**Supporting Information**

# Potentiation of *Francisella* Resistance to Conventional Antibiotics through Small Molecule Adjuvants

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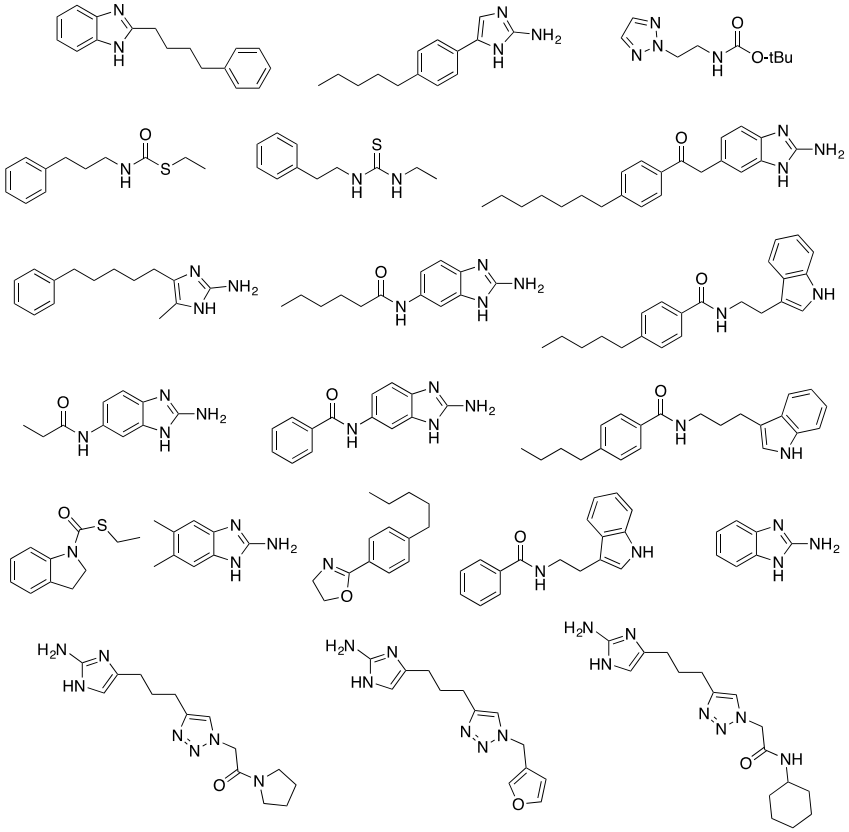
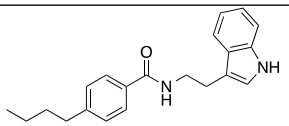
**Initial pilot screen.**[1-5]

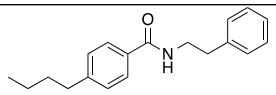
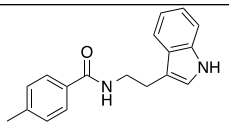
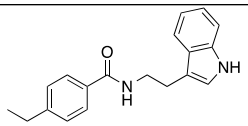
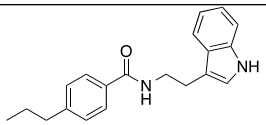
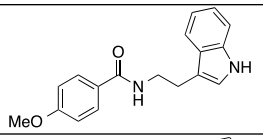
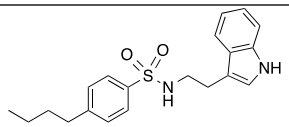
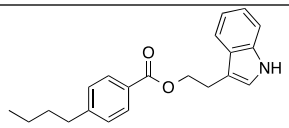
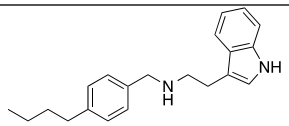
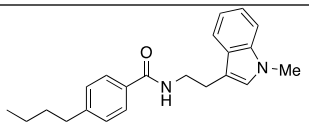
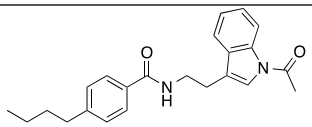
**SI Figure 1** Compounds from initial pilot screen.



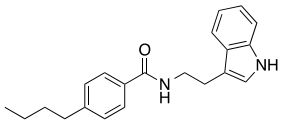
**MIC Results of SAR study.**

**SI Table 1** MIC results of SAR study.

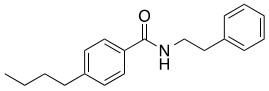
| Compound | Structure | MIC (μM) | Concentration tested (μM) | Colistin (μg/mL) |
|---|---|---|---|---|
| 5 |  | >200 | 50 | 8 |

| | | | | |
|---|---|---|---|---|
| 9 |  | >200 | 50 | 256 |
| 8 |  | 100 | 25 | 256 |
| 7 |  | 100 | 25 | 256 |
| 6 |  | 50 | 12.5 | 256 |
| 15 |  | >200 | 50 | 512 |
| 12 |  | 50 | 12.5 | 256 |
| 11 |  | >200 | 50 | 256 |
| 10 |  | 25 | 6.25 | 256 |
| 13 |  | >200 | 50 | 256 |
| 14 |  | >200 | 50 | 256 |

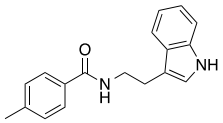
**Synthetic procedures and compound characterization**



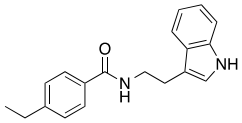
***N*-(2-(1*H*-indol-3-yl)ethyl)-4-butylbenzamide (5).** White solid; yield 93%; $^{1}$H NMR (300 MHz, $CDCl_3$), δ 8.43 (br, 1H), 7.66-7.59 (m, 3H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.24-7.10 (m, 4H), 7.03 (s, 1H), 6.32 (br, 1H), 3.79 (q, *J* = 6 Hz, 2H), 3.08 (t, *J* = 6.6 Hz, 2H), 2.62 (t, *J* = 7.2 Hz, 2H), 1.58 (q, *J* = 8.1 Hz, 2H), 1.34 (sext, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 168.0, 147.1, 136.9, 132.4, 129.0, 127.7, 127.3, 122.7, 122.6, 119.8, 119.1, 113.3, 111.8, 40.7, 35.9, 33.8, 25.7, 22.7, 14.3; HRMS (ESI) calcd. for $C_{21}H_{24}N_2O$ $[M+H]^+$: 321.19614, found: 321.19576.



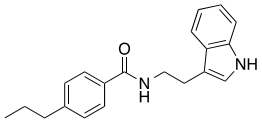
**4-butyl-*N*-phenethylbenzamide (9)**. White solid; yield 93%; $^1$H NMR (300 MHz, $CDCl_3$), δ 7.60 (d, $J$ = 8.1 Hz, 2H), 7.35-7.31 (m, 2H), 7.26-7.19 (m, 5H), 6.14 (br, 1H), 3.71 (q, $J$ = 6.6 Hz, 2H), 2.93 (t, $J$ = 6.9 Hz, 2H), 2.63 (t, $J$ = 7.5 Hz, 2H), 1.64-1.54 (m, 2H), 1.34 (sext, $J$ = 7.2 Hz, 2H), 0.92 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.7, 147.0, 139.2, 132.2, 129.1, 128.9, 128.8, 127.0, 126.8, 41.3, 36.0, 35.7, 33.6, 22.5, 14.1; HRMS (ESI) calcd. for $C_{19}H_{23}NO$ $[M+H]^+$: 282.18524, found: 282.18477.



