Ruthenium(II)-Catalyzed C–N, C–O and C–C Formations by C–H Activation

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vorgelegt von

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aus

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Erklärung

Ich versichere, dass ich die vorliegende Dissertation in der Zeit
von October 2012 bis January 2017 am

Institut für Organische und Biomolekulare Chemie
der Georg-August-Universität zu Göttingen

auf Anregung und unter Anleitung von

Herrn Prof. Dr. Lutz Ackermann

selbständig durchgeführt und keine anderen als die angegebenen
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I DEDICATE THIS WORK TO MY BELOVED MOTHER AND FATHER.

Abbreviations

Ac	acetyl
Ad	adamantyl
Alk	alkyl
AQ	8-Aminoquinoline
Ar	aryl
ARB	Angiotension Receptor Blocker
ASTM	American Society for Testing and Materials
BHT	butylated hydroxytoluene
Bn	benzyl
n-Bu	*n*-butyl
t-Bu	*tert*-butyl
calcd.	calculated
cat.	catalytic
CMD	concerted metalation-deprotonation
COSY	correlated spectroscopy
Cy	Cyclohexyl
d	doublet
δ	chemical shift
DCE	1,2-Dichloroethane
DFT	density function theory
DG	directing group

Ed.	editor
EI	electron ionization
equiv	equivalents
ESI	electronspray ionization
Et	ethyl
ET	electron transfer
eV	electron volt
FT	Fourier transform
g	gram
GC	gas chromatography
h	hour
HASPO	heteroatom substituted secondary phosphine oxide
HMBC	heteronuclear multiple bond correlation
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum coherence
Hz	Hertz
IR	infrared spectroscopy
J	coupling constant
KIE	kinetic isotope effect
$[M^+]$	molecular ion peak
m	meta
m	multiplet
Me	methyl

Mes	mesityl
min	minute
mL	milliliter
mmol	millimol
m. p.	melting point
MSP	methyl-phenyl-sulfoximine
MPV	membrane pump vacuum
MS	mass spectrometry
m/*z*	mass/charge
NMP	*N*-Methyl-2-pyrrolidone
NMR	nuclear magnetic resonance spectroscopy
NOESY	nuclear Overhauser enhancement spectroscopy
NR	no reaction
o	*ortho*
OPV	oil pump vacuum
p	*para*
Ph	phenyl
Piv	pivaloyl
ppm	parts per million
pza	2-pyrazole-5-ylaniline
i-Pr	*iso*-propyl
R	rest
s	singlet

SET	single-electron-transfer
SPO	secondary phosphine oxide
SPS	solvent purification system
t	time
t	triplet
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
Tf	triflyl
TLC	thin layer chromatography
TM	transition metal
TS	transition state
Ts	tosyl
UV	ultraviolet

Contents

Introduction:

1.1 Transition Metal-Catalyzed Direct C–H Bond Functionalization

The selective construction of heterocyclic structural motifs is of key importance for many state of the art applications of synthetic organic chemistry. Heteroaromatic compounds with exiguous chemical and biological properties are used as pharmaceuticals, agrochemicals and materials (Figure1.1).[1-4]

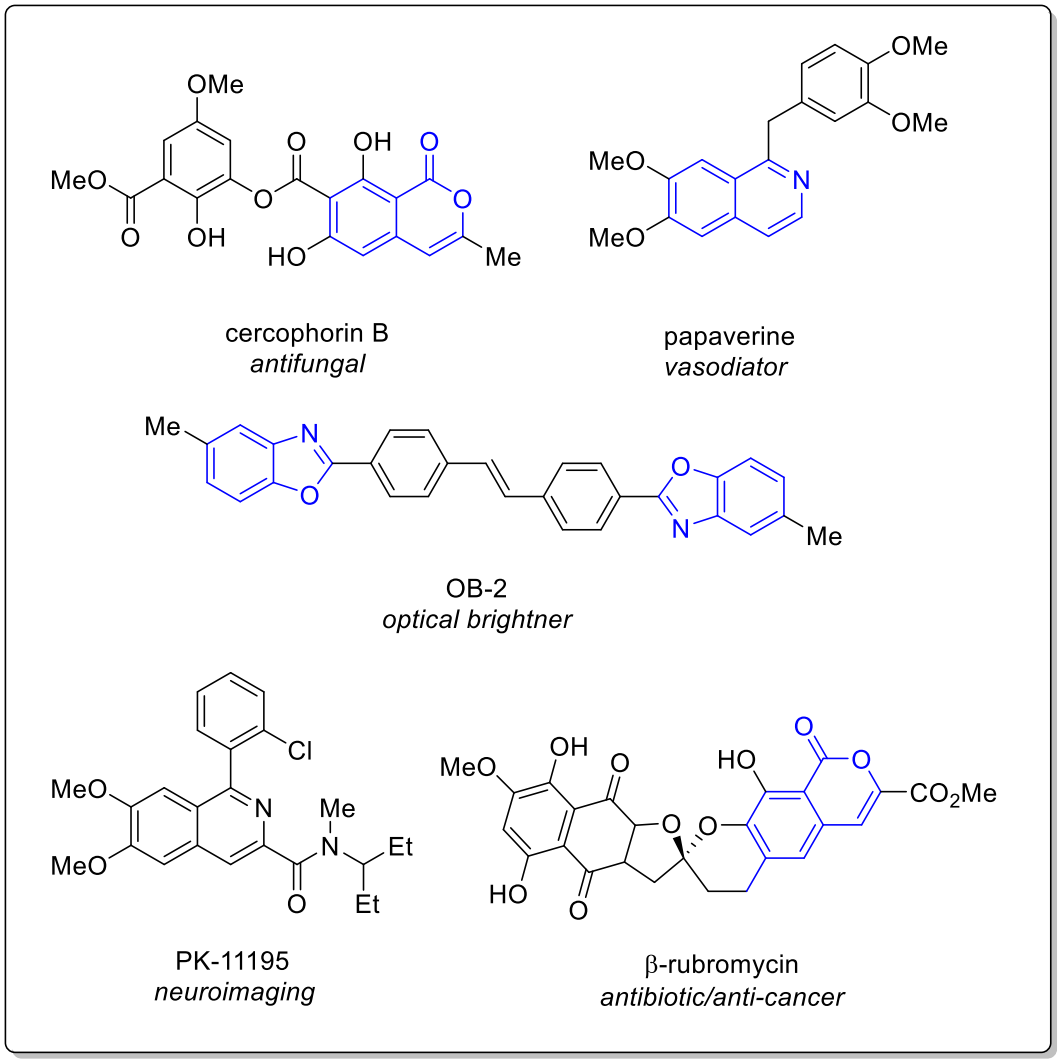
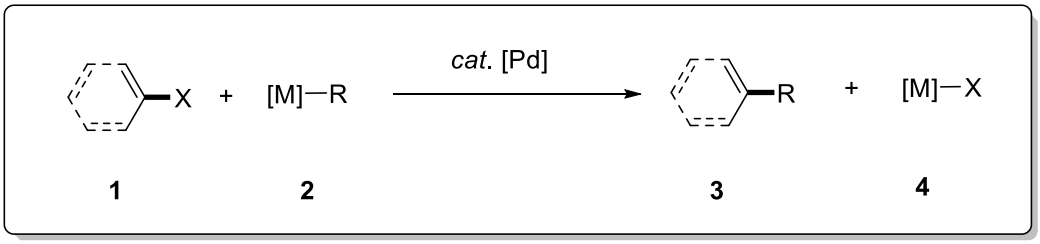


Figure 1.1: Examples of naturally occurring and bioactive heterocycles.

The de novo synthesis of naturally occurring molecules containing heteroatoms on large scale is a challenging task and a perpetual driving force for the development of new synthetic methodologies. Especially the chemo- and site-selective formation of C–C bonds remains as an ongoing inspiration of synthetic organic chemists. As a result, considerable progress was

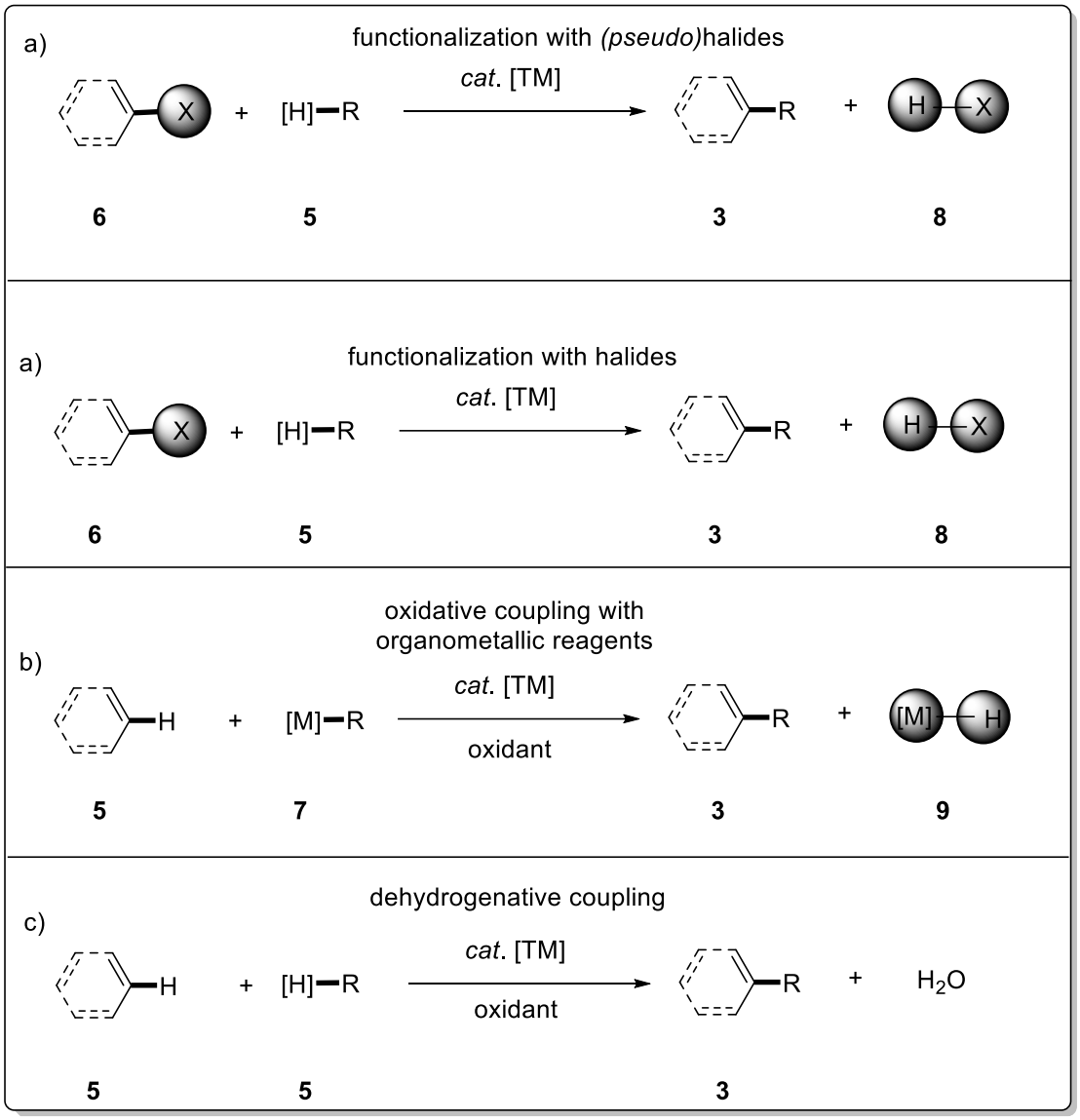
made on transition metal-catalyzed C–C coupling reactions during the past decades.[5-9] In this context, it is important to mention that in 2010 the Nobel prize in chemistry was awarded jointly to *R. F. Heck*, *E. Negishi* and *A. Suzuki* for their significant contributions to the development of palladium-catalyzed cross-coupling reactions.[10]

In these transformations, the palladium catalyst promotes the reaction between an aryl- or vinyl(pseudo)halide **1** and an organometallic reagent **2** to the cross-coupled product **3** (Scheme 1.1). Other metals are also known to achieve these transformations by their catalytic mode of actions in reactions, for example nickel or copper. Although these reactions are very efficient, they feature a significant disadvantage, namely that prefunctionalized starting materials are a prerequisite. Generally, the compounds were prepared in several steps starting from the unfunctionalized molecules.[11-12]



Scheme 1.1: Palladium-catalyzed cross-coupling reactions.

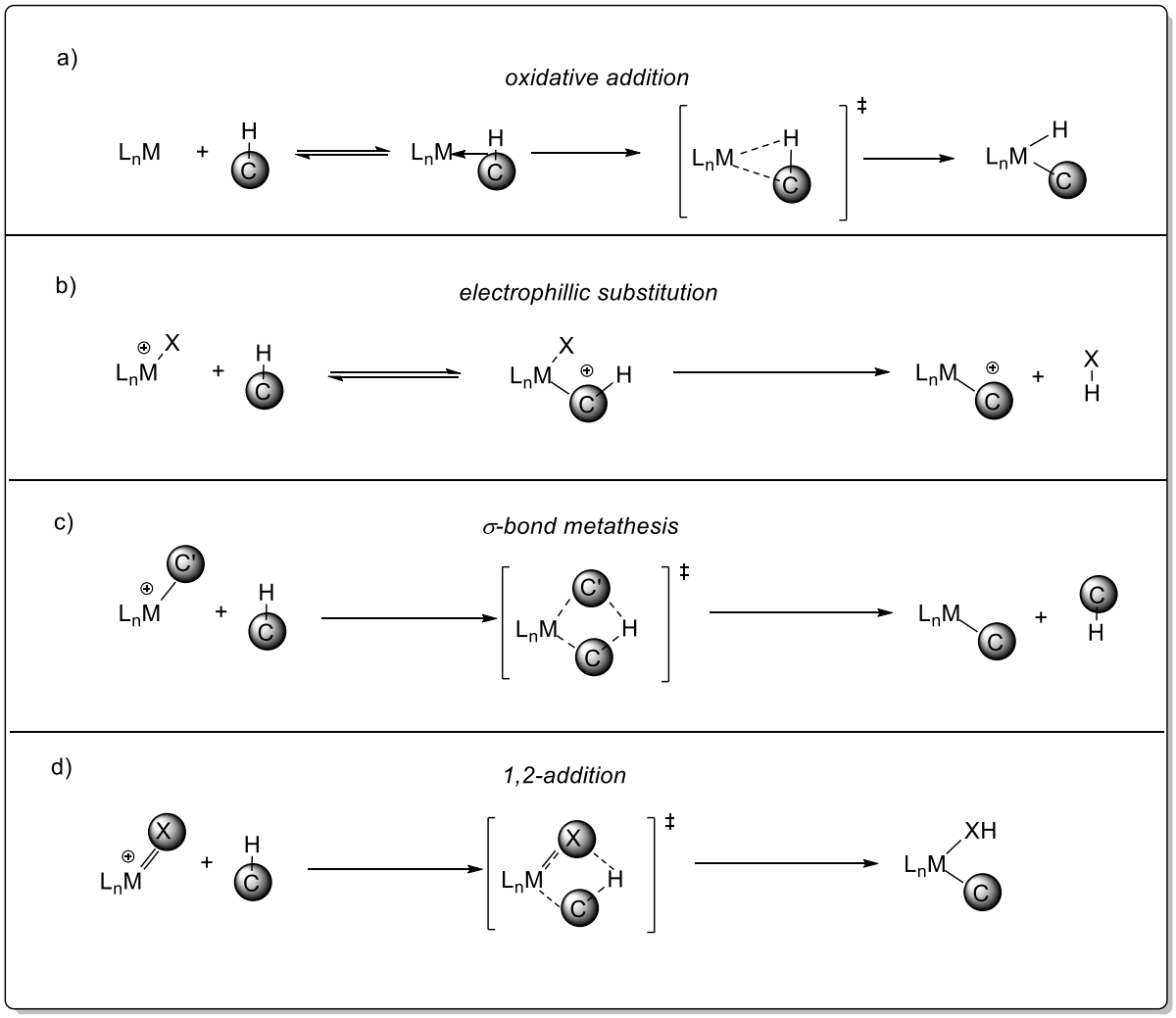
With respect to ecological and economical aspects of organic synthesis, new concepts for more sustainable transition metal-catalyzed direct C–H functionalizations have been conceived.[13,14] The direct C–H functionalization has the advantage that the prefunctionalization of the starting materials is not required, which is accompanied with a significant reduction of waste material **4**. The Scheme 1.2 shows the three different strategies that are widely used for the transformations in transition metal-catalyzed direct C–H functionalizations.[15] The direct cleavage of C–H bonds and their transformation into C–Het bonds has become a compelling research area in modern chemistry geared to achieving complex target structures. These protocols offer appealingly short routes to natural products, pharmaceuticals, and agrochemicals.



Scheme 1.2: Strategies for the transition metal-catalyzed direct C–H functionalizations.

In analogy to traditional cross-coupling chemistry, Scheme 1.2a shows the coupling between **5** with an unactivated C–H bond and an aryl- or vinyl(pseudo)halide and halides **6**. The reaction demonstrated in (Scheme 1.2b) works inversely: The C–H bond in an aryl- or vinyl-substrate is functionalized with an organometallic reagent **7**. For these kind of reactions, however, the use of an oxidant is mandatory. The Scheme 1.2c describes the dehydrogenative coupling between substrates **5** through activation of two C–H bonds and the formal generation of dihydrogen. However, an oxidant is also needed for this type of reactions. Although a number of transformations in which a C–H bond is functionalized with participation of a transition metal-activated ligand *via* a transition metal-induced radical-chain mechanism are known, *Shilov* classifies only specific types of reactions as "true C–H activation".[16] In these reactions, the metal is directly involved in the cleavage of the C–H bond and a M–C σ–bond is formed.

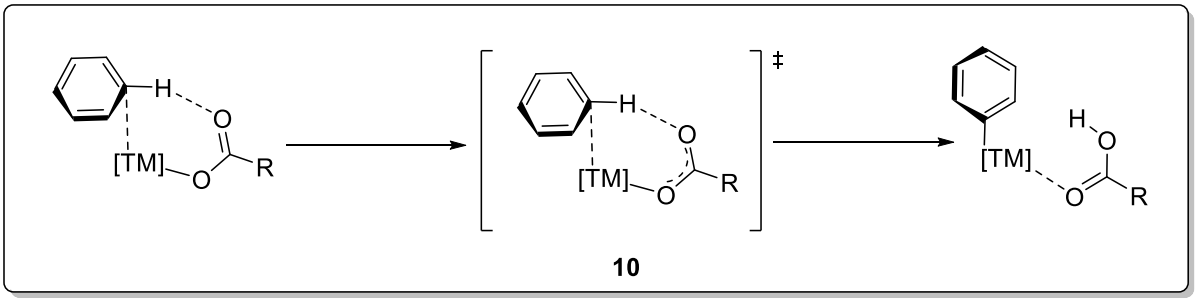
Different mechanistic pathways, four of which are shown in Scheme 1.3 as the traditionally most generally accepted ones, can take place for these processes.[17-20]



Scheme 1.3: Different mechanisms for transition metal-catalyzed C–H activation.

The first pathway shown in Scheme 1.3a is the oxidative addition of a C–H bond to the metal center. This process can occur for electron-rich and low-valent late transition metals, such as rhenium, iron, ruthenium, osmium, iridium and platinum. If late- or post-transition metals are employed in high oxidation stages, including palladium(II), platinum(II), platinum(IV), mercury(II), the mechanism is frequently shifted towards an electrophilic substitution (Scheme 1.3b). However, early group 3 and 4 transition metals as well as lanthanides cannot undergo oxidative addition. For these metals σ–bond metathesis (SBM) usually takes place (Scheme 1.3c). C–H activation can also proceed *via* 1,2-addition to unsaturated Π=X bonds (Scheme 1.3d). As a novel mode of action, an increasing mode of C–H activation, many of reactions proceeds *via* "base-assisted" C–H activation.[19] For instance, a carboxylate-ligand on the transition metal can act as base to promote the abstraction of the proton, along with an

electrophilic activation of the C–H bond by the metal. Proton abstraction by the carboxylate and C–M bond formation take place simultaneously. Such transition states **10** have been described as "concerted-metalation-deprotonation" (CMD)[20] or "amphiphilic metal-ligand activation" (AMLA)[17] and the mechanism can be generalized as shown in Scheme 1.4.[19,21-23]



Scheme 1.4: Mechanism for the carboxylate-assisted C–H activation.

Various calculations showed that a six-membered transition state, where the carboxylate is still bound to the transition metal, is favored over a four-membered transition state as for example, shown in the differences in energy between the potential transition-states of the iridium-catalyzed C–H activation in benzene (Figure 1.2).[35b,35c]

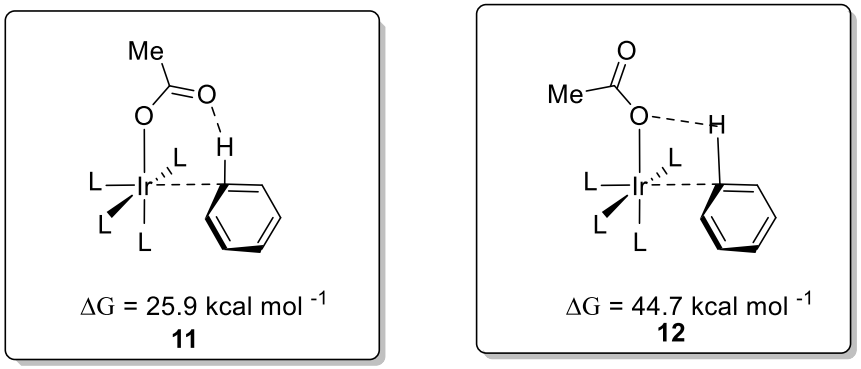


Figure 1.2: Differences in energy between a 4-membered and 6-membered TS.

Nevertheless, in case of hydroxyl- or alkoxyl-ligands only 4-membered transition states are possible. This transition state appears to be a SBM (Scheme 1.3c). However, calculations by *Goddard III et al.* revealed that, in contrast to SBM, the M–O bond is based on a different orbital than the newly formed H–O bond.[25,26] Herein, a four-membered transition state was proposed and mechanistic pathway is termed as "internal electrophilic substitution" (IES)[26].
In this context, theoretical calculations have offered new insight into the mechanism of base-assisted C–H metalation. Based on computational studies, *Davies* and *Macgregor* described

such reaction as an "ambiphilic metal-ligand activation" (AMLA)[35a] whereas *Fagnou* used the term "concerted-metalation-deprotonation" (CMD)[36]. Both proposals favor a similar six-membered transition state, however, *Davies* and *Macgregor* suggested an agostic interaction between the metal center and the C–H bond (Figure 1.3). An activation or strained model was used to compare the performance of hydroxide and acetate, whether the later can access the both four-membered and six-membered transition states (Scheme 1.4).[35b] Although the computed barriers of >40kcal mol^{-1} are rather high for different processes involved, the different transition state geometries show the domination by interaction with base.[35c] This can be rationalized as base(acetate)-assisted-intermolecular electrophilic substitution-type (BIES) C−H metalation event.[51b,55]

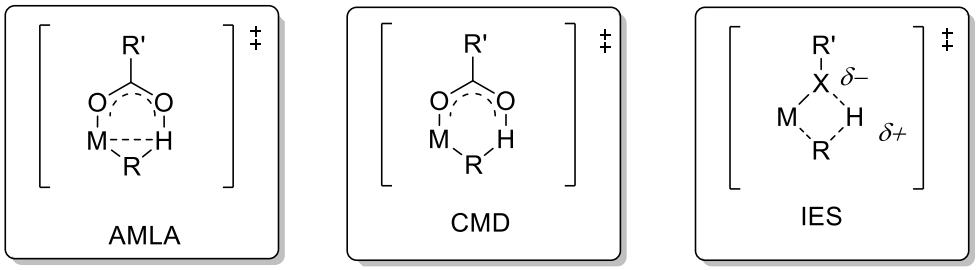
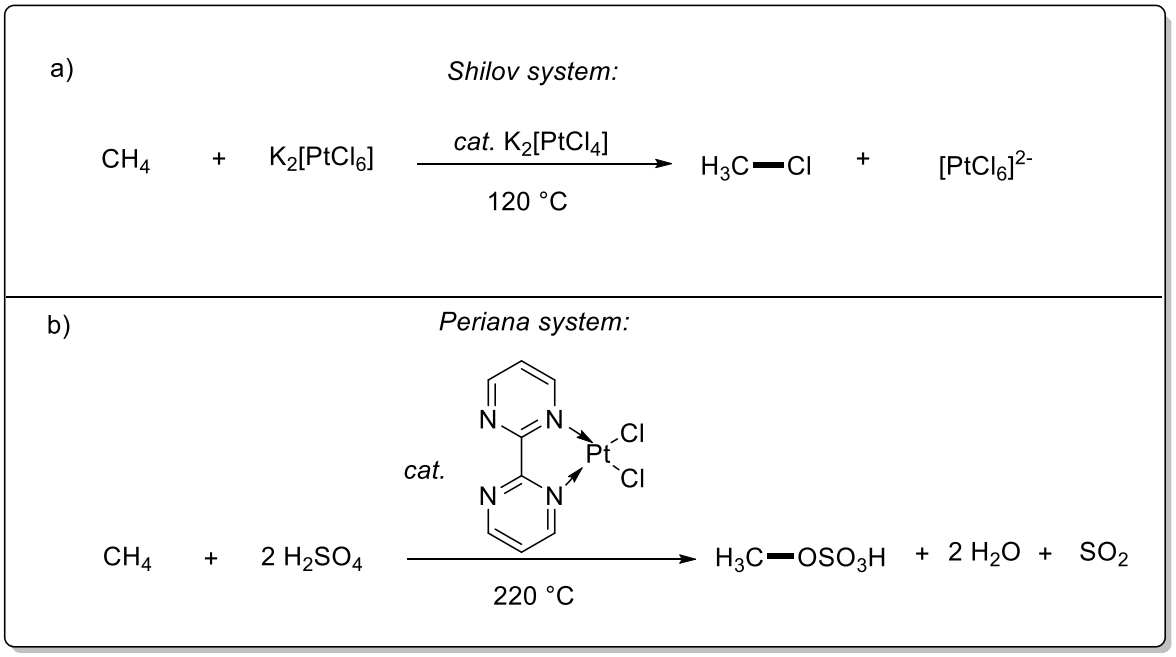


Figure 1.3: Proposed transition state for base-assisted C–H activation.

1.2 Site-Selectivity and Directing Groups in C–H Bond Functionalization

The main challenge in C–H activation chemistry is the chemo- and site-selective cleavage of specific C–H bonds. The selective conversion of methane to methanol, for instance, is of great importance with respect to the potential use of methanol as a fuel.[27] However, the chemoselective oxidation of alkanes is still a challenging task, as alcohols and aldehydes tend to be more reactive than the hydrocarbons themselves thus resulting in overoxidation. Radical-based reactions, on the other side, are often not selective enough and lead to product mixtures. Scheme 1.5a shows the early catalytic system which was developed by *Shilov* for the selective methane activation.[16]

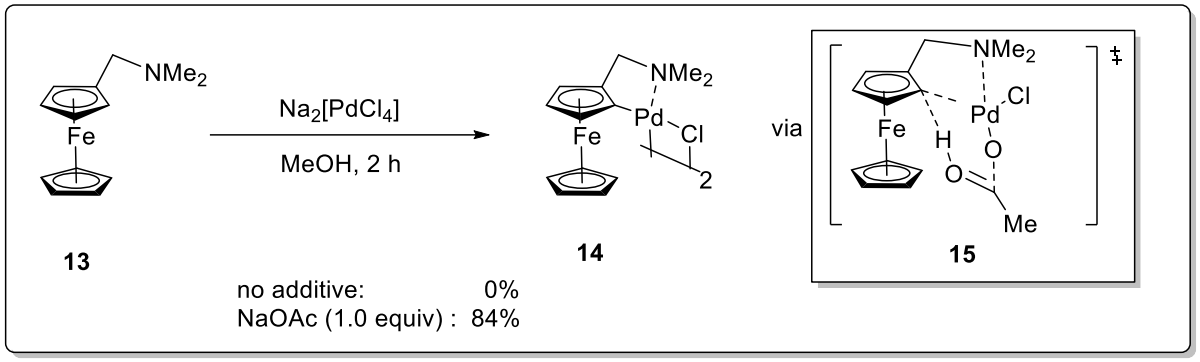


Scheme 1.5: Methane activation by *Shilov* and *Periana*.

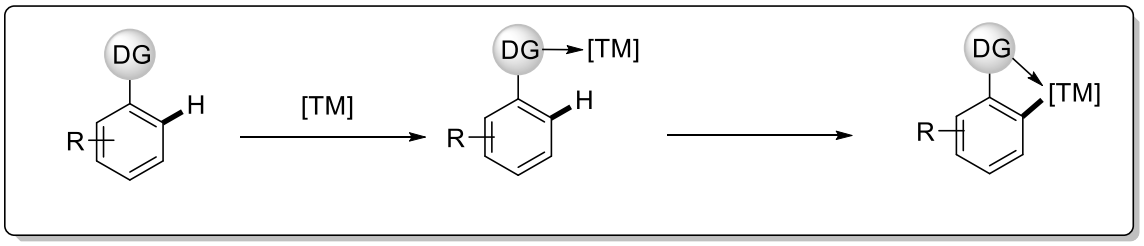
Besides the selective C–H activation of aliphatic compounds, the selective functionalization of aromatic and heteroaromatic C–H bonds is of significant importance, as an ample number of fine chemicals consists of aromatic moieties. On the one hand, C–H activation on aromatic system might be accelerated due to the precoordination of the aromatic π–system to the transition metal.[29-31] On the other hand, the site-selective C–H bond cleavage of functionalized arenes and heteroarenes remains a challenging task.

In the early 1970s, work by *Shaw* and *Gaunt* highlighted the importance of stoichiometric amounts of NaOAc for successful cyclometalation of *N*, *N*-dimethylaminomethylferrocene (**13**) (Scheme 1.6).[32] Subsequently, *Reutov* and co-workers found that carboxylic acids are competent additives for the same transformation.[33,34] More importantly, a transition state of concerted carboxylate-assisted intermolecular deprotonation (**15**)[19,32-34] was specifically proposed.

The most common way to achieve site-selectivity in direct C–H bond activation on arenes is the use of a directing group, which is usually placed in the *ortho*-position to the C–H bond to be functionalized (Scheme 1.7). The directing group bears a heteroatom with a lone pair of electrons and can thus coordinate to the transition metal complex [TM].



S**cheme 1.6:** Base-assisted cyclometalation and proposed transition state **15**.



Scheme 1.7: Principle of a directing group in transition metal-catalyzed C–H activation.

In the past decade, a variety of different directing groups, some of which are shown in Figure 1.4, have been successfully applied for palladium-, nickel-, rhodium-, ruthenium- or iridium-catalyzed direct C–C and C–heterobond reactions.[14,15,30–32]

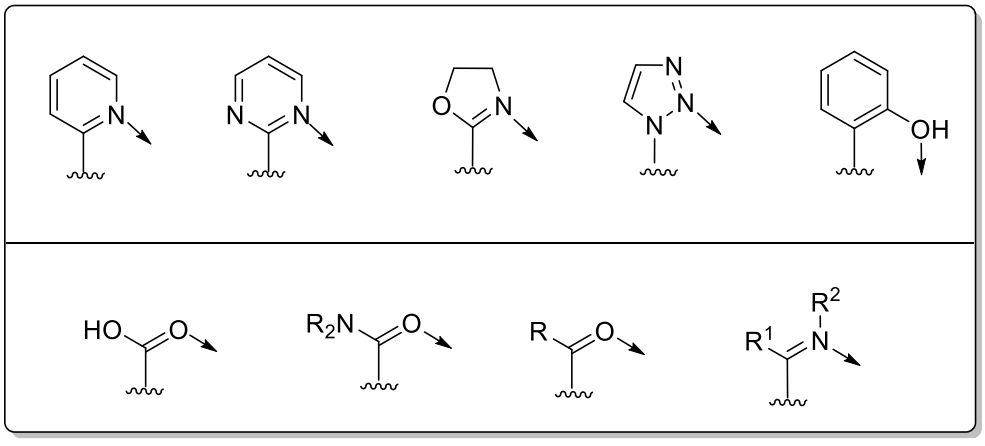
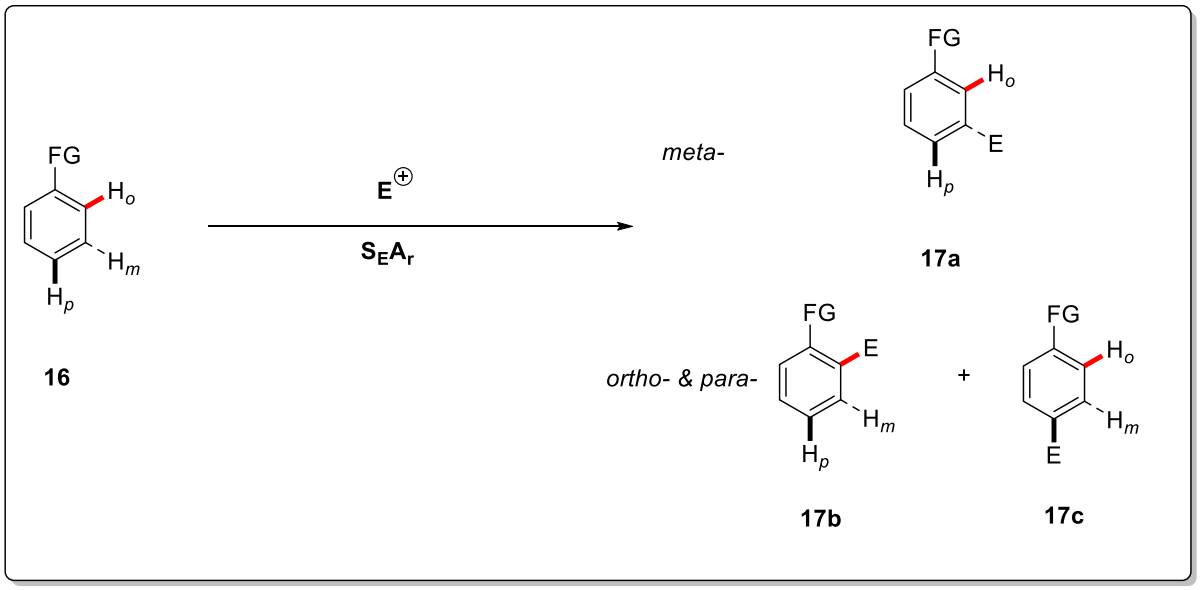


Figure 1.4: Different directing-groups in transition-metal catalyzed C–H activation.

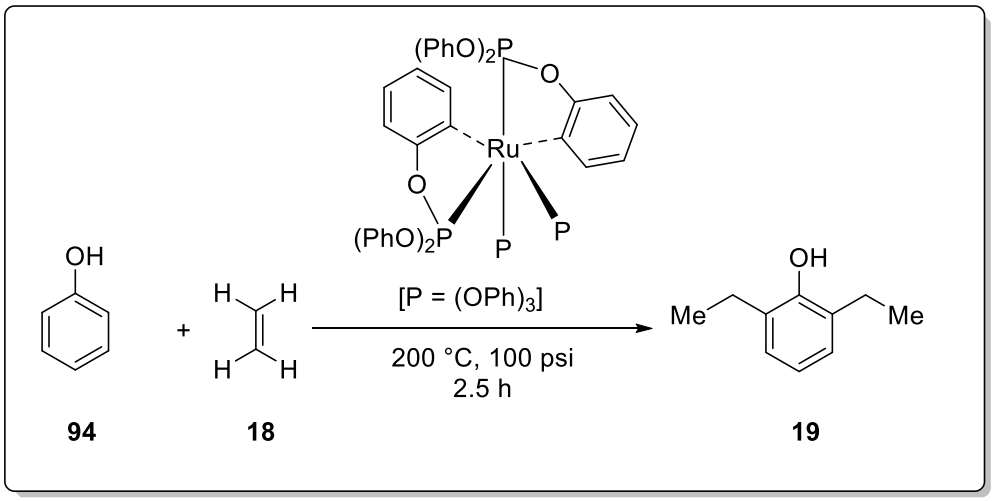
C–H bonds are ubiquitous in nature, a feature which on the one hand facilitates their usage as starting material for elaboration of more complex structures. However, on the other hand, this makes controlling the site-selectivity of C–H functionalization a great challenge. In

electrophilic aromatic substitution, it has been well established that electron-donating substituents direct incoming electrophiles to the *ortho*- (**17b**) and *para*-positions (**17c**), whereas electron-withdrawing substituents lead to the *meta*- position (**17a**) (Scheme 1.8).



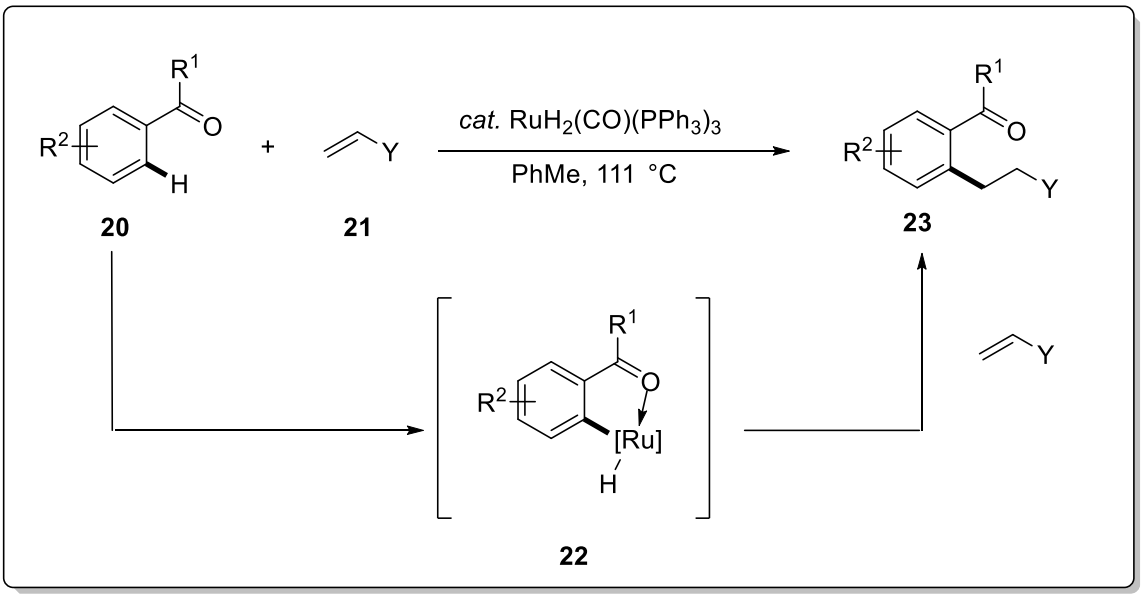
Scheme 1.8: Site-selectivity in electrophilic aromatic substitution.

Based on pioneering work by *Lewis*,[37] in 1993 *Murai et al.* described the first example of a directed catalytic C–H bond functionalization of aromatic ketones **20** (Scheme 1.9). This reaction can also be considered as a hydroarylation of olefin **21**.



Scheme 1.8a: Hydroarylation by *Lewis*.

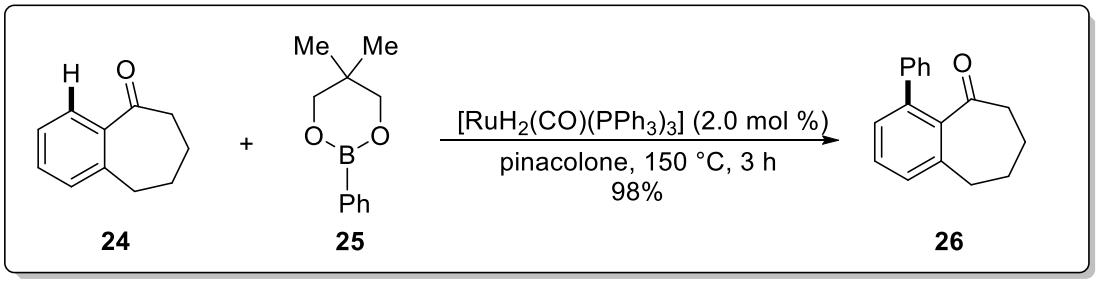
Herein the carbonyl-functionality served as the directing group for the ruthenium-catalyst. Further intermediate developments showed that also other directing groups and other ruthenium catalysts can be used for these hydroarylations, with recent advances from the groups of *Genet* and *Ackermann*.[38-43]



Scheme 1.9: Hydroarylation by *Murai*.

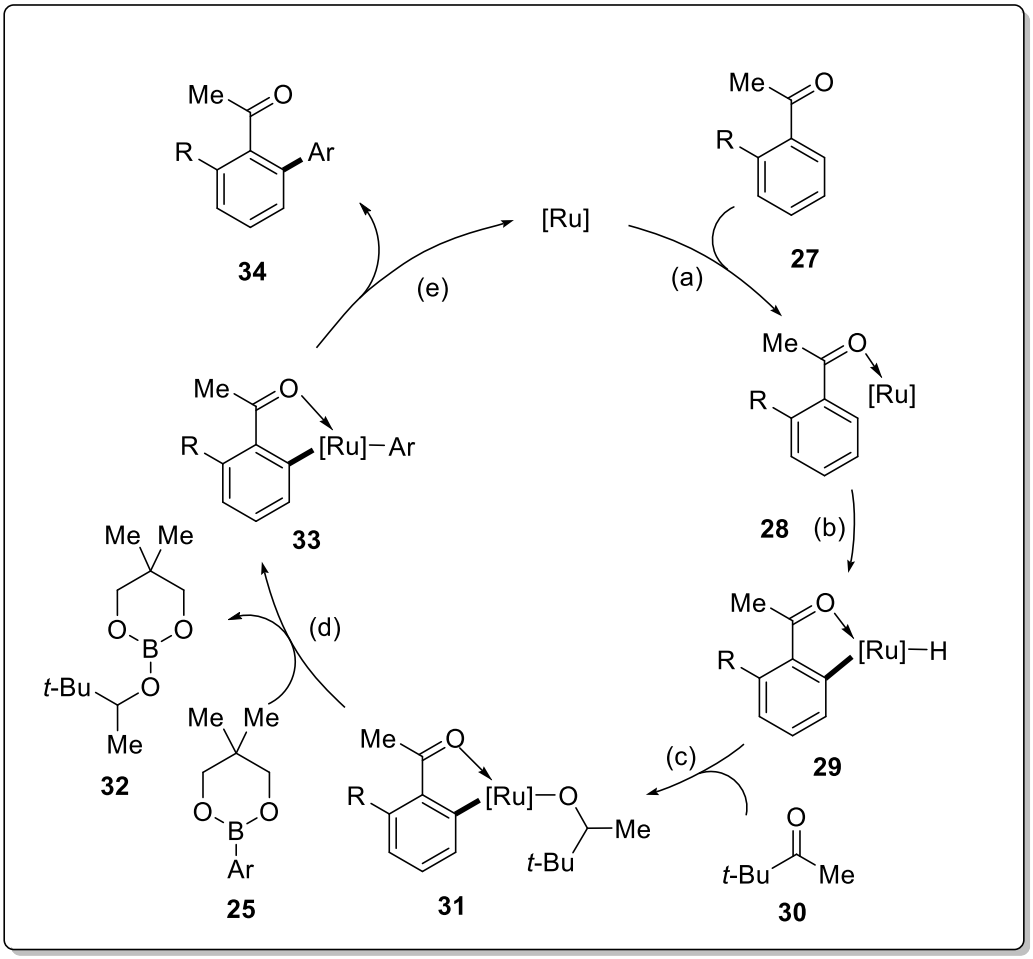
1.3 Ruthenium-Catalyzed Direct Arylations with Organometallic Reagents

A ruthenium-catalyzed[41b] chelation-assisted approach was developed based on the use of arylboronates[41c] as arylating agents.[41] Thereby, a regioselective ruthenium-catalyzed arylation of substrates bearing an oxygen-containing directing group was achieved. A variety of aromatic ketones were efficiently arylated in pinacolone using aryl boronates **25** with both electron-donating, as well as electron-withdrawing substituents (Scheme 1.10).



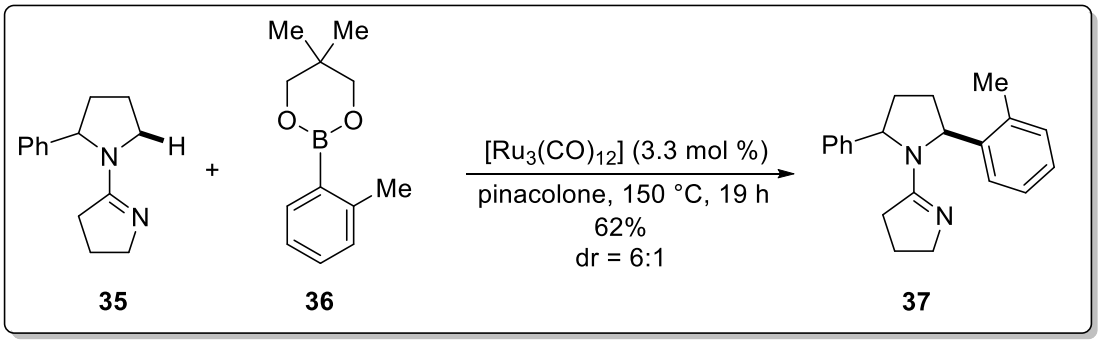
Scheme 1.10. Ruthenium-catalyzed arylation of ketone in pinacolone.

Mechanistic studies revealed that pinacolone acts here not only as the solvent, but also as an oxidizing agent. Additionally, inter- and intramolecular competition experiments with deuterium-labeled ketones provided evidence for a pre-coordination of the ruthenium catalyst by the oxygen of the aryl ketone.[41d] Thus, a mechanism was elaborated consisting of (a) coordination, (b) oxidative addition to yield an *ortho*-metalated ruthenacycle, (c) insertion of pinacolone into the [Ru]–H bond, (d) transmetalation, and finally (e) reductive elimination (Scheme 1.11).[41e]



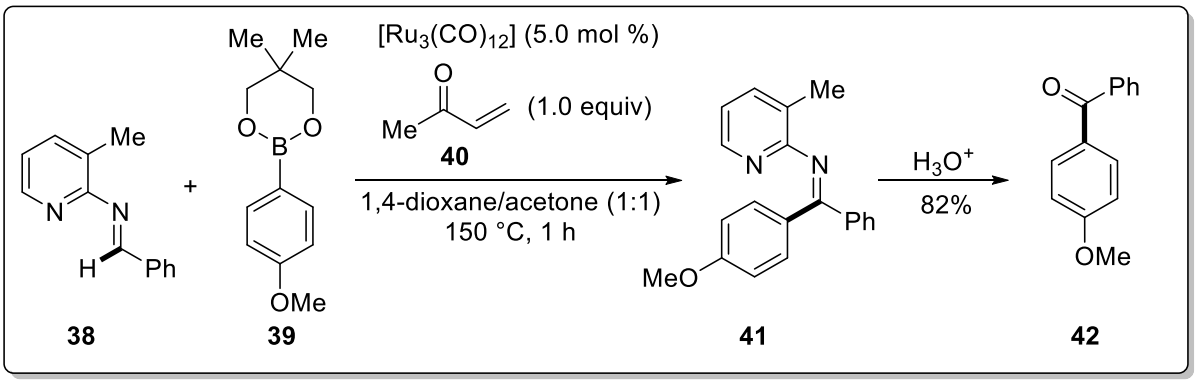
Scheme 1.11. Proposed mechanism for ruthenium-catalyzed arylations of ketones **24**.

An extension of this reaction to the functionalization of C(sp^3)–H bonds was more recently reported. Thus, pyrrolidines **35** were efficiently arylated with substituted arylboronates in pinacolone, yielding, however, often mixtures of diastereomers (Scheme 1.12).[41f]



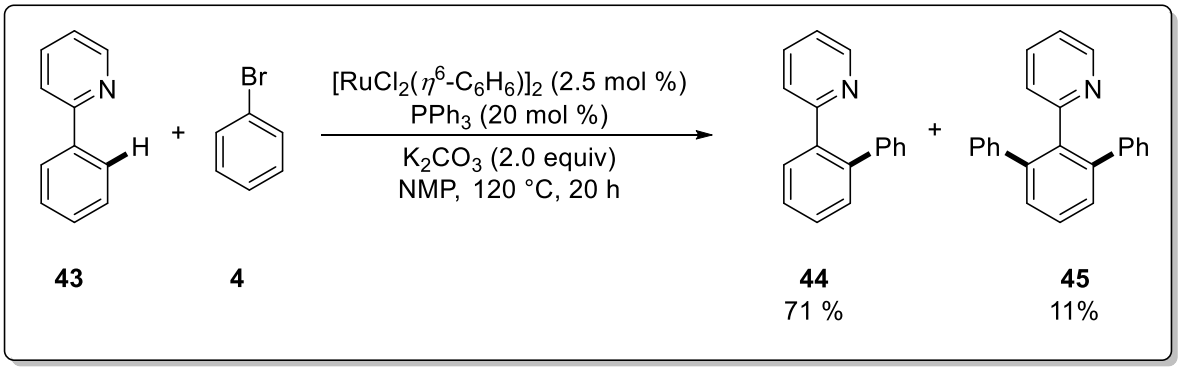
Scheme 1.12. Ruthenium-catalyzed functionalization of a C(sp^3)–H bond in pyrrolidine **35**.

Jun and coworkers used a related approach for a ruthenium-catalyzed arylation of aldimines.[41g] Here, a pyridyl-substituent allowed for the selective arylation with arylboronates **39**. Methyl vinyl ketone (**40**) as additive led to high isolated yields of the corresponding ketones (Scheme 1.13).



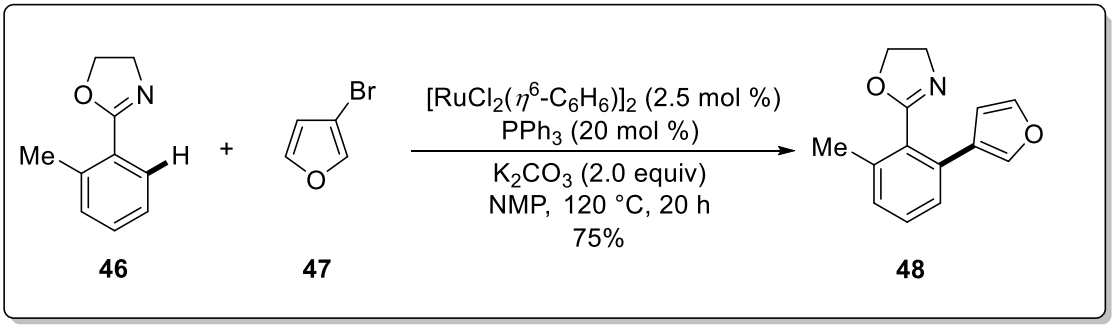
Scheme 1.13. Ruthenium-catalyzed direct arylation of aldimine **38**.

A catalytic system comprising $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$ and PPh_3 was developed by *Oi*, *Inoue* and coworkers for direct arylations of pyridine derivatives using aryl bromides as the electrophiles in NMP as the solvent (Scheme 1.14).[41h]



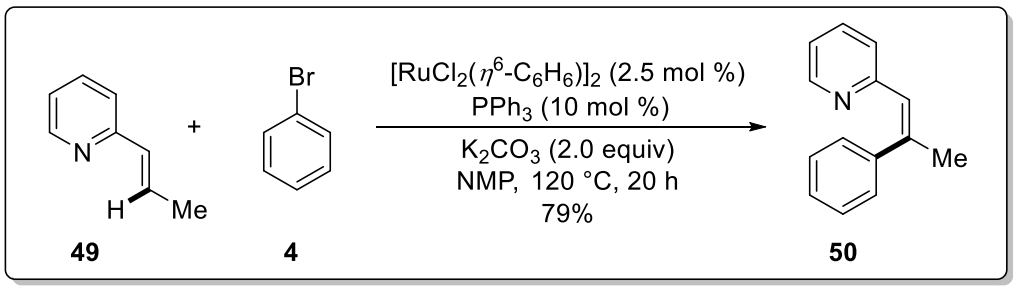
Scheme 1.14. Ruthenium-catalyzed direct arylation of pyridine **43** with bromide **4**.

The same protocol proved applicable to directed arylations of imines, imidazolines and oxazolines as pronucleophilic starting materials in NMP (Scheme 1.15).[41i] Transformations of the later substrates should prove useful, since 2-oxazolinyl substituents **46** can be easily converted into a variety of valuable functionalities.[41j]



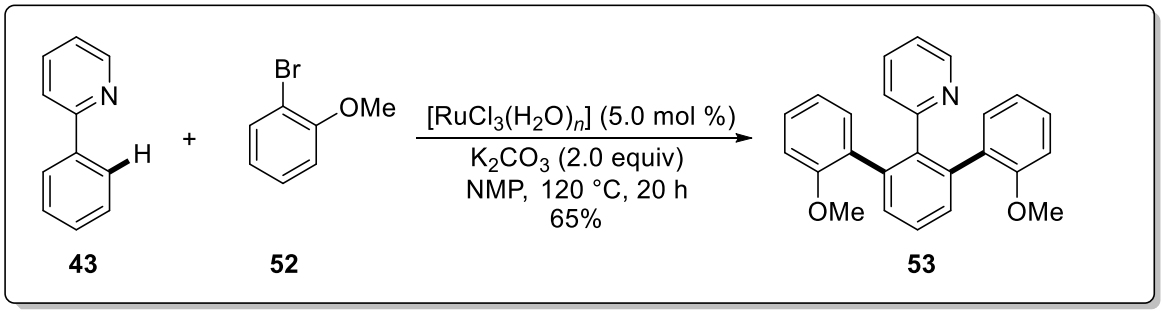
Scheme 1.15. Ruthenium-catalyzed direct arylation with heteroaryl bromide **47**.

Also alkenyl C–H bonds were directly functionalyzed with aryl bromides **47** using this catalytic system in NMP, yielding regio- and stereoselectively functionalized alkenes (Scheme 1.16).[41k]



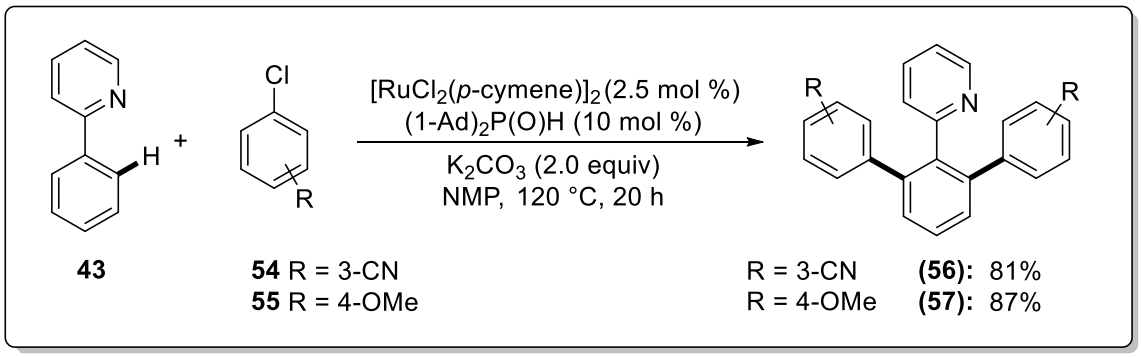
Scheme 1.16. Ruthenium-catalyzed direct arylation of alkene **49**.

A phosphine ligand-free ruthenium-catalyzed direct arylation with aryl bromides as electrophiles **4** was disclosed. Notably, the use of inexpensive $RuCl_3 \cdot (H_2O)_n$ as catalyst allowed for economically attractive C–H functionalizations of pyridine **43**, oxazoline **46** and pyrazole **51** derivatives, also with more sterically hindered *ortho*-substituted aryl bromides (Scheme 1.15).[41l,41m]



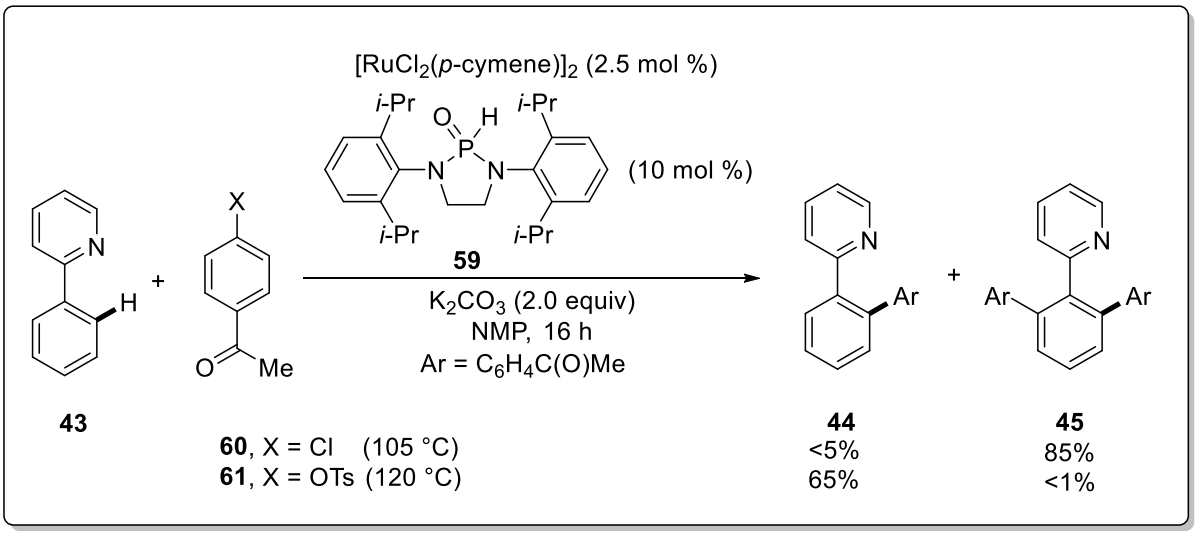
Scheme 1.17. Ruthenium-catalyzed phosphine free direct arylation of pyridine **43**.

Among aryl halides, chlorides are the most useful simple class of electrophilic substrates, due to their lower cost and wide diversity of commercially available compounds.[41] The direct arylations with aryl chlorides were until recently only generally applicable in palladium-catalyzed *intramolecular* transformations.[41n] However, a broadly applicable Intermolecular C–H arylation of various arenes with aryl chlorides was accomplished by Ackermann with a ruthenium complex derived from secondary phosphine oxide (SPO) $(1\text{-Ad})_2P(O)H$ as preligand (Scheme 1.18).[41o] Thereby, pyridine and ketimine derivatives were efficiently C–H arylated with functionalized electron-deficient, and electron-rich, thus for an oxidative addition electronically deactivated, aryl chlorides.



Scheme 1.18. Ruthenium-catalyzed direct arylation with aryl chlorides **54** and **55**.

Importantly, tosylates **61** are more stable towards hydrolysis than triflates. Thus, protocols for traditional cross-coupling reactions were developed by the group of *Ackermann* using ruthenium complex derived from heteroatom-substituted secondary phosphine oxide (HASPO) preligand **59**[41p] allowed for C–H arylations with various tosylates **58**.[41q]. Selective mono- or diarylation reactions could be achieved through the judicious choice of the corresponding electrophile (Scheme 1.19). Thus, while aryl chlorides **60** gave rise to diarylated products, the use of aryl tosylates **61** cleanly afforded the corresponding monoarylated derivatives.



Scheme 1.19. Selective ruthenium-catalyzed direct arylations through choice of electrophile.

