Silicon amine reagents for the photocatalytic synthesis of piperazines from aldehydes and ketones

Supporting Information

Sheng-Ying Hsieh and Jeffrey W. Bode*

Laboratorium für Organische Chemie, Department of Chemistry and Applied Biosciences
ETH Zürich, Zürich 8093, Switzerland

bode@org.chem.ethz.ch

Table of Contents

1. General information

Reactions with anhydrous solvents were carried out in oven-dried glassware under N_2 using standard manifold techniques.[1]

1.1 Materials

Compounds that are not described in the experimental part were synthesized according to literature procedures. Unless otherwise stated, chemicals were purchased from ABCR, Acros, Alfa Aesar, Apollo Scientific, Fluorochem, Maybridge, Merck, Sigma-Aldrich, Strem, or TCI, and were used without further purification. Common organic solvents were used as supplied (ACS or HPLC grade). Anhydrous MeCN, CH_2Cl_2, and THF (HPLC grade) were freshly dried by passage over activated alumina under an inert atmosphere of N_2. 1,1,1,3,3,3-Hexafluoro-2-propanol is abbreviated to HFIP, and 2,2,2-trifluoroethanol to TFE.

All the synthesized SLAP reagents were stored under 4 °C to avoid the decomposition.

1.2 Blue light reactor and the photocatalytic reaction

Nichia LumiFlex LED strip (blue light, λ_{max} = 467 nm, 6 W for 30 LEDs) were purchased from Lumitronix® LED-Technik (http://www.leds.de/) and assembled in a 15×12×12 cm^3 metal case with total 150 blue LEDs (**maximum power: 30 W**). The case was also equipped with a cooling fan (12×12 cm^2) to maintain the temperature at room temperature. Detailed specification of the blue LEDs can be found in this webpage: http://www.leds.de/en/LED-strips-modules-oxid-oxid-oxid/Flexible-LED-strips/LumiFlex-LED-Leiste-30-LEDs-50cm-24V-blue.html.

Photocatalytic reactions were carried out in closed glass vials (sizes depended on reaction scales), neither degassed beforehand nor conducted under dry conditions. The vials were exposed next to the blue LEDs as shown in Figure S1.

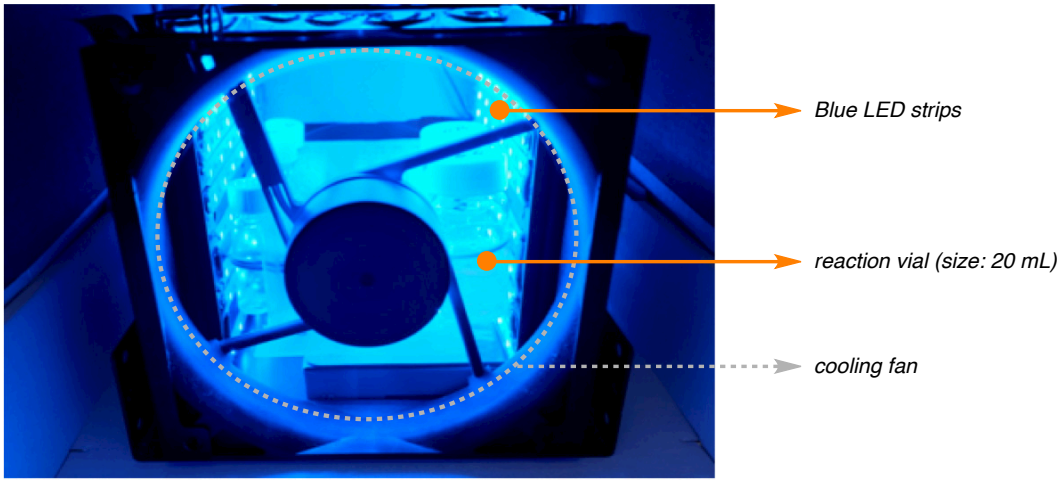


Figure S1. Blue light reactor/reaction setup. We thank Mr. Benedikt Wanner from the Bode group of Laboratorium für Organische Chemie at ETH Zürich for the construction of this blue reactor.

(1) Leonard, J.; Lygo, B.; Procter, G. *Advanced Practical Organic Chemistry*, Taylor & Francis, 1998.

1.3 Reaction monitoring and purification

Thin layer chromatography (TLC) was performed on glass-backed plates pre-coated with silica gel (*Merck*, Silica Gel 60 F254), and visualized by UV quenching and by staining with basic $KMnO_4$, ninhydrin solution, or phosphomolybdic acid.

Flash column chromatography[2] was performed on silica gel (*Silicycle* SiliaFlash F60, 230–400 mesh) using a forced flow of eluent at 0.4–0.5 bar.

1.4 Characterization instruments

NMR spectra were recorded on *Bruker* Avance 400 MHz, and Varian Mercury 300 MHz spectrometers using $CDCl_3$ as the solvent unless indicated otherwise. The residual signal of the $CDCl_3$ was used as the internal standard (7.26 ppm in ^1H and 77.160 ppm in ^{13}C NMR). No additional internal standard was used in the measurement of ^{19}F NMR. Peaks of ^{13}C NMR from the major rotamer were marked with asterisks if able to be recognized.

Infrared (IR) data was obtained on a *JASCO* FT-IR-4100 spectrometer with only major peaks being reported.

Optical rotations were measured on a *JASCO* P-2000 polarimeter operating with Tungsten-Halogen (WI) lamp at 589 nm through a 100 mm path length cell.

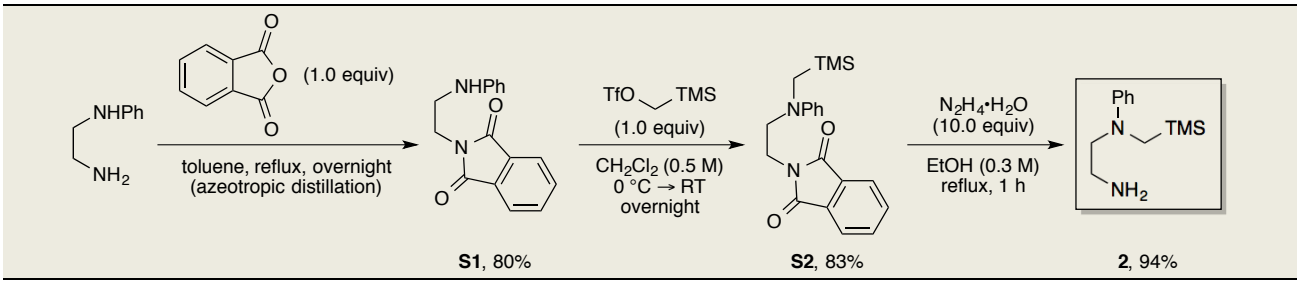
Melting points (m.p.) were measured on an *Electrothermal Mel-Temp* melting point apparatus and were uncorrected.

High resolution mass spectra were measured by the Mass Spectrometry Service Facility of Laboratorium für Organische Chemie at ETH Zürich on a Bruker Daltonics maXis for ESI-Q-TOF spectrometer (ESI-MS).

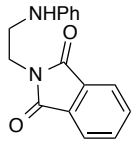
(2) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

2. Preparation of SLAP reagents

2.1 Synthesis of SLAP reagent 2



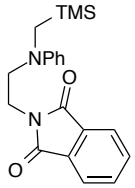
2-(2-(Phenylamino)ethyl)isoindoline-1,3-dione (S1)



The procedure was modified from the literature.[3] A mixture of *N*-phenylethane-1,2-diamine (2.62 mL, 20.00 mmol, 1.00 equiv) and phthalic anhydride (2.96 g, 20.00 mmol, 1.00 equiv) in toluene (20 mL) was heated for reflux with Dean–Stark apparatus overnight. The reaction was cooled and condensed under *vacuo*. Treated with the mixture of EtOAc and hexanes, the desired product was obtained as a white solid (4.24 g, 80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.84 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.17–7.12 (m, 2 H), 6.69–6.61 (m, 3 H), 4.03 (br, 1 H), 3.97 (t, *J* = 6.1 Hz, 2 H), 3.44 (t, *J* = 6.1 Hz, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.7, 147.7, 134.2, 132.1, 129.4, 123.5, 117.7, 112.8, 43.1, 37.6; **HRMS** (ESI): calculated for $[C_{16}H_{15}N_2O_2]^+$: m/z = 267.1128, found: m/z = 267.1129.

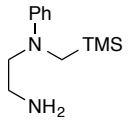
2-(2-(Phenyl((trimethylsilyl)methyl)amino)ethyl)isoindoline-1,3-dione (S2)



The procedure was modified from the literature.[4] To an ice-cooled solution of **S1** (1.07 g, 4.00 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (10 mL, 0.50 M) under N_2 was slowly added (trimethylsilyl)methyl trifluoromethanesulfonate[5] (0.82 mL, 4.00 mmol, 1.00 equiv). The reaction was allowed to warm to room temperature and stirred overnight. After quenched by 5% $NaOH_{(aq)}$ (10 mL), the mixture was extracted by CH_2Cl_2 (3×10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product (1.17 g, 83%) as a yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.80 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.18–7.12 (m, 2 H), 6.79 (apparent d, *J* = 7.9 Hz, 2 H), 6.55 (apparent t, *J* = 7.2 Hz, 1 H), 3.90–3.86 (m, 2 H), 3.61–3.57 (m, 2 H), 2.93 (s, 2 H), 0.11 (s, 9 H).; **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.3, 148.8, 134.0, 132.1, 129.1, 123.2, 115.7, 112.4, 50.0, 41.7, 33.9, –1.1; **HRMS** (ESI): calculated for $[C_{20}H_{25}N_2O_2Si]^+$: m/z = 353.1680, found: m/z = 353.1678; **IR** (ν/cm^{-1}, neat): 3060, 2952, 2897, 1772, 1714, 1597, 1505, 1394, 1249, 1184, 1122, 1039, 1022, 854, 719.

***N*^{1}-phenyl-*N*^{1}-((trimethylsilyl)methyl)ethane-1,2-diamine (2)**

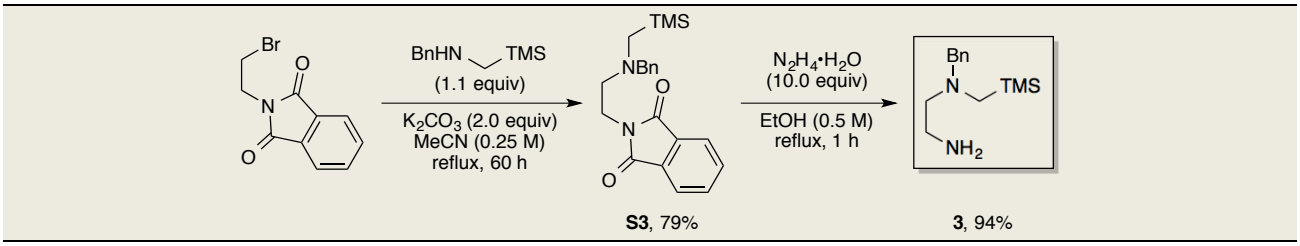


Hydrazine monohydrate (1.62 mL, 33.20 mmol, 10.00 equiv) was added to a solution of **S2** (1.17 g, 3.30 mmol, 1.00 equiv) in EtOH (10 mL, 0.30 M). The mixture was heated under reflux for 1 h and the white solids precipitated during the reaction. The reaction was cooled to room temperature and sufficient amount of 5% $NaOH_{(aq)}$ was added to dissolved the white precipitates. EtOH was removed under *vacuo* and the remained aqueous layer was extracted by CH_2Cl_2 (3×10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product (0.69 g, 94%) as a colorless oil without further purification.

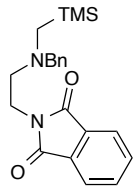
(3) Cul, A.; Daïch, A.; Decroix, B.; Sanz, G.; Van Hijfte, L. *Tetrahedron* **2004**, *60*, 11029–11039.
(4) Kawanishi, N.; Shirai, N.; Sato, Y.; Hatano, K.; Kurono, Y. *J. Org. Chem.* **1995**, *60*, 4272–4275.
(5) (a) The reagent was prepared from (trimethylsilyl)methanol and triflate anhydride by the procedure reported in Anderson, W. K.; Milowsky, A. S. *J. Med. Chem.* **1986**, *29*, 2241–2249; (b) d = 1.16 g/mL.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.22–7.17 (m, 2 H), 6.69 (dt, *J* = 7.8, 1.0 Hz, 2 H), 6.63 (tt, *J* = 7.1, 1.0 Hz, 1 H), 3.37 (t, *J* = 6.9 Hz, 2 H), 2.91 (t, *J* = 6.9 Hz, 2 H), 2.90 (s, 2 H), 1.14 (br, 2 H), 0.08 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 149.4, 129.0, 115.4, 112.4, 55.9, 42.5, 38.9, –0.9; **HRMS** (ESI): calculated for $[C_{12}H_{23}N_2Si]^+$: m/z = 223.1625, found: m/z = 223.1627; **IR** (ν/cm^{-1}, neat): 3366, 3296, 3060, 2952, 1597, 1505, 1382, 1248, 1193, 1034, 990, 850, 744, 693.

2.2 Synthesis of SLAP reagent 3



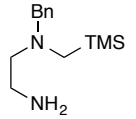
2-(2-(Benzyl((trimethylsilyl)methyl)amino)ethyl)isoindoline-1,3-dione (S3)



A mixture of 2-(2-bromoethyl)isoindoline-1,3-dione (7.62 g, 30.00 mmol, 1.00 equiv), *N*-benzyl-1-(trimethylsilyl)methanamine (7.25 mL, 33.00 mmol, 1.10 equiv), and K_2CO_3 (8.29 g, 60.00 mmol, 2.00 equiv) in MeCN (120 mL, 0.25 M) was heated under reflux for 2 days. The reaction was cooled to room temperature, filtered, washed with CH_2Cl_2. The combined filtrate was condensed and the residue was purified by flash column chromatography to afford the desired product (8.63 g, 79%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.81 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.17–7.09 (m, 5 H), 3.77 (t, *J* = 6.3 Hz, 2 H), 3.54 (s, 2 H), 2.60 (t, *J* = 6.3 Hz, 2 H), 2.09 (s, 2 H), 0.03 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.2, 139.8, 133.8, 132.4, 128.8, 128.1, 126.8, 123.1, 61.9, 54.9, 46.3, 36.0, –1.2; **HRMS** (ESI): calculated for $[C_{21}H_{27}N_2O_2Si]^+$: m/z = 367.1836, found: m/z = 367.1838; **IR** (ν/cm^{-1}, neat): 2952, 2793, 1772, 1714, 1395, 1248, 1085, 1069, 1018, 855, 721.

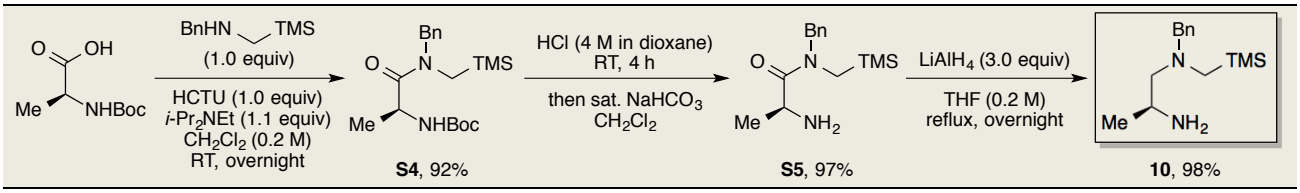
N^1-benzyl-N^1-((trimethylsilyl)methyl)ethane-1,2-diamine (3)



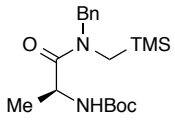
Hydrazine monohydrate (11.15 mL, 228.70 mmol, 10.00 equiv) was added to a solution of **S3** (8.36 g, 22.90 mmol, 1.00 equiv) in EtOH (46 mL, 0.50 M). The mixture was heated under reflux for 1 h and the white solids precipitated during the reaction. The reaction was cooled to room temperature and sufficient amount of 5% $NaOH_{(aq)}$ was added to dissolved the white precipitates. EtOH was removed under *vacuo* and the remained aqueous layer was extracted by CH_2Cl_2 (3×50 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product (5.12 g, 94%) as a colorless oil without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.35–7.23 (m, 5 H), 3.53 (s, 2 H), 2.72 (t, *J* = 5.9 Hz, 2 H), 2.39 (t, *J* = 5.9 Hz, 2 H), 2.00 (s, 2 H), 1.30 (br, 2 H), 0.10 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 140.2, 128.9, 128.3, 126.9, 62.4, 60.4, 46.4, 39.8, –1.2; **HRMS** (ESI): calculated for $[C_{13}H_{25}N_2Si]^+$: m/z = 237.1782, found: m/z = 237.1785; **IR** (ν/cm^{-1}, neat): 3369, 3028, 2952, 2789, 1585, 1453, 1248, 1028, 854, 738, 699.

2.3 Synthesis of SLAP reagent 10



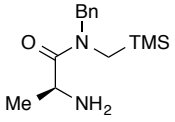
(*S*)-*tert*-Butyl (1-(benzyl((trimethylsilyl)methyl)amino)-1-oxopropan-2-yl)carbamate (S4)



The procedure was modified from the literature.[6] To a mixture of *N*-Boc-L-alanine (3.78 g, 20.00 mmol, 1.00 equiv) and *N*,*N*,*N*′,*N*′-tetramethyl-*O*-(6-chloro-1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (HCTU, 9.10 g, 22.00 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (100 mL, 0.20 M) was sequentially added $^{i}Pr_2NEt$ (7.61 mL, 44.00 mmol, 2.20 equiv) and *N*-benzyl-1-(trimethylsilyl)methanamine (4.40 mL, 20.00 mmol, 1.00 equiv). The mixture was stirred under N_2 at room temperature overnight. The reaction was washed with 1 N $HCl_{(aq)}$ (3×50 mL), sat. $NaHCO_{3(aq)}$ (1×50 mL), and brine. The final organic layer was dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product (6.68 g, 92%) as a colorless oil.

$[\alpha]_D^{24}$ (c = 1.0, $CHCl_3$) = –27.7; the ratio of rotamers was 75:25 as determined by ^{1}H NMR at room temperature; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.38–7.26 (m, 3.00 H), 7.20–7.15 (m, 2.00 H), 5.57 (d, *J* = 8.2 Hz, 0.25 H), 5.44 (d, *J* = 8.2 Hz, 0.75 H), 5.03 (d, *J* = 14.8 Hz, 0.25 H), 4.73–4.65 (m, 1.00 H), 4.66 (d, *J* = 16.5 Hz, 0.75 H), 4.57 (d, *J* = 16.5 Hz, 0.75 H), 4.19 (d, *J* = 14.8 Hz, 0.25 H), 2.87 (s, 1.50 H), 2.83 (s, 0.50 H), 1.45 (s, 2.25 H), 1.43 (s, 6.75 H), 1.36 (d, *J* = 6.7 Hz, 0.75 H), 1.27 (d, *J* = 6.8 Hz, 2.25 H), 0.13 (s, 2.25 H), 0.06 (s, 6.75 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 172.7, 172.3*, 155.2*, 155.0, 136.9, 136.4*, 129.0, 128.7*, 127.8, 127.7*, 127.5*, 126.8, 79.5*, 79.4, 53.2*, 50.2, 46.4, 46.0*, 38.7*, 38.1, 28.44, 28.43*, 19.5*, 19.4, –1.2*, –1.6; **HRMS** (ESI): calculated for $[C_{19}H_{32}N_2NaO_3Si]^+$: m/z = 387.2074, found: m/z = 387.2074; **IR** (ν/cm^{-1}, neat): 3424, 3311, 2978, 1713, 1634, 1453, 1366, 1249, 1169, 1028, 854, 731, 698.

(*S*)-2-Amino-*N*-benzyl-*N*-((trimethylsilyl)methyl)propanamide (S5)

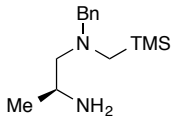


The procedure was modified from the literature.[6] A solution of HCl in dioxane (4.0 M, 30.9 mL, 123.4 mmol, 15.0 equiv) was added to **S4** (3.0 g, 8.2 mmol, 1.0 equiv), and the mixture was stirred at room temperature for 4 h. The reaction was condensed under *vacuo* to remove the excess HCl in dioxane, and the residue was basified and partitioned with sat. $NaHCO_{3(aq)}$ and CH_2Cl_2. The organic layer was separated and the basic aqueous layer was extracted with CH_2Cl_2 for twice. Organic extracts were combined, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the deprotected amine (2.1 g, 97%) as a colorless oil without further purification.

$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = –50.2; the ratio of rotamers was 75:25 as determined by ^{1}H NMR at room temperature; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.36–7.24 (m, 3 H), 7.16–7.12 (m, 2 H), 5.10 (d, *J* = 14.8 Hz, 0.25 H), 4.63 (d, *J* = 16.7 Hz, 0.75 H), 4.37 (d, *J* = 16.7 Hz, 0.75 H), 4.06 (d, *J* = 14.8 Hz, 0.25 H), 3.78–3.70 (m, 1 H), 3.15 (d, *J* = 14.9 Hz, 0.75 H), 2.83 (d, *J* = 16.3 Hz, 0.25 H), 2.68 (d, *J* = 16.3 Hz, 0.25 H), 2.57 (d, *J* = 14.9 Hz, 0.75 H), 1.70 (br, 2 H), 1.27 (d, *J* = 6.8 Hz, 0.75 H), 1.27 (d, *J* = 6.7 Hz, 2.25 H), 0.10 (s, 2.25 H), 0.04 (s, 6.75 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 176.1, 175.7*, 137.3, 136.6*, 129.0*, 128.7, 127.81, 127.77*, 127.4, 126.4*, 52.8*, 50.3, 47.0, 46.9*, 38.9*, 37.6, 22.2*, 21.4, –1.2*, –1.5; **HRMS** (ESI): calculated for $[C_{14}H_{25}N_2OSi]^+$: m/z = 265.1731, found: m/z = 265.1734; **IR** (ν/cm^{-1}, neat): 3364, 3297, 2953, 2897, 1633, 1453, 1248, 995, 851, 732, 697.

(6) Fang, Y.-Q.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2008**, *130*, 5660–5661.

(*S*)-*N*^{1}-Benzyl-*N*^{1}-((trimethylsilyl)methyl)propane-1,2-diamine (10)

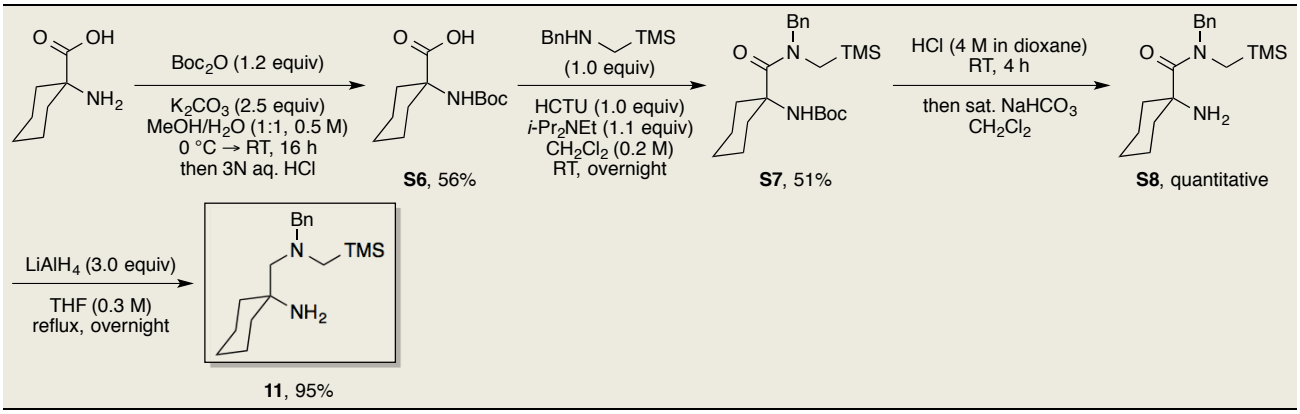


To an ice-cooled solution of **S5** (1.85 g, 7.00 mmol, 1.00 equiv) in anhydrous THF (35 mL, 0.20 M), $LiAlH_4$ (0.80 g, 21.00 mmol, 3.00 equiv) was added slowly and portionwise (CAUTION![7]). After the addition was complete, the mixture was heated under reflux overnight. The reaction was cooled to room temperature and quenched with 20% $NaOH_{(aq)}$ before filtered and washed with EtOAc. The combined filtrate was condensed under *vacuo*, and the desired product was obtained as a colorless oil without further purification (1.71 g, 98%).

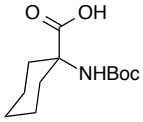
$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = +85.8; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.32–7.27 (m, 4 H), 7.24–7.20 (m, 1 H), 3.73 (d, *J* = 13.5 Hz, 1 H), 3.26 (d, *J* = 13.5 Hz, 1 H), 3.02–2.94 (m, 1 H), 2.17 (dd, *J* = 12.2, 9.1 Hz, 1 H), 2.11 (dd, *J* = 12.2, 4.4 Hz, 1 H), 2.10 (d, *J* = 14.8 Hz, 1 H), 1.88 (br, 2 H), 1.85 (d, *J* = 14.8 Hz, 1 H), 0.97 (d, *J* = 6.4 Hz, 3 H), 0.07 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 140.0, 129.0, 128.3, 127.0, 66.7, 62.7, 47.0, 44.6, 21.0, –1.1; **HRMS** (ESI): calculated for $[C_{14}H_{27}N_2Si]^+$: m/z = 251.1938, found: m/z = 251.1941; **IR** (ν/cm^{-1}, neat): 3359, 2956, 2790, 1585, 1453, 1365, 1248, 1062, 840, 740, 699.

(7) The addition of $LiAlH_4$ must be slow. Stop the addition if the reaction is too drastic, and continue the addition while the reaction returns gentle.

2.4 Synthesis of SLAP reagent 11



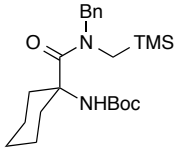
1-((*tert*-Butoxycarbonyl)amino)cyclohexanecarboxylic acid (S6)



The procedure was modified from the literature.[8] K_2CO_3 (34.6 g, 250.0 mmol, 2.5 equiv) was added to a solution of 1-aminocyclohexanecarboxylic acid (14.3 g, 100.0 mmol, 1.0 equiv) in MeOH (50 mL) and H_2O (100 mL). A solution of Boc_2O (26.2 g, 120.0 mmol, 1.2 equiv) in MeOH (50 mL) was added dropwise at 0 °C. The mixture was allowed to warm to room temperature and stirred for 16 h before condensed under *vacuo*. The residue was cooled to 0 °C, acidified with 3 N $HCl_{(aq)}$ to pH = 5 (ca. 180 mL), and extracted with EtOAc (4×150 mL). The extracts were combined, washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the crude product. After washed with Et_2O, the pure product was obtained as a white solid (13.7 g, 56%).

^{1}H NMR (400 MHz, CD_3OD): δ [ppm] = 4.88 (br, 2 H), 2.02–1.98 (m, 2 H), 1.78 (ddd, *J* = 13.8, 12.6, 4.2 Hz, 2 H), 1.53–1.45 (m, 5 H), 1.43 (s, 9 H), 1.37–1.22 (m, 1H); **^{13}C NMR** (100 MHz, CD_3OD): δ [ppm] = 178.8, 157.3, 80.1, 59.8, 33.6, 28.8, 26.5, 22.5.

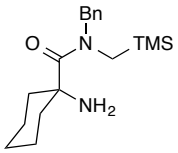
tert-Butyl (1-(benzyl((trimethylsilyl)methyl)carbamoyl)cyclohexyl)carbamate (S7)



The procedure was modified from the literature.[6] To a mixture of **S6** (4.87 g, 20.00 mmol, 1.00 equiv) and *N*,*N*,*N*′,*N*′-tetramethyl-*O*-(6-chloro-1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (HCTU, 9.10 g, 22.00 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (100 mL, 0.20 M) was sequentially added ^{i}Pr$_2$NEt (7.61 mL, 44.00 mmol, 2.20 equiv) and *N*-benzyl-1-(trimethylsilyl)methanamine (4.40 mL, 20.00 mmol, 1.00 equiv). The mixture was stirred under N_2 at room temperature overnight. The reaction was washed with 1 N $HCl_{(aq)}$ (3×50 mL), sat. $NaHCO_{3(aq)}$ (1×50 mL), and brine. The final organic layer was dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product (4.24 g, 51%) as a white solid.

m.p.: 120–121 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.36–7.20 (m, 5 H), 4.90 (s, 2 H), 4.77 (br, 1 H), 2.76 (s, 2 H), 2.11 (apparent d, *J* = 13.8 Hz, 2 H), 1.96 (apparent dt, *J* = 13.8, 6.8 Hz, 2 H), 1.72–1.59 (m, 3 H), 1.42 (s, 9 H), 1.35–1.29 (m, 3 H), 0.04 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 172.3, 153.7, 137.5, 128.7, 127.3, 127.2, 79.7, 59.1, 53.3, 39.4, 33.2, 28.5, 25.3, 21.7, –0.8; **HRMS** (ESI): calculated for $[C_{23}H_{39}N_2O_3Si]^+$: m/z = 419.2724, found: m/z = 419.2721; **IR** (ν/cm^{-1}, neat): 3286, 2931, 1693, 1619, 1496, 1390, 1366, 1247, 1163, 853, 731.

1-Amino-*N*-benzyl-*N*-((trimethylsilyl)methyl)cyclohexanecarboxamide (S8)



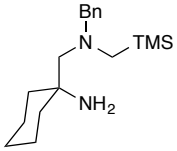
The procedure was modified from the literature.[6] A solution of HCl in dioxane (4.0 M, 60.0 mL, 240.0 mmol, 15.0 equiv) was added to **S7** (6.7 g, 16.0 mmol, 1.0 equiv), and the mixture was stirred at room temperature for 4 h. The reaction was condensed under *vacuo*

(8) Prozymex A/S; Pedersen, J.; Lauritzen, C. WO2012/119941 A1, **2012**.

to remove the excess HCl in dioxane, and the residue was basified and partitioned with sat. $NaHCO_{3(aq)}$ and CH_2Cl_2. The organic layer was separated and the basic aqueous layer was extracted with CH_2Cl_2 for twice. Organic extracts were combined, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the deprotected amine (5.1 g, quantitative) as a white solid without further purification.

m.p.: 65–66 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.36–7.31 (m, 2 H), 7.27–7.23 (m, 1 H), 7.19–7.16 (m, 2 H), 5.22 (s, 2 H), 2.73 (s, 2 H), 2.03 (ddd, *J* = 13.9, 10.5, 3.7 Hz, 1 H), 1.67–1.29 (m, 10 H), 0.04 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 175.3, 138.4, 128.7, 127.1, 126.8, 58.4, 54.4, 39.8, 37.4, 25.6, 22.2, –0.8; **HRMS** (ESI): calculated for $[C_{18}H_{31}N_2OSi]^+$: m/z = 319.2200, found: m/z = 319.2201; **IR** (ν/cm^{-1}, neat): 2925, 2857, 1620, 1452, 1246, 853, 728, 697.

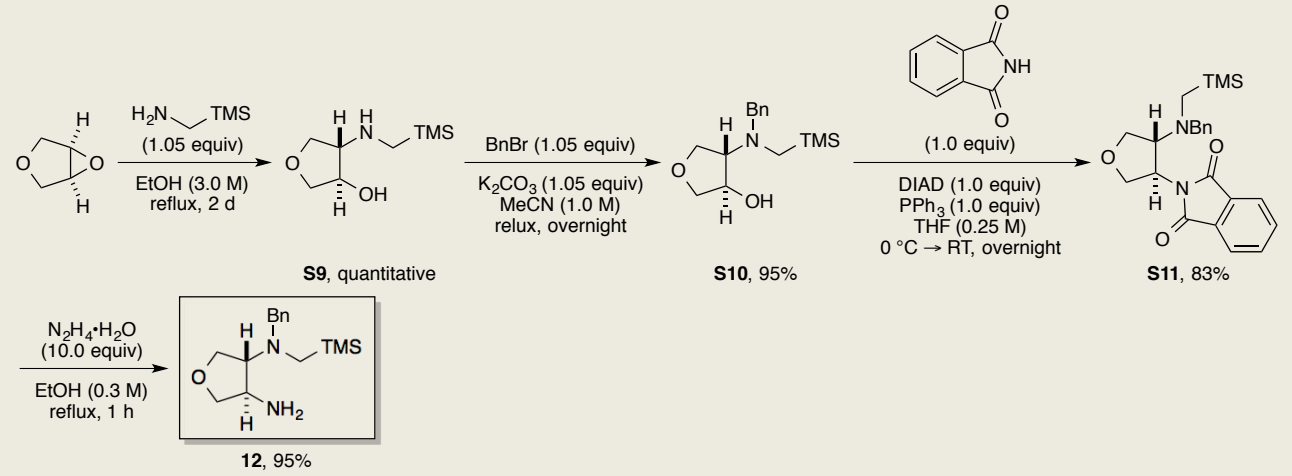
1-((Benzyl((trimethylsilyl)methyl)amino)methyl)cyclohexanamine (11)



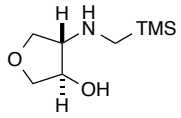
To an ice-cooled solution of **S8** (4.78 g, 15.00 mmol, 1.00 equiv) in anhydrous THF (45 mL, 0.30 M), $LiAlH_4$ (1.71 g, 45.00 mmol, 3.00 equiv) was added slowly and portionwise (CAUTION![7]). After the addition was complete, the mixture was heated under reflux overnight. The reaction was cooled to room temperature and quenched with 20% $NaOH_{(aq)}$ before filtered and washed with EtOAc. The combined filtrate was condensed under *vacuo*, and the desired product was obtained as colorless oil without further purification (4.34 g, 95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.36–7.29 (m, 4 H), 7.26–7.22 (m, 1 H), 3.61 (s, 2 H), 2.37 (s, 2 H), 2.23 (s, 2 H), 1.52–1.35 (m, 5 H), 1.29–1.18 (m, 7 H), 0.12 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 140.4, 129.2, 128.2, 126.9, 69.6, 64.5, 52.0, 50.8, 37.6, 26.2, 22.0, -0.8; **HRMS** (ESI): calculated for $[C_{18}H_{33}N_2Si]^+$: m/z = 305.2408, found: m/z = 305.2407; **IR** (ν/cm^{-1}, neat): 2926, 2853, 1495, 1450, 1363, 1247, 1068, 855, 741, 699.

2.5 Synthesis of SLAP reagent 12



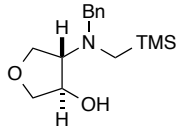
trans-4-(((Trimethylsilyl)methyl)amino)tetrahydrofuran-3-ol (S9)



To a solution of 3,4-epoxytetrahydrofuran (2.15 mL, 30.00 mmol, 1.00 equiv) in EtOH (10 mL, 3.00 M) was added (trimethylsilyl)methanamine (4.22 mL, 31.50 mmol, 1.05 equiv). The mixture was heated under reflux for 2 days. The reaction was cooled to room temperature and condensed under *vacuo* to afford the desired product (5.67 g, quantitative) as a colorless oil without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 4.13 (ddd, *J* = 4.3, 2.7, 1.3 Hz, 1 H), 4.04 (dd, *J* = 9.1, 5.6 Hz, 1 H), 3.95 (dd, *J* = 9.8, 4.6 Hz, 1 H), 3.65 (dd, *J* = 9.8, 2.7 Hz, 1 H), 3.55 (dd, *J* = 9.1, 3.4 Hz, 1 H), 3.08 (ddd, *J* = 5.6, 3.4, 1.3 Hz, 1 H), 2.20 (br, 2 H), 2.05 (s, 2 H), 0.02 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 76.1, 74.2, 72.3, 70.7, 38.4, –2.6; **HRMS** (ESI): calculated for $[C_8H_{20}NO_2Si]^+$: m/z = 190.1258, found: m/z = 190.1262; **IR** (ν/cm^{-1}, neat): 3390, 2953, 2871, 1660, 1464, 1421, 1249, 1074, 856.

