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Pyrroloindolone Synthesis via a Cp*Co^{III}-Catalyzed Redox-Neutral Directed C−H Alkenylation/Annulation Sequence

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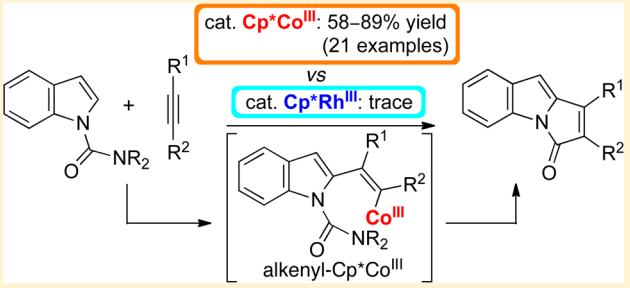
Supporting Information

ABSTRACT: A unique synthetic utility of a Cp*Co^{III} catalyst in comparison with related Cp*Rh^{III} catalysts is described. A C2-selective indole alkenylation/annulation sequence proceeded smoothly with catalytic amount of a $[Cp^*Co^{III}(C_6H_6)](PF_6)_2$ complex and KOAc. Intramolecular addition of an alkenyl-Cp*Co species to a carbamoyl moiety gave pyrroloindolones in 58−89% yield in one pot. Clear difference was observed between the catalytic activity of the Cp*Co^{III} complex and those of Cp*Rh^{III} complexes, highlighting the unique nucleophilic activity of the organocobalt species. The Cp*Co^{III} catalysis was also suitable for simple alkenylation process of *N*-carbamoyl indoles, and broad range of alkynes, including terminal alkynes, were applicable to give C2-alkenylated indoles in 50−99% yield. Mechanistic studies on C−H activation step under Cp*Co^{III} catalysis with the aid of an acetate unit as well as evaluation of the difference between organo-Co^{III} species and organo-Rh^{III} species are also described.



1. INTRODUCTION

Transition metal-catalyzed direct C−H bond functionalization has emerged as a powerful synthetic methodology.[1] Catalytic C−H bond functionalization processes do not require preactivated substrates such as haloarenes and stoichiometric amounts of organometallic reagents, and thus the process has become an increasingly viable alternative to traditional cross-coupling processes. The indole skeleton is an attractive platform for developing regioselective C−H bond functionalization reactions because of its utility in the design and synthesis of biologically active compounds.[2] Tremendous efforts have been focused on these reactions over the last several years, leading to a variety of transition metal-catalyzed direct C−H arylation,[3] alkylation,[4] oxidative alkenylation,[5] and redox-neutral direct alkenylation[6−8] processes of indoles. On the other hand, applications of the indole C−H functionalization process to cascade reactions, providing access to more functionalized *N*-fused indole cores, have been rare.[9] Among *N*-fused indole cores, a pyrrolo[1,2-*a*]indole bearing a 6−5−5 tricyclic skeleton is an important structural motif found in many biologically active natural products and pharmaceuticals, such as antitumor mitomycin C, antimalarial flinderole B, antinociceptive melatonin analogues, and psychotropic compounds (Figure 1).[10] Thus, methods for efficiently providing a pyrrolo[1,2-*a*]indole unit from readily available starting materials via a C−H activation process are in great demand. Here, we describe the C2-selective C−H alkenylation/annulation cascade of *N*-carbamoyl indoles to afford pyrroloindolones in one-pot.

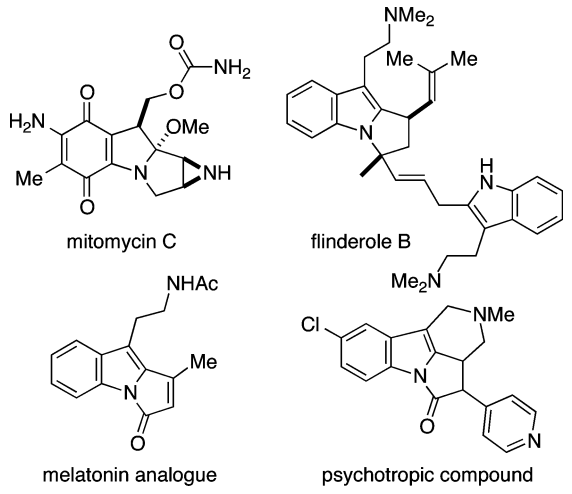


Figure 1. Biologically active natural and unnatural compounds bearing a pyrrolo[1,2-*a*]indole core.

