博士論文

論文題目　Development of Cp*Co^{III}-Catalyzed C-H Bond Addition Reactions to Electrophiles
(Cp^*Co^{III} 触媒による C-H 結合の求電子剤への付加反応の開発)

氏　　名　吉野　達彦　(Tatsuhiko Yoshino)

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Abbreviation

Ac	acetyl
Ad	1-adamantyl
aq.	aqueous solution
Ar	aryl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bu	butyl
Bz	benzoyl
Cbz	benzoyloxycarbonyl
CMD	concerted metalation-deprotonation
Cp	cyclopentadienyl
Cp*	pentamethylcyclopentadienyl
Cp^{Et5}	pentaethylcyclopentadienyl
Cp^{Me4}	tetramethylcyclopentadienyl
Cp^{tt}	1,3-di-*tert*-butylcylopentadienyl
d	day(s)
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DG	directing group
DMA	*N*,*N*-dimethylacetamide
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
EDTA	ethylenediamine tetraacetic acid
eq	equivalent(s)
Et	ethyl
h	hour(s)
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
IPr·HCl	1,3-Diisopropylimidazolium chloride
*i*Pr	2-propyl
KIE	kinetic isotope effect
L	ligand
Me	methyl
min	minute(s)
MS 3A	molecular sieves 3A

NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
*o*Ns	2-nitrobenzenesulfonyl
PG	protecting group
Ph	phenyl
Piv	pivaloyl
PMP	4-methoxyphenyl
*p*Ns	4-nitrobenzenesulfonyl
Pym	2-pyrimidyl
rt	room temperature
S_EAr	electrophilic aromatic substitution
SEM	2-(trimethylsilyl)ethoxymethyl
*t*Bu	*tert*-butyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
tmp	2,2,6,6-tetramethylpiperidide
TMS	trimethylsilyl
TON	turnover number
Ts	*p*-toluenesulfonyl

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Chapter 1 Investigation of New Cobalt Catalysts for C-H Bond Addition to Electrophiles

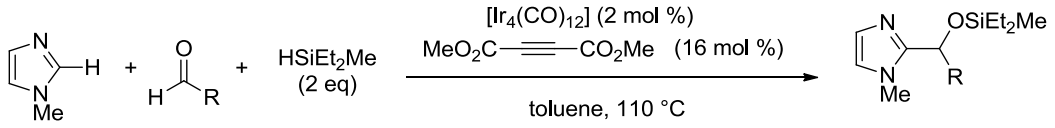
1.1 Background

1.1.1 Transition Metal-Catalyzed C-H Bond Activation and Reactions with Electrophiles

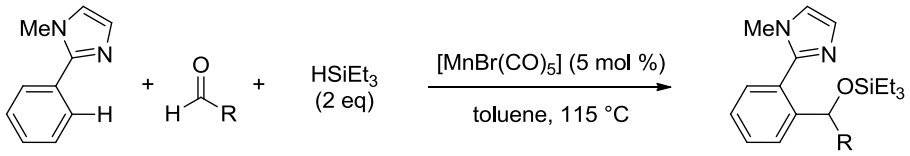
Nucleophilic addition of organometallic reagents to polar electrophiles, such as aldehydes, imines, and Michael acceptors, is a fundamental C-C bond-forming reaction in organic synthesis. Although it is a reliable method, there are several drawbacks in terms of atom economy[1] and functional group compatibility. The generation of nucleophilic organometallic reagents generally requires stoichiometric amounts of strong bases and/or reducing metals, such as Mg and Li, which inevitably produce stoichiometric amounts of salt waste. Moreover, the strongly basic nature of the required bases as well as the organometallic nucleophiles themselves often damages various functional groups.

The transition metal-catalyzed C-H bond functionalization reaction is an attractive method for addressing these issues.[2] The formation of organotransition metal species via aromatic and aliphatic C-H bond activation assisted by coordinating functional groups, which are called directing groups, has been extensively studied over the past few decades. Reactions with polar electrophiles such as aldehydes, imines and Michael acceptors, however, are not as well studied as those with alkenes and alkynes.[2i] Addition reactions of aromatic C-H bonds to aldehydes have been achieved using Ir[3] and Mn[4] catalysts and stoichiometric amounts of silanes as trapping reagents of the produced alcohols to achieve catalytic turnover (Scheme 1). Yoshikai and co-workers reported a Co-catalyzed addition reaction of aromatic C-H bonds to imines in the presence of heteroaromatic rings as directing groups.[5] The reaction also required a stoichiometric amount of a Grignard reagent (Scheme 2). In most of these catalytic systems, C-H bond activation is thought to be achieved by the oxidative addition of C-H bonds to low-valent transition metal catalysts to afford metal hydride complexes. Difficulties in reductive elimination to form heteroatom-hydrogen bonds,[6] however, might be problematic for achieving a fully catalytic process without stoichiometric amounts of additives.

Scheme 1 Transition metal-catalyzed C-H bond addition to aldehydes with silanes

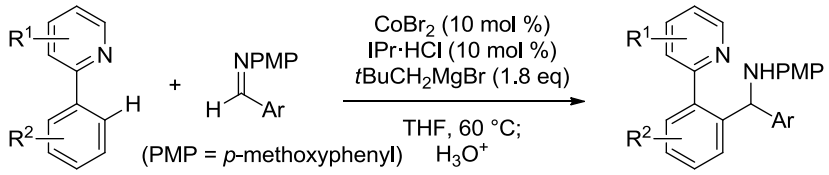


Murai, S. *et al. Angew., Chem. Int. Ed.* **2002**, *41*, 2779.



Kuninobu, Y.; Takai, K. *et al. Angew., Chem. Int. Ed.* **2007**, *46*, 6518.

Scheme 2 Co-NHC-catalyzed C-H bond addition to imines

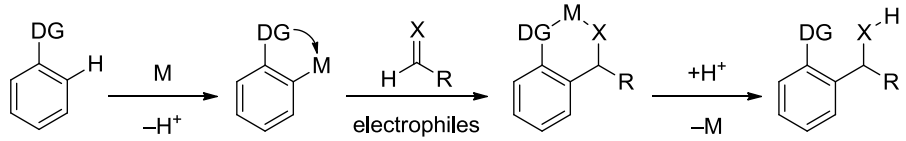


Yoshikai, N. *et al. Chem. Commun.* **2012**, *48*, 4305.

1.1.2 Cp*Rh-Catalyzed C-H Bond Activation and Addition Reactions to Electrophiles

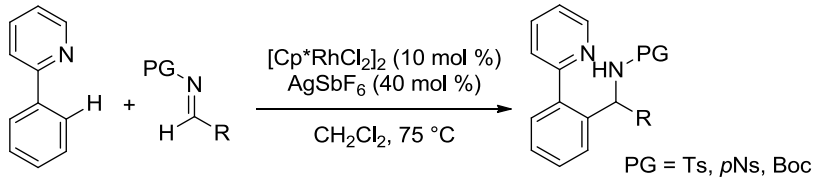
A thorough catalytic version of the reaction could be realized if C-H bond activation proceeded via net deprotonation and the catalytic cycle was completed by protonation after the insertion of electrophiles (Scheme 3).

Scheme 3 Nucleophilic addition of C-H bonds to electrophiles



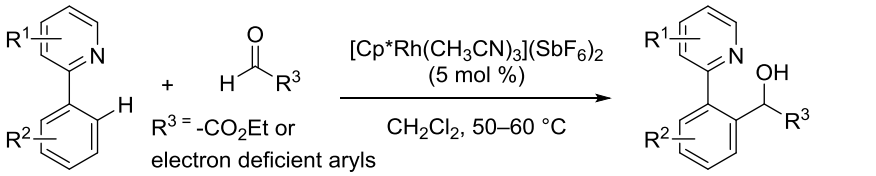
Cp^*Rh^{III} catalysts (Cp* = pentamethylcyclopentadienyl) recently emerged as privileged catalysts for this type of transformation. These catalysts were first introduced into the field of directing group-assisted catalytic C-H bond functionalization by Satoh, Miura, and co-workers for oxidative cyclization reactions.[7] Several oxidative C-H bond functionalization reactions using the Cp^*Rh^{III} catalysts have been developed over the past few years.[8] In 2011, Bergman, Ellman, and co-workers reported that the cationic Cp^*Rh^{III} catalyst generated from $[Cp^*RhCl_2]_2$ and $AgSbF_6$ in situ effectively promotes addition reactions of 2-phenypyridines to imines (Scheme 4).[9a,c] Around the same time, Shi's group reported similar reaction conditions.[9b,d] These reaction conditions are quite atom-economical and do not require stoichiometric amounts of reagents. These findings were soon followed by reactions with aldehydes,[10] isocyanates,[11] and α,β-unsaturated carbonyl compounds[12] under similar conditions were reported. Selected examples are summarized in Scheme 5.

Scheme 4 Cp^*Rh^{III}-catalyzed addition of 2-phenylpyridines to imines

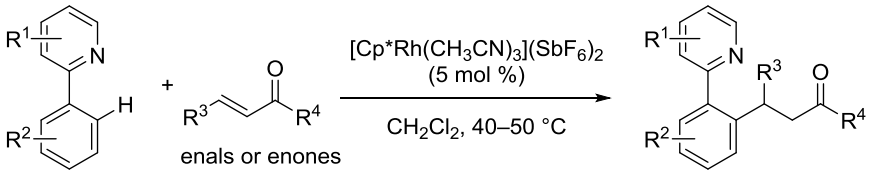


Bergman, R. G.; Ellman, J. A. *et al. J. Am. Chem. Soc.* **2011**, *133*, 1248.

Scheme 5 Cp*Rh^{III}-catalyzed addition reactions to other electrophiles



Li, C.-J. *et al. Adv. Synth. Catal.* **2011**, *353*, 1269.



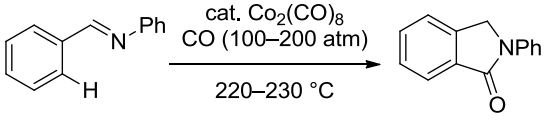
Li, C.-J. *et al. Org. Biomol. Chem.* **2011**, *9*, 7176.

Although Cp*Rh^{III}-catalyzed processes are useful and versatile, the need for expensive and precious rhodium sources is economically and environmentally disadvantageous. A recent report indicated similar catalytic activity of Ru^{II} for addition reactions to isocyanates and α,β-unsaturated ketones.[13] More easily accessible first-row transition metal catalysts, however, have not yet developed for this type of transformation.[14]

1.1.3 Cobalt Catalysts for C-H Bond Functionalization

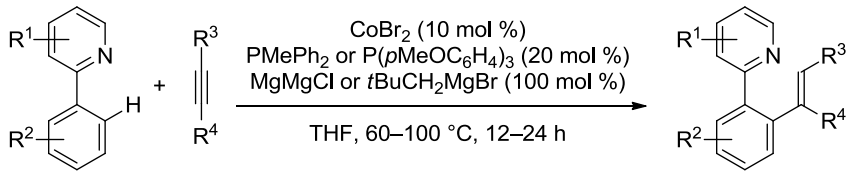
Cobalt is homologous to rhodium and iridium, which are often utilized for catalytic C-H bond functionalization reactions, but it is a more abundant first-row transition metal. Therefore, cobalt is a highly promising candidate as an alternative catalyst of C-H bond functionalization reactions. The history of cobalt-catalyzed C-H bond functionalization reactions dates back to the 1950's, when Murahashi *et al.* reported a reaction between a Schiff base and carbon monoxide using $Co_2(CO)_8$ as the catalyst under harsh conditions (Scheme 6).[15] Nevertheless, cobalt-catalyzed C-H bond functionalization reactions, especially C-C bond-forming reactions were scarcely investigated until very recently.[16] Yoshikai and co-workers made notable progress in 2010, demonstrating the ability of a low-valent cobalt catalyst prepared in situ via reduction of a Co^{II} salt by Grignard reagents for chelation-assisted C-H bond functionalization reactions (Scheme 7).[17] C-H bond activation is proposed to proceed via oxidative addition of C-H bonds to a low-valent cobalt species in these reactions. Since these pioneering studies, cobalt/Grignard reagent catalytic systems have been intensively exploited for several types of C-H bond functionalization reactions[18] by Yoshikai's group as well as other researchers.

Scheme 6 $Co_2(CO)_8$-catalyzed carbonylation of Schiff base

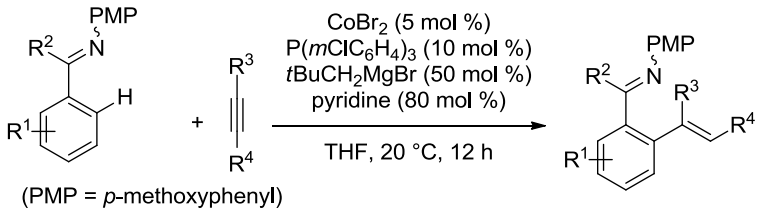


Murahashi, S. *J. Am. Chem. Soc.* **1955**, *77*, 6403.

Scheme 7 $CoBr_2$-Grignard reagent catalytic system for C-H bond alkenylation



Yoshikai, N. *et al. J. Am. Chem. Soc.* **2010**, *132*, 12250.



(PMP = *p*-methoxyphenyl)

Yoshikai, N. *et al. J. Am. Chem. Soc.* **2011**, *133,* 17283.

1.1.4 Cyclopentadienylcobalt(III) as Catalyst Candidates

In contrast to low-valent cobalt catalysis, high-valent electrophilic cobalt catalysts have not been investigated in C-H bond functionalization reactions, although there are some reports of stoichiometric processes, including C-H bond metalation via electrophilic C-H bond activation by Co^{III} species.[19] Considering the mechanism of C-H bond addition reactions, in which cyclometalated intermediates react with electrophiles, three or more available coordination sites with a facial geometry are necessary. The most straightforward design of the catalyst candidates based on the reported Cp^*Rh^{III} catalysts[9,10] are dicationic cyclopentadienylcobalt complexes with weakly coordinating dissociable ligands (Figure 1). Among the $CpCo^{III}$ (Cp = cyclopentadienyl) and Cp^*Co^{III} complexes reported in the literature, I focused on the dicationic cyclopentadienylcobalt arene complexes (Figure 1, right). Although the synthesis, structure, ligand exchange, and electronic properties of these complexes have been studied,[20] they have never before been utilized as catalysts or reagents for organic transformation. Ligand exchange from an arene to other arenes or polar solvent molecules reportedly occurs, and these complexes are thus considered to have enough available coordination sites. Based on this background, I began my investigation by synthesizing dicationic cyclopentadienylcobalt complexes and evaluating their catalytic activity for C-H bond functionalization reactions.

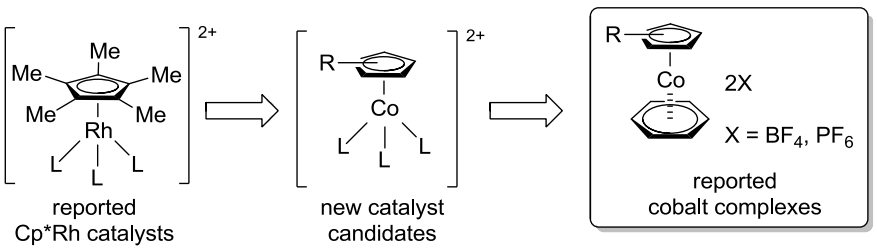


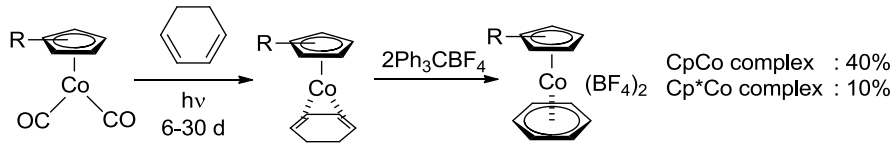
Figure 1 Structure of catalyst candidates for C-H bond addition reactions

1.2 Synthesis of Dicationic Cyclopentadienylcobalt Complexes

1.2.1 Synthesis of $[Cp^*Co(C_6H_6)](PF_6)_2$ (1a)

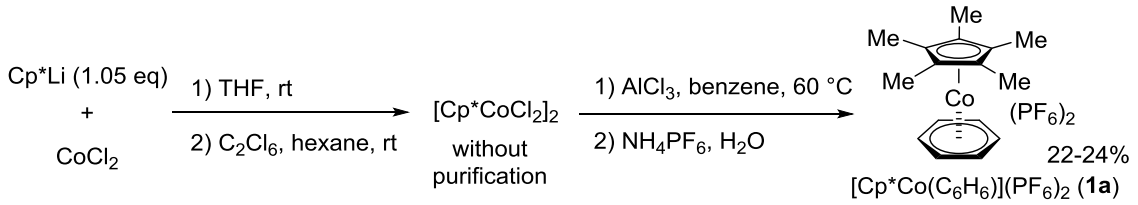
Because $[CpCo(C_6H_6)](BF_4)_2$ is quite unstable and difficult to store over a long period of time,[20b] the Cp^*Co^{III} complex was selected as the first candidate. Preparation of $[CpCo(C_6H_6)](BF_4)_2$ was reported by Fischer[20a] and the same method was used for the synthesis of $[Cp^*Co(C_6H_6)](BF_4)_2$ (Scheme 8).[20b] These methods, however, are not attractive for practical preparation due to the long reaction time under photo-irradiated conditions and the low yield, especially in the case of the Cp^*Co^{III} complex.

Scheme 8 Reported synthetic method of dicationic cobalt-arene complexes



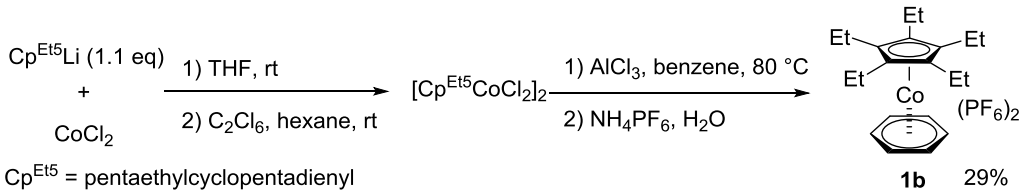
A more practical synthesis from the corresponding dichloride dimer[21] was established by Kölle and co-workers.[20c] I obtained $[Cp^*Co(C_6H_6)](PF_6)_2$ (**1a**) as an air- and moisture-stable yellow powder without purification of any intermediates (Scheme 9). After complexation of Cp*Li and $CoCl_2$, oxidation by hexachloroethane afforded crude $[Cp^*CoCl_2]_2$ as an air-stable green solid. Abstraction of the coordinating chloride using $AlCl_3$ in benzene and subsequent anion exchange with NH_4PF_6 in water resulted in **1a** as a water-insoluble precipitate.

Scheme 9 Synthesis of $[Cp^*Co(C_6H_6)](PF_6)_2$ (1a)



Pentaethylcyclopentadienyl complex **1b** was also synthesized by the same procedure using pentaethylcyclopentadienyllithium[22] (Scheme 10).

Scheme 10 Synthesis of $[Cp^{Et5}Co(C_6H_6)](PF_6)_2$ (1b)



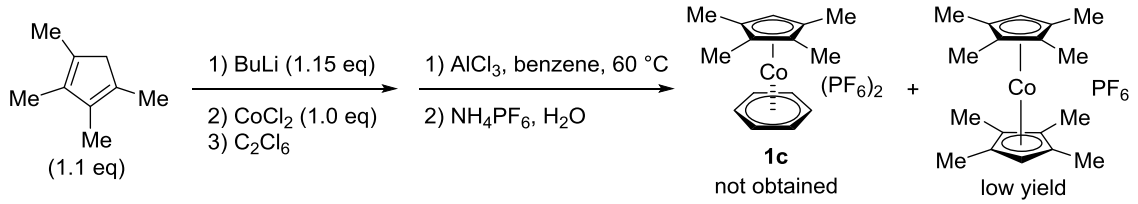
Cp^{Et5} = pentaethylcyclopentadienyl

1b 29%

1.2.2 Synthesis of Other Cyclopentadienylcobalt Complexes from $Co_2(CO)_8$

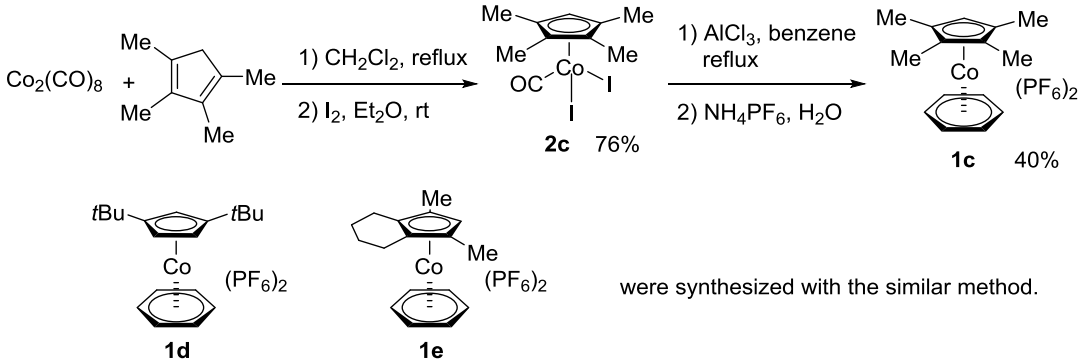
Although the above-method is convenient, it could not be used to synthesize other types of cylopentadienylcobalt complexes. For example, synthesis of tetramethylcyclopentadienylcobalt complex **1c** failed and only the cobaltocenium salt was isolated (Scheme 11).

Scheme 11 Unsuccessful synthesis of tetramethylcyclopentadienylcobalt complex 1c



I speculated that the failed synthesis might be due to an unsuccessful complexation step and therefore examined alternative cyclopentadienylcobalt halide precursors. Tetramethylcyclopentadienylcobalt diiodide carbonyl complex **2c**, which could be obtained from $Co_2(CO)_8$ and tetramethylcyclopentadiene according to the literature,[23] was a good precursor for the cationic complex **1c** (Scheme 12). The same conditions for halide abstraction and anion exchange successfully afforded **1c** in acceptable yield. Complexes **1d** and **1e** could be similarly synthesized using the corresponding dienes[24] and $Co_2(CO)_8$.

Scheme 12 Synthesis of 1 from $Co_2(CO)_8$

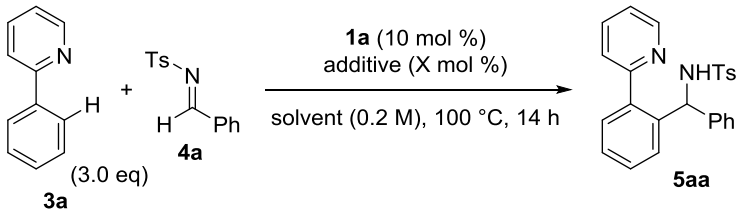


1.3 Addition of 2-Phenylpyridine to Imines

1.3.1 Optimization of the Reaction Conditions

The addition reaction of 2-phenylpyridine **3a** to *N*-tosylimine **4a** was selected as a model reaction. The results of the initial trials using [Cp*Co(C_6H_6)](PF_6)$_2$ (**1a**) as a catalyst are summarized in Table 1. A mixture of imine **4a**, 2-phenylpyridine **3a** (3.0 eq), and **1a** (10 mol %) was heated in various solvents at 100 °C (entries 1-5). When DCE was used as a solvent, the desired product **5aa** was afforded albeit in low yield (30%, entry 4). Although prolonging the reaction time slightly improved the yield, the result remained unsatisfactory (entry 6). The addition of some basic or acidic additives negatively affected the reactivity (entries 7-9). These negative effects might be due to the coordinating ability of these additives because the addition of a coordinating solvent, CH_3CN, clearly inhibited the desired reaction (entry 10).

Table 1 Initial trials with *N*-tosylimine

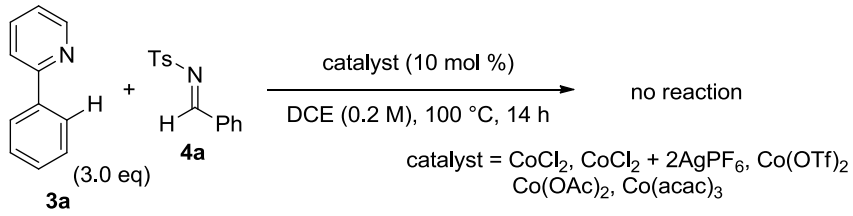


entry	solvent	additive (X mol %)	yield (%)[a]
1	CH_3CN	–	< 5
2	toluene	–	< 5
3	$PhCF_3$	–	< 5
4	DCE	–	30
5	*tert*-amyl-alcohol	–	< 5
6[b]	DCE	–	44
7	DCE	CsOAc (10)	22
8	DCE	CsOPiv (10)	7
9	DCE	PivOH (10)	22
10	DCE	CH_3CN (200)	< 5

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard. [b] Reaction time 60 h

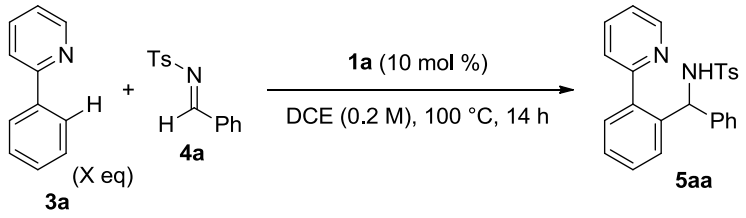
Control experiments confirmed the importance of the cationic Cp*Co^{III} catalyst: no reaction proceeded with various commercially available Co^{II} and Co^{III} compounds (Scheme 13).

Scheme 13 Control experiments with various cobalt sources



A substrate inhibition effect by **3a** was observed (Table 2). While almost no difference was observed in the yields of **5aa** with 1.5 or 3.0 equivalents of **3a** (entries 1, 2), further increasing the amount of **3a** led to a significant decrease in the reactivity (entry 3). The same substrate inhibition effect was reported in the Cp*Rh^{III}-catalyzed reaction[9c] and the authors explained that the coordination of 2-phenypyridine **3a** to the cyclometalated intermediate likely impeded the coordination and insertion of the imine. A similar explanation is plausible in this case.

Table 2 Substrate inhibition by 3a



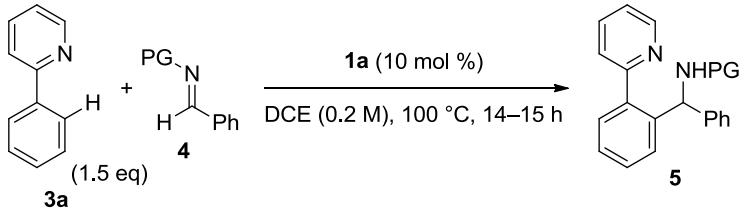
entry	amount of **3a** (X eq)	yield (%)[a]
1	1.5	33
2	3.0	30
3	6.0	20

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.

Next, I screened several protecting groups of imines (Table 3). Bergmann and Ellman revealed that the addition of **3a** to *N*-tosylimine **4a** in the presence of the Cp*Rh^{III} catalyst is reversible and the equilibrium constant is not sufficient to achieve a high yield.[9a] Although they found that the problem could be avoided by using *N*-Boc imine **4b**, only a complex mixture was obtained under the conditions used (entry 2), probably because the *N*-Boc group was not tolerated in Lewis acidic metal-catalyzed reaction conditions at a high temperature. *N*-Diphenylphosphinoylimine **4c** showed no reactivity (entry 3). Other arylsulfonyl protecting groups, which would have stronger electron-withdrawing effects than the tosyl group, were also investigated. While nosyl

groups and 2-pyridinesulfonyl group were not suitable due to their coordinating properties (entries 4, 5, 7), *N*-2-thiophenesulfonylimine **4g**[25] afforded the product in an improved yield (44%, entry 6).

Table 3 Screening of imines

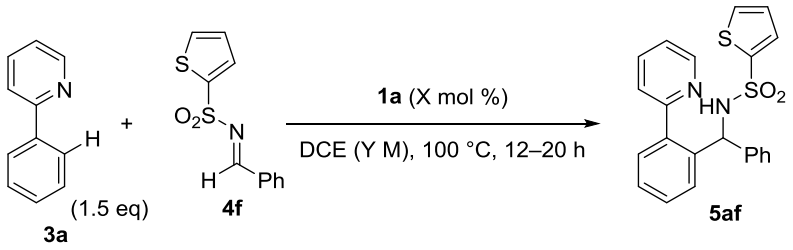


entry	PG	imine	product	yield (%)[a]
1	Ts	**4a**	**5aa**	33
2	Boc	**4b**	**5ab**	messy
3	$Ph_2P(O)$-	**4c**	**5ac**	0
4	*p*Ns	**4d**	**5ad**	0
5	*o*Ns	**4e**	**5ae**	16
6	2-thienyl-SO_2-	**4f**	**5af**	44
7	2-pyridyl-SO_2-	**4g**	**5ag**	0

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.

