Pd-Catalyzed Heck Cyclization and *in-situ* Hydrocarboxylation or Hydromethenylation via A Borrowing Hydrogen Strategy

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Supporting Information

**General Information.** All reactions were carried out under a nitrogen atmosphere unless the reaction procedure states otherwise. Tetrahydrofuran (THF) was distilled from sodium-benzophenone in a continuous still under an atmosphere of N₂. Dioxane was distilled from sodium-benzophenone under an atmosphere of N₂. Dichloromethane were distilled from calcium hydride in a still under and atmosphere of nitrogen. Room temperature reactions were carried out between 20-25 °C. Flash column chromatography was performed using 40-63 μm silica gel as the stationary phase. ¹H and ¹³C NMR spectra were recorded on a Bruker AC-400 FT spectrometer using solvent CDCl₃ residue as an internal reference (7.26 ppm for ¹H NMR and 77.00 ppm for ¹³C NMR). Electron spray ionization (ESI) mass spectrometry data were acquired using a Thermo LTQ Orbitrap XL instrument.
Table S1. Full Results for Reaction Condition Optimization$^a$

![Image](image.png)

<table>
<thead>
<tr>
<th>entry</th>
<th>Pd</th>
<th>ligand</th>
<th>solvent</th>
<th>CHCl\textsubscript{3} (equiv)</th>
<th>T/°C</th>
<th>yield (%)</th>
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<td>dioxane/H\textsubscript{2}O</td>
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$^a$ The reaction was carried out at 0.10 mmol scale of iodide, Pd (5 mol%), ligand (15 mol%), KOH (8.0 equiv) in 1.0 ml of solvent for 1 h; dioxane/H\textsubscript{2}O = 1:4, THF/H\textsubscript{2}O = 1:4. $^b$ TFP = tri(2-furyl)phosphine (5 mol%).
Table S2. Conditions Optimization for the Reaction with Hyrazones$^a$

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<th>Pd</th>
<th>ligand (mol %)</th>
<th>solvent</th>
<th>base</th>
<th>T/$^o$C</th>
<th>yield (%)</th>
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$^a$ The reaction was carried out at 0.10 mmol scale of iodide, Pd (5 mol%), base (3.0 equiv) in 1.5 ml of solvent at indicated temperature for 1 h.
Compounds 1a was prepared following the literature [1].

**Preparation of 1b:**

Oxalyl dichloride (0.61 ml, 7.20 mmol, 2.4 equiv) was added to a solution of (E)-2-methylbut-2-enoic acid (0.36 g, 3.60 mmol, 1.2 equiv) with a drop of DMF in CH$_2$Cl$_2$ (10.0 ml) at room temperature dropwise. The reaction was maintained at room temperature for 30 min and the excess oxalyl dichloride and CH$_2$Cl$_2$ was carefully removed by evaporation.

The above acid chloride in CH$_2$Cl$_2$ (10.0 ml) was added to a mixture of 2-iodoaniline (0.66 g, 2.00 mmol, 1.0 equiv), DMAP (18.3 mg, 0.15 mmol, 0.05 equiv), Et$_3$N (0.84 ml, 6.00 mmol, 2.0 equiv) in CH$_2$Cl$_2$ (10.0 ml) at -20 °C dropwise. After stirring at -20 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO$_3$, extracted with CH$_2$Cl$_2$, washed with brine, and dried over Na$_2$SO$_4$. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.36 g, 60% in mineral oil, 9.00 mmol, 3.0 equiv) was added to a solution of the above amide in DMF (10.0 ml) at room temperature for portions. After stirring for 20 min at room temperature BnBr (0.53 ml, 4.50 mmol, 1.5 equiv) was added dropwise and the reaction mixture was allowed to stir for additional 3 hours. The reaction was quenched by the addition of water, diluted with ethyl acetate (100 ml), washed with water. The organic layer was dried over Na$_2$SO$_4$, concentrated and purified by column chromatography on silica (hexanes: ethyl acetate = 20: 1) to afford 1b (0.41 g, 1.04 mmol, 35% three steps). Solid, 63.1 °C (ethyl acetate/hexanes).

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.86 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.6$ Hz, 1H), 7.26-7.16 (m, 5H), 7.12 (td, $J_1 = 7.8$ Hz, $J_2 = 1.2$ Hz, 1H), 6.92 (td, $J_1 = 7.6$ Hz, $J_2 = 1.6$ Hz, 1H), 6.66 (d, $J = 7.6$ Hz, 1H), 5.76 (bs, 1H), 5.64 (bd, $J = 12.8$ Hz, 1H), 4.14 (bd, $J = 14.0$ Hz, 1H), 1.65 (s, 3H), 1.43 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.8, 144.7, 140.0, 137.0, 132.1, 131.4, 129.9, 129.3, 128.9, 128.5, 128.3, 127.4, 99.8, 51.8, 14.2, 13.3. HRMS (ESI) calcd. for C$_{18}$H$_{19}$NOI$^+$ (M+H)$^+$ 392.0506, found 392.0507.

**Preparation of 1c:**

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.86 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.6$ Hz, 1H), 7.26-7.16 (m, 5H), 7.12 (td, $J_1 = 7.8$ Hz, $J_2 = 1.2$ Hz, 1H), 6.92 (td, $J_1 = 7.6$ Hz, $J_2 = 1.6$ Hz, 1H), 6.66 (d, $J = 7.6$ Hz, 1H), 5.76 (bs, 1H), 5.64 (bd, $J = 12.8$ Hz, 1H), 4.14 (bd, $J = 14.0$ Hz, 1H), 1.65 (s, 3H), 1.43 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.8, 144.7, 140.0, 137.0, 132.1, 131.4, 129.9, 129.3, 128.9, 128.5, 128.3, 127.4, 99.8, 51.8, 14.2, 13.3. HRMS (ESI) calcd. for C$_{18}$H$_{19}$NOI$^+$ (M+H)$^+$ 392.0506, found 392.0507.
The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.20 g, 2.00 mmol, 1.2 equiv)] in CH$_2$Cl$_2$ (6.0 ml) was added to a mixture of 2-iodo-4-methylaniline (0.38 g, 1.60 mmol, 1.0 equiv), DMAP (9.8 mg, 0.08 mmol, 0.05 equiv), Et$_3$N (0.45 ml, 3.20 mmol, 2.0 equiv) in CH$_2$Cl$_2$ (6.0 ml) at -20 °C dropwise. After stirring at -20 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO$_3$, extracted with CH$_2$Cl$_2$, washed with brine, and dried over Na$_2$SO$_4$. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.19 g, 60% in mineral oil, 4.80 mmol, 3.0 equiv) was added to a solution of the above amide in THF (10.0 ml) at 0 °C for portions. After stirring at 0 °C for 20 min MeI (0.21 ml, 3.20 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at 50 °C for 2 hours. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine, dried over Na$_2$SO$_4$, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1c (0.26 g, 0.78 mmol, 49% three steps) as oil. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.68 (s, 1H), 7.11 (d, $J$ = 7.2 Hz, 1H), 6.99 (d, $J$ = 8.4 Hz, 1H), 5.80 (bs, 1H), 3.19 (s, 3H), 2.30 (s, 3H), 1.60 (bs, 3H), 1.45 (bs, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 173.3, 144.5 (bs), 140.4, 139.1, 132.2, 130.0, 128.9, 126.2, 98.7, 37.1 (bs), 20.4, 14.0, 13.3. HRMS (ESI) calcd. for C$_{13}$H$_{17}$NOI$^+$ (M+H)$^+$ 330.0349, found 330.0341.

Preparation of 1d:

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.60 g, 6.00 mmol, 1.2 equiv)] in CH$_2$Cl$_2$ (10.0 ml) was added to a mixture of 2-iodo-4-methoxyaniline [2] (1.25 g, 5.00 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (10.0 ml) at 0 °C, followed by Et$_3$N (2.8 ml, 20.00 mmol, 4.0 equiv) added to the mixture dropwise. After stirring at 0 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO$_3$, extracted with CH$_2$Cl$_2$, washed with brine, and dried over Na$_2$SO$_4$. After filtration and concentration, the crude amide was used in next step without further purification. Sodium hydride (0.40 g, 60% in mineral oil, 10.00 mmol, 2.0 equiv) was added to a solution of the above amide in THF (20.0 ml) at 0 °C for portions. After stirring for 30 min at 0 °C MeI (0.62 ml, 10.00 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine, dried over Na$_2$SO$_4$, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1d (1.02 g, 3.95 mmol, 59% three steps). Solid, 107.8-112.3 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.35 (d, $J$ = 2.0 Hz, 1H), 7.02 (d, $J$ = 8.0 Hz, 1H), 6.85 (d, $J$ = 7.6 Hz, 1H), 5.80 (bs, 1H), 3.79 (s, 3H), 3.18 (s, 3H), 1.60 (bs, 3H), 1.47 (bs, 3H); $^{13}$C NMR
(100 MHz, CDCl₃): δ 173.4, 158.5, 140.0, 132.3, 129.7, 129.5, 124.5, 115.0, 99.3, 55.6, 37.2, 14.1, 13.3. HRMS (ESI) calcd. for C₁₃H₁₆INO₂Na⁺ (M+Na)⁺ 368.0123, found 368.0121.