As a part of our ongoing research projects on first-row transition metal catalysis,[11,12] we recently demonstrated the utility of a cationic high valent Cp*Co^{III} complex, $[Cp^*Co^{III}(C_6H_6)](PF_6)_2$ (Cp*Co-**1a**), in C−H bond functionalization processes.[13] The nucleophilicity of the aryl-Co species generated in situ via C−H bond activation featured the

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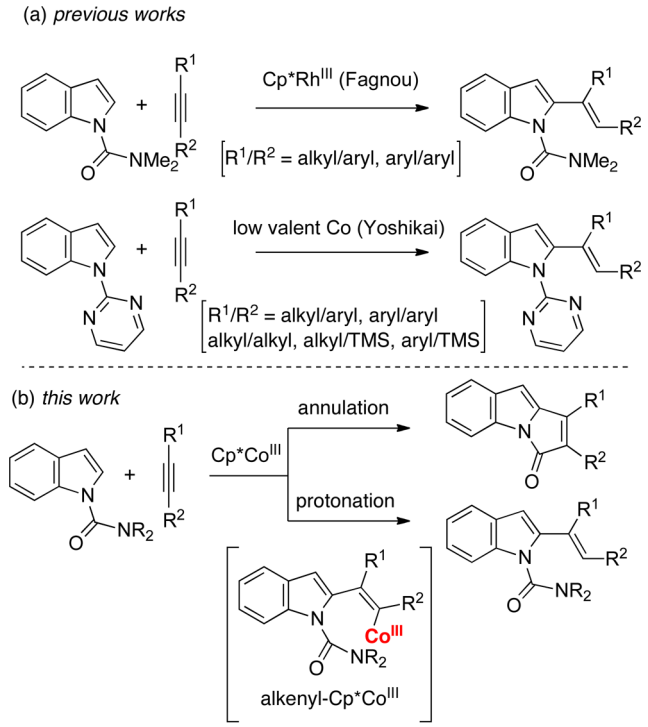
Cp^*Co^{III} catalysis, enabling nucleophilic addition to polar electrophiles such as imines and enones. Previous reports from our group, however, just demonstrated that the Cp^*Co^{III} catalyst could promote the reactions already established with Cp^*Rh^{III} catalysts.[14] To further expand the utility of the Cp^*Co^{III} catalysis, we explored a unique reaction in which only the Cp^*Co^{III} catalyst could efficiently promote the reaction. On the basis of the large difference in electronegativity between Co and Rh, we envisioned that the alkenyl-Cp^*Co^{III} species, generated via C2-selective C−H activation of indoles followed by insertion to alkyne, would be nucleophilic enough to react with an even less electrophilic *N*-carbamoyl directing group,[15,16] giving pyrroloindolones in one pot (Scheme 1; this work). By adjusting the reaction conditions, Cp^*Co^{III} also successfully gave simply C2-alkenylated indoles from broad range of alkynes, including terminal alkynes.

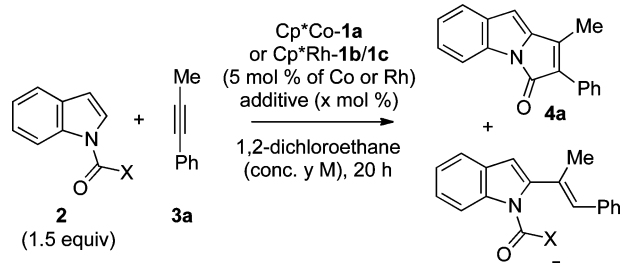
Scheme 1. (a) Previous Works: C2-Alkenylation of Indoles and (b) This Work: C2-Alkenylation/Annulation Sequence for Pyrroloindolone Synthesis



2. RESULTS AND DISCUSSION

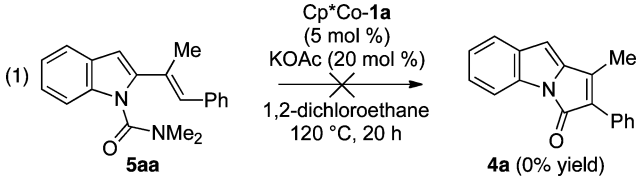
2.1. Cp^*Co^{III}-Catalyzed Pyrroloindolone Synthesis. Optimization studies toward pyrroloindolone synthesis are summarized in Table 1. No reaction of *N*-dimethylcarbamoyl indole **2a** with alkyne **3a** was promoted by 5 mol % of Cp*Co-**1a** alone at 80 °C (entry 1), while simply alkenylated product **5aa** was obtained in 90% yield in the presence of KOAc (10 mol %, entry 2). Desired pyrroloindolone **4a**, however, was not obtained at 80 °C. At 120 °C, the desired annulation proceeded to give **4a** in 22% yield (entry 3), together with **5aa** (41% yield). Increasing the amount of KOAc improved the yield of **4a** (33%), but **5aa** was still obtained as a major product (entry 4). As shown in eq 1, **4a** was not obtained when treating **5aa** under identical reaction conditions (120 °C, with 5 mol % of Cp*Co-**1a**, 20 mol % KOAc). The result suggested that **4a** was