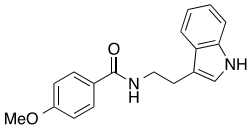
***N*-(2-(1*H*-indol-3-yl)ethyl)-4-methylbenzamide (8)**. White solid; yield 55%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.36 (br, 1H), 7.65-7.57 (m, 3H), 7.38 (d, $J$ = 7.8 Hz, 1H), 7.24-7.10 (m, 4H), 7.04 (s, 1H), 6.32 (br, 1H), 3.79 (q, $J$ = 6.3 Hz, 2H), 3.09 (t, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.7, 141.9, 136.6, 131.8, 129.3, 127.4, 127.2, 127.0, 122.3, 122.2, 119.5, 118.8, 113.0, 111.5, 40.4, 25.4, 21.5; HRMS (ESI) calcd. for $C_{18}H_{18}N_2O$ $[M+H]^+$: 279.14914, found: 279.14879.



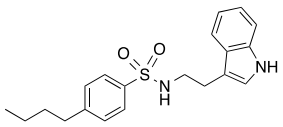
***N*-(2-(1*H*-indol-3-yl)ethyl)-4-ethylbenzamide (7)**. Tan solid; yield 90%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.22 (br, 1H), 7.67-7.59 (m, 3H), 7.38 (d, $J$ = 8.4 Hz, 1H), 7.25-7.11 (m, 4H), 7.06 (s, 1H), 6.25 (br, 1H), 3.80 (q, $J$ = 6.6 Hz, 2H), 3.09 (t, $J$ = 6.6 Hz, 2H), 2.66 (q, $J$ = 7.8 Hz, 2H), 1.23 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.7, 148.1, 136.6, 132.1, 128.1, 127.4, 127.1, 122.3, 122.2, 119.5, 118.8, 112.9, 111.5, 40.4, 28.8, 25.4, 15.4; HRMS (ESI) calcd. for $C_{19}H_{20}N_2O$ $[M+H]^+$: 293.16484, found: 293.16430.



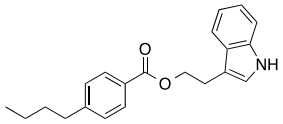
***N*-(2-(1*H*-indol-3-yl)ethyl)-4-propylbenzamide (6)**. White solid; yield 89%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.12 (br, 1H), 7.66 (d, $J$ = 6.9 Hz, 1H), 7.59 (d, $J$ = 7.8 Hz, 2H), 7.39 (d, $J$ = 8.4 Hz, 1H), 7.25-7.11 (m, 4H), 7.08 (s, 1H), 6.21 (br, 1H), 3.80 (q, $J$ = 6.3 Hz, 2H), 3.10 (t, $J$ = 6.6 Hz, 2H), 2.60 (t, $J$ = 7.2 Hz, 2H), 1.63 (q, $J$ = 7.2 Hz, 2H), 0.92 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.9, 146.7, 136.7, 132.3, 128.9, 127.6, 127.1, 122.5, 122.4, 119.7, 119.0, 113.1, 111.6, 40.5, 38.1, 25.6, 24.6, 14.0; HRMS (ESI) calcd. for $C_{20}H_{22}N_2O$ $[M+H]^+$: 307.18049, found: 307.17997.



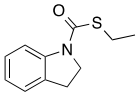
***N*-(2-(1*H*-indol-3-yl)ethyl)-4-methoxybenzamide (15)**. White solid; yield 79%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.32 (br, 1H), 7.64 (d, $J$ = 8.7 Hz, 3H), 7.38 (d, $J$ = 8.1 Hz, 1H), 7.24-7.09 (m, 3H), 7.04 (s, 1H), 6.86 (d, $J$ = 6.0 Hz, 2H), 6.27 (br, 1H), 3.82-3.75 (m, 5H), 3.08 (t, $J$ = 6.6 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.2, 162.2, 136.6, 128.8, 127.4, 126.9, 122.3, 119.6, 118.9, 113.8, 113.1, 111.5, 55.5, 40.4, 25.5; HRMS (ESI) calcd. for $C_{18}H_{18}N_2O_2$ $[M+H]^+$: 295.14410, found: 295.14353.



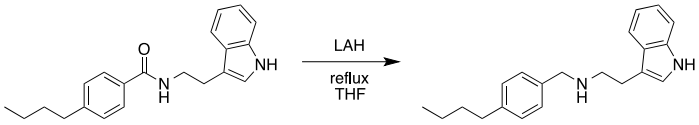
***N*-(2-(1*H*-indol-3-yl)ethyl)-4-butylbenzenesulfonamide (12)**. White solid; yield 92%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.12 (br, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.24-7.16 (m, 3H), 7.09-7.03 (m, 1H), 6.96 (s, 1H), 3.28-3.27 (m, 2H), 2.93 (t, *J* = 6.3 Hz, 2H), 2.65 (t, *J* = 7.5 Hz, 2H), 1.65-1.55 (m, 2H), 1.41-1.31 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 148.4, 137.0, 136.5, 129.1, 127.1, 127.0, 122.8, 122.3, 119.6, 118.6, 111.6, 111.5, 43.2, 35.6, 33.3, 25.6, 22.4, 14.0; HRMS (ESI) calcd. for $C_{20}H_{24}N_2O_2S$ $[M+H]^+$: 357.16313, found: 357.16223.



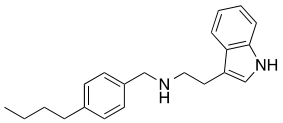
**2-(1*H*-indol-3-yl)ethyl 4-butylbenzoate (11)**. Yellow solid; yield 62%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.05 (br, 1H), 7.97 (d, *J* = 7.5 Hz, 2H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.26-7.10 (m, 5H), 4.60 (t, *J* = 6.9 Hz, 2H), 3.25 (t, *J* = 7.2 Hz, 2H), 2.67 (t, *J* = 8.1 Hz, 2H), 1.62 (quin, *J* = 7.8 Hz, 2H), 1.36 (sext, *J* = 6.3 Hz, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.0, 148.7, 136.4, 129.9, 128.7, 128.1, 127.7, 122.4, 122.3, 119.7, 119.1, 112.4, 111.4, 65.1, 36.0, 33.5, 25.2, 22.6, 14.2; HRMS (ESI) calcd. for $C_{21}H_{23}NO_2$ $[M+Na]^+$: 344.16210, found: 344.16145.