Preparation of 1e:

[Diagram]

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.60 g, 6.00 mmol, 1.2 equiv)] in CH₂Cl₂ (10.0 ml) was added to a mixture of 2-iodo-4-(trifluoromethyl)aniline (1.44 g, 5.00 mmol, 1.0 equiv) in CH₂Cl₂ (10.0 ml) at 0 °C, followed by Et₃N (2.8 ml, 20.00 mmol, 4.0 equiv) added to the mixture dropwise. After stirring at 0 °C for 30 min and room temperature overnight, the reaction mixture was quenched by the addition of water, extracted with ethyl acetate, washed with brine, and dried over Na₂SO₄. After filtration and concentration, the crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 7: 1 to 5: 1) to afford 1e (0.36 g, 0.93 mmol, 19% three steps). Solid, 69.8-71.5 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 8.12 (s, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 5.81 (bs, 1H), 3.24 (s, 3H), 1.68 (bs, 3H), 1.51 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 172.9, 150.6, 137.1 (q, J = 3.6 Hz), 131.8, 131.1, 130.6 (d, J = 33.1 Hz), 129.4, 126.4 (q, J = 2.9 Hz), 122.5 (q, J = 271.0 Hz), 98.8, 37.1, 14.0, 13.4; ¹⁹F NMR (376 MHz, CDCl₃): δ -62.6. HRMS (ESI) calcd. for C₁₃H₁₃F₃INONa⁺ (M+Na)⁺ 405.9892, found 405.9892.

Preparation of 1f:

[Diagram]

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.60 g, 6.00 mmol, 1.2 equiv)] in CH₂Cl₂ (10.0 ml) was added to a mixture of 2-iodo-4-fluoroaniline (1.44 g, 5.00 mmol, 1.0 equiv) in CH₂Cl₂ (10.0 ml) at 0 °C, followed by Et₃N (2.8 ml, 20.00 mmol, 4.0 equiv) added to the mixture dropwise. After stirring at 0 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO₃, extracted with CH₂Cl₂, washed with brine, and dried over Na₂SO₄. After filtration and concentration, the crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 7: 1 to 5: 1) to afford 1f (0.36 g, 0.93 mmol, 19% three steps). Solid, 69.8-71.5 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 8.12 (s, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 5.81 (bs, 1H), 3.24 (s, 3H), 1.68 (bs, 3H), 1.51 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 172.9, 150.6, 137.1 (q, J = 3.6 Hz), 131.8, 131.1, 130.6 (d, J = 33.1 Hz), 129.4, 126.4 (q, J = 2.9 Hz), 122.5 (q, J = 271.0 Hz), 98.8, 37.1, 14.0, 13.4; ¹⁹F NMR (376 MHz, CDCl₃): δ -62.6. HRMS (ESI) calcd. for C₁₃H₁₃INO₂Na⁺ (M+Na)⁺ 405.9892, found 405.9892.
with brine, and dried over Na₂SO₄. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.40 g, 60% in mineral oil, 10.00 mmol, 2.0 equiv) was added to a solution of the above amide in THF (20.0 ml) at 0 °C for portions. After stirring for 30 min at 0 °C MeI (0.62 ml, 10.00 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine, dried over Na₂SO₄, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1f (0.42 g, 1.26 mmol, 25% three steps). Solid, 95.7-98.0 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.58 (bd, J = 5.2 Hz, 1H), 7.21-6.96 (m, 2H), 5.79 (bs, 1H), 3.20 (s, 3H), 1.63 (bs, 3H), 1.48 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 173.1, 160.4 (d, J = 252.0 Hz), 143.5 (bs), 131.9, 130.2, 129.8, 126.6 (d, J = 24.0 Hz), 116.2 (d, J = 22.0 Hz), 98.7, 37.0 (bs), 14.0, 13.2; ¹⁹F NMR (376 MHz, CDCl₃) : δ -112.6. HRMS (ESI) calcd. for C₁₂H₁₄FINO⁺ (M+H)⁺ 334.0104, found 334.0100.

**Preparation of 1g:**

![Diagram](image)

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enolic acid (0.24 g, 2.40 mmol, 1.2 equiv)] in CH₂Cl₂ (8.0 ml) was added to a mixture of 4-chloro-2-iodoaniline (0.51 g, 2.00 mmol, 1.0 equiv), DMAP (12.2 mg, 0.10 mmol, 0.05 equiv), Et₃N (0.56 ml, 4.00 mmol, 2.0 equiv) in CH₂Cl₂ (8.0 ml) at -20 °C dropwise. After stirring at -20 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO₃, extracted with CH₂Cl₂, washed with brine, and dried over Na₂SO₄. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.24 g, 60% in mineral oil, 6.00 mmol, 3.0 equiv) was added to a solution of the above amide in THF (10.0 ml) at 0 °C for portions. After stirring for 20 min at 0 °C MeI (0.25 ml, 4.00 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at 50 °C for 3 hours. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine, dried over Na₂SO₄, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1g (0.24 g, 0.69 mmol, 34% three steps). Solid, 76.3-81.0 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.84 (d, J = 2.4 Hz, 1H), 7.30 (dd, J₁ = 8.4 Hz, J₂ = 2.0 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 5.78 (bs, 1H), 3.18 (s, 3H), 1.64 (bs, 3H), 1.48 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 172.1, 145.0 (bs), 138.4, 132.5, 131.0, 129.6 (bs), 128.8, 128.5, 98.2, 36.1 (bs), 13.1, 12.4. HRMS (ESI) calcd. for C₁₂H₁₄NOI⁺Cl⁻ (M+H⁻)⁻ 349.9803, found 349.9797.

**Preparation of 1h:**
The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.33 g, 3.30 mmol, 1.1 equiv)] in CH$_2$Cl$_2$ (7.0 ml) was added to a mixture of 4-bromo-2-iodoaniline (0.88 g, 3.00 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (7.0 ml) at 0 °C dropwise, followed by Et$_3$N (1.60 ml, 12.00 mmol, 4.0 equiv) added to the mixture dropwise. After stirring at -20 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO$_3$, extracted with CH$_2$Cl$_2$, washed with brine, and dried over Na$_2$SO$_4$. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.24 g, 60% in mineral oil, 6.00 mmol, 2.0 equiv) was added to a solution of the above amide in DMF (10.0 ml) at 0 °C for portions. After stirring for 30 min at room temperature MeI (0.37 ml, 6.00 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water, diluted with ethyl acetate, washed with water and brine, dried over Na$_2$SO$_4$, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1h (0.42 g, 1.07 mmol, 35% three steps). Solid, 95.1-97.3 °C (ethyl acetate/hexanes).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.01 (d, $J = 2.0$ Hz, 1H), 7.46 (dd, $J_1 = 8.4$ Hz, $J_2 = 2.0$ Hz, 1H), 7.00 (d, $J = 8.4$ Hz, 1H), 5.80 (bs, 1H), 3.20 (s, 3H), 1.65 (bs, 3H), 1.50 (bs, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 172.8, 146.3 (bs), 141.9, 132.3, 131.8, 130.5, 130.1, 121.2, 99.6, 36.9 (bs), 14.0, 13.3. HRMS (ESI) calcd. for C$_{12}$H$_{13}$N$_8$I$_2$BrINONa$^+$ (M+Na)$^+$ 415.9123, found 415.9122.

Preparation of 1i:

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.44 g, 4.40 mmol, 1.5 equiv)] in CH$_2$Cl$_2$ (10.0 ml) was added to a mixture of 2-iodo-5-methoxyaniline $^3$ (0.72 g, 2.90 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (10.0 ml) at 0 °C, followed by Et$_3$N (0.81 ml, 5.80 mmol, 2.0 equiv) added to the mixture dropwise. After stirring at 0 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO$_3$, extracted with CH$_2$Cl$_2$, washed with brine, and dried over Na$_2$SO$_4$. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.15 g, 60% in mineral oil, 3.80 mmol, 1.3 equiv) was added to a solution of the above amide in THF (15.0 ml) at 0 °C for portions. After stirring for 30 min at 0 °C MeI (0.36 ml, 5.80 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine,
dried over Na₂SO₄, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 5: 1) to afford 1i (0.34 g, 0.98 mmol, 34% three steps). Solid, 82.7-89.5 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.71 (d, J = 8.8 Hz, 1H), 6.70 (bs, 1H), 6.60 (d, J = 7.2 Hz, 1H), 5.84 (bs, 1H), 3.77 (s, 3H), 3.22 (bs, 3H), 1.66 (bs, 3H), 1.49 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 173.2, 160.6, 148.0, 140.2, 132.2, 130.2, 115.4, 115.1, 87.3, 55.6, 37.1, 14.1, 13.4. HRMS (ESI) calcd. for C₁₃H₁₆INO₂Na⁺ (M+Na)⁺ 368.0123, found 368.0124.

**Preparation of 1j:**

![Chemical Reaction Diagram]

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.60 g, 6.00 mmol, 1.2 equiv)] in CH₂Cl₂ (10.0 ml) was added to a mixture of 5-chloro-2-iodoaniline (1.27 g, 5.00 mmol, 1.0 equiv) in CH₂Cl₂ (10.0 ml) at 0 °C, followed by Et₃N (2.8 ml, 20.00 mmol, 4.0 equiv) added to the mixture dropwise. After stirring at 0 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO₃, extracted with CH₂Cl₂, washed with brine, and dried over Na₂SO₄. After filtration and concentration, the crude amide was used in next step without further purification.