Table 1. Optimization of the Alkenylation/Annulation Sequence



entry	Indole: X (**2**)	cat.	additive (x mol %)	conc. (y M)	temp. (z °C)	% yield[a] **4a**	**5**
1	Me_2N- **2a**	Cp*Co-**1a**	none	0.5	80	0	0
2	Me_2N- **2a**	Cp*Co-**1a**	KOAc (10)	0.5	80	0	90[b]
3	Me_2N- **2a**	Cp*Co-**1a**	KOAc (10)	0.5	120	22	41
4	Me_2N- **2a**	Cp*Co-**1a**	KOAc (20)	0.5	120	33	55
5	Me_2N- **2a**	Cp*Co-**1a**	KOAc (20)	0.3	120	46	44
6	Me_2N- **2a**	Cp*Co-**1a**	KOAc (20)	0.1	120	61	33
7	Me_2N- **2a**	Cp*Rh-**1b**	PivOH (500)	0.1	120	<1	>95
8	Me_2N- **2a**	Cp*Rh-**1b**	KOAc (20)	0.1	120	0	5
9	Me_2N- **2a**	Cp*Rh-**1b**	CsOPiv (20)	0.1	120	0	20
10	iPr_2N- **2b**	Cp*Co-**1a**	KOAc (20)	0.1	120	0	15
11	 **2c**	Cp*Co-**1a**	KOAc (20)	0.1	120	57	36
12	 **2d**	Cp*Co-**1a**	KOAc (20)	0.1	120	34	24
13	 **2e**	Cp*Co-**1a**	KOAc (20)	0.1	120	73	9
14	**2e**	Cp*Rh-**1b**	PivOH (500)	0.1	120	<1	90
15	**2e**	Cp*Rh-**1b**	KOAc (20)	0.1	120	0	3
16	**2e**	Cp*Rh-**1b**	CsOPiv (20)	0.1	120	0	4
17	**2e**	Cp*Rh-**1c**	PivOH (500)	0.1	120	0	>95
18	**2e**	Cp*Rh-**1c**	KOAc (20)	0.1	120	0	11
19	**2e**	Cp*Rh-**1c**	CsOPiv (20)	0.1	120	0	9
20	**2e**	Cp*Co-**1a**	KOAc (20)	0.1	130	82(78)[c]	8

[a]Determined by ^{1}H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as an internal standard unless otherwise noted. [b]Isolated yield after purification by silica gel column chromatography. Regioisomeric ratio (rr) of **5** was 17:1. [c]Number in parentheses is the isolated yield of pure **4a** (single regioisomer) after purification by silica gel column chromatography.



obtained directly from the alkenyl-Cp^*Co^{III} intermediate via an intramolecular nucleophilic addition, while **5aa** was obtained via irreversible proto-demetalation. The concentration of the reaction was important to decelerate the intermolecular protonation pathway (entries 4−6), and **4a** was obtained in 61% yield at 0.1 M (entry 6). As shown in entries 7−9, Cp*Rh-**1b** was not suitable for the desired alkenylation/annulation sequence. Under the Fagnou's conditions optimized for alkenylation with 5 equiv of PivOH,[6] **5aa** was obtained in

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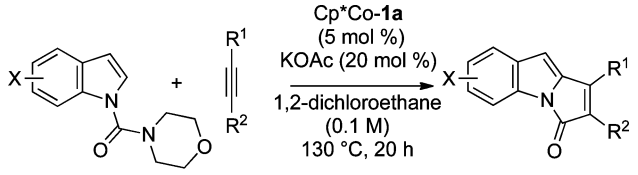
Table 2. Pyrroloindolone Synthesis via Cp*Co-Catalyzed C−H Alkenylation/Annulation[a]



Cp*Co-**1a** = $[Cp^*Co(C_6H_6)](PF_6)_2$

entry	X	2	R^1	R^2	3	4	% yield[b]
1	H	**2e**	Me	Ph	**3a**	**4a**	78
2	H	**2e**	Me	4-Me-C_6H_4	**3b**	**4b**	75
3	H	**2e**	Me	4-MeO-C_6H_4	**3c**	**4c**	89
4	H	**2e**	Me	4-Cl-C_6H_4	**3d**	**4d**	77
5	H	**2e**	Me	4-Br-C_6H_4	**3e**	**4e**	68
6	H	**2e**	Me	4-CO_2Et-C_6H_4	**3f**	**4f**	63
7	H	**2e**	Me	2-naphthyl	**3g**	**4g**	89
8	H	**2e**	Me	6-MeO-naphth-2-yl	**3h**	**4h**	73
9	H	**2e**	Et	Ph	**3i**	**4i**	71
10	H	**2e**	*n*-Bu	1-thienyl	**3j**	**4j**	78
11	H	**2e**	Ph	Ph	**3k**	**4k**	72
12	H	**2e**	4-Br-C_6H_4	4-Br-C_6H_4	**3l**	**4l**	58
13	4-Me	**2f**	Me	2-naphthyl	**3g**	**4m**	83
14	5-Me	**2g**	Me	2-naphthyl	**3g**	**4n**	78
15	5-MeO	**2h**	Me	2-naphthyl	**3g**	**4o**	88
16	5-Cl	**2i**	Me	2-naphthyl	**3g**	**4p**	85
17	5-Br	**2j**	Me	2-naphthyl	**3g**	**4q**	73
18	5-CO_2Me	**2k**	Me	2-naphthyl	**3g**	**4r**	61
19[c]	H	**2e**	$BnO_2C(CH_2)_3$	Ph	**3m**	**4s**	75[d]
20	H	**2e**	$TBDPSO(CH_2)_3$	Ph	**3n**	**4t**	82
21	H	**2e**	Ph	4-CO_2Et-C_6H_4	**3o**	**4u**	72[e]
22	H	**2e**	Et	Et	**3p**	**4v**	0[f]
23	H	**2e**	H	4-Br-C_6H_4	**3q**	**4w**	0[f]

