2), 21.5 (CH_3). *Minor isomer:* δ = 159.7 (C_q), 143.4 (C_q), 140.2 (CH), 137.6 (C_q), 137.1 (C_q), 132.7 (C_q), 131.3 (CH), 131.1 (CH), 129.6 (CH), 127.9 (CH), 126.4 (CH), 125.4 (CH), 115.4 (CH), 111.9 (CH), 106.1 (CH), 65.8 (CH_3), 39.8 (CH_2), 29.5 (CH_2), 15.2 (CH_3). **IR** (ATR) ν = 3274, 2918, 1599, 1518, 1324, 1156, 1093, 1041, 813, 661 cm^{-1}. **MS** (ESI) m/z (relative intensity): 817 (10) $[2M+Na]^+$, 420 (20) $[M+Na]^+$, 398 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{24}N_3O_3S$ $[M+H]^+$: 398.1533, found: 398.1537.



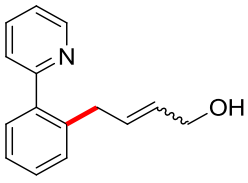
4-[2-(4-Bromo-1*H*-pyrazol-1-yl)phenyl]but-2-en-1-ol (111ea): The general procedure **H** was followed using 2-[2-(4-bromo-1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168e**) (70.3 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **111ea** (39.0 mg, 53%, *E*/*Z* = 5.9/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, *J* = 0.7 Hz, 0.15H), 7.64 (d, *J* = 0.7 Hz, 0.85H), 7.60 (d, *J* = 0.7 Hz, 0.15H), 7.59 (d, *J* = 0.7 Hz, 0.85H), 7.43–7.34 (m, 1H), 7.43–7.21 (m, 3H), 5.66 (dtt, *J* = 15.2, 6.5, 1.2 Hz, 1H), 5.49 (dtt, *J* = 15.2, 5.8, 1.5 Hz, 1H), 4.09 (d, *J* = 6.5 Hz, 0.29H), 4.02 (d, *J* = 6.5 Hz, 1.71H), 3.35 (dd, *J* = 6.5, 1.5 Hz, 0.29H), 3.31 (dd, *J* = 6.5, 1.5 Hz, 1.71H), 1.62 (brs, 0.15H), 1.41 (brs, 0.85H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 140. 9 (CH), 139.1 (C_q), 135.8 (C_q), 130.9 (CH), 130.8 (CH), 129.8 (CH), 129.8 (CH), 129.2 (CH), 127.3 (CH), 126.4 (CH), 94.5 (C_q), 63.3 (CH_2), 34.2 (CH_2). *Minor isomer:* δ = 141.0 (CH), 138.9 (C_q), 136.3 (C_q), 130.8 (CH), 130.5 (CH), 129.9 (CH), 129.8 (CH), 129.4 (CH), 127.2 (CH), 126.5 (CH), 94.3 (C_q), 58.2 (CH_2), 29.4 (CH_2). **IR** (ATR) ν = 3357, 2916, 1494, 1405, 1328, 954, 764, 614 cm^{-1}. **MS** (ESI) m/z (relative intensity): 317 (100) $[M+Na]^+$ (^{81}Br), 315 (100) $[M+Na]^+$ (^{79}Br), 295 (20) $[M+H]^+$ (^{81}Br), 293 (20) $[M+H]^+$ (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{13}H_{14}{}^{81}BrN_2O$ $[M+H]^+$: 295.0265, found: 295.0260; $C_{13}H_{14}{}^{79}BrN_2O$ $[M+H]^+$: 293.0284, found: 293.0280.



4-[2-(1*H*-Indazol-1-yl)phenyl]but-2-en-1-ol (111fa): The general procedure **H** was followed using 2-[2-(1*H*-indazol-1-yl)phenyl]propan-2-ol (**168f**) (63.1 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **111fa** (39.2 mg, 59%, *E*/*Z* = 4.6/1.0 by ^{1}H NMR) as a colorless oil.

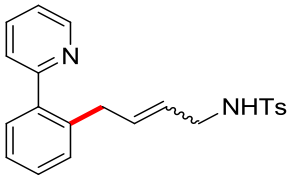
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 (d, *J* = 0.9 Hz, 0.18H), 8.18 (d, *J* = 0.9 Hz, 0.82H), 7.83–7.7 (m, 1H), 7.52–7.30 (m, 5H), 7.23–7.11 (m, 2H), 5.46 (dtt, *J* = 15.3, 6.7, 1.2 Hz, 1H), 5.43–5.38 (m, 0.18H), 5.20 (dtt, *J* = 15.3, 5.9, 1.4 Hz, 0.82H), 3.81 (d, *J* = 5.6 Hz, 0.36H), 3.75 (d, *J* = 5.6 Hz, 1.64H), 3.34–3.19 (m, 2H), 1.73 (brs, 0.18H), 1.13 (brs, 0.82H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 140.6 (C_q), 138.1 (C_q), 137.8 (C_q), 134.5 (CH), 130.9 (CH), 130.4 (CH), 129.8 (CH), 129.1 (CH), 127.8 (CH), 127.3 (CH), 126.8 (CH), 123.9 (C_q), 121.1 (CH), 121.0 (CH), 110.0 (CH), 63.2 (CH_2), 34.6 (CH_2). *Minor isomer:* δ = 140.6 (C_q), 138.2 (C_q), 137.6 (C_q), 134.6 (CH), 130.5 (CH), 129.7 (CH), 129.5 (CH), 129.2 (CH), 127.9 (CH), 127.2 (CH), 126.9 (CH), 123.9 (C_q), 121.2 (CH), 121.0 (CH), 110.0 (CH), 58.0 (CH_2), 29.5 (CH_2). **IR** (ATR) *v* = 3372, 2917, 1615, 1500, 1414, 1200, 984, 744 cm^{-1}. **MS** (ESI) m/z (relative intensity): 287 (100) $[M+Na]^+$, 265 (30) $[M+H]^+$, 247 (80). **HR-MS** (ESI) m/z calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1335, found: 265.1336.



4-[2-(Pyridin-2-yl)phenyl]but-2-en-1-ol (111ga): The general procedure **H** was followed using 2-[2-(pyridin-2-yl)phenyl]propan-2-ol (**168g**) (53.4 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **111ga** (47.9 mg, 85%, *E*/*Z* = 7.2/1.0 by ^{1}H NMR) as a colorless oil.

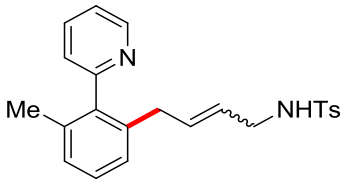
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.71–8.61 (m, 1H), 7.84–7.65 (m, 1H), 7.43–7.15 (m, 6H), 5.67 (dtt, *J* = 15.3, 6.6, 1.4 Hz, 0.87H), 5.61–5.54 (m, 0.26H), 5.40 (dtt, *J* = 15.3, 5.9, 1.6 Hz, 0.87H), 4.02–3.98 (m,

0.24H), 3.94 (dq, *J* = 5.9, 1.2 Hz, 1.76H), 3.53–3.48 (m, 0.24H), 3.45 (dt, *J* = 6.6, 1.2 Hz, 1.76H), 1.82 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 159.8 (C_q), 149.0 (CH), 140.3 (C_q), 137.7 (C_q), 136.2 (CH), 131.4 (CH), 130.1 (CH), 130.0 (CH), 129.8 (CH), 128.5 (CH), 126.3 (CH), 124.1 (CH), 121.8 (CH), 63.3 (CH_2), 35.9 (CH_2). *Minor isomer:* δ = 159.9 (C_q), 148.9 (CH), 140.0 (C_q), 138.2 (C_q), 136.5 (CH), 131.3 (CH), 130.0 (CH), 129.7 (CH), 129.0 (CH), 128.6 (CH), 126.3 (CH), 124.3 (CH), 121.8 (CH), 58.0 (CH_2), 31.1 (CH_2). **IR** (ATR) *v* = 3321, 2851, 1586, 1468, 1426, 1092, 972, 753 cm^{-1}. **MS** (ESI) m/z (relative intensity): 248 (100) $[M+Na]^+$, 226 (70) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{15}H_{16}NO$ $[M+H]^+$: 226.1226, found: 226.1226.



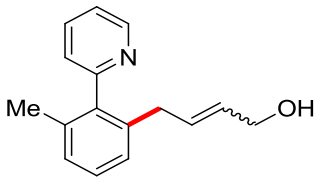
4-Methyl-*N*-[4-(2-(pyridin-2-yl)phenyl)but-2-en-1-yl)benzenesulfonamide (111gg): The general procedure **H** was followed using 2-[2-(pyridin-2-yl)phenyl]propan-2-ol (**168g**) (53.4 mg, 0.25 mmol) and 3-tosyl-5-vinyloxazolidin-2-one (**110g**) (133.7 mg, 0.50 mmol). Purification by column chromatography on silica gel (Hexane/EtOAc/Et_3N: 3/1/0.3) yielded **111gg** (81.4 mg, 86%, *E*/*Z* = 3.2/1.0 by ^{1}H NMR) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.68–8.52 (m, 1H), 7.85–7.61 (m, 3H), 7.43–7.09 (m, 8H), 5.09 (dtt, *J* = 15.2, 6.3, 1.5 Hz, 1H), 5.21 (dtt, *J* = 10.4, 7.0, 1.5 Hz, 0.24H), 5.53 (dtt, *J* = 15.2, 6.7, 1.3 Hz, 0.76H), 4.99 (t, *J* = 6.0 Hz, 0.24H), 4.59 (t, *J* = 6.0 Hz, 0.76H), 3.65–3.26 (m, 4H), 2.39 (s, 0.71H), 2.38 (s, 2.29H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 159.6 (C_q), 148.9 (CH), 143.1 (C_q), 140.2 (C_q), 137.2 (C_q), 136.9 (C_q), 136.1 (CH), 133.3 (CH), 129.9 (CH), 129.7 (CH), 129.5 (CH), 128.3 (CH), 127.0 (CH), 126.3 (CH), 125.5 (CH), 124.0 (CH), 121.7 (CH), 45.1 (CH_2), 35.9 (CH_2), 21.5 (CH_3). *Minor isomer:* δ = 159.7 (C_q), 148.9 (CH), 143.1 (C_q), 140.0 (C_q), 137.6 (C_q), 137.1 (C_q), 136.4 (CH), 132.7 (CH), 129.9 (CH), 129.6 (CH), 129.5 (CH), 128.5 (CH), 127.0 (CH), 126.3 (CH), 124.5 (CH), 124.1 (CH), 121.8 (CH), 39.9 (CH_2), 31.2 (CH_2), 21.5 (CH_3). **IR** (ATR) *v* = 3274, 2922, 1587, 1426, 1325, 1156, 1093, 754, 661, 550 cm^{-1}. **MS** (ESI) m/z (relative intensity): 779 (10) $[2M+Na]^+$, 401 (40) $[M+Na]^+$, 379 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{22}H_{22}N_2O_2S$ $[M+H]^+$: 379.1475, found: 379.1478.



4-Methyl-*N*-{4-[3-methyl-2-(pyridin-2-yl)phenyl]but-2-en-1-yl}benzenesulfon-amide (111hg): The general procedure **H** was followed using 2-[3-methyl-2-(pyridin-2-yl)phenyl]propan-2-ol (**168h**) (56.8 mg, 0.25 mmol) and 3-tosyl-5-vinyloxazolidin-2-one (**110g**) (133.7 mg, 0.50 mmol). Purification by column chromatography on silica gel (Hexane/EtOAc/Et_3N: 3/1/0.3) yielded **111hg** (55.0 mg, 56%, *E*/*Z* = 2.8/1.0 by ^{1}H NMR) as a colorless oil.

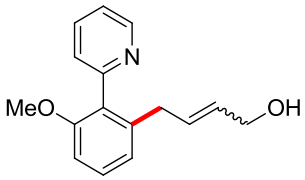
^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.06–8.55 (m, 1H), 7.72 (td, *J* = 7.7, 1.8 Hz, 1H), 7.68–7.60 (m, 2H), 7.35–7.13 (m, 5H), 7.13–7.03 (m, 1H), 7.03–6.93 (m, 1H), 5.45 (dtt, *J* = 15.3, 6.9, 1.3 Hz, 1H), 5.16 (dtt, *J* = 10.6, 7.1, 1.7 Hz, 0.26H), 4.98 (dtt, *J* = 15.3, 6.4, 1.5 Hz, 0.74H), 4.89 (t, *J* = 6.0 Hz, 0.26H), 4.59 (t, *J* = 6.0 Hz, 0.74H), 3.35 (t, *J* = 6.0 Hz, 1.47H), 3.25 (t, *J* = 6.0 Hz, 0.53H), 3.06–2.95 (m, 2H), 2.40 (s, 0.79H), 2.38 (s, 2.21H), 1.99 (s, 2.21H), 1.97 (s, 0.79H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 159.1 (C_q), 149.4 (CH), 143.1 (C_q), 140.1 (C_q), 137.1 (C_q), 136.9 (C_q), 136.1 (C_q), 136.1 (CH), 133.1 (CH), 129.5 (CH), 128.1 (CH), 128.0 (CH), 127.0 (CH), 126.8 (CH), 125.3 (CH), 124.6 (CH), 121.8 (CH), 45.1 (CH_2), 36.5 (CH_2), 21.5 (CH_3), 20.3 (CH_3). *Minor isomer:* δ = 159.1 (C_q), 149.5 (CH), 143.1 (C_q), 139.9 (C_q), 137.4 (C_q), 137.1 (C_q), 136.2 (CH), 136.1 (C_q), 132.4 (CH), 129.5 (CH), 128.2 (CH), 128.0 (CH), 126.9 (CH), 126.5 (CH), 124.7 (CH), 124.3 (CH), 121.8 (CH), 39.7 (CH_2), 31.7 (CH_2), 21.5 (CH_3), 20.3 (CH_3). **IR** (ATR) *v* = 3275, 3063, 1570, 1459, 1324, 1155, 1092, 970, 660 cm^{-1}. **MS** (ESI) m/z (relative intensity): 415 (20) $[M+Na]^+$, 393 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{24}N_2O_2S$ $[M+H]^+$: 393.1631, found: 393.1634.



4-[3-Methyl-2-(pyridin-2-yl)phenyl]but-2-en-1-ol (111ha): The general procedure **H** was followed using 2-[3-methyl-2-(pyridin-2-yl)phenyl]propan-2-ol (**168h**) (56.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on

silica gel (*n*-hexane/EtOAc: 1/3) yielded **111ha** (44.9 mg, 75%, *E*/*Z* = 3.3/1.0 by ^{1}H NMR) as a colorless oil.

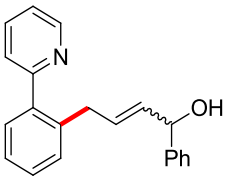
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.72–8.64 (m, 1H), 8.79–8.69 (m, 1H), 7.34–7.18 (m, 3H), 7.15–7.04 (m, 2H), 5.53 (dtt, *J* = 15.2, 6.6, 1.4 Hz, 0.77H), 5.52–5.43 (m, 0.46H), 5.09 (dtt, *J* = 15.2, 6.6, 1.4 Hz, 0.77H), 3.91 (ddd, *J* = 5.8, 1.1, 1.1 Hz, 1.53H), 3.83 (d, *J* = 5.8 Hz, 0.47H), 3.15–3.00 (m, 2H), 2.06 (brs, 1H), 2.01 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 159.2 (C_q), 149.3 (CH), 140.0 (C_q), 137.7 (C_q), 136.1 (CH), 136.0 (C_q), 131.1 (CH), 129.9 (CH), 128.1 (CH), 128.0 (CH), 126.8 (CH), 124.7 (CH), 121.8 (CH), 63.3 (CH_2), 36.6 (CH_2), 20.3 (CH_3). *Minor isomer:* δ = 159.3 (C_q), 149.5 (CH), 139.9 (C_q), 137.9 (C_q), 136.2 (CH), 136.1 (C_q), 130.8 (CH), 128.8 (CH), 128.2 (CH), 128.0 (CH), 126.5 (CH), 124.8 (CH), 121.8 (CH), 58.0 (CH_2), 31.7 (CH_2), 20.3 (CH_3). **IR** (ATR) *v* = 3306, 2917, 1720, 1585, 1459, 1424, 970, 751 cm^{-1}. **MS** (ESI) m/z (relative intensity): 501 (50) $[2M+Na]^+$, 262 (45) $[M+Na]^+$, 240 (100) $[M+H]^+$, 222 (30). **HR-MS** (ESI) m/z calcd for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1383, found: 240.1383.



4-[3-Methoxy-2-(pyridin-2-yl)phenyl]but-2-en-1-ol (111ia): The general procedure **H** was followed using 2-[3-methoxy-2-(pyridin-2-yl)phenyl]propan-2-ol (**168i**) (60.8 mg, 0.25 mmol) and 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol). Purification by column chromatography on silica gel (Hexane/EtOAc/Et_3N: 3/1/0.3) yielded **111ia** (37.0 mg, 58%, *E*/*Z* = 4.1/1.0 by ^{1}H NMR) as a colorless oil.

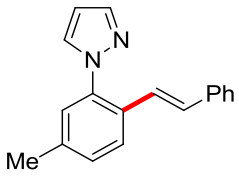
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.72–8.58 (m, 1H), 7.76–7.62 (m, 1H), 7.44–7.12 (m, 3H), 6.97–6.74 (m, 2H), 5.53 (dtt, *J* = 15.2, 6.8, 1.5 Hz, 0.82H), 5.50–5.45 (m, 0.36H), 5.29 (dtt, *J* = 15.2, 5.8, 1.3 Hz, 0.82H), 3.88 (dq, *J* = 5.9, 1.1 Hz, 1.62H), 3.84 (dq, *J* = 5.9, 1.1 Hz, 0.38H), 3.67 (s, 3H), 3.16 (d, *J* = 6.2 Hz, 0.38H), 3.12 (d, *J* = 6.2 Hz, 1.62H), 2.38 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 156.9 (C_q), 156.5 (C_q), 149.0 (CH), 139.7 (C_q), 135.6 (CH), 130.7 (CH), 130.0 (CH), 129.5 (C_q), 129.1 (CH), 125.8 (CH), 121.8 (CH), 121.7 (CH), 108.9 (CH), 63.2 (CH_2), 55.8 (CH_3), 36.1 (CH_2). *Minor isomer:* δ = 156.9 (C_q), 156.5 (C_q), 149.1 (CH), 140.0 (C_q), 135.8 (CH), 130.5 (CH), 129.5 (C_q), 129.2 (CH), 129.0 (CH), 126.0 (CH), 121.7 (CH), 121.5 (CH), 108.9 (CH), 63.2 (CH_2), 57.8 (CH_3), 31.2 (CH_2). **IR** (ATR)

v = 3306, 2835, 1579, 1466, 1255, 1061, 971, 780, 745 cm^{-1}. **MS** (ESI) m/z (relative intensity): 533 (40) $[2M+Na]^+$, 278 (30) $[M+Na]^+$, 272 (40), 256 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{18}NO_2$ $[M+H]^+$: 256.1332, found: 256.1334.