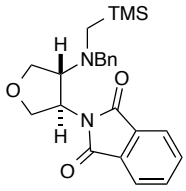
trans-4-(Benzyl((trimethylsilyl)methyl)amino)tetrahydrofuran-3-ol (S10)



A mixture of **S9** (5.67 g, 30.00 mmol, 1.00 equiv), BnBr (3.74 mL, 31.50 mmol, 1.05 equiv) and K_2CO_3 (4.57 g, 31.50 mmol, 1.05 equiv) in MeCN (30 mL, 1.00 M) was heated under reflux overnight. The reaction was cooled to room temperature, filtered, and washed with CH_2Cl_2. The combined filtrate was condensed under vacuo to afford the desired product (7.93 g, 95%) as a yellowish oil without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.39–7.32 (m, 4 H), 7.29–7.25 (m, 1 H), 4.42 (ddd, *J* = 5.8, 4.2, 3.0 Hz, 1 H), 3.96 (dd, *J* = 9.8, 5.8 Hz, 1 H), 3.91 (dd, *J* = 9.6, 7.8 Hz, 1 H), 3.71 (dd, *J* = 9.6, 5.5 Hz, 1 H), 3.65 (apparent d, *J* = 3.2 Hz, 2 H), 3.58 (dd, *J* = 9.8, 4.2 Hz, 1 H), 3.26 (ddd, *J* = 7.8, 5.5, 3.0 Hz, 1 H), 2.20 (br, 1 H), 2.12 (d, *J* = 14.8 Hz, 1 H), 2.04 (d, *J* = 14.8 Hz, 1 H), 0.10 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 139.8, 128.6, 128.4, 127.1, 75.1, 72.9, 71.7, 69.1, 59.4, 42.4, –1.3; **HRMS** (ESI): calculated for $[C_{15}H_{26}NO_2Si]^+$: m/z = 280.1727, found: m/z = 280.1728; **IR** (ν/cm^{-1}, neat): 3410, 2952, 2860, 1495, 1454, 1422, 1365, 1249, 1074, 856, 740, 699.

2-(*trans*-4-(Benzyl((trimethylsilyl)methyl)amino)tetrahydrofuran-3-yl)isoindoline-1,3-dione (S11)

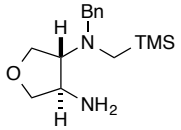


S10 (5.55 g, 20.00 mmol, 1.00 equiv), phthalimide (2.94 g, 20.00 mmol, 1.00 equiv), and PPh_3 (5.25 g, 20.00 mmol, 1.00 equiv) were dissolved in anhydrous THF (80 mL, 0.25 M) under N_2. This clear solution was cooled to 0 °C and diisopropyl azodicarboxylate (DIAD, 3.94 mL, 20.00 mmol, 1.00 equiv) was added dropwise. The reaction was allowed to warm to room temperature and stirred under N_2 overnight. After the solvent was removed under *vacuo*, the residue was purified by flash column chromatography to afford the *trans*

product[9] (6.67 g, 83%) as a yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.84–7.79 (m, 2 H), 7.75–7.71 (m, 2 H), 7.10–7.00 (m, 5 H), 4.96 (ddd, *J* = 8.7, 8.7, 4.6 Hz, 1 H), 4.14–4.07 (m, 2 H), 3.99–3.84 (m, 3 H), 3.68 (d, *J* = 13.9 Hz, 1 H), 3.40 (d, *J* = 13.9 Hz, 1 H), 2.16 (d, *J* = 14.8 Hz, 1 H), 2.03 (d, *J* = 14.8 Hz, 1 H), 0.03 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 167.8, 139.4, 134.2, 131.8, 128.3, 128.2, 127.0, 123.3, 70.9, 68.9, 65.1, 58.8, 49.4, 40.5, –1.4; **HRMS** (ESI): calculated for $[C_{23}H_{29}N_2O_3Si]^+$: m/z = 409.1942, found: m/z = 409.1943; **IR** (ν/cm^{-1}, neat): 2953, 2877, 1773, 1714, 1387, 1248, 1088, 924, 857, 720.

trans-N^3-Benzyl-N^3-((trimethylsilyl)methyl)tetrahydrofuran-3,4-diamine (12)

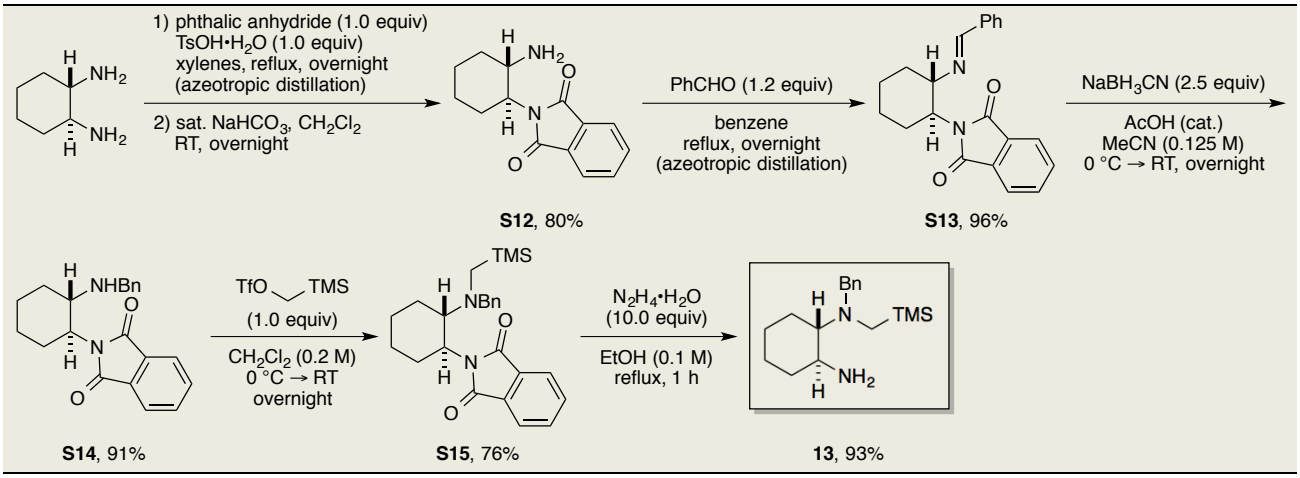


Hydrazine monohydrate (2.98 mL, 61.20 mmol, 10.00 equiv) was added to a solution of **S11** (2.50 g, 6.10 mmol, 1.00 equiv) in EtOH (18 mL, 0.30 M). The mixture was heated under reflux for 1 h and the white solids precipitated during the reaction. The reaction was cooled to room temperature and sufficient amount of 5% $NaOH_{(aq)}$ was added to dissolved the white precipitates. EtOH was removed under *vacuo* and the remained aqueous layer was extracted by CH_2Cl_2 (3×20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product (1.62 g, 95%) as a colorless oil without further purification.

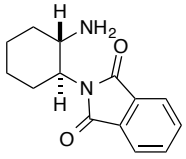
^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.36–7.29 (m, 4 H), 7.26–7.21 (m, 1 H), 4.00 (dd, *J* = 9.0, 6.7 Hz, 1 H), 3.84–3.77 (m, 2 H), 3.69 (d, *J* = 14.1 Hz, 1 H), 3.52 (d, *J* = 14.1 Hz, 1 H), 3.50 (apparent td, *J* = 6.7, 4.9 Hz, 1 H), 3.28 (dd, *J* = 9.0, 6.7 Hz, 1 H), 3.02 (apparent dt, *J* = 7.4, 5.6 Hz, 1 H), 2.05 (s, 2 H), 1.25 (br, 2 H), 0.07 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 140.0, 128.5, 128.4, 127.1, 75.3, 71.7, 67.8, 59.5, 53.5, 41.7, –1.3; **HRMS** (ESI): calculated for $[C_{15}H_{27}N_2OSi]^+$: m/z = 279.1887, found: m/z = 279.1887; **IR** (ν/cm^{-1}, neat): 3368, 2951, 2853, 1602, 1494, 1453, 1247, 1052, 838, 738, 698.

(9) The reaction went through aziridinium intermediate.

2.6 Synthesis of SLAP reagent 13



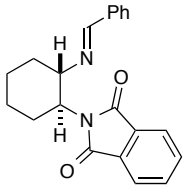
2-(*trans*-2-Aminocyclohexyl)isoindoline-1,3-dione (S12)



The procedure was modified from the literature.[10] A stirred suspension of *p*-TsOH•H_2O (7.6 g, 40.0 mmol, 1.0 equiv) in xylenes (200 mL) was heated to reflux to remove water azeotropically (c.a. 1–2 h). The resulting solution was allowed to cool to room temperature, followed by the addition of *trans*-cyclohexane-1,2-diamine (4.6 g, 40.0 mmol, 1.0 equiv) and phthalic anhydride (5.9 g, 40.0 mmol, 1.0 equiv). The mixture was again heated to remove water azeotropically overnight and allowed to cool to room temperature. The monoprotected **S12**•*p*-TsOH was obtained by recrystallization from hexanes/xylenes (a white solid, 16.0 g, 96%). **S12**•*p*-TsOH was dissolved in CH_2Cl_2 (100 mL) and stirred with sat. $NaHCO_{3(aq)}$ (100 mL) at room temperature overnight. After the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3×100 mL). The combined organics were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product **S12** without further purification (a white solid, 7.8 g, 80% from diamine).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.82 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.69 (dd, *J* = 5.4, 3.1 Hz, 2 H), 3.79 (ddd, *J* = 12.4, 10.5, 3.9 Hz, 1 H), 3.41 (ddd, *J* = 11.3, 10.5, 4.1 Hz, 1 H), 2.19 (dddd, *J* = 12.6, 12.6, 12.4, 3.5 Hz, 1 H), 2.07–2.01 (m, 1 H), 1.84–1.73 (m, 1 H), 1.49–1.28 (m, 4 H), 1.19 (dddd, *J* = 12.8, 11.3, 3.6 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.9, 134.0, 132.1, 123.3, 58.7, 51.0, 36.8, 29.5, 25.8, 25.2.

2-(*trans*-2-(Benzylideneamino)cyclohexyl)isoindoline-1,3-dione (S13)

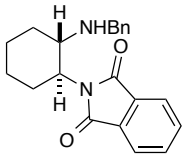


The procedure was followed by the literature.[10a] A solution of **S12** (9.77 g, 40.00 mmol, 1.00 equiv) and benzaldehyde (4.87 mL, 48.00 mmol, 1.20 equiv) in benzene (100 mL) with Dean–Stark apparatus overnight. The reaction was allowed to cool to room temperature and poured into hexanes. The desired product was obtained from the recrystallization as a white solid (12.79 g, 96%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.63 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.50 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.47–7.45 (m, 2 H), 7.22–7.15 (m, 3 H), 4.33 (ddd, *J* = 12.7, 10.6, 3.8 Hz, 1 H), 3.96 (ddd, *J* = 10.6, 10.6, 4.3 Hz, 1 H), 2.17 (dddd, *J* = 12.7, 12.7, 11.8, 3.0 Hz, 1 H), 1.82–1.61 (m, 5 H), 1.49–1.35 (m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.6, 160.9, 136.3, 133.8, 131.9, 130.6, 128.5, 128.2, 123.1, 69.5, 55.8, 34.3, 28.9, 25.7, 24.3.

(10) (a) Kaik, M.; Gawroński, J. *Tetrahedron: Asymmetry* **2003**, *14*, 1559–1563; (b) Bui, T.; Syed, S.; Barbas, C. F. *J. Am. Chem. Soc.* **2009**, *131*, 8758–8759.

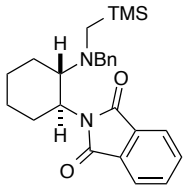
2-(*trans*-2-(Benzylamino)cyclohexyl)isoindoline-1,3-dione (S14)



The procedure was modified from the literature.[10a] To a solution of imine **S13** (9.97 g, 30.00 mmol, 1.00 equiv) in dry MeCN (240 mL, 0.13 M) at 0 °C was added $NaBH_3CN$ (4.71 g, 75.00 mmol, 2.50 equiv) and AcOH (0.17 mL, 3.00 mmol, 0.10 equiv) sequentially. The reaction was allowed to warm to room temperature and stirred overnight. After solvent was removed under *vacuo*, the residue was extracted with CH_2Cl_2 and sat. $NaHCO_{3(aq)}$. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product (9.14 g, 91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.80 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.10–7.04 (m, 5 H), 3.96 (ddd, *J* = 12.4, 11.0, 3.9 Hz, 1 H), 3.81 (d, *J* = 13.2 Hz, 1 H), 3.59 (d, *J* = 13.2 Hz, 1 H), 3.26 (td, *J* = 11.0, 4.1 Hz, 1 H), 2.31–2.20 (m, 2 H), 1.84–1.77 (m, 3 H), 1.45–1.29 (m, 2 H), 1.18–1.08 (m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.9, 141.2, 133.8, 132.2, 128.2, 128.0, 126.7, 123.2, 56.5, 56.1, 50.7, 33.3, 29.6, 25.8, 25.2.

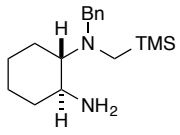
2-(*trans*-2-(Benzyl((trimethylsilyl)methyl)amino)cyclohexyl)isoindoline-1,3-dione (S15)



The procedure was modified from the literature.[4] To an ice-cooled solution of **S14** (3.00 g, 9.00 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (45 mL, 0.20 M) under N_2 was slowly added (trimethylsilyl)methyl trifluoromethanesulfonate[5] (1.83 mL, 9.00 mmol, 1.00 equiv). The reaction was allowed to warm to room temperature and stirred overnight. After quenched by 5% $NaOH_{(aq)}$ (10 mL), the mixture was extracted by CH_2Cl_2 (3×20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product (2.88 g, 76%) as a white solid.

m.p.: 78–79 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.80–7.78 (m, 2 H), 7.73–7.70 (m, 2 H), 7.17–7.13 (m, 1 H), 7.09– 7.05 (m, 2 H), 6.96–6.94 (m, 2 H), 4.20 (ddd, *J* = 12.1, 10.8, 3.9 Hz, 1 H), 3.74 (d, *J* = 13.6 Hz, 1 H), 3.25 (d, *J* = 13.6 Hz, 1 H), 3.25–3.20 (m, 1 H), 2.35–2.24 (m, 1 H), 2.13 (d, *J* = 14.2 Hz, 1 H), 2.06–2.02 (m, 1 H), 1.91 (d, *J* = 14.2 Hz, 1 H), 1.86–1.75 (m, 3 H), 1.36–1.24 (m, 3 H), –0.05 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = **168.5**, **168.1**, 140.2, 133.7, **132.7**, **132.2**, 128.6, 128.0, 126.7, **123.1**, **122.8**, 59.7, 57.0, 51.9, 40.9, 29.8, 26.0, 25.2, 22.5, –1.2; **HRMS** (ESI): calculated for $[C_{25}H_{33}N_2O_2Si]^+$: m/z = 421.2306, found: m/z = 421.2307; **IR** (ν/cm^{-1}, neat): 2933, 1767, 1708, 1389, 1246, 1076, 847, 718.

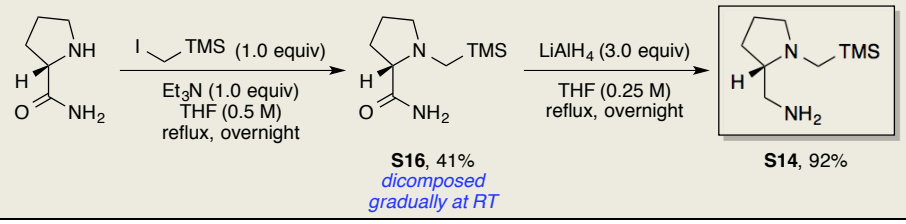
***trans*-N^1-Benzyl-N^1-((trimethylsilyl)methyl)cyclohexane-1,2-diamine (13)**



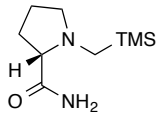
Hydrazine monohydrate (5.85 mL, 120.00 mmol, 10.00 equiv) was added to a solution of **S15** (5.05 g, 12.00 mmol, 1.00 equiv) in EtOH (120 mL, 0.10 M). The mixture was heated under reflux for 1 h and the white solids precipitated during the reaction. The reaction was cooled to room temperature and sufficient amount of 5% $NaOH_{(aq)}$ was added to dissolved the white precipitates. EtOH was removed under *vacuo* and the remained aqueous layer was extracted by CH_2Cl_2 (3×50 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product (3.25 g, 93%) as a colorless oil without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.30 (d, *J* = 4.4 Hz, 4 H), 7.25–7.20 (m, 1 H), 3.83 (d, *J* = 13.6 Hz, 1 H), 3.27 (d, *J* = 13.6 Hz, 1 H), 2.60 (ddd, *J* = 10.4, 10.4, 4.2 Hz, 1 H), 2.12–2.04 (m, 1 H), 2.07 (d, *J* = 14.6 Hz, 1 H), 1.93 (d, *J* = 14.6 Hz, 1 H), 1.99–1.84 (m, 4 H), 1.81–1.76 (m, 1 H), 1.65–1.60 (m, 1 H), 1.25–1.07 (m, 3 H), 1.04–0.93 (m, 1 H), 0.06 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 140.6, 128.8, 128.4, 126.8, 67.0, 56.9, 51.6, 41.1, 35.2, 25.8, 25.3, 21.0, –1.1; **HRMS** (ESI): calculated for $[C_{17}H_{31}N_2Si]^+$: m/z = 291.2251, found: m/z = 291.2250; **IR** (ν/cm^{-1}, neat): 3359, 2928, 2856, 1585, 1450, 1364, 1248, 1070, 839, 740. 689.

2.7 Synthesis of SLAP reagent 14



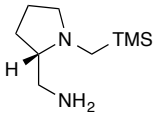
(*S*)-1-((Trimethylsilyl)methyl)pyrrolidine-2-carboxamide (S16)



(*S*)-Pyrrolidine-2-carboxamide (2.28 g, 20.00 mmol, 1.00 equiv), (iodomethyl)trimethylsilane (2.97 mL, 20.00 mmol, 1.00 equiv), and Et_3N (2.78 mL, 20.00 mmol, 1.00 equiv) were mixed in anhydrous THF (40 mL, 0.50 M) and heated to reflux under N_2 overnight. The reaction was cooled to room temperature and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product[11] (1.65 g, 41%) as a colorless oil.

$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = –112.7; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.08 (br, 1 H), 6.52 (br, 1 H), 3.13–3.08 (m, 1 H), 2.83 (dd, *J* = 10.1, 5.2 Hz, 1 H), 2.25–2.18 (m, 1 H), 2.24 (d, *J* = 14.2 Hz, 1 H), 2.19–2.08 (m, 1 H), 1.84 (d, *J* = 14.2 Hz, 1 H), 1.81–1.71 (m, 3 H), 0.02 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 178.8, 72.3, 56.6, 47.3, 30.4, 24.8, –1.6; **HRMS** (ESI): calculated for $[C_9H_{21}N_2OSi]^+$: m/z = 201.1418, found: m/z = 201.1418; **IR** (ν/cm^{-1}, neat): 3430, 3258, 2954, 2790, 1682, 1574, 1249, 1107, 853, 763, 693.

(*S*)-(1-((Trimethylsilyl)methyl)pyrrolidin-2-yl)methanamine (14)

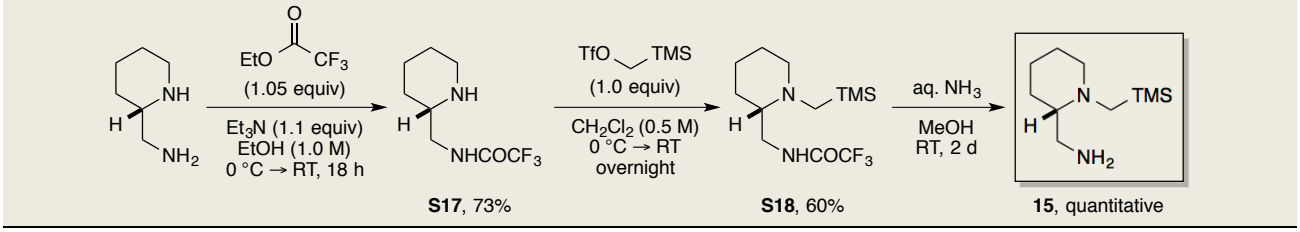


To an ice-cooled solution of **S16** (1.50 g, 7.50 mmol, 1.00 equiv) in anhydrous THF (30 mL, 0.25 M), $LiAlH_4$ (0.85 g, 22.50 mmol, 3.00 equiv) was added slowly and portionwise (CAUTION![7]). After the addition was complete, the mixture was heated under reflux overnight. The reaction was cooled to room temperature and quenched with 20% $NaOH_{(aq)}$ before being filtered and washed with EtOAc. The combined filtrate was condensed under *vacuo*, and the desired product was obtained as colorless oil without further purification (1.28 g, 92%).

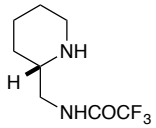
$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = –83.3; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 3.05 (ddd, *J* = 8.9, 4.4, 4.4 Hz, 1 H), 2.69 (dd, *J* = 13.0, 5.1 Hz, 1 H), 2.59 (dd, *J* = 13.0, 2.7 Hz, 1 H), 2.24 (d, *J* = 14.2 Hz, 1 H), 2.14 (dddd, *J* = 7.4, 5.1, 4.9, 2.7 Hz, 1 H), 2.07 (ddd, *J* = 8.9, 8.6, 8.6 Hz, 1H), 1.79–1.72 (m, 1 H), 1.69–1.53 (m, 3 H), 1.54 (d, *J* = 14.2 Hz, 1 H), 1.25 (br, 2 H), 0.01 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 69.8, 57.3, 45.4, 43.4, 27.2, 23.3, –1.3; **HRMS** (ESI): calculated for $[C_9H_{23}N_2Si]^+$: m/z = 187.1625, found: m/z = 187.1627; **IR** (ν/cm^{-1}, neat): 3369, 2953, 2777, 1582, 1461, 1418, 1248, 1113, 850, 762, 692.

(11) The product was found to decompose gradually at room temperature over a few weeks.

2.8 Synthesis of SLAP reagent 15



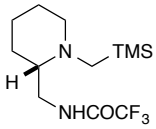
2,2,2-Trifluoro-*N*-(piperidin-2-ylmethyl)acetamide (S17)



The procedure was modified from the literature.[12] To an ice-cooled solution of piperidin-2-ylmethanamine (3.64 mL, 30.00 mmol, 1.00 equiv) and Et_3N (4.59 mL, 33.00 mmol, 1.10 equiv) in EtOH (30 mL, 1.00 M), ethyl 2,2,2-trifluoroacetate (3.75 mL, 31.50 mmol, 1.05 equiv) was added dropwise under N_2. The reaction was allowed to warm to room temperature and stirred for 18 h. After the solvents were removed under *vacuo*, the residue was further recrystallized with Et_2O/hexanes to afford the desired product (4.63 g, 73%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.19 (br, 1 H), 3.40 (dd, *J* = 13.7, 4.2 Hz, 1 H), 3.16 (dd, *J* = 13.7, 7.5 Hz, 1 H), 3.07 (dddd, *J* = 12.4, 4.1, 2.1, 2.1 Hz, 1 H), 2.75 (dddd, *J* = 10.9, 7.5, 4.2, 2.8 Hz, 1 H), 2.65–2.59 (m, 1 H), 1.87–1.80 (m, 1 H), 1.83 (br, 1 H), 1.68–1.58 (m, 2 H), 1.47–1.29 (m, 2 H), 1.20–1.10 (m, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 157.6 (q, *J* = 36.8 Hz), 116.0 (q, *J* = 287.7 Hz), 55.0, 46.5, 45.0, 30.3, 26.5, 24.1; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –75.8.

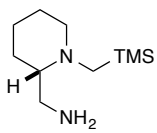
2,2,2-Trifluoro-*N*-((1-((trimethylsilyl)methyl)piperidin-2-yl)methyl)acetamide (S18)



The procedure was modified from the literature.[4] To an ice-cooled solution of **S17** (3.15 g, 15.00 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (30 mL, 0.50 M) under N_2 was slowly added (trimethylsilyl)methyl trifluoromethanesulfonate[5] (3.05 mL, 15.00 mmol, 1.00 equiv). The reaction was allowed to warm to room temperature and stirred overnight. After quenched by 5% $NaOH_{(aq)}$ (20 mL), the mixture was extracted by CH_2Cl_2 (3×30 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired product (2.66 g, 60%) as a yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.19 (br, 1 H), 3.48 (dd, *J* = 13.9, 4.8 Hz, 1 H), 3.29 (dd, *J* = 13.9, 3.2 Hz, 1 H), 2.95 (ddd, *J* = 12.0, 3.8, 3.8 Hz, 1 H), 2.30–2.25 (m, 1 H), 2.21 (d, *J* = 14.3 Hz, 1 H), 2.10 (ddd, *J* = 12.0, 10.8, 2.7 Hz, 1 H), 1.72–1.67 (m, 1 H), 1.63 (d, *J* = 14.3 Hz, 1 H), 1.62–1.57 (m, 2 H), 1.47–1.27 (m, 3 H), 0.05 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 157.6 (q, *J* = 37.1 Hz), 116.1 (q, *J* = 287.8 Hz), 60.9, 54.8, 44.7, 41.6, 28.5, 24.7, 23.6, –1.2; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –75.9; **HRMS** (ESI): calculated for $[C_{12}H_{24}F_3N_2OSi]^+$: m/z = 297.1605, found: m/z = 297.1607; **IR** (ν/cm^{-1}, neat): 3341, 2939, 2859, 2788, 1727, 1525, 1250, 1165, 1065, 861, 702.

(1-((Trimethylsilyl)methyl)piperidin-2-yl)methanamine (15)



To a solution of **S18** (2.4 g, 8.1 mmol, 1.0 equiv) in MeOH (20 mL, 0.4 M), *ca.* 25% $NH_{3(aq)}$ (20 mL, 131.3 mmol, 16.2 equiv) was added. The mixture was stirred at room temperature for 2 days before the solvents were removed under *vacuo*. The residue was extracted with CH_2Cl_2 and sat. $NaHCO_{3(aq)}$. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product (1.6 g, quantitative) as a colorless oil without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 2.93–2.88 (m, 2 H), 2.61 (dd, *J* = 13.3, 3.4 Hz, 1 H), 2.32 (d, *J* = 14.4 Hz, 1 H), 2.09 (ddd, *J* = 12.1, 11.4, 3.3 Hz, 1 H), 2.09 (ddd, *J* = 11.7, 11.4, 3.1 Hz, 1 H), 2.02–1.96 (m,

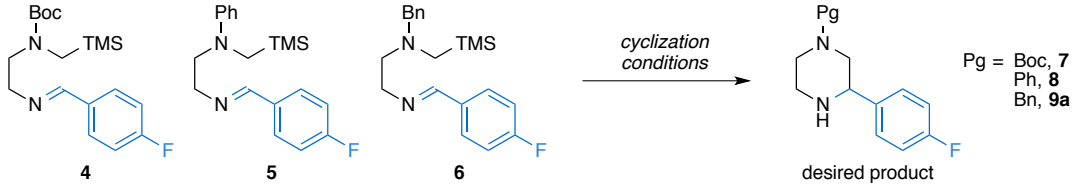
(12) Fujita, M.; Chiba, K.; Tominaga, Y.; Hino, *Chem. Pharm. Bull.* **1998**, *46*, 787–796.

3 H), 1.70–1.64 (m, 1 H), 1.62 (d, J = 14.4 Hz, 1 H), 1.56–1.43 (m, 4 H), 1.32–1.21 (m, 1 H), 0.03 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 65.6, 55.7, 44.7, 43.6, 28.0, 25.1, 24.0, –0.9; **HRMS** (ESI): calculated for $[C_{10}H_{25}N_2Si]^+$: m/z = 201.1782, found: m/z = 201.1783; **IR** (ν/cm^{-1}, neat): 3369, 2933, 2857, 2778, 1683, 1582, 1462, 1248, 1201, 1130, 838, 692.

3. Photocatalytic synthesis of piperazines with SLAP reagents

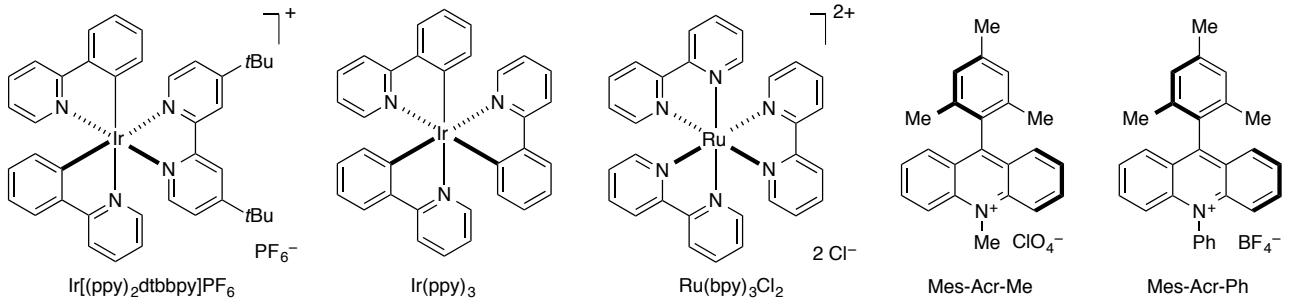
3.1 Optimized conditions for cyclization

Table S1. Screening of cyclization conditions

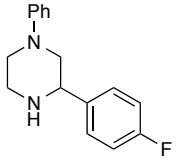


entry	imine[a]	condition	result
1	**4**	$Cu(OTf)_2$ (1.0 equiv), 2,6-lutidine (1.0 equiv), 1,2-dichloroethane/HFIP (1:1, 0.10 M), RT, 16 h	imine recovered
2	**4**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN (0.05 M), blue light, RT, 16 h	imine recovered
3	**5**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN (0.05 M), blue light, RT, 3 h	**8**, 73%[b]
4	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN (0.05 M), blue light, RT, 3 h	**9a**, N.D.[b] (59%[c])
5	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN/MeOH (9:1, 0.05 M), blue light, RT, 3 h	**9a**, 62%[b] (67%[c])
6	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN/HFIP (9:1, 0.05 M), blue light, RT, 3 h	**9a**, 67%[b] (71%[c])
7	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN/TFE (9:1, 0.05 M), blue light, RT, 3 h	**9a**, 70%[b]
8	**6**	No catalyst, MeCN (0.05 M), blue light, RT, 3 h	imine recovered
9	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeCN (0.05 M), dark, RT, 3 h	imine recovered
10	**6**	$Ir(ppy)_3$ (1 mol %), MeCN (0.05 M), blue light, RT, 3 h	imine recovered + unidentified products
11	**6**	$Ru(bpy)_3Cl_2 \cdot 6H_2O$ (1 mol %), MeCN (0.05 M), blue light, RT, 3 h	fully desilylated unidentified products
12	**6**	Mes-Acr-Me (5 mol %), MeCN (0.05 M), blue light, RT, 3 h	imine recovered
13	**6**	Mes-Acr-Ph (5 mol %), MeCN (0.05 M), blue light, RT, 3 h	imine recovered
14	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), MeOH (0.05 M), blue light, RT, 3 h	**9a**, N.D.[b] (55%[c])
15	**6**	$Ir[(ppy)_2dtbbpy]PF_6$ (1 mol %), HFIP (0.05 M), blue light, RT, 3 h	imine recovered + trace of hydrolysis

[a]Imine formation was performed with *p*-fluorobenzaldehyde and MS 4A in MeCN. [b]Isolated yield under 0.5 mmol scale. [c]Calculated yield from crude ^1H NMR spectrum under 0.1 mmol scale with 1,3,5-trimethoxybenzene as an internal standard. N.D. = not determined.



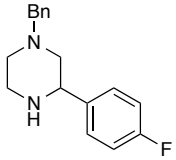
3-(4-Fluorophenyl)-1-phenylpiperazine (8) (Table 1, entry 3)



A mixture of the **2** (112.2 mg, 0.5 mmol, 1.0 equiv) and 4-fluorobenzaldehyde (53.6 µL, 0.5 mmol, 1.0 equiv), and MS 4A (100.0 mg) in MeCN (1.0 mL, 0.5 M) under N_2 was stirred overnight at room temperature. The reaction was filtered through Celite and washed with CH_2Cl_2. The filtrate was condensed under *vacuo* and the residue was re-dissolved in MeCN (10 mL, 0.05 M) in a vial (20 mL), followed by the addition of $Ir[(ppy)_2dtbbpy]PF_6$[13] (4.6 mg, 5.0 µmol, 0.01 equiv). The reaction was stirred at room temperature under the exposure of blue LEDs with a cooling fan to maintain the temperature. H_2O (0.1 mL) was added and the reaction was stirred for another 5 min. After the solvents were removed under *vacuo*, the residue was dissolved in CH_2Cl_2, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) to afford the desired product (93.9 mg, 73%) as a yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.47 (ddd, *J* = 8.5, 5.3, 2.6 Hz, 2 H), 7.33–7.28 (m, 2 H), 7.11–7.07 (m, 2 H), 7.00–6.97 (m, 2 H), 6.91 (tt, *J* = 7.2, 1.0 Hz, 1 H), 4.01 (dd, *J* = 10.4, 2.9 Hz, 1 H), 3.67–3.62 (m, 2 H), 3.27 (ddd, *J* = 11.4, 3.5, 2.2 Hz, 1 H), 3.19 (td, *J* = 11.4, 3.0 Hz, 1 H), 2.94 (td, *J* = 11.4, 3.5 Hz, 1H), 2.74 (dd, *J* = 11.8, 10.4 Hz, 1 H), 2.41 (br, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 162.3 (d, *J* = 245.8 Hz), 151.3, 137.8 (d, *J* = 3.1 Hz), 129.2, 128.8 (d, *J* = 7.9 Hz), 119.9, 116.3, 115.4 (d, *J* = 21.2 Hz), 59.8, 57.1 (d, *J* = 1.4 Hz), 49.4, 46.2; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –114.6; **HRMS** (ESI): calculated for $[C_{16}H_{18}FN_2]^+$: m/z = 257.1449, found: m/z = 257.1448; **IR** (ν/cm^{-1}, neat): 3037, 2947, 2821, 1671, 1600, 1508, 1449, 1333, 1234, 1141, 964, 837, 759, 693.

1-Benzyl-3-(4-fluorophenyl)piperazine (9a) (Table 1, entry 5–7)



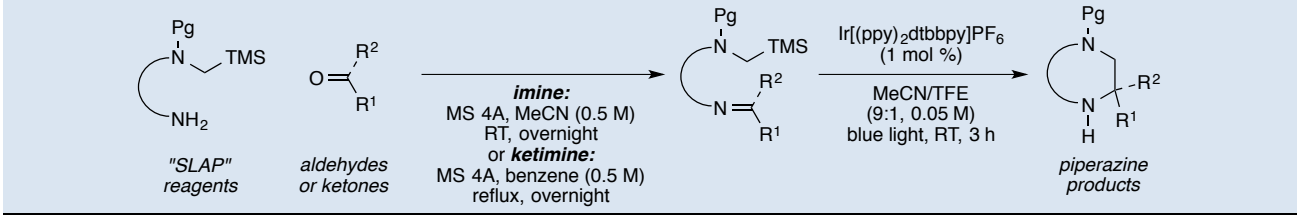
A mixture of the **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and 4-fluorobenzaldehyde (53.6 µL, 0.5 mmol, 1.0 equiv), and MS 4A (100.0 mg) in MeCN (1.0 mL, 0.5 M) under N_2 was stirred overnight at room temperature. The reaction was filtered through Celite and washed with CH_2Cl_2. The filtrate was condensed under *vacuo* and the residue was re-dissolved in MeCN/MeOH (9:1, 10 mL, 0.05 M) in a vial (20 mL), followed by the addition of $Ir[(ppy)_2dtbbpy]PF_6$[13] (4.6 mg, 5.0 µmol, 0.01 equiv). The reaction was stirred at room temperature under the exposure of blue LEDs with a cooling fan to maintain the temperature. H_2O (0.1 mL) was added and the reaction was stirred for another 5 min. After the solvents were removed under *vacuo*, the residue was dissolved in CH_2Cl_2, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) to afford the desired product (83.7 mg, 62%) as a yellowish oil. (Entry 5)

- The photocatalytic reaction was conducted under MeCN/HFIP (9:1, 10 mL, 0.05 M) for 3 h at room temperature. The desired product was obtained by flash column chromatography (90.7 mg, 67%). (Entry 6)
- The photocatalytic reaction was conducted under MeCN/TFE (9:1, 10 mL, 0.05 M) for 3 h at room temperature. The desired product was obtained by flash column chromatography (94.2 mg, 70%). (Entry 7)

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.39–7.33 (m, 6 H), 7.30–7.27 (m, 1 H), 7.04–6.99 (m, 2 H), 3.90 (dd, *J* = 10.2, 2.8 Hz, 1 H), 3.57 (s, 2 H), 3.12–3.04 (m, 2 H), 2.93–2.84 (m, 2 H), 2.22 (ddd, *J* = 11.0, 9.7, 4.8 Hz, 1 H), 2.21 (br, 1 H), 2.07 (t, *J* = 10.2 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 162.1 (d, *J* = 245.2 Hz), 138.5 (d, *J* = 3.1 Hz), 138.0, 129.3, 128.6 (d, *J* = 7.9 Hz), 128.3, 127.1, 115.2 (d, *J* = 21.1 Hz), 63.3, 61.4 (d, *J* = 1.2 Hz), 59.7, 53.2, 46.2; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –115.2; **HRMS** (ESI): calculated for $[C_{17}H_{20}FN_2]^+$: m/z = 271.1605, found: m/z = 271.1608; **IR** (ν/cm^{-1}, neat): 3262, 2939, 2806, 1604, 1509, 1453, 1318, 1223, 1133, 1026, 836, 699.