[a]Reaction was run using **2** (1.5 equiv), **3** (0.20 mmol), $[Cp^*Co(C_6H_6)](PF_6)_2$ (5 mol %), KOAc (20 mol %) in 1,2-dichloroethane (0.1 M) under Ar at 130 °C unless otherwise noted. [b]Isolated yield of pure **4** (single regioisomer) after purification by silica gel column chromatography. [c]Reaction was run at 160 °C using $[Cp^*Co(C_6H_6)](PF_6)_2$ (10 mol %) and KOAc (40 mol %). [d]Isolated yield of **4s** and its regioisomer (r.r. = 18:1). [e]Isolated yield of **4u** and its regioisomer (r.r. = 1:1.2). [f]Simply alkenylated products were obtained.

excellent yield, but annulation adduct **4a** was obtained in less than 1% (entry 7). We also attempted reactions with Cp*Rh-**1b** in the presence of either KOAc or CsOPiv, but none of them produced the desired **4a** (entries 8−9). To further accelerate the desired alkenylation/annulation pathway over the undesired alkenylation/protonation pathway, the *N*-carbamoyl group was modified (entries 10−13), and the best yield of **4a** was obtained with *N*-carbamoyl indole **2e** bearing a morpholine unit (entry 13, 73%). To reconfirm that the present alkenylation/annulation sequence is a characteristic process under the Cp^*Co^{III} catalysis, we again attempted the reaction of indole **2e** with Cp*Rh-**1b**, and only trace if any **4a** was obtained (entries 14−16). To exclude the possible adverse effects of acetonitrile in Cp*Rh-**1b** as well as different counterions, we additionally attempted to use $[Cp^*RhCl_2]_2$ with $AgPF_6$ (Cp*Rh-**1c**), but still desired **4a** was not obtained (entries 17−19). Finally, **4a** was obtained in 82% (78% isolated yield) from **2e** at 130 °C after 20 h (entry 20) under Cp*Co-**1a** catalysis.

The optimal reaction conditions were then applied to various alkynes and indoles as summarized in Table 2. The alkenylation/annulation sequence of indole **2e** proceeded well with various aryl/alkyl- and diaryl-substituted alkynes (entries 1−12). The scope of indole is summarized in entries 13−18. Both electron-donating and electron-withdrawing substituents were compatible, and various 4- or 5-substituted indoles showed good reactivity. In entries 1−10 and 13−18, each annulation adduct was obtained as a single isomer. A minor regioisomer of the alkenyl-Cp^*Co^{III} intermediate was predominantly protonated to afford alkenylated adduct **5** in each entry (<10%). The alkenylation/annulation sequence proceeded even with a functionalized alkyne **3m** and **3n** bearing either an ester unit or a silyl ether unit, giving **4s** and **4t** in 75% yield (18:1 regioisomeric ratio, entry 19) and 82% yield (single isomer, entry 20). With unsymmetrical diaryl-alkyne **3o**, the annulation adduct **4u** was obtained, but in poor regioisomeric ratio (entry 21). Annulation adducts, however, were not obtained from dialkyl-substituted alkynes and terminal alkynes, because protonation of the alkenyl-Cp^*Co^{III} intermediate preferentially gave simply alkenylated products **5** (entries 22 and 23).

To demonstrate the synthetic utility of the present reaction, we transformed pyrroloindolones, as summarized in Scheme 2. Removal of the benzyl group in **4s** (95%) followed by activation of the carboxylic acid gave *N*-fused indole **6** bearing a 6−5−5−6 tetracyclic skeleton (57%). Hydrogenation of **4a** with Pt/C gave *cis*-substituted pyrroloindolone **7** in 79% yield.

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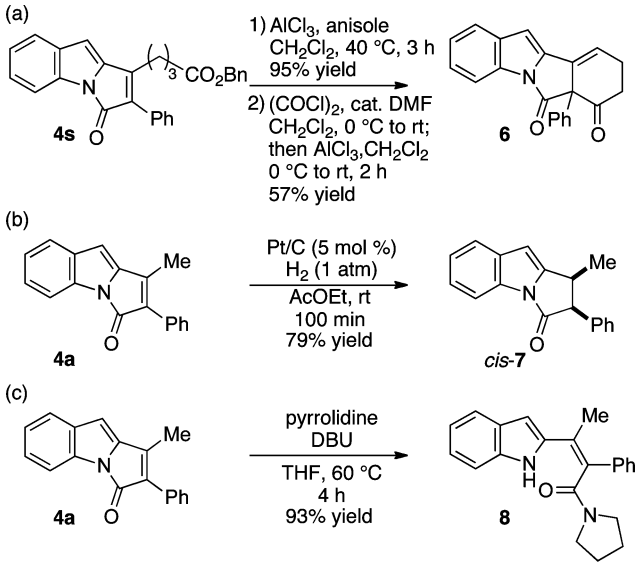
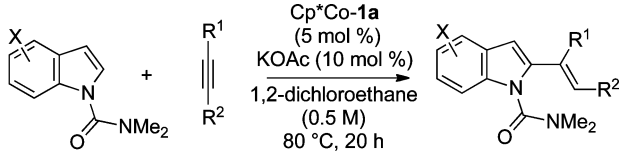
Scheme 2. Transformation of Pyrroloindolones



Ring-opening of the pyrroloindolone core was also readily performed, and fully substituted α,β-unsaturated amide **8** was obtained in 93% yield from **4a**.