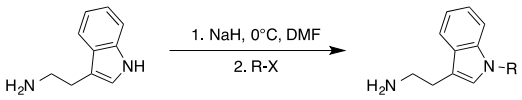
***S*-ethyl indoline-1-carbothioate (2)**. Colorless oil; yield 95%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.03 (d, *J* = 7.8 Hz, 1H), 7.21-7.14 (m, 2H), 7.01-6.96 (m, 1H), 3.99 (t, *J* = 9.0 Hz, 2H), 3.16 (t, *J* = 8.1 Hz, 2H), 2.99 (q, *J* = 7.2 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 165.7, 142.9, 131.1, 127.6, 124.8, 123.6, 115.9, 47.3, 27.9, 24.6, 15.4; HRMS (ESI) calcd. for $C_{11}H_{13}NOS$ $[M+H]^+$: 208.07906, found: 208.07872.




**SI Scheme 1.** Synthetic scheme for the synthesis of amine **10**.

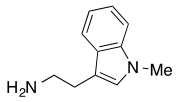


***N*-(4-butylbenzyl)-2-(1*H*-indol-3-yl)ethan-1-amine (10)**. In a flame dried round bottom under $N_2$ atmosphere was added amide **5** (200.0 mg, 0.62 mmol) and anhydrous THF (10 mL). The reaction mixture was cooled to 0°C and LAH (3.12 mL, 6.24 mmol) was added dropwise. The reaction was allowed to warm to rt before being heated to reflux. After the reaction was complete the reaction was cooled to 0°C and slowly quenched with $H_2O$. After quenching, a sat. solution of Rochelle's salt was added and the mixture was stirred until two visible layers were observed. The aq. layer was extracted with EtOAc (3 x 10 mL) and the combined organic layers were washed with brine (1 x 10 mL) and dried over $Na_2SO_4$, then filtered. The solvent was removed *in vacuo* and the residue was purified by flash chromatography using DCM/2% MeOH/2% TEA to deliver product as a yellow oil (130.1 mg, 68%). $^1$H NMR (300 MHz, $CDCl_3$), δ 8.09 (br, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.22-7.17 (m, 3H), 7.13-7.09 (m, 3H), 7.02 (s, 1H), 3.79 (s, 2H), 3.06 (s, 3H) 2.58 (t, *J* = 7.2 Hz, 2H), 1.63-1.53 (m, 2H), 1.40-1.31 (m, 2H), 1.23-1.18 (m, 2H), 0.92 (t, *J* = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 141.7, 137.2, 136.5, 128.6, 128.3, 127.6, 122.1, 119.4, 119.1, 114.0, 111.3, 53.7, 49.4, 46.1, 35.4, 33.8, 25.8, 22.5, 14.1; HRMS (ESI) calcd. for $C_{21}H_{26}N_2$ $[M+H]^+$: 307.21688, found: 307.21658.

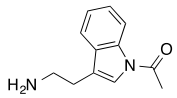



**SI Scheme 2.** Synthetic scheme for the synthesis of tryptamines derivatives **16** and **17**.

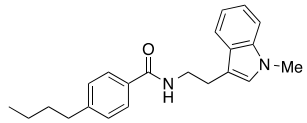
**General procedure for indole alkylation or acylation:**
In a flame dried round bottom under $N_2$ atmosphere was added tryptamine (300 mg, 1.87 mmol) and anhydrous DMF (10 mL). The reaction mixture was cooled to 0°C and NaH (82.4 mg, 2.06 mmol) was added in a single portion. The reaction was stirred for 30 min before MeI (128 µL, 2.06 mmol) was added dropwise. After completion the reaction was poured into $H_2O$ and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (1 x 5 mL) and dried over $Na_2SO_4$, then filtered. The solvent was removed *in vacuo* and the resulting residue was purified by flash chromatography using DCM/2% MeOH/2% TEA to afford pure product as a yellow oil (176.0 mg, 54%).



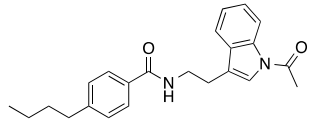

**2-(1-methyl-1*H*-indol-3-yl)ethan-1-amine (16)**. Yellow Oil; yield 54%; $^1$H NMR (300 MHz, $CDCl_3$), δ 7.64-7.60 (m, 1H), 7.32-7.21 (m, 2H), 7.14-7.09 (m, 1H), 6.90 (s, 1H), 3.75 (s, 3H), 3.04-3.00 (m, 2H), 2.96-2.89 (m, 2H), 1.90 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 137.2, 128.0, 127.0, 121.7, 119.1, 118.8, 112.0, 109.3, 42.5, 32.7, 29.2; HRMS (ESI) calcd. for $C_{11}H_{14}N_2$ $[M+H]^+$: 175.12298, found: 175.12294.



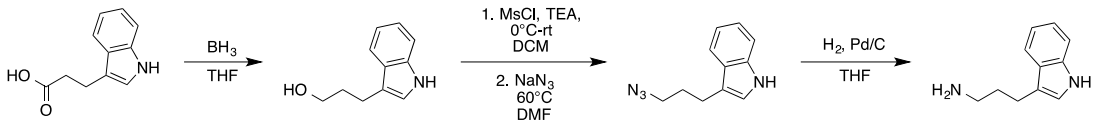

**1-(3-(2-aminoethyl)-1*H*-indol-1-yl)ethan-1-one (17)**. Orange oil; yield 60%; $^1$H NMR (300 MHz, $CDCl_3$), δ 7.59 (d, *J* = 6 Hz, 1H), 7.38-7.36 (m, 1H), 7.21-7.17 (m, 1H), 7.12-7.08 (m, 1H), 7.02 (s, 1H), 3.61-3.55 (m, 2H), 2.98-2.92 (m, 2H), 2.58 (s, 3H), 1.91 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 170.3, 136.5, 127.4, 122.3, 122.2, 119.4, 118.7, 112.8, 111.5, 39.9, 25.4, 23.5; HRMS (ESI) calcd. for $C_{12}H_{14}N_2O$ $[M+H]^+$: 203.11789, found: 203.11755.



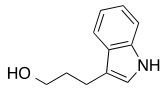

**4-butyl-*N*-(2-(1-methyl-1*H*-indol-3-yl)ethyl)benzamide (13)**. White solid; yield 91%; $^1$H NMR (300 MHz, $CDCl_3$), δ 7.66-7.59 (m, 3H), 7.34-7.10 (m, 5H), 6.92 (s, 1H), 6.27 (br, 1H), 3.81-3.75 (m, 5H), 3.08 (t, *J* = 6.6 Hz, 2H), 2.63 (t, *J* = 7.5 Hz, 2H), 1.59 (quin, *J* = 7.5 Hz, 2H), 1.41-1.28 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 167.8, 147.0, 137.6, 132.5, 128.9, 128.2, 127.3, 122.2, 119.4, 119.3, 112.0, 109.8, 40.9, 35.9, 33.8, 33.1, 25.7, 22.7, 14.3; HRMS (ESI) calcd. for $C_{22}H_{26}N_2O$ $[M+H]^+$: 335.21179, found: 335.21105.



