Ruthenium- and Cobalt-Catalyzed Chelation-Assisted C−H Functionalizations

Dissertation

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Contents

Abbreviations

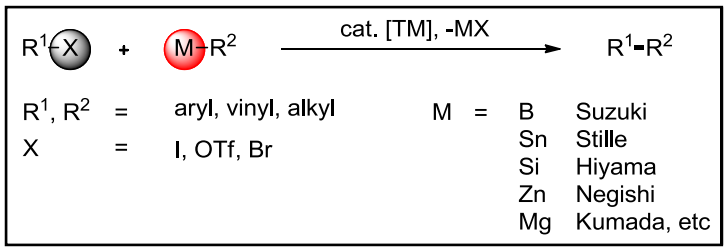
Ac	acetyl
Ad	adamantly
Alk	alkyl
AMLA	ambiphilic metal-ligand activation
aq.	aqueous
Ar	aryl
ARBs	angiotensin-II-receptor blockers
atm	*atmospheric pressure*
Bn	benzyl
Bu	butyl
calc.	calculated
CAN	ceric ammonium nitrate
cat.	catalyst
CMD	concerted-metalation-deprotonation
conv.	conversion
Cp*	pentamethylcyclopentadienyl
Cy	cyclohexyl
d	doublet
DCE	1,2-dichloroethane
dd	doublet of doublet
DG	directing group
DMA	*N*,*N*-dimethylacetamide
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
DMPU	*N,N'*-dimethyl-*N,N'*-propylene urea
dt	doublet of triplet
Ed.	editor
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
FG	functional group
g	gram
GC	gas chromatography
h	hour
Het	hetero(aryl)
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	Hertz
i	*iso*
IES	intramolecular electrophilic
J	coupling constant
KIE	kinetic isotope effect
L	ligand
m	meta
m	multiplet
M	molar, metal
$[M]^+$	molecular ion peak
Me	methyl
Mes	mesityl
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mmol	millimol
M. p.	melting point
MPV	membrane pump vacuum
MS	mass spectrometry
m/z	mass-to-charge ratio
MVK	methyl vinyl ketone
n	*normal*
NHC	*N*-heterocyclic carbene
NMP	*N*-methylpyrrolidinone
Ph	phenyl
Piv	pivaloyl
PMB	*para*-methoxybenzyl
PMP	*para*-methoxyphenyl
py	pyridyl
PyO	2-aminopyridine-1-oxide
pym	pyrimidyl
Pyr	pyrrole
Q	quinoline
r	removable
R_L	R_{Large}
R_S	R_{Small}
δ	chemical shift
T	temperature
TBS	*tert*-butyldimethylsilyl
THF	Tetrahydrofuran
TM	transition metal
Ts	*para*-toluenesulfonyl
X	(pseudo)halide

	substitution		
IPr	1,3-bis(2,6-diisopropylphenyl)	XPhos	2-dicyclohexylphosphino-2',4',6'-triiso propylbiphenyl
IR	infrared spectroscopy		

1 Introduction

1.1 Transition-Metal-Catalyzed C−H Functionalizations

A long-standing challenge in synthetic organic chemistry is the development of methods for the direct conversion of unactivated carbon−hydrogen bonds into carbon−carbon, carbon−nitrogen, carbon−halogen, or carbon−oxygen bonds among others. Mild and selective transformations of this type will undoubtedly obtain a wide range of potential applications in varies applied fields. During the last few decades of the previous century, a new family of C−C bond forming reactions based on transition-metal catalysts has emerged as a powerful tool and experienced a remarkable progress which played a vital role in the synthesis of pharmaceuticals, natural products, agrochemicals, polymers and feedstock commodity chemicals.[1] Among them, transition-metal-catalyzed cross-coupling reactions are arguably the most prominent approach to the construction of C−C bonds (Scheme 1.1).[1a,2]



Scheme 1.1. Transition-metal-catalyzed cross-coupling reactions.

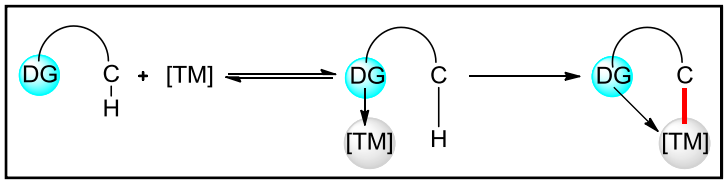
However, the formation of such bonds relies on prefunctionalized starting materials, such as organoboron, organozinc or organotin compounds, which add costly chemical steps to the overall synthesis. Circumventing the disadvantages of the traditional approaches will not only improve atom economy,[3] but also increase the overall efficiency of multistep synthetic sequences. In recent decades, transition-metal-catalyzed C−H bond functionalizations became

[1] a) *Transition Metals for Organic Synthesis* (Eds.: M. Beller and C. Bolm), 2nd ed., Wiley-VCH, Weinheim, **2004**; b) *Metal-Catalyzed Cross-Coupling Reactions and More*; (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, **2014**.

[2] a) Metal-Catalyzed Cross-Coupling Reactions, (Eds: A. de Meijere and F. Diederich), 2nd ed. Wiley-VCH, Weinheim, **2004**. For selected reviews on C–C bond formation via traditional cross-coupling reactions, see: b) C. C. C. J. Seechum, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062–5085; c) H. Li, C. C. C. J. Seechum, T. J. Colacot, *ACS Catal.* **2012**, *2*, 1147–1164; d) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A. M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev.* **2011**, *111*, 1346–1416; e) G. Cahiez, A. Moyeux, *Chem. Rev.* **2010**, *110*, 1435–1462; f) A. Roglans, A. Pla-Quintana, M. Moreno-Mañas, *Chem. Rev.* **2006**, *106*, 4622–4643; g) J. P. Corbet, G. Mignani, *Chem. Rev.* **2006**, *106*, 2651–2710, and references cited therein.

[3] B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695–705.

an attractive strategy to streamline chemical synthesis.[4] Due to its high atom- and step-economy, intensive research efforts have led to the remarkable progress for challenging C−H bond functionalization.[5]



Scheme 1.2. Regioselective intermolecular cleavage of C−H bonds through the use of a directing group (DG).

Direct C−H bond functionalizations are limited by mainly two challenging issues: (i) The requirement to control site-selectivity of the C−H functionalization in a molecule that contains various potentially reactive C−H bond; and (ii) the requirement to achieve selective functionalization of a single C−H bond within a complex molecule. The most common strategy involves the use of substrates that contain a directing group (DG). These directing groups coordinate to the metal center and selectively bring the metal to the proximity of a C−H bond (Scheme 1.2)[6] and subsequently allow its activation and cleavage. Many transition metals, including, ruthenium, rhodium, palladium and cobalt, undergo stoichiometric cyclometalations.[5,6b,7] By far, a large remarkable progress in organometallic chemistry has set the stage for the development of increasingly viable metal catalysts for C−H bond

[4] a) *Handbook of C—H Transformations* (Ed: G. Dyker), Wiley-VCH, Weinheim, **2005**; b) F.Kakiuchi, N. Chatani, *Adv. Synth. Catal*. **2003**, *345*, 1077–1101; c) M. Miura, M. Nomura, *Top. Curr. Chem*. **2002**, *219*, 212–237; d) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev*. **2002**, *102*, 1731-1770; e) L. Ackermann, *Synlett* **2007**, *4*, 507–526.

[5] a) *Modern Arylation Methods*, (Ed: L. Ackermann), Wiley-VCH, Weinheim, **2009**; For recent representative general reviews on C—H bond functionalizations, see: b) J. Mo, L. Wang, Y. Liu, X. Cui, *Synthesis* **2015**, *47*, 439–459; c) G. Qiu, J. Wu, *Org. Chem. Front*. **2015**, *2*, 169–178; d) J. Yang, *Org. Biomol. Chem*. **2015**, *13*, 1930-1941; e) L. Ackermann, *Org. Process Res. Dev*. **2015**, *18*, 260-269; f) F. Zhang, D. R. Spring, *Chem. Soc. Rev*. **2014**, *43*, 6906–6919; g) A. F. M. Noisier, M. A. Brimble, *Chem. Rev*. **2014**, *114*, 8775–8806; h) V. S. Thirunavukkarasu, S. I. Kozhushkov, L. Ackermann, *Chem. Commun*. **2014**, *50*, 29–39; i) L. Ackermann, *Acc. Chem. Res*. **2014**, *47*, 281–295; j) K. Gao, N. Yoshikai, *Acc. Chem. Res*. **2014**, *47*, 1208–1219; k) L. Ackermann, *J.Org. Chem*. **2014**, *79*, 8948-8954; l) J. J. Mousseau, A. B. Charrette, *Acc. Chem. Res*. **2013**, *46*, 412-424; m) K. M. Engle, T. S. Mei, M. Wasa, J. Q. Yu, *Acc. Chem. Res*. **2012**, *45*, 788–802; n) S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res*. **2012**, *45*, 936-946; o) J. Wencel-Delord, T. Droege, F. Glorius, *Chem. Soc. Rev*. **2011**, *40*, 4740–4761; p) C. S. Yeung, V. M. Dong, *Chem. Rev*. **2011**, *111*, 1215-1292; q) L. Ackermann, *Chem. Rev*. **2011**, *111*, 1315–1345; r) M. C. Willis, *Chem. Rev*. **2010**, *110*, 725-748; s) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev*. **2010**, *110*, 624-655; t) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev*. **2007**, *107*, 174–238; u) P. Sehnal, R. J. K. Taylor, I. J. S. Fairlamb, *Chem. Rev*. **2010**, *110*, 824–889, and the references therein.

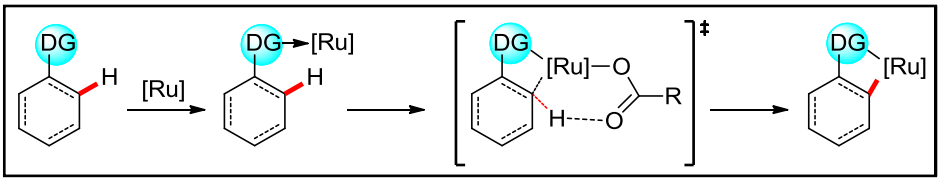
[6] a) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed*. **2009**, *48*, 9792–9826; b) L. Ackermann, *Top. Organomet. Chem*. 2007, *24*, 35–60; c) I. Omae, *Coord. Chem. Rev*. **2004**, *248*, 995–1023.

[7] a) N. Kuhl, N. Schroeder, F. Glorius, *Adv. Synth. Catal*. **2014**, *356*, 1443–1460; b) S. D. Sarkar, W. Liu, S. I. Kozhushkov, L. Ackermann, *Adv. Synth. Catal*. **2014**, *356*, 1461–1479; c) S. I. Kozhushkov, L. Ackermann, *Chem. Sci*. **2013**, *4*, 886–896; d) T. S. Mei, L. Kou, S. Ma, K. M. Engle, J. Q. Yu, *Synthesis* **2012**, *44*, 1778–1791, and references cited therein.

functionalization reactions.[5–7]

1.2 Carboxylate-Assisted Ruthenium-Catalyzed C–H Functionalizations

Looking at the development in the area of utilizing unreactive C–H bonds in chemical synthesis *via* transition metal catalysis, one can easily realize that the majority of achievements in C–H functionalization reactions rely on noble metal catalysts, typically based on palladium, rhodium or ruthenium.[5b–5i,5l–5u,8] The pivotal metalation step of C–H bond activation reactions, was proposed to proceeded by oxidative addition, electrophilic substitution, σ-bond metathesis or 1,2-addition.[5i,5q] A few early reports indicated another potential possibility, which suggests that the reactions proceed *via* base-assisted metalation.[5i,5q] An early stoichiometric cyclometalation reactions of ruthenium was disclosed by Davies and coworkers, and revealed the beneficial effect of NaOAc.[9] However, the first ruthenium(II)-catalyzed C–H bond functionalization with carboxylate assistance was reported by Ackermann in 2008 (Scheme 1.3).[10] Since then, the use of various carboxylates as cocatalytic additives for ruthenium catalysis became popular and widespread.



Scheme 1.3. Proposed rationalization for base-assisted C–H ruthenation.

1.2.1 Carboxylate-Assisted Ruthenium-Catalyzed Oxidative Alkyne Annulations and Oxidative Alkenylations *via* C–H Functionalization

Since Ackermann and coworkers suggested that ruthenium-catalyzed direct arylation involves reversible C–H bond activations *via* carboxylate-assisted and subsequent deprotonative ruthenations, carboxylates were also explored as cocatalytic additives for ruthenium-catalyzed oxidative C–H bond functionalizations[11]. The Ackermann group developed ruthenium

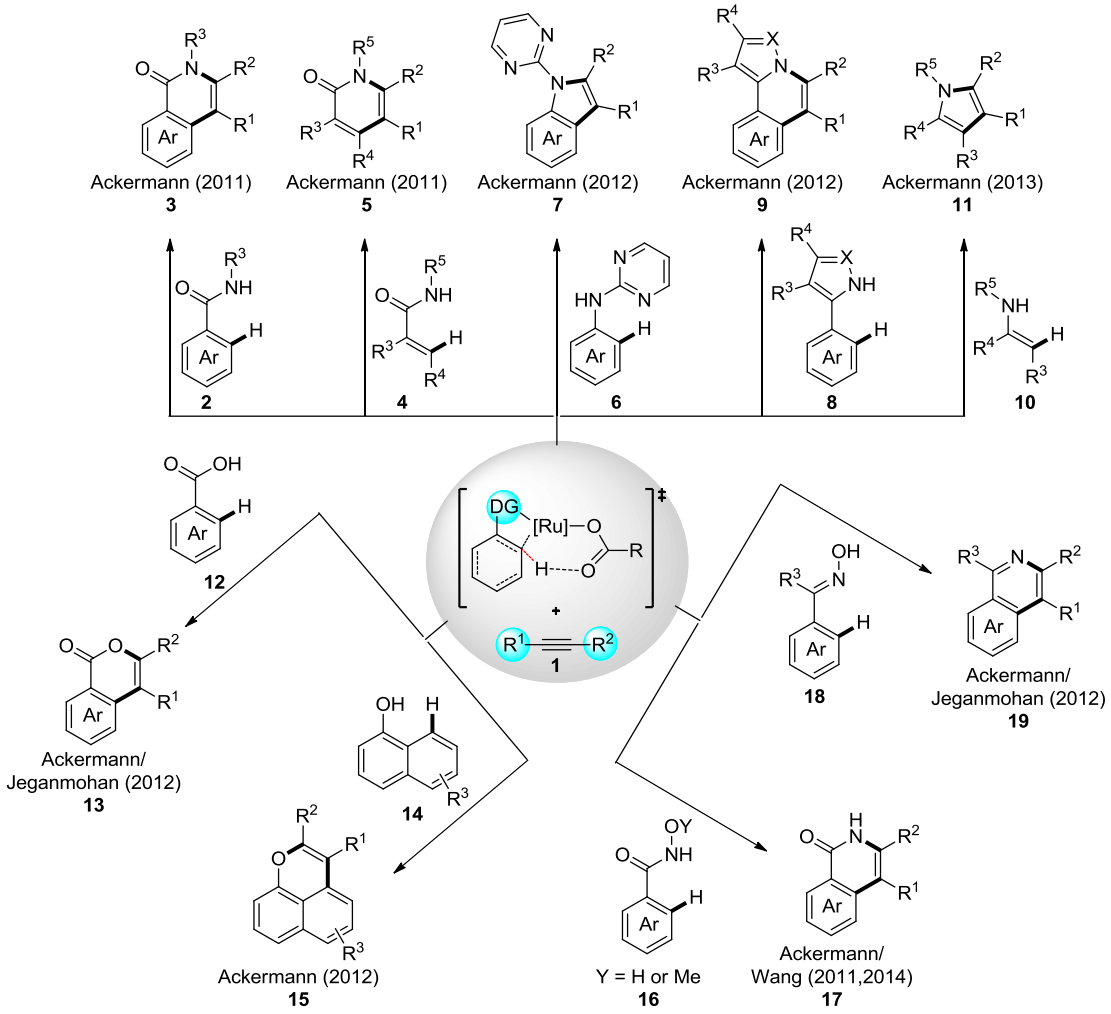
[8] Recent examples for C–H functionalizations. **Pd**: a) K. S. L. Chan, H.-Y. Fu, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, *137*, 2042-2046. **Rh**: b) S. Yu, S. Liu, Y. Lan, B. Wan, X. Li, *J. Am. Chem. Soc.* **2015**, *137*, 1623–1631; c) G. Zhang, H. Yu, G. Qin, H. Huang, *Chem. Commun.* **2014**, *50*, 4331–4334. **Ru**: d) S. Warratz, C. Kornhaass, A. Cajaraville, B. Niepoetter, D. Stalke, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, 5513–5517; e) F. Yang, K. Rauch, K. Kettelhoit, L. Ackermann, *Angew. Chem. Int. Ed.* **2014**, *53*, 11285–11288.

[9] D. L. Davies, O. Al-Duaij, J. Fawcett, M. Giardiello, S. T. Hilton, D. R. Russell, *Dalton Trans.* **2003**, 4132–4138.

[10] L. Ackermann, R. Vicente, A. Althammer, *Org. Lett.* **2008**, *10*, 2299–2302.

[11] a) H. Weissman, X. Song, D. Milstein, *J. Am. Chem. Soc.* **2001**, *123*, 337–338; b) T. Ueyama, S. Mochida, T.

catalytic systems for oxidative alkyne annulations, with the assistance of various directing groups. As a consequence, the first ruthenium-catalyzed oxidative annulations of alkynes through C−H and N−H bond cleavages for the synthesis of bioactive isoquinolones were reported in 2011.[12]



Scheme 1.4. The synthesis of heterocycles through alkyne annulations *via* ruthenium-catalyzed C−H bond cleavage.

Further mechanistic studies proposed the ruthenium-catalyzed oxidative annulations to proceed by an initial carboruthenation *via* acetate-assisted C−H bond cleavage, followed by migratory insertion, reductive elimination and reoxidation of the ruthenium(0) species.[5i,12] Thereafter, additional evidence was provided, through synthesis and isolation of key intermediates.[8f,13] Notably, during the last few years, the scope of alkyne annulations by

Fukutani, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2011**, *13*, 706–708.

[12] L. Ackermann, A. V. Lygin, N. Hofmann, *Angew. Chem. Int. Ed.* **2011**, *50*, 6379–6382.

[13] a) B. Li, H. Feng, N. Wang, J. Ma, H. Song, S. Xu, B. Wang, *Chem. Eur. J.* **2012**, *18*, 12873–12879; b) B. Li, T.

C−H/Het−H bond functionalization have witnessed significant progress in the following aspects: oxidative alkyne annulations through (i) C−H/N−H bonds cleavages;[12, 14] (ii) C−H/O−H bonds cleavages; [15] (iii) C−H/N−O bonds cleavages. [16] Therefore, ruthenium(II)-catalyzed annulations of alkynes are among the most important approaches for the preparation of heterocyclic molecules (Scheme 1.4).

In the meantime, carboxylate-assisted ruthenium-catalyzed direct oxidative alkenylations were also developed in recent years, although the first ruthenium-catalyzed oxidative alkenylation can be traced back to 2001, as reported by Milstein and coworkers. They employed molecular oxygen as the terminal oxidant, and obtained a rather narrow and limited scope under these harsh reaction conditions.[11a] A carboxylate-assisted procedure for the successful ruthenium-catalyzed direct alkenylation of heteroaromatic[11b] and aromatic[17] acids was reported in 2011 by Miura and coworkers as well as by Ackermann and coworkers. Further mechanistic studies showed the importance of acetates to be dominated for efficient C−H bond metalations.[17] Thereafter, the groups of Miura and Ackermann independently revealed the powerful ruthenium-catalyzed direct oxidative alkenylation of *N,N*-di-[18] and *N*-monoalkylated benzamides **2**.[19]

The direct alkenylation of acrylamides **4** with alkenes was reported by Zhang and Loh.[20] Similarly, Wang and coworkers described an alkenylation reaction of *N*-methoxybenzamides **2** bearing an internal oxidizing directing group.[21]

Roisnel, C. Darcel, P. H. Dixneuf, *Dalton Trans*. **2012**, *41*, 10934–10937.

[14] a) L. Ackermann, A. V. Lygin, N. Hofmann, *Org. Lett*. **2011**, *13*, 3278–3281; b) L. Ackermann, A. V. Lygin, *Org. Lett*. **2012**, *14*, 764–767; c) L. Ackermann, L. Wang, A. V. Lygin, *Chem. Sci*. **2012**, *3*, 177–180; d) W. Ma, K. Graczyk, L. Ackermann, *Org. Lett*. **2012**, *14*, 6318–6321; e) L. Wang, L. Ackermann, *Org. Lett*. **2013**, *15*, 176–179.

[15] a) M. Deponti, S. I. Kozhushkov, D. S. Yufit, L. Ackermann, *Org. Biomol. Chem*. **2013**, *11*, 142–148, and references cited therein; b) L. Ackermann, J. Pospech, K. Graczyk, K. Rauch, *Org. Lett*. **2012**, *14*, 930–933; c) R. K. Chinnagolla, M. Jeganmohan, *Chem. Commun*. **2012**, *48*, 2030–2032; d) V. S. Thirunavuarasu, M. Donati, L. Ackermann, *Org. Lett*. **2012**, *14*, 4210–4213.

[16] a) L. Ackermann, S. Fenner, *Org. Lett*. **2011**, *13*, 6548–6551; b) B. Li, H. Feng, S. Xu, B. Wang, *Chem. Eur. J*. **2011**, *17*, 12573–12577; c) K. Parthasarathy, N. Senthilkumar, J. Jayakumar, C.-H. Cheng, *Org. Lett*. **2012**, *14*, 3478–3481; d) C. Kornhaass, J. Li, L. Ackermann, *J. Org. Chem*. **2012**, *77*, 9190–9198; e) R.K. Chinnagolla, S. Pimparkar, M. Jeganmohan, *Org. Lett*. **2012**, *14*, 3032–3035; f) F. Yang, L. Ackermann, *J. Org. Chem*. **2014**, *79*, 12070–12082.

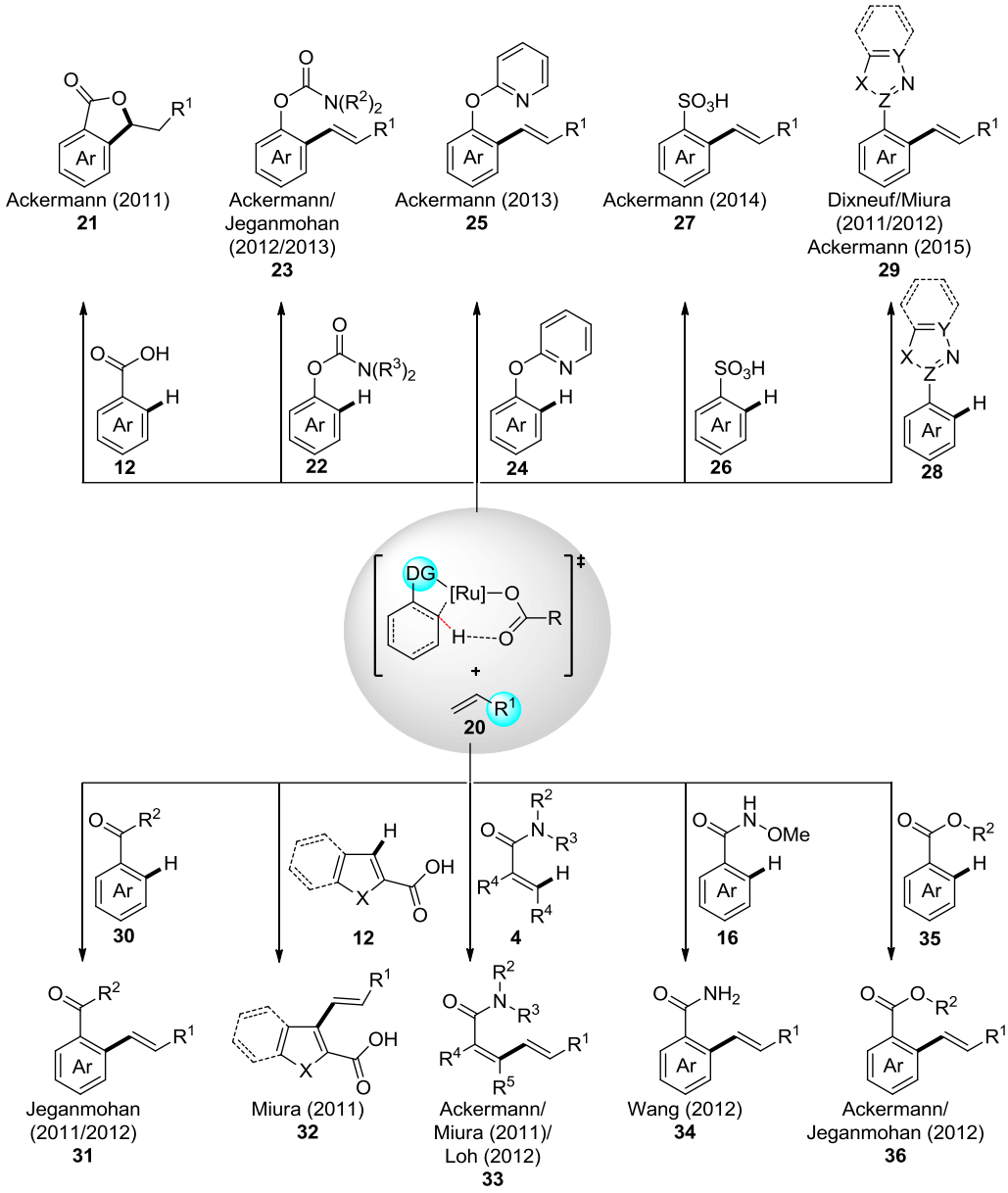
[17] L. Ackermann, J. Pospech, *Org. Lett*. **2011**, *13*, 4153–4155.

[18] Y. Hashimoto, T. Ortloff, K. Hirano, T. Satoh, C. Bolm, M. Miura, *Chem. Lett*. **2012**, *41*, 151–153.

[19] L. Ackermann, L. Wang, R. Wolfram, A. V. Lygin, *Org. Lett*. **2012**, *14*, 728–731.

[20] J. Zhang, T.-P. Loh, *Chem. Commun*. **2012**, *48*, 11232–11234.

[21] B. Li, J. Ma, N. Wang, H. Feng, S. Xu, B. Wang, *Org. Lett*. **2012**, *14*, 736–739.



Scheme 1.5. Carboxylate-assisted ruthenium-catalyzed oxidative C−H bond alkenylations.

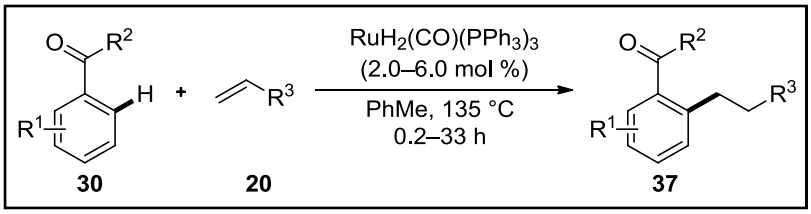
Based on these contributions, the following research for the mentioned ruthenium(II) catalytic system came to extend the scope of directing groups, to include ester (**35**),[22–23] ketone (**30**),[24] aldehyde,[25] carbamate (**22**),[26–27] 2-pyridyloxy (**24**),[28] sulfonic acid (**26**),[29] oxazole (**28**),[30]

[22] K. Graczyk, W. Ma, L. Ackermann, *Org. Lett*. **2012**, *14*, 4110–4113.
[23] K. Padala, S. Pimparkar, P. Madasamy, M. Jeganmohan, *Chem. Commun*. **2012**, *48*, 7140–7142.
[24] K. Padala. M. Jeganmhan, *Org. Lett*. **2011**, *13*, 6144–6147.
[25] K. Padala. M. Jeganmhan, *Org. Lett*. **2012**, *14*, 1134–1137.
[26] J. Li, C. Kornhaass, L. Ackermann, *Chem. Commun*. **2012**, *48*, 11343–11345.
[27] M. C. Reddy, M. Jeganmohan, *Eur. J. Org. Chem*. **2013**, 1150–1157.
[28] W. Ma, L. Ackermann, *Chem. Eur. J*. **2013**, *19*, 1150–1157.
[29] W. Ma, R. Mei, G. Tenti, L. Ackermann, *Chem. Eur. J*. **2014**, *20*, 15248–15251.
[30] B. Li, K. Devaraj, C. Darcel, P. Dixneuf, *Green Chem*. **2012**, *14*, 2706–2709.

triazole,[31] among others. (Scheme 1.5).[32]

1.2.2 Carboxylate-Assisted Ruthenium-Catalyzed Hydroarylations *via* C−H Bond Functionalization

As discussed above, the carboxylate-assisted ruthenium-catalyzed oxidative C−H bond functionalizations can be used as one of the reliable methods for C−C bond formation. Meanwhile, the developments of ruthenium-catalyzed hydroarylation reactions in an atom- and step-economical way, under mild reaction conditions were also achieved. Pioneering finding by Lewis, indicated the first *ortho*-hydroarylation of alkenes with phenol.[33] A further breakthrough was made in 1993 by Murai and coworkers, when they reported on the ruthenium(0)-catalyzed direct hydroarylation of alkenes **20** *via* chelation-assisted C−H bond activation in aromatic ketones **30** (Scheme 1.6).[34] The reaction can be considered to constitute an ideal pathway, not only in terms of atom- and step-economy, but also because of its high site-selectivity. A series of hydroarylation reactions were reported by Murai and coworkers in the following years,[35 – 36] including a direct alkylation with decorated vinylsilanes **20**, as reported by Trost.[37]



Scheme 1.6. Ruthenium(0)-catalyzed direct hydroarylation by Murai.

Subsequently, progress was made by Genet, Darses and coworkers utilizing a more flexible and practical $[RuCl_2(p\text{-cymene})]_2$ precursor, in association with sodium formiate and a

[31] C. Tirler, L. Ackermann, *Tetrahedron* **2015**, DOI:10.1016/j.tet.2015.02.033.

[32] a) Y. Hashimoto, T. Ueyama, T. Fukutani, K. Hirano, T. Satoh, M. Miura, *Chem. Lett*. **2011**, *40*, 1165–1166; b) P. B. Arockiam, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *Green Chem*. **2011**, *13*, 3075-3078; c) L.-Q. Zhang, S. Yang, X. Huang, J. You, F. Sodirectng, *Chem. Commun*. **2013**, *49*, 8830–8832; d) B. Li, J. Ma, W. Xie, H. Song, S. Xu, B. Wang, *J. Org. Chem*. **2013**, *78*, 9345–9353.

[33] L. N. Lewis, J. F. Smith, *J. Am. Chem. Soc.* **1986**, *108*, 2728–2735.

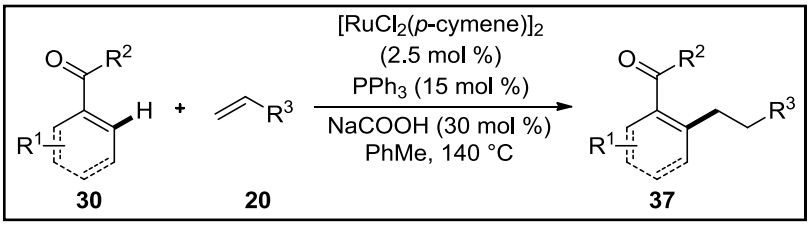
[34] S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Nature* **1993**, *366*, 529–531.

[35] a) M. Sonoda, F. Kakiuchi, A. Kamatani, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 109–110; b) F. Kakiuchi, M. Yamauchi, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 111–112; c) T. Sato, F. Kakiuchi, N. Chatani, S. Murai, *Chem. Lett.* **1998**, 893–894; d) F. Kakiuchi, T. Sato, M. Yanauchi, N. Chatani, S. Murai, *Chem. Lett*. **1999**, 19–20.

[36] a) F. Kakiuchi, T. Sato, K. Igi, N. Chatani, S. Murai, *Chem. Lett*, **2001**, 386–387. Selected reviews: b) J. R. Andreatta, B. A. McKeown, T. B. Gunnoe, *J. Organomet. Chem*. **2011**, *696*, 305–315; c) F. Kakiuchi, *Top. Organomet. Chem*. **2007**, 24, 1–33.

[37] B. M. Trost, K. Imi, I. W. Davies, *J. Am. Chem. Soc.* **1995**, *117*, 5371–5372.

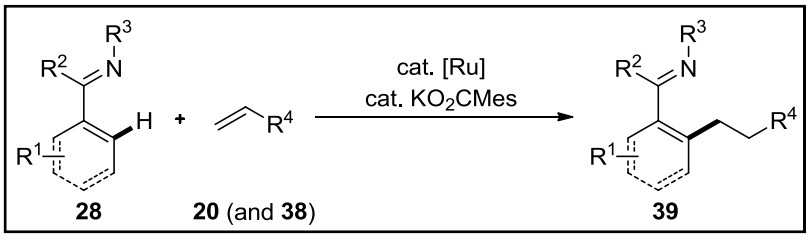
phosphine ligand (Scheme 1.7).[38]



Scheme 1.7. In-situ ruthenium(0) catalyst for hydroarylation by Genet and Darses.

Meanwhile, the Ackermann group disclosed a ruthenium-based catalytic system, consisting of $[RuCl_2(cod)]_n$ and XPhos, that promoted the addition of arenes to various methylenecyclopropanes **38**.[39]

Nevertheless, among the many strategies available, carboxylate-assisted ruthenium(II)-catalyzed C−H bond functionalizations were successfully utilized in the hydroarylations by Ackermann and coworkers in 2013.[40–41] The reaction unveiled a highly efficient and broadly applicable ruthenium(II)biscarboxylate catalyst for additions of C−H bonds to methylenecyclopanes and even unactivated alkenes (Scheme 1.8). Very recently, a highly efficient ruthenium-catalyzed α-alkylation of a C(sp^3)−H bonds in pyrrolidines was also reported by Ackermann and coworkers.[42]



Scheme 1.8. Carboxylate-assisted ruthenium(II)-catalyzed direct hydroarylation.

Despite these notable advances, the hydroarylation with olefins bearing functional groups remained challenging, especially those of more important families of acceptors, such as α,β-unsaturated acceptors. Moreover, sporadic early reports were limited to the use of rather

[38] a) R. Martinez, R. Chevalier, S. Darses, J. P. Genet, *Angew. Chem. Int. Ed*. **2006**, *45*, 8232–8235; b) R. Martinez, J. P. Genet, S. Darses, *Chem. Commun*. **2008**, 3855–3857; c) R. Martinez, M. O. Simon, R. Chevalier, C. Pautigny, J. P. Genet, S. Darses, *J. Am. Chem. Soc.* **2009**, *131*, 7887–7895; d) M.-O. Simon, R. Martinez, J.-P. Genet, S. Darses, *Adv. Synth. Catal*. **2009**, *351*, 153–157; e) M. O. Simon, R. Martinez, J. P. Genet, S. Darses, *J. Org. Chem*. **2010**, *75*, 208–210; f) M.-O. Simon, S. Darses, *J. Org. Chem*. **2013**, *78*, 9981–9985.

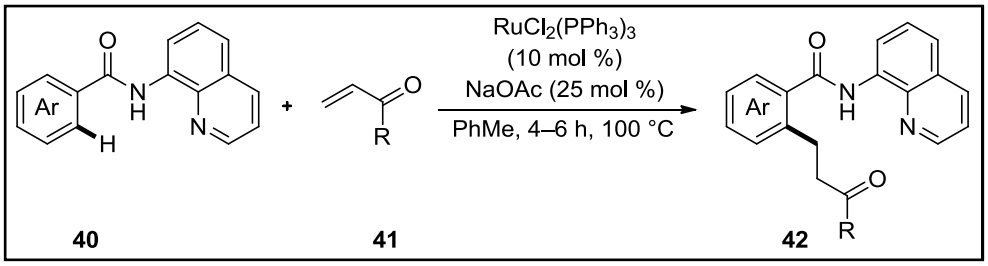
[39] a) S. I. Kozhushkov, D. S. Yufit, L. Ackermann, *Org. Lett*. **2008**, *10*, 3409–3412; b) L. Ackermann, S. I. Kozhushkov, D. S. Yufit, *Chem. Eur. J*. **2012**, *18*, 12068–12077.

[40] M. Schinkel, I. Marek, L. Ackermann, *Angew. Chem. Int. Ed*. **2013**, *52*, 3977–3980.

[41] M. Schinkel, J. Wallbaum, S.I. Kozhushkov, I. Marek, L. Ackermann, *Org. Lett*. **2013**, *15*, 4482–4484.

[42] M. Schinkel, L. Wang, K. Bielefeld, L. Ackermann, *Org. Lett*. **2014**, *16*, 1876–1879.

expensive[43] rhodium[44] or rhenium[45] catalysts. Until the introduction of bidentate-chelation assistance, Chatani and coworkers described a new ruthenium-catalyzed C−H hydroarylation of aromatic amides (**40**) with a wide range of *α,β*-unsaturated ketones (**41**) *via* bidentate-chelation assistance (Scheme 1.9).[46]



Scheme 1.9. Ruthenium(II)-catalyzed direct hydroarylation of aromatic amides **40** with *α,β*-unsaturated ketones **41**.

In spite of the significant progress achieved in the last two decades in the area of ruthenium-catalyzed direct hydroarylation, a great deal of work, such as improving the tolerance of a range of functional groups, still has to be done in this field of catalysis.

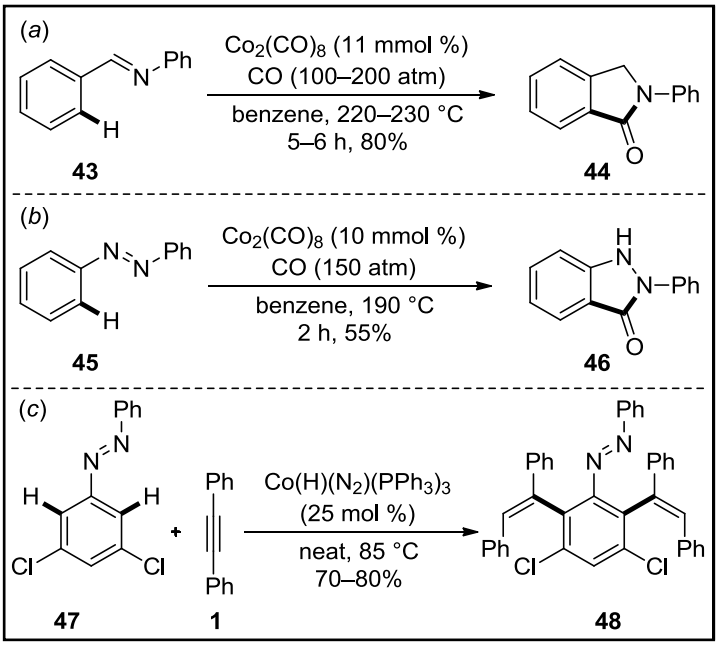
1.3 Cobalt-Catalyzed C−H Bond Functionalizations

Over the last few decades, most of the remarkable advances in transition metal-catalyzed C−H bond functionalization were achieved employing the expensive[43] second-row transition metals. The development of catalysts based on the naturally more abundant first-row transition metals and complexes, which would enable C−H bond functionalization to be accomplished under mild reaction conditions, would present a more activation strategy. Consequently, the use of 3d transition metal catalysts has witnessed considerable recent attention.[47]

Among the first-row transition metals, the notable power of cobalt salts as effective catalysts

[43] The price of transition metals: see a) http://www.platinum.matthey.com/; b) http://www.chemicool.com/ (20.05.2015).
[44] a) S. G. Lim, J. A. Ahn, C. H. Jun, *Org. Lett*. **2004**, *6*, 4687–4690; b) L. Yang, C. Correia, C. Li, *Org. Biomol. Chem*. **2011**, *9*, 7176–7179; c) L. Yang, B. Qian, H. Huang, *Chem. Eur. J*. **2012**, *18*, 9511–9515.
[45] Y. Kuninobu, Y. Nishina, K. Okaguchi, M. Shouho, K. Takai, *Bull. Chem. Soc. Jpn*. **2008**, *81*, 1393–1401.
[46] G. Rouquet, N. Chatani, *Chem. Sci*. **2013**, *4*, 2201–2208.
[47] a) B. Su, Z.-C. Cao, Z.-J. Shi, *Acc. Chem. Res*. **2015**, *48*, 886–896; b) E. Nakamura, T. Hatakeyama, S. Ito, K. Ishizuka, L. Ilies, M. Nakamura, *Org. React*. **2014**, *83*, 1–209; c) J. Yamaguchi, K. Muto, K. Itami, *Eur. J. Org. Chem*. **2013**, 19–30; d) N. Yoshikai, *Synlett* **2011**, 1047–1051; e) Y. Nakao, *Chem. Rec*. **2011**, *11*, 242–251; f) E. Nakamura, N. Yoshikai, *J. Org. Chem*. **2010**, *75*, 6061–6067; f) A. Kulkami, O. Daugulis, *Synthesis* **2009**, 4087–4109.

for homocouplings of Grignard reagents was pioneered by Kharasch and Fields in 1941.[48] The first example of cobalt used in chelation-assisted C−H functionalization was developed in 1955 by Murahashi who revealed an *ortho*-carbonylation reaction of aldimine **43** using dicobalt octacarbonyl as the catalyst, giving phthalimidine **44** again under rather harsh reaction conditions, however under high temperature and pressure (Scheme 1.10a).[49] Later, Murahashi and Horiie showed that azobenzene **45** could undergo a similar direct metalation furnishing the indazolone **46** (Scheme 1.10b).[50] In the next few decades, the application of cobalt in chelation-assisted C−H bond functionalization was stagnant until 1994, when a $Co(H)(N_2)(PPh_3)_3$-catalyzed *ortho*-alkenylation of azobenzene derivative **47** with tolane (**1**) was reported (Scheme 1.10c).[51] Meanwhile, Klein and coworkers described the first example of a well-defined stoichiometric cyclometalation, employing azobenzene and $Co(Me)(PMe_3)_4$.[52]

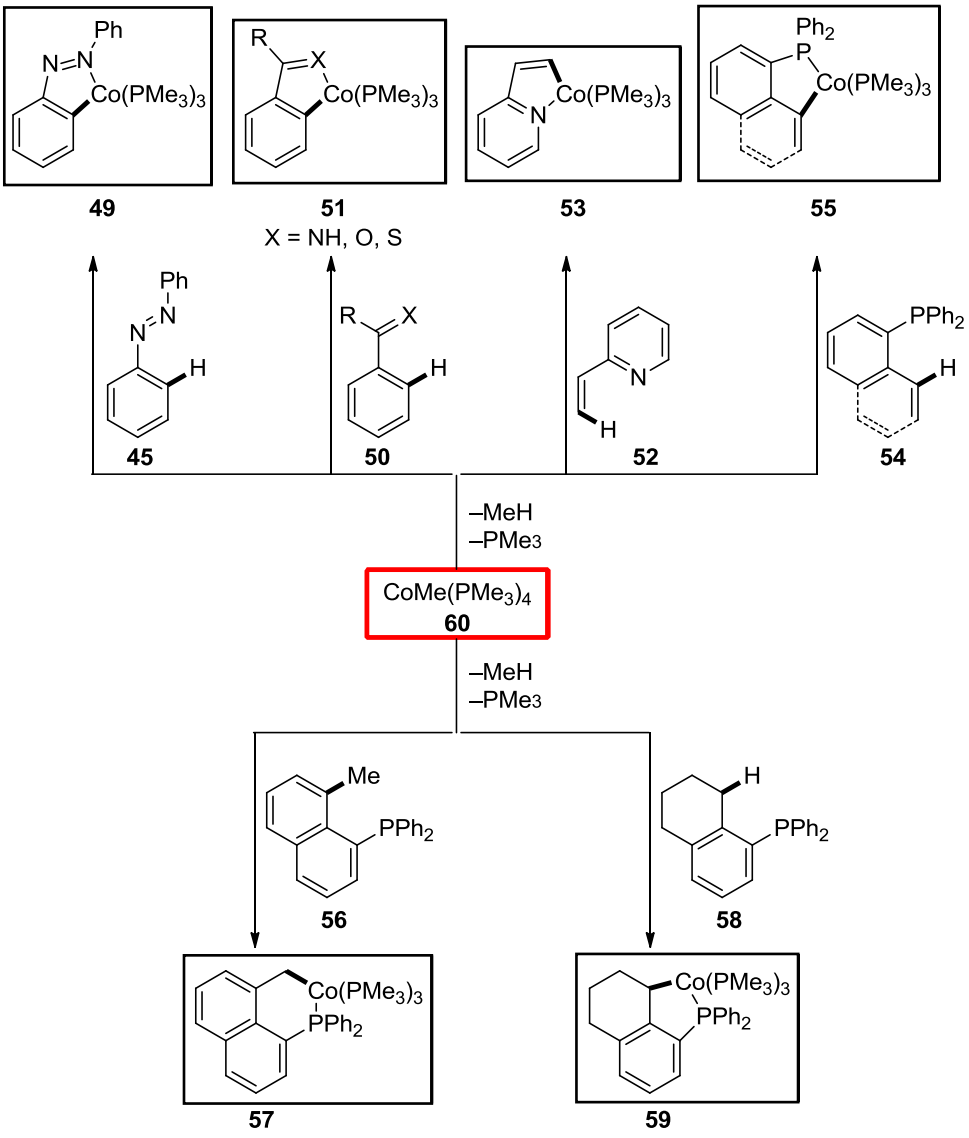


Scheme 1.10. Cobalt-mediated chelation-assisted C−H bond functionalizations reported before 1995.

Further research provided a series of aromatic and olefinic substrates bearing various

[48] M. S. Kharasch, E. K. Fields, *J. Am. Chem. Soc.* **1941**, *63*, 2316–2320.
[49] S. Murahashi, *J. Am. Chem. Soc.* **1955**, 77, 6403–6404.
[50] S. Murahashi, S. Horiie, *J. Am. Chem. Soc.* **1956**, *78*, 4816–4817.
[51] G. Halbritter, F. Knoch, A. Wolski, H. Kisch, *Angew. Chem. Int. Ed.* **1994**, *33*, 1603–1605.
[52] H.-F. Klein, M. Helwig, U. Koch, U. Flörke, H.-J. Haupt, *Z. Naturforsch. B: Chem. Sci.* **1993**, *48*, 778–784.

directing groups containing nitrogen,[52–53] oxygen,[54] sulfur[55] and phosphorus[56–57,58] atoms, which could assist the stoichimetric oxidative addition of the *ortho* C–H bond to the cobalt complex, with concomitant reductive elimination of methane. In particular, both the five- and six-membered cobaltocycles can be formed with phosphorus chelating ligands *via* C–H bond activation, including a C(sp^3)–H bond (Scheme 1.11).[54] All of this knowledge implied that complexes of cobalt could potentially allow for mild C–H bond functionalization although still facing many challenges.

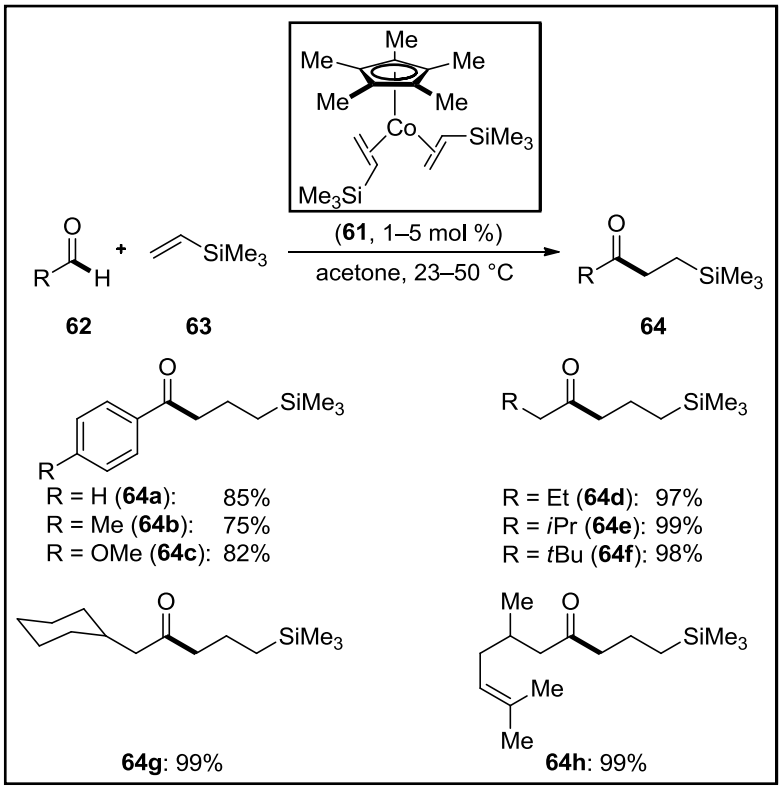


Scheme 1.11. Stoichiometric cyclometalation with cobalt complex **60**.

[53] H.-F. Klein, S. Camadanli, R. Beck, D. Leukel, U. Flörke, *Angew. Chem. Int. Ed.* **2005**, *44*, 975–977.
[54] S. Camadanli, R. Beck, U. Flörke, H.-F. Klein, *Dalton Trans.* **2008**, 5701–5704.
[55] R. Beck, H. Sun, X. Li, S. Camadanli, H.-F. Klein, *Eur. J. Inorg. Chem.* **2008**, 3253–3257.
[56] H.-F. Klein, S. Schneider, M. He, U. Flörke, H.-J. Haupt, *Eur. J. Inorg. Chem.* **2000**, 2295–2301.
[57] H.-F. Klein, R. Beck, U. Flörke, H.-J. Haupt, *Eur. J. Inorg. Chem.* **2003**, 1380–1387.
[58] R. Beck, H. Sun, X. Li, H.-F. Klein, *Z. Anorg. Allg. Chem.* **2009**, *635*, 99–105.

1.3.1 Cobalt-Catalyzed C−H Bond Functionalizations in Aldehydes

Based on early contributions, functionalization of the aldehyde C−H bond was first reported by Brookhart and coworkers in 1997. The Cp*Co(CH_2=$CHSiMe_3$)$_2$ (**61**) catalyst succeeded in the hydroacylation of olefins (Scheme 1.12).[59−60] Further research described clear evidence for the oxidative addition of C(sp^2)−H bonds to the Cp*Co(I) moiety.[61]

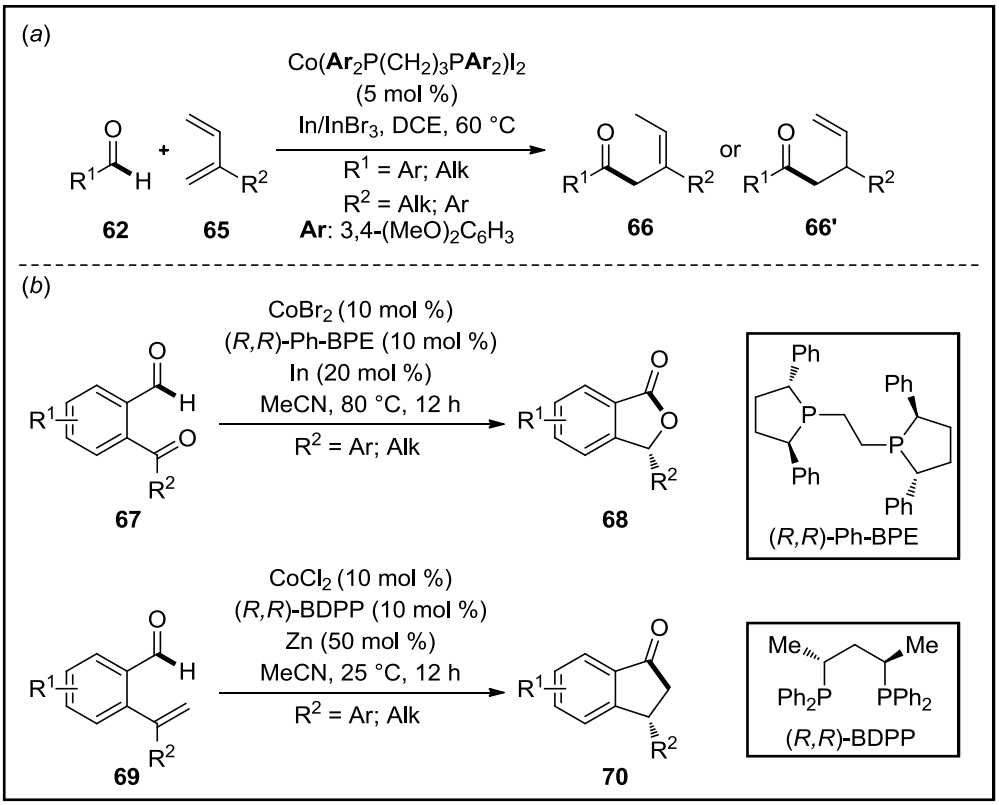


Scheme 1.12. Cobalt-catalyzed formyl C−H functionalization in aldehydes **62** reported before 2014.

Recent progress in the formyl−H bond functionalization of aldehydes was made in 2014 by Dong and Yoshikai. Dong and coworkers described a cobalt-catalyzed hydroacylation of 1,3-dienes **65** with aldehydes **62**, and proposed an oxidative cyclization mechanism that involved a cobaltacycle intermediate, which predetermined the regio- and stereoselectivity of the transformation (Scheme 1.13a).[62] Taking in consideration this recent work on cobalt and the previously reported contributions on enantioselective Rh-catalyzed transformations,[63]

[59] C. P. Lenges, M. Brookhart, *J. Am. Chem. Soc.* **1997**, *119*, 3165–3166.
[60] C. P. Lenges, P. S. White, M. Brookhart, *J. Am. Chem. Soc.* **1998**, *120*, 6965–6979.
[61] C. P. Lenges, M. Brookhart, B. E. Grant, *J. Organomet. Chem.* **1997**, *528*, 199–203.
[62] Q.-A. Chen, D. K. Kim, V. M. Dong, *J. Am. Chem. Soc.* **2014**, *136*, 3772–3775.
[63] a) D. H. Phan, K. G. M. Kou, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 16354–16355; b) M. M. Coulter, K. G. M. Kou, B. Galligan, V. M. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 16330–16333; c) D. H. T. Phan, B. Kim, V. M. Dong, *J.*

Yoshikai and coworkers reported the first chiral cobalt-diphosphine catalytic system, which allowed for intramolecular hydroacylation of 2-acylbenzaldehydes **67** and 2-alkenylbenzaldehydes **69**, to generate phthalides **68** or indanones **70** derivatives, respectively (Scheme 1.13b).[64]



Scheme 1.13. a) Cobalt-catalyzed hydroacylation by oxidative cyclization. b) Cobalt-catalyzed enantioselective intramolecular hydroacylation.

1.3.2 Low-Valent Cobalt-Catalyzed Chelation-Assisted C−H Bond Functionalizations

The chelation-assisted direct conversion of C−H bonds into C−C bonds using low-valent cobalt catalysts was studied independently by the research groups of Yoshikai,[65] Nakamura,[66]

Am. Chem. Soc. **2009**, *131*, 15608–15609; d) K. Kundu, J. V. McCullagh, A. T. Jr. Morehead, *J. Am. Chem. Soc.* **2005**, *127*, 16042–16043.

[64] J. Yang, N. Yoshikai, *J. Am. Chem. Soc.* **2014**, *136*, 16748–16751.

[65] Selected representative examples: a) W. Xu, N. Yoshikai, *Angew. Chem. Int. Ed.* **2014**, *53*, 14166–14170; b) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2013**, *52*, 8574–8578; c) K. Gao, N. Yoshikai, *J. Am. Chem. Soc.* **2013**, *135*, 9279–9282; d) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2012**, *51*, 4698–4701; e) P.-S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2011**, *133*, 17283–17295; f) K. Gao, P.-S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2010**, *132*, 12249–12251.

[66] a) Q. Chen, L. Ilies, N. Yoshikai, E. Nakamura, *Org. Lett.* **2011**, *13*, 3232–3234; b) L. Ilies, Q. Chen, X. Zeng, E. Nakamura, *J. Am. Chem. Soc.* **2011**, *133*, 5221–5223; c) Q. Chen, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2011**, *133*, 428–429.

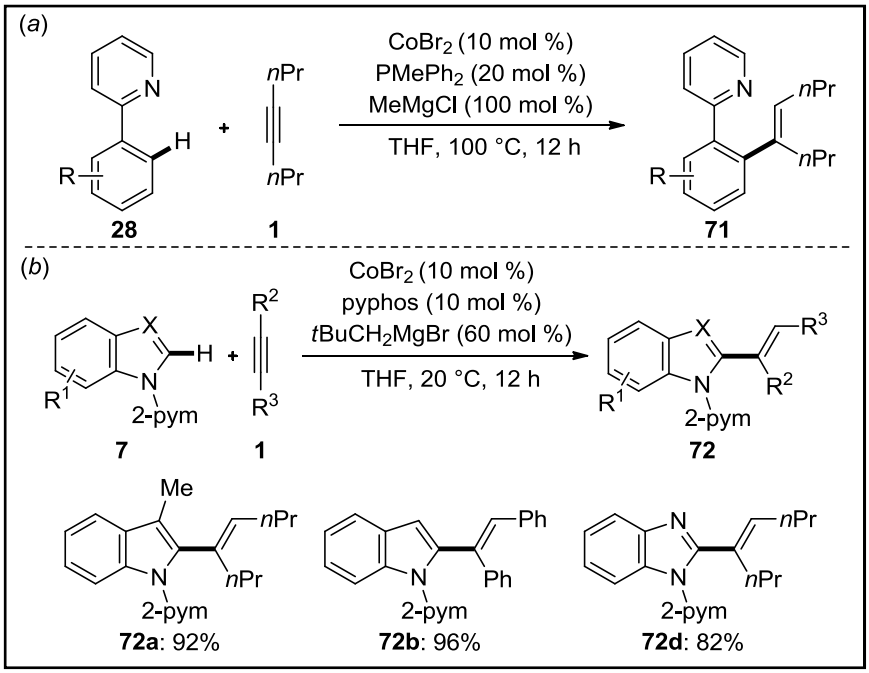
and Ackermann.[67–68]

1.3.2.1 Low-Valent Cobalt-Catalyzed C−H Bond Functionalizations

According to the two different types of developed cobalt-catalyzed C−H bond functionalization, the subsequent discussion in this section will be divided in two topics:

(a) Cobalt-catalyzed hydroarylation of alkynes and olefins

Based on Kisch's report on the first cobalt(I)-catalyzed *ortho*-dialkenylation reactions,[51] Yoshikai and coworkers devised a ternary catalytic system consisted of $CoBr_2$, phosphine ligand ($PMePh_2$) and a reductant (MeMgCl), which catalyzed the hydroarylation reaction between 2-arylpyridines **28** and oct-4-yne **1** to yield the desired hydroarylated product **71** (Scheme 1.14a).[65f] The scope of cobalt-catalysis was further expanded to use pyrimidin-2-yl as a removable directing group.[69] Remarkably, the C2-selective alkenylation of *N*-pyrimidylindoles **7** with internal alkynes **1** was catalyzed by low-valent cobalt at ambient temperature (Scheme 1.14b).[65d]



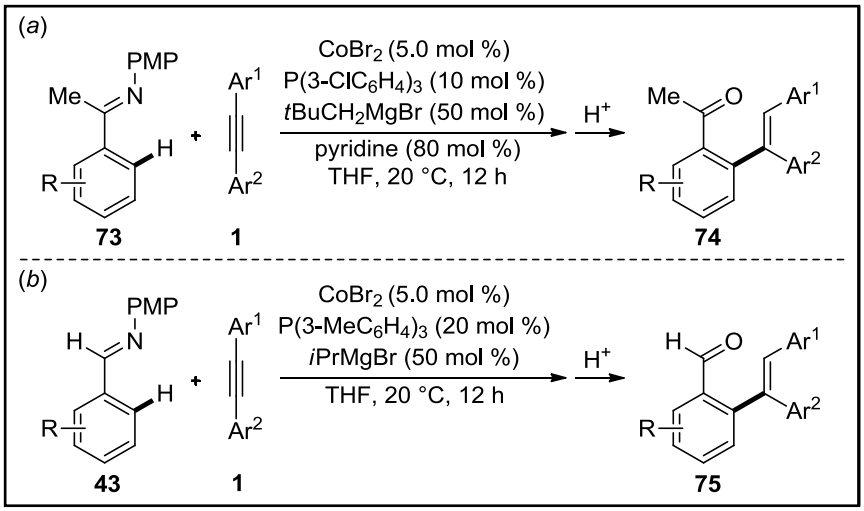
Scheme 1.14. Cobalt-catalyzed hydroarylation *via* C−H bond activation in 2-arylpyridines **28** and *N*-(pyrimidin-2-yl)indoles **7**.

[67] a) B. Punji, W. Song, G. Shevchenko, L. Ackermann, *Chem. E. J.* **2013**, 19, 10605–10610; b) W. Song, L. Ackermann, *Angew. Chem. Int. Ed.* **2012**, *51*, 8251–8254.

[68] See also: a) L. Grigorjeva, O. Daugulis, *Org. Lett.* **2014**, *16*, 4688-4690; b) L. Griorjeva, O. Daugulis, *Org. Lett.* **2014**, *16*, 4684–4687; c) L. Grigorjeva, O. Daugulis, *Angew. Chem. Int. Ed.* **2014**, *53*, 10209–10212.

[69] L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764-767.

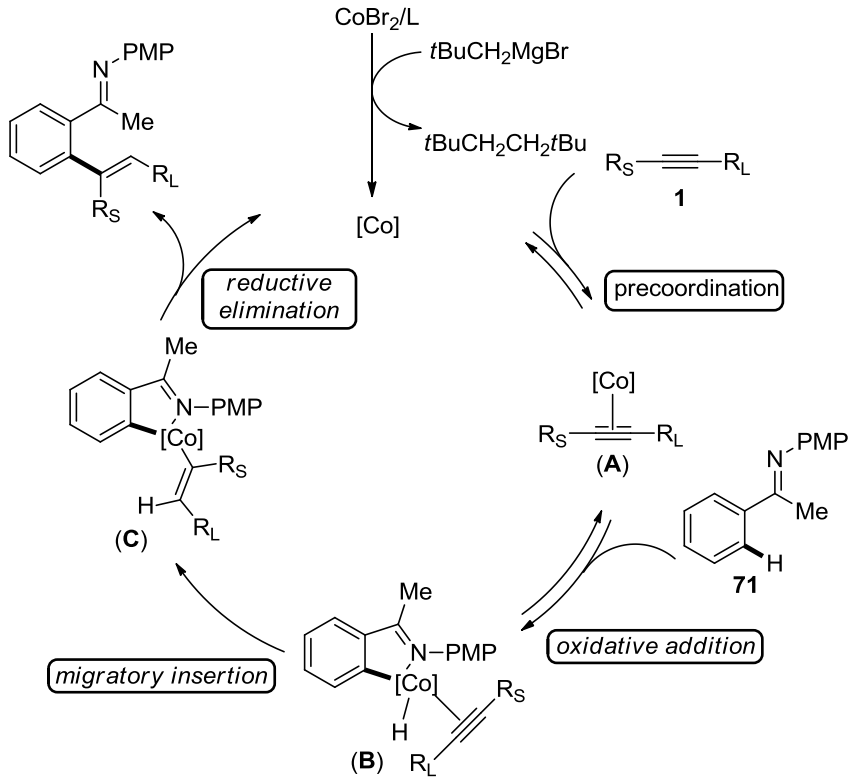
Schiff bases (**73** and **43**) as directing groups behaved in a similar fashion to phenylpyridine (**28**). The additions of aryl ketimines **73** and aldimines **43** to internal alkynes were achieved by a catalytic system of $CoBr_2$, phosphine ligand, Grignard reagent and pyridine.[67e] Under acidic reaction conditions, the diarylacetylenes **1** afforded the corresponding ketones **74** (Scheme 1.15a) and aldehydes **75** (Scheme 1.15b), while the products of dialkyl- and alkylarylacetylenes underwent cyclization to give benzofulvene derivatives.[65e,70]



Scheme 1.15. Cobalt-catalyzed hydroarylations with aryl ketimines **73** and aldimines **43** *via* C−H activation.

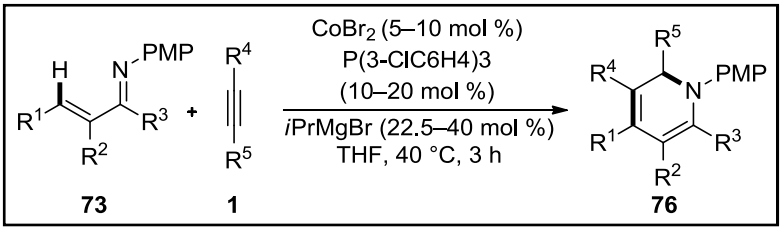
The proposed catalytic cycle of these novel cobalt-catalyzed direct hydroarylations began with the reduced form of the active cobalt catalyst, which was generated from the cobalt(II) precatalyst and an excess of tBuCH$_2$MgBr. Precoordination of the alkyne **1** to the active cobalt species was followed by oxidative addition of the *ortho* C−H bond in **73** to the cobalt complex **A**. Intramolecular hydrocobaltation in complex **B** and subsequent reductive elimination in the intermediate **C** furnished the desired product and regenerated the cobalt catalyst (Scheme 1.16).[5j,65e] In the case of unsymmertrical alkynes **1**, the product *via* C–C bond formation at the less hindered acetylenic carbon was formed predominantly. Such a regioselectivity was rationalized in terms of significant steric interactions on the cobalt center upon the transformation **B**→**C**.

[70] T. Yamakawa, N. Yoshikai, *Tetrahedron* **2013**, *69*, 4459–4465.



Scheme 1.16. Plausible catalytic cycle for the cobalt-catalyzed hydroarylation with internal alkynes **1**.

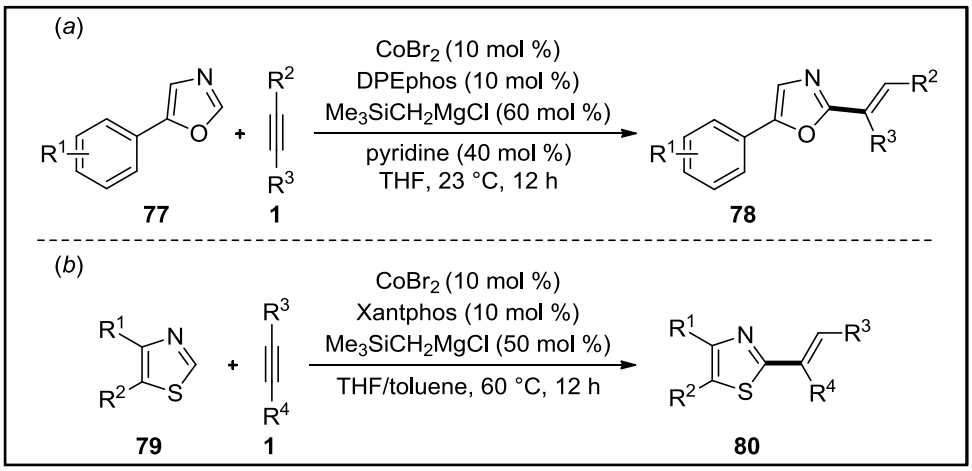
Notably, the hydroarylation proceeded not only on aryl imines but also on olefins *via* alkenyl C−H activation. Thus, dihydropyridine derivatives **76** were generated by annulations of *α,β*-unsaturated imines (Scheme 1.17).[71]



Scheme 1.17. Annulation of alkynes **1** with *α,β*-unsaturated imines **73**.

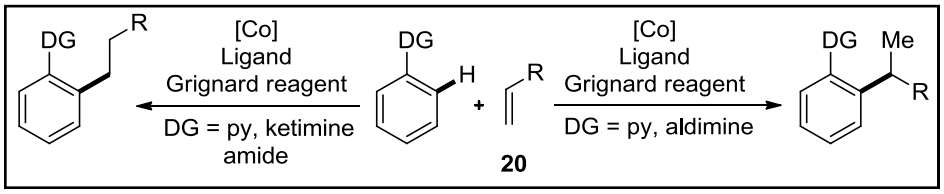
Utilizing the differences in bond acidities of diversely positioned C−H bonds is another viable approach to perform site-selective C−H bond functionalizations in heteroaromatic compounds. Thus, Yoshikai and coworkers developed a cobalt-based catalytic system for the *syn*-additions of (benzo)azoles **77** or **79** to internal alkynes *via* C−H bond functionalization with high chemo-, regio- and stereoselectivities under mild conditions (Scheme 1.18).[72]

[71] T. Yamakawa, N. Yoshikai, *Org. Lett*. **2013**, *15*, 196–199.
[72] a) Z. Ding, N. Yoshikai, *Org. Lett*. **2010**, *12*, 4180–4183; b) Z. Ding, N. Yoshikai, *Synthesis* **2011**, 2561–2566.



Scheme 1.18. Alkenylations of azoles **77** and **79** with alkynes **1**.

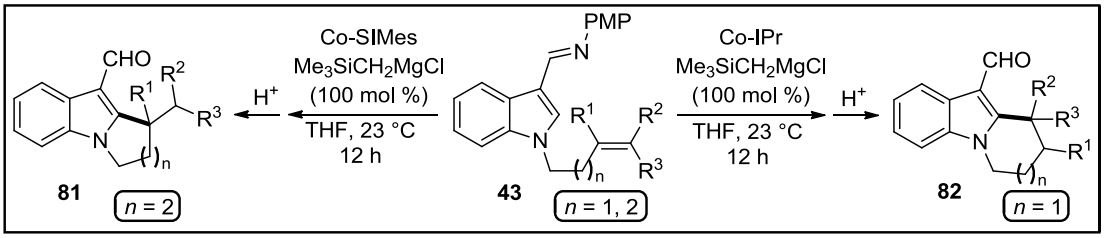
Considering the remarkabe high efficacy of alkyne hydroarylation, Yoshikai and coworkers next became intrigued by the development of analogous novel reactions for styrenes. So far, the low-valent cobalt have already successfully catalyzed pyridinyl- (**28**),[73] benzamide- (**2**)[66b] and imine-assisted (**73**)[65a–65b,74] C–H bond hydroarylation with good regioselectivity (Scheme 1.19).



Scheme 1.19. Various directing groups assisted hydroarylations of olefins.

The first example of intramolecular cobalt catalysis, namely the cobalt/NHC-catalyzed intramolecular hydroarylation of alkene moieties after C–H bond activation on C2 position of indole fragments, was investigated by Yoshikai's group (Scheme 1.20).[65b] The reaction allowed for the direct transformation of indole derivatives **43** into dihydropyrroloindoles **81** or tetrahydropyridoindoles **82** under mild conditions. Interestingly, the size of the formed cycle was not only dependent on the length of the olefin tether, but also controlled by the steric properties of the NHC ligand. Thus, the cobalt-IPr catalyst promoted the regioselective intramolecular cyclizations of olefins to tetrahydropyridoindole **82**, whereas the cobalt-SIMes analogue switched regioselectivity toward the formation of dihydropyrroloindole **81**.

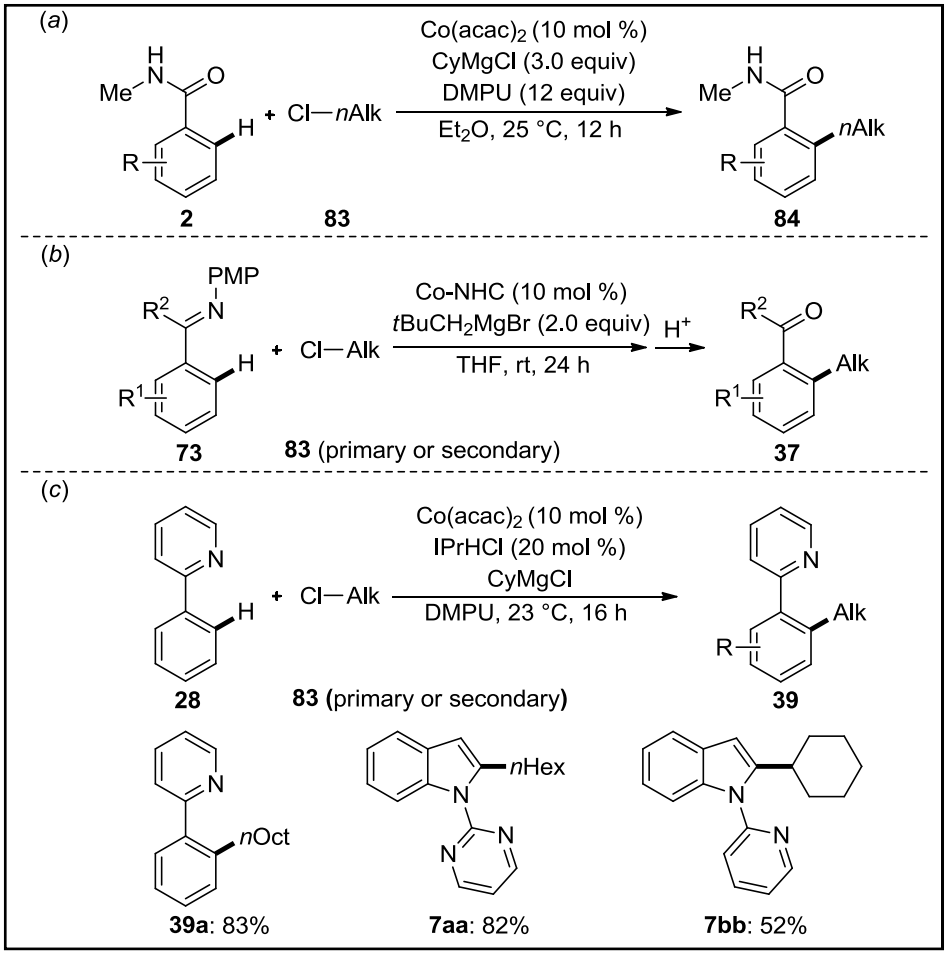
[73] K. Gao, N. Yoshikai, *J. Am. Chem. Soc*. **2011**, *133*, 400–402.
[74] a) K. Gao, N. Yoshikai, *Angew. Chem. Int. Ed*. **2011**, *50*, 6888-6892; b) P.-S. Lee, N. Yoshikai, *Angew. Chem. Int. Ed*. **2013**, *52*, 1240–1244; c) T. Yamakawa, N. Yoshikai, *Chem. Asian. J*. **2014**, *9*, 1242–1246.



Scheme 1.20. Cobalt/NHC-catalyzed intramolecular hydroarylation leading to dihydropyrroloindoles **81** or tetrahydropyridoindoles **82**.

(b) Cobalt-catalyzed coupling reactions with organic electrophiles

In recent years, some examples of cobalt-catalyzed C−H coupling reactions with organic electrophiles have been reported. Cobalt-catalyzed *ortho*-alkylation of benzamides **2** with primary alkyl chlorides **81** was reported by Nakamura and coworkers (Scheme 1.21a),[66c]

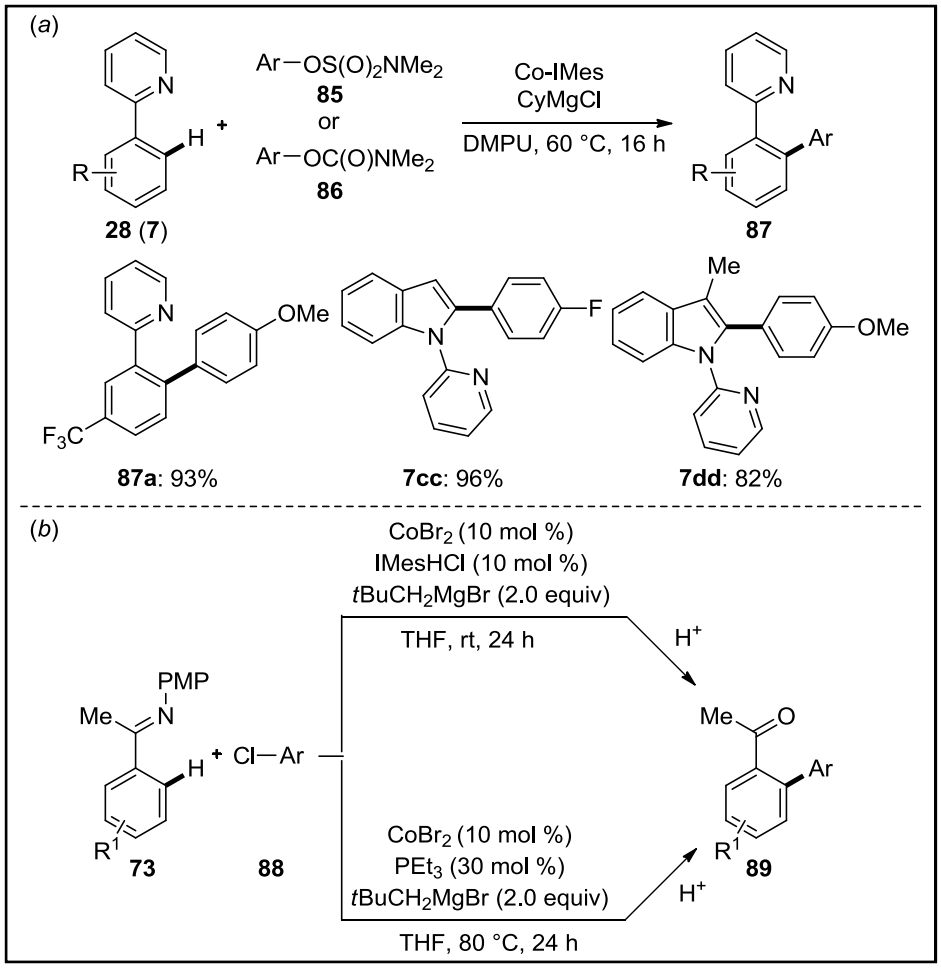


Scheme 1.21. Cobalt-catalyzed C−H alkylation with diverse directing groups.

The reaction could also be performed with ketimine- (**73**),[65c] pyridyl- and pyrimidyl-assistance (**28**),[67a] thus achieving direct alkylation with a broad range of primary and secondary alkyl chlorides and bromides through C−H bond activation (Schemes

1.21b–1.21c). In addition, oxidative *ortho*-alkylation of benzamides **2** and 2-arylpyridines **28** with alkyl Grignard reagents was also reported by Nakamura and coworkers.[66a]

The cobalt-catalyzed functionalization of C−H bonds could be applied to challenging direct arylation. Ackermann and coworkers initially developed a cobalt-IMes catalytic system for direct C−H arylations of arenes with the electronically deactivated aryl sulfamates **85** and aryl carbamates **86**.[67b] These direct functionalizations chemoselectively delivered the monoarylated products **87** (Scheme 1.22a). The versatile cobalt catalyst was not limited to 2-arylpyridines **28** but also set the stage for the synthesis of potentially bioactive *N*-substituted indoles **7**.

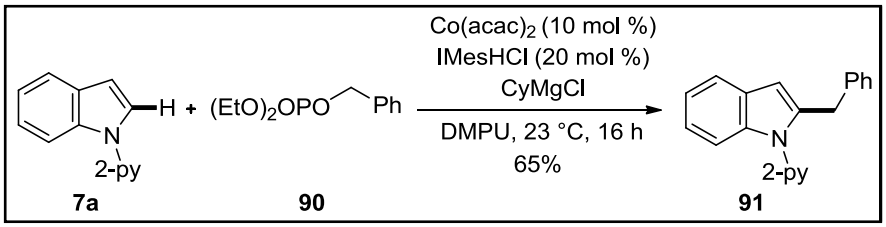


Scheme 1.22. Cobalt/NHC-catalyzed C−H bond arylations with diverse directing groups.

Aryl chlorides **88** are the ideal electrophilic aryl halides for direct arylation reactions, since they are cost-effective, whilst being widely available. Ackermann and Yoshikai explored a cobalt-based catalytic system that allowed the direct arylation of aryl pyridines **28** and ketimines **73** with decorated chlorobenzene at ambient or elevated temperatures in the

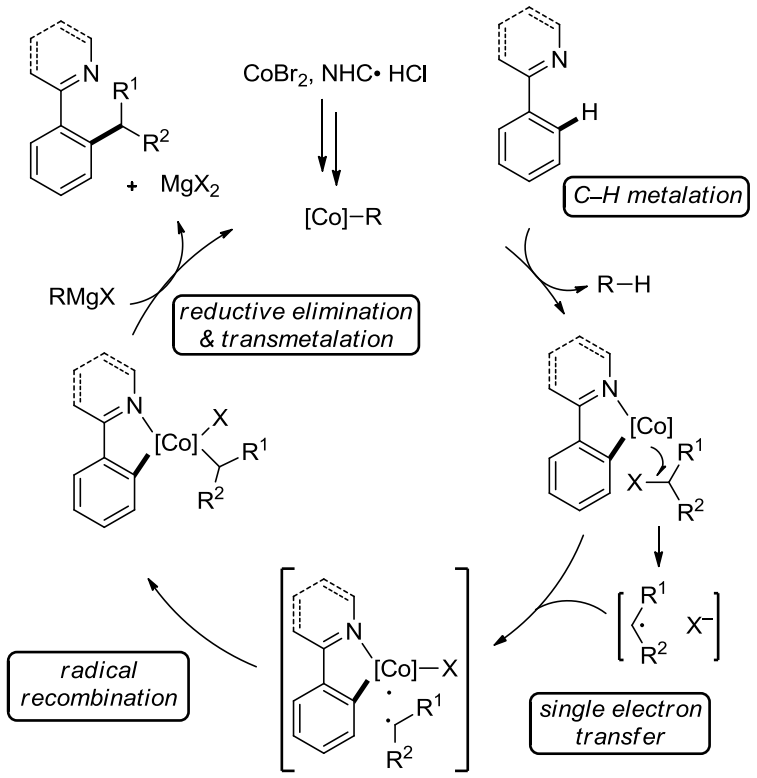
presence of NHC or phosphine ligands, respectively. After hydrolysis, biarylketones **89** were obtained (Scheme 1.22b).[67a,75] In contrast, oxidative arylation of 2-arylpyridines with aryl Grignard reagents was reported by Shi and coworkers.[76]

Meanwhile, the cobalt-IMes catalyst was not restricted to the synthesis of biaryl compounds, but also enabled effective C−H bond benzylation reactions on indole **7a** with benzyl phosphates **90** as electrophiles at ambient temperature (Scheme 1.23).[67b]



Scheme 1.23. Cobalt-catalyzed C−H benzylation of indole **7**.

The general consensus is that the cobalt-catalyzed C−H alkylation involves a radical intermediate. Thus, a proposed catalytic cycle is shown below (Scheme 1.24).[5j−5k]



Scheme 1.24. Proposed catalytic cycle for the cobalt-catalyzed C−H bond functionalization.

The cycle is initiated by a C−H cyclocobaltation and subsequent single electron transfer (SET)

[75] K. Gao, P.-S. Lee,C. Long, N. Yoshikai, *Org. Lett.* **2011**, *14*, 4234–4237.
[76] B. Li, Z.-H. Wu, Y.-F. Gu, C.-L. Sun, B.-Q. Wang, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2011**, *50*, 1109–1113.

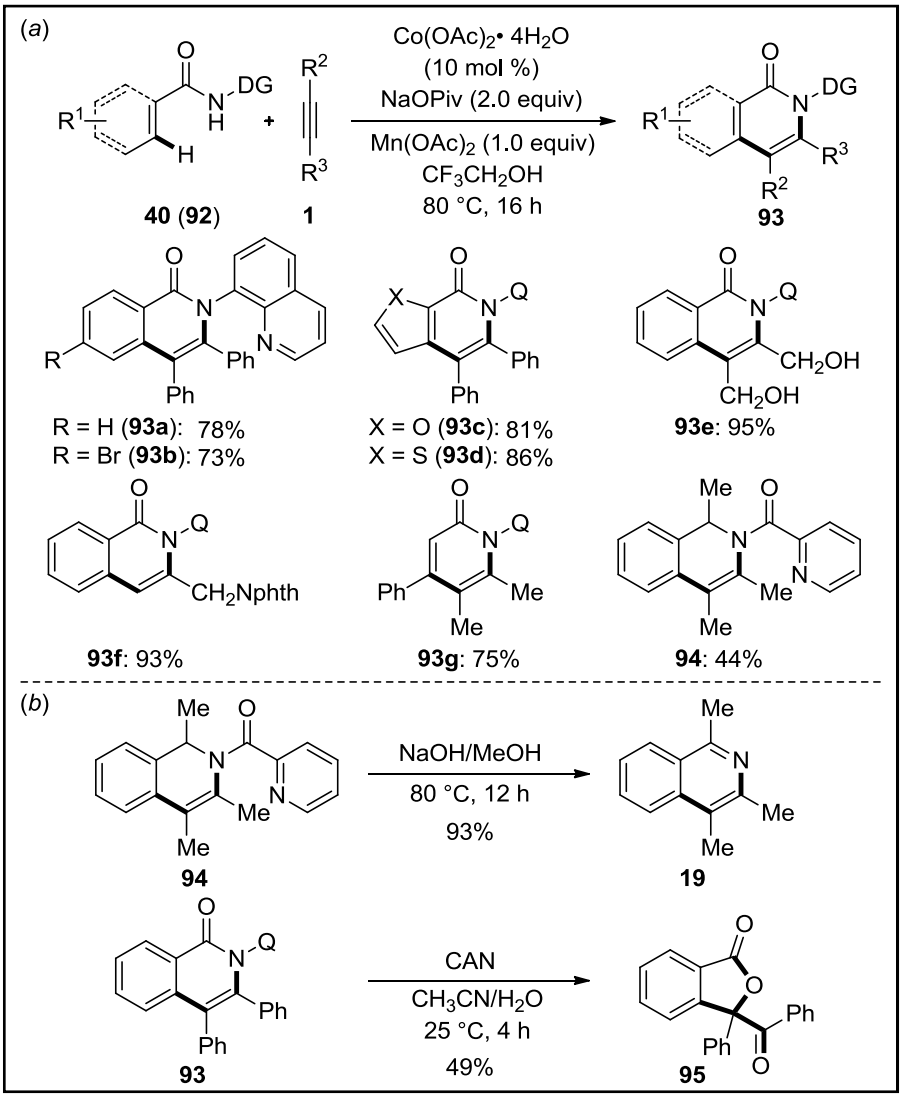
from the cobalt center to the alkyl halide **83**. The desired product resulted from radical C−C coupling followed by reductive elimination, and the alkyl cobalt species was regenerated after the transmetalation of cobalt halide with the Grignard reagent.

1.3.2.2 Cobalt-Catalyzed Oxidative C−H Bond Functionalizations

Since Daugulis initially devised the 2-aminoquinoline and picolinamide directing groups for the palladium-catalyzed arylation of C(sp^3)−H bonds in 2005,[77] the bidentate-type directing groups have quickly emerged as a new tool in exploring C−H activation reactions.[78] Interestingly, another remarkable progress was made by Daugulis and coworkers, by reporting an approach for cobalt-catalyzed direct oxidative alkyne annulation *via* aminoquinoline **40** and picolinamide **92** as bidentate-chelation assistance. The reaction was successful with both terminal and internal alkynes. This approach provided expedient access to diversely decorated isoquinolin-1-ones **93** with ample scope of substrates, such as heteroarenes and vinyl amide **40** (Scheme 1.25a). Furthermore, it allowed the subsequent removal of the directing groups under simple reaction conditions (Scheme 1.25b).[68c]

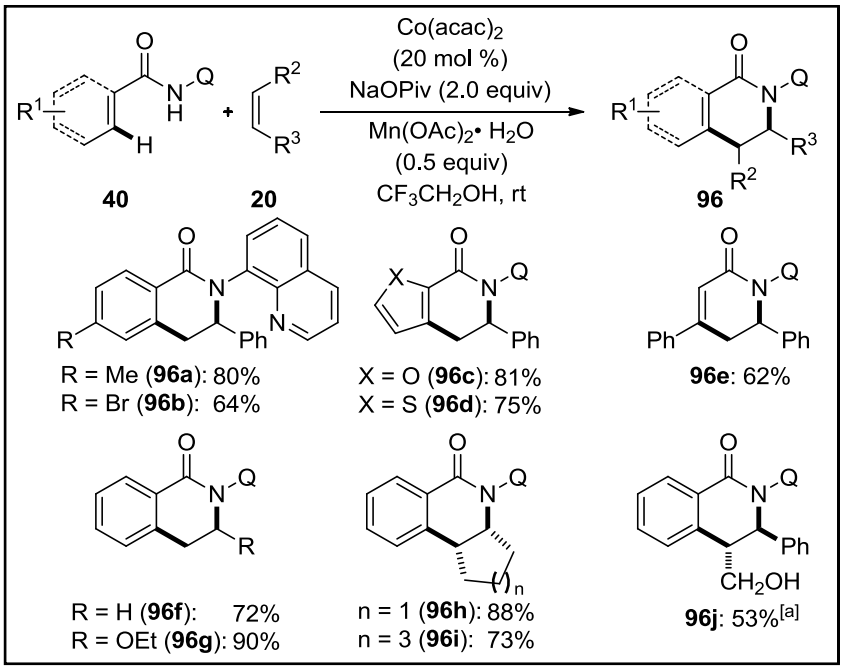
[77] V. G. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2005**, *127*, 13154–13155.

[78] Recent reviews on C—H activation with bidentate directing groups: a) O. Daugulis, J. Roane, L. D. Tran, *Acc. Chem. Res.* **2015**, *48*, 1053–1064; b) L. C. M. Castro, N. Chatani, *Chem. Lett.* **2015**, *44*, 410–421; c) M. Corbet, F. De Campo, *Angew. Chem. Int. Ed.* **2013**, *52*, 9896–9898; d) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11942–11959. Selected recent examples demonstrating the power of bidentate directing groups: e) Q. Gu, H. H. Al Mamari, K. Graczyk, E. Diers, L. Ackermann, *Angew. Chem. Int. Ed.* **2014**, *53*, 3868–3871; f) W. Song, S. Lackner, L. Ackermann, *Angew. Chem. Int. Ed.* **2014**, *53*, 2477–2480; g) Y. Aihara, N. Chatani, *J. Am. Chem. Soc.* **2014**, *136*, 898–901.



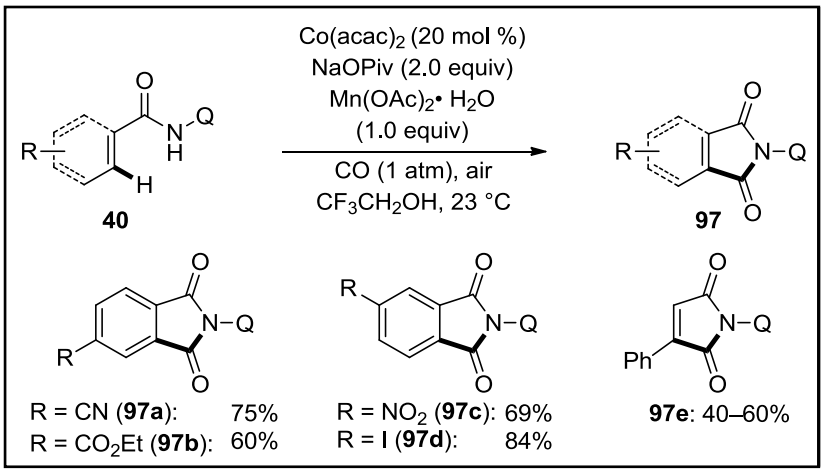
Scheme 1.25. (a) Substrate scope for cobalt-catalyzed C−H annulations. (b) Directing group removal.

After the successful development of cobalt-catalyzed oxidative cyclizations with alkyne **1**, further studies indicated that the cobalt catalytic system was not restricted to alkynes, but also exhibited notable power in C(sp^2)−H bond coupling with alkenes. Upon further investigations of the reaction of *N*-(quinolin-8-yl)benzamide (**40**) and styrene (**20**), employing $Co(acac)_2$ as a catalyst, $Mn(OAc)_3 \cdot 2H_2O$ as a co-catalyst, and oxygen from air as a terminal oxidant, a remarkable scope of aminoquinoline-protected amides of benzoic, heteroaromatic and acrylic acids furnished products **96** in good yields (Scheme 1.26).[68b]



Scheme 1.26. Substrate scope for cobalt-catalyzed alkene annulations through C−H bond activation. [a] $Co(acac)_2$ (50 mol %), 80 °C.

Based on the high catalytic efficacy of the cobalt catalyst in oxidative annulations of alkynes **1** and alkenes **20**, Daugulis and coworkers thereafter developed a cobalt-catalyzed direct carbonylation of benzoic- and acrylic acid-derivatives amides **40** with carbon monoxide through bidentate-chelation assistance. The entire scope was completed at ambient temperature and afforded the desired phthal- and succinimides **97** in good yields (Scheme 1.27a).[68a]

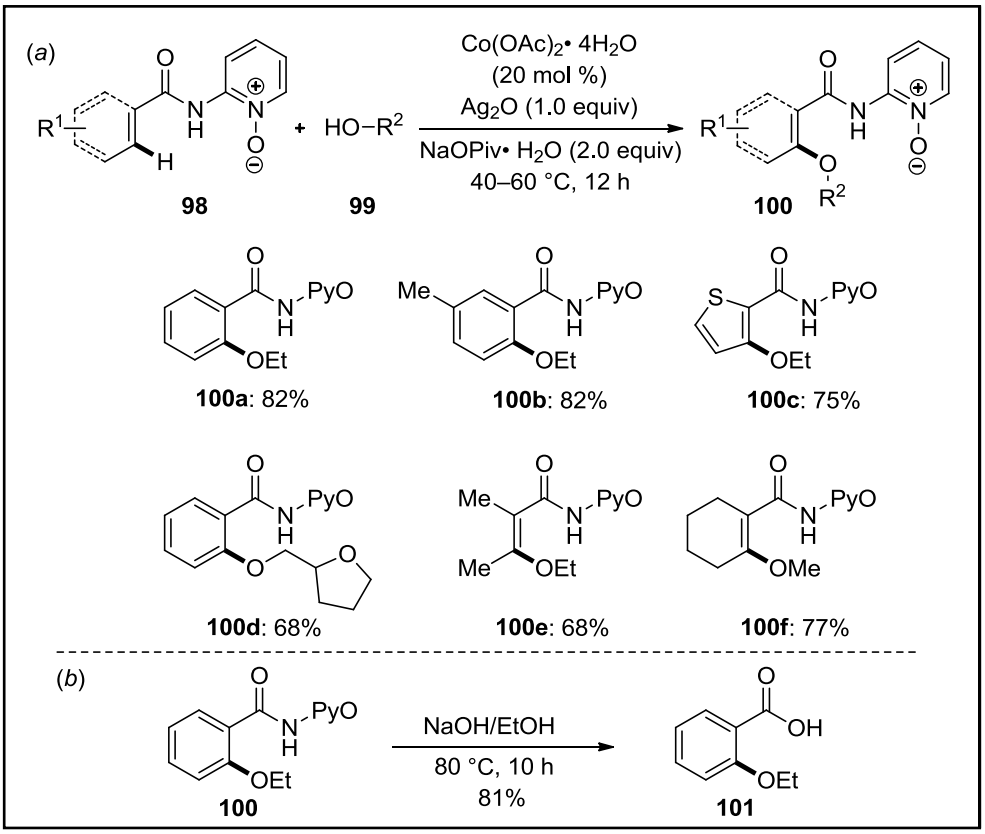


Scheme 1.27. Carbonylation of aminoquinoline-derived amides **40**.

A wide range of functional groups, such as halogen, nitrile, ester and cyano substituents, can

be tolerated under the optimizaed reaction conditions. Intramolecular competition experiments with *meta*-substituted arenes exhibited high levels of site-selectivity (Scheme 1.27).[68a] The directing group can be easily removed by treatment with methanolic ammonia, and the desired phthalimide **97** were obtained in high yield.

Meanwhile, very recently Song and coworkers developed the cobalt-catalyzed C−H bond alkoxylation with alcohols in benzamides **98** derived from 2-aminopyridine-1-oxide through a *N,O*-bidentate-type directing groups.[79] The reaction proceeded under mild conditions using $Co(OAc)_2 \cdot 4H_2O$ as the catalyst and with a wide range of substituted alcohols as well as of benzamides, heteroarenes and substituted vinyl amides **98** decorated with a variety of functional groups (Scheme 1.28a).[79]



Scheme 1.28. (a) Substrate scope for cobalt-catalyzed C−H alkoxylation. (b) Directing group removal.