(13) (a) The iridium photocatalyst can be purchased from Sigma-Aldrich or prepared according to the literature: Ladouceur, S.; Fortin, D.; Zysman-Colman, E. *Inorg. Chem.* **2011**, *50*, 11514–11526; (b) Abbreviations: dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine; ppy = 2-phenylpyridine.

3.2 General procedure



** Protecting groups (Pg) can be alkyl or aryl substituents.*

General condition for imine formation:

A mixture of a SLAP reagent (0.5 mmol), an aldehyde (0.5 mmol), and MS 4A (100.0 mg) in MeCN (1.0 mL, 0.5 M) under N_2 was stirred at room temperature overnight.[14] The reaction was filtered through Celite and washed with CH_2Cl_2. The filtrate was condensed under *vacuo* and used directly for cyclization.

General condition for ketimine formation:

A mixture of a SLAP reagent (0.5 mmol), a ketone (0.5 mmol), and MS 4A (100.0 mg) in benzene (1.0 mL, 0.5 M) under N_2 was stirred at reflux overnight. The reaction was filtered through Celite and washed with CH_2Cl_2. The filtrate was condensed under *vacuo* and used directly for cyclization.

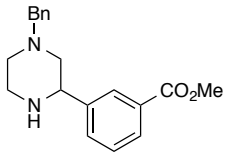
General condition for photocatalytic cyclization:

The reaction was carried out in a closed vial (20 mL) with no need to be degased beforehand or under dry conditions. To a solution of the corresponding imine or ketimine (0.5 mmol, 1.00 equiv) in MeCN/TFE (9:1, 10.0 mL, 0.05 M), $Ir[(ppy)_2dtbbpy]PF_6$[13] (4.6 mg, 5.0 μmol, 0.01 equiv) was added. The reaction was stirred at room temperature under the exposure of blue LEDs (30 W) with a cooling fan to maintain the temperature. H_2O (0.1 mL) was added and the reaction was stirred for another 5 min. After the solvents were removed under *vacuo*, the residue was dissolved in CH_2Cl_2, dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography to afford the desired piperazine product.

(14) If necessary, reaction time for imine formation can be shortened to 2–4 h.

3.3 Substrate scope

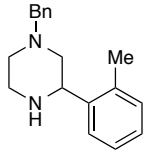
Methyl 3-(4-benzylpiperazin-2-yl)benzoate (9b) (Scheme 2)



The photocatalytic synthesis of **9b** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and methyl 3-formylbenzoate (82.1 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a yellowish oil (102.1 mg, 66%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 8.08 (t, *J* = 1.6 Hz, 1 H), 7.95 (dt, *J* = 7.8, 1.6 Hz, 1 H), 7.61 (dt, *J* = 7.7, 1.6 Hz, 1 H), 7.39 (apparent t, *J* = 7.8 Hz, 1 H), 7.36–7.24 (m, 5 H), 3.97 (dd, *J* = 10.2, 2.9 Hz, 1 H), 3.91 (s, 3 H), 3.56 (s, 2 H), 3.13–3.03 (m, 2 H), 2.93–2.84 (m, 2 H), 2.69 (br, 1 H), 2.25 (td, *J* = 10.7, 4.2 Hz, 1 H), 2.12 (dd, *J* = 11.0, 10.2 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 167.0, 142.7, 137.8, 131.8, 130.3, 129.2, 128.8, 128.5, 128.30, 128.27, 127.2, 77.2, 63.3, 60.9, 60.0, 53.0, 52.1, 46.0; **HRMS** (ESI): calculated for $[C_{19}H_{23}N_2O_2]^+$: m/z = 311.1754, found: m/z = 311.1755; **IR** (ν/cm^{-1}, neat): 3327, 3028, 2948, 2807, 1715, 1673, 1435, 1287, 1204, 1105, 1027, 1001, 818, 737.

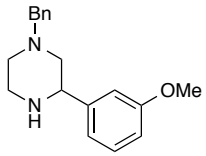
1-Benzyl-3-(*o*-tolyl)piperazine (9c) (Scheme 2)



The photocatalytic synthesis of **9c** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and 2-methylbenzaldehyde (57.8 μL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a yellowish oil (73.6 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.56 (d, *J* = 7.6 Hz, 1 H), 7.37–7.31 (m, 4 H), 7.28–7.24 (m, 1 H), 7.22–7.12 (m, 3 H), 4.13 (dd, *J* = 10.0, 2.6 Hz, 1 H), 3.60 (d, *J* = 13.1 Hz, 1 H), 3.55 (d, *J* = 13.1 Hz, 1 H), 3.13 –3.10 (m, 2 H), 2.91–2.86 (m, 2 H), 2.48 (br, 1 H), 2.35 (s, 3 H), 2.26 (ddd, *J* = 11.2, 9.2, 5.4 Hz, 1 H), 2.03 (dd, *J* = 11.2, 10.0 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 140.3, 138.0, 135.4, 130.4, 129.3, 128.3, 127.12, 127.11, 126.3, 126.2, 63.3, 59.9, 56.4, 53.3, 46.4, 19.3; **HRMS** (ESI): calculated for $[C_{18}H_{23}N_2]^+$: m/z = 267.1856, found: m/z = 267.1858; **IR** (ν/cm^{-1}, neat): 3322, 3026, 2938, 2804, 1493, 1453, 1316, 1133, 1101, 1025, 756, 699.

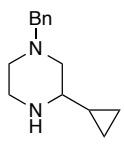
1-Benzyl-3-(3-methoxyphenyl)piperazine (9d) (Scheme 2)



The photocatalytic synthesis of **9d** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and 3-methoxybenzaldehyde (60.8 μL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a yellowish oil (98.9 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.38–7.32 (m, 4 H), 7.30–7.23 (m, 2 H), 7.01–6.98 (m, 2 H), 6.83 (ddd, *J* = 8.2, 2.5, 1.2 Hz, 1 H), 3.92 (dd, *J* = 10.5, 2.8 Hz, 1 H), 3.82 (s, 3 H), 3.58 (s, 2 H), 3.13–3.04 (m, 2 H), 2.95 (ddd, *J* = 11.0, 2.8, 1.7 Hz, 1 H), 2.87 (ddd, *J* = 10.7, 2.3, 2.3 Hz, 1 H), 2.55 (br, 1 H), 2.24 (ddd, *J* = 10.7, 10.7, 4.2 Hz, 1 H), 2.13 (dd, *J* = 10.5, 10.5 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 159.7, 144.1, 138.0, 129.4, 129.3, 128.3, 127.1, 119.5, 113.1, 112.5, 63.3, 61.1, 60.4, 55.3, 53.1, 46.2; **HRMS** (ESI): calculated for $[C_{18}H_{23}N_2O]^+$: m/z = 283.1805, found: m/z = 283.1803; **IR** (ν/cm^{-1}, neat): 3324, 2939, 2806, 1673, 1585, 1454, 1317, 1250, 1131, 1048, 910, 740, 699.

1-Benzyl-3-cyclopropylpiperazine (9e) (Scheme 2)

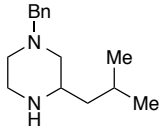


The photocatalytic synthesis of **9e** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and cyclopropanecarboxaldehyde (37.4 μL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (49.9 mg, 46%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 8.13 (br, 1 H), 7.35–7.25 (m, 5 H), 3.61 (d, *J* = 13.1 Hz, 1 H), 3.54 (d, *J* = 13.1 Hz, 1 H), 3.35 (ddd, *J* = 12.4, 2.9, 2.9 Hz, 1 H), 3.06–2.99 (m, 2 H), 2.83 (dd, *J* = 12.4, 1.9 Hz, 1 H), 2.60 (ddd, *J* = 11.9, 11.8, 2.9 Hz, 1 H), 2.53 (dd, *J* = 12.1, 10.0 Hz, 1 H), 2.38 (ddd, *J* = 10.0, 9.7, 3.1 Hz,

1 H), 1.19 (apparent dddd, *J* = 12.9, 9.7, 8.1, 4.8 Hz, 1 H), 0.76 (dddd, *J* = 9.6, 5.1, 5.1, 4.9 Hz, 1 H), 0.69–0.56 (m, 2 H), 0.28 (dddd, *J* = 10.2, 4.9, 4.7, 4.7 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 137.3, 129.0, 128.5, 127.5, 62.4, 61.0, 55.7, 49.4, 43.9, 11.8, 4.1, 3.9; **HRMS** (ESI): calculated for $[C_{14}H_{21}N_2]^+$: m/z = 217.1699, found: m/z = 217.1699; **IR** (ν/cm^{-1}, neat): 3399, 2927, 2810, 2714, 2482, 1590, 1453, 1314, 1055, 1015, 741, 700.

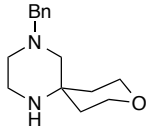
1-Benzyl-3-isobutylpiperazine (9f) (Scheme 2)



The photocatalytic synthesis of **9f** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and 3-methylbutanal (54.1 µL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (36.0 mg, 37%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.30–7.27 (m, 4 H), 7.25–7.21 (m, 1 H), 4.43 (br, 1 H), 3.49 (apparent q, *J* = 13.0 Hz, 2 H), 3.03 (apparent dt, *J* = 12.1, 2.9 Hz, 1 H), 2.94– 2.87 (m, 2 H), 2.81–2.73 (m, 2 H), 2.15 (apparent td, *J* = 11.3, 3.2 Hz, 1 H), 1.85 (dd, *J* = 11.3, 9.9 Hz, 1 H), 1.66 (apparent dh, *J* = 7.8, 6.6 Hz, 1 H), 1.36 (apparent dt, *J* = 14.0, 7.1 Hz, 1 H), 1.23 (ddd, *J* = 14.0, 7.8, 6.3 Hz, 1 H), 0.88 (d, *J* = 2.6 Hz, 3 H), 0.86 (d, *J* = 2.6 Hz, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 137.9, 129.2, 128.3, 127.2, 63.3, 59.2, 53.2, 52.8, 45.3, 42.7, 24.3, 23.0, 22.6; **HRMS** (ESI): calculated for $[C_{15}H_{25}N_2]^+$: m/z = 233.2012, found: m/z = 233.2018; **IR** (ν/cm^{-1}, neat): 3398, 2957, 2822, 2718, 2482, 1590, 1454, 1368, 1318, 1140, 922, 736, 700.

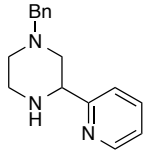
4-Benzyl-9-oxa-1,4-diazaspiro[5.5]undecane (9g) (Scheme 2)



The photocatalytic synthesis of **9g** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and dihydro-2*H*-pyran-4(3*H*)-one (46.2 µL, 0.5 mmol, 1.0 equiv). The photocatalytic cyclization was carried out in MeCN/MeOH (9:1, 10.0 mL, 0.05 M). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (41.1 mg, 33%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.35–7.26 (m, 5 H), 6.47 (br, 1 H), 3.83 (dt, *J* = 12.0, 4.9 Hz, 2 H), 3.53 (s, 2 H), 3.41 (dt, *J* = 12.0, 6.0 Hz, 2 H), 3.11 (apparent t, *J* = 5.2 Hz, 2 H), 2.65 (dd, *J* = 6.8, 3.8 Hz, 2 H), 2.50 (apparent br, 2 H), 1.93 (apparent t, *J* = 5.5 Hz, 4 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 137.9, 128.8, 128.5, 127.4, 63.3, 62.6, 58.9, 52.7, 52.5, 39.9, 33.6; **HRMS** (ESI): calculated for $[C_{15}H_{23}N_2O]^+$: m/z = 247.1805, found: m/z = 247.1805; **IR** (ν/cm^{-1}, neat): 3397, 2947, 2851, 2809, 2488, 1587, 1454, 1363, 1239, 1152, 1107, 1029, 912, 850, 736, 700.

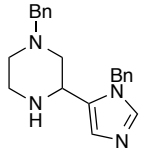
1-Benzyl-3-(pyridin-2-yl)piperazine (9h) (Scheme 2)



The photocatalytic synthesis of **9h** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and pyridine-2-carbaldehyde (47.8 µL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (81.5 mg, 64%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 8.51 (ddd, *J* = 4.9, 1.3, 1.2 Hz, 1 H), 7.60 (ddd, *J* = 7.7, 7.5, 1.8 Hz, 1 H), 7.34–7.20 (m, 6 H), 7.13 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1 H), 4.50 (br, 1 H), 4.09 (dd, *J* = 10.1, 3.0 Hz, 1 H), 3.54 (s, 2 H), 3.14 (ddd, *J* = 12.3, 2.9, 2.9 Hz, 1 H), 3.09–3.02 (m, 2 H), 2.84–2.79 (m, 1 H), 2.28–2.20 (m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 159.6, 149.2, 137.7, 136.7, 129.2, 128.3, 127.2, 122.6, 121.7, 63.2, 60.3, 58.8, 52.8, 45.2; **HRMS** (ESI): calculated for $[C_{16}H_{20}N_3]^+$: m/z = 254.1652, found: m/z = 254.1654; **IR** (ν/cm^{-1}, neat): 3390, 2938, 2810, 2713, 2472, 1592, 1435, 1317, 1149, 1106, 912, 777, 743, 700.

1-Benzyl-3-(1-benzyl-1*H*-imidazol-5-yl)piperazine (9i) (Scheme 2)

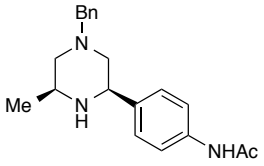


The photocatalytic synthesis of **9i** followed the general procedure with **3** (118.2 mg, 0.5 mmol, 1.0 equiv) and 1-benzyl-1*H*-imidazole-5-carbaldehyde (93.1 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in

CH_2Cl_2) as a yellowish solid (125.0 mg, 75%).

m.p.: 112–113 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.45 (d, *J* = 1.0 Hz, 1 H), 7.35–7.23 (m, 8 H), 7.08–7.06 (m, 2 H), 7.01 (apparent br, 1 H), 5.30 (d, *J* = 15.7 Hz, 1 H), 5.15 (d, *J* = 15.7 Hz, 1 H), 3.80 (ddd, *J* = 10.0, 2.8, 0.7 Hz, 1 H), 3.49 (s, 2 H), 2.94 (dt, *J* = 12.6, 3.0 Hz, 1 H), 2.88–2.81 (m, 2 H), 2.72 (apparent dq, *J* = 11.0, 2.5 Hz, 1 H), 2.31 (br , 1 H), 2.18 (dd, *J* = 10.0, 10.0 Hz, 1 H), 2.08 (apparent td, *J* = 11.0, 3.3 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 138.2, 137.6, 136.7, 132.2, 129.2, 129.0, 128.3, 128.0, 127.1, 126.9, 126.8, 63.3, 58.4, 53.7, 50.6, 48.7, 45.5; **HRMS** (ESI): calculated for $[C_{21}H_{25}N_4]^+$: m/z = 333.2074, found: m/z = 333.2073; **IR** (ν/cm^{-1}, neat): 3303, 2811, 1668, 1496, 1454, 1342, 1316, 1267, 1225, 1111, 909, 814, 732.

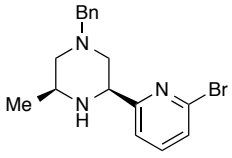
_N_-(4-((2_R_,6_S_)-4-Benzyl-6-methylpiperazin-2-yl)phenyl)acetamide (16a) (Scheme 3)



The photocatalytic synthesis of **16a** followed the general procedure with **10** (125.2 mg, 0.5 mmol, 1.0 equiv) and *N*-(4-formylphenyl)acetamide (81.6 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (149.7 mg, 93%, dr > 20:1). The relative stereochemistry was assigned by NOESY.

$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = +10.1; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 8.11 (s, 1 H), 7.46–7.43 (m, 2 H), 7.35–7.25 (m, 7 H), 3.94 (dd, *J* = 10.7, 2.8 Hz, 1 H), 3.58 (d, *J* = 13.1 Hz, 1 H), 3.53 (d, *J* = 13.1 Hz, 1 H), 3.10 (dqd, *J* = 10.6, 6.3, 2.8 Hz, 1 H), 2.88 (d, *J* = 10.9 Hz, 1 H), 2.82 (d, *J* = 10.8 Hz, 1 H), 2.62 (br, 1 H), 2.13 (s, 3 H), 2.04 (dd, *J* = 10.9, 10.7 Hz, 1 H), 1.82 (dd, *J* = 10.8, 10.6 Hz, 1 H), 1.10 (d, *J* = 6.3 Hz, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 168.9, 138.0, 137.9, 137.4, 129.3, 128.3, 127.7, 127.1, 120.2, 63.1, 60.4, 60.0, 60.0, 51.1, 24.4, 19.8; **HRMS** (ESI): calculated for $[C_{20}H_{26}N_3O]^+$: m/z = 324.2070, found: m/z = 324.2071; **IR** (ν/cm^{-1}, neat): 3298, 3261, 3060, 3030, 2962, 2932, 2810, 1667, 1604, 1541, 1517, 1317, 1130, 909, 836, 732, 700.

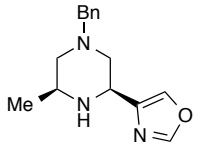
(3_S_,5_S_)-1-Benzyl-3-(6-bromopyridin-2-yl)-5-methylpiperazine (16b) (Scheme 3)



The photocatalytic synthesis of **16b** followed the general procedure with **10** (125.2 mg, 0.5 mmol, 1.0 equiv) and 5-bromopyridine-2-carbaldehyde (93.0 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (89.4 mg, 52%, dr > 20:1). The relative stereochemistry was determined by analogy to **16a**.

$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = +20.3; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.48 (t, *J* = 7.7 Hz, 1 H), 7.36–7.24 (m, 7 H), 4.07 (dd, *J* = 10.5, 3.0 Hz, 1 H), 3.58 (d, *J* = 13.1 Hz, 1 H), 3.54 (d, *J* = 13.1 Hz, 1 H), 3.12–3.04 (m, 2 H), 2.84 (dd, *J* = 10.8, 2.9 Hz, 1 H), 2.20 (br, 1 H), 2.02 (dd, *J* = 10.6, 10.5 Hz, 1 H), 1.75 (dd, *J* = 10.8, 10.7 Hz, 1 H), 1.11 (d, *J* = 6.4 Hz, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 162.5, 141.6, 138.9, 138.0, 129.2, 128.3, 127.1, 126.8, 120.2, 63.1, 60.5, 60.3, 58.7, 50.5, 19.9; **HRMS** (ESI): calculated for $[C_{17}H_{21}BrN_3]^+$: m/z = 346.0913, found: m/z = 346.0912; **IR** (ν/cm^{-1}, neat): 3287, 2960, 2805, 1581, 1555, 1435, 1407, 1315, 1119, 1061, 985, 791, 739, 699.

4-((2_S_,6_S_)-4-Benzyl-6-methylpiperazin-2-yl)oxazole (16c) (Scheme 3)

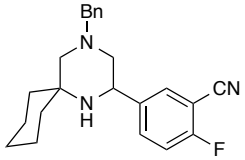


The photocatalytic synthesis of **16c** followed the general procedure with **10** (125.2 mg, 0.5 mmol, 1.0 equiv) and 1,3-oxazole-4-carboxaldehyde (48.5 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (87.6 mg, 68%, dr > 20:1). The relative stereochemistry was determined by analogy to **16a**.

$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = +7.0; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.82 (d, *J* = 1.0 Hz, 1 H), 7.55 (t, *J* = 1.0 Hz, 1 H), 7.36–7.24 (m, 5 H), 4.04 (dd, *J* = 10.6, 3.0 Hz, 1 H), 3.56 (s, 2 H), 3.12–3.04 (m, 2 H), 2.84 (dd, *J* = 10.9, 2.9 Hz, 1 H), 2.20 (br, 1 H), 2.08 (dd, *J* = 10.6, 10.5 Hz, 1 H), 1.77 (dd, *J* = 10.9, 10.1 Hz, 1 H), 1.08 (d, *J* = 6.4 Hz, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 151.0, 141.2, 137.9, 134.5, 129.2,

128.3, 127.2, 63.1, 60.5, 57.7, 52.5, 50.7, 19.8; **HRMS** (ESI): calculated for $[C_{15}H_{20}N_3O]^+$: m/z = 258.1601, found: m/z = 258.1603; **IR** (ν/cm^{-1}, neat): 3287, 2961, 2810, 1669, 1510, 1455, 1317, 1137, 1100, 1061, 914, 744, 700.

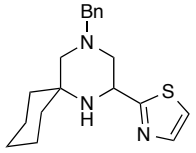
5-(4-Benzyl-1,4-diazaspiro[5.5]undecan-2-yl)-2-fluorobenzonitrile (17a) (Scheme 3)



The photocatalytic synthesis of **17a** followed the general procedure with **11** (152.3 mg, 0.5 mmol, 1.0 equiv) and 2-fluoro-5-formylbenzonitrile (74.6 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (1–10% EtOAc in hexanes) as a yellowish oil (94.1 mg, 52%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.76 (dd, *J* = 6.2, 2.3 Hz, 1 H), 7.67 (ddd, *J* = 8.8, 5.2, 2.3 Hz, 1 H), 7.39–7.33 (m, 4 H), 7.30–7.27 (m, 1 H), 7.16 (t, *J* = 8.7 Hz, 1 H), 4.22 (dd, *J* = 10.5, 3.2 Hz, 1 H), 3.57 (d, *J* = 13.4 Hz, 1 H), 3.45 (d, *J* = 13.4 Hz, 1 H), 2.87 (dd, *J* = 10.6, 3.2 Hz, 1 H), 2.79 (d, *J* = 11.0 Hz, 1 H), 1.90 (dd, *J* = 10.6, 10.5 Hz, 2 H), 1.89 (br, 1 H), 1.81 (d, *J* = 11.0 Hz, 1 H), 1.56 – 1.34 (m, 10 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 162.3 (d, *J* = 258.2 Hz), 140.6 (d, *J* = 3.5 Hz), 138.6, 134.1 (d, *J* = 8.2 Hz), 132.2, 128.7, 128.3, 127.1, 116.1 (d, *J* = 19.3 Hz), 114.2, 101.2 (d, *J* = 15.4 Hz), 62.9, 62.1, 62.0, 53.3, 52.0, 38.8, 32.1, 26.4, 22.0, 21.8; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –108.9; **HRMS** (ESI): calculated for $[C_{23}H_{27}FN_3]^+$: m/z = 364.2184, found: m/z = 364.2183; **IR** (ν/cm^{-1}, neat): 2926, 2854, 2801, 2235, 1611, 1497, 1454, 1266, 1110, 834, 739, 699.

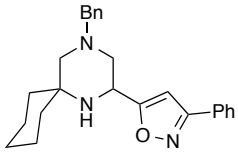
2-(4-Benzyl-1,4-diazaspiro[5.5]undecan-2-yl)thiazole (17b) (Scheme 3)



The photocatalytic synthesis of **17b** was followed by the general procedure with **11** (152.3 mg, 0.5 mmol, 1.0 equiv) and thiazole-2-carbaldehyde (43.9 μL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (5–30% EtOAc in hexanes) as a yellowish oil (61.4 mg, 37%).

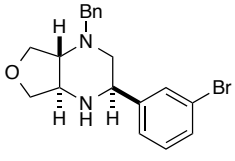
^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.73 (d, *J* = 3.3 Hz, 1 H), 7.38–7.31 (m, 4 H), 7.29–7.25 (m, 1 H), 7.26 (d, *J* = 3.3 Hz, 1 H), 4.62 (dd, *J* = 10.5, 3.4 Hz, 1 H), 3.62 (d, *J* = 13.4 Hz, 1 H), 3.46 (d, *J* = 13.4 Hz, 1 H), 3.24 (dd, *J* = 10.6, 3.4 Hz, 1 H), 2.80 (d, *J* = 11.0 Hz, 1 H), 2.09 (dd, *J* = 10.6, 10.5 Hz, 1H), 1.88 (apparent t, *J* = 6.0 Hz, 2 H), 1.81 (d, *J* = 11.0 Hz, 1 H), 1.58–1.48 (m, 2 H), 1.47–1.32 (m, 7 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 173.5, 142.3, 138.7, 128.8, 128.3, 127.1, 118.6, 62.9, 62.0, 60.9, 52.9, 52.3, 38.6, 32.2, 26.5, 22.0, 21.8; **HRMS** (ESI): calculated for $[C_{19}H_{26}N_3S]^+$: m/z = 328.1842, found: m/z = 328.1846; **IR** (ν/cm^{-1}, neat): 2926, 2854, 2800, 1673, 1453, 1327, 1129, 781, 736, 698.

5-(4-Benzyl-1,4-diazaspiro[5.5]undecan-2-yl)-3-phenylisoxazole (17c) (Scheme 3)



The photocatalytic synthesis of **17c** followed the general procedure with **11** (152.3 mg, 0.5 mmol, 1.0 equiv) and 3-phenylisoxazole-5-carbaldehyde (86.6 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (1–5% EtOAc in hexanes) as a yellowish oil (71.2 mg, 38%)

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.80–7.78 (m, 2 H), 7.45–7.42 (m, 3 H), 7.37–7.31 (m, 4 H), 7.29–7.25 (m, 1 H), 6.48 (s, 1 H), 4.47 (dd, *J* = 10.6, 2.6 Hz, 1 H), 3.60 (d, *J* = 13.3 Hz, 1 H), 3.46 (d, *J* = 13.3 Hz, 1 H), 3.15 (dd, *J* = 10.5, 2.6 Hz, 1 H), 2.79 (d, *J* = 11.1 Hz, 1 H), 2.15 (dd, *J* = 10.6, 10.5 Hz, 1 H), 1.90–1.81 (m, 2 H), 1.81 (d, *J* = 11.1 Hz, 1 H), 1.56–1.49 (m, 2 H), 1.45–1.33 (m, 7 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 174.1, 162.3, 138.5, 130.0, 129.2, 128.9, 128.8, 128.4, 127.2, 126.9, 98.7, 62.9, 62.0, 58.5, 52.1, 47.9, 38.5, 32.0, 26.4, 21.9, 21.8; **HRMS** (ESI): calculated for $[C_{25}H_{30}N_3O]^+$: m/z = 388.2383, found: m/z = 388.2383; **IR** (ν/cm^{-1}, neat): 3061, 3028, 2928, 2854, 2803, 1603, 1579, 1454, 1442, 1406, 1308, 1144, 910, 768, 735, 695.



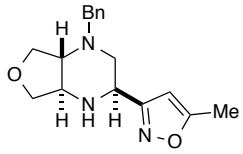
(*trans*,*cis*)-1-Benzyl-3-(3-bromophenyl)octahydrofuro[3,4-*b*]pyrazine (18a) (Scheme 3)

The photocatalytic synthesis of **18a** followed the general procedure with **12** (139.2 mg, 0.5 mmol, 1.0 equiv) and 3-bromobenzaldehyde (58.3 μL, 0.5 mmol, 1.0 equiv).

The desired product was obtained by flash column chromatography (10–50% EtOAc in hexanes) as a yellowish oil (120.6 mg, 65%, dr > 20:1). The relative stereochemistry was determined by analogy to **18b**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.59 (t, *J* = 2.0 Hz, 1 H), 7.41 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1 H), 7.34–7.26 (m, 6 H), 7.18 (t, *J* = 7.9 Hz, 1 H), 4.06–4.02 (m, 2 H), 4.01 (dd, *J* = 10.6, 3.1 Hz, 1 H), 3.71 (dd, *J* = 10.6, 7.2 Hz, 1 H), 3.65 (d, *J* = 13.1 Hz, 1 H), 3.59 (dd, *J* = 10.5, 7.0 Hz, 1 H), 3.36 (d, *J* = 13.1 Hz, 1 H), 3.27 (ddd, *J* = 10.6, 9.2, 7.2 Hz, 1 H), 2.92 (dd, *J* = 11.4, 3.1 Hz, 1 H), 2.51 (ddd, *J* = 10.5, 9.2, 7.0 Hz, 1 H), 2.05 (dd, *J* = 11.4, 10.6 Hz, 1 H), 2.04 (br, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 144.0, 137.5, 130.9, 130.4, 130.1, 129.2, 128.4, 127.5, 126.1, 122.6, 69.9, 69.8, 68.2, 62.0, 61.8, 61.0, 60.9; **HRMS** (ESI): calculated for $[C_{19}H_{22}BrN_2O]^+$: m/z = 373.0190, found: m/z = 373.0906; **IR** (ν/cm^{-1}, neat): 3299, 2938, 2868, 2820, 1676, 1568, 1453, 1324, 1034, 892, 785, 741, 698.

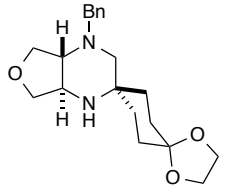
(*trans*,*cis*)-1-Benzyl-3-(5-methylisoxazol-3-yl)octahydrofuro[3,4-*b*]pyrazine (18b) (Scheme 3)



The photocatalytic synthesis of **18b** followed the general procedure with **12** (139.2 mg, 0.5 mmol, 1.0 equiv) and 5-methylisoxazole-3-carbaldehyde (55.6 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a yellowish oil (107.7 mg, 72%, dr > 20:1). The relative stereochemistry was assigned by NOESY.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.33–7.23 (m, 5 H), 5.96 (d, *J* = 1.0 Hz, 1 H), 4.19 (dd, *J* = 11.0, 3.2 Hz, 1 H), 4.02 (dd, *J* = 7.3, 7.3 Hz, 1 H), 3.99 (dd, *J* = 7.5, 6.7 Hz, 1 H), 3.64 (d, *J* = 13.2 Hz, 1 H), 3.62 (dd, *J* = 10.7, 7.3 Hz, 1 H), 3.55 (dd, *J* = 10.5, 7.5 Hz, 1 H), 3.35 (d, *J* = 13.2 Hz, 1 H), 3.23 (ddd, *J* = 10.7, 9.1, 7.3 Hz, 1 H), 3.05 (dd, *J* = 11.2, 3.2 Hz, 1 H), 2.43 (ddd, *J* = 10.5, 9.1, 6.7 Hz, 1H), 2.37 (d, *J* = 1.0 Hz, 3 H), 2.13 (dd, *J* = 11.2, 11.0 Hz, 1 H), 2.06 (br, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 169.5, 163.9, 137.3, 129.1, 128.3, 127.4, 100.0, 69.6, 69.4, 68.2, 61.7, 61.7, 57.9, 53.4, 12.2; **HRMS** (ESI): calculated for $[C_{17}H_{22}N_3O_2]^+$: m/z = 300.1707, found: m/z = 300.1706; **IR** (ν/cm^{-1}, neat): 3290, 2939, 2869, 1673, 1604, 1453, 1322, 1146, 1087, 1025, 893, 799, 745, 701.

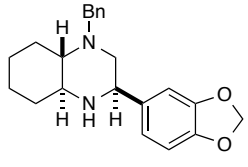
(*trans*)-4'-Benzylhexahydro-1'*H*-spiro[cyclohexane-1,2'-furo[3,4-*b*]pyrazin]-4-one ethylene ketal (18c) (Scheme 3)



The photocatalytic synthesis of **18c** followed the general procedure with **12** (139.2 mg, 0.5 mmol, 1.0 equiv) and 1,4-dioxaspiro[4.5]decan-8-one (78.1 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a white solid (72.0 mg, 42%).

m.p.: 135–136 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.32–7.21 (m, 5 H), 3.96 (dd, *J* = 7.1, 7.1 Hz, 1 H), 3.96 (dd, *J* = 7.0, 7.0 Hz, 1 H), 3.92–3.85 (m, 4 H), 3.59 (d, *J* = 13.3 Hz, 1 H), 3.55–3.48 (m, 2 H), 3.31 (ddd, *J* = 10.7, 9.4, 7.1 Hz, 1 H), 3.19 (d, *J* = 13.3 Hz, 1 H), 2.72 (d, *J* = 11.5 Hz, 1 H), 2.22 (ddd, *J* = 10.5, 9.4, 7.0 Hz, 1 H), 2.12–2.06 (m, 1 H), 1.80–1.67 (m, 3 H), 1.71 (d, *J* = 11.5 Hz, 1 H) , 1.58–1.41 (m, 5 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 138.2, 128.7, 128.3, 127.3, 109.0, 70.2, 69.8, 69.6, 64.3, 64.3, 63.0, 61.5, 56.8, 52.8, 35.7, 30.5, 30.4, 29.3; **HRMS** (ESI): calculated for $[C_{20}H_{29}N_2O_3]^+$: m/z = 345.2173, found: m/z = 345.2175; **IR** (ν/cm^{-1}, neat): 2945, 2872, 1736, 1675, 1453, 1370, 1094, 1033, 938 888, 740, 700.

(*trans*,*cis*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-1-benzyldecahydroquinoxaline (19a) (Scheme 3)

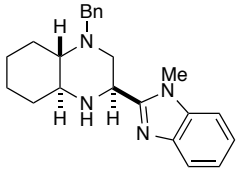


The photocatalytic synthesis of **19a** followed the general procedure with **13** (145.3 mg, 0.5 mmol, 1.0 equiv) and benzo[*d*][1,3]dioxole-5-carbaldehyde (75.1 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (10–50% EtOAc in hexanes) as a yellowish oil (150.3 mg, 86%, dr > 20:1). The relative stereochemistry was assigned by NOESY.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.31 (d, *J* = 4.4 Hz, 4 H), 7.29–7.21 (m, 1 H), 6.89 (d, *J* = 1.6 Hz, 1 H), 6.80 (dd, *J* = 8.0, 1.6 Hz, 1 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 5.91 (s, 2 H), 4.15 (d, *J* = 13.6 Hz, 1 H), 3.88 (dd, *J* = 10.9, 2.8 Hz, 1 H), 3.25 (d, *J* = 13.6 Hz, 1 H), 2.83 (dd, *J* = 10.9, 2.8 Hz, 1 H), 2.67 (ddd, *J* = 10.6,

8.7, 3.9 Hz, 1 H), 2.33–2.29 (m, 1 H), 2.12 (dd, *J* = 10.9, 10.9 Hz, 1 H), 1.99 (ddd, *J* = 10.6, 8.6, 3.6 Hz, 1H), 1.88–1.84 (m, 1 H), 1.78–1.71 (m, 3 H), 1.49–1.33 (m, 3 H), 1.30–1.19 (m, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 147.5, 146.7, 138.8, 136.9, 129.2, 128.2, 126.8, 120.2, 108.0, 107.7, 100.9, 65.6, 61.1, 60.8, 60.2, 57.2, 32.8, 29.1, 25.4, 24.9; **HRMS** (ESI): calculated for $[C_{22}H_{27}N_2O_2]^+$: m/z = 351.2067, found: m/z = 351.2069; **IR** (ν/cm^{-1}, neat): 2926, 2856, 2799, 1502, 1487, 1442, 1250, 1039, 934, 808, 735, 699.

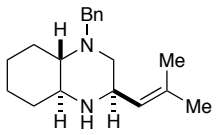
(*trans*,*cis*)-1-Benzyl-3-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)decahydroquinoxaline (19b) (Scheme 3)



The photocatalytic synthesis of **19b** followed the general procedure with **13** (145.3 mg, 0.5 mmol, 1.0 equiv) and 1-methyl-1*H*-benzo[*d*]imidazole-2-carbaldehyde (80.1 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a yellowish oil (153.2 mg, 85%). Relative stereochemistry was determined by analogy to **19a**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.75–7.71 (m, 1 H), 7.35–7.27 (m, 4 H), 7.25–7.20 (m, 4 H), 4.32 (dd, *J* = 10.7, 2.9 Hz, 1 H), 4.22 (d, *J* = 13.4 Hz, 1 H), 3.67 (s, 3 H), 3.21 (d, *J* = 13.4 Hz, 1 H), 3.03 (dd, *J* = 11.6, 2.9 Hz, 1 H), 2.69 (ddd, *J* = 10.8, 8.7, 3.4 Hz, 1 H), 2.44 (dd, *J* = 11.6, 10.7 Hz, 1 H), 2.35–2.31 (m, 1 H), 2.18 (br, 1 H), 1.98 (ddd, *J* = 10.8, 8.7, 3.5 Hz, 1 H), 1.91–1.83 (m, 2 H), 1.81–1.77 (m, 1 H), 1.45–1.32 (m, 3 H), 1.29–1.19 (m, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 153.8, 142.2, 138.7, 135.6, 129.0, 128.2, 126.9, 122.4, 121.9, 119.5, 109.1, 67.1, 60.3, 57.4, 57.0, 52.6, 32.5, 29.8, 29.0, 25.3 (two carbons); **HRMS** (ESI): calculated for $[C_{23}H_{29}N_4]^+$: m/z = 361.2387, found: m/z = 361.2390; **IR** (ν/cm^{-1}, neat): 3257, 2931, 2857, 2802, 1472, 1443, 1332, 1132, 909, 742.

