Ruthenium- and Manganese-Catalyzed C−O and C−C Formation *via* C−H Activation

Dissertation

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Contents

List of Abbreviations

Ac	acetyl
acac	acetyl acetonate
Ad	adamantyl
Alk	alkyl
Am	amyl
AMLA	ambiphilic metal-ligand activation
aq.	aqueous
Ar	aryl
APT	attached proton test
atm	atmospheric pressure
ATR	attenuated total reflectance
BBN	9-borabicyclo(3.3.1)nonane
BDMAEE	bis(2-dimethylaminoethyl)ether
BHT	2,6-di-*tert*-butyl-4-methylphenol
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
BQ	benzoquinoline
Bu	butyl
Bz	benzoyl
c-	cyclo
calc.	calculated
CAN	ceric ammonium nitrate
cat.	catalytic
CMD	concerted-metalation-deprotonation
cod	1,5-cyclooctadiene
conv.	conversion
Cp*	cyclopentadienyl
Cy	cyclohexyl
δ	chemical shift
d	doublet
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublet

DFT	density functional theory
DG	directing group
DIPEA	*N*,*N*-diisopropylethylamine
DMA	*N*,*N*-dimethylacetamide
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DPPBz	1,2-bis(diphenylphosphino)benzene
dt	doublet of triplet
E	electrophile
Ed.	edition
EI	electron ionization
equiv	equivalent
ESI	electronspray ionization
Et	ethyl
FG	functional group
g	gram
GC	gas chromatography
h	hour
Hal	halogen
Het	hetero(aryl)
Hept	heptyl
Hex	hexyl
HPLC	high performance liquid chromatography
HR-MS	high resolution mass spectrometry
Hz	Hertz
i	*iso*
IR	infrared spectroscopy
J	coupling constant
KIE	kinetic isotope effect
L	ligand
LDA	lithium diisopropylamide
LiHMDS	lithium bis(trimethylsilyl)amide
m	*meta*
m	multiplet
M	molar
$[M]^+$	molecular ion peak

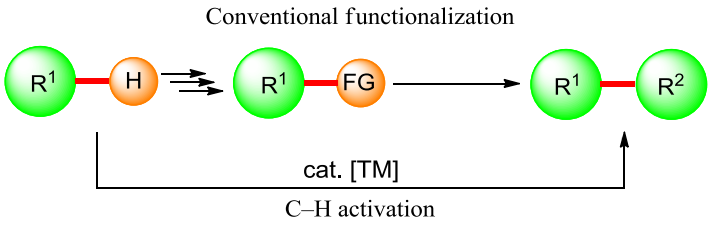
Me	methyl
Mes	mesityl
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mmol	millimol
M. p.	melting point
MS	mass spectrometry
MTBE	methyl *tert*-butyl ether
m/z	mass-to-charge ratio
NCTS	*N*-cyano-4-methyl-*N*-phenyl benzenesulfonamide
NMP	*N*-methylpyrrolidinone
NMR	nuclear magnetic resonance
o	*ortho*
OPV	oil pump vacuum
p	*para*
pent	pentyl
Ph	phenyl
PMP	*para*-methoxyphenyl
Piv	pivaloyl
ppm	parts per million
Pr	propyl
Py	pyridyl
q	quartet
*r*DG	removable directing group
ref.	reference
RT	room temperature
s	singlet
salen	*N*,*N*'-bis(salicylidene)ethylenediamine
sat.	saturated
S_E^{Ar}	electrophilic aromatic subsititution
SOD	superoxide dismutase
SPS	solvent purification system
t	*tert*
t	triplet
T	temperature
tacn	1,4,7-triazacyclononane

TEMPO	2,2,6,6-tetramethylpiperidine-*N*-oxide
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TLC	thin layer chromatography
TM	transition metal
TMP	2,2,6,6-tetramethylpiperidine
TMS	trimethylsilyl
TPP	tetraphenylporphyrin
Ts	*para*-toluenesulfonyl
TS	transition state
wt%	weight by volume
X	(pseudo)halide

1 Introduction

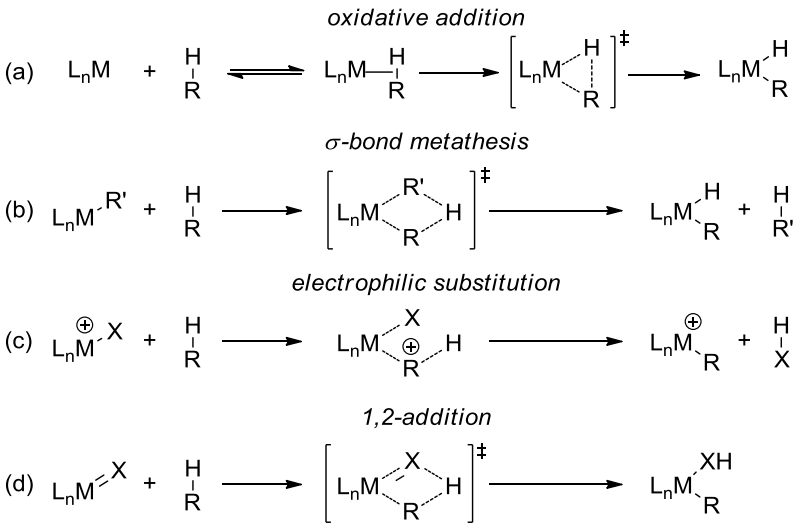
1.1 Transition Metal-Catalyzed C–H Activation

In the past several decades, transition metal-catalyzed cross-coupling reactions have been proved to be one of the most useful and reliable tools for C−C bond formation,[1] such as Negishi,[2] Suzuki-Miyaura,[3] Kumada-Corriu,[4] Stille,[5] and Hiyama cross couplings.[6] These reactions have already been widely applied in pharmaceutical, agrochemical, and fine chemical industries, as well as academic research.[7] However, the prefunctionalized organometallic substrates are often sensitive to air and water, relatively expensive and generate stoichiometric byproducts, all of which remain major disadvantages and limit their applications. According to the guideline of the twelve principles of green chemistry,[8] direct C−H activations are emerging as potential alternatives to conventional cross-coupling reactions due to their atom- and step-economy, which compares favorably to traditional organic synthesis (Scheme 1.1.1). Indeed, C−H activation has been identified to be a powerful tool for constructing complicated molecules from simple precursors.[9]



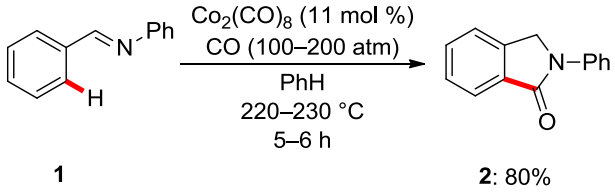
Scheme 1.1.1 C−H Activation versus Conventional Functionalization

The C–H bond metalation step can be accomplished by the active metal species L_nM, four generally accepted modes of these mechanisms have been summarized by Eisenstein and co-workers,[10] including (a) oxidative addition with electron-rich late transition metals, (b) σ-bond metathesis with early transition metals, (c) electrophilic activation with electron-deficient late transition metals, and (d) 1,2-addition to unsaturated M−X bonds (Scheme 1.1.2).



Scheme 1.1.2 Possible Mechanisms for C−H Bond Metalation

As early as 1955, Murahashi reported a cobalt-catalyzed chelation-assisted C–H bond functionalization of (*E*)-*N*,1-diphenylmethanimine (**1**) for the formation of 2-phenylisoindolin-1-one (**2**) under high pressures of CO (100–200 atm). This carbonylation reaction is identified as an early example of transition metal-catalyzed C–H activation reaction (Scheme 1.1.3).[11]



Scheme 1.1.3 Cobalt-Catalyzed C–H Carbonylation

Thereafter, a variety of catalyzed C–H activation reactions were successfully explored, using palladium, platinum, rhodium, ruthenium and iridium, as well as the inexpensive, naturally abundant 3d base metals, such as iron, cobalt, nickel and copper. [9c-w]

1.2 Transition Metal-Catalyzed C–H Cyanation with *N*-Cyano-4-methyl-*N*-phenyl benzenesulfonamide (NCTS)

Aromatic nitriles **3** serve as one of the most important structural motifs in pharmaceuticals, dyes, agrochemicals and natural products.[12] Selected examples from the pharmaceutical and agrochemical industries are shown in Figure 1.2.1.[13]

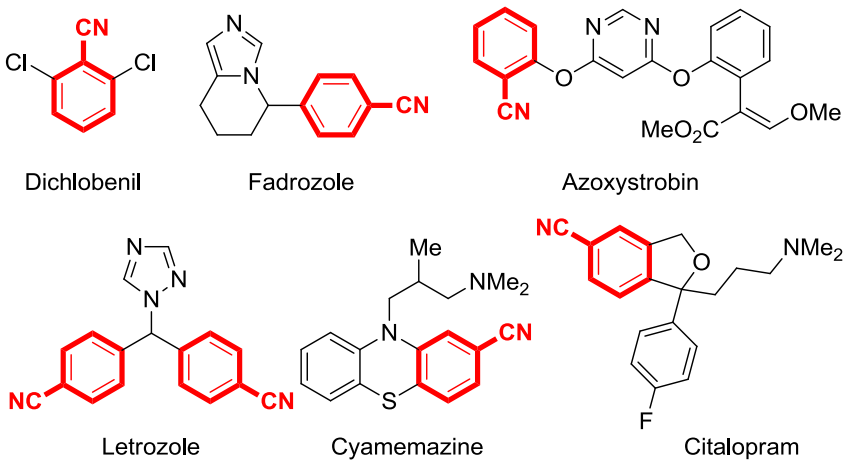
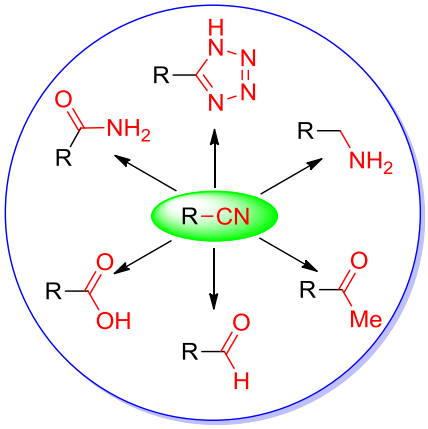


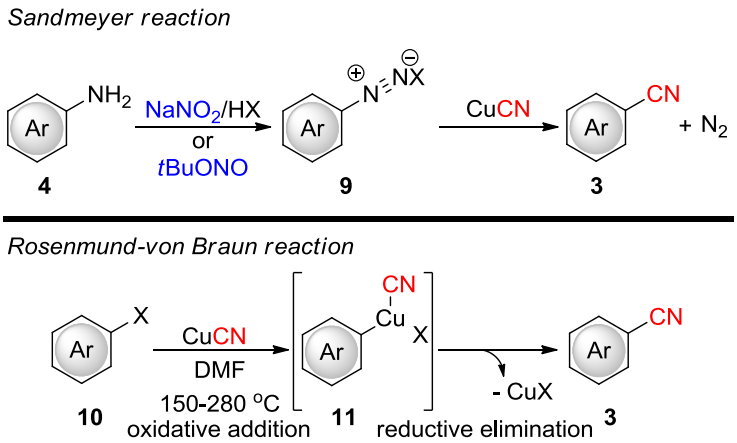
Figure 1.2.1 Selected Examples from Pharmaceutical and Agrochemical Industries

Moreover, nitriles are versatile chemical intermediates, because the cyano group can be readily diversificated into amines **4**, ketones **5**, acids **6**, aldehydes **7**, amides **8**, among others (Scheme 1.2.1).[14]



Scheme 1.2.1 Transformation of Cyano Group

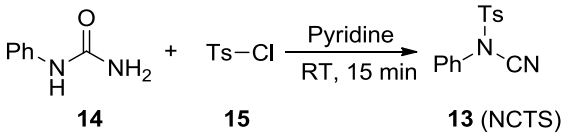
The earlier preparation of aryl nitriles **3** relied on classical approaches, such as the Sandmeyer[15] or the Rosenmund–von Braun reaction (Scheme 1.2.2),[16] and thus have been applied in laboratory and industry for more than a century. However, the use of stoichiometric or even super-stoichiometric amounts of toxic metal cyanides, such as CuCN, or $Zn(CN)_2$, under harsh conditions do not meet today's criteria of sustainable synthesis.[8b]



Scheme 1.2.2 General Process of the Sandmeyer and Rosenmund-von Braun Reactions

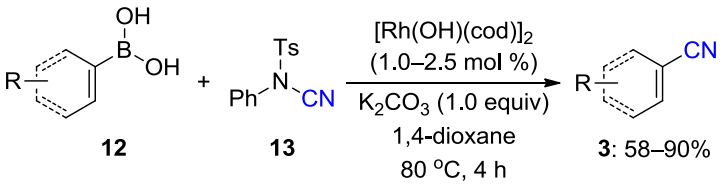
Recent alternative methods include transition-metal-catalyzed cyanations[12b, 17] of aryl halides **10** or boronic acids **12** with metal cyanides.[14a, 18] Indeed, these strategies proceed under milder reaction conditions and display improved functional group tolerance, but toxic metal cyanides are still necessary. Later on, the groups of Buchwald, Beller, Chang, Jiao, Yu, and others have developed the cyanation by the use of more benign and user-friendly cyano sources, such as $K_4Fe(CN)_6$,[19] *N*,*N*-dimethylformamide (DMF),[20] NH_3/DMF,[21] CH_3NO_2[22] in the presence of stoichiometric amounts of oxidants. These approaches are limited to prefunctionalized substrates or electron-rich arenes.

In recent years, the bench stable readily accessible and user-friendly *N*-cyano-4-methyl-*N*-phenyl benzenesulfonamide (NCTS, **13**) has emerged as a versatile cyanation reagent.[23] Notably, it can be easily prepared from inexpensive commercial available phenylurea (**14**) by dehydrative tosylation with *p*-toluenesulfonyl chloride (**15**) in high efficacy, as reported by Kurzer (Scheme 1.2.3).



Scheme 1.2.3 The Preparation of NCTS (**13**)

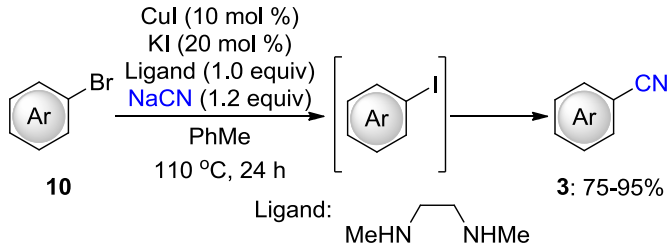
Although it was first synthesized as early as 1949 by Kurzer,[23] the NCTS (**13**) was used as the cyanation reagent until 2011 by the group of Beller.[24] They have demonstrated the first rhodium-catalyzed cyanation of prefunctionalized aryl and alkenyl boronic acids **12** by the use of NCTS (**13**) as the cyanation reagent. Aryl or alkenyl boronic acids **12** with various functional groups, such as chloro, bromo, ketone, ether or anilide, underwent the cyanation process to give the aromatic or vinyl nitriles **3** in good yields under mild conditions. It is noteworthy that various nitriles **3** could be readily accessed *via* the combination of direct borylations of arenes or hydroborations of alkynes with the developed cyanation procedure (Scheme 1.2.4).[24]



Scheme 1.2.4 Rhodium-Catalyzed Cyanation of Aryl and Alkenyl Boronic Acids **12** with NCTS (**13**)

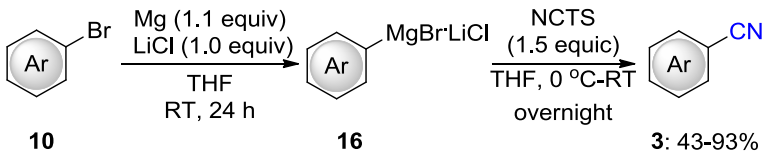
Hartwig and co-workers described a two-step iridium-catalyzed borylation and copper-mediated cyanation of arenes in 2010.[14a] In contrast to the work of Hartwig, the catalytic amounts of rhodium catalyst and user-friendly NCTS (**13**) were used instead of the stoichiometric amounts of copper source and toxic $Zn(CN)_2$ in this strategy. [24]

The Rosenmund–von Braun reaction requires super-stoichiometric amounts of toxic metal cyanides under harsh reaction conditions.[16] In order to address these limitations, Buchwald and co-workers developed the copper-catalyzed domino halide exchange-cyanation of aryl bromides **10** (Scheme 1.2.5). This new method showed significant improvements, include *i)* milder reaction condition, *ii)* good functional group tolerance, and *iii)* the use of polar solvents, which made the isolation and purification of the nitrile products simpler.[18d]



Scheme 1.2.5 Copper-Catalyzed Cyanation of Aryl Brimides **10** with NaCN

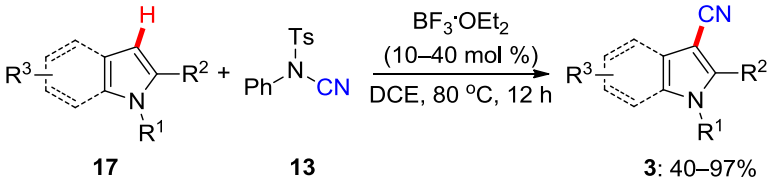
This approach provided significant improvements, but the toxic NaCN is used in this procedure.[18d] Therefore, Beller and co-workers developed a novel synthesis of various (hetero)aryl nitriles **3** from (hetero)aryl bromides **10** *via in situ* generation of Grignard reagents, with subsequent treatment with NCTS (**13**) in good to excellent yields (Scheme 1.2.6).[25] The toxic NaCN was replaced by the user-friendly NCTS (**13**) cyanation reagent. However, due to the required formation of Grignard reagents, important functional groups, such as ester, ketone, amino and alcohols were not suitable for this cyanation reaction.



Scheme 1.2.6 Cyanation *via* in situ Generation Grignard Reagents with NCTS (**13**)

In the same year, Wang and co-workers disclosed the Lewis-acid-catalyzed electrophilic cyanation of indoles **17** and pyrroles **18** with NCTS (**13**) as the cyanation reagent in an S_EAr

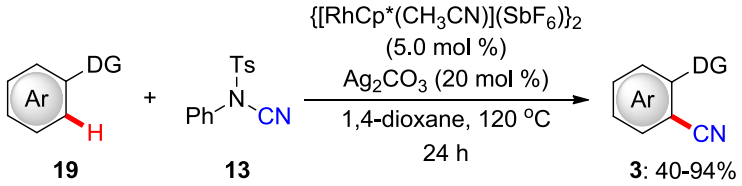
reaction (Scheme 1.2.7).[26] The corresponding cyanation products were obtained in 40–97% yields with excellent regioselectivities, including NH free indoles. However, this cyanation procedure was limited to electron-rich substrates **17**, and the electron-poor substrates failed to give the corresponding products because of the electrophilic nature of this reaction.



17 **13** **3**: 40–97%

Scheme 1.2.7 Lewis-Acid-Catalyzed Electrophilic Cyanation of Indoles **17** and Pyrroles **18** with NCTS (**13**)

To overcome these restrictions, Fu and coworkers developed a rhodium-catalyzed directed C–H cyanation of arenes with NCTS (**13**).[27] This strategy furnished a number of aromatic and heteroaromatic nitriles in moderate to excellent yields under mild conditions, with good tolerance of various synthetically important functional groups. Furthermore, many different directing groups, such as oxime, pyridine or pyrazole, proved to be suitable in this C−H cyanation process (Scheme 1.2.8).

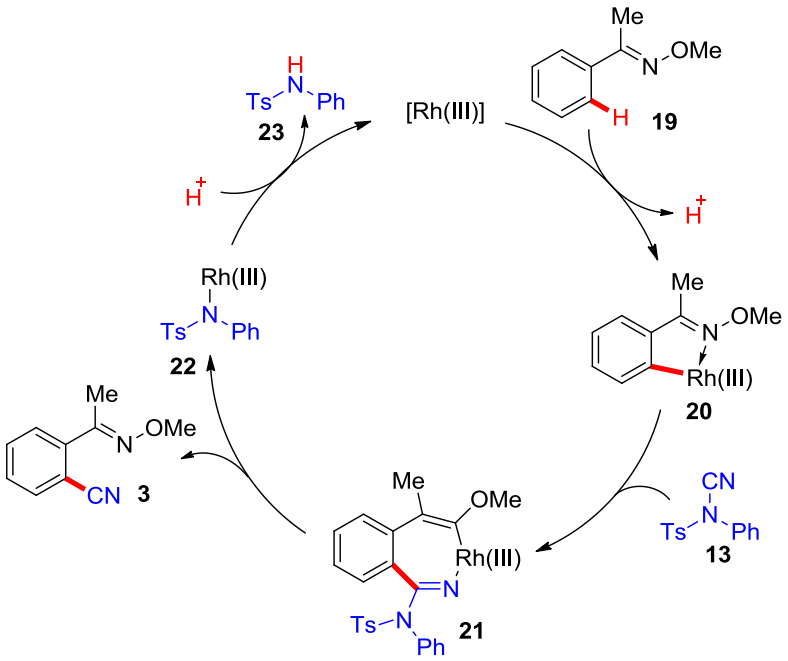


19 **13** **3**: 40-94%

DG = oxime, pyridine, pyrazole, imidazole, oxazoline

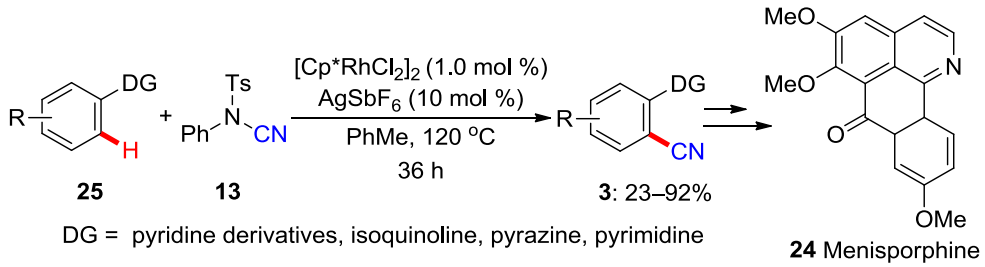
Scheme 1.2.8 Rhodium-Catalyzed Directed C–H Cyanation of Arenes with NCTS (**13**)

A plausible catalytic cycle for this rhodium-catalyzed C–H cyanation was proposed to be initiated by concerted metalation–deprotonation,[28] thus forming the five-membered rhodacycle intermediate **20**. Subsequently, seven-membered rhodacycle **21** is formed *via* NCTS (**13**) coordination and migratory insertion into the carbon–rhodium bond. Then, *β*-elimination furnishes the desired cyanation product **3** and a tosylaniline-coordinated Rh(III) complex **22**. Finally, proto-demetalation of the Rh(III) complex **22** regenerates the active Rh(III) complex (Scheme 1.2.9).[27]



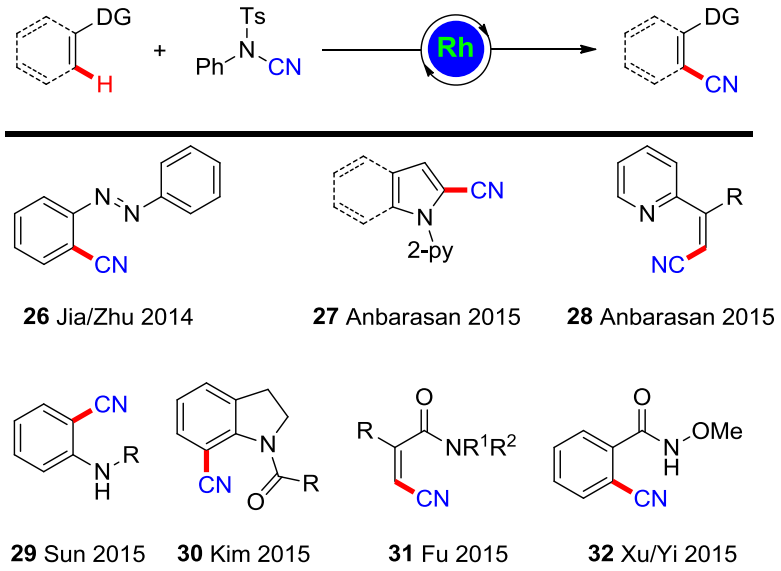
Scheme 1.2.9 Proposed Catalytic Cycle for Rhodium-Catalyzed C–H Cyanation with NCTS (**13**)

Related work on rhodium-catalyzed directed C–H cyanation with NCTS (**13**) as the cyanation reagent was reported by Anbarasan in the same year (Scheme 1.2.10).[29] As in the work by Fu,[27] pyridine derivatives were used as a directing group. However, the key intermediate for the synthesis of naturally available alkaloid menisporphine,[30] which is isolated from *Menispermum dauricum DC* (Menispermaceae, **24**),[31] could be readily synthesized by the use of this methodology.[29]



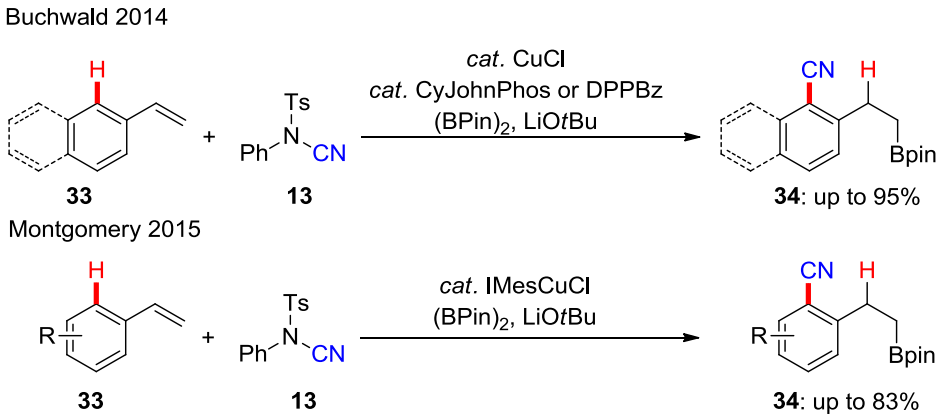
Scheme 1.2.10 Rhodium-Catalyzed Directed C–H Cyanation of Arenes with NCTS (**13**)

Subsequently, various rhodium-catalyzed directed C–H cyanations were reported using NCTS (**13**) as the efficient cyanation reagent from the groups of Jia/Zhu,[32] Anbarasan,[33] Sun,[34] Kim,[35] Fu,[36] Xu/Yi.[37] They independently investigated the cyanations with different substrates. Importantly, some of them achieved the cyanation on alkenes[33a, 36] and at the C-7 position[35] of indolines (Scheme 1.2.11).



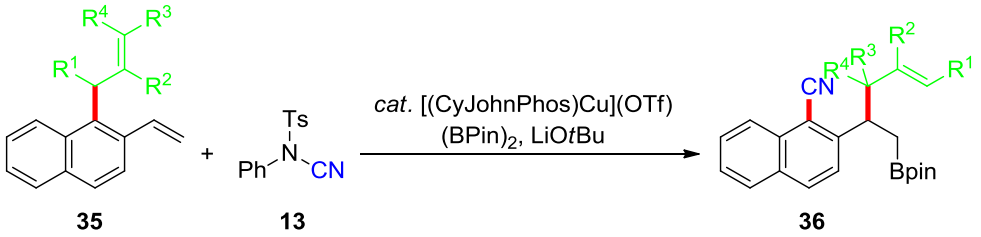
Scheme 1.2.11 Rhodium-Catalyzed C–H Cyanation with Different Directing Groups

This class of C–H cyanation catalysts was not limited to rhodium complexes, as the C–H cyanation could also be achieved by using copper catalysis. Two copper-catalyzed regioselective borylation/*ortho*-cyanation of vinylarenes **33** with NCTS (**13**) were more recently achieved by Buchwald[38] and Montgomery,[39] wherein the vinyl group underwent formal hydroboration simultaneously along with *ortho*-cyanation of the arene (Scheme 1.2.12).



Scheme 1.2.12 Copper-Catalyzed Borylation/*ortho*-Cyanation of Vinylarenes **33** with NCTS (**13**)

Furthermore, based on the previous work,[38] Yang reported a copper-catalyzed borylation/*ortho*-cyanation/allyl group transfer cascade reaction. This process was suggested to be initiated by an unconventional copper-catalyzed electrophilic dearomatization. Subsequently, an rearomatization-driven Cope rearrangement occurred which featured regio- and stereospecific 1,3-transposition of the allyl fragment. Adjacent tertiary and quaternary stereocenters were constructed with excellent diastereocontrol through this copper-catalyzed cascade reaction (Scheme 1.2.13).[40]

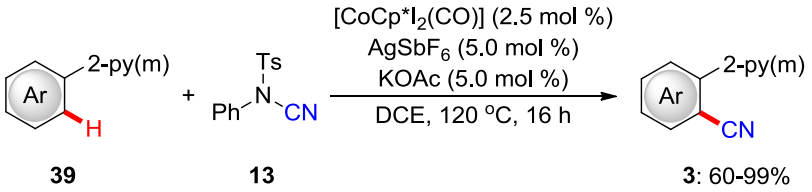


35 **13** **36**

Scheme 1.2.13 Copper-Catalyzed Borylation/*ortho*-Cyanation/Allyl Transfer Cascade Transformation with NCTS (**13**)

Since the Kanai group published the cobalt(III)-catalyzed hydroarylation of imines **37** and *α*,*β*-unsaturated ketones **38** in 2103,[41] the high valent cobalt catalyzed C–H activation has emerged as a salient alternative to those rhodium catalyzed C–H activation.[42]

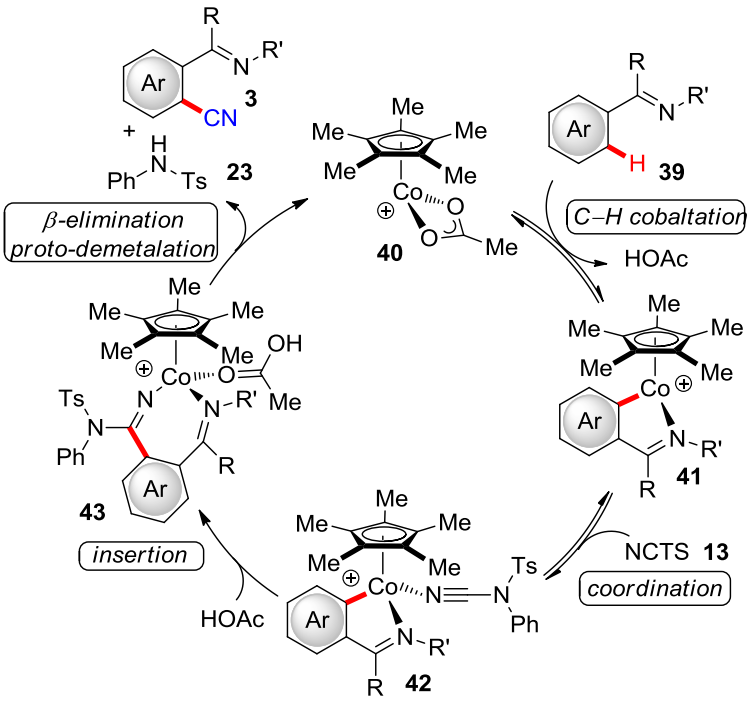
The cobalt-catalyzed C–H cyanation of arenes and heteroarenes was independently explored by the groups of Ackermann[43] and Glorius.[44] These carboxylate-assisted[28] cobalt-catalyzed C–H cyanation proved to have excellent chemoselectivity with high functional group tolerance, in that ester, ketone, bromo, fluoro and amido group were well tolerated.[43] Furthermore, this cobalt catalytic system was not restricted to the typical 2-phenyl pyridine derivatives. Indeed, the biologically relevant indole heterocycles **39** [9x, 45] also proved to be suitable substrates and efficiently achieved the desired cyanation products **3** (Scheme 1.2.14). It is noteworthy that the directing group was shown to be removable, providing ready access to a variety of substituted cyanated NH-free indoles.[43]



39 **13** **3**: 60-99%

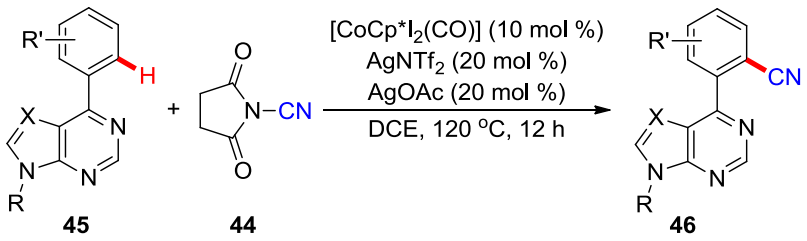
Scheme 1.2.14 Cobalt-Catalyzed C–H Cyanation with NCTS (**13**)

Based on the experimental mechanistic studies, Ackermann and co-workers proposed the catalytic cycle to be initiated by a reversible and fast C–H metalation (intermolecular: k_H/k_D = 1.0), thus forming the cyclometalated complex **41**. The seven-membered cobaltacycle complex **43** then undergoes migratory insertion with NCTS (**13**). Subsequently, *β*-elimination affords the cyanation product **3**, while proto-demetalation regenerates the catalytically active cobalt(III) carboxylate catalyst **40** (Scheme 1.2.15).[43]



Scheme 1.2.15 Proposed Mechanism for Cobalt-Catalyzed C–H Cyanation with NCTS (**13**)

A related cobalt-catalyzed C−H cyanation work was later reported by Chang and co-workers.[46] They used the *N*-cyanosuccinimide (**44**) as an electrophilic cyanation reagent in place of NCTS (**13**), providing the monocyanated products with high selectivity and excellent functional group tolerance. Notably, the substrate scope was found to be broad, and a wide range of heterocycles, including 6-arylpurines **45**, underwent the cyanation process in high efficacy (Scheme 1.2.16).[46]



Scheme 1.2.16 Cobalt-Catalyzed C–H Cyanation with *N*-Cyanosuccinimide (**44**)

1.3 Ruthenium-Catalyzed C–H Hydroxylation

Oxygenated aromatic molecules can be found in a variety of useful pharmaceuticals, agrochemicals, polymers, and biologically active compounds (Figure 1.3.1), and are key intermediates in organic synthesis.[47] The importance of substituted phenols in these areas has resulted in a continued demand for developing versatile methods for the synthesis of substituted phenols. Direct catalytic C–H oxygenation represents an environmentally benign as well as step-economical approach to substituted phenols.[9j, 48]

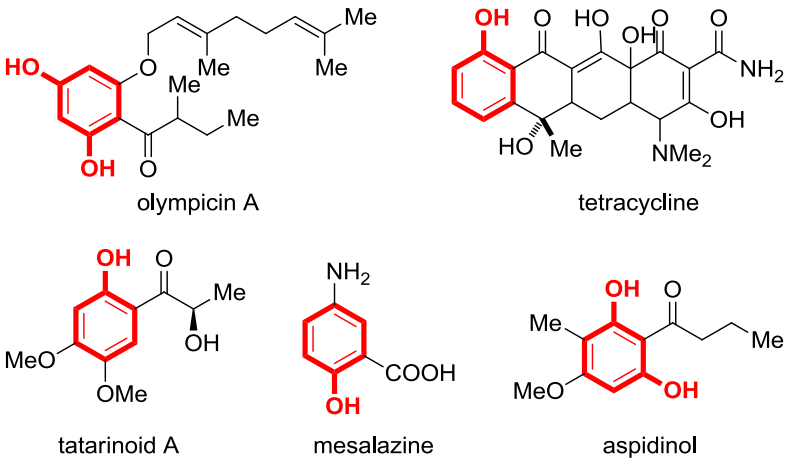
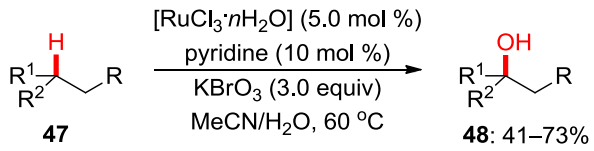


Figure 1.3.1 Selected Biologically Active Compounds

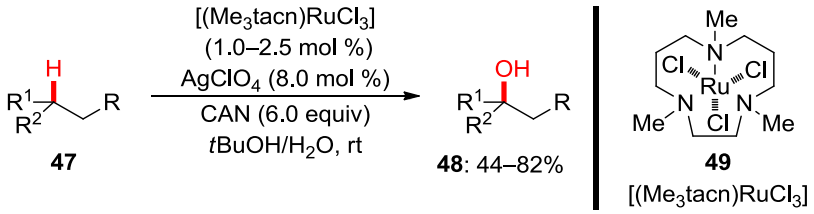
Since the early achievements reported by Breslow[49] and Fujiwara,[50] synthetically useful methods for catalytic direct oxygenation of alkanes and arenes has been broadly investigated, mostly using palladium,[48a, 48b, 51] or iron catalysts.[52] In contrast, readily available ruthenium complexes-catalyzed C–H oxygenations have been underdeveloped until recently.[9j]

The recent ruthenium-catalyzed unactivated tertiary C–H bond oxygenations were successfully achieved by Du Bois and co-workers (Scheme 1.3.1).[53] They found that the catalytic efficacy of this ruthenium-catalyzed hydroxylation was promoted by the combination of catalytic [$RuCl_3.nH_2O$][54] and pyridine in the presence of stoichiometric amounts of $KBrO_3$. Various functional groups, such as ester, epoxide, sulfone, oxazolidinone, carbamate, and sulfamate, could be tolerated in this oxygenation, affording the tertiary alcohol products in synthetically acceptable yields. Moreover, the use of $H_2{}^{18}O$ as a co-solvent resulted in the nearly quantitative incorporation of ^{18}O into the corresponding alcohol, thus providing a convenient method for ^{18}O-atom incorporation [53b]



Scheme 1.3.1 Ruthenium-Catalyzed Tertiary C–H Hydroxylation

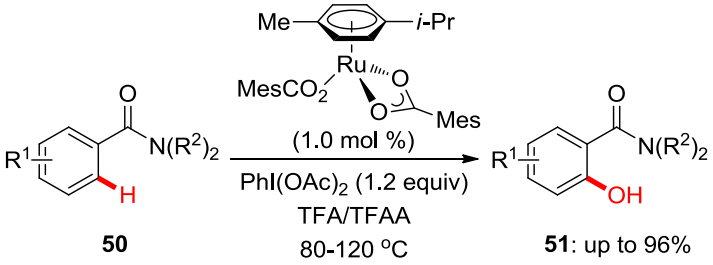
After further investigations, the same group discovered that the yield could be improved using a combination of [(Me_3tacn)$RuCl_3$] (**49**) as the catalyst, $AgClO_4$ as an additive and CAN as the oxidant, allowing for a reduction of the catalyst loading, as well as reduced reaction temperatures (Scheme 1.3.2).[53a]



Scheme 1.3.2 Ruthenium-Catalyzed Tertiary C–H Hydroxylation

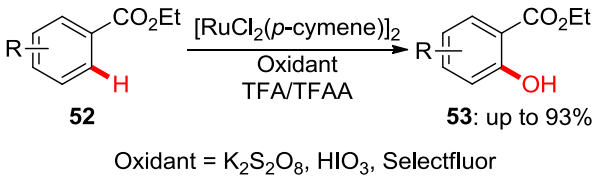
In recent years, numerous direct oxygenation of more stable C(sp^2)–H bonds in arenes and heteroarenes with readily accessible ruthenium catalysts have been devised, with key contributions coming from the groups of Ackermann,[55] Rao[56] and others.[57]

In 2012, the group of Ackermann reported the ruthenium-catalyzed, weakly-coordinating directing group directed C–H hydroxylations.[55e] The C–O bond formation process proceeded smoothly with the user-friendly and inexpensive [$RuCl_3(H_2O)_n$] catalyst, in addition to $PhI(OAc)_2$ as an oxidant (Scheme 1.3.5). However, the most satisfactory results were obtained when the well-defined ruthenium(II) biscarboxylate [$Ru(O_2CMes)_2$(*p*-cymene)] was used as the catalyst. Remarkably, the corresponding phenols with a variety of valuable functional groups could be provided through this highly efficient C(sp^2)–H hydroxylation at a reasonably low catalyst loading of only 1.0 mol % (Scheme 1.3.3).[55e]



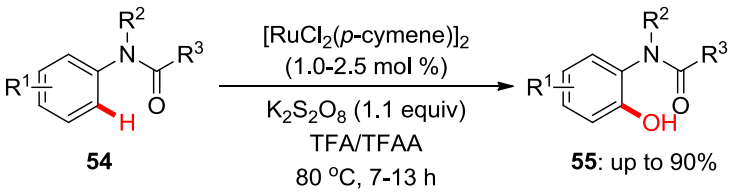
Scheme 1.3.3 Ruthenium(II)-Catalyzed Amide-Directed C–H Hydroxylation

A ruthenium(II)-catalyzed *ortho*-hydroxylation of benzoates **52** has been developed by Rao and coworkers.[56d] A variety of functionalized *ortho*-hydroxylyzed benzoates could be accessed *via* this ester-directed C–H oxygenation process. It is noteworthy that a TFA/TFAA co-solvent system was found to be ideal, and potassium persulfate, Selectfluor, or iodic acid was used as oxidants in this C–O bond formation. Moreover, important biologically compounds, such as Mesalazine could be synthesized in a step-economical manner by the ruthenium(II)-catalyzed hydroxylation product (Scheme 1.3.4).



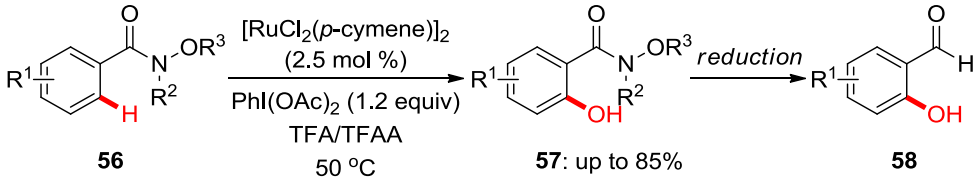
Scheme 1.3.4 Ruthenium(II)-Catalyzed C–H Hydroxylation of Benzoates **52**

Ruthenium(II)-catalyzed anilide-directed oxidative C–O bond formations were reported by Rao. An efficient synthesis of mono- and dihydroxylated anilides by C(sp^2)–H oxygenation was accomplished, featuring excellent site-selectivities and good functional group tolerance (Scheme 1.3.5).[56c]



Scheme 1.3.5 Ruthenium(II)-Catalyzed Anilide-Directed C–H Hydroxylation

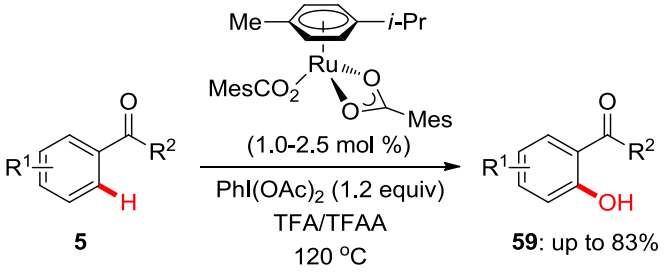
The *N*-Methoxy-*N*-methylamides–Weinreb amides **56**, which can be chemoselectively transformed into the corresponding ketones **5** and aldehydes **7**, have been shown to be important in synthetic organic chemistry.[58] Based on their previous investigation,[55e] Ackermann and co-workers reported the C–H oxygenation of aryl Weinreb amides **56**[55c] using $[RuCl_2(p\text{-cymene})]_2$ as the catalyst and $PhI(OAc)_2$ as the oxidant, which was found to enable the C–H hydroxylation of aryl Weinreb amides **56**, affording the corresponding phenols **57** with ample scope under mild reaction conditions. Furthermore, the *ortho*-hydroxyaldehyde such as **58** could be obtained *via* a facile reduction process of the ruthenium-catalyzed C–H bond oxygenation product (Scheme 1.3.6).[55c]



Scheme 1.3.6 Ruthenium(II)-Catalyzed C–H Hydroxylation of Weinreb Amides **56**

This ruthenium-catalyzed hydroxylation was not limited to relatively strongly coordinating directing groups. Indeed, the much weaker coordinating directing ketones **5** (Scheme 1.3.7)[55f] and aldehydes **7** [55b] were also shown to be applicable. It is noteworthy that when using ketone **5** directed C–H hydroxylations, there were three related palladium-catalyzed ketone directed C–H hydroxylation published almost at the same time.[51c, 51f, 51g] However, the inexpensive ruthenium-catalyzed C–H hydroxylation is obviously more attractive comparing to palladium

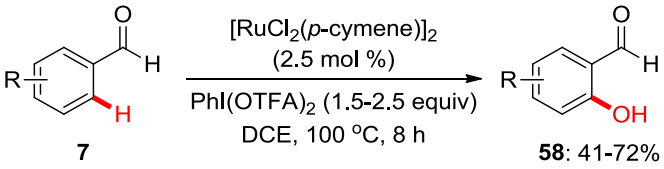
catalytic system.



Scheme 1.3.7 Ruthenium(II)-Catalyzed Ketone-Directed C–H Hydroxylation

The ruthenium-catalyzed C–H hydroxylation bearing very weakly coordinating directing group aldehydes **7** should be highlighted,[55b] because of the inherent tendency of aldehydes to undergo over-oxidation to the corresponding carboxylic acid under the oxidizing reaction conditions usually, restricting the utility of aldehyde-directed C–H hydroxylation.

Significantly, Ackermann and co-workers reported the first ruthenium-catalyzed C–H oxygenation by assistance of very weakly coordinating aldehydes **7**.[55b] The site-selective hydroxylation of various benzaldehydes **7** with ample scope was accomplished efficiently in the presence of an inexpensive and a user-friendly ruthenium(II) complex, providing products which could be easily converted into various valuable heterocycles (Scheme 1.3.8).



Scheme 1.3.8 Ruthenium(II)-Catalyzed Aldehyde-Directed C–H Hydroxylation

1.4 Manganese-Catalyzed C–H Activation

During the past decade, catalytic C–H activation reactions were successfully achieved by using rare and expensive 4d or 5d transition metals, such as ruthenium, rhodium, palladium, iridium and rhenium.[9c-p, 9r-w] In contrast, C–H activation reactions catalyzed by naturally abundant 3d transition metal complexes are considerably less explored until more recently, despite their high abundance and low cost. Recently, the 3d transition metals, such as iron, cobalt and nickel, catalyzed C–H bond activation reactions developed enormously.[42, 59]

Manganese is the twelfth most abundant element and the third most abundant transition metal after iron and titanium in the earth's crust.[60] In addition, it is an essential trace element for life on earth. Thus, several manganese-containing enzymes are needed to metabolize carbohydrates, cholesterol and amino acids in the human body, such as arginase and manganese-containing superoxide dismutase (Mn-SOD).[61] Moreover, the less toxic[62] and lower cost[63] as compared

to 4d and 5d transition metals mean that manganese has the potential to be a successful alternative to typically used transition metals, such as platinum, palladium, rhodium, iridium or ruthenium (Figure 1.4.1).

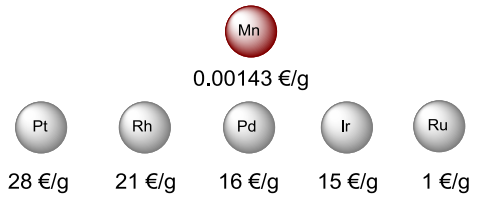
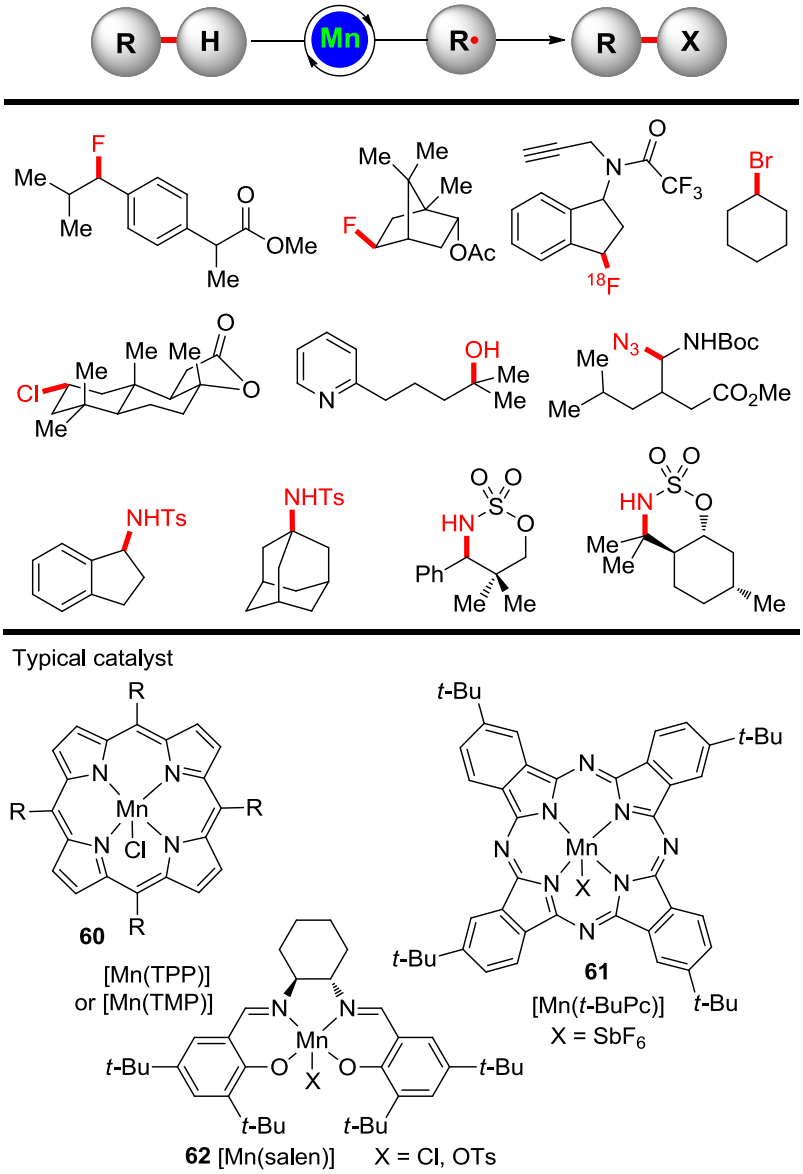


Figure 1.4.1 Price of Selected Transition Metals[63]

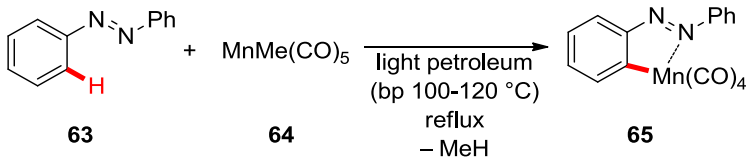


Scheme 1.4.1 Manganese-Catalyzed C–H Functionalization by Homolytic C–H Cleavage

In consideration of these advantages, manganese-catalyzed C–H oxygenations,[64] nitrogenations[65] and halogenations[66] have been well explored with high-valent manganese[67]

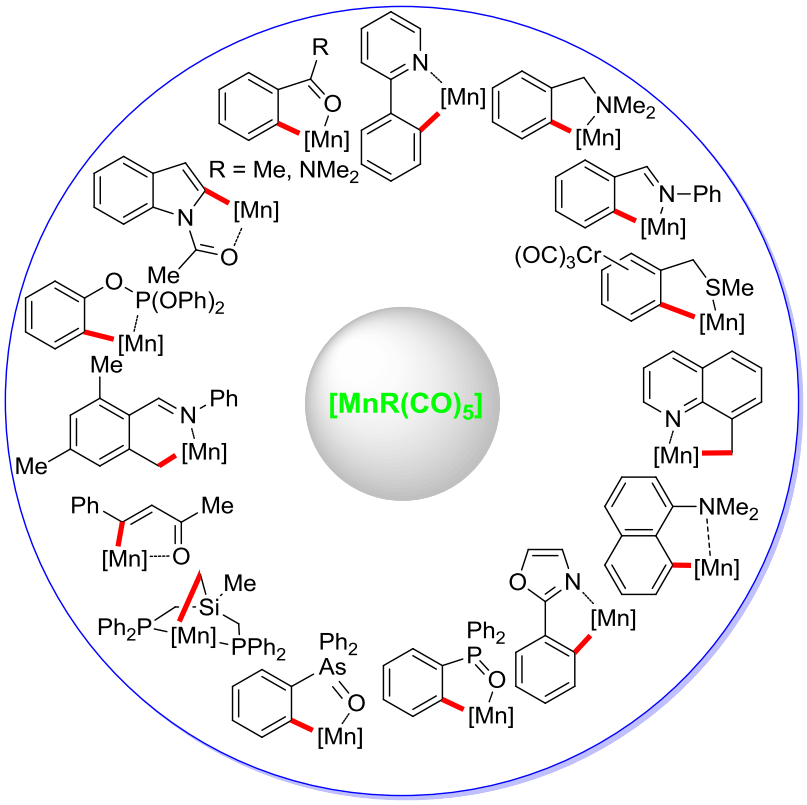
species *via* a radical-type mechanism (Scheme 1.4.1). In contrast, manganese-catalyzed organometallic C–H activation[68] reactions are scarce.[69]

An early example of stoichiometric manganese-mediated C–H activation was demonstrated on azobenzene (**63**), to produce the five-membered manganacycle complex **65** formation, as was reported by Stone, Bruce and co-workers.[70] This relatively stable complex could be isolated by column chromatography and was characterized by ^{1}H NMR and IR spectroscopy (Scheme 1.4.2).



Scheme 1.4.2 Stoichiometric Manganese-Mediated C–H Activation

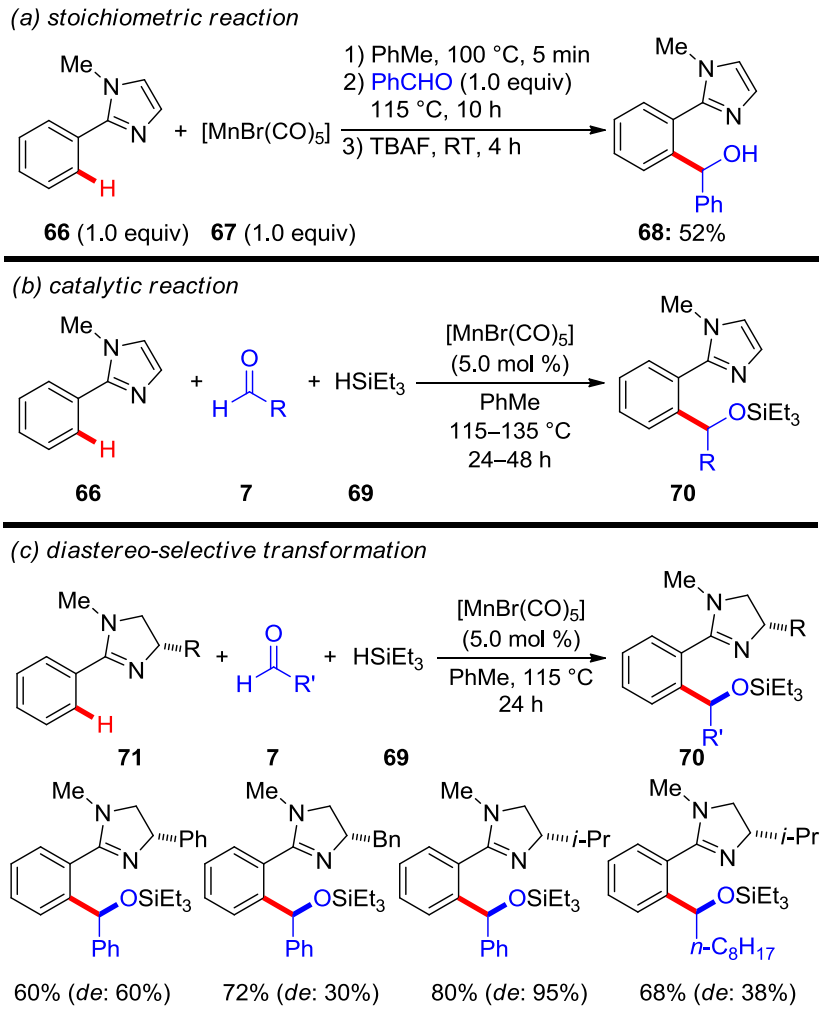
Thereafter, a variety of manganacycle complexes were successfully prepared in the presence of stoichiometric amounts of $MnR(CO)_5$ *via* C–H activation. It is noteworthy that the directing groups were necessary for the site-selective formation of the manganacycle complexes.[70-71]



Scheme 1.4.3 Representative Manganacycle Complexes (R = Me, Bn, Ph, etc)

With the successful preparation of a set of manganacycle, the transformations of these complexes were investigated by the groups of Nicholson/Main,[72] Woodgate,[73] Liebeskind,[74] among others.

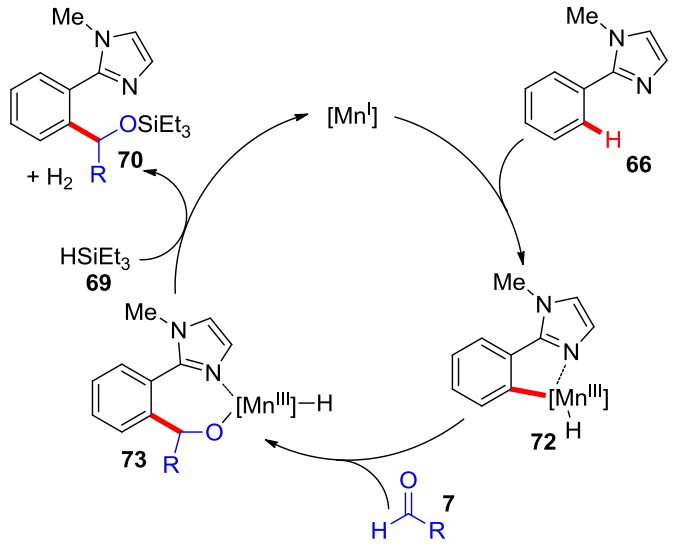
To date, only a few examples of manganese-catalyzed organometallic C–H bond activation have been reported. Significant progress on manganese-catalyzed organometallic C–H activation was achieved in 2007 by the group of Kuninobu/Takai,[75] although the first stoichiometric manganese-mediated C–H bond activation was disclosed by Stone, Bruce and co-workers as early as 1970.[70] Thus, Kuninobu/Takai reported the manganese-catalyzed, imidazole-directed aromatic C–H bond addition to the polar C=O bond in aldehydes **7**.[75]
They initiated their investigations by examing the stoichiometric manganese C–H activation reaction.[75] The polar C=O bond insertion into the aromatic C–H bond of 1-methyl-2-phenyl-1*H*imidazole (**66**) reaction was conducted with stoichiometric amounts of [MnBr(CO)$_5$] (**67**) and provided the corresponding benzyl alcohol **68** in 52% yield (Scheme 1.4.4a). Only a trace amount of desired product was obtained in the presence of catalytic amounts of [MnBr(CO)$_5$]. They found that catalyst turnover could be achieved in this polar C=O bond insertion reaction when Et$_3$SiH (**69**) was introduced as the additive, therefore affording the corresponding silylethers **70** (Scheme 1.4.4b).



Scheme 1.4.4 Manganese-Catalyzed C–H Addition to Aldehydes **7**

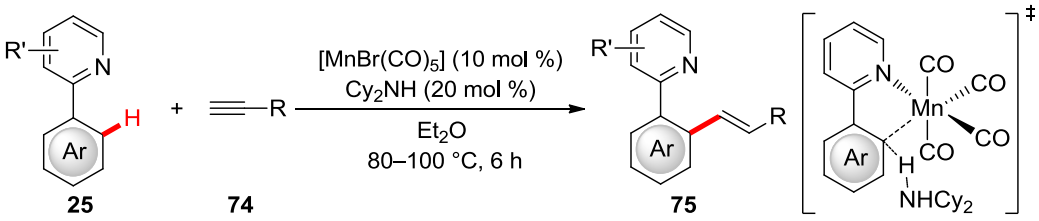
They also screened some other transition metal catalysts in this C–H transformation. However, only $[Mn_2(CO)_{10}]$ showed comparable catalytic activities, while $MnCl_2$, $Mn(acac)_3$, $ReBr(CO)_5$, $Ru_3(CO)_{12}$, $RuH_2(CO)(PPh_3)_3$, $RhCl(PPh_3)_3$, and $Ir_4(CO)_{12}$ failed to give any conversions. Remarkably, this manganese-catalyzed C–H activation reaction could be directly applied to diastereo-selective transformations, and the diastereomeric excess silylethers **70** were obtained when using chiral imidazoline as the directing groups (Scheme 1.4.4c).

The catalytic cycle proposed by Kuninobu/Takai suggested that the C–H activation is accelerated by the coordination of the nitrogen atom of the imidazole to the manganese center, which then undergoes C=O bond insertion into the manganese–carbon bond, to form seven-membered manganese complex **73**. Finally, the silylethers **70** is formed *via* release of H_2 gas and regeneration of the manganese(I) catalyst by the action of Et_3SiH (**69**) (Scheme 1.4.5).



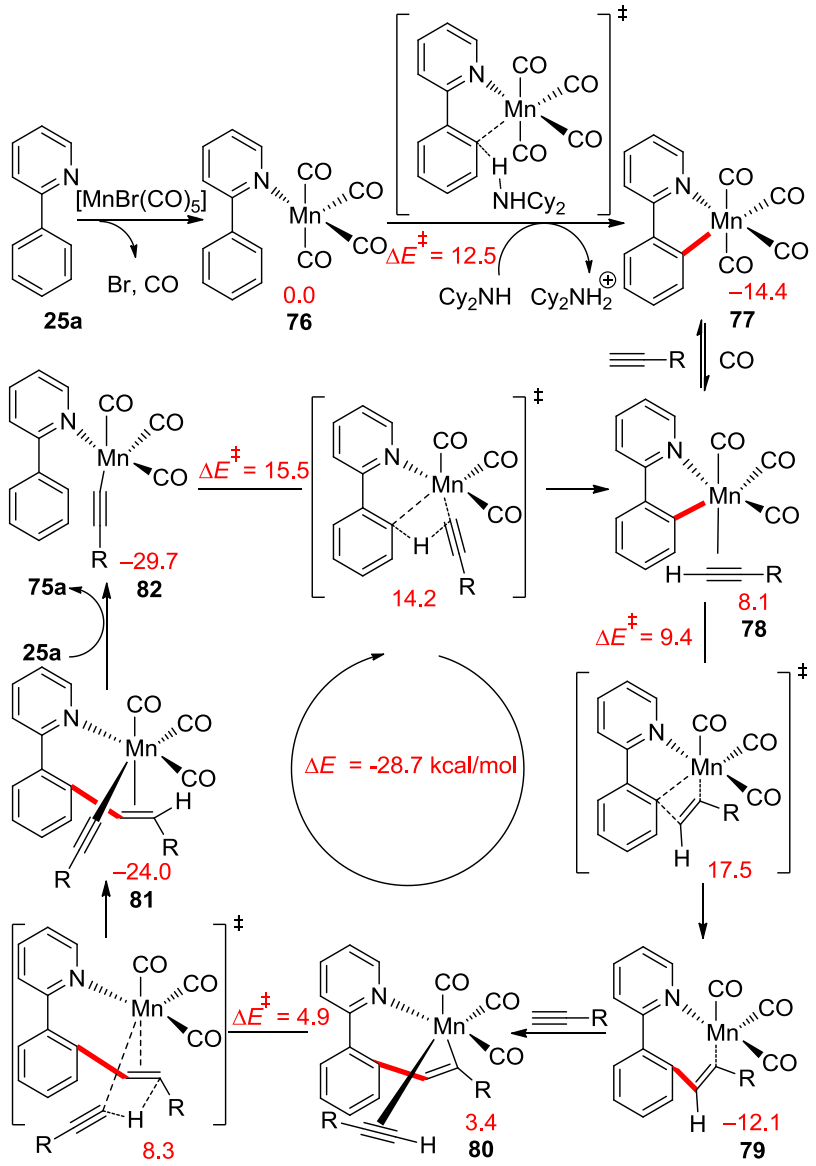
Scheme 1.4.5 Proposed Catalytic Cycle for Manganese(I)-Catalyzed C–H Addition to Aldehydes **7**

The group of Wang reported that manganese-catalyzed C–H bond addition was not restricted to C–Het multiple bonds.[76] They developed a novel C–H alkenylation *via* hydroarylation of terminal alkynes **74** in the presence of $[MnBr(CO)_5]$ as the catalyst.[76] Various aromatic and aliphatic alkynes **74** with a wide range of functional groups, including fluoro, chloro, bromo, iodo, ester and nitro substitutents, underwent the C–H alkenylation process to provide facile access to the *anti*-Markovnikov *E*-configured olefins **75** in a highly chemo-, regio-, and stereoselective fashion (Scheme 1.4.6). However, this C–H alkenylation protocol was limited to terminal alkynes **74**.



Scheme 1.4.6 Manganese-Catalyzed C–H Alkenylation with Terminal Alkynes **73**

A proposed catalytic cycle for the manganese-catalyzed C–H addition onto C–C triple bond was established based on their experimental studies and DFT calculations (Scheme 1.4.7).

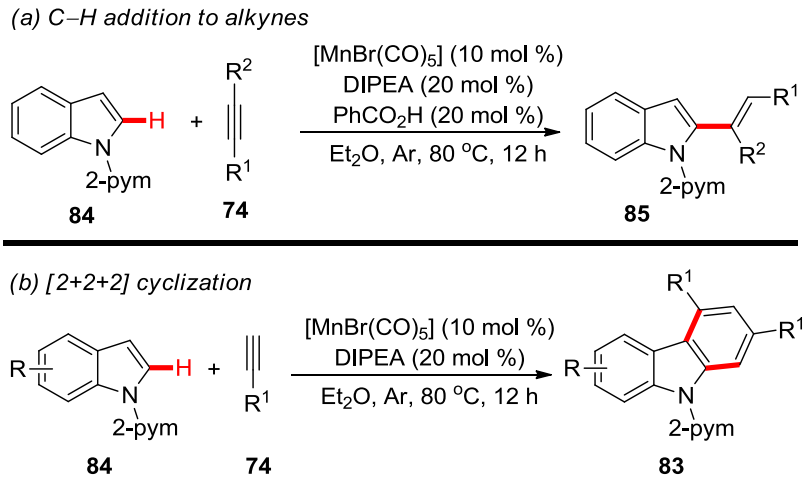


Scheme 1.4.7 Proposed Catalytic Cycle for Manganese(I)-Catalyzed C–H Alkenylation

The reaction was initiated by base-assisted deprotonative C−H activation in the presence of the manganese catalyst and $HNCy_2$. The resulting five-membered manganacycle **77** subsequently

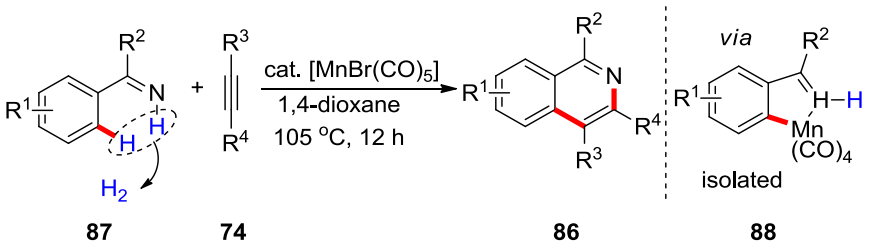
undergoes insertion of the alkyne to provide a seven-membered manganacycle **79**. Then, the alkenylation product **75** is furnished from intermediate **79** *via* a ligand-to-ligand H-transfer process, along with the formation of manganese species **82**. Complex **78** was regenerated through alkynyl-assisted C−H activation.

A related work on manganese-catalyzed C–H alkenylation with alkynes **74** was published by Li and co-workers.[77] Compared to Wang's work,[76] this C–H alkenylation was not restricted to the terminal alkynes.[77] Indeed, both terminal and internal alkynes **74** proved to be suitable substrates in this protocol, providing the bis/trisubstituted indolyl-alkenes with a catalytic amount of acid as additive (Scheme 1.4.8a). Notably, carbazoles **83** were obtained *via* a [2+2+2] cyclization process in the absence of acid **6** (Scheme 1.4.8b). This suggested that $PhCO_2H$ (**6**) was key to success in the chemo-selectivity *via* an H-transfer process.



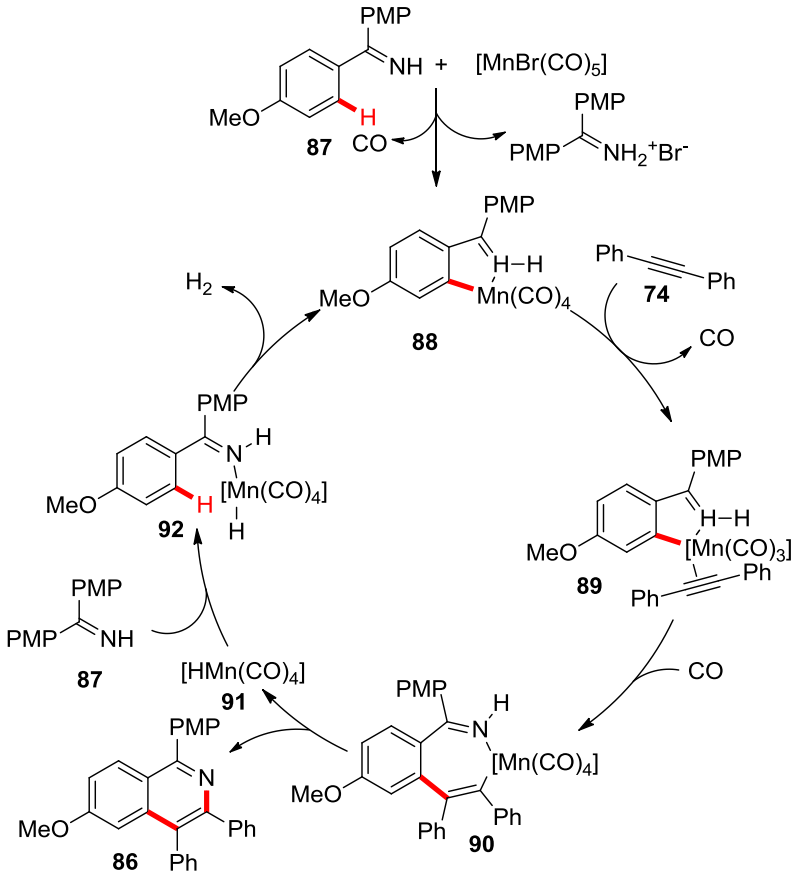
Scheme 1.4.8 Manganese(I)-Catalyzed C–H Alkenylation and Cyclization of Indoles **84**

Isoquinolines **86** are key building blocks in organic synthesis and often present significant bioactivity, such as anti-inflammatory or antimalarial properties.[78] Developing new strategies for the efficient isoquinolines preparation is therefore in high demand. In 2014, Wang and coworkers described a highly atom-economical strategy to access isoquinoline derivatives *via* dehydrogenative [4+2] annulation of N−H imines **87** with alkynes **74** in the presence of $MnBr(CO)_5$ (Scheme 1.4.9).[79] In contrast to other well known isoquinoline synthesis through the noble 4d or 5d transition-metal catalyzed C−H activation,[80] this manganese-catalyzed C−H transformation produced H_2 as the sole byproduct without any oxidants, ligands, or additives. Diaryl, aryl alkyl imines, aromatic and aliphatic acetylenes **74** with a wide range of functional groups underwent the C–H annulations to furnish the corresponding isoquinolines in high yields. Importantly, terminal alkynes **74**, which are often challenging substrates in transition-metal catalyzed isoquinoline **86** synthesis,[80] were found to be suitable substrates in this manganese-catalyzed C–H annulation reaction.[79]



Scheme 1.4.9 Manganese(I)-Catalyzed C−H Annulation of N−H Imines **87** with Alkynes **74**

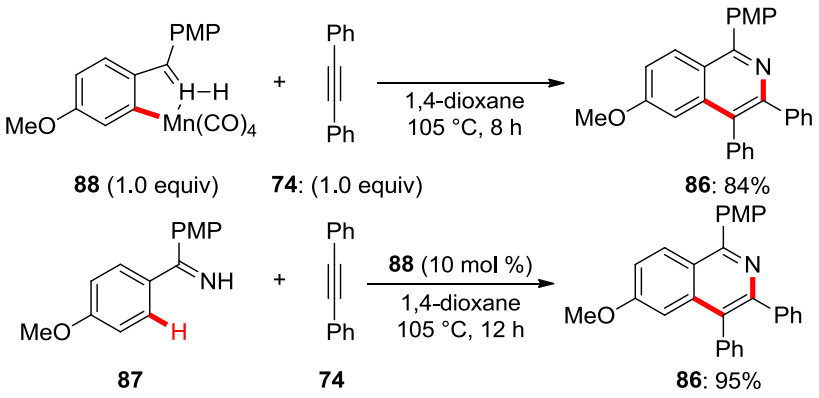
Based on their experimental mechanistic studies, Wang and co-workers proposed two catalytic cycles, the more favored process is shown in Scheme 1.4.10. The five-membered manganacycle complex **88** was formed through C–H manganation, followed by seven-membered manganacycle complex **90** formation *via* alkyne coordination and insertion into manganese–carbon bond of the manganese species **89**. Subsequently, elimination of the product and generates manganese hydride species [$HMn(CO)_4$] (**91**). The active manganese complex **88** was regenerated by coordination of the N–H imine **87** with [$HMn(CO)_4$] (**91**), along with the release of H_2.