The conditions were optimized using **4g** as an electrophile (Table 4). The yield was improved under more concentrated conditions (entry 2), in which the equilibrium should shift to the right side. More significant improvement was achieved by changing the work-up procedure from short silica gel chromatography to acidic quenching, followed by an aqueous work-up using EDTA solution (entry 3). The latter work-up method was beneficial to obtain a better yield with improved reproducibility. The reason for the improvement, however, is not yet clear. I suspect that the intermediate shown in Figure 2 was too stable to be protonated during the work-up on silica gel and some amount of the product could not be recovered by eluting AcOEt. Next, I tried to reduce the catalyst amount, but the reactivity was not adequate with 5 mol % of **1a** (entry 4). The addition of hexafluoroisopropanol (HFIP) as a proton source with weaker coordinating ability than carboxylic acids, which was anticipated to accelerate the protonation step, did not significantly affect the reactivity (entry 6).

Table 4 Miscellaneous optimization



entry	catalyst loading (X mol %)	concentration (Y M)	work-up method	yield (%)[a]
1	10	0.2	A	44
2	10	1	A	59
3	10	1	B	80
4	5	1	B	63
5[b]	5	1	B	67

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.
[b] HFIP (1 eq) was added.

work-up A : filitered through a short pad of silica gel with AcOEt as eluent
B : quenched by the addition AcOH, then *aq.*work-up with CH_2Cl_2/EDTA aq.

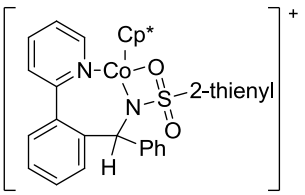
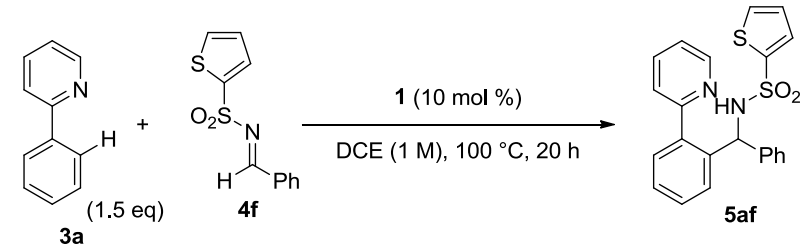
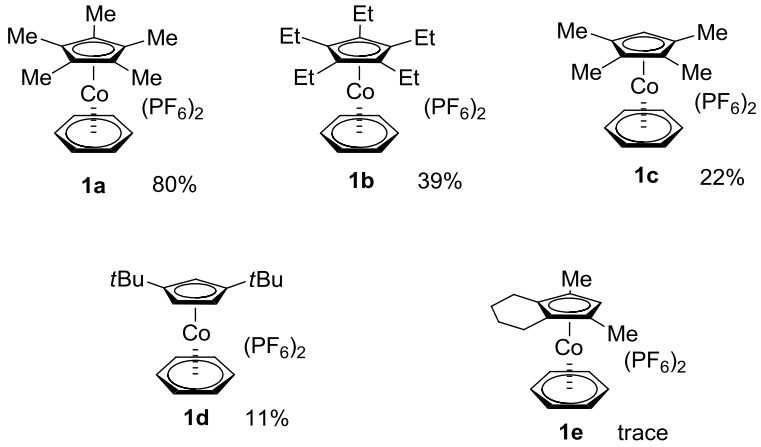


Figure 2 Intermediate before protonation

To achieve a more efficient catalytic turnover, other dicationic cyclopentadienylcobalt complexes were evaluated as catalysts (Table 5). The activity of all the other complexes, however, was inferior to that of **1b**. Poor yields with sterically more hindered catalysts (**1b**, **1e**, and probably **1d**) would result from the decreased reactivity due to steric repulsion between the ligands and substrates. It is much more difficult to explain the lower turnover number (TON) of **1c,** but the catalyst seemed to decompose because some unidentified precipitates appeared after the reaction. Complex **1a** was determined to be the best catalyst in terms of the balance between the reactivity and stability.

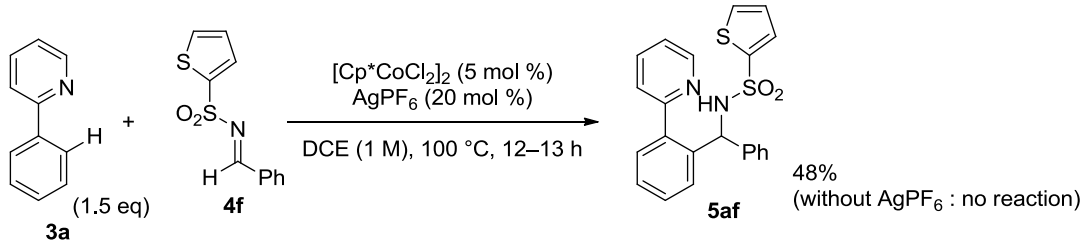
Table 5 Catalyst screening





Although a catalyst prepared in situ from $[Cp^*CoCl_2]_2$ and $AgPF_6$ could also promote the reaction, the yield was rather moderate, probably due to the inefficient formation of the active species via chloride abstraction and/or some impurities in $[Cp^*CoCl_2]_2$.[i] The non-cationic complex $[Cp^*CoCl_2]_2$ alone did not promote the reaction.

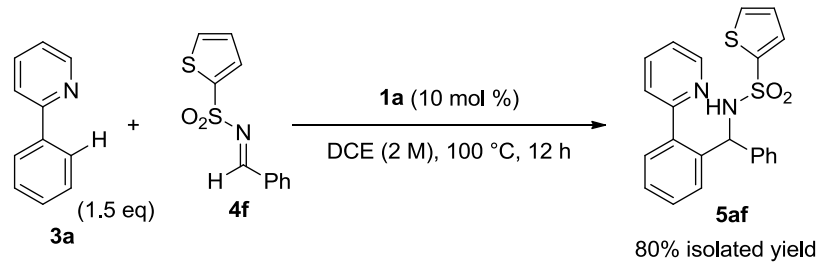
Scheme 14 Catalyst prepared in situ



Finally, product **5af** was isolated in 80% yield under the optimized reaction conditions shown in Scheme 15.

[i] Because purification was not successful, crude $[Cp^*CoCl_2]_2$ obtained in Scheme 9 was directly used. ^1H NMR analysis was also difficult due to some paramagnetic impurities.

Scheme 15 Optimized reaction conditions for addition to imine



1.3.2 Scope and Limitations

The scope of aromatic imines is shown in Table 6. Both electron-deficient (entries 3-6) and electron-rich (entries 7-9) aromatic imines afforded the desired products **5** in moderate to good yields. The yield was decreased to some extent by a strongly electron-donating methoxy group (entry 8), probably due to decreased electrophilicity and the relatively small equilibrium constant. No significant difference in reactivity was observed for sterically hindered *ortho*-substituted imine **9**. The reaction also proceeded with imines derived from electron-rich heteroaromatic aldehydes in moderate yields (entries 10, 11).

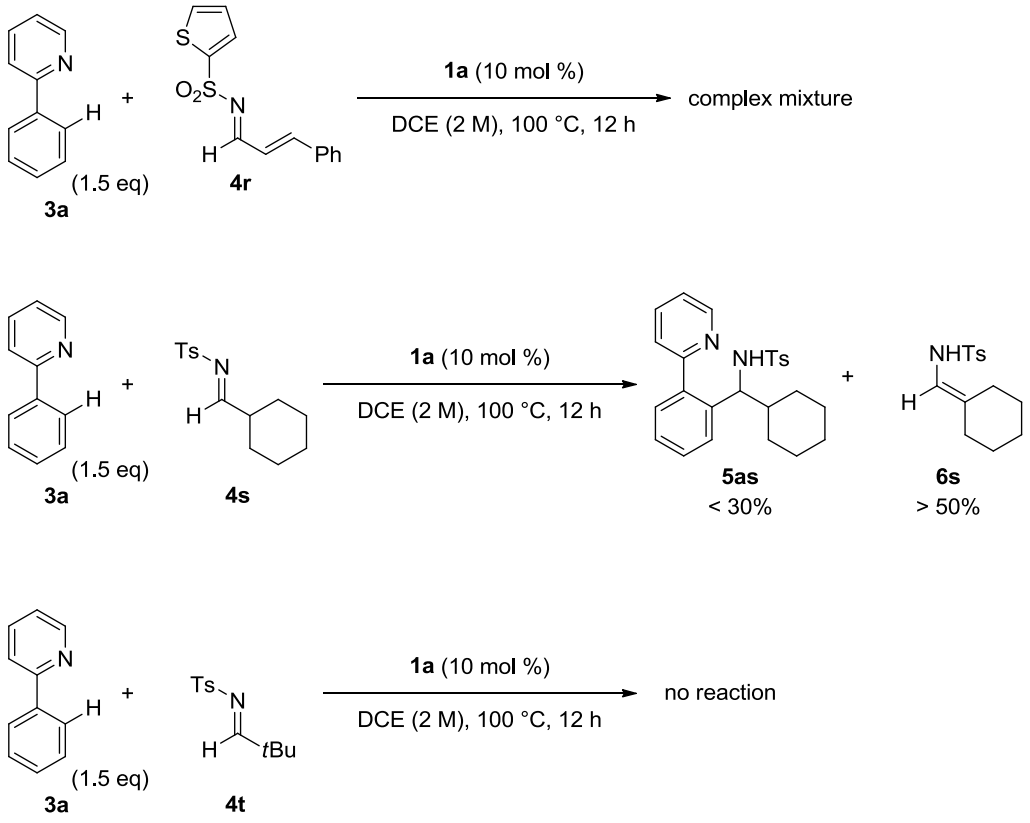
Table 6 Scope of aromatic imines

entry	R : imine **4**		product	yield (%)
1	Ph	**4f**	**5af**	80
2	2-naphthyl	**4h**	**5ah**	79
3	*p*ClC$_6$H$_4$-	**4i**	**5ai**	83
4	*p*BrC$_6$H$_4$-	**4j**	**5aj**	72
5	*p*CF$_3$C$_6$H$_4$-	**4k**	**5ak**	64
6	*m*ClC$_6$H$_4$-	**4l**	**5al**	76
7	*p*MeC$_6$H$_4$-	**4m**	**5am**	76
8	*p*MeOC$_6$H$_4$-	**4n**	**5an**	57
9	*o*MeC$_6$H$_4$-	**4o**	**5ao**	71
10	2-thienyl	**4p**	**5ap**	69
11	2-furyl	**4q**	**5aq**	66

In contrast to aromatic imines, alkenyl and alkyl imines did not give satisfactory results (Scheme 16). When α,β-unsaturated imine **4r** was utilized, conjugate addition and other side reactions competed, and therefore only a complex mixture was obtained. Aliphatic imines **4s** and **4t** were also examined as electrophiles. A tosyl group was selected as the protecting group for the aliphatic imines because the reversibility would be less problematic than for aromatic imines and 2-thiophenesulfonyl-protected aliphatic imines were rather unstable. In the case of imine **4s** bearing an α-proton, isomerization to the corresponding enamide **6s** occurred faster than the desired addition reaction. Therefore, aliphatic imine without an α-proton

4t was investigated. In this case, however, the reaction did not proceed at all and only the starting materials were recovered. Imine **4t** might be too sterically crowded to insert into the metalacycle intermediate.

Scheme 16 Limitations



1.3.3 Reaction Mechanism

A plausible reaction mechanism based on the reported Cp^*Rh^{III}-catalyzed reaction[9] is depicted in Figure 3. Initially, the coordinating benzene of **1a** would dissociate upon heating, and 2-phenylpyridine complex **I** would be generated. L_N indicates coordination of another 2-phenylpyridine or solvent molecule. The process of C-H activation is assumed to proceed via an electrophilic aromatic substitution (S_EAr) or a concerted metalation-deprotonation mechanism (CMD)[26] intermolecularly assisted by another 2-phenylpyridine as an external base[27] to form cyclometalated intermediate **II**. Although it is difficult to determine the mechanism by which the C-H activation step proceeded, S_EAr would be less likely because 2-phenylpyridine **3a** is an electron-deficient aromatic compound and the electronic effects of substrates **3** on the reactivity toward a Michael addition were not clear (discussed below). After ligand exchange (**III)** and the insertion of electrophiles (**IV**), proto-demetalation from **V** with another 2-phenylpyridine **3a** (or with acidic proton captured at the step from **I** to **II**) would dissociate the products and regenerate the key intermediate **II**. The observation that a large amount of 2-phenylpyridine **3a** decreased the reaction rate (1.3.1 Table 2, entry 3) implies that intermediate **I** with 2-phenylpyridine **3a** as an extra ligand exists as a resting state.

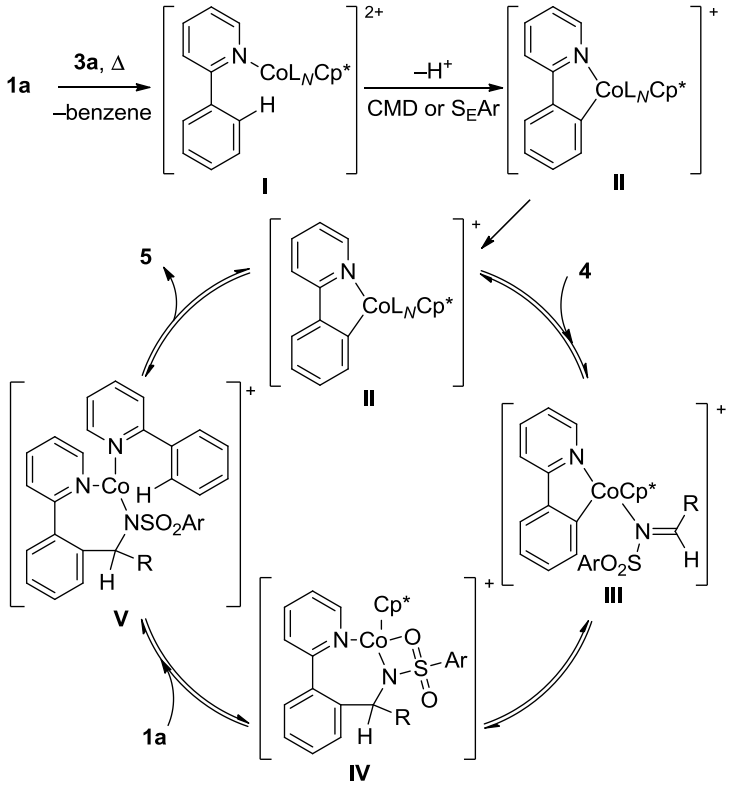
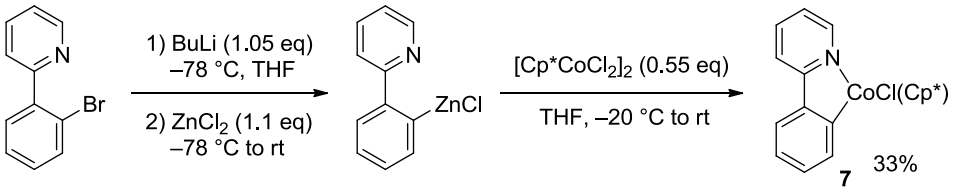


Figure 3 A plausible reaction mechanism

Several experiments were performed to confirm the intermediacy of cyclometalated species **II**. Attempts to directly observe intermediates by ^{1}H NMR under catalytic and stoichiometric reaction conditions did not provide any information due to severe broadening of the NMR signals caused by unidentified paramagnetic species. The synthesis and isolation of cyclometalated complex **7** via transmetalation from the corresponding arylzinc reagent, however, were successful. Complex **7** was quite air- and moisture-stable, and moderately stable toward silica gel column chromatography. A single crystal suitable for X-ray analysis was successfully obtained from toluene/CH_2Cl_2/hexane solution. The ORTEP diagram of **7** and the selected bond lengths and angles compared with those of the corresponding Cp*Rh^{III} complex[28] are shown in Figure 4 and Table 7. Cobalt complex **7** has a piano stool structure very similar to those of the rhodium and iridium complexes[28] but the bond lengths around the cobalt center are about 0.1 Å shorter (Table 7), reflecting the smaller ionic radius of Co^{III}. The difference in the M-C bond lengths between **7** and the rhodium complex (0.092 Å) was smaller than that of M-N bond lengths (0.137 Å), which indicates that Cp*Co^{III} forms a weaker M-C bond compared with Cp*Rh^{III}.

Scheme 17 Synthesis of a cyclometalated complex 7



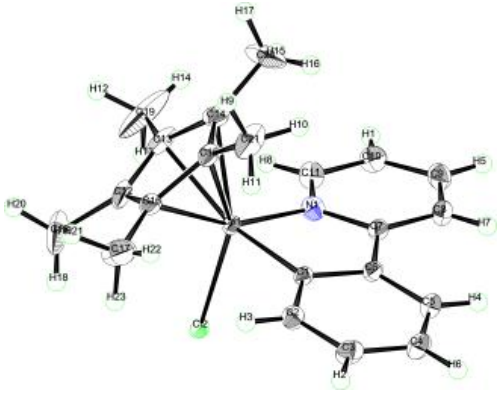


Figure 4 ORTEP diagram of 7 at the 50% probability level

Table 7 Selected bond lengths and angles of 7 and the corresponding Rh complex

	bond lengths of **7** [Å]	bond lengths of Cp*Rh^{III} [a] [Å]
M – N	1.955 (2)	2.092 (1)
M – C	1.944 (2)	2.036 (1)
M – Cl	2.2829 (9)	2.3917 (4)

	bond angles of **7** [deg]	bond angles of Cp*Rh^{III} [a] [deg]
N – M – C	82.50 (8)	78.71 (5)
C – M – Cl	90.91 (6)	88.34 (4)
Cl – M – N	93.13 (6)	87.87 (3)

[a] reported in ref[28], compound **2b**.

The catalytic activity of **7** was evaluated in the presence of $AgPF_6$ (Scheme 18). Although the reactivity was lower than that of cationic complex **1a**, the addition reaction proceeded with a moderate TON. The intermediacy of the cyclometalated intermediate **II** is clearly supported by this result. The observed lower reactivity in these reaction conditions implies that proto-demetalation from **V** is promoted by the acidic proton captured at the step between **I** and **II,** as well as another 2-phenylpyridine **3a**.

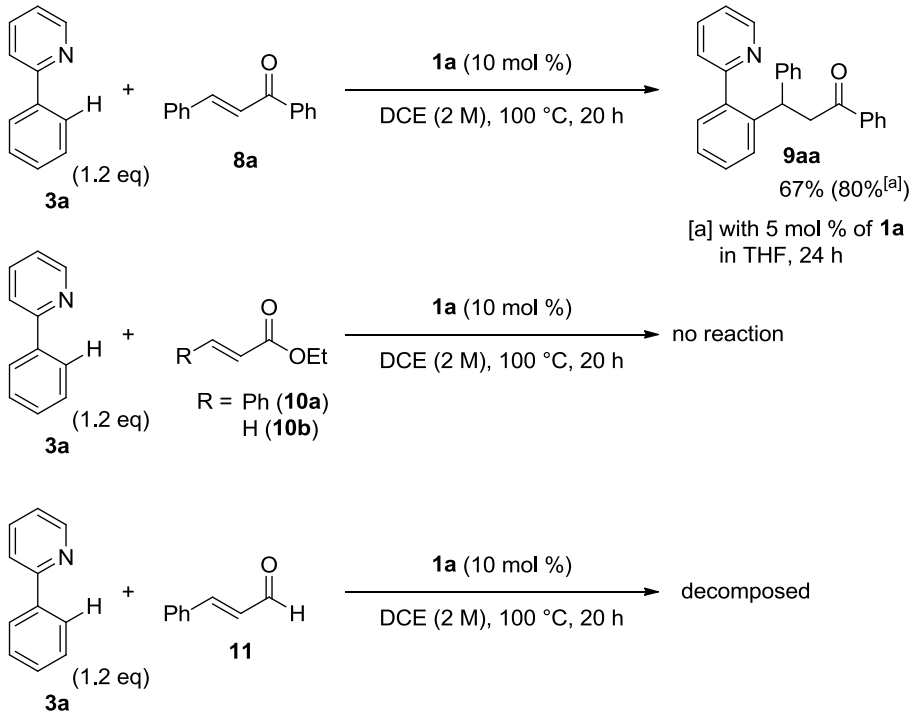
Scheme 18 Catalytic activity of 7

1.4 Addition of 2-Phenylpyridines to Michael Acceptors

1.4.1 Addition to α,β-Unsaturated Ketones

Conjugate addition reactions to α,β-unsaturated carbonyl compounds were also investigated to confirm the generality of the Cp^*Co^{III} catalysis. As initial trials, several Michael acceptors were subjected to almost the same conditions for imines (Scheme 19). Chalcone **8a** was a suitable substrate and the desired product **9aa** was isolated in 67% yield. The isolated yield was further improved to 80% by changing the solvent to THF and decreasing the catalyst loading to 5 mol %. By these slight modification of the reaction conditions, the formation of some byproducts that might be derived from chalcone **8a** was suppressed. On the other hand, α,β-unsaturated esters **10** afforded no detectable products, presumably because of their lower electrophilicity. In addition, more reactive α,β-unsaturated aldehyde **11** also failed to give the desired product. Aldehyde **11** was unstable under the reaction conditions and decomposition of **11** was observed.

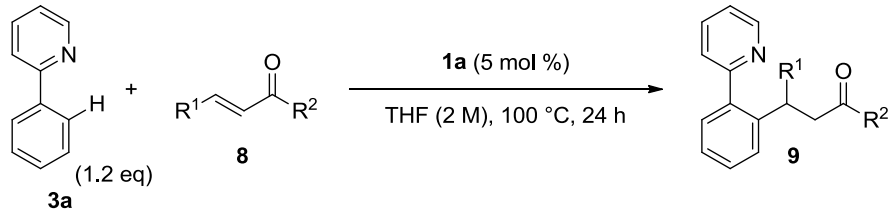
Scheme 19 Reactions with various Michael acceptors



The scope of enones is summarized in Table 8 and Scheme 20. Chalcone and its

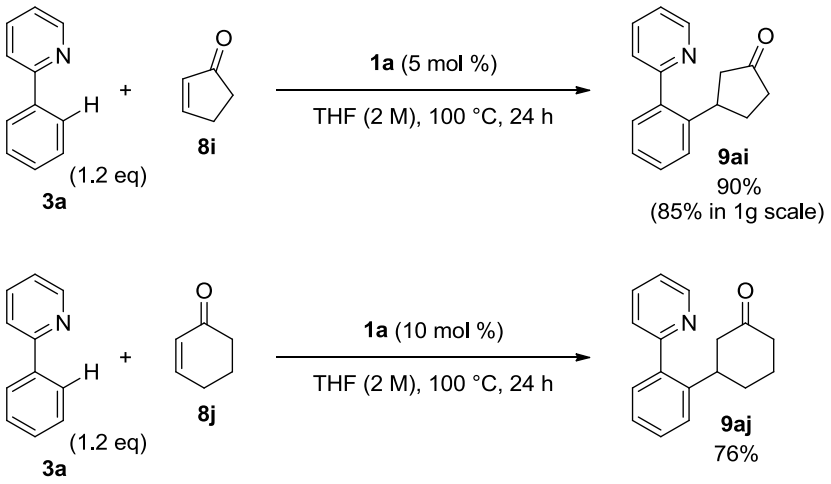
derivatives bearing either electron-donating or electron-withdrawing substituents gave the products in 67%-80% yield (Table 8, entries 1-5). Other acyclic alkyl substituted enones (entries 6-8) as well as cyclic enones (Scheme 20) also gave products **9af**-**9aj** in 76%-90% yield. Alkyl-substituted enones other than **8j** generally tend to afford a better yield than aromatic-substituted enones. The reaction was also successfully performed in preparative scale (5.0 mmol) without significant loss of the yield (**6ai**).

Table 8 Scope of acyclic enones



entry	R^1	R^2	enone	product	yield (%)
1	Ph	Ph	**8a**	**9aa**	80
2	*p*ClC_6H_4-	Ph	**8b**	**9ab**	75
3	*p*$MeOC_6H_4$-	Ph	**8c**	**9ac**	67
4	Ph	*p*BrC_6H_4-	**8d**	**9ad**	75
5	Ph	*m*$MeOC_6H_4$-	**8e**	**9ae**	76
6	Ph	Me	**8f**	**9af**	78
7	Me	Ph	**8g**	**9ag**	84
8	Me	Et	**8h**	**9ah**	84

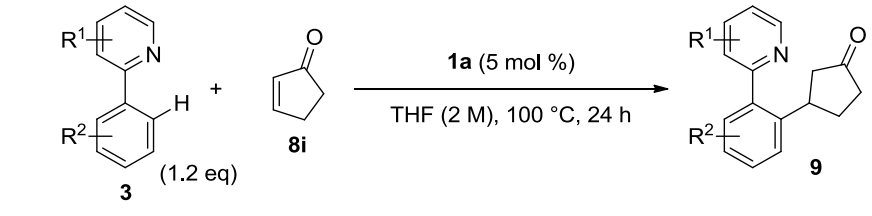
Scheme 20 Reactions with cyclic enones

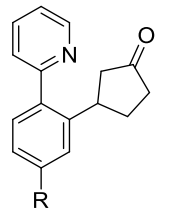


The effects of substituents on 2-phenylpyridine **3** were evaluated using 2-cyclopenten-1-one **8i** as an electrophile (Table 9). Donors with both electron-withdrawing and electron-donating groups at the *para*-position to the directing

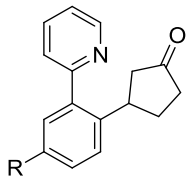
2-pyridyl group afforded the products in good yields (**9bi**-**9di**). Notably, the present Cp*Co^{III} catalysis showed good functional group compatibility. Acetyl group (**9ei**), free-phenolic hydroxy group (**9fi**), and tertiary amino group (**9gi**) did not interfere with the desired reactions. In addition, meta-substituted donors showed modest reactivity with perfect regio-selectivity. Only less hindered C-H bonds reacted under the current conditions and products **9hi**-**9ji** were predominantly obtained. While a methyl substituent at the 3-position of the directing pyridine ring was compatible (**9ki**), 3-methyl- and 6-methyl-substituted substrates showed dramatically decreased reactivity toward addition reactions to imine **4f** or enone **8i** and less than 10% yield was obtained in all attempts. Coordination of 2-phenylpyridines **3** to the cobalt center or formation of the metalacycle intermediate would be much less favorable in the presence of such substituents.

Table 9 Scope of 2-phenylpyridines



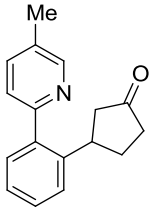


R = Me (**9bi**) : 80%
OMe (**9ci**) : 87%
Br (**9di**) : 74%
Ac (**9ei**) : 78%
OH (**9fi**) : 80%
NMe_2 (**9gi**) : 73%



R = Me (**9hi**) : 67%
(10 mol % of **1a** was used.)

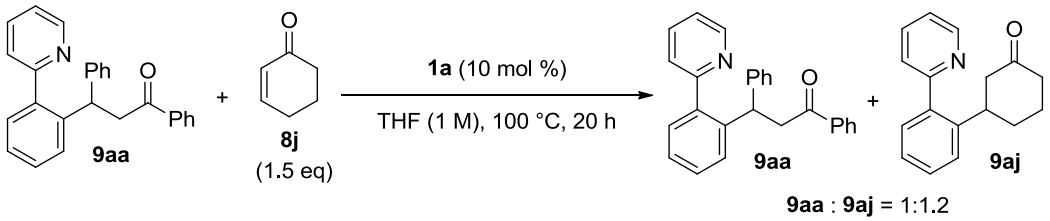
OMe (**9ii**) : 70%
Cl (**9ji**) : 76%



9ki, 83%

A crossover experiment was also conducted. The reaction of **9aa** and enone **8j** with **1a** afforded a mixture of **9aa** and **9aj** accompanied by the formation of chalcone **9a** (Scheme 21). This result indicates that the conjugate addition reaction to enones **8** was also reversible under the Cp*Co^{III} catalysis.