2.2. Cp*Co^{III}-Catalyzed C2-Alkenylation of Indoles. Because simple C−H alkenylation also proceeded smoothly under the reaction conditions in entry 2 of Table 1 (90% yield), the substrate scope of the redox-neutral C−H alkenylation was investigated in detail to compare the potential for Cp*Co^{III} catalysis with previous examples using either the Cp*Rh^{III} or low valent Co-catalysis (see Scheme 1).[6,7] As summarized in Table 3, the scope of applicable alkynes was broad. Not only aryl/alkyl- and diaryl-substituted alkynes (entries 1−8), but also dialkyl-substituted alkynes (entries 9−16) gave the products in good yield. Terminal alkynes are often rather difficult substrates in hydroarylation reactions because of their relatively acidic protons and problematic self-di- or trimerization under transition metal catalysis. It is, therefore, noteworthy that alkenylation proceeded even with terminal alkynes, giving products in 68−78% yield with a >30:1 regioisomeric ratio (entries 17−20).[17] Limitations of the present system are shown in entries 21−23. Sterically hinderd alkynes such as **3t** and **3u** gave only trace, if any, products (entries 21 and 22).

Table 3. Cp*Co-Catalyzed C−H Alkenylation of Indoles[a]



2 (1.5 equiv) **3** **5**

Cp*Co-**1a** = $[Cp^*Co(C_6H_6)](PF_6)_2$

entry	X	2	R^1	R^2	3	5	r.r.[b]	% yield[c]
1	H	**2a**	Me	Ph	**3a**	**5aa**	17:1	90
2	H	**2a**	Me	4-Me-C_6H_4	**3b**	**5ab**	14:1	71
3	H	**2a**	Me	4-MeO-C_6H_4	**3c**	**5ac**	15:1	50
4	H	**2a**	Me	4-Cl-C_6H_4	**3d**	**5ad**	15:1	84
5	H	**2a**	Me	4-Br-C_6H_4	**3e**	**5ae**	14:1	96
6	H	**2a**	Me	4-CO_2Et-C_6H_4	**3f**	**5af**	17:1	88
7	H	**2a**	Et	Ph	**3i**	**5ai**	10:1	90
8	H	**2a**	4-Br-C_6H_4	4-Br-C_6H_4	**3l**	**5al**	–	83
9	H	**2a**	Et	Et	**3p**	**5ap**	–	93
10	H	**2a**	Pr	Pr	**3r**	**5ar**	–	97
11	5-Me	**2l**	Pr	Pr	**3r**	**5lr**	–	99
12	5-MeO	**2m**	Pr	Pr	**3r**	**5mr**	–	92
13	5-BnO	**2n**	Pr	Pr	**3r**	**5nr**	–	99
14	5-Cl	**2o**	Pr	Pr	**3r**	**5or**	–	96
15	5-Br	**2p**	Pr	Pr	**3r**	**5pr**	–	92
16	5-CO_2Me	**2q**	Pr	Pr	**3r**	**5qr**	–	93
17[d]	H	**2a**	H	4-Br-C_6H_4	**3q**	**5aq**	>30:1	73
18[d,e]	H	**2a**	H	Ph	**3s**	**5as**	>30:1	68
19[d]	5-Me	**2l**	H	4-Br-C_6H_4	**3q**	**5lq**	>30:1	73
20[d]	5-Cl	**2o**	H	4-Br-C_6H_4	**3q**	**5oq**	>30:1	78
21	H	**2a**	TMS	Ph	**3t**	**5at**	–	0
22	H	**2a**	*i*Pr	Me	**3u**	**5au**	–	trace
23	H	**2a**	Pr	Me	**3v**	**5av**	1.2:1	90

[a]Reaction was run using **2** (1.5 equiv), **3** (0.30 mmol), $[Cp^*Co(C_6H_6)](PF_6)_2$ **1a** (5 mol %), and KOAc (10 mol %) in 1,2-dichloroethane (0.5 M) at 80 °C under Ar unless otherwise noted. [b]Determined by ^{1}H NMR analysis of the crude reaction mixture. [c]Isolated yield after purification by silica gel column chromatography was shown for each entry. [d]Reaction was run at 130 °C in 0.15 M. [e]Reaction was run using 2 equiv of **2a**, $[Cp^*Co(C_6H_6)](PF_6)_2$ **1a** (10 mol %), and KOAc (20 mol %).

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Unsymmetrical dialkyl-alkyne **3v** gave product in 90% yield, but in poor regioisomeric ratio (1:1.2, entry 23).