Scheme 1.4.10 Suggested Catalytic Cycle for Manganese(I)-Catalyzed C−H/N–H Annulation of N−H Imines **87** with Alkynes **74**

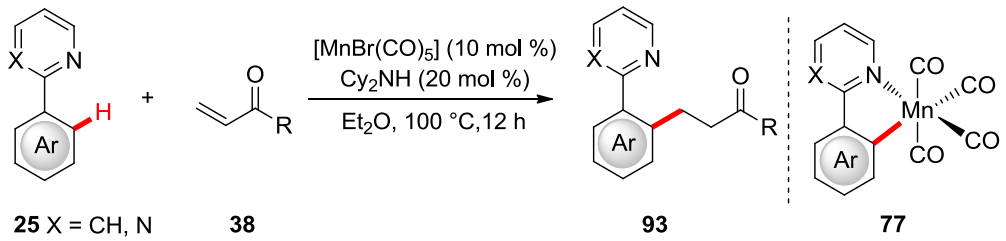
Notably, the five-membered manganacycle complex **88**, which can be prepared from arene **87**

in the presence of stoichiometric amounts of [$MnBr(CO)_5$], proved to be the key active intermediate through the use of catalytic or stoichiometric amounts of **88** in these C−H annulations (Scheme 1.4.11). Furthermore, the formation of H_2 and CO was confirmed by GC analysis of the atmosphere above the reaction mixture.



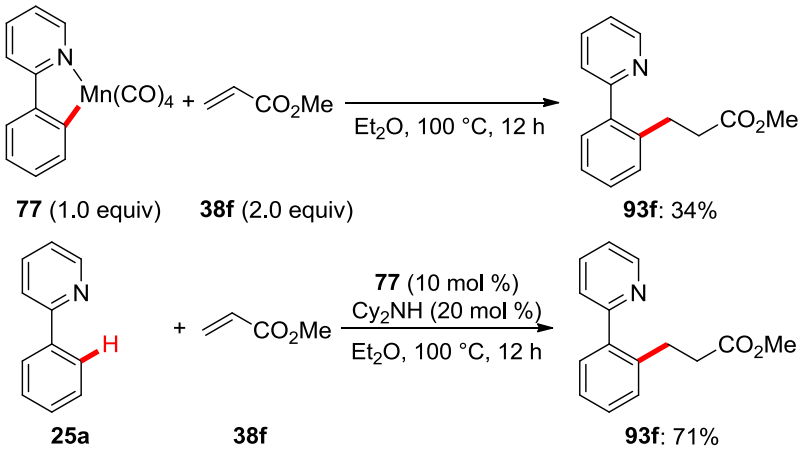
Scheme 1.4.11 C–H Annulation of N−H Imines **87** with Cyclometalated Complex **88**

The extension of these C–H addition strategies from C≡C or polar C=Het multiple bonds to polar C=C double bonds was accomplished by Wang and co-workers. The hydroarylation of *α,β*-unsaturated carbonyls **38** were achieved through a olefin insertion into the manganese−carbon bond step.[81] The addition reaction showed a broad substrate scope, good functional group tolerance, and complete mono-selectivity (Scheme 1.4.12).



Scheme 1.4.12 Manganese(I)-Catalyzed C–H Addition to *α,β*-Unsaturated Carbonyls **38**

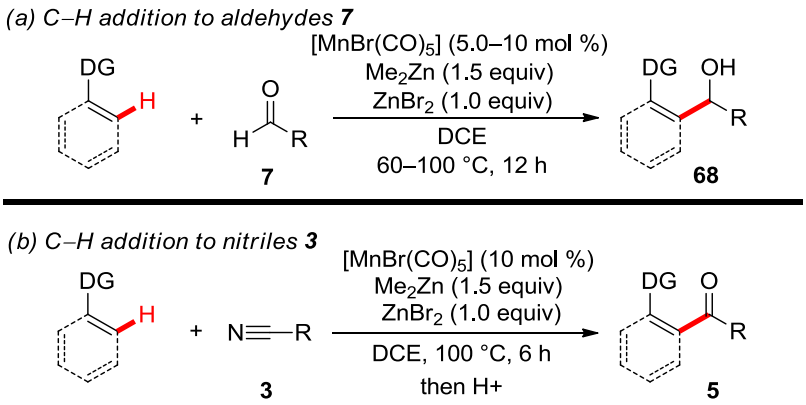
Moreover, mechanistic studies indicated that the five-membered manganacycle complex **77** was likely the crucial intermediate in this transformation, and the key C–H cleavage step was reversible and accelerated by the assistance of catalytic amounts of a base, such as $HNCy_2$. (Scheme 1.4.13).



Scheme 1.4.13 C–H Addition to *α,β*-Unsaturated Carbonyls **38** with Cyclometalated Complex **77**

Recently, transition metal catalyzed nucleophilic C–H addition to aldehydes **7** and nitriles **3** have been well explored.[82] However, external silanes **69** needed to be introduced to ensure catalytic turnover, therefore affording the corresponding silylethers **70**[75, 82c, 82e, 82f] as the final product, or these methods were limited to electron-rich and electron-neutral arenes.[83]

In 2015, the group of Wang developed a manganese-catalyzed nucleophilic C(sp^2)–H addition to aldehydes **7** and nitriles **3** leading to the benzyl alcohols **68** or ketones **5** with 38–95% yields and excellent regio- and stereoselectivity (Scheme 1.4.14).[84]

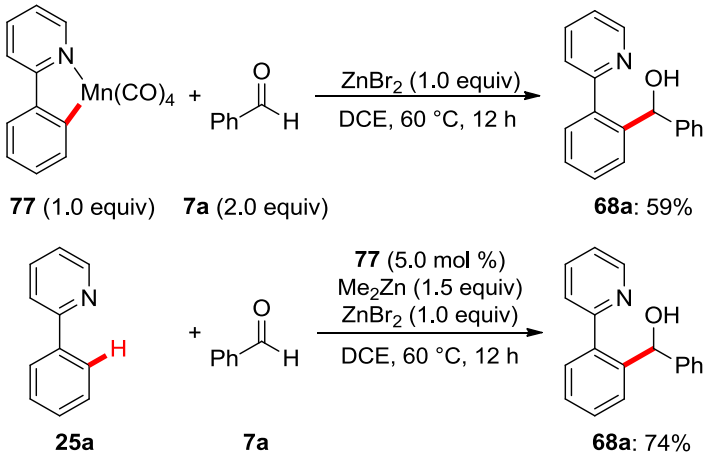


Scheme 1.4.14 Manganese-Catalyzed C–H Addition to Aldehydes **7** and Nitriles **3**

Herein, the benzyl alcohols **68** were conveniently accessed as the final products, and a broad range of electron-donating, -neutral and -withdrawing functional groups, such as methoxy, amine, fluoro, chloro, bromo, iodo, ester, trifluoromethyl were well tolerated.[84] It is noteworthy that both aromatic and olefinic C–H bonds were suitable to this catalytic system, as well as aliphatic aldehydes **7** and nitriles **3**.

In comparison to the work of Kuninobu/Takai,[75] they did not obtain the corresponding silylethers **70** as the final products.[84] In addition, the reaction was not limited to C=O bond

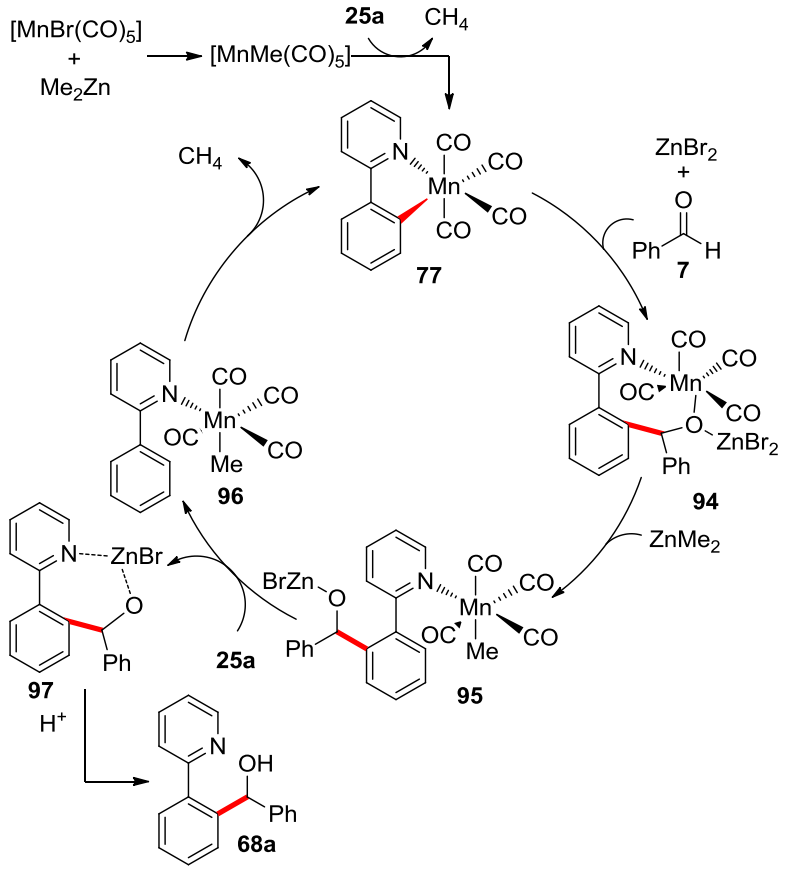
insertion, as the nucleophilic addition of C–H bond could also be applied to the relatively low propensity of the C≡N bond efficiently.



Scheme 1.4.15 C–H Addition to Aldehydes **7** with Cyclometalated Complex **77**

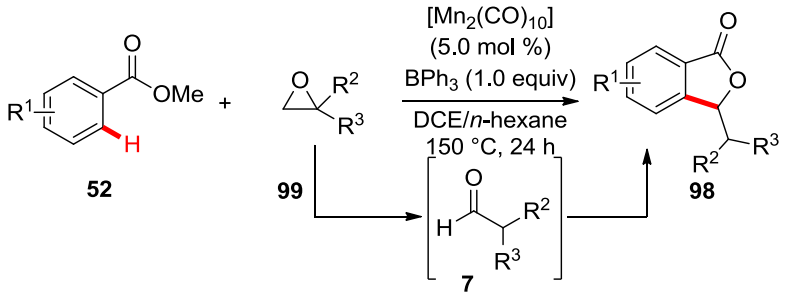
Importantly, the formation of methane was observed by GC analysis, and $ZnMe_2$ and $ZnBr_2$ were found to be essential for the product formation. Furthermore, the manganacycle complex **77** was successfully prepared from stoichiometric manganese C–H activation, and was shown to be the key intermediate from the observation of comparable catalytic efficiency in both catalytic and stoichiometric procedures (Scheme 1.4.15).

Then, Wang and co-workers proposed a catalytic cycle for this nucleophilic C–H addition reaction (Scheme 1.4.16). The manganese species $[MnMe(CO)_5]$ (**64**) is generated from $[MnBr(CO)_5]$ (**67**) in the presence of $ZnMe_2$, which subsequently undergoes cyclomanganation with substrate **25a** to afford the catalytically active manganacycle **77**. Then the C=O bond undergoes insertion into the manganese–carbon bond by the assistance of Lewis-acid $ZnBr_2$, forming the seven-membered manganacycle complex **94**. The methylmanganese species **95** was formed through ligand metathesis of **94** with Me_2Zn, which reacted with **25a** to generate **95** and furnished zinc species **97**. Finally, intermediate **97** was hydrolyzed to give the benzyl alcohols **68a**, along with intramolecular C–H activation of complex **96** to regenerate catalyst **77** with release of CH_4.



Scheme 1.4.16 Proposed Catalytic Cycle for Manganese(I)-catalyzed C–H Addition to Aldehydes **7**

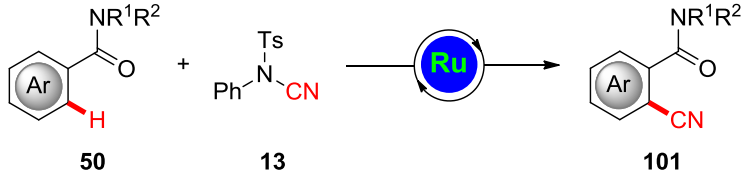
Recently, the manganese-catalyzed synthesis of isobenzofuranones **98** from aromatic esters **52** and oxiranes **99** *via* C−H bond activation was developed by Kuninobu and co-workers by the assistance of Lewis-acid BPh_3 (**100**) (Scheme 1.4.17).[85] This C−H annulation occurred with aromatic, heteroaromatic, and olefinic C−H bonds in moderate to good yields and with high functional group tolerance. Importantly, this is the first example of oxygen-directed organometallic manganese-catalyzed C−H activation. The use of BPh_3 (**100**) is essential to improve the efficiency by cooperation with the manganese catalyst. The reaction process likely occurs by oxirane isomerization to aldehyde **7** under Lewis acidic condition, then undergoing the C=O bond insertion into the formed manganese−carbon bond[85] as was demonstration previously in the field (*vide supra*).[75, 84]



Scheme 1.4.17. Manganese(I)-Catalyzed Isobenzofuranones **98** Synthesis

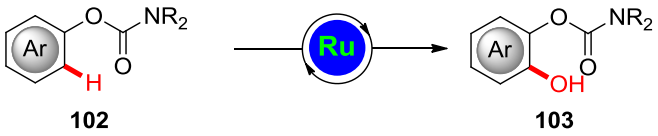
2 Objectives

Aromatic nitriles **3** constitute key structural motifs of important pharmaceuticals, dyes, agrochemicals and natural products.[12-13] The cyano group serves as a versatile functional group that can easily be transformed into amine, ketone, acid, aldehyde, amide, among others.[14] Recently, rhodium-catalyzed C–H cyanations of arenes were established with rather strongly coordinating directing groups.[27, 29] Herein, an alternative strategy was envisioned, which involves C–H cyanation with relatively inexpensive ruthenium catalyst bearing only weakly coordinating directing groups by the use of bench stable, less toxic and readily accessible *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS, **13**) (Scheme 2.1).[86]



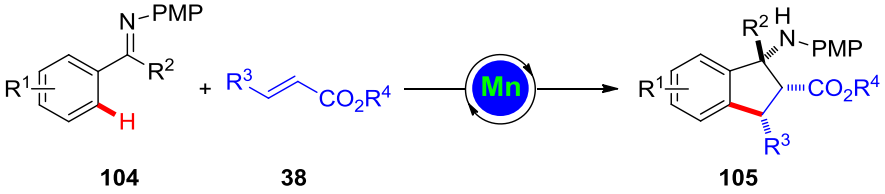
Scheme 2.1 Ruthenium(II)-Catalyzed C–H Cyanations of Benzamides **50**

The catalytic direct oxygenation of otherwise unreactive C(sp^2)–H bonds was shown to be the most step-economical approach to substituted phenols.[48] Although ruthenium-catalyzed C(sp^2)–H bonds direct oxygenation on arenes were reported, these notable progresses were mainly focused on oxygenation on electron-deficient substrates bearing electron- withdrawing directing groups. Therefore, a ruthenium-catalyzed C(sp^2)–H bond oxygenation of the electron-rich phenol derivatives was wished to be demonstrated (Scheme 2.2).[55d]



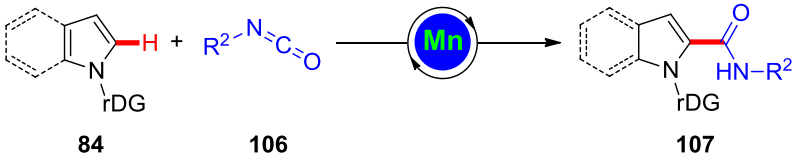
Scheme 2.2 Ruthenium-Catalyzed C(sp^2)–H Oxygenations of Carbamates **102**

Carbocyclic *β*-amino acids can be found in natural products and pharmaceuticals, such as cispentacin and icofungipen, which possess noteworthy antifungal or antibacterial activities, and they are also a versatile intermediate in organic synthesis.[87] Moreover, manganese-catalyzed organometallic C–H activation reactions are scarce and only scattered examples have been reported.[69] Obviously, developing new methods for the efficient preparation of substituted *β*-amino acids is of significant importance, particularly exploiting the inexpensive and less toxic manganese catalyst (Scheme 2.3).[88]



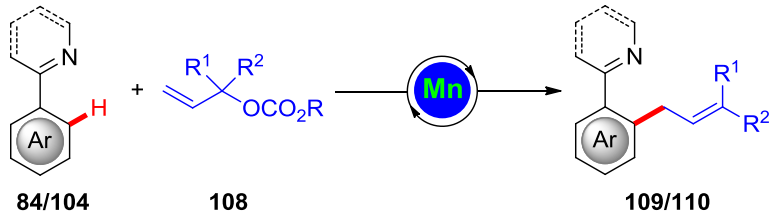
Scheme 2.3 Manganese-Catalyzed Synthesis of *cis*-*β*-Amino Acid Esters **105** through Organometallic C–H Activation of Ketimines **104**

The easily accessible isocyanates **106** contain polar double bonds, and have been successfully applied to step-economical aryl amide formation through C–H activation with expensive rhodium,[89] rhenium,[90] ruthenium[91] or relatively inexpensive Cp*Co(III) complex.[92] Here, a manganese-catalyzed C–H bond addition to the C=N bond of isocyanates **106** for the access to aryl amide was planned (Scheme 2.4).[93]



Scheme 2.4 Manganese(I)-Catalyzed C–H Amino Carbonylation of Heteroarenes with Isocyanates **106**

The allyl group is one of the most important and useful functionalities in organic synthesis because they provide readily access to various functional groups.[94] Furthermore, allyl arenes exist in various natural products and pharmaceuticals.[94] Due to the importance of the allyl group, it is significant to develop a new versatile C–H allylation in the presence of less toxic and inexpensive manganese catalyst, although transition metal catalyzed direct C–H allylation[95] reactions have been previously explored (Scheme 2.5).[96]



Scheme 2.5 Manganese(I)-Catalyzed Substitutive C–H Allylation

3 Results and Discussion

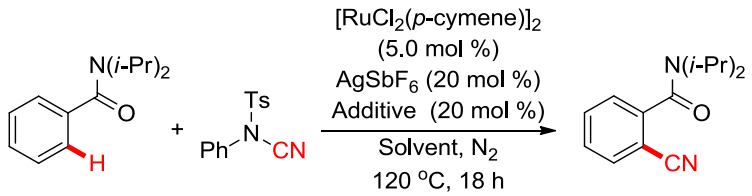
3.1 Ruthenium(II)-Catalyzed C–H Cyanations of Benzamides

Aromatic nitriles are widely found in pharmaceuticals, agrochemicals and natural products,[12-13] and cyano groups can be readily transformed into many valuable functional groups, such as amines, ketones, amides, acids or aldehydes, among others.[14] Hence, it is important to develop new methods to introduce the cyano group onto aromatic ring.

3.1.1 Optimization of Ruthenium(II)-Catalyzed C–H Cyanation with Benzamides

The ruthenium(II)-catalyzed C–H cyanation was initiated by using *N*,*N*-diisopropylbenzamide (**50a**) and *N*-cyano-4-methyl-*N*-phenylbenzenesulfonamide (NCTS, **13**) in the presence of $[RuCl_2(p\text{-cymene})]_2$ as the catalyst. The effect of different additives and solvents was investigated in this reaction (Table 3.1.1). The desired cyanation product was formed in 70% yield with 20 mol % of AgOAc and $AgSbF_6$ as additives in DCE (entry 1). The cyanation efficacy could not be increased with a higher amount of the additive, but less than 5% product conversion was observed without $AgSbF_6$ (entries 2–4). Next, different solvents were screened and DCE was found to be the ideal (entries 1, 5–8). The background reaction experiment was then performed, and clearly showed that this C–H activation process did not occur without a ruthenium catalyst (entry 9). Subsequently, a variety of metal acetate additives were tested to investigate the influence of different additives, and it turned out that the NaOAc provided the highest catalytic efficacy (entries 10–14).

Table 3.1.1 Optimization of Ruthenium(II)-Catalyzed C–H Cyanations with Benzamides **50**[a]



50a **13** **101a**

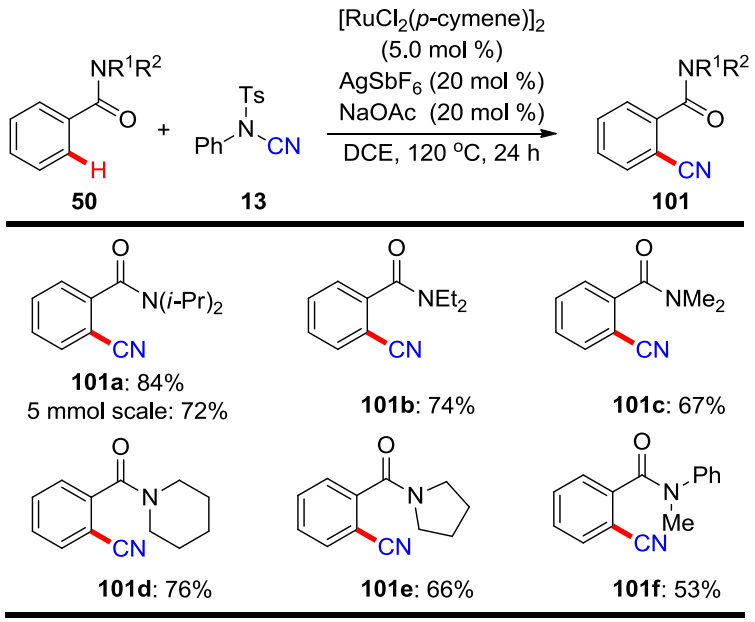
Entry	Additive	Solvent	Yield (%)
1	AgOAc	DCE	77 (70)
2[b]	AgOAc	DCE	80 (67)
3[c]	AgOAc	DCE	67 (54)
4[d]	AgOAc	DCE	< 5
5	AgOAc	1,4-dioxane	38

6	AgOAc	*o*-xylene	21
7	AgOAc	PhMe	23
8	AgOAc	DMF	< 2
9[e]	AgOAc	DCE	< 2
10	$Cu(OAc)_2$	DCE	30
11	KOAc	DCE	< 5
12	CsOAc	DCE	17
13	**NaOAc**	**DCE**	**90 (80)**
14[f]	**NaOAc**	**DCE**	**95 (84)**

[a] Reaction conditions: **50a** (0.5 mmol), **13** (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), additive (20 mol %), solvent (2.0 mL), under N_2, 120 ℃, 18 h; GC-conversion, isolated yields are given in parentheses. [b] AgOAc (30 mol %). [c] $AgSbF_6$ (30 mol %). [d] Without $AgSbF_6$. [e] Without $[RuCl_2(p\text{-cymene})]_2$. [f] 24 h.

3.1.2 Effect of *N*-Substituents on C–H Cyanations

Subsequently, the effect of the *N*-substituent at the amide moiety under the optimized system was studied (Table 3.1.1, entry 14). A set of tertiary amides **50a**–**50f** proved to be suitable substrates in this ruthenium(II)-catalyzed C–H cyanation system, thus affording the corresponding products **101** in good yields. This cyanation reaction is not limited to a 0.5 mmol scale. Indeed, a 5 mmol scale reaction also afforded a comparable yield of 72% (Scheme 3.1.1).

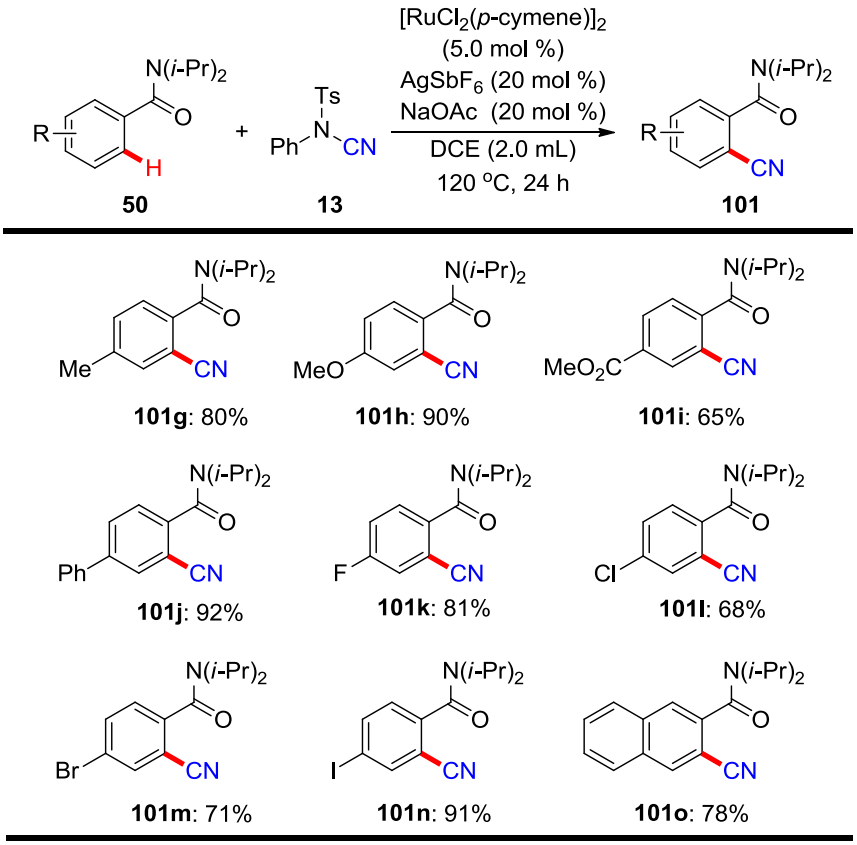


Reaction conditions: **50** (0.5 mmol), **13** (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), NaOAc (20 mol %), DCE (2.0 mL), under N_2, 120 °C, 24 h.

Scheme 3.1.1 Effect of *N*-Substituents on C–H Cyanations

3.1.3 Scope of Ruthenium-Catalyzed C–H Cyanation with Amides

Next, the substrate scope of the ruthenium-catalyzed C–H cyanations of amides **100** was explored (Scheme 3.1.2). Under the optimized reaction conditions, various substituted aromatic amides **50** could undergo the cyanation process to provide the desired products **101** in high chemo-selectivity and good to excellent yields. Various valuable functional groups, such as ester, fluoro, chloro, bromo, even iodo, were well tolerated affording the corresponding products **101**, which should allow for further diversification of the cyanation products **101**.



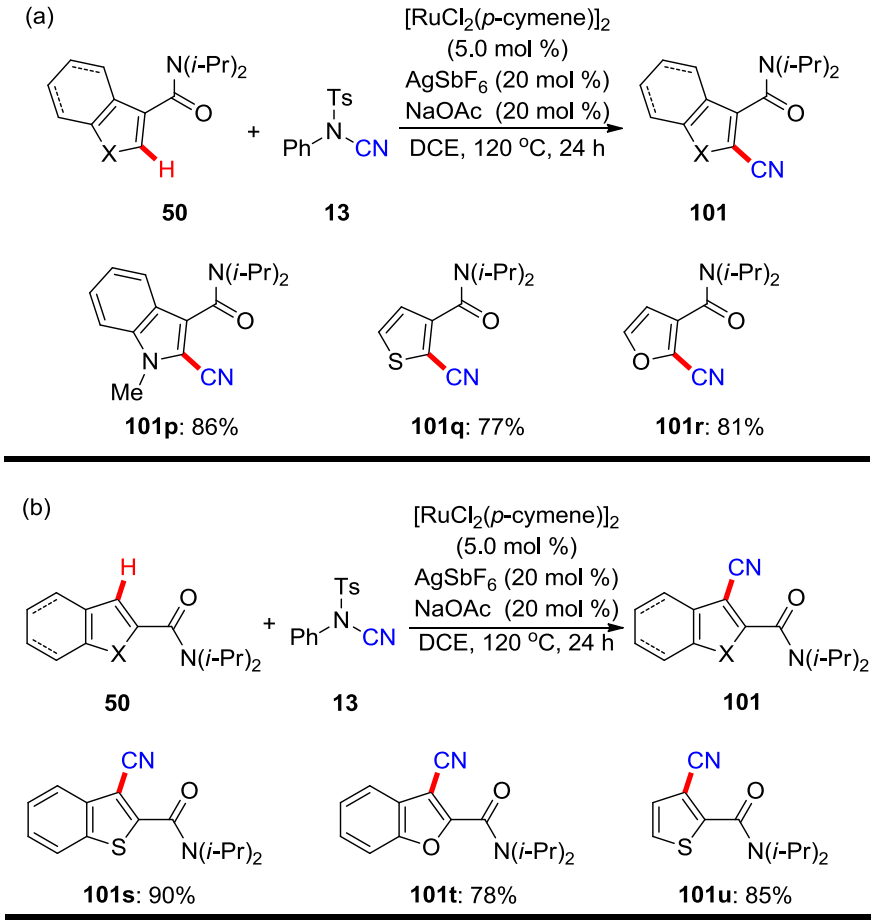
Reaction conditions: **50** (0.5 mmol), **13** (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), NaOAc (20 mol %), DCE (2.0 mL), under N_2, 120 °C, 24 h.

Scheme 3.1.2 Scope of Ruthenium-Catalyzed C–H Cyanations with Amides **50**

3.1.4 C–H Cyanation with Heteroaromatic Amides

The powerful carboxylate-assisted ruthenium(II)-catalyzed direct C–H cyanation was not limited to simple aromatic amides **50**, but also proved viable for more attractive heteroaromatic amides **50**. For the challenging heteroaromatic amides, either C2 (Scheme 3.1.3a) or C3 (Scheme 3.1.3b) position could be cyanated by this C–H activation strategy, thereby furnishing cyanated thiophenes (**101q**, **101u**), furanes (**101r**), benzothiophenes (**101s**), benzofuranes (**101t**) and indoles (**101p**) in good yields and excellent chemo- and

site-selectivities.

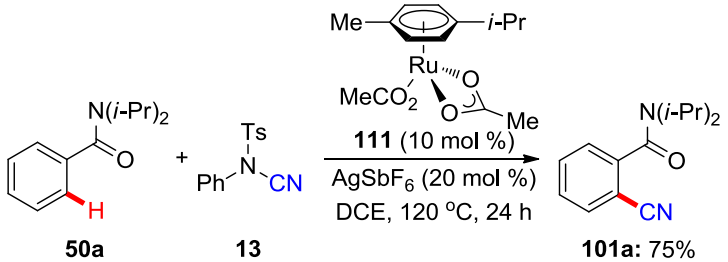


Reaction conditions: **50** (0.5 mmol), **13** (1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %), NaOAc (20 mol %), DCE (2.0 mL), under N_2, 120 °C, 24 h.

Scheme 3.1.3 C–H Cyanations of Heteroaromatic Amides **50**

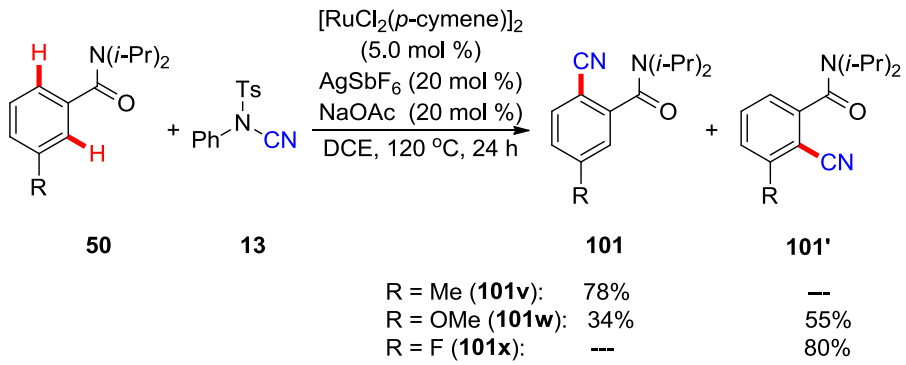
3.1.5 Mechanistic Studies

In order to gain details on this useful and unique chemo-selective C–H cyanation reaction, some mechanistic experiments were performed. First, the ruthenium(II) biscarboxylate complex **111** was prepared according to a literature procedure.[97] The comparable catalytic efficacy in 75% yield was observed when conducting the cyanation reaction in the presence of catalytic amount of complex **111** without NaOAc (Scheme 3.1.4).



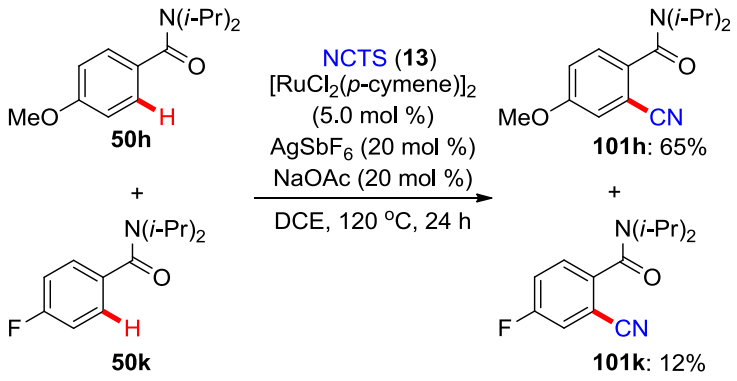
Scheme 3.1.4 Well-Defined Complex **111** as Catalyst

Intramolecular competition experiments with *meta*-substituted amides **50v**–**50x** demonstrated that the site-selectivity was controlled by steric interactions, since the C–H activation occurred predominantly at the less hindered position. In case of the *meta*-methoxy and fluoro substituted benzamides **50w** and **50x**, a secondary directing group effect[10] was noted (Scheme 3.1.5).



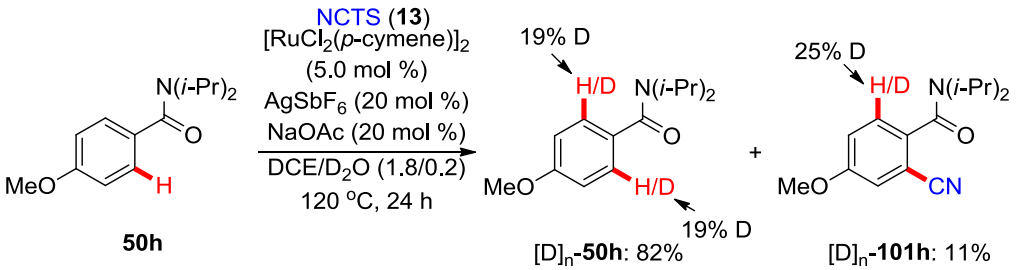
Scheme 3.1.5 Intramolecular Competition Experiments with *meta*-Substituted Arenes

Subsequently, an intermolecular competition experiment between electron-rich and electron-deficient amides was conducted. The results clearly showed the higher activity of electron-rich arenes, which indicated an base-assisted electrophilic-type (BIES)[98] C–H activation by the cationic ruthenium species.



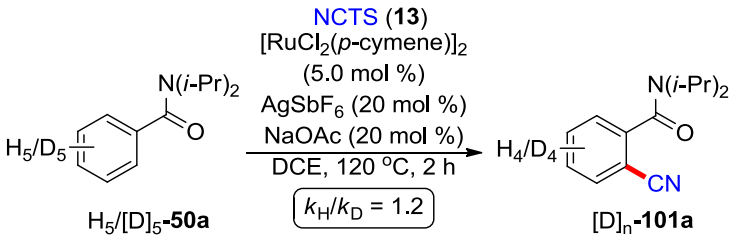
Scheme 3.1.6 Intermolecular Competition Experiment between Arenes **50**

Furthermore, this ruthenium(II)-catalyzed C–H cyanation reaction was carried out in the presence of D_2O as co-solvent. H/D exchange was observed by reisolation of the starting material $[D]_n$-**50h** and the cyanation product $[D]_n$-**101** (Scheme 3.1.7). These observations supported a reversible C–H activation step.



Scheme 3.1.7 H/D Exchange Experiment

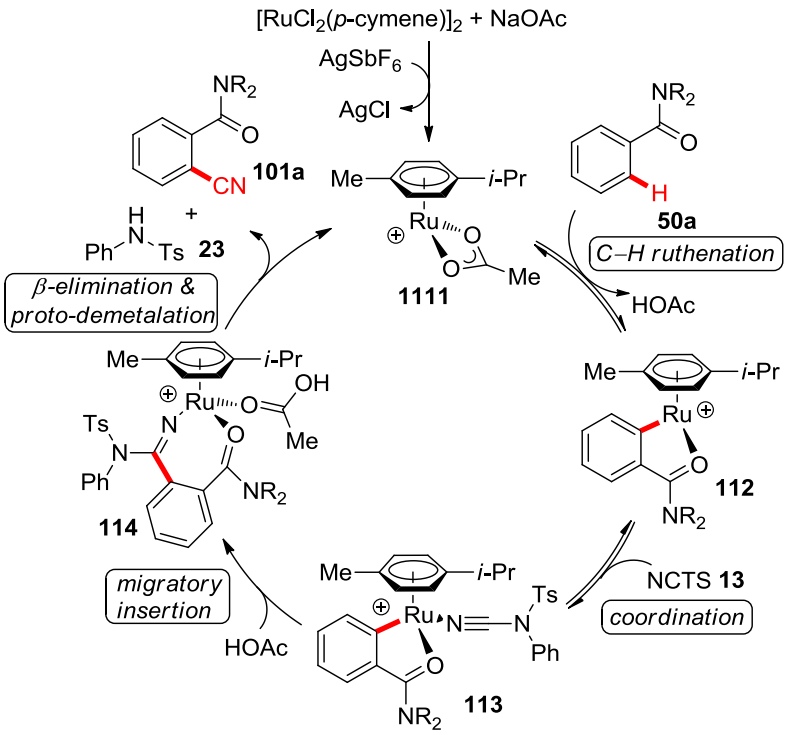
The intermolecular kinetic isotope effect (KIE) from a one pot reaction between substrates **50a** and $[D]_5$-**50a** was found to be rather low ($k_H/k_D \approx 1.2$) (Scheme 3.1.8). These experimental results indicated that the C–H ruthenation process is not the rate-determining step.



Scheme 3.1.8 Kinetic Isotope Effect Study

3.1.6 Plausible Catalytic Cycle

Based on these mechanistic studies, a plausible catalytic cycle was proposed for this ruthenium(II)-catalyzed C–H cyanation (Scheme 3.1.9). After reversible and fast C–H bond ruthenation on amide **50** with the cationic ruthenium carboxylate species **111**, the resulting cationic ruthenium complex **112** undergoes coordination and insertion of NCTS (**13**), and thus affords the intermediate **114**. Finally, the desired cyanation product is formed and the cationic ruthenium(II) carboxylate catalyst is regenerated after *β*-elimination and proto-demetalation.



Scheme 3.1.9 Plausible Catalytic Cycle

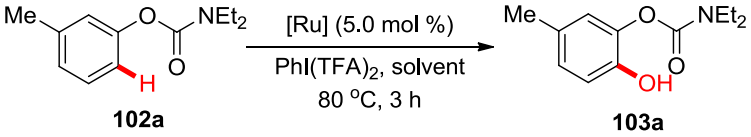
3.2 *Ortho*- and *Para*-Selective Ruthenium(II)-Catalyzed C(sp^2)–H Oxygenations of Phenol Derivatives

The catalytic oxygenation of otherwise unreactive C(sp^2)–H bonds proved to be one of the most step-economical approaches for the synthesis of substituted phenols.[48] The ruthenium-catalyzed C(sp^2)–H bond oxygenation on arenes bearing weakly coordinating directing groups, such as amides, esters, ketones, and aldehydes were previously reported by Ackermann[55] and Rao.[56] However, these notable advances only focused on direct oxygenation on electron-deficient substrates bearing electron-withdrawing directing groups.

3.2.1 Optimization of Ruthenium(II)-Catalyzed C–H Oxygenations of Carbamates

At the outset of this investigations on the ruthenium(II)-catalyzed C–H oxygenations of carbamates **102**, *m*-tolyl diethylcarbamate (**102a**) was selected as the model substrate and [bis(trifluoroacetoxy)iodo]benzene (PIFA) as the oxidant to exam the effects of different ruthenium catalysts and solvents (Table 3.2.1). The background reaction experiment showed that the desired oxygenation product could not be obtained in the absence of a ruthenium catalyst (entry 1), while 39% yield of the corresponding phenol was formed in the presence of catalytic amounts of [$Ru_3(CO)_{12}$] in DCE (entry 2). These findings clearly indicated that this C–H oxygenation process was catalyzed by a ruthenium catalyst. Then, different ruthenium catalyst precursors were tested, with [$RuCl_2$(*p*-cymene)]$_2$ showing the highest catalytic efficacy and giving the desired oxygenation product in 65% (entries 2–6). Furthermore, other solvents and oxidants were explored, and $PhI(TFA)_2$ and DCE proved to be the best choice among the tested solvents and oxidants, respectively (entries 6–9). It is noteworthy that the ruthenium-catalyzed C–H bond oxygenation could occur at a rather low reaction temperature under the optimized condition in a comparable yield (entry 10).

Table 3.2.1 Optimization of C–H Oxygenation with Carbamate **102a**[a]



102a **103a**

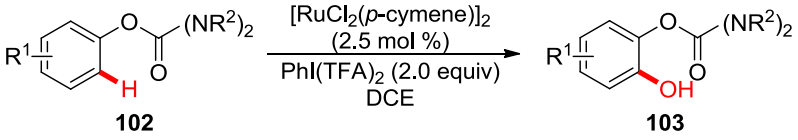
Entry	[Ru]	Solvent	Yield (%)
1	---	DCE	---
2	[$Ru_3(CO)_{12}$]	DCE	39
3	[$Ru(O_2CMes)_2$(*p*-cymene)]	DCE	46
4	[$RuCl_2(PPh_3)_3$]	DCE	53
5	[$RuCl_3(H_2O)_n$]	DCE	54

6	$[RuCl_2(p\text{-cymene})]_2$	DCE	65
7	$[RuCl_2(p\text{-cymene})]_2$	TFA/TFAA	30[b]
8	$[RuCl_2(p\text{-cymene})]_2$	1,4-dioxane	24[c]
9	$[RuCl_2(p\text{-cymene})]_2$	PhMe	57
10	$[RuCl_2(p\text{-cymene})]_2$	DCE	67[d]

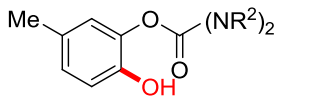
[a] Reaction conditions: **102a** (0.5 mmol), $PhI(TFA)_2$ (1.0 mmol), [Ru] (5.0 mol %), solvent (2.0 mL), 80 ℃, 3 h, isolated yield. [b] $K_2S_2O_8$ (2.0 equiv) instead of $PhI(TFA)_2$. [c] ^{1}H-NMR conversions with CH_2Br_2 as internal standard. [d] 50 ℃, 24 h.

3.2.2 Scope of *ortho*-Selective C–H Oxygenation with Carbamates

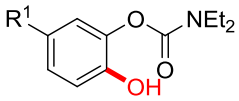
With the optimized catalytic system in hand, the substrate scope of carbamates **102** was investigated (Scheme 3.2.1).



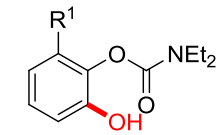
102 → **103**



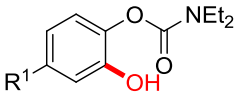
R^2 = Et (**103a**): 67%[a]
R^2 = Me (**103b**): 63%[a]
R^2 = *i*-Pr(**103c**): 63%[a]



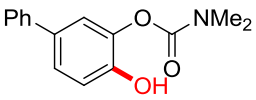
R^1 = OMe (**103d**): 46%[a]
R^1 = Br (**103e**): 66%[c]
R^1 = I (**103f**): 71%[b]



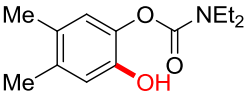
R^1 = Me (**103g**): 67%[b]
R^1 = Ph (**103h**): 79%[c]
R^1 = *i*-Pr (**103i**): 76%[b]
R^1 = F (**103j**): 58%[c]
R^1 = Cl (**103k**): 52%[c]
R^1 = Br (**103l**): 57%[c]
R^1 = I (**103m**): 42%[c]



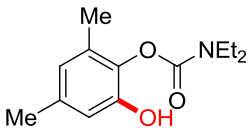
R^1 = H (**103n**): 42%[c]
R^1 = Ph (**103o**): 51%[c]
R^1 = OMe (**103p**): 46%[b]
R^1 = F (**103q**): 48%[c]



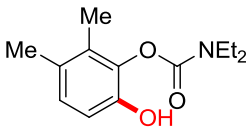
103r: 75%[a]



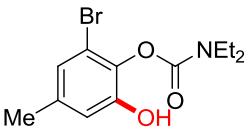
103s: 52%[b]



103t: 73%[c]



103u: 66%[b]



103v: 53%[c]

[a] 50 °C, 24 h. [b] 80 °C, 3 h. [c] 80 °C, 6 h.

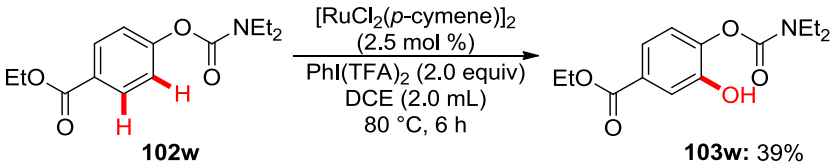
Scheme 3.2.1 Scope of *ortho*-Selective C–H Oxygenation with Carbamates **102**

Fortunately, *para*-, *meta*-, and even more sterically hindered *ortho*-substituted aryl carbamates **102** could be converted to corresponding phenols in moderate to good yields under this optimized ruthenium(II)-catalyzed *ortho*-selective C–H oxygenation. Moreover, a variety of valuable functional groups, such as fluoro, chloro, bromo, or iodo, were well tolerated,

affording the corresponding phenol products **103** efficiently. Notably, this transformation showed high chemo- and site-selectivities to furnish the *ortho*-substituted phenols **103**.

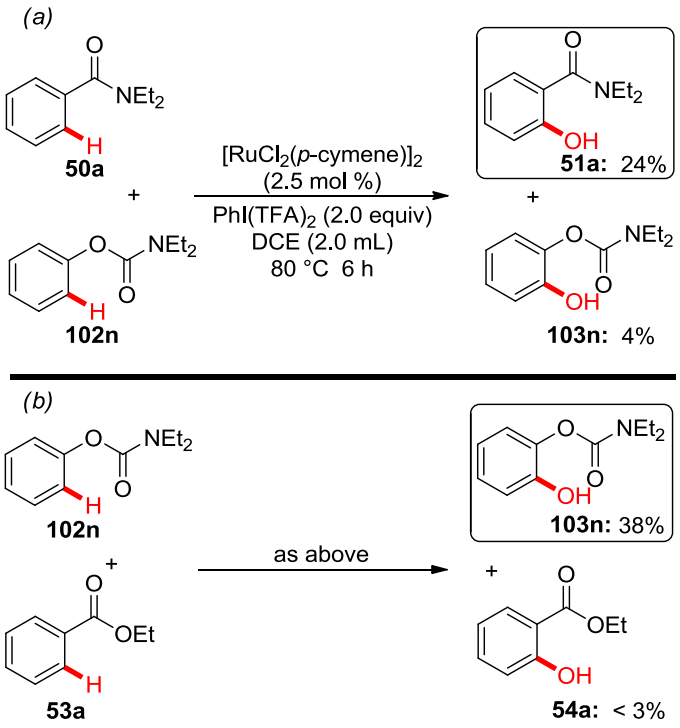
3.2.3 Competition Experiments

The group of Rao reported ester directed ruthenium(II)-catalyzed C–H oxygenation to deliver the corresponding phenol products.[56d] Thus, it is interesting to find out the directing abilities of different directing groups in this oxygenation reaction system through either intramolecular or intermolecular competition experiments. First, an intramolecular competition experiment was conducted with benzoate **102w** which contains two directing groups, ester and carbamate. The carbamate directed oxygenation product was detected as the sole product **103w** in 39% yield, which indicated the carbamate as the more powerful directing group as compared to ester in this case (Scheme 3.2.2). This selectivity suggested that the less favorable six-membered cycle might be the crucial intermediate in this carbamate directed C–H activation mode.



Scheme 3.2.2 Intramolecular Competition Experiment

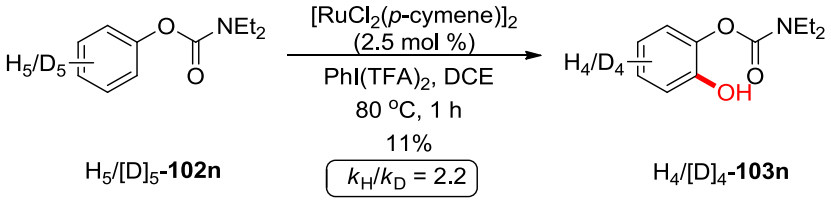
Then, intermolecular competition experiments between substrates with different directing groups were performed. From the competition experiment between amide **50** and carbamate **102**, the amide directed oxygenation product **51a** was isolated in 24% as well as 4% of the oxygenated carbamate **103a** (Scheme 3.2.3a). One further competition experiment showed that carbamate reacted faster than ester, which is in good agreement with the intramolecular competition experiment (Scheme 3.2.3b). These results provided the following directing ability order: amide > carbamate > ester.



Scheme 3.2.3 Intermolecular Competition Experiments

3.2.4 Kinetic Isotope Effect Study

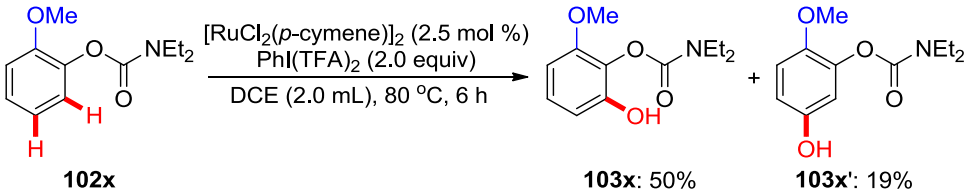
Subsequently, a kinetic isotope effect (KIE) study experiment was carried out to gain a deeper understanding of this carbamate directed ruthenium(II)-catalyzed C–H oxygenation reaction. The KIE of $k_H/k_D \approx 2.2$ by using **102n** and $[D]_5$-**102n** was obtained in a one-pot reaction, and revealed the C–H metalation step to be kinetically relevant (Scheme 3.2.4).[99]



Scheme 3.2.4 Kinetic Isotope Effect Study

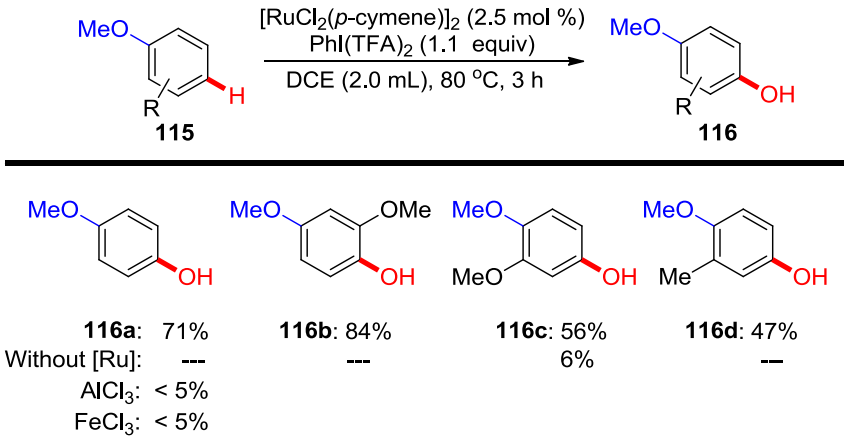
3.2.5 *para*-Selective C–H Oxygenation of Anisoles

When 2-methoxyphenyl diethylcarbamate (**102x**) was used as the starting material in this oxygenation system, not only the desired *ortho*-oxygenation product could be observed in 50% yield, but also the *meta*-oxygenation product as the byproduct in 19% yield (Scheme 3.2.5). It appears that the methoxy group has a significant influence and changed the substrate reactivity, directing the oxygenation in *para*-position to the methoxy group.



Scheme 3.2.5 C–H Oxygenation on Arene **102x**

Interestingly, this ruthenium-catalyzed C–H oxygenation could take place on simple anisole derivatives **115** as well, delivering *para*-oxygenated products **116** in moderate to good yields. Only 1,2-dimethoxybenzene (**115c**) could provide the corresponding oxygenation product in a very low yield without the ruthenium catalyst (Scheme 3.2.6). Moreover, under otherwise identical reaction conditions by the use of Lewis acids $AlCl_3$ or $FeCl_3$ as the catalyst furnished only <5% of product **116a**, as determined by GC analysis.



Scheme 3.2.6 *para*-Selective C–H Oxygenation of Anisoles **115**

3.3 Manganese-Catalyzed Synthesis of *cis*-*β*-Amino Acid Esters through Organometallic C–H Activation of Ketimines

Carbocyclic *β*-amino acids are widely found in many natural products and antibiotics, and certain carbocyclic *β*-amino acids, such as cispentacin, icofungipen, and BAY Y9379, possess important antifungal or antibacterial activities, while tilidin, a phenyl-substituted cyclohexene amino ester, is an analgetic.[87, 100] Amipurimycin with a five-membered carbocyclic *β*-amino acid motif is an important antibiotic (Figure 3.3.1).[87, 100]

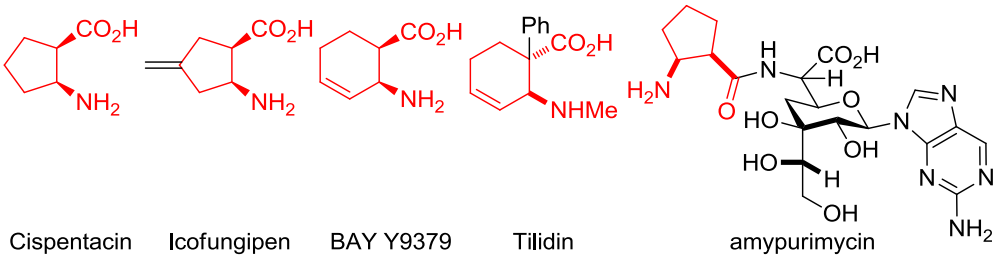


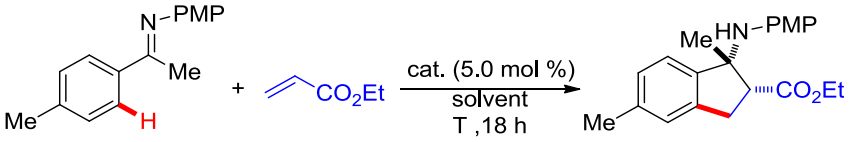
Figure 3.3.1 Selected Biologically Active *β*-Amino Acids

Moreover, *β*-amino acids are key structural motifs in non-natural *β*-peptides and versatile intermediates in organic synthesis.[87] Therefore, developing new methods for efficient preparation of substituted *β*-amino acids is of significant importance.

3.3.1 Optimization of Manganese-Catalyzed C–H Annulation of Acrylates by Imines

At the outset of the studies, a variety of reaction conditions for the envisioned manganese-catalyzed C–H activation of ketimine **104a** were tested with ethyl acrylate **38a** as the substrate (Table 3.1).

Table 3.3.1 Optimization of Manganese-Catalyzed C–H Annulation of Acrylate **38a**[a]



104a **38a** **105aa**

Entry	Catalyst	Solvent	*T* [°C]	Yield (%)
1	$Mn_2(CO)_{10}$	PhMe	100	59
2	$Mn_2(CO)_{10}$	PhMe	140	45
3	**$Mn_2(CO)_{10}$**	**PhMe**	**120**	**87**
4	$MnBr(CO)_5$	PhMe	120	11[b]
5	$MnCl_2$	DCE	120	--[b]

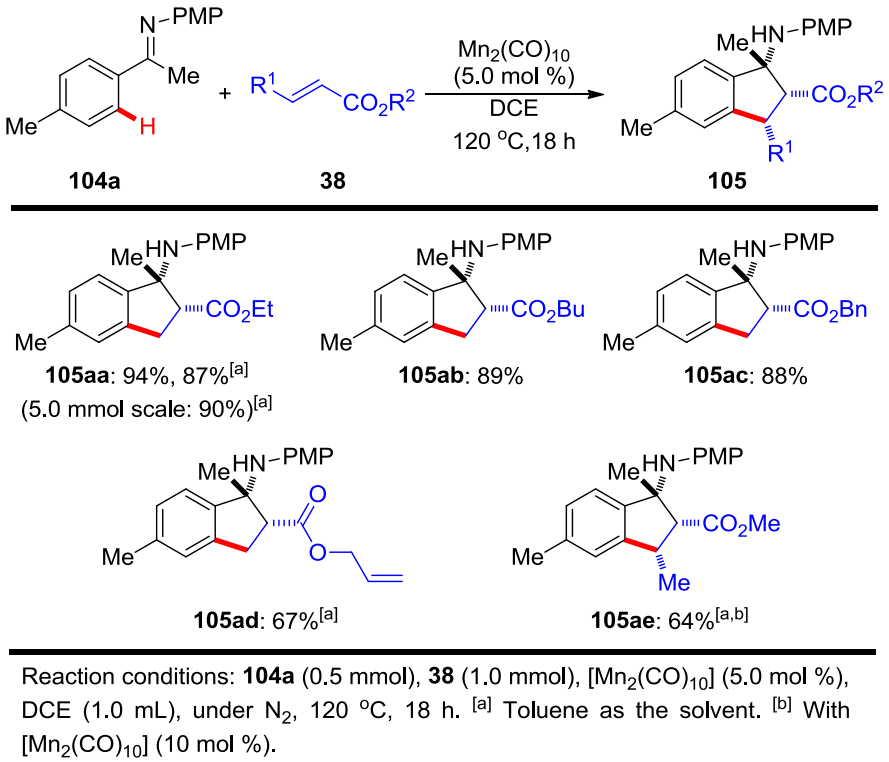
6	**$Mn_2(CO)_{10}$**	**DCE**	**120**	**94**
7	$Mn_2(CO)_{10}$	1,4-dioxane	120	77
8	---	DCE	120	---
9	$Co_2(CO)_8$	DCE	120	<3
10	$Ni(cod)_2$	DCE	120	--[b]

[a] Reaction conditions: **104a** (0.5 mmol), **38a** (1.0 mmol), catalyst (5.0 mol %), solvent (1.0 mL), under N_2, 120 ℃, 18 h, isolated yield. [b] Catalyst (10 mol %).

We were delighted to observe that the formation of *cis*-*β*-amino acid ester **105aa** occurred in the presence of catalytic amount of $Mn_2(CO)_{10}$ (entry 1). Subsequently, the effect of the reaction temperature was explored, and 120 ^oC was found to be ideal (entries 1–3). Notably, additional additives such as amines or metal acetates were not necessary in this manganese-catalyzed C–H annulation of imines **104a** with acrylates **38a**. The following optimization studies showed that other manganese catalysts were less efficient, and toluene and DCE were the optimal solvents (entry 4–7). A control experiment revealed that the C–H bond activation did not occur in the absence of $Mn_2(CO)_{10}$ (entry 8). No or only trace amounts of the desired product were observed in the presence of $Co_2(CO)_8$ or $Ni(cod)_2$ as the catalysts (entries 9 and 10).

3.3.2 Scope of Manganese-Catalyzed C–H Activation with Acrylates

With the optimized catalytic system in hand, the scope of *α,β*-unsaturated esters **38** for the manganese-catalyzed the C–H activation of imine **104a** was explored (Scheme 3.3.1). A variety of *α,β*-unsaturated esters **38a**–**38d** were suitable substrates, affording the desired *β*-amino esters **105** in good yields with excellent regio- and diastereoselectivity. A comparably high yield could be achieved even on a larger 5 mmol scale. It is noteworthy that not only terminal acrylates **38** but also the internal acrylate (*E*)-**38e** was successfully applied to generate the desired product **105ae** in good yield with excellent stereocontrol of all three contiguous stereocenters. However, the reactions with (*Z*)-crotonate (**38g**), cinnamic acid ester (**38h**) and methacrylate (**38i**) only gave traces of the desired products.

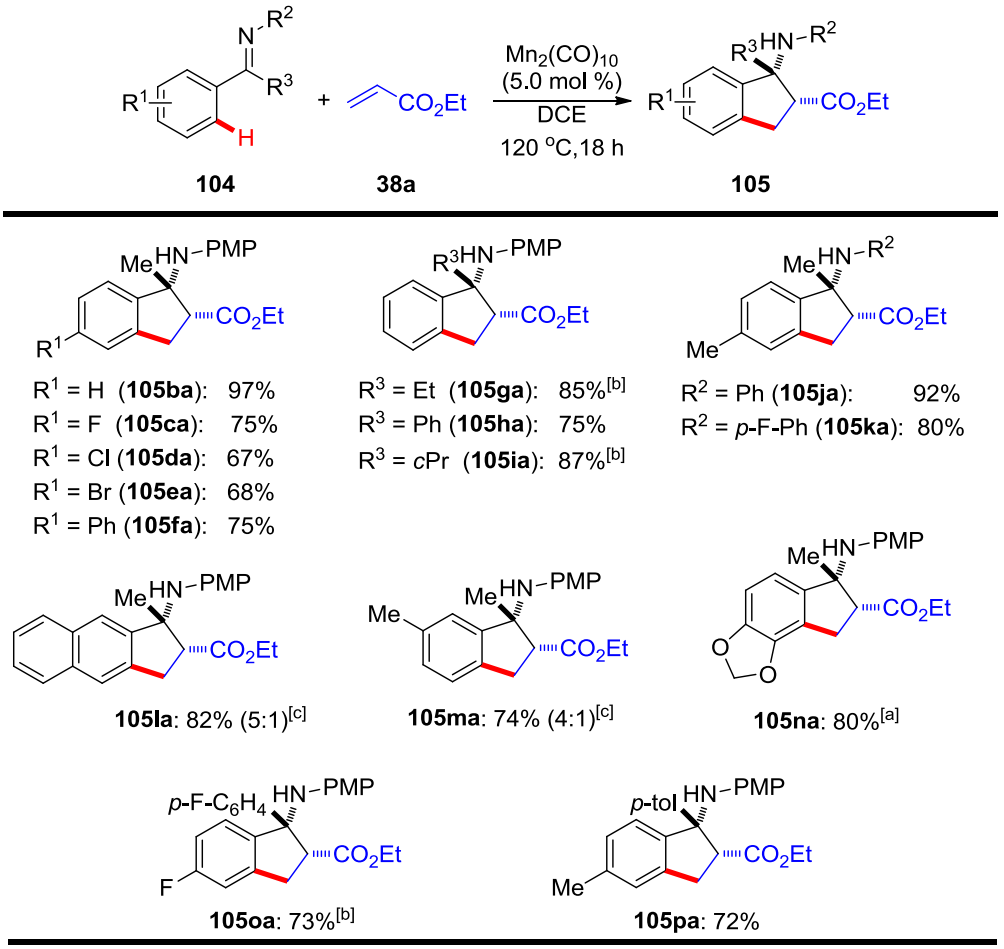


Reaction conditions: **104a** (0.5 mmol), **38** (1.0 mmol), $[Mn_2(CO)_{10}]$ (5.0 mol %), DCE (1.0 mL), under N_2, 120 °C, 18 h. [a] Toluene as the solvent. [b] With $[Mn_2(CO)_{10}]$ (10 mol %).

Scheme 3.3.1 Manganese-Catalyzed C–H Activation with Alkenes **38**

3.3.3 Scope of Manganese-Catalyzed C–H Activation with Imines

Next, the scope of the imine **104** under the optimized catalytic conditions was explored (Scheme 3.3.2). Many valuable functional groups, such as fluoro, chloro, bromo and cyclopropyl, were well tolerated by the catalytic system, which is instrumental for further derivatizations of compounds **105**. Both aryl alkyl and diaryl imines **104** afforded the desired products **105** in good yields, whereas aldimines only gave traces of corresponding product. Further examination of the electronic effect of ketone group showed that electron efficient ones were preferable to the electron deficient substrates (**105aa, 105ja, 105ka**). The selectivity of *meta*-substituted arenes **104l** and **104m** was controlled by steric interactions, since the C–H activation occurred predominantly at the less hindered position (**105la, 105ma**).

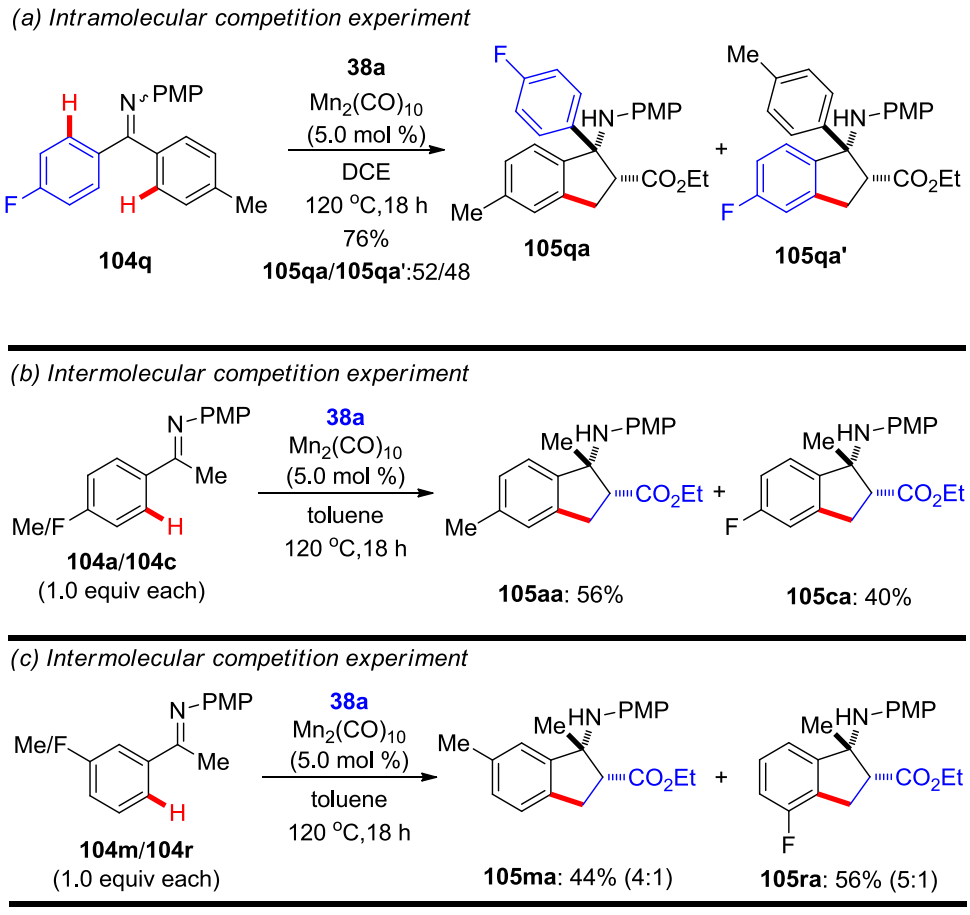


Reaction conditions: **104** (0.5 mmol), **38a** (1.0 mmol), [$Mn_2(CO)_{10}$] (5.0 mol %), DCE (1.0 mL), under N_2, 120 °C, 18 h. [a] Toluene as the solvent. [b] [$Mn_2(CO)_{10}$] (10 mol %). [c] Regioselectivity determined by ^{1}H NMR spectroscopy.

Scheme 3.3.2 Manganese-Catalyzed C–H Activation with Imines **104**

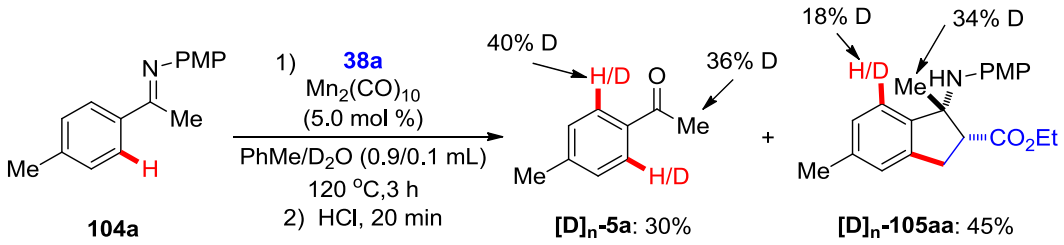
3.3.4 Mechanistic Studies

In order to shed light on the course of this new manganese-catalyzed C–H activation, a set of experiments towards elucidation of its mechanistic aspects were performed. First, in the intramolecular competition experiment with imine **104q**, no significant chemoselectivity was observed, and the almost 1:1 ratio of the products **105qa** and **105qa'** revealed that electron-rich and electron-poor arenes have comparable activities (Scheme 3.3.3a). Second, intermolecular competition experiment between *meta*- or *para*-substituted methyl- and fluoroacetophenonimines showed that there is no significant electronic effect in this manganese-catalyzed C–H bond activation (Scheme 3.3.3b and c). Both intra- and intermolecular competition experiments indicated that the electronic effects of imines **104** had only a minor influence on the manganese-catalyzed alkene annulation process.