1-Phenyl-4-[2-(pyridin-2-yl)phenyl]but-2-en-1-ol (111jb): The general procedure **H** was followed using phenyl [2-(pyridin-2-yl)phenyl]methanol (**168j**) (65.3 mg, 0.25 mmol) and (*trans*)-4-phenyl-5-vinyl-1,3-dioxolan-2-one (**110b**) (95.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/1) yielded **111jb** (56.7 mg, 75%, *E*/*Z* = 1.5/1.0 by ^{1}H NMR) as a colorless oil.

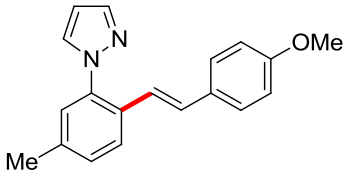
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 0.4H), 8.61 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 0.6H), 7.73 (td, *J* = 7.7, 1.8 Hz, 0.4H), 7.62 (td, *J* = 7.7, 1.8 Hz, 0.6H), 7.44–7.13 (m, 11H), 5.73 (dtd, *J* = 15.2, 6.6, 1.1 Hz, 0.6H), 5.67–5.56 (m, 0.8H), 5.40 (ddt, *J* = 15.2, 7.0, 1.5 Hz, 1H), 5.01 (d, *J* = 6.9 Hz, 0.6H), 3.85–3.73 (m, 0.4H), 3.57–3.44 (m, 1.6H), 2.45 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) *Major isomer:* δ = 159.6 (C_q), 148.9 (CH), 143.1 (C_q), 140.3 (C_q), 137.6 (C_q), 136.2 (CH), 133.5 (CH), 130.8 (CH), 130.1 (CH), 129.8 (CH), 128.5 (CH), 128.3 (CH), 127.3 (CH), 126.4 (CH), 126.1 (CH), 124.1 (CH), 121.7 (CH), 74.7 (CH), 36.0 (CH_2). *Minor isomer:* δ = 159.9 (C_q), 148.9 (CH), 143.5 (C_q), 140.0 (C_q), 138.1 (C_q), 136.6 (CH), 132.7 (CH), 130.4 (CH), 130.0 (CH), 129.8 (CH), 128.7 (CH), 128.4 (CH), 127.2 (CH), 126.3 (CH), 125.9 (CH), 124.4 (CH), 121.9 (CH), 69.0 (CH), 31.4 (CH_2). **IR** (ATR) *v* = 3311, 3024, 1586, 1468, 1443, 1023, 969, 750, 699 cm^{-1}. **MS** (ESI) m/z (relative intensity): 625 (30) $[2M+Na]^+$, 324 (20) $[M+Na]^+$, 318 (40), 302 (45) $[M+H]^+$, 300 (70), 284 (100). **HR-MS** (ESI) m/z calcd for $C_{21}H_{20}NO$ $[M+H]^+$: 302.1539, found: 302.1540.



(*E*)-1-(5-Methyl-2-styrylphenyl)-1*H*-pyrazole (74co): The general procedure **I** was followed using phenyl 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and ethynylbenzene (**8o**) (51.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74co** (45.0 mg, 69%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 1.8 Hz, 1H), 7.67–7.58 (m, 2H), 7.47–7.34 (m, 2H), 7.34–7.13 (m, 5H), 7.00 (d, *J* = 16.3 Hz, 1H), 6.90 (d, *J* = 16.3 Hz, 1H), 6.45 (d, *J* = 2.1 Hz, 1H), 2.39 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 140.5 (CH), 138.5 (C_q), 138.3 (C_q), 137.1 (C_q), 131.4 (CH), 130.3 (C_q), 129.9 (CH), 129.1 (CH), 128.5 (CH), 127.6 (CH), 126.8 (CH), 126.5 (CH), 126.3 (CH), 123.8 (CH), 106.4 (CH), 21.1 (CH_3). **IR** (ATR) *v* = 3024, 1515, 1449, 1391, 1097, 1042, 951, 813, 753, 691 cm^{-1}. **MS** (ESI) m/z (relative intensity): 283 (70) $[M+Na]^+$, 261 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{17}N_2$ $[M+H]^+$: 261.1386, found: 261.1385.

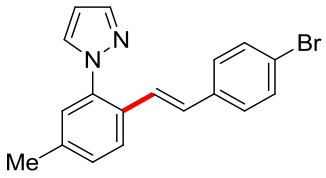
The analytical data were in accordance with those reported in the literature.[202]



(*E*)-1-[2-(4-Methoxystyryl)-5-methylphenyl]-1*H*-pyrazole (74cq): The general procedure **I** was followed using phenyl2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 1-ethynyl-4-methoxybenzene (**8q**) (66.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **74cq** (43.0 mg, 59%) as a white solid.

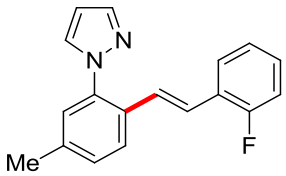
M.p. = 70–72 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 1.8 Hz, 1H), 7.66–7.57 (m, 2H), 7.35–7.27 (m, 2H), 7.26–7.14 (m, 2H), 6.94 (d, *J* = 16.3 Hz, 1H), 6.88–6.80 (m, 2H), 6.75 (d, *J* = 16.3 Hz, 1H), 6.44 (dd, *J* = 2.4, 1.8 Hz, 1H), 3.79 (s, 3H), 2.38 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 159.3 (C_q), 140.4 (CH), 138.3 (C_q), 137.9 (C_q), 131.4 (CH), 130.3 (C_q), 130.0 (C_q), 129.8 (CH), 129.1 (CH), 127.7 (CH), 126.7 (CH), 126.1 (CH), 121.6 (CH), 114.0 (CH), 106.3 (CH), 55.3 (CH_3), 21.0 (CH_3). **IR** (ATR) *v* = 2916, 1603, 1511, 1457, 1248, 1174, 1033, 951, 826, 754 cm^{-1}. **MS** (ESI) m/z (relative intensity): 313

(100) $[M+Na]^+$, 291 (50) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{19}N_2O$ $[M+H]^+$: 291.1492, found: 291.1491.



(*E*)-1-[2-(4-Bromostyryl)-5-methylphenyl]-1*H*-pyrazole (74cr): The general procedure **I** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 1-bromo-4-ethynylbenzene (**8r**) (90.5 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74cr** (61.1 mg, 72%) as a colorless oil.

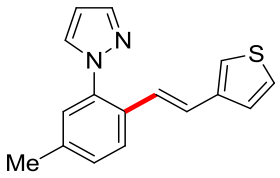
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 (s, 1H), 7.67–7.54 (m, 2H), 7.45–7.37 (m, 2H), 7.27–7.18 (m, 4H), 6.92 (d, J = 16.3 Hz, 1H), 6.86 (d, J = 16.3 Hz, 1H), 6.45 (d, J = 2.1 Hz, 1H), 2.39 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 140.6 (C_q), 138.6 (C_q), 138.5 (C_q), 136.0 (CH), 131.6 (CH), 131.3 (CH), 129.6 (C_q), 129.1 (CH), 128.8 (CH), 127.9 (CH), 126.8 (CH), 126.2 (CH), 124.5 (CH), 121.3 (C_q), 106.5 (CH), 21.0 (CH_3). **IR** (ATR) ν = 3026, 2918, 1613, 1515, 1485, 1390, 1191, 1071, 950, 750 cm^{-1}. **MS** (ESI) m/z (relative intensity): 363 (30) $[M+Na]^+$ (^{81}Br), 361 (30) $[M+Na]^+$ (^{79}Br), 341 (100) $[M+H]^+$ (^{81}Br), 339 (100) $[M+H]^+$ (^{79}Br). **HR-MS** (ESI) m/z calcd for $C_{18}H_{16}N_2{}^{81}Br$ $[M+H]^+$: 341.0472, found: 341.0474, $C_{18}H_{16}N_2{}^{79}Br$ $[M+H]^+$: 339.0491, found: 339.0491.



(*E*)-1-[2-(2-Fluorostyryl)-5-methylphenyl]-1*H*-pyrazole (74cs): The general procedure **I** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 1-ethynyl-2-fluorobenzene (**8s**) (60.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74cs** (60.5 mg, 87%) as a colorless oil.

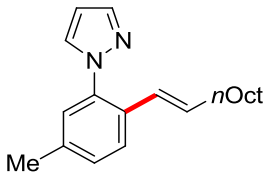
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.68 (s, 1H), 7.63–7.53 (m, 2H), 7.33 (td, J = 7.7, 1.7 Hz, 1H), 7.22–7.07 (m, 4H), 7.01–6.87 (m, 3H), 6.38 (s, 1H), 2.32 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 160.3 (d, $^1J_{C\text{-}F}$ = 251.3 Hz, C_q), 138.8 (C_q), 138.7 (C_q), 129.8 (C_q), 125.1 (d, $^2J_{C\text{-}F}$ = 12.0 Hz, C_q), 129.2 (CH), 129.2 (CH),

128.9 (d, $^{3}J_{C\text{-}F}$ = 8.4 Hz, CH), 126.9 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz, CH), 126.7 (CH), 126.4 (CH), 126.4 (CH), 125.9 (d, $^{3}J_{C\text{-}F}$ = 4.8 Hz, CH), 124.1 (d, $^{4}J_{C\text{-}F}$ = 3.7 Hz, CH), 122.2 (d, $^{3}J_{C\text{-}F}$ = 3.8 Hz, CH), 115.6 (d, $^{2}J_{C\text{-}F}$ = 22.2 Hz, CH), 106.5 (CH), 20.9 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -118.13 (ddd, J = 10.8, 7.7, 5.3 Hz). **IR** (ATR) ν = 3065, 1615, 1516, 1455, 1230, 1095, 1038, 950, 751 cm^{-1}. **MS** (ESI) m/z (relative intensity): 301 (30) $[M+Na]^+$, 279 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{16}N_2F$ $[M+H]^+$: 279.1292, found: 279.1293.



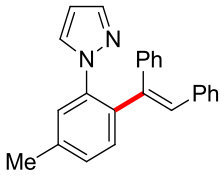
(*E*)-1-{5-Methyl-2-[2-(thiophen-3-yl)vinyl]phenyl}-1*H*-pyrazole (74ct): The general procedure **I** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 3-ethynylthiophene (**8t**) (54.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74ct** (40.2 mg, 60%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75 (s, 1H), 7.63 (d, J = 2.3 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.28–7.17 (m, 4H), 7.14 (dd, J = 5.0, 1.3 Hz, 1H), 7.00 (d, J = 16.2 Hz, 1H), 6.73 (d, J = 16.2 Hz, 1H), 6.44 (d, J = 2.3, 1.8 Hz, 1H), 2.38 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 140.6 (CH), 140.1 (C_q), 138.5 (C_q), 138.3 (C_q), 131.5 (CH), 130.1 (C_q), 129.3 (CH), 126.9 (CH), 126.2 (CH), 126.1 (CH), 125.0 (CH), 124.5 (CH), 123.9 (CH), 122.7 (CH), 106.5 (CH), 21.2 (CH_3). **IR** (ATR) ν = 3104, 2918, 1677, 1517, 1401, 1044, 951, 755, 623 cm^{-1}. **MS** (ESI) m/z (relative intensity): 289 (20) $[M+Na]^+$, 267 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{15}N_2S$ $[M+H]^+$: 267.0950, found: 267.0949.



(*E*)-1-[2-(*dec*-1-En-1-yl)-5-methylphenyl]-1*H*-pyrazole (74cu): The general procedure **I** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and dec-1-yne (**8u**) (69.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74cu** (39.5 mg, 56%) as a colorless oil.

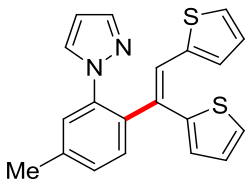
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 (d, *J* = 2.2 Hz, 1H), 7.53 (d, *J* = 2.2 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.14 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.36 (t, *J* = 2.1 Hz, 1H), 6.09 (d, *J* = 15.7 Hz, 1H), 6.08–6.03 (m, 1H), 2.29 (s, 3H), 2.05 (td, *J* = 7.3, 5.4 Hz, 2H), 1.51 (s, 1H), 1.33 (t, *J* = 7.3 Hz, 2H), 1.28–1.07 (m, 9H), 0.80 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 140.3 (CH), 137.8 (C_q), 137.4 (C_q), 133.2 (CH), 131.3 (CH), 130.5 (C_q), 129.0 (CH), 126.7 (CH), 126.5 (CH), 124.8 (CH), 106.1 (CH), 33.1 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 22.6 (CH_2), 20.8 (CH_3), 14.0 (CH_3). **IR** (ATR) *v* = 2923, 2853, 1517, 1457, 1042, 950, 748, 624 cm^{-1}. **MS** (ESI) m/z (relative intensity): 319 (20) $[M+Na]^+$, 297 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{29}N_2$ $[M+H]^+$: 297.2325, found: 297.2328.



(*E*)-1-[2-(1,2-Diphenylvinyl)-5-methylphenyl]-1*H*-pyrazole (74ca): The general procedure **I** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 1,2-diphenylethyne (**8a**) (89.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74ca** (60.6 mg, 72%) as a colorless oil.

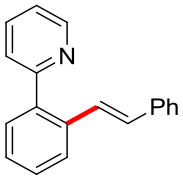
^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.40 (d, *J* = 2.4 Hz, 1H), 7.34 (d, *J* = 1.8 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 1.3 Hz, 1H), 7.12 (dd, *J* = 7.7, 1.8, Hz, 1H), 7.04–6.91 (m, 8H), 6.89–6.84 (m, 2H), 6.54 (s, 1H), 6.02 (dd, *J* = 2.4, 1.8 Hz, 1H), 2.32 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 140.0 (CH), 139.9 (C_q), 139.2 (C_q), 139.0 (C_q), 138.6 (C_q), 137.2 (C_q), 137.0 (C_q), 131.5 (CH), 130.8 (CH), 130.6 (CH), 129.6 (CH), 129.3 (CH), 128.8 (CH), 127.9 (CH), 127.8 (CH), 127.2 (CH), 127.1 (CH), 126.8 (CH), 106.2 (CH), 21.1 (CH_3). **IR** (ATR) *v* = 3022, 1517, 1445, 1400, 1100, 952, 826, 747, 695 cm^{-1}. **MS** (ESI) m/z (relative intensity): 359 (10) $[M+Na]^+$, 337 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{24}H_{21}N_2$ $[M+H]^+$: 337.1699, found: 337.1700.

The analytical data were in accordance with those reported in the literature.[203]



(*Z*)-1-{2-[1,2-Di(thiophen-2-yl)vinyl]-5-methylphenyl}-1*H*-pyrazole (74cj): The general procedure **I** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 1,2-di(thiophen-2-yl)ethyne (**8j**) (95.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74cj** (47.1 mg, 54%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 (d, *J* = 1.8 Hz, 1H), 7.56 (dd, *J* = 2.4 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.31–7.27 (m, 2H), 7.20 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.11 (dd, *J* = 5.0, 1.2 Hz, 1H), 6.92–6.86 (m, 3H), 6.83 (dd, *J* = 3.5, 1.2 Hz, 1H), 6.68 (s, 1H), 6.26 (dd, *J* = 2.4, 1.8 Hz, 1H), 2.40 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 140.4 (C_q), 140.1 (C_q), 140.0 (CH), 139.0 (C_q), 138.7 (C_q), 135.9 (C_q), 131.0 (CH), 130.7 (CH), 130.3 (C_q), 129.7 (CH), 129.0 (CH), 128.6 (CH), 127.5 (CH), 127.0 (CH), 126.6 (CH), 126.5 (CH), 126.4 (CH), 121.5 (CH), 106.7 (CH), 21.1 (CH_3). **IR** (ATR) *v* = 3098, 1518, 1400, 1036, 950, 841, 750, 699 cm^{-1}. **MS** (ESI) m/z (relative intensity): 371 (30) $[M+Na]^+$, 349 (100) $[M+H]^+$, 252 (10). **HR-MS** (ESI) m/z calcd for $C_{20}H_{17}N_2S_2$ $[M+H]^+$: 349.0828, found: 349.0831.

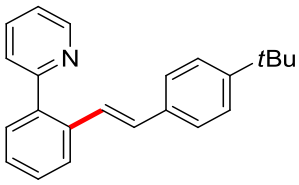


(*E*)-2-(2-Styrylphenyl)pyridine (74jo): The general procedure **I** was followed using phenyl 2-[2-(pyridin-2-yl)phenyl]propan-2-ol (**168j**) (53.3 mg, 0.25 mmol) and ethynylbenzene (**8o**) (51.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (DCM: 100% → *n*-hexane/EtOAc: 8/1) yielded **74jo** (46.3 mg, 72%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.75 (dt, *J* = 4.1, 1.2 Hz, 1H), 7.91–7.68 (m, 2H), 7.56 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.50–7.34 (m, 5H), 7.34–7.16 (m, 5H), 7.05 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.9 (C_q), 149.5 (CH), 139.6 (C_q), 137.5 (C_q), 135.9 (CH), 135.7 (C_q), 130.2 (CH), 130.0 (CH), 128.6 (CH), 128.6 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 126.5 (CH), 126.2 (CH), 125.0 (CH), 121.8 (CH). **IR** (ATR) v = 3056, 1583, 1459, 1424, 1150, 962, 761, 750, 692 cm^{-1}. **MS** (ESI) m/z (relative intensity):

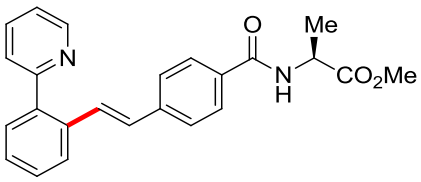
537 (20) $[2M+Na]^+$, 515 (30) $[2M+H]^+$, 280 (30) $[M+Na]^+$, 258 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{16}N$ $[M+H]^+$: 258.1277, found: 258.1277.

