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Cobalt(III)-Catalyzed C−C Coupling of Arenes with 7-Oxabenzonorbornadiene and 2-Vinyloxirane via C−H Activation

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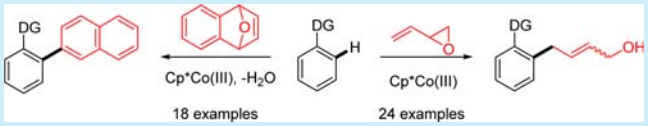
Ⓢ *Supporting Information*

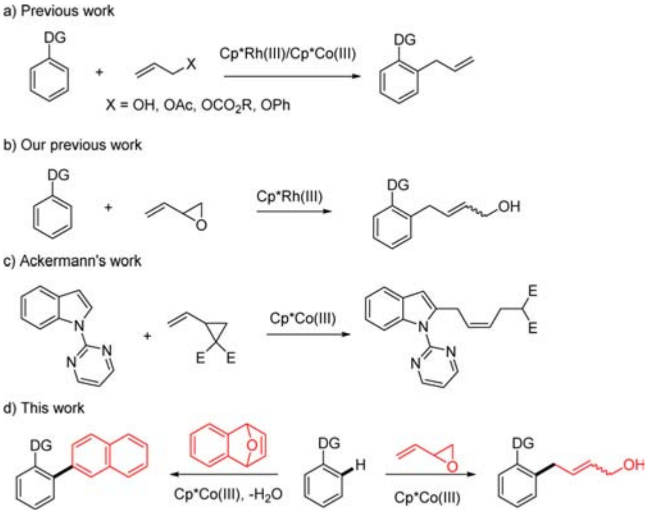
ABSTRACT: Co(III)-catalyzed mild C−C couplings of arenes with strained rings such as 7-oxabenzonorbornadienes and 2-vinyloxirane have been realized. The transformation is proposed to undergo *ortho* C−H activation, olefin insertion, and subsequent *β*-oxygen elimination. A broad range of synthetically useful functional groups are compatible, thus providing a new entry to access diversely 2-functionalized indoles.



Over the past decades, transition-metal-catalyzed direct C−H functionalization and C−C/C−heteroatom bond formation have received increasing attention because of their high activity, broad substrate scope, and functional group compatibility. This strategy has enabled the development of a plethora of useful synthetic methods to access complex structures.[1] Despite these attractive features, most of the achievements have been accomplished with expensive second- and third-row transition-metal catalysts, particularly ruthenium, rhodium, and palladium complexes. Thus, the development of comparable and even more efficient systems with earth-abundant first-row transition-metal catalysts is highly desirable. Recently, Matsunaga and Kanai pioneered applications of high-valent Cp*Co(III) complexes[2] as earth-abundant and less toxic metal catalysts for C−H activation of arenes. The high efficiency originated from the higher Lewis acidity of the Co(III) and enhanced metal−substrate corporation.[3] Afterward, the groups of Glorius,[4] Ackermann,[5] Ellman,[6] Daugulis,[7] Chang,[8] and others[9] have made progress in Co(III) catalysis.

Allylation of arenes is one of the most fundamental and useful transformations in organic synthesis because the allyl moiety can be further converted into a wide variety of functional groups.[10] Allylarenes are traditionally prepared by rearrangements and electrophilic and nucleophilic substitutions. These methods often suffer from harsh reaction conditions, low regioselectivity, overallylation, and limited substrate scope.[11] Therefore, the development of inexpensive and efficient methods for the direct allylation of arenes in a green and atom-economical fashion is highly desirable. In this regard, transition-metal-catalyzed C−H bond functionalization has exhibited tremendous potential for the direct allylation of aromatic C−H bonds (Scheme 1a).[12] These reactions are thought to proceed via C−H metalation, olefin insertion, and subsequent *β*-elimination of oxygen-containing functional groups. However, the leaving groups lower the atom economy of the reactions. To overcome this limitation, our group developed an allylarene synthesis via Rh(III)-catalyzed C−H activation of arenes and coupling with vinyloxirane (Scheme 1b).[13] Lately, Ackermann and co-workers reported a cobalt(III)-catalyzed coupling of indoles and vinylcyclopropane via C−H/C−C functionalization (Scheme 1c).[14] In this process, olefin insertion into a Rh−C bond is followed by *β*-C elimination under exceedingly mild conditions. As part of our ongoing studies and expansion of the utility of Cp*Co(III) catalysis, we now report the Co(III)-catalyzed coupling of indoles with 7-oxabenzonorbornadienes and 2-vinyloxirane to access 2-substituted indoles.

