Supporting Information

Rhodium(III)-Catalyzed C–H Allylation of Indoles with Allyl Alcohols via β-Hydroxide Elimination

Xiaowei Wu†, Haitao Ji†, ‡, *

†Drug Discovery Department, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, Florida 33612-9416, United States
‡Departments of Oncologic Sciences and Chemistry, University of South Florida, Tampa, Florida 33612, United States

E-mail: Haitao.Ji@moffitt.org

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(A) General Information

The reagents (chemicals) were purchased from commercial sources and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness). All products were characterized by their NMR and MS spectra. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane (TMS). Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd) and broad (br). High-resolution mass spectra (HRMS) were measured on Micromass Ultra Q-TOF spectrometer. All N-carbamoylindoles 1 were prepared by following the procedure as described in the literature. Allyl alcohols 2a, 2b, 2c, 2d, 2e, 2f, 2g, 2h, 2i, 2j, 2k, 2l, 2n, 2o, and 2p are commercial materials.
(B) General Procedures

General Procedure for C-H activation:

To a dry tube was equipped with N-ethoxy-indole-1-carboxamides 1 (0.2 mmol, 1 equiv), allylic alcohols 2 (0.3 mmol, 1.5 equiv), [Cp*RhCl₂]₂ (0.01 mmol, 0.05 equiv), NaOAc (0.12 mmol, 0.6 equiv) and 2 mL 1,2-dichloroethane. The resulting mixture was stirred at room temperature for 2~6 h under Ar atmosphere. Then, the solution was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na₂SO₄, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 6/1 ~ 4/1, v/v) to give desired products 3.
(C) The Gram-scale Preparation of 3i

With Cp*Rh$^{III}$ catalyst: To a dry round bottom flask was equipped with N-ethoxy-indole-1-carboxamides 1i (1.0 g, 4.58 mmol, 1 equiv), allylic alcohols 2a (922 mg, 6.87 mmol, 1.5 equiv), [Cp*RhCl$_2$]$_2$ (85.0 mg, 0.13 mmol, 0.03 equiv), NaOAc (225.5 mg, 2.75 mmol, 0.6 equiv) and 40 mL 1,2-dichloroethane. The resulting mixture was stirred at room temperature for 6 h under Ar atmosphere. Then, the solution was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na$_2$SO$_4$, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 6/1 ~ 4/1, v/v) to give the desired product 3i (1.13 g, 74% yield).

With Ru$^{II}$ catalyst: To a dry round bottom flask was equipped with N-ethoxy-indole-1-carboxamides 1i (1.0 g, 4.58 mmol, 1 equiv), allylic alcohols 2a (922 mg, 6.87 mmol, 1.5 equiv), [{RuCl$_2$(p-cymene)}$_2$] (140.3 mg, 0.23 mmol, 0.05 equiv), NaOAc (375.9 mg, 4.58 mmol, 1 equiv) and 40 mL 1,2-dichloroethane. The resulting mixture was stirred at 45 $^\circ$C for 6 h under Ar atmosphere. Then, the solution was diluted with dichloromethane and washed by water. The combined organic layers were dried with Na$_2$SO$_4$, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 6/1 ~ 4/1, v/v) to give the desired product 3i (597.0 mg, 39% yield).

Removal of the Directing Group:

The optimization of reaction conditions for removal of the directing group$^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>base</th>
<th>T ($^\circ$C)</th>
<th>4a Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF/H$_2$O = 3/1 (v/v)</td>
<td>LiOH (4.0 equiv)</td>
<td>60</td>
<td>NR</td>
</tr>
<tr>
<td>2</td>
<td>THF/H$_2$O = 3/1 (v/v)</td>
<td>NaOH (4.0 equiv)</td>
<td>60</td>
<td>NR</td>
</tr>
<tr>
<td>3</td>
<td>THF/H$_2$O = 3/1 (v/v)</td>
<td>KOH (4.0 equiv)</td>
<td>60</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>THF/H$_2$O = 3/1 (v/v)</td>
<td>KOH (4.0 equiv)</td>
<td>80</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>THF/H$_2$O = 3/1 (v/v)</td>
<td>KOH (4.0 equiv)</td>
<td>100</td>
<td>NR</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>t-BuOK (2.0 equiv)</td>
<td>rt</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>t-BuONa (2.0 equiv)</td>
<td>rt</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>EtOH</td>
<td>KOH (4.0 equiv)</td>
<td>100</td>
<td>NR</td>
</tr>
<tr>
<td>9</td>
<td>n-propanol/H$_2$O = 1/2 (v/v)</td>
<td>KOH (4.0 equiv)</td>
<td>100</td>
<td>NR</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: 3a (0.2 mmol, 1 equiv), base, in 4 mL solvent, Ar atmosphere.
Condition 10

![Condition 10 Reaction](image)

**Conditions:**
- To a solution of 3i (0.52 g, 1.55 mmol, 1 equiv) in dry DMF (20 mL) was added NaH (74.6 mg, 60%, dispersion in mineral oil, 1.2 equiv) portionwise at 0 °C. The resulting mixture was stirred for 30 mins at room temperature, and then Mel (441.0 mg, 2 equiv) was added into the solution. The reaction was stirred for 6 hours at room temperature. Then, the reaction was quenched with saturated NH₄Cl solution. The solution was diluted with EtOAc and washed by brine. The combined organic layers were dried with Na₂SO₄, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 15/1 ~ 10/1, v/v) to give the desired product 3ia (498.0 mg, 92% yield). 

**1H NMR (500 MHz, CDCl₃) δ** 7.53 – 7.46 (m, 1H), 7.38 – 7.34 (m, 1H), 7.31 – 7.26 (m, 3H), 7.26 – 7.16 (m, 4H), 6.44 (d, J = 15.8 Hz, 1H), 6.25 (dt, J = 15.8, 6.5 Hz, 1H), 3.96 – 3.70 (m, 4H), 3.19 (s, 3H), 2.29 (s, 3H), 1.12 (t, J = 7.1 Hz, 3H) ppm. 

**13C NMR (126 MHz, CDCl₃) δ** 153.89, 137.30, 135.42, 134.10, 131.54, 130.00, 128.64, 127.36, 127.08, 126.18, 123.02, 121.31, 118.72, 113.24, 111.95, 69.69, 37.64, 28.55, 13.70, 8.81 ppm. 

**HRMS (ESI) m/z:** calculated for C₂₂H₂₅N₂O₂⁺ [M + H]⁺: 349.1916, found: 349.1909.

Condition 11

**Conditions:**
- To a solution of 3ia (50.0 mg, 0.14 mmol, 1 equiv) in anhydrous THF (5 mL) was added LiAlH₄ (27.2 mg, 5 equiv) portionwise at room temperature. The resulting mixture was stirred for 30 mins, and then the reaction was heated to 60 °C for 12 hours under Ar atmosphere. The reaction was quenched with saturated NH₄Cl solution. The solution was diluted with EtOAc and washed by brine. The combined organic layers were dried with Na₂SO₄, filtered, concentrated and purified by column chromatography on silica gel (hexanes/EtOAc = 15/1 ~ 10/1, v/v) to give the product 4a (21.0 mg, 59% yield). 

**1H NMR (500 MHz, CDCl₃) δ** 7.75 (s, 1H), 7.55 – 7.48 (m,
1H), 7.38 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 7.27 – 7.19 (m, 2H), 7.17 – 7.06 (m, 2H), 6.51 (d, $J = 15.8$ Hz, 1H), 6.33 (dt, $J = 15.8$, 6.6 Hz, 1H), 3.65 (dd, $J = 6.6$, 1.2 Hz, 2H), 2.28 (s, 3H) ppm. $^{13}$C NMR (126 MHz, CDCl$_3$) δ 137.12, 135.49, 132.21, 132.07, 129.54, 128.76, 127.60, 126.68, 126.32, 121.42, 119.24, 118.40, 110.45, 107.69, 29.94, 8.61 ppm. HRMS (ESI) m/z: calculated for C$_{18}$H$_{18}$N$^+$ [M + H]$^+$: 248.1439, found: 248.1430.
(D) MECHANISTIC EXPERIMENTS