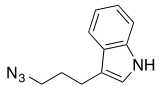

***N*-(2-(1-acetyl-1*H*-indol-3-yl)ethyl)-4-butylbenzamide (14)**. Yellow solid; yield 70%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.05 (br, 1H), 7.36-7.30 (m, 4H), 7.17-7.12 (m, 3H), 7.02-6.97 (m, 2H), 4.10-4.05 (m, 2H), 3.06 (t, *J* = 8.4 Hz, 2H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.19 (s, 3H), 1.65-1.56 (m, 2H), 1.36 (sext, 7.5 Hz, 2H), 0.95 (t, *J* = 6.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 174.8, 173.7, 148.1, 136.3, 132.8, 128.8, 128.6, 127.5, 122.7, 122.1, 119.5, 118.8, 112.5, 111.2, 47.3, 35.7, 33.4, 26.3, 25.0, 22.4, 14.0; HRMS (ESI) calcd. for $C_{23}H_{26}N_2O_2$ $[M+H]^+$: 363.20670, found: 363.20564.



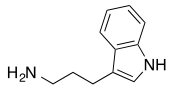

**SI Scheme 3.** Synthetic scheme for the synthesis of amine **20**.



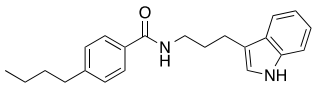
**3-(1*H*-indol-3-yl)propan-1-ol (18)**. 3-indolepropionic acid (1.00 g, 5.29 mmol) was dissolved in THF (20 mL) and cooled to 0°C before dropwise addition of $BH_3$*THF (22.0 mL, 21.76 mmol). The reaction was allowed to warm to rt and stir for 48 hr. The reaction was quenched at 0°C with EtOH and was poured into $H_2O$ (40 mL) and EtOAc (40 mL). A cloudy emulsion formed and sat. $NaHCO_3$ (20 mL) was added. The layers were separated and the organic layer was washed with brine (1 x 40 mL) and dried over $Na_2SO_4$, then filtered. The solvent was removed *in vacuo* and the residue was purified by flash chromatography using 1:1 Hex/EtOAc to afford the product as a yellow oil (627.3 mg, 68% yield). $^1$H NMR (300 MHz, $CDCl_3$), δ 8.04 (br, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.22-7.09 (m, 2H), 7.00 (s, 1H), 3.74 (t, *J* = 6.3 Hz, 2H), 2.97 (s, 1H), 2.90-2.84 (m, 2H), 2.00 (quin, *J* = 6.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 136.5, 127.6, 122.1, 121.4, 119.3, 119.0, 116.1, 111.2, 62.8, 33.0, 21.5; HRMS (ESI) calcd. for $C_{11}H_{13}NO$ $[M+H]^+$: 176.10699, found: 176.10695.



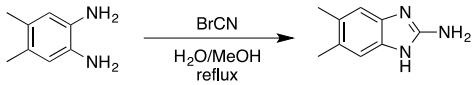

**3-(3-azidopropyl)-1*H*-indole (19)**. In a flame dried round bottom under $N_2$ atmosphere was added alcohol **18** (620.0 mg, 3.54 mmol), TEA (1.0 mL, 7.08 mmol), and anhydrous DCM (10 mL). The reaction mixture was cooled to 0°C, MsCl (301 µL, 3.89 mmol) was added dropwise and allowed to warm to rt for 3 hr. The reaction was washed with brine (1 x 5 mL), and dried over $Na_2SO_4$, then filtered. The solvent was removed *in vacuo* and the residue was dissolved in anhydrous DMF (10 mL) and $NaN_3$ (460.0 mg, 7.08 mmol) was added in a single portion. The reaction was heated to 60°C and allowed to stir overnight. After completion the reaction was cooled to rt and poured into $H_2O$ and extracted with EtOAc (3 x 10 mL). The combined organics were washed with brine (1 x 10 mL) and dried over $Na_2SO_4$, then filtered. The solvent was removed *in vacuo* and the residue was purified by flash chromatography using 8:1 Hex/EtOAc to give the product as a yellow oil (490.0 mg, 69% yield). $^1$H NMR (300 MHz, $CDCl_3$), δ 7.95 (br, 1H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.39-7.36 (m, 1H), 7.25-7.12 (m, 2H), 7.01 (s, 1H), 3.34 (t, *J* = 6.9 Hz, 2H), 2.89 (t, 7.2 Hz, 2H), 2.02 (quin, *J* = 6.9 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 136.6, 127.6, 122.3, 121.8, 119.6, 119.1, 115.3, 111.4, 51.3, 29.5, 22.4.



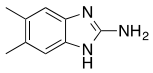

**3-(1*H*-indol-3-yl)propan-1-amine (20)**. The azide **19** (470.0 mg, 2.35 mmol) was dissolved in THF (10 mL) and 10% Pd/C (100.0 mg) was added. The atmosphere was removed under vacuum and back filled with a $H_2$ balloon. The reaction was stirred overnight and then filtered through a pad of celite. The solvent was removed *in vacuo* and the residue was used directly in the next step.




***N*-(3-(1*H*-indol-3-yl)propyl)-4-butylbenzamide (4)**. White solid; yield 45%; $^1$H NMR (300 MHz, $CDCl_3$), δ 8.19 (br, 1H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.26-7.09 (m, 4H), 7.00 (s, 1H), 6.19 (br, 1H), 3.54-3.52 (m, 2H), 2.90-2.85 (m, 2H), 2.65-2.60 (m, 2H), 2.04 (quin, *J* = 6.6 Hz, 2H), 1.59 (quin, *J* = 6.3 Hz, 2H), 1.40-1.31 (m, 2H), 0.94 (t, *J* = 6.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 168.0, 147.1, 136.9, 132.3, 128.9, 127.6, 127.2, 122.4, 122.1, 119.7, 119.2, 115.8, 111.7, 40.4, 35.9, 33.8, 30.1, 23.3, 22.7, 14.4; HRMS (ESI) calcd. for $C_{22}H_{26}N_2O$ $[M+H]^+$: 335.21179, found: 335.21103.