Scheme 3.3.3 Intra/Intermolecular Competition Experiments

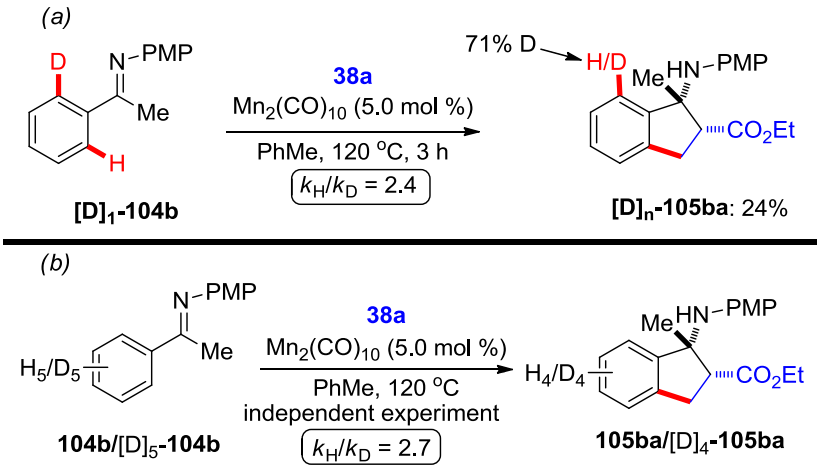
Additionally, C–H bond activation performed in the presence of D_2O as co-solvent revealed a reversible H/D-exchange, as was observed for the reisolation of the labeled substrate $[D]_n$-**5a** after acidic work-up as well as for the labeled product $[D]_n$-**105aa**(Scheme 3.3.4).



Scheme 3.3.4 H/D Exchange Experiment

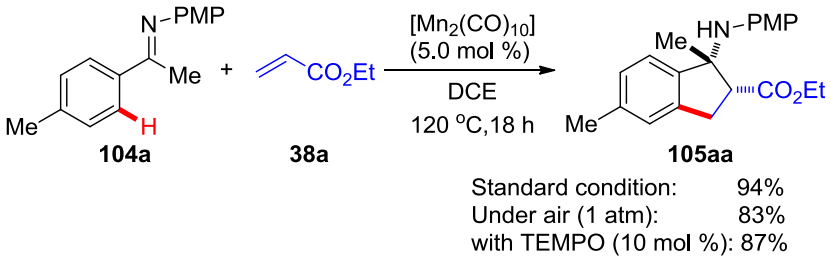
Furthermore, the kinetic isotope effect (KIE) of the manganese-catalyzed C–H activation was found to be $k_H/k_D \approx 2.4$, as was determined by the intramolecular competition experiment with isotopically labeled substrate $[D]_1$-**104b** (Scheme 3.3.5a), and the intermolecular KIE of $k_H/k_D \approx 2.1$ which was determined by independent experiments of substrates **104b** and $[D]_1$-**104b** (Scheme 3.3.5b). Both experimental results supported a kinetically relevant C–H

manganesation step.



Scheme 3.3.5 Kinetic Isotope Effect Studies

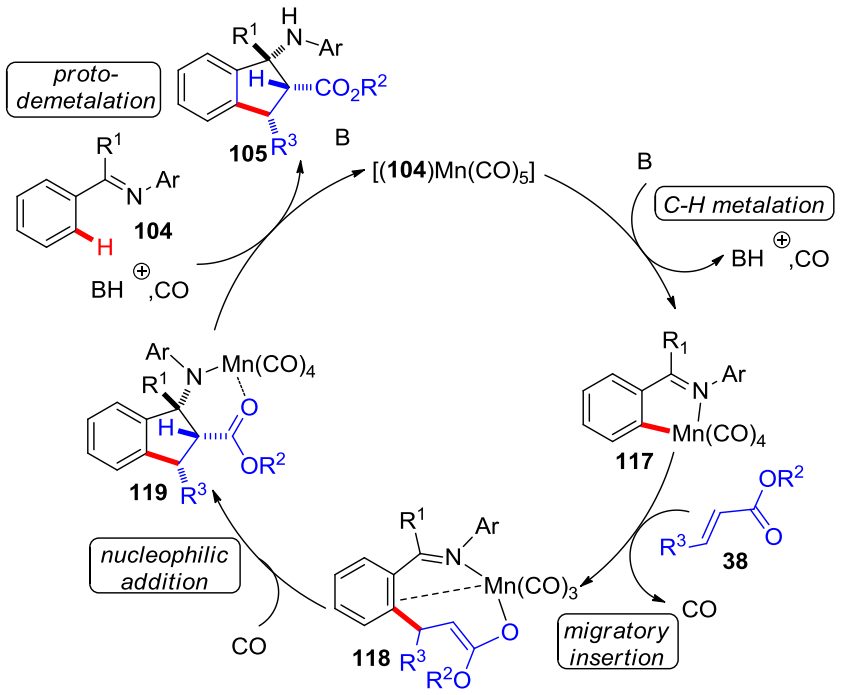
Moreover, a radical pathway was excluded by conducting the experiment either under an atmosphere of aif or in the presence of the radical scavenger TEMPO (Scheme 3.3.6). These findings strongly supported the organometallic C–H activation mode.



Scheme 3.3.6 C–H activation in the Presence of Radical Scavengers

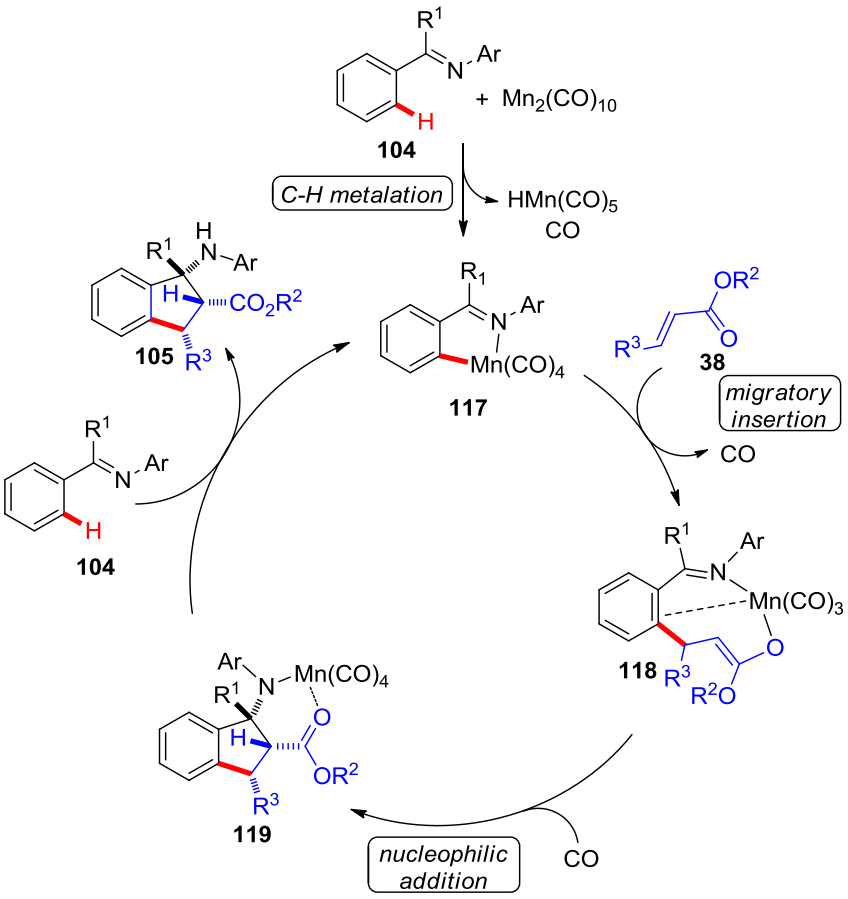
3.3.5 Proposed Mechanism

Based on these mechanistic studies, two plausible catalytic cycles were proposed for this manganese-catalyzed *cis*-selective *β*-amino ester formation.



Scheme 3.3.7 Proposed Mechanism

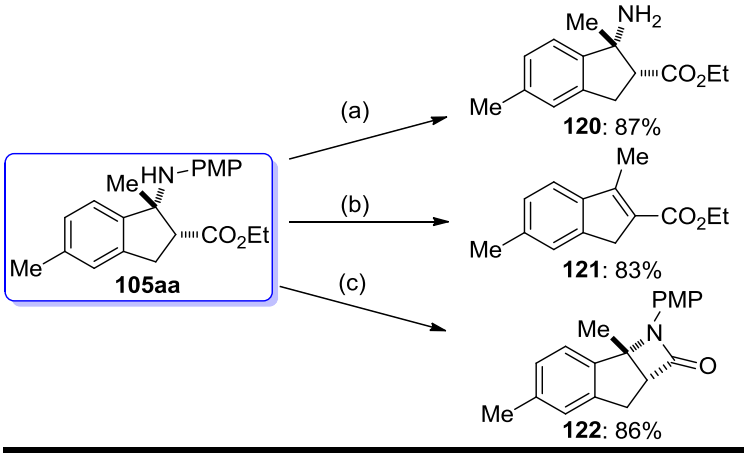
The initial rate-determining C–H metalation of ketimine **104** was proposed to generate intermediate **117** through base assistance, then the intermediate manganese enolate **118** is afforded *via* migratory insertion of *α,β*-unsaturated ester **38**, which subsequently undergo the intramolecular cyclization by nucleophilic attack at the carbon of imine group, thereby affording complex **119**. Finally, proto-demetalation furnishes the desired *β*-amino ester **105** and regenerates the active manganese complex (Scheme 3.3.7). Another possibility is that the intermediate **117** is formed *via* release of $HMn(CO)_5$ and CO, then the intermediate manganese enolate **118** is formed *via* migratory insertion of *α,β*-unsaturated ester **38** into the manganese–carbon bond of **117**. This intermediate subsequently undergoes the intramolecular cyclization by nucleophilic attack, affording complex **119**. Finally, the desired product **105** is obtained through complex **119** reacting with **104**, along with regeneration active manganese complex **117** (Scheme 3.3.8).



Scheme 3.3.8 Alternative Mechanism

3.3.6 Diversification of C–H Activation Product

Finally, the utility of the obtained *N*-protected *β*-amino esters **105** was investigated (Scheme 3.3.9).



(a) CAN (2.5 equiv), CH_3CN:H_2O (1:1), 23 °C, 3h. (b) PhMe, 160 °C, 14 h. (c) LiHMDS (1.5 equiv), THF, 0 °C-23 °C, 10 h.

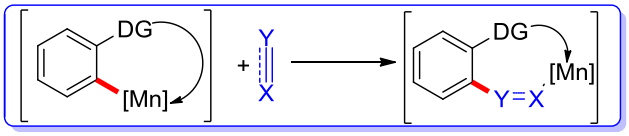
Scheme 3.3.9 Diversification of Product **105aa**

As can be seen from Scheme 3.3.9, compound **105aa** can be selectively deprotected by removing the PMP group to give *β*-amino ester **120**, which displays the free amino group (a). Important organic building blocks, indenecarboxylate**121** (b) and *β*-lactam derivative **122** (c), can readily be obtained from **105aa** in good yields as well.

3.4 Manganese(I)-Catalyzed C–H Aminocarbonylation of Heteroarenes

The step-economical aryl amide formation through C–H activation using easily accessible isocyanates **110** has been successfully achieved with rather expensive 4d or 5d transition metals, such as rhodium,[89] rhenium,[90] ruthenium[91] or Cp*Co^{III} complexes[92] from the groups of Kuninobu/Takai, Bergman/Ellman, Cheng, Li and Ackermann. Although manganese is the third most abundant transition metal in the earth crust, the organometallic C–H bond activation with manganese catalyst is still less explored compared to the noble transition metals.

The triple or polar double bond can be inserted into the manganese-carbon bond (Scheme 3.4.1),[75-77, 79, 81, 88] and we became attracted by the isocyanates **106** which contain polar C=Het double bonds. It might undergo the insertion process to form amide in the presence of a manganese catalyst.

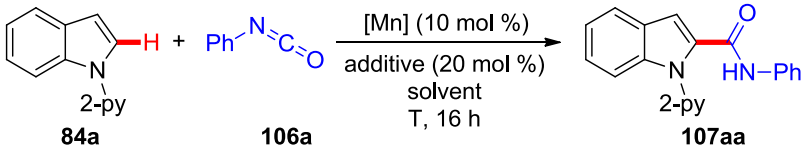


Scheme 3.4.1 Insertion into Manganese–Carbon Bond by Polar Multiple Bond

3.4.1 Optimization of Manganese-Catalyzed C–H Aminocarbonylation

Based on this hypothesis, studies with 1-(pyridin-2-yl)-1*H*-indole (**84a**) and phenyl isocyanate (**106a**) as the model substrates were initiated (Table 3.4.1).

Table 3.4.1 Optimization of Manganese-Catalyzed C–H Activation[a]



84a **106a** **107aa**

Entry	[Mn]	Additive	Solvent	*T* [°C]	Yield [%][b]
1	$[Mn_2(CO)_{10}]$	---	PhMe	120	56[c]
2	$[Mn_2(CO)_{10}]$	NaOAc	PhMe	120	47[c]
3	$[MnBr(CO)_5]$	NaOAc	PhMe	120	70[c]
4	$[MnBr(CO)_5]$	NEt_3	PhMe	120	79[c]
5	$[MnBr(CO)_5]$	PPh_3	PhMe	120	< 3[c]
6	$[Mn_2(CO)_{10}]$	NaOAc	Et_2O	100	76
7	$[Mn_2(CO)_{10}]$	NaOAc	1,4-dioxane	100	33[d]
8	$[Mn_2(CO)_{10}]$	NaOAc	DME	100	14[d]
9	$[MnBr(CO)_5]$	NaOAc	Et_2O	100	84

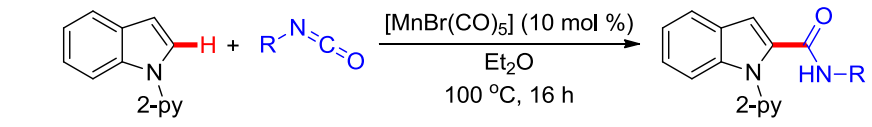
10	$[MnBr(CO)_5]$	---	PhMe	120	61
11	$[MnBr(CO)_5]$	---	THF	100	78
12	$[MnBr(CO)_5]$	---	MTBE	100	80
13	$[MnBr(CO)_5]$	---	nBu$_2$O	100	91
14	$[MnBr(CO)_5]$	---	Et_2O	100	95
15	$[MnBr(CO)_5]$	---	---	100	83
16	$[Mn_2(CO)_{10}]$	---	Et_2O	100	89
17	---	---	Et_2O	100	---
18	$MnCl_2$	---	Et_2O	100	---
19	$Mn(OAc)_2$	---	Et_2O	100	---

[a] Reaction conditions: **84a** (0.50 mmol), **106a** (0.55 mmol), [Mn] (10 mol %), additive (20 mol %), solvent (1.0 mL), under N_2, 100 °C, 16 h, isolated yield. [b] Isolated yield. [c] **84a** (1.0 mmol). [d] NMR conversions using CH_2Br_2 as internal standard.

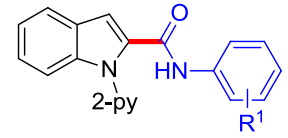
With $[Mn_2(CO)_{10}]$ as the catalyst and toluene as the solvent, the desired product **107aa** was formed in 56% yield (entry 1). Notably, this manganese-catalyzed C–H aminocarbonylation worked without any additional ligand or additive, in contrast to cobalt-catalyzed approaches.[92] Next, the influence of additives was investigated, and it was found that the yield was slightly improved in the presence of $[MnBr(CO)_5]$ as the catalyst and a tertiary amine as additive (entries 2–5). Different solvents were tested, and etheral solvents were found to be ideal (entries 6–13). Finally, $[MnBr(CO)_5]$ as catalyst together with ethers as solvent without any additive were identified as the optimal reaction conditions (entries 12–16). Furthermore, the control experiments clearly showed that the C–H activation reaction did not occur without the catalyst or with simple manganese salts, such as $MnCl_2$, $Mn(OAc)_2$ (entries 17–19).

3.4.2 Scope of Manganese-Catalyzed C–H Aminocarbonylation with Isocyanates

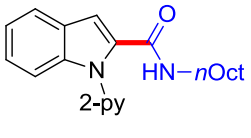
With the optimized catalytic conditions in hand (Table 3.4.1, entries 13 and 14), the C–H aminocarbonylation scope with isocyanates **106** was investigated (Scheme 3.4.1). Under the optimized conditions, various valuable functional groups on substituted aryl isocyanates **106**, such as fluoro, chloro, iodo and methoxy substituents, were tolerated to give the corresponding products **107** in good to excellent yields, which highlights the potential for functional groups further diversifications. It is noteworthy that the more challenging electron-rich and sterically hindered secondary alkyl isocyanates **106k** and **106l** were also suitable for this manganese(I) catalysis with acceptable to good yields. Moreover, the *ortho*-substituted aryl isocyanate, 1-naphthaleneisocyanate **106m** and the heteroaromatic substrate, 2-furanisocyanate **106n**, were converted into the corresponding products **107am** and **107an** with comparable catalytic efficacy (Scheme 3.4.2).



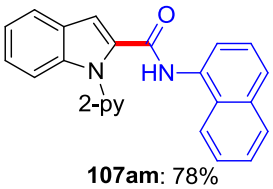
84a **106** **107**



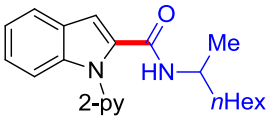
R^1 = H (**107aa**): 95%, 91%[a]
R^1 = 4-F (**107ab**): 92%, 82%[a]
R^1 = 4-Me (**107ac**): 69%
R^1 = 4-MeO (**107ad**): 94%
R^1 = 4-CF_3 (**107ae**): 76%
R^1 = 3-Cl (**107af**): 79%
R^1 = 3-I (**107ag**): 74%
R^1 = 2-MeO (**107ah**): 86%
R^1 = 2-Me (**107ai**): 70%
R^1 = 2-I (**107aj**): 79%, 72%[a]



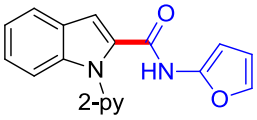
107ak: 61%



107am: 78%



107al: 71%[b]



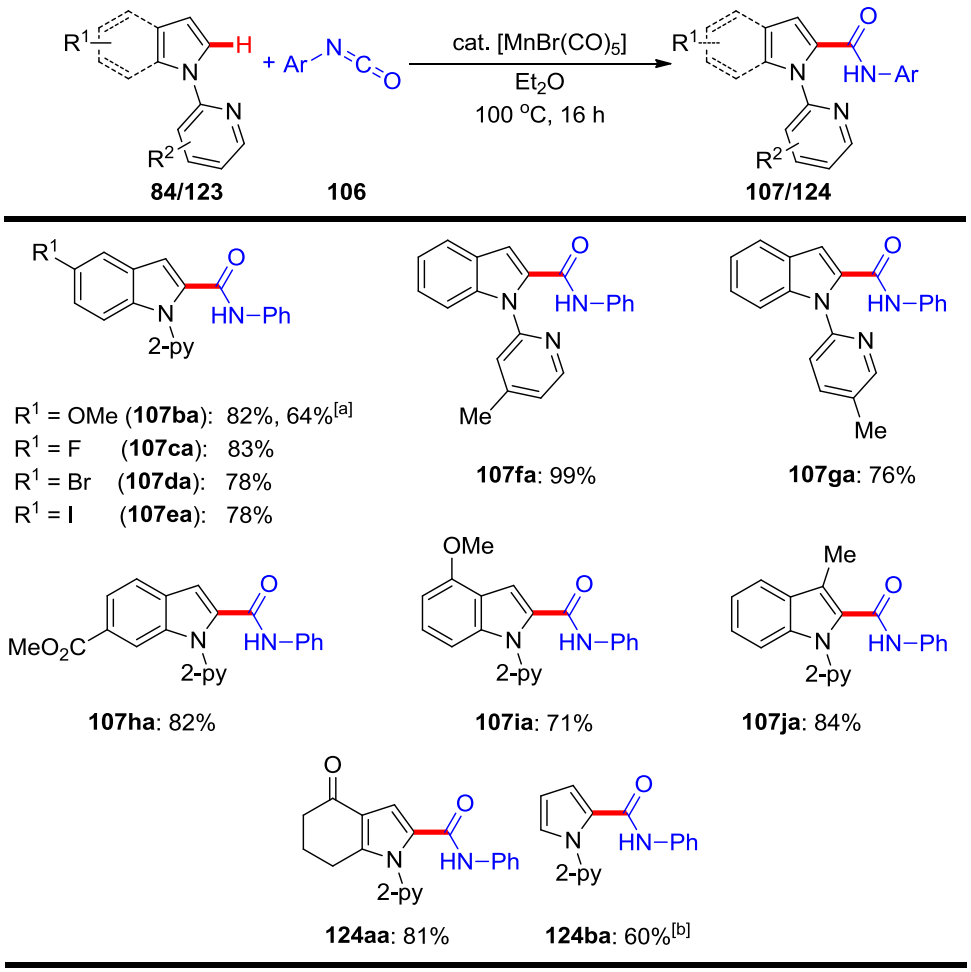
107an: 62%

Reaction conditions: **84a** (0.50 mmol), **106** (0.55 mmol), [$MnBr(CO)_5$] (10 mol %), Et_2O (1.0 mL), under N_2, 100 °C, 16 h. [a] nBu_2O as solvent. [b] **106** (2.0 equiv).

Scheme 3.4.2 Manganese-Catalyzed C–H Activation with Isocyanates **106**

3.4.3 Scope of Manganese-Catalyzed C–H Amidation with Indoles and Pyrroles

The scope of indoles **84** and pyrroles **123** under the optimized conditions was next explored. The indoles **84** showed high reactivity and chemoselectivity. Besides, a variety of valuable functional groups, such as bromo, iodo, ester and ketone, were well tolerated in this catalytic system. Furthermore, the more sterically hindered C3-substituted substrate **84j** was also found to be suitable in this manganese-catalyzed C–H aminocarbonylation process to afford the corresponding product in high yields. Notably, the manganese-catalyzed C–H activation protocol was not limited to indole substrates. Thus, pyrroles **123** underwent the process with high catalytic efficacy as well (Scheme 3.4.3).

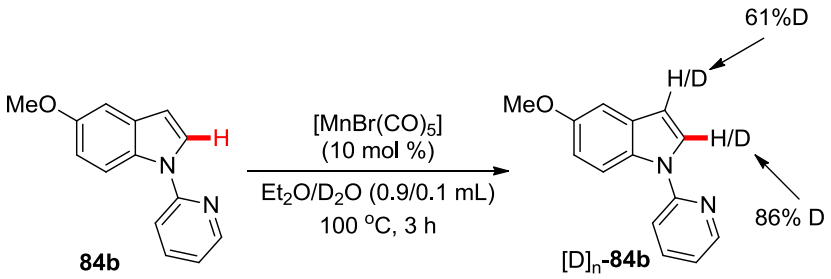


Reaction conditions: **84/123** (0.50 mmol), **106** (0.55 mmol), $[MnBr(CO)_5]$ (10 mol %), Et_2O (1.0 mL), under N_2, 100 °C, 16 h. [a] *n*-Bu_2O as solvent. [b] **123b** (2.0 equiv), $[MnBr(CO)_5]$ (20 mol %).

Scheme 3.4.3 Manganese-Catalyzed C–H Amidation with Indoles **84** and Pyrroles **123**

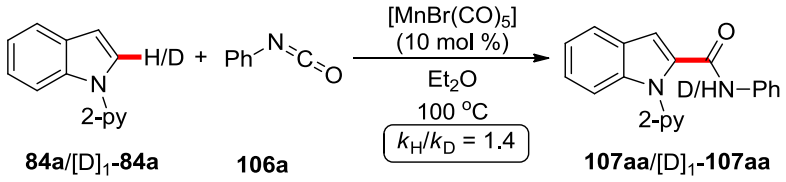
3.4.4 Mechanistic Studies

In order to gain deeper understanding on the manganese-catalyzed C–H aminocarbonylation process, a set of mechanistic experiments was performed. First, H/D exchange reaction under the manganese(I) catalytic system was conducted in the presence of D_2O as a co-solvent. Here, the corresponding product was not observed. Then, the reaction in the presence of D_2O as co-solvent but without the isocyanate was performed, H/D exchange was detected in the C2 and C3 positions of the indole substrate in the reisolated $[D]_n$-**84b**. This finding revealed that the C–H manganesation process is reversible (Scheme 3.4.4).



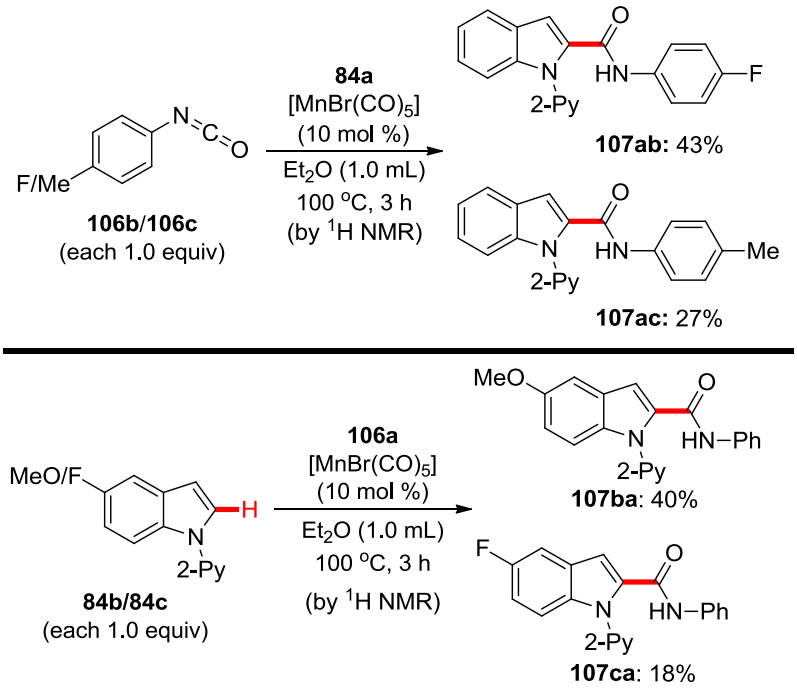
Scheme 3.4.4 H/D Exchange Experiment

Next, the kinetic isotope effect (KIE) of the manganese-catalyzed C–H activation was determined by independent experiments of substrates **84a** and [D]$_1$-**84a** to be $k_H/k_D \approx 1.4$ (Scheme 3.4.5). These experimental result indicated a fast C–H manganesation step.



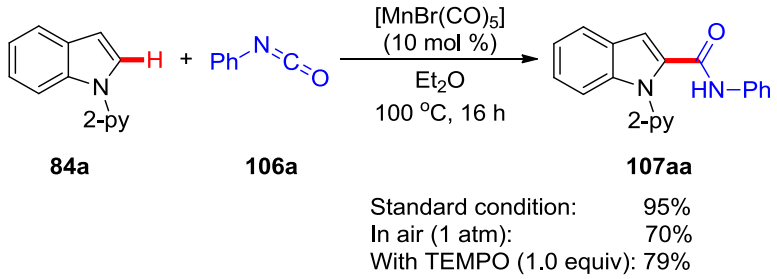
Scheme 3.4.5 Kinetic Isotope Effect Study

Subsequently, the intermolecular competition experiments between electron-rich and electron-deficient isocyanates **106** and indoles **84** were conducted. These competition experiments clearly showed electron-deficient isocyanates **110** and electron-rich indoles **83** to be preferentially converted (Scheme 3.4.6), which indicated that the insertion of the isocyanate C=N double bond into the manganese-carbon bond was the rate-determining step.



Scheme 3.4.6 Intermolecular Competition Experiments

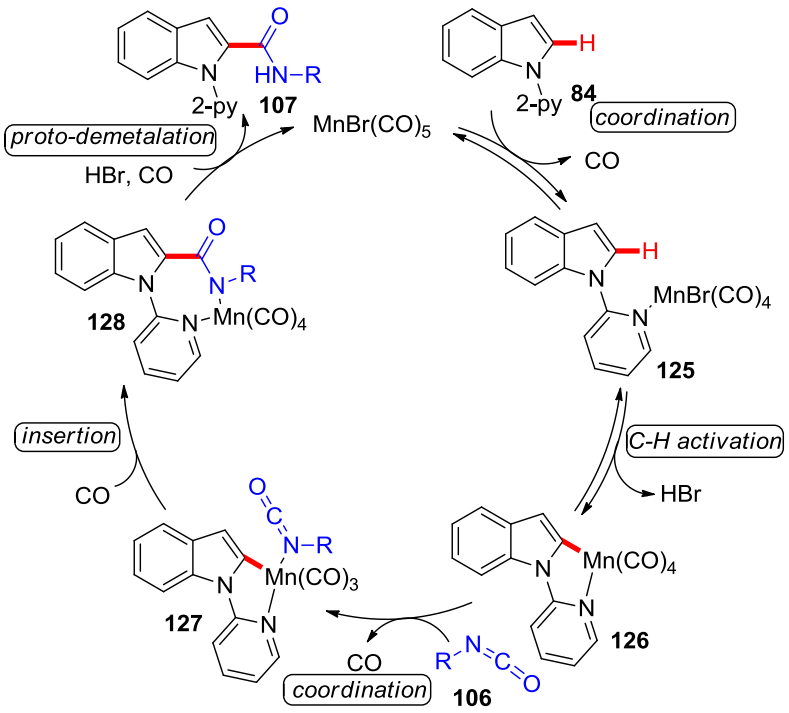
Additionally, the comparable catalytic efficiency of the manganese(I)-catalyzed C–H functionalizations was highlighted when conducting the experiments either under an atmosphere of air or in the presence of stoichiometric amounts of the radical scavenger TEMPO (Scheme 3.4.7). These results strongly supported the organometallic C–H activation mode.



Scheme 3.4.7 C–H Activation Under Air or in the Presence of Radical Scavengers

3.4.5 Proposed Mechanism

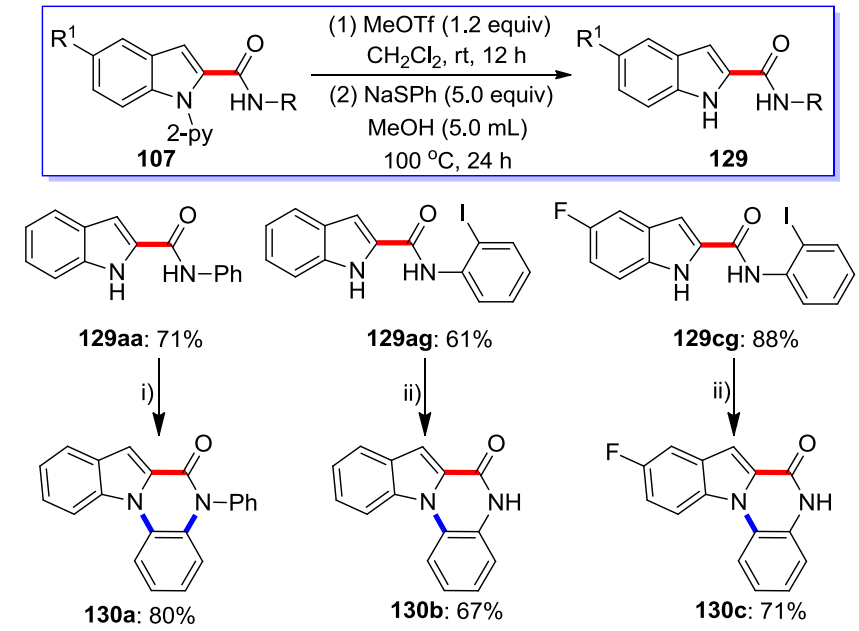
Based on the mechanistic studies, we proposed a plausible catalytic cycle for this manganese(I)-catalyzed C–H aminocarbonylation process (Scheme 3.4.8). The catalytic cycle for this manganese(I)-catalyzed C–H aminocarbonylation was proposed to be initiated by the coordination of the pyridine moiety to the manganese catalyst. Subsequently, complex **125** undergoes a reversible and fast C–H bond metalation, forming the cyclometalated complex **126**. The seven-membered manganacycle complex **128** was formed after coordination and rate-determining insertion of the C=N bond of isocyanate **106** into the manganese-carbon bond. Finally, proto-demetalation released the desired product and regenerated the manganese(I) catalyst.



Scheme 3.4.8 Proposed Mechanism

3.4.6 Diversification of Aminocarbonylation Product

Finally, in order to show the utility of the products obtained from aminocarbonylation, several further diversifications have been performed (Scheme 3.4.9).



i) 1-Fluoro-2-nitrobenzene, Cs_2CO_3, CH_3CN, 90 °C, 12 h.
ii) CuI (cat.), L-proline (cat.), NaH, DMF, 150 °C, μw, 5 min.

Scheme 3.4.9 Diversification of C–H Activation Product

First, the traceless removal of the pyridyl directing group was successfully achieved to release the NH-free indole **129** in good yield. Furthermore, the important quinoxalinones **130** can be conveniently synthesized from the late-stage diversification of amides **107** in a single step.

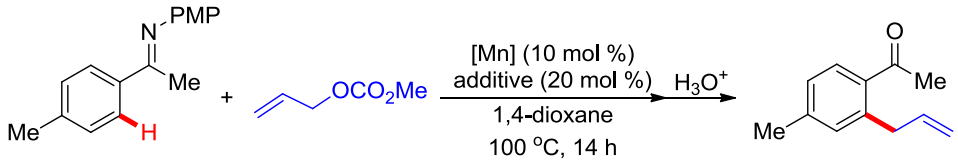
3.5 Manganese(I)-Catalyzed Substitutive C–H Allylation

The allyl group is one of the most important and useful functionalities in organic synthesis because it provides easy access to various functional groups.[94] Because of this importance of the allyl group, developing new allylation reactions has drawn the attention of chemist for a long time. Although cross-coupling reactions with prefunctionalized arenes have proven to be a viable method,[101] direct C–H allylation is obviously more attractive. This approach provides a straightforward way to introduce allyl units because of its atom- and step-economy. The classical Lewis acid-mediated Friedel-Crafts-type allylation of electron rich arenes is known and widely used for many years.[102] But there are several limitations, including: *i*) limited substarte scope, to electron-rich substrates; *ii*) poor regioselectivities; and *iii*) over allylation.
In the recent years, transition metal-catalyzed direct C–H allylations were developed by different research groups. However, these reactions only occurred in the presence of rare and expensive 4d or 5d transition metals, such as ruthenium,[95i, 103] rhodium,[95e-g, 104] palladium,[95h, 105] iridium[106] and rhenium[107] in most cases. Recently, C–H allylations catalyzed by inexpensive 3d metal, such as iron,[95a, 108] cobalt,[44, 95b, 95c, 109] nickel[95d, 110] and copper[111] have also been developed. In contrast, even though manganese is the twelfth most abundant element and the third most abundant transition metal after iron and titanium in earth crust, there is no report about allylation by manganese catalysis so far.

3.5.1 Optimization of Manganese-Catalyzed C–H Allylation with Carbonate

The studies were initiated by exploring the allylation of ketimine **104a** with allyl methyl carbonate **108a**, and various reaction conditions were tested (Table 3.5.1).

Table 3.5.1 Optimization of Manganese-Catalyzed C–H Allylation with Carbonate **108a**[a]



104a **108a** **109aa**

Entry	[Mn]	Additive	Yield (%)
1	---	NaOAc	---
2	$MnCl_2$	NaOAc	---
3	$Mn(OAc)_2$	NaOAc	---
4	$MnBr(CO)_5$	NaOAc	76
5	$MnBr(CO)_5$	NaOMe	78
6	$MnBr(CO)_5$	---	11
7	$MnBr(CO)_5$	KOAc	78

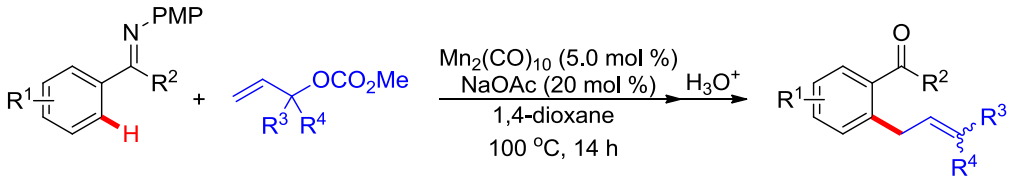
8	$MnBr(CO)_5$	LiOAc	34
9	$MnBr(CO)_5$	NaOPiv	83
10	**$MnBr(CO)_5$**	**KO_2CMes**	**86**
11	$Mn_2(CO)_{10}$	---	67
12	$Mn_2(CO)_{10}$	KO_2CMes	51
13	$Mn_2(CO)_{10}$	NaOPiv	75
14	$Mn_2(CO)_{10}$	KOAc	81
15	**$Mn_2(CO)_{10}$**	**NaOAc**	**88**
16	**$Mn_2(CO)_{10}$**	**NaOAc**	**84**[b]

[a] Reaction conditions: **104a** (0.5 mmol), **108a** (1.5 mmol), [Mn] (10 mol %), additive (20 mol %), 1,4-dioxane (1.0 mL), under N_2, 14 h, isolated yield. [b] 10 mmol scale.

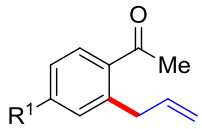
The desired allylation product **109aa** was not obtained in the absence of a manganese catalyst or when employing simple manganese salts, such as $MnCl_2$ and $Mn(OAc)_2$ (entries 1–3). To our delight, when $MnBr(CO)_5$ was used as the catalyst in the presence of catalytic amounts of NaOAc, the desired product **109aa** was isolated in 76% yield after hydrolysis of the allylated ketimine (entry 4). Then, different additives were investigated (entries 5, 7–10), and KO_2CMes was found to be the optimal additive. The catalytic efficiency decreased dramatically without additives (entry 6). Likewise, the dimeric complex $Mn_2(CO)_{10}$ showed a comparable catalytic efficacy in the presence of NaOAc as the additive (entry 12). Subsequently, the reactions with different additives or without additive were probed, and these results indicated that NaOAc was ideal (entries 11–15). Notably, the optimal catalytic system could be used on a 5 mmol scale in a comparable high yield (entry 16).

3.5.2 Scope of Manganese-Catalyzed C–H Allylation of Imines

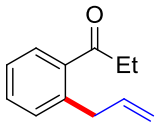
With the optimized catalytic system in hand (Table 1, entries 10 and 15), the scope of the carboxylate-assisted manganese(I)-catalyzed C–H allylation of imines **104** with various allyl carbonates **108** was studied (Scheme 3.5.1). A large variety of imines **104** were suitable for this transformation. Different valuable functional groups, such as amine, fluoro, chloro, bromo, iodo and nitrile, were tolerated to give the corresponding products. When *meta*-substituted arenes **104n**–**104p** were employed in the allylation reaction, the regioselectivity was largely controlled by steric interactions except for substrates with a secondary directing group influence. Notably, this manganese-catalyzed C–H allylation was not restricted to the non-substituted allyl carbonates **108**. Indeed, substitution on the *α*-position of allyl carbonates **108b** and **108c** proved to be suitable in this protocol to give linear allylation products in good yields with excellent diastereoselectivities. In all cases, a double-bond isomerization to the thermodynamically more stable structure derivative was not observed.



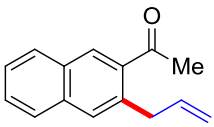
104 **108** **109**



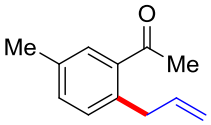
R^1 = H (**109ba**): 86%
R^1 = OMe (**109sa**): 72%
R^1 = NMe_2 (**109ta**): 64%
R^1 = Ph (**109fa**): 78%
R^1 = F (**109ca**): 78%
R^1 = Cl (**109da**): 81%
R^1 = Br (**109ea**): 73%
R^1 = I (**109ua**): 83%
R^1 = CN (**109va**): 87%



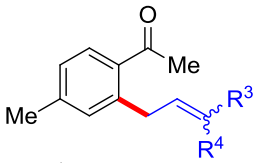
109ga: 91%



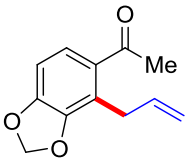
109na: 86% (12:1)[c]



109oa: 76% (6:1)[b,c]



R^3 = Me, R^4 = H (**109ab**): 66% (10:1)[a]
R^3 = *n*Bu, R^4 = H (**109ac**): 62% (12:1)[a]



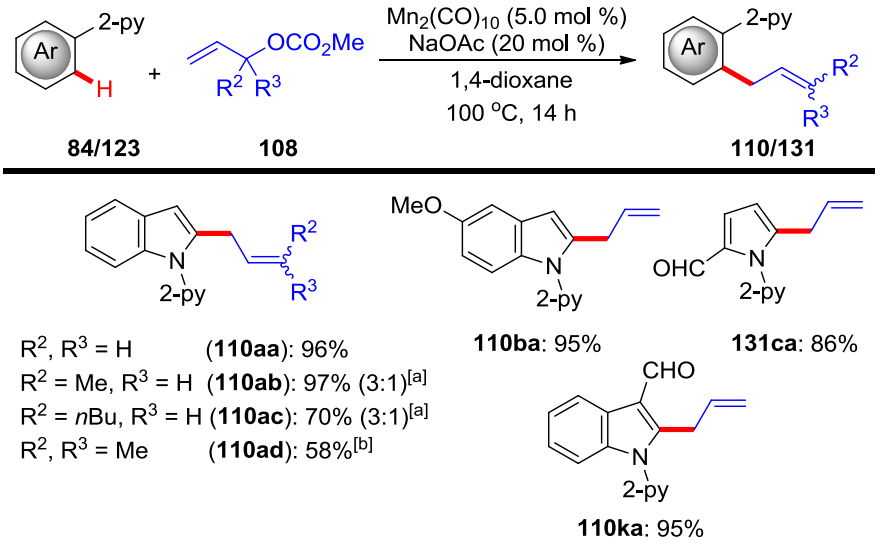
109pa: 68%

Reaction conditions: **104** (0.5 mmol), **108** (1.5 mmol), [$Mn_2(CO)_{10}$] (5.0 mol %), NaOAc (20 mol %), 1,4-dioxane (1.0 mL), under N_2, 14 h. [a] *E*/*Z* ratio of the products in parentheses. [b] 120 °C. [c] Major regioisomer shown; regioisomeric ratio in parentheses.

Scheme 3.5.1 C–H Allylation of Imines **104** with Allyl Carbonates **108**

3.5.3 Scope of Manganese-Catalyzed C–H Allylation of Heteroarenes

To further highlight the power of the carboxylate-assisted manganese(I)-catalyzed direct C–H allylation *via* C–O cleavage, the reaction was further explored with the biologically relevant indole heterocycles **84**,[9x, 45] which also proved to be suitable for the C−H allylation (Scheme 3.5.2). The indoles **84** showed excellent reactivity, and methoxy, fluoro, bromo or iodo groups were well tolerated. Particularly, indole-3-carbaldehyde **84k** was also found to be a suitable substrate, and gave the desired product with excellent yield. Thus, the less stable formyl C–H bond remained untouched, highlighting the organometallic C–H activation process. Not only the non-substituted ally carbonates were suitable in this manganese-catalyzed C–H functionalization, but also the α-substituted allyl carbonates **104** were proved to be suitable substrates giving linear allylation indoles **110** with good yield. Notably, this manganese catalytic system was not restricted to indole substrates, but the pyrrole **123** underwent the C–H allylation with good yields as well.

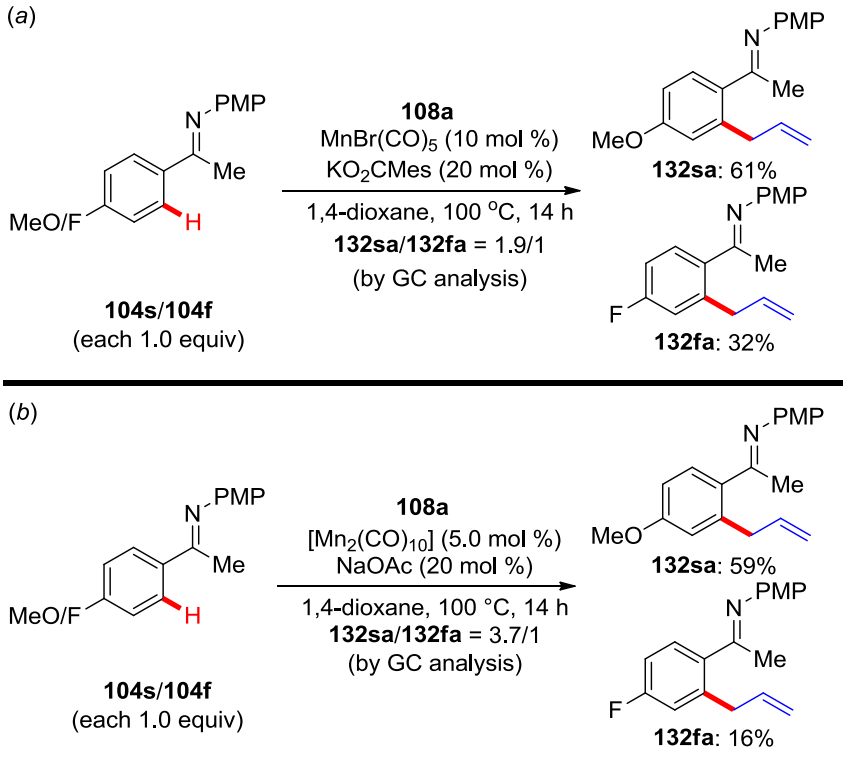


Reaction conditions: **84/123** (0.5 mmol), **108** (1.0 mmol), [$Mn_2(CO)_{10}$] (10 mol %), NaOAc (20 mol %), 1,4-dioxane (1.0 mL), under N_2, 14 h. [a] *E/Z* ratio of the products in parentheses. [b] With [$Mn_2(CO)_{10}$] (10 mol%), NaOAc (40 mol %), 120 °C.

Scheme 3.5.2 C–H Allylation of Heteroarenes **84/123** with Allyl Carbonates **108**

3.5.4 Mechanistic Studies

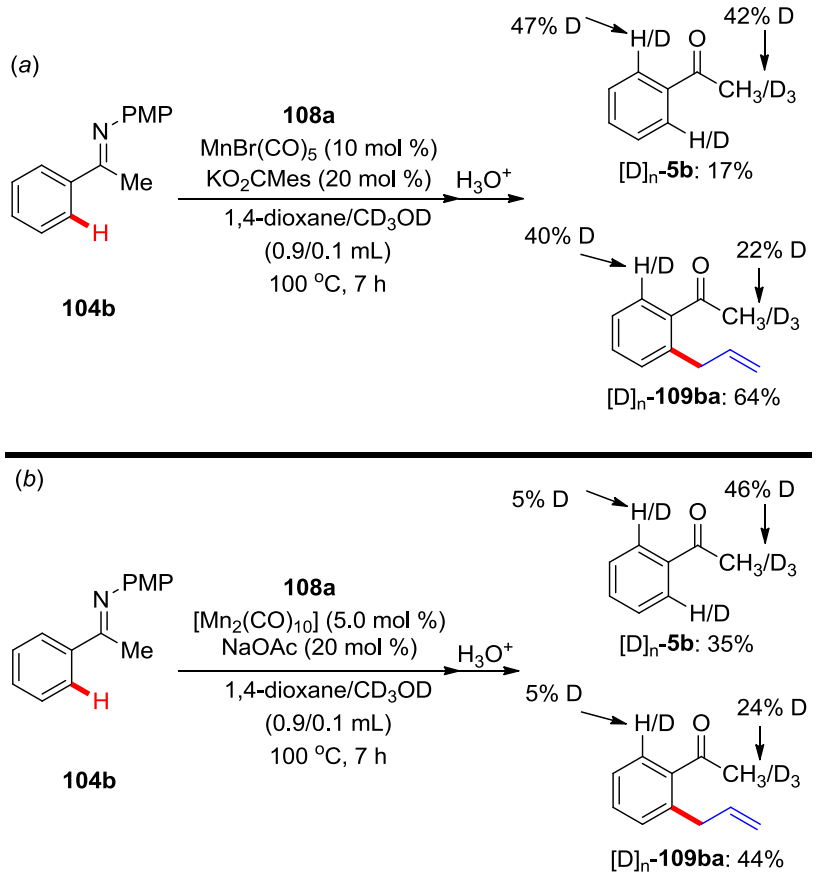
In order to gain insights into the manganese-catalyzed C–H activation reaction, a set of experiments towards elucidation of its mechanism were performed.



Scheme 3.5.3 Intermolecular Competition Experiments

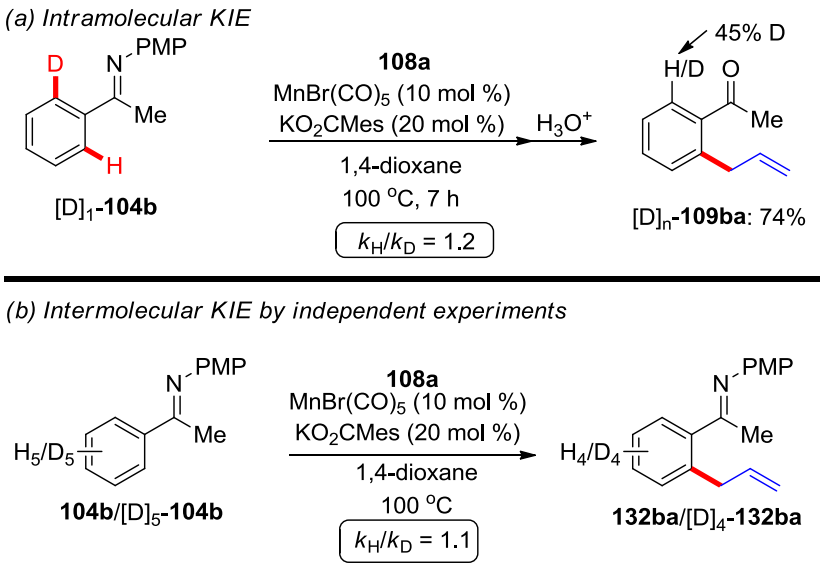
The intermolecular competition experiment between electron-rich and electron-deficient imines **104** showed that electron-rich arenes were preferentially converted either with $MnBr(CO)_5/KO_2CMes$ (Scheme 3.5.3a) or $Mn_2(CO)_{10}$/NaOAc as the catalytic systems (Scheme 3.5.3b).

Subsequently, the manganese(I)-catalyzed C–H allylation reaction was conducted in the presence of CD_3OD as the co-solvent, which revealed a reversible H/D exchange reaction, as was observed by reisolation of the labeled $[D]_n$-**5b** and the labeled product $[D]_n$-**109ba** (Scheme 3.5.4a). However, almost no H/D exchange in $C(sp^2)$–H was observed in the $Mn_2(CO)_{10}$/NaOAc system (Scheme 3.5.4b). These observations revealed that the C–H activation might be different between the two systems.



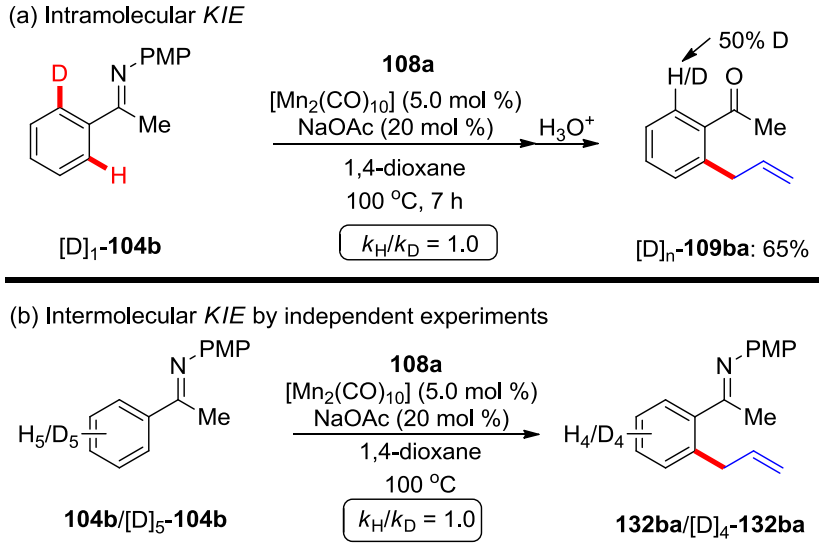
Scheme 3.5.4 H/D Exchange Experiments

The intramolecular kinetic isotope effect (KIE) was found to be $k_H/k_D \approx 1.2$ (Scheme 3.5.5a). Moreover, a similar rather low KIE of $k_H/k_D \approx 1.1$ was observed in independent reactions between substrates **104b** and $[D]_1$-**104b** (Scheme 3.5.5b) in the $MnBr(CO)_5/KO_2CMes$ system.



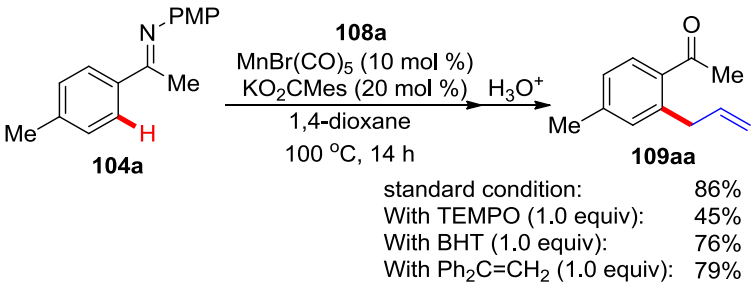
Scheme 3.5.5 KIE Studies

The similar KIE values were obtained in the $Mn_2(CO)_{10}$/NaOAc system, namely intramolecular $k_H/k_D \approx 1.0$ and intermolecular $k_H/k_D \approx 1.0$ (Scheme 3.5.6). These experimental findings indicated that the C–H manganesation process was not the rate-determining step in both catalytic systems.



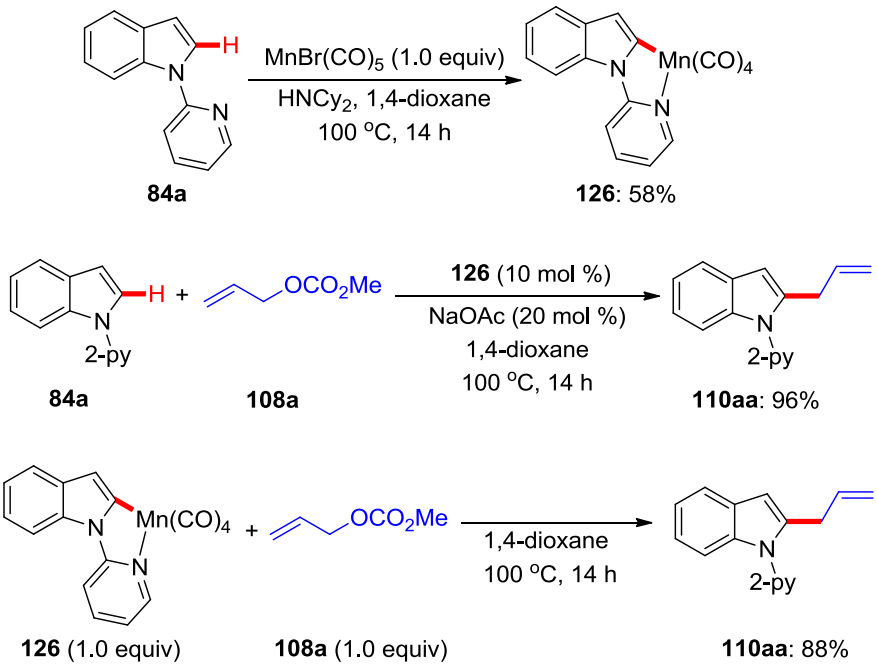
Scheme 3.5.6 KIE Study Experiments in $Mn_2(CO)_{10}$/NaOAc System

Furthermore, a radical pathway could be excluded by conducting the experiment in the presence of stoichiometric amounts of radical scavengers, such as TEMPO, BHT or $Ph_2C{=}CH_2$ (Scheme 3.5.7). These results strongly supported the organometallic C–H activation mode.



Scheme 3.5.7 Evidence for an Organometallic C–H Activation Mode

Additionally, the potential intermediate **126** was prepared by stoichiometric amounts of [$MnBr(CO)_5$] through C–H activation in moderate yield. Notably, cyclometalated complex **126** showed a high activity to afford the corresponding allylation product not only with catalytic amounts but also stoichiometric experiment (Scheme 3.5.8). These results reveled that this cyclometalated complex is the key intermediate of this C–H allylation.

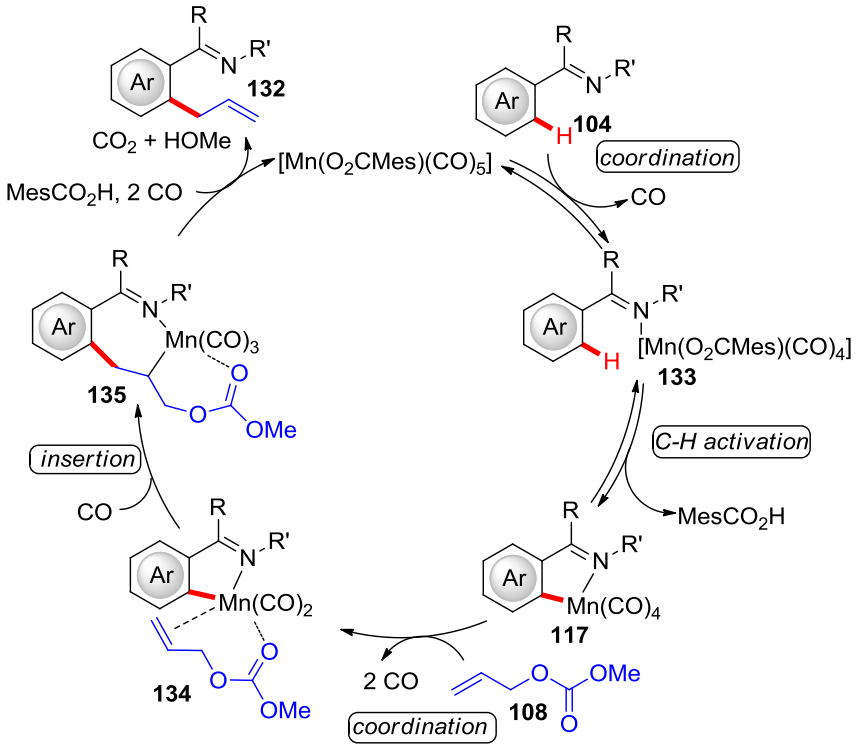


Scheme 3.5.8 C–H Allylations with Cyclometalated Complex **126**

3.5.5 Proposed Mechanism

Based on these mechanistic studies, we proposed a plausible catalytic cycle for this allylation protocol, which is shown for the system comprising of $MnBr(CO)_5$ and KO_2CMes. The active manganese catalyst [$Mn(O_2CMes)(CO)_5$] was formed and then the nitrogen of substrate **104** coordinates to the manganese center to generate the complex **133**, which is followed by the fast C–H manganesation producing the key intermediate cyclometalated complex **117**. Subsequently, migratory insertion of electrophile **135** occurs. The activation of the allyl carbonate **108** *via* an oxidative addition procedure could be an alternative pathway. Finally,

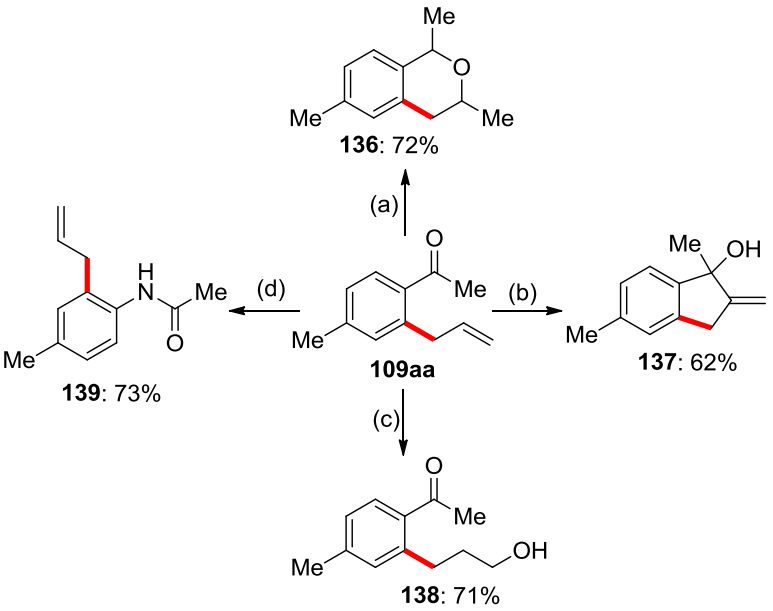
β-oxygen elimination, decarboxylation and MeOH release affords the allylation product **132** as well as regenerates the active manganese catalyst (Scheme 3.5.9).



Scheme 3.5.9 Proposed Mechanism

3.5.6 Diversification of C–H Activation Products

Finally, in order to show the synthetic utility of the allylation products of the manganese-catalyzed C–H allylation, several further diversifications were completed (Scheme 3.5.8). The synthetically useful cyclic ether **136**, indanol **137**, alcohol **138**, or anilide **139** were accessed efficiently.



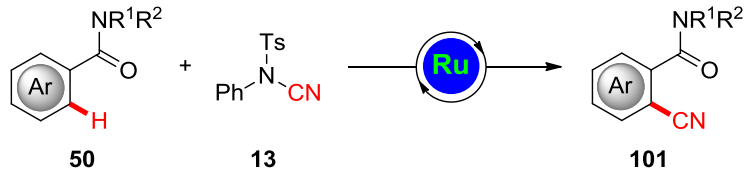
(a) 1) $LiAlH_4$ (2.1 equiv), Et_2O, 23 °C, 12 h. 2) KO*t*Bu (3.0 equiv), NMP, 100 °C, 1 h. (b) $AlMe_3$ (1.0 equiv), $Ni(cod)_2$ (20 mol %), PCy_3 (20 mol %), THF, 23 °C, 15 min. (c) 1) 9-BBN (1.05 equiv), THF, 23 °C, 24 h. 2) aq. H_2O_2, 2 N NaOH, THF, 23 °C, 2 h. (d) 1) $NH_2OH{\cdot}HCl$ (2.3 equiv), NaOAc (2.5 equiv), $MeOH/H_2O$, 100 °C, 1 h. 2) cyanuric chloride (5.0 mol %), $ZnCl_2$ (10 mol %), MeCN, 90 °C, 2 h.

Scheme 3.5.8 Diversification of C–H Activation Product

3.6 Summary

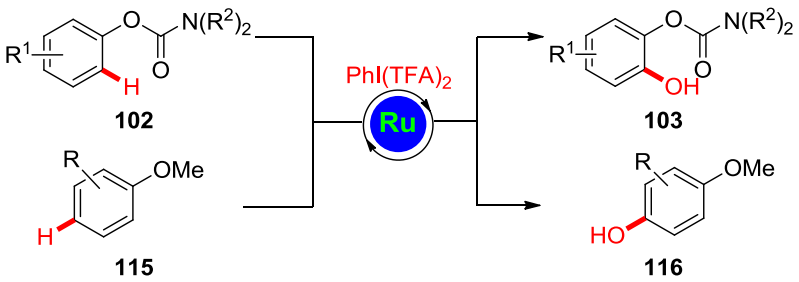
This thesis focused on the development of new methods for ruthenium- and manganese-catalyzed C–H activation.

First, an unprecedented ruthenium(II)-catalyzed C–H cyanation on arenes by using bench stable, readily accessible and user-friendly *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS, **13**) as the cyanation reagent was accomplished (Scheme 3.6.1). This direct C–H cyanation on synthetically useful (hetero)aromatic amides **50** tolerated a variety of valuable functional groups with good site-selectivity and broad scope. Due to the importance of the cyano group which can be readily transformed to many other valuable functional groups, this present C–H cyanation reaction may provide a new strategy for the rapid modification of functional molecules.[86]



Scheme 3.6.1 Ruthenium(II)-catalyzed C–H Cyanations of Benzamides **50**

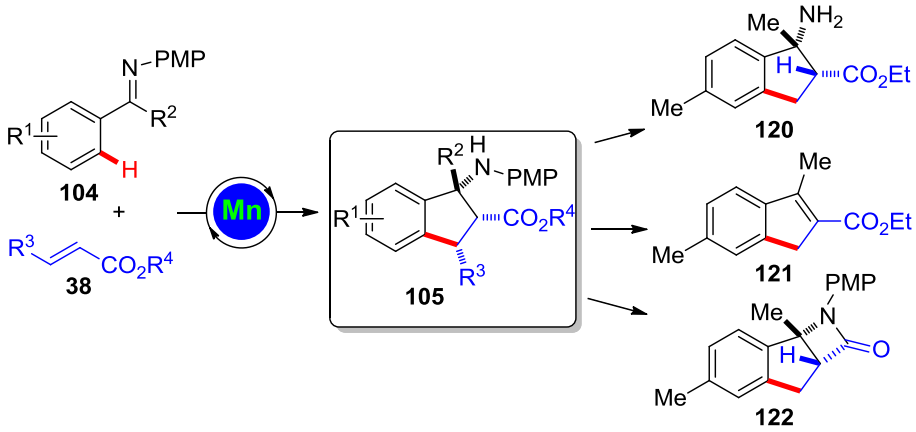
Second, an *ortho*- and *para*-selective ruthenium-catalyzed C(sp^2)–H oxygenation of phenol derivatives was developed, which provides a new strategy for the synthesis of phenol derivatives (Scheme 3.6.2). The site-selectivity could be controlled through the substrate modification. The *ortho*-C–H oxygenation proceeded on aryl carbamates **102**, while C–H *para*-oxygenation occurred on anisole derivatives **115** under the ruthenium(II) catalysis. Furthermore, the directing group ability order was established through competition experiments to be amide > carbamate > ester.[55d]



Scheme 3.6.2 *Ortho*- and *Para*-Selective Ruthenium-Catalyzed C(sp^2)–H Oxygenations of Phenol Derivatives

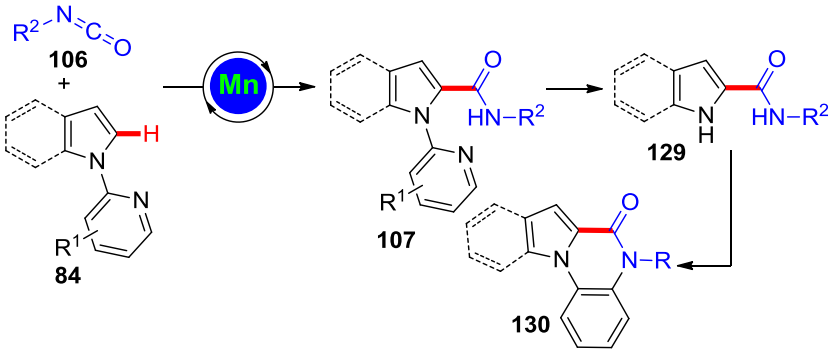
Third, a novel type of manganese-catalyzed annulation of acrylates by imines *via* organometallic C–H bond activation was developed, which provided a new approach to valuable carbocyclic *β*-amino acid derivatives with high efficacy, good functional group

tolerance and excellent *cis*-diastereoselectivity (Scheme 3.6.3). Furthermore, the unprotected *β*-amino ester **120** and important organic building blocks were readily accessed from these C–H annulation products.[88]



Scheme 3.6.3 Manganese-Catalyzed Synthesis of *cis*-*β*-Amino Acid Esters **105** through Organometallic C–H Activation of Ketimines **104**

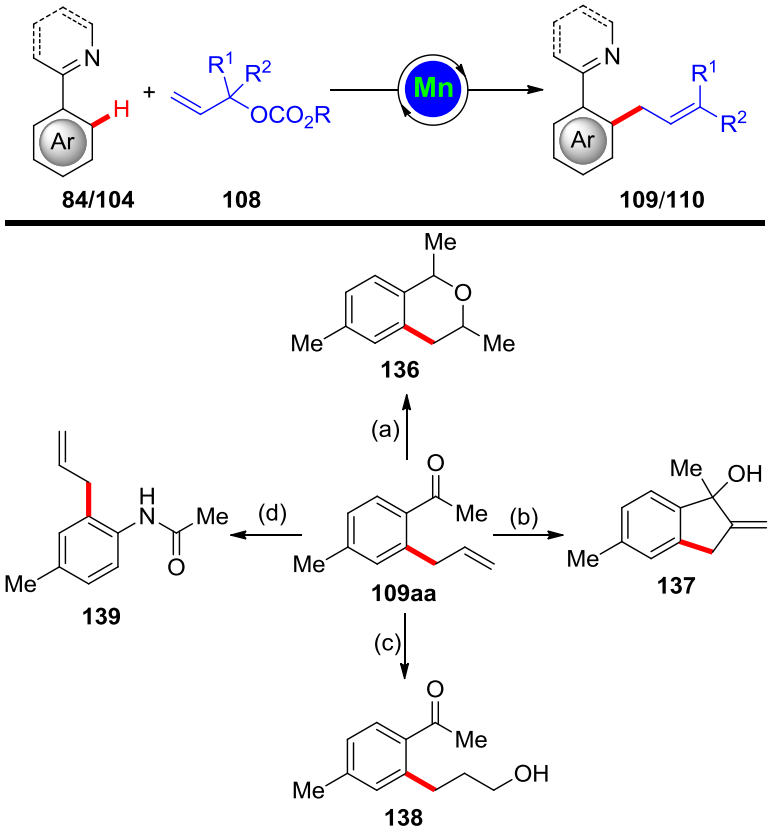
Fourth, the first manganese-catalyzed C–H aminocarbonylation with good yields, highly functional group tolerance and broad substrate scope was developed (Scheme 3.6.4). Moreover, the valuable quinoxalinones can be conveniently accessed from the C–H activation products after removal of the pyridyl group in one step. Mechanistic studies strongly suggested an organometallic C–H activation process, as well as a rate-determining migratory insertion step.[93]



Scheme 3.6.4 Manganese(I)-Catalyzed C–H Amino Carbonylation of Heteroarenes **84** with Isocyanates **106**

Fifth, a versatile manganese(I)-catalyzed allylation of inert C–H bond with allyl carbonates by C–O bond cleavage has been developed (Scheme 3.6.5). A set of valuable functional groups, such as amine, fluoro, chloro, bromo, iodo and nitrile substituents can be tolerated to give the corresponding products. Notably, the reaction was not limited to ketimines **104**, and the biologically relevant heterocycles **84** also proved to be suitable for the C−H allylation.