Sodium hydride (0.40 g, 60% in mineral oil, 10.00 mmol, 2.0 equiv) was added to a solution of the above amide in THF (20.0 ml) at 0 °C for portions. After stirring for 30 min at 0 °C MeI (0.62 ml, 10.00 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine, dried over Na₂SO₄, concentrated. The crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1j (0.60 g, 1.72 mmol, 34% three steps). Solid, 103.3-107.8 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.78 (d, J = 8.4 Hz, 1H), 7.14 (s, 1H), 6.99 (d, J = 7.6 Hz, 1H), 5.81 (bs, 1H), 3.21 (s, 3H), 1.68 (bs, 3H), 1.51 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 172.9, 148.3 (bs), 140.7, 134.9, 131.8, 130.7, 129.5, 129.1, 96.3, 37.0 (bs), 14.0, 13.4. HRMS (ESI) calcd. for C₁₂H₁₃₃(Cl)NNONa⁺ (M+Na)⁺ 371.9628, found 371.9623.

**Preparation of 1k:**

A mixture of 4-methoxyphenylboronic acid (3.65 g, 24.00 mmol, 1.2 equiv), 4-bromo-2-nitroaniline (4.34 g, 20.00 mmol, 1.0 equiv), Pd(PPh₃)₄ (1.15 g, 1.00 mmol, 0.05 equiv) in 2 M K₂CO₃ (aq.) (30.0 ml) and DMF (30.0 ml) was heated at 100 °C for 3 days. Then the mixture was filtered through a pad of celite and extracted with ethyl acetate (300 ml), washed with water and brine, dried over Na₂SO₄. After
filtration and concentration, the crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 4'-methoxy-3-nitrobiphenyl-4-amine (4.59 g, 18.80 mmol, 94%).

To a solution of p-TsOH·H2O (8.56 g, 45.00 mmol, 3.0 equiv) in MeCN (200 mL) was added the aromatic amine (3.66 g, 15.00 mmol, 1.0 equiv) and stirred for 2 min. After being cooled to 10-15 °C the resulting suspension was added a solution of NaNO2 (2.07 g, 30.00 mmol, 2.0 equiv) and KI (6.23 g, 37.50 mmol, 2.5 equiv) in H2O (25.0 mL) gradually. The reaction mixture was stirred for 10 min before warmed to room temperature and stirred overnight. To the reaction mixture was added H2O, saturated NaHCO3 and Na2S2O3. After filtered through a pad of celite, extracted with ethyl acetate and dried over Na2SO4. After filtration and concentration, the crude iodide was obtained[4].

Iron power (4.12 g, 75.00 mmol, 5.0 equiv) was added to a mixture of the crude iodide in AcOH (50.0 ml) and EtOH (50.0 ml) at room temperature. The mixture was stirred at 100 °C for 1.3 hours. After cooling to room temperature, AcOH and EtOH were removed by evaporation and the residue was neutralized with saturated NaHCO3. Then the mixture was filtered through a pad of celite, extracted with ethyl acetate and dried over Na2SO4. After filtration and concentration, the residue was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford S1[5] (3.31 g, 10.2 mmol, 68%). Solid, 160.0-162.8 °C (ethyl acetate/hexanes). 1H NMR (400 MHz, CDCl3): δ 7.65 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.00-6.87 (m, 3H), 6.68 (dd, J1 = 8.0 Hz, J2 = 2.0 Hz, 1H), 4.14 (bs, 2H), 3.84 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 159.3, 146.9, 142.3, 139.1, 132.8, 127.9, 118.7, 114.2, 112.9, 82.1, 55.3. HRMS (ESI) calcd. for C13H13INO+ (M+H)+ 326.0042, found 326.0034.

Sodium cyanoborohydride (0.23 g, 3.60 mmol, 1.2 equiv) was added to a stirred mixture of 4-iodo-4'-methoxybiphenyl-3-amine (0.98 g, 3.00 mmol, 1.0 equiv), zinc(II) chloride (0.49 g, 3.6 mmol, 1.2 equiv) and benzaldehyde (0.37 mL, 3.60 mmol, 1.2 equiv) in methanol (30.0 mL), and the reaction mixture was refluxed under nitrogen for 2 hours. After cooling to room temperature, the reaction mixture was diluted with 10% aq. NaOH (15 mL) and methanol was removed by evaporation. Then the mixture was extracted with ethyl acetate, dried over Na2SO4 and concentrated, the crude N-benzyl-4-iodo-4'-methoxybiphenyl-3-amine was used in next step without further purification.[6]

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.36 g, 3.60 mmol, 1.2 equiv)] in CH2Cl2 (15.0 ml) was added to the crude N-benzyl-4-iodo-4'-methoxybiphenyl-3-amine in CH2Cl2 (15.0 ml) at 0 °C, followed by Et3N (2.8 ml, 20.00 mmol, 4.0 equiv) added to the mixture dropwise. After stirring
at 0 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO₃, extracted with ethyl acetate, washed with brine, and dried over Na₂SO₄. After filtration and concentration, the crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10:1) to afford 1k (0.30 g, 0.60 mmol, 20% three steps). Solid, 109.8-114.5 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.86 (d, J = 8.0 Hz, 1H), 7.20-7.13 (m, 2H), 6.76 (s, 1H), 5.83 (bs, 1H), 5.72 (d, J = 13.2 Hz, 1H), 4.14 (d, J = 13.2 Hz, 1H), 3.81 (s, 3H), 1.68 (bs, 3H), 1.44 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃) rotaters : δ 174.3, 172.5, 159.3 (bs), 144.6, 141.1, 140.2, 139.8, 136.9, 135.4, 134.0, 132.0, 131.0, 129.7, 129.3, 129.2, 127.8, 127.5, 127.2, 126.8, 114.0, 97.0, 55.1, 51.5 (bs), 14.1, 13.8, 13.1, 13.0. HRMS (ESI) calcd. for C₂₅H₂₄INO₂Na⁺ (M+Na)⁺ 520.0749, found 520.0756.

Preparation of 1l:

Sodium hydride (0.34 g, 60% in mineral oil, 8.60 mmol, 2.0 equiv) was added to a solution of the amide [7] (1.20 g, 4.30 mmol, 1.0 equiv) in THF (20.0 ml) and DMF (3.0 ml) at 0 °C for portions. After stirring for 30 min at 0 °C 5-bromopent-1-ene (0.76 g, 5.10 mmol, 1.2 equiv) was added dropwise and the reaction mixture was allowed to stir at 65 °C for 24 hours. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with water and brine, dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica (hexanes: ethyl acetate = 10:1) to afford 1l (1.29 g, 3.50 mmol, 81%) as oil. ¹H NMR (100 MHz, CDCl₃): δ 7.87 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.98 (t, J = 7.2 Hz, 1H), 5.86-5.62 (m, 2H), 5.07-4.84 (m, 2H), 4.10 (bs, 1H), 3.23 (bs, 1H), 2.16-1.95 (m, 2H), 1.85-1.53 (m, 5H), 1.42 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 172.7, 145.3 (bs), 140.2, 137.7, 132.3, 130.8, 129.7, 128.8, 114.9, 100.0, 48.7 (bs), 31.1, 26.3, 14.1, 13.3. HRMS (HESI) calcd. for C₁₆H₂₁NO⁺ (M+H)⁺ 370.0662, found 370.0664.

Preparation of 1m [8]:

Potassium hydroxide (0.36 g, 6.40 mmol, 2.0 equiv) and ⁴Bu₄NHSO₄ (54.3 mg, 0.16 mmol, 0.05 equiv) was added to a solution of the amide (0.96 g, 3.20 mmol, 1.0 equiv) in toluene (20.0 ml) at room temperature successively. After stirred at room temperature for 3 hours, 3-methylbut-3-enyl 4-methylbenzenesulfonylate (0.78 g, 3.20 mmol, 1.0 equiv) was added and the mixture was stirred at 80 °C for 6 hours. The
reaction was quenched by the addition of water, extracted with ethyl acetate, dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford 1m (0.68 g, 1.8 mmol, 58%). Solid, 45.7-47.9 °C (ethyl acetate/hexanes) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.88 (d, J = 6.8 Hz, 1H), 7.43-7.29 (m, 1H), 7.12 (d, J = 6.0 Hz, 1H), 7.06-6.92 (m, 1H), 5.72 (s, 1H), 4.76 (s, 1H), 4.71 (bs, 1H), 4.30 (bs, 1H), 3.30 (bs, 1H), 2.47-2.16 (m, 2H), 1.71 (bs, 3H), 1.62 (s, 3H), 1.43 (bs, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 172.8, 143.1, 140.2, 132.4, 131.0, 129.7, 128.85, 128.80, 128.76, 111.6, 100.0, 47.5, 35.1, 22.6, 14.1, 13.3. HRMS (ESI) calcd. for C₁₆H₂₀INONa⁺ (M+Na)⁺ 392.0487, found 392.0485.

