## 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 N<sub>2</sub>. Dioxane was distilled from sodium-benzophenone under an atmosphere of N<sub>2</sub>. 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. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AC-400 FT spectrometer using solvent CDCl<sub>3</sub> residue as an internal reference (7.26 ppm for <sup>1</sup>H NMR and 77.00 ppm for <sup>13</sup>C NMR). Electron spray ionization (ESI) mass spectrometry data were acquired using a Thermo LTQ Orbitrap XL instrument.

	$ \begin{array}{c}                                     $								
entry	1a Pd	lligand	solvent	2a CHCl <sub>2</sub>	T/ºC	vield			
entry	1 u	inguna	sorvent	(equiv)	17 0	(%)			
1	$Pd(PPh_3)_2Cl_2$	none	dioxane/H <sub>2</sub> O	4.0	80	13			
2	$Pd(OAc)_2$	$\mathrm{TFP}^{b}$	dioxane/H <sub>2</sub> O	4.0	80	57			
3	$Pd(OAc)_2$	TFP	dioxane/H <sub>2</sub> O	4.0	60	67			
4	$Pd(OAc)_2$	TFP	THF	4.0	60	Trace			
5	$Pd(PPh_3)_2Cl_2$	none	THF/H <sub>2</sub> O	4.0	60	<10			
6	$Pd(PPh_3)_2Cl_2$	PPh <sub>3</sub>	THF/H <sub>2</sub> O	4.0	60	<10			
7	$Pd(OAc)_2$	TFP	dioxane/H <sub>2</sub> O	4.0	90	75			
8	$Pd(OAc)_2$	PPh <sub>3</sub>	dioxane/H <sub>2</sub> O	4.0	90	65			
9	$Pd(OAc)_2$	PPh <sub>3</sub>	dioxane/H <sub>2</sub> O	4.0	80	52			
10	$Pd(OAc)_2$	PPh <sub>3</sub>	dioxane/H <sub>2</sub> O	4.0	70	68			
11	$Pd(OAc)_2$	TFP	dioxane/H <sub>2</sub> O	4.0	80	79			
12	$Pd(OAc)_2$	TFP	dioxane/H <sub>2</sub> O	8.0	80	80			
13	$Pd(OAc)_2$	TFP	dioxane/H <sub>2</sub> O	0.2 ml	80	16			

 Table S1. Full Results for Reaction Condition Optimization<sup>a</sup>

<sup>*a*</sup> 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<sub>2</sub>O = 1:4, THF/H<sub>2</sub>O = 1:4. <sup>*b*</sup> TFP = tri(2-furyl)phosphine (5 mol%).

	N Me Me 1a	+ TSHNN	Pd, base OMe	Me N Me	4f	Me
entry	Pd	ligand (mol %)	solvent	base	T/°C	yield (%)
1	Pd(OAc) <sub>2</sub>	PPh <sub>3</sub> (10)	MeCN	<sup>t</sup> BuOLi	80	<10
2	$Pd(OAc)_2$	$PPh_3(5)$	MeCN	<sup>t</sup> BuOLi	80	45
3	$Pd(OAc)_2$	PPh <sub>3</sub> (2.5)	MeCN	<sup>t</sup> BuOLi	80	50
4	$Pd(OAc)_2$	$PPh_3(1)$	MeCN	<sup>t</sup> BuOLi	80	42
5	$Pd(OAc)_2$	$PPh_3(5)$	dioxane	KOH	80	<10
6	$Pd(OAc)_2$	$PPh_3(5)$	toluene	<sup>t</sup> BuOLi	80	<10
7	PdCl <sub>2</sub>	$PPh_3(5)$	MeCN	<sup>t</sup> BuOLi	80	61
8	Pd(MeCN) <sub>2</sub> Cl <sub>2</sub>	$PPh_3(5)$	MeCN	<sup>t</sup> BuOLi	80	49
9	$Pd(PPh_3)_2Cl_2$	none	MeCN	<sup>t</sup> BuOLi	80	66
10	$Pd(PPh_3)_2Cl_2$	none	MeCN	<sup>t</sup> BuOK	80	<10
11	$Pd(PPh_3)_2Cl_2$	none	MeCN	<sup>t</sup> BuONa	80	42
12	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub>	none	dioxane	<sup>t</sup> BuOLi	80	77
13	$Pd(PPh_3)_2Cl_2$	none	THF	<sup>t</sup> BuOLi	80	92
14	$Pd(PPh_3)_2Cl_2$	none	DME	<sup>t</sup> BuOLi	80	84
15	$Pd(PPh_3)_2Cl_2$	none	THF	<sup>t</sup> BuOLi	70	88

**Table S2.** Conditions Optimization for the Reaction with Hydrazones<sup>*a*</sup>

<sup>*a*</sup> 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 <sup>[1]</sup>.

