## Highly Efficient Syntheses of Azetidines, Pyrrolidines and Indolines via Palladium

# Catalyzed Intramolecular Amination of $C(sp^3)$ and $C(sp^2)$ -H Bonds at $\gamma$ and $\delta$ Positions

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1. **Reagents**: All commercial materials were used as received unless otherwise noted. The following solvents were obtained from a JC Meyer solvent dispensing system and used without further purification: THF, DMF, DCM and toluene. Flash chromatography was performed using 230-400 mesh SiliaFlash 60® silica gel (Silicycle Inc.). PhI(OAc)<sub>2</sub> (98%, Aldrich), Pd(OAc)<sub>2</sub> (98%, Aldrich), AcOH (99.7%, Mallinckrodt Chemicals) were used in the Pd-catalyzed reactions.

2. **Instruments**: NMR spectra were recorded on Bruker CDPX-300, DPX-300, DRX-400 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, br s = broad singlet, m = multiplet. High resolution ESI mass experiments were operated on a Waters LCT Premier instrument.

3. General procedure A for the preparation of picolinamide substrates 1, 8, 10, 16, 18, 21, 24, 26, 30, 35, 37, 44.



A mixture of amine (1.0 eq), picolinic acid (1.1 eq), EDCI (1.1 eq), HOBtH<sub>2</sub>O (1.1 eq), and DIPEA (3.0 eq) in anhydrous DCM (0.2 M) was stirred at rt overnight. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give the desired picolinamide product.

4. General procedure B for the preparation of picolinamide substrates 5, 13, 28.



A mixture of amino alcohol (1.0 eq), picolinic acid (1.0 eq), EDCI (1.1 eq), and HOBtH<sub>2</sub>O (1.1 eq) in anhydrous DMF (0.2 M) was stirred at room temperature overnight. Water was added and the mixture was extracted with ethyl acetate. The combined organic layers was washed with water and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The resulting residue was dissolved in DCM; Ac<sub>2</sub>O (2.0 eq) and Et<sub>3</sub>N (2.0 eq) were added to the resulting solution. After stirring at rt for 8 hours, the solvent was removed and the residue was purified by silica gel flash chromatography to give the desired picolinamide product.

5. General procedure C: Synthesis of azetidines via Pd-catalyzed intramolecular amination of  $\gamma$ -C(sp<sup>3</sup>)–H bonds.

A mixture of picolinamide substrate (0.2 mmol, 1.0 eq),  $Pd(OAc)_2$  (2.2 mg, 0.01 mmol, 0.05 eq),  $PhI(OAc)_2$  (161 mg, 0.5 mmol, 2.5 eq), and AcOH (23  $\mu$ L, 0.4 mmol, 2.0 eq) in anhydrous toluene (2 mL) in a 10 mL glass vial (purged with Ar, sealed with PTFE cap) was heated at 110 °C for 24 hours. The reaction mixture was cooled to rt, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give the cyclized azetidine product.

6. General procedure D: Synthesis of pyrrolidines via Pd-catalyzed intramolecular amination of  $\delta$ -C(sp<sup>3</sup>)–H bonds.

A mixture of picolinamide (0.2 mmol, 1.0 eq),  $Pd(OAc)_2$  (2.2 mg, 0.01 mmol, 0.05 eq),  $PhI(OAc)_2$  (161 mg, 0.5 mmol, 2.5 eq), AcOH (115  $\mu$ L, 2.0 mmol, 10.0 eq) in anhydrous toluene (2 mL) in a 10 mL glass vial (purged with Ar, sealed with PTFE cap) was heated at 110 °C for 24 hours. The reaction mixture was cooled to rt, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give the cyclized pyrrolidine product.

7. General procedure E: Synthesis of indolines via Pd-catalyzed intramolecular amination of  $\delta$ -C(sp<sup>2</sup>)–H bonds.

A mixture of picolinamide (0.4 mmol, 1.0 eq),  $Pd(OAc)_2$  (1.8 mg, 0.008 mmol, 0.02 eq),  $PhI(OAc)_2$  (322 mg, 1.0 mmol, 2.5 eq), and toluene (4 mL) in a 10 mL glass vial (purged with Ar, sealed with PTFE cap) was heated at 60 °C for 24 hours. The reaction mixture was cooled to rt,

and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give the cyclized product.

8. <sup>1</sup>H-NMR assay for the screening reactions of substrate 1.



The screening reactions of substrate 1 were carried out following the general procedure C under the conditions specified in Table 1 in a 10 mL glass vial (purged with different gas, sealed with PTFE cap) (0.2 mmol scale). The reaction mixture was then cooled to rt, diluted with CHCl<sub>3</sub>, filtered through a short celite pad, and concentrated *in vacuo*. The resulting residue was dissolved in 0.5 mL of CDCl<sub>3</sub> and 0.2 mmol of Cl<sub>2</sub>CHCHCl<sub>2</sub> was added as an internal standard. The distributions of compounds 1, 2(cis and trans isomers), 3, 4 were analyzed based on the distinct chemical shifts of  $\beta$ -Hs of different products in <sup>1</sup>H-NMR of the resulting mixture. More than 2 experiments were performed for each condition.

## 9. Characterization of compounds 1-45:

All the azetidine and pyrrolidine products show two sets of rotamer signals in <sup>1</sup>H and <sup>13</sup>C-NMR spectra at rt. The <u>ratio</u> of these two sets of signal changes in different solvent such as  $CDCl_3$  and  $DMSO-d_6$ .



Compound **1** was prepared following the standard coupling procedure A in 90% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.61 (m, 2H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.87 (m, 1H), 7.48 (m, 1H), 4.78 (dd, *J* = 5.1, 9.1 Hz, 1H), 3.79 (s, 3H), 2.37 (m, 1H), 1.05 (d, *J* = 2.1 Hz, 3H), 1.03 (d, *J* = 2.1 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  172.35, 164.42, 149.67, 148.55, 137.59, 126.67, 122.48, 57.58, 52.33, 31.70, 19.38, 18.14; HRMS Calcd for C<sub>12</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 237.1239; Found: 237.1218.



Compound 2-cis isomer was isolated in 74% yield following the general procedure C with 2.5 mol% of Pd(OAc)<sub>2</sub>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: 2.5/1)  $\delta$  8.57 (d, J = 4.6 Hz, 0.28H), 8.43 (m, 0.72H), 8.14 (m, 1H), 7.80 (m, 1H), 7.37 (m, 1H), 5.08 (d, J = 4.9 Hz, 0.72H), 4.94 (dd, J = 9.3, 8.9 Hz, 0.28H), 4.51 (d, J =4.9 Hz, 0.28H), 4.42 (m, 0.72H), 4.29 (dd, J = 5.4, 10.0 Hz, 0.28H), 3.78 (s, 0.86H), 3.77 (m, 0.72H), 3.64 (s, 2.14H), 2.76 (m, 1H), 1.41 (m, 3H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz) δ 171.47, 170.96, 164.92, 164.50, 151.47, 151.28, 148.06, 147.42, 136.87, 136.68, 125.49, 125.41, 123.97, 123.53, 72.28, 66.57, 60.37, 54.05, 52.25, 51.94, 30.75, 30.52, 19.43, 19.19; HRMS Calcd for  $C_{12}H_{15}N_2O_3$  [M+H<sup>+</sup>]: 235.1083; Found: 235.1090.

Compound **2**-trans isomer was isolated in 12% yield following the general procedure C with 2.5 mol% of Pd(OAc)<sub>2</sub>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: 2.5/1)  $\delta$  8.58 (d, *J* = 4.0 Hz, 0.31H), 8.46 (m, 0.78H), 8.17 (m, 1H), 7.83 (m, 1H), 7.39 (m, 1H), 5.62 (dd, *J* = 0.8, 9.2 Hz, 0.77H), 5.05 (d, *J* = 9.5 Hz, 0.29H), 4.85 (dd, *J* = 8.4, 10.0 Hz, 0.29H), 4.40 (m, 0.29H), 4.34 (dd, *J* = 8.6, 9.8 Hz, 0.75H), 3.91 (m, 0.76H), 3.81 (s, 0.8H), 3.64 (s, 2.2H), 3.22 (m, 1H), 1.19 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  170.59, 164.91, 151.90, 148.52, 147.98, 137.30, 137.16, 125.92, 125.80, 124.47, 124.04, 70.26, 64.39, 54.95, 52.35, 52.03, 31.38, 28.83, 28.46, 15.54, 15.20; HRMS Calcd for C<sub>12</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 235.1083; Found: 235.1064.