Scheme 21 Reversibility of addition to enones

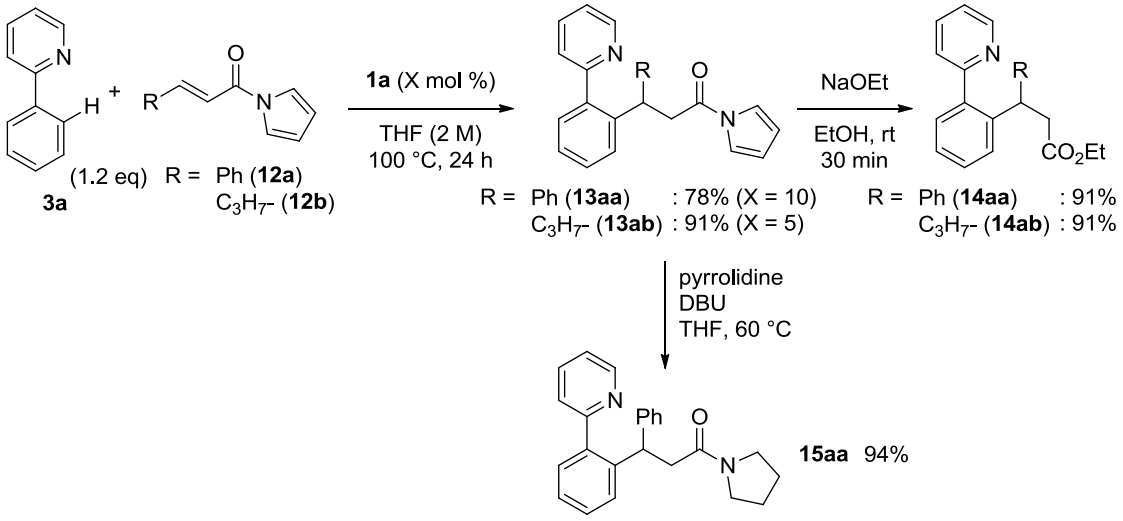


9aa : **9aj** = 1:1.2

1.4.2 Addition to α,β-Unsaturated *N*-Acylpyrroles

Because no successful result was obtained in addition reactions of α,β-unsaturated esters and an enal, I next investigated the use of α,β-unsaturated *N*-acylpyrroles **12** as ester surrogates. α,β-Unsaturated-*N*-acylpyrroles **12** are expected to have high electrophilicity, similar to α,β-unsaturated ketones. Moreover, the *N*-acylpyrrole moiety of the products can be easily converted to several functional groups, such as ester and amide. Hence, many synthetic reactions, including asymmetric conjugate addition reactions using α,β-unsaturated *N*-acylpyrroles as electrophiles have been reported to date.[29] The conjugate addition reactions of 2-phenylpyridine **3a** successfully proceeded under the same conditions for α,β-unsaturated ketones, as expected (Scheme 22). Both β-aryl and β-alkyl substituted substrates afforded the products **13** in good yields and the products were readily converted to the corresponding esters **14** by treatment with NaOEt at room temperature. Transformation of **13aa** to the corresponding amide **15aa** was also accomplished using pyrrolidine and DBU.

Scheme 22 Conjugate addition reactions to α,β-unsaturated *N*-acylpyrroles 12 and subsequent transformations to esters and an amide



Chapter 2. C2-Selective Addition of Indoles to Imines

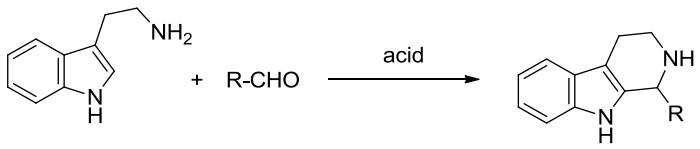
2.1 Background

2.1.1 Conventional Methods for C2-Selective Functionalization of Indoles

Indoles are abundant structural motifs found in a variety of biologically active natural and unnatural compounds. The synthesis and functionalization of indoles have, therefore, been extensively studied over the last several decades.[30] Indoles are electron-rich heteroaromatic compounds that react with a wide range of polar electrophiles (E^+), predominantly at the C3-position via electrophilic aromatic substitution.[31]

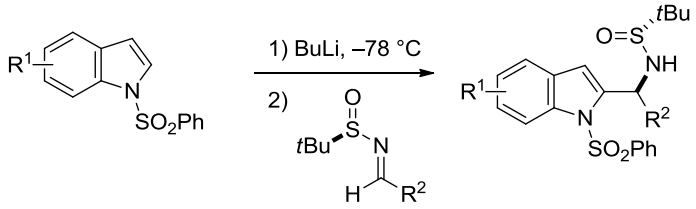
The C2-selective functionalization of indole derivatives with polar electrophiles, in contrast, is a much more formidable task. The Pictet-Spengler reaction (Scheme 23) is frequently used to synthesize various indole alkaloids, in which C2-selective functionalization can be achieved, although the diversity of the products is limited.

Scheme 23 Pictet-Spengler reaction



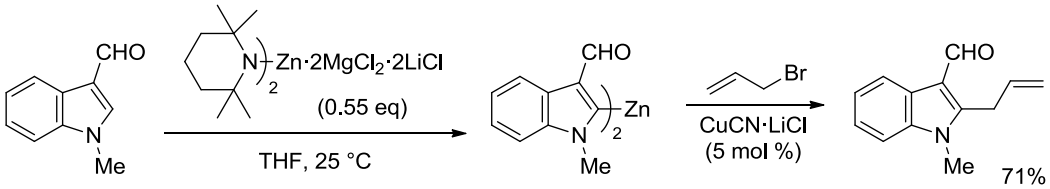
Lithiation and subsequent trapping by electrophiles can realize a more general synthesis of C2-functionalized indoles.[32] The proton at the C2 position is the most acidic in *N*-protected indoles, so high C2-selectivity is generally observed. Diastereoselective addition of 2-lithioindoles to chiral *N*-sufinylimines, for example, was reported by Liu, Chen, and co-workers (Scheme 24).[32e] These protocols, however, essentially require stoichiometric amounts of alkyllithium reagents, which are not compatible with several functional groups on the indoles. C2-Selective metalation by milder bases was also developed.[33] Among them, $(tmp)_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ developed by the Knochel group,[33c] realized high chemoselectivity (Scheme 25). The use of stoichiometric amounts of metal reagents and salt waste production, however, remain problematic in terms of atom-economy.

Scheme 24 Diastereoselective addition of 2-lithioindoles to *N*-sulfinylimines



Liu, L.; Chen, Y.-L. *et al. Tetrahedron: Asymmetry* **2007**, *18*, 1833.

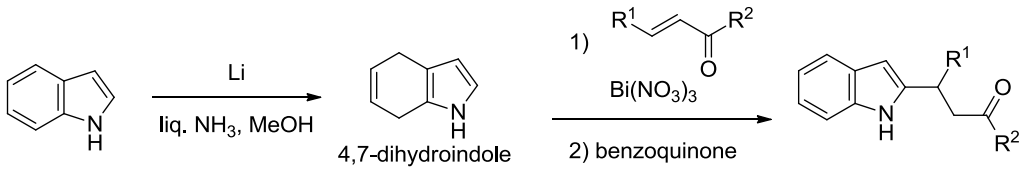
Scheme 25 Zincation of indoles under mild conditions



Knochel, P. *et al. Angew. Chem., Int. Ed.* **2007**, *46*, 7685.

An alternative method using 4,7-dihydroindoles was developed by Saraçoglu and co-worker (Scheme 26).[34a] They reported that 4,7-dihydroindoles selectively react with Michael acceptors at the C2-position under Lewis acid-catalyzed conditions. C2-functionalized indoles were obtained after oxidative rearomatization. Based on their report, other groups developed catalytic asymmetric Friedel-Crafts alkylation reactions of 4,7-dihydroindoles with Michael acceptors[34b-d,f] and imines.[34e] The strongly reducing conditions using Li in liquid ammonia to synthesize 4,7-dihydroindoles, however, seem to limit the scope of nucleophiles. In addition, the reduction/S_EAr/oxidation sequence is not desirable in terms of atom-economy and step-economy.[35]

Scheme 26 Utilization of 4,7-dihydroindoles as nucleophiles

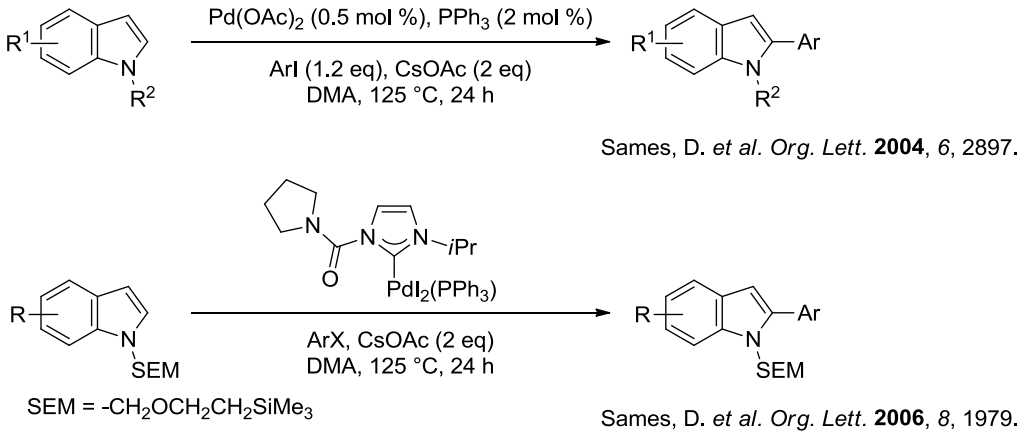


Saraçoglu, N. *et al. Tetrahedron* **2005**, *61*, 2401.

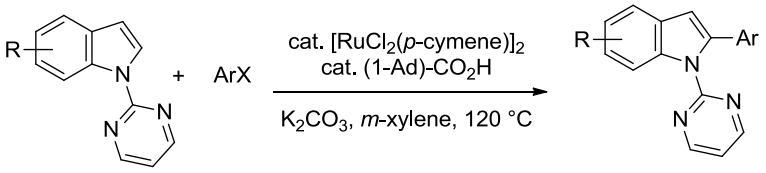
2.1.2 Transition Metal-Catalyzed C2-Selective Functionalization of Indoles

On the other hand, transition metal-catalyzed C2-selective functionalization reactions of indoles have attracted much attention[36] and C2-selective arylation reactions are particularly well investigated. The pioneering studies by Sames and co-workers demonstrated that C2-selective arylation of indoles using arylhalides could effectively proceed in the presence of Pd catalysts (Scheme 27).[37] They explained that C2-selectivity is obtained as the result of palladium migration from the C3- to the C2-position based on several KIE experiments.[37b] These reports led to the development of C2-arylation reactions using various transition metal catalysts.[38] The introduction of directing groups on the nitrogen atom of indoles often facilitates C2-selective functionalization (Scheme 28).[38f,g]

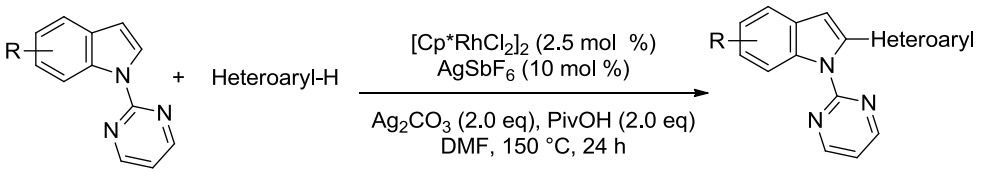
Scheme 27 Pioneering studies of C2-arylation of indoles by Sames *et al.*



Scheme 28 Directing group-assisted C2-arylation of indoles



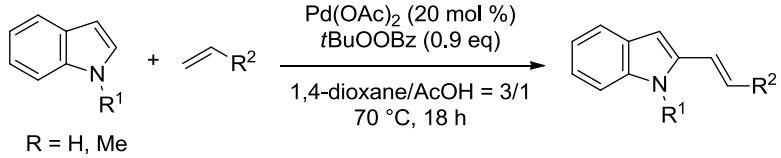
Ackermann, L. *et al. Org. Lett.* **2011**, *13*, 3332.



You, J.; Lan, J. *et al. Chem. Sci.* **2013**, *4*, 1964.

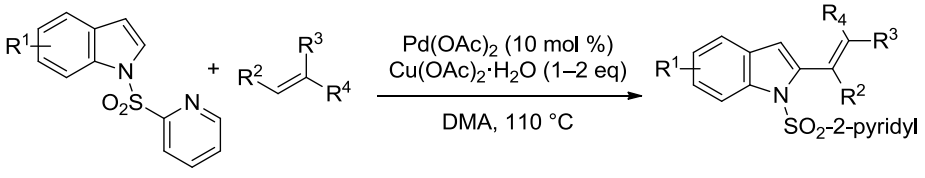
In addition to arylation reactions, alkenylation using alkenes under oxidative conditions, called the oxidative Heck reaction, are also well explored with or without directing group assistance (Scheme 29).[39]

Scheme 29 C2-Selective oxidative Heck reactions of indoles



R = H, Me

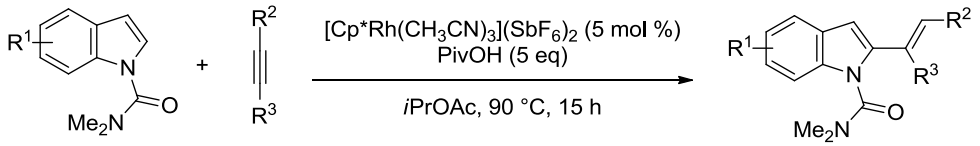
Gaunt, M. J. *et al. Angew. Chem., Int. Ed.* **2005**, *44*, 3125.



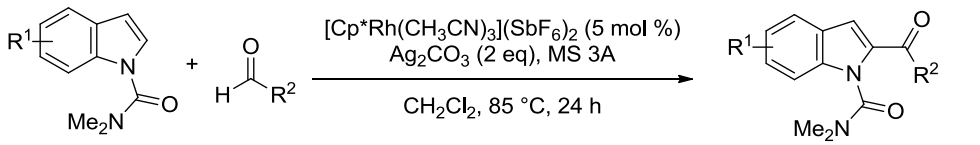
Gómez Arrayás, R.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 6511.

Other types of reactions, such as alkylation,[40] non-oxidative alkenylation using alkynes,[18d,41] acylation,[42] and amidation,[43] were also investigated. Among them, examples of Cp*Rh^{III}-catalyzed reactions are summarized in Scheme 30. These reactions demonstrated that appropriate directing groups can facilitate C2-selective metalation under Cp*Rh^{III} catalysis.

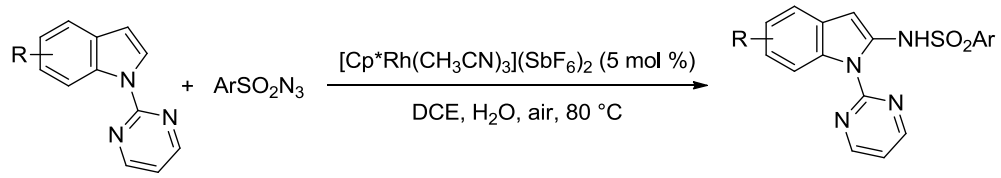
Scheme 30 Directing group-assisted C2-functionalization of indoles catalyzed by Cp*Rh^{III}



Schipper, D. J.; Fagnou, K. *et al. J. Am. Chem. Soc.* **2010**, *132*, 6910.



Li, Y. *et al. Chem. Commun.* **2012**, *48*, 5163.

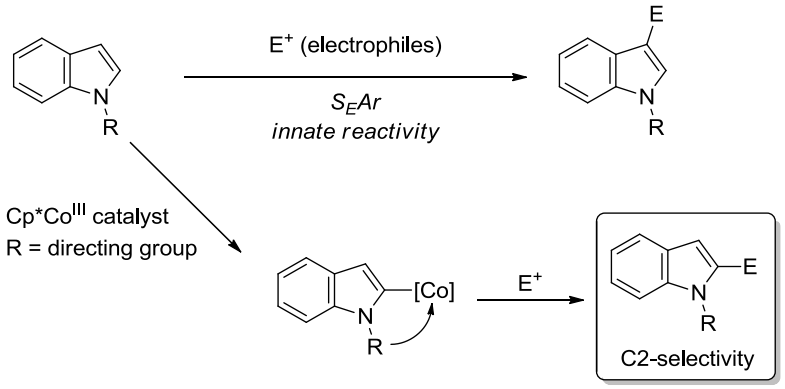


Zhou, B.; Li, Y. *et al. Org. Biomol. Chem.* **2012**, *10*, 8953.

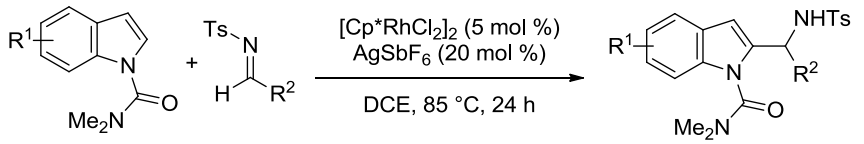
The objective of this study was to achieve C2-selective alkylation of indoles using carbon electrophiles (Scheme 31). While C3-selective alkylation is expected under conventional acid-catalyzed Friedel-Crafts alkylation conditions due to the innate reactivity of indoles mentioned above, C2-selective reaction using the Cp*Co^{III} catalyst would be possible via directing group-assisted C2-metalation, which is known in several transition metal catalyses, including Cp*Rh^{III} explained in this section.

During my research, Zhou, Li, and co-workers reported a Cp*Rh^{III}-catalyzed C2-selective addition reaction of indoles to imines (Scheme32),[44] but several problems remained to be solved, especially the high catalyst loading (10 mol % of "Rh" and 20 mol % of Ag), and low TON of the precious Cp*Rh^{III} catalyst (TON: 4-7 based on "Rh"). These problems encouraged me to continue my investigation of the Cp*Co^{III} catalyst.

Scheme 31 Cp*Co^{III}-catalyzed C2-selective functionalization of indoles with electrophiles



Scheme 32 Cp*Rh^{III}-catalyzed C2-selective addition of indoles to imines



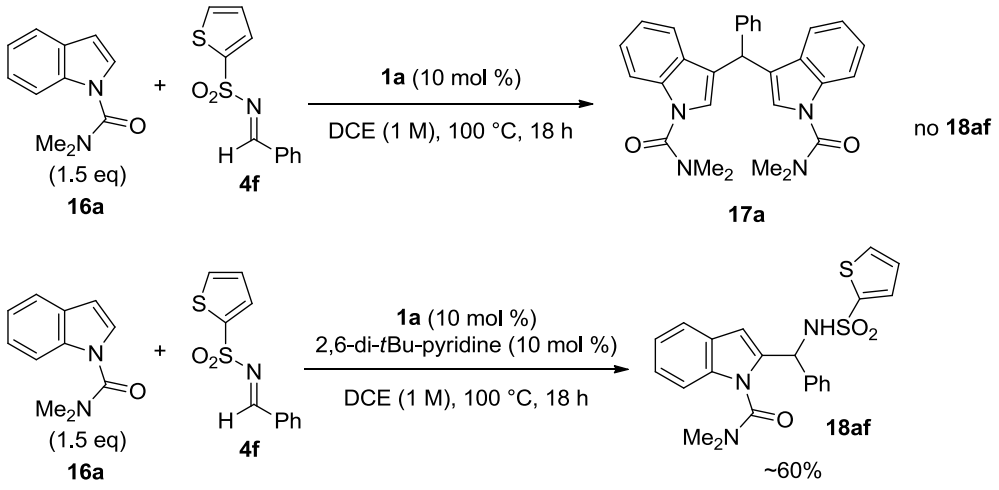
Zhou, B.; Li, Y. *et al. Adv. Synth. Catal.* **2013**, *355*, 360.

2.2 Optimization of the Reaction Conditions

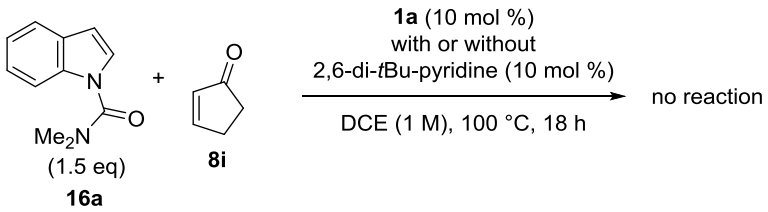
Initial attempts using *N*-carbamoyl-protected indole **16a** and imine **4f** afforded unexpected results, as shown in Scheme 33. When only catalyst **1a** was used, no desired product was obtained and 3,3'-bisindolylmethane **17** formed as a sole product. On the other hand, the addition of a non-coordinating base, 2,6-di-*tert*-butyl-pyridine, dramatically affected the reaction outcome and desired product **18af** was observed as a major product in moderate yield without the formation of **17** or any other regioisomers. I speculated that the formation of 3,3'-bisindolylmethane **17** is promoted by protic acids generated during the metalation step because acid-catalyzed formation of 3,3'-bisindolylmethanes from indoles and imines have been reported.[45] The addition of a base to trap the protic acids could accordingly suppress the formation of **17** and the desired product could be obtained as a major product. It is also possible that the base facilitates C2-selective metalation via the CMD mechanism, but this is less likely because 2,6-di-*tert*-butyl-pyridine would be too bulky to participate in the metalation step.

Michael acceptor **8i** was also examined as an electrophile under the same conditions, but failed to afford any products and the starting materials were recovered (Scheme 34). Therefore, I attempted to optimize the reaction conditions for imines.

Scheme 33 Initial trials using *N*-cabamoyl-protected imine 16a

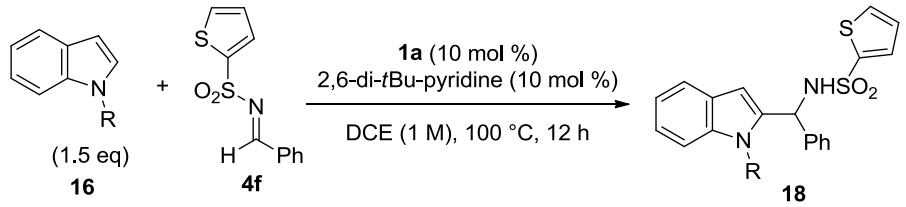


Scheme 34 Unsuccessful results using enone8i



First, I examined the effect of directing groups of indoles (Table 10). The strong coordination ability of the carbamoyl group was determined to be quite important. *N*-Acetyl indole **16b** afforded the product but in diminished yield (entry 2). No reaction proceeded with less coordinating substrates like Boc- (**16c**), Cbz- (**16d**) and tosyl- (**16e**) protected indoles (entries 3-5). 2-Pyridinesulfonyl-protected indole (**16f**) was used in anticipation of its coordination ability, but still no reaction occurred (entry 6).

Table 10 Effect of directing groups of indoles



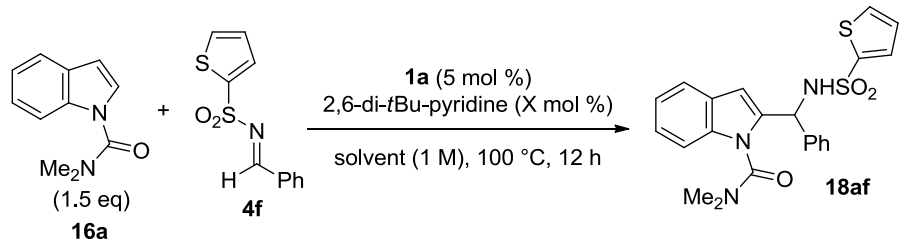
entry	R	indole	product	yield (%)[a]
1	-CONMe$_2$	**16a**	**18af**	62
2	Ac	**16b**	**18bf**	24
3	Boc	**16c**	**18cf**	0
4	Cbz	**16d**	**18df**	0
5	Ts	**16e**	**18ef**	0
6	-SO$_2$-2-pyridyl	**16f**	**18ff**	0

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.

Further optimization was conducted using **16a** as a substrate and the results are summarized in Table 11. Catalyst loading was decreased to 5 mol % at this stage, but the yield was unchanged (entry 1). The amount of base had little effect on the reactivity (entries 1-3). Although the yield slightly improved when 5 mol % of the base was used (entry 1), the amounts of observed unidentified byproducts were slightly larger than that in entries 2 and 3. Therefore, I used 10 mol % of the base for further investigation. Solvent screening did not improve the yield, as shown in entries 4-7. Both non-polar and ether type solvents could not be utilized. In the case of *t*BuOH, a complex mixture

was obtained due to the decomposition and reaction of the solvent. The yield was increased by using 2.0 eq of **16a**, but not sufficiently (entry 8).

Table 11 Amount of the base and solvent effect

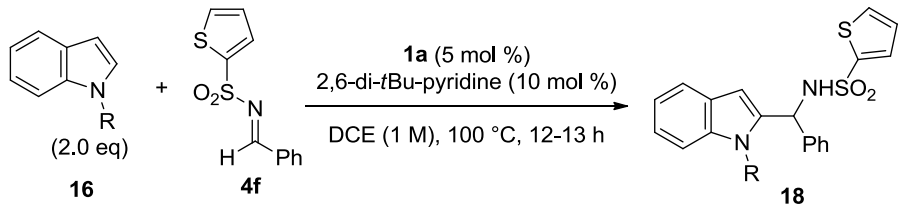


entry	base (X mol %)	solvent	yield (%)[a]
1	5	DCE	67
2	10	DCE	59
3	100	DCE	58
4	10	toluene	0
5	10	THF	0
6	10	1,4-dioxane	0
7	10	*t*BuOH	messy
8[b]	10	DCE	69

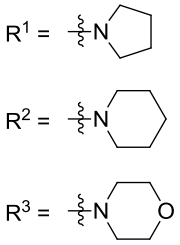
[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.
[b] 2.0 eq of **16a** was used.

Because no significant improvement was achieved by changing various reaction conditions, I then screened directing groups again (Table 12). Various carbamoyl-protected indoles **16b**-**16j** demonstrated only comparable or lower reactivity than **1a** (entries 2-5). Notable improvement was achieved when *N*-(2-pyridyl)-indole **16k** or *N*-(2-pyrimidyl)-indole **16l** was used as a substrate and the yield was increased to around 80% (entries 6-7). Because of its removability,[38f] 2-pyrmidyl-protected indole **16l** was selected as an optimal substrate.

Table 12 Reinvestigation of directing groups



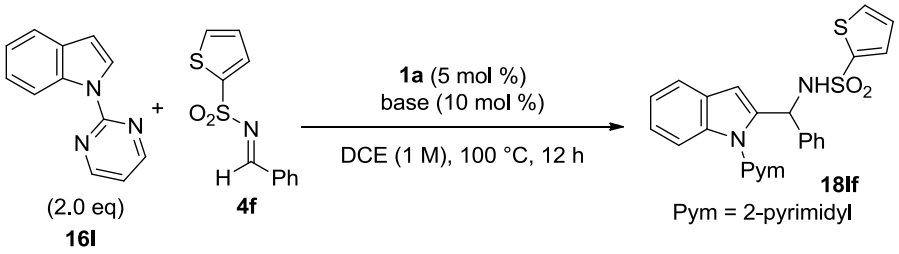
entry	R	indole	product	yield (%)[a]
1	-$CONMe_2$	**16a**	**18af**	69
2	-$CONiPr_2$	**16g**	**18gf**	trace
3	-COR^1	**16h**	**18hf**	53
4	-COR^2	**16i**	**18if**	67
5	-COR^3	**16j**	**18jf**	27
6	2-pyridyl	**16k**	**18kf**	81
7	2-pyrimidyl	**16l**	**18lf**	80



[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.

Bases were also screened (Table 13) in an attempt to reduce the amount of unidentified byproducts that were observed even in the presence of 10 mol % of 2,6-di-*t*Bu-pyridine (entry 1). In contrast to the results of the initial trials shown in Scheme 33, C2-adduct **18lf** was afforded as a major product without any additional bases together with several byproducts (entry 2). In this case, the 2-pyrimidyl moiety of **16l** presumably works as a base to trap the protons generated during the reaction. Nevertheless, the additional base was beneficial based on the results in entries 1 and 2. While inorganic bases were less effective (entries 3-5), acetate bases showed relatively better results (entries 6-8). Addition of NaOAc or KOAc suppressed the formation of byproducts more efficiently than 2,6-di-*t*Bu-pyridine. Although the addition of CsOPiv also decreased the formation of byproducts, reactivity significantly declined (entry 9). Coordinating bases were not suitable (entries 10, 11). Among them, KOAc was the best additive in terms of reactivity and suppression of byproduct formation.

Table 13 Base screening

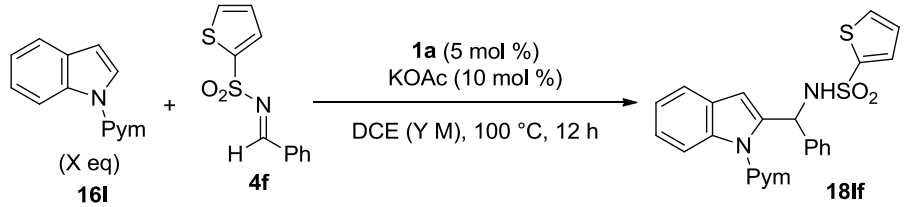


entry	base	yield (%)[a]	entry	base	yield (%)[a]
1	2,6-di-*t*Bu-pyridine	80	7	NaOAc	77
2	none	72	8	KOAc	82
3	K_2CO_3	65	9	CsOPiv	46
4	Cs_2CO_3	32	10	*i*PrNEt$_2$	11
5	K_3PO_4	63	11	pyridine	< 5
6	LiOAc	71	12	2,6-lutidine	77

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard.