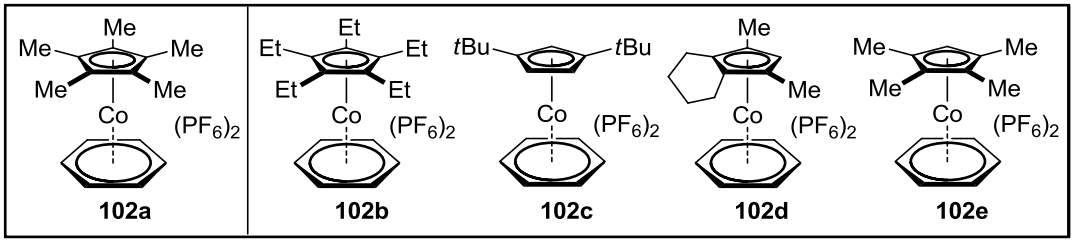
In addition, the reaction showed a high site-selectivity when *meta*-substituted substrates were employed. The mechanistic studies revealed that a radical pathway was involved. Further,

[79] L.-B. Zhang, X.-Q. Hao, S.-K. Zhang, Z.-J. Liu, X.-X. Zheng, J.-F. Gong, J.-L. Niu, M.-P. Song, *Angew. Chem. Int. Ed.* **2015**, *54*, 272–275.

kinetic isotope effect (KIE) studies suggested the C−H bond activation not to be the rate-limiting step. The 2-aminopyridine-1-oxide directing group can easily be removed affording benzoic acid **101** (Scheme 1.28b).

1.3.3 High-Valent Cobalt-Catalyzed C−H Bond Functionalizations

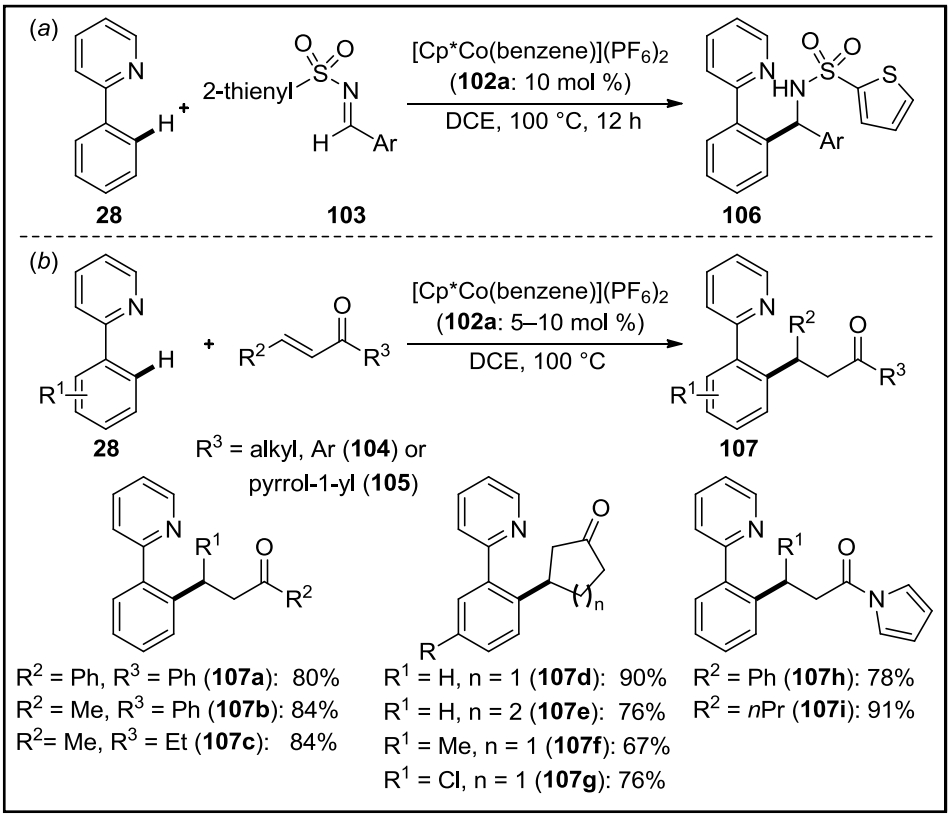
In recent years, Cp*Rh(III) complexes have been involved in the rapidly progregressing step-economical[80] C−H bonds functionalizations.[5b,7a] However, a number of analogous Cp*Co(III) complexes have been prepared and characterized up to now (Scheme 1.29).[81]



Scheme 1.29. Selected synthesized cationic high-valent cobalt(III) complexes.

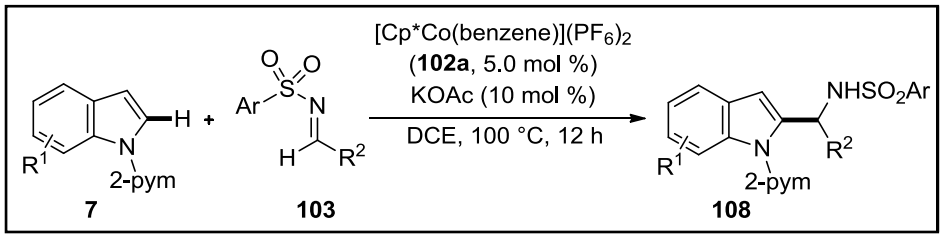
Kanai and coworkers chose cobalt, which is isoelectronic to rhodium, but less expensive and more abundant, and tried to emulate the reactivity of Cp*Rh(III). In 2013, they reported on the application of a variety of Cp*Co(III) complexes (Scheme 1.29) for synthetic organic transformations, and the [Cp*Co(benzene)]$(PF_6)_2$ complex (**102a**) appeared to be successful in promoting the addition of 2-arylpyridines **28** onto multiple bonds in imines **103** (Scheme 1.30a) as well as in α,β-unsaturated enones **104**, and 1-pyrrolylenones **105** (Scheme 1.30b).[82]

[80] P. A. Wender, V. A. Verma, T. J. Paxton, T. H. Pillow, *Acc. Chem. Res*. **2008**, *41*, 40–49.
[81] a) E. O. Fischer, R. D. Fisher, *Naturforsch. B* **1961**, *16*, 556–557; b) G. Fairhurst, C. White, *J. Chem. Soc.*, *Dalton Trans*. **1979**, 1531–1538; c) U. Koelle, B. Fuss, M. V. Rajasekharan, B. L. Ramakrishna, J. H. Ammeter, M. C. Boehm, *J. Am. Chem. Soc*, **1984**, *106*, 4252–4160.
[82] T. Yoshino, H. Ikemoto, S. Matsunaga, M. Kanai, *Angew. Chem. Int. Ed*. **2013**, *52*, 2207–2211.



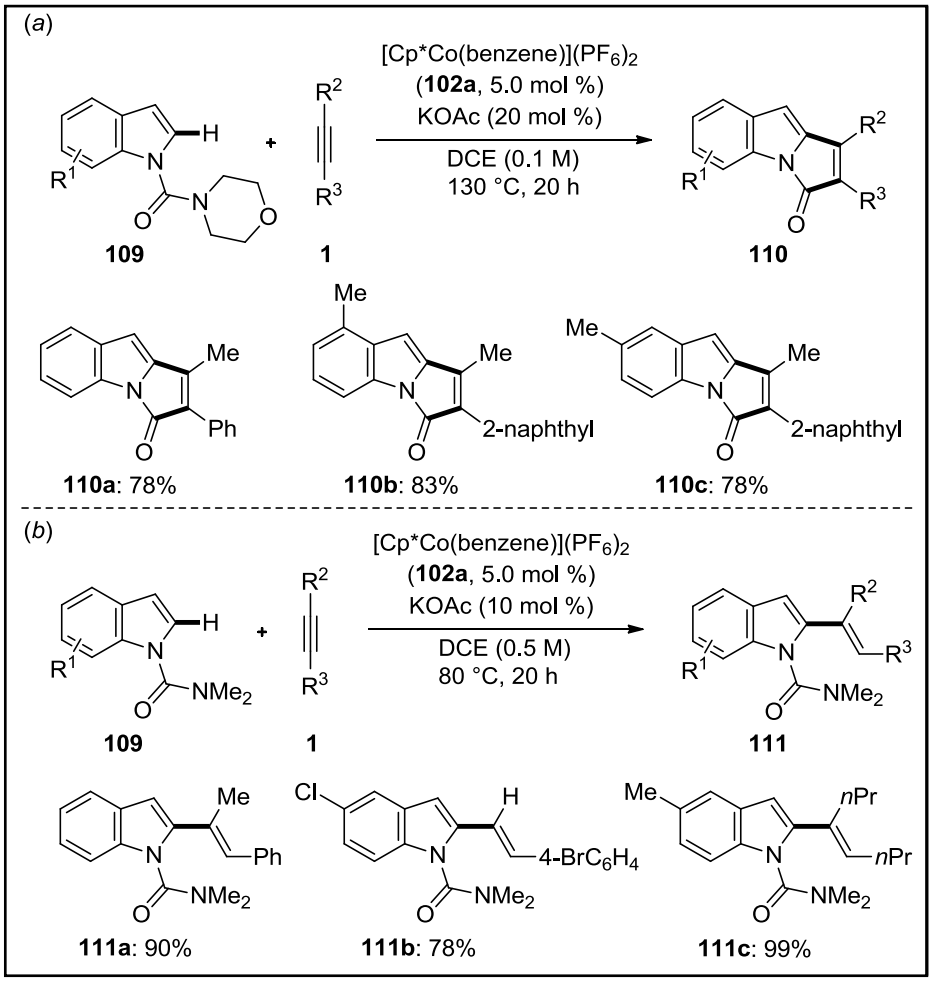
Scheme 1.30. Cobalt(III)-catalyzed addition of 2-aryl pyridines to imines **103**, *α,β*-unsaturated enones **104** and **105**.

Taking into consideration the important biological activity of indole and its derivatives, their modification and functionalization have extensively been studied *inter alia* by Kanai group applying the high-valent [Cp*Co(benzene)$(PF_6)_2$] complex (**102a**). The catalyst efficiently promoted the C2-selective hydroindolation of imines **103** with broad scope (Scheme 1.31).[83] The pyrimid-2-yl directing group can be easily removed upon treatment with NaOEt, yielding the NH-free indole derivative in a high yield.[69]



Scheme 1.31. Cobalt(III)-catalyzed addition of *N*-(pyrimidin-2-yl)indoles **7** to imines **102**.

[83] T. Yoshino, H. Ikemnto, S. Matsunaga, M. Kanai, *Chem. Eur. J.* **2013**, *19*, 9142–9146.



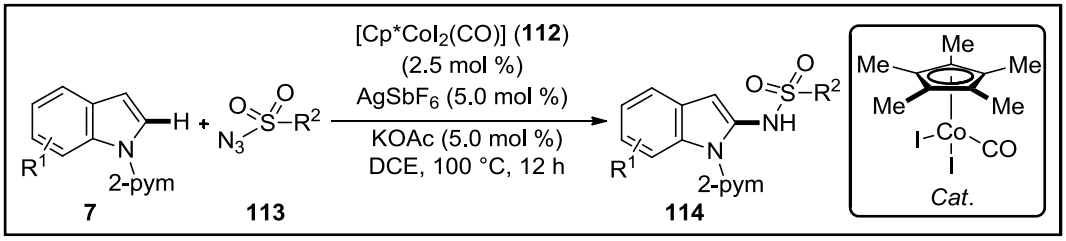
Scheme 1.32. Cobalt(III)-catalyzed annulations and alkenlations of indoles **109** *via* C−H bond alkenylation.

Further studies with Cp*Co(III) complexes were extended to catalyze the annulations and alkenylations of *N*-carbamoylindoles **109** *via* direct C−H activation in reactions with internal alkynes **1** to afford pyrroloindolones **110**. The results demonstrated that the Cp*Co(III) complexes possess the characteristic reactivity similar to those of the Cp*Rh(III) system (Scheme 1.32).[84] Furthermore, intensive mechanistic studies revealed the difference in the mode of catalytic activity between the Cp*Co(III) and Cp*Rh(III) complexes, thus highlighted the unique nucleophilic activity of the latter.[84]

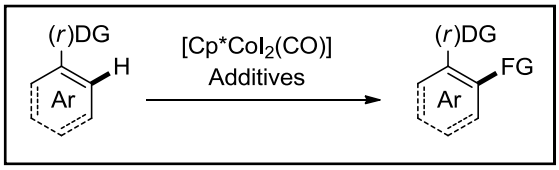
Besides their contributions on developing catalytically efficient Cp*Co(III) complexes, recently the Kanai group successfully applied the air-stable [Cp*CoI_2(CO)] complex **112**, prepared by Li and Jin as early as 2004,[85] for the C2-selective C−H bond amidation in

[84] H. Ikemoto, T. Yoshino, K. Sakata, S. Matsunaga, M. Kanai, *J. Am. Chem. Soc.* **2014**, *136*, 5424–5431.
[85] W. Li, L. Weng, G. Jin, *Inorg. Chem. Commun.* **2004**, *7*, 1174–1177.

indoles **7** (Scheme 1.33).[86]



Scheme 1.33. Cobalt(III)-catalyzed C−H bond amidation of indoles **7**.



Scheme 1.34. Cp*CoI_2(CO) catalyzed C−H bond functionalizations.

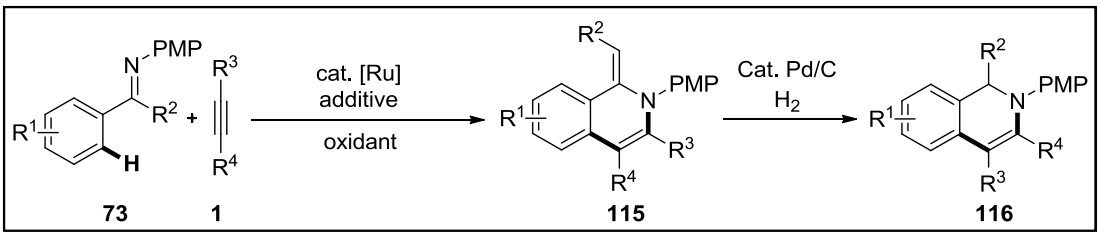
The use of the [Cp*CoI_2(CO)] complex (**112**) attracts an increasing attention in the past several months (Scheme 1.34). Thus, more examples of C−H bond amidation were reported using acetoxycarbamates as convenient nitrogen sources, as reported by the Chang group.[87] Likewise the direct C−H phosphoramidation was developed by the Kanai group.[88] Moreover, the cobalt(III)-catalyzed direct C−H cyanations, halogenations, allylations were developed by the Ackermann,[89] Glorius,[90] and Chang groups.[91] Very recently, Glorius and coworkers provided a reactive modular route towards a new class of conjugated polycyclic hydrocarbons using diazo compounds carbine precursors.[92] The Kanai group also reported on Cp*Co(III)-catalyzed oxidative alkenylation of bezamides **2** and acetanilides with ethyl acrylate.[93]

[86] B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, *Adv. Synth. Catal*. **2014**, *356*, 1491–1495.
[87] P. Patel, S. Chang, *ACS Catal*. **2015**, *5*, 853–858.
[88] B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, *Chem. Commun*. **2015**, *51*, 4659–4661.
[89] J. Li, L. Ackermann, *Angew. Chem. Int. Ed*. **2015**, *54*, 3635–3638.
[90] D.-G. Yu, T. Gensch, F. de Azambuja, S. Vásquez-Céspedes, F. Glorius, *J. Am. Chem. Soc*. **2014**, *136*, 17722–17725.
[91] A. B. Pawar, S. Chang, *Org. Lett*. **2015**, *17*, 660–663.
[92] D. Zhao, J. H. Kim, L. Stegemann, C. A. Strassert, F. Glorius, *Angew. Chem. Int. Ed*. **2015**, *54*, 4508–4511.
[93] Y. Suzuki, B. Sun, T. Yoshino, M. Kanai, S. Matsunaga, *Tetrahedron*, **2015**, DOI: 10.1016/j.tet.2015.02.032.

2 Objectives

Over the last decade, remarkable advances in transition-metal-catalyzed C–H bond functionalization have been achieved, which provided a more straightforward pathway for the development of chemo- and site-selective syntheses of valuable organic molecules. As a consequence, the center of gravity in researches of *Prof. Dr*. Lutz Ackermann and coworkers mainly focused on the development of synthetically useful transition-metal catalyzed C–H bond functionalizations. Within this context, major efforts were made to develop further applications of ruthenium and cobalt complexes in catalyzed C–H activation.

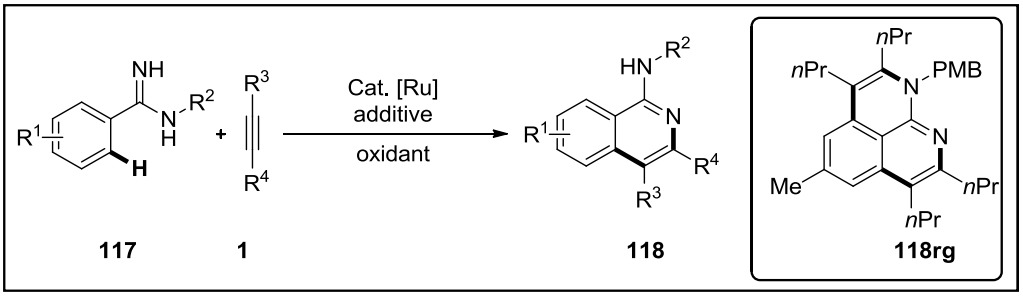
Isoquinolines are key structural motifs of various heterocyclic compounds with diverse bioactivities. The new efficient methods for the selective preparation of these heterocycles are in strong demand. As a consequence, the method to synthesize decorated isoquinolines through annulations of alkynes with *ortho*-halosubstituted aromatic imines under transition netal catalysis has been reported.[94] However, a more step- and atom-economical approach by the transition-metal-catalyzed oxidative C–H functionalization has been recognized as an increasingly viable tool for the preparation of substituted heterocycles. Therefore, a new protocol for ruthenium-catalyzed oxidative alkyne annulations by C–H bond activation of ketimines **73** was the prime focus of the first project (Scheme 2.1).



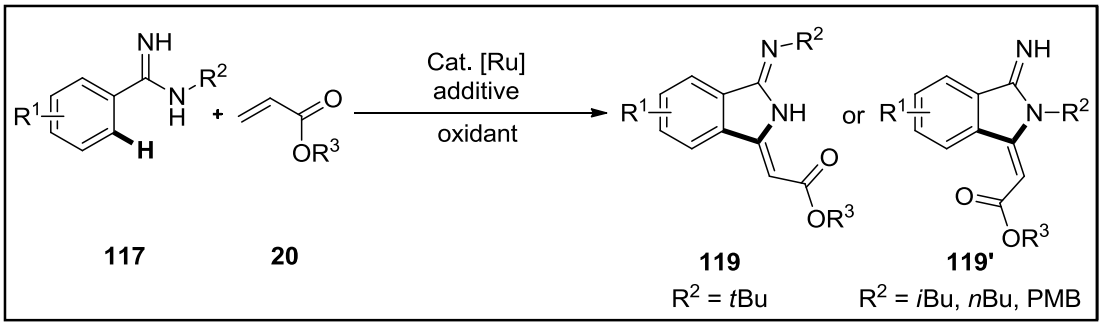
Scheme 2.1. Oxidative C–H bond functionalizations with decorated ketimines **73** and alkynes **1**.

As was mentioned above, we were going to manage the extension of isoquinolines to decorated 1-aminoisoquinolines **118** and isoindolines **119**. One of the reasons for the significance of these heterocycles is that they constitute important structural motifs of various compounds with activities of relevance to biology or medicinal chemistry. For example, the aminoisoquinoline moiety was found in nonbenzamidine factor VIIa inhibitors against nonthromboembolic cardiovascular disease (Scheme 2.2 and Scheme 2.3).

[94] R. C. Larock, *Top. Organomet. Chem*. **2005**, *14*, 147–182.

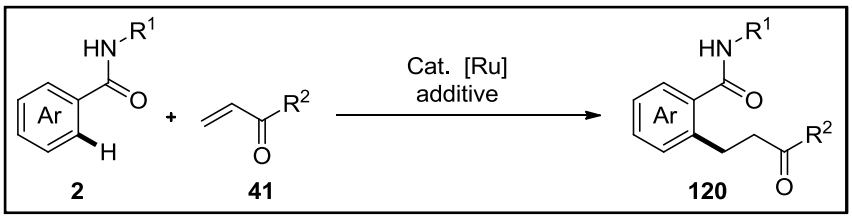


Scheme 2.2. Oxidative annulations of alkynes **1** with decorated amidines **117** through C–H activation.



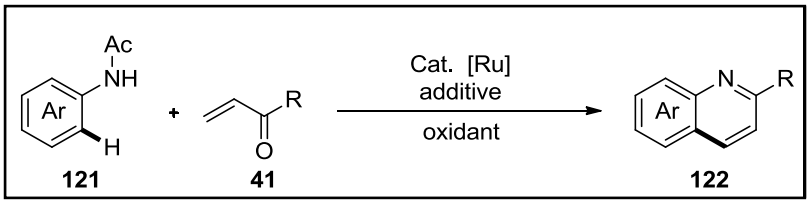
Scheme 2.3. Oxidative alkenylation of decorated amidines **117** with acrylated **20** through C–H bond activation.

The synthetic utility of the transition-metal-catalyzed hydroarylation *via* C–H bond activation was illustrated by Murai.[34] Despite the remarkable progress achieved during the last decade, *α,β*-unsaturated acceptors still could not be utilized for such alkylations until 8-aminoquinoline was introduced as a removable bidentate directing group by Chatani.[46] We planned to establish ruthenium-catalyzed direct hydroarylation of *α,β*-unsaturated ketones **41** with aromatic amides **2** *via* monodentate coordination in an environmentally friendly medium (Scheme 2.4).



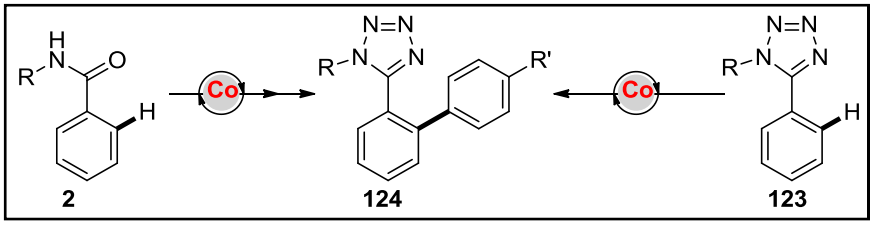
Scheme 2.4. Hydroarylation of *α,β*-unsaturated ketones **41** with mono-dentate amides **2**.

Meanwhile, oxidative annulations of *α,β*-unsaturated ketones **41** with acetanilides **121** to synthesize decorated quinolines **122** were also envisioned (Scheme 2.5).



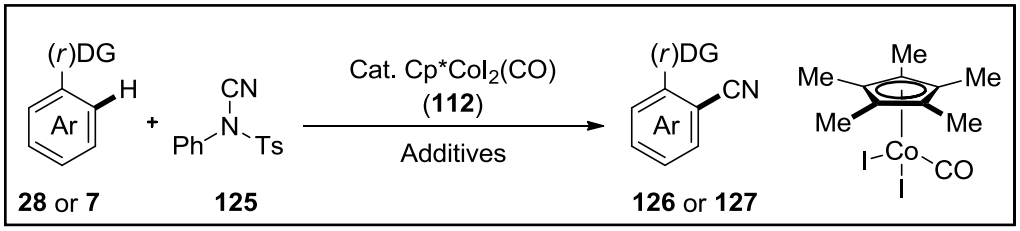
Scheme 2.5. Oxidative annulations of α,β-unsaturated ketones **41** with acetanilides **121**.

Biaryls constitute the key structural motifs of biologically active and naturally occurring compounds, for example, in angiotensin-II-receptor blockers (ARBs).[5e] The synthesis of these structural moiety mostly relied on palladium(0)-catalyzed cross-coupling reactions. Recently, the development of catalysts based on the naturally more abundant and less expensive first-row transition metals and their complexes has witnessed considerable growth.[47] Among them, inexpensive cobalt catalysts have been recognized as increasingly viable tools for C–H bond activations during the last years. Consequently, the use of cobalt complexes were another focus in this context to develop a new step- and atom-economic strategy for the synthesis of ARBs **124** and derivatives, as shown in Scheme 2.6.



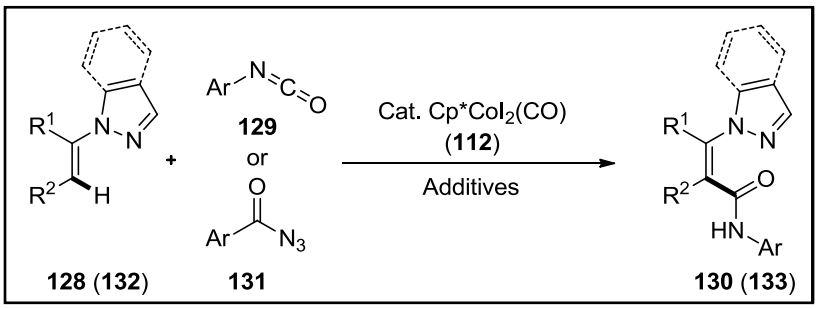
Scheme 2.6. Strategy for the synthesis of ARBs and derivatives.

Generally, many cobalt catalytic systems required Grignard reagents as the base and the reductant to generate the reactive low-valent cobalt catalysts. Hence, most of the functional groups could not be tolerated under these reaction conditions. In order to avoid these disadvantages, the research groups of Kanai, Ackermann, Daugulis and Song developed milder reaction conditions with cobalt catalysts, including high-valent Cp*Co(III) derivatives. Based on this progress, we set out to develop an unprecedented cobalt(III)-catalyzed C–H cyanation of arenes **28** and heteroarenes **7** as the fifth project. (Scheme 2.7).



Scheme 2.7. Cobalt(III)-catalyzed C–H cyanation.

In the last few years, transition-metal-catalyzed direct insertion of isocyanates into C–H bonds is in great demand, because this approach efficiently provides synthetically valuable amides. However, acyl azides were only found to work as amino sources in the iridium- and ruthenium-catalyzed amidation reactions. Moreover, further application of acyl azides was strongly limited by the difficulty in controlling the dual reactivity of acyl azides, as the reaction results in C–C and C–N bond formations and often affords a mixture of products. For this reason, it was our goal to develop the first cobalt(III)-catalyzed C–H aminocarbonylation with isocyanates **129** and acyl azides **131** (Scheme 2.8).



Scheme 2.8. Cobalt(III)-catalyzed aminocarbonylation of C–H bonds.

3 Ruthenium(II)-Catalyzed Oxidative Alkyne Annulation by C–H Bond Activation on Ketimines

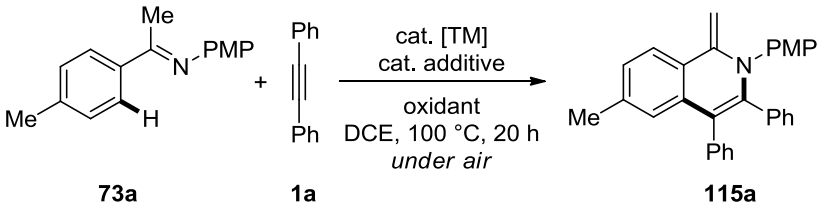
Isoquinolines are key structural moieties of various practically useful compounds. One of the most efficient methods for their preparation has been so far the transition-metal-catalyzed oxidative annulation of alkynes with *ortho*-halo-substituted aromatic imines with alkynes to furnish these heterocycles.[95] Herein, we established a more straightforward approach to decorated isoquinolines **115** through ruthenium(II)-catalyzed oxidative alkyne annulations with easily accessible ketimines **73** as the starting materials. The reaction provided an expedient access to *exo*-methylene-1,2-dihydroisoquinolines **116**.[96]

3.1 Optimization studies

At the outset of our studies, we explored various reaction conditions for the envisioned ruthenium(II)-catalyzed annulations of tolane (**1a**) with ketimine **73a**, along with $Cu(OAc)_2 \cdot H_2O$ as the oxidant (Table 3.1). Preliminary experiments indicated DCE to be the solvent of choice, while significantly lower yields were obtained with *t*-AmOH, MeOH, H_2O, DMF or toluene. Furthermore, KPF_6 and $MesCO_2K$ proved to be suitable as cocatalytic additives. Yet, the most effective catalysis was achieved with $AgSbF_6$ (Table 3.1, entries 1–4), which is likely due to the *in situ* formation of a cationic ruthenium catalyst. It is worth noting that the C–H bond functionalization proceeded efficiently under an ambient atmosphere of air, which highlights the user-friendly system (entry 5). While $CuBr_2$ as the oxidant shut down the oxidative alkyne annulation completely (entry 6), interestingly, the catalytic activity was restored through the addition of metal acetates, indicating carboxylate assistance to be of major importance for the C–H bond functionalization (entries 7–9).[5q,97] Additionally, we found that the ruthenium(II) catalyst outcompeted typical rhodium or palladium complexes (Table 3.1, entries 5, 10, and 11).

Table 3.1. Optimization of the oxidative annulations with ketimine **73a**.[a]

[95] R. C. Larock, *Top. Organomet. Chem*. **2005**, *14*, 147–182.
[96] J. Li, L. Ackermann, *Tetrahedron* **2014**, *70*, 3342–3348.
[97] L. Ackermann, *Chem. Commun*. **2010**, *46*, 4866–4877.



73a **1a** **115a**

Entry	Catalyst	Additive	Oxidant	Yield [%][b]
1	--	--	$Cu(OAc)_2 \cdot H_2O$	0
2	$[RuCl_2(p\text{-cymene})]_2$	KPF_6	$Cu(OAc)_2 \cdot H_2O$	51[c]
3	$[RuCl_2(p\text{-cymene})]_2$	$MesO_2K$	$Cu(OAc)_2 \cdot H_2O$	61[c]
4	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	67[c]
5	***$[RuCl_2(p\text{-cymene})]_2$***	***$AgSbF_6$***	***$Cu(OAc)_2 \cdot H_2O$***	***71***
6	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$	0
7	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$/NaOAc	54[d]
8	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$/KOAc	53[d]
9	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$/CsOAc	37[d]
10	$[RhCpCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	46
11	$PdCl_2(PPh_3)_2$	$AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	0

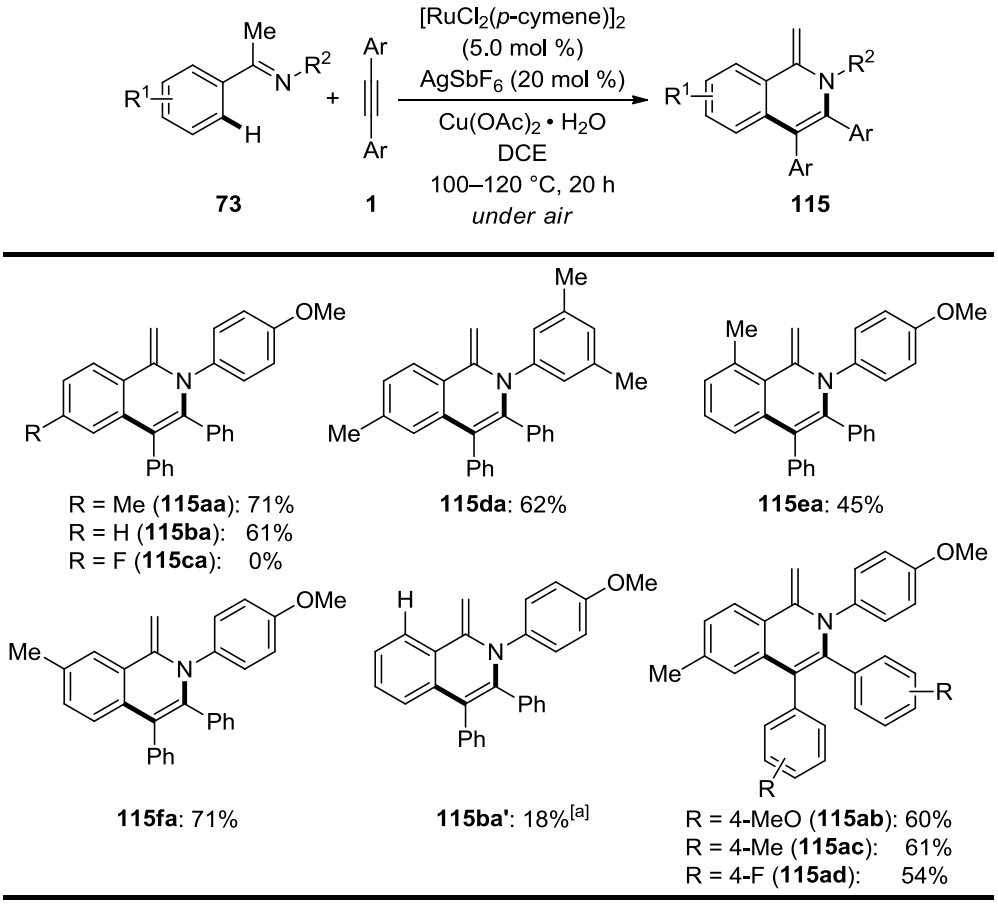
[a] General reaction conditions: **73a** (0.50 mmol), **1a** (1.00 mmol), catalyst (5.0 mol %), additive (20–30 mol %), oxidant (0.50 mmol), DCE (2.0 mL), under ambient air, 100 ℃ , 20 h. [b] Isolated yields. [c] Under an atmosphere of N_2. [d] MOAc (1.0 mmol).

3.2 Scope and Limitations

3.2.1 Scope of Aromatic Alkyne Annulation

With the optimized reaction conditions in hand, we explored its scope and limitations in the oxidative C–H functionalization with differently substituted ketimines **73** and alkynes **1** (Scheme 3.1). The oxidative annulation efficiently occurred with acetophenonimines **73** bearing substituents on the *N*-aryl moiety. Notably, transformations of electron-rich-methylsubstituted ketimines **73a** and **73d** proceeded very smoothly (**115aa**, **115da**), whereas substrate **73c** with the electron-deficient fluoro group provided only a negligible conversion under the optimized conditions. Furthermore, a more sterically hindered

substrate **73e** bearing an *ortho*-methyl substituent was also converted, albeit with a relatively low isolated yield of product **115ea**. Intramolecular competition experiments with substrate **73f** bearing a *meta*-methyl group was controlled by steric interaction to deliver the product **115fa**, which can be rationalized in terms of significant steric interactions. Compound **115ba'** was obtained in low yield when (*E*)-*N*-[1-(2-bromophenyl)ethylidene]-4-methoxyaniline (**73g**) was employed. Meanwhile, substituted tolane derivatives **1b**–**1d** were found to be viable substrates as well, thereby delivering the desired products **115ab**–**115ad**, respectively. Yields of the desired products can be affected by different electronic factors in the substituted alkynes. Thus, compounds **1b** and **1c** with electron-rich methyl and methoxyl groups delivered the target products in relatively better yields.

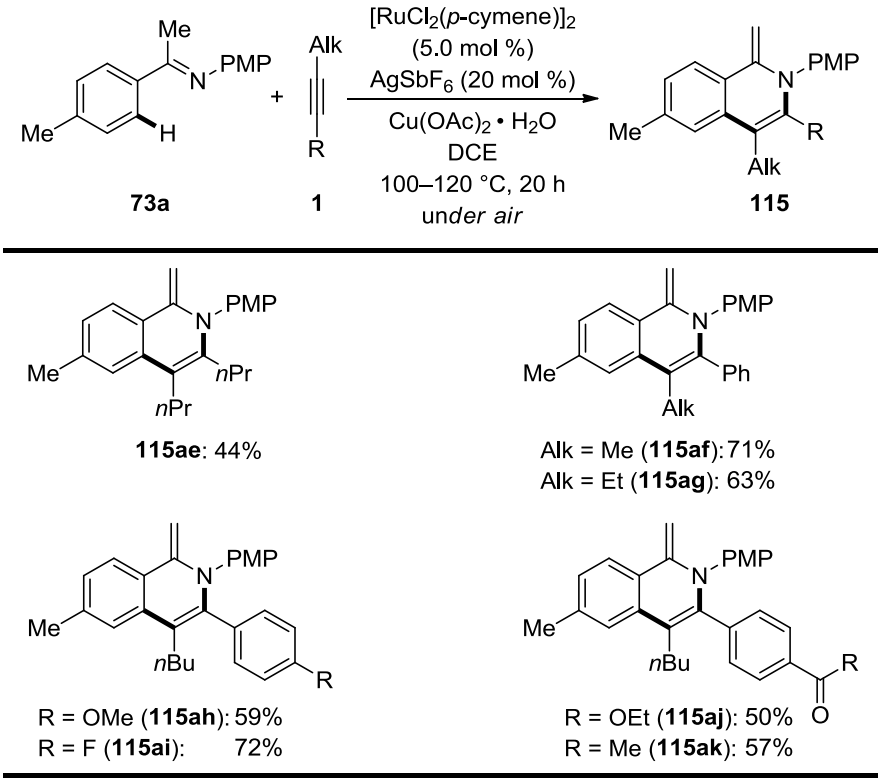


Scheme 3.1. Oxidative C–H functionalization of aromatic ketimines **73**. [a] (*E*)-*N*-[1-(2-bromophenyl)ethylidene]-4-methoxyaniline (**73g**, 0.5 mmol) was used.

3.2.2 Scope of the Annulation with Alkyl Alkynes

Fortunately, the optimized catalytic system was not restricted to the use of diarylalkynes **1** as

starting materials (Scheme 3.1). We initially tested dialkylsubstituted substrate **1e**, which delivered the desired product **115ae** in acceptable yield (Scheme 3.2). Here, we particularly focused our efforts on the use of unsymmetrical substrates **1** to probe the challenging regiocontrol in the oxidative annulation. We were delighted to observe that the C–H bond functionalizations proceeded with perfect regioselectivities, placing the aromatic substituent proximal to the nitrogen atom, which can be ascribed to the steric hindrance of the alkyl groups. Furthermore, the ruthenium catalyst displayed high chemoselectivity in which oxidative annulations of alkynes **1j** and **1k** bearing an ester or a ketone group solely took place through chelation assistance by the ketimine moiety to furnish products **115aj** and **115ak** in moderate yields (Scheme 3.2).

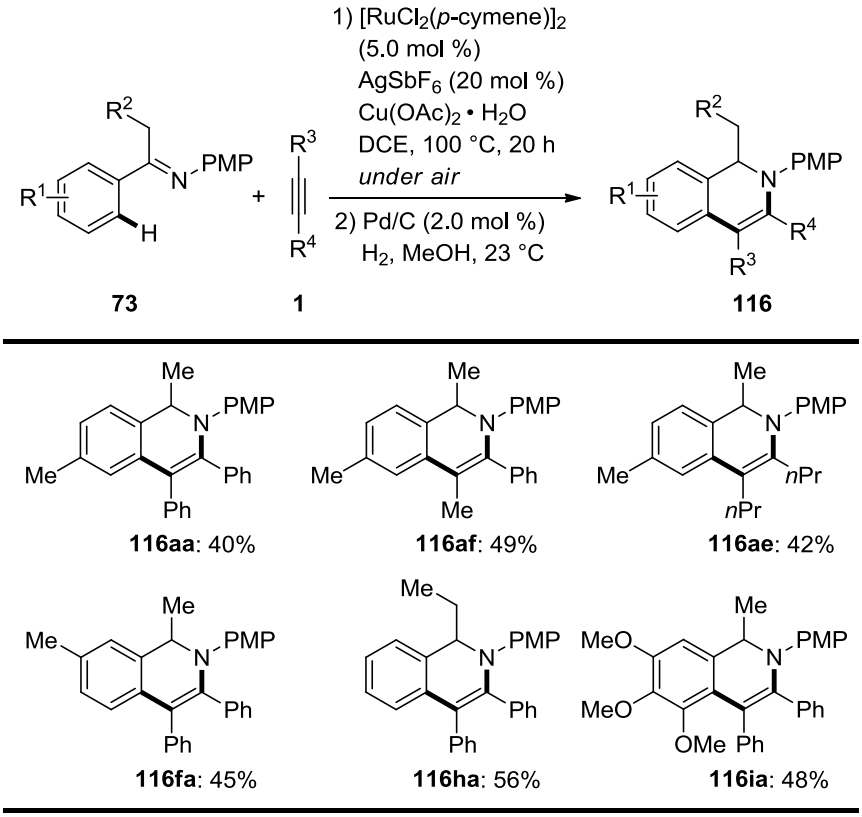


Scheme 3.2. Oxidative C–H functionalization with alkylalkynes **1**.

3.2.3 Multicatalytic Synthesis of Dihydroisoquinolines

Considering that the 2-substituted isoquinoline moiety plays an important role in various heterocyclic compounds with different bioactivities as key structural motifs, we subsequently devised a two-step reaction sequence consisting of the initial ruthenium(II)-catalyzed C–H bond functionalization followed by the palladium-catalyzed hydrogenation in a one-pot

fashion (Scheme 3.3). The multicatalytic approach set the stage for the efficient preparation of the decorated products **116**, again occurring with excellent regio- and chemo-selectivities (**116af**, **116fa**). It is noteworthy that a more sterically congested ketimine **73h** gave the ethyl-substituted dihydroisoquinoline **116ha** in a comparable yield.

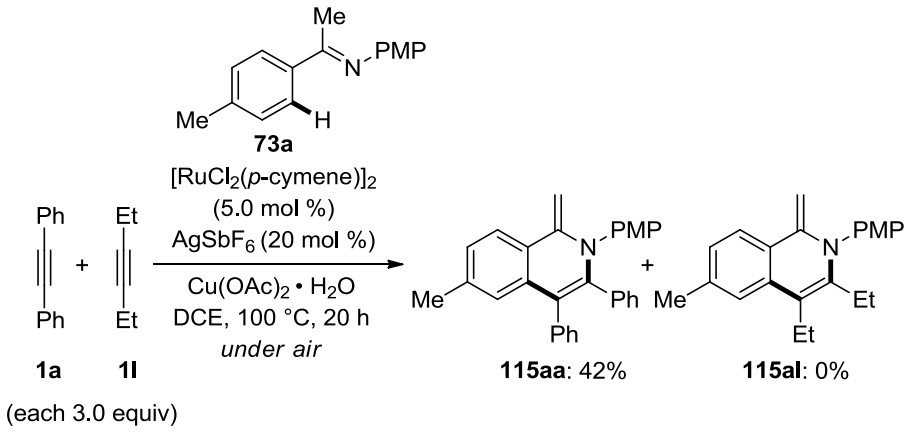


Scheme 3.3. Multicatalytic synthesis of 1,2-dihydroisoquinolines **116**.

3.3 Mechanistic Studies

3.3.1 Intermolecular Competition Experiment

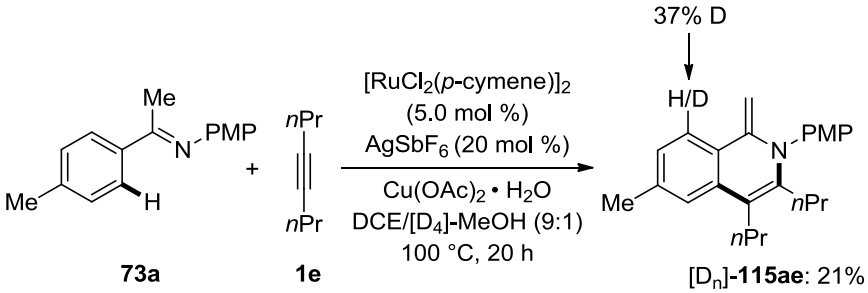
Given the unique selectivity and outstanding efficacy of our ruthenium(II)-catalyzed C–H bond functionalization approach, we became interested in exploring its mode of action. Hence, keeping this purpose in mind, a competition experiment between arylalkyne **1a** and alkylalkyne **1l** was performed and revealed the former to be solely converted (Scheme 3.4).



Scheme 3.4. Competition experiment between alkynes **1a** and **1l**.

3.3.2 Reaction in the Presence of Isotopically Labeled Solvent

Furthermore, significant H/D exchange was observed in the presence of the deuterated cosolvent [D_4]-MeOH, which can be rationalized in terms of a reversible carboxylate-assisted C–H bond metalation step by the ruthenium(II) complex (Scheme 3.5).

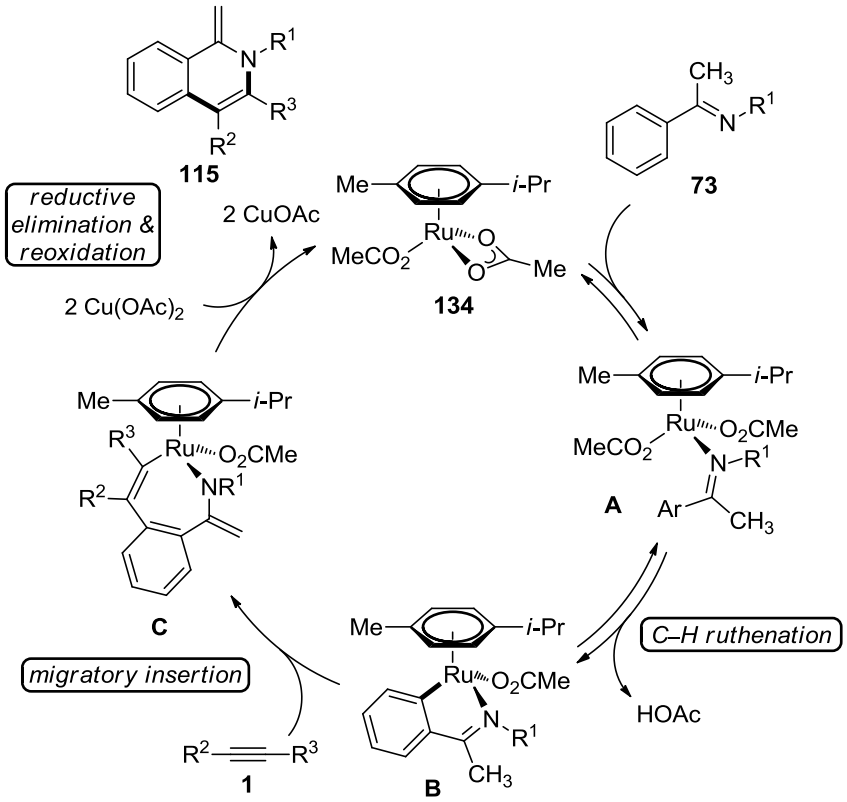


Scheme 3.5. C–H bond functionalization in the presence of deuterated cosolvent [D_4]-MeOH.

3.4 Proposed Catalytic Cycle

Based on these mechanistic studies, we propose the following catalytic cycle for the ruthenium(II)-catalyzed oxidative annulation, which commences with a reversible chelation-assisted C(sp^2)–H bond ruthenation (Scheme 3.6) with a loss of one molecular acetic acid thereby affording intermediate **B**. Subsequently, a two-step sequence started from coordination of alkyne **1** and followed by regioselective migratory insertion[5i] along with tautomerization[98] occurred. Thus, a seven-membered key intermediate **C** is generated. Finally, the desired product **115** was furnished *via* reductive elimination, while the catalytically active species **134** was regenerated through oxidation by $Cu(OAc)_2$.

[98] Y. Boutadla, O. Al-Duaij, D. L. Davies, G. A. Griffith, K. Singh, *Organometallics* **2009**, *28*, 433–440.



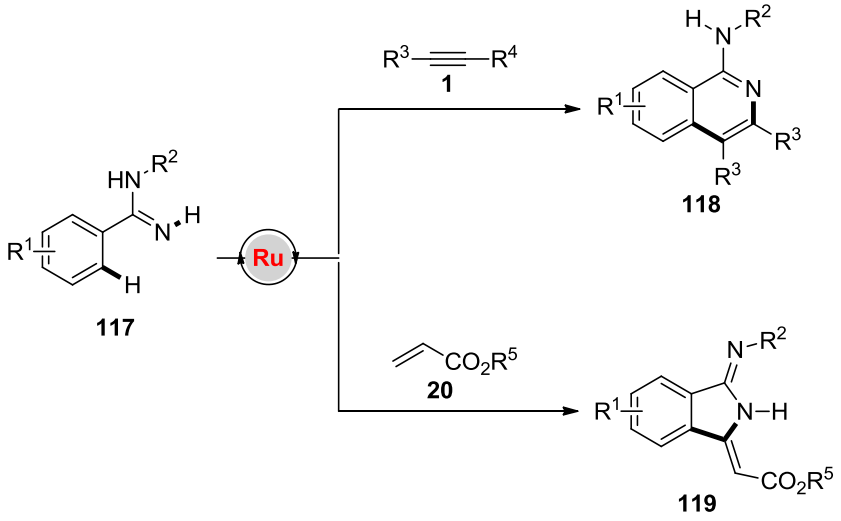
Scheme 3.6. Proposed catalytic cycle.

3.5 Conclusion

In summary, we have reported on a novel ruthenium(II)-catalyzed oxidative alkyne annulation to furnish exo-methylene-1,2-dihydroisoquinolines by C–H activation on ketimines. Particularly, carboxylate-assisted ruthenium(II) catalysis proved to be decisive for the success of the synthesis of diversely decorated products in high yields. Compounds **115** can easily be transformed into heterocycles **116** *via* palladium-catalyzed hydrogenation in a one-pot fashion. The ruthenium(II)-catalyzed C–H bond functionalizations proceeded with excellent chemo-, site-, and regio-selectivities under an ambient atmosphere of air. Mechanistic studies were indicative of a reversible C–H bond metalation step.

4 Amidines for Versatile Ruthenium(II)-Catalyzed Oxidative C–H Bond Activation with Internal Alkynes and Acrylates

Aminoisoquinolines and isoindolines are among the most abundant heterocycles and represent indispensable structural motifs in bioactive compounds (see Chapter **1.2**).[99] With the successful utilization of ruthenium(II) catalysts for oxidative C–H bond activations, we were interested to establish the first ruthenium-catalyzed oxidative C–H bond functionalizations with benzamidines **117**.[100]



Scheme 4.1. Ruthenium(II)-catalyzed C–H bond activation on amidines **117**.

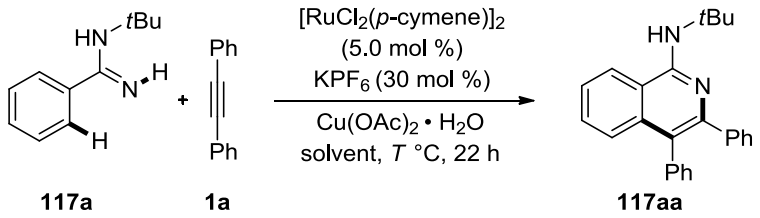
4.1 Oxidative Alkyne Annulation

4.1.1 Optimization Studies

We initiated our studies by testing different reaction conditions for the desired oxidative annulation of tolane (**1a**) with benzamidine **117a**. Preliminary experiments proved $[RuCl_2(p\text{-cymene})]_2$ as the ideal metal complex and KPF_6 as the cocatalytic additive of choice, while significantly lower yields were obtained with $AgSbF_6$ or AgOAc. Among a set of representative solvents, DME provided optimal results (Table 4.1, entries 1–5 and 8). However, it is worth noting that inexpensive, non-toxic H_2O[101,5o] was found to be a viable reaction medium as well (entries 6 and 7).

[99] a) R. Alajarin, C. Burgoes, *in Modern Heterocyclic Chemistry* (Eds.: J. Alvarez-Builla, J. J. Vaquero, J. Barluenga), Wiley-VCH, Weinheim, **2011**, 1527–1629; b) N. L. Subasinghe, J. Lanter, T. Markotan, E. Opas, S. McKenney, C. Crysler, C. Hou, J. O'Neill, D. Johnson, Z. Sui, *Bioorg. Med. Chem. Lett*. **2013**, *23*, 1063–1069.
[100] J. Li, M. John, L. Ackermann, *Chem. Eur. J*. **2014**, *20*, 5403–5408.
[101] B. Li, P. H. Dixneuf, *Chem. Soc. Rev*. **2013**, *42*, 5744–6337.

Table 4.1. Optimization of oxidative annulation with benzamidine **117a**.[a]



117a **1a** **117aa**

Entry	***T*** [°C]	**Solvent**	**Yield** [%][b]
1	100	DMF	7
2	100	PhMe	21
3	100	*m*-xylene	25
4	100	1,4-dioxane	20
5	100	DME	58
6	100	H_2O	46[c]
7	120	H_2O	76[c]
8	***120***	***DME***	***86***[c]

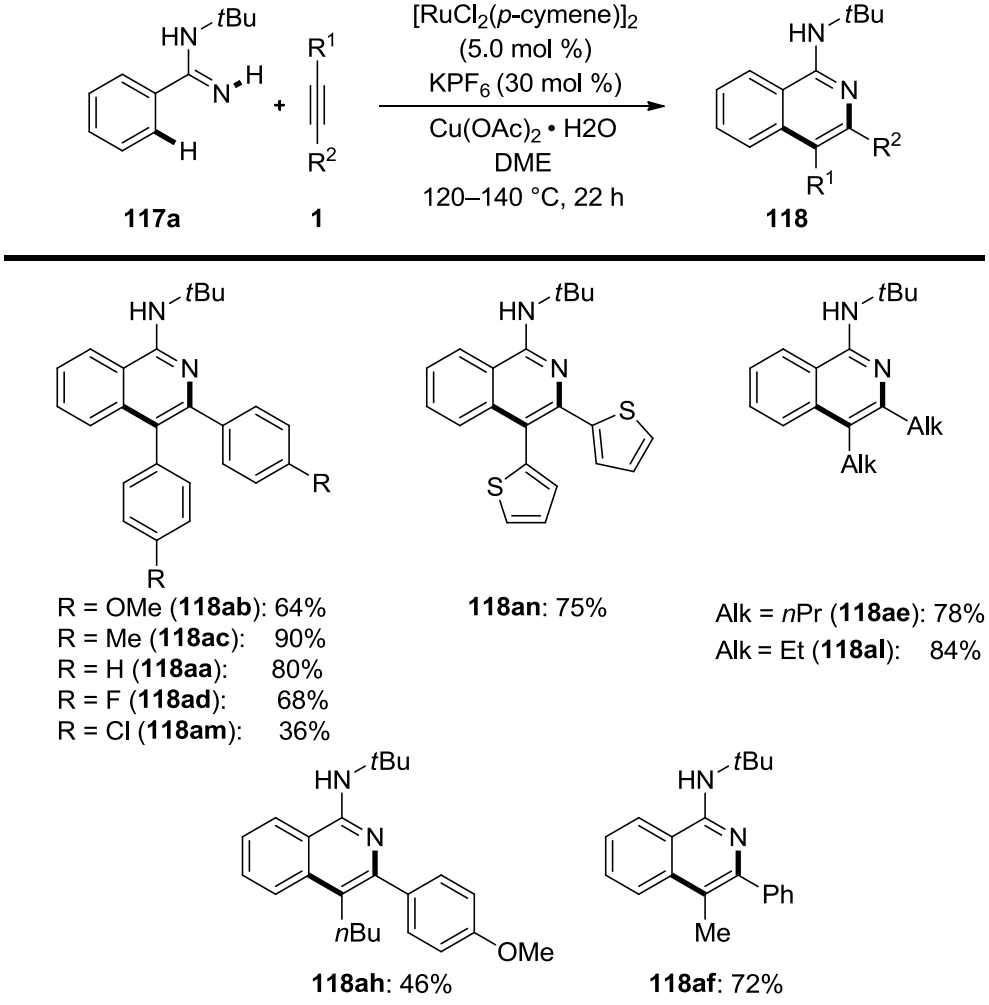
[a] Reaction conditions: **117a** (0.5 mmol), **1a** (0.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), KPF_6 (30 mol%), solvent (2.0 mL). [b] Yields of isolated products. [c] 2.0 equiv of alkyne **1a**.

4.1.2 Scope and Limitations

4.1.2.1 Scope of Annulations with Alkynes

Thereafter, with the optimized catalytic system in hand, we probed its scope and limitations in the oxidative annulation of differently decorated alkynes **1** (Scheme 4.2). We were delighted to find that arylalkynes **1b**–**1d** and **1m** bearing different functional groups were well tolerated by the ruthenium catalyst, though slightly lower yields were obtained when the electron-rich (**1b**) or electron-deficient diarylalkynes **1d** and **1m** as well as alkyne with sulfur-containing heteroaromatic moieties in substrate **1n** were employed. The catalytic system was not limited to the use of diarylalkynes, but also allowed for the efficient conversion of the more challenging dialkylalkynes **1e** and **1l**. Unsymmetrically substituted alkynes **1h** and **1f** were

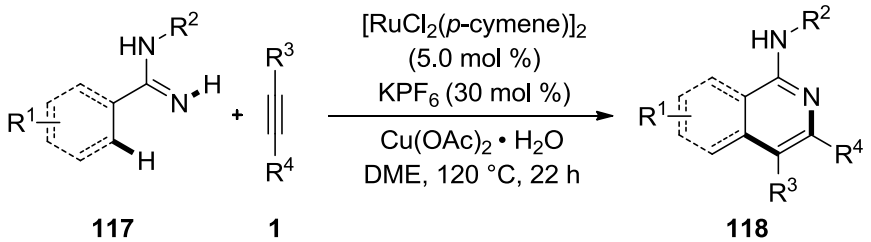
converted with high regioselectivity, furnishing solely the products **118ah** and **118af**, respectively, with the aromatic substitutents in the neighbouring position to the nitrogen atom.

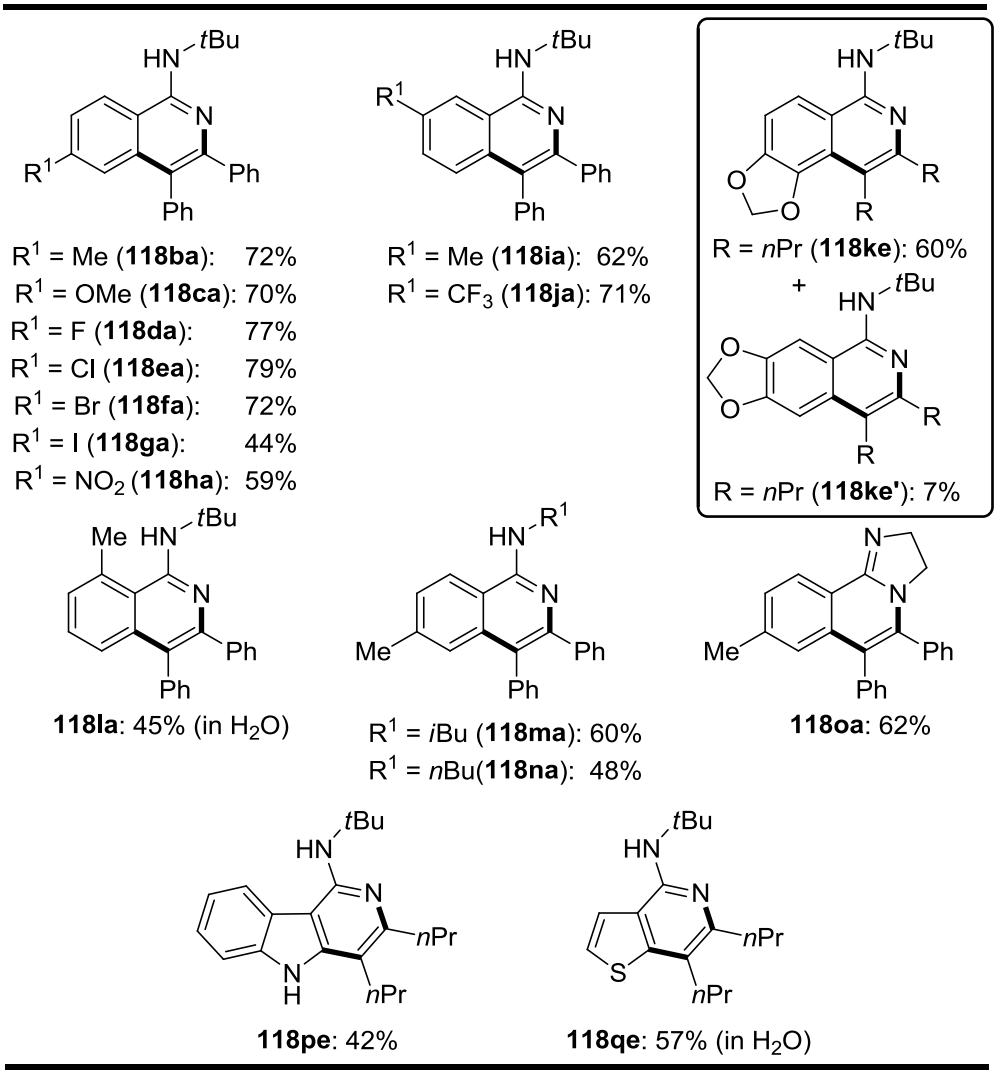


Scheme 4.2. Ruthenium(II)-catalyzed oxidative annulation with alkynes **1**.

4.1.2.2 Scope of Annulations with Substituted Amidines

Next, the tolerance of various electrophilic functional groups was investigated under this catalytic system. Substituted benzamidines **117b–117h** bearing fluoro, chloro, bromo, iodio, or nitro substituents were well tolerated by the robust ruthenium(II) catalyst (Scheme 4.3).



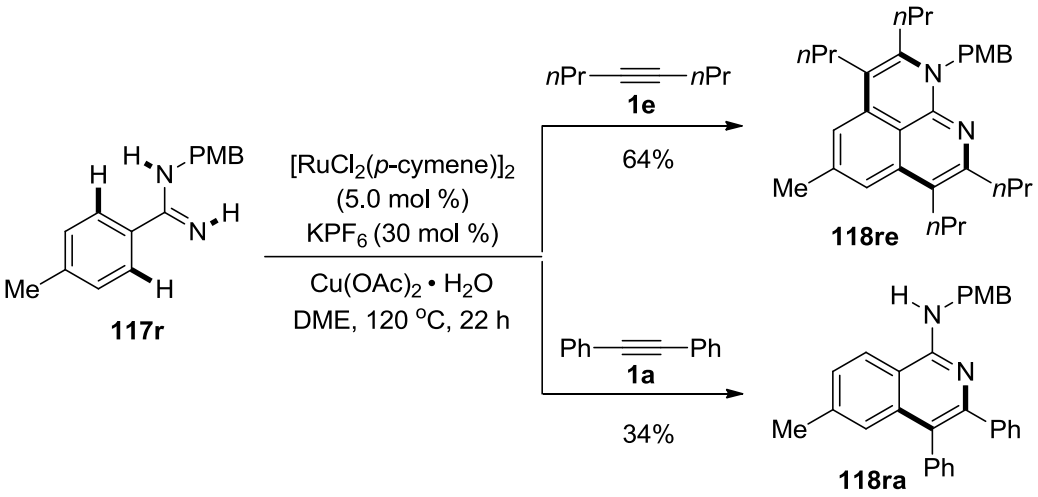


Scheme 4.3. Scope of annulation with substituted amidines **117**.

Intramolecular competition experiments with substrates **117i** and **117j** bearing *meta*-methyl or *meta*-trifluoromethyl substituents were controlled by steric interactions to deliver the sole products **118ia** and **118ja**, respectively. In contrast, the functionalization occurred predominantly at the more sterically congested C–H bond when there is a secondary directing-group installed on the amidine **117k**. Substrate **117l** bearing a sterically hindering *ortho*-substituent gave the desired product **117la** in a slightly reduced yield, as was also observed when using substrates **117n** with a less bulky *N*-substitution pattern. It is worth noting that cyclic amidine **117o** also proved to be viable starting materials and underwent the efficient conversion into product **118oa**. Moreover, indole and thiophene derivatives **117p** and **117q** gave the desired products of the C–H/N–H bonds functionalization as well, thus delivering γ-carboline **118pe** and annulated azabenzothiophene **118qe**.

Interestingly, a cascade twofold C–H/N–H bonds functionalization occurred when utilizing

the *para*-methoxybenzyl (PMB)-substituted benzamidine **117r** and dialkylalkyne **1e** as the starting materials, thereby highlighting the ability of the 1-aminoisoquinolines **118** themselves to serve as useful substrates for directed C–H bond transformations. In contrast, the arylalkyne **1a** uniquely furnished the product **118ra** through a single C–H/N–H bonds functionalization (Scheme 4.4).

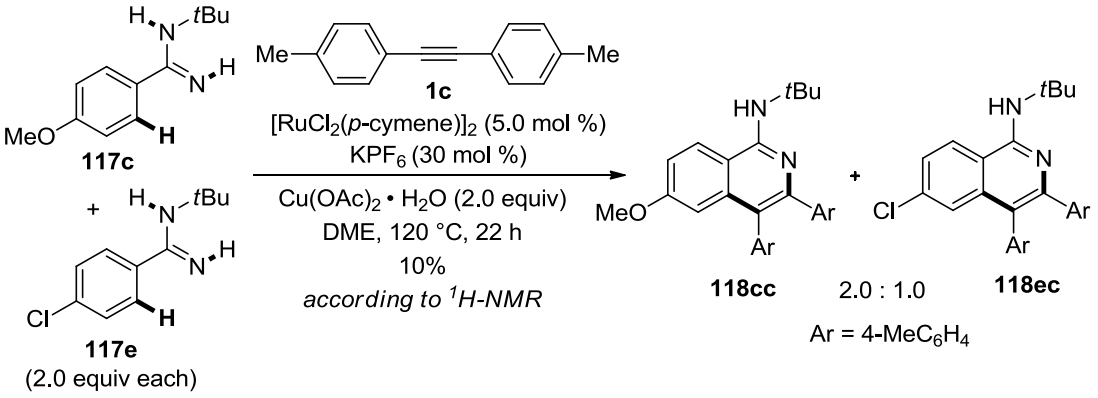


Scheme 4.4. Cascade twofold vs single C–H/N–H bonds functionalizations.

4.1.3 Mechanistic Studies

4.1.3.1 Intermolecular Competition Experiments

Given the remarkable activity of the alkyne-annulation catalyst, we performed mechanistic studies to delineate its mode of action. To this end, intermolecular competition experiments revealed electron-rich benzamidine **117c** to be preferentially converted (Scheme 4.5).

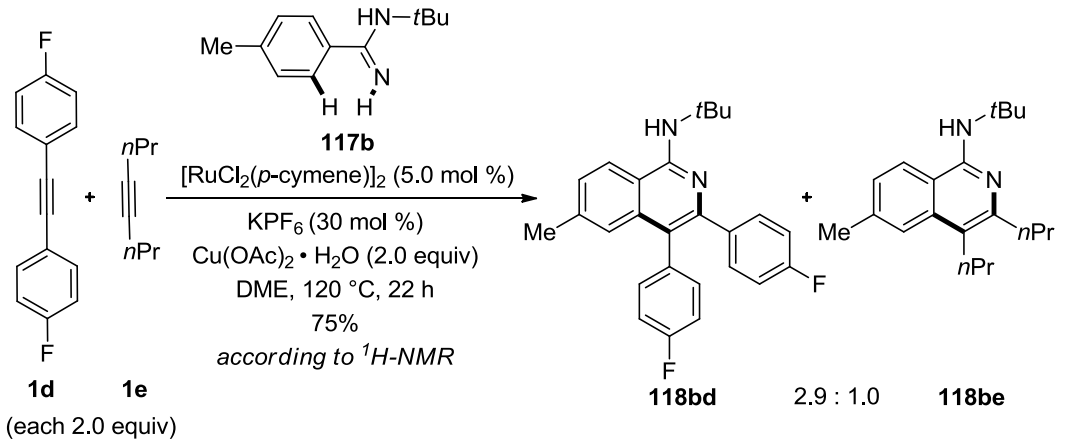


Scheme 4.5. Intermolecular competition experiment with benzamidines **117c** and **117e**.

This observation is in good agreement with the *in situ* generated cationic ruthenium(II)

complex operating by an electrophilic-type activation mode.

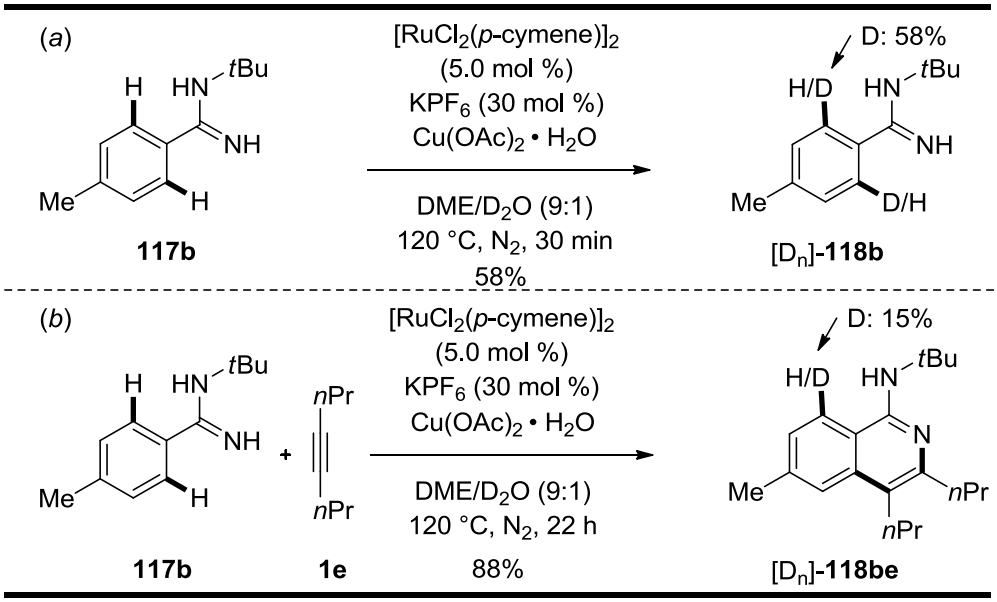
Additionally, a competition experiment between diarylalkyne **1d** and dialkylalkyne **1e** highlighted that aromatic alkynes outperformed the corresponding alkyl-substituted substrate (Scheme 4.6).



Scheme 4.6. Intermolecular competition experiment between alkynes **1**.

4.1.3.2 Reactions in the Presence of Isotopically Labeled Solvent

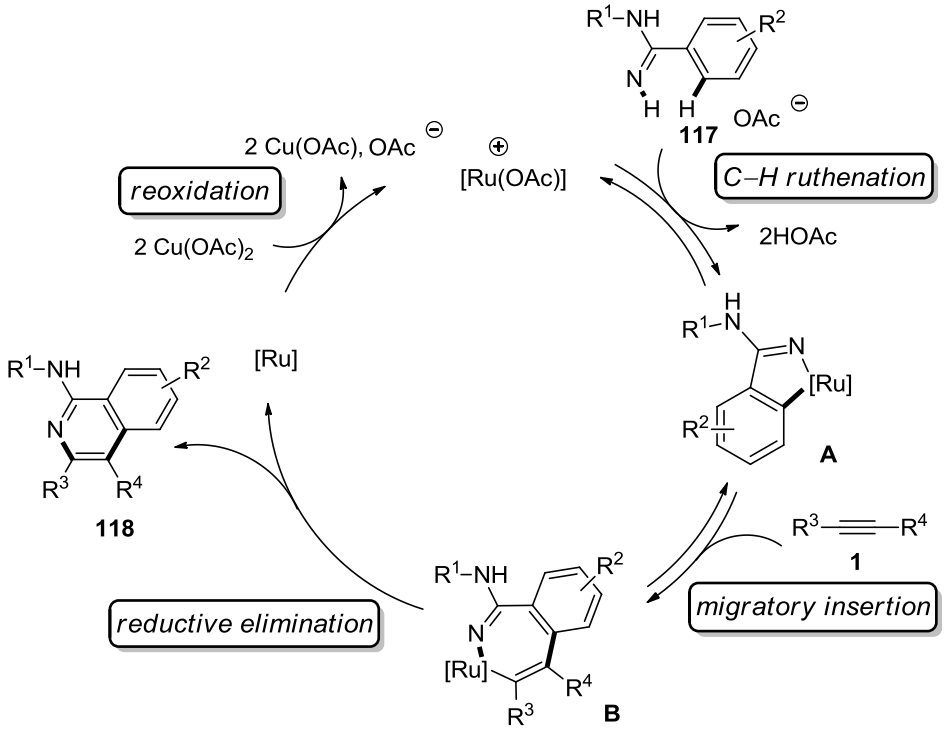
Subsequently, we explored the catalytic C–H bond functionalization on benzamidine **117b** in the presence of isotopically labeled water (D_2O) as the cosolvent. These studies demonstrated a significant H/D exchange in the *ortho*-positions of both the reisolated starting material **117b** (Scheme 4.7a) and the product **118**, albeit with a considerably reduced deuterium incorporation when performing the reaction in the presence of alkyne **1e** (Scheme 4.7b).



Scheme 4.7. H/D exchange reactions: (a) In the absence of **1**. (b) In the presence of **1e**.

4.1.4 Proposed Catalytic Cycle

Given our mechanistic studies and the literature precedents,[5i] we proposed a plausible catalytic cycle which involves an initial reversible C–H bond activation in substrate **117**, along with subsequent migratory insertion of alkyne **1** into intermediate **A** (Scheme 4.8). Thereafter, reductive elimination in ruthenacycle **B** delivered the desired product **118**, while reoxidation regenerated the catalytically active ruthenium(II) complex.



Scheme 4.8. Plausible mode of the catalyst action.

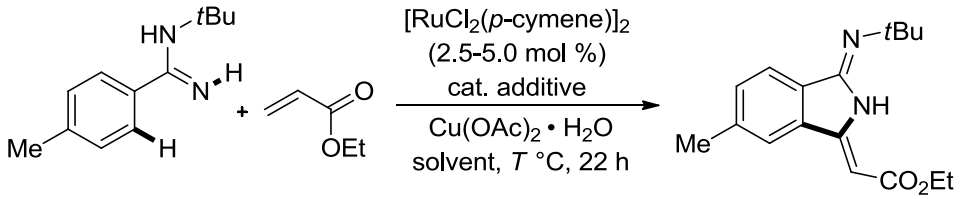
4.2 Oxidative Alkenylation

4.2.1 Optimization Studies

Taking into consideration the high catalytic efficacy of the ruthenium(II)-catalyzed oxidative annulation of alkynes **1**, we became intrigued by developing novel oxidative twofold C–H bond functionalizations with alkenes **20**. Therefore, we initially studied the effect exerted by representative additives and solvents on the cross-dehydrogenative coupling of alkene **20a** with amidine **117b** (Table 4.2). Apparently, employing the catalytic system previously optimized for the oxidative alkyne annulation catalytic system delivered 3-alkylydene-1-iminoisoindoline **119ba** in unsatisfactorily low yield (entry 1). This was caused by the formation of an undesired by-product stemming from *N*-deprotection, which

could be isolated in 43% yield.

Table 4.2. Optimization of oxidative annulation with alkene **20a**.[a]



117b **20a** **119ba**

Entry	Additive ([equiv])	*T* [℃]	Solvent	Yield [%][b]
1	KPF_6 (0.3)	120	DME	18[c]
2	$AgSbF_6$ (0.2)	120	DME	41
3	KPF_6 (0.3)	120	DCE	63
4	$AgSbF_6$ (0.2)	120	DCE	66
5	$AgPF_6$ (0.2)	120	DCE	13
6	CF_3CO_2Ag (0.2)	120	DCE	59
7	AgOAc (0.3)	120	DCE	70
8	AgOAc (0.5)	120	DCE	75
9	***AgOAc (0.5)***	***100***	***DCE***	***73[d]***
10	AgOAc (0.5)	80	DCE	69[d]
11	AgOAc (0.5)	60	DCE	64[d]

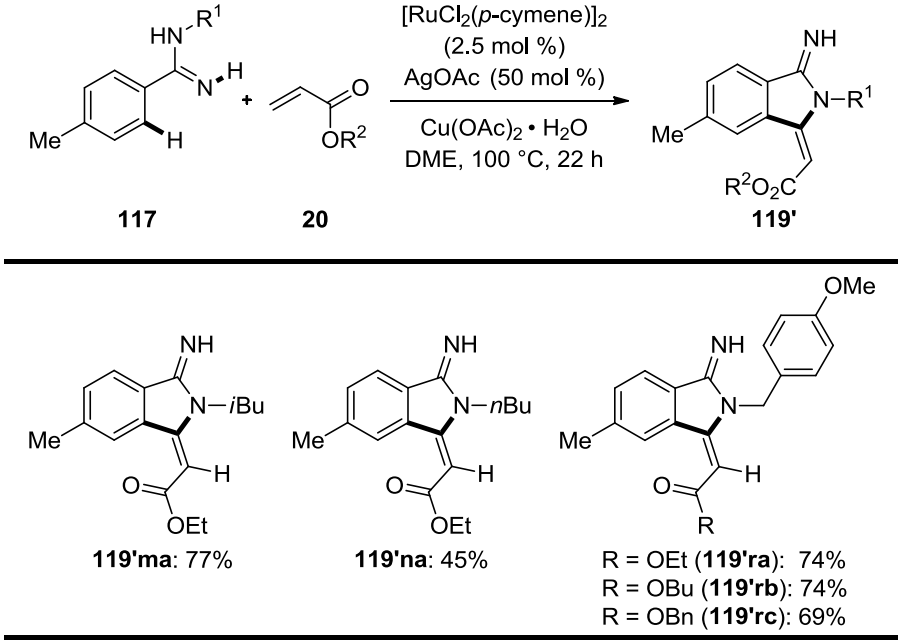
[a] Reaction conditions: **117b** (0.5 mmol), **20a** (1.5 equiv), $Cu(OAc)_2 \cdot H_2O$ (2.0 equiv), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol%), cat. additive, solvent (2.0 mL), 18–22 h. [b] Yields of isolated products. [c] Along with 43% of the corresponding *N*-deprotected product. [d] $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %).

However, we were pleased to observe that the efficacy of the oxidative alkenylation process was remarkably improved when using $AgSbF_6$ as the additive in DCE as the solvent (entries 2 and 3). Among a series of silver(I) salts (entries 4–8), 50 mol % of AgOAc gave the product in optimal yields (entries 8 and 9). This allowed for efficient catalysis to occur at a reduced catalyst loading and at reaction temperatures as low as 60 ℃ .[5o] Various oxidants other than $Cu(OAc)_2 \cdot H_2O$, such as $CuBr_2$, $K_2S_2O_8$, or $PhI(OAc)_2$, did not furnish the desired product **119ba**.

4.2.2 Scope and Limitations

4.2.2.1 Scope of *N*-Substituents on Amidines

In order to test the range of our optimized catalytic system for the oxidative alkenylation, we initially evaluated the influence exerted by the different steric bulk of the *N*-substituent in benzamidines **117** (Scheme 4.9). Among the less sterically hindered *iso*- or *n*-butyl-substituted substrates, amidines **117m** and **117n** (Scheme 4.9) delivered inferior results as compared to the *tert*-butyl analogue **117b** (Table 4.2). It is worth noting that detailed spectroscopic studies on the product's connectivity revealed that the reduced steric bulk of the *N*-substituent strongly influenced the chemo- and diastereoselectivity of the isoindoline formation in that the substituted nitrogen atom of the amidine underwent the C–N bond formation. Furthermore, the PMB-substituted benzamidine **117r** gave the desired products **119'ra–119'uc** in high yields as well.

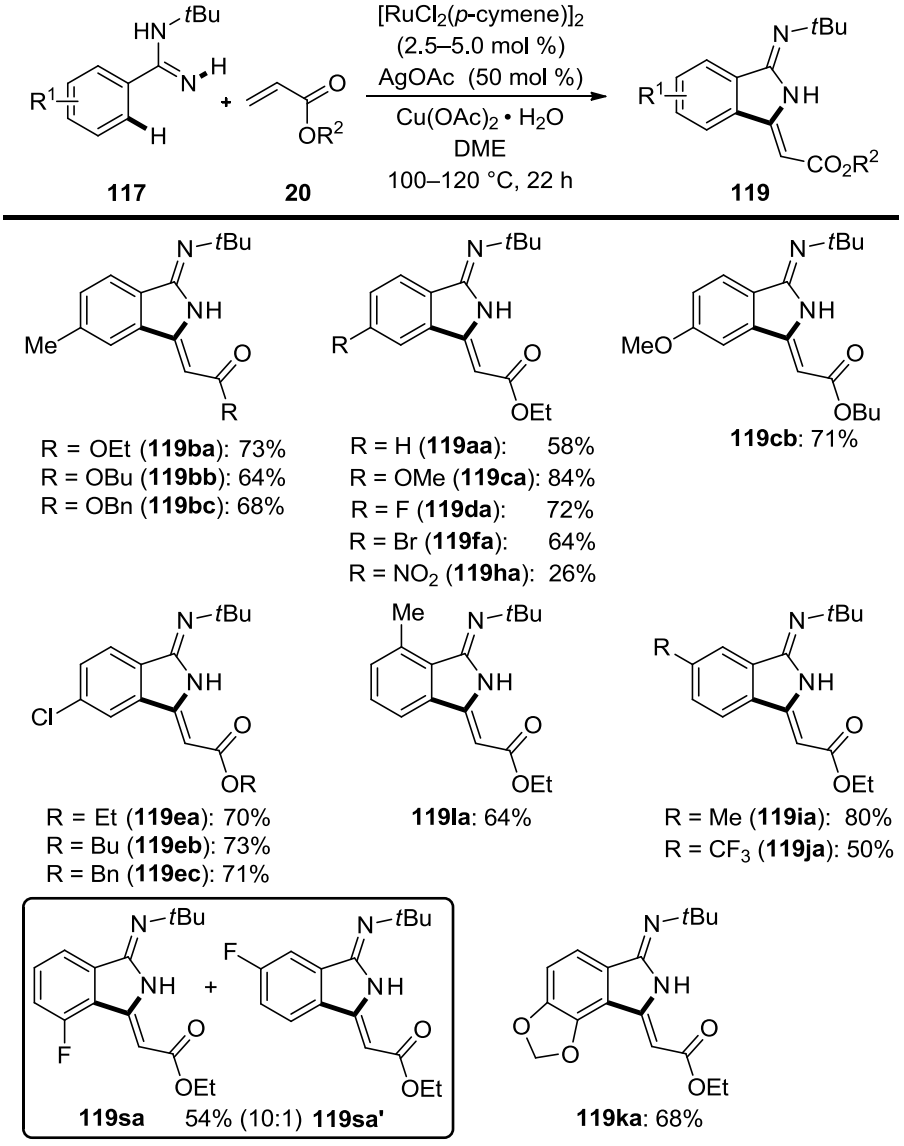


Scheme 4.9. Reactivity of benzamidines **117** with less bulky *N*-substituents.

4.2.2.2 Scope of the Oxidative Alkenylation with Aromatic Amidines and Acrylates

Thereafter, we examined the scope of the ruthenium(II)-catalyzed cross-dehydrogenative alkenylation with different substituted benzamidines **117** and alkenes **20** (Scheme 4.10a). Remarkably, the ruthenium(II) catalyst turned out to be widely applicable and tolerated various electrophilic functional groups, such as fluoro, chloro, bromo, and nitro substituents,

albeit with a low yield of the desired product **119ha** in the latter case. The C–H bond functionalizations occurred efficiently with *para*- and more sterically hindered *ortho*-substituted amidines **117b**, **117c** and **117l**.



Scheme 4.10. Scope of oxidative synthesis of 1-iminoisoindolines **119**.

Intramolecular competition experiments with *meta*-substituted amidines **117i** and **117j** were also tested and disclosed the formation of products **119ia** and **119ja** to be controlled predominantly by steric interactions. Yet, when using substrates having heteroatom substituents with a secondary directing group chelation effect[102] (substrate **117s**) or the fluoro substituent possessing the *ortho*-orienting effect (substrate **117k**),[103] sterically more hindered

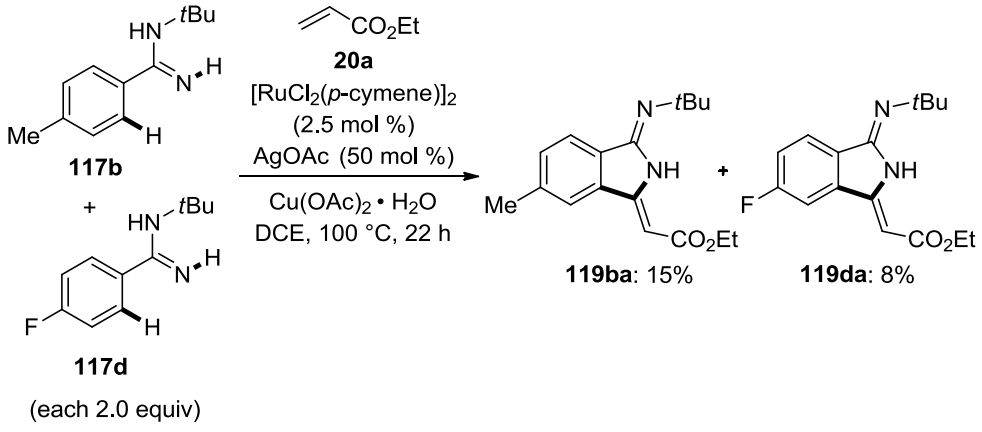
[102] D. Balcells, E. Clot, O. Eisenstein, *Chem. Rev.* **2010**, *110*, 749–823.
[103] E. Clot, O. Eisenstein, N. Jasim, S. A. Macgregor, J. E. McGrady, N. Perutz, *Acc. Chem. Res*. **2011**, *44*, 333–348.

compounds **119sa** and **119ka** were obtained as the major or the sole product, respectively (Scheme 4.10). The results of **119sa** revealed a considerable secondary directing group effect exerted by fluoro and methylenedioxy present in benzamidines **117s** and **117k**, respectively (Scheme 4.10).

4.2.3 Mechanistic Studies

4.2.3.1 Intermolecular Competition Experiments

To understand the working mode of our novel 1-imino-isoindoline (**119**) synthes, we performed intermolecular competition experiments between differently substituted benzamidines **117**. These studies revealed that the electron-rich substrate **117b** is inherently more reactive (Scheme 4.11), which coincides with the observation made within the ruthenium-catalyzed oxidative alkyne annulation (see above).

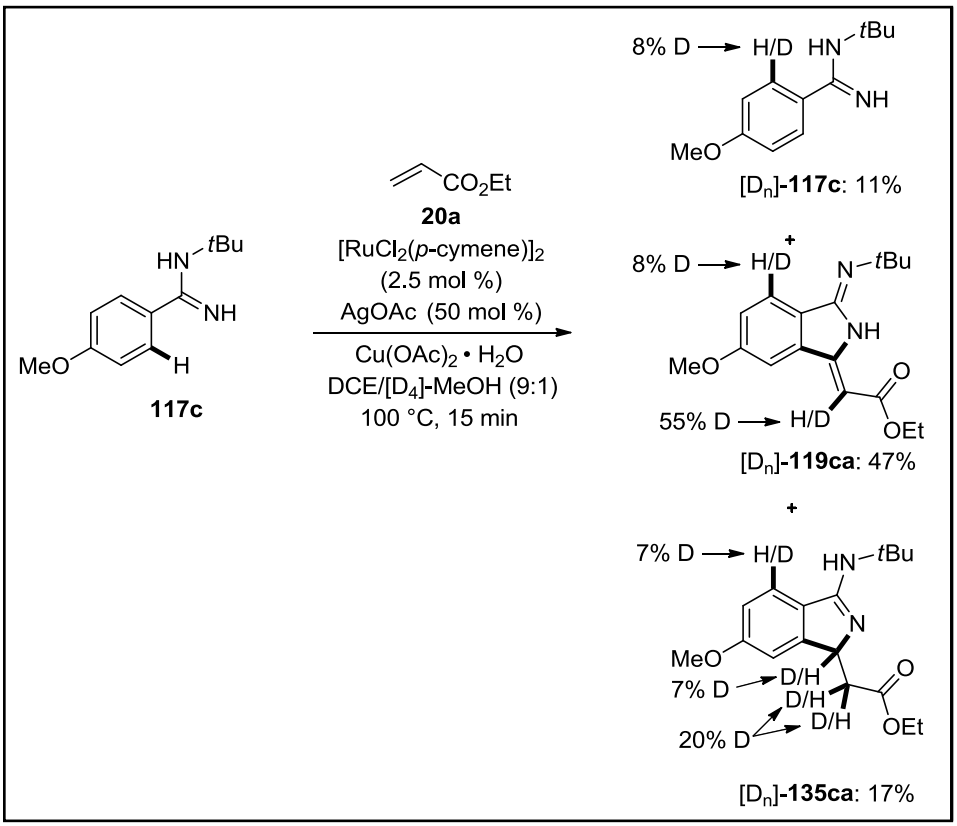


Scheme 4.11. Intermolecular competition experiment.

4.2.3.2 Experiment in the Presence of Isotopically Labeled Solvent

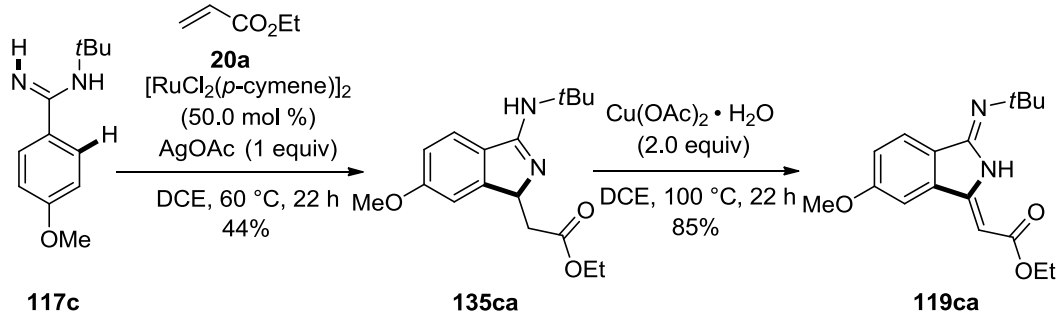
In addition, we performed reactions with the isotopically labeled cosolvent [D_4]-MeOH. These experiments revealed the high efficiency of the optimized catalytic system with cationic ruthenium(II) catalyst by giving a remarkable conversion of the substrate **117c** within only 15 min. Obvious evidence of H/D scrambling on both of the recycled starting material [D_n]-**117c** and desired product [D_n]-**119ca** was gathered (Scheme 4.12), which unraveled that the ruthenium(II)-catalyzed alkenylation is undergoing a reversible C–H bond metalation step. Notably, an important intermediate **135ca** was also isolated from the reaction mixture, thus indicating the reaction sequence to comprise an initial oxidative alkenylation followed by

subsequent intramolecular aza-Michael reaction. Both products **119ca** and **135ca** showed deuterium incorporation in the α-position to the carbonyl group, which is likely owing to the rapid H/D exchange on the N–H-acidic amidine group prior to the intramolecular conjugate addition.



Scheme 4.12. C–H bond activation in the presence of [D_4]-MeOH.

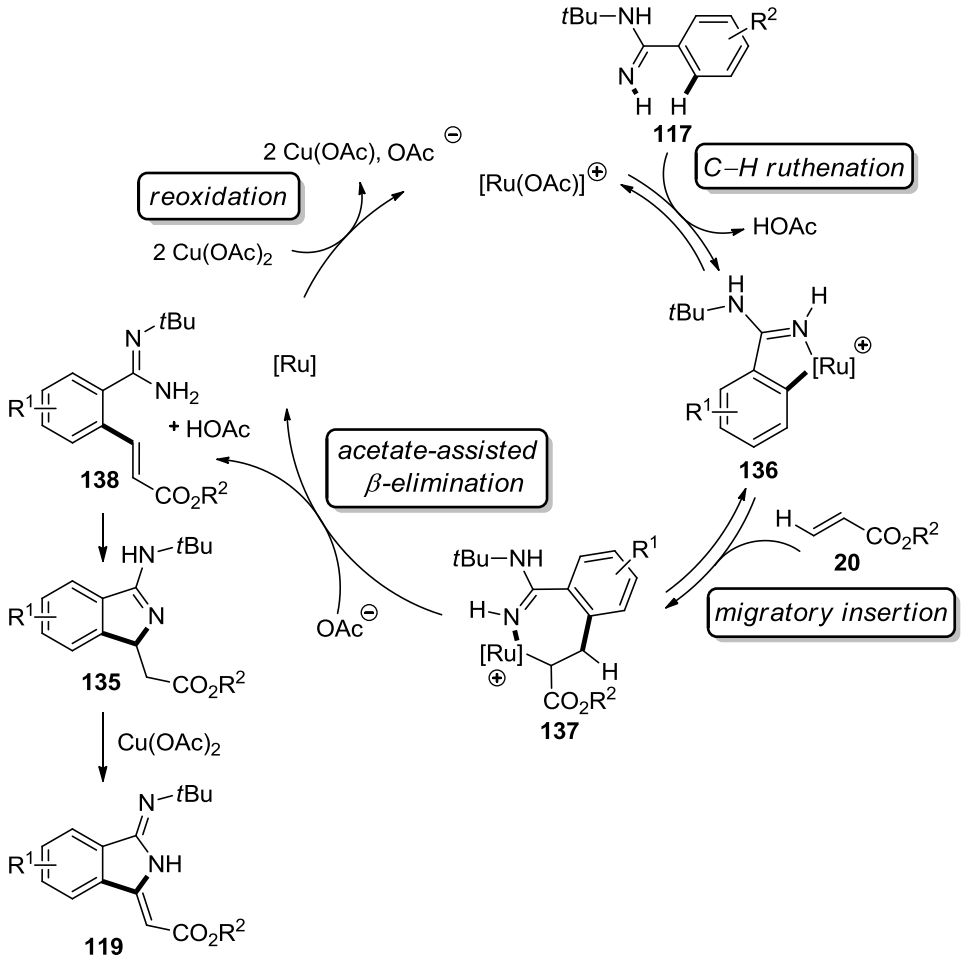
The intermediate **135ca** was obtained as a sole product by performing the cyclization without copper(II) acetate. Moreover, we established that the dehydrogenative formation of product **119ca** from **135ca** was indeed viable in the absence of the ruthenium catalyst, thus solely being mediated by the copper(II) oxidant (Scheme 4.13).



Scheme 4.13. Synthesis of intermediate **135ca** and copper(II)-mediated oxidative alkene formation.

4.2.4 Proposed Catalytic Cycle

Based on our mechanistic studies, we propose the initial C–H bond activation to involve a reversible acetate-assisted cycloruthenation of amidine **117** with the cationic species to form complex **136** (Scheme 4.14), which then undergoes a migratory insertion of alkene **20** to give the intermediate **137**. Subsequently, acetate-assisted *β*-hydride elimination gives rise to the product of oxidative alkenylation **138**, while reductive elimination and reoxidation by $Cu(OAc)_2 \cdot H_2O$ regenerates the catalytically active ruthenium(II) complex. The desired product **119** is yielded through an intramolecular aza-Michael addition of compound **138**, followed by dehydrogenation of the obtained intermediate **135**.



Scheme 4.14. Proposed catalytic cycle.

4.2.5 Conclusion

In summary, we have reported on the unprecedented ruthenium(II)-catalyzed oxidative C–H bond functionalization on easily accessible aryl amidines **117** with alkynes **1** and alkenes **20**.

Thus, *in situ* formed cationic ruthenium(II) complexes allowed for alkyne annulations by C–H/N–H bonds functionalizations to give diversely substituted 1-aminoisoquinolines **118**, which served as viable substrates for catalyzed C–H bond activation reactions themselves. Furthermore, novel oxidative alkenylations of benzamidines proved to be viable with versatile cationic ruthenium(II) complexes and, thereby, provided access to structurally diverse iminoisoindolines **119**. Detailed mechanistic studies indicated the reversibility of the key C–H bond activation step in both cases.