Moreover, the synthetically useful cycle ether **136**, indanol **137**, alcohol **138** or anilide **139** were accessed from the C–H allylation products. Mechanistic studies strongly supported an organometallic C–H activation process. Importantly, the well-defined cyclometalated complex was prepared, and found to be the key intermediate in the process.[96]



Scheme 3.6.5 Manganese(I)-Catalyzed Substitutive C–H Allylation

4 Experimental Section

4.1 General Remarks

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

Solvents

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

Solvent	**Drying Method**
Water (**H_2O**)	Degassed before its use applying repeated Freeze-Pump-Thaw degassing procedure.
1,2-Dichloroethane (**DCE**) **Dimethylacetamide** (**DMA**)	Dried over CaH_2 for 8 h, degassed and distilled under reduced pressure.
Dichloromethane (**DCM**) **Tetrahydrofuran** (**THF**) **Et_2O**	Purified using a solvent purification system (SPS) from MBRAUN.
Methanol (**MeOH**)	Distilled from Mg
PhMe	Pre-dried over KH followed by distillation from sodium benzophenone ketyl.
1,4-Dioxane ***n*Bu$_2$O**	Dried by distillation from sodium benzophenone ketyl.

Vacuum

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

Melting Points (M. p.)

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

Chromatography

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60F-plates (MACHEREY-NAGEL) with 254 nm fluorescent indicator from MERCK. Plates were visualized under UV-light or developed by treatment with a $KMnO_4$ solution followed by

carefully applying a heat gun. Chromatographic purification of products was accomplished by column chromatography on MERCK silica gel, grade 60 (0.040–0.063 mm and 0.063–0.200 mm).

Gas Chromatograpgy (GC)

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

Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance (NMR) spectroscopy was performed at 300, 400 or 600 MHz (^{1}H NMR), 75 or 125 MHz (^{13}C NMR, APT) and 283 MHz (^{19}F NMR) on BRUKER *AM 250*, VARIAN *Unity-300* and *Inova 500* instruments. Chemical shifts are reported as δ-values in ppm relative to the residual proton peak of the deuterated solvent or its carbon atom, respectively, or the standard tetramethylsilane (TMS) resonance. For characterization of the observed resonance multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), dt (doublet of triplet), or analogue representations. The coupling constants *J* are reported in Hertz (Hz).

Infrared Spectroscopy (IR)

Infrared spectra were recorded on a BRUKER *Alpha-P* ATR-spectrometer. Liquid probes were measured as film and solid samples neat. Analysis of the spectral data was done by using the OPUS 6. Absorption ($\tilde{\nu}$) is given in wave numbers (cm^{-1}). Spectra were recorded in the range of 4000 to 400 cm^{-1}. *In situ*-IR: ReactIR™ 15, METTLER TOLEDO, iC IR 4.3 Software.

Mass Spectrometry (MS)

MS (EI) and HR-MS (EI) were measured on a *Time-of-Flight* mass spectrometer *AccuTOF* from JOEL. ESI-mass spectra were recorded on an *Ion-Trap* mass spectrometer *LCQ* from FINNIGAN or on a *Time-of-Flight* mass spectrometer *microTOF* from BRUKER. ESI-HR-MS spectra were recorded on a BRUKER *APEX IV* or a BRUKER *DALTONIC*, Fourier Transform Ion Cyclotron Resonance (FTICR)] mass spectrometer. The ratios of mass to charge (*m/z*) are indicated, intensities relative to the base peak (I = 100) are written in parentheses.

Reagents

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

Benzamides **9** and [**D**]$_5$**-9a**,[112] **3**,[24] aryl carbamates **101**,[113] [**D**]$_5$**-101a**,[113-114] ketimines

105,[115] $[D]_1$-**105b**,[115b, 116] $[D]_5$-**105b**,[115b, 117] indoles **83**,[118] $[D]_1$-**83a**,[118a] **129a**,[119] **129b**,[120] **110b**–**110o**,[91a, 121] **114b**–**114d**,[122] **114e**.[123]

4.2 General Procedures

General Procedure A: Versatile Ruthenium(II)-Catalyzed C–H Cyanations of Benzamides 50.

Benzamides **50** (0.50 mmol), *N*-cyano-*N*-phenyl-4-methylbenzenesulfonamide (**13**) (272 mg, 1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.4 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), NaOAc (8.2 mg, 20 mol %) and DCE (2.0 mL) were placed in a 20 mL sealed tube under N_2 and stirred at 120 ℃ for 24 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel to afford the desired products **101**.

General Procedure B: *ortho*-Selective Ruthenium(II)-Catalyzed C(sp^2)–H Oxygenations of Carbamates 102.

$[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), carbamate **102** (0.50 mmol), $PhI(TFA)_2$ (430 mg, 1.0 mmol) and DCE (2.0 mL) were placed into a 25 mL Schlenk tube equipped with a septum under N_2. The tube was then placed into an oil bath and the reaction mixture was stirred at 50–80 ℃ for 3–24 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel to afford the desired products **103**.

General Procedure C: *para*-Selective Ruthenium(II)-Catalyzed C(sp^2)–H Oxygenations of Anisoles 115.

$[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), **115** (0.50 mmol), $PhI(TFA)_2$ (240 mg, 0.55 mmol) and DCE (2.0 mL) were placed into a 25 mL Schlenk tube equipped with a septum under N_2. The reaction mixture was stirred at 80 ℃ for 3 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel to afford the desired products **116**.

General Procedure D: Manganese-Catalyzed Synthesis of *cis*-*β*-Amino Acid Esters through Organometallic C–H Activation

Ketimines **104** (0.5 mmol), acrylates **38** (1.0 mmol), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %) and DCE or toluene (1.0 mL) were placed in a 25 mL Schlenk tube under N_2. The mixture was stirred at 120 ℃ for 18 h. At ambient temperature, the reaction mixture was transferred into a round flask with EtOAc and concentrated under reduced pressure, purified by column

chromatography on silica gel to afford the desired products **105**.

General Procedure E: Manganese(I)-Catalyzed C–H Aminocarbonylation of Heteroarenes 84.

Heteroarenes **84** (0.50 mmol), isocyanates **106** (0.55 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %) and Et_2O or nBu_2O (1.0 mL) were placed in a 20 mL sealed tube or 25 mL Schlenk tube under N_2. The mixture was stirred at 100 ℃ for 16 h. At ambient temperature, the reaction mixture was transferred into a round flask with CH_2Cl_2 (50 mL) and concentrated under reduced pressure and purified by column chromatography on silica gel using a mixture of *n*-hexane, EtOAc, CH_2Cl_2 and Et_3N to afford the desired products **107**.

General Procedure F: Manganese(I)-Catalyzed C–H Allylation of Ketimines 104.

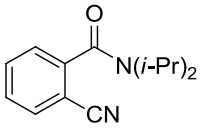
Ketimines **104** (0.5 mmol), allyl carbonates **108** (1.5 mmol, 3.0 equiv), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %), NaOAc (8.2 mg, 20 mol %) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2. The mixture was stirred at 100 ℃ for 14 h. At ambient temperature, the reaction mixture was diluted with Et_2O (5 mL). Then, HCl (5 mL, 1 M) was added, the mixture was vigorously stirred at ambient temperature for 20 min, and the resulting mixture was extracted with Et_2O (3 × 10 mL). The combined organic layer was washed with brine (10 mL), and then dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel afforded the desired products **109**.

General Procedure G: Manganese-Catalyzed C–H Allylation of Heteroarenes 84 or 123.

Heteroarenes **84** or **123** (0.5 mmol), allyl carbonates **108** (1.0 mmol, 2.0 equiv), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %), NaOAc (8.2 mg, 20 mol %) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2. The mixture was stirred at 100 ℃ for 14 h. At ambient temperature, the reaction mixture was transferred into a round flask with EtOAc and concentrated under reduced pressure, purified by column chromatography on silica gel to afford the desired products **110** or **131.**

4.3 Versatile Ruthenium(II)-Catalyzed C–H Cyanations of Benzamides

Characterization Data of Products 101



2-Cyano-*N*,*N*-diisopropylbenzamide (101a): The representative procedure was followed using *N*,*N*-diisopropylbenzamide (**50a**) (103 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→2/1) yielded **101a** (97 mg, 84%) as a colorless solid.

M.p. = 109–111 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.62 (ddd, J = 7.7, 1.3, 0.6 Hz, 1H), 7.57 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 7.40 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 7.29 (ddd, J = 7.7, 1.3, 0.6 Hz, 1H), 3.52 (hept, J = 6.7 Hz, 2H), 1.56 (d, J = 6.7 Hz, 6H), 1.15 (s_{br}, 6H).

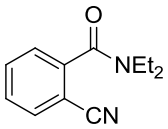
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.7 (C_q), 142.4 (C_q), 133.0 (CH), 132.8 (CH), 128.5 (CH), 125.7 (CH), 116.8 (C_q), 108.9 (C_q), 51.4 (CH), 46.1 (CH), 20.6 (CH_3), 20.2 (CH_3).

IR (neat): 2964, 2225, 1625, 1437, 1341, 1031, 788, 552 cm^{-1}.

MS (EI) *m/z* (relative intensity): 230 (5) [M^+], 187 (24), 173 (25), 130 (100), 102 (36).

HR-MS (EI) *m/z* calcd for $C_{14}H_{18}N_2O$ [M^+] 230.1419, found 230.1424.

The spectral data are in accordance with those reported in the literature.[124]



2-Cyano-*N*,*N*-diethylbenzamide (101b): The representative procedure was followed using *N*,*N*-diethylbenzamide (**50b**) (89 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→2/1) yielded **101b** (75 mg, 74%) as a colorless oil.

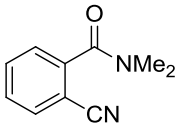
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.63 (ddd, J = 7.7, 1.3, 0.6 Hz, 1H), 7.58 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 7.42 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 7.35 (ddd, J = 7.7, 1.3, 0.6 Hz, 1H), 3.53 (q, J = 7.1 Hz, 2H), 3.12 (q, J = 7.1 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H), 1.03 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.0 (C_q), 140.9 (C_q), 132.8 (CH), 132.7 (CH), 129.0 (CH), 126.6 (CH), 116.5 (C_q), 109.6 (C_q), 43.0 (CH_2), 39.1 (CH_2), 13.9 (CH_3), 12.4 (CH_3).

IR (neat): 2976, 2228, 1628, 1429, 1292, 1080, 762, 546 cm^{-1}.

MS (EI) *m/z* (relative intensity): 202 (20) [M^+], 173 (15), 130 (100), 102 (40).

HR-MS (ESI) *m/z* calcd for $C_{12}H_{14}N_2NaO$ [M + Na^+] 225.1004, found 225.0998.



2-Cyano-*N*,*N*-dimethylbenzamide (101c): The representative procedure was followed using *N*,*N*-dimethylbenzamide (**50c**) (75 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→1/1) yielded **101c** (58 mg, 67%) as a colorless oil.

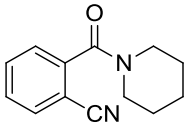
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.66–7.57 (m, 2H), 7.47–7.39 (m, 2H), 3.10 (s, 3H), 2.88 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.5 (C_q), 140.3 (C_q), 133.0 (CH), 132.7 (CH), 129.4 (CH), 127.4 (CH), 116.7 (C_q), 109.7 (C_q), 38.5 (CH_3), 34.9 (CH_3).

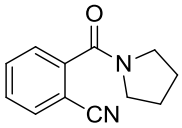
IR (neat): 2933, 2228, 1632, 1396, 1069, 760, 542 cm^{-1}.

MS (EI) *m/z* (relative intensity): 174 (35) [M^+], 130 (100), 102 (65), 75 (23).

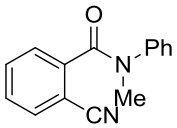
HR-MS (ESI) *m/z* calcd for $C_{10}H_{11}N_2O$ [M + H^+] 175.0871, found 175.0866.
The spectral data are in accordance with those reported in the literature.[125]



2-(Piperidine-1-carbonyl)benzonitrile (**101d**): The representative procedure was followed using phenyl(piperidin-1-yl)methanone (**50d**) (95 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→2/1) yielded **101d** (81 mg, 76%) as a colorless solid.
M.p. = 108–110 ℃.
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.7 Hz, 1H), 7.59 (dd, *J* = 7.7, 7.6 Hz, 1H), 7.43 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 3.72–3.69 (m, 2H), 3.18 (t, *J* = 5.6 Hz, 2H), 1.64–1.62 (m, 4H), 1.54–1.48 (m, 2H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.0 (C_q), 140.5 (C_q), 132.9 (CH), 132.8 (CH), 129.2 (CH), 127.1 (CH), 116.8 (C_q), 109.6 (C_q), 48.1 (CH_2), 42.9 (CH_2), 26.2 (CH_2), 25.2 (CH_2), 24.2 (CH_2).
IR (neat): 2928, 2228, 1621, 1437, 1292, 1254, 779, 554 cm^{-1}.
MS (EI) *m/z* (relative intensity): 214 (45) [M^+], 213 (100), 130 (100), 102 (50), 84 (23).
HR-MS (ESI) *m/z* calcd for $C_{13}H_{15}N_2O$ [M + H^+] 215.1184, found 215.1179.



2-(Pyrrolidine-1-carbonyl)benzonitrile (101e): The representative procedure was followed using phenyl(pyrrolidin-1-yl)methanone (**50e**) (88 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→1/1) yielded **101e** (67 mg, 66%) as a colorless oil.
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.68–7.52 (m, 2H), 7.46–7.40 (m, 2H), 3.60 (t, *J* = 6.8 Hz, 2H), 3.22 (t, *J* = 6.4 Hz, 2H), 1.96–1.79 (m, 4H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 141.2 (C_q), 132.9 (CH), 132.8 (CH), 129.4 (CH), 127.1 (CH), 116.9 (C_q), 109.5 (C_q), 48.3 (CH_2), 45.8 (CH_2), 25.9 (CH_2), 24.1 (CH_2).
IR (neat): 2973, 2879, 2228, 1623, 1594, 1448, 760, 650 cm^{-1}.
MS (EI) *m/z* (relative intensity): 200 (55) [M^+], 171 (35), 130 (100), 102 (65), 70 (50).
HR-MS (EI) *m/z* calcd for $C_{12}H_{12}N_2O$ [M^+] 200.0950, found 200.0951.



2-Cyano-*N*-methyl-*N*-phenylbenzamide (101f): The representative procedure was followed

using *N*-methyl-*N*-phenylbenzamide (**50f**) (106 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→2/1) yielded **101f** (63 mg, 53%) as a colorless solid.

M.p. = 75–77 °C.

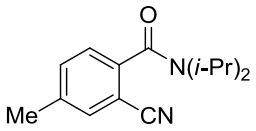
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.48–7.08 (m, 9H), 3.49 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.4 (C_q), 142.8 (C_q), 140.8 (C_q), 132.7 (CH), 132.0 (CH), 129.2 (CH), 129.1 (CH), 128.4 (CH), 127.3 (CH), 127.0 (CH), 117.1 (C_q), 110.5 (C_q), 37.7 (CH_3).

IR (neat): 3053, 2227, 1632, 1592, 1495, 1380, 769, 699, 553 cm^{-1}.

MS (EI) *m/z* (relative intensity): 236 (35) [M^+], 143 (22), 130 (100), 102 (35), 77 (18).

HR-MS (EI) *m/z* calcd for $C_{15}H_{12}N_2O$ [M^+] 236.0950, found 236.0946.



2-Cyano-*N*,*N*-diisopropyl-4-methylbenzamide (101g): The representative procedure was followed using *N*,*N*-diisopropyl-4-methylbenzamide (**50g**) (110 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→2/1) yielded **101g** (98 mg, 80%) as a colorless solid.

M.p. = 92–94 °C.

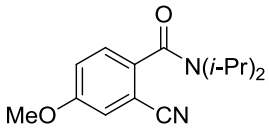
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42 (s, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 1H), 3.52 (hept, *J* = 6.8 Hz, 2H), 2.34 (s, 3H), 1.52 (d, *J* = 6.8 Hz, 6H), 1.12 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.0 (C_q), 139.7 (C_q), 138.8 (C_q), 133.7 (CH), 133.0 (CH), 125.6 (CH), 116.9 (C_q), 108.8 (C_q), 51.3 (CH), 46.0 (CH), 20.8 (CH_3), 20.6 (CH_3), 20.2 (CH_3).

IR (neat): 2970, 1617, 1440, 1342, 1037, 822, 597 cm^{-1}.

MS (EI) *m/z* (relative intensity): 244 (10) [M^+], 201 (50), 187 (22), 144 (100), 116 (20), 89 (18).

HR-MS (EI) *m/z* calcd for $C_{15}H_{20}N_2O$ [M^+] 244.1576, found 244.1571.



2-Cyano-*N*,*N*-diisopropyl-4-methoxybenzamide (101h): The representative procedure was followed using *N*,*N*-diisopropyl-4-methoxybenzamide (**50h**) (118 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→1/1) yielded **101h** (117 mg, 90%) as a colorless solid.

M.p. = 118–120 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 2.6 Hz, 1H), 7.07 (dd, *J* = 8.0, 2.6 Hz, 1H), 3.78 (s, 3H), 3.53 (s_{br}, 2H), 1.50 (s_{br}, 6H), 1.12 (s_{br}, 6H).

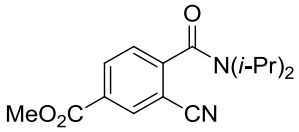
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.8 (C_q), 159.0 (C_q), 134.9 (C_q), 127.2 (CH), 119.2 (CH),

117.3 (CH), 116.7 (C_q), 109.9 (C_q), 55.6 (CH_3), 51.3 (CH), 46.0 (CH), 20.4 (CH_3), 20.3 (CH_3).

IR (neat): 2978, 2228, 1622, 1441, 1372, 1248, 1026, 848, 593 cm^{-1}.

MS (EI) *m/z* (relative intensity): 260 (10) [M^+], 217 (50), 160 (100), 117 (15), 77 (10).

HR-MS (EI) *m/z* calcd for $C_{15}H_{20}N_2O_2$ [M^+] 260.1525, found 260.1532.



Methyl 3-cyano-4-(diisopropylcarbamoyl)benzoate (101i): The representative procedure was followed using methyl 4-(diisopropylcarbamoyl)benzoate (**50i**) (132 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→2/1) yielded **101i** (94 mg, 65%) as a colorless solid.

M.p. = 81–83 ℃.

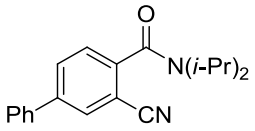
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 1.6 Hz, 1H), 8.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 3.89 (s, 3H), 3.52 (hept, *J* = 6.7 Hz, 1H), 3.44 (hept, *J* = 6.7 Hz, 1H), 1.52 (d, *J* = 6.8 Hz, 6H), 1.13 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 164.5 (C_q), 145.8 (C_q), 134.0 (CH), 133.9 (CH), 130.6 (C_q), 126.0 (CH), 115.9 (C_q), 109.5 (C_q), 52.6 (CH_3), 51.5 (CH), 46.3 (CH), 20.5 (CH_3), 20.1 (CH_3).

IR (neat): 2958, 2231, 1719, 1635, 1433, 1295, 1261, 1107, 769, 555 cm^{-1}.

MS (EI) *m/z* (relative intensity): 288 (10) [M^+], 245 (65), 231 (50), 188 (100), 101 (10).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{21}N_2O_3$ [M + H^+] 289.1552, found 289.1547.



3-Cyano-*N*,*N*-diisopropyl-[1,1'-biphenyl]-4-carboxamide (101j): The representative procedure was followed using *N*,*N*-diisopropyl-[1,1'-biphenyl]-4-carboxamide **(50j)** (141 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc/Et_3N: 200/10/1→200/60/1) yielded **101j** (140 mg, 92%) as a colorless solid.

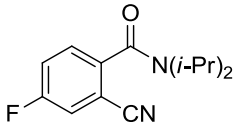
M.p. = 114–116 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 1.8 Hz, 1H), 7.77 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.53–7.34 (m, 6H), 3.64 (hept, *J* = 6.7 Hz, 1H), 3.56 (hept, *J* = 6.7 Hz, 1H), 1.58 (d, *J* = 6.8 Hz, 6H), 1.18 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 141.7 (C_q), 140.8 (C_q), 138.0 (C_q), 131.5 (CH), 131.1 (CH), 129.0 (CH), 128.4 (CH), 126.8 (CH), 126.2 (CH), 116.8 (C_q), 109.5 (C_q), 51.4 (CH), 46.1 (CH), 20.6 (CH_3), 20.2 (CH_3).

IR (neat): 2970, 1627, 1442, 1342, 1034, 753, 695 cm^{-1}.

MS (EI) *m/z* (relative intensity): 306 (10) [M^+], 263 (60), 206 (100), 151 (15).
HR-MS (EI) *m/z* calcd for $C_{20}H_{22}N_2O$ [M^+] 306.1732, found 306.1730.



2-Cyano-4-fluoro-*N*,*N*-diisopropylbenzamide (101k): The representative procedure was followed using 4-fluoro-*N*,*N*-diisopropylbenzamide **(50k)** (112 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **101k** (101 mg, 81%) as a colorless solid.

M.p. = 129–131 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.37–7.29 (m, 3H), 3.54 (hept, J = 6.7 Hz, 2H), 1.55 (d, J = 6.7 Hz, 6H), 1.17 (s_{br}, 6H).

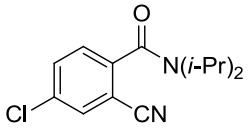
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 161.3 ($^1J_{C–F}$ = 256 Hz, C_q), 138.9 ($^4J_{C–F}$ = 4 Hz, C_q), 128.0 ($^3J_{C–F}$ = 8 Hz, CH), 120.7 ($^2J_{C–F}$ = 21 Hz, CH), 119.7 ($^2J_{C–F}$ = 24 Hz, CH), 115.6 ($^4J_{C–F}$ = 3 Hz, C_q), 110.7 ($^3J_{C–F}$ = 9 Hz, C_q), 51.6 (CH), 46.4 (CH), 20.8 (CH_3), 20.3 (CH_3).

^{19}F-NMR (283 MHz, $CDCl_3$): δ = –(110.0–110.1) (m).

IR (neat): 2973, 2231, 1617, 1443, 1372, 1342, 1156, 1032, 829, 597 cm^{-1}.

MS (EI) *m/z* (relative intensity): 248 (5) [M^+], 205 (35), 191 (40), 148 (100), 120 (25), 58 (17).

HR-MS (EI) *m/z* calcd for $C_{14}H_{17}FN_2O$ [M^+] 248.1325, found 248.1323.



4-Chloro-2-cyano-*N*,*N*-diisopropylbenzamide (101l): The representative procedure was followed using 4-chloro-*N*,*N*-diisopropylbenzamide **(50l)** (120 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc/Et_3N: 100/10/1→100/20/1) yielded **101l** (91 mg, 68%) as a colorless solid.

M.p. = 131–133 ℃.

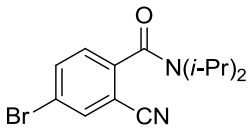
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, J = 1.6 Hz, 1H), 7.57 (dd, J = 8.2, 1.6 Hz, 1H), 7.28 (d, J = 8.2 Hz, 1H), 3.53 (hept, J = 6.0 Hz, 2H), 1.55 (d, J = 6.0 Hz, 6H), 1.17 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.7 (C_q), 140.7 (C_q), 134.5 (C_q), 133.3 (CH), 132.4 (CH), 127.2 (CH), 115.5 (C_q), 110.7 (C_q), 51.6 (CH), 46.4 (CH), 20.8 (CH_3), 20.3 (CH_3).

IR (neat): 2981, 2231, 1626, 1442, 1339, 1033, 847, 589 cm^{-1}.

MS (EI) *m/z* (relative intensity): 264 (5) [M^+], 221 (48), 207 (45), 164 (100), 136 (20), 100 (10).

HR-MS (EI) *m/z* calcd for $C_{14}H_{17}ClN_2O$ [M^+] 264.1029, found 264.1028.



4-Bromo-2-cyano-*N*,*N*-diisopropylbenzamide (101m): The representative procedure was followed using 4-bromo-*N*,*N*-diisopropylbenzamide (**50m**) (142 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc/Et_3N: 100/10/1→100/20/1) yielded **101m** (110 mg, 71%) as a colorless solid.

M.p. = 121–123 ℃.

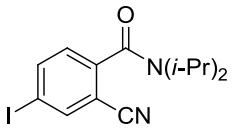
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 2.0 Hz, 1H), 7.72 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 3.53 (hept, *J* = 6.7 Hz, 2H), 1.55 (d, *J* = 6.7 Hz, 6H), 1.16 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 141.2 (C_q), 136.3 (CH), 135.3 (CH), 127.3 (CH), 122.1 (C_q), 115.5 (C_q), 110.9 (C_q), 51.6 (CH), 46.4 (CH), 20.7 (CH_3), 20.3 (CH_3).

IR (neat): 2966, 2218, 1630, 1443, 1344, 1037, 850, 554 cm^{-1}.

MS (EI) *m/z* (relative intensity): 310 (10) [M^+] (^{81}Br), 308 (10) [M^+] (^{79}Br), 267 (55) (^{81}Br), 265 (55) (^{79}Br), 210 (100) (^{81}Br), 208 (100) (^{79}Br), 182 (20) (^{81}Br), 180 (20) (^{79}Br).

HR-MS (EI) *m/z* calcd for $C_{14}H_{17}BrN_2O$ [M^+] 308.0524, found 308.0529.



2-Cyano-4-iodo-*N*,*N*-diisopropylbenzamide (101n): The representative procedure was followed using 4-iodo-*N*,*N*-diisopropylbenzamide (**50n**) (166 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/CH_2Cl_2: 1/1) yielded **101n** (162 mg, 91%) as a colorless solid.

M.p. = 157–159 ℃.

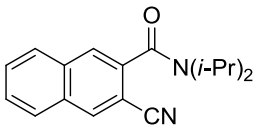
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 1.6 Hz, 1H), 7.88 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 3.50 (hept, *J* = 6.6 Hz, 2H), 1.50 (d, *J* = 6.6 Hz, 6H), 1.12 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.8 (C_q), 141.9 (CH), 141.5 (C_q), 140.8 (CH), 127.1 (CH), 115.1 (C_q), 110.8 (C_q), 92.8 (C_q), 51.4 (CH), 46.2 (CH), 20.6 (CH_3), 20.1 (CH_3).

IR (neat): 2966, 2223, 1631, 1439, 1338, 1034, 825, 557 cm^{-1}.

MS (EI) *m/z* (relative intensity): 356 (15) [M^+], 313 (80), 299 (40), 256 (100), 227 (12), 101 (17).

HR-MS (EI) *m/z* calcd for $C_{14}H_{17}IN_2O$ [M^+] 356.0386, found 356.0388.



3-Cyano-*N*,*N*-diisopropyl-2-naphthamide (101o): The representative procedure was followed using *N*,*N*-diisopropyl-2-naphthamide (**50o**) (128 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→2/1) yielded **101o** (109 mg, 78%) as a colorless solid.

M.p. = 133–135 ℃.

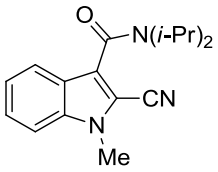
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.20 (s, 1H), 7.83 (d, J = 8.5 Hz, 2H), 7.74 (s, 1H), 7.64–7.53 (m, 2H), 3.36–3.54 (m, 2H), 1.60 (d, J = 6.0 Hz, 6H), 1.16 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.0 (C_q), 136.5 (C_q), 135.1 (CH), 134.1 (C_q), 131.4 (C_q), 129.6 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 124.9 (CH), 117.1 (C_q), 106.7 (C_q), 51.4 (CH), 46.1 (CH), 20.5 (CH_3), 20.3 (CH_3).

IR (neat): 2972, 2229, 1617, 1474, 1342, 1152, 901, 756, 481 cm^{-1}.

MS (EI) *m/z* (relative intensity): 280 (20) [M^+], 237 (45), 180 (100), 152 (40).

HR-MS (EI) *m/z* calcd for $C_{18}H_{20}N_2O$ [M^+] 280.1576, found 280.1576.



2-Cyano-*N*,*N*-diisopropyl-1-methyl-1*H*-indole-3-carboxamide (101p): The representative procedure was followed using *N*,*N*-diisopropyl-1-methyl-1*H*-indole-3-carboxamide (**50p**) (129 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→10/3) yielded **101p** (122 mg, 86%) as a colorless solid.

M.p. = 202–204 ℃.

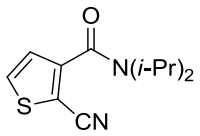
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, J = 8.1 Hz, 1H), 7.38 (dd, J = 8.3, 6.7 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 7.20 (dd, J = 8.1, 6.7 Hz, 1H), 3.83 (s, 3H), 3.73 (hept, J = 6.7 Hz, 2H), 1.39 (s_{br}, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.2 (C_q), 137.2 (C_q), 126.4 (CH), 124.0 (C_q), 123.9 (C_q), 121.9 (CH), 120.9 (CH), 112.2 (C_q), 110.2 (CH), 107.1 (C_q), 48.8 (CH), 31.5 (CH_3), 20.9 (CH_3).

IR (neat): 2979, 2224, 1616, 1536, 1371, 1311, 1045, 745 cm^{-1}.

MS (EI) *m/z* (relative intensity): 283 (10) [M^+], 240 (15), 183 (100), 128 (10).

HR-MS (EI) *m/z* calcd for $C_{17}H_{21}N_3O$ [M^+] 283.1685, found 283.1679.



2-Cyano-*N*,*N*-diisopropylthiophene-3-carboxamide (101q): The representative procedure was followed using *N*,*N*-diisopropylthiophene-3-carboxamide (**50q**) (106 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→3/1) yielded **101q** (91 mg, 77%) as a colorless solid.

M.p. = 76–78 ℃.

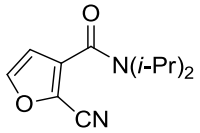
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.58 (d, J = 5.0 Hz, 1H), 7.05 (d, J = 5.0 Hz, 1H), 3.59 (s_{br}, 2H), 1.52 (s_{br}, 6H), 1.20 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 163.0 (C_q), 148.3 (C_q), 132.8 (CH), 126.1 (CH), 112.7 (C_q), 106.2 (C_q), 51.4 (CH), 46.4 (CH), 20.7 (CH_3), 20.5 (CH_3).

IR (neat): 3072, 2221, 1629, 1444, 1323, 1203, 1038, 776 cm^{-1}.

MS (EI) *m/z* (relative intensity): 236 (5) [M^+], 221 (15), 193 (25), 179 (45), 136 (100), 58 (8).

HR-MS (EI) *m/z* calcd for $C_{12}H_{16}N_2OS$ [M^+] 236.0983, found 236.0981.



2-Cyano-*N*,*N*-diisopropylfuran-3-carboxamide (101r): The representative procedure was followed using *N*,*N*-diisopropylfuran-3-carboxamide (**50r**) (98 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **101r** (89 mg, 81%) as a colorless oil.

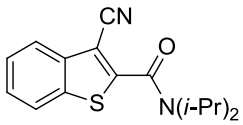
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, J = 1.9 Hz, 1H), 6.50 (d, J = 1.9 Hz, 1H), 3.66 (s_{br}, 2H), 1.29 (s_{br}, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.6 (C_q), 146.9 (CH), 133.8 (C_q), 123.2 (C_q), 110.7 (CH), 110.2 (C_q), 51.3 (CH), 46.5 (CH), 20.6 (CH_3).

IR (neat): 2973, 2229, 1628, 1484, 1372, 1336, 1026, 1019, 754 cm^{-1}.

MS (EI) *m/z* (relative intensity): 220 (10) [M^+], 205 (20), 177 (23), 163 (70), 120 (100), 64 (8).

HR-MS (EI) *m/z* calcd for $C_{12}H_{16}N_2O_2$ [M^+] 220.1212, found 220.1207.



3-Cyano-*N*,*N*-diisopropylbenzo[*b*]thiophene-2-carboxamide (101s): The representative procedure was followed using *N*,*N*-diisopropylbenzo[*b*]thiophene-2-carboxamide (**50s**) (131 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/CH_2Cl_2: 1/1) yielded **101s** (129 mg, 90%) as a colorless solid.

M.p. = 134–136 °C.

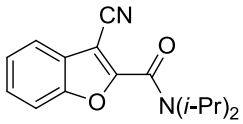
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.85 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.55–7.45 (m, 2H), 3.72 (s_{br}, 2H), 1.40 (s_{br}, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.5 (C_q), 149.2 (C_q), 137.3 (C_q), 136.8 (C_q), 126.7 (CH), 126.4 (CH), 122.8 (CH), 122.7 (CH), 113.0 (C_q), 104.0 (C_q), 20.6 (CH_3). $\underline{C}H(CH_3)_2$ is not detectable.

IR (neat): 2969, 2224, 1633, 1452, 1343, 1316, 1037, 751, 611 cm^{-1}.

MS (EI) *m/z* (relative intensity): 286 (8) [M^+], 271 (10), 243 (15), 186 (75), 158 (13), 114 (15), 43 (100).

HR-MS (EI) *m/z* calcd for $C_{16}H_{18}N_2OS$ [M^+] 286.1140, found 286.1149.



3-Cyano-*N*,*N*-diisopropylbenzofuran-2-carboxamide (101t): The representative procedure was followed using *N*,*N*-diisopropylbenzofuran-2-carboxamide (**50t**) (123 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc/Et_3N: 100/5/1→100/20/1) yielded **101t** (105 mg, 78%) as a colorless solid.

M.p. = 99–101 °C.

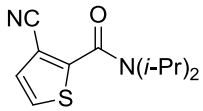
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.70–7.67 (m, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.48–7.36 (m, 2H), 3.80 (s_{br}, 2H), 1.40 (s_{br}, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 157.6 (C_q), 156.9 (C_q), 153.1 (C_q), 127.5 (CH), 125.2 (CH), 125.1 (C_q), 120.5 (CH), 112.2 (CH), 111.7 (C_q), 94.1 (C_q), 50.7 (CH), 47.4 (CH), 20.5 (CH_3).

IR (neat): 2972, 2233, 1626, 1440, 1321, 1181, 1036, 738 cm^{-1}.

MS (EI) *m/z* (relative intensity): 270 (10) [M^+], 227 (30), 213 (45), 170 (100), 114 (30), 43 (45).

HR-MS (EI) *m/z* calcd for $C_{16}H_{18}N_2O_2$ [M^+] 270.1368, found 270.1368.



3-Cyano-*N*,*N*-diisopropylthiophene-2-carboxamide (101u): The representative procedure was followed using *N*,*N*-diisopropylthiophene-2-carboxamide (**50u**) (106 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→*5*/1) yielded **101u** (100 mg, 85%) as a colorless solid.

M.p. = 99–101 °C.

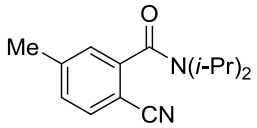
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 5.2 Hz, 1H), 7.16 (d, *J* = 5.2 Hz, 1H), 3.71–3.62 (m, 2H), 1.36 (s_{br}, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.5 (C_q), 148.1 (C_q), 128.4 (CH), 126.3 (CH), 113.8 (C_q), 108.2 (C_q), 49.6 (CH), 20.6 (CH_3).

IR (neat): 2980, 2227, 1627, 1455, 1328, 1207, 1029, 766 cm^{-1}.

MS (EI) *m/z* (relative intensity): 236 (5) [M^+], 221 (18), 193 (23), 179 (50), 136 (100), 58 (10).

HR-MS (EI) *m/z* calcd for $C_{12}H_{16}N_2OS$ [M^+] 236.0983, found 236.0982.



2-Cyano-*N*,*N*-diisopropyl-5-methylbenzamide (101v): The representative procedure was followed using *N*,*N*-diisopropyl-3-methylbenzamide (**50v**) (110 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→3/1) yielded **101v** (95 mg, 78%) as a colorless solid.

M.p. = 147–149 ℃.

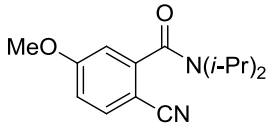
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.12 (s, 1H), 3.57 (hept, *J* = 7.0 Hz, 1H), 3.54 (hept, *J* = 7.0 Hz, 1H), 2.40 (s, 3H), 1.57 (d, *J* = 6.7 Hz, 6H), 1.17 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.0 (C_q), 144.2 (C_q), 142.4 (C_q), 132.7 (CH), 129.3 (CH), 126.3 (CH), 117.1 (C_q), 105.9 (C_q), 51.4 (CH), 46.1 (CH), 21.8 (CH_3), 20.7 (CH_3), 20.3 (CH_3).

IR (neat): 2978, 2228, 1628, 1443, 1338, 1038, 843, 550 cm^{-1}.

MS (EI) *m/z* (relative intensity): 244 (20) [M^+], 229 (20), 201 (60), 187 (35), 144 (100), 116 (23), 89 (17).

HR-MS (EI) *m/z* calcd for $C_{15}H_{20}N_2O$ [M^+] 244.1576, found 244.1566.



The representative procedure was followed using *N*,*N*-diisopropyl-3-methoxybenzamide (**50w**) (118 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→1/1) yielded **101w** (45 mg, 34%) and **101w'** (72 mg, 55%) as colorless solids.

2-Cyano-*N*,*N*-diisopropyl-3-methoxybenzamide (101w):

M.p. = 163–165 ℃.

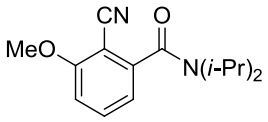
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.7 Hz, 1H), 6.89 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H), 3.56 (hept, *J* = 6.8 Hz, 1H), 3.52 (hept, *J* = 6.8 Hz, 1H), 1.54 (d, *J* = 6.8 Hz, 6H), 1.15 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.6 (C_q), 162.9 (C_q), 144.3 (C_q), 134.7 (CH), 117.2 (C_q), 114.4 (CH), 111.4 (CH), 100.5 (C_q), 55.7 (CH_3), 51.4 (CH), 46.2 (CH), 20.7 (CH_3), 20.2 (CH_3).

IR (neat): 2964, 2224, 1630, 1457, 1337, 1242, 1027, 850, 680 cm^{-1}.

MS (EI) *m/z* (relative intensity): 260 (20) [M^+], 217 (50), 203 (35), 160 (100), 117 (14).

HR-MS (EI) *m/z* calcd for $C_{15}H_{20}N_2O_2$ [M^+] 260.1525, found 260.1523.



2-Cyano-*N*,*N*-diisopropyl-5-methoxybenzamide (101w'):

M.p. = 165–167 ℃.

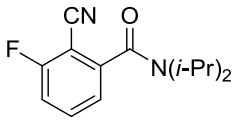
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.49 (dd, J = 8.6, 7.6 Hz, 1H), 6.90 (d, J = 8.6 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 3.88 (s, 3H), 3.56 (hept, J = 6.8 Hz, 1H), 3.49 (hept, J = 6.8 Hz, 1H), 1.52 (d, J = 6.8 Hz, 6H), 1.12 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.5 (C_q), 161.4 (C_q), 143.8 (C_q), 134.5 (CH), 117.2 (CH), 114.3 (C_q), 110.7 (CH), 98.3 (C_q), 56.1 (CH_3), 51.3 (CH), 46.0 (CH), 20.5 (CH_3), 20.1 (CH_3).

IR (neat): 2971, 2227, 1625, 1461, 1342, 1276, 1030, 800, 605 cm^{-1}.

MS (EI) *m/z* (relative intensity): 260 (13) [M^+], 217 (50), 203 (25), 160 (100), 117 (18).

HR-MS (EI) *m/z* calcd for $C_{15}H_{20}N_2O_2$ [M^+] 260.1525, found 260.1523.



2-Cyano-3-fluoro-*N*,*N*-diisopropylbenzamide (101x): The representative procedure was followed using 3-fluoro-*N*,*N*-diisopropylbenzamide (**50x**) (112 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→1/1) yielded **101x** (100 mg, 80%) as a colorless solid.

M.p. = 148–150 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.58 (ddd, J = 8.5, 7.6, 5.4 Hz, 1H), 7.15 (td, J = 8.5, 1.0 Hz, 1H), 7.08 (dd, J = 7.6, 0.9 Hz, 1H), 3.52 (hept, J = 6.7 Hz, 2H), 1.52 (d, J = 6.7 Hz, 6H), 1.14 (s_{br}, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.3 ($^4J_{C–F}$ = 2 Hz, C_q), 163.1 ($^1J_{C–F}$ = 261 Hz, C_q), 143.9 (C_q), 135.2 ($^3J_{C–F}$ = 9 Hz, CH), 121.3 ($^4J_{C–F}$ = 3 Hz, CH), 115.8 ($^2J_{C–F}$ = 19 Hz, CH), 111.9 (C_q), 98.5 ($^2J_{C–F}$ = 16 Hz, (C_q), 51.5 (CH), 46.2 (CH), 20.5 (CH_3), 20.1 (CH_3).

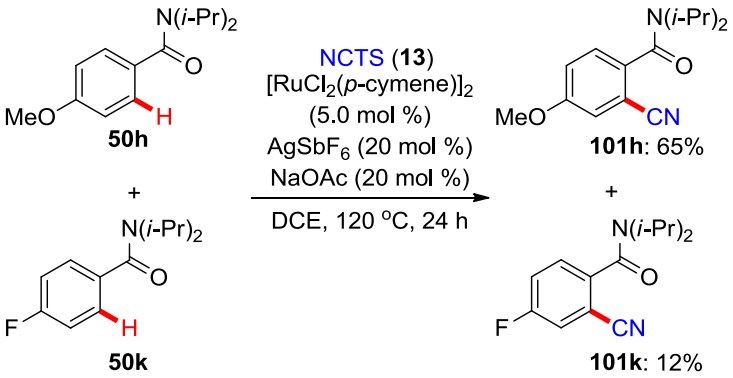
^{19}F-NMR (283 MHz, $CDCl_3$): δ = –105.0 (q).

IR (neat): 2980, 1629, 1442, 1344, 1256, 809, 583 cm^{-1}.

MS (EI) *m/z* (relative intensity): 248 (8) [M^+], 205 (50), 191 (70), 148 (100), 120 (28).

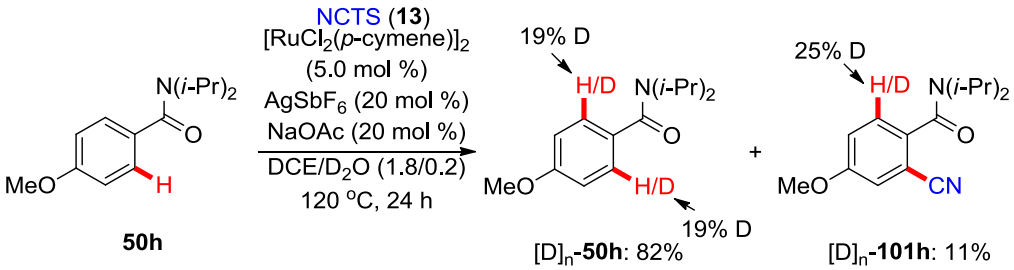
HR-MS (EI) *m/z* calcd for $C_{14}H_{17}FN_2O$ [M^+] 248.1325, found 248.1333.

Intermolecular Competition Experiment between 50h and 50k

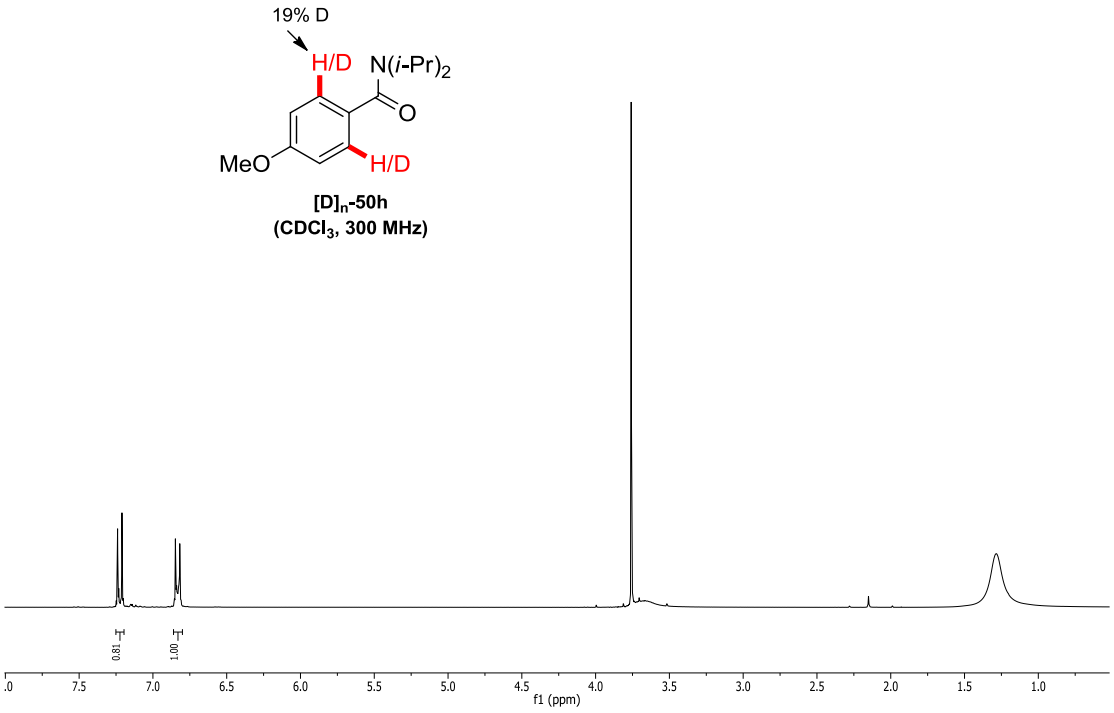


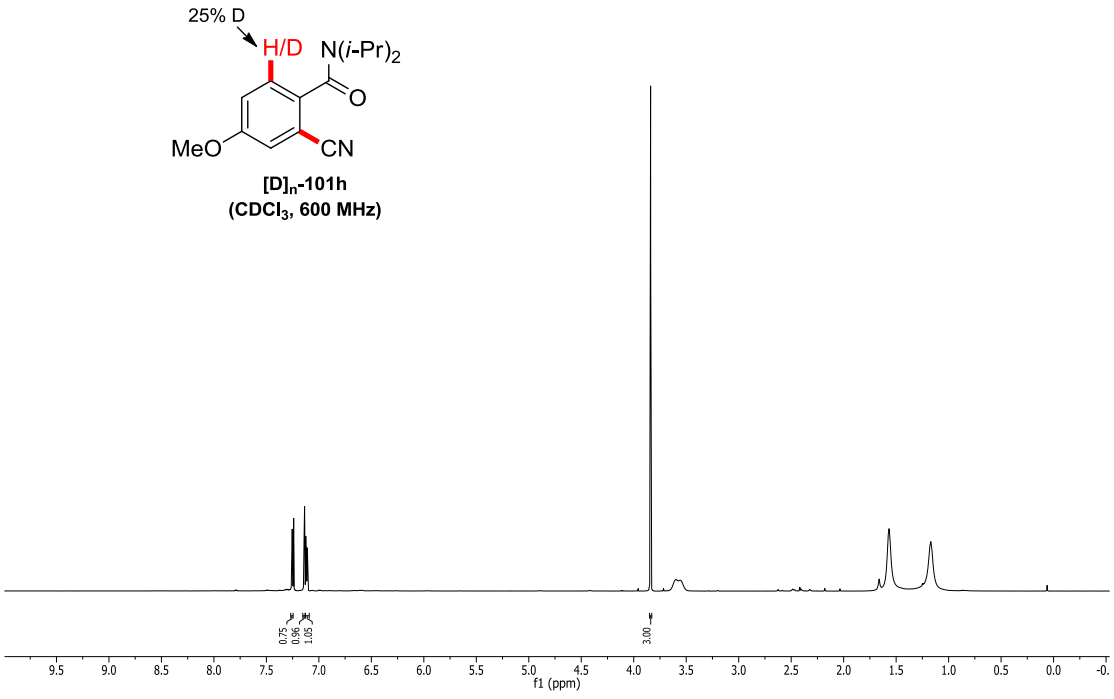
N,*N*-Diisopropyl-4-methoxybenzamide **(50h)** (118 mg, 0.50 mmol), 4-fluoro-*N*,*N*-diisopropylbenzamide (**50k**) (112 mg, 0.50 mmol), NCTS (**13**) (136 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.4 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), NaOAc (8.2 mg, 20 mol %) and DCE (2.0 mL) were placed into a 20 mL sealed tube under N_2 and stirred at 120 ℃ for 24 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1→1/1) to afford the products **101h** (84 mg, 65%) and **101k** (15 mg, 12%).

Ruthenium-Catalyzed H/D Exchange in 50h with D_2O as the Co-Solvent

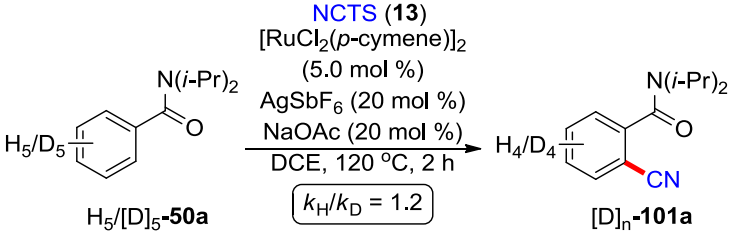


N,*N*-Diisopropyl-4-methoxybenzamide **(50h)** (0.50 mmol), NCTS (**13**) (272 mg, 1.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.4 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20 mol %), NaOAc (8.2 mg, 20 mol %), DCE (1.8 mL) and D_2O (0.2 mL) were placed into a 20 mL sealed tube under N_2 and stirred at 120 ℃ for 24 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel to afford $[D]_n$-**50h** (97 mg, 82%) and $[D]_n$-**101h** (15 mg, 11%). The deuterium incorporation was estimated by ^{1}H-NMR spectroscopy.


19% D
H/D
N(i-Pr)2
O
MeO
H/D
[D]n-50h
(CDCl3, 300 MHz)
0.81
1.00
f1 (ppm)


25% D
H/D
N(i-Pr)2
O
MeO
CN
[D]n-101h
(CDCl3, 600 MHz)
0.75
0.95
1.05
3.00
f1 (ppm)

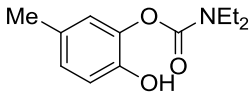
Kinetic Isotope Effect



N,*N*-Diisopropylbenzamide **(50a)** (51 mg, 0.25 mmol), $[D]_5$-*N*,*N*-diisopropylbenzamide **(**$[D]_5$**-50a)** (53 mg, 0.25 mmol), NCTS (**13**) (68 mg, 0.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 5.0 mol %), $AgSbF_6$ (17 mg, 20 mol %), NaOAc (4.1 mg, 20 mol %) and DCE (2.0 mL) were placed into a 20 mL sealed tube under N_2 and stirred at 120 ℃ for 2 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel to afford $[D]_n$-**101a** (36 mg, 62%). The kinetic isotope effect of this reaction was determined to be $k_H/k_D \approx 1.2$ as estimated by ^{1}H-NMR spectroscopy.

4.4 *Ortho*- and *Para*-Selective Ruthenium(II)-Catalyzed C(sp^2)–H Oxygenations of Phenol Derivatives

Characterization Data of Products 103



2-Hydroxy-5-methylphenyl diethylcarbamate (103a): The representative procedure was followed using *m*-tolyl diethylcarbamate (**102a**) (103.5 mg, 0.50 mmol), and the reaction mixture was stirred at 50 ℃ for 24 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103a** (67%) as a colorless solid.

M.p. = 80–82 ℃.

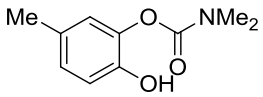
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.92 (s, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.82 (s, 1H), 3.46 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 2.26 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.7 (C_q), 145.3 (C_q), 139.8 (C_q), 130.3 (C_q), 126.9 (CH), 122.3 (CH), 118.9 (CH), 42.5 (CH_2), 42.3 (CH_2), 20.3 (CH_3), 14.1 (CH_3), 13.2 (CH_3).

IR (neat): 3333, 2974, 1684, 1163, 783 cm^{-1}.

MS (EI) *m/z* (relative intensity): 223 (33) [M^+], 123 (13), 100 (100), 72 (76), 44 (33).

HR-MS (EI) *m/z* calcd for $C_{12}H_{17}NO_3$ [M^+] 223.1208, found 223.1206.



2-Hydroxy-5-methylphenyl dimethylcarbamate (103b): The representative procedure was followed using *m*-tolyl dimethylcarbamate (**102b**) (89.5 mg, 0.50 mmol), and the reaction mixture was stirred at 50 ℃ for 24 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103b** (63%) as a colorless solid.

M.p. = 98–100 ℃.

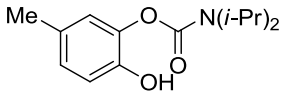
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.87–6.81 (m, 4H), 3.10 (s, 3H), 3.00 (s, 3H), 2.24 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 155.1 (C_q), 145.3 (C_q), 139.6 (C_q), 130.4 (C_q), 127.0 (CH), 122.5 (CH), 118.8 (CH), 36.8 (CH_3), 36.6 (CH_3), 20.4 (CH_3).

IR (neat): 3262, 2950, 1684, 1295, 1179, 796, 578 cm^{-1}.

MS (EI) *m/z* (relative intensity): 195 (25) [M^+], 123 (5), 95 (3), 72 (100), 42 (8).

HR-MS (EI) *m/z* calcd for $C_{10}H_{13}NO_3$ [M^+] 195.0895, found 195.0891.



2-Hydroxy-5-methylphenyl di-*iso*propylcarbamate (103c): The representative procedure was followed using *m*-tolyl di-*iso*propylcarbamate (**102c**) (117.5 mg, 0.50 mmol), and the reaction mixture was stirred at 50 ℃ for 24 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103c** (63%) as a colorless solid.

M.p. = 113–115 ℃.

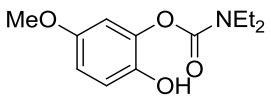
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.11 (s, 1H), 6.89–6.85 (m, 3H), 4.17–3.94 (m, 2H), 2.27 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 6H), 1.30 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.2 (C_q), 145.4 (C_q), 139.8 (C_q), 130.3 (C_q), 126.9 (CH), 122.2 (CH), 119.1 (CH), 47.2 (CH), 46.6 (CH), 21.4 (CH_3), 20.3 (CH_3), 20.2 (CH_3).

IR (neat): 3286, 2971, 1665, 1287, 1146, 1110, 813, 611 cm^{-1}.

MS (EI) *m/z* (relative intensity): 251 (15) [M^+], 128 (80), 124 (73), 86 (100), 43 (84).

HR-MS (EI) *m/z* calcd for $C_{14}H_{21}NO_3$ [M^+] 251.1521, found 251.1520.



2-Hydroxy-5-methoxyphenyl diethylcarbamate (103d): The representative procedure was followed using 3-methoxyphenyl diethylcarbamate (**102d**) (111.5 mg, 0.50 mmol), and the reaction mixture was stirred at 50 ℃ for 24 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103d** (46%) as a colorless solid.

M.p. = 79–81 ℃.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.89 (d, *J* = 8.8 Hz, 1H), 6.82 (s, 1H), 6.64 (dd, *J* = 8.8, 2.8 Hz,

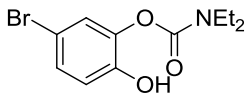
1H), 6.59 (d, *J* = 2.8 Hz, 1H), 3.73 (s, 3H), 3.46 (q, *J* = 7.1 Hz, 2H), 3.38 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.4 (C_q), 153.7 (C_q), 141.6 (C_q), 140.4 (C_q), 119.7 (CH), 111.8 (CH), 107.8 (CH), 55.8 (CH_3), 42.5 (CH_2), 42.3 (CH_2), 14.1 (CH_3), 13.2 (CH_3).

IR (neat): 3343, 2981, 1694, 1518, 1274, 1147, 1031, 752 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 (15) [M^+], 139 (5), 100 (100), 72 (62), 44 (13).

HR-MS (EI) *m/z* calcd for $C_{12}H_{17}NO_4$ [M^+] 239.1158, found 239.1161.



5-Bromo-2-hydroxyphenyl diethylcarbamate (103e): The representative procedure was followed using 3-bromophenyl diethylcarbamate (**102e**) (135.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103e** (66%) as a colorless oil.

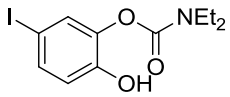
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 2.4 Hz, 1H), 7.11 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.01 (s, 1H), 6.74 (d, *J* = 8.6 Hz, 1H), 3.44 (q, *J* = 7.1 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.4 (C_q), 147.5 (C_q), 140.5 (C_q), 129.3 (CH), 125.2 (CH), 120.3 (CH), 111.4 (C_q), 42.7 (CH_2), 42.4 (CH_2), 14.0 (CH_3), 13.1 (CH_3).

IR (neat): 3269, 2976, 1683, 1426, 1274, 1159, 964, 628 cm^{-1}.

MS (EI) *m/z* (relative intensity): 287 (5) [M^+], 160 (5), 100 (100), 72 (55), 43 (17).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}BrNO_3$ [M^+] 287.0157, found 287.0169.



2-Hydroxy-5-iodophenyl diethylcarbamate (103f): The representative procedure was followed using 3-iodophenyl diethylcarbamate (**102f**) (159.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 3 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103f** (71%) as a colorless solid.

M.p. = 106–108 ℃.

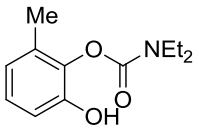
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.41–7.37 (m, 2 H), 7.34 (d, *J* = 2.1 Hz, 1H), 6.80 (dd, *J* = 8.5, 1.7 Hz, 1H), 3.46 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.4 (C_q), 148.4 (C_q), 140.7 (C_q), 135.3 (CH), 130.9 (CH), 120.8 (CH), 80.6 (C_q), 42.6 (CH_2), 42.4 (CH_2), 14.0 (CH_3), 13.2 (CH_3).

IR (neat): 3269, 2979, 1700, 1273, 1157, 825, 601 cm^{-1}.

MS (EI) *m/z* (relative intensity): 335 (20) [M^+], 206 (10), 100 (100), 72 (65), 44 (20).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}INO_3$ [M^+] 335.0018, found 335.0018.



2-Hydroxy-6-methylphenyl diethylcarbamate (103g): The representative procedure was followed using *o*-tolyl diethylcarbamate (**102g**) (103.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 3 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103g** (67%) as a colorless oil.

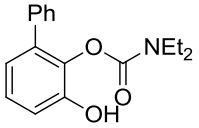
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.96 (s, 1H), 6.87 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.71–6.66 (m, 2H), 3.49 (q, *J* = 7.1 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 2.21 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.2 (C_q), 148.2 (C_q), 138.5 (C_q), 130.9 (C_q), 125.7 (CH), 122.1 (CH), 116.0 (CH), 42.4 (CH_2), 42.0 (CH_2), 16.5 (CH_3), 14.0 (CH_3), 13.2 (CH_3).

IR (neat): 3304, 2976, 1685, 1424, 1275, 1179, 1159, 769, 726 cm^{-1}.

MS (EI) *m/z* (relative intensity): 223 (8) [M^+], 123 (5), 100 (100), 72 (50), 44 (8).

HR-MS (EI) *m/z* calcd for $C_{12}H_{17}NO_3$ [M^+] 223.1208, found 223.1208.



3-Hydroxy-[1,1'-biphenyl]-2-yl diethylcarbamate (103h): The representative procedure was followed using [1,1'-biphenyl]-2-yl diethylcarbamate (**102h**) (134.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolated by column chromatography (*n*-hexane/EtOAc: 3/1) yielded **103h** (79%) as a colorless oil.

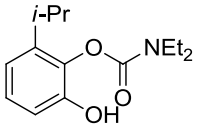
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.43–7.31 (m, 6H), 7.06–7.01 (m, 1H), 6.89–6.84 (m, 2H), 3.32 (q, *J* = 7.1 Hz, 2H), 3.17 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.6 (C_q), 148.9 (C_q), 138.1 (C_q), 137.2 (C_q), 135.9 (C_q), 128.9 (CH), 127.9 (CH), 127.1 (CH), 126.0 (CH), 121.9 (CH), 117.7 (CH), 42.2 (CH_2), 41.8 (CH_2), 13.5 (CH_3), 13.0 (CH_3).

IR (neat): 3282, 2976, 1685, 1424, 1271, 1193, 902, 755, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity): 285 (20) [M^+], 139 (10), 128 (15), 100 (100), 72 (60), 44 (25).

HR-MS (EI) *m/z* calcd for $C_{17}H_{19}NO_3$ [M^+] 285.1365, found 285.1362.



2-Hydroxy-6-isopropylphenyl diethylcarbamate (103i): The representative procedure was followed using 2-isopropylphenyl diethylcarbamate (**102i**) (117.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 3 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103i** (76%) as a colorless solid.

M.p. = 85–87 °C.

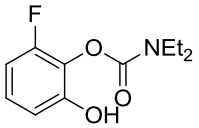
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.92 (dd, *J* = 7.9, 7.9 Hz, 1H), 6.86 (s, 1H), 6.77 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.64 (dd, *J* = 7.9, 1.7 Hz, 1H), 3.49 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 3.10 (hept, *J* = 6.9 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 6H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.6 (C_q), 148.2 (C_q), 141.1 (C_q), 137.6 (C_q), 125.9 (CH), 117.3 (CH), 115.9 (CH), 42.4 (CH_2), 42.0 (CH_2), 27.6 (CH), 22.8 (CH_3), 13.9 (CH_3), 13.2 (CH_3).

IR (neat): 3174, 2965, 1685, 1148, 1181, 964, 782, 732 cm^{-1}.

MS (EI) *m/z* (relative intensity): 251 (5) [M^+], 137 (3), 100 (100), 72 (45), 43 (20).

HR-MS (EI) *m/z* calcd for $C_{14}H_{21}NO_3$ [M^+] 251.1521, found 251.1515.



2-Fluoro-6-hydroxyphenyl diethylcarbamate (103j): The representative procedure was followed using 2-fluorophenyl diethylcarbamate (**102j**) (105.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103j** (58%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.61 (s, 1H), 6.93–6.85 (m, 1H), 6.66–6.59 (m, 2H), 3.47 (q, *J* = 7.1 Hz, 2H), 3.38 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H).

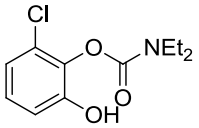
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 155.1 ($^{1}J_{C-F}$ = 248 Hz, C_q), 154.2 (C_q), 150.1 ($^{3}J_{C-F}$ = 3 Hz, C_q), 128.5 ($^{2}J_{C-F}$ = 13 Hz, C_q), 125.7 ($^{3}J_{C-F}$ = 10 Hz, CH), 113.7 ($^{4}J_{C-F}$ = 3 Hz, CH), 107.6 ($^{2}J_{C-F}$ = 19 Hz, CH), 42.7 (CH_2), 42.5 (CH_2), 13.8 (CH_3), 13.1 (CH_3).

^{19}F-NMR (283 MHz, $CDCl_3$) δ = –(130.1–130.2) (m).

IR (neat): 3277, 2979, 1692, 1474, 1013, 768, 562 cm^{-1}.

MS (EI) *m/z* (relative intensity): 227 (10) [M^+], 128 (15), 100 (100), 72 (77), 44 (32).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}FNO_3$ [M^+] 227.0958, found 227.0956.



2-Chloro-6-hydroxyphenyl diethylcarbamate (103k): The representative procedure was followed using 2-chlorophenyl diethylcarbamate (**102k**) (113.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103k** (52%) as a colorless solid.

M.p. = 75–77 ℃.

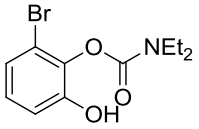
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.50 (s, 1H), 6.92–6.80 (m, 2H), 6.68 (dd, *J* = 7.3, 2.4 Hz, 1H), 3.52 (q, *J* = 7.1 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 153.9 (C_q), 150.1 (C_q), 136.5 (C_q), 127.2 (C_q), 126.3 (CH), 121.0 (CH), 116.9 (CH), 42.6 (CH_2), 42.3 (CH_2), 13.9 (CH_3), 13.1 (CH_3).

IR (neat): 3298, 2981, 1694, 1425, 1211, 1159, 910, 773, 718 cm^{-1}.

MS (EI) *m/z* (relative intensity): 243 (10) [M^+], 144 (15), 100 (100), 72 (75), 44 (33).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}ClNO_3$ [M^+] 243.0662, found 243.0655.



2-Bromo-6-hydroxyphenyl diethylcarbamate (103l): The representative procedure was followed using 2-bromophenyl diethylcarbamate (**102l**) (135.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103l** (57%) as a colorless solid.

M.p. = 107–109 ℃.

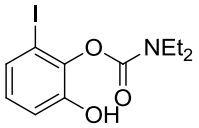
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.39 (s, 1H), 7.06 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.84 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.7 Hz, 1H), 3.56 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 153.8 (C_q), 149.9 (C_q), 137.8 (C_q), 127.0 (CH), 124.3 (CH), 118.0 (CH), 116.4 (C_q), 42.6 (CH_2), 42.3 (CH_2), 14.0 (CH_3), 13.1 (CH_3).

IR (neat): 3177, 2979, 1690, 1424, 1209, 1162, 885, 751 cm^{-1}.

MS (EI) *m/z* (relative intensity): 287 (3) [M^+], 188 (3), 100 (100), 72 (40), 44 (5).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}BrNO_3$ [M^+] 287.0157, found 287.0163.



2-Hydroxy-6-iodophenyl diethylcarbamate (103m): The representative procedure was followed using 2-iodophenyl diethylcarbamate (**102m**) (159.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103m** (42%) as a colorless solid.

M.p. = 118–120 ℃.

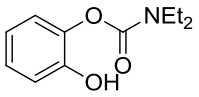
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.31 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.76 (s, 1H), 6.73 (dd, *J* = 8.0, 8.0 Hz, 1H), 3.62 (q, *J* = 7.1 Hz, 2H), 3.42 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 153.7 (C_q), 148.9 (C_q), 140.5 (C_q), 130.5 (CH), 127.9 (CH), 119.1 (CH), 90.6 (C_q), 42.5 (CH_2), 42.4 (CH_2), 14.1 (CH_3), 13.1 (CH_3).

IR (neat): 3207, 2978, 1688, 1422, 1207, 1160, 871, 749 cm^{-1}.

MS (EI) *m/z* (relative intensity): 335 (6) [M^+], 235 (5), 206 (4), 100 (100), 72 (37).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}INO_3$ [M^+] 335.0018, found 335.0034.



2-Hydroxyphenyl diethylcarbamate (103n): The representative procedure was followed using phenyl diethylcarbamate (**102n**) (96.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103n** (42%) as a colorless solid.

M.p. = 69–71 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.31 (s, 1H), 7.07–6.93 (m, 3H), 6.88–6.82 (m, 1H), 3.46 (q, *J* = 7.2 Hz, 2H), 3.39 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H).

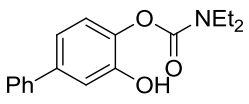
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.7 (C_q), 147.9 (C_q), 140.2 (C_q), 126.5 (CH), 122.0 (CH), 120.7 (CH), 119.3 (CH), 42.6 (CH_2), 42.3 (CH_2), 14.1 (CH_3), 13.2 (CH_3).

IR (neat): 3289, 2976, 1684, 1278, 1161, 1097, 938, 744 cm^{-1}.

MS (EI) *m/z* (relative intensity): 209 (15) [M^+], 110 (15), 100 (100), 72 (80), 44 (36).

HR-MS (EI) *m/z* calcd for $C_{11}H_{15}NO_3$ [M^+] 209.1052, found 209.1054.

The spectral data are in accordance with those reported in the literature.[126]



3-Hydroxy-[1,1'-biphenyl]-4-yl diethylcarbamate (103o): The representative procedure was followed using [1,1'-biphenyl]-4-yl diethylcarbamate (**102o**) (134.5 mg, 0.50 mmol), and the

reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1) yielded **103o** (51%) as a colorless solid.

M.p. = 81–83 ℃.

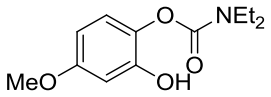
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.57 (s, 1H), 7.51–7.47 (m, 2H), 7.42–7.29 (m, 3H), 7.22 (d, *J* = 1.7 Hz, 1H), 7.11–7.04 (m, 2H), 3.50 (q, *J* = 7.1 Hz, 2H), 3.43 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.8 (C_q), 148.0 (C_q), 140.1 (C_q), 139.7 (C_q), 139.5 (C_q), 128.5 (CH), 127.1 (CH), 126.9 (CH), 122.2 (CH), 119.2 (CH), 117.7 (CH), 42.6 (CH_2), 42.3 (CH_2), 14.0 (CH_3), 13.2 (CH_3).

IR (neat): 3213, 2978, 1681, 1413, 1240, 1167, 754, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 285 (10) [M^+], 128 (8), 100 (100), 72 (47), 44 (10).

HR-MS (EI) *m/z* calcd for $C_{17}H_{19}NO_3$ [M^+] 285.1365, found 285.1364.



2-Hydroxy-4-methoxyphenyl diethylcarbamate (103p): The representative procedure was followed using 4-methoxyphenyl diethylcarbamate (**102p**) (111.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 3 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103p** (46%) as a colorless solid.

M.p. = 86–88 ℃.

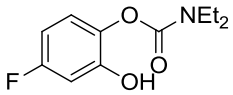
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.51 (s, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 6.47 (d, *J* = 3.0 Hz, 1H), 6.38 (dd, *J* = 8.8, 3.0 Hz, 1H), 3.69 (s, 3H), 3.44 (q, *J* = 7.1 Hz, 2H), 3.37 (q, *J* = 7.1 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 158.0 (C_q), 155.2 (C_q), 148.6 (C_q), 134.1 (C_q), 122.2 (CH), 106.3 (CH), 104.2 (CH), 55.4 (CH_3), 42.6 (CH_2), 42.3 (CH_2), 14.1 (CH_3), 13.2 (CH_3).

IR (neat): 3212, 2983, 1671, 1428, 1205, 1166, 1030, 833 cm^{-1}.

MS (EI) *m/z* (relative intensity): 239 (15) [M^+], 111 (12), 100 (100), 72 (65), 43 (25).

HR-MS (EI) *m/z* calcd for $C_{12}H_{17}NO_4$ [M^+] 239.1158, found 239.1155.



4-Fluoro-2-hydroxyphenyl diethylcarbamate (103q): The representative procedure was followed using 4-fluorophenyl diethylcarbamate (**102q**) (105.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103q** (48%) as a colorless solid.

