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Cobalt(III)-Catalyzed Fast and Solvent-Free C−H Allylation of Indoles Using Mechanochemistry

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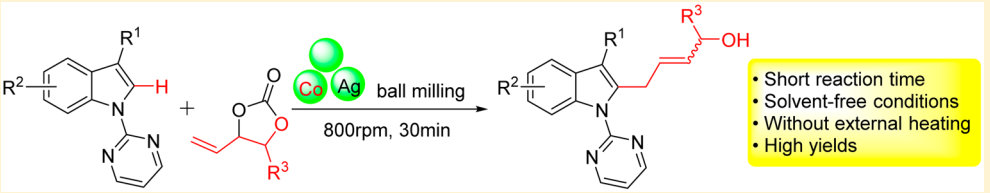
Supporting Information

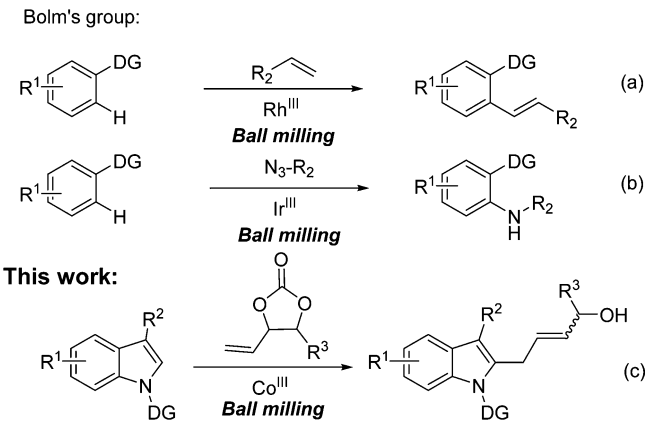


ABSTRACT: Mechanochemical conditions have been applied to a highly efficient cobalt(III)-catalyzed C−H bond activation for the first time. In a subsequent step to the olefin insertion and *β*-oxygen elimination, *N*-pyrimidinylindoles were allylated with vinylethylene carbonates in the absence of organic solvent under high-speed ball-milling condition. As the reaction afforded the desired products in up to 98% yields within a short time, this method constitutes an environmentally friendly and powerful alternative to the common solution-based approaches.

The presence of an allylic alcohol building block offers the molecule tremendous potential for further modification and great opportunity to transform into a wide variety of pharmaceutical and biologically active compounds.[1] The integration of allylic alcohol into a privileged scaffold, such as indole, is of great interest.[2] However, traditional synthesis of allylic aromatic compounds bearing a hydroxyl group at the allylic position is realized by nucleophilic ring opening of vinyl epoxides with organometallic reagents, which is restricted by narrow substrate scope and limited functional group compatibility.[3] Over the past decades, noble transition metals such as rhodium-,[4,5] iridium-,[6] palladium-,[7] and ruthenium[8]-catalyzed directed C−H activation have received increasing attention.[9] Recently, cost-effective Cp*Co(III) complexes have also been identified as powerful catalysts in C−H activation, as reported by Matsunaga and Kanai,[10] Ackermann,[11] Ellman,[12] Glorius,[13] Jiao,[14] Li,[15] Maji,[16] Wang,[17] Zhang,[18] and others.[19] Therefore, transition-metal-catalyzed coupling reactions have been developed as a new strategy to synthesize allylic aromatic scaffolds. For instance, Wang[4b] and Kim[4c] developed Rh(III)-catalyzed C−H directed allylation with 4-vinyl-1,3-dioxolan-2-ones. Li and co-workers developed Rh(III)-[4a] and Co(III)[15a]-catalyzed C−C couplings of arenes with 2-vinyloxirane. However, the usage of toxic solvents, such as 1,2-dichloroethane (DCE), and relative long reaction time (typically over 10 h) are still posing potential limitations for the wide application of such methods.

In recent years, the application of mechanochemistry, especially ball-milling reaction, has successfully drawn much attention.[20] Bolm and co-workers first reported the Rh(III)-catalyzed C−H functionalization of acetanilides with acrylate under solventless conditions in a ball-mill machine (Scheme 1a).[21] Subsequently, in 2016, the same group reported Ir(III)-catalyzed mechanochemical C−H bond amidation of benzamides with sulfonyl azides (Scheme 1b).[22] Compared to the traditional solvent reaction system, ball-milling reactions are believed to significantly improve the reaction efficiency.[23] Inspired by these continuous findings as well as our ongoing studies of mechanochemistry,[24] we herein report a solvent-free ball-milling approach to synthesize allylic alcohol-substituted

Scheme 1. Mechanochemical Functionalization of Arenes in Ball Mills



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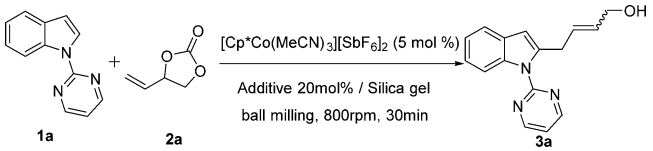
indoles more environmentally friendly and efficiently. As far as we know, this is the first example of Co(III)-catalyzed C−H bond activation using mechanochemistry (Scheme 1c).

At the commencement, *N*-pyrimidinylindole **1a** was chosen for primary reaction optimization (Table 1). Considering the

Table 1. Reaction Optimization[a]



entry	catalyst (mol %)	additive	yield of **3a**[b] (%)
1[c]	$Cp^*Co(MeCN)_3[SbF_6]_2$ (5)	CsOAc	72
2	$Cp^*Co(MeCN)_3[SbF_6]_2$ (5)	CsOAc	92
3	$Cp^*Co(MeCN)_3[SbF_6]_2$ (5)		79
4	$Cp^*Co(MeCN)_3[SbF_6]_2$ (5)	KOAc	97
5	$Cp^*Co(MeCN)_3[SbF_6]_2$ (5)	NaOAc	98
6	$Cp^*Co(MeCN)_3[SbF_6]_2$ (5)	AgOAc	98
7	$Cp^*Co(MeCN)_3[SbF_6]_2$ (2.5)	NaOAc	69
8	$CoCl_2$ (5)	NaOAc	0
9	$Co(acac)_2$ (5)	NaOAc	0
10	$[(p\text{-cymene})RuCl_2]_2$ (2.5) $AgSbF_6$ (5)	KOAc	29

[a]Unless otherwise noted, all reactions were carried out with **1a** (0.6 mmol), **2** (1.2 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (0.03 mmol, 5 mol %), additives (0.12 mmol, 20 mol %), using stainless steel grinding balls (4 mm diameter × 36) in a 45 mL stainless steel vial. Cp* = pentamethyl cyclopentadienyl. [b]Isolated yield. All cases provided 2.5:1 to 3:1 of *Z*/*E* ratio, which were determined by ^{1}H NMR. [c]Balls (6 mm diameter × 16) at 600 rpm were used.