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Compound **3** as diastereomeric mixture was isolated in 2% yield following the general procedure C with 2.5 mol% of Pd(OAc)<sub>2</sub>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.62 (m, 1H), 8.21 (m, 1H), 7.90 (m, 1H), 7.49 (m, 1H), 4.96 (m, 1H), 4.20 (m, 2H), 3.80 (s, 3H), 2.65 (m, 1H), 2.19 (m, 3H), 1.11 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  172.17, 172.02, 171.24, 164.86, 149.71, 148.71, 137.78, 126.88, 122.81, 66.03, 54.88, 53.80, 52.93, 52.82, 36.10, 35.93, 31.38, 21.35, 21.28, 14.48, 12.66; HRMS Calcd for C<sub>14</sub>H<sub>19</sub>N<sub>2</sub>O<sub>5</sub> [M+H<sup>+</sup>]: 295.1294; Found: 295.1291.



Compound **4** was isolated in 8% yield following the general procedure C with 2.5 mol% of Pd(OAc)<sub>2</sub>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  8.58 (m, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.86 (m, 1H), 7.48 (m, 1H), 5.14 (dd, *J* = 4.2, 9.1 Hz, 1H), 4.33 (dd, *J* = 5.9, 11.7 Hz, 1H), 4.21 (m, 3H), 3.79 (s, 3H), 2.86 (m, 1H), 2.14 (s, 3H), 2.08 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz):  $\delta$  171.52, 171.10, 170.97, 164.88, 149.48, 148.69, 137.84, 127.02, 122.87, 62.34, 62.24, 53.12, 51.77, 40.25, 21.23, 21.20; HRMS Calcd for C<sub>16</sub>H<sub>21</sub>N<sub>2</sub>O<sub>7</sub> [M+H<sup>+</sup>]: 253.1349; Found: 253.1347.

Compound **5** was prepared following the standard procedure B in 40% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  8.56 (m, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.86 (td, *J* = 7.7, 1.6 Hz, 1H), 7.44 (m, 1H), 4.28 (m, 3H), 2.04 (s, 3H), 2.01 (m, 1H), 1.02 (d, *J* = 4.0 Hz, 3H), 1.00 (d, *J* = 4.0 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  171.31, 164.55, 150.08, 148.46, 137.71,

126.57, 122.67, 64.97, 53.65, 29.99, 21.20, 19.85, 18.84; HRMS Calcd for  $C_{13}H_{19}N_2O_3$  [M+H<sup>+</sup>]: 251.1396; Found: 251.1388.

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Compound **6** was prepared in 82% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1.3:1</u>)  $\delta$  8.55 (d, *J* = 4.7 Hz, 2.3H), 8.07 (d, *J* = 7.9 Hz, 2.3H), 7.80 (td, *J* = 7.7, 1.8 Hz, 2.3H), 7.35 (m, 2.3H), 4.81 (m, 2.3H), 4.55-4.20 (m, 6.9H), 4.08 (dd, *J* = 5.5, 10.2 Hz, 1.3H), 3.68 (dd, *J* = 4.6, 10.2 Hz, 1H), 2.59 (m, 2.3H), 2.07 (s, 3.9H), 2.00 (s, 3H), 1.32 (d, *J* = 7.0 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 3.9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  171.30, 171.23, 166.39, 166.11, 152.26, 152.13, 148.48, 148.46, 137.30, 137.16, 125.92, 125.78, 124.39, 124.19, 71.02, 67.17, 65.53, 64.09, 60.33, 54.17, 29.21, 28.59, 21.28, 21.19, 19.56, 19.19; HRMS Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 249.1239; Found: 249.1221.

Compound **8** was prepared in 63% yield following the standard coupling procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.66 (s, 1H), 8.63 (d, *J* = 4.6 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.89 (t, *J* = 7.7 Hz, 1H), 7.48 (m, 1H), 4.69 (d, *J* = 9.8Hz, 1H), 3.78 (s, 3H), 1.10 (s, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  172.02, 164.29, 149.76, 148.62, 137.64, 126.69, 122.62, 60.62, 52.10, 35.33, 26.69; HRMS Calcd for C<sub>13</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 251.1396; Found: 251.1384.

Compound **9** was prepared in 91% yield following the standard procedure **C**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ratio of rotamers: <u>1:0.36</u>):  $\delta$  8.56 (d, J = 4.8 Hz, 0.36H), 8.43 (m, 1H), 8.16 (m, 1.36H), 7.80 (m, 1.36H), 7.36 (dd, J = 4.9, 7.4 Hz, 0.36H), 7.30 (m, 1H), 5.18 (s, 1H), 4.60 (s, 0.36H), 4.50 (d, J = 9.7 Hz, 0.36H), 4.38 (d, J = 9.8 Hz, 0.36H), 3.97 (d, J = 9.6 Hz, 1H), 3.87 (d, J = 9.5 Hz, 1H), 3.78 (s, 1.08H), 3.62 (s, 3H), 1.46 (s, 3H), 1.43 (s, 1.08H), 1.19 (s, 1.08H), 1.16 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  170.58, 169.78, 165.45, 165.17, 151.97, 151.86, 148.46, 147.89, 137.27, 137.12, 125.92, 125.81, 124.37, 123.96, 75.84, 69.99, 66.39, 60.34, 52.23, 51.96, 36.34, 36.02, 28.66, 28.40, 23.03, 22.73; HRMS Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 249.1239; Found: 249.1234.

Compound **10** was prepared in 84% yield following the standard procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.58 (m, 1H), 8.49 (d, *J* = 6.8 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 (m, 1H), 4.79 (m, 1H), 3.76 (s, 3H), 2.06-1.97 (m, 1H), 1.95-1.81 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  172.87, 164.43, 149.75, 148.59, 137.63,

126.70, 122.56, 53.74, 52.61, 26.09, 10.10; HRMS Calcd for  $C_{11}H_{15}N_2O_3$  [M+H<sup>+</sup>]: 223.1083; Found: 223.1069.

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Compound **11** was prepared in 25% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: 2.5:1)  $\delta$  8.59 (d, *J* = 4.4 Hz, 0.4H), 8.45 (d, *J* = 4.6 Hz, 1H), 8.16 (m, 1.4H), 7.83 (m, 1.4H), 7.40 (m, 1.4H), 5.55 (dd, *J* = 5.4, 9.3 Hz, 1H), 4.99 (dd, *J* = 5.4, 9.4 Hz, 0.4H), 4.88 (m, 0.4H), 4.76 (m, 0.4H), 4.38 (m, 1H), 4.24 (m, 1H), 3.81 (s, 1.2H), 3.67 (s, 3H), 2.76 (m, 1.4H), 2.36 (m, 1.4H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  172.33, 171.86, 165.14, 164.78, 151.84, 151.67, 148.57, 147.92, 137.36, 137.17, 125.98, 125.90, 124.39, 123.94, 65.96, 60.34, 54.07, 52.77, 52.45, 47.76, 22.09, 21.83; HRMS Calcd for C<sub>11</sub>H<sub>13</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 221.0926; Found: 221.0924.

Compound **12** was prepared in 70% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.65 (d, J = 7.8 Hz, 1H), 8.58 (d, J = 4.7 Hz, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.86 (t, J = 7.7 Hz, 1H), 7.45 (t, J = 6.5 Hz, 1H), 4.94 (m, 1H), 4.26 (m, 2H), 3.78 (s, 3H), 2.38 (m, 1H), 2.26 (m, 1H), 2.05 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  172.34, 171.10, 164.57, 149.53, 148.63, 137.74, 126.90, 122.66, 61.06, 52.91, 50.33, 31.32, 21.18; HRMS Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O<sub>5</sub> [M+H<sup>+</sup>]: 281.1137; Found: 281.1116.