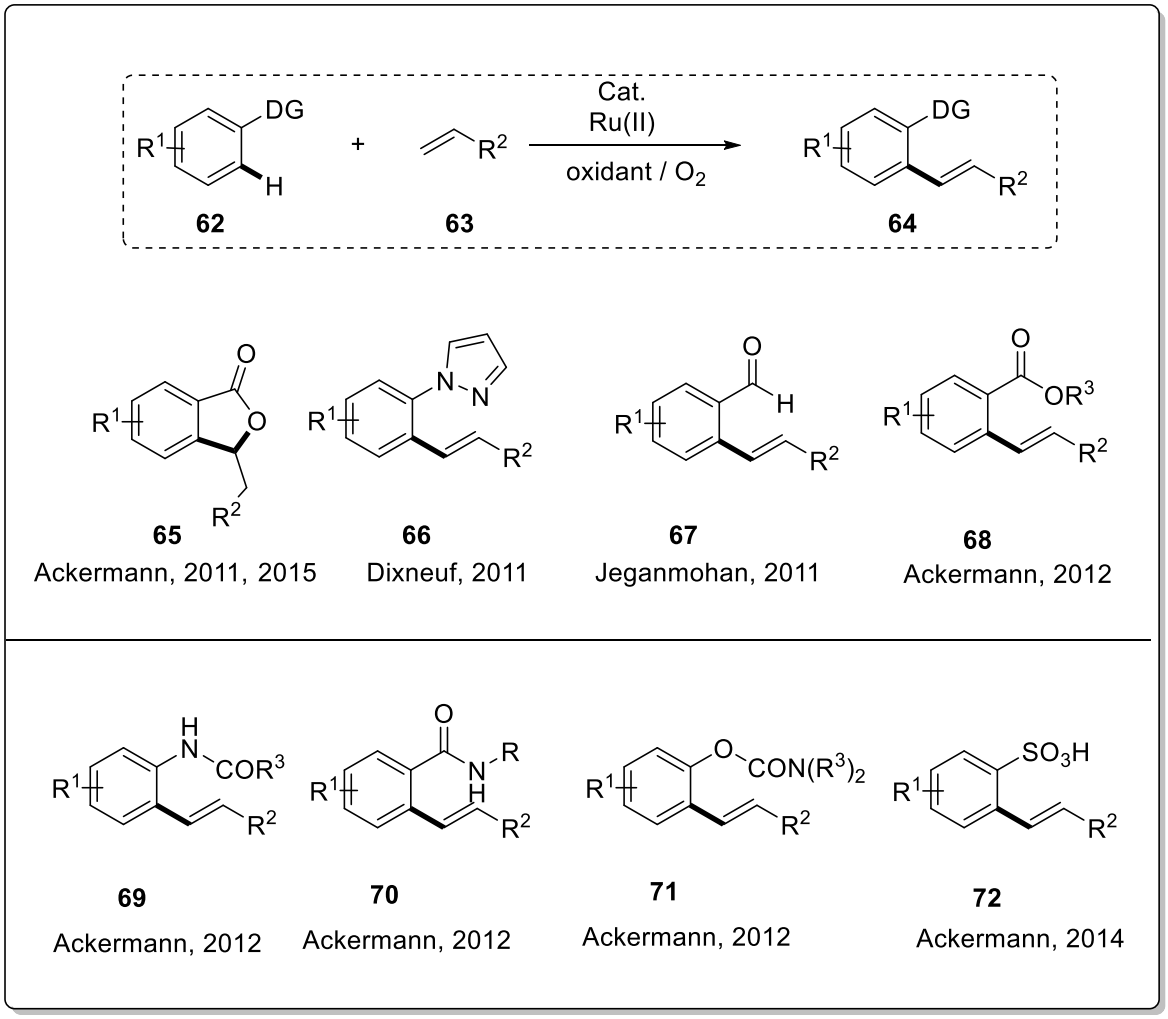
Direct arylations of pronucleophiles with inexpensive aryl chlorides **60** proceeded with high efficacy and excellent diastereoselectivity using either ruthenium carbenes or a ruthenium complex derived from air-stable secondary phosphine oxide preligand $(1\text{-Ad})_2P(O)H$ as catalyst (Scheme 1.19).[41r]

1.3 Transition Metal-Catalyzed Oxidative C–H functionalization with Alkenes and Alkynes

1.3.1 Transition Metal-Catalyzed Oxidative C–H Alkenylation

Palladium-catalyzed oxidative cross-coupling reactions were discovered by *Fujiwara* and *Moritani* in the late 1960s.[44] Recent years have witnessed its wide application in the preparation of numerous synthetically and practically useful heterocycles, such as isoquinolines, isoquinolones, isocoumarins, α-pyrones and 2-pyridines.[47] In 1979, *Hong et al*. reported rhodium-catalyzed styrene synthesis using simple arenes and ethylene in the presence of CO.[48] In 2007, *Satoh* and *Miura* reported the rhodium-catalyzed oxidative alkenylation of easily accessible benzoic acid using acrylates, acryl amides or nitriles as alkenylating reagent. The oxidant was stoichiometric amounts of $Cu(OAc)_2 \cdot H_2O$ in the presence of catalytic $Cu(OAc)_2 \cdot H_2O$.[49] Later, *Glorius* and coworkers reported the rhodium-catalyzed alkenylations of acetanilides,[50] acetophenones and benzamides.[51] In contrast, *Ackermann* reported

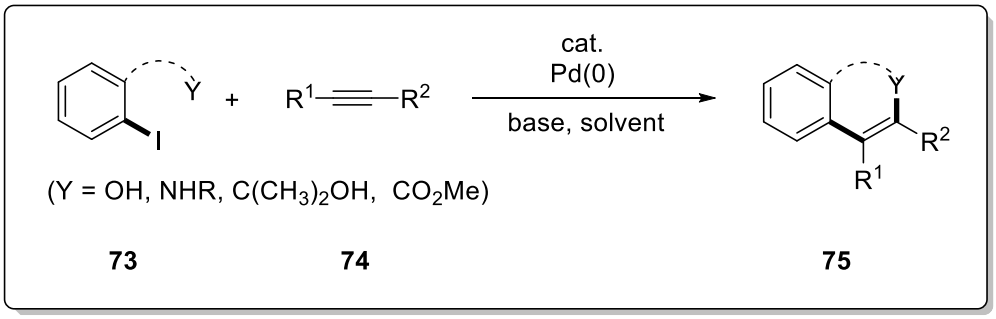
independently C–H alkenylation of acetanilide **69**, benzamide **70**, carbamates **71**, and sulfonic acid derivatives **72** (Scheme 1.20) with inexpensive ruthenium(II) catalysts.[51b-51e,174]



Scheme 1.20: Selected examples of ruthenium(II)-catalyzed oxidative alkenylations.

1.5 Transition Metal-Catalyzed Oxidative Alkyne Annulation

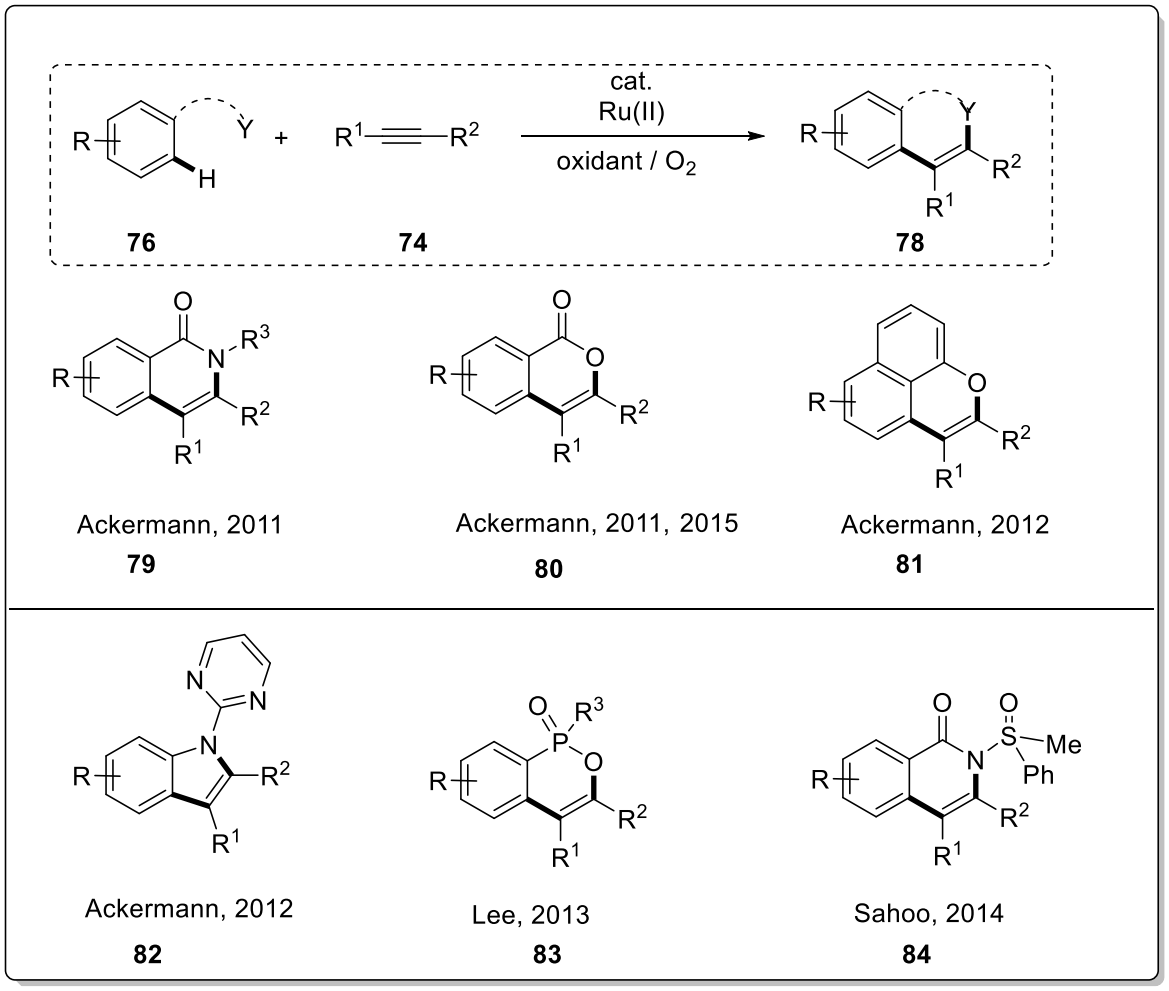
Larock et al. in 1991 reported the efficient palladium-catalyzed alkyne annulation with substituted haloarenes.[52] Thus, a number of synthetically valuable protocols have been developed based on the *Larock-type* heterocyle synthesis (Scheme 1.21)[53]



Scheme 1.21: *Larock* alkyne annulation.

It has become a challenging research target to combine transition metal-catalyzed C–H bond metalation and alkyne annulation in a one pot fashion. Various procedures (Scheme. 1.22) have been reported with rhodium as the catalyst and $Cu(OAc)_2 \cdot H_2O$ as the oxidant.[54]

Later, the *Ackermann* group as well as the group of *Lee* and *Sahoo* accomplished the ruthenium(II)-catalyzed direct C–H olefinations of benzamide **79**, carboxylic acids **80**, phenol **81**, phosphates **83** and sulfoximines **84**.[57a-57c]

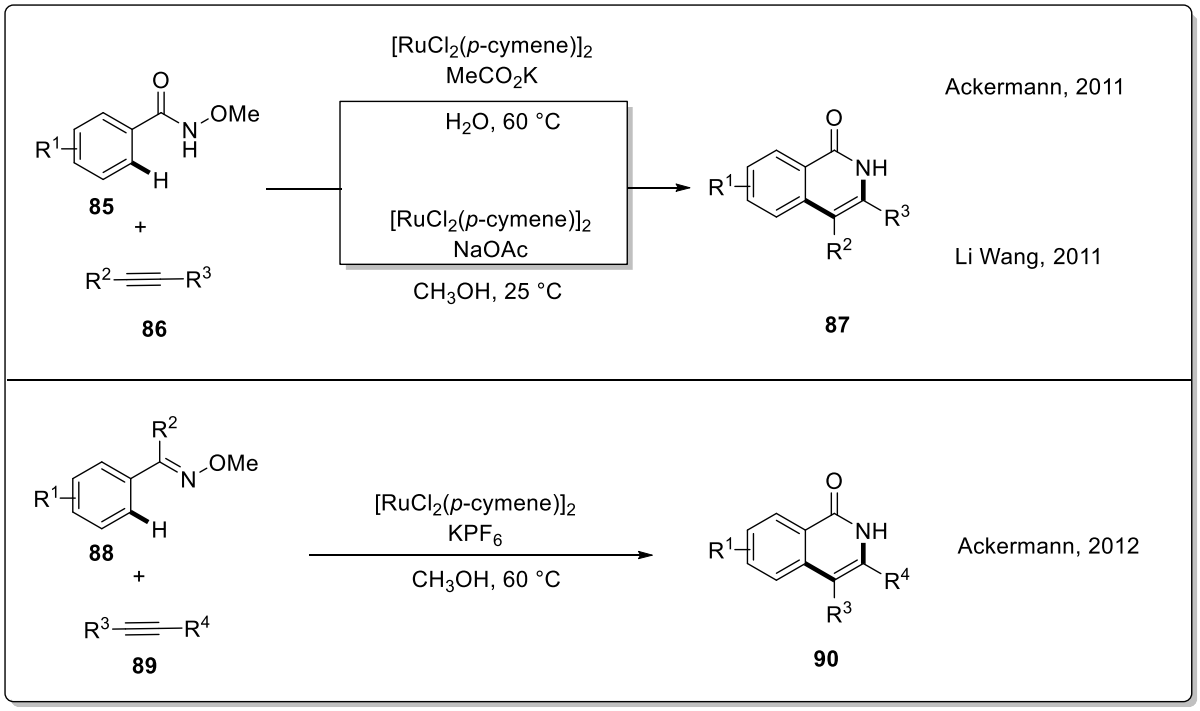


Scheme 1.22: Selected examples of ruthenium(II)-catalyzed oxidative annulations.

1.5 Transition Metal-Catalyzed Alkenylation and Alkyne Annulation by C–H/N–O Cleavage

To the development of oxidative alkenylation and alkyne annulations subsequently utilized C–H/N–O cleavages. The advantage of this method is that the substrate itself acts as an 'internal oxidant' via N–O cleavage. Thus external oxidants such as $Cu(OAc)_2 \cdot H_2O$ are no longer needed. *Fagnou* and coworkers initiated the rhodium(III)-catalyzed C–H alkyne annulation with hydroxamic acid esters substrates. Later, the *Fagnou* group as well as the *Glorius* group accomplished the rhodium(III)-catalyzed direct C–H olefinations of benzhydroxamic acid esters with "oxidizing directing group" methods.[55-57]

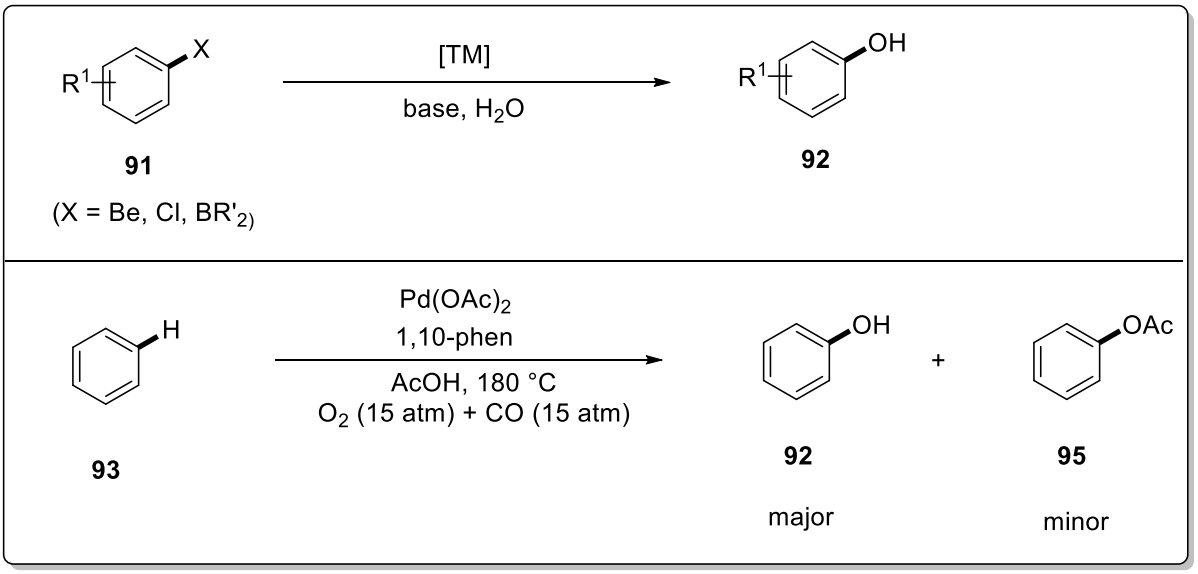
Versatile ruthenium(II)-catalyzed alkyne annulations were discovered by the research group of *Ackermann* as well as explored by the groups of *Li* and *Wang* in 2011.[58-59] Oximes **88** proved to be effective internal oxidants. In 2012, *Ackermann* and co-workers reported the first cationic ruthenium(II) catalysts for alkyne annulations with oximes through C–H/N–O clevages (Scheme 1.23). Ruthenium(II)-catalyzed oxidative C–H bond alkenylation of *N*-methoxybenzamides was reported by *Li* and *Wang* employing both activated and unactivated alkenes.[60-61]



Scheme 1.23: Ruthenium(II)-catalyzed annulation by C–H/N–O bond functionalization.

1.6 Transition Metal-Catalyzed C–O Formations by C–H Activation

Oxygenated aromatic molecules are key intermediates in organic synthesis and important structural components of useful pharmaceuticals, agrochemicals, polymers, and biologically active compounds.[62] For instance, phenol is a central commodity chemical in industry, which is largely produced in a three step synthesis (cumene process) starting from benzene and propylene. Although during recent years transition metal-catalyzed coupling of halogenated or boronated arenes (**91**) to phenol (**92**) have been discovered,[63-65] direct C–H oxygenation should be the optimal choice considering the atom-economy aspect of oxygenation reactions and its importance in further transformations in organic synthesis (Scheme 1.24).

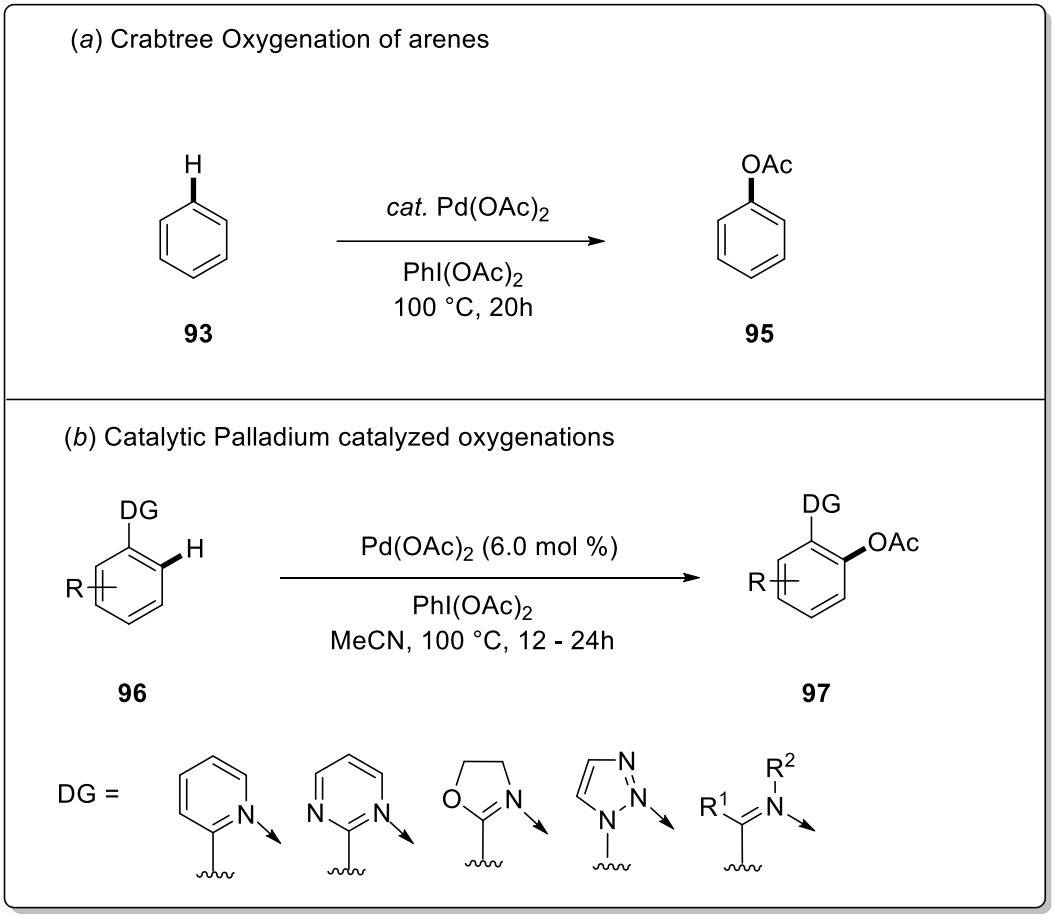


Scheme 1.24: Selected examples of metal-mediated phenol synthesis **92**.

Jintoku and *Fujiwara* in the early 1990's, reported the palladium-catalyzed transformation of benzene (**93**) and molecular oxygen to phenol **92** (Scheme 1.24).[66] The palladium precursor was modified by the addition of 1,10-phenanthroline and dissolved in a mixture of benzene and acetic acid. The reaction proceeded at 180 °C under an atmosphere of oxygen (15 atm) and carbon monoxide (15 atm). The acetylated phenol (**95**) was monitored as a side product.

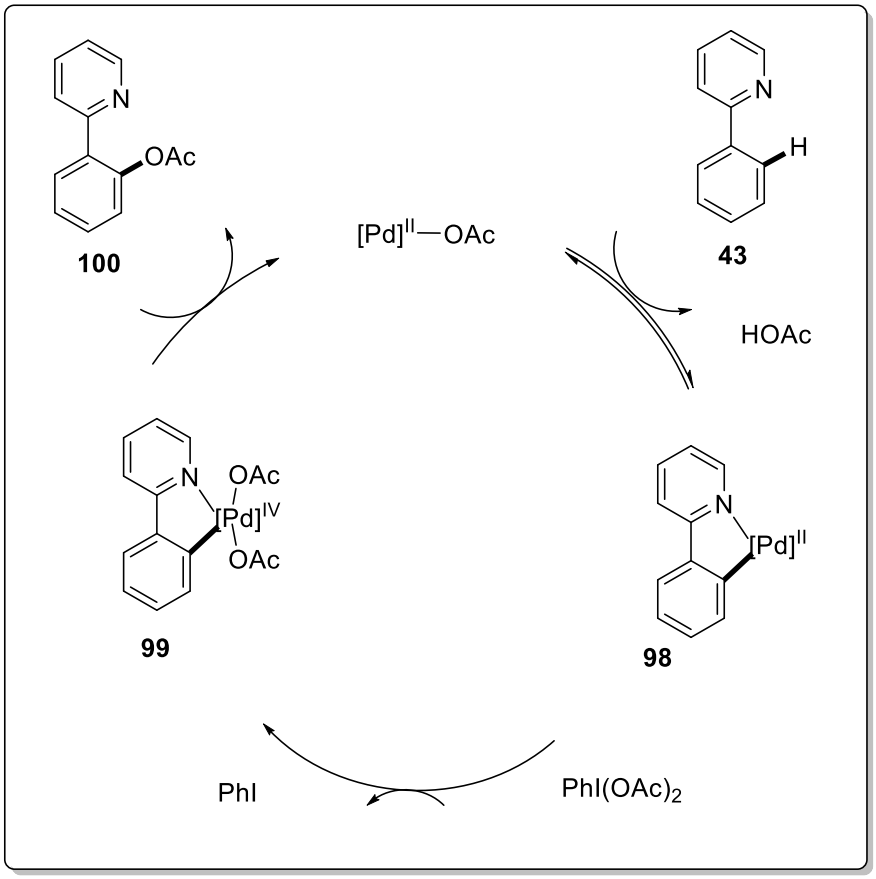
Early examples of palladium-catalyzed ligand-directed C(sp^2)–H bond oxygenation were reported by Crabtree and Sanford using $PhI(OAc)_2$ as the stoichiometric oxidant (Scheme 1.25).[67,174] A variety of pyridine derivatives (**96**) and other well decorated nitrogen-based substituents served as excellent DG, delivering *ortho*-acetoxylated products (**97**) in excellent yields. However, simple ketones and aldehydes did not undergo *ortho*-acetoxylation under these conditions, presumably because these are weakly-coordinating ligands for palladium.

Moreover, $PhI(OAc)_2$ could also be utilized in palladium-catalyzed ligand-directed $C(sp^3)$–H bond oxygenation.[68]



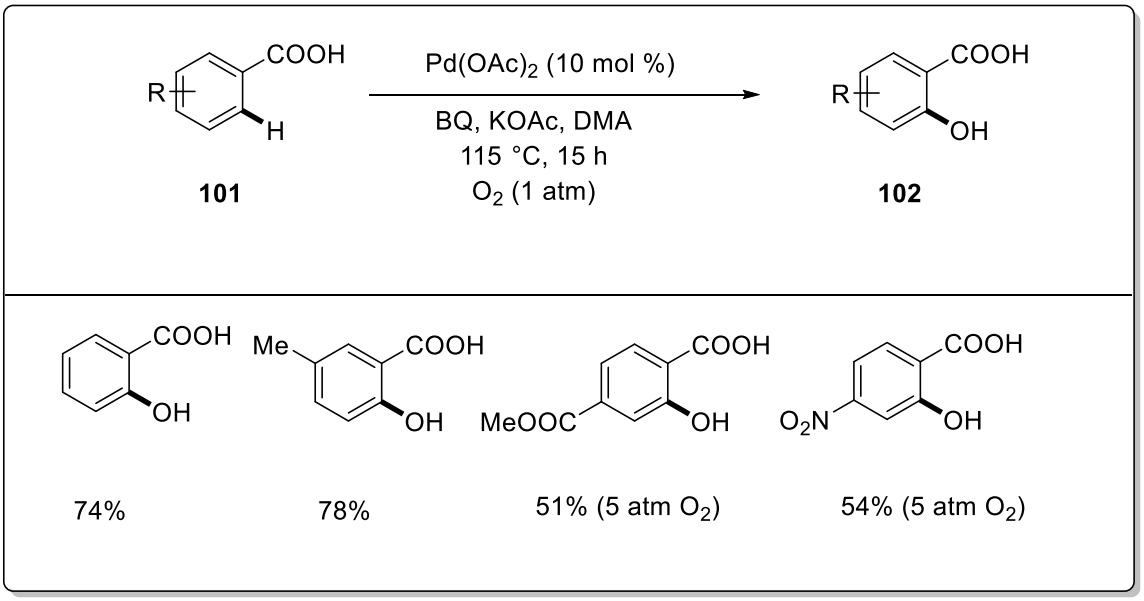
Scheme 1.25: Palladium-catalyzed $C(sp^2)$–H bond oxygenation.

Based on their mechanistic studies,[71,72] *Sanford* and coworkers proposed the catalytic cycle for palladium-catalyzed *ortho*-acetoxylation as shown in Scheme 1.26. First, ligand-directed C–H activation generates a cyclopalladated intermediate **98**. Second, two-electron oxidation of the palladacycle generates the palladium(IV) species **99**. Third, reductive elimination releases the product **100** and regenerates the palladium(II) catalyst.[73,74]



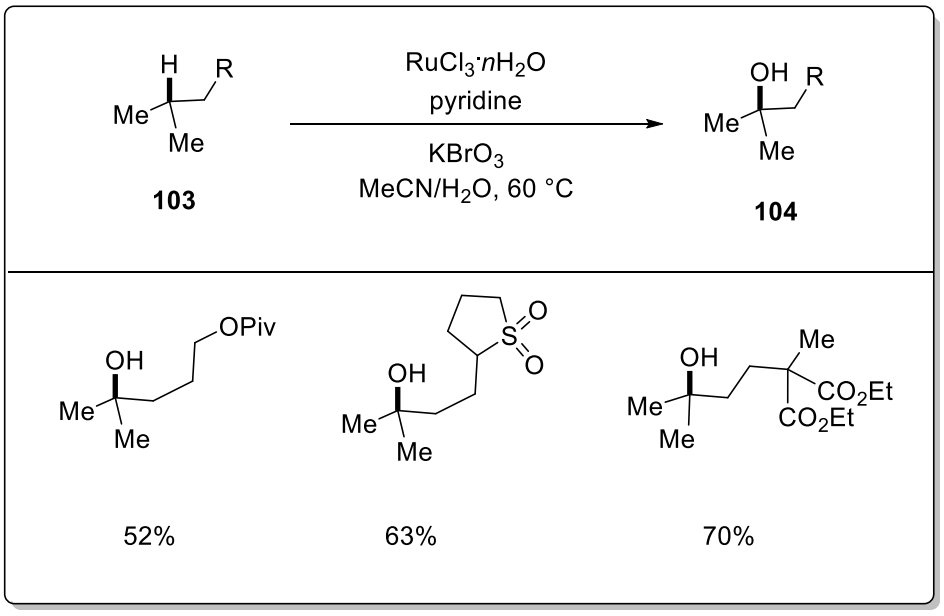
Scheme 1.26: Proposed mechanism for palladium-catalyzed *ortho*-acetoxylation **100**.

Oxgenations reactions have been studied thoroughly using inorganic peroxides, such as Oxone and $K_2S_2O_8$.[71] Yet, molecular oxygen is the optimal oxygen source considering the atom-economy aspect. Recently, the group of *Yu* described a palladium(II)-based catalytic system that fetched the regioselective *ortho*-hydroxylation of potassium benzoates with the environmentally friendly molecular oxygen as the oxidant (Scheme 1.27).[73] The reaction rates were significantly increased in presence of stoichiometric benzoquinone (BQ) and thereby converted substrates (**101**) into desired *ortho*-hydroxylated product **102** in satisfying yield with atmospheric O_2. They confirmed that the oxygen-atom incorporated with labeling experiments. into the hydroxylated product originated from molecular oxygen $^{18}O_2$.



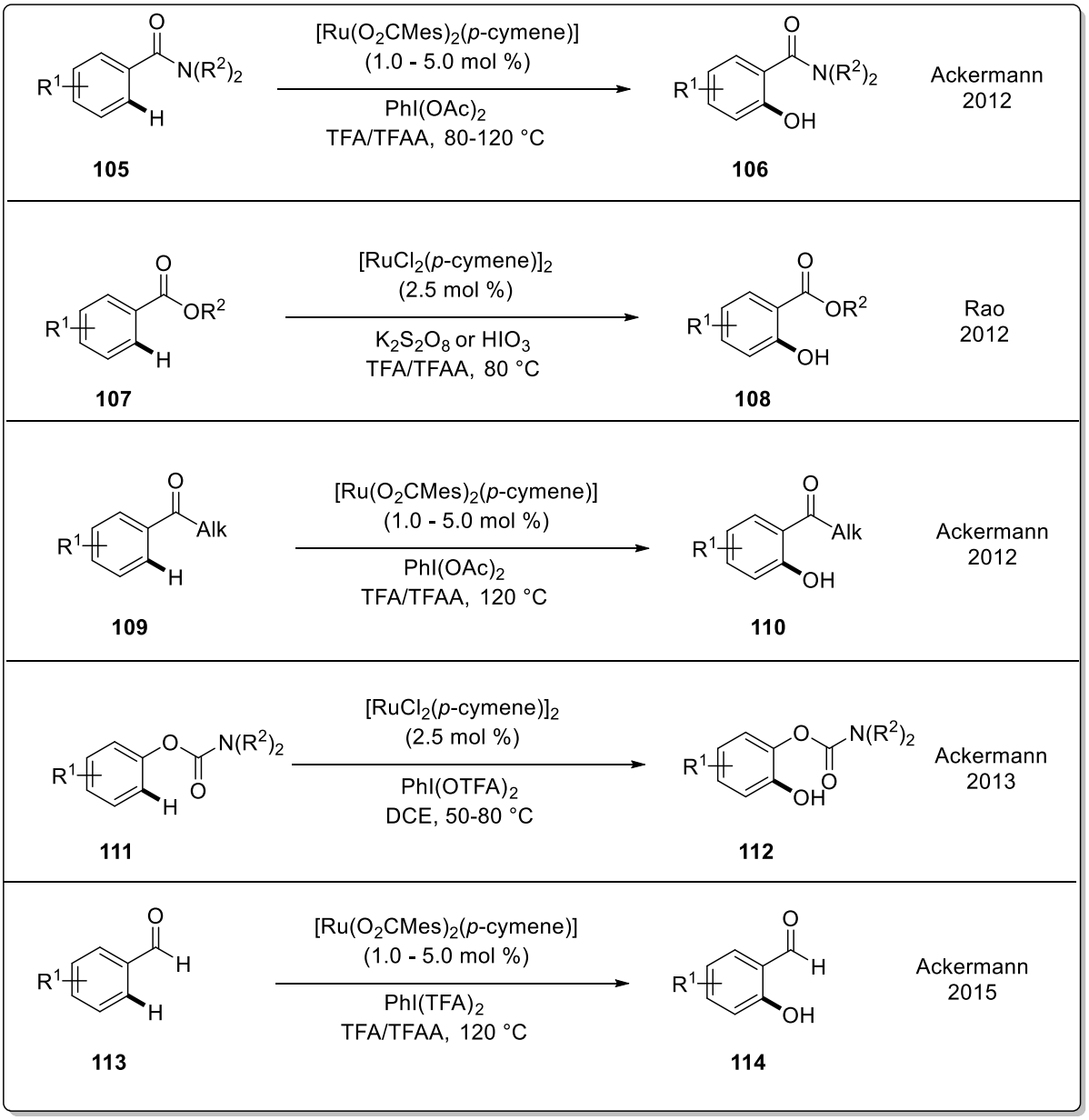
Scheme 1.27: Palladium-catalyzed C(sp^2)–H bond oxygenation.

Recently, ruthenium-catalyzed hydroxylations of C–H bonds have been developed. Previous reports illustrated the RuO_4-mediated hydroxylation of unactivated tertiary C(sp^3)–H bonds in hydrocarbons (**103**).[74-75] *Du Bois* and coworkers disclosed the C(sp^3)–H hydroxylation with catalytic $RuCl_3 \cdot nH_2O$ using $KBrO_3$ as the stoichiometric oxidant, allowing the oxygenation of the weakest C–H bonds in substrates **103** (Scheme1.28).[76] Thus, this method is largely limited to tertiary alkyl C–H bonds.



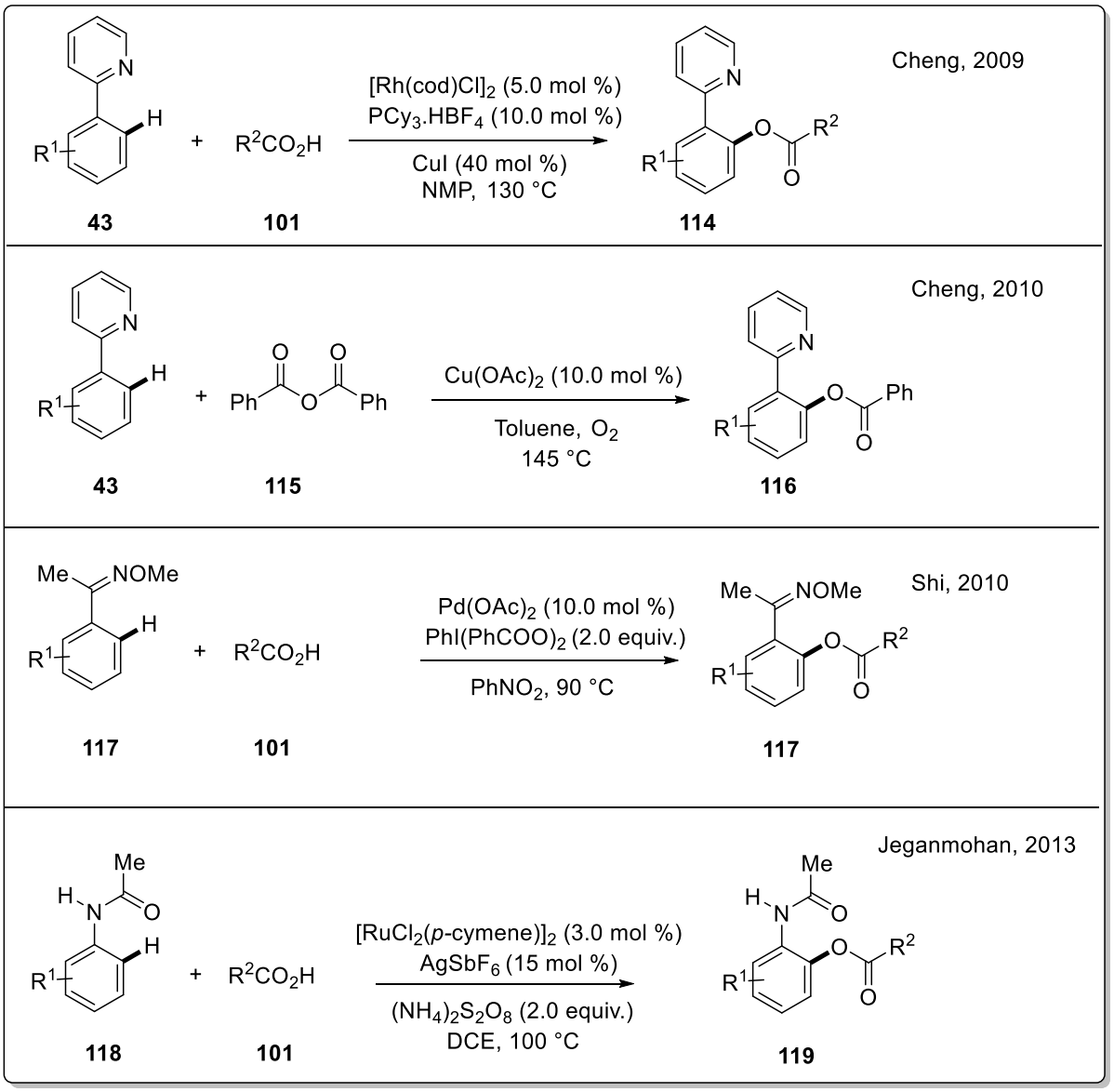
Scheme 1.28: Ruthenium-catalyzed C(sp^3)–H bond oxygenation.

During the past few years a tremendous development in the ruthenium-catalyzed direct hydroxylation of stronger C(sp^2)–H bonds in (hetro)arenes has been witnessed.[62] *Rao* and coworkers disclosed ruthenium-catalyzed *ortho*-hydroxylation with benzoic acid using $K_2S_2O_8$ or HIO_3 as the oxidant,[77] while *Ackermann* and coworkers employed the well-defined ruthenium(II)–biscarboxylate complex [Ru($O_2CMes)_2$(*p*-cymene)] as well as inexpensive $RuCl_3 \cdot nH_2O$ in the hydroxylation reactions using hypervalent iodine reagents as the oxidant.[78] The acidic reaction medium turned out to be crucial for chelation-assisted *ortho*-hydroxylations on (hetro)arene **43** with ester **107**, amide **105**, or even weakly-coordinated ketone **109** as the directing groups.[79-80] While previous studies had focused on arenes bearing electron-withdrawing directing groups, the group of *Ackermann*[81] independently explored ruthenium-catalyzed carbamate **111** as well as weakly co-ordinating aldehyde **113** *ortho*-hydroxylation with excellent site-selectivities. This mode of reaction could be used in further post-synthetic functionalizations of electron-rich phenol **111** and aldehyde **113** to respective valuable heterocycles (Scheme. 1.29).[82]



Scheme 1.29: Selected examples of Ruthenium(II)-catalyzed C(sp^2)–H bond hydroxylation.

Whilst previous studies on ruthenium(II)-catalyzed C(sp^2)–H bond oxygenation of arenes bearing electron-withdrawing or electron-donating directing groups are limited to acetoxylation and hydroxylations of aromatics[78-81] the group of *Sanford* reported benzoxylation of 2-phenylpyridines with benzoate iodonium salts in the presence of a palladium catalyst.[83] In 2009, *Cheng's* group demonstrated benzoxylation of 2-phenyl-pyridines with benzoic acids in the presence of a rhodium catalyst.[84] A very recent report from the group of *Jeganmohan* showed the use of aryl-carboxylic acids **101** in ruthenium(II) catalysis to achieve the aryloxylation[87] of acetanilides **113** using inorganic oxidants (Scheme 1.30).[88]

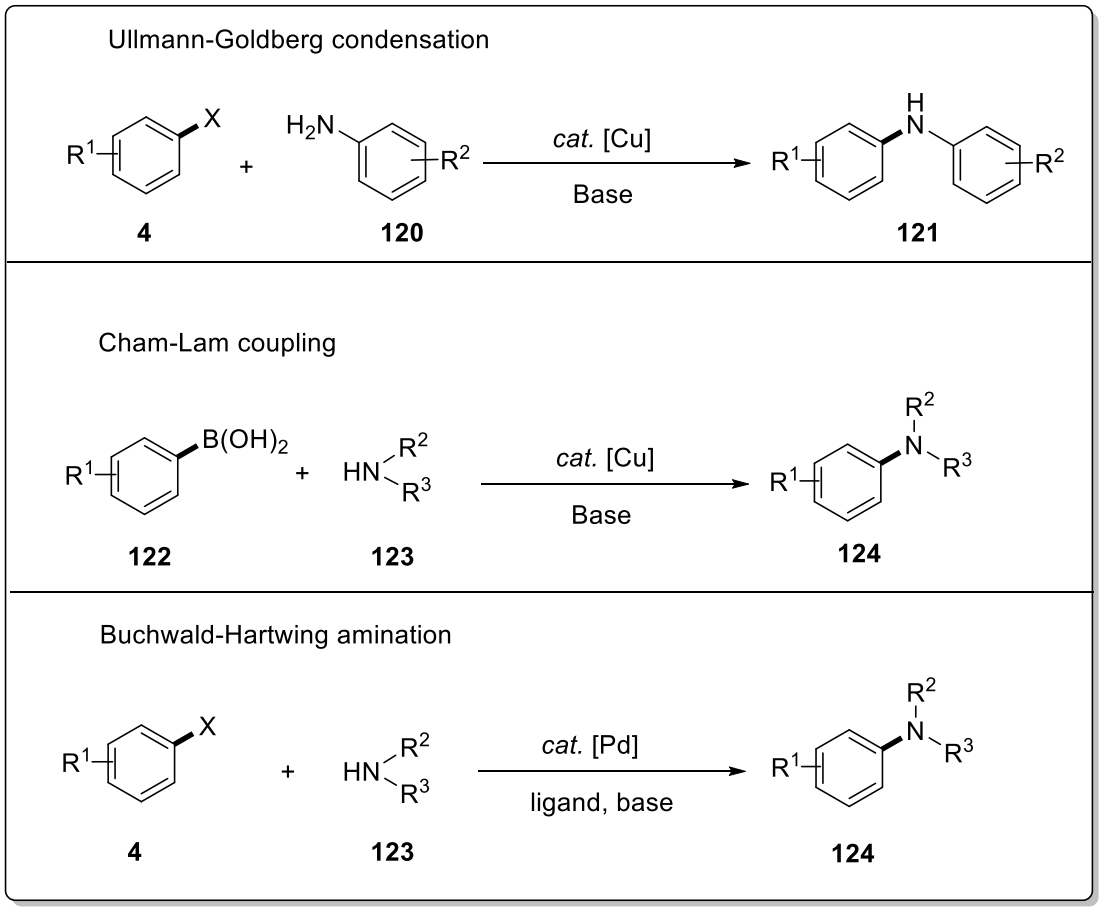


Scheme 1.30: Selected examples of metal-catalyzed C(sp^2)–H bond benzoxylation.

1.7 Transition Metal-Catalyzed C–N Bond Formations

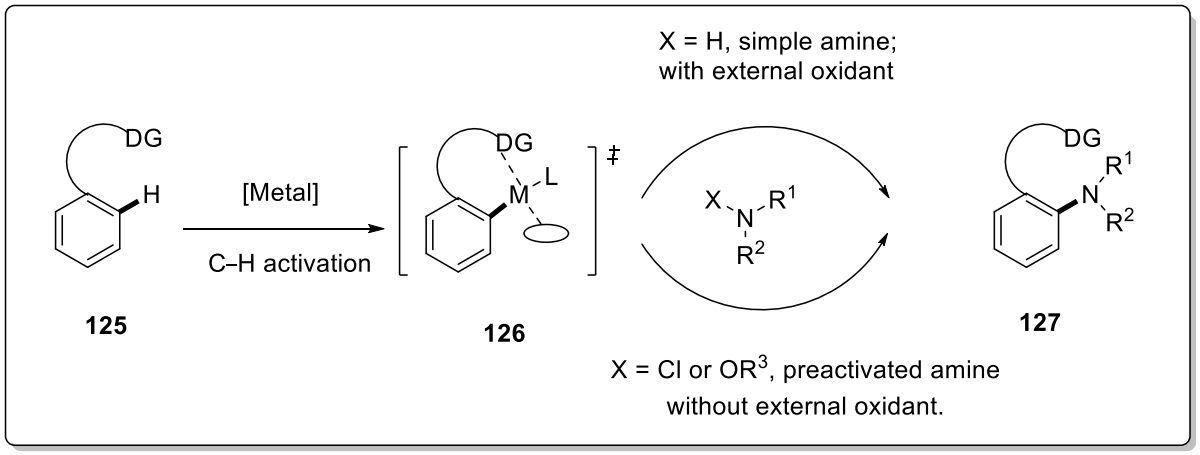
Aromatic amines are of significant importance owing to their widespread existence in natural products and artificial organic compounds.[89,90] Because of their unique properties, they have found broad applications in the prepration of various materials, such as agrochemicals, pharmaceutical agents, dyes, pigments, and polymers[91,92] As a consequence, developing practical and efficient preparations of amines has always been one of the central research topics in both academic and industrial areas.[62,93-97]

As many efforts have been devoted to their synthesis, substantial achievements have been made over the past decades, and a large amount of different catalytic systems have been successfully established. The *Ullmann–Goldberg* condensation **121**,[97-101] *Chan–Lam* coupling **124**,[102-106] and *Buchwald–Hartwig* amination **124**,[107-111] reactions are among the classic methodologies, which provide increasingly viable and practical tools for C–N bond formation (Scheme1.31). However, in all these cases, prefunctionalization of the arenes, such as for aryl halides, pseudo halides (**4**), or boronic acids (**122**) is necessary and the accompanying generation of undesired stoichiometric byproducts (hydrogen halides or the corresponding salts) cannot be avoided. Nowadays, with economic and environmental considerations becoming increasingly important, it is highly desirable to explore new strategies to circumvent those inherent limitations.



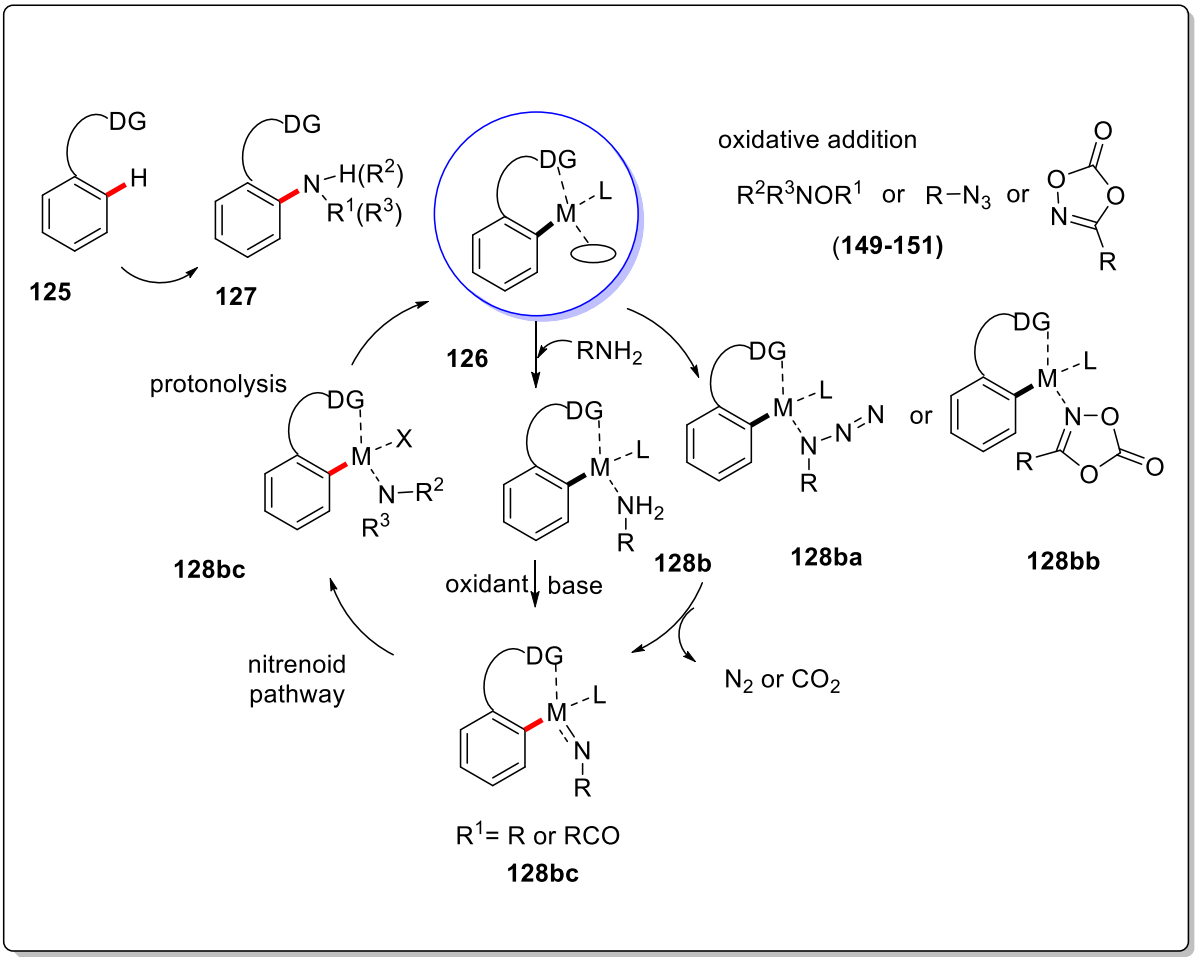
Scheme 1.31: Early examples of metal-catalyzed C(sp^2)–H bond amination.

Transition-metal-catalyzed direct C–H functionalization opens a new avenue for diverse C–N bond construction in a step and atom-economical way, without the requirement of prefunctionalization of the C–H coupling partners. With the assistance of various directing groups with different coordination abilities, the cyclometalation of numerous transition-metal catalysts can regioselectively occur on the *ortho*-position through the C–H activation process. Subsequently, a variety of amino sources have been successfully employed as effective coupling partners to install a nitrogen-containing functional group. In general, there are two approaches to fulfill the transformation. The first employs simple neutral amines, amides, or sulfonamides as effective aminating reagents. In this process, external oxidants are always required to facilitate the formation of the C–N bond. The second strategy utilizes preactivated amino sources, including *N*-chloroamine, *N*-hydroxycarbamate, *O*-acylhydroxylamine, nitrosobenzene, *N*-fluorobenzenesulfonimide (NFSI), azides, and 1,4,2-dioxazol-5-one, under redox-neutral conditions (Scheme 1.32).[19,46,112-118]

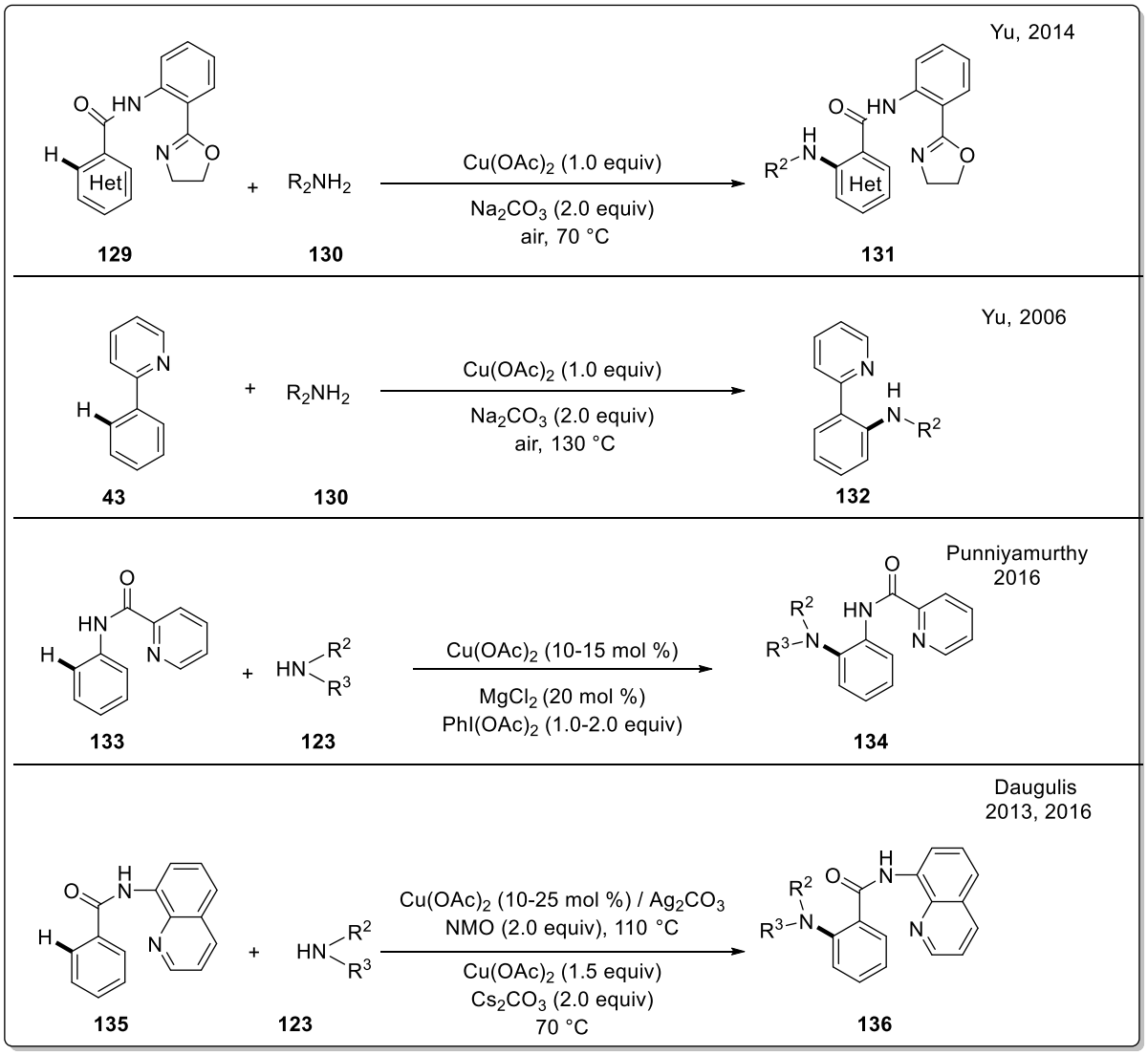


Scheme 1.32: Directing group assisted *ortho*- C–H amination.

A more detailed mechanistic consideration is illustrated in Scheme 1.32a. Starting from the reactive metallacycle species **126**, a variety of amidating reagents can coordinate to the metal center to form **128a**, **128b**, or **128c**. Several classical amidating reagents were selected to describe the following different catalytic cycles. In general, there are two kinds of possible key intermediates involved in the above amidation process. One is a nitrene intermediate whereas the other is an imido intermediate. For the first case, organic azide and 1,4,2-dioxazol-5-one are the most widely used amino source, which release compound **128bb**, although some primary amines could also deliver the nitrene intermediate **128ba**, which subsequently proceeded through a stepwise nitrenoid transfer pathway to yield product **127** from **128ba**. For the second type, some secondary amines in the presence of external oxidant and base could generate **128bc** by direct metalation. The oxidative addition of secondary *N*-benzoate alkylamine to the metal center followed by reductive elimination yields **127**. Finally, protonolysis by another molecule of the starting material **125** or acid would afford the final aminated product **127** and regenerate the reactive species **126**.



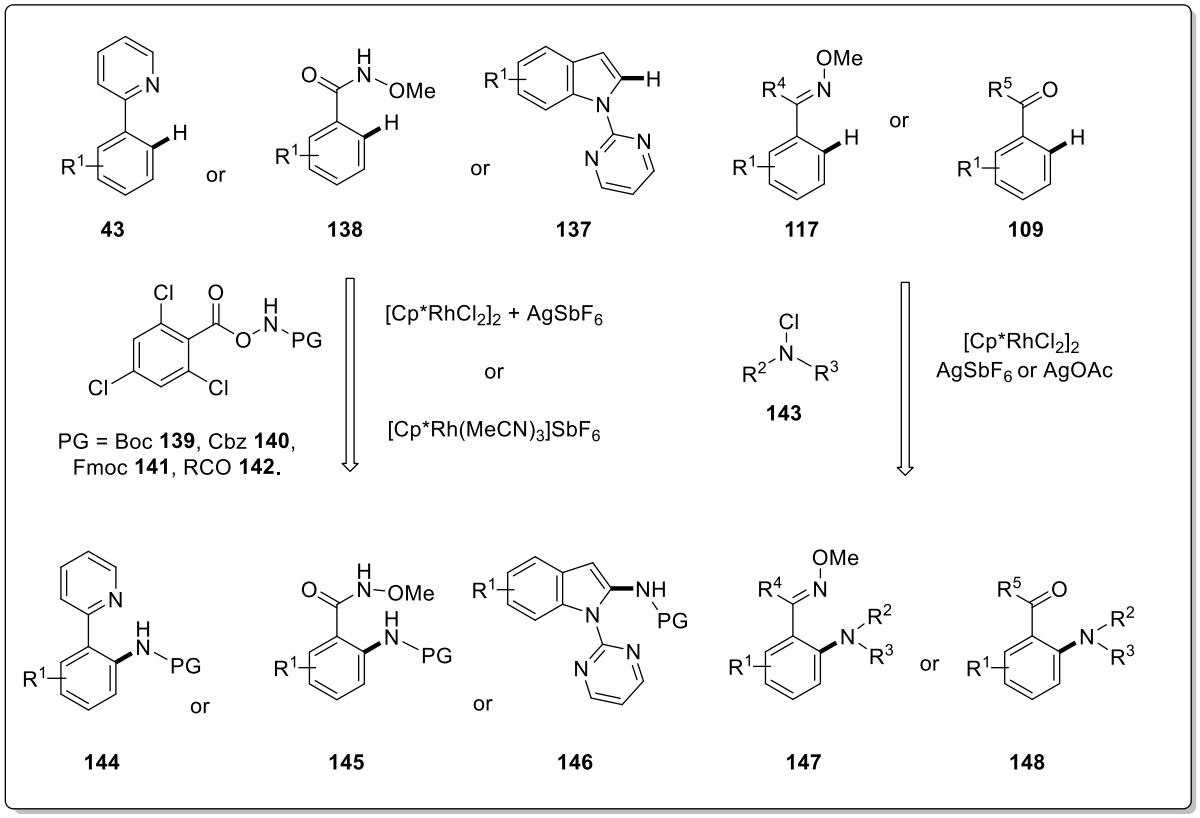
Scheme 1.32a: Catalytic cycles for transition-metal-catalyzed *ortho*- C–H aminations.



Scheme 1.33: Selected examples of copper mediated C–H amination.