Preparation of 1n:

To a solution of p-TsOH·H₂O (6.33 g, 33.3 mmol, 3.0 equiv) in MeCN (200 mL) was added 2-nitro-4-(phenylethynyl)aniline [⁹] (2.65 g, 11.10 mmol, 1.0 equiv) and stirred for 2 min. After being cooled to 10-15 °C, the resulting suspension was added a solution of NaNO₂ (1.53 g, 22.20 mmol, 2.0 equiv) and KI (4.61 g, 27.80 mmol, 2.5 equiv) in H₂O (25.0 ml) gradually. The reaction mixture was stirred for 10 min before warmed to room temperature and stirred overnight and quenched by the addition of H₂O, saturated NaHCO₃ and Na₂S₂O₃. After filtered through a pad of celite, the filtrate was extracted with ethyl acetate, dried over Na₂SO₄. Filtration and concentration gave the crude iodide, which was used in next step without further purification.

Iron power (3.10 g, 55.50 mmol, 5.0 equiv) was added to a mixture of the crude iodide in AcOH (40.0 ml) and EtOH (40.0 ml) at room temperature. The mixture was stirred at 100 °C for 1.5 hours. After cooling to room temperature AcOH and EtOH was removed by evaporation, the residue was neutralized with saturated NaHCO₃ and filtered through a pad of celite. The filtrate was extracted with ethyl acetate and dried over Na₂SO₄. After filtration and concentration, the residue was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford S2 (2.21 g, 6.90 mmol, 63%). Solid, 70.3 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.61 (d, J = 8.0 Hz, 1H), 7.56-7.45 (m, 2H), 7.41-7.29 (m, 3H), 6.91 (s, 1H), 6.65 (d, J = 8.0 Hz, 1H), 4.12 (bs, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 146.6, 138.9, 131.6, 128.4, 128.3, 124.2, 123.03, 123.01, 117.1, 89.8, 88.7, 84.2. HRMS (ESI) calcd. for C₁₄H₁₁IN⁺ (M+H)⁺ 319.9936, found 319.9934.
The crude acid chloride [prepared as above from (E)-2-methylbut-2-enoic acid (0.45 g, 4.50 mmol, 1.5 equiv)] in CH$_2$Cl$_2$ (10.0 ml) was added to a mixture of S2 (0.96 g, 3.0 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (10.0 ml) at 0 °C, followed by Et$_3$N (0.84 ml, 6.00 mmol, 2.0 equiv) added to the mixture dropwise. After stirring at 0 °C for 30 min and room temperature overnight, the mixture was quenched with the addition of saturated NaHCO$_3$, extracted with CH$_2$Cl$_2$, washed with brine and dried over Na$_2$SO$_4$. Filtration and concentration gave the crude amide, which was used in next step without further purification.

Sodium hydride (0.16 g, 60% in mineral oil, 3.90 mmol, 1.3 equiv) was added to a solution of the above amide in THF (15.0 ml) at 0 °C for portions. After stirring for 30 min at 0 °C MeI (0.37 ml, 6.00 mmol, 2.0 equiv) was added dropwise and the reaction mixture was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water, extracted with ethyl acetate, washed with brine, dried over Na$_2$SO$_4$, concentrated and purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford In (0.46 g, 1.10 mmol, 36% three steps). Solid, 111.6-116.0 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.84 (d, $J$ = 8.0 Hz, 1H), 7.58-7.48 (m, 2H), 7.42-7.33 (m, 3H), 7.30 (s, 1H), 7.12 (d, $J$ = 8.0 Hz, 1H), 5.83 (bs, 1H), 3.23 (s, 3H), 1.69 (bs, 3H), 1.50 (bs, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 173.0, 147.4 (bs), 140.1, 132.0, 131.9, 131.60, 131.56, 130.7, 128.8, 128.4, 124.7, 122.4, 99.0, 91.5, 87.4, 37.0 (bs), 14.2, 13.4. HRMS (ESI) calcd. for C$_{20}$H$_{18}$INONa$^+$ (M+Na)$^+$ 438.0331, found 438.0330.

Preparation of 1o:

A solution of S3 $^{[10]}$ (1.16 g, 6.00 mmol, 1.2 equiv), Pd(OAc)$_2$ (11.0 mg, 0.05 mmol, 1 mol %), SPhos (26.7 mg, 0.065 mmol, 1.3 mol %), 4-Methoxyphenylboronic acid (0.76 g, 5.00 mmol, 1.0 equiv), K$_3$PO$_4$ (1.38 g, 6.50 mmol, 1.3 equiv) in THF (40 ml) was stirred at 40 °C for 24 hours. The reaction mixture was diluted with water and extracted with ethyl acetate, dried over MgSO$_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexanes: ethyl acetate = 50: 1) to afford the crude cross-coupling ester $^{[11]}$ (0.34 g, 31%). Then to a solution of the above crude ester (0.34 g, 1.50 mmol, 1.0 equiv) in EtOH (10 mL, 95%) was added 10% aq. NaOH (4 ml). The mixture was stirred at 55 °C for 2 hours. After being cooled to room temperature, EtOH was removed by evaporation. The residue mixture was diluted with ethyl acetate (50 ml), washed with 10% aq. NaOH (10 ml×2). The water layer was acidified with 2 M HCl, extracted with ethyl acetate. The organic layer was dried over Na$_2$SO$_4$, concentrated and the residue was used in next step without purification.
The crude acid chloride [prepared as above from S4 (1.50 mmol, 1.0 equiv)] in THF (5.0 ml) was added to a mixture of 2-iodo-N-methylaniline (0.35 g, 1.50 mmol, 1.0 equiv) and K₂CO₃ (0.42 g, 3.00 mmol, 2.0 equiv) in THF (10.0 ml) at room temperature dropwise. After stirring at room temperature overnight, the mixture was quenched with the addition of saturated NaHCO₃, extracted with ethyl acetate, washed with brine, and dried over Na₂SO₄. After filtration and concentration, the crude amide was purified by column chromatography on silica (hexanes: ethyl acetate = 8: 1 to 10: 1) to afford 1o (0.23 g, 0.56 mmol, 38%) as viscous oil.

\[ {^1}H \text{ NMR (400 MHz, CDCl}_3 \text{): } \delta 7.69 (d, J = 8.0 \text{ Hz, } 1\text{H}), 7.05 (t, J = 7.6 \text{ Hz, } 1\text{H}), 6.84 (td, J_1 = 8.0 \text{ Hz, } J_2 = 0.8 \text{ Hz, } 1\text{H}), 6.72-6.62 (m, 5\text{H}), 6.34 (q, J = 6.8 \text{ Hz, } 1\text{H}), 3.76 (s, 3\text{H}), 3.19 (s, 3\text{H}), 1.57 (d, J = 7.2 \text{ Hz, } 3\text{H}); \]
\[ {^{13}}C \text{ NMR (100 MHz, CDCl}_3 \text{): } \delta 171.6, 158.4, 145.7, 139.6, 138.5, 131.3, 130.0, 129.7, 128.7, 128.6, 127.7, 113.3, 99.2, 55.2, 36.8, 14.3. \]
HRMS (ESI) calcd. for C₁₈H₁₈INO₂Na⁺ (M+Na)⁺ 430.0280, found 430.0284.

Preparation of 1p:

To a solution of S5[¹²] (1.57 g, 4.64 mmol, 1.0 equiv) in MeCN (10 mL) was added a solution of BnNH₂ (1.0 ml, 9.28 mmol, 2.0 equiv) in MeCN (5 mL) and stirred at 50 °C for overnight. After being cooled to room temperature, MeCN was removed by evaporation. The residue mixture was neutralized with 10% aq. NaOH, extracted with ethyl acetate, dried over Na₂SO₄. After filtration and concentration, the crude product was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1 to 5: 1) to afford S6 (0.71 g, 2.60 mmol, 56%) as oil. \[ {^1}H \text{ NMR (400 MHz, CDCl}_3 \text{): } \delta 7.39-7.30 (m, 4\text{H}), 7.29-7.23 (m, 1\text{H}), 6.27 (q, J = 1.6 \text{ Hz, } 1\text{H}), 5.94-5.82 (m, 1\text{H}), 3.71 (s, 2\text{H}), 3.38 (dd, J_1 = 1.2 \text{ Hz, } J_2 = 0.8 \text{ Hz, } 2\text{H}); \]
\[ {^{13}}C \text{ NMR (100 MHz, CDCl}_3 \text{): } \delta 139.7, 128.4, 128.3, 127.1, 126.4, 113.4, 60.1, 51.3. \]
HRMS (ESI) calcd. for C₁₀H₁₃INa⁺ (M+Na)⁺ 274.0093, found 274.0086.

The crude acid chloride [prepared as above from (E)-2-methylbut-2-enioic acid (0.50 g, 3.90 mmol, 1.5 equiv)] in CH₂Cl₂ (5.0 ml) was added to a mixture of S6 (0.71 g, 2.60 mmol, 1.0 equiv) and Et₃N (0.72 ml, 5.20 mmol, 2.0 equiv) in CH₂Cl₂ (10.0 ml) at 0 °C dropwise. After stirring at room temperature overnight, the mixture was quenched with the addition of saturated NaHCO₃, extracted with CH₂Cl₂, washed
with brine, and dried over Na₂SO₄. After filtration and concentration, the crude amide was purified by column chromatography on silica (hexanes: ethyl acetate = 15: 1 to 10: 1) to afford 1p (0.75 g, 2.11 mmol, 81%) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.24 (m, 3H), 7.23-7.12 (m, 2H), 6.15 (bs, 1H), 5.93 (s, 1H), 5.77 (bs, 1H), 4.59 (s, 2H), 4.10 (bs, 2H), 1.90 (t, J = 1.2 Hz, 3H), 1.70 (dd, J₁ = 6.8 Hz, J₂ = 1.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 174.1, 136.4, 131.5, 128.6, 127.5, 127.4, 126.1, 106.3 (bs), 58.9 (bs), 53.2 (bs), 51.1 (bs), 46.0 (bs), 14.3, 13.1. HRMS (ESI) calcd. for C₁₅H₁₉INO⁺ (M+H)⁺ 356.0511, found 356.0511.