Compound **13** was prepared in 32% yield using the standard procedure **B**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.56 (m, 1H), 8.20 (td, J = 1.0, 7.9 Hz, 1H), 8.13 (d, J = 6.1 Hz, 1H), 7.86 (td, J = 7.7, 1.7 Hz, 1H), 7.44 (m, 1H), 4.30 (m, 3H), 2.03 (s, 3H), 1.81 (m, 1H), 1.64 (m, 1H), 1.29 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  171.31, 164.41, 150.09, 148.44, 137.68, 126.53, 122.63, 64.79, 52.61, 36.53, 25.72, 21.19, 15.87, 11.67; HRMS Calcd for C<sub>14</sub>H<sub>21</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 265.1552; Found: 265.1547.



Compound **14** was isolated in 70% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1.3:1</u>)  $\delta$  8.56 (m, 2.3H), 8.07 (m, 2.3H), 7.82 (td, *J* = 7.7, 1.7 Hz, 2.3H), 7.37 (m, 2.3H), 5.33 (m, 1H), 4.84 (m, 1.3H), 4.65-4.47 (m, 4.9H), 4.37-4.24 (m, 3.3H), 3.84 (t, *J* = 8.3 Hz, 1H), 2.93-2.72 (m, 2.3H), 2.07 (s, 3.9H), 1.96 (s, 3H), 1.75-1.56 (m, 4.6H), 0.92 (m, 6.9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  170.99, 170.84, 166.25, 165.85, 152.33, 152.27,

148.54, 148.42, 137.27, 137.17, 125.86, 125.76, 124.30, 124.22, 66.17, 63.01, 61.88, 61.77, 59.72, 54.04, 35.70, 35.51, 22.20, 22.12, 21.38, 21.23, 12.14, 12.10; HRMS Calcd for  $C_{14}H_{19}N_2O_3$  [M+H<sup>+</sup>]: 263.1396; Found: 263.1396.

Compound **15** was isolated in 8% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.56 (m, 1H), 8.36 (d, *J* = 9.5 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.88 (td, *J* = 7.7, 7.7 Hz, 1H), 7.46 (m, 1H), 4.61 (m, 1H), 4.27 (d, *J* = 5.4 Hz, 2H), 4.22 (m, 1H), 4.12 (m, 1H), 2.11 (s, 3H), 2.05 (s, 3H), 2.02 (m, 1H), 1.63 (m, 1H), 1.47 (m, 1H), 1.03 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  171.41, 171.36, 164.45, 150.00, 148.51, 137.86, 126.75, 122.82, 64.46, 64.26, 49.55, 41.61, 21.38, 21.30, 21.25, 12.29; HRMS Calcd for C<sub>16</sub>H<sub>23</sub>N<sub>2</sub>O<sub>5</sub> [M+H<sup>+</sup>]: 323.1607; Found: 323.1605.

Compound **16** was prepared in 95% yield following the standard procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.68 (d, *J* = 9.0 Hz, 1H), 8.62 (d, *J* = 4.7 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.2 Hz, 1H), 7.44 (m, 1H), 4.71 (d, *J* = 9.4 Hz, 1H), 4.35 (m, 1H), 3.73 (s, 3H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.17 (s, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  171.57, 165.18, 149.92, 148.79, 137.53, 126.65, 122.67, 74.48, 68.05, 58.46, 52.56, 28.73, 21.31; HRMS Calcd for C<sub>15</sub>H<sub>23</sub>N<sub>2</sub>O<sub>4</sub> [M+H<sup>+</sup>]: 295.1658; Found: 295.1635.

Compound **17** was isolated in 79% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ratio of rotamers: <u>3:1</u>)  $\delta$  8.57 (d, *J* = 4.6 Hz, 1H), 8.45 (d, *J* = 4.7 Hz, 3H), 8.14 (m, 4H), 7.80-7.75 (m, 4H), 7.36-7.29 (m, 4H), 5.64 (dd, *J* = 1.0, 7.5 Hz, 3H), 5.09 (d, *J* = 7.7 Hz, 1H), 4.98 (dd, *J* = 6.6, 10.0 Hz, 1H), 4.74 (m, 4H), 4.65 (m, 1H), 4.41 (dd, *J* = 7.1, 10.1 Hz, 3H), 4.21 (m, 3H), 3.79 (s, 3H), 3.65 (s, 9H), 1.17 (s, 36H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  169.22, 168.34, 165.10, 164.95, 151.90, 151.65, 148.49, 148.09, 137.26, 137.11, 125.93, 125.86, 124.31, 123.90, 75.51, 75.40, 73.99, 68.66, 64.27, 63.46, 63.07, 58.81, 52.26, 52.07, 31.28, 28.21; HRMS Calcd for C<sub>15</sub>H<sub>21</sub>N<sub>2</sub>O<sub>4</sub> [M+H<sup>+</sup>]: 293.1501; Found: 293.1484.

# NHPA 18

Compound **18** was prepared in 67% yield following the standard procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.53 (d, J = 4.1 Hz, 1H), 8.20 (d, J = 7.8 Hz, 1H), 8.11 (s, 1H), 7.85 (td, J = 7.7, 5.2 Hz, 1H), 7.41 (dd, J = 5.2, 6.9 Hz, 1H), 3.44-3.23 (m, 2H), 1.72 (m, 1H), 1.51 (m, 1H), 1.26 (m, 1H), 0.96 (m, 6H); ); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  164.23, 150.02, 147.93, 137.25, 125.95,

122.12, 44.96, 35.05, 27.00, 17.22, 11.28; HRMS Calcd for  $C_{11}H_{17}N_2O$  [M+H<sup>+</sup>]: 193.1341; Found: 193.1322.

Compound **19** was isolated in 68% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, no rotamers observed)  $\delta$  8.58 (d, J = 4.4 Hz, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.82 (td, J = 7.7, 1.6 Hz, 1H), 7.37 (m, 1H), 4.78 (dd, J = 9.5, 10.7 Hz, 1H), 4.33 (m, 2H), 3.86 (dd, J = 5.6, 10.2 Hz, 1H), 2.61 (m, 1H), 1.71 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  165.18, 152.03, 147.90, 136.61, 125.03, 123.61, 59.81, 53.83, 31.48, 27.28, 11.06; HRMS Calcd for C<sub>11</sub>H<sub>15</sub>N<sub>2</sub>O [M+H<sup>+</sup>]: 191.1184; Found: 191.1168.



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Compound **20** was isolated in 12% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.56 (m, 1H), 8.36 (s, 1H), 8.21 (dd, J = 0.7, 5.9 Hz, 1H), 7.88 (m, 1H), 7.45 (m, 1H), 4.24 (dd, J = 4.4, 11.3 Hz, 1H), 4.10 (dd, J = 4.9, 11.3 Hz, 1H), 3.64 (m, 1H), 3.48 (m, 1H), 2.12 (s, 3H), 1.97 (m, 1H), 1.50 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  171.20, 164.39, 148.02, 137.31, 126.08, 122.18, 65.52, 40.69, 39.65, 22.03, 20.89, 11.34; HRMS Calcd for C<sub>13</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 251.1396; Found: 251.1380.

Compound **21** was prepared in 87% yield following the standard coupling procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.58 (m, 1H), 8.36 (d, *J* = 7.6 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.85 (t, *J* = 7.7 Hz, 1H), 7.44 (m, 1H), 4.85 (m, 1H), 3.75 (s, 3H), 1.79-1.69 (m, 3H), 0.98 (t, *J* = 4.5 Hz, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  173.47, 164.45, 149.69, 148.56, 137.64, 126.71, 122.62, 52.58, 51.11, 41.89, 25.22, 23.20, 22.15; HRMS Calcd for C<sub>13</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 251.1396; Found: 251.1383.