Scheme 1. Allylation of Arenes



At the outset of our study, we examined the C−H arylation of *N*-pyrimidinylindole (**1a**) with 7-oxabenzonorbornadiene (**2a**), which has been applied as a naphthylating reagent by us under Rh(III) catalysis.[13a] When the reaction was conducted in DCE using $[Cp^*CoCl_2]_2/AgSbF_6$ (4 mol %/16 mol %) as the catalyst at 50 °C, traces of product were obtained (Table 1,

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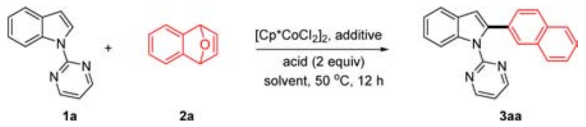
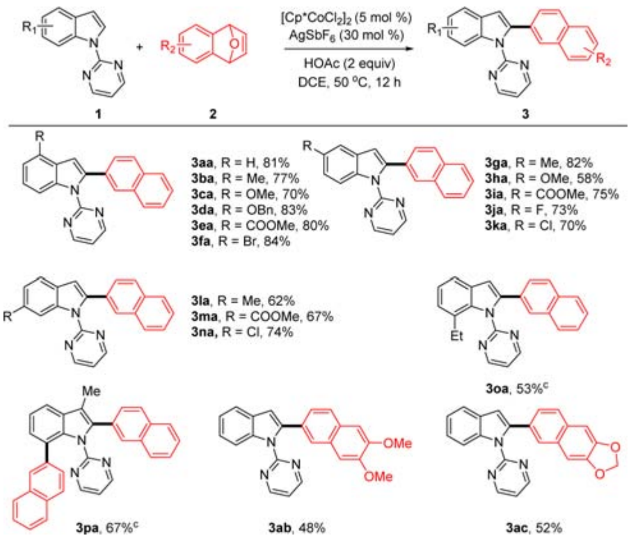
Table 1. Optimization of the Reaction Conditions[a]



entry	cat. (mol %)	additive (mol %)	solvent	yield (%)[b]
1	$[Cp^*CoCl_2]_2$ (4)	$AgSbF_6$ (16)	DCE	<5
2	$[Cp^*CoCl_2]_2$ (4)	$AgSbF_6$ (16)	DCE	56
3[c]	$[Cp^*CoCl_2]_2$ (4)	$AgSbF_6$ (16)	DCE	45
4	$[Cp^*CoCl_2]_2$ (4)	$AgNTf_2$ (16)	DCE	51
5	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (16)	DCE	67
6	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (20)	DCE	75
7	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (30)	DCE	81
8	$[Cp^*CoCl_2]_2$ (4)	$AgSbF_6$ (30)	DCE	70
9	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (30)	dioxane	71
10	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (30)	THF	42
11	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (30)	TFE	56
12	–	$AgSbF_6$ (30)	DCE	0
13[d]	$[Cp^*CoCl_2]_2$ (5)	$AgSbF_6$ (30)	DCE	52

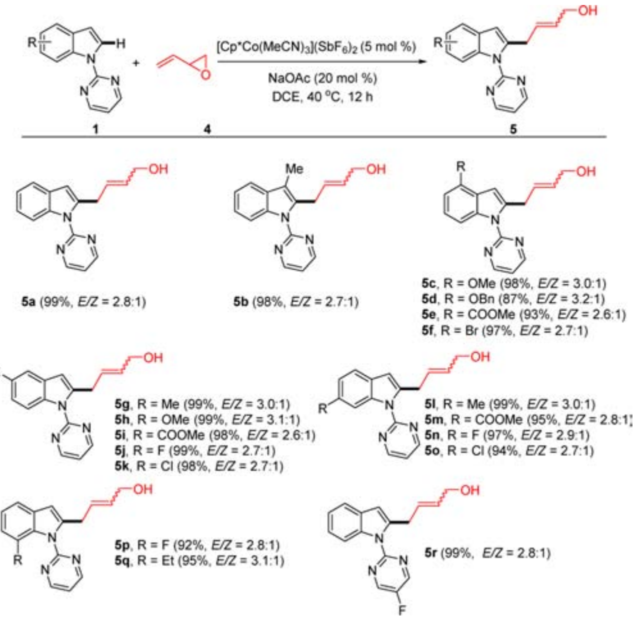
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), HOAc (2 equiv), solvent (2 mL), 50 °C, 12 h, pressure tube under N_2. [b] Isolated yields after chromatography. [c] PivOH (2 equiv) was used. [d] 9-(Toluene-4-sulfonyl)-1,4-dihydro-1,4-epiazanonaphthalene (2 equiv) was used

Scheme 2. Dehydrative Coupling with 7-Oxabenzonorbornadienes[a,b]



[a] Reaction conditions: indole (0.2 mmol), 7-oxabenzonorbornadiene (0.4 mmol), $[Cp^*CoCl_2]_2$ (5 mol %), $AgSbF_6$ (30 mol %), HOAc (2 equiv), DCE (2 mL), 50 °C, 12 h, pressure tube under N_2. [b] Isolated yields after chromatography are shown. [c] AgOAc (30 mol %), 110 °C.