The amount of indole **16l** and the concentration were eventually optimized (Table 14). More concentrated conditions tended to give higher yields (entries 1-3) and larger amounts of indoles also led to higher conversion of imine **4f** (entries3-5). This tendency is likely due to thermodynamic control of the yield under these conditions. The reversibility of this reaction is discussed in the following section. The conditions in entry 3 (2.0 eq of **16l**, 2 M) were finally adopted as the best conditions.

Table 14 Final Optimization



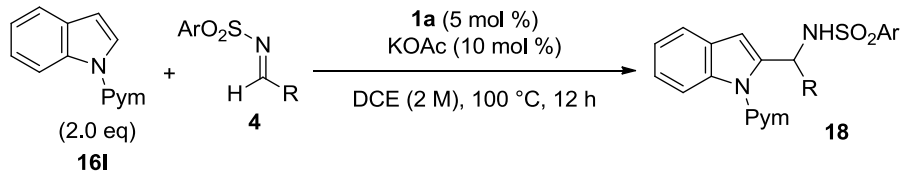
entry	indole (X eq)	concentration (Y M)	yield (%)[a]
1	2.0	1	82
2	2.0	0.5	73
3	2.0	2	89 (83)
4	1.5	2	82
5	1.2	2	78

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture using dibenzylether as an internal standard. Number in parenthesis is the isolated yield.

2.3 Substrate Scope

After optimizing the conditions, I examined the substrate scope. The scope of aromatic imines is shown in Table 15. Imines with electron-withdrawing groups (**4i**-**4l**, **4u**) generally gave high yields (entries 3-7), while lower yields were obtained with electron-rich imines (**4m**-**4o**, entries 8-10). Electron-rich heteroaromatic imines **4p** and **4q** were also applicable despite affording moderate yields (entries 11, 12). In addition, tosylimine **4a** also afforded satisfactory yield under the optimized conditions (entry 13) as well as 2-thiophenesulfonylimines.

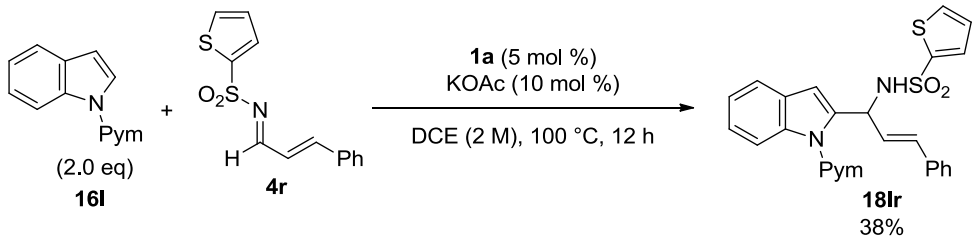
Table 15 Scope of aromatic imines



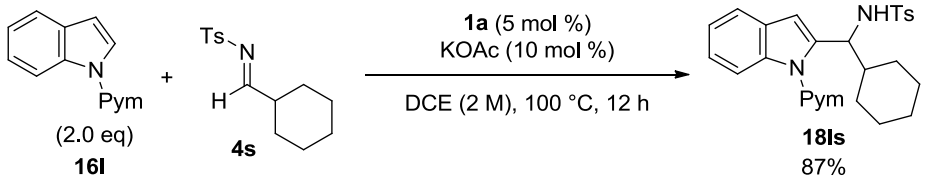
entry	R	Ar	imine	product	yield (%)
1	Ph	2-thienyl	**4f**	**18lf**	83
2	2-naphthyl	2-thienyl	**4h**	**18lh**	78
3	*p*ClC$_6$H$_4$-	2-thienyl	**4i**	**18li**	89
4	*p*BrC$_6$H$_4$-	2-thienyl	**4j**	**18lj**	91
5	*p*CF$_3$C$_6$H$_4$-	2-thienyl	**4k**	**18lk**	93
6	pCO$_2$MeC$_6$H$_4$-	2-thienyl	**4u**	**18lu**	90
7	*m*ClC$_6$H$_4$-	2-thienyl	**4l**	**18ll**	90
8	*p*MeC$_6$H$_4$-	2-thienyl	**4m**	**18lm**	71
9	*p*MeOC$_6$H$_4$-	2-thienyl	**4n**	**18ln**	48
10	*o*MeC$_6$H$_4$-	2-thienyl	**4o**	**18lo**	74
11	2-thienyl	2-thienyl	**4p**	**18lp**	58
12	2-furyl	2-thienyl	**4q**	**18lq**	64
13	Ph	*p*MeC$_6$H$_4$-	**4a**	**18la**	78

Although α,β-unsaturated imine **4r** resulted in a relatively low yield (38%, Scheme 35) due to the competitive conjugate addition reaction, the reaction was much cleaner than that using 2-phenylpyridine **3a** (1.3.2, Scheme 16). Furthermore, it is noteworthy that aliphatic imine **4s** successfully afforded a high yield without isomerization to the corresponding enamide (Scheme 36). These significant differences between the addition reaction of 2-phenylpyridine **3a** and that of indole **16l** are attributed to the difference in the basicity of pyridine and pyrimidine or moderate Lewis acidity of the cationic Cp*Co^{III} catalyst attenuated by the addition of KOAc.

Scheme 35 Reaction with α,β-unsaturated imine 4r

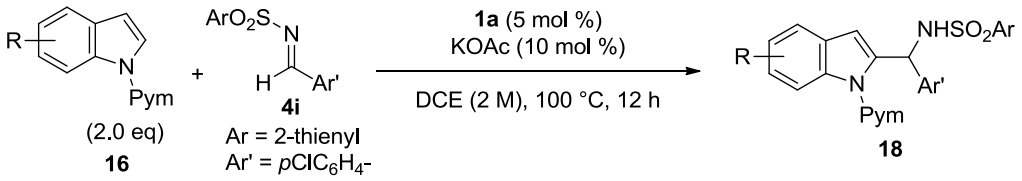


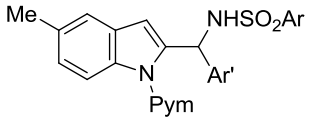
Scheme 36 Reaction with aliphatic imine 4s



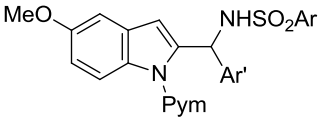
Next, the scope of indoles was investigated using imine **4i** as an electrophile and the results are shown in Table 16. Both electron-donating and electron-withdrawing substituents were compatible and various 4-, 5-, or 6-substituted indoles showed good reactivity. Because CO_2Me-substituted indole **16q** had lower reactivity than the others, the reaction was performed at 120 °C to afford product **18qi** in 77% yield. The observed functional group compatibility in Table 16 is synthetically useful because indoles bearing a Cl- or Br-substituent may be problematic in conventional methods using alkyllithium[32] reagents or Birch reduction conditions[34] due to chemoselectivity issues.

Table 16 Scope of indoles

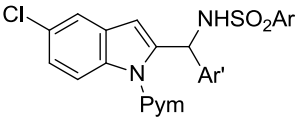




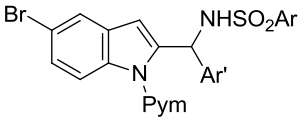
18mi, 89%



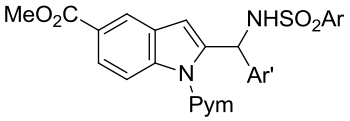
18ni, 84%



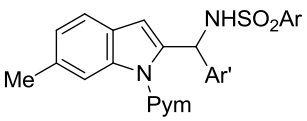
18oi, 88%



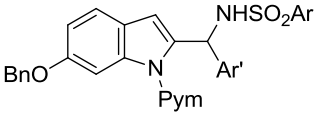
18pi, 87%



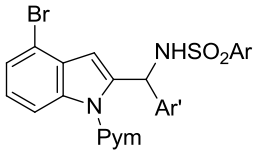
18qi, 77% (120 °C)



18ri, 89%



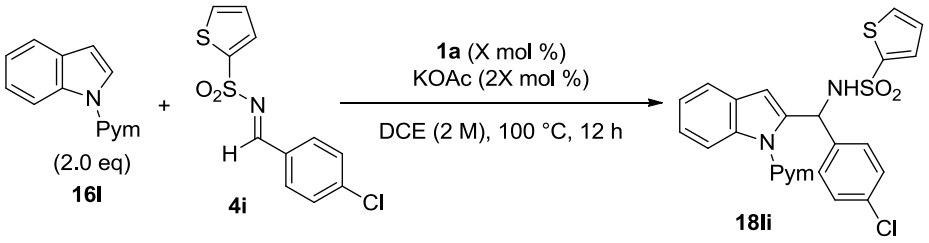
18si, 62%



18ti, 88%

I tried to reduce the catalyst loading to evaluate the efficiency of the Cp*Co^{III} catalyst (Table 17). The amount of the catalyst was successfully decreased to 0.5 mol % without any loss of reactivity (entries 1-3). Further decrease of the catalyst loading, however, diminished the yield (entry 4). Nevertheless, the observed TON in entries 6, up to around 180, was much higher than that observed with Cp*Rh^{III} catalysts in related addition reactions to imines under non-oxidative conditions.[9,44]

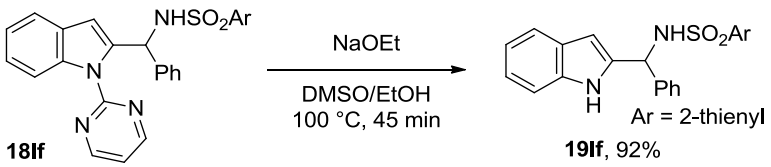
Table 17 Catalyst loading



entry	catalyst loading (X mol %)	yield (%)	TON
1	5	89	18
2	1	91	91
3	0.5	91	180
4	0.1	< 25	< 250

The 2-pyrimidyl directing group in product **18lf** was successfully removed by treatment with NaOEt,[38f] affording N-H free indole **19lf** in 92% yield (Scheme 37).

Scheme 37 Removal of 2-pyrimidyl group



2.4 Reaction Mechanism

It is reasonable to speculate that the reaction mechanism of C2-selective addition of pyrimidyl-protected indoles **16** to imines **4** is similar to that of 2-phenylpyridines **3**, described in Chapter 1. A plausible catalytic cycle is shown in Figure 5. As an initiation step, thermal dissociation of the benzene ligand of **1a** and ligand exchange to acetate generates the catalytically active species **I**. After coordination of the pyrimidyl group of indole **16** (**II**), regioselective C-H metalation occurs at the C2-position via either S_EAr or a CMD mechanism to afford intermediate **III**. Coordination of imine **4** (**IV**) followed by addition to the C-N double bond affords **V**. Protonation of **V** with AcOH then gives product **18** and regenerates active species **I**. Direct proton abstraction from **16** by Co-N bond of **V** to afford **18** is an alternative possible reaction pathway.

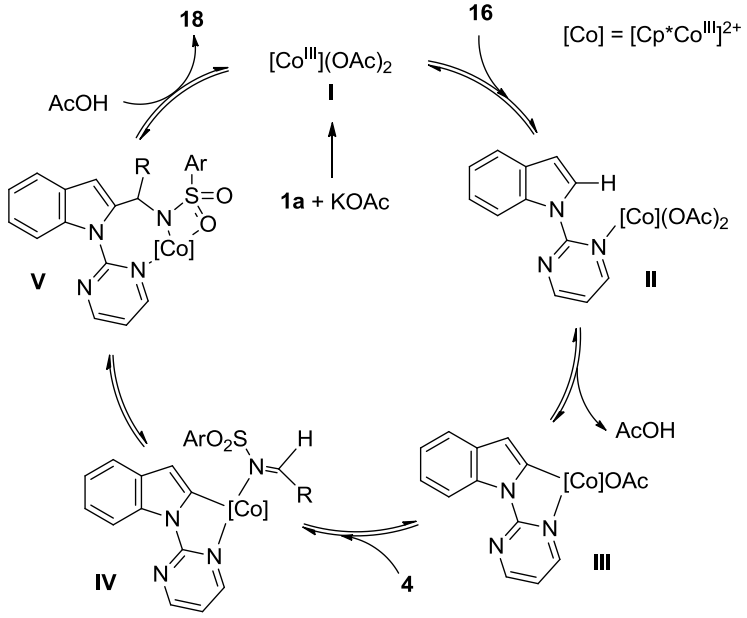
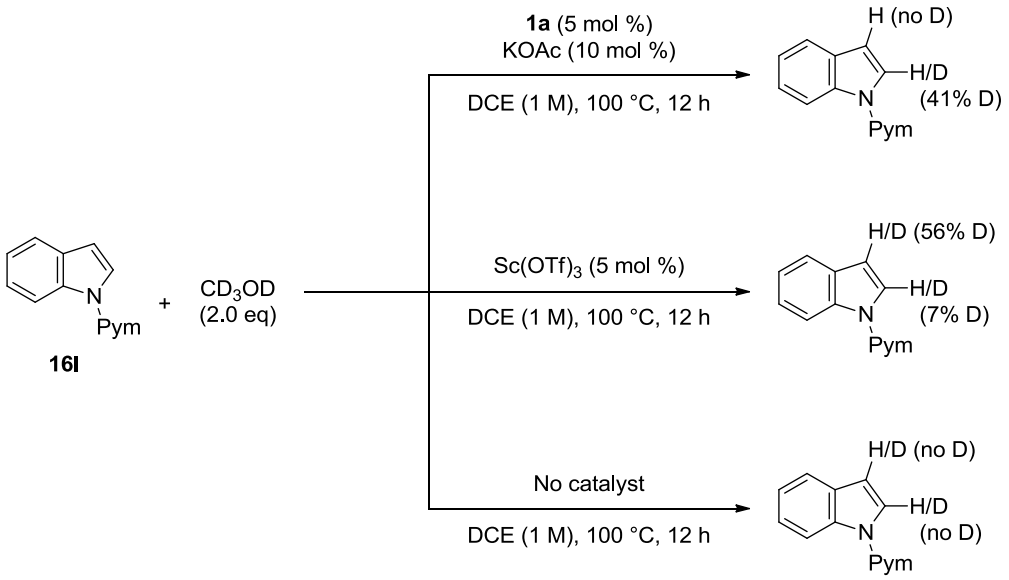


Figure 5 One of the Plausible Catalytic Cycles

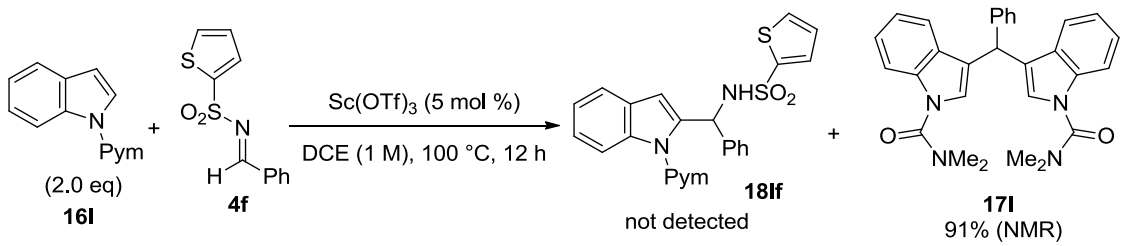
Several experiments were performed to gain insight into the reaction mechanism. The results of H/D exchange experiments of **16l** with CD_3OD (2.0 eq) are summarized in Scheme 38. Under the Cp^*Co^{III} catalysis, a site-selective H/D exchange ocurred at the C2-position of the indole (41% D) and deuterium incorporation was not detected at the C3-position. In contrast, a simple Lewis acid, $Sc(OTf)_3$, preferentially promoted H/D exchange at the C3-position (56% D) while, in the absence of catalysts, deuterium incorporation was not detected at either the C2- or C3-position (<5%). These

results suggest that reversible C2-selective C-H activation and metalation occurred under the Cp*Co^{III} catalysis, overriding the intrinsic reactivity of indoles under simple Lewis acidic conditions. The Lewis acidic conditions using a catalytic amount of $Sc(OTf)_3$ actually gave 3,3'-bisindolylmethane **17l** without the formation of C2-products (Scheme 39).

Scheme 38 H/D exchange experiments



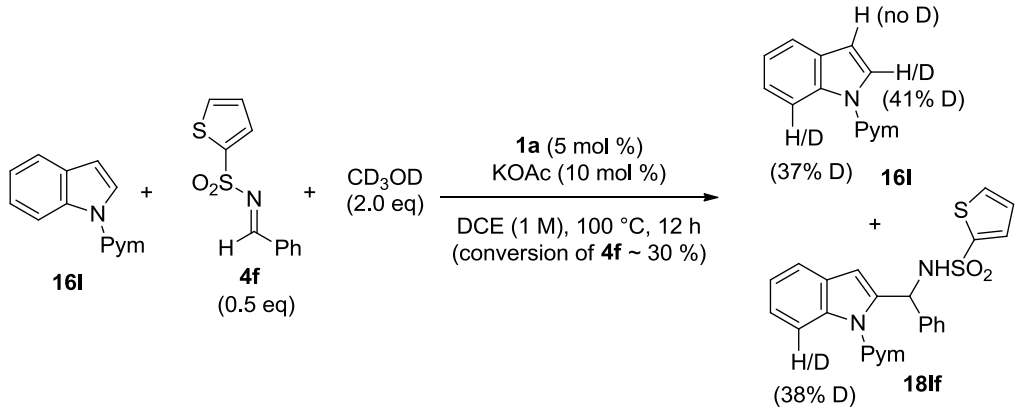
Scheme 39 Reaction using $Sc(OTf)_3$ as Lewis acid



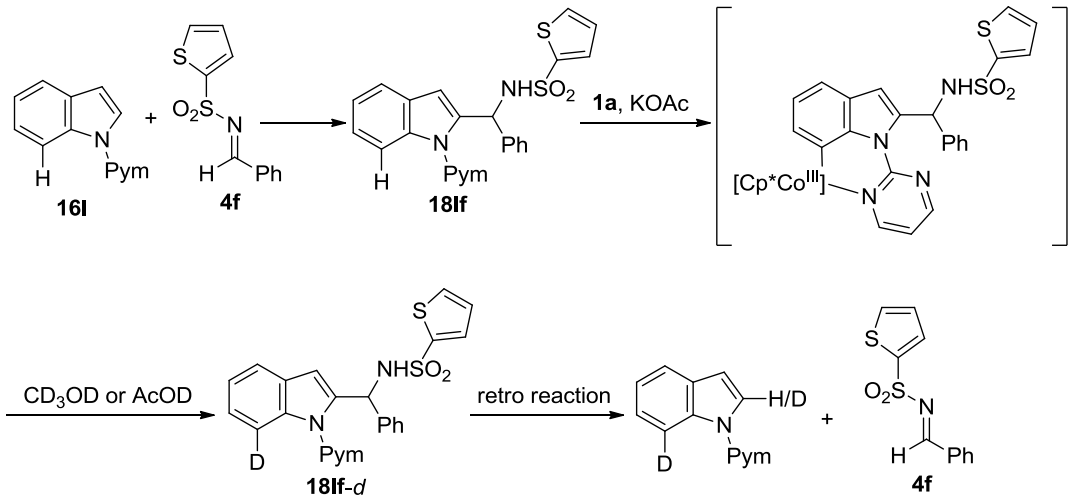
An unexpected result was obtained when the same experiment was conducted in the presence of imine **4f** (Scheme 40). In addition to the expected deuteration at the C2-position of the recovered starting material **16l**, deuterium incorporation at the C7-positions of both **16l** and the product **18lf** was observed. Because H/D exchange at the C7-position did not occur in the absence of imine **4f** (Scheme39), I speculate that C7-metalation/proto-demetalation proceeded after C2-selective addition to imine **4f** followed by a retro addition reaction to afford C7-deuterated indole **16l** (Scheme 41). In

this case, C7-metalation would be facilitated because the cobalt center would not be able to approach the C2-position due to steric hindrance and would instead be located near the C7-position. The reversibility was confirmed by a crossover experiment using **18lf** and imine **4l**, as shown in Scheme 42. The formation of imine **4f** and adduct **18ll** clearly indicated that the C2-selective addition reaction of pyrimidyl-protected indoles to imine **4** is reversible under the optimized reaction conditions.

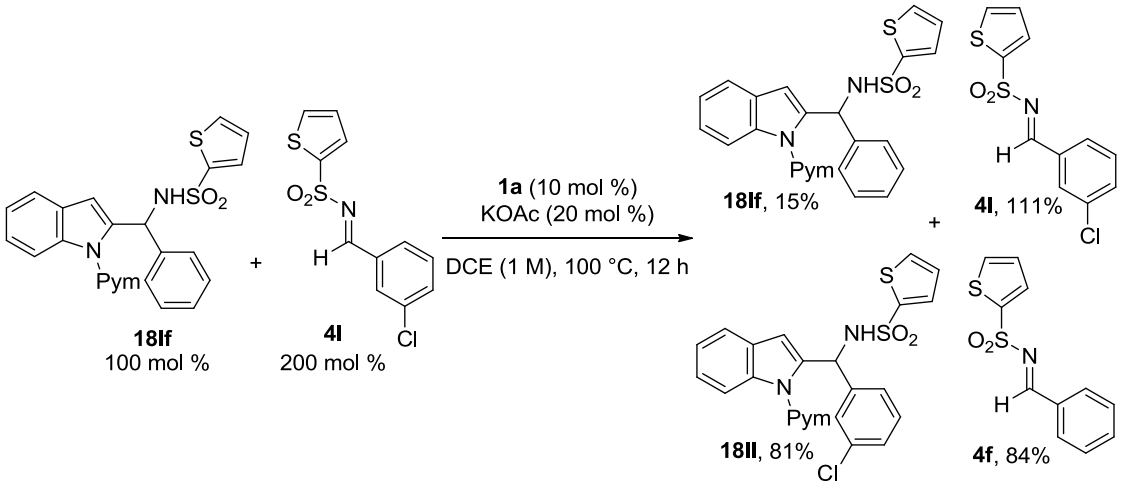
Scheme 40 H/D exchange experiment in the presence of imine 4f



Scheme 41 Possible mechanism of unexpected H/D exchange at the C7-position

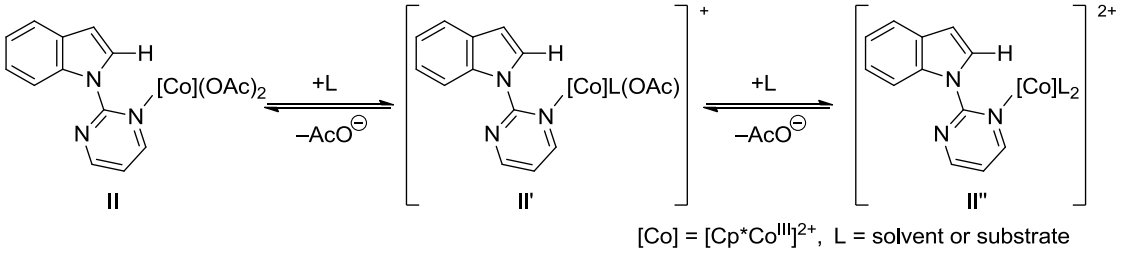


Scheme 42 Crossover Experiment



The detailed mechanism of the C-H activation step and the precise structure of the intermediate that undergoes C-H activation remain unclear. Although the intermediate **II** in Figure 5 is depicted as a non-cationic complex with two acetoxy ligands, there would be ligand exchange equilibrium between dicationic, monocationic, and non-cationic species (Figure 6). It should be pointed out that the addition of KOAc is not essential and similar results were obtained with non-coordinating bases or even without any bases (2.2, Table 13). It is difficult to conclude that activation of C-H bond proceeds via S_EAr or a CMD mechanism assisted by the coordinating acetoxy ligands or the pyrimidyl group of another substrate in an intermolecular manner. To elucidate the actual mechanism, further studies, including computational chemistry approach, are necessary.

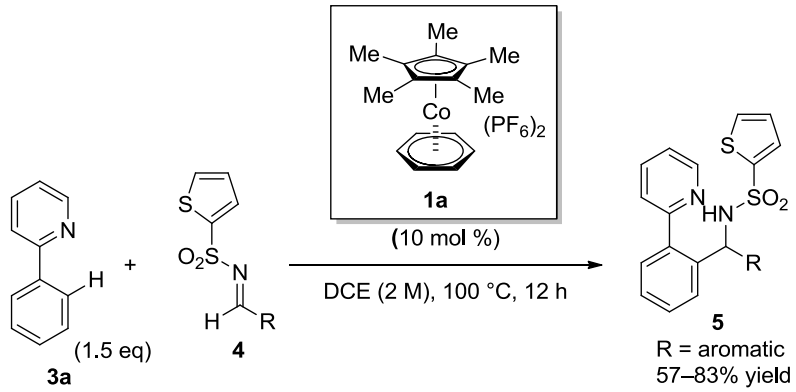
Scheme 43 Possible ligand exchange before C-H activation



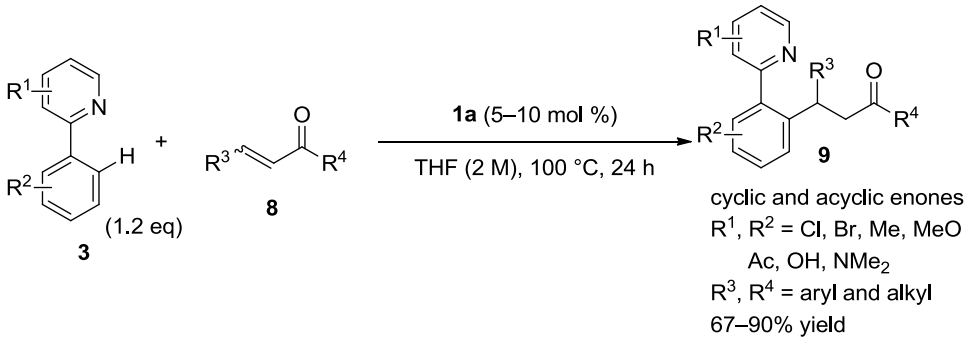
Summary and Perspective

In summary, $[Cp^*Co(C_6H_6)](PF_6)_2$ **1a** was an efficient catalyst for an addition reaction of C-H bonds to polar electrophiles in the presence of pyridine as a directing group (Scheme 44-46). The reaction likely proceeded via the same mechanism as that reported for Cp^*Rh^{III} catalysis,[9-11] but used much more accessible cobalt catalyst **1a**. Catalyst **1a** also promoted a C2-selective addition reaction of 2-pyrimidyl-protected indoles **16** to imines **4** with high efficiency. The remarkable functional group compatibility observed in both reactions is synthetically useful because conventional C-H metalation methods using strong bases like alkyllithium reagents are not compatible with several functional groups.

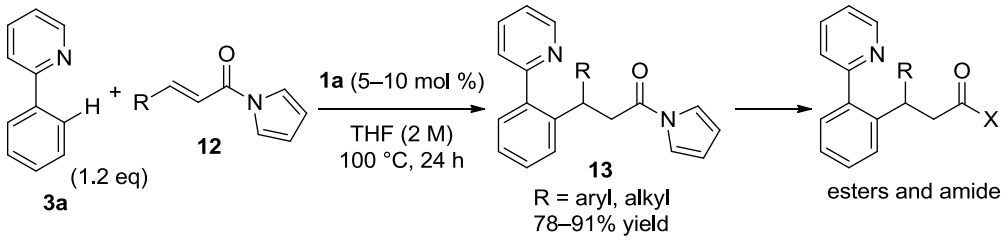
Scheme 44 Addition of 2-phenylpyridine to imines



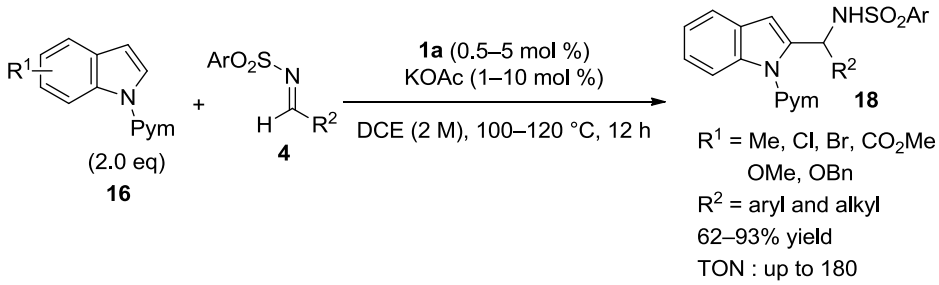
Scheme 45 Addition of 2-phenylpyridines to α,β-unsaturated ketones



Scheme 46 Addition 2-phenylpyridine to α,β-unsaturated *N*-acylpyrroles



Scheme 47 C2-Selective addition of indoles to imines



Catalytic stereocontrol is a crucial problem in C-H bond addition reactions to polar electrophiles catalyzed by transition metals. The reversibility observed in the Cp*Rh^{III} catalyzed reactions and in my investigation of the Cp*Co^{III} catalyst, however, makes stereocontrol much more difficult despite recent progress in asymmetric catalysis by designed chiral cyclopentadienylrhodium complexes.[46] If thermodynamic stability of the products is not adequate in comparison with that of the staring materials, a retro reaction occurs as quickly as the desired reaction and racemization is inevitable. Therefore, the structure of the reaction components should be carefully selected although this might reduce the generality. A tandem reaction is a good solution to suppress a retro reaction, as Bergman and Ellman demonstrated in an addition reaction to aldehydes.[10d] A smaller ionic radius of cobalt than of rhodium would be advantageous for asymmetric induction by chiral cyclopentadienyl ligands.