#### **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  $CH_2Cl_2$  (10.0 ml) at room temperature dropwise. The reaction was maintained at room temperature for 30 min and the excess oxalyl dichloride and  $CH_2Cl_2$  was carefully removed by evaporation.



The above acid chloride in  $CH_2Cl_2$  (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<sub>3</sub>N (0.84 ml, 6.00 mmol, 2.0 equiv) in  $CH_2Cl_2$  (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<sub>3</sub>, extracted with  $CH_2Cl_2$ , washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.86 (dd,  $J_I = 8.0$  Hz,  $J_2 = 1.6$  Hz, 1H), 7.26-7.16 (m, 5H), 7.12 (td,  $J_I = 7.8$  Hz,  $J_2 = 1.2$  Hz, 1H), 6.92 (td,  $J_I = 7.6$  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 = 14.0Hz, 1H), 1.65 (s, 3H), 1.43 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>18</sub>H<sub>19</sub>NOI<sup>+</sup> (M+H)<sup>+</sup> 392.0506, found 392.0507.

**Preparation of 1c:** 



The crude acid chloride [prepared as above from (*E*)-2-methylbut-2-enoic acid (0.20 g, 2.00 mmol, 1.2 equiv)] in  $CH_2Cl_2$  (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<sub>3</sub>N (0.45 ml, 3.20 mmol, 2.0 equiv) in  $CH_2Cl_2$  (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<sub>3</sub>, extracted with  $CH_2Cl_2$ , washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, 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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>13</sub>H<sub>17</sub>NOI<sup>+</sup> (M+H)<sup>+</sup> 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<sub>2</sub>Cl<sub>2</sub> (10.0 ml) was added to a mixture of 2-iodo-4-methoxyaniline <sup>[2]</sup> (1.25 g, 5.00 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  735 (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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>13</sub>H<sub>16</sub>INO<sub>2</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 368.0123, found 368.0121.

#### **Preparation of 1e:**



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<sub>2</sub>Cl<sub>2</sub> (10.0 ml) was added to a mixture of 2-iodo-4-(trifluoromethyl)aniline (1.44 g, 5.00 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, concentrated. 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -62.6. HRMS (ESI) calcd. for C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>INONa<sup>+</sup> (M+Na)<sup>+</sup> 405.9892, found 405.9892.

#### **Preparation of 1f:**



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<sub>2</sub>Cl<sub>2</sub> (10.0 ml) was added to a mixture of 2-iodo-4-fluoroaniline (1.44 g, 5.00 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed

with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) :  $\delta$  -112.6. HRMS (ESI) calcd. for C<sub>12</sub>H<sub>14</sub>FINO<sup>+</sup> (M+H)<sup>+</sup> 334.0104, found 334.0100.

#### **Preparation of 1g:**



The crude acid chloride [prepared as above from (*E*)-2-methylbut-2-enoic acid (0.24 g, 2.40 mmol, 1.2 equiv)] in  $CH_2Cl_2$  (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), Et<sub>3</sub>N (0.56 ml, 4.00 mmol, 2.0 equiv) in  $CH_2Cl_2$  (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 NaHCO<sub>3</sub>, extracted with  $CH_2Cl_2$ , washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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 Na<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ 7.84 (d, *J* = 2.4 Hz, 1H), 7.30 (dd, *J*<sub>1</sub> = 8.4 Hz, *J*<sub>2</sub> = 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>12</sub>H<sub>14</sub>NOI<sup>35</sup>CI<sup>+</sup> (M+H)<sup>+</sup> 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  $CH_2Cl_2$  (7.0 ml) was added to a mixture of 4-bromo-2-iodoaniline (0.88 g, 3.00 mmol, 1.0 equiv) in  $CH_2Cl_2$  (7.0 ml) at 0 °C dropwise, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.01 (d, *J* = 2.0 Hz, 1H), 7.46 (dd, *J<sub>I</sub>* = 8.4 Hz, *J<sub>2</sub>* = 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>12</sub>H<sub>13</sub><sup>81</sup>BrINONa<sup>+</sup> (M+Na)<sup>+</sup> 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<sub>2</sub>Cl<sub>2</sub> (10.0 ml) was added to a mixture of 2-iodo-5-methoxyaniline <sup>[3]</sup> (0.72 g, 2.90 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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 Na<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>13</sub>H<sub>16</sub>INO<sub>2</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 368.0123, found 368.0124.