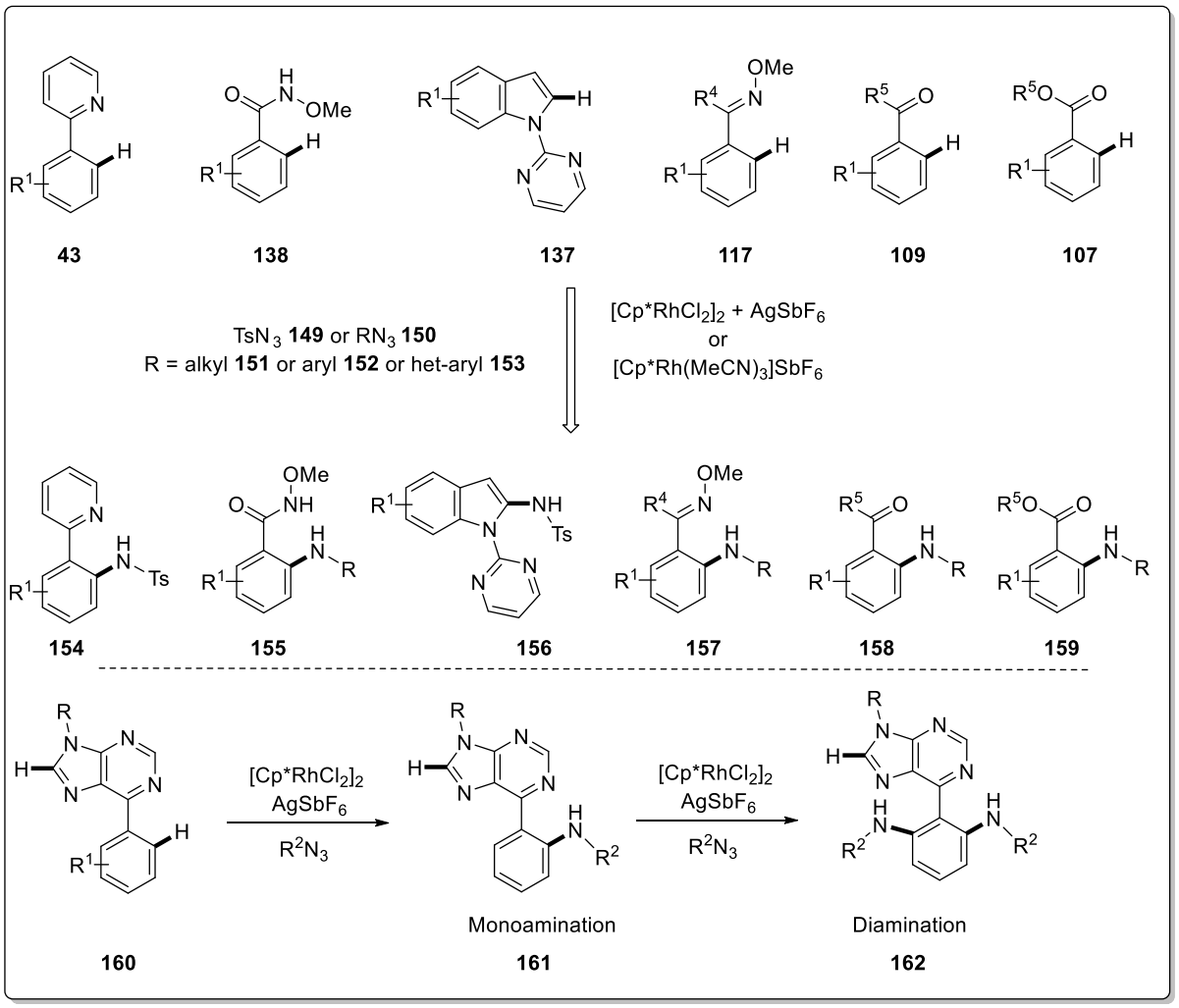
In 2006, *Yu's* group rendered the stoichiometric direct C–H amination of 2-phenylpyridine (**43**) with amine (**130**).[119] One equivalent of copper(II)-acetate was used as the catalyst and air acted as the oxidant (Scheme 1.33). However, in this preliminary work, only one example was provided without any substrate scope exploration. Later, a similar system was demonstrated by *Chatani*, albeit with lower efficiency. [120] Subsequently, several other groups developed different catalytic systems independently. Four years later, *Li* and co-workers developed an amidation of 2-arylpyridine derivatives **43** with amides by using a catalytic amount of CuBr in combination with *tert*-butyl peroxide (TBP) as the oxidant under neat conditions. This is a ligand and base-free transformation.[121] Satisfying yields were achieved for the secondary amides. However, when primary amides or $TsNH_2$ were utilized, comparatively lower yields were obtained. Simultaneously, *Nicholas*' group reported that a catalytic amount of $Cu(OAc)_2$

mediated the amidation of 2-phenylpyridine (**43**) by using molecular oxygen as the terminal oxidant. A broad range of primary *N*-reagents, such as sulfonamides, carboxamides, and anilines, could all participate in the reaction, providing the expected amination products in moderate to good yields.[122] A trace amount of DMSO was added at high reaction temperatures of 160 °C to enable high catalytic turnover. In 2014, *Shen* reported a copper-catalyzed C–H amidation of *N*-pyrimidyl/pyridyl indoles **137** and arylpyridines **43** under aerobic conditions by using phthalimide as an aminating reagent.[123] Once again, the high reaction temperature of 150 °C is the main limitation of this strategy. The *Bolm* group disclosed a rapid access to *N*-arylated sulfoximines by copper-mediated C–H amination of 2-arylpyridines with sulfoximines. A stoichiometric amount of copper salt was required to ensure the efficiency when oxygen was used as the oxidant.[124]. Very recently, *Li*, *Chen* and coworkers presented a copper(I)bromide-catalyzed intermolecular dehydrogenative amidation of arenes with amides by using air as the terminal oxidant. A wide range of amides such as *N*-aryl amides, *N*-alkyl amides, benzamide derivatives, imides, and lactams all proved to be good coupling partners.[125]



Scheme 1.34: Selected examples of rhodium(III)–catalyzed C–H bond amination.

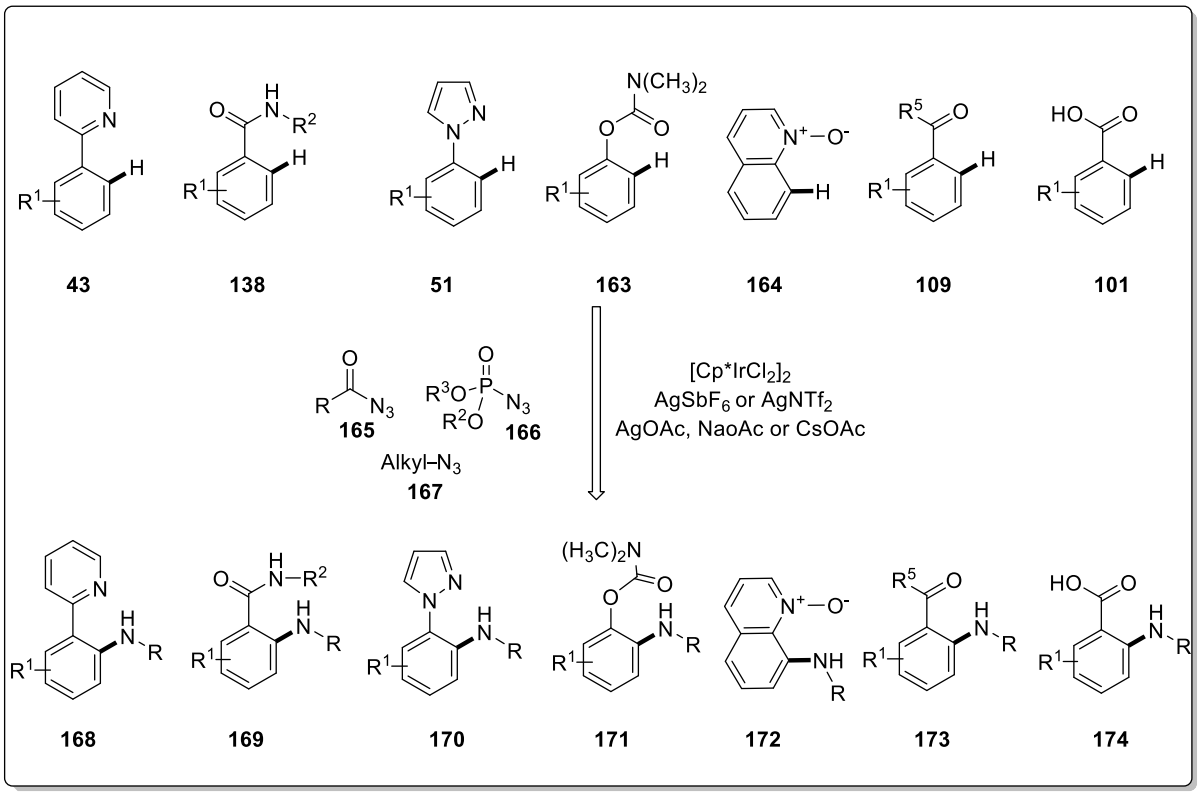
Besides free amines which were explored using copper catalysts[119-125] *N*-chloroamine **143**,[119-120] *N*-aroyloxyamide **142** are another kind of efficient preactivated amino source. In 2013, the *Glorius* group reported a rhodium(III)-catalyzed C–H amidation using electron-deficient aroyloxycarbamates **139** as an efficient electrophilic nitrogen source (Scheme 1.34).[126] Both pyridine **43** and *O*-methyl hydroxamic acids served as efficient directing groups to give access to *N*-carbamate protected arylamines **140** under mild reaction conditions. The group of *Yi*, *Xu* and co-workers extended this type of preactivated amino reagent to include *N*-(2,4,6-trichlorobenzoyloxy)amides, which proved to be effective coupling partners for the rhodium(III)–catalyzed direct regioselective C2-amidation of indoles bearing an *N*-2-pyrimidyl directing group **146**.[127]



Scheme 1.35: Selected examples of rhodium(III)–catalyzed C–H bond amination.

The group of *Chang* disclosed the amidation of 2-phenylpyridine (**43**) with tosyl azide **149** (TsN_3) which was efficiently catalyzed by a cationic Cp*Rh(III)–species and which was generated in situ by treating $[RhCp^*Cl_2]_2$ with a silver salt (Scheme 1.35).[128] Besides pyridine

43, quinoline **135**, pyrazole **51**, and oxime **117** as well as purine **160** could also be used as good chelation groups to promote the amidation with moderate to good yields. In addition, the reaction could be scaled up.[129] Since then, TsN_3 **149** has become a popular amidating reagent for various amidation processes. For instance, *Zhou, Li et al.* developed a rhodium-catalyzed direct C2-amidation of indoles bearing a 2-pyrimidyl unit as a directing group through C–H activation by using sulfonyl azides **149-153** as the amine source.[130] In their work, ten equivalents of water were added as an additive to enhance the efficiency. Recently, our group also made some contributions to this area.



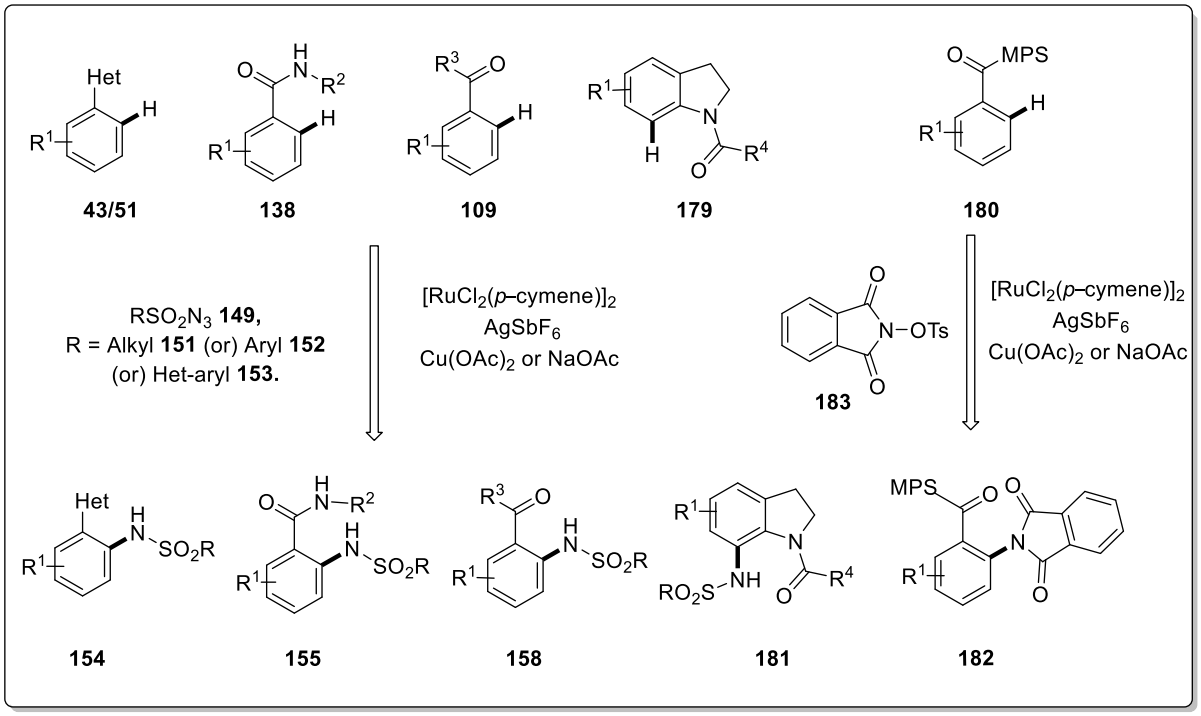
Scheme 1.36: Selected examples of Iridium(III)-catalyzed C–H bond amination.

Besides rhodium catalysis, it is reasonable to investigate the catalytic ability of iridium, which is in group 9 and just below rhodium in the periodic table.[131] Among others *Chang's* group continued to explore [Cp*Ir(III)]-catalyzed C–H aminations by using organoazides **165-167**.[132-141] Because the catalyst precursor, $[IrCp^*Cl_2]_2$ is structurally and electronically comparable the previously used $[RhCp^*Cl_2]_2$ (Scheme 1.35).[121-125] They succeeded in the iridium–catalyzed intermolecular C–H amidation of arene assisted by various conventional directing groups, including benzamide **138**, removable carbamate **163**, ketoxime **117**, pyridine **43**, pyrazole **51**, oxazoline **46**, benzoxazole **175**, isoquinoline **176**, and acyl anilide **113**. (Scheme 1.36)[132-141] *Bolm* and co-workers extended this methodology in mechanochemistry

under solvent-free conditions in a ball mill.[133] Furthermore, by adding an acid additive to accelerate the rate-determining, product-releasing step, they succeeded in a remote regioselective C–H amidation of quinoline *N*-oxides **164** at the 8-position under mild conditions.[134,135] In addition, by the combination of acetic acid and lithium carbonate as additives, iridium was able to catalyze the direct C–H amidation of weakly coordinating esters **107** and ketones **109** with various sulfonyl azides **149-153**. Moreover, carboxylic acid **101** could also be utilized as a traceless directing group in the Ir-catalyzed direct C–H amidation with sulfonyl azide **149**. (Scheme 1.36).[136,137] Subsequent protodecarboxylation of the *ortho*-amidated benzoic acid **174** product could be mediated by $Pd(OAc)_2$ under heating. The two tandem reactions were compatible to enable a convenient one-pot, two-step process for the preparation of meta-substituted (*N*-sulfonyl)aniline derivatives, which are not easily accessible by other ways. *Wu* and *Cui* showed that 1,2,3-triazole **177** and nitrone **178** could be efficient directing groups for the iridium-catalyzed amidation of azide **149**.[138,139] It was noteworthy that the regio-selectivity and reactivity could be greatly improved by installation of *N*-oxide motif on the triazole group. After the reaction, the *N*-oxide **164** could be readily reduced by PCl_3.[132,136] *Huestis* and *Chen* developed a benzylic primary amine directed orthosulfonamidation of aryl C–H bonds with sulfonyl azides **149** by using a commercially available iridium(III) complex as the catalyst.[141]

Later, they used phosphoryl azides **166** to synthesize phosphoramidates by Ir(III)-catalyzed intermolecular C–H amidation with the assistance of NaOAc as the additive.[142,143] Both benzamide **138** and ketone **109** proved to be suitable substrates for the transformation. In the meantime, *Zhu's* group independently applied phosphoryl azides **166** in the direct C–H phosphoramidation of 2-arylpyridines **43** and 1-arylpyazoles **51**.[144] In this transformation AgOAc was used as the additive to enhance the efficacy. Recently, *Lu* and co-workers disclosed an iridium-catalyzed C–H amination of benzamides **138** by using alkyl azides **151** as the primary alkylamine source **130**. A wide range of alkyl azides, including linear, branched, and cyclic alkyl azides were suitable coupling partners. Even biologically relevant molecules, such as amino acids, peptides, steroids, sugars, and thymidine derivatives could also be installed with high efficiency and complete chiral retention.[145] It was found that the CsOAc additive was vital for success and governed both the reactivity and the regioselectivity for this transformation. The group of *Chang* and *Li* group independently developed Ir(III)-catalyzed regioselective direct C7-amidation and amination of indolines **179** with various organoazides **149**, such as sulfonyl, acyl, aryl, and alkyl azides **149-153** (Scheme 1.37).[146,147] In *Chang's* work, easily removable *N*-protecting groups such as *N*-Boc or *N*-Cbz could readily be

employed as efficient directing groups. *Li* showed that the 7-aminoindoline product could be oxidized by MnO_2 to afford 7-aminoindole in situ in a one-pot operation.[147]



Scheme 1.37: Ruthenium(II)–catalyzed C–H bond amidation.

Compared with rhodium and iridium, ruthenium is significantly less expensive (rhodium 800 USD, iridium 700 USD, ruthenium 40 USD per troy oz) and it has been used more and more in transition-metal-catalyzed direct C–H functionalizations.[7,15,30,32,45] The groups of *Sahoo*[150] and *Jiao*[151] reported the ruthenium-catalyzed intermolecular *ortho* C–H amidation of weakly co-ordinating acyclic aromatic ketones with sulfonyl azides **149** (Scheme 1.37). At the same time, *Chang's* group[152] also described the ruthenium-catalyzed intermolecular C–H amidation by using sulfonyl azides **150** as the amino source. In *Chang's* work, not only weakly coordinating ketones **109**, but also benzamide **138** and various heterocycles could act as efficient directing groups to promote the transformation. *Kim* and co-workers successfully extended the substrate scope to cyclic ketones **109** including xanthones and chromones.[153] A wide range of sulfonyl azides **151** were suitable for the amidation. However, benzoyl azide and phenyl azide **152** show no reactivity under the standard reaction conditions.

Ackermann et al.[154] reported a ruthenium(II)-catalyzed direct amidation of arenes displaying heteroaromatic groups with a broad range of alkyl and aryl sulfonyl azides **149**. Pyrazole **51**, pyrimidine **137**, and pyridine **43** proved to be efficient DGs to provide satisfying yields. Later, *Ding*, *Luo* and co-workers[155] demonstrated that benzothiazole **175** also could facilitate the

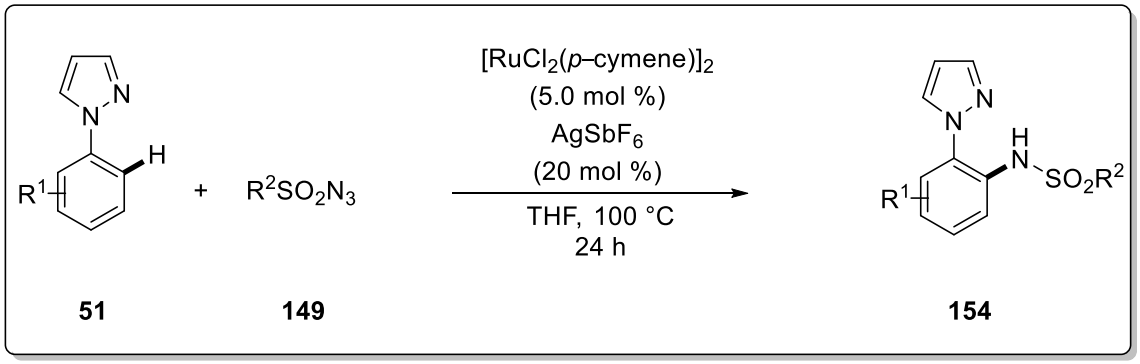
ruthenium(II)-catalyzed direct amidation of sulfonyl azides **149**. Furthermore, *Liang's* group[156] studied the mechanism by employing ruthenium-catalyzed amidation of 2-phenylpyridine (**43**) with 4-methylbenzenesulfonyl azide as a model reaction. Two ruthenium intermediates were isolated and fully characterized by X–ray crystallography. A ruthenium–imido species was proposed to explain the formation of the azacyclopropane analog. The *Zhu's* group[157] developed a ruthenium-catalyzed regioselective direct C7-amidation of indoline **179** with sulfonyl azides **149**. The *N*-acyl group was employed to accomplish the C–H amidation process. *Sahoo* demonstrated ruthenium-catalyzed sulfoximine **180** directed intermolecular C–H amidation of methyl-phenyl sulfoximine (MPS) **180** with sulfonyl azides **152** or *N*–OTs phthalimide **183**. Stoichiometric KOAc or Ag_2O as base additives were required to enhance to the efficiency (Scheme 1.37)[158,159]

2 Objectives

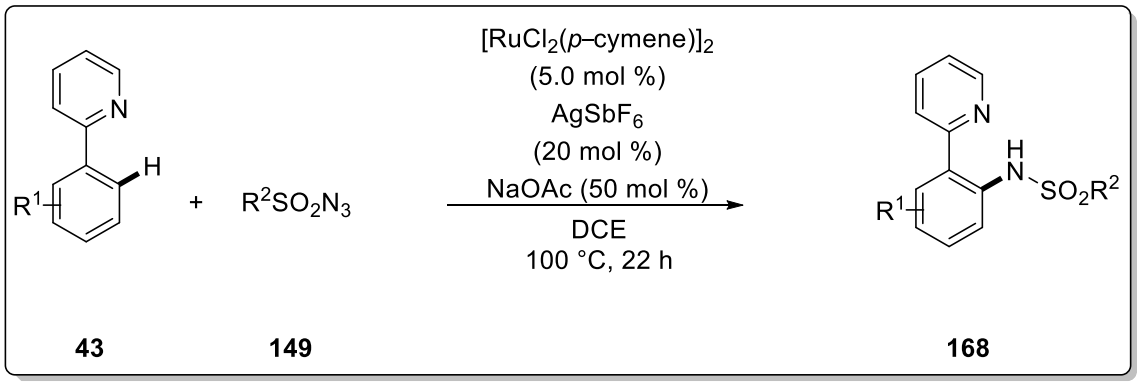
Transition-metal-catalyzed C–H bond functionalizations are attractive tools for improving the atom- and step-economy of organic synthesis.[7,19,30,32,41] In recent years, ruthenium(II)-complexes have been identified as powerful catalysts for the direct transformation of otherwise unreactive C–H bonds into C–C bonds.[41] On the contrary, ruthenium(II)–catalyzed C(sp^2)–heteroatom bond forming processes continue to be scarce.[154]

The mono-selective C–H amination of arenes received considerable attention, as a key structural frameworks in drug discovery.[165,166] In this context, it should take advantage of the less expensive ruthenium for the demanding direct amination of heteroarenes (**43** and **51**) in a broadly applicable and highly selective fashion (Scheme 1.38).

Herein, we disclose the heteroatom-assistance in directed C–H bond amidations, in which the versatile ruthenium(II)-catalysts overrode the inherent substrate-controlled heteroatom oxidation by chelation-controlled aromatic C–H activation.[113] It is noteworthy that the acetate-assistance leading to pyridine-amidated products can be easily converted to other useful building blocks in organic synthesis.[160-162]



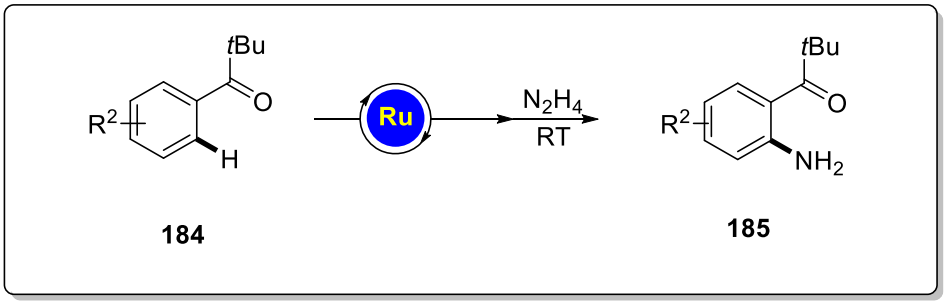
Scheme 1.38: Ruthenium-catalyzed C–H amidation with pyrazoles **51**.



Scheme 1.39: Ruthenium(II)-catalyzed C–H amidation with pyridine **43**.

It is a challenging project for C–H nitrogenations with weakly co-ordinating directing groups[7,39,163,164] Amines are readily available ready to be transformed into valuable heterocycles like indoles, quinolines and quinoxalines, which are very useful synthons for industries.

Aminophenones **185** are key motifs in natural product synthesis,[165,166] medicinal chemistry, crop protection, or material sciences, and they represent versatile intermediates in organic synthesis.[167] As a consequence, methods that allow for the efficient prepration for well-decorated aminophenones continue to be in high demand in organic chemistry.[168] It should take advantage of the less expensive ruthenium for the demanding direct amination of ketones **184**.The transformative nature of our C–H activation platform provides a step-economical access to decorated primary aminophenones as a key intermediate in the synthesis of various bioactive heterocycles.



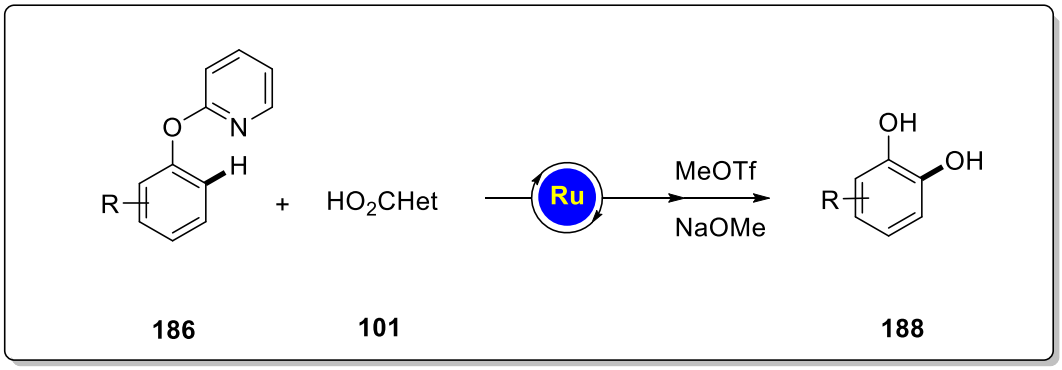
Scheme 1.40: Envisioned facile access to primary aminophenones **185**.

Although the *Ackermann* group has developed weakly coordinated ketones for site-selective C–H oxygenations, heteroarenes are doubtless much more challenging as a substrate in C–H oxygenations.[79-82] Ruthenium(II)-catalyzed C–H oxygenations by 2-pyridyloxyarene and sulfoximine benzamides assistance has proven thus far elusive. Taking advantage of the unique characteristics of ruthenium catalysis, the formyl group could possibly serve as a directing group rather than a substrate in the ruthenium-catalyzed C–H oxygenations.

Whilst previous studies of ruthenium(II)-catalyzed C(sp^2)–H bond oxygenation of arenes bearing electron-withdrawing or electron-donating directing groups are limited to acetoxylation and hydroxylations of aromatics.[78-81]

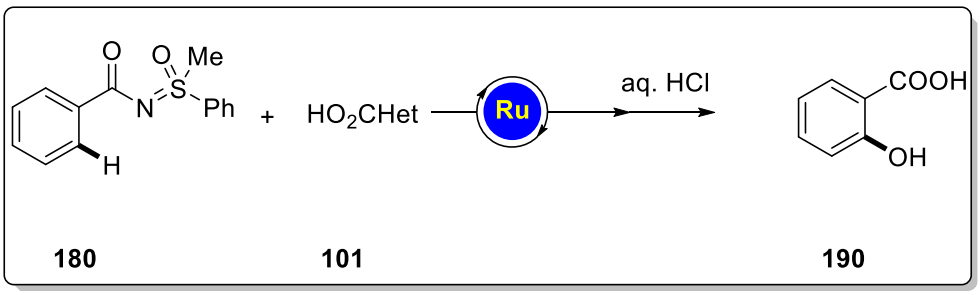
The catalytic direct oxygenation of otherwise unreactive C(sp^2)–H bonds was shown to be the most step-economical approach to substituted phenols.[169] Although ruthenium-catalyzed direct C(sp^2)–H bonds direct oxygenation of arenes were reported, these notable progresses were mainly focused on oxygenation of electron-deficient substrates bearing electron-

withdrawing directing groups.[170-172] Therefore, a ruthenium-catalyzed C(sp^2)–H bond oxygenation of phenol derivatives envisioned (Scheme 1.41). The major limitation in the synthesis of heteroarene-containing products is largely due to the facile *N*-oxidation of these heterocycles by hyper-valent iodine(III) reagents in ruthenium(II) catalyzed oxygenation reactions. In addition, despite their significant practical importance, reports of ruthenium-catalyzed C–H oxygenations of substrates displaying removable directing groups for C–C bond formation is well established.[173-174]



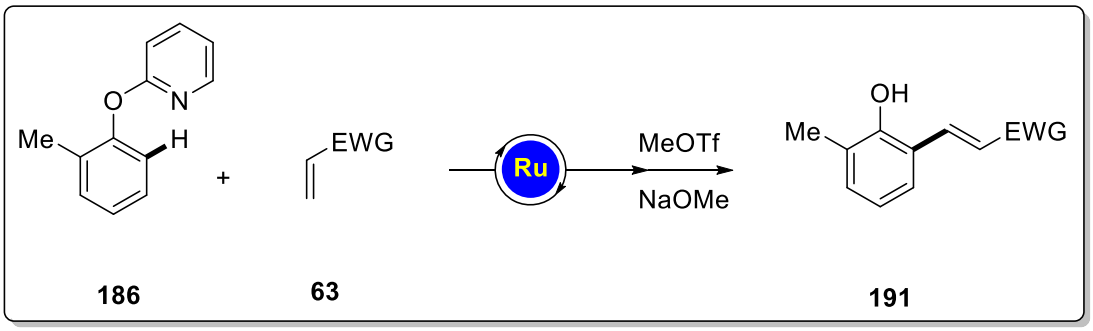
Scheme 1.41: Removable auxiliary assistance for ruthenium(II) catalyzed oxygenations.

In spite of these significant advances, the use of non–removable and non–modifiable DGs and the lack of generality limit the broad synthetic application of this transformation and unfortunately continue to be scarce. In addition, highly chemoselective functionalization in the presence of a variety of C–H bonds remains elusive. The incorporation of easily removable and robust DGs can overcome some of these limitations.[176-178] For instance, we have devised reaction conditions for step-economical direct oxygenation via use of phenyl-methyl-sulfoximine as reusable auxiliary.[180-185]



Scheme 1.42: Reusable auxiliary assistance for ruthenium(II) catalyzed oxygenations **180**.

In the transition metal-catalyzed alkenylations, directing groups were usually introduced to achieve site-selective C–H functionalization.[38-43] Recently, major progress in the development of ruthenium-catalyzed oxidative C–H alkenylation reactions has been done by the *Ackermann* research group and others.[88,186-189] The previously described alkenylations with oximes and *N*-methoxybenzamides require external oxidant. To perform the reaction at a reduced temperature and to avoid a second transition metal, it was decided to use a dioxygen as a trigger and air or molecular oxygen as the terminal oxidant.[190] Herein, the well-studied reaction between arenes and activated alkenes should serve as a modelsystem.[191-195] However, the commonly applied DGs are usually difficult to remove or modify under mild conditions. Herein, we devise ruthenium(II)-catalyzed oxidative alkenylations with 2-aryloxypyridines **186** as a preparative approach to the synthetically valuable alkenylated phenols **94**.[196-199]



Scheme 1.43: Ruthenium(II)-catalyzed oxidative alkenylation with O_2 as oxidant.

3 Results and Discussions

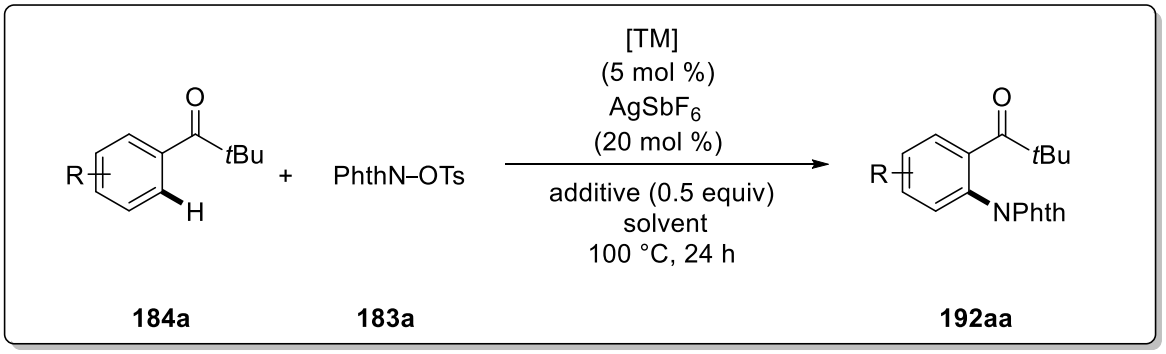
3.1 Ketone-assisted ruthenium(II)-catalyzed C–H imidation: access to primary aminoketones by weak coordination

It is a challenging project to perform C–H amination with weakly coordinating directing groups.[160-164] The *Ackermann* group has made great achievements by utilizing ketones for site-selective ruthenium(II)-catalyzed C–H oxygenations, as well as the formyl group assisted C–H oxygenations.[210] But the direct access to aminophenones has unfortunately proven elusive thus far. Aminophenones **185** are key structural motifs in natural product syntheses, medicinal chemistry, crop protection, or material sciences,[165] and they represent versatile intermediates in organic synthesis.[167] As a consequence, methods that allow for the efficient preparation of decorated aminophenones **185** continue to be in high demand.[92,168] The development of new chemical transformations based on the catalytic functionalization of otherwise inert C–H bonds has the potential to dramatically simplify the synthesis of complex molecules.[14,15] For instance, transition metal-catalyzed C–H amidations have emerged as an increasingly viable alternative to the palladium-catalyzed aminations of aryl halides. Particularly, ruthenium(II)-complexes have in recent years been identified as powerful tools for C–H nitrogenations, largely exploiting strongly coordinating directing groups that are difficult to remove or modify.[179-181] Herein we disclose the first direct access to aminophenones via versatile ruthenium(II)-catalyzed C–H activation.

3.1.1 Optimization of ruthenium(II)–catalyzed imidation of ketones

It is known that acetophenone is very prone to α–oxidation, thus substrate **184a** was the best substrate for the optimization. The previously used organic azides **149** were declined as the nitrogen source. The results summarized in entries 1-10 (Table 1) showed that the 1,4-dioxane was the best reaction medium and $AgSbF_6$ was found to be most suitable for this transformation, giving the desired product **192** in 34% yield. The dimeric complex $[RuCl_2(p\text{-cymene})]_2$ outperformed $[Ru(O_2CMes)_2(p\text{-cymene})]$, $[Ru_2(hp)_4Cl]$ and $[Ru_2(OAc)_4Cl]$ (entries 8–12, Table 1). Typical $[Cp^*CoI_2(CO)]$, $[Cp^*Rh(Cl)_2]_2$ and $Pd(OAc)_2$ catalysts failed in delivering the desired product **192** (entries 13–15, Table 1), highlighting the challenging nature of the ketone-assisted C–H nitrogenation.

Table 1: Screening of catalysts and solvents.

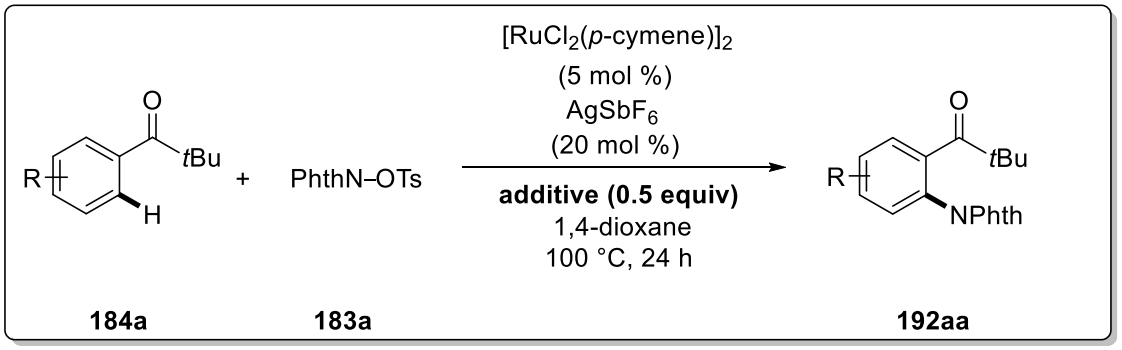


Entry	Catalyst	Additive	Solvent	Time (h)	Yield (%)[a]
1	$[RuCl_2(p\text{-cymene})]_2$	---	toluene	22	8
2	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	*t*-AmOH	22	NR
3	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DME	22	NR
4	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	*t*-AmOH	22	NR
5	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	H_2O	22	8
6	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	22	23
7	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	1,4-dioxane	22	34
8	$RuCl_3\cdot(H_2O)_n$	$AgSbF_6$	1,4-dioxane	22	16
9	$[RuBr_2(p\text{-cymene})]_2$	$AgSbF_6$	1,4-dioxane	22	64[b]
10	$[Ru(O_2CMes)_2(p\text{-cymene})]$	$AgSbF_6$	1,4-dioxane	22	34
11	$[Ru_2(hp)_4Cl]$	$AgSbF_6$	1,4-dioxane	24	9[b]
12	$[Ru_2(OAc)_4Cl]$	$AgSbF_6$	1,4-dioxane	22	37[b]
13	$[Cp^*CoI_2(CO)]$	$AgSbF_6$	1,4-dioxane	24	16[b]
14	$[Cp^*Rh(Cl)_2]_2$	$AgSbF_6$	1,4-dioxane	22	42[b]
15	$Pd(OAc)_2$	$AgSbF_6$	1,4-dioxane	24	NR[b]
16	**$[RuCl_2(p\text{-cymene})]_2$**	**$AgSbF_6$**	**1,4-dioxane**	**24**	**78[b]**
17	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	1,4-dioxane	22	63

[a] Reaction conditions: **184a** (0.5 mmol), **183a** (1.2 mmol), catalyst (5.0 mol %), solvent (2.0 mL), under N_2, 100 °C, 24 h, isolated yield, [b] $Cu(OAc)_2\cdot H_2O$ (0.5 equiv).

As the next step, optimization studies to identify the optimal additive and ratio of reagents for the efficient direct amidation of arene **184** with pthalimide **183** were performed. The results are summarized in Table 2.

Table 2: Effect of acetates on C–H imidation



Entry	Additive (0.5 equiv)	Solvent	Yield [a]
1	$Cu(OAc)_2 \cdot H_2O$	1,4-dioxane	54
2	**$Cu(OAc)_2 \cdot H_2O$**	1,4-dioxane	**78**
3	LiOAc	1,4-dioxane	25
4	CsOAc	1,4-dioxane	34
5	NaOAc	1,4-dioxane	23
6	NaOAc	1,4-dioxane	14
7	NH_4OAc	1,4-dioxane	16
8	KOAc	1,4-dioxane	18

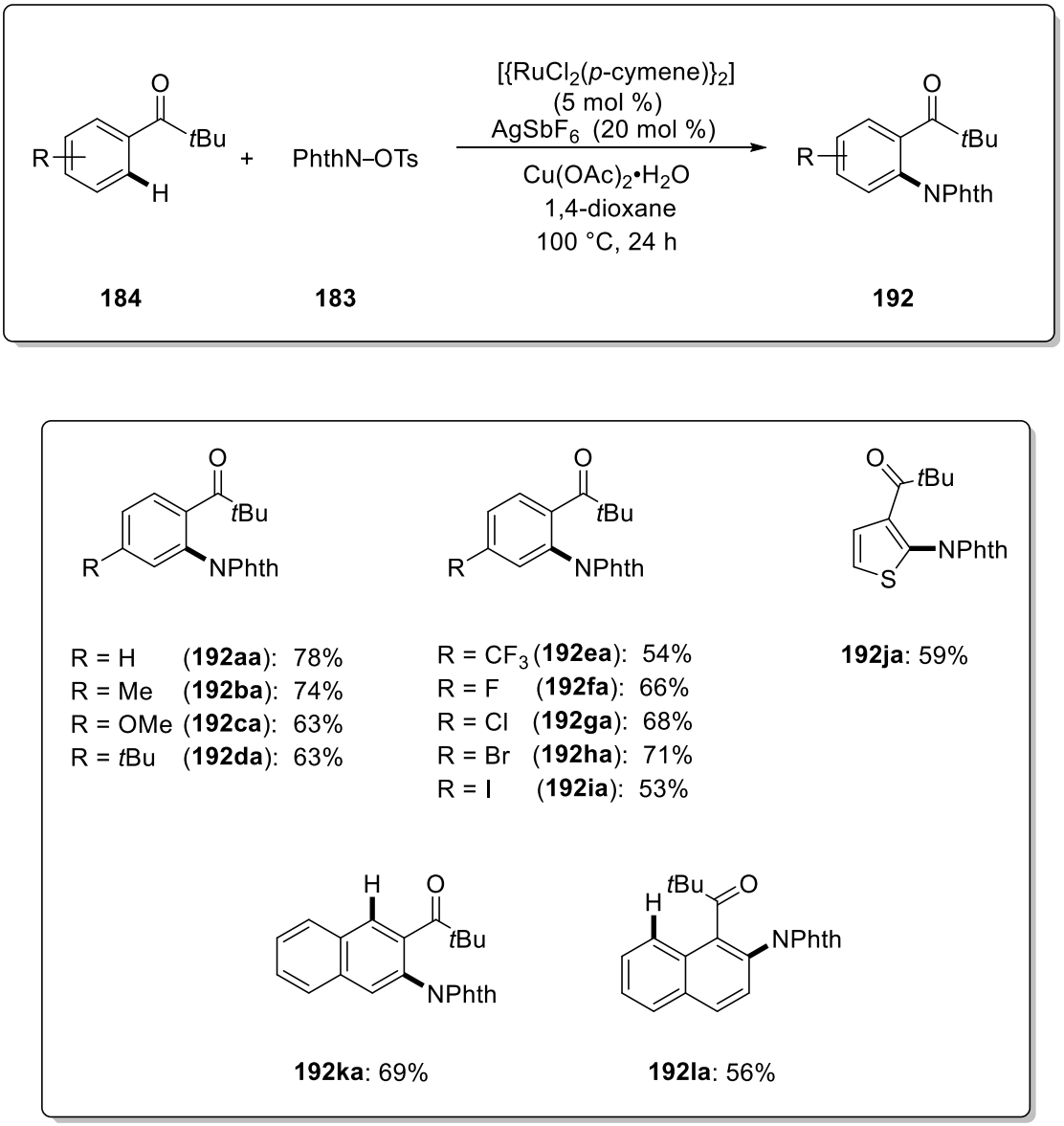
[a] Reaction conditions: **184a** (0.5 mmol), **183a** (0.6 mmol), catalyst (5.0 mol %), solvent (2.0 mL), under N_2, 100 °C, 22 h, isolated yield, isolated yield; $Cu(OAc)_2 \cdot H_2O$ (0.5 equiv).

With the dimeric complex $[RuCl_2(p\text{-cymene})]_2$ as the catalyst, stoichiometric amount of $Cu(OAc)_2 \cdot H_2O$ as additive and 1,4-dioxane as solvent, the desired product **192** was formed in 54% yield entry **1** (Table 2). Different additives were tested (Table 2, entries 3–8) and notably, the lower loading of $Cu(OAc)_2 \cdot H_2O$ (entry 2) was found to be the optimal condition for the ruthenium(II)-catalyzed C–H bond imidation reaction.

3.1.2 Scope of ruthenium(II)-catalyzed imidation of ketones 184

With the optimized catalytic conditions in hand (Table 2, entry 2), the C–H imidation scope with well decorated ketones **184** and pthalimide **183** was investigated (Scheme. 1.44). The ruthenium(II)-catalyzed C–H bond imidation reaction gave the best results when the *para*-substituted arylketone **184** was bearing both an electron-withdrawing groups, such as trifluoromethyl, fluoro, chloro and bromo substituents (Scheme 1.44) as well as electron-donating groups, such as methoxy and *tert*-butyl groups **184** (Scheme 1.44), thus

showing robustness of the versatile synthetic methodology which should prove instrumental for postsynthetic diversifications of thus obtained imidophenones **192**

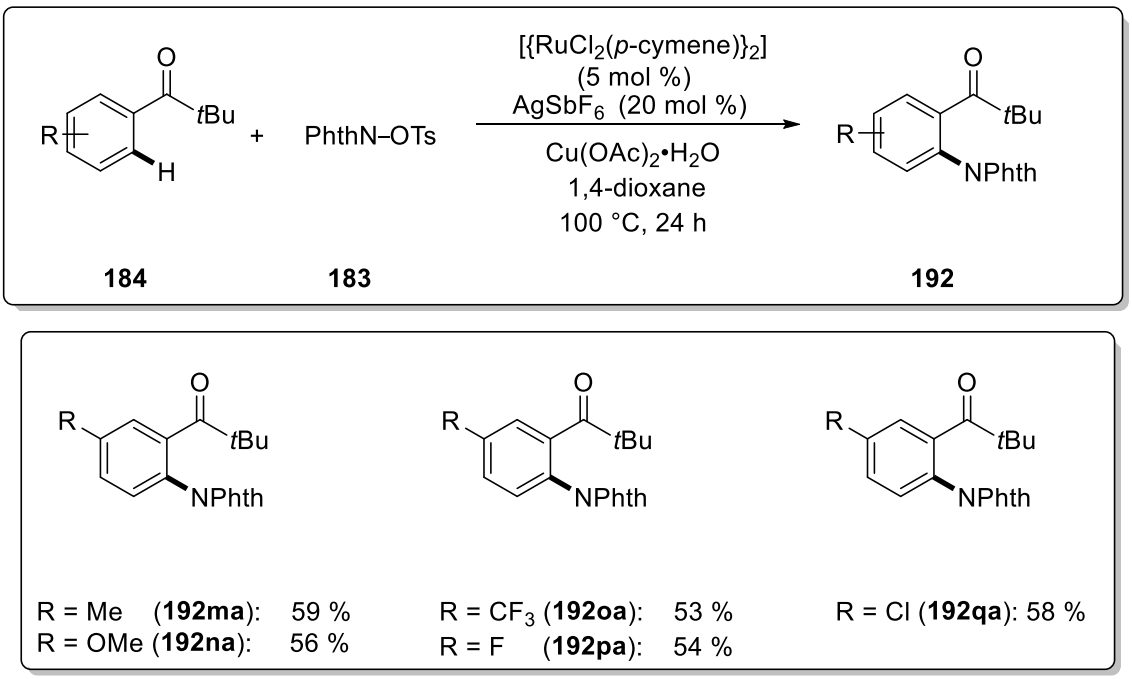


Scheme 1.44: Scope of ruthenium(II)-catalyzed imidation of ketones **184**.

The naphthalene substituted aryl-ketones **184k** and **184l** were employed in the ruthenium(II)-catalyzed C–H bond imidation reactions with excellent positional selectivity of C–H bond functionalization protocol in these products **192ka** and **192la**. Yet, the robust ruthenium(II) catalyst was not limited to carbocyclic aromatic compounds. Indeed, the C–H imidation of thiophene **192ja** proved viable as well, occurring with good site-selectivity (Scheme 1.44).

3.1.2 Scope of ruthenium(II)-catalyzed imidation of *meta*-substituted ketones 184

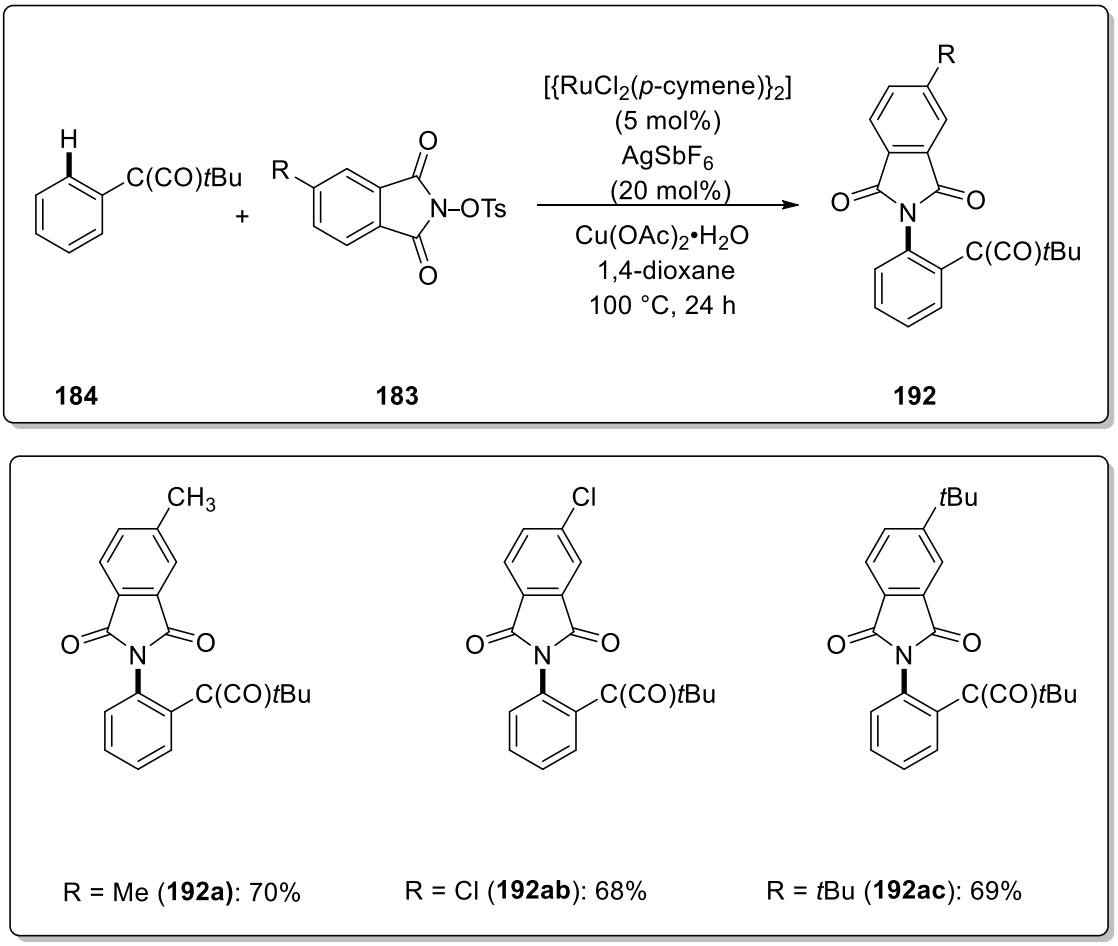
Afterwards we investigated the site-selectivity of the ruthenium(II)-catalyzed C–H bond imidation reactions using *meta*-substituted arylketones **192m** (Scheme 1.45). The steric factor was found important for controlling the *site*-selectivities. High levels of site-selectivity were observed within the reaction and functional groups like methoxy and trifluoromethyl substituents were well imidated to deliver products **192** (Scheme 1.45). It is noteworthy that the synthetically useful 3-chloro and 3-fluoro substituted ketones **192pa** and **192qa** delivered comparable yields.



Scheme 1.45: Scope of ruthenium(II)-catalyzed imidation of *meta*-substituted ketones **184**.

3.1.2 Scope of ruthenium(II)-catalyzed C–H imidation with phthalimides

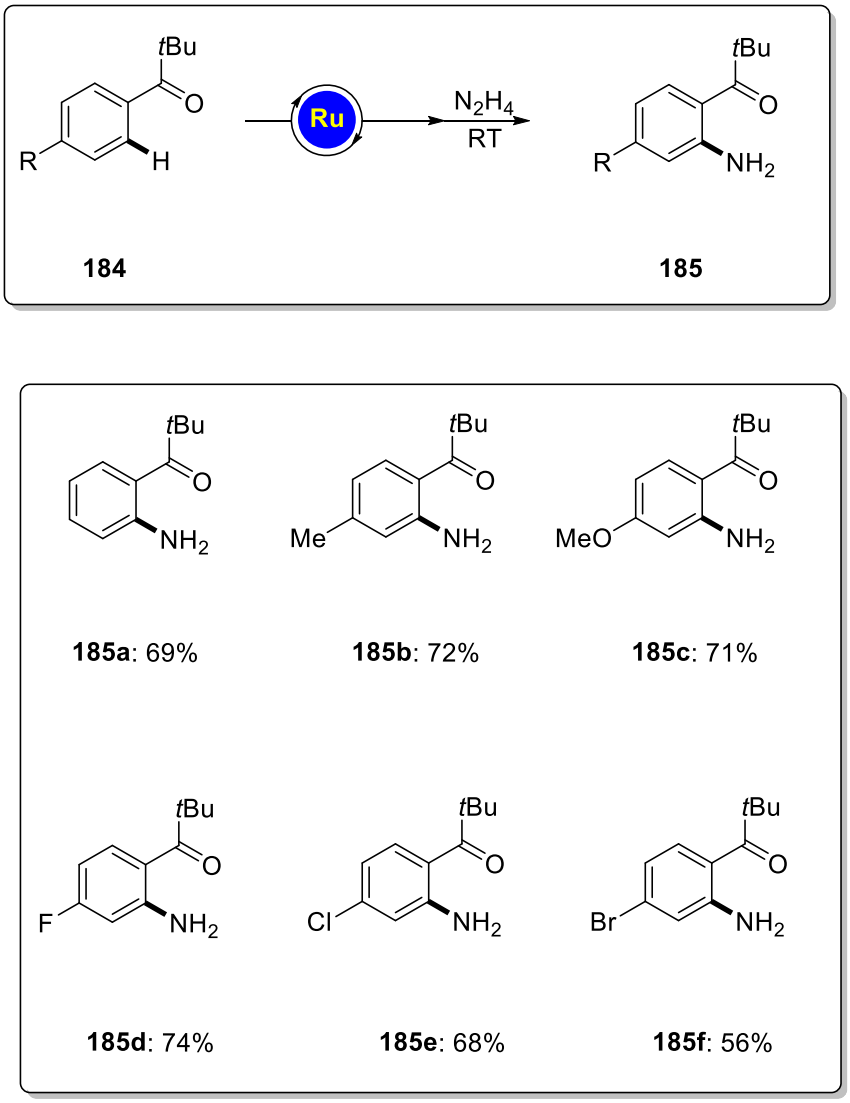
Moreover, this catalytic system could be applied to differently substituted phthalimides **183**. Chloro, methyl and electron rich *tert*-butyl groups were well tolerated to give imidated products in acceptable yields **192aa-192ac (**Scheme 1.46).



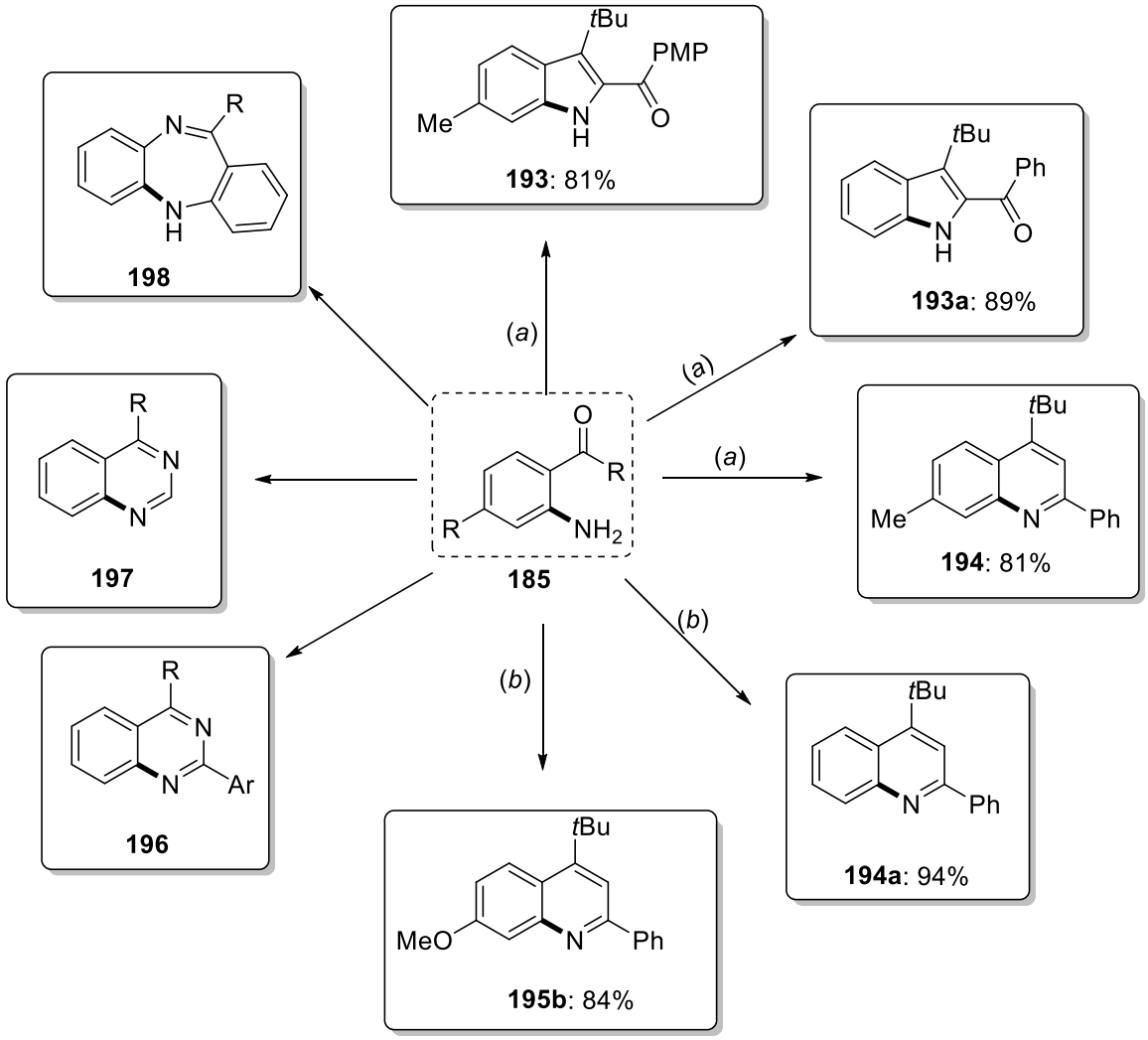
Scheme 1.46: Scope of ruthenium(II)-catalyzed C–H imidation with phthalimides **183**.

3.1.3 Facile acess to primary aminopheneones 185

The synthetic utility of the ruthenium(II)-catalyzed amidation protocol was reflected by providing efficient access to the synthetically useful primary aminophenones. Furthermore, we were delighted to find that the versatile imidated products could be very easily transformed to free anilines by deprotedtion of pthalimido group thereby, yielding the desired *ortho*-aminophenones **185**. Useful functional groups, such as, fluoro, chloro, or bromo groups, were well tolerated by ruthenium catalyst (Scheme 1.47).



Scheme 1.47: Facile access to primary aminopheneones **185.**



Scheme 1.48: Diversification of products **193-198**. (*a*) 4, $ArCOCH_2Br$, DMF, 100 °C, 16 h. (*b*) 4, ArC≡CH, $InCl_3$ (20 mol %), CH_3CN, 90 °C, 24 h.