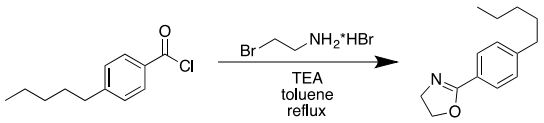



**SI Scheme 4.** Synthetic scheme for the synthesis of amine **1**.

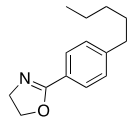



**5,6-dimethyl-1*H*-benzo[*d*]imidazol-2-amine (1)**. 4,5-dimethylbenzene-1,2-diamine (1.00 g, 7.34 mmol) was dissolved in $H_2O$ (100 mL) and MeOH (100 mL). BrCN (3.11 g, 29.36 mmol) was added in a single portion and the reaction was heated to reflux. After cooling the solvent was removed *in-vacuo* and basified with 1M NaOH (40 mL). The aq. layer was extracted with EtOAc (3 x 30 mL). The organic layer was washed with brine and dried over $Na_2SO_4$, then filtered. The solvent was removed and the solid was dissolved in MeOH (10 mL) and acidified with conc. HCl. The solvent was removed a final time to give a brown solid (1.21 g, 83% yield). $^1$H NMR (300 MHz, DMSO-$d_6$), δ 8.45 (s, 2H), 7.12 (s,

2H), 2.21 (s, 6H); $^{13}$C NMR (100 MHz, DMSO-$d_6$), δ 150.1, 131.2, 127.7, 111.9, 19.6; HRMS (ESI) calcd. for $C_9H_{11}N_3$ $[M+H]^+$: 162.10257, found: 162.10244.

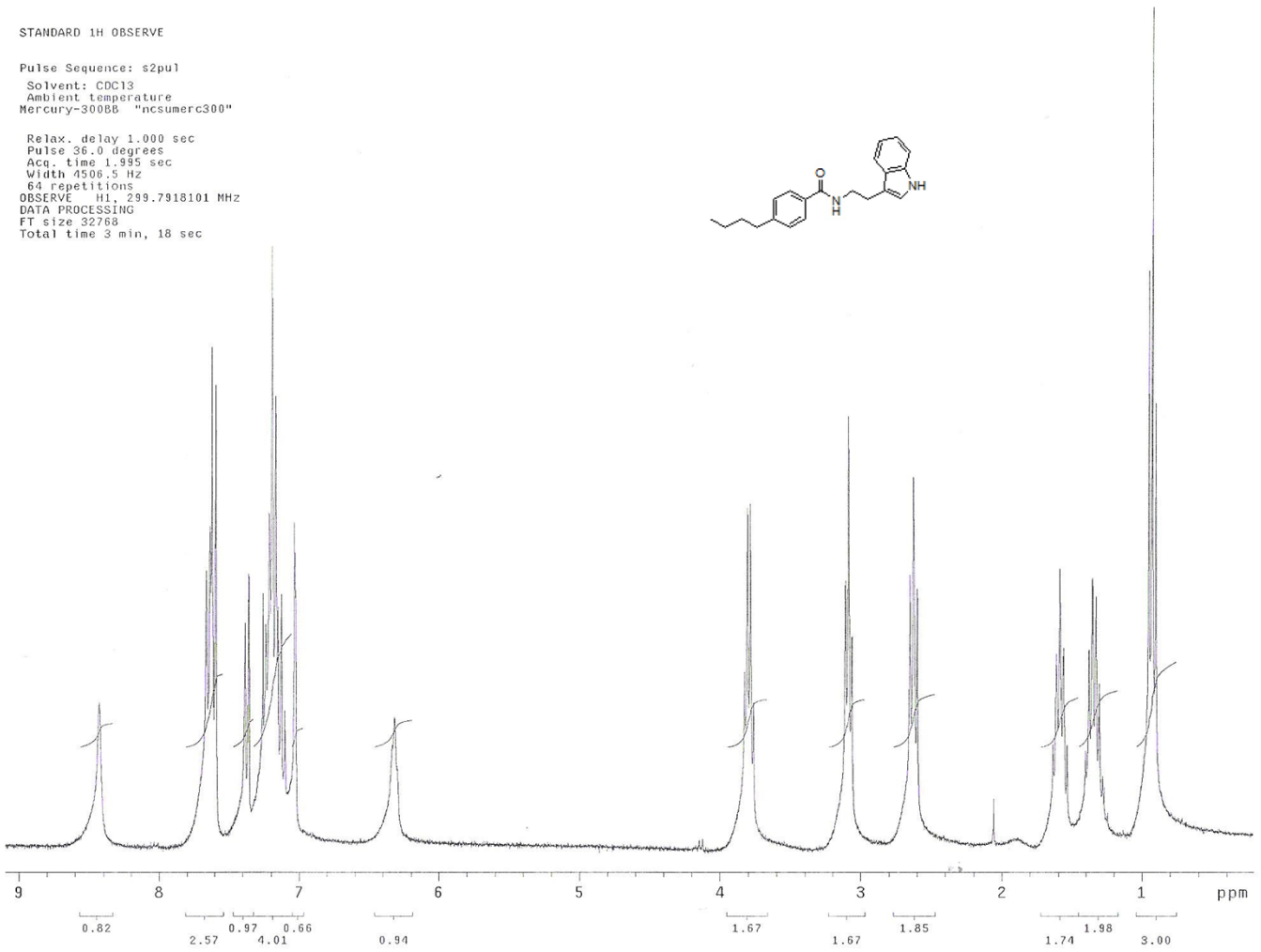



**SI Scheme 5.** Synthetic scheme for the synthesis of amine **3**.




**2-(4-pentylphenyl)-4,5-dihydrooxazole (3)**. 2-Bromoethylamine hydrobromide (265.2 mg, 1.29 mmol) was dissolved in anhydrous toluene (7 mL) in a round bottom flask. To this solution, TEA (894 µL, 6.45 mmol) was added and the solution was stirred for 5 min. 4-pentylbenzoyl chloride (290 µL, 1.42 mmol) was then added dropwise to reaction and stirred at ambient temperature for 2 hr, then at 135 °C for 22 hr. The round bottom flask was cooled to room temperature, rinsed with EtOAc (20 mL) and $H_2O$ (15 mL). The organic layer was extracted, dried over $Na_2SO_4$, filtered, and concentrated to dryness. The crude oil was then purified via flash column chromatography using 5:1 Hex/EtOAc to 3:1 Hex/EtOAc to give a colorless oil (212.0 mg, 76% yield). $^1$H NMR (300 MHz, $CDCl_3$), δ 7.84 (d, $J$ = 8.4 Hz, 2H), 7.20 (d, $J$ = 8.1 Hz, 2H), 4.43-4.36 (m, 2H), 4.06-3.99 (m, 2H), 2.62 (t, $J$ = 7.5 Hz, 2H), 1.63-1.58 (m, 2H), 1.32-1.27 (m, 4H), 0.87 (t, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$), δ 164.8, 146.7, 129.8, 128.7, 128.3, 127.1, 125.2, 67.6, 55.0, 35.9, 31.5, 31.0, 22.6, 14.1; HRMS (ESI) calcd. for $C_{14}H_{19}NO$ $[M+H]^+$: 218.15394, found: 218.15378.