practicability, inexpensive vinylethylene carbonate (VEC), which is widely used as a film-forming additive in lithium-ion batteries, was used as allylation reagent in place of 2-vinyloxirane. Owing to the inert nature of VEC, monomeric Co(III) catalyst $[Cp^*Co(MeCN)_3][SbF_6]_2$ (5 mol %) along with CsOAc (20 mol %) was used to establish the module reaction. To our delight, 72% of 2-allylated *N*-pyrimidinylindole **3a** was obtained after 30 min grinding at 800 rpm (entry 1). Smaller balls (4 mm × 36) and higher rotational speed (800 rpm) improved the yield to 92% (entry 2). In the absence of additive, only 79% of **3a** was isolated under the same condition, indicating the important presence of acetates (entry 3). Several additives were also examined. It turned out that NaOAc and AgOAc gave the highest isolated yields (entries 4−6). Decreasing the loading of $[Cp^*Co(MeCN)_3][SbF_6]_2$ to 2.5 mol %, the yield of **3a** dropped to 69% (entry 7). When low-valent cobalt catalysts $Co(acac)_2$ and $CoCl_2$ were used, **3a** was not detected (entries 9 and 10). Other transition metal catalysts, such as $[(p\text{-cymene})RuCl_2]_2$, produced only 29% of **3a** (entry 10). In some cases, such as **3j**, AgOAc gave higher yield (95%) than NaOAc (47%). Therefore, the optimized reaction conditions were **1** (0.6 mmol), **2** (2 equiv), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (5 mol %), AgOAc (20 mol %), and silica gel placed in a 45 mL of stainless steel vial with stainless steel grinding balls (4 mm diameter × 36) and ball-milling at 800 rpm for 30 min.[25]

With the optimized conditions in hand, the scopes and limitations of this reaction were then investigated (Scheme 2). To our delight, *N*-pyrimidinylindoles bearing electron-donating groups, including methyl (**3b−d**), methoxy (**3e** and **3f**), and benzyloxy (**3g**) groups at different positions, all coupled with vinylethylene carbonate efficiently, and the corresponding products were obtained in 81−93% yields. The introduction of a cyano group inhibited the reaction as a result of its coordination with cobalt complex and lower electron density on the indole ring (**3h**). The indoles substituted by the different type of halogens, such as fluorine, chlorine, and bromine, at various positions could also give the corresponding product (**3i−3o**) in good yields. To extend the scope of this methodology further, fourth position substituted vinylethylene carbonates **2b** and **2c** were synthesized and subjected to the reaction. We were pleased to find that the corresponding products **3p** and **3q** were obtained in excellent yields under standard reactions condition (Scheme 3). Scaling up of the model reaction to gram level still gave 94% of **3a**, which was obtained using 0.8 mol % catalytic system and prolonged grinding time to 60 min (Scheme 4).

To gain insight into the reaction mechanism, a set of control experiments were carried out (Scheme 5). When substrate **1a** and CD_3OD were subjected to the optimized ball-milling conditions, H/D scrambling at C-2 and C-3 positions indicated an organometallic mode of C−H activation (Scheme 5a). Intermolecular competition experiments of different substituted *N*-pyrimidinylindoles revealed a reactivity for the electron-poor substrate **1i** lower than that of the electron-rich **1e**. The reaction shows **3e** and **3i** in a 1.9:1 ratio (determined by ^{1}H NMR analysis), indicating cationic cobalt species acted as electrophiles in the C−H activation process (Scheme 5b). In addition, the competitive coupling of an equimolar mixture of **1a** and **1a**-[D] with vinylethylene carbonate determined by the initial rate gave a kinetic isotope effect (KIE) value of K_H/K_D = 1.9 under solvent-free mechanochemical conditions. These findings indicated a base-assisted internal electophilic substitution (BIES)-type C−H functionalization[26] (Scheme 5c).

Based on our mechanistic studies and previous literature,[27] a tentative mechanism has been proposed for this reaction (Scheme 6). Initially, a cationic cobalt(III) acetate complex **I** was generated upon treatment of $Cp^*Co(MeCN)_3[SbF_6]_2$ with AgOAc. C−H activation at 2-position of indole took place under the assistance of pyrimidine group leading to a five-member metal acyclic intermediate **II** with the elimination of HOAc. Then vinylethylene carbonate coordinated to the Co center of **II** and subsequently generated seven-member intermediate **IV**. Subsequently, *β*-oxygen elimination occurred to form intermediate **V** with new double bond bearing an allylic hydroxyl group while releasing CO_2. Protonolysis of intermediate **V** regenerated the active cobalt complex and afforded the desired product.

In summary, by using vinylethylene carbonate as a coupling partner, we have developed a cobalt(III)-catalyzed mechanochemical process for the allylation of indoles under solvent-free conditions. Mechanochemical strategy possesses two significant aspects compared to solvent-based methods: first, these reactions were conducted under solvent-free conditions, kept away from the usage of highly toxic solvents. Second, high-speed ball-milling could significantly reduce reaction time (only 30 min) without external heating by contrast to the similar reactions under solvent condition (typically over 10 h). In view of these advantages, the applications of such a reaction to achieve the facile synthesis of bioactive compounds are currently underway.

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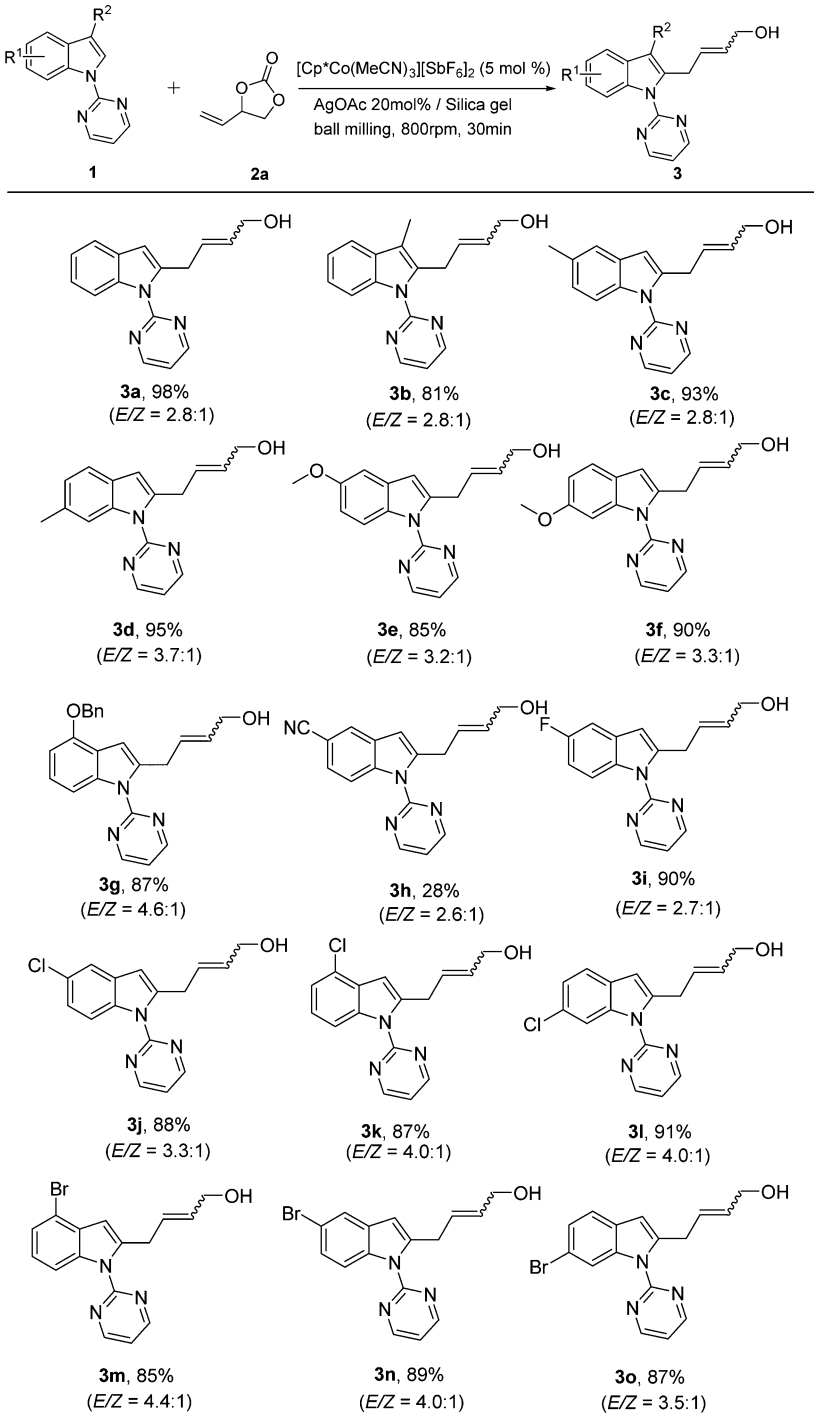
Scheme 2. Co(III)-Catalyzed C−H Allylation with Vinylethylene Carbonate 2a[a]