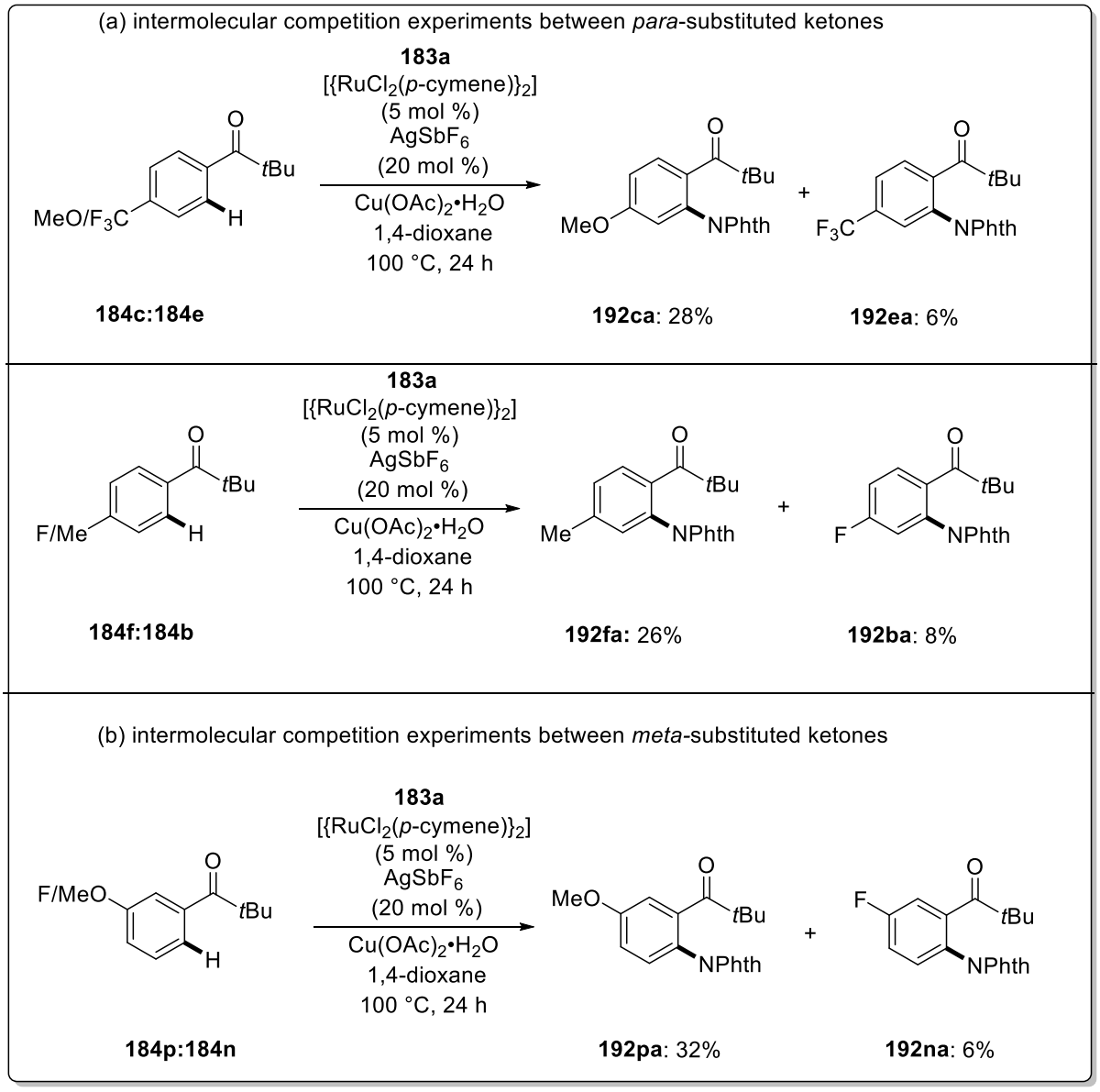
3.1.4 Mechanistic Studies

To shed light on the course of this new ruthenium(II)-catalyzed amidation protocol, a set of experiments were performed.

3.1.4.1 Competition experiments

First, the intermolecular competition experiment between *para*-substituted ketones **184c**/**184e** highlighted electronic effects, while *meta*-substituted ketones **184p**/**184m** showed primarily the influence on *site*-selectivity of the C–H bond functionalization. The results of the electron-

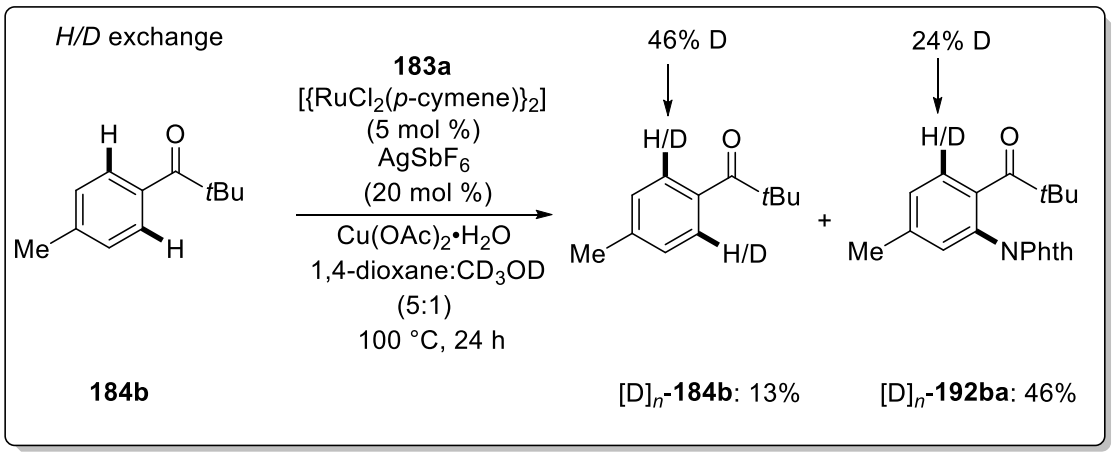
rich and electron-deficient arenes are presented herein. The competition between *para*-(trifluoromethyl)-substituted arene **184e** and *para*-methoxy-substituted arene **184c** indicated that the electron-rich arene reacted faster, (Scheme 1.49a). Also in the second reaction between *para*-methyl-substituted arene **184b** and *para*-fluoro-substituted arene **184f**, a significant larger amount of the electron-rich amidated product was observed (Scheme 1.49b). Finally, the third experiment to reveal the high level of positional-selectivity between *meta*-fluoro-substituted arene **184p** and *meta*-methoxy-substituted arene **184n** was conducted and revealed the similar reactivity profile (Scheme 1.49c). These experiments clearly showed that electron-rich ketones reacted faster than electron-deficient ones.



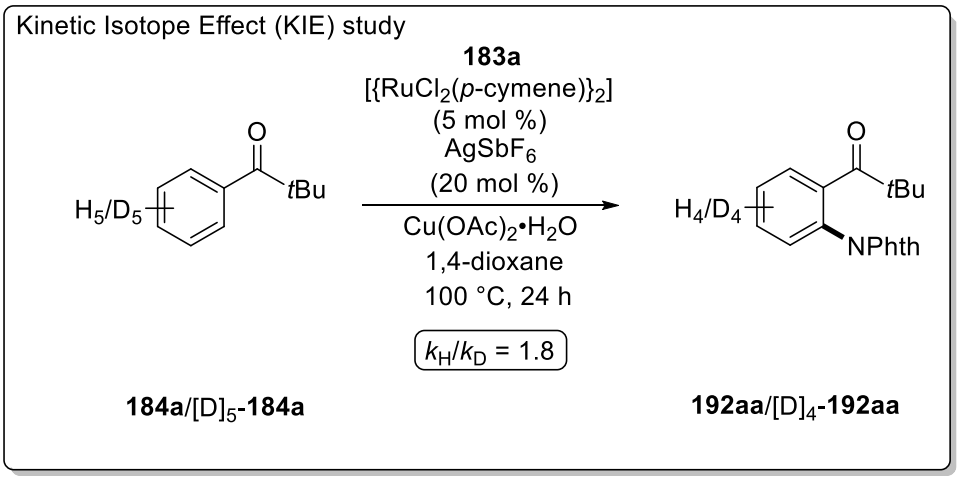
Scheme 1.49: Competition experiments between ketones **184**.

3.1.4.1 Studies with isotopically labelled compounds

In consideration of the unique selectivity features displayed by competition experiments by the ketone-assisted ruthenium(II)-catalyzed C–H amidation, we performed experiments with isotopically labelled substrates **184b** (Scheme 1.50). As C–H and C–D bonds differ in their bond strength and energy, this approach is of great importance for determining the kinetics of reactions involving C–H bond cleavages.[212] In presence of pthalimide **183a**, 54% hydrogen of ketone **184b** was replaced by deuterium and 76% of hydrogen on the amidated product **184ba** was replaced by deuterium, using CD_3OD as the co-solvent. Thus the C–H bond cleavage is most likely reversible and thus not the turnover determining step of the catalytic cycle. Finally, a competition experiment between **184a** and **[D]$_n$-184a** revealed a low kinetic isotope effect (KIE) of 1.8 (Scheme 1.51).



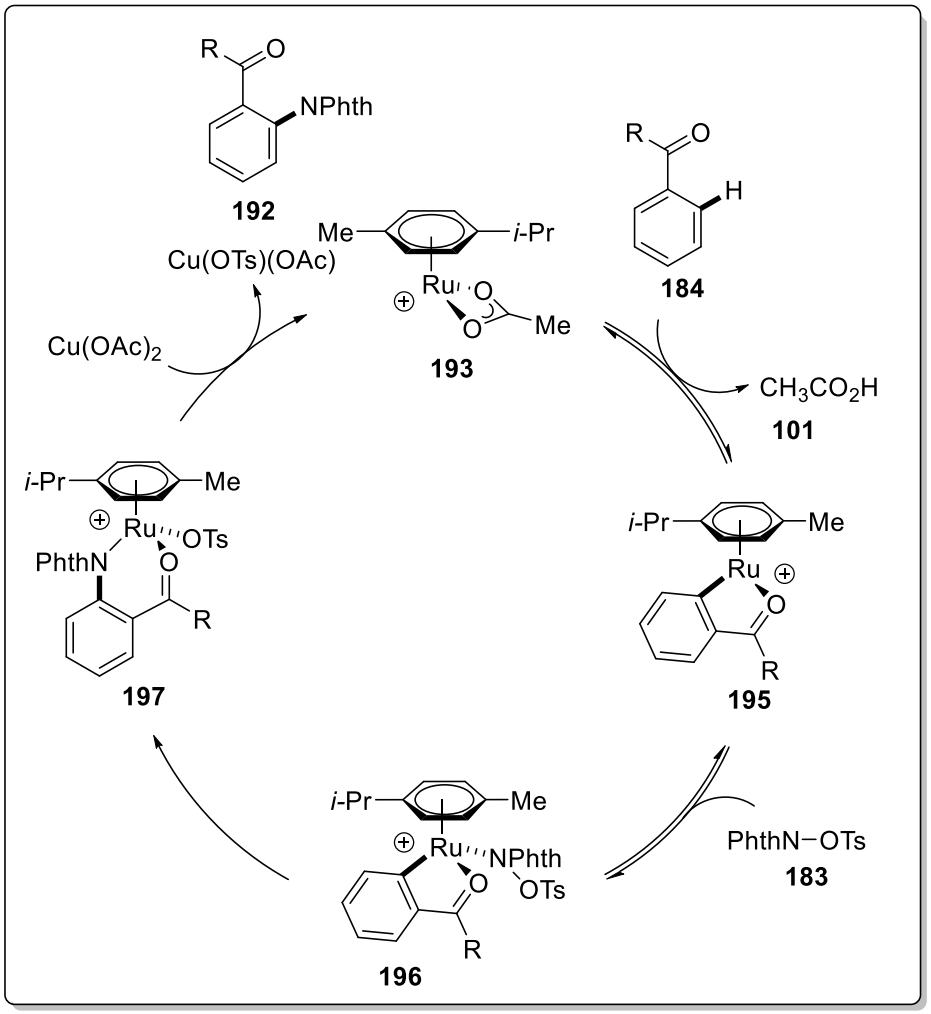
Scheme 1.50: Studies with isotopically labeled co-solvent **184a**.



Scheme 1.51: Independent KIE experiment.

3.1.4.3 Plausible catalytic cycle

Summarizing the information, a reaction mechanism can be plausibly proposed for the ruthenium(II)-catalyzed C–H amidation (Scheme 1.52). First, the catalytically active cationic ruthenium species **193** is formed by abstraction of one chloride-ligand assisted by $AgSbF_6$. Then the coordination of in-situ generated ruthenium(II)-carboxylate complex **193** by ketone **184** to generate complex **195** and carboxylic acid. Second, the cyclometalated intermediate **195** is subsequently coordinated by amidating reagent **183**. Thereafter, N–O bond cleavage delivers the cationic complex **197**, which finally regenerates the catalytically active species **193**, thereby liberating the desired amidated product **192** (Scheme 1.52). Here, it is proposed that the acetate facilitates the C–H bond cleavage, which serves as a catalytic proton shuttle from the transition state of the BIES process to the insoluble base.[51b,55]



Scheme 1.52: Plausible mechanism of ruthenium(II)-catalyzed C–H amidation.

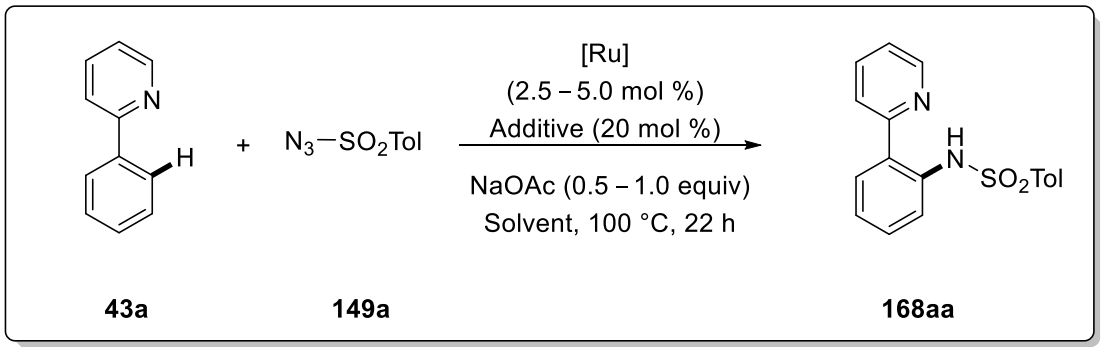
3.2 Ruthenium(II)-Catalyzed C–H Amidation of Heteroarenes

Aromatic amines are widely found in pharmaceuticals, agrochemicals and natural products,[92] and amino groups can be readily transformed into many valuable functional groups, such as amides, acids, nitriles, or azides among others.[209] Hence, it is important to develop new methods to introduce the group onto an aromatic ring.

3.2.1 Optimization of ruthenium(II)-catalyzed C–H nitrogenation of heteroarenes

At the outset of the studies, a variety of reaction conditions were screened for the envisioned ruthenium(II)-catalyzed C–H nitrogenation of arenes **43** with organic azide **149** as a suitable nitrogen source. The optimal reaction conditions for this direct amidation in the most efficient and selective way was established. Attempted reactions in THF, *t*-AmOH, DME, toluene, DMF, NMP or water, gave only traces of the amidated product **168aa** (Table 3, entries 3-7). Yet, switching the solvent to DCE dramatically increased the yield (entriy 9). Even the carboxylate assistance did not change the efficacy (entry 12). Among a set of representative ruthenium complexes, the dimeric ruthenium(II)-complex $[RuCl_2(p\text{-cymene})]_2$ was then shown to be the best ruthenium source in combination with $AgSbF_6$ (entry 9). The best conditions were found to be in presence of NaOAc (50 mol %), with DCE at 100 °C for 22 hours (entry 15).

Table 3: Optimization of ruthenium(II)-catalyzed C–H nitrogenation of pyridine **43a**

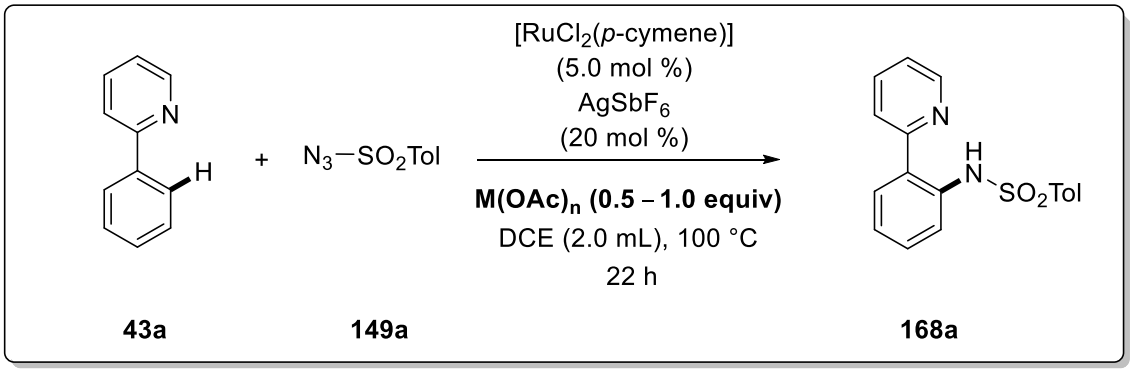


Entry	[Ru]	Additive	Solvent	Time (h)	Yield (%)[a]
1	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	THF	22	41
2	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	*t*-AmOH	22	31
3	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DME	22	22
4	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	toluene	22	38
5	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DMF	22	NR
6	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	NMP	22	NR
7	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	NMP·H_2O	22	26
8	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	H_2O	22	23
9	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	22	54
10	$RuCl_3\cdot(H_2O)_n$	$AgSbF_6$	DCE	22	16
11	$[RuBr_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	22	64
12	$[Ru(O_2CMes)_2(p\text{-cymene})]$	KO_2CMes	DCE	22	34
13	$[RuCl_2(p\text{-cymene})]_2$	$AgBF_4$	DCE	22	37
14	$[RuCl_2(p\text{-cymene})]_2$ (2.5) mol %	$AgSbF_6$	DCE	22	42
15	**$[RuCl_2(p\text{-cymene})]_2$**	**$AgSbF_6$**	**DCE**	22	**84**[b]
16	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	22	63[c]
17	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	22	54[d]

[a] Reaction conditions: **43a** (0.5 mmol), **149a** (0.75 mmol), catalyst (5.0 mol %), DCE (2.0 mL), under N_2, 100 °C, 22 h, isolated yield, [b] NaOAc (0.5 equiv); [c] NaOAc (1.0 equiv) [d] NaOAc (0.3 equiv).

Next, optimization studies to identify the optimal acetate source and ratio of reagent for the efficient direct amidation of arene **43** with organic azide **149** were performed (Table 4).

Table 4: Effect of acetates on C–H amidation.



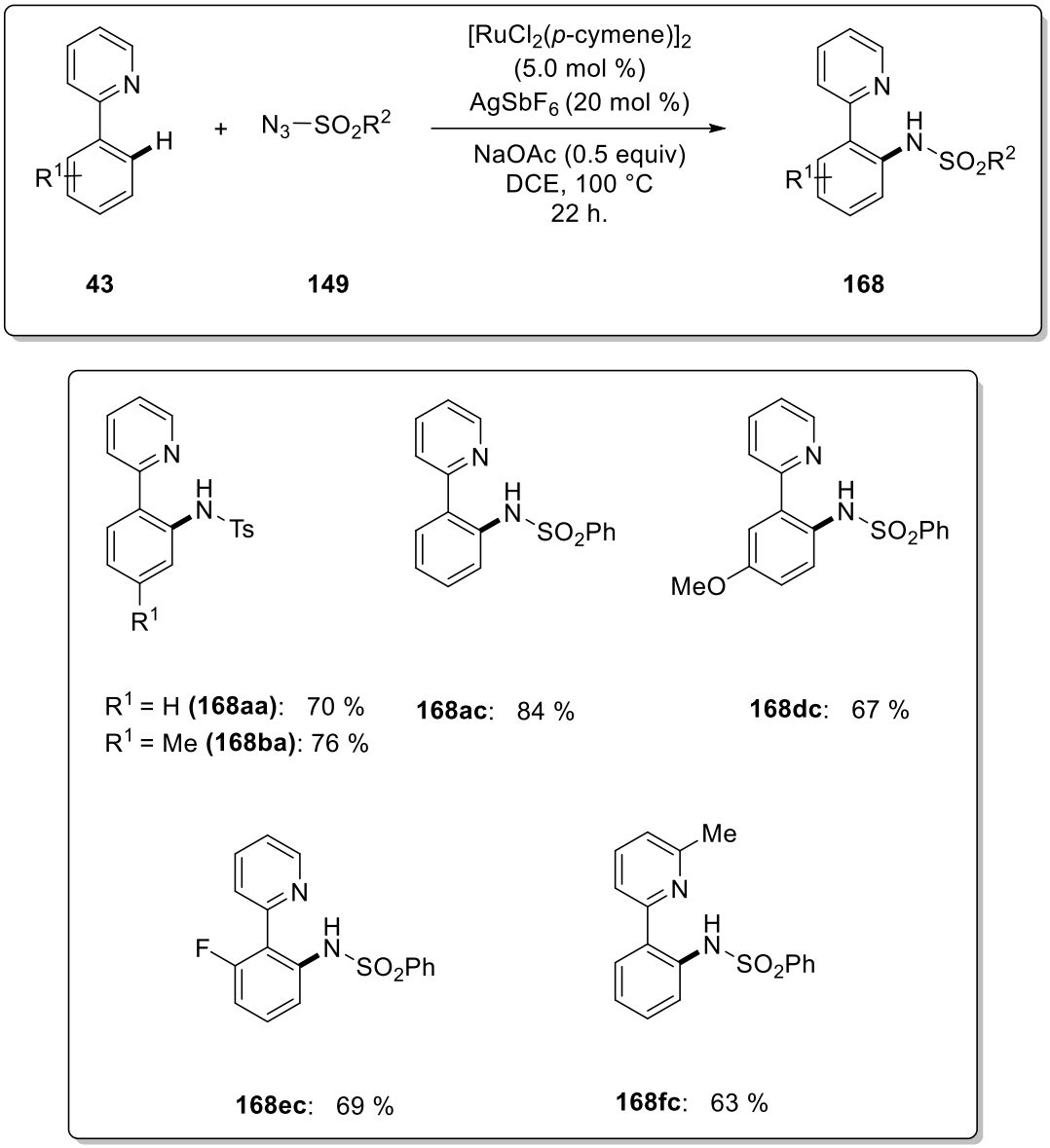
Entry	Acetate (0.5 equiv)	Solvent	Yield (%)[a]
1	$Cu(OAc)_2 \cdot H_2O$	DCE	52[b]
2	$Cu(OAc)_2 \cdot H_2O$	DCE	63
3	LiOAc	DCE	45
4	CsOAc	DCE	54
5	NaOAc	DCE	63
6	**NaOAc**	**DCE**	**84**
7	NH_4OAc	DCE	46
8	KOAc	DCE	58

[a] Reaction conditions: **43a** (0.5 mmol), **149a** (0.75 mmol), catalyst (5.0 mol %), solvent (2.0 mL), under N_2, 100 C, 22 h, isolated yield, isolated yield; [b] $Cu(OAc)_2 \cdot H_2O$ (1.0 equiv).

With the dimeric complex $[RuCl_2(p\text{-cymene})]_2$ as the catalyst stoichiometric amounts of $Cu(OAc)_2 \cdot H_2O$ as additive and 1,4-dioxane as solvent, the desired product **168a** was formed in 52% yield (Table 4, entry 1). Different additives were tested (entries 2-5) and notably NaOAc (entry 6) was found to be the best.

3.2.2 Scope of Ruthenium(II)-catalyzed amidation of pyridines 43.

Under the optimized conditions the direct amidation of various substitutes hetero-arenes **43** was explored (Scheme 1.53). Notably, a variety of functional groups on the arenes **43** were well tolerated by the effective catalytic system to furnish the corresponding amidated products **168**, even bearing sterically hindered substituent (Scheme 1.53).



Scheme 1.53: Scope of ruthenium(II)-catalyzed amidation of pyridines **43**.

Then, we evaluated the versatility of the C–H amidation with *para*-methyl-substituted heteroarenes and 76% yield of the amidated product were isolated. Generally, the catalytic system showed high chemoselectivity, exclusively yielding the mono-amidated products **168a-168f** (Scheme 1.53).

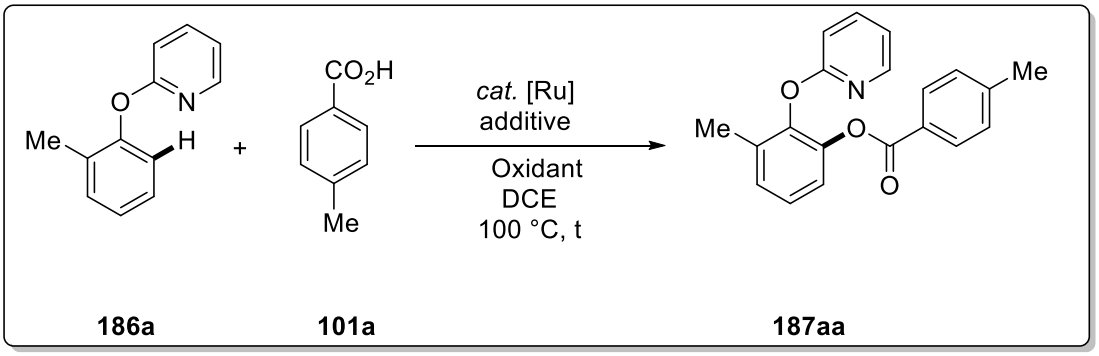
3.3 Ruthenium(II)-Catalyzed C–H Oxygenations of phenols 94.

In recent years, a number of DGs for the C–H oxygenation reaction catalyzed by ruthenium(II)-complexs have been explored.[62] However, the transformation of these directing groups in a number of cases remains a major problem, whereas the methods that exploited removable directing groups are scarce.[174,175] First, it should be examined if the carboxylate assistance could promote the direct oxygenation of substrates forming six membered ruthenacycle as an intermediate as well. Successful solution of this problem could open the way for a novel strategy of using removable DGs. Therefore, we developed ruthenium-catalyzed twofold C–H functionalization with arenes and heteroarenes using easily cleavable pyridin-2-yloxy directing groups **186**.[175] Based on these studies we became interested in developing a C–H oxygenation reaction with a reusable directing groups.[59,158]

3.3.1 Optimization of ruthenium(II)-catalyzed C–H oxygenation of phenols 94.

Initially, we selected 2-(*o*-tolyloxy)-pyridine (**186a**) and *para*-methylbenzoic acid (**101a**) as the substrates to test the reaction conditions (Table 5). While additives were found to be mandatory for of ruthenium(II)-catalyzed acyloxylations with carboxylic acids, they proved to be effective for the desired C–O bond formation of product **187aa** (Table 5, entries 2-7). Among a variety of additives that were examined $AgSbF_6$ proved to be superior, which can be rationalized by the in-situ generation of a cationic ruthenium(II)-species (Table 5, entries 7-10).

Table 5: Optimization of ruthenium(II)-catalyzed oxygenation of phenol **186a**.

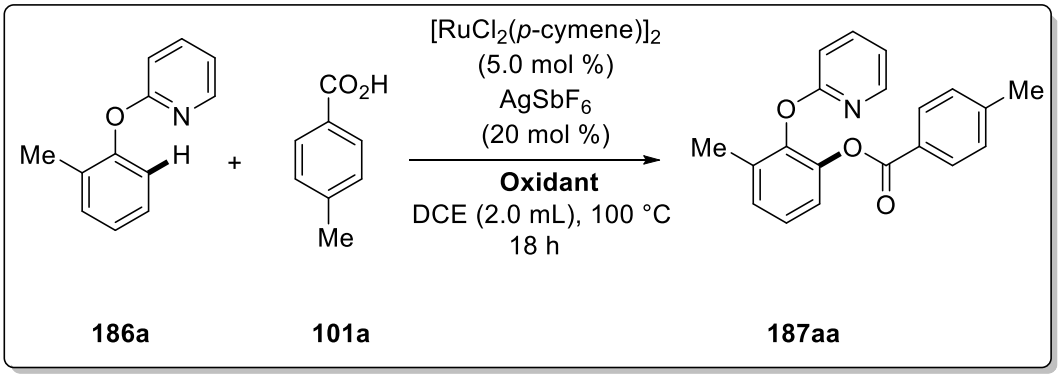


Entry	Catalyst	Additive	Solvent	Yield (%)[a]
1	$[RuCl_2(p\text{-cymene})]_2$	--	DCE	NR
2	$[RuCl_2(p\text{-cymene})]_2$	KOAc	DCE	NR
3	$[RuCl_2(p\text{-cymene})]_2$	Ag_2CO_3	DCE	28
4	$[RuCl_2(p\text{-cymene})]_2$	$AgPF_6$	DCE	24
5	$[RuCl_2(p\text{-cymene})]_2$	$AgBF_4$	DCE	42
6	$[RuCl_2(p\text{-cymene})]_2$	KPF_6	DCE	53[b]
7	**$[RuCl_2(p\text{-cymene})]_2$**	**$AgSbF_6$**	**DCE**	**78[c]**
8	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	43[c 12h]
9	$RuCl_3(H_2O)_n$	$AgSbF_6$	DCE	55[c, d]
10	$[Ru(O_2CMes)_2(p\text{-cymene})]$	KO_2CMes	DCE	34
11	$[Ru_2(hp)_4Cl]$	$AgBF_4$	DCE	46
12	$[Ru_2(OAc)_4Cl]$	$AgSbF_6$	DCE	42
13	$[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %)	$AgSbF_6$	DCE	63[c]

[a] Reaction conditions: **186a** (1.0 mmol), **101a** (0.5 mmol), catalyst (5.0 mol %), $K_2S_2O_8$ (1.0 mmol), solvent (2.0 mL), under N_2, 100 °C, 18 h, isolated yield, [b] KPF_6 (40 mol %); [c] $K_2S_2O_8$ (1.0 mmol), [d] $RuCl_3 \cdot (H_2O)_n$ (10 mol %).

As the next step, optimization studies were performed. to identify the optimal ratio and oxidant for the efficient direct C–H acyloxylation of arene **186** with carboxylic acid **101** The results are summarized in Table 6.

Table 6: Effect of oxidants on C–H acyloxylation.



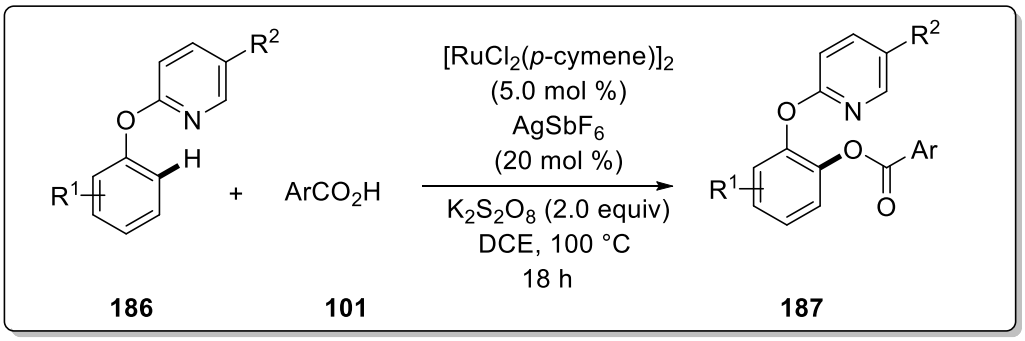
Entry	Oxidant (2.0 equiv)	Solvent	Yield (%)[a]
1	Ag_2CO_3	DCE	28
2	Ag_2O	DCE	32
3	K_2CO_3	DCE	14
4	Na_2CO_3	DCE	16
5	Oxone	DCE	55
6	**$K_2S_2O_8$**	**DCE**	**78[a]**
7	$(NH_4)_2S_2O_8$	DCE	46
8	$K_2S_2O_8$	DCE	58[b]

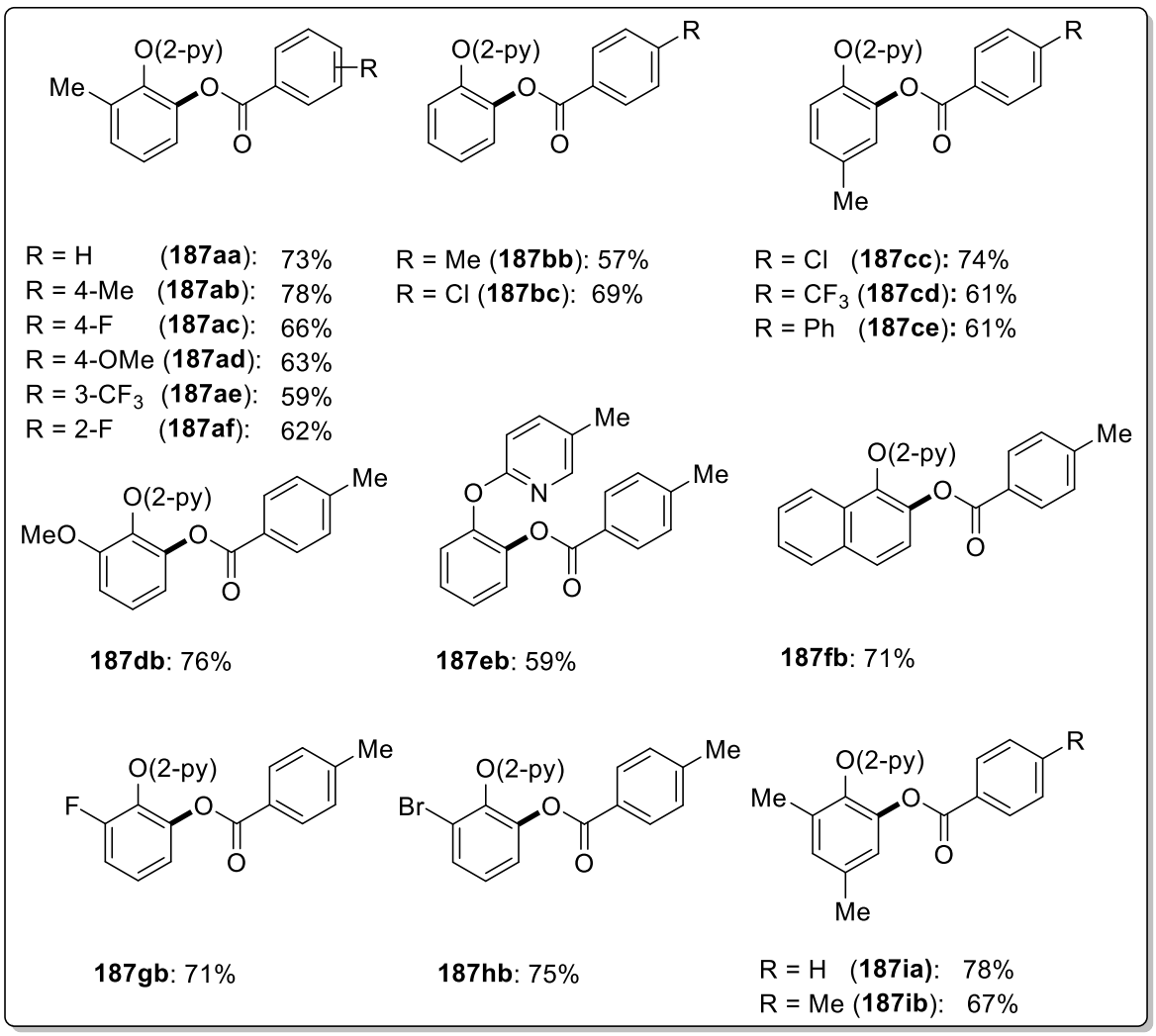
[a] Reaction conditions: **186a** (1.0 mmol), **101a** (0.5 mmol), catalyst (5.0 mol %), $K_2S_2O_8$ (1.0 mmol), solvent (2.0 mL), under N_2, 100 °C, 18 h, isolated yield, [b] $K_2S_2O_8$ (1.0 equiv).

Subsequently, a set of common sacrificial oxidants such as Ag_2CO_3 and Ag_2O were tested (Table 6, entries 1 and 2), and the utilization of K_2CO_3, Na_2CO_3 as bases failed to deliver the good yield of product **187aa** under otherwise identical reaction conditions (entries 3–5). Furthermore, the application of Oxone, $K_2S_2O_8$, $(NH_4)_2S_2O_8$ successfully implemented (entries 6 and 7), which revealed that the combination of the peroxydisulfate moiety and the potassium cation plays a crucial role for this C–H transformation. and 2.0 equivalent of $K_2S_2O_8$ was identified as the optimal reaction oxidant (entry 6).

3.3.2 Scope of ruthenium(II)-catalyzed C–H oxygenation with arene **186**.

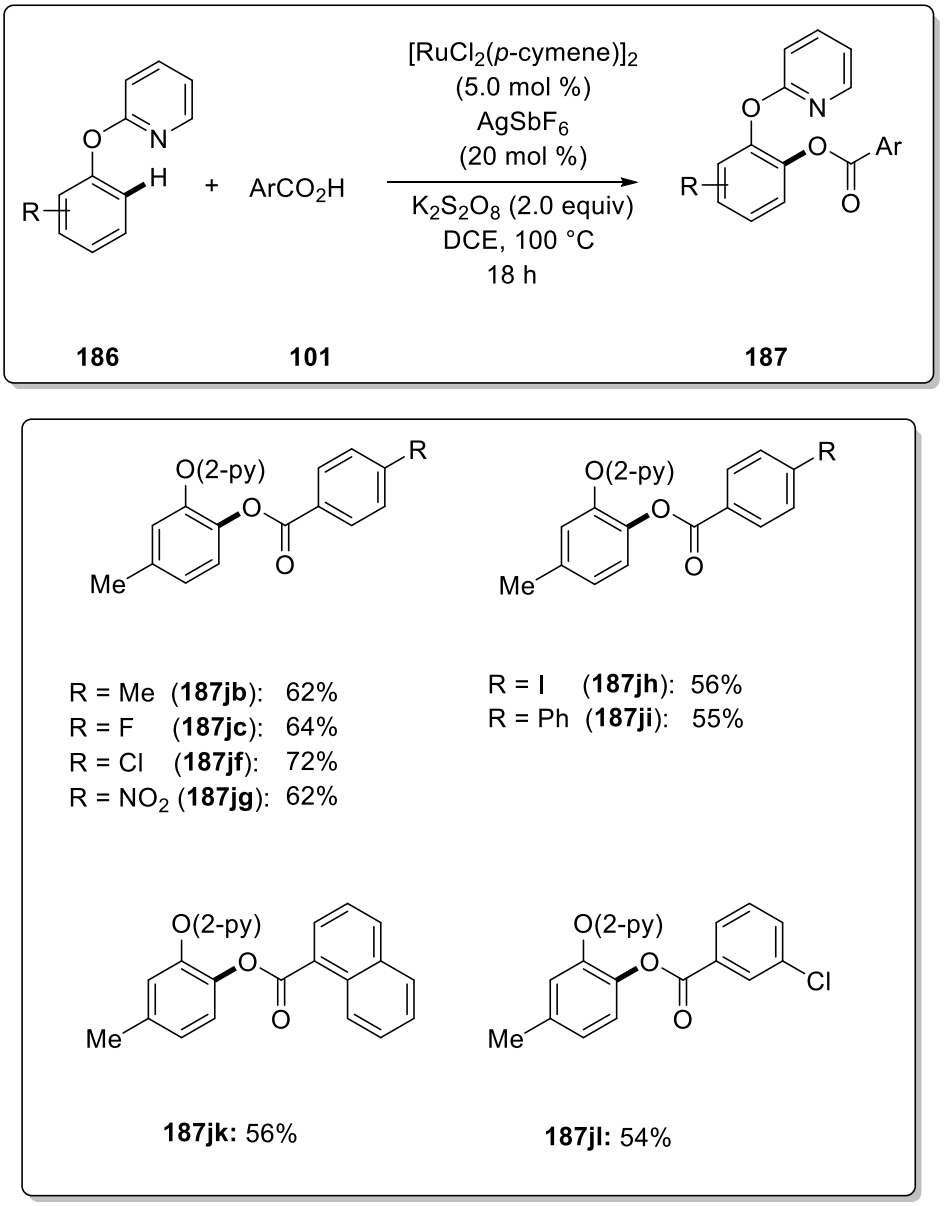
With the optimized catalytic system in hand, we tested its versatility with a set of representative arenes **186** and carboxylic acids **101** (Scheme 1.54). When using *mono*-substituted or *para*-di-substituted arenes **186a-186i**, the C–H acyloxylations proceeded with excellent levels of chemoselectivity, such that the *mono*-oxygenated products were obtained in high to excellent yields **187**.





Scheme 1.54: Scheme of ruthenium(II)-catalyzed acyloxylation of arene **186**.

The robust ruthenium(II)-catalyst proved to be tolerant of various functional groups, including fluoro, chloro and bromo substituents the latter of which should prove valuable for further functionalizations of the products **187**. Interestingly, placing an additional electron-donating substituent on the pyridyl-oxy auxiliary did not give an improved yield of the corresponding oxygenated product **187hb**.

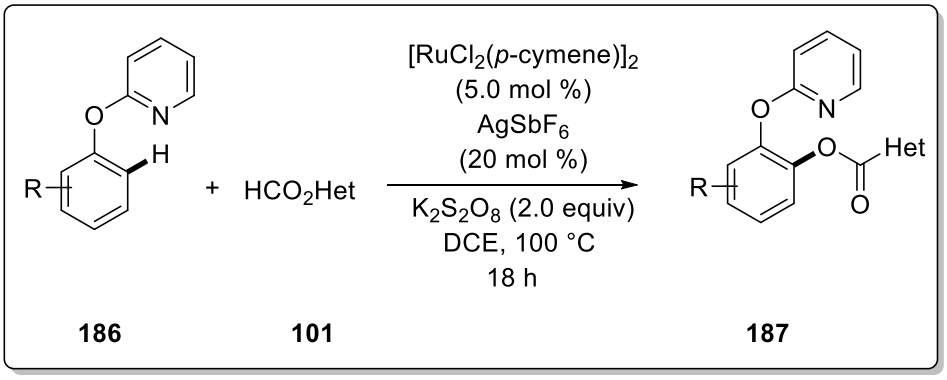


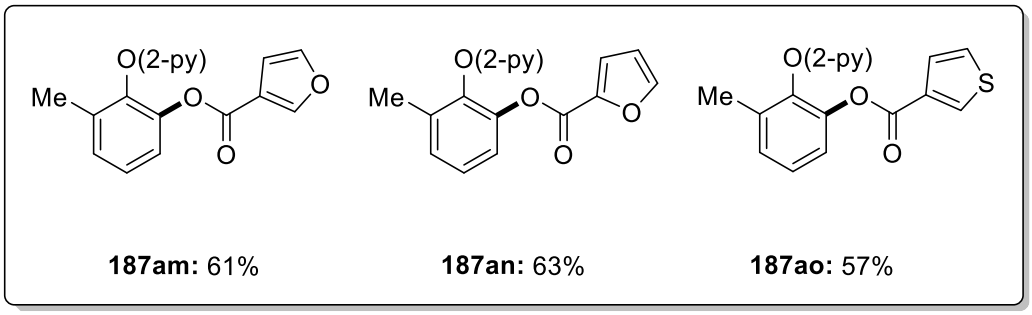
Scheme 1.55: Positional selectivity in ruthenium(II)-catalyzed acyloxylation of arene **186**.

Subsequently, the regioselectivity of the C–H acyloxylations was explored with the *meta*-substituted arene **186j** and a variety of carboxylic acids **101** (Scheme 1.55). The

regioselectivity was governed by steric interactions, thereby delivering **187ja-187jl** as the sole products. This ruthenium(II)-catalyzed C–H acyloxylation displayed excellent chemoselectivity by tolerating various electrophilic functional groups, including fluoro, chloro, iodo and even sensitive nitro groups (Scheme 1.55).

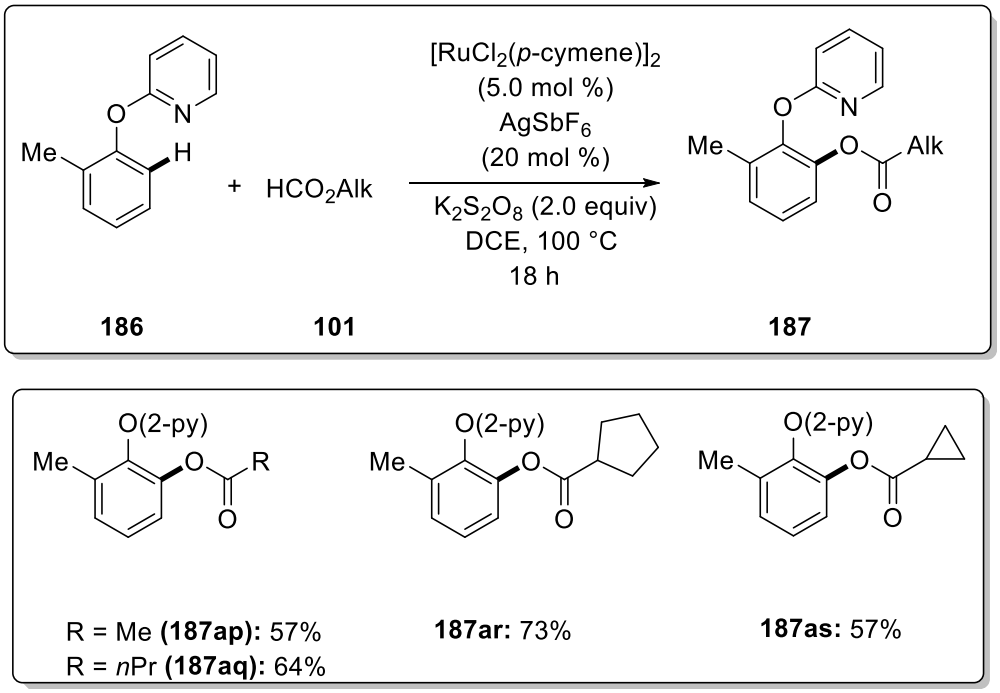
The cationic ruthenium(II)-catalyst was found to have a broad substrate scope for the C–H acyloxylations reaction. Thus, heteroaromatic acids **101m-101o**, including the thiophene derivative **101o**, were also identified as viable substrates. (Scheme 1.56). The 2,3-furyl substituted carboxylic acids also underwent the acyloxylation and showed the versatility of the reaction **187am-187ao** (Scheme 1.56).





Scheme 1.56: Ruthenium(II)-catalyzed acyloxylation with heteroaromatic acids **186**.

The unique power of the C–H acyloxylations was highlighted by the successful use of alkyl carboxylic acids **101p-101s**, which have hitherto proven to be particularly challenging substrates (Scheme 1.57).



Scheme 1.57: Ruthenium(II)-catalyzed acyloxylation with aliphatic carboxylic acids **101**.

3.3.3 Mechanistic studies

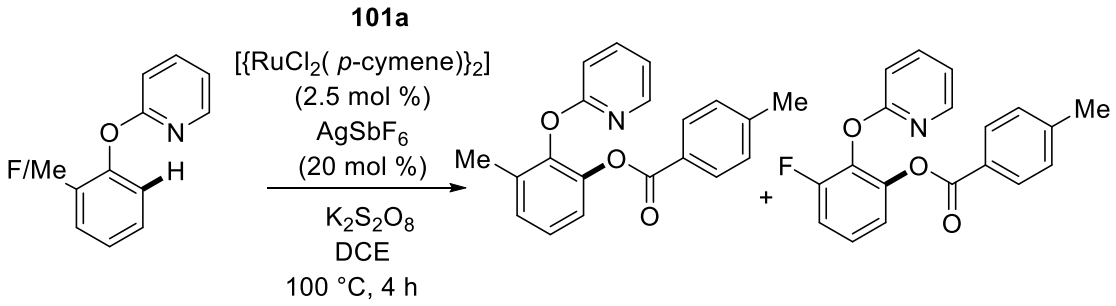
To shed light on the course of this new ruthenium(II)-catalyzed oxygenation protocol, a set of experiments were performed to elucide its mechanistic aspects.

3.3.3.1 Competition experiments

First, the intermolecular competition experiment between *ortho*-substituted arenes **186g** highlighted electronic effects. The results of the electron-rich and electron-deficient arenes are presented herein. The competition between *ortho*-methyl-substituted arene **186a** and *ortho*-fluoro-substituted arene **186g** indicated that the electron-rich arene reacted faster (Scheme 1.58a). Also in the second reaction between *meta*-methyl-substituted arene **186j** and *meta*-fluoro-substituted arene **187k** a significant larger amount of the electron-rich amidated product was observed (Scheme 1.58b). The third experiment to reveal the high level of positional-selectivity between aliphatic carboxylic acid **101r** and aromatic carboxylic acid **101b** was conducted and revealed a similar profile (Scheme 1.58c). Finally, the fourth experiment between *para*-methyl-substituted carboxylic acid **101b** and *para*-nitro-

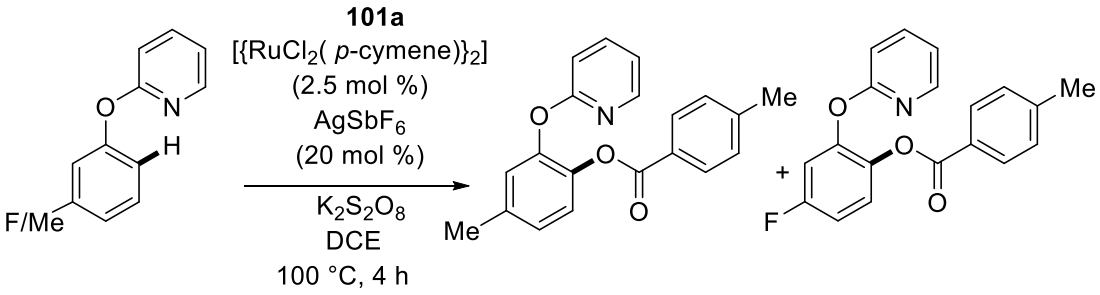
substituted arene **101g** was conducted (Scheme 1.58d). Overall, these experiments clearly showed that electron-rich arenes reacted faster than electron-deficient ones.

(a) intermolecular competition experiments between *ortho*-substituted arenes **186**



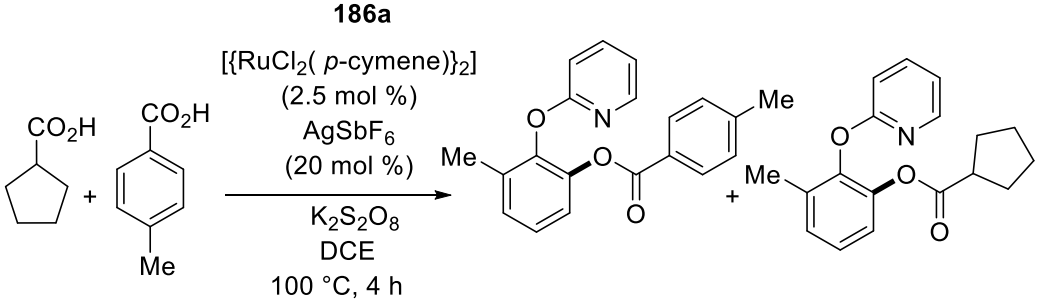
186g/186a **187ab:** 23% **187gb:** 2%

(b) intermolecular competition experiments between *meta*-substituted arenes **186**

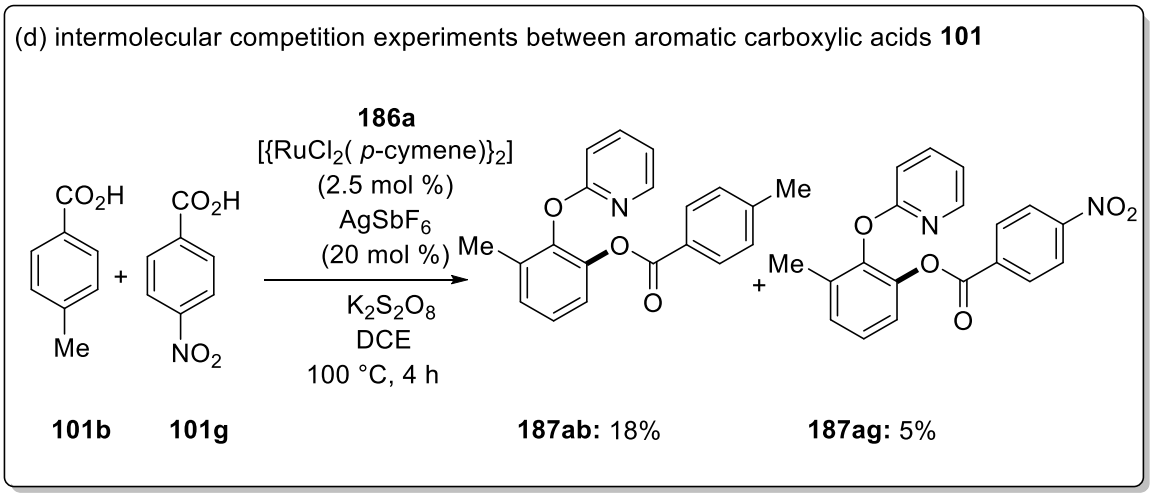


186i/186j **187ib:** 31% **187jb:** 7%

(c) intermolecular competition experiments between aliphatic/aromatic carboxylic acids **101**



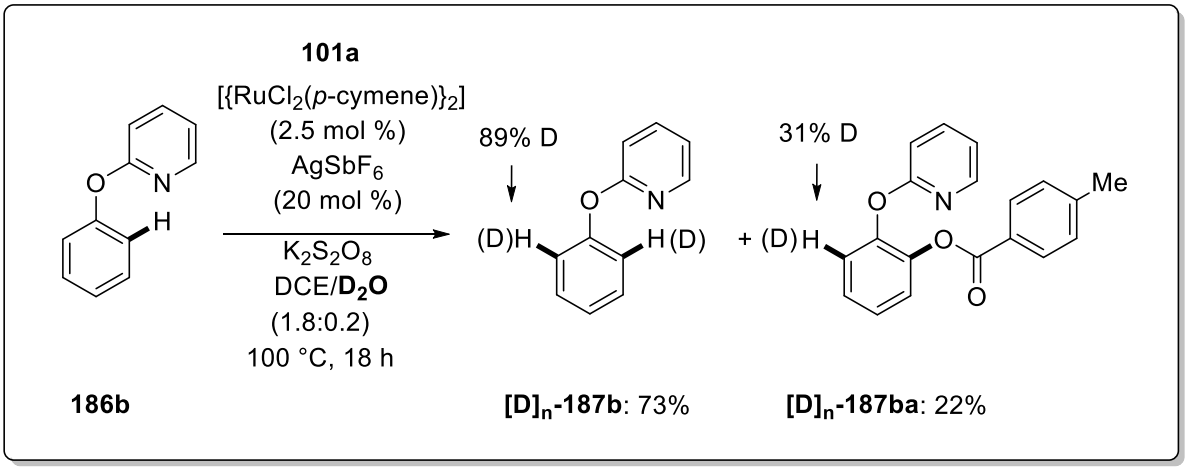
101r **101b** **187ab:** 28% **187ar:** 4%



Scheme 1.58: Competition experiments with arenes **187a**.

3.3.3.2 Studies with isotopically labeled compounds

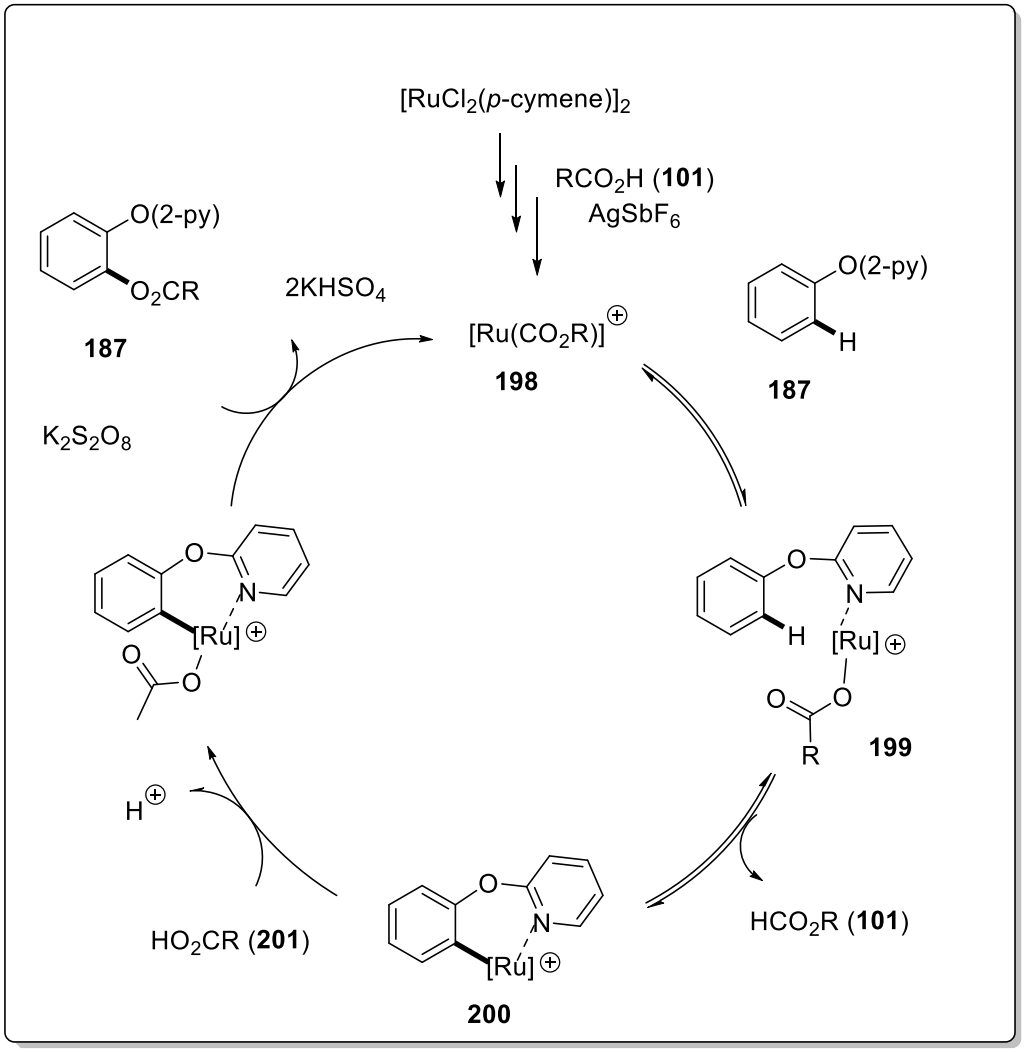
In consideration of the unique selectivity features displayed by competition experiments by the removable auxiliary-assisted ruthenium(II)-catalyzed C–H oxygenation, we performed experiments with isotopically labelled substrates (Scheme 1.59). In presence of carboxylic acid **101b**, 89% hydrogen of arene **186b** was replaced by deuterium and 31% hydrogen on the oxygenated product **187** was changed to deuterium using CD_3OD as a co-solvent. These results suggest that the C–H bond cleavage is most likely reversible and thus not the turnover determining step of the catalytic cycle.



Scheme 1.59: Reversible H/D exchange in presence of D_2O

3.3.3.3 Plausible catalytic cycle

Based on these mechanistic studies, a plausible catalytic cycle was proposed for this ruthenium(II)-catalyzed C–H oxygenation (Scheme 1.60). After reversible and fast C–H bond ruthenation on arene **187** by the cationic ruthenium carboxylate species **199**, the resulting cationic ruthenium complex **199** undergoes coordination and insertion of aryl carboxylic acid **101**, and thus affords the intermediate **201**. Finally, the desired oxygenated product is formed and the cationic ruthenium(II)-carboxylate catalyst is regenerated after *β*-elimination and proto-demetalation.



Scheme 1.60: Plausible mechanism of ruthenium(II)-catalyzed C–H oxygenation.

3.4 Reusable auxiliary assistance for ruthenium(II)-catalyzed C–H oxygenation of sulfoximines

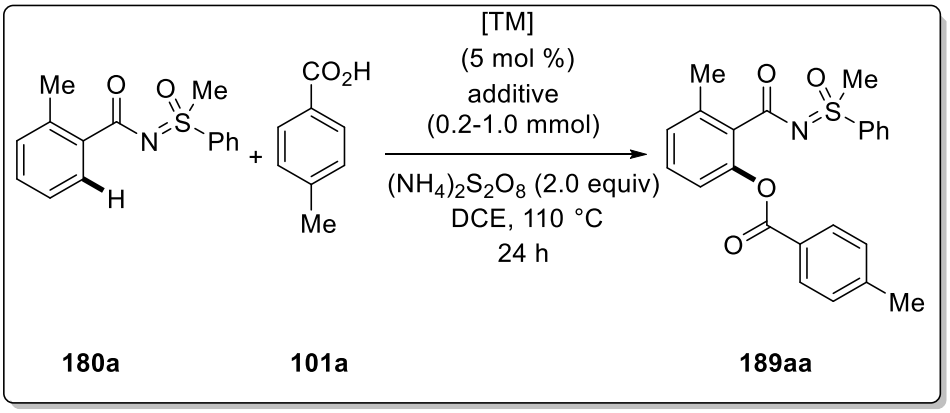
Recently, the independent studies from *Bolm* and *Sahoo* revealed the synthetic utility of the well-established reusable sulfoximines[158,159] which have been employed for the efficient C–H oxidation of arenes.[165] In recent years, the group of Ackermann developed number of directing groups for the C–H oxygenation reaction catalyzed by ruthenium(II)-complex.[62] A ruthenium(II)-catalyzed intermolecular C–H oxygenation assisted by removable auxiliary provided step-economical access to synthetically meaningful salicylic acid derivatives. The first iodine(III)- and silver-free C–H oxygenation strategy occurred by ruthenium(II)-catalysis with ample scope and high functional group tolerance to efficiently deliver densely substituted arenes employing the readily available benzoic acids as coupling partners exploiting removable auxiliary assistance in oxygenations.