3-(1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2a):

Typical Procedure: Chloroform (65 μl, 0.80 mmol, 4.0 equiv) was added to a mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)₂ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) under nitrogen, followed by H₂O (1.60 ml) was added. After stirring at room temperature for 0.5 min, dioxane (0.40 ml) was added and the reaction mixture was stirred at room temperature for additional 1 min before heated to 80 °C for 1 hour. After complete consumption of starting material, the mixture was cooled to room temperature, quenched with 1 M HCl (6 ml) and extracted with EtOAc (3×20 ml). The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1) to afford 2a (36.7 mg, 79%) and 3 (6.3 mg, 17%).

2a: Solid, 119.6-121.8 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.27 (m, 1H), 7.18 (d, J = 7.2 Hz, 1H), 7.07 (t, J = 7.2 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 3.21 (s, 3H), 2.28-2.17 (m, 1H), 2.14-2.03 (m, 2H), 2.00-1.85 (m, 1H), 1.38 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 179.9, 177.8, 143.2, 132.8, 128.0, 123.8, 122.5, 115.2, 108.2, 47.50, 32.65, 29.20, 26.20, 23.53. The spectra were identical with the reported data. [13]

3: Oil. ¹H NMR (400 MHz, CDCl₃): δ 7.29 (td, J₁ = 7.6 Hz, J₂ = 1.2 Hz, 1H), 7.19 (ddd, J₁ = 7.2 Hz, J₂ = 1.2 Hz, J₃ = 0.8 Hz, 1H), 7.09 (td, J₁ = 7.6 Hz, J₂ = 1.2 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 5.95 (dd, J₁ = 17.2 Hz, J₂ = 10.4 Hz, 1H), 5.19-5.09 (m, 2H), 3.21 (s, 3H), 1.49 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 178.7, 143.0, 138.0, 132.7, 128.0, 123.8, 122.5, 115.2, 108.2, 51.2, 26.3, 22.4. The spectra were identical with the reported data. [14]

The reaction with carbon monoxide:
An autoclave containing Pd(PPh₃)₂Cl₂ (14.0 mg, 0.02 mmol, 5 mol %), PPh₃ (21.0 mg, 0.08 mmol, 20 mol %), 1a (0.126 g, 0.40 mmol, 1.0 equiv), NEt₃ (0.22 ml, 1.60 mmol, 4.0 equiv) and DMF/H₂O (4.0 ml/0.40 ml) filled with CO at 5 atm and evacuated (this sequence was repeated three times). The autoclave was warmed up to 80 °C and stirred for 1.5 hours. The mixture was then cooled to room temperature and diluted with ethyl acetate (100 ml). The mixture was washed with 10 % aq. NaOH (3×10 ml).

The combined aqueous phase was then extracted with ethyl acetate (1×10 ml). All of the organic layer was combined, dried over Na₂SO₄, concentrated and purified by column chromatography on silica (ethyl acetate: hexanes = 1: 10) to afford 3 (11.7 mg, 16%).

The water layer was acidified with 2 M HCl till pH ~ 1, extracted with ethyl acetate (3×30 ml). The organic layer was dried over Na₂SO₄, concentrated and the residue was purified by column chromatography on silica (dichloromethane: ethyl acetate = 20: 3) to afford 2a′ (30.2 mg, 32%) and 2a (44.1 mg, 47%) (ethyl acetate: hexanes: AcOH = 50: 50: 1).

2a′: Viscous oil. ¹H NMR (400 MHz, CDCl₃): δ 7.34 (td, J₁ = 7.6 Hz, J₂ = 1.6 Hz, 1H), 7.23-7.13 (m, 2H), 6.94 (d, J = 7.6 Hz, 1H), 3.30 (s, 3H), 3.10 (q, J = 7.2 Hz, 1H), 1.53 (s, 3H), 0.97 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 181.7, 174.7, 142.5, 132.2, 128.7, 124.2, 122.2, 109.0, 49.6, 48.3, 26.6, 22.6, 13.3. HRMS (ESI) calcd. for C₁₃H₁₅NO₃Na⁺ (M+Na)⁺ 256.0950, found 256.0953.

3-(N-benzyl-3'-methyl-2'-oxoindolin-3'-yl)propanoic acid (2b):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1b (78.2 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)₂ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H₂O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2b (35.5 mg, 57%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1) as viscous oil. ¹H NMR (400 MHz, CDCl₃): δ 7.36-7.22 (m, 5H), 7.21-7.11 (m, 2H), 7.03 (t, J = 7.2 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 4.94 (d, J = 15.6 Hz, 1H), 4.89 (d, J = 15.6 Hz, 1H), 2.37-2.22 (m, 1H), 2.21-2.06 (m, 2H), 2.02-1.87 (m, 1H), 1.44 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 180.0, 178.2, 142.2, 135.8, 132.7, 128.8, 128.1, 127.6, 127.2, 122.7, 109.2, 47.5, 43.7, 32.6, 29.3, 23.9. HRMS (ESI) calcd. for C₁₉H₁₈NO₃⁻ (M-H)⁻ 308.1281, found 308.1286.

3-(1',3',5'-trimethyl-2'-oxoindolin-3'-yl)propanoic acid (2c):

S16
The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1e (65.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2e (30.7 mg, 62%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 90.8-96.7 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.06 (d, $J$ = 7.6 Hz, 1H), 6.98 (s, 1H), 6.73 (d, $J$ = 7.6 Hz, 1H), 3.18 (s, 3H), 2.23 (s, 3H), 2.23-2.17 (m, 1H), 1.97-1.81 (m, 1H), 1.36 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 179.9, 178.1, 140.7, 132.8, 128.3, 123.5, 107.9, 47.6, 32.7, 29.3, 26.2, 23.5, 21.1. HRMS (ESI) calcd. for C$_{14}$H$_{16}$NO$_3$ (M-H) 246.1125, found 246.1132.

3-(5'-methoxy-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2d):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1d (69.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2d (35.1 mg, 68%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 138.8-140.4 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.85-6.70 (m, 3H), 3.80 (s, 3H), 3.18 (s, 3H), 2.30-2.14 (m, 1H), 2.14-1.99 (m, 2H), 1.97-1.81 (m, 1H), 1.36 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 179.5, 178.1, 156.2, 136.6, 134.1, 112.2, 110.2, 108.5, 55.7, 48.0, 32.7, 29.3, 26.3, 23.6. HRMS (ESI) calcd. for C$_{14}$H$_{17}$NO$_3$Na$^+$ (M+Na)$^+$ 286.1055, found 286.1057.

3-(1',3'-dimethyl-2'-oxo-5'-trifluoromethyl)indolin-3'-yl)propanoic acid (2e):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1e (76.6 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2e (38.7 mg, 64%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 139.8-143.9 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.56 (d, $J$ = 8.4 Hz, 1H), 7.40 (s, 1H), 6.92 (d, $J$ = 8.4 Hz, 1H), 3.24 (s, 3H), 2.33-2.18 (m, 1H), 2.18-2.03 (m, 2H), 1.98-1.83 (m, 1H), 1.41 (s, 3H). $^{13}$F NMR (376 MHz, CDCl$_3$): $\delta$ -61.41. HRMS (ESI) calcd. for C$_{14}$H$_{14}$F$_3$NO$_3$Na$^+$ (M+Na)$^+$ 324.0823, found 324.0823.
3-(5'-fluoro-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2f):

![Chemical Structure](image)

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1f (66.6 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2f (33.7 mg, 67%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 146.2-150.3 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.01-6.89 (m, 2H), 6.77 (dd, $J_1 = 8.4$ Hz, $J_2 = 4.0$ Hz, 1H), 3.20 (s, 3H), 2.29-2.17 (m, 1H), 2.15-2.00 (m, 2H), 1.37 (s, 3H); $^13$C NMR (100 MHz, CDCl$_3$): δ 179.5, 178.1, 159.4 (d, J = 239.7 Hz), 139.0 (d, J = 1.8 Hz), 134.5 (d, J = 7.8 Hz), 114.4 (d, J = 23.3 Hz), 110.9 (d, J = 24.5 Hz), 108.7 (d, J = 8.1 Hz), 48.0 (d, J = 1.6 Hz), 32.6, 29.2, 26.3, 23.4. $^{19}$F NMR (376 MHz, CDCl$_3$): δ -120.1. HRMS (ESI) calcd. for C$_{14}$H$_{14}$FNO$_3$Na$^+$ (M+Na)$^+$ 274.0855, found 274.0855.

3-(5'-chloro-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2g):

![Chemical Structure](image)

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1g (69.9 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2g (37.4 mg, 70%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 140.6-144.6 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.26-7.22 (m, 1H), 7.15 (d, J = 2.0 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 3.19 (s, 3H), 2.29-2.18 (m, 1H), 2.16-2.02 (m, 2H), 1.98-1.84 (m, 1H), 1.37 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 179.4, 177.9, 141.7, 134.5, 128.2, 128.1, 123.3, 109.1, 47.8, 32.6, 29.2, 26.3, 23.4. HRMS (ESI) calcd. for C$_{13}$H$_{14}$NO$_3^{15}$Cl (M-H) -141.0579, found 141.0579.