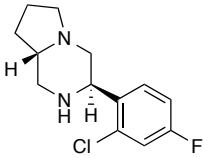
(*trans*,*cis*)-1-Benzyl-3-(2-methylprop-1-en-1-yl)decahydroquinoxaline (19c) (Scheme 3)



The photocatalytic synthesis of **19c** followed the general procedure with **13** (145.3 mg, 0.5 mmol, 1.0 equiv) and 3-methyl-2-butenal (48.2 μL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (57.0 mg, 40%, dr > 20:1). The relative stereochemistry was determined by analogy to **19a**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.31–7.20 (m, 5 H), 5.06 (d, *J* = 8.8 Hz, 1 H), 4.10 (d, *J* = 13.5 Hz, 1 H), 3.69–3.63 (m, 1 H), 3.19 (d, *J* = 13.5 Hz, 1 H), 2.58–2.65 (m, 1 H), 2.65 (dd, *J* = 11.7, 3.1 Hz, 1 H), 2.29–2.24 (m, 1 H), 2.09–2.01 (m, 2 H), 1.86–1.76 (m, 2 H), 1.73–1.68 (m, 1 H), 1.63 (d, *J* = 1.4 Hz, 3 H), 1.61 (d, *J* = 1.4 Hz, 3 H), 1.47– 1.10 (m, 5 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 138.7, 136.5 (br), 129.2, 128.3, 127.0, 123.6 (br), 64.8, 60.3, 57.5, 57.0, 54.0, 31.7, 29.1, 25.9, 25.1, 24.9, 18.5; **HRMS** (ESI): calculated for $[C_{19}H_{29}N_2]^+$: m/z = 285.2325, found: m/z = 285.2326; **IR** (ν/cm^{-1}, neat): 3308, 2929, 2856, 2795, 1673, 1447, 1375, 1135, 1084, 749, 739, 699.

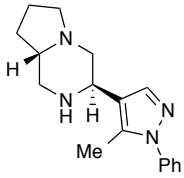
(3*R*,8a*S*)-3-(2-Chloro-4-fluorophenyl)octahydropyrrolo[1,2-*a*]pyrazine (20a) (Scheme 3)



The photocatalytic synthesis of **20a** followed the general procedure with **14** (93.2 mg, 0.5 mmol, 1.0 equiv) and 2-chloro-4-fluorobenzaldehyde (79.3 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (71.8 mg, 56%, dr > 20:1). The relative stereochemistry was determined by analogy to **21b**.

$[\alpha]_D^{26}$ (c = 1.0, $CHCl_3$) = –58.3; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.61 (dd, *J* = 8.7, 6.3 Hz, 1 H), 7.07 (dd, *J* = 8.6, 2.7 Hz, 1 H), 6.94 (ddd, *J* = 8.7, 8.3, 2.7 Hz, 1 H), 4.34 (dd, *J* = 10.1, 2.9 Hz, 1 H), 3.25 (dd, *J* = 11.0, 2.9 Hz, 1 H), 3.20 (dd, *J* = 10.6, 2.9 Hz, 1 H), 3.09 (ddd, *J* = 8.7, 8.6, 2.3 Hz, 1 H), 2.72 (dd, *J* = 11.0, 10.0 Hz, 1 H), 2.24 (br, 1 H), 2.16 (ddd, *J* = 8.8, 8.8, 8.7 Hz, 1H), 2.09 (dddd, *J* = 10.0, 6.5, 6.0, 2.9 Hz, 1 H), 2.00 (dd, *J* = 10.6, 10.1 Hz, 1 H), 1.89–1.80 (m, 2 H), 1.78–1.70 (m, 1 H), 1.50–1.40 (m, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 161.6 (d, *J* = 249.0 Hz), 135.6 (d, *J* = 3.5 Hz), 133.8 (d, *J* = 10.1 Hz), 129.4 (d, *J* = 8.6 Hz), 116.8 (d, *J* = 24.5 Hz), 114.2 (d, *J* = 20.6 Hz), 62.8, 58.3, 55.4, 53.5, 51.0, 27.4, 21.3; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –113.5; **HRMS** (ESI): calculated for $[C_{13}H_{17}ClFN_2]^+$: m/z = 255.1059, found: m/z = 255.1061; **IR** (ν/cm^{-1}, neat): 3254, 2962, 2798, 1675, 1604, 1581, 1489, 1232, 1166, 1136, 1040, 911, 857, 822.

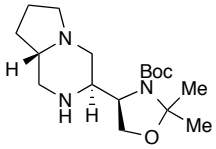
(3*R*,8a*S*)-3-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)octahydropyrrolo[1,2-*a*]pyrazine (20b) (Scheme 3)



The photocatalytic synthesis of **20b** followed the general procedure with **14** (93.2 mg, 0.5 mmol, 1.0 equiv) and 5-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (93.1 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (91.9 mg, 63%, dr > 20:1). The relative stereochemistry was determined by analogy to **21b**.

$[\alpha]_D^{25}$ (c = 1.0, $CHCl_3$) = –20.0; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.67 (s, 1 H), 7.45–7.32 (m, 5 H), 3.93 (dd, *J* = 10.5, 3.1 Hz, 1 H), 3.74 (br, 1 H), 3.22 (dd, *J* = 11.6, 2.8 Hz, 1 H), 3.14 (dd, *J* = 10.8, 3.1 Hz, 1 H), 3.12–3.07 (m, 1 H), 2.67 (dd, *J* = 11.6, 10.1 Hz, 1 H), 2.35 (dd, *J* = 10.8, 10.5 Hz, 1 H), 2.30 (s, 3 H), 2.22 (ddd, *J* = 8.9, 8.9, 8.9 Hz, 1 H), 2.14 (dddd, *J* = 10.2, 6.0, 3.6, 2.8 Hz, 1 H), 1.91–1.81 (m, 2 H), 1.79–1.70 (m, 1 H), 1.45–1.43 (m, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 139.9, 138.5, 136.4, 129.1, 127.8, 125.1, 119.8, 62.5, 58.7, 53.6, 51.3, 50.8, 27.4, 21.1, 11.1; **HRMS** (ESI): calculated for $[C_{17}H_{23}N_4]^+$: m/z = 283.1917, found: m/z = 283.1919; **IR** (ν/cm^{-1}, neat): 3294, 2952, 2800, 1599, 1504, 1453, 1391, 1170, 1110, 943, 858, 765, 696.

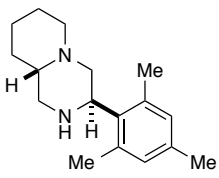
(*R*)-*tert*-Butyl 2,2-dimethyl-4-((3*S*,8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-3-yl)oxazolidine-3-carboxylate (20c) (Scheme 3)



The photocatalytic synthesis of **20c** followed the general procedure with **14** (93.2 mg, 0.5 mmol, 1.0 equiv) and (*S*)-(–)-3-(*tert*-butoxycarbonyl)-4-formyl-2,2-dimethyl-1,3-oxazolidine (114.6 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (94.7 mg, 58%, dr > 20:1). The relative stereochemistry was determined by analogy to **21b**.

$[\alpha]_D^{26}$ (c = 1.0, $CHCl_3$) = –31.5; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 4.15 (br, 1 H), 4.07 (br, 1 H), 3.95 (br, 1 H), 3.87 (dd, *J* = 9.4, 6.4 Hz, 1 H), 3.28 (d, *J* = 10.6 Hz, 1 H), 3.18 (d, *J* = 10.6 Hz, 1 H), 3.14–3.09 (m, 2 H), 2.65 (dd, *J* = 10.9, 10.9 Hz, 1 H), 2.26 (ddd, *J* = 8.8, 8.2, 8.2 Hz, 1 H), 2.17–2.13 (m, 2 H), 1.87–1.71 (m, 3 H), 1.54 (s, 3 H), 1.45–1.39 (m, 13 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 153.0*, 152.3, 94.3, 93.9*, 80.6, 64.2, 62.8, 59.3*, 58.9, 56.0, 53.5, 53.2*, 52.8, 49.9, 28.5, 27.0, 26.9*, 26.1, 23.9*, 22.4, 21.0;[15] **HRMS** (ESI): calculated for $[C_{17}H_{32}N_3O_3]^+$: m/z = 326.2438, found: m/z = 326.2438; **IR** (ν/cm^{-1}, neat): 3319, 2975, 2938, 2879, 2807, 1696, 1378, 1365, 1256, 1172, 1088, 848, 734.

***cis*-3-Mesityloctahydro-1*H*-pyrido[1,2-*a*]pyrazine (21a) (Scheme 3)**

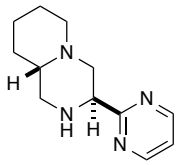


The photocatalytic synthesis of **21a** followed the general procedure with **15** (100.2 mg, 0.5 mmol, 1.0 equiv) and 2,4,6-trimethylbenzaldehyde (73.7 µL, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) as a yellowish oil (87.5 mg, 68%, dr > 20:1). The relative stereochemistry was determined by analogy to **21b**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 6.79 (s, 2 H), 4.58 (dd, *J* = 11.2, 3.2 Hz, 1 H), 3.01 (dd, *J* = 11.6, 2.9 Hz, 1 H), 2.92 (d, *J* = 11.6 Hz, 1 H), 2.83 ddt, *J* = 11.6, 10.9 Hz, 1 H), 2.75 (dd, *J* = 11.5, 3.2 Hz, 1 H), 2.66 (dd, *J* = 11.5, 11.2 Hz, 1 H), 2.50 (s, 6 H), 2.21 (s, 3 H), 2.27–2.17 (m, 2 H), 1.83–1.79 (m, 2 H), 1.69–1.58 (m, 2 H), 1.48–1.30 (m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 137.4, 136.7, 133.4, 130.3, 62.2, 57.6, 56.8, 55.6, 52.5, 29.0, 24.9, 23.8, 21.7, 20.7; **HRMS** (ESI): calculated for $[C_{17}H_{27}N_2]^+$: m/z = 259.2169, found: m/z = 259.2170; **IR** (ν/cm^{-1}, neat): 3321, 2932, 2857, 2797, 1611, 1448, 1327, 1124, 1096, 1064, 924, 851, 733.

(15) Peaks from rotamers are underlined paired with asterisks indicating the major ones.

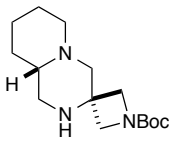
cis-3-(Pyrimidin-2-yl)octahydro-1_H_-pyrido[1,2-_a_]pyrazine (21b) (Scheme 3)



The photocatalytic synthesis of **21b** followed the general procedure with **15** (100.2 mg, 0.5 mmol, 1.0 equiv) and pyrimidine-2-carboxaldehyde (54.0 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 20% MeOH in CH_2Cl_2) as a brownish oil (56.6 mg, 52%, dr > 10:1), which can be recrystallized with CH_2Cl_2/EtOAc/hexanes as a yellowish solid. The relative stereochemistry was assigned by NOESY.

m.p.: compound decomposes at T > 180 °C; **^{1}H NMR** (400 MHz, CD_2Cl_2): δ [ppm] = 8.68 (d, *J* = 4.9 Hz, 2 H), 7.17 (td, *J* = 4.9, 0.5 Hz, 1 H), 4.12 (dd, *J* = 10.6, 3.1 Hz, 1 H), 3.18 (dd, *J* = 11.1, 3.1 Hz, 1 H), 2.97 (dd, *J* = 12.4, 3.0 Hz, 1 H), 2.81 (apparent dtd, *J* = 11.2, 3.6, 1.5 Hz, 1 H), 2.65 (dd, *J* = 12.4, 10.2 Hz, 1 H), 2.55 (br, 1 H), 2.11–2.03 (m, 2 H), 1.85 (dddd, *J* = 10.4, 10.2, 3.0, 2.7 Hz, 1 H), 1.78–1.73 (m, 1 H), 1.64–1.57 (m, 2 H), 1.56–1.51 (m, 1 H), 1.37–1.16 (m, 2 H); **^{13}C NMR** (100 MHz, CD_2Cl_2): δ [ppm] = 169.7, 157.4, 119.9, 62.9, 61.2, 61.0, 56.7, 52.3, 30.0, 26.3, 24.8.; **HRMS** (ESI): calculated for $[C_{12}H_{19}N_4]^+$: m/z = 219.1604, found: m/z = 219.1607; **IR** (ν/cm^{-1}, neat): 3396, 2936, 1672, 1568, 1425, 1330, 1200, 1128, 925, 800, 730.

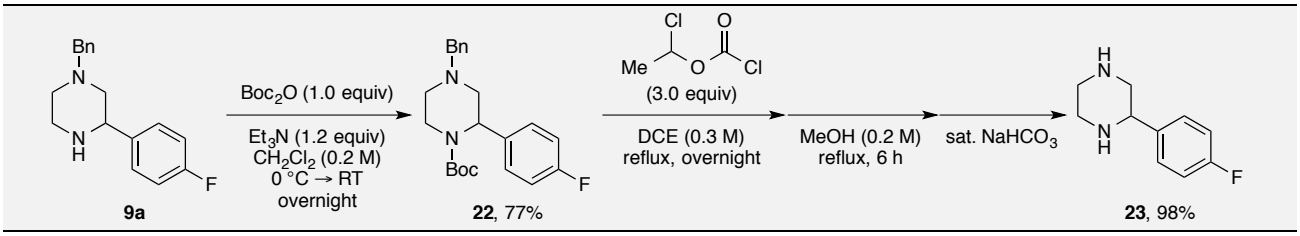
***tert*-Butyl octahydrospiro[azetidine-3,3'-pyrido[1,2-*a*]pyrazine]-1-carboxylate (21c) (Scheme 3)**



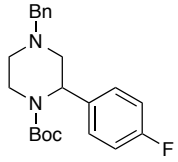
The photocatalytic synthesis of **21c** followed the general procedure with **15** (100.2 mg, 0.5 mmol, 1.0 equiv) and *tert*-butyl 3-oxoazetidine-1-carboxylate (85.6 mg, 0.5 mmol, 1.0 equiv). The desired product was obtained by flash column chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2) as a yellowish oil (46.2 mg, 33%).

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 3.97 (d, *J* = 8.9 Hz, 1 H), 3.71 (d, *J* = 8.9 Hz, 1 H), 3.66 (d, *J* = 9.2 Hz, 1 H), 3.54 (d, *J* = 9.2 Hz, 1 H), 2.83 (d, *J* = 11.1 Hz, 1 H), 2.74–2.69 (m, 2 H), 2.48 (t, *J* = 11.0, 11.0 Hz, 1 H), 2.13 (d, *J* = 11.1 Hz, 1 H), 2.02 (ddd, *J* = 11.2, 11.1, 4.3 Hz, 1 H), 1.81 (apparent t, *J* = 10.5 Hz, 1 H), 1.75–1.69 (m, 1 H), 1.61–1.51 (m, 2 H), 1.49–1.42 (m, 1 H), 1.41 (s, 9 H), 1.31–1.20 (m, 2 H), 1.16–1.10 (m, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 156.6, 79.5, 63.0, 61.4, 60.8 (br), 58.8 (br), 56.0, 52.4, 48.6, 29.4, 28.5, 25.6, 24.1; **HRMS** (ESI): calculated for $[C_{15}H_{28}N_3O_2]^+$: m/z = 282.2176, found: m/z = 282.2175; **IR** (ν/cm^{-1}, neat): 3308, 2933, 2874, 2803, 1702, 1406, 1169, 1114, 860, 771, 733.

3.4 Procedure for *N*-Bn deprotection



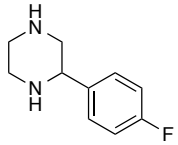
***tert*-Butyl 4-benzyl-2-(4-fluorophenyl)piperazine-1-carboxylate (22)**



A solution of Boc_2O (436.5 mg, 2.0 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added dropwise to a stirred mixture of **9a** (540.7 mg, 2.0 mmol, 1.0 equiv) and Et_3N (333.6 μL, 2.4 mmol, 1.2 equiv) in CH_2Cl_2 (5.0 mL) under N_2 at 0 °C. The reaction was allowed to warm to room temperature and stirred overnight before washed with sat. $NaHCO_{3(aq)}$ (1×50 mL) and brine. The organic layer was dried over Na_2SO_4, filtered, and condensed under *vacuo*. The residue was purified by flash column chromatography (2%–8% EtOAc in hexanes) to afford the desired product (569.2 mg, 77%) as a yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.43–7.39 (m, 2 H), 7.35–7.25 (m, 5 H), 7.01–6.95 (m, 2 H), 5.21 (apparent s, 1 H), 3.90 (apparent d, J = 13.5 Hz, 1 H), 3.58 (d, J = 13.0 Hz, 1 H), 3.45 (d, J = 13.0 Hz, 1 H), 3.22 (apparent d, J = 12.0, 1 H), 3.00 (dt, J = 13.5, 7.1 Hz, 1 H), 2.83 (apparent d, J = 11.2 Hz, 1 H), 2.42 (dd, J = 12.0, 4.2 Hz, 1 H), 2.18 (apparent t, J = 11.2 Hz, 1 H), 1.48 (s, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 161.9 (d, J = 245.0 Hz), 155.0, 137.9 (apparent s), 136.4, 129.6 (d, J = 7.8 Hz), 129.3, 128.4, 127.4, 114.9 (d, J = 21.0 Hz), 80.2, 63.2, 55.2, 53.4, 52.8, 39.9, 28.6; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –116.3; **HRMS** (ESI): calculated for $[C_{22}H_{28}FN_2O_2]^+$: m/z = 371.2129, found: m/z = 371.2131; **IR** (ν/cm^{-1}, neat): 2976, 2930, 2810, 2768, 1691, 1604, 1509, 1454, 1415, 1365, 1301, 1225, 1171, 1117, 1025, 844, 771.

2-(4-Fluorophenyl)piperazine (23)



The procedure was modified from the literature.[16] To a stirred solution of **22** (120.0 mg, 0.32 mmol, 1.0 equiv) in 1,2-dichloroethane (1.0 mL) at room temperature was added 1-chloroethylchloroformate (104.8 μL, 0.97 mmol, 3.0 equiv). This reaction was conducted in a closed vial (size: 3 mL). The reaction was heated under reflux overnight and cooled to room temperature before condensed under *vacuo*. The residue was dissolved in MeOH (2 mL) and the mixture was heated under reflux for additional 6 h. The reaction was cooled to room temperature and condensed under *vacuo*. The residue was dissolved in CH_2Cl_2 (5 mL) and stirred with sat. $NaHCO_{3(aq)}$ (5 mL) at room temperature. After the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The combined organics were washed with brine, dried over Na_2SO_4, filtered, and condensed under *vacuo* to afford the desired product **23** without further purification (a white solid, 57.1 mg, 98%).

m.p.: 98–99 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ [ppm] = 7.33 (ddd, J = 8.6, 5.4, 2.6 Hz, 2 H), 7.01–6.95 (m, 2 H), 3.71 (dd, J = 10.2, 2.8 Hz, 1 H), 3.10–3.05 (m, 1 H), 2.99–2.91 (m, 3 H), 2.88–2.81 (m, 1 H), 2.64 (dd, J = 12.1, 10.2 Hz, 1 H), 1.79 (br, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ [ppm] = 162.2 (d, J = 245.1 Hz), 138.7 (d, J = 3.1 Hz), 128.5 (d, J = 7.9 Hz), 115.3 (d, J = 21.2 Hz), 61.4, 54.5, 47.9, 46.1; **^{19}F NMR** (377 MHz, $CDCl_3$): δ [ppm] = –115.3 ; **HRMS** (ESI): calculated for $[C_{10}H_{14}FN_2]^+$: m/z = 181.1136, found: m/z = 181.1134; **IR** (ν/cm^{-1}, neat): 3244, 3198, 2939, 2827, 1604, 1510, 1327, 1224, 1155, 1137, 879, 828.

(16) (a) Olofson, R. A.; Martz, J. T.; Senet, J. P.; Piteau, M.; Malfroot, T. *J. Org. Chem.* **1984**, *49*, 2081–2082; (b) Yokoshima, S.; Watanabe, K.; Uehara, F.; Usui, Y.; Tanaka, H. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5749–5751; (c) Firth, J. D.; O'Brien, P., Ferris, L. *J. Am. Chem. Soc.* **2016**, *138*, 651–659.

4. X-ray crystallography

Crystals of **18c** (CCDC 1445313) were obtained by recrystallization from Et_2O/EtOAc. The X-ray data was collected to confirm the relative stereochemistry.

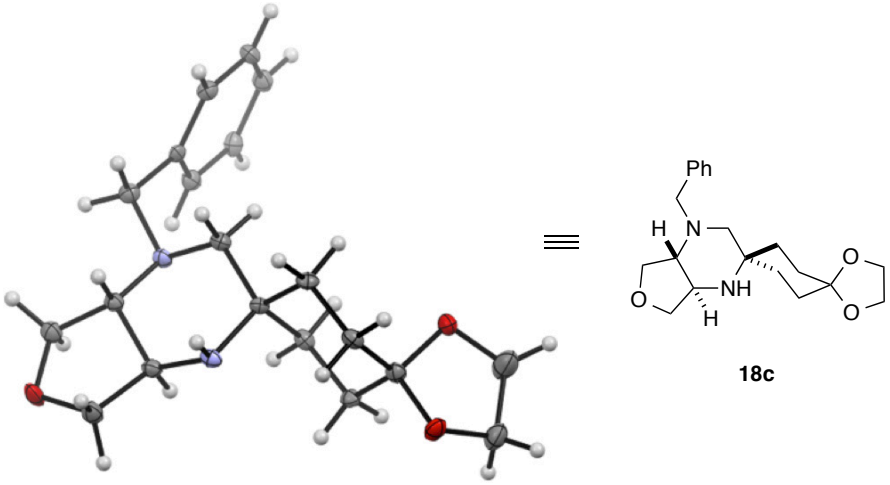


Figure S2. ORTEP representation of **18c**. Ellipsoids include 50% of the electron density. We thank Dr. Nils Trapp from the X-ray crystallographic service of the Laboratorium für Organische Chemie at ETH Zürich for performing the experiments.

Experimental

A suitable single crystal of **18c** [$C_{20}H_{28}N_2O_3$, code: mo_jb141015_1_1_0m] was selected and measured on a Bruker Apex2 Duo (Mo) diffractometer. The crystal was kept at 100.0(2) K during data collection. Using Olex2,[17] the structure was solved with the XT[18] structure solution program using Direct Methods and refined with the XL[19] refinement package using Least Squares minimization.

(17) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339–341.
(18) Sheldrick, G. M. *Acta Cryst.* **2015**, *A71*, 3–8.
(19) Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112–122.

Table S2. Crystal data and structure refinement for **18c**.

Identification code	mo_jb141015_1_1_0m
Empirical formula	$C_{20}H_{28}N_2O_3$
Formula weight	344.44
Temperature/K	100.0(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.7442(9)
b/Å	6.1717(5)
c/Å	14.9524(13)
α/°	90
β/°	90.609(2)
γ/°	90
Volume/Å^3	899.16(14)
Z	2
ρ_{calc}g/cm^3	1.272
μ/mm^{-1}	0.085
F(000)	372.0
Crystal size/mm^3	0.16 × 0.07 × 0.04
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.18 to 54.974
Index ranges	-12 ≤ h ≤ 12, -3 ≤ k ≤ 8, -19 ≤ l ≤ 18
Reflections collected	5498
Independent reflections	3053 [R_{int} = 0.0394, R_{sigma} = 0.0639]
Data/restraints/parameters	3053/2/229
Goodness-of-fit on F^2	1.014
Final R indexes [I>=2σ (I)]	R_1 = 0.0448, wR_2 = 0.0886
Final R indexes [all data]	R_1 = 0.0662, wR_2 = 0.0969
Largest diff. peak/hole / e Å^{-3}	0.34/-0.26
Flack parameter	-0.6(10)

Table S3. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **18c**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O1	-799(2)	8764(4)	8856.0(14)	23.6(5)
O2	2037(2)	8208(3)	3910.2(14)	21.0(5)
O3	3664(2)	5987(4)	4487.8(14)	19.1(5)
N1	469(2)	6762(4)	6701.0(16)	15.0(6)
N2	2169(2)	5437(4)	8247.7(16)	15.0(6)
C1	4607(3)	1449(5)	8701.4(19)	17.3(7)
C2	6012(3)	1041(5)	8685(2)	20.5(7)
C3	6936(3)	2665(5)	8901(2)	19.9(7)
C4	6458(3)	4725(5)	9118.4(19)	18.9(7)
C5	5063(3)	5121(5)	9128.8(19)	17.7(7)
C6	4120(3)	3493(5)	8930.5(19)	15.1(6)
C7	2598(3)	3968(5)	8976(2)	17.3(7)
C8	755(3)	6161(5)	8349.1(19)	14.4(6)
C9	395(3)	7538(6)	9148(2)	19.6(7)
C10	-942(3)	8617(6)	7890(2)	21.1(7)
C11	415(3)	7704(5)	7588.9(19)	15.7(6)

C12	2236(3)	4291(5)	7383.0(19)	15.4(6)
C13	1810(3)	5671(5)	6569.8(19)	12.6(6)
C14	1663(3)	4163(5)	5767.8(19)	15.0(6)
C15	1328(3)	5355(5)	4898(2)	15.9(6)
C16	2409(3)	7038(5)	4707(2)	16.2(7)
C17	2611(3)	8595(5)	5489.4(19)	15.5(6)
C18	2917(3)	7379(5)	6361.6(19)	15.2(6)
C19	4362(4)	7384(7)	3893(3)	39.1(10)
C20	3299(3)	8966(6)	3539(2)	26.7(8)

Table S4. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **18c**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	22.1(12)	30.7(13)	17.9(12)	-1.7(11)	2.8(9)	14.8(11)
O2	18.5(11)	27.0(13)	17.3(12)	8.3(10)	-0.8(8)	2.0(9)
O3	16.1(11)	19.3(11)	21.9(12)	1.9(10)	5.5(9)	3.0(9)
N1	11.4(12)	14.3(13)	19.1(14)	-1.0(11)	-1(1)	1(1)
N2	12.3(12)	17.4(14)	15.2(13)	0.7(11)	-0.1(10)	4.2(11)
C1	19.4(15)	16.4(16)	16.0(16)	2.2(13)	0.5(13)	2.0(13)
C2	23.4(17)	18.8(16)	19.4(17)	1.6(15)	6.0(13)	9.4(15)
C3	16.6(16)	26.0(17)	17.1(16)	1.0(15)	1.6(12)	5.4(15)
C4	19.8(16)	23.2(16)	13.6(16)	-0.7(14)	1.7(13)	-1.1(14)
C5	20.9(16)	19.6(16)	12.6(16)	-0.4(14)	-1.0(12)	4.5(14)
C6	18.2(15)	18.8(16)	8.3(14)	3.5(13)	0.5(11)	6.0(13)
C7	17.8(15)	17.4(16)	16.6(16)	1.6(14)	0.0(12)	1.0(13)
C8	12.1(14)	13.6(14)	17.4(16)	-0.2(13)	0.8(11)	0.7(13)
C9	16.7(15)	22.4(16)	19.8(17)	0.8(15)	1.4(12)	3.5(14)
C10	20.7(16)	25.7(18)	16.9(16)	0.0(15)	-0.1(12)	7.9(14)
C11	14.2(15)	13.8(15)	19.0(17)	1.2(13)	0.1(12)	2.2(13)
C12	16.0(15)	13.1(15)	16.9(16)	-0.3(13)	0.5(12)	2.1(13)
C13	12.6(14)	11.3(15)	13.9(15)	0.5(12)	-0.8(11)	1.6(12)
C14	16.9(15)	10.1(14)	18.0(15)	-1.4(13)	-2.1(12)	-0.8(12)
C15	14.4(15)	16.5(15)	16.8(15)	-3.2(13)	-2.4(12)	2.0(13)
C16	14.8(15)	18.7(17)	15.2(16)	0.2(13)	-0.8(12)	2.3(13)
C17	14.8(15)	12.0(14)	19.6(16)	2.3(14)	1.4(12)	-0.4(13)
C18	13.5(14)	15.9(15)	16.1(16)	-3.2(13)	-0.1(12)	1.5(13)
C19	26.8(19)	52(3)	38(2)	22(2)	8.3(16)	8.8(19)
C20	22.6(17)	34(2)	23.7(18)	9.9(17)	3.5(13)	-1.6(16)

Table S5. Bond Lengths for **18c**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C9	1.451(3)	C4	C5	1.382(4)
O1	C10	1.453(4)	C5	C6	1.391(4)
O2	C16	1.436(4)	C6	C7	1.514(4)
O2	C20	1.432(4)	C8	C9	1.510(4)
O3	C16	1.426(3)	C8	C11	1.517(4)
O3	C19	1.418(4)	C10	C11	1.511(4)
N1	C11	1.451(4)	C12	C13	1.538(4)
N1	C13	1.485(3)	C13	C14	1.524(4)

N2	C7	1.475(4)	C13	C18	1.542(4)
N2	C8	1.459(3)	C14	C15	1.526(4)
N2	C12	1.476(4)	C15	C16	1.509(4)
C1	C2	1.393(4)	C16	C17	1.525(4)
C1	C6	1.392(4)	C17	C18	1.531(4)
C2	C3	1.383(5)	C19	C20	1.515(5)
C3	C4	1.394(4)			

Table S6. Bond Angles for **18c**.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
C9	O1	C10	109.5(2)	N1	C11	C10	117.5(2)
C20	O2	C16	106.0(2)	C10	C11	C8	101.3(2)
C19	O3	C16	106.6(2)	N2	C12	C13	114.4(2)
C11	N1	C13	110.1(2)	N1	C13	C12	112.1(2)
C7	N2	C12	109.7(2)	N1	C13	C14	107.8(2)
C8	N2	C7	111.9(2)	N1	C13	C18	109.6(2)
C8	N2	C12	106.8(2)	C12	C13	C18	110.8(2)
C6	C1	C2	120.4(3)	C14	C13	C12	107.8(2)
C3	C2	C1	120.2(3)	C14	C13	C18	108.6(2)
C2	C3	C4	119.8(3)	C13	C14	C15	113.2(2)
C5	C4	C3	119.7(3)	C16	C15	C14	110.5(2)
C4	C5	C6	121.2(3)	O2	C16	C15	109.5(2)
C1	C6	C7	121.5(3)	O2	C16	C17	110.4(2)
C5	C6	C1	118.7(3)	O3	C16	O2	104.3(2)
C5	C6	C7	119.7(3)	O3	C16	C15	109.4(2)
N2	C7	C6	110.8(2)	O3	C16	C17	111.0(2)
N2	C8	C9	118.8(2)	C15	C16	C17	111.9(2)
N2	C8	C11	108.2(2)	C16	C17	C18	111.6(3)
C9	C8	C11	100.9(2)	C17	C18	C13	112.1(2)
O1	C9	C8	104.4(2)	O3	C19	C20	106.3(3)
O1	C10	C11	104.1(2)	O2	C20	C19	104.0(3)
N1	C11	C8	115.1(3)				

Table S7. Torsion Angles for **18c**.

A	**B**	**C**	**D**	**Angle/°**	**A**	**B**	**C**	**D**	**Angle/°**
O1	C10	C11	N1	162.0(2)	C9	C8	C11	C10	-43.9(3)
O1	C10	C11	C8	35.7(3)	C10	O1	C9	C8	-14.5(3)
O2	C16	C17	C18	176.3(2)	C11	N1	C13	C12	44.7(3)
O3	C16	C17	C18	-68.5(3)	C11	N1	C13	C14	163.2(2)
O3	C19	C20	O2	-4.9(4)	C11	N1	C13	C18	-78.8(3)
N1	C13	C14	C15	62.3(3)	C11	C8	C9	O1	36.2(3)
N1	C13	C18	C17	-62.8(3)	C12	N2	C7	C6	69.8(3)
N2	C8	C9	O1	154.3(2)	C12	N2	C8	C9	-175.6(3)
N2	C8	C11	N1	62.7(3)	C12	N2	C8	C11	-61.5(3)
N2	C8	C11	C10	-169.4(2)	C12	C13	C14	C15	-176.4(2)
N2	C12	C13	N1	-50.6(3)	C12	C13	C18	C17	173.0(2)
N2	C12	C13	C14	-169.1(2)	C13	N1	C11	C8	-52.6(3)
N2	C12	C13	C18	72.2(3)	C13	N1	C11	C10	-171.9(3)
C1	C2	C3	C4	-1.2(4)	C13	C14	C15	C16	57.0(3)

C1	C6	C7	N2	-110.9(3)	C14	C13	C18	C17	54.7(3)
C2	C1	C6	C5	1.0(4)	C14	C15	C16	O2	-177.2(2)
C2	C1	C6	C7	-178.4(3)	C14	C15	C16	O3	69.0(3)
C2	C3	C4	C5	0.9(4)	C14	C15	C16	C17	-54.4(3)
C3	C4	C5	C6	0.4(4)	C15	C16	C17	C18	54.1(3)
C4	C5	C6	C1	-1.3(4)	C16	O2	C20	C19	25.0(3)
C4	C5	C6	C7	178.1(3)	C16	O3	C19	C20	-17.3(4)
C5	C6	C7	N2	69.7(3)	C16	C17	C18	C13	-54.6(3)
C6	C1	C2	C3	0.3(4)	C18	C13	C14	C15	-56.3(3)
C7	N2	C8	C9	64.4(3)	C19	O3	C16	O2	33.0(3)
C7	N2	C8	C11	178.5(2)	C19	O3	C16	C15	150.1(3)
C7	N2	C12	C13	-180.0(2)	C19	O3	C16	C17	-86.0(3)
C8	N2	C7	C6	-172.0(2)	C20	O2	C16	O3	-36.3(3)
C8	N2	C12	C13	58.7(3)	C20	O2	C16	C15	-153.3(3)
C9	O1	C10	C11	-13.5(3)	C20	O2	C16	C17	83.0(3)
C9	C8	C11	N1	-171.8(2)					

Table S8. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **18c**.

Atom	***x***	***y***	***z***	**U(eq)**
H1	-200(30)	5760(40)	6626(19)	18
H1A	3977	326	8555	21
H2	6337	-356	8526	25
H3	7894	2377	8901	24
H4	7088	5851	9259	23
H5	4741	6530	9274	21
H7A	2077	2595	8929	21
H7B	2387	4640	9560	21
H8	126	4882	8319	17
H9A	175	6621	9670	24
H9B	1162	8518	9310	24
H10A	-1109	10064	7623	25
H10B	-1709	7642	7720	25
H11	1101	8908	7613	19
H12A	1632	3003	7408	18
H12B	3186	3773	7296	18
H14A	926	3101	5888	18
H14B	2529	3349	5694	18
H15A	1281	4304	4399	19
H15B	421	6065	4946	19
H17A	1773	9479	5562	19
H17B	3381	9588	5359	19
H18A	2971	8432	6860	18
H18B	3820	6654	6317	18
H19A	4765	6546	3396	47
H19B	5108	8166	4211	47
H20A	3505	10459	3741	32
H20B	3260	8941	2877	32

5. NMR spectra

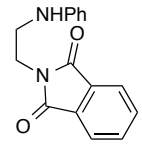
Table of contents

2-(2-(Phenylamino)ethyl)isoindoline-1,3-dione (S1)

57-24-03-bhsieh.10.fid
Sample fly-09-088
group bode
PRO CDCl3 /opt/v bhsieh 57

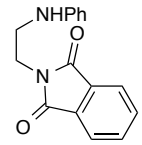
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86, 7.86, 7.85, 7.84, 7.83, 7.83, 7.82, 7.81, 7.73, 7.73, 7.73, 7.72, 7.71, 7.71, 7.70, 7.69, 7.69, 7.69, 7.17, 7.16, 7.16, 7.16, 7.15, 7.15, 7.14, 7.14, 7.14, 7.13, 7.13, 7.12, 7.12, 6.69, 6.69, 6.68, 6.67, 6.67, 6.66, 6.65, 6.65, 6.65, 6.64, 6.64, 6.64, 6.63, 6.63, 6.62, 6.62, 6.62, 6.61, 4.03, 3.98, 3.97, 3.95, 3.45, 3.44, 3.42.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.17–7.12 (m, 2 H), 6.69–6.61 (m, 3 H), 4.03 (br, 1 H), 3.97 (t, *J* = 6.1 Hz, 2 H), 3.44 (t, *J* = 6.1 Hz, 2 H).



57-24-03-bhsieh.11.fid
Sample fly-09-088
group bode
CAR CDCl3 /opt/v bhsieh 57

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 147.7, 134.2, 132.1, 129.4, 123.5, 117.7, 112.8, 43.1, 37.6.