3.4.1 Optimization of ruthenium(II)-catalyzed C–H oxygenation of sulfoximines

With the promising success with removable directing group in ruthenium(II)-catalyzed acyloxylations we became interested in developing a novel methodology for the RDG in C–O forming reactions. Initially, we selected *N*-(*o*-methylbenzoyl) **180** and *para*-methylbenzoic acid **101a** as substrates to test the reaction conditions (Table 7).

Additives proved to be effective for the desired C–O bond formation of **189** (Table 7). Among a variety of additives that were examined KPF_6 proved to be superior, which can be rationalized by the in-situ generation of a cationic ruthenium(II)species (entries 7-11). The direct C–H oxygenation of arene **180** with carboxylic acid **101** were performed. The results are summarized in Table 7.

Table 7: Optimization of ruthenium(II)-catalyzed oxygenation of **180**.

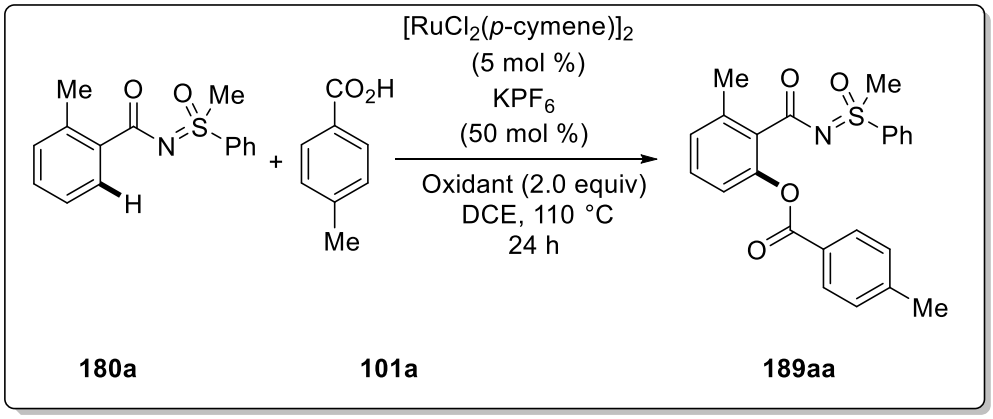


Entry	Catalyst	Additive	Solvent	Time (h)	Yield (%)[a]
1	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	DME	24	21
2	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	*t*-AmOH	24	8
3	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	1,4-dioxane	24	16
4	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	toluene	24	NR
5	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	DMF	24	NR
6	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	NMP	24	NR
7	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	DCE	24	26
8	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgSbF_6$	DCE	24	23
9	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgBF_6$	DCE	24	24
10	[{$RuCl_2$(*p*-cymene)}$_2$]	$AgPF_6$	DCE	24	16
11	[{$RuCl_2$(*p*-cymene)}$_2$]	KPF_6	DCE	24	81[a]
12	[$RuCl_3 \cdot n H_2O$]	KPF_6	DCE	24	23[b]
13	[$MnBr(CO)_5$]	KPF_6	DCE	24	NR
14	----	KPF_6	DCE	24	NR
15	[{RhCp*Cl_2}$_2$]	KPF_6	DCE	24	NR
16	[Cp*Co(CO)I_2]	KPF_6	DCE	24	NR

[a] Reaction conditions: **180a** (0.5 mmol), **101a** (0.60 mmol), catalyst (5.0 mol %), $(NH_4)_2S_2O_8$ (1.0 mmol), solvent (2.0 mL), under N_2, 100 °C, 24 h, isolated yield, [b] $(NH_4)_2S_2O_8$ (1.5 mmol).

Next step, optimization studies to identify the optimal oxidant source for the efficient direct amidation of arene **180** with carboxylic acid **101** were performed. The results are summarized in Table 8.

Table 8: Exploring oxidants



Entry	Oxidant (2.0 equiv)	Solvent	Yield (%)[a]
1	$K_2S_2O_8$	DCE	11
2	$PhI(OAc)_2$	DCE	NR
4	$KHSO_5$	DCE	16
5	Ag_2O	DCE	NR
6	$PhI(TFA)_2$	DCE	NR
7	Oxone	DCE	16
8	**$(NH_4)_2S_2O_8$**	**DCE**	**81**
9	$(NH_4)_2S_2O_8$	DCE	54[b]
10	$(NH_4)_2S_2O_8$	DCE	38[c]

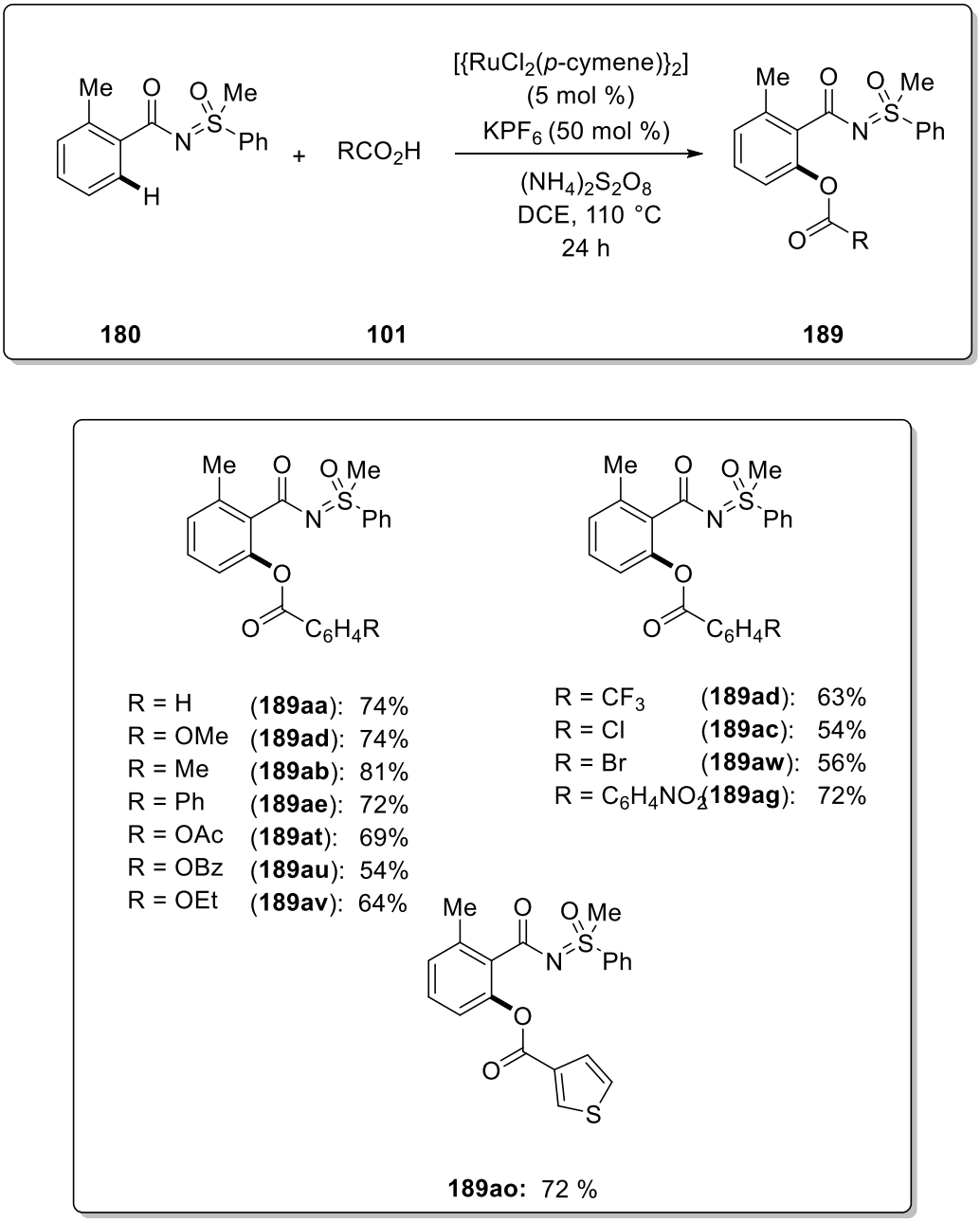
[a] Reaction conditions: **180a** (0.5 mmol), **101a** (0.6 mmol), catalyst (5.0 mol %), $(NH_4)_2S_2O_8$ (1.0 mmol), solvent (2.0 mL), under N_2, 100 °C, 18 h, isolated yield, [b] KPF_6 (0.3 equiv), [c] KPF_6 (0.2 equiv).

A set of common sacrificial oxidants $K_2S_2O_8$, $PhI(OAc)_2$, $KHSO_5$, Ag_2O, $PhI(TFA)_2$, oxone and $(NH_4)_2S_2O_8$ were tested and $(NH_4)_2S_2O_8$ was identified as the optimal reaction oxidant (entries 1-7).

3.4.2 Scope of ruthenium(II)-catalyzed C–H oxygenation of arene **180**.

With an optimized catalytic system in hand, we then tested its versatility with a set of representative arenes **180** and carboxylic acids **101** (Scheme 1.62). When using *mono*-substituted or *para*-substituted arenes**180c** the C–H oxygenation proceeded with excellent

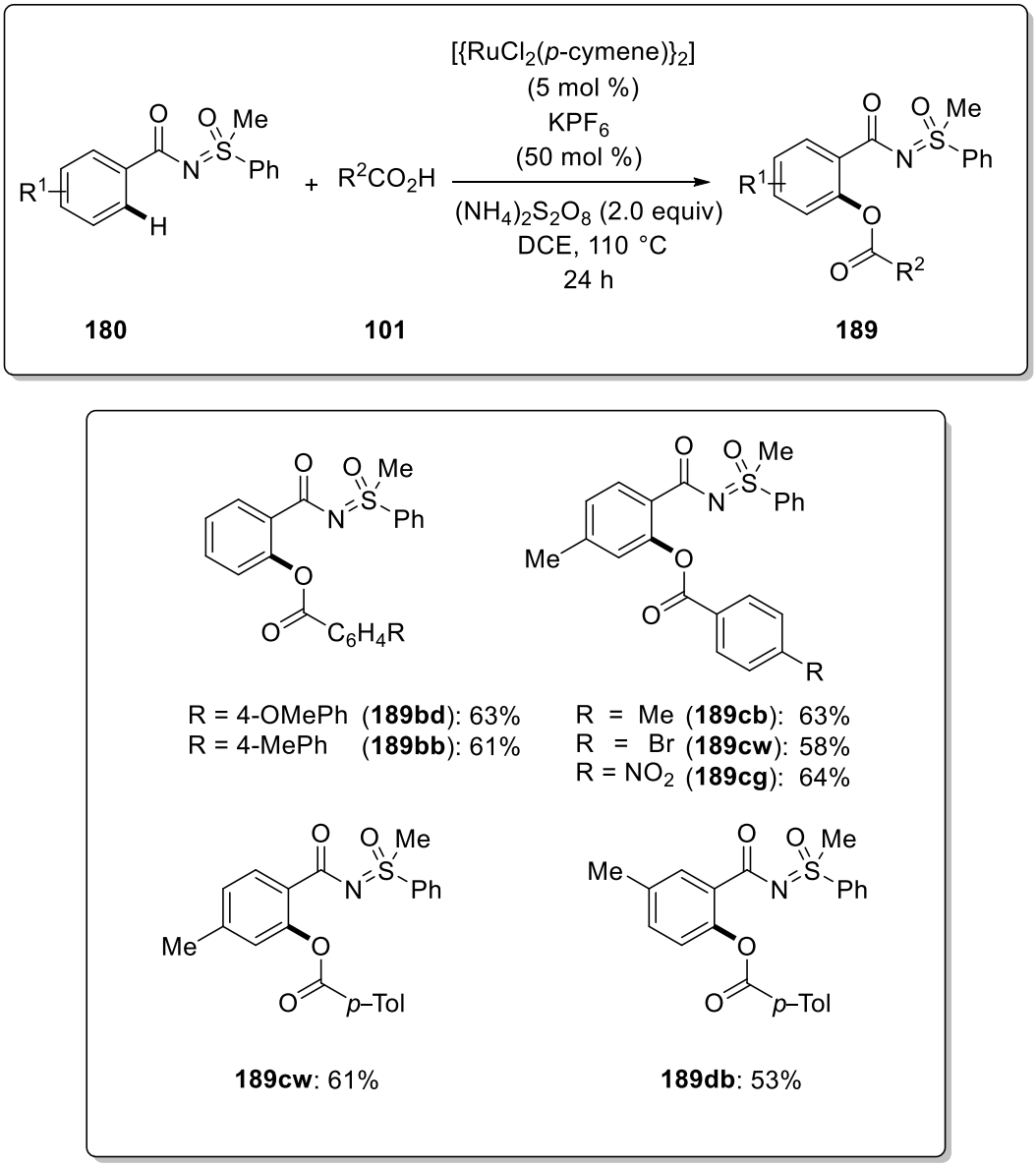
levels of chemoselectivity, such that the *mono*-oxygenated products were obtained in high to excellent yield **189cb** (Scheme 1.62).



Scheme 1.62: Scope of ruthenium(II)-catalyzed acyloxylation of acids **101**.

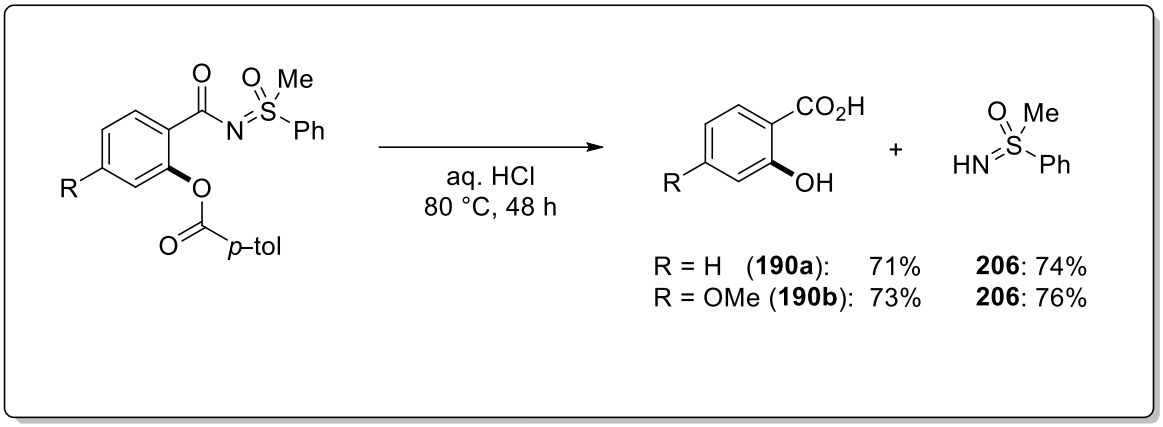
The robust ruthenium(II) catalyst proved to be tolerant of various functional groups, including fluoro, chloro, and bromo substituents, the latter of which should prove valuable for further functionalization of the products **189** (Scheme 1.62). To our delight, thiophene-

3-carboxylic acid was successfully installed as a coupling partner **101o** to give product **189ao** in 72 %.



Scheme 1.63: Scope of ruthenium(II)-catalyzed acyloxylation of arene **180**.

High levels of positional selectivity were observed with *para*-substituted arenes **180c** as well. Substitutions on the aromatic moiety *N*–aroyl MPS **180** were likewise tolerated under the optimized reaction conditions. The widely applicable ruthenium(II) catalyst was not limited to aromatic substrates. Indeed, the C–H oxygenation of *para*- and *meta*- substitueted products **180db** proved viable, occurring with excellent levels of positional control (Scheme 1.63).



Scheme 1.64. Reusability of directing group.

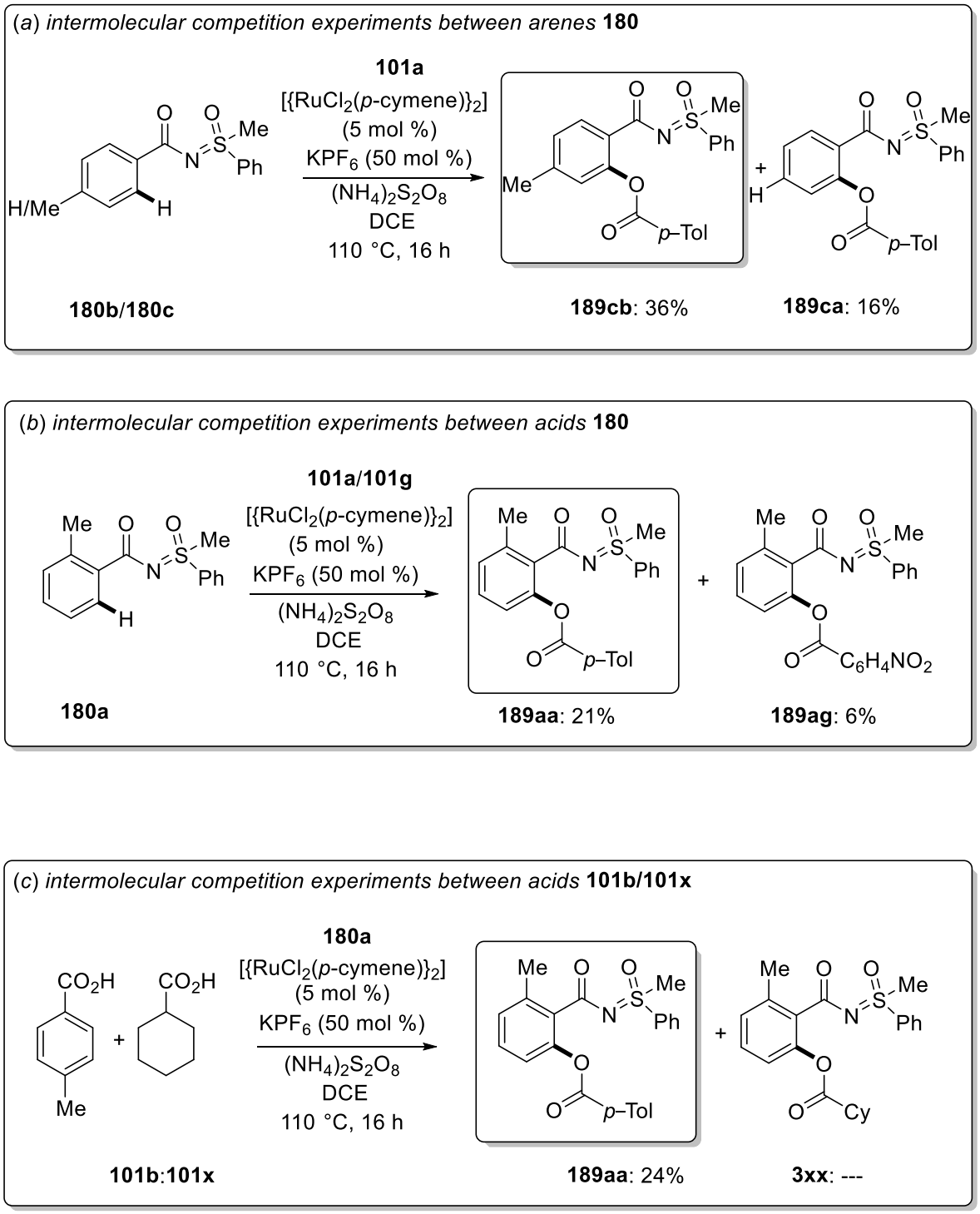
Finally, hydrolysis of the oxygenated products with aqueous HCl readily cleaved the removable DG in a traceless fashion. Thus, the desired *ortho*-hydroxy carboxylic acids **102a** (71%) and **102b** (73%) were obtained respectively, with the recovery of the DG (Scheme 1.64). The synthetic utility of the ruthenium(II)-catalyzed oxygenation protocol was reflected by providing efficient access to the synthetically useful salicylic acid derivatives **190a** and **190b** (Scheme 1.64).

3.4.3 Mechanistic studies

To shed light on the course of this ruthenium(II)-catalyzed oxygenation protocol a set of experiments were performed.

3.4.3.1 Competition experiments

First, intermolecular competition experiment between *para*-substituted arenes **180c** highlighted electronic effects on *site*-selectivity of the C–H bond functionalization. The competition between *para*-methyl-substituted arene **180c** and the un-substituted arene **180b**, showed that the electron-rich arene reacted faster. (Scheme 1.65a). Also in the second reaction between *para*-methyl-benzoic acid **189cb** and *para*-nitro-benzoic acid **189ca**, a significant larger amount of the electron-rich oxygenated product was observed (Scheme 1.65b). The third experiment was conducted to reveal the high level of positional-selectivity between aliphatic carboxylic acid **101x** and aromatic carboxylic acid **101b** and revealed the challenging nature of aliphatic carboxylic acids (Scheme 1.65c). These experiments clearly showed that the electron-rich arenes reacted faster than the electron-deficient ones.

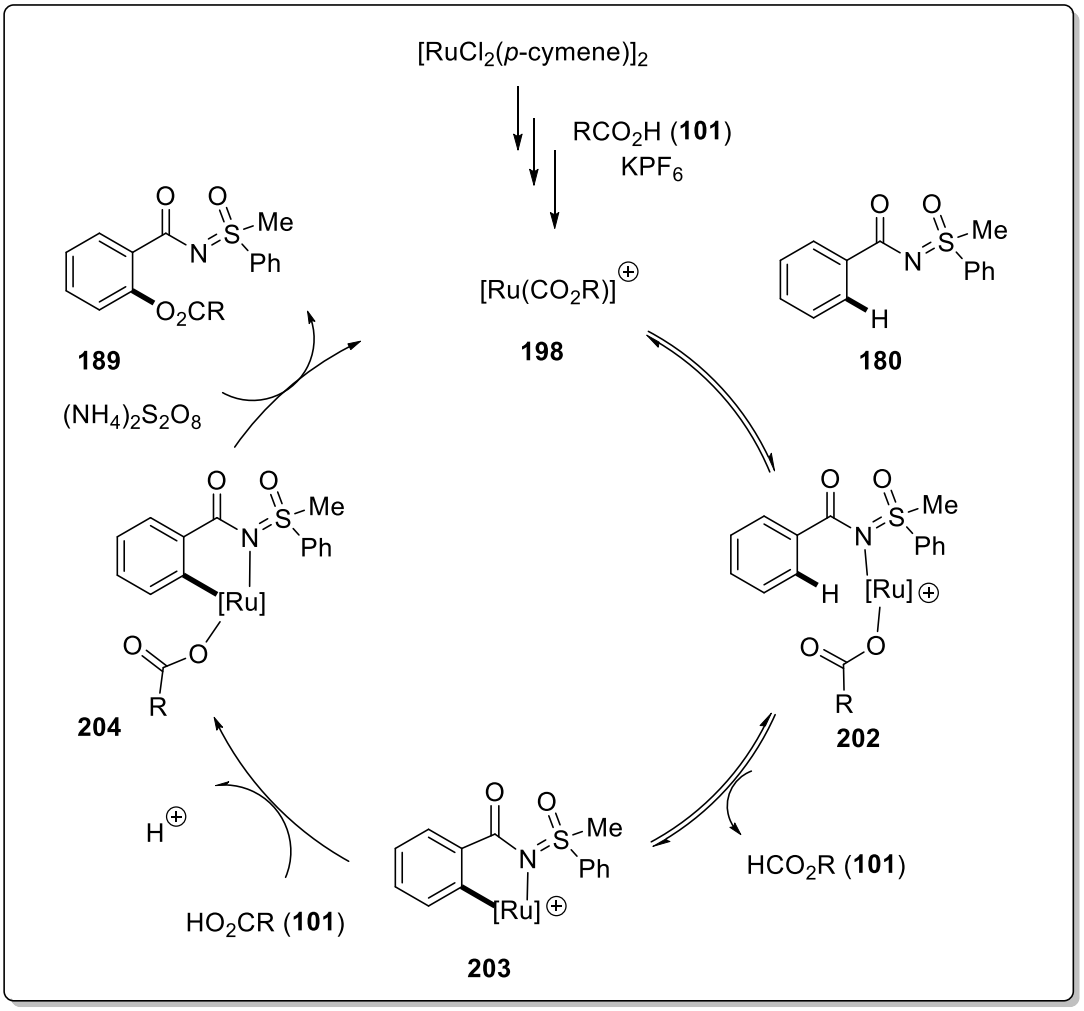


Scheme 1.65: Competition experiments between arenes **180** and acids **101**.

3.4.3.3 Plausible catalytic cycle

Based on these mechanistic studies a plausible catalytic cycle was proposed for this ruthenium(II)-catalyzed C–H oxygenation (Scheme 1.66). After reversible and fast C–H bond

ruthenation on arene **180** with the cationic ruthenium carboxylate species **198**, the resulting cationic ruthenium complex **202** undergoes coordination and insertion of aryl carboxylic acid **203**, and thus affords the intermediate **204**. Finally, the desired oxygenated product is formed and the cationic ruthenium(II)-carboxylate catalyst is regenerated after reductive elimination. The operationally simple protocol featured high catalytic efficacy and excellent functional group tolerance. These observations, and particularly the preferential transformation of electron-rich arenes, can be rationalized in terms of a base-assisted intramolecular electrophilic substitution-type (BIES)[51b,55] C–H metalation event to be operative.



Scheme 1.66: Plausible mechanism of ruthenium(II)-catalyzed C–H oxygenation **180**.

3.5 Ruthenium(II)-catalyzed C–H alkenylation of arenes bearing removable directing group with O_2 as the oxidant

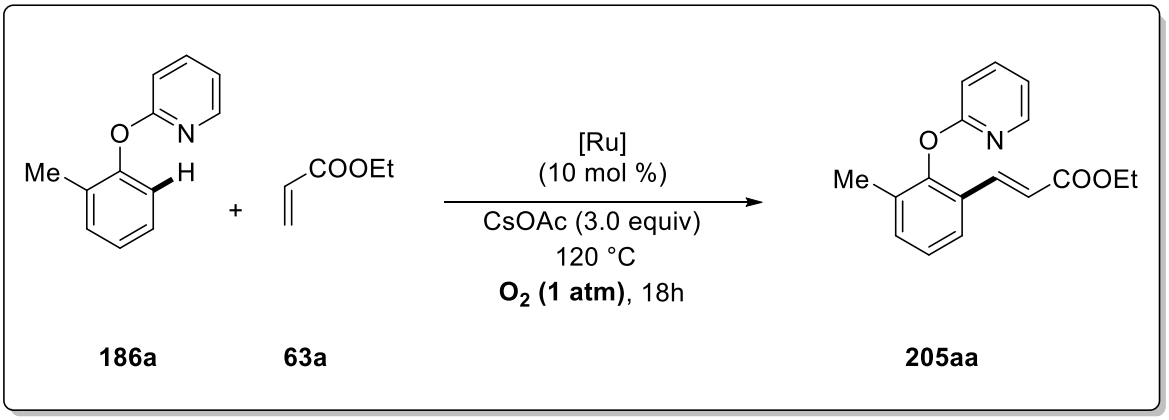
Oxidative alkenylation by twofold C–H activation[15,19] represents the most efficient and step-economical strategy for the assembly of selectively substituted olefins.[39,164] Based on pioneering studies by *Fujiwara* and *Moritani*,[44-46] tremendous progress has been made in metal-catalyzed cross-dehydrogenative olefinations, most notably in palladium catalysis.[213] In contrast, versatile ruthenium(II)-complexes[62] have only recently emerged as powerful catalysts for oxidative C–H functionalizations. Despite these indisputable advances, ruthenium(II)-catalyzed oxidative alkenylations using chelation assistance have been thus far limited to the use of antibacterial copper(II) or expensive silver(I) salts as the oxidants.[32,42] Thereby, undesired metal waste is generated, which contradicts the sustainable nature of C–H activation technology. A notable elegant exception was developed by *Milstein* and co-workers, which indicated the potential of ruthenium catalysis.[214] Unfortunately, the catalyst was severely limited to rather harsh reaction conditions, such as high pressure reactions with CO at 8 atm and a reaction temperature of 180 °C. Moreover, mixtures of regioisomeric products which were difficult to separate were largely obtained when using substituted arenes. In contrast, we have very recently identified the beneficial effect of carboxylates for aerobic alkyne annulations. We then became interested in developing the first ruthenium(II)-catalyzed positional selective alkenylations with O_2 as the sole oxidant.

3.5.1 Optimization studies

Initially, we selected 2-(*o*-tolyloxy)pyridine **186** and ethyl acrylate **63** as the substrates to test the reaction conditions (Table 9). While carboxylate additives were found to be mandatory for ruthenium-catalyzed direct arylations with aryl halides, **4** and proved to be effective for the desired oxidative C–H bond alkenylation of **205** (entries 1–3). To our delight, the coupled product **205** was isolated in 68% yield when using the well defined ruthenium catalyst [Ru(O_2CMes)$_2$(*p*-cymene)] **198** (10 mol %) and 3.0 mmol of **63** (entry 5). Importantly, this alkenylation product was also obtained in 32% yield with PEG as the solvent. Molecular dioxygen served as the sacrificial oxidant (entry 6). Furthermore, control experiments verified that no desired product was observed in the absence ruthenium-catalyst. Lowering the amount of acrylate as a coupling partner in this solvent-free transformation resulted in lower isolated

yields (entries 4-7). The well-defined ruthenium(II)-carboxylate catalyst outcompeted the $RuCl_3 \cdot H_2O$, $RuI_3 \cdot H_2O$ and $[Ru_2(hp)_4Cl]$ in delivering the alkenylated product in exceedingly good yields in ruthenium(II)-oxidase catalysis (entries 8-11).

Table 9: Optimization of ruthenium(II)-catalyzed C–H alkenylation.



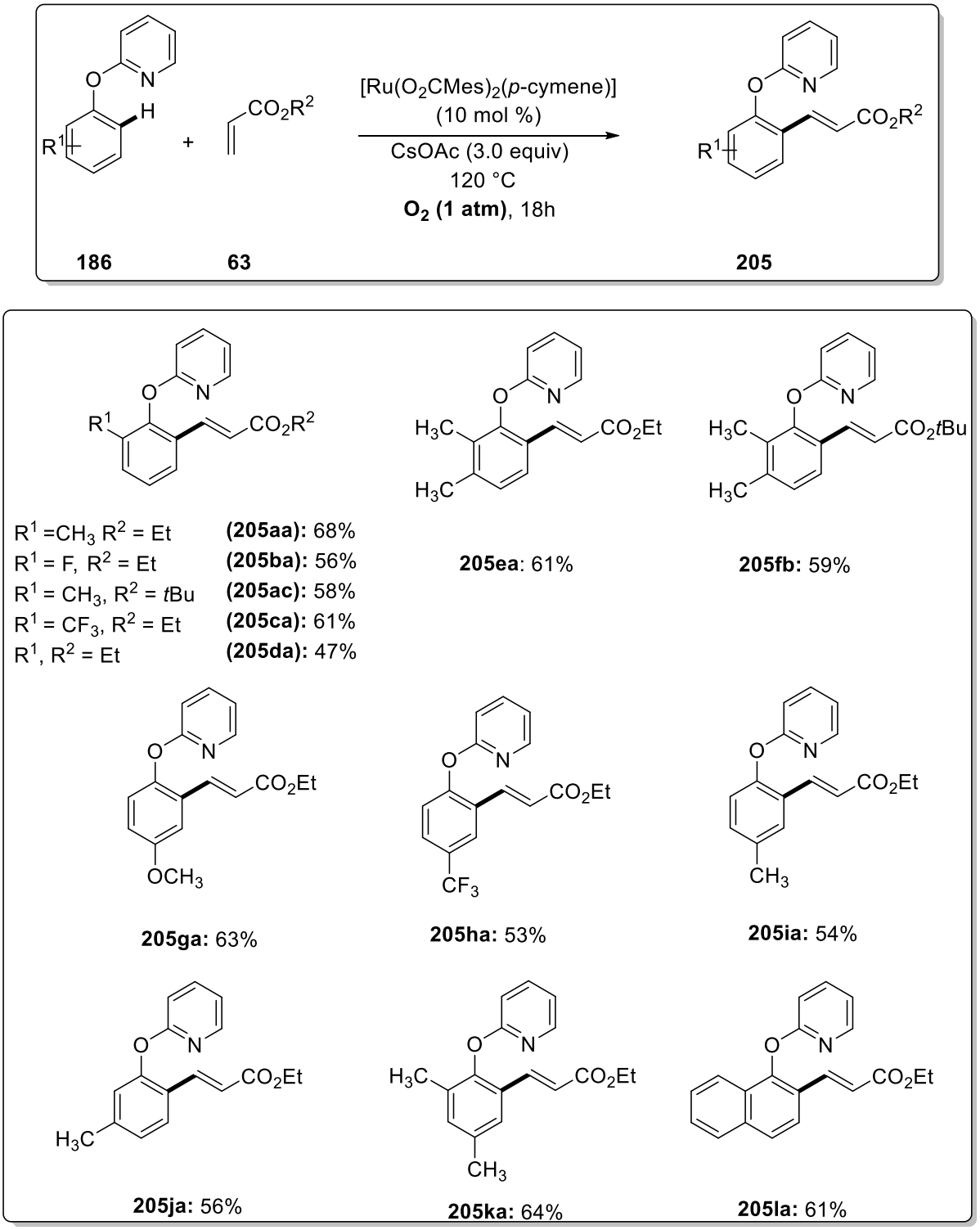
Entry	Catalyst	Additive	Solvent	Time (h)	Yield (%)[a]
1	$[Ru(O_2CMes)_2(p\text{-cymene})]$	CsOAc	PEG	18	32
2	$[Ru(O_2CMes)_2(p\text{-cymene})]$	CsOAc	CH_3OH:PEG (1:1)	18	28
3	$[Ru(O_2CMes)_2(p\text{-cymene})]$	CsOAc	*t*-BuOH	18	34
4	$[Ru(O_2CMes)_2(p\text{-cymene})]$	-----	H_2O	18	18
5	$[Ru(O_2CMes)_2(p\text{-cymene})]$	CsOAc	acrylate	18	54[a]
6	$[Ru(O_2CMes)_2(p\text{-cymene})]$	CsOAc	acrylate	18	26[b]
7	$[Ru(O_2CMes)_2(p\text{-cymene})]$	CsOAc	acrylate	18	**68[c]**
8	$RuCl_3.H_2O$ (10 %)	CsOAc	acrylate	18	36[c]
9	$RuI_3.H_2O$ (10 %)	CsOAc	acrylate	18	NR
10	----	CsOAc	acrylate	18	NR
11	$[Ru_2(hp)_4Cl]$ (5 %)	CsOAc	acrylate	18	41

[a] Reaction conditions: **186a** (0.5 mmol), **63a** (2.5 mmol), catalyst (10.0 mol %), under O_2, 120 °C, 18 h, isolated yield [b] **63a** (1.0 mmol); [c] **63a** (1.5 mmol).

With the optimized conditions in hand, we explored the versatility of this C–H monoalkenylation reaction (Scheme 1.67). Gratifyingly, substrates with both electron-donating (products **205aa-205fa**) and electron-withdrawing substituents **205ha** at the *ortho* and *para* position of the phenyl ring were viable and furnished the desired products **205ia** in

high isolated yields, thus indicating the general applicability of phenoxylpyridine substrates **205la**.

3.5.2 Scope of ruthenium(II)-catalyzed C–H alkenylation of phenol derivatives **186**.

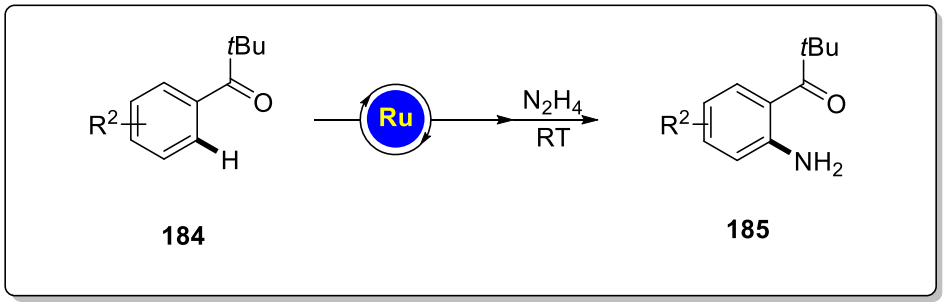


Scheme 1.67: Scope of aerobic ruthenium(II)-catalyzed C–H alkenylation of phenol derivatives **186**

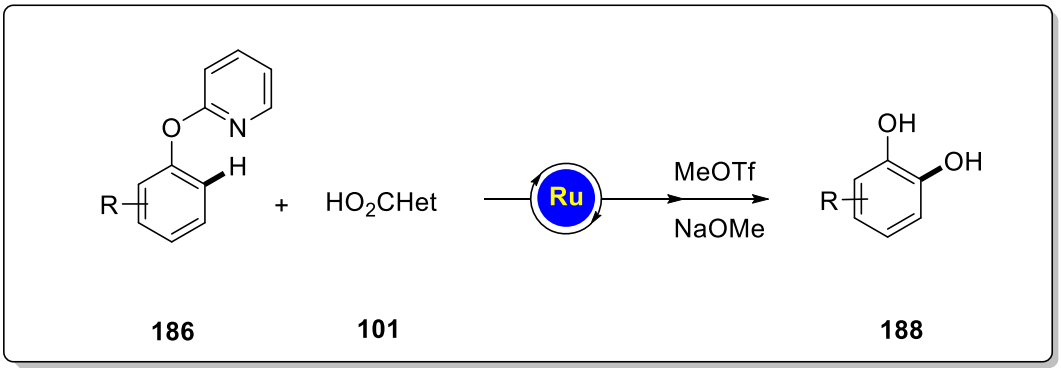
Notably, halogen substituents at the *ortho* and *para* position of the phenyl ring in substrates **168g** and **168h** were also tolerated under this catalytic system (Scheme 1.67). This could provide a versatile synthetic handle for further functionalization of the products **205ha**. Furthermore, oxidative alkenylations with naphthol derivative **205la**, respectively, delivered the desired alkenylated products with excellent site selectivity. Importantly, the catalytic C–H bond functionalizations occurred with excellent diastereoselectivities, delivering the *E* diastereomers as the sole products in all cases. The site-selectivity of the oxidative C–H bond functionalization with *meta*-substituted phenol derivatives **168j** was largely controlled by steric interactions, thus delivering the alkenylated product **205ja** in good yield

4 Summary and Outlook

Phenols and amines are key structural motifs of numerous bioactive compounds of relevance to agrochemicals and drug discovery, among others. Transition metal-catalyzed direct functionalization processes of otherwise inert C–H bonds emerged as a more sustainable alternative to the classically used cross-coupling reactions for the synthesis of substituted phenol and derivatives. For this reason, the research was focused on the development of novel methods for efficient and selective direct C–H transformations to construct C–O and C–N bond scaffolds in an atom- and step-economical manner.



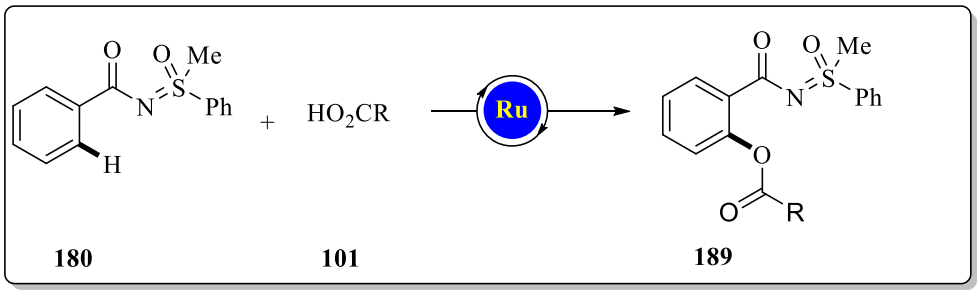
Scheme 1.68: Facile access to primary aminopheneones **185**.



Scheme 1.69: Removable auxiliary assistance for ruthenium(II) catalyzed oxygenations **186**.

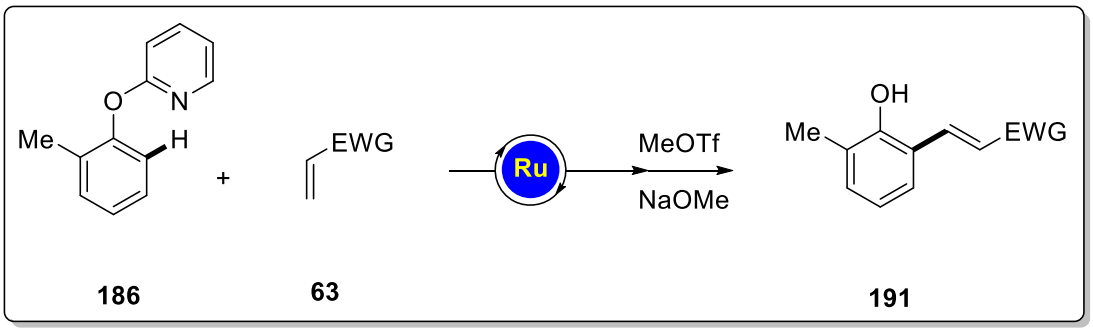
The first part of this thesis described an efficient and generally applicable method for the ruthenium(II)-catalyzed oxidative C–N bond formation of ketone **184** accomplished with different nitrogen sources (Scheme 1.68). The high activity of the catalytic system was not restricted to aromatic carboxalic acids **101** as coupling partners, but enabled the first ruthenium(II)-catalyzed direct C–N formation of 2-phenylpyridine **43**. An *in situ* generated

cationic ruthenium(II)-catalyst promoted the highly chemo- and mono-selective C–H funtionalization in excellent yields with a broad substrate scope. Here, electron-donating and -withdrawing groups on the arene of both ketone and aromatic azide **149** based reagents were compatible with this transformation to set the stage after removal of the pthalimido group for valuable 2-aminoketones **185**, which are key structural frameworks in drugs and biologically relevant heterocycles.



Scheme 1.70: Reusable auxiliary assistance for ruthenium(II)-catalyzed oxygenations.

A straight forward synthesis starting from benzoic acid derivatives **101** by applying C–O bond formation approach as the key reaction and subsequent removal of the DG group provides the corresponding synthetically useful salicylic acid derivatives **190** in a highly economical manner (Scheme 1.70).



Scheme 1.71: Ruthenium(II)-catalyzed oxidative alkenylation

We then became interested in developing the first ruthenium(II)-catalyzed positional selective alkenylations with O_2 as the sole oxidant. Use of the versatile ruthenium oxidase catalysis by direct dioxygen-coupled turnover include: a) an unparalleled broad substrate scope in aerobic alkenylations, b) sustainable aerobic C–H activations that produce H_2O as the only by-product, c) exceedingly mild reaction conditions, and d) oxidative olefinations with weakly coordinating or removable directing groups.

5 Experimental Section

5.1 General Remarks

All reactions involving moisture- or air-sensitive reagents or products were conducted under an atmosphere of nitrogen, using standard Schlenk techniques and pre-dried glassware. Syringes for handling of dry solvents or liquid reagents were evacuated and purged with nitrogen threefold prior to use. Analytical data of substances that are known in the literature were compared with those described in the literature.

5.1.1 Solvents

All solvents for reactions were purified using a MBRAUN Solvent Purification System 800 (MB SPS 800) or were dried, degassed, distilled and stored under an inert atmosphere (argon or nitrogen) according to following standard procedures.

***t*-Amyl alcohol** (*t*-AmOH) was dried over Na for 5 h and distilled under ambient pressure.

***t*-Butyl alcohol** (*t*-BuOH) was dried over Na and distilled under ambient pressure and stored over molecular sieves (4 Å).

1,2-Dichloroethane (DCE) was dried over CaH_2 for 8 h and distilled under ambient pressure.

1,2-Dimethoxyethane (DME) was dried over Na for 12h and distilled over Na/benzophenone under ambient pressure.

1,4-Dioxane was dried over CaH_2 and distilled under reduced pressure.

Methanol (MeOH) was dried over $Mg(OEt)_2$ for 3 h and distilled under ambient pressure.

***N*-Methyl-2-pyrrolidone** (NMP) was stirred for 6 h over CaH_2 and subsequently distilled under reduced pressure.

Tetrahydrofuran (THF) was purified using a MB SPS 800 and distilled under ambient pressure.

Toluene (PhMe) was dried over Na and distilled over Na/benzophenone under ambient pressure.

Water (H_2O) was degassed for 2 h and ultrasonicated.

***o*-Xylene** was distilled over Na/benzophenone under reduced pressure.

5.1.2 Vacuum

Following pressures were measured on the used vacuum pumps and are not corrected: membrane pump vacuum (MPV): 5.0 mbar, oil pump vacuum (OPV): 0.1 mbar.

5.1.3 Melting Point

Melting points were measured using a Stuart® *Melting Point Apparatus SMP3* (Barloworld Scientific).

5.1.4 Chromatography

Analytical TLC was performed on 0.25 mm silica gel 60F plates (Macherey-Nagel) with 254 nm fluorescent indicator from Merck. Plates were visualized under ultraviolet light. 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, 70–230 mesh ASTM).

5.1.5 Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance (NMR) spectra were recorded at 300, 400, 500, 600 MHz (^{1}H-NMR), at 75, 126 MHz (^{13}C-NMR, APT) and at 282 MHz (^{19}F-NMR) respectively, on Bruker *Avance III HD* 400 and 500, or Varian *Mercury* 300, *Inova* 500 and 600 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.

^{1}H-NMR	^{13}C-NMR
$CDCl_3$ 7.26 ppm	77.16 ± 0.06 ppm
DMSO-d_6 2.50 ppm	39.52 ± 0.06 ppm

For the characterization of the observed signal multiplicities, the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), hept (heptet), m (multiplet). Coupling constants *J* are reported in Hertz (Hz).

5.1.6 Infrared Spectroscopy

Infrared spectra were recorded using a Bruker *Alpha-P ATR FT-IR* spectrometer. Liquid samples were measured as a film, and solid samples were measured neat. The analysis of the spectra was carried out using the software from Bruker *OPUS 6*. The absorption is given in wave numbers (cm^{-1}) and the spectra were recorded in the range of 4000–400 cm^{-1}.

5.1.7 Mass Spectrometry

EI- and EI-HRMS spectra 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-HRMS spectra were recorded on a Bruker *APEX IV* mass spectrometer. The ratio of mass to charge areindicated, intensities relative to the base peak (I = 100) are given in parentheses.

5.1.8 Reagents

Chemicals obtained from commercial sources (purity > 95%) were used without further purification. The following compounds were synthesized by known literature procedures: [{$RuCl_2$(*p*-cymene)}$_2$] and [Ru(O_2CMes)$_2$(*p*-cymene)] by the courtesy of *Karsten Rauch*.

5.2 General Procedures

5.2.1 Representative procedure A: Ruthenium(II)−catalyzed C−H omidations with weakly coordinating ketones 192: A suspension of 2,2-dimethyl-1-phenylpropan-1-one (**184**), (81.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183**), (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv) in 1,4-dioxane (2.0 mL) was stirred in a sealed tube under N_2 at 100 °C for 24 h. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and passed through celite with CH_2Cl_2 (100 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1) to yield **192** (120 mg, 78%) as a colorless solid.

5.2.2 Representative procedure B: Ruthenium(II) catalyzed C–H imidations with weakly coordinating ketones: A suspension of 2,2-dimethyl-1-phenylpropan-1-one (**184**), (81.0 mg, 0.50 mmol), 5-methyl-1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183**), (200 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv) in 1,4-dioxane (2.0 mL) was stirred in a sealed tube under N_2 at 100 °C for 24 h. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and passed through celite with CH_2Cl_2 (100 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1) to yield **192** (120 mg, 70%) as a colorless solid.

5.2.3 Representative procedure C: Access to primary aminoketones: A suspension of 2-(2-ivaloylphenyl)isoindoline-1,3-dione (**192**), (307 mg, 1.0 mmol) and hydrazine (2.0 mL), was stirred at ambient temperature for 4 h. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and passed through celite with CH_2Cl_2 (50 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) to yield **185** (122 mg, 69%) as an orange liquid.

5.2.4 Representative procedure D Access indoles and quinolines: A suspension of *ortho*-aminoketone (**185**), (88.5 mg. 0.5 mmol), 2-bromo-1-phenylethan-1-one (149 mg, 1.5 equiv),

and anhydrous DMF (2.0 mL) was added and stirred at 100 °C for 16 h. At ambient temperature, the reaction mixture was diluted with Et_2O (20 mL) and passed through celite with Et_2O (100 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) to yield **193** (112 mg, 81%) as a yellow solid.

5.2.5 Representative procedure E Access indoles and quinolines: A suspension of *ortho*-aminoketone (**185**), (88.5 mg. 0.50 mmol), 2-bromo-ethynylbenzene (77.0 mg, 1.5 equiv), $InCl_3$ (14.8 mg, 20 mol %) and anhydrous CH_3CN (2.0 mL) was added and stirred at 90 °C for 24 h. At ambient temperature, the reaction mixture was diluted with EtOAc (20 mL) and passed through celite with CH_2Cl_2 (100 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) to yield **194a** (124 mg, 94%) as a yellow solid.

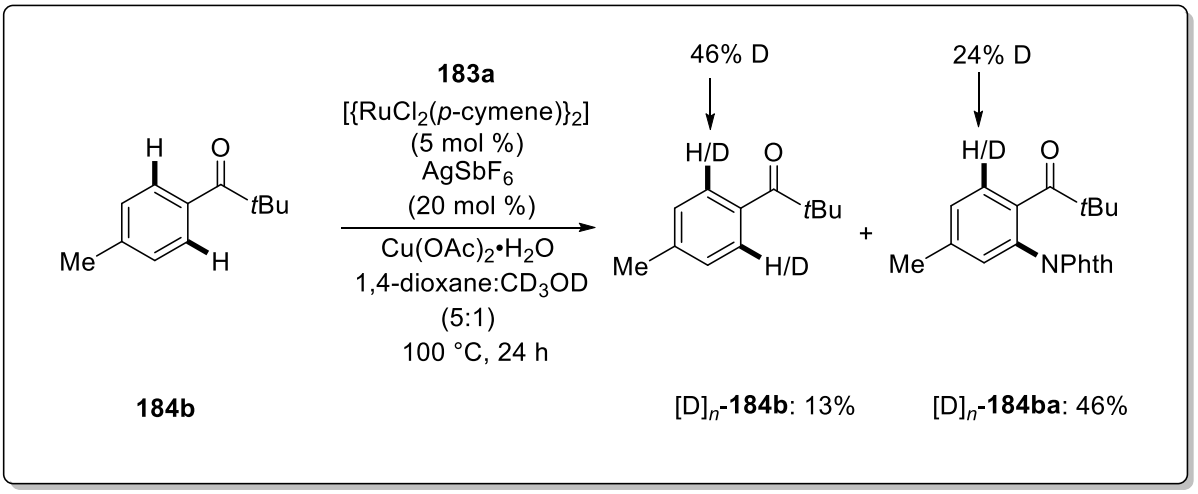
5.2.6 Representative Procedure E1: Ruthenium-catalyzed C–H amidation of pyridines 43 : In a 20 mL flame-dried screw-capped sealed tube, 2-phenylpyridine (**43**), (71 mg, 0.50 mmol), 4-methyl benzenesulfonyl azide (**149**), (183 mg, 2.0 equiv), $[RuCl_2(p\text{-cymene})]_2$ (15.0 mg, 5.0 mol %), $AgSbF_6$ (34.0 mg, 20.0 mol %), NaOAc (21 mg, 0.5 equiv) in DCE (2.0 mL) were stirred at 100 °C for 24 h. At ambient temperature, the reaction mixture was diluted with H_2O (75 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine (50 mL) and 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: 4:1) to yield **168** (113 mg, 70%) as a colorless solid.

5.2.7 Representative procedure F: Ruthenium-catalyzed oxidative oxygenation of substituted pyridines 186: A suspension of 2-(*o*-tolyloxy)pyridine (**186)**, (185.4 mg, 1.00 mmol), *p*-toluic acid (**101a)**, (68.4 mg, 0.50 mmol), $[\{RuCl_2\text{-}(p\text{-cymene})\}_2]$ (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol) in DCE (2.0 mL) was stirred in a sealed tube under N_2 at 100 °C for 18 h. At ambient temperature, the reaction mixture was diluted with 20 mL CH_2Cl_2 (20 mL) and passed through celite with CH_2Cl_2 (100 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1) to yield **187** (124.8 mg, 78%) as a colorless solid.

5.2.8 Representative procedure G: Ruthenium(II)−catalyzed C−H oxygenation of arenes 180: A suspension of sulfoximine benzamide (**180**), (137 mg, 0.50 mmol), carboxylic acid (**101a**), (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.00 mmol) in DCE (2.0 mL) was degassed with N_2 five times and stirred in a sealed tube under N_2 at 110 °C for 24 h. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and passed through Celite with CH_2Cl_2 (150 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:3) to yield **189** (164 mg, 81%) as a colorless solid.

5.2.9 Representative procedure H: Remove and reuse of sulfoximine 202: *N*-[2-(4-Methylbenzoyloxy-4-methoxy)]-*S*-methyl-*S*-phenylsulfoximine **(189)** (211 mg, 0.50 mmol) was dissolved in aqueous HCl (12 N, 5.0 mL) and stirred at 80 °C for 48 h. The reaction mixture was extracted with CH_2Cl_2, and aqueous layer was basified with 40% NaOH and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under vacuum to give sulfoximine **202** (130 mg, 74%) as a colorless liquid dried over Na_2SO_4, and concentrated under vacuum to give the corresponding 4-methoxy-2-hydroxy benzoic acid **190a** (139 mg, 71%).

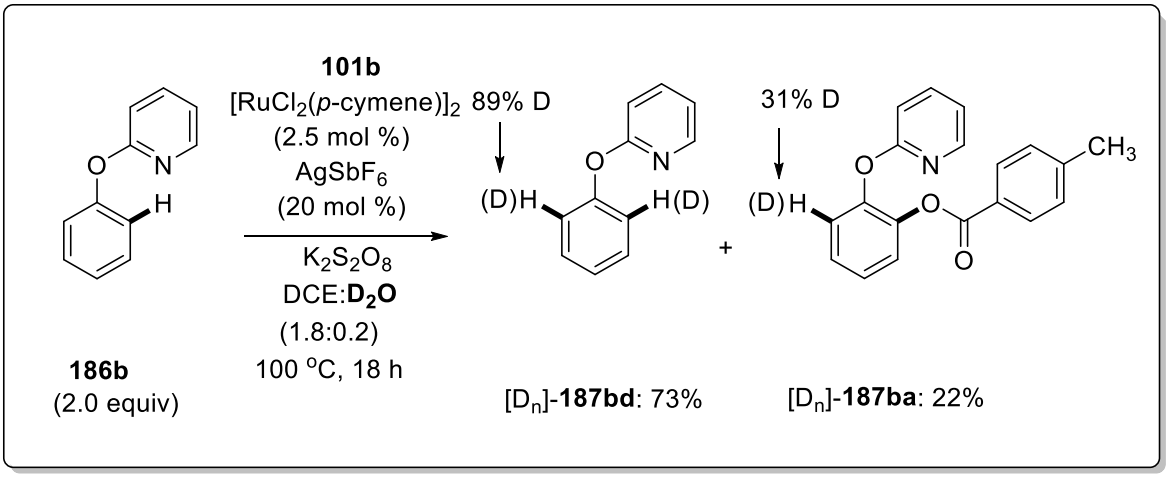
5.2.10 Representative Procedure I: Aerobic ruthenium(II)-catalyzed oxidative alkenylation with O_2 as oxidant 186: A suspension of 2-(aryloxy)pyridine (**186**) (0.50 mmol, 1.0 equiv), acrylate (**63**) (2.5 mmol, 5.0 equiv), Ru(O_2CMes)$_2$(p-cymene)] (28.0 mg, 0.05 mmol, 10.0 mol %) and CsOAc (288 mg, 1.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The flask was evacuated and flushed with O_2 three times. The reaction mixture was stirred at 120 °C for 18 h under O_2 (1 atm). At ambient temperature, the reaction mixture was diluted with saturated aq. NH_4Cl (10 mL) and extracted with EtOAc (3 x 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation in vacuo, the product was purified by column chromatography on silica gel (nhexane/EtOAc).



Scheme 1.71: H/D-Exchange experiments of weakly co-ordinating ketone **184**.

5.3.1 Procedure J: H/D-Exchange experiments of weakly co-ordinating ketone (Scheme 1.50). A suspension of 2,2-dimethyl-1-phenylpropan-1-one (**184**) (81.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv) in 1,4-dioxane:CD_3OD (5:1, 2.0 mL) was stirred in a sealed tube under N_2 at 100 °C for 24 h. At ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and passed through celite with CH_2Cl_2 (100 mL). The organic layer was dried over Na_2SO_4. After evaporation of the solvents in *vaccuo*, the crude product was purified by column chromatography on silica gel (n-hexane/EtOAc: 10:1) to yield **[D]$_n$-184** 13% and **[D] $_n$-184ba** 46%.

5.3.2 Ruthenium-Catalyzed H/D Exchange in Substrates 186b with D_2O as the cosolvent.

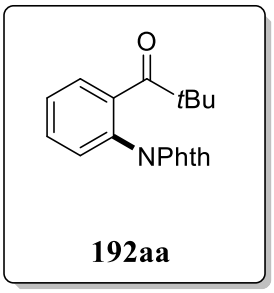


Scheme 1.72 H/D-Exchange experiments of arene **186**.

5.3.3 Procedure K: H/D-Exchange experiments of 2-phenoxypyridine (Scheme 1.59): A suspension of 2-phenoxypyridine **186b** (171 mg, 1.0 mmol), *p-t*oluic acid **101b** (68.4 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol%), $AgSbF_6$ (34.4 mg, 20 mol%) and $K_2S_2O_8$ (270 mg, 2.0 mmol) in DCE:D_2O (1.8:0.2, 2 0 mL) was stirred in a sealed tube under N_2 at 100 °C for 18 h. At ambient temperature, the reaction mixture was diluted with 20 mL CH_2Cl_2 and passed with celite with 100 mL CH_2Cl_2. The organic layer was dried over Na_2SO_4. After evaporation of the solvents in *vaccuo*, the crude product was purified by column chromatography on silica gel (n-hexane/EtOAc: 10:1) to yield **[D]$_n$-187bd** 73% and **[D]$_n$-187ba** 22%.

6 Analytical Data:

Synthesis of 2-(2-Pivaloylphenyl)isoindoline-1,3-dione (192aa)



192aa

The representative procedure **A** was followed using 2,2-dimethyl-1-phenylpropan-1-one (**184a**) (81.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192aa** (120 mg, 78%) as a white solid.

M. p.: 125–126 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 7.3, 0.6 Hz, 2H), 7.77 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.68 (ddd, *J* = 7.7, 1.6, 0.5 Hz, 1H), 7.58–7.52 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.45 (td, *J* = 7.6, 1.3 Hz, 1H), 7.35 (ddd, *J* = 7.9, 1.3, 0.5 Hz, 1H), 1.30 (s, 9H).

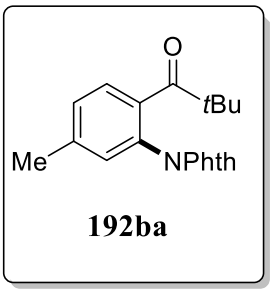
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 209.7 (C_q), 167.5 (C_q), 137.8 (C_q), 134.3 (CH), 131.9 (C_q), 130.6 (CH), 130.2 (CH), 129.4 (C_q), 127.9 (CH), 126.9 (CH), 123.7 (CH), 44.4 (C_q), 28.4 (CH_3).

IR (ATR): 2943, 1720, 1650, 1372, 1060, 982, 830, 509 cm^{-1}.

MS (EI) *m/z* (relative intensity) 307 (65) [M^+], 192 (100), 161 (55), 142 (35).

HR-MS (ESI) *m/z* for $C_{19}H_{18}NO_3$ [$M+H^+$] calcd.: 308.1208.
found: 308.1211.

Synthesis of 2-(5-Methyl-2-pivaloylphenyl)isoindoline-1,3-dione (192ba)



192ba

The representative procedure **A** was followed using 2,2-dimethyl-1-(*p*-tolyl)propan-1-one (**184b**) (88.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ba** (118 mg, 74%) as a white solid.

M.p.: 136–137 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.83 (dd, *J* = 7.6, 0.5 Hz, 1H), 7.70 (d, *J* = 8.6, Hz, 2H), 7.55 (d, *J* = 7.9 Hz 2H), 7.4 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36–7.32 (m, 1H), 2·54 (s, 3H), 1.31 (s, 9H).