[a]Isolated yield. *Z*/*E* ratios were determined by ^{1}H NMR.

EXPERIMENTAL SECTION

General Information. All chemicals were obtained from commercial soures and were used as received unless otherwise noted. *N*-Pyrimidine indole,[28] vinylethylene carbonates **2b** and **2c**,[29] **1a**-$[D]_1$,[30] $[Cp^*Co(CO)I_2]$,[10b] and $[Cp^*Co(MeCN)_3][SbF_6]_2$[15a] were prepared by following literature reports. All reactions were performed using grinding vessels in a FRITSCH Planetary micro mill model "Pulverisette 7 premium line". Both vessels (45 mL) and balls were made of stainless steel. Column chromatography was performed on silica gel (300−400 mesh) using ethyl acetate (EA)/hexane (Hex). NMR spectra were recorded on a 600 MHz NMR spectrometer in the solvent indicated. Chemical shifts are reported downfield from TMS (=0) or $CDCl_3$ (=7.26) for ^{1}H NMR. For ^{13}C NMR, chemical shifts are reported in the scale relative to $CDCl_3$ (=77.0). Mass spectra were measured with a low-resolution MS instrument using ESI ionization. HRMS spectra were recorded on an electrospray ionization quadrupole time-of-flight (ESI-Q-TOF) mass spectrometer. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

General Procedures for the Synthesis of Compound 3. *N*-Pyrimidinylindole **1** (0.6 mmol), vinylethylene carbonate **2** (1.2 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (0.03 mmol, 5 mol %), AgOAc (0.12 mmol, 20 mol %), and silica gel (600 mg, grinding auxiliary)

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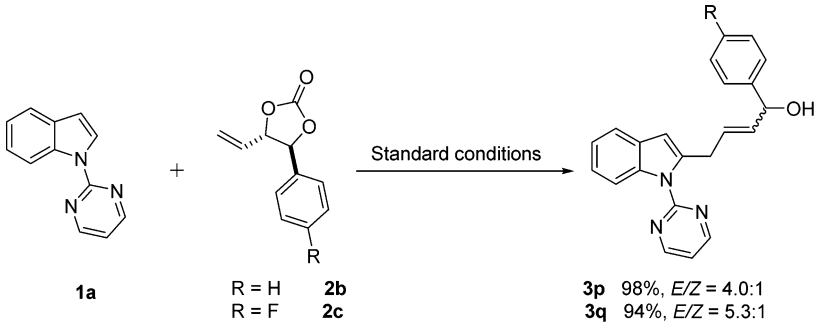
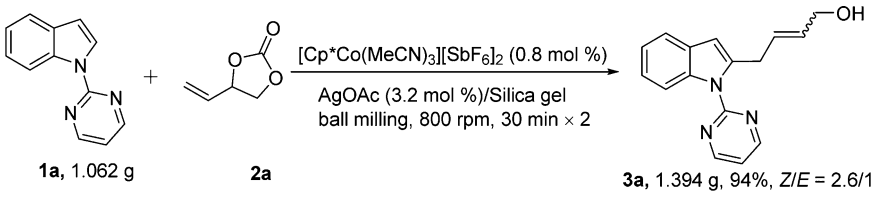
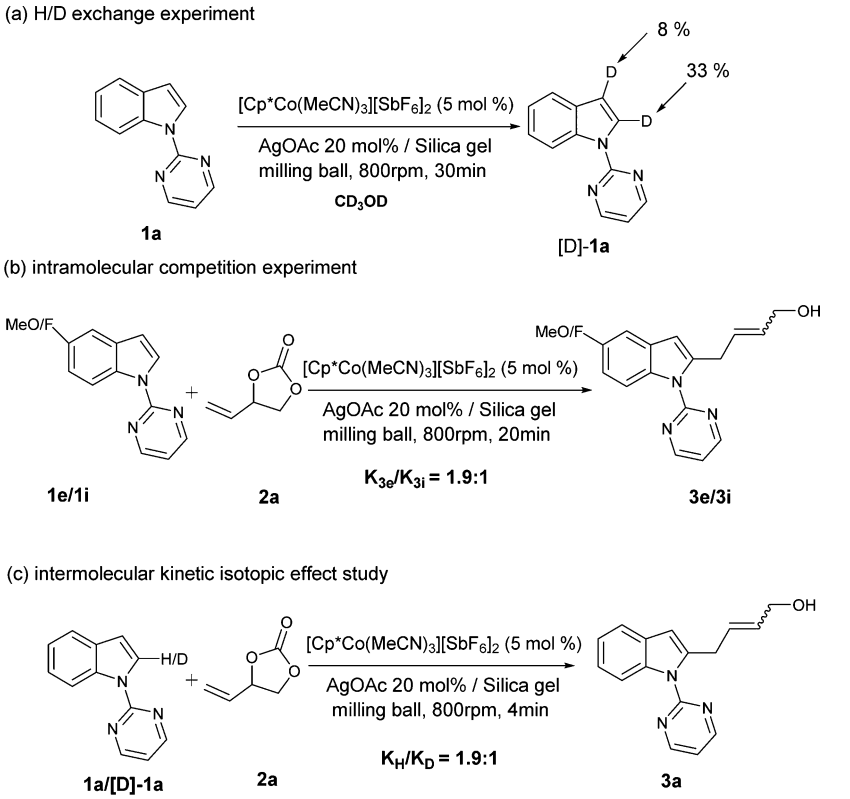
Scheme 3. Co(III)-Catalyzed C−H Allylation with Substituted Vinylethylene Carbonates



Scheme 4. Gram-Scale Reaction



Scheme 5. Mechanistic Studies



were transferred to a ball-milling vessel (stainless steel, 45 mL) loaded with 36 grinding balls (stainless steel, 4 mm diameter). The milling vessel was placed in the ball mill (800 rpm, 30 min). The crude product was collected by washing the vessel and the balls with EtOAc (3 × 20 mL). The mixture was concentrated in vacuum and purified by flash chromatography (Hexane/EtOAc = 4:1 to 1:1).