M.p. = 83–85 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.76 (s, 1H), 6.94 (dd, *J* = 8.6, 5.7 Hz, 1H), 6.59–6.51 (m, 2H),

3.46 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

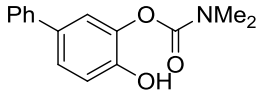
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 160.5 ($^1J_{C–F}$ = 243 Hz, C_q), 154.9 (C_q), 149.2 ($^3J_{C–F}$ = 13 Hz, C_q), 136.2 ($^4J_{C–F}$ = 3 Hz, C_q), 122.6 ($^3J_{C–F}$ = 13 Hz, CH), 106.8 ($^2J_{C–F}$ = 24 Hz, CH), 106.1 ($^2J_{C–F}$ = 24 Hz, CH), 42.6 (CH_2), 42.3 (CH_2), 14.0 (CH_3), 13.2 (CH_3).

^{19}F-NMR (283 MHz, $CDCl_3$) δ = –(115.8–115.9) (m).

IR (neat): 3170, 2984, 1675, 1426, 1227, 1154, 963, 850, 561 cm^{-1}.

MS (EI) *m/z* (relative intensity): 227 (8) [M^+], 128 (12), 100 (100), 72 (83), 44 (40).

HR-MS (EI) *m/z* calcd for $C_{11}H_{14}FNO_3$ [M^+] 227.0958, found 227.0957.



4-Hydroxy-[1,1'-biphenyl]-3-yl dimethylcarbamate (103r): The representative procedure was followed using [1,1'-biphenyl]-3-yl dimethylcarbamate (**102r**) (120.5 mg, 0.50 mmol), and the reaction mixture was stirred at 50 ℃ for 24 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103r** (75%) as a colorless solid.

M.p. = 127–129 ℃.

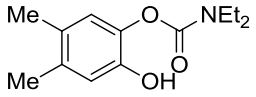
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.52 (d, *J* = 7.2 Hz, 2H), 7.43–7.38 (m, 2H), 7.33–7.26 (m, 3H), 7.02 (d, *J* = 8.7 Hz, 1H), 3.16 (s, 3H), 3.06 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 155.2 (C_q), 147.3 (C_q), 140.2 (C_q), 140.1 (C_q), 134.2 (C_q), 128.7 (CH), 126.8 (CH), 126.6 (CH), 125.2 (CH), 120.7 (CH), 119.4 (CH), 36.9 (CH_3), 36.8 (CH_3).

IR (neat): 3210, 1682, 1296, 1180, 752, 690 cm^{-1}.

MS (EI) *m/z* (relative intensity): 257 (15) [M^+], 157 (8), 128 (10), 72 (100), 42 (6).

HR-MS (EI) *m/z* calcd for $C_{15}H_{15}NO_3$ [M^+] 257.1052, found 257.1059.



2-Hydroxy-4,5-dimethylphenyl diethylcarbamate (103s): The representative procedure was followed using 3,4-dimethylphenyl diethylcarbamate (**102s**) (110.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 3 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103s** (52%) as a colorless solid.

M.p. = 82–84 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.08 (s, 1H), 6.78 (s, 1H), 6.74 (s, 1H), 3.46 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 2.15 (s, 3H), 2.14 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).

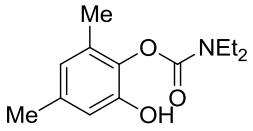
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.9 (C_q), 145.2 (C_q), 137.6 (C_q), 134.6 (C_q), 128.6 (C_q),

122.6 (CH), 120.2 (CH), 42.5 (CH_2), 42.2 (CH_2), 19.1 (CH_3), 18.7 (CH_3), 14.1 (CH_3), 13.2 (CH_3).

IR (neat): 3270, 2977, 1690, 1417, 1305, 1165, 1084, 883, 758 cm^{-1}.

MS (EI) *m/z* (relative intensity): 237 (25) [M^+], 137 (10), 100 (100), 72 (75), 44 (22).

HR-MS (EI) *m/z* calcd for $C_{13}H_{19}NO_3$ [M^+] 237.1365, found 237.1359.



2-Hydroxy-4,6-dimethylphenyl diethylcarbamate (103t): The representative procedure was followed using 2,4-dimethylphenyl diethylcarbamate (**102t**) (110.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103t** (73%) as a colorless solid.

M.p. = 109–111 ℃.

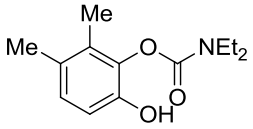
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.88 (s, 1H), 6.52 (d, *J* = 2.6 Hz, 1H), 6.52 (d, *J* = 2.6 Hz, 1H), 3.50 (q, *J* = 7.1 Hz, 2H), 3.41 (q, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 2.17 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.5 (C_q), 147.7 (C_q), 136.4 (C_q), 135.5 (C_q), 130.3 (C_q), 122.9 (CH), 116.7 (CH), 42.4 (CH_2), 42.0 (CH_2), 20.8 (CH_3), 16.5 (CH_3), 14.0 (CH_3), 13.2 (CH_3).

IR (neat): 3253, 2981, 1673, 1276, 1157, 831, 569 cm^{-1}.

MS (EI) *m/z* (relative intensity): 237 (25) [M^+], 137 (30), 100 (100), 72 (65), 44 (15).

HR-MS (EI) *m/z* calcd for $C_{13}H_{19}NO_3$ [M^+] 237.1365, found 237.1364.



2-Hydroxy-5,6-dimethylphenyl diethylcarbamate (103u): The representative procedure was followed using 2,3-dimethylphenyl diethylcarbamate (**102u**) (110.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 3 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103u** (66%) as a colorless solid.

M.p. = 81–83 ℃.

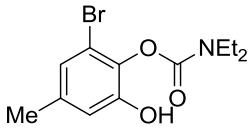
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.81 (d, *J* = 8.1 Hz, 1H), 6.64 (d, *J* = 8.1 Hz, 1H), 6.51 (s, 1H), 3.52 (q, *J* = 7.2 Hz, 2H), 3.41 (q, *J* = 7.2 Hz, 2H), 2.20 (s, 3H), 2.12 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.2 (C_q), 146.0 (C_q), 138.4 (C_q), 129.3 (C_q), 129.0 (C_q), 126.9 (CH), 114.9 (CH), 42.3 (CH_2), 42.0 (CH_2), 19.4 (CH_3), 14.1 (CH_3), 13.2 (CH_3), 12.8 (CH_3).

IR (neat): 3337, 2977, 1684, 1423, 1274, 1159, 1025, 729, 654 cm^{-1}.

MS (EI) *m/z* (relative intensity): 237 (10) [M^+], 137 (5), 100 (100), 72 (50), 44 (10).

HR-MS (EI) *m/z* calcd for $C_{13}H_{19}NO_3$ [M^+] 237.1365, found 237.1372.



2-Bromo-6-hydroxy-4-methylphenyl diethylcarbamate (103v): The representative procedure was followed using 2-bromo-4-methylphenyl diethylcarbamate (**102v**) (142.5 mg, 0.50 mmol), and the reaction mixture was stirred at 80 ℃ for 6 h. Isolation by column chromatography (*n*-hexane/EtOAc: 5/1→3/1) yielded **103v** (54%) as a colorless solid.

M.p. = 83–85 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42 (s, 1H), 6.87 (d, J = 1.9 Hz, 1H), 6.50 (d, J = 1.9 Hz, 1H), 3.55 (q, J = 7.1 Hz, 2H), 3.41 (q, J = 7.1 Hz, 2H), 2.14 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H).

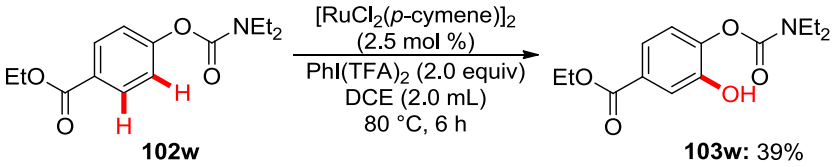
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 154.1 (C_q), 149.4 (C_q), 137.0 (C_q), 135.4 (C_q), 124.4 (CH), 118.4 (CH), 115.8 (C_q), 42.6 (CH_2), 42.3 (CH_2), 20.6 (CH_3), 14.0 (CH_3), 13.2 (CH_3).

IR (neat): 3239, 2976, 1686, 1426, 1305, 1269, 800, 577 cm^{-1}.

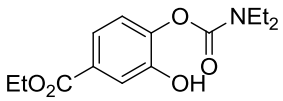
MS (EI) *m/z* (relative intensity): 301 (3) [M^+], 200 (3), 100 (100), 72 (45), 43 (36).

HR-MS (EI) *m/z* calcd for $C_{12}H_{16}BrNO_3$ [M^+] 301.0314, found 301.0304.

Intramolecular Competition Experiment



$[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), $PhI(TFA)_2$ (430 mg, 1.0 mmol), **102w** (132.5 mg, 0.50 mmol) and DCE (2.0 mL) were placed into a 25 mL schlenk tube equipped with a septum under N_2. The reaction mixture was stirred at 80 ℃ for 6 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→3/1) to afford the desired product **103w** (39%) as a colorless oil.



Ethyl 4-[(diethylcarbamoyl)oxy]-3-hydroxybenzoate (103w):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.64 (d, *J* = 2.0 Hz, 1H), 7.56 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.47 (s, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.47 (q, *J* = 7.1 Hz, 2H), 3.40 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

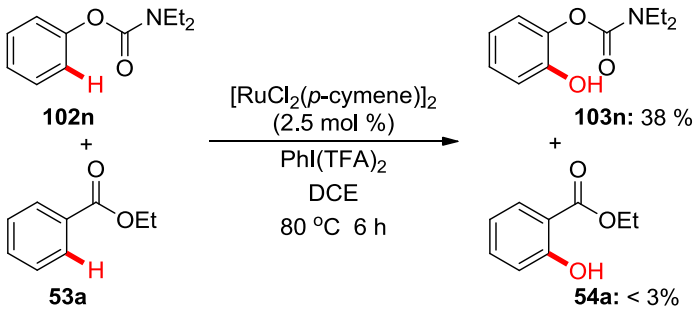
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 165.8 (C_q), 154.1 (C_q), 147.8 (C_q), 143.6 (C_q), 128.5 (C_q), 122.1 (CH), 122.0 (CH), 120.1 (CH), 61.0 (CH_2), 42.7 (CH_2), 42.5 (CH_2), 14.3 (CH_3), 14.1 (CH_3), 13.3 (CH_3).

IR (neat): 3274, 2979, 1687, 1427, 1279, 1214, 1094, 759 cm^{-1}.

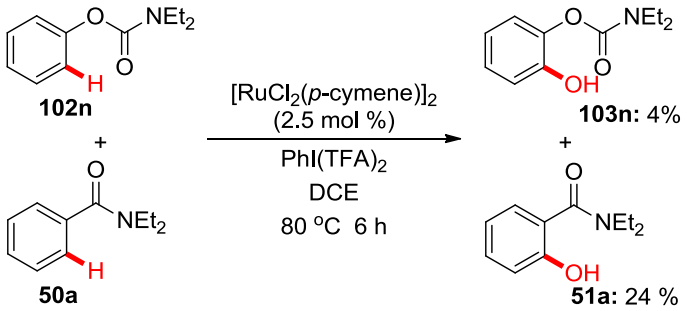
MS (EI) *m/z* (relative intensity): 281 (3) [M^+], 236 (5), 100 (100), 72 (50), 44 (10).

HR-MS (EI) *m/z* calcd for $C_{14}H_{19}NO_5$ [M^+] 281.1263, found 281.1264.

Intermolecular Competition Experiments

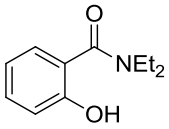


$[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), $PhI(TFA)_2$ (430 mg, 1.0 mmol), **102n** (96.5 mg, 0.50 mmol), **53a** (75.0 mg, 0.50 mmol) and DCE (2.0 mL) were placed into a 25 mL Schlenk tube equipped with a septum under N_2. The reaction mixture was stirred at 80 ℃ for 6 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→3/1) to afford the desired product **103n** (38%).



$[RuCl_2(p\text{-cymene})]_2$ (7.65 mg, 2.5 mol %), $PhI(TFA)_2$ (430 mg, 1.0 mmol), **102n** (96.5 mg, 0.50 mmol), **50a** (88.5 mg, 0.50 mmol) and DCE (2.0 mL) were placed into a 25 mL Schlenk

tube equipped with a septum under N_2. The reaction mixture was stirred at 80 °C for 6 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→3/1) to afford the desired products **51a** (24%) and **103n** (4%).



***N*,*N*-Diethyl-2-hydroxybenzamide (51a):**

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.44 (s, 1H), 7.27–7.19 (m, 2H), 6.93 (dd, *J* = 8.3, 1.3 Hz, 1H), 6.82 (dd, *J* = 8.2, 6.9 Hz, 1H), 3.46 (q, *J* = 7.1 Hz, 4H), 1.22 (t, *J* = 7.1 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 171.2 (C_q), 157.9 (C_q), 131.9 (CH), 127.2 (CH), 118.6 (C_q), 118.5 (CH), 117.7 (CH) 42.0, (CH_2), 13.3 (CH_3).

IR (neat): 3165, 2978, 1610, 1582, 1247, 881 cm^{-1}.

MS (EI) *m/z* (relative intensity): 193 (35) [M^+], 192 (55), 121 (100).

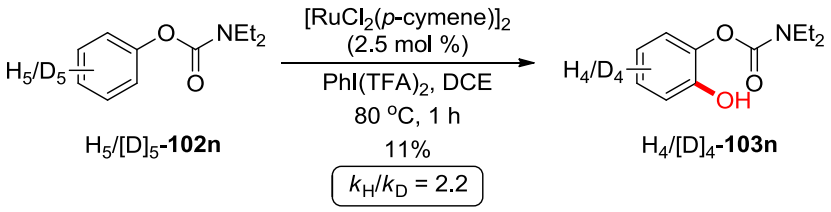
HR-MS (EI) *m/z* calcd for $C_{11}H_{14}NO_2$ [M^+] 193.1103, found 193.1103.

The spectral data are in accordance with those reported in the literature.[55e]

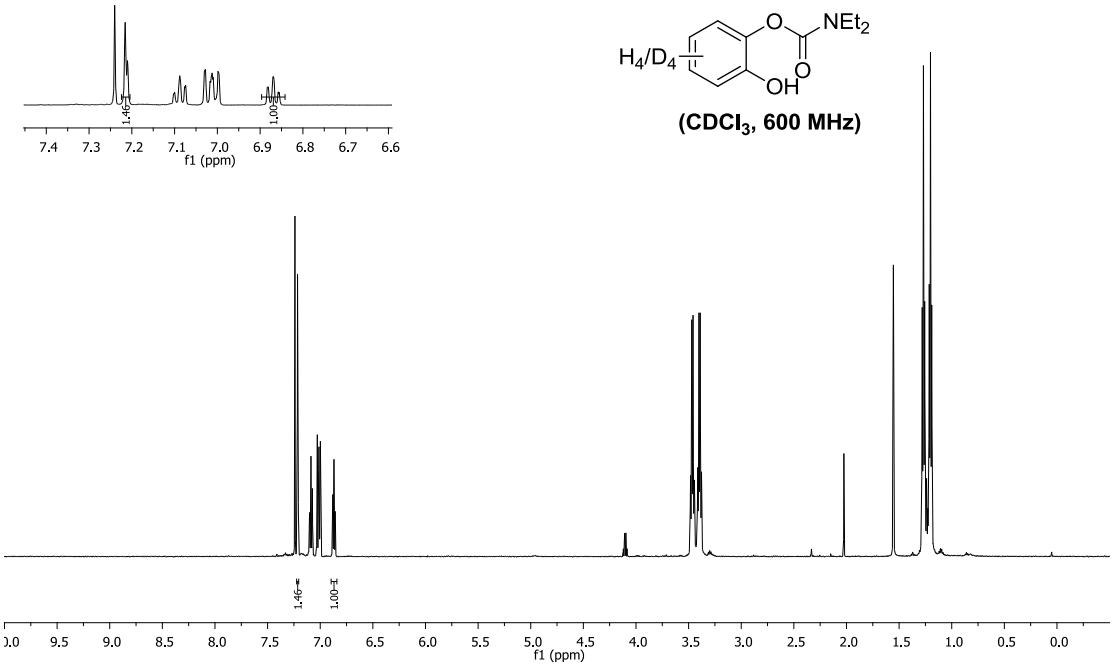
Preparation of the substrate [D]$_5$-102n[113-114]

A sealed tube equipped with a magnetic stirring bar was charged with CuI (37.8 mg, 10 mol %) and NaI (59.6 mg, 20 mol %). The tube was evacuated and back-filled with nitrogen. Then [D]$_5$-bromobenzene (322.0 mg, 2.0 mmol, 1.0 equiv), DMEDA (88.5 mg, 1.0 mol) and 1,4-dioxane (2.0 mL) were added. The tube was sealed under N_2, and the reaction mixture was stirred at 110 °C. After 6 h, under a stream of N_2, $CsOH \cdot H_2O$ (1008 mg, 6.0 mol) and D_2O (2 mL) were added. The tube was sealed under N_2, stirred and heated to 130 °C for 24 h. At ambient temperature, CH_2Cl_2 (10 mL) and HCl (2 mL, 37%) were added. The reaction mixture was stirred for 2 h, then extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation of the solvents *in vacuo*, the crude product was obtained without further purification. The crude product was dissolved in DMF (5.0 mL). Then NaH (125 mg, 60% dispersion, 3.0 mmol) was added, the solution was stirred for 15 min at ambient temperature and diethylcarbamoyl chloride (272 mg, 2.0 mmol) was added. After stirring for 2 h at ambient temperature, the reaction mixture was carefully reacted with ice and extracted with Et_2O (3 x 15 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1) to yield [D]$_5$-**102n** (95% [D]) (45%) as a colorless oil.

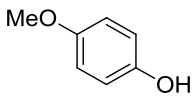
Kinetic Isotope Effect



$[RuCl_2(p\text{-cymene})]_2$ (3.9 mg, 2.5 mol %), $PhI(TFA)_2$ (215 mg, 0.50 mmol), $[D_5]$-**102n** (50.0 mg, 0.25 mmol), **102n** (48.5 mg, 0.25 mmol), DCE (2.0 mL) were placed into a 25 mL Schlenk tube equipped with a septum under N_2. The reaction mixture was stirred at 80 ℃ for 1 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1→3/1) to afford the desired product $[D_n]$-**103n** (11%). The ratio of **103n**/$[D]_5$-**103n** was determined to be 50/23 by ^{1}H-NMR spectroscopy.



Characterization Data of Products 116



4-Methoxyphenol (116a): The representative procedure was followed using anisole (**115a**) (54.0 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded

116a (71%) as a colorless solid.

M.p. = 56–58 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.80 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 5.47 (s_{br}, 1H), 3.77 (s, 3H).

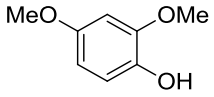
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 153.6 (C_q), 149.5 (C_q), 116.1 (CH), 114.9 (CH), 55.8 (CH_3).

IR (neat): 3401, 2953, 1512, 1277, 1235, 1039, 807, 736 cm^{-1}.

MS (EI) *m/z* (relative intensity): 124.1 (90) [M^+], 109.0 (100), 81 (50), 53 (27).

HR-MS (EI) *m/z* calcd for $C_7H_8O_2$ [M^+] 124.0524, found 124.0528.

The spectral data are in accordance with those reported in the literature.[127]



2,4-Dimethoxyphenol (116b): The representative procedure was followed using 1,3-dimethoxybenzene (**115b**) (69.0 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **116b** (84%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.82 (d, *J* = 8.6 Hz, 1H), 6.48 (d, *J* = 2.8 Hz, 1H), 6.37 (dd, *J* = 8.6, 2.8 Hz, 1H), 5.32 (s_{br}, 1H), 3.83 (s, 3H), 3.74 (s, 3H).

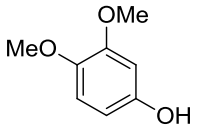
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 153.4 (C_q), 147.0 (C_q), 139.7 (C_q), 114.0 (CH), 104.1 (CH), 99.4 (CH), 55.8 (CH_3), 55.7 (CH_3).

IR (neat): 3437, 2940, 1506, 1201, 1150, 1026, 789 cm^{-1}.

MS (EI) *m/z* (relative intensity): 154 (100) [M^+], 139 (95), 111 (85), 96 (15), 79 (15), 53 (15).

HR-MS (EI) *m/z* calcd for $C_{118}H_{10}O_3$ [M^+] 154.0630, found 154.0629.

The spectral data are in accordance with those reported in the literature.[127]



3,4-Dimethoxyphenol (116c): The representative procedure was followed using 1,2-dimethoxybenzene (**115c**) (69.0 mg, 0.50 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **116c** (56%) as a colorless solid.

M.p. = 79–81 °C.

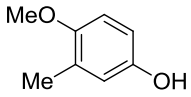
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.70 (d, *J* = 8.6 Hz, 1H), 6.44 (d, *J* = 2.8 Hz, 1H), 6.33 (dd, *J* = 8.6, 2.8 Hz, 1H), 5.48 (s_{br}, 1H), 3.78 (s, 3H), 3.77 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 150.2 (C_q), 149.8 (C_q), 142.9 (C_q), 112.4 (CH), 105.8 (CH), 100.6 (CH), 56.5 (CH_3), 55.7 (CH_3).

IR (neat): 3417, 2937, 1509, 1220, 1195, 1024, 952, 765 cm^{-1}.

MS (EI) *m/z* (relative intensity): 154 (100) [M^+], 139 (87), 111 (75), 96 (15), 55 (15).

HR-MS (EI) *m/z* calcd for $C_{118}H_{10}O_3$ [M^+] 154.0630, found 154.0634.
The spectral data are in accordance with those reported in the literature.[127]



4-Methoxy-3-methylphenol (116d): The representative procedure was followed using 1-methoxy-2-methylbenzene (**115d**) (61.0 mg, 0.50 mmol), $PhI(TFA)_2$ (430 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1) yielded **116d** (47%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.68 (d, *J* = 8.5 Hz, 1H), 6.64 (d, *J* = 2.9 Hz, 1H), 6.60 (dd, *J* = 8.5, 2.9 Hz, 1H), 4.29 (s_{br}, 1H), 3.76 (s, 3H), 2.16 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 151.9 (C_q), 149.0 (C_q), 128.0 (C_q), 117.9 (CH), 112.5 (CH), 111.3 (CH), 56.0 (CH_3), 16.2 (CH_3).

IR (neat): 3382, 2950, 1503, 1465, 1219, 1035, 738 cm^{-1}.

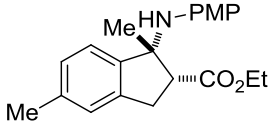
MS (EI) m/z (relative intensity): 138 (85) [M^+], 123 (100), 95 (15), 77 (15), 67 (17).

HR-MS (EI) m/z calcd for $C_8H_{10}O_2$ [M^+] 138.0681, found 138.0677.

The spectral data are in accordance with those reported in the literature.[127]

4.5 Manganese(I)-Catalyzed Synthesis of *cis*-*β*-Amino Acid Esters through Organometallic C–H Activation

Characterization Data of Products 105



Ethyl 1-[(4-methoxyphenyl)amino]-1,5-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105aa): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105aa** (159 mg, 94%) as a colorless solid.

M.p. = 64–65 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.15–6.84 (m, 3H), 6.58 (dd, *J* = 8.8, 1.8 Hz, 2H), 6.32 (dd, *J* = 8.8, 1.8 Hz, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.79 (s_{br}, 1H), 3.70 (s, 3H), 3.27–3.13 (m, 2H), 3.09–2.91 (m, 1H), 2.37 (s, 3H), 1.76 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

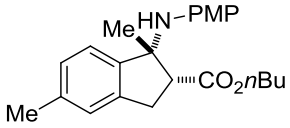
^{13}C-NMR (125 MHz, $CDCl_3$) δ = 172.5 (C_q), 154.3 (C_q), 143.2 (C_q), 141.1 (C_q), 138.6 (C_q), 137.8 (C_q), 127.3 (CH), 125.2 (CH), 123.6 (CH), 122.9 (CH), 113.4 (CH), 67.4 (C_q), 60.4 (CH_2),

55.5 (CH_3), 55.3 (CH), 33.0 (CH_2), 28.4 (CH_3), 21.4 (CH_3), 14.2 (CH_3).

IR (neat): 2984, 1722, 1504, 1222, 1180, 1030, 806, 569 cm^{-1}.

MS (EI) *m/z* (relative intensity): 339 (5) [M^+], 216 (60), 171 (20), 143 (100), 128 (75), 108 (53).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{25}NO_3$ [M^+] 339.1834, found 339.1832.



***n*-Butyl 1-[(4-methoxyphenyl)amino]-1,5-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ab)**: The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and *n*-butyl acrylate (**38b**) (128 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ab** (163 mg, 89%) as a colorless oil.

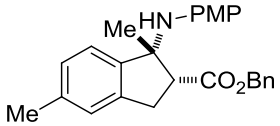
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.07–6.97 (m, 3H), 6.59 (dd, *J* = 8.9, 1.2 Hz, 2H), 6.32 (dd, *J* = 8.9, 1.2 Hz, 2H), 4.12 (d, *J* = 6.7 Hz, 2H), 3.80 (s_{br}, 1H), 3.70 (s, 3H), 3.30–3.15 (m, 2H), 3.09–2.97 (m, 1H), 2.38 (s, 3H), 1.76 (s, 3H), 1.63 (tt, *J* = 7.9, 5.9 Hz, 2H), 1.48–1.35 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.7 (C_q), 154.4 (C_q), 143.2 (C_q), 141.2 (C_q), 138.6 (C_q), 137.8 (C_q), 127.3 (CH), 125.2 (CH), 123.6 (CH), 123.1 (CH), 113.4 (CH), 67.4 (C_q), 64.3 (CH_2), 55.4 (CH_3), 55.1 (CH), 32.9 (CH_2), 30.5 (CH_2), 28.2 (CH_3), 21.3 (CH_3), 19.2 (CH_2), 13.6 (CH_3).

IR (neat): 2958, 1721, 1507, 1462, 1234, 1182, 1036, 817 cm^{-1}.

MS (EI) *m/z* (relative intensity): 367 (35) [M^+], 244 (60), 143 (95), 123 (100), 108 (70), 80 (40).

HR-MS (ESI) *m/z* calcd for $C_{23}H_{29}NO_3$ [M^+] 367.2147, found 367.2161.



Benzyl 1-[(4-methoxyphenyl)amino]-1,5-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ac): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and benzyl acrylate (**38c**) (150 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ac** (176 mg, 88%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.44–7.34 (m, 4H), 7.10–7.01 (m, 3H), 6.60–6.56 (m, 2H), 6.32–6.27 (m, 2H), 5.17 (s, 2H), 3.80 (s_{br}, 1H), 3.72 (s, 3H), 3.39–3.21 (m, 2H), 3.06 (dd, *J* = 16.3, 8.4 Hz, 1H), 2.41 (s, 3H), 1.81 (s, 3H).

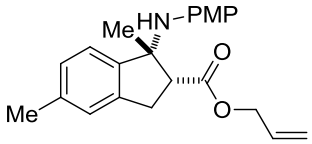
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.4 (C_q), 154.4 (C_q), 143.2 (C_q), 141.1 (C_q), 138.5 (C_q), 137.9 (C_q), 135.8 (C_q), 128.4 (CH), 128.2 (CH), 128.1 (CH), 127.5 (CH), 125.2 (CH), 123.6 (CH), 122.9 (CH), 113.5 (CH), 67.6 (C_q), 66.3 (CH_2), 55.4 (CH_3), 55.2 (CH), 33.0 (CH_2), 28.4

(CH_3), 21.3 (CH_3).

IR (neat): 2934, 1725, 1507, 1233, 1178, 1036, 813, 747, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 401 (15) [M^+], 279 (10), 233 (15), 123 (75), 91 (100).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{27}NO_3$ [M^+] 401.1991, found 401.1980.



Allyl 1-[(4-methoxyphenyl)amino]-1,5-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ad): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl) ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and allyl acrylate (**38d**) (133 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ad** (118 mg, 67%) as a colorless solid.

M.p. = 63–64 ℃.

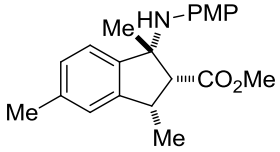
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.04 (s, 1H), 7.02–6.95 (m, 2H), 6.58–6.54 (m, 2H), 6.31–6.27 (m, 2H), 5.90 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.33 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.23 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.58 (dt, *J* = 5.7, 1.4 Hz, 2H), 3.75 (s_{br}, 1H), 3.68 (s, 3H), 3.29–3.16 (m, 2H), 3.00 (dd, *J* = 15.7, 8.3Hz, 1H), 2.35 (s, 3H), 1.76 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 172.4 (C_q), 154.5 (C_q), 143.2 (C_q), 141.1 (C_q), 138.5 (C_q), 137.9 (C_q), 132.2 (CH), 127.5 (CH), 125.3 (CH), 123.7 (CH), 123.1 (CH), 118.2 (CH_2), 113.5 (CH), 67.6 (C_q), 65.2 (CH_2), 55.5 (CH_3), 55.3 (CH), 33.0 (CH_2), 28.3 (CH_3), 21.3 (CH_3).

IR (neat): 2946, 1725, 1504, 1439, 1222, 1178, 1031, 818, 569 cm^{-1}.

MS (EI) *m/z* (relative intensity): 351 (15) [M^+], 229 (40), 144 (85), 129 (43), 123 (100), 108 (20).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{25}NO_3$ [M^+] 351.1834, found 351.1825.



Methyl-1-[(4-methoxyphenyl)amino]-1,3,5-trimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ae): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol), methyl (*E*)-but-2-enoate (**38e**) (107 μL, 1.0 mmol) and $Mn_2(CO)_{10}$ (19.6 mg, 10 mol %). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ae** (108 mg, 64%) as a colorless solid.

M.p. = 99–100 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.15 (d, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.99 (s, 1H), 6.73 (s, 4H), 4.30 (s_{br}, 1H), 3.75 (s, 3H), 3.57–3.44 (m, 5H), 2.37 (s, 3H), 1.61 (s, 3H), 1.32 (d,

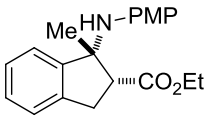
J = 6.5 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.6 (C_q), 153.6 (C_q), 145.9 (C_q), 143.9 (C_q), 139.2 (C_q), 137.7 (C_q), 127.8 (CH), 123.7 (CH), 122.0 (CH), 121.0 (CH), 114.0 (CH), 66.6 (C_q), 61.4 (CH), 55.5 (CH_3), 50.9 (CH_3), 39.4 (CH), 26.7 (CH_3), 21.4 (CH_3), 15.1 (CH_3).

IR (neat): 3398, 2966, 1730, 1508, 1246, 1162, 808, 555, 514 cm^{-1}.

MS (EI) *m/z* (relative intensity): 339 (15) [M^+], 216 (45), 157 (100), 142 (55), 123 (65), 108 (45).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{26}NO_3$ [M + H^+] 340.1913, found 340.1907.



Ethyl 1-[(4-methoxyphenyl)amino]-1-methyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ba): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-phenylethan-1-imine (**104b**) (113 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ba** (158 mg, 97%) as a colorless oil.

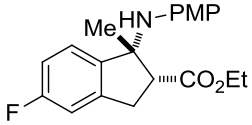
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.30–7.17 (m, 3H), 7.08 (d, *J* = 7.3 Hz, 1H), 6.57 (d, *J* = 8.9 Hz, 2H), 6.29 (d, *J* = 8.9 Hz, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 1H), 3.69 (s, 3H), 3.29–3.18 (m, 2H), 3.10–2.99 (m, 1H), 1.79 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.6 (C_q), 154.5 (C_q), 146.1 (C_q), 141.0 (C_q), 138.5 (C_q), 128.1 (CH), 126.5 (CH), 124.6 (CH), 123.9 (CH), 123.1 (CH), 113.4 (CH), 67.7 (C_q), 60.4 (CH_2), 55.2 (CH_3), 55.2 (CH), 33.0 (CH_2), 28.1 (CH_3), 14.1 (CH_3).

IR (neat): 2977, 1719, 1507, 1224, 1181, 1034, 826, 758 cm^{-1}.

MS (EI) *m/z* (relative intensity): 325 (15) [M^+], 202 (25), 129 (100), 123 (95), 108 (48), 80 (20).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{23}NO_3$ [M^+] 325.1678, found 325.1688.



Ethyl 5-fluoro-1-[(4-methoxyphenyl)amino]-1-methyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ca): The representative procedure was followed using 1-(4-fluorophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104c**) (122 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ca** (129 mg, 75%) as a colorless solid.

M.p. = 78–79 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.01–6.96 (m, 1H), 6.93–6.83 (m, 2H), 6.57 (dd, *J* = 8.8, 1.6 Hz, 2H), 6.27 (dd, *J* = 8.8, 1.6 Hz, 2H), 4.15 (q, *J* = 7.4 Hz, 2H), 3.74 (s_{br}, 1H), 3.69 (s, 3H),

3.29–3.12 (m, 2H), 3.00 (dd, *J* = 16.0, 8.4 Hz, 1H), 1.76 (s, 3H), 1.26 (t, *J* = 7.4 Hz, 3H).

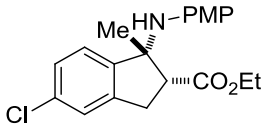
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.3(C_q), 162.9 ($^1J_{C-F}$ = 244 Hz, C_q), 154.7 (C_q), 143.3 ($^3J_{C-F}$ = 9 Hz, C_q), 141.7 ($^4J_{C-F}$ = 2 Hz, C_q), 138.3 (C_q), 125.2 ($^3J_{C-F}$ = 9 Hz, CH), 123.5 (CH), 113.6 ($^2J_{C-F}$ = 23 Hz, CH), 113.5 (CH), 111.5 ($^2J_{C-F}$ = 22 Hz, CH,), 67.1 (C_q), 60.6 (CH_2), 55.5 (CH_3), 55.3 (CH), 32.9 ($^4J_{C-F}$ = 2 Hz, CH_2), 28.2 (CH_3), 14.1 (CH_3).

^{19}F-NMR (283 MHz, $CDCl_3$) δ = -(114.5–114.6) (m).

IR (neat): 2988, 1719, 1505, 1238, 1181, 827, 807, 699 cm^{-1}.

MS (EI) *m/z* (relative intensity): 343 (15) [M^+], 221 (20), 147 (65), 123 (100), 108 (25).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{22}FNO_3$ [M^+] 343.1584, found 343.1591.



Ethyl 5-chloro-1-[(4-methoxyphenyl)amino]-1-methyl-2,3-dihydro-1*H*-indene-2-carboxylate (105da): The representative procedure was followed using 1-(4-chlorophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104d**) (130 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→*5*/1) yielded **105da** (120 mg, 67%) as a colorless solid.

M.p. = 79–80 ℃.

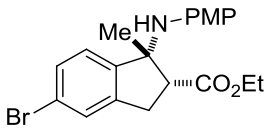
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.21 (d, *J* = 2.0 Hz, 1H), 7.15 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.58 (dd, *J* = 8.6, 2.0 Hz, 2H), 6.30 (dd, *J* = 8.6, 2.0 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.72 (s_{br}, 1H), 3.70 (s, 3H), 3.27–3.16 (m, 2H), 3.06–2.95 (m, 1H), 1.74 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.2 (C_q), 154.8 (C_q), 144.7 (C_q), 142.9 (C_q), 138.1 (C_q), 133.7 (C_q), 126.8 (CH), 125.1 (CH), 124.8 (CH), 123.5 (CH), 113.6 (CH), 67.2 (C_q), 60.6 (CH_2), 55.3 (CH_3), 55.3 (CH), 32.8 (CH_2), 28.0 (CH_3), 14.1 (CH_3).

IR (neat): 2984, 1718, 1505, 1437, 1222, 1180, 1030, 823, 806, 567, 459 cm^{-1}.

MS (EI) *m/z* (relative intensity): 359 (15) [M^+], 236 (40), 163 (90), 128 (75), 123 (100), 108 (65).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{23}ClNO_3$ [M + H^+] 360.1366, found 360.1361.



Ethyl 5-bromo-1-[(4-methoxyphenyl)amino]-1-methyl-2,3-dihydro-1H-indene-2-carboxylate (105ea): The representative procedure was followed using 1-(4-bromophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104e**) (152 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→*5*/1) yielded

105ea (137 mg, 68%) as a colorless solid.

M.p. = 65–66 ℃.

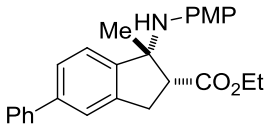
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.37 (s, 1H), 7.30 (d, J = 8.2 Hz, 1H), 6.88 (dd, J = 8.2, 1.5 Hz, 1H), 6.58 (dd, J = 8.8, 1.7 Hz, 2H), 6.31 (dd, J = 8.8, 1.7 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.71 (s_{br}, 1H), 3.69 (s, 3H), 3.27–3.17 (m, 2H), 3.06–2.95 (m, 1H), 1.73 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.1 (C_q), 154.8 (C_q), 145.2 (C_q), 143.3 (C_q), 138.0 (C_q), 129.6 (CH), 127.8 (CH), 125.5 (CH), 123.5 (CH), 121.8 (C_q), 113.6 (CH), 67.3 (C_q), 60.6 (CH_2), 55.3 (CH_3), 55.2 (CH), 32.8 (CH_2), 27.9 (CH_3), 14.1 (CH_3).

IR (neat): 2985, 1718, 1504, 1221, 1179, 1030, 824, 697, 454 cm^{-1}.

MS (EI) *m/z* (relative intensity): 405 (8) [M^+] (^{81}Br), 403 (10) [M^+] (^{79}Br), 282 (30) (^{81}Br), 280 (30) (^{79}Br), 209 (45) (^{81}Br), 207 (45) (^{79}Br), 128 (100), 123 (85).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{23}BrNO_3$ [M + H^+] 404.0861, found 404.0856.



Ethyl 1-[(4-methoxyphenyl)amino]-1-methyl-5-phenyl-2,3-dihydro-1*H*-indene-2-carboxylate (105fa): The representative procedure was followed using 1-([1,1'-biphenyl]-4-yl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104f**) (151 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105fa** (151 mg, 75%) as a colorless oil.

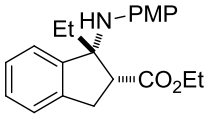
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.63–7.60 (m, 2H), 7.48–7.42 (m, 4H), 7.37–7.33 (m, 1H), 7.14 (dd, J = 7.8, 0.6 Hz, 1H), 6.59 (dd, J = 9.0, 2.3 Hz, 2H), 6.37 (dd, J = 9.0, 2.3 Hz, 2H), 4.23–4.10 (m, 2H), 3.81 (s_{br}, 1H), 3.70 (s, 3H), 3.34–3.27 (m, 2H), 3.14–3.07 (m, 1H), 1.82 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 172.6 (C_q), 154.6 (C_q), 145.3 (C_q), 141.7 (C_q), 141.3 (C_q), 141.0 (C_q), 138.5 (C_q), 128.7 (CH), 127.2 (CH), 127.1 (CH), 125.7 (CH), 124.2 (CH), 123.3 (CH), 123.2 (CH), 113.5 (CH), 67.5 (C_q), 60.5 (CH_2), 55.5 (CH_3), 55.3 (CH), 33.1 (CH_2), 28.1 (CH_3), 14.2 (CH_3).

IR (neat): 2976, 1720, 1507, 1227, 1182, 1034, 827, 762, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 401 (5) [M^+], 278 (70), 205 (100), 123 (30), 108 (30).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{27}NO_3$ [M^+] 401.1991, found 401.1992.



Ethyl 1-ethyl-1-[(4-methoxyphenyl)amino]-2,3-dihydro-1*H*-indene-2-carboxylate (105ga): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-phenylpropan-1-imine (**104g**) (120 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ga** (144 mg, 85%) as a colorless oil.

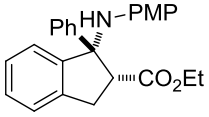
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.29–7.16 (m, 3H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.56 (d, *J* = 8.8 Hz, 2H), 6.28 (d, *J* = 8.8 Hz, 2H), 4.05 (q, *J* = 7.1 Hz, 2H), 3.91 (s_{br}, 1H), 3.68 (s, 3H), 3.44–3.36 (m, 1H), 3.30–3.22 (m, 1H), 3.08 (dd, *J* = 16.2, 8.7 Hz, 1H), 2.28–2.08 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 173.0 (C_q), 153.9 (C_q), 143.9 (C_q), 141.8 (C_q), 138.5 (C_q), 128.1 (CH), 126.4 (CH), 124.6 (CH), 124.4 (CH), 121.7 (CH), 113.5 (CH), 71.8 (C_q), 60.4 (CH_2), 55.3 (CH_3), 50.7 (CH), 33.3 (CH_2), 31.9 (CH_2), 14.0 (CH_3), 8.8 (CH_3).

IR (neat): 2967, 1720, 1507, 1233, 1179, 1036, 756 cm^{-1}.

MS (EI) *m/z* (relative intensity): 339 (35) [M^+], 310 (25), 143 (90), 123 (100).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{25}NO_3$ [M^+] 339.1834, found 339.1843.



Ethyl 1-[(4-methoxyphenyl)amino]-1-phenyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ha): The representative procedure was followed using *N*-(4-methoxyphenyl)-1,1-diphenylmethanimine (**104h**) (144 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ha** (145 mg, 75%) as a colorless solid.

M.p. = 117–118 °C.

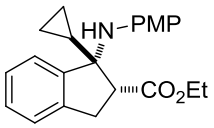
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 8.0 Hz, 2H), 7.40–7.18 (m, 6H), 7.13–7.08 (m, 1H), 6.58 (dd, *J* = 9.1, 1.0 Hz, 2H), 6.41 (dd, *J* = 9.0, 1.0 Hz, 2H), 4.77 (s, 1H), 4.17–3.99 (m, 2H), 3.67 (s, 3H), 3.63–3.51 (m, 2H), 3.27 (dd, *J* = 15.8, 7.6 Hz, 1H), 1.13 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.6 (C_q), 152.7 (C_q), 145.2 (C_q), 143.8 (C_q), 141.2 (C_q), 138.8 (C_q), 128.1 (CH), 128.0 (CH), 127.0 (CH), 127.0 (CH), 126.3 (CH), 125.5 (CH), 124.7 (CH), 118.6 (CH), 113.8 (CH), 73.5 (C_q), 60.7 (CH_2), 58.9 (CH_2), 55.4 (CH), 34.2 (CH_2), 13.9 (CH_3).

IR (neat): 2926, 1717, 1508, 1225, 820, 751, 701, 523 cm^{-1}.

MS (EI) *m/z* (relative intensity): 387 (20) [M^+], 265 (100), 191 (60), 123 (65), 115 (40).

HR-MS (ESI) *m/z* calcd for $C_{25}H_{25}NO_3$ [M^+] 387.1834, found 387.1844.



Ethyl 1-cyclopropyl-1-[(4-methoxyphenyl)amino]-2,3-dihydro-1*H*-indene-2-carboxylate (105ia): The representative procedure was followed using 1-cyclopropyl-*N*-(4-methoxyphenyl)-1-phenyl methanimine (**104i**) (126 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→5/1) yielded **105ia** (154 mg, 87%) as a colorless oil.

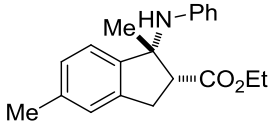
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.30–7.16 (m, 4H), 6.57 (dd, *J* = 8.3, 1.3 Hz, 2H), 6.39 (dd, *J* = 8.3, 1.3 Hz, 2H), 4.17 (s, 1H), 4.02–3.83 (m, 2H), 3.68 (s, 3H), 3.35–3.22 (m, 2H), 3.12 (dd, *J* = 15.7, 8.3 Hz, 1H), 1.63–1.53 (m, 1H), 1.12 (t, *J* = 7.4 Hz, 3H), 0.59–0.41 (m, 3H), 0.28–0.20 (m, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 173.2 (C_q), 153.0 (C_q), 143.5 (C_q), 141.8 (C_q), 139.3 (C_q), 128.2 (CH), 126.3 (CH), 124.7 (CH), 124.5 (CH), 119.8 (CH), 113.6 (CH), 71.0 (C_q), 60.4 (CH_2), 55.3 (CH_3), 53.4 (CH), 33.9 (CH_2), 22.3 (CH), 13.9 (CH_3), 1.9 (CH_2), 1.4 (CH_2).

IR (neat): 2981, 1720, 1507, 1233, 1179, 1036, 821, 759 cm^{-1}.

MS (EI) *m/z* (relative intensity): 351 (10) [M^+], 228 (30), 155 (100), 123 (55), 108 (45).

HR-MS (ESI) *m/z* calcd for $C_{22}H_{26}NO_3$ [M + H^+] 352.1913, found 352.1907.



Ethyl 1,5-dimethyl-1-(phenylamino)-2,3-dihydro-1*H*-indene-2-carboxylate (105ja): The representative procedure was followed using *N*-phenyl-1-(*p*-tolyl)ethan-1-imine (**104j**) (105 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→10/1) yielded **105ja** (142 mg, 92%) as a colorless oil.

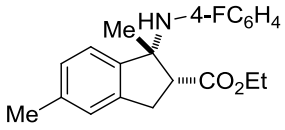
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.25–7.06 (m, 3H), 7.03–6.98 (m, 2H), 6.76–6.72 (m, 1H), 6.41–6.38 (m, 2H), 4.14 (s, 1H), 4.03 (dq, *J* = 7.1, 1.8 Hz, 2H), 3.37–3.30 (m, 2H), 3.12–3.05 (m, 1H), 2.40 (s, 3H), 1.83 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 172.6 (C_q), 145.8 (C_q), 143.4 (C_q), 140.9 (C_q), 138.0 (C_q), 128.3 (CH), 127.7 (CH), 125.3 (CH), 123.3 (CH), 119.4 (CH), 118.5 (CH), 67.2 (C_q), 60.4 (CH_2), 55.3 (CH), 33.3 (CH_2), 29.8 (CH_3), 21.3 (CH_3), 13.9 (CH_3).

IR (neat): 2977, 1718, 1599, 1495, 1184, 1034, 748, 693 cm^{-1}.

MS (EI) *m/z* (relative intensity): 309 (5) [M^+], 216 (40), 143 (100), 128 (55), 93 (45).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{23}NO_2$ [M^+] 309.1729, found 309.1733.



Ethyl 1-[(4-fluorophenyl)amino]-1,5-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ka): The representative procedure was followed using *N*-(4-fluorophenyl)-1-(*p*-tolyl)ethan-1-imine (**104k**) (114 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→10/1) yielded **105ka** (131 mg, 80%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.13–6.99 (m, 3H), 6.70 (td, *J* = 8.7, 1.4 Hz, 2H), 6.29 (ddd, *J* = 8.9, 4.7, 1.4 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.97 (s, 1H), 3.31–3.17 (m, 2H), 3.04 (dd, *J* = 14.9, 7.6 Hz, 1H), 2.38 (s, 3H), 1.79 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H).

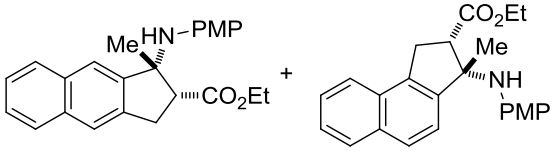
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.5 (C_q), 157.5 ($^{1}J_{C\text{-}F}$ = 240 Hz, C_q), 142.9 (C_q), 141.6 ($^{4}J_{C\text{-}F}$ = 2 Hz, C_q), 141.1 (C_q), 138.1 (C_q), 127.6 (CH), 125.3 (CH), 123.5 (CH), 121.5 ($^{3}J_{C\text{-}F}$ = 8 Hz, CH), 114.7 ($^{2}J_{C\text{-}F}$ = 22 Hz, CH), 67.4 (C_q), 60.5 (CH_2), 55.4 (CH), 33.2 (CH_2), 29.0 (CH_3), 21.4 (CH_3), 14.2 (CH_3).

^{19}F-NMR (283 MHz, $CDCl_3$) δ = –(124.0–124.2) (m).

IR (neat): 2977, 1719, 1505, 1212, 1186, 1035, 818 cm^{-1}.

MS (EI) *m/z* (relative intensity): 327 (10) [M^+], 216 (65), 171 (20), 143 (100), 128 (75), 111 (55).

HR-MS (ESI) *m/z* calcd for $C_{20}H_{23}FNO_2$ [M + H^+] 328.1713, found 328.1707.



The representative procedure was followed using *N*-(4-methoxyphenyl) -1-(naphthalen-2-yl)ethan-1-imine (**104l**) (138 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105la** and **105la'** (154 mg, 82%, 5:1) as a colorless oil.

IR (neat): 2977, 1720, 1506, 1235, 1176, 1033, 828, 746, 477 cm^{-1}.

MS (EI) *m/z* (relative intensity): 375 (30) [M^+], 253 (55), 179 (100), 165 (65), 123 (88), 108 (15).

HR-MS (ESI) *m/z* calcd for $C_{24}H_{25}NO_3$ [M^+] 375.1834, found 375.1818.

Ethyl 1-[(4-methoxyphenyl)amino]-1-methyl-2,3-dihydro-1*H*-cyclopenta[*b*]naphthalene -2-carboxylate (105la, major product**)**:

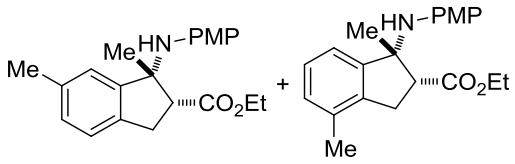
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.80 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.69 (s, 1H), 7.47 (s, 1H), 7.46–7.39 (m, 2H), 6.59–6.56 (m, 2H), 6.39–6.36 (m, 2H), 4.24–4.12 (m, 2H), 3.89 (s_{br}, 1H), 3.68 (s, 3H), 3.48–3.41 (m, 1H), 3.33 (dd, *J* = 9.1, 8.0 Hz, 1H), 3.23 (dd, *J* = 16.0, 8.0 Hz, 1H), 1.86 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 172.4 (C_q), 154.6 (C_q), 145.2 (C_q), 139.4 (C_q), 138.2 (C_q), 133.6 (C_q), 132.5 (C_q), 128.1 (CH), 127.3 (CH), 125.6 (CH), 125.0 (CH), 123.7 (CH), 122.7 (CH), 122.4 (CH), 113.5 (CH), 67.2 (C_q), 60.6 (CH_2), 55.9 (CH_3), 55.3 (CH), 32.9 (CH_2), 27.5 (CH_3), 14.3 (CH_3).

Ethyl 3-[(4-methoxyphenyl)amino]-3-methyl-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalene-2-carboxylate (105la', minor product**)**:

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.89 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.56–7.48 (m, 2H), 7.28 (d, *J* = 8.4 Hz, 1H), 6.51–6.47 (m, 2H), 6.29–6.22 (m, 2H), 4.24–4.12 (m, 2H), 3.89 (s_{br}, 1H), 3.64 (s, 3H), 3.53–3.41 (m, 3H), 1.88 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 172.4 (C_q), 154.1 (C_q), 142.9 (C_q), 138.6 (C_q), 136.9 (C_q), 133.5 (C_q), 129.9 (C_q), 128.3 (CH), 127.4 (CH), 126.1 (CH), 125.6 (CH), 124.3 (CH), 122.2 (CH), 121.9 (CH), 113.5 (CH), 68.7 (C_q), 60.6 (CH_2), 55.3 (CH_3), 54.9 (CH), 31.5 (CH_2), 29.5 (CH_3), 14.2 (CH_3).



The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*m*-tolyl) ethan-1-imine (**104m**) (120 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 10/1→5/1) yielded **105ma** and **105ma'** (126 mg, 74%, 4:1) as a colorless solid.

M.p. = 63–64 ℃.

IR (neat): 2977, 1720, 1507, 1231, 1171, 1035, 812, 449 cm^{-1}.

MS (EI) m/z (relative intensity): 339 (20) [M^+], 217 (25), 143 (65), 123 (100), 108 (15).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{25}NO_3$ [M^+] 339.1834, found 339.1827.

Ethyl 1-[(4-methoxyphenyl)amino]-1,6-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ma):

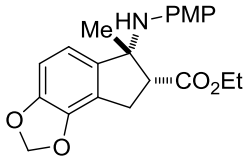
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.12–7.10 (m, 2H), 6.96 (s, 1H), 6.58 (dd, *J* = 8.9, 1.7 Hz, 2H), 6.29 (dd, *J* = 8.9, 1.7 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 1H), 3.70 (s, 3H), 3.25 (dd, *J* = 8.5, 8.8 Hz, 1H), 3.16–2.96 (m, 2H), 2.34 (s, 3H), 1.79 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.7 (C_q), 154.4 (C_q), 146.2 (C_q), 138.5 (C_q), 138.1 (C_q), 136.2 (C_q), 129.0 (CH), 124.4 (CH), 124.3 (CH), 122.7 (CH), 113.4 (CH), 67.6 (C_q), 60.4 (CH_2), 55.2 (CH_3), 55.2 (CH), 32.7 (CH_2), 28.3 (CH_3), 21.3 (CH_3), 14.1 (CH_3).

Ethyl 1-[(4-methoxyphenyl)amino]-1,4-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ma'):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.16–7.08 (m, 2H), 6.94 (d, *J* = 7.4 Hz, 1H), 6.58 (dd, *J* = 8.9, 1.7 Hz, 2H), 6.29 (dd, *J* = 8.9, 1.7 Hz, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 1H), 3.70 (s, 3H), 3.25 (dd, *J* = 8.5, 8.8 Hz, 1H), 3.16–2.96 (m, 2H), 2.28 (s, 3H), 1.78 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.7 (C_q), 154.5 (C_q), 145.8 (C_q), 139.8 (C_q), 138.3 (C_q), 133.9 (C_q), 128.8 (CH), 126.7 (CH), 123.1 (CH), 121.3 (CH), 113.4 (CH), 68.0 (C_q), 60.5 (CH_2), 54.9 (CH_3), 54.9 (CH), 31.7 (CH_2), 28.1 (CH_3), 18.7 (CH_3), 14.1 (CH_3).



Ethyl 6-[(4-methoxyphenyl)amino]-6-methyl-7,8-dihydro-6*H*-indeno[4,5-*d*][1,3] dioxole-7-carboxylate (105na): The representative procedure was followed using 1-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104n**) (135 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→10/1) yielded **105na** (147 mg, 80%) as a colorless solid.

M.p. = 85–86 ℃.

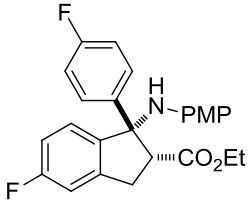
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 6.67 (d, *J* = 7.9 Hz, 1H), 6.59 (dd, *J* = 8.2, 2.3 Hz, 2H), 6.52 (d, *J* = 7.9 Hz, 1H), 6.33 (dd, *J* = 8.2, 2.3 Hz, 2H), 5.98 (d, *J* = 11 Hz, 1H), 5.97 (d, *J* = 11 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.73 (s_{br}, 1H), 3.70 (s, 3H), 3.25 (t, *J* = 8.8 Hz, 1H), 3.15–2.97 (m, 2H), 1.73 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.3 (C_q), 154.6 (C_q), 147.4 (C_q), 142.9 (C_q), 141.5 (C_q), 138.3 (C_q), 123.4 (CH), 121.7 (C_q), 116.7 (CH), 113.5 (CH), 106.9 (CH), 101.0 (CH_2), 67.4 (C_q), 60.5 (CH_2), 55.9 (CH_3), 55.2 (CH), 28.8 (CH_2), 28.1 (CH_3), 14.1 (CH_3).

IR (neat): 2976, 1721, 1508, 1462, 1233, 1035, 823, 513 cm^{-1}.

MS (EI) *m/z* (relative intensity): 369 (20) [M^+], 247 (75), 173 (100), 143 (40), 123 (70), 108 (55), 80 (30).

HR-MS (ESI) *m/z* calcd for $C_{21}H_{23}NO_5$ [M^+] 369.1576, found 369.1578.



Ethyl 5-fluoro-1-(4-fluorophenyl)-1-[(4-methoxyphenyl)amino]-2,3-dihydro-1*H*-indene-2-carboxylate (105oa): The representative procedure was followed using 1,1-bis(4-fluorophenyl)-*N*- (4-methoxyphenyl)methanimine (**104o**) (162 mg, 0.50 mmol),

ethyl acrylate (**38a**) (107 μL, 1.0 mmol) and $Mn_2(CO)_{10}$ (19.6 mg, 10 mol %). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→*5*/1) yielded **105oa** (154 mg, 73%) as a colorless solid.

M.p. = 141–142 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.54–7.49 (m, 2H), 7.08–6.95 (m, 4H), 6.80–6.74 (m, 1H), 6.58 (dd, *J* = 9.0, 1.1 Hz, 2H), 6.37 (dd, *J* = 9.0, 1.1 Hz, 2H), 4.66 (s_{br}, 1H), 4.20–4.01 (m, 2H), 3.66 (s, 3H), 3.65–3.48 (m, 2H), 3.25–3.13 (m, 1H), 1.15 (t, *J* = 7.2 Hz, 3H).

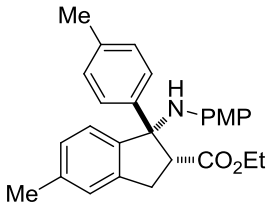
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.0 (C_q), 162.7 ($^1J_{C\text{-}F}$ = 246 Hz, C_q), 162.0 ($^1J_{C\text{-}F}$ = 246 Hz, C_q), 153.0 (C_q), 143.5 ($^3J_{C\text{-}F}$ = 8 Hz, C_q), 140.6 ($^4J_{C\text{-}F}$ = 3 Hz, C_q), 139.4 ($^4J_{C\text{-}F}$ = 3 Hz, C_q), 138.6 (C_q), 128.9 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 126.6 ($^3J_{C\text{-}F}$ = 9 Hz, CH), 119.0 (CH), 115.0 ($^2J_{C\text{-}F}$ = 22 Hz, CH), 113.9 (CH), 113.3 ($^2J_{C\text{-}F}$ = 23 Hz, CH), 112.9 ($^2J_{C\text{-}F}$ = 23 Hz, CH), 72.4 (C_q), 60.9 (CH_2), 59.7 (CH_3), 55.4 (CH), 33.8 ($^4J_{C\text{-}F}$ = 2 Hz, CH_2), 14.0 (CH_3).

^{19}F-NMR (283 MHz, $CDCl_3$) δ = –(114.2–114.3) (m), –(115.6–115.8) (m).

IR (neat): 3359, 1718, 1511, 1241, 1180, 1037, 810, 574, 475 cm^{-1}.

MS (EI) *m/z* (relative intensity): 423 (10) [M^+], 300 (45), 227 (100), 201 (25), 123 (35), 108 (30).

HR-MS (ESI) *m/z* calcd for $C_{25}H_{23}F_2NO_3$ [M^+] 423.1646, found 423.1643.



Ethyl-1-[(4-methoxyphenyl)amino]-5-methyl-1-(*p*-tolyl)-2,3-dihydro-1*H*-indene-2-carboxylate (105pa): The representative procedure was followed using *N*-(4-methoxyphenyl)-1,1-di-*p*-tolylmethanimine (**104p**) (158 mg, 0.50 mmol) and ethyl acrylate (**38a**) (107 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→*5*/1) yielded **105pa** (149 mg, 72%) as a colorless solid.

M.p. = 118–119 ℃.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.46 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.11–7.09 (m, 2H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.59 (dd, *J* = 9.0, 2.2 Hz, 2H), 6.42 (dd, *J* = 9.0, 2.2 Hz, 2H), 4.74 (s_{br}, 1H), 4.14–4.04 (m, 2H), 3.67 (s, 3H), 3.63 (dd, *J* = 8.4, 7.8 Hz, 1H), 3.52 (dd, *J* = 16.0, 8.4 Hz, 1H), 3.22 (dd, *J* = 16.0, 7.8 Hz, 1H), 2.39 (s, 3H), 2.32 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H).

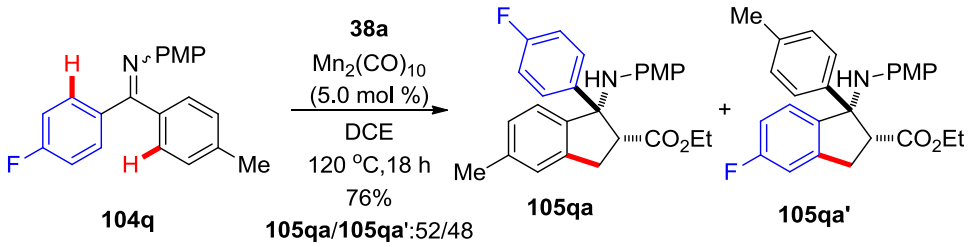
^{13}C-NMR (125 MHz, $CDCl_3$) δ = 172.6 (C_q), 152.3 (C_q), 142.6 (C_q), 141.1 (C_q), 141.0 (C_q), 139.1 (C_q), 137.5 (C_q), 136.3 (C_q), 128.7 (CH), 127.0 (CH), 126.8 (CH), 125.2 (CH), 125.1 (CH), 118.2 (CH), 113.7 (CH), 72.9 (C_q), 60.6 (CH_2), 59.1 (CH_3), 55.4 (CH), 34.1 (CH_2), 21.2 (CH_3), 21.0 (CH_3), 14.1 (CH_3).

IR (neat): 2984, 1711, 1510, 1229, 1183, 1037, 823, 809, 528 cm^{-1}.

MS (EI) *m/z* (relative intensity): 415 (8) [M^+], 293 (100), 220 (55), 205 (35), 123 (30).

HR-MS (ESI) *m/z*calcd for $C_{27}H_{29}NO_3$ [M^+] 415.2147, found 415.2135.

Intramolecular Competition Experiment of 104q



N-[(4-Fluorophenyl)(*p*-tolyl)methylene]-4-methoxyaniline (**104q**) (160 mg, 0.5 mmol), ethyl acrylate (**38a**) (107 μL, 1.0 mmol), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %) and DCE (1.0 mL) were placed in a 25 mL Schlenk tube under N_2 and then stirred at 120 ℃ for 18 h. At ambient temperature, the crude GC-MS was measured to obtain the product ratio of 52:48. Then, the reaction mixture was transferred into a round bottom flask with EtOAc (20 mL) and concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1→5/1) to afford the mixture of products **105qa** and **105qa'** (160 mg, 76%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.53–7.49 (m, 2H), 7.43–7.39 (m, 2H), 7.18–7.14 (m, 2H), 7.10–6.88 (m, 7H), 6.80–6.73 (m, 1H), 6.59–6.53 (m, 4H), 6.40–6.34 (m, 4H), 4.68 (s, 2H), 4.17–3.98 (m, 4H), 3.69–3.41 (m, 10H), 3.24–3.12 (m, 2H), 2.37 (s, 3H), 2.30 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 172.3 (C_q), 172.2 (C_q), 162.6 ($^1J_{C\text{-}F}$ = 244 Hz, C_q), 161.8 ($^1J_{C\text{-}F}$ = 245 Hz, C_q), 152.7 (C_q), 152.6 (C_q), 143.3 ($^3J_{C\text{-}F}$ = 8 Hz, C_q), 142.0 (C_q), 141.2 (C_q), 141.1 ($^4J_{C\text{-}F}$ = 2 Hz, C_q), 140.8 (C_q), 139.6 ($^4J_{C\text{-}F}$ = 3 Hz, C_q), 138.8 ($^3J_{C\text{-}F}$ = 8 Hz, C_q), 137.8 (C_q), 136.6 (C_q), 128.9 (CH), 128.8 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 127.1 (CH), 126.8 (CH), 126.5 ($^3J_{C\text{-}F}$ = 8 Hz, CH), 125.4 (CH), 125.1 (CH), 118.7 (CH), 118.4 (CH), 114.8 ($^2J_{C\text{-}F}$ = 22 Hz, CH), 113.8 (CH), 113.3 ($^2J_{C\text{-}F}$ = 22 Hz, CH), 111.6 ($^2J_{C\text{-}F}$ = 22 Hz, CH), 72.7 (C_q), 72.6 (C_q), 60.8 (CH_2), 60.7 (CH_2), 59.6 (CH_3), 59.2 (CH_3), 55.5 (CH), 55.4 (CH), 34.1 (CH_2), 34.0 (CH_2), 21.3 (CH_3), 21.1 (CH_3), 14.1 (CH_3), 14.1 (CH_3).

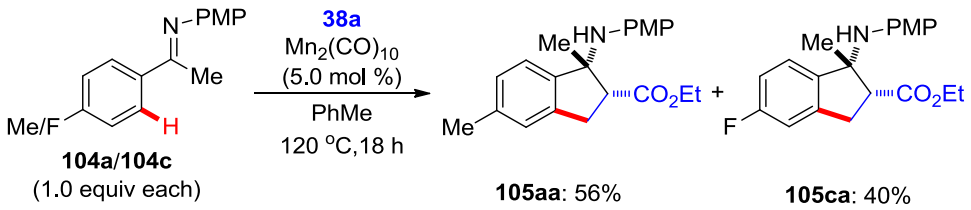
^{19}F-NMR (283 MHz, $CDCl_3$) δ = – (114.6–114.7) (m), – (116.0–116.1) (m).

IR (neat): 3369, 3306, 1712, 1509, 1240, 1179, 1032, 818, 526 cm^{-1}.

MS (EI) *m/z* (relative intensity): 419 (10) [M^+], 297 (100), 224 (55), 209 (30), 123 (35).

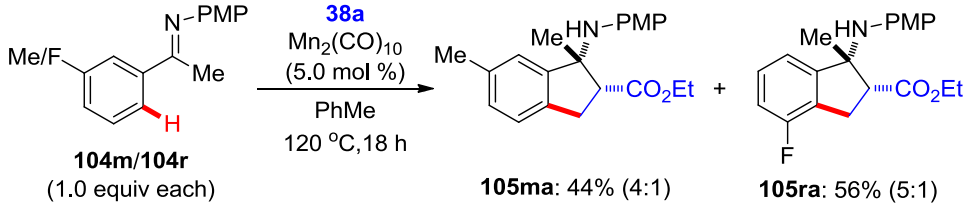
HR-MS (ESI) *m/z*calcd for $C_{26}H_{26}FNO_3$ [M^+] 419.1897, found 419.1892.

Intermolecular Competition Experiment between 104a and 104c

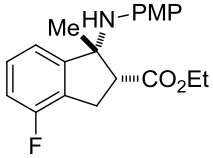


(*E*)-4-Methoxy-*N*-[1-(*p*-tolyl)ethylidene]aniline (**104a**) (120 mg, 0.5 mmol), (*E*)-*N*-[1-(4-fluorophenyl)ethylidene]-4-methoxyaniline (**104c**) (122 mg, 0.5 mmol), ethyl acrylate (**38a**) (54 μL, 0.5 mmol), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %) and toluene (2.0 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 120 ℃ for 18 h. At ambient temperature, the reaction mixture was transferred into a round bottom flask with EtOAc (20 mL) and concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1→5/1) to afford the products **105aa** (95 mg, 56%) and **105ca** (69 mg, 40%).

Intermolecular Competition Experiment between 104m and 104r



(*E*)-*N*-(4-methoxyphenyl)-1-(*m*-tolyl)ethan-1-imine (**104m**) (120 mg, 0.5 mmol), (*E*)-1-(3-fluorophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104r**) (122 mg, 0.5 mmol), ethyl acrylate (**38a**) (54 μL, 0.5 mmol), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %) and toluene (2.0 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 120 ℃ for 18 h. At ambient temperature, the crude GC was measured to obtain the GC conversion of the products (**105ma**+**105ma**') [44%, (4:1)] and (**105ra**+**105ra**') [56%, (5:1)], the ratio of (**105ma**+**105ma**'):(**105ra**+**105ra**') = 1:1.3.



Ethyl-4-fluoro-1-[(4-methoxyphenyl)amino]-1-methyl-2,3-dihydro-1*H*-indene-2-carboxylate (105ra):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.22–7.15 (m, 1H), 6.97 (dd, *J* = 8.9, 8.4 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.64–6.55 (m, 2H), 6.39–6.25 (m, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.78 (s_{br}, 1H), 3.71 (s, 3H), 3.33–3.12 (m, 3H), 1.79 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 172.2 (C_q), 159.5 ($^1J_{C-F}$ = 244 Hz, C_q), 154.8 (C_q), 149.8 ($^3J_{C-F}$ = 6 Hz, C_q), 138.2 (C_q), 128.6 ($^3J_{C-F}$ = 7 Hz, CH), 127.4 ($^2J_{C-F}$ = 19 Hz, C_q), 123.4 (CH), 119.7 ($^4J_{C-F}$ = 3 Hz, CH), 114.5 ($^2J_{C-F}$ = 21 Hz, CH), 113.7 (CH), 68.1 ($^4J_{C-F}$ = 2 Hz, C_q), 60.7 (CH_2), 55.4 (CH_3), 55.3 ($^4J_{C-F}$ = 1 Hz, CH), 29.0 (CH_2), 28.2 (CH_3), 14.2 (CH_3).

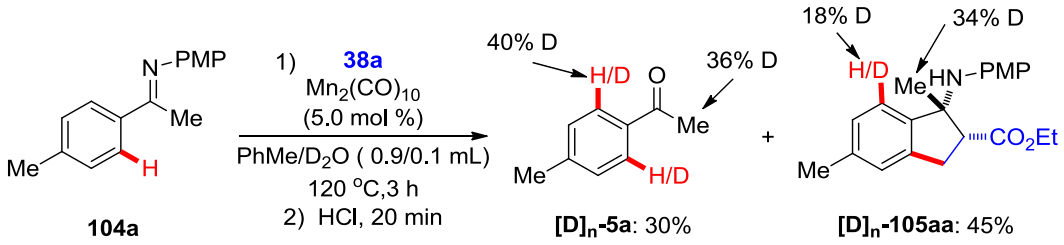
^{19}F-NMR (283 MHz, $CDCl_3$) δ = –(118.3–114.4) (m).

IR (neat): 2988, 1722, 1508, 1238, 905, 725 cm^{-1}.