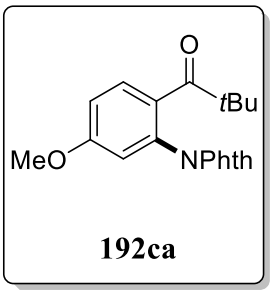
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.5 (C_q), 167.5 (C_q), 145.5 (C_q), 137.8 (C_q), 134.8 (CH), 132.2 (C_q), 130.5 (CH), 129.4 (C_q), 127.7 (CH), 124.1 (CH), 123.5 (CH), 44.4 (C_q), 28.4 (CH_3), 22.1 (CH_3).

IR (ATR): 2953, 1725, 1675, 1378, 1110, 824, 531 cm^{-1}.

MS (EI) *m/z* (relative intensity) 321 (40) [M^+], 281 (100), 184 (65), 165 (45).

HR-MS (ESI) *m/z* for $C_{20}H_{20}NO_3$ [M+H^+] calcd.: 322.1365.
found: 322.1369.

Synthesis of 2-(5-Methoxy-2-pivaloylphenyl)isoindoline-1,3-dione (192ca)



192ca

The representative procedure **A** was followed using 1-(4-methoxyphenyl)-2,2-dimethylpropan-1-one (**184c**) (96.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ca** (119 mg, 63%) as a white solid.

M. p: 186–187 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 5.4, 3.1 Hz, 1H), 7.85 (dd, *J* = 5.4, 3.1 Hz, 1H), 7.74 (ddd, *J* = 5.6, 3.0, 1.7 Hz, 2H), 7.69 (d, *J* = 8.7 Hz, 1H), 6.94 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.86 (d, *J* = 2.6 Hz, 1H), 3.84 (s, 3H), 1.29 (s, 9H).

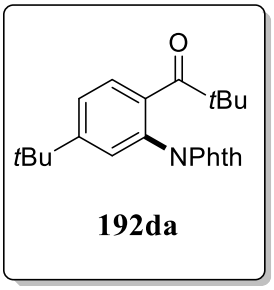
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.6 (C_q), 167.8 (C_q), 161.0 (C_q), 134.3 (CH), 134.3 (CH), 132.6 (C_q), 132.0 (CH), 131.5 (C_q), 129.8 (C_q), 128.6 (CH), 124.0 (CH), 123.5 (CH), 55.6 (CH_3), 44.4 (C_q), 28.5 (CH_3).

IR (ATR): 2962, 1719, 1259, 1084, 1012, 792, 644 cm^{-1}.

MS (EI) *m/z* (relative intensity) 337 (65) [M^+], 289 (100), 161 (55), 142 (45).

HR-MS (ESI) *m/z* for $C_{20}H_{20}NO_4$ [M+H^+] calcd.: 338.1314.
found: 338.1317.

Synthesis of 2-[(5-(*tert*-Butyl)-2-pivaloylphenyl)]isoindoline-1,3-dione (192da)



192da

The representative procedure **A** was followed using 1-[4-(tert-butyl)phenyl)]-2,2-dimethylpropan-1-one (**184d**) (109 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192da** (114 mg, 63%) as a white solid.

M.p.: 164–165 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.64 (dd, *J* = 8.2, 0.4 Hz, 1H), 7.44 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.32 (d, *J* = 2.0 Hz, 1H), 1.33 (s, 9H), 1.30 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.5 (C_q), 167.7 (C_q), 154.3 (C_q), 134.7 (C_q), 134.0 (CH) 132.0 (C_q), 129.3 (CH), 127.3 (CH), 126.9 (CH), 124.9 (CH), 123.6 (C_q), 45.0 (C_q), 34.9 (C_q), 31.0 (CH_3), 28.4 (CH_3).

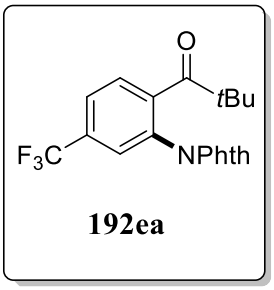
IR (**ATR):** 2956, 1717, 1685, 1378, 1117, 1088, 964, 736 cm^{-1}.

MS (EI) *m/z* (relative intensity) 363 (45) [M^+], 187 (100), 214 (65), 105 (35).

HR-MS (ESI) *m/z* for $C_{23}H_{26}NO_4$ [M+H^+] calcd.: 364.0734.

found: 364.0709.

Synthesis of 2-[(2-Pivaloyl-5-(trifluoromethyl)phenyl)]isoindoline-1,3-dione (192ea)



192ea

The representative procedure **A** was followed using 2,2-dimethyl-1-[(4-(trifluoromethyl)phenyl)]propan-1-one (**184e**) (115 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ea** (101 mg, 54%) as a white solid.

M.p.:114–115 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93–7.89 (m, 2H), 7.80–7.75 (m, 3H), 7.73–7.68 (m, 1H), 7.64 (dt, *J* = 1.9, 0.7 Hz, 1H), 1.31 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.6 (C_q), 166.9 (C_q), 141.0 (CH), 134.0 (C_q), 132.6 (q, $^2J_{C\text{-}F}$ = 35 Hz, C_q), 132.4 (CH), 131.0 (q, $^1J_{C\text{-}F}$ = 272 Hz, C_q), 127.3 (CH), 126.0 (C_q), 125.2 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 124.8 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 121.2 (CH), 44.5 (C_q), 28.3 (CH_3).

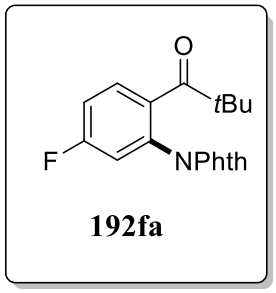
^{19}F-NMR (283 MHz, $CDCl_3$) δ = -63.0 (s).

IR (ATR): 2973, 1714, 1379, 1292, 1115, 1076, 884, 702 cm^{-1}.

MS (EI) *m/z* (relative intensity) 341 (45) [M^+], 287 (100), 226 (70), 134 (45).

HR-MS (ESI) *m/z* for $C_{20}H_{16}F_3NO_3$ [M+H^+] calcd.: 376.1182.
found: 376.1179.

Synthesis of 2-(5-Fluoro-2-pivaloylphenyl)isoindoline-1,3-dione (192fa)



192fa

The representative procedure **A** was followed using 1-(4-fluorophenyl)-2,2-dimethylpropan-1-one (**184f**) (90.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192fa** (107 mg, 66%) as a white solid.

M.p.: 137–138 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.89 (ddd, J = 5.5, 2.9, 0.4 Hz, 2H), 7.77 (d, J = 0.4 Hz, 1H), 7.77–7.74 (m, 1H), 7.70 (ddt, J = 8.6, 5.9, 0.4 Hz, 1H), 7.18 (dd, J = 2.6, 0.4 Hz, 1H), 7.16–7.08 (m, 1H), 1.30 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.4 (C_q), 166.9 (C_q), 163.0 (q, $^1J_{C\text{-}F}$ = 238 Hz, C_q), 161.7 (CH), 133.7 (q, $^4J_{C\text{-}F}$ = 4 Hz, C_q), 131.7 (CH), 131.5 (q, $^3J_{C\text{-}F}$ = 10 Hz, CH), 128.6 (q, $^3J_{C\text{-}F}$ = 10 Hz, C_q), 123.8 (CH), 117.8 (q, $^2J_{C\text{-}F}$ = 22 Hz, CH), 114.8 (q, $^2J_{C\text{-}F}$ = 22 Hz, CH), 44.5 (C_q), 28.5 (CH_3).

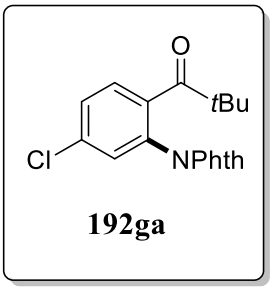
^{19}F-NMR (283 MHz, $CDCl_3$) δ = -107.7 (s).

IR (ATR): 2971, 1736, 1658, 1325, 1120, 821, 536 cm^{-1}.

MS (EI) *m/z* (relative intensity) 325 (65) [M^+], 221 (100), 148 (60), 139 (50).

HR-MS (ESI) *m/z* for $C_{20}H_{17}FNO_3$ [M+H^+] calcd.: 326.1114.
found: 326.1116.

Synthesis of 2-(5-Chloro-2-pivaloylphenyl)isoindoline-1,3-dione (192ga)



192ga

The representative procedure **A** was followed using 1-(4-chlorophenyl)-2,2-dimethylpropan-1-one (**184g**) (98.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ga** (116 mg, 68%) as a white solid.

M.p.: 126–127 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.84 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.73–7.68 (m, 2H), 7.55 (ddd, *J* = 7.6, 1.5 Hz, 1H), 7.46 (td, *J* = 7.6, 1.3 Hz, 1H), 7.34 (ddd, *J* = 7.9, 1.3, 0.5 Hz, 1H), 1.29 (s, 9H).

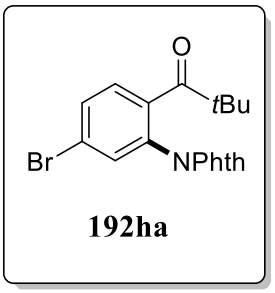
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.7 (C_q), 166.6 (C_q), 141.1 (C_q), 137.6 (C_q), 134.4 (CH), 133.6 (C_q), 130.8 (CH), 130.1 (CH), 129.2 (CH), 127.1 (C_q), 125.0 (CH), 44.5 (C_q), 28.4 (CH_3).

IR (ATR): 2990, 1836, 1725, 1429, 1185, 970, 715, 534 cm^{-1}.

MS (EI) *m/z* (relative intensity) 341 (65) [M^+], 281 (100), 162 (55), 139 (45).

HR-MS (ESI) *m/z* for $C_{19}H_{17}ClNO_3$ [M+H^+] calcd.: 342.0836.
found: 342.0839.

Synthesis of 2-(5-Bromo-2-pivaloylphenyl)isoindoline-1,3-dione (192ha)



192ha

The representative procedure **A** was followed using 1-(4-bromophenyl)-2,2-dimethylpropan-1-one (**184h**) (120 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ha** (136.7 mg, 71%) as a white solid.

M.p.:111–112 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.91–7.87 (m, 2H), 7.78–7.75 (m, 2H), 7.58 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.56–7.52 (m, 2H), 1.29 (s, 9H).

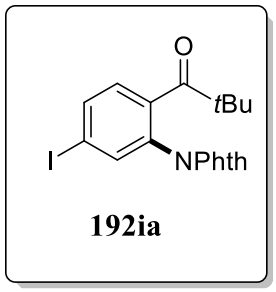
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.6 (C_q), 166.9 (C_q), 136.3 (C_q), 134.4 (CH), 133.2 (CH), 131.6 (CH), 131.0 (C_q), 130.7 (C_q), 128.0 (CH), 124.0 (CH), 123.8 (C_q), 44.5 (C_q), 28.4 (CH_3).

IR (ATR) 2930, 1820, 1735, 1502, 1112, 725, 435 cm^{-1}.

MS (EI) *m/z* (relative intensity) 385 (40) [^{79}Br, M^+], 388 (40) [^{81}Br, M^+], 217 (100), 138 (60), 140 (50).

HR-MS (ESI) *m/z* for $C_{19}H_{17}BrNO_3$ [$M+H^+$] calcd.: 386.0374.
found: 386.0375.

Synthesis of 2-(5-Iodo-2-pivaloylphenyl)isoindoline-1,3-dione (192ia)



192ia

The representative procedure **A** was followed using 1-(4-iodophenyl)-2,2-dimethylpropan-1-one (**184i**) (144 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ia** (115 mg, 53%) as a white solid.

M.p.: 108–109 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.91–7.88 (m, 2H), 7.79 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.76 (dd, *J* = 6.5, 2.1 Hz, 2H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 1.28 (s, 9H).

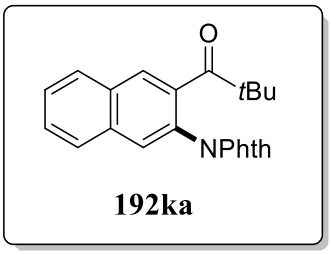
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.7 (C_q), 167.0 (C_q), 138.9 (CH), 137.0 (C_q), 136.8 (CH), 134.4 (CH), 131.6 (C_q), 130.4 (C_q), 128.0 (CH), 123.8 (CH), 95.6 (C_q), 44.5 (C_q), 28.4 (CH_3).

IR (ATR): 2958, 1713, 1676, 1367, 952, 712, 529 cm^{-1}.

MS (EI) *m/z* (relative intensity) 433 (25) [M^+], 328 (100), 276 (55), 115 (35).

HR-MS (ESI) *m/z* for $C_{19}H_{17}INO_3$ [M+H^+] calcd.: 434.0235.
found: 434.0237.

Synthesis of 2-(3-Pivaloylnaphthalen-2-yl)isoindoline-1,3-dione (192ka)



192ka

The representative procedure **A** was followed using 2,2-dimethyl-1-(naphthalen-2-yl)propan-1-one (**184k**) (106 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ka** (123 mg, 69%) as a white solid.

M.p.: 113–114 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.16 (s, 1H), 7.92– (dd, *J* = 7.2, 1.2 Hz, 3H), 7.88–7.85 (m, 1H), 7.84 (s, 1H), 7.77 (dd, *J* = 7.3, 1.2 Hz, 2H), 7.59 (dd, *J* = 7.3, 1.2 Hz, 2H), 1.39 (s, 9H).

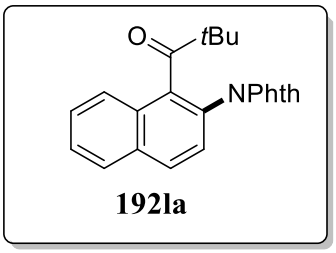
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.5 (C_q), 167.8 (C_q), 134.4 (C_q), 134.3 (CH), 133.5 (C_q), 132·0 (C_q), 131.6 (C_q), 129.6 (CH), 128.5 (CH), 128.1 (CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 126.7 (C_q), 123.7 (CH), 44.6 (C_q), 28.7 (CH_3).

IR (ATR): 2923, 1718, 1687, 1466, 1171, 1074, 832, 747 cm^{-1}.

MS (EI) *m/z* (relative intensity) 357 (25) [M^+], 308 (100), 276 (55), 115 (35).

HR-MS (ESI) *m/z* for $C_{23}H_{20}NO_3$ [M+H^+] calcd.: 358.1465.
found: 358.1460.

Synthesis of 2-(1-Pivaloylnaphthalen-2-yl)isoindoline-1,3-dione (192la)



192la

The representative procedure **A** was followed using 2,2-dimethyl-1-(naphthalen-1-yl)propan-1-one (**184l**) (106 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192la** (100 mg, 56%) as a white solid.

M.p.:112–113 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.16 (dd, *J* = 6.3, 0.7 Hz, 2H), 7.94–7.91 (m, 2H), 7.89–7.83 (m, 2H), 7.78–7.75 (m, 2H), 7.61–7.57 (m, 2H), 1.39 (s, 9H).

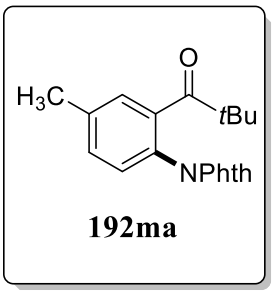
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.5 (C_q), 167.8 (C_q), 134.5 (C_q), 134.3 (CH), 133.5 (C_q), 132.0 (C_q), 131.6 (C_q), 129.7 (CH), 128.5 (CH), 128.1 (CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 126.8 (C_q), 123.7 (CH), 44.6 (C_q), 28.7 (CH_3).

IR (neat): 2926, 1869, 1726, 1518, 1327, 1248, 1057, 892 cm^{-1}.

MS (EI) *m/z* (relative intensity) 357 (55) [M^+], 318 (100), 221 (55), 108 (35).

HR-MS (ESI) *m/z* for $C_{23}H_{20}NO_3$ [M+H^+] calcd.: 358.1365.
found: 358.1370.

Synthesis of 2-(4-methyl-2-pivaloylphenyl)isoindoline-1,3-dione (192ma)



192ma

The representative procedure **A** was followed using 2,2-dimethyl-1-(3-tolyl)propan-1-one (**184m**) (115 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ma** (104 mg, 59%) as a white solid.

M.p.:138–139 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.45 (s, 1H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.22 (d, *J* = 7.3 Hz, 1H), 2.43 (s, 3H), 1.28 (s, 9H).

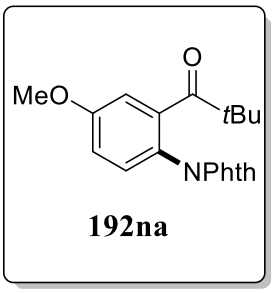
^{13}C NMR (126 MHz, $CDCl_3$): δ = 210.0 (C_q), 167.6 (C_q), 138.2 (C_q), 137.8 (C_q), 134.3 (CH), 131.9 (CH), 131.2 (C_q), 130.0 (CH), 127.4 (CH), 126.6 (C_q), 123.7 (CH), 44.4 (C_q), 28.3 (CH_3), 21.4 (CH_3).

IR (ATR): 2953, 1736, 1358, 1106, 1086, 982, 838, 509 cm^{-1}.

MS (EI) *m/z* (relative intensity) 321 (45) [M^+], 280 (100), 189 (55), 145 (40).

HR-MS (ESI) *m/z* for $C_{20}H_{20}NO_3$ [M+H^+] calcd.: 322.1456.
found: 322.1451.

Synthesis of 2-(4-Methoxy-2-pivaloylphenyl)isoindoline-1,3-dione (192na)



192na

The representative procedure **A** was followed using 1-(3-methoxyphenyl)-2,2-dimethylpropan-1-one (**184n**) (96.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192na** (98.0 mg, 56%) as a white solid.

M.p.:184–185 °C**.**

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 5.4, 3.0 Hz, 1H), 7.88 (dd, *J* = 5.4, 3.0 Hz, 1H), 7.72 (ddd, *J* = 5.3, 2·8, 1.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 1H), 6.95 (dd, *J* = 8.4, 2·3 Hz, 1H), 6.86 (s, 1H), 3.82 (s, 3H), 1.27 (s, 9H).

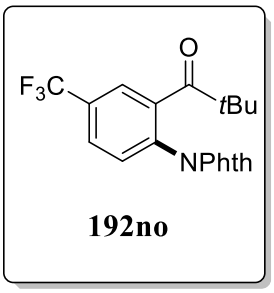
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.6 (C_q), 167.9 (C_q), 161.0 (C_q), 134.3 (CH), 134.0 (CH), 132·6 (C_q), 132·0 (CH), 131.9 (C_q), 129.8 (C_q), 123.6 (CH), 123.6 (CH), 55.6 (CH_3), 44.4 (C_q), 28.5 (CH_3).

IR (neat): 2981, 1664, 1219, 1120, 1027, 735, 656 cm^{-1}.

MS (EI) *m/z* (relative intensity) 337 (65) [M^+], 264 (100), 236 (60), 193 (50), 152 (30).

HR-MS (ESI) *m/z* for $C_{20}H_{20}NO_4$ [M+H^+] calcd.: 338.1374.
found: 338.1369.

Synthesis of 2-[(2-Pivaloyl-4-(trifluoromethyl)phenyl)]isoindoline-1,3-dione (192no)



192no

The representative procedure **A** was followed using 2,2-dimethyl-1-[(3-(trifluoromethyl)phenyl)]propan-1-one (**184n**) (124 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192no** (99.3 mg, 53%) as a white solid.

M.p.:124–124 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.93–7.89 (m, 3H), 7.80–7.76 (m, 3H), 7.53 (s, 1H), 1.33 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.2 (C_q), 166.8 (C_q), 138.0 (C_q), 134.6 (CH), 132.0 (q, $^2J_{C\text{-}F}$ = 35 Hz, C_q), 130.6 (q, $^1J_{C\text{-}F}$ = 272 Hz, C_q), 127.4 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 126.3 (CH), 125.2 (CH), 124.0 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 123.8 (C_q), (q, $^4J_{C\text{-}F}$ = 2 Hz, C_q), 44.5 (C_q), 28.4 (CH_3).

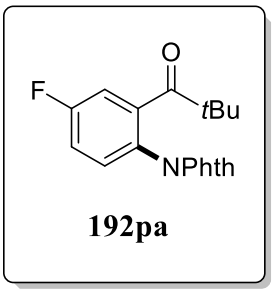
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -62.8 (s).

IR (ATR): 2964, 1895, 1325, 1263, 1126, 1054, 823, 728 cm^{-1}.

MS (EI) *m/z* (relative intensity) 375 (45) [M^+], 287 (100), 226 (70), 134 (45).

HR-MS (ESI) *m/z* for $C_{20}H_{16}F_3NO_3$ [M+H^+] calcd.: 376.1184.
found: 376.1179.

Synthesis of 2-(4-Fluoro-2-pivaloylphenyl)isoindoline-1,3-dione (192pa)



192pa

The representative procedure **A** was followed using 1-(3-fluorophenyl)-2,2-dimethylpropan-1-one (**184p**) (90.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192pa** (86.0 mg, 54%) as a white solid.

M.p.:116–118 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.82 (ddd, J = 5.5, 2.9, 0.4 Hz, 2H), 7.70 (d, J = 0.4 Hz, 2H), 7.71–7.69 (m, 2H), 7.16 (s, 1H), 1.30 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.3 (C_q), 166.8 (C_q), 163.8 (q, $^1J_{C\text{-}F}$ = 243 Hz, C_q), 161.7 (CH), 134.1 (CH), 133.6 (q, $^4J_{C\text{-}F}$ = 4 Hz, C_q), 131.6 (q, $^3J_{C\text{-}F}$ = 9 Hz, C_q), 128.5 (q, $^3J_{C\text{-}F}$ = 9 Hz, CH), 128.5 (CH), 117.8 (q, $^2J_{C\text{-}F}$ = 23 Hz, CH), 114.8 (C_q), 44.5 (C_q), 28.5 (CH_3).

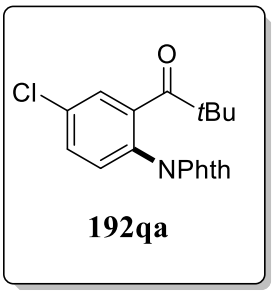
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -107.8 (s).

IR (ATR): 2969, 1782, 1257, 1127, 1028, 985, 844, 744 cm^{-1}.

MS (EI) *m/z* (relative intensity) 325 (55) [M^+], 223 (100), 118 (65), 142 (50).

HR-MS (ESI) *m/z* for $C_{20}H_{16}FNO_3$ [M+H^+] calcd.: 326.1164.
Found: 326.1159.

Synthesis of 2-(4-Chloro-2-pivaloylphenyl)isoindoline-1,3-dione (192qa)



192qa

The representative procedure **A** was followed using 2,2-dimethyl-1-(3-[(chloromethyl)phenyl)]propan-1-one (**184q**) (115 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192qa** (99.0 mg, 58%) as a white solid.

M.p.:114–115 °C**.**

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.97–7.83 (m, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.62 (d, *J* = 6.3 Hz, 1H), 7.52 (dd, *J* = 8.5, 0.7 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 1.30 (s, 9H).

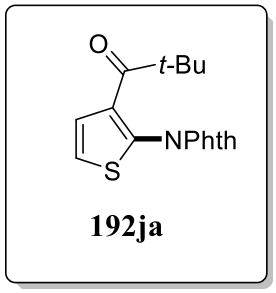
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.2 (C_q), 167.1(C_q), 138.9 (C_q), 134.4 (CH), 133.9 (C_q), 131.7 (CH), 131.3 (C_q), 130.6 (CH), 127.8 (CH), 127.0 (C_q), 123.8 (CH), 44.6 (C_q), 28.4 (CH_3).

IR (ATR): 2970, 1722, 1676, 1357, 1089, 734, 688 cm^{-1}.

MS (EI) *m/z* (relative intensity) 341 (45) [M^+], 284 (100), 168 (65), 135 (50).

HR-MS (ESI) *m/z* for $C_{19}H_{17}ClNO_3$ [M+H^+] calcd.: 342.0849.
found: 342.0852.

Synthesis of 2-(4-Pivaloylthiophen-3-yl)isoindoline-1,3-dione (192ja)



192ja

The representative procedure **A** was followed using 2,2-dimethyl-1-(thiophen-3-yl)propan-1-one (**184j**) (84.0 mg, 0.50 mmol), 1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183a**) (190 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ja** (101 mg, 59%) as a white solid.
M.p.:118–119 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.92 (ddd, *J* = 5.5, 3.2, 0.3 Hz, 2H), 7.78–7.75 (m, 2H), 7.46 (d, *J* = 5.8 Hz, 1H), 7.34 (d, *J* = 5.8 Hz, 1H), 1.29 (s, 9H).

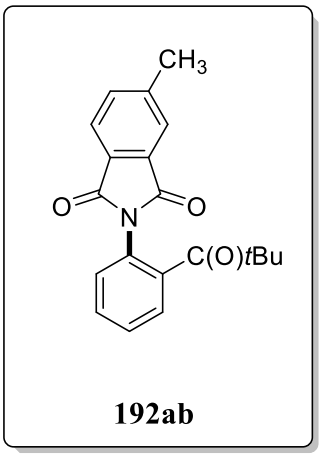
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 202.9 (C_q), 166.4 (C_q), 135.5 (CH), 135.2 (C_q), 134.5 (CH), 131.9 (C_q), 126.0 (CH), 124.0 (C_q), 123.7 (CH), 44.5 (C_q), 27.4 (CH_3).

IR (ATR): 2975, 1713, 1673, 1377, 759, 718, 530 cm^{-1}.

MS (EI) *m/z* (relative intensity) 313 (35) [M^+], 256 (100), 157 (60), 172 (55), 104 (30), 43 (10).

HR-MS (ESI) *m/z* for $C_{17}H_{16}NO_3S$ [$M+H^+$] calcd.: 314.0873
found: 314.0875.

Synthesis of 5-Methyl-2-(2-pivaloylphenyl)isoindoline-1,3-dione (192ab)



192ab

The representative procedure **B** was followed using 2,2-dimethyl-1-phenylpropan-1-one (**184a**) (82.0 mg, 0.50 mmol), 5-methyl-1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183b**) (199 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ab** (112 mg, 70%) as a white solid.

M.p.:154–156 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 7.6, 0.5 Hz, 1H), 7.69–7.64 (m, 2H), 7.55–7.51 (m, 2H), 7.43 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36–7.32 (m, 1H), 2.50 (s, 3H), 1.29 (s, 9H).

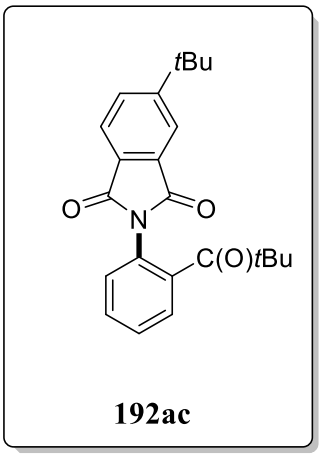
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.5 (C_q), 167.5 (C_q), 167.4 (C_q), 145.5 (C_q), 137.8 (C_q), 134.8 (CH), 132.2 (C_q), 130.5 (CH), 129.4 (C_q), 129.2 (C_q), 128.3 (CH), 127.7 (CH), 126.8 (CH), 124.1 (CH), 123.5 (CH), 44.4 (C_q), 28.4 (CH_3), 22.1 (CH_3).

IR (ATR): 2979, 1704, 1678, 1379, 1086, 965, 740 cm^{-1}.

MS (EI) *m/z* (relative intensity) 321 (55) [M^+], 281 (100), 286 (65), 256 (50), 193 (35).

HR-MS (ESI) *m/z* for $C_{20}H_{20}NO_3$ [M+H^+] calcd.: 322.1456
found: 322.1459.

Synthesis of 5-(*tert*-Butyl)-2-(2-pivaloylphenyl)isoindoline-1,3-dione (192ac)



192ac

The representative procedure **B** was followed using 2,2-dimethyl-1-phenylpropan-1-one (**184a**) (85.0 mg, 0.50 mmol), 5-(*tert*-butyl)-1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183c**) (224 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ac** (126 mg, 69%) as a white solid.

M.p.:172–173 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.82–7.75 (m, 2H), 7.68 (ddd, *J* = 7.7, 1.5, 0.5 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.46–7.42 (m, 1H), 7.33 (ddd, *J* = 7.8, 1.3, 0.5 Hz, 1H), 1.37 (s, 9H), 1.30 (s, 9H).

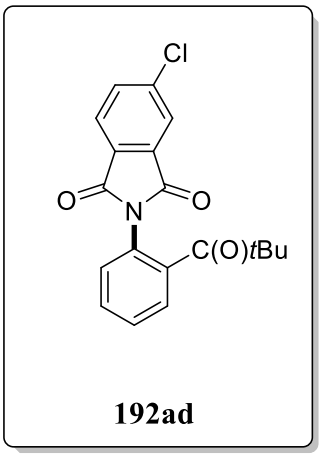
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 209.8 (C_q), 167.9 (C_q), 167.5 (CH), 159.0 (C_q), 137.8 (C_q), 132.1 (C_q), 131.4 (CH), 130.6 (CH), 130.2 (CH), 129.5 (C_q), 129.2 (CH), 127.8 (CH), 126.9 (C_q), 123.5 (C_q), 120.9 (CH), 44.4 (C_q), 35.8 (C_q), 31.1 (CH_3), 28.4 (CH_3).

IR (ATR): 2915, 1821, 1632, 1259, 1105, 1026, 862, 749 cm^{-1}.

MS (EI) *m/z* (relative intensity) 363 (35) [M^+], 284 (100), 286 (60), 256 (50), 193 (30), 43 (10).

HR-MS (ESI) *m/z* for $C_{23}H_{26}NO_4$ [M+H^+] calcd.: 364.0721,
found: 364.0729.

Synthesis of 5-Chloro-2-(2-pivaloylphenyl)isoindoline-1,3-dione (192ad)



192ad

The representative procedure **B** was followed using 2,2-dimethyl-1-phenylpropan-1-one (**184a**) (85.0 mg, 0.50 mmol), 5-chloro-1,3-dioxoisoindolin-2-yl-4-methylbenzenesulfonate (**183d**) (210 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (14.0 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $Cu(OAc)_2 \cdot H_2O$ (49.0 mg, 0.50 equiv). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **192ad** (115 mg, 68%) as a white solid.

M.p.: = 174–175 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 7.2, 1.5 Hz, 2H), 7.79 (dd, *J* = 7.3, 1.3 Hz, 2H), 7.62 (d, *J* = 7.3 Hz, 1H), 7.52 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.33–7.23 (m, 1H), 1.30 (s, 9H).

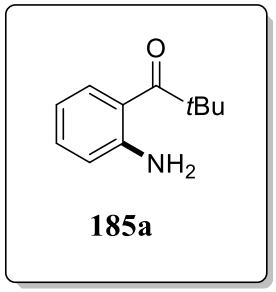
^{13}C-NMR (126 MHz $CDCl_3$): δ = 208.2 (C_q), 167.1 (C_q), 166.5 (C_q), 138.8 (C_q), 134.4 (CH), 134.0 (C_q), 132.8 (C_q), 131.5 (CH), 131.2 (C_q), 130.6 (CH), 128.8 (CH), 127.5 (CH), 127.0 (C_q), 123.8 (CH), 44.6 (C_q), 28.4 (CH_3).

IR (ATR): 2872, 1729, 1635, 1345, 1023, 721, 635 cm^{-1}.

MS (EI) *m/z* (relative intensity) 341 (45) [M^+], 306 (100), 307 (60), 291 (50), 276 (35), 57 (10).

HR-MS (ESI) *m/z* for $C_{19}H_{17}ClNO_3$ [M+H^+] calcd.: 342.0869.
found: 342.0871.

Synthesis of 1-(2-Aminophenyl)-2,2-dimethylpropan-1-one (185a)



185a

The representative procedure **C** was followed using a suspension of 2-(2-pivaloylphenyl)isoindoline-1,3-dione (**192aa**) (307 mg, 1.0 mmol) and hydrazine (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **185a** 1-(2-aminophenyl)-2,2-dimethylpropan-1-one (120 mg, 69%) as a orange liquid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.20–7.14 (m, 1H), 6.68 (ddd, *J* = 8.6, 2.0, 0.4 Hz, 2H), 5.63 (s, 2H), 1.37 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 209.5 (C_q), 149.4 (C_q), 132.4 (CH), 130.3 (CH), 118.8 (C_q), 117.8 (CH), 115.2 (CH), 44.8 (C_q), 29.0 (CH_3).

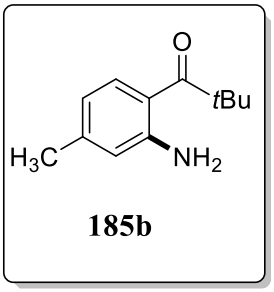
IR (ATR): 3472, 3341, 2953, 1620, 1465, 970, 805, 519 cm^{-1}.

MS (EI) *m/z* (relative intensity) 177 (55) [M^+], 120 (100), 149 (65), 149 (55), 92 (25), 57 (10).

HR-MS (ESI) *m/z* for $C_{11}H_{16}NO$ [$M+H^+$] calcd.:178.1259.
found: 178.1263.

The analytical data are in accordance with those reported in the literature[119].

Synthesis of 1-(2-Amino-4-methylphenyl)-2,2-dimethylpropan-1-one (185b)



185b

The representative procedure **C** was followed using a suspension of 2-(5-methyl-2-pivaloylphenyl)isoindoline-1,3-dione (**192ba**) (321 mg, 1.0 mmol) and hydrazine (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **185b** (137 mg, 72%) as a colorless liquid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.3 Hz, 1H), 6.48 (dd, *J* = 7.2, 1.3 Hz, 1H), 6.42 (dd, *J* = 6.8, 1.2 Hz, 1H), 5.81 (s, 2H), 2.23 (s, 3H), 1.37 (s, 9H).

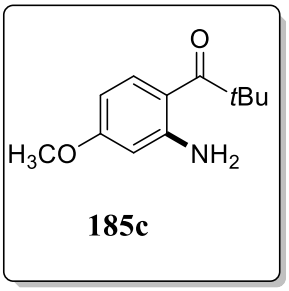
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.7 (C_q), 143.4 (C_q), 131.0 (CH), 130.8 (C_q), 118.0 (CH), 116.5 (CH), 115.8 (C_q), 44.6 (C_q), 29.0 (CH_3), 21.4 (CH_3).

IR (ATR): 3474, 3347, 2965, 1618, 1547, 1475, 1183, 970 cm^{-1}.

MS (EI) *m/z* (relative intensity) 190 (35) [M^+], 134 (100), 135 (60), 106 (55), 77 (25), 43 (10).

HR-MS (ESI) *m/z* for $C_{12}H_{17}ClNO$ [$M+H^+$] calcd.: 191.1301.
found: 191.1311.

Synthesis of 1-(2-Amino-4-methoxyphenyl)-2,2-dimethylpropan-1-one (185c)



185c

The representative procedure **C** was followed using a suspension of 2-(5-methoxy-2-pivaloylphenyl)isoindoline-1,3-dione (**192ca**) (337 mg, 1.0 mmol) and hydrazine (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **185c** (147 mg, 71%) as a colorless liquid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.3 Hz, 1H), 6.18 (dd, *J* = 7.2, 2.3 Hz, 2H), 6.1 (s, 2H), 3.77 (s, 3H), 1.37 (s, 9H).

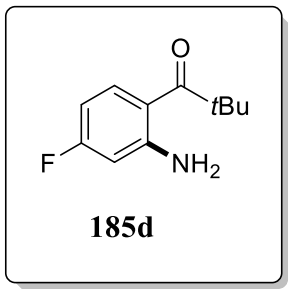
^{13}C-NMR (126 MHz $CDCl_3$): δ = 207.3 (C_q), 163.0 (C_q), 153.3 (C_q), 133.3 (CH), 111.6 (C_q), 103.1 (CH), 100.3 (CH), 55.1 (CH_3), 44.3 (C_q), 29.1 (CH_3).

IR (ATR): 3421, 2935, 1747, 1527, 1436, 1417, 1183 cm^{-1}.

MS (EI) *m/z* (relative intensity) 206 (35) [M^+], 150 (100), 151 (60), 122 (55), 107 (30), 95 (10).

HR-MS (ESI) *m/z* for $C_{18}H_{18}NO_2$ [$M+H^+$] calcd.: 207.1223
found: 207.1235.

Synthesis of 1-(2-Amino-4-fluorophenyl)-2,2-dimethylpropan-1-one (185d)



185d

The representative procedure **C** was followed using a suspension of 2-(5-fluoro-2-pivaloylphenyl)isoindoline-1,3-dione (**192da**) (325 mg, 1.0 mmol) and hydrazine (2.0 mL). Purification by column chromatography on silica on silica gel (*n*-hexane/EtOAc: 5:1) yielded **185d** (144 mg, 74%) as a yellow liquid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.88–7.79 (m, 1H), 6.36–6.26 (m, 2H), 6.00 (s, 2H), 1.37 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 208.4 (C_q), 166.2 (C_q), 164.2 (C_q), 133.5 (CH), 116.5 (C_q), 114.7 (CH), 103.3 (CH), 44.6 (C_q), 29.0 (CH_3).

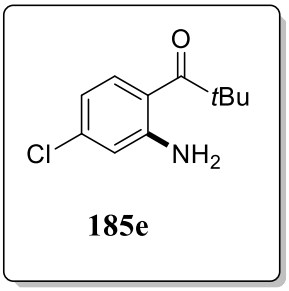
^{19}F NMR (282 MHz, $CDCl_3$): δ = ‑106.6.

IR (ATR): 3487, 3361, 2928, 1681, 1254, 1142, 783, 541 cm^{-1}.

MS (EI) *m/z* (relative intensity) 195 (45) [M^+], 195 (100), 165 (65), 142 (50), 112 (30), 86 (10).

HR-MS (ESI) *m/z* for $C_{11}H_{15}FNO$ [$M+H^+$] calcd.: 196.1059.
found: 196.1062.

Synthesis of 1-(2-Amino-4-chlorophenyl)-2,2-dimethylpropan-1-one (185e)



185e

The representative procedure **C** was followed using a suspension of 2-(5-chloro-2-pivaloylphenyl)isoindoline-1,3-dione (**192ea**) (342 mg, 1.0 mmol) and hydrazine (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **185e** (144 mg, 68%) as a red liquid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.7 Hz, 1H), 6.65 (dd, *J* = 7.1, 1.3 Hz, 1H), 6.57 (dd, *J* = 8.7, 2.1 Hz, 1H), 5.82 (s, 2H), 1.36 (s, 9H).

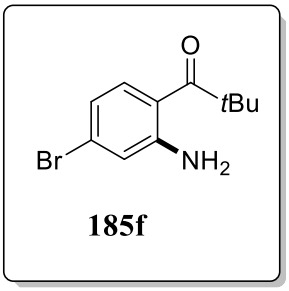
^{13}C-NMR (126 MHz $CDCl_3$): δ = 208.6 (C_q), 151.0 (C_q), 138.4 (C_q), 132.0 (CH), 117.0 (CH), 116.6 (CH), 115.4 (C_q), 44.7 (C_q), 28.8 (CH_3).

IR (ATR): 3469, 3347, 3967, 1602, 1535, 1178, 953, 766 cm^{-1}.

MS (EI) *m/z* (relative intensity) 210 (10) [M^+], 154 (100), 156 (70), 126 (55), 99 (30), 69 (10).

HR-MS (ESI) *m/z* for $C_{11}H_{15}ClNO$ [$M+H^+$] calcd.: 211.0764.
found: 211.0766.

Synthesis of 1-(2-Amino-4-bromophenyl)-2,2-dimethylpropan-1-one (185f)



185f

The representative procedure **C** was followed using a suspension of 2-(2-pivaloylphenyl)isoindoline-1,3-dione (**192fa**) (386 mg, 1.0 mmol) and hydrazine (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **185f** (143 mg, 56%) as a orange liquid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.3 Hz, 1H), 6.83 (dd, *J* = 7.3, 1.4 Hz, 1H), 6.72 (dd, *J* = 8.3, 2.0, Hz, 1H), 5.78 (s, 2H), 1.35 (s, Hz, 9H).

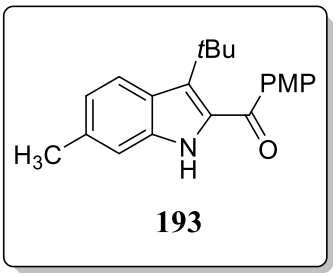
^{13}C-NMR (126 MHz $CDCl_3$): δ = 208.8 (C_q), 150.9 (C_q), 131.8 (CH), 126.9 (C_q), 120.1 (CH), 118.3 (CH), 117.1 (C_q), 44.8 (C_q), 28.7 (CH_3).

IR (ATR): 3462, 3254, 2915, 1578, 1364, 851, 816, 470 cm^{-1}.

MS (EI) *m/z* (relative intensity) 255 (40) [M^+], 198 (100), 170 (60), 296 (50), 143 (30), 91 (10).

HR-MS (ESI) *m/z* for $C_{11}H_{15}BrNO$ [$M+H^+$] calcd.: 256.1430.
found: 256.1434.

Synthesis of [(3-(*tert*-Butyl)-6-methyl-1H-indol-2-yl)](4-methoxyphenyl)methanone (193)



193

The representative procedure **D** was followed using a suspension of 1-(2-amino-4-methylphenyl)-2,2-dimethylpropan-1-one (**185b**) (95.5 mg. 0.50 mmol), 2-bromo-1-(4-methoxyphenyl)ethan-1-one (170 mg, 1.5 equiv), and anhydrous DMF (2 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **193** (130 mg, 81%) as a yellow solid.

M.p.: 203–204 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.4 Hz, 2H), 7.78 (d, *J* = 7.4 Hz, 2H), 7.09 (s, 1H), 6.98 (dd, *J* = 7.3, 1.2, Hz, 1H), 6.93–6.89 (m, 1H), 3.86 (s, 3H), 2.44 (s, 3H), 1.44 (s, 9H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 192.0 (C_q), 164.0 (C_q), 136.4 (C_q), 133.2 (C_q), 132.4 (CH), 131.7 (C_q), 129.6 (CH), 127.1 (C_q), 124.6 (C_q), 122.7 (CH), 120.3 (CH), 113.8 (CH), 111.2 (CH), 55.6 (CH_3), 33.3 (C_q), 31.7 (CH_3), 21.5 (CH_3).

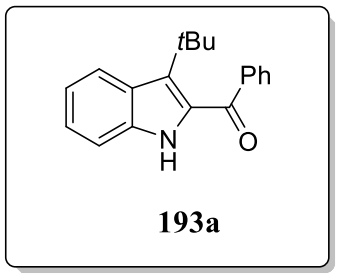
IR (ATR): 3217, 2930, 1600, 1253, 1107, 984, 681 cm^{-1}.

MS (EI) *m/z* (relative intensity) 320 (45) [M^+], 135 (100), 306 (65), 296 (50), 107 (30), 85 (10).

HR-MS (ESI) *m/z* for $C_{21}H_{23}NO_2$ [M+H^+] calcd.: 321.1729.
found: 321.1736.

The analytical data are in accordance with those reported in the literature[110].

Synthesis of [(3-(*tert*-Butyl)-1H-indol-2-yl)](phenyl)methanone (193a)



193a

The representative procedure **D** was followed using a suspension of 1-(2-aminophenyl)-2,2-dimethylpropan-1-one (**185a**) (88.5 mg. 0.50 mmol), 2-bromo-1-phenylethan-1-one (149 mg, 1.5 equiv) and anhydrous DMF (2 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **193a** (123 mg, 89%) as a yellow solid.

M.p.: 203–204 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 (s, 1H), 7.98 (dd, J = 8.5, 1.0 Hz, 1H), 7.81 (dd, J = 8.3, 1.4 Hz, 2H), 7.60–7.57 (m, 1H), 7.45 (dd, J = 8.2, 1.3 Hz, 2H), 7.32–7.30 (m, 1H), 7.26–7.22 (m, 1H), 7.14 (ddd, J = 8.2, 1.9, 1.1 Hz, 1H), 1.47 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 193.2 (C_q), 138.6 (C_q), 136.0 (C_q), 133.6 (CH), 130.0 (CH), 129.7 (CH), 12
8.0 (C_q), 126.7 (C_q), 125.6 (CH), 123.5 (CH), 123.2 (CH), 119.7 (CH), 111.6 (CH), 33.4 (C_q), 31.7 (CH_3).

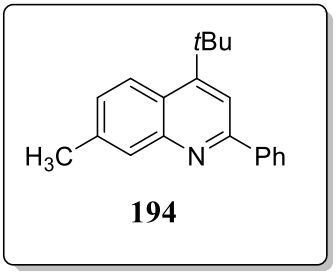
IR (ATR): 3345, 2955, 1642, 1261, 1127, 742, 681, 595 cm^{-1}.

MS (EI) *m/z* (relative intensity) 276 (45) [M^+], 262 (100), 247 (80), 105 (60), 234 (25), 43 (10).

HR-MS (ESI) *m/z* for $C_{19}H_{20}NO$ [$M+H^+$] calcd.: 277.1467.
found: 277.1462

The analytical data are in accordance with those reported in the literature[110].

Synthesis of 4-(*tert*-Butyl)-7-methyl-2-phenylquinoline (194)



194

The representative procedure **E** was followed using a suspension of 1-(2-amino-4-methylphenyl)-2,2-dimethylpropan-1-one (**185b**) (95.5 mg. 0.50 mmol), 2-bromo-ethynylbenzene (77.0 mg, 1.5 equiv), $InCl_3$ (14.8 mg, 20 mol %) and anhydrous CH_3CN (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) yielded **194** (111 mg, 81%) as a yellow solid.

M.p.:179–180 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.28 (d, J = 8.7 Hz, 1H), 8.12–8.10 (m, 2H), 7.99 (s, 1H), 7.75 (s, 1H), 7.52–7.48 (m, 2H), 7.45 (dd, J = 8.2, 1.7, Hz, 1H), 7.33 (ddd, J = 8.9, 2.0, 0.6 Hz, 1H), 2·54 (s, 3H), 1.64 (s, 9H).

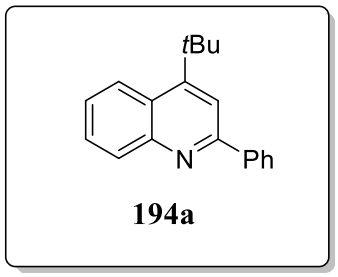
^{13}C NMR (126 MHz, $CDCl_3$): δ = 157.0 (C_q), 156.5 (C_q), 148.5 (CH), 138.7 (CH), 131.0 (C_q), 129.7 (C_q), 128.0 (CH), 127.5 (CH), 126.2 (C_q), 125.9 (C_q), 124.8 (CH), 119.3 (CH), 116.1 (CH), 115.4 (CH), 36.3 (C_q), 31.2 (CH_3), 28.4 (CH_3).

IR (ATR): 2927, 1543, 1056, 1219, 981, 786, 647 cm^{-1}.

MS (EI) *m/z* (relative intensity) 274 (55) [M^+], 260 (100), 43 (40), 244 (35), 219 (25), 58 (10).

HR-MS (ESI) *m/z* for $C_{20}H_{21}N$ [$M+H^+$] calcd.: 275.1674.
found: 275.1680.

Synthesis of 4-(*tert*-Butyl)-2-phenylquinoline (194a)



194a

The representative procedure **E** was followed using a suspension of 1-(2-aminophenyl)-2,2-dimethylpropan-1-one (**185a**) (88.5 mg. 0.50 mmol), 2-bromo-ethynylbenzene (77.0 mg, 1.5 equiv), $InCl_3$ (14.8 mg, 20 mol %) and anhydrous CH_3CN (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) to yielded **194a** (123 mg, 94%) as a yellow solid.

M.p.:183–184 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.42 (dd, J = 8.3, 1.3 Hz, 1H), 8.24 (dd, J = 8.4, 1.4 Hz, 2H), 8.17–8.15 (m, 2H), 7.67 (ddd, J = 8.2, 5.3, 1.3 Hz, 2H), 7.55–7.45 (m, 3H), 1.68 (s, 9H).

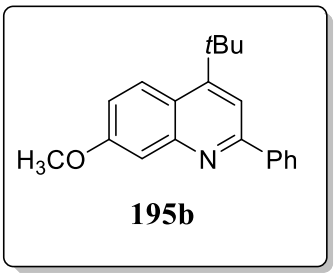
^{13}C NMR (126 MHz, $CDCl_3$): δ = 157.0 (C_q), 156.2 (C_q), 149.6 (C_q), 140.2 (C_q), 131.4 (CH), 129.1 (CH), 128.2 (CH), 127.5 (CH), 126.3 (CH), 125.9 (C_q), 124.8 (CH), 119.3 (CH), 116.2 (CH), 36.3 (C_q), 31.3 (CH_3).

IR (ATR): 2957, 1586, 1227, 761, 691 cm^{-1}.

MS (EI) *m/z* (relative intensity) 260 (65) [M^+], 258 (100), 243 (90), 115 (65), 226 (25), 53 (10).

HR-MS (ESI) *m/z* for $C_{19}H_{19}N$ [$M+H^+$] calcd.: 261.1517.
found: 261.1521.

Synthesis of 4-(*tert*-Butyl)-7-methoxy-2-phenylquinoline (195b)



195b

The representative procedure **E** was followed using a suspension of 1-(2-amino-4-methoxyphenyl)-2,2-dimethylpropan-1-one (**185c**) (103 mg. 0.50 mmol), 2-bromo-ethynylbenzene (77.0 mg, 1.5 equiv), $InCl_3$ (14.8 mg, 20 mol %) and anhydrous CH_3CN (2.0 mL). Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 5:1) to yielded **195b** (122 mg, 84%) as a yellow solid.

M.p.:189–190 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, J = 7.5 Hz, 1H), 8.12–8.08 (m, 2H), 7.68 (s, 1H), 7.55 (dd, J = 7.5, 1.3 Hz, 2H), 7.45–7.43 (m, 1H), 7.15 (dd, J = 7.3, 1.2 Hz, 2H), 3.96 (s, 3H), 1.64 (s, 9H).

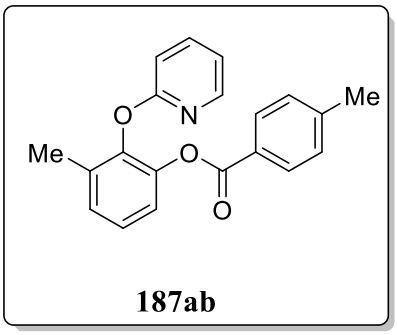
^{13}C-NMR (101 MHz, $CDCl_3$): δ = 159.4 (C_q), 157.5 (C_q), 156.3 (C_q), 151.6 (C_q), 140.5 (C_q), 129.0 (CH), 128.7 (CH), 127.5 (CH), 123.4 (CH), 121.0 (C_q), 117.7 (CH), 114.4 (CH), 109.2 (CH), 55.5 (CH_3), 36.3 (C_q), 31.3 (CH_3).

IR (ATR): 2957, 1591, 1024, 1276, 924, 726, 689 cm^{-1}.

MS (EI) *m/z* (relative intensity) 290 (80) [M^+], 276 (100), 290 (30), 235 (30), 191 (10).

HR-MS (ESI) *m/z* for $C_{20}H_{21}NO$ [$M+H^+$] calcd.: 291.1623.
found: 291.1620.

Synthesis of 3-Methyl-2-{(pyridin-2-yloxy)phenyl 4-methyl}benzoate (187ab)



187ab

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine (**186a)** (185.4 mg, 1.0 mmol) and *p*-toluic acid (**101b)** (68.4 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **186ab** (124 mg, 78%) as a white solid.

M.p.: 90–92 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.13 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.51 (dd, *J* = 8.2, 5.2, Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.13–7.10 (m, 3H), 6.95–6.72 (m, 1H), 6.82 (d, *J* = 8, 6.2 Hz, 2H), 2.36 (s, 3H), 2.33 (s, 3H).

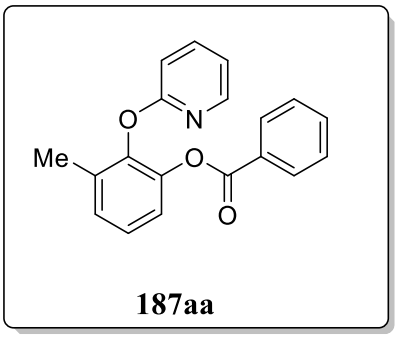
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.0 (C_q), 162.8 (C_q), 147.1(CH), 144.7 (C_q), 143.8 (C_q), 140.2 (C_q), 138.9 (CH), 136.4 (C_q), 129.6 (CH), 128.6 (CH), 126.0 (C_q), 125.8 (CH), 123.3 (CH), 123.1 (CH), 118.1 (CH), 110.6 (CH), 21.2 (CH_3), 20.7 (CH_3).

IR (ATR): 2922, 1726, 1428, 1288, 1270, 1176, 1017, 776 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (79) $[C_{12}H_{10}NO]^+$, 172 (4), 119 (100), 91 (41), 78 (7), 65 (13), 51(5).

HR-MS (ESI) *m/z* for $C_{20}H_{18}NO_3$ $[M+H]^+$ calcd.: 320.1287.
found: 320.1283.

Synthesis of 3-Methyl-2-{(pyridin-2-yloxy)phenyl 4-methyl}benzoate (187aa)



187aa

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine (**186a)** (185.4 mg, 1.0 mmol) and benzoic acid (**101a)** (61.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187aa** (112 mg, 73%) as a white solid.

M.p.: 98–100 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (dd, *J* = 5.0, 1.7, 0.8 Hz, 1H), 7.81 (dd, *J* = 8.5, 1.1 Hz, 2H), 7.61–7.46 (m, 2H), 7.40–7.29 (m, 2H), 7.21–7.10 (m, 3H), 6.89 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.85–6.77 (m, 1H), 2.26 (s, 3H).

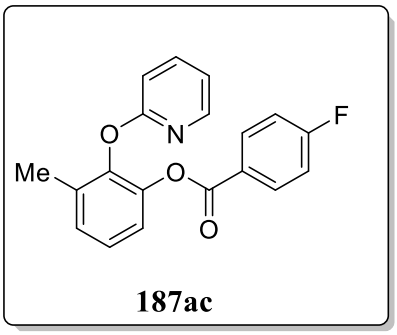
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.1 (C_q), 162.9 (C_q), 147.4 (CH), 145.3 (C_q), 144.1 (C_q), 142.8 (C_q), 139.1 (CH), 129.9 (CH), 128.9 (CH), 126.6 (C_q), 126.2 (CH), 125.4 (CH), 123.8 (CH), 123.1 (CH), 118.4 (CH), 110.9 (CH), 21.7 (CH_3).

IR (ATR): 1758, 1578, 1415, 1397, 1284, 1125, 1043, 742 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 172 (10), 105 (100), 78 (15), 77 (60), 66 (5), 51 (19).

HR-MS (ESI) *m/z* for $C_{19}H_{16}NO_3$ $[M+H]^+$ calcd.: 306.1130.
found: 306.1126.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl 4-fluorobenzoate (187ac)



187ac

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and 4-flourobenzoic acid **(101c)** (70.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ac** (107 mg, 66%) as a white solid.

M.p.:116–118 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.81 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.53 (dd, *J* = 8.3, 5.2, Hz, 1H), 7.18 (d, *J* = 2.7 Hz, 3H), 6.99 (dd, *J* = 8.9, 8.4 Hz, 2H), 6.88 (dd, *J* = 7.2, 5.0, Hz, 1H), 6.79 (d, *J* = 8.3, 0.9 Hz, 1H), 2.25 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 166.8 (C_q), 164.7 (C_q), 163.1 (d, $^1J_{C\text{-}F}$ = 250 Hz, C_q), 147.4 (CH), 143.3 (C_q), 143.0 (d, $^2J_{C\text{-}F}$ = 20 Hz, CH), 139.1 (CH), 133.0 (C_q), 132.3 (CH), 133.5 (d, $^3J_{C\text{-}F}$ = 10 Hz, CH), 128.4 (CH), 125.2 (d, $^4J_{C\text{-}F}$ = 3 Hz, C_q), 120.9 (CH), 118.0 (CH), 115.4 (d, $^2J_{C\text{-}F}$ = 20 Hz, CH), 110.1 (CH), 16.4 (CH_3).

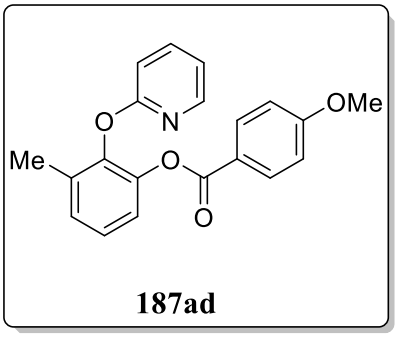
^{19}F-NMR (283 MHz, $CDCl_3$) δ = -104.6 (s).

IR (neat): 1733, 1601, 1462, 1426, 1276, 1228, 1085, 850, 812 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (83) $[C_7H_4FO_2]^+$, 123 (100), 95 (34), 78 (6), 111 (30), 78 (10), 51 (5), 43 (13).

HR-MS (ESI) *m/z* for $C_{19}H_{15}FNO_3$ $[M+H]^+$ calcd.: 324.1036.
found: 324.1034.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl 4-methoxybenzoate (187ad)



187ad

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and 4-methoxybenzoic acid **(101d)** (76.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ad** (106 mg, 63%) as a white solid.

M.p.:102–104 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16 (dd, *J* = 5.0, 2.0, Hz, 1H), 7.81–7.71 (m, 2H), 7.60 (dd, *J* = 8.3, 7.2, Hz, 1H), 7.27–7.14 (m, 3H), 6.95–6.74 (m, 4H), 3.72 (s, 3H), 2.47 (s, 3H).

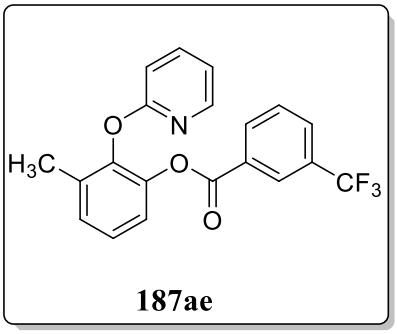
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.9 (C_q), 163.5 (C_q), 162.8 (C_q), 147.4 (CH), 143.5 (C_q), 143.2 (C_q), 139.0 (CH), 133.0 (C_q), 132.0 (CH), 128.2 (CH), 125.2 (CH), 121.3 (C_q), 121.1 (CH), 118.0 (CH), 113.4 (CH), 110.2 (CH), 55.4 (CH_3), 16.4 (CH_3).

IR (ATR): 1730, 1428, 1262, 1234, 1095, 1076, 773, 747 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (40) $[C_{12}H_{10}NO]^+$, 136 (12), 135 (100), 107 (10), 86 (11), 84 (19), 77 (15) 51 (5).

HR-MS (ESI) *m/z* for $C_{20}H_{18}NO_4$ $[M+H]^+$ calcd.: 336.1236.
found 336.1238.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl 3-(trifluoromethyl)benzoate (187ae)



187ae

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and 3-(triflouromethyl)benzoic acid **(101e)** (95.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ae** (110 mg, 59%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16 (d, *J* = 4.6, 2.3 Hz, 1H), 8.09–8.01 (m, 1H), 8.01–7.95 (m, 1H), 7.83 (dd, *J* = 8.3, 3.3 Hz, 1H), 7.61–7.45 (m, 2H), 7.28–7.19 (m, 3H), 6.95–6.80 (m, 2H), 2.29 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.1 (C_q), 162.9 (C_q), 147.4 (CH), 145.3 (C_q), 144.1 (CH), 142.8 (CH), 139.1 (C_q), 128.9 (q, $^2J_{C\text{-}F}$ = 33 Hz, C_q), 129.9 (CH), 126.4 (C_q), 126.2 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 125.4 (C_q), 125.4 (CH), 123.8 (q, $^1J_{C\text{-}F}$ = 272 Hz, C_q), 123.1 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 118.4 (CH), 110.9 (CH), 21.7 (CH_3).