2.3. Mechanistic Studies. In the present reaction, the Cp*Co^{III}-**1a** promoted the alkenylation/annulation sequence, while the Cp*Rh^{III}-**1b** and Cp*Rh^{III}-**1c** promoted only the alkenylation. We initially hypothesized that the carbon−metal bond of the alkenyl-Cp*Co^{III} species would be more polarized than that of the Cp*Rh^{III} species, and thus be more nucleophilic to react well, even with a poorly electrophilic carbamoyl group.[15] To evaluate the difference between the postulated alkenyl-Cp*Co^{III} species and the alkenyl-Cp*Rh^{III} species, we tried to isolate the key intermediate but failed. Thus, we instead isolated more stable cobaltacyclic aryl-Cp*Co^{III} species derived from 2-phenylpyridine (Figure 2),

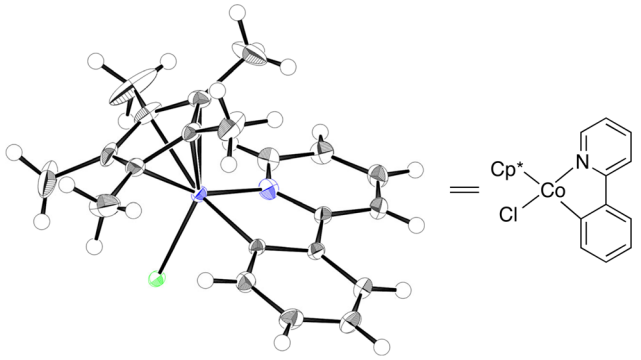


Figure 2. ORTEP of cobaltacyclic compound derived from 2-phenylpyridine.

because a corresponding aryl-Cp*Rh^{III} species has already been fully characterized.[18] Each atomic charge was then estimated by natural population analysis.[19] As shown in Figure 3, the C−

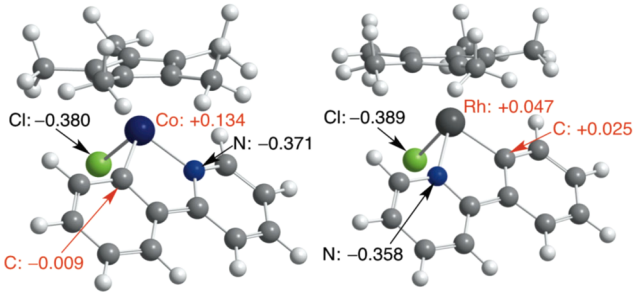
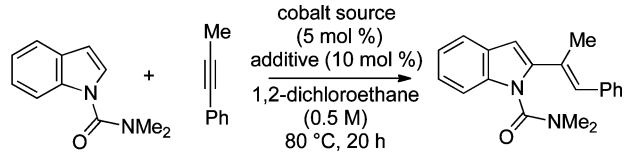


Figure 3. Atomic charge of aryl-Cp*Co^{III} species and aryl-Cp*Rh^{III} species estimated by natural population analysis (B3LYP/6-31LAN).

Co^{III} bond in the cobaltacycle was more polarized than the C−Rh^{III} bond in the rhodacycle. Thus, we assume, by analogy, the similar difference in carbon−metal bond between the alkenyl-Cp*Co^{III} species and that of Cp*Rh^{III}.

As to the alkenylation process, KOAc was important to promote the reaction (Table 1, entry 1 vs entry 2). Several negative control experiments either without cobalt salt or with different cobalt sources (Table 4, entries 1−5) indicated that the cationic Co^{III} was essential to promote the reaction. On the other hand, potassium ion was not essential because other metal acetates were somewhat effective to promote the alkenylation (entries 6−8). To gain insight into the reaction mechanism, H/D exchange experiments were performed in the presence of CD_3OD (Scheme 3a−c). Under the Cp*Co^{III}

Table 4. Negative Control Experiments



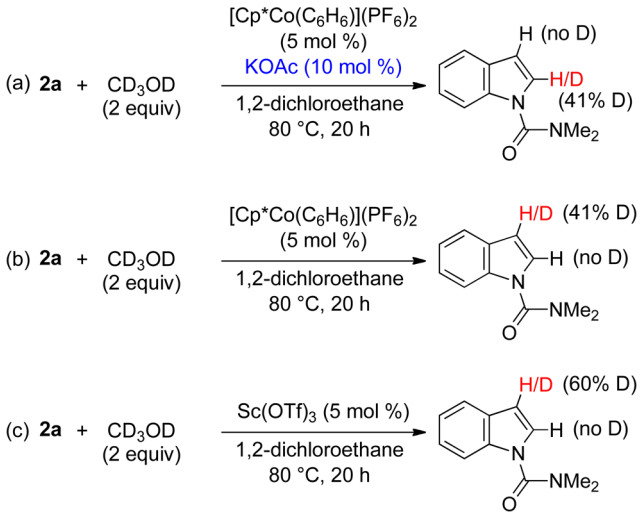
2 (1.5 equiv) **3** **5aa**

Cp*Co-**1a** = [Cp*Co(C_6H_6)](PF_6)$_2$

entry	cobalt source	additive	% yield[a]
1	none	KOAc	0
2	Co^{II}(OAc)$_2$	none	0
3	Co^{II}Cl$_2$	$AgPF_6$ + KOAc	0
4	Co^{III}(acac)$_3$	KOAc	0
5	[Co^{III}(NH_3)$_6$]Cl$_3$	KOAc	0
6	[Cp*Co^{III}(C_6H_6)](PF_6)$_2$	LiOAc	0
7	[Cp*Co^{III}(C_6H_6)](PF_6)$_2$	NaOAc	57
8	[Cp*Co^{III}(C_6H_6)](PF_6)$_2$	CsOAc	66