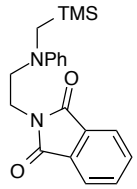


2-(2-(Phenyl((trimethylsilyl)methyl)amino)ethyl)isoindoline-1,3-dione (S2)

41-27-10-bhsieh.10.fid
Sample fly-10-037
group bode

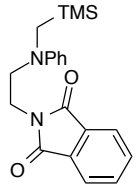
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83, 7.82, 7.81, 7.81, 7.80, 7.79, 7.78, 7.78, 7.71, 7.71, 7.70, 7.69, 7.68, 7.67, 7.67, 7.17, 7.17, 7.17, 7.16, 7.16, 7.15, 7.15, 7.14, 7.13, 7.13, 7.12, 6.80, 6.78, 6.57, 6.55, 6.53, 3.90, 3.89, 3.88, 3.88, 3.88, 3.87, 3.86, 3.61, 3.60, 3.60, 3.59, 3.57, 2.93, 0.11.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.18–7.12 (m, 2 H), 6.79 (apparent d, *J* = 7.9 Hz, 2 H), 6.55 (apparent t, *J* = 7.2 Hz, 1 H), 3.90–3.86 (m, 2 H), 3.61–3.57 (m, 2 H), 2.93 (s, 2 H), 0.11 (s, 9 H).



41-27-10-bhsieh.11.fid
Sample fly-10-037
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 148.8, 134.0, 132.1, 129.1, 123.2, 115.7, 112.4, 50.0, 41.7, 33.9, -1.1.

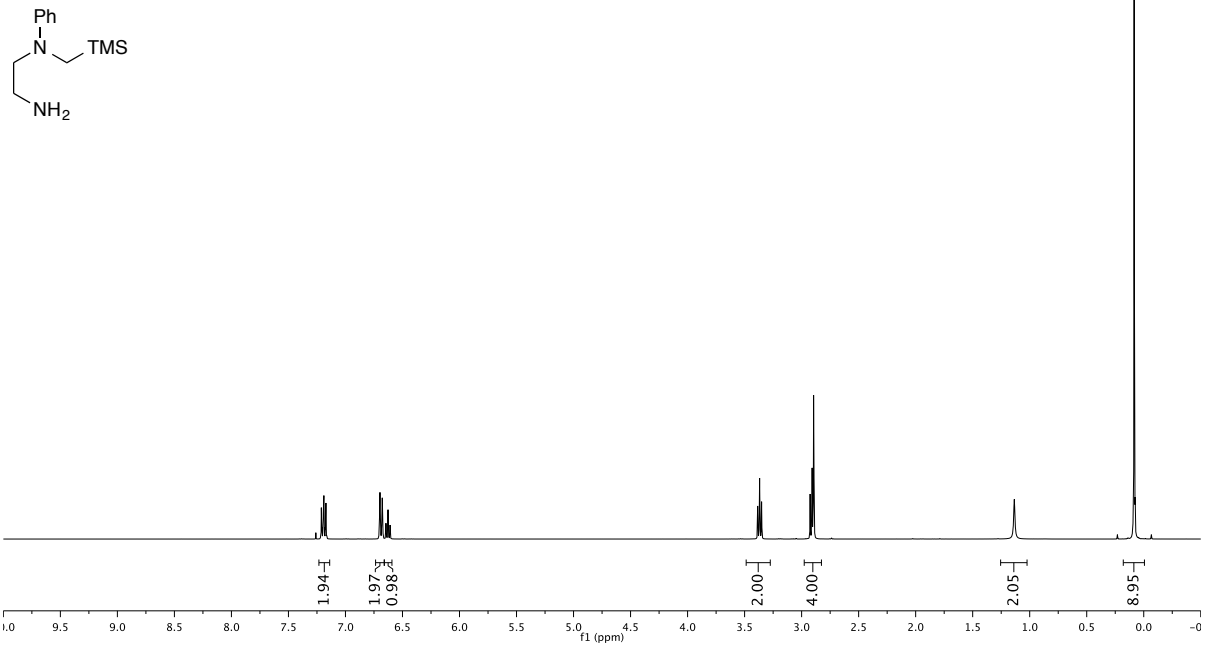


N^1-phenyl-N^1-((trimethylsilyl)methyl)ethane-1,2-diamine (2)

21-13-06-bhsieh.10.fid
Sample fly-10-038
group bode

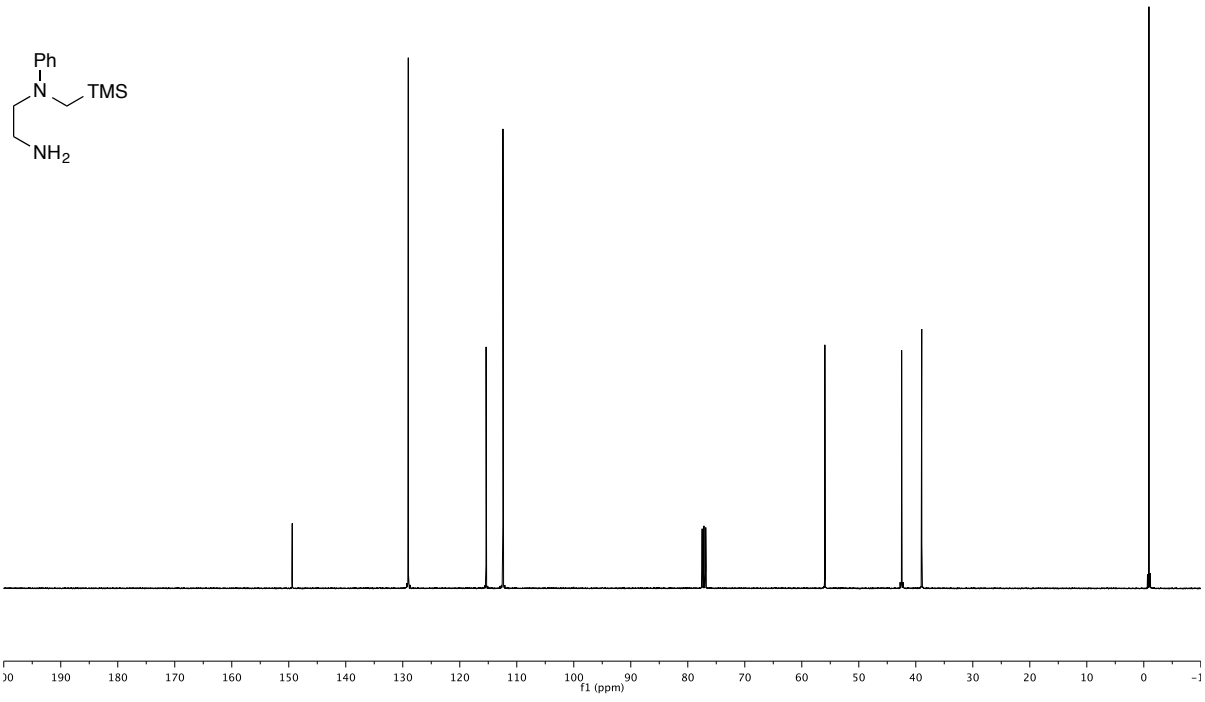
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22, 7.21, 7.21, 7.21, 7.20, 7.19, 7.19, 7.18, 7.18, 7.17, 7.17, 6.70, 6.70, 6.70, 6.69, 6.69, 6.68, 6.68, 6.68, 6.68, 6.65, 6.65, 6.64, 6.63, 6.63, 6.62, 6.61, 6.61, 6.61, 3.39, 3.37, 3.35, 2.93, 2.91, 2.90, 2.89, 1.14, 0.08.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22–7.17 (m, 2 H), 6.69 (dt, *J* = 7.8, 1.0 Hz, 2 H), 6.63 (tt, *J* = 7.1, 1.0 Hz, 1 H), 3.37 (t, *J* = 6.9 Hz, 2 H), 2.91 (t, *J* = 6.9 Hz, 2 H), 2.90 (s, 2 H), 1.14 (br, 2 H), 0.08 (s, 9 H).



21-13-06-bhsieh.11.fid
Sample fly-10-038
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4, 129.0, 115.4, 112.4, 55.9, 42.5, 38.9, -0.9.

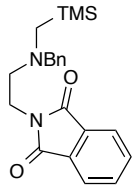


2-(2-(Benzyl((trimethylsilyl)methyl)amino)ethyl)isoindoline-1,3-dione (S3)

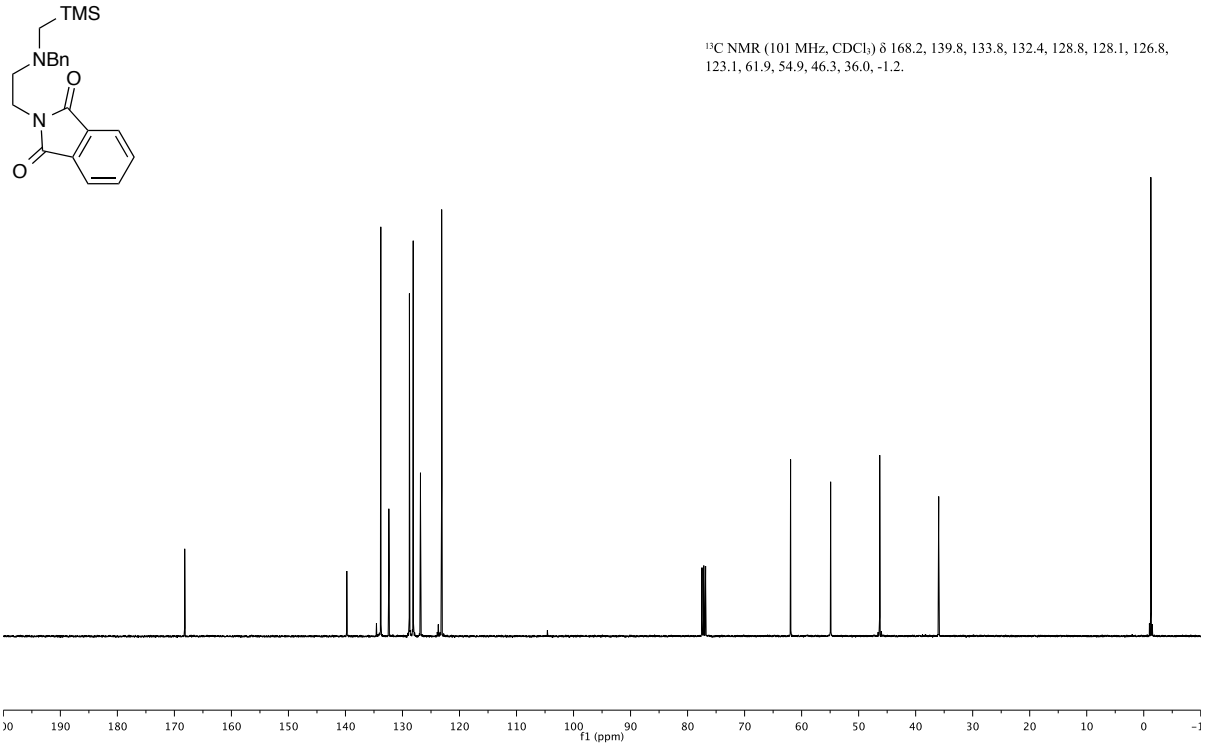
41-17-10-bhsieh.10.fid
Sample fly-10-129
group bode

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82, 7.82, 7.81, 7.80, 7.72, 7.71, 7.70, 7.69, 7.17, 7.17, 7.16, 7.16, 7.15, 7.15, 7.14, 7.13, 7.13, 7.12, 7.12, 7.12, 7.11, 7.11, 7.10, 7.09, 3.79, 3.77, 3.75, 3.54, 2.62, 2.60, 2.58, 2.09, 0.03.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.17–7.09 (m, 5 H), 3.77 (t, *J* = 6.3 Hz, 2 H), 3.54 (s, 2 H), 2.60 (t, *J* = 6.3 Hz, 2 H), 2.09 (s, 2 H), 0.03 (s, 9 H).



41-17-10-bhsieh.11.fid
Sample fly-10-129
group bode



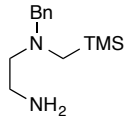
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 139.8, 133.8, 132.4, 128.8, 128.1, 126.8, 123.1, 61.9, 54.9, 46.3, 36.0, -1.2.

N^1-benzyl-N^1-((trimethylsilyl)methyl)ethane-1,2-diamine (3)

5-20-08-bhsieh.10.fid
Sample fly-10-151
group bode
PRO CDCl3 /opt/v bhsieh 5

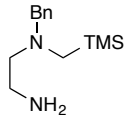
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35, 7.35, 7.34, 7.33, 7.32, 7.32, 7.32, 7.31, 7.30, 7.30, 7.28, 7.27, 7.26, 7.26, 7.25, 7.25, 7.24, 7.24, 7.24, 7.23, 7.23, 3.53, 2.74, 2.72, 2.71, 2.40, 2.39, 2.38, 2.00, 1.30, 0.10.

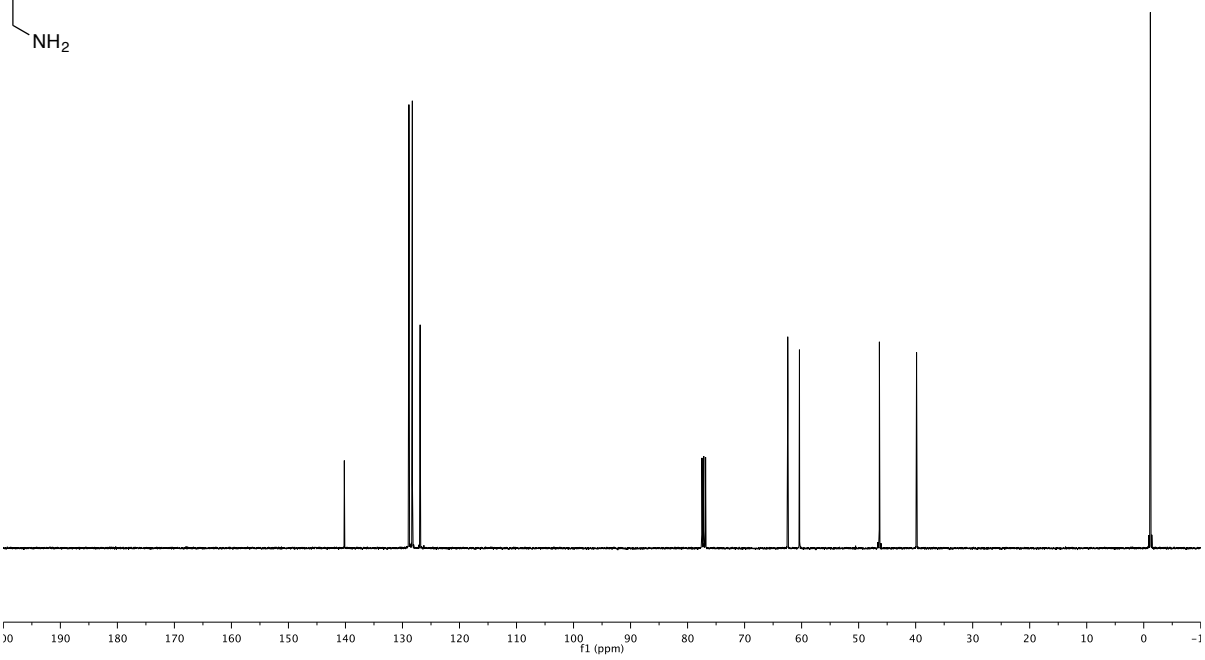
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35–7.23 (m, 5 H), 3.53 (s, 2 H), 2.72 (t, *J* = 5.9 Hz, 2 H), 2.39 (t, *J* = 5.9 Hz, 2 H), 2.00 (s, 2 H), 1.30 (br, 2 H), 0.10 (s, 9 H).



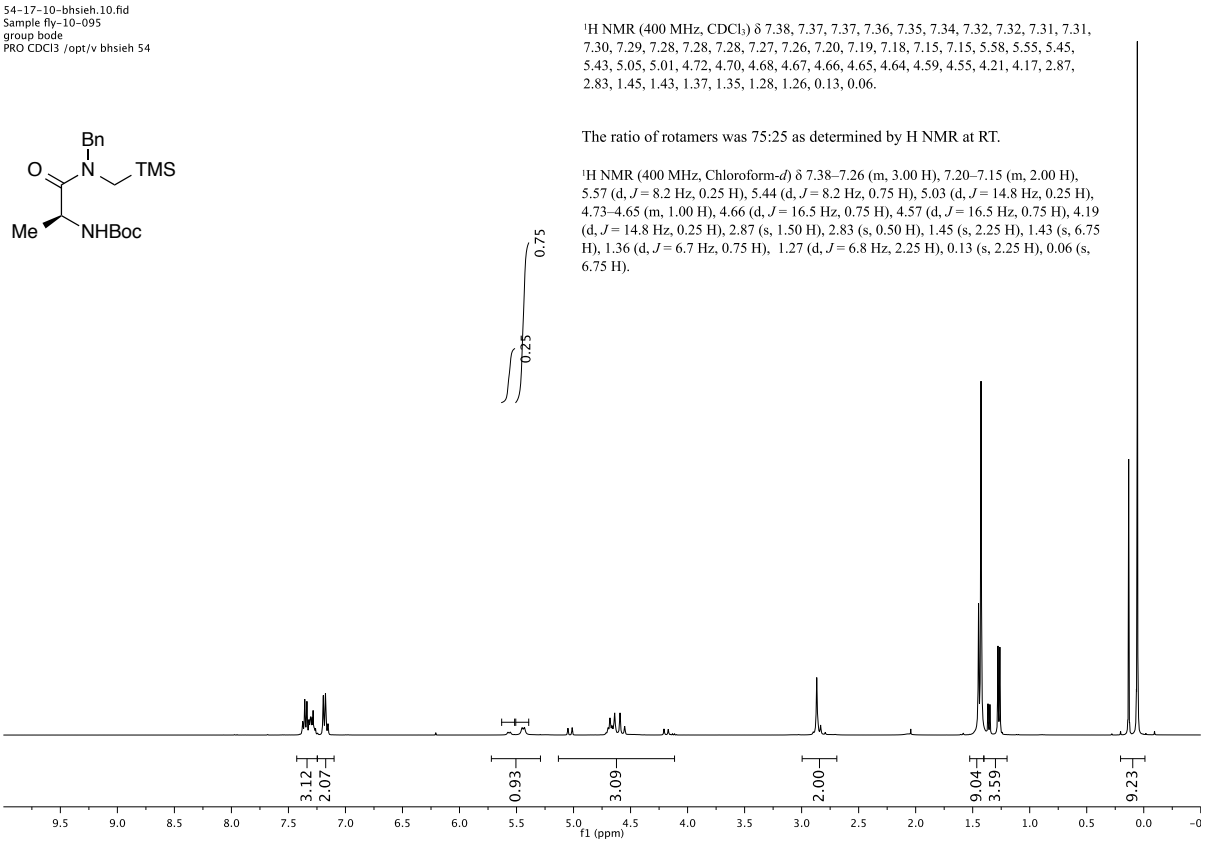
5-20-08-bhsieh.11.fid
Sample fly-10-151
group bode
CAR CDCl3 /opt/v bhsieh 5

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 128.9, 128.3, 126.9, 62.4, 60.4, 46.4, 39.8, -1.2.





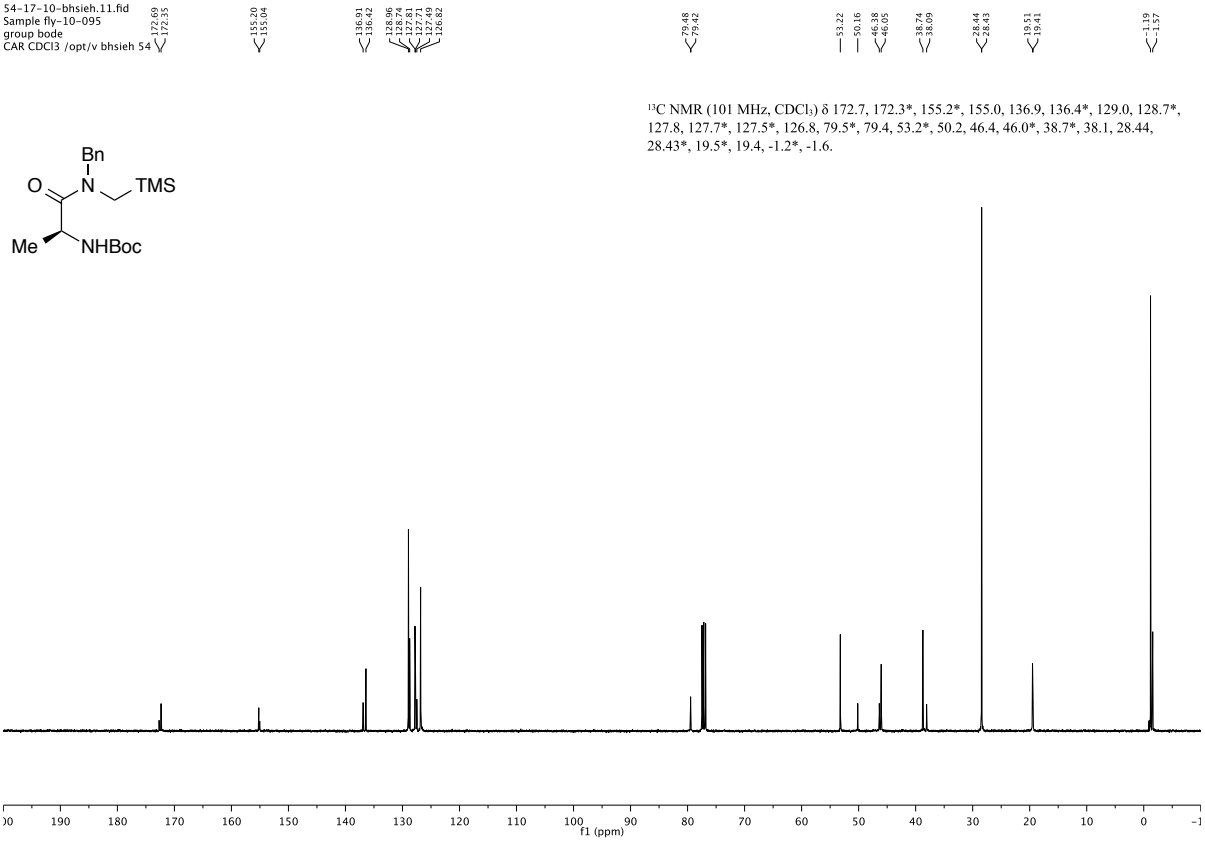
(*S*)-*tert*-Butyl (1-(benzyl((trimethylsilyl)methyl)amino)-1-oxopropan-2-yl)carbamate (S4)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38, 7.37, 7.37, 7.36, 7.35, 7.34, 7.32, 7.32, 7.31, 7.31, 7.30, 7.29, 7.28, 7.28, 7.28, 7.27, 7.26, 7.20, 7.19, 7.18, 7.15, 7.15, 5.58, 5.55, 5.45, 5.43, 5.05, 5.01, 4.72, 4.70, 4.68, 4.67, 4.66, 4.65, 4.64, 4.59, 4.55, 4.21, 4.17, 2.87, 2.83, 1.45, 1.43, 1.37, 1.35, 1.28, 1.26, 0.13, 0.06.

The ratio of rotamers was 75:25 as determined by H NMR at RT.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38–7.26 (m, 3.00 H), 7.20–7.15 (m, 2.00 H), 5.57 (d, *J* = 8.2 Hz, 0.25 H), 5.44 (d, *J* = 8.2 Hz, 0.75 H), 5.03 (d, *J* = 14.8 Hz, 0.25 H), 4.73–4.65 (m, 1.00 H), 4.66 (d, *J* = 16.5 Hz, 0.75 H), 4.57 (d, *J* = 16.5 Hz, 0.75 H), 4.19 (d, *J* = 14.8 Hz, 0.25 H), 2.87 (s, 1.50 H), 2.83 (s, 0.50 H), 1.45 (s, 2.25 H), 1.43 (s, 6.75 H), 1.36 (d, *J* = 6.7 Hz, 0.75 H), 1.27 (d, *J* = 6.8 Hz, 2.25 H), 0.13 (s, 2.25 H), 0.06 (s, 6.75 H).

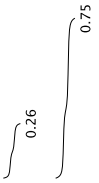


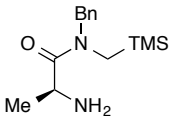
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 172.3*, 155.2*, 155.0, 136.9, 136.4*, 129.0, 128.7*, 127.8, 127.7*, 127.5*, 126.8, 79.5*, 79.4, 53.2*, 50.2, 46.4, 46.0*, 38.7*, 38.1, 28.44, 28.43*, 19.5*, 19.4, -1.2*, -1.6.

(*S*)-2-Amino-*N*-benzyl-*N*-((trimethylsilyl)methyl)propanamide (S5)

42-17-10-bhsieh.10.fid
Sample fly-10-135
group bode

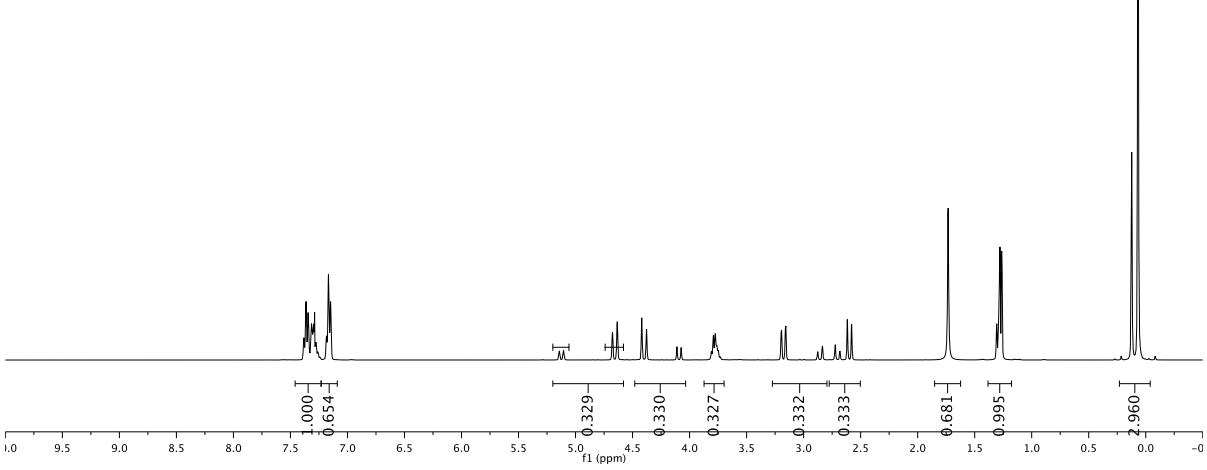
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36, 7.36, 7.35, 7.35, 7.34, 7.34, 7.33, 7.32, 7.32, 7.32, 7.31, 7.29, 7.29, 7.29, 7.28, 7.28, 7.28, 7.27, 7.26, 7.25, 7.25, 7.24, 7.16, 7.15, 7.14, 7.14, 7.14, 7.13, 7.12, 7.12, 7.12, 5.11, 5.08, 4.65, 4.61, 4.39, 4.35, 4.08, 4.05, 3.78, 3.77, 3.76, 3.75, 3.74, 3.73, 3.72, 3.72, 3.70, 3.17, 3.13, 2.85, 2.85, 2.85, 2.84, 2.81, 2.81, 2.81, 2.80, 2.70, 2.69, 2.66, 2.65, 2.59, 2.59, 2.59, 2.55, 2.55, 2.55, 1.70, 1.28, 1.26, 1.25, 1.23, 0.10, 0.04.





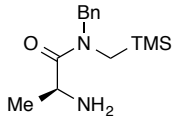
The ratio of rotamers was 75:25 as determined by H NMR at RT.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36–7.24 (m, 3 H), 7.16–7.12 (m, 2 H), 5.10 (d, *J* = 14.8 Hz, 0.25 H), 4.63 (d, *J* = 16.7 Hz, 0.75 H), 4.37 (d, *J* = 16.7 Hz, 0.75 H), 4.06 (d, *J* = 14.8 Hz, 0.25 H), 3.78–3.70 (m, 1 H), 3.15 (d, *J* = 14.9 Hz, 0.75 H), 2.83 (d, *J* = 16.3 Hz, 0.25 H), 2.68 (d, *J* = 16.3 Hz, 0.25 H), 2.57 (d, *J* = 14.9 Hz, 0.75 H), 1.70 (br, 2 H), 1.27 (d, *J* = 6.8 Hz, 0.75 H), 1.27 (d, *J* = 6.7 Hz, 2.25 H), 0.10 (s, 2.25 H), 0.04 (s, 6.75 H).



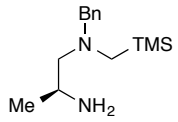
42-17-10-bhsieh.11.fid
Sample fly-10-135
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 175.7*, 137.3, 136.6*, 129.0*, 128.7, 127.81, 127.77*, 127.4, 126.4*, 52.8*, 50.3, 47.0, 46.9*, 38.9*, 37.6, 22.2*, 21.4, -1.2*, -1.5.



(*S*)-N^1-Benzyl-N^1-((trimethylsilyl)methyl)propane-1,2-diamine (10)

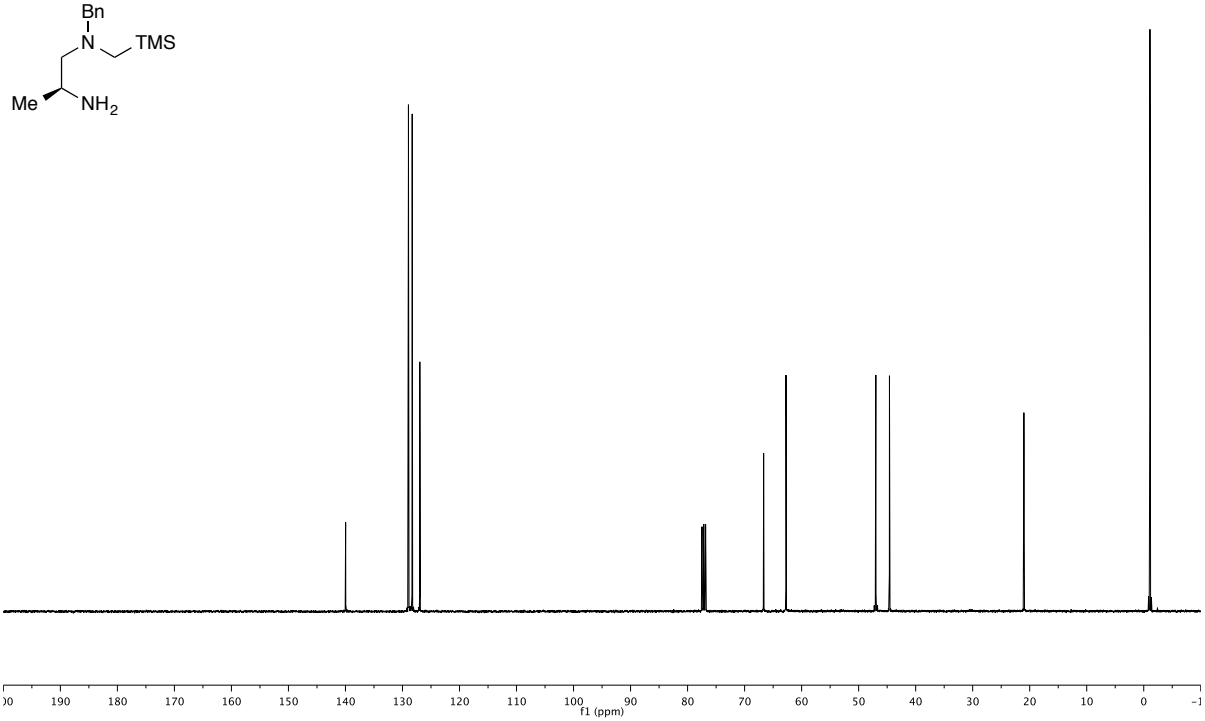
43-17-10-bhsieh.10.fid
Sample fly-10-137
group bode



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32, 7.31, 7.30, 7.29, 7.29, 7.29, 7.28, 7.28, 7.27, 7.27, 7.25, 7.24, 7.24, 7.23, 7.23, 7.23, 7.22, 7.22, 7.22, 7.21, 7.21, 7.21, 7.20, 3.74, 3.71, 3.28, 3.24, 3.02, 3.01, 3.01, 3.00, 3.00, 2.99, 2.99, 2.98, 2.97, 2.97, 2.96, 2.96, 2.95, 2.94, 2.20, 2.17, 2.17, 2.14, 2.13, 2.12, 2.10, 2.09, 2.08, 1.88, 1.86, 1.83, 0.97, 0.96, 0.07.

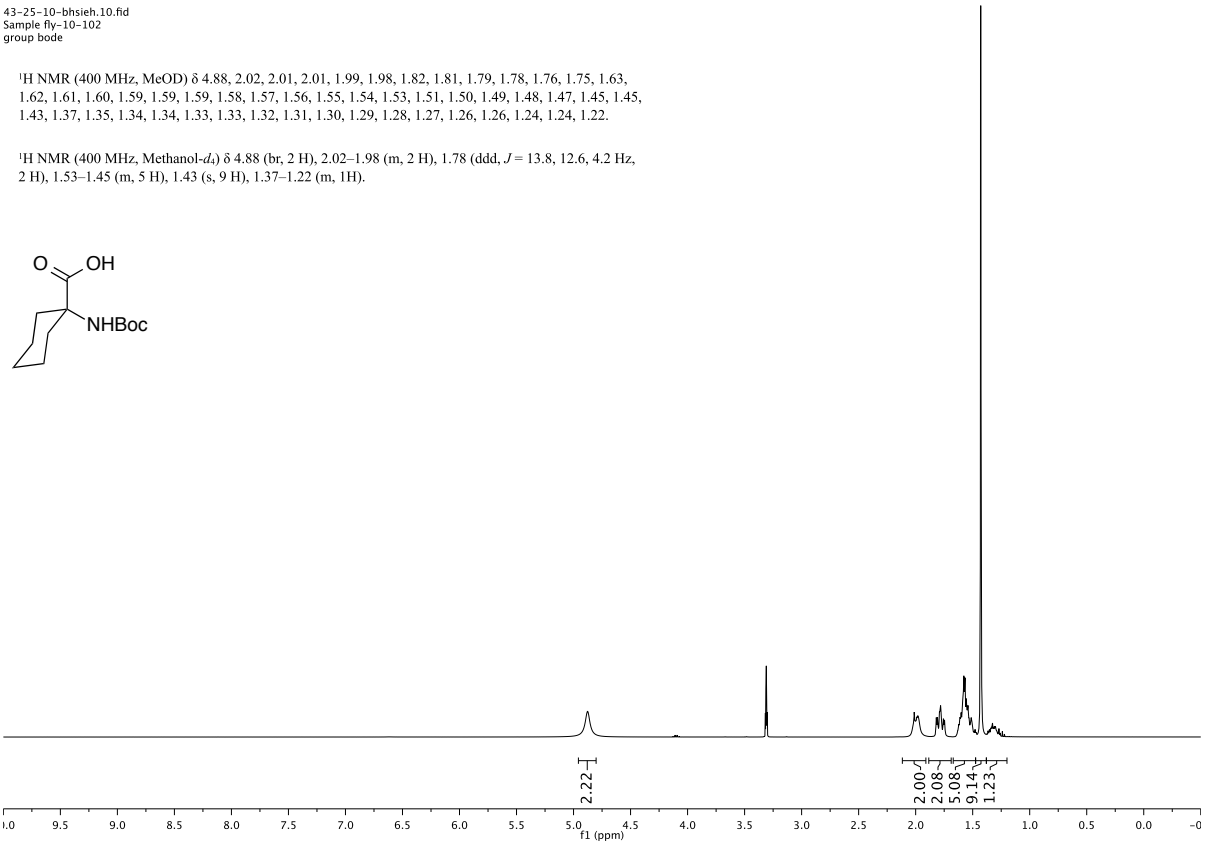
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32–7.27 (m, 4 H), 7.24–7.20 (m, 1 H), 3.73 (d, *J* = 13.5 Hz, 1 H), 3.26 (d, *J* = 13.5 Hz, 1 H), 3.02–2.94 (m, 1 H), 2.17 (dd, *J* = 12.2, 9.1 Hz, 1 H), 2.11 (dd, *J* = 12.2, 4.4 Hz, 1 H), 2.10 (d, *J* = 14.8 Hz, 1 H), 1.88 (br, 2 H), 1.85 (d, *J* = 14.8 Hz, 1 H), 0.97 (d, *J* = 6.4 Hz, 3 H), 0.07 (s, 9 H).