5 Ruthenium(II)-Catalyzed C–H Bond Hydroarylation and Oxidative Annulation with *α,β*-Unsaturated Ketones *via* Monodentate Directing Group

Early development of ruthenium-catalyzed C–H bond hydroarylation was started by Lewis and Smith,[33] as well as Murai and coworkers who published a report on the "ruthenium-catalyzed *ortho*-C–H bond hydroarylation of aromatic ketones with olefins *via* a chelation assisted strategy" in 1993.[46] Advances were subsequently made with the more flexible and practical ruthenium complex $[RuCl_2(p\text{-cymene})]_2$. However, despite of a few examples in the literature which were rather rare and limited to the use expensive rhodium[44] or rhenium[45] catalysts, several important families of acceptors, such as *α,β*-unsaturated ketones, could thus far not be utilized. In recent years, bidentate directing groups have emerged as a new powerful tool in C–H functionalization. A major progress was achieved by Daugulis,[68c,77,104] Chatani,[105] and Ackermann[78e,f,106] *et al*. Thus, Chatani and coworkers developed the ruthenium-catalyzed C–H hydroarylation of aromatic substrates with *α,β*-unsaturated ketones *via* a removable 8-aminoquinoline bidentate directing group.[46] Herein, we developed ruthenium-catalyzed C–H bond hydroarylation and oxidative annulation with *α,β*-unsaturated ketones *via* more atom-economical monodentate directing group.

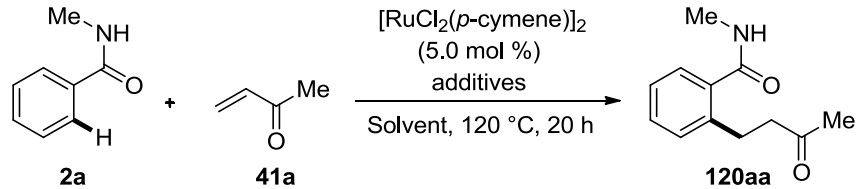
5.1 Optimization Studies

We initiated our studies by testing the feasibility of the ruthenium(II)-catalyzed C–H bond hydroarylation of methyl vinyl ketone (**41a**) with benzamide **2a** (Table 5.1). Thus far, the reported ruthenium-catalyzed direct hydroarylation with MVK by Chatani was accomplished with $RuCl_2(PPh_3)_3$ as the catalyst.[46] However, catalyst delivered no desired product with the assistance of monodentate amide (entries 1–2). Similar observations were made when employing combinations of $[RuCl_2(p\text{-cymene})]_2$ and additives (entries 3–5). A significant breakthrough was made using $MesCO_2K$ and $MesCO_2H$ as the cocatalysts (entry 6).

[104] a) D. Shabashov, O. Daugulis, *J. Am. Chem. Soc*. **2010**, *132*, 3965–3972; b) E. T. Nadres, O. Daugulis, *J. Am. Chem. Soc*. **2012**, *134*, 7–10; c) L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc*. **2012**, *134*, 18237–18240.
[105] a) Y. Aihara, N. Chatani, *J. Am. Chem. Soc*. **2013**, *135*, 5308–5311; b) Y. Aihara, N. Chatani, *Chem. Sci*. **2013**, *4*, 664-670; c) Y. Ano, M. Tobisu, N. Chatani, *Org. Lett*. **2012**, *14*, 354–357; d) Y. Ano, M. Tobisu, N. Chatani, *J. Am. Chem. Soc*. **2011**, *133*, 12984–12986.
[106] H. H. Al Mamari, E. Diers, L. Ackermann, *Chem. Eur. J*. **2014**, *20*, 9739–9743.

Stoichiometric $MesCO_2H$ loading provided the optimal result (entry 7). Notably, omission of either of the two additives, or employing [Ru($MesCO_2$)$_2$(*p*-cymene)] as the catalyst, or reducing the catalyst loading resulted in significantly reduced yield of the desired product **120aa** (entries 8–11). Furthermore, it is worth noting that the combination of KOAc and HOAc was found to be suitable as well, albeit with lower efficacy (entry 12).

Table 5.1. Optimization of ruthenium(II)-catalyzed C–H bond hydroarylation in benzamide **2a**.[a]



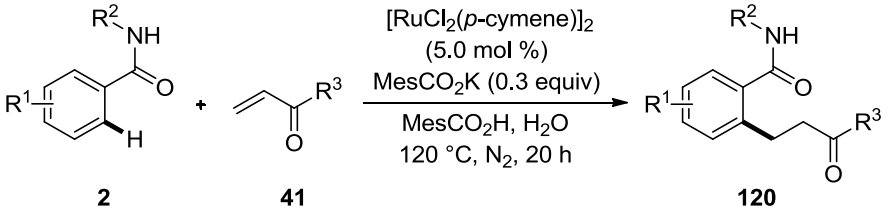
2a **41a** **120aa**

Entry	Additive **A** [equiv]	Additive **B** [equiv]	Solvent	Yield [%][b]
1	NaOAc (0.3)	--	PhMe	0[c]
2	NaOAc (0.3)	--	H_2O	0[c]
3	KPF_6 (0.2)	--	H_2O	0
4	KPF_6 (0.2)	NaOAc (2.0)	H_2O	0
5	PPh_3 (0.15)	NaO_2CH (0.3)	PhMe	0
6	$MesCO_2K$ (0.3)	$MesCO_2H$ (0.3)	H_2O	69
7	***$MesCO_2K$ (0.3)***	***$MesCO_2H$ (1.0)***	***H_2O***	***80***
8	$MesCO_2K$ (0.3)	--	H_2O	51
9	--	$MesCO_2H$ (1.0)	H_2O	29
10	--	--	H_2O	58[d]
11	$MesCO_2K$ (0.3)	$MesCO_2H$ (1.0)	H_2O	46[e]
12	KOAc (1.0)	HOAc (1.0)	H_2O	64

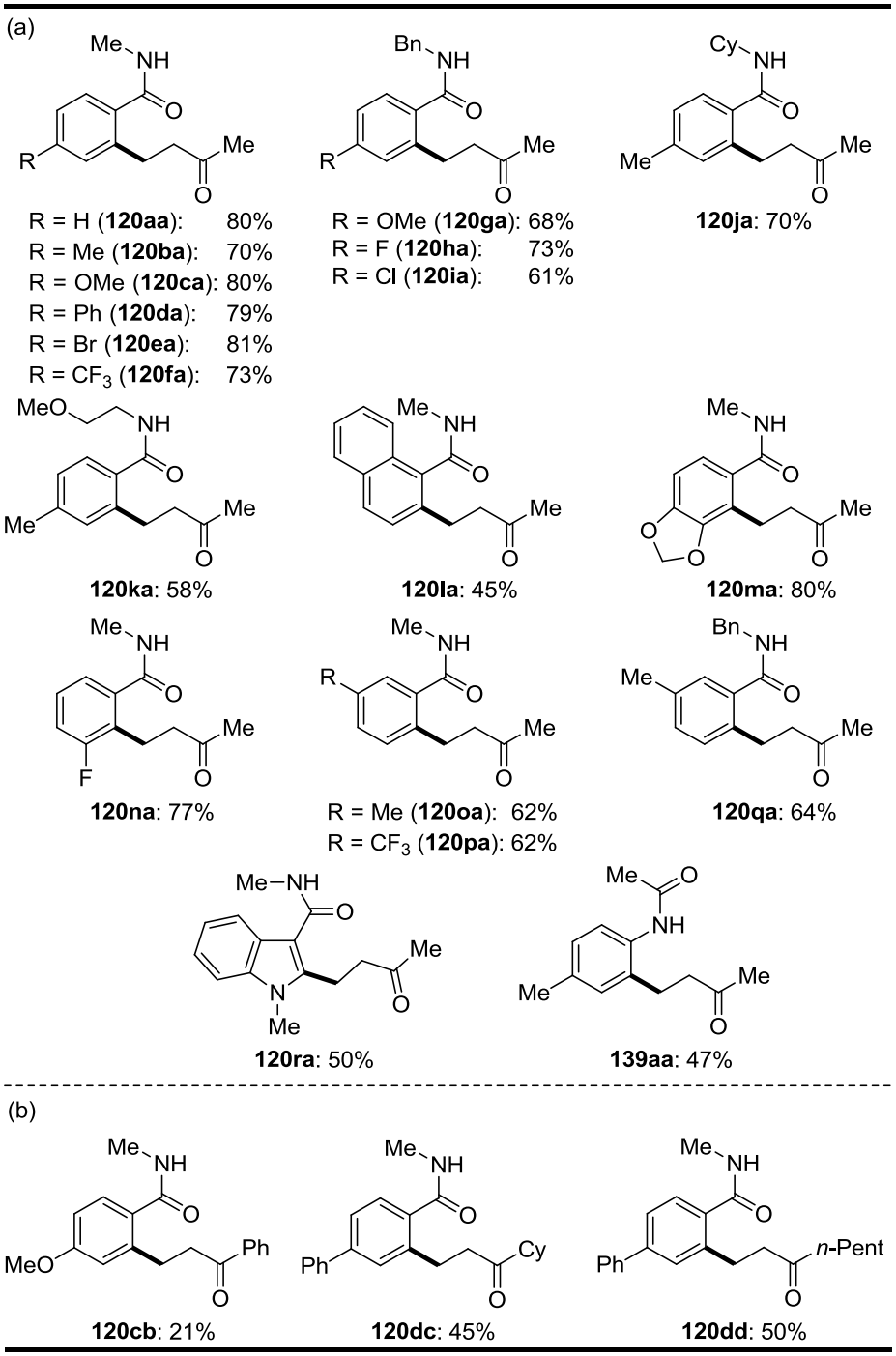
[a]General reaction conditions: **2a** (0.5 mmol), **41a** (1.0 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (5.0 mol %), $MesCO_2K$ (0.3 equiv), $MesCO_2H$ (1.0 equiv), H_2O (2.0 mL), under N_2, 120 ℃ , 20 h. [b] Isolated yields. [c] $RuCl_2(PPh_3)_3$ (10 mol %). [d] [Ru($MesCO_2$)$_2$(*p*-cymene)] (10 mol %). [e] [$RuCl_2$(*p*-cymene)]$_2$ (2.5 mol %).

5.2 Scope of the Alkylation with *α,β*-unsaturated Ketones

With the optimized ruthenium(II) catalyst in hand, we tested its versatility in the C–H bond hydroarylation with weakly-coordinating[7b] benzamides **2** (Scheme 5.1). Notably, in these chelation-assisted direct hydroarylations, both electron-rich and electron-poor *para*-substituted benzamides **2a**–**2f** were identified as viable substrates. Furthermore, a variation of the substitution pattern on the nitrogen atom was also investigated, such as benzyl (**2g**–**2i**), cyclohexyl (**2j**) and methoxyethyl (**2k**), which proved to be suitable and did not significantly alter the catalytic efficacy. More sterically hindered *ortho*-substituted benzamide **2l** was successfully employed as well, albeit furnishing the desired product in a slightly reduced yield. Intramolecular competition experiments with *meta*-substituted benzamides **2m** and **2n** featured a considerable secondary directing group effect[102] or *ortho*-orienting effect,[103] respectively, thus leading to a site-selective formation of sterically more hindered compounds **120ma** and **120na** as the sole product. In contrast, the conversion of the *meta*-methyl and *meta*-trifluoromethyl substituted arenes **2o**–**2q** was largely governed by steric interactions to deliver the products **120oa**–**120qa** at the less sterically hindered position. The widely applicable ruthenium(II) catalyst was not limited to aromatic benzamides. Indeed, the reaction of the heteroaromatic indole derivative **2r** also led to the site-selective hydroarylation in modest yield. Interestingly, *N*-(*p*-tolyl)acetamide (**121a**) was proved to be a suitable substrate as well, although a modest yield was obtained under the optimal conditions. However, among a set of varied *α,β*-unsaturated ketones, the aromatic ketone **41b** only delivered the desired product **120cb** in only low yield, presumably due to a polymerization tendency of the ketone. Yet, vinyl alkyl ketones **41c** and **41d** gave the alkylated products **120dc** and **120dd**, respectively, in relatively high yields.



2 **41** **120**



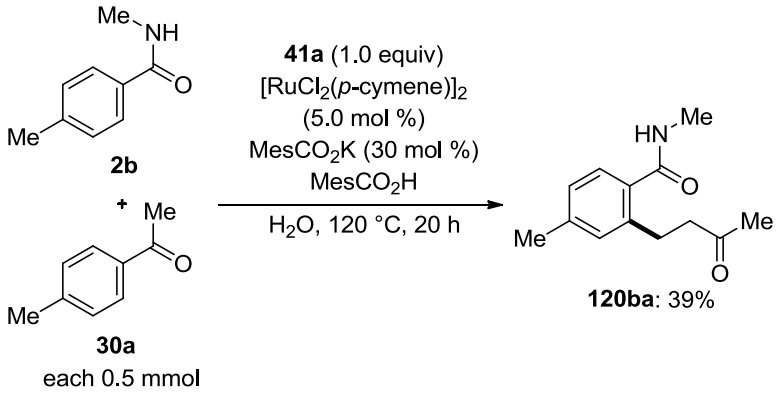
Scheme 5.1. Ruthenium(II)-catalyzed hydroarylation of *α,β*-unsaturated ketones **41** with substituted benzamides **2**.

5.3 Mechanistic Studies

5.3.1 Comparison of the Directing Group Power

Intermolecular competition experiments between arenes with different directing groups clearly highlighted the amide as directing group is more powerful than the ketone in the

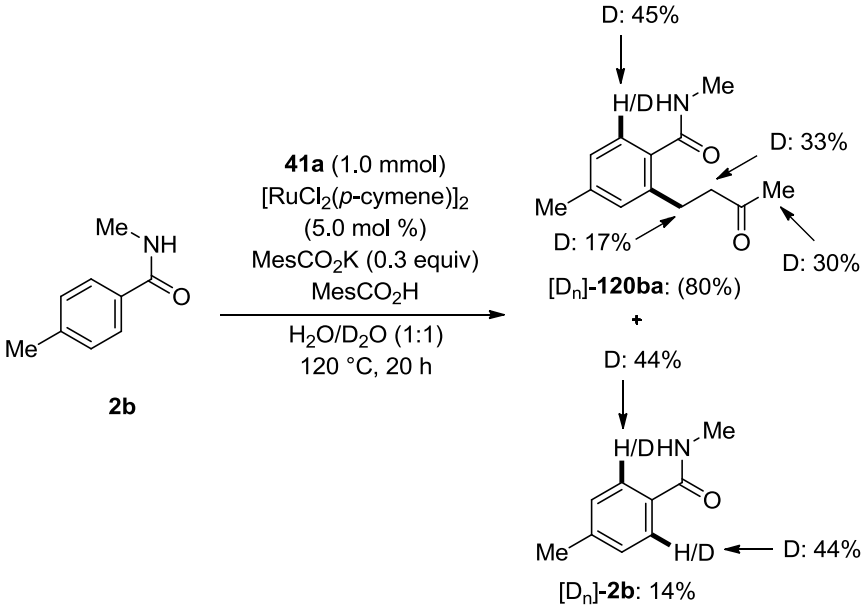
chelation-assisted C–H hydroarylation under the standard reaction conditions (Scheme 5.2).



Scheme 5.2. Competition experiments between aromatic amide **2b** and ketone **30a**.

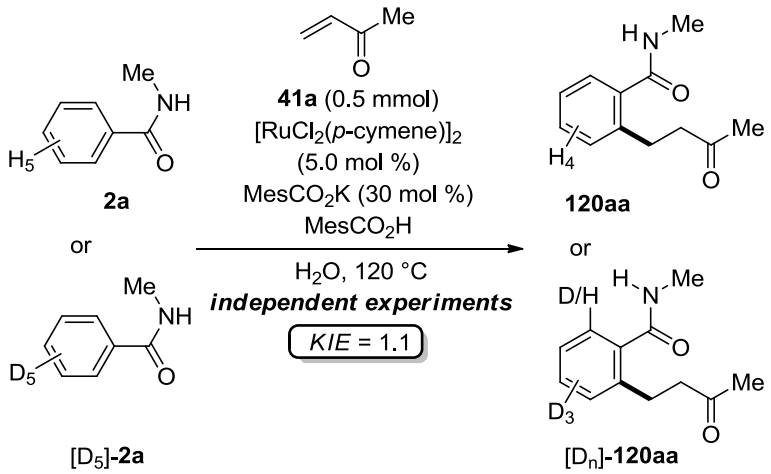
5.3.2 Reaction in the Presence of Isotopically Labeled Solvent

Obvious evidence of H/D exchange on both the reisolated starting material [D_n]-**2b** and the desired profuct [D_n]-**120ba** was obtained with the deuterated cosolvent D_2O (Scheme 5.3), which can be rationalized in terms of a reversible C–H bond metalation step in the ruthenium(II)-catalyzed C–H hydroarylations.



Scheme 5.3. H/D exchange experiments.

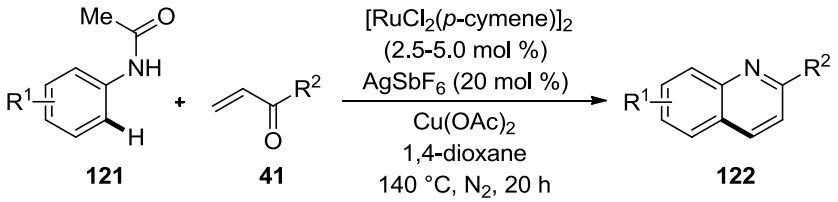
Moreover, ruthenium(II)-catalyzed hydroarylations with the product compound and the isotopically labeled substrate [D_5]-**2a** disclosed a significant kinetic isotope effect (KIE) of $k_H/k_D \approx 1.1$ for the intermolecular KIE experiment (Scheme 5.4). This data is in agreement with the C–H bond metalation not to be the rate-determining step.

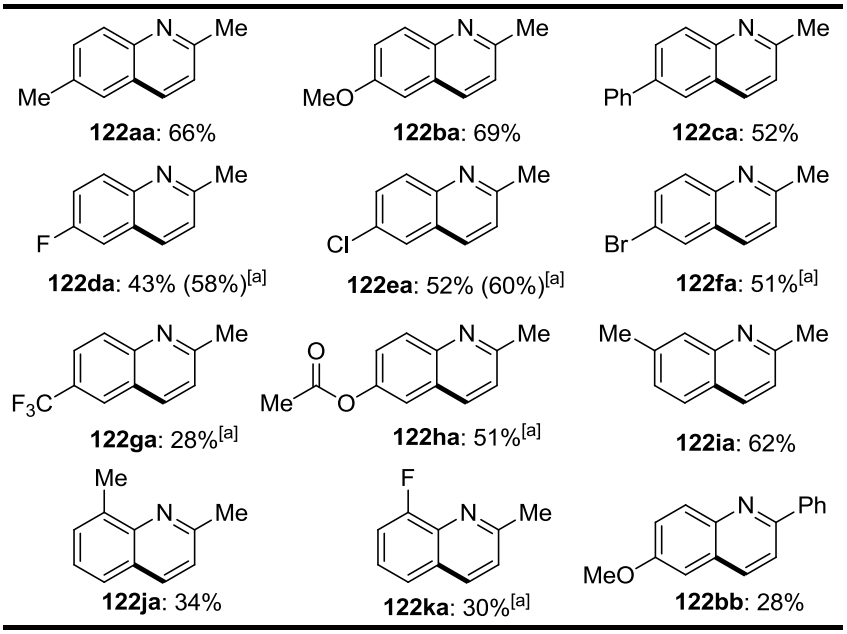


Scheme 5.4. Kinetic isotope effect (KIE) studies.

5.4 Scope of the Oxidative Annulation with *α,β*-Unsaturated Ketone

Thereafter, inspired by our previous work on oxidative alkenylations,[5,7,100] we probed the oxidative annulation of differently decorated acetanilides **121** in the presence of cocatalytic $AgSbF_6$ and stoichimetric $Cu(OAc)_2$ (Scheme 5.5). Importantly, the catalytic system was not limited to the use of electron-rich *N*-phenyleacetanilides **121a**–**121c**, but also allowed for the transformation of electron-poor substrates. Valuable electrophilic functional groups, such as fluoro, chloro, bromo, trifluoro and ester substituents, were well tolerated by the ruthenium(II) catalytic system when utilizing substituted acetanilides **121d**–**121h**. Upon intramolecular competition experiment with substrate **121i** bearing a *meta*-methyl substituent, the cyclization was governed by steric interaction to deliver the product **122ia** in a good yield. However, substrates **121j** and **121k** bearing an *ortho*-substituent provided the desired products **122ja** and **122ka**, respectively, in lower yields. Phenyl vinyl ketone ketone (**41b**) demonstrated again a lower reactivity.



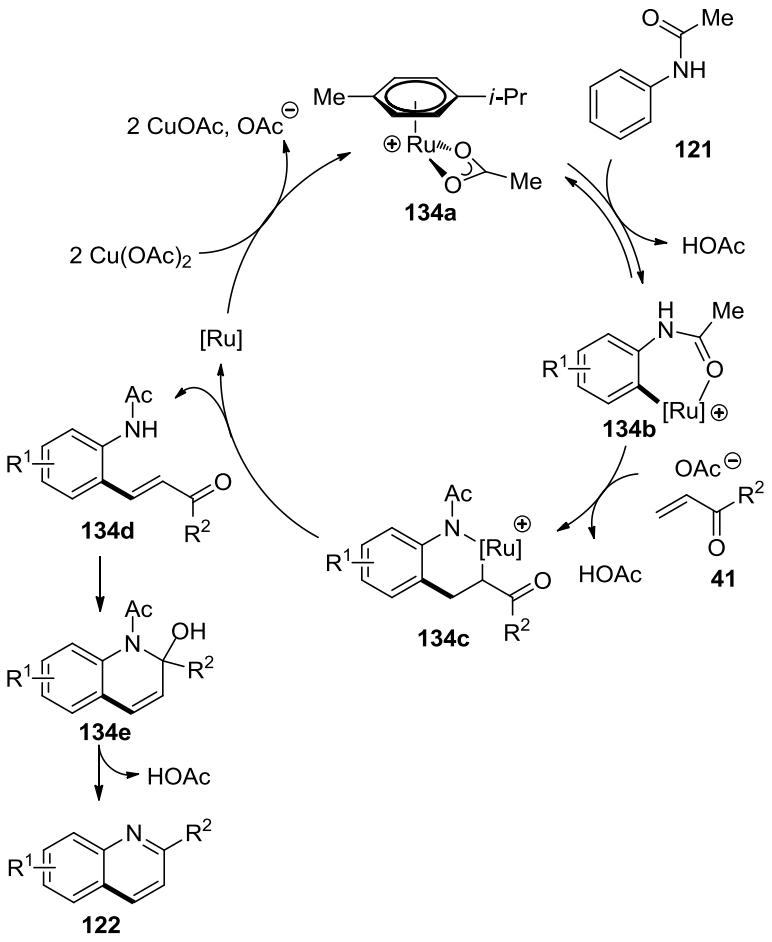


Scheme 5.5. Scope of oxidative annulations with substituted *N*-phenylacetanilides **121**. [a] $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %).

5.5 Proposed Catalytic Cycle

Based on our previous work,[7, 107] we propose the initial C–H ruthenation formed cycloruthenated complex **134b** then followed by a migratory insertion with alkene **41** to generate the intermediate **134c**. Subsequently, *β*-hydrideelimination furnish the product of oxidative alkenylation **134d**, the catalytically active ruthenium(II) complex is regenerated after reductive elimination and reoxidation, while the desired product **122** is obtained through an intramolecular nucleophilic addition of compound **134d**, followed by elimination of acetic acid to furnish desired product **122**.

[107] L. Ackermann, L. Wang, R. Wolfram, A. V. Lygin, *Org. Lett.* **2012**, *14*, 728-731.

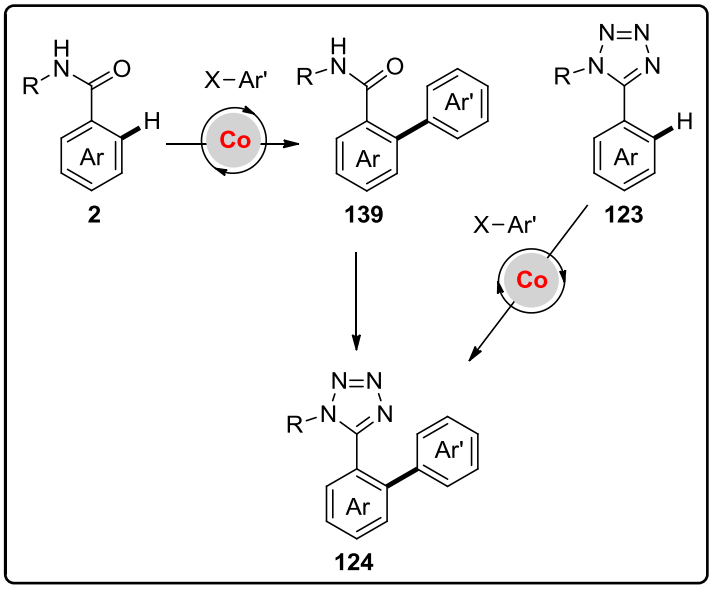


5.6 Conclusion

In summary, we have developed the first ruthenium(II)-catalyzed hydroarylation and oxidative annulation of *α,β*-unsaturated ketones **41** with easily accessible monodentate benzamides **2**, acetanilides **121** under simple reaction conditions. Furthermore, inexpensive, non-toxic H_2O was proved to be the suitable reaction medium in the C–H bond *ortho*-alkylation. This methodology highlighted the fact that monodentate directing groups can be used to achieve these challenging transformations. The latter proceeded only with difficulty when traditional methods were used and represent the utilization of *α,β*-unsaturated ketones **41** in the ruthenium(II)-catalyzed direct C–H bond hydroarylation, which was only realized with bidentate directing groups as of yet. Detailed KIE experiments indicated C–H metalation to be not the rate-determining step. Moreover, novel oxidative annulations of *N*-phenylacetanilides **121** with *α,β*-unsaturated ketones **41** to deliver decorated quinolines **122** were also viable with the versatile ruthenium(II) catalyst.

6 Cobalt-Catalyzed C–H Arylation with Weakly-Coordinating Amides and Tetrazoles: Expedient Route to Angiotensin-II-Receptor Blockers

Angiotensin-II-Receptor Blockers (ARBs), such as Valsartan, Losartanare or Candesartan, are important antihypertensives.[108,5e] As of yet, the biaryl moieties in ARBs were predominantly synthesized through palladium-catalyzed cross-coupling reactions.[109] A significant advance to access these building blocks has been accomplished with ruthenium(II) catalysts through direct C–H bond arylation reactions.[5e,110] In consideration of the progress in cobalt-catalyzed direct C–H bond arylation,[67,75] we devised cobalt-catalyzed C–H bond arylations with weakly-coordinating[7b] benzamides **2** as well as direct arylations of aryl tetrazoles **123**. Our strategy for the synthesis of derivatives **139** as ARBs constituents is depicted in scheme 6.1.[111]



Scheme 6.1. Strategies for the synthesis of derivatives **124** as ARBs building blocks.

6.1 Optimization

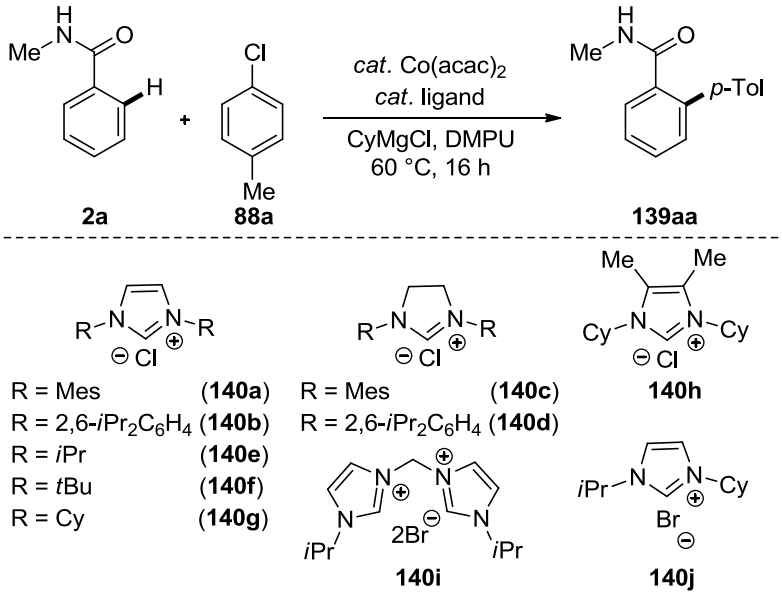
6.1.1 Optimization Studies

We initialed our studies by probing different reaction conditions for the envisioned C–H bond

[108] a) J. H. Kim, J. H. Lee, S. H. Paik, J. H. Kim, Y. H. Chi, *Arch. Pharmacal Res*. **2012**, *35*, 1123–1126; b) A. R. De Caterina, A. R. Harper, F. Cuculi, *Vasc. Health Risk Manage*. **2012**, *8*, 299–305.
[109] a) S. Aalla, G. Gilla, Y. Bojja, R. R. Anumula, P. R. Vummenthala, P. R. Padi, *Org. Process Res. Dev*. **2012**, *16*, 682–686; b) G. Wang, B. Sun, C. Peng, *Org. Process Res. Dev*. **2011**, *15*, 986–988.
[110] a) M. Seki, *ACS Catal*. **2014**, *4*, 4047–4050; b) E. Diers, N. Y. P. Kumar, T. Mejuch, I. Marek, L. Ackermann, *Tetrahedron* **2013**, *69*, 4445–4453; c) M. Seki, M. Nagahama, *J. Org. Chem*. **2011**, *76*, 10198–10206.
[111] J. Li, L. Ackermann, *Chem. Eur. J*. **2015**, *21*, 5718–5722.

arylation of weakly-coordinating benzamide **2a** with inexpensive *p*-tolylchloride (**88a**) (Table 6.1).

Table 6.1. Optimization of cobalt-catalyzed C–H bond arylation.[a]



Entry	[$Co(acac)_2$] [mol %]	Ligand	Yield[b] [%]
1	10.0	IMesHCl (**140a**)	23[c]
2	10.0	IPrHCl (**140b**)	<5[c]
3	10.0	sIMesHCl (**140c**)	16[c]
4	10.0	sIPrHCl (**140d**)	0[c]
5	10.0	PPh_3	13[c]
6	10.0	**140e**	29[c]
7	10.0	**140f**	<5[c]
8	10.0	**140g**	47[c]
9	***5.0***	***140g***	***78***
10	--	**140g**	0
11	5.0	**140h**	32
12	5.0	**140i**	<5
13	5.0	**140j**	26

[a] General reaction conditions: **2a** (0.5 mmol), **88a** (0.6 mmol), *cat*. $Co(acac)_2$, ligand (5 mol %), CyMgCl (3.0 equiv), DMPU (1.0 mL), 60 °C, 16 h. [b] Yield of isolated product. [c] **88a** (0.75

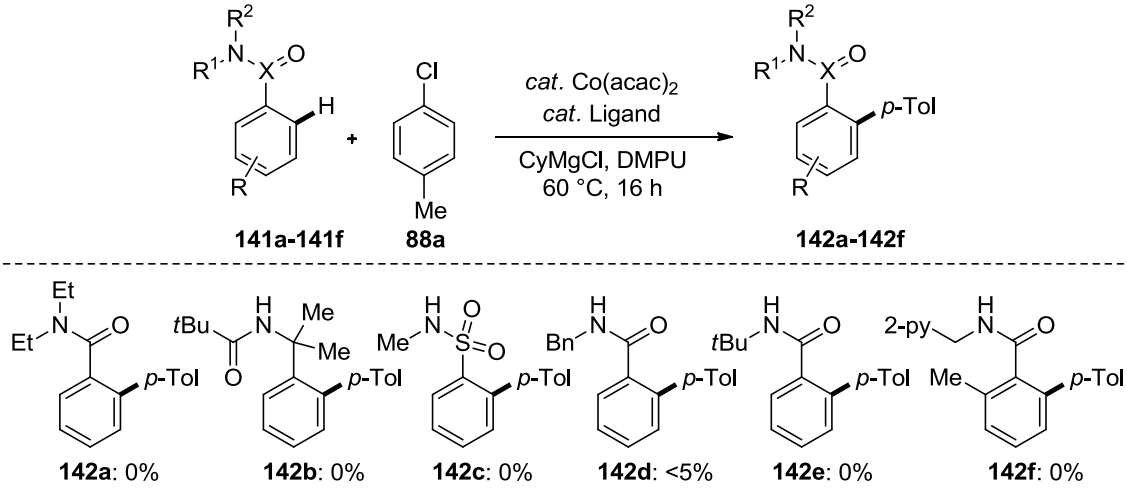
mmol), ligand (20 mol %).

Thus far, all reported cobalt-catalyzed direct arylations with organic (pseudo)halides were accomplished with one of the two *N*-heterocyclic carbene (NHC)[112–113] preligands IMesHCl (**140a**) or IPrHCl (**140b**).[67,75] However, preligands **140a** and **140b** delivered the desired product **139aa** in only unsatisfactory low yields, even with a relatively high catalyst loading of 10 mol % (entries 1 and 2). A similar observation was made when employing the saturated analogues sIMesHCl (**140c**), and sIPrHCl (**140d**) (entries 3 and 4), or the tertiary phosphine PPh_3 (entry 5). Cobalt catalysts derived from isopropyl-substituted NHC **140e** were previously shown to be effective for direct alkylations,[65c] but proved unsuitable for the C–H bond arylation with benzamides **2a** (entries 6 and 7), thus highlighting the challenge associated with the use of weakly-coordinating amides. In contrast, among various NHC precursors, ICyHCl (**140g**) proved to be optimal with an ideal ligand to cobalt ratio of 1:1 (entries 8 and 9). Under these reaction conditions the catalyst loading could also be significantly reduced (entry 9). The more electron-rich pre-NHC **140h**, the bidentate derivative **140i** and the unsymmetrically substituted pre-NHC **140j** failed to improve the catalytic efficacy (entries 10–13).

6.1.2 Effect of the Directing Groups

Notably, we also tried the cobalt-catalyzed C–H bond arylation with differently substituted aryl amides **141a**–**141f** (Scheme 6.2). These test reactions under the optimized reaction conditions verified the crucial importance of the amide directing group. For substrates without free N–H moieties or with sterically demanding directing group, no catalytic reaction was observed. The same result was obtained with benzenesulfonamide **141c** or with substrate **141f** bearing a bidentate-type directing groups as well.

[112] M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485–496.
[113] S. Díez-González, N. Marion, S. P. Nolan, *Chem. Rev.* **2009**, *109*, 3612–3676.

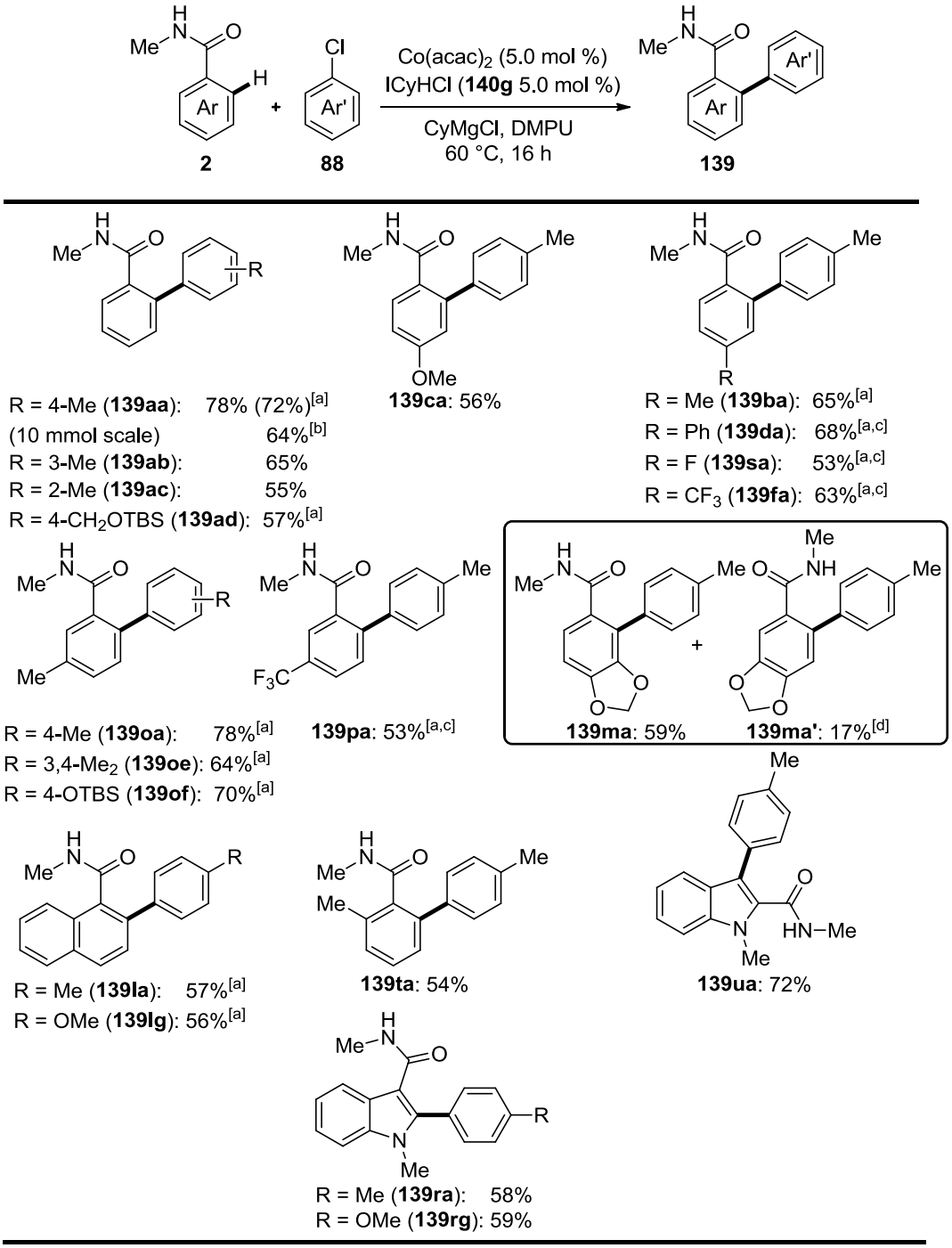


Scheme 6.2. Screening of directing groups for the arylation reactions.

6.2 Scope and Limitations

Having identified a highly effective catalyst for the selective arylation of *N*-methylbenzamide (**2a**) with 4-chlorotoluene (**88a**), we further extended the reaction scope to include other benzamides with a broad range of aryl chlorides (Scheme 6.3). In order to test the efficiency of the cobalt-catalyzed direct arylation, we subsequently set up a 10 mmol scale reaction of **2a** with **88a** which provided biaryl product **139aa** in 64% yield when employing 2.0 mol % of $Co(acac)_2$ and ICyHCl in DMPU at 60 ℃ for 16 h. Notably, various aryl chlorides **88a**–**88g** were successfully employed. The TBS-protected (4-chlorophenyl)methanol **88d** and 4-chlorophenol **88f** were readily converted to the corresponding biaryl products **139ad** and **139of** in good yields of 57% and 70%, respectively. The arylation with sterically more demanding *ortho* substituent *o*-tolylchloride afforded the target product **139ac** as well, albeit in a modest yield (55%). Similarly lower yields were observed for benzamides **2s**, **2f**, and **2p** with electron-deficient functional groups, even when employing an increased loading of $Co(acac)_2$ and carbene preligand. Likewise, we exploited the use of the amide group for the direct arylation of the biologically active indole[114] derivatives, delivering the desired products **139ua**, **139ra** and **139rg** were isolated in good yields. Upon arylation of *meta*-substituted benzamide **2m**, an influence of the secondary directing group chelation effect[102] was minor.

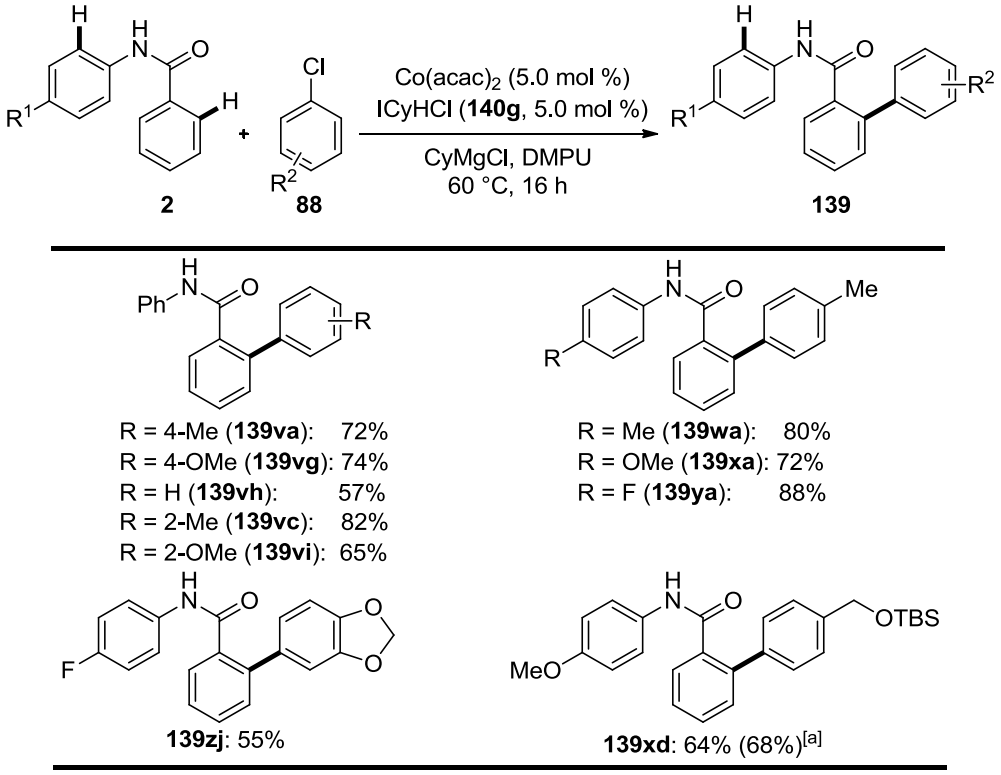
[114] *Modern Heterocyclic Chemistry* (Eds.: J. Alvarez-Builla, J. J. Vaquero, J. Barluenga,), Wiley-VCH, Weinheim, **2011**.



Scheme 6.3. Substrate scope of cobalt-catalyzed C–H bond arylation. [a] 0.5 h. [b] $Co(acac)_2$ (2.0 mol %), **140g** (2.0 mol %). [c] $Co(acac)_2$ (10 mol %), **140g** (10 mol %).

Thereafter, the substrate scope was extended to competition experiments of various benzamides **2** (Scheme 6.4). Remarkably, the cobalt-catalyzed C–H functionalizations occurred on the benzamides **2** with excellent chemo-selectivity. Both electron-donating and electron-withdrawing substituents on the aryl chloride **88** were tolerated selectively delivering the *mono*-arylated biaryls **139va–139xd** in good yields. Moreover, chlorobenzenes with

sterically hindered substituents in the *ortho*-position also delivered the desired products **139** with high catalytic efficacy.

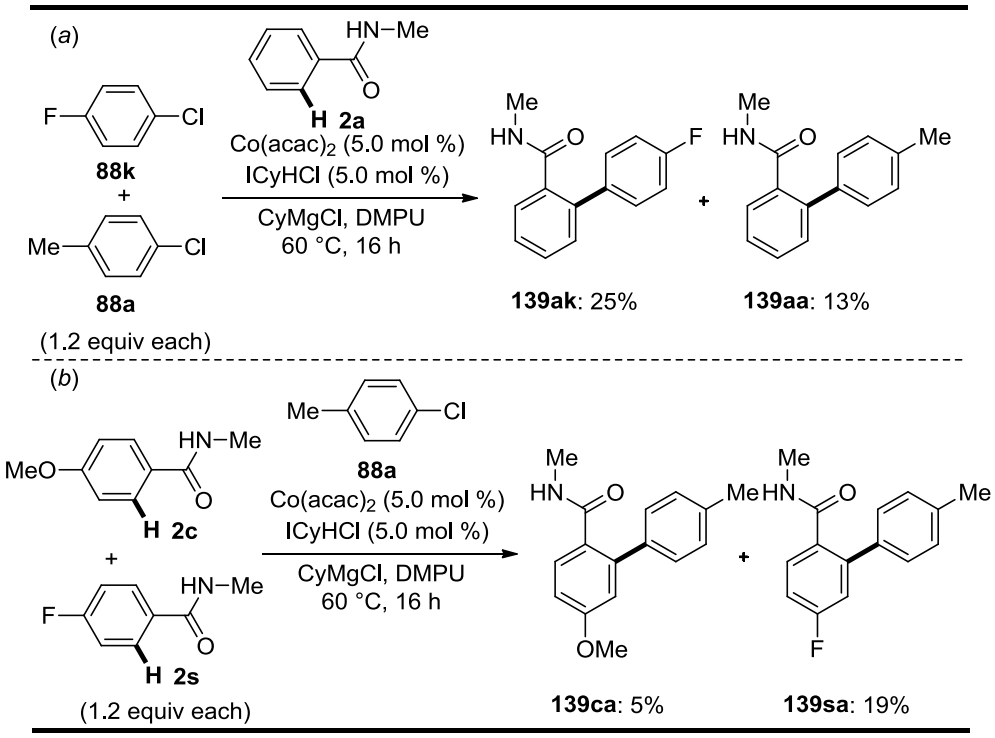


Scheme 6.4. Cobalt-catalyzed direct C–H bond arylation of anilides **2**. [a]: 0.5 h.

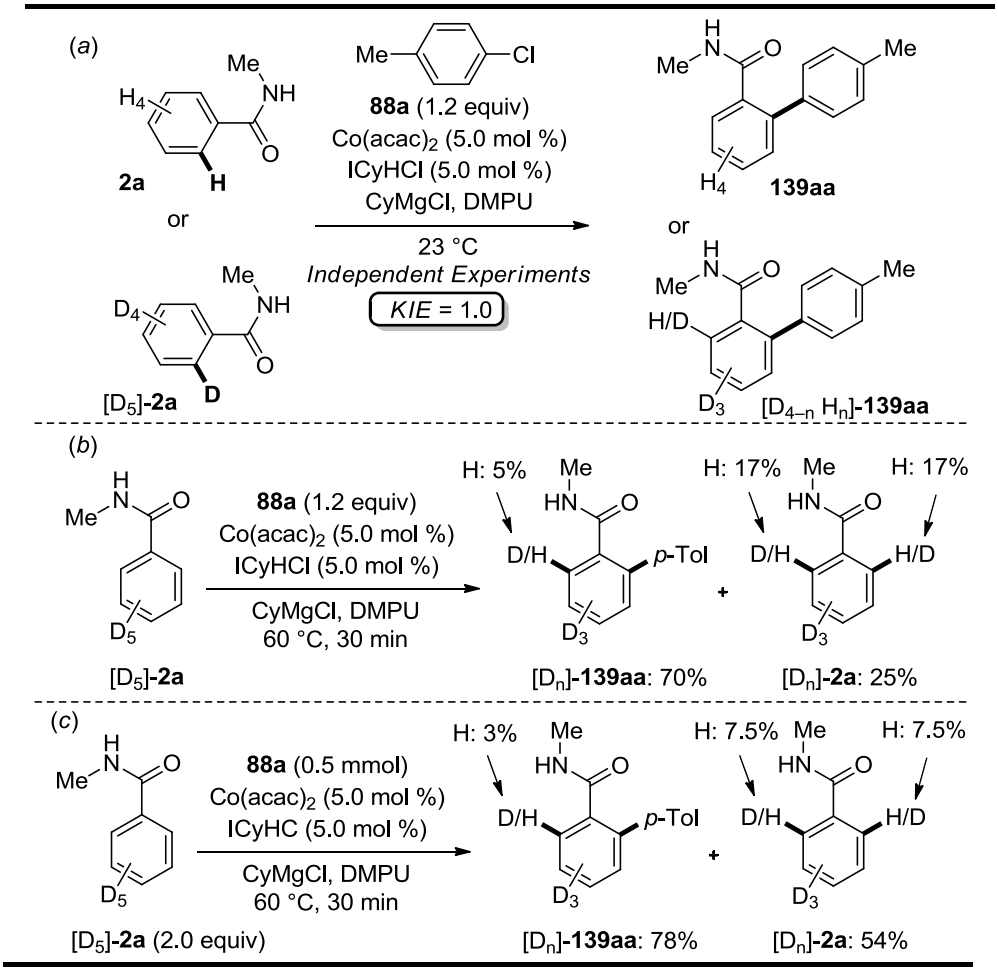
6.3 Mechanistic Studies

The results of a set of intermolecular competition experiments revealed electron-deficient benzamides **2** and electron-deficient aryl chlorides **88** to be more reactive than their electron-rich counterparts (Scheme 6.5).

Thereafter, we performed studies to delineate the catalyst working mode. Independent experiments with isotopically labeled substrates indicated the C–H bond cobaltation not to be kinetically relevant (KIE ≈ 1.0), and provided evidence for a reversible D/H exchange reaction (Scheme 6.6).



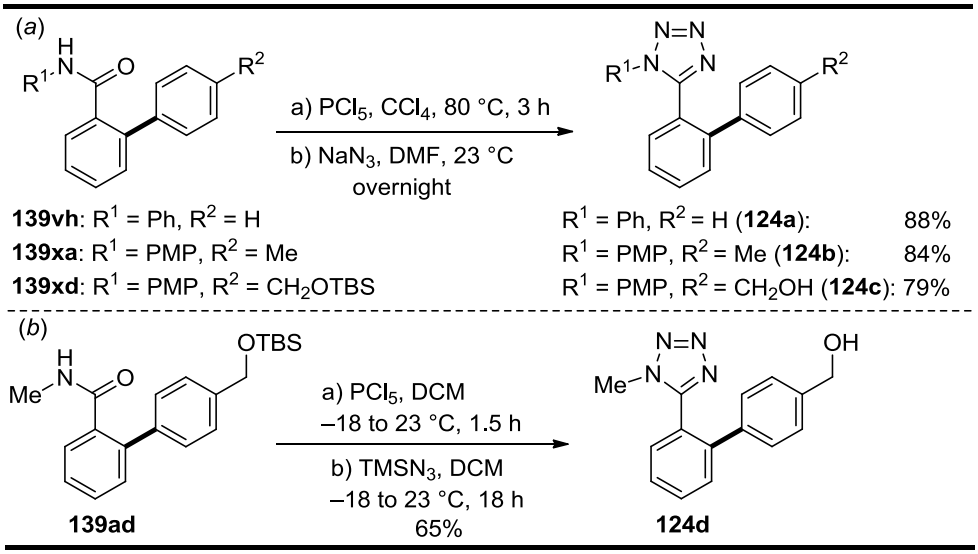
Scheme 6.5. (a) Competition experiments between aryl chlorides **88**, (b) and different aryl amides **2**.



Scheme 6.6. (a) Kinetic isotope effect (KIE) study. (b, c) Cobalt-catalyzed H/D exchange experiments with deuterated **2a**.

6.4 Synthesis of Biaryl Tetrazoles

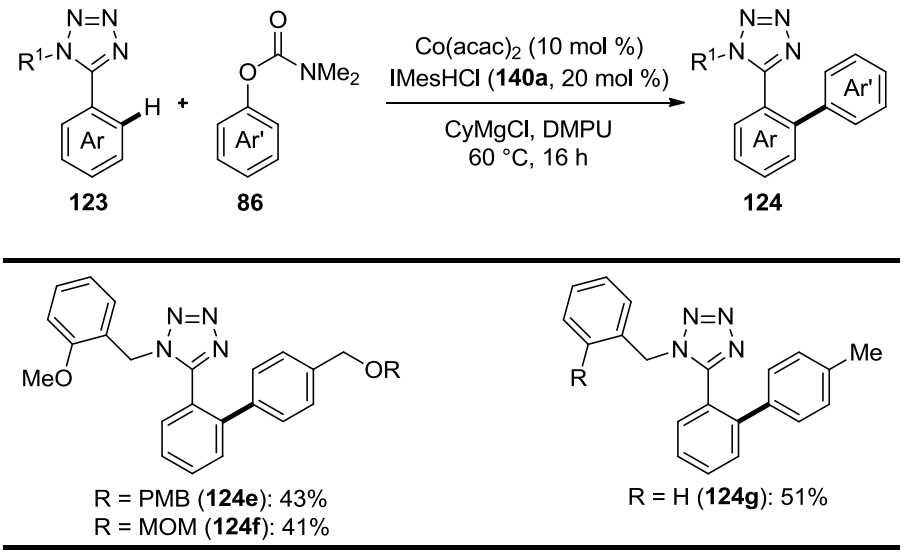
As discussed above, benzamides can be easy transformed into phenyl tetrazoles according to the previously published protocols.[115] Consequently, a simple route to synthesize ARBs building blocks and derivatives **124a**–**124d** was designed *via* initial cobalt-catalyzed direct C–H bond arylation by weak assistance of amides group in substrates **2** (Scheme 6.3) followed by the transformation of the amido substituent into the tetrazole moiety (Scheme 6.7).



Scheme 6.7. Facile preparation of biaryl tetrazoles **124**.

Alternatively, we explored the possibility of devising an even more step-economical approach to biaryl tetrazoles **124** through the unprecedented cobalt-catalyzed C–H bond activation by tetrazole assistance in substrates **123**. Intriguingly, a low-valent cobalt catalyst derived from preligand **140a** proved effective here, thereby chemo-selectively delivering the desired products **124**. It is noteworthy that the tetrazole-assisted C–H bond arylation proceeded by C–H/C–O bonds cleavages with challenging aryl carbamates **86** as the electrophiles (Scheme 6.8), although the products **124** were obtained in rather modest yields.

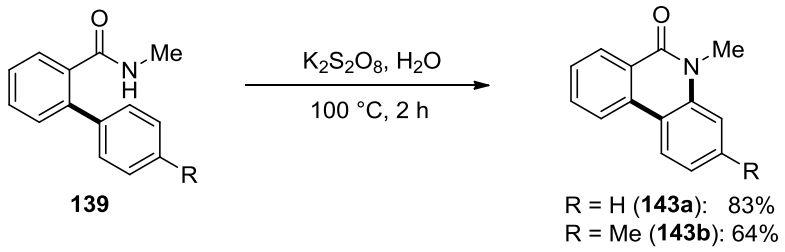
[115] S. N. Rao, T. Ravisankar, J. Latha, K. S. Babu, *Pharma Chem*. **2012**, *4*, 1093–1103.



Scheme 6.8. Tetrazole-assisted C–H bond arylation with carbamates **86**.

6.5 Oxidative Annulation

Finally, we successfully exploited the products of direct arylation **139** for the synthesis of substituted phenanthridin-6(*5H*)-ones **143a** and **143b**, which were obtained in 83 and 64% yield, respectively (Scheme 6.9).



Scheme 6.9. Oxidative annulations of **139** to phenanthridin-6(*5H*)-ones **143**.

6.6 Conclusion

In summary, we have developed novel strategies for cobalt-catalyzed syntheses of biaryl tetrazoles **124** through C–H bond functionalization. Thus, NHC-ligated low-valent cobalt catalysts enabled the first direct arylation assisted by weak coordination. The arylated benzamides **139** were formed with high site- and chemo-selectivities as well as ample scope. This reaction provided expedient access to biaryl tetrazoles, which represent key scaffolds of ARB blockbuster drugs. The results of mechanistic studies were in line with a reversible C–H bond cobaltation and a rate-determining reductive elimination. The power of the user-friendly

cobalt catalysis was further illustrated by unprecedented tetrazole-assisted C–H bond activations with 3d transition metal complexes, thus constituting an alternative approach to ARBs building blocks.

7 Cobalt(III)-Catalyzed C–H Bond Cyanation of Arenes and Heteroarenes

Functionalizations of otherwise inert C–H bonds provide an approach for improving the atom- and step-economy in organic synthesis. While most of the achievements were accomplished with expensive second-row transition-metal catalysts, largely focused on ruthenium, rhodium and palladium complexes, further applications of these methods are limited.[5,7,116] Inexpensive cobalt catalysts, for C–H bonds activations have been recognized as an increasingly viable tool for organic syntheses, also in the field of C–H bond activation including arylations, alkylations, alkenylations, benzylations and hydroarylations.[5j–5k] The general cobalt catalytic systems for most of these studies were assisted by phosphine or *N*-heterocyclic carbene (NHC) ligands, along with a strong base. Grignard reagents were used as base and reductants to generate the reactive low-valent cobalt-catalysts, which devised methods for new C–C bonds formation. Although several functional groups can be tolerated, the Grignard reagents could induce some other undesirable byproducts. Therefore, in order to avoid these kinds of disadvantages, the research groups of Kanai, Ackermann, Daugulis and Song developed other mild reaction systems with cobalt catalysts, including high-valent [Cp*Co(III)] derivatives, which allowed for the oxidative alkyne annulations, oxidative alkenylations and alkoxylation under mild reaction conditions without Grignard reagents.[68,79,82–84,86] Based on this progress, we hence became interested in developing unprecedented cobalt(III)-catalyzed C–H bond cyanations of arenes and heteroarenes, which are discussed below in this Chapter.[89]

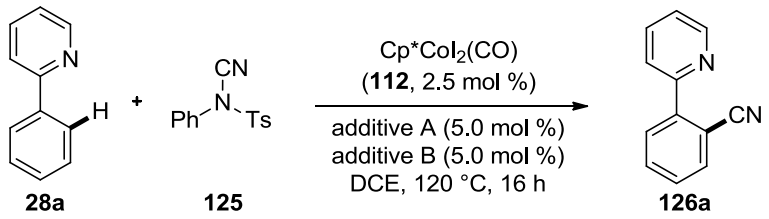
7.1 Optimization Studies

Initially we probed various reaction conditions for the desired cobalt-catalyzed C–H bond functionalization utilizing 2-phenylpyridine (**28a**) and *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (**125**, NCTS) as the cyanating reagent. Preliminary experiments identified [Cp*CoI_2(CO)] to be the efficient metal catalyst of choice, along with $AgSbF_6$ and NaOAc as the cocatalytic additives (Table 7.1, entries 1-4, 10). Experiments without this additive or with AgOAc instead of $AgSbF_6$ inhibited the reaction immediately (entries 6 and

[116] L. Ackermann, *Top. Curr. Chem.* **2010**, *292*, 211–229, and references cited therein.

8). Among a representative set of acetate source, KOAc provided optimal yields (entries 1, 5, 7 and 9). A C–H bond cyanation with an excess of substrate **125** formed the monocyanated product **126a** as the sole product (entry 11), which unraveled the prominent chemoselectivity of the cobalt(III) catalyst.

Table 7.1 Optimization of cobalt-catalyzed C–H bond cyanation.[a]



28a **125** **126a**

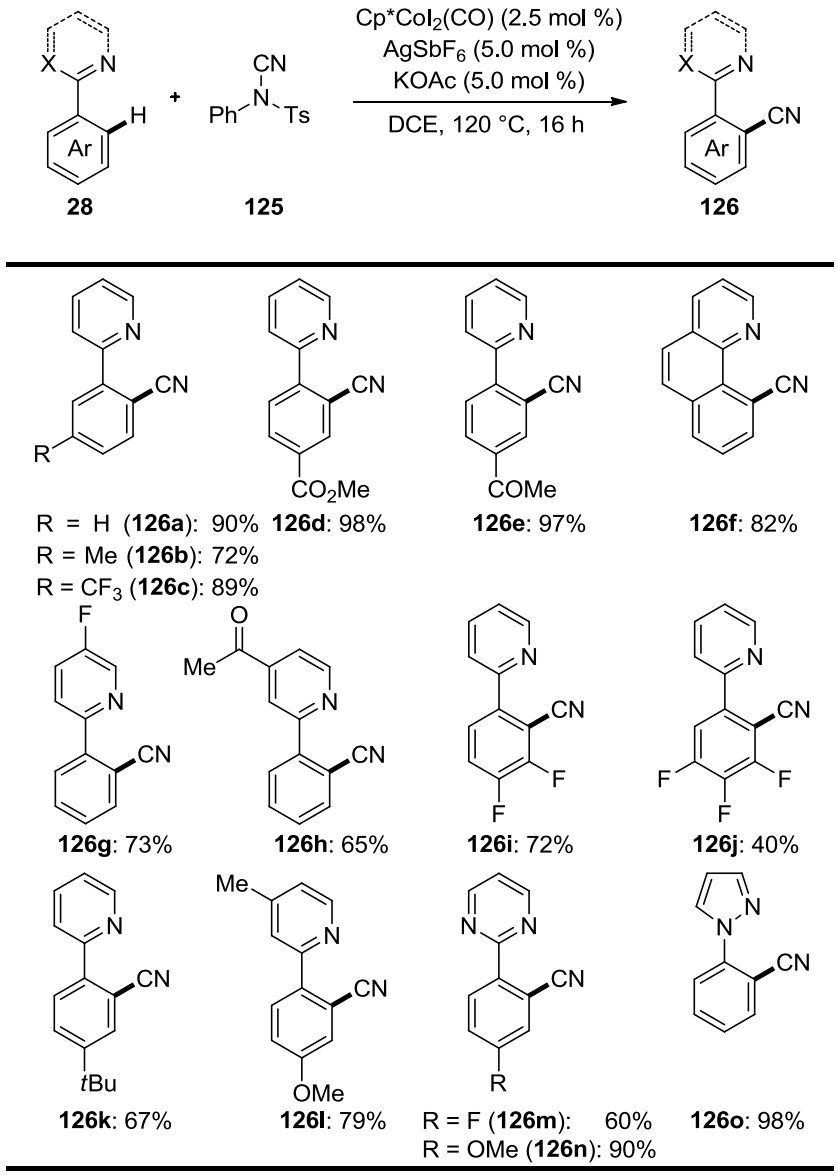
Entry	[Co]	Additive A	Additive B	Yield (%)[b]
1	***[Cp*CoI$_2$(CO)]***	***AgSbF$_6$***	***NaOAc***	***83***
2	CoI_2	$AgSbF_6$	NaOAc	0
3	$Co(acac)_2$	$AgSbF_6$	NaOAc	0
4	$[Cp^*CoCl_2]_2$	$AgSbF_6$	NaOAc	30
5	***[Cp*CoI$_2$(CO)]***	***AgSbF$_6$***	***KOAc***	***90***
6	[Cp*CoI$_2$(CO)]	AgOAc	NaOAc	0
7	[Cp*CoI$_2$(CO)]	$AgSbF_6$	AgOAc	66
8	[Cp*CoI$_2$(CO)]	--	KOAc	0
9	[Cp*CoI$_2$(CO)]	$AgSbF_6$	--	33
10	--	$AgSbF_6$	KOAc	0
11	[Cp*CoI$_2$(CO)]	$AgSbF_6$	KOAc	93[c]
12	[Cp*CoI$_2$(CO)]	$AgSbF_6$	KOAc	39[d]

[a] Reaction conditions: **28a** (0.5 mmol), **2** (0.75 mmol), [Cp*CoI$_2$(CO)] (**112**, 2.5 mol %), additive A (5.0 mol %), additive B (5.0 mol %), DCE (2.0 mL), 120 ℃ , 16 h. [b] Yield of isolated product. [c] **125** (1.5 mmol). [d] 4.0 h.

7.2 Scope and Limitations

7.2.1 Substrate Scope of Cobalt-Catalyzed C–H Bond Cyanation

With the optimized catalytic system in hand, the scope of the cyanation was evaluated (Scheme 7.1).



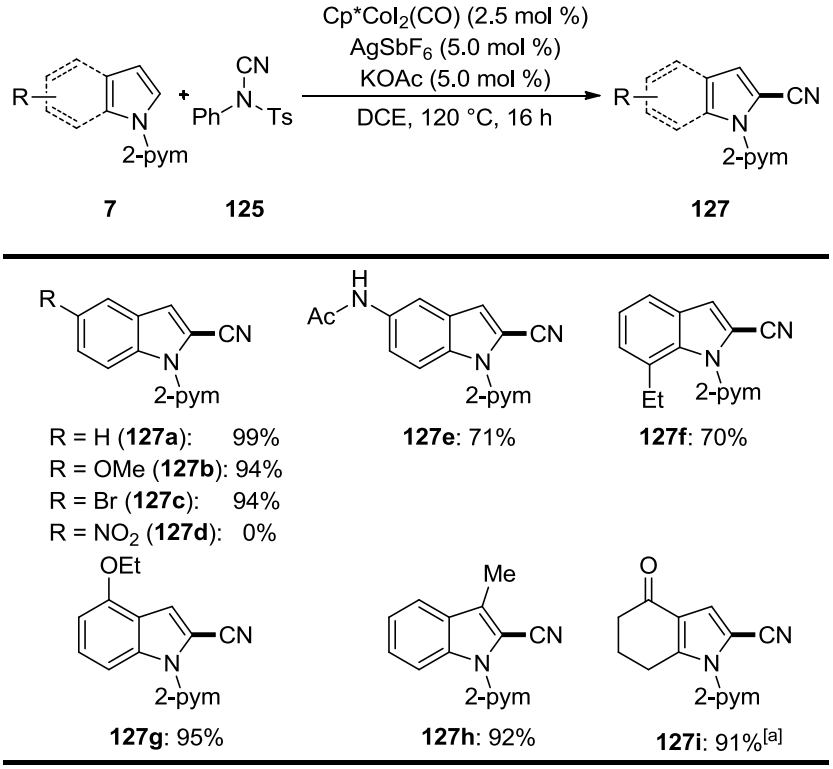
Scheme 7.1. Substrate scope of cobalt-catalyzed C–H bond cyanation.

The chelation-assisted C–H bond functionalization of *meta*-disubstituted arenes **28a**–**28c** proceeded with excellent site-selectivity at the less sterically hindered position. Significantly, the cobalt(III) catalyst displayed a remarkable chemo-selectivity, and a number of valuable electrophilic groups such as esters (**126d**) or ketones (**126e** and **126h**) were well tolerated. Cyanation of the substrate **28i** with a fluorine substituent featured a considerable secondary directing group effect,[102] thereby leading to the site-selectively afforded the more sterically hindered compound **126i** as the sole product in good yield.[103] However, the 3,4,5-trifluorosubstituted substrate **28j** delivered the corresponding product **126j** with an inferior result. Subsequently, a variation of the substitution pattern on the Lewis-basic

pyridine moiety proved to be viable, but did not significantly alter the catalytic efficacy. We were delighted to observe that synthetically useful substrates substituted with heterocyclic moieties, such as pyridyl (py), pyrimidinyl (pym), and pyrazolyl, could be utilized as the selectivity-ensuring entities. In contrast, other directing groups, such as oximes or esters, have been thus far not been suitable substrates.

7.2.2 Scope of the C–H Bond Cyanation with Indoles

Thereafter, we examined the use of the removable pyrimidine directing group for the cyanation of biologically active indole[117] derivatives **7**[118] (Scheme 7.2).



Scheme 7.2. Cobalt-catalyzed C–H bond cyanation of indoles **7**. [a] [Cp*CoI_2(CO)] (**112**, 5.0 mol %), $AgSbF_6$ (10 mol %), KOAc (10 mol %).

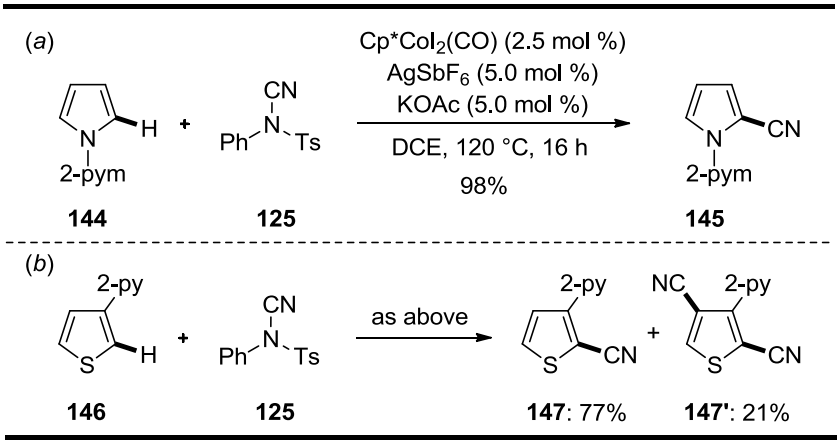
Applying this method, the parent compound **127a** was synthesized in virtually quantitative yield. Remarkably, 5-substituted indoles bearing various functional groups, such as methoxy (**7b**), bromo (**7c**) or amido (**7e**), were efficiently cyanated, which allowed the synthesis of serotonin derivatives in a step-economical fashion. Unfortunately, the reaction with 5-nitro

[117] *Modern Heterocyclic Chemistry* (Eds.: J. Alvarez-Builla, J. J. Vaquero, J. Barluenga), Wiley-VCH, Weinheim, **2011**.
[118] L. Ackermann, A. V. Lygin, *Org. Lett*. **2011**, *13*, 3332–3335.

substituted indole **7d** was not successful. Generally, substitution on the carbocyclic moiety of the substrates **7** was well tolerated by the C–H bond functionalization catalyst. Interestingly, the sterically more congested 3-methyl indole derivative **7h** delivered the desired cyanated product **127h** in excellent isolated yield as well. Even the sensitive ketone functionality on the tetrahydroindolone **7i** was cyanated with remarkably high efficacy.

7.2.3 Scope of the C–H Bond Cyanation with Heteroarenes

The versatile cobalt(III) catalyst was not limited to cyanations on the indole heterocycle. Indeed, the direct C–H bond cyanation of pyrroles (**144**, Scheme 7.3a) and thiophenes (**146**, Scheme 7.3b) occurred with excellent levels of efficacy and positional selectivity as well.

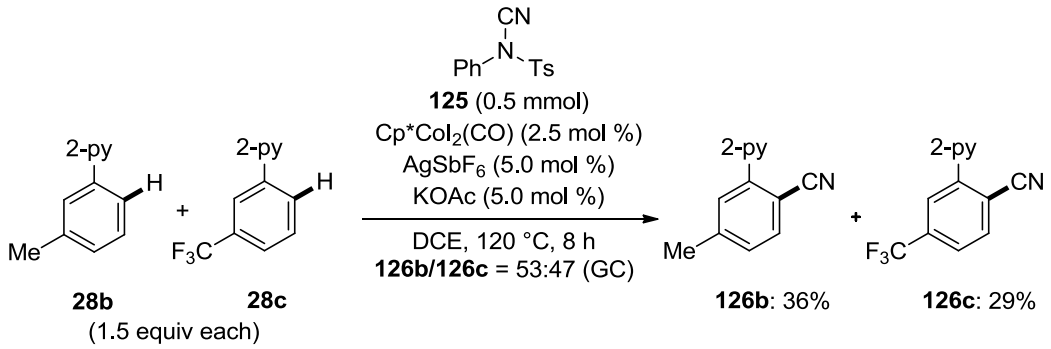


Scheme 7.3. Cobalt-catalyzed C–H bond cyanation of the heteroarenes **144** and **146**.

7.3 Mechanistic Studies

7.3.1 Intermolecular Competition Experiments

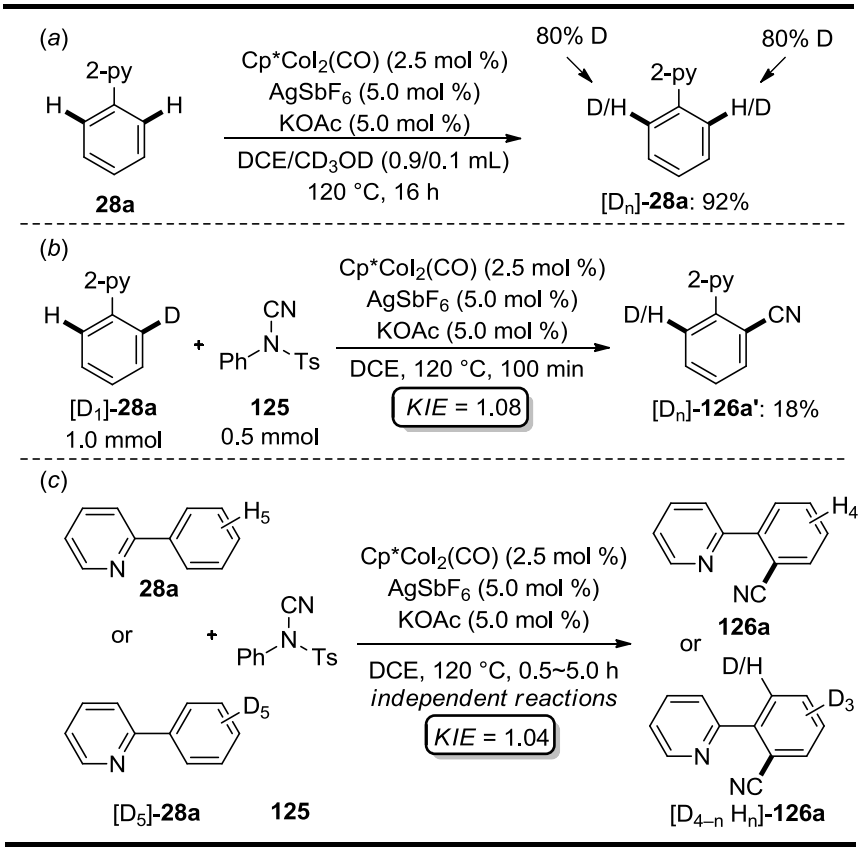
Intrigued by the outstanding activity of the cobalt catalyst through for cobalt mechanistically unusual carboxylate assistance, we sought to unravel the mode of action. To this end, intermolecular competition experiments between the differently substituted arenes **28b** and **28c** highlighted a slight preference in the C–H bond cyanation for the more electron-rich substrate (Scheme 7.4).



Scheme 7.4. Competition experiment between differently substituted arenes **28b** and **28c**.

7.3.2 Reactions with Isotopically Labelled Reagents

The use of a deuterated cosolvent clearly indicated a significant H/D exchange solely occurring in the *ortho* position of arene **28a** (Scheme 7.5a).

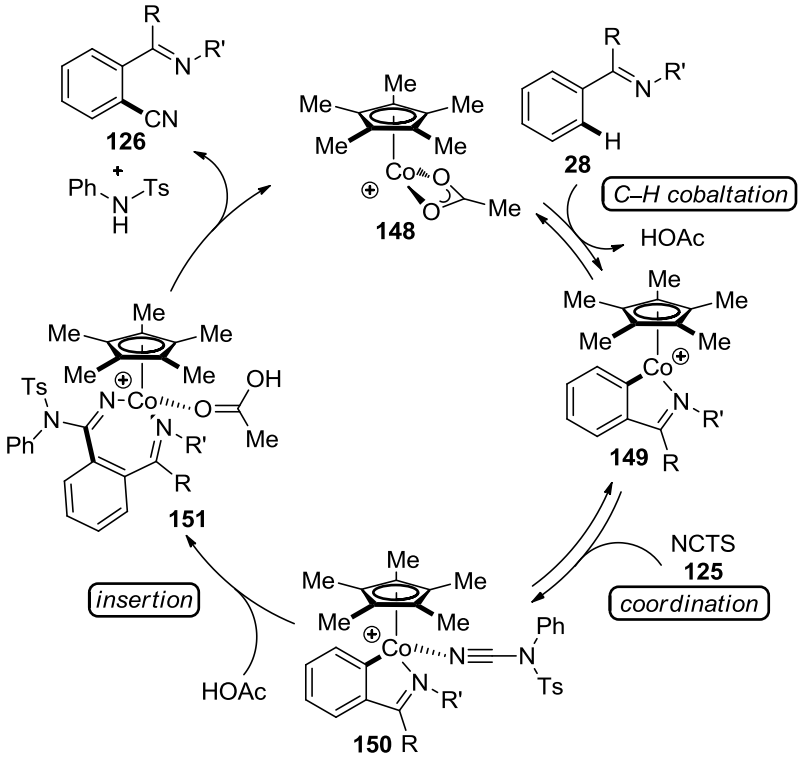


Scheme 7.5. Cobalt-catalyzed H/D exchange and determination of KIE values with arene **28a**.

Accordingly, cobalt-catalyzed C–H bond cyanations with isotopically labeled substrates led to a minor kinetic isotope effect (KIE) values of $k_H/k_D \approx 1.0$ and $k_H/k_D \approx 1.1$ for the inter- and intramolecular KIE-determination experiments, respectively (Scheme 7.5b and Scheme 7.5c). These data were in agreement with the C–H bond metalation step not being rate-determining.

Moreover, a Hammett plot correlation[119] (See Chapter **10**) indicated a change in the rate-determining reaction step depending on the substitution pattern of the arene.

7.3.3 Proposed Catalytic Cycle



Scheme 7.6. Proposed catalytic cycle.

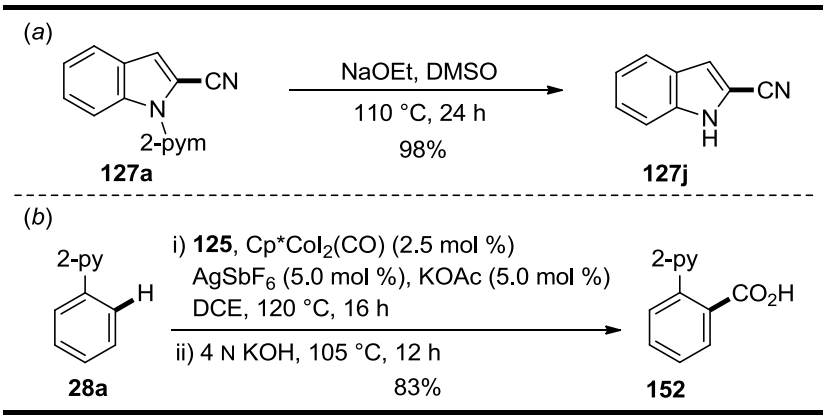
Based on our mechanistic studies, we proposed the catalytic cycle initiated by a reversible carboxylate-assisted C–H bond metalation, thus yielding the cyclometalated complex **149** (Scheme 7.6). Subsequent coordination and insertion of **125** furnished the key intermediates **150** and **151**, respectively. Finally, *β*-elimination provides the desired product **126**, while proto-demetalation regenerates the catalytically active cobalt(III) carboxylate catalyst **148**.

7.4 Application

To illustrate the unique potential of the cobalt(III)-catalyzed cyanation protocol, we removed the directing group on the indole **127a** (Scheme 7.7a),[118] and devised a reaction sequence which resulted in the formal direct carboxylation of unactivated C–H bonds.[120] Thus, a

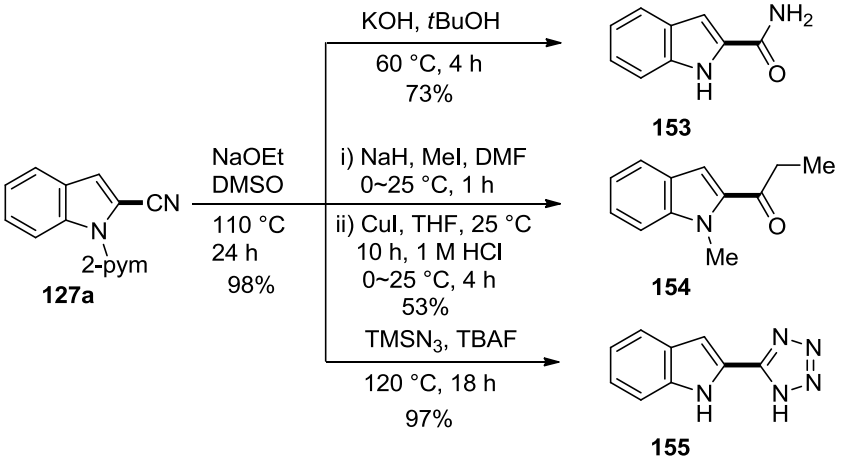
[119] a) L. P. Hammett, *J. Am. Chem. Soc*, **1937**, *59*, 96–103; b) Y. Aihara, N. Chatani, *Chem. Sci*. **2011**, *4*, 664–670.
[120] a) B. Yu, L.-N. He, *ChemSusChem* **2015**, *8*, 52–62; b) M. T. Johnson, O. F. Wendt, *J. Organomet. Chem*. **2014**, *751*, 213–220; c) L. Ackermann, *Angew. Chem. Int. Ed*. **2011**, *50*, 3842–3844; d) K. Huang, C.-L. Sunwa, Z.-J. Shi, *Chem. Soc. Rev*. **2011**, *40*, 2435–2452.

one-pot procedure initiated by the cobalt-catalyzed C–H bond cyanation, along with a facile base-mediated saponification, delivered the desired carboxylic acid **152** in high yield (Scheme 7.7b).



Scheme 7.7. (a) Removal of directing group. (b) Cobalt-catalyzed one-pot synthesis of the carboxylic acid **152**.

Finally, we exploited the cobalt-catalyzed C–H bond cyanation for the synthesis of the functionalized indoles **153**–**155** (Scheme 7.8).[118, 121] Particularly, the high-yielding preparation of the 2-tetrazolyl derivative **153** should prove instrumental for the design of novel bioactive drugs.



Scheme 7.8. Cobalt-catalyzed C–H bond activation towards substituted indoles.

7.5 Conclusion

In summary, we have reported on the first cobalt-catalyzed cyanation of unactivated C–H

[121] a) M. Chaitanya, D. Yadagiri, P. Anbarasan, *Org. Lett*. **2013**, *15*, 4960–4963; b) S. M. Kim, J. H. Park, Y. K. Kang, Y. K. Chung, *Angew. Chem. Int. Ed*. **2009**, *48*, 4543–4545; c) D. Amantini, R. Beleggia, F. Fringuelli, F. Pizzo, L. Vaccaro, *J. Org. Chem*. **2004**, *69*, 2896–2898.

bonds in arenes **28** and heteroarenes **7**, **144** and **146**. Thus, carboxylate assistance led to an enhanced activity of cationic cobalt(III) catalyst towards the direct cyanation of arenes and heteroarenes with ample scope. The optimized catalytic system tolerated various functional groups and proved applicable with removable directing groups. Mechanistic studies revealed an effecient cobalt-catalyzed site-selective *ortho* deuteration of heteroarylarenes by reversible C–H bond activation.

8 Cobalt(III)-Catalyzed Aryl- and Alkenyl-C–H Bond Aminocarbonylation with Isocyanates and Acyl Azides

In recent years, transition-metal-catalyzed direct insertion of isocyanates into C–H bonds is in high demand, because they efficiently provide synthetically valuable amide moieties.[122] Theoretically, acyl azides can be employed as precursors for isocyanates *via* the "Curtius rearrangement" at elevated temperature.[123] To the best of our knowledge, acyl azides were only found to work as amino sources in the iridium- and ruthenium-catalyzed amidation.[124–125] Another sole example of the use of acyl azides was developed applying rhodium catalysts.[125] However, further application of acyl azides was strongly limited by the difficulty in controlling their dual reactivity, leading to a mixture of products with C–C and C–N bond formation. Described herein is the first cobalt(III)-catalyzed C–H bond aminocarbonylation with isocyanates and acyl azides.[126]

8.1 Optimization

We commenced our studies by exploring the reaction conditions for the cobalt(III)-catalyzed C–H bond aminocarbonylations of 1-phenylpyrazole (**128a**) with phenyl isocyanate (**129a**) (Table 8.1). With a combination of $AgNTf_2$ or $AgPF_6$ and AgOAc, the desired product **130aa** was obtained in low yields (entries 1–2). Among a set of representative carboxylate salts, AgOPiv provided the optimal results (entries 3–9). The nature of the silver salts appeared to be crucial, and both $AgSbF_6$ and $AgNTf_2$ combined with AgOPiv gave the best yields (entries 10–13). Moreover, omission of either of the catalyst's components or replacement of the $[Cp^*CoI_2(CO)]$[85–86] by other cobalt sources failed to deliver the desired product (entries 14–19), whereas reducing the amount of isocyanate **129a** or changing the reaction media resulted in significantly reduced yields or inhibited the reaction (entries 20–22).

Table 8.1. Optimization of cobalt(III)-catalyzed C–H bond aminocarbonylation.[a]

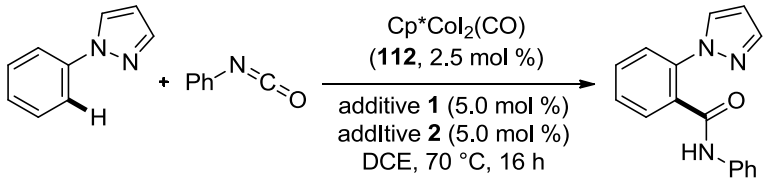
[122] a) S. D. Sarkar, L. Ackermann, *Chem. Eur. J.* **2014**, *20*, 13932–13936; b) B. Zhou, W. Hou, Y. Yang, Y. Li, *Chem. Eur. J.* **2013**, *19*, 4701–4706; c) K. D. Hesp, R. G. Bergman, J. Ellman, *J. Am. Chem. Soc.* **2013**, *135*, 11430–11433; d) K. Muralirajan, K. Parthasarathy, C. H. Cheng, *Org. Lett.* **2012**, *14*, 4262–4265; e) Y. Kuninobu, Y. Tokunaga, A. Kawata, K. Takai, *J. Am. Chem. Soc.* **2006**, *128*, 202–209.

[123] T. Curtius, *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 3023–3033.

[124] J. Ryu, J. Kwak, K. Shin, D. Lee, S. Chang, *J. Am. Chem. Soc.* **2013**, *135*, 12861–12868.

[125] K. Shin, J. Ryu, S. Chang, *Org. Lett.* **2014**, *16*, 2022–2025.

[126] J. Li, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, (DOI: 10.1002/anie.201501926).



128a **129a** **130aa**

Entry	[Co]	Additive 1	Additive 2	Yield (%)[b]
1	[Cp*CoI$_2$(CO)]	AgNTf$_2$	AgOAc	35
2	[Cp*CoI$_2$(CO)]	AgPF$_6$	AgOAc	23
3	[Cp*CoI$_2$(CO)]	AgPF$_6$	AgCO$_2$Ad	25
4	[Cp*CoI$_2$(CO)]	AgPF$_6$	AgOPiv	42
5	[Cp*CoI$_2$(CO)]	AgPF$_6$	KOAc	24
6	[Cp*CoI$_2$(CO)]	KPF$_6$	AgOAc	0
7	[Cp*CoI$_2$(CO)]	AgPF$_6$	CsOAc	0
8	[Cp*CoI$_2$(CO)]	AgPF$_6$	KOPiv	0
9	[Cp*CoI$_2$(CO)]	AgPF$_6$	NaOPiv	0
10	[Cp*CoI$_2$(CO)]	AgSbF$_6$	AgOPiv	46
11	[Cp*CoI$_2$(CO)]	AgNTf$_2$	AgOPiv	57
12	[Cp*CoI$_2$(CO)]	AgPF$_6$	AgOPiv	64[c]
13	***[Cp*CoI$_2$(CO)]***	***AgSbF$_6$***	***AgOPiv***	***67[c]***
14	[Cp*CoI$_2$(CO)]	AgPF$_6$	--	0
15	[Cp*CoI$_2$(CO)]	--	AgOPiv	0
16	--	AgPF$_6$	AgOPiv	0
17	CoI$_2$	AgSbF$_6$	AgOPiv	0
18	Co(OAc)$_2$	AgSbF$_6$	AgOPiv	0
19	Co(acac)$_2$	AgSbF$_6$	AgOPiv	0
20	[Cp*CoI$_2$(CO)]	AgSbF$_6$	AgOPiv	53[c,d]
21	[Cp*CoI$_2$(CO)]	AgPF$_6$	AgOPiv	0[e]
22	[Cp*CoI$_2$(CO)]	AgPF$_6$	AgOPiv	0[f]

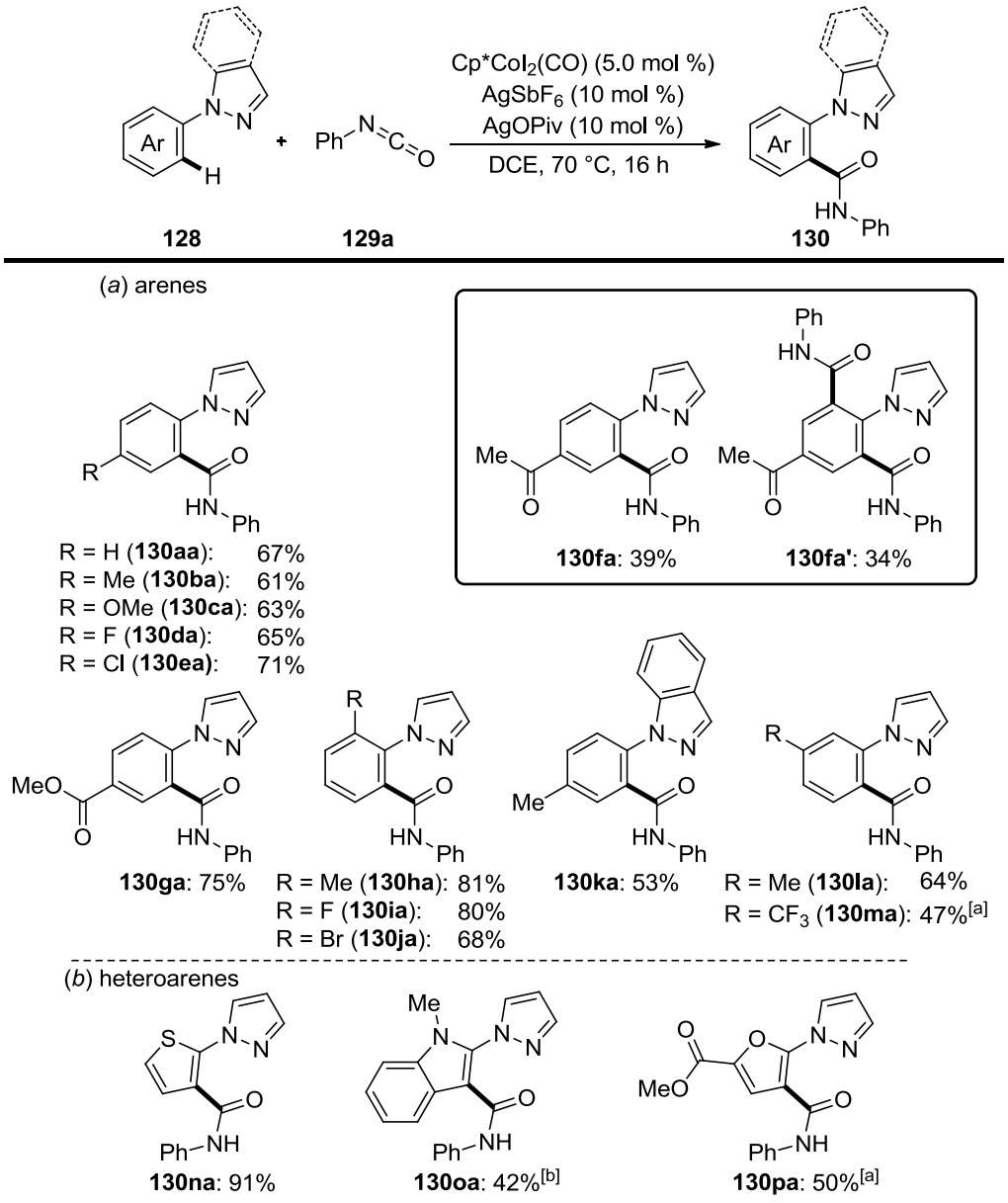
[a] General reaction conditions: **128a** (0.5 mmol), **129a** (1.0 mmol), Cp*CoI$_2$(CO) (**112**, 2.5 mol %), AgSbF$_6$ (5.0 mol %), KOAc (5.0 mol %), DCE (2.0 mL), 70 °C, 16 h. [b] Isolated yields.

[c] [Cp*CoI_2(CO)] (5.0 mol %), additives (10 mol %). [d] **129a** (0.75 mmol). [e] NMP (2.0 mL). [f] PhMe (2.0 mL).

8.2 Scope and Limitations

8.2.1 Scope of Aminocarbonylation with Substrates 128

With the optimized cobalt(III) catalytic system in hand, we explored its substrate scope with various *N*-heteroarenes (Scheme 8.1).

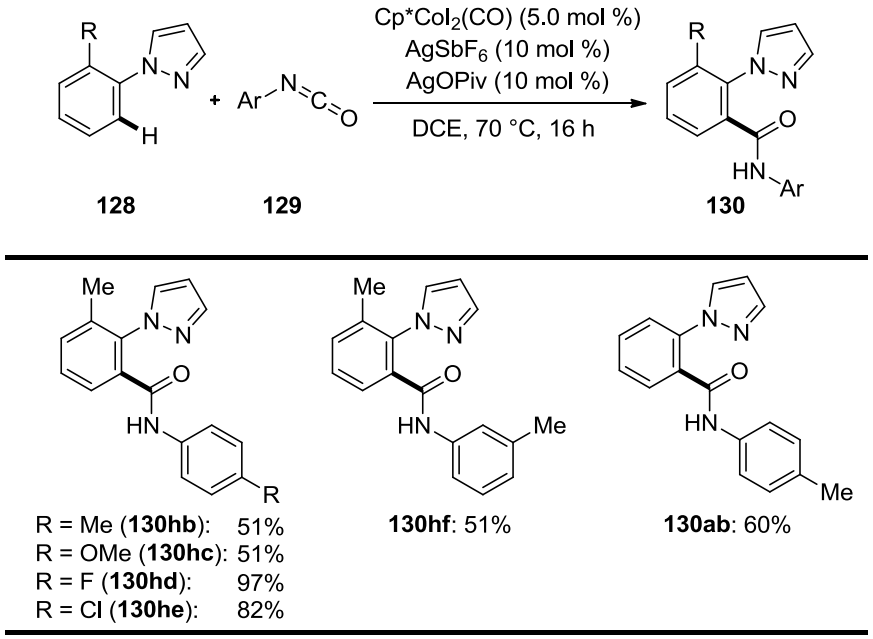


Scheme 8.1. Scope of cobalt-catalyzed aminocarbonylation of C–H bonds. [a] [Cp*CoI_2(CO)] (10 mol %), $AgSbF_6$ (20 mol %), AgOPiv (20 mol %). [b] [Cp*CoI_2(CO)] (10 mol %), $AgNTf_2$ (20 mol %), AgOPiv (20 mol %).

Notably, the chelation-assisted C–H bond aminocarbonylation proved to be broadly applicable. Both electron-rich as well as electron-deficient arylpyrazoles were converted into nitriles with moderate to high isolated yields **130aa**–**130ea**. Importantly, the cobalt(III) catalyst displayed an excellent chemoselectivity, wherein a number of valuable electrophilic groups, such as ketones or esters, were well tolerated. Interestingly, a certain amount of disubstituted products like **130fa'** were also isolated. Furthermore, a set of more sterically hindered substrates bearing an *ortho*-methyl, fluoro or bromo group generated the desired products in good yields **130ha**–**130ja**. We were delighted to observe that synthetically useful indazoles **28k** could be utilized as the selectivity ensuring entity. In intramolecular competition experiments with *meta*-substituted arenes **28l** and **28m**, the site-selectivities were largely governed by steric interactions. The widely applicable cobalt catalyst was not limited to transformations of only aromatic pyrazoles. Indeed, heteroaromatic thiophene, indole and furan derivatives **128n**–**128p** also led to site-selective C–H bond aminocarbonylations.

8.2.2 Scope of Aminocarbonylation with Decorated Isocyanates 129

Next, we were pleased to observe that isocyanates **129b**–**129f** bearing various functional groups were well tolerated by the cobalt catalyst (Scheme 8.2).



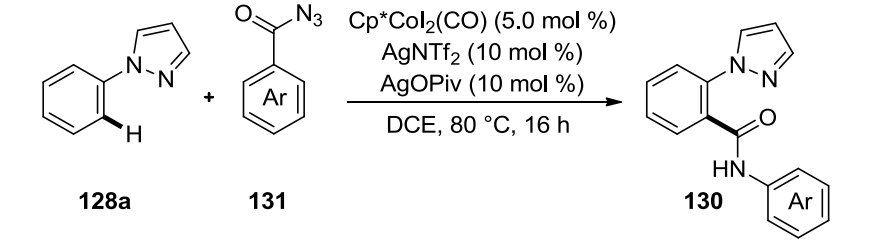
Scheme 8.2. Cobalt-catalyzed aminocarbonylation of C–H bonds.