*4-(1-(Pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3a**).* Product **3a** was obtained as a colorless oil (156.0 mg, 98%, *E*/*Z* = 2.8:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.4 Hz, 2H), 8.27−8.21 (m, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.25−7.16 (m, 2H), 7.14 (t, *J* = 4.4 Hz, 1H), 6.48 (s, 1H), 5.88−5.61 (m, 2H), 4.25 (d, *J* = 6.0 Hz, 0.52H), 4.03 (d, *J* = 5.6 Hz, 1.48H), 3.99−3.92 (m, 2H), 1.48 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.1, 158.1, 139.6, 137.0, 131.0, 129.5, 129.1, 122.7, 121.8, 119.8, 117.1, 113.7, 106.4, 63.4, 32.4; minor isomer δ 139.6, 137.0, 130.1, 129.1, 122.8, 121.9, 113.8, 106.3, 58.6, 28.1; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{16}N_3NaO$ $[M + Na]^+$ 288.1107, found 288.1100.

*Gram-Scale Synthesis of **3a**:* *N*-Pyrimidinylindole **1a** (1.062 g, 5.4 mmol), vinylethylene carbonate **2a** (1.232 g, 10.8 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (32.3 mg, 0.0043 mmol, 0.8 mol %), AgOAc (28.8 mg, 0.173 mmol, 3.2 mol %), and silica gel (2.000 g, grinding auxiliary) were transferred to a ball-milling vessel (stainless steel, 45 mL) loaded with 36 grinding balls (stainless steel, 4 mm diameter). The milling vessel was placed in the ball mill (800 rpm, 30 min ×2 + 10 min

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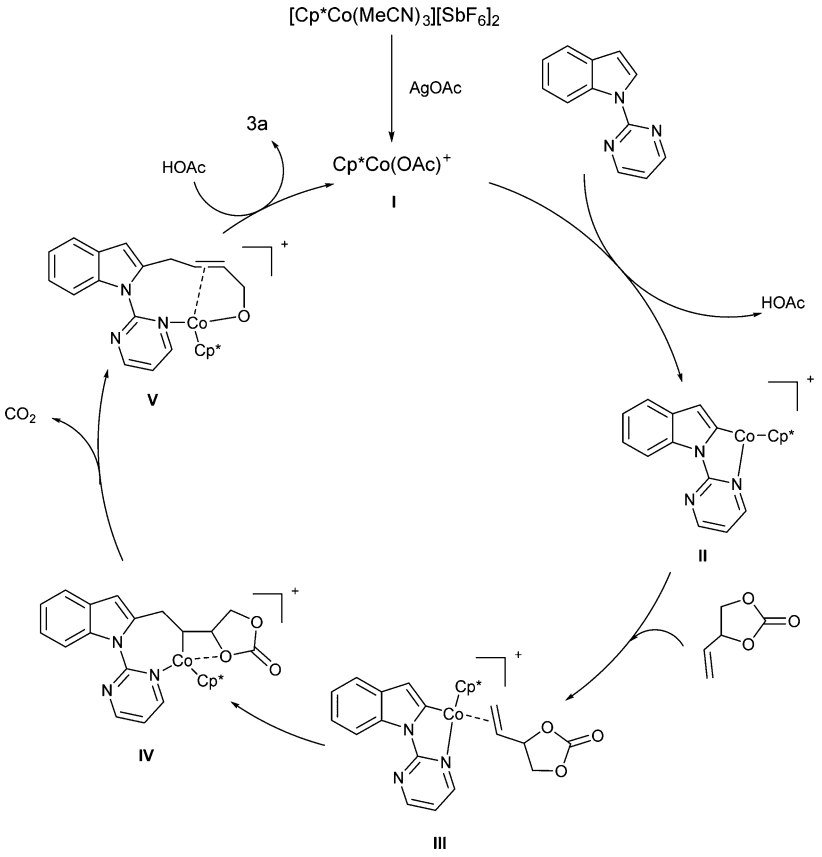
Scheme 6. Proposed Mechanism



break). The crude product was collected by washing the vessel and the balls with EtOAc (3 × 40 mL). The mixture was concentrated in vacuum and purified by flash chromatography (Hexane/EtOAc = 4:1 to 1:1) to afford **3a** as a colorless oil (1.349g, 94%, *Z*/*E* = 2.6/1 by ^{1}H NMR).

*4-(3-Methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3b**).* Product **3b** was obtained as a colorless oil (135.8 mg, 81%, *E*/*Z* = 2.8:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.8, 2H), 8.25−8.21 (m, 1H), 7.54−7.51 (m, 1H), 7.25−7.18 (m, 2H), 7.07 (t, *J* = 4.8 Hz, 1H), 5.76−5.44 (m, 1H), 4.18 (d, *J* = 5.8 Hz, 0.52H), 3.96 (d, *J* = 5.9 Hz, 0.52H), 3.93 (d, *J* = 6.0 Hz, 1.48H), 3.88 (d, *J* = 5.9 Hz, 1.48H), 2.29 (s, 3H), 1.51 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.1, 136.1, 134.0, 130.2, 129.9, 129.7, 128.6, 122.9, 121.4, 118.0, 116.8, 113.3, 113.3, 63.3, 28.9, 8.8; minor isomer δ 158.0, 136.2, 134.5, 130.2, 129.8, 123.0, 121.5, 118.0, 116.8, 113.6, 113.4, 58.5, 25.0, 8.8. The NMR data were consistent with those in a literature report.[31]

*4-[5-Methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl]but-2-en-1-ol (**3c**).* Product **3c** was obtained as a colorless oil (155.9 mg, 93%, *E*/*Z* = 2.8:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.8 Hz, 2H), 8.20−8.14 (m, 1H), 7.33 (s, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 7.04−6.99 (m, 1H), 6.40 (s, 1H), 5.85−5.58 (m, 2H), 4.21 (d, *J* = 6.1 Hz, 0.47H), 3.98 (d, *J* = 5.3 Hz, 1.53H), 3.96−3.87 (m, 2H), 2.46 (s, 3H), 2.26 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 157.90, 157.9, 139.6, 135.2, 131.0, 130.8, 129.4, 129.3, 124.0, 119.6, 116.8, 113.5, 106.2, 63.1, 32.5, 21.2; minor isomer δ 158.0, 139.6, 135.2, 131.1, 130.0, 129.4, 128.7, 124.0, 116.7, 113.7, 106.0, 58.4, 28.1; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{17}N_3NaO$ $[M + Na]^+$ 302.1264, found 302.1269.