As for reactivity of the Cp*Co^{III} catalysis, there is much room for investigation considering the outstanding utility of Cp*Rh^{III} catalysis. Although the C-H activation step would be more difficult compared with Cp*Rh^{III} because the Co-C bond would be weaker than the Rh-C bond, the reactivity of the cyclometalated intermediates to electrophiles would be higher due to the polar nature of the Co-C bond. Therefore, a higher generality of the electrophilic reaction components is expected in the Cp*Co^{III} catalysis. To overcome the obstacles in C-H activation and realize more synthetically useful reactions, the design of appropriate directing groups that can be easily introduced and removed or converted to other functional groups is needed.

Experimental Section

General

Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on JEOL JNM-ECS400 spectrometers and JNM-ECX500 spectrometers. Chemical shifts in $CDCl_3$, CD_3OD, DMSO-d_6 were reported in the scale relative to tetramethylsilane, CHD_2OD, DMSO-d_5 (0.00, 3.31, 2.49 ppm for ^{1}H NMR) and $CDCl_3$, CD_3OD DMSO-d_6 (77.0, 49.0, 39.5) ppm for ^{13}C NMR) as an internal reference, respectively. ESI mass spectra were measured on JEOL JMS-T100LC AccuTOF spectrometer. Column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM).

Materials

Commercially available anhydrous tetrahydrofuran (THF) and hexane (Wako Ltd., deoxygenated grade) were dried over activated molecular sieves 4A under argon atmosphere. 1,2-Dichloroethane (DCE) was distilled from CaH_2, purged with argon for over 30 min and stored over activated molecular sieves 4A under argon atmosphere. Commercially available anhydrous benzene, toluene, Et_2O, 1,4-dioxane, CH_2Cl_2, DMSO, EtOH, *t*BuOH (Kanto Ltd. or Wako Ltd.) were used without further manipulation. Anhydrous $CoCl_2$ was purchased from Strem Chemicals Inc. $Co_2(CO)_8$ was purchased from Kanto Ltd. All the other commercially available reagents were used as received unless otherwise stated. Substrates were synthesized according to the literatures or purchased as listed below.

2-Phenylpyridine derivatives (**3**): a) Liu, C.; Yang, W. *Chem. Commun.* **2009**, *45*, 6267; b) Liu, C.; Han, N.; Song, X.; Qiu, J. *Eur. J. Org. Chem.* **2010**, 5548. Commercially available compounds were purchased and distilled before use.

Aromatic and α,β-unsaturated sulfonylimines (**4a**, **4d-4r**): Morimoto, H.; Lu, Gang.; Aoyama, N.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 9588.

Aliphatic sulfonylimines (**4s**, **4t**): Chemla, F.; Hebbe, V.; Normant, J.-F. *Synthesis* **2000**, 75.

Boc-protected imine (**4b**): Yang, J. W.; Pan, S. C.; List, B. *Org. Synth.* **2009**, *89*, 11.

Diphenylphosphinoylimine (**4c**): Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561.

α,β-Unsaturated ketones (**8**): Pore, D. M.; Desai, U. V.; Thopate, T. S.; Wadgaonkar, P. P. *Russ. J. Org. Chem.* **2007**, *43*, 1088. Commercially available compounds were purchased and purified by distillation or recrystallization before use.

α,β-Unsaturated esters (**10**): They were purchased and purified by distillation before use.

α,β-Unsaturated *N*-acylpyrroles (**11**): Matsunaga, S.; Kinoshita, T.; Okada, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 7559.

N-Carbamoylindoles (**16a**, **16g**-**16j**): Schipper, D. J.; Hutchinson, M.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*, 6910.

N-Acetylindole (**16b**): A commercially available reagent was used as received.

N-Boc- or *N*-Cbz-protected indoles (**16c**, **16d**): Weedon, A. C.; Zhang, B. *Synthesis* **1992**, 95.

N-Tosylindole (**16e**): Wagger, J.; Svete. J.; Stanovnik, B. *Synthesis* **2009**, 1436.

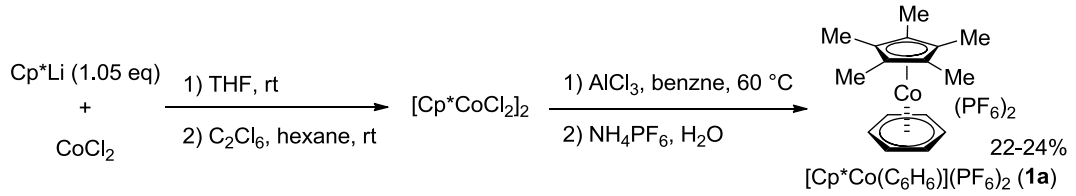
N-(2-Pyridinesulfonyl)indole (**16f**): García-Rubia, A.; Gómez Arrayás, R.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 6511.

N-(2-Pyridyl)indole (**16k**): Cano, R.; Ramón, D. J.; Yus, M. *J. Org. Chem.* **2011**, *76*, 654.

N-(2-Pyrimidyl)indoles (**16l**-**16t**): Ackermann, L.; Lygin, A. V. *Org. Lett.* **2011**, *13*, 3332.

Experimental Procedures

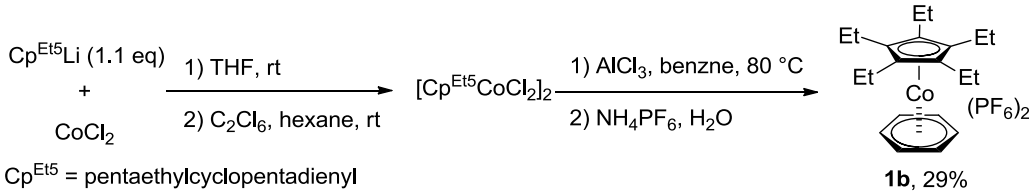
Preparation of Cobalt Complex 1a



To a well-dried 1-L flask were added pentamethylcyclopentadienyllithium (Kölle, U.; Fuss, B. *Chem. Ber.* **1984**, *117*, 743; 17.9 g, 126 mmol), THF (500 mL), and $CoCl_2$ (15.6 g, 120 mmol) successively under argon atmosphere. After stirring for 15 min at room temperature, the solvent was removed in vacuo. The residue was extracted with hexane (250 mL x 4), and the extracts were filtered through a glass filter under argon atmosphere. To the filtrate containing highly air-sensitive $[Cp^*CoCl]_2$ was added hexachloroethane (50 g, 210 mmol), and the mixture was stirred for 15 min at room temperature. [The following manipulations can be carried out under air because Cp^*Co^{III} complexes were not sensitive to air and moisture.] Resulting green precipitates were collected by filtration, washed with hexane (100 mL x 5), and then dried in vacuo to give crude $[Cp^*CoCl_2]_2$ (16.3 g, 51% based on $CoCl_2$).

To another flame-dried flask were added the crude $[Cp^*CoCl_2]_2$ (10.6 g, 20 mmol), $AlCl_3$ (53 g, 400 mmol), and benzene (200 mL). The suspension was stirred at 60 °C for 90 min until the color of the mixture turned to yellow-orange. Then excess $AlCl_3$ was carefully hydrolyzed by adding water (500 mL) at 0 °C. After removal of insoluble materials by filtration through a pad of celite, layers were separated. To the yellow aqueous layer was added NH_4PF_6 (26 g) in minimum amount of water. Yellow precipitates were collected by filtration and successively washed with water, CH_2Cl_2, and Et_2O. After re-precipitation with acetone/Et_2O, **1a** was obtained as an air-stable yellow solid (9.68 g, 43% from $[Cp^*CoCl_2]_2$, 22% overall yield). IR (KBr) ν 3099, 2926, 1470, 1447, 1423, 1382, 1083, 1020, 882, 833 cm^{-1}; ^1H NMR (CD_3NO_2, 400 MHz) δ 2.22 (s, 15H), 7.37 (s, 6H); ^{13}C NMR (CD_3NO_2, 100 MHz) δ 11.7, 106.9, 112.7; Anal. calculated for $C_{16}H_{21}CoF_{12}P_2$: C, 34.18; H, 3.76, found: C, 34.05; H, 3.92.

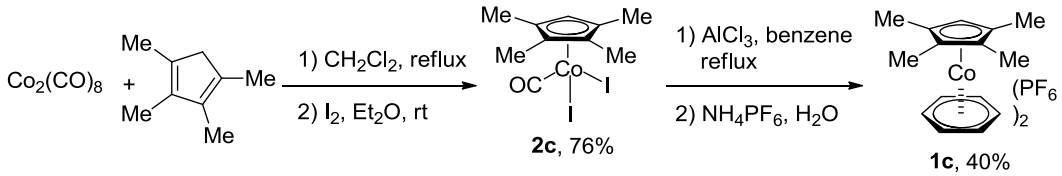
Preparation of Cobalt Complex 1b



To a well-dried 50-mL flask were added pentaethylcyclopentadienyllithium (Stein, D.; Sitzmann, H. *J. Organomet. Chem.* **1991**, *402*, C1; 353 mg, 1.66 mmol), THF (5 mL), and $CoCl_2$ (196 mg, 1.51 mmol) successively under argon atmosphere. After stirring for 5 h at room temperature, the solvent was removed in vacuo. The residue was extracted with hexane (6 mL x 3), and the extracts were filtered through a glass filter under argon atmosphere. To the filtrate was added hexachloroethane (715 mg, 3 mmol), and the mixture was stirred for 15 min at room temperature. Resulting green precipitates were collected by filtration, washed with hexane, and then dried in vacuo.

To another flame-dried flask were added thus obtained green solid, $AlCl_3$ (1.9 g, 125 mmol) and benzene (10 mL). The suspension was stirred at 80 °C for 1 h until the color of the mixture turned to yellow-orange. Then excess $AlCl_3$ was carefully hydrolyzed by adding water (50 mL) at 0 °C. After the organic layer was separated and discarded, the aqueous layer was filtered through a pad of celite. To the obtained aqueous solution was added NH_4PF_6 (600 mg) in minimum amount of water. Yellow precipitates were collected by filtration and successively washed with water, CH_2Cl_2, and Et_2O. After re-precipitation with acetone/Et_2O, **1b** was obtained as a yellow solid (281 mg, 29%). IR (KBr) ν 3090, 2989, 2947, 1474, 1446, 1406, 1048, 873, 834 cm^{-1}; ^1H NMR (CD_3NO_2, 500 MHz) δ 1.35 (t, *J* = 7.7 Hz, 15H), 2.90 (q, *J* = 7.7 Hz, 10H) 7.36 (s, 6H); ^{13}C NMR (CD_3NO_2, 125 MHz) δ 14.8, 20.4, 107.1, 116.9.

Preparation of Cobalt Complex 1c

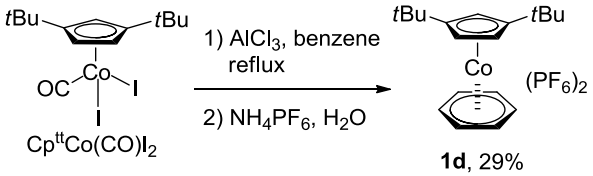


To a well-dried 2-necked 50-mL flask were successively added $Co_2(CO)_8$ (800 mg, 2.34 mmol), degassed CH_2Cl_2 (20 mL), and tetramethylcyclopentadiene (0.89 mL, 5.9 mmol). The mixture was refluxed under argon stream for 4 h and then cooled to room temperature. The solvent was removed in vacuo. The residue was dissolved in degassed Et_2O (10 mL), and then iodine (1.5 g, 5.9 mmol) in degassed Et_2O (10 mL) was added

dropwise at room temperature with stirring. [Caution: During the addition, the mixture was refluxed due to the exothermic reaction, and CO gas evolution was observed.] After the mixture was stirred at room temperature for 1 h, the solvent was evaporated. The residue was purified by silica gel column chromatography (hexane then CH_2Cl_2/hexane=4/1) to afford **2c** as a deep purple crystalline solid (1.64 g, 76%). IR (KBr) ν 2030, 1458, 1374, 1007 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.22 (s, 6H), 2.30 (s, 6H) 5.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 11.7, 12.7, 89.3, 99.5, 104.9, 198.8.

To a flame-dried 50-mL flask were successively added **2c** (231 mg, 0.50 mmol), benzene (10 mL), and $AlCl_3$ (1.3 g, 10 mmol). The mixture was refluxed for 19 h. Then excess $AlCl_3$ was carefully hydrolyzed by adding water (25 mL) at 0 °C. After removal of some insoluble materials by filtration through celite, the layers were separated. To the aqueous layer was added NH_4PF_6 (1 g) in minimum amount of water. Precipitates were collected by filtration and washed with water. After twice re-precipitation with acetone/Et_2O, **1e** was obtained as a brown solid (110 mg, 40%). IR (KBr) ν 3104, 1459, 836 cm^{-1}; ^1H NMR (CD_3NO_2, 500 MHz) δ 2.21–2.33 (m, 12H), 6.61 (brs, 1H) 7.46 (brs, 6H); Clear ^{13}C NMR spectrum was not obtained due to the severe signal broadening and the instability in CD_3NO_2.

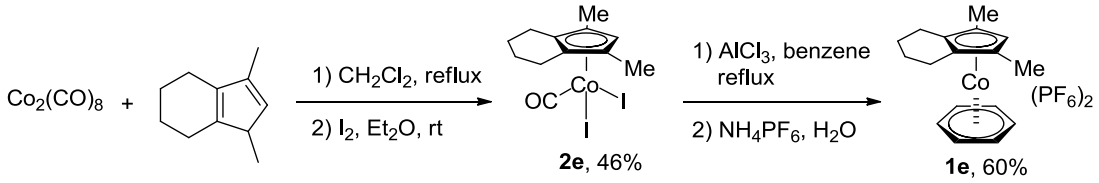
Preparation of Cobalt Complex 1d



1d, 29%

To a flame-dried 100-mL flask were successively added $Cp^{tt}Co(CO)I_2$ (Li, W.; Weng, L.-H.; Jin, G.-X. *Inorg. Chem. Commun.* **2004**, *7*, 1174; 259 mg, 0.50 mmol), benzene (10 mL), and $AlCl_3$ (1.8 g, 13 mmol). The mixture was refluxed for 3 h. Then excess $AlCl_3$ was carefully hydrolyzed by adding water (15 mL) at 0 °C. After the organic layer was separated and discarded, the aqueous layer was filtered through a pad of celite. To the obtained aqueous solution was added NH_4PF_6 (1.0 g) in minimum amount of water. Yellow precipitates were collected by filtration and washed with water. After twice re-precipitation with acetone/Et_2O, **1c** was obtained as a yellow solid (141 mg, 29%). IR (KBr) ν 3108, 2979, 1489, 1457, 1378, 1256, 1165, 1085, 837 cm^{-1}; ^1H NMR (CD_3NO_2, 400 MHz) δ 1.48 (s, 18H), 6.71 (t, J = 1.6 Hz, 1H), 6.78 (d, J = 1.6 Hz, 2H), 7.81 (s, 6H); ^{13}C NMR (CD_3NO_2, 125 MHz) δ 30.2, 34.7, 86.4, 88.8, 106.0, 136.1.

Preparation of Cobalt Complex 1e



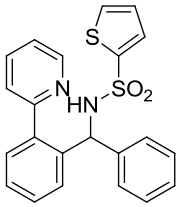
To a well-dried 2-necked 100-mL flask were successively added $Co_2(CO)_8$ (1.4 g, 4.1 mmol), degassed CH_2Cl_2 (10 mL), and 1,3-dimethyl-4,5,6,7-tetrahydroindene (Austin, R. N.; Clark, T. J.; Dickson, T. E.; Killian, C. M.; Nile, T. A.; Schabacker, D. J.; McPhail, A. T. *J. Organomet. Chem.* **1995**, *491*, 11; 1.6 g, 11 mmol) in degassed CH_2Cl_2 (10 mL). The mixture was refluxed under argon stream for 4 h and then cooled to room temperature. The solvent was removed in vacuo. The residue was dissolved in degassed Et_2O (25 mL), and then iodine (2.5 g, 10 mmol) in degassed Et_2O (20 mL) was added dropwise at room temperature with stirring. [Caution: During the addition, the reaction mixture was refluxed due to the exothermic reaction, and CO gas evolution was observed.] After the mixture was stirred at room temperature overnight, the solvent was evaporated. The residue was purified by silica gel column chromatography (hexane then CH_2Cl_2/hexane = 4/1) and recrystallization from CH_2Cl_2/hexane to afford **2e** as a deep purple crystalline solid (1.8 g, 46%). IR (KBr) ν 2941, 2030, 1473, 1417 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.68–1.80 (m, 2H), 1.83–1.97 (m, 2H), 2.19 (brs, 6H), 2.41–2.55 (m, 2H), 3.00–3.13 (m, 2H), 5.46 (brs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.0, 21.0, 22.1, 91.0, 95.5, 108.5, 199.4.

To a flame-dried 300-mL flask were successively added **2e** (1.53 g, 3.1 mmol), benzene (60 mL), and $AlCl_3$ (8.4 g, 63 mmol). The mixture was refluxed for 2 h. Then, excess $AlCl_3$ was carefully hydrolyzed by adding water (100 mL) at 0 °C. After the organic layer was separated and discarded, the aqueous layer was filtered through a pad of celite. To the obtained aqueous solution was added NH_4PF_6 (5 g) in minimum amount of water, and the mixture was cooled to 0 °C for 15 min. Precipitates were collected by filtration and washed with cold water. After re-precipitation with acetone/Et_2O, **1e** was obtained as a yellow solid (1.06 g, 60%). IR (KBr) ν 3101, 2944, 1448, 1419, 1024, 834 cm^{-1}; ^1H NMR (CD_3NO_2, 500 MHz) δ 1.88–2.28 (m, 10H), 2.30–2.46 (m, 2H), 2.67–2.82 (m, 2H), 6.60 (brs, 1H), 7.50 (brs, 6H); Clear ^{13}C NMR spectrum was not obtained due to the severe signal broadening and the instability in CD_3NO_2

General Procedure of Cobalt^{III}-catalyzed Addition Reaction of 2-Phenylpyridine to Imines

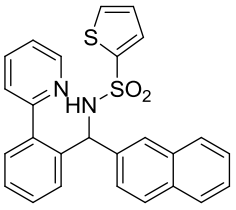
To a dried screw-capped vial were added imine **4** (0.40 mmol), 2-phenylpyridine

2a (85 μL, 0.60 mmol), **1a** (11.2 mg, 0.040 mmol), and 1,2-dichloroethane (0.20 mL) under Ar atmosphere. The vial was capped, and the mixture was heated at 100 °C for 12 h with stirring. After the mixture was cooled to room temperature, acetic acid (ca. 0.1 mL) was added under air, and the mixture was stirred for over 15 min. After dilution with CH_2Cl_2, saturated EDTA·2Na aq. was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (x 2). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation, obtained crude mixture was purified by silica gel column chromatography to give a corresponding product **5**.



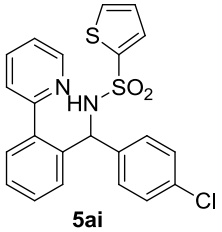
5af

***N*-(Phenyl(2-(pyridin-2-yl)phenyl)methyl)thiophene-2-sulfonamide (5af):** a colorless solid; IR (KBr) ν 3277, 3088, 1592, 1430, 1336, 1153, 1092, 1071, 1017, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.77–5.84 (m, 1H), 6.82–6.88 (m, 1H), 6.90–6.96 (m, 6H), 7.05–7.11 (m, 1H), 7.17–7.34 (m, 4H), 7.35–7.39 (m, 1H), 7.40–7.49 (m, 2H), 8.49–8.55 (m, 1H), 9.17 (d, *J* = 9.4 Hz , 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 61.7, 121.9, 124.4, 125.8, 126.2, 126.7, 127.3, 128.0, 128.3, 130.9, 131.4, 131.5, 137.0, 139.4, 139.6, 140.4, 143.1, 147.3, 159.6; HRMS (ESI): *m*/*z* calculated for $C_{22}H_{18}N_2NaO_2S_2^+$ [M+Na^+]: 429.0702, found: 429.0697.



5ah

***N*-(Naphthalen-2-yl(2-(pyridin-2-yl)phenyl)methyl)thioph ene-2-sulfonamide (5ah):** a colorless solid; IR (KBr) ν 3055, 1589, 1426, 1330, 1154, 1092, 1023, 758, 725 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.95 (d, *J* = 9.4 Hz 1H), 6.82–6.88 (m, 2H), 6.92–6.98 (m, 1H), 6.99–7.05 (m, 1H), 7.21–7.29 (m, 4H), 7.30–7.40 (m, 5H), 7.40–7.46 (m, 2H), 7.46–7.55 (m, 1H), 7.58–7.65 (m, 1H), 8.51–8.56 (m, 1H), 9.26 (d, *J* = 9.4 Hz , 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 61.8, 122.0, 124.3, 124.3, 124.5, 125.4, 125.7, 126.8, 127.1, 127.2, 127.7, 128.1, 128.4, 130.9, 131.0, 131.5, 131.5, 131.8, 132.5, 136.9, 137.5, 139.3, 139.5, 143.0, 147.2, 159.5; HRMS (ESI): *m*/*z* calculated for $C_{26}H_{20}N_2NaO_2S_2^+$ [M+Na^+]: 479.0859, found: 479.0854.

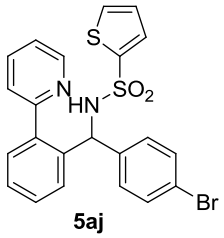


5ai

***N*-((4-Chlorophenyl)(2-(pyridin-2-yl)phenyl)methyl)thiophene-2 -sulfonamide (5ai):** a colorless solid; IR (KBr) ν 3085, 1590, 1491, 1429, 1337, 1152, 1092, 1015, 766, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.71–5.77 (m, 1H), 6.84–6.98 (m, 5H), 7.09–7.24 (m, 3H), 7.24–7.43 (m, 5H), 7.48–7.56 (m, 1H), 8.48–8.54 (m, 1H), 9.27 (d, *J* = 9.4 Hz , 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 61.3, 122.1, 124.4,

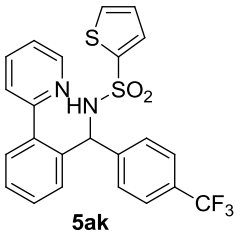
126.8, 127.2, 127.4, 128.2, 128.4, 130.9, 131.0, 131.5, 131.6, 132.0, 137.2, 139.0, 139.1, 139.2, 142.9, 147.3, 159.4; HRMS (ESI): *m*/*z* calculated for $C_{22}H_{17}ClN_2NaO_2S_2^+$ [M+Na^+]: 463.0313, found: 463.0310.

***N*-((4-Bromophenyl)(2-(pyridin-2-yl)phenyl)methyl)thiophene-2-sulfonamide (5aj):** a pale yellow solid; IR (KBr) ν 3083, 1590, 1488, 1471, 1152, 1092, 1011, 854, 797, 764, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.71 (d, *J* = 9.4 Hz, 1H), 6.80–6.89 (m, 3H), 6.93–6.98 (m, 1H), 7.02–7.08 (m, 2H), 7.10–7.44 (m, 7H), 7.52 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.51 (brd, *J* = 4.9 Hz , 1H), 9.27 (d, *J* = 9.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 61.3, 120.2, 122.2, 124.4, 126.8, 127.6, 128.2, 128.5, 130.3, 131.0, 131.1, 131.5, 131.6, 137.3, 139.0, 139.2, 139.7, 142.9, 147.3, 159.4; HRMS (ESI): *m*/*z* calculated for $C_{22}H_{17}BrN_2NaO_2S_2^+$ [M+Na^+]: 506.9808, found: 506.9802.



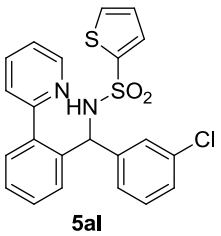
5aj

***N*-((2-(Pyridin-2-yl)phenyl)(4-(trifluoromethyl)phenyl)methyl) thiophene-2-sulfonamide (5ak):** a colorless solid; IR (KBr) ν 3075, 1 328, 1161, 1118, 1093, 1067, 1017, 761, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.81 (brd, *J* = 9.7 Hz, 1H), 6.85–6.89 (m, 1H), 6.89–6.94 (m, 1H), 7.06–7.11 (m, 3H), 7.16–7.24 (m, 4H), 7.25–7.30 (m, 1H), 7.32–7.37 (m, 1H), 7.37–7.41 (m, 1H), 7.42–7.49 (m, 2H), 8.48–8.52 (m, 1H), 9.30 (brd, *J* = 9.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 61.6, 122.2, 123.9 (q, $^1J_{CF}$ = 271.9 Hz), 124.2 (q, $^3J_{CF}$ = 3.6 Hz), 124.4, 126.2, 126.9, 128.4, 128.4 (q, $^2J_{CF}$ = 32.4 Hz), 128.6, 131.1, 131.1, 131.6, 131.6, 137.2, 138.9, 139.2, 142.9, 144.8, 147.3, 159.4; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{17}F_3N_2NaO_2S_2^+$ [M+Na^+]: 497.0576, found:497.0578.



5ak

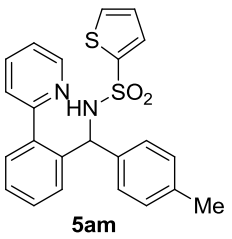
***N*-((3-Chlorophenyl)(2-(pyridin-2-yl)phenyl)methyl)thiophene-2-sulfonamide (5al):** a pale yellow solid; IR (KBr) ν 3274, 3061, 1593, 1473, 1427, 1337, 1226, 1156, 1092, 1017, 753, 718, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.74 (d, *J* = 9.8 Hz, 1H), 6.81–6.91 (m, 5H), 6.93–6.97 (m, 1H), 7.10–7.18 (m, 2H), 7.19–7.24 (m, 1H), 7.25–7.29 (m, 1H), 7.31–7.36 (m, 1H), 7.36–7.40 (m, 1H), 7.41–7.44 (m, 1H), 7.50 (ddd, *J* = 8.0, 8.0, 1.7 Hz, 1H), 8.54 (dd, *J* = 5.2, 1.7 Hz, 1H) 9.23 (d, *J* = 9.8 Hz , 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 61.4, 122.1, 124.2, 124.4, 126.0, 126.4, 126.8, 128.3, 128.5, 128.6, 131.0, 131.1, 131.5, 131.5, 133.3, 137.2, 138.9, 139.2, 142.6,



5al

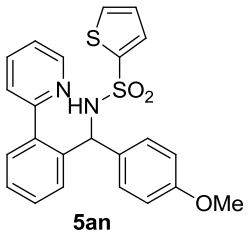
142.9, 147.3, 159.4; HRMS (ESI): *m*/*z* calculated for $C_{22}H_{17}ClN_2NaO_2S_2^+$ [M+Na^+]: 463.0313, found: 463.0310.

***N*-((2-(Pyridin-2-yl)phenyl)(*p*-tolyl)methyl)thiophene-2-sulfonamide (5am):** a colorless solid; IR (KBr) ν 3084, 1591, 1429, 1334, 1151, 1093, 1018, 854, 760, 732, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.12 (s, 3H), 5.77 (d, *J* = 9.2 Hz, 1H), 6.70–6.76 (m, 2H), 6.77–6.83 (m, 2H), 6.83–6.88 (m, 1H), 6.92–6.98 (m, 1H), 7.05–7.14 (m, 1H), 7.17–7.34 (m, 4H), 7.34–7.43 (m, 2H), 7.44–7.52 (m, 1H), 8.49–8.55 (m, 1H), 9.04 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.7, 61.4 121.9, 124.4, 125.7, 126.7, 127.8, 128.0, 128.3, 130.7, 130.8, 131.4, 131.4, 135.7, 137.0, 137.3, 139.3, 139.6, 143.0, 147.3, 159.6; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{20}N_2NaO_2S_2^+$ [M+Na^+]: 443.0859, found: 443.0860.