Compound **22-trans** was isolated in 72% yield following the standard procedure **D**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1:0.86</u>)  $\delta$  8.61 (dd, J = 1.0, 5.4 Hz, 0.86H), 8.47 (m, 1H), 8.07 (d, J = 7.9 Hz, 1H), 7.93 (d, J = 7.9 Hz, 0.86H), 7.83 (m, 1.86H), 7.39 (m, 1.86H), 5.18 (m, 1H), 4.75 (dd, J = 2.6, 8.8 Hz, 0.86H), 4.13 (m, 1.86H), 3.78 (s, 2.6H), 3.66 (s, 3H), 3.60 (dd, J = 9.0, 11.0 Hz, 0.86H), 3.36 (dd, J = 9.2, 11.9 Hz, 1H), 2.50 (m, 1.86H), 2.27 (m, 1H), 2.16 (m, 0.86H), 1.99 (m, 1.86H), 1.13 (d, J = 6.5 Hz, 3H), 1.07 (d, J = 6.6 Hz, 2.6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.91, 173.10, 165.55, 165.74, 153.72, 152.93, 148.26, 147.49, 137.31, 137.23, 125.50, 124.99, 124.78, 62.53, 60.57, 56.91, 55.47, 52.63, 52.41, 39.82, 36.77, 33.31, 30.01, 17.62, 17.46; HRMS Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 249.1239; Found: 249.1232.

Compound **22**-cis was isolated in 10% yield following the standard procedure **D**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1:1.4</u>)  $\delta$  8.63 (d, *J* = 3.4 Hz, 1.4H), 8.47 (d, *J* = 4.6 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1.4H), 7.82 (m, 2.4H), 7.39 (m, 2.4H), 5.28 (t, *J* = 8.4 Hz, 1H), 4.66 (dd, *J* = 7.7, 9.8 Hz, 1.4H), 4.25 (m, 2.5H), 3.78 (s, 4.2H), 3.58 (m, 1.4H), 3.51 (s, 3H), 3.30 (t, *J* = 10.0 Hz, 1H), 2.62 (m, 2.4H), 2.37 (m, 2.4H), 1.74 (m, 2.4H), 1.14 (dd, *J* = 8.0, 6.7 Hz, 7.2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.89, 173.11, 166.49, 165.92, 153.63, 153.35, 148.41, 147.43, 137.39, 137.21, 125.53, 125.40, 125.08, 124.84, 62.30, 61.09, 57.15, 55.72, 52.68, 52.31, 40.33, 37.30, 34.79, 31.53, 17.53, 17.01; HRMS Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 249.1239; Found: 249.1225.

Compound **24** was prepared in 99% yield following the standard coupling procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.57 (dd, J = 0.7, 4.1 Hz, 1H), 8.31 (d, J = 8.2 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H), 7.85 (td, J = 7.8, 1.6 Hz, 1H), 7.43 (m, 1H), 4.85 (m, 1H), 3.73 (s, 3H), 1.94 (m, 1H), 1.72 (m, 1H), 0.99 (s, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  173.85, 164.16, 149.73, 148.61, 137.65, 126.71, 122.65, 52.69, 50.34, 46.38, 31.07, 29.94; HRMS Calcd for C<sub>14</sub>H<sub>21</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 265.1552; Found: 265.1528.

Compound **25** was isolated in 86% yield following the standard procedure C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ratio of rotamers: <u>1:1.3</u>)  $\delta$  8.61 (d, *J* = 4.7 Hz, 1.3H), 8.45 (d, *J* = 4.7 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.93 (d, *J* = 7.9 Hz, 1.3H), 7.80 (m, 2.3H), 7.36 (m, 1.3H), 7.31 (m, 1H), 5.36 (t, *J* = 8.4 Hz, 1H), 4.73 (dd, *J* = 8.1, 9.5 Hz, 1.3H), 3.85 (m, 1H), 3.77 (m, 2.6H), 3.76 (s, 3.9H), 3.50 (s, 3H), 3.48 (d, *J* = 11.8 Hz, 1H), 2.24 (m, 1H), 2.11 (dd, *J* = 8.0, 12.5 Hz, 1.3H), 1.91 (m, 2.3H), 1.63 (m, 9.9H), 1.03 (s, 3.9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.99, 173.13, 166.75, 166.09, 153.51, 153.26, 148.39, 147.39, 137.35, 137.18, 125.53, 125.39, 125.10, 124.90, 62.72, 61.76, 61.18, 60.35, 52.66, 52.31, 45.76, 42.55, 39.66, 36.40, 26.76, 26.34, 26.30, 26.11; HRMS Calcd for C<sub>14</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 263.1396; Found: 263.1387.

Compound **26** was prepared in 71% yield following the standard coupling method **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.57 (m, 1H), 8.44 (d, *J* = 10.4 Hz, 1H), 8.16 (d, *J* = 6.9 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.43 (m, 1H), 4.81 (m, 1H), 3.74 (s, 3H), 1.96 (m, 2H), 1.46 (m, 1H), 0.95 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.11, 164.40, 149.70, 148.57, 137.64, 126.72, 122.57, 56.62, 52.39, 34.92, 19.09, 13.97; HRMS Calcd for C<sub>12</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 237.1239; Found: 237.1230.



Compound **27** was isolated in 17% yield following the standard procedure **D**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ratio of rotamer: <u>1:0.8</u>)  $\delta$  8.60 (m, 0.8H), 8.47 (m, 1H), 8.59 (dd, *J* = 0.9, 7.9 Hz, 1H), 7.92 (dd, *J* = 0.9, 7.9 Hz, 0.8H), 7.81 (m, 1.8H), 7.37 (m, 1.8H), 5.16 (m, 1H), 4.70 (m, 0.8H), 4.04-3.80 (m, 3.6H), 3.78 (s, 2.4H), 3.64 (s, 3H), 2.32-2.22 (m, 1.8H), 2.18-2.13 (m, 1H), 2.10-2.00 (m, 1.4H), 1.99-1.92 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.84, 173.04, 166.60, 165.85, 153.71, 153.06, 148.27, 147.49, 137.29, 137.17, 125.47, 124.90, 124.71, 61.95, 60.46, 52.57, 52.36, 50.10, 48.64, 32.17, 29.23, 25.82, 22.35; HRMS Calcd for C<sub>12</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 235.1083; Found: 235.1075.

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Compound **28** was prepared in 49% yield following the standard procedure **B**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.55 (d, *J* = 4.3 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.86 (t, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 6.2 Hz, 1H), 4.98 (m, 1H), 4.17 (d, *J* = 4.8 Hz, 2H), 2.06 (s, 3H), 1.72 (m, 1H), 1.60 (m, 1H), 1.46 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  171.32, 164.33, 150.09, 148.43, 137.72, 126.57, 122.67, 66.88, 46.85, 41.05, 25.17, 23.46, 22.44, 21.20; HRMS Calcd for C<sub>14</sub>H<sub>21</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 265.1552; Found: 265.1545.



Compound **29** was prepared in 72% yield following the standard procedure **D**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1:1.6</u>)  $\delta$  8.58 (m, 2.6H), 7.86 (m, 5.2H), 7.35 (m, 2.6H), 5.15 (m, 1H), 4.62 (m, 1.6H), 4.35 (m, 3.2H), 4.05 (m, 2.6H), 3.94 (m, 2H), 3.33 (m, 2.6H), 2.50 (m, 2.6H), 2.06 (s, 4.8H), 2.02 (m, 2.6H), 1.87 (s, 3H), 1.81 (m, 2.6H), 1.13 (d, *J* = 6.5 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 4.8H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  171.34, 170.95, 167.52, 166.83, 154.70, 154.41, 148.41, 148.25, 137.34, 137.29, 125.27, 125.18, 124.74, 124.25, 65.87, 64.37, 57.41, 57.06, 56.68, 54.63, 37.65, 35.60, 32.64, 29.69, 21.38, 21.15, 18.73, 18.22; HRMS Calcd for C<sub>14</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 263.1396; Found: 263.1371.