Scheme 3. C−H Allylation of Heterocycles[a,b]



[a] Reaction conditions: indole (0.2 mmol), 2-vinyloxirane (0.4 mmol), $[Cp^*Co(MeCN)_3](SbF_6)_2$ (5 mol %), NaOAc (20 mol %), DCE (2 mL), 40 °C, 12 h, pressure tube under N_2. [b] Isolated yields after chromatography are shown.

entry 1). Fortunately, the product **3aa** was isolated in 56% yield when HOAc (2 equiv) was introduced (entry 2). Switching the acid to HOPiv lowered the yield to 45% (entry 3). The amount of the silver additive had a significant effect on the reaction efficiency. The isolated yield of **3aa** was dramatically improved to 81% when the ratio of $AgSbF_6$ to $[Cp^*CoCl_2]_2$ was increased to 6:1 (entry 7), where the excess of $AgSbF_6$ likely activates the 7-oxabenzonorbornadiene substrate as a Lewis acid.[13a] Solvent screening revealed that DCE was the most optimal medium (entries 9−11). No product was observed when the cobalt catalyst was omitted (entry 12). The product was also obtained using 9-(toluene-4-sulfonyl)-1,4-dihydro-1,4-epiazanonaphthalene in 52% yield (entry 13). While a Co(III) catalyst is not unique for this reaction, the Rh(III)-catalyzed system required a temperature of 130 °C,[13a] indicating the higher efficiency of the Co(III) catalyst.

With the set of optimized reaction conditions in hand, the scope and limitations of this reaction were next explored (Scheme 2). Much to our delight, *N*-pyrimidinylindoles bearing both electron-donating and -withdrawing substituents, including methyl (**3ba**, **3ga**, and **3la**), methoxy (**3ca** and **3ha**), benzyloxy (**3da**), an ester group (**3ea**, **3ia**, and **3ma**), fluoro (**3ja**), chloro (**3ka** and **3na**), and bromo (**3fa**) at different positions all coupled smoothly with 7-oxabenzonorbornadiene, and the corresponding products were isolated in 53−84% yield. Unfortunately, the introduction of substituents at the 3- and 7-positions of the indole inhibited the reaction as a result of steric hindrance. When a catalytic amount of AgOAc was added and the temperature was raised, **3oa** was obtained in 53% yield. Similarly, the diarylation product **3pa** was isolated in a moderate yield (67%) when a 3-substituted indole substrate was used. Naphthylated products **3ab** and **3ac** were also isolated in moderate yields when substituted 7-oxabenzonorbornadienes were used.

With the development of these dehydrative naphthylation reactions, we next extended the strained olefins to 2-vinyloxirane (Scheme 3). *N*-(2-Pyrimidyl)indoles bearing a large variety of electron-donating (Me, OMe, and OBn) and -withdrawing (F, Cl, Br, and COOMe) groups in the benzene ring all coupled smoothly with 2-vinyloxirane in excellent yields. Of note, only a 5 mol % loading of the monomeric Co(III) catalyst sufficed. The introduction of substituents at the 3- and 7-positions of the indole ring and on the pyrimidine ring had minimal influence (**5b**, **5p**, **5q**, and **5r**), indicative of tolerance of steric effects, and the coupled products were isolated in consistently excellent yields (92−98%). In all cases,

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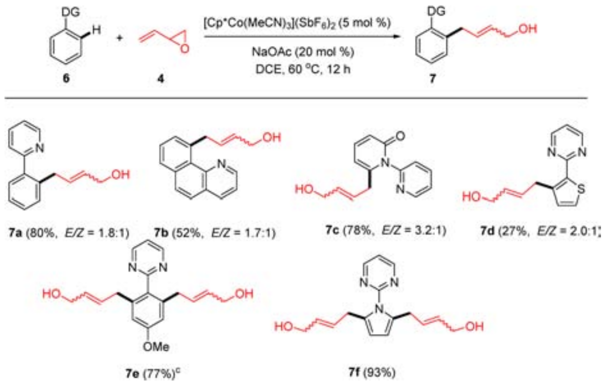
the stereoselectivity of the reaction was low (*trans*/*cis* = 2.6:1−3.2:1).