**Representative NMR spectra.**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Ambient temperature
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Pulse 36.0 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
64 repetitions
OBSERVE H1, 299.7918101 MHz
DATA PROCESSING
FT size 32768
Total time 3 min, 18 sec
O
N
H
NH
9
8
7
6
5
4
3
2
1
ppm
0.82
2.57
0.97
0.66
4.01
0.94
1.67
1.67
1.85
1.74
1.98
3.00

13C OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "ncsumerc400"

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Acq. time 1.199 sec
Width 25000.0 Hz
4416 repetitions
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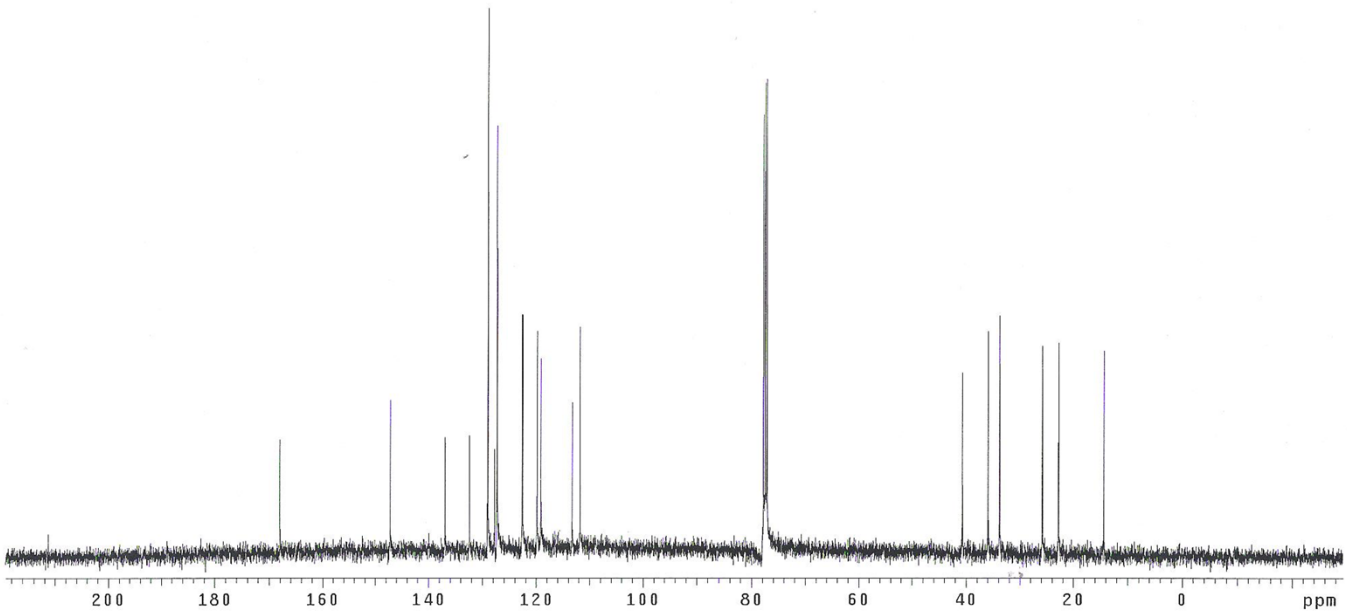
DECOUPLE H1, 400.1266027 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 34 min, 55 sec



STANDARD 1H OBSERVE

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Solvent: CDCl3
Ambient temperature
Mercury-300BB "ncsumerc300"

Relax. delay 1.000 sec
Pulse 36.0 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
16 repetitions
OBSERVE H1, 299.7918101 MHz
DATA PROCESSING
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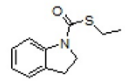
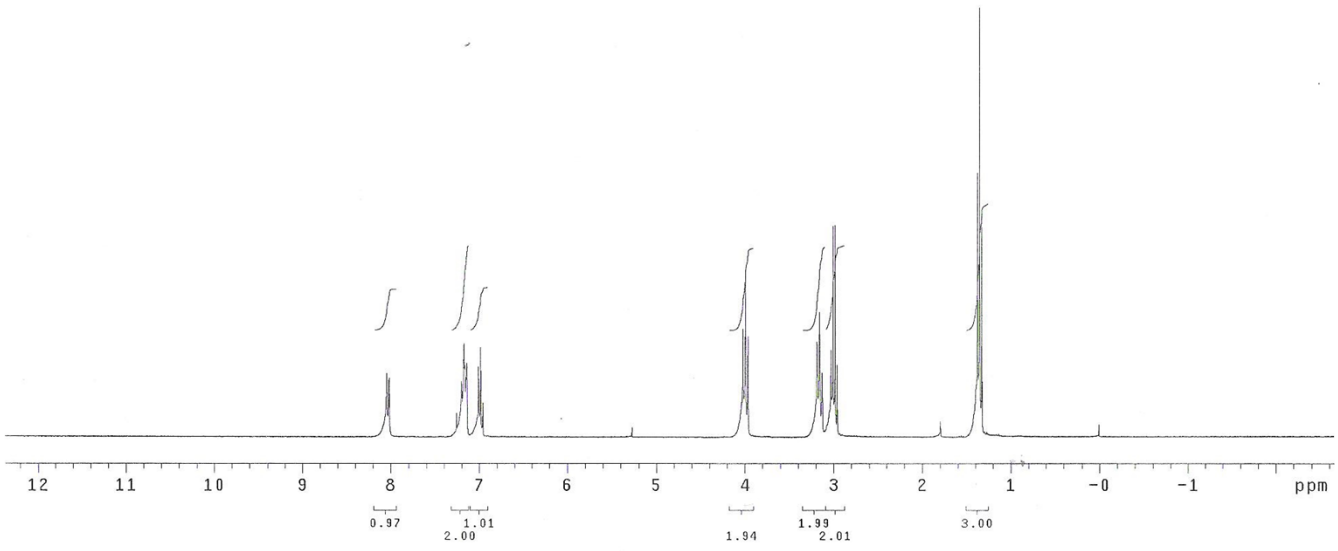
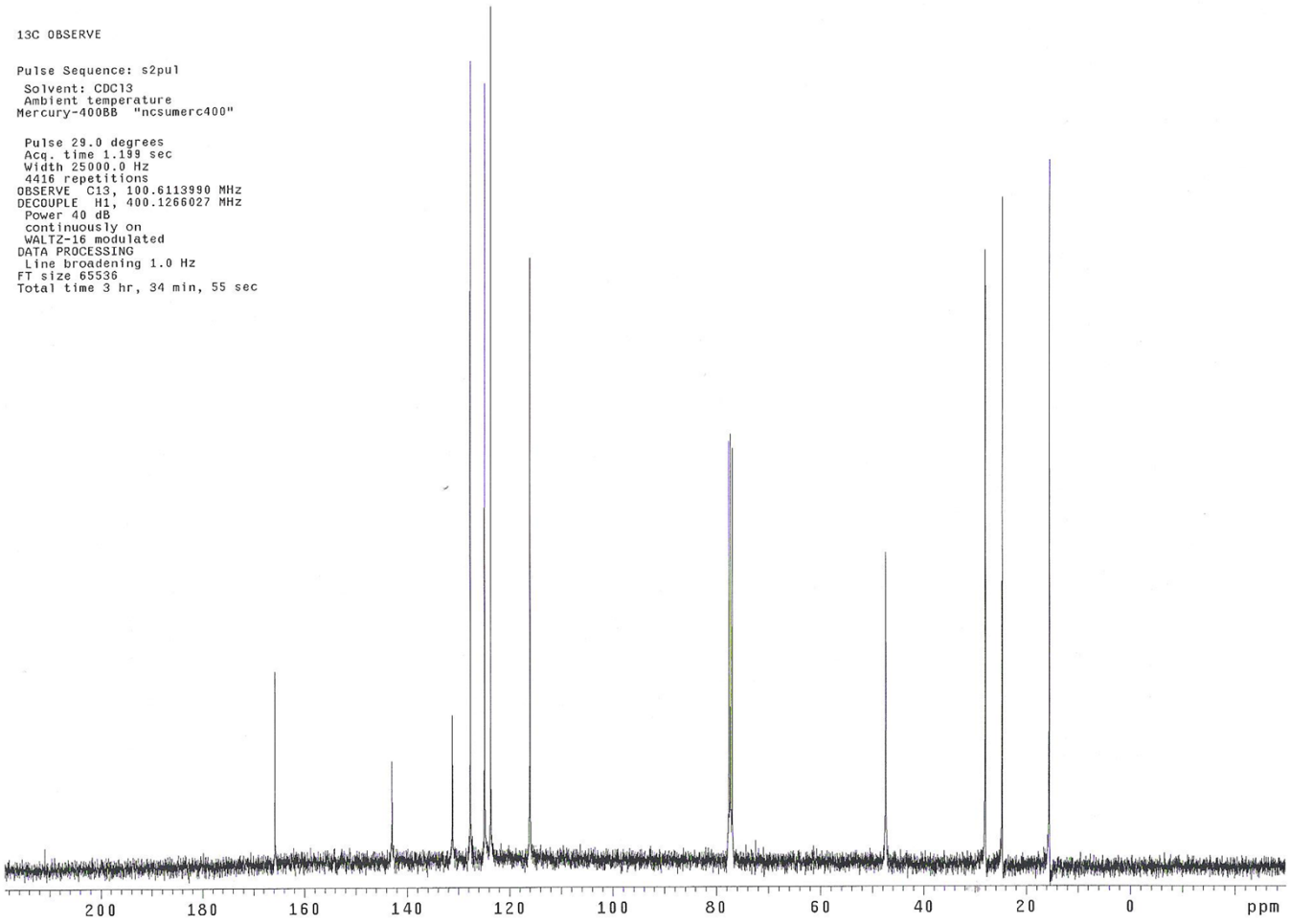
Total time 0 min, 49 sec