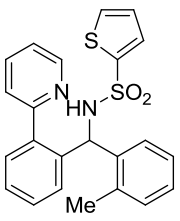
5am

***N*-((4-Methoxyphenyl)(2-(pyridin-2-yl)phenyl)methyl)thiophene-2-sulfonamide (5an):** a colorless solid; IR (KBr) ν 3270, 3061, 2836, 1589, 1510, 1335, 1250, 1155, 1024, 756, 723, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.64 (s, 3H), 5.75 (d, *J* = 9.7 Hz, 1H), 6.45–6.50 (m, 2H), 6.81–6.87 (m, 3H), 6.936.98 (m, 1H), 7.06–7.11 (m, 1H), 7.16–7.23 (m, 2H), 7.23–7.27 (m, 1H), 7.27–7.34 (m, 1H), 7.34–7.38 (m, 1H), 7.38–7.42 (m, 1H), 7.45–7.52 (m, 1H), 8.50–8.54 (m, 1H), 9.04 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.1, 61.2, 112.8, 121.9, 124.4, 126.8, 127.0, 127.9, 128.3, 130.7, 130.9/, 131.5, 131.5, 132.6, 137.1, 139.4, 139.7, 143.0, 147.4, 157.9, 159.7; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{20}N_2NaO_3S_2^+$ [M+Na^+]: 459.0808, found: 459.0805.



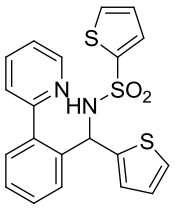
5an

***N*-((2-(Pyridin-2-yl)phenyl)(*o*-tolyl)methyl)thiophene-2-sulfonamide (5ao):** a colorless solid; IR (KBr) ν 3277, 3060, 2930, 1587, 1561, 1460, 1427, 1406, 1334, 1155, 1018, 757, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.88 (s, 3H), 6.00 (d, *J* = 8.6 Hz, 1H), 6.69–6.75 (m, 1H), 6.80–6.94 (m, 5H), 7.18–7.24 (m, 3H), 7.25–7.30 (m, 2H), 7.37–7.41 (m, 2H), 7.43–7.55 (m, 2H), 8.63–8.67 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.8, 58.5, 122.1, 123.9, 124.9, 126.4, 126.8, 126.9, 127.5, 128.0, 130.1, 130.3, 130.9, 131.1, 131.8, 135.1, 136.8, 137.7, 138.0, 139.9, 142.5, 148.2, 159.5; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{20}N_2NaO_2S_2^+$ [M+Na^+]: 443.0859, found: 443.0863.



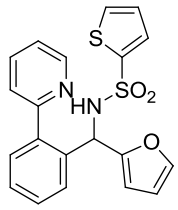
5ao

***N*-((2-(Pyridin-2-yl)phenyl)(thiophen-2-yl)methyl)thiophene-2-sulfonamide (5ap):** a colorless solid; IR (KBr) ν 3097, 2852, 1591, 1469, 1428, 1406, 1224, 1155, 1013, 850, 756, 730, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.92 (d, *J* = 9.5 Hz, 1H), 6.36–6.39 (m, 1H), 6.52–6.56 (m, 1H), 6.82–6.86 (m, 1H), 6.87–6.91 (m, 1H), 7.10–7.15 (m, 2H), 7.20–7.24 (m, 2H), 7.30–7.38 (m, 3H), 7.41–7.44 (m, 1H), 7.55–7.61 (m, 1H), 8.51–8.56 (m, 1H), 9.55 (d, *J* = 9.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 59.4, 121.9, 124.3, 124.4, 124.6, 126.0, 126.8, 128.4, 128.5, 130.5, 131.1, 131.6, 131.7, 137.2, 139.0, 139.4, 142.8, 145.6, 147.5, 159.6; HRMS (ESI): *m*/*z* calculated for $C_{20}H_{16}N_2NaO_2S_3^+$ [M+Na^+]: 435.0267, found: 435.0269.



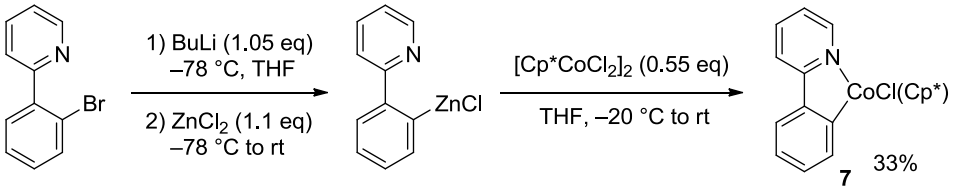
5ap

***N*-(Furan-2-yl(2-(pyridin-2-yl)phenyl)methyl)thiophene-2-sulfonamide (5aq):** a colorless solid; IR (KBr) ν 3161, 3088, 1593, 1438, 1405, 1338, 1156, 1095, 1007, 755, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.71–5.75 (m, 1H), 5.77 (d, *J* = 9.4 Hz, 1H), 5.91 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.86 (dd, *J* = 4.9, 3.6 Hz, 1H), 6.94–7.00 (m, 1H), 7.13–7.46 (m, 8H), 7.62 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.54–8.61 (m, 1H), 8.98 (d, *J* = 9.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 57.2, 106.7, 109.9, 122.1, 124.1, 126.8, 128.3, 128.5, 130.4, 131.1, 131.2, 131.6, 137.1, 137.2, 139.5, 141.3, 142.7, 147.4, 152.6, 159.5; HRMS (ESI): *m*/*z* calculated for $C_{20}H_{16}N_2NaO_3S_2^+$ [M+Na^+]: 419.0495, found: 419.0491.



5aq

Synthesis of Cyclometalated Complex 7



7 33%

To a flame-dried test tube was added 2-(2-bromophenyl)pyridine (Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 11483; 224 mg, 0.96 mmol) and THF (3.0 mL). The solution was cooled to –78 °C, and BuLi (2.65 M in hexane, 0.38 mL, 1.0 mmol) was added dropwise. The mixture was stirred for 30 min at –78 °C, and then $ZnCl_2$ (144 mg, 1.06 mmol) in THF (1.2 mL) was slowly added. After stirred at the same temperature for 10 min, the mixture was warmed to room temperature to afford a solution of the arylzinc reagent as a clear red solution.

To another flame-dried 30 mL-flask was added $[Cp^*CoCl_2]_2$ (281 mg, 0.53 mmol) and THF (7.0 mL). The solution was cooled with ice/salt bath and the above

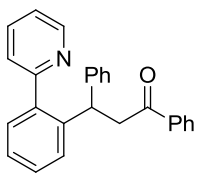
prepared arylzinc reagent solution was added dropwise. After the mixture was stirred for 30 min at the same temperature and then 1 h at room temperature, the solvent was removed by evaporation. The residue was dissolved in CH_2Cl_2 and loaded onto a silica gel column cooled with dry ice. A deep purple band was quickly eluted with CH_2Cl_2/AcOEt = 1/1 and the solvent was evaporated. After recrystallization from CH_2Cl_2/hexane, cyclometalated complex **7** was obtained as a deep purple crystal (120 mg, 33%). IR (KBr) ν 3034, 2979, 2908, 2205, 1600, 1574, 1477, 1414, 1014, 921, 759, 734 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.28 (s, 15H), 7.06–7.15 (m, 2H), 7.32 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.61–7.67 (m, 2H), 8.25–8.30 (m, 1H), 9.20–9.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 9.4, 93.4, 118.1, 121.4, 122.9, 123.0, 129.4, 136.8, 140.1, 146.4, 153.7, 167.3, 181.2; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{23}NCo^+$ [M-Cl^+]: 348.1157, found: 348.1145.

A single crystal suitable for X-ray analysis was obtained by slow vapor diffusion of hexane to a solution of **7** in toluene/CH_2Cl_2. The crystallographic data are attached at the last of the experimental section.

General Procedure of Cobalt^{III}-catalyzed Addition Reaction to Michael Acceptors

To a dried screw-capped vial were added α,β-unsaturated ketones **8** or α,β-unsaturated *N*-acylpyrrole **12** (0.40 mmol), 2-phenylpyridine **3** (0.48 mmol), **1a** (5.6 mg, 0.020 mmol), and THF (0.20 mL) under Ar atmosphere. The vial was capped and the mixture was heated at 100 °C for 24 h with stirring. After the mixture was cooled to room temperature, acetic acid (ca. 0.1 mL) was added under air, and the mixture was stirred for over 15 min. After dilution with CH_2Cl_2, saturated EDTA·2Na aq. was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layers were dried over Na_2SO_4. After filtration and evaporation, the crude residue was purified by silica gel column chromatography to give a corresponding product **9** or **13**.

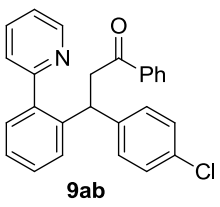
1,3-Diphenyl-3-(2-(pyridin-2-yl)phenyl)propan-1-one (9aa): a colorless oil; IR (neat) ν 3059, 3026, 1685, 1584, 1448, 1426, 1238, 1205, 1024, 986, 751, 698 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.74 (d, *J* = 7.2 Hz, 2H), 5.19 (t, *J* = 7.2 Hz, 1H), 7.03–7.12 (m, 3H), 7.13–7.19 (m, 2H), 7.21–7.43 (m, 8H), 7.49–7.55 (m, 1H), 7.67 (ddd, *J* = 7.9, 7.9, 2.0 Hz, 1H), 7.85–7.91 (m, 2H), 8.62–8.67 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 41.4, 44.9, 121.7, 124.3, 125.9, 126.2. 127.7, 127.8, 128.0, 128.1, 128.4, 128.5, 130.0, 132.8, 136.1, 136.8, 140.5, 142.2, 143.7, 149.0, 159.9, 197.8; HRMS (ESI): *m*/*z* calculated for



9aa

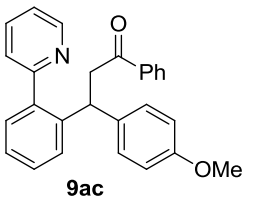
$C_{26}H_{21}NNaO^+$ [M+Na^+]: 386.1516, found: 386.1504.

3-(4-Chlorophenyl)-1-phenyl-3-(2-(pyridin-2-yl)phenyl)propan-1-one (9ab): a pale yellow oil; IR (neat) ν 3059, 3017, 1685, 1585, 1490, 1238, 1092, 1014, 753, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.65–3.80 (m, 2H), 5.15–5.23 (m, 1H), 6.96–7.02 (m, 2H), 7.08–7.14 (m, 2H), 7.21–7.44 (m, 8H), 7.49–7.56 (m, 1H), 7.69 (ddd, *J* = 7.5, 7.5, 1.8 Hz, 1H), 7.84–7.91 (m, 2H), 8.61–8.67 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.8, 44.7, 121.8, 124.3, 126.4, 127.5, 127.9, 128.2, 128.4, 128.5, 129.2, 130.0, 131.6, 132.9, 136.3, 136.6, 140.3, 141.7, 142.3, 148.9, 159.7, 197.6; HRMS (ESI): *m*/*z* calculated for $C_{26}H_{20}ClNNaO^+$ [M+Na^+]: 420.1126, found: 420.1117.



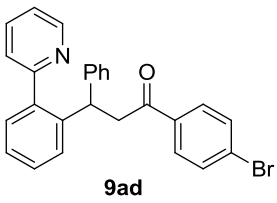
9ab

3-(4-Methoxyphenyl)-1-phenyl-3-(2-(pyridin-2-yl)phenyl)propan-1-one (9ac): a pale yellow oil; IR (neat) ν 3006, 2835, 1685, 1584, 1510, 1468, 1249, 1179, 1035, 755, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.68–3.74 (m, 5H), 5.12 (dd, *J* = 7.4 Hz, 7.4 Hz, 1H), 6.67–6.73 (m, 2H), 6.93–7.01 (m, 2H), 7.21–7.43 (m, 8H), 7.48–7.56 (m, 1H), 7.68 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 7.83–7.91 (m, 2H), 8.64 (brd, *J* = 4.9 Hz ,1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.6, 45.1, 55.0, 113.5, 121.7, 124.3, 126.1, 127.5, 128.0, 128.4, 128.5, 128.7, 129.9, 132.8, 135.8, 136.1, 136.8, 140.3, 142.5, 148.9, 157.6, 159.8, 198.0; HRMS (ESI): *m*/*z* calculated for $C_{27}H_{23}NNaO_2^+$ [M+Na^+]: 416.1621, found: 416.1609.



9ac

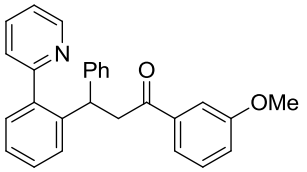
1-(4-Bromophenyl)-3-phenyl-3-(2-(pyridin-2-yl)phenyl)propan-1-one (9ad): a yellow oil; IR (neat) ν 3059, 3025, 1686, 1584, 1469, 1425, 1397, 1291, 1240, 1203, 1071, 1010, 984, 795, 755, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.64–3.75 (m, 2H), 5.17 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.03–7.12 (m, 3H), 7.13–7.2 0 (m, 2H), 7.21–7.38 (m, 6H), 7.50–7.56 (m, 2H), 7.64–7.76 (m, 3H), 8.61–8.67 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 41.4, 44.8, 121.7, 124.2,125.9, 126.2, 127.6, 127.7, 127.8, 128.1, 128.4, 129.5, 129.9, 131.6, 135.4, 136.1, 140.3, 141.9, 143.4, 148.8, 159.7, 196.9; HRMS (ESI): *m*/*z* calculated for $C_{26}H_{20}BrNNaO^+$ [M+H^+]: 442.0802, found: 442.0803.



9ad

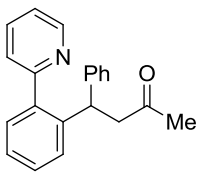
1-(3-Methoxyphenyl)-3-phenyl-3-(2-(pyridin-2-yl)phenyl)propan-1-one (9ae): a colorless solid; IR (KBr) ν 3057, 3026, 1684, 1594, 1426, 1260, 1165, 786 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.73 (d, *J* = 7.6 Hz, 2H), 3.80 (s, 3H), 5.18 (t, *J* = 7.6 Hz, 1H), 7.02–

7.12 (m, 4H), 7.12–7.19 (m, 2H), 7.21–7.37 (m, 7H), 7.39 (brs, 1H), 7.46–7.50 (m, 1H), 7.68 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.62–8.67 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 41.5, 45.0, 55.4, 112.1, 119.6, 120.7, 121.8, 124.4, 126.0, 126.3, 127.7, 127.8, 128.2, 128.5, 129.4, 130.0, 136.3, 138.3, 140.4, 142.1, 143.7, 148.9, 159.7, 159.8, 197.7; HRMS (ESI): *m*/*z* calculated for $C_{27}H_{23}NNaO_2^+$ [M+Na$^+$]: 416.1621, found: 416.1625.



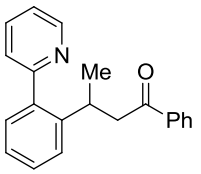
9ae

4-Phenyl-4-(2-(pyridin-2-yl)phenyl)butan-2-one (9af): a colorless solid; IR (KBr) ν 3026, 3000, 1712, 1586, 1561, 1490, 1430, 1356, 1161, 1023, 758, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.01 (s, 3H), 3.14 (dd, *J* = 16.2, 8.3 Hz, 1H), 3.19 (dd, *J* = 16.2, 6.6 Hz, 1H) , 5.02 (dd, *J* = 8.3, 6.6 Hz, 1H), 7.00–7.14 (m, 2H), 7.08–7.12 (m, 1H), 7.14–7.19 (m, 2H), 7.24–7.37 (m, 6H), 7.70 (ddd, *J* = 7.3, 7.3, 2.0 Hz, 1H), 8.67–8.71 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.8, 41.3, 50.0, 121.8, 124.4, 126.0, 126.2, 127.5, 127.7, 128.2, 128.5, 130.0, 136.2, 140.3, 141.8, 143.4, 148.9, 159.9, 206.9; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{19}NNaO^+$ [M+Na$^+$]: 324.1359, found: 324.1366.



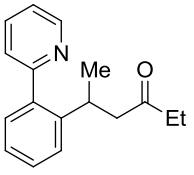
9af

1-Phenyl-3-(2-(pyridin-2-yl)phenyl)butan-1-one (9ag): a pale yellow solid; IR (KBr) ν 2973, 2907, 1677, 1582, 1468, 1426, 1362, 1256, 1203, 987, 798, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26 (d, *J* = 6.7 Hz, 3H), 3.04 (dd, *J* = 15.9, 9.4 Hz, 1H), 3.41 (dd, *J* = 15.9, 4.9 Hz, 1H), 3.64–3.78 (m, 1H), 7.22–7.55 (m, 9H), 7.73 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.79–7.86 (m, 2H), 8.61–8.68 (m, 1H),; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 31.2, 47.3, 121.7, 124.2, 126.0, 126.1, 128.1, 128.3, 128.6, 129.8, 132.7, 136.2, 136.8, 140.0, 144.3, 149.0, 160.0, 199.1; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{19}NNaO^+$ [M+Na$^+$]: 324.1359, found: 324.1366.



9ag

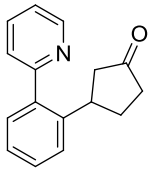
5-(2-(Pyridin-2-yl)phenyl)hexan-3-one (9ah): a pale yellow oil; IR (neat) ν 2972, 2939, 1712, 1585, 1469, 1426, 1112, 1024, 989, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.95 (t, *J* = 7.4 Hz, 3H), 1.20 (d, *J* = 7.2 Hz, 3H), 2.27 (q, *J* = 7.4 Hz, 2H), 2.54 (dd, *J* = 15.9, 8.6 Hz, 1H), 2.82 (dd, *J* = 15.9, 5.6 Hz, 1H) 3.51–3.63 (m, 1H), 7.22–7.46 (m, 6H), 7.77 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.65–8.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 7.6, 21.6, 30.6, 35.9, 50.7, 121.7, 124.2, 125.8, 125.9, 128.5, 129.8, 136.1, 139.9, 144.1, 149.0, 159.9, 210.3; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{19}NNaO^+$ [M+Na$^+$]: 276.1359,



9ah

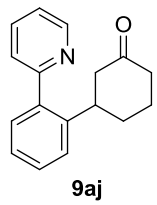
found: 276.1354.

3-(2-(pyridin-2-yl)phenyl)cyclopentanone (9ai): a pale orange oil; IR (neat) ν 3060, 2961, 2896, 1739, 1585, 1469, 1426, 1138, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.97–2.09 (m, 1H), 2.11–2.20 (m, 1H), 2.23–2.32 (m, 2H), 2.37–2.45 (m, 1H), 2.46–2.54 (m, 1H), 3.67–3.76 (m, 1H) 7.25–7.37 (m, 3H), 7.38–7.47 (m, 3H), 7.78 (ddd, *J* = 7.6, 7.6, 2.0 Hz, 1H), 8.66–8.70 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 30.9, 38.3, 38.8, 46.5, 121.9, 124.0, 125.7, 126.4, 128.7, 130.0, 136.4, 140.7, 140.8, 149.1, 160.0, 218.6; HRMS (ESI): *m*/*z* calculated for $C_{16}H_{15}NNaO^{+}$ [M+Na^{+}]: 260.1046, found: 260.1054.



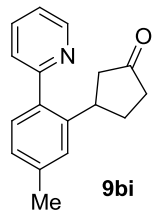
9ai

3-(2-(Pyridin-2-yl)phenyl)cyclohexanone (9aj): a pale yellow solid; IR (KBr) ν 2933, 2849, 1703, 1583, 1469, 1441, 1425, 1221, 797, 773, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.52–1.64 (m, 1H), 1.78–1.88 (m, 1H), 2.01–2.10 (m, 2H), 2.28–2.42 (m, 2H), 2.48–2.57 (m, 2H), 3.25–3.36 (m, 1H) 7.24–7.37 (m, 4H), 7.39–7.44 (m, 2H), 7.75 (ddd, *J* = 7.7, 7.7, 1.7 Hz, 1H), 8.64–8.69 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 25.4, 32.7, 40.0, 41.1, 48.7, 121.8, 124.0, 126.0, 126.3, 128.7, 130.0, 136.3, 139.9, 142.1, 149.1, 159.7, 211.0; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{17}NNaO^{+}$ [M+Na^{+}]: 274.1203, found: 274.1201.



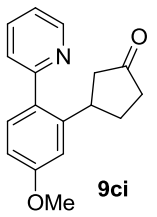
9aj

3-(5-Methyl-2-(pyridin-2-yl)phenyl)cyclopentanone (9bi): a pale yellow solid; IR (KBr) ν 2963, 2880, 1738, 1581, 1466, 1430, 1403, 1228, 795, 759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.99–2.04 (m, 1H), 2.10–2.20 (m, 1H), 2.26–2.31 (m, 2H), 2.38–2.43 (m, 1H), 2.41 (s, 3H), 2.48–2.52 (m, 1H), 3.69–3.73 (m, 1H) 7.10–7.13 (m, 1H), 7.21–7.28 (m, 3H), 7.37–7.40 (m, 1H), 7.75 (ddd, *J* = 7.8, 7.8, 2.0 Hz, 1H), 8.62–8.65 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.3, 30.9, 38.2, 38.8, 46.5, 121.6, 124.0, 126.3, 127.1, 129.9, 136.3, 137.9, 138.4, 140.7, 149.1, 160.0, 218.7; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{17}NNaO^{+}$ [M+Na^{+}]: 274.1203, found: 274.1200.



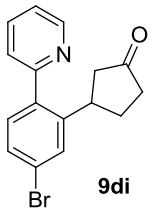
9bi

3-(5-Methoxy-2-(pyridin-2-yl)phenyl)cyclopentanone (9ci): a pale yellow solid; IR (KBr) ν 2950, 2842, 1730, 1607, 1584, 1470, 1432, 1288, 1227, 1043, 879, 790 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.94–2.07 (m, 1H), 2.10–2.33 (m, 3H), 2.36–2.55 (m, 2H), 3.72–3.83 (m, 1H), 3.86 (s, 3H), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.95 (d, *J* = 2.5 Hz, 1H), 7.22–7.27 (m, 1H), 7.28–7.32 (m, 1H), 7.33–7.38 (m, 1H), 7.71–7.78 (m, 1H), 8.63–8.70 (m, 1H); ^{13}C



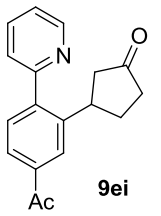
9ci

NMR ($CDCl_3$, 100 MHz) δ 30.8, 38.4, 38.8, 46.4, 55.2, 111.0, 112.0, 121.5, 124.0, 131.3, 133.4, 136.4, 142.5, 149.0, 159.7, 159.8, 218.5; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{17}NNaO_2^+$ [M+Na^+]: 290.1152, found: 290.1157.



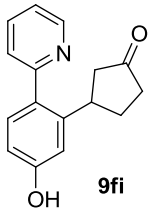
9di

3-(5-Bromo-2-(pyridin-2-yl)phenyl)cyclopentanone (9di): a pale yellow oil; IR (neat) ν 2963, 1740, 1589, 1465, 1428, 1138, 1093, 1024, 789, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.75–2.06 (m, 1H), 2.10–2.33 (m, 3H), 2.37–2.52 (m, 2H), 3.65–3.75 (m, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.28–7.33 (m, 1H), 7.33–7.38 (m, 1H), 7.45 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.55 (d, *J* = 1.9 Hz, 1H), 7.78 (ddd, *J* = 7.5, 7.5, 1.7 Hz, 1H), 8.65–8.70 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 30.7, 38.3, 38.7, 46.3, 122.2, 122.9, 123.9, 129.0, 129.5, 131.6, 136.6, 139.6, 143.3, 149.3, 158.9, 217.7; HRMS (ESI): *m*/*z* calculated for $C_{16}H_{14}BrNNaO^+$ [M+Na^+]: 338.0151, found: 338.0156.



9ei

3-(5-Acetyl-2-(pyridin-2-yl)phenyl)cyclopentanone (9ei): a pale orange solid; IR (KBr) ν 3051, 2960, 1742, 1684, 1584, 1462, 1432, 1242, 1139, 828, 791, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.04–2.23 (m, 2H), 2.25–2.35 (m, 2H), 2.40–2.54 (m, 2H), 2.65 (s, 3H), 3.70–3.79 (m, 1H), 7.31–7.36 (m, 1H), 7.38–7.43 (m, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.81 (ddd, *J* = 7.5, 7.5, 1.7 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.7 Hz, 1H), 8.07 (d, *J* = 1.7 Hz, 1H), 8.69–8.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 26.6, 30.8, 38.3, 38.7, 46.4, 122.4, 123.9, 125.6, 126.5, 130.3, 136.6, 137.1, 141.7, 145.1, 149.3, 158.8, 197.6, 217.8; HRMS (ESI): *m*/*z* calculated for $C_{18}H_{17}NNaO_2^+$ [M+Na^+]: 302.1152, found: 302.1156.

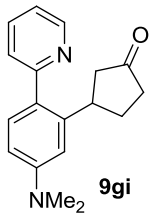


9fi

3-(5-Hydroxy-2-(pyridin-2-yl)phenyl)cyclopentanone (9fi): a colorless solid; IR (KBr) ν 3457, 2954, 1741, 1607, 1472, 1431, 1305, 1241, 1001, 873, 836, 790, 751 cm^{-1}; ^1H NMR (CD_3OD, 500 MHz) δ 1.92–2.06 (m, 1H), 2.08–2.44 (m, 5H), 3.52–3.61 (m, 1H), 6.75 (dd, *J* = 8.4, 2.9 Hz, 1H), 6.91 (d, *J* = 2.9 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.35–7.40 (m, 1H), 7.43–7.47 (m, 1H), 7.89 (ddd, *J* = 7.6, 7.6, 1.7 Hz, 1H), 8.55–8.59 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ 32.1, 39.5, 39.8, 47.1, 113.6, 114.4, 123.3, 126.2, 132.3, 133.1, 138.6, 144.0, 149.5, 159.4, 161.2, 220.8; HRMS (ESI): *m*/*z* calculated for $C_{16}H_{15}NNaO_2^+$ [M+Na^+]: 276.0995, found: 276.0994.

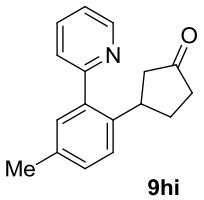
3-(5-(Dimethylamino)-2-(pyridin-2-yl)phenyl)cyclopentanone (9gi): a yellow solid; IR (KBr) ν 2899, 2805, 1736, 1605, 1585, 1465, 1429, 1348, 1142, 1119, 790 cm^{-1}; ^1H

NMR ($CDCl_3$, 400 MHz) δ 1.98–2.10 (m, 1H), 2.12–2.24 (m, 1H), 2.25–2.36 (m, 2H), 2.37–2.47 (m, 1H), 2.49–2.60 (m, 1H) 3.01 (s, 6H), 3.82–3.95 (m, 1H), 6.66–6.73 (m, 2H), 7.17–7.24 (m, 1H), 7.26–7.30 (m, 1H), 7.32–7.38 (m, 1H), 7.71 (ddd, *J* = 7.6, 7.6, 1. 8 Hz, 1H), 8.61–8.66 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 31.0, 38.5, 38.9, 40.4, 46.6, 109.2, 110.5, 120.9, 123.9, 129.1, 131.1, 136.2, 141.7, 148.9, 150.6, 160.3, 219.1; HRMS (ESI): *m*/*z* calculated for $C_{18}H_{20}N_2NaO^+$ [M+Na^+]: 303.1468, found: 303.1477.



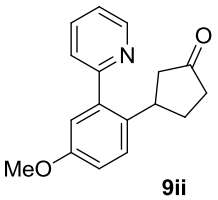
9gi

3-(4-Methyl-2-(pyridin-2-yl)phenyl)cyclopentanone (9hi): a pale orange oil; IR (neat) ν 2960, 2926, 1740, 1586, 1469, 1427, 1142, 824, 792, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.94–2.06 (m, 1H), 2.08–2.32 (m, 3H), 2.32–2.54 (m, 2H), 2.37 (s, 3H), 3.60–3.71 (m, 1H), 7.15–7.19 (m, 1H) 7.21–7.32 (m, 3H), 7.35–7.40 (m, 1H), 7.76 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.66–8.70 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.8, 31.0, 38.0, 38.8, 46.6, 121.8, 123.9, 125.6, 129.4, 130.6, 135.9, 136.3, 137.8, 140.5, 149.1, 160.0, 218.8; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{17}NNaO^+$ [M+Na^+]: 274.1203, found: 274.1200.