Compound **30** was prepared in 57% yield following the standard coupling procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  10.24 (s, 1H), 8.56 (d, *J* = 4.2 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 7.84 (td, *J* = 7.7, 1.3 Hz, 1H), 7.41 (m, 2H), 7.23 (M, 1H), 7.09 (m, 1H), 1.42 (s, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  161.74, 150.14, 148.12, 141.01, 137.63, 135.40, 126.78, 126.38, 126.29, 125.17, 124.96, 122.48, 34.48, 30.48; HRMS Calcd for C<sub>16</sub>H<sub>19</sub>N<sub>2</sub>O [M+H<sup>+</sup>]: 255.1497; Found: 255.1475.



Compound **31** was isolated in 61% yield following the standard procedure **D** with 10 mol% of Pd(OAc)<sub>2</sub>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, no rotamers observed)  $\delta$  8.58 (d, *J* = 4.5 Hz, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.85 (m, 2H), 7.35(t, *J* = 5.2 Hz, 1H), 7.23 (m, 1H), 7.13 (m, 2H), 4.02 (s, 2H), 1.25 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  154.91, 148.46, 142.39, 141.85, 137.49, 128.01, 125.45, 125.09, 124.73, 122.29, 118.35, 65.46, 41.03, 28.61; HRMS Calcd for C<sub>16</sub>H<sub>17</sub>N<sub>2</sub>O [M+H<sup>+</sup>]: 253.1341; Found: 253.1323.



Compound 33

Compound **32** was prepared from compound **32-0** based on the known procedure.<sup>1</sup> Compound **33** was isolated in 56% yield following the standard procedure **D**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1:1.2</u>)  $\delta$  8.67 (t, *J* = 4.7 Hz, 2.2H), 8.00 (m, 2.2H), 7.84 (m, 2.2H), 7.40 (dd, *J* = 5.0, 6.6 Hz, 2.2H), 7.29 (m, 2.2H), 6.93 (d, *J* = 7.5 Hz, 1.2H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.77 (dd, *J* = 2.5, 8.1 Hz, 2.2H), 5.22 (s, 2H), 5.13 (s, 2.4H), 5.04 (s, 2.4H), 4.99 (s, 2H), 3.85 (s, 3H), 3.81 (s, 3.6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  166.91, 166.57, 155.43, 155.06, 154.17, 148.57, 148.34, 139.74, 137.79, 137.32, 137.29, 129.65, 129.62, 126.01, 125.39, 125.34, 124.71, 124.46, 124.26, 115.20, 114.84, 109.12, 109.03, 55.78, 55.72, 55.61, 54.29, 53.36, 52.10; HRMS Calcd for C<sub>15</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>]: 255.1134; Found: 255.1116.

#### Compound **34**

Compound **34** was isolated in 30% yield following the standard procedure **D**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.50 (dd, J = 0.7, 3.9 Hz, 1H), 8.38 (s, 1H), 8.21 (d, J = 7.8 Hz, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.40 (m, 1H), 7.31 (m, 1H), 7.02 (d, J = 7.4 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 5.35 (s, 2H), 4.77 (d, J = 5.9 Hz, 1H), 3.90 (s, 3H), 2.05 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  171.12, 164.15, 158.91, 150.53, 148.43, 137.69, 136.37, 129.32, 126.43, 126.00, 122.92, 122.70, 111.46, 65.02, 56.24, 35.13, 21.44; HRMS Calcd for C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O<sub>4</sub> [M+H<sup>+</sup>]: 315.1345; Found: 315.1345.

Compound **35** was prepared in 98% yield following the standard amide coupling procedure **A**. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.55 (m, 1H), 8.49 (d, *J* = 8.0 Hz, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.43 (m, 1H), 7.30 (m, 3H), 7.20 (m, 2H), 5.10 (m, 1H), 3.72 (s, 3H), 3.29 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$ 172.18, 164.41, 149.63, 148.72, 137.69, 136.49, 129.68, 128.99, 127.48, 126.84, 122.62, 53.90, 52.73, 38.62; HRMS Calcd for C<sub>16</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 285.1239; Found: 285.1226.



Compound **36** was isolated in 81% yield following the standard procedure **E**. <sup>1</sup>H NMR (DMSOd<sub>6</sub>, 300 MHz, no rotamers observed)  $\delta$  8.56 (d, *J* = 4.3 Hz, 1H), 8.28 (d, *J* = 8.2 Hz, 1H), 8.03 (m, 2H), 7.58 (m, 1H), 7.53 (m, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 5.67 (dd, *J* = 2.3, 10.9 Hz, 1H), 3.70 (m, 1H), 3.60 (s, 3H), 3.19 (dd, *J* = 2.3, 16.8 Hz, 1H); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 100 MHz)  $\delta$  173.05, 165.84, 153.40, 148.20, 144.26, 138.59, 130.66, 128.25, 128.11, 126.71, 125.51, 125.19, 118.00, 62.94, 52.95, 33.98; HRMS Calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>]: 283.1083; Found: 283.1063.



Compound **37** was prepared in 97% yield following the standard amide coupling procedure A. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.55 (m, 1H), <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.51 (d, *J* = 4.3 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.14 (s, 1H), 7.85 (td, *J* = 7.7, 1.5 Hz, 1H), 7.41 (m, 1H), 7.33 (m, 2H), 7.26 (m, 3H), 3.76 (dd, *J* = 6.8, 13.5 Hz, 2H), 2.97 (t, *J* = 7.3 Hz, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  164.75, 150.30, 148.47, 139.39, 137.67, 129.17, 128.99, 126.85, 126.51, 122.51, 41.20, 36.30; HRMS Calcd for C<sub>14</sub>H<sub>15</sub>N<sub>2</sub>O [M+H<sup>+</sup>]: 227.1184; Found: 227.1179.



Compound **38** was isolated in 90% yield following the standard procedure **E**. <sup>1</sup>H NMR (DMSOd<sub>6</sub>, 300 MHz)  $\delta$  8.66 (d, *J* = 4.5 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 8.03 (td, *J* = 7.8, 1.6 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.58 (dd, *J* = 5.3, 6.9 Hz, 1H), 7.30 (m, 2H), 7.10 (m, 1H), 4.20 (t, *J* = 8.3 Hz, 2H), 3.13 (t, *J* = 8.3 Hz, 2H); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 75.5 MHz)  $\delta$  166.57, 155.07, 149.07, 143.78, 138.34, 133.39, 127.83, 126.13, 125.81, 125.01, 124.39, 117.77, 50.83, 28.82; HRMS Calcd for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>O [M+H<sup>+</sup>]: 225.1028; Found: 225.1021.



Compound **38** (50 mg, 0.22 mmol, 1.0 eq) was dissolved in a mixture of THF/MeOH/H<sub>2</sub>O (1/0.5/0.5 mL); NaOH (14 mg, 0.33 mmol, 1.5 eq) was then added. The mixture was heated to 50 °C and stirred for 24 hours. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography to give the desired product **39**<sup>2</sup> in 83% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  7.15 (d, *J* = 7.2 Hz, 1H), 7.07 (m, 1H), 6.75 (m, 2H), 3.66 (s, 1H), 3.59 (t, *J* = 8.4 Hz, 2H), 3.08 (t, *J* = 8.3 Hz, 2H).

#### 10. Application of the more easily removable PAre group.



Compound **43** was prepared in 84% yield using the standard amide coupling procedure **A** with compound **42**<sup>3</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.53 (d, *J* = 8.3 Hz, 1H), 8.45 (d, *J* = 3.8 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 1H), 7.48 (dd, *J* = 4.7, 7.8 Hz, 1H), 5.29 (s, 2H), 4.75 (m, 1H), 3.75 (s, 3H), 1.78 (m, 3H), 0.96 (s, 15H), 0.13 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  173.75, 165.85, 146.10, 144.47, 140.32, 135.66, 126.59, 62.06, 52.65, 50.99, 41.84, 26.38, 25.36, 23.24, 22.36, 18.74, -4.95; HRMS Calcd for C<sub>20</sub>H<sub>35</sub>N<sub>2</sub>O<sub>4</sub>Si [M+H<sup>+</sup>]: 395.2366; Found: 395.2357.