#### **Preparation of 1j:**



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<sub>2</sub>Cl<sub>2</sub> (10.0 ml) was added to a mixture of 5-chloro-2-iodoaniline (1.27 g, 5.00 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ 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 C<sub>12</sub>H<sub>13</sub><sup>35</sup>CIINONa<sup>+</sup> (M+Na)<sup>+</sup> 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(PPh<sub>3</sub>)<sub>4</sub> (1.15 g, 1.00 mmol, 0.05 equiv) in 2 M K<sub>2</sub>CO<sub>3</sub> (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 Na<sub>2</sub>SO<sub>4</sub>. 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·H<sub>2</sub>O (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 NaNO<sub>2</sub> (2.07 g, 30.00 mmol, 2.0 equiv) and KI (6.23 g, 37.50 mmol, 2.5 equiv) in H<sub>2</sub>O (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 H<sub>2</sub>O, saturated NaHCO<sub>3</sub> and Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>. After filtered through a pad of celite, extracted with ethyl acetate and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration, the crude iodide was obtained <sup>[4]</sup>.

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 NaHCO<sub>3</sub>. Then the mixture was filtered through a pad of celite, extracted with ethyl acetate and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration, the residue was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford **S1**<sup>[5]</sup> (3.31 g, 10.2 mmol, 68%). Solid, 160.0-162.8 °C (ethyl acetate/hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 2.0 Hz, 1H), 4.14 (bs, 2H), 3.84 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>13</sub>H<sub>13</sub>INO<sup>+</sup> (M+H)<sup>+</sup> 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 Na<sub>2</sub>SO<sub>4</sub> and concentrated, the crude *N*-benzyl-4-iodo-4'-methoxybiphenyl-3-amine was used in next step without further purification. <sup>[6]</sup>

The crude acid chloride [prepared as above from (*E*)-2-methylbut-2-enoic acid (0.36 g, 3.60 mmol, 1.2 equiv)] in CH<sub>2</sub>Cl<sub>2</sub> (15.0 ml) was added to the crude *N*-benzyl-4-iodo-4'-methoxybiphenyl-3-amine in CH<sub>2</sub>Cl<sub>2</sub> (15.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with ethyl acetate, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.86 (d, *J* = 8.0 Hz, 1H), 7.32-7.20 (m, 5H), 7.20-7.13 (m, 2H), 7.10 (dd, *J*<sub>1</sub> = 8.4, *J*<sub>2</sub> = 2.0 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) rotaters :  $\delta$  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 C<sub>25</sub>H<sub>24</sub>INO<sub>2</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 520.0749, found 520.0756.

#### **Preparation of 11:**



Sodium hydride (0.34 g, 60% in mineral oil, 8.60 mmol, 2.0 equiv) was added to a solution of the amide <sup>[7]</sup> (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 Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford **11** (1.29 g, 3.50 mmol, 81%) as oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>16</sub>H<sub>21</sub>NOI<sup>+</sup> (M+H)<sup>+</sup> 370.0662, found 370.0664.

#### **Preparation of 1m**<sup>[8]</sup>:



Potassium hydroxide (0.36 g, 6.40 mmol, 2.0 equiv) and  ${}^{n}Bu_{4}NHSO_{4}$  (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-methylbenzenesulfonate (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 Na<sub>2</sub>SO<sub>4</sub> 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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>16</sub>H<sub>20</sub>INONa<sup>+</sup> (M+Na)<sup>+</sup> 392.0487, found 392.0485.