3-(5'-bromo-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2h):

![Chemical Structure](image)

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1h (78.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2h (35.7 mg, 58%) (dichloromethane: ethyl
acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 134.7-138.9 °C (ethyl acetate/hexanes). 1H NMR (400 MHz, CDCl3): δ 7.39 (dd, J1 = 8.4 Hz, J2 = 2.0 Hz, 1H), 7.28 (d, J = 2.0 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 3.19 (s, 3H), 2.29-2.17 (m, 1H), 2.16-2.02 (m, 2H), 1.98-1.84 (m, 1H), 1.37 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 179.2, 178.1, 142.2, 134.8, 131.0, 126.0, 115.5, 109.6, 47.8, 32.5, 29.2, 26.3, 23.4. HRMS (ESI) calcd. for C13H1479BrNO3Na+ (M+Na)+ 334.0055, found 334.0054.

3-(6'-methoxy-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2i):

The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), 1i (69.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)2 (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H2O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1.5 hours afforded 2i (34.1 mg, 65%) (dichloromethane: ethyl acetate: hexanes: AcOH = 50: 50: 1) as viscous oil. 1H NMR (400 MHz, CDCl3): δ 7.05 (d, J = 8.4 Hz, 1H), 6.55 (d, J = 7.2 Hz, 1H), 6.43 (s, 1H), 3.81 (s, 3H), 3.18 (s, 3H), 2.27-2.13 (m, 1H), 2.13-1.98 (m, 2H), 1.97-1.80 (m, 1H), 1.35 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 180.5, 178.4, 160.2, 144.4, 124.6, 123.2, 106.5, 96.2, 55.5, 47.0, 32.8, 29.3, 26.2, 23.7. HRMS (ESI) calcd. for C14H17NO4Na+ (M+Na)+ 286.1055, found 286.1057.

3-(6'-chloro-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2j):

The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), 1j (69.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)2 (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H2O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2j (30.9 mg, 58%) (dichloromethane: ethyl acetate: hexanes: AcOH = 50: 50: 1) as viscous oil. 1H NMR (400 MHz, CDCl3): δ 7.08 (d, J = 8.0 Hz, 1H), 7.03 (dd, J = 1.6 Hz, 1H), 6.84 (d, J = 1.6 Hz, 1H), 3.19 (s, 3H), 2.27-2.15 (m, 1H), 2.13-2.01 (m, 2H), 1.97-1.83 (m, 1H), 1.36 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 179.8, 178.2, 144.4, 133.9, 131.0, 123.6, 122.5, 108.9, 47.3, 32.5, 29.2, 26.3, 23.5. HRMS (ESI) calcd. for C13H1435ClNO3Na+ (M+Na)+ 290.0560, found 290.0559.

3-(N-benzyl-6'-(4''-methoxyphenyl)-3'-methyl-2'-oxoindolin-3'-yl)propanoic acid (2k):
The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1k (99.5 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2k (37.8 mg, 45%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes). Solid, 134.6-138.9 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.38 (d, $J = 8.4$ Hz, 2H), 7.36-7.24 (m, 5H), 7.20 (s, 2H), 6.90 (s, 1H), 4.99 (d, $J = 15.6$ Hz, 1H), 4.93 (d, $J = 15.6$ Hz, 1H), 3.84 (s, 3H), 2.37-2.24 (m, 1H), 2.30-2.10 (m, 2H), 2.08-1.93 (m, 1H), 1.47 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 180.2, 178.4, 159.3, 142.8, 141.3, 135.9, 133.4, 131.0, 128.8, 128.1, 127.7, 127.2, 122.9, 121.3, 114.2, 107.7, 55.3, 47.3, 43.7, 32.6, 29.4, 23.9. HRMS (ESI) calcd. for C$_{26}$H$_{25}$NO$_4$Na$^+$ (M+Na)$^+$ 438.1678, found 438.1678.

3-(3'-methyl-2'-oxo-N-(pent-4''-enyl)indolin-3'-yl)propanoic acid (2l):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1l (73.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2l (34.5 mg, 60%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes). Solid, 67.3-71.8 °C (ethyl acetate/hexanes). $^1$H NMR (400 MHz, CDCl$_3$): δ 7.39-7.22 (m, 1H), 7.17 (d, $J = 6.8$ Hz, 1H), 7.05 (t, $J = 7.2$ Hz, 1H), 6.85 (d, $J = 7.8$ Hz, 1H), 5.91-5.75 (m, 1H), 5.13-4.93 (m, 2H), 3.80-3.63 (m, 2H), 2.28-2.18 (m, 1H), 2.18-2.02 (m, 4H), 1.88 (t, $J = 11.2$ Hz, 1H), 1.83-1.70 (m, 2H), 1.37 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 179.7, 178.2, 142.5, 137.2, 132.9, 128.1, 122.8, 122.6, 115.6, 108.4, 47.4, 39.4, 32.6, 31.0, 29.2, 26.6, 23.7. HRMS (ESI) calcd. for C$_{17}$H$_{21}$NO$_3$Na$^+$ (M+Na)$^+$ 310.1419, found 310.1419.

3-(3'-methyl-N-(3''-methylbut-3''-enyl)-2'-oxoindolin-3'-yl)propanoic acid (2m):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1m (73.8 mg, 0.20
mmol, 1.0 equiv), Pd(OAc)₂ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H₂O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2m (30.0 mg, 52%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.29-7.23 (m, 1H), 7.17 (d, J = 7.2 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 4.77 (s, 1H), 4.66 (s, 1H), 3.89 (dt, J₁ = 14.4 Hz, J₂ = 7.2 Hz, 1H), 3.79 (dt, J₁ = 14.0 Hz, J₂ = 7.2 Hz, 1H), 2.37 (t, J = 7.6 Hz, 2H), 2.25-2.16 (m, 1H), 1.92-1.83 (m, 1H), 1.82 (s, 3H), 1.36 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 179.7, 178.2, 142.3, 142.0, 132.9, 128.1, 122.8, 122.5, 112.8, 110.9, 89.5, 89.0, 47.5, 38.2, 35.3, 32.5, 29.2, 23.9, 22.1. HRMS (ESI) calcd. for C₁₇H₂₁NO₃Na⁺ (M+Na)⁺ 310.1419, found 310.1413.

3-(1',3'-dimethyl-2'-oxo-6'-[(phenylethynyl]indolin-3'-yl)propanoic acid (2n):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1n (83.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)₂ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H₂O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded 2n (42.4 mg, 64%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 158.5-162.4 °C (ethyl acetate/hexanes). ¹H NMR (400 MHz, CDCl₃): δ 7.58-7.49 (m, 2H), 7.41-7.32 (m, 3H), 7.29-7.23 (m, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.00 (s, 1H), 3.22 (s, 3H), 2.31-2.18 (m, 1H), 2.17-2.03 (m, 2H), 2.00-1.85 (m, 1H), 1.38 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 179.7, 178.1, 143.2, 133.0, 131.6, 128.4, 128.3, 126.4, 123.1, 122.9, 122.6, 110.9, 89.5, 89.0, 47.5, 32.5, 29.2, 26.2, 23.3. HRMS (ESI) calcd. for C₂₁H₁₉NO₃Na⁺ (M+Na)⁺ 356.1263, found 356.1266.

3-(3-(4-methoxyphenyl)-1-methyl-2-oxoindolin-3-yl)propanoic acid (2o):

The reaction of chloroform (32 μl, 0.40 mmol, 4.0 equiv), 1o (40.7 mg, 0.10 mmol, 1.0 equiv), Pd(OAc)₂ (1.1 mg, 0.005 mmol, 5 mol %), KOH (44.9 mg, 0.80 mmol, 8.0 equiv) and TFP (3.5 mg, 0.015 mmol, 15 mol %) in H₂O (0.80 ml)/dioxane (0.20 ml) at 80 °C for 1 hour afforded 2o (12.7 mg, 39%) as viscous oil (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.20 (m, 4H), 7.11 (td, J = 7.6, 1.2 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.86-6.79 (m, 2H), 3.76 (s, 3H), 3.22 (s, 3H), 2.73-2.62 (m, 1H), 2.55-2.43 (m, 1H), 2.19-2.13 (m, 1H), 1.94 (s, 3H); ¹³C NMR (100 MHz,
3-(1-benzyl-3-methyl-4-methylene-2-oxypyrrolidin-3-yl)-N-phenylpropanamide (S7) and (Z)-N-benzyl-2-methyl-N-(2-(phenylcarbamoyl)allyl)but-2-enamide (S8):

The reaction of chloroform (65 μl, 0.80 mmol, 4.0 equiv), 1p (71.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)$_2$ (2.2 mg, 0.01 mmol, 5 mol %), KOH (89.8 mg, 1.60 mmol, 8.0 equiv) and TFP (7.0 mg, 0.03 mmol, 15 mol %) in H$_2$O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded a mixture of acids (2p/2p' = 2:1, 21.2 mg, 39%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1).