#### Compound 44-trans (51%).

Compound **44-trans** was isolated in 51% yield following the standard procedure **D** without 10 equiv of AcOH. **44-cis** isomer was also obtained in 7% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz, ratio of rotamers: <u>1:1.8</u>)  $\delta$  8.46 (d, J = 4.7 Hz, 1.8H), 8.34 (d, J = 4.7 Hz, 1H), 8.02 (d, J = 7.9 Hz, 2.8H), 7.37 (m, 2.8H), 5.04 (m, 5.6H), 4.81 (dd, J = 2.0, 8.5 Hz, 1H), 4.72 (dd, J = 2.1, 8.9 Hz, 1.8H), 4.07 (dd, J = 7.8, 11.8 Hz, 1H), 3.76 (s, 5.4H), 3.57 (m, 1.8H), 3.53 (s, 3H), 3.28 (m, 2.8H), 2.49 (m, 2.8H), 2.17 (m, 2.8H), 1.97 (m, 2.8H), 1.12 (d, J = 6.6 Hz, 3H), 1.00 (d, J = 6.6 Hz, 5.4H), 0.93 (s, 25.2H), 0.11 (d, J = 2.8 Hz, 16.8H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.43, 172.78, 166.97, 166.94, 151.01, 149.96, 147.10, 146.10, 138.10, 136.67, 135.42, 135.21, 124.95, 124.87, 61.50, 61.49, 61.23, 59.47, 55.77, 54.08, 52.71, 52.51, 39.41, 37.29, 32.94, 30.65, 26.35, 18.76, 18.74, 17.84, 17.31, -4.93, -4.99; HRMS Calcd for C<sub>20</sub>H<sub>33</sub>N<sub>2</sub>O<sub>4</sub>Si [M+H<sup>+</sup>]: 393.2210; Found: 393.2212.

#### Compound 45.

Compound 44 (40 mg, 0.1 mmol, 1.0 eq) was dissolved in dioxane (2 mL), and aq. HCl (1 M) (0.5 mL, 0.5 mmol, 5.0 eq) was added. The mixture was stirred at rt for 24 hours. NaHCO<sub>3</sub> (84 mg, 1.0 mmol, 10.0 eq) and CbzCl (22  $\mu$ L, 0.15 mmol, 1.5 eq) were added and the resulting mixture was stirred at rt for another 3 hours. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography to give product 45 in 73% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  7.37 (m, 5H), 5.20 (m, 2H), 4.45 (m, 1H), 3.82 (m, 1H), 3.73 (s, 1.5H), 3.58 (s, 1.5H), 3.07 (m, 1H), 2.46 (m, 1H), 2.13 (m, 1H), 1.91 (m, 1H), 1.06 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  173.68, 173.52, 155.29, 154.63, 137.12, 137.07, 128.89, 128.82, 128.40, 128.33, 128.30, 128.17, 67.45, 67.33, 59.78, 59.47, 54.07, 53.71, 52.68, 52.50, 38.92, 38.00, 32.49, 31.58, 17.74, 17.69;

### Compound **46**<sup>4</sup>

Compound 45 (21 mg, 0.076 mmol, 1.0 eq) was dissolved in ethyl acetate (1 mL), Boc<sub>2</sub>O (20 mg, 0.091 mmol, 1.2eq) and Pd/C (2 mg) was added. The mixture was stirred under H<sub>2</sub> (1 atm.) at rt for 12 hours. The reaction mixture was filtered through a pad of celite; the filtrate was concentrated in vacuo. The residue was then dissolved in a mixture of THF/MeOH/H2O (1/0.3/0.3 mL), and LiOH.H<sub>2</sub>O (6 mg, 0.15 mmol, 2.0 eq) was added. The resulting mixture was stirred at rt for 12 hours, aq. HCl (1 M) was added to pH = 2, then extracted with ethyl acetate. The combined organic layers was washed with water and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was dissolved in anhydrous DMF (1 mL), and treated with K<sub>2</sub>CO<sub>3</sub> (21 mg, 0.15 mmol, 2.0 eq), BnBr (14 µL, 0.11 mmol, 1.5 eq) and KI (cat). After stirring at rt for 3 hours, water was added and the mixture was extracted with ethyl acetate. The combined organic layers was washed with water and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was purified by silica gel flash chromatography to give product **46** in 62% yield. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz) δ 7.34 (m, 5H), 5.26 (m, 2H), 4.44 (dd, J = 2.1, 8.7 Hz, 0.4 H), 4.32 (dd, J = 2.8, 8.8 Hz, 0.6 H), 3.75 (m, 1H), 3.00 (m, 1H), 2.41 (m, 1H), 1.00 (m, 1H), 2.41 (m, 1H), 1.00 (m, 1H), 1.02.10 (m, 1H), 1.90 (m, 1H), 1.46 (s, 3.6H), 1.34 (s, 5.4H), 1.04 (m, 3H). HRMS Calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>4</sub> [M+H<sup>+</sup>]: 278.1392; Found: 278.1379.

11. Substrate deuteration experiments.



**General procedure F**: Picolinamide substrate (0.1 mmol),  $Pd(OAc)_2$  (2.2 mg, 0.01 mmol, 10 mol%), AcOD (1 mmol, 10 equiv) in anhydrous toluene (1 mL) in a 10 mL glass vial (purged with Ar, sealed with PTFE cap) was heated at 110 °C for 24 hours (No PhI(OAc)<sub>2</sub> was added). The reaction mixture was cooled to rt, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give the deuterated product. The resulting compound was dissolved in CDCl<sub>3</sub> and analyzed by <sup>1</sup>H-NMR.

<sup>&</sup>lt;sup>1</sup> Zhao, Y.; Chen, G. Org. Lett. **2011**, 13, 4850-4853.

<sup>&</sup>lt;sup>2</sup> Huang, Y.-B.; Yang, C.-T.; Yi, J.; Deng, X.-J.; Fu, Y.; Liu, L. J. Org. Chem. 2011, 76, 800-810.

<sup>&</sup>lt;sup>3</sup> He, G.; Chen, G. Angew. Chem. Int. Ed. 2011, 50, 5192-5196.

<sup>&</sup>lt;sup>4</sup> Xie, W.; Zou, B.; Pei, D.; Ma, D. Org. Lett. 2005, 7, 2775-2777.











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ppm \_ Integral ppm 8.4329 ۰ 8.4311 8.4293 8.4211 0.3596 8.4192 1.0018 8.4174 1.3650 8.1559 ω 8.1541 1.3705 8.1365 0.3681 7.7770 1.0136 7.7741 7.3209 Chemical Formula: C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub> 7.3089 Molecular Weight: 248.2777 7.3045 Exact Mass: 248.1161 7.3021 7.2899 σ 7.2602 <sup>∕</sup>CO₂Me 5.1832 4.5971 1.0000 G 9 4.4936 4.4693 0.3545 4.3785 0.3578 4.3540 0.3589 3.9660 1.0085 3.9421 Ь 1.0065 3.8682 1.1154 3.8444 3.0537 3.7788 3.6177 ω 3.6166 2.1530 n. 1.7999 3.0062 1.4640 1.1236 1.4317 1.1158 1.1858 3.0590 1.1638 -0.0148 -0.0168 - 
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 F1P
 3801.24 1

 F2P
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 F2
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TD SOLVENT NS NS NS SWH FIDHES AG DW AG DW TE TE PROBHD PULPROG SI SSB CB PC PL1 SF01 EXPN0 PROCNO INSTRUM Time Date Current Data Parameters NAME 1004hg3-116-1H F2 - Acquisition Parameters Processing parameters J 300.0 K 1.00000000 sec 400.1300089 MHz 400.1324710 MHz CHANNEL f1 ======: 1H mm 88I 1H-20.00 cm 9.500 ppm 3801.24 Hz -0.500 ppm -200.07 Hz 0.50000 ppm/cm 200.06500 Hz/cm 16 2 8278.146 Hz 0.126314 Hz 3.9584243 sec 20111004 60.400 usec 6.00 usec COC 13 724.1 65536 32768 spect 6.45 usec 0.00 dB 13.15 0.00 1.00 2g30 Ηz