#### **Preparation of 1n:**



To a solution of *p*-TsOH·H<sub>2</sub>O (6.33 g, 33.3 mmol, 3.0 equiv) in MeCN (200 mL) was added to 2-nitro-4-(phenylethynyl)aniline <sup>[9]</sup> (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 NaNO<sub>2</sub> (1.53 g, 22.20 mmol, 2.0 equiv) and KI (4.61 g, 27.80 mmol, 2.5 equiv) in H<sub>2</sub>O (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 H<sub>2</sub>O, saturated NaHCO<sub>3</sub> and Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>. After filtered through a pad of celite, the filtrate was extracted with ethyl acetate, dried over Na<sub>2</sub>SO<sub>4</sub>. 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 NaHCO<sub>3</sub> and filtered through a pad of celite. The filtrate was extracted with ethyl acetate and dried over Na<sub>2</sub>SO<sub>4</sub>. 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>14</sub>H<sub>11</sub>IN<sup>+</sup> (M+H)<sup>+</sup> 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<sub>2</sub>Cl<sub>2</sub> (10.0 ml) was added to a mixture of **S2** (0.96 g, 3.0 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10.0 ml) at 0 °C, followed by Et<sub>3</sub>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<sub>3</sub>, extracted with CH<sub>2</sub>Cl<sub>2</sub>, washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub>, concentrated and purified by column chromatography on silica (hexanes: ethyl acetate = 10: 1) to afford **1n** (0.46 g, 1.10 mmol, 36% three steps). Solid, 111.6-116.0 °C (ethyl acetate/hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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 = 8.0Hz, 1H), 5.83 (bs, 1H), 3.23 (s, 3H), 1.69 (bs, 3H), 1.50 (bs, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>20</sub>H<sub>18</sub>INONa<sup>+</sup> (M+Na)<sup>+</sup> 438.0331, found 438.0330.

#### **Preparation of 10:**



A solution of **S3** <sup>[10]</sup> (1.16 g, 6.00 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (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<sub>3</sub>PO<sub>4</sub> (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 MgSO4, 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 <sup>[11]</sup> (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<sub>2</sub>SO<sub>4</sub>, 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 K<sub>2</sub>CO<sub>3</sub> (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 NaHCO<sub>3</sub>, extracted with ethyl acetate, washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration, the crude amide was purified by column chromatography on silica (hexanes: ethyl acetate = 8: 1 to 10: 1) to afford **10** (0.23 g, 0.56 mmol, 38%) as viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.69 (d, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.84 (td, *J<sub>I</sub>* = 8.0 Hz, *J<sub>2</sub>* = 0.8 Hz, 1H), 6.72-6.62 (m, 5H), 6.34 (q, *J* = 6.8 Hz, 1H), 3.76 (s, 3H), 3.19 (s, 3H), 1.57 (d, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>18</sub>H<sub>18</sub>INO<sub>2</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 430.0280, found 430.0284.

#### **Preparation of 1p:**



To a solution of **S5** <sup>[12]</sup> (1.57 g, 4.64 mmol, 1.0 equiv) in MeCN (10 mL) was added a solution of BnNH<sub>2</sub> (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 Na<sub>2</sub>SO<sub>4</sub>. 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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.39-7.30 (m, 4H), 7.29-7.23 (m, 1H), 6.27 (q, *J* = 1.6 Hz, 1H), 5.94-5.82 (m, 1H), 3.71 (s, 2H), 3.38 (dd, *J*<sub>1</sub> = 1.2 Hz, *J*<sub>2</sub> = 0.8 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  139.7, 128.4, 128.3, 127.1, 126.4, 113.4, 60.1, 51.3. HRMS (ESI) calcd. for C<sub>10</sub>H<sub>13</sub>INNa<sup>+</sup> (M+Na)<sup>+</sup> 274.0093, found 274.0086.