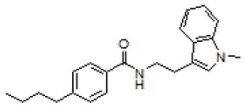



13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "ncsumerc400"
Pulse 29.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
4416 repetitions
OBSERVE C13, 100.6113990 MHz
DECOUPLE H1, 400.1266027 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 34 min, 55 sec
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300BB "ncsumerc300"

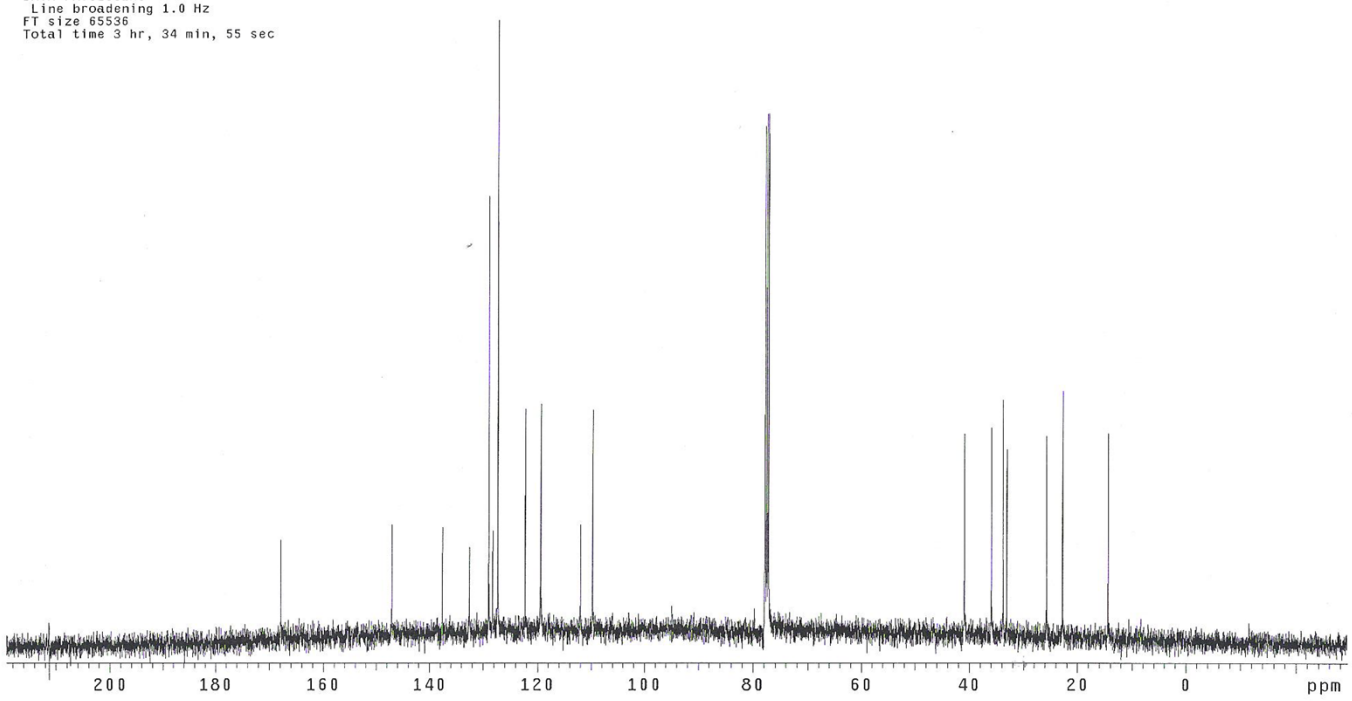
Relax. delay 1.000 sec
Pulse 36.0 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
16 repetitions
OBSERVE H1, 299.7918101 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 49 sec



13C OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "ncsumerc400"

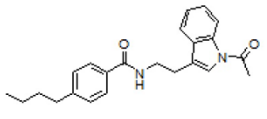
Pulse 29.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
5248 repetitions
OBSERVE C13, 100.6113609 MHz
DECOUPLE H1, 400.1266027 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 34 min, 55 sec



STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300BB "ncsumerc300"