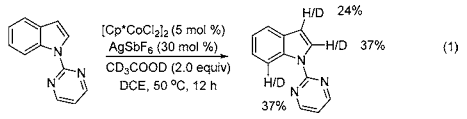
The arene substrate was not restricted to *N*-(2-pyrimidyl)-indoles (Scheme 4). The coupling of 2-phenylpyridine and benzo[*h*]quinoline with 2-vinyloxirane delivered allylic alcohols **7a** and **7b**, respectively, in good yields. Although this coupling has been reported using Rh(III) catalysts,[13b] the coupling of 2-phenylpyridine proceeded with low mono/di selectivity. Furthermore, the arene substrate has been extended to a 2-pyridone (**7c**) and a thiophene (**7d**). Diallylation products (**7e** and **7f**) were isolated in good to high yields when a pyrimidyl directing group was used. In all cases, the reactions proceeded smoothly under the standard or slightly modified conditions.

Scheme 4. Substrate Scope of Other Arenes[a,b]

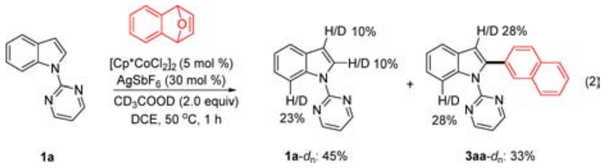


[a] Arene (0.2 mmol), 2-vinyloxirane (0.4 mmol), [Cp*Co(MeCN)$_3$]-(SbF$_6$)$_2$ (5 mol %), NaOAc (20 mol %), DCE (2 mL), 60 °C, 12 h, pressure tube under N$_2$. [b] Isolated yields after chromatography are shown. [c] The reaction was conducted at 100 °C.

To briefly gain details of the reaction, **1a** was subjected to the present cobalt-catalyzed system in CD$_3$COOD with or without a 7-oxabenzonorbornadiene substrate (eqs 1 and 2). Significant levels of deuterium incorporation (10% and 37%, respectively) at the 2-position of the recovered **1a** were observed. In addition, deuteration at the 3- and 7-positions was also observed in both cases, indicating the reversibility of the C−H bond cleavage. Moreover, a competition experiment between **1i** and **1h** was performed, and the more electron-deficient indole reacted at a higher rate (eq 3), thus suggesting that the C−H activation probably occurs via a concerted metalation−deprotonation (CMD) mechanism.



(1)

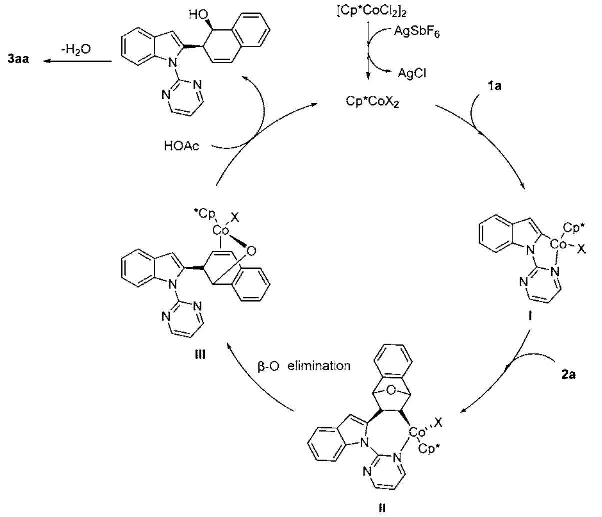


(2)

On the basis of previous reports,[8a,13] a plausible mechanism is proposed for the coupling of an indole with 7-oxabenzonorbornadiene (Scheme 5). Initially, the cationic Cp*Co(III) catalyst is generated with the assistance of AgSbF$_6$. Cyclometalation of the *N*-pyrimidinylindole affords five-membered metallacyclic intermediate **I**. Coordination of the bicyclic alkene to the Co center of **I** and subsequent insertion into the C=C bond generate intermediate **II** with a seven-membered ring. Intermediate **II** undergoes *β*-oxygen elimination to give alkoxide intermediate **III**. Protonolysis of **III** regenerates the active catalyst and releases the dihydronaphthol intermediate, which is then dehydrated to give the product **3aa**.

(3)

Scheme 5. Proposed Mechanism of Naphthylation



In conclusion, we have demonstrated cobalt(III)-catalyzed C−C couplings of *N*-pyrimidinylindoles with strained rings such as 7-oxabenzonorbornadienes and 2-vinyloxirane under mild conditions. The coupling of 7-oxabenzonorbornadienes resulted in 2-naphthylation of the *N*-pyrimidinylindoles, and the coupling of 2-vinyloxirane yielded allylic alcohol products. The reaction pathway likely involves the Co-catalyzed *ortho* C−H activation, olefin insertion, and subsequent *β*-oxygen elimination. The Co(III)-catalyzed coupling systems are advantageous in terms of selectivity and efficiency. These catalytic systems expand the synthetic utility of cobalt-catalyzed C−H activation reactions. In view of the mild conditions, broad scope, and high catalytic activity, this method may find applications in the synthesis of complex structures.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01806.

Experimental details, characterization data, and copies of NMR spectra of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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