The crude acid chloride [prepared as above from (*E*)-2-methylbut-2-enoic acid (0.50 g, 3.90 mmol, 1.5 equiv)] in  $CH_2Cl_2$  (5.0 ml) was added to a mixture of **S6** (0.71 g, 2.60 mmol, 1.0 equiv) and  $Et_3N$  (0.72 ml, 5.20 mmol, 2.0 equiv) in  $CH_2Cl_2$  (10.0 ml) at 0 °C dropwise. After stirring at room temperature overnight, the mixture was quenched with the addition of saturated NaHCO<sub>3</sub>, extracted with  $CH_2Cl_2$ , washed

with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. 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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J*<sub>1</sub> = 6.8 Hz, *J*<sub>2</sub> = 1.2 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>15</sub>H<sub>19</sub>INO<sup>+</sup> (M+H)<sup>+</sup> 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 H<sub>2</sub>O (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 Na<sub>2</sub>SO<sub>4</sub> 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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  179.9, 177.8, 143.2, 132.8, 128.2, 122.8, 122.7, 108.2, 47.50, 32.65, 29.20, 26.20, 23.53. The spectra were identical with the reported data. <sup>[13]</sup>

**3**: Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.29 (td,  $J_1$  = 7.6 Hz,  $J_2$  = 1.2 Hz, 1H), 7.19 (ddd,  $J_1$  = 7.2 Hz,  $J_2$  = 1.2 Hz,  $J_3$  = 0.8 Hz, 1H), 7.09 (td,  $J_1$  = 7.6 Hz,  $J_2$  = 1.2 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 5.95 (dd,  $J_1$  = 17.2 Hz,  $J_2$  = 10.4 Hz, 1H), 5.19-5.09 (m, 2H), 3.21 (s, 3H), 1.49 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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. <sup>[14]</sup>

#### The reaction with carbon monoxide:



An autoclave containing Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (14.0 mg, 0.02 mmol, 5 mol %), PPh<sub>3</sub> (21.0 mg, 0.08 mmol, 20 mol %), **1a** (0.126 g, 0.40 mmol, 1.0 equiv), NEt<sub>3</sub> (0.22 ml, 1.60 mmol, 4.0 equiv) and DMF/H<sub>2</sub>O (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 ( $1 \times 10$  ml). All of the organic layer was combined, dried over Na<sub>2</sub>SO<sub>4</sub>, 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 ( $3 \times 30$  ml). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, 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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.34 (td,  $J_1 = 7.6$  Hz,  $J_2 = 1.6$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>13</sub>H<sub>15</sub>NO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 256.0950, found 256.0953.



The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **1b** (78.2 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>O (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.0, 178.2, 142.2, 135.8, 132.7, 128.8, 128.1, 127.6, 127.2, 122.8, 122.7, 109.2, 47.5, 43.7, 32.6, 29.3, 23.9. HRMS (ESI) calcd. for C<sub>19</sub>H<sub>18</sub>NO<sub>3</sub><sup>-</sup> (M-H)<sup>-</sup> 308.1281, found 308.1286.

2b

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



The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **1c** (65.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded **2c** (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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.06 (d, *J* = 7.6 Hz, 1H), 6.98 (s, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 3.18 (s, 3H), 2.33 (s, 3H), 2.25-2.17 (m, 1H), 2.13-2.01 (m, 2H), 1.96-1.82 (m, 1H), 1.36 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  179.9, 178.1, 140.7, 132.8, 132.4, 128.3, 123.5, 107.9, 47.6, 32.7, 29.3, 26.2, 23.5, 21.1. HRMS (ESI) calcd. for C<sub>14</sub>H<sub>16</sub>NO<sub>3</sub><sup>-</sup> (M-H)<sup>-</sup> 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)<sub>2</sub> (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<sub>2</sub>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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>14</sub>H<sub>17</sub>NO<sub>4</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 286.1055, found 286.1057.

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



The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **1e** (76.6 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  179.8, 178.2, 146.2, 133.3, 126.1 (q, *J* = 3.8 Hz), 125.0 (q, *J* = 32.6 Hz), 124.3 (q, *J* = 270.0 Hz), 119.8 (q, *J* = 3.4 Hz), 108.0, 47.5, 32.4, 29.2, 26.4, 23.4. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -61.41. HRMS (ESI) calcd. for C<sub>14</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 324.0823, found 324.0823.

#### 3-(5'-fluoro-1',3'-dimethyl-2'-oxoindolin-3'-yl)propanoic acid (2f):



The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **1f** (66.6 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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), 1.95-1.82 (m, 1H), 1.37 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -120.1. HRMS (ESI) calcd. for C<sub>13</sub>H<sub>14</sub>FNO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 274.0855, found 274.0855.

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



The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **1g** (69.9 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>13</sub>H<sub>13</sub>NO<sub>3</sub><sup>35</sup>Cl<sup>-</sup> (M-H)<sup>-</sup> 266.0579, found 266.0586.