*4-(6-Methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3d**).* Product **3d** was obtained as a colorless oil (159.2 mg, 95%, *E*/*Z* = 3.7:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8, 2H), 8.07−8.03 (m, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.42 (s, 1H), 5.88−5.61 (m, 2H), 4.25 (d, *J* = 6.2 Hz, 0.43H), 4.03 (d, *J* = 6.7 Hz, 1.57H), 3.98−3.89 (m, 2H), 2.47 (s, 3H), 1.56 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 158.1, 138.9, 137.4, 132.6, 130.8, 129.8, 126.9, 123.3, 119.4, 117.0, 113.7, 106.3, 63.4, 32.4, 22.0; minor isomer δ 139.0, 137.4, 132.6, 130.0, 129.3, 126.9, 123.4, 119.4, 117.0, 113.8, 106.2, 58.6, 28.1; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{17}N_3NaO$ $[M + Na]^+$ 302.1264, found 302.1271.

*4-(5-Methoxy-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3e**).* Product **3e** was obtained as a colorless oil (150.6 mg, 85%, *E*/*Z* = 3.2:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, *J* = 3.7 Hz, 2H), 8.20−8.15 (m, 1H), 7.02−6.97 (m,2H), 6.87−6.84 (m, 1H), 6.39 (s, 1H), 5.85−5.57 (m, 2H), 4.20 (d, *J* = 5.8 Hz, 0.48H), 3.98 (d, *J* = 5.8 Hz, 1.52H), 3.95−3.88 (m, 2H), 3.82 (s, 3H), 2.37 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 157.8, 157.8, 155.1, 140.3, 131.7, 130.9, 129.7, 129.0, 116.7, 114.7, 111.3, 106.2, 102.1, 62.9, 55.5, 32.5; minor isomer δ 157.8, 155.4, 140.3, 132.0, 130.1, 129.7, 128.5, 116.6, 114.9, 111.4, 106.1, 102.1, 58.2, 28.2; MS (ESI) *m*/*z* (relative intensity) 296.2 (100) $[M + H]^+$, 318.2 (69) $[M + Na]^+$. The NMR data agree with those in a literature report.[31]

*4-(6-Methoxy-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3f**).* Product **3f** was obtained as a colorless oil (159.5 mg, 90%, *E*/*Z* = 3.3:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.8 Hz, 2H), 7.91−7.86 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 6.39 (s, 1H), 5.85−5.58 (m, 2H), 4.23 (d, *J* = 6.0 Hz, 0.46H), 4.01 (d, *J* = 6.7 Hz, 1.54H), 3.96−3.88 (m, 2H), 3.86 (s, 3H), 1.66 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer 158.2, 158.1, 156.8, 138.6, 137.9, 130.8, 129.7, 123.3, 120.1, 116.9, 110.6, 106.3, 99.0, 63.3, 55.8, 32.5; minor isomer δ 138.6, 137.9, 130.0, 129.3, 123.3, 120.0, 116.9, 110.5, 106.2, 99.2, 58.5, 28.2; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{17}N_3NaO_2$ $[M + Na]^+$ 318.1213, found 318.1221.

*4-(4-(Benzyloxy)-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3g**).* Product **3g** was obtained as a colorless oil (193.9 mg, 87%, *E*/*Z* = 4.6:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.8 Hz, 2H), 7.91−7.85 (m, 1H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.44−7.40 (m, 2H), 7.38−7.34 (m, 1H), 6.73−6.67 (m, 2H), 5.85−5.59 (m, 2H),

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5.23 (s, 2H), 4.21 (d, J = 6.4 Hz, 0.36H), 3.99 (d, J = 5.7 Hz, 1.64H), 3.96−3.90 (m, 2H), 1.95 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 158.1, 151.6, 138.5, 138.3, 137.5, 131.1, 129.4, 128.6, 127.9, 127.5, 123.5, 119.8, 117.4, 107.3, 103.7, 103.5, 70.1, 63.3, 32.5; minor isomer δ 151.5, 138.5, 138.3, 137.5, 130.3, 128.9, 127.5, 123.5, 117.3, 107.5, 103.8, 103.3, 58.5, 28.1; HRMS (ESI) m/z calcd for $C_{23}H_{21}N_3NaO_2$ $[M + Na]^+$ 394.1526, found 394.1524.

*2-(4-Hydroxybut-2-en-1-yl)-1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (**3h**).* Product **3h** was obtained as a colorless sticky oil (48.8 mg, 28%, E/Z = 2.6:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, J = 4.8, 2H), 8.29−8.23 (m, 1H), 7.85−7.83 (m, 1H), 7.46−7.43 (m, 1H), 7.31−7.25 (m, 1H), 6.53 (s, 1H), 5.86−5.63 (m, 2H), 4.26 (d, J = 6.3 Hz, 0.55H), 4.06 (d, J = 5.8 Hz, 1.45H), 3.99−3.92 (m, 2H), 1.61 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.4, 157.4, 142.3, 138.7, 131.7, 128.9, 128.3, 125.7, 124.7, 120.4, 118.2, 114.5, 105.9, 104.7, 63.2, 32.3; minor isomer δ 138.7, 130.8, 128.0, 125.8, 120.3, 118.1, 114.6, 105.8, 104.8, 58.5, 28.0; HRMS (ESI) m/z calcd for $C_{17}H_{14}N_4NaO$ $[M + Na]^+$ 313.1060, found 313.1062.

*4-(5-Fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3i**).* Product **3i** was obtained as a white solid (161.6 mg, 90%, E/Z = 2.7:1 by ^{1}H NMR): mp 94−96 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (d, J = 4.8 Hz, 2H), 8.27−8.15 (m, 1H), 7.16 (d, J = 9.0 Hz, 1H), 7.12 (t, J = 4.8 Hz, 1H), 6.94 (t, J = 9.1 Hz, 1H), 6.42 (s, 1H), 5.86−5.61(m, 2H), 4.23 (d, J = 5.3 Hz, 0.54H), 4.02 (d, J = 5.8 Hz, 1.46H), 3.97−3.90 (m, 2H), 1.83 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.7 (d, J_{C-F} = 269.2 Hz), 158.1, 158.0, 141.4, 133.4, 131.2, 129.8 (d, J_{C-F} = 10.0 Hz), 129.0, 117.2, 114.8 (d, J_{C-F} = 9.1 Hz), 110.3 (d, J_{C-F} = 25.0 Hz), 106.2 (d, J_{C-F} = 4.0 Hz), 105.0 (d, J_{C-F} = 23.5 Hz), 63.2, 32.6; minor isomer δ 130.3, 128.6, 117.2, 115.0 (d, J_{C-F} = 9.1 Hz), 110.3 (d, J_{C-F} = 24.9 Hz), 106.0 (d, J_{C-F} = 3.9 Hz), 58.4, 28.2; HRMS (ESI) m/z calcd for $C_{16}H_{14}N_3FNaO$ $[M + Na]^+$ 306.1013, found 306.1021.

*4-(5-Chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3j**).* Product **3j** was obtained as a colorless oil (158.3 mg, 88%, E/Z = 3.3:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (d, J = 4.8 Hz, 2H), 8.27−8.13 (m, 1H), 7.47 (d, J = 1.7 Hz, 1H), 7.20−7.11 (m, 2H), 6.41 (s, 1H), 5.89−5.62 (m, 2H), 4.26 (d, J = 4.6 Hz, 0.47H), 4.05 (d, J = 5.6 Hz, 1.53H), 3.99−3.90 (m, 2H), 1.99 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 157.9, 141.2, 135.4, 131.3, 130.3, 129.1, 127.3, 122.7, 119.2, 117.4, 115.0, 105.8, 63.3, 32.6; minor isomer δ 130.4, 128.8, 127.3, 122.8, 119.2, 117.4, 115.2, 105.7, 58.6, 28.2; HRMS (ESI) m/z calcd for $C_{16}H_{14}N_3ClNaO$ $[M + Na]^+$ 322.0718, found 322.0728.