The analytical data were in accordance with those reported in the literature.[77]



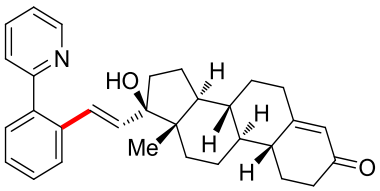
(*E*)-2-{2-[4-(*tert*-Butyl)styryl]phenyl}pyridine (74jv): The general procedure **I** was followed using phenyl 2-(2-(pyridin-2-yl)phenyl)propan-2-ol (**168j**) (53.3 mg, 0.25 mmol) and 1-(*tert*-butyl)-4-ethynylbenzene (**8v**) (79.2 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **74jv** (62.7 mg, 80%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.75 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 7.70 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.75 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.55 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.44 (ddd, *J* = 7.8, 1.2, 1.0 Hz, 1H), 7.41 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.37 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.34–7.31 (m, 4H), 7.26 (ddd, *J* = 7.4, 4.8, 1.2 Hz, 1H), 7.20 (d, *J* = 16.2 Hz, 1H), 7.04 (d, *J* = 16.2 Hz, 1H), 1.31 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.9 (C_q), 150.7 (C_q), 149.5 (CH), 139.5 (C_q), 135.9 (CH), 135.9 (C_q), 135.0 (C_q), 130.2 (CH), 129.9 (CH), 128.6 (CH), 127.5 (CH), 126.8 (CH), 126.3 (CH), 126.2 (CH), 125.5 (CH), 125.1 (CH), 121.8 (CH), 34.6 (C_q), 31.2 (CH_3). **IR** (ATR) ν = 2961, 1584, 1460, 1424, 1268, 965, 818, 750 cm^{-1}. **MS** (ESI) m/z (relative intensity): 336 (10) $[M+Na]^+$, 314 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{23}H_{24}N$ $[M+H]^+$: 314.1903, found: 314.1906.



(*S,E*)-Methyl 2-{4-[2-(pyridin-2-yl)styryl]benzamido}propanoate (74jw): The general procedure **I** was followed at 120 °C using phenyl 2-(2-(pyridin-2-yl)phenyl)propan-2-ol (**168j**) (53.3 mg, 0.25 mmol) and (*S*)-methyl 2-(4-ethynylbenzamido)propanoate (**8w**) (115.6 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **74jw** (60.0 mg, 62%) as a colorless oil.

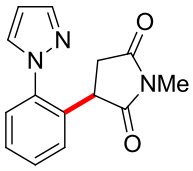
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.73 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.90–7.67 (m, 4H), 7.64–7.50 (m, 1H), 7.49–7.32 (m, 5H), 7.32–7.20 (m, 2H), 7.04 (d, *J* = 16.2 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 4.77 (dt, *J* = 14.4, 7.2 Hz, 1H), 3.76 (s, 3H), 1.49 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 173.5 (C_q), 166.2 (C_q), 158.6 (C_q), 149.4 (CH), 140.9 (C_q), 139.7 (C_q), 136.0 (CH), 135.1 (C_q), 132.4 (C_q), 130.2 (CH), 129.6 (CH), 128.7 (CH), 128.6 (CH), 128.0 (CH), 127.3 (CH), 126.5 (CH), 126.2 (CH), 124.8 (CH), 121.9 (CH), 52.5 (CH), 48.5 (CH_3), 18.7 (CH_3). **IR** (ATR) *v* = 3323, 2951, 1742, 1641, 1536, 1501, 1458, 1213, 1167, 752 cm^{-1}. **MS** (ESI) m/z (relative intensity): 795 (10) $[2M+Na]^+$, 773 (30) $[M+H]^+$, 409 (10) $[M+Na]^+$, 387 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{24}H_{23}N_2O_3$ $[M+H]^+$: 387.1703, found: 387.1702.



(*8R*,*9S*,*10R*,*13S*,*14S*,*17R*)-17-Hydroxy-13-methyl-17-[(*E*)-2-(pyridin-2-yl)styryl]-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[a]phenanthren-3(2*H*)-one (74jx): The general procedure **I** was followed at 80 °C using phenyl 2-(2-(pyridin-2-yl)phenyl)propan-2-ol (**168j**) (53.3 mg, 0.25 mmol) and (*8R*,*9S*,*10R*,*13S*,*14S*,*17R*)-17-ethynyl-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[a]phenanthren-3(2*H*)-one (**8x**) (149.2 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **74jx** (62.4 mg, 55%) as a colorless oil.

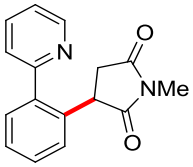
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.65 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.68 (td, *J* = 7.9, 1.8 Hz, 1H), 7.54 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.46 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.39 (dt, *J* = 7.9, 1.2 Hz, 1H), 7.37–7.27 (m, 2H), 7.22 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.57 (d, *J* = 16.0 Hz, 1H), 6.26 (d, *J* = 16.0 Hz, 1H), 5.80 (s, 1H), 2.50–2.32 (m, 2H), 2.30–2.15 (m, 3H), 2.10–2.00 (m, 1H), 1.97–1.75 (m, 5H), 1.62–1.43 (m, 3H), 1.41–1.15 (m, 5H), 1.07–0.97 (m, 1H), 0.94 (s, 3H), 0.84–0.70 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 199.8 (C_q), 166.5 (C_q), 159.0 (C_q), 149.3 (CH), 139.2 (C_q), 136.4 (CH), 135.9 (CH), 135.6 (C_q), 130.0 (CH), 128.5 (CH), 127.4 (CH), 127.1 (CH), 126.6 (CH), 124.7 (CH), 124.5 (CH), 121.8 (CH), 84.0 (C_q), 49.2 (CH), 48.7 (CH), 47.2 (C_q), 42.5 (CH), 41.1 (CH), 36.5 (CH_2), 36.2 (CH_2), 35.5 (CH_2), 32.1 (CH_2), 30.8 (CH_2),

26.5 (CH_2), 26.1 (CH_2), 23.3 (CH_2), 14.1 (CH_3). **IR** (ATR) ν = 3436, 2927, 2867, 1660, 1461, 1425, 1260, 1014, 910, 730 cm^{-1}. **MS** (ESI) m/z (relative intensity): 907 (30) $[2M+H]^+$, 476 (15) $[M+Na]^+$, 454 (100) $[M+H]^+$, 436 (30). **HR-MS** (ESI) m/z calcd for $C_{31}H_{36}NO_2$ $[M+H]^+$: 454.2741, found: 454.2747.



3-[2-(1*H*-Pyrazol-1-yl)phenyl]-1-methylpyrrolidine-2,5-dione (102af): The general procedure **J** was followed using 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol) and 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 3/2) yielded **102af** (43.4 mg, 68%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.70 (d, J = 2.4 Hz, 1H), 7.61 (d, J = 1.8 Hz, 1H), 7.43–7.36 (m, 2H), 7.34–7.29 (m, 1H), 7.29–7.23 (m, 1H), 6.41 (dd, J = 2.4, 1.8 Hz, 1H), 4.12 (dd, J = 9.6, 5.6 Hz, 1H), 3.07 (dd, J = 18.4, 9.6 Hz, 1H), 2.92 (s, 3H), 2.82 (dd, J = 18.4, 5.6 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 177.5 (C_q), 176.2 (C_q), 140.8 (CH), 139.6 (C_q), 133.0 (C_q), 131.2 (CH), 129.9 (CH), 129.0 (CH), 128.7 (CH), 126.6 (CH), 107.1 (CH), 43.3 (CH), 37.8 (CH_2), 25.1 (CH_3). **IR** (ATR) ν = 3136, 1694, 1518, 1435, 1382, 1280, 1144, 1003, 760 cm^{-1}. **MS** (ESI) m/z (relative intensity): 533 (100) $[2M+Na]^+$, 278 (70) $[M+Na]^+$, 256 (40) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{14}H_{14}N_3O_2$ $[M+H]^+$: 256.1081, found: 256.1077.

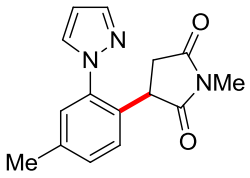


1-Methyl-3-[2-(pyridin-2-yl)phenyl]pyrrolidine-2,5-dione (102jf): The general procedure **J** was followed using phenyl 2-(2-(pyridin-2-yl)phenyl)propan-2-ol (**168j**) (53.3 mg, 0.25 mmol) and 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **102jf** (60.6 mg, 91%) as a colorless oil.

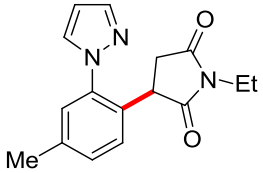
^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.52 (d, J = 4.8 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.54 (dd, J = 7.8, 1.0 Hz, 1H), 7.47–7.43 (m, 1H), 7.41–7.35 (m, 2H), 7.29–7.15 (m, 2H), 4.34 (dd, J = 9.6, 5.6 Hz, 1H), 3.14 (dd,

J = 18.4, 9.6 Hz, 1H), 2.92 (s, 3H), 2.89 (dd, *J* = 18.4, 9.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 178.3 (C_q), 176.5 (C_q), 158.9 (C_q), 148.4 (CH), 140.0 (C_q), 136.8 (CH), 135.4 (C_q), 130.5 (CH), 129.4 (CH), 129.0 (CH), 127.9 (CH), 124.1 (CH), 122.0 (CH), 44.9 (CH), 38.6 (CH_2), 25.0 (CH_3). **IR** (ATR) *v* = 3057, 1696, 1436, 1382, 1282, 1120, 953, 757 cm^{-1}. **MS** (ESI) m/z (relative intensity): 555 (100) $[2M+Na]^+$, 289 (70) $[M+Na]^+$, 267 (90) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{15}N_2O_2$ $[M+H]^+$: 267.1128, found: 267.1126.

The analytical data were in accordance with those reported in the literature.[204]

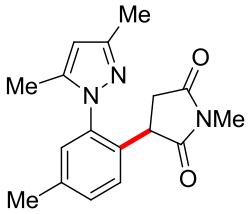


1-Methyl-3-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]pyrrolidine-2,5-dione (102cf): The general procedure **J** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **102cf** (43.1 mg, 64%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 2.2 Hz, 1H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.24 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.20–7.14 (m, 2H), 6.44 (dd, *J* = 2.2, 1.8 Hz, 1H), 4.10 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.09 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.96 (s, 3H), 2.83 (dd, *J* = 18.4, 5.6 Hz, 1H), 2.40 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 177.7 (C_q), 176.3 (C_q), 140.7 (CH), 139.4 (C_q), 139.0 (C_q), 131.1 (CH), 129.9 (C_q), 129.7 (CH), 129.6 (CH), 127.2 (CH), 106.9 (CH), 42.9 (CH), 37.8 (CH_2), 25.1 (CH_3), 20.8 (CH_3). **IR** (ATR) *v* = 3118, 2924, 1694, 1434, 1381, 1279, 1118, 950, 757 cm^{-1}. **MS** (ESI) m/z (relative intensity): 561 (30) $[2M+Na]^+$, 292 (100) $[M+Na]^+$, 270 (80) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{15}H_{16}N_3O_2$ $[M+H]^+$: 270.1237, found: 270.1239.



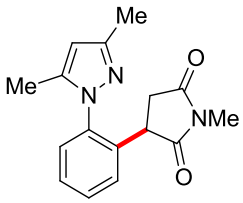
1-Ethyl-3-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]pyrrolidine-2,5-dione (102cg): The general procedure **J** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg,

0.25 mmol) and 1-ethyl-1*H*-pyrrole-2,5-dione (**11g**) (62.6 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **102cg** (44.0 mg, 62%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 2.4 Hz, 1H), 7.66 (d, *J* = 1.8 Hz, 1H), 7.24 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.19 (d, *J* = 1.3 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.45 (dd, *J* = 2.4, 1.8 Hz, 1H), 4.09 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.55 (qd, *J* = 7.2, 3.7 Hz, 2H), 3.07 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.76 (dd, *J* = 18.4, 5.6 Hz, 1H), 2.40 (s, 3H), 1.19 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 177.4 (C_q), 175.9 (C_q), 140.7 (CH), 139.4 (C_q), 138.8 (C_q), 131.1 (CH), 129.9 (C_q), 129.7 (CH), 129.1 (CH), 127.1 (CH), 106.9 (CH), 42.7 (CH), 37.8 (CH_2), 34.0 (CH_2), 20.9 (CH_3), 13.0 (CH_3). **IR** (ATR) *v* = 3119, 2939, 1698, 1402, 1351, 1222, 1126, 1044, 752 cm^{-1}. **MS** (ESI) m/z (relative intensity): 589 (40) $[2M+Na]^+$, 306 (98) $[M+Na]^+$, 284 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{18}N_3O_2$ $[M+H]^+$: 284.1394, found: 284.1395.



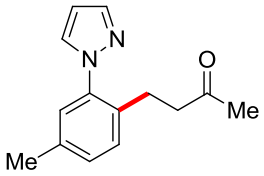
3-[2-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-4-methylphenyl]-1-methylpyrrolidine-2,5-dione (102kf): The general procedure **J** was followed using 2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-4-methylphenyl]propan-2-ol (**168k**) (61.1 mg, 0.25 mmol) and 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.5 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **102kf** (60.0 mg, 85%) as a white solid.

M.p. = 127–129 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.23–7.12 (m, 2H), 7.00 (dt, *J* = 1.5, 0.7 Hz, 1H), 5.87 (s, 1H), 3.83 (dd, *J* = 8.6, 6.5 Hz, 1H), 3.00 (s, 1H), 2.98 (d, *J* = 3.3 Hz, 1H), 2.81 (s, 3H), 2.34 (s, 3H), 2.16 (s, 3H), 2.09 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 177.3 (C_q), 176.1 (C_q), 148.8 (C_q), 141.3 (C_q), 138.6 (C_q), 137.9 (C_q), 132.6 (C_q), 130.2 (CH), 130.0 (CH), 129.2 (CH), 105.6 (CH), 43.4 (CH), 37.9 (CH_2), 25.0 (CH_3), 20.9 (CH_3), 13.4 (CH_3), 11.5 (CH_3). **IR** (ATR) *v* = 2925, 1693, 1433, 1283, 1119, 835, 778, 689 cm^{-1}. **MS** (ESI) m/z (relative intensity): 320 (40) $[M+Na]^+$, 298 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{17}H_{20}N_3O_2$ $[M+H]^+$: 298.1550, found: 298.1547.



3-[2-(3,5-Dimethyl-1*H*-pyrazol-1-yl)phenyl]-1-methylpyrrolidine-2,5-dione (102lf): The general procedure **J** was followed using 2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168l**) (57.6 mg, 0.25 mmol) and 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.5 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 1/1) yielded **102lf** (58.1 mg, 82%) as a white solid.

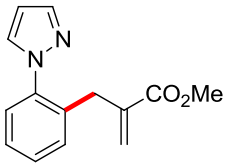
M.p. = 100–102 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.43–7.33 (m, 2H), 7.32–7.13 (m, 2H), 5.88 (s, 1H), 3.88 (dd, *J* = 9.0, 6.1 Hz, 1H), 3.15–2.89 (m, 2H), 2.80 (s, 3H), 2.15 (s, 3H), 2.08 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 177.2 (C_q), 176.1 (C_q), 148.9 (C_q), 141.4 (C_q), 138.1 (C_q), 135.8 (C_q), 130.6 (CH), 129.3 (CH), 128.6 (CH), 128.5 (CH), 105.8 (CH), 43.8 (CH), 37.7 (CH_2), 24.9 (CH_3), 13.3 (CH_3), 11.4 (CH_3). **IR** (ATR) *v* = 1691, 1508, 1436, 1380, 1279, 1121, 951, 766 cm^{-1}. **MS** (ESI) m/z (relative intensity): 306 (70) $[M+Na]^+$, 284 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{18}N_3O_2$ $[M+H]^+$: 284.1394, found: 284.1386.



4-[4-Methyl-2-(1*H*-pyrazol-1-yl)phenyl]butan-2-one (102ch): The general procedure **J** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol) and but-3-en-2-one (**11h**) (35.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **102ch** (43.4 mg, 76%) as a colorless oil.

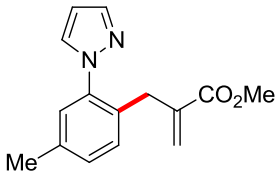
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.67 (d, *J* = 1.3 Hz, 1H), 7.57 (d, *J* = 1.8 Hz, 1H), 7.20–7.07 (m, 3H), 6.40 (t, *J* = 2.1 Hz, 1H), 2.75 (t, *J* = 7.6 Hz, 2H), 2.53 (t, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 2.02 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 207.6 (C_q), 140.1 (CH), 139.3 (C_q), 136.8 (C_q), 133.7 (C_q), 130.4 (CH), 130.2 (CH), 129.3 (CH), 127.0 (CH), 106.2 (CH), 44.4 (CH_2), 29.8 (CH_3), 25.5 (CH_2), 20.7 (CH_3). **IR** (ATR) *v* = 2923, 1713, 1516, 1405, 1162, 1044, 951, 817, 754, 623 cm^{-1}. **MS** (ESI) m/z (relative intensity): 251 (50) $[M+Na]^+$, 229 (100) $[M+H]^+$, 171 (30). **HR-MS** (ESI) m/z calcd for $C_{14}H_{17}N_2O$ $[M+H]^+$:

229.1335, found: 229.1344.



Methyl 2-[2-(1*H*-pyrazol-1-yl)benzyl]acrylate (202aa): The general procedure **K** was followed using 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol) and methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **202aa** (48.3 mg, 80%) as a colorless oil.