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



The reaction of chloroform (65  $\mu$ l, 0.80 mmol, 4.0 equiv), **1h** (78.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.39 (dd,  $J_1$  = 8.4 Hz,  $J_2$  = 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>13</sub>H<sub>14</sub><sup>79</sup>BrNO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 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)<sub>2</sub> (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<sub>2</sub>O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1.5 hours afforded **2i** (34.1 mg, 65%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1) as viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>14</sub>H<sub>17</sub>NO<sub>4</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 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)<sub>2</sub> (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<sub>2</sub>O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded **2j** (30.9 mg, 58%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 85.5-88.6 °C (ethyl acetate/hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.08 (d, *J* = 7.6 Hz, 1H), 7.03 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>1</sub> = 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>13</sub>H<sub>14</sub><sup>35</sup>CINO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 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)<sub>2</sub> (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<sub>2</sub>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: AcOH = 50: 50: 1). Solid, 134.6-138.9 °C (ethyl acetate/hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.38 (d, *J* = 8.4 Hz, 2H), 7.36-7.24 (m, 5H), 7.20 (s, 2H), 6.95 (d, *J* = 8.4 Hz, 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>26</sub>H<sub>25</sub>NO<sub>4</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 438.1681, found 438.1678.

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



The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **11** (73.8 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>O (1.60 ml)/dioxane (0.40 ml) at 80 °C for 1 hour afforded **21** (34.5 mg, 60%) (dichloromethane: ethyl acetate = 20: 3 to ethyl acetate: hexanes: AcOH = 50: 50: 1). Solid, 67.3-71.8 °C (ethyl acetate/hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.29-7.22 (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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>17</sub>H<sub>21</sub>NO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 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)<sub>2</sub> (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<sub>2</sub>O (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J<sub>I</sub>* = 14.4 Hz, *J<sub>2</sub>* = 7.2 Hz, 1H), 3.79 (dt, *J<sub>I</sub>* = 14.0 Hz, *J<sub>2</sub>* = 7.2 Hz, 1H), 2.37 (t, *J* = 7.2 Hz, 2H), 2.25-2.16 (m, 1H), 2.15-2.01 (m, 2H), 1.92-1.83 (m, 1H), 1.82 (s, 3H), 1.36 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  179.7, 178.2, 142.3, 142.0, 132.9, 128.1, 122.8, 122.5, 112.8, 108.4, 47.4, 38.2, 35.3, 32.5, 29.2, 23.9, 22.1. HRMS (ESI) calcd. for C<sub>17</sub>H<sub>21</sub>NO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 310.1419, found 310.1413.





The reaction of chloroform (65 µl, 0.80 mmol, 4.0 equiv), **1n** (83.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>O (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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>21</sub>H<sub>19</sub>NO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 356.1263, found 356.1266.

#### 3-(3-(4-methoxyphenyl)-1-methyl-2-oxoindolin-3-yl)propanoic acid (20):



The reaction of chloroform (32 µl, 0.40 mmol, 4.0 equiv), **1o** (40.7 mg, 0.10 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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 H<sub>2</sub>O (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). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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), 2.06-1.94 (m, 1H); <sup>13</sup>C NMR (100 MHz,

CDCl<sub>3</sub>):  $\delta$  178.1, 178.0, 158.9, 143.7, 131.3, 131.2, 128.5, 127.9, 124.7, 122.9, 114.0, 108.5, 55.2, 55.0, 32.3, 29.4, 26.4. HRMS (ESI) calcd. for C<sub>19</sub>H<sub>19</sub>NO<sub>4</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 348.1212, found 342.1213.

# 3-(1-benzyl-3-methyl-4-methylene-2-oxopyrrolidin-3-yl)-*N*-phenylpropanam ide (S7) and (Z)-*N*-benzyl-2-methyl-N-(2-(phenylcarbamoyl)allyl)but-2-enamide (S8):



The reaction of chloroform (65  $\mu$ l, 0.80 mmol, 4.0 equiv), **1p** (71.0 mg, 0.20 mmol, 1.0 equiv), Pd(OAc)<sub>2</sub> (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<sub>2</sub>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<sub>2</sub> (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<sub>2</sub>O, extracted with ethyl acetate, and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration, the crude amide was purified by column chromatography on silica (hexanes: ethyl acetate = 2: 1) to afford S7 (18.1 mg, 66%) and S8 (7.6 mg, 28%).