EDCI (18.0 mg, 0.094 mmol, 1.2 equiv) and PhNH$_2$ (8.5μl, 0.094 mmol, 1.2 equiv) was added to a solution of the above acids, DMAP (11.5 mg, 0.094 mmol, 1.2 equiv) in DCM (1 ml) at 0 °C subsequently. The reaction was stirred at room temperature for overnight and quenched with the addition of H$_2$O, extracted with ethyl acetate, and dried over Na$_2$SO$_4$. After filtration and concentration, the crude amide was purified by column chromatography on silica (hexanes: ethyl acetate = 2: 1) to afford

S7: Viscous oil. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.65 (bs, 1H), 7.49 (d, $J$ = 8.0 Hz, 2H), 7.40-7.27 (m, 5H), 7.27-7.20 (m, 2H), 7.08 (t, $J$ = 7.2 Hz, 1H), 5.10 (s, 1H), 5.09 (s, 1H), 4.55 (d, $J$ = 14.4 Hz, 1H), 4.50 (d, $J$ = 14.8 Hz, 1H), 3.87 (d, $J$ = 14.0 Hz, 1H), 2.40-2.27 (m, 1H), 2.27-2.11 (m, 2H), 2.08-1.97 (m, 1H), 1.30 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 177.3, 170.8, 145.6, 138.1, 135.9, 128.88, 128.85, 128.1, 127.8, 124.0, 119.6, 108.5, 50.1, 48.1, 46.3, 34.3, 33.5, 24.7. HRMS (ESI) calcd. for C$_{22}$H$_{24}$N$_2$O$_2$Na$^+$ (M+Na)$^+$ 371.1725, found 371.1726.

S8: Viscous oil. $^1$H NMR (400 MHz, CDCl$_3$): 9.87 (bs, 1H), 7.78 (d, $J$ = 8.0 Hz, 2H), 7.46-1.29 (m, 5H), 7.20 (d, $J$ = 7.2 Hz, 2H), 7.10 (t, $J$ = 7.6 Hz, 1H), 6.53 (s, 1H), 5.83-5.63 (m, 1H), 5.42 (s, 1H), 4.60 (s, 2H), 4.40 (s, 2H), 1.82 (s, 3H), 1.66 (d, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 175.4, 162.8 (bs), 138.6, 137.7(bs), 135.4(bs), 131.3, 129.9(bs), 129.1, 128.8, 127.9, 127.0, 126.4, 124.1, 120.1, 50.3, 43.9, 14.3, 13.2. HRMS (ESI) calcd. for C$_{22}$H$_{24}$N$_2$O$_2$Na$^+$ (M+Na)$^+$ 371.1735, found 371.1735.
3-cinnamyl-1,3-dimethylindolin-2-one (4a):

**Typical Procedure:** Under N\textsubscript{2} atmosphere a flame-dried schlenk tube was added 1\textsubscript{a} (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (7.0 mg, 0.01 mmol, 5 mol %), N\textsuperscript{\prime}-benzylidene-4-methylbenzenesulfonohydrazide (0.110 g, 0.40 mmol, 2.0 equiv), LiO\textsubscript{Bu} (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 h. After consumption of starting material, the mixture was cooled to room temperature and quenched by the addition of water, extracted with EtOAc, washed with brine. The organic layer was dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated, and the residue was purified by column chromatography on silica (10% ethyl acetate/hexanes) to afford 4\textsubscript{a} (38.6 mg, 70%) as oil. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.36-7.19 (m, 7H), 7.13 (dt, \textit{J} = 7.6 Hz, \textit{J} \textsubscript{1} = 0.8 Hz, 1H), 6.88 (d, \textit{J} = 8.0 Hz, 1H), 6.41 (d, \textit{J} = 15.6 Hz, 1H), 6.01-5.88 (m, 1H), 3.24 (s, 3H), 2.78-2.64 (m, 2H), 1.48 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 180.2, 143.1, 137.2, 133.6, 133.5, 128.4, 127.8, 127.1, 126.1, 124.2, 122.9, 122.4, 108.0, 48.6, 41.6, 26.1, 22.5. The spectra were identical with the reported data \cite{15}.

3-cinnamyl-1,3,5-trimethylindolin-2-one (4b):

A mixture of 1\textsubscript{b} (65.8 mg, 0.20 mmol, 1.0 equiv), Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (7.0 mg, 0.01 mmol, 5 mol %), N\textsuperscript{\prime}-benzylidene-4-methylbenzenesulfonohydrazide (0.110 g, 0.40 mmol, 2.0 equiv), LiO\textsubscript{Bu} (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4\textsubscript{b} (38.3 mg, 66%) (hexanes: acetone = 20: 1) as oil. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.33-7.19 (m, 5H), 7.12 (m, 2H), 6.76 (d, \textit{J} = 7.6 Hz, 1H), 6.42 (d, \textit{J} = 16.0 Hz, 1H), 5.92 (dt, \textit{J} = 15.6 Hz, \textit{J} \textsubscript{1} = 7.6 Hz, 1H), 3.21 (s, 3H), 2.70 (dd, \textit{J} = 7.6 Hz, \textit{J} \textsubscript{1} = 0.8 Hz, 2H), 2.42 (s, 3H), 1.46 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 180.1, 140.7, 137.3, 133.6, 133.5, 131.8, 128.3, 128.0, 127.8, 127.1, 126.1, 124.2, 124.3, 123.7, 107.7, 48.6, 41.6, 26.1, 22.6, 21.2. HRMS (ESI) calcd. for C\textsubscript{20}H\textsubscript{21}NONa\textsuperscript{+} (M+Na\textsuperscript{+}) 314.1521, found 314.1523.

5-chloro-3-cinnamyl-1,3-dimethylindolin-2-one (4c)

5-chloro-3-cinnamyl-1,3-dimethylindolin-2-one (4c)
A mixture of 1g (69.9 mg, 0.20 mmol, 1.0 equiv), Pd(PPh₃)₂Cl₂ (7.0 mg, 0.01 mmol, 5 mol %), N'-benzylidene-4-methylbenzenesulfonohydrazide (0.110 g, 0.40 mmol, 2.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4c (37.9 mg, 61%) (hexanes: dichloromethane: ethyl acetate = 20: 20: 1) as oil.

1H NMR (400 MHz, CDCl₃): δ 7.34-7.22 (m, 7H), 6.79 (d, J = 8.4 Hz, 1H), 6.42 (d, J = 15.6 Hz, 1H), 5.88 (dt, J₁ = 15.6 Hz, J₂ = 7.6 Hz, 1H), 3.22 (s, 3H), 2.77-2.64 (m, 2H), 1.47 (s, 3H); 13C NMR (100 MHz, CDCl₃): δ 179.6, 141.7, 137.0, 135.2, 134.0, 128.4, 127.7, 127.3, 126.1, 123.5, 123.4, 108.9, 49.0, 41.5, 26.2, 22.5. HRMS (ESI) calcd. for C₁₉H₁₈NO₃₅ClNa⁺ (M+Na)⁺ 334.0999, found 334.0996.

(E)-3-(3'-(4''-chlorophenyl)allyl)-1,3-dimethylindolin-2-one (4d)

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh₃)₂Cl₂ (7.0 mg, 0.01 mmol, 5 mol %), N'-4-chlorobenzylidene)-4-methylbenzenesulfonohydrazide (0.124 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4d (58.0 mg, 87%) (hexanes: ethyl acetate = 10: 1) as oil.

1H NMR (400 MHz, CDCl₃): δ 7.30-7.24 (m, 1H), 7.24-7.16 (m, 3H), 7.13-7.05 (m, 3H), 6.82 (d, J = 7.6 Hz, 1H), 6.29 (d, J = 16.0 Hz, 1H), 5.84 (dt, J₁ = 15.6 Hz, J₂ = 7.6 Hz, 1H), 3.18 (s, 3H), 2.64 (dd, J₁ = 7.6 Hz, J₂ = 1.2 Hz, 2H), 1.42 (s, 3H); 13C NMR (100 MHz, CDCl₃): δ 180.1, 143.1, 135.7, 133.4, 132.8, 128.5, 127.9, 127.3, 124.9, 122.8, 122.4, 108.0, 48.6, 41.6, 26.1, 22.5. HRMS (HEI) calcd. for C₁₉H₁₉NO₃₅Cl⁺ (M+H)⁺ 312.1150, found 312.1148.

(E)-3-(3-(4-tert-butylphenyl)allyl)-1,3-dimethylindolin-2-one (4e)

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh₃)₂Cl₂ (7.0 mg, 0.01 mmol, 5 mol %), N'-4-tert-butylbenzylidene)-4-methylbenzenesulfonohydrazide (0.132 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4e (59.0 mg, 88%) (hexanes: acetone = 20: 1) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.21 (m, 4H), 7.15 (d, J = 8.4 Hz, 2H), 7.06 (t, J = 7.2 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.33 (d, J = 15.6 Hz, 1H), 5.86 (dt, J₁ = 15.6 Hz, J₂ = 7.6 Hz, 1H), 3.19 (s, 3H), 2.72-2.57 (m, 2H), 1.41 (s, 3H), 1.29 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 180.2, 150.2, 143.1, 135.7, 133.4, 132.8, 132.4, 128.5, 127.9, 127.3, 124.9, 122.8, 122.4, 108.0, 48.6, 41.6, 26.1, 22.6. HRMS (HEI) calcd. for C₂₃H₂₈NO⁺ (M+H)⁺ 334.2165, found 334.2161.
A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh₃)Cl₂ (7.0 mg, 0.01 mmol, 5 mol %), N'-((4-methoxybenzylidene)-4-methylbenzenesulfonohydrazide (0.122 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4f (56.6 mg, 92%) (hexanes: ethyl acetate = 10: 1 to 5: 1) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.29-7.20 (m, 2H), 7.16-7.11 (m, 2H), 7.07 (td, J₁ = 7.6 Hz, J₂ = 0.8 Hz, 1H), 6.86-6.74 (m, 3H), 6.29 (d, J = 15.6 Hz, 1H), 5.74 (dt, J₁ = 15.6 Hz, J₂ = 7.2 Hz, 1H), 3.77 (s, 3H), 3.18 (s, 3H), 2.69-2.56 (m, 2H), 1.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 180.3, 156.5, 143.1, 133.6, 133.0, 130.1, 127.7, 127.2, 122.9, 122.3, 121.9, 113.8, 107.9, 55.2, 48.7, 41.6, 26.1, 22.4. HRMS (HESI) calcd. for C₂₀H₂₂NO₂⁺ (M+H)⁺ 308.1645, found 308.1640.