S31

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75	248.2777 248.2777 248.2777 248.277 248.277 248.277 27.601 77.601 77.175 75.842 69.991 66.393
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<pre>waltz16</pre>	Data Parameters 1006hg3-116-1 3331 1 20111005 20111005 19.38 spect 5 mm GNP 1H/1 20536 CDC13 11264 16795.92 Hz 0.266819 Hz 0.266819 Hz 0.266819 Hz 0.266819 Hz 28.600 usec 6.00 usec 0.0000000 sec 0.0000000 sec 13C 13C 5.25 usec 5.25 usec 5.4106357 MHz

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S46







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S57



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ndd Integral ppm -8.62960 G 8.61829 8.46619 1.4397 -8.45074 1.0645 8.05513 8.02883 1.0880 ш 7.92374 1.4590 7.89810 2.5259 -7.81931 7.79394 2.7900 -7.76841 22-7.38905 Chemical Formula: C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub> Exact Mass: 248.1161 Molecular Weight: 248.2777 7.37122 7.34791 7.33912 7.32268 σ 7.29560 ''C.O<sub>2</sub>Me -5.28020 5.25216 4.65985 1.0000 -4.63414 σı 4.62732 4.60138 1.3803 4.20512 4.18188 2.4517 4.16643 -4.14273 4.5343 3.77744 -3.58039 4.5828 -3.54386 1.0971 -3.50812 ω -3.29618 -3.26280 -2.48944 2.5996 2.46801 2.5884 -2.44924 1.3006 ъ 2.33068 -2.31616 2.5748 -2.29633 2.27682 2.16863 7.8093 1.66229 1.62437 1.58800 1.13841 1.11163 0 1.08914 0.00034 1D NMA plot parameters CX 20.00 F1P 9.500 F1 2848.76 F2P -0.500 F2 -149.93 PPMCM 0.50000 HZCM 149.93500 F2 -SI SSB CB FC FIDRES AG RG DW DE TE TE P1 PL1 SF01 TD SOLVENT NS DS SWH NUC 1 PROBHD PULPROG Current Data Parameters NAME 0525hg2-286B EXPNO 2 INSTRUM Time PROCNO F2 - Acquisition Parameters Date\_\_\_\_\_20110525 Processing parameters ບາ == CHANNEL f1 ====== 1H 12.10 usec 0.00 dB 299.8718518 MHz 16 2 5172.839 Hz 5.3084660 sec 181 81.000 usec 6.00 usec 300.0 K 299.8699997 MHz mm 1.00000000 sec 0.50000 ppm/cm 149.93500 Hz/cm 20.00 cm 9.500 ppm 2848.76 Hz QNP 1H/1 -0.500 ppm -149.93 Hz zg30 65536 CDC13 spect 18.19 32768 no 0.00 1.00 Ηz 11 11 11 11 11

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 1D NMR plot parameters

 CX
 20.00 cm

 F1P
 9.500 ppm

 F1
 3801.24 Hz

 F2P
 -0.500 ppm

 F2P
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TD SOLVENT SSLVENT SSH SWH FIDRES AG RG DW DE TE TE SI SF WDW SSB SSB CB CB NUC1 P1 PL1 SF01 PPMCM HZCM PULPROG PROBHD INSTRUM EXPNO Time F2 - Acquisition Parameters Date\_ 20110504 PROCNO Current Data Parameters NAME 0504hg2-260 Processing parameters -----: CHANNEL f1 ======: 1H 6.45 usec 0.00 dB ഗ 400.1300084 MHz 0 0.00 Hz 1.00 60.400 usec 6.00 usec 300.0 K 1.00000000 sec mm BBI 1H-B 400.1324710 MHz 3.9584243 sec 71.8 16 2 8278.146 Hz 0.126314 Hz 0.50000 ppm/cm 200.06500 Hz/cm zg30 65536 CDC13 spect 18.33 32768

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HZCM	۲ ۲2 ۲2	1D NMA CX F1P	PC	GB	LB	NDM MDM	, SF	IS	F2 - Pr	SF02	PL13	PL12		NUCZ	CPDPAG2	8	SF01	PL1	P1	NUC1		D12	D11	D1	T F		RG	AQ	FIDRES	SMH US	NS	SOLVENT	TD	ם וון סטאמ	INS HUM	Time	Date_	F2 - Ac	PAOCNO	EXPNO	Current
-794.02 HZ 11.50000 ppm/cm 867.12695 Hz/cm	16588.51 Hz -10.000 ppm	plot parameters 20.00 cm 220.000 ppm	1.40	0	0 00 Hz	on	75.4023410 MHz	32768	ocessing parameters	299.8711995 MHz	19.70 dB	19.70 dB	0.00 dB		waltz16	CHANNEL f2	75.4106357 MHz	-6.00 dB	5.25 usec	13C	===== CHANNEL f1 ===================================	0.00002000 sec	0.03000000 sec	2.0000000 sec	300.0 K	26.600 usec	1024	1.7433076 sec	0.286819 Hz	4 COD 30704	304	- COC13	95239 955453		s mm OND 11/1	19.24	20111011	quisition Parameters	ĻÅ	96601	: Data Parameters 1011hq3-122C

ppm 7 Integral ppm 8.5662 ഗ 8.5634 8.5611 8.5582 1.0371 ≥ ‡ 8.5504 0.9040 0.9997 8.5476 œ 8.5453 8.5424 1.0083 8.1598 1.0025 8.1567 8.1367 8.1337 7.8178 Chemical Formula: C12H16N2O3 Molecular Weight: 236.2670 7.8122 Exact Mass: 236.1161 7.4267 7.4108 7.2601 σ "'CO2Me 4.8152 4.7974 S 4.7884 1.0000 4.7703 -4.7610 4.7431 Δ 3.0658 3.7418 1.9645 1.9162 ω 1.9060 1.8878 1.8169 1.7996 1.7960 N 2.2468 1.7702 1.4574 1.4500 2.0589 1.4275 1.4170 3.0937 1.4043 1.3955 1.3802 0.9535 0.9291 0 0.9046 -0.0329 ۲2 ۲2 ۲2 F1P ST ST WDW SSB CB PC NUC1 PL1 SF01 NS DS SWH FIDRES AQ PG DW DE TE TE TD SOLVENT PPMCM HZCM 1D NMR plot parameters CX 20.00 PROBHD EXPN0 PROCNO PULPROG INSTRUM Time F2 - Acquisition Parameters Date\_\_\_\_\_20110516 Current Data Parameters NAME 0516hg2-274H Processing parameters сı -= CHANNEL f1 ======: 1H 12.10 usec 0.00 dB 299.8718518 MHz 6172.839 Hz 0.094190 Hz 5.3084660 sec 128 81.000 usec 6.00 usec 300.0 K 1.00000000 sec m 299.8700101 MHz 0.50000 ppm/cm 149.93500 Hz/cm QNP 1H/1 20.00 cm 9.500 ppm 2848.76 Hz -0.500 ppm -149.93 Hz 32768 CDC13 65536 spect 13.39 0.00 1.00 2930 0 0 ∿ີ ອີ N Ηz





mqq		, mad
200		
175		173.835 173.042 166.602 165.850
150 		-153.709 153.057 -148.273 -147.489 -137.289
125		-137.166 -125.474 -124.904 -124.708
	Chemical Fo Exact M	70.007
75	N N N N N N N N N N N N N N N N N N N	77.870 77.670 77.243 61.948 60.457
50		52.565 52.356 50.104 48.644
25		32.173 29.227 25.824 22.352
CPDPHG2 PCPD2 PCPD2 PL12 PL13 SFD2 SFD SFD SF SF SF SF SF SF SF SF SF SF SF SF SF	PULPROG TD SSLVENT DS SWH FIDRES AG D1 D1 D1 D1 D1 D1 D1 D1 D1 D1 D1 D1 D1	Current Dat NAME EXPNO PROCNO F2 - Acquis Date_ Time INSTRUM 50000 5
= CHANNEL f2 ======= waltz16 115.00 usec 0.00 dB 19.70 dB 19.70 dB 19.70 dB 299.8711995 MHz 32768 75.4023410 MHz 75.4023410 MHz 0 0.00 Hz 0 0.00 Hz 1.40 parameters 20.000 cm 220.000 ppm 46588.51 Hz -754.02 Hz 11.50000 ppm/cm	zgpg3 55536 CDC13 203 18796.992 Hz 0.286819 Hz 1.7433076 sec 406.4 26.600 usec 6.00 usec 0.0300000 sec 0.0300000 sec 0.00002000 sec 13C 5.25 usec 5.25 usec 5.25 usec 75.4106357 MHz	a Parameters 1009hg3-97C 334 1 ition Parameters 20111009 14.31 spect mm GNP 1H/1