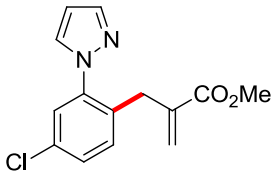
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.57 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.38–7.28 (m, 4H), 6.39 (dd, *J* = 2.4, 1.9 Hz, 1H), 6.13 (td, *J* = 1.2, 1.0 Hz, 1H), 5.20 (td, *J* = 1.5, 1.3 Hz, 1H), 3.67 (s, 3H), 3.62 (dd, *J* = 1.5, 1.0 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.9 (C_q), 140.3 (CH), 139.8 (C_q), 138.7 (C_q), 134.4 (C_q), 130.9 (CH), 130.6 (CH), 128.5 (CH), 127.3 (CH), 126.6 (CH), 126.5 (CH_2), 106.2 (CH), 51.9 (CH_3), 33.5 (CH_2). **IR** (ATR) *v* = 2950, 1716, 1517, 1394, 1194, 1138, 1045, 939, 751 cm^{-1}. **MS** (ESI) m/z (relative intensity): 265 (75) $[M+Na]^+$, 243 (100) $[M+H]^+$, 211 (15). **HR-MS** (ESI) m/z calcd for $C_{14}H_{15}N_2O_2$ $[M+H]^+$: 243.1128, found: 243.1126.



Methyl 2-[4-methyl-2-(1*H*-pyrazol-1-yl)benzyl]acrylate (202ca): The general procedure **K** was followed using 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (53.8 mg, 0.25 mmol) and methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **202ca** (46.1 mg, 72%) as a colorless oil.

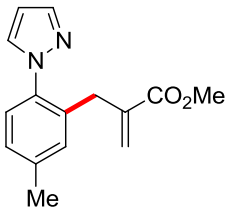
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.56 (dd, *J* = 2.3, 0.7 Hz, 1H), 7.20–7.11 (m, 3H), 6.37 (dd, *J* = 2.3, 1.9 Hz, 1H), 6.11 (td, *J* = 1.9, 0.5 Hz, 1H), 5.20 (td, *J* = 1.5, 1.4 Hz, 1H), 3.66 (s, 3H), 3.57 (dd, *J* = 1.5, 1.1 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 167.1 (C_q), 140.3 (CH), 139.7 (C_q), 139.1 (C_q), 137.3 (C_q), 131.1 (C_q), 130.8 (CH), 130.6 (CH), 129.3 (CH), 127.2 (CH), 126.4 (CH_2), 106.2 (CH), 51.8 (CH_3), 33.1 (CH_2), 20.8 (CH_3). **IR** (ATR) *v* = 2950, 1718, 1516, 1436, 1196, 1174, 1136, 952,

753 cm^{-1}. **MS** (ESI) m/z (relative intensity): 279 (100) $[M+Na]^+$, 257 (50) $[M+H]^+$, 225 (45), 197 (10). **HR-MS** (ESI) m/z calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$: 257.1285, found: 257.1280.



Methyl 2-[4-chloro-2-(1*H*-pyrazol-1-yl)benzyl]acrylate (202ma): The general procedure **K** was followed using 2-[4-chloro-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168m**) (59.2 mg, 0.25 mmol) and methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **202ma** (57.3 mg, 83%) as a colorless oil.

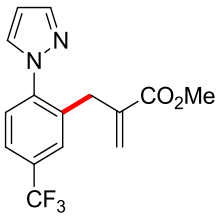
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.56 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.30–7.28 (m, 1H), 7.27–7.21 (m, 2H), 6.39 (dd, *J* = 2.4, 1.9 Hz, 1H), 6.16 (td, *J* = 1.9, 0.5 Hz, 1H), 5.27 (td, *J* = 1.5, 1.2 Hz, 1H), 3.67 (s, 3H), 3.59 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.6 (C_q), 140.6 (CH), 138.3 (C_q), 138.0 (C_q), 136.4 (C_q), 134.1 (C_q), 130.7 (CH), 130.6 (CH), 127.8 (CH), 127.4 (CH), 127.2 (CH_2), 106.6 (CH), 52.0 (CH_3), 33.4 (CH_2). **IR** (ATR) *v* = 2932, 1717, 1517, 1490, 1394, 1195, 1142, 939, 819, 753 cm^{-1}. **MS** (ESI) m/z (relative intensity): 299 (70) $[M+Na]^+$, 277 (100) $[M+H]^+$, 245 (10). **HR-MS** (ESI) m/z calcd for $C_{14}H_{14}ClN_2O_2$ $[M+H]^+$: 277.0738, found: 277.0742.



Methyl 2-[5-methyl-2-(1*H*-pyrazol-1-yl)benzyl]acrylate (202ba): The general procedure **K** was followed using 2-[5-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168b**) (54.1 mg, 0.25 mmol) and methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **202ba** (54.4 mg, 85%) as a colorless oil.

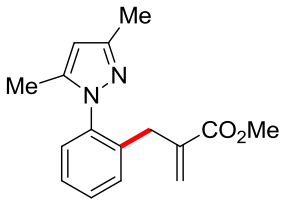
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.66 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.53 (dd, *J* = 2.3, 0.7 Hz, 1H), 7.22–7.16

(m, 1H), 7.13–7.07 (m, 2H), 6.36 (dd, *J* = 2.3, 1.9 Hz, 1H), 6.13 (td, *J* = 2.0, 0.5 Hz, 1H), 5.21 (td, *J* = 1.5, 1.3 Hz, 1H), 3.67 (s, 3H), 3.56 (m, 2H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 167.1 (C_q), 140.2 (CH), 138.9 (C_q), 138.5 (C_q), 137.6 (C_q), 134.2 (C_q), 131.5 (CH), 130.7 (CH), 128.0 (CH), 126.6 (CH_2), 126.5 (CH), 106.1 (CH), 51.8 (CH_3), 33.3 (CH_2), 21.1 (CH_3). **IR** (ATR) *v* = 2949, 1717, 1519, 1436, 1395, 1201, 1143, 819, 752 cm^{-1}. **MS** (ESI) m/z (relative intensity): 279 (45) $[M+Na]^+$, 257 (100) $[M+H]^+$, 225 (10). **HR-MS** (ESI) m/z calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$: 257.1285, found: 257.1294.



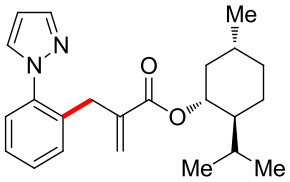
Methyl 2-[2-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)benzyl]acrylate (202na): The general procedure **K** was followed using 2-[2-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)phenyl]propan-2-ol (**168n**) (53.8 mg, 0.25 mmol) and methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **202na** (34.3 mg, 57%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.72 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.63 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.60–7.55 (m, 2H), 7.47–7.41 (m, 1H), 6.44 (dd, *J* = 2.4, 1.8 Hz, 1H), 6.17 (td, *J* = 1.9, 0.5 Hz, 1H), 5.25 (td, *J* = 1.5, 1.1 Hz, 1H), 3.73 (dd, *J* = 1.5, 1.0 Hz, 2H), 3.68 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.5 (C_q), 142.5 (C_q), 141.0 (CH), 137.9 (C_q), 135.2 (C_q), 130.6 (CH), 130.4 (q, $^{2}J_{C–F}$ = 32.7 Hz, C_q), 128.1 (q, $^{3}J_{C–F}$ = 3.6 Hz, CH), 127.2 (CH_2), 126.8 (CH), 124.4 (q, $^{3}J_{C–F}$ = 3.6 Hz, CH), 123.6 (q, $^{1}J_{C–F}$ = 273.5 Hz, C_q), 107.0 (CH), 52.0 (CH_3), 33.7 (CH_2). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -62.58 (s). **IR** (ATR) *v* = 2953, 1718, 1522, 1395, 1335, 1126, 940, 753 cm^{-1}. **MS** (ESI) m/z (relative intensity): 333 (100) $[M+Na]^+$, 311 (70) $[M+H]^+$, 291 (15), 279 (35), 251 (10). **HR-MS** (ESI) m/z calcd for $C_{15}H_{14}N_2O_2F_3$ $[M+H]^+$: 311.1002, found: 311.1000.



Methyl 2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)benzyl]acrylate (202la): The general procedure **K** was followed using 2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168l**) (57.6 mg, 0.25 mmol) and methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 4/1) yielded **202la** (49.1 mg, 73%) as a colorless oil.

^{1}**H NMR** (300 MHz, $CDCl_3$) δ = 7.35–7.23 (m, 3H), 7.16 (ddd, *J* = 7.5, 7.5, 1.2 Hz, 1H), 6.09 (td, *J* = 1.4, 0.7 Hz, 1H), 5.91 (s, 1H), 5.20 (td, *J* = 1.4, 1.4 Hz, 1H), 3.64 (s, 3H), 3.47 (m, 2H), 2.25 (s, 3H), 2.02 (d, *J* = 0.7 Hz, 3H). ^{13}**C NMR** (125 MHz, $CDCl_3$) δ = 166.9 (C_q), 148.3 (C_q), 140.2 (C_q), 138.5 (C_q), 138.1 (C_q), 137.1 (C_q), 130.5 (CH), 128.8 (CH), 128.0 (CH), 127.0 (CH), 126.8 (CH_2), 105.1 (CH), 51.8 (CH_3), 33.4 (CH_2), 13.6 (CH_3), 11.5 (CH_3). **IR** (ATR) *v* = 2950, 1719, 1502, 1437, 1204, 1142, 948, 780 cm^{-1}. **MS** (ESI) m/z (relative intensity): 293 (20) $[M+Na]^+$, 271 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{16}H_{19}N_2O_2$ $[M+H]^+$: 271.1441, found: 271.1450.

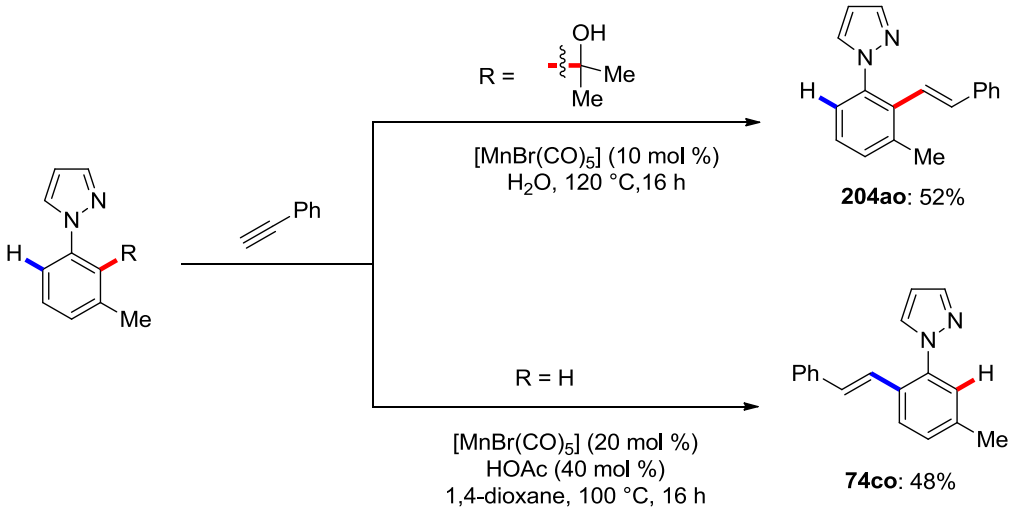


(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 2-[2-(1*H*-pyrazol-1-yl)benzyl]acrylate (202ab): The general procedure **K** was followed using 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol) and (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl)} acrylate (**201b**) (136.2 mg, 0.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 9/1 → 4/1) yielded **202ab** (83.4 mg, 91%) as a colorless oil.

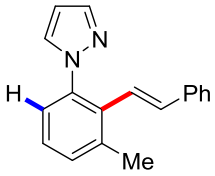
^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 7.67 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.56 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.38–7.25 (m, 4H), 6.38 (dd, *J* = 2.4, 1.9 Hz, 1H), 6.12 (td, *J* = 1.4, 1.3 Hz, 1H), 5.21 (td, *J* = 1.5, 1.4 Hz, 1H), 4.64 (td, *J* = 10.9, 4.4 Hz, 1H), 3.60 (m, 2H), 1.93–1.85 (m, 1H), 1.72–1.53 (m, 3H), 1.50–1.36 (m, 2H), 1.34–1.25 (m, 1H), 1.07–0.93 (m, 1H), 0.89–082 (m, 4H), 0.79 (d, *J* = 7.0 Hz, 3H), 0.64 (d, *J* = 7.0 Hz, 3H). ^{13}**C NMR** (100 MHz, $CDCl_3$) δ = 166.1 (C_q), 140.3 (CH), 139.9 (C_q), 139.3 (C_q), 134.7 (C_q), 130.7

(CH), 130.6 (CH), 128.4 (CH), 127.2 (CH), 126.5 (CH), 126.2 (CH_2), 106.2 (CH), 74.6 (CH), 47.0 (CH), 40.7 (CH_2), 34.2 (CH_2), 33.6 (CH_2), 31.3 (CH), 26.1 (CH), 23.4 (CH_2), 22.0 (CH_3), 20.8 (CH_3), 16.2 (CH_3). **IR** (ATR) ν = 2953, 2924, 2868, 1709, 1517, 1454, 1393, 1252, 1141, 939, 759 cm^{-1}. **MS** (ESI) m/z (relative intensity): 389 (30) $[M+Na]^+$, 367 (100) $[M+H]^+$, 229 (35). **HR-MS** (ESI) m/z calcd for $C_{23}H_{31}N_2O_2$ $[M+H]^+$: 367.2380, found: 367.2377.

Postion-selective Manganese(I)-Catalyzed C–C Activation Highlighting benefits over C–H Activation



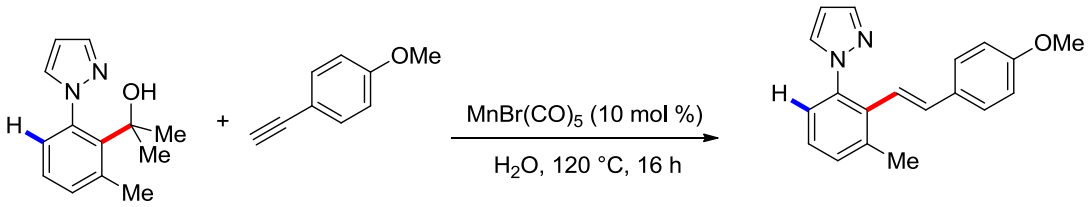
A suspension of 2-[2-methyl-6-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**203a**) (54.1 mg, 0.25 mmol), ethynylbenzene (**8o**) (66.1 mg, 0.50 mmol), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **204ao** (33.9 mg, 52%) as a colorless oil.



(*E*)-1-(3-Methyl-2-styrylphenyl)-1*H*-pyrazole (204ao) **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.70 (d, *J* = 1.9 Hz, 1H), 7.58 (d, *J* = 2.1 Hz, 1H), 7.36–7.20 (m, 8H), 6.88 (d, *J* = 16.7 Hz, 1H), 6.36 (dd, *J* = 2.1, 1.9 Hz, 1H), 6.29 (d, *J* = 16.7 Hz, 1H), 2.49 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 140.0 (CH), 139.1 (C_q),

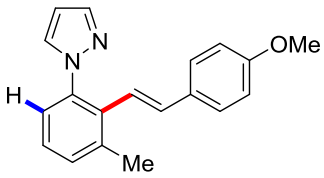
137.6 (C_q), 137.1 (C_q), 134.3 (CH), 133.0 (C_q), 131.3 (CH), 130.5 (CH), 128.5 (CH), 127.7 (CH), 127.2 (CH), 126.3 (CH), 124.5 (CH), 123.1 (CH), 106.3 (CH), 21.2 (CH_3). **IR** (ATR) ν = 3024, 1473, 1393, 1043, 970, 953, 752 cm^{-1}. **MS** (ESI) m/z (relative intensity): 363 (10), 283(30) $[M+Na]^+$, 261 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{18}H_{17}N_2$ $[M+H]^+$: 261.1386, found: 261.1384.

A suspension of 1-(*m*-tolyl)-1*H*-pyrazole (**20c**) (39.6 mg, 0.25 mmol), ethynylbenzene (**8o**) (66.1 mg, 0.50 mmol), HOAc (6.0 µL, 40 mol %), $[MnBr(CO)_5]$ (13.7 mg, 20.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 100 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74co** (31.3 mg, 48%) as a colorless oil. The data has been reported above.



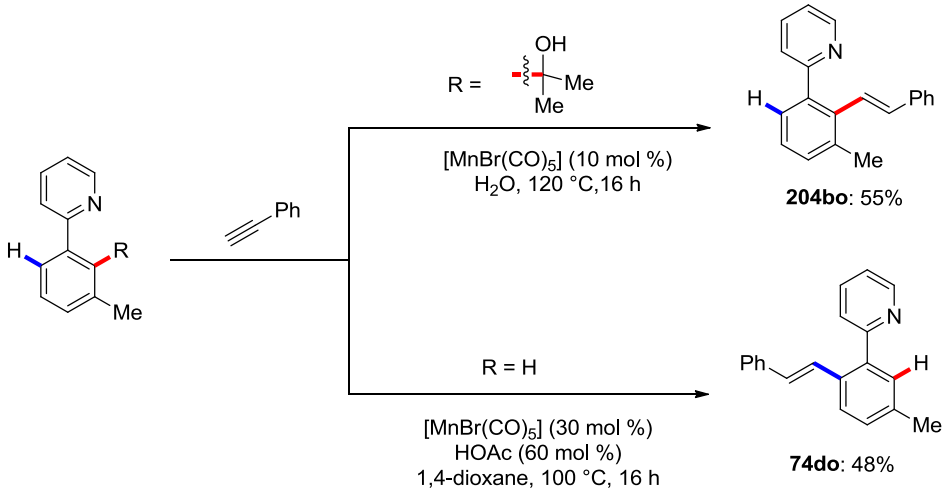
203a **8q** **204aq**: 59%

A suspension of 2-[2-methyl-6-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**203a**) (54.1 mg, 0.25 mmol), 1-ethynyl-4-methoxybenzene (**8q**) (66.1 mg, 0.50 mmol), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) yielded **204aq** (43.0 mg, 59%) as a colorless oil.