*4-(4-Chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3k**).* Product **3k** was obtained as a colorless oil (156.5 mg, 87%, E/Z = 4.0:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (d, J = 4.8 Hz, 2H), 8.15−8.09 (m, 1H), 7.19−7.11 (m, 3H), 6.59 (s, 1H), 5.88−5.61 (m, 2H), 4.25 (d, J = 5.4 Hz, 0.4H), 4.03 (d, J = 6.8 Hz, 1.6H), 3.98−3.90 (m, 2H), 1.70 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 157.8, 140.5, 137.6, 131.4, 128.8, 127.7, 125.0, 123.2, 121.5, 117.6, 112.3, 104.3, 63.3, 32.4; minor isomer δ 140.5, 137.6, 130.5, 128.5, 123.3, 121.6, 117.6, 112.4, 104.2, 58.5, 28.1; HRMS (ESI) m/z calcd for $C_{16}H_{14}ClN_3NaO$ $[M + Na]^+$ 322.0718, found 322.0715.

*4-(6-Chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3l**).* Product **3l** was obtained as a colorless oil (163.6 mg, 91%, E/Z = 4.0:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (d, J = 4.8 Hz, 2H), 8.34−8.29 (m, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.19−7.14 (m, 1H), 6.44 (s, 1H), 5.88−5.63 (m, 2H), 4.26 (d, J = 5.2 Hz, 0.4H) 4.05 (d, J = 5.8 Hz, 1.6H), 3.99−3.90 (m, 2H), 1.59 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 157.8, 140.5, 137.3, 131.2, 129.1, 128.5, 127.6, 122.3, 120.4, 117.4, 114.1, 106.2, 63.3, 32.5; minor isomer δ 157.8, 137.3, 130.3, 128.8, 128.6, 122.4, 117.4, 114.2, 106.0, 58.5, 28.2; HRMS (ESI) m/z calcd for $C_{16}H_{14}ClN_3NaO$ $[M + Na]^+$ 322.0718, found 322.0706.

*4-(4-Bromo-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3m**).* Product **3m** was obtained as a colorless oil (175.1 mg, 85%, E/Z = 4.4:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (d, J = 4.8 Hz, 2H), 8.18−8.12 (m, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.17−7.13 (m, 1H), 7.09−7.04 (m, 1H), 6.53 (s, 1H), 5.85−5.60 (m, 2H), 4.23 (d, J = 5.2 Hz, 0.37H), 4.02 (d, J = 5.1 Hz, 1.63H), 3.96−3.89 (m, 2H), 1.79 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 157.7, 140.5, 137.1, 131.4, 129.5, 128.6, 124.6, 123.5, 117.6, 113.6, 112.8, 105.9, 63.2, 32.4; minor isomer δ 140.6, 137.2, 130.5, 129.5, 128.3, 124.6, 123.5, 117.6, 112.9, 105.8, 58.4, 28.0; MS (ESI) m/z (relative intensity) 366.2 (100) $[M + Na]^+$. The NMR data agree with those in a literature report.[31]

*4-(5-Bromo-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3n**).* Product **3n** was obtained as a pale yellow oil (183.8 mg, 89%, E/Z = 4.0:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (d, J = 4.7 Hz, 2H), 8.27−8.13 (m, 1H), 7.61−7.56 (m, 1H), 7.29−7.24 (m, 1H), 7.09−7.05 (m, 1H), 6.35 (s, 1H), 5.80−5.55 (m, 2H), 4.18 (d, J = 4.7 Hz, 0.4H), 3.97 (d, J = 5.4 Hz, 1.6H), 3.91−3.80 (m, 2H), 2.26 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 157.7, 141.2, 135.7, 131.4, 130.9, 128.7, 125.3, 122.3, 117.5, 115.5, 115.0, 105.6, 63.1, 32.5; minor isomer δ 130.6, 128.4, 125.4, 117.5, 115.7, 115.0, 105.5, 58.4, 28.2; HRMS (ESI) m/z calcd for $C_{16}H_{14}N_3BrNaO$ $[M + Na]^+$ 366.0212, found 366.0220.

*4-(6-Bromo-1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3o**).* Product **3o** was obtained as a colorless oil (179.6 mg, 87%, E/Z = 3.5:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (d, J = 4.8 Hz, 2H), 8.48−8.44 (m, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.30−7.27 (m, 1H), 7.15 (t, J = 4.8 Hz, 1H), 6.43 (s, 1H), 5.86−5.61 (m, 2H), 4.24 (d, J = 4.6 Hz, 0.44H), 4.03 (d, J = 5.5 Hz, 1.56H), 3.96−3.89 (m, 2H), 1.51 (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.2, 157.8, 140.4, 137.6, 131.2, 129.1, 128.0, 125.0, 120.8, 117.4, 116.9, 116.3, 106.2, 63.3, 32.5; minor isomer 137.6, 130.4, 128.7, 125.0, 117.4, 117.1, 116.3, 106.1, 58.5, 28.2; HRMS (ESI) m/z calcd for $C_{16}H_{14}BrN_3NaO$ $[M + Na]^+$ 366.0212, found 366.0206.

*2-Phenyl-4-(1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3p**).* Product **3p** was obtained as a yellow oil (200.5 mg, 98%, E/Z = 4.0:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (d, J = 4.8 Hz, 0.4H), 8.66 (d, J = 4.8 Hz, 1.6H), 8.28 (d, J = 8.3 Hz, 0.2H), 8.19 (d, J = 8.4 Hz, 1.8H), 7.52 (d, J = 7.3 Hz, 1H), 7.39−7.15 (m, 7H), 7.09 (t, J = 4.8 Hz, 0.2H), 6.99 (t, J = 4.8 Hz, 0.8H), 6.47 (d, J = 5.6 Hz, 1H), 5.89−5.58 (m, 2H), 5.06 (d, J = 6.8 Hz, 1H), 4.19−4.14 (m, 0.2H), 4.0−3.91 (m, 1.8H), 2.11 (s, 0.2H), 1.98 (s, 0.8H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 158.0, 157.9, 142.9, 139.3, 137.0, 134.2, 129.1, 129.0, 128.4, 127.4, 126.1, 122.7, 121.8, 119.8, 117.1, 113.7, 106.6, 74.8, 32.4; minor isomer δ 158.1, 143.3, 139.4, 137.1, 133.5, 129.1, 128.5, 127.5, 126.0, 122.8, 121.9, 119.9, 113.9, 69.6, 28.4; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_3NaO$ $[M + Na]^+$ 364.1420, found 364.1429.