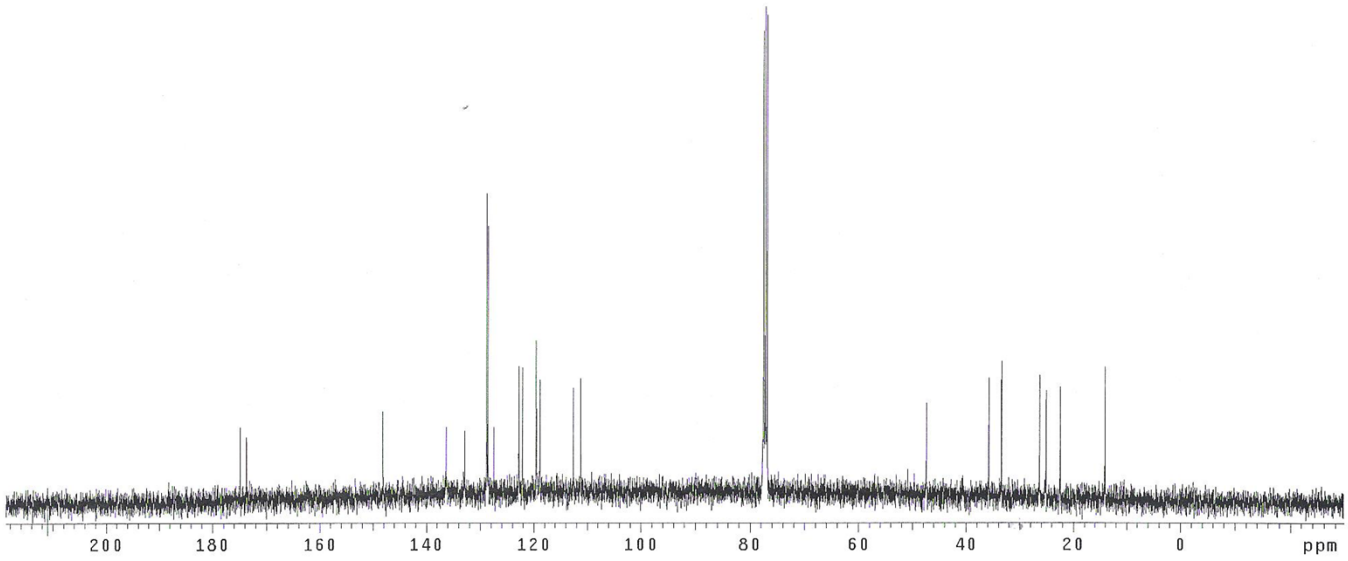
Relax. delay 1.000 sec
Pulse 36.0 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
16 repetitions
OBSERVE H1, 299.7918101 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 49 sec



13C OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "ncsumerc400"

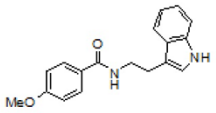
Pulse 29.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2624 repetitions
OBSERVE C13, 100.6113906 MHz
DECOUPLE H1, 400.1266027 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 9 min, 47 sec

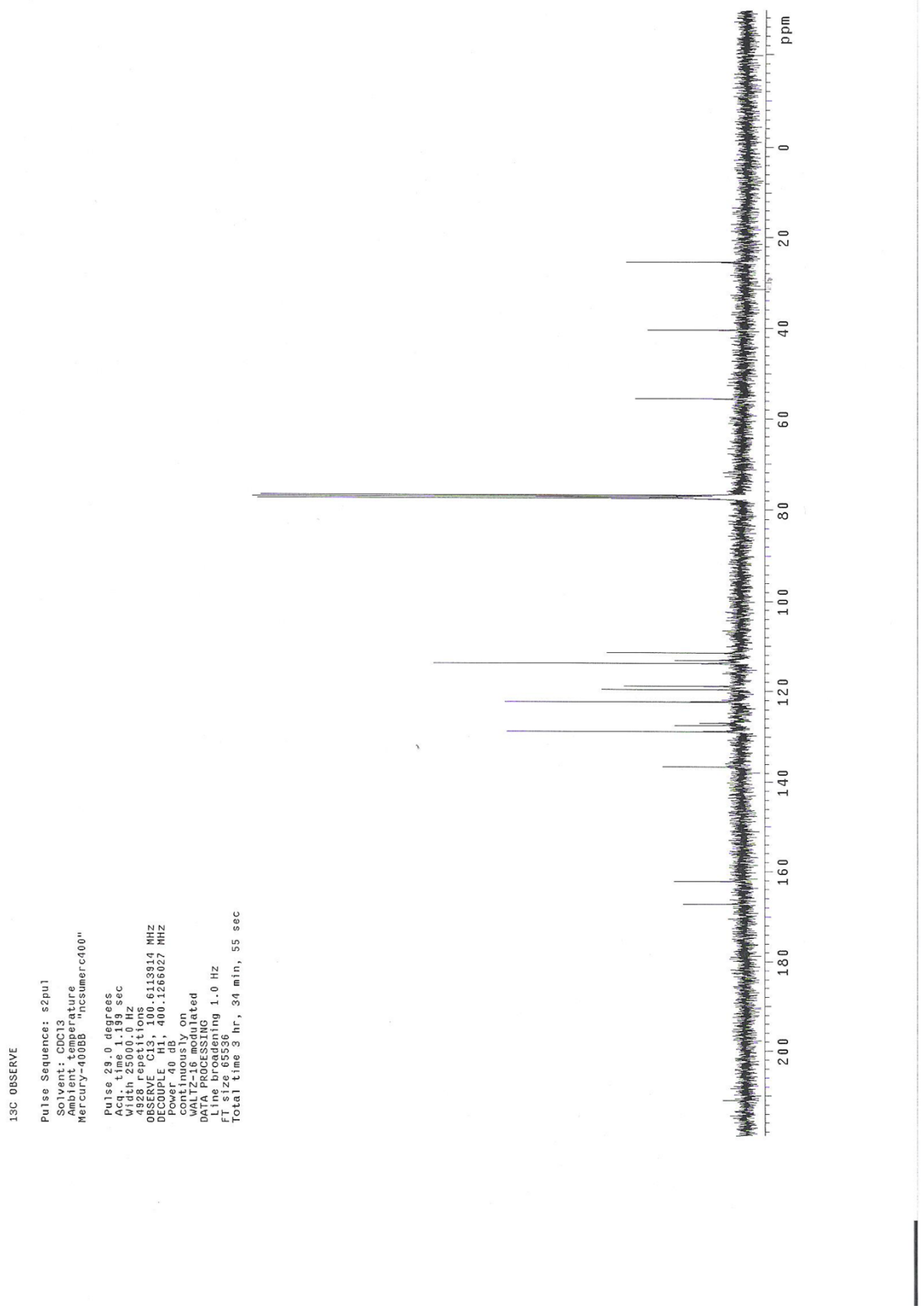


STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300BB "ncsumerc300"

Relax. delay 1.000 sec
Pulse 36.0 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
32 repetitions
OBSERVE H1, 299.7918101 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec



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3. Z. Su, S. A. Rogers, W. S. McCall, A. C. Smith, S. Ravishankar, T. Mullikin and C. Melander, *Org. Biomol. Chem.*, 2010, **8** (12), 2814-2822.
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5. S. A. Rogers and C. Melander, *Angew. Chem.*, 2008, **47**, (28), 5229-5231.