43-17-10-bhsieh.11.fid
Sample fly-10-137
group bode



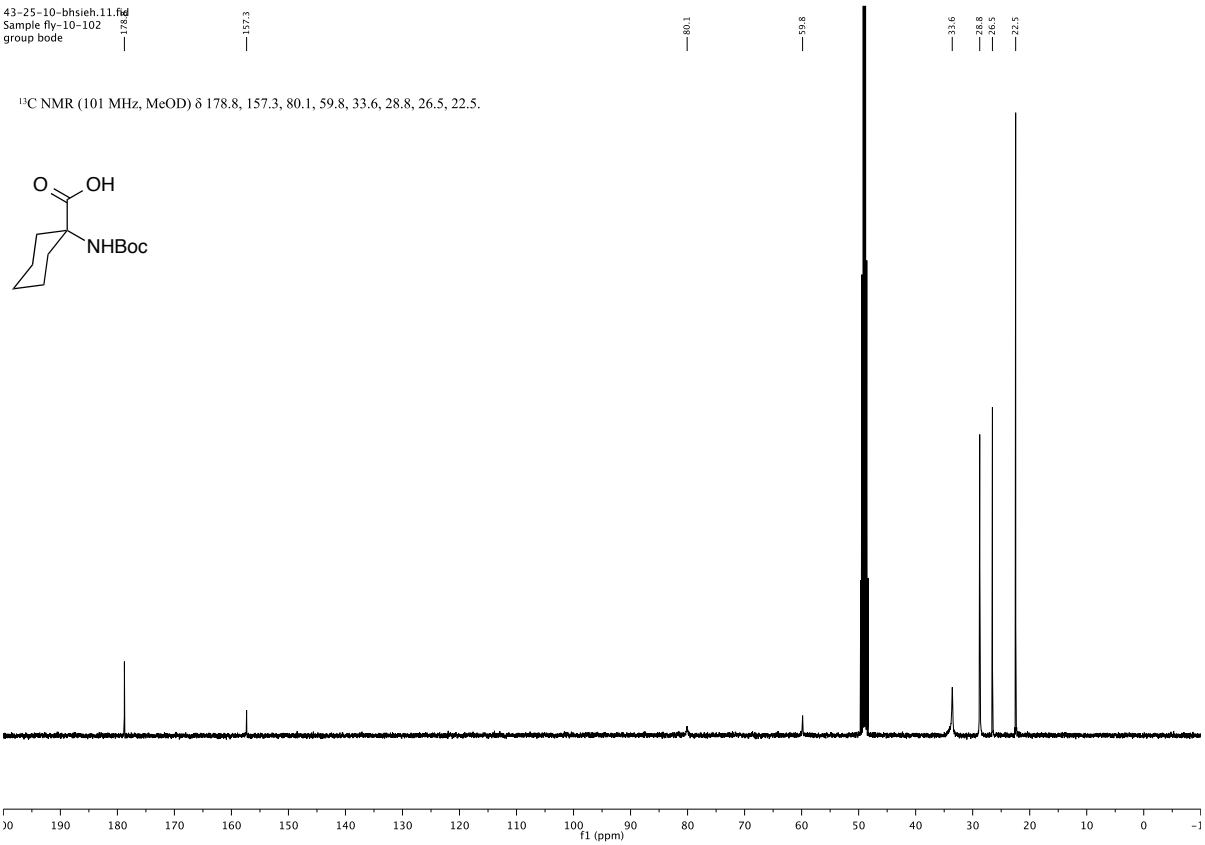
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 129.0, 128.3, 127.0, 66.7, 62.7, 47.0, 44.6, 21.0, -1.1.

1-((*tert*-Butoxycarbonyl)amino)cyclohexanecarboxylic acid (S6)



^{1}H NMR (400 MHz, MeOD) δ 4.88, 2.02, 2.01, 2.01, 1.99, 1.98, 1.82, 1.81, 1.79, 1.78, 1.76, 1.75, 1.63, 1.62, 1.61, 1.60, 1.59, 1.59, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53, 1.51, 1.50, 1.49, 1.48, 1.47, 1.45, 1.45, 1.43, 1.37, 1.35, 1.34, 1.34, 1.33, 1.33, 1.32, 1.31, 1.30, 1.29, 1.28, 1.27, 1.26, 1.26, 1.24, 1.24, 1.22.

^{1}H NMR (400 MHz, Methanol-d_4) δ 4.88 (br, 2 H), 2.02–1.98 (m, 2 H), 1.78 (ddd, J = 13.8, 12.6, 4.2 Hz, 2 H), 1.53–1.45 (m, 5 H), 1.43 (s, 9 H), 1.37–1.22 (m, 1H).



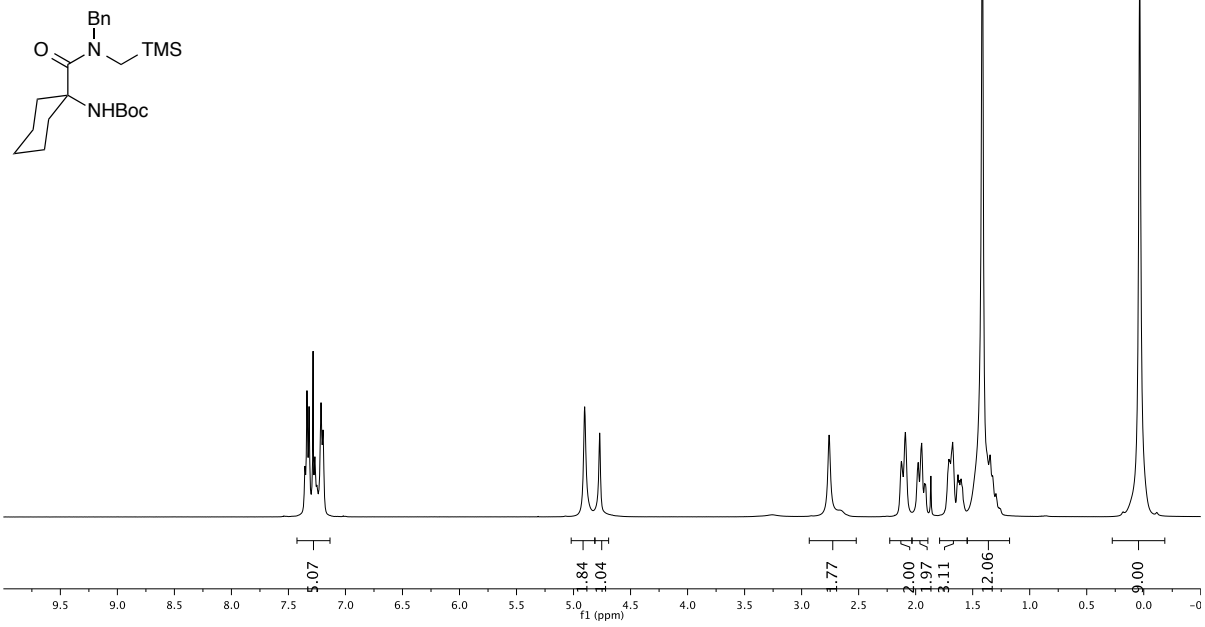
^{13}C NMR (101 MHz, MeOD) δ 178.8, 157.3, 80.1, 59.8, 33.6, 28.8, 26.5, 22.5.

tert-Butyl (1-(benzyl((trimethylsilyl)methyl)carbamoyl)cyclohexyl)carbamate (S7)

55-17-10-bhsieh.10.fid
Sample fly-10-111
group bode
PRO CDCl3 /opt/v bhsieh 55

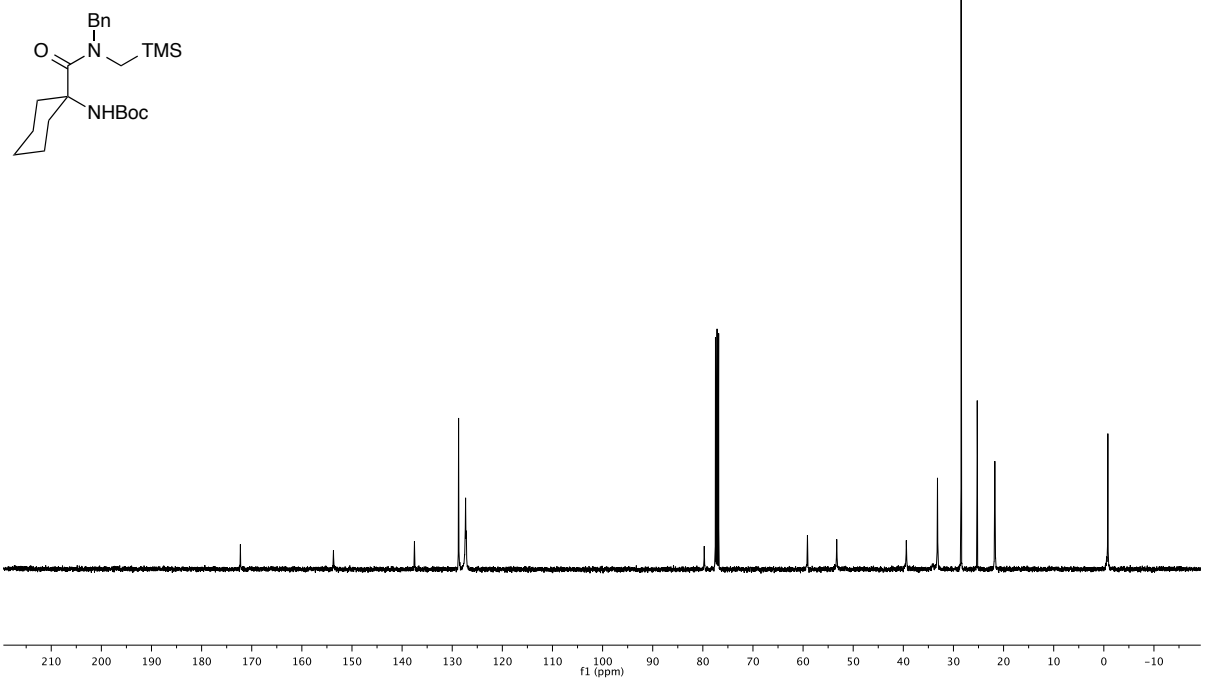
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36, 7.34, 7.32, 7.29, 7.28, 7.27, 7.25, 7.21, 7.20, 4.90, 4.77, 2.76, 2.13, 2.09, 1.99, 1.98, 1.96, 1.95, 1.92, 1.91, 1.72, 1.71, 1.70, 1.69, 1.67, 1.67, 1.64, 1.63, 1.62, 1.61, 1.60, 1.59, 1.42, 1.35, 1.32, 1.32, 1.30, 1.29, 0.04.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36–7.20 (m, 5 H), 4.90 (s, 2 H), 4.77 (br, 1 H), 2.76 (s, 2 H), 2.11 (apparent d, *J* = 13.8 Hz, 2 H), 1.96 (apparent dt, *J* = 13.8, 6.8 Hz, 2 H), 1.72–1.59 (m, 3 H), 1.42 (s, 9 H), 1.35–1.29 (m, 3 H), 0.04 (s, 9 H).



55-17-10-bhsieh.11.fid
Sample fly-10-111
group bode
CAR CDCl3 /opt/v bhsieh 55

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 153.7, 137.5, 128.7, 127.3, 127.2, 79.7, 59.1, 53.3, 39.4, 33.2, 28.5, 25.3, 21.7, -0.8.

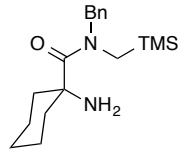


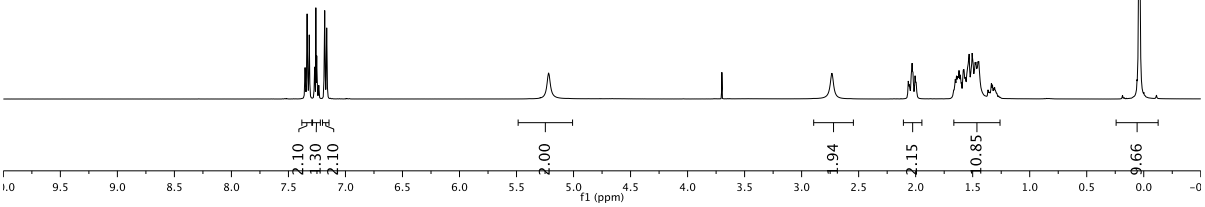
1-Amino-*N*-benzyl-*N*-((trimethylsilyl)methyl)cyclohexanecarboxamide (S8)

44-17-10-bhsieh.10.fid
Sample fly-10-153
group bode

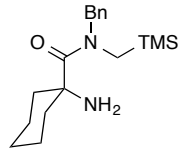
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36, 7.35, 7.35, 7.34, 7.34, 7.33, 7.32, 7.32, 7.31, 7.27, 7.27, 7.27, 7.26, 7.25, 7.25, 7.24, 7.23, 7.23, 7.19, 7.18, 7.18, 7.17, 7.17, 7.16, 5.22, 2.73, 2.07, 2.06, 2.04, 2.03, 2.02, 2.01, 2.00, 1.67, 1.66, 1.65, 1.65, 1.64, 1.64, 1.63, 1.62, 1.61, 1.60, 1.58, 1.58, 1.56, 1.55, 1.54, 1.54, 1.53, 1.51, 1.50, 1.50, 1.49, 1.48, 1.47, 1.45, 1.45, 1.44, 1.37, 1.36, 1.35, 1.35, 1.34, 1.34, 1.33, 1.33, 1.32, 1.31, 1.31, 1.30, 1.30, 1.29, 0.04.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36–7.31 (m, 2 H), 7.27–7.23 (m, 1 H), 7.19–7.16 (m, 2 H), 5.22 (s, 2 H), 2.73 (s, 2 H), 2.03 (ddd, *J* = 13.9, 10.5, 3.7 Hz, 1 H), 1.67–1.29 (m, 10 H), 0.04 (s, 9 H).

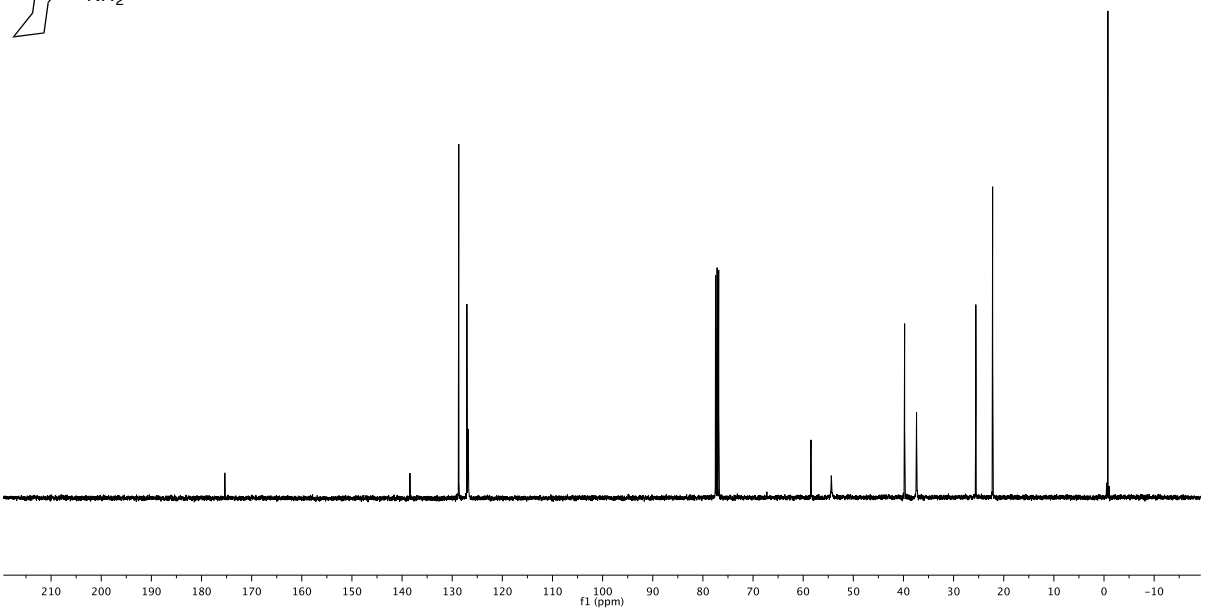




44-17-10-bhsieh.11.fid
Sample fly-10-153
group bode



^{13}C NMR (101 MHz, $CDCl_3$) δ 175.3, 138.4, 128.7, 127.1, 126.8, 58.4, 54.4, 39.8, 37.4, 25.6, 22.2, -0.8.

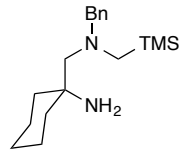


1-((Benzyl((trimethylsilyl)methyl)amino)methyl)cyclohexanamine (11)

16-21-08-bhsieh.10.fid
Sample fly-10-159
group bode
PRO CDCl3 /opt/v bhsieh 16

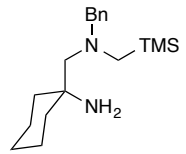
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36, 7.35, 7.35, 7.34, 7.33, 7.33, 7.32, 7.31, 7.31, 7.31, 7.30, 7.29, 7.29, 7.26, 7.25, 7.25, 7.24, 7.24, 7.23, 7.22, 3.61, 2.37, 2.23, 1.52, 1.51, 1.50, 1.50, 1.49, 1.49, 1.48, 1.47, 1.47, 1.46, 1.45, 1.44, 1.44, 1.43, 1.41, 1.40, 1.38, 1.37, 1.36, 1.35, 1.29, 1.28, 1.28, 1.26, 1.24, 1.24, 1.22, 1.22, 1.21, 1.20, 1.20, 1.19, 1.19, 1.18, 0.12.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36–7.29 (m, 4 H), 7.26–7.22 (m, 1 H), 3.61 (s, 2 H), 2.37 (s, 2 H), 2.23 (s, 2 H), 1.52–1.35 (m, 5 H), 1.29–1.18 (m, 7 H), 0.12 (s, 9 H).



16-21-08-bhsieh.11.fid
Sample fly-10-159
group bode
CAR CDCl3 /opt/v bhsieh 16

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 129.2, 128.2, 126.9, 69.6, 64.5, 52.0, 50.8, 37.6, 26.2, 22.0, -0.8.

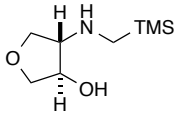


trans-4-(((Trimethylsilyl)methyl)amino)tetrahydrofuran-3-ol (S9)

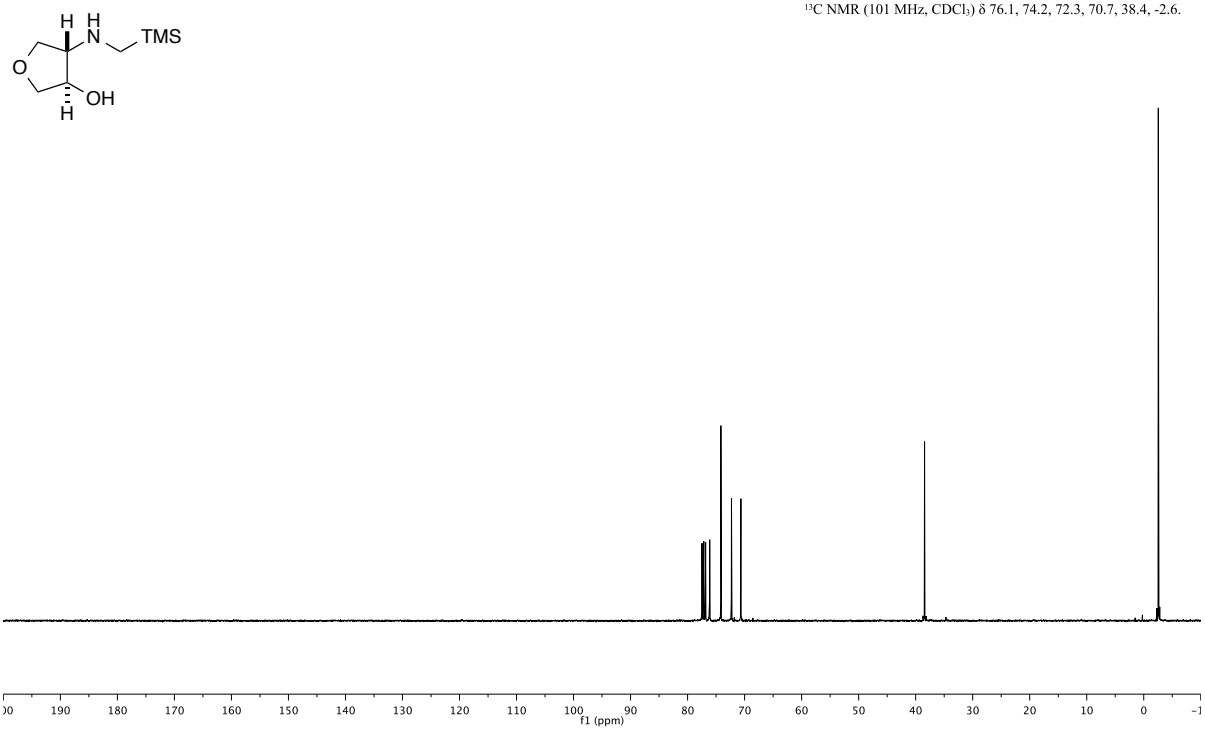
48-17-10-bhsieh.10.fid
Sample fly-10-024
group bode
PRO CDCl3 /opt/v bhsieh 48

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14, 4.14, 4.14, 4.13, 4.13, 4.13, 4.12, 4.06, 4.05, 4.04, 4.02, 3.97, 3.95, 3.94, 3.93, 3.66, 3.66, 3.64, 3.63, 3.57, 3.56, 3.54, 3.53, 3.10, 3.09, 3.09, 3.08, 3.08, 3.08, 3.07, 2.20, 2.05, 0.02.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.13 (ddd, *J* = 4.3, 2.7, 1.3 Hz, 1 H), 4.04 (dd, *J* = 9.1, 5.6 Hz, 1 H), 3.95 (dd, *J* = 9.8, 4.6 Hz, 1 H), 3.65 (dd, *J* = 9.8, 2.7 Hz, 1 H), 3.55 (dd, *J* = 9.1, 3.4 Hz, 1 H), 3.08 (ddd, *J* = 5.6, 3.4, 1.3 Hz, 1 H), 2.20 (br, 2 H), 2.05 (s, 2 H), 0.02 (s, 9 H).



48-17-10-bhsieh.11.fid
Sample fly-10-024
group bode
CAR CDCl3 /opt/v bhsieh 48



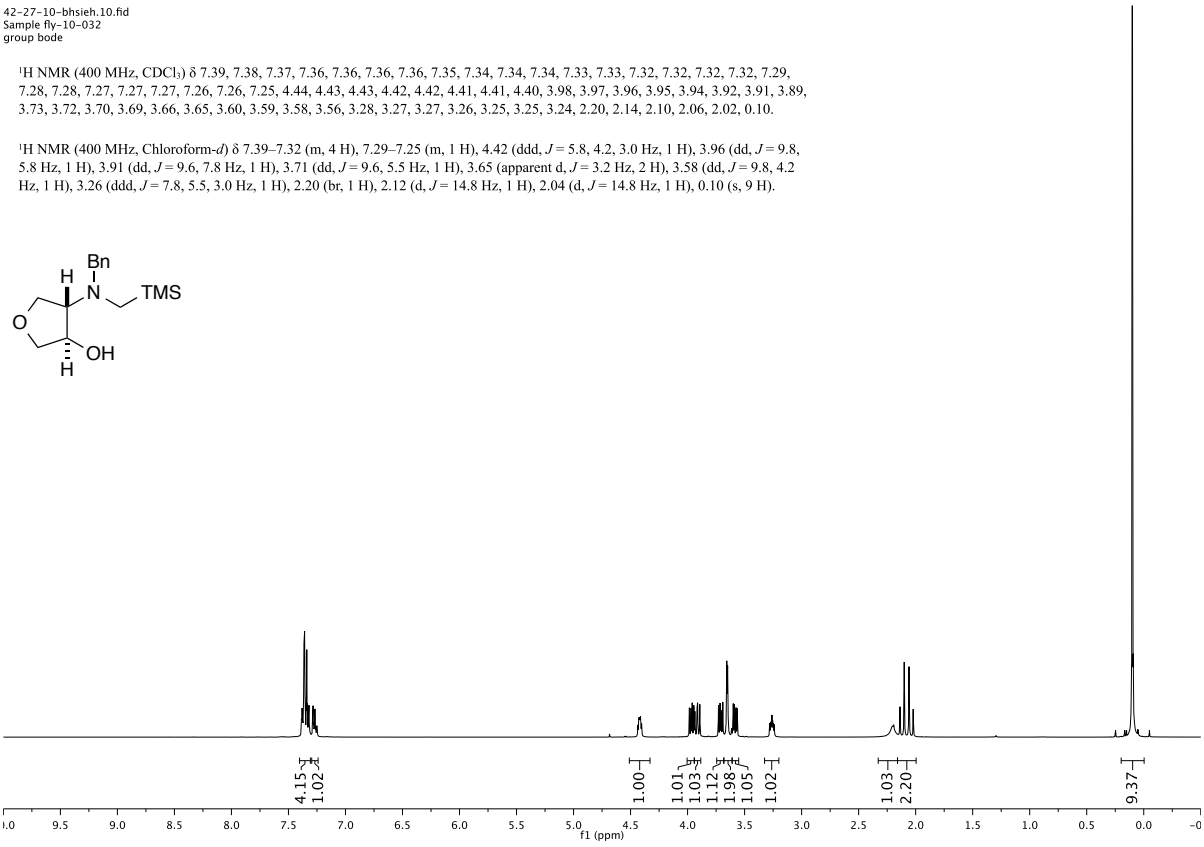
^{13}C NMR (101 MHz, $CDCl_3$) δ 76.1, 74.2, 72.3, 70.7, 38.4, -2.6.

trans-4-(Benzyl((trimethylsilyl)methyl)amino)tetrahydrofuran-3-ol (S10)

42-27-10-bhsieh.10.fid
Sample fly-10-032
group bode

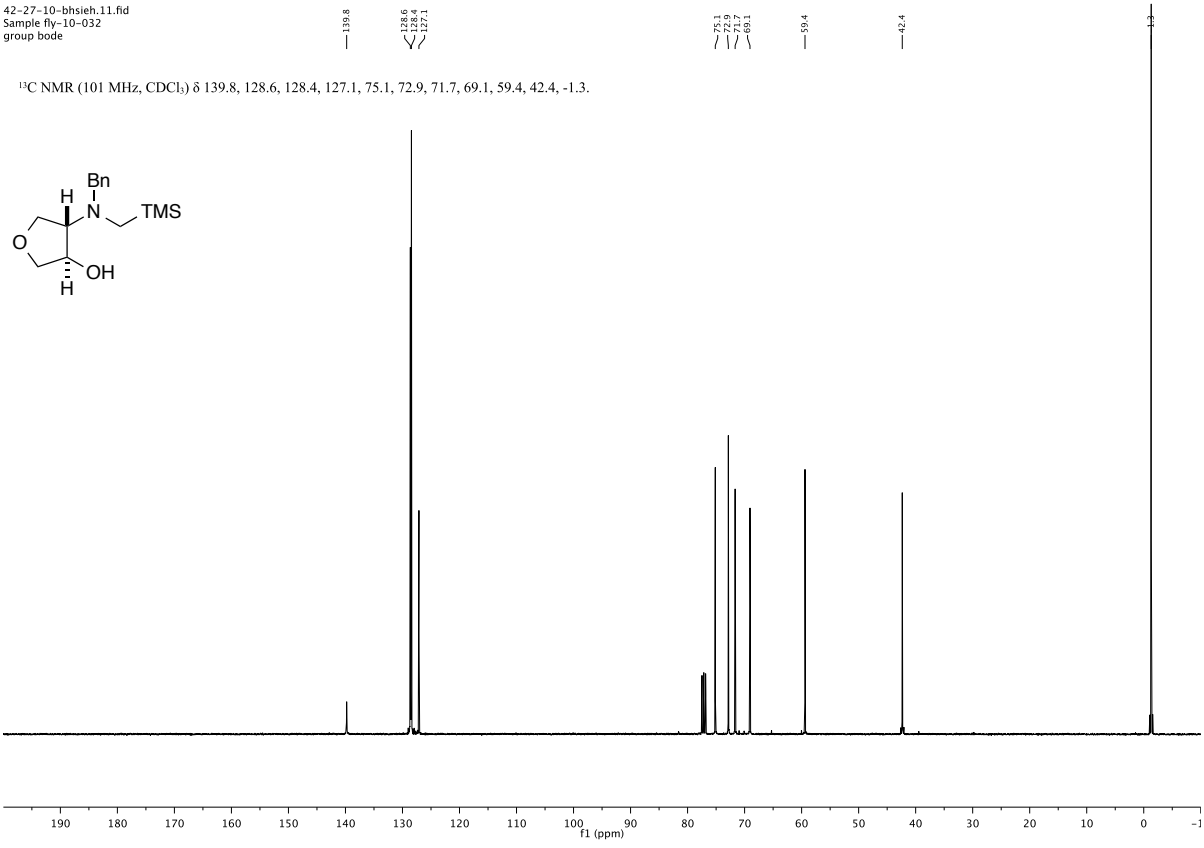
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39, 7.38, 7.37, 7.36, 7.36, 7.36, 7.36, 7.35, 7.34, 7.34, 7.34, 7.33, 7.33, 7.32, 7.32, 7.32, 7.32, 7.29, 7.28, 7.28, 7.27, 7.27, 7.27, 7.26, 7.26, 7.25, 4.44, 4.43, 4.43, 4.42, 4.42, 4.41, 4.41, 4.40, 3.98, 3.97, 3.96, 3.95, 3.94, 3.92, 3.91, 3.89, 3.73, 3.72, 3.70, 3.69, 3.66, 3.65, 3.60, 3.59, 3.58, 3.56, 3.28, 3.27, 3.27, 3.26, 3.25, 3.25, 3.24, 2.20, 2.14, 2.10, 2.06, 2.02, 0.10.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39–7.32 (m, 4 H), 7.29–7.25 (m, 1 H), 4.42 (ddd, *J* = 5.8, 4.2, 3.0 Hz, 1 H), 3.96 (dd, *J* = 9.8, 5.8 Hz, 1 H), 3.91 (dd, *J* = 9.6, 7.8 Hz, 1 H), 3.71 (dd, *J* = 9.6, 5.5 Hz, 1 H), 3.65 (apparent d, *J* = 3.2 Hz, 2 H), 3.58 (dd, *J* = 9.8, 4.2 Hz, 1 H), 3.26 (ddd, *J* = 7.8, 5.5, 3.0 Hz, 1 H), 2.20 (br, 1 H), 2.12 (d, *J* = 14.8 Hz, 1 H), 2.04 (d, *J* = 14.8 Hz, 1 H), 0.10 (s, 9 H).



42-27-10-bhsieh.11.fid
Sample fly-10-032
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 128.6, 128.4, 127.1, 75.1, 72.9, 71.7, 69.1, 59.4, 42.4, -1.3.

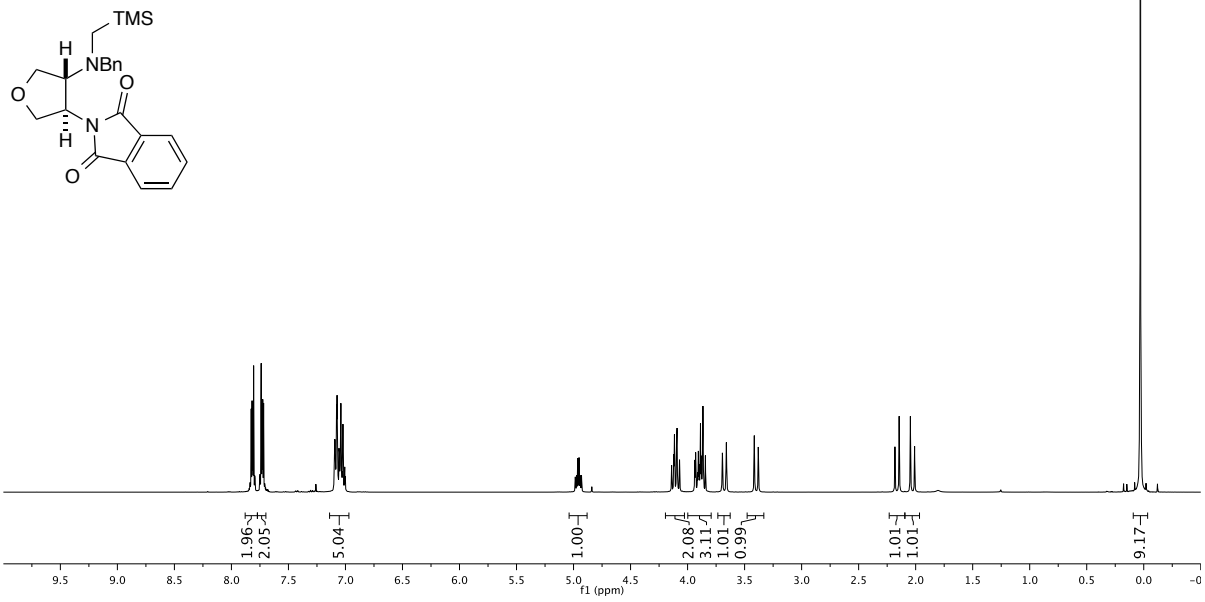


2-(*trans*-4-(Benzyl((trimethylsilyl)methyl)amino)tetrahydrofuran-3-yl)isoindoline-1,3-dione (S11)

43-27-10-bhsieh.10.fid
Sample fly-10-039
group bode

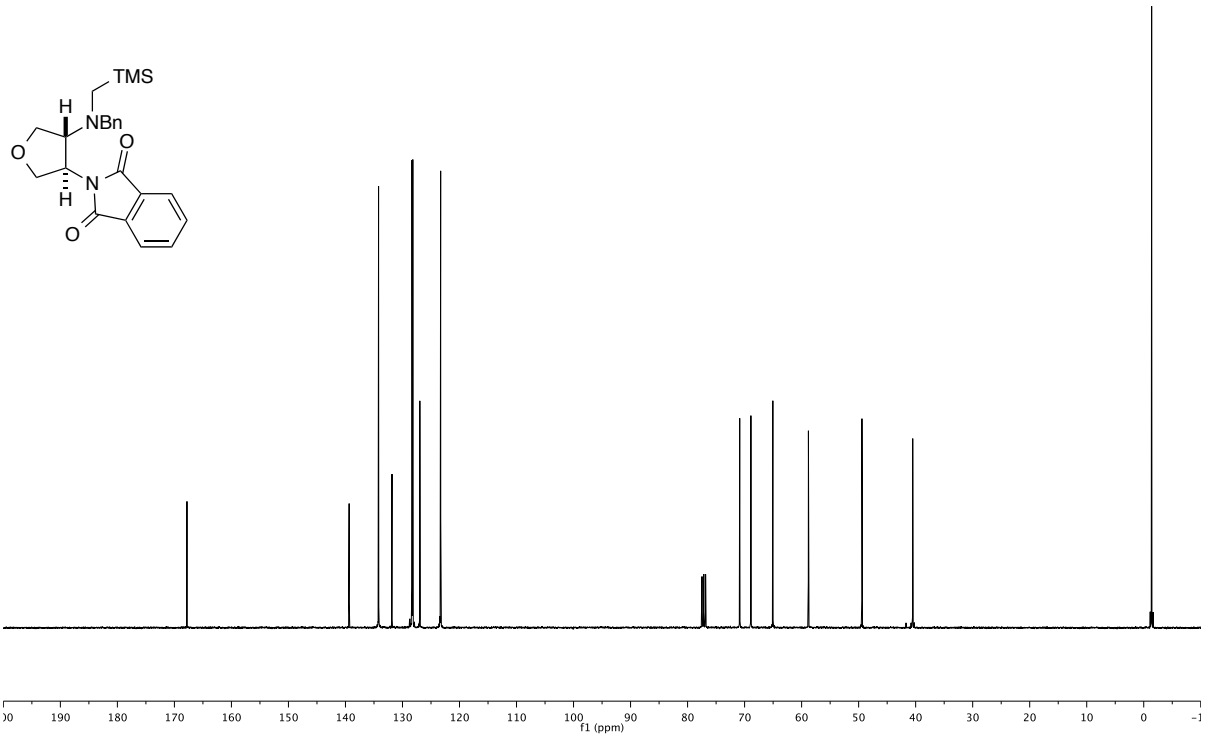
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84, 7.83, 7.82, 7.81, 7.81, 7.81, 7.80, 7.79, 7.75, 7.75, 7.74, 7.73, 7.73, 7.73, 7.72, 7.71, 7.10, 7.09, 7.09, 7.08, 7.08, 7.07, 7.07, 7.06, 7.06, 7.05, 7.05, 7.05, 7.04, 7.04, 7.04, 7.03, 7.03, 7.02, 7.02, 7.01, 7.01, 7.00, 4.98, 4.97, 4.96, 4.95, 4.94, 4.93, 4.14, 4.12, 4.12, 4.10, 4.09, 4.07, 3.94, 3.93, 3.91, 3.91, 3.90, 3.89, 3.89, 3.88, 3.87, 3.87, 3.86, 3.84, 3.70, 3.66, 3.42, 3.38, 2.18, 2.15, 2.05, 2.01, 0.03.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84–7.79 (m, 2 H), 7.75–7.71 (m, 2 H), 7.10–7.00 (m, 5 H), 4.96 (ddd, *J* = 8.7, 8.7, 4.6 Hz, 1 H), 4.14–4.07 (m, 2 H), 3.99–3.84 (m, 3 H), 3.68 (d, *J* = 13.9 Hz, 1 H), 3.40 (d, *J* = 13.9 Hz, 1 H), 2.16 (d, *J* = 14.8 Hz, 1 H), 2.03 (d, *J* = 14.8 Hz, 1 H), 0.03 (s, 9 H).