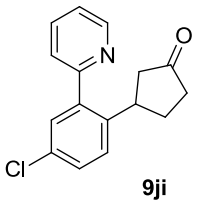
9hi

3-(4-Methoxy-2-(pyridin-2-yl)phenyl)cyclopentanone (9ii): a pale yellow oil; IR (neat) ν 2959, 1739, 1586, 1471, 1227, 1031, 789, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.91–2.08 (m, 1H), 2.08–2.31 (m, 3H), 2.35–2.52 (m, 2H), 3.54–3.68 (m, 1H), 3.83 (s, 3H), 6.89 (d, *J* = 2.7 Hz, 1H), 6.97 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.25–7.36 (m, 2H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.78 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.69 (brd, *J* = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 31.1, 37.7, 38.8, 46.6, 55.3, 114.5, 115.1, 122.0, 123.9, 126.8, 132.9, 136.4, 141.6, 149.1, 157.7, 159.7, 218.8; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{17}NNaO_2^+$ [M+Na^+]: 290.1152, found: 290.1143.



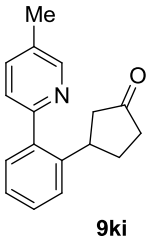
9ii

3-(4-Chloro-2-(pyridin-2-yl)phenyl)cyclopentanone (9ji): a pale yellow oil; IR (neat) ν 3056, 2963, 1741, 1584, 1467, 1427, 1404, 1140, 1099, 822, 796, 780, 751 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.93–2.05 (m, 1H), 2.10–2.31 (m, 3H), 2.35–2.51 (m, 2H), 3.63–3.72 (m, 1H), 7.27–7.41 (m, 5H), 7.76–7.82 (m, 1H), 8.66–8.70 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 30.8, 37.9, 38.7, 46.3, 122.3, 123.9, 127.2, 128.7, 129.8, 131.9, 136.6, 139.5, 142.2, 149.3, 158.5, 218.0; HRMS (ESI): *m*/*z* calculated for $C_{16}H_{14}ClNNaO^+$ [M+Na^+]: 294.0657, found: 294.0665.



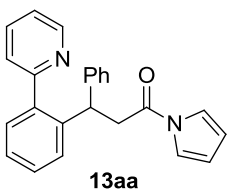
9ji

3-(2-(5-Methylpyridin-2-yl)phenyl)cyclopentanone (9ki): a colorless oil; IR (neat) ν 2960, 1739, 1457, 1136, 839, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.95–2.09 (m, 1H), 2.10–2.33 (m, 3H), 2.36–2.53 (m, 2H), 2.41 (s, 3H), 3.66–3.79 (m, 1H), 7.25–7.36 (m, 3H), 7.39–7.45 (m, 2H), 7.59 (dd, *J* = 7.9, 2.0 Hz, 1H), 8.51 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.1, 30.8, 38.3, 38.8, 46.4, 123.4, 125.6, 126.3, 128.5, 129.9, 131.3, 137.0, 140.6, 140.8, 149.4, 157.0, 218.7; HRMS (ESI): *m*/*z* calculated for $C_{17}H_{17}NNaO^+$ [M+Na^+]: 274.1203, found: 274.1196.



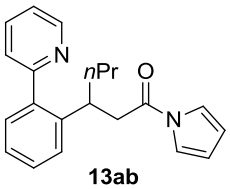
9ki

3-Phenyl-3-(2-(pyridin-2-yl)phenyl)-1-(1H-pyrrol-1-yl)propan-1-one (13aa): a pale yellow oil; IR (neat) ν 3060, 3031, 1717, 1585, 1469, 1271, 1112, 1073, 924, 744, 699 cm^{-1}; ^1H NMR (acetone-d_6, 400 MHz) δ 3.76 (dd, *J* = 16.7, 6.3 Hz, 1H), 3.85 (dd, *J* = 16.7, 8.7 Hz, 1H), 5.33 (dd, *J* = 8.7, 6.3 Hz, 1H), 6.20–6.27 (m, 2H), 7.07–7.53 (m, 13H), 7.81 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1H), 8.62–8.69 (m, 1H); ^{13}C NMR (acetone-d_6, 100 MHz) δ 40.8, 42.2, 113.3, 119.9, 122.7, 125.2, 126.8, 127.0, 128.7, 128.9, 128.9, 129.2, 130.8, 137.3, 141.4, 143.0, 144.6, 149.6, 160.8, 169.4; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{20}N_2NaO^+$ [M+Na^+]: 375.1468, found: 375.1464.



13aa

3-(2-(Pyridin-2-yl)phenyl)-1-(1H-pyrrol-1-yl)hexan-1-one (13ab): a colorless oil; IR (neat) ν 2956, 2926, 1715, 1585, 1469, 1335, 1272, 1071, 925, 745 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.69 (dd, *J* = 7.5, 7.5 Hz, 3H), 0.95–1.14 (m, 2H), 1.58–1.72 (m, 2H), 3.00 (dd, *J* = 15.3, 8.6 Hz, 1H), 3.28 (dd, *J* = 15.3, 5.7 Hz, 1H), 3.52–3.61 (m, 1H), 6.21–6.24 (m, 2H), 7.23–7.34 (m, 5H), 7.36–7.43 (m, 3H), 7.73 (ddd, *J* = 7.8, 7.8, 1.7 Hz, 1H), 8.62–8.66 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.8, 20.3, 36.7, 37.7, 42.4, 112.7, 119.1, 121.7, 124.3, 126.1, 126.2, 128.7, 129.8, 136.2, 140.9, 141.8, 148.9, 160.0, 169.4; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{22}N_2NaO^+$ [M+Na^+]: 341.1625, found: 341.1627.

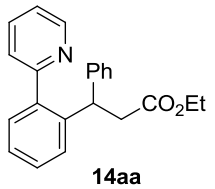


13ab

Transformation of *N*-Acylpyrrole 13aa to Corresponding Ester 14aa

To a solution of **13aa** (73.3 mg, 0.208 mmol) in EtOH (1.0 mL) was added NaOEt (29 mg, 0.42 mmol) at 0 °C. After the mixture was stirred at room temperature for 30 min, saturated *aq*. NH_4Cl was added. The mixture was extracted with AcOEt (x 3), and

the combined organic layers were dried over Na_2SO_4. After filtration and evaporation, the crude residue was purified by silica gel column chromatography (hexane/AcOEt = 8/1 then 4/1) to afford **14aa** as a pale yellow oil (62.9 mg, 91%).

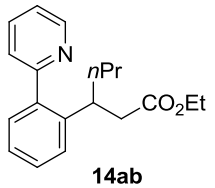


14aa

Ethyl 3-phenyl-3-(2-(pyridin-2-yl)phenyl)propanoate (14aa): a pale yellow oil; IR (neat) ν 2979, 1733, 1585, 1469, 1426, 1252, 1151, 1024, 754, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06 (dd, *J* = 7.2, 7.2 Hz, 3H), 3.00 (dd, *J* = 15.5, 9.0 Hz, 1H), 3.08 (dd, *J* = 15.5, 7.2 Hz, 1H), 3.90–4.03 (m, 2H), 4.93–5.02 (m, 1H), 7.00–7.20 (m, 5H), 7.21–7.40 (m, 6H), 7.63–7.72 (m, 1H), 8.66–8.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 40.9, 42.1, 60.2, 121.7, 124.3, 126.0, 126.3, 127.4, 127.7, 128.1, 128.4, 130.0, 136.1, 140.6, 141.3, 143.4, 149.0, 159.8, 171.6; HRMS (ESI): *m*/*z* calculated for $C_{22}H_{21}NNaO_2^+$ [M+Na^+]: 354.1465, found: 354.1466.

Transformation of *N*-Acylpyrrole 13ab to Corresponding Ester 14ab

The same procedure as the transformation of **13aa** to **14aa** gave **13ab** from **14ab** as a pale yellow oil in 91% yield.



14ab

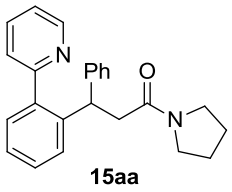
Ethyl 3-(2-(pyridin-2-yl)phenyl)hexanoate (14ab): a pale yellow oil; IR (neat) ν 2957, 2926, 2871, 1733, 1585, 1467, 1426, 1243, 1025, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.69 (dd, *J* = 7.5, 7.5 Hz, 3H), 0.98–1.12 (m, 2H), 1.12 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.47–1.64 (m, 2H), 2.55 (dd, *J* = 15.2, 7.7 Hz, 1H), 2.69 (dd, *J* = 15.2, 7.2 Hz, 1H), 3.39–3.47 (m, 1H), 3.95–4.06 (m, 2H), 7.22–7.29 (m, 2H), 7.31–7.35 (m, 2H), 7.35–7.40 (m, 1H), 7.43–7.47 (m, 1H), 7.74 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 8.66–8.71 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.8, 14.1, 20.2, 36.4, 38.6, 41.4, 60.1, 121.6, 124.4, 126.0, 126.1, 128.5, 129.7, 135.9, 141.0, 142.1, 149.1, 159.9, 172.5; HRMS (ESI): *m*/*z* calculated for $C_{19}H_{23}NNaO_2^+$ [M+Na^+]: 320.1621, found: 320.1629.

Transformation of *N*-Acylpyrrole 13aa to Corresponding Amide 15aa

To a solution of **13aa** (31.7 mg, 0.090 mmol) in THF (0.30 mL) were added DBU (40 μL, 0.27 mmol) and pyrrolidine (23 μL, 0.27 mmol) at room temperature. After the mixture was stirred at 60 °C for 4 h, saturated *aq*. NH_4Cl was added at room temperature. The mixture was extracted with AcOEt (x 3), and combined organic layers were dried over Na_2SO_4. After filtration and evaporation, the crude residue was purified by silica gel column chromatography (hexane/AcOEt = 1/1; AcOEt/MeOH = 50/1;

AcOEt/MeOH = 30/1) to afford **15aa** as a pale yellow oil (30.2 mg, 94%).

3-(2-(Pyridin-2-yl)phenyl)-1-(pyrrolidin-1-yl)hexan-1-one (15aa): a pale yellow oil; IR (neat) ν 2972, 2872, 1638, 1585, 1427, 1024, 755, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.67–1.85 (m, 4H), 2.94–3.04 (m, 2H), 3.08–3.16 (m, 1H), 3.25–3.38 (m, 3H), 5.01–5.07 (m, 1H), 6.98–7.02 (m, 2H), 7.04–7.09 (m, 1H), 7.10–7.15 (m, 2H), 7.19–7.25 (m, 1H), 7.25–7.33 (m, 3H), 7.35–7.41 (m, 2H), 7.66 (ddd, *J* = 7.7, 7.7, 1.9 Hz, 1H), 8.62–8.66 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 24.2, 26.0, 41.1, 42.3, 45.5, 46.5, 121.7, 124.5, 125.8, 126.2, 127.3, 127.8, 128.0, 128.3, 130.1, 136.0, 140.8, 141.9, 144.2, 148.9, 159.7, 169.5; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{26}N_2NaO^+$ [M+Na^+]: 379.1781, found: 379.1776.

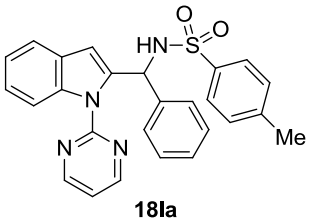


15aa

General Procedure of Cobalt^{III}-catalyzed C2-Selective Addition Reaction of Indoles to Imines

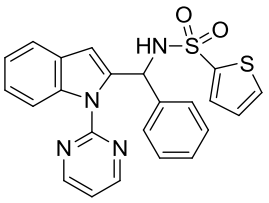
To a dried screw-capped vial were added indole **16** (0.80 mmol), imine **4** (0.40 mmol), **1a** (11 mg, 0.020 mmol), KOAc (3.9 mg, 0.040 mmol), and 1,2-dichloroethane (0.20 mL) under Ar atmosphere. The vial was capped and the mixture was heated at 100 °C for 12 h with stirring. After the mixture was cooled to room temperature, acetic acid (ca. 0.1 mL) was added under air, and the mixture was stirred for over 15 min. After dilution with CH_2Cl_2, saturated EDTA·2Na aq. was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (x 2). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation, obtained crude mixture was purified by silica gel column chromatography to give a corresponding product **18**.

4-Methyl-*N*-(phenyl(1-(pyrimidin-2-yl)-*1H*-indol-2-yl)methyl)benzenesulfonamide (18la): a colorless solid; IR (KBr) ν 3279, 1568, 1456, 1433, 1325, 1159, 1092, 813, 750, 676 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.16 (s, 3H), 6.18 (d, *J* = 9.7 Hz, 1H), 6.32 (s, 1H), 6.91–6.96 (m, 3H), 6.98–7.07 (m, 3H), 7.13–7.21 (m, 3H), 7.22–7.27 (m, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.54–7.59 (m, 2H), 7.66 (brd, *J* = 9.7 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 8.51 (d, *J* = 5.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.2, 55.9, 111.3, 114.3, 116.9, 120.4, 122.2, 123.9, 125.9, 126.7, 126.8, 127.9, 128.2, 128.9, 136.4, 137.0, 137.9, 139.2, 142.7, 156.9, 157.7; HRMS (ESI): *m*/*z* calculated for $C_{26}H_{22}N_4NaO_2S^+$ [M+Na^+]: 477.1356, found: 477.1347.



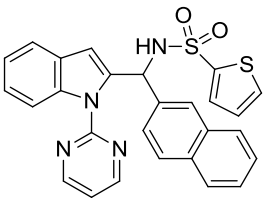
18la

***N*-(Phenyl(1-(pyrimidin-2-yl)-*1H*-indol-2-yl)methyl)thiophen e-2-sulfonamide (18lf):** a colorless solid; IR (KBr) ν 3296, 3255, 3087, 1567, 1454, 1423, 1332, 1154, 752, 668 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.30 (d, *J* = 9.5 Hz, 1H), 6.50 (s, 1H), 6.78–6.83 (m, 1H), 6.93 (t, *J* = 4.9 Hz, 1H), 6.99–7.08 (m, 3H), 7.12–7.16 (m, 2H), 7.18–7.24 (m, 1H), 7.24–7.32 (m, 2H), 7.45–7.52 (m, 2H), 7.80 (brd, *J* = 9.5 Hz, 1H), 8.21 (d, *J* = 8.1 Hz, 1H), 8.52 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.0, 111.1, 114.4, 116.9, 120.6, 122.3, 124.1, 125.9, 126.8, 126.9, 127.9, 128.2, 131.3, 131.9, 136.5, 137.1, 138.9, 142.2, 156.9, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{18}N_4NaO_2S_2^+$ [M+Na^+]: 469.0764, found: 469.0759.



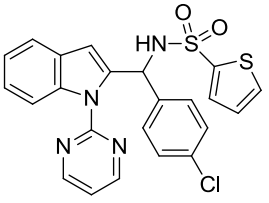
18lf

***N*-(Naphthalen-2-yl(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl) thiophene-2-sulfona mide (18lh):** a colorless solid; IR (KBr) ν 3276, 3051, 1566, 1454, 1430, 1338, 1157, 748, 671 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.47 (d, *J* = 9.2 Hz, 1H), 6.56 (s, 1H), 6.78 (dd, *J* = 4.9, 3.7 Hz 1H), 6.82 (t, *J* = 4.8 Hz, 1H), 7.21–7.32 (m, 4H), 7.33–7.39 (m, 2H), 7.46–7.49 (m, 1H), 7.50–7.62 (m, 4H), 7.63–7.69 (m, 1H), 7.88 (brd, *J* = 9.2 Hz, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 8.46 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 56.2, 111.2, 114.5, 116.9, 120.6, 122.3, 124.1, 124.2, 124.9, 125.8, 125.9, 126.7, 127.3, 127.8, 128.2, 131.3, 132.0, 132.2, 132.7, 136.4, 136.5, 136.6, 137.2, 142.1, 156.8, 157.6; HRMS (ESI): *m*/*z* calculated for $C_{27}H_{20}N_4NaO_2S_2^+$ [M+Na^+]: 519.0920, found: 519.0908.



18lh

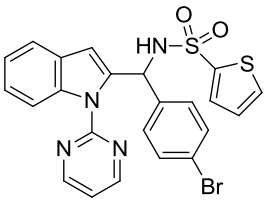
***N*-((4-Chlorophenyl)(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18li):** a colorless solid; IR (KBr) ν 3298, 3122, 3043, 1577, 1566, 1455, 1426, 1334, 1146, 852, 802, 728 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.23 (d, *J* = 9.7 Hz, 1H), 6.49 (s, 1H), 6.81 (dd, *J* = 5.2, 4.0 Hz 1H), 6.98 (t, *J* = 4.8 Hz, 1H), 7.01–7.05 (m, 2H), 7.07–7.12 (m, 2H), 7.19–7.24 (m, 1H), 7.27–7.33 (m, 2H), 7.45–7.52 (m, 2H), 7.86 (brd, *J* = 9.7 Hz, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 8.55 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.5, 111.4, 114.5, 117.1, 120.6, 122.4, 124.2, 126.8, 127.4, 128.0, 128.1, 131.5, 132.0, 132.7, 135.8, 137.1, 137.7, 141.9, 156.8, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{17}ClN_4NaO_2S_2^+$ [M+Na^+]: 503.0374, found: 503.0366.



18li

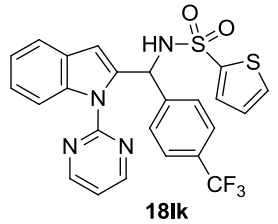
***N*-((4-Bromophenyl)(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfona**

mide (18lj): a colorless solid; IR (KBr) ν 3276, 3093, 1568, 1455, 1431, 1334, 1156, 1074, 1010, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.20 (d, *J* = 9.2 Hz, 1H), 6.48 (s, 1H), 6.79–6.84 (m, 1H), 6.98–7.01 (m, 1H), 7.02–7.07 (m, 2H), 7.17–7.33 (m, 5H), 7.44–7.52 (m, 2H), 7.85 (brd, *J* = 9.2 Hz, 1H), 8.25 (d, *J* = 8.6 Hz, 1H), 8.53–8.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.7, 111.6, 114.6, 117.1, 120.7, 121.0, 122.5, 124.3, 126.8, 127.7, 128.1, 131.1, 131.5, 132.1, 135.7, 137.2, 138.4, 142.0, 156.9, 157.9; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{17}BrN_4NaO_2S_2^+$ [M+Na^+]: 546.9869, found: 546.9855.



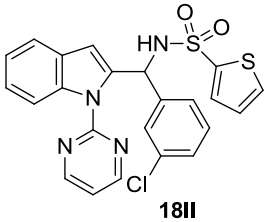
18lj

***N*-((1-(Pyrimidin-2-yl)-1*H*-indol-2-yl)(4-(trifluoromethyl)phe nyl)methy l)thiophene-2-sulfonamide (18lk):** a colorless solid; IR (KBr) ν 3292, 3092, 1568, 1456, 1432, 1324, 1156, 1125, 1066, 1016, 728, 669 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.29 (d, *J* = 9.8 Hz, 1H), 6.51 (s, 1H), 6.80-6.84 (m, 1H), 6.97 (t, *J* = 4.8 Hz, 1H), 7.20-7.26 (m, 1H), 7.28–7.36 (m, 6H), 7.46–7.53 (m, 2H), 7.87 (brd, *J* = 9.8 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 8.54 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.9, 111.8, 114.7, 117.1, 120.7, 122.6, 123.8 (q, $^1J_{CF}$ = 272.3 Hz), 124.5, 125.0 (q, $^3J_{CF}$ = 3.2 Hz), 126.4, 126.9, 128.1, 129.2 (q, $^2J_{CF}$ = 32.4 Hz), 131.6, 132.2, 135.4, 137.2, 142.0, 143.4, 156.8, 157.9; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{17}F_3N_4NaO_2S_2^+$ [M+Na^+]: 537.0638, found: 537.0630.



18lk

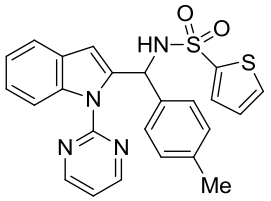
***N*-((3-Chlorophenyl)(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18ll):** a colorless solid; IR (KBr) ν 3093, 1567, 1454, 1433, 1335, 1160, 750, 713, 671 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.24 (d, *J* = 9.7 Hz, 1H), 6.49 (s, 1H), 6.80 (dd, *J* = 4.9, 3.6 Hz 1H), 6.93–7.04 (m, 4H), 7.18–7.33 (m, 4H), 7.43–7.52 (m, 2H), 7.83 (brd, *J* = 9.7 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.56 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.6, 111.4, 114.6, 117.0, 120.6, 122.4, 124.1, 124.2, 126.2, 126.8, 127.1, 128.0, 129.2, 131.5, 132.1, 134.0, 135.6, 137.1, 141.2, 141.8, 156.7, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{17}ClN_4NaO_2S_2^+$ [M+Na^+]: 503.0374, found: 503.0364.



18ll

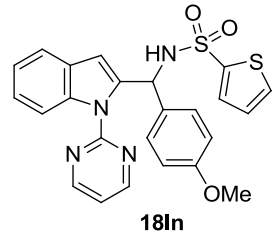
***N*-((1-(Pyrimidin-2-yl)-1*H*-indol-2-yl)(*p*-tolyl)methyl)thiophene-2-sulfonamide (18lm):** a colorless solid; IR (KBr) ν 3268, 3096, 3039, 2918, 1568, 14 55, 1430, 1331, 1154, 724, 672 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.16 (s, 3H), 6.27 (d, *J* = 9.2 Hz, 1H),

6.50 (s, 1H), 6.77–6.81 (m, 1H), 6.82–6.87 (m, 2H), 6.95 (t, *J* = 4.8 Hz, 1H), 6.98–7.03 (m, 2H), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.25–7.31 (m, 2H), 7.44–7.52 (m, 2H), 7.75 (brd, *J* = 9.2 Hz, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 8.54 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.8, 55.9, 111.0, 114.4, 116.9, 120.6, 122.3, 124.0, 125.9, 126.7, 128.2, 128.7, 131.3, 131.9, 136.0, 136.5, 136.8, 137.2, 142.3, 157.0, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{20}N_4NaO_2S_2^+$ [M+Na$^+$]: 483.0920, found: 483.0909.



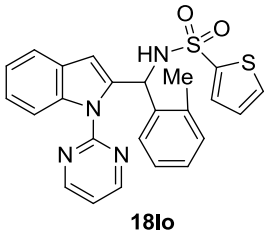
18lm

***N*-((4-Methoxyphenyl)(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18ln):** a pale yellow solid; IR (KBr) ν 3274, 3095, 2956, 2926, 2835, 1566, 1510, 1455, 1430, 1337, 1250, 1157, 1022, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.63 (s, 3H), 6.28 (d, *J* = 9.2 Hz, 1H), 6.49 (s, 1H), 6.53–6.58 (m, 2H), 6.79 (dd, J = 4.9, 3.7 Hz, 1H), 6.93 (t, *J* = 4.8 Hz, 1H), 6.98–7.04 (m, 2H), 7.19 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.23–7.31 (m, 2H), 7.43–7.50 (m, 2H), 7.72 (brs, 1H), 8.20 (d, *J* = 7.5 Hz, 1H), 8.52 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.1, 55.6, 111.8, 113.3, 114.3, 117.0, 120.6, 122.3, 124.0, 126.8, 127.2, 128.2, 131.0, 131.3, 131.9, 136.9, 137.2, 142.2, 157.0, 157.8, 158.4; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{20}N_4NaO_3S_2^+$ [M+Na$^+$]: 499.0870, found: 499.0865.



18ln

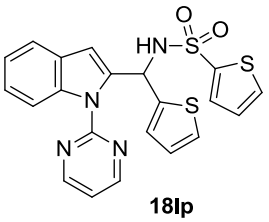
***N*-((1-(Pyrimidin-2-yl)-1*H*-indol-2-yl)(*o*-tolyl)methyl)thiophene-2-sulfonamide (18lo):** a colorless solid; IR (KBr) ν 3276, 3091, 3048, 1566, 1455, 1428, 1346, 1155, 1017, 729, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.36 (s, 3H), 5.74 (d, *J* = 8.6 Hz, 1H), 6.34 (s, 1H), 6.82 (dd, *J* = 5.2, 4.0 Hz, 1H), 6.85–6.93 (m, 2H), 7.01–7.10 (m, 4H), 7.14–7.20 (m, 1H), 7.23–7.28 (m, 1H), 7.33–7.37 (m, 2H), 7.43 (d, *J* = 7.5 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.67 (d, *J* = 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.2, 53.6, 109.5, 114.1, 117.2, 120.5, 122.0, 123.8, 125.7, 126.8, 126.9, 127.6, 128.1, 130.4, 131.4, 131.9, 136.3, 136.8, 137.4, 138.3, 142.1, 157.4, 158.0; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{20}N_4NaO_2S_2^+$ [M+Na$^+$]: 483.0920, found: 483.0913.



18lo

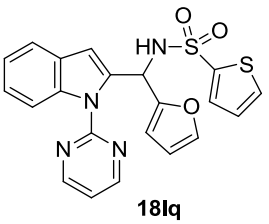
***N*-((1-(Pyrimidin-2-yl)-1*H*-indol-2-yl)(thiophen-2-yl)methyl)thiophene-2-sulfonamide (18lp):** a pale yellow solid; IR (KBr) ν 3274, 3091, 1567, 1455, 1430, 1338, 1158, 717 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.40 (d, *J* = 9.2 Hz, 1H), 6.43–6.47 (m, 1H), 6.57 (s,

1H), 6.59 (dd, *J* = 5.2, 3.4, 1H), 6.79 (dd, *J* = 4.9, 3.7 Hz, 1H), 6.95–7.00 (m, 2H), 7.18–7.23 (m, 1H), 7.27–7.32 (m, 2H), 7.48–7.52 (m, 2H), 8.18 (brd, *J* = 9.2 Hz, 1H), 8.26 (d, *J* = 9.2 Hz, 1H), 8.58 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 53.4, 111.0, 114.6, 116.9, 120.8, 122.4, 124.3, 124.3, 124.8, 126.5, 126.8, 128.1, 131.5, 132.1, 136.0, 137.2, 142.0, 144.2, 157.1, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{16}N_4NaO_2S_3^+$ [M+Na$^+$]: 475.0328, found: 475.0318.



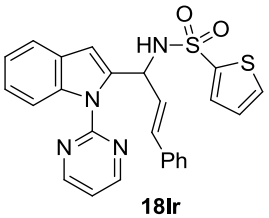
18lp

***N*-(Furan-2-yl(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18lq):** a pale yellow solid; IR (KBr) ν 3245, 1568, 1454, 1431, 1336, 1161, 1021, 742, 728 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.95–6.00 (m, 1H), 6.07 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.41–6.46 (m, 1H), 6.55 (s, 1H), 6.80–6.85 (m, 1H), 7.04–7.07 (m, 1H), 7.09 (t, *J* = 4.8 Hz, 1H), 7.17–7.23 (m, 1H), 7.26–7.36 (m, 2H), 7.44–7.53 (m, 3H), 8.24–8.30 (m, 1H), 8.67 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.5, 107.3, 110.3, 110.6, 114.4, 117.1, 120.8, 122.3, 124.3, 126.8, 128.1, 131.5, 132.0, 135.0, 137.3, 141.8, 142.1, 151.2, 157.3, 157.9; HRMS (ESI): *m*/*z* calculated for $C_{21}H_{16}N_4NaO_3S_2^+$ [M+Na$^+$]: 459.0557, found: 459.0549.



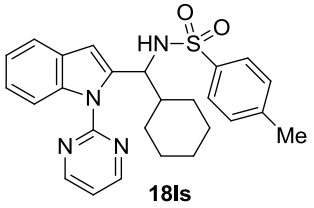
18lq

(*E*)-*N*-(3-Phenyl-1-(1-(pyrimidin-2-yl)-1H-indol-2-yl)allyl)thiophene-2-sulfonamide (18lp): a pale yellow solid; IR (KBr) ν 3443, 3274, 3091, 3048, 1565, 1454, 1429, 1345, 1157, 748, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.85 (ddd, *J* = 9.4, 4.5, 1.8 Hz, 1H), 6.11 (dd, *J* = 16.1, 4.5 Hz, 1H), 6.31 (dd, *J* = 16.1, 1.8 Hz, 1H), 6.49 (s, 1H), 6.77 (dd, *J* = 5.2, 3.8 Hz, 1H), 7.03 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.08 (t, *J* = 4.9 Hz, 1H), 7.10–7.30 (m, 6H), 7.45–7.52 (m, 2H), 7.70 (brd, *J* = 9.4 Hz, 1H), 8.24 (d, *J* = 7.6 Hz, 1H), 8.72 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 54.3, 110.1, 114.3, 117.4, 120.6, 122.3, 124.1, 126.2, 126.8, 127.6, 127.7, 128.3, 128.3, 131.3, 131.3, 132.0, 136.0, 136.5, 137.3, 142.3, 157.3, 158.1; HRMS (ESI): *m*/*z* calculated for $C_{25}H_{20}N_4NaO_2S_2^+$ [M+Na$^+$]: 495.0920, found: 495.0907.