mqq			maa
		Chemical Formula: C Exact Mass: 262 Molecular Weight 2	171.343 170.945 167.522 166.834 154.704 154.406 148.408 148.250 137.339 137.287 125.270 125.183 124.740 124.245
		262.3043	77.994 77.569 77.145 65.866 64.373 57.410 57.058 56.678 54.632 37.651 35.599 32.644 29.693 21.379 21.151 18.734 18.218
1D    NMR plot parameters      1D    NMR plot parameters      CX    20.00 ppm      F1P    220.000 ppm      F1P    16588.51 Hz      F2P    -10.000 ppm      F2    -754.02 Hz      PPMCM    11.50000 ppm/cm      HZCM    867.12695 Hz/cm	 =====      CHANNEL      f1      =========      sec        NUC1      13C      5.25      usec        PL1      -6.00      dB        SF01      75.4106357      MHz	PULPHUG      ZSQS30        TD      E5536        SOLVENT      CDC13        NS      701        DS      4        SWH      18796.992 Hz        AQ      1.7433076 sec        PG      512        DE      6.00 usec        DE      6.00 usec        DE      300.0 K        D11      0.03000000 sec        D12      0.00022000 sec	Current Data Parameters NAME 1011hg2-123C EXPNO 96601 PROCNO 1 F2 - Acquisition Parameters Date_ 2011011 Time 20.06 INSTRUM Spect


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mdd					ppm
200					
175					<u> </u>
150					
125					
			Chemical Fo Exact M Molecular V		125.506 125.194 118.000
			rmula: C <sub>16</sub> H <sub>1</sub> ass: 282.100 Veight: 282.2	36	
75			4N2O3 940	æ	
					62.942 52.954 
					40.817 40.608 40.400 40.191
					39.982 39.774 33.984
0-					
1D NMA P CX F1P F1 F2P F2P F2 F2 F2 F2 F2 F2 F2 F2 F2 F2 F2 F2 F2	F2 - Pro SI - Pro WDW SSB LB GB PC	**************************************	P1 PL1 SF01	SWH FIDRES AG DW DE DE TE TE d11 d12	Current NAME EXPNO PROCNO F2 - Acg Date_ Time INSTRUM PROBHD PDULPROG TD PULPROG TD SOLVENT NS
<pre>ilot parameters</pre>	cessing parameters 32768 100.6127290 MHz EM 0 1.00 Hz 0 1.40	CHANNEL f2 waltz16 1H 114.00 usec 0.00 dB 24.00 dB 24.00 dB 24.00 dB 24.00 dB 24.00 dB	CHANNEL f1 13C 16.35 usec -6.00 dB 100.6237959 MHz	25125.629 Hz 1.3042164 sec 16384 19.900 usec 6.00 usec 300.0 K 2.00000000 sec 0.03000000 sec	Data Parameters 1105hg3-142C 1 1 20111105 5 mm BBI 1H- 29930 65536 DMS0 289
			14 19 19		Si



m dd			ppm
200			
175			
150		-	150.304 148.472 139.387 137.674
125			129.171 128.993 126.846 126.506 122.506
100		Chemical Fo Exact M Molecular	
		HN 0 HN 0 n n n HN 0 HN 0 HN 0 HN 0 HN 0 HN 226.1106 ass: 226.1106 ass: 226.2738	77.909 77.477
50			41.195 36.295
0			
1D NMA plot CX F1P F2P F2P F2P F2P F2P F2P F2P F2P	PCPDPR62 PCPD2 PCPD2 PL12 PL13 SF02 SF02 SF SI SSB SSB SSB SSB SSB SSB SSB SSB SSB	SWH FIDRES AG DW DE D1 D1 D1 D1 D1 D1 D1 D1 D1 D1 D1 D1 D1	Current Dat NAME EXPNO PROCNO F2 - Acquis Date_ Time INSTRUM PROBHD 5 PULPROG TD SOLVENT NS
parameters 20.00 cm 215.000 ppm 16211.50 Hz -5.000 ppm -377.01 Hz 11.00000 ppm/cm 829.42578 Hz/cm	- LHANNEL 12 Waltz14 115.00 Usec 0.00 dB 19.70 dB 19.70 dB 299.8711995 MHz 32768 75.4023410 MHz 0 0.00 Hz 0.00 Hz 1.40	18796.923 Hz 0.286819 Hz 1.7433076 sec 512 26.600 usec 300.0 K 2.00000000 sec 0.0300000 sec 0.0300000 sec 0.00002000 sec 0.00002000 sec 5.25 usec 5.25 usec -6.00 dB 75.4106357 MHz	20 Parameters 102Bhg2-256A 350 1 120111028 20111028 17.24 Spect 17.24 55536 65536 65536 CDC13 11

ppm ] Integral ppm 8.6579 ۰ 8.6429 8.1749 0.9713 8.1488 7.9995 0.8677 7.9944 ω-1.0211 7.9737 7.9687 0.9470 7.7927 1.0560 7.7665 1.9289 7.5752 0.9654 7.5577 7.5522 Chemical Formula: C14H12N20 Molecular Weight: 224.2579 7.5350 38 Exact Mass: 224.0950 7.3029 7.2787 7.2370 **m**-7.0777 υı 4.1994 4.1719 2.0000 4.1435 3.3389 3.1337 3.1059 1.9911 ω 3.0781 2.5060 2.5002 2.4946 N 0 -0.0047 -F2 - Processing parameters SI 32768 SF 299.8700050 MHz WDW 0 SSB 0.00 Hz GB 0.00 Hz GB 0 PC 1.00 F1P F1 F2P F2 F2 F2 F2 HZCM NUC1 PL1 SF01 TD SOLVENT NS DS DS SWH FIDRES AG AG AG AG DW DE TE PROBHD PULPROG 1D NMR plot parameters CX 20.00 Time INSTRUM EXPNO F2 - Acquisition Parameters Date\_\_\_\_\_20111028 PROCNO Current Data Parameters NAME 1028hg3-137 ----- CHANNEL f1 -------1H 12.10 usec 0.00 dB ហ 6172.839 Hz 0.094190 Hz 5.3084660 sec 362 81.000 usec 6.00 usec 300.0 K 1.00000000 sec 299.8718518 MHz ШШ 0.50000 ppm/cm 149.93500 Hz/cm 9.500 ppm 2848.76 Hz QNP 1H/1 na 0.00 Hz 1.00 -0.500 ppm -149.93 Hz 20.00 cm 2930 5536 DMS0 16 15.09 spect

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200		· · · ·	
1 150			
	Molecular Wei	Chemical Formula 2004	
100	ght 277.1314	bz 'CO2Me <b>46</b>	
		77.908 77.483 77.059 67.448 67.327 59.781	
		59.468 54.067 53.711 52.682 52.500	
		38.921 38.000 32.489 31.578 17.739 17.694	
	•		
F 1 F 2 F 2 PPMCM HZCM	D11 D12 P1 SF01 PL1 PL1 PL1 PL1 PL12 PL12 PL12 PL12 PL	NAME EXPNO PROCNO Date_ Time INSTRUM PROBHD PULPROG TD SOLVENT NS SOLVENT SOLVENT FIDRES AG AG AG DW DI	Current D
220.000 cm 220.000 ppm 16588.51 Hz -10.000 ppm -754.02 Hz 11.50000 ppm/cm 867.12695 Hz/cm		1103hg3-145-1C 1 1 1 1 1 20111103 18.21 20111103 18.21 20111103 18.21 2099 18.21 2099 1971 2099 18796.92 1.7433076 sec 1024 26.00 usec 300.0 k 2.0000000 sec	ata Parameters