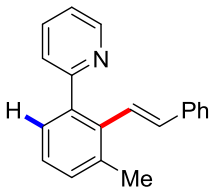


(*E*)-1-[2-(4-Methoxystyryl)-3-methylphenyl]-1*H*-pyrazole (204aq) ^{1}**H NMR** (600 MHz, $CDCl_3$) δ = 7.70 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.58 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.35–7.27 (m, 2H), 7.26–7.20 (m, 3H), 6.89–6.82 (m, 2H), 6.74 (d, *J* = 16.7 Hz, 1H), 6.36 (dd, *J* = 2.4, 1.9 Hz, 1H), 6.23 (d, *J* = 16.7 Hz, 1H),

3.80 (s, 3H), 2.48 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 159.3 (C_q), 140.0 (CH), 139.1 (C_q), 137.5 (C_q), 133.8 (CH), 133.3 (C_q), 131.3 (CH), 130.4 (CH), 130.0 (C_q), 127.5 (CH), 126.9 (CH), 124.5 (CH), 120.9 (CH), 114.0 (CH), 106.2 (CH), 55.3 (CH_3), 21.3 (CH_3). **IR** (ATR) ν = 2835, 1605, 1509, 1472, 1393, 1247, 1173, 1031, 752 cm^{-1}. **MS** (ESI) m/z (relative intensity): 313 (10) $[M+Na]^+$, 291 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{19}H_{19}N_2O$ $[M+H]^+$: 291.1492, found: 291.1486.



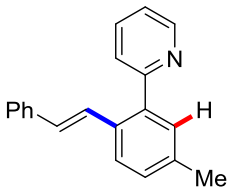
A suspension of 2-[2-methyl-6-(pyridin-2-yl)phenyl]propan-2-ol (**203b**) (56.8 mg, 0.25 mmol), ethynylbenzene (**8o**) (66.1 mg, 0.50 mmol), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **204bo** (37.3 mg, 55%) as a colorless oil.



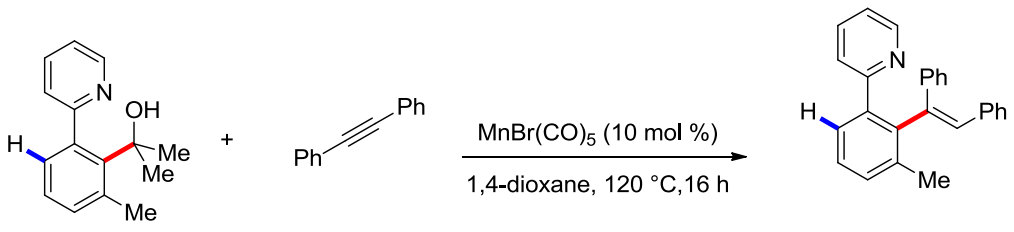
(*E*)-2-(3-Methyl-2-styrylphenyl)pyridine (204bo) **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.66 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.60 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1H), 7.43–7.36 (m, 2H), 7.30–7.23 (m, 6H), 7.22–7.17 (m, 1H), 7.15 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.10 (d, *J* = 16.6 Hz, 1H), 6.28 (d, *J* = 16.6 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 160.1 (C_q), 149.1 (CH), 140.2 (C_q), 137.4 (C_q), 136.6 (C_q), 135.6 (C_q), 135.5 (CH), 134.9 (CH), 130.4 (CH), 128.4 (CH), 127.9 (CH), 127.3 (CH), 126.9 (CH), 126.7 (CH), 126.1 (CH), 125.1 (CH), 121.3 (CH), 21.2 (CH_3). **IR** (ATR) ν = 3057, 1585, 1452, 1426, 967, 749, 732

cm^{-1}. **MS** (ESI) m/z (relative intensity): 272 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{18}N$ $[M+H]^+$: 272.1434, found: 272.1430.

A suspension of 2-(*m*-tolyl)pyridine (**20d**) (42.3 mg, 0.25 mmol), ethynylbenzene (**8o**) (66.1 mg, 0.50 mmol), HOAc (9.0 µL, 60 mol %), $[MnBr(CO)_5]$ (20.6 mg, 20.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 100 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **74do** (17.0 mg, 25%) as a colorless oil.



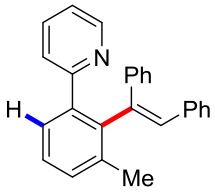
(*E*)-2-(5-Methyl-2-styrylphenyl)pyridine (74do) **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.77–8.66 (m, 1H), 7.71 (ddd, *J* = 7.7, 7.7, 1.6 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.38–7.35 (m, 3H), 7.33–7.15 (m, 6H), 7.00 (d, *J* = 16.2 Hz, 1H), 2.40 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 158.9 (C_q), 149.5 (CH), 139.5 (C_q), 137.7 (C_q), 137.6 (C_q), 135.9 (CH), 132.8 (C_q), 130.7 (CH), 129.5 (CH), 129.2 (CH), 128.6 (CH), 127.4 (CH), 127.3 (CH), 126.5 (CH), 126.2 (CH), 125.1 (CH), 121.8 (CH), 21.2 (CH_3). **IR** (ATR) ν = 3023, 1585, 1565, 1497, 1462, 964, 750, 693 cm^{-1}. **MS** (ESI) m/z (relative intensity): 272 $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{20}H_{18}N$ $[M+H]^+$: 272.1434, found: 272.1430.



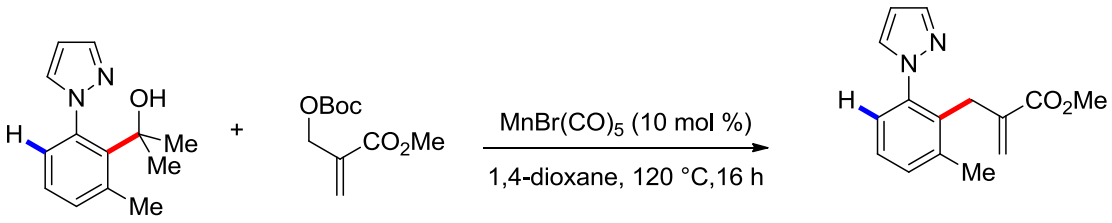
203b **8a** **204ba**: 71%

A suspension of 2-[2-methyl-6-(pyridin-2-yl)phenyl]propan-2-ol (**203b**) (56.8 mg, 0.25 mmol), methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**8a**) (89.1 mg, 0.50 mmol) and $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL)

and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) yielded **204ba** (61.4 mg, 71%) as a colorless oil.

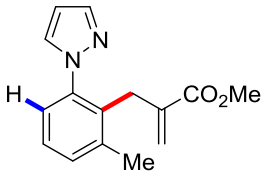


(*E*)-2-[2-(1,2-Diphenylvinyl)-3-methylphenyl]pyridine (204ba) **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.50 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.48 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1H), 7.44–7.38 (m, 2H), 7.32 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.27 (ddd, *J* = 7.5, 1.6, 0.7 Hz, 1H), 7.17–7.09 (m, 3H), 7.07–6.94 (m, 8H), 6.49 (s, 1H), 2.26 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 160.0 (C_q), 148.9 (CH), 142.2 (C_q), 141.2 (C_q), 140.0 (C_q), 139.6 (C_q), 137.6 (C_q), 137.0 (C_q), 135.1 (CH), 131.9 (CH), 130.4 (CH), 129.9 (CH), 128.9 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 127.3 (CH), 126.7 (CH), 126.6 (CH), 124.3 (CH), 121.1 (CH), 20.8 (CH_3). **IR** (ATR) *v* = 3055, 3020, 1586, 1492, 1444, 909, 772, 732, 695 cm^{-1}. **MS** (ESI) m/z (relative intensity): 348 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{26}H_{22}N$ $[M+H]^+$: 348.1747, found: 348.1744.

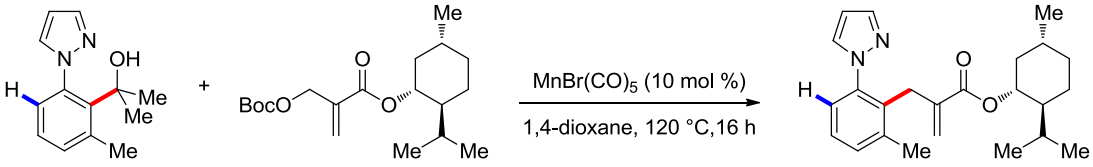


203a **201a** **205aa**: 82%

A suspension of 2-[2-methyl-6-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**203a**) (54.1 mg, 0.25 mmol), methyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate (**201a**) (108.1 mg, 0.50 mmol), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 6/1) yielded **205aa** (52.7 mg, 82%) as a colorless oil.

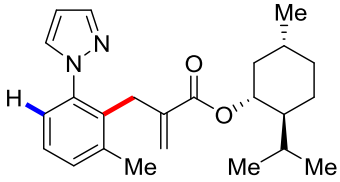


Methyl 2-[2-methyl-6-(1*H*-pyrazol-1-yl)benzyl]acrylate (205aa) **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.63 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.45 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.25–7.21 (m, 2H), 7.18 (dd, *J* = 6.6, 2.4 Hz, 1H), 6.33 (dd, *J* = 2.4, 1.8 Hz, 1H), 6.14 (td, *J* = 1.8, 0.9 Hz, 1H), 5.04 (td, *J* = 1.1, 0.9 Hz, 1H), 3.71 (s, 3H), 3.46 (dd, *J* = 1.8, 1.1 Hz, 2H), 2.26 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 167.0 (C_q), 140.7 (C_q), 140.2 (CH), 138.8 (C_q), 138.4 (C_q), 132.7 (C_q), 130.6 (CH), 130.6 (CH), 127.1 (CH), 124.9 (CH_2), 124.7 (CH), 106.0 (CH), 52.0 (CH_3), 30.1 (CH_2), 19.7 (CH_3). **IR** (ATR) *v* = 2950, 1715, 1516, 1394, 1278, 1255, 1135, 947, 749 cm^{-1}. **MS** (ESI) m/z (relative intensity): 279 (65) $[M+Na]^+$, 257 (100) $[M+H]^+$, 225 (10). **HR-MS** (ESI) m/z calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$: 257.1285, found: 257.1280.



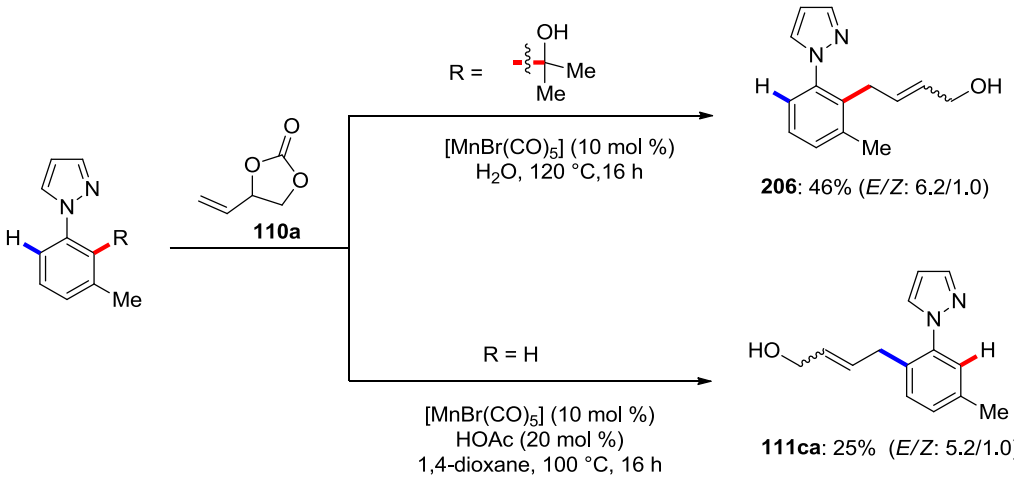
203a + **201b** → **205ab**: 91%

A suspension of 2-[2-methyl-6-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**203a**) (54.0 mg, 0.25 mmol), (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-{[(tert-butoxycarbonyl)oxy]methyl)} acrylate (**201b**) (136.2 mg, 0.50 mmol), and [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 9/1→6/1) yielded **205ab** (86.6 mg, 91%) as a colorless oil.

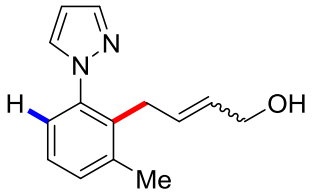


(*1R,2S,5R*)-2-Isopropyl-5-methylcyclohexyl 2-[2-methyl-6-(1*H*-pyrazol-1-yl)benzyl]acrylate (205ab) **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.63 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.45 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.27–7.18

(m, 3H), 6.34–6.30 (m, 1H), 6.11 (td, *J* = 1.7, 1.2 Hz, 1H), 5.02 (td, *J* = 2.1, 1.2 Hz, 1H), 4.71 (ddd, *J* = 10.9, 10.9, 4.4 Hz, 1H), 3.45 (dd, *J* = 2.1, 1.7 Hz, 2H), 2.28 (s, 3H), 2.01–1.94 (m, 1H), 1.75 (heptd, *J* = 6.9, 2.7 Hz, 1H), 1.70–1.61 (m, 2H), 1.48 (tdt, *J* = 12.0, 6.7, 3.3 Hz, 1H), 1.40–1.34 (m, 1H), 1.10–1.00 (m, 1H), 0.96 (td, *J* = 12.1, 10.9 Hz, 1H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.86–0.84 (m, 4H), 0.72 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.1 (C_q), 140.6 (C_q), 140.1 (CH), 139.1 (C_q), 138.7 (C_q), 133.2 (C_q), 130.7 (CH), 130.6 (CH), 127.0 (CH), 124.7 (CH), 124.4 (CH_2), 105.9 (CH), 74.7 (CH), 47.1 (CH), 40.8 (CH_2), 34.3 (CH_2), 31.4 (CH), 30.1 (CH_2), 26.5 (CH), 23.6 (CH_2), 22.1 (CH_3), 20.8 (CH_3), 19.7 (CH_3), 16.5 (CH_3). **IR** (ATR) *v* = 2953, 2927, 2869, 1708, 1516, 1476, 1393, 1250, 1132, 746 cm^{-1}. **MS** (ESI) m/z (relative intensity): 783 (58) $[2M+Na]^+$, 403 (60) $[M+Na]^+$, 381 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{24}H_{33}N_2O_2$ $[M+H]^+$: 381.2537, found: 381.2533.



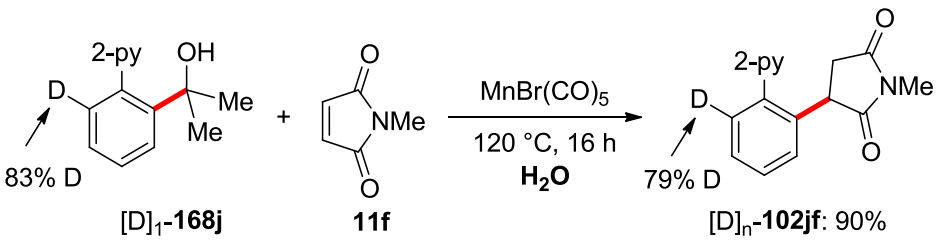
A suspension of 2-[2-methyl-6-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (54.1 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, EtOAc (10 mL) was added and the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **206** (26.1 mg, 46%, *E*/*Z* = 6.2/1.0 by ^{1}H NMR) as a colorless oil.



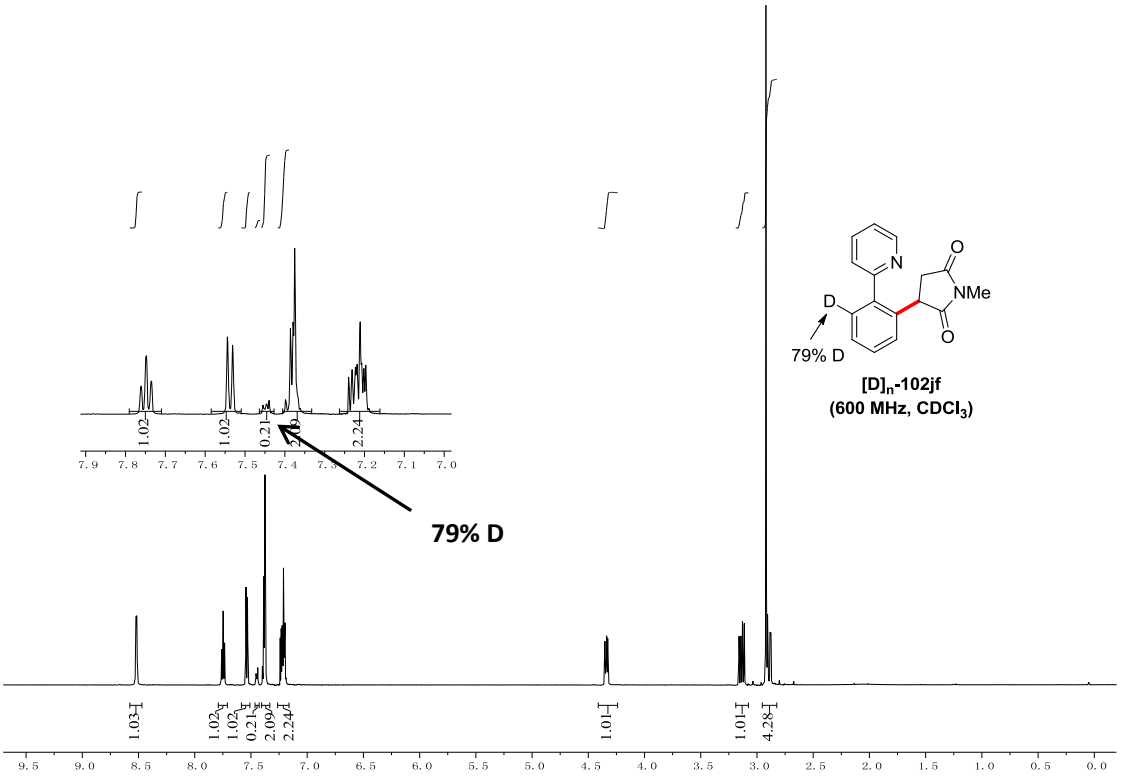
4-[2-Methyl-6-(1*H*-pyrazol-1-yl)phenyl]but-2-en-1-ol (206) **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.71–7.69 (*J* = 1.9, 0.7 Hz, 0.14H), 7.66 (*J* = 1.9, 0.7 Hz, 0.86H), 7.57–7.49 (m, 1H), 7.25–7.09 (m, 3H), 6.41 (dd, *J* = 2.1, 1.9 Hz, 0.14H), 6.37 (dd, *J* = 2.1, 1.9 Hz, 0.86H), 5.64 (dtt, *J* = 15.4, 6.4, 1.4 Hz, 0.86H), 5.53 (dtt, *J* = 15.4, 6.4, 1.4 Hz, 0.14H), 5.40 (dtt, *J* = 15.4, 6.4, 1.4 Hz, 0.14H), 5.34 (dtt, *J* = 15.4, 6.4, 1.4 Hz, 0.86H), 3.97 (dt, *J* = 5.9, 1.2 Hz, 1.72H), 3.93 (dd, *J* = 5.9, 1.2 Hz, 0.28H), 3.26 (dd, *J* = 5.9, 1.5 Hz, 0.28H), 3.19 (dd, *J* = 5.9, 1.5 Hz, 1.72H), 2.37 (s, 0.42H), 2.35 (s, 2.58H), 1.92 (brs, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) *Major isomer:* δ = 140.1 (C_q), 134.0 (CH), 138.4 (C_q), 134.3 (C_q), 131.0 (CH), 130.7 (CH), 130.0 (CH), 129.4 (CH), 126.6 (CH), 124.7 (CH), 105.9 (CH), 63.3 (CH_2), 30.9 (CH_2), 19.9 (CH_3). *Minor isomer:* δ = 140.2 (CH), 139.9 (C_q), 138.1 (C_q), 135.2 (C_q), 131.2 (CH), 130.9 (CH), 129.2 (CH), 129.1 (CH), 126.5 (CH), 124.8 (CH), 106.1 (CH), 58.0 (CH_2), 26.9 (CH_2), 19.9 (CH_3). **IR** (ATR) *v* = 3335, 2856, 1514, 1475, 1395, 1046, 973, 754 cm^{-1}. **MS** (ESI) m/z (relative intensity): 251 (60) $[M+Na]^+$, 229 (30) $[M+H]^+$, 211 (100). **HR-MS** (ESI) m/z calcd for $C_{14}H_{17}N_2O$ $[M+H]^+$: 229.1335, found: 229.1333.