*2-(4-Fluorophenyl)-4-(1-(pyrimidin-2-yl)-1H-indol-2-yl)but-2-en-1-ol (**3q**).* Product **3q** was obtained as a yellow oil (202.9 mg, 94%, E/Z = 5.3:1 by ^{1}H NMR): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (d, J = 4.8 Hz, 0.32H), 8.71 (d, J = 4.8 Hz, 1.68H), 8.30 (d, J = 8.3 Hz, 0.16H), 8.22 (d, J = 8.3 Hz, 0.84H), 7.56−7.51 (m, 1H), 7.38−7.12 (m, 5H), 7.08−6.94 (m, 3H), 6.47 (s, 1H), 5.91−5.56 (m, 2H), 5.07 (d, J = 6.8 Hz, 1H), 4.19−4.12 (m, 0.19H), 4.01−3.95 (m, 1.71H), 2.05 (s, 0.16H), 1.88 (s, 0.84H); ^{13}C NMR (151 MHz, $CDCl_3$) major isomer δ 162.1 (d, J_{C-F} = 245.5 Hz), 158.0, 158.0, 139.2, 138.7 (d, J_{C-F} = 2.9 Hz), 137.0, 134.0, 129.2, 129.0, 127.7 (d, J_{C-F} = 8.1 Hz), 122.8, 121.9, 119.9, 117.1, 115.2 (d, J_{C-F} = 21.3 Hz), 113.7, 74.2, 32.4; minor isomer 162.1 (d, J_{C-F} = 245.6 Hz), 158.2, 158.1, 139.3, 139.0 (d, J_{C-F} = 2.8 Hz), 137.1, 133.4, 129.1, 128.6, 127.6 (d, J_{C-F} = 8.2 Hz), 122.9, 122.0, 119.9, 117.1, 115.3 (d, J_{C-F} = 21.4 Hz), 114.0, 106.7, 69.0, 28.4; HRMS (ESI) m/z calcd for $C_{22}H_{18}FN_3NaO$ $[M + Na]^+$ 382.1326, found 382.1333.

Experiment of H/D Exchange. Indole **1a** (0.6 mmol), CD_3OD (1.2 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (0.03 mmol, 5 mol %), AgOAc (0.12 mmol, 20 mol %), and silica gel (600 mg, grinding auxiliary) were transferred to a ball-milling vessel (stainless steel, 45 mL) loaded with 36 grinding balls (stainless steel, 4 mm). The milling vessel was placed in the ball mill (800 rpm, 30 min). The crude product was isolated by washing the vessel and the balls with EtOAc (3× 20 mL). The mixture was concentrated in vacuum and purified by flash chromatography (Hexane/EtOAc = 4:1 to 2:1). Recovery: 98% of **1a** and **1a**-$[D]_n$.

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Competitive Experiment. Indole **1e** (0.6 mmol), indole **1h** (0.6 mmol), vinylethylene carbonate **2** (0.6 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (0.03 mmol, 5 mol %), AgOAc (0.12 mmol, 20 mol %), and silica gel (600 mg, grinding auxiliary) were transferred to a ball-milling vessel (stainless steel, 45 mL) loaded with 36 grinding balls (stainless steel, 4 mm). The milling vessel was placed in the ball mill (800 rpm, 20 min). The crude product was isolated by washing the vessel and the balls with EtOAc (3× 20 mL). The mixture was concentrated in vacuum and purified by flash chromatography (Hexane/EtOAc = 4:1 to 2:1) to give mixture (**3e** and **3h**). The ratio of the two products was determined by the integration of signals in ^{1}H NMR resulting K_{3e}/K_{3h} = 1.98/1.03 = 1.9:1.

KIE Experiment. Indole **1a** (0.3 mmol), indole **1a**-$[D]_1$ (0.3 mmol), vinylethylene carbonate 2 (0.6 mmol), $[Cp^*Co(MeCN)_3][SbF_6]_2$ (0.03 mmol, 5 mol %), AgOAc (0.12 mmol, 20 mol %), and silica gel (600 mg, grinding auxiliary) were transferred to a ball-milling vessel (stainless steel, 45 mL) loaded with 36 grinding balls (stainless steel, 4 mm). The milling vessel was placed in the ball mill (800 rpm, 5 min). The crude product was isolated by washing the vessel and the balls with EtOAc (3 × 20 mL). The mixture was concentrated in vacuum and purified by flash chromatography (Hexane/EtOAc = 4:1). Recovery indole **1a** and **1a**-$[D]_1$ 174.6 mg (88%), $K_{(H)}/K_{(D)}$ = (1−0.457)/0.457 = 1.89:1.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01695.

^{1}H and ^{13}NMR spectra of all products (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Tan, Q.-W.; Ouyang, M.-A.; Wu, Z.-J. *Nat. Prod. Res.* **2012**, *26*, 1375.

(2) Sundararaju, B.; Achard, M.; Bruneau, C. *Chem. Soc. Rev.* **2012**, *41*, 4467.

(3) (a) Larock, R. C.; Ilkka, S. J. *Tetrahedron Lett.* **1986**, *27*, 2211. (b) Echavarren, A. M.; Tueting, D. R.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039. (c) Lentz, N. L.; Peet, N. P. *Tetrahedron Lett.* **1990**, *31*, 811. (d) Herron, J. R.; Russo, V.; Valente, E. J.; Ball, Z. T. *Chem. - Eur. J.* **2009**, *15*, 8713.

(4) (a) Yu, S.; Li, X. *Org. Lett.* **2014**, *16*, 1200. (b) Zhang, S.-S.; Wu, J.-Q.; Lao, Y.-X.; Liu, X.-G.; Liu, Y.; Lv, W.-X.; Tan, D.-H.; Zeng, Y.-F.; Wang, H. *Org. Lett.* **2014**, *16*, 6412. (c) Sharma, S.; Shin, Y.; Mishra, N. K.; Park, J.; Han, S.; Jeong, T.; Oh, Y.; Lee, Y.; Choi, M.; Kim, I. S. *Tetrahedron* **2015**, *71*, 2435. (d) Debbarma, S.; Bera, S. S.; Maji, M. S. *J. Org. Chem.* **2016**, *81*, 11716.

(5) For reviews on Rh-catalyzed C−H bond functionalization, see the following references: (a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (b) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (c) Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*, 1308.

(6) Conejero, S.; Paneque, M.; Poveda, M. L.; Santos, L. L.; Carmona, E. *Acc. Chem. Res.* **2010**, *43*, 572.

(7) (a) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (b) Minami, Y.; Hiyama, T. *Acc. Chem. Res.* **2016**, *49*, 67.

(8) Ruiz, S.; Villuendas, P.; Urriolabeitia, E. P. *Tetrahedron Lett.* **2016**, *57*, 3413.

(9) (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (b) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (c) Guo, X.-X.; Gu, D.-W.; Wu, Z.; Zhang, W. *Chem. Rev.* **2015**, *115*, 1622. (d) Murakami, K.; Yamada, S.; Kaneda, T.; Itami, K. *Chem. Rev.* **2017**, *117*, 9302. (e) Qin, Y.; Zhu, L.; Luo, S. *Chem. Rev.* **2017**, *117*, 9433.