43-27-10-bhsieh.11.fid
Sample fly-10-039
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 139.4, 134.2, 131.8, 128.3, 128.2, 127.0, 123.3, 70.9, 68.9, 65.1, 58.8, 49.4, 40.5, -1.4.

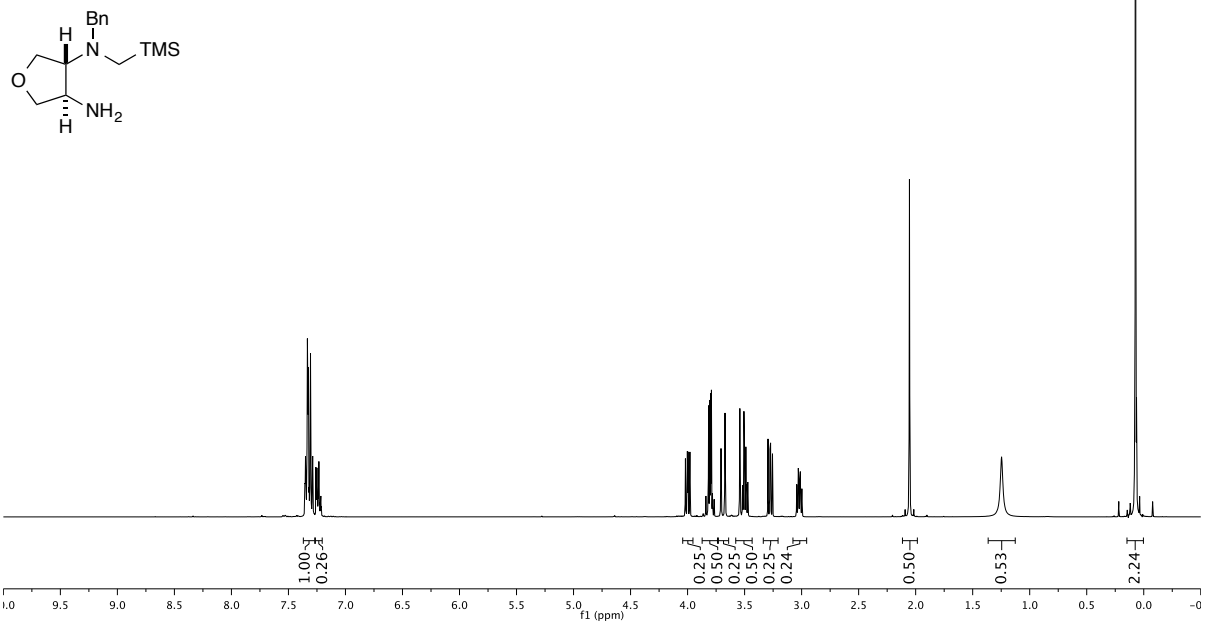


trans-N^3-Benzyl-N^3-((trimethylsilyl)methyl)tetrahydrofuran-3,4-diamine (12)

40-17-06-bhsieh.10.fid
Sample fly-10-042
group bode

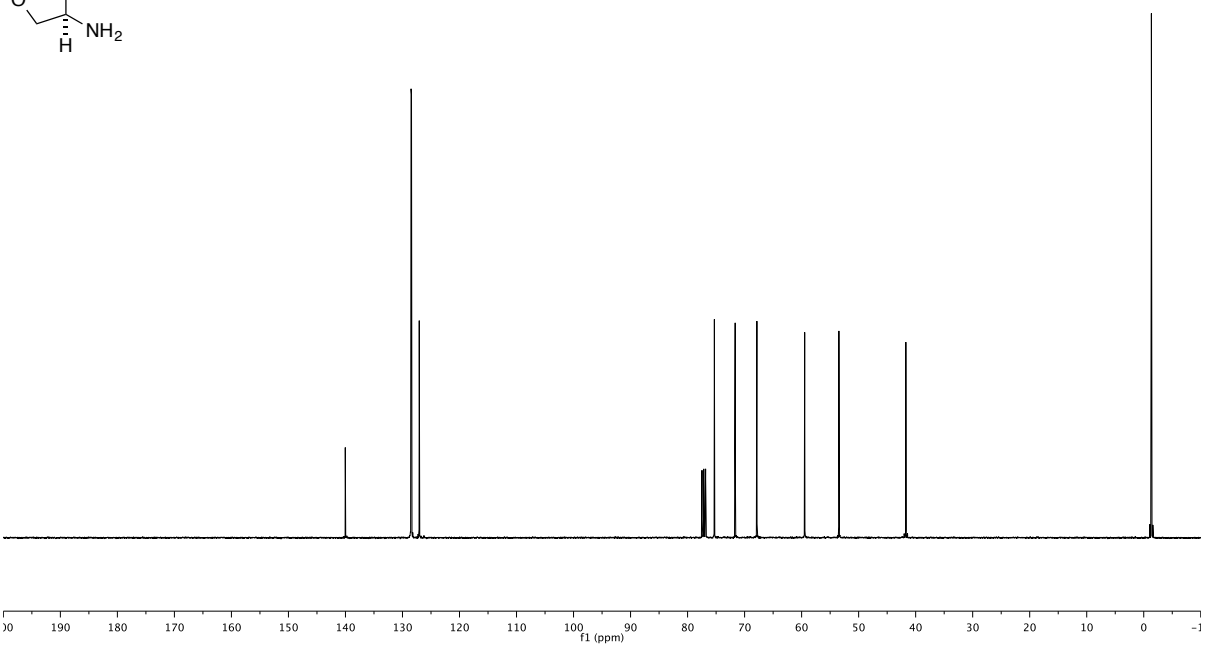
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36, 7.35, 7.35, 7.34, 7.33, 7.33, 7.33, 7.32, 7.32, 7.32, 7.31, 7.31, 7.31, 7.30, 7.29, 7.29, 7.29, 7.28, 7.26, 7.25, 7.25, 7.24, 7.24, 7.23, 7.23, 7.22, 7.22, 7.21, 4.02, 4.00, 4.00, 3.98, 3.84, 3.82, 3.82, 3.81, 3.80, 3.79, 3.78, 3.77, 3.71, 3.67, 3.54, 3.52, 3.51, 3.50, 3.49, 3.48, 3.47, 3.29, 3.28, 3.27, 3.26, 3.04, 3.03, 3.02, 3.02, 3.01, 3.00, 2.05, 1.25, 0.07.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36–7.29 (m, 4 H), 7.26–7.21 (m, 1 H), 4.00 (dd, *J* = 9.0, 6.7 Hz, 1 H), 3.84–3.77 (m, 2 H), 3.69 (d, *J* = 14.1 Hz, 1 H), 3.52 (d, *J* = 14.1 Hz, 1 H), 3.50 (apparent td, *J* = 6.7, 4.9 Hz, 1 H), 3.28 (dd, *J* = 9.0, 6.7 Hz, 1 H), 3.02 (apparent dt, *J* = 7.4, 5.6 Hz, 1 H), 2.05 (s, 2 H), 1.25 (br, 2 H), 0.07 (s, 9 H).

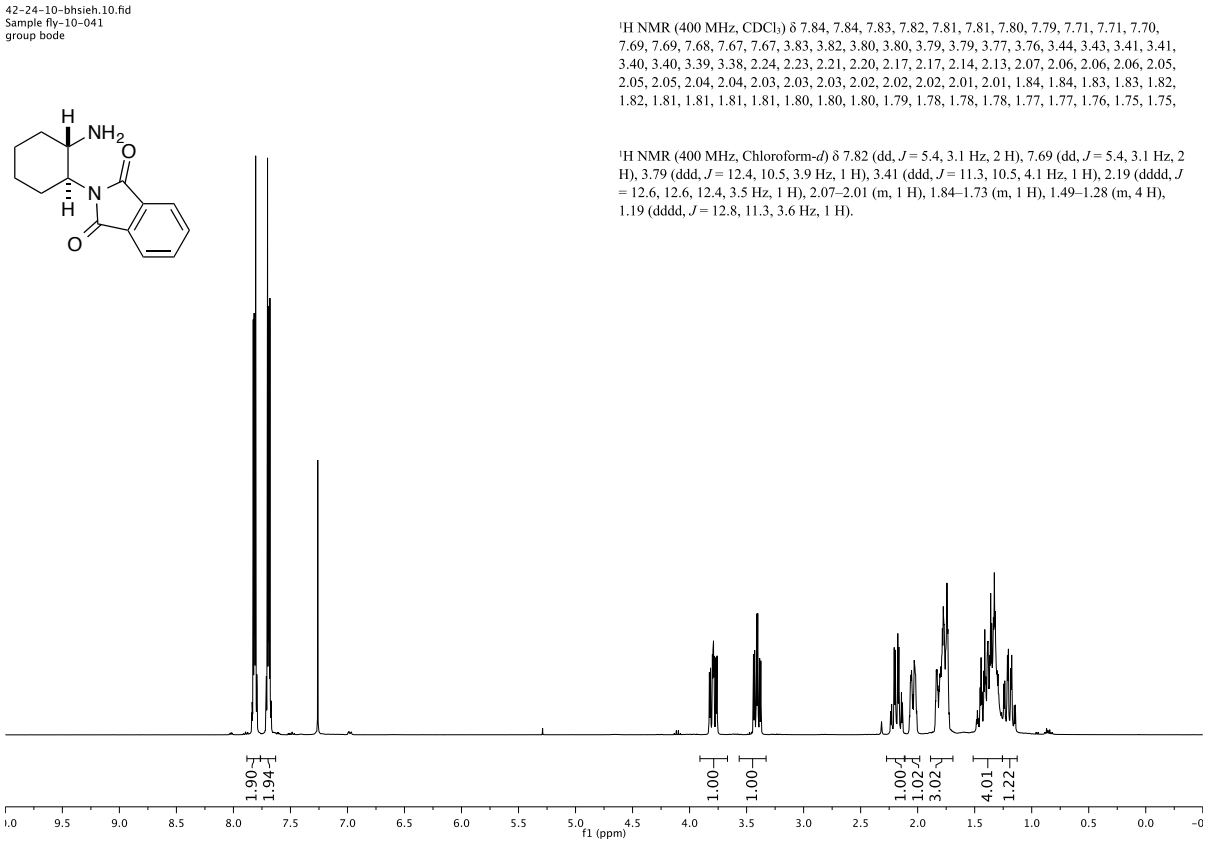


40-17-06-bhsieh.11.fid
Sample fly-10-042
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 128.5, 128.4, 127.1, 75.3, 71.7, 67.8, 59.5, 53.5, 41.7, -1.3.

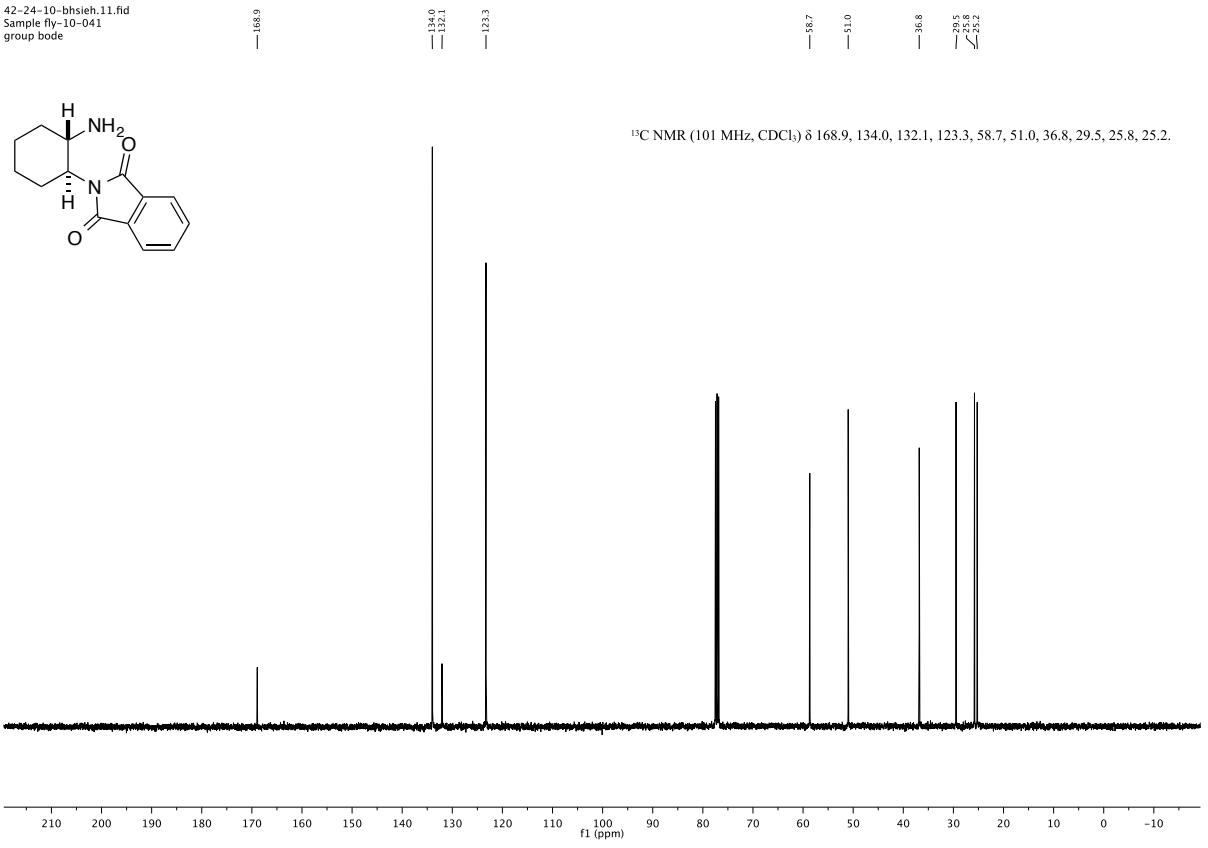


2-(*trans*-2-Aminocyclohexyl)isoindoline-1,3-dione (S12)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84, 7.84, 7.83, 7.82, 7.81, 7.81, 7.80, 7.79, 7.71, 7.71, 7.70, 7.69, 7.69, 7.68, 7.67, 7.67, 3.83, 3.82, 3.80, 3.80, 3.79, 3.79, 3.77, 3.76, 3.44, 3.43, 3.41, 3.41, 3.40, 3.40, 3.39, 3.38, 2.24, 2.23, 2.21, 2.20, 2.17, 2.17, 2.14, 2.13, 2.07, 2.06, 2.06, 2.06, 2.05, 2.05, 2.05, 2.04, 2.04, 2.03, 2.03, 2.03, 2.02, 2.02, 2.02, 2.01, 2.01, 1.84, 1.84, 1.83, 1.83, 1.82, 1.82, 1.81, 1.81, 1.81, 1.81, 1.80, 1.80, 1.80, 1.79, 1.78, 1.78, 1.78, 1.77, 1.77, 1.76, 1.75, 1.75,

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.69 (dd, *J* = 5.4, 3.1 Hz, 2 H), 3.79 (ddd, *J* = 12.4, 10.5, 3.9 Hz, 1 H), 3.41 (ddd, *J* = 11.3, 10.5, 4.1 Hz, 1 H), 2.19 (dddd, *J* = 12.6, 12.6, 12.4, 3.5 Hz, 1 H), 2.07–2.01 (m, 1 H), 1.84–1.73 (m, 1 H), 1.49–1.28 (m, 4 H), 1.19 (dddd, *J* = 12.8, 11.3, 3.6 Hz, 1 H).



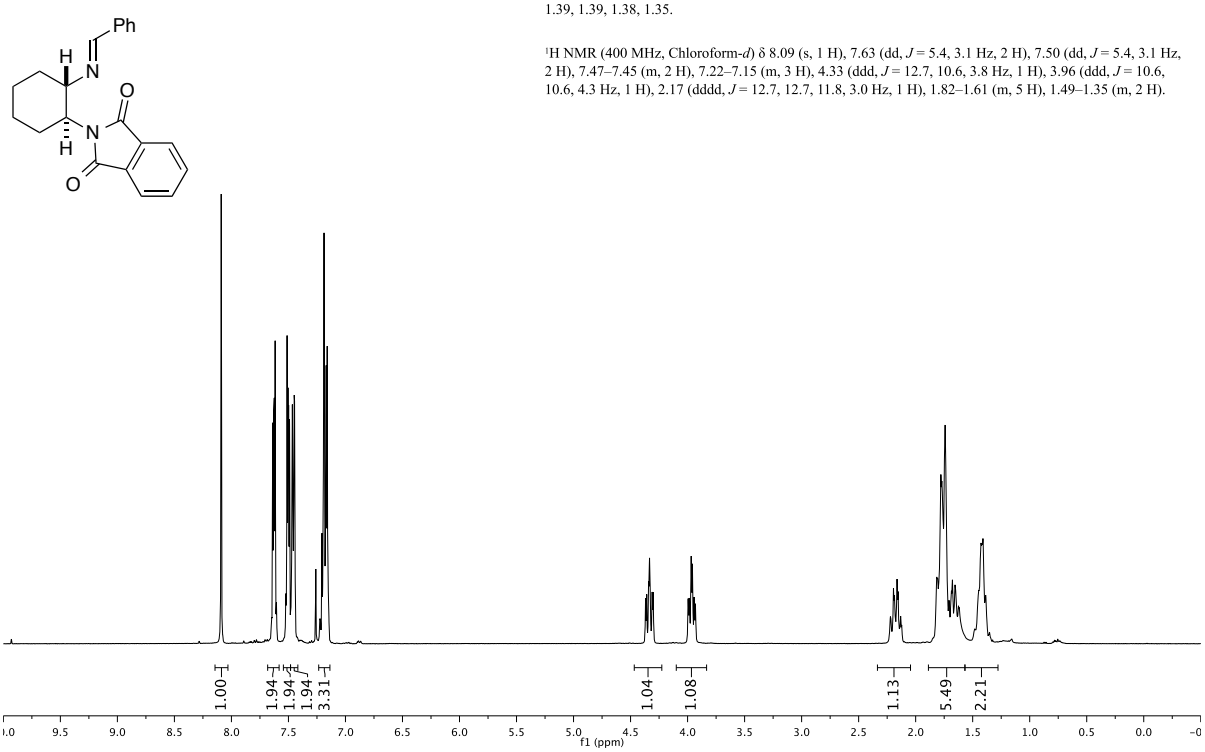
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 134.0, 132.1, 123.3, 58.7, 51.0, 36.8, 29.5, 25.8, 25.2.

2-(*trans*-2-(Benzylideneamino)cyclohexyl)isoindoline-1,3-dione (S13)

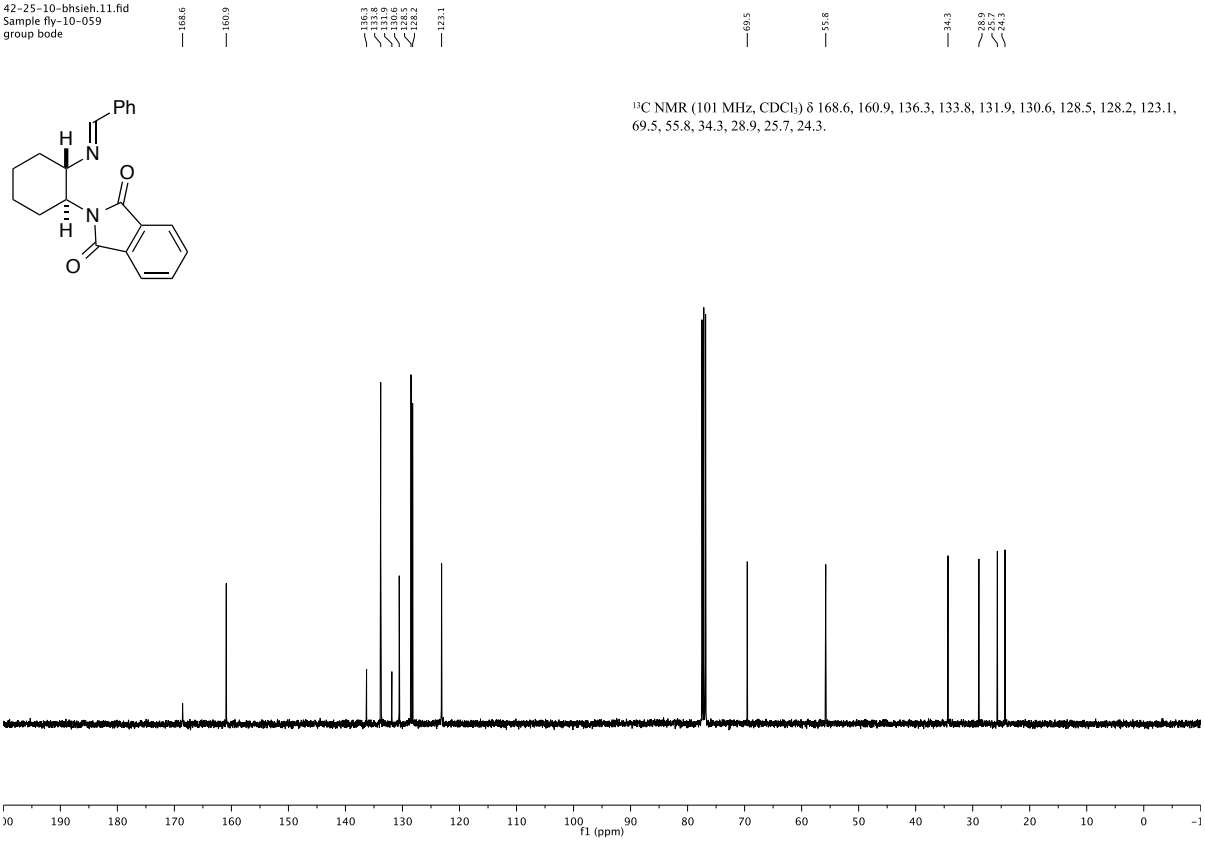
42-25-10-bhsieh.10.fid
Sample fly-10-059
group bode

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09, 7.64, 7.63, 7.62, 7.62, 7.51, 7.50, 7.50, 7.49, 7.47, 7.47, 7.45, 7.45, 7.22, 7.22, 7.21, 7.19, 7.17, 7.16, 7.15, 7.15, 4.37, 4.36, 4.34, 4.33, 4.33, 4.31, 4.30, 4.00, 3.98, 3.97, 3.96, 3.94, 3.93, 2.22, 2.22, 2.20, 2.19, 2.16, 2.15, 2.14, 2.13, 2.12, 1.82, 1.81, 1.80, 1.78, 1.77, 1.76, 1.75, 1.74, 1.73, 1.72, 1.71, 1.69, 1.69, 1.68, 1.66, 1.65, 1.62, 1.61, 1.49, 1.48, 1.46, 1.45, 1.45, 1.44, 1.43, 1.43, 1.42, 1.41, 1.39, 1.39, 1.38, 1.35.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (s, 1 H), 7.63 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.50 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.47–7.45 (m, 2 H), 7.22–7.15 (m, 3 H), 4.33 (ddd, *J* = 12.7, 10.6, 3.8 Hz, 1 H), 3.96 (ddd, *J* = 10.6, 10.6, 4.3 Hz, 1 H), 2.17 (dddd, *J* = 12.7, 12.7, 11.8, 3.0 Hz, 1 H), 1.82–1.61 (m, 5 H), 1.49–1.35 (m, 2 H).



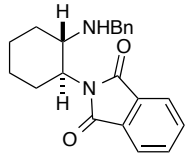
42-25-10-bhsieh.11.fid
Sample fly-10-059
group bode



^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 160.9, 136.3, 133.8, 131.9, 130.6, 128.5, 128.2, 123.1, 69.5, 55.8, 34.3, 28.9, 25.7, 24.3.

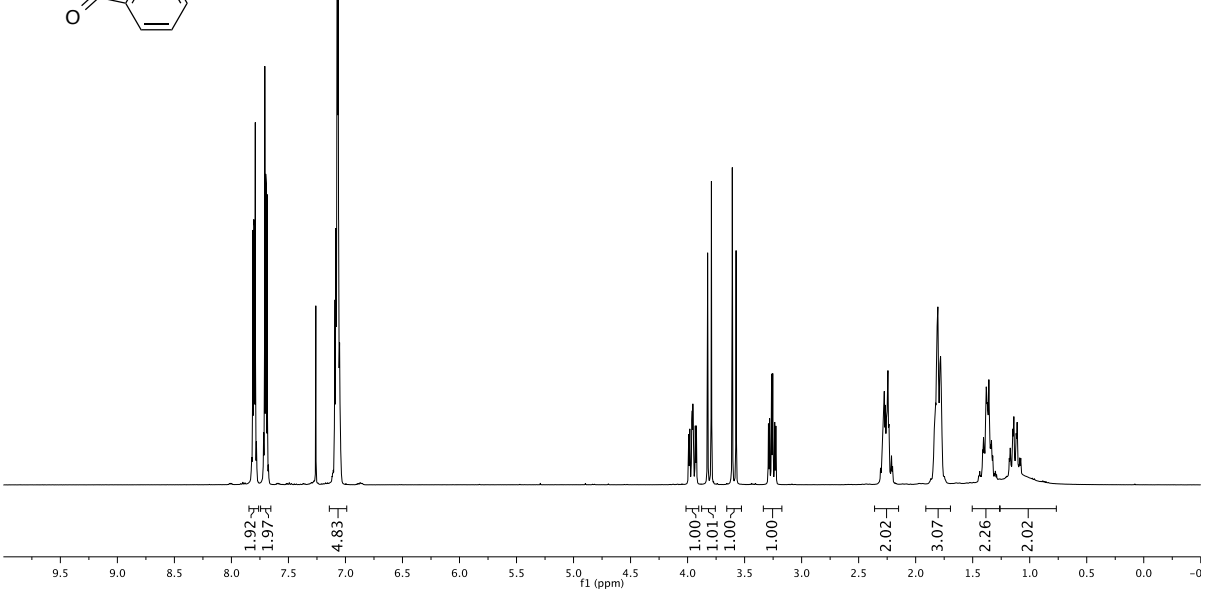
2-(*trans*-2-(Benzylamino)cyclohexyl)isoindoline-1,3-dione (S14)

5-25-08-bhsieh.10.fid
Sample fly-10-063-CC-washed
group bode
PRO CDCl3 /opt/v bhsieh 5

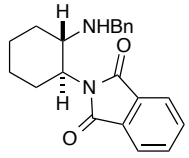


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81, 7.80, 7.80, 7.79, 7.71, 7.70, 7.69, 7.69, 7.10, 7.10, 7.09, 7.09, 7.08, 7.08, 7.07, 7.07, 7.06, 7.06, 7.05, 7.05, 7.05, 7.05, 7.04, 3.99, 3.98, 3.96, 3.96, 3.95, 3.95, 3.93, 3.92, 3.82, 3.79, 3.61, 3.57, 3.29, 3.28, 3.26, 3.25, 3.24, 3.23, 2.31, 2.30, 2.29, 2.28, 2.28, 2.27, 2.27, 2.26, 2.25, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 1.84, 1.84, 1.83, 1.82, 1.82, 1.82, 1.81, 1.80, 1.79, 1.79, 1.78, 1.78, 1.77, 1.77, 1.45, 1.44, 1.43, 1.41, 1.41, 1.40, 1.40, 1.39, 1.38, 1.37, 1.37, 1.36, 1.36, 1.35, 1.34, 1.34, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.18, 1.18, 1.17, 1.17, 1.16, 1.15, 1.15, 1.14, 1.14, 1.12, 1.12, 1.11, 1.11, 1.09, 1.09, 1.08.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.10–7.04 (m, 5 H), 3.96 (ddd, *J* = 12.4, 11.0, 3.9 Hz, 1 H), 3.81 (d, *J* = 13.2 Hz, 1 H), 3.59 (d, *J* = 13.2 Hz, 1 H), 3.26 (td, *J* = 11.0, 4.1 Hz, 1 H), 2.31–2.20 (m, 2 H), 1.84–1.77 (m, 3 H), 1.45–1.29 (m, 2 H), 1.18–1.08 (m, 2 H).



5-25-08-bhsieh.11.fid
Sample fly-10-063-CC-washed
group bode
CAR CDCl3 /opt/v bhsieh 5



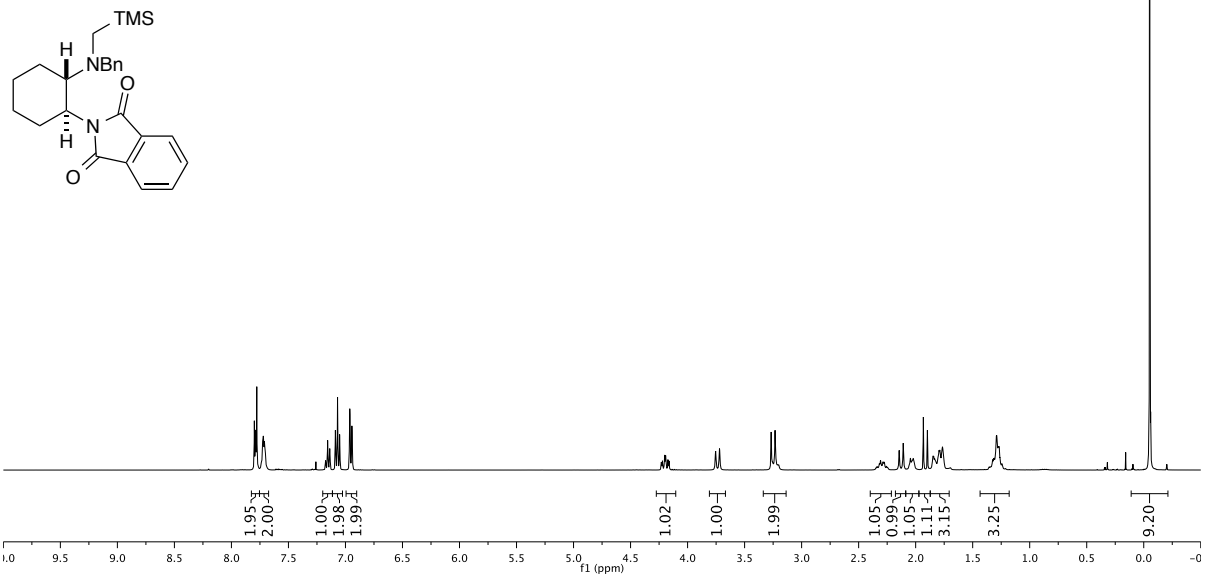
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 141.2, 133.8, 132.2, 128.2, 128.0, 126.7, 123.2, 56.5, 56.1, 50.7, 33.3, 29.6, 25.8, 25.2.

2-(*trans*-2-(Benzyl((trimethylsilyl)methyl)amino)cyclohexyl)isoindoline-1,3-dione (S15)

41-19-06-bhsieh.10.fid
Sample fly-10-050-CC
group bode

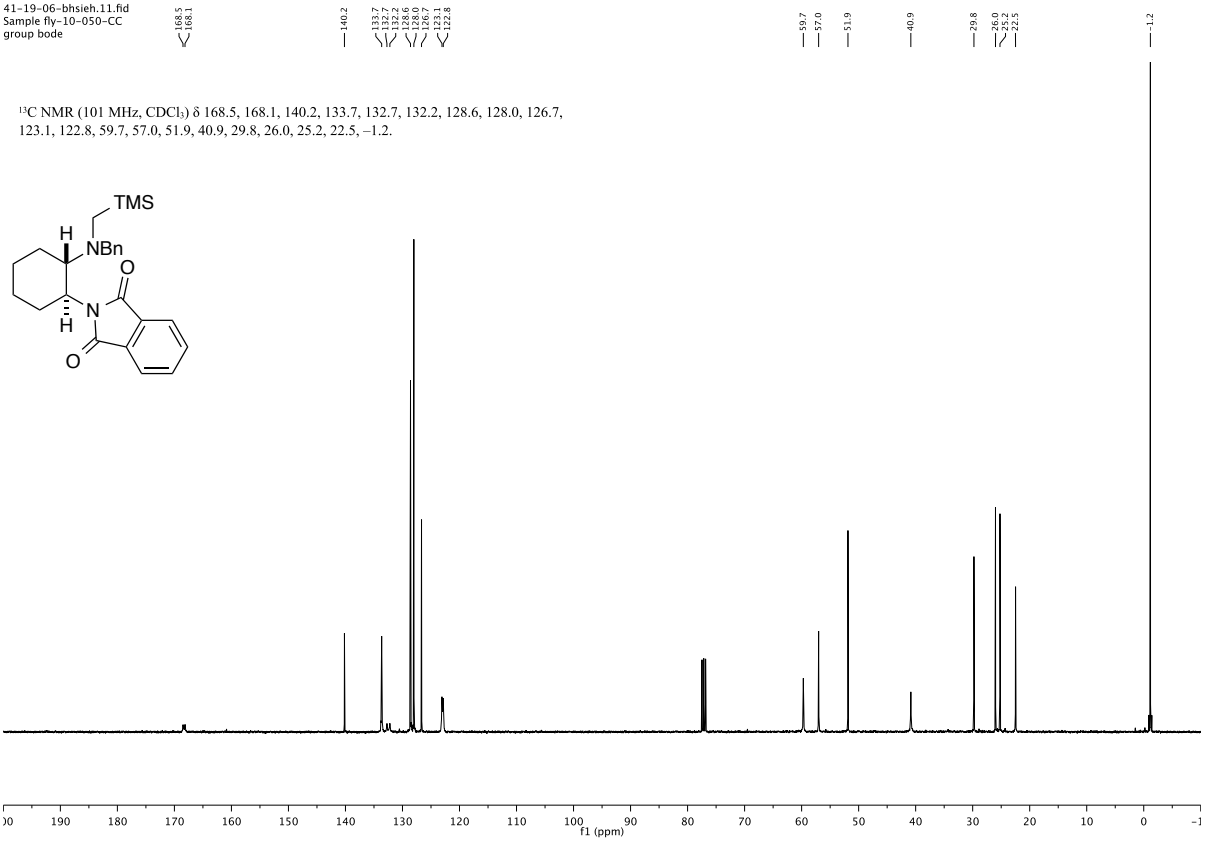
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80, 7.79, 7.78, 7.73, 7.72, 7.72, 7.72, 7.71, 7.70, 7.70, 7.17, 7.16, 7.16, 7.15, 7.14, 7.14, 7.13, 7.09, 7.08, 7.07, 7.07, 7.07, 7.06, 7.05, 7.05, 7.05, 6.96, 6.96, 6.96, 6.95, 6.94, 6.94, 4.23, 4.22, 4.20, 4.20, 4.19, 4.19, 4.17, 4.16, 3.75, 3.72, 3.27, 3.25, 3.23, 3.21, 3.20, 2.35, 2.34, 2.33, 2.32, 2.31, 2.29, 2.28, 2.27, 2.26, 2.26, 2.25, 2.24, 2.14, 2.11, 2.06, 2.05, 2.05, 2.04, 2.03, 2.02, 1.93, 1.90, 1.86, 1.85, 1.84, 1.83, 1.83, 1.82, 1.80, 1.80, 1.79, 1.78, 1.77, 1.76, 1.76, 1.75, 1.36, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.30, 1.29, 1.29, 1.28, 1.27, 1.26, 1.26, 1.25, 1.24, 1.24, -0.05.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80–7.78 (m, 2 H), 7.73–7.70 (m, 2 H), 7.17–7.13 (m, 1 H), 7.09– 7.05 (m, 2 H), 6.96–6.94 (m, 2 H), 4.20 (ddd, *J* = 12.1, 10.8, 3.9 Hz, 1 H), 3.74 (d, *J* = 13.6 Hz, 1 H), 3.25 (d, *J* = 13.6 Hz, 1 H), 3.25–3.20 (m, 1 H), 2.35–2.24 (m, 1 H), 2.13 (d, *J* = 14.2 Hz, 1 H), 2.06–2.02 (m, 1 H), 1.91 (d, *J* = 14.2 Hz, 1 H), 1.86–1.75 (m, 3 H), 1.36–1.24 (m, 3 H), –0.05 (s, 9 H).