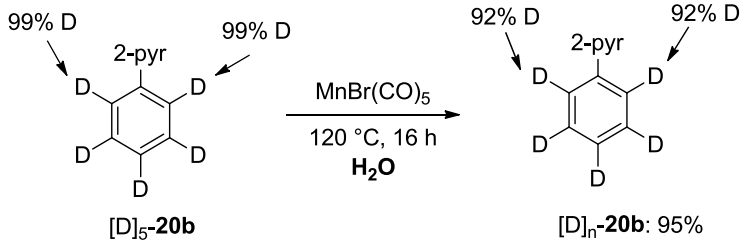
A suspension of 1-(*m*-tolyl)-1*H*-pyrazole (**20c**) (39.6 mg, 0.25 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (48.0 µL, 0.50 mmol), HOAc (3.0 µL, 20 mol %), $[MnBr(CO)_5]$ (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 100 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 2/1) yielded **111ca** (14.3 mg, 25%, *E*/*Z* = 5.2/1.0 by ^{1}H NMR) as a colorless oil.

C–C versus C–H Activation Experiments



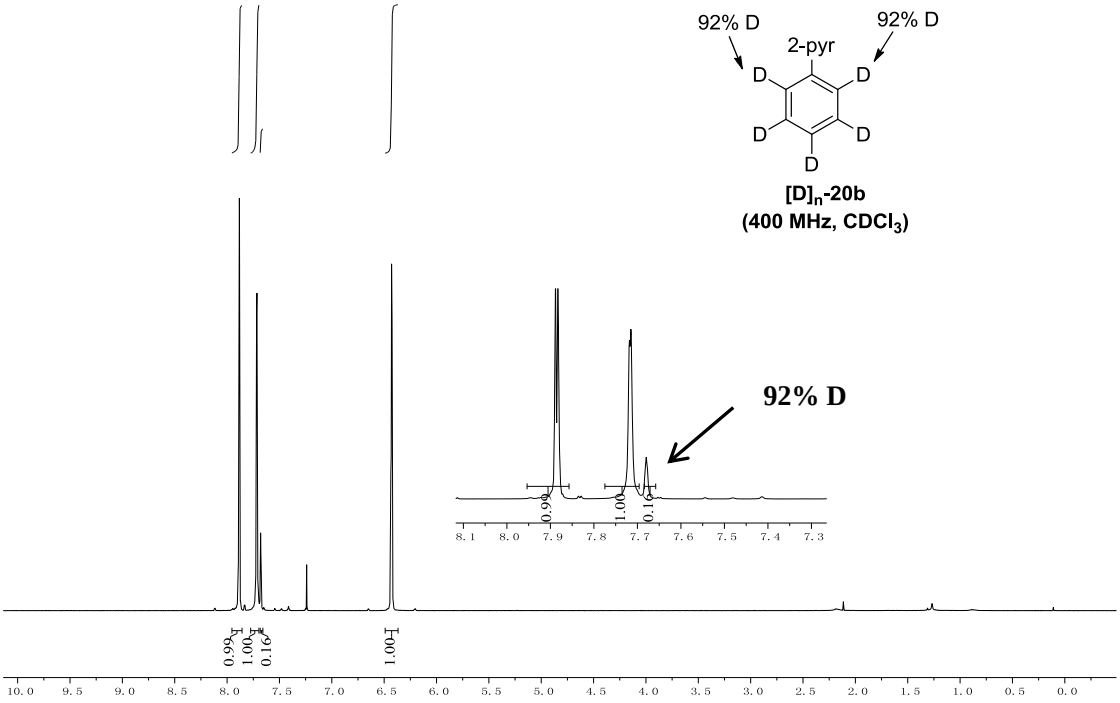
A suspension of 2-[2-(pyridin-2-yl)phenyl]propan-2-ol ([D]$_1$-**168j**) (53.5 mg, 0.25 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol), [MnBr(CO)$_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded [D]$_n$-**102jf** (60.0 mg, 90%). The deuterium incorporation was determined by ^{1}H NMR spectroscopy.

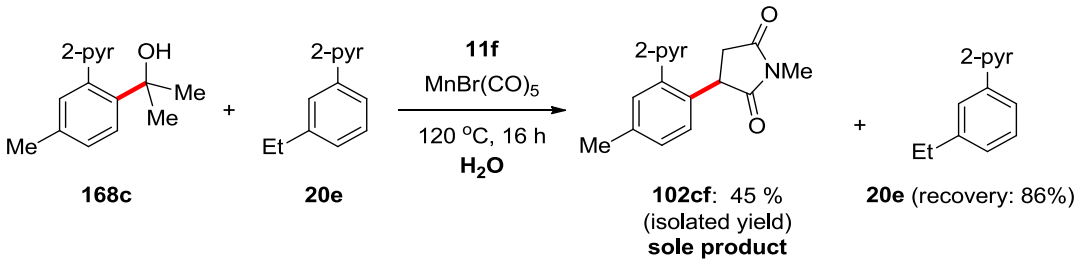




A suspension of 1-phenyl-1*H*-pyrazole ([D]$_5$-**20b**) (37.3 mg, 0.25 mmol), [MnBr(CO)$_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in*

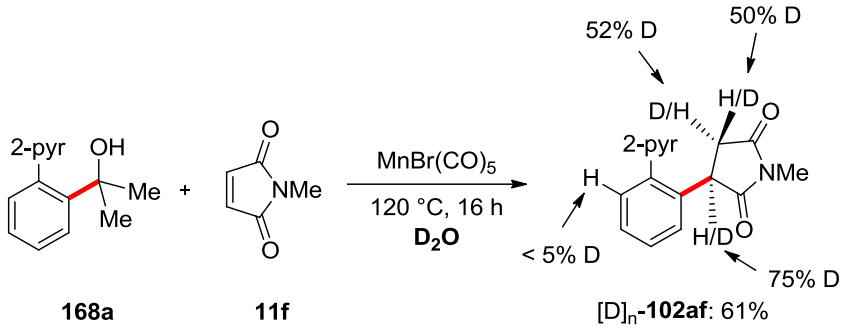
vacuo. Purification by column chromatography on silica gel afforded $[D]_n$-**20b** (35.4 mg, 95%). The deuterium incorporation was determined by ^1H NMR spectroscopy.



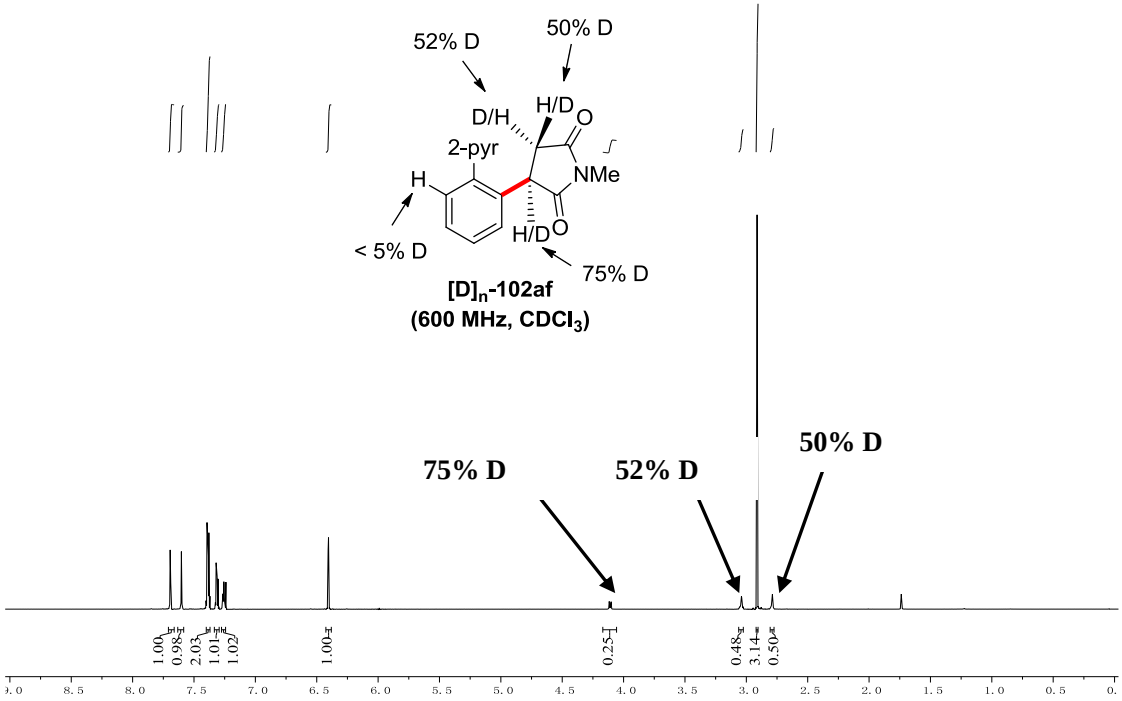


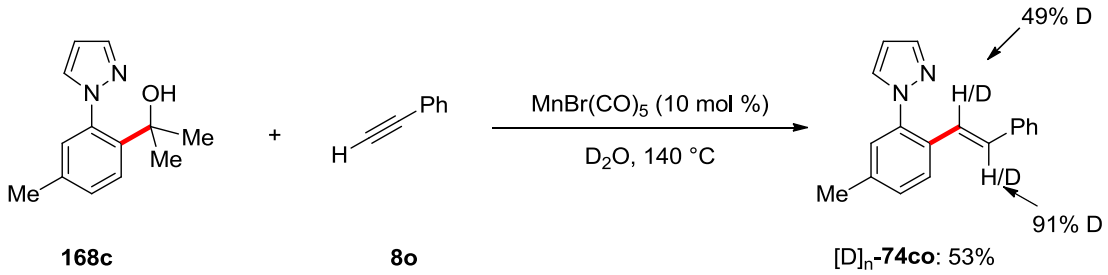
A suspension of 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (108.2 mg, 0.50 mmol), 1-(3-ethylphenyl)-1*H*-pyrazole (**20e**) (86.2 mg, 0.50 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded **102cf** (61.0 mg, 45%) and **20e** (74.0 mg, 86% recovered).

H/D Exchange Experiments



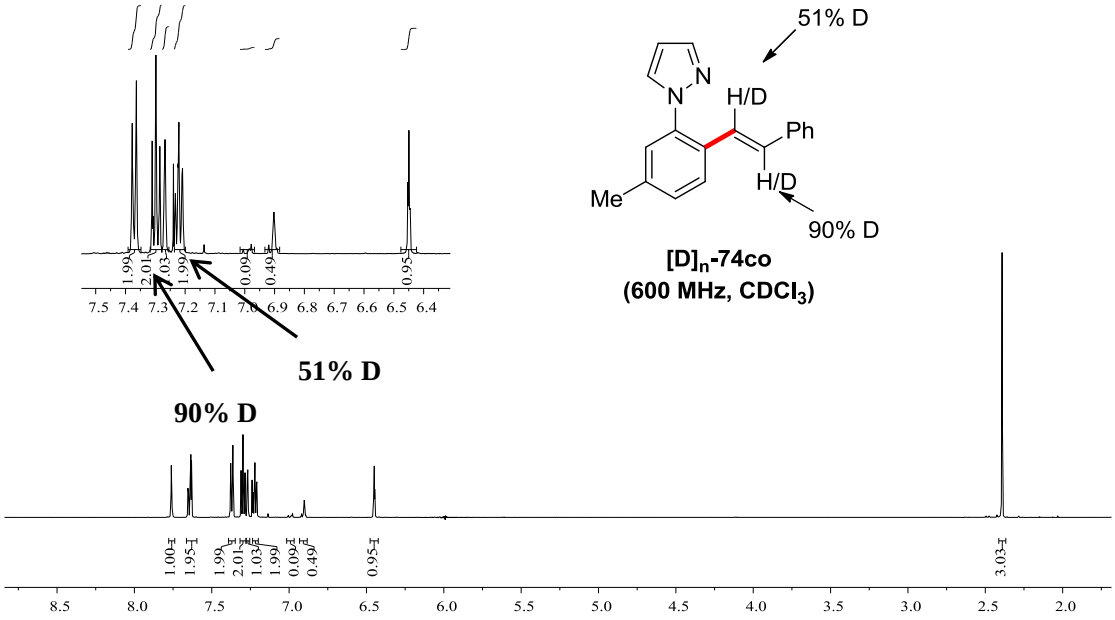
A suspension of 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in D_2O (1.0 mL) was stirred at 120 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded $[D]_n$-**102af** (39.0 mg, 61%). The deuterium incorporation was determined by ^1H NMR spectroscopy.

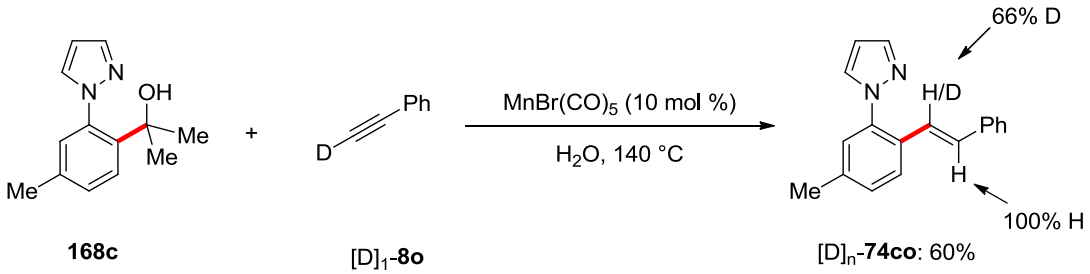




168c **8o** [D]$_n$-**74co**: 53%

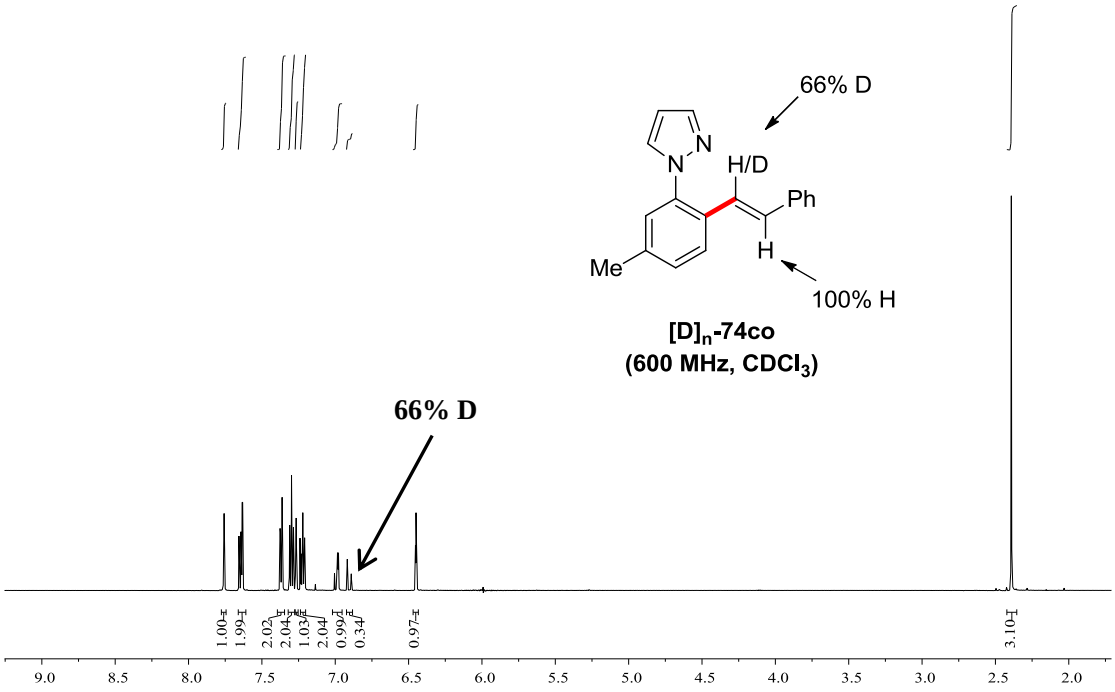
A suspension of 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol), ethynylbenzene (**8o**) (51.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in D_2O (1.0 mL) was stirred at 140 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded [D]$_n$-**74co** (35.0 mg, 53%). The deuterium incorporation was determined by ^1H NMR spectroscopy.