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

Scheme 3. H/D Exchange Experiments (a) with Cp*Co^{III}-1a + KOAc, (b) with Cp*Co^{III}-1a Alone, and (c) with Sc(OTf)$_3$



catalysis in the presence of KOAc, the site-selective H/D exchange occurred at the C2-position of the indole (41% D), and no detectable deuterium incorporation was observed at the C3-position (a). In contrast, the Cp*Co-**1a** alone selectively promoted H/D exchange at the C3-position (b, 41% D). The tendency in Scheme 3b was similar with that with a simple Lewis acid, such as Sc(OTf)$_3$, which also preferably promoted H/D exchange at the C3-position (c, 60% D). These results supported the mechanism that reversible C2-selective C−H activation and metalation occurred under the Cp*Co^{III} catalysis with the aid of acetate moiety.

The key role of an acetate unit in C−H activation step was supported by DFT calculations with Gaussian09[20] (B3LYP/6-31G**)[21] as shown in Figure 4. Previous theoretical studies showed the importance of an acetate unit in the C−H activation with Ir^{III}, Rh^{III}, and Pd^{II} complexes.[22,23] Among some conformations examined for the complex [Cp*Co^{III}(κ^2-OAc)-(**2a**)]$^+$, the singlet-state structure ^{1}**A**, in which the oxygen atom of a carbamoyl group coordinates to the Co atom, is in the

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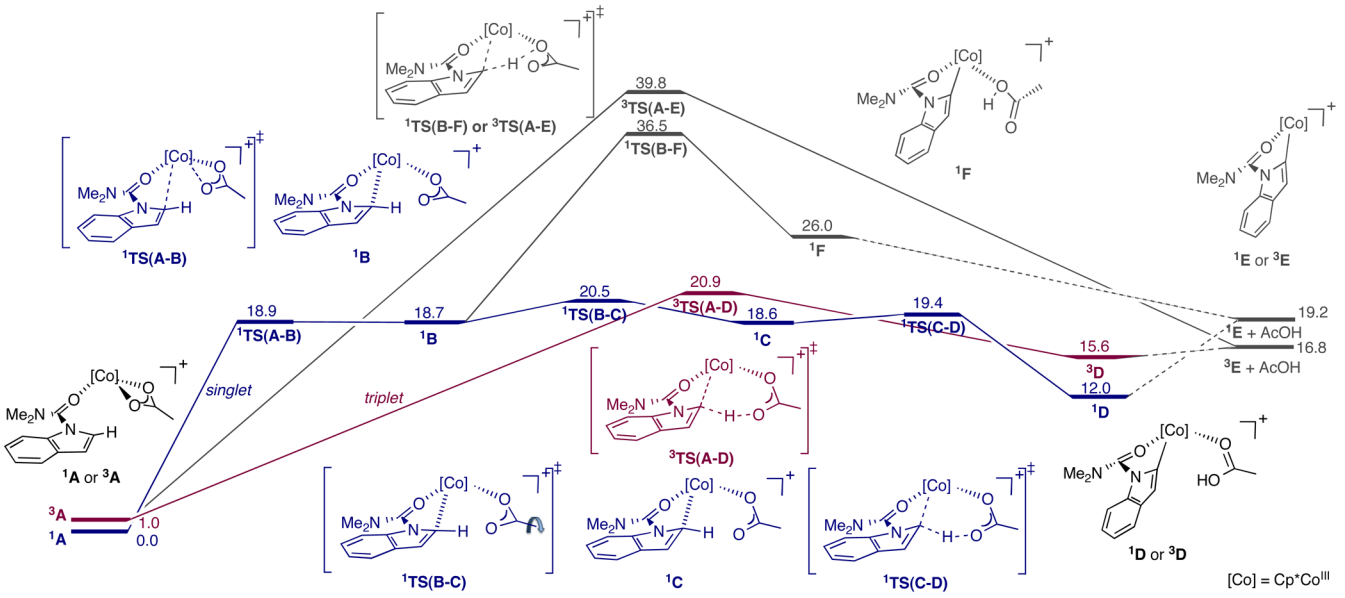

Figure 4. Relative Gibbs free-energy diagram (298.15 K) for acetate-assisted C−H activation pathways with the Cp^*Co^{III}-catalyst (kcal/mol).