**S7:** Viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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), 3.82 (d, J = 14.4 Hz, 1H), 2.40-2.27 (m, 1H), 2.27-2.11 (m, 2H), 2.08-1.97 (m, 1H), 1.30 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>22</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 371.1735, found 371.1726.

**S8:** Viscous oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>22</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 371.1735, found

371.1740.

3-cinnamyl-1,3-dimethylindolin-2-one (4a):



**Typical Procedure:** Under N<sub>2</sub> atmosphere a flame-dried schlenk tube was added **1a** (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N*'-benzylidene-4-methylbenzenesulfonohydrazide (0.110 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 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<sub>2</sub>SO<sub>4</sub> and concentrated, and the residue was purified by column chromatography on silica (10% ethyl acetate/hexanes) to afford **4a** (38.6 mg, 70%) as oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.36-7.19 (m, 7H), 7.13 (dt, *J*<sub>1</sub> = 7.6 Hz, *J*<sub>1</sub> = 0.8 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.41 (d, *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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 <sup>[15]</sup>.

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



A mixture of **1b** (65.8 mg, 0.20 mmol, 1.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N'*-benzylidene-4-methylbenzenesulfonohydrazide (0.110 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 **4b** (38.3 mg, 66%) (hexanes: acetone = 20: 1) as oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.33-7.19 (m, 5H), 7.12 (m, 2H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.92 (dt, *J*<sub>1</sub> = 15.6 Hz, *J*<sub>2</sub> = 7.6 Hz, 1H), 3.21 (s, 3H), 2.70 (dd, *J*<sub>1</sub> = 7.6 Hz, *J*<sub>2</sub> = 0.8 Hz, 2H), 2.42 (s, 3H), 1.46 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.1, 140.7, 137.3, 133.6, 133.5, 131.8, 128.3, 128.0, 127.1, 126.1, 124.3, 123.7, 107.7, 48.6, 41.6, 26.1, 22.6, 21.2. HRMS (ESI) calcd. for C<sub>20</sub>H<sub>21</sub>NONa<sup>+</sup> (M+Na)<sup>+</sup> 314.1521, found 314.1523.

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



A mixture of **1g** (69.9 mg, 0.20 mmol, 1.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N*'-benzylidene-4-methylbenzenesulfonohydrazide (0.110 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 **4c** (37.9 mg, 61%) (hexanes: dichloromethane: ethyl acetate = 20: 20: 1) as oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J<sub>I</sub>* = 15.6 Hz, *J<sub>2</sub>* = 7.6 Hz, 1H), 3.22 (s, 3H), 2.77-2.64 (m, 2H), 1.47 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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 C<sub>19</sub>H<sub>18</sub>NO<sup>35</sup>ClNa<sup>+</sup> (M+Na)<sup>+</sup> 334.0999, found 334.0996.





A mixture of **1a** (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J*<sub>1</sub> = 15.6 Hz, *J*<sub>2</sub> = 7.6 Hz, 1H), 3.18 (s, 3H), 2.64 (dd, *J*<sub>1</sub> = 7.6 Hz, *J*<sub>2</sub> = 1.2 Hz, 2H), 1.42 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.1, 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, 22.5. HRMS (HESI) calcd. for C<sub>19</sub>H<sub>19</sub>NO<sup>35</sup>Cl<sup>+</sup> (M+H)<sup>+</sup> 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(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J*<sub>1</sub> = 15.6 Hz, *J*<sub>2</sub> = 7.6 Hz, 1H), 3.19 (s, 3H), 2.72-2.57 (m, 2H), 1.41 (s, 3H), 1.29 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.2, 150.2, 143.1, 134.5, 133.6, 133.4, 127.8, 125.9, 125.3, 123.3, 122.9, 122.3, 107.9, 48.6, 41.6, 34.4, 31.2, 26.1, 22.6. HRMS (HESI) calcd. for C<sub>23</sub>H<sub>28</sub>NO<sup>+</sup> (M+H)<sup>+</sup> 334.2165, found 334.2161.