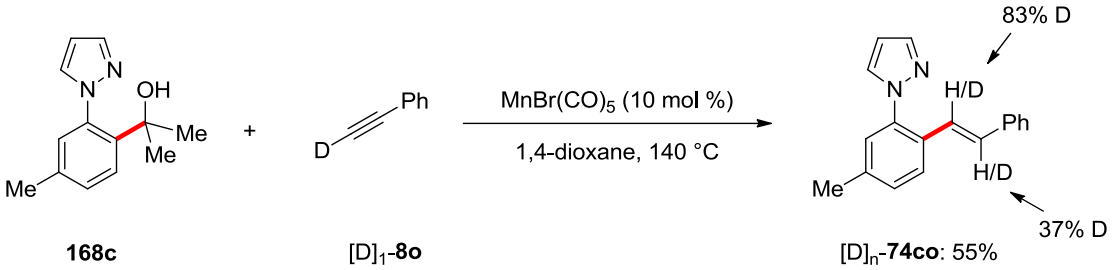




168c $[D]_1$-**8o** $[D]_n$-**74co**: 60%

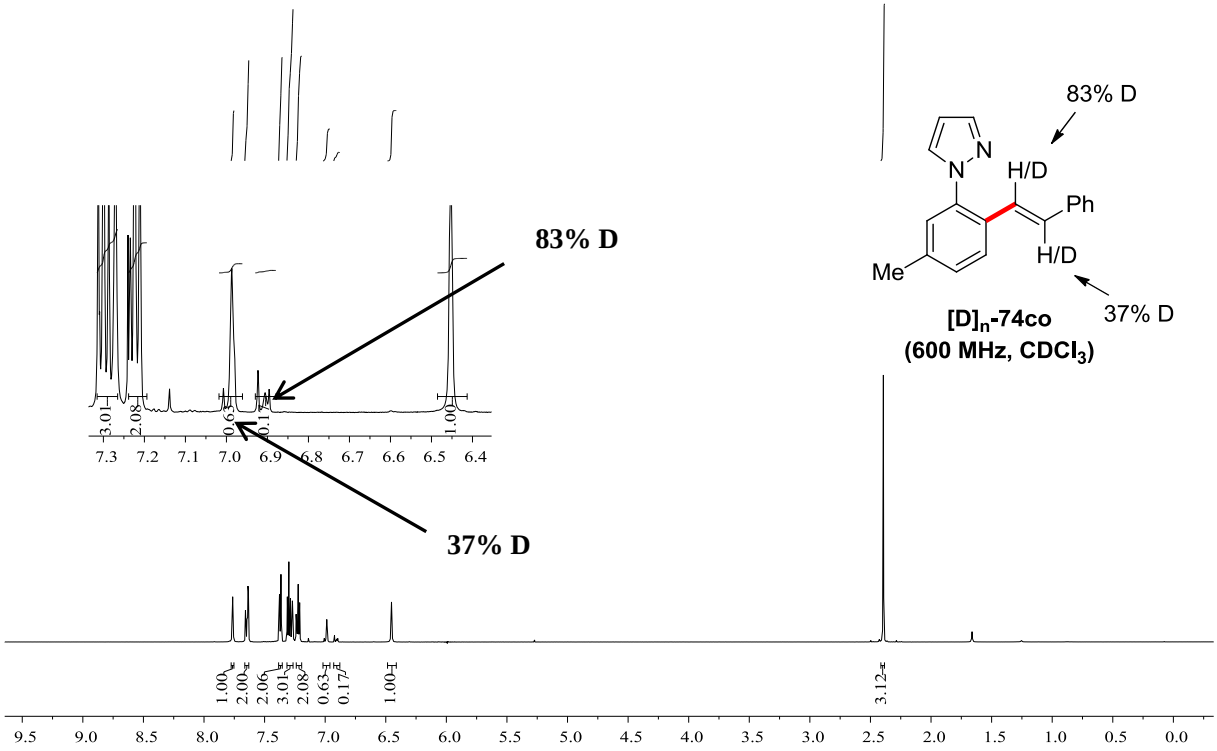
A suspension of 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol), $[D]_1$-ethynylbenzene ($[D]_1$-**8o**) (51.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 140 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded $[D]_n$-**74co** (39.1 mg, 60%). The deuterium incorporation was determined by ^1H NMR spectroscopy.

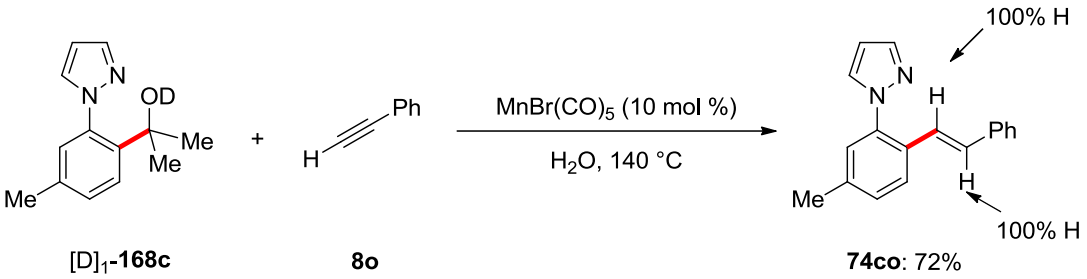




168c [D]$_1$-**8o** [D]$_n$-**74co**: 55%

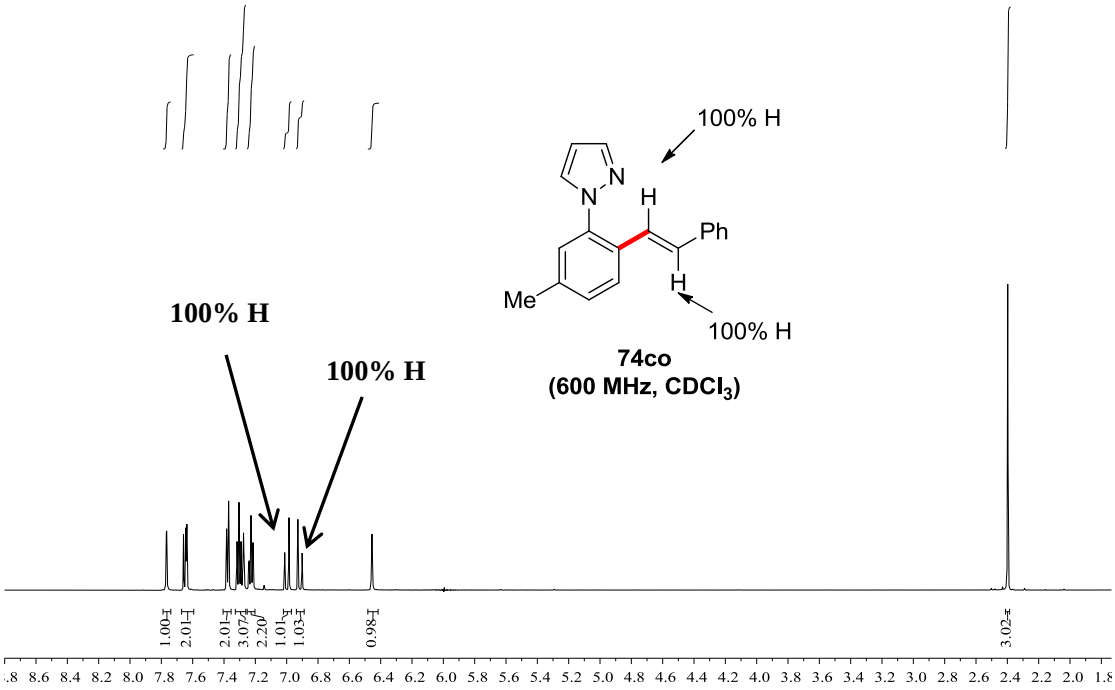
A suspension of 2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168c**) (54.1 mg, 0.25 mmol), [D]$_1$-ethynylbenzene ([D]$_1$-**8o**) (51.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in 1,4-dioxane (1.0 mL) was stirred at 140 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was transferred into a round bottom flask with CH_2Cl_2 (20 mL) and concentrated in *vacuo*. Purification by column chromatography on silica gel afforded [D]$_n$-**74co** (35.9 mg, 55%). The deuterium incorporation was determined by ^{1}H NMR spectroscopy.



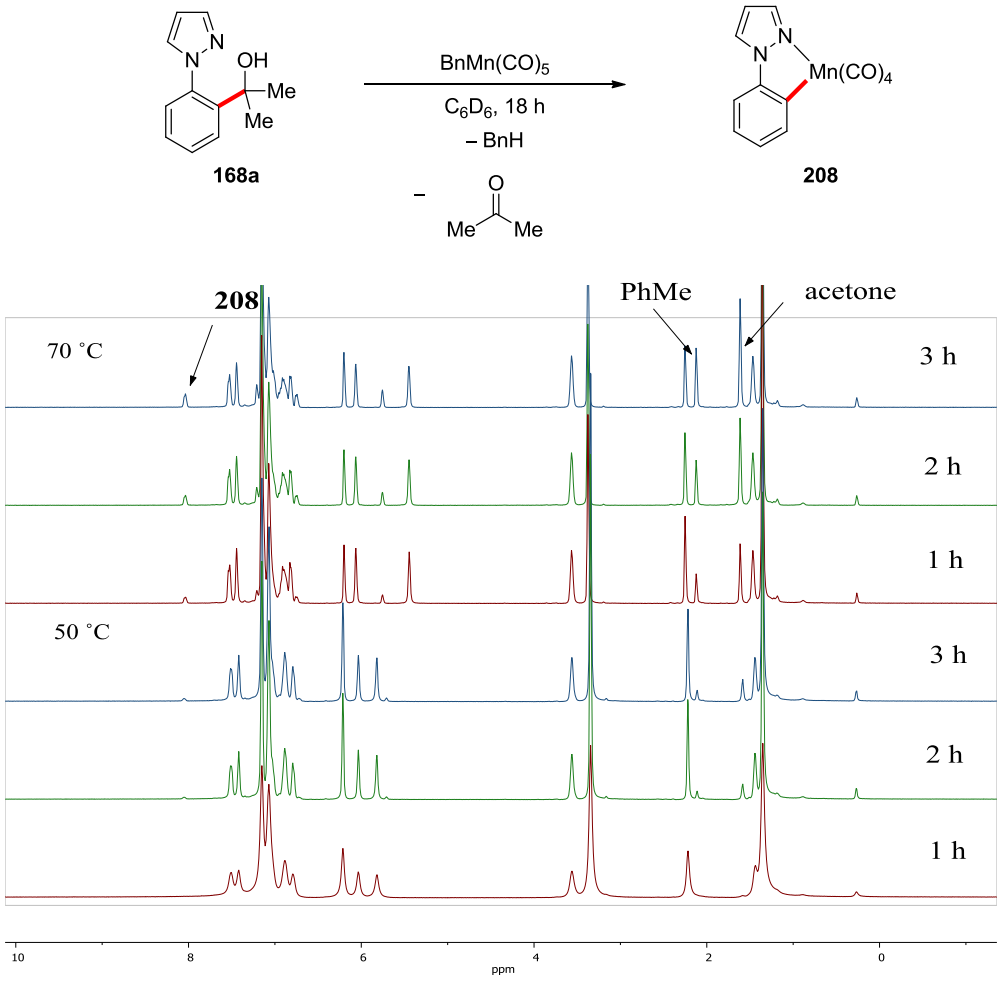


$[D]_1$-**168c** **8o** **74co**: 72%

A suspension of $[D]_1$-2-[4-methyl-2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol ($[D]_1$-**168c**) (54.1 mg, 0.25 mmol), ethynylbenzene (**8o**) (51.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (6.9 mg, 10.0 mol %) in H_2O (1.0 mL) was stirred at 140 °C for 16 h under N_2. After cooling to ambient temperature, the mixture was dried over Na_2SO_4, washed with EtOAc (30 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded $[D]_n$-**74co** (46.7 mg, 72%). The deuterium incorporation was determined by ^{1}H NMR spectroscopy.

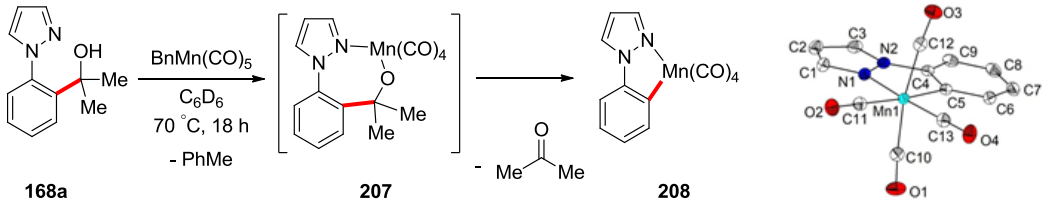


^{1}H NMR Studies: Temperature Dependence on the C–C Cleavage



Preparation of the sample: inside glovebox, an oven dried NMR tube was charged with 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (10.2 mg, 0.05 mmol), $BnMn(CO)_5$ (14.3 mg, 0.05 mmol), 1,3,5-trimethoxybenzene (2.8 mg, 0.017 mmol) and C_6D_6 (0.6 mL). The tube was transferred out of the glove box and the reaction was monitored at 60, 120 and 180 min by ^{1}H NMR at 25, 50 and 70 °C. Toluene and acetone were progressively formed and quantified at 2.33 ppm and 1.55 ppm, respectively.

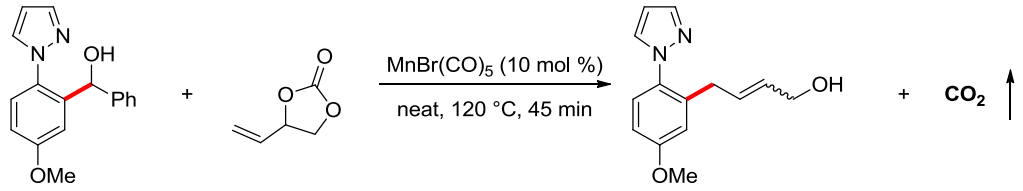
Synthesis of Complex C'



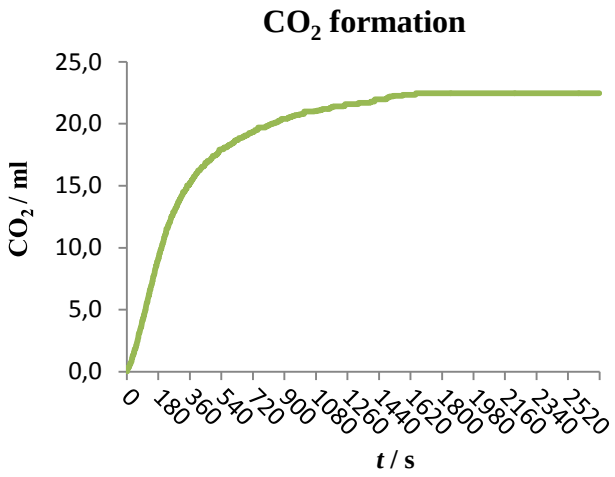
168a **207** **208**

A 10 mL oven-dried Schlenk-tube was charged with 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (70.1 mg, 0.25 mmol), $MnBn(CO)_5$ (71.6 mg, 0.25 mmol) and C_6D_6 (1.0 mL). The mixture was stirred at 70 °C for 18 h under N_2 in the glovebox. After cooling to ambient temperature, the solution was filtered to through a pipette packed with cotton wool, and removal of solvent under reduced pressure yielded a yellow solid (56.6 mg, 73%). Crystals suitable for X-ray diffraction were obtained by slow evaporation from *n*-hexane, providing light yellow crystals **208**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.11 (d, *J* = 2.7 Hz, 1H), 7.96–7.91 (m, 1H), 7.71 (d, *J* = 2.1 Hz, 1H), 7.36–7.09 (m, 3H), 6.51 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 219.7 (CO), 214.6 (CO), 211.9 (CO), 157.1 (C_q), 143.5 (C_q), 143.2 (CH), 142.5 (CH), 126.9 (CH), 126.4 (CH), 124.5 (CH), 111.8 (CH), 109.3 (CH).

Detection of the CO_2 Formation

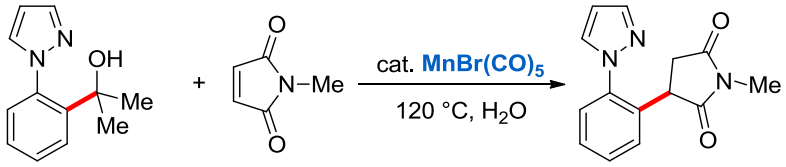


168d' **110a** **111da**: 66%



A 10 mL oven-dried Schlenk-tube was charged with [5-methoxy-2-(1*H*-pyrazol-1-yl)phenyl](phenyl)methanol (**168d'**) (280.3 mg, 1.0 mmol), 4-vinyl-1,3-dioxolan-2-one (**110a**) (228.2 mg, 2.0 mmol), $MnBr(CO)_5$ (27.5 mg, 10 mol %). The mixture was connected to a gas detection system (GM5-KONT). Subsequently, the reaction was placed in a preheated oil bath at 120 °C. The generation of CO_2 was detected.