18lr

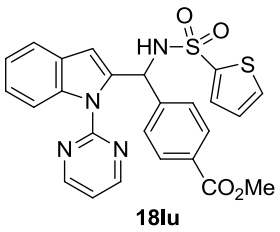
***N*-(Cyclohexyl(1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)-4-methylbenzenesulfonamide (18ls) :** a pale colorless solid; IR (KBr) ν 3261, 2925, 2851, 1577, 1564, 1454, 1429, 1348, 1325, 1162, 1092, 809, 741 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.71-0.88 (m, 2H), 0.96–1.18 (m, 4H), 1.23–1.38 (m,



18ls

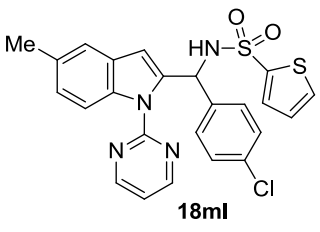
1H), 1.42–1.55 (m, 2H), 1.68–1.79 (m, 1H), 2.06 (s, 3H), 2.15–2.27 (m, 1H), 4.49 (brs, 1H), 6.01 (s, 1H), 6.79–6.84 (m, 2H), 7.10–7.15 (m, 1H), 7.22–7.27 (m, 1H), 7.30 (d, *J* = 6.9 Hz, 1H), 7.43–7.49 (m, 2H), 8.13 (d, *J* = 8.6 Hz, 1H), 8.84 (d, *J* = 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.0, 25.6, 25.7, 26.0, 29.9, 30.3, 41.2, 58.8, 110.5, 114.1, 117.3, 120.0, 122.0, 123.4, 126.6, 128.2, 128.6, 136.9, 137.0, 137.9, 142.4, 157.6, 158.2; HRMS (ESI): *m*/*z* calculated for $C_{26}H_{28}N_4NaO_2S^+$ [M+Na^+]: 483.1825, found: 483.1836.

Methyl 4-((1-(pyrimidin-2-yl)-1*H*-indol-2-yl)(thiophene-2-sulfonamido)methyl)benzoate (18lu): a colorless solid; IR (KBr) ν 3270, 3100, 2948, 1718, 1567, 1455, 1431, 1346, 1282, 1158 , 1112, 1017, 730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.83 (s, 3H), 6.28 (d, *J* = 9.4 Hz, 1H), 6.51 (s, 1H), 6.81 (dd, *J* = 5.2, 3.8 Hz, 1H), 6.94 (t, *J* = 4.9 Hz, 1H), 7.20-7.34 (m, 5H), 7.46–7.53 (m, 2H), 7.71–7.76 (m, 2H), 7.92 (brd, *J* = 9.4 Hz, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 8.51 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.9, 55.9, 111.5, 114.6, 117.0, 120.6, 122.4, 124.2, 125.9, 126.8, 128.0, 128.7, 129.2, 131.4, 132.0, 135.6, 137.0, 141.9, 144.4, 156.6, 157.8, 166.5; HRMS (ESI): *m*/*z* calculated for $C_{25}H_{20}N_4NaO_2S_2^+$ [M+Na^+]: 527.0819, found: 527.0818.



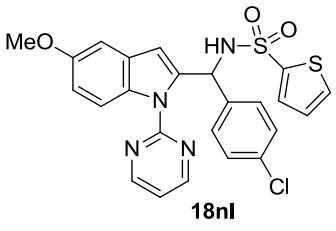
18lu

***N*-((4-Chlorophenyl)(5-methyl-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18ml):** a colorless solid; IR (KBr) ν 3290, 3100, 2918, 2856, 1577, 1430, 1335, 1157, 1091, 1014, 807, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.45 (s, 3H), 6.18 (d, *J* = 9.6 Hz, 1H), 6.41 (s, 1H), 6.80-6.86 (m, 1H), 6.96 (t, *J* = 4.9 Hz, 1H), 7.00-7.15 (m, 5H), 7.28 (brs, 1H), 7.30-7.38 (m, 1H), 7.45–7.50 (m, 1H), 7.90 (brd, *J* = 9.6 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.53 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 55.6, 111.4, 114.5, 116.8, 120.4, 125.8, 126.8, 127.3, 128.1, 128.3, 131.5, 132.0, 132.1, 132.7, 135.5, 135.7, 137.9, 142.0, 156.9, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{19}ClN_4NaO_2S_2^+$ [M+Na^+]: 517.0531, found: 517.0523.



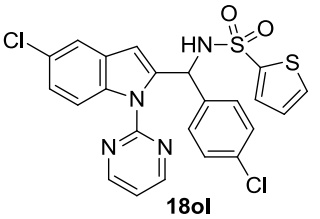
18ml

***N*-((4-Chlorophenyl)(5-methoxy-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18nl):** a colorless solid; IR (KBr) ν 3448, 1577, 1432, 1339, 1206, 1158, 1091, 805, 722, 670 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400



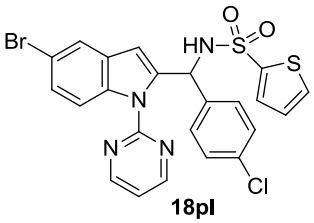
18nl

MHz) δ 3.87 (s, 3H), 6.19 (d, *J* = 9.4 Hz, 1H), 6.44 (s, 1H), 6.82 (dd, *J* = 5.4, 4.0 Hz, 1H), 6.90-6.99 (m, 3H), 7.01–7.06 (m, 2H), 7.07–7.13 (m, 2H), 7.32 (dd, *J* = 5.4, 1.4 Hz, 1H), 7.47 (dd, *J* = 4.0, 1.4 Hz, 1H), 7.89 (brd, *J* = 9.4 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.52 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.7, 55.7, 102.6, 111.6, 113.5, 115.9, 116.8, 126.8, 127.4, 128.1, 128.9, 131.5, 132.0, 132.0, 132.8, 136.3, 137.9, 142.0, 155.7, 156.7, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{19}ClN_4NaO_3S_2^+$ [M+Na$^+$]: 533.0480, found: 533.0471.



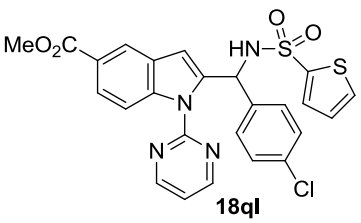
18ol

***N*-((5-Chloro-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)(4-chlorophenyl)methyl)thiophene-2-sulfonamide (18ol):** a colorless solid; IR (KBr) ν 3439, 3274, 1563, 1448, 1428, 1336, 1158, 1069, 804 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.23 (d, *J* = 9.6 Hz, 1H), 6.43 (s, 1H), 6.84 (dd, *J* = 4.9, 4.0 Hz, 1H), 7.00-7.10 (m, 5H), 7.24 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.35 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.45–7.50 (m, 2H), 7.75 (brd, *J* = 9.6 Hz, 1H), 8.19 (d, *J* = 9.0 Hz, 1H), 8.56 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.5, 110.4, 115.9, 117.4, 119.9, 124.3, 126.9, 127.3, 127.8, 128.1, 129.2, 131.6, 132.1, 132.9, 135.4, 137.4, 137.4, 141.8, 156.5, 157.9; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{16}Cl_2N_4NaO_2S_2^+$ [M+Na$^+$]: 536.9984, found: 536.9976.



18pl

***N*-((5-Bromo-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)(4-chlorophenyl)methyl)thiophene-2-sulfonamide (18pl):** a colorless solid; IR (KBr) ν 3434, 3295, 1578, 1562, 1443, 1428, 1335, 1148, 801 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.23 (d, *J* = 9.7 Hz, 1H), 6.43 (s, 1H), 6.82–6.87 (m, 1H), 7.00–7.10 (m, 5H), 7.33–7.40 (m, 2H), 7.46–7.50 (m, 1H), 7.62 (d, *J* = 1.8 Hz, 1H), 7.74 (brd, *J* = 9.7 Hz, 1H), 8.14 (d, *J* = 9.0 Hz, 1H), 8.56 (d, *J* = 5.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.4, 110.3, 115.5, 116.3, 117.4, 123.0, 126.9, 127.0, 127.3, 128.2, 129.7, 131.6, 132.1, 132.9, 135.8, 137.2, 137.4, 141.8, 156.5, 157.9; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{16}BrClN_4NaO_2S_2^+$ [M+Na$^+$]: 580.9479, found: 580.9475.

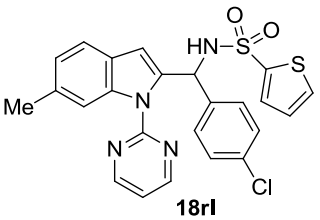


18ql

Methyl 2-((4-chlorophenyl)(thiophene-2-sulfonamido)methyl)-1-(pyrimidin-2-yl)-1*H*-indole-5-carboxylate (18ql): a pale yellow solid; IR (KBr) ν 3255, 3100, 2950, 1714, 1566, 1427, 1345, 1308, 1158, 1092, 1014, 769 cm^{-1}; ^{1}H

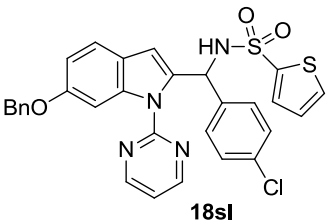
NMR ($CDCl_3$, 500 MHz) δ 3.95 (s, 3H), 6.27 (d, *J* = 9.5 Hz, 1H), 6.55 (s, 1H), 6.82 (dd, *J* = 4.9, 3.7 Hz, 1H), 7.02–7.11 (m, 5H), 7.32 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.48 (dd, *J* = 3.7, 1.4 Hz, 1H), 7.71 (brd, *J* = 9.5 Hz, 1H), 7.98 (dd, *J* = 8.9, 1.4 Hz, 1H), 8.20-8.25 (m, 2H), 8.59 (d, *J* = 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 52.0, 55.4, 111.4, 114.2, 117.7, 123.1, 124.3, 125.3, 126.9, 127.4, 127.7, 128.2, 131.6, 132.1, 133.0, 137.3, 137.6, 139.7, 141.8, 156.5, 158.0, 167.4; HRMS (ESI): *m*/*z* calculated for $C_{25}H_{19}ClN_4NaO_4S_2^+$ [M+Na^+]: 561.0429, found: 561.0425.

***N*-((4-Chlorophenyl)(6-methyl-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)methyl)thiophene-2-sulfonamide (18rl):** a pale yellow solid; IR (KBr) ν 3276, 3100, 2918, 2856, 1567, 1490, 1431, 1340, 1158, 1091, 1013, 822, 720, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.47 (s, 3H), 6.17 (d, *J* = 9.5 Hz, 1H), 6.41 (s, 1H), 6.83 (dd, *J* = 4.9, 3.7 Hz, 1H), 6.98 (t, *J* = 5.0 Hz, 1H), 7.00-7.11 (m, 5H), 7.33 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.48 (dd, *J* = 3.7, 1.4 Hz, 1H), 7.88 (brd, *J* = 9.5 Hz, 1H), 8.04 (s, 1H), 8.55 (d, *J* = 5.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.0, 55.5, 111.3, 114.4, 117.0, 120.3, 124.1, 125.8, 126.8, 127.4, 128.0, 131.5, 132.0, 132.7, 134.3, 135.1, 137.5, 137.9, 142.1, 156.9, 157.8; HRMS (ESI): *m*/*z* calculated for $C_{24}H_{19}ClN_4NaO_2S_2^+$ [M+Na^+]: 517.0531, found: 517.0520.



18rl

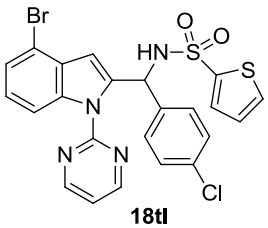
***N*-((6-(Benzyloxy)-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)(4-chlorophenyl)methyl)thiophene-2-sulfonamide (18sl):** a pale yellow solid; IR (KBr) ν 3310, 3091, 2878, 1577, 1489, 1427, 1337, 1150, 1014, 849, 725, 700, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.09 (d, *J* = 11.7 Hz, 1H), 5.13 (d, *J* = 11.7 Hz, 1H), 6.16 (d, *J* = 10.0 Hz, 1H), 6.40 (s, 1H), 6.81 (dd, *J* = 4.9, 3.7 Hz, 1H), 6.95 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.98 (t, *J* = 4.8 Hz, 1H), 7.01–7.05 (m, 2H), 7.08–7.13 (m, 2H), 7.30–7.42 (m, 5H), 7.44–7.50 (m, 3H), 7.83 (brd, *J* = 10.0 Hz, 1H), 7.95 (d, *J* = 1.9 Hz, 1H), 8.53 (d, *J* = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.7, 70.6, 100.5, 111.7, 112.3, 117.0, 121.1, 122.4, 126.8, 127.4, 127.6, 128.0, 128.2, 128.6, 131.5, 132.1, 132.8, 134.7, 137.2, 138.0, 138.1, 142.1, 157.0, 157.1, 157.9; HRMS (ESI): *m*/*z* calculated for $C_{30}H_{23}ClN_4NaO_3S_2^+$ [M+Na^+]: 609.0793, found: 609.0783.



18sl

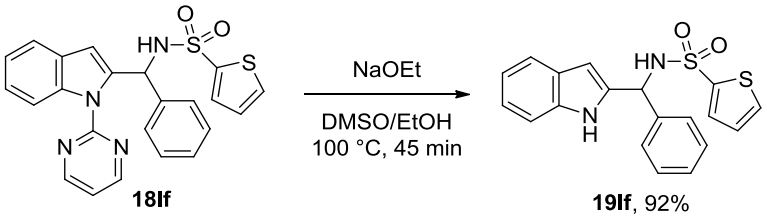
***N*-((4-Bromo-1-(pyrimidin-2-yl)-1*H*-indol-2-yl)(4-chlorophenyl)methyl)thiophene-2-sulfonamide (18tl):** a pale yellow solid; IR (KBr) ν 3448, 3276, 3100, 1577, 1561, 1433, 1341, 1159, 1091, 1014, 718 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.23 (d, *J* = 9.2

Hz, 1H), 6.47 (s, 1H), 6.84 (dd, *J* = 4.9, 3.8 Hz, 1H), 7.01–7.06 (m, 3H), 7.08–7.17 (m, 3H), 7.32 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.50 (dd, *J* = 3.8, 1.4 Hz, 1H), 7.74 (brd, *J* = 9.2 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 8.57 (d, *J* = 5.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.4, 110.8, 113.6, 114.3, 117.6, 125.1, 125.2, 126.9, 127.3, 128.2, 128.6, 131.6, 132.3, 132.9, 136.6, 137.3, 137.3, 141.7, 156.6, 158.0; HRMS (ESI): *m*/*z* calculated for $C_{23}H_{16}BrClN_4NaO_2S_2^+$ [M+Na$^+$]: 580.9479, found: 580.9486.



18tl

Removal of 2-pyrimidyl group



18lf **19lf**, 92%

To a solution of **18lf** (134 mg, 0.30 mmol) in DMSO (2.0 mL) were added NaOEt in EtOH (prepared from EtOH and Na, ca. 3M, 0.3 mL) at room temperature. After the mixture was stirred at 100 °C for 45 min, saturated *aq.* NH_4Cl was added at room temperature. The mixture was extracted with AcOEt (x 2), and the combined organic layers were washed with water, brine, and dried over Na_2SO_4. After filtration and evaporation, the crude residue was dissolved in CH_2Cl_2 (2 mL). To the solution was added hexane (5 mL), and precipitated solids were collected, washed with hexane, and dried in vacuo to afford **19lf** as a colorless solid (89.5 mg, 81%). The filtrate was concentrated, and subjected to preparative TLC (hexane/AcOEt = 2/1) to afford **19lf** (12.6 mg, 11%).

***N*-((1*H*-Indol-2-yl)(phenyl)methyl)thiophene-2-sulfonamide (19lf):** a colorless solid; IR (KBr) ν 3416, 3259, 3085, 3058, 1494, 1456, 1420, 1402, 1322, 1299, 1162, 1024, 752, 718, 701, 674 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 5.75 (brs, 1H), 6.11–6.14 (m, 1H), 6.89–6.94 (m, 2H), 6.98–7.04 (m, 1H), 7.16–7.32 (m, 6H), 7.35 (dd, *J* = 3.7, 1.4 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.70 (dd, *J* = 4.9, 1.4 Hz, 1H), 9.06 (brs, 1H), 10.90 (brs, 1H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 55.8, 99.7, 111.2, 118.9, 119.8, 121.0, 127.1, 127.2, 127.3, 127.5, 128.1, 131.5, 132.2, 136.2, 138.9, 140.0, 142.2; HRMS (ESI): *m*/*z* calculated for $C_{19}H_{16}N_2NaO_2S_2^+$ [M+Na$^+$]: 391.0546, found: 391.0538.

H/D-Exchange Experiments (Scheme 38, Scheme 40)

To a dried screw-capped vial were added indole **16l** (78 mg, 0.40 mmol),

appropriate catalysts, 1,2-dichloroethane (0.20 mL), CD_3OD (32 μL, 0.80 mmol), and imine **4f** (not added in Scheme 38; 50 mg, 0.20 mmol for Scheme 40) under Ar atmosphere. The vial was capped, and the mixture was heated at 100 °C for 12 h with stirring. After dilution with CH_2Cl_2, saturated EDTA·2Na aq. (for Co catalyst) or saturated $NaHCO_3$ aq. (for $Sc(OTf)_3$) was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (x 2). The combined organic layers were dried over Na_2SO_4. After filtration and evaporation, deuterium incorporation was evaluated by ^1H NMR analysis of the crude mixture in Scheme 38. In Scheme 40, deuterium incorporation was evaluated by ^1H NMR analysis of the recovered starting material and the isolated product after silica gel column chromatography.

X-ray Crystallographic Data of 7

Table S1. Crystal data and structure refinement for cpcocl

Identification code	cpcocl	
Empirical formula	C21 H23 Cl Co N	
Formula weight	383.78	
Temperature	93(2) K	
Wavelength	0.71075 Å	
Crystal system	monoclinic	
Space group	P21/c	
Unit cell dimensions	a = 7.177(3) Å	α= 90°.
	b = 14.812(5) Å	β= 99.963(6)°.
	c = 16.726(6) Å	γ = 90°.
Volume	1751.3(11) $Å^3$	
Z	4	
Density (calculated)	1.456 Mg/m^3	
Absorption coefficient	1.134 mm^{-1}	
F(000)	800	
Crystal size	0.18 x 0.16 x 0.15 mm^3	
Theta range for data collection	3.02 to 27.55°.	
Index ranges	-9<=h<=9, -19<=k<=19, -21<=l<=21	
Reflections collected	27269	
Independent reflections	4020 [R(int) = 0.0426]	
Completeness to theta = 27.55°	99.3 %	
Max. and min. transmission	0.8484 and 0.8220	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4020 / 0 / 222	
Goodness-of-fit on F^2	1.064	
Final R indices [I>2sigma(I)]	R1 = 0.0365, wR2 = 0.0964	
R indices (all data)	R1 = 0.0391, wR2 = 0.0989	
Largest diff. peak and hole	0.882 and -0.626 $e.Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for cpcocl. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Co(1)	1751(1)	7621(1)	1852(1)	13(1)
Cl(2)	4454(1)	8265(1)	1570(1)	15(1)
C(1)	2414(3)	6473(1)	1413(1)	14(1)
N(1)	3044(3)	7094(1)	2870(1)	21(1)
C(7)	3526(3)	6202(1)	2821(1)	17(1)
C(10)	4145(3)	7045(2)	4311(1)	24(1)
C(3)	2770(3)	5378(2)	378(1)	25(1)
C(2)	2192(3)	6218(2)	608(1)	21(1)
C(5)	3863(3)	5008(2)	1777(1)	23(1)
C(14)	-789(3)	7744(2)	2271(1)	22(1)
C(16)	-450(3)	8098(2)	966(1)	22(1)
C(9)	4525(3)	6129(2)	4267(1)	25(1)
C(4)	3600(3)	4766(2)	965(2)	26(1)
C(15)	-1118(3)	7427(1)	1454(1)	18(1)
C(13)	61(3)	8620(2)	2280(2)	27(1)
C(8)	4239(3)	5704(2)	3520(1)	22(1)
C(12)	240(3)	8829(2)	1478(2)	29(1)
C(11)	3404(3)	7504(2)	3607(1)	23(1)
C(21)	-2131(4)	6579(2)	1165(2)	37(1)
C(19)	549(4)	9253(3)	2982(2)	67(1)
C(20)	-1394(4)	7282(3)	2968(2)	50(1)
C(18)	971(4)	9698(2)	1197(3)	63(1)
C(17)	-613(4)	8102(3)	61(2)	49(1)
C(6)	3265(3)	5861(1)	1993(1)	17(1)

Table S3. Bond lengths [Å] and angles [°] for cpcocl.

Co(1)-C(1)	1.944(2)
Co(1)-N(1)	1.955(2)
Co(1)-C(15)	2.071(2)
Co(1)-C(14)	2.072(2)
Co(1)-C(16)	2.093(2)
Co(1)-C(13)	2.115(2)
Co(1)-C(12)	2.130(2)
Co(1)-Cl(2)	2.2829(9)
C(1)-C(2)	1.380(3)
C(1)-C(6)	1.389(3)
N(1)-C(11)	1.358(3)
N(1)-C(7)	1.373(3)
C(7)-C(8)	1.402(3)
C(7)-C(6)	1.454(3)
C(10)-C(11)	1.384(3)
C(10)-C(9)	1.388(3)
C(3)-C(2)	1.388(3)
C(3)-C(4)	1.391(3)
C(5)-C(4)	1.386(3)
C(5)-C(6)	1.403(3)
C(14)-C(15)	1.425(3)
C(14)-C(13)	1.433(3)
C(14)-C(20)	1.481(3)
C(16)-C(12)	1.417(3)
C(16)-C(15)	1.421(3)
C(16)-C(17)	1.497(3)
C(9)-C(8)	1.382(3)
C(15)-C(21)	1.490(3)
C(13)-C(12)	1.403(4)
C(13)-C(19)	1.497(4)
C(12)-C(18)	1.496(3)
C(1)-Co(1)-N(1)	82.50(8)
C(1)-Co(1)-C(15)	92.99(8)

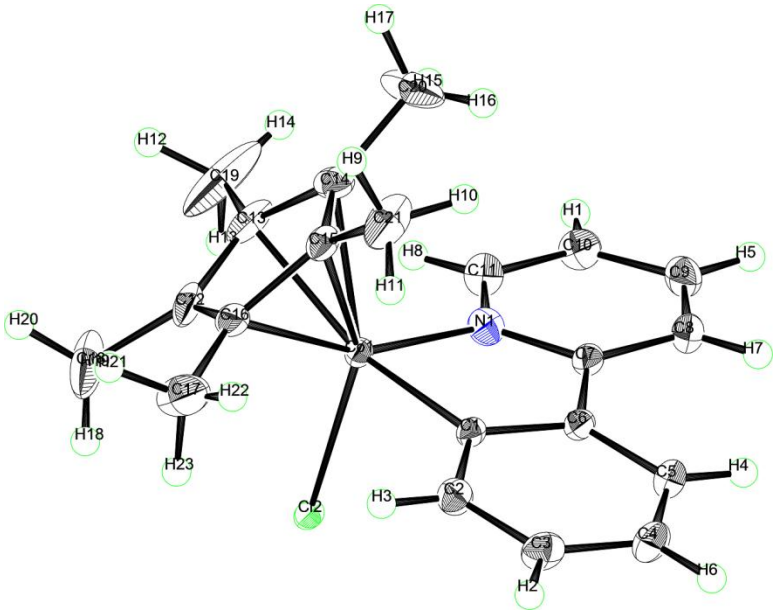
N(1)-Co(1)-C(15)	121.30(8)
C(1)-Co(1)-C(14)	119.45(9)
N(1)-Co(1)-C(14)	93.02(9)
C(15)-Co(1)-C(14)	40.23(9)
C(1)-Co(1)-C(16)	103.43(9)
N(1)-Co(1)-C(16)	159.63(8)
C(15)-Co(1)-C(16)	39.90(9)
C(14)-Co(1)-C(16)	66.99(9)
C(1)-Co(1)-C(13)	158.73(9)
N(1)-Co(1)-C(13)	101.40(9)
C(15)-Co(1)-C(13)	66.98(9)
C(14)-Co(1)-C(13)	40.01(10)
C(16)-Co(1)-C(13)	66.20(9)
C(1)-Co(1)-C(12)	140.38(10)
N(1)-Co(1)-C(12)	137.00(10)
C(15)-Co(1)-C(12)	66.09(9)
C(14)-Co(1)-C(12)	65.91(9)
C(16)-Co(1)-C(12)	39.19(10)
C(13)-Co(1)-C(12)	38.60(10)
C(1)-Co(1)-Cl(2)	90.91(6)
N(1)-Co(1)-Cl(2)	93.13(6)
C(15)-Co(1)-Cl(2)	145.57(7)
C(14)-Co(1)-Cl(2)	149.56(7)
C(16)-Co(1)-Cl(2)	106.10(7)
C(13)-Co(1)-Cl(2)	109.58(7)
C(12)-Co(1)-Cl(2)	89.78(7)
C(2)-C(1)-C(6)	117.77(18)
C(2)-C(1)-Co(1)	127.76(15)
C(6)-C(1)-Co(1)	114.44(15)
C(11)-N(1)-C(7)	118.30(19)
C(11)-N(1)-Co(1)	126.83(16)
C(7)-N(1)-Co(1)	114.77(14)
N(1)-C(7)-C(8)	121.0(2)
N(1)-C(7)-C(6)	113.46(18)
C(8)-C(7)-C(6)	125.49(19)
C(11)-C(10)-C(9)	119.1(2)

C(2)-C(3)-C(4)	120.1(2)
C(1)-C(2)-C(3)	121.7(2)
C(4)-C(5)-C(6)	119.3(2)
C(15)-C(14)-C(13)	107.9(2)
C(15)-C(14)-C(20)	125.5(3)
C(13)-C(14)-C(20)	126.4(3)
C(15)-C(14)-Co(1)	69.88(12)
C(13)-C(14)-Co(1)	71.64(13)
C(20)-C(14)-Co(1)	128.42(18)
C(12)-C(16)-C(15)	107.7(2)
C(12)-C(16)-C(17)	124.5(2)
C(15)-C(16)-C(17)	127.5(2)
C(12)-C(16)-Co(1)	71.80(13)
C(15)-C(16)-Co(1)	69.23(12)
C(17)-C(16)-Co(1)	129.34(17)
C(8)-C(9)-C(10)	119.5(2)
C(5)-C(4)-C(3)	119.5(2)
C(16)-C(15)-C(14)	107.74(19)
C(16)-C(15)-C(21)	126.7(2)
C(14)-C(15)-C(21)	125.4(2)
C(16)-C(15)-Co(1)	70.87(12)
C(14)-C(15)-Co(1)	69.89(12)
C(21)-C(15)-Co(1)	128.54(16)
C(12)-C(13)-C(14)	107.4(2)
C(12)-C(13)-C(19)	124.3(3)
C(14)-C(13)-C(19)	128.1(3)
C(12)-C(13)-Co(1)	71.26(13)
C(14)-C(13)-Co(1)	68.35(13)
C(19)-C(13)-Co(1)	129.34(17)
C(9)-C(8)-C(7)	119.4(2)
C(13)-C(12)-C(16)	109.2(2)
C(13)-C(12)-C(18)	125.8(3)
C(16)-C(12)-C(18)	124.9(3)
C(13)-C(12)-Co(1)	70.14(13)
C(16)-C(12)-Co(1)	69.01(12)
C(18)-C(12)-Co(1)	128.79(17)

N(1)-C(11)-C(10)	122.5(2)
C(1)-C(6)-C(5)	121.6(2)
C(1)-C(6)-C(7)	114.05(18)
C(5)-C(6)-C(7)	124.27(19)

Symmetry transformations used to generate equivalent atoms:

Figure S1 ORTEP diagram of **7**



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