Deuterium Incorporation Experiment A:

To a dry tube was equipped with N-ethoxy-1H-indole-1-carboxamide (1a, 0.2 mmol), 5 mol% [Cp*RhCl₂]₂, and NaOAc (0.12 mmol, 0.6 equiv), followed by adding DCE (2 mL) and CD₃OD (2 mmol, 10 equiv). The mixture was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the product. Found H/D exchange occurred at the C2-position of the indole (40% D) and the C7-position of the indole (40% D).

¹H NMR of the product 1a-Dₙ of the reaction
Deuterium Incorporation Experiment B:

To a reaction tube was added N-ethoxy-1H-indole-1-carboxamide (1a, 0.2 mmol), 5 mol% [Cp*RhCl₂]₂, and dry DCE (2 mL). Then, CD₃OD (2 mmol, 10 equiv) was added and the mixture was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the crude product. *No obvious H/D exchange was detected at the C2-position and the C7-position of the indole.*

¹H NMR of the product 1a-Dₙ of this reaction.

Deuterium Incorporation Experiment C:

To a dry tube was equipped with N-ethoxy-1H-indole-1-carboxamide (1a, 0.2 mmol), 2a (0.3 mmol, 1.5 equiv), 5 mol% [Cp*RhCl₂]₂ and NaOAc (0.12 mmol, 0.6 equiv),
followed by adding DCE (2 mL) and CD$_3$OD (2 mmol, 10 equiv). The reaction tube was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the crude product. *Found H/D exchange occurred at the C7-position of the indole (25% D).*

$^1$H NMR of the product 3a-D$_n$

Deuterium Incorporation Experiment D:

![Deuterium Incorporation Experiment D](image)

Synthesis of compound 2a-D. To a solution of 2aa (150.0 mg, 1.13 mmol, 1 equiv) in methanol was added CeCl$_7$H$_2$O (1.13 mmol, 1 equiv). The resulting mixture was cooled to 0 °C and then NaBD$_4$ (42.9 mg, 1 equiv) was added portionwise. The mixture was stirred for 1 h and then saturated NH$_4$Cl aqueous solution was added. The resulting mixture was diluted with dichloromethane and washed by water. The
combined organic layers were dried with Na$_2$SO$_4$, concentrated and purified by column chromatography on silica gel to give the product 2a-D (92.0 mg, 60% yield). 

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.42 – 7.28 (m, 5H), 6.14 – 5.99 (m, 1H), 5.36 (dd, $J$ = 17.1, 1.4 Hz, 1H), 5.21 (dd, $J$ = 10.3, 1.4 Hz, 1H), 1.91 (s, 1H).

To a dry tube was equipped with N-ethoxy-1H-indole-1-carboxamide (1a, 41.0 mg, 0.2 mmol), 2a-D (0.3 mmol, 1.5 equiv), 5 mol % [Cp*RhCl$_2$]$_2$ and NaOAc (0.12 mmol, 0.6 equiv), followed by adding DCE (2 mL) and CD$_3$OD (2 mmol, 10 equiv). The reaction tube was stirred at room temperature for 2 h under Ar atmosphere. The resulting mixture was directly concentrated and purified by column chromatography on silica gel to give the corresponding product 3a-D (48.0 mg, 75% yield). 

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.24 (br, 1H), 7.73 (dd, $J$ = 8.2, 0.6 Hz, 1H), 7.52 (d, $J$ = 7.5 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.32 – 7.27 (m, 2H), 7.25 – 7.17 (m, 3H), 6.47 (d, $J$ = 0.7 Hz, 1H), 6.40 (t, $J$ = 6.3 Hz, 1H), 4.10 (q, $J$ = 7.0 Hz, 2H), 3.90 (d, $J$ = 6.6 Hz, 2H), 1.32 (t, $J$ = 7.0 Hz, 3H) ppm.