Kinetic Analysis

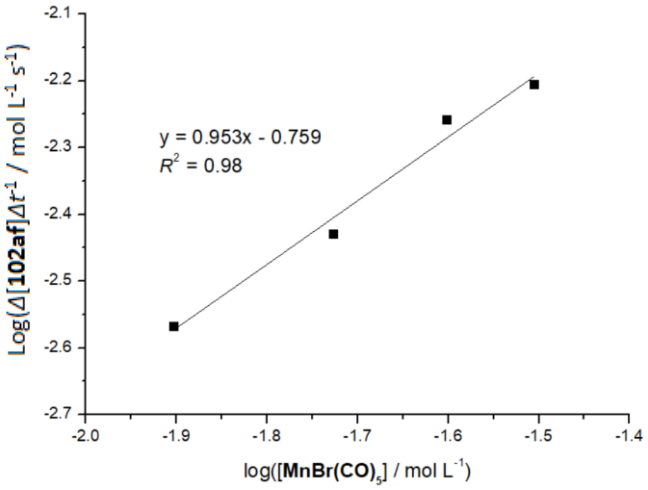


168a **11f** **102af**

Order with respect to [$MnBr(CO)_5$]

The reaction order with respect to [$MnBr(CO)_5$] was examined using the initial rate method.[11] A Schlenk-tube was charged with 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.50 mmol), [$MnBr(CO)_5$] (5.0, 7.5, 10.0, 12.5 mol %) and 1,3,5-trimethoxybenzene (14.0 mg, 0.083 mmol). H_2O (1.0 mL) was added and the mixture was stirred at 120 °C. Six parallel reactions with the same amount of $MnBr(CO)_5$ were performed. A reaction was stopped every 5 min and cooled to 0 °C immediately. The mixture was diluted with EtOAc (1.0 mL), filtered through a short plug of silica gel and analyzed by gas chromatography.

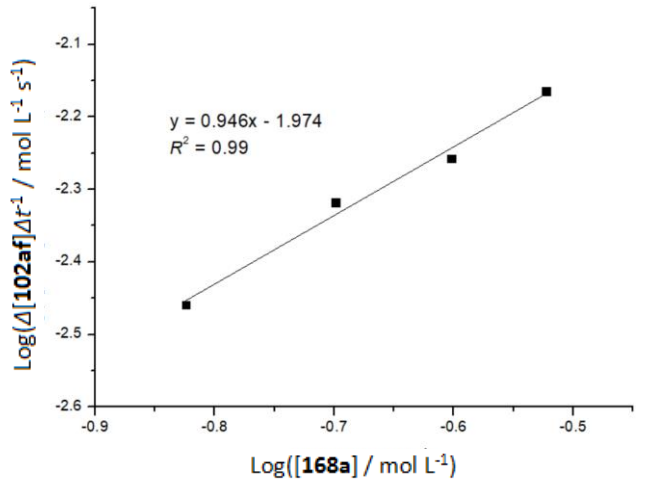
$MnBr(CO)_5$ / mol %	Δ[**102af**] Δt^{-1}/ 10^{-3} mol L^{-1} s^{-1}	log(c / mol L^{-1})	log(Δ[**102af**] Δt^{-1}/ mol L^{-1} s^{-1})
5.0	2.71	-1.90	-2.57
7.5	3.73	-1.73	-2.43
10.0	5.53	-1.60	-2.26
12.5	6.24	-1.51	-2.20



Order with respect to 168a

The reaction order with respect to **168a** was examined using the initial rate method.[9] A Schlenk-tube was charged with 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (0.15, 0.20, 0.25, 0.30 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (55.6 mg, 0.5 mmol), [$MnBr(CO)_5$] (6.9 mg, 0.025 mmol) and 1,3,5-trimethoxybenzene (14.0 mg, 0.083 mmol). H_2O (1.0 mL) was added and the mixture was stirred at 120 °C. Six parallel reactions with the same amount of **168a** were performed. A reaction was stopped every 5 min and cooled to 0 °C immediately. The mixture was diluted with EtOAc (1.0 mL), filtered through a short plug of silica gel and analyzed by gas chromatography.

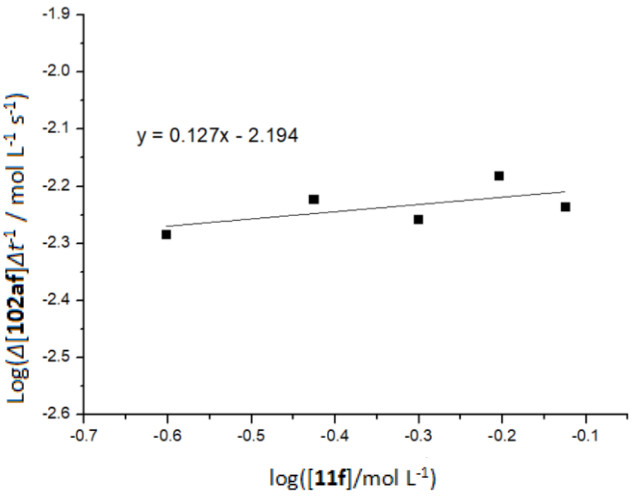
168a / mmol	Δ[**102af**] Δt^{-1}/ 10^{-3} mol L^{-1} s^{-1}	log(c / mol L^{-1})	log(Δ[**102af**] Δt^{-1}/ mol L^{-1} s^{-1})
0.15	2.46	-0.82	-2.46
0.20	4.80	-0.70	-2.32
0.25	5.53	-0.60	-2.26
0.30	6.84	-0.52	-2.17



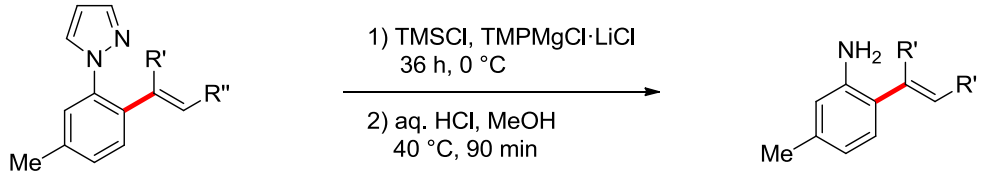
Order with respect to 11f

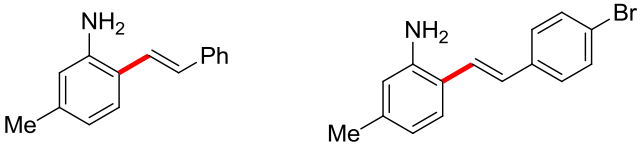
The reaction order with respect to **11f** was examined using the initial rate method.[9] A Schlenk-tube was charged with 2-[2-(1*H*-pyrazol-1-yl)phenyl]propan-2-ol (**168a**) (50.6 mg, 0.25 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (**11f**) (1.0, 1.5, 2.0, 2.5, 3.0 equiv), [$MnBr(CO)_5$] (6.9 mg, 0.025 mmol) and 1,3,5-trimethoxybenzene (14.0 mg, 0.083 mmol). H_2O (1.0 mL) was added and the mixture was stirred at 120 °C. Six parallel reactions with the same amount of **11f** were performed. A reaction was stopped every 5 min and cooled to 0 °C immediately. The mixture was diluted with EtOAc (1.0 mL), filtered through a short plug of silica gel and analyzed by gas chromatography.

11f / equiv	Δ[**102af**] Δt^{-1}/ 10^{-3} mol L^{-1} s^{-1}	log(c / mol L^{-1})	log(Δ[**102af**] Δt^{-1}/ mol L^{-1} s^{-1})
1.0	5.21	-0.60	-2.28
1.5	6.00	-0.43	-2.22
2.0	5.53	-0.30	-2.26
2.5	6.60	-0.20	-2.18
3.0	5.81	-0.13	-2.24



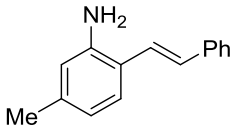
Removal of Pyrazole Group



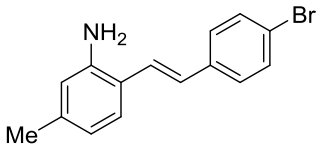


209a: 72% **209b**: 53% **209c**: 59%

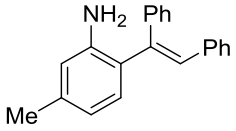
To a solution of **74** (1.0 mmol) and TMSCl (217.3 mg, 2.0 mmol) in THF (5.0 mL) was added TMPMgCl·LiCl in THF (1.0 M, 4.0 mmol) dropwise, and the mixture was stirred for 36 h at 0 ºC. Then, water was added, and the mixture was then extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude material was dissolved in MeOH (30 mL), mixed with aq. HCl 2M (15 mL) and stirred for 1.5 h at 40 ºC. After this period, the mixture was neutralized with saturated aq. $NaHCO_3$ (15 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1→20/1) yielded **209**.



(*E*)-5-Methyl-2-styrylaniline (209a) (150.5 mg, 72% yield) White solid, **M.p.** = 79–81 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.49 (d, *J* = 7.4 Hz, 2H), 7.43–7.28 (m, 3H), 7.27–7.20 (m, 1H), 7.14 (d, *J* = 16.1 Hz, 1H), 6.95 (d, *J* = 16.1 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 6.54 (s, 1H), 3.75 (brs, 2H), 2.28 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 143.8 (C_q), 138.7 (C_q), 137.8 (C_q), 129.3 (CH), 128.6 (CH), 127.3 (CH), 127.1 (CH), 126.3 (CH), 124.2 (CH), 121.1 (C_q), 120.1 (CH), 116.9 (CH), 21.2 (CH_3). **IR** (ATR) *v* = 3437, 3360, 3031, 1609, 1505, 1343, 966, 800, 753, 689 cm^{-1}. **MS** (ESI) m/z (relative intensity) 210 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{15}H_{16}N$ $[M+H]^+$: 210.1277, found: 210.1277.



(*E*)-2-(4-Bromostyryl)-5-methylaniline (209b) (152.7 mg, 53% yield) Pale yellow solid, **M.p.** = 124–125 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 16.1 Hz, 1H), 6.86 (d, *J* = 16.1 Hz, 1H), 6.62 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.54 (s, 1H), 3.84 (brs, 2H), 2.26 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 143.7 (C_q), 139.1 (C_q), 136.7 (C_q), 131.7 (CH), 127.9 (CH), 127.8 (CH), 127.1 (CH), 124.9 (CH), 121.0 (C_q), 120.8 (C_q), 120.3 (CH), 117.1 (CH), 21.3 (CH_3). **IR** (ATR) *v* = 3433, 3357, 1612, 1484, 1268, 1072, 970, 867, 815, 511 cm^{-1}. **MS** (ESI) m/z (relative intensity) 288 (100) $[M+H]^+$ (^{79}Br), 290 (98) $[M+H]^+$ (^{81}Br). **HR-MS** (ESI) m/z calcd for $C_{15}H_{15}{}^{79}BrN$ $[M+H]^+$: 288.0382, found: 288.0384; m/z calcd for $C_{15}H_{15}{}^{81}BrN$ $[M+H]^+$: 290.0362, found: 290.0364.

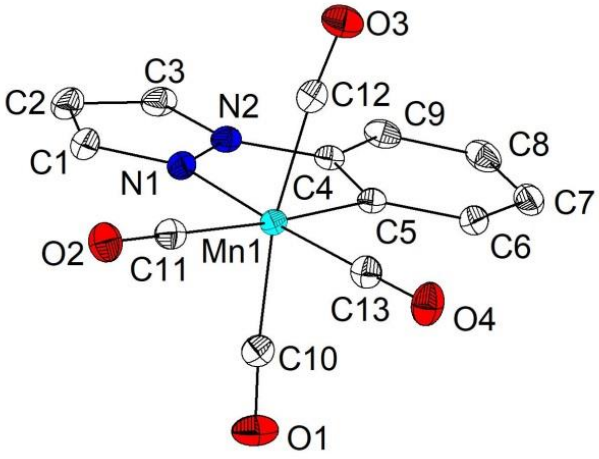


(*E*)-2-(1,2-Diphenylvinyl)-5-methylaniline (209c) (168.4 mg, 59% yield) White solid, **M.p.** = 142–143 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.28–7.22 (m, 5H), 7.19–7.12 (m, 3H), 7.12–7.07 (m, 2H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 6.59 (dd, *J* = 7.7, 1.7Hz, 1H), 6.50–6.47 (m, 1H), 3.54 (brs, 2H), 2.28 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 144.1 (C_q), 140.7 (C_q), 139.9 (C_q), 138.8 (C_q), 137.4 (C_q), 131.0 (CH), 130.2 (CH), 129.7 (CH), 129.4 (CH), 128.6 (CH), 128.0 (CH), 127.5 (CH), 127.2 (C_q), 126.7 (CH), 119.2 (CH), 116.6 (CH), 21.2 (CH_3). **IR** (ATR) *v* = 3478, 3390, 1613, 1443, 1315, 1257, 1074, 777, 715 cm^{-1}. **MS** (ESI) m/z (relative intensity) 286 (100) $[M+H]^+$. **HR-MS** (ESI) m/z calcd for $C_{21}H_{20}N$ $[M+H]^+$: 286.1590, found: 286.1590.

Single-Crystal Structure Analysis

Crystal Data for $C_{13}H_7MnN_2O_4$ (*M* =310.15 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 8.5614(4) Å, *b* = 6.8901(3) Å, *c* = 21.4151(11) Å, *β* = 92.838(2) , *V* = 1261.70(10) Å^3, *Z* = 4, *T* = 99.97 K, μ(MoKα) = 1.060 mm^{-1}, D_{calc} = 1.633 g/cm^3, 18532 reflections measured (6.212 ≤ 2Θ ≤ 60.992), 3828 unique (R_{int} = 0.0179, R_{sigma} = 0.0147) which were used in all calculations. The final R_1 was 0.0213 (I >

2σ(I)) and wR_2 was 0.0596 (all data).



Molecular structure of 208 in the crystal. (Anisotropic displacement parameters are depicted at the 50 % probability level.)

Crystal data and structure refinement for 208:

Compound	**208**
Empirical formula	$C_{13}H_7MnN_2O_4$
Identification code	0455_CG_0m
Empirical formula	$C_{13}H_7MnN_2O_4$
Formula weight	310.15
Temperature/K	99.97
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.5614(4)
b/Å	6.8901(3)
c/Å	21.4151(11)
α/°	90
β/°	92.838(2)
γ/°	90
Volume/Å^3	1261.70(10)
Z	4
ρ_{calc}g/cm^3	1.633
μ/mm^{-1}	1.06
F(000)	624

Crystal size/mm^3	0.452 × 0.202 × 0.174
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.212 to 60.992
Index ranges	-11 ≤ h ≤ 12, -9 ≤ k ≤ 9, -30 ≤ l ≤ 30
Reflections collected	18532
Independent reflections	3828 [R_{int} = 0.0179, R_{sigma} = 0.0147]
Data/restraints/parameters	3828/0/181
Goodness-of-fit on F^2	1.056
Final R indexes [I>=2σ (I)]	R_1 = 0.0213, wR_2 = 0.0591
Final R indexes [all data]	R_1 = 0.0220, wR_2 = 0.0596
Largest diff. peak/hole / e Å^{-3}	0.44/-0.39

Bond lengths [Å] for 208:

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Mn1	N1	2.0351(8)	N1	C1	1.3368(12)
Mn1	C5	2.0584(9)	N2	C3	1.3538(12)
Mn1	C10	1.8630(10)	N2	C4	1.4179(12)
Mn1	C11	1.8423(10)	C1	C2	1.4003(15)
Mn1	C12	1.8546(11)	C2	C3	1.3770(16)
Mn1	C13	1.8032(10)	C4	C5	1.3992(12)
O1	C10	1.1321(13)	C4	C9	1.3889(13)
O2	C11	1.1408(13)	C5	C6	1.3998(13)
O3	C12	1.1361(13)	C6	C7	1.3944(14)
O4	C13	1.1451(13)	C7	C8	1.3889(15)
N1	N2	1.3588(11)	C8	C9	1.3860(15)

Bond angles [°] for 208:

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N1	Mn1	C5	79.10(3)	C3	N2	N1	110.99(8)
C10	Mn1	N1	91.87(4)	C3	N2	C4	132.88(9)

C10	Mn1	C5	86.35(4)	N1	C1	C2	110.27(9)
C11	Mn1	N1	92.24(4)	C3	C2	C1	105.62(9)
C11	Mn1	C5	171.34(4)	N2	C3	C2	107.11(9)
C11	Mn1	C10	93.88(4)	C5	C4	N2	114.95(8)
C11	Mn1	C12	95.85(4)	C9	C4	N2	121.04(8)
C12	Mn1	N1	91.87(4)	C9	C4	C5	124.01(9)
C12	Mn1	C5	84.65(4)	C4	C5	Mn1	114.01(6)
C12	Mn1	C10	169.43(4)	C4	C5	C6	115.46(8)
C13	Mn1	N1	172.85(4)	C6	C5	Mn1	130.52(7)
C13	Mn1	C5	93.77(4)	C7	C6	C5	121.83(9)
C13	Mn1	C10	87.16(4)	C8	C7	C6	120.42(9)
C13	Mn1	C11	94.89(4)	C9	C8	C7	119.63(9)
C13	Mn1	C12	87.91(4)	C8	C9	C4	118.62(9)
N2	N1	Mn1	115.76(6)	O1	C10	Mn1	175.19(9)
C1	N1	Mn1	138.22(7)	O2	C11	Mn1	178.43(9)
C1	N1	N2	106.01(8)	O3	C12	Mn1	175.27(9)
N1	N2	C4	116.11(7)	O4	C13	Mn1	177.70(9)

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Curriculum Vitae

Personal Information

Name:	Hui Wang
Date of Birth:	03.10.1987
Place of Birth:	Hefei, Anhui (P. R. China.)
Gender:	Male
Nationality:	Chinese

Academic Education

10/2014-03/2019 **PhD Candidate in Organic Chemistry**

Institut für Organische und Biomolekulare Chemie,

Georg-August-Universität Göttingen

Supervisor: Prof. Dr. Lutz Ackermann

Thesis: Cobalt(III)- and Manganese(I)-Catalyzed C–H and C–C Activations

09/2011-07/2014 **M. Sc. in Organic Chemistry**

College of Chemistry and Molecular Engineering

Zhengzhou University

Supervisor: Prof. Dr. Xiuling Cui

Thesis: Direct Dimerization and Phosphonation of Heteroaromatic Compounds under Metal- and External Oxidant- Free Conditions

09/2007-07/2011 **B.Sc. in Chemistry**

Department of Chemistry

Zhengzhou University

Conferences

24-29/09, 2017	Poster of the 1st Summer School on Organic Catalysis for Energy Conversion, Göttingen, Germany.
19-20/09, 2016	Poster of the 4th NikaS Symposium, TU Braunschweig, Germany.
17-20/10, 2013.	8th National Conference on Organic Chemistry, Chongqing, China.

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(+ Equal contribution)