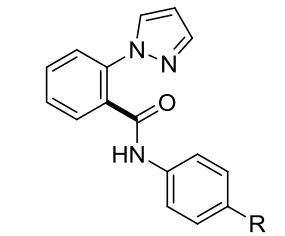
Acceptable yields were obtained with electron-rich substituted isocyanates **129b** and **129c**,

whereas electron-deficient reagents **129d** were found to be most reactive, and the desired product **130hd** was produced in virtually quantitative yield. Likewise a chloro substituent in isocyanate **129e** was also found to be tolerated by the catalytic system, which can be useful for further functionalizations by cross-coupling chemistry.

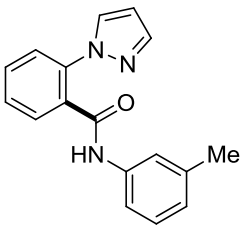
8.2.3 Scope of Aminocarbonylation with Acyl Azides 131

As discussed above, acyl azides **131** can either be employed as aminocarbonylation reagents or precursors for isocyanates **129**. Yet, the synthetic approach to acyl azides is much simpler than those to isocyanates. Thus, we were delighted to explore that a wide substrate scope was observed to be competent when employing differently decorated acyl azides **131** (Scheme 8.3). Good yields were obtained with *para*-substituted electron-rich acyl azides **131b**, **131c** and **131g** as well as with azides **130ah** and **130ai** bearing electron-withdrawing substituents. Finally, *meta*- and *ortho*-substituted acyl azides **131f** and **131j** were tested, delivering the desired products **130af** and **130aj**, respectively, in high isolated yields.

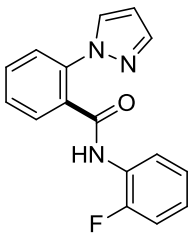




R = Me (**130ab**): 52%
R = OMe (**130ac**): 60%
R = Ph (**130ag**): 57%
R = Br (**130ah**): 63%
R = CF_3 (**130ai**): 66%



130af: 63%



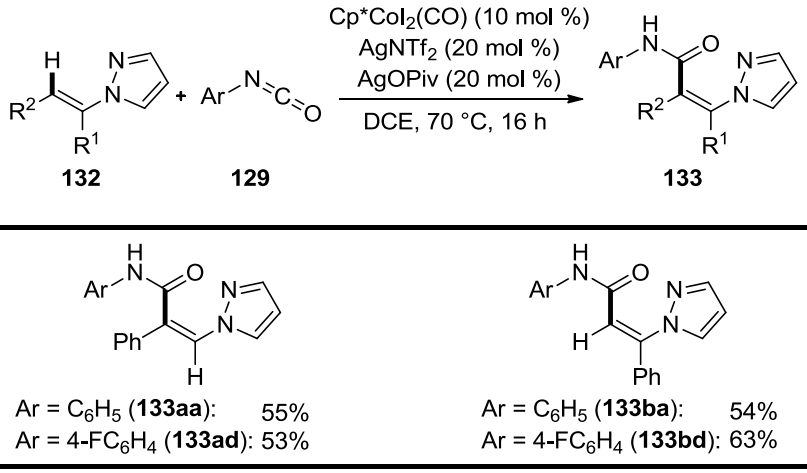
130aj: 78%

Scheme 8.3. Cobalt-catalyzed C–H bond aminocarbonylation with acyl azides **131**.

8.2.4 Scope of Aminocarbonylation with Vinyl Pyrazole 132

Interestingly, cobalt(III)-catalyzed aminocarbonylation was not only applicable on (hetero)arenes, but also successfully on olefins *via* alkenyl C–H bond activation (Scheme 8.4).

Both (*E*)-1-styryl-1*H*-pyrazole (**132a**) and 1-(1-phenylvinyl)-1*H*-pyrazole (**132b**) as well as un- or *para*-substituted aryl isocyanates showed good reactivity in direct aminocarbonylations under remarkable mild reaction conditions, thereby furnishing the thermodynamically less stable *Z*-olefins as the sole products **133**.



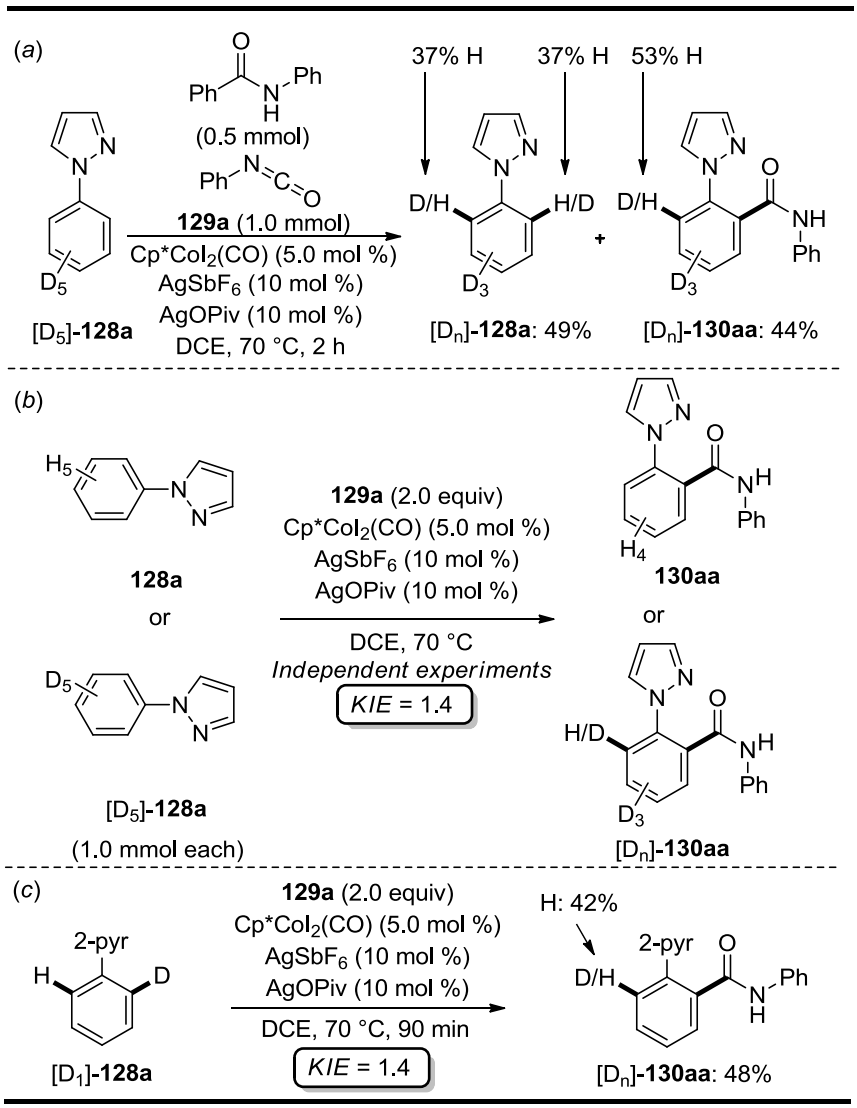
Scheme 8.4. Cobalt-catalyzed C–H bond aminocarbonylation with vinyl pyrazoles **133**.

8.3 Mechanistic Studies

8.3.1 H/D Exchange Experiments and Kinetic Isotope Experiments

Intrigued by the outstanding catalytic activity of this cobalt catalyst through for cobalt mechanistically unusual carboxylate assistance, we performed studies to delineate its working mode. To this end, an experiment with deuterated substrate [D_5]-**128a** clearly demonstrated a significant H/D exchange solely occurring in the *ortho* position of [D_n]-**128a** and [D_n]-**130aa** (Scheme 8.5a).

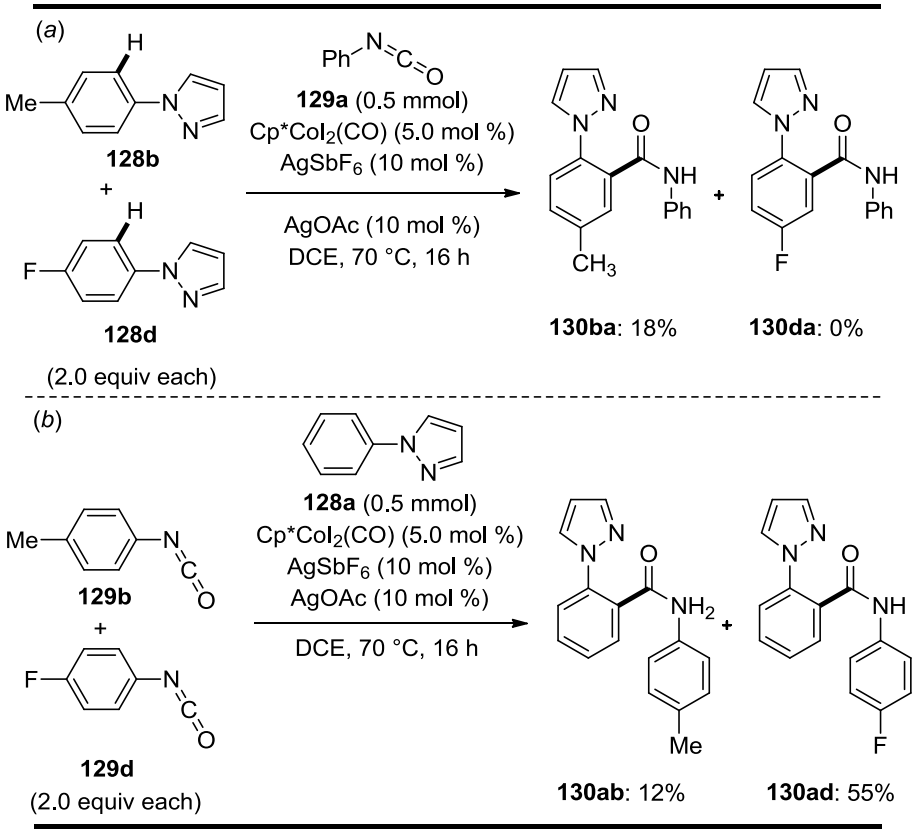
Independent experiments with isotopically labeled substrates indicated the C–H bond cobaltation can be characterized with a kinetic isotope effect (KIE) value of k_H/k_D = 1.4 (Scheme 8.5b). A similar KIE value was also obtained in the intramolecular KIE-determination experiment (Scheme 8.5c).



Scheme 8.5. Mechanistic studies. (a) H/D exchange reaction. (b) Intermolecular competition experiment: Determination of kinetic isotope effect (KIE). (c) Intramolecular competition experiment: Determination of kinetic isotope effect (KIE).

8.3.2 Competition Experiments

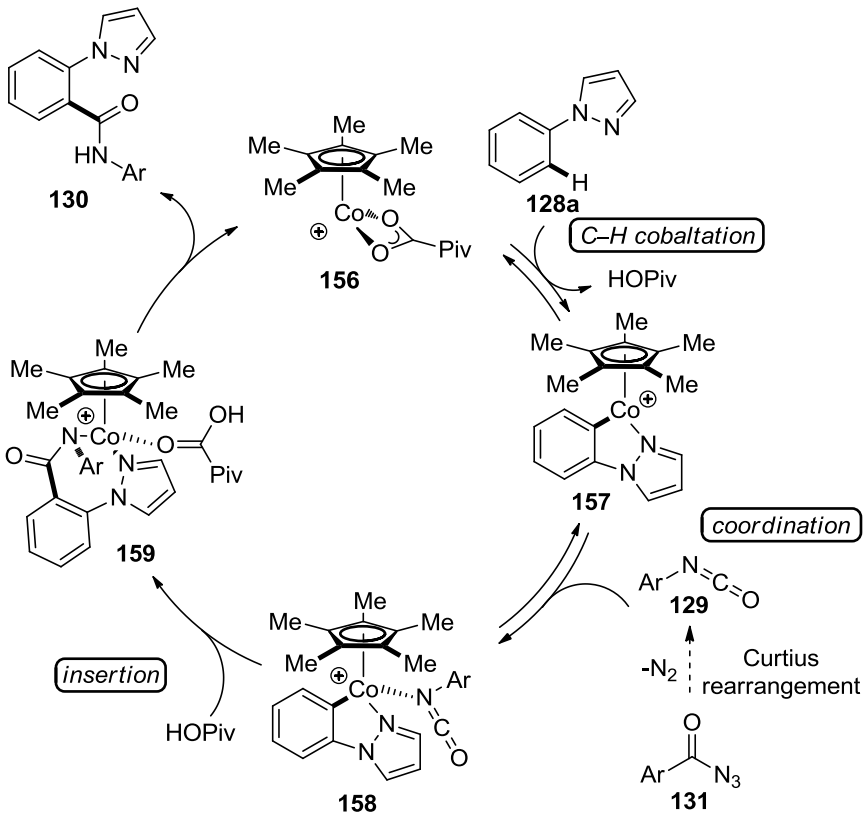
A set of intermolecular competition experiments between the differently substituted arenes **128** revealed a distinct preference in the C–H bond aminocarbonylation for the more electron-rich substrate **128b** (Scheme 8.6a). On the contrary, the results from the competition experiments between differently substituted isocyanates **129** showed the latter as an electron-deficient one to be more reactive than its electron-rich counterparts (Scheme 8.6b).



Scheme 8.6. (a) Competition experiment with different arenes **128**. (b) Competition experiment with different isocyanates **129**.

8.3.3 Proposed Catalytic Cycle

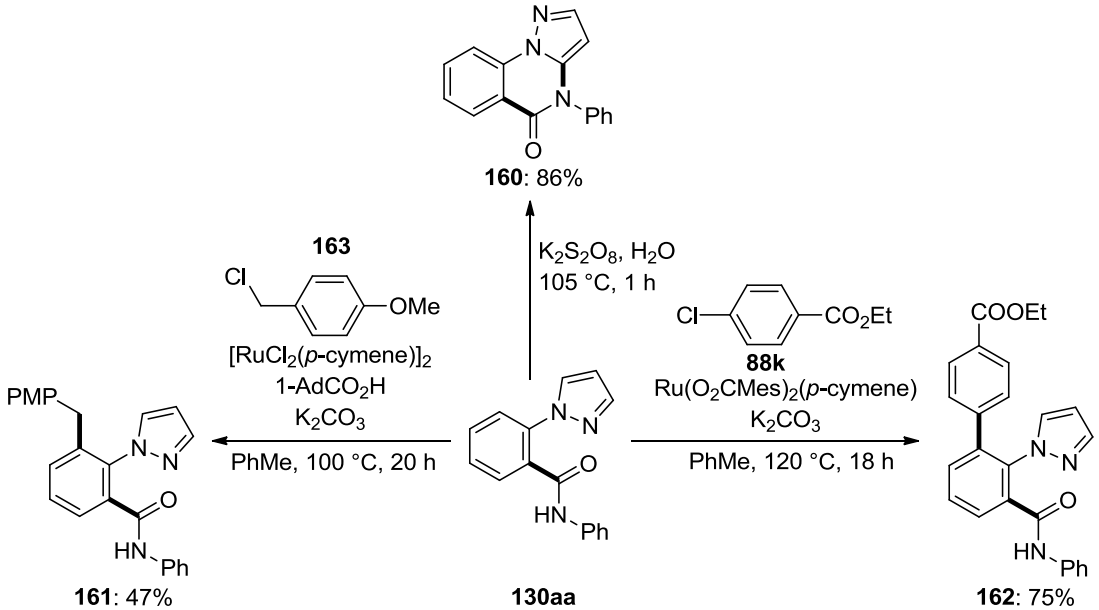
Based on our mechanistic studies, we proposed the catalytic cycle to be initiated by a reversible C–H bond metalation, thus yielding the cyclometalated complex **157** (Scheme 8.7). Subsequent coordination and insertion of isocyanate **129** furnish the key intermediates **158** and **159**, respectively. Finally, proto-demetalation regenerates the catalytically active cobalt(III) carboxylate catalyst **156** and provides the desired product **130**.



Scheme 8.7. Proposed catalytic cycle.

8.4 Applications

To demonstrate the synthetic versatility of the products synthesized by this method, several derivatization reactions were performed (Scheme 8.8).



Scheme 8.8. Derivatization of products **130** obtained by cobalt-catalyzed C–H bond aminocarbonylation.

Oxidative annulation of **130aa** afforded the heterocyclic product **160**. Direct C–H bond benzylation[127] and arylation[128] using ruthenium(II) catalysts delivered the corresponding products **161** and **162** in modest to good yields, respectively.

8.5 Conclusion

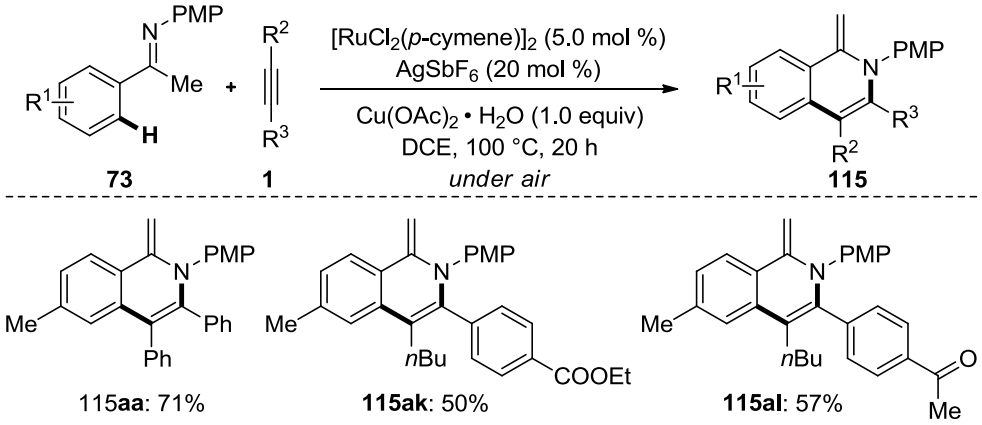
In summary, we have established the first cobalt-catalyzed aminocarbonylation of unactivated C–H bonds with isocyanates **129** and acyl azides **131**. Thus, carboxylate assistance led to a highly active cationic cobalt(III) catalyst for the direct aminocarbonylation of arenes **128** and alkenes **132** with ample scope. The optimized catalytic system tolerated various functional groups and proved applicable to olefins *via* alkenyl C–H bond activation. Mechanistic studies revealed an effective *site*-selective cobalt catalyst for the *site*-selective *ortho* deuteration of heteroarylarenes by reversible C–H bond activation.

[127] L. Ackermann, P. Novák, *Org. Lett.* **2009**, *11*, 4966–4969.
[128] L. Ackermann, R. Vicente, H. K. Potukuchi, V. Pirovano, *Org. Lett.* **2010**, *12*, 5032-5035.

9 Summary and Outlook

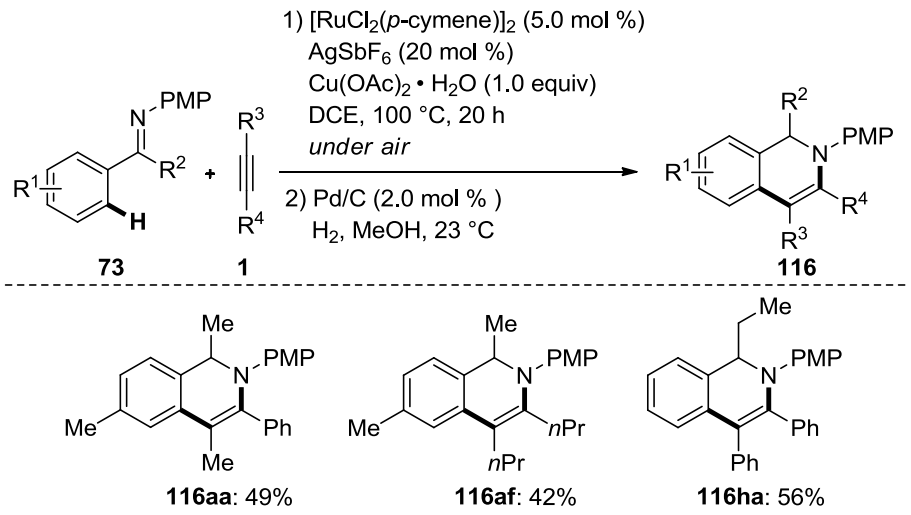
To improve the atom- and step-economy of organic syntheses, major efforts have been made on transformations of inert carbon–hydrogen (C–H) bonds into carbon–carbon (C–C) or carbon–heteroatom (C–N, C–O, C–Hal) bonds. Significant advances in organometallic chemistry have set the stage for the development of increasingly viable metal catalysts for C–H bond activation reactions and their applications in the preparation of pharmaceutical, agrochemical and functional materials. Thus, the work presented within this thesis focused on the development of versatile ruthenium- and cobalt-catalyzed direct C–H bond functionalizations.

In the first project, an effective protocol for the oxidative annulation of ketimines **73** with internal alkynes **1** was established, and the catalytic system consisting of $[RuCl_2(p\text{-cymene})]_2$, $AgSbF_6$ and $Cu(OAc)_2 \cdot H_2O$ tolerated well various functional groups (Scheme 9.1).



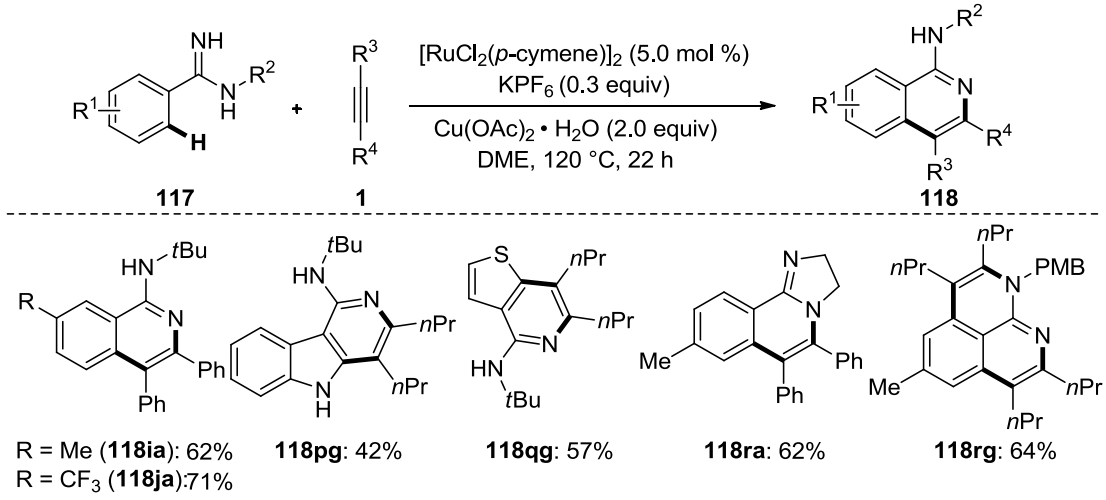
Scheme 9.1. Oxidative C–H bond functionalization with decorated ketimines and alkynes.

In order to access the corresponding reduced 1,2-dihydroisoquinolines **116**, we subsequently devised a two-step reaction sequence consisting of an initial ruthenium(II)-catalyzed C–H bond activation followed by palladium-catalyzed hydrogenation (Scheme 9.2).



Scheme 9.2. Multicatalytic synthesis of 1,2-dihydroisoquinolines **116**.

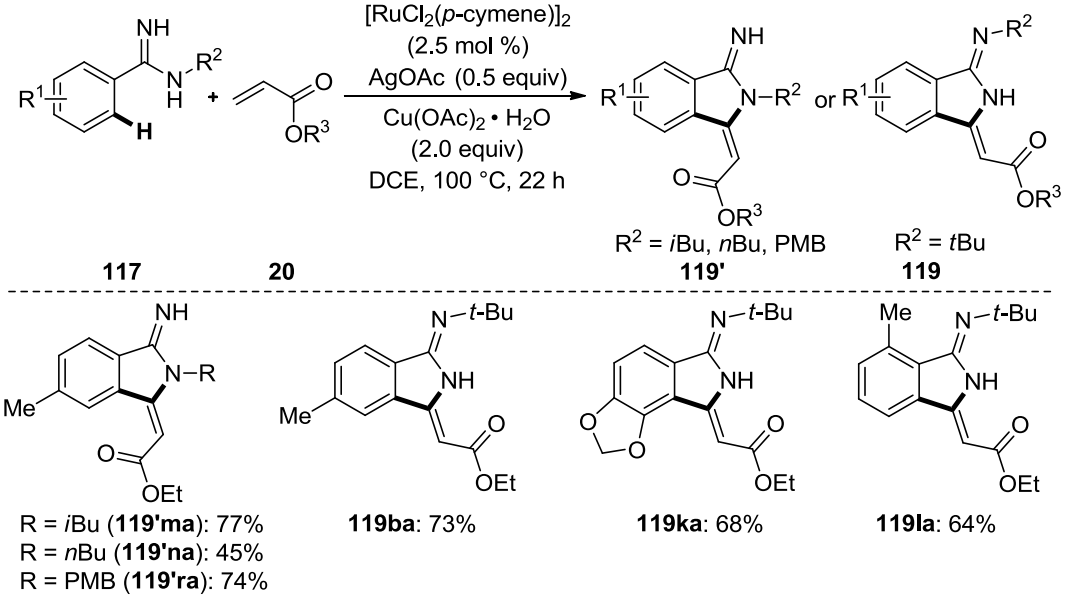
Based on the above findings, we managed to expand the scope of aromatic substrates to particularly challenging (hetero)aryl amidines **117**. A method for ruthenium(II)-catalyzed oxidative C–H bond annulations was developed by employing amidines and internal alkynes **1**. The reaction provided expedient access to differently decorated aminoisoquinolines **118** with ample scope. In addition, intramolecular competition experiments with substrates bearing *meta*-methyl or *meta*-trifluoromethyl substituents proceeded with excellent levels of site selectivity, producing aminoisoquinolines substituted at the less sterically hindered position (Scheme 9.3)



Scheme 9.3. Substrates scope for ruthenium(II)-catalyzed oxidative C–H bond annulations.

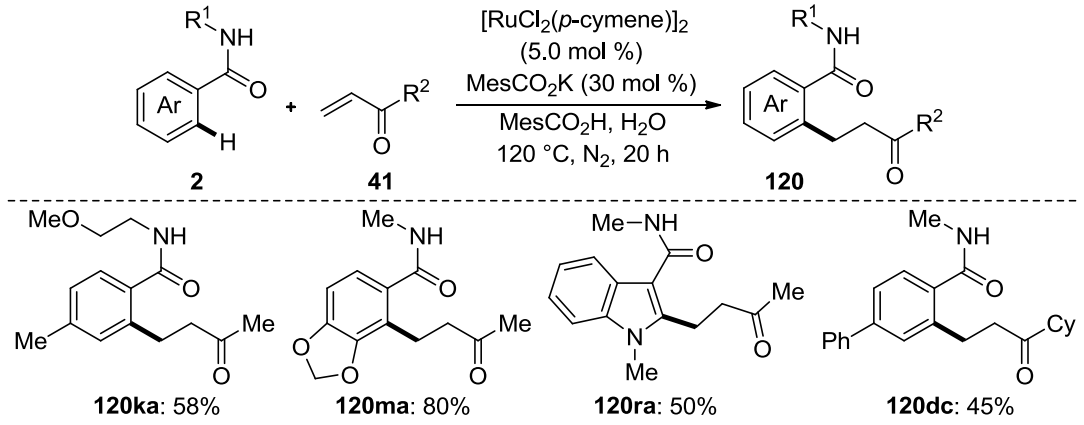
Inspired by the successful synthesis of aminoisoquinolines **118**, we subsequently became interesting in developing novel oxidative twofold C–H bond functionalizations with alkenes

20. The reaction proceeded not only with excellent chemo-, site-, and regio-selectivities, but also with perfect diastereoselectivity (Scheme 9.4).

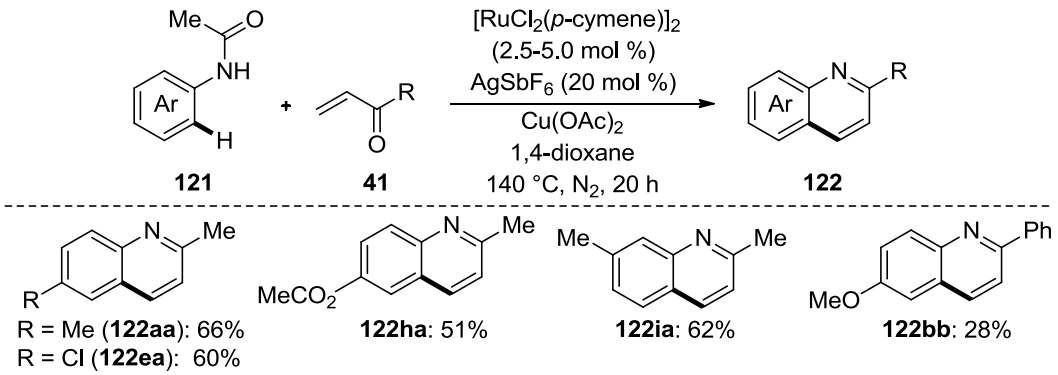


Scheme 9.4. Ruthenium(II)-catalyzed oxidative C–H bond alkenylation.

We subsequently established ruthenium(II)-catalyzed direct hydroarylation of α,β-unsaturated ketones **41** with aromatic amides **2** through monodentate coordination (Scheme 9.5). Meanwhile, oxidative annulations of α,β-unsaturated ketones **41** with acetanilides **121** furnished decorated quinolines **122** (Scheme 9.6).

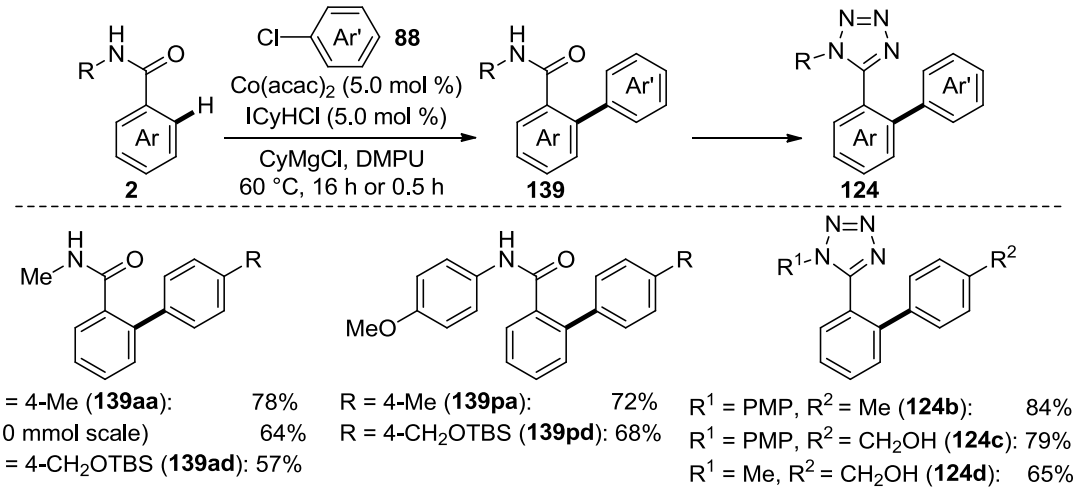


Scheme 9.5. Direct C–H bond hydroarylation of α,β-unsaturated ketones **41** with decorated amides **2**.



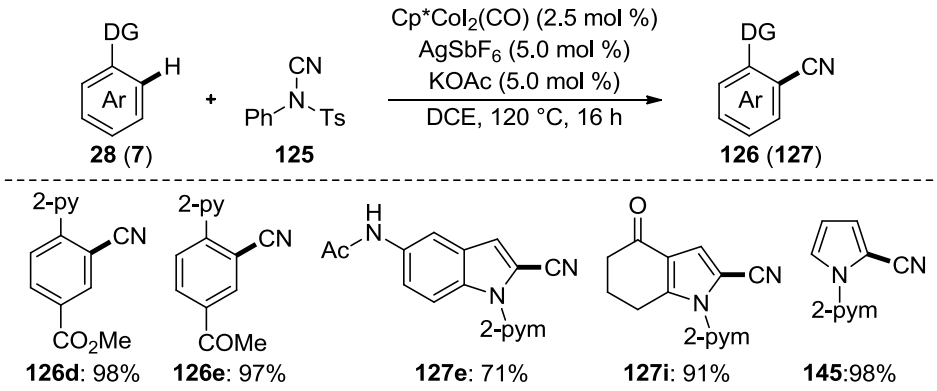
Scheme 9.6. Oxidative annulations of α,β-unsaturated ketones **41** with acetanilides **121**.

Thereafter, we developed cobalt-catalyzed direct C–H bond arylation with weakly-coordinating benzamides. Various aryl chlorides **88** as well as un- or *para*-substituted benzamides **2** were identified as viable substrates for direct arylations under remarkably mild reaction conditions. Moreover, the unique synthetic utility of this reaction was illustrated by the facile transformation of the *ortho*-arylated benzamides **139** to the desired biaryl tetrazoles **124** (Scheme 9.7).



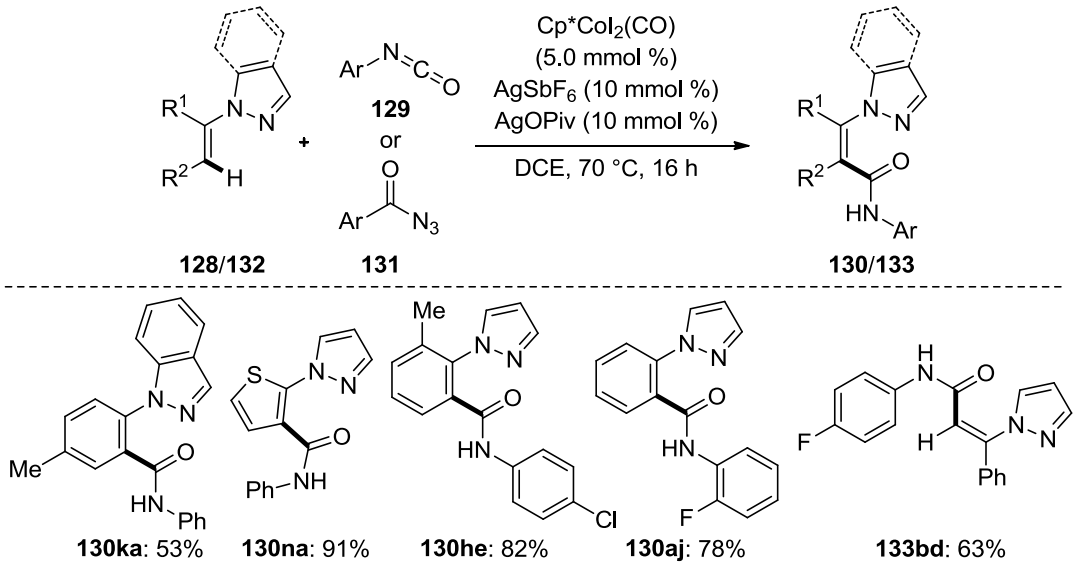
Scheme 9.7. Scope of cobalt-catalyzed C–H bond arylation and facile transformation of arylated benzamides **139** to biaryl tetrazoles **124**.

Very recently, inexpensive high-valent [Cp*Co(III)] derivatives have been identified as efficient catalysts for the site-selective functionalization of unactivated C–H bonds. We developed first cobalt(III)-catalyzed C–H bond cyanation of arenes and heteroarenes. The chelation-assisted C–H bond cyanation proceeded with excellent site- and chemo-selectivity, and a wide range of functional groups, such as halogens, ketones, esters and amides, were tolerated under the optimized reaction conditions (Scheme 9.8).



Scheme 9.8. Cobalt-catalyzed C–H bond cyanation.

Finally, described herein is the first cobalt(III)-catalyzed C–H bond aminocarbonylation with isocyanates **129** or acyl azides **131** as an electrophilic partner (Scheme 9.9). Notably, a broad scope of isocyanates **129** or acyl azides **131** makes this strategy especially attractive.



Scheme 9.9. Cobalt-catalyzed aminocarbonylation of C–H bonds.

In summary, major efforts in this thesis were focused on step- and atom-economical synthetic strategies based on transition-metal-catalyzed direct C–H bond functionalizations. In this context, we have developed ruthenium- and cobalt-catalyzed chelation-assisted direct C–H bond annulations, hydroarylations, arylations, cyanations and aminocarbonylations. Considering the rapid expansion of transition-metal-catalyzed C–H bond functionalizations, the researches towards further applications of the cobalt(III) is actively undertaken in the Ackermann group, more exciting progress is expected.

10 Experimental Section

10.1 General Remarks

Unless otherwise noted, all reactions were performed under N_2 or Ar atmosphere using pre-dried glassware and standard Schlenk techniques.

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-Dimethoxyether** (DME) and ***tert*-amylalcohol** (*t*-AmOH) were used as supplied by Merck or stirred over sodium chips for 5 h at 120 °C and then distilled at ambient pressure.

Water (H_2O) was degassed before its use applying repeated freeze-pump-thaw degassing procedure.

1,2-Dichloroethane (DCE) and **1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone** (DMPU) were dried over CaH_2 for 8 h, degassed and distilled under reduced pressure.

Dichloromethane (DCM), ***N*,*N*-dimethylformamide** (DMF) and **tetrahydrofuran** (THF) were purified using a solvent purification system (SPS) from MBRAUN. ***N*-Methyl-2-pyrrolidone** (NMP) was dried over CaH_2 for 4 h at 150 °C and subsequently distilled under reduced pressure.

Methanol (MeOH) was distilled from magnesium methanolate.

Toluene was pre-dried over KH followed by distillation from sodium benzophenone ketyl.

1,4-Dioxane was dried over sodium benzophenone ketyl and distilled afterwards.

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. Reported values are uncorrected.

Chromatography

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60F-plates

(Merck) with 254 nm fluorescent indicator from MERCK. Plates were visualized under UV-light or developed by treatment with a $KMnO_4$ solution followed by carefully heating. 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 Chromatography (GC)

The conversion of the reactions was monitored by 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, Ø 0.25 m).

High Performance Liquid Chromatography (HPLC)

Preparative and analytical separations were performed on an HPLC-System from KNAUER (*Smartline Pump 100*, Dynamic Mixing Chamber, Injection- and Control-Valve, *Smartline UV Detector 2500*). Separation normal phase column (250 × 10 mm) from MACHEREY-NAGEL (MN) was used. Organic solvents of HPLC grade were employed. All samples were filtered through Polytetrafluoroethylene Filter from ROTH (Ø 25 mm, 0.2 µm) or VWR (Ø 13 mm, 0.2 µm) prior to separation.

Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance (NMR) spectroscopy was performed at 300, 400, 500 or 600 MHz (^{1}H NMR), 75, 100 or 125 MHz (^{13}C NMR, APT) and 282 MHz (^{19}F NMR) on BRUKER *AM 250*, VARIAN *Unity-300* and *Inova 500* instruments. Chemical shifts are reported as δ-values in ppm relative to the residual proton peak of the deuterated solvent or its carbon atom, respectively, or the standard trimethylsilyl (TMS) peak. For characterization of the observed resonance multiplicities the following abbreviations were applied: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *m* (multiplet), *dd* (doublet of doublet), *dt* (doublet of triplet), or analogue representations. The coupling constants *J* are reported in Hertz (Hz).

Infrared Spectroscopy (IR)

Infrared spectra were recorded on a BRUKER *Alpha-P* ATR-spectrometer. Liquid probes have been measured as films between the plates of NaCl and solid probes neat applying Attenuated Total Reflection (ATR) technique which enables the samples to be examined

directly. Analysis of the spectral data has been done by using the *OPUS 3.1* software from BRUKER, respectively *OPUS 6*. Absorption ($\tilde{\nu}$) is given in wave numbers (cm^{-1}). Spectra were recorded in the range of 4000 to 400 cm^{-1}.

Mass Spectrometry (MS)

MS (EI) and HR-MS (EI) were measured on a *Time-of-Flight* mass spectrometer *AccuTOF* from JOEL. ESI-mass spectra were recorded on an *Ion-Trap* mass spectrometer *LCQ* from FINNIGAN or on a *Time-of-Flight* mass spectrometer *microTOF* from BRUKER. ESI-HR-MS 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, intensities relative to the base peak (I = 100) are written in parentheses.

Reagents

Chemicals obtained from commercial sources with purity above 95% were used without further purification.

10.2 Synthesis of the Starting Materials

The following starting materials were synthesized according to previously described methods: ketimines **73a**–**73i**;[129] alkynes **1b**–**1d**, **1d**–**1g**, **1h**–**1k**, **1i**; amidines **117a**–**117r**;[130] aryl amides **2a**–**2z**, [D_5]-**2a**;[131] acetanilides **121a**–**121k**;[132] α,β-unsaturated ketones **41b**–**41c**;[133] aryl tetrazoles **123a**–**123b**;[110c] aryl chlorides **88d**, **88f**;[134] carbamates **86**;[135] phenylpyridines **28a**–**28e**, **28g**–**28l**, **146**, phenyl pyrimidines **28m**–**28n**;[136] (pyrimidin-2-yl)-1*H*-indoles **7a**–**7h**, **144**;[137] *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (**125**, NCTS);[138] 2-[D]-phenylpyridine [D_1]-**28a**;[139] Cp*$Co^{III}I_2$(CO) (**112**);[85,86] aryl pyrazoles **128b**–**128i**, **128k**–**128n**, **128p**,

[129] G. Ghattas, D. Chen, F. Pan, J. Klankermayer, *Dalton Trans*. **2012**, *41*, 9026–9028.
[130] a) X. H. Wei, M. Zhao, Z. Y. Du, X. W. Li, *Org. Lett*. **2011**, *13*, 4636–4639; b) Y. Wang, H. G. Wang, J. L. Peng, Q. Zhu, *Org. Lett*. **2011**, *13*, 4604–4607.
[131] Q. Tang, D. Xia, X. Jin, Q. Zhang, X.-Q. Sun, C. Wang, *J. Am. Chem. Soc*. **2013**, *135*, 4628–4631.
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[134] H. M. L. Davies, S. J. Hedley, B. R. Bohall, *J. Org. Chem*. **2005**, *70*, 10737–10742.
[135] X. Sun, Y. Sun, C. Zhang, Y. Rao, *Chem. Commun*. **2014**, *50*, 1262–1264.
[136] V. P. W. Böhm, T. Weskamp, C. W. K. Gstöttmayr, W. A. Herrmann, *Angew. Chem. Int. Ed*. **2000**, *39*, 1602–1604.
[137] L. Ackermann, A. V. Lygin, *Org. Lett*. **2011**, *13*, 3332–3335.
[138] P. Anbarasan, H. Neumann, M. Beller, *Chem. Eur. J*. **2011**, *17*, 4217–4222.
[139] C. Xu, Q. Shen, *Org. Lett*. **2014**, *16*, 2046–2049.

[D_5]-**128a**;[140] **128j**;[141] **128o**;[142] **132a**;[143] **132b**;[144] 2-[D]-1-phenyl-1*H*-pyrazole ([D_1]-**128a**);[141,139] isocyanates **129b**–**129c**, **129e**-**129f** and acyl azides **131**.[145]

10.3 General Procedures

General procedure A for the ruthenium(II)-catalyzed oxidative alkyne annulation with ketimines

A suspension of ketimine **73** (0.50 mmol), alkyne **1** (1.00 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20.0 mol %), and $Cu(OAc)_2 \cdot H_2O$ (99.5 mg, 0.50 mmol) in DCE (2.0 mL) was stirred at 100 ℃ for 20 h under an atmosphere of air. After cooling down to ambient temperature, the reaction mixture was extracted with EtOAc (3 × 20 mL), washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (*n*-hexane/EtOAc/Et_3N) to afford product **115**.

General procedure B for Multicatalytic Synthesis of Dihydroisoquinolines

A suspension of ketimine **73** (0.50 mmol), alkyne **1** (1.00 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20.0 mol %), and $Cu(OAc)_2 \cdot H_2O$ (99.5 mg, 0.50 mmol) in DCE (2.0 mL) was stirred at 100 ℃ for 20 h under an atmosphere of air. After cooling to ambient temperature, the reaction mixture was filtrated, and Pd/C (10 % w/w) was added. The reaction mixture was stirred at ambient temperature for 24 h under an atmosphere of H_2. The reaction mixture was extracted with EtOAc (3 × 20 mL), washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (*n*-hexane/EtOAc) to afford product **116**.

General procedure C for the ruthenium(II)-catalyzed oxidative alkyne annulation with amidines

A suspension of amidine **117** (0.50 mmol), alkyne **1** (1.00 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %), KPF_6 (27.6 mg, 30 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in DME (2.0 mL) was stirred at 120 °C for 22 h under an atmosphere of N_2. At ambient temperature,

[140] A. Correa, C. Bolm, *Adv. Synth. Catal*. **2007**, *349*, 2673–2676.
[141] F. Diness, D. P. Fairlie, *Angew. Chem. Int. Ed*. **2012**, *51*, 8102–8106.
[142] W.-B. Wu, J.-M. Huang, *Org. Lett*. **2012**, *14*, 5832–5835.
[143] J. Mao, Q. Hua, J. Guo, D. Shi, S. Ji, *Synlett* **2008**, *13*, 2011–2016.
[144] Q. Liao, Y. Wang, L. Zhang, C. Xi, *J. Org. Chem*. **2009**, *74*, 6371–6373.
[145] K. Shi, J. Ryu, S. Chang, *Org. Lett*. **2014**, *16*, 2022–2025.

H_2O (20 mL) was added, and the reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc) to yield products **118**.

General procedure D for the ruthenium(II)-catalyzed oxidative alkenylation of amidines

A suspension of amidine **117** (0.50 mmol), alkene **20** (0.75 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7−15.3 mg, 2.5−5.0 mol %), AgOAc (41.5 mg, 50 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in DCE (2.0 mL) was stirred at 100−120 °C for 22 h under an atmosphere of N_2. At ambient temperature, the reaction mixture was extracted with EtOAc (3 × 20 mL), washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc) to yield products **119**.

General procedure E for the ruthenium(II)-catalyzed C−H hydroarylation with aromatic amides

A suspension of aryl amides **2** or acetanilides **121** (0.50 mmol), *α,β*-unsaturated ketones **41** (1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30 mol %) and $MesCO_2H$ (82 mg, 1.0 equiv) in degassed H_2O (2.0 mL) was stirred at 120 °C for 20 h under an atmosphere of N_2. At ambient temperature, aq. Sat. NaCl solution (15 mL) was added, the reaction mixture was extracted with EtOAc (3 × 20 mL) and the combined organic phases were dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc) yielded products **120**.

General procedure F for the ruthenium(II)-catalyzed oxidative annulation by acetanilides

A suspension of respective acetanilide **121** (0.50 mmol), *α,β*-unsaturated ketone **41** (1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), $AgSbF_6$ (17.2 mg, 20 mol %) and $Cu(OAc)_2$ (190.0 mg, 2.1 equiv) in 1,4-dioxane (2,0 mL) was stirred at 140 °C for 20 h under an atmosphere of N_2. At ambient temperature, H_2O (15 mL) was added. The reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc) yielded products

122.

General procedure G for the cobalt-catalyzed C−H bond arylation by aromatic amides

A suspension of $Co(acac)_2$ (6.5 mg, 5.0 mol %), ICyHCl (6.8 mg, 5.0 mol %), aryl amide **2** (0.50 mmol) and DMPU (1.0 mL) was stirred for 5 min at 0 °C. To this mixture, a 2-Me-THF solution of CyMgCl (1.0 M solution in 2-Me-THF, 1.5 mL, 3.0 equiv) was added dropwise at the same temperature, followed by addition of aryl chloride **88** (1.2 equiv). Then the mixture was stirred at 60 °C for 16 h (or for 30 min in the indicated cases) under an atmosphere of argon. At ambient temperature, aq. sat. NH_4Cl solution (2.0 mL) and H_2O (15 mL) were added. The reaction mixture was extracted with MTBE (3 × 20 mL), the combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc) yielded products **139**.

General procedure H for the cobalt-catalyzed C−H bond arylation in aryl tetrazoles

A suspension of $Co(acac)_2$ (12.9 mg, 10.0 mol %), IMesHCl (34.0 mg, 20.0 mol %), aryl tetrazole **123** (0.50 mmol), aryl carbamate **86** (1.2 equiv) and DMPU (1.0 mL) was stirred for 5 min at 0 °C. To this mixture, a 2-Me-THF solution of CyMgCl (1.0 M solution in 2-Me-THF, 0.8 mL, 1.6 equiv) was added dropwise at the same temperature. Then the mixture was stirred at 60 °C for 16 h under an atmosphere of argon. At ambient temperature, aq. Sat. NH_4Cl solution (2.0 mL) and H_2O (15 mL) were added. The reaction mixture was extracted with MTBE (3 × 20 mL), the combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc) yielded products **124**.

General procedure I for the cobalt-catalyzed C−H bond cyanation by (hetero)arenes

A suspension of **28** or **7** (0.50 mmol), NCTS (**125**) (204 mg, 0.75 mmol), [Cp*CoI_2(CO)] (**1**12, 6.0 mg, 2.5 mol %), $AgSbF_6$ (8.6 mg, 5.0 mol %) and KOAc (2.5 mg, 5.0 mol %) in DCE (2.0 mL) was stirred at 120 °C for 16 h under an atmosphere of argon. At ambient temperature, the solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc/ CH_2Cl_2/Et_3N) to yield products **126** or **127**.

General procedure J for the cobalt-catalyzed C−H bond carbonylation by isocyanates

A suspension of **128** (0.50 mmol), aryl isocyanate **129** (1.00 mmol), [Cp*CoI_2(CO)] (**112**,

12.0 mg, 5.0 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and AgOPiv (10.4 mg, 10.0 mol %) in DCE (2.0 mL) was stirred at 70 °C for 16 h under an atmosphere of argon. At ambient temperature, the solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N) to yield products **130**.

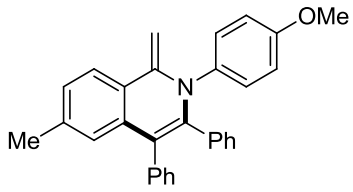
General procedure K for the cobalt-catalyzed C−H bond carbonylation by acyl azides

A suspension of **128** (0.50 mmol), acyl azide **131** (1.0 mmol), Cp*CoI_2(CO) (**112**, 12.0 mg, 5.0 mol %), $AgNTf_2$ (19.9 mg, 10.0 mol %) and AgOPiv (10.4 mg, 10.0 mol %) in DCE (2.0 mL) was stirred at 80 °C for 16 h under an atmosphere of argon. At ambient temperature, the solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/ CH_2Cl_2/EtOAc/Et_3N) to yield products **130**.

10.4 Analytical Data

10.4.1 Analytical Data for the Product of Ruthenium(II)-Catalyzed Oxidative Alkyne Annulation with Ketimines

2-(4-Methoxyphenyl)-6-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (115aa)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178.0 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2:1:0.05) yielded **115aa** (147 mg, 71%) as a yellow solid. M. p.: 190–192 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.66 (d, J = 8.2 Hz, 1H), 7.14 (m, 2H),7.01–7.04 (m, 6H), 6.84–6.94 (m, 5H), 6.76 (d, J = 8.8 Hz, 2H), 6.41 (s, 1H), 4.46 (s, 1H), 3.63 (s, 3H), 3.07 (s, 1H), 2.13 (s, 3H).

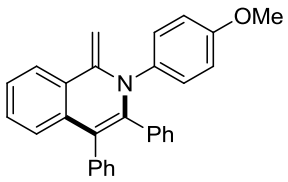
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.5 (C_q), 147.2 (C_q), 142.0 (C_q), 138.0 (C_q), 137.4 (C_q), 135.9 (C_q), 134.8 (C_q), 133.6 (C_q), 131.8 (CH), 131.6 (CH), 130.7 (CH), 127.7 (CH), 127.1 (CH), 126.7 (CH), 126.5 (CH), 125.9 (CH), 124.7 (C_q), 124.0 (CH), 123.8 (CH), 114.3 (CH), 112.1 (C_q), 79.2 (CH_2), 55.0 (CH_3), 20.9 (CH_3).

IR (ATR): 3024, 1654, 1507, 1245, 1028, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 415 (55) [M^+], 414 (100), 400 (45), 383 (15), 370 (10), 294 (10).

HR-MS (ESI) *m/z* calcd for $C_{30}H_{25}NO$ [M+H^+] 416.2009, found 416.2014.

2-(4-Methoxyphenyl)-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (115ba)



The general procedure **A** was followed using **73b** (112.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2:1:0.02) yielded **115ba** (122 mg, 61%) as an off white solid. M. p.: 189–190 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.76 (m, 1H), 7.20–6.85 (m, 14H), 6.77 (d, J = 8.7 Hz, 2H), 6.61 (m, 1H), 4.52 (s, 1H), 3.63 (s, 3H), 3.13 (s, 1H).

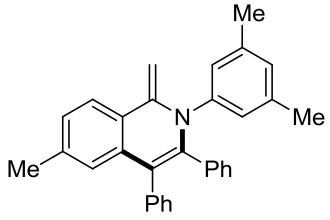
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.3 (C_q), 147.0 (C_q), 141.8 (C_q), 137.2 (C_q), 135.5 (C_q), 134.6 (C_q), 133.4 (C_q), 131.6 (CH), 131.4 (CH), 130.5 (CH), 128.7 (CH), 127.6 (CH), 127.0 (C_q), 126.6 (CH), 126.4 (CH), 125.9 (CH), 125.8 (CH), 123.8 (CH), 123.6 (CH), 114.3 (CH), 112.1 (C_q), 80.1 (CH_2), 54.9 (CH_3).

IR (ATR): 2993, 1621, 1507, 1244, 758, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity) 401 (50) [M^+], 400 (100), 388 (10), 356 (5), 209 (10).

HR-MS (EI) *m/z* calcd for $C_{29}H_{22}NO$ [M-H^+] 400.1701, found 400.1699.

2-(3,5-Dimethylphenyl)-6-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (115da)



The general procedure **A** was followed using **73d** (118.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 5:1:0.01→5:1:0.02) yielded **115da** (125 mg, 62%) as an off white solid. M. p.: 194–196 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.65 (d, J = 8.3 Hz, 1H), 7.17–7.00 (m, 6H), 6.94–6.83 (m, 5H), 6.72 (br s, 3H), 6.41 (s, 1H), 4,45 (s, 1H), 3.12 (s, 1H), 2.14 (s, 3H), 2.10 (s, 6H).

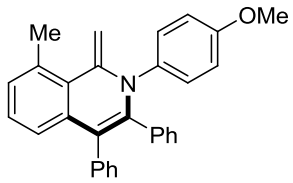
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 146.6 (C_q), 141.8 (C_q), 141.6 (C_q), 138.0 (C_q), 137.8 (C_q), 137.4 (C_q), 135.7 (C_q), 133.5 (C_q), 131.7 (CH), 130.6 (CH), 128.1 (CH), 127.9 (CH), 127.6 (CH), 127.0 (CH), 126.4 (CH), 126.3 (CH), 125.8 (CH), 124.7 (C_q), 123.9 (CH), 123.6 (CH), 112.1 (C_q), 79.6 (CH_2), 20.7 (CH_3), 20.3 (CH_3).

IR (ATR): 3011, 1738, 1600, 1481, 1302, 698 cm^{-1}.

MS (EI) *m/z* (relative intensity) 413 (5) [M^+], 400 (10), 291 (5).131 (5), 69 (30), 44 (100).

HR-MS (ESI) *m/z* calcd for $C_{31}H_{26}N$ [M-H^+] 412.2060, found 412.2069.

2-(4-Methoxyphenyl)-8-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (115ea)



The general procedure **A** was followed using **73e** (119.5 mg, 0.50mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3:1:0.02) yielded **115ea** (94 mg, 45%) as a yellow solid. M. p.: 186–188 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.08–7.18 (m, 5H), 7.02 (d, J = 8.7 Hz, 2H), 7.00–6.97 (m, 2H), 6.91–6.89 (m, 5H), 6.75 (d, J = 8.7 Hz, 2H), 6.42 (dd, J = 7.6, 1.5 Hz, 1H), 4,31 (s, 1H), 3.92 (s, 1H), 3.65 (s, 3H), 2.52 (s, 3H).

^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.1 (C_q), 146.3 (C_q), 142.1 (C_q), 137.9 (C_q), 135.8 (C_q), 135.7 (C_q), 135.1 (C_q), 133.8 (C_q), 131.7 (CH), 131.1 (CH), 130.3 (CH), 129.2 (CH), 127.6 (CH), 127.3 (CH), 126.8 (C_q), 126.6 (CH), 126.3 (CH), 125.7 (CH), 120.7 (CH), 114.1 (CH),

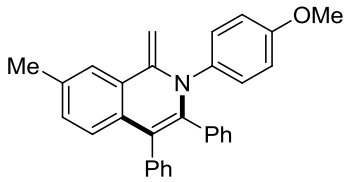
113.7 (C_q), 96.1 (CH_2), 54.9 (CH_3), 22.5 (CH_3).

IR (ATR): 2959, 1616, 1507, 1239, 1034, 760 cm^{-1}.

MS (EI) *m/z* (relative intensity) 415 (75) [M^+], 400 (100), 369 (10), 294 (5), 279 (5), 121 (10).

HR-MS (EI) *m/z* calcd for $C_{30}H_{25}NO$ [M^+] 415.1936, found 415.1927.

2-(4-Methoxyphenyl)-7-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (115fa)



The general procedure **A** was followed using **73f** (119.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1:1:0.01→1:1:0.03) yielded **115fa** (148 mg, 71%) as an off white solid. M. p.: 148–150 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.60 (s, 1H), 7.12 (d, J = 7.3 Hz, 2H), 7.07–6.84 (m, 11H), 6.77 (d, J = 8.6 Hz, 2H), 6.53 (d, J = 8.0 Hz, 1H), 4,50 (s, 1H), 3.64 (s, 3H), 3.11 (s, 1H), 2.31 (s, 3H).

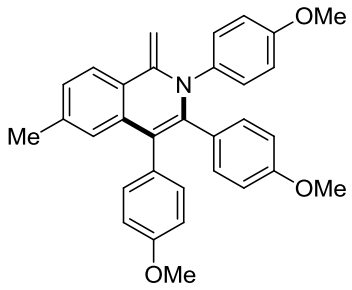
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.5 (C_q), 147.1 (C_q), 141.0 (C_q), 137.5 (C_q), 135.9 (C_q), 135.3 (C_q), 134.9 (C_q), 131.7 (CH), 131.6 (CH), 131.1 (C_q), 130.7 (CH), 129.7 (C_q), 127.7 (CH), 127.0 (C_q), 126.7 (CH), 126.4 (CH), 125.9 (CH), 124.0 (CH), 123.8 (CH), 114.4 (CH), 112.1 (C_q), 79.7 (CH_2), 55.0 (CH_3), 20.8 (CH_3).

IR (ATR): 2997, 1621, 1507, 1244, 1030, 698 cm^{-1}.

MS (EI) *m/z* (relative intensity) 415 (100) [M^+], 414 (85), 400 (45), 383 (10), 369 (10), 306 (5).

HR-MS (ESI) *m/z*calcd for $C_{30}H_{26}NO$ [$M+H^+$] 416.2009, found 416.2014.

2,3,4-Tris(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (115ab)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and 1,2-bis(4-methoxyphenyl)acetylene (**1b**) (238 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2:1:0→2:1:0.05) yielded **115ab** (142 mg, 60%) as a yellow solid. M. p.: 125–126 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.63 (d, J = 8.5 Hz, 1H), 7.01 (d, J = 8.9 Hz, 3H), 6.93 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 6.78 (d, J = 8.9 Hz, 2H), 6.72 (d, J = 8.9 Hz, 2H), 6.44 (d, J = 8.9 Hz, 2H), 6.42 (s, 1H), 4,42 (s, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 3.52 (s, 3H), 3.01 (s, 1H), 2.14 (s, 3H).

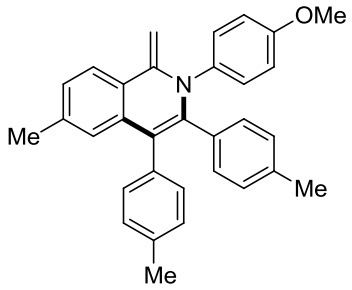
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.4 (C_q), 157.1 (C_q), 157.0 (C_q), 147.3 (C_q), 141.9 (C_q), 137.9 (C_q), 135.1 (C_q), 134.1 (C_q), 132.7 (CH), 131.8 (CH), 131.5 (CH), 129.7 (C_q), 128.5 (C_q), 126.9 (CH), 124.7 (C_q), 124.0 (CH), 123.7 (CH), 114.4 (CH), 113.2 (CH), 112.2 (CH), 111.8 (C_q), 79.0 (CH_2), 55.0 (CH_3), 54.7 (CH_3), 54.5 (CH_3), 20.9 (CH_3).

IR (ATR): 2955, 1737, 1605, 1506, 1235, 807 cm^{-1}.

MS (EI) *m/z* (relative intensity) 475 (65) [M^+], 474 (100), 460 (20), 443 (5), 366 (5), 240 (5).

HR-MS (ESI) *m/z* calcd for $C_{32}H_{30}NO_3$ [M+H$^+$] 476.2220, found 476.2226.

2-(4-Methoxyphenyl)-6-methyl-1-methylene-3,4-di-*p*-tolyl-1,2-dihydroisoquinoline (115ac)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and 1,2-bis(4-methylphenyl)ethylne (**1c**) (206 mg, 1.00 mmol). Purification by column

chromatography (*n*-hexane/EtOAc/Et_3N: 1:1:0→1:1:0.03) yielded **115ac** (134 mg, 61%) as a yellow solid. M. p.: 163–165 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.63 (d, J = 8.3 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.96 (m, 1H), 6.95 (d, J = 8.1 Hz, 2H), 6.90 (d, J = 8.1 Hz, 2H), 6.81 (d, J = 7.8 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 6.68 (d, J = 8.1 Hz, 2H), 6.41 (s, 1H), 4,43 (s, 1H), 3.63 (s, 3H), 3.03 (s, 1H), 2.18 (s, 3H), 2.12 (s, H), 1.99 (s, 3H).

^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.4 (C_q), 147.3 (C_q), 141.9 (C_q), 137.9 (C_q), 135.2 (C_q), 135.0 (C_q), 134.6 (C_q), 134.5 (C_q), 133.9 (C_q), 133.2 (C_q), 131.6 (CH), 131.5 (CH), 130.5 (CH), 128.4 (CH), 127.4 (CH), 126.9 (CH), 124.7 (C_q), 124.0 (CH), 123.7 (CH), 114.3 (CH), 112.0 (C_q), 79.1 (CH_2), 54.9 (CH_3), 20.9 (CH_3), 20.6 (CH_3), 20.5 (CH_3).

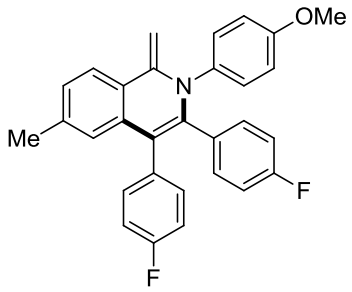
IR (ATR): 2956, 1606, 1506, 1239, 1033, 804 cm^{-1}.

MS (EI) *m/z* (relative intensity) 443 (40) [M^+], 430 (100), 411 (5), 386 (5), 342 (15), 237 (60).

HR-MS (EI) *m/z* calcd for $C_{32}H_{28}NO$ [M-H^+] 442.2171, found 442.2179.

HR-MS (EI) *m/z* calcd for $C_{30}H_{22}N^{35}Cl_2O$ [M-H^+] 482.1078, found 482.1069.

3,4-Bis(4-fluorophenyl)-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (115ad)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and 1,2-bis(4-fluorophenyl)ethyne (**1d**) (214 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2:1:0→2:1:0.05) yielded **115ad** (122 mg, 54%) as an off white solid. M. p.: 196–198 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.67 (d, J = 8.1 Hz, 1H), 7.06–6.97 (m, 9H), 6.79 (d, J = 8.9 Hz, 2H), 6.73 (t, J = 8.9 Hz, 2H), 6.40 (s, 1H), 4,48 (s, 1H), 3.65 (s, 3H), 3.08 (s, 1H), 2.15 (s, 3H).

^{13}C-NMR (75 MHz, DMSO-d_6): δ = 160.9 (C_q, $J_{C\text{-}F}$ = 243.0 Hz), 159.8 (C_q, $J_{C\text{-}F}$ = 243.0 Hz),

157.6 (C_q), 147.0 (C_q), 141.3 (C_q), 138.2 (C_q), 134.7 (C_q), 133.6 (CH, J_{C-F} = 8.2 Hz), 133.5 (C_q), 132.8 (CH, J_{C-F} = 8.2 Hz), 132.3 (C_q), 132.3 (C_q), 131.5 (CH), 127.3 (CH), 124.7 (C_q), 123.9 (CH), 123.8 (CH), 114.7 (CH, J_{C-F} = 21.1 Hz), 114.5 (CH), 113.7 (CH, J_{C-F} = 21.7 Hz), 111.3 (C_q), 79.4 (CH_2), 55.0 (CH_3), 20.8 (CH_3).

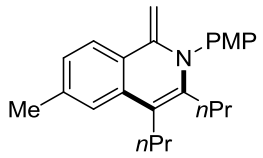
^{19}F-NMR (282 MHz, DMSO-d_6): δ = -109.9, -111.4.

IR (ATR): 2971, 1601, 1505, 1213, 828 cm^{-1}.

MS (EI) *m/z* (relative intensity) 451 (75) [M^+], 450 (100), 436 (45), 419 (15), 406 (5), 330 (5).

HR-MS (EI) *m/z* calcd for $C_{30}H_{22}NOF_2$ [M-H^+] 450.1669, found 450.1672.

2-(4-Methoxyphenyl)-6-methyl-1-methylene-3,4-di-*n*-propyl-1,2-dihydroisoquinoline (115ae)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and oct-4-yne (**1e**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3:1:0.01→3:1:0.05) yielded **115ae** (77 mg, 44%) as a yellow oil.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.50 (d, J = 8.1 Hz, 1H), 7.15 (d, J = 8.9 Hz, 2H), 7.08 (d, J = 8.9 Hz, 2H), 7.04 (s, 1H), 6.93 (d, J = 8.1 Hz, 1H), 4.24 (s, 1H), 3.81 (s, 3H), 2.81 (s, 1H), 2.43–2.38 (m, 2H), 2.31 (s, 3H), 2.06–2.00 (m, 2H), 1.52–1.44 (m, 2H), 1.33–1.25 (m, 2H), 1.00 (t, J = 7.8 Hz, 3H), 0.62 (t, J = 8.0 Hz, 3H).

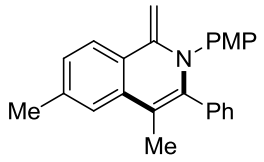
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 158.3 (C_q), 147.4 (C_q), 140.4 (C_q), 138.0 (C_q), 134.7 (C_q), 132.7 (C_q), 131.0 (CH), 126.1 (CH), 124.8 (C_q), 132.7 (CH), 121.9 (CH), 115.1 (CH), 106.1 (C_q), 78.1 (CH_2), 55.2 (CH_3), 31.6 (CH_2), 28.9 (CH_2), 22.8 (CH_2), 21.9 (CH_2), 21.1 (CH_3), 14.1 (CH_2), 14.0 (CH_3).

IR (ATR): 2957, 1650, 1506, 1241, 1031, 827 cm^{-1}.

MS (EI) *m/z* (relative intensity) 347 (55) [M^+], 334 (65), 320 (100), 304 (50), 291 (45), 176 (45).

HR-MS (EI) *m/z* calcd for $C_{24}H_{28}NO$ [M-H^+] 346.2171, found 346.2167.

2-(4-Methoxyphenyl)-4,6-dimethyl-1-methylene-3-phenyl-1,2-dihydroisoquinoline (115af)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and prop-1-yn-1-ylbenzene (**1f**) (116 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1:2:0→1:2:0.03) yielded **115af** (125 mg, 69%) as an off white solid. M. p.: 121–123 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.62 (d, J = 8.9 Hz, 1H), 7.17–7.05 (m, 7H), 6.97 (d, J = 8.9 Hz, 2H), 6.95 (d, J = 8.9 Hz, 2H), 4,35 (s, 1H), 3.64 (s, 3H), 2.96 (s, 1H), 2.34 (s, 3H)), 1.66 (s, 3H).

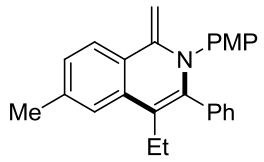
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.4 (C_q), 147.1 (C_q), 141.0 (C_q), 138.3 (C_q), 136.6 (C_q), 135.2 (C_q), 133.3 (C_q), 131.7 (CH), 130.1 (CH), 127.5 (CH), 127.0 (CH), 126.9 (CH), 125.2 (C_q), 123.5 (CH), 122.6 (CH), 114.2 (CH), 102.5 (C_q), 78.1 (CH_2), 55.0 (CH_3), 21.0 (CH_3), 14.4 (CH_3).

IR (ATR): 2920, 1609, 1506, 1298, 1242, 698 cm^{-1}.

MS (EI) *m/z* (relative intensity) 353 (45) [M^+], 352 (100), 340 (40), 321 (10), 244 (15), 217 (15).

HR-MS (ESI) *m/z* calcd for $C_{25}H_{22}NO$ [M-H^+] 352.1701, found 352.1761.

4-Ethyl-2-(4-methoxyphenyl)-6-methyl-1-methylene-3-phenyl-1,2-dihydroisoquinoline (115ag)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and but-1-yn-1-ylbenzene (**1g**) (130 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1:1:0→1:1:0.03) yielded **115ag** (116 mg, 63%) as an off white solid. M. p.: 199–201 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.62 (d, J = 8.5 Hz, 1H), 7.18–7.08 (m, 6H), 7.02 (d, J = 8.5 Hz, 1H), 6.96 (d, J = 9.0 Hz, 2H), 6.74 (d, J = 9.0 Hz, 2H), 4,33 (s, 1H), 3.63 (s, 3H), 2.92 (s, 1H), 2.34 (s, 3H), 2.08 (q, J = 7.1 Hz, 2H), 0.92 (t, J = 7.1 Hz, 3H).

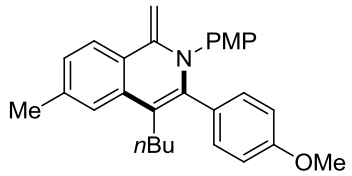
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.4 (C_q), 147.2 (C_q), 141.0 (C_q), 138.2 (C_q), 136.3 (C_q), 135.1 (C_q), 132.0 (C_q), 131.7 (CH), 129.9 (CH), 127.5 (CH), 127.1 (CH), 126.8 (CH), 125.5 (C_q), 123.9 (CH), 122.4 (CH), 114.2 (CH), 108.8 (C_q), 78.0 (CH_2), 54.9 (CH_3), 21.0 (CH_3), 20.6 (CH_2), 14.3 (CH_3).

IR (ATR): 2970, 1737, 1584, 1508, 1229, 1027, 736 cm^{-1}.

MS (EI) *m/z* (relative intensity) 367 (50) [M$^+$], 366 (100), 352 (25), 336 (5), 320 (5), 244 (5).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{26}NO$ [M+H$^+$] 368.2014, found 368.2010.

4-*n*-Butyl-2,3-bis(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (115ah)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and 1-(hex-1-yn-1-yl)-4-methoxybenzene (**1h**) (188 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et$_3$N: 3:1:0.01→3:1:0.05) yielded **115ah** (125 mg, 59%) as an off white solid. M. p.: 133–133 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.60 (d, J = 8.3 Hz, 1H), 7.10 (s, 1H), 6.99 (m, 1H), 6.99 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 6.71 (d, J = 8.8 Hz, 2H), 4,31 (s, 1H), 3.65 (s, 6H), 2.90 (s, 1H), 2.33 (s, 3H), 2.05 (t, J = 7.3 Hz, 2H), 1.34 (m, 2H), 1.16 (m, 2H), 0.71 (t, J = 7.3 Hz, 3H).

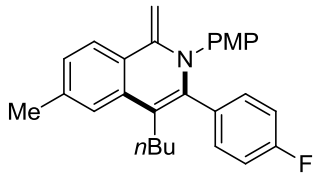
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.6 (C_q), 157.1 (C_q), 147.1 (C_q), 140.9 (C_q), 138.0 (C_q), 135.3 (C_q), 132.3 (C_q), 131.5 (CH), 131.1 (CH), 128.5 (C_q), 126.6 (CH), 125.3 (C_q), 123.7 (CH), 122.3 (CH), 114.2 (CH), 112.7 (CH), 108.0 (C_q), 77.9 (CH_2), 54.9 (CH_3), 54.7 (CH_3), 31.6 (CH_2), 27.2 (CH_2), 22.1 (CH_2), 21.1 (CH_3), 13.4 (CH_3).

IR (ATR): 2928, 1737, 1507, 1240, 1033, 829 cm^{-1}.

MS (EI) *m/z* (relative intensity) 425 (65) [M^+], 424 (100), 412 (25), 384 (75), 274 (5), 240 (10).

HR-MS (EI) *m/z* calcd for $C_{29}H_{31}NO_2$ [M^+] 425.2355, found 425.2344.

4-*n*-Butyl-3-(4-fluorophenyl)-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoqui-noline (115ai)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and 1-fluoro-4-(hex-1-yn-1-yl)benzene (**1i**) (176 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3:1:0→3:1:0.05) yielded **115ai** (148 mg, 72%) as an off white solid. M. p.: 96–98 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.62 (d, J = 8.4 Hz, 1H), 7.16–7.11 (m, 3H), 7.02–6.96 (m, 5H), 6.77 (d, J = 8.8 Hz, 2H), 4,34 (s, 1H), 3.65 (s, 3H), 2.93 (s, 1H), 2.34 (s, 3H), 2.04 (t, J = 7.2 Hz, 2H), 1.34 (m, 2H), 1.15 (m, 2H), 0.70 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, DMSO-d_6): δ = 160.6 (C_q $J_{C\text{-}F}$ = 245 Hz), 157.3 (C_q), 147.0 (C_q), 140.0 (C_q), 138.1 (C_q), 135.0 (C_q), 132.6 (C_q, $J_{C\text{-}F}$ = 3.5 Hz), 132.4 (C_q), 132.3 (CH, $J_{C\text{-}F}$ = 8.0 Hz), 131.5 (CH), 126.8 (CH), 125.3 (C_q), 123.7 (CH), 122.4 (CH), 114.3 (CH, $J_{C\text{-}F}$ = 21.5 Hz), 114.2 (CH), 108.0 (C_q), 78.1 (CH_2), 55.0 (CH_3), 31.5 (CH_2), 27.1 (CH_2), 22.0 (CH_2), 20.9 (CH_3), 13.4 (CH_3).

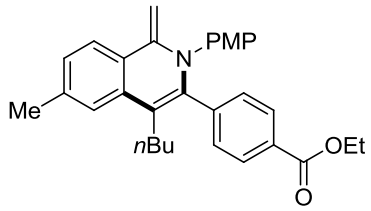
^{19}F-NMR (282 MHz, DMSO-d_6): δ = -114.4.

IR (ATR): 2954, 1599, 1507, 1243, 1033, 825 cm^{-1}.

MS (EI) *m/z* (relative intensity) 413 (50) [M^+], 412 (100), 398 (20), 372 (40), 354 (10), 262 (10).

HR-MS (ESI) *m/z* calcd for $C_{28}H_{29}NOF$ [M+H^+] 414.2233, found 414.2228.

Ethyl 4-[4-*n*-Butyl-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinolin-3-yl]benzoate (115aj)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and ethyl 4-(hex-1-ynyl)benzoate (**1j**) (230 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3:1:0→3:1:0.05) yielded **115aj** (116 mg, 50%) as an off white solid. M. p.: 151–153 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.75 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 2H), 7.13 (s, 1H), 7.05 (d, J = 8.5 Hz, 1H), 6.99 (d, J = 9.0 Hz, 2H), 6.75 (d, J = 9.0 Hz, 2H), 4,36 (s, 1H), 4.26 (q, J = 7.2 Hz, 2H), 3.63 (s, 3H), 2.98 (s, 1H), 2.35 (s, 3H), 2.02 (m, 2H), 1.34 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H), 1.12 (m, 2H), 0.68 (t, J = 7.2 Hz, 3H).

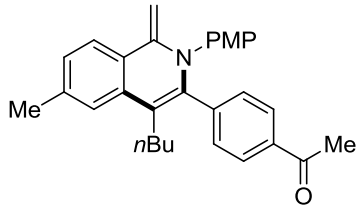
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 165.1 (C_q), 157.5 (C_q), 147.0 (C_q), 141.1 (C_q), 140.0 (C_q), 138.1 (C_q), 134.8 (C_q), 132.0 (C_q), 131.6 (CH), 130.5 (CH), 128.3 (C_q), 128.1 (CH), 127.0 (CH), 125.5 (C_q), 123.8 (CH), 122.4 (CH), 114.3 (CH), 107.9 (C_q), 78.3 (CH_2), 60.5 (CH_2), 54.9 (CH_3), 31.4 (CH_2), 26.9 (CH_2), 21.8 (CH_2), 20.9 (CH_3), 13.8 (CH_3), 13.2 (CH_3).

IR (ATR): 2928, 1718, 1507, 1272, 1098, 747 cm^{-1}.

MS (EI) *m/z* (relative intensity) 467 (60) [M^+], 466 (100), 452 (20), 438 (20), 424 (10), 394 (10).

HR-MS (ESI) *m/z* calcd for $C_{31}H_{34}NO_3$ [M+H^+] 468.2539, found 468.2533.

1-{4-[4-*n*-Butyl-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinolin-3-yl]phenyl}ethan-1-one (115ak)



The general procedure **A** was followed using **73a** (119.5 mg, 0.50 mmol) and 1-(4-(hex-1-ynyl)phenyl)ethanone (**1k**) (200 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3:1:0.01→3:1:0.03) yielded **115ak** (125 mg,

57%) as an off white solid. M. p.: 129–131 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.75 (d, J = 8.3 Hz, 2H), 7.56 (s, 1H), 7.27 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.5 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 4,41 (s, 1H), 3.63 (s, 3H), 3.00 (s, 1H), 2.49 (s, 3H), 2.33 (s, 3H), 1.98 (m, 2H), 1.33 (m, 2H), 1.11 (m, 2H), 0.68 (t, J = 7.6 Hz, 3H).

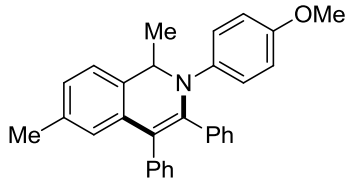
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 197.3 (C_q), 157.5 (C_q), 147.1 (C_q), 141.2 (C_q), 139.2 (C_q), 135.3 (C_q), 135.2 (C_q), 135.0 (C_q), 131.7 (CH), 130.6 (CH), 130.0 (CH), 129.6 (C_q), 127.9 (C_q), 127.3 (CH), 124.1 (CH), 122.5 (CH), 114.4 (CH), 108.0 (C_q), 79.0 (CH_2), 55.0 (CH_3), 31.6 (CH_2), 27.2 (CH_2), 26.5 (CH_3), 22.0 (CH_2), 20.8 (CH_2), 13.4 (CH_3).

IR (ATR): 2929, 1681, 1507, 1243, 1028, 830 cm^{-1}.

MS (EI) *m/z* (relative intensity) 437 (60) [M^+], 436 (85), 424 (100), 408 (10), 396 (20), 354 (90).

HR-MS (EI) *m/z* calcd for $C_{30}H_{30}NO_2$ [M-H$^+$] 436.2277, found 436.2286.

2-(4-Methoxyphenyl)-1,6-dimethyl-3,4-diphenyl-1,2-dihydroisoquinoline (116aa)



The general procedure **B** was followed using **73a** (119.5 mg, 0.50 mmol) and **1a** (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 120:1) yielded **116aa** (83 mg, 40%) as a white solid. M. P.: 168–170 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.32–7.24 (m, 4H), 7.24–7.05 (m, 4H), 6.99–6.91 (m, 5H), 6.90–6.86 (m, 2H), 6.63–6.57 (m, 2H), 5.02 (q, J = 6.8 Hz, 1H), 3.65 (d, J = 0.9 Hz, 3H), 2.26 (s, 3H), 1.67 (d, J = 6.8 Hz, 3H).

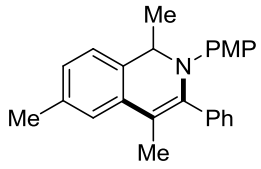
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.6 (C_q), 140.9 (C_q), 138.6 (C_q), 137.8 (C_q), 137.6 (C_q), 136.2 (C_q), 132.1 (C_q), 132.1 (CH), 131.0 (CH), 130.7 (C_q), 127.8 (CH), 127.0 (CH), 126.9 (CH), 126.6 (CH), 126.0 (CH), 124.8 (CH), 123.8 (CH), 123.6 (CH), 121.7 (C_q), 113.6 (CH), 60.2 (CH), 55.3 (CH_3), 22.5 (CH_3), 21.5 (CH_3).

IR (ATR): 2980, 1755, 1510, 1243, 1027, 750 cm^{-1}.

MS (EI) *m/z* (relative intensity) 417 (10) [M^+], 402 (100), 387 (5), 358 (10), 294 (5).

HR-MS (EI) *m/z* calcd for $C_{30}H_{27}NO$ [M^+] 417.2093, found 417.2085.

2-(4-Methoxyphenyl)-1,4,6-trimethyl-3-phenyl-1,2-dihydroisoquinoline (116af)



The general procedure **B** was followed using **73a** (119.5 mg, 0.50 mmol) and prop-1-ynylbenzene (**1f**) (116 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100:1) yielded **116af** (87 mg, 49%) as a white solid. M. p.: 150–152 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.16–7.28 (m, 4H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 8.7 Hz, 2H), 4.90 (q, *J* = 7.0 Hz, 1H), 3.63 (s, 3H), 2.40 (s, 3H), 2.23 (s, 3H), 1.50 (d, *J* = 7.0 Hz, 3H).

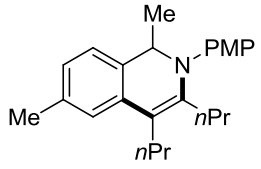
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.3 (C_q), 141.5 (C_q), 137.9 (C_q), 136.2 (C_q), 136.1 (C_q), 133.7 (C_q), 132.1 (C_q), 130.8 (CH), 127.5 (CH), 127.1 (CH), 126.8 (CH), 124.5 (CH), 123.3 (CH), 122.9 (CH), 113.9 (C_q), 113.6 (CH), 60.1 (CH), 55.3 (CH_3), 22.0 (CH_3), 21.5 (CH_3), 15.3 (CH_3).

IR (ATR): 2964, 1738, 1505, 1229, 1033, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity) 355 (15) [M^+], 340 (100), 325 (5), 296 (10), 282 (5).

HR-MS (EI) *m/z* calcd for $C_{25}H_{25}NO$ [M^+] 355.1936, found 355.1939.

2-(4-Methoxyphenyl)-1,6-dimethyl-3,4-di-*n*-propyl-1,2-dihydroisoquinoline (116ae)



The general procedure **B** was followed using **73a** (119.5 mg, 0.50 mmol) and oct-4-yne (**1e**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 50:1) yielded **116ae** (75 mg, 42%) as a green oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.08 (s, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 9.2 Hz, 2H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 9.2 Hz, 2H), 4.60 (q, *J* = 6.8 Hz, 1H), 3.74 (s, 3H),

2.70–2.47 (m, 2H), 2.42–2.34 (m, 1H), 2.34 (s, 3H), 2.16–2.06 (m, 1H), 1.41-1.68 (m, 4H), 1.32 (d, J = 6.8 Hz, 3H), 1.05 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H).

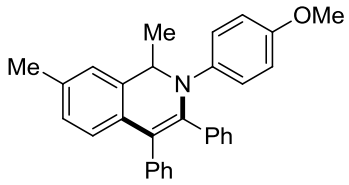
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 155.0 (C_q), 141.5 (C_q), 137.6 (C_q), 135.8 (C_q), 132.0 (C_q), 131.7 (C_q), 126.0 (CH), 124.7 (CH), 124.0 (CH), 121.9 (CH), 118.3 (C_q), 113.9 (CH), 60.3 (CH), 55.4 (CH_3), 31.4 (CH_2), 29.8 (CH_2), 23.4 (CH_2), 22.1 (CH_3), 22.1 (CH_2), 21.6 (CH_3), 14.6 (CH_3), 14.2 (CH_3).

IR (ATR): 2958, 2869, 1505, 1237, 1035, 827cm^{-1}.

MS (EI) *m/z* (relative intensity) 349 (10) [M$^+$], 334 (100), 320 (10), 304 (5), 290 (5), 276 (5).

HR-MS (EI) *m/z* calcd for $C_{24}H_{31}NO$ [M$^+$] 349.2406, found 349.2410.

2-(4-Methoxyphenyl)-1,7-dimethyl-3,4-diphenyl-1,2-dihydroisoquinoline (116fa)



The general procedure **B** was followed using **73f** (119.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100:1) yielded **116fa** (94 mg, 45%) as an off white solid. M. p.: 160–163 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, J = 4.4 Hz, 4H), 7.22–7.09 (m, 4H), 7.00–6.89 (m, 4H), 6.86 (d, J = 8.9 Hz, 3H), 6.86 (s, 1H), 6.58 (d, J = 8.9 Hz, 2H), 4.98 (q, J = 6.7 Hz, 1H), 2.29 (s, 3H), 1.65 (d, J = 6.7 Hz, 3H).

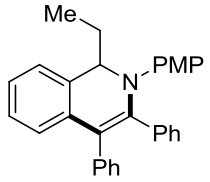
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.5 (C_q), 141.0 (C_q), 138.7 (C_q), 137.6 (C_q), 136.8 (C_q), 135.9 (C_q), 133.6 (C_q), 131.9 (CH), 131.0 (CH), 129.7 (C_q), 127.8 (CH), 127.5 (CH), 127.0 (CH), 126.5 (CH), 126.0 (CH), 125.5 (CH), 123.5 (CH), 123.3 (CH), 122.1 (C_q), 113.7 (CH), 60.4 (CH), 55.3 (CH_3), 22.4 (CH_3), 21.1 (CH_3).

IR (ATR): 2972, 1756, 1509, 1243, 1027, 749 cm^{-1}.

MS (EI) *m/z* (relative intensity) 417 (10) [M$^+$], 402 (100), 387 (5), 358 (10), 294 (5).

HR-MS (EI) *m/z* calcd for $C_{30}H_{27}NO$ [M$^+$] 417.2093, found 417.2088.

1-Ethyl-2-(4-methoxyphenyl)-3,4-diphenyl-1,2-dihydroisoquinoline (116ha)



The general procedure **B** was followed using **73h** (119.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100:1) yielded **116ha** (116 mg, 56%) as an off white solid. M. p.: 100–103 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.32–7.27 (m, 5H), 7.22–7.14 (m, 5H), 6.99-6.89 (m, 6H), 6.60 (dd, J = 9.0, 1.3 Hz, 2H), 4.68 (dd, J = 6.9, 6.9 Hz, 1H), 3.65 (d, J = 1.4 Hz, 3H), 2.18–2.08 (m, 1H), 1.92–1.83 (m, 1H), 1.23 (t, J = 7.6 Hz, 3H).

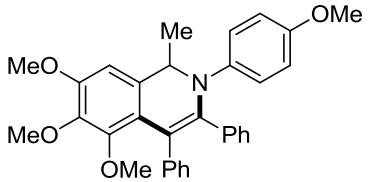
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.7 (C_q), 141.2 (C_q), 138.6 (C_q), 138.5 (C_q), 137.6 (C_q), 132.4 (C_q), 131.9 (CH), 131.8 (C_q), 131.3 (CH), 127.8 (CH), 127.0 (CH), 126.7 (CH), 126.7 (CH), 126.1 (CH), 125.8 (CH), 125.8 (CH), 124.1 (CH), 123.2 (CH), 112.7 (C_q), 113.7 (CH), 67.0 (CH), 55.3 (CH_3), 28.6 (CH_2), 11.2 (CH_3).

IR (ATR): 2953, 1738, 1505, 1229, 1028, 700 cm^{-1}.

MS (EI) *m/z* (relative intensity) 417 (65) [M$^+$], 388 (100), 372 (5), 344 (10), 280 (5), 252 (5).

HR-MS (EI) *m/z* calcd for $C_{30}H_{27}NO$ [M$^+$] 417.2093, found 417.2081.

5,6,7-Trimethoxy-2-(4-methoxyphenyl)-1-methyl-3,4-diphenyl-1,2-dihydroisoquinoline (116ia)



The general procedure **B** was followed using **73i** (157.5 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100:1) yielded **116ia** (118 mg, 48%) as an off white solid. M. p.: 138–140 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.38–7.33 (m, 2H), 7.29–7.24 (m, 2H), 7.17–7.07 (m, 2H),

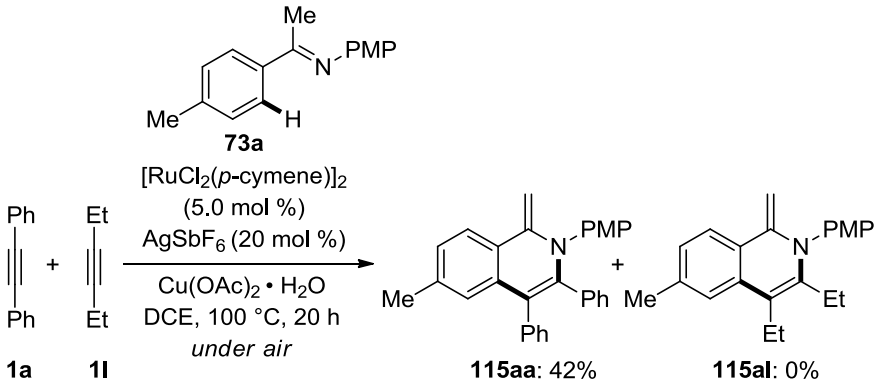
7.07–7.00 (m, 1H), 7.00–6.89 (m, 3H), 6.86 (d, J = 9.0 Hz, 2H), 6.59 (d, J = 8.9 Hz, 2H), 6.39 (s, 1H), 4.91 (q, J = 6.7 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.63 (s, 3H), 2.99 (s, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 154.3 (C_q), 152.3 (C_q), 150.5 (C_q), 141.8 (C_q), 140.7 (C_q), 140.5 (C_q), 137.4 (C_q), 137.3 (C_q), 132.4 (CH), 132.1 (C_q), 131.1 (CH), 126.8 (CH), 126.7 (CH), 126.3 (CH), 125.5 (CH), 122.6 (CH), 121.8 (C_q), 120.5 (C_q), 113.7 (CH), 103.9 (CH), 60.5 (CH), 60.2 (CH_3), 59.7 (CH_3), 55.9 (CH_3), 55.3 (CH_3), 21.9 (CH_3).

IR (ATR): 2987, 1742, 1511, 1226, 708 cm^{-1}.

MS (EI) *m/z* (relative intensity) 493 (5) [M^+], 478 (100), 463 (5), 448 (10), 417 (5).

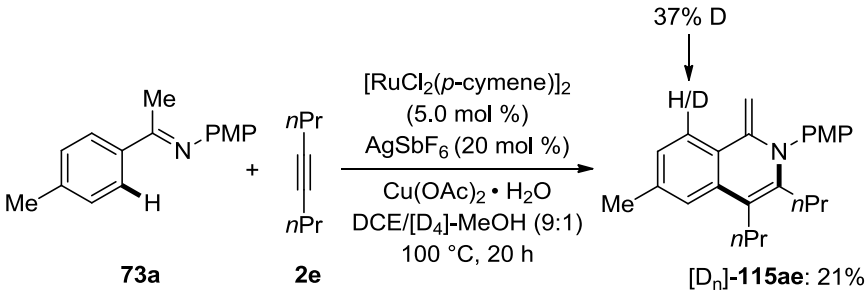
HR-MS (EI) *m/z* calcd for $C_{32}H_{31}NO_4$ [M^+] 493.2253, found 493.2259.

Intermolecular Competition Experiment Between Alkynes Substrates 1a and 1l:



A suspension of (*E*)-4-methoxy-*N*-[1-(*p*-tolyl)ethylidene]aniline (**73a**) (120 mg, 0.50 mmol), 1,2-diphenylethyne (**1a**) (178 mg, 1.00 mmol), hex-3-yne (**1l**) (82.0 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (100 mg, 0.50 mmol) in DCE (2.0 mL) was stirred at 100 ℃ for 20 h under an atmosphere of air. At ambient temperature, H_2O (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc/Et_3N: 20:1:0.05) to yield **115aa** (78 mg, 42%) as the sole product.

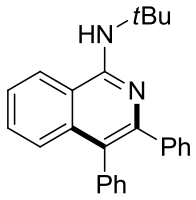
Ruthenium(II)-Catalyzed H/D Exchange with Substrate 73a in [D_4]-MeOH as the cosolvent in the Presence of Alkyne 1e:



A suspension of (*E*)-4-methoxy-*N*-[1-(*p*-tolyl)ethylidene]aniline (**73a**) (120 mg, 0.50 mmol), oct-4-yne (**1e**) (110 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (100 mg, 0.50 mmol) in a solvent mixture of DCE and $[D_4]$-MeOH (1.8/0.2 mL) was stirred at 100 °C for 20 h under an atmosphere of air. At ambient temperature, H_2O (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography (*n*-hexane/EtOAc/Et_3N: 1:2:0.03) to yield $[D_n]$-**115ae** (32.0 mg, 21%) as an off white solid. The D-incorporation in $[D_n]$-**115ae** was estimated by ^{1}H-NMR spectroscopy.

10.4.2 Analytical Data for the Products of the Ruthenium(II)-Catalyzed Oxidative C-H Activation with Internal Alkynes and Acrylates

***N*-(*tert*-Butyl)-3,4-diphenylisoquinolin-1-amine (118aa)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1a** (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100:1) yielded **118aa** (141 mg, 80%) as a yellow solid. M. p.: 139−142 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, J = 7.9 Hz, 1H), 7.55 (d, J = 7.3 Hz, 1H), 7.48−7.41 (m, 4H), 7.35−7.30 (m, 3H), 7.26−7.23 (m, 2H), 7.18−7.16 (m, 3H), 5.23 (s, 1H), 1.66 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.3 (C_q), 148.0 (C_q), 141.9 (C_q), 138.8 (C_q), 137.4 (C_q), 132.1 (CH), 130.4 (CH), 129.1 (CH), 128.2 (CH), 127.1 (CH), 126.5 (CH), 126.4 (CH), 126.3 (CH), 125.2 (CH), 121.0 (CH), 120.2 (C_q), 117.0 (C_q), 51.9 (C_q), 29.4 (CH_3).

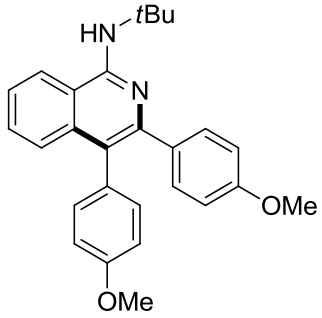
IR (ATR): 3437, 2956, 1515, 1416, 1210, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 352 (30) [M^+], 337 (15), 296 (100), 278 (25), 190 (10), 165 (10).

HR-MS (EI) *m/z* calcd for $C_{25}H_{24}N_2$ [M^+] 352.1939, found 352.1934.

The spectral data were in accordance with those reported in the literature.[146]

***N*-(*tert*-Butyl)-3,4-bis(4-methoxyphenyl)isoquinolin-1-amine (118ab)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1b** (238 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1→50/1) yielded **118ab** (131 mg, 64%) as a white solid. M. p.: 176−179 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 6.9, 1.4 Hz, 1H), 7.41−7.35 (m, 3H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.16 (s, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 1.63 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.2 (C_q), 158.1 (C_q), 153.1 (C_q), 147.6 (C_q), 137.9 (C_q), 134.5 (C_q), 133.0 (CH), 131.6 (CH), 131.2 (C_q), 129.0 (CH), 126.2 (CH), 124.9 (CH), 121.0 (CH), 119.2 (C_q), 116.9 (C_q), 113.8 (CH), 112.6 (CH), 55.2 (CH_3), 55.1 (CH_3), 51.8 (C_q), 29.4 (CH_3).

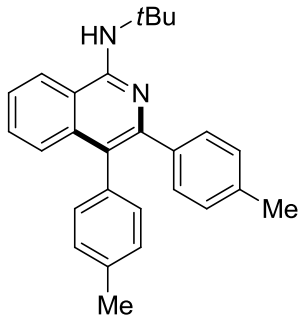
IR (ATR): 3439, 2949, 1512, 1417, 1234, 763 cm^{-1}.