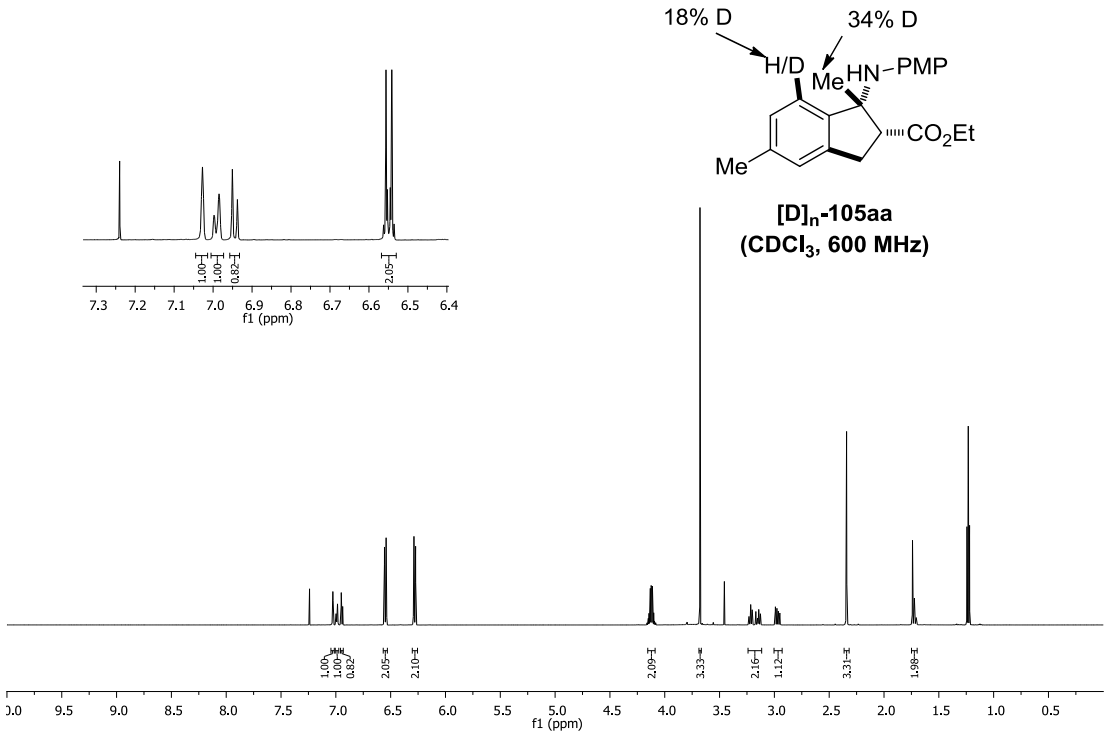
MS (EI) *m/z* (relative intensity): 343 (30) [M^+], 221 (10), 149 (50), 123 (100), 108 (30).

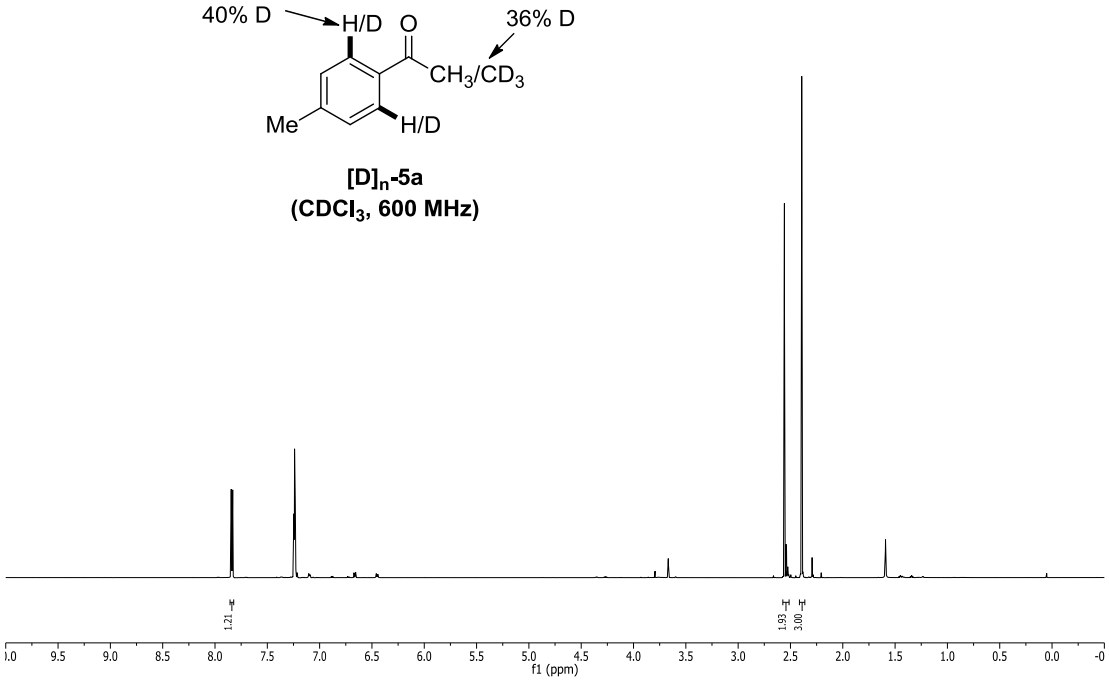
HR-MS (ESI) *m/z* calcd for $C_{20}H_{22}FNO_3$ [M^+] 343.1584, found 343.1591.

Manganese-Catalyzed H/D Exchange Experiment

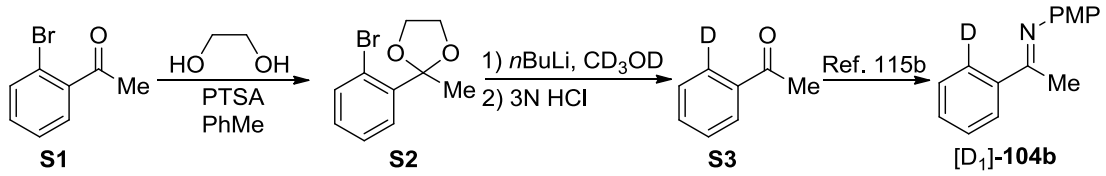


(*E*)-4-Methoxy-*N*-[1-(*p*-tolyl)ethylidene]aniline (**104a**) (120 mg, 0.5 mmol), ethyl acrylate (**38a**) (107 µL, 1.0 mmol), $Mn_2(CO)_{10}$ (9.8 mg, 5.0 mol %), toluene (0.9 mL) and D_2O (0.1 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 120 ℃ for 3 h. At ambient temperature, 1 M HCl (5.0 mL) was added and the mixture was stirred at ambient temperature for 20 min. The reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 15/1→5/1) yielded [D_n]-**5a** (20 mg, 30%) and [D]$_n$-**105aa** (76 mg, 45%).


18% D
34% D
H/D
Me
HN–PMP
CO2Et
Me
[D]n-105aa
(CDCl3, 600 MHz)
f1 (ppm)


40% D
H/D
O
36% D
CH3/CD3
Me
H/D
[D]n-5a
(CDCl3, 600 MHz)
f1 (ppm)

Preparation of $[D]_1$-**104b**[115b, 116]

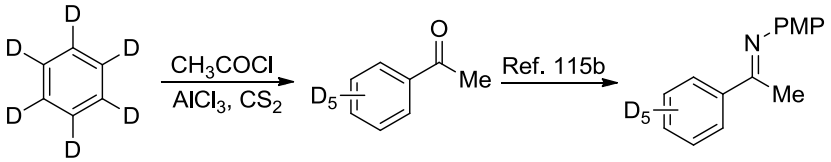


To a solution of 1-(2-bromophenyl)ethanone (10 mmol) in toluene (100 mL) was added ethane-1,2-diol (20 mmol) and *para*-toluenesulfonic acid monohydrate (2.0 mol %). The resulting mixture was stirred at 130 ℃ for 18 h using a Dean-Stark apparatus, and then cooled to ambient temperature and quenched by the addition of saturated $NaHCO_3$ solution (10 mL). The mixture was extracted with Et_2O (3 × 25 mL) and the combined organic phase was dried over Na_2SO_4, and filtered. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) afforded 2-(2-bromophenyl)-2-methyl-1,3-dioxolane (2.06 g, 85 %) as a colorless oil.

To a solution of 2-(2-bromophenyl)-2-methyl-1,3-dioxolane (1.95 g, 8.0 mmol) in Et_2O (15 mL) was slowly added a solution of *n*BuLi in hexane (3.5 mL, 8.8 mmol, 2.5 M) at −78 ℃. The mixture was stirred at the same temperature for 1 h and then CD_3OD (1.0 mL) was added. The reaction mixture was allowed to warm to 0 ℃ and stirred for 1.5 h. Then the mixture was diluted with H_2O (15 mL) and diethyl ether (15 mL). The organic phase was separated and HCl (3 N, 15 mL) was added. The resulting mixture was vigorously stirred for 12 h and the organic phase was separated, which was then washed with brine (10 mL) and dried over Na_2SO_4. The solvents were evaporated and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) to afford $[D]_1$-acetophenone (806 mg, 83 %) as a colorless oil.

The substrate $[D]_1$-**104b** was synthesized from $[D]_1$-acetophenone according to previously described methods.[115b]

Preparation of $[D]_5$-**104b**[115b, 117]

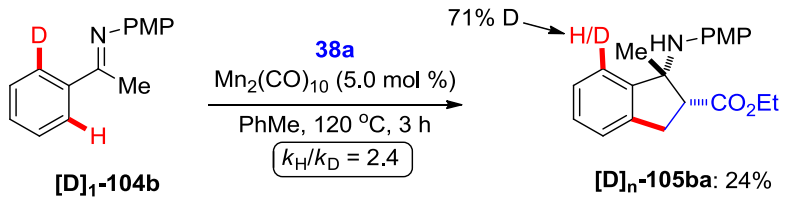


$[D]_6$-Benzene (1.2 ml, 12.8mmol), $AlCl_3$ (2.14 g, 16mmol), and anhydrous CS_2 (3.0 mL) were added to a 25-mL flask under N_2 atmosphere. To the mixture was dropwise added a solution of acetyl chloride (1.26 g, 16 mmol) in anhydrous CS_2 (5.0 mL) at 0 ℃. The resulting mixture was allowed to warm to ambient temperature and was stirred for 5 h. Then the mixture was heated to 50 ℃ for 3 h. After cooling to ambient temperature, the resulting mixture was poured into ice water and extracted with CH_2Cl_2 (3 × 30 mL). The organic layer was washed with saturated aqueous Na_2CO_3 (30 mL) and brine (20 mL), and then dried over Na_2SO_4.

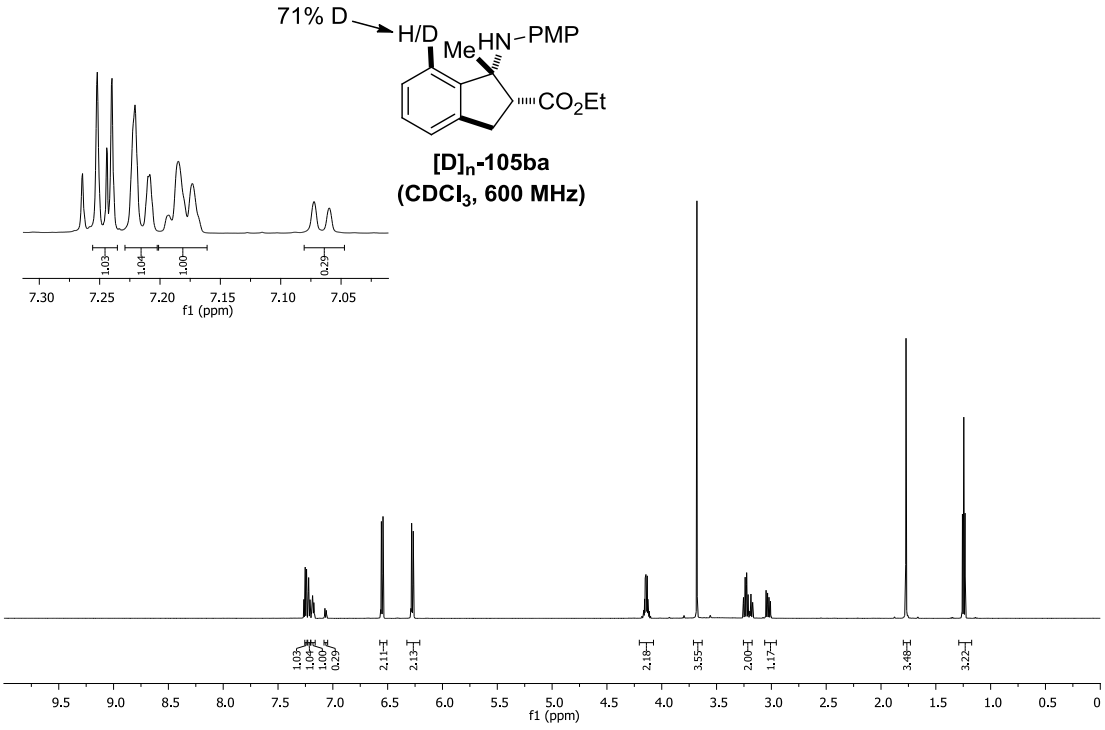
After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) afforded $[D]_5$-acetophenone (1.39 g, 87 %) as colorless oil.

The compound $[D]_5$-**104b** was synthesized from $[D]_5$-acetophenone according to previously described methods.[115b]

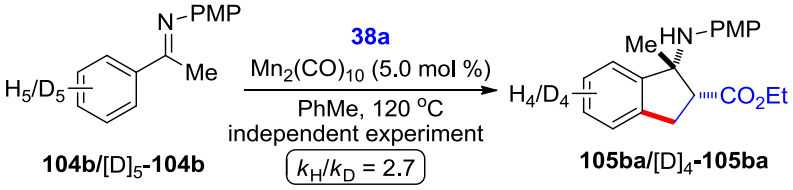
Kinetic Isotope Effect



$[D]_1$-4-Methoxy-*N*-[1-(*p*-tolyl)ethylidene]aniline ($[D]_1$-**104b**) (226 mg, 1.0 mmol), ethyl acrylate (**38a**) (214 μL, 2.0 mmol), $Mn_2(CO)_{10}$ (19.6 mg, 5.0 mol %) and toluene (3.0 mL) were placed in a 25 mL Schlenk tube under N_2, and then stirred at 120 ℃ for 3 h. At ambient temperature, the reaction mixture was transferred into a round flask with EtOAc and concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1→5/1) to afford the $[D]_n$-**105ba** (77 mg, 24%). The kinetic isotope effect of this reaction was determined to be $k_H/k_D \approx 2.4$ as estimated by ^{1}H-NMR spectroscopy.



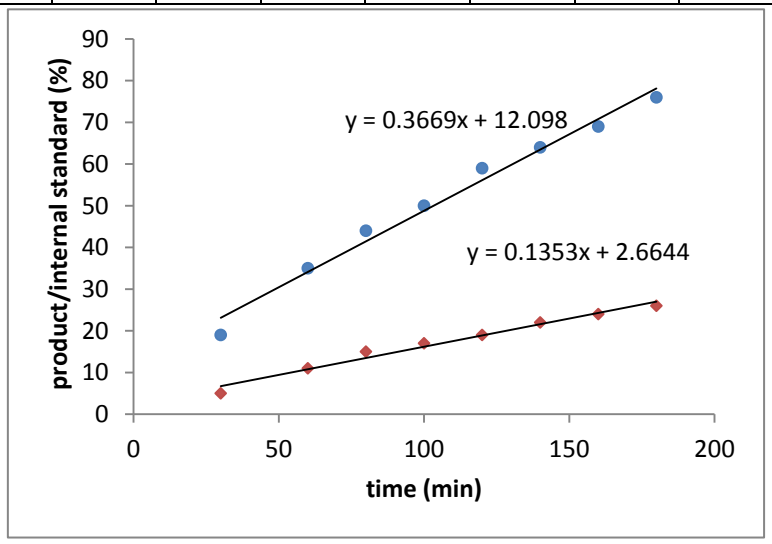
KIE Determined by GC



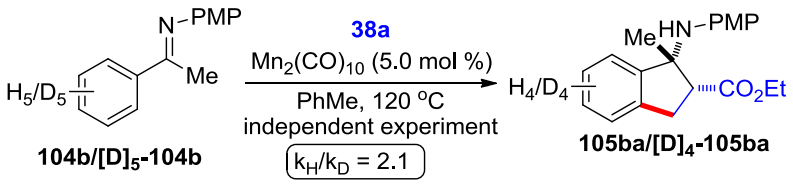
104b/[D]$_5$-**104b** **105ba**/[D]$_4$-**105ba**

Two parallel reactions of **38a** with **104b** and [D]$_5$-**104b** respectively were performed to determine the corresponding KIE value. **104b** (225 mg, 1.0mmol) or [D]$_5$-**104b** (230 mg, 1.0 mmol), ethyl acrylate (**38a**) (214 μL, 2.0 mmol), $Mn_2(CO)_{10}$ (19.6 mg, 5.0 mol %), 1,3,5-trimethoxybenzene (168 mg, 1.0 mmol) and toluene (3.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 120 ℃, a periodic aliquot (0.05 mL) was taking out by syringe and analyzed by GC to provide the following conversions:

Time (min)	30	60	80	100	120	140	160	180
105ba	19	35	44	50	59	64	69	76
[D]$_4$-**105ba**	5	11	15	17	19	22	24	26



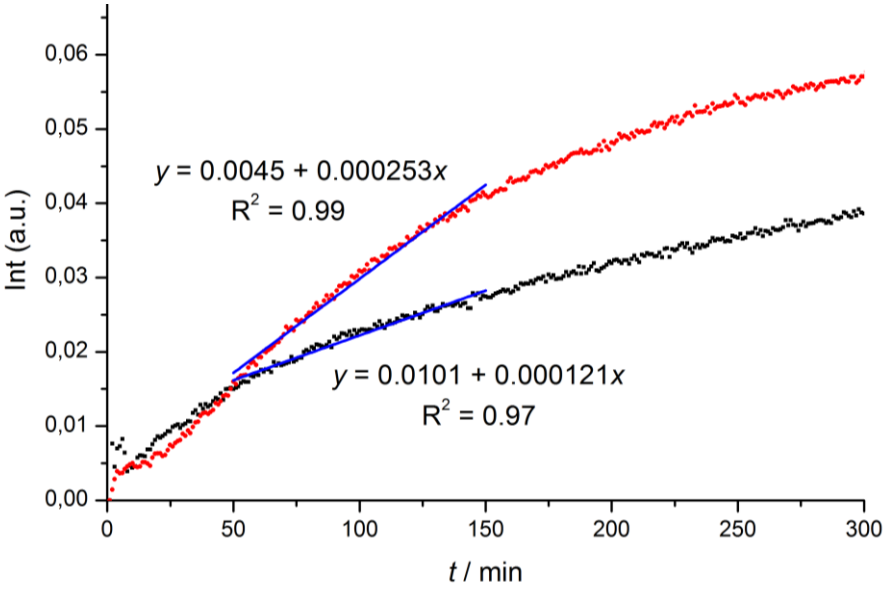
KIE Determined by *in situ* react IR



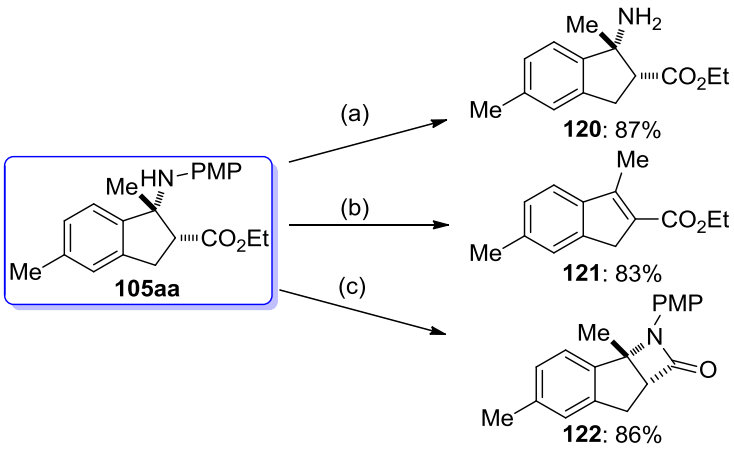
104b/[D]$_5$-104b **105ba/[D]$_4$-105ba**

Two parallel reactions of **38a** with **104b** and [D]$_5$-**104b**, respectively, were performed to determine the corresponding KIE value. **104b** (225 mg, 1.0mmol) or [D]$_5$-**104b** (230mg, 1.0 mmol), ethyl acrylate (**38a**) (214 μL, 2.0 mmol), $Mn_2(CO)_{10}$ (19.6 mg, 5.0 mol %), and toluene (3.0 mL) were placed in a 25 mL Schlenk tube, which was then equipped with the *in situ* react

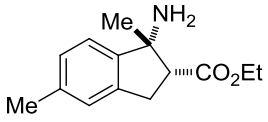
IR under N_2. The mixture was stirred at 120 ℃. The reaction rate was followed by integration of a vibrational band at 1350−1335 cm^{-1}. The kinetic isotope effect of this reaction was determined to be $k_H/k_D \approx 2.1$.



Diversification of Product 105aa



Reaction a: A solution of **105aa** (85 mg, 0.25 mmol) in MeCN (8 mL) was added dropwise within 10 min to a solution of CAN (343 mg, 2.5 equiv) in H_2O (8 mL) at 0 ℃. After 3 h stirring at ambient temperature, the reaction mixture was basified with NaOH (1 N) to pH = 12. Then the solution was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were acidified with HCl (1 N) until pH = 2, and then washed by HCl (1 N, 3 × 10 mL). The aqueous phase was basified with Na_2CO_3 solid to pH = 12, and then extracted with CH_2Cl_2 (4 × 10 mL). The combined organic phases were then dried over Na_2SO_4, and the solvent was removed under reduced pressure to afford the product **120** (51 mg, 87%) as colorless oil.



Ethyl 1-amino-1,5-dimethyl-2,3-dihydro-1*H*-indene-2-carboxylate (120):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.15 (d, *J* = 8.3 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 7.02 (s, 1H) 4.27–4.17 (m, 2H), 3.36 (dd, *J* = 15.8, 8.8 Hz, 2H), 3.15 (dd, *J* = 8.8, 8.1 Hz, 1H), 2.97 (dd, *J* = 15.8, 8.1 Hz, 1H), 2.32 (s, 3H), 1.69 (s_{br}, 2H), 1.64 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H).

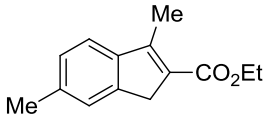
^{13}C-NMR (125 MHz, $CDCl_3$) δ = 172.7 (C_q), 145.7 (C_q), 140.2 (C_q), 137.6 (C_q), 127.8 (CH), 125.3 (CH), 121.9 (CH), 63.0 (C_q), 60.5 (CH_2), 56.3 (CH), 32.4 (CH_2), 28.6 (CH_3), 21.3 (CH_3), 14.5 (CH_3).

IR (neat): 2975, 1725, 1371, 1191, 1158, 1034, 815 cm^{-1}.

MS (EI) *m/z* (relative intensity): 233 (15) [M^+], 218 (100), 158 (30), 145 (85), 128 (30), 115 (20).

HR-MS (ESI) *m/z* calcd for $C_{14}H_{19}NO_2$ [M^+] 233.1416, found 233.1424.

Reaction b: **105aa** (85 mg, 0.25 mmol) and toluene (0.5 mL) were placed in a 25 mL sealed tube under N_2 and then stirred at 160 ℃ for 14 h. At ambient temperature, the reaction mixture was transferred into a round bottom flask with EtOAc (20 mL) and concentrated under reduced pressure, purified by column chromatography on silica gel (*n*-hexane/EtOAc: 50/1) to afford the product **121** (45 mg, 83%) as colorless oil.



Ethyl 3,6-dimethyl-1*H*-indene-2-carboxylate (121):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.38 (d, *J* = 7.8 Hz, 1H), 7.29 (s, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 3.62 (q, *J* = 2.5 Hz, 2H), 2.54 (t, *J* = 2.5 Hz, 3H), 2.43 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 165.9 (C_q), 151.3 (C_q), 143.7 (C_q), 142.7 (C_q), 137.6 (C_q), 128.7 (C_q), 127.3 (CH), 124.6 (CH), 120.7 (CH), 59.8 (CH_2), 38.5 (CH_2), 21.7 (CH_3), 14.5 (CH_3), 12.5 (CH_3).

IR (neat): 2980, 1696, 1253, 1197, 1051, 812, 755 cm^{-1}.

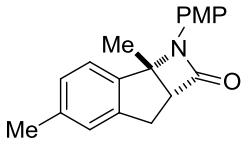
MS (EI) *m/z* (relative intensity): 216 (50) [M^+], 171 (23), 143 (100), 128 (65), 115 (23).

HR-MS (ESI) *m/z* calcd for $C_{14}H_{16}O_2$ [M^+] 216.1150, found 216.1150.

The spectral data are in accordance with those reported in the literature.[128]

Reaction c: A solution of LiHMDS (1.5 equiv, 0.38 mL, 1 N in THF) was slowly added to a solution of **105aa** (85 mg, 0.25 mmol) in THF (3 mL) at 0 ℃. The mixture was stirred for 1 h at 0 ℃, and then stirred at ambient temperature for 9 h and reacted with HCl (1 N, 10 mL). The

mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic phases were dried over Na_2SO_4 and filtered. The solvent was removed in vacuo. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1→1/1) afforded product **122** (63 mg, 86%) as a colorless oil.



1-(4-Methoxyphenyl)-5,7*b*-dimethyl-1,2*a*,3,7*b*-tetrahydro-2*H*-indeno[1,2-*b*]azet-2-one (122):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.42 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.07 (s, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 3.74 (s, 3H), 3.69 (d, *J* = 10.2 Hz, 1H), 3.33 (d, *J* = 17.4 Hz, 1H), 3.09 (dd, *J* = 17.3, 10.2 Hz, 1H), 2.31 (s, 3H), 1.96 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 167.1 (C_q), 156.1 (C_q), 144.4 (C_q), 139.0 (C_q), 138.5 (C_q), 130.4 (C_q), 127.5 (CH), 127.0 (CH), 124.1 (CH), 119.7 (CH), 114.2 (CH), 71.8 (C_q), 59.4 (CH_3), 55.4 (CH), 29.9 (CH_2), 21.4 (CH_3), 20.5 (CH_3).

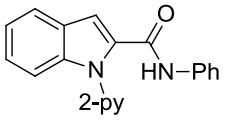
IR (neat): 2926, 1726, 1507, 1368, 1238, 1029, 824, 518 cm^{-1}.

MS (EI) *m/z* (relative intensity): 293 (8) [M^+], 145 (45), 144 (100), 129 (95), 128 (58), 78 (13).

HR-MS (ESI) *m/z* calcd for $C_{19}H_{19}NO_2$ [M^+] 293.1416, found 293.1426.

4.6 Manganese(I)-Catalyzed C–H Aminocarbonylation of Heteroarenes

Characterization Data of Products 107 and 124



***N*-Phenyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107aa)**: The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107aa** (149 mg, 95%) as a white solid. The reaction using *n*Bu_2O instead of Et_2O yielded **107aa** (142 mg, 91%).

M.p. = 176–177 ℃.

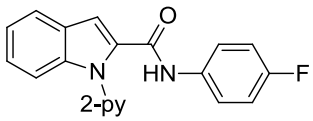
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 9.32 (s, 1H), 8.54 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H), 7.87 (td, *J* = 7.7, 1.9 Hz, 1H), 7.51–7.41 (m, 3H), 7.36–7.26 (m, 3H), 7.25–7.13 (m, 3H), 7.07–6.99 (m, 2H), 6.98 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 160.0 (C_q), 151.2 (C_q), 149.1 (CH), 138.6 (C_q), 138.5 (CH), 137.9 (C_q), 133.7 (C_q), 128.7 (CH), 126.8 (C_q), 125.0 (CH), 124.2 (CH), 122.5 (CH), 122.0 (CH), 121.8 (CH), 121.1 (CH), 120.5 (CH), 110.6 (CH), 108.7 (CH).

IR (neat): 3242, 1661, 1593, 1542, 1470, 1435, 1308, 1218, 739, 688, 508 cm^{-1}.

MS (EI) *m/z* (relative intensity): 313 (5) [M^+], 221 (100), 192 (20).

HR-MS (EI) *m/z* calcd for $C_{20}H_{15}N_3O$ [M^+] 313.1215, found 313.1221.



***N*-(4-Fluorophenyl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ab):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-fluoro-4-isocyanatobenzene (**106b**) (76 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ab** (152 mg, 92%) as a white solid. The reaction using nBu_2O instead of Et_2O yielded **107ab** (136 mg, 82%).

M.p. = 197–198 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.55 (s, 1H), 8.51 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.91 (dt, *J* = 7.7, 1.9 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.45–7.13 (m, 6H), 7.00 (dt, *J* = 7.4, 1.1 Hz, 1H), 6.95 (s, 1H), 6.89–6.83 (m, 2H).

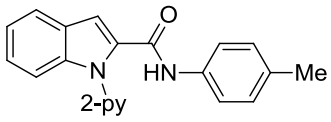
^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.4 (C_q), 158.1 ($^1J_{C–F}$ = 240 Hz, C_q), 150.9 (C_q), 148.8 (CH), 138.5 (CH), 137.8 (C_q), 135.3 ($^4J_{C–F}$ = 3 Hz, C_q), 133.5 (C_q), 126.4 (C_q), 124.9 (CH), 122.4 (CH), 122.0 (CH), 121.6 ($^3J_{C–F}$ = 7 Hz, CH), 121.5 (CH), 120.6 (CH), 115.1 ($^2J_{C–F}$ = 20 Hz, CH), 111.2 (CH), 108.3 (CH).

^{19}F-NMR (283 MHz, DMSO-d_6) δ = –(118.9–119.0) (m).

IR (neat): 3184, 1662, 1569, 1541, 1502, 1469, 1201, 888, 734, 711, 513 cm^{-1}.

MS (EI) *m/z* (relative intensity): 331 (5) [M^+], 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}FN_3O$ [M^+] 331.1121, found 331.1121.



1-(Pyridin-2-yl)-*N*-(*p*-tolyl)-1*H*-indole-2-carboxamide (107ac): The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanato-4-methylbenzene (**106c**) (74 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ac** (113 mg, 69%) as a white solid.

M.p. = 192–193 ℃.

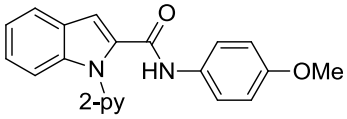
^{1}H-NMR (300 MHz, DMSO-d_6) δ = 10.49 (s, 1H), 8.63–8.47 (m, 1H), 7.98 (td, *J* = 7.7, 2.0 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.55–7.35 (m, 4H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.21 (dd, *J* = 8.4, 6.4 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 2.24 (s, 3H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.3 (C_q), 150.9 (C_q), 148.7 (CH), 138.4 (CH), 137.8 (C_q), 136.4 (C_q), 133.8 (C_q), 132.4 (C_q), 128.9 (CH), 126.5 (C_q), 124.8 (CH), 122.3 (CH), 121.9 (CH), 121.5 (CH), 120.6 (CH), 119.8 (CH), 111.1 (CH), 108.1 (CH), 20.4 (CH_3).

IR (neat): 3017, 1659, 1591, 1534, 1470, 1442, 1307, 801, 737, 511 cm^{-1}.

MS (EI) *m/z* (relative intensity): 327 (8) [M$^+$], 221 (100), 192 (18), 98 (18).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O$ [M$^+$] 327.1372, found 327.1358.



***N*-(4-Methoxyphenyl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ad):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanato-4-methoxybenzene (**106d**) (82 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ad** (162 mg, 94%) as a white solid.

M.p. = 164–165 ℃.

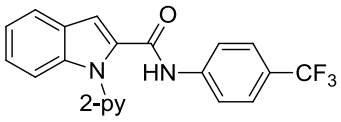
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.34 (s, 1H), 8.51 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.87 (ddd, *J* = 7.7, 7.8, 1.9 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.38–7.14 (m, 6H), 7.01 (dd, *J* = 7.3, 7.1 Hz, 1H), 6.92 (s, 1H), 6.70 (d, *J* = 9.0 Hz, 2H), 3.71 (s, 3H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.1 (C_q), 155.4 (C_q), 150.9 (C_q), 148.7 (CH), 138.4 (CH), 137.8 (C_q), 133.9 (C_q), 132.0 (C_q), 126.5 (C_q), 124.7 (CH), 122.3 (CH), 121.9 (CH), 121.5 (CH), 121.3 (CH), 120.6 (CH), 113.7 (CH), 111.1 (CH), 107.9 (CH), 55.1 (CH_3).

IR (neat): 3272, 1651, 1538, 1436, 1243, 1021, 824, 738, 550 cm^{-1}.

MS (EI) *m/z* (relative intensity): 343 (8) [M$^+$], 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O_2$ [M$^+$] 343.1321, found 343.1320.



1-(Pyridin-2-yl)-*N*-[4-(trifluoromethyl)phenyl]-1*H*-indole-2-carboxamide (107ae): The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanato-4-(trifluoromethyl)benzene (**106e**) (103 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ae** (144 mg, 76%) as a white solid.

M.p. = 229–230 ℃.

^{1}H-NMR (300 MHz, DMSO-d_6) δ = 10.86 (s, 1H), 8.63–8.49 (m, 1H), 8.02 (td, *J* = 7.7, 1.9 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.81 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.53–7.39 (m, 3H), 7.33 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.29–7.20 (m, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.9 (C_q), 150.8 (C_q), 148.8 (CH), 142.6 (C_q), 138.5

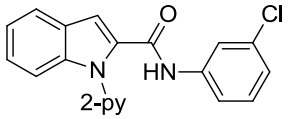
(CH), 138.0 (C_q), 133.1 (C_q), 126.4 (C_q), 125.8 (q, $^3J_{C-F}$ = 3.8 Hz, CH), 125.4 (t, $^1J_{C-F}$ = 270 Hz, C_q), 125.2 (CH), 123.5 (m, C_q), 122.5 (CH), 122.1 (CH), 121.6 (CH), 120.7 (CH), 119.6 (CH), 111.1 (CH), 108.9 (CH).

^{19}F-NMR (282 MHz, DMSO-d_6) δ = -55.64.

IR (neat): 2998, 1669, 1592, 1537, 1470, 1441, 1310, 1107, 824, 738, 415 cm^{-1}.

MS (EI) *m/z* (relative intensity): 381 (8) [M^+], 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{21}H_{14}F_3N_3O$ [M^+] 381.1089, found 381.1071.



***N*-(3-Chlorophenyl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107af):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-chloro-3-isocyanatobenzene (**106f**) (85 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107af** (137 mg, 79%) as a white solid.

M.p. = 184–185 ℃.

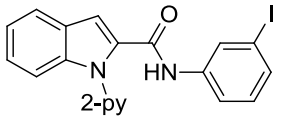
^{1}H-NMR (500 MHz, DMSO-d_6) δ = 10.70 (s, 1H), 8.57 (ddd, *J* = 4.8, 2.0, 0.9 Hz, 1H), 8.03 (td, *J* = 7.7, 1.9 Hz, 1H), 7.87 (s, 1H), 7.81 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.62 (ddd, *J* = 8.3, 2.0, 0.9 Hz, 1H), 7.56 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.50–7.41 (m, 3H), 7.40–7.28 (m, 2H), 7.25 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.14 (ddd, *J* = 8.0, 2.2, 0.9 Hz, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.7 (C_q), 150.7 (C_q), 148.8 (CH), 140.4 (C_q), 138.5 (CH), 137.9 (C_q), 133.2 (C_q), 132.9 (C_q), 130.2 (CH), 126.4 (C_q), 125.1 (CH), 123.1 (CH), 122.5 (CH), 122.1 (CH), 121.6 (CH), 120.6 (CH), 119.1 (CH), 118.1 (CH), 111.1 (CH), 108.7 (CH).

IR (neat): 3229, 1662, 1588, 1529, 1469, 1420, 1303, 1287, 776, 737, 569 cm^{-1}.

MS (EI) *m/z* (relative intensity): 347 (8) [M^+], 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}ClN_3O$ [M^+] 347.0825, found 347.0818.



***N*-(3-Iodophenyl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ag):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-iodo-3-isocyanatobenzene (**106g**) (135 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ag** (162 mg, 74%) as a white solid.

M.p. = 160–161 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.23 (s, 1H), 8.56 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.97–7.86 (m,

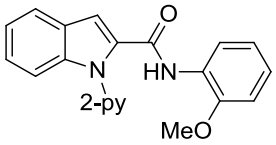
2H), 7.50 (dt, *J* = 8.0, 0.9 Hz, 1H), 7.40–7.31 (m, 5H), 7.26–7.18 (m, 1H), 7.06 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.01 (s, 1H), 6.90 (t, *J* = 8.0 Hz, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.6 (C_q), 150.8 (C_q), 148.8 (CH), 140.4 (C_q), 138.5 (CH), 137.9 (C_q), 133.2 (C_q), 132.0 (CH), 130.6 (CH), 127.8 (CH), 126.4 (C_q), 125.1 (CH), 122.4 (CH), 122.1 (CH), 121.6 (CH), 120.6 (CH), 118.9 (CH), 111.1 (CH), 108.7 (CH), 94.3 (C_q).

IR (neat): 3239, 1651, 1583, 1527, 1468, 1439, 1188, 772, 737, 551 cm^{-1}.

MS (EI) *m/z* (relative intensity): 439 (8) [M^+], 221 (100), 192 (15), 43 (16).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}IN_3O$ [M^+] 439.0182, found 439.0191.



***N*-(2-Methoxyphenyl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ah):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanato-2-methoxybenzene (**106h**) (82 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ah** (148 mg, 86%) as a white solid.

M.p. = 146–147 ℃.

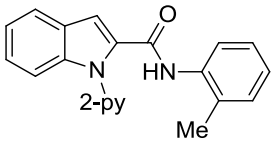
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.67 (s, 1H), 8.64–8.58 (m, 1H), 8.38 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.87 (td, *J* = 7.7, 2.0 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.34–7.30 (m, 2H), 7.28–7.19 (m, 2H), 7.05 (td, *J* = 7.8, 1.7 Hz, 1H), 6.99–6.84 (m, 2H), 3.88 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 159.2 (C_q), 151.2 (C_q), 149.2 (CH), 147.8 (C_q), 138.9 (C_q), 138.1 (CH), 133.8 (C_q), 127.6 (C_q), 126.8 (C_q), 125.2 (CH), 123.7 (CH), 122.4 (CH), 122.0 (CH), 121.7 (CH), 121.1 (CH), 120.9 (CH), 119.6 (CH), 111.3 (CH), 109.8 (CH), 108.2 (CH), 55.6 (CH_3).

IR (neat): 3398, 3057, 1660, 1530, 1435, 1220, 1025, 734, 535 cm^{-1}.

MS (EI) *m/z* (relative intensity): 343 (3) [M^+], 221 (100), 192 (20).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O_2$ [M^+] 343.1321, found 343.1319.



1-(Pyridin-2-yl)-*N*-(*o*-tolyl)-1*H*-indole-2-carboxamide (107ai): The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanato-2-methylbenzene (**106i**) (74 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ai** (111 mg, 70%) as a white solid.

M.p. = 157–158 ℃.

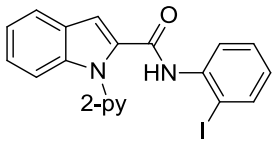
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.53 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 8.32 (s, 1H), 7.84 (ddd, *J* = 8.0, 7.5, 1.9 Hz, 1H), 7.77 (d, *J* = 7.0 Hz, 1H), 7.64–7.55 (m, 1H), 7.46 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.43–7.38 (m, 1H), 7.33–7.25 (m, 2H), 7.22–7.11 (m, 4H), 7.06 (td, *J* = 7.4, 1.4 Hz, 1H), 2.25 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 159.8 (C_q), 151.2 (C_q), 149.2 (CH), 138.7 (C_q), 138.3 (CH), 135.5 (C_q), 133.7 (C_q), 130.4 (CH), 129.4 (C_q), 126.8 (C_q), 126.6 (CH), 125.2 (CH ×2), 123.1 (CH), 122.5 (CH), 122.0 (CH), 121.8 (CH), 121.1 (CH), 111.1 (CH), 108.4 (CH), 17.7 (CH_3).

IR (neat): 3240, 3018, 1654, 1544, 1444, 1431, 1294, 1264, 739, 680, 436 cm^{-1}.

MS (EI) *m/z* (relative intensity): 327 (5) [M^+], 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O$ [M^+] 327.1372, found 327.1370.



***N*-(2-Iodophenyl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107aj):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-iodo-2-isocyanatobenzene (**106j**) (135 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107aj** (173 mg, 79%) as a white solid. When using nBu_2O instead of Et_2O yielded **107aj** (158 mg, 72%).

M.p. = 199–200 ℃.

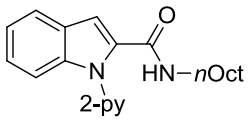
^{1}H-NMR (500 MHz, DMSO-d_6) δ = 10.11 (s, 1H), 8.59 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H), 8.02–7.98 (m, 1H), 7.92 (dd, *J* = 7.9, 1.30 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.53 (dt, *J* = 8.0, 0.9 Hz, 1H), 7.50–7.39 (m, 5H), 7.32 (ddd, *J* = 8.4, 7.0, 1.2 Hz, 1H), 7.24 (td, *J* = 7.5, 7.0, 1.0 Hz, 1H), 7.03 (td, *J* = 7.6, 1.7 Hz, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.6 (C_q), 150.9 (C_q), 148.7 (CH), 139.1 (C_q), 138.8 (CH), 138.4 (CH), 138.0 (C_q), 133.1 (C_q), 128.6 (CH), 128.0 (CH), 127.8 (CH), 126.4 (C_q), 124.9 (CH), 122.4 (CH), 122.0 (CH), 121.6 (CH), 120.9 (CH), 111.4 (CH), 108.3 (CH), 97.6 (C_q).

IR (neat): 3199, 3040, 1660, 1592, 1543, 1440, 1203, 830, 733, 515, 480 cm^{-1}.

MS (EI) *m/z* (relative intensity): 439 (5) [M^+], 312 (5), 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}N_3OI$ [M^+] 439.0182, found 439.0185.



***N*-*n*-Octyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ak):** The representative

procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanatooctane (**106k**) (86 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ak** (106 mg, 61%) as a white solid.

M.p. = 125–126 ℃.

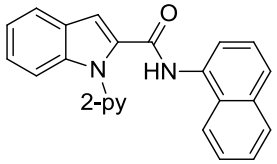
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.56 (s, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.38 (dd, *J* = 8.1, 6.0 Hz, 2H), 7.30–7.21 (m, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 6.97 (s, 1H), 6.76 (s, 1H), 3.30–3.22 (m, 2H), 1.53–1.41 (m, 2H), 1.32–1.19 (m, 10H), 0.91–0.85 (m, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 161.7 (C_q), 151.4 (C_q), 148.9 (CH), 138.4 (C_q), 138.1 (CH), 133.9 (C_q), 126.9 (C_q), 124.6 (CH), 122.4 (CH), 121.8 (CH), 121.4 (CH), 121.2 (CH), 111.0 (CH), 107.3 (CH), 39.6 (CH_2), 31.7 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.8 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (neat): 3297, 2919, 2850, 1642, 1548, 1471, 1439, 1273, 1225, 733, 720, 685, 525, 443 cm^{-1}.

MS (EI) *m/z* (relative intensity): 349 (8) [M^+], 221 (100), 192 (20).

HR-MS (EI) *m/z* calcd for $C_{22}H_{27}N_3O$ [M^+] 349.2154, found 349.2155.



***N*-(Naphthalen-1-yl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107am)**: The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 1-isocyanatonaphthalene (**106m**) (93 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107am** (141 mg, 78%) as a white solid.

M.p. = 225–226 ℃.

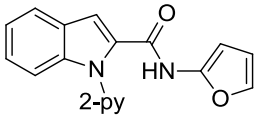
^{1}H-NMR (500 MHz, DMSO-d_6) δ = 10.64 (s, 1H), 8.63 (dd, *J* = 5.0, 1.7 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 8.01 (t, *J* = 7.7 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.86–7.83 (m, 2H), 7.72–7.47 (m, 7H), 7.43 (dd, *J* = 7.4, 4.9 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 160.6 (C_q), 150.9 (C_q), 148.8 (CH), 138.4 (CH), 137.7 (C_q), 133.9 (C_q), 133.7 (C_q), 133.2 (C_q), 128.8 (C_q), 127.9 (CH), 126.7 (C_q), 126.0 (CH), 125.9 (CH), 125.8 (CH), 125.4 (CH), 124.8 (CH), 123.3 (CH), 123.1 (CH), 122.3 (CH), 122.0 (CH), 121.5 (CH), 120.6 (CH), 111.1 (CH), 108.2 (CH).

IR (neat): 3217, 3012, 1650, 1536, 1466, 1271, 1209, 795, 738, 550 cm^{-1}.

MS (EI) *m/z* (relative intensity): 363 (8) [M^+], 221 (100), 192 (15).

HR-MS (EI) *m/z* calcd for $C_{24}H_{17}N_3O$ [M^+] 363.1372, found 363.1364.



***N*-(Furan-2-yl)-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107an):** The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), 2-isocyanatofuran (**106n**) (60 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107an** (94 mg, 62%) as a white solid.

M.p. = 190–191 °C.

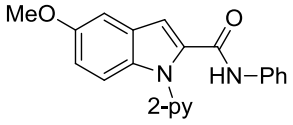
^{1}H-NMR (300 MHz, DMSO-d_6) δ = 11.36 (s, 1H), 8.56 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H), 8.01 (ddd, *J* = 8.0, 7.4, 1.9 Hz, 1H), 7.83–7.72 (m, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.48–7.35 (m, 4H), 7.34–7.26 (m, 1H), 7.22 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 6.44 (dd, *J* = 3.3, 2.0 Hz, 1H), 6.18 (dd, *J* = 3.3, 0.9 Hz, 1H).

^{13}C-NMR (75 MHz, DMSO-d_6) δ = 157.6 (C_q), 150.8 (C_q), 148.8 (CH), 146.2 (C_q), 138.5 (CH), 138.1 (C_q), 135.8 (CH), 132.2 (C_q), 126.3 (C_q), 125.1 (CH), 122.5 (CH), 122.1 (CH), 121.5 (CH), 120.9 (CH), 111.2 (CH), 111.1 (CH), 108.8 (CH), 95.2 (CH).

IR (neat): 2992, 1660, 1551, 1472, 1441, 1295, 1274, 1236, 1145, 739, 593 cm^{-1}.

MS (EI) *m/z* (relative intensity): 303 (5) [M^+], 221 (100), 192 (15).

HR-MS (ESI) *m/z* calcd for $C_{18}H_{13}N_3O_2Na$ [M+Na^+] 326.0899, found 326.0900.



5-Methoxy-*N*-phenyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ba): The representative procedure was followed using 5-methoxy-1-(pyridin-2-yl)-1*H*-indole (**84b**) (112 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **111ba** (140 mg, 82%) as a white solid. When using nBu_2O instead of Et_2O yielded **107ba** (110 mg, 64%).

M.p. = 160–161 °C.

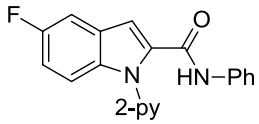
^{1}H-NMR (500 MHz, DMSO-d_6) δ = 10.50 (s, 1H), 8.55 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.99 (ddd, *J* = 8.0, 7.7, 1.9 Hz,1H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.45–7.37 (m, 2H), 7.35–7.29 (m, 3H), 7.27 (d, *J* = 2.5 Hz, 1H), 7.08 (tt, *J* = 7.4, 1.2 Hz, 1H), 6.96 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.82 (s, 3H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.5 (C_q), 154.9 (C_q), 151.0 (C_q), 148.7 (CH), 138.9 (C_q), 138.4 (CH), 134.0 (C_q), 133.0 (C_q), 128.5 (CH), 127.0 (C_q), 123.4 (CH), 122.2 (CH), 120.4 (CH), 119.8 (CH), 115.2 (CH), 112.2 (CH), 108.1 (CH), 103.0 (CH), 55.4 (CH_3).

IR (neat): 3054, 1649, 1547, 1462, 1437, 1294, 1181, 1121, 757, 690, 546, 505 cm^{-1}.

MS (EI) *m/z* (relative intensity): 343 (10) [M^+], 251 (100), 208 (20), 179 (10).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O_2$ [M^+] 343.1321, found 343.1334.



5-Fluoro-*N*-phenyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ca): The representative procedure was followed using 5-fluoro-1-(pyridin-2-yl)-1*H*-indole (**84c**) (106 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ca** (137 mg, 83%) as a white solid.

M.p. = 173–174 ℃.

^{1}H-NMR (300 MHz, DMSO-d_6) δ = 10.56 (s, 1H), 8.56 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 8.01 (td, *J* = 7.7, 1.9 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.60 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.56–7.41 (m, 3H), 7.39 (s, 1H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.17 (td, *J* = 9.3, 2.6 Hz, 1H), 7.08 (t, *J* = 7.3 Hz, 1H).

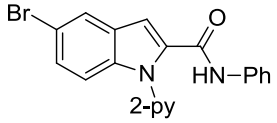
^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.2 (C_q), 157.9 ($^1J_{C–F}$ = 234 Hz, C_q), 150.6 (C_q), 148.8 (CH), 138.8 (C_q), 138.6 (CH), 135.2 (C_q), 134.4 (C_q), 128.5 (CH), 126.8 ($^3J_{C–F}$ = 10 Hz, C_q), 123.6 (CH), 122.6 (CH), 120.6 (CH), 119.8 (CH), 113.2 ($^2J_{C–F}$ = 26 Hz, CH), 112.6 ($^3J_{C–F}$ = 9 Hz, CH), 108.0 ($^4J_{C–F}$ = 4 Hz, CH), 106.5 ($^2J_{C–F}$ = 23 Hz, CH).

^{19}F-NMR (283 MHz, DMSO-d_6) δ = –(121.9–122.0) (m).

IR (neat): 3064, 1645, 1593, 1547, 1462, 1443, 1319, 1201, 777, 542 cm^{-1}.

MS (EI) *m/z* (relative intensity): 331 (5) [M^+], 239 (100), 210 (15).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}FN_3O$ [M^+] 331.1121, found 331.1117.



5-Bromo-*N*-phenyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107da): The representative procedure was followed using 5-bromo-1-(pyridin-2-yl)-1*H*-indole (**84d**) (137 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107da** (152 mg, 78%) as a white solid.

M.p. = 196–197 ℃.

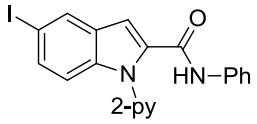
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.71 (s, 1H), 8.51 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.92 (td, *J* = 7.7, 1.9 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.44–7.26 (m, 5H), 7.19–7.07 (m, 3H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.78 (s, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.1 (C_q), 150.4 (C_q), 148.8 (CH), 138.8 (C_q), 138.7 (CH), 136.4 (C_q), 134.8 (C_q), 128.5 (CH), 128.3 (C_q), 127.4 (CH), 124.1 (CH), 123.6 (CH), 122.7 (CH), 120.6 (CH), 119.8 (CH), 113.8 (C_q), 113.3 (CH), 107.4 (CH).

IR (neat): 3291, 1655, 1530, 1436, 1378, 1181, 744, 688, 503 cm^{-1}.

MS (EI) *m/z* (relative intensity): 393 (5) [M^+] (^{81}Br), 391 (5) [M^+] (^{79}Br), 301 (100) (^{81}Br), 299 (100) (^{79}Br), 220 (15), 192 (35).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}BrN_3O$ [M^+] 391.0320, found 391.0321.



5-Iodo-*N*-phenyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ea): The representative procedure was followed using 5-iodo-1-(pyridin-2-yl)-1*H*-indole (**84e**) (160 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ea** (171 mg, 78%) as a white solid.

M.p. = 199–200 ℃.

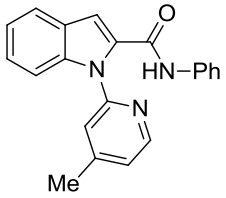
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.76 (s, 1H), 8.53 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H), 7.91 (td, *J* = 7.8, 1.9 Hz, 1H), 7.51–7.42 (m, 3H), 7.40–7.36 (m, 2H), 7.33 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H), 7.12 (dd, *J* = 8.5, 7.2 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 1H), 6.99–6.93 (m, 1H), 6.76 (s, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.1 (C_q), 150.4 (C_q), 148.8 (CH), 138.8 (C_q), 138.6 (CH), 136.8 (C_q), 134.3 (C_q), 132.8 (CH), 130.3 (CH), 129.0 (C_q), 128.5 (CH), 123.6 (CH), 122.6 (CH), 120.6 (CH), 119.8 (CH), 113.6 (CH), 107.2 (CH), 85.3 (C_q).

IR (neat): 3292, 1656, 1596, 1530, 1435, 1379, 1312, 1181, 786, 746, 688, 502 cm^{-1}.

MS (EI) *m/z* (relative intensity): 439 (8) [M^+], 347 (100), 220 (35), 192 (20), 78 (10).

HR-MS (EI) *m/z* calcd for $C_{20}H_{14}IN_3O$ [M^+] 439.0182, found 439.0191.



1-(4-Methylpyridin-2-yl)-*N*-phenyl-1*H*-indole-2-carboxamide (107fa): The representative procedure was followed using 1-(4-methylpyridin-2-yl)-1*H*-indole (**84f**) (104 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107fa** (162 mg, 99%) as a white solid.

M.p. = 178–179 ℃.

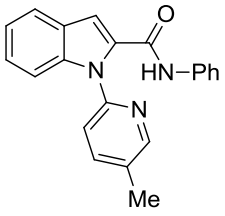
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.29 (s, 1H), 8.43 (d, *J* = 5.1 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.30–7.13 (m, 4H), 7.11–7.01 (m, 3H), 2.45 (s, 3H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.5 (C_q), 150.9 (C_q), 149.5 (C_q), 148.4 (CH), 139.0 (C_q), 137.8 (C_q), 133.8 (C_q), 128.5 (CH), 126.4 (C_q), 124.7 (CH), 123.4 (CH), 123.3 (CH), 121.9 (CH), 121.4 (CH), 121.0 (CH), 119.8 (CH), 111.1 (CH), 108.0 (CH), 20.4 (CH_3).

IR (neat): 3054, 1659, 1597, 1538, 1440, 1308, 1237, 737, 689, 509 cm^{-1}.

MS (EI) *m/z* (relative intensity): 327 (5) [M^+], 235 (100), 208 (15), 43 (40).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O$ [M^+] 327.1372, found 327.1377.



1-(5-Methylpyridin-2-yl)-*N*-phenyl-1*H*-indole-2-carboxamide (107ga): The representative procedure was followed using 1-(5-methylpyridin-2-yl)-1*H*-indole (**84g**) (104 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ga** (125 mg, 76%) as a white solid.

M.p. = 184–185 ℃.

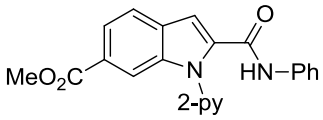
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 9.46 (s, 1H), 8.35 (s, 1H), 7.66 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.23–7.10 (m, 3H), 7.03–6.99 (m, 2H), 6.96 (s, 1H), 2.35 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 160.1 (C_q), 149.2 (CH), 148.9 (C_q), 139.1 (CH), 138.5 (C_q), 138.0 (C_q), 133.5 (C_q), 132.3 (C_q), 128.6 (CH), 126.6 (C_q), 124.8 (CH), 124.0 (CH), 121.9 (CH), 121.5 (CH), 120.6 (CH), 120.5 (CH), 110.5 (CH), 108.4 (CH), 18.0 (CH_3).

IR (neat): 3337, 3050, 1663, 1596, 1520, 1484, 1437, 1313, 1186, 751, 689, 542, 503 cm^{-1}.

MS (EI) *m/z* (relative intensity): 327 (5) [M^+], 235 (100), 206 (5), 192 (5).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O$ [M^+] 327.1372, found 327.1376.



Methyl 2-(phenylcarbamoyl)-1-(pyridin-2-yl)-1*H*-indole-6-carboxylate (107ha): The representative procedure was followed using methyl 1-(pyridin-2-yl)-1*H*-indole-6-carboxylate (**84h**) (126 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ha** (153 mg, 82%) as a white solid.

M.p. = 201–202 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 10.07 (s, 1H), 8.49 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.96–7.86 (m, 2H), 7.52 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.48 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.38 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.31 (ddd, *J* = 7.5, 4.9, 0.9 Hz, 1H), 7.09 (dd, *J* = 8.5, 7.2 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.99–6.90 (m, 1H), 6.78 (s, 1H), 3.90 (s, 3H).

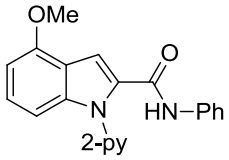
^{13}C-NMR (126 MHz, DMSO-d_6) δ = 166.5 (C_q), 159.0 (C_q), 150.3 (C_q), 149.0 (CH), 138.8

(CH), 138.7 (C_q), 137.0 (C_q), 136.6 (C_q), 130.1 (C_q), 128.6 (CH), 125.7 (C_q), 123.8 (CH), 123.0 (CH), 122.1 (CH), 121.9 (CH), 120.9 (CH), 119.9 (CH), 112.9 (CH), 107.8 (CH), 52.0 (CH_3).

IR (neat): 3283, 2945, 1721, 1657, 1514, 1426, 1229, 1187, 1090, 748, 688, 550 cm^{-1}.

MS (EI) *m/z* (relative intensity): 371 (5) [M^+], 279 (100), 220 (5), 192 (10).

HR-MS (EI) *m/z* calcd for $C_{22}H_{17}N_3O_3$ [M^+] 371.1270, found 371.1258.



4-Methoxy-*N*-phenyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (107ia): The representative procedure was followed using 4-methoxy-1-(pyridin-2-yl)-1*H*-indole (**84i**) (112 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→10/2/2/1) yielded **107ia** (122 mg, 71%) as a white solid.

M.p. = 195–196 ℃.

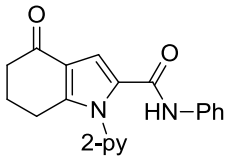
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.03 (s, 1H), 8.55 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.87 (td, *J* = 7.7, 2.0 Hz, 1H), 7.49–7.43 (m, 3H), 7.30 (dd, *J* = 7.7, 7.3 Hz, 1H), 7.26–7.09 (m, 4H), 7.06–6.97 (m, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.45 (d, *J* = 7.8 Hz, 1H), 3.86 (s, 3H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.2 (C_q), 153.7 (C_q), 151.1 (C_q), 148.7 (CH), 139.4 (C_q), 139.0 (C_q), 138.4 (CH), 132.0 (C_q), 128.5 (CH), 126.2 (CH), 123.4 (CH), 122.5 (CH), 120.9 (CH), 119.7 (CH), 117.1 (C_q), 105.6 (CH), 104.1 (CH), 101.4 (CH), 55.3 (CH_3).

IR (neat): 3298, 1659, 1591, 1529, 1438, 1258, 1193, 1183, 779, 755, 690, 556 cm^{-1}.

MS (EI) *m/z* (relative intensity): 343 (15) [M^+], 251 (100), 236 (30), 180 (10).

HR-MS (EI) *m/z* calcd for $C_{21}H_{17}N_3O_2$ [M^+] 343.1321, found 343.1316.



4-Oxo-*N*-phenyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-indole-2-carboxamide (124aa): The representative procedure was followed using 1-(pyridin-2-yl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (**123a**) (106 mg, 0.50 mmol), isocyanatobenzene (**106a**) (66 mg, 0.55 mmol) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 5/1/1/1→5/5/5/1) yielded **124aa** (134 mg, 81%) as a white solid.

M.p. = 274–275 ℃.

^{1}H-NMR (500 MHz, DMSO-d_6) δ = 10.12 (s, 1H), 8.54 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.99 (td, *J* = 7.7, 1.9 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.55–7.46 (m, 2H), 7.40 (s, 1H), 7.26 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 2.62 (t, *J* = 6.1 Hz, 2H), 2.44 (dd, *J* = 7.2, 5.5 Hz, 2H),

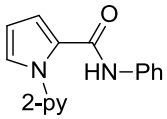
2.06–2.01 (m, 2H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 193.2 (C_q), 158.3 (C_q), 150.3 (C_q), 148.6 (CH), 147.8 (C_q), 138.9 (C_q), 138.4 (CH), 128.9 (C_q), 128.4 (CH), 123.6 (CH), 123.2 (CH), 121.6 (CH), 119.7 (CH), 119.6 (C_q), 110.0 (CH), 37.5 (CH_2), 22.9 (CH_2), 21.9 (CH_2).

IR (neat): 3284, 2949, 1651, 1593, 1454, 1463, 1435, 1314, 1186, 757, 691, 507 cm^{-1}.

MS (EI) *m/z* (relative intensity): 331 (5) [M$^+$], 239 (100), 183 (15), 78 (15).

HR-MS (EI) *m/z* calcd for $C_{20}H_{17}N_3O_2$ [M$^+$] 331.1321, found 331.1323.



***N*-Phenyl-1-(pyridin-2-yl)-1*H*-pyrrole-2-carboxamide (124ba):** The representative procedure was followed using 2-(1*H*-pyrrol-1-yl)pyridine (**123b**) (72 mg, 0.50 mmol), isocyanatobenzene (**106a**) (119 mg, 1.00 mmol), $MnBr(CO)_5$ (27.4 mg, 20 mol %) and Et_2O (1.0 mL). Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2/Et_3N: 10/1/1/1→5/1/1/1) yielded **124ba** (79 mg, 60%) as a white solid.

M.p. = 142–143 ℃.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.76 (s, 1H), 8.49 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H), 7.77 (td, *J* = 7.8, 1.9 Hz, 1H), 7.55–7.45 (m, 2H), 7.32 (dt, *J* = 8.0, 0.9 Hz, 1H), 7.29–7.21 (m, 3H), 7.17 (dd, *J* = 2.9, 1.7 Hz, 1H), 7.10–7.00 (m, 1H), 6.90 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.28 (dd, *J* = 3.7, 2.8 Hz, 1H).

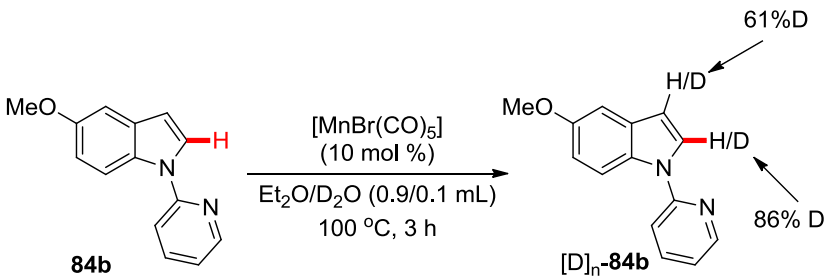
^{13}C-NMR (125 MHz, $CDCl_3$) δ = 159.2 (C_q), 152.1 (C_q), 148.2 (CH), 138.4 (CH), 138.2 (C_q), 128.9 (CH), 127.9 (C_q), 127.2 (CH), 123.9 (CH), 122.5 (CH), 119.9 (CH), 119.3 (CH), 116.4 (CH), 109.7 (CH).

IR (neat): 3232, 3060, 1666, 1576, 1479, 1440, 1317, 1136, 786, 727, 522 cm^{-1}.

MS (EI) *m/z* (relative intensity): 263 (5) [M$^+$], 171 (100), 116 (20), 78 (20).

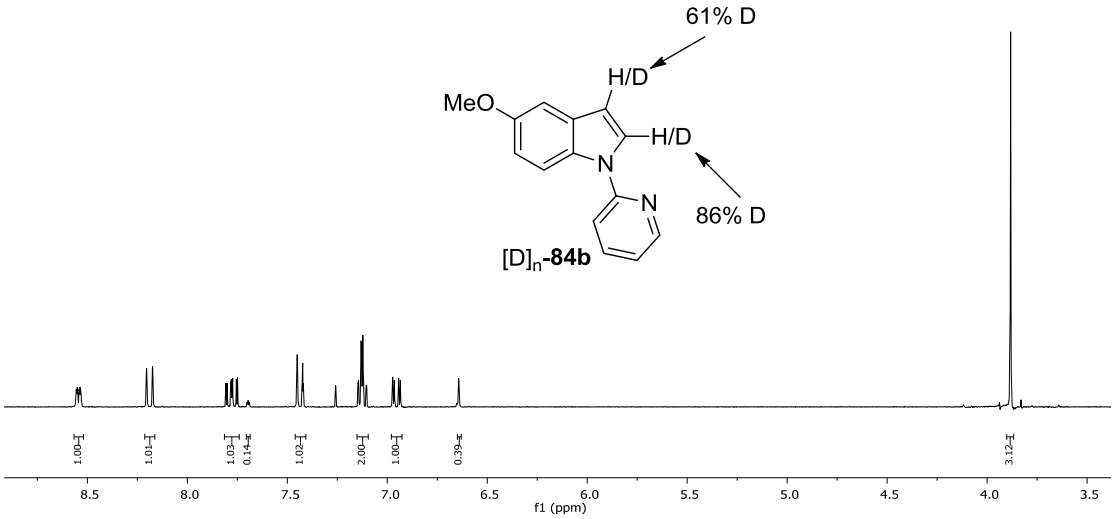
HR-MS (EI) *m/z* calcd for $C_{16}H_{13}N_3O$ [M$^+$] 263.1059, found 263.1057.

Manganese-Catalyzed H/D Exchange Experiment

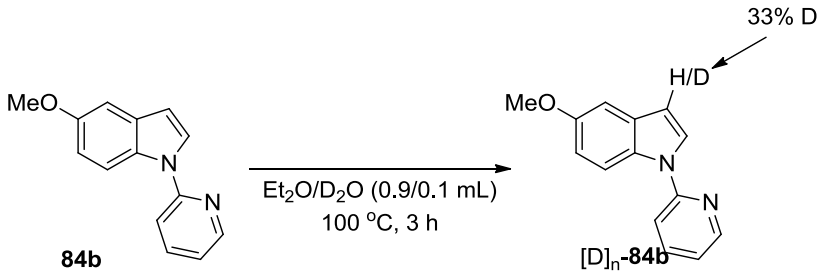


5-Methoxy-1-(pyridin-2-yl)-1*H*-indole (**84b**) (112 mg, 0.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %), Et_2O (0.9 mL) and D_2O (0.1 mL) were placed in a 20 mL sealed tube under N_2 and were then stirred at 100 ℃ for 3 h. At ambient temperature, the reaction mixture was diluted

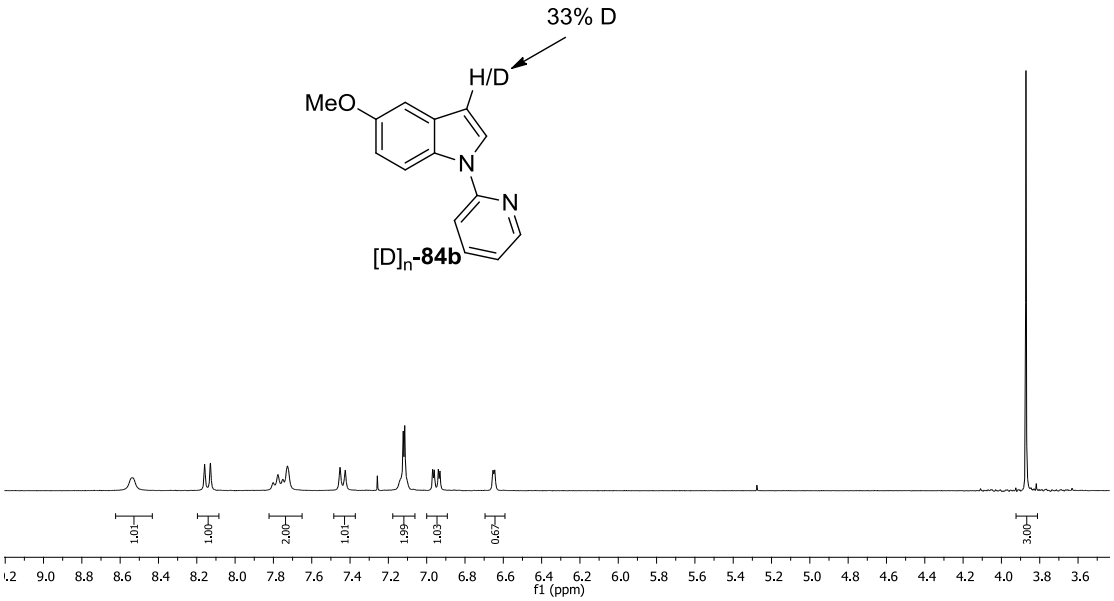
with H_2O (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography on silica gel (*n*-hexane/EtOAc:10/1) yielded $[D]_n$-**84b** (106 mg, 95%). The D incorporation was determined by ^{1}H-NMR spectroscopy.



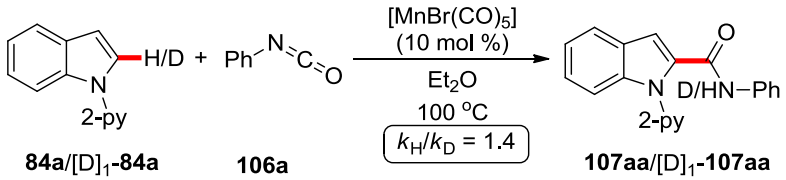
Manganese-Free H/D Exchange Experiment



5-Methoxy-1-(pyridin-2-yl)-1*H*-indole (**84b**) (112 mg, 0.5 mmol), Et_2O (0.9 mL) and D_2O (0.1 mL) were placed in a 20 mL sealed tube under N_2 and were then stirred at 100 ℃ for 3 h. At ambient temperature, the reaction mixture was diluted with EtOAc (15 mL) and was dried with Na_2SO_4 then concentrated under reduced pressure yielded $[D]_n$-**84b** (110 mg, 98%). The D incorporation was determined by ^{1}H-NMR spectroscopy.