(E)-3-(3'-2''-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (4g):

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh₃)Cl₂ (7.0 mg, 0.01 mmol, 5 mol %), N'-((2-methoxybenzylidene)-4-methylbenzenesulfonohydrazide (0.122 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 80 °C for 1 hour afforded 4g (57.9 mg, 94%) (hexanes: ethyl acetate = 10: 1) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.22 (m, 2H), 7.22-7.13 (m, 2H), 7.10-7.03 (m, 1H), 6.89-6.77 (m, 3H), 6.65 (d, J = 16.0 Hz, 1H), 5.91 (dt, J₁ = 16.0 Hz, J₂ = 8.0 Hz, 1H), 3.77 (s, 3H), 3.20 (s, 3H), 2.75-2.58 (m, 2H), 1.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 180.3, 156.5, 143.1, 133.8, 128.5, 128.2, 122.9, 122.3, 121.9, 113.8, 107.9, 55.4, 48.6, 42.0, 26.1, 22.3. HRMS (HESI) calcd. for C₂₀H₂₂NO₂⁺ (M+H)⁺ 308.1645, found 308.1647.

(E)-1,3-dimethyl-3-(3'-m-tolylallyl)indolin-2-one (4h):

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh₃)Cl₂ (7.0 mg, 0.01 mmol, 5 mol %), N'-((3-methylbenzylidene)-4-methylbenzenesulfonohydrazide (0.115 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4h (49.6 mg, 85%) (hexanes: acetone = 20: 1) as oil. ¹H NMR (400 MHz, CDCl₃): δ 7.30-7.21 (m, 2H), 7.14 (t, J = 7.6 Hz, 1H), 7.08 (td, J₁ = 7.6 Hz, J₂ = 0.8 Hz, 1H), 7.05-6.98 (m, 3H), 6.83 (d, J = 8.0 Hz, 1H), 6.32 (d, J = 15.6 Hz, 1H), 5.90 (dt, J₁ = 15.6 Hz, J₂ = 7.2 Hz, 1H), 3.19 (s, 3H), 2.71-2.58 (m, 2H), 2.30 (s, 3H), 1.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ
180. 2, 143.1, 137.9, 137.2, 133.6, 128.3, 128.0, 127.8, 126.9, 123.9, 123.2, 122.9, 122.4, 108.0, 48.6, 41.6, 26.1, 22.5, 21.3. HRMS (HESI) calcd. for C_{20}H_{22}NO^+ (M+H)^+ 298.1696, found 298.1696.

(E)-3-(3''-(3''-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (4i):

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh$_3$)$_2$Cl$_2$ (7.0 mg, 0.01 mmol, 5 mol %), N'-3-methoxybenzylidene)-4-methylbenzenesulfonylhydrazone (0.122 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 80 °C for 1 hour afforded 4i (41.7 mg, 68%) (hexanes: acetone = 40: 3) as oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.30-7.20 (m, 2H), 7.19-7.13 (m, 1H), 7.07 (td, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz, 1H), 6.85-6.77 (m, 2H), 6.76-6.70 (m, 2H), 6.32 (d, $J$ = 15.6 Hz, 1H), 5.88 (dt, $J_1$ = 15.6 Hz, $J_2$ = 7.6 Hz, 1H), 3.77 (s, 3H), 3.18 (s, 3H), 2.70-2.59 (m, 2H), 1.42 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 180.1, 159.6, 143.1, 138.7, 133.53, 133.48, 129.3, 127.8, 124.5, 122.9, 122.4, 118.8, 112.6, 111.6, 108.0, 55.1, 48.6, 41.5, 26.1, 22.5. HRMS (HESI) calcd. for C$_{20}$H$_{22}$NO$_2$^+ (M+H)$^+$ 308.1645, found 308.1642.

(E)-3-(3''-(3'',4''-dimethoxyphenyl)allyl)-1,3-dimethylindolin-2-one (4j):

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh$_3$)$_2$Cl$_2$ (7.0 mg, 0.01 mmol, 5 mol %), N'-3,4-dimethoxybenzylidene)-4-methylbenzenesulfonylhydrazone (0.134 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 80 °C for 1 hour afforded 4j (47.5 mg, 70%) (hexanes: ethyl acetate = 5: 1 to 3: 1) as oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.32-7.22 (m, 2H), 7.09 (td, $J_1$ = 7.6 Hz, $J_2$ = 1.2 Hz, 1H), 6.84 (d, $J$ = 8.0 Hz, 1H), 6.78-6.71 (m, 3H), 6.29 (d, $J$ = 15.6 Hz, 1H), 5.77 (dt, $J_1$ = 15.2 Hz, $J_2$ = 7.6 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.20 (s, 3H), 2.71-2.59 (m, 2H), 1.44 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 180.2, 148.7, 148.4, 143.0, 133.6, 133.2, 130.3, 127.7, 122.9, 122.2, 118.9, 110.9, 108.8, 107.9, 55.8, 55.7, 48.6, 41.5, 26.1, 22.4. HRMS (ESI) calcd. for C$_{21}$H$_{23}$NO$_3$Na$^+$ (M+Na)$^+$ 360.1576, found 360.1581.

(E)-1,3-dimethyl-3-(3''-(naphthalen-2''-yl)allyl)indolin-2-one (4k):

A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh$_3$)$_2$Cl$_2$ (7.0 mg, 0.01 mmol, 5 mol %), N'-(3,4-dimethoxybenzylidene)-4-methylbenzenesulfonylhydrazone (0.134 g, 0.40 mmol, 2.0 equiv), LiO'Bu (48.0 mg, 0.60 mmol, 3.0 equiv) and in 3.0 mL of THF was stirred at 80 °C for 1 hour afforded 4k (47.5 mg, 70%) (hexanes: ethyl acetate = 5: 1 to 3: 1) as oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.32-7.22 (m, 2H), 7.09 (td, $J_1$ = 7.6 Hz, $J_2$ = 1.2 Hz, 1H), 6.84 (d, $J$ = 8.0 Hz, 1H), 6.78-6.71 (m, 3H), 6.29 (d, $J$ = 15.6 Hz, 1H), 5.77 (dt, $J_1$ = 15.2 Hz, $J_2$ = 7.6 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.20 (s, 3H), 2.71-2.59 (m, 2H), 1.44 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 180.2, 148.7, 148.4, 143.0, 133.6, 133.2, 130.3, 127.7, 122.9, 122.2, 118.9, 110.9, 108.8, 107.9, 55.8, 55.7, 48.6, 41.5, 26.1, 22.4. HRMS (ESI) calcd. for C$_{21}$H$_{23}$NO$_3$Na$^+$ (M+Na)$^+$ 360.1576, found 360.1581.
A mixture of 1a (63.0 mg, 0.20 mmol, 1.0 equiv), LiO\textsuperscript{t}Bu(48.0 mg, 0.60 mmol, 3.0 equiv), N'-(naphthalen-2-ylmethylene)-4-methylbenzenesulfonohydrazide (0.130 g, 0.40 mmol, 2.0 equiv), Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (7.0 mg, 0.01 mmol, 5 mol %) in 3.0 mL of THF was stirred at 70 °C for 1 hour afforded 4k (42.0 mg, 64%) (hexanes: ethyl acetate = 10: 1) as viscous oil. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.80-7.68 (m, 3H), 7.57 (s, 1H), 7.47-7.37 (m, 3H), 7.31-7.23 (m, 2H), 7.10 (t, \textit{J} = 7.6 Hz, 1H), 6.83 (d, \textit{J} = 7.6 Hz, 1H), 6.51 (d, \textit{J} = 16.0 Hz, 1H), 6.03 (dt, \textit{J} = 15.6 Hz, J\textsubscript{2} = 7.6 Hz, 1H), 3.19 (s, 3H), 2.72 (d, \textit{J} = 7.6 Hz, 2H), 1.46 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 180.2, 143.1, 134.6, 133.8, 133.6, 133.5, 132.8, 128.0, 127.8, 127.5, 126.1, 125.8, 125.6, 124.6, 123.5, 122.9, 122.4, 108.0, 48.7, 41.8, 26.1, 22.5. HRMS (HESI) calcd. for C\textsubscript{23}H\textsubscript{22}NO\textsuperscript{+} (M+H)\textsuperscript{+} 328.1696, found 328.1692.

References:
S47
\[ \text{4a} \]

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