lowest Gibbs free energy at 298.15 K (see the Supporting Information). The cleavage of a Co−O(acetate) bond in **^{1}A** gives the structure of κ^1-complex $[Cp^*Co^{III}(\kappa^1\text{-OAc})(\mathbf{2a})]^+$, **^{1}B**, via the transition state **^{1}TS(A−B)**. In **^{1}B**, weak interaction between the C2 atom at indole and the Co atom exists (the distance is 2.345 Å). After the transformation of **^{1}B** to the other conformation of κ^1-complex **^{1}C**, the abstraction of the hydrogen atom at the C2-position by the oxygen atom at acetate and the formation of the C−Co bond simultaneously occur through the six-membered transition state **^{1}TS(C−D)** to afford the complex **^{1}D**. The bond distance between the C2 atom at indole and the Co atom is 1.932 Å in **^{1}D**. Thus, there are three transition states, **^{1}TS(A−B)** (ΔG = 18.9 kcal/mol), **^{1}TS(B−C)** (ΔG = 20.5 kcal/mol), and **^{1}TS(C−D)** (ΔG = 19.4 kcal/mol), and two intermediates, **^{1}B** and **^{1}C**, along the singlet-state acetate-assisted pathway from **^{1}A** to **^{1}D**, and the reaction step is endothermic by 12.0 kcal/mol. The four-membered transition state, **^{1}TS(B−F)**, has much higher free energy (ΔG = 36.5 kcal/mol).[22a,b]

On the other hand, the triplet-state structure **^{3}A** is located slightly higher, 1.0 kcal/mol, than the singlet structure **^{1}A**. In the case of triplet state, the hydrogen atom at the C2-position in **^{3}A** is directly transferred into the oxygen atom at acetate via the six-membered transition state **^{3}TS(A−D)** to afford the complex **^{3}D**. The relative free energy of **^{3}TS(A−D)** (20.9 kcal/mol) is almost the same as those of the transition states in the singlet-state pathway. The four-membered transition state **^{3}TS(A−E)** has also higher free energy (ΔG = 39.8 kcal/mol), and the oxidative addition of Co−H bond in the complex $[Cp^*Co^{III}(\kappa^2\text{-OAc})(\mathbf{2a})]^+$ was not found. Therefore, the acetate-assisted C−H bond activation step goes through the six-membered transition states in both singlet and triplet states.

A plausible catalytic cycle with a Cp^*Co^{III} complex in the presence of KOAc is shown in Figure 5. As the initial step, thermal dissociation of the benzene ligand of $[Cp^*Co(C_6H_6)](PF_6)_2$ as well as ligand exchange to acetate (or substrate) would generate catalytically active monocationic species **I**, in equilibrium with a resting neutral diacetate complex. After coordination of the carbamoyl group of indole **2** (**II**), regioselective C−H metalation at the C2-position would

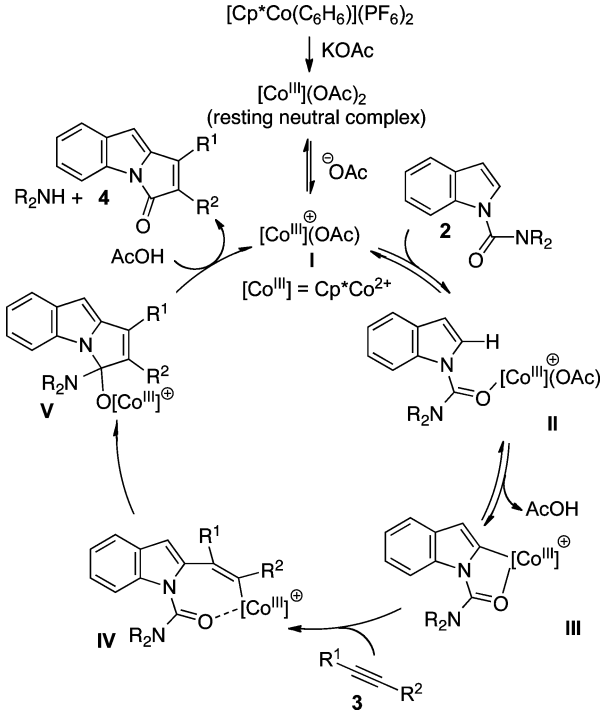

Figure 5. Postulated catalytic cycle.

occur via a concerted metalation−deprotonation mechanism[23] to afford indolyl-Co species **III**. Insertion of alkyne **3** then generates the key alkenyl-Co intermediate (**IV**). Annulation (**V**) followed by release of morpholine gives product **4**. On the other hand, proto-demetalation of **IV** with AcOH gives product **5** and regenerates the active species **I**.

3. CONCLUSION

In summary, we demonstrated the characteristic reactivity of a Cp^*Co^{III} catalyst compared with related Cp^*Rh^{III} catalysts. The C2-selective indole alkenylation/annulation sequence proceeded smoothly in the presence of $[Cp^*Co^{III}(C_6H_6)](PF_6)_2$ and KOAc, giving pyrroloindolones in 58−89% yield.[24]

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The clear difference in the catalytic activity between the Cp^*Co^{III} complex and Cp^*Rh^{III} complexes highlighted the unique nucleophilic activity of the organocobalt species. The Cp^*Co^{III} catalysis was also suitable for simple alkenylation process, and broad range of alkynes including terminal alkynes were applicable to give alkenylated products in 50−99% yield. Further studies to apply the unique properties of first-row transition metal catalysis to other reactions are ongoing.

■ ASSOCIATED CONTENT

Supporting Information

Experimetal details, including procedures, syntheses and characterization of new products, ^1H and ^{13}C NMR charts, CIF, and computational details for supporting mechanism. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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