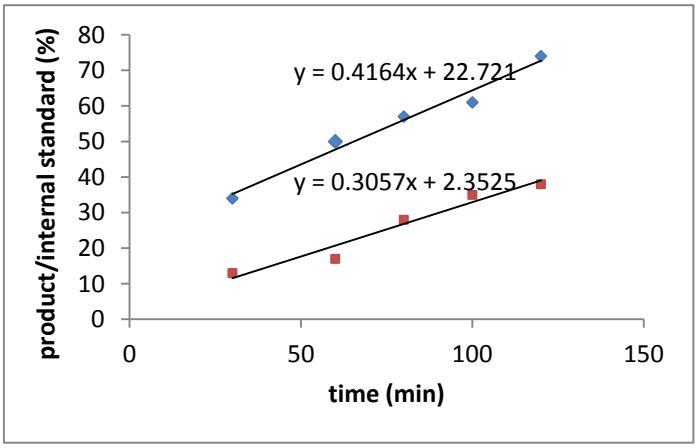
KIE Study



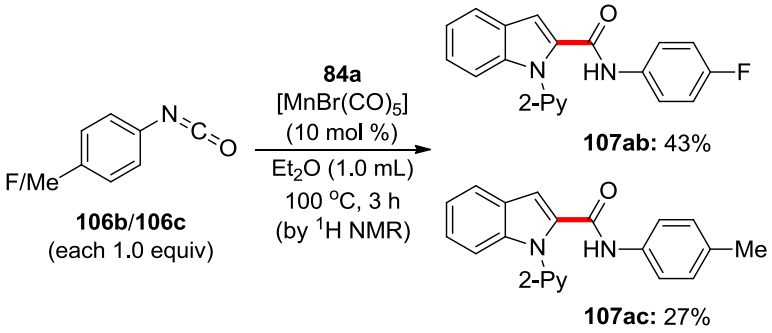
84a/[D]$_1$-**84a** **106a** **107aa**/[D]$_1$-**107aa**

Five parallel independent reactions of **84a** or [D]$_1$-**84a** with **106a** respectively were performed to determine the corresponding KIE value. **84a** (97 mg, 0.50 mmol) or [D]$_1$-**84a** (97 mg, 0.50 mmol), **107a** (66 mg, 0.55 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %), and Et_2O (1.0 mL) were placed in 20 mL sealed tubes. The mixtures were stirred at 100 ℃. After cooling to ambient temperature, the GC conversions were measured by using 2-phenylpyridine as the standard:

Time (min)	30	60	80	100	120
107aa	34	50	57	61	74
[D]$_1$-**107aa**	13	17	28	35	38

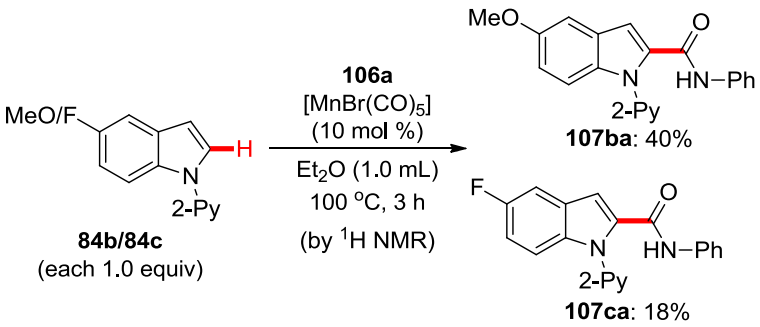


Intermolecular Competition Experiment between 106b and 106c



1-Fluoro-4-isocyanatobenzene (**106b**) (68.5 mg, 0.5 mmol), 1-isocyanato-4-methyl benzene (**106c**) (65.5 mg, 0.5 mmol), 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %) and Et_2O (1.0 mL) were placed in a 20 mL sealed tube under N_2 and were then stirred at 100 ℃ for 3 h. At ambient temperature, the reaction mixture was filtered through a short pad of silica gel (CH_2Cl_2/EtOAc: 1/1) and the solvent was evaporated *in vacuo* to give the crude products. The NMR conversion was determined by ^{1}H-NMR spectroscopy using CH_2Br_2 (17.6 μL) as the standard to give **107ab** (43%) and **107ac** (27%).

Intermolecular Competition Experiment between 84b and 84c

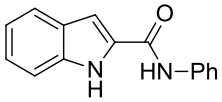


5-Methoxy-1-(pyridin-2-yl)-1*H*-indole (**84b**) (112 mg, 0.5 mmol), 5-fluoro-1-(pyridin-2-yl)-1*H*-indole (**84c**) (106 mg, 0.5 mmol), isocyanatobenzene (**106a**) (55

μL, 0.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %) and Et_2O (1.0 mL) were placed in a 20 mL sealed tube under N_2 and were then stirred at 100 ℃ for 3 h. At ambient temperature, the reaction mixture was filtered through a short pad of silica gel (CH_2Cl_2/EtOAc: 1/1) and the solvent was evaporated *in vacuo* to give the crude products. The NMR conversion was determined by ^{1}H-NMR spectroscopy using CH_2Br_2 (17.6 μL) as the standard to give **107ba** (40%) and **107ca** (18%).

Removal of Directing Group

Methyl trifluoromethanesulfonate (0.36 mmol, 1.2 equiv) was added dropwise to a solution of **107** (0.30 mmol, 1.0 equiv) in CH_2Cl_2 (7.5 mL) at 0 ℃, and the resulting solution was stirred for 12 h at ambient temperature. The solvent was removed *under vacuo*. Then, PhSNa (200 mg, 5.0 equiv) and MeOH (5.0 mL) were added and the resulting mixture was stirred at 100 ℃ for 24 h with a reflux condenser. The solvents were removed, and the resulting residue was acidified until pH = 7 by using HCl (1.0 M), then extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography to afford **129**.



***N*-Phenyl-1*H*-indole-2-carboxamide (129aa)**: Isolation by column chromatography (*n*-hexane/EtOAc/CH_2Cl_2: 20/1/1→5/1/1) yielded **129aa** (50 mg, 71%) as a white solid.

M.p. = 188–189 ℃.

^{1}H-NMR (500 MHz, DMSO-d_6) δ = 11.71 (s, 1H), 10.17 (s, 1H), 7.82 (dd, *J* = 8.6, 1.2 Hz, 2H), 7.68 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.49 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.43 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.37 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.23 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.15–7.02 (m, 2H).

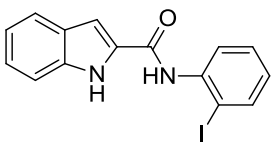
^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.7 (C_q), 138.9 (C_q), 136.8 (C_q), 131.4 (C_q), 128.6 (CH), 127.0 (C_q), 123.7 (CH), 123.4 (CH), 121.6 (CH), 120.1 (CH), 119.8 (CH), 112.3 (CH), 103.8 (CH).

IR (neat): 3419, 3339, 1642, 1595, 1525, 1444, 1308, 1225, 815, 743, 617, 478 cm^{-1}.

MS (EI) *m/z* (relative intensity): 236 (70) [M^+], 144 (100), 116 (25), 89 (47).

HR-MS (EI) *m/z* calcd for $C_{15}H_{12}N_2O$ [M^+] 236.0950, found 236.0949.

The spectral data are in accordance with those reported in the literature.[129]



***N*-(2-Iodophenyl)-1*H*-indole-2-carboxamide (129ag)**: Isolation by column chromatography

(*n*-hexane/EtOAc/CH_2Cl_2: 20/1/1→10/1/1) yielded **129ag** (67 mg, 61%) as a light yellow solid.

M.p. = 234–235 °C.

^{1}H-NMR (500 MHz, DMSO-d_6) δ = 11.73 (s, 1H), 9.92 (s, 1H), 7.95 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.54 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.49–7.44 (m, 2H), 7.38 (d, *J* = 1.6 Hz, 1H), 7.24–7.21 (m, 1H), 7.09–7.05 (m, 2H).

^{13}C-NMR (125 MHz, DMSO-d_6) δ = 159.7 (C_q), 139.3 (C_q), 138.8 (CH), 136.8 (C_q), 131.1 (C_q), 128.7 (CH), 128.1 (CH), 128.0 (CH), 127.0 (C_q), 123.7 (CH), 121.6 (CH), 119.9 (CH), 112.3 (CH), 103.8 (CH), 98.2 (C_q).

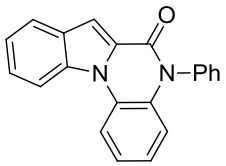
IR (neat): 3379, 3292, 1662, 1576, 1526, 1421, 1342, 1232, 1195, 1009, 731, 549 cm^{-1}.

MS (EI) *m/z* (relative intensity): 362 (25) [M^+], 235 (100), 144 (75), 89 (50).

HR-MS (EI) *m/z* calcd for $C_{15}H_{11}IN_2O$ [M^+] 361.9916, found 361.9914.

The spectral data are in accordance with those reported in the literature.[130]

C–H Activation Product Diversification



5-(Phenyl)indolo[1,2-a]quinoxalin-6(5*H*)-one (130a): A mixture of *N*-phenyl-1*H*-indole-2-carboxamide (**129aa**) (47.3 mg, 0.2 mmol), 1-fluoro-2-nitrobenzene (34 mg, 0.24 mmol) and $CsCO_3$ (228 mg, 0.7 mmol) in MeCN (3 mL) was stirred in 90 °C for 12h. Then, the mixture was cooled to ambient temperature, diluted with brine (12 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried with Na_2SO_4 and evaporated *under vacuo*. Isolation by column chromatgraphy (*n*-hexane/EtOAc/CH_2Cl_2: 20/1/1→10/1/1) yielded **130a** (50 mg, 80%) as a colorless solid.

M.p. = 214–215 °C.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.42 (dd, *J* = 8.4, 1.3 Hz, 1H), 8.35 (dd, *J* = 8.6, 0.9 Hz, 1H), 7.94 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.67 (d, *J* = 0.9 Hz, 1H), 7.65–7.60 (m, 2H), 7.58–7.52 (m, 2H), 7.43–7.36 (m, 3H), 7.33 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.12 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 6.74 (dd, *J* = 8.3, 1.4 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 156.6 (C_q), 136.8 (C_q), 134.6 (C_q), 131.3 (C_q), 130.3 (CH), 129.5 (C_q), 129.5 (CH), 129.2 (CH), 128.5 (C_q), 126.6 (C_q), 125.7 (CH), 124.0 (CH) 123.6 (CH), 123.5 (CH), 122.7 (CH), 117.8 (CH), 115.6 (CH), 114.4 (CH), 107.7 (CH).

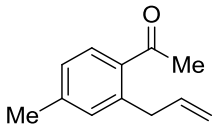
IR (neat): 3054, 1661, 1589, 1390, 1299, 748, 709, 525, 434 cm^{-1}.

MS (EI) *m/z* (relative intensity): 310 (100) [M^+], 173 (10).

HR-MS (EI) *m/z* calcd for $C_{21}H_{14}N_2O$ [M^+] 310.1106, found 310.1104.

4.7 Manganese(I)-Catalyzed Substitutive C–H Allylation

Characterization Data of Products 109, 110 and 131



1-(2-Allyl-4-methylphenyl)ethan-1-one (109aa): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 µL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109aa** (77 mg, 88%) as a colorless oil.

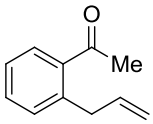
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 8.3 Hz, 1H), 7.08–7.05 (m, 2H), 5.97 (ddt, *J* =17.8, 11.2, 6.5 Hz, 1H), 5.00 (ddt, *J* =11.2, 1.6, 1.6 Hz, 1H), 4.98 (ddt, *J* =17.8, 1.6, 1.6 Hz, 1H), 3.64 (dt, *J* = 6.5, 1.6 Hz, 2H), 2.53 (s, 3H), 2.34 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 201.2 (C_q), 142.1 (C_q), 140.2 (C_q), 137.6 (CH), 134.8 (C_q), 131.9 (CH), 129.7 (CH), 126.7 (CH), 115.4 (CH_2), 38.1 (CH_2), 29.4 (CH_3), 21.3 (CH_3).

IR (neat): 2920, 1679, 1608, 1431, 1354, 1257, 911, 814 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 175 (100) [M+H$^+$].

HR-MS (ESI) *m/z* calcd for $C_{12}H_{15}O$ [M+H$^+$] 175.1117, found 175.1116.



1-(2-Allylphenyl)ethan-1-one (109ba): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-phenylethan-1-imine (**104b**) (113 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 µL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109ba** (69 mg, 86%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.62 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.3, 1.4 Hz, 1H), 7.31–7.18 (m, 2H), 5.97 (ddt, *J* = 16.7, 10.2, 6.5 Hz, 1H), 5.01 (ddt, *J* = 10.2, 1.5, 1.5 Hz, 1H), 4.98 (ddt, *J* = 16.7, 1.5, 1.5 Hz, 1H), 3.63 (dt, *J* = 6.5, 1.5 Hz, 2H), 2.54 (s, 3H).

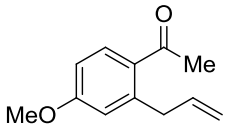
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 202.0 (C_q), 139.6 (C_q), 138.0 (C_q), 137.4 (CH), 131.4 (CH), 131.1 (CH), 128.9 (CH), 126.1 (CH), 115.6 (CH_2), 37.9 (CH_2), 29.7 (CH_3).

IR (neat): 3074, 1683, 1355, 1249, 955, 913, 757, 598 cm^{-1}.

MS (EI) *m/z* (relative intensity): 160 (5) [M$^+$], 145 (100), 127 (20), 115 (45), 91 (20).

HR-MS (ESI) *m/z* calcd for $C_{11}H_{13}O$ [M+H$^+$] 161.0961, found 161.0961.

The spectral data are in accordance with those reported in the literature.[131]



1-(2-Allyl-4-methoxyphenyl)ethan-1-one (109sa): The representative procedure was followed using *N*,1-bis(4-methoxyphenyl)ethan-1-imine (**104s**) (128 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→10/1) yielded **109sa** (69 mg, 72%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 8.1 Hz, 1H), 6.76 (d, *J* = 2.5 Hz, 1H), 6.75 (dd, *J* = 8.1, 2.5 Hz, 1H), 5.97 (ddt, *J* = 17.7, 9.5, 6.5 Hz, 1H), 5.02 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.99 (dd, *J* = 17.7, 1.5 Hz, 1H), 3.81 (s, 3H), 3.69 (d, *J* = 6.5 Hz, 2H), 2.51 (s, 3H).

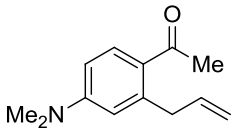
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 199.6 (C_q), 162.0 (C_q), 143.5 (C_q), 137.3 (CH), 132.4 (CH), 129.8 (C_q), 116.7 (CH), 115.6 (CH_2), 110.8 (CH), 55.2 (CH_3), 38.6 (CH_2), 29.2 (CH_3).

IR (neat): 2970, 2839, 1673, 1600, 1566, 1235, 1133, 913, 809 cm^{-1}.

MS (EI) *m/z* (relative intensity): 189 (5) [M-H$^+$], 175 (100), 160 (25), 147 (20), 115 (15), 91 (15).

HR-MS (EI) *m/z* calcd for $C_{12}H_{14}O$ [M$^+$] 190.0994, found 190.0994.

The spectral data are in accordance with those reported in the literature.[132]



1-[2-Allyl-4-(dimethylamino)phenyl]ethan-1-one (109ta): The representative procedure was followed using 4-{1-[(4-methoxyphenyl)imino]ethyl}-*N*,*N*-dimethylaniline (**104t**) (134 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→10/1) yielded **109ta** (65 mg, 64%) as a colorless solid.

M. p. = 43–44 ℃.

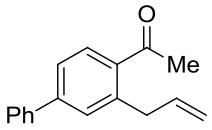
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 8.2 Hz, 1H), 6.50 (dd, *J* = 8.2, 2.8 Hz, 1H), 6.48 (d, *J* = 2.8 Hz, 1H), 6.03 (ddt, *J* = 16.7, 10.1, 6.5 Hz, 1H), 5.01 (ddt, *J* = 16.7, 1.5, 1.4 Hz, 1H), 4.99 (ddt, *J* = 10.1, 1.5, 1.4 Hz, 1H), 3.76 (dt, *J* = 6.5, 1.5 Hz, 2H), 3.01 (s, 6H), 2.50 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 198.3 (C_q), 152.4 (C_q), 143.6 (C_q), 138.1 (CH), 133.2 (CH), 124.1 (C_q), 114.9 (CH_2), 113.7 (CH), 108.3 (CH), 39.9 (CH_3), 39.5 (CH_2), 28.7 (CH_3).

IR (neat): 2899, 1648, 1595, 1543, 1370, 1261, 1199, 1052, 843, 814 cm^{-1}.

MS (EI) *m/z* (relative intensity): 203 (25) [M$^+$], 188 (100), 173 (20), 160 (30), 144 (15), 115 (15).

HR-MS (EI) *m/z* calcd for $C_{13}H_{17}NO$ [M$^+$] 203.1310, found 203.1303.



1-[3-Allyl-(1,1'-biphenyl)-4-yl]ethan-1-one (109fa): The representative procedure was followed using 1-[(1,1'-biphenyl)-4-yl]-*N*-(4-methoxyphenyl)ethan-1-imine (**104f**) (151 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109fa** (92 mg, 78%) as a colorless oil.

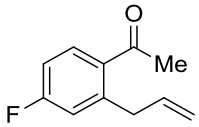
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 8.5 Hz, 1H), 7.65–7.58 (m, 2H), 7.52 (s, 1H), 7.51–7.34 (m, 4H), 6.05 (ddt, *J* = 17.5, 9.5, 6.5 Hz, 1H), 5.07 (ddt, *J* = 17.5, 1.5, 1.5 Hz, 1H), 5.05 (ddt, *J* = 9.5, 1.5, 1.5 Hz, 1H), 3.76 (dt, *J* = 6.5, 1.5 Hz, 2H), 2.60 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 201.3 (C_q), 144.2 (C_q), 140.6 (C_q), 139.8 (C_q), 137.3 (CH), 136.3 (C_q), 130.0 (CH), 129.9 (CH), 128.8 (CH), 128.0 (CH), 127.1 (CH), 124.6 (CH), 115.8 (CH_2), 38.2 (CH_2), 29.6 (CH_3).

IR (neat): 3031, 1679, 1604, 1354, 1248, 913, 761, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 236 (5) [M^+], 221 (100), 178 (35), 165 (25), 115 (13).

HR-MS (ESI) *m/z* calcd for $C_{17}H_{16}O$ [M^+] 236.1201, found 236.1213.



1-(2-Allyl-4-fluorophenyl)ethan-1-one (109ca): The representative procedure was followed using 1-(4-fluorophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104c**) (122 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109ca** (69 mg, 78%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 8.4, 5.8 Hz, 1H), 7.03–6.82 (m, 2H), 5.93 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.04 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.00 (ddt, *J* = 16.8, 1.5 Hz, 1H), 3.65 (d, *J* = 6.5 Hz, 2H), 2.53 (s, 3H).

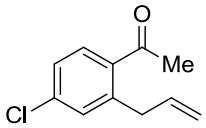
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 200.1 (C_q), 164.1 (C_q, $^{1}J_{C\text{-}F}$ = 253 Hz), 143.9 (C_q, $^{3}J_{C\text{-}F}$ = 8 Hz), 136.5 (CH), 133.8 (C_q, $^{4}J_{C\text{-}F}$ = 3 Hz), 131.7 (CH, $^{3}J_{C\text{-}F}$ = 9 Hz), 118.0 (CH, $^{2}J_{C\text{-}F}$ = 22 Hz), 116.4 (CH_2), 112.9 (CH, $^{2}J_{C\text{-}F}$ = 22 Hz), 38.0 (CH_2, $^{4}J_{C\text{-}F}$ = 2 Hz), 29.6 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$) δ = –(107.5–107.6) (m).

IR (neat): 3081, 1683, 1581, 1415, 1355, 1233, 977, 816, 583 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 179 (100) [M+H^+].

HR-MS (ESI) *m/z* calcd for $C_{11}H_{12}FO$ [M+H^+] 179.0867, found 179.0862.



1-(2-Allyl-4-chlorophenyl)ethan-1-one (109da): The representative procedure was followed using 1-(4-chlorophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104d**) (130 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109da** (79 mg, 81%) as a colorless oil.

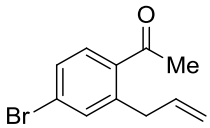
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 2.1 Hz, 1H), 7.23 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.91 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.04 (ddt, *J* = 10.1, 1.6, 1.6 Hz, 1H), 4.99 (ddt, *J* = 16.8, 1.6, 1.6 Hz, 1H), 3.60 (dt, *J* = 6.5, 1.6 Hz, 2H), 2.52 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 200.6 (C_q), 142.1 (C_q), 137.4 (C_q), 136.4 (CH), 136.0 (C_q), 131.1 (CH), 130.5 (CH), 126.2 (CH), 116.4 (CH_2), 37.7 (CH_2), 29.6 (CH_3).

IR (neat): 3083, 2979, 1684, 1590, 1558, 1355, 1246, 1104, 959, 917, 815 cm^{-1}.

MS (EI) *m/z* (relative intensity): 193 (5) [M-H^+], 179 (100), 144 (40), 115 (50).

HR-MS (ESI) *m/z* calcd for $C_{11}H_{12}ClO$ [M+H^+] 195.0571, found 195.0564.



1-(2-Allyl-4-bromophenyl)ethan-1-one (109ea): The representative procedure was followed using 1-(4-bromophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104e**) (152 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109ea** (87 mg, 73%) as a colorless oil.

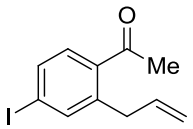
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.49 (d, *J* = 8.1 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.39 (dd, *J* = 8.1, 2.0 Hz, 1H), 5.91 (ddt, *J* = 16.7, 10.1, 6.5 Hz, 1H), 5.04 (ddt, *J* = 10.1, 1.5, 1.5 Hz, 1H), 4.99 (ddt, *J* = 16.7, 1.5, 1.5 Hz, 1H), 3.59 (dt, *J* = 6.5, 1.5 Hz, 2H), 2.51 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 200.8 (C_q), 142.1 (C_q), 136.5 (C_q), 136.4 (CH), 134.0 (CH), 130.5 (CH), 129.2 (CH), 126.0 (C_q), 116.4 (CH_2), 37.6 (CH_2), 29.6 (CH_3).

IR (neat): 3079, 1683, 1584, 1554, 1354, 1250, 1094, 957, 916, 813, 595 cm^{-1}.

MS (EI) *m/z* (relative intensity): 237 (5) [M^+], 223 (95), 144 (100), 116 (70), 89 (15).

HR-MS (ESI) *m/z* calcd for $C_{11}H_{11}BrNaO$ [M+Na^+] 260.9885, found 260.9885.



1-(2-Allyl-4-iodophenyl)ethan-1-one (109ua): The representative procedure was followed using 1-(4-iodophenyl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104u**) (176 mg, 0.50 mmol) and

allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109ua** (118 mg, 83%) as a colorless oil.

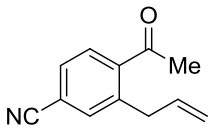
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.62 (d, *J* = 1.8 Hz, 1H), 7.61 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 5.90 (ddt, *J* = 16.7, 10.1, 6.5 Hz, 1H), 5.04 (ddt, *J* = 10.1, 1.6, 1.6 Hz, 1H), 4.99 (ddt, *J* = 16.7, 1.6, 1.6 Hz, 1H), 3.56 (dt, *J* = 6.5, 1.6 Hz, 2H), 2.50 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 201.1 (C_q), 141.8 (C_q), 140.0 (CH), 137.1 (C_q), 136.5 (CH), 135.2 (CH), 130.3 (CH), 116.4 (CH_2), 98.7 (C_q), 37.5 (CH_2), 29.6 (CH_3).

IR (neat): 3076, 2977, 1682, 1578, 1547, 1476, 1249, 955, 915, 811, 595 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 309 (100) [M+Na^+].

HR-MS (ESI) *m/z* calcd for $C_{11}H_{11}INaO$ [M+Na^+] 308.9747, found 308.9745.



4-Acetyl-3-allylbenzonitrile (109va): The representative procedure was followed using 4-{1-[(4-methoxyphenyl)imino]ethyl}benzonitrile (**104v**) (125 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 30/1→10/1) yielded **109va** (81 mg, 87%) as a colorless oil.

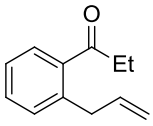
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.63 (d, *J* = 8.7 Hz, 1H), 7.56 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.54 (d, *J* = 1.7 Hz, 1H), 5.88 (ddt, *J* = 17.0, 10.6, 6.5 Hz, 1H), 5.09 (ddt, *J* = 10.6, 1.4, 1.4 Hz, 1H), 4.99 (ddt, *J* = 17.0, 1.4, 1.4 Hz, 1H), 3.58 (dt, *J* = 6.3, 1.4 Hz, 2H), 2.54 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 201.1 (C_q), 142.1 (C_q), 140.3 (C_q), 135.7 (CH), 134.4 (CH), 129.8 (CH), 128.6 (CH), 117.9 (C_q), 117.2 (C_q), 114.6 (CH_2), 37.1 (CH_2), 29.9 (CH_3).

IR (neat): 3083, 2232, 1691, 1357, 1248, 917, 830, 613 cm^{-1}.

MS (EI) *m/z* (relative intensity): 184 (5) [M-H^+], 170 (100), 142 (20), 115 (30), 89 (10).

HR-MS (ESI) *m/z* calcd for $C_{12}H_{12}NO$ [M+H^+] 186.0913, found 186.0911.



1-(2-Allylphenyl)propan-1-one (109ga): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-phenylpropan-1-imine (**104g**) (120 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109ga** (79 mg, 91%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.54 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.37 (ddd, *J* = 8.0, 7.1, 1.5 Hz, 1H), 7.29–7.17 (m, 2H), 5.95 (ddt, *J* = 16.8, 10.3, 6.5 Hz, 1H), 5.01 (ddt, *J* = 10.3, 1.6, 1.6 Hz, 1H), 4.96 (ddt, *J* = 16.8, 1.6, 1.6 Hz, 1H), 3.57 (dt, *J* = 6.5, 1.6 Hz, 2H), 2.86 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H).

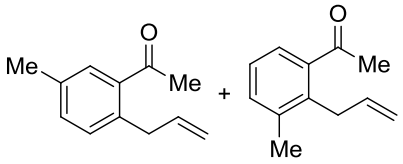
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 205.5 (C_q), 139.1 (C_q), 138.6 (C_q), 137.4 (CH), 131.0 (CH), 130.9 (CH), 127.8 (CH), 126.0 (CH), 115.6 (CH_2), 37.8 (CH_2), 35.0 (CH_2), 8.2 (CH_3).

IR (neat): 2978, 2938, 1687, 1435, 1222, 954, 915, 753 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 175 (100) $[M+H^+]$.

HR-MS (ESI) *m/z* calcd for $C_{12}H_{15}O$ $[M+H^+]$ 175.1117, found 175.1117.

The spectral data are in accordance with those reported in the literature.[133]



109oa + 109oa'

The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*m*-tolyl) ethan-1-imine (**104o**) (120 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109oa** and **109oa'** (66 mg, 76%, 6:1) as a colorless oil.

IR (neat): 3002, 2921, 1682, 1431, 1265, 996, 911, 828, 613 cm^{-1}.

MS (EI) *m/z* (relative intensity): 174 (5) $[M^+]$, 159 (100), 131 (30), 115 (25), 91 (20), 43 (25).

HR-MS (EI) *m/z* calcd for $C_{12}H_{14}O$ $[M^+]$ 174.1045, found 174.1036.

1-(2-Allyl-5-methylphenyl)ethan-1-one (109oa):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.42 (s, 1H), 7.28–7.12 (m, 2H), 5.95 (ddt, *J* = 16.8, 10.4, 6.4 Hz, 1H), 4.99 (ddt, *J* = 10.4, 1.5, 1.5 Hz, 1H), 4.96 (ddt, *J* = 16.8, 1.5, 1.5 Hz, 1H), 3.58 (dt, *J* = 6.4, 1.5 Hz, 2H), 2.53 (s, 3H), 2.35 (s, 3H).

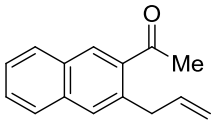
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 202.2 (C_q), 138.0 (C_q), 137.6 (CH), 136.5 (C_q), 135.6 (C_q), 132.1 (CH), 131.1 (CH), 129.5 (CH), 115.3 (CH_2), 37.5 (CH_2), 29.7 (CH_3), 20.9 (CH_3).

The spectral data are in accordance with those reported in the literature.[131]

1-(2-Allyl-3-methylphenyl)ethan-1-one (109oa'):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.38 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.28–7.12 (m, 2H), 5.95 (ddt, *J* = 16.8, 10.4, 6.4 Hz, 1H), 4.90–4.80 (m, 2H), 3.55 (dt, *J* = 6.4, 1.5 Hz, 2H), 2.52 (s, 3H), 2.32 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 203.6 (C_q), 139.9 (C_q), 138.4 (C_q), 136.3 (CH), 136.1 (C_q), 132.9 (CH), 129.5 (CH), 125.8 (CH), 115.0 (CH_2), 33.5 (CH_2), 30.4 (CH_3), 19.7 (CH_3).



1-(3-Allylnaphthalen-2-yl)ethan-1-one (109na): The representative procedure was followed using *N*-(4-methoxyphenyl)-1- (naphthalen-2-yl)ethan-1-imine (**104n**) (138 mg, 0.50 mmol)

and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **109na** (90 mg, 86%, 12:1) as a colorless oil.

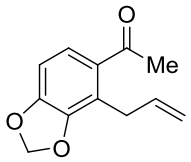
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.16 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.66 (s, 1H), 7.60–7.38 (m, 2H), 6.06 (ddt, *J* = 16.5, 10.1, 6.4 Hz, 1H), 5.08 (ddt, *J* = 10.1, 1.1, 1.1 Hz, 1H), 5.03 (ddt, *J* = 16.5, 1.1, 1.1 Hz, 1H), 3.82 (dt, *J* = 6.4, 1.1 Hz, 2H), 2.67 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 201.7 (C_q), 137.6 (CH), 136.4(C_q), 136.1 (C_q), 134.6 (C_q), 131.1 (C_q), 130.2 (CH), 129.5 (CH), 128.4 (CH), 128.1 (CH), 127.2 (CH), 126.1 (CH), 115.8 (CH_2), 38.0 (CH_2), 29.6 (CH_3).

IR (neat): 3057, 1678, 1494, 1354, 1268, 1164, 885, 745, 475 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 211 (100) [M+H$^+$].

HR-MS (ESI) *m/z* calcd for $C_{15}H_{15}O$ [M+H$^+$] 211.1117, found 211.1115.



1-(4-Allylbenzo[*d*][1,3]dioxol-5-yl)ethan-1-one (109pa): The representative procedure was followed using 1-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(4-methoxyphenyl)ethan-1-imine (**104p**) (135 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→10/1) yielded **109pa** (70 mg, 68%) as a colorless solid.

M. p. = 58–59 ℃.

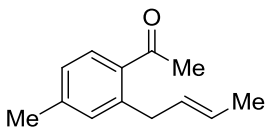
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.34 (d, *J* = 8.2 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 5.99 (s, 2H), 5.98 (ddt, *J* = 17.1, 10.1, 6.2 Hz, 1H), 4.98 (ddt, *J* = 17.1, 1.6, 1.6 Hz, 1H), 4.96 (ddt, *J* = 10.1, 1.6, 1.6 Hz, 1H), 3.64 (dt, *J* = 6.2, 1.6 Hz, 2H), 2.50 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 199.2 (C_q), 149.8 (C_q), 147.3 (C_q), 136.0 (CH), 131.6 (C_q), 125.8 (CH), 122.2 (C_q), 115.1 (CH_2), 105.5 (CH), 101.5 (CH_2), 30.7 (CH_2), 29.1 (CH_3).

IR (neat): 2915, 1662, 1595, 1447, 1260, 1050, 1008, 919, 810, 570 cm^{-1}.

MS (EI) *m/z* (relative intensity): 204 (5) [M$^+$], 189 (50), 161 (30), 131 (32), 103 (25), 43 (100).

HR-MS (EI) *m/z* calcd for $C_{12}H_{12}O_3$ [M$^+$] 204.0786, found 204.0788.



(*E*)-1-[2-(But-2-en-1-yl)-4-methylphenyl]ethan-1-one (*E*-109ab): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and but-3-en-2-yl methyl carbonate (**108b**) (195 mg, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded (*E*/*Z*)-**109ab** (62 mg, 66%, *E*/*Z* = 10/1 by ^{1}H NMR) as a colorless oil.

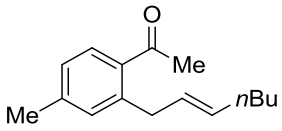
^{1}H-NMR (600 MHz, $CDCl_3$) δ = 7.55 (d, *J* = 8.6 Hz, 1H), 7.06 (s, 1H), 7.04 (d, *J* = 8.6 Hz, 1H), 5.58 (dtq, *J* = 15.4, 6.5, 1.4 Hz, 1H), 5.45 (dqt, *J* = 15.4, 6.2, 1.3 Hz, 1H), 3.55 (dd, *J* = 6.5, 1.4 Hz, 2H), 2.53 (s, 3H), 2.34 (s, 3H), 1.64 (dd, *J* = 6.2, 1.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 201.5 (C_q), 141.9 (C_q), 141.1 (C_q), 135.0 (C_q), 131.8 (CH), 130.0 (CH), 129.5 (CH), 126.5 (CH), 126.1 (CH), 36.9 (CH_2), 29.6 (CH_3), 21.4 (CH_3), 17.9 (CH_3).

IR (neat): 2917, 1680, 1608, 1435, 1354, 1255, 966, 814 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 189 (100) [$M+H^+$].

HR-MS (ESI) *m/z* calcd for $C_{13}H_{17}O$ [$M+H^+$] 189.1274, found 189.1272.



(*E*)-1-[2-(Hept-2-en-1-yl)-4-methylphenyl]ethan-1-one (*E*-109ac): The representative procedure was followed using *N*-(4-methoxyphenyl)-1-(*p*-tolyl)ethan-1-imine (**104a**) (120 mg, 0.50 mmol) and hept-1-en-3-yl methyl carbonate (**108c**) (258 mg, 1.5 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded (*E/Z*)-**109ac** (72 mg, 62%, *E*/*Z* = 12/1 by ^{1}H NMR) as a colorless oil.

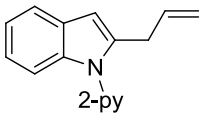
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.54 (d, *J* = 7.7 Hz, 1H), 7.07 (s, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 5.54 (dt, *J* = 15.4, 6.2 Hz, 1H), 5.43 (dt, *J* = 15.4, 6.8 Hz, 1H), 3.56 (d, *J* = 6.2 Hz, 2H), 2.52 (s, 3H), 2.34 (s, 3H), 2.05–1.84 (m, 2H), 1.40–1.19 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 201.5 (C_q), 141.9 (C_q), 141.2 (C_q), 135.1 (C_q), 131.9 (CH), 131.8 (CH), 129.4 (CH), 128.7 (CH), 126.4 (CH), 36.9 (CH_2), 32.2 (CH_2), 31.6 (CH_2), 29.6 (CH_3), 22.2 (CH_2), 21.4 (CH_3), 13.9 (CH_3).

IR (neat): 2957, 2925, 1681, 1608, 1354, 1256, 968, 813, 577 cm^{-1}.

MS (EI) *m/z* (relative intensity): 230 (10) [M^+], 215 (35), 159 (100), 145 (20).

HR-MS (ESI) *m/z* calcd for $C_{16}H_{23}O$ [$M+H^+$] 231.1743, found 231.1736.



2-Allyl-1-(pyridin-2-yl)-1*H*-indole (110aa): The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (116 μL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/CH_2Cl_2: 3/1→1/1) yielded **110aa** (112 mg, 96%) as a colorless solid.

M. p. = 79–81 ℃.

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.64 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.86 (ddd, *J* = 8.1, 7.5, 2.0 Hz, 1H), 7.61–7.52 (m, 1H), 7.43 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.38–7.26 (m, 2H), 7.18–7.07 (m,

2H), 6.46 (d, *J* = 0.9 Hz, 1H), 5.89 (ddt, *J* = 16.8, 10.5, 6.5 Hz, 1H), 4.99 (ddt, *J* = 10.5, 1.3, 1.3 Hz, 1H), 4.95 (ddt, *J* = 16.8, 1.3, 1.3 Hz, 1H), 3.64 (dt, *J* = 6.6, 1.3 Hz, 2H).

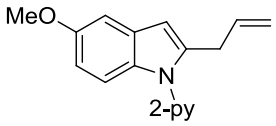
^{13}C-NMR (75 MHz, $CDCl_3$) δ = 151.4 (C_q), 149.5 (CH), 139.0 (C_q), 138.2 (CH), 137.3 (C_q), 134.8 (CH), 128.5 (C_q), 122.0 (CH), 121.8 (CH), 121.0 (CH), 120.6 (CH), 120.0 (CH), 116.5 (CH_2), 110.1 (CH), 103.1 (CH), 32.1 (CH_2).

IR (neat): 3049, 1578, 1553, 1470, 1455, 1436, 1352, 908, 745, 601 cm^{-1}.

MS (EI) *m/z* (relative intensity): 234 (32) [M^+], 219 (100), 78 (15).

HR-MS (EI) *m/z* calcd for $C_{16}H_{14}N_2$ [M^+] 234.1157, found 234.1165.

The spectral data are in accordance with those reported in the literature.[95b]



2-Allyl-5-methoxy-1-(pyridin-2-yl)-1*H*-indole (110ba): The representative procedure was followed using 5-methoxy-1-(pyridin-2-yl)-1*H*-indole (**84b**) (112 mg, 0.50 mmol) and allyl methyl carbonate (**108a**) (116 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/CH_2Cl_2: 3/1→1/1) yielded **110ba** (125 mg, 95%) as a colorless oil.

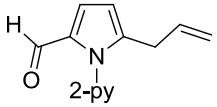
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.67–8.55 (m, 1H), 7.83 (ddd, *J* = 8.0, 2.0, 0.5 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.31–7.19 (m, 2H), 7.05 (d, *J* = 2.5 Hz, 1H), 6.79 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.39 (s, 1H), 5.89 (ddt, *J* = 17.0, 10.7, 6.5 Hz, 1H), 4.99 (ddt, *J* = 10.7, 1.2, 1.2 Hz, 1H), 4.96 (ddt, *J* = 17.0, 1.2, 1.2 Hz, 1H), 3.84 (s, 3H), 3.63 (dt, *J* = 6.5, 1.2 Hz, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 154.7 (C_q), 151.4 (C_q), 149.4 (CH), 139.5 (C_q), 138.1 (CH), 134.8 (CH), 132.3 (C_q), 129.0 (C_q), 121.7 (CH), 120.6 (CH), 116.5 (CH_2), 111.3 (CH), 110.9 (CH), 103.0 (CH), 102.2 (CH), 55.8 (CH_3), 32.2 (CH_2).

IR (neat): 2940, 1580, 1468, 1434, 1201, 1170, 1032, 913, 743, 570 cm^{-1}.

MS (EI) *m/z* (relative intensity): 264 (35) [M^+], 249 (100), 206 (15), 78 (15).

HR-MS (EI) *m/z* calcd for $C_{17}H_{16}N_2O$ [M^+] 264.1263, found 264.1262.



5-Allyl-1-(pyridin-2-yl)-1*H*-pyrrole-2-carbaldehyde (131ca): The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-pyrrole-2-carbaldehyde (**123c**) (86 mg, 0.50 mmol), allyl methyl carbonate (**108a**) (116 µL, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 20/1→5/1) yielded **131ca** (91 mg, 86%) as a colorless oil.

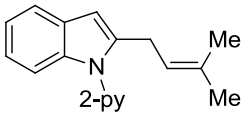
^{1}H-NMR (300 MHz, $CDCl_3$) δ = 9.40 (s, 1H), 8.56 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H), 7.80 (ddd, *J* = 7.7, 7.7, 1.9 Hz, 1H), 7.35 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.02 (d, *J* = 3.9 Hz, 1H), 6.18 (d, *J* = 3.9 Hz, 1H), 5.75 (ddt, *J* = 16.7, 10.1, 6.7 Hz, 1H), 4.96 (dd, *J* = 10.1, 1.5 Hz, 1H), 4.89 (dd, *J* = 16.7, 1.5 Hz, 1H), 3.26 (d, *J* = 6.7 Hz, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 177.9 (CHO), 150.6 (C_q), 148.9 (CH), 142.2 (C_q), 137.9 (CH), 133.5 (CH), 132.9 (C_q), 123.6 (CH), 123.4 (CH), 122.8 (CH), 117.2 (CH_2), 110.1 (CH), 31.1 (CH_2).

IR (neat): 2781, 1662, 1472, 1445, 1323, 809, 786 cm^{-1}.

MS (EI) *m/z* (relative intensity): 212 (95) [M^+], 197 (50), 183 (100), 169 (80), 78 (90), 51 (55).

HR-MS (EI) *m/z* calcd for $C_{13}H_{12}N_2O$ [M^+] 212.0950, found 212.0945.



2-(3-Methylbut-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indole (110ad): The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol), methyl (2-methylbut-3-en-2-yl) carbonate (**108d**) (144 μL, 1.0 mmol), $Mn_2(CO)_{10}$ (19.6 mg, 10 mol %) and NaOAc (16.4 mg, 40 mol %). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded **110ad** (76 mg, 58%) as a colorless oil.

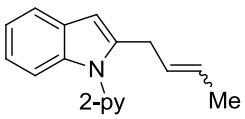
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.66 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.86 (ddd, *J* = 8.1, 7.5, 2.0 Hz, 1H), 7.60–7.54 (m, 1H), 7.43 (ddd, *J* = 8.0, 1.0, 1.0 Hz, 1H), 7.36–7.26 (m, 2H), 7.16–7.10 (m, 2H), 6.45 (d, *J* = 0.9 Hz, 1H), 5.25 (t, *J* = 7.1 Hz, 1H), 3.56 (dd, *J* = 7.2, 0.9 Hz, 2H), 1.68 (s, 3H), 1.57 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 151.5 (C_q), 149.6 (CH), 140.6 (C_q), 138.1 (CH), 137.4 (C_q), 133.5 (C_q), 128.6 (C_q), 121.9 (CH), 121.5 (CH), 121.1 (CH), 120.6 (CH), 120.5 (CH), 119.9 (CH), 110.0 (CH), 102.4 (CH), 26.7 (CH_2), 25.6 (CH_3), 17.7 (CH_3).

IR (neat): 2971, 1585, 1468, 1454, 1435, 1148, 780, 736 cm^{-1}.

MS (EI) *m/z* (relative intensity): 262 (25) [M^+], 247 (22), 219 (100), 206 (20).

HR-MS (EI) *m/z* calcd for $C_{18}H_{18}N_2$ [M^+] 262.1470, found 262.1464.



The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol) and but-3-en-2-yl methyl carbonate (**108b**) (130 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded (*E/Z*)-**110ab** (120 mg, 97%, *E*/*Z* = 3/1 by ^{1}H NMR) as a colorless oil.

IR (neat): 2914, 1711, 1585, 1468, 1455, 1435, 1316, 1210, 965, 735 cm^{-1}.

MS (EI) *m/z* (relative intensity): 248 (75) [M^+], 233 (35), 219 (100), 206 (20), 78 (15).

HR-MS (EI) *m/z* calcd for $C_{17}H_{16}N_2$ [M^+] 248.1313, found 248.1310.

(*E*)-2-(But-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indole (*E*-110ab):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.65 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.91–7.77 (m, 1H), 7.64–7.53 (m, 1H), 7.49–7.20 (m, 3H), 7.20–7.06 (m, 2H), 6.47 (d, *J* = 0.9 Hz, 1H), 5.52 (dtq, *J*

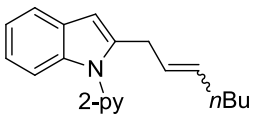
= 15.1, 6.5, 1.4 Hz, 1H), 5.52 (dqt, *J* = 15.1, 6.1, 1.1 Hz, 1H), 3.57 (dd, *J* = 6.5, 1.1 Hz, 2H), 1.60 (dd, *J* = 6.1, 1.4 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 151.3 (C_q), 149.3 (CH), 139.9 (C_q), 137.9 (CH), 137.2 (C_q), 128.5 (C_q), 127.1 (CH), 127.0 (CH), 121.8 (CH), 121.6 (CH), 120.9 (CH), 120.5 (CH), 119.9 (CH), 110.0 (CH), 102.7 (CH), 31.0 (CH_2), 17.8 (CH_3).

(*Z*)-2-(But-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indole (*Z*-110ab):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.65 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.91–7.77 (m, 1H), 7.64–7.53 (m, 1H), 7.49–7.20 (m, 3H), 7.20–7.06 (m, 2H), 6.48 (d, *J* = 0.9 Hz, 1H), 5.62–5.28 (m, 2H), 3.65 (dd, *J* = 6.5, 1.1 Hz, 2H), 1.61 (d, *J* = 6.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 152.4 (C_q), 149.5 (CH), 139.8 (C_q), 138.0 (CH), 137.3 (C_q), 128.5 (C_q), 126.4 (CH), 125.6 (CH), 121.8 (CH), 121.6 (CH), 120.9 (CH), 120.5 (CH), 119.9 (CH), 109.9 (CH), 102.6 (CH), 25.7 (CH_2), 12.8 (CH_3).



The representative procedure was followed using 1-(pyridin-2-yl)-1*H*-indole (**84a**) (97 mg, 0.50 mmol) and hept-1-en-3-yl methyl carbonate (**108c**) (172 mg, 1.0 mmol). Isolation by column chromatography (*n*-hexane/EtOAc: 50/1→20/1) yielded (***E*/*Z***)-**110ac** (102 mg, 70%, *E*/*Z* = 3/1 by ^{1}H NMR) as a colorless oil.

IR (neat): 2955, 1585, 1468, 1455, 1435, 1272, 1211, 1022, 779, 734 cm^{-1}.

MS (EI) *m/z* (relative intensity): 290 (50) [M^+], 247 (45), 233 (25), 219 (100), 206 (50).

HR-MS (EI) *m/z* calcd for $C_{20}H_{22}N_2$ [M^+] 290.1783, found 290.1785.

(*E*)-2-(Hept-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indole (*E*-110ac):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.64 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.84 (ddd, *J* = 7.6, 5.4, 2.0 Hz, 1H), 7.63–7.52 (m, 1H), 7.47–7.38 (m, 1H), 7.38–7.26 (m, 2H), 7.17–7.08 (m, 2H), 6.45 (d, *J* = 0.7 Hz, 1H), 5.51–5.43 (m, 1H), 5.33 (dt, *J* = 15.4, 6.4 Hz, 1H), 3.58 (d, *J* = 6.4 Hz, 2H), 1.91 (ddd, *J* = 7.2, 6.2, 6.2 Hz, 2H), 1.34–1.16 (m, 4H), 0.93–0.81 (m, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 151.5 (C_q), 149.5 (CH), 140.1 (C_q), 138.1 (CH), 137.3 (C_q), 132.8 (CH), 128.5 (C_q), 125.9 (CH), 121.9 (CH), 121.6 (CH), 121.0 (CH), 120.6 (CH), 120.0 (CH), 110.1 (CH), 102.9 (CH), 32.1 (CH_2), 31.5 (CH_2), 31.0 (CH_2), 22.1 (CH_2), 13.9 (CH_3).

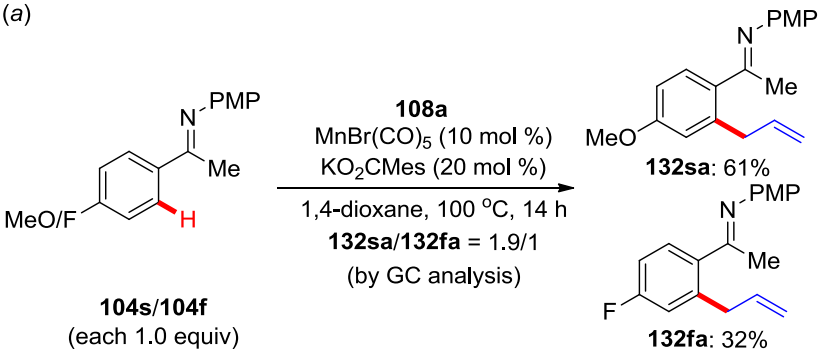
(*Z*)-2-(hept-2-en-1-yl)-1-(pyridin-2-yl)-1*H*-indole (*Z*-110ac):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 8.66 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.86 (ddd, *J* = 7.6, 5.4, 2.0 Hz, 1H), 7.63–7.52 (m, 1H), 7.47–7.38 (m, 1H), 7.38–7.26 (m, 2H), 7.17–7.08 (m, 2H), 6.46 (d, *J* = 0.7 Hz, 1H), 5.54–5.26 (m, 2H), 3.62 (d, *J* = 5.6 Hz, 2H), 1.99 (ddd, *J* = 7.2, 6.2, 6.2 Hz, 2H), 1.32–1.27 (m, 4H), 0.93–0.81 (m, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 151.5 (C_q), 149.6 (CH), 140.0 (C_q), 138.2 (CH), 137.3 (C_q), 131.8 (CH), 128.6 (C_q), 125.4 (CH), 122.0 (CH), 121.6 (CH), 121.1 (CH), 120.6 (CH), 120.0 (CH), 110.0 (CH), 102.6 (CH), 31.7 (CH_2), 26.9 (CH_2), 25.9 (CH_2), 22.3 (CH_2), 14.0 (CH_3).

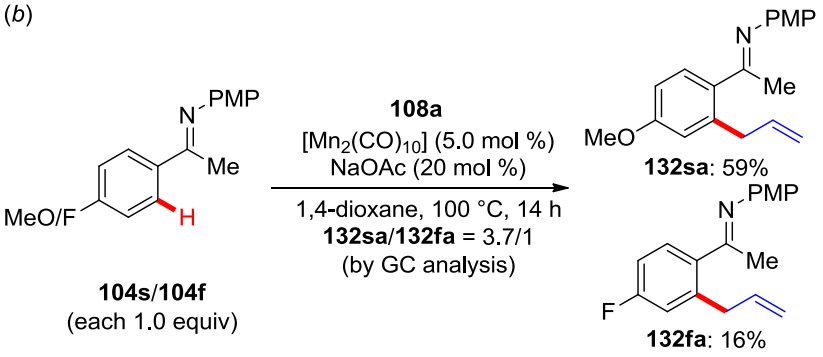
Intermolecular Competition Experiments between Arenes 104s and 104f

(*a*)



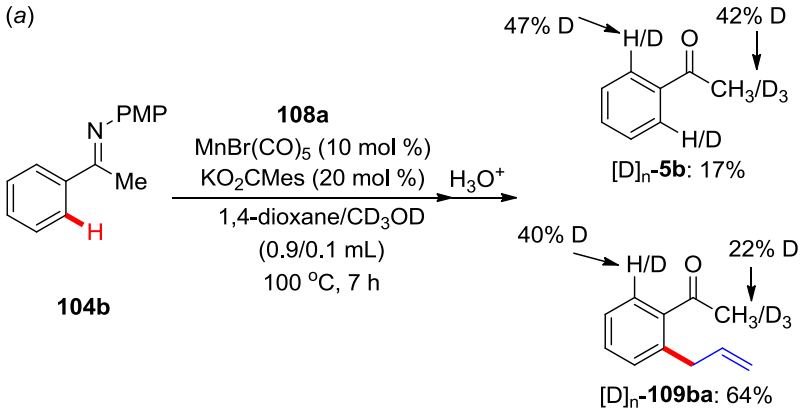
4-Methoxy-*N*-[1-(4-methoxyphenyl)ethylidene]aniline (**104s**) (128 mg, 0.5 mmol), *N*-[1-(4-fluorophenyl)ethylidene]-4-methoxyaniline (**104f**) (122 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (58 μL, 0.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %), KO_2CMes (20.2 mg, 20 mol %) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 100 ℃ for 14 h. At ambient temperature, the reaction mixture was diluted with EtOAc (10 mL), then 1,3,5-trimethoxybenzene (84 mg, 0.5 mmol) was added as internal standard, the crude mixture was analyzed to obtain the GC conversion of the products **132sa** (61%) and **132fa** (32%).

(*b*)

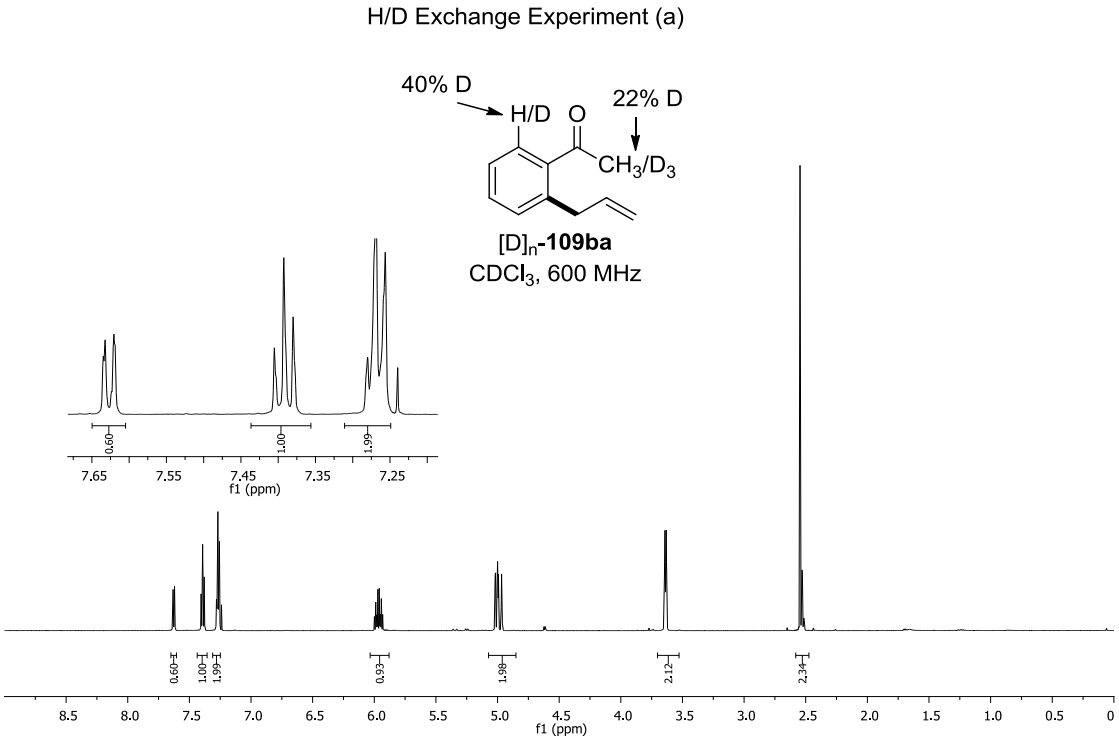


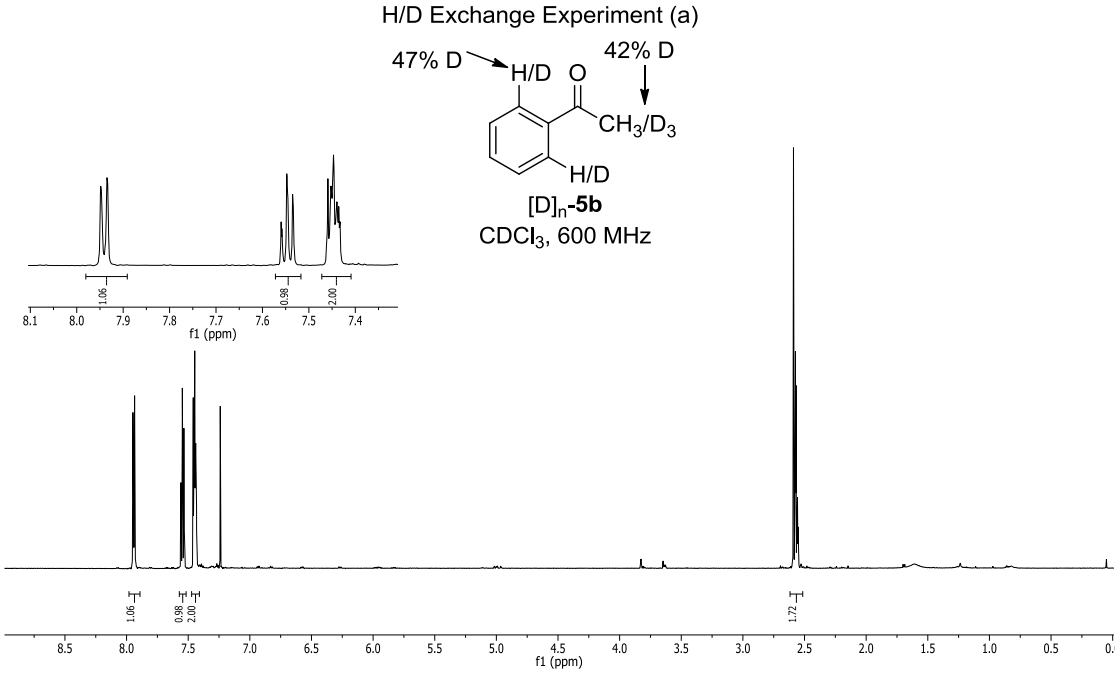
4-Methoxy-*N*-[1-(4-methoxyphenyl)ethylidene]aniline (**104s**) (128 mg, 0.5 mmol), *N*-[1-(4-fluorophenyl)ethylidene]-4-methoxyaniline (**104f**) (122 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (58 μL, 0.5 mmol), $[Mn_2(CO)_{10}]$ (9.8 mg, 5.0 mol %), NaOAc (8.2 mg, 20 mol %) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 100 ℃ for 14 h. At ambient temperature, the reaction mixture was diluted with EtOAc (10 mL), then 1,3,5-trimethoxybenzene (84 mg, 0.5 mmol) was added as internal standard, the crude mixture was analyzed to obtain the GC conversion of the products **132sa** (59%) and **132fa** (16%).

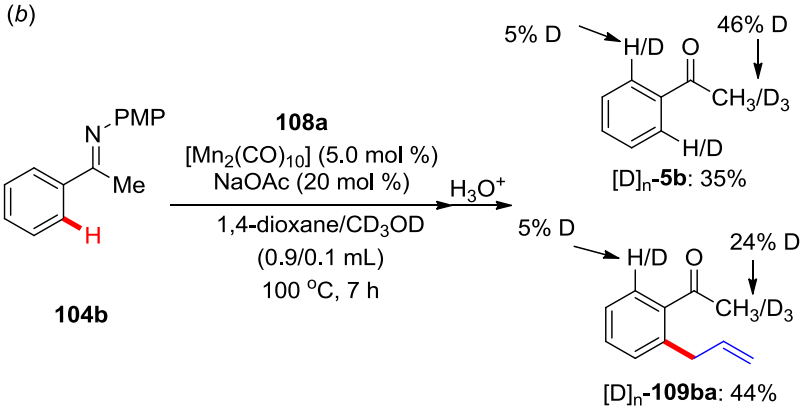
Manganese-Catalyzed H/D Exchange Experiments



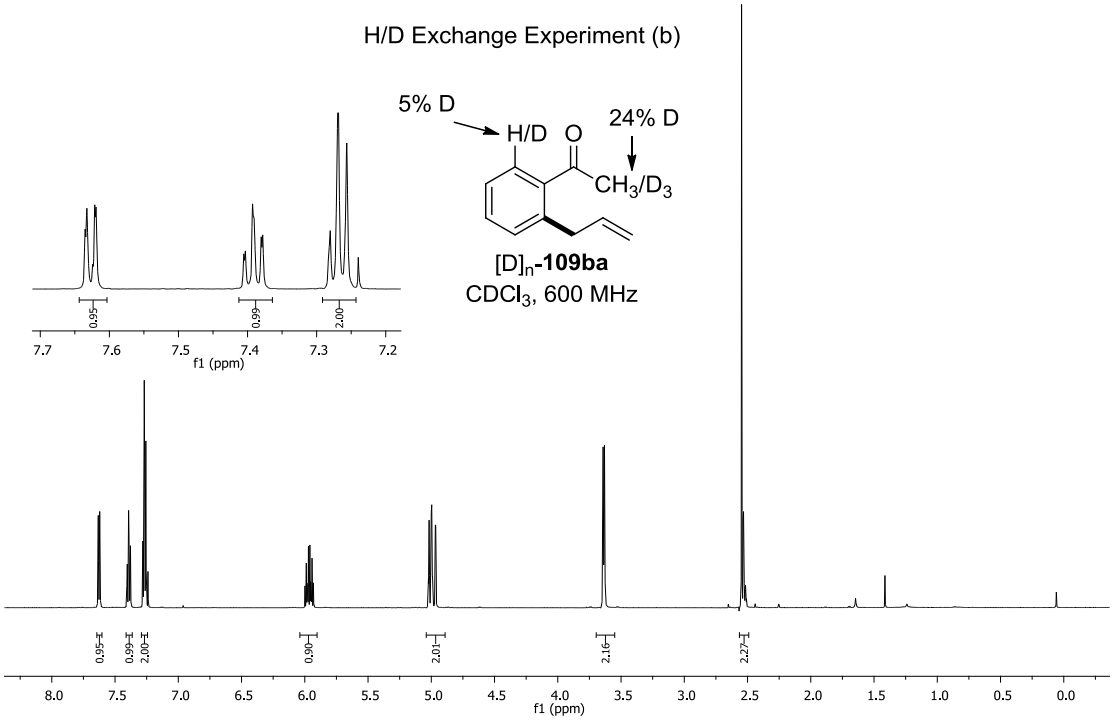
(*E*)-4-Methoxy-*N*-(1-phenylethylidene)aniline (**104b**) (113 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %), KO_2CMes (20.2 mg, 20 mol %), 1,4-dioxane (0.9 mL) and CD_3OD (0.1 mL) were placed in a 25 mL Schlenk tube under N_2 and were stirred at 100 ℃ for 7 h. At ambient temperature, the reaction mixture was diluted with Et_2O (5 mL), then HCl (5 mL, 1 M) was added, the mixture was vigorously stirred at ambient temperature for 20 min, and the resulting mixture was extracted with Et_2O (3 × 10 mL). The combined organic layer was washed with brine (10 mL) and dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 50/1→20/1) yielded $[D]_n$-**5b** (10 mg, 17%) and $[D]_n$-**109ba** (52 mg, 64%).

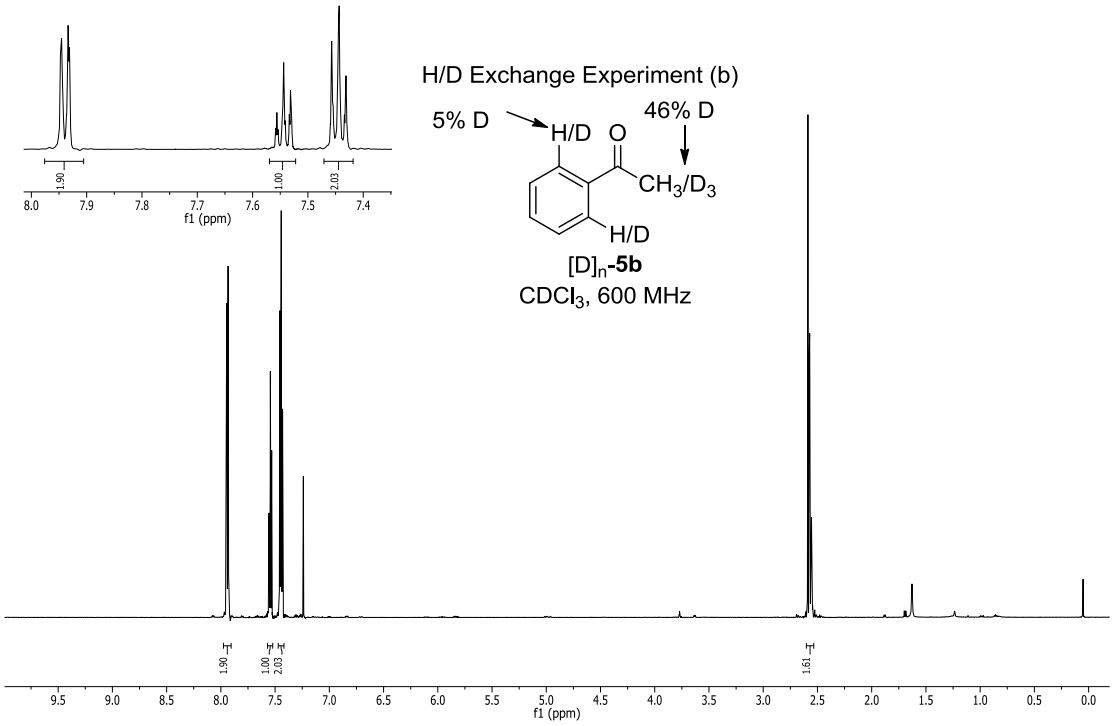






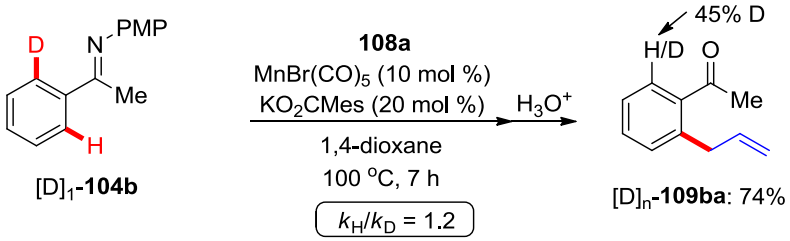
(*E*)-4-Methoxy-*N*-(1-phenylethylidene)aniline (**104b**) (113 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol), $[Mn_2(CO)_{10}]$ (9.8 mg, 5.0 mol %), NaOAc (8.2 mg, 20 mol %), 1,4-dioxane (0.9 mL) and CD_3OD (0.1 mL) were placed in a 25 mL Schlenk tube under N_2 and were stirred at 100 ℃ for 7 h. At ambient temperature, the reaction mixture was diluted with Et_2O (5 mL), then HCl (5 mL, 1 M) was added, the mixture was vigorously stirred at ambient temperature for 20 min, and the resulting mixture was extracted with Et_2O (3×10 mL). The combined organic layer was washed with brine (10 mL) and dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 50/1→20/1) yielded $[D]_n$-**5b** (21 mg, 35%) and $[D]_n$-**109ba** (35 mg, 44%).


H/D Exchange Experiment (b)
5% D
H/D
O
24% D
CH3/D3
[D]n-109ba
CDCl3, 600 MHz
f1 (ppm)

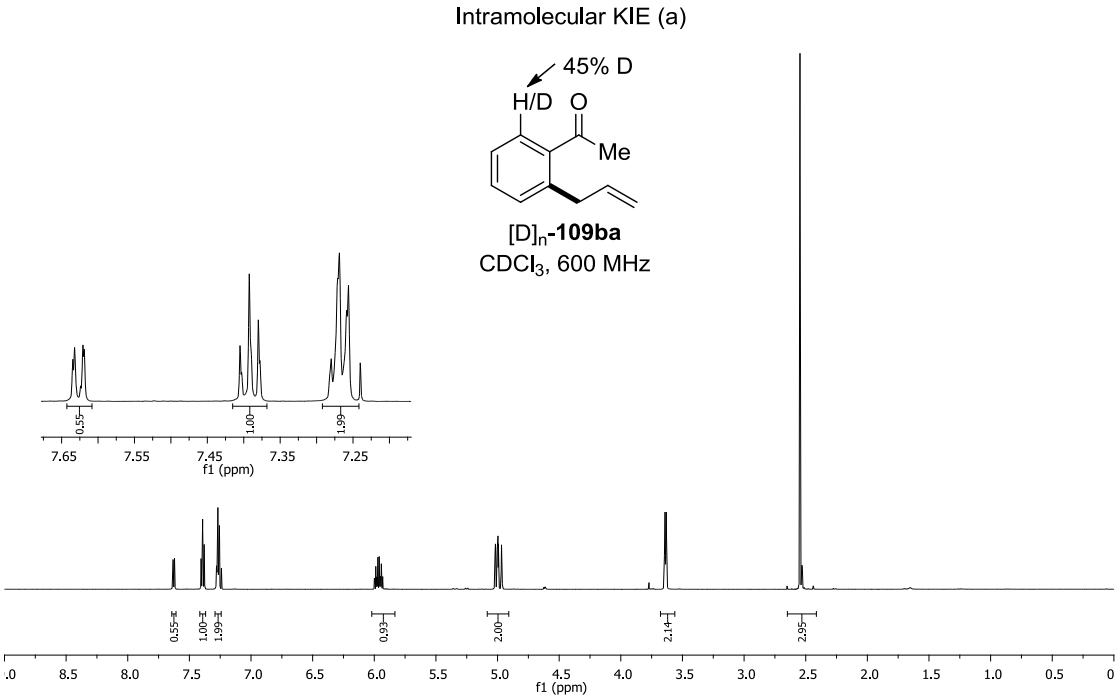

H/D Exchange Experiment (b)
5% D
H/D
O
46% D
CH3/D3
H/D
[D]n-5b
CDCl3, 600 MHz
f1 (ppm)

Kinetic Isotope Effect

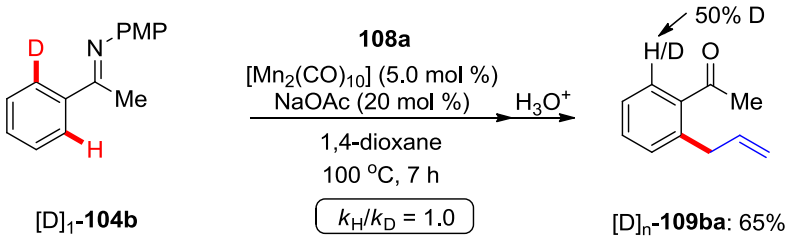
Intramolecular KIE (a)



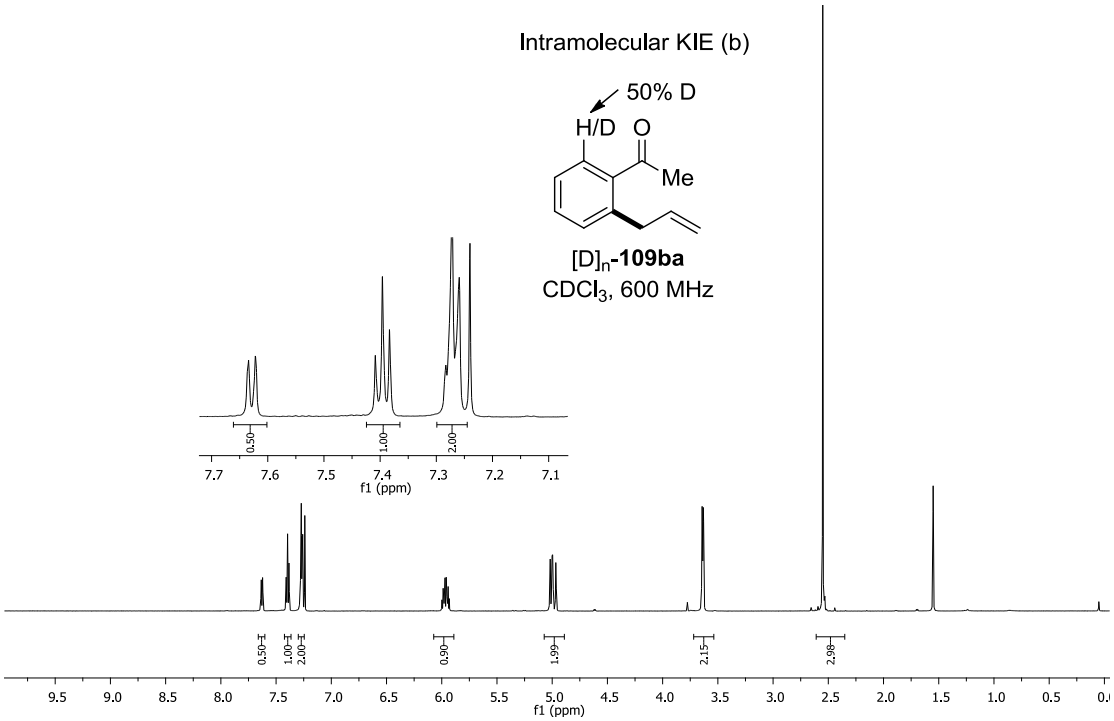
[D]$_1$-(*E*)-4-Methoxy-*N*-(1-phenylethylidene)aniline ([D]$_1$-**104b**) (113 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %), KO_2CMes (20.2 mg, 20 mol %), and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2, and then stirred at 100 ℃ for 7 h. At ambient temperature, the reaction mixture was diluted by Et_2O (5 mL), then HCl (5 mL, 1 M) was added, the mixture was stirred vigorously at ambient temperature for 20 min, the resulting mixture was extracted with Et_2O (3 × 10 mL). The combined organic layer was washed with brine (10 mL), and then dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 50/1→20/1) afforded the [D]$_n$-**109ba** (60 mg, 74%). The kinetic isotope effect of this reaction was determined to be $k_H/k_D \approx 1.2$ as estimated by ^{1}H-NMR spectroscopy.