(10) (a) Yoshino, T.; Ikemoto, H.; Matsunaga, S.; Kanai, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 2207. (b) Sun, B.; Yoshino, T.; Matsunaga, S.; Kanai, M. *Adv. Synth. Catal.* **2014**, *356*, 1491. (c) Sun, B.; Yoshino, T.; Kanai, M.; Matsunaga, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 12968. (d) Bunno, Y.; Murakami, N.; Suzuki, Y.; Kanai, M.; Yoshino, T.; Matsunaga, S. *Org. Lett.* **2016**, *18*, 2216.

(11) (a) Sauermann, N.; González, M. J.; Ackermann, L. *Org. Lett.* **2015**, *17*, 5316. (b) Li, J.; Tang, M.; Zang, L.; Zhang, X.; Zhang, Z.; Ackermann, L. *Org. Lett.* **2016**, *18*, 2742. (c) Zell, D.; Bu, Q.; Feldt, M.; Ackermann, L. *Angew. Chem., Int. Ed.* **2016**, *55*, 7408. (d) Nakanowatari, S.; Mei, R.; Feldt, M.; Ackermann, L. *ACS Catal.* **2017**, *7*, 2511. (e) Wang, H.; Lorion, M. M.; Ackermann, L. *Angew. Chem., Int. Ed.* **2017**, *56*, 6339. (f) Wang, H.; Lorion, M. M.; Ackermann, L. *ACS Catal.* **2017**, *7*, 3430.

(12) (a) Hummel, J. R.; Ellman, J. A. *Org. Lett.* **2015**, *17*, 2400. (b) Hummel, J. R.; Ellman, J. A. *J. Am. Chem. Soc.* **2015**, *137*, 490.

(13) (a) Gensch, T.; Klauck, F. J. R.; Glorius, F. *Angew. Chem., Int. Ed.* **2016**, *55*, 11287. (b) Lerchen, A.; Knecht, T.; Daniliuc, C. G.; Glorius, F. *Angew. Chem., Int. Ed.* **2016**, *55*, 15166. (c) Wang, X.; Lerchen, A.; Glorius, F. *Org. Lett.* **2016**, *18*, 2090.

(14) Liang, Y.; Liang, Y.-F.; Tang, C.; Yuan, Y.; Jiao, N. *Chem. - Eur. J.* **2015**, *21*, 16395.

(15) (a) Kong, L.; Yu, S.; Tang, G.; Wang, H.; Zhou, X.; Li, X. *Org. Lett.* **2016**, *18*, 3802. (b) Kong, L.; Yu, S.; Zhou, X.; Li, X. *Org. Lett.* **2016**, *18*, 588. (c) Kong, L.; Zhou, X.; Li, X. *Org. Lett.* **2016**, *18*, 6320. (d) Li, L.; Wang, H.; Yu, S.; Yang, X.; Li, X. *Org. Lett.* **2016**, *18*, 3662. (e) Zhou, X.; Pan, Y.; Li, X. *Angew. Chem., Int. Ed.* **2017**, *56*, 8163.

(16) Bera, S. S.; Debbarma, S.; Ghosh, A. K.; Chand, S.; Maji, M. S. *J. Org. Chem.* **2017**, *82*, 420.

(17) Liu, X.-G.; Zhang, S.-S.; Wu, J.-Q.; Li, Q.; Wang, H. *Tetrahedron Lett.* **2015**, *56*, 4093.

(18) (a) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107. (b) Liu, Y.; Wang, C.; Lv, N.; Liu, Z.; Zhang, Y. *Adv. Synth. Catal.* **2017**, *359*, 1351. (c) Yu, W.; Zhang, W.; Liu, Y.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2017**, *4*, 77.

(19) (a) Moselage, M.; Li, J.; Ackermann, L. *ACS Catal.* **2016**, *6*, 498. (b) Wei, D.; Zhu, X.; Niu, J.-L.; Song, M.-P. *ChemCatChem* **2016**, *8*, 1242. (c) Yoshino, T.; Matsunaga, S. *Adv. Synth. Catal.* **2017**, *359*, 1245.

(20) (a) Beyer, M. K.; Clausen-Schaumann, H. *Chem. Rev.* **2005**, *105*, 2921. (b) Hernández, J. G.; Bolm, C. *J. Org. Chem.* **2017**, *82*, 4007.

(21) Hermann, G. N.; Becker, P.; Bolm, C. *Angew. Chem., Int. Ed.* **2015**, *54*, 7414.

(22) Hermann, G. N.; Becker, P.; Bolm, C. *Angew. Chem., Int. Ed.* **2016**, *55*, 3781.

(23) (a) James, S. L.; Adams, C. J.; Bolm, C.; Braga, D.; Collier, P.; Friić, T.; Grepioni, F.; Harris, K. D. M.; Hyett, G.; Jones, W.; Krebs, A.; MacK, J.; Maini, L.; Orpen, A. G.; Parkin, I. P.; Shearouse, W. C.; Steed, J. W.; Waddell, D. C. *Chem. Soc. Rev.* **2012**, *41*, 413. (b) James, S. L.; Friščić, T. *Chem. Soc. Rev.* **2013**, *42*, 7494. (c) Hernández, J. G.; Friščić, T. *Tetrahedron Lett.* **2015**, *56*, 4253. (d) Lou, S.-J.; Mao, Y.-J.; Xu, D.-Q.; He, J.-Q.; Chen, Q.; Xu, Z.-Y. *ACS Catal.* **2016**, *6*, 3890.

(24) (a) Yu, J.; Li, Z.; Jia, K.; Jiang, Z.; Liu, M.; Su, W. *Tetrahedron Lett.* **2013**, *54*, 2006. (b) Yu, J.; Jiang, Z.; Su, W. *RSC Green Chemistry* **2015**, *31*, 96. (c) Jiang, Z. J.; Li, Z. H.; Yu, J. B.; Su, W. K. *J. Org. Chem.*

DOI: 10.1021/acs.joc.7b01695
J. Org. Chem. XXXX, XXX, XXX−XXX

2016, *81*, 10049. (d) Yu, J. B.; Zhang, Y.; Jiang, Z. J.; Su, W. K. *J. Org. Chem.* **2016**, *81*, 11514.
(25) The temperature in the reaction vessel might increase 10−20 °C after 30 min ball-milling.
(26) (a) Zell, D.; Müller, V.; Dhawa, U.; Bursch, M.; Presa, R. R.; Grimme, S.; Ackermann, L. *Chem. - Eur. J.* **2017**, *23*, 12145. (b) Ma, W. B.; Mei, R. H.; Tenti, G.; Ackermann, L. *Chem. - Eur. J.* **2014**, *20*, 15248.
(27) Simmons, E. M.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2012**, *51*, 3066.
(28) Qiu, R.; Reddy, V. P.; Iwasaki, T.; Kambe, N. *J. Org. Chem.* **2015**, *80*, 367.
(29) Yoshida, Y.; Endo, T. *Polymer* **2016**, *102*, 167.
(30) Zhu, X.; Su, J.-H.; Du, C.; Wang, Z.-L.; Ren, C.-J.; Niu, J.-L.; Song, M.-P. *Org. Lett.* **2017**, *19*, 596.
(31) Kong, L.; Yu, S.; Tang, G.; Wang, H.; Zhou, X.; Li, X. *Org. Lett.* **2016**, *18*, 3802.

DOI: 10.1021/acs.joc.7b01695
J. Org. Chem. XXXX, XXX, XXX−XXX