#### (E)-3-(3'-(4''-methoxyphenyl)allyl)-1,3-dimethylindolin-2-one (4f)



A mixture of **1a** (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N'*-(4-methoxybenzylidene)-4-methylbenzenesulfonohydrazide (0.122 g, 0.40 mmol, 2.0 equiv), LiO<sup>*t*</sup>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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.29-7.20 (m, 2H), 7.16-7.11 (m, 2H), 7.07 (td,  $J_1$  = 7.6 Hz,  $J_2$  = 0.8 Hz, 1H), 6.86-6.74 (m, 3H), 6.29 (d, J = 15.6 Hz, 1H), 5.74 (dt,  $J_1$  = 15.6 Hz,  $J_2$  = 7.2 Hz, 1H), 3.77 (s, 3H), 3.18 (s, 3H), 2.69-2.56 (m, 2H), 1.41 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.3, 158.9, 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 C<sub>20</sub>H<sub>22</sub>NO<sub>2</sub><sup>+</sup> (M+H)<sup>+</sup> 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(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J*<sub>1</sub> = 16.0 Hz, *J*<sub>2</sub> = 8.0 Hz, 1H), 3.77 (s, 3H), 3.20 (s, 3H), 2.75-2.58 (m, 2H), 1.42 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.3, 156.5, 143.1, 133.8, 128.5, 128.2, 127.7, 126.7, 126.5, 124.9, 123.1, 122.3, 120.5, 110.8, 107.8, 55.4, 48.6, 42.0, 26.1, 22.3. HRMS (HESI) calcd. for C<sub>20</sub>H<sub>22</sub>NO<sub>2</sub><sup>+</sup> (M+H)<sup>+</sup> 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(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N'*-(3-methylbenzylidene)-4-methyl-benzenesulfonohydrazide (0.115 g, 0.40 mmol, 2.0 equiv), LiO<sup>*t*</sup>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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.30-7.21 (m, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.08 (td, *J*<sub>1</sub> = 7.6 Hz, *J*<sub>2</sub> = 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, *J*<sub>1</sub> = 15.6 Hz, *J*<sub>2</sub> = 7.2 Hz, 1H), 3.19 (s, 3H), 2.71-2.58 (m, 2H), 2.30 (s, 3H), 1.42 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ 

180. 2, 143.1, 137.9, 137.2, 133.8, 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)<sup>+</sup> 298.1696, found 298.1696.



A mixture of **1a** (63.0 mg, 0.20 mmol, 1.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N'*-(3-methoxybenzylidene)-4-methylbenzenesulfonohydrazide (0.122 g, 0.40 mmol, 2.0 equiv), LiO<sup>*t*</sup>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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.30-7.20 (m, 2H), 7.19-7.13 (m, 1H), 7.07 (td, *J*<sub>1</sub> = 7.6 Hz, *J*<sub>1</sub> = 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*<sub>1</sub> = 15.6 Hz, *J*<sub>2</sub> = 7.6 Hz, 1H), 3.77 (s, 3H), 3.18 (s, 3H), 2.70-2.59 (m, 2H), 1.42 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>20</sub>H<sub>22</sub>NO<sub>2</sub><sup>+</sup> (M+H)<sup>+</sup> 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<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.0 mg, 0.01 mmol, 5 mol %), *N'*-(3,4-dimethoxybenzylidene)-4-methylbenzenesulfonohydrazide (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  180.2, 148.7, 148.4, 143.0, 133.6, 133.2, 130.3, 127.7, 122.9, 122.3, 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<sub>21</sub>H<sub>23</sub>NO<sub>3</sub>Na<sup>+</sup> (M+Na)<sup>+</sup> 360.1576, found 360.1581.





A mixture of **1a** (63.0 mg, 0.20 mmol, 1.0 equiv), LiO<sup>*t*</sup>Bu(48.0 mg, 0.60 mmol, 3.0 quiv), *N*'-(naphthalen-2-ylmethylene)-4-methylbenzenesulfonohydrazide (0.130 g, 0.40 mmol, 2.0 equiv), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (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. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  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, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.03 (dt, *J<sub>I</sub>* = 15.6 Hz, *J<sub>2</sub>* = 7.6 Hz, 1H), 3.19 (s, 3H), 2.72 (d, *J* = 7.6 Hz, 2H), 1.46 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  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<sub>23</sub>H<sub>22</sub>NO<sup>+</sup> (M+H)<sup>+</sup> 328.1696, found 328.1692.

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