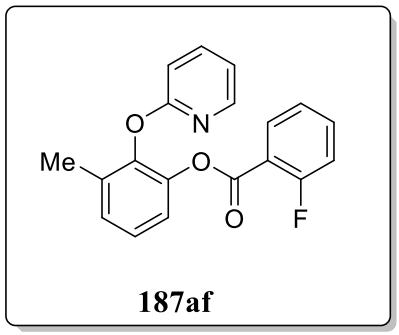
^{19}F-NMR (283 MHz, $CDCl_3$) δ = -62.81.

IR (ATR): 1746, 1465, 1428, 1334, 1242, 1170, 906, 726 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 173 (59), 145 (46), 126 (4), 83 (9), 78 (9) 51 (5), 43 (20).

HR-MS (ESI) *m/z* for $C_{20}H_{15}F_3NO_3$ $[M+H]^+$ calcd.: 374.1004.
found: 374.0999.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl 2-fluorobenzoate (187af)



187af

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and 2-fluorobenzoic acid **(101f)** (70.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187af** (92 mg, 62%) as a white solid.

M.p.:118–120. °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16 (ddd, J = 5.0, 2.0, 0.8 Hz, 1H), 7.70–7.61 (m, 1H), 7.61 (dd, J = 8.3, 5.2, Hz, 1H), 7.53–7.44 (m, 1H), 7.21-7.18 (m, 3H), 7.15–7.02 (m, 2H), 6.96–6.81 (m, 2H), 2.47 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.0 (d, $^1J_{C\text{-}F}$ = 272 Hz, C_q), 162.6 (C_q), 161.4 (d, $^3J_{C\text{-}F}$ = 4 Hz, C_q), 147.4 (CH), 142.9 (C_q), 143.1 (C_q), 139.1 (CH), 134.9 (d, $^3J_{C\text{-}F}$ = 10 Hz, CH), 133.1 (C_q), 132.1 (CH), 128.9 (CH), 125.3 (CH), 123.7 (d, $^4J_{C\text{-}F}$ = 4 Hz, CH), 120.9 (CH), 118.0 (d, $^2J_{C\text{-}F}$ = 10 Hz, C_q), 117.5 (CH), 116.9 (d, $^2J_{C\text{-}F}$ = 22 Hz, CH), 110.0 (CH), 16.4 (CH_3).

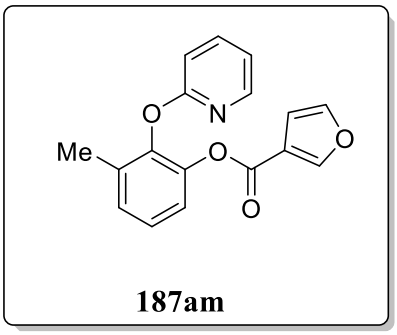
^{19}F-NMR (283 MHz, $CDCl_3$) δ = -108.7.

IR (ATR): 1737, 1717, 1426, 1271, 1185, 879, 816, 747 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (88) $[C_{12}H_{10}NO]^+$, 172 (5), 123 (100), 95 (26), 66 (4), 51 (6).

HR-MS (ESI) *m/z* for $C_{19}H_{15}FNO_4$ $[M+H]^+$ calcd.: 323.0958.
found: 323.0951.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl furan-3-carboxylate (187am)



187am

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and furan-3-carboxylic acid **(101m)** (56.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187am** (90 mg, 61%) as a white solid.

M.p.:102–104 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16–8.08 (m, 1H), 7.77–7.69 (m, 1H), 7.59 (ddd, *J* = 10.5, 5.3, 3.7, 2.0 Hz, 1H), 7.35 (d, *J* = 5.3, 1.8 Hz, 1H), 7.29–7.14 (m, 3H), 6.97–6.80 (m, 2H), 6.59 (dd, *J* = 5.1, 1.8, Hz, 1H), 2.51 (s, 3H).

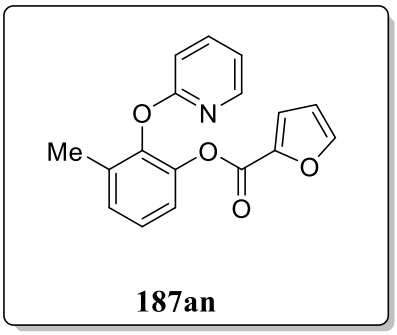
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 162.7 (C_q), 160.3 (C_q), 148.3 (CH), 147.5 (CH), 143.6 (CH), 143.4 (C_q), 142.7 (C_q), 139.1 (CH), 133.0 (C_q), 128.4 (CH), 125.2 (CH), 121.0 (CH), 118.1 (C_q), 118.0 (CH), 110.1 (CH), 109.8 (CH), 16.4 (CH_3).

IR (ATR): 2921, 2852, 1739, 1465, 1426, 1156, 1113, 771 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 172 (5), 119 (2), 102 (3), 96 (4), 95 (74) 78 (11), 67 (4) 51 (5).

HR-MS (ESI) *m/z* for $C_{17}H_{14}NO_4$ $[M+H]^+$ calcd.: 296.0923.
found: 296.0924.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl furan-2-carboxylate (187an)



187an

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and furan-2-carboxylic acid **(101n)** (56.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187an** (93 mg, 63%) as an off-white solid.

M.p.: 101–103 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, J = 4.5, 1.9 Hz, 1H), 7.65–7.46 (m, 2H), 7.21 (d, J = 5.1 Hz, 3H), 6.97–6.75 (m, 3H), 6.47–6.36 (m, 1H), 2.62 (s, 3H).

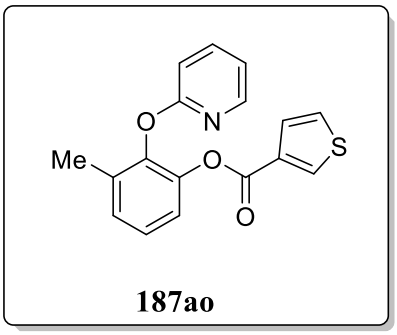
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 162.6 (C_q), 155.8 (C_q), 147.4 (CH), 146.9 (CH), 143.4 (C_q), 142.4 (C_q), 139.0 (CH), 133.1 (C_q), 128.5 (CH), 125.2 (CH), 120.9 (CH), 119.0 (CH), 118.0 (C_q), 111.7 (CH), 110.1 (CH), 16.4 (CH_3).

IR (neat): 1724, 1464, 1427, 1289, 1273, 1095, 767, 748 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 172 (6), 119 (2), 102 (3), 96 (4), 95 (76) 78 (9), 67 (4) 51 (6).

HR-MS (ESI) *m/z* for $C_{17}H_{14}NO_4$ $[M+H]^+$ calcd.: 296.0923.
found: 296.0920.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl thiophene-3-carboxylate (187ao)



187ao

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and thiophene-3-carboxylic acid **(101o)** (64.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ao** (89 mg, 57%) as a white solid.

M.p.: 95–97 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (dd, *J* = 5.1, 2.0 Hz, 1H), 7.79–7.68 (m, 1H), 7.61–7.43 (m, 2H), 7.33–7.18 (m, 2H), 7.14–7.02 (m, 2H), 6.91 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.81 (d, *J* = 8.3, 0.9 Hz, 1H), 2.49 (s, 3H).

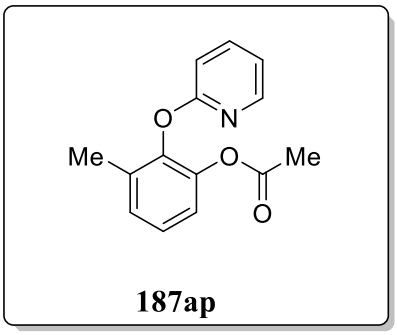
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 162.9 (C_q), 160.0 (C_q), 147.4 (CH), 144.8 (C_q), 140.0 (C_q), 139.1 (CH), 136.8 (C_q), 133.6 (CH), 132.2 (C_q), 127.9 (CH), 126.0 (CH), 125.8 (CH), 123.5 (CH), 123.2 (CH), 118.3 (CH), 110.9 (CH), 21.1 (CH_3).

IR (ATR): 1724, 1234, 1178, 1090, 1061, 853, 788, 420 cm^{-1}.

HR-MS (EI) *m/z* (relative intensity) 184 (79) $[C_{12}H_{10}NO]^+$, 172 (6), 111 (100), 91 (4), 83 (12), 78 (10), 51 (7), 43 (19).

HR-MS (ESI) *m/z* for $C_{17}H_{14}NO_3S$ $[M+H]^+$ calcd.: 312.0694.
found: 312.0693.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl acetate (187ap)



187ap

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and acetic acid **(101p)** (1 mL, 17 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol) for 30 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ap** (139 mg, 57%) as a white solid.

M.p.: 101–103 °C.

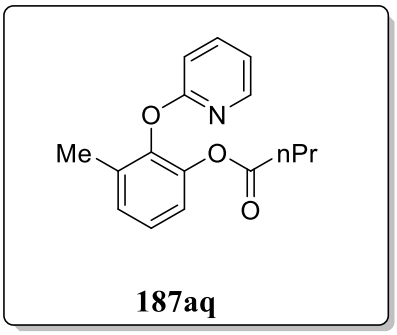
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.18–8.10 (ddd, *J* = 5.0, 2.0, 1.0 Hz, 1H), 7.71–7.62 (m, 1H), 7.20–7.13 (m, 2H), 7.08–7.02 (m, 1H), 6.99–6.86 (m, 2H), 2.23 (s, 3H), 1.96 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 168.3 (C_q), 162.6 (C_q), 147.5 (CH), 143.3 (C_q), 143.0 (C_q), 139.2 (CH), 133.0 (C_q), 128.2 (CH), 125.2 (CH), 120.8 (CH), 118.0 (CH), 109.8 (CH), 20.4 (CH_3), 16.3 (CH_3). IR (neat): 2923, 1759, 1571, 1401, 1211, 1173, 1077, 768 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 201 (20), 172 (18), 79 (7), 78 (14), 66 (4), 51 (7), 43 (13).

HR-MS (ESI) *m/z* for $C_{14}H_{14}NO_3$ $[M+H]^+$ calcd.: 244.0895.
found: 244.0973.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl butanoate (187aq)



187aq

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and butyric acid **(101q)** (44.5 mg, 0.50 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187aq** (87 mg, 64%) as an off-white solid.

M.p.: 58–60 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.26–8.04 (m, 1H), 7.75–7.60 (m, 1H), 7.21–7.11 (m, 2H), 7.08–7.01 (m, 1H), 6.99–6.85 (m, 2H), 2.27 (t, *J* = 7.4 Hz, 2H), 2.19 (s, 3H), 1.61–1.43 (m, 2H), 0.96 (s, 3H).

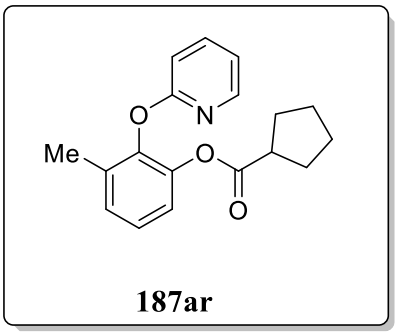
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 171.1 (C_q), 162.7 (C_q), 147.6 (CH), 143.2 (C_q), 139.2 (CH), 133.0 (C_q), 128.3 (CH), 125.3 (CH), 121.0 (CH), 118.0 (CH), 109.9 (CH), 35.8 (CH_2), 18.3 (CH_2), 16.4 (CH_3), 13.6 (CH_3).

IR (ATR): 2965, 1760, 1463, 1426, 1270, 1235, 775 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 201 (23), 172 (6), 79 (3), 71 (11), 66 (4), 51 (5), 43 (18).

HR-MS (ESI) *m/z* for $C_{16}H_{18}NO_3$ $[M+H]^+$ calcd.: 272.1278.
found: 272.1289.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl cyclopentanecarboxylate (187ar)



187ar

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and cyclopentanecarboxylic acid **(101r)** (57.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ar** (108 mg, 73%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.17–8.10 (m, 1H), 7.65 (ddd, *J* = 10.4, 6.3, 2.1 Hz, 1H), 7.19–7.13 (m, 2H), 7.04 (dd, *J* = 6.2, 3.5 Hz, 1H), 6.99–6.84 (m, 2H), 2.77–2.69 (m, 1H), 2.20 (d, *J* = 1.8 Hz, 3H), 1.77–1.46 (m, 8H).

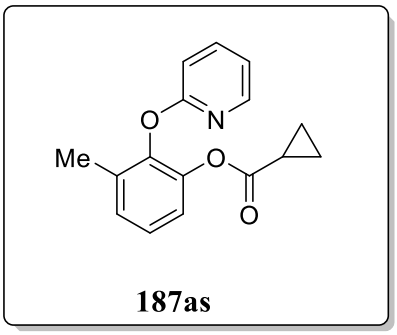
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 174.1 (C_q), 162.7 (C_q), 147.6 (CH), 143.4 (C_q), 143.4 (C_q), 139.1 (CH), 133.0 (C_q), 128.2 (CH), 125.3 (CH), 120.9 (CH), 118.0 (CH), 109.9 (CH), 43.6 (CH), 29.8 (CH_2), 25.8 (CH_2), 16.4 (CH_3).

IR (ATR): 2955, 2871, 1755, 1463, 1462, 1271, 1119, 774 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 201 (27), 172 (6), 144 (4), 78 (7), 69 (22), 51 (6), 41 (10).

HR-MS (ESI) *m/z* for $C_{18}H_{20}NO_3$ $[M+H]^+$ calcd.: 298.1443.
found: 298.1444.

Synthesis of 3-Methyl-2-(pyridin-2-yloxy)phenyl cyclopropanecarboxylate (187as)



187as

The representative procedure **F** was followed using 2-(*o*-tolyloxy)pyridine **(186a)** (185.4 mg, 1.0 mmol) and cyclopropanecarboxylic acid **(101s)** (43.0 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187as** (78 mg, 58%) as a white solid.

M.p.: 59–61 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.65 (dd, *J* = 8.3, 5.2, Hz, 1H), 7.16–7.11 (m, 2H), 7.07–7.00 (m, 1H), 6.97–6.86 (m, 2H), 2.19 (s, 3H), 1.54 (t, *J* = 7.9, Hz, 1H), 0.93–0.85 (m, 2H), 0.82–0.73 (m, 2H).

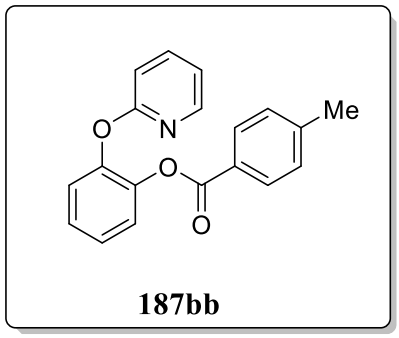
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.2 (C_q), 162.7 (C_q), 147.5 (CH), 143.3 (C_q), 143.1 (C_q), 139.1 (CH), 132.9 (C_q), 128.2 (CH), 125.2 (CH), 120.9 (CH), 118.0 (CH), 110.0 (CH), 16.4 (CH_2), 12.8 (CH_3), 8.8 (CH_2).

IR (ATR): 2923, 2854, 1740, 1426, 1271, 1426, 1271, 1136, 774, 378 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 201 (22), 172 (5), 78 (10), 69 (33), 66 (4), 51 (6), 41 (22).

HR-MS (ESI) *m/z* for $C_{16}H_{16}NO_3$ $[M+H]^+$ calcd.: 270.1130.
found: 270.1131.

Synthesis of 2-(Pyridin-2-yloxy)phenyl 4-methylbenzoate (187bb)



187bb

The representative procedure **F** was followed using 2-phenoxypyridine **(186b)** (171.1 mg, 1.0 mmol), 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol) and [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187bb** (87 mg, 57%) as a white solid.

M.p.: 97–99 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (dd, *J* = 4.8, 2.1 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.60–7.52 (m, 4H), 7.39–7.24 (m, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 6.96–6.89 (m, 1H), 6.84 (dd, *J* = 8.3, 0.9 Hz, 1H), 2.44 (s, 3H).

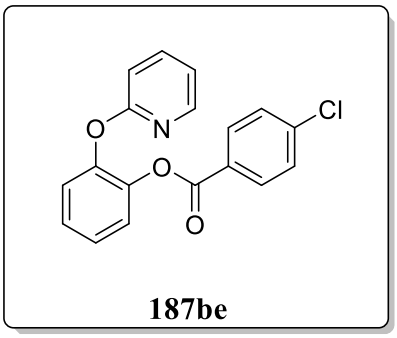
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.0 (C_q), 162.9 (C_q), 147.4 (CH), 145.3 (C_q), 144.1 (C_q), 142.8 (C_q), 139.1 (CH), 129.9 (CH), 128.9 (CH), 126.6 (C_q), 126.1 (CH), 125.4 (CH), 123.8 (CH), 123.1 (CH), 118.4 (CH), 110.9 (CH), 21.7 (CH_3).

IR (ATR): 1738, 1472, 1455, 13857, 1244, 1144, 1015, 984, 742 cm^{-1}.

MS (EI) *m/z* (relative intensity) 170 (41) $[C_{11}H_8NO]^+$, 120 (10), 119 (100), 91 (31), 78 (5), 65 (10), 51 (4).

HR-MS (ESI) *m/z* for $C_{19}H_{16}NO_3$ $[M+H]^+$ calcd.: 306.1130.
found: 306.1124.

Synthesis of 2-(Pyridin-2-yloxy)phenyl 4-chlorobenzoate (187be)



187be

The representative procedure **F** was followed using 2-phenoxypyridine **(186b)** (171.1 mg, 1.0 mmol) and 4-chlorobenzoic acid **(101e)** (78.2 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol) in DCE (2.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187be** (112 mg, 69%) as a white solid.

M.p.: 116–118 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.56 (ddd, *J* = 8.4, 7.2, 2.0 Hz, 1H), 7.39–7.26 (m, 6H), 6.91 (dd, *J* = 7.2, 3.8, Hz, 1H), 6.85–6.80 (m, 1H).

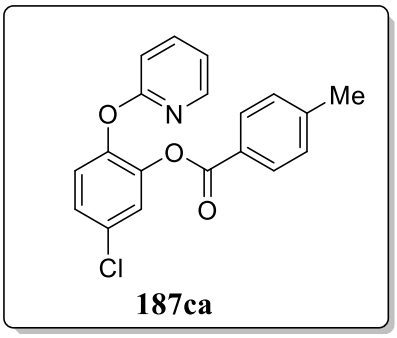
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.3 (C_q), 162.9 (C_q), 147.5 (CH), 145.3 (C_q), 142.6 (C_q), 139.9 (C_q), 139.3 (CH), 131.3 (CH), 128.7 (CH), 127.4 (C_q), 127.0 (CH), 125.6 (CH), 123.2 (CH), 123.2 (CH), 118.5 (CH), 110.9 (CH).

IR (ATR): 1738, 1588, 1465, 1427, 1244, 1225, 1053, 742 cm^{-1}.

MS (EI) *m/z* (relative intensity) 170 (82) $[C_{11}H_8NO]^+$, 141 (35), 139 (100), 111 (36), 75 (11), 51 (8).

HR-MS (ESI) *m/z* for $C_{18}H_{13}ClNO_3$ $[M+H]^+$ calcd.: 326.0584.
found: 326.0580.

Synthesis of 5-Chloro-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187ca)



187ca

The representative procedure **F** was followed using 2-(4-chlorophenoxy)pyridine **(186c)** (205.6 mg, 1.0 mmol), 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{RuCl-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ca** (125 mg, 74%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.56 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.37 (d, *J* = 2.3 Hz, 1H), 7.3 –7.21 (m, 2H), 7.1 –7.11 (m, 2H), 6.96–6.81 (m, 2H), 2.42 (s, 3H).

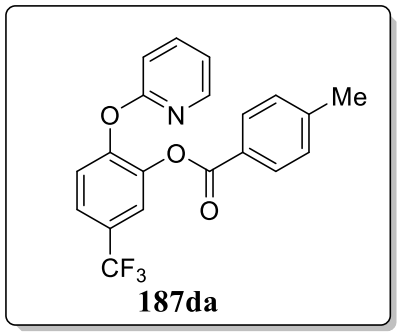
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.8 (C_q), 162.7 (C_q), 147.4 (CH), 144.5 (C_q), 144.1 (C_q), 143.2 (C_q), 139.4 (CH), 130.2 (CH), 130.0 (C_q), 129.1 (CH), 126.8 (CH), 125.7 (C_q), 124.3 (CH), 124.0 (CH), 118.7 (CH), 111.0 (CH), 21.7 (CH_3).

IR (ATR): 1738, 1486, 1465, 1427, 1244, 1173, 1053, 862, 742 cm^{-1}.

MS (EI) *m/z* (relative intensity) 204 (28) $[C_{11}H_7ClNO]^+$, 192 (4), 119 (100), 91 (34), 78 (8) 65 (12), 51 (6).

HR-MS (ESI) *m/z* for $C_{19}H_{15}ClNO_3$ $[M+H]^+$ calcd.: 340.0740.
found: 340.0736.

Synthesis of 2-(Pyridin-2-yloxy)-5-(trifluoromethyl)phenyl 4-methylbenzoate (187da)



187da

The representative procedure **F** was followed using 2-(4-(trifluoromethyl)phenoxy)pyridine **(186d)** (239.1.6 mg, 1.0 mmol), 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol) in DCE (2.0 mL) were stirred in a sealed tube under N_2 at 100 °C for 18 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187da** (114 mg, 61%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 (d, J = 4.6, 2.1 Hz, 1H), 7.8 –7.74 (m, 2H), 7.65–7.55 (m, 3H), 7.45–7.38 (m, 1H), 7.25 (d, J = 2.3 Hz, 1H), 7.19 (dd, J = 8.3, 2.3 Hz, 1H), 6.97 (dd, J = 6.4, 2.8 Hz, 1H), 6.9 (dd, J = 8.3, 2.3 Hz, 1H), 2.45 (s, 3H).

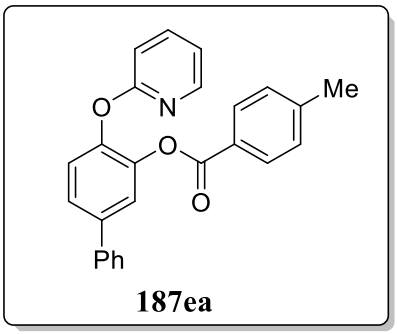
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.7 (C_q), 162.2 (CH), 148.3 (C_q), 147.4 (CH), 144.6 (C_q), 142.7 (C_q), 139.5 (CH), 130.0 (CH), 129.1 (CH), 127.7 (q, $^2J_{C\text{-}F}$ = 33 Hz, C_q), 124.5 (q, $^1J_{C\text{-}F}$ = 280 Hz, C_q), 123.9 (q, $^3J_{C\text{-}F}$ = 4 Hz, CH), 123.3 (CH), 121.6 (q, $^4J_{C\text{-}F}$ = 2 Hz, C_q), 119.1 (CH), 111.4 (CH), 21.8 (CH_3).^{19}F-NMR (282 MHz, $CDCl_3$) δ = -62.1 (s).

IR (ATR): 1742, 1590, 1428, 1328, 1256, 1115, 1053 cm^{-1}.

HR-MS (EI) *m/z* (relative intensity) 238 (20) [$C_{12}H_7F_3NO$]$^+$, 226 (4), 119 (100), 91 (31), 78 (7), 65 (12), 51 (6).

HR-MS (ESI) *m/z* for $C_{20}H_{15}F_3NO_3$ $[M+H]^+$ calcd.: 374.1004.
found: 374.0996.

Synthesis of 4-(Pyridin-2-yloxy)-[1,1'-biphenyl]-3-yl 4-methylbenzoate (187ea)



187ea

The representative procedure **F** was followed using 2-([1,1'-biphenyl]-4-yloxy)pyridine **(186e)** (247.2, 1.0 mmol), 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded 1**87ea** (116 mg, 61%) as a white solid.

M.p.: 101–103 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.15 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.64–7.50 (m, 5H), 7.47–7.30 (m, 4H), 7.20–7.13 (d, *J* = 8.0, 0.7 Hz, 2H), 6.96–6.85 (m, 2H), 2.35 (s, 3H).

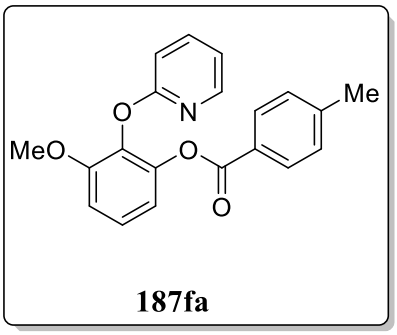
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.1 (C_q), 162.9 (C_q), 147.4 (CH), 144.5 (C_q), 144.1 (C_q), 142.8 (CH), 139.7 (C_q), 139.2 (C_q), 138.8 (CH), 129.9 (CH), 128.9 (CH), 128.6 (CH), 127.3 (CH), 127.0 (CH), 126.1 (CH), 125.2 (CH), 123.3 (CH), 122.5 (CH), 118.5 (CH), 111.0 (CH), 21.7 (CH_3).

IR (ATR): 1733, 1466, 1430, 1273, 1244, 1059, 758, 746 cm^{-1}.

MS (EI) *m/z* (relative intensity) 246 (65) $[C_{17}H_{12}NO]^+$, 234 (4), 119 (100), 102 (3), 91 (30), 78 (5) 65 (7), 51 (3).

HR-MS (ESI) *m/z* for $C_{25}H_{19}NO_3$ $[M]^+$ calcd.: 381.1365.
found: 381.1358.

Synthesis of 3-Methoxy-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187fa)



187fa

The representative procedure **F** was followed using 2-(2-methoxyphenoxy)pyridine **(186f)** (247.2, 1.0 mmol) and 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187fa** (127 mg, 76%) as a white solid.

M.p.: 150–152 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.10 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.76–7.72 (m, 2H), 7.53 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.28–7.19 (m, 1H), 7.13 (d, *J* = 8.0, 0.7 Hz, 2H), 6.99–6.81 (m, 4H), 3.80 (s, 3H), 2.36 (s, 3H).

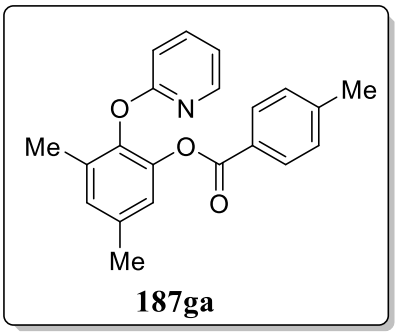
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.1 (C_q), 162.8 (C_q), 153.2 (C_q), 147.3 (CH), 144.3 (C_q), 144.1 (C_q), 138.9 (CH), 134.6 (C_q), 129.1 (CH), 128.9 (CH), 126.2 (C_q), 125.2 (CH), 118.1 (CH), 115.6 (CH), 110.4 (CH), 110.1 (CH), 56.4 (CH_3), 21.7 (CH_3).

IR (ATR): 1729, 1598, 1464, 1427, 1262, 1095, 773, 746 cm^{-1}.

MS (EI) *m/z* (relative intensity) 200 (55) $[C_{12}H_{10}NO_2]^+$, 173 (4), 119 (100), 91 (35), 78 (5) 65 (10), 51 (4).

HR-MS (ESI) *m/z* for $C_{20}H_{17}NO_4$ $[M]^+$ calcd.: 335.1158.
found: 335.1151.

Synthesis of 3,5-Dimethyl-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187ga)



187ga

The representative procedure **F** was followed using 2-(2,4-dimethylphenoxy)pyridine **(186g)** (199.2, 1.0 mmol) and 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ga** (98 mg, 59%) as a white solid.

M.p.: 100–102 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.12 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.52 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.12 (dt, *J* = 8.1, 0.7 Hz, 2H), 6.99–7.21 (m, 2H), 6.87 (ddd, *J* = 7.1, 5.0, 0.9 Hz, 1H), 6.79 (d, *J* = 8.3, 0.9 Hz, 1H), 2.36 (s, 3H), 2.35 (s, 3H), 2.21 (s, 3H).

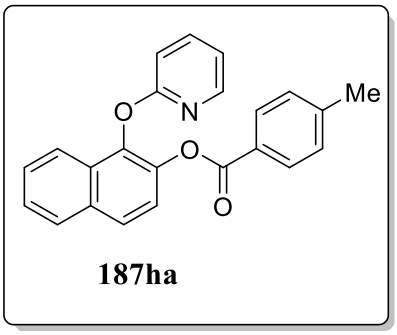
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.3 (C_q), 162.9 (C_q), 147.4 (CH), 143.9 (C_q), 142.8 (C_q), 141.0 (C_q), 138.9 (CH), 135.1 (C_q), 132.3 (C_q), 129.8 (CH), 128.9 (CH), 128.8 (CH), 126.3 (C_q), 121.5 (CH), 117.8 (C_q), 110.1 (CH), 21.7 (CH_3), 21.1 (CH_3), 16.3 (CH_3).

IR (ATR): 1738, 1467, 1265, 1249, 1079, 863, 778, 745 cm^{-1}.

MS (EI) *m/z* (relative intensity) 198 (83) $[C_{13}H_{12}NO]^+$, 186 (4), 143 (3), 119 (100), 91 (32), 78 (6) 65 (12), 51 (4).

HR-MS (ESI) *m/z* for $C_{21}H_{20}NO_3$ $[M+H]^+$ calcd.: 334.1443.
found: 334.1438.

Synthesis of 1-(Pyridin-2-yloxy)naphthalen-2-yl 4-methylbenzoate (187ha)



187ha

The representative procedure **F** was followed using 2-(naphthalen-1-yloxy)pyridine **(186h)** (221.2, 1.0 mmol), 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ha** (126 mg, 71%) as an orange solid.

M.p.: 145–147 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.07 (dd, *J* = 16.5, 4.6, 2.3 Hz, 2H), 7.96–7.89 (m, 1H), 7.86–7.72 (m, 3H), 7.63–7.44 (m, 4H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.01 (ddd, *J* = 9.8, 6.6, 3.1 Hz, 2H), 2.47 (s, 3H).

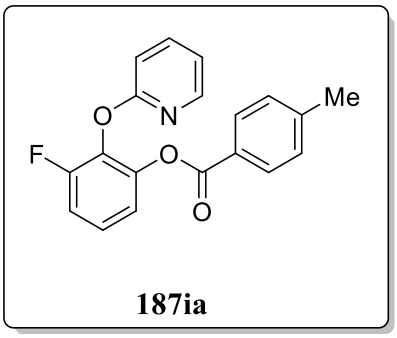
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.2 (C_q), 163.3 (C_q), 147.6 (CH), 144.2 (C_q), 139.7 (C_q), 139.6 (C_q), 139.2 (CH), 132.5 (C_q), 129.9 (CH), 128.9 (C_q), 127.8 (CH), 126.5 (C_q), 126.3 (CH), 126.2 (CH), 126.0 (CH), 125.6 (CH), 122.1 (CH), 122.0 (CH), 118.3 (CH), 110.2 (CH), 21.7 (CH_3).

IR (ATR): 1731, 1594, 1426, 1249, 1228, 1084, 774, 744 cm^{-1}.

MS (EI) *m/z* (relative intensity) 220 (65) $[C_{15}H_{10}NO]^+$, 192 (6), 119 (100), 102 (3), 91 (31), 78 (8) 65 (7), 51 (4).

HR-MS (ESI) *m/z* for $C_{23}H_{18}NO_3$ $[M+H]^+$ calcd.: 356.1287.
found: 356.1281.

Synthesis of 3-Fluoro-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187ia)



187ia

The representative procedure **F** was followed using 2-(2-fluorophenoxy)pyridine **(186i)** (189.1, 1.0 mmol) and 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ia** (115 mg, 71%) as a white solid.

M.p.: 86–88 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.08 (ddd, J = 5.0, 2.0, 0.8 Hz, 1H), 7.79 (d, J = 8.2 Hz, 2H), 7.63–7.54 (m, 1H), 7.32–7.08 (m, 5H), 6.99–6.87 (m, 2H), 2.39 (s, 3H).

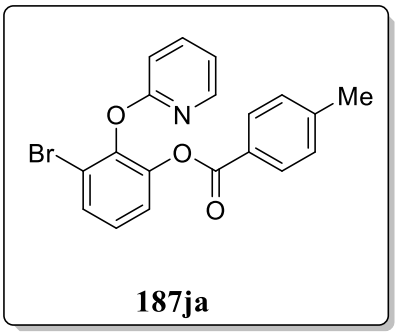
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.9 (C_q), 162.1 (C_q), 156.0 (d, $^1J_{C\text{-}F}$ = 253 Hz, C_q), 147.2 (CH), 144.8 (C_q), 144.6 (d, $^3J_{C\text{-}F}$ = 4 Hz, C_q), 139.3 (CH), 133.5 (d, $^2J_{C\text{-}F}$ = 14 Hz, C_q), 129.0 (CH), 125.9 (C_q), 125.1 (d, $^3J_{C\text{-}F}$ = 9 Hz, CH), 119.0 (d, $^4J_{C\text{-}F}$ = 2 Hz, CH) 118.9 (CH), 114.1 (d, $^2J_{C\text{-}F}$ = 20 Hz, CH), 113.9 (CH), 110.5 (CH), 21.8 (CH_3).

IR (ATR): 1737, 1591, 1463, 1426, 1227, 1075, 986, 741 cm^{-1}.

^{19}F-NMR (283 MHz, $CDCl_3$) δ = -126.43 (s). MS (EI) *m/z* (relative intensity) 188 (39) $[C_{11}H_7FNO]^+$, 176 (5), 120 (15), 119 (100), 91 (45), 78 (11) 65 (16), 51 (8).

HR-MS (ESI) *m/z* for $C_{19}H_{15}FNO_3$ $[M+H]^+$ calcd.: 324.1036.
found: 324.1032.

Synthesis of 3-Bromo-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187ja)



187ja

The representative procedure **F** was followed using 2-(2-bromophenoxy)pyridine **(187j)** (250.2, 1.0 mmol) and 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol) in DCE (2.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ja** (144 mg, 75%) as a light yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16–8.12 (m, 1H), 7.73 (dd, *J* = 8.3, 2.2 Hz, 2H), 7.63–7.55 (m, 1H), 7.48–7.36 (m, 2H), 7.27–7.20 (m, 1H), 7.19–7.13 (m, 1H), 6.98–6.92 (m, 2H), 6.89–6.83 (m, 1H), 2.38 (s, 3H).

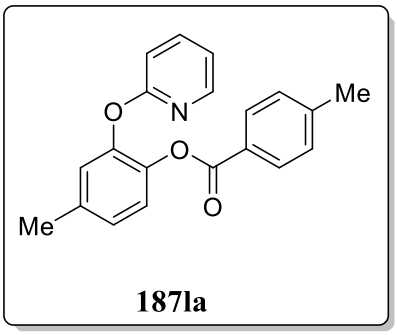
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.8 (C_q), 162.4 (C_q), 147.4 (CH), 146.0 (C_q), 144.4 (C_q), 142.0 (C_q), 139.4 (CH), 134.4 (CH), 132.1 (CH), 130. (CH), 129.0 (CH), 128.4 (CH), 126.4 (CH), 125.9 (CH), 125.0 (C_q), 118.9 (CH), 118.8 (C_q), 111.1 (CH), 21.8 (CH_3).

IR (ATR): 1737, 1483, 1464, 1245, 1171, 1053, 907, 742 cm^{-1}.

MS (EI) *m/z* (relative intensity) 248 (18) $[C11H_7{}^{79}BrNO]^+$, 296 (5), 340 (4), 119 (100), 91 (32), 78 (9) 65 (8), 51 (7).

HR-MS (ESI) *m/z* for $C_{19}H_{16}{}^{79}BrNO_3$ $[M+H]^+$ calcd.: 384.0257.
found: 384.0223.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187la)



187la

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **(186l)** (185.2, 1.0 mmol) and 4-methylbenzoic acid **(101a)** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187la** (99 mg, 62%) as a white solid.

M.p.: 94–96 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.17–8.11 (m, 1H), 7.75–7.69 (m, 2H), 7.65 (ddd, *J* = 8.2, 7.1, 2.0 Hz, 1H), 7.28–7.14 (m, 5H), 6.93–6.87 (m, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 2.40 (s, 3H), 2.31 (s, 3H).

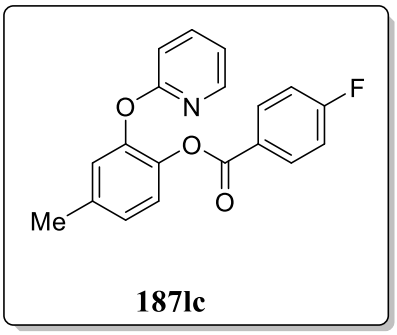
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.0 (C_q), 162.8 (C_q), 147.1 (CH), 144.7 (C_q), 143.8 (C_q), 140.2 (C_q), 138.9 (CH), 136.5 (C_q), 129.6 (CH), 128.6 (CH), 126.0 (C_q), 125.8 (CH), 123.3 (CH), 123.1 (CH), 118.1 (CH), 110.6 (CH), 21.3 (CH_3), 20.7 (CH_3).

IR (ATR): 1726, 1428, 1270, 1240, 1071, 867, 746 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (79) $[C_{12}H_{10}NO]^+$, 172 (4), 119 (100), 91 (41), 78 (7), 66 (13), 51 (10).

HR-MS (ESI) *m/z* for $C_{20}H_{18}NO_3$ $[M+H]^+$ calcd.: 320.1208.
found: 320.1283.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 4-fluorobenzoate (187lc)



187lc

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine (**186l)** (185.2, 1.0 mmol) and 4-fluorobenzoic acid (**101c)** (70.0 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187lc** (103 mg, 64%) as a white solid.

M.p.: 102–104 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.84 (dd, *J* = 8.9, 5.5 Hz, 2H), 7.54 (dd, *J* = 8.3, 5.2, Hz, 1H), 7.25–7.18 (m, 1H), 7.12–6.95 (m, 4H), 6.89 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.81 (d, *J* = 8.3, 0.9 Hz, 1H), 2.30 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 166.7 (C_q), 165.0 ($^1J_{C\text{-}F}$ = 270 Hz, C_q), 163.2 ($^2J_{C\text{-}F}$ = 33 Hz, CH), 162.9 (C_q), 147.4 (CH), 144.7 (C_q), 140.1 (C_q), 139.1 (CH), 136.9 (C_q), 132.5 ($^3J_{C\text{-}F}$ = 10 Hz, CH), 126.1 (CH), 125.3 ($^4J_{C\text{-}F}$ = 3 Hz, C_q), 123.5 (CH), 118.3 (CH), 115.4 ($^2J_{C\text{-}F}$ = 25 Hz, CH), 110.8 (CH), 21.1 (CH_3).

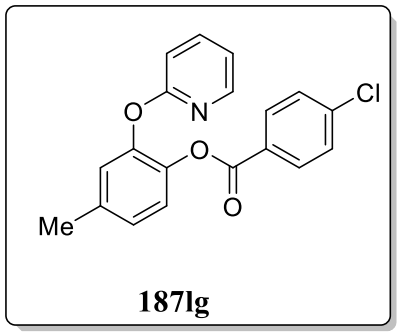
IR (ATR): 1736, 1507, 1467, 1431, 1259, 1065, 795, 778 cm^{-1}.

^{19}F-NMR (282 MHz, $CDCl_3$) δ = -106.7.

HR-MS (EI) *m/z* (relative intensity) 184 (100) $[C_7H_4FO_2]^+$, 172 (6), 123 (60), 113 (10), 95 (32), 78 (7), 51 (5), 43 (14).

HR-MS (ESI) *m/z* for $C_{19}H_{15}FNO_3$ $[M+H]^+$ calcd.: 324.1036.
found: 324.1033.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 4-chlorobenzoate (187lg)



187lg

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **186l** (185.2, 1.0 mmol) and 4-chlorobenzoic acid **101g** (77.5 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187lg** (122 mg, 72%) as a white solid.

M.p.: 104–106 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.11 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.41 (m, 1H), 7.35–7.27 (m, 2H), 7.20 (d, *J* = 8.1 Hz, 1H), 7.12–7.03 (m, 2H), 6.97–6.77 (m, 2H), 2.33 (s, 3H).

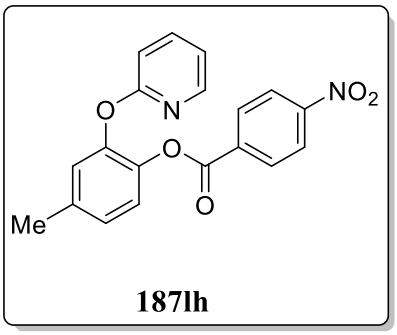
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.3 (C_q), 162.9 (C_q), 147.4 (CH), 144.6 (C_q), 140.1 (C_q), 139.7 (C_q), 139.2 (CH), 137.0 (C_q), 131.2 (CH), 128.5 (CH), 127.4 (C_q), 126.1 (CH), 123.6 (CH), 123.1 (CH), 118.3 (CH), 110.8 (CH), 21.1 (CH_3).

IR (ATR): 1737, 1593, 1258, 1238, 1066, 1014, 748, 395cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_7H_4ClO_2]^+$, 172 (7), 139 (60), 113 (10), 111 (30), 78 (10), 66 (5), 51 (7).

HR-MS (ESI) *m/z* for $C_{19}H_{15}ClNO_3$ $[M+H]^+$ calcd.: 340.0740.
found: 340.0648.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 4-nitrobenzoate (187lh)



187lh

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **186l** (185.2, 1.0 mmol) and 4-nitrobenzoic acid **101h** (83.5 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187lh** (108 mg, 62%) as a white solid.

M.p.: 140–142 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.21– 8.14 (m, 2H), 8.10 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 2H), 7.55 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.27–7.19 (d, *J* = 8.0 Hz, 1H), 7.13–7.04 (m, 2H), 6.98–6.79 (m, 2H), 2.42 (s, 3H).

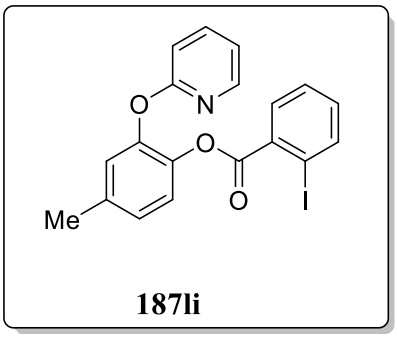
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 162.7 (C_q), 162.3 (C_q), 150.5 (C_q), 147.4 (CH), 144.4 (C_q), 139.8 (C_q), 139.3 (CH), 137.4 (C_q), 134.3 (C_q), 130.8 (CH), 126.1 (CH), 123.6 (CH), 123.3 (CH), 122.8 (CH), 118.5 (CH), 110.8 (CH), 21.1 (CH_3).

IR (ATR): 1742, 1522, 1427, 1276, 1260, 876, 780, 712 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}O]^+$, 172 (110), 150 (31), 120 (9), 104 (24), 92 (12) 76 (14) 51 (6).

HR-MS (ESI) *m/z* for $C_{19}H_{15}N_2O_5$ $[M+H]^+$ calcd.: 351.0981.
found: 351.0978.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 2-iodobenzoate (187li)



187li

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **186l** (185.2, 1.0 mmol) and 2-iodobenzoic acid **101i** (124.0 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187li** (120 mg, 56%) as a white solid.

M.p.: 68–70 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.19 (dd, *J* = 4.9, 2.0 Hz, 1H), 8.09 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.64–7.50 (m, 2H), 7.29 (ddd, *J* = 7.7, 4.7, 2.7 Hz, 2H), 7.16–7.09 (m, 2H), 7.03–6.85 (m, 3H), 2.35 (s, 3H).

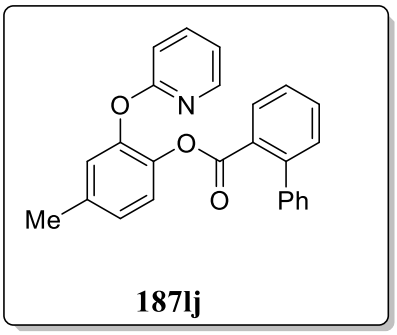
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.6 (C_q), 162.9 (C_q), 147.4 (CH), 144.6 (C_q), 141.3 (CH), 140.0 (C_q), 139.2 (CH), 137.0 (C_q), 133.2 (C_q), 132.9 (CH), 131.1 (CH), 127.6 (CH), 126.1 (CH), 123.5 (CH), 123.1 (CH), 118.4 (CH), 110.9 (CH), 94.7 (C_q), 21.1 (CH_3).

IR (ATR): 1745, 1428, 1274, 1236, 1187, 1082, 778, 747 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (80) $[C_{12}H_{10}NO]^+$, 231 (98), 203 (24), 101 (3), 76 (15), 66 (4) 51 (5).

HR-MS (ESI) *m/z* for $C_{19}H_{15}INO_3$ $[M+H]^+$ calcd.: 432.0097.
found: 432.0095.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 2-iodobenzoate (187lj)



187lj

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **187l** (185.2, 1.0 mmol), [1,1'-biphenyl]-4-carboxylic acid **101j** (99.0 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187lj** (105 mg, 55%) as a white solid.

M.p.: 98–100 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.17 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.66–7.57 (m, 2H), 7.53–7.46 (m, 1H), 7.39–7.27 (m, 7H), 7.04–6.82 (m, 5H), 2.30 (s, 3H).

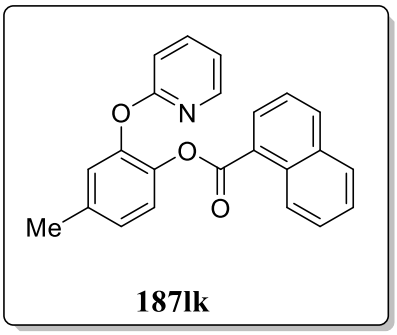
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 165.6 (C_q), 163.0 (C_q), 147.5 (CH), 144.8 (C_q), 143.0 (C_q), 140.7 (C_q), 140.1 (C_q), 139.1 (CH), 136.7 (C_q), 131.4 (CH), 130.7 (CH), 129.9 (C_q), 129.5 (CH), 128.4 (CH), 127.8 (CH), 127.1 (CH), 126.8 (CH), 125.9 (CH), 123.3 (CH), 122.8 (CH), 118.4 (CH), 110.9 (CH), 21.0 (CH_3).

IR (ATR): 1749, 1465, 1427, 1232, 1191, 1032, 744, 697 cm^{-1}.

MS (EI) *m/z* (relative intensity) 181 (100) $[C_{13}H_9O]^+$, 153 (27), 152 (31), 127 (5), 78 (4), 51 (3).

HR-MS (ESI) *m/z* for $C_{25}H_{20}NO_3$ $[M+H]^+$ calcd.: 382.1443.
found: 382.1442.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 1-naphthoate (187lk)



187lk

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **186l** (185.2, 1.0 mmol) and 1-naphthoic acid **101k** (86.0 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187lk** (99 mg, 56%) as a white solid.

M.p.: 91–93 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.96–8.91 (m, 1H), 8.22–8.17 (m, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.94 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.89–7.83 (m, 1H), 7.62–7.50 (m, 3H), 7.41–7.33 (t, *J* = 7.8 Hz, 2H), 7.21–7.11 (m, 2H), 6.96–6.83 (m, 2H), 2.31 (s, 3H).

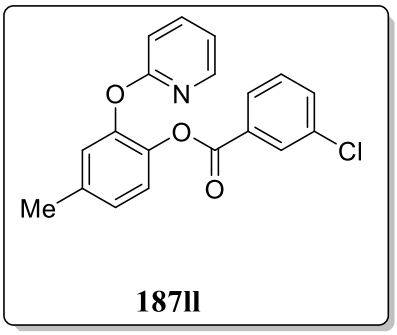
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.7 (C_q), 163.0 (C_q), 147.4 (CH), 144.9 (C_q), 140.4 (C_q), 139.2 (CH), 136.9 (C_q), 133.9 (C_q), 133.6 (CH), 131.4 (C_q), 130.8 (CH), 128.4 (CH), 127.8 (CH), 126.2 (CH), 126.1 (CH), 125.6 (C_q), 125.4 (CH), 124.2 (CH), 123.7 (CH), 123.4 (CH), 118.3 (CH), 111.0 (CH), 21.1 (CH_3).

IR (ATR): 1737, 1496, 1466, 1421, 1234, 1171, 1058, 743 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (36) $[C_{12}H_{10}NO]^+$, 155 (100), 127 (51), 101 (3), 78 (6), 66 (3) 51 (4).

HR-MS (ESI) *m/z* for $C_{23}H_{18}NO_3$ $[M+H]^+$ calcd.: 356.1287.
found: 356.1283.

Synthesis of 4-Methyl-2-(pyridin-2-yloxy)phenyl 3-chlorobenzoate (187ll)



187ll

The representative procedure **F** was followed using 2-(*m*-tolyloxy)pyridine **186l** (185.2, 1.0 mmol) and 3-chlorobenzoic acid **101l** (67.5 mg, 0.5 mmol), [{$RuCl_2$-(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ll** (128 mg, 76%) as a white solid.

M.p.: 108–110 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.21–8.13 (m, 1H), 7.81–7.71 (m, 2H), 7.63–7.55 (m, 1H), 7.53–7.46 (m, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.27–7.22 (m, 1H), 7.05 (d, *J* = 7.4 Hz, 2H), 7.01 (dd, *J* = 7.2, 5.0 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 2.30 (s, 3H).

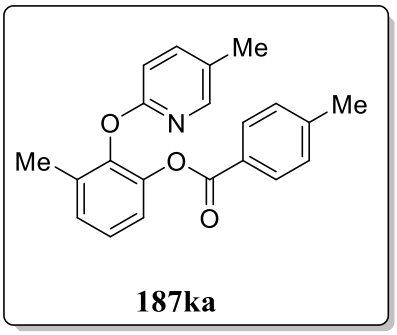
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 163.0 (C_q), 162.8 (C_q), 147.3 (CH), 144.6 (C_q), 139.9 (C_q), 139.2 (CH), 137.0 (C_q), 134.2 (C_q), 133.2 (CH), 130.6 (C_q), 129.7 (CH), 129.4 (CH), 127.9 (CH), 126.0 (CH), 123.5 (CH), 122.9 (CH), 118.4 (CH), 110.8 (CH), 21.05 (CH_3) .

IR (ATR): 1741, 1431, 1261, 1193, 1100, 1058, 788, 739 cm^{-1}.

MS (EI) *m/z* (relative intensity) 184 (100) $[C_{12}H_{10}NO]^+$, 172 (5), 139 (60), 113 (8), 111 (28), 78 (9) 51 (5).

HRMS (ESI) *m/z* for $C_{19}H_{15}ClNO_3$ $[M+H]^+$ calcd.: 340.0762.
found: 340.0739.

Synthesis of 3-Methyl-2-((5-methylpyridin-2-yl)oxy)phenyl 4-methylbenzoate (187ka)



187ka

The representative procedure **F** was followed using 5-methyl-2-(*o*-tolyloxy)pyridine **186k** (199.2, 1.0 mmol) and 4-methylbenzoic acid **101a** (67.5 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ka** (110 mg, 67%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.90 (d, *J* = 2.5, 0.8 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.31 (ddd, *J* = 8.4, 2.5, 0.7 Hz, 1H), 7.20–7.09 (m, 5H), 6.69 (dd, *J* = 8.3, 0.7 Hz, 1H), 2.37 (s, 3H), 2.23 (s, 3H), 2.19 (s, 3H).

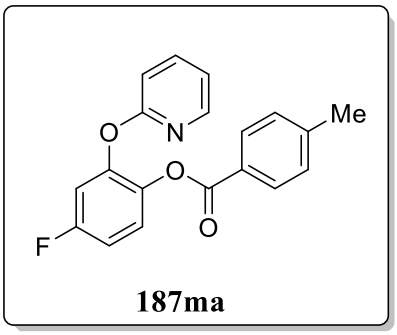
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.2 (C_q), 161.0 (C_q), 146.9 (CH), 143.9 (C_q), 143.7 (C_q), 143.2 (C_q), 139.9 (CH), 133.0 (C_q), 129.9 (CH), 128.8 (CH), 128.2 (CH), 127.0 (C_q), 126.3 (C_q), 125.1 (CH), 121.0 (CH), 109.5 (CH), 21.7 (CH_3), 17.4 (CH_3), 16.4 (CH_3).

IR (ATR): 1732, 1464, 1269, 1231, 1085, 1070, 746, 395 cm^{-1}.

MS (EI) *m/z* (relative intensity) 198 (100) $[C_{13}H_{12}NO]^+$, 171 (17), 142 (61), 118 (18), 111 (30), 78 (10), 65 (8), 51 (7).

HR-MS (ESI) *m/z* for $C_{21}H_{20}NO_3$ $[M+H]^+$ calcd.: 334.1365.
found: 334.1351.

Synthesis of 4-Fluoro-2-(pyridin-2-yloxy)phenyl 4-methylbenzoate (187ma)



187ma

The representative procedure **F** was followed using 2-(3-fluorophenoxy)pyridine **186m** (189.1, 1.0 mmol), and 4-methylbenzoic acid **101a** (68.4 mg, 0.5 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187ma** (93 mg, 58%) as a white solid.

M.p.: 97-99 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.14 (ddd, J = 5.0, 2.0, 0.8 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.59 (ddd, J = 8.3, 7.2, 2.0 Hz, 1H), 7.31–7.23 (m, 1H), 7.18–7.12 (m, 2H), 7.08–6.81 (m, 3H), 2.41(s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 164.3 (C_q), 162.5 (C_q), 160.4 (d, $^1J_{C\text{-}F}$ = 280 Hz, C_q), 158.6 (CH), 147.5 (CH), 146.1 (d, $^4J_{C\text{-}F}$ = 3 Hz, C_q), 144.4 (C_q), 139.5 (CH), 138.9 (d, $^3J_{C\text{-}F}$ = 4 Hz, C_q), 130.0 (CH), 129.0 (CH), 126.0 (C_q), 124.3 (d, $^3J_{C\text{-}F}$ = 10 Hz, CH), 124.3 (CH), 118.9 (CH), 112.0 (d, $^2J_{C\text{-}F}$ = 20 Hz, CH), 111.9 (d, $^2J_{C\text{-}F}$ = 25 Hz, CH), 110.6 (CH), 21.7 (CH_3).

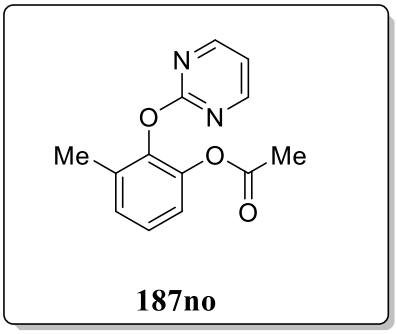
^{19}F-NMR (283 MHz, $CDCl_3$) δ = -114.3.

IR (ATR): 1737, 1496, 1466, 1421, 1234, 1171, 1140, 1058, 743 cm^{-1}.

MS (EI) *m/z* (relative intensity) 188 (45) $[C_{11}H_7FNO]^+$, 176 (4), 120 (12), 91 (30), 78 (6), 65 (10) 51 (4).

HR-MS (ESI) *m/z* for $C_{19}H_{15}FNO_3$ $[M+H]^+$ calcd.: 324.1036.
found: 324.1031.

Synthesis of 3-Methyl-2-(pyrimidin-2-yloxy)phenyl acetate (187no)



187no

A suspension of 2-(*o*-tolyloxy)pyrimidine **186n** (186.2, 1.0 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (7.6 mg, 2.5 mol %), $AgSbF_6$ (34.4 mg, 20 mol %) and $K_2S_2O_8$ (270 mg, 2.0 mmol) in DCE:AcOH (3:1) (2.0 mL) were stirred in a sealed tube under N_2 at 100 °C for 18 h. At ambient temperature, the reaction mixture was diluted with 20 mL CH_2Cl_2 (20 mL) and passed through celite with 100 mL CH_2Cl_2. The organic layer was dried over Na_2SO_4. After evaporation of the solvent in vaccuo, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1) to yield Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **187no** (157 mg, 64%) as a white solid.

M.p.: 96–98 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.71 (d, J = 4.8 Hz, 2H), 7.23–7.14 (m, 2H), 7.12–6.94 (m, 2H), 2.19 (s, 3H), 2.06 (s, 3H).

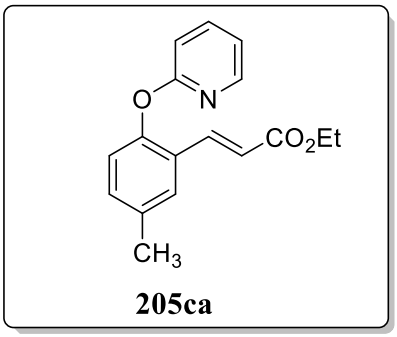
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 168.2 (C_q), 164.3 (C_q), 159.7 (CH), 142.7 (C_q), 142.6 (C_q), 132.6 (C_q), 128.3 (CH), 125.7 (CH), 120.9 (CH), 116.1 (CH), 20.6 (CH_3), 16.3 (CH_3).

IR (ATR): 2923, 2854, 1758, 1571, 1402, 1174, 1030, 876cm^{-1}.

HR-MS (EI) *m/z* (relative intensity) 185 (85) [$C_{11}H_9N_2O$]$^+$, 202 (100), 160 (12), 147 (9), 134 (15), 79 (11), 53 (13).

HR-MS (ESI) *m/z* calcd.: for $C_{13}H_{13}N_2O_3$ [M+H]$^+$ calcd.: 245.0926.
found. 245.0922.

Synthesis of *(E)*-Ethyl-3-{3-methyl-2-(pyridin-2-yloxy)phenyl}acrylate (205ca)



205ca

Representative procedure **H** was followed using 2-(4-methylphenoxy)pyridine(**186c**) (93.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ca** (100 mg, 68%) as a colourless solid.

M.p.: = 115–117 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.08 (ddd, , *J*=5.0, 2.0, 0.8 Hz, 1H), 7.76 (d, *J*=16.1 Hz, 1H), 7.66 (ddd, *J*=8.1, 7.2, 2.0, 1H), 7.70 – 7.63 (m, 1H), 7.52 – 7.49 (m, 1H), 7.29 – 7.24 (m, 1H), 7.16 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.95 – 6.90 (m, 2H), 6.40 (d, *J* = 16.1, Hz, 1H), 4.16 (q, *J* = 7.1Hz, 2H), 2.08 (s, 3H), 1.24 (*J* = 7.1Hz, 3H).

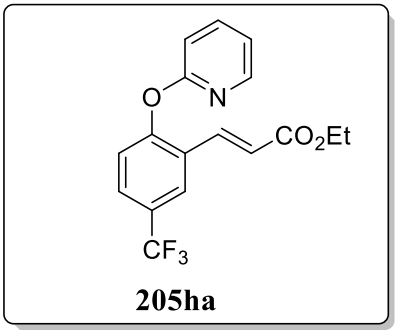
^{13}C NMR (76 MHz, $CDCl_3$) δ = 166.8 (C_q), 163.2 (C_q), 150.7 (C_q), 147.8 (CH), 139.6 CH), 139.2 (CH), 133.1(CH), 132.3 (C_q), 128.3 (C_q), 125.6 (CH), 125.3 (CH), 119.7 (CH), 118.1 (CH), 110.3 (CH), 60.3 (CH_2), 16.6 (CH_3), 14.2 (CH_3).

IR (ATR): 2975, 2929, 1699, 1629, 1422, 1243, 1175, 774 cm^{-1}.

MS (EI) *m/z*(relative intensity): 282 (15) [M+], 254 (10), 238 (15), 210 (10), 180 (10), 167 (15), 131 (10), 78 (20).

HR-MS (EI) *m/z* for $C_{17}H_{17}NO_3$ [M+] calcd.: 283.1208.
found: 283.1211.

Synthesis of *(E)*-Ethyl-3-{2-(pyridin-2-yloxy)-5-(trifluoromethyl)phenyl}acrylate (205ha):



205ha

Representative procedure **H** was followed using 2-{4-(trifluoromethyl)phenoxy}pyridine (**186h**) (118.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), $[Ru(O_2CMes)_2(p\text{-cymene})]$ (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ha** (86.0 mg, 53%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.22 – 8.14 (m, 1H), 7.96 – 7.86 (m, 2H), 7.77 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 7.66 – 7.58 (m, 1H), 7.21 (dt, *J* = 8.6, 0.9 Hz, 1H), 7.11 – 7.01 (m, 2H), 6.54 (d, *J* = 16.1 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.4 (C_q), 162.6 (C_q), 155.3 (C_q), 147.7 (CH), 140.0 (CH), 137.4 (CH), 127.7 (C_q), 127.6 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 127.1 ($^2J_{C\text{-}F}$ = 33 Hz, C_q), 125.3 ($^3J_{C\text{-}F}$ = 4 Hz, CH), 123.7 ($^1J_{C\text{-}F}$ = 272 Hz, C_q), 122.5 (CH), 121.4 (CH), 119.6 (CH), 112.3 (CH), 60.7 (CH_2), 14.2 (CH_3).