MS (EI) *m/z* (relative intensity) 412 (30) [M^+], 397 (15), 356 (100), 341 (10), 312 (10).

HR-MS (EI) *m/z* calcd for $C_{27}H_{28}N_2O_2$ [M^+] 412.2151, found 412.2141.

***N*-(*tert*-Butyl)-3,4-di-*p*-tolylisoquinolin-1-amine (118ac)**

[146] X. H. Wei, M. Zhao, Z. Y. Du, X. W. Li, *Org. Lett.* **2011**, *13*, 4636−4639.



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1c** (206 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 150/1) yielded **118ac** (171 mg, 90%) as a white solid. M. p.: 173−174 °C.

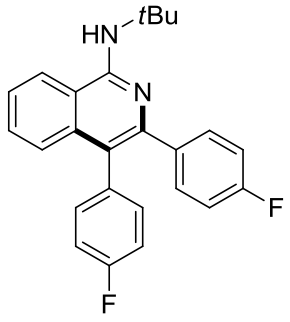
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, J = 8.0 Hz, 1H), 7.53 (dd, J = 8.1, 2.1 Hz, 1H), 7.46−7.39 (m, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 6.98 (d, J = 8.1 Hz, 2H), 5.18 (s, 1H), 2.39 (s, 3H), 2.31 (s, 3H), 1.64 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.0 (C_q), 147.7 (C_q), 139.0 (C_q), 137.6 (C_q), 135.9 (C_q), 135.9 (C_q), 135.8 (C_q), 131.6 (CH), 130.0 (CH), 129.0 (CH), 128.9 (CH), 127.7 (CH), 126.2 (CH), 124.7 (CH), 121.0 (CH), 119.8 (C_q), 116.9 (C_q), 51.8 (C_q), 29.5 (CH_3), 21.4 (CH_3), 21.3 (CH_3).

IR (ATR): 3452, 2989, 1573, 1512, 1210, 762 cm^{-1}.

MS (EI) *m/z* (relative intensity) 380 (35) [M^+], 365 (15), 324 (100), 308 (10), 291 (5). **HR-MS** (EI) *m/z* calcd for $C_{27}H_{28}N_2$ [M^+] 380.2252, found 380.2250.

***N*-(*tert*-Butyl)-3,4-bis(4-fluorophenyl)isoquinolin-1-amine (118ad)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1d** (214 mg, 1.00 mmol) at 140 °C. Purification by column chromatography (*n*-hexane/EtOAc: 120/1) yielded **118ad** (131 mg, 68%) as a yellow solid. M. p.: 195−198 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, J = 7.9 Hz, 1H), 7.49−7.40 (m, 3H), 7.36−7.31 (m,

2H), 7.17−7.12 (m, 2H), 7.06 (t, J = 8.8 Hz, 2H), 6.88 (t, J = 8.8 Hz, 2H), 5.24 (s, 1H), 1.64 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 161.9 (C_q, J_{C-F} = 245.5 Hz), 161.2 (C_q, J_{C-F} = 245.5 Hz), 153.3 (C_q), 147.2 (C_q), 137.7 (C_q, J_{C-F} = 3.5 Hz), 137.3 (C_q), 134.4 (C_q, J_{C-F} = 3.5 Hz), 133.4 (CH, J_{C-F} =7.9 Hz), 131.9 (CH, J_{C-F} = 7.9 Hz), 129.3 (CH), 125.9 (CH), 125.3 (CH), 121.1 (CH), 118.8 (C_q), 117.0 (C_q), 115.3 (CH, J_{C-F} = 21.4 Hz), 114.1 (CH, J_{C-F} = 21.4 Hz), 51.9 (C_q), 29.4 (CH_3).

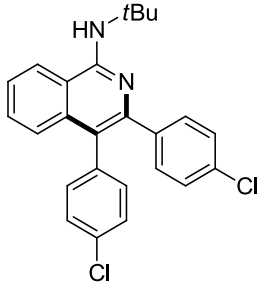
^{19}F-NMR (282 MHz, $CDCl_3$): δ = −(115.75−115.83) (m), −(115.85−116.00) (m).

IR (ATR): 3472, 2963, 1506, 1417, 1214, 825 cm^{-1}.

MS (EI) *m/z* (relative intensity) 388 (30) [M$^+$], 373 (15), 332 (100), 331 (95), 314 (20), 294 (5).

HR-MS (EI) *m/z* calcd for $C_{25}H_{22}N_2F_2$ [M$^+$] 388.1751, found 388.1746.

***N-tert*-Butyl-3,4-bis(4-chlorophenyl)isoquinolin-1-amine (118am)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1m** (246 mg, 1.00 mmol) at 140 °C. Purification by column chromatography (*n*-hexane/EtOAc: 120/1) yielded **118am** (76 mg, 36%) as an off white solid. M. p.: 198−200 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.74 (m, 1H, ArH), 7.41−7.47 (m, 3H), 7.27−7.33 (m, 4H), 7.12−7.17 (m, 4H), 5.24 (s, 1H), 1.61 (s, 9H).

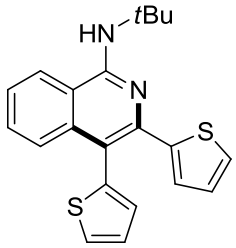
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.5 (C_q), 147.0 (C_q), 140.1 (C_q), 137.1 (C_q), 137.0 (C_q), 133.3 (CH), 132.7 (C_q), 132.6 (C_q), 131.6 (CH), 129.5 (CH), 128.6 (CH), 127.5 (CH), 125.9 (CH), 125.6 (CH), 121.2 (CH), 118.9 (C_q), 117.1 (C_q), 51.9 (C_q), 29.3 (CH_3).

IR (ATR): 3450, 2952, 1517, 1418, 1088, 763 cm^{-1}.

MS (EI) m/z (relative intensity) 420 (25) [M$^+$], 405 (15), 364 (100), 328 (30), 311 (15), 292 (10).

HR-MS (EI) *m/z* calcd for $C_{25}H_{22}N_2Cl_2$ [M^+] 420.1160, found 420.1149.

***N*-(*tert*-Butyl)-3,4-di(thiophen-2-yl)isoquinolin-1-amine (118an)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1n** (190 mg, 1.00 mmol) at 140 °C. Purification by column chromatography (*n*-hexane/EtOAc: 120/1) yielded **118an** (142 mg, 75%) as an off white solid. M. p.: 165−168 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.2 Hz, 1H), 7.55 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.48−7.44 (m, 2H), 7.41−7.36 (m, 1H), 7.27−7.25 (m, 2H), 7.03 (dd, *J* = 3.8, 1.2 Hz, 1H), 6.89−6.86 (m, 1H), 6.46 (dd, *J* = 3.8, 1.2 Hz, 1H), 5.30 (s, 1H), 1.70 (s, 9H).

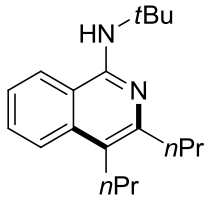
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.2 (C_q), 146.9 (C_q), 143.0 (C_q), 139.5 (C_q), 139.0 (C_q), 129.7 (CH), 128.9 (CH), 127.8 (CH), 127.8 (CH), 127.1 (CH), 126.9 (CH), 126.4 (CH), 126.1 (CH), 125.2 (CH), 120.9 (CH), 117.1 (C_q), 109.4 (C_q), 52.0 (C_q), 29.0 (CH_3).

IR (ATR): 3444, 2962, 1513, 1426, 1223, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity) 364 (60) [M^+], 349 (20), 308 (100), 290 (10), 275 (40), 263 (10).

HR-MS (EI) *m/z* calcd for $C_{21}H_{20}N_2S_2$ [M^+] 364.1068, found 364.1064.

***N*-(*tert*-Butyl)-3,4-dipropylisoquinolin-1-amine (118ae)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1e** (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 150/1) yielded **118ae** (112 mg, 78%) as a green oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.58−7.52

(m, 1H), 7.38−7.32 (m, 1H), 4.95 (s, 1H), 2.87−2.75 (m, 4H), 1.89−1.79 (m, 2H), 1.66−1.57 (m, 2H), 1.60 (s, 9H), 1.07 (t, J = 7.3 Hz, 3H), 1.01 (t, J = 7.3 Hz, 3H).

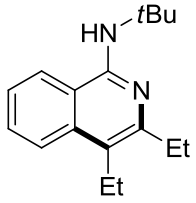
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 152.3 (C_q), 150.4 (C_q), 136.7 (C_q), 128.7 (CH), 123.8 (CH), 123.7 (CH), 121.6 (CH), 117.1 (C_q), 116.5 (C_q), 51.5 (C_q), 37.1 (CH_2), 29.5 (CH_2), 29.4 (CH_3), 24.1 (CH_2), 22.7 (CH_2), 14.6 (CH_3), 14.4 (CH_3).

IR (ATR): 3482, 2957, 1518, 1416, 1209, 758 cm^{-1}.

MS (EI) *m/z* (relative intensity) 284 (20) [M^+], 269 (15), 255 (10), 228 (25), 213 (10), 199 (100).

HR-MS (EI) *m/z* calcd for $C_{19}H_{28}N_2$ [M^+] 284.2252, found 284.2239.

***N*-(*tert*-Butyl)-3,4-diethylisoquinolin-1-amine (118al)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1l** (82 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118al** (107 mg, 84%) as a green oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, J = 8.5 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H,), 7.53 (ddd, J = 8.5, 6.8, 1.1 Hz, 1H), 7.33 (ddd, J = 8.5, 6.8, 1.1 Hz, 1H), 4.94 (s, 1H), 2.89 (q, J = 7.6 Hz, 2H), 2.81 (q, J = 7.6 Hz, 2H), 1.58 (s, 9H), 1.33 (t, J = 7.6 Hz, 3H), 1.21 (t, J = 7.6 Hz, 3H).

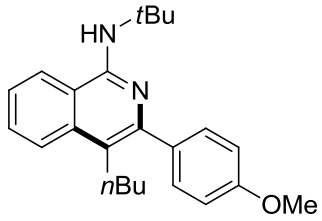
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.4 (C_q), 151.2 (C_q), 136.4 (C_q), 128.8 (CH), 123.8 (CH), 123.4 (CH), 121.6 (CH), 117.3 (C_q), 117.1 (C_q), 51.5 (C_q), 29.3 (CH_3), 28.0 (CH_2), 20.2 (CH_2), 15.2 (CH_3), 14.1 (CH_3).

IR (ATR): 3458, 2961, 1518, 1417, 1210, 758 cm^{-1}.

MS (EI) *m/z* (relative intensity) 256 (20) [M^+], 241 (20), 228 (10), 200 (45), 185 (100), 171 (60).

HR-MS (EI) *m/z* calcd for $C_{17}H_{24}N_2$ [M^+] 256.1939, found 256.1946.

***N*-(*tert*-Butyl)-4-*n*-butyl-3-(4-methoxyphenyl)isoquinolin-1-amine (118ah)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1h** (188 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118ah** (83 mg, 46%) as a white solid. M. p.: 115−117 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.99 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.59 (dd, J = 8.8, 7.2 Hz, 1H), 7.52 (d, J = 8.4, 7.2 Hz, 2H), 7.41 (d, J = 7.8 Hz, 1H), 6.97 (d, J = 8.6 Hz, 2H), 5.01 (s, 1H), 3.87 (s, 3H), 2.93−2.87 (m, 2H), 1.69−1.56 (m, 2H), 1.55 (s, 9H), 1.42−1.35 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H).

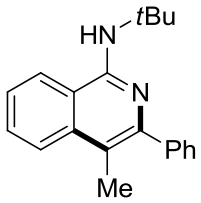
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.5 (C_q), 152.0 (C_q), 149.0 (C_q), 136.9 (C_q), 135.4 (C_q), 130.4 (CH), 128.7 (CH), 124.6 (CH), 124.4 (CH), 121.4 (CH), 117.8 (C_q), 117.3 (C_q), 112.9 (CH), 55.2 (CH_3), 51.4 (C_q), 33.4 (CH_2), 29.4 (CH_3), 27.8 (CH_2), 22.8 (CH_2), 14.0 (CH_3).

IR (ATR): 3448, 2953, 1510, 1419, 1228, 830 cm^{-1}.

MS (EI) *m/z* (relative intensity) 362 (30) [M^+], 347 (10), 319 (10), 306 (35), 263 (100), 248 (20).

HR-MS (EI) *m/z* calcd for $C_{24}H_{30}N_2O$ [M^+] 362.2358, found 362.2347.

***N*-(*tert*-Butyl)-4-methyl-3-phenylisoquinolin-1-amine (118af)**



The general procedure **C** was followed using **117a** (88.0 mg, 0.50 mmol) and **1f** (116 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 150/1) yielded **118af** (105 mg, 72%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70−7.66 (m, 2H), 7.65−7.62 (m, 1H), 7.49−7.43 (m, 3H), 7.40−7.34 (m, 1H), 5.05 (s, 1H),

2.53 (s, 3H), 1.60 (s, 9H).

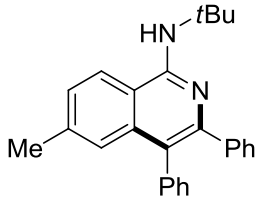
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.2 (C_q), 149.0 (C_q), 142.5 (C_q), 137.7 (C_q), 130.1 (CH), 129.2 (CH), 127.5 (CH), 126.8 (CH), 124.9 (CH), 124.4 (CH), 121.5 (CH), 117.6 (C_q), 112.2 (C_q), 51.7 (C_q), 29.4 (CH_3), 15.2 (CH_3).

IR (ATR): 3452, 2960, 1517, 1421, 1211, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity) 290 (25) [M^+], 275 (15), 273 (95), 234 (100), 216 (20).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{23}N_2$ [M+H^+] 291.1861, found 291.1856.

***N*-(*tert*-Butyl)-6-methyl-3,4-diphenylisoquinolin-1-amine (118ba)**



The general procedure **C** was followed using **117b** (95.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 150/1) yielded **118ba** (131 mg, 72%) as a yellow solid. M. p.: 92−95 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 8.9 Hz, 1H), 7.40−7.25 (m, 7H), 7.22−7.12 (m, 5H), 5.15 (s, 1H), 2.36 (s, 3H), 1.63 (s, 9H).

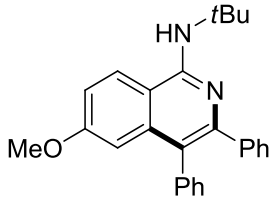
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.3 (C_q), 148.1 (C_q), 142.1 (C_q), 139.2 (C_q), 139.0 (C_q), 137.6 (C_q), 132.1 (CH), 130.3 (CH), 128.1 (CH), 127.1 (CH), 127.0 (CH), 126.4 (CH), 126.3 (CH), 125.3 (CH), 121.0 (CH), 120.0 (C_q), 115.2 (C_q), 51.9 (C_q), 29.4 (CH_3), 21.9 (CH_3).

IR (ATR): 3456, 2957, 1573, 1415, 1206, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 366 (40) [M^+], 351 (20), 310 (100), 309 (95), 292 (20), 277 (20).

HR-MS (EI) *m/z* calcd for $C_{26}H_{26}N_2$ [M^+] 366.2096, found 366.2086.

***N*-(*tert*-Butyl)-6-methoxy-3,4-diphenylisoquinolin-1-amine (118ca)**



The general procedure **C** was followed using **117c** (103 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118ca** (133 mg, 70%) as a white solid. M. p.: 138−139 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.66 (d, J = 9.4 Hz, 1H), 7.40−7.38 (m, 1H), 7.37 (d, J = 1.5 Hz, 1H), 7.34−7.25 (m, 3H), 7.22−7.19 (m, 2H), 7.16−7.12 (m, 3H), 7.03 (dd, J = 9.0, 2.6 Hz, 1H), 6.85 (d, J = 2.6 Hz, 1H), 5.08 (s, 1H), 3.68 (s, 3H), 1.62 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.1 (C_q), 153.3 (C_q), 148.7 (C_q), 142.0 (C_q), 139.4 (C_q), 139.0 (C_q), 132.0 (CH), 130.4 (CH), 128.2 (CH), 127.0 (CH), 126.5 (CH), 126.4 (CH), 123.0 (CH), 120.0 (C_q), 116.3 (CH), 112.1 (C_q), 105.6 (CH), 55.1 (CH_3), 51.8 (C_q), 29.5 (CH_3).

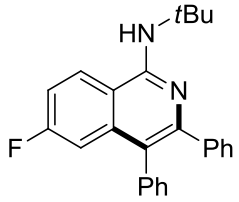
IR (ATR): 3426, 2954, 1610, 1515, 1417, 1213, 703 cm^{-1}.

MS (EI) *m/z* (relative intensity) 382 (25) [M^+], 367 (15), 326 (100), 308 (10), 293 (10), 282 (15).

HR-MS (EI) *m/z* calcd for $C_{26}H_{26}N_2O$ [M^+] 382.2045, found 382.2047.

The spectral data were in accordance with those reported in the literature.[146]

***N*-(*tert*-Butyl)-6-fluoro-3,4-diphenylisoquinolin-1-amine (118da)**



The general procedure **C** was followed using **117d** (97.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 120/1) yielded **118da** (142 mg, 77%) as a yellow solid. M. p.: 175−176 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.77−7.72 (m, 1H), 7.40−7.37 (m, 2H), 7.37−7.28 (m, 3H), 7.20−7.12 (m, 7H), 5.15 (s, 1H), 1.63 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.0 (C_q, J_{C-F} = 249.0 Hz), 153.1 (C_q), 149.2 (C_q), 141.5 (C_q), 139.7 (C_q, J_{C-F} = 9.1 Hz), 138.3 (C_q), 131.9 (CH), 130.3 (CH), 128.4 (CH), 127.1 (CH), 126.8 (CH), 126.7 (CH), 123.9 (CH, J_{C-F} = 8.1 Hz), 120.0 (C_q), 114.6 (CH, J_{C-F} = 24.8 Hz), 114.0 (C_q), 110.2 (CH, J_{C-F} = 22.2 Hz), 52.0 (C_q), 29.4 (CH_3).

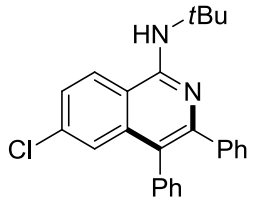
^{19}F-NMR (282 MHz, $CDCl_3$): δ = −(109.9−110.0), (m).

IR (ATR): 3432, 2970, 1575, 1519, 1208, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity) 370 (30) [M^+], 355 (15), 314 (95), 313 (100), 296 (20), 208 (5).

HR-MS (EI) *m/z* calcd for $C_{25}H_{23}FN_2$ [M^+] 370.1845, found 370.1842.

***N*-(*tert*-Butyl)-6-chloro-3,4-diphenylisoquinolin-1-amine (118ea)**



The general procedure **C** was followed using **117e** (105 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 120/1) yielded **118ea** (152 mg, 79%) as a yellow solid. M. p.: 175−176 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 2.1 Hz, 1H), 7.39−7.29 (m, 6H), 7.20−7.13 (m, 5H), 5.15 (s, 1H), 1.62 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.1 (C_q), 149.4 (C_q),141.5 (C_q), 138.8 (C_q), 138.1 (C_q), 135.6 (C_q), 131.9 (CH), 130.3 (CH), 128.4 (CH), 127.2 (CH), 126.8 (CH), 126.7 (CH), 125.8 (CH), 125.2 (CH), 122.9 (CH), 119.5 (C_q), 115.2 (C_q), 52.1 (C_q), 29.4 (CH_3).

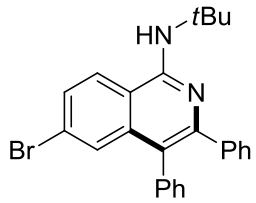
IR (ATR): 3465, 2963, 1571, 1414, 1211, 695 cm^{-1}.

MS (EI) *m/z* (relative intensity) 386 (35) [M^+], 371 (15), 330 (100), 312 (25), 277 (20), 199 (5).

HR-MS (EI) *m/z* calcd for $C_{25}H_{23}ClN_2$ [M^+] 386.1550, found 386.1538.

The spectral data were in accordance with those reported in the literature.[146]

6-Bromo-*N*-(*tert*-butyl)-3,4-diphenylisoquinolin-1-amine (118fa)



The general procedure **C** was followed using **117f** (127 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography

(*n*-hexane/EtOAc: 150/1) yielded **118fa** (154 mg, 72%) as a yellow solid. M. p.: 176−178 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, J = 1.8 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.50 (dd, J = 8.8, 1.8 Hz, 1H), 7.40−7.31 (m, 5H), 7.21−7.15 (m, 5H), 5.17 (s, 1H), 1.64 (s, 9H).

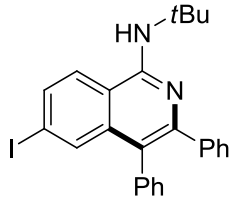
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.2 (C_q), 149.4 (C_q), 141.5 (C_q), 139.0 (C_q), 138.0 (C_q), 131.9 (CH), 130.3 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 127.2 (CH), 126.8 (CH), 126.7 (CH), 124.1 (C_q), 122.9 (CH), 119.3 (C_q), 115.5 (C_q), 52.1 (C_q), 29.3 (CH_3).

IR (ATR): 3443, 2965, 1568, 1414, 1211, 695 cm^{-1}.

MS (EI) *m/z* (relative intensity) 430, 432 (30) [M^+], 415, 417 (15), 374, 376 (100), 356, 358 (10), 293, 295 (10), 277 (25).

HR-MS (ESI) *m/z* calcd for $C_{25}H_{24}N_2Br$ [$M+H^+$] 431.1123, found 431.1113.

***N*-(*tert*-Butyl)-6-iodo-3,4-diphenylisoquinolin-1-amine (118ga)**



The general procedure **C** was followed using **117g** (151 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 120/1) yielded **118ga** (105 mg, 44%) as white solid. M. p.: 179−181 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.89 (d, J = 1.8 Hz, 1H), 7.67 (dd, J = 8.8, 1.8 Hz, 1H), 7.44 (dd, J = 8.8 Hz, 1H), 7.38−7.29 (m, 5H), 7.19−7.13 (m, 5H), 5.15 (s, 1H), 1.62 (s, 9H).

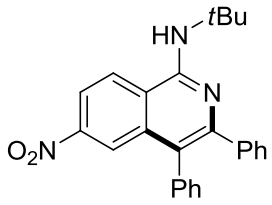
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.3 (C_q), 149.2 (C_q), 141.5 (C_q), 139.2 (C_q), 138.0 (C_q), 135.0 (CH), 133.8 (CH), 132.0 (CH), 130.3 (CH), 128.4 (CH), 127.1 (CH), 126.8 (CH), 126.7 (CH), 122.7 (CH), 119.0 (C_q), 115.8 (C_q), 96.5 (C_q), 52.0 (C_q), 29.3 (CH_3).

IR (ATR): 3452, 2958, 1566, 1413, 1210, 693 cm^{-1}.

MS (EI) *m/z* (relative intensity) 478 (50) [M^+], 463 (15), 422 (100), 421 (90), 404 (5), 277 (20).

HR-MS (EI) *m/z* calcd for $C_{25}H_{23}N_2I$ [M^+] 478.0906, found 478.0905.

***N*-(*tert*-Butyl)-6-nitro-3,4-diphenylisoquinolin-1-amine (118ha)**



The general procedure **C** was followed using **117h** (111 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 80/1) yielded **118ha** (99 mg, 59%) as a red solid. M. p.: 200–202 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.44 (d, J = 2.3 Hz, 1H), 8.14 (dd, J = 9.0, 2.3 Hz, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.39–7.33 (m, 5H), 7.20–7.16 (m, 5H), 5.32 (s, 1H), 1.64 (s, 9H).

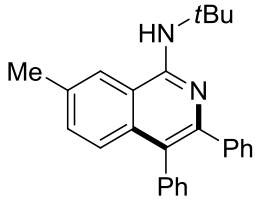
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.9 (C_q), 148.1 (C_q), 140.9 (C_q), 137.6 (C_q), 137.2 (C_q), 131.8 (CH), 130.3 (CH), 128.7 (CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 123.3 (CH), 122.9 (C_q), 122.4 (CH), 121.0 (C_q), 119.0 (C_q), 118.5 (CH), 52.4 (C_q), 29.2 (CH_3).

IR (ATR): 3444, 2916, 1530, 1342, 1210, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 397 (30) [M^+], 382 (10), 341 (100), 311 (20), 294 (30), 277 (20).

HR-MS (EI) *m/z* calcd for $C_{25}H_{23}N_3O_2$ [M^+] 397.1790, found 397.1793.

***N*-(*tert*-Butyl)-7-methyl-3,4-diphenylisoquinolin-1-amine (118ia)**



The general procedure **C** was followed using **117i** (95.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118ia** (113 mg, 62%) as a white solid. M. p.: 215–217 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.50 (s, 1H), 7.44 (d, J = 8.6 Hz, 1H), 7.41–7.38 (m, 2H), 7.34–7.27 (m, 4H), 7.22–7.19 (m, 2H), 7.16–7.11 (m, 3H), 5.15 (s, 1H), 2.51 (s, 3H), 1.64 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.9 (C_q), 147.0 (C_q), 141.9 (C_q), 139.0 (C_q), 135.4 (C_q), 135.0 (C_q), 132.0 (CH), 131.0 (CH), 130.3 (CH), 128.1 (CH), 127.1 (CH), 126.4 (CH), 126.3 (CH), 126.2 (CH), 120.3 (CH), 120.2 (C_q), 117.1 (C_q), 51.8 (C_q), 29.4 (CH_3), 21.7 (CH_3).

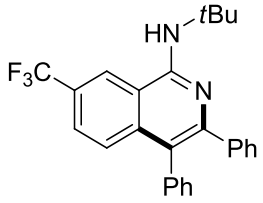
IR (ATR): 3461, 2953, 1570, 1419, 1205, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity) 366 (30) [M^+], 351 (15), 310 (100), 309 (80), 292 (15), 277 (15).

HR-MS (EI) *m/z* calcd for $C_{26}H_{26}N_2$ [M^+] 366.2096, found 366.2078.

The spectral data were in accordance with those reported in the literature.[146]

***N*-(*tert*-Butyl)-7-(trifluoromethyl)-3,4-diphenylisoquinolin-1-amine (118ja)**



The general procedure **C** was followed using **117j** (122 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 150/1) yielded **118ja** (149 mg, 71%) as a yellow solid. M. p.: 176−177 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.98 (s, 1H), 7.65−7.58 (m, 2H), 7.40−7.37 (m, 2H), 7.34−7.29 (m, 3H), 7.19 (d, J = 2.1 Hz, 1H), 7.17 (d, J = 2.0 Hz, 2H), 7.15 (d, J = 2.8 Hz, 2H), 5.24 (s, 1H), 1.64 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.4 (C_q), 150.3 (C_q), 141.2 (C_q), 139.3 (C_q), 138.0 (C_q), 131.8 (CH), 130.3 (CH), 128.3 (CH), 127.2 (CH, $J_{C\text{-}F}$ = 6.0 Hz), 127.2 (CH), 126.8 (CH), 126.8 (CH), 126.2 (C_q, $J_{C\text{-}F}$ = 32.0 Hz), 124.8 (CH, $J_{C\text{-}F}$ = 3.5 Hz), 124.5 (C_q, $J_{C\text{-}F}$ = 271.3 Hz), 119.9 (C_q), 118.9 (CH, $J_{C\text{-}F}$ = 4.5 Hz), 115.9 (C_q), 52.3 (C_q), 29.4 (CH_3).

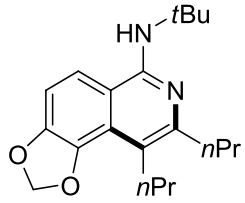
^{19}F-NMR (282 MHz, $CDCl_3$): δ = −61.96 (s).

IR (ATR): 3474, 2960, 1524, 1303, 1105, 692 cm^{-1}.

MS (EI) *m/z* (relative intensity) 420 (30) [M^+], 405 (15), 364 (100), 363 (95), 346 (15), 277 (10).

HR-MS (EI) *m/z* calcd for $C_{26}H_{23}N_2F_3$ [M-H^-] 419.1735, found 419.1733.

***N*-(*tert*-Butyl)-8,9-di-*n*-propyl-[1,3]dioxolo[4,5-*f*]isoquinolin-6-amine (118ke)**



The general procedure **C** was followed using **117k** (110 mg, 0.50 mmol) and 4-octyne (**1e**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1→80/1) yielded **118ke** (100 mg, 60%) and **118ke'** (10 mg, 7%) as a green oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.22 (d, J = 8.9 Hz, 1H), 6.97 (d, J = 8.9 Hz, 1H), 6.04 (s, 2H), 4.79 (s, 1H), 2.90−2.85 (m, 2H), 2.72−2.67 (m, 2H), 1.85−1.73 (m, 2H), 1.58−1.50 (m, 2H), 1.54 (s, 9H), 0.99 (t, J = 7.3 Hz, 6H).

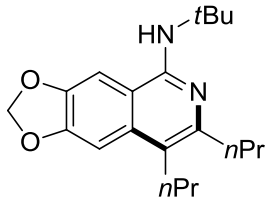
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 151.9 (C_q), 151.0 (C_q), 146.3 (C_q), 141.4 (C_q), 124.4 (C_q), 116.2 (CH), 114.6 (C_q), 114.1 (C_q), 107.7 (CH), 100.7 (CH_2), 51.6 (C_q), 36.5 (CH_2), 30.7 (CH_2), 29.4 (CH_3), 25.1 (CH_2), 22.8 (CH_2), 14.4 (CH_3), 14.4 (CH_3).

IR (ATR): 3459, 2958, 1525, 1442, 1210, 738 cm^{-1}.

MS (EI) *m/z* (relative intensity) 328 (55) [M^+], 313 (15), 299 (25), 272 (30), 243 (100), 227 (5).

HR-MS (EI) *m/z* calcd for $C_{20}H_{28}N_2O_2$ [M^+] 328.2151, found 328.2151.

***N*-(*tert*-Butyl)-7,8-di-*n*-propyl-[1,3]dioxolo[4,5-*g*]isoquinolin-5-amine (118ke')**



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.11 (s, 1H), 6.97 (s, 1H), 5.99 (s, 2H), 4.50 (s, 1H), 2.75−2.68 (m, 4H), 1.83−1.76 (m, 2H), 1.60−1.50 (m, 2H), 1.53 (s, 9H), 1.03 (t, J = 7.2 Hz, 3H), 0.99 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 151.7 (C_q), 149.6 (C_q), 149.4 (C_q), 145.8 (C_q), 134.4 (C_q), 116.9 (C_q), 112.6 (C_q), 101.1 (CH_2), 100.8 (CH), 98.9 (CH), 51.5 (C_q), 37.0 (CH_2), 30.0 (CH_2), 29.5 (CH_3), 23.9 (CH_2), 22.8 (CH_2), 14.6 (CH_3), 14.4 (CH_3).

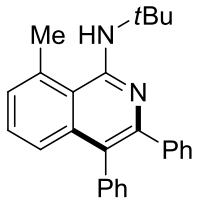
IR (ATR): 3444, 2929, 1634, 1357, 1056, 694 cm^{-1}.

MS (EI) *m/z* (relative intensity) 328 (30) [M^+], 328 (40), 313 (25), 299 (10), 272 (45), 243

(100).

HR-MS (EI) *m/z* calcd for $C_{20}H_{28}N_2O_2$ [M^+] 328.2151, found 328.2151.

***N*-(*tert*-Butyl)-8-methyl-3,4-diphenylisoquinolin-1-amine (118la)**



The general procedure **C** was followed using **117l** (95.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol) in H_2O. Purification by column chromatography (*n*-hexane/EtOAc: 200/1) yielded **118la** (83 mg, 45%) as an off white solid. M. p.: 136−139 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42−7.38 (m, 2H), 7.36−7.26 (m, 4H), 7.24−7.20 (m, 2H), 7.19-7.12 (m, 5H), 5.57 (s, 1H), 2.96 (s, 3H), 1.63 (s, 9H).

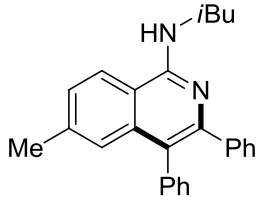
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.4 (C_q), 147.5 (C_q), 141.8 (C_q), 139.5 (C_q), 139.4 (C_q), 132.5 (C_q), 132.2 (CH), 130.3 (CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 127.1 (CH), 126.4 (CH), 126.4 (CH), 124.6 (CH), 120.2 (C_q), 117.8 (C_q), 52.3 (C_q), 29.4 (CH_3), 25.0 (CH_3).

IR (ATR): 3510, 2963, 1503, 1406, 1222, 705 cm^{-1}.

MS (EI) *m/z* (relative intensity) 366 (20) [M^+], 351 (10), 310 (100), 309 (65), 292 (20), 277 (10).

HR-MS (EI) *m/z* calcd for $C_{26}H_{26}N_2$ [M^+] 366.2096, found 366.2093.

***N*-Isobutyl-6-methyl-3,4-diphenylisoquinolin-1-amine (118ma)**



The general procedure **C** was followed using **117m** (95.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118ma** (110 mg, 60%) as a yellow solid. M. p.: 83−86 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, J = 8.4 Hz, 1H), 7.41−7.30 (m, 7H), 7.23−7.20 (m,

2H), 7.16−7.13 (m, 3H), 5.31 (t, *J* = 5.6 Hz, 1H), 3.56−3.52 (m, 2H), 2.38 (s, 3H), 2.13−2.04 (m, 1H), 1.07 (d, *J* = 6.5 Hz, 6H).

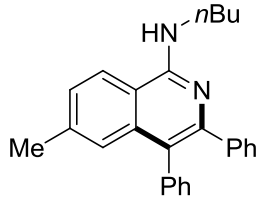
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.9 (C_q), 148.3 (C_q), 141.7 (C_q), 139.4 (C_q), 138.8 (C_q), 137.6 (C_q), 132.0 (CH), 130.3 (CH), 128.1 (CH), 127.2 (CH), 127.2 (CH), 127.1 (CH), 126.4 (CH), 125.3 (CH), 120.8 (CH), 120.2 (C_q), 114.8 (C_q), 49.2 (CH_2), 28.6 (CH), 22.0 (CH_3), 20.7 (CH_3).

IR (ATR): 2957, 1573, 1318, 1055, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 366 (15) [M^+], 351 (15), 323 (20), 310 (55), 293 (70), 222 (55), 105 (100).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{27}N_2$ [$M+H^+$] 367.2174, found 367.2169.

***N*-*n*-Butyl-6-methyl-3,4-diphenylisoquinolin-1-amine (118na)**



The general procedure **C** was followed using **117n** (95.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **117na** (88 mg, 48%) as a yellow solid. M. p.: 93−96 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.5 Hz, 1H), 7.41−7.39 (m, 1H), 7.32−7.27 (d, *J* = 1.9 Hz, 1H), 7.31 (m, 5H), 7.21−7.18 (m, 2H), 7.16−7.11 (m, 3H), 5.20 (s, 1H), 3.74−3.68 (m, 2H), 2.36 (s, 3H), 1.80−1.70 (m, 2H), 1.57−1.44 (m, 2H), 0.99 (t, *J* = 7.3 Hz, 3H).

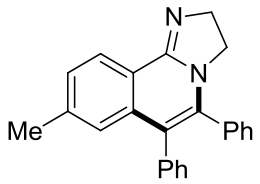
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.9 (C_q), 148.3 (C_q), 141.7 (C_q), 139.4 (C_q), 138.8 (C_q), 137.5 (C_q), 132.0 (CH), 130.3 (CH), 128.0 (CH), 127.2 (CH), 127.1 (CH), 126.5 (CH), 126.4 (CH), 125.2 (CH), 120.9 (CH), 120.3 (C_q), 114.8 (C_q), 41.4 (CH_2), 32.1 (CH_2), 22.0 (CH_3), 20.5 (CH_2), 14.1 (CH_3).

IR (ATR): 2958, 1599, 1573, 1448, 1318, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 366 (15) [M^+], 351 (20), 323 (30), 310 (100), 294 (25).

HR-MS (EI) *m/z* calcd for $C_{26}H_{26}N_2$ [M^+] 366.2096, found 366.2091.

8-Methyl-5,6-diphenyl-2,3-dihydroimidazo[2,1-a]isoquinoline (118oa)



The general procedure **C** was followed using **117o** (80.0 mg, 0.50 mmol) and diphenylacetylene (**1a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0→3/1/0.1) yielded **118oa** (105 mg, 62%) as an off white solid. M. p.: 234−237 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.14 (d, J = 8.1 Hz, 1H), 7.26 (d, J = 1.5 Hz, 1H), 7.21−7.14 (m, 8H), 7.07−7.04 (m, 2H), 6.82 (s, 1H), 3.99 (t, J = 9.5 Hz, 2H), 3.74 (t, J = 9.5 Hz, 2H), 2.28 (s, 3H).

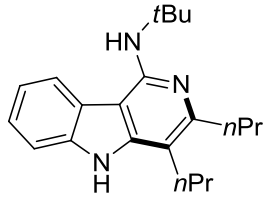
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 157.2 (C_q), 141.9 (C_q), 139.1 (C_q), 137.0 (C_q), 136.4 (C_q), 134.8 (C_q), 131.8 (CH), 129.4 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 126.5 (CH), 126.3 (CH), 125.2 (CH), 119.0 (C_q), 113.6 (C_q), 51.6 (CH_2), 50.4 (CH_2), 22.0 (CH_3).

IR (ATR): 3045, 2869, 1623, 1419, 1274, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity) 336 (80) [M^+], 335 (100) [$M-H^-$].

HR-MS (EI) *m/z* calcd for $C_{24}H_{20}N_2$ [M^+] 336.1626, found 336.1615.

***N*-(*tert*-Butyl)-3,4-dipropyl-5*H*-pyrido[4,3-*b*]indol-1-amine (118pe)**



The general procedure **C** was followed using **117p** (108 mg, 0.50 mmol) and 4-octyne (**1e**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **118pe** (68 mg, 42%) as a yellow solid. M. p.: 88−91 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.96 (br s, 1H), 7.73 (d, J = 7.7 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.35−7.29 (m, 1H), 7.27−7.21 (m, 1H), 4.67 (s, 1H), 2.79−2.70 (m, 4H), 1.92−1.80 (m, 2H), 1.71−1.58 (m, 2H), 1.65 (s, 9H), 1.07−0.98 (m, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.4 (C_q), 151.6 (C_q), 145.2 (C_q), 138.3 (CH), 123.6 (CH),

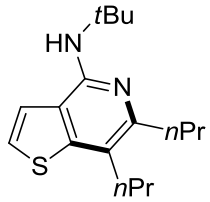
122.5 (C_q), 120.0 (CH), 119.3 (CH), 110.3 (CH), 107.2 (C_q), 102.5 (C_q), 51.7 (C_q), 36.4 (CH_2), 29.9 (CH_3), 29.1 (CH_2), 23.5 (CH_2), 22.8 (CH_2), 14.4 (CH_3), 14.3 (CH_3).

IR (ATR): 3448, 2957, 1582, 1439, 1238, 733 cm^{-1}.

MS (EI) *m/z* (relative intensity) 323 (60) [M^+], 308 (70), 267 (100), 252 (60), 238 (100), 224 (35), 211 (80).

HR-MS (EI) *m/z* calcd for $C_{21}H_{29}N_3$ [M^+] 323.2361, found 323.2364.

***N*-(*tert*-Butyl)-6,7-dipropylthieno[3,2-*c*]pyridin-4-amine (118qe)**



The general procedure **C** was followed using **117q** (91.0 mg, 0.50 mmol) and 4-octyne (**1e**) (110 mg, 1.00 mmol) in H_2O. Purification by column chromatography (*n*-hexane/EtOAc: 120/1→100/1) yielded **118qe** (83 mg, 57%) as a yellow oil.

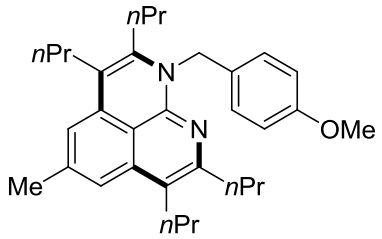
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.18 (d, J = 5.5 Hz, 1H), 7.10 (d, J = 5.5 Hz, 1H), 4.43 (s, 1H), 2.73−2.67 (m, 4H), 1.85−1.77 (m, 2H), 1.69−1.61 (m, 2H), 1.53 (s, 9H), 1.03−0.96 (m, 6H). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 150.8 (C_q), 150.8 (C_q), 149.3 (C_q), 122.8 (CH), 120.8 (C_q), 119.9 (CH), 117.2 (C_q), 51.6 (C_q), 36.1 (CH_2), 33.2 (CH_2), 29.5 (CH_3), 22.9 (CH_2), 22.7 (CH_2), 14.5 (CH_3), 14.3 (CH_3).

IR (ATR): 3443, 2957, 1556, 1489, 1419, 1215, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity) 290 (60) [M^+], 275 (75), 234 (75), 219 (35), 205 (100), 178 (40).

HR-MS (EI) *m/z* calcd for $C_{17}H_{26}N_2S$ [M^+] 290.1817, found 290.1821.

1-(4-Methoxybenzyl)-5-methyl-2,3,7,8-tetrapropyl-1*H*-benzo[*de*][1,8]naphthyridine (118re)



The general procedure **C** was followed using **118r** (127 mg, 0.50 mmol) and oct-4-yne (**1e**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118re** (150 mg, 64%) as a yellow solid. M. p.: 107−108 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.07 (d, J = 8.6 Hz, 2H), 6.92 (s, 1H), 6.83 (d, J = 8.6 Hz, 2H), 6.70 (s, 1H), 5.44 (br s, 2H), 3.68 (s, 3H), 2.64−2.43 (m, 8H), 2.40 (s, 3H), 1.61−1.45 (m, 8H), 1.02−0.92 (m, 9H), 0.80 (t, J = 7.4 Hz, 3H).

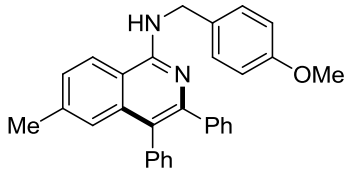
^{13}C-NMR (75 MHz, DMSO-d_6): δ = 157.9 (C_q), 150.9 (C_q), 149.5 (C_q), 141.3 (C_q), 140.7 (C_q), 138.1 (C_q), 135.4 (C_q), 130.7 (C_q), 127.2 (CH), 117.4 (C_q), 116.3 (C_q), 113.9 (CH), 113.7 (CH), 112.5 (CH), 112.1 (C_q), 54.9 (CH_3), 45.7 (CH_2), 36.0 (CH_2), 30.7 (CH_2), 29.1 (CH_2), 28.8 (CH_2), 22.6 (CH_2), 22.4 (CH_3), 21.8 (CH_2), 21.7 (CH_2), 20.9 (CH_2), 14.1 (CH_3), 14.0 (CH_3), 13.9 (CH_3), 13.8 (CH_3).

IR (ATR): 2954, 1624, 1513, 1345, 1252, 829 cm^{-1}.

MS (EI) *m/z* (relative intensity) 470 (40) [M^+], 441 (5), 349 (45), 306 (10), 277 (10), 121 (100).

HR-MS (EI) *m/z* calcd for $C_{32}H_{42}N_2O$ [M^+] 470.3297, found 470.3293.

***N*-(4-Methoxybenzyl)-6-methyl-3,4-diphenylisoquinolin-1-amine (118ra)**



The general procedure **C** was followed using **117r** (127 mg, 0.50 mmol) and **1a** (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **118ra** (73 mg, 34%) as a yellow solid. M. p.: 97−98 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ7.70 (d, J = 8.8 Hz, 2H), 7.44−7.27 (m, 9H), 7.25−7.13 (m, 5H), 6.92 (dd, J = 8.3, 2.4 Hz, 2H), 5.42 (t, J = 5.0 Hz, 1H), 4.86 (d, J = 5.0 Hz, 2H), 3.82 (s,

3H), 2.38 (s, 3H).

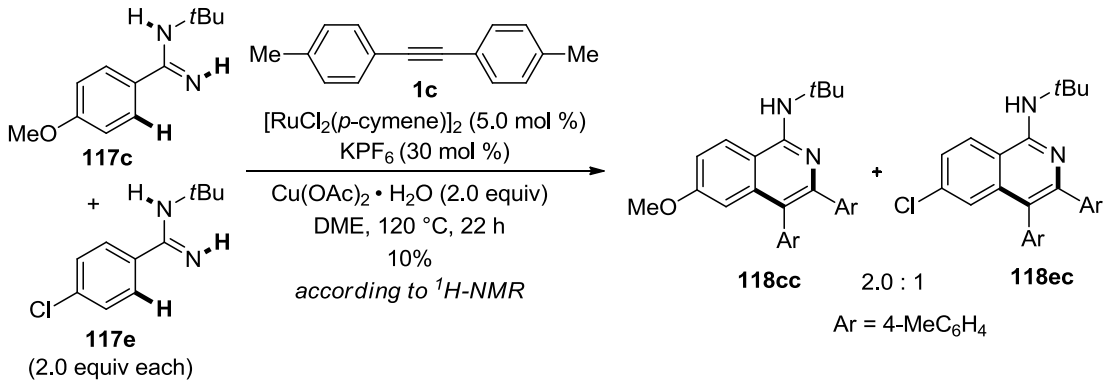
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 158.8 (C_q), 153.5 (C_q), 148.2 (C_q), 141.6 (C_q), 139.6 (C_q), 138.7 (C_q), 132.1 (C_q), 132.0 (CH), 130.3 (CH), 129.5 (CH), 128.1 (CH), 127.3 (CH), 127.1 (CH), 126.5 (CH), 126.4 (CH), 125.3 (CH), 121.0 (CH), 120.9 (C_q), 114.8 (C_q), 113.9 (CH), 55.4 (CH_3), 45.5 (CH_2), 22.0 (CH_3).

IR (ATR): 3436, 2910, 1573, 1509, 1245, 699 cm^{-1}.

MS (EI) m/z (relative intensity) 430 (100) [M^+], 415 (20), 309 (15), 294 (30), 136 (35), 121 (70).

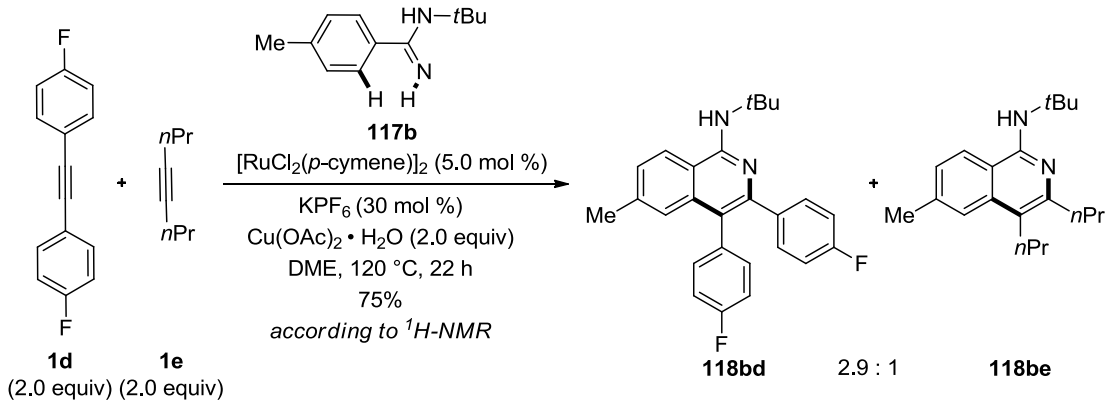
HR-MS (EI) m/z calcd for $C_{30}H_{26}N_2O$ [M^+] 430.2045, found 430.2051.

Intermolecular Competition Experiment between Substrates 117c and 117e:



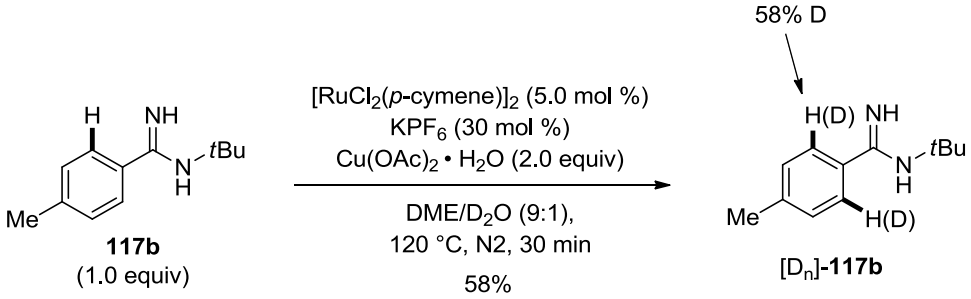
A suspension of 1,2-di-*p*-tolylethyne (**1c**) (103 mg, 0.50 mmol), *N*-(*tert*-butyl)-4-methoxybenzimidamide (**117c**) (206 mg, 1.00 mmol), *N*-(*tert*-butyl)-4-chlorobenzimidamide (**117e**) (210 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), KPF_6 (27.6 mg, 30 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in DME (2.0 mL) was stirred at 120 ℃ for 22 h under an atmosphere of N_2. At ambient temperature, H_2O (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 100/1) to yield a mixture of **118cc** and **118ec** (21 mg, 10%) as a solid. The ratio was estimated by ^{1}H-NMR spectroscopy.

Intermolecular Competition Experiment Between Alkynes Substrates 1d and 1e:



A suspension of *N*-(*tert*-butyl)-4-methylbenzimidamide (**117b**) (95.0 mg, 0.50 mmol), 1,2-bis(4-fluorophenyl)ethyne (**1d**) (214 mg, 1.00 mmol), 4-octyne (**1e**) (110 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), KPF_6 (27.6 mg, 30 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in DME (2.0 mL) was stirred at 120 ℃ for 22 h under an atmosphere of N_2. At ambient temperature, H_2O (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 150:1→120:1) to yield a mixture products of **118bd** and **118be** (141 mg, 75%) as a solid. The ratio was estimated by ^{1}H-NMR spectroscopy.

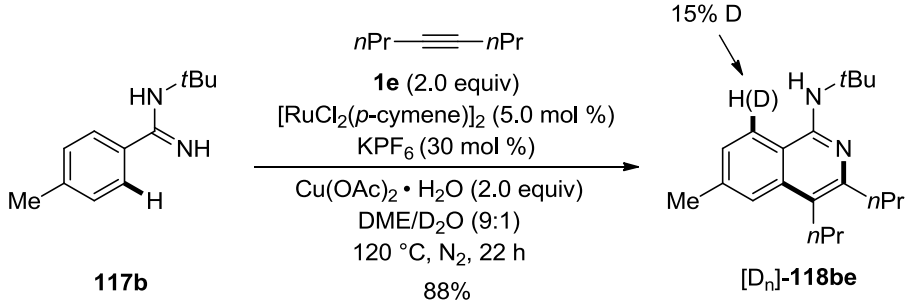
Ruthenium(II)-Catalyzed H/D Exchange in Substrate 117b with D_2O as the Cosolvent in the Absence of Alkyne:



A suspension of *N*-(*tert*-butyl)-4-methylbenzimidamide (**117b**) (95.0 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), KPF_6 (27.6 mg, 30 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in a solvent mixture of DME and D_2O (1.8/0.2 mL) was stirred at 120 ℃ for 0.5 h under an atmosphere of N_2. At ambient temperature, H_2O (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were

washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography (*n*-hexane/EtOAc/Et_3N: 1/1/0.02) to yield [D_n]-**117b** (55.0 mg, 58%) as a white solid. The D-incorporation in [D_n]-**117b** was estimated by ^{1}H-NMR spectroscopy.

Ruthenium-Catalyzed H/D Exchange in Substrate 117b with D_2O as the Cosolvent in the Presence of Alkyne:

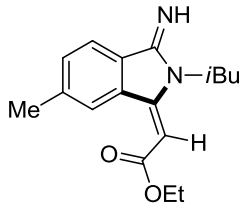


117b [D_n]-**118be**

A suspension of *N*-(*tert*-butyl)-4-methylbenzimidamide (**117b**) (95.0 mg, 0.50 mmol), oct-4-yne (**1e**) (110 mg, 1.00 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %), KPF_6 (27.6 mg, 30 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in a solvent mixture of DME and D_2O (1.8/0.2 mL) was stirred at 120 ℃ for 22 h under an atmosphere of N_2. At ambient temperature, H_2O (20 mL) was added, and the mixture was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 100/1) to yield [D_n]-**118be** (131 mg, 88%) as a green oil. The D-incorporation in [D_n]-**118be** was estimated by ^{1}H-NMR spectroscopy.

Analytical Data for the Products of the Ruthenium(II)-Catalyzed Oxidative C–H Bond Activation with Acrylates

Ethyl (*E*)-2-(3-imino-2-isobutyl-6-methylisoindolin-1-ylidene)acetate (119'ma)



The general procedure **D** was followed using **117m** (95.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75

mmol) and $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 8/1) yielded **119'ma** (110 mg, 77%) as a white solid. M.p.: 68−71 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.96 (s, 1H), 7.68 (br s, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 5.42 (s, 1H), 4.21 (q, J = 7.0 Hz, 2H), 3.66 (d, J = 7.7 Hz, 2H), 2.45 (s, 3H), 2.24−2.15 (m, 1H), 1.31 (t, J = 7.0 Hz, 3H), 0.93 (d, J = 6.8 Hz, 6H).

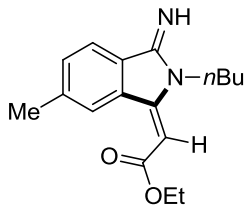
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.8 (C_q), 162.3 (C_q), 151.4 (C_q), 142.2 (C_q), 133.0 (C_q), 131.2 (CH), 128.3 (CH), 127.9 (C_q), 120.4 (CH), 93.5 (CH), 59.9 (CH_2), 47.2 (CH_2), 26.9 (CH), 22.0 (CH_3), 20.1 (CH_3), 14.4 (CH_3).

IR (ATR): 3385, 3228, 2961, 1640, 1157, 1069, 826 cm^{-1}.

MS (EI) *m/z* (relative intensity) 286 (20) [M^+], 241 (15), 213 (100), 197 (15), 185 (15), 158 (35), 142 (10).

HR-MS (EI) *m/z* calcd for $C_{17}H_{22}N_2O_2$ [M^+] 286.1681, found 286.1678.

Ethyl (*E*)-2-(2-*n*-butyl-6-methylisoindolin-3-imino-1-ylidene)acetate (119'na)



The general procedure **D** was followed using **117n** (95.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 8/1) yielded **119'na** (64 mg, 45%) as a white solid. M. p.: 101−102 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.97 (s, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 7.6 Hz, 1H), 5.43 (s, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.81 (t, J = 7.7 Hz, 2H), 2.46 (s, 3H), 1.68−1.57 (m, 2H), 1.45−1.30 (m, 2H), 1.33 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.3 Hz, 3H).

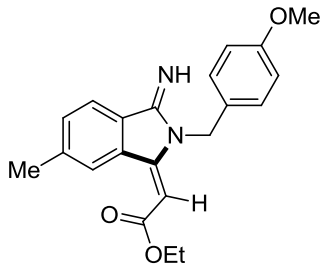
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.9 (C_q), 161.8 (C_q), 151.0 (C_q), 142.2 (C_q), 133.2 (C_q), 131.1 (CH), 128.4 (CH), 128.0 (C_q), 120.3 (CH), 93.1 (CH), 59.9 (CH_2), 40.0 (CH_2), 29.3 (CH_2), 22.1 (CH_3), 20.2 (CH_2), 14.4 (CH_3), 13.8 (CH_3).

IR (ATR): 3235, 2934, 1598, 1153, 1069, 822 cm^{-1}.

MS (EI) *m/z* (relative intensity) 286 (5) [M^+], 241 (10), 213 (100), 185 (15), 158 (20), 142 (10).

HR-MS (EI) *m/z* calcd for $C_{17}H_{22}N_2O_2$ [M^+] 286.1681, found 286.1684.

Ethyl (*E*)-2-{3-imino-2-(4-methoxybenzyl)-6-methylisoindolin-1-ylidene}acetate (119'ra)



The general procedure **D** was followed using **117r** (127 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 °C. Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **117'ra** (129 mg, 74%) as a white solid. M. p.: 165−166 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 7.58 (d, J = 7.9 Hz, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.15 (d, J = 8.9 Hz, 2H), 6.82 (d, J = 8.9 Hz, 2H), 5.44 (s, 1H), 5.03 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 2.49 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H).

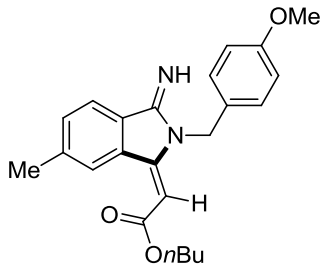
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.7 (C_q), 162.1 (C_q), 158.7 (C_q), 150.8 (C_q), 142.5 (C_q), 142.5 (C_q), 133.3 (C_q), 131.4 (CH), 128.6 (CH), 128.3 (C_q), 127.9 (CH), 120.6 (CH), 114.1 (CH), 94.4 (CH), 59.9 (CH_2), 55.2 (CH_3), 43.2 (CH_2), 22.1 (CH_3), 14.4 (CH_3).

IR (ATR): 3261, 2955, 1604, 1115, 1035, 819 cm^{-1}.

MS (EI) *m/z* (relative intensity) 350 (70) [M^+], 335 (5), 277 (60), 185 (100), 121 (45).

HR-MS (EI) *m/z* calcd for $C_{21}H_{22}N_2O_3$ [M^+] 350.1630, found 350.1627.

***n*-Butyl (*E*)-2-{3-imino-2-(4-methoxybenzyl)-6-methylisoindolin-1-ylidene}acetate (119'rb)**



The general procedure **D** was followed using **117r** (127 mg, 0.50 mmol), **20b** (96.0 mg, 0.75 mmol) $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 5/1) to afford **119'rb** (140 mg, 74%) as a white solid. M.p.: 111−113 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 7.58 (d, J = 7.9 Hz, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.15 (d, J = 8.9 Hz, 2H), 6.82 (d, J = 8.9 Hz, 2H), 5.44 (s, 1H), 5.03 (s, 2H), 4.17 (q, J = 6.8 Hz, 2H), 3.75 (s, 3H), 2.49 (s, 3H), 1.65 (m, 2H), 1.39 (m, 2H), 0.94 (t, J =7.1 Hz, 3H).

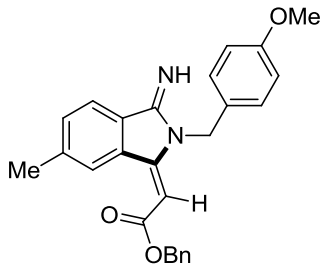
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.8 (C_q), 162.1 (C_q), 158.8 (C_q), 150.8 (C_q), 142.5 (C_q), 142.0 (C_q), 133.4 (C_q), 131.5 (CH), 128.6 (CH), 128.3 (C_q), 127.9 (CH), 120.6 (CH), 114.1 (CH), 94.5 (CH), 64.0 (CH_2), 55.2 (CH_3), 43.2 (CH_2), 30.8 (CH_2), 22.1 (CH_3), 19.2 (CH_2), 13.8 (CH_3).

IR (ATR): 3250, 2965, 1596, 1247, 1097, 822 cm^{-1}.

MS (EI) *m/z* (relative intensity) 378 (55) [M^+], 363 (5), 277 (45), 185 (100), 121 (65).

HR-MS (EI) *m/z* calcd for $C_{23}H_{26}N_2O_3$ [M^+] 378.1943, found 378.1942.

Benzyl (*E*)-2-{3-imino-2-(4-methoxybenzyl)-6-methylisoindolin-1-ylidene}acetate (119'rc).



The general procedure **D** was followed using **117r** (127 mg, 0.50 mmol), **20c** (122 mg, 0.75 mmol) $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **119'rc** (142 mg, 69%) as a white solid. M. p.:

136−137 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.30−7.39 (m, 6H), 7.13 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 5.50 (s, 1H), 5.17 (s, 2H), 5.03 (s, 2H), 3.75 (s, 3H), 2.48 (s, 3H).

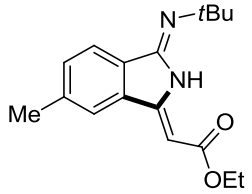
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.5 (C_q), 162.1 (C_q), 158.8 (C_q), 151.3 (C_q), 142.6 (C_q), 136.4 (C_q), 133.3 (C_q), 131.5 (CH), 128.7 (CH), 128.5 (CH), 128.2 (CH), 128.2 (C_q), 128.2 (C_q), 128.1 (CH), 127.9 (CH), 120.6 (CH), 114.1 (CH), 93.9 (CH), 65.8 (CH_2), 55.2 (CH_3), 43.2 (CH_2), 22.1 (CH_3).

IR (ATR): 3255, 2832, 1707, 1637, 1120, 824 cm^{-1}.

MS (EI) *m/z* (relative intensity) 412 (10) [M^+], 321 (10), 277 (25), 185 (100), 142 (5), 121 (45).

HR-MS (EI) *m/z* calcd for $C_{26}H_{24}N_2O_3$ [M^+] 412.1787, found 412.1790.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-methylisoindolin-1-ylidene}acetate (119ba)



The general procedure **D** was followed using **119b** (95.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 °C. Purification by column chromatography (*n*-hexane/EtOAc: 12/1) yielded **119ba** (105 mg, 73%) as a white solid. M.p.: 142−144 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.88 (s, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.39 (s, 1H), 7.32 (d, J = 7.8 Hz, 1H), 5.45 (s, 1H), 4.25 (q, J = 7.2 Hz, 2H), 2.44 (s, 3H), 1.46 (s, 9H), 1.34 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.6 (C_q), 151.9 (C_q), 148.0 (C_q), 140.7 (C_q), 134.5 (C_q), 132.9 (C_q), 132.1 (CH), 122.4 (CH), 120.9 (CH), 84.0 (CH), 59.9 (C_q), 54.1 (CH_2), 30.5 (CH_3), 21.7 (CH_3), 14.5 (CH_3).

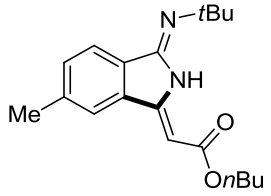
IR (ATR): 3397, 2969, 1637, 1193, 1053, 801 cm^{-1}.

MS (EI) *m/z* (relative intensity) 286 (10) [M^+], 271 (100), 225 (90), 184 (30), 158 (45), 143

(15).

HR-MS (EI) *m/z* calcd for $C_{17}H_{22}N_2O_2$ [M^+] 286.1681, found 286.1676.

***n*-Butyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-methylisoindolin-1-ylidene}acetate (119bb)**



The general procedure **D** was followed using **119b** (95.0 mg, 0.50 mmol), **20b** (75.0 mg, 0.75 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **119bb** (100 mg, 64%) as a white solid. M.p.: 75−78 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.87 (s, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.38 (s, 1H), 7.30 (d, J = 7.9 Hz, 1H), 5.45 (s, 1H), 4.17 (t, J = 6.7 Hz, 2H), 2.43 (s, 3H), 1.72−1.62 (m, 2H), 1.45 (s, 9H), 1.50−1.36 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H).

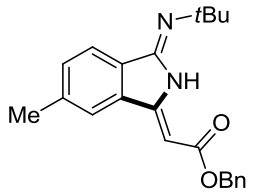
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.7 (C_q), 151.9 (C_q), 148.0 (C_q), 140.7 (C_q), 134.5 (C_q), 132.8 (C_q), 132.1 (CH), 122.4 (CH), 120.9 (CH), 84.0 (CH), 63.9 (C_q), 54.0 (CH_2), 30.8 (CH_2), 30.4 (CH_3), 21.7 (CH_3), 19.2 (CH_2), 13.7 (CH_3).

IR (ATR): 3396, 2968, 1634, 1189, 1051, 702 cm^{-1}.

MS (EI) *m/z* (relative intensity) 314 (10) [M^+], 299 (100), 285 (5), 225 (85), 185 (20), 158 (25).

HR-MS (EI) *m/z* calcd for $C_{19}H_{26}N_2O_2$ [M^+] 314.1994, found 314.1996.

Benzyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-methylisoindolin-1-ylidene}acetate (119bc)



The general procedure **D** was followed using **117b** (95.0 mg, 0.50 mmol), **20c** (75.0 mg, 0.75 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **119bc** (119 mg, 68%) as a white solid. M. p.:

126−127 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.82 (s, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.42−7.30 (m, 7H), 5.52 (s, 1H), 5.25 (s, 2H), 2.42 (s, 3H), 1.44 (s, 9H).

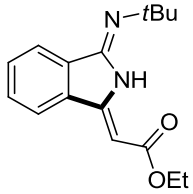
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.1 (C_q), 152.2 (C_q), 147.9 (C_q), 140.7 (C_q), 136.2 (C_q), 134.4 (C_q), 132.8 (C_q), 132.2 (CH), 128.6 (CH), 128.2 (CH), 128.1 (CH), 122.4 (CH), 120.9 (CH), 83.6 (CH), 65.8 (C_q), 54.1 (CH_2), 30.4 (CH_3), 21.7 (CH_3).

IR (ATR): 3396, 2968, 1634, 1189, 1050, 754 cm^{-1}.

MS (EI) *m/z* (relative intensity) 348 (10) [M^+], 333 (100), 225 (80), 185 (15), 158 (25), 91 (60).

HR-MS (EI) *m/z* calcd for $C_{22}H_{24}N_2O_2$ [M^+] 348.1838, found 348.1831.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)isoindolin-1-ylidene}acetate (119aa)



The general procedure **D** was followed using **117a** (88.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 12/1) yielded **119aa** (79 mg, 58%) as a white solid. M. p.: 68−70 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.92 (s, 1H), 7.85−7.82 (m, 1H), 7.58−7.56 (m, 1H), 7.51−7.42 (m, 2H), 5.47 (s, 1H), 4.22 (q, J = 7.2 Hz, 2H), 1.45 (s, 9H), 1.31 (t, J = 7.2 Hz, 3H).

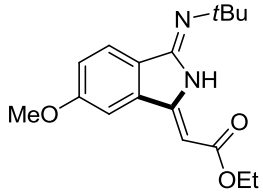
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.4 (C_q), 151.7 (C_q), 147.8 (C_q), 135.3 (C_q), 134.2 (C_q), 131.0 (CH), 130.2 (CH), 122.6 (CH), 120.5 (CH), 84.2 (CH), 59.9 (C_q), 54.1 (CH_2), 30.4 (CH_3), 14.4 (CH_3).

IR (ATR): 3387, 2971, 1656, 1179, 1058, 808 cm^{-1}.

MS (EI) *m/z* (relative intensity) 272 (15) [M^+], 257 (100), 211 (95), 170 (35), 144 (40), 128 (20).

HR-MS (EI) *m/z* calcd for $C_{16}H_{20}N_2O_2$ [M^+] 272.1525, found 272.1522.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-methoxyisoindolin-1-ylidene}acetate (119ca)



The general procedure **D** was followed using **117c** (103 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 ℃ . Purification by column chromatography (*n*-hexane/EtOAc: 4/1) yielded **119ca** (127 mg, 84%) as a white solid. M. p.: 100−101 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.81 (s, 1H), 7.72 (d, J = 9.2 Hz, 1H), 7.02 (d, J = 2.2 Hz, 1H), 7.00 (dd, J = 9.2, 2.2 Hz, 1H), 5.41 (s, 1H), 4.22 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H), 1.43 (s, 9H), 1.30 (t, J = 7.2 Hz, 3H).

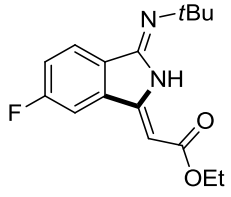
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.4 (C_q), 161.8 (C_q), 151.6 (C_q), 147.6 (C_q), 135.9 (C_q), 128.0 (C_q), 123.8 (CH), 118.0 (CH), 104.6 (CH), 84.0 (CH), 59.9 (C_q), 55.6 (CH_3), 54.0 (CH_2), 30.5 (CH_3), 14.4 (CH_3).

IR (ATR): 3418, 2969, 1634, 1490, 1282, 1057, 800 cm^{-1}.

MS (EI) *m/z* (relative intensity) 302 (15) [M^+], 287 (100), 241 (90), 200 (30), 174 (40), 158 (20).

HR-MS (EI) *m/z* calcd for $C_{17}H_{22}N_2O_3$ [M^+] 302.1630, found 302.1636.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-fluoroisoindolin-1-ylidene}acetate (119da)



The general procedure **D** was followed using **117d** (97.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 ℃ . Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **119da** (105 mg, 72%) as a white solid. M.p.: 87−88 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.90 (s, 1H), 7.81 (dd, J = 8.4, 5.0 Hz, 1H), 7.23 (dd, J =

8.4, 2.1 Hz, 1H), 7.17 (dd, *J* = 8.4, 2.1 Hz, 1H), 5.42 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.44 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H).

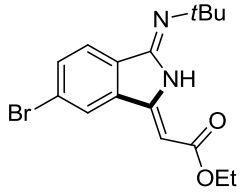
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.3 (C_q), 164.3 (C_q, $J_{C\text{-}F}$ = 250.2 Hz), 150.6 (C_q, $J_{C\text{-}F}$ = 4.1 Hz), 146.8 (C_q), 136.2 (C_q, $J_{C\text{-}F}$ = 10.0 Hz), 131.3 (C_q), 124.5 (CH, $J_{C\text{-}F}$ = 9.4 Hz), 118.6 (CH, $J_{C\text{-}F}$ = 23.6 Hz), 107.5 (CH, $J_{C\text{-}F}$ = 24.6 Hz), 84.7 (CH), 60.1 (C_q), 54.2 (CH_2), 30.4 (CH_3), 14.2 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -(109.5−109.6). (m). IR (ATR): 3391, 2970, 1667, 1210, 1054, 799 cm^{-1}.

MS (EI) *m/z* (relative intensity) 290 (5) [M^+], 275 (100), 229 (90), 188 (25), 162 (35), 146 (20).

HR-MS (EI) *m/z* calcd for $C_{16}H_{19}N_2O_2F$ [M^+] 290.1431, found 290.1423.

Ethyl 2-{(1*Z*,3*Z*)-6-Bromo-3-(*tert*-butylimino)isoindolin-1-ylidene}acetate (119fa)



The general procedure **D** was followed using **119f** (127 mg, 0.50 mmol), ethyl acrylate (**20a)** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 ℃ . Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **119fa** (112 mg, 64%) as a white solid. M. p.: 115−116 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.92 (s, 1H), 7.75−7.72 (m, 2H), 7.64 (d, *J* = 8.1 Hz, 1H), 5.46 (s, 1H), 4.26 (q, *J* = 6.8 Hz, 2H), 1.46 (s, 9H), 1.34 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.3 (C_q), 150.3 (C_q), 146.9 (C_q), 136.1 (C_q), 134.2 (CH), 134.0 (C_q), 124.5 (CH), 124.1 (C_q), 123.7 (CH), 85.1 (CH), 60.1 (C_q), 54.3 (CH_2), 30.4 (CH_3), 14.4 (CH_3).

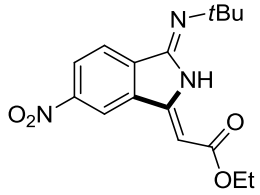
IR (ATR): 3382, 2970, 1647, 1197, 1046, 799 cm^{-1}.

MS (EI) *m/z* (relative intensity) 350; 352 (5) [M^+], 335; 337 (100), 289; 291 (70), 222; 224 (20), 207; 209 (15).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2{}^{79}Br$ [M+H^+] 351.0708; 353.0688, found 351.0703;

353.0683.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-nitroisoindolin-1-ylidene}acetate (119ha)



The general procedure **D** was followed using **117h** (111 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 ℃. Purification by column chromatography (*n*-Hexane/EtOAc: 20/1) yielded **119ha** (42 mg, 26%) as a white solid. M. p.: 190−191 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 10.09 (s, 1H), 8.44 (d, J = 1.9 Hz, 1H), 8.35 (dd, J = 8.6, 1.9 Hz, 1H), 7.99 (d, J = 8.6 Hz, 1H), 5.60 (s, 1H), 4.26 (q, J = 7.2 Hz, 2H), 1.45 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H).

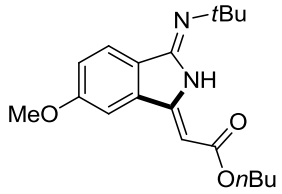
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.1 (C_q), 149.5 (C_q), 149.5 (C_q), 145.8 (C_q), 140.4 (C_q), 135.2 (C_q), 125.9 (CH), 123.7 (CH), 116.3 (CH), 86.3 (CH), 60.4 (C_q), 54.8 (CH_2), 30.2 (CH_3), 14.4 (CH_3).

IR (ATR): 3339, 2966, 1623, 1259, 1030, 800 cm^{-1}.

MS (EI) *m/z* (relative intensity) 317 (10) [M^+], 302 (100), 272 (30), 256 (75), 226 (20), 189 (20), 57 (25).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{20}N_3O_4$ [$M+H^+$] 318.1454, found 318.1449.

***n*-Butyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-methoxyisoindolin-1-ylidene}acetate (119cb)**



The general procedure **D** was followed using **117c** (103 mg, 0.50 mmol), **20b** (96.0 mg, 0.75 mmol) $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 ℃. Purification by column chromatography (*n*-hexane/EtOAc: 8/1) yielded **119cb** (117 mg, 71%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.83 (s, 1H), 7.74 (d, J = 8.6 Hz, 1H), 7.06−7.02 (m, 2H),

5.45 (s, 1H), 4.17 (t, J = 6.6 Hz, 2H), 3.85 (s, 3H), 1.72−1.62 (m, 2H), 1.44 (s, 9H), 1.49−1.36 (m, 2H), 1.31 (t, J = 7.4 Hz, 3H).

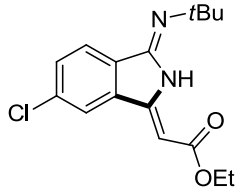
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.6 (C_q), 161.8 (C_q), 151.7 (C_q), 147.7 (C_q), 135.9 (C_q), 128.1 (C_q), 123.8 (CH), 118.1 (CH), 104.6 (CH), 84.1 (CH), 63.9 (C_q), 55.7 (CH_3), 54.0 (CH_2), 30.9 (CH_2), 30.5 (CH_3), 19.2 (CH_2), 13.8 (CH_3).

IR (ATR): 3399, 2962, 1621, 1157, 1053, 800 cm^{-1}.

MS (EI) *m/z* (relative intensity) 330 (10) [M^+], 315 (100), 274 (5), 241 (75), 200 (25), 174 (30), 158 (20).

HR-MS (EI) *m/z* calcd for $C_{19}H_{26}N_2O_3$ [M^+] 330.1943, found 330.1947.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-chloroisoindolin-1-ylidene}acetate (119ea)



The general procedure **D** was followed using **117e** (105 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **119ea** (107 mg, 70%) as a white solid. M. p.: 120−121 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.91 (s, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.54 (d, J = 1.8 Hz, 1H), 7.45 (dd, J = 8.1, 1.8 Hz, 1H), 5.44 (s, 1H), 4.23 (q, J = 7.2 Hz, 2H), 1.44 (s, 9H), 1.32 (t, J = 7.2 Hz, 3H).

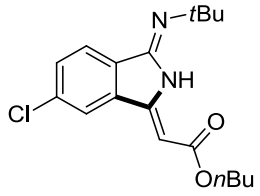
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.2 (C_q), 150.4 (C_q), 146.8 (C_q), 136.5 (C_q), 135.8 (C_q), 133.7 (C_q), 131.2 (CH), 123.9 (CH), 120.7 (CH), 85.1 (CH), 60.1 (C_q), 54.3 (CH_2), 30.3 (CH_3), 14.4 (CH_3).

IR (ATR): 3382, 2967, 1643, 1176, 1049, 800 cm^{-1}.

MS (EI) *m/z* (relative intensity) 306 (5) [M^+], 291 (85), 245 (60), 204 (20), 178 (25), 43 (100).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2{}^{35}Cl$ [M^+] 306.1135, found 306.1096.

***n*-Butyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-chloroisoindolin-1-ylidene}acetate (119eb)**



The general procedure **D** was followed using **117e** (105 mg, 0.50 mmol), **20b** (96.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **119eb** (123 mg, 74%) as a white solid. M. p.: 81−82 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.91 (s, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.54 (d, J = 1.9 Hz, 1H), 7.45 (dd, J = 8.2, 1.9 Hz, 1H), 5.45 (s, 1H), 4.17 (t, J = 6.6 Hz, 2H), 1.72−1.62 (m, 2H), 1.44 (s, 9H), 1.45−1.37 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H).

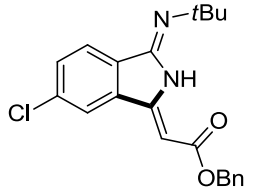
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.4 (C_q), 150.4 (C_q), 146.9(C_q), 136.5 (C_q), 135.8 (C_q), 133.7 (C_q), 131.2 (CH), 124.0 (CH), 120.7 (CH), 85.1 (CH), 64.1 (C_q), 54.3 (CH_2), 30.8 (CH_2), 30.3 (CH_3), 19.2 (CH_2), 13.7 (CH_3).

IR (ATR): 3367, 2958, 1651, 1172, 1061, 828 cm^{-1}.

MS (EI) *m/z* (relative intensity) 334 (5) [M^+], 319 (100), 245 (75), 204 (20), 178 (20), 163 (15).

HR-MS (EI) *m/z* calcd for $C_{18}H_{23}N_2O_2{}^{35}Cl$ [M^+] 334.1448, found 334.1445.

Benzyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-6-chloroisoindolin-1-ylidene}acetate (119ec)



The general procedure **D** was followed using **117e** (105 mg, 0.50 mmol), **20c** (122 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **119ec** (130 mg, 71%) as a white solid. M. p.: 114−116 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.85 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 1.8 Hz, 1H), 7.47 (dd, J = 8.4, 1.8 Hz, 1H), 7.41−7.33 (m, 5H), 5.51 (s, 1H), 5.23 (s, 2H), 1.42 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 168.9 (C_q), 150.8 (C_q), 146.7 (C_q), 136.5 (C_q), 136.0 (C_q),

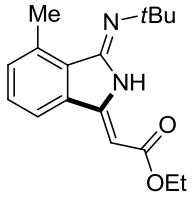
135.7 (C_q), 133.7 (C_q), 131.3 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 123.9 (CH), 120.8 (CH), 84.7 (CH), 66.0 (C_q), 54.3 (CH_2), 30.8 (CH_3).

IR (ATR): 3385, 2970, 1638, 1161, 1048, 602 cm^{-1}.

MS (EI) *m/z* (relative intensity) 368 (10) [M^+], 353 (100), 309 (5), 245 (80), 205 (20), 178 (20).

HR-MS (EI) *m/z* calcd for $C_{21}H_{21}N_2O_2Cl$ [M^+] 368.1292, found 368.1297.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-4-methylisoindolin-1-ylidene}acetate (119la)



The general procedure **D** was followed using **117l** (95.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 °C. Purification by column chromatography (*n*-hexane/EtOAc: 20/1) yielded **119la** (91 mg, 64%) as a white solid. M. p.: 91–92 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.85 (s, 1H), 7.42 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.31 (dd, *J* = 9.0, 9.0 Hz, 1H), 7.25 (dd, *J* = 9.0, 3.0 Hz, 1H), 5.42 (s, 1H), 4.23 (q, *J* = 6.0 Hz, 2H), 2.69 (s, 3H), 1.44 (s, 9H), 1.32 (t, *J* = 6.0 Hz, 3H).

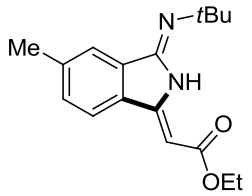
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.7 (C_q), 152.1 (C_q), 148.3 (C_q), 137.3 (C_q), 134.8 (C_q), 133.6 (CH), 131.8 (C_q), 129.3 (CH), 118.1 (CH), 82.7 (CH), 59.8 (C_q), 54.4 (CH_2), 30.3 (CH_3), 18.4 (CH_3), 14.5 (CH_3).

IR (ATR): 3400, 2965, 1618, 1178, 1054, 780 cm^{-1}.

MS (EI) *m/z* (relative intensity) 286 (55) [M^+], 271 (50), 225 (100), 184 (90), 156 (30), 142 (15).

HR-MS (EI) *m/z* calcd for $C_{17}H_{22}N_2O_2$ [M^+] 286.1681, found 286.1685.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-5-methylisoindolin-1-ylidene}acetate (119ia)



The general procedure **D** was followed using **117i** (95.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %) at 100 °C. Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **119ia** (114 mg, 80%) as a white solid. M. p.: 79–81 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.88 (br s, 1H), 7.65 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 5.42 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.45 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

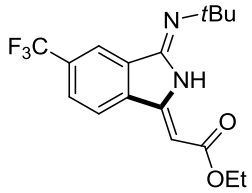
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.6 (C_q), 151.9 (C_q), 148.1 (C_q), 141.7 (C_q), 135.5 (C_q), 131.7 (C_q), 131.3 (CH), 122.8 (CH), 120.4 (CH), 83.8 (CH), 59.9 (CH_2), 54.0 (C_q), 30.4 (CH_3), 21.6 (CH_3), 14.4 (CH_3).

IR (ATR): 3406, 2962, 1214, 1161, 1030, 796 cm^{-1}.

MS (EI) *m/z* (relative intensity) 286 (10) [M^+], 271 (100), 225 (90), 185 (25), 158 (30).

HR-MS (EI) *m/z* calcd for $C_{17}H_{22}N_2O_2$ [M^+] 286.1681, found 286.1681.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-5-(trifluoromethyl)isoindolin-1-ylidene}acetate (119ja)



The general procedure **D** was followed using **117j** (122 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **119ja** (85 mg, 50%) as a white solid. M. p.: 139–140 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 10.0 (br s, 1H), 8.13 (s, 1H), 7.74 (dd, J = 8.0, 1.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 5.55 (s, 1H), 4.25 (q, J = 7.2 Hz, 2H), 1.46 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H).

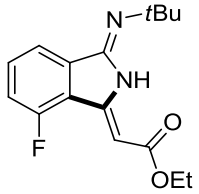
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.2 (C_q), 150.3 (C_q), 146.5 (C_q), 137.2 (C_q), 136.0 (C_q), 133.1 (C_q, $J_{C\text{-}F}$ = 32.8 Hz), 127.2 (CH, $J_{C\text{-}F}$ = 7.4 Hz), 123.8 (C_q, $J_{C\text{-}F}$ = 273.0 Hz), 121.1 (CH), 120.1 (CH, $J_{C\text{-}F}$ = 7.6 Hz), 85.8 (CH), 60.3 (CH_2), 54.5 (C_q), 30.3 (CH_3), 14.4 (CH_3).

IR (ATR): 3278, 2942, 1725, 1642, 1184, 1050, 778 cm^{-1}.

MS (EI) *m/z* (relative intensity) 340 (10) [M^+], 325 (80), 279 (85), 238 (15), 212 (15), 43 (100).

HR-MS (ESI) *m/z* calcd for $C_{17}H_{20}F_3N_2O_2$ [M+H^+] 341.1477 found 341.1471.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-7-fluoroisoindolin-1-ylidene}acetate (119sa)



The general procedure **D** was followed using **117s** (97.0 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 120 ℃ . Purification by column chromatography (*n*-hexane/EtOAc: 15/1) yielded **119sa** (71 mg, 49%) and **119sa'** (7 mg, 5%) as a white solids. **119sa**: M. p.: 101−102 °C.

^{1}H{^{19}F}-NMR (300 MHz, $CDCl_3$): δ = 10.10 (s, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.53 (dd, J = 8.2, 7.6 Hz, 1H), 7.23 (d, J = 8.2 Hz, 1H), 5.80 (s, 1H), 4.32 (q, J = 7.2 Hz, 2H), 1.53 (s, 9H), 1.41 (t, J = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.6 (C_q), 158.3 (C_q, $J_{C\text{-}F}$ = 256.7 Hz), 148.6 (C_q, $J_{C\text{-}F}$ = 3.6 Hz), 147.1 (C_q, $J_{C\text{-}F}$ = 2.7 Hz), 138.2 (C_q, $J_{C\text{-}F}$ = 3.3 Hz), 132.4 (CH, $J_{C\text{-}F}$ = 7.5 Hz), 121.3 (C_q, $J_{C\text{-}F}$ = 14.1 Hz), 118.6 (CH, $J_{C\text{-}F}$ = 3.6 Hz), 117.4 (CH, $J_{C\text{-}F}$ = 19.8 Hz), 89.1 (CH, $J_{C\text{-}F}$ = 7.3 Hz), 60.1 (C_q), 54.2 (CH_2), 30.2 (CH_3), 14.4 (CH_3).

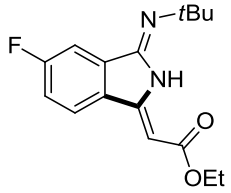
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -(116.9−117.0). (m).

IR (ATR): 3388, 2970, 1634, 1210, 1073, 812 cm^{-1}.

MS (EI) *m/z* (relative intensity) 290 (10) [M^+], 275 (90), 229 (100), 188 (30), 162 (30), 147 (15).

HR-MS (EI) *m/z* calcd for $C_{16}H_{19}N_2O_2F$ [M^+] 290.1431, found 290.1428.

Ethyl 2-{(1*Z*,3*Z*)-3-(*tert*-Butylimino)-5-fluoroisoindolin-1-ylidene}acetate (119sa')



M. p.: 96–97 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.99 (s, 1H), 7.58 (dd, J = 8.4, 4.6 Hz, 2H), 7.19 (td, J = 8.6, 2.4 Hz, 1H), 5.45 (s, 1H), 4.27 (q, J = 7.1 Hz, 2H), 1.48 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H).

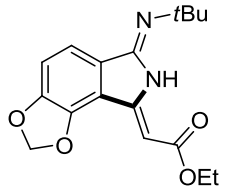
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.4 (C_q), 165.3 (C_q, $J_{C\text{-}F}$ = 251.7 Hz), 150.9 (C_q), 146.7 (C_q), 138.0 (C_q), 129.0 (C_q), 122.4 (CH, $J_{C\text{-}F}$ = 9.5 Hz), 118.2 (CH, $J_{C\text{-}F}$ = 28.2 Hz), 109.5 (CH, $J_{C\text{-}F}$ = 23.0 Hz), 84.0 (CH), 60.1 (C_q), 54.3 (CH_2), 30.3 (CH_3), 14.4 (CH_3).

IR (ATR): 3382, 2967, 1628, 1207, 1053, 798 cm^{-1}.

MS (EI) *m/z* (relative intensity) 290 (10) [M^+], 275 (100), 229 (95), 188 (30), 162 (30), 147 (15).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2F$ [M^+] 290.1431, found 290.1391.

Ethyl(*Z*)-2-{(*Z*)-6-(*tert*-Butylimino)-6,7-dihydro-8*H*-[1,3]dioxolo[4,5-*e*]isoindol-8-ylidene} acetate (119ka)



The general procedure **D** was followed using **117k** (110 mg, 0.50 mmol), **20a** (75.0 mg, 0.75 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) at 100 ℃ . Purification by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **119ka** (108 mg, 68%) as a white solid. M. p.: 181−182 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.79 (s, 1H), 7.37 (d, J = 8.0 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 6.11 (s, 2H), 5.52 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 1.43 (s, 9H), 1.31 (t, J = 7.2 Hz, 3H).

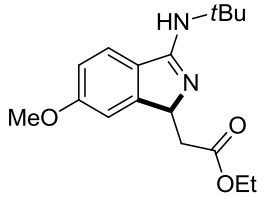
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.5 (C_q), 150.1 (C_q), 148.9 (C_q), 147.4 (C_q), 142.4 (C_q), 129.6 (C_q), 116.3 (CH), 116.1 (C_q), 110.5 (CH), 102.7 (C H_2), 87.6 (CH), 59.9 (C_q), 54.0 (CH_2), 30.4 (CH_3), 14.4 (CH_3).

IR (ATR): 3400, 2981, 1620, 1178, 1036, 800 cm^{-1}.

MS (EI) *m/z* (relative intensity) 316 (15) [M^+], 301 (95), 255 (100), 214 (35), 188 (45), 173 (10).

HR-MS (EI) *m/z* calcd for $C_{17}H_{20}N_2O_4$ [M^+] 316.1423, found 316.1424.

Ethyl 2-{3-(tert-Butylamino)-6-methoxy-1*H*-isoindol-1-yl}acetate (135ca)



A suspension of *N*-(*tert*-butyl)-4-methoxybenzimidamide (**117c**) (15.30 mg, 0.075 mmol), **20a** (7.500 mg, 0.075 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (23.0 mg, 50.0 mol %) and AgOAc (12.50 mg, 0.075 mmol) in DCE (1.0 mL) was stirred at 60 °C for 22 h under an atmosphere of N_2. At ambient temperature, the reaction mixture was extracted with EtOAc (3 × 10 mL), washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc/Et_3N: 5/1/0.05) to afford **135ca** (10 mg, 44%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 8.9 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.86 (dd, *J* = 8.9, 2.0 Hz, 1H), 5.06 (dd, *J* = 8.5, 6.4 Hz, 1H), 4.41 (br s, 1H), 4.19–4.11 (m, 2H), 3.82 (s, 3H), 2.99 (dd, *J* = 15.6, 6.2 Hz, 1H), 2.48 (dd, *J* = 15.6, 8.6 Hz, 1H), 1.48 (s, 9H), 1.24 (t, *J* = 7.2 Hz, 1H).

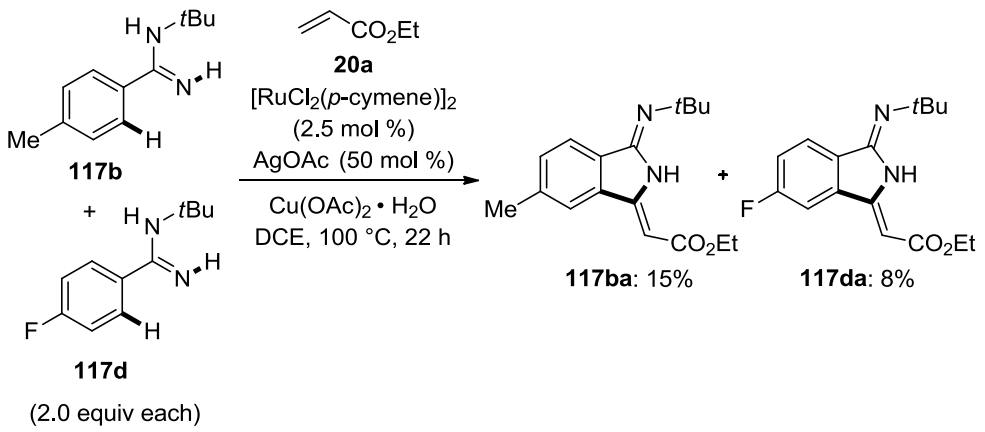
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 171.9 (C_q), 160.5 (C_q), 160.1 (C_q), 154.2 (C_q), 128.8 (C_q), 118.8 (CH), 113.4 (CH), 107.7 (CH), 66.7 (CH), 60.3 (C_q), 55.5 (CH_3), 51.4 (CH_2), 39.7 (CH_2), 29.0 (CH_3), 14.2 (CH_3).

IR (film): 3402, 2965, 1725, 1605, 1480, 1242, 1023 cm^{-1}.

MS (ESI) *m/z* (relative intensity) 305 (90) [M+H^+], 291 (100), 249 (5), 235 (10), 161 (5).

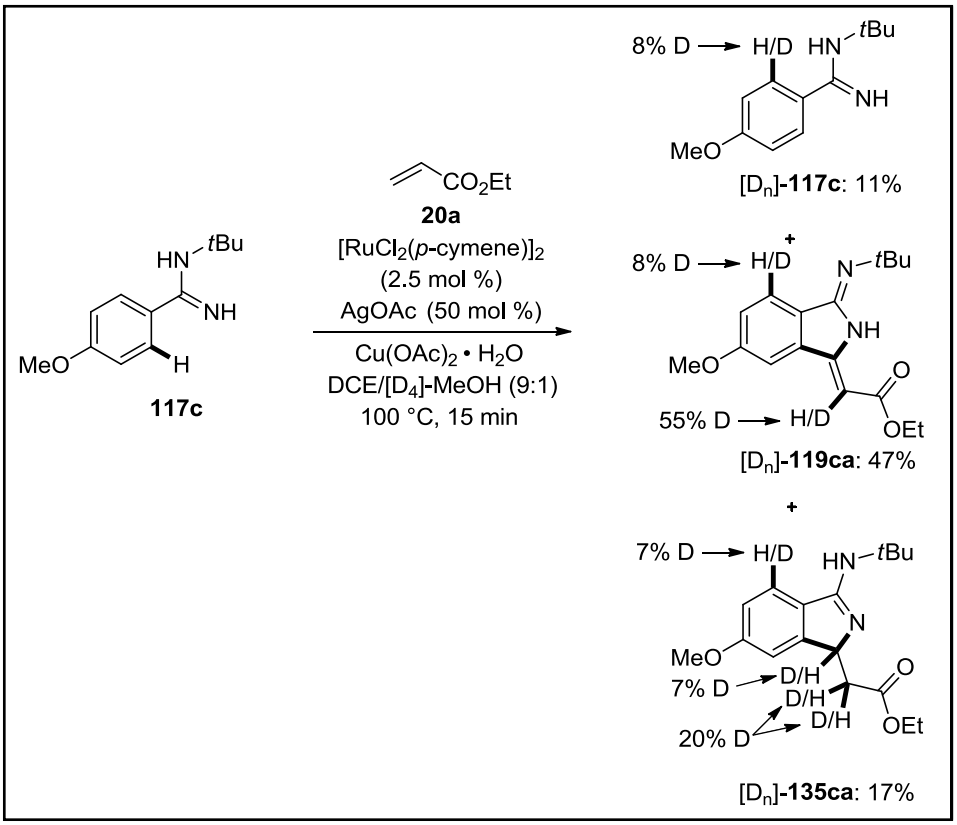
HR-MS (ESI) *m/z* calcd for $C_{17}H_{25}N_2O_3$ [M+H^+] 305.1865, found 305.1862.

Intermolecular Competition Experiment between Substrates 117b and 117d:



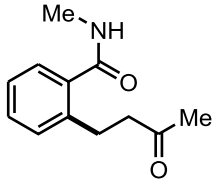
A suspension of *N*-(*tert*-butyl)-4-methylbenzimidamide (**117b**) (190 mg, 1.00 mmol), *N*-(*tert*-butyl)-4-fluorobenzimidamide (**117d**) (194 mg, 1.00 mmol), **20a** (50.0 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), AgOAc (41.5 mg, 50 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) in DCE (2.0 mL) was stirred at 100 °C for 22 h under an atmosphere of N_2. At ambient temperature, the reaction mixture was extracted with EtOAc (3 × 20 mL), washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1→10/1) to yield **119ba** (21.0 mg, 15%) and **119da** (11.0 mg, 8%) as colorless solids.

Ruthenium(II)-Catalyzed H/D Exchange with Substrate 117c in CD_3OD as the Cosolvent: A suspension of *N*-(*tert*-butyl)-4-methoxybenzimidamide (**117c**) (103 mg, 0.50 mmol), ethyl acrylate (**20a**) (100 mg, 0.75 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), AgOAc (41.5 mg, 50 mol %) and $Cu(OAc)_2 \cdot H_2O$ (199 mg, 1.00 mmol) was stirred at 100 °C for 22 h in a solvent mixture of DCE and CD_3OD (1.8/0.2 mL) as the solvent under an atmosphere of N_2. At ambient temperature, the reaction mixture was extracted with EtOAc (3 × 20 mL), washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc/Et_3N: 5/1/0→1/1/0.02) yielded $[D_n]$-**119ca** (71.0 mg, 47%) as a green oil, $[D_n]$-**135ca** (26.0 mg, 17%) as a green oil and reisolated starting material $[D_n]$-**117c** (11.0 mg, 11%) as a colorless solid. The D-incorporation in $[D_n]$-**119ca**, $[D_n]$-**135ca** and $[D_n]$-**117c** was estimated by ^{1}H-NMR spectroscopy.