$^1$H NMR of 2a-D
\(^1\)H NMR of the product 3a-D

![NMR spectrum](image)

### Determination of the Kinetic Isotope Effect (KIE):

1a (21.0 mg, 0.1 mmol) was allowed to react with 2a (21.0 mg, 0.15 mmol) in dry DCE (2 mL) in the presence of NaOAc (0.6 equiv) and 5 mol % [Cp*RhCl\(_2\)]. The mixture was stirred at room temperature under Ar atmosphere. The reaction was stopped after 10 min, and the crude mixture was purified using column chromatography on silica gel to give the corresponding product 3a (18.0 mg, 28\% yield).

1a-D (21.0 mg, 0.1 mmol, 95\% D) was allowed to react with 2a (21.0 mg, 0.15 mmol) in dry DCE (2 mL) in the presence of NaOAc (0.6 equiv) and 5 mol % [Cp*RhCl\(_2\)]. The mixture was stirred at room temperature under Ar atmosphere. The reaction was stopped after 10 min, and the crude mixture was purified using column chromatography on silica gel to give the corresponding product 3a (22.5 mg, 35\% yield). A kinetic isotopic effect of these two reactions was thus determined to be \(k_\text{H}/k_\text{D} = 0.76\).
(E) Copies of NMR Spectra for the Products.

2-cinnamyl-N-ethoxy-1H-indole-1-carboxamide (3a)
2-cinnamyl-N-ethoxy-5-fluoro-1H-indole-1-carboxamide (3b)
5-chloro-2-cinnamyl-N-ethoxy-1H-indole-1-carboxamide (3c)
5-bromo-2-cinnamyl-N-ethoxy-1H-indole-1-carboxamide (3d)
4-chloro-2-cinnamyl-N-ethoxy-1H-indole-1-carboxamide (3e)
2-cinnamyl-N-ethoxy-6-fluoro-1H-indole-1-carboxamide (3f)
2-cinnamyl-N-ethoxy-5-methyl-1H-indole-1-carboxamide (3g)
2-cinnamyl-N-ethoxy-5-methoxy-1H-indole-1-carboxamide (3h)
2-cinnamyl-N-ethoxy-3-methyl-1H-indole-1-carboxamide (3i)
2-cinnamyl-N-ethoxy-3-phenyl-1H-indole-1-carboxamide (3j)
(E)-N-ethoxy-2-(3-(4-fluorophenyl)allyl)-1H-indole-1-carboxamide (3k)
(E)-2-(3-(4-chlorophenyl)allyl)-N-ethoxy-1H-indole-1-carboxamide (3l)
(E)-2-(3-(4-bromophenyl)allyl)-N-ethoxy-1H-indole-1-carboxamide (3m)
(E)-N-ethoxy-2-(3-(p-tolyl)allyl)-1H-indole-1-carboxamide (3n)
(E)-N-ethoxy-2-(3-(4-methoxyphenyl)allyl)-1H-indole-1-carboxamide (3o)
(E)-N-ethoxy-2-(3-(4-(trifluoromethyl)phenyl)allyl)-1H-indole-1-carboxamide (3p)
(E)-N-ethoxy-2-(3-(thiophen-2-yl)allyl)-1H-indole-1-carboxamide (3q)
(E)-N-ethoxy-2-(3-(naphthalen-2-yl)allyl)-1H-indole-1-carboxamide (3r)
(E)-N-ethoxy-2-(pent-2-en-1-yl)-1H-indole-1-carboxamide (3s)
(E)-N-ethoxy-2-(hex-2-en-1-yl)-1H-indole-1-carboxamide (3t)
2-allyl-N-ethoxy-1H-indole-1-carboxamide (3u)
N-ethoxy-2-(3-methylbut-2-en-1-yl)-1H-indole-1-carboxamide (3v)
2-cinnamyl-N-ethoxy-N,3-dimethyl-1H-indole-1-carboxamide (3ia)
2-cinnamyl-3-methyl-1H-indole (4a)
**Supplementary References.**