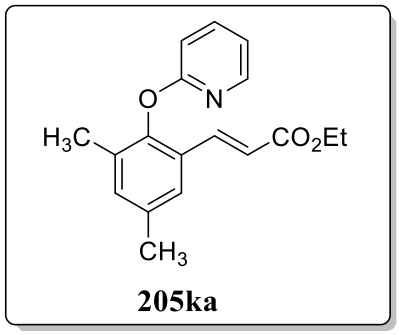
^{19}F-NMR ($CDCl_3$) δ = -62.4 (s).

IR (ATR): 2983, 1716, 1641, 1267, 1162, 1123, 1073, 773 cm^{-1}.

MS (EI) *m/z* (relative intensity): 336 (10) [M+], 308 (15), 292 (17), 264 (100), 248 (7), 236 (15), 215 (10), 167 (13).

HR-MS (EI) *m/z* for $C_{17}H_{14}F_3NO_3$ [M+] calcd.: 337.0926.
found: 337.0917.

Synthesis of *(E)*-Ethyl-3-{3,5-dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (205ka):



205ka

Representative procedure **H** was followed using 2-(2,4-dimethylphenoxy)pyridine (**186k**) (97.5 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ka** (101.5 mg, 64%) as a colourless solid.

M.p.: 73 – 75 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 (ddd, *J* = 4.9, 2.0, 1.0 Hz, 1H), 7.75 (d, *J* = 16.1 Hz, 1H), 7.67 (ddd, *J* = 8.2, 7.2, 2.0 Hz, 1H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 6.96 – 6.91 (m, 2H), 6.41 (d, *J* = 16.1 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 2.06 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

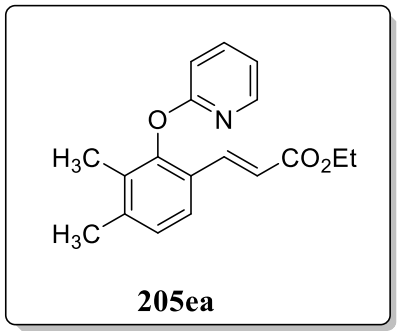
^{13}C NMR (76 MHz, $CDCl_3$) δ = 166.9 (C_q), 163.3 (C_q), 148.5 (C_q), 147.7 (CH), 139.5 (CH), 139.3 (CH), 135.0 (C_q), 134.0 (CH), 131.8 (C_q), 127.7 (C_q), 125.7 (CH), 119.5 (CH), 118.0 (CH), 110.3 (CH), 60.2 (CH_2), 20.9 (CH_3), 16.5 (CH_3), 14.2 (CH_3).

IR (ATR): 2982, 1698, 1428, 1281, 1234, 1202, 1040, 774 cm^{-1}.

MS (EI) *m/z* (relative intensity): 296 (30) [M+], 268 (150), 280 (10), 268 (15), 252 (25), 224 (100), 203 (30) 175 (25).

HR-MS (EI) *m/z* for $C_{18}H_{19}NO_3$ [M+] calcd.: 297.1365.
found: 297.1369.

Synthesis of *(E)*-Ethyl-3-{3,4-dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (205ea):



205ea

Representative procedure **H** was followed using 2-(2,3-dimethylphenoxy)pyridine (**186e**) (100.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ea** (86.7 mg, 61%) as a colourless solid.

M.p.: 127 –129 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 – 8.09 (m, 1H), 7.74 (d, *J* = 16.1 Hz, 1H), 7.68 (ddd, *J* = 9.3, 7.2, 2.0 Hz 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.96 – 6.92 (m, 2H), 6.38 (d, *J* = 16.1 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.33 (s, 3H), 2.02 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 3H).

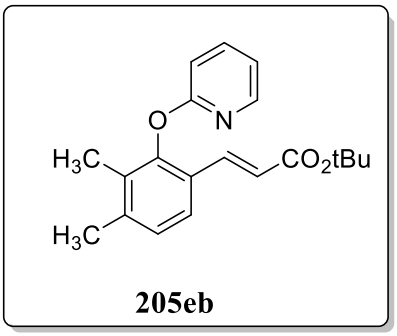
^{13}C NMR (76 MHz, $CDCl_3$) δ = 167.0 (C_q), 163.4 (C_q), 150.5 (C_q), 147.8(CH), 141.1 (C_q), 139.6 (CH), 139.5 (CH), 130.8 (C_q), 127.4 (CH), 125.8 (C_q), 124.5 (CH), 118.6 (CH), 118.0 (CH), 110.3 (CH), 60.2 (CH_2), 20.4 (CH_3), 14.2 (CH_3), 12.9 (CH_3).

IR (ATR): 2982, 1711, 1254, 1236, 1200, 1168, 1141, 782 cm^{-1}.

MS (EI) *m/z* (relative intensity): 296 (30) [M+], 268 (150), 252 (20), 224 (100), 203 (15), 181 (15), 115 (10) 78 (20).

HR-MS (EI) *m/z* for $C_{18}H_{19}NO_3$ [M+] calcd.: 297.1365.
found: 297.1360.

Synthesis of *(E)*-*tert*-Butyl-3-{3,4-dimethyl-2-(pyridin-2-yloxy)phenyl}acrylate (205eb):



205eb

Representative procedure **H** was followed using 2-(2,3-dimethylphenoxy)pyridine (**186e**) (100.0 mg, 0.50 mmol), *tert*-butyl acrylate (**63b**) (325.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205eb** (96 mg, 59%) as a colourless solid.

M.p.: 114 –116 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 (dd, *J* = 5.4, 2.1 Hz, 1H), 7.65 (d, J = 16.0 Hz, 2H), 7.71 – 7.65 (m, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.07(d, *J* = 8.1 Hz, 1H), 6.99 – 6.85 (m, 2H), 6.31 (d, *J* = 16.0 Hz, 1H), 2.02 (s, 3H), 2.02 (s, 3H), 1.45 (s, 9H).

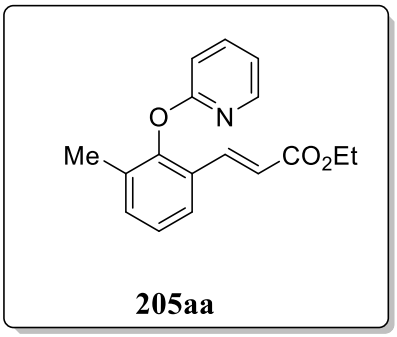
^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.3 (C_q), 163.5 (C_q) 150.4 (C_q), 147.8 (CH), 140.8 (C_q), 139.5 (CH), 138.4 (CH), 130.7 (C_q), 127.3 (CH), 125.9 (C_q), 124.3 (CH), 120.4 (CH), 117.9 (CH), 110.3 (CH), 80.1 (C_q), 28.1 (CH_3), 20.4 (CH_3), 12.9 (CH_3).

IR (ATR): 2974, 1698, 1256, 1234, 1150, 987, 824, 782 cm^{-1}.

MS (EI) *m/z* (relative intensity): 324 (10) [M+], 268 (10), 252 (20), 224 (100), 208 (10), 194 (5), 175 (15) 115 (7).

HR-MS (EI) *m/z* for $C_{20}H_{23}NO_3$ [M+] calcd.: 297.1365.
found: 297.1360.

Synthesis of *(E)*-Ethyl-3-{3-methyl-2-(pyridin-2-yloxy)phenyl}acrylate (205aa)



205aa

Representative procedure **H** was followed using 2-(*o*-tolyloxy)pyridine(**186a**) (93.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205aa** (100 mg, 68%) as a colourless solid.

M.p.: 115 –117 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.08 (ddd, , *J*=5.0, 2.0, 0.8 Hz, 1H), 7.76 (d, *J* = 16.1 Hz, 1H), 7.66 (ddd, *J* = 8.1, 7.2, 2.0, 1H), 7.70 –7.63 (m, 1H), 7.52 – 7.49 (m. 1H), 7.29 – 7.24 (m, 1H), 7.16 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.95 – 6.90 (m, 2H), 6.40 (d, *J* = 16.1, Hz, 1H), 4.16 (q, *J* = 7.1Hz, 2H), 2.08 (s, 3H), 1.24 (*J* = 7.1Hz, 3H).

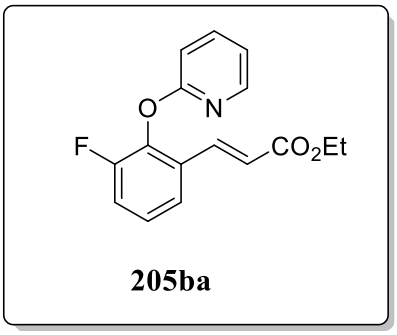
^{13}C NMR (76 MHz, $CDCl_3$) δ = 166.8 (C_q), 163.2 (C_q), 150.7 (C_q), 147.8 (CH), 139.6 (CH), 139.2 (CH), 133.1(CH), 132.3 (C_q), 128.3 (C_q), 125.6 (CH), 125.3 (CH), 119.7 (CH), 118.1 (CH), 110.3 (CH), 60.3 (CH_2), 16.6 (CH_3), 14.2 (CH_3).

IR (ATR): 2975, 2929, 1699, 1629, 1422, 1243, 1175, 774 cm^{-1}.

MS (EI) *m/z*(relative intensity): 282 (15) [M+], 254 (10), 238 (15), 210 (10), 180 (10), 167 (15), 131 (10), 78 (20).

HR-MS (EI) *m/z* for $C_{17}H_{17}NO_3$ [M+] calcd.: 283.1208.
found: 283.1211.

Synthesis of *(E)*-Ethyl-3-{3-fluoro-2-(pyridin-2-yloxy)phenyl}acrylate (205ba)



205ba

Representative procedure **H** was followed using 2-(2-fluorophenoxy) pyridine(**186b**) (158.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ba** (88.5 mg, 56%) as a yellow solid.

M.p.: 75 – 77 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.09 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.82 (d, *J* = 16.1 Hz, 1H), 7.73 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.25 – 7.21 (m, 1H), 7.21 – 7.14 (m, 1H), 7.08 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.01 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.49 (d, *J* = 16.2 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

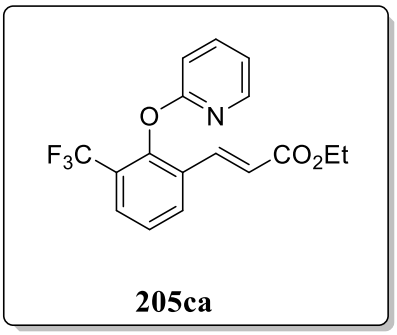
^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.6 (C_q), 162.6 (Cq) , 155.5 ($^1J_{C\text{-}F}$ = 251 Hz, C_q), 147.4 (CH) , 140.0 ($^2J_{C\text{-}F}$ =12.7 Hz, C_q), 139.6 (CH), 137.8 ($^4J_{C\text{-}F}$ = 4 Hz, CH), 130.3 ($^3J_{C\text{-}F}$ = 2 Hz, C_q), 125.8 ($^3J_{C\text{-}F}$ = 8.0 Hz, CH), 122.9 ($^4J_{C\text{-}F}$ = 3.4 Hz, CH), 121.0 (CH), 118.9 (CH), 117.8 ($^2J_{C\text{-}F}$ = 19 Hz, CH), 110.7 (CH), 60.6 (CH_2), 14.2 (CH_3) ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -126.2 (s).).

IR (ATR): 2987, 1710, 1426, 1325, 1265, 1226, 1171, 980, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 286 (10) [M+], 258 (15), 242 (15), 214 (100), 185 (20), 136 (10), 107 (15), 78 (55).

HR-MS (EI) *m/z* for $C_{16}H_{14}FNO_3$ [M+] calcd.: 287.0958.
found: 287.0925.

Synthesis of *(E)*-Ethyl-3-{2-(pyridin-2-yloxy)-3-(trifluoromethyl)phenyl}acrylate (205ca)



205ca

Representative procedure **H** was followed using 2-{2-(trifluoromethyl)phenoxy}pyridine (**186c**) (118.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ca** (88 mg, 58%) as a colourless solid.

M.p.: 43 – 45 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.01 (ddd, *J* = 5.1, 2.0, 0.8 Hz, 1H), 7.84 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.76 – 7.66 (m, 2H), 7.61 (d, *J* = 16.1 Hz, 1H), 7.36 (tt, *J* = 8.0, 0.9 Hz, 1H), 7.05 (dt, *J* = 8.3, 0.9 Hz, 1H), 6.95 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.40 (d, *J* = 16.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H).

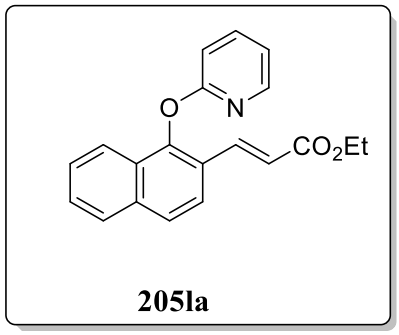
^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.2 (C_q), 163.5 (C_q), 149.8 (q, $^3J_{C\text{-}F}$ = 1.7 Hz, C_q), 147.3 (CH), 139.7 (CH), 137.5 (CH), 131. (CH), 130.9 (C_q), 128.6 (q, $^3J_{C\text{-}F}$ = 5.0 Hz, CH), 125.6 (CH), 125.0 (q, $^2J_{C\text{-}F}$ = 31.6 Hz, C_q), 122.9 (q, $^1J_{C\text{-}F}$ = 273 Hz, C_q), 121.2 (CH), 118.7 (CH), 110.7 (CH), 60.5 (CH_2), 14.1 (CH_3). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -61.7 (s).

IR (ATR): 2987, 1707, 1425, 1328, 1231, 1136, 1104, 778 cm^{-1}.

MS (EI) *m/z* (relative intensity): 336 (20) [M+], 292 (20), 264 (100), 244 (25), 196 (15), 167 (10), 51 (15).

HR-MS (EI) *m/z* for $C_{17}H_{14}F_3NO_3$ [M+] calcd.: 337.0926.
found: 337.0919.

Synthesis of *(E)*-Ethyl-3-{1-(pyridin-2-yloxy)naphthalen-2-yl}acrylate (205la)



205la

Representative procedure **H** was followed using 2-(naphthalen-1-yloxy)pyridine (**186l**) (110.5 mg, 0.50 mmol), ethyl acrylate (**63a**) (250.0 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol.). Purification by column chromatography (n-hexane/EtOAc: 15:1) yielded **205la** (97.0 mg, 61%) as a colourless solid.

M.p.: 155–157 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.06 (ddd, J = 5.0, 2.0, 0.8 Hz, 1H), 8.00 (d, J = 16.1 Hz, 1H), 7.91 – 7.79 (m,2H), 7.75 (s, 2H), 7.71 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.50 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.42 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.03 (dt, *J* = 8.3, 0.8 Hz, 1H), 6.96 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.54 (d, *J* = 16.1 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

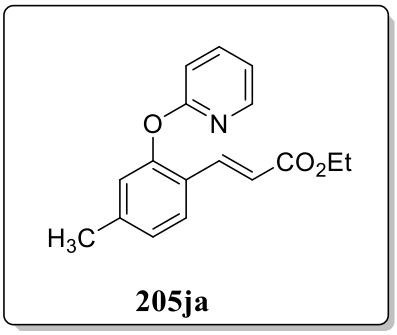
^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.8 (C_q), 164.2 (C_q), 148.8 (C_q), 147.9 (CH), 139.7 (CH), 138.6 (CH), 135.6 (C_q), 128.0 (CH), 128.0 (C_q), 127.4 (CH), 126.8 (CH), 126.0 (CH), 124.2 (C_q), 123.3 (CH), 123.2 (CH), 119.8 (CH), 118.4 (CH), 110.2 (CH), 60.4 (CH_2), 14.2 (CH_3).

IR (ATR): 2987, 1712, 1292, 1256, 1234, 1174, 1138, 783 cm^{-1}.

MS (EI) *m/z* (relative intensity) 318 (10) [M+], 290 (25), 274 (15), 246 (65), 225 (100), 197 (80), 168 (20), 139 (30).

HR-MS (EI) *m/z* for $C_{20}H_{17}NO_3$ [M+] calcd.: 319.1208.
found: 319.1217.

Synthesis of *(E)*-Ethyl-3-{4-methyl-2-(pyridin-2-yloxy)phenyl}acrylate (205ja)



205ja

Representative procedure **H** was followed using 2-(m-tolyloxy)pyridine (**186j**) (93.0 mg, 0.50 mmol), ethyl acrylate (**63a**) (250 mg, 5.0 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (28.0 mg, 10.0 mol %) and CsOAc (288.0 mg, 1.5 mmol) purification by column chromatography (*n*-hexane/EtOAc: 15:1) yielded **205ja** (80.0 mg, 56%) as a colourless solid.

M.p.: 44–46 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.15 (ddd, *J* = 5.0, 2.0, 0.7 Hz, 1H), 7.83 (d, *J* = 16.1 Hz, 1H), 7.68 (ddd, *J* = 8.2, 7.2, 2.0 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.04 – 6.99 (m, 1H), 6.97 (ddd, *J*= 7.3, 4.9, 1.0 Hz, 1H), 6.95 – 6.93 (m, 1H), 6.88 (d, *J* = 1.6 Hz, 1H), 6.41 (d, *J* = 16.1 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H).

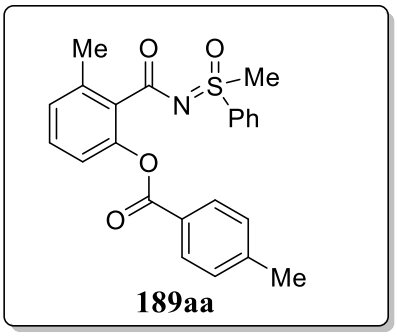
^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.0 (C_q), 163.4 (C_q), 152.8 (C_q), 147.8 (CH), 142.0 (C_q), 139.5 (CH), 138.8 (CH), 127.8 (CH), 126.2 (CH), 124.5 (C_q), 122.8 (CH), 118.6 (CH), 118.6 (CH), 111.6 (CH), 60.3 (CH_2), 21.4 (CH_3), 14.2 (CH_3).

IR (ATR): 2980, 1709, 1316, 1234, 1172, 1103, 1029, 781 cm^{-1}.

MS (EI) m/z (relative intensity) 282 (40) [M+], 254 (45), 238 (35), 210 (100), 194 (20), 182 (25), 167 (35), 78 (35).

HR-MS (EI) *m/z* for $C_{17}H_{17}NO_3$ [M+] calcd.: 283.1208.
found: 283.1214.

Synthesis of *N*-[2-(4-Methylbenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189aa):



189aa

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101a**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol%), KPF_6 (43.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.00 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ab** (164 mg, 81%) as a white solid.

M.p.: = 114-115 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.0 Hz, 2H), 7.81 (ddt, *J* = 8.3, 7.2, 1.0 Hz, 2H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.24–7.15 (m, 3H), 7.07–6.96 (m, 2H), 3.02 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H).

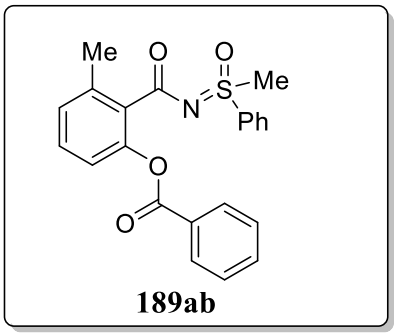
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 175.0 (C_q), 165.1 (C_q), 147.7 (C_q), 144.3 (CH), 138.3 (C_q), 137.3 (C_q), 133.7 (CH), 132.0 (C_q), 130.4 (C_q), 130.2 (CH), 129.4 (CH), 129.3 (CH), 129.2 (CH), 128.1 (CH), 127.1 (CH), 120.4 (C_q), 44.0 (CH_3), 21.7 (CH_3), 19.7 (CH_3).

IR (ATR): 2925, 1763, 1671, 1609, 1406, 1309, 1173, 1020, 755 cm^{-1}.

MS (EI) *m/z* (relative intensity) 407 (60) [M^+], 287 (100), 138 (50), 149 (30).

HR-MS (ESI): *m/z* for $C_{23}H_{21}NO_4S$ [$M+H^+$] calcd 408.1225.
found 408.1233.

Synthesis of *N*-[2-(4-Benzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ab):



189ab

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101b**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ab** (145 mg, 74%) as a white solid.

M.p.: = 125-126 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 7.2 Hz, 2H), 7.80 (d, *J* = 7.5 Hz, 2H), 7.59 (ddt, *J* = 8.2, 7.2, 1.0 Hz, 2H), 7.54 (d, *J* = 7.4 Hz, 2H), 7.46 (dd, *J* = 7.6, 0.9 Hz, 2H), 7.39–7.35 (m, 2H), 7.27 (dd, *J* = 8.4, 7.4 Hz, 1H), 3.06 (s, 3H), 2.42 (s, 3H).

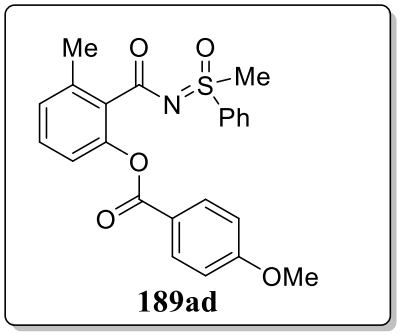
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 174.6 (C_q), 164.8 (C_q), 147.4 (C_q), 138.0 (C_q), 137.2 (C_q), 133.5 (CH), 133.4 (CH), 131.8 (C_q), 130.1 (CH), 129.5 (C_q), 129.3 (CH), 129.1 (CH), 128.4 (CH), 128.0 (CH), 126.8 (CH), 120.1 (CH), 43.9 (CH_3), 19.7 (CH_3).

IR (neat): 2925, 1731, 1627, 1577, 1446, 1245, 1128, 1019, 835 cm^{-1}.

MS (EI) *m/z* (relative intensity) 393 (45) [M^+], 279 (100), 178 (60), 148 (25).

HR-MS (ESI): *m/z* for $C_{22}H_{19}NO_4S$ [M+H^+] calcd.: 394.1068.
found: 394.1069.

Synthesis of *N*-[2-(4-Methoxybenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ad):



189ad

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101d**) (91.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ad** (156 mg, 74%) as a white solid.

M.p.: = 110–112 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 7.4 Hz, 2H), 7.57 (ddt, *J* = 8.7, 7.4, 1.2 Hz, 2H), 7.41 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.30–7.23 (m, 2H), 7.08 (d, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 2H), 3.84 (s, 3H), 3.08 (s, 3H), 2.42 (s, 3H).

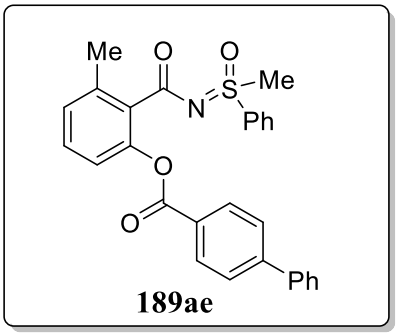
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 175.0 (C_q), 164.8 (C_q), 163.8 (C_q), 147.7 (C_q), 138.3 (C_q), 137.2 (C_q), 133.7 (CH), 132.4 (CH), 132.0 (C_q), 129.4 (CH), 129.2 (CH), 128.0 (CH), 127.1 (CH), 122.0 (C_q), 120.4 (CH), 113.8 (CH), 55.5 (CH_3), 44.0 (CH_3), 19.7 (CH_3).

IR (ATR): 2943, 1730, 1508, 1246, 1178, 1066, 917, 766 cm^{-1}.

MS (EI) *m/z* (relative intensity) 423 (50) [M^+], 279 (100), 145 (50), 122 (20).

HR-MS (ESI): *m/z* for $C_{23}H_{21}NO_5S$ [M+H^+] calcd.: 424.1174.
found: 424.1178.

Synthesis of *N*-[2-(4-Phenylbenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ae):



189ae

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101e**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ae** (164 mg, 81%) as a white solid.

M.p.: = 111-113 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 7.3 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.64–7.60 (m, 2H), 7.52 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.47 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.42–7.37 (m, 3H), 7.29 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.14–7.06 (m, 2H), 3.12 (s, 3H), 2.45 (s, 3H).

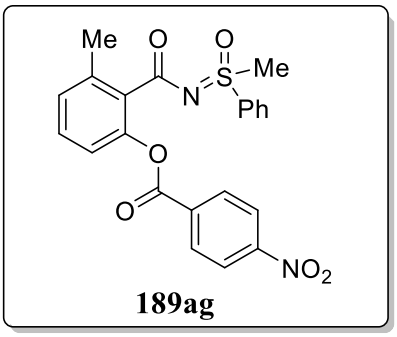
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 174.6 (C_q), 164.7 (C_q), 147.5 (C_q), 145.9 (C_q), 139.5 (C_q), 138.1 (C_q), 137.2 (C_q), 133.5 (CH), 131.8 (C_q), 130.7 (CH), 130.0 (CH), 129.5 (CH), 129.3 (CH), 129.0 (CH), 128.8 (CH), 128.2 (C_q), 128.0 (CH), 127.1 (CH), 126.8 (CH), 126.8 (CH), 44.0 (CH_3), 19.7 (CH_3).

IR (ATR): 2927, 1762, 1624, 1476, 1447, 1305, 1147, 1050, 920 cm^{-1}.

MS (EI) *m/z* (relative intensity) 469 (55) [M^+], 286 (100), 124 (60), 146 (30).

HR-MS (ESI): *m/z* for $C_{28}H_{23}N_2O_4S$ [$M+H^+$] calcd.: 470.1381.
found: 470.1379.

Synthesis of *N*-[2-(4-Nitrobenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ag):



189ag

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101g**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ag** (145 mg, 68%) as a white solid.

M.p.: = 125-126 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 8.6 Hz, 2H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.85–7.82 (m, 2H), 7.61 (dt, *J* = 8.1, 0.8 Hz, 1H), 7.45 (dd, *J* = 7.4, 1.4 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.4 Hz, 2H), 7.08 (d, *J* = 7.4 Hz, 1H), 3.21 (s, 3H), 2.45 (s, 3H).

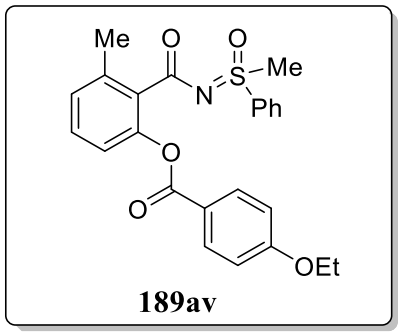
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 174.2 (C_q), 163.2 (C_q), 150.5 (C_q), 147.4 (C_q), 138.1 (C_q), 137.3 (C_q), 134.9 (C_q), 133.7 (CH), 131.4 (C_q), 131.2 (CH), 129.4 (CH), 129.3 (CH), 128.4 (CH), 126.8 (CH), 123.4 (CH), 120.0 (CH), 44.2 (CH_3), 19.8 (CH_3).

IR (ATR): 2925, 1764, 1681, 1609, 1446, 1308, 1172, 1019, 836 cm^{-1}.

MS (EI) *m/z* (relative intensity) 438 (60) [M^+], 288 (100), 159 (50), 119 (15).

HR-MS (ESI): *m/z* for $C_{22}H_{18}N_2O_6S$ [M+H^+] calcd.: 439.0919.
found. 439.0920.

Synthesis of *N*-[2-{4-(Ethoxy)benzoyloxy-6-methyl}]-*S*-methyl-*S*-phenylsulfoximine (189av):



189av

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101v**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189av** (142 mg, 64%) as a white solid.

M.p.: = 106-107 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 7.4 Hz, 2H), 7.57 (ddt, *J* = 8.0, 1.6, 0.9, Hz, 1H), 7.44 (dd, *J* = 7.6, 0.6 Hz, 2H), 7.26 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.03 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.07 (q, *J* = 7.0 Hz, 2H), 3.08 (s, 3H), 2.42 (s, 3H), 1.41 (t, *J* = 7.0 Hz, 3H).

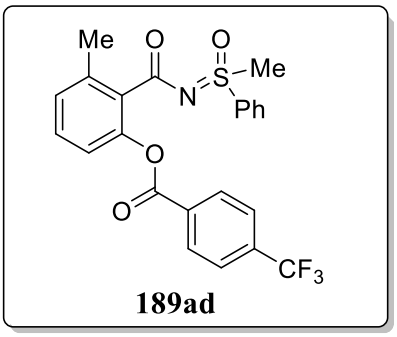
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 174.8 (C_q), 164.6 (C_q), 163.1 (C_q), 147.6 (C_q), 138.2 (C_q), 137.1 (C_q), 133.5 (CH), 132.2 (CH), 131.8 (C_q), 129.3 (CH), 129.1 (CH), 127.8 (CH), 126.7 (CH), 121.6 (C_q), 120.3 (CH), 114.2 (CH), 63.8 (CH_2), 44.0 (CH_3), 20.0 (CH_3), 14.7 (CH_3).

IR (ATR): 2936, 1745, 1607, 1462, 1348, 1264, 1130, 976 cm^{-1}.

MS (EI) *m/z* (relative intensity) 437 (55) [M^+], 296 (100), 132 (50), 112 (35).

HR-MS (ESI): *m/z* for $C_{24}H_{23}NO_5S$ [$M+H^+$] calcd.: 438.1330.
found: 438.1334.

Synthesis of *N*-[2-{4-(Trifluoromethy)lbenzoyloxy-6-methyl}]-*S*-methyl-*S*-phenylsulfoximine (189ad):



189ad

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101d**) (114.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ad** (164.0 mg, 81%) as a white solid.

M.p.: = 88-89 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.1 Hz, 2H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.60–7.55 (m, 3H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.33 (ddt, *J* = 8.3, 2.4, 1.2 Hz, 1H), 7.15–7.10 (m, 1H), 7.06 (dd, *J* = 8.1, 1.1 Hz, 1H), 3.16 (s, 3H), 2.45 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$): δ = 174.3 (C_q), 163.7 (C_q), 147.4 (C_q), 138.0 (C_q), 137.2 (q, $^1J_{C\text{-}F}$ = 238 Hz, C_q), 134.4 (q, $^2J_{C\text{-}F}$ = 35 Hz, C_q), 133.5 (CH), 132.7 (C_q), 131.5 (C_q), 130.5 (CH), 129.4 (q, $^3J_{C\text{-}F}$ = 10 Hz, CH), 129.2 (CH), 128.2 (CH), 126.7 (CH), 125.2 (q, $^4J_{C\text{-}F}$ = 4 Hz, CH), 120.0 (CH), 44.0 (CH_3), 19.8 (CH_3).

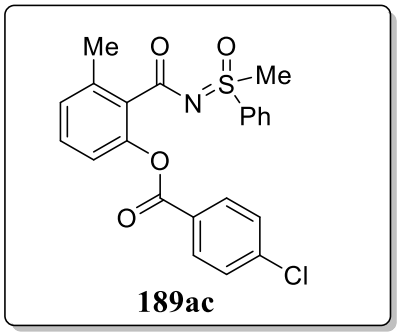
^{19}F-NMR (283 MHz, $CDCl_3$): δ = -63.1 (s).

IR (ATR): 2936, 1727, 1579, 1421, 1222, 1166, 1064, 977, 763 cm^{-1}.

MS (EI) *m/z* (relative intensity) 461 (70) [M^+], 286 (100), 169 (50), 181 (40).

HR-MS (ESI): *m/z* for $C_{23}H_{18}F_3NO_4S$ [$M+H^+$] calcd.: 462.0942.
found: 462.0946.

Synthesis of *N*-[2-(4-Chlorobenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ac):



189ac

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101c**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ac** (115 mg, 54%) as a white solid.

M.p.: = 125-126 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.83 (dd, *J* = 7.4, 0.9 Hz, 1H), 8.45 (d, *J* = 7.2 Hz, 1H), 8.38 (dd, *J* = 7.4, 0.9, Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.57–7.54 (m, 1H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.32 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.14 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.07 (ddd, *J* = 8.1, 1.1, 0.6 Hz, 1H), 3.24 (s, 3H), 2.46 (s, 3H).

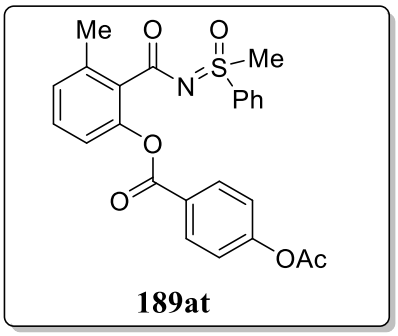
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 174.4 (C_q), 164.2 (C_q), 147.4 (C_q), 138.1 (C_q), 137.2 (C_q), 133.6 (CH), 131.8 (CH), 131.6 (C_q), 129.5 (CH), 129.3 (C_q), 129.2 (CH), 128.4 (CH), 128.3 (C_q), 128.1 (CH), 126.8 (CH), 120.1 (CH), 44.1 (CH_3), 19.8 (CH_3).

IR (ATR): 2983, 1770, 1605, 1509, 1422, 1315, cm^{-1}.

MS (EI) *m/z* (relative intensity) 427 (55) [M^+], 246 (100), 121 (50), 182 (30).

HR-MS (ESI): *m/z* for $C_{19}H_{18}NO_3$ [$M+H^+$] calcd.: 428.0616.
found: 428.0619.

Synthesis of *N*-[2-(4-Acetyloxybenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189at):



189at

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101t**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189at** (115.0 mg, 69%) as a white solid.

M.p.: = 105–106 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.7 Hz, 2H), 7.78 (dd, *J* = 8.5, 1.3 Hz, 2H), 7.55–7.51 (m, 1H), 7.37 (dd, *J* = 8.3, 0.9 Hz, 2H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 2H), 7.09 (d, *J* = 7.7 Hz, 1H), 7.03 (dd, *J* = 8.3, 0.9 Hz, 1H), 3.10 (s, 3H), 2.43 (s, 3H), 2.30 (s, 3H).

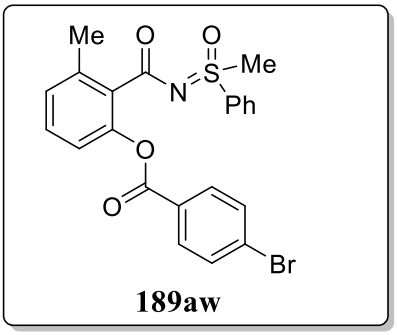
^{13}C-NMR (126 MHz, $CDCl_3$) δ = 174.5 (C_q), 168.5 (C_q), 164.0 (C_q), 154.5 (C_q), 147.3 (C_q), 138.0 (C_q), 137.1 (C_q), 133.6 (CH), 131.7 (C_q), 131.7 (CH), 129.3 (CH), 129.1 (CH), 128.0 (CH), 127.0 (C_q), 126.7 (CH), 121.7 (CH), 120.1 (CH), 44.0 (CH_3), 21.1 (CH_3), 19.7 (CH_3).

IR (ATR): 2925, 1760, 1705, 1612, 1577, 1454, 1318, 1215, 1106, 990 cm^{-1}.

MS (EI) *m/z* (relative intensity) 451 (55) [M^+], 281 (100), 197 (60), 168 (25).

HR-MS (ESI): *m/z* for $C_{24}H_{21}NO_6S$ [M+H^+] calcd.: 452.1090
found: 452.1093.

Synthesis of *N*-[2-(4-Bromobenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189aw):



189aw

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101w**) (116 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189aw** (131 mg, 56%) as a white solid.

M.p.: = 106-108 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 7.8 Hz, 1H), 8.09 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.83 (d, *J* =7.8, 2H), 7.69 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.46 (dt, *J* = 7.6, 0.9 Hz, 2H), 7.30 (dt, *J* = 8.3, 7.5 Hz, 2H), 7.12 (d, *J* = 7.6, 0.9 Hz, 1H), 7.03 (dt, *J* = 8.1, 0.8 Hz, 1H), 3.16 (s, 3H), 2.45 (s, 3H).

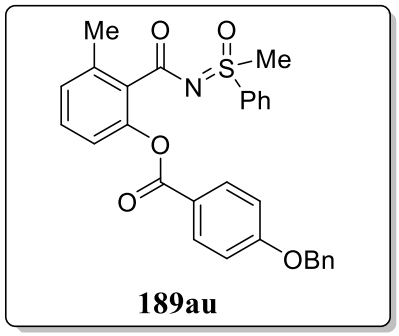
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.6 (C_q), 163.8 (C_q), 147.5 (C_q), 138.2 (C_q), 137.6 (C_q), 136.3 (CH), 133.8 (CH), 133.1 (CH), 131.7 (C_q), 131.6 (C_q), 130.1 (CH), 129.5 (CH), 128.4 (CH), 126.9 (CH), 122.5 (C_q), 120.2 (CH), 44.1 (CH_3), 19.8 (CH_3).

IR (ATR): 2926, 1731, 1519, 1447, 1280, 1194, 1129, 1066, 918, 674 cm^{-1}.

MS (EI) *m/z* (relative intensity) 471 (40) [^{79}Br, M^+], 373 (40) [^{81}Br, M^+], 471 (55) [M^+], 269 (100), 184 (65), 112 (45).

HR-MS (ESI): *m/z* for $C_{22}H_{18}BrNO_4S$ [$M+H^+$] calcd.: 472.0140.
found: 472.0143.

Synthesis of *N*-[2-{4-(Benzoyloxy)benzoyloxy-6-methyl}]-*S*-methyl-*S*-phenylsulfoximine (189au):



189au

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101u**) (120 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189au** (131 mg, 56%) as a white solid.

M.p.: = 104-105 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.6, Hz, 2H), 7.84 (d, *J* = 8.6, Hz, 2H), 7.54 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.45–7.35 (m, 6H), 7.30 (ddt, *J* = 8.0, 2.3, 1.0 Hz, 1H), 7.14 (dd, *J* = 7.4, 0.8 Hz, 2H), 7.03–6.98 (m, 3H), 5.14 (s, 2H), 3.09 (s, 3H), 2.44 (s, 3H).

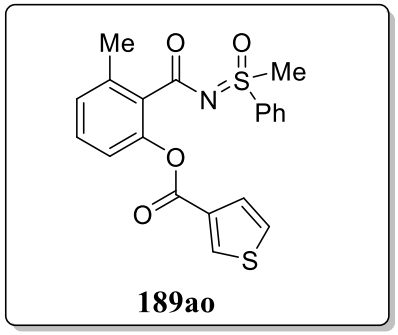
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 174.6 (C_q), 164.4 (C_q), 162.6 (C_q), 147.4 (C_q), 137.9 (C_q), 136.9 (C_q), 135.8 (CH), 133.4 (CH), 132.1 (C_q), 131.8 (CH), 129.1 (C_q), 128.9 (CH), 128.4 (CH), 127.9 (CH), 127.7 (C_q), 127.2 (CH), 126.7 (CH), 121.8 (CH), 120.1 (CH), 114.5 (CH), 70.0 (CH_2), 43.8 (CH_3), 19.6 (CH_3).

IR (ATR): 2925, 1763, 1621, 1570, 1446, 1308, 1209, 1132, 976 cm^{-1}.

MS (EI) *m/z* (relative intensity) 499 (55) [M^+], 216 (100), 124 (60), 137 (30).

HR-MS (ESI): *m/z* for $C_{29}H_{25}NO_5S$ [$M+H^+$] calcd.: 500.1453.
found: 500.1458.

Synthesis of *N*-[2-(4-Thienoyl-3-oxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ao):



189ao

The representative procedure **G** was followed using sulfoximine benzamide (**180a**) (137 mg, 0.50 mmol), carboxylic acid (**101o**) (77.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ao** (144 mg, 72%) as a colourless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.26 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.87–7.90 (m, 2H), 7.61 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.58 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.46–7.42 (m, 2H), 7.31 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.29 (d, 7.5, 2.3, 1H), 7.09 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 3.13 (s, 3H), 2.43 (s, 3H).

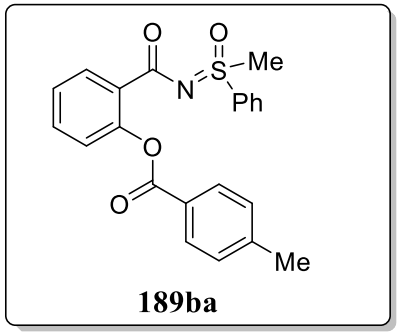
^{13}C-NMR (150 MHz, $CDCl_3$): δ = 174.7 (C_q), 160.8 (C_q), 147.3 (C_q), 138.3 (C_q), 137.2 (C_q), 134.1 (CH), 133.6 (CH), 133.0 (C_q), 131.8 (C_q), 129.4 (CH), 129.1 (CH), 128.2 (CH), 128.0 (CH), 126.9 (CH), 126.2 (CH), 120.2 (CH), 44.1(CH_3), 19.8 (CH_3).

IR (ATR): 2926, 1761, 1715, 1446, 1302, 1147, 976, 686 cm^{-1}.

MS (EI) *m/z* (relative intensity) 399 (50) [M^+], 268 (100), 137 (50), 158 (40).

HR-MS (ESI): *m/z* for $C_{20}H_{17}NO_4S$ [M+H^+] calcd.: 400.0599.
found.: 400.0593.

Synthesis of *N*-[2-(4-Methylbenzoyloxy)]-*S*-methyl-*S*-phenylsulfoximine (189ba):



189ba

The representative procedure **G** was followed using sulfoximine benzamide (**180b**) (130 mg, 0.50 mmol), carboxylic acid (**101a**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ba** (119 mg, 61%) as a white solid.

M.p.: = 111-113 °C.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.11–8.09 (dd, *J* = 8.6, 2.0, Hz, 1H), 8.07 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.86 (dd, *J* = 7.8, 1.2, Hz, 1H), 7.57 (d, *J* = 6.9. 0.9, Hz, 1H), 7.53–7.51 (m, 1H), 7.50 (d, 7.3, 0.9, 1H), 7.31 (ddt, 8.3, 1.7, 0.9, 3H), 7.22 (d, *J* = 7.1 Hz, 1H), 7.16 (dd, *J* = 8.1, 1.2 Hz, 2H), 2.88 (s, 3H), 2.40 (s, 3H).

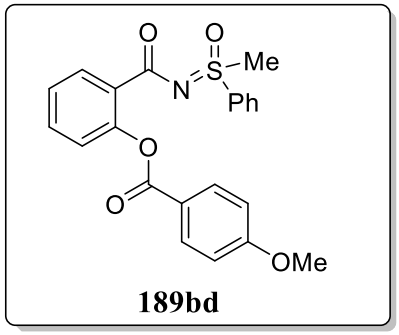
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 172.6 (C_q), 165.6 (C_q), 150.1 (C_q), 144.1 (C_q), 138.4 (C_q), 133.5 (CH), 132.7 (CH), 131.9 (CH), 130.4 (CH), 129.5 (C_q), 129.2 (CH), 129.1 (CH), 127.3 (C_q), 127.1 (CH), 125.9 (CH), 123.5 (CH), 44.0 (CH_3), 21.7 (CH_3).

IR (ATR): 2926, 1737, 1603, 1503, 1413, 1369, 1268, 1159, 1066, 975 cm^{-1}.

MS (EI) *m/z* (relative intensity) 393 (65) [M^+], 214 (100), 181 (60), 112 (25).

HR-MS (ESI): *m/z* for $C_{22}H_{19}NO_4S$ [M+H^+] calcd.:394.1035.
found: 394.1039.

Synthesis of *N*-[2-(4-Methoxybenzoyloxy)]-*S*-methyl-*S*-phenylsulfoximine (189bd):



189bd

The representative procedure **G** was followed using sulfoximine benzamide (**180b**) (130 mg, 0.50 mmol), carboxylic acid (**101d**) (77.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189bd** (125 mg, 63%) as a white solid.

M.p.: = 107-109 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.83 (dd, *J* = 8.4, 0.8 Hz, 1H), 8.46 (dd, *J* = 8.4, 0.8 Hz, 1H), 8.37 (ddd, *J* = 8.3, 2.4, 1.1 Hz, 1H), 7.85–7.81 (m, 2H), 7.64 (d, *J* = 7.8, 0.9 Hz, 1H), 7.47–7.42 (m, 2H), 7.32 (dd, *J* = 8.0, 1.0, Hz, 1H), 7.14 (d, *J* = 7.8, 0.9 Hz, 2H), 7.07 (dd, *J* = 7.8, 1.0 Hz, 1H), 3.24 (s, 3H), 2.46 (s, 3H).

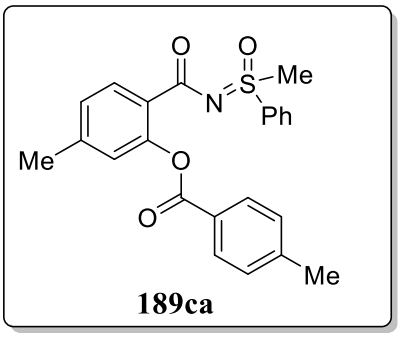
^{13}C-NMR (126 MHz, $CDCl_3$): δ = 174.3 (C_q), 163.0 (C_q), 148.1 (C_q), 147.5 (C_q), 138.1 (C_q), 137.6 (C_q), 136.0 (CH), 133.7 (CH), 131.3 (C_q), 130.0 (CH), 129.4 (CH), 128.6 (CH), 127.5 (CH), 126.8 (CH), 125.0 (CH), 120.1 (CH), 44.2 (CH_3), 20.0 (CH_3).

IR (ATR): 2938, 1713, 1605, 1462, 1405, 1274, 1188, 1020, 920 cm^{-1}.

MS (EI) *m/z* (relative intensity) 409 (55) [M^+], 292 (100), 128 (60), 139 (30).

HR-MS (ESI): *m/z* for $C_{22}H_{19}NO_5S$ [M+H^+] calcd.: 410.0984.
found: 410.0981.

Synthesis of *N*-[2-(4-Methylbenzoyloxy-4-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ca):



189ca

The representative procedure **G** was followed using sulfoximine benzamide (**180c**) (130 mg, 0.50 mmol), carboxylic acid (**101a**) (77.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ca** (128 mg, 63%) as a white solid.

M.p.: = 102-103 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.4 Hz, 2H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.57–7.54 (m, 1H), 7.44 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.29–7.26 (m, 3H), 7.12–7.04 (d, *J* = 7.6 Hz, 2H), 3.09 (s, 3H), 2.44 (s, 3H), 2.42 (s, 3H).

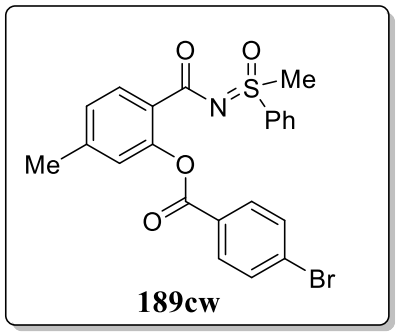
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 173.5 (C_q), 164.5 (C_q), 147.5 (C_q), 144.5 (C_q), 138.3 (C_q), 137.2 (CH), 133.6 (CH), 131.9 (C_q), 130.7 (C_q), 130.2 (CH), 129.4 (CH), 129.3 (C_q), 129.2 (CH), 128.1 (CH), 127.1 (CH), 126.9 (CH), 43.7 (CH_3), 21.9 (CH_3), 20.1 (CH_3).

IR (ATR): 2924, 1772, 1615, 1517, 1401, 1306, 1218, 1026, 919, 753 cm^{-1}.

MS (EI) *m/z* (relative intensity) 407 (40) [M^+], 258 (100), 181 (65), 125 (30).

HR-MS (ESI): *m/z* for $C_{23}H_{21}NO_4S$ [$M+H^+$] calcd.: 408.1191.
found: 408.1196.

Synthesis of *N*-[2-(4-Bromobenzoyloxy-4-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189cw):



189cw

The representative procedure **G** was followed using sulfoximine benzamide (**180c**) (137 mg, 0.50 mmol), carboxylic acid (**101w**) (119 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189cw** (136.0 mg, 58%) as a white solid.

M.p.: = 103-105 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.92–7.89 (m, 3H), 7.70 (dd, *J* = 7.6, 1.0 Hz, 2H), 7.52–7.49 (m, 3H), 7.35 (dd, *J* = 7.9, 1.1 Hz, 2H), 7.02 (dd, *J* = 7.6, 1.0 Hz, 2H), 2.95 (s, 3H), 2.41 (s, 3H).

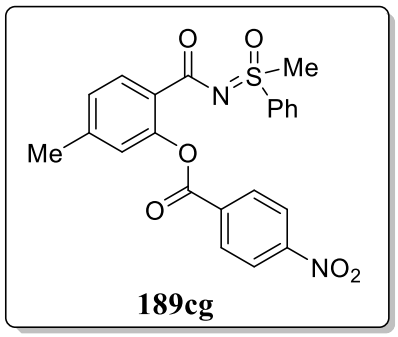
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.6 (C_q), 164.2 (C_q), 149.1 (C_q), 144.0 (C_q), 141.5 (C_q), 137.8 (CH), 133.4 (CH), 132.0 (CH), 131.0 (CH), 131.6 (CH), 129.1 (CH), 128.5 (C_q), 128.0 (C_q), 126.9 (CH), 122.0 (C_q), 121.7 (CH), 43.7 (CH_3), 21.5 (CH_3).

IR (neat): 2925, 1764, 1608, 1576, 1426, 1308, 1216, 1139, 1019, 755 cm^{-1}.

MS (EI) *m/z* (relative intensity) 471 (45) [^{79}Br, M^+], 373 (40) [^{81}Br, M^+], 294 (100), 261 (60), 159 (25).

HR-MS (ESI): *m/z* for $C_{22}H_{18}BrNO_4S$ [$M+H^+$] calcd.: 472.0140.
found: 472.0148.

Synthesis of *N*-[2-(4-Nitrobenzoyloxy-4-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189cg):



189cg

The representative procedure **G** was followed using sulfoximine benzamide (**180c**) (137 mg, 0.50 mmol), carboxylic acid (**101g**) (100 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189cg** (140 mg, 64%) as a white solid.

M.p.: = 96-97 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.26–8.24 (m, 2H), 8.22–8.19 (m, 2H), 7.83 (dt, *J* = 7.2, 1.3 Hz, 2H), 7.58 (td, *J* = 7.4, 1.3 Hz, 1H), 7.46 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 3.21 (s, 3H), 2.45 (s, 3H).

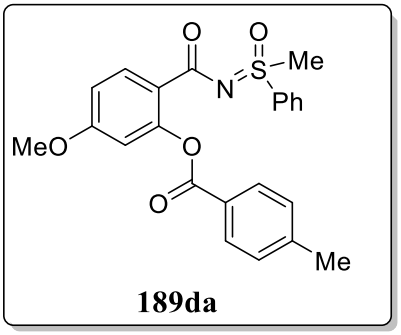
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 163.2 (C_q), 150.5 (C_q), 147.4 (C_q), 138.1 (C_q), 137.4 (C_q), 134.9 (C_q), 133.7 (CH), 131.4 (CH), 131.2 (C_q), 129.4 (CH), 129.3 (CH), 128.4 (CH), 126.8 (CH), 123.4 (CH), 120.0 (CH), 44.2 (CH_3), 20.0 (CH_3).

IR (ATR): 2928, 1734, 1605, 1510, 1447, 1280, 1218, 1096, 976, 763 cm^{-1}.

MS (EI) *m/z* (relative intensity) 438 (75) [M^+], 229 (100), 169 (50), 118 (25).

HR-MS (ESI): *m/z* for $C_{22}H_{18}N_2O_6S$ [M+H^+] calcd.: 439.0886
found: 439.0889.

Synthesis of *N*-[2-(4-Methylbenzoyloxy-4-methoxy)]-*S*-methyl-*S*-phenylsulfoximine (189da):



189da

The representative procedure **G** was followed using sulfoximine benzamide (**180d**) (145 mg, 0.50 mmol), carboxylic acid (**101a**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189da** (129 mg, 61%) as a white solid.

M.p.: = 110-111 °C.

^{1}H-NMR (600 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 8.6, 3H), 7.79 (dd, *J* = 7.4, 0.9 Hz, 2H), 7.36 (dd, *J* = 7.4, 1.0 Hz, 2H), 7.21 (dd, *J* = 7.4, 0.9 Hz, 2H), 6.89 (d, *J* = 7.4 Hz, 2H), 6.87 (d, *J* = 7.4 Hz, 1H), 3.85 (s, 3H), 2.95 (s, 3H), 1.54 (s, 3H).

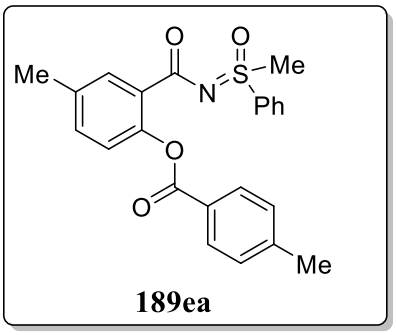
^{13}C-NMR (150 MHz, $CDCl_3$) δ = 171.0 (C_q), 164.4 (C_q), 163.6 (C_q), 149.1 (C_q), 138.1 (C_q), 137.5 (C_q), 133.3 (CH), 132.4 (CH), 130.0 (C_q), 127.0 (CH), 125.0 (CH), 125.6 (C_q), 121.7 (CH), 120.7 (CH), 120.4 (CH), 113.7 (CH), 55.5 (CH_3), 44.0 (CH_3), 21.0 (CH_3).

IR (ATR): 2936, 1745, 1624, 1530, 1416, 1350, 1254, 1116, 976, 784 cm^{-1}.

MS (EI) *m/z* (relative intensity) 423 (75) [M^+], 159 (100), 135 (70), 128 (30).

HR-MS (ESI): *m/z* for $C_{23}H_{21}NO_5S$ [$M+H^+$] calcd.: 424.1140
found: 424.1135.

Synthesis of *N*-[2-(4-Methylbenzoyloxy-5-methyl)]-*S*-methyl-*S*-phenylsulfoximine (189ea):



189ea

The representative procedure **G** was followed using 3 sulfoximine benzamide (**180e**) (137 mg, 0.50 mmol), carboxylic acid (**101a**) (82.0 mg, 0.60 mmol), [{$RuCl_2$(*p*-cymene)}$_2$] (15.3 mg, 5.0 mol %), KPF_6 (46.0 mg, 50 mol %) and $(NH_4)_2S_2O_8$ (114 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/3) yielded **189ea** (123 mg, 61%) as a white solid.

M.p.: = 110-111 °C.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 6.3 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.52 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.37–7.30 (m, 1H), 7.24 (s, 1H), 7.22 (*J* = 8.3 Hz, 2H), 7.01 (dd, *J* = 7.6, 0.9 Hz, 2H), 3.02 (s, 3H), 2.36 (s, 3H), 2.34 (s, 3H).

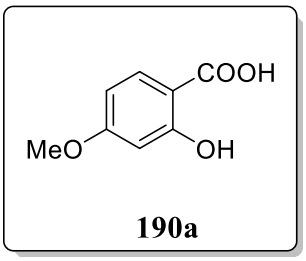
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.5 (C_q), 165.1 (C_q), 147.7 (C_q), 144.2 (C_q), 138.3 (C_q), 137.3 (C_q), 133.7 (C_q), 132.0 (CH), 130.4 (CH), 129.5 (CH), 129.0 (C_q), 129.2 (CH), 128.1 (CH), 127.1 (CH), 126.9 (CH), 120.3 (CH), 44.0 (CH_3), 21.7 (CH_3), 20.0 (CH_3).

IR (ATR): 2924, 1742, 1626, 1524, 1410, 1215, 1126, 1016, 830, 684 cm^{-1}.

MS (EI) *m/z* (relative intensity) 407 (45) [M^+], 152 (100), 135 (45), 222 (35).

HR-MS (ESI): *m/z* for $C_{23}H_{21}NO_4S$ [M+H^+] calcd.: 408.1191
found: 408.1196.

Synthesis of 2-hydroxy-4-methoxybenzoic acid (190a):



190a

N-[2-(4-Methylbenzoyloxy-4-methoxy)]-*S*-methyl-*S*-phenylsulfoximine **(189db)** (211 mg, 0.50 mmol) was dissolved in aqueous HCl (12 N, 5.0 mL) and stirred at 80 °C for 48 h. The reaction mixture was extracted with CH_2Cl_2, and aqueous layer was basified with 40% NaOH and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under vacuum to give sulfoximine **202** (130 mg, 74%) as a colorless liquid dried over Na_2SO_4, and concentrated under vacuum to give the corresponding 4-methoxy-2-hydroxy benzoic acid **190a** (139 mg, 71%).

M.p.: = 152-153 °C.

^{1}H-NMR (600 MHz, DMSO-d_6): δ = 7.70 (dd, J = 8.6, 0.6 Hz, 1H), 6.48 (dd, J = 8.6, 2.5 Hz, 1H), 6.46 (dd, J = 2.5, 0.6 Hz, 1H), 3.78 (s, 3H).

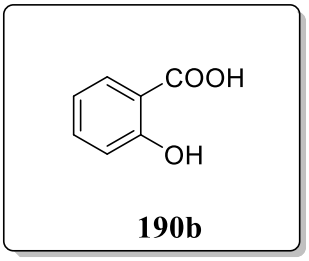
^{13}C-NMR (126 MHz, DMSO-d_6): δ = 171.6 (C_q), 164.9 (C_q), 163.2 (C_q), 131.4 (CH), 106.8 (C_q), 105.5 (CH), 100.6 (CH), 55.4 (CH_3).

IR (ATR): 3415, 2976, 1356, 1271, 1139, 1093, 964 cm^{-1}.

MS (EI) *m/z* (relative intensity) 167 (40) [M^+], 110 (100), 67 (35).

HR-MS (ESI): *m/z* for $C_8H_8O_4$ [M+H^+] calcd.: 168.1480
found: 168.1486.

Synthesis of 2-hydroxybenzoic acid (190b):



190b

N-[2-(4-Methylbenzoyloxy-6-methyl)]-*S*-methyl-*S*-phenylsulfoximine **(189aa)** (183 mg, 0.50 mmol) was dissolved in aqueous HCl (12 N, 5.0 mL) and stirred at 80 °C for 48 h. The reaction mixture was extracted with CH_2Cl_2, and aqueous layer was basified with 40% NaOH and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under vacuum to give sulfoximine **202** (130 mg, 74%) as a colorless liquid dried over Na_2SO_4, and concentrated under vacuum to give the corresponding *o*-hydroxy benzoic acid **190b** (119 mg, 71%).

M.p.: = 158-159 °C.

^{1}H-NMR (600 MHz, DMSO-d_6): δ = 7.82 (dd, J = 8.0, 1.7 Hz, 1H), 7.47 (ddd, J = 8.0, 7.2, 1.7 Hz, 1H), 6.93 (dd, J = 8.3, 1.1 Hz, 1H), 6.89 (ddd, J = 8.3, 7.2, 1.1 Hz, 1H).

^{13}C-NMR (126 MHz, DMSO-d_6): δ = 171.7 (C_q), 161.1 (C_q), 135.4 (CH), 130.1 (CH), 119.0 (CH), 117.0 (CH), 113.0 (C_q).

IR (ATR): 3250, 1750, 1500, 1250, 1129, 1036, 964 cm^{-1}.

MS (EI) *m/z* (relative intensity) 137 (35) [M^+], 105 (100), 69 (35).

HR-MS (ESI): *m/z* for $C_7H_6O_3$ [M+H^+] calcd.: 138.1220.
found: 138.1226.

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3). "*Ruthenium(II)-Catalyzed Decarboxylative C–H-Activation: Versatile Routes to meta-Alkenylated Arenes*" N. Y. P. Kumar, **Keshav Raghuvanshi**, A. Bechtoldt, Prof. Dr. L. Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 6929-6932.

4). "*Ruthenium Oxidase Catalysis for Site-Selective C–H Alkenylations with Ambient O*2 *as the Sole Oxidant*" A. Bechtoldt, C. Tirler, **K. Raghuvanshi**, S. Warratz, C. Kornhaaß, Prof. Dr. L. Ackermann *Angew. Chem. Int. Ed.* **2016**, *55*, 264-267.

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