10.4.3 Analytical Data for the Products of Ruthenium(II)-Catalyzed C–H Bond Hydroarylation and Oxidative Annulation with α,β-Unsaturated Ketones *via* Monodentate Coordination

***N*-Methyl-2-(3-oxobutyl)benzamide (120aa)**



The general procedure **E** was followed using **2a** (68 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120aa** (82 mg, 80%) as a colorless solid. M. p.: = 117−119 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 2H), 7.21–7.13 (m, 2H), 6.36 (br s, 1H), 2.96 (d, J = 4.9 Hz, 3H), 2.93 (t, J = 6.0 Hz, 2H), 2.87 (t, J = 6.0 Hz, 2H), 2.10 (s, 3H).

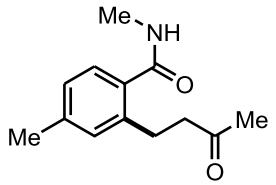
^{13}C-NMR (125MHz, $CDCl_3$): δ = 208.6 (C_q), 170.6 (C_q), 138.9 (C_q), 136.7 (C_q), 129.9 (CH), 129.7 (CH), 127.2 (CH), 126.2 (CH), 45.2 (CH_2), 30.0 (CH_3), 27.2 (CH_2), 26.6 (CH_3).

IR (ATR): 3290, 1707, 1631, 1368, 1166, 661 cm^{-1}.

MS (EI) m/z (relative intensity) 205 (10) [M^+], 175 (10), 162 (100), 144 (10), 131 (45), 103 (5).

HR-MS (ESI) m/z calcd for $C_{12}H_{16}NO_2$ [M+H^+] 206.1181, found 206.1177.

N,4-Dimethyl-2-(3-oxobutyl)benzamide (120ba)



The general procedure **E** was followed using **2b** (75 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **120ba** (77 mg, 70%) as a colorless solid. M. p.: = 108−109 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.24 (dd, J = 7.1, 1.4 Hz, 1H), 7.00 (s, 1H), 6.99 (d, J = 7.1 Hz, 1H), 6.26 (br s, 1H), 2.96 (d, J = 4.9 Hz, 3H), 2.90 (t, J = 6.0 Hz, 2H), 2.89 (t, J = 6.0 Hz, 2H), 2.30 (s, 3H), 2.11 (s, 3H).

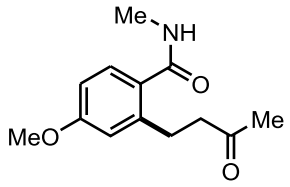
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.5 (C_q), 170.5 (C_q), 139.9 (C_q), 139.0 (C_q), 133.6 (C_q), 130.5 (CH), 127.1 (CH), 126.8 (CH), 45.4 (CH_2), 30.0 (CH_3), 27.3 (CH_2), 26.7 (CH_3), 21.3 (CH_3).

IR (ATR): 3287, 1710, 1632, 1542, 1164, 693 cm^{-1}.

MS (EI) m/z (relative intensity) 219 (10) [M^+], 189 (5), 176 (100), 161 (10), 145 (45), 115 (15).

HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_2$ [M^+] 219.1259, found 219.1256.

4-Methoxy-*N*-methyl-2-(3-oxobutyl)benzamide (120ca)



The general procedure **E** was followed using **2c** (83 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120ca** (94 mg, 80%) as a colorless solid. M. p.: = 107−109 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.29 (dd, J = 8.1, 0.8 Hz, 1H), 6.70 (s, 1H), 6.66 (d, J = 8.1 Hz, 1H), 6.34 (br s, 1H), 3.76 (s, 3H), 2.93 (d, J = 5.1 Hz, 3H), 2.93 (t, J = 6.4 Hz, 2H), 2.86 (t, J = 6.4 Hz, 2H), 2.10 (s, 3H).

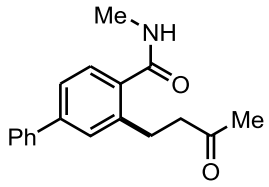
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.6 (C_q), 170.3 (C_q), 160.6 (C_q), 141.4 (C_q), 128.9 (C_q), 128.9 (CH), 115.4 (CH), 111.2 (CH), 55.2 (CH_3), 45.2 (CH_2), 29.9 (CH_3), 27.5 (CH_2), 26.6 (CH_3).

IR (ATR): 3288, 1705, 1543, 1247, 1157, 696 cm^{-1}.

MS (EI) m/z (relative intensity) 235 (15) [M^+], 205 (10), 192 (100), 177 (5), 161 (60), 135 (10).

HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_3$ [M^+] 235.1208, found 235.1206.

N-Methyl-3-(3-oxobutyl)-[1,1'-biphenyl]-4-carboxamide (120da)



The general procedure **E** was followed using **2d** (106 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120da** (111 mg, 79%) as a colorless solid. M. p.: = 153−155 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.60–7.48 (m, 2H), 7.48–7.38 (m, 5H), 7.38–7.28 (m, 1H), 6.42 (br s, 1H), 3.10–3.00 (m, 2H), 2.98 (d, J = 4.9 Hz, 3H), 2.96–2.83 (m, 2H), 2.12 (s, 3H).

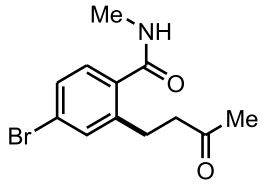
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 208.5 (C_q), 170.4 (C_q), 142.8 (C_q), 140.1 (C_q), 139.6 (C_q), 135.3 (C_q), 128.8 (CH), 128.6 (CH), 127.7 (CH), 127.7 (CH), 127.1 (CH), 124.9 (CH), 45.3 (CH_2), 29.9 (CH_3), 27.4 (CH_2), 26.6 (CH_3).

IR (ATR): 3287, 1709, 1630, 1543, 1160, 697 cm^{-1}.

MS (EI) m/z (relative intensity) 281 (15) [M^+], 250 (5), 238 (100), 207 (40), 178 (20), 165 (15).

HR-MS (EI) m/z calcd for $C_{18}H_{19}NO_2$ [M^+] 281.1416, found 281.1417.

4-Bromo-*N*-methyl-2-(3-oxobutyl)benzamide (120ea)



The general procedure **E** was followed using **2e** (107 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **120ea** (113 mg, 81%) as a colorless solid. M. p.: = 132−134 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 2H), 7.27–7.21 (m, 1H), 6.52 (br s, 1H), 2.99–2.92 (m, 4H), 2.92 (d, J = 1.6 Hz, 3H), 2.15 (s, 3H).

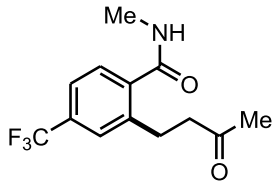
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.0 (C_q), 169.5 (C_q), 141.1 (C_q), 135.6 (C_q), 132.4 (CH), 129.3 (CH), 128.8 (CH), 124.0 (C_q), 44.8 (CH_2), 30.0 (CH_3), 26.8 (CH_2), 26.8 (CH_3).

IR (ATR): 3287, 1705, 1639, 1543, 1167, 686 cm^{-1}.

MS (EI) m/z (relative intensity) 283 (5) [M^+], 240 (100), 225 (10), 211 (35), 183 (10), 102 (20).

HR-MS (ESI) m/z calcd for $C_{12}H_{14}NO_2{}^{79}Br$ [M+] 283.0208, found 283.0210.

***N*-Methyl-2-(3-oxobutyl)-4-(trifluoromethyl)benzamide (120fa)**



The general procedure **E** was followed using **2f** (102 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120fa** (99 mg, 73%) as a colorless solid. M. p.: = 117−119 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.45 (s, 3H), 6.58 (br s, 1H), 2.99 (d, J = 4.9 Hz, 3H), 2.96 (t, J = 5.0 Hz, 2H), 2.94 (t, J = 5.0 Hz, 2H), 2.13 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$,): δ = 207.9 (C_q), 169.2 (C_q), 140.1 (C_q), 139.6 (C_q), 131.8 (C_q, $J_{C\text{-}F}$ = 32.4 Hz), 127.8 (CH), 126.2 (CH, $J_{C\text{-}F}$ = 3.7 Hz), 124.0 (C_q, $J_{C\text{-}F}$ = 271.5 Hz), 123.1 (CH, J = 3.7 Hz), 44.68 (CH_2), 30.02 (CH_3), 26.8 (CH_2), 26.8 (CH_3).

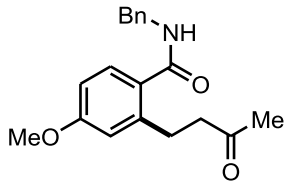
^{19}F-NMR ($CDCl_3$, 282 MHz): δ -62.9 (s).

IR (ATR): 3294, 1713, 1550, 1333, 1114, 696 cm^{-1}.

MS (EI) m/z (relative intensity) 273 (5) [M^+], 254 (5), 230 (60), 199 (20), 151 (10), 43 (100).

HR-MS (EI) m/z calcd for $C_{13}H_{14}F_3NO_2$ [M^+] 273.0977, found 273.0973.

***N*-Benzyl-4-methoxy-2-(3-oxobutyl)benzamide (120ga)**



The general procedure **E** was followed using **2g** (121 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **120ga** (106 mg, 68%) as a colorless solid. M. p.: = 131−133 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.37–7.31 (m, 5H), 7.32–7.25 (m, 1H), 6.74 (d, J = 2.5 Hz, 1H), 6.70 (dd, J = 8.4, 2.6 Hz, 1H), 6.44 (br s, 1H), 4.59 (d, J = 5.8 Hz, 2H), 3.78 (s, 3H), 2.99 (t, J = 7.1 Hz, 2H), 2.86 (t, J = 7.1 Hz, 2H), 2.09 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.3 (C_q), 169.4 (C_q), 160.8 (C_q), 141.9 (C_q), 138.3 (C_q), 128.8 (CH), 128.8 (CH), 128.6 (C_q), 127.8 (CH), 127.5 (CH), 115.7 (CH), 111.3 (CH), 55.3 (CH_3), 45.3 (CH_2), 44.0 (CH_2), 29.9 (CH_3), 27.7 (CH_2).

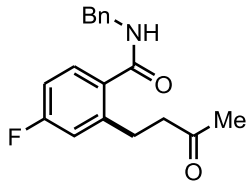
IR (ATR): 3280, 1706, 1628, 1268, 1025, 694 cm^{-1}.

MS (EI) m/z (relative intensity) 311 (15) [M^+], 268 (45), 205 (20), 161 (30), 106 (25), 91 (100).

HR-MS (ESI) m/z calcd for $C_{19}H_{22}NO_3$ [M+H^+] 312.1600, found 312.1600.

The spectral data were in accordance with those reported in the literature.[147]

***N*-Benzyl-4-fluoro-2-(3-oxobutyl)benzamide (120ha)**



The general procedure **E** was followed using **2h** (115 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1→2:1) yielded **120ha** (109 mg, 73%) as a colorless solid. M. p.: = 112−114 °C.

[147] R. Manoharan, M. Jeganmohan, *Chem. Commun.* **2015**, *51*, 2929–2932.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.40–7.25 (m, 6H), 6.93–6.81 (m, 2H), 6.74 (t, J = 5.8 Hz, 1H), 4.57 (d, J = 5.8 Hz, 2H), 2.94 (t, J = 6.6 Hz, 2H), 2.83 (t, J = 6.6 Hz, 2H), 2.07 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 208.0 (C_q), 168.9 (C_q), 163.4 (C_q, $J_{C\text{-}F}$ = 249.7 Hz), 142.3 (C_q, $J_{C\text{-}F}$ = 7.8 Hz), 138.1 (C_q), 132.5 (C_q, $J_{C\text{-}F}$ = 3.1 Hz), 129.3 (CH, $J_{C\text{-}F}$ = 8.8 Hz), 128.8 (CH), 127.8 (CH), 127.6 (CH), 116.6 (CH, $J_{C\text{-}F}$ = 21.4 Hz), 113.2 (CH, $J_{C\text{-}F}$ = 21.6 Hz), 44.7 (CH_2), 44.0 (CH_2), 29.9 (CH_3), 27.1 (CH_2, $J_{C\text{-}F}$ = 1.6 Hz).

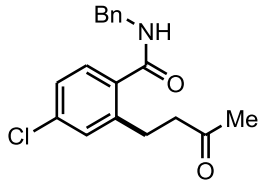
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -110.4 (ddd, J = 9.8, 8.1, 5.8 Hz).

IR (ATR): 3281, 1709, 1635, 1234, 1168, 694 cm^{-1}.

MS (EI) m/z (relative intensity) 299 (10) [M^+], 256 (30), 193 (10), 149 (25), 106 (65), 91 (100).

HR-MS (EI) m/z calcd for $C_{18}H_{18}FNO_2$ [M^+] 299.1322, found 299.1323.

***N*-Benzyl-4-chloro-2-(3-oxobutyl)benzamide (120ia)**



The general procedure **E** was followed using **2i** (123 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **120ia** (97 mg, 62%) as a colorless solid. M. p.: = 125−126 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.37–7.25 (m, 6H), 7.20–7.18 (m, 1H), 7.16 (dd, J = 8.1, 2.1 Hz, 1H), 6.67 (d, J = 6.4 Hz, 1H), 4.59 (d, J = 5.8 Hz, 2H), 2.93 (t, J = 6.6 Hz, 2H), 2.85 (t, J = 6.6 Hz, 2H), 2.09 (s, 3H).

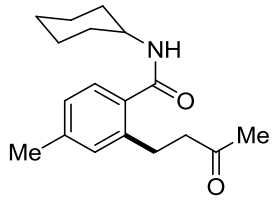
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 207.7 (C_q), 168.6 (C_q), 141.2 (C_q), 137.9 (C_q), 135.8 (C_q), 134.7 (C_q), 129.8 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.6 (CH), 126.4 (CH), 44.8 (CH_2), 44.1 (CH_2), 30.0 (CH_3), 27.0 (CH_2).

IR (ATR): 3279, 1708, 1637, 1541, 1163, 692 cm^{-1}.

MS (EI) m/z (relative intensity) 315 (10) [M^+], 272 (30), 209 (5), 165 (15), 106 (75), 91 (100).

HR-MS (EI) m/z calcd for $C_{18}H_{18}N^{35}ClO_2$ [M^+] 315.1026, found 315.1030.

***N*-Cyclohexyl-4-methyl-2-(3-oxobutyl)benzamide (120ja)**



The general procedure **E** was followed using **2j** (109 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **120ja** (100 mg, 70%) as a colorless solid. M. p.: = 143−145 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.30–7.20 (m, 1H), 7.02 (s, 1H), 7.01 (d, J = 6.8 Hz, 1H), 6.04 (d, J = 8.2 Hz, 1H), 4.13–3.82 (m, 1H), 2.96 (t, J = 6.2 Hz, 2H), 2.87 (t, J = 6.2 Hz, 2H), 2.32 (s, 3H), 2.12 (s, 3H), 2.13–2.02 (m, 2H), 1.88–1.69 (m, 3H), 1.54–1.32 (m, 2H), 1.31–1.09 (m, 3H).

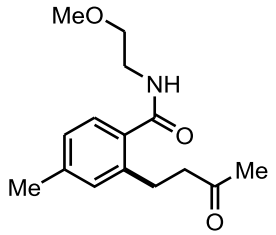
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.2 (C_q), 169.0 (C_q), 139.8 (C_q), 138.9 (C_q), 134.1 (C_q), 130.5 (CH), 127.0 (CH), 126.8 (CH), 48.6 (CH), 45.4 (CH_2), 33.2 (CH_2), 30.0 (CH_3), 27.4 (CH_2), 25.6 (CH_2), 25.0 (CH_2), 21.3 (CH_3).

IR (ATR): 3278, 2923, 1712, 1631, 1537, 699 cm^{-1}.

MS (EI) m/z (relative intensity) 287 (35) [M^+], 244 (100), 189 (70), 162 (70), 145 (60).

HR-MS (EI) m/z calcd for $C_{18}H_{25}NO_2$ [M^+] 287.1885, found 287.1879.

***N*-(2-Methoxyethyl)-4-methyl-2-(3-oxobutyl)benzamide (120ka)**



The general procedure **E** was followed using **2k** (97 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120ka** (76 mg, 58%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, J = 7.7 Hz, 1H), 7.01 (s, 1H), 7.00 (d, J = 7.7 Hz, 1H), 6.40 (br s, 1H), 3.60 (dt, J = 7.8, 1.7 Hz, 2H), 3.53 (dt, J = 7.8, 1.7 Hz, 2H), 3.35 (s, 3H), 2.95 (dt, J = 6.0, 1.3 Hz, 2H), 2.83 (dt, J = 6.0, 1.3 Hz, 2H), 2.31 (s, 3H), 2.11 (s, 3H).

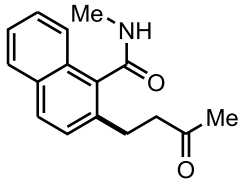
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.1 (C_q), 169.8 (C_q), 140.1 (C_q), 139.3 (C_q), 133.4 (C_q), 130.8 (CH), 127.1 (CH), 126.8 (CH), 71.2 (CH_2), 58.8 (CH_3), 45.6 (CH_2), 39.6 (CH_2), 30.0 (CH_3), 27.6 (CH_2), 21.3 (CH_3).

IR (ATR): 3313, 2928, 1640, 1530, 1302, 1121 cm^{-1}.

MS (EI) m/z (relative intensity) 263 (5) [M^+], 248 (10), 231 (10), 220 (30), 189 (75), 145 (100).

HR-MS (EI) m/z calcd for $C_{15}H_{21}NO_3$ [M^+] 263.1521, found 263.1524.

***N*-Methyl-2-(3-oxobutyl)-1-naphthamide (120la)**



The general procedure **E** was followed using **2l** (93 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **120la** (57 mg, 45%) as a colorless solid. M. p.: = 153−155 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.91–7.62 (m, 3H), 7.54–7.35 (m, 2H), 7.25 (d, J = 8.3 Hz, 1H), 6.46 (br s, 1H), 3.08 (d, J = 5.4 Hz, 3H), 3.01–2.78 (m, 4H), 2.09 (s, 3H).

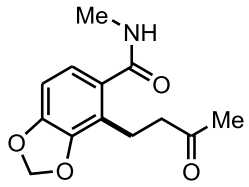
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.0 (C_q), 170.1 (C_q), 134.6 (C_q), 134.1 (C_q), 131.8 (C_q), 130.2 (C_q), 129.1 (CH), 127.8 (CH), 126.8 (CH), 126.3 (CH), 125.6 (CH), 124.8 (CH), 44.7 (CH_2), 30.1 (CH_3), 27.4 (CH_2), 26.6 (CH_3).

IR (ATR): 3261, 1704, 1627, 1260, 745, 448 cm^{-1}.

MS (EI) m/z (relative intensity) 255 (20) [M^+], 224 (10), 212 (100), 197 (20), 181 (50), 155 (25).

HR-MS (EI) m/z calcd for $C_{16}H_{17}NO_2$ [M^+] 255.1259, found 255.1261.

***N*-Methyl-4-(3-oxobutyl)benzo[*d*][1,3]dioxole-5-carboxamide (120ma)**



The general procedure **E** was followed using **2m** (90 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120ma** (100 mg, 80%) as a colorless solid. M. p.: = 139−141 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.93 (d, J = 8.0 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.47 (br s, 1H), 5.95 (s, 2H), 2.94 (d, J = 4.9 Hz, 3H), 2.94–2.88 (m, 4H), 2.15 (s, 3H).

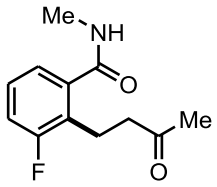
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.7 (C_q), 169.5 (C_q), 148.1 (C_q), 146.2 (C_q), 131.0 (C_q), 121.5 (CH), 121.1 (C_q), 106.2 (CH), 101.1 (CH_2), 43.0 (CH_2), 29.9 (CH_3), 26.7 (CH_3), 21.7 (CH_2).

IR (ATR): 3301, 1706, 1543, 1251, 1040, 705 cm^{-1}.

MS (EI) m/z (relative intensity) 249 (25) [M^+], 218 (15), 206 (100), 188 (5), 175 (65), 149 (15).

HR-MS (EI) m/z calcd for $C_{13}H_{15}NO_4$ [M^+] 249.1001, found 249.1006.

3-Fluoro-*N*-methyl-2-(3-oxobutyl)benzamide (120na)



The general procedure **E** was followed using **2n** (77 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **120na** (86 mg, 70%) as a colorless solid. M. p.: = 123−125 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.21–7.11 (m, 2H), 7.09–6.93 (m, 1H), 6.55 (br s, 1H), 2.96 (d, J = 4.9 Hz, 3H), 2.94 (t, J = 5.4 Hz, 2H), 2.89 (t, J = 5.4 Hz, 2H), 2.12 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 208.7 (C_q), 169.3 (C_q, J = 3.2 Hz), 161.4 (C_q, J = 246.1 Hz), 139.1 (C_q, J = 4.3 Hz), 127.8 (CH, J = 8.9 Hz), 126.1 (C_q, J = 16.7 Hz), 122.9 (CH, J = 3.4 Hz), 116.7 (CH, J = 23.0 Hz), 43.5 (CH_2, J = 2.4 Hz), 29.8 (CH_3), 26.7 (CH_3), 21.1 (CH_2, J = 2.9 Hz).

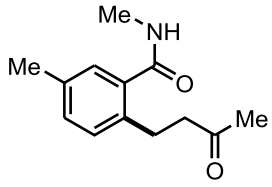
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -116.1 (dd, J = 10.2, 4.4 Hz).

IR (ATR): 3291, 1703, 1547, 1319, 1163, 710 cm^{-1}.

MS (EI) m/z (relative intensity) 223 (10) [M^+], 180 (100), 165 (15), 149 (60), 121 (15), 101 (15).

HR-MS (EI) m/z calcd for $C_{12}H_{14}NO_2F$ [M^+] 223.1009, found 223.1006.

***N*,5-Dimethyl-2-(3-oxobutyl)benzamide (120oa)**



The general procedure **E** was followed using **2o** (75 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **120oa** (68 mg, 62%) as a colorless solid. M. p.: = 112−114 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.15 (d, J = 1.8 Hz, 1H), 7.10 (dd, J = 7.9, 1.8 Hz, 1H), 7.07 (d, J = 7.9 Hz, 1H), 6.41 (br s, 1H), 2.98 (d, J = 4.9 Hz, 3H), 2.89 (t, J = 5.0 Hz, 2H), 2.87 (t, J = 5.0 Hz, 2H), 2.30 (s, 3H), 2.12 (s, 3H).

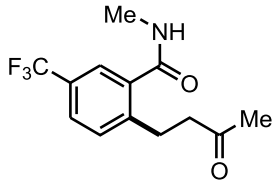
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 208.6 (C_q), 170.6 (C_q), 136.4 (C_q), 135.8 (C_q), 135.6 (C_q), 130.6 (CH), 129.5 (CH), 127.8 (CH), 45.3 (CH_2), 30.1 (CH_3), 26.7 (CH_2), 26.7 (CH_3), 20.9 (CH_3).

IR (ATR): 3285, 1709, 1541, 1319, 1160, 697 cm^{-1}.

MS (EI) m/z (relative intensity) 219 (15) [M^+], 189 (5), 176 (100), 161 (10), 145 (60), 117 (15).

HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_2$ [M^+] 219.1259, found 219.1252.

***N*-Methyl-2-(3-oxobutyl)-5-(trifluoromethyl)benzamide (120pa)**



The general procedure **E** was followed using **2p** (102 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120pa** (85 mg, 62%) as a colorless solid. M. p.: = 96−98 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.60 (dt, J = 1.6, 0.7 Hz, 1H), 7.56–7.49 (m, 1H), 7.32 (dt, J = 8.3, 0.8 Hz, 1H), 6.61 (br s, 1H), 2.98 (d, J = 5.2 Hz, 3H), 2.97 (t, J = 5.8 Hz, 2H), 2.89 (t, J = 5.8 Hz, 2H), 2.11 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 207.9 (C_q), 169.0 (C_q), 142.9 (C_q, $J_{C\text{-}F}$ = 1.7 Hz), 137.2

(C_q), 130.1 (CH), 128.6 (C_q, J_{C-F} = 32.8 Hz), 126.4 (CH, J_{C-F} = 3.7 Hz), 124.3 (CH, J_{C-F} = 3.8 Hz), 123.2 (C_q, J_{C-F} = 271.5 Hz), 44.7 (CH_2), 30.0 (CH_3), 26.9 (CH_2), 26.8 (CH_3).

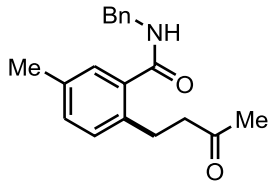
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.6 (s).

IR (ATR): 3286, 1705, 1552, 1311, 1115, 641 cm^{-1}.

MS (EI) m/z (relative intensity) 273 (5) [M^+], 243 (5), 230 (100), 215 (10), 199 (35), 189 (10).

HR-MS (EI) m/z calcd for $C_{13}H_{14}NO_2F_3$ [M^+] 273.0977, found 273.0979.

***N*-Benzyl-5-methyl-2-(3-oxobutyl)benzamide (120qa)**



The general procedure **E** was followed using **2q** (113 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **120qa** (94 mg, 64%) as a colorless solid. M. p.: = 130−132 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.43–7.25 (m, 5H), 7.17 (d, J = 0.9 Hz, 1H), 7.14–7.06 (m, 2H), 6.52 (br s, 1H), 4.60 (d, J = 5.8 Hz, 2H), 3.01 (dt, J = 6.8, 1.5 Hz, 2H),, 2.82 (dt, J = 6.8, 1.5 Hz, 2H), 2.29 (s, 3H), 2.07 (s, 3H).

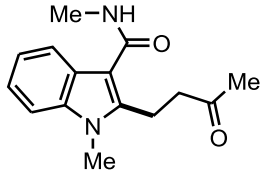
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 208.5 (C_q), 169.9 (C_q), 138.2 (C_q), 136.2 (C_q), 136.0 (C_q), 136.0 (C_q), 130.8 (CH), 129.9 (CH), 128.8 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 45.4 (CH_2), 44.0 (CH_2), 29.9 (CH_3), 26.9 (CH_2), 20.8 (CH_3).

IR (ATR): 3242, 1707, 1634, 1311, 821, 702 cm^{-1}.

MS (EI) m/z (relative intensity) 295 (20) [M^+], 252 (40), 189 (5), 145 (20), 106 (30), 91 (100).

HR-MS (EI) m/z calcd for $C_{19}H_{21}NO_2$ [M^+] 295.1572, found 295.1580.

***N*,1-Dimethyl-2-(3-oxobutyl)-1*H*-indole-3-carboxamide (120ra)**



The general procedure **E** was followed using **2r** (94 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **120ra** (65 mg, 50%) as a colorless solid. M. p.: = 151−153 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.67 (m, 1H), 7.35–7.29 (m, 1H), 7.26–7.15 (m, 2H), 6.08 (br s, 1H), 3.74 (s, 3H), 3.35 (t, *J* = 7.5 Hz, 2H), 3.04 (d, *J* = 4.9 Hz, 3H), 2.93 (t, *J* = 7.5 Hz, 2H),, 2.15 (s, 3H).

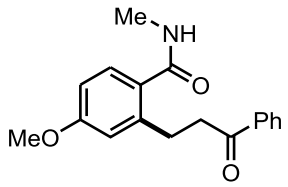
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 207.8 (C_q), 166.6 (C_q), 144.9 (C_q), 136.6 (C_q), 124.8 (C_q), 121.8 (CH), 121.2 (CH), 118.4 (CH), 110.0 (CH), 107.6 (C_q), 43.3 (CH_2), 29.9 (CH_3), 29.6 (CH_3), 26.3 (CH_3), 19.8 (CH_2).

IR (ATR): 3293, 1711, 1619, 1539, 1167, 734 cm^{-1}.

MS (EI) m/z (relative intensity) 258 (55) [M^+], 227 (15), 215 (80), 200 (10), 184 (100), 172 (15), 158 (85).

HR-MS (EI) m/z calcd for $C_{15}H_{18}N_2O_2$ [M^+] 258.1368, found 258.1363.

4-Methoxy-*N*-methyl-2-(3-oxo-3-phenylpropyl)benzamide (120cb)



The general procedure **E** was followed using **2c** (83 mg, 0.5 mmol) and **41b** (132 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120cb** (31 mg, 21%) as a colorless solid. M. p.: = 130−132 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.97–7.88 (m, 2H), 7.51 (ddt, *J* = 8.3, 6.6, 1.4 Hz, 1H), 7.45–7.36 (m, 2H), 7.31 (d, *J* = 8.5 Hz, 1H), 6.77 (d, *J* = 2.6 Hz, 1H), 6.69 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.38 (br s, 1H), 3.75 (s, 3H), 3.42 (t, *J* = 7.3 Hz, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 2.94 (d, *J* = 4.9 Hz, 3H).

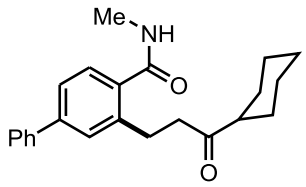
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 199.8 (C_q), 170.4 (C_q), 160.6 (C_q), 141.6 (C_q), 136.8 (C_q), 133.0 (CH), 129.1 (C_q), 128.9 (CH), 128.5 (CH), 128.1 (CH), 115.5 (CH), 111.3 (CH), 55.2 (CH_3), 40.5 (CH_2), 28.1 (CH_2), 26.7 (CH_3).

IR (ATR): 3277, 1681, 1545, 1277, 1039, 690 cm^{-1}.

MS (EI) m/z (relative intensity) 297 (15) [M^+], 266 (10), 223 (10), 192 (100), 177 (30), 161 (35).

HR-MS (ESI) m/z calcd for $C_{18}H_{20}NO_3$ [M+H^+] 298.1443, found 298.1437.

3-(3-Cyclohexyl-3-oxopropyl)-*N*-methyl-[1,1'-biphenyl]-4-carboxamide (120dc)



The general procedure **E** was followed using **2d** (106 mg, 0.5 mmol) and **41c** (138 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **120dc** (79 mg, 45%) as a colorless solid. M. p.: = 155−157 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, J = 7.4 Hz, 2H), 7.50–7.30 (m, 6H), 6.56 (br s, J = 4.9 Hz, 1H), 3.00 (d, J = 4.9 Hz, 3H), 2.99 (t, J = 5.7 Hz, 2H), 2.94 (t, J = 5.7 Hz, 2H), 2.34 – 2.25 (m, 1H), 1.82 – 1.68 (m, 4H), 1.34–1.10 (m, 6H).

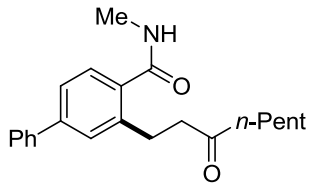
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 213.7 (C_q), 170.3 (C_q), 142.6 (C_q), 140.2 (C_q), 139.6 (C_q), 135.4 (C_q), 128.7 (CH), 128.3 (CH), 127.8 (CH), 127.6 (CH), 127.0 (CH), 124.8 (CH), 50.9 (CH), 42.2 (CH_2), 28.5 (CH_2), 27.3 (CH_2), 26.8 (CH_3), 25.9 (CH_2), 25.7 (CH_2).

IR (ATR): 3289, 2927, 1699, 1630, 1538, 1312, 697 cm^{-1}.

MS (EI) m/z (relative intensity) 349 (20) [M^+], 318 (5), 238 (100), 209 (40), 178 (15), 165 (15).

HR-MS (EI) m/z calcd for $C_{23}H_{27}NO_2$ [M^+] 349.2042, found 249.2039.

***N*-Methyl-3-(3-oxooctyl)-[1,1'-biphenyl]-4-carboxamide (120dd)**



The general procedure **E** was followed using **2d** (106 mg, 0.5 mmol) and **41d** (126 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **120dd** (84 mg, 50%) as a colorless solid. M. p.: = 128−130 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.57–7.50 (m, 2H), 7.46–7.38 (m, 5H), 7.37–7.32 (m, 1H), 6.46 (br s, J = 4.9 Hz, 1H), 3.03 (t, J = 7.2 Hz, 2H), 3.00 (d, J = 4.9 Hz, 3H), 2.90 (t, J = 7.2 Hz, 2H), 2.36 (t, J = 7.5 Hz, 2H), 1.52 (p, J = 7.5 Hz, 2H), 1.31–1.13 (m, 4H), 0.83 (t, J = 7.1 Hz, 3H).

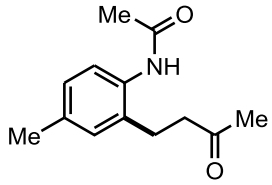
^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 211.1 (C_q), 170.4 (C_q), 142.8 (C_q), 140.2 (C_q), 139.6 (C_q), 135.5 (C_q), 128.8 (CH), 128.5 (CH), 127.9 (CH), 127.7 (CH), 127.1 (CH), 124.9 (CH), 44.2 (CH_2), 43.0 (CH_2), 31.4 (CH_2), 27.3 (CH_2), 26.7 (CH_3), 23.5 (CH_2), 22.4 (CH_2), 13.9 (CH_3).

IR (ATR): 3287, 1710, 1632, 1542, 1164, 693 cm^{-1}.

MS (EI) m/z (relative intensity) 337 (5) [M^+], 281 (25), 238 (100), 223 (5), 207 (35), 178 (15).

HR-MS (EI) m/z calcd for $C_{22}H_{27}NO_2$ [M^+] 337.2042, found 337.2048.

***N*-(4-Methyl-2-(3-oxobutyl)phenyl)acetamide (139aa)**



The general procedure **E** was followed using **121a** (75 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and KO_2CMes (51 mg, 50 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **139aa** (51 mg, 47%) as a colorless solid. M. p.: = 124−126 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.84 (br s, 1H), 7.62 (d, J = 8.2 Hz, 1H), 6.99 (dd, J = 8.0, 2.0 Hz, 1H), 6.89 (d, J = 2.1 Hz, 1H), 2.87 (dt, J = 6.0, 1.5 Hz, 2H), 2.75 (dt, J = 6.0, 1.5 Hz, 2H), 2.26 (s, 3H), 2.24 (s, 3H), 2.12 (s, 3H).

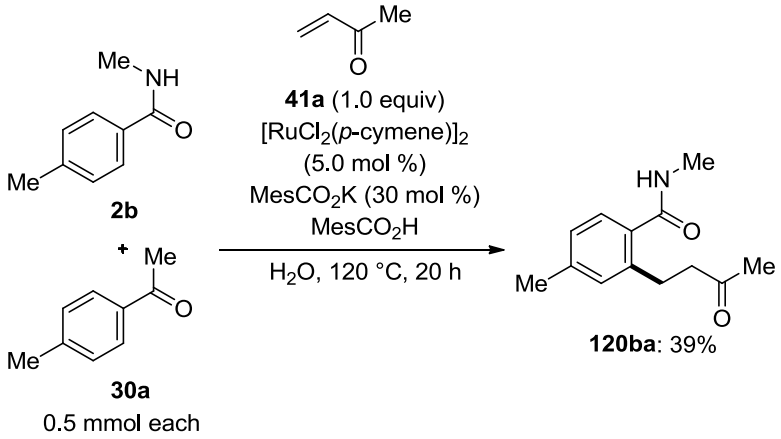
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 210.3 (C_q), 168.8 (C_q), 134.7 (C_q), 133.0 (C_q), 132.6 (C_q), 130.3 (CH), 127.7 (CH), 124.4 (CH), 45.3 (CH_2), 29.9 (CH_3), 24.2 (CH_3), 23.8 (CH_2), 20.8 (CH_3).

IR (ATR): 3282, 1709, 1641, 1522, 1287, 811 cm^{-1}.

MS (EI) m/z (relative intensity) 219 (60) [M^+], 176 (75), 162 (40), 134 (100), 120 (85), 107 (10).

HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_2$ [M^+] 219.1259, found 219.1259.

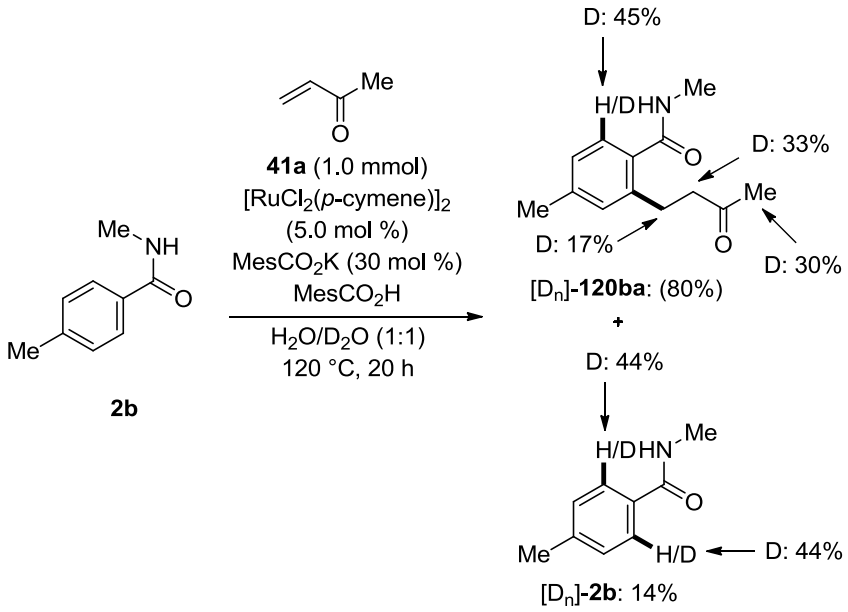
Intermolecular Competition Experiments Between Arenes with Different Directing Groups:



A suspension of MVK (**41a**) (35 mg, 0.5 mmol), *N*,4-dimethylbenzamide (**2b**) (75 mg, 0.5 mmol), 1-(*p*-tolyl)ethanone (**30a**) (67 mg, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30.0 mol %) and $MesCO_2H$ (82 mg, 1.0 equiv) in H_2O (2.0 mL) was stirred at 120 °C for 20 h under an atmosphere of Ar. At ambient temperature, aq. sat. NaCl (15 mL) was added. The reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 1:1) yielded products **120ba** (43 mg, 39%) as the sole product.

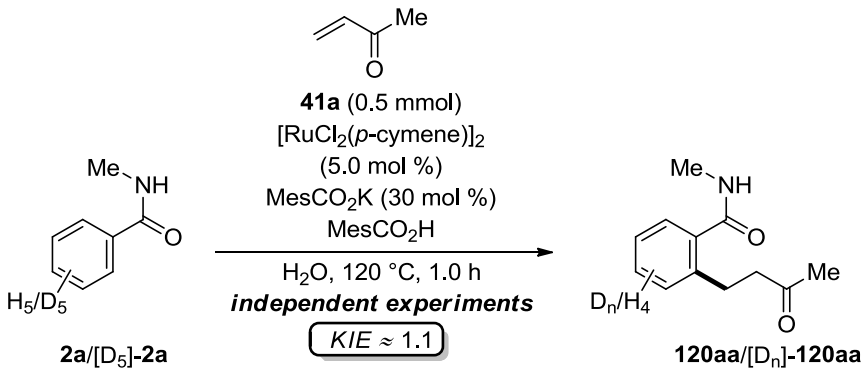
H/D Exchange Experiments:

Ruthenium(II)-Catalyzed H/D Exchange with Substrate III-1b in D_2O as the cosolvent:

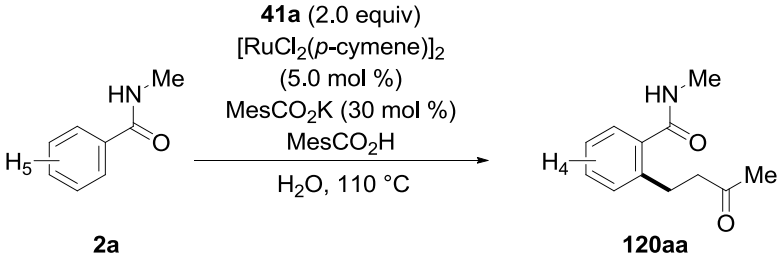


A suspension of MVK (**41a**) (70 mg, 1.0 mmol), *N*,4-dimethylbenzamide (**2b**) (75 mg, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30.0 mol %) and $MesCO_2H$ (82 mg, 1.0 equiv) in a solvent mixture of H_2O and D_2O (1.0/1.0 mL) was stirred at 120 °C for 20 h under an atmosphere of Ar. At ambient temperature, aq. sat. NaCl (15 mL) was added. The reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 1:1→1:2) yielded product [D_n]-**120ba** (88 mg, 80%) as a colorless solid, and reisolated starting material [D_n]-**2b** (11 mg, 14%) as a colorless solid. The D-incorporation in [D_n]-**120ba** and [D_n]-**2b** was estimated by ^{1}H-NMR spectroscopy.

Kinetic Isotope Effect:

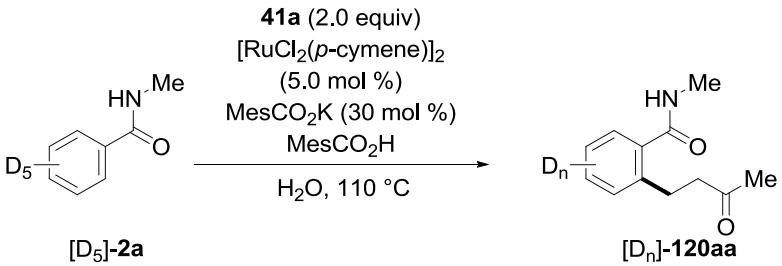


Two independent reactions with **2a** or deuterated substrate [D_5]-**2a** under the standard conditions were performed: Suspensions of MVK (**41a**) (70 mg, 1.0 mmol), substrates **2a** (68 mg, 0.5 mmol) or [D_5]-**2a** (70 mg, 0.5 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30.0 mol %) and $MesCO_2H$ (82 mg, 0.5 mmol) in H_2O (2.0 mL) were stirred at 110 °C for 0.5 h, 1.5 h, 2.0 h, 2.5 h, 3.5 h, 4.5 h, 5.0 h under an atmosphere of argon, respectively. The consumption of substrate **2a** or [D_5]-**2a** and the appearance of the products **120aa** or [D_n]-**120aa** were monitored by GC analysis. These experiments indicated that the C–H bond activation is not the turnover-limiting step of the ruthenium(II)-catalyzed C–H alkylation reaction.



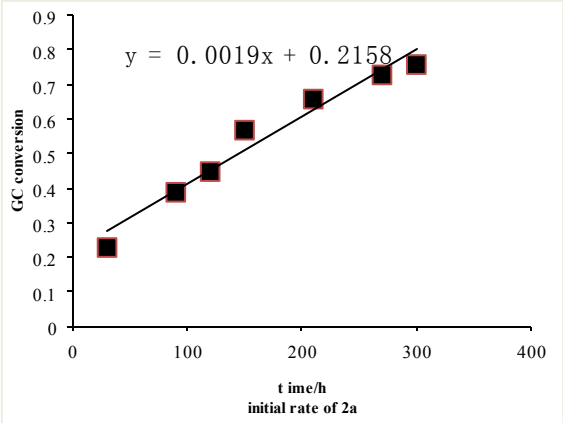
2a **120aa**

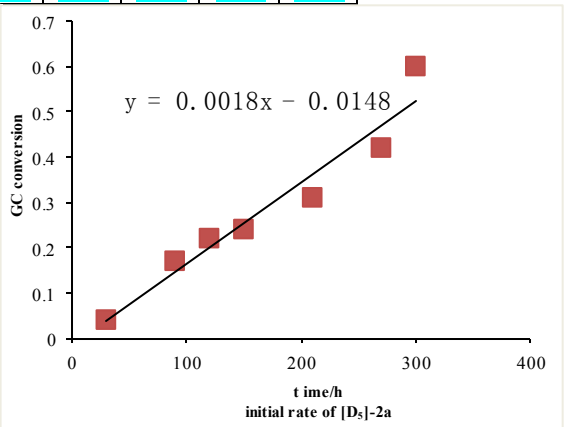
t/(h)	0.5	1.5	2.0	2.5	3.5	4.5	5.0
120aa	0.23	0.39	0.57	0.45	0.66	0.73	0.76
2a	0.77	0.61	0.43	0.55	0.34	0.27	0.24



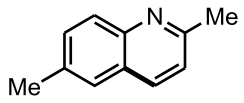
[D_5]-**2a** [D_n]-**120aa**

t/(h)	0.5	1.5	2.0	2.5	3.5	4.5	5.0
[D_n]-**120aa**	0.04	0.17	0.22	0.24	0.31	0.42	0.60
[D_5]-**2a**	0.96	0.83	0.78	0.76	0.69	0.58	0.40





,6-Dimethylquinoline (122aa)



The general procedure **F** was followed using **121a** (75 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **122aa** (52 mg, 66%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.91 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 9.0 Hz, 1H), 7.49 (s, 1H), 7.48 (dd, J = 7.6, 1.8 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 2.69 (s, 3H), 2.48 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.9 (C_q), 146.4 (C_q), 135.5 (CH), 135.3 (C_q), 131.6 (CH), 128.2 (CH), 126.4 (C_q), 126.3 (CH), 121.9 (CH), 25.2 (CH_3), 21.4 (CH_3).

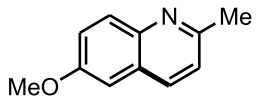
IR (film): 2917, 1601, 1495, 1119, 825, 592 cm^{-1}.

MS (EI) m/z (relative intensity) 157 (100) [M^+], 142 (20), 128 (10), 115 (20), 89 (10), 77 (10).

HR-MS (EI) m/z calcd for $C_{11}H_{11}N$ [M^+] 157.0891, found 157.0884.

The spectral data were in accordance with those reported in the literature.[148]

6-Methoxy-2-methylquinoline (122ba)



The general procedure **F** was followed using **121b** (83 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **III-6ba** (60 mg, 69%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.94–7.90 (m, 1H), 7.89–7.85 (m, 1H), 7.30 (dd, J = 9.2, 2.8 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 2.8 Hz, 1H), 3.88 (s, 3H), 2.67 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 157.1 (C_q), 156.3 (C_q), 143.9 (C_q), 135.0 (CH), 130.0 (CH), 127.3 (C_q), 122.2 (CH), 121.8 (CH), 105.2 (CH), 55.4 (CH_3), 25.0 (CH_3).

IR (ATR): 2937, 1602, 1498, 1229, 1029, 830 cm^{-1}.

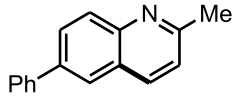
[148] a). Y. Matsubara, S. Hirakawa, Y. Yamaguchi, Z.-i. Yoshida, *Angew. Chem. Int. Ed.*, 2011, **50**, 7670–7673; b) V. Sridharan, C. Avendaño, J. C. Menéndez, *Tetrahedron*, 2007, **63**, 673–681.

MS (EI) m/z (relative intensity) 173 (100) [M^+], 158 (50), 143 (5), 130 (80), 115 (5), 103 (20).

HR-MS (ESI) m/z calcd for $C_{11}H_{12}NO$ [$M+H^+$] 174.0919, found 174.0921.

The spectral data were in accordance with those reported in the literature.[148]

2-Methyl-6-phenylquinoline (122ca)



The general procedure **F** was followed using **121c** (106 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122ca** (57 mg, 52%) as an off white solid. M. p.: = 92−93 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.09 (dd, J = 8.9, 2.1 Hz, 2H), 7.99–7.91 (m, 2H), 7.76–7.65 (m, 2H), 7.50 (d, J = 7.5 Hz, 1H), 7.48 (d, J = 6.6 Hz, 1H), 7.43–7.35 (m, 1H), 7.31 (d, J = 8.4 Hz, 1H), 2.77 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.0 (C_q), 147.3 (C_q), 140.5 (C_q), 138.4 (C_q), 136.3 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 127.5 (CH), 127.4 (CH), 126.6 (C_q), 125.2 (CH), 122.4 (CH), 25.4 (CH_3).

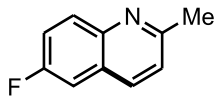
IR (ATR): 2998, 1595, 1488, 1314, 892, 764 cm^{-1}.

MS (EI) m/z (relative intensity) 219 (100) [M^+], 204 (5), 191 (5), 176 (5), 152 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{13}N$ [M^+] 219.1048, found 219.1049.

The spectral data were in accordance with those reported in the literature.[149]

6-Fluoro-2-methylquinoline (122da)



The general procedure **E** was followed using **121d** (77 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122da** (47 mg, 58%) as an off white solid. M. p.: = 51−53 °C.

[149] F. Mongin, L. Mojovic, B. Guillamet, F. Trécourt, G. Quéguiner, *J. Org. Chem*., 2002, **67**, 8991–8994.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.05–7.91 (m, 2H), 7.42 (ddd, J = 9.1, 8.4, 2.8 Hz, 1H), 7.36 (dd, J = 8.9, 2.8 Hz, 1H), 7.27 (dd, J = 8.4, 0.8 Hz, 1H), 2.71 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.9 (C_q, $J_{C\text{-}F}$ = 250.1 Hz), 158.3 (C_q), 144.9 (C_q), 135.5 (CH, $J_{C\text{-}F}$ = 5.1 Hz), 131.0 (CH, $J_{C\text{-}F}$ = 9.0 Hz), 126.9 (C_q, $J_{C\text{-}F}$ = 10.1 Hz), 122.7 (CH), 119.4 (CH, $J_{C\text{-}F}$ = 25.6 Hz), 110.5 (CH, $J_{C\text{-}F}$ = 21.8 Hz), 25.2 (CH_3).

^{19}F-NMR ($CDCl_3$, 282 MHz): δ -115.0 (td, J = 8.6, 5.3 Hz).

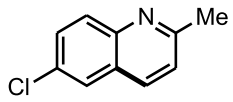
IR (ATR): 3058, 1652, 1439, 1329, 749, 509 cm^{-1}.

MS (EI) m/z (relative intensity) 161 (100) [M^+], 146 (5), 133 (10).

HR-MS (EI) m/z calcd for $C_{10}H_8NF$ [M^+] 161.0641, found 161.0638.

The spectral data were in accordance with those reported in the literature.[148a,150]

6-Chloro-2-methylquinoline (122ea)



The general procedure **F** was followed using **121e** (85 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122ea** (53 mg, 60%) as an off white solid. M. p.: = 95–97 ℃ .

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.9 (d, J = 8.6 Hz, 2H), 7.7 (d, J = 2.4 Hz, 1H), 7.57 (dd, J = 9.0, 2.3 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 2.70 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.3 (C_q), 146.2 (C_q), 135.2 (CH), 131.2 (C_q), 130.2 (CH), 130.2 (CH), 127.0 (C_q), 126.1 (CH), 122.8 (CH), 25.3 (CH_3).

IR (ATR): 3050, 1597, 1468, 1067, 830, 641 cm^{-1}.

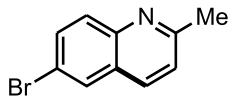
MS (EI) m/z (relative intensity) 177 (100) [M^+], 162 (10), 142 (15), 133 (15), 115 (15), 105 (5).

HR-MS (EI) m/z calcd for $C_{10}H_8NCl$ [M^+] 177.0345, found 177.0341.

The spectral data were in accordance with those reported in the literature.[148a,150]

6-Bromo-2-methylquinoline (122fa)

[150] C. Ramesh, V. Kavala, C.-W. Kuo, C.-F. Yao, *Tetrahedron Lett.*, 2010, **51**, 5234–5237.



The general procedure **F** was followed using **121f** (107 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122fa** (56 mg, 51%) as an off white solid. M. p.: = 98−100 °C .

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.95–7.90 (m, 1H), 7.89 (d, J = 2.2 Hz, 1H), 7.87–7.82 (m, 1H), 7.71 (dd, J = 9.0, 2.2 Hz, 1H), 7.27 (d, J = 8.5 Hz, 1H), 2.70 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.5 (C_q), 146.4 (C_q), 135.1 (CH), 132.8 (CH), 130.4 (CH), 129.5 (CH), 127.6 (C_q), 122.8 (CH), 119.3 (C_q), 25.4 (CH_3).

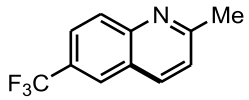
IR (ATR): 3048, 1594, 1488, 1300, 1071, 828 cm^{-1}.

MS (EI) m/z (relative intensity) 221 (100) [M^+], 205 (5), 142 (20), 115 (30).

HR-MS (EI) m/z calcd for $C_{10}H_8N^{79}Br$ [M^+] 220.9840, found 220.9838.

The spectral data were in accordance with those reported in the literature.[148a,150]

2-Methyl-6-(trifluoromethyl)quinoline (122ga)



The general procedure **F** was followed using **121g** (101 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122ga** (30 mg, 28%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.21–8.04 (m, 3H), 7.83 (dd, J = 8.8, 2.1 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 2.77 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.5 (C_q), 148.9 (C_q), 136.8 (CH), 129.8 (CH), 127.6 (C_q, $J_{C\text{-}F}$ = 32.5 Hz), 124.1 (C_q, $J_{C\text{-}F}$ = 273.3 Hz), 125.5 (CH, $J_{C\text{-}F}$ = 4.4 Hz), 125.4 (C_q), 125.1 (CH, $J_{C\text{-}F}$ = 3.2 Hz), 123.2 (CH), 25.5 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.2 (s).

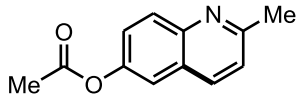
IR (ATR): 1605, 1484, 1291, 1109, 903, 705 cm^{-1}.

MS (EI) m/z (relative intensity) 211 (100) [M^+], 193 (5), 168 (5).

HR-MS (ESI) m/z calcd for $C_{11}H_9NF_3$ [M+H$^+$] 212.0687, found 212.0687.

The spectral data were in accordance with those reported in the literature.[151]

2-Methylquinolin-6-yl acetate (**122ha**)



The general procedure **F** was followed using **121h** (97 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **122ha** (51 mg, 51%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.99 (d, = 8.8 Hz, 1H), 7.96 (d, = 8.5 Hz, 1H), 7.48 (d, J = 2.5 Hz, 1H), 7.38 (dd, J = 9.0, 2.6 Hz, 1H), 7.28–7.22 (m, 1H), 2.71 (s, 3H), 2.32 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.4 (C_q), 158.8 (C_q), 147.8 (C_q), 145.8 (C_q), 135.8 (CH), 130.1 (CH), 126.6 (C_q), 124.4 (CH), 122.5 (CH), 118.1 (CH), 25.2 (CH_3), 21.1 (CH_3).

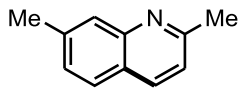
IR (ATR): 1713, 1598, 1504, 1429, 1234, 832 cm^{-1}.

MS (EI) m/z (relative intensity) 201 (5) [M$^+$], 159 (100), 130 (10), 103 (5).

HR-MS (EI) m/z calcd for $C_{12}H_{11}NO_2$ [M$^+$] 201.0790, found 201.0789.

The spectral data were in accordance with those reported in the literature.[152]

2,7-Dimethylquinoline (**122ia**)



The general procedure **F** was followed using **121i** (75 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122ia** (49 mg, 62%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 0.8 Hz, 1H), 7.63 (d, J = 8.3 Hz, 1H), 7.29 (dd, J = 8.3, 1.7 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 2.70 (s, 3H), 2.52 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.9 (C_q), 148.1 (C_q), 139.6 (C_q), 135.8 (CH), 127.8 (CH),

[151] K. K. H. Chandrashekarappa, K. M. Mahadevan, K. B. Manjappa, *Tetrahedron Letters* **2013**, *54*, 1368–1370.
[152] K. Jyothish, R. R. Avirah, D. Ramaiah, *Org. Lett.* **2006**, *8*, 111–114.

127.7 (CH), 127.1 (CH), 124.5 (C_q), 121.1 (CH), 25.3 (CH_3), 21.9 (CH_3).

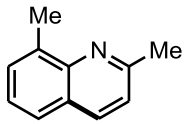
IR (ATR): 2916, 1601, 1505, 1305, 835, 776 cm^{-1}.

MS (EI) m/z (relative intensity) 157 (100) [M^+], 142 (20), 128 (5), 115 (15), 89 (5).

HR-MS (EI) m/z calcd for $C_{11}H_{11}N$ [M^+] 157.0891, found 157.0889.

The spectral data were in accordance with those reported in the literature.[148a]

2,8-Dimethylquinoline (122ja)



The general procedure **E** was followed using **121j** (75 mg, 0.5 mmol) and methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122ja** (27 mg, 34%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, J = 8.4 Hz, 1H), 7.59 (d, J = 8.4, 1H), 7.51 (ddd, J = 7.0, 1.6, 0.9 Hz, 1H), 7.34 (dd, J = 8.0, 7.0 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 2.80 (s, 3H), 2.75 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 157.8 (C_q), 146.9 (C_q), 136.5 (C_q), 136.2 (CH), 129.4 (CH), 126.3 (C_q), 125.4 (CH), 125.2 (CH), 121.6 (CH), 25.6 (CH_3), 17.9 (CH_3).

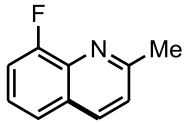
IR (ATR): 2919, 1604, 1500, 1424, 829, 758 cm^{-1}.

MS (EI) m/z (relative intensity) 157 (100) [M^+], 142 (20), 128 (5), 115 (15), 89 (5).

HR-MS (EI) m/z calcd for $C_{11}H_{11}N$ [M^+] 157.0891, found 157.0883.

The spectral data were in accordance with those reported in the literature.[149]

8-Fluoro-2-methylquinoline (122ka)



The general procedure **F** was followed using **121k** (77 mg, 0.5 mmol), methyl vinyl ketone (**41a**) (70 mg, 1.0 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **122ka** (24 mg, 30%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.03 (dd, J = 8.5, 1.6 Hz, 1H), 7.58–7.48 (m, 1H), 7.44–7.34 (m, 2H), 7.32 (d, J = 8.6 Hz, 1H), 2.77 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.5 (C_q, $J_{C\text{-}F}$ = 1.6 Hz), 157.6 (C_q, $J_{C\text{-}F}$ = 255.3 Hz), 138.0 (C_q, $J_{C\text{-}F}$ = 11.2 Hz), 135.8 (CH, $J_{C\text{-}F}$ = 3.2 Hz), 128.1 (C_q, $J_{C\text{-}F}$ = 2.7 Hz), 125.3 (CH, $J_{C\text{-}F}$ = 8.0 Hz), 123.1 (CH, $J_{C\text{-}F}$ = 4.8 Hz), 123.0 (CH), 113.5 (CH, $J_{C\text{-}F}$ = 19.2 Hz), 25.5 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -126.4 (ddd, J = 9.9, 5.3, 1.6 Hz).

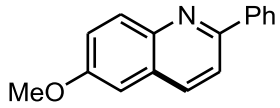
IR (ATR): 3057, 1606, 1503, 1234, 1081, 831 cm^{-1}.

MS (EI) m/z (relative intensity) 161 (100) [M^+], 146 (10), 132 (5).

HR-MS (EI) m/z calcd for $C_{10}H_8NF$ [M^+] 161.0641, found 161.0645.

The spectral data were in accordance with those reported in the literature.[151]

6-Methoxy-2-phenylquinoline (122bb)



The general procedure **F** was followed using **121b** (83 mg, 0.5 mmol), **41b** (132 mg, 1.0 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **122bb** (33 mg, 28%) as a colorless solid. M. p.: = 129−131 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.15–8.00 (m, 4H), 7.81 (d, J = 8.6 Hz, 1H), 7.62–7.46 (m, 2H), 7.46–7.41 (m, 1H), 7.37 (dd, J = 9.2, 2.8 Hz, 1H), 7.07 (d, J = 2.8 Hz, 1H), 3.93 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 157.6 (C_q), 155.0 (C_q), 144.3 (C_q), 139.8 (C_q), 135.5 (CH), 131.2 (CH), 128.9 (CH), 128.8 (CH), 128.1 (C_q), 127.2 (CH), 122.3 (CH), 119.2 (CH), 105.0 (CH), 55.5 (CH_3).

IR (ATR): 1596, 1490, 1227, 1020, 831, 699 cm^{-1}.

MS (EI) m/z (relative intensity) 235 (100) [M^+], 220 (35), 192 (60), 165 (5).

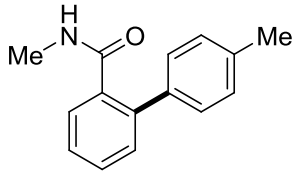
HR-MS (EI) m/z calcd for $C_{16}H_{13}NO$ [M^+] 235.0997, found 235.1000.

The spectral data were in accordance with those reported in the literature.[153]

[153] K. A. Reynolds, D. J. Young, W. A. Loughlin, *Synthesis* **2010**, 3645–3648.

10.4.4 Analytically Data for the Products of Cobalt-Catalyzed Direct Arylation of Aromatic Amides

***N*,4'-Dimethylbiphenyl-2-carboxamide (139aa)**



The general procedure **G** was followed using **2a** (68 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h (or 0.5 h). Purification by column chromatography (*n*-hexane/EtOAc 10:1→2:1) yielded **139aa** (88 mg, 78%) and **139aa'** (14 mg, 9%) as colorless solids, (or 81 mg, 72% yield of **139aa** as the sole product). **139aa**: M. p.: = 108−110 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.67 (ddd, J = 7.5, 1.6, 0.6 Hz, 1H), 7.49–7.40 (m, 1H), 7.40–7.35 (m, 1H), 7.33 (ddd, J = 7.2, 1.6, 0.6 Hz, 1H), 7.28 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 5.20 (s, 1H), 2.67 (d, J = 5.0 Hz, 3H), 2.37 (s, 3H).

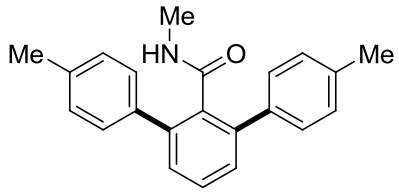
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.3 (C_q), 139.3 (C_q), 137.5 (C_q), 137.1 (C_q), 135.5 (C_q), 130.1 (CH), 130.1 (CH), 129.3 (CH), 128.8 (CH), 128.5 (CH), 127.3 (CH), 26.7 (CH_3), 21.2 (CH_3).

IR (ATR): 3252, 2921, 1625, 1564, 1020, 801 cm^{-1}.

MS (EI) m/z (relative intensity) 225 (40) [M^+], 208 (15), 195 (100), 165 (50), 152 (45), 115 (5).

HR-MS (EI) m/z calcd for $C_{15}H_{15}NO$ [M^+] 225.1154, found 225.1160.

***N*,4,4''-Trimethyl-[1,1':3',1''-terphenyl]-2'-carboxamide (139aa')**



M. p.: = 223−225 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.43 (dd, J = 8.3, 7.0 Hz, 1H), 7.34 (d, J = 8.1 Hz, 4H), 7.31 (dd, J = 7.7, 0.6 Hz, 2H), 7.20–7.15 (m, 4H), 5.21 (s, 1H), 2.49 (d, J = 5.0 Hz, 3H), 2.36 (s, 6H).

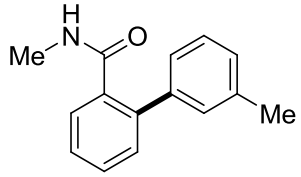
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 169.9 (C_q), 140.0 (C_q), 137.5 (C_q), 137.0 (C_q), 135.6 (C_q), 128.9 (CH), 128.9 (CH), 128.9 (CH), 128.3 (CH), 26.6 (CH_3), 21.3 (CH_3).

IR (ATR): 3253, 2921, 1625, 1564, 1020, 801 cm^{-1}.

MS (EI) m/z (relative intensity) 315 (40) [M^+], 298 (5), 285 (100), 267 (10), 242 (20), 226 (10).

HR-MS (EI) m/z calcd for $C_{22}H_{21}NO$ [M^+] 315.1623, found 315.1615.

***N*,3'-Dimethylbiphenyl-2-carboxamide (139ab)**



The general procedure **G** was followed using **2a** (68 mg, 0.5 mmol) and 3-chlorotoluene (**88b**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→2:1) yielded **139ab** (73 mg, 65%) as a colorless solid. M. p.: = 144−146 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.67 (dd, J = 7.4, 1.5 Hz, 1H), 7.46–7.31 (m, 3H), 7.27 (d, J = 7.4 Hz, 1H), 7.20–7.14 (m, 3H), 5.20 (s, 1H), 2.66 (d, J = 5.1 Hz, 3H), 2.37 (s, 3H).

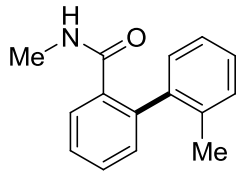
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.1 (C_q), 140.0 (C_q), 139.3 (C_q), 138.2 (C_q), 135.5 (C_q), 130.0 (CH), 129.9 (CH), 129.2 (CH), 128.8 (CH), 128.4 (CH), 128.4 (CH), 127.4 (CH), 125.6 (CH), 26.7 (CH_3), 21.5 (CH_3).

IR (ATR): 3284, 1632, 1313, 757, 700, 449 cm^{-1}.

MS (EI) m/z (relative intensity) 225 (35) [M^+], 208 (10), 195 (100), 165 (50), 152 (45), 115 (5).

HR-MS (EI) m/z calcd for $C_{15}H_{15}NO$ [M^+] 225.1154, found 225.1157.

***N*,2'-Dimethylbiphenyl-2-carboxamide (139ac)**



The general procedure **G** was followed using **2a** (68 mg, 0.5 mmol) and 2-chlorotoluene (**88c**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→2:1) yielded **139ac** (62 mg, 55%) as a colorless solid. M. p.: = 95−96 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.92–7.88 (m, 1H), 7.52–7.37 (m, 2H), 7.32–7.22 (m, 3H), 7.20–7.12 (m, 2H), 5.22 (s, 1H), 2.60 (d, J = 4.9 Hz, 3H), 2.09 (s, 3H).

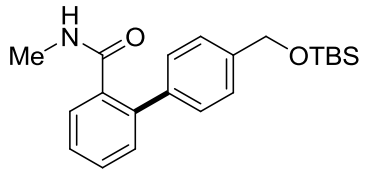
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 168.7 (C_q), 140.1 (C_q), 139.0 (C_q), 136.0 (C_q), 134.7 (C_q), 130.3 (CH), 130.2 (CH), 130.2 (CH), 129.2 (CH), 129.0 (CH), 128.1 (CH), 127.6 (CH), 126.1 (CH), 26.7 (CH_3), 20.1 (CH_3).

IR (ATR): 3318, 1629, 1548, 1310, 755, 467 cm^{-1}.

MS (EI) m/z (relative intensity) 225 (15) [M^+], 210 (20), 195 (100), 165 (50), 152 (25), 139 (5).

HR-MS (EI) m/z calcd for $C_{15}H_{15}NO$ [M^+] 225.1154, found 225.1152.

4'-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-*N*-methyl-[1,1'-biphenyl]-2-carboxamide (139ad)



The general procedure **G** was followed using **2a** (68 mg, 0.5 mmol) and *tert*-butyl{(4-chlorobenzyl)oxy}dimethylsilane (**88d**) (154 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→2:1) yielded **139ad** (102 mg, 57%) as a colorless solid. M. p.: = 91−93 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.68 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 7.44 (td, *J* = 7.5, 1.5 Hz, 1H), 7.38 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.36 (s, 4H), 7.34 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 5.16 (d, *J* = 5.0 Hz, 1H), 4.77 (s, 2H), 2.65 (d, *J* = 5.0 Hz, 3H), 0.93 (s, 9H), 0.09 (s, 6H).

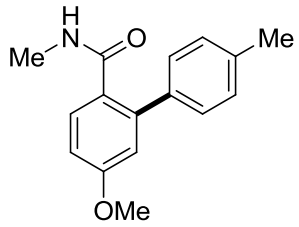
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.3 (C_q), 141.1 (C_q), 139.2 (C_q), 138.7 (C_q), 135.6 (C_q), 130.1 (CH), 130.1 (CH), 128.9 (CH), 128.5 (CH), 127.5 (CH), 126.2 (CH), 64.7 (CH_2), 26.7 (CH_3), 25.9 (CH_3), 18.4 (C_q), -5.2 (CH_3).

IR (ATR): 3304, 2929, 1630, 1252, 834, 759 cm^{-1}.

MS (EI) m/z (relative intensity) 355 (5) [M^+], 340 (5), 298 (100), 224 (35), 195 (10), 165 (20).

HR-MS (ESI) m/z calcd for $C_{21}H_{30}NO_2Si$ [M+H^+] 356.2046, found 356.2040.

5-Methoxy-*N*,4'-dimethylbiphenyl-2-carboxamide (139ca)



The general procedure **G** was followed using **2c** (83 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→3:2) yielded **139ca** (72 mg, 56%) as a colorless solid. M. p.: = 128−129 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.6 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 6.88 (dd, J = 8.6, 2.6 Hz, 1H), 6.80 (d, J = 2.6 Hz, 1H), 5.15 (s, 1H), 3.82 (s, 3H), 2.64 (d, J = 4.9 Hz, 3H), 2.37 (s, 3H).

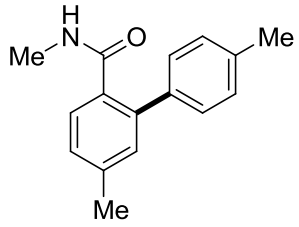
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 169.6 (C_q), 160.5 (C_q), 141.1 (C_q), 137.6 (C_q), 137.2 (C_q), 130.8 (CH), 129.2 (CH), 128.4 (CH), 127.8 (C_q), 115.3 (CH), 112.7 (CH), 55.4 (CH_3), 26.7 (CH_3), 21.2 (CH_3).

IR (ATR): 3304, 1633, 1536, 1287, 1179, 824 cm^{-1}.

MS (EI) m/z (relative intensity) 255 (35) [M^+], 238 (5), 225 (100), 210 (5), 182 (15), 165 (10).

HR-MS (EI) m/z calcd for $C_{16}H_{17}NO_2$ [M^+] 255.1259, found 255.1263.

N,4',5-Trimethylbiphenyl-2-carboxamide (139ba)



The general procedure **G** was followed using **2b** (75 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→2:1) yielded **139ba** (78 mg, 65%) as a colorless solid. M. p.: = 137−139 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 8.1 Hz, 2H), 7.21–7.10 (m, 4H), 5.16 (d, J = 5.0 Hz, 1H), 2.66 (d, J = 4.9 Hz, 3H), 2.38 (s, 3H), 2.37 (s, 3H).

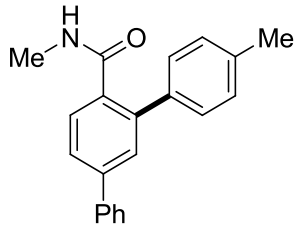
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.3 (C_q), 140.2 (C_q), 139.3 (C_q), 137.4 (C_q), 137.3 (C_q), 132.6 (C_q), 130.8 (CH), 129.2 (CH), 129.0 (CH), 128.5 (CH), 128.1 (CH), 26.7 (CH_3), 21.3 (CH_3), 21.2 (CH_3).

IR (ATR): 3243, 1627, 1563, 1322, 841, 519 cm^{-1}.

MS (EI) m/z (relative intensity) 239 (40) [M^+], 222 (10), 209 (100), 181 (15), 165 (45), 152 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{17}NO$ [M^+] 239.1310, found 239.1302.

***N*,4''-Dimethyl-[1,1':3',1''-terphenyl]-4'-carboxamide (139da)**



The general procedure **G** was followed using **2d** (106 mg, 0.5 mmol), 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol), $Co(acac)_2$ (12.9 mg, 10 mol %) and ICyHCl (13.5 mg, 10 mol %) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→3:2) yielded **139da** (102 mg, 68%) as a colorless solid. M. p.: = 170−172 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.0 Hz, 1H), 7.64–7.57 (m, 3H), 7.55 (d, J = 1.8 Hz, 1H), 7.43 (ddd, J = 7.7, 6.7, 1.2 Hz, 2H), 7.39–7.35 (m, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.26–7.21 (m, 2H), 5.28 (d, J = 4.9 Hz, 1H), 2.70 (d, J = 4.9 Hz, 3H), 2.39 (s, 3H).

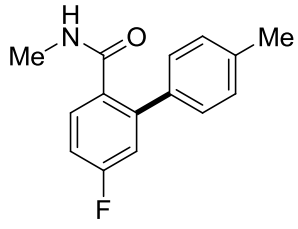
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 169.9 (C_q), 142.8 (C_q), 140.0 (C_q), 139.7 (C_q), 137.6 (C_q), 137.1 (C_q), 134.1 (C_q), 129.4 (CH), 129.3 (CH), 128.8 (CH), 128.8 (CH), 128.5 (CH), 127.8 (CH), 127.1 (CH), 125.9 (CH), 26.7 (CH_3), 21.3 (CH_3).

IR (ATR): 3301, 1639, 1530, 1304, 757, 719 cm^{-1}.

MS (EI) m/z (relative intensity) 301 (40) [M^+], 284 (10), 271 (100), 241 (10), 228 (30), 165 (10).

HR-MS (EI) m/z calcd for $C_{21}H_{19}NO$ [M^+] 301.1467, found 301.1460.

5-Fluoro-*N*,4'-dimethylbiphenyl-2-carboxamide (139sa)



The general procedure **G** was followed using **2s** (77 mg, 0.5 mmol), 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol), $Co(acac)_2$ (12.9 mg, 10 mol %) and ICyHCl (13.5 mg, 10 mol %) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1→1:1) yielded **139sa** (64 mg, 53%) as a colorless solid. M. p.: = 144−145 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.70 (dd, J = 8.4, 6.0 Hz, 1H), 7.29 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.11–7.02 (m, 2H), 5.17 (s, 1H), 2.68 (d, J = 4.8 Hz, 3H), 2.40 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.2 (C_q), 163.1 (C_q, $J_{C\text{-}F}$ = 250.0 Hz), 141.8 (C_q, $J_{C\text{-}F}$ = 8.3 Hz), 138.1 (C_q), 136.0 (C_q, $J_{C\text{-}F}$ = 1.8 Hz), 131.5 (C_q, $J_{C\text{-}F}$ = 3.2 Hz), 131.2 (CH, $J_{C\text{-}F}$ = 9.0 Hz), 129.4 (CH), 128.3 (CH), 116.7 (CH, $J_{C\text{-}F}$ = 22.1 Hz), 114.3 (CH, $J_{C\text{-}F}$ = 22.1 Hz), 26.8 (CH_3), 21.3 (CH_3).

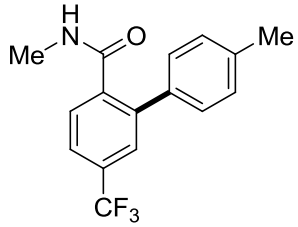
^{19}F-NMR ($CDCl_3$, 376 MHz): δ -110.4 – -110.5 (m).

IR (ATR): 3243, 1630, 1557, 1176, 835, 607 cm^{-1}.

MS (EI) m/z (relative intensity) 243 (5) [M^+], 213 (20), 183 (5), 165 (5), 58 (25), 43 (100).

HR-MS (EI) m/z calcd for $C_{15}H_{14}NFO$ [M^+] 243.1059, found 243.1065.

***N*,4'-Dimethyl-5-(trifluoromethyl)biphenyl-2-carboxamide (139fa)**



The general procedure **G** was followed using **2f** (102 mg, 0.5 mmol), 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol), $Co(acac)_2$ (12.9 mg, 10 mol %) and ICyHCl (13.5 mg, 10 mol %) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 6:1→2:1) yielded **139fa** (93 mg, 63%) as a colorless solid. M. p.: = 157−159 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.74 (d, J = 8.6 Hz, 1H), 7.61 (d, J = 8.6 Hz, 1H), 7.60 (s, 1H), 7.29 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 5.31 (s, 1H), 2.69 (d, J = 4.9 Hz, 3H), 2.38 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 168.9 (C_q), 139.9 (C_q), 138.6 (C_q), 138.3 (C_q), 135.6 (C_q), 131.9 (C_q, $J_{C\text{-}F}$ = 32.8 Hz), 129.5 (CH), 129.3 (CH), 128.3 (CH), 126.9 (CH, $J_{C\text{-}F}$ = 7.5 Hz), 124.0 (CH, $J_{C\text{-}F}$ = 7.5 Hz), 123.5 (C_q, $J_{C\text{-}F}$ = 271.9 Hz), 26.8 (CH_3), 21.3 (CH_3).

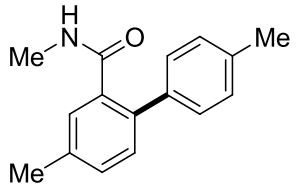
^{19}F-NMR (376 MHz, $CDCl_3$): δ = -62.9 (s).

IR (ATR): 3280, 1643, 1335, 1117, 814, 545 cm^{-1}.

MS (EI) m/z (relative intensity) 293 (35) [M^+], 263 (100), 235 (10), 215 (20), 165 (30).

HR-MS (EI) m/z calcd for $C_{16}H_{14}NOF_3$ [M^+] 293.1027, found 293.1034.

***N*,4,4'-Trimethylbiphenyl-2-carboxamide (139oa)**



The general procedure **G** was followed using **2o** (75 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **139oa** (93 mg, 78%) as a colorless solid. M. p.: = 144−146 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.48 (s, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 8.2 Hz, 2H), 5.18 (s, 1H), 2.66 (d, J = 4.9 Hz, 3H), 2.37 (s, 3H), 2.36 (s, 3H).

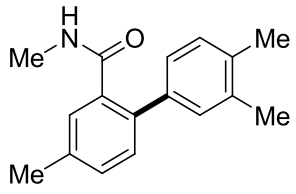
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.5 (C_q), 137.3 (C_q), 137.2 (C_q), 137.1 (C_q), 136.4 (C_q), 135.3 (C_q), 130.8 (CH), 130.1 (CH), 129.4 (CH), 129.2 (CH), 128.5 (CH), 26.6 (CH_3), 21.1 (CH_3), 20.9 (CH_3).

IR (ATR): 3320, 1633, 1533, 1309, 810, 531 cm^{-1}.

MS (EI) m/z (relative intensity) 239 (45) [M^+], 222 (10), 209 (100), 181 (15), 165 (50), 152 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{17}NO$ [M^+] 239.1310, found 239.1308.

***N*,3',4,4'-Tetramethylbiphenyl-2-carboxamide (139oe)**



The general procedure **G** was followed using **2o** (75 mg, 0.5 mmol) and 4-chloro-1,2-dimethylbenzene (**88e**) (84 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **139oe** (82 mg, 64%) as a colorless solid. M. p.: = 123−125 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.77–7.71 (m, 1H), 7.29–7.26 (m, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.07 (dd, J = 7.5, 1.4 Hz, 1H), 7.05 (d, J = 7.7 Hz, 1H), 6.98 (s, 1H), 5.24 (s, 1H), 2.60 (d, J = 4.9 Hz, 3H), 2.40 (s, 3H), 2.32 (s, 3H), 2.03 (s, 3H).

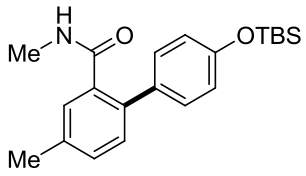
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 168.9 (C_q), 139.9 (C_q), 137.3 (C_q), 136.2 (C_q), 135.6 (C_q), 134.2 (C_q), 133.0 (C_q), 131.0 (CH), 130.2 (CH), 130.2 (CH), 129.8 (CH), 129.8 (CH), 128.7 (CH), 26.8 (CH_3), 21.1 (CH_3), 21.0 (CH_3), 19.5 (CH_3).

IR (ATR): 3281, 1634, 1551, 1319, 823, 468 cm^{-1}.

MS (EI) m/z (relative intensity) 253 (40) [M^+], 238 (70), 222 (100), 208 (15), 195 (50), 179 (55).

HR-MS (EI) m/z calcd for $C_{17}H_{19}NO$ [M^+] 253.1467, found 253.1473.

4'-{(*tert*-Butyldimethylsilyl)oxy}-*N*,4-dimethyl-[1,1'-biphenyl]-2-carboxamide (139of)



The general procedure **G** was followed using **2o** (75 mg, 0.5 mmol) and *tert*-butyl(4-chlorophenoxy)dimethylsilane (**88f**) (145 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **139of** (125 mg, 70%) as a colorless solid. M. p.: = 70–72 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.49 (d, J = 1.5 Hz, 1H), 7.23–7.21 (m, 4H), 6.85 (dd, J = 8.6, 0.6 Hz, 2H), 5.10 (d, J = 5.0 Hz, 1H), 2.65 (d, J = 5.0 Hz, 3H), 2.37 (d, J = 0.7 Hz, 3H), 0.98 (s, 9H), 0.20 (s, 6H).

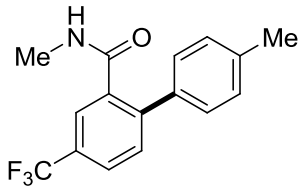
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.5 (C_q), 155.4 (C_q), 137.1 (C_q), 136.1 (C_q), 135.3 (C_q), 133.1 (C_q), 130.8 (CH), 129.9 (CH), 129.8 (CH), 129.5 (CH), 120.2 (CH), 26.6 (CH_3), 25.7 (CH_3), 20.9 (CH_3), 18.3 (C_q), -4.4 (CH_3).

IR (ATR): 3251, 2930, 1621, 1254, 911, 777 cm^{-1}.

MS (EI) m/z (relative intensity) 355 (45) [M^+], 298 (35), 267 (100), 239 (5), 211 (5), 165 (10).

HR-MS (EI) m/z calcd for $C_{21}H_{29}NO_2Si$ [M^+] 355.1968, found 355.1960.

***N*,4'-Dimethyl-4-(trifluoromethyl)biphenyl-2-carboxamide (139pa)**



The general procedure **G** was followed using **2p** (102 mg, 0.5 mmol) 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol), $Co(acac)_2$ (12.9 mg, 10 mol %) and ICyHCl (13.5 mg, 10 mol %) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **139pa** (78 mg, 53%) as a colorless solid. M. p.: = 161−163 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.31 (d, J = 7.9 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 5.26 (s, 1H), 2.72 (d, J = 4.8 Hz, 3H), 2.41 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 168.7 (C_q), 142.7 (C_q), 138.4 (C_q), 136.0 (C_q), 135.7 (C_q), 130.6 (CH), 129.6 (C_q, $J_{C\text{-}F}$ = 32.6 Hz), 129.5 (CH), 128.3 (CH), 126.6 (CH, $J_{C\text{-}F}$ = 7.2 Hz), 126.0 (CH, $J_{C\text{-}F}$ = 7.2 Hz), 123.7 (C_q, $J_{C\text{-}F}$ = 272.4 Hz), 26.8 (CH_3), 21.3 (CH_3).

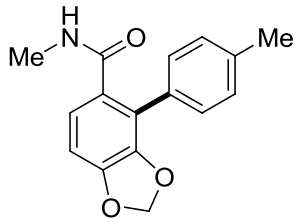
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -62.7 (s).

IR (ATR): 3241, 1633, 1364, 1263, 1125, 825 cm^{-1}.

MS (EI) m/z (relative intensity) 293 (30) [M^+], 263 (100), 249 (5), 235 (10), 215 (20), 165 (35).

HR-MS (EI) m/z calcd for $C_{16}H_{14}NOF_3$ [M^+] 293.1027, found 293.1027.

***N*-Methyl-4-*p*-tolylbenzo[*d*][1,3]dioxole-5-carboxamide (139ma)**



general procedure **G** was followed using **2m** (90 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→2:1) yielded **139ma** (93 mg, 59%) and **139ma'** (23 mg, 17%) as colorless solids. **IV-5ia**: M. p.: = 166−168 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 7.9 Hz, 1H), 7.21 (d, J = 8.1 Hz, 2H), 6.79 (d, J = 7.9 Hz, 1H), 5.97 (s, 2H), 5.25 (s, 1H), 2.63 (d, J = 4.9 Hz, 3H), 2.36 (s, 3H).

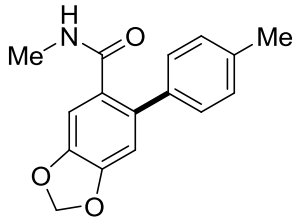
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 168.9 (C_q), 148.6 (C_q), 145.2 (C_q), 138.0 (C_q), 130.5 (C_q), 129.5 (C_q), 129.2 (CH), 129.0 (CH), 123.5 (CH), 121.4 (C_q), 107.3 (CH), 101.3 (CH_2), 26.7 (CH_3), 21.3 (CH_3).

IR (ATR): 3238, 1637, 1443, 1243, 830, 526 cm^{-1}.

MS (EI) m/z (relative intensity) 269 (55) [M^+], 252 (10), 239 (100), 209 (20), 181 (40), 153 (35).

HR-MS (EI) m/z calcd for $C_{16}H_{15}NO_3$ [M^+] 269.1052, found 269.1050.

***N*-Methyl-6-*p*-tolylbenzo[*d*][1,3]dioxole-5-carboxamide (139ma')**



M. p.: = 190−192 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.22 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 8.2 Hz, 3H), 7.18 (s, 1H), 6.00 (s, 2H), 5.07 (d, J = 4.9 Hz, 1H), 2.61 (d, J = 4.9 Hz, 3H), 2.36 (s, 3H).

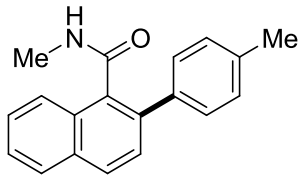
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 169.4 (C_q), 148.9 (C_q), 146.9 (C_q), 137.4 (C_q), 137.0 (C_q), 134.3 (C_q), 129.2 (CH), 129.2 (C_q), 128.5 (CH), 109.9 (CH), 109.1 (CH), 101.6 (CH_2), 26.8 (CH_3), 21.2 (CH_3).

IR (ATR): 3341, 1635, 1480, 1232, 820, 577 cm^{-1}.

MS (EI) m/z (relative intensity) 269 (100) [M^+], 252 (25), 239 (100), 224 (10), 209 (55), 181 (60).

HR-MS (ESI) m/z calcd for $C_{16}H_{16}NO_3$ [M+H^+] 270.1130, found 270.1127.

***N*-Methyl-2-(*p*-tolyl)-1-naphthamide (139la)**



The general procedure **G** was followed using **2l** (93 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **139la** (78 mg, 57%) as a colorless solid. M. p.: = 196−198 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.08–7.97 (m, 1H), 7.90–7.87 (d, J = 8.8 Hz, 1H), 7.86–7.82 (m, 1H), 7.57–7.46 (m, 3H), 7.46–7.43 (m, 2H), 7.25–7.21 (m, 2H), 5.40 (d, J = 5.0 Hz, 1H), 2.77 (d, J = 5.0 Hz, 3H), 2.39 (s, 3H).

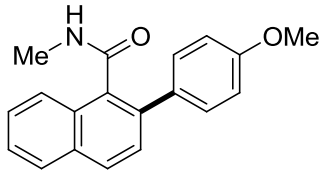
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.3 (C_q), 137.4 (C_q), 137.4 (C_q), 136.3 (C_q), 133.3 (C_q), 132.4 (C_q), 130.4 (C_q), 129.4 (CH), 129.2 (CH), 128.6 (CH), 127.9 (CH), 127.5 (CH), 127.2 (CH), 126.2 (CH), 125.6 (CH), 26.8 (CH_3), 21.2 (CH_3).

IR (ATR): 3280, 1632, 1538, 1292, 811, 548 cm^{-1}.

MS (EI) m/z (relative intensity) 275 (50) [M^+], 258 (5), 245 (100), 230 (5), 215 (25), 202 (55).

HR-MS (EI) m/z calcd for $C_{19}H_{17}NO$ [M^+] 275.1310, found 275.1305.

2-(4-Methoxyphenyl)-*N*-methyl-1-naphthamide (139lg)



The general procedure **G** was followed using **2l** (93 mg, 0.5 mmol) and 1-chloro-4-methoxybenzene (**88g**) (85 mg, 0.6 mmol) for 0.5 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **139lg** (81 mg, 56%) as a colorless solid. M. p.: = 190−191 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 8.5, 1.6 Hz, 1H), 7.61–7.37 (m, 5H), 6.95 (d, J = 8.5 Hz, 2H), 5.45 (d, J = 5.1 Hz, 1H), 3.83 (s, 3H), 2.77 (d, J = 5.1 Hz, 3H).

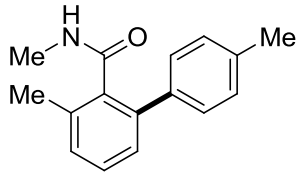
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.3 (C_q), 159.1 (C_q), 135.8 (C_q), 133.0 (C_q), 132.6 (C_q), 132.1 (C_q), 130.4 (C_q), 129.8 (CH), 129.3 (CH), 127.8 (CH), 127.4 (CH), 127.1 (CH), 126.1 (CH), 125.4 (CH), 113.9 (CH), 55.3 (CH_3), 26.8 (CH_3).

IR (ATR): 3288, 1633, 1541, 1243, 820, 555 cm^{-1}.

MS (EI) m/z (relative intensity) 291 (60) [M^+], 274 (5), 261 (100), 218 (15), 202 (10), 189 (35).

HR-MS (EI) m/z calcd for $C_{19}H_{17}NO_2$ [M^+] 291.1259, found 291.1264.

***N*,3,4'Trimethylbiphenyl-2-carboxamide (139ta)**



The general procedure **G** was followed using **2t** (75 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **139ta** (64 mg, 54%) as a colorless solid. M. p.: = 185−186 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 7.6 Hz, 1H), 7.20–7.14 (m, 4H), 5.23 (d, J = 6.0 Hz, 1H), 2.64 (d, J = 4.9 Hz, 3H), 2.39 (s, 3H), 2.35 (s, 3H).

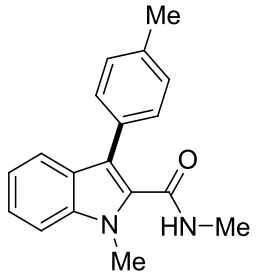
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.6 (C_q), 138.9 (C_q), 137.4 (C_q), 137.0 (C_q), 136.2 (C_q), 135.6 (C_q), 129.0 (CH), 129.0 (CH), 128.8 (CH), 128.2 (CH), 127.1 (CH), 26.5 (CH_3), 21.2 (CH_3), 19.6 (CH_3).

IR (ATR): 3228, 1625, 1543, 786, 710, 543 cm^{-1}.

MS (EI) m/z (relative intensity) 239 (65) [M^+], 224 (10), 209 (100), 195 (5), 181 (20), 165 (65).

HR-MS (ESI) m/z calcd for $C_{16}H_{18}NO$ [$M+H^+$] 240.1388, found 240.1380.

***N*,1-Dimethyl-3-*p*-tolyl-1*H*-indole-2-carboxamide (139ua)**



The general procedure **G** was followed using **2u** (94 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **139ua** (100 mg, 72%) as a colorless solid. M. p.: = 167−169 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, J = 8.1 Hz, 1H), 7.41–7.38 (m, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.31 (dd, J = 8.1, 1.2 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 7.12 (dd, J = 8.1, 1.2 Hz, 1H), 5.64 (s, 1H), 4.02 (s, 3H), 2.77 (d, J = 5.1 Hz, 3H), 2.42 (s, 3H).

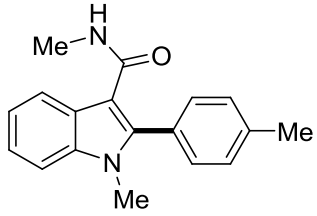
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.2 (C_q), 137.7 (C_q), 136.9 (C_q), 130.7 (C_q), 129.9 (CH), 129.5 (CH), 129.1 (C_q), 126.2 (C_q), 124.1 (CH), 120.6 (CH), 120.4 (CH), 118.2 (C_q), 109.9 (CH), 31.6 (CH_3), 26.4 (CH_3), 21.3 (CH_3).

IR (ATR): 3242, 1639, 1567, 1365, 751, 517 cm^{-1}.

MS (EI) m/z (relative intensity) 278 (100) [M^+], 262 (5), 248 (30), 233 (15), 221 (15), 204 (20).

HR-MS (EI) m/z calcd for $C_{18}H_{18}N_2O$ [M^+] 278.1419, found 278.1414.

***N*,1-Dimethyl-2-*p*-tolyl-1*H*-indole-3-carboxamide (139ra)**



The general procedure **G** was followed using **2r** (94 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **139ra** (80 mg, 58%) as a colorless solid. M. p.: = 170−171 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.36 (d, J = 7.3 Hz, 1H), 7.35 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 7.31 (m, 1H), 7.29 (dd, J = 6.8, 1.5 Hz, 1H), 7.26 (m, 1H), 5.24 (s, 1H), 3.49 (s, 3H), 2.73 (d, J = 4.7 Hz, 3H), 2.46 (s, 3H).

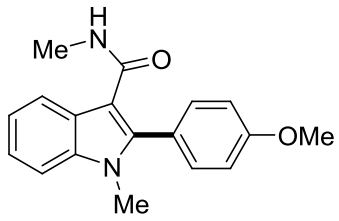
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.0 (C_q), 140.9 (C_q), 139.8 (C_q), 136.6 (C_q), 130.4 (CH), 129.8 (CH), 127.9 (C_q), 127.0 (C_q), 122.6 (CH), 122.0 (CH), 121.5 (CH), 109.3 (CH), 108.9 (C_q), 30.6 (CH_3), 26.0 (CH_3), 21.4 (CH_3).

IR (ATR): 3338, 1623, 1524, 1222, 750, 511 cm^{-1}.

MS (EI) m/z (relative intensity) 278 (30) [M^+], 248 (100), 233 (5), 218 (5), 204 (10), 190 (5).

HR-MS (EI) m/z calcd for $C_{18}H_{18}N_2O$ [M^+] 278.1419, found 278.1422.

2-(4-Methoxyphenyl)-*N*,1-dimethyl-*1H*-indole-3-carboxamide (139rg)



The general procedure **G** was followed using **2r** (94 mg, 0.5 mmol) and 1-chloro-4-methoxybenzene (**88g**) (85 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded **139rg** (87 mg, 59%) as a colorless solid. M. p.: = 146−147 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.41–8.30 (m, 1H), 7.36 (d, J = 8.7 Hz, 2H), 7.33–7.19 (m, 3H), 7.06 (d, J = 8.7 Hz, 2H), 5.28 (s, 1H), 3.89 (s, 3H), 3.49 (s, 3H), 2.74 (d, J = 4.8 Hz, 3H).

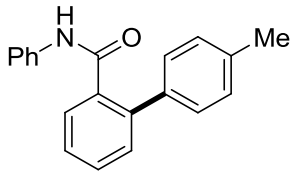
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.9 (C_q), 160.4 (C_q), 140.6 (C_q), 136.5 (C_q), 131.8 (CH), 126.9 (C_q), 122.8 (C_q), 122.6 (CH), 121.9 (CH), 121.5 (CH), 114.5 (CH), 109.2 (CH), 108.8 (C_q), 55.4 (CH_3), 30.6 (CH_3), 26.1 (CH_3).

IR (ATR): 3338, 1619, 1542, 1247, 752, 531 cm^{-1}.

MS (EI) m/z (relative intensity) 294 (45) [M^+], 264 (100), 249 (5), 234 (5), 221 (5), 192 (10).

HR-MS (ESI) m/z calcd for $C_{18}H_{19}N_2O_2$ [$M+H^+$] 295.1447, found 295.1445.

4'-Methyl-*N*-phenylbiphenyl-2-carboxamide (139va)



The general procedure **G** was followed using **2v** (99 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **139va** (103 mg, 72%) as a colorless solid. M. p.: = 154−155 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.86 (dd, J = 7.5, 1.5 Hz, 1H), 7.64–7.37 (m, 3H), 7.35 (d, J = 8.1 Hz, 2H), 7.24–7.16 (m, 4H), 7.11 (dd, J = 8.1, 1.5 Hz, 2H), 7.08–6.98 (m, 1H), 6.92 (s, 1H), 2.37 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.0 (C_q), 139.5 (C_q), 137.9 (C_q), 137.5 (C_q), 136.9 (C_q), 135.1 (C_q), 130.6 (CH), 130.3 (CH), 129.6 (CH), 129.5 (CH), 128.7 (CH), 128.6 (CH), 127.6 (CH), 124.2 (CH), 119.8 (CH), 21.2 (CH_3).