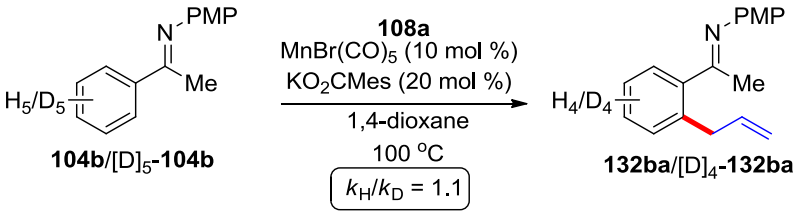
Intramolecular KIE (b)



[D]$_1$-(*E*)-4-Methoxy-*N*-(1-phenylethylidene)aniline ([D]$_1$-**104b**) (113 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol), [$Mn_2(CO)_{10}$] (9.8 mg, 5.0 mol %), NaOAc (8.2 mg, 20 mol %), and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2, and then stirred at 100 ℃ for 7 h. At ambient temperature, the reaction mixture was diluted by Et_2O (5 mL), then HCl (5 mL, 1 M) was added, the mixture was stirred vigorously at ambient temperature for 20 min, the resulting mixture was extracted with Et_2O (3 × 10 mL). The combined organic layer was washed with brine (10 mL), and then dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 50/1→20/1) afforded the [D]$_n$-**109ba** (52 mg, 65%). The kinetic isotope effect of this reaction was determined to be $k_H/k_D \approx 1.0$ as estimated by ^{1}H-NMR spectroscopy.

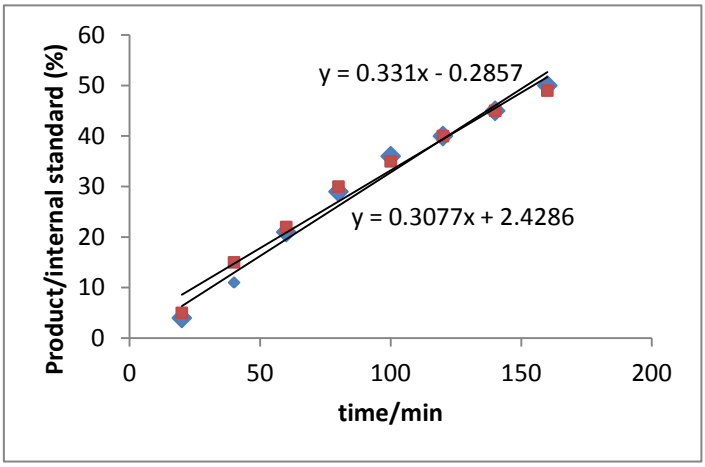


Intermolecular KIE by Independent Experiments (a)

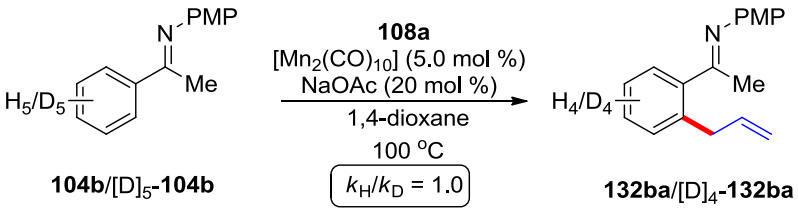


Two parallel reactions of **108a** with **104b** and [D]$_5$-**104b** respectively were performed to determine the corresponding KIE value. **104b** (113 mg, 0.5 mmol) or [D]$_5$-**104b** (115 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol), $MnBr(CO)_5$ (13.7 mg, 10 mol %), KO_2CMes (20.2 mg, 20 mol %), 1,3,5-trimethoxybenzene (84 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 100 ℃, a periodic aliquot (0.02 mL) was removed by syringe and analyzed by GC to provide the following conversions:

Time (min)	20	40	60	80	100	120	140	160
132ba	4	11	21	29	36	40	45	50
[D]$_4$-**132ba**	5	14	22	30	35	40	45	49



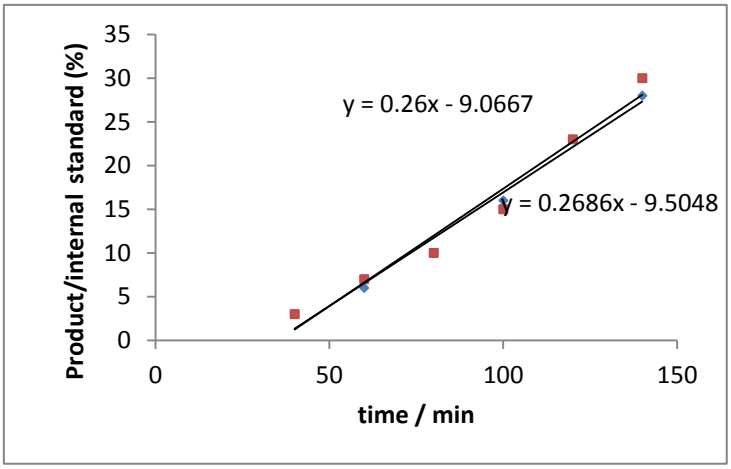
Intermolecular KIE by Independent Experiments (b)



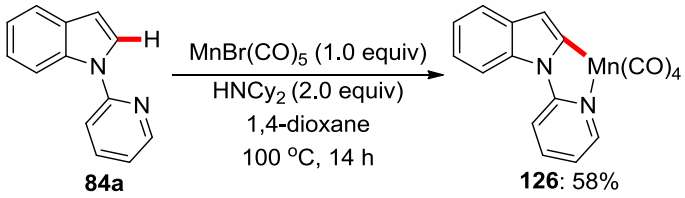
Two parallel reactions of **108a** with **104b** and [D]$_5$-**104b** respectively were performed to determine the corresponding KIE value. **104b** (113 mg, 0.5 mmol) or [D]$_5$-**104b** (115 mg, 0.5 mmol), allyl methyl carbonate (**108a**) (174 μL, 1.5 mmol), $[Mn_2(CO)_{10}]$ (9.8 mg, 5.0 mol %),

NaOAc (8.2 mg, 20 mol %), 1,3,5-trimethoxybenzene (84 mg, 0.5 mmol) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube. The mixture was stirred at 100 ℃, a periodic aliquot (0.02 mL) was removed by syringe and analyzed by GC to provide the following conversions:

Time (min)	40	60	80	100	120	140
132ba	3	6	10	16	23	28
[D]$_4$-**132ba**	3	7	10	15	23	30



C–H Allylations with Cyclometalated Complex 126



84a **126**: 58%

$MnBr(CO)_5$ (1.0 mmol, 274 mg), 1-(pyridin-2-yl)-1*H*-indole **84a** (1.0 mmol, 194 mg), dicyclohexylamine (362 mg, 2.0 mmol) and 1,4-dioxane (2.0 mL) were placed in a 25 mL Schlenk tube under N_2 and then stirred at 100 ℃ for 14 h. At ambient temperature, the mixture was diluted with EtOAc (20 ml) and filtered through a short pad of celite. The solvent was removed by rotary evaporation and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1) afforded **126** (210 mg, 58%).

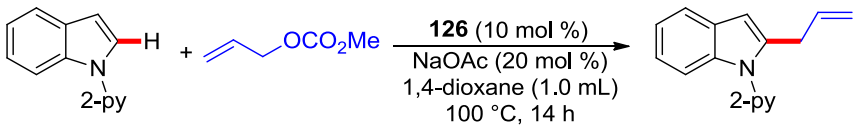
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.44 (dd, *J* = 5.7, 1.7 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.85 (ddd, *J* = 8.5, 7.0, 1.7 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.49 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.18 (dd, *J* = 7.6, 7.1 Hz, 1H), 7.11 (ddd, *J* = 7.6, 7.2, 1.3 Hz, 1H), 6.91 (ddd, *J* = 7.0, 5.6, 1.3 Hz, 1H), 6.82 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ = 218.9 (C_q), 213.3 (C_q), 211.2 (C_q), 166.3 (C_q), 156.9 (C_q), 153.9 (CH), 140.1 (CH), 137.8 (C_q), 136.5 (C_q), 121.9 (CH), 120.1 (CH), 118.1 (CH), 117.8 (CH), 117.6 (CH), 110.7 (CH), 110.6 (CH).

IR (neat): 2076, 1968, 1925, 1483, 1441, 791, 733, 653, 618 cm^{-1}.

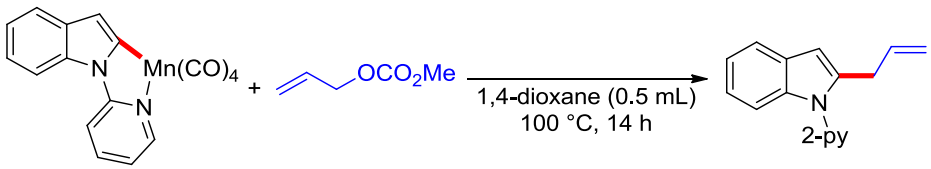
MS (EI) *m/z* (relative intensity): 360 (5) [M^+], 248 (30), 194 (100), 167 (15), 89 (15).

HR-MS (EI) *m/z* calcd for $C_{17}H_9MnN_2O_4$ [M^+] 359.9943, found 359.9955.



84a **108a** **110aa:** 96%

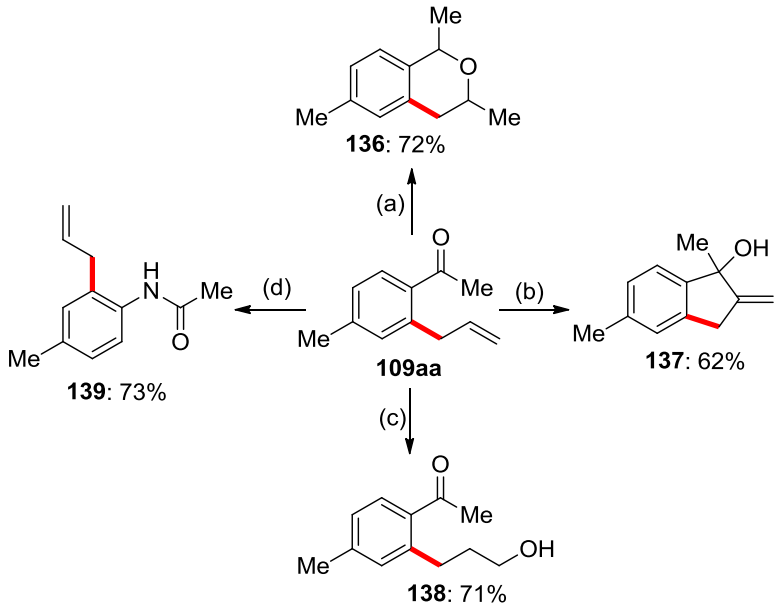
1-(Pyridin-2-yl)-1*H*-indole **84a** (97 mg, 0.5 mmol), allyl methyl carbonate **108a** (116 μL, 1.0 mmol), **126** (18 mg, 10 mol %), NaOAc (8.2 mg, 20 mol %) and 1,4-dioxane (1.0 mL) were placed in a 25 mL Schlenk tube under N_2. The mixture was stirred at 100 ℃ for 14 h. At ambient temperature, the reaction mixture was transferred into a round flask with EtOAc and concentrated under reduced pressure. Purification by column chromatography on silica gel afforded the desired product **110aa** (124 mg, 96% based on 0.55 mmol).



126 **108a** **110aa:** 88%

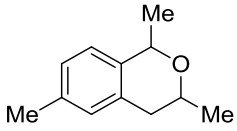
126 (72 mg, 0.2 mmol), allyl methyl carbonate **108a** (24 μL, 0.2 mmol), and 1,4-dioxane (0.5 mL) were placed in a 25 mL Schlenk tube under N_2. The mixture was stirred at 100 ℃ for 14 h. At ambient temperature, the reaction mixture was transferred into a round flask with EtOAc and concentrated under reduced pressure. Purification by column chromatography on silica gel afforded product **110aa** (41 mg, 88%).

Diversification of C–H Activation Products



Reaction (a): i) A solution of **109aa** (174 mg, 1.0 mmol) in Et_2O (4 mL) was added to a stirred suspension of $LiAlH_4$ (80 mg, 2.1 mmol) in Et_2O (4 mL), and the reaction was stirred at ambient temperature for 12 h under N_2 atmosphere. Then the reaction was treated with NaOH (10 mL, 1 M) and stirred for additional 10 min, the white precipitate was removed by filtration and the filtrate was extracted with Et_2O (3×10 mL). The combined organic layer was washed with brine (10 mL), and then dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1→5/1) afforded the corresponding alcohol 1-(2-allyl-4-methylphenyl)ethan-1-ol (156 mg, 89%) as a colorless oil.

ii) 1-(2-Allyl-4-methylphenyl)ethan-1-ol (71 mg, 0.4 mmol), KO*t*Bu (135 mg, 1.5 mmol) and NMP (5.0 mL) were placed in a 25 mL Schlenk tube under N_2. The mixture was stirred at 100 ℃ for 2 h. At ambient temperature, the reaction mixture was quenched with H_2O (10 mL), and the resulting mixture extracted with Et_2O (3×10 mL). The combined organic layer was washed with brine (10 mL), and dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 50/1→20/1) afforded the desired product **136** [57 mg, 81% (dr = 3:1)] as a colorless oil.



1,3,6-Trimethylisochromane (136):

IR (neat): 2972, 2927, 1616, 1446, 1381, 1135, 1099, 812, 557 cm^{-1}.

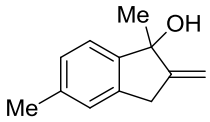
MS (EI) *m/z* (relative intensity): 176 (5) [M^+], 161 (100), 143 (30), 132 (20), 117 (25), 91 (15).

HR-MS (EI) *m/z* calcd for $C_{12}H_{16}O$ [M^+] 176.1201, found 176.1199.

Major isomer: **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 7.00–6.89 (m, 3H), 5.01 (q, *J* = 6.7 Hz, 1H), 4.14–3.96 (m, 1H), 2.76–2.51 (m, 2H), 2.30 (s, 3H), 1.51 (d, *J* = 6.7 Hz, 3H), 1.31 (d, *J* = 6.2 Hz, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ = 136.1 (C_q), 135.6 (C_q), 133.0 (C_q), 129.2 (CH), 126.7 (CH), 125.1 (CH), 70.6 (CH), 63.8 (CH), 36.0 (CH_2), 22.2 (CH_3), 21.3 (CH_3), 20.9 (CH_3).

Minor isomer: **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 7.00–6.89 (m, 3H), 4.84 (q, *J* = 6.6 Hz, 1H), 3.86–3.75 (m, 1H), 2.76–2.51 (m, 2H), 2.30 (s, 3H), 1.53 (d, *J* = 6.6 Hz, 3H), 1.35 (d, *J* = 6.1 Hz, 3H). **^{13}C-NMR** (75 MHz, $CDCl_3$) δ = 136.4 (C_q), 135.7 (C_q), 133.7 (C_q), 129.1 (CH), 126.9 (CH), 124.2 (CH), 73.0 (CH), 70.5 (CH), 36.6 (CH_2), 21.8 (CH_3), 21.3 (CH_3), 20.9 (CH_3).

Reaction (b): To a solution of **109aa** (87 mg, 0.5 mmol), $Ni(cod)_2$ (27.5 mg, 20 mol %) and PCy_3 (28 mg, 20 mol %) in THF (5 mL) was added drop wise $AlMe_3$ (0.5 mL, 1.0 M in heptane). The reaction mixture was stirred at ambient temperature for 15 min, and then quenched with MeOH (1 mL). The solution was transferred into a round bottom flask with Et_2O and concentrated under reduced pressure. Purification by column chromatography on silica gel (*n*-hexane/EtOAc: 20/1→5/1) afforded the desired product **137** (54 mg, 62%) as a colorless oil.



1,5-Dimethyl-2-methylene-2,3-dihydro-1*H*-inden-1-ol (137):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.30 (d, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 5.44 (t, *J* = 2.3 Hz, 1H), 5.16 (t, *J* = 2.3 Hz, 1H), 3.62 (d, *J* = 2.3 Hz, 2H), 2.35 (s, 3H), 1.96 (s, 1H), 1.54 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ = 157.4 (C_q), 145.2 (C_q), 139.4 (C_q), 138.3 (C_q), 128.1 (CH), 125.1 (CH), 123.0 (CH), 107.9 (CH_2), 79.8 (C_q), 36.0 (CH_2), 28.8 (CH_3), 21.4 (CH_3).

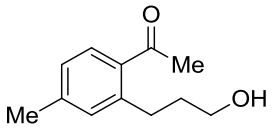
IR (neat): 3392, 2969, 1614, 1426, 1118, 1081, 871, 816, 586 cm^{-1}.

MS (EI) *m/z* (relative intensity): 174 (5) [M^+], 159 (100), 131 (25), 115 (20), 91 (15), 43 (25).

HR-MS (EI) *m/z* calcd for $C_{12}H_{14}O$ [M^+] 174.1045, found 174.1039.

Reaction (c): A solution of **109aa** (87 mg, 0.5 mmol) in THF (1 mL) was treated with 9-BBN (1.05 mL, 1.05 equiv, 0.5 M in THF,) at ambient temperature, and then the mixture was stirred for 24 h at ambient temperature. The crude product was followed by successive additions of aq. NaOH (2.2 mL, 2 M) and aq. H_2O_2 (30%, 1.1 mL) at 0 ^oC, the reaction mixture was allowed to warm to ambient temperature and stirred for further 24 h. Then the mixture was treated with saturated aq. $Na_2S_2O_3$ (5 mL) and stirred for another 10 min. The mixture was extracted with Et_2O (3×10 mL), the combined organic layer was washed with brine (10 mL), and dried over Na_2SO_4. After concentration under reduced pressure, purification by column chromatography

on silica gel (*n*-hexane/EtOAc: 20/1→5/1) afforded the desired product **138** (68 mg, 71%) as a colorless oil.



1-[2-(3-Hydroxypropyl)-4-methylphenyl]ethan-1-one (138):

^{1}H-NMR (300 MHz, $CDCl_3$) δ = 7.58 (d, J = 7.8 Hz, 1H), 7.07 (s, 1H), 7.05 (d, J = 7.8 Hz, 1H), 3.57 (t, J = 5.9 Hz, 2H), 2.90 (t, J = 7.4 Hz, 2H), 2.76 (s, 1H), 2.54 (s, 3H), 2.33 (s, 3H), 1.92–1.70 (m, 2H).

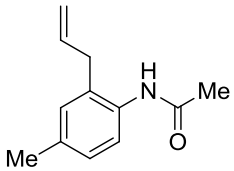
^{13}C-NMR (125 MHz, $CDCl_3$) δ = 201.9 (C_q), 142.4 (C_q), 142.2 (C_q), 134.7 (C_q), 132.1 (CH), 129.9 (CH), 126.5 (CH), 61.5 (CH_2), 34.6 (CH_2), 29.7 (CH_3), 29.6 (CH_2), 21.4 (CH_3).

IR (neat): 3411, 2924, 1675, 1355, 1251, 1229, 1054, 814, 731, 576 cm^{-1}.

MS (EI) *m/z* (relative intensity): 192 (5) [M^+], 177 (25), 159 (100), 146 (55), 131 (58), 105 (30), 91 (35).

HR-MS (EI) *m/z* calcd for $C_{12}H_{16}O_2$ [M^+] 192.1150, found 192.1148.

Reaction (d): Hydroxylamine hydrochloride (79 mg, 1.15 mmol), **109aa** (87 mg, 0.5 mmol), NaOAc (103 mg, 1.25 mmol), MeOH (1 mL) and H_2O (0.5 mL) were added to a 25 mL Schlenk tube. The reaction mixture was stirred at 100 ℃ for 1 h. At ambient temperature, the mixture was extracted with Et_2O (3×10 mL) and the combined organic layer was washed with brine and dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was dissolved in MeCN (3.0 mL) and added to a Schlenk tube which contained cyanuric chloride (4.5 mg, 0.025 mmol) and $ZnCl_2$ (6.8 mg, 0.05 mmol). The reaction mixture was stirred at 90 ℃ for 2 h. At ambient temperature, the mixture was extracted with Et_2O (3×10 mL) and the combined organic layer was washed with brine, dried over Na_2SO_4 and filtered. After concentration under reduced pressure, purification by column chromatography on silica gel (*n*-hexane/EtOAc: 10/1→5/1) afforded the desired product **139** (62 mg, 73%) as a colorless solid.



***N*-(2-Allyl-4-methylphenyl)acetamide (139)**:

M. p. = 107–108 ℃.

^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.56 (d, J = 8.1 Hz, 1H), 7.25 (d, J = 2.0 Hz, 1H), 7.01 (dd, J = 8.1, 2.0 Hz, 1H), 6.95 (d, J = 2.0 Hz, 1H), 5.92 (ddt, J = 17.2, 10.1, 6.2 Hz, 1H), 5.12 (ddt, J =

10.1, 1.7, 1.7 Hz, 1H), 5.05 (ddt, *J* = 17.2, 1.7, 1.7 Hz, 1H), 3.30 (dt, *J* = 6.2, 1.7 Hz, 2H), 2.27 (s, 3H), 2.09 (s, 3H).

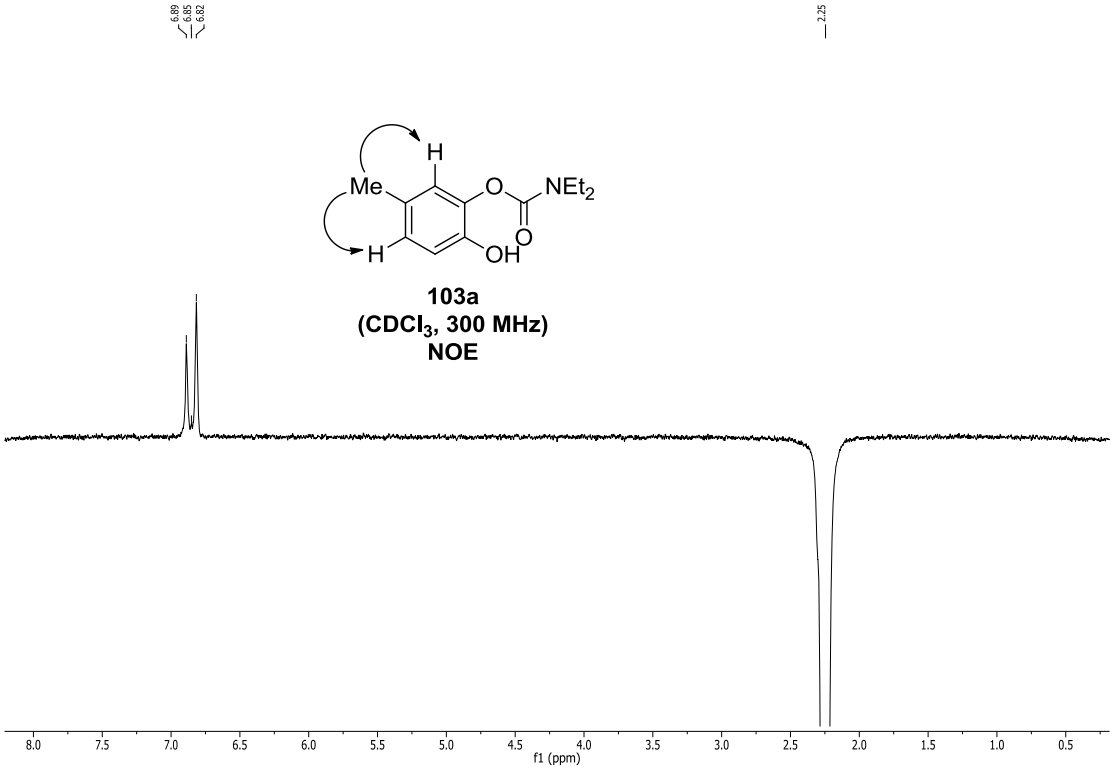
^{13}C-NMR (100 MHz, $CDCl_3$) δ = 168.4 (C_q), 136.4 (CH), 135.1 (C_q), 133.2 (C_q), 130.7 (C_q), 130.6 (CH), 127.8 (CH), 124.3 (CH), 116.2 (CH_2), 36.7 (CH_2), 24.0 (CH_3), 20.8 (CH_3).

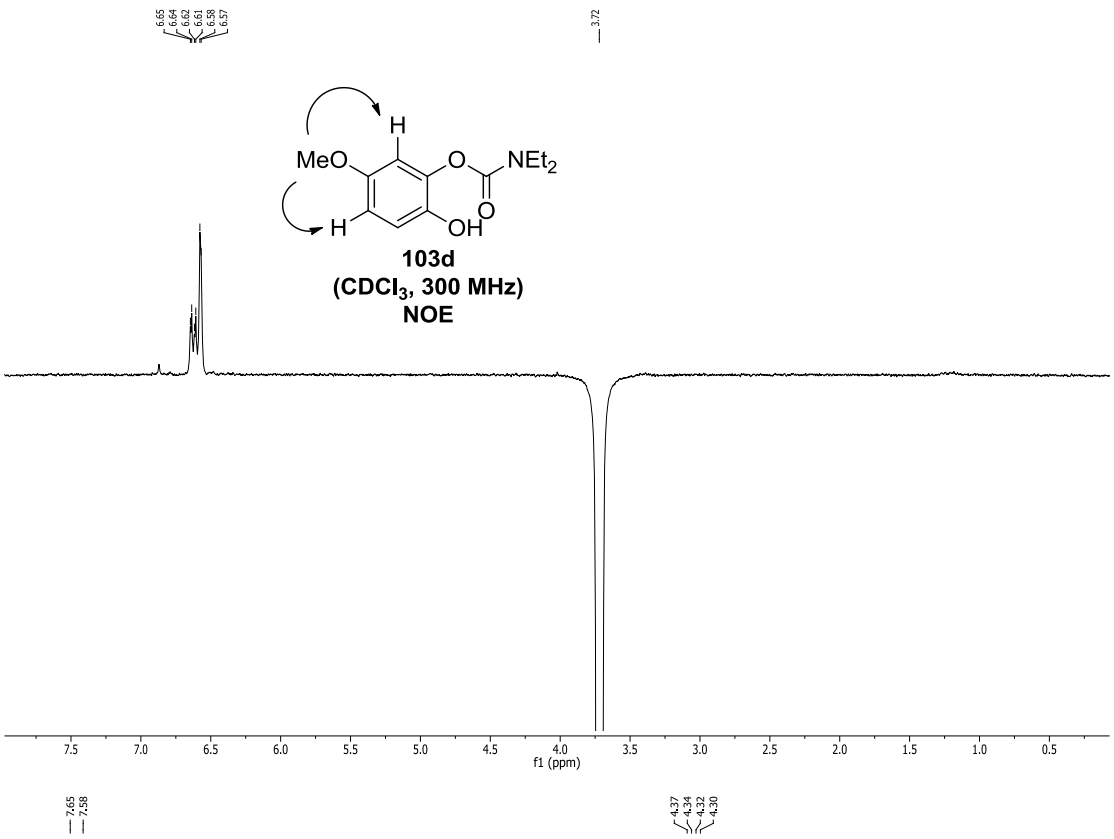
IR (neat): 3270, 2916, 1637, 1526, 1364, 1285, 993, 907, 811, 703, 605, 505 cm^{-1}.

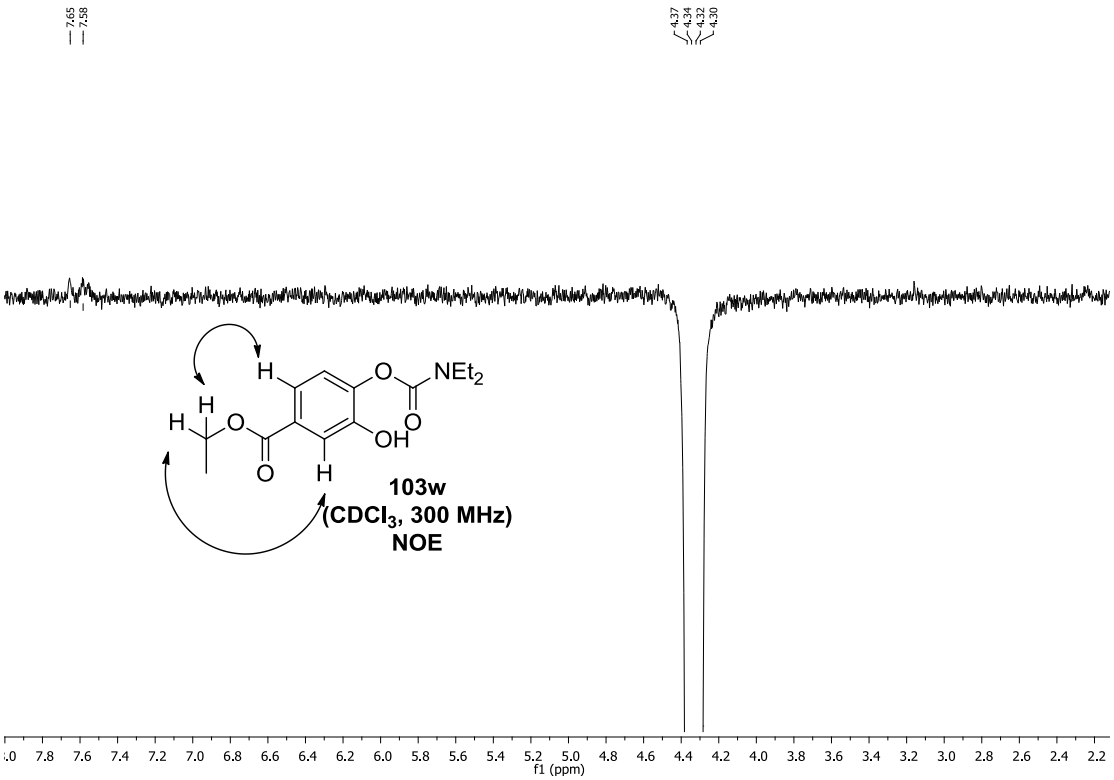
MS (EI) *m/z* (relative intensity): 189 (25) [M^+], 146 (70), 132 (50), 58 (30), 43 (100).

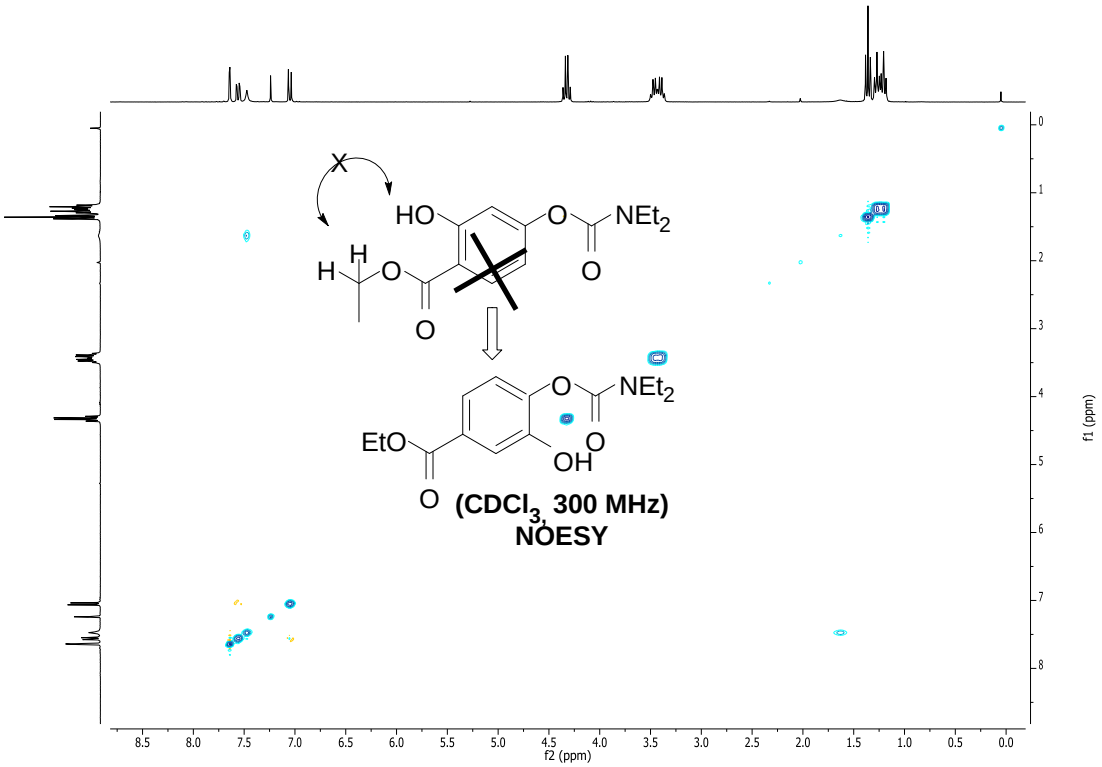
HR-MS (EI) *m/z* calcd for $C_{12}H_{15}NO$ [M^+] 189.1154, found 189.1145.

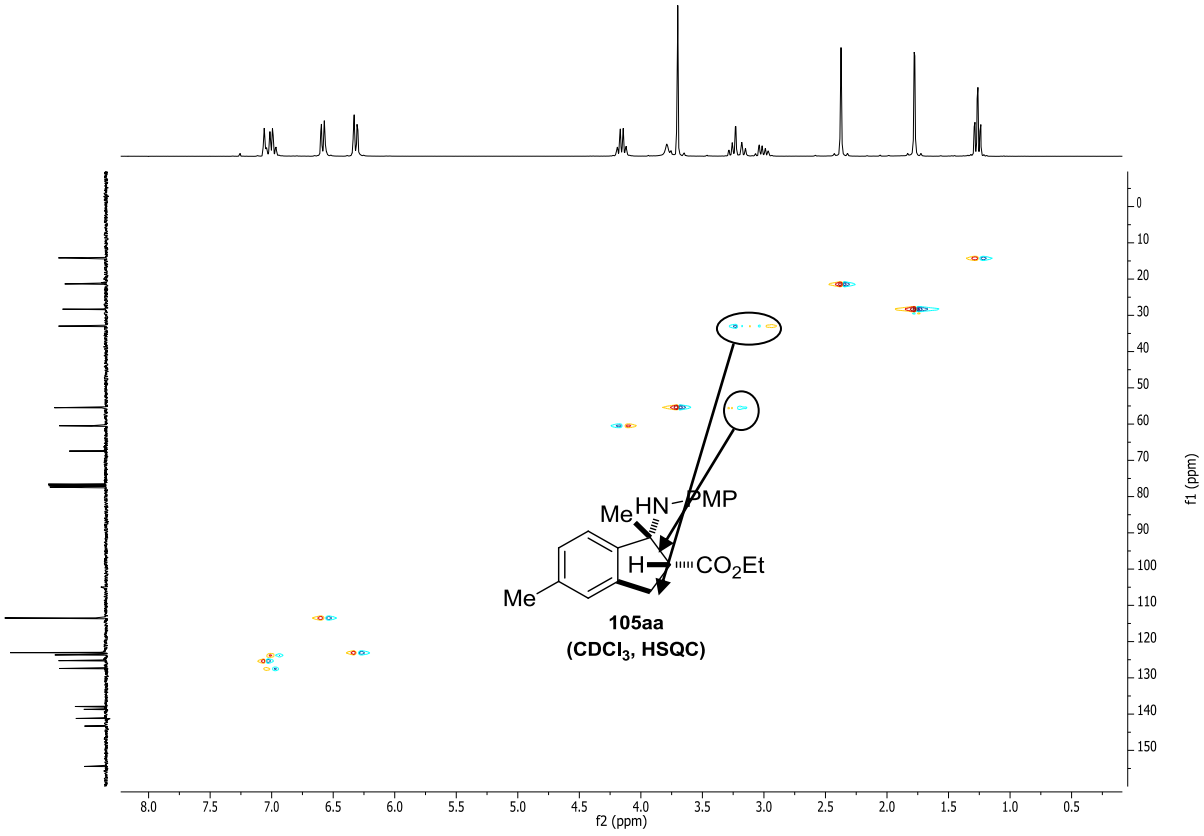
4.8 Selected NMR Spectra

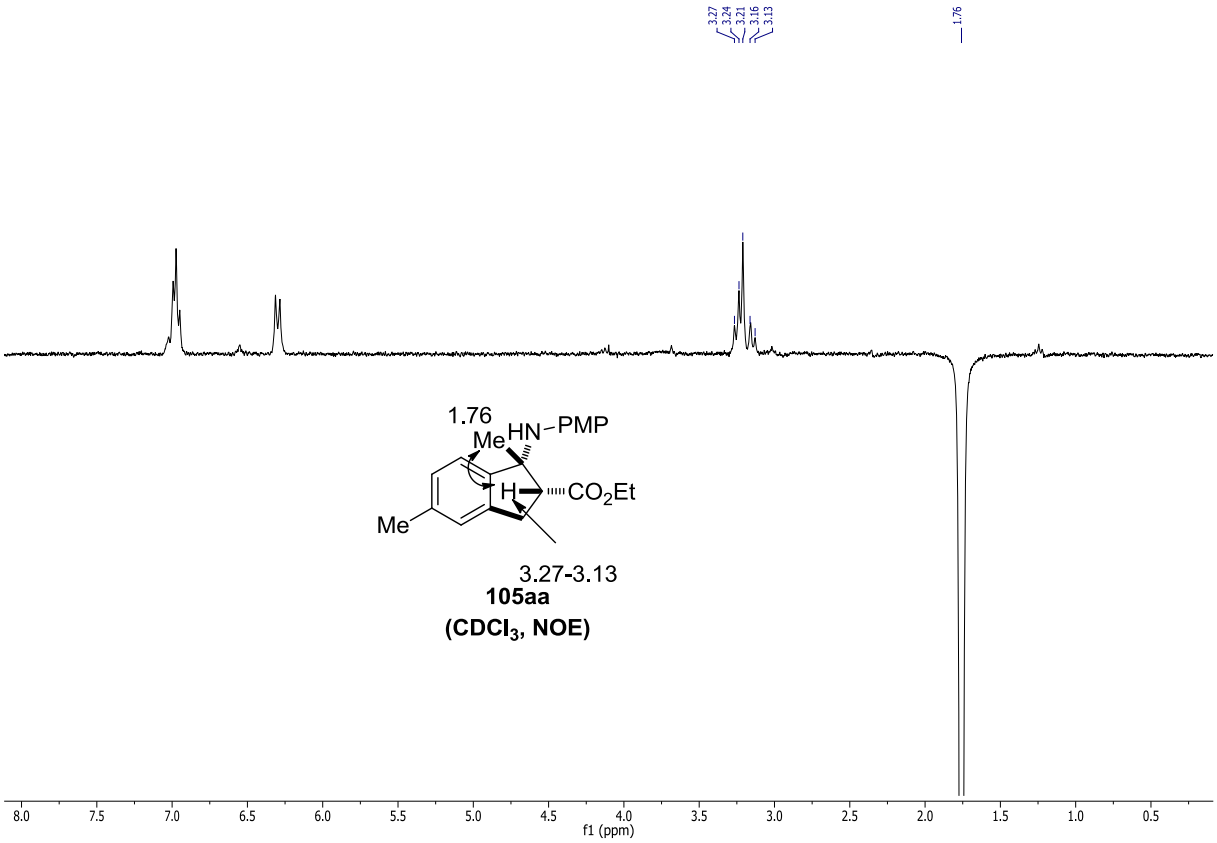


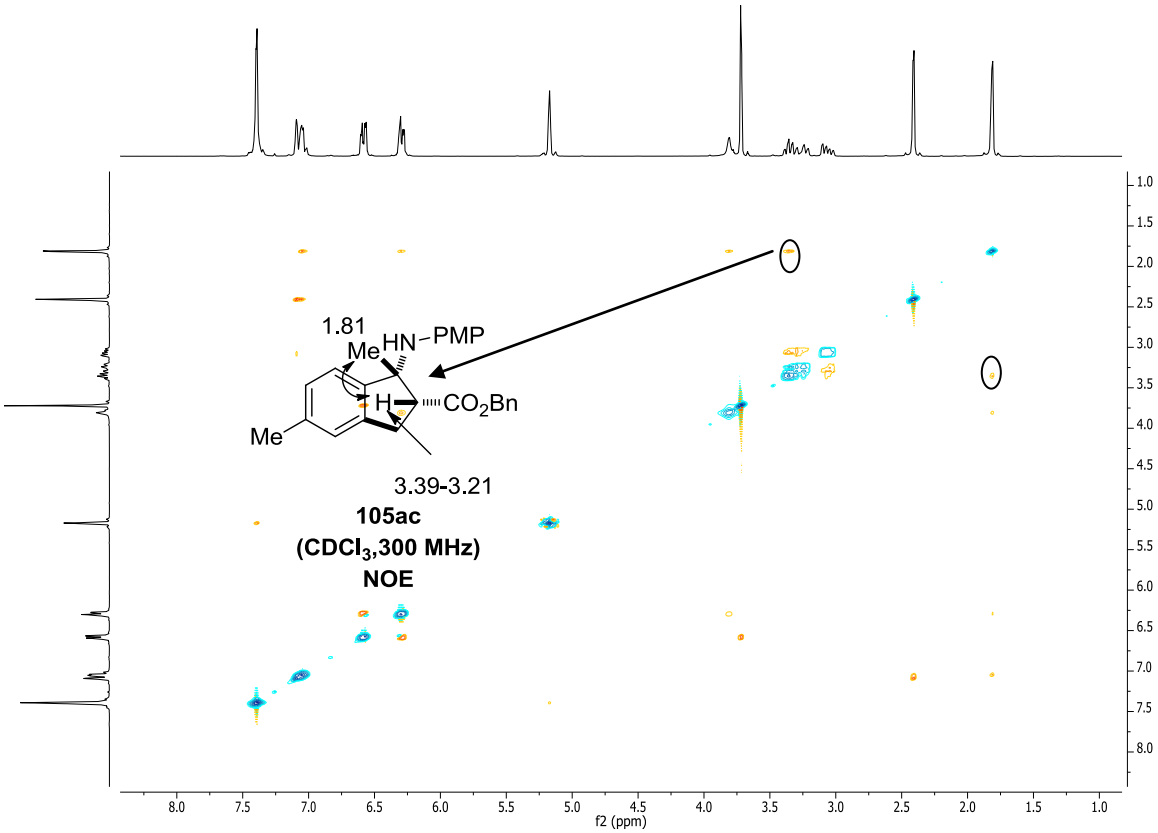

6.65
6.64
6.62
6.61
6.59
6.57
3.72
H
MeO
O
NEt2
O
H
OH
103d
(CDCl3, 300 MHz)
NOE
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

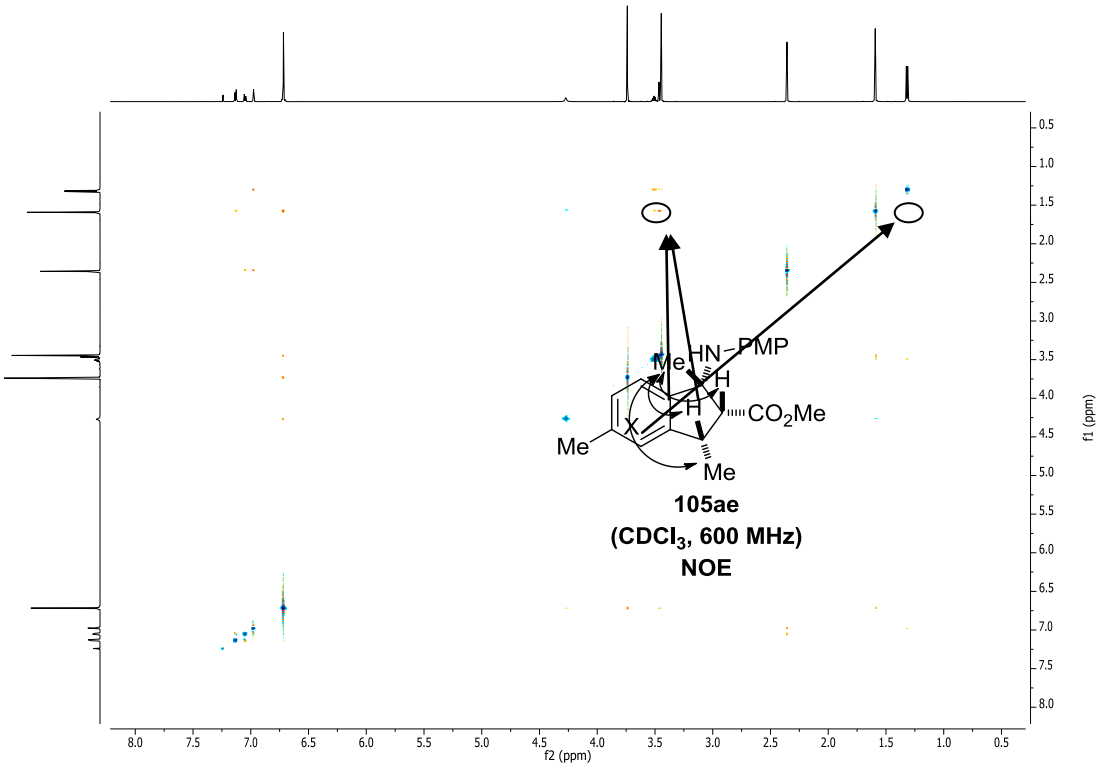

7.65
7.58
4.37
4.34
4.32
4.30
H
O
NEt2
H
H
O
O
OH
O
H
103w
(CDCl3, 300 MHz)
NOE
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
f1 (ppm)

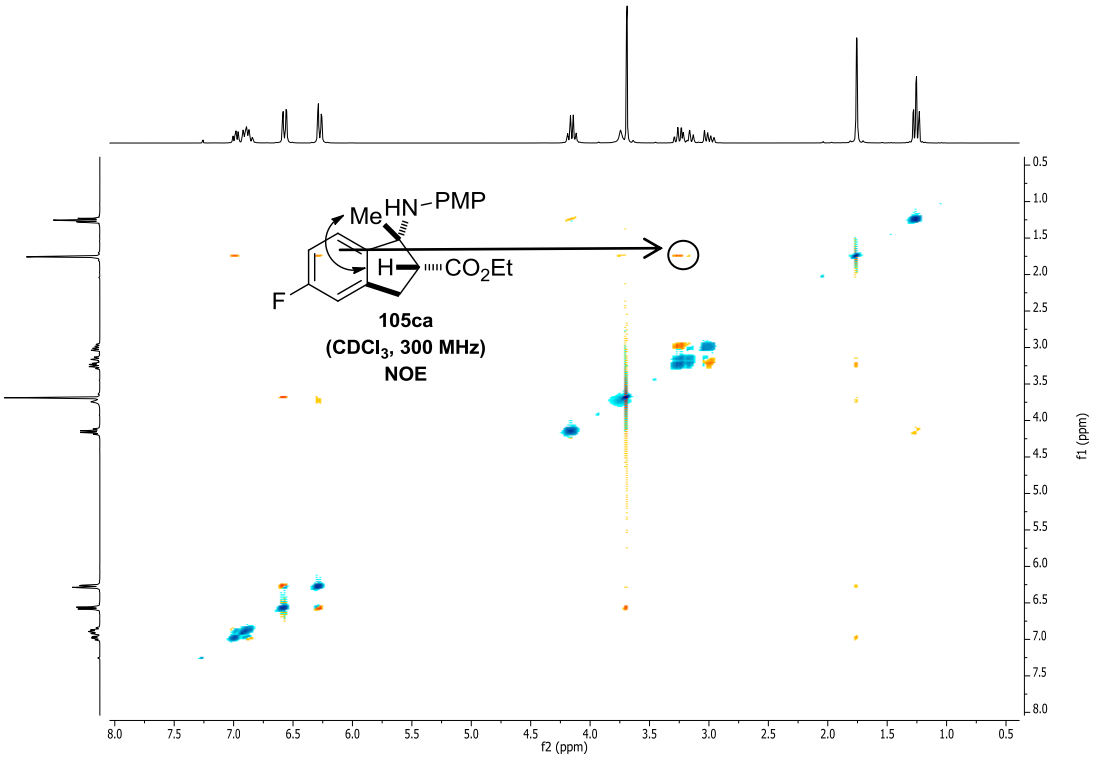

HO
O
NEt2
H
O
O
O
NEt2
EtO
O
OH
O
(CDCl3, 300 MHz)
NOESY
f2 (ppm)
f1 (ppm)

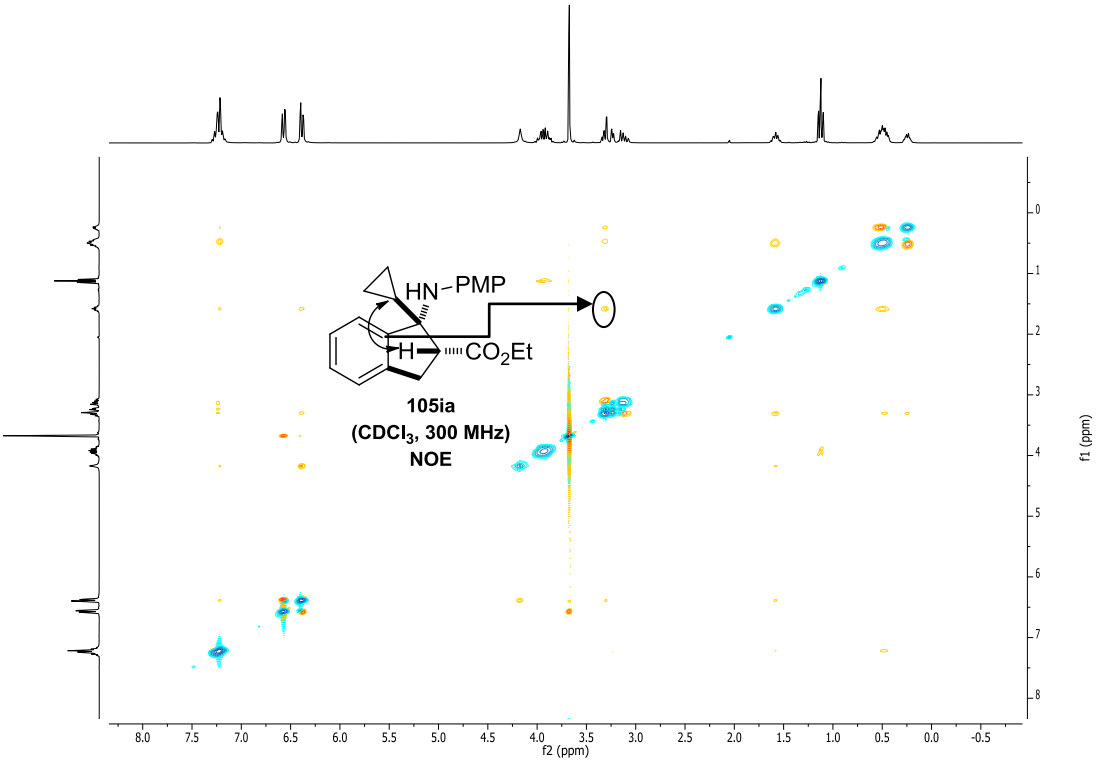

Me
HN
PMP
H
CO2Et
Me
105aa
(CDCl3, HSQC)
f2 (ppm)
f1 (ppm)

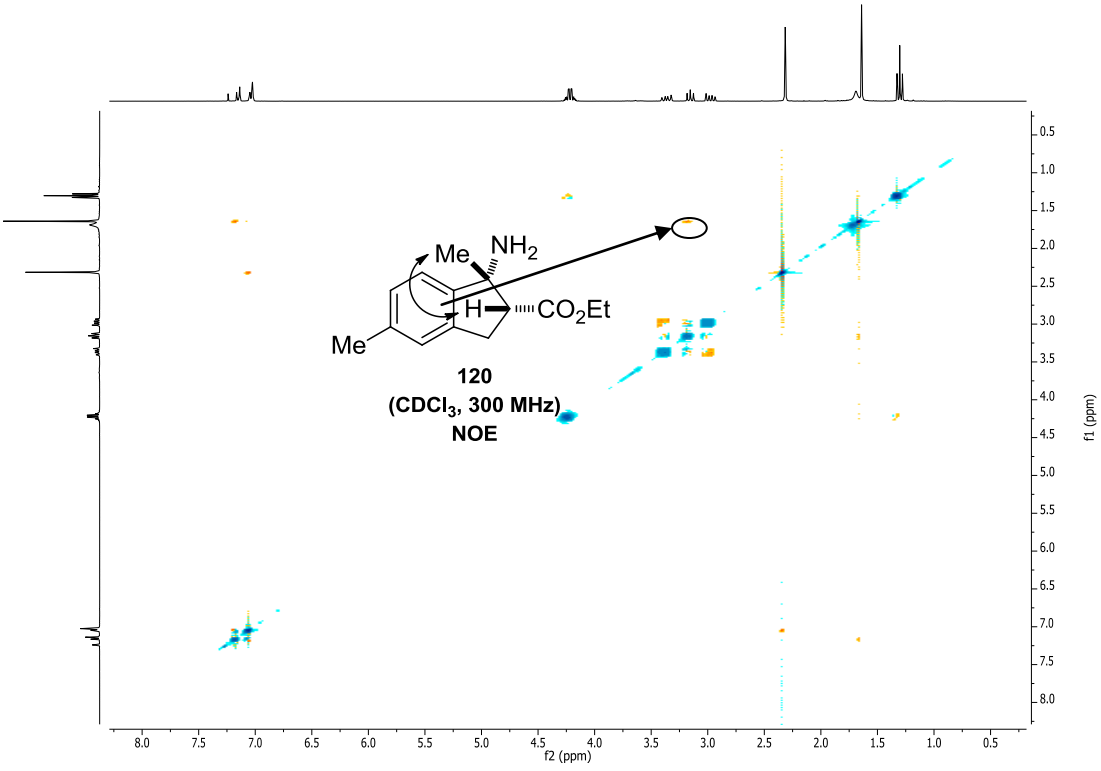

3.27
3.24
3.21
3.16
3.13
1.76
1.76
Me
HN–PMP
H
CO2Et
Me
3.27-3.13
105aa
(CDCl3, NOE)
f1 (ppm)

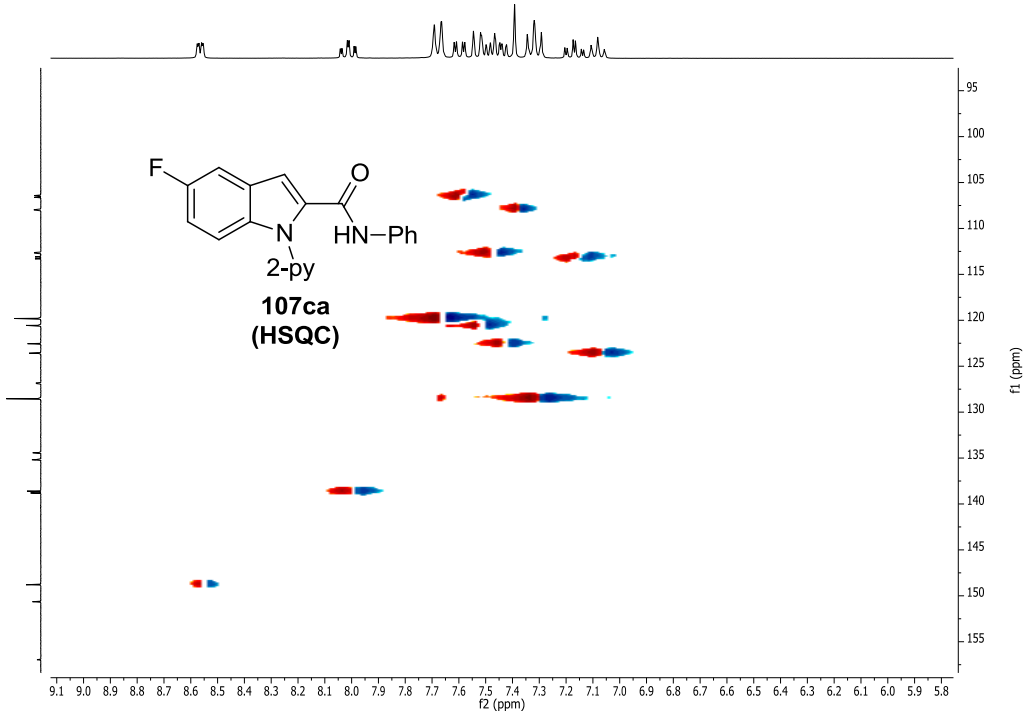

1.81
Me
HN–PMP
H
CO2Bn
Me
3.39-3.21
105ac
(CDCl3,300 MHz)
NOE
f2 (ppm)

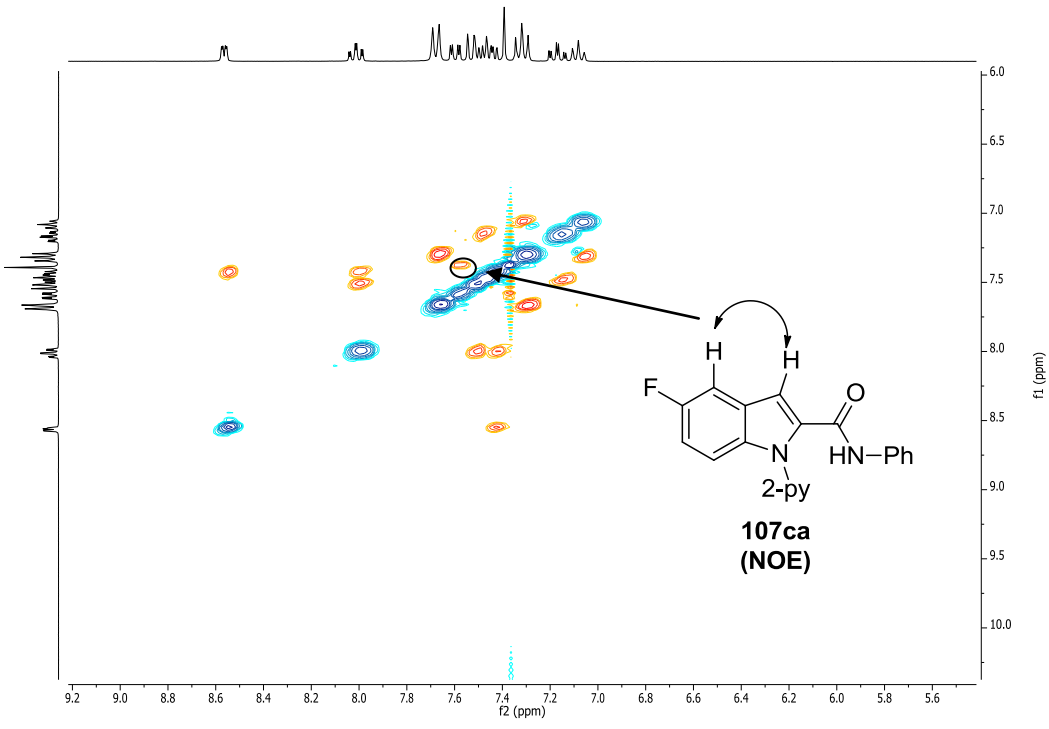

Me
HN–PMP
H
H
CO2Me
X
Me
Me
105ae
(CDCl3, 600 MHz)
NOE
f2 (ppm)
f1 (ppm)

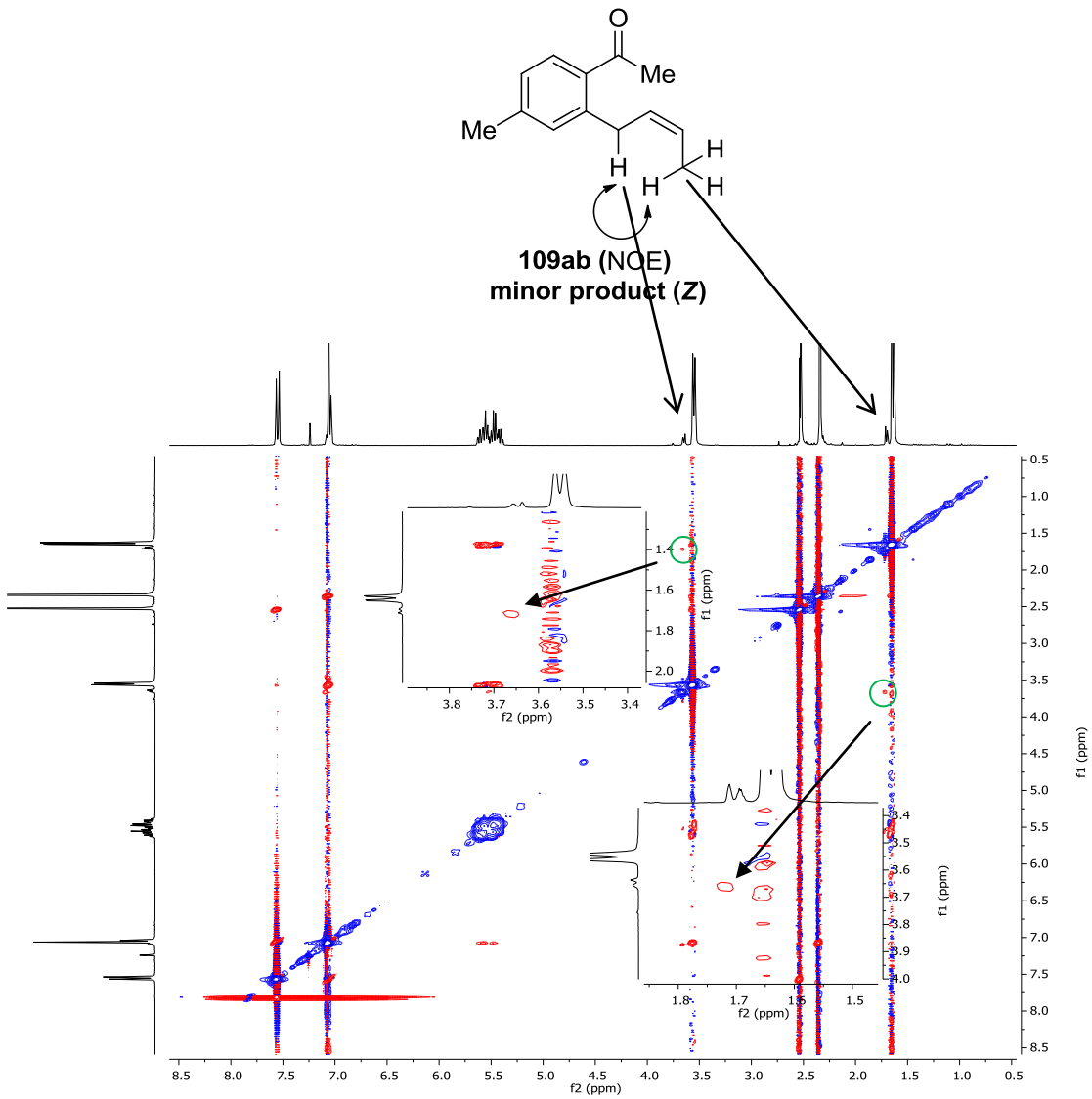

Me
HN–PMP
H
CO2Et
F
105ca
(CDCl3, 300 MHz)
NOE
f2 (ppm)
f1 (ppm)

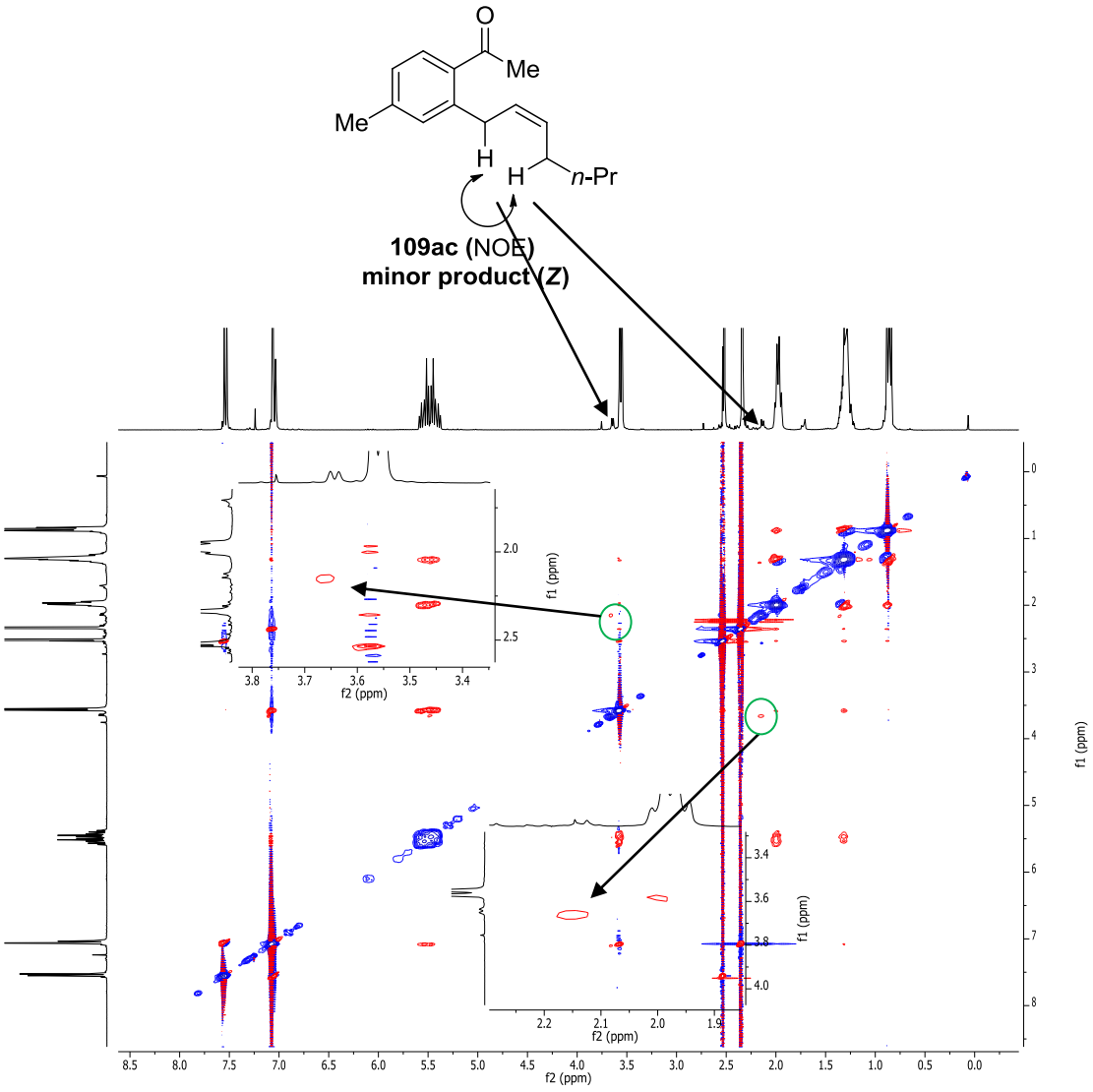

HN–PMP
H
CO2Et
105ia
(CDCl3, 300 MHz)
NOE
f2 (ppm)
f1 (ppm)

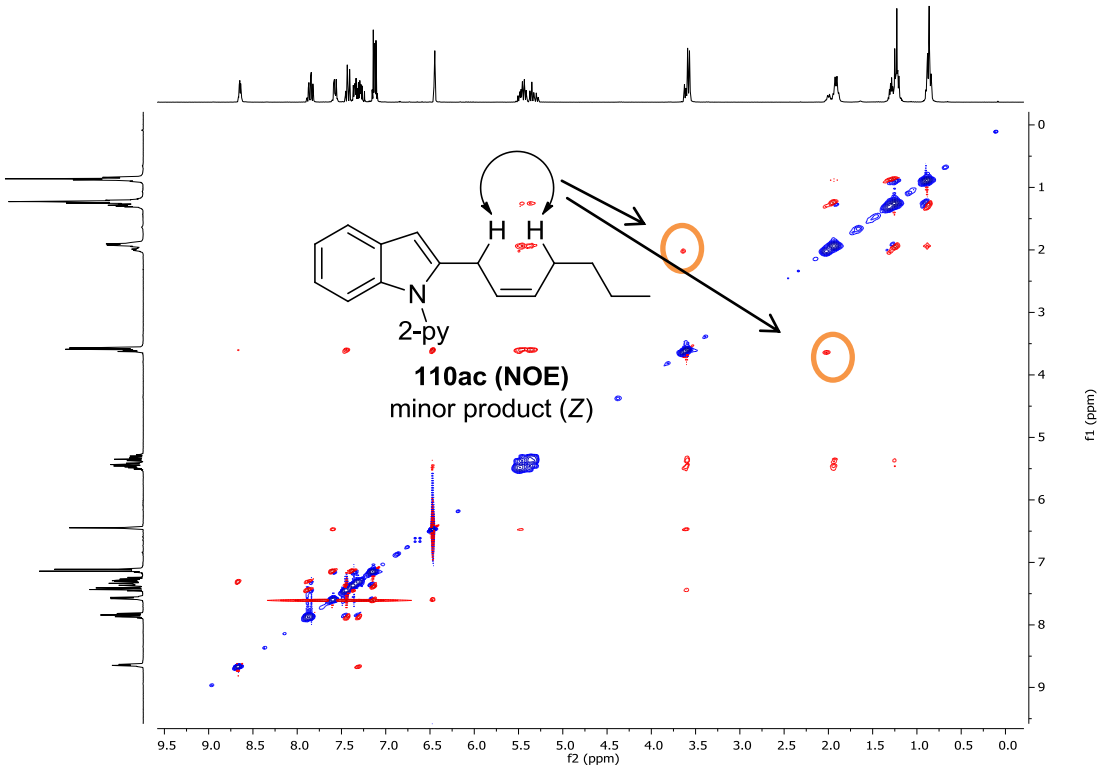

Me
NH2
H
CO2Et
Me
120
(CDCl3, 300 MHz)
NOE
f2 (ppm)
f1 (ppm)


F
O
N
HN−Ph
2-py
107ca
(HSQC)
f2 (ppm)
f1 (ppm)


H
H
F
O
N
HN−Ph
2-py
107ca
(NOE)
f2 (ppm)
f1 (ppm)


O
Me
Me
H
H
H
H
109ab (NOE)
minor product (Z)
f2 (ppm)
f1 (ppm)


O
Me
Me
H
H
n-Pr
109ac (NOE)
minor product (Z)
f2 (ppm)
f1 (ppm)


H H
N
2-py
110ac (NOE)
minor product (Z)
f2 (ppm)
f1 (ppm)

5 References

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Posters & Conferences

- ✧ 1) Lower Saxony Catalysis Symposium (Nikas). 16th–17th October 2014, Goettingen, Germany.
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