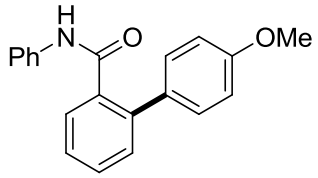
IR (ATR): 3058, 1652, 1439, 1329, 749, 509 cm^{-1}.

MS (EI) m/z (relative intensity) 287 (35) [M^+], 195 (100), 165 (40), 152 (40).

HR-MS (EI) m/z calcd for $C_{20}H_{17}NO$ [M^+] 287.1310, found 287.1304.

The spectral data were in accordance with those reported in the literature.[154]

4'-Methoxy-*N*-phenylbiphenyl-2-carboxamide (139vg)



The general procedure **G** was followed using **2v** (99 mg, 0.5 mmol) and 1-chloro-4-methoxybenzene (**88g**) (85 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **139vg** (112 mg, 74%) as a colorless solid. M.p.: = 146−148 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84 (dd, J = 7.5, 1.4 Hz, 1H), 7.53–7.37 (m, 5H), 7.25–7.13 (m, 4H), 7.07–7.01 (m, 1H), 6.97–6.91 (d, J = 8.8 Hz, 3H), 3.81 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.3 (C_q), 159.5 (C_q), 139.1 (C_q), 137.6 (C_q), 135.1 (C_q), 132.1 (C_q), 130.6 (CH), 130.4 (CH), 130.0 (CH), 129.4 (CH), 128.8 (CH), 127.4 (CH), 124.3 (CH), 119.9 (CH), 114.4 (CH), 55.4 (CH_3).

IR (ATR): 3238, 1653, 1434, 1238, 755, 526 cm^{-1}.

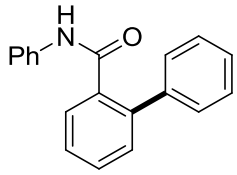
[154] S. E. Havlik, J. M. Simmons, V. J. Winton, J. B. Johnson, *J. Org. Chem*. **2011**, *76*, 3588–3593.

MS (EI) m/z (relative intensity) 303 (20) [M^+], 211 (100), 196 (5), 183 (5), 168 (20), 152 (5).

HR-MS (EI) m/z calcd for $C_{20}H_{17}NO_2$ [M^+] 303.1259, found 303.1260.

The spectral data were in accordance with those reported in the literature.[154]

***N*-Phenyl-[1,1'-biphenyl]-2-carboxamide (139vh)**



The general procedure **G** was followed using **2v** (99 mg, 0.5 mmol) and chlorobenzene (**88h**) (67 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) and recrystallization (*n*-hexane/EtOAc) yielded **139vh** (78 mg, 57%) as a colorless solid. M. p.: = 111−113 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, J = 7.2, 1.6 Hz, 1H), 7.60–7.37 (m, 8H), 7.22 (d, J = 8.5 Hz, 1H), 7.19 (d, J = 7.2 Hz, 1H), 7.13–6.95 (m, 3H), 6.88 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.9 (C_q), 139.8 (C_q), 139.4 (C_q), 137.4 (C_q), 135.2 (C_q), 130.6 (CH), 130.2 (CH), 129.5 (CH), 128.9 (CH), 128.7 (CH), 128.7 (CH), 128.0 (CH), 127.8 (CH), 124.3 (CH), 119.8 (CH).

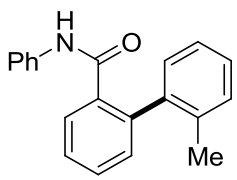
IR (ATR): 3331, 1664, 1516, 1433, 741, 688 cm^{-1}.

MS (EI) m/z (relative intensity) 273 (50) [M^+], 181 (100), 152 (60), 127 (5).

HR-MS (EI) m/z calcd for $C_{19}H_{15}NO$ [M^+] 273.1154, found 273.1153.

The spectral data were in accordance with those reported in the literature.[154]

2'-Methyl-*N*-phenylbiphenyl-2-carboxamide (139vc)



The general procedure **G** was followed using **2v** (99 mg, 0.5 mmol) and 2-chlorotoluene (**88c**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **139vc** (118 mg, 82%) as a colorless solid. M. p.: = 134−136 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.12 (dd, J = 7.1, 2.0 Hz, 1H), 7.57–7.48 (m, 2H), 7.41–7.30 (m, 4H), 7.26 (dd, J = 7.3, 2.1 Hz, 1H), 7.20 (d, J = 7.3 Hz, 1H), 7.17 (d, J = 7.1 Hz, 1H), 7.10 (s, 1H), 7.01 (d, J = 6.9 Hz, 2H), 7.00–6.98 (m, 1H), 2.11 (s, 3H).

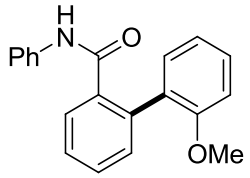
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.5 (C_q), 139.9 (C_q), 138.9 (C_q), 137.5 (C_q), 136.5 (C_q), 134.2 (C_q), 130.9 (CH), 130.8 (CH), 130.4 (CH), 130.1 (CH), 129.2 (CH), 128.7 (CH), 128.6 (CH), 128.0 (CH), 126.6 (CH), 124.1 (CH), 119.6 (CH), 20.1 (CH_3).

IR (ATR): 3063, 1647, 1546, 1329, 752, 512 cm^{-1}.

MS (EI) m/z (relative intensity) 287 (5) [M^+], 195 (100), 165 (20), 152 (15), 93 (25).

HR-MS (EI) m/z calcd for $C_{20}H_{17}NO$ [M^+] 287.1310, found 287.1308.

2'-Methoxy-*N*-phenylbiphenyl-2-carboxamide (139vi)



The general procedure **G** was followed using **2v** (99 mg, 0.5 mmol) and 1-chloro-2-methoxybenzene (**88i**) (85 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **139vi** (99 mg, 65%) as a colorless solid. M. p.: = 139−141 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.90 (dd, J = 7.3, 1.8 Hz, 1H), 7.59–7.42 (m, 2H), 7.41–7.27 (m, 4H), 7.24–7.12 (m, 4H), 7.08 (td, J = 7.5, 1.1 Hz, 1H), 7.05–6.98 (m, 1H), 6.90 (dd, J = 8.2, 1.0 Hz, 1H), 3.65 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.7 (C_q), 156.2 (C_q), 137.8 (C_q), 137.8 (C_q), 135.9 (C_q), 135.7 (C_q), 130.9 (CH), 130.6 (CH), 130.6 (CH), 129.8 (CH), 128.9 (CH), 128.7 (CH), 127.8 (CH), 123.9 (CH), 121.2 (CH), 119.4 (CH), 111.0 (CH), 55.6 (CH_3).

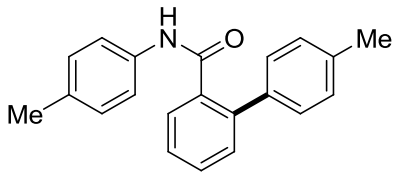
IR (ATR): 3237, 1653, 1434, 1238, 756, 515 cm^{-1}.

MS (EI) m/z (relative intensity) 303 (5) [M^+], 272 (10), 211 (100), 196 (20), 168 (10), 139 (10).

HR-MS (EI) m/z calcd for $C_{20}H_{17}NO_2$ [M^+] 303.1259, found 303.1255.

The spectral data were in accordance with those reported in the literature.[154]

4'-Methyl-*N*-*p*-tolylbiphenyl-2-carboxamide (139wa)



The general procedure **G** was followed using **2w** (105 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **139wa** (120 mg, 80%) as a colorless solid. M. p.: = 134−136 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (dd, J = 7.5, 1.5 Hz, 1H), 7.55–7.45 (m, 2H), 7.42–7.39 (m, 1H), 7.37 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.03 (s, 4H), 6.91 (s, 1H), 2.39 (s, 3H), 2.28 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.0 (C_q), 139.4 (C_q), 137.8 (C_q), 136. 9 (C_q), 135.2 (C_q), 134.9 (C_q), 133.9 (C_q), 130.4 (CH), 130.2 (CH), 129.5 (CH), 129.4 (CH), 129.2 (CH), 128.6 (CH), 127.5 (CH), 119. 9 (CH), 21.2 (CH_3), 20.9 (CH_3).

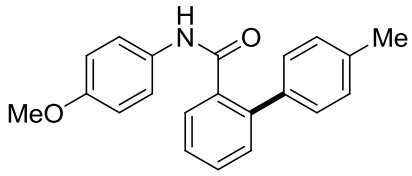
IR (ATR): 3044, 1649, 1510, 1327, 755, 510 cm^{-1}.

MS (EI) m/z (relative intensity) 301 (15) [M^+], 285 (5), 195 (100), 165 (20), 152 (20).

HR-MS (EI) m/z calcd for $C_{21}H_{19}NO$ [M^+] 301.1467, found 301.1478.

The spectral data were in accordance with those reported in the literature.[155]

***N*-(4-Methoxyphenyl)-4'-methyl-[1,1'-biphenyl]-2-carboxamide (139xa)**



The general procedure **G** was followed using **2x** (114 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **139xa** (115 mg, 72%) as a colorless solid. M. p.: = 152−154 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.84 (ddd, J = 7.6, 1.6, 0.5 Hz, 1H), 7.50 (td, J = 7.5, 1.5 Hz, 1H), 7.43 (td, J = 7.5, 1.5 Hz, 1H), 7.38 (ddd, J = 7.6, 1.5, 0.5 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H),

[155] U. A. Shah, N. K. Wagh,.H. S. Deokar, S. S. Kadam, V. M. Kulkarni, *Int. J. Pharm. Bio Sci*. **2010**, *1*, 501–511.

7.22 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 6.81 (s, 1H), 6.75 (d, J = 9.0 Hz, 2H), 3.74 (s, 3H), 2.38 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.0 (C_q), 156.3 (C_q), 139.4 (C_q), 137.8 (C_q), 137.0 (C_q), 135.2 (C_q), 130.7 (C_q), 130.4 (CH), 130.2 (CH), 129.5 (CH), 129.4 (CH), 128.6 (CH), 127.5 (CH), 121.7 (CH), 113.9 (CH), 55.5 (CH_3), 21.5 (CH_3).

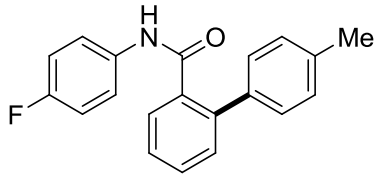
IR (ATR): 3250, 1650, 1506, 1239, 836, 515 cm^{-1}.

MS (EI) m/z (relative intensity) 317 (40) [M^+], 195 (100), 165 (30), 152 (35), 122 (5).

HR-MS (EI) m/z calcd for $C_{21}H_{19}NO_2$ [M^+] 317.1416, found 317.1408.

The spectral data were in accordance with those reported in the literature.[155]

***N*-(4-Fluorophenyl)-4'-methylbiphenyl-2-carboxamide (139ya)**



The general procedure **G** was followed using **2y** (108 mg, 0.5 mmol) and 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **139ya** (134 mg, 88%) as a colorless solid. M. p.: = 160−162 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84 (dd, J = 7.5, 1.6 Hz, 1H), 7.54–7.38 (m, 3H), 7.34 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.07–7.03 (m, 2H), 6.93–6.87 (m, 3H), 2.39 (s, 3H), 2.38 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.1 (C_q), 159.3 (C_q, $J_{C\text{-}F}$ = 243.0 Hz), 139.4 (C_q), 137.9 (C_q), 136.9 (C_q), 134.9 (C_q), 133.5 (C_q, $J_{C\text{-}F}$ = 2.7 Hz), 130.6 (CH), 130.3 (CH), 129.6 (CH), 129.5 (CH), 128.6 (CH), 127.6 (CH), 121.6 (CH, $J_{C\text{-}F}$ = 7.9 Hz), 115.4 (CH, $J_{C\text{-}F}$ = 22.5 Hz), 21.2 (CH_3).

^{19}F-NMR ($CDCl_3$, 282 MHz): δ -117.9 – -118.0 (m).

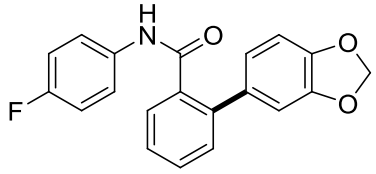
IR (ATR): 3026, 1650, 1505, 1212, 755, 514 cm^{-1}.

MS (EI) m/z (relative intensity) 305 (20) [M^+], 267 (5), 239 (5), 195 (100), 165 (40), 152 (40).

HR-MS (EI) m/z calcd for $C_{20}H_{16}NFO$ [M^+] 305.1216, found 305.1209.

The spectral data were in accordance with those reported in the literature.[155]

2-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-(4-fluorophenyl)benzamide (139zj)



The general procedure **G** was followed using **2z** (108 mg, 0.5 mmol) and 5-chlorobenzo[*d*][1,3]dioxole (**88j**) (94 mg, 0.6 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **139zj** (92 mg, 55%) as a colorless solid. M. p.: = 123−125 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.80 (dd, J = 7.5, 1.5 Hz, 1H), 7.63–7.40 (m, 2H), 7.38 (dd, J = 7.5, 1.5 Hz, 1H), 7.18 (m, 2H), 7.03 (br s, 1H), 7.00–6.81 (m, 5H), 5.98 (s, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.2 (C_q), 159.3 (C_q, J_{C-F} = 245.4 Hz), 148.0 (C_q), 147.5 (C_q), 139.0 (C_q), 135.0 (C_q), 133.7 (C_q), 133.5 (C_q, J_{C-F} = 2.8 Hz), 130.6 (CH), 130.2 (CH), 129.2 (CH), 127.6 (CH), 122.2 (CH), 121.7 (CH, J_{C-F} = 7.9 Hz), 115.5 (CH, J_{C-F} = 22.6 Hz), 109.2 (CH), 108.6 (CH), 101.3 (CH_2).

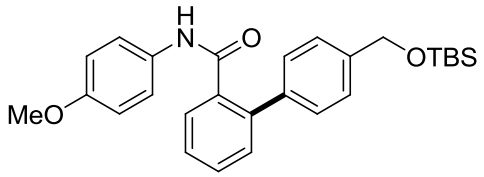
^{19}F-NMR (376 MHz, $CDCl_3$): δ = -117.7 – -117.8 (m).

IR (ATR): 3235, 1646, 1505, 1223, 761, 517 cm^{-1}.

MS (EI) m/z (relative intensity) 335 (40) [M^+], 278 (40), 248 (15), 225 (40), 195 (100), 167 (40).

HR-MS (EI) m/z calcd for $C_{20}H_{14}NO_3$ [M^+] 335.0958, found 335.0962.

4'-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-*N*-(4-methoxyphenyl)-[1,1'-biphenyl]-2-carboxamide (139xd)



The general procedure **G** was followed using **2x** (114 mg, 0.5 mmol) and *tert*-butyl{(4-chlorobenzyl)oxy}dimethylsilane (**88d**) (154 mg, 0.6 mmol) for 16 h (or 0.5 h).

Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **139xd** (143 mg, 64%; or 152 mg, 68%) as a colorless solid. M. p.: = 97–99 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.84 (ddd, J = 7.6, 1.5, 0.5 Hz, 1H), 7.50 (td, J = 7.5, 1.5 Hz, 1H), 7.46–7.41 (m, 3H), 7.41–7.36 (m, 3H), 7.00 (d, J = 8.9 Hz, 2H), 6.80 (s, 1H), 6.74 (d, J = 9.0 Hz, 2H), 4.76 (t, J = 0.8 Hz, 2H), 3.73 (s, 3H), 0.93 (s, 9H), 0.09 (s, 6H).

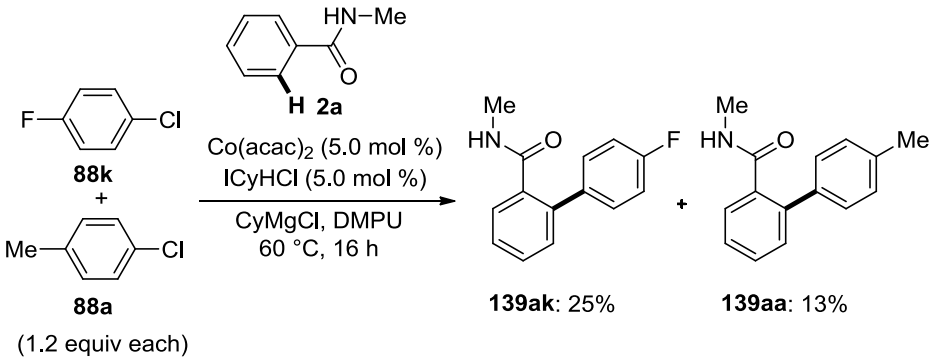
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.1 (C_q), 156.5 (C_q), 141.4 (C_q), 139.3 (C_q), 138.5 (C_q), 135.4 (C_q), 130.6 (C_q), 130.5 (CH), 130.3 (CH), 129.5 (CH), 128.7 (CH), 127.7 (CH), 126.5 (CH), 121.8 (CH), 114.0 (CH), 64.6 (CH_2), 55.4 (CH_3), 25.9 (CH_3), 18.4 (C_q), -5.3 (CH_3).

IR (ATR): 3312, 2928, 1646, 1509, 1243, 1087, 823 cm^{-1}.

MS (EI) m/z (relative intensity) 447 (20) [M$^+$], 390 (100), 375 (5), 316 (15), 195 (10), 165 (30).

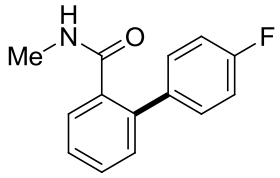
HR-MS (EI) m/z calcd for $C_{27}H_{33}NO_3Si$ [M$^+$] 447.2230, found 447.2223.

a) Intermolecular Competition Experiment between Substrates 88k and 88a:



A suspension of *N*-methylbenzamide (**2a**) (68 mg, 0.5 mmol), 4-chlorotoluene (**88a**) (76 mg, 0.6 mmol), 1-chloro-4-fluorobenzene (**88k**) (78 mg, 0.6 mmol), $Co(acac)_2$ (6.5 mg, 5.0 mol %), and ICyHCl (**140g**) (6.8 mg, 5.0 mol %) in DMPU (1.0 mL) was stirred for 5 min at 0 °C. To this mixture, a 1.0 M solution of CyMgCl in THF (1.5 mL, 3.0 equiv) was added dropwise at the same temperature. The reaction mixture was stirred at 60 °C for 16 h under an atmosphere of Ar. At ambient temperature, aq. sat. NH_4Cl solution (2.0 mL) and H_2O (15 mL) were added, and the resulting mixture was extracted with MTBE (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 3:2→2:1) yielded **139ak** (29 mg, 25%) and **139aa** (15 mg, 13%) as colorless solids.

4'-Fluoro-*N*-methyl-[1,1'-biphenyl]-2-carboxamide (139ak)



M. p.: = 131−133 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.61 (ddd, J = 7.4, 1.6, 0.5 Hz, 1H), 7.45 (td, J = 7.4, 1.6 Hz, 1H), 7.41–7.33 (m, 3H), 7.33–7.29 (m, 1H), 7.08 (t, J = 8.7 Hz, 2H), 5.26 (s, 1H), 2.69 (d, J = 4.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.0 (C_q), 162.3 (C_q, $J_{C\text{-}F}$ = 246.9 Hz), 138.2 (C_q), 136.0 (C_q, $J_{C\text{-}F}$ = 3.4 Hz), 135.8 (C_q), 130.1 (CH, $J_{C\text{-}F}$ = 8.1 Hz), 130.0 (CH), 130.0 (CH), 128.5 (CH), 127.6 (CH), 115.5 (CH, $J_{C\text{-}F}$ = 21.4 Hz), 26.7 (CH_3).

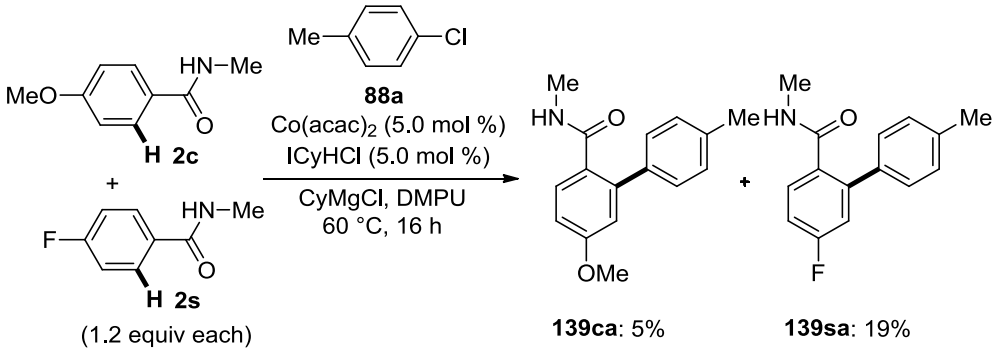
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -114.49 – -114.62 (m).

IR (ATR): 3320, 1633, 1533, 1309, 810, 531 cm^{-1}.

MS (EI) m/z (relative intensity) 229 (30) [M^+], 212 (5), 199 (100), 170 (55), 151 (10).

HR-MS (EI) m/z calcd for $C_{14}H_{12}NFO$ [M^+] 229.0903, found 229.0906.

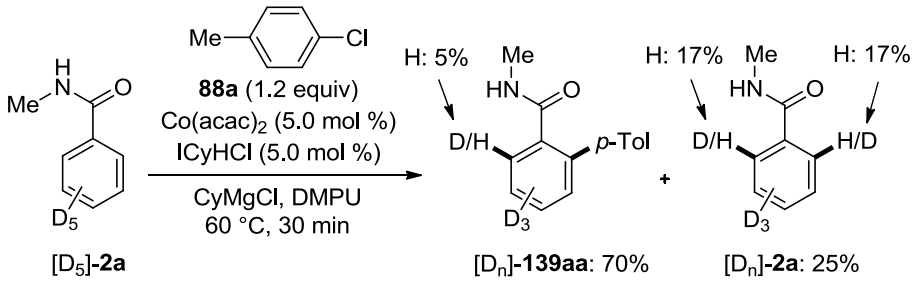
b) Intermolecular Competition Experiment between Substrates 2c and 2s:



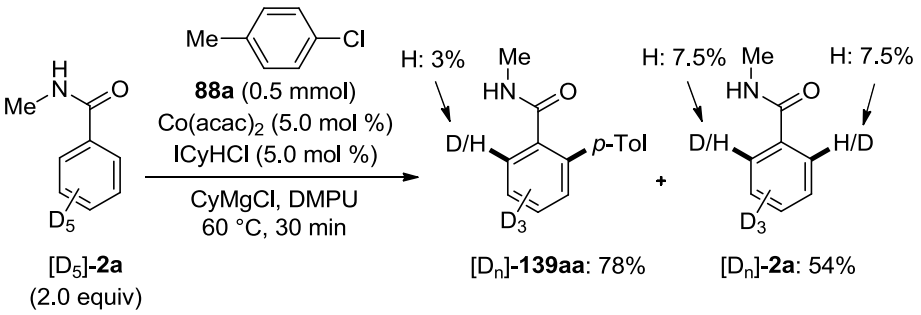
A suspension of 4-methoxy-*N*-methylbenzamide (**2c**) (99 mg, 0.6 mmol), 4-fluoro-*N*-methylbenzamide (**2s**) (92 mg, 0.6 mmol), 4-chlorotoluene (**88a**) (63 mg, 0.5 mmol), $Co(acac)_2$ (6.5 mg, 5.0 mol %), and ICyHCl (**140g**) (6.8 mg, 5.0 mol %) in DMPU (1.0 mL) was stirred for 5 min at 0 °C. To this mixture, a 1.0 M solution of CyMgCl in THF (2.2 mL, 4.4 equiv) was added dropwise at the same temperature. Then the reaction mixture

was stirred at 60 °C for 16 h under an atmosphere of Ar. At ambient temperature, aq. sat. NH_4Cl solution (2.0 mL) and H_2O (15 mL) were added and the reaction mixture was extracted with MTBE (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 2:1→1:1) yielded **139ca** (6 mg, 5%) and **139sa** (23 mg, 19%) as colorless solids.

Cobalt-Catalyzed H/D Exchange in Substrate [D_5]-2a under the Standard Reaction Conditions:

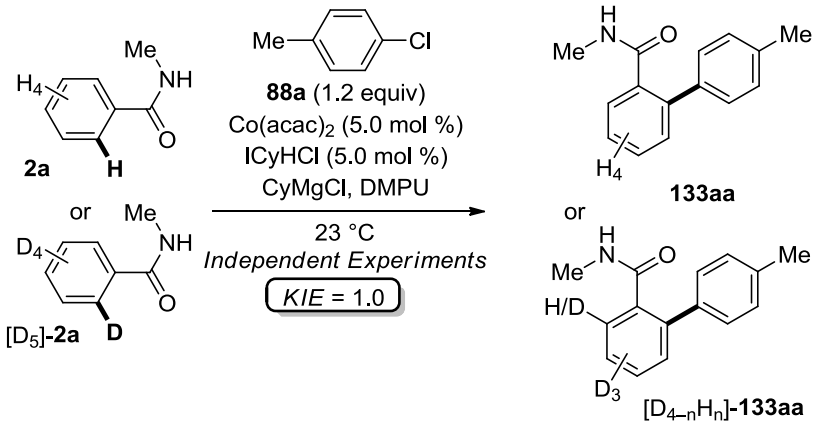


A suspension of $Co(acac)_2$ (6.5 mg, 5.0 mol %), ICyHCl (**140g**) (6.8 mg, 5.0 mol %), [D_5]-**2a** (70 mg, 0.5 mmol) and DMPU (1.0 mL) was stirred for 5 min at 0 °C. To this mixture, a 1.0 M solution of CyMgCl in THF (1.5 mL, 3.0 equiv) was added dropwise at the same temperature followed by 4-chlorotoluene **88a** (76 mg, 1.2 equiv). Then the reaction mixture was stirred at 60 °C for 30 min under an atmosphere of Ar. At ambient temperature, aq. sat. NH_4Cl solution (2.0 mL) and H_2O (15 mL) were added. The reaction mixture was extracted with MTBE (3 × 20 mL). The combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 2:1) yielded product [D_n]-**139aa** (81 mg, 70%) and starting material [D_n]-**2a** (18 mg, 25%) as colorless solids. The D-incorporation in [D_n]-**139aa** and [D_n]-**2a** was estimated by ^{1}H-NMR spectroscopy.



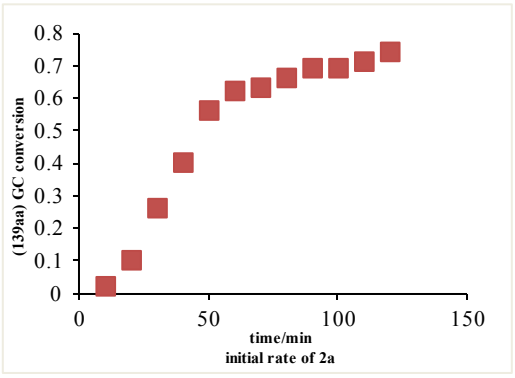
Under the same reaction conditions, from [D_5]-**2a** (140 mg, 1.0 mmol) and 4-chlorotoluene **88a** (63 mg, 0.5 mmol) trated with 1.0 M solution of CyMgCl in THF (2.0 mL, 4.0 equiv) in the presence of $Co(acac)_2$ (6.5 mg, 5.0 mol %) and ICyHCl (**140g**) (6.8 mg, 5.0 mol %) in DMPU (1.0 mL), product [D_n]-**139aa** (89 mg, 78%) and starting material [D_n]-**2a** (76 mg, 54%) were obtained as colorless solids after the same workup and column chromatography on silica gel (*n*-hexane/EtOAc 2:1). The degree of deuterium incorporation in [D_n]-**139aa** and [D_n]-**2a** were estimated by ^{1}H-NMR spectroscopy.

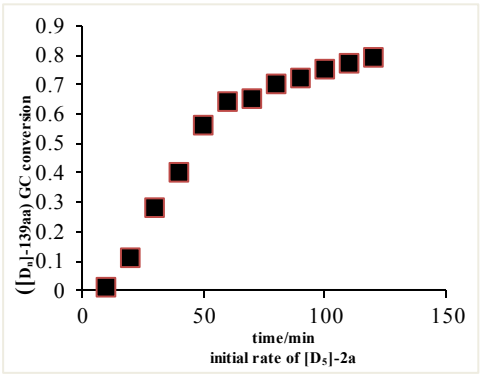
KIE Determination Experiments with 2a and [D_5]-2a as Substrates:

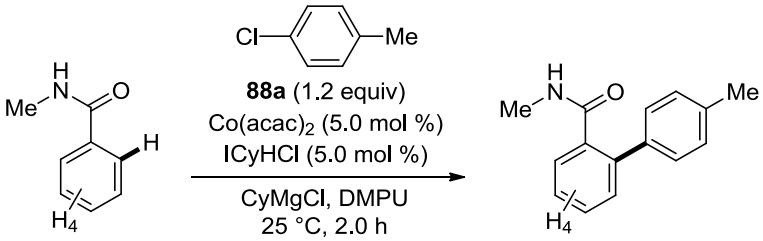


Two parallel reactions with substrate **2a** and deuterated substrate [D_5]-**2a** were performed under the standard conditions **G**: In each case, a suspension of 4-chlorotoluene (**88a**) (151 mg, 1.2 mmol), substrates **2a** (135 mg, 1.0 mmol) or [D_5]-**2a** (140 mg, 1.0 mmol), respectively, $Co(acac)_2$ (12.9 mg, 5.0 mol %), ICyHCl (**140g**) (13.5 mg, 5.0 mol %) and 1,3,5-trimethoxybenzene (168 mg, 1.0 mmol) in DMPU (2.0 mL) was stirred for 5 min at 0 °C. To each mixture was added a 1.0 M solution of CyMgCl in THF (3.0 mL, 3.0 equiv) dropwise at the same temperature, and then the reaction mixtures were stirred at 23 °C for 2.0 h. For both reactions, an aliquot (0.2 mL) was removed by syringe every 10 min. The

consumption of substrate **2a** or [D_5]-**2a** and the appearance of the product **139aa** or [D_n]-**139aa** were monitored by GC analysis. These experiments indicated that the C–H bond activation was not the rate-limiting step of the cobalt-catalyzed C–H bond arylation reaction.

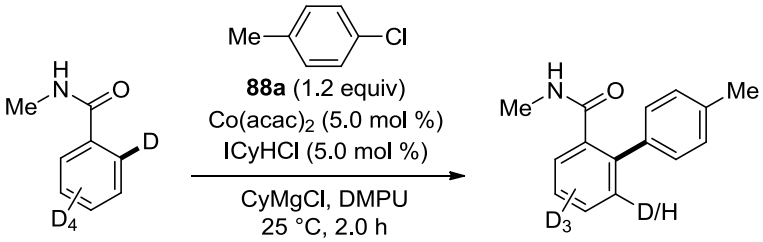






2a **139aa**

Time/(min)	10	20	30	40	50	60	70	80	90	100	110	120
139aa	**0.02**	**0.1**	**0.26**	**0.4**	**0.56**	**0.62**	**0.63**	**0.66**	**0.69**	**0.69**	**0.71**	**0.74**
2a	**0.98**	**0.9**	**0.74**	**0.6**	**0.44**	**0.38**	**0.37**	**0.34**	**0.31**	**0.31**	**0.29**	**0.26**

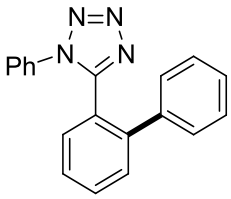


[D_5]-**2a** [$D_{4-n}H_n$]-**139aa**

Time/(min)	10	20	30	40	50	60	70	80	90	100	110	120
[D_n]-**139aa**	**0.01**	**0.11**	**0.28**	**0.4**	**0.56**	**0.64**	**0.65**	**0.7**	**0.72**	**0.75**	**0.77**	**0.79**
[D_5]-**2a**	**0.99**	**0.89**	**0.72**	**0.6**	**0.44**	**0.36**	**0.35**	**0.3**	**0.28**	**0.25**	**0.23**	**0.21**

Synthesis of Biaryl Tetrazoles

5-([1,1'-Biphenyl]-2-yl)-1-phenyl-1*H*-tetrazole (124a)



To a stirred solution of compound **139vh** (205 mg, 0.75 mmol) in CCl_4 (10 mL) was added PCl_5 (312 mg, 1.5 mmol) under an atmosphere of Ar. The reaction mixture was stirred at 80 °C for 3 h. After completion of the reaction, the solvent was removed under reduced pressure. To the residue was added DMF (5.0 mL) at 0 °C under an atmosphere of Ar, and the mixture was stirred for 10 min to get a clear solution. The obtained iminoyl chloride solution was added dropwise to the stirred suspension of NaN_3 (153 mg, 2.35 mmol) in DMF (5.0 mL) at 0 °C, then the mixture was stirred at 23 °C overnight. After completion of the reaction as was indicated by TLC monitoring, the reaction mixture was cooled to 0 °C, diluted with H_2O (15.0 mL)[115] and extracted with EtOAc (3 × 20 mL) and the combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) yielded product **124a** (197 mg, 88%) as a colorless solid. M. p.: = 124−126 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.79 (ddd, J = 7.4, 1.6, 0.5 Hz, 1H), 7.63–7.51 (m, 2H), 7.31 (ddd, J = 7.6, 1.5, 0.5 Hz, 1H), 7.27–7.21 (m, 1H), 7.16–7.06 (m, 3H), 7.03–6.95 (m, 2H), 6.66–6.51 (m, 4H).

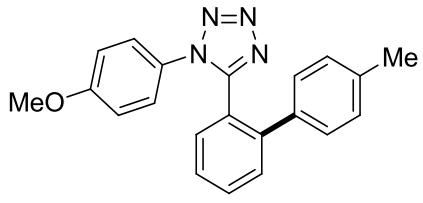
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 153.9 (C_q), 141.7 (C_q), 138.6 (C_q), 133.5 (C_q), 131.5 (CH), 131.2 (CH), 130.3 (CH), 128.9 (CH), 128.9 (CH), 128.3 (CH), 128.1 (CH), 127.9 (CH), 127.1 (CH), 123.2 (CH), 122.7 (C_q).

IR (ATR): 1503, 1454, 1103, 760, 684, 550 cm^{-1}.

MS (EI) m/z (relative intensity) 298 (15) [M^+], 297 (55), 269 (100), 241 (5), 178 (5), 152 (15).

HR-MS (ESI) m/z calcd for $C_{19}H_{15}N_4$ [M+H^+] 299.1297, found 299.1294.

1-(4-Methoxyphenyl)-5-(4'-methyl-[1,1'-biphenyl]-2-yl)-*1H*-tetrazole (124b)



From the compound **139xa** (222 mg, 0.70 mmol) in CCl_4 (10 mL) was added PCl_5 (292 mg, 1.40 mmol) and NaN_3 (137 mg, 2.10 mmol), product **124b** (202 mg, 84%) was obtained as a

colorless solid after column chromatography on silica gel (*n*-hexane/EtOAc 4:1) applying the same protocol as indicated above. M. p.: = 143−145 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.56 (td, *J* = 7.5, 1.6 Hz, 1H), 7.49 (td, *J* = 7.5, 1.6 Hz, 1H), 7.30 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.59 (d, *J* = 9.0 Hz, 2H), 6.55–6.44 (m, 4H), 3.75 (s, 3H), 2.26 (s, 3H).

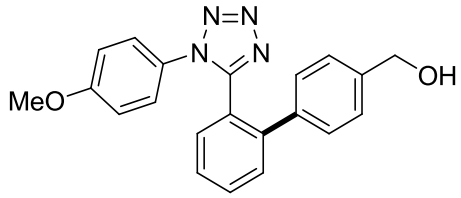
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.8 (C_q), 154.0 (C_q), 141.8 (C_q), 137.0 (C_q), 135.9 (C_q), 131.3 (CH), 131.1 (CH), 130.1 (CH), 128.9 (CH), 128.0 (CH), 127.6 (CH), 126.6 (C_q), 124.7 (CH), 122.8 (C_q), 113.9 (CH), 55.6 (CH_3), 21.1 (CH_3).

IR (ATR): 2919, 1515, 1252, 1103, 831, 756 cm^{-1}.

MS (EI) m/z (relative intensity) 342 (10) [M^+], 313 (95), 299 (100), 284 (10), 271 (10), 192 (45).

HR-MS (EI) m/z calcd for $C_{21}H_{18}N_4O$ [M^+] 342.1481, found 342.1484.

{2'-[1-(4-Methoxyphenyl)-1*H*-tetrazol-5-yl]-[1,1'-biphenyl]-4-yl}methanol (**124c**)



From the compound **139xd** (224 mg, 0.50 mmol), PCl_5 (312 mg, 1.50 mmol) and NaN_3 (102 mg, 1.60 mmol), product **124c** (142 mg, 79%) was obtained as a colorless oil after column chromatography on silica gel (*n*-hexane/EtOAc 4:1) applying the same protocol as indicated above.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.59 (tdd, *J* = 7.6, 1.5, 0.4 Hz, 1H), 7.54 (tdd, *J* = 7.6, 1.4, 0.4 Hz, 1H), 7.31 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.63 (d, *J* = 8.2 Hz, 2H), 6.61 (d, *J* = 9.0 Hz, 2H), 6.51 (d, *J* = 9.0 Hz, 2H), 4.23 (s, 2H), 3.75 (s, 3H).

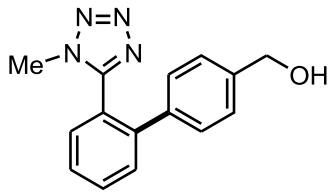
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 160.0 (C_q), 153.8 (C_q), 141.1 (C_q), 139.0 (C_q), 134.6 (C_q), 131.5 (CH), 131.4 (CH), 130.3 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 126.6 (C_q), 124.6 (CH), 122.9 (C_q), 114.2 (CH), 55.6 (CH_3), 54.3 (CH_2).

IR (ATR): 2099, 1512, 1250, 1025, 831, 694 cm^{-1}.

MS (EI) m/z (relative intensity) 358 (20) [M^+], 357 (100), 329 (20), 311 (10), 300 (10), 270 (10).

HR-MS (ESI) m/z calcd for $C_{21}H_{19}N_4O$ [M+H^+] 359.1508, found 359.1511.

{2'-(1-Methyl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl}methanol (124d)



To a solution of compound **139ad** (178 mg, 0.50 mmol) in CH_2Cl_2 (10 mL) was added phosphorous pentachloride (125 mg, 0.60 mmol) at –18 to –20 °C under an atmosphere of Ar, then the reaction mixture was warmed to 23 °C for 1 h. The solvent was removed under reduced pressure (bath temperature under 23 °C). The residue was dissolved in DCM (10 mL), and $TMSN_3$ (98.0 mg, 0.85 mmol) was added dropwise to this solution at –18 to –20 °C under stirring. The reaction mixture was stirred at 23 °C for 18 h, the reaction was quenched by careful addition of aq. sat. $NaHCO_3$ solution (15 mL).[110c] After extraction with DCM (3 × 20 mL), the combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 1:1) to yield products **124d** (87.0 mg, 65%) as a colorless solid. M. p.: = 143−145 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.63 (ddd, J = 7.6, 1.5, 0.5 Hz, 1H), 7.58–7.53 (m, 2H), 7.49 (td, J = 7.5, 1.4 Hz, 1H), 7.25 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 4.65 (s, 2H), 3.21 (s, 3H), 2.53 (s, 1H).

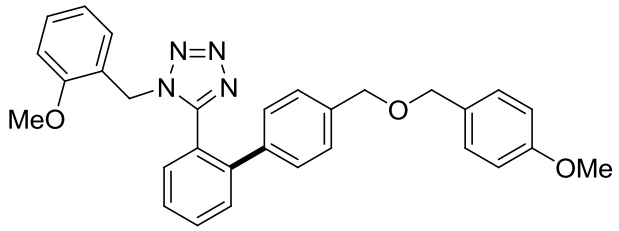
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.1 (C_q), 141.5 (C_q), 141.1 (C_q), 137.9 (C_q), 131.7 (CH), 131.3 (CH), 130.3 (CH), 128.5 (CH), 127.9 (CH), 127.3 (CH), 122.2 (C_q), 64.3 (CH_2), 33.5 (CH_3).

IR (ATR): 3390, 1474, 1206, 1006, 780, 526 cm^{-1}.

MS (EI) m/z (relative intensity) 266 (20) [M^+], 265 (100), 237 (45), 219 (10), 208 (20), 178 (20).

HR-MS (ESI) m/z calcd for $C_{15}H_{15}N_4O$ [M+H^+] 267.1246, found 267.1238.

1-(2-Methoxybenzyl)-5-{4'-[(4-methoxybenzyloxy)methyl]-[1,1'-biphenyl]-2-yl}-1*H*-tetrazole (124e)



The general procedure **H** was followed using **123a** (133 mg, 0.5 mmol) and 4-{(4-methoxybenzyloxy)methyl}phenyl dimethylcarbamate (**86a**) (189 mg, 0.6 mmol). Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **124e** (107 mg, 43%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.61 (ddd, J = 7.8, 6.4, 2.3 Hz, 1H), 7.54 (ddd, J = 7.8, 1.3, 0.7 Hz, 1H), 7.46–7.39 (m, 2H), 7.27 (ddd, J = 8.6, 8.2, 0.6 Hz, 4H), 7.17 (ddd, J = 8.3, 7.3, 1.9 Hz, 1H), 7.12–7.08 (m, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.77 (ddd, J = 7.6, 1.9, 0.4 Hz, 1H), 6.73 (td, J = 7.4, 1.1 Hz, 1H), 6.68–6.63 (m, 1H), 4.71 (s, 2H), 4.49 (s, 2H), 4.49 (s, 2H), 3.80 (s, 3H), 3.48 (s, 3H).

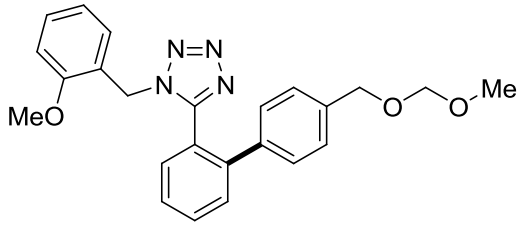
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.2 (C_q), 156.7 (C_q), 154.6 (C_q), 141.5 (C_q), 138.2 (C_q), 138.2 (C_q), 138.2 (C_q), 131.1 (CH), 131.1 (CH), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.3 (CH), 128.6 (CH), 128.0 (CH), 127.4 (CH), 123.1 (C_q), 121.5 (C_q), 120.4 (CH), 113.8 (CH), 110.2 (CH), 72.1 (CH_2), 71.2 (CH_2), 55.3 (CH_3), 55.1 (CH_3), 46.1 (CH_2).

IR (ATR): 2962, 1720, 1257, 1083, 1022, 795 cm^{-1}.

MS (EI) m/z (relative intensity) 492 (5) [M^+], 356 (30), 250 (10), 235 (10), 207 (20), 121 (100).

HR-MS (ESI) m/z calcd for $C_{30}H_{29}N_4O_3$ [M+H^+] 493.2240, found 493.2225.

1-(2-Methoxybenzyl)-5-{4'-[(methoxymethoxy)methyl]-[1,1'-biphenyl]-2-yl}-1*H*-tetrazole (124f)



The general procedure **H** was followed using **123b** (133 mg, 0.5 mmol) and 4-{(methoxymethoxy)methyl}phenyl dimethylcarbamate (**84b**) (143 mg, 0.6 mmol). Purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **124f** (85 mg, 41%) as a colorless solid. M. p.: = 98−100 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.61 (ddd, J = 7.8, 6.7, 2.0 Hz, 1H), 7.54 (ddd, J = 7.8, 1.3, 0.6 Hz, 1H), 7.47–7.38 (m, 2H), 7.30–7.25 (m, 2H), 7.17 (ddd, J = 8.4, 7.4, 1.9 Hz, 1H), 7.10 (d, J = 8.4 Hz, 2H), 6.78 (ddd, J = 7.5, 1.9, 0.5 Hz, 1H), 6.74 (td, J = 7.4, 1.0 Hz, 1H), 6.69–6.64 (m, 1H), 4.72 (s, 2H), 4.70 (s, 2H), 4.56 (s, 2H), 3.49 (s, 3H), 3.40 (s, 3H).

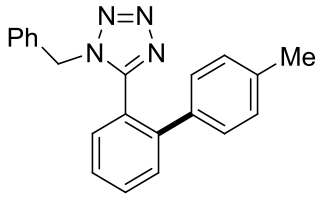
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 156.6 (C_q), 154.6 (C_q), 141.5 (C_q), 138.3 (C_q), 137.7 (C_q), 131.1 (CH), 131.1 (CH), 130.1 (CH), 130.0 (CH), 129.9 (CH), 128.6 (CH), 128.1 (CH), 127.5 (CH), 123.1 (C_q), 121.5 (C_q), 120.4 (CH), 110.2 (CH), 95.9 (CH_2), 68.7 (CH_2), 55.5 (CH_3), 55.1 (CH_3), 46.1 (CH_2).

IR (ATR): 2950, 1728, 1496, 1249, 1040, 769 cm^{-1}.

MS (EI) m/z (relative intensity) 416 (20) [M^+], 415 (30), 355 (10), 298 (5), 205 (30), 121 (100).

HR-MS (ESI) m/z calcd for $C_{24}H_{25}N_4O_3$ [M+H^+] 417.1927, found 417.1917.

1-Benzyl-5-(4'-methyl-[1,1'-biphenyl]-2-yl)-1*H*-tetrazole (124g)



The general procedure **H** was followed using **123c** (118 mg, 0.5 mmol) and *p*-tolyl dimethylcarbamate (**84c**) (107 mg, 0.6 mmol). Purification by column chromatography (*n*-hexane/EtOAc 5:1) and recrystallization (*n*-hexane) yielded **124g** (83 mg, 51%) as a colorless solid. M. p.: = 109−111 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.66–7.47 (m, 2H), 7.44–7.27 (m, 2H), 7.22–7.10 (m, 3H), 7.08 (d, J = 8.2 Hz, 2H), 7.01 (d, J = 8.2 Hz, 2H), 6.74 (d, J = 7.8 Hz, 2H), 4.75 (s, 2H), 2.32 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.6 (C_q), 141.5 (C_q), 137.9 (C_q), 135.8 (C_q), 133.1 (C_q), 131.4 (CH), 131.2 (CH), 130.1 (CH), 129.6 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 127.7 (CH), 127.5 (CH), 122.6 (C_q), 50.8 (CH_2), 21.2 (CH_3).

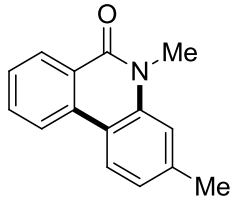
IR (ATR): 1435, 1240, 1095, 839, 721, 533 cm^{-1}.

MS (EI) m/z (relative intensity) 326 (55) [M$^+$], 325 (100), 297 (45), 192 (30), 178 (35), 91 (85).

HR-MS (ESI) m/z calcd for $C_{21}H_{19}N_4$ [M+H$^+$] 327.1610, found 327.1609.

The spectral data were in accordance with those reported in the literature.[109b]

3,5-Dimethylphenanthridin-6(*5H*)-one (143a)



A suspension of *N*,4'-dimethyl-[1,1'-biphenyl]-2-carboxamide (**139aa**) (113 mg, 0.5 mmol) and $K_2S_2O_8$ (270 mg, 1.0 mmol) in H_2O (5.0 mL) was stirred at 105 °C for 2.0 h. After completion of the reaction, at ambient temperature the reaction mixture was extracted with MTBE (3 × 20 mL) at ambient temperature. The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc 4:1) yielded **143a** (93 mg, 83%) as a colorless solid. M. p.: = 123−125 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.53 (dd, *J* = 8.1, 0.7 Hz, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.73 (ddt, *J* = 8.4, 7.1, 1.4 Hz, 1H), 7.55 (ddt, *J* = 7.3, 5.8, 1.3 Hz, 1H), 7.29–7.17 (m, 1H), 7.13 (ddd, *J* = 8.1, 1.6, 0.8 Hz, 1H), 3.80 (d, *J* = 1.2 Hz, 3H), 2.51 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.6 (C_q), 139.8 (C_q), 137.9 (C_q), 133.6 (C_q), 132.2 (CH), 128.8 (CH), 127.3 (CH), 125.1 (C_q), 123.5 (CH), 123.0 (CH), 121.3 (CH), 116.8 (C_q), 115.3 (CH), 30.0 (CH_3), 22.0 (CH_3).

IR (ATR): 1644, 1606, 1310, 1098, 769 cm^{-1}.

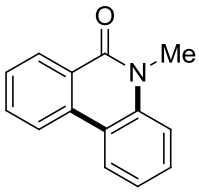
MS (EI) m/z (relative intensity) 223 (100) [M+], 208 (10), 192 (20), 178 (5), 165 (15), 152 (10).

HR-MS (EI) m/z calcd for $C_{15}H_{13}NO$ [M$^+$] 223.0997, found 223.0994.

The spectral data were in accordance with those reported in the literature.[156]

[156] S. A. Glover, A. Goosen, *J. Chem. Soc., Perkin Trans. 1* **1978**, 653–657.

5-Methylphenanthridin-6(*5H*)-one (143b)



Under the same conditions as above, from *N*-methyl-[1,1'-biphenyl]-2-carboxamide (**139ah**) (106.0 mg, 0.50 mmol) and $K_2S_2O_8$ (270.0 mg, 1.00 mmol), compound **143b** (6.0 mg, 64%) was obtained as a colorless solid after column chromatography (*n*-hexane/EtOAc 4:1). M. p.: = 116−118 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.54 (dd, J = 8.1, 1.3 Hz, 1H), 8.25 (m, 2H), 7.74 (m, 1H), 7.55 (m, 2H), 7.39 (dd, J = 8.6, 1.1 Hz, 2H), 7.30 (m, 1H), 3.80 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.4 (C_q), 137.9 (C_q), 133.4 (C_q), 132.2 (CH), 129.4 (CH), 128.7 (CH), 127.8 (CH), 125.5 (C_q), 123.1 (CH), 122.3 (CH), 121.5 (CH), 119.1 (C_q), 114.9 (CH), 30.0 (CH_3).

IR (ATR): 2918, 1639, 1599, 1300, 1088, 723 cm^{-1}.

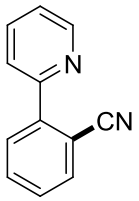
MS (EI) m/z (relative intensity) 209 (100) [M+], 178 (40), 166 (5), 152 (25), 139 (10).

HR-MS (EI) m/z calcd for $C_{14}H_{11}NO$ [M^+] 209.0841, found 209.0843.

The spectral data were in accordance with those reported in the literature.[157]

10.4.5 Analytical Data for the Products of Cobalt(III)-Catalyzed C−H Bond Cyanation of (Hetero)Arenes

2-(Pyridin-2-yl)benzonitrile (126a)



The general procedure **I** was followed using **28a** (78 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **126a** (81 mg, 90%) as a slight yellow solid. M. p.: = 63−65 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.84–8.71 (m, 1H), 7.91–7.73 (m, 4H), 7.68 (dd, J = 7.5,

[157] H. Iwasaki, T. Eguchi, N. Tsutsui, H. Ohno, T, Tanaka, *J. Org. Chem*. **2008**, *73*, 7145–7152.

1.4 Hz, 1H), 7.49 (td, *J* = 7.6, 1.3 Hz, 1H), 7.34 (ddd, *J* = 7.2, 4.8, 1.5 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.1 (C_q), 149.8 (CH), 143.4 (C_q), 136.7 (CH), 134.0 (CH), 132.7 (CH), 129.9 (CH), 128.6 (CH), 123.2 (CH), 123.1 (CH), 118.6 (C_q), 111.0 (C_q).

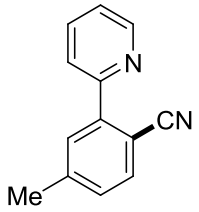
IR (ATR): 3350, 2224, 1560, 1464, 758, 509 cm^{-1}.

MS (EI) m/z (relative intensity) 180 (100) [M^+], 154 (5), 140 (5), 126 (5), 102 (5), 75 (5).

HR-MS (EI) m/z calcd for $C_{12}H_8N_2$ [M^+] 180.0687, found 180.0684.

The spectral data were in accordance with those reported in the literature.[158]

4-Methyl-2-(pyridin-2-yl)benzonitrile (126b)



The general procedure **I** was followed using **28b** (85 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2 1:1) yielded **126b** (70 mg, 72%) as a colorless solid. M. p.: = 62−63 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.76 (dd, *J* = 5.0, 1.4 Hz, 1H), 8.00–7.74 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.44–7.27 (m, 2H), 2.48 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.2 (C_q), 149.8 (CH), 143.7 (C_q), 143.2 (C_q), 136.6 (CH), 133.9 (CH), 130.6 (CH), 129.4 (CH), 123.2 (CH), 123.1 (CH), 118.9 (C_q), 107.9 (C_q), 21.9 (CH_3).

IR (ATR): 3002, 2218, 1587, 1462, 791, 586 cm^{-1}.

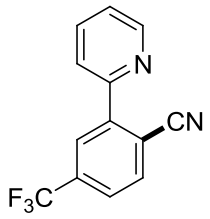
MS (EI) m/z (relative intensity) 194 (100) [M^+], 179 (10), 167 (30), 152 (5), 140 (10), 114 (5).

HR-MS (EI) m/z calcd for $C_{13}H_{10}N_2$ [M^+] 194.0844, found 194.0849.

The spectral data were in accordance with those reported in the literature.[159]

2-(Pyridin-2-yl)-4-(trifluoromethyl)benzonitrile (126c)

[158] X. Chen, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, *J. Am. Chem. Soc.* **2006**, *128*, 6790–6791.
[159] J. Kim, S. Chang, *J. Am. Chem. Soc.* **2010**, *132*, 10272–10274.



The general procedure **I** was followed using **28c** (112 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 1:1:0→1:1:0.1) yielded **126c** (110 mg, 89%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$):δ = 8.79 (dt, J = 4.8, 1.4 Hz, 1H), 8.14 (d, J = 1.8 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.90–7.80 (m, 2H), 7.75 (dd, J = 8.1, 1.8 Hz, 1H), 7.40 (ddd, J = 6.8, 4.8, 1.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 153.6 (C_q), 150.1 (CH), 144.2 (C_q), 137.0 (CH), 134.6 (CH), 134.6 (C_q, $J_{C\text{-}F}$ = 33.0 Hz), 127.0 (CH, $J_{C\text{-}F}$ = 3.8 Hz), 125.3 (CH, $J_{C\text{-}F}$ = 3.8 Hz), 123.9 (CH), 123.2 (CH), 123.0 (C_q, $J_{C\text{-}F}$ = 253.6 Hz), 117.4 (C_q), 114.3 (C_q, $J_{C\text{-}F}$ = 1.5 Hz).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -63.43 (s).

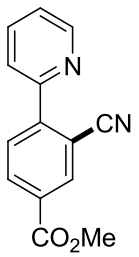
IR (ATR): 3056, 2232, 1568, 1335, 1128, 792 cm^{-1}.

MS (EI) m/z (relative intensity) 248 (100) [M^+], 226 (25), 209 (10), 179 (25), 152 (10).

HR-MS (EI) m/z calcd for $C_{13}H_7N_2F_3$ [M^+] 248.0561, found 248.0551.

The spectral data were in accordance with those reported in the literature.[160]

Methyl 3-cyano-4-(pyridin-2-yl)benzoate (126d)



The general procedure **I** was followed using **28d** (107 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **126d** (117 mg, 98%) as a colorless solid. M. p.: = 106−108 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.78 (ddd, J = 4.8, 1.8, 1.1 Hz, 1H), 8.45 (dd, J = 1.8, 0.5

[160] X. Jia, D. Yang, W. Wang, F. Luo, J. Cheng, *J. Org. Chem*. **2009**, *74*, 9470–9474.

Hz, 1H), 8.30 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.93 (dd, *J* = 8.2, 0.5 Hz, 1H), 7.89–7.79 (m, 2H), 7.38 (ddd, *J* = 6.7, 4.8, 1.8 Hz, 1H), 3.96 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.8 (C_q), 154.1 (C_q), 150.0 (CH), 146.8 (C_q), 136.9 (CH), 135.3 (CH), 133.5 (CH), 130.6 (C_q), 130.2 (CH), 123.8 (CH), 123.3 (CH), 117.8 (C_q), 111.4 (C_q), 52.7 (CH_3).

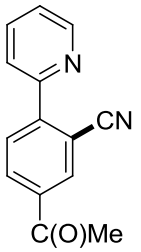
IR (ATR): 3085, 2230, 1725, 1448, 1294, 756 cm^{-1}.

MS (EI) m/z (relative intensity) 238 (85) [M^+], 207 (100), 179 (70), 152 (40), 125 (15), 89 (15).

HR-MS (EI) m/z calcd for $C_{14}H_{10}N_2O_2$ [M^+] 238.0742, found 238.0734.

The spectral data were in accordance with those reported in the literature.[159]

5-Acetyl-2-(pyridin-2-yl)benzonitrile (126e)



The general procedure **I** was followed using **28e** (98 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **126e** (108 mg, 97%) as a colorless solid. M. p.: = 107−108 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.79 (ddd, *J* = 4.8, 1.8, 1.1 Hz, 1H), 8.35 (dd, *J* = 1.8, 0.6 Hz, 1H), 8.22 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.96 (dd, *J* = 8.2, 0.6 Hz, 1H), 7.90–7.78 (m, 2H), 7.39 (ddd, *J* = 6.7, 4.8, 1.8 Hz, 1H), 2.66 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 195.4 (C_q), 154.0 (C_q), 150.0 (CH), 146.8 (C_q), 136.9 (CH), 136.8 (C_q), 134.1 (CH), 132.0 (CH), 130.4 (CH), 123.9 (CH), 123.3 (CH), 117.9 (C_q), 111.6 (C_q), 26.7 (CH_3).

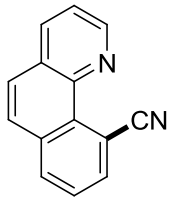
IR (ATR): 3077, 2227, 1685, 1467, 1260, 786 cm^{-1}.

MS (EI) m/z (relative intensity) 222 (70) [M^+], 207 (100), 179 (70), 152 (35), 125 (15), 78 (15).

HR-MS (EI) m/z calcd for $C_{14}H_{10}N_2O$ [M^+] 222.0793, found 222.0790.

The spectral data were in accordance with those reported in the literature.[91]

Benzo[*h*]quinoline-10-carbonitrile (126f)



The general procedure **I** was followed using **28f** (90 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:4:1:0.01) yielded **126f** (84 mg, 82%) as a colorless solid. M. p.: = 138−140 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.13 (dd, J = 4.4, 1.8 Hz, 1H), 8.21 (dd, J = 8.1, 1.8 Hz, 1H), 8.13 (ddd, J = 11.8, 7.7, 1.4 Hz, 2H), 7.83–7.79 (m, 2H), 7.74 (m, 1H), 7.62 (dd, J = 8.1, 4.4 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 148.4 (CH), 144.4 (C_q), 136.2 (CH), 135.7 (CH), 134.0 (C_q), 132.7 (CH), 130.7 (C_q), 127.3 (CH), 127.2 (CH), 127.1 (CH), 126.9 (C_q), 123.0 (CH), 120.8 (C_q), 108.9 (C_q).

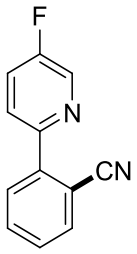
IR (ATR): 2207, 1618, 1422, 829, 714, 664 cm^{-1}.

MS (EI) m/z (relative intensity) 204 (100) [M$^+$], 177 (20), 150 (10), 124 (5), 102 (5).

HR-MS (EI) m/z calcd for $C_{14}H_8N_2$ [M$^+$] 204.0687, found 204.0685.

The spectral data were in accordance with those reported in the literature.[159]

2-(5-Fluoropyridin-2-yl)benzonitrile (126g)



The general procedure **I** was followed using **28g** (87 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 1:1:0.05) yielded **126g** (72 mg, 73%) as a colorless solid. M. p.: = 102−105 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, J = 2.9 Hz, 1H), 7.78 (m, 3H), 7.67 (td, J = 7.7, 1.4

Hz, 1H), 7.58–7.42 (m, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.1 (C_q, $J_{C\text{-}F}$ = 258.5 Hz), 151.3 (C_q, $J_{C\text{-}F}$ = 4.3 Hz), 142.3 (C_q), 138.3 (CH, $J_{C\text{-}F}$ = 24.0 Hz), 134.0 (CH), 132.8 (CH), 129.8 (CH), 128.7 (CH), 124.1 (CH, $J_{C\text{-}F}$ = 4.7 Hz), 123.5 (CH, $J_{C\text{-}F}$ = 20.8 Hz), 118.5 (C_q), 110.9 (C_q).

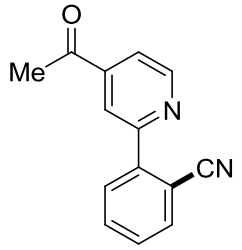
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -126.8 (dd, J = 8.0, 4.3 Hz).

IR (ATR): 3043, 2220, 1584, 1446, 1223, 750 cm^{-1}.

MS (EI) m/z (relative intensity) 198 (100) [M^+], 179 (5), 171 (10), 151 (5), 128 (5), 99 (5).

HR-MS (EI) m/z calcd for $C_{12}H_7N_2F$ [M^+] 198.0593, found 198.0585.

2-(4-Acetylpyridin-2-yl)benzonitrile (126h)



The general procedure **I** was followed using **28h** (99 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-Hexane/CH_2Cl_2/EtOAc 1:1:0.05) yielded **126h** (72 mg, 65%) as a colorless solid. M. p.: = 124−125 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.29 (dd, J = 2.3, 0.9 Hz, 1H), 8.36 (dd, J = 8.2, 2.2 Hz, 1H), 7.91–7.85 (m, 2H), 7.82 (ddd, J = 7.5, 1.4, 0.6 Hz, 1H), 7.71 (dd, J = 7.5, 1.4 Hz, 1H), 7.55 (td, J = 7.5, 1.4 Hz, 1H), 2.67 (s, 3H).

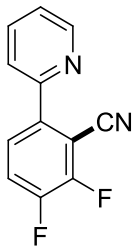
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.0 (C_q), 158.6 (C_q), 149.9 (CH), 142.1 (C_q), 136.4 (CH), 134.3 (CH), 132.8 (CH), 131.3 (C_q), 130.0 (CH), 129.5 (CH), 122.9 (CH), 118.3 (C_q), 111.2 (C_q), 26.9 (CH_3).

IR (ATR): 2224, 1676, 1582, 1370, 1269, 761 cm^{-1}.

MS (EI) m/z (relative intensity) 222 (70) [M^+], 207 (100), 179 (50), 152 (65), 125 (15), 102 (10).

HR-MS (EI) m/z calcd for $C_{14}H_{10}N_2O$ [M^+] 222.0793, found 222.0800.

2,3-Difluoro-6-(pyridin-2-yl)benzonitrile (126i)



The general procedure **I** was followed using **28i** (96 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-Hexane/CH_2Cl_2/EtOAc 2:1:0.1) yielded **126i** (78 mg, 72%) as a slight yellow solid. M. p.: = 67–68 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.82–8.77 (m, 1H), 7.85 (td, J = 7.8, 1.7 Hz, 1H), 7.61–7.56 (m, 2H), 7.41 (ddd, J = 7.8, 4.9, 1.2 Hz, 1H), 7.31 (td, J = 8.9, 7.4 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 153.4 (C_q, $J_{C\text{-}F}$ = 259.0, 13.4 Hz), 150.1 (CH), 149.3 (C_q, $J_{C\text{-}F}$ = 2.9 Hz), 148.5 (C_q, $J_{C\text{-}F}$ = 259.0, 13.4 Hz), 136.6 (CH), 134.1 (C_q, $J_{C\text{-}F}$ = 13.4 Hz), 130.5 (CH, $J_{C\text{-}F}$ = 7.8, 4.7 Hz), 125.2 (CH, $J_{C\text{-}F}$ = 3.7 Hz), 124.2 (CH), 117.9 (CH, $J_{C\text{-}F}$ = 18.5 Hz), 116.5 (C_q), 109.5 (C_q, $J_{C\text{-}F}$ = 3.7 Hz).

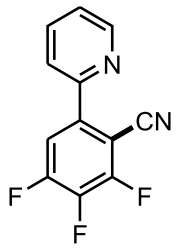
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -126.9 (m), -138.33 (m).

IR (ATR): 3089, 2235, 1570, 1426, 1275, 745 cm^{-1}.

MS (EI) m/z (relative intensity) 216 (100) [M^+], 197 (15), 189 (15), 163 (10), 136 (5), 88 (5).

HR-MS (EI) m/z calcd for $C_{12}H_6N_2F_2$ [M^+] 216.0499, found 216.0492.

2,3,4-trifluoro-6-(pyridin-2-yl)benzonitrile (126j)



The general procedure **I** was followed using **28j** (105 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-Hexane/CH_2Cl_2/EtOAc 2:1:0.1) yielded **126j** (47 mg, 40%) as a slight yellow solid. M. p.: = 61–63 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.75 (ddd, J = 4.8, 1.7, 1.0 Hz, 1H), 7.92–7.82 (m, 1H), 7.78 (dt, J = 8.0, 1.1 Hz, 1H), 7.56 (ddd, J = 10.4, 6.9, 2.1 Hz, 1H), 7.40 (ddd, J = 7.4, 4.8, 1.3 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 153.6 (C_q, ddd, J_{C-F} = 259.7, 16.5, 3.2 Hz), 153.6 (C_q, ddd, J_{C-F} = 260.1, 15.8, 2.2 Hz), 152.1 (C_q), 150.1 (CH), 140.0 (C_q, dd, J_{C-F} = 8.1, 4.3 Hz), 139.7 (C_q, ddd, J_{C-F} = 257.6, 15.9, 2.1 Hz), 137.1 (CH), 124.2 (CH), 122.9 (CH), 114.2 (CH, dd, J_{C-F} = 19.8, 3.3 Hz), 111.8 (C_q, t, J_{C-F} = 2.7 Hz), 98.0 (C_q, dd, J_{C-F} = 13.3, 3.7 Hz).

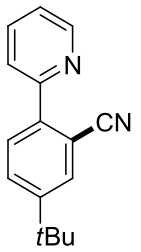
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -122.84 – -123.12 (m), -124.79 (ddd, J = 20.0, 11.8, 2.2 Hz), -156.60 (ddd, J = 21.3, 19.9, 6.9 Hz).

IR (ATR): 3068, 2235, 1520, 1397, 1072, 789 cm^{-1}.

MS (EI) m/z (relative intensity) 234 (100) [M$^+$], 215 (25), 207 (20), 181 (15), 157 (5).

HR-MS (EI) m/z calcd for $C_{12}H_5N_2F_3$ [M$^+$] 234.0405, found 2344.0408.

5-(*tert*-Butyl)-2-(pyridin-2-yl)benzonitrile (126k)



The general procedure **I** was followed using **28k** (106 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 1:1:0→1:1:0.1) yielded **126k** (79 mg, 67%) as a colorless solid. M. p.: = 68−71 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.74 (ddd, J = 4.8, 1.8, 1.0 Hz, 1H), 7.83–7.73 (m, 4H), 7.68 (dd, J = 8.3, 2.1 Hz, 1H), 7.31 (ddd, J = 7.3, 4.8, 1.4 Hz, 1H), 1.34 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 155.2 (C_q), 152.3 (C_q), 149.9 (CH), 140.6 (C_q), 136.7 (CH), 131.1 (CH), 130.2 (CH), 129.7 (CH), 123.0 (CH), 123.0 (CH), 119.2 (C_q), 110.6 (C_q), 34.8 (C_q), 31.0 (CH_3).

IR (ATR): 2964, 2223, 1602, 1461, 897, 789 cm^{-1}.

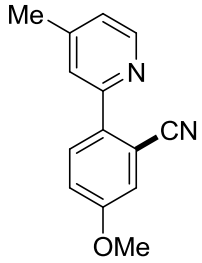
MS (EI) m/z (relative intensity) 236 (30) [M$^+$], 221 (100), 205 (10), 193 (25), 166 (5), 152 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{16}N_2$ [M$^+$] 236.1313, found 236.1314.

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

[161] X. Kou, M. Zhao, X. Qiao, Y. Zhu, X. Tong, Z. Shen, *Chem. Eur. J.* **2013**, *19*, 16880–16886.

5-Methoxy-2-(4-methylpyridin-2-yl)benzonitrile (126l)



The general procedure **I** was followed using **28l** (100 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **126l** (88 mg, 79%) as a colorless solid. M. p.: = 109−111 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.55 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.72 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.51 (dt, *J* = 1.7, 0.8 Hz, 1H), 7.22 (d, *J* = 2.7 Hz, 1H), 7.16 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.09 (ddd, *J* = 5.1, 1.5, 0.8 Hz, 1H), 3.84 (s, 3H), 2.40 (s, 3H).

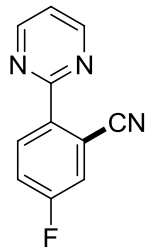
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.3 (C_q), 154.8 (C_q), 149.5 (CH), 147.8 (C_q), 136.2 (C_q), 131.2 (CH), 123.7 (CH), 123.7 (CH), 119.3 (CH), 118.6 (C_q), 118.3 (CH), 111.7 (C_q), 55.7 (CH_3), 21.1 (CH_3).

IR (ATR): 2925, 2225, 1608, 1466, 1276, 820 cm^{-1}.

MS (EI) m/z (relative intensity) 224 (100) [M^+], 209 (25), 194 (10), 181 (60), 166 (20), 154 (25).

HR-MS (EI) m/z calcd for $C_{14}H_{12}N_2O$ [M^+] 224.0950, found 224.0952.

5-Fluoro-2-(pyrimidin-2-yl)benzonitrile (126m)



The general procedure **I** was followed using **28m** (87 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **126m** (60 mg, 60%) as a colorless solid. M. p.: = 170−171 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.90 (d, *J* = 4.9 Hz, 2H), 8.42 (dd, *J* = 8.9, 5.6 Hz, 1H),

7.54 (dd, J = 8.1, 2.7 Hz, 1H), 7.46–7.36 (m, 1H), 7.32 (t, J = 4.9 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.9 (C_q, $J_{C\text{-}F}$ = 253.4 Hz), 161.8 (C_q), 157.2 (C_q), 136.5 (CH, $J_{C\text{-}F}$ = 3.7 Hz), 132.7 (CH, $J_{C\text{-}F}$ = 8.7 Hz), 121.8 (CH, $J_{C\text{-}F}$ = 24.8 Hz), 120.0 (CH, $J_{C\text{-}F}$ = 10.5 Hz), 120.0 (CH), 117.6 (C_q, $J_{C\text{-}F}$ = 2.7 Hz), 113.5 (C_q, $J_{C\text{-}F}$ = 9.4 Hz).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -108.8 (td, J = 7.9, 5.5 Hz).

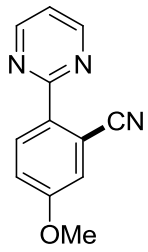
IR (ATR): 3062, 2231, 1560, 1415, 1227, 810 cm^{-1}.

MS (EI) m/z (relative intensity) 119 (100) [M^+], 172 (15), 146 (90), 119 (25), 100 (10), 75 (10).

HR-MS (EI) m/z calcd for $C_{11}H_6N_3F$ [M^+] 199.0546, found 199.0538.

The spectral data were in accordance with those reported in the literature.[162]

5-Methoxy-2-(pyrimidin-2-yl)benzonitrile (126n)



The general procedure **I** was followed using **28n** (93 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 6:1→4:1) yielded **126n** (95 mg, 90%) as a colorless solid. M. p.: = 127−129 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.84 (d, J = 4.8 Hz, 2H), 8.32 (d, J = 8.9 Hz, 1H), 7.30 (d, J = 2.7 Hz, 1H), 7.25–7.22 (m, 1H), 7.19 (dd, J = 8.9, 2.7 Hz, 1H), 3.88 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.4 (C_q), 160.6 (C_q), 157.1 (CH), 132.6 (C_q), 131.9 (CH), 119.7 (CH), 119.4 (CH), 118.8 (C_q), 118.7 (CH), 112.9 (C_q), 55.8 (CH_3).

IR (ATR): 3082, 2222, 1552, 1404, 1288, 803 cm^{-1}.

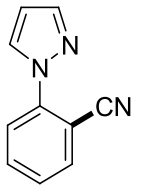
MS (EI) m/z (relative intensity) 211 (100) [M^+], 196 (15), 168 (10), 158 (40), 128 (10), 115 (10).

HR-MS (EI) m/z calcd for $C_{12}H_9N_3O$ [M^+] 211.0746, found 211.0752.

The spectral data were in accordance with those reported in the literature.[162]

[162] X. Hong, H. Wang, G. Qian, Q. Tan, B. Xu, *J. Org. Chem*. **2014**, *79*, 3228–3237.

2-(1*H*-Pyrazol-1-yl)benzonitrile (126o)



The general procedure **I** was followed using **128a** (72 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 20:7:1:0.01) yielded **126o** (83 mg, 98%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, J = 2.6 Hz, 1H), 7.77 (m, 3H), 7.68 (td, J = 7.6, 1.8 Hz, 1H), 7.40 (td, J = 7.6, 1.2 Hz, 1H), 6.53 (dd, J = 2.6, 1.8 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 142.2 (CH), 142.0 (C_q), 134.4 (CH), 134.0 (CH), 129.5 (CH), 127.2 (CH), 124.3 (CH), 117.0 (C_q), 108.5 (CH), 105.3 (C_q).

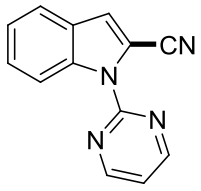
IR (ATR): 3124, 2161, 1700, 1392, 933, 749 cm^{-1}.

MS (EI) m/z (relative intensity) 169 (100) [M^+], 142 (55), 129 (15), 115 (25), 102 (30), 75 (20).

HR-MS (EI) m/z calcd for $C_{10}H_7N_3$ [M^+] 169.0640, found 169.0644.

The spectral data were in accordance with those reported in the literature.[160]

1-(Pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (7a)



The general procedure **I** was followed using **7a** (98 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2 3:2) yielded **127a** (109 mg, 99%) as a colorless solid. M. p.: = 125−127 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.82 (d, J = 4.8 Hz, 2H), 8.68 (dq, J = 8.6, 0.9 Hz, 1H), 7.67 (ddd, J = 8.0, 1.3, 0.8 Hz, 1H), 7.49 (ddd, J = 8.5, 7.1, 1.3 Hz, 1H), 7.46 (d, J = 0.8 Hz, 1H), 7.31 (ddd, J = 8.0, 7.1, 1.0 Hz, 1H), 7.22 (t, J = 4.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.2 (CH), 156.4 (C_q), 136.5 (C_q), 127.7 (C_q), 127.4 (CH),

123.4 (CH), 121.9 (CH), 120.9 (CH), 117.9 (CH), 116.1 (CH), 114.1 (C_q), 108.9 (C_q).

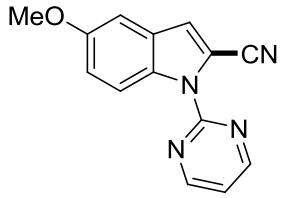
IR (ATR): 3100, 2225, 1565, 1423, 1333, 738 cm^{-1}.

MS (EI) m/z (relative intensity) 220 (100) [M^+], 194 (15), 169 (25), 141 (15), 114 (25), 79 (30).

HR-MS (ESI) m/z calcd for $C_{13}H_9N_4$ [M+H^+] 221.0827, found 221.0825.

The spectral data were in accordance with those reported in the literature.[91]

5-Methoxy-1-(pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (127b)



The general procedure **I** was followed using **7b** (113 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 2:1:0.01) yielded **127b** (118 mg, 94%) as a colorless solid. M. p.: = 185−187 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 4.8 Hz, 2H), 8.59 (dt, *J* = 9.3, 0.7 Hz, 1H), 7.36 (d, *J* = 0.8 Hz, 1H), 7.19 (t, *J* = 4.8 Hz, 1H), 7.11 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.07–7.00 (m, 1H), 3.86 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.1 (CH), 156.4 (C_q), 156.2 (C_q), 131.5 (C_q), 128.4 (C_q), 120.4 (CH), 117.8 (CH), 117.7 (CH), 117.2 (CH), 114.2 (C_q), 109.0 (C_q), 102.5 (CH), 55.7 (CH_3).

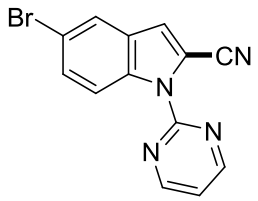
IR (ATR): 2985, 2219, 1568, 1437, 1211, 805 cm^{-1}.

MS (EI) m/z (relative intensity) 250 (100) [M^+], 235 (80), 207 (75), 180 (15), 154 (5), 79 (40).

HR-MS (EI) m/z calcd for $C_{14}H_{10}N_4O$ [M^+] 250.0855, found 250.0850.

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

5-Bromo-1-(pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (127c)



The general procedure **I** was followed using **7c** (137 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:4:1:0.01) yielded **127c** (140 mg, 94%) as a colorless solid. M. p.: = 234−236 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.80 (d, J = 4.8 Hz, 2H), 8.56 (dt, J = 9.1, 0.7 Hz, 1H), 7.78 (dd, J = 2.0, 0.7 Hz, 1H), 7.53 (dd, J = 9.1, 2.0 Hz, 1H), 7.35 (d, J = 0.7 Hz, 1H), 7.22 (t, J = 4.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.4 (CH), 156.3 (C_q), 135.1 (C_q), 130.4 (CH), 129.3 (C_q), 124.4 (CH), 119.7 (CH), 118.3 (CH), 117.8 (CH), 116.8 (C_q), 113.6 (C_q), 110.0 (C_q).

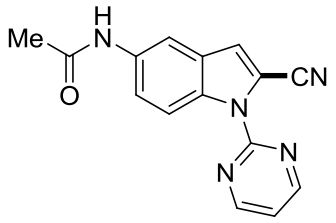
IR (ATR): 3140, 2216, 1576, 1441, 1253, 801 cm^{-1}.

MS (EI) m/z (relative intensity) 298 (100) [M^+], 273 (5), 247 (10), 219 (30), 166 (10), 140 (30).

HR-MS (EI) m/z calcd for $C_{13}H_7N_4{}^{79}Br$ [M^+] 297.9854, found 297.9860.

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

***N*-{2-Cyano-1-(pyrimidin-2-yl)-1*H*-indol-5-yl}acetamide (127e)**



The general procedure **I** was followed using **7e** (126 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **127e** (98 mg, 71%) as an off white solid. M. p.: = 284−286 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ= 10.04 (s, 1H), 8.95 (dd, J = 4.9, 0.7 Hz, 2H), 8.64–8.40 (m, 1H), 8.20 (d, J = 2.2 Hz, 1H), 7.81 (s, 1H), 7.55 (dd, J = 9.2, 2.1 Hz, 1H), 7.49 (td, J = 4.9, 0.7 Hz, 1H), 2.08 (s, 3H).

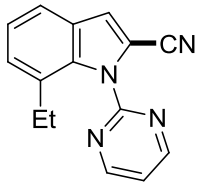
^{13}C-NMR (125 MHz, DMSO-d_6): δ = 168.0 (C_q), 158.7 (CH), 155.3 (C_q), 135.0 (C_q), 132.0 (C_q), 127.4 (C_q), 120.9 (CH), 120.1 (CH), 118.6 (CH), 115.7 (CH), 113.6 (C_q), 110.9 (CH), 108.1 (C_q), 23.9 (CH_3).

IR (ATR): 3216, 2215, 1659, 1424, 1260, 809 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (45) [M^+], 235 (100), 207 (10), 183 (5), 156 (10), 129 (5).

HR-MS (EI) m/z calcd for $C_{15}H_{11}N_5O$ [M^+] 277.0964, found 277.0973.

7-Ethyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (127f)



The general procedure **I** was followed using **7f** (112 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2 2:1) yielded **127f** (87 mg, 70%) as a slight yellow oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.89 (d, J = 4.8 Hz, 2H), 7.54 (d, J = 1.4 Hz, 1H), 7.41 (s, 1H), 7.39 (t, J = 4.9 Hz, 1H), 7.30–7.27 (m, 1H), 7.26–7.22 (t, J = 7.5 Hz, 1H), 2.53 (q, J = 7.5 Hz, 2H), 0.95 (t, J = 7.5 Hz, 3H).

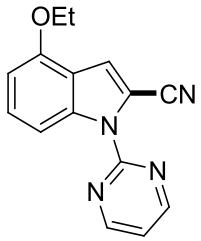
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.6 (CH), 156.8 (C_q), 135.7 (C_q), 129.6 (C_q), 128.0 (C_q), 127.5 (CH), 123.2 (CH), 120.1 (CH), 120.0 (CH), 118.5 (CH), 113.4 (C_q), 111.2 (C_q), 26.3 (CH_2), 13.6 (CH_3).

IR (ATR): 2969, 2223, 1561, 1411, 1267, 743 cm^{-1}.

MS (EI) m/z (relative intensity) 248 (100) [M^+], 233 (100), 220 (10), 206 (5), 179 (15), 155 (25).

HR-MS (ESI) m/z calcd for $C_{15}H_{13}N_4$ [$M+H^+$] 249.1140, found 249.1135.

4-Ethoxy-1-(pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (127g)



The general procedure **I** was followed using **7g** (119 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2 1:1) yielded **127g** (125 mg, 95%) as a colorless solid. M. p.: = 170−172 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.80 (d, J = 4.8 Hz, 2H), 8.24–8.09 (m, 1H), 7.59 (t, J = 0.6

Hz, 1H), 7.37 (dd, *J* = 8.6, 7.9 Hz, 1H), 7.20 (t, *J* = 4.8 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 4.18 (d, *J* = 7.0 Hz, 2H), 1.49 (t, *J* = 7.0 Hz, 3H).

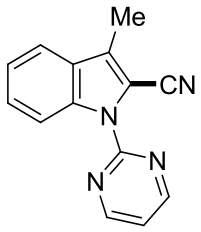
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.1 (CH), 156.5 (C_q), 152.7 (C_q), 137.7 (C_q), 128.6 (CH), 119.1 (C_q), 118.6 (CH), 117.8 (CH), 114.3 (C_q), 108.5 (CH), 107.2 (C_q), 103.6 (CH), 63.8 (CH_2), 14.8 (CH_3).

IR (ATR): 2977, 2221, 1567, 1431, 1348, 769 cm^{-1}.

MS (EI) m/z (relative intensity) 264 (60) [M^+], 236 (100), 210 (10), 207 (35), 180 (10), 79 (30).

HR-MS (EI) m/z calcd for $C_{15}H_{12}N_4O$ [M^+] 264.1011, found 264.1011.

3-Methyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (127h)



The general procedure **I** was followed using **7h** (105 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:4:1:0.01) yielded **127h** (108 mg, 92%) as a colorless solid. M. p.: = 167−169 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 4.8 Hz, 2H), 8.69 (dt, *J* = 8.5, 1.0 Hz, 1H), 7.63 (ddd, *J* = 8.0, 1.3, 0.7 Hz, 1H), 7.49 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.32 (ddd, *J* = 8.0, 7.2, 1.0 Hz, 1H), 7.16 (t, *J* = 4.8 Hz, 1H), 2.57 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.1 (CH), 156.5 (C_q), 136.4 (C_q), 131.5 (C_q), 128.6 (C_q), 127.6 (CH), 123.0 (CH), 120.1 (CH), 117.3 (CH), 116.2 (CH), 113.9 (C_q), 107.2 (C_q), 10.0 (CH_3).

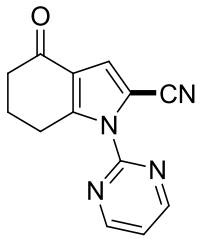
IR (ATR): 3049, 2215, 1567, 1424, 812, 731 cm^{-1}.

MS (EI) m/z (relative intensity) 234 (100) [M^+], 219 (5), 206 (10), 180 (10), 155 (40), 128 (15).

HR-MS (ESI) m/z calcd for $C_{14}H_{11}N_4$ [$M+H^+$] 235.0984, found 235.0978.

The spectral data were in accordance with those reported in the literature.[163]

4-Oxo-1-(pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-indole-2-carbonitrile (127i)



The general procedure **I** was followed using **7i** (107 mg, 0.5 mmol), NCTS (204 mg, 0.75 mmol), Cp*CoI_2(CO) (**112**, 12.0 mg, 5.0 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and KOAc (5.0 mg, 10 mol %). Purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **127i** (108 mg, 91%) as a yellow solid. M. p.: = 238−241 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.83 (d, J = 4.8 Hz, 1H), 7.38 (s, 1H), 7.36 (t, J = 4.8 Hz, 1H), 3.25 (t, J = 6.2 Hz, 2H), 2.60–2.52 (m, 2H), 2.24–2.12 (m, 2H).

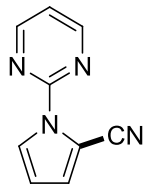
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 193.3 (C_q), 158.6 (CH), 155.2 (C_q), 147.9 (C_q), 122.8 (C_q), 120.9 (CH), 119.9 (CH), 113.1 (C_q), 105.5 (C_q), 37.7 (CH_2), 25.4 (CH_2), 23.3 (CH_2).

IR (ATR): 2963, 2217, 1677, 1577, 1410, 825 cm^{-1}.

MS (EI) m/z (relative intensity) 238 (80) [M^+], 223 (5), 210 (15), 196 (10), 182 (100), 155 (5).

HR-MS (EI) m/z calcd for $C_{13}H_{10}N_4O$ [M^+] 238.0855, found 238.0853.

1-(Pyrimidin-2-yl)-1*H*-pyrrole-2-carbonitrile (145)



The general procedure **I** was followed using **144** (73 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **145** (83 mg, 98%) as a colorless solid. M. p.: = 120−122 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.71 (d, J = 4.8 Hz, 2H), 7.96 (dd, J = 3.2, 1.7 Hz, 1H), 7.20 (t, J = 4.8 Hz, 1H), 7.05 (dd, J = 3.7, 1.7 Hz, 1H), 6.35 (dd, J = 3.7, 3.2 Hz, 1H).

[163] S. Xu, X. Huang, X. Hong, B. Xu, *Org. Lett.* **2012**, *14*, 4614-4617.

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.4 (CH), 155.0 (C_q), 126.0 (CH), 124.9 (CH), 118.8 (CH), 114.0 (C_q), 111.7 (CH), 102.8 (C_q).

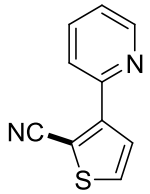
IR (ATR): 3165, 2219, 1564, 1429, 1177, 742 cm^{-1}.

MS (EI) m/z (relative intensity) 170 (100) [M^+], 144 (10), 118 (10), 91 (5), 79 (40), 52 (20).

HR-MS (EI) m/z calcd for $C_9H_6N_4$ [M^+] 170.0592, found 170.0589.

The spectral data were in accordance with those reported in the literature.[163]

3-(Pyridin-2-yl)thiophene-2-carbonitrile (147)



The general procedure **I** was followed using **146** (81 mg, 0.5 mmol) and NCTS (204 mg, 0.75 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 2:1:0:0→8:4:1:0.01) yielded **147** (72 mg, 77%) and **147'** (22 mg, 21%) as slight yellow solids.

147: M. p.: = 43–45 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.70 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.02–7.88 (m, 1H), 7.79 (ddd, J = 8.0, 7.5, 1.8 Hz, 1H), 7.66 (d, J = 5.2 Hz, 1H), 7.59 (d, J = 5.2 Hz, 1H), 7.30 (ddd, J = 7.5, 4.8, 0.9 Hz, 1H).

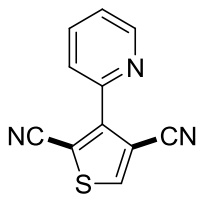
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 150.8 (C_q), 149.9 (CH), 149.8 (C_q), 136.9 (CH), 131.6 (CH), 128.2 (CH), 123.5 (CH), 121.8 (CH), 114.6 (C_q), 106.2 (C_q).

IR (ATR): 3101, 2210, 1582, 1430, 894, 735 cm^{-1}.

MS (EI) m/z (relative intensity) 186 (100) [M^+], 159 (30), 142 (20), 129 (5), 114 (10), 78 (10).

HR-MS (ESI) m/z calcd for $C_{10}H_7N_2S$ [$M+H^+$] 187.0330, found 187.0326.

3-(Pyridin-2-yl)thiophene-2,4-dicarbonitrile (147')



M. p.: = 153–155 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.85–8.78 (m, 1H), 8.21 (s, 1H), 7.95–7.84 (m, 2H), 7.43 (ddd, J = 6.4, 4.8, 2.4 Hz, 1H).

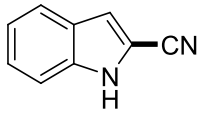
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 150.2 (CH), 150.0 (C_q), 148.2 (C_q), 140.8 (CH), 137.2 (CH), 124.8 (CH), 122.9 (CH), 113.4 (C_q), 112.5 (C_q), 112.2 (C_q), 109.4 (C_q).

IR (ATR): 3088, 2218, 1586, 1465, 993, 744 cm^{-1}.

MS (EI) m/z (relative intensity) 211 (100) [M$^+$], 184 (65), 167 (10), 158 (15), 139 (5), 78 (10).

HR-MS (EI) m/z calcd for $C_{11}H_5N_3S$ [M$^+$] 211.0204, found 211.0205.

1*H*-Indole-2-carbonitrile (127j)



A mixture of **127a** (242 mg, 1.10 mmol), NaOEt (300 mg, 4.40 mmol) and DMSO (6.0 mL) was stirred at 110 °C under an Ar atmosphere for 24 h. At ambient temperature, the reaction mixture was diluted with EtOAc (30 mL) and washed with brine (30 mL). The aqueous phase was extracted with EtOAc (2 × 30 mL), and the combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) to yield **127j** (153 mg, 98%) as a colorless solid. M. p.: 97–98 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.64 (br s, 1H), 7.66 (dd, J = 8.1, 0.9 Hz, 1H), 7.46–7.32 (m, 2H), 7.23–7.18 (m, 2H).

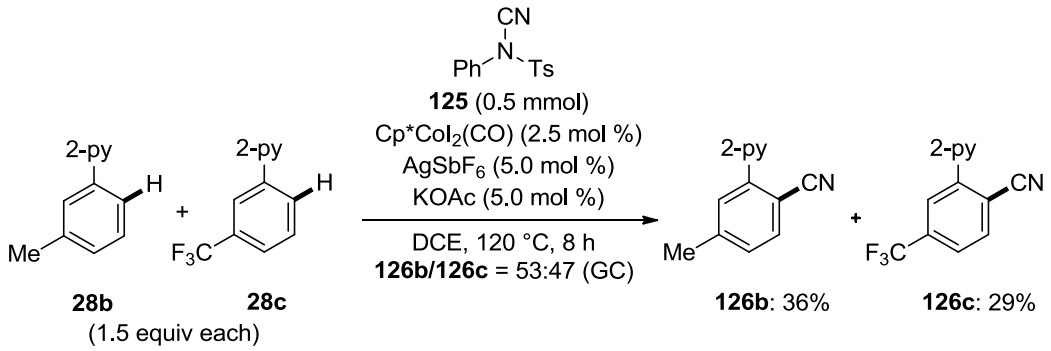
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 136.7 (C_q), 126.2 (CH), 126.1 (C_q), 122.0 (CH), 121.7 (CH), 114.4 (CH), 114.1 (C_q), 111.6 (CH), 106.2 (C_q). IR (ATR): 3273, 2235, 1521, 1409, 1224, 806, 732, 652 cm^{-1}.

MS (EI) m/z (relative intensity) 142 (100) [M$^+$], 115 (40), 98 (5), 89 (10), 74 (5), 63 (10).

HR-MS (EI) m/z calcd for $C_9H_6N_2$ [M$^+$] 142.0531, found 142.0528.

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

Intermolecular Competition Experiment between Substrates 28b and 28c:

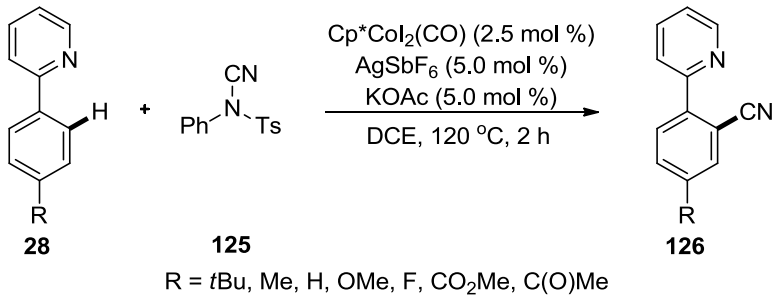


A suspension of NCTS (**125**) (136 mg, 0.50 mmol), 2-(*m*-tolyl)pyridine (**28b**) (127 mg, 0.75 mmol), 2-{3-(trifluoromethyl)phenyl}pyridine (**28c**) (167 mg, 0.75 mmol), Cp*CoI_2(CO) (**112**, 6.0 mg, 2.5 mol %), $AgSbF_6$ (8.6 mg, 5.0 mol %) and KOAc (2.5 mg, 5.0 mol %) in DCE (2.0 mL) was stirred at 120 °C for 8 h under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2/EtOAc 1:1:0.1) to yield **126b** (35 mg, 36%) and **126c** (36 mg, 29%).

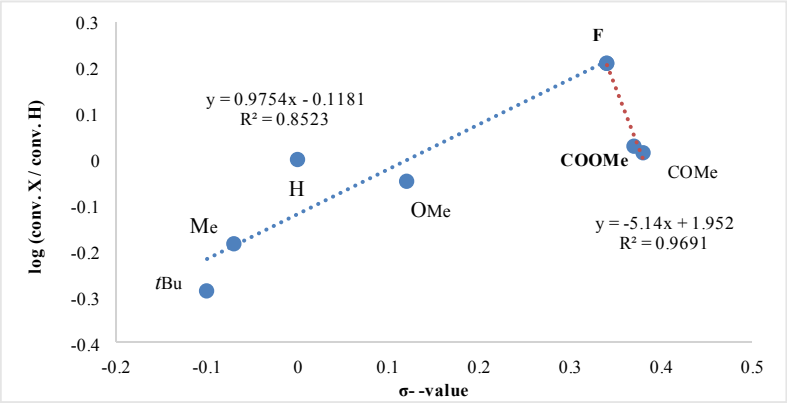
Hammett plot of Reactions of 2-(4-R-Phenyl)pyridines 28 with NCTS (125):

To an oven-dried 25 mL screw-capped vials, respective 2-(4-R-phenyl)pyridines (0.25 mmol), NCTS (**125**, 102 mg, 0.38 mmol), Cp*CoI_2(CO) (**112**, 3.0 mg, 2.5 mol %), $AgSbF_6$ (4.3 mg, 5.0 mol %) and KOAc (1.3 mg, 5.0 mol %) and DCE (1.0 mL) were added under a gentle stream of Ar. The reaction mixtures were stirred for 2 h at 120 °C. After the reaction was finished, the screw-capped vials were cooled with an ice bath. The mixtures were filtered through a pad of Celite each and concentrated *in vacuo*. The residues were analyzed by ^{1}H-NMR spectroscopy. Conversions of starting materials were determined using dibromomethane (43.5 mg, 0.25 mmol) as an internal standard.

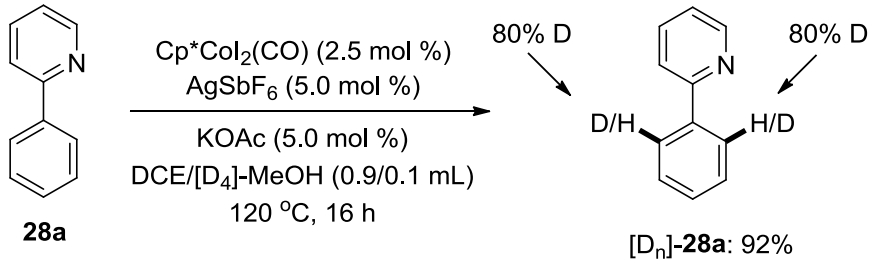
Table **10. 1**.



	P	SM	NMR Conv.	σ_m-	Log(conv. X/conv. H)
R = *t*Bu	13%	85%	15%	–0.1	–0.2863
R = Me	17%	81%	19%	–0.07	–0.1836
R = H	29%	71%	29%	0	0
R = OMe	25%	74%	26%	0.12	–0.0474
R = F	44%	53%	47%	0.34	0.2097
R = CO_2Me	29%	69%	31%	0.37	0.0290
R = COMe	29%	70%	30%	0.38	0.0147



Cobalt-Catalyzed H/D Exchange in Substrate 28a with CD_3OD as the Cosolvent without NCTS:

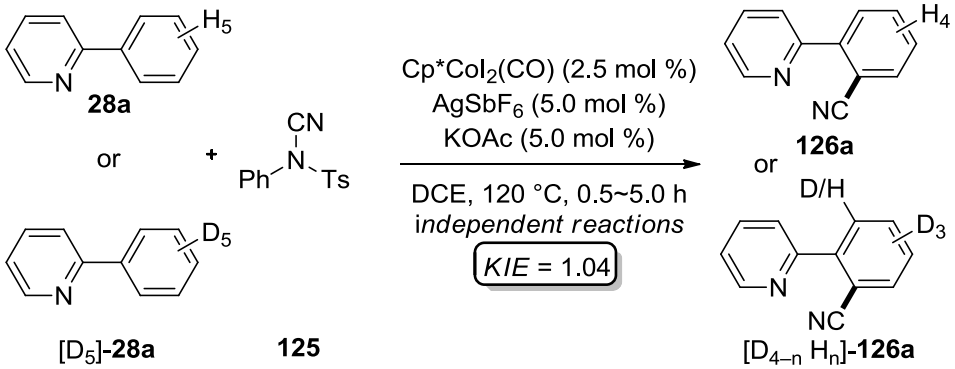


28a

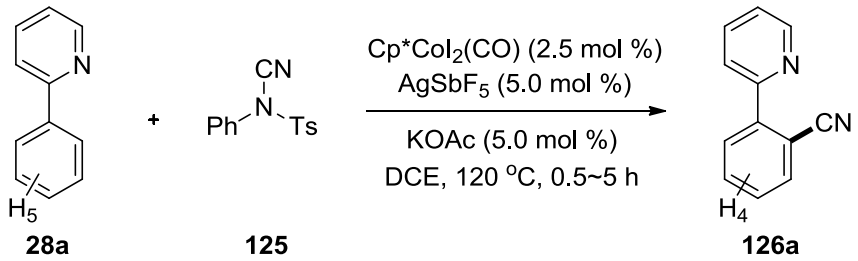
[D_n]-**28a**: 92%

A suspension of 2-phenylpyridine (**28a**) (78 mg, 0.50 mmol), Cp*CoI_2(CO) (**112**, 6.0 mg, 2.5 mol %), $AgSbF_6$ (8.6 mg, 5.0 mol %) and KOAc (2.5 mg, 5.0 mol %) in a solvent mixture of DCE and CD_3OD (0.9/0.1 mL) was stirred at 120 °C for 16 h under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc) to yield [D_n]-**28a** (72 mg, 92%) as a slightly yellow oil. The D-incorporation in [D_n]-**28a** was estimated by ^{1}H-NMR spectroscopy.

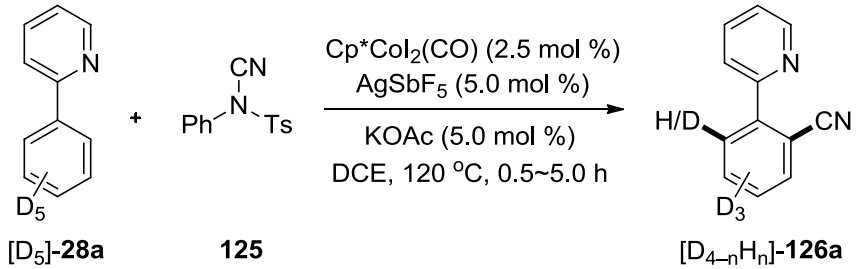
KIE experiments with V-1a and [D_5]-V-1a as substrates:



Two parallel reactions with **28a** and deuterated substrate [D_5]-**28a** under the standard conditions were performed: A suspensions of NCTS (**125**) (102 mg, 0.38 mmol), substrates **28a** (39.0 mg, 0.25 mmol) or [D_5]-**28a** (40.0 mg, 0.25 mmol), Cp*CoI_2(CO) (**112**, 3.0 mg, 2.5 mol %), $AgSbF_6$ (4.3 mg, 5.0 mol %) and KOAc (1.3 mg, 5.0 mol %) in DCE (1.0 mL) was stirred at 120 °C under an atmosphere of Ar. The consumption of substrates **V-1a** or [D_5]-**28a** and the appearance of the products **126a** or [D_n]-**126a** were monitored by GC analysis (with 0.25 mmol dodecane as an internal standard) after 0.5 h, 1.0 h, 1.5 h, 2.0 h, 2.5 h, 3.0 h, 3.5 h, 4.0 h, 5.0 h, respectively. The consumption of substrate **28a** or [D_5]-**28a** and the appearance of the products **126a** or [D_n]-**126a** were monitored by GC analysis (with 0.25 mmol dodecane as an internal standard).

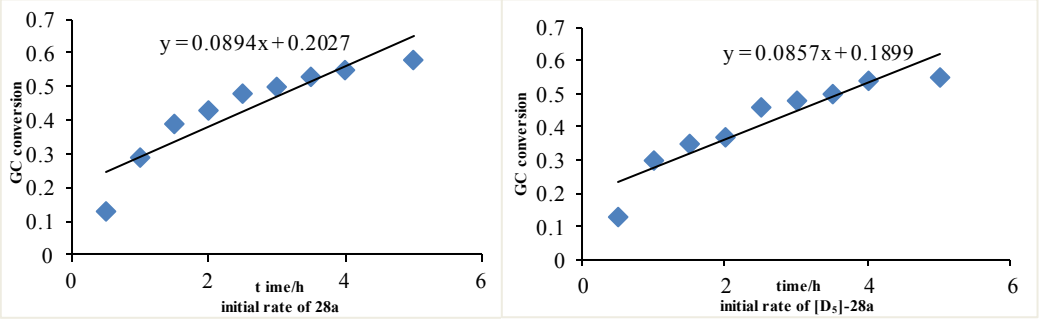


t/(h)	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	5.0
126a	0.13	0.29	0.39	0.43	0.48	0.50	0.53	0.55	0.58
28a	0.84	0.69	0.56	0.52	0.50	0.45	0.47	0.43	0.42

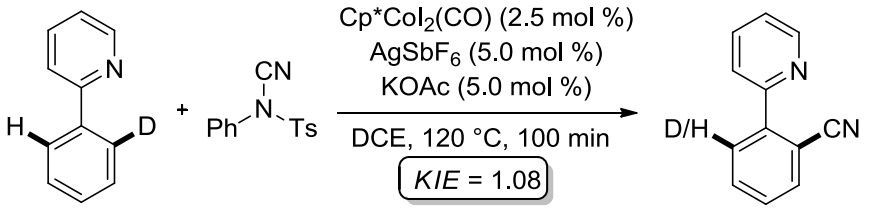


t/(h)	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	5.0
[D_n]-**126a**	0.13	0.30	0.35	0.37	0.46	0.48	0.50	0.54	0.55

[D_5]-**28a**	0.88	0.67	0.64	0.54	0.50	0.50	0.45	0.43	0.40

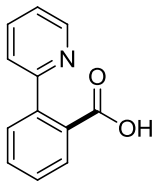


Intramolecular competition experiment: Kinetic isotope effect (KIE):



A suspension of NCTS (**125**) (136 mg, 0.50 mmol), 2-[D]-phenylpyridine ([D_1]-**28a**) (156 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 6.0 mg, 2.5 mol %), $AgSbF_6$ (8.6 mg, 5.0 mol %) and KOAc (2.5 mg, 5.0 mol %) in DCE (2.0 mL) was stirred at 120 °C for 100 min under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 6:1) to yield [D_n]-**126a'** (16 mg, 18%) as a solid. The D-incorporation in [D_n]-**126a'** was estimated by ^{1}H-NMR spectroscopy.

2-(Pyridin-2-yl)benzoic acid (**152**)



A suspension of 2-(pyridin-2-yl)benzonitrile (**126a**) (90 mg, 0.5 mmol), which was prepared according to the general procedure **I** as indicated above, and KOH (180 mg, 5.0 mmol, 1.25 mL of a 4 N aq. solution) was stirred at 105 °C for 12 h. After completion of the reaction, the

reaction mixture was neutralized by HCl aq. (2 N, 2.8 mL). Then the reaction was extracted with CH_2Cl_2 (200 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and the solid was washed with Et_2O (3 × 10 mL) to afford product **152** (92 mg, 83%, calculated from **28a**) as a colorless solid. M. p.: = 201–204 ℃ .

^{1}H-NMR (500 MHz, CD_3OD): δ = 8.53 (ddd, J = 5.1, 1.8, 1.0 Hz, 1H), 7.92 (ddd, J = 7.7, 1.4, 0.5 Hz, 1H), 7.88 (td, J = 7.7, 1.8 Hz, 1H), 7.62 (td, J = 7.5, 1.4 Hz, 1H), 7.57–7.51 (m, 2H), 7.50 (ddd, J = 7.6, 1.4, 0.5 Hz, 1H), 7.39 (ddd, J = 7.6, 5.0, 1.1 Hz, 1H).

^{13}C-NMR (125 MHz, CD_3OD): δ = 171.2 (C_q), 160.3 (C_q), 149.1 (CH), 142.0 (C_q), 138.5 (C_q), 133.1 (CH), 132.4 (CH), 131.3 (CH), 131.2 (CH), 129.7 (CH), 125.2 (CH), 123.7 (CH).

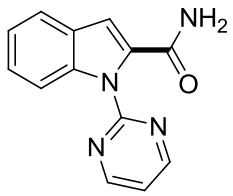
IR (ATR): 2405, 1715, 1429, 1255, 1004, 797 cm^{-1}.

MS (EI) m/z (relative intensity) 199 (5) [M^+], 182 (10), 155 (100), 127 (20), 115 (5), 102 (5).

HR-MS (ESI) m/z calcd for $C_{12}H_8NO_2$ [M-H^+] 198.0555, found 198.0555.

The spectral data were in accordance with those reported in the literature.[164]

1-(Pyrimidin-2-yl)-1*H*-indole-2-carboxamide (153)



To a solution of 1-(pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (**127a**) (66 mg, 0.3 mmol) in *t*BuOH (5.0 mL) was added KOH (336 mg, 6.0 mmol) in small portions. The reaction mixture was stirred at 60 °C for 4 h. Then the reaction was cooled to ambient temperature and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo* and purified by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **153** (52 mg, 72%, calculated from **7a**) as a colorless solid. M. p.: = 254−256 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 9.37 (br s, 1H), 8.70 (br s, 1H), 8.68 (d, J = 4.8 Hz, 2H), 7.69 (dd, J = 8.1, 1.0 Hz, 1H), 7.46 (dd, J = 8.3, 1.1 Hz, 1H), 7.33 (ddd, J = 8.3, 7.0, 1.1 Hz,

[164] M. Chaitanya, D. Yadagiri, P. Anbarasan, *Org. Lett.* **2013**, *15*, 4960–4963.

1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.12 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.06 (t, *J* = 4.8 Hz, 1H).

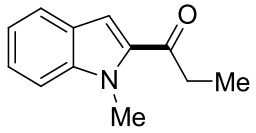
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.4 (CH), 158.4 (C_q), 157.3 (C_q), 136.9 (C_q), 130.1 (C_q), 127.5 (C_q), 125.5 (CH), 122.4 (CH), 121.0 (CH), 116.8 (CH), 112.0 (CH), 104.2 (CH).

IR (ATR): 3388, 3238, 1688, 1573, 1428, 739 cm^{-1}.

MS (EI) m/z (relative intensity) 238 (90) [M^+], 210 (40), 143 (100), 115 (50), 89 (60).

HR-MS (EI) m/z calcd for $C_{13}H_{10}N_4O$ [M^+] 238.0855, found 238.0864.

1-(1-Methyl-1*H*-indol-2-yl)propan-1-one (154)



To the mixture of 1-methyl-1*H*-indole-2-carbonitrile (31.0 mg, 0.20 mmol), prepared from 1*H*-indole-2-carbonitrile (**127j**) according to previously described methods in 99% yield, and CuI (1.0 mg, 5.2 µmol) in anhydrous THF (5 mL) was added EtMgBr (0.21 mmol, 70 µL of a 3 N solution in THF), and the reaction mixture was stirred at ambient temperature for 10 h. Then 1 N HCl aq. solution (3.0 mL) was added at 0 °C, and the resulting mixture was stirred at room temperature for another 4 h. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (*n*-hexane/EtOAc 20:1) yielded **154** (20 mg, 52%, calculated from **7a**) as a slightly yellow solid. M. p.: = 55−57 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.71–7.65 (d, *J* = 8.0 Hz, 1H), 7.40–7.33 (m, 2H), 7.28 (d, *J* = 0.7 Hz, 1H), 7.14 (ddd, *J* = 8.0, 5.6, 2.2 Hz, 1H), 4.07 (s, 3H), 3.00 (q, *J* = 7.4 Hz, 2H), 1.23 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 194.9 (C_q), 139.9 (C_q), 134.6 (C_q), 125.7 (C_q), 125.6 (CH), 122.7 (CH), 120.6 (CH), 110.8 (CH), 110.3 (CH), 33.1 (CH_2), 32.2 (CH_3), 9.0 (CH_3).

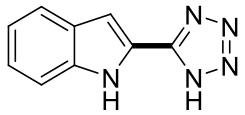
IR (ATR): 2951, 1663, 1511, 1315, 1155, 731 cm^{-1}.

MS (EI) m/z (relative intensity) 187 (50) [M^+], 158 (100), 144 (5), 130 (25), 115 (5), 89 (50).

HR-MS (EI) m/z calcd for $C_{12}H_{13}NO$ [M^+] 187.0997, found 187.0995.

The spectral data were in accordance with those reported in the literature.[165]

2-(1*H*-Tetrazol-5-yl)-1*H*-indole (155)



To the vial equipped with a magnetic bar, TBAF·3H_2O (32 mg, 0.1 mmol), 1*H*-indole-2-carbonitrile (29 mg, 0.2 mmol) and $TMSN_3$ (34.5 mg, 0.3 mmol) were added. The vial was sealed and heated under vigorous stirring at 120 °C for 18 h. The crude reaction mixture was diluted with EtOAc (20 mL) and TBAF was removed by washing the organic phase with 1 N aq. HCl aqueous solution (3 × 5 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude solid was washed with a 2:1 *n*-hexane/Et_2O mixture (2 × 10 mL) to afford **155** (36 mg, 94%, calculated from **7a**) as a colorless solid. M. p.: = 232−234 °C.

^{1}H-NMR (500 MHz, CD_3OD): δ = 7.63 (dt, J = 8.0, 1.0 Hz, 1H), 7.49 (dd, J = 8.3, 0.9 Hz, 1H), 7.23 (ddd, J = 8.3, 7.0, 1.0 Hz, 1H), 7.12 (d, J = 0.9 Hz, 1H), 7.09 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H).

^{13}C-NMR (125 MHz, CD_3OD): δ = 152.3 (C_q), 139.1 (C_q), 129.4 (C_q), 125.1 (CH), 122.9 (C_q), 122.3 (CH), 121.5 (CH), 113.0 (CH), 105.1 (CH).

IR (ATR): 3226, 1618, 1339, 1084, 924, 744 cm^{-1}.

MS (EI) m/z (relative intensity) 185 (70) [M^+], 157 (100), 142 (35), 130 (40), 115 (20), 103 (70).

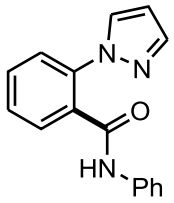
HR-MS (EI) m/z calcd for $C_9H_7N_5$ [M^+] 185.0701, found 185.0705.

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

10.4.6 Analytical Data for the Products of Cobalt(III)-Catalyzed Aryl and Alkenyl C−H Bond Aminocarbonylation with Isocyanates and Acyl Azides

***N*-Phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130aa)**

[165] Y.-T. Hong, A. Barchuk, M. J. Krische, *Angew. Chem. Int. Ed.* **2006**, *45*, 6885–6888.



The general procedure **J** was followed using **128a** (72 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130aa** (88 mg, 67%) as a colorless solid. M. p.: = 167−169 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.47 (br s, 1H), 7.93–7.86 (m, 1H), 7.79–7.74 (m, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.57–7.48 (m, 2H), 7.45–7.35 (m, 3H), 7.25 (t, J = 7.6 Hz, 2H), 7.06 (ddt, J = 7.8, 6.9, 1.2 Hz, 1H), 6.44 (t, J = 2.2 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.4 (C_q), 141.4 (CH), 137.8 (C_q), 137.2 (C_q), 133.0 (C_q), 131.9 (CH), 131.3 (CH), 130.6 (CH), 129.1 (CH), 128.8 (CH), 126.7 (CH), 124.4 (CH), 120.0 (CH), 107.8 (CH).

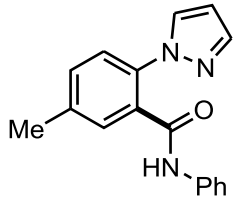
IR (ATR): 3245, 1650, 1541, 1326, 942, 755 cm^{-1}.

MS (EI) m/z (relative intensity) 263 (5) [M$^+$], 171 (100), 144 (5), 130 (5), 116 (20), 89 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{13}N_3O$ [M$^+$] 263.1059, found 263.1061.

The spectral data were in accordance with those reported in the literature.[166]

5-Methyl-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130ba)



The general procedure **J** was followed using **128b** (79 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130ba** (84 mg, 61%) as a colorless solid. M. p.: = 168−170 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.33 (br s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.80–7.75 (m, 1H), 7.67 (d, J = 2.4 Hz, 1H), 7.40 (d, J = 7.3 Hz, 2H), 7.36–7.31 (m, 1H), 7.28–7.24 (m, 2H), 7.22–7.21 (m, 1H), 7.09–6.96 (m, 1H), 6.44 (t, J = 2.1 Hz, 1H), 2.43 (s, 3H).

[166] K. Muralirajan, K. Parthasarathy, C.-H. Cheng, *Org. Lett.* **2012**, *14*, 4262–4265.

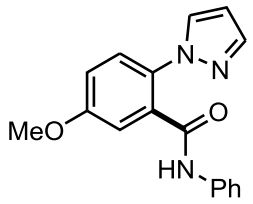
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.3 (C_q), 142.2 (C_q), 141.3 (CH), 138.0 (C_q), 137.1 (C_q), 132.1 (CH), 130.8 (CH), 130.2 (C_q), 130.0 (CH), 128.8 (CH), 127.6 (CH), 124.3 (CH), 120.0 (CH), 107.7 (CH), 21.1 (CH_3).

IR (ATR): 3244, 1650, 1543, 1325, 952, 757 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (5) [M^+], 185 (100), 167 (5), 142 (5), 130 (10), 103 (10).

HR-MS (EI) m/z calcd for $C_{17}H_{15}N_3O$ [M^+] 277.1215, found 277.1216.

5-Methoxy-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130ca)



The general procedure **J** was followed using **128c** (87 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ca** (92 mg, 63%) as a colorless solid. M. p.: = 122−124 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.54 (br s, 1H), 7.78 (dd, J = 1.9, 0.7 Hz, 1H), 7.62 (dd, J = 2.4, 0.7 Hz, 1H), 7.45 (d, J = 3.0 Hz, 1H), 7.43–7.37 (m, 2H), 7.28 (d, J = 8.7 Hz, 1H), 7.27–7.23 (m, 2H), 7.08–7.05 (m, 1H), 7.05–7.02 (m, 1H), 6.42 (t, J = 2.2 Hz, 1H), 3.88 (s, 3H).

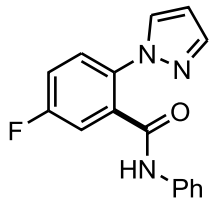
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.9 (C_q), 160.0 (C_q), 141.2 (CH), 137.8 (C_q), 134.5 (C_q), 132.6 (CH), 130.2 (C_q), 128.8 (CH), 128.7 (CH), 124.4 (CH), 120.0 (CH), 117.7 (CH), 114.7 (CH), 107.5 (CH), 55.8 (CH_3).

IR (ATR): 3244, 1653, 1555, 1444, 1037, 753 cm^{-1}.

MS (EI) m/z (relative intensity) 293 (5) [M^+], 201 (100), 186 (15), 174 (5), 158 (10), 146 (5).

HR-MS (ESI) m/z calcd for $C_{17}H_{16}N_3O_2$ [$M+H^+$] 294.1243, found 294.1237.

5-Fluoro-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130da)



The general procedure **J** was followed using **128d** (81 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130da** (91 mg, 65%) as a colorless solid. M. p.: = 142−144 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.53 (br s, 1H), 7.80 (dd, J = 2.0, 0.6 Hz, 1H), 7.71–7.57 (m, 2H), 7.45–7.32 (m, 3H), 7.31–7.16 (m, 3H), 7.11–7.02 (m, 1H), 6.46 (dd, J = 2.4, 1.9 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.0 (C_q, $J_{C\text{-}F}$ = 251.6 Hz), 162.7 (C_q), 141.6 (CH), 137.6 (C_q), 135.3 (C_q, $J_{C\text{-}F}$ = 7.8 Hz), 133.4 (C_q, J = 3.4 Hz), 132.4 (CH), 129.3 (CH, $J_{C\text{-}F}$ = 8.5 Hz), 128.9 (CH), 124.7 (CH), 120.1 (CH), 118.4 (CH, $J_{C\text{-}F}$ = 22.8 Hz), 117.9 (CH, $J_{C\text{-}F}$ = 24.6 Hz), 108.0 (CH).

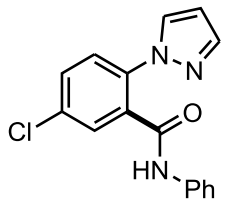
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –(110.2 – 110.3) (m).

IR (ATR): 3270, 1650, 1490, 1326, 1045, 732 cm^{-1}.

MS (EI) m/z (relative intensity) 281 (5) [M^+], 189 (100), 162 (5), 148 (5), 134 (10), 107 (10).

HR-MS (EI) m/z calcd for $C_{16}H_{12}N_3OF$ [M^+] 281.0964, found 281.0972.

5-Chloro-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130ea)



The general procedure **J** was followed using **128e** (89 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130ea** (106 mg, 71%) as a colorless solid. M. p.: = 137−139 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.63 (br s, 1H), 7.85 (d, J = 2.2 Hz, 1H), 7.78–7.75 (m, 1H), 7.68 (dd, J = 2.4, 0.7 Hz, 1H), 7.47 (dd, J = 8.6, 2.5 Hz, 1H), 7.39 (dd, J = 8.6, 1.2 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 7.28–7.21 (m, 1H), 7.13–7.01 (m, 1H), 6.45 (dd, J = 2.2, 1.8 Hz, 1H).

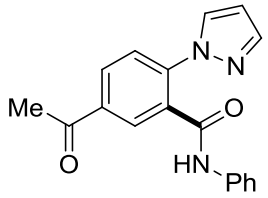
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.1 (C_q), 141.7 (CH), 137.6 (C_q), 135.7 (C_q), 135.0 (C_q), 134.2 (C_q), 131.9 (CH), 131.3 (CH), 130.6 (CH), 128.9 (CH), 127.9 (CH), 124.7 (CH), 120.1 (CH), 108.1 (CH).

IR (ATR): 3115, 1656, 1552, 1324, 944, 748 cm^{-1}.

MS (EI) m/z (relative intensity) 297 (5) [M^+], 205 (100), 178 (5), 150 (10), 142 (5), 123 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{13}N_3OCl$ [M+H$^+$] 298.0747, found 298.0742.

5-Acetyl-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130fa)



The general procedure **J** was followed using **128f** (93 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 5:1:1) yielded **130fa** (60 mg, 39%) and **130fa'** (72 mg, 34%) as off white solids. **130fa**: M. p.: = 173−175 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.68 (br s, 1H), 8.34 (d, J = 1.9 Hz, 1H), 8.07 (dd, J = 8.3, 1.9 Hz, 1H), 7.84–7.73 (m, 2H), 7.57–7.40 (m, 3H), 7.36–7.18 (m, 2H), 7.08 (d, J = 7.3 Hz, 1H), 6.48 (dd, J = 1.9,1.8 Hz, 1H), 2.60 (s, 3H).

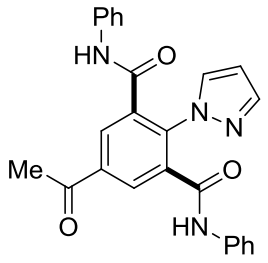
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.2 (C_q), 164.1 (C_q), 142.0 (CH), 140.4 (C_q), 137.6 (C_q), 136.5 (C_q), 132.2 (C_q), 131.3 (CH), 130.9 (CH), 130.7 (CH), 128.9 (CH), 126.0 (CH), 124.7 (CH), 120.1 (CH), 108.5 (CH), 26.7 (CH_3).

IR (ATR): 3289, 1677, 1651, 1594, 1243, 935, 750 cm^{-1}.

MS (EI) m/z (relative intensity) 305 (5) [M$^+$], 213 (100), 170 (10), 143 (5), 115 (5).

HR-MS (EI) m/z calcd for $C_{18}H_{15}N_3O_2$ [M$^+$] 305.1164, found 305.1172.

5-Acetyl-*N*1,*N*3-diphenyl-2-(1*H*-pyrazol-1-yl)isophthalamide (130fa')



M. p.: = 89–91 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 11.29 (s, 1H), 7.95 (d, J = 2.0 Hz, 1H), 7.86 (dd, J = 8.5, 2.0 Hz, 1H), 7.82 (dd, J = 1.8, 0.6 Hz, 1H), 7.71 (d, J = 2.6 Hz, 1H), 7.63–7.56 (m, 2H), 7.31 (t, J = 8.0 Hz, 2H), 7.27 (d, J = 8.7 Hz, 1H), 7.14–6.99 (m, 4H), 6.81 (s, 2H), 6.55 (dd, J = 2.6, 1.7 Hz, 1H), 2.55 (s, 3H).

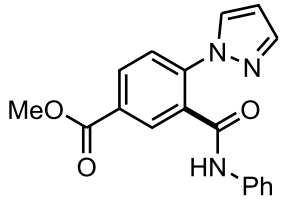
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 195.5 (C_q), 151.6 (C_q), 151.6 (C_q), 142.4 (CH), 138.6 (C_q), 137.7 (C_q), 137.7 (C_q), 137.1 (C_q), 134.4 (C_q), 130.2 (CH), 129.7 (CH), 129.5 (CH), 129.0 (CH), 129.0 (CH), 128.6 (CH), 128.4 (CH), 124.2 (CH), 120.2 (CH), 109.1 (CH), 26.5 (CH_3).

IR (ATR): 3067, 1714, 1521, 1226, 935, 752 cm^{-1}.

MS (EI) m/z (relative intensity) 425 (5) [M^+], 213 (100), 170 (10), 143 (5), 119 (35).

HR-MS (ESI) m/z calcd for $C_{25}H_{21}N_4O_3$ [M+H^+] 425.1614 found 425.1608.

Methyl 3-(phenylcarbamoyl)-4-(1*H*-pyrazol-1-yl)benzoate (130ga)



The general procedure **J** was followed using **128g** (101 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ga** (121 mg, 75%) as a colorless solid. M. p.: = 163−165 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, J = 2.0 Hz, 1H), 8.32 (br s, 1H), 8.18 (dd, J = 8.3, 2.0 Hz, 1H), 7.78 (d, J = 2.1 Hz, 2H), 7.53 (d, J = 8.3 Hz, 1H), 7.48–7.40 (m, 2H), 7.28 (t, J = 7.9 Hz, 2H), 7.16–7.03 (m, 1H), 6.47 (dd, J = 2.0, 2.1 Hz, 1H), 3.95 (s, 3H).

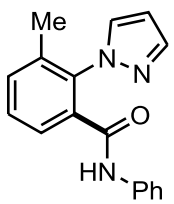
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.4 (C_q), 164.0 (C_q), 142.0 (CH), 140.5 (C_q), 137.6 (C_q), 132.3 (C_q), 132.3 (CH), 131.9 (CH), 131.4 (CH), 130.2 (C_q), 129.0 (CH), 126.0 (CH), 124.8 (CH), 120.1 (CH), 108.4 (CH), 52.6 (CH_3).

IR (ATR): 3281, 1714, 1547, 1303, 1121, 742 cm^{-1}.

MS (EI) m/z (relative intensity) 321 (5) [M^+], 290 (5), 229 (100), 197 (5), 170 (5).

HR-MS (EI) m/z calcd for $C_{18}H_{15}N_3O_3$ [M^+] 321.1113, found 321.1122.

3-Methyl-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130ha)



The general procedure **J** was followed using **128h** (79 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 12:1:1:1%) yielded **130ha** (112 mg, 81%) as a colorless solid. M. p.: = 109−111 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.85 (dd, J = 2.0, 0.6 Hz, 1H), 7.82 (br s, 1H), 7.80–7.76 (m, 1H), 7.56 (dd, J = 2.4, 0.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.45–7.41 (m, 1H), 7.35–7.30 (m, 2H), 7.25–7.21 (m, 2H), 7.09–6.98 (m, 1H), 6.46 (dd, J = 2.0, 2.2 Hz, 1H), 2.05 (s, 3H).

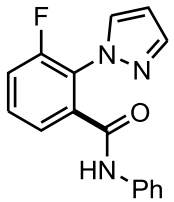
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 164.3 (C_q), 141.6 (CH), 137.8 (C_q), 137.2 (C_q), 136.1 (C_q), 135.1 (C_q), 133.1 (CH), 132.8 (CH), 129.9 (CH), 128.8 (CH), 128.2 (CH), 124.4 (CH), 119.9 (CH), 107.6 (CH), 17.1 (CH_3).

IR (ATR): 3107, 1668, 1542, 1441, 1319, 752 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (5) [M^+], 185 (100), 156 (5), 142 (5), 130 (10), 103 (10).

HR-MS (ESI) m/z calcd for $C_{17}H_{16}N_3O$ [M+H^+] 278.1293, found 278.1288.

3-Fluoro-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130ia)



The general procedure **J** was followed using **128i** (81 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130ia** (112 mg, 80%) as a colorless solid. M. p.: = 175−177 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.64 (br s, 1H), 7.89–7.86 (m, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.68 (td, J = 1.6, 0.7 Hz, 1H), 7.58–7.48 (m, 1H), 7.43–7.38 (m, 2H), 7.34 (ddd, J = 9.1, 8.3, 1.4 Hz, 1H), 7.29–7.20 (m, 2H), 7.12–6.97 (m, 1H), 6.51 (dd, J = 2.5, 1.9 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.8 (C_q, J_{C-F} = 3.2 Hz), 157.4 (C_q, J_{C-F} = 253.5 Hz), 142.0 (CH), 137.7 (C_q), 136.3 (C_q), 133.7 (CH, J_{C-F} = 1.9 Hz), 130.9 (CH, J_{C-F} = 8.2 Hz), 128.9 (CH), 126.2 (CH, J_{C-F} = 3.7 Hz), 125.7 (C_q, J_{C-F} = 13.8 Hz), 124.6 (CH), 120.0 (CH), 118.7 (CH, J_{C-F} = 20.6 Hz), 107.9 (CH).

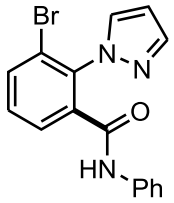
^{19}F-NMR (376 MHz, $CDCl_3$): δ = -121.9 (dd, J = 9.3, 5.1 Hz).

IR (ATR): 3243, 1651, 1543, 1308, 977, 752 cm^{-1}.

MS (EI) m/z (relative intensity) 281 (5) [M^+], 189 (100), 162 (5), 148 (5), 134 (10), 107 (10).

HR-MS (EI) m/z calcd for $C_{16}H_{13}N_3OF$ [M+H^+] 282.1043, found 282.1037.

3-Bromo-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130ja)



The general procedure **J** was followed using **128j** (111 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 12:1:1:1%) yielded **130ja** (116 mg, 68%) as a colorless solid. M. p.: = 123−124 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.44 (br s, 1H), 7.89–7.83 (m, 2H), 7.77 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.63 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.37–7.32 (m, 2H), 7.20 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.12–6.98 (m, 1H), 6.52–6.47 (m, 1H).

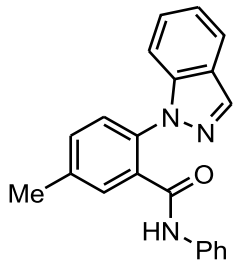
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.0 (C_q), 141.8 (CH), 137.6 (C_q), 137.1 (C_q), 136.2 (C_q), 135.4 (CH), 133.3 (CH), 131.0 (CH), 129.6 (CH), 128.7 (CH), 124.5 (CH), 123.2 (C_q), 120.0 (CH), 107.7 (CH).

IR (ATR): 3244, 1656, 1540, 1440, 1318, 749 cm^{-1}.

MS (EI) m/z (relative intensity) 341 (5) [M^+], 249 (100), 222 (5), 194 (5), 170 (10), 142 (10).

HR-MS (EI) m/z calcd for $C_{16}H_{14}N_3O^{79}Br$ [M+H^+] 342.0242, found 342.0237.

2-(1*H*-Indazol-1-yl)-5-methyl-*N*-phenylbenzamide (130ka)



The general procedure **J** was followed using **128k** (104 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 12:1:1:1%) yielded **130ka** (87 mg, 53%) as a colorless solid. M. p.: = 128–130 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.42 (br s, 1H), 8.27 (d, J = 1.0 Hz, 1H), 7.91–7.85 (m, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.42 (ddd, J = 8.2, 2.1, 0.9 Hz, 1H), 7.36 (ddd, J = 8.6, 6.9, 1.1 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.28 (dd, J = 8.5, 1.0 Hz, 1H), 7.26–7.23 (m, 2H), 7.18 (m, 3H), 7.07–6.94 (m, 1H), 2.49 (s, 3H).

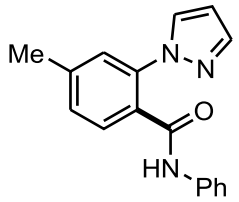
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.4 (C_q), 141.4 (C_q), 139.7 (C_q), 137.7 (C_q), 135.7 (CH), 133.9 (C_q), 133.3 (C_q), 132.3 (CH), 131.9 (CH), 128.7 (CH), 128.0 (CH), 127.8 (CH), 124.3 (C_q), 124.3 (CH), 121.9 (CH), 121.2 (CH), 120.0 (CH), 110.2 (CH), 21.2 (CH_3).

IR (ATR): 3059, 1648, 1547, 1330, 831, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 327 (5) [M^+], 235 (100), 220 (10), 208 (10), 192 (10), 180 (10).

HR-MS (EI) m/z calcd for $C_{21}H_{17}N_3O$ [M^+] 327.1372, found 327.1368.

4-Methyl-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (130la)



The general procedure **J** was followed using **128l** (79 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 12:1:1:1%) yielded **130la** (91 mg, 66%) as a colorless solid. M. p.: = 130−132 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.52 (br s, 1H), 7.76 (d, J = 1.9 Hz, 1H), 7.74–7.69 (m, 1H), 7.65 (d, J = 2.4 Hz, 1H), 7.43–7.38 (m, 2H), 7.35–7.29 (m, 1H), 7.28–7.20 (m, 3H), 7.09–7.01 (m, 1H), 6.42 (s, 1H), 2.43 (s, 3H).

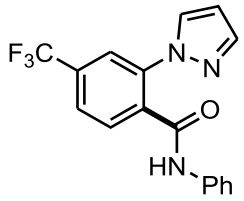
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.5 (C_q), 141.2 (CH), 139.5 (C_q), 137.9 (C_q), 134.8 (C_q), 132.7 (C_q), 132.1 (CH), 131.9 (CH), 131.1 (CH), 128.8 (CH), 126.8 (CH), 124.4 (CH), 120.0 (CH), 107.6 (CH), 21.0 (CH_3).

IR (ATR): 3241, 1661, 1543, 1323, 1025, 748 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (5) [M^+], 185 (100), 258 (5), 142 (5), 130 (10), 103 (10).

HR-MS (ESI) m/z calcd for $C_{17}H_{16}N_3O$ [$M+H^+$] 278.1293, found 278.1288.

***N*-Phenyl-2-(1*H*-pyrazol-1-yl)-4-(trifluoromethyl)benzamide (130ma)**



The general procedure **J** was followed using **128m** (106 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 10 mol%), $AgNTf_2$ (39.0 mg, 20 mol%) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ma** (78 mg, 42%) as a colorless solid. M. p.: = 142−144 °C.

^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.39 (s, 1H), 8.26 (d, J = 2.5 Hz, 1H), 8.05 (s, 1H), 7.86 (d, J = 1.1 Hz, 2H), 7.70 (d, J = 1.8 Hz, 1H), 7.62–7.53 (m, 2H), 7.31 (t, J = 7.9 Hz, 2H), 7.16–7.04 (m, 1H), 6.51 (dd, J = 2.5, 1.8 Hz, 1H).

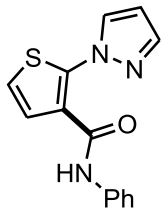
^{13}C-NMR (125 MHz, DMSO-d_6): δ = 164.5 (C_q), 141.4 (CH), 138.7 (C_q), 137.6 (C_q), 135.0 (C_q), 130.7 (C_q, $J_{C\text{-}F}$ = 32.6 Hz), 130.4 (CH), 130.2 (CH), 128.6 (CH), 123.3 (C_q, $J_{C\text{-}F}$ = 273.1 Hz), 123.7 (CH), 120.2 (CH, $J_{C\text{-}F}$ = 3.9 Hz), 119.6 (CH), 107.8 (CH).

IR (ATR): 3041, 1649, 1449, 1314, 1126, 758 cm^{-1}.

MS (EI) m/z (relative intensity) 331 (5) [M$^+$], 312 (5), 239 (100), 212 (5), 198 (5), 184 (5).

HR-MS (EI) m/z calcd for $C_{17}H_{12}N_3F_3O$ [M$^+$] 331.0932, found 331.0941.

***N*-Phenyl-2-(1*H*-pyrazol-1-yl)thiophene-3-carboxamide (130na)**



The general procedure **J** was followed using **128n** (75 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130na** (123 mg, 91%) as a colorless solid. M. p.: = 129−131 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 10.31 (br s, 1H), 7.88 (dd, J = 2.0, 0.6 Hz, 1H), 7.80 (dd, J = 2.5, 0.7 Hz, 1H), 7.61–7.57 (m, 2H), 7.56 (d, J = 5.8 Hz, 1H), 7.30 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.14 (d, J = 5.8 Hz, 1H), 7.07 (tt, J = 7.4, 1.2 Hz, 1H), 6.52 (dd, J = 2.5, 2.0 Hz, 1H).

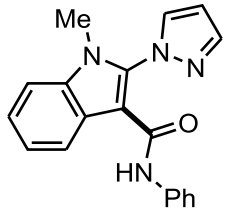
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.5 (C_q), 142.0 (CH), 139.6 (C_q), 138.3 (C_q), 133.8 (CH), 131.0 (C_q), 130.1 (CH), 128.9 (CH), 124.2 (CH), 121.2 (CH), 119.8 (CH), 108.6 (CH).

IR (ATR): 3225, 1660, 1534, 1312, 1057, 751 cm^{-1}.

MS (EI) m/z (relative intensity) 269 (15) [M^+], 177 (100), 150 (5), 122 (10), 105 (5).

HR-MS (EI) m/z calcd for $C_{14}H_{11}N_3OS$ [M^+] 269.0623, found 269.0612.

1-Methyl-*N*-phenyl-2-(1*H*-pyrazol-1-yl)-1*H*-indole-3-carboxamide (130oa)



The general procedure **J** was followed using **128o** (106 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 10 mol%), $AgNTf_2$ (39.0 mg, 20 mol%) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130oa** (66 mg, 42%) as a yellow oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.40 (ddd, *J* = 8.0, 1.3, 0.9 Hz, 1H), 8.08 (br s, 1H), 8.01 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.78 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.46–7.42 (m, 2H), 7.40 (ddd, *J* = 8.3, 6.7, 1.3 Hz, 1H), 7.37–7.31 (m, 2H), 7.28–7.24 (m, 2H), 6.63 (dd, *J* = 2.5, 1.9 Hz, 1H), 3.50 (s, 3H).

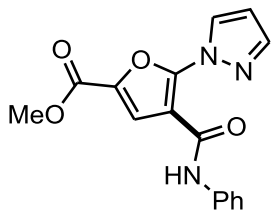
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.3 (C_q), 143.1 (CH), 138.5 (C_q), 134.4 (C_q), 134.3 (CH), 133.3 (C_q), 128.8 (CH), 125.3 (C_q), 124.42 (CH), 123.6 (CH), 122.6 (CH), 122.5 (CH), 119.5 (CH), 109.7 (CH), 108.5 (CH), 107.3 (C_q), 29.6 (CH_3).

IR (ATR): 1658, 1528, 1449, 1245, 1103, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 316 (15) [M^+], 224 (100), 209 (5), 196 (5), 169 (10).

HR-MS (EI) m/z calcd for $C_{19}H_{16}N_4O$ [M^+] 316.1324, found 316.1333.

Methyl 4-(phenylcarbamoyl)-5-(1*H*-pyrazol-1-yl)furan-2-carboxylate (130pa)



The general procedure **J** was followed using **128p** (96 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 10 mol %), $AgSbF_6$ (34.4 mg, 20 mol%) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130pa** (78 mg, 50%) as a colorless solid. M. p.: = 140−142 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 12.3 (br s, 1H), 8.26 (dd, *J* = 2.8, 0.6 Hz, 1H), 7.93 (d, *J* = 1.7 Hz, 1H), 7.83 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.34 (dd, *J* = 8.4, 7.5 Hz, 2H), 7.10 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.60 (dd, *J* = 2.8, 1.7 Hz, 1H), 3.91 (s, 3H).

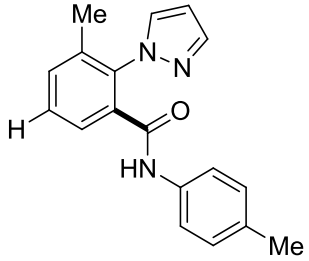
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.1 (C_q), 157.3 (C_q), 144.2 (C_q), 142.2 (CH), 138.5 (C_q), 138.3 (C_q), 130.2 (CH), 129.0 (CH), 124.2 (CH), 122.7 (CH), 120.0 (CH), 110.0 (C_q), 108.9 (CH), 52.3 (CH_3).

IR (ATR): 3027, 1739, 1557, 1317, 1147, 748 cm^{-1}.

MS (EI) m/z (relative intensity) 311 (25) [M^+], 280 (5), 243 (5), 219 (100), 187 (5), 151 (15).

HR-MS (EI) m/z calcd for $C_{16}H_{13}N_3O_4$ [M^+] 311.0906, found 311.0903.

3-Methyl-2-(1*H*-pyrazol-1-yl)-*N*-(*p*-tolyl)benzamide (130hb)



The general procedure **J** was followed using **128h** (79 mg, 0.5 mmol) and **129b** (133 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 12:1:1:1%) yielded **130hb** (74 mg, 51%) as a colorless solid. M. p.: = 149−151 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.79 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.73 (br s, 1H), 7.55 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.47 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.42 (ddd, *J* = 7.6, 1.7, 0.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.45 (dd, *J* = 2.2, 1.6 Hz, 1H), 2.26 (s, 3H), 2.05 (s, 3H).

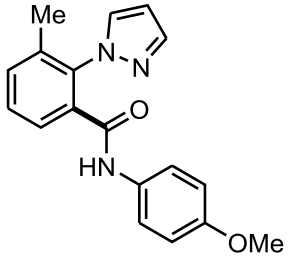
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.2 (C_q), 141.5 (CH), 137.1 (C_q), 136.1 (C_q), 135.2 (C_q), 135.2 (C_q), 134.0 (C_q), 133.0 (CH), 132.7 (CH), 129.8 (CH), 129.3 (CH), 128.1 (CH), 120.0 (CH), 107.5 (CH), 20.8 (CH_3), 17.1 (CH_3).

IR (ATR): 3244, 1672, 1523, 1317, 1050, 751 cm^{-1}.

MS (EI) m/z (relative intensity) 291 (5) [M^+], 185 (100), 158 (5), 142 (5), 130 (10), 103 (5).

HR-MS (EI) m/z calcd for $C_{18}H_{17}N_3O$ [M^+] 291.1372, found 291.1381.

***N*-(4-Methoxyphenyl)-3-methyl-2-(1*H*-pyrazol-1-yl)benzamide (130hc)**



The general procedure **J** was followed using **128h** (79 mg, 0.5 mmol) and **129c** (149 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130hc** (78 mg, 51%) as colorless solids. M. p.: = 98−100 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.83 (dd, J = 2.0, 0.6 Hz, 1H), 7.76 (dd, J = 7.6, 1.1 Hz, 1H), 7.71 (br s, 1H), 7.55 (dd, J = 2.4, 0.6 Hz, 1H), 7.47 (dd, J = 7.6, 7.6 Hz, 1H), 7.43–7.39 (m, 1H), 7.22 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 9.0 Hz, 2H), 6.46 (t, J = 2.1 Hz, 1H), 3.74 (s, 3H), 2.04 (s, 3H).

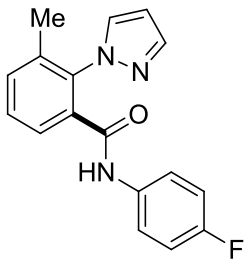
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.1 (C_q), 156.4 (C_q), 141.4 (CH), 137.1 (C_q), 136.1 (C_q), 135.2 (C_q), 132.9 (CH), 132.8 (CH), 130.9 (C_q), 129.8 (CH), 128.1 (CH), 121.7 (CH), 113.9 (CH), 107.5 (CH), 55.4 (CH_3), 17.1 (CH_3).

IR (ATR): 3103, 1659, 1511, 1243, 1035, 759 cm^{-1}.

MS (EI) m/z (relative intensity) 307 (5) [M^+], 185 (100), 156 (5), 142 (5), 130 (5), 103 (5).

HR-MS (EI) m/z calcd for $C_{18}H_{17}N_3O_2$ [M^+] 307.1321, found 307.1327.

***N*-(4-Fluorophenyl)-3-methyl-2-(1*H*-pyrazol-1-yl)benzamide (130hd)**



The general procedure **J** was followed using **128h** (79 mg, 0.5 mmol) and **129d** (114 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130hd** (143 mg, 97%) as a colorless solid. M. p.: = 144−146 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.94 (br s, 1H), 7.83 (dd, J = 2.0, 0.6 Hz, 1H), 7.78–7.71 (m, 1H), 7.55 (dd, J = 2.4, 0.6 Hz, 1H), 7.46 (dd, J = 7.6, 7.6 Hz, 1H), 7.43–7.39 (m, 1H), 7.31–7.25 (m, 2H), 7.01–6.77 (m, 2H), 6.46 (dd, J = 2.4, 1.9 Hz, 1H), 2.04 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.3 (C_q), 159.3 (C_q, $J_{C\text{-}F}$ = 243.7 Hz), 141.4 (CH), 137.1 (C_q), 136.1 (C_q), 134.9 (C_q), 133.8 (C_q, $J_{C\text{-}F}$ = 2.9 Hz), 133.1 (CH), 132.8 (CH), 129.8 (CH), 128.1 (CH), 121.7 (CH, $J_{C\text{-}F}$ = 7.9 Hz), 115.4 (CH, $J_{C\text{-}F}$ = 22.4 Hz), 107.5 (CH), 17.1 (CH_3).

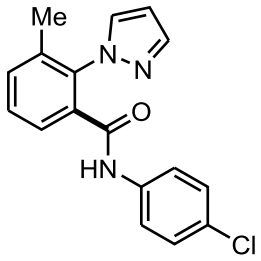
^{19}F-NMR (376 MHz, $CDCl_3$): δ = -117.8 (td, J = 8.4, 4.5 Hz).

IR (ATR): 3056, 1673, 1508, 1211, 1055, 754 cm^{-1}.

MS (EI) m/z (relative intensity) 295 (5) [M^+], 185 (100), 156 (5), 142 (5), 130 (10), 103 (5).

HR-MS (EI) m/z calcd for $C_{17}H_{14}N_3FO$ [M^+] 295.1121, found 295.1123.

***N*-(4-Chlorophenyl)-3-methyl-2-(1*H*-pyrazol-1-yl)benzamide (130he)**



The general procedure **J** was followed using **128h** (79 mg, 0.5 mmol) and **129e** (153 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%→10:2:1:0) yielded **130he** (128 mg, 82%) as a colorless solid. M. p.: = 153−155 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 (br s, 1H), 7.83 (dd, J = 1.8, 0.6 Hz, 1H), 7.75 (ddd, J = 7.6, 1.8, 0.6 Hz, 1H), 7.55 (dd, J = 2.4, 0.6 Hz, 1H), 7.47 (dd, J = 7.6, 7.6 Hz, 1H), 7.44–7.41 (m, 1H), 7.28 (d, J = 8.9 Hz, 2H), 7.17 (d, J = 8.9 Hz, 2H), 6.46 (dd, J = 2.4, 1.9 Hz, 1H), 2.04 (s, 3H).

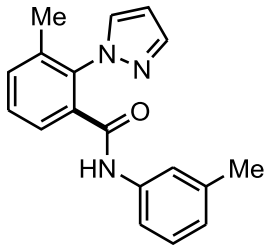
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.3 (C_q), 141.5 (CH), 137.2 (C_q), 136.4 (C_q), 136.1 (C_q), 134.8 (C_q), 133.3 (CH), 132.9 (CH), 129.9 (CH), 129.2 (C_q), 128.8 (CH), 128.1 (CH), 121.1 (CH), 107.6 (CH), 17.1 (CH_3).

IR (ATR): 3236, 1678, 1491, 1397, 1312, 753 cm^{-1}.

MS (EI) m/z (relative intensity) 311 (5) [M^+], 185 (100), 156 (5), 142 (5), 130 (10), 103 (5).

HR-MS (EI) m/z calcd for $C_{17}H_{14}N_3OCl$ [M^+] 311.0825, found 311.0826.

3-Methyl-2-(1*H*-pyrazol-1-yl)-*N*-(*m*-tolyl)benzamide (130hf)



The general procedure **J** was followed using **128h** (79 mg, 0.5 mmol) and **129f** (133 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130hf** (74 mg, 51%) as a colorless solid. M. p.: = 119−121 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.79 (br s, 1H), 7.76 (ddd, *J* = 7.7, 1.8, 0.7 Hz, 1H), 7.55 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.47 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.42 (ddd, *J* = 7.6, 1.8, 0.7 Hz, 1H), 7.25 (dd, *J* = 1.3, 0.7 Hz, 1H), 7.16–7.08 (m, 1H), 7.05 (m, 1H), 6.91–6.75 (m, 1H), 6.46 (dd, *J* = 2.4, 1.9 Hz, 1H), 2.28 (s, 3H), 2.05 (s, 3H).

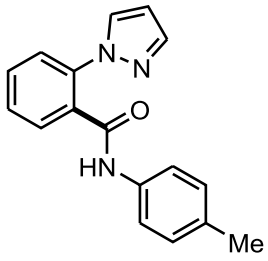
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.3 (C_q), 141.5 (CH), 138.7 (C_q), 137.7 (C_q), 137.2 (C_q), 136.1 (C_q), 135.2 (C_q), 133.0 (CH), 132.7 (CH), 129.8 (CH), 128.5 (CH), 128.1 (CH), 125.1 (CH), 120.5 (CH), 117.0 (CH), 107.5 (CH), 21.4 (CH_3), 17.1 (CH_3).

IR (ATR): 3111, 1656, 1551, 1323, 944, 748 cm^{-1}.

MS (EI) m/z (relative intensity) 291 (5) [M^+], 185 (100), 156 (5), 142 (5), 130 (10), 103 (5).

HR-MS (EI) m/z calcd for $C_{18}H_{17}N_3O$ [M^+] 291.1372, found 291.1375.

2-(1*H*-pyrazol-1-yl)-*N*-(*p*-tolyl)benzamide (130ab)



The general procedure **J** (or **K**) was followed using **128a** (72 mg, 0.5 mmol) and **129b** (133 mg, 1.0 mmol) (or **131b**, 161 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130ab** (83 mg, 60%; or 72 mg, 52%) as a colorless solid. M. p.: = 167−169 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.22 (br s, 1H), 7.98–7.87 (m, 1H), 7.80–7.76 (m, 1H), 7.69 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.62–7.48 (m, 2H), 7.46–7.38 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 6.44 (d, *J* = 2.5, 2.2 Hz, 1H), 2.28 (s, 3H).

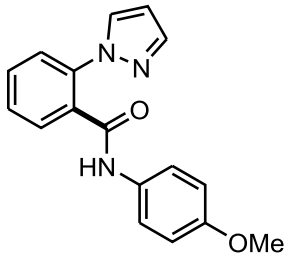
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.1 (C_q), 141.3 (CH), 137.2 (C_q), 135.2 (C_q), 134.1 (C_q), 133.0 (C_q), 131.9 (CH), 131.2 (CH), 130.6 (CH), 129.3 (CH), 129.1 (CH), 126.8 (CH), 120.0 (CH), 107.7 (CH), 20.9 (CH_3).

IR (ATR): 3245, 1650, 1541, 1325, 1040, 753 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (5) [M^+], 171 (100), 144 (5), 130 (5), 116 (15), 89 (10).

HR-MS (EI) m/z calcd for $C_{17}H_{15}N_3O$ [M^+] 277.1215, found 277.1208.

***N*-(4-Methoxyphenyl)-2-(1*H*-pyrazol-1-yl)benzamide (130ac)**



The general procedure **K** was followed using **128a** (72 mg, 0.5 mmol) and **131c** (177 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ac** (88 mg, 60%) as a colorless solid. M. p.: = 130−132 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.22 (br s, 1H), 7.94–7.88 (m, 1H), 7.77 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.70 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.60–7.46 (m, 2H), 7.43–7.38 (m, 1H), 7.30 (d, *J* = 9.0 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 2H), 6.45 (dd, *J* = 2.4, 1.9 Hz, 1H), 3.75 (s, 3H).

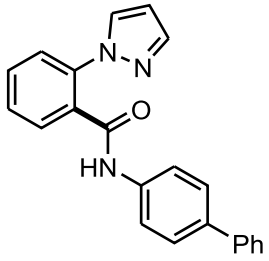
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.2 (C_q), 156.5 (C_q), 141.3 (CH), 137.2 (C_q), 133.1 (C_q), 132.0 (CH), 131.2 (CH), 130.9 (C_q), 130.6 (CH), 129.1 (CH), 126.8 (CH), 121.8 (CH), 114.0 (CH), 107.7 (CH), 55.4 (CH_3).

IR (ATR): 3049, 1665, 1510, 1243, 1031, 764 cm^{-1}.

MS (EI) m/z (relative intensity) 293 (10) [M^+], 171 (100), 144 (5), 116 (15).

HR-MS (EI) m/z calcd for $C_{17}H_{15}N_3O_2$ [M^+] 293.1164, found 293.1167.

***N*-([1,1'-Biphenyl]-4-yl)-2-(1*H*-pyrazol-1-yl)benzamide (130ag)**



The general procedure **K** was followed using **128a** (72 mg, 0.5 mmol) and **131g** (223 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ag** (97 mg, 57%) as a colorless solid. M. p.: = 168−169 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.63 (br s, 1H), 7.91 (dd, J = 7.2, 2.1 Hz, 1H), 7.80 (d, J = 1.9 Hz, 1H), 7.71 (d, J = 2.4 Hz, 1H), 7.61–7.45 (m, 8H), 7.44–7.35 (m, 3H), 7.33–7.25 (m, 1H), 6.46 (t, J = 2.1 Hz, 1H).

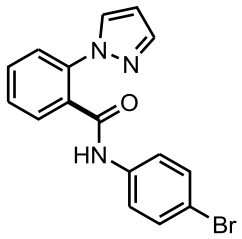
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.4 (C_q), 141.4 (CH), 140.5 (C_q), 137.3 (C_q), 137.2 (C_q), 137.2 (C_q), 132.9 (C_q), 132.0 (CH), 131.4 (CH), 130.7 (CH), 129.1 (CH), 128.7 (CH), 127.5 (CH), 127.0 (CH), 126.8 (CH), 126.8 (CH), 120.3 (CH), 107.8 (CH).

IR (ATR): 3243, 1656, 1518, 1303, 840, 734 cm^{-1}.

MS (EI) m/z (relative intensity) 339 (5) [M^+], 171 (100), 144 (5), 130 (5), 116 (10).

HR-MS (ESI) m/z calcd for $C_{22}H_{17}N_3O$ [M+H^+] 339.1372, found 339.1376.

***N*-(4-Bromophenyl)-2-(1*H*-pyrazol-1-yl)benzamide (130ah)**



The general procedure **K** was followed using **128a** (72 mg, 0.5 mmol) and **131h** (225 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ah** (107 mg, 63%) as a colorless solid. M. p.: = 148−150 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.64 (br s, 1H), 7.90 (dd, J = 7.5, 1.9 Hz, 1H), 7.77 (d, J = 1.9 Hz, 1H), 7.68 (d, J = 2.4 Hz, 1H), 7.61–7.47 (m, 2H), 7.40–7.28 (m, 5H), 6.45 (t, J = 2.2 Hz, 1H).

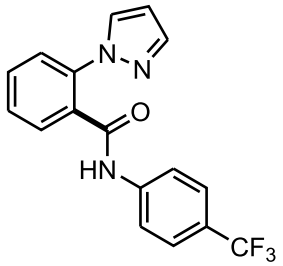
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.3 (C_q), 141.4 (CH), 137.2 (C_q), 137.0 (C_q), 132.8 (C_q), 132.1 (CH), 131.8 (CH), 131.5 (CH), 130.8 (CH), 129.2 (CH), 126.9 (CH), 121.5 (CH), 117.0 (C_q), 107.9 (CH).

IR (ATR): 3249, 1662, 1518, 1318, 1073, 750 cm^{-1}.

MS (EI) m/z (relative intensity) 341 (5) [M^+], 171 (100), 144 (5), 116 (10), 89 (5).

HR-MS (EI) m/z calcd for $C_{16}H_{12}N_3O^{79}Br$ [M^+] 341.0164, found 341.0164.

2-(1*H*-Pyrazol-1-yl)-*N*-{4-(trifluoromethyl)phenyl}benzamide (130ai)



The general procedure **K** was followed using **128a** (72 mg, 0.5 mmol) and **131i** (215 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130ai** (110 mg, 66%) as a colorless solid. M. p.: = 168−170 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.03 (br s, 1H), 7.88 (dd, J = 6.9, 2.5 Hz, 1H), 7.79 (d, J = 1.9 Hz, 1H), 7.69 (d, J = 2.5 Hz, 1H), 7.62–7.41 (m, 6H), 7.35 (dd, J = 7.0, 2.2 Hz, 1H), 6.47 (dd, J = 2.2, 1.9 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.7 (C_q), 141.4 (CH), 141.0 (C_q), 137.2 (C_q), 132.6 (C_q), 132.1 (CH), 131.7 (CH), 130.9 (CH), 129.2 (CH), 126.9 (CH), 126.1 (CH, $J_{C\text{-}F}$ = 7.5 Hz), 126.1 (C_q, $J_{C\text{-}F}$ = 32.9 Hz) 124.0 (C_q, $J_{C\text{-}F}$ = 271.5 Hz), 119.5 (CH), 108.0 (CH).

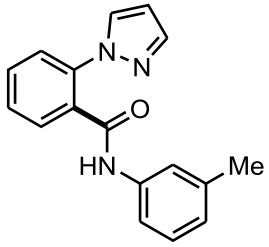
^{19}F-NMR ($CDCl_3$, 282 MHz): δ = -62.2 (s).

IR (ATR): 3255, 1668, 1538, 1318, 1109, 749 cm^{-1}.

MS (EI) m/z (relative intensity) 331 (5) [M^+], 171 (100), 144 (5), 130 (5), 116 (15), 89 (10).

HR-MS (EI) m/z calcd for $C_{17}H_{12}N_3OF_3$ [M^+] 331.0932, found 331.0936.

2-(1*H*-Pyrazol-1-yl)-*N*-(*m*-tolyl)benzamide (130af)



The general procedure **K** was followed using **128a** (72 mg, 0.5 mmol) and **131f** (161 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **130af** (87 mg, 63%) as a colorless solid. M. p.: = 127−129 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.29 (br s, 1H), 7.94–7.86 (m, 1H), 7.77 (d, J = 1.9 Hz, 1H), 7.70 (d, J = 2.4 Hz, 1H), 7.53 (m, 2H), 7.41 (dd, J = 7.5, 1.7 Hz, 1H), 7.31 (s, 1H), 7.16–7.12 (m, 2H), 6.88 (ddd, J = 4.5, 3.0, 1.1 Hz, 1H), 6.44 (t, J = 2.2 Hz, 1H), 2.29 (s, 3H).

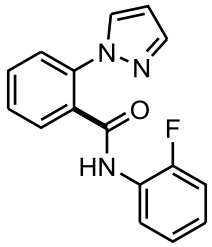
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.4 (C_q), 141.4 (CH), 138.8 (C_q), 137.7 (C_q), 137.2 (C_q), 133.1 (C_q), 131.9 (CH), 131.3 (CH), 130.6 (CH), 129.1 (CH), 128.6 (CH), 126.8 (CH), 125.3 (CH), 120.7 (CH), 117.1 (CH), 107.8 (CH), 21.5 (CH_3).

IR (ATR): 3240, 1663, 1548, 1311, 1042, 742 cm^{-1}.

MS (EI) m/z (relative intensity) 277 (5) [M^+], 171 (100), 144 (5), 116 (15).

HR-MS (ESI) m/z calcd for $C_{17}H_{16}N_3O$ [M+H^+] 278.1293, found 278.1286.

***N*-(2-Fluorophenyl)-2-(1*H*-pyrazol-1-yl)benzamide (130aj)**



The general procedure **K** was followed using **128a** (72 mg, 0.5 mmol) and **131j** (165 mg, 1.0 mmol). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **130aj** (110 mg, 78%) as a colorless solid. M. p.: = 135−137 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.42 (br s, 1H), 8.36 – 8.26 (m, 1H), 7.90 (dd, J = 7.5, 1.7 Hz, 1H), 7.74 (d, J = 1.9 Hz, 1H), 7.71 (d, J = 2.4 Hz, 1H), 7.62–7.48 (m, 2H), 7.43 (dd, J = 7.3, 1.9 Hz, 1H), 7.09 (ddd, J = 8.2, 5.6, 3.1 Hz, 1H), 7.05 – 6.97 (m, 2H), 6.46–6.36 (m, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.8 (C_q), 152.6 (C_q, J_{C-F} = 245.3 Hz), 141.6 (CH), 137.5 (C_q), 132.3 (C_q), 131.5 (CH), 131.2 (CH), 130.6 (CH), 128.9 (CH), 126.4 (CH), 126.3 (C_q, J_{C-F} = 10.5 Hz), 124.7 (CH, J_{C-F} = 7.5 Hz), 124.4 (CH, J_{C-F} = 3.7 Hz), 122.0 (CH), 114.9 (CH, J_{C-F} = 19.1 Hz), 107.8 (CH).

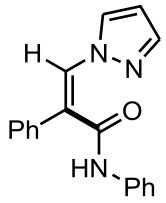
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -129.0 (ddd, J = 8.2, 2.8 Hz).

IR (ATR): 3254, 1657, 1450, 1317, 1039, 749 cm^{-1}.

MS (EI) m/z (relative intensity) 281 (5) [M^+], 171 (100), 144 (5), 130 (5), 116 (10).

HR-MS (EI) m/z calcd for $C_{16}H_{12}N_3OF$ [M^+] 281.0964, found 281.0976.

(*Z*)-*N*,2-Diphenyl-3-(1*H*-pyrazol-1-yl)acrylamide (133aa)



The general procedure **J** was followed using **132a** (85 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 10 mol%), $AgNTf_2$ (39.8 mg, 20 mol%) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) yielded **133aa** (80 mg, 55%) as a colorless solid. M. p.: = 180−181 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.87 (s, 1H), 7.87 (d, J = 2.6 Hz, 1H), 7.60 (d, J = 1.8 Hz, 1H), 7.54 (dd, J = 8.6, 1.2 Hz, 2H), 7.52–7.48 (m, 2H), 7.43–7.28 (m, 6H), 7.18–7.07 (m, 1H), 6.33 (dd, J = 2.6, 1.8 Hz, 1H).

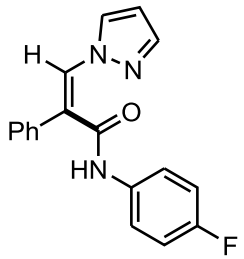
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.4 (C_q), 141.8 (CH), 137.5 (C_q), 134.9 (C_q), 130.0 (CH), 129.1 (CH), 129.0 (CH), 128.6 (CH), 126.6 (CH), 126.5 (C_q), 126.2 (CH), 124.9 (CH), 120.2 (CH), 108.1 (CH).

IR (ATR): 3250, 1646, 1540, 1439, 953, 750 cm^{-1}.

MS (EI) m/z (relative intensity) 289 (5) [M^+], 221 (5), 197 (100), 169 (40), 115 (10).

HR-MS (ESI) m/z calcd for $C_{18}H_{15}N_3O$ [M^+] 289.1215, found 289.1216.

(*Z*)-*N*-(4-Fluorophenyl)-2-phenyl-3-(1*H*-pyrazol-1-yl)acrylamide (133ad)



The general procedure **J** was followed using **132a** (85 mg, 0.5 mmol) and **129d** (137 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, mg, 10 mol %), $AgNTf_2$ (39.8 mg, 20 mol %) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%→5:1:0:0) yielded **133ad** (81 mg, 53%) as a colorless solid. M. p.: = 184−185 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.99 (br s, 1H), 7.81 (d, J = 2.6 Hz, 1H), 7.60 (d, J = 1.8 Hz, 1H), 7.55–7.43 (m, 4H), 7.40–7.34 (m, 3H), 7.33 (s, 1H), 7.01 (t, J = 8.7 Hz, 2H), 6.34 (t, J = 2.2 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.4 (C_q), 159.7 (C_q, $J_{C\text{-}F}$ = 244.3 Hz), 141.8 (CH), 134.9 (C_q), 133.5 (C_q, $J_{C\text{-}F}$ = 2.9 Hz), 130.2 (CH), 129.0 (CH), 128.6 (CH), 126.6 (CH), 126.5 (C_q), 126.1 (CH), 122.1 (CH, $J_{C\text{-}F}$ = 8.0 Hz), 115.7 (CH, $J_{C\text{-}F}$ = 22.6 Hz), 108.0 (CH).

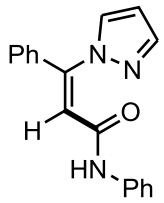
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -117.2 (tt, J = 8.2, 4.8 Hz).

IR (ATR): 3240, 1636, 1505, 1391, 1211, 747 cm^{-1}.

MS (EI) m/z (relative intensity) 307 (5) [M^+], 239 (5), 197 (100), 169 (45), 142 (5), 115 (10).

HR-MS (EI) m/z calcd for $C_{18}H_{14}FN_3O$ [M^+] 307.1121, found 307.1125.

(*Z*)-*N*,3-Diphenyl-3-(1*H*-pyrazol-1-yl)acrylamide (133ba)



The general procedure **J** was followed using **132b** (85 mg, 0.5 mmol) and **129a** (119 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 10 mol%), $AgNTf_2$ (39.8 mg, 20 mol%) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%) yielded **133ba** (78 mg, 54%) as a colorless solid. M. p.: = 159−161 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.69 (br s, 1H), 7.85 (d, J = 2.0 Hz, 1H), 7.51–7.45 (m, 3H), 7.43–7.31 (m, 3H), 7.30–7.18 (m, 4H), 7.12–7.01 (t, J = 2.2 Hz, 1H), 6.45 (t, J = 2.2 Hz, 1H), 6.37 (s, 1H).

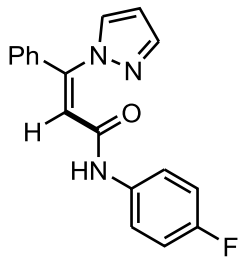
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.0 (C_q), 142.8 (C_q), 141.2 (CH), 138.0 (C_q), 136.4 (C_q), 133.0 (CH), 130.4 (CH), 128.8 (CH), 128.8 (CH), 127.6 (CH), 124.2 (CH), 119.8 (CH), 119.2 (CH), 107.7 (CH).

IR (ATR): 3054, 1658, 1539, 1440, 1085, 755 cm^{-1}.

MS (EI) m/z (relative intensity) 289 (5) [M^+], 197 (65), 169 (5), 129 (100), 102 (10), 77 (15).

HR-MS (EI) m/z calcd for $C_{18}H_{15}N_3O$ [M^+] 289.1215, found 289.1214.

(*Z*)-*N*-(4-Fluorophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)acrylamide (133bd)



The general procedure **J** was followed using **132b** (85 mg, 0.5 mmol) and **129d** (137 mg, 1.0 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 10 mol%), $AgNTf_2$ (39.8 mg, 20 mol%) and AgOPiv (20.8 mg, 20 mol %). Purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 8:1:1:1%→5:1:0:0) yielded **133bd** (97 mg, 63%) as a colorless solid. M. p.: = 150−152 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 9.92 (br s, 1H), 7.94–7.82 (m, 1H), 7.53 (dd, J = 2.5, 0.6 Hz, 1H), 7.52–7.48 (m, 2H), 7.48–7.45 (m, 1H), 7.44–7.38 (m, 2H), 7.30–7.25 (m, 2H), 7.01 (dd, J = 9.1, 8.3 Hz, 2H), 6.52 (dd, J = 2.5, 1.9 Hz, 1H), 6.40 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.0 (C_q), 159.2 (C_q, $J_{C\text{-}F}$ = 243.4 Hz), 143.0 (C_q), 141.1 (CH), 136.3 (C_q), 134.1 (C_q, $J_{C\text{-}F}$ = 2.9 Hz), 133.0 (CH), 130.5 (CH), 128.8 (CH), 127.6 (CH), 121.5 (CH, $J_{C\text{-}F}$ = 7.8 Hz), 118.8 (CH), 115.4 (CH, $J_{C\text{-}F}$ = 22.5 Hz), 107.7 (CH).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = -118.0 (tt, J = 8.3, 4.8 Hz).

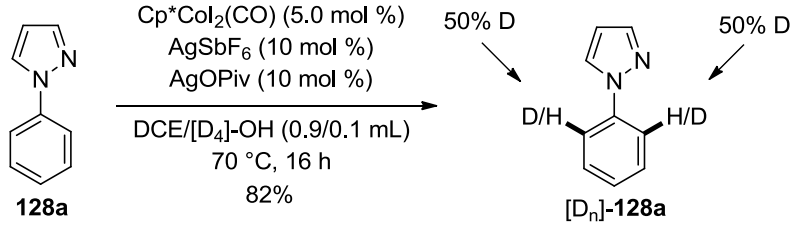
IR (ATR): 3006, 1659, 1508, 1210, 921, 761 cm^{-1}.

MS (EI) m/z (relative intensity) 307 (5) [M^+], 197 (80), 169 (5), 129 (100), 102 (10).

HR-MS (ESI) m/z calcd for $C_{18}H_{14}N_3FO$ [M+H^+] 307.1121, found 307.1118.

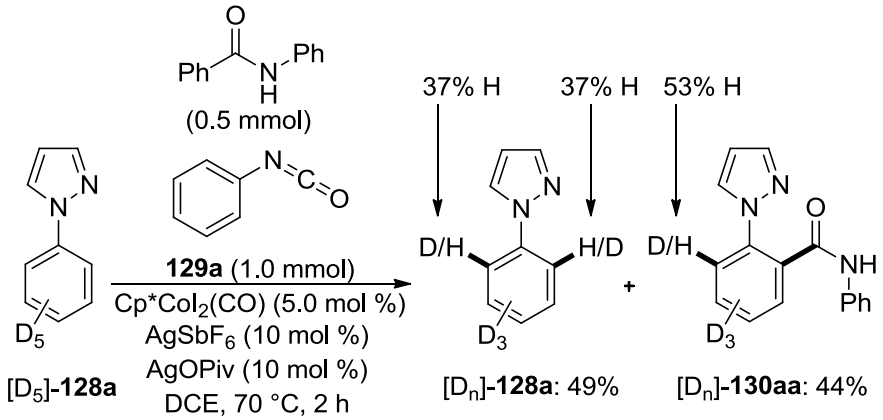
H/D Exchange Experiments:

Cobalt-Catalyzed H/D Exchange in Substrate 128a with [D_4]-MeOH as the Cosolvent without Isocyanate 129:



A suspension of 1-phenyl-1*H*-pyrazole (**128a**) (72 mg, 0.50 mmol), Cp*CoI_2(CO) (**112**, 12 mg, 5.0 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and AgOPiv (10.4 mg, 10.0 mol %) in a solvent mixture of DCE and CD_3OD (0.9/0.1 mL) was stirred at 70 °C for 16 h under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc) to yield [D_n]-**128a** (59 mg, 82%) as a slightly yellow oil. The D-incorporation in [D_n]-**128a** was estimated by ^{1}H-NMR spectroscopy.

Scheme S-2. Cobalt-Catalyzed H/D Exchange in Substrate [D_5]-128a with Isocyanate 129a:

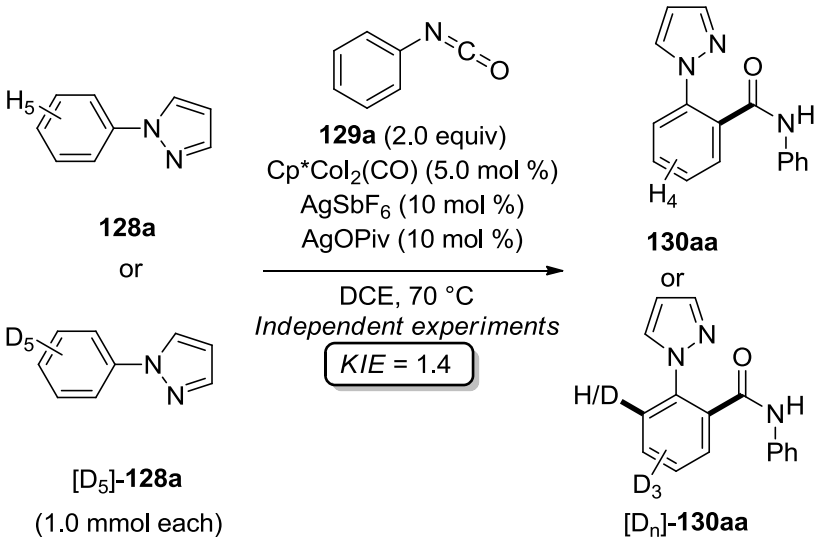


A suspension of [D_5]-**128a** (74 mg, 0.5 mmol), **129a** (119 mg, 1.0 mmol), *N*-phenylbenzamide (99 mg, 0.5 mmol), Cp*CoI_2(CO) (**112**, 12 mg, 5.0 mmol %), $AgSbF_6$ (17.2 mg, 10 mol %) and AgOPiv (10.4 mg, 10 mmol %) in DCE (2.0 mL) was stirred at 70 °C for 2 h under an atmosphere of Ar. At ambient temperature, the solvent was evaporated *in vacuo* and the

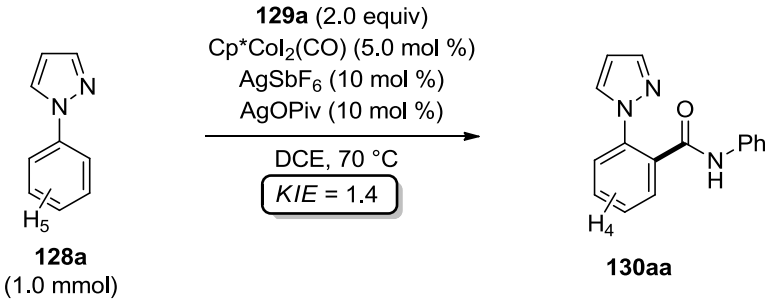
residue was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) to recover starting material [D_n]-**128a** (36 mg, 49%) as a slight yellow oil and yield product [D_n]-**130aa** (58 mg, 44%) as a colorless solid. The D-incorporation in [D_n]-**128a** and [D_n]-**130aa** was estimated by ^{1}H-NMR spectroscopy.

KIE Determination Experiments:

KIE Determination Experiments with 128a and [D_5]-128a as Substrates:



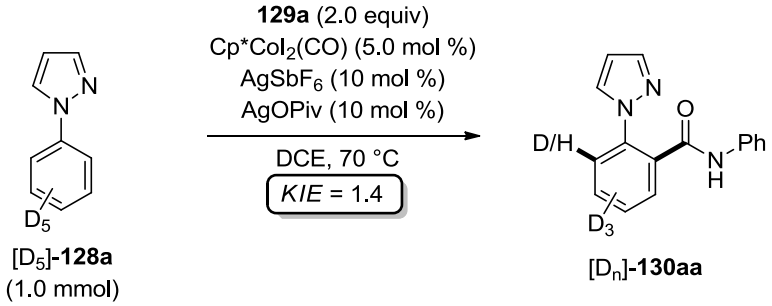
1). Two independent reactions with **128a** or deuterated substrate [D_5]-**128a** under the standard conditions were performed: Two reaction mixtures each containing phenyl isocyanate (**129a**) (338 mg, 2.0 mmol), substrates **128a** (144 mg, 1.00 mmol) or [D_5]-**128a** (149 mg, 1.00 mmol), Cp*CoI_2(CO) (**112**, 24 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 10.0 mol %) and AgOPiv (20.8 mg, 10.0 mol %) in DCE (4.0 mL) were stirred at 70 °C under an atmosphere of Ar. The consumption of substrates **128a** or [D_5]-**128a** and the appearance of the products **130a** or [D_n]-**130a** were monitored by GC analysis after 0.5 h, 1.0 h, 1.25 h, 1.5 h, 1.75 h, 2.0 h, 2.25 h, 2.5 h, 2.75 h, 3.0 h, respectively. These experiments indicated that the C–H bond activation is not the rate-limiting step of the cobalt-catalyzed C–H bond aminocarbonylation reaction.



128a
(1.0 mmol)

130aa

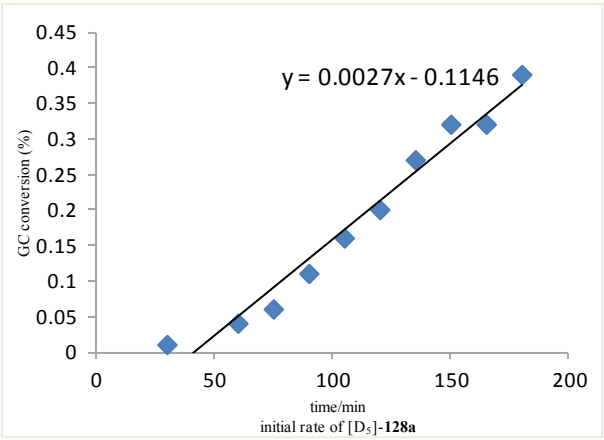
t/(h)	0.5	1.0	1.25	1.5	1.75	2.0	2.25	2.5	2.75	3.0
130aa	0.06	0.16	0.22	0.28	0.35	0.39	0.47	0.56	0.56	0.61
128a	0.94	0.84	0.78	0.72	0.65	0.61	0.53	0.44	0.44	0.49

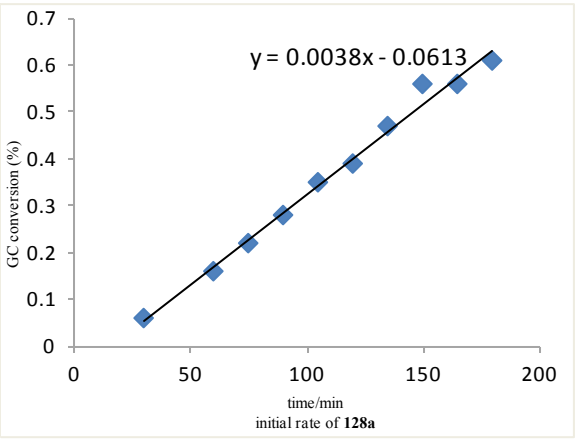


[D_5]-128a
(1.0 mmol)

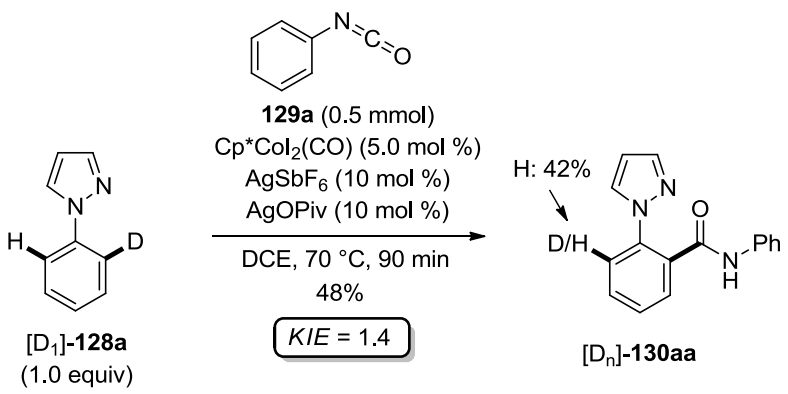
[D_n]-130aa

t/(h)	0.5	1.0	1.25	1.5	1.75	2.0	2.25	2.5	2.75	3.0
[D_n]-**130aa**	0.01	0.04	0.06	0.11	0.16	0.20	0.27	0.32	0.32	0.39
[D_5]-**128a**	0.99	0.96	0.94	0.89	0.84	0.80	0.73	0.68	0.68	0.61



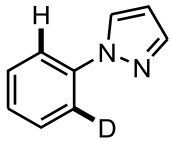


Intramolecular Competition Experiment: Kinetic Isotope Effect (KIE):



2). 1-(Phenyl-2-*d*)-1*H*-pyrazole ([D_1]-**128a**) (73.0 mg, 0.50 mmol), phenyl isocyanate (**129a**) (60.0 mg, 0.50 mmol), Cp*CoI_2(CO) (**112**, 12.0 mg, 5.0 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and AgOPiv (10.4 mg, 10.0 mol %) in DCE (2.0 mL) was stirred at 70 °C for 90 min under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:0.01) to yield [D_n]-**130aa** (63.0 mg, 48%) as a colorless solid. The degree of deuterium incorporation in [D_n]-**130aa** was estimated by ^{1}H-NMR spectroscopy.

1-(Phenyl-2-*d*)-1*H*-pyrazole ([D_1]-**128a**)



^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.91 (dd, J = 2.5, 0.6 Hz, 1H), 7.71 (dd, J = 1.8, 0.7 Hz, 1H), 7.70–7.67 (m, 1H), 7.51–7.36 (m, 2H), 7.27 (td, J = 7.5, 1.1 Hz, 1H), 6.45 (dd, J = 2.5, 1.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 141.0 (CH), 140.2 (C_q), 129.4 (CH), 129.4 (CH), 126.7 (CH), 126.4 (CH, J = 1.6 Hz), 119.2 (CH), 119.2 (CH), 107.6 (CH).

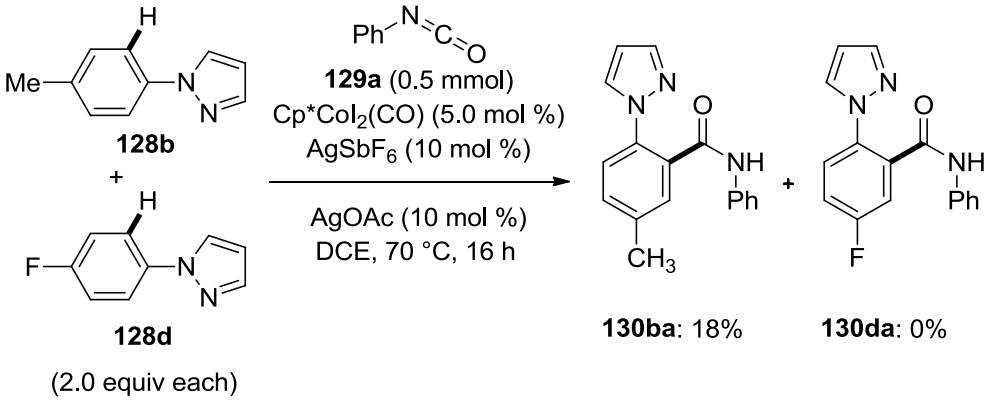
IR (ATR): 3066, 1593, 1391, 1045, 936, 742 cm^{-1}.

MS (EI) m/z (relative intensity) 145 (100) [M^+], 118 (30), 91 (25), 78 (45).

HR-MS (EI) m/z calcd for $C_9H_7DN_2$ [M^+] 145.0750, found 145.0752.

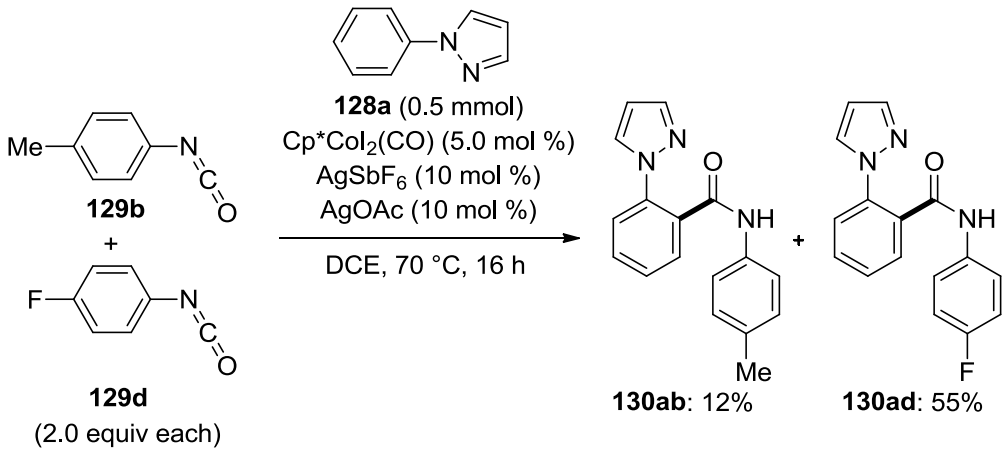
Competition Experiments:

Intermolecular Competition Experiment between Substrates VI-1b and VI-1d:



A suspension of phenyl isocyanate (**129a**) (60 mg, 0.5 mmol), 1-*p*-tolyl-1*H*-pyrazole (**128b**) (158 mg, 1.00 mmol), 1-(4-fluorophenyl)-1*H*-pyrazole (**128d**) (162 mg, 1.00 mmol), Cp*CoI_2(CO) (**112**, 12 mg, 5.0 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and AgOPiv (10.8 mg, 10.0 mol %) in DCE (2.0 mL) was stirred at 70 °C for 16 h under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:0.01) to yield **130ba** (25 mg, 18%) as a colorless solid.

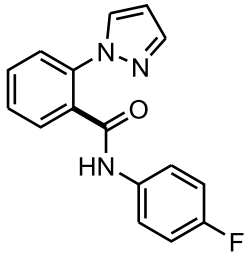
Intermolecular Competition Experiment between Substrates 129b and 129d:



A suspension of 1-phenyl-1*H*-pyrazole (**128a**) (72 mg, 0.5 mmol), 1-isocyanato-4-methylbenzene (**129b**) (133 mg, 1.00 mmol), 1-fluoro-4-isocyanatobenzene (**129d**) (137 mg, 1.00 mmol), Cp*CoI_2(CO) (**112**, 12 mg, 5.0 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and AgOPiv (10.8 mg, 10.0 mol %) in DCE (2.0 mL) was stirred at 70 °C for 16 h under an atmosphere of Ar. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel

(*n*-hexane/CH_2Cl_2/EtOAc/Et_3N 10:1:1:1%) to yield **130ab** (17 mg, 12%) and **130ad** (77 mg, 55%) as colorless solids.

***N*-(4-Fluorophenyl)-2-(1*H*-pyrazol-1-yl)benzamide (130ad)**



M. p.: = 130−132 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.58 (br s, 1H), 7.96–7.84 (m, 1H), 7.77 (d, J = 1.9 Hz, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.62–7.46 (m, 2H), 7.43–7.30 (m, 3H), 6.94 (dd, J = 9.1, 8.3 Hz, 2H), 6.46 (t, J = 2.2 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.4 (C_q), 159.4 (C_q, $J_{C\text{-}F}$ = 243.9 Hz), 141.3 (CH), 137.2 (C_q), 133.9 (C_q, $J_{C\text{-}F}$ = 2.9 Hz), 132.8 (C_q), 132.0 (CH), 131.4 (CH), 130.7 (CH), 129.2 (CH), 126.8 (CH), 121.8 (CH, $J_{C\text{-}F}$ = 7.9 Hz), 115.5 (CH, $J_{C\text{-}F}$ = 22.4 Hz), 107.8 (CH).

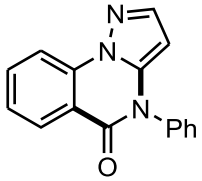
^{19}F-NMR (282 MHz, $CDCl_3$): δ = -117.8 (tt, J = 8.2, 4.8 Hz).

IR (ATR): 3258, 1652, 1507, 1209, 832, 754 cm^{-1}.

MS (EI) m/z (relative intensity) 281 (5) [M^+], 171 (100), 144 (5), 130 (10), 116 (15).

HR-MS (EI) m/z calcd for $C_{16}H_{12}N_3OF$ [M^+] 281.0964, found 281.0961.

4-Phenylpyrazolo[1,5-a]quinazolin-5(4*H*)-one (160)



A suspension of *N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (**130aa**) (53 mg, 0.2 mmol) and $K_2S_2O_8$ (81 mg, 0.3 mmol) in H_2O (5.0 mL) was stirred at 105 °C for 1.0 h. After completion of the reaction, at ambient temperature the reaction mixture was extracted with MTBE (3 × 10 mL) at ambient temperature. The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography

(*n*-Hexane/EtOAc 4:1) yielded **160** (45 mg, 85%) as a colorless solid. M. p.: = 160−162 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.36–8.32 (m, 1H), 8.23–8.18 (m, 1H), 7.81 (ddd, *J* = 8.3, 7.3, 1.5 Hz, 1H), 7.64 (d, *J* = 2.0 Hz, 1H), 7.59–7.54 (m, 2H), 7.52–7.47 (m, 1H), 7.47–7.40 (m, 3H), 5.47 (d, *J* = 2.0 Hz, 1H).

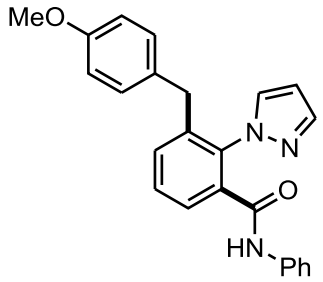
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.6 (C_q), 141.7 (CH), 141.5 (C_q), 137.7 (C_q), 136.8 (C_q), 135.0 (CH), 130.0 (CH), 129.4 (CH), 129.3 (CH), 127.8 (CH), 125.5 (CH), 116.3 (CH), 114.7 (C_q), 90.9 (CH).

IR (ATR): 1668, 1553, 1482, 1127, 757, 684 cm^{-1}.

MS (EI) m/z (relative intensity) 261 (100) [M^+], 234 (10), 205 (5), 128 (10), 103 (10), 77 (25).

HR-MS (EI) m/z calcd for $C_{16}H_{11}N_3O$ [M^+] 261.0902, found 261.0903.

3-(4-Methoxybenzyl)-*N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (161)



According to the established protocol, a suspension of *N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (**130aa**) (66 mg, 0.25 mmol), 1-(chloromethyl)-4-methoxybenzene (**163**, 78 mg, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.8 mg, 5.0 mol %), 1-AdCO_2H (13.5 mg, 30 mol %) and K_2CO_3 (69 mg, 0.5 mmol) in PhMe (1.0 mL) was stirred at 100 °C for 20 h.[167] At ambient temperature, the reaction mixture was extracted with MTBE (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc 5:1) yielded **161** (45 mg, 47%) as a colorless solid. M. p.: = 133−135 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 1.9 Hz, 1H), 7.80 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.73 (br s, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.42–7.35 (m, 2H), 7.35–7.29 (m, 2H), 7.25 (m, 1H), 7.22 (d, *J* = 8.3 Hz, 1H), 7.11–6.97 (m, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 3.75 (s, 3H), 3.64 (s, 2H).

[167] L. Ackermann, P. Novák, R. Vicente, N. Hofmann, *Angew. Chem. Int. Ed.* **2009**, *48*, 6045–6048.

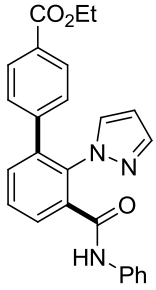
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.3 (C_q), 158.2 (C_q), 141.6 (CH), 140.6 (C_q), 137.7 (C_q), 135.8 (C_q), 135.5 (C_q), 133.4 (CH), 133.0 (CH), 131.3 (C_q), 130.1 (CH), 129.7 (CH), 128.8 (CH), 128.5 (CH), 124.4 (CH), 119.9 (CH), 113.9 (CH), 107.5 (CH), 55.2 (CH_3), 35.8 (CH_2).

IR (ATR): 3274, 1650, 1508, 1245, 1025, 750 cm^{-1}.

MS (EI) m/z (relative intensity) 383 (15) [M^+], 290 (80), 262 (100), 247 (25), 234 (5), 219 (15).

HR-MS (EI) m/z calcd for $C_{24}H_{21}N_3O_2$ [M^+] 383.1634, found 383.1629.

Ethyl 3'-(Phenylcarbamoyl)-2'-(1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-carboxylate (162)



According to the established protocol, a suspension of *N*-phenyl-2-(1*H*-pyrazol-1-yl)benzamide (**130aa**) (63 mg, 0.24 mmol), which was prepared according the general procedure **J**, ethyl 4-chlorobenzoate (**88k**) (37 mg, 0.2 mmol), [Ru($MesCO_2$)$_2$(*p*-cymene)] (5.6 mg, 5.0 mol %) and K_2CO_3 (55 mg, 0.4 mmol) in PhMe (1.0 mL) was stirred at 120 °C for 20 h under an atmosphere of Ar.[168] At ambient temperature, the reaction mixture was extracted with MTBE (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-hexane/EtOAc 5:1) and HPLC yielded product **162** (62 mg, 75%) as a colorless solid. M. p.: = 147−149 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.55 (br s, 1H), 8.04 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 2H), 7.76–7.71 (m, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.63 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.49–7.38 (m, 2H), 7.34–7.25 (m, 3H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.14–7.03 (m, 1H), 6.25 (dd, *J* = 2.4, 1.9 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.2 (C_q), 164.0 (C_q), 142.1 (C_q), 141.0 (CH), 140.0 (C_q), 137.9 (C_q), 135.8 (C_q), 134.9 (C_q), 133.7 (CH), 132.8 (CH), 130.6 (CH), 130.1 (CH), 129.8 (C_q), 129.4 (CH), 128.9 (CH), 128.3 (CH), 124.5 (CH), 120.0 (CH), 107.8 (CH), 61.1 (CH_2),

[168] L. Ackermann, R. Vicente, H. K. Potukuchi, V. Pirovano, *Org. Lett.* **2010**, *12*, 5032–5035.

14.3 (CH_3).

IR (ATR): 3279, 1708, 1551, 1278, 1106, 756 cm^{-1},

MS (ESI) m/z (relative intensity) 412 (10) [$M+H^+$], 434 [$M+Na^+$], 450 [$M+K^+$], 845 [$2M+Na^+$].

HR-MS (EI) m/z calcd for $C_{25}H_{22}N_3O_3$ [$M+H^+$] 412.1661, found 412.1656.

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