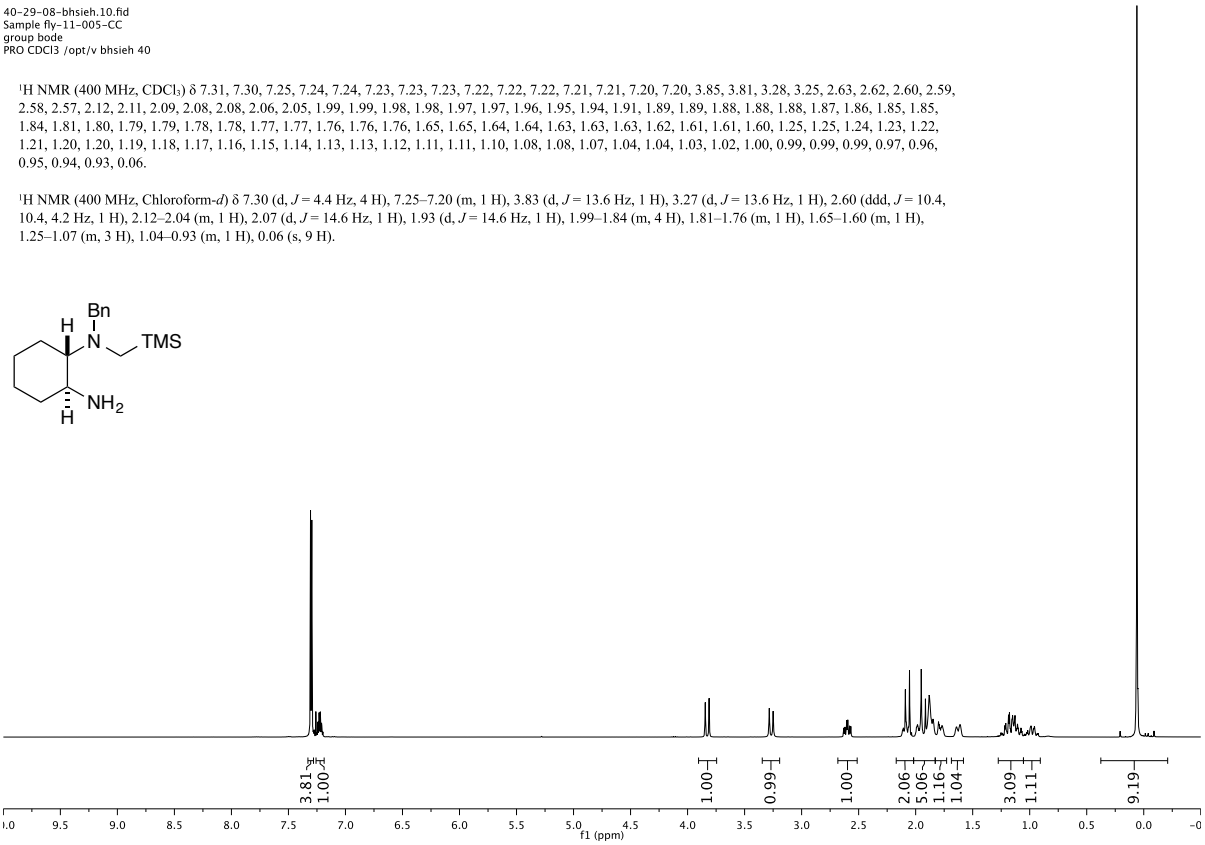


41-19-06-bhsieh.11.fid
Sample fly-10-050-CC
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 168.1, 140.2, 133.7, 132.7, 132.2, 128.6, 128.0, 126.7, 123.1, 122.8, 59.7, 57.0, 51.9, 40.9, 29.8, 26.0, 25.2, 22.5, –1.2.

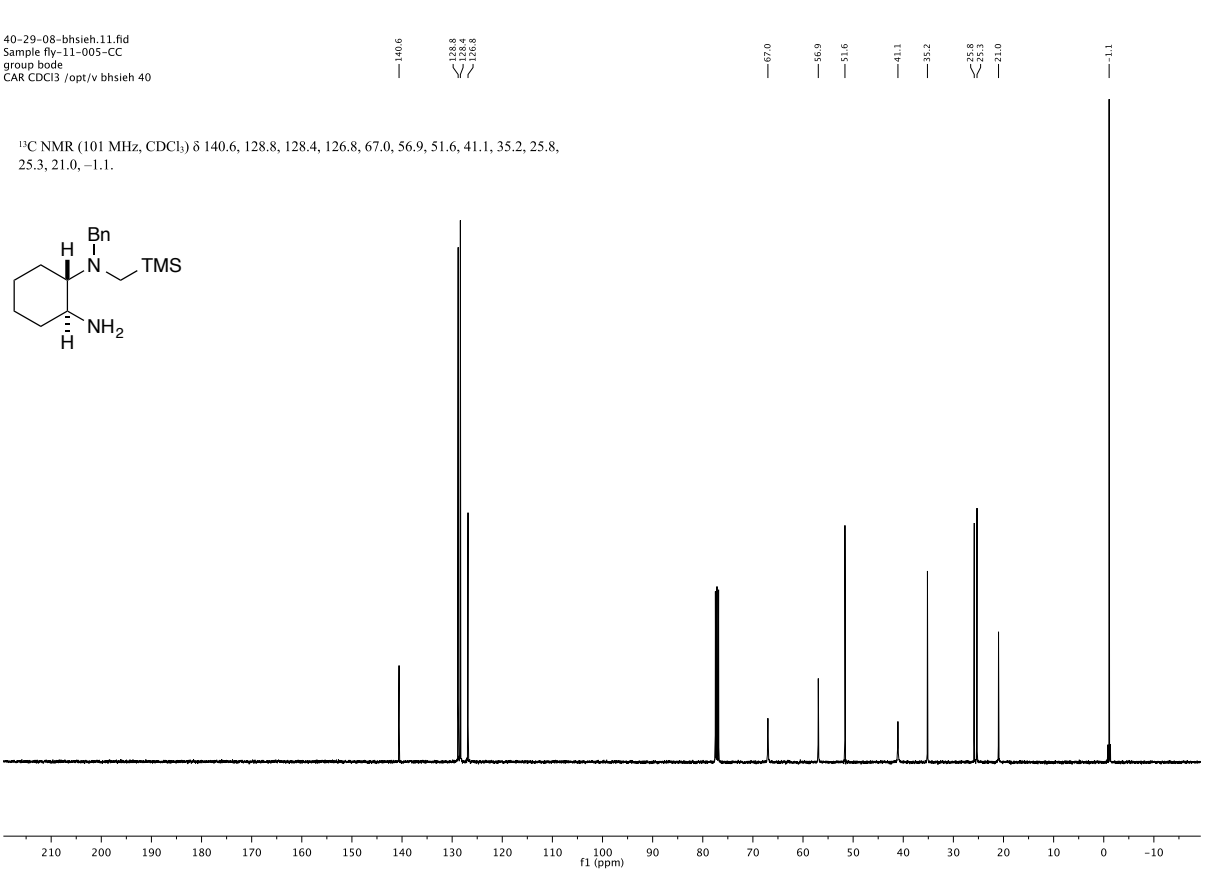


trans-N^1-Benzyl-N^1-((trimethylsilyl)methyl)cyclohexane-1,2-diamine (13)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31, 7.30, 7.25, 7.24, 7.24, 7.23, 7.23, 7.23, 7.22, 7.22, 7.22, 7.21, 7.21, 7.20, 7.20, 3.85, 3.81, 3.28, 3.25, 2.63, 2.62, 2.60, 2.59, 2.58, 2.57, 2.12, 2.11, 2.09, 2.08, 2.08, 2.06, 2.05, 1.99, 1.99, 1.98, 1.98, 1.97, 1.97, 1.96, 1.95, 1.94, 1.91, 1.89, 1.89, 1.88, 1.88, 1.88, 1.87, 1.86, 1.85, 1.85, 1.84, 1.81, 1.80, 1.79, 1.79, 1.78, 1.78, 1.77, 1.77, 1.76, 1.76, 1.76, 1.65, 1.65, 1.64, 1.64, 1.63, 1.63, 1.63, 1.62, 1.61, 1.61, 1.60, 1.25, 1.25, 1.24, 1.23, 1.22, 1.21, 1.20, 1.20, 1.19, 1.18, 1.17, 1.16, 1.15, 1.14, 1.13, 1.13, 1.12, 1.11, 1.11, 1.10, 1.08, 1.08, 1.07, 1.04, 1.04, 1.03, 1.02, 1.00, 0.99, 0.99, 0.99, 0.97, 0.96, 0.95, 0.94, 0.93, 0.06.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 4.4 Hz, 4 H), 7.25–7.20 (m, 1 H), 3.83 (d, *J* = 13.6 Hz, 1 H), 3.27 (d, *J* = 13.6 Hz, 1 H), 2.60 (ddd, *J* = 10.4, 10.4, 4.2 Hz, 1 H), 2.12–2.04 (m, 1 H), 2.07 (d, *J* = 14.6 Hz, 1 H), 1.93 (d, *J* = 14.6 Hz, 1 H), 1.99–1.84 (m, 4 H), 1.81–1.76 (m, 1 H), 1.65–1.60 (m, 1 H), 1.25–1.07 (m, 3 H), 1.04–0.93 (m, 1 H), 0.06 (s, 9 H).



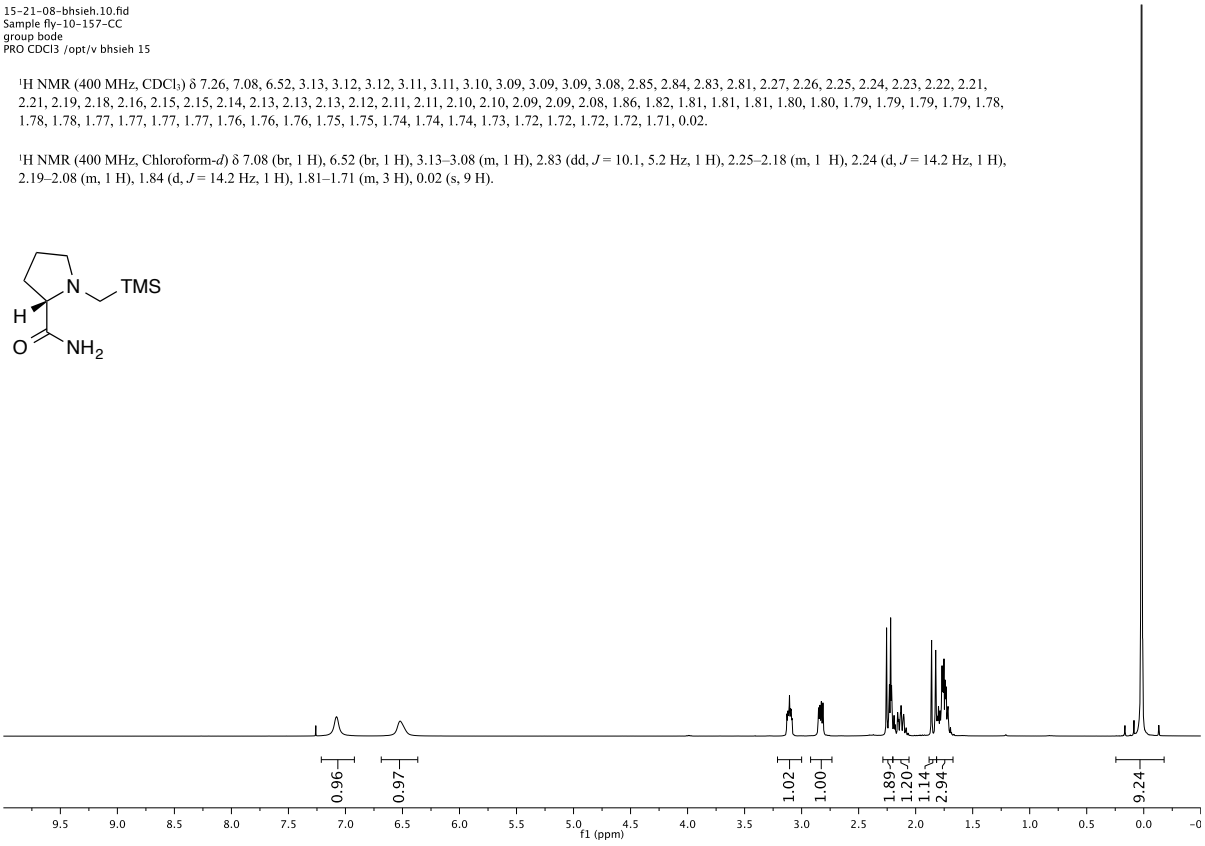
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 128.8, 128.4, 126.8, 67.0, 56.9, 51.6, 41.1, 35.2, 25.8, 25.3, 21.0, –1.1.

(*S*)-1-((Trimethylsilyl)methyl)pyrrolidine-2-carboxamide (S16)

15-21-08-bhsieh.10.fid
Sample fly-10-157-CC
group bode
PRO CDCl3 /opt/v bhsieh 15

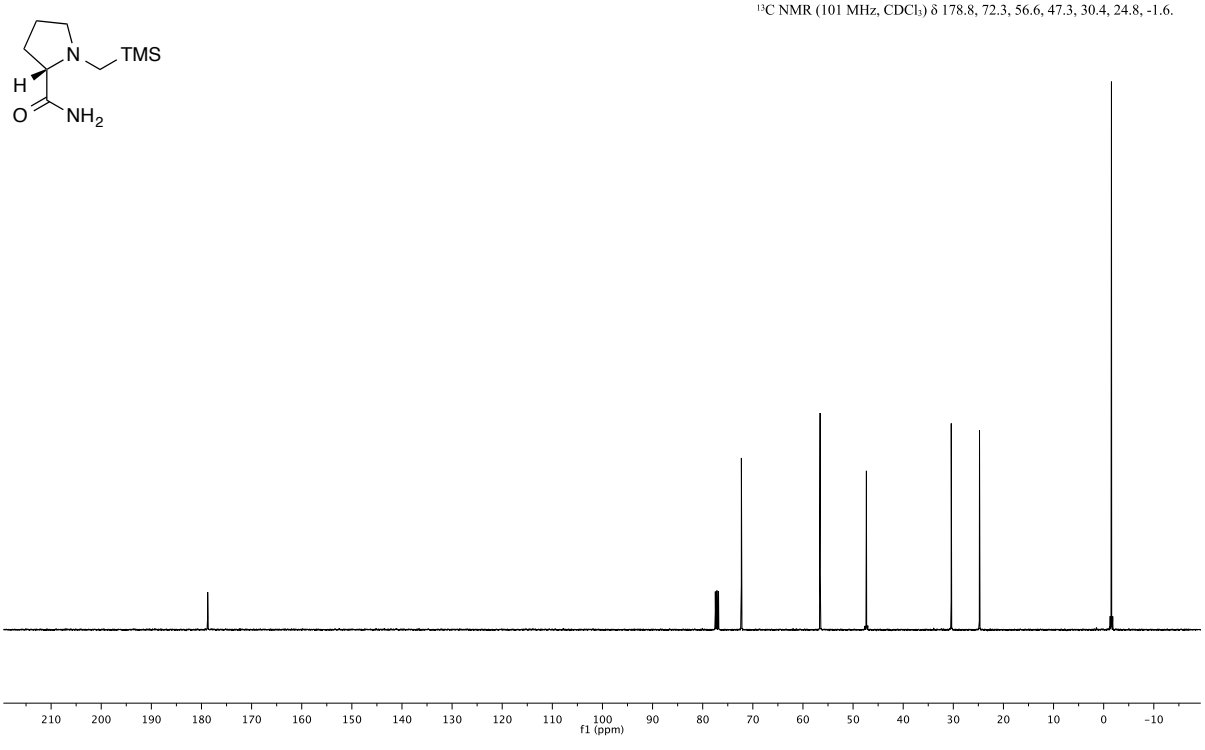
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26, 7.08, 6.52, 3.13, 3.12, 3.12, 3.11, 3.11, 3.10, 3.09, 3.09, 3.09, 3.08, 2.85, 2.84, 2.83, 2.81, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.21, 2.19, 2.18, 2.16, 2.15, 2.15, 2.14, 2.13, 2.13, 2.13, 2.12, 2.11, 2.11, 2.10, 2.10, 2.09, 2.09, 2.08, 1.86, 1.82, 1.81, 1.81, 1.81, 1.80, 1.80, 1.79, 1.79, 1.79, 1.79, 1.78, 1.78, 1.78, 1.77, 1.77, 1.77, 1.77, 1.76, 1.76, 1.76, 1.75, 1.75, 1.74, 1.74, 1.74, 1.73, 1.72, 1.72, 1.72, 1.72, 1.71, 0.02.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.08 (br, 1 H), 6.52 (br, 1 H), 3.13–3.08 (m, 1 H), 2.83 (dd, *J* = 10.1, 5.2 Hz, 1 H), 2.25–2.18 (m, 1 H), 2.24 (d, *J* = 14.2 Hz, 1 H), 2.19–2.08 (m, 1 H), 1.84 (d, *J* = 14.2 Hz, 1 H), 1.81–1.71 (m, 3 H), 0.02 (s, 9 H).



15-21-08-bhsieh.11.fid
Sample fly-10-157-CC
group bode
CAR CDCl3 /opt/v bhsieh 15

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.8, 72.3, 56.6, 47.3, 30.4, 24.8, -1.6.

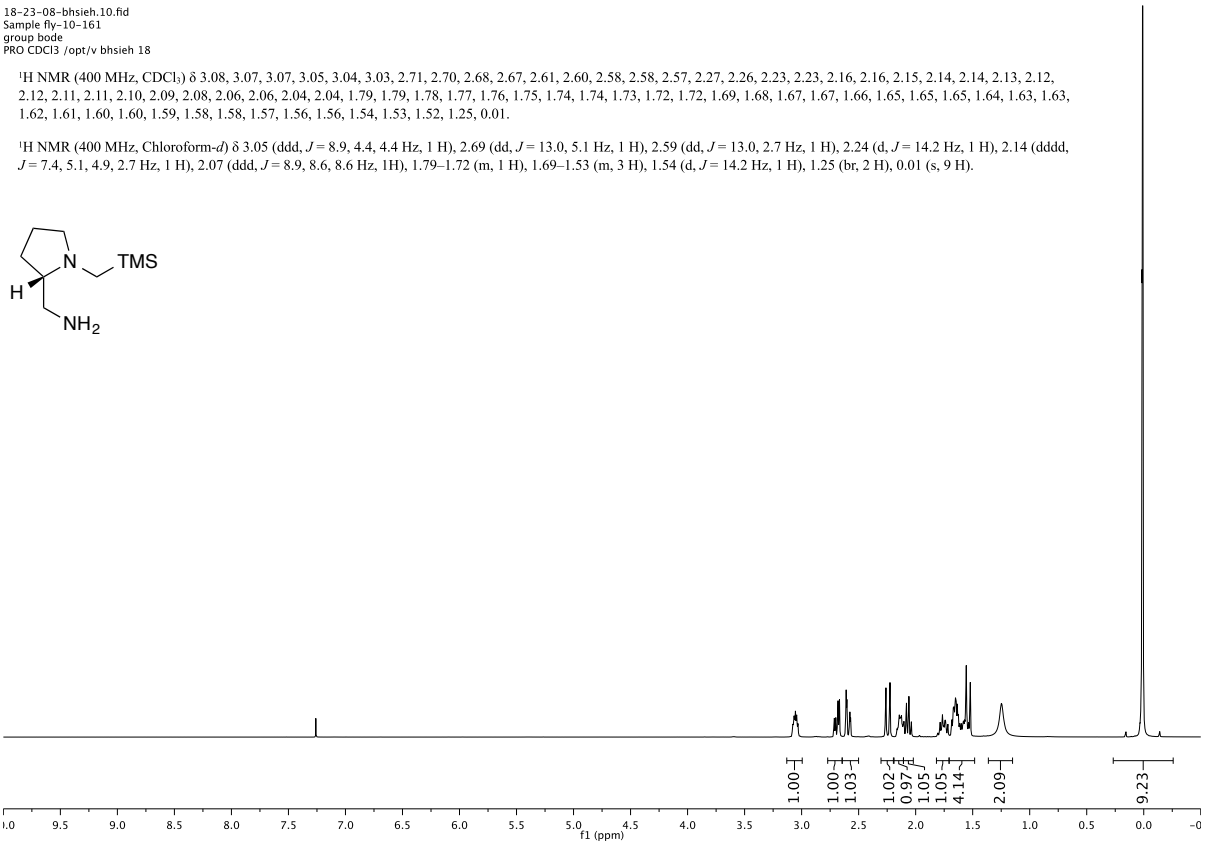


(*S*)-(1-((Trimethylsilyl)methyl)pyrrolidin-2-yl)methanamine (14)

18-23-08-bhsieh.10.fid
Sample fly-10-161
group bode
PRO CDCl3 /opt/v bhsieh 18

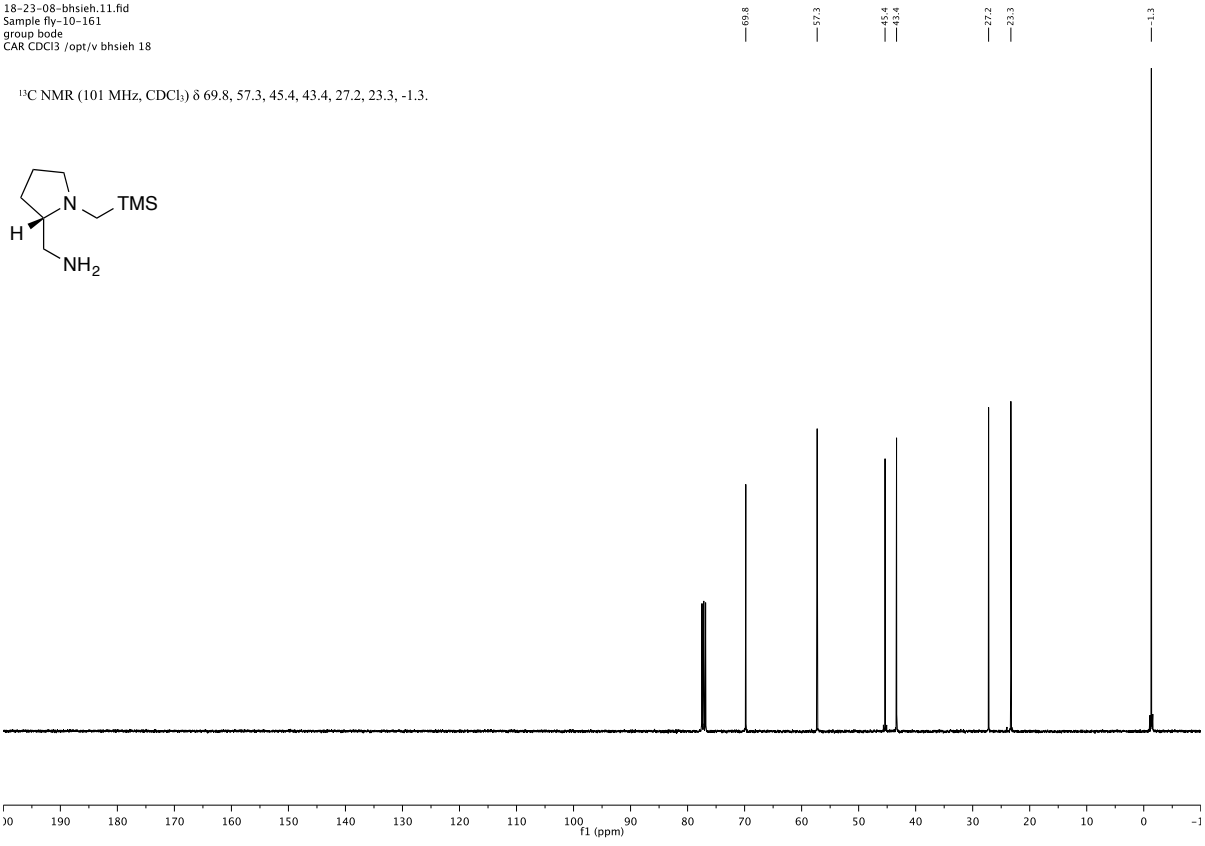
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08, 3.07, 3.07, 3.05, 3.04, 3.03, 2.71, 2.70, 2.68, 2.67, 2.61, 2.60, 2.58, 2.58, 2.57, 2.27, 2.26, 2.23, 2.23, 2.16, 2.16, 2.15, 2.14, 2.14, 2.13, 2.12, 2.12, 2.11, 2.11, 2.10, 2.09, 2.08, 2.06, 2.06, 2.04, 2.04, 1.79, 1.79, 1.78, 1.77, 1.76, 1.75, 1.74, 1.74, 1.73, 1.72, 1.72, 1.69, 1.68, 1.67, 1.67, 1.66, 1.65, 1.65, 1.65, 1.64, 1.63, 1.63, 1.62, 1.61, 1.60, 1.60, 1.59, 1.58, 1.58, 1.57, 1.56, 1.56, 1.54, 1.53, 1.52, 1.25, 0.01.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.05 (ddd, *J* = 8.9, 4.4, 4.4 Hz, 1 H), 2.69 (dd, *J* = 13.0, 5.1 Hz, 1 H), 2.59 (dd, *J* = 13.0, 2.7 Hz, 1 H), 2.24 (d, *J* = 14.2 Hz, 1 H), 2.14 (dddd, *J* = 7.4, 5.1, 4.9, 2.7 Hz, 1 H), 2.07 (ddd, *J* = 8.9, 8.6, 8.6 Hz, 1H), 1.79–1.72 (m, 1 H), 1.69–1.53 (m, 3 H), 1.54 (d, *J* = 14.2 Hz, 1 H), 1.25 (br, 2 H), 0.01 (s, 9 H).



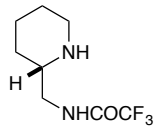
18-23-08-bhsieh.11.fid
Sample fly-10-161
group bode
CAR CDCl3 /opt/v bhsieh 18

^{13}C NMR (101 MHz, $CDCl_3$) δ 69.8, 57.3, 45.4, 43.4, 27.2, 23.3, -1.3.



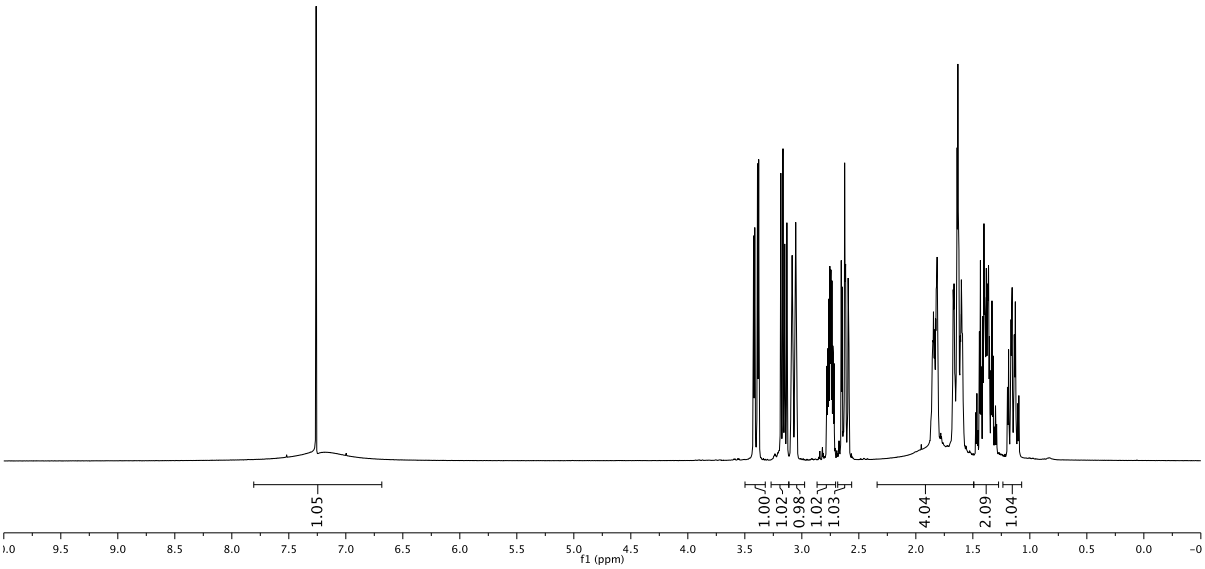
2,2,2-Trifluoro-*N*-(piperidin-2-ylmethyl)acetamide (S17)

41-24-10-bhsieh.10.fid
Sample fly-10-154
group bode

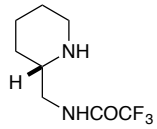


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19, 3.42, 3.41, 3.39, 3.38, 3.18, 3.17, 3.15, 3.13, 3.10, 3.09, 3.08, 3.08, 3.07, 3.06, 3.06, 3.05, 3.05, 3.04, 2.78, 2.77, 2.77, 2.76, 2.75, 2.74, 2.74, 2.73, 2.72, 2.72, 2.65, 2.65, 2.62, 2.62, 2.62, 2.59, 2.59, 1.87, 1.86, 1.86, 1.86, 1.85, 1.85, 1.85, 1.84, 1.84, 1.83, 1.83, 1.82, 1.82, 1.81, 1.81, 1.80, 1.68, 1.67, 1.67, 1.66, 1.66, 1.66, 1.65, 1.65, 1.64, 1.64, 1.63, 1.62, 1.62, 1.61, 1.61, 1.60, 1.60, 1.60, 1.59, 1.59, 1.58, 1.47, 1.46, 1.46, 1.44, 1.43, 1.42, 1.41, 1.40, 1.40, 1.39, 1.39, 1.39, 1.38, 1.38, 1.37, 1.37, 1.36, 1.36, 1.35, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.20, 1.19, 1.17, 1.16, 1.16, 1.15, 1.14, 1.13, 1.13, 1.12, 1.11, 1.10.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (br, 1 H), 3.40 (dd, *J* = 13.7, 4.2 Hz, 1 H), 3.16 (dd, *J* = 13.7, 7.5 Hz, 1 H), 3.07 (dddd, *J* = 12.4, 4.1, 2.1, 2.1 Hz, 1H), 2.75 (dddd, *J* = 10.9, 7.5, 4.2, 2.8 Hz, 1 H), 2.65–2.59 (m, 1 H), 1.87–1.80 (m, 1 H), 1.83 (br, 1 H), 1.68–1.58 (m, 2 H), 1.47–1.29 (m, 2 H), 1.20–1.10 (m, 1 H).

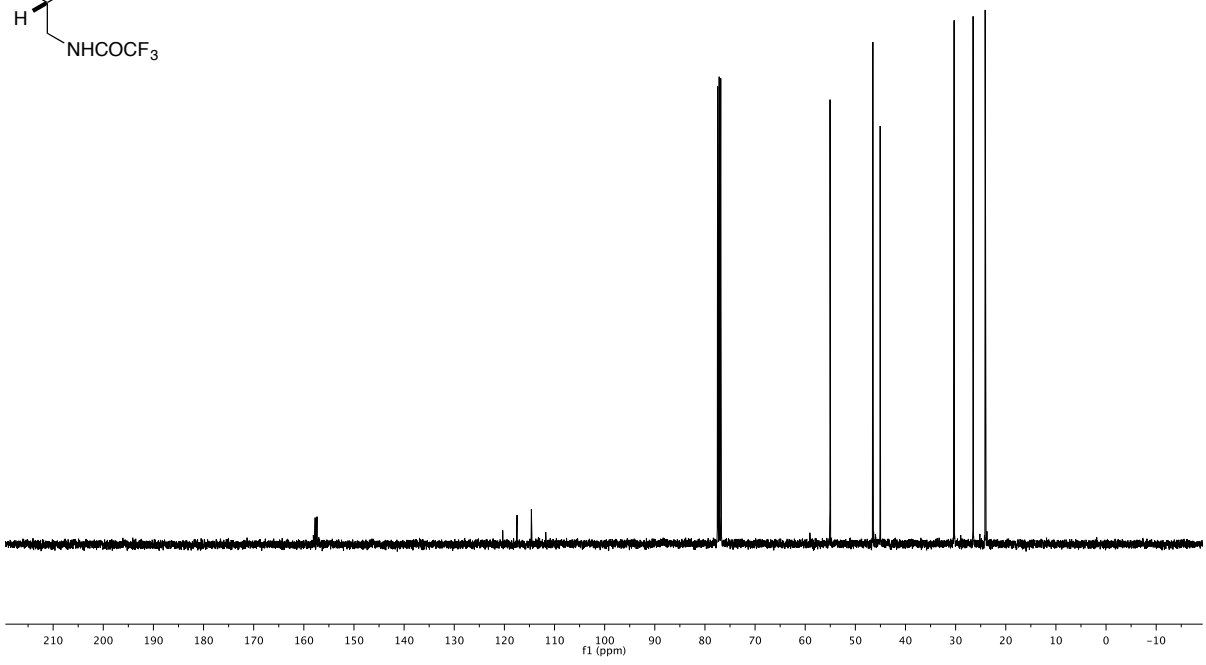


41-24-10-bhsieh.11.fid
Sample fly-10-154
group bode



^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 157.7, 157.4, 157.0, 120.3, 117.5, 114.6, 111.8, 55.0, 46.5, 45.0, 30.3, 26.5, 24.1.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.6 (q, *J* = 36.8 Hz), 116.0 (q, *J* = 287.7 Hz), 55.0, 46.5, 45.0, 30.3, 26.5, 24.1.

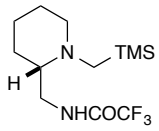


2,2,2-Trifluoro-*N*-((1-((trimethylsilyl)methyl)piperidin-2-yl)methyl)acetamide (S18)

50-24-08-bhsieh.10.fid
Sample fly-10-156-CC
group bode
PRO CDCl3 /opt/v bhsieh 50

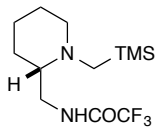
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19, 3.51, 3.50, 3.47, 3.46, 3.32, 3.31, 3.28, 3.27, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.30, 2.29, 2.28, 2.28, 2.27, 2.27, 2.26, 2.25, 2.25, 2.23, 2.20, 2.13, 2.12, 2.10, 2.10, 2.09, 2.09, 2.07, 2.06, 1.72, 1.71, 1.71, 1.70, 1.69, 1.68, 1.67, 1.65, 1.62, 1.62, 1.61, 1.61, 1.60, 1.59, 1.59, 1.58, 1.58, 1.57, 1.57, 1.47, 1.46, 1.46, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.40, 1.39, 1.39, 1.38, 1.37, 1.37, 1.36, 1.36, 1.35, 1.35, 1.34, 1.33, 1.33, 1.32, 1.32, 1.31, 1.30, 1.30, 1.29, 1.28, 1.27, 0.05.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (br, 1 H), 3.48 (dd, *J* = 13.9, 4.8 Hz, 1 H), 3.29 (dd, *J* = 13.9, 3.2 Hz, 1 H), 2.95 (ddd, *J* = 12.0, 3.8, 3.8 Hz, 1 H), 2.30–2.25 (m, 1 H), 2.21 (d, *J* = 14.3 Hz, 1 H), 2.10 (ddd, *J* = 12.0, 10.8, 2.7 Hz, 1 H), 1.72–1.67 (m, 1 H), 1.63 (d, *J* = 14.3 Hz, 1 H), 1.62–1.57 (m, 2 H), 1.47–1.27 (m, 3 H), 0.05 (s, 9 H).



50-24-08-bhsieh.11.fid
Sample fly-10-156-CC
group bode
CAR CDCl3 /opt/v bhsieh 50

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.6 (q, *J* = 37.1 Hz), 116.1 (q, *J* = 287.8 Hz), 60.9, 54.8, 44.7, 41.6, 28.5, 24.7, 23.6, -1.2.

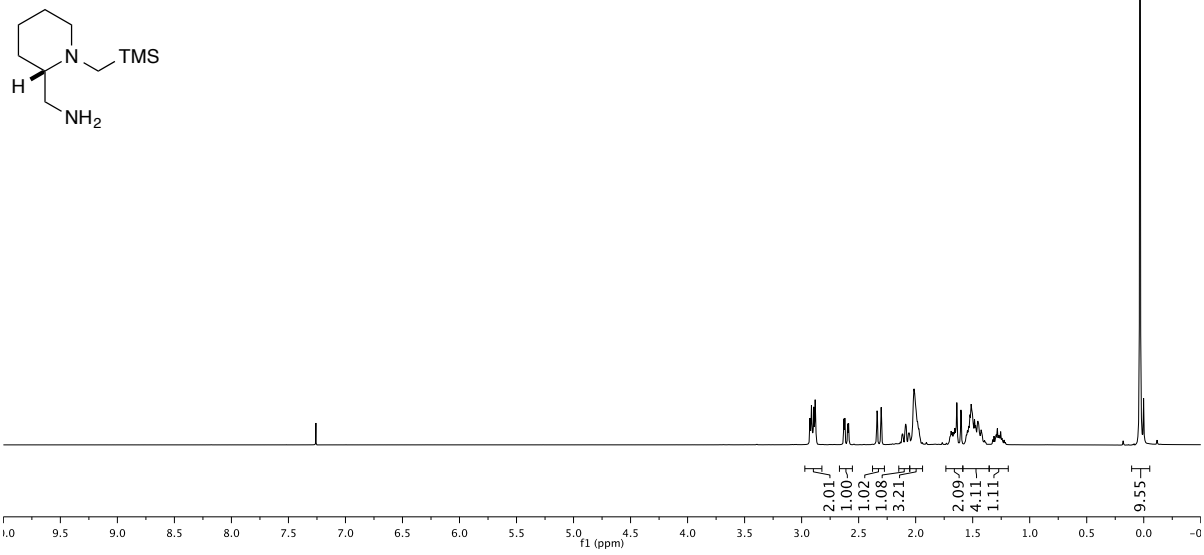


(1-((Trimethylsilyl)methyl)piperidin-2-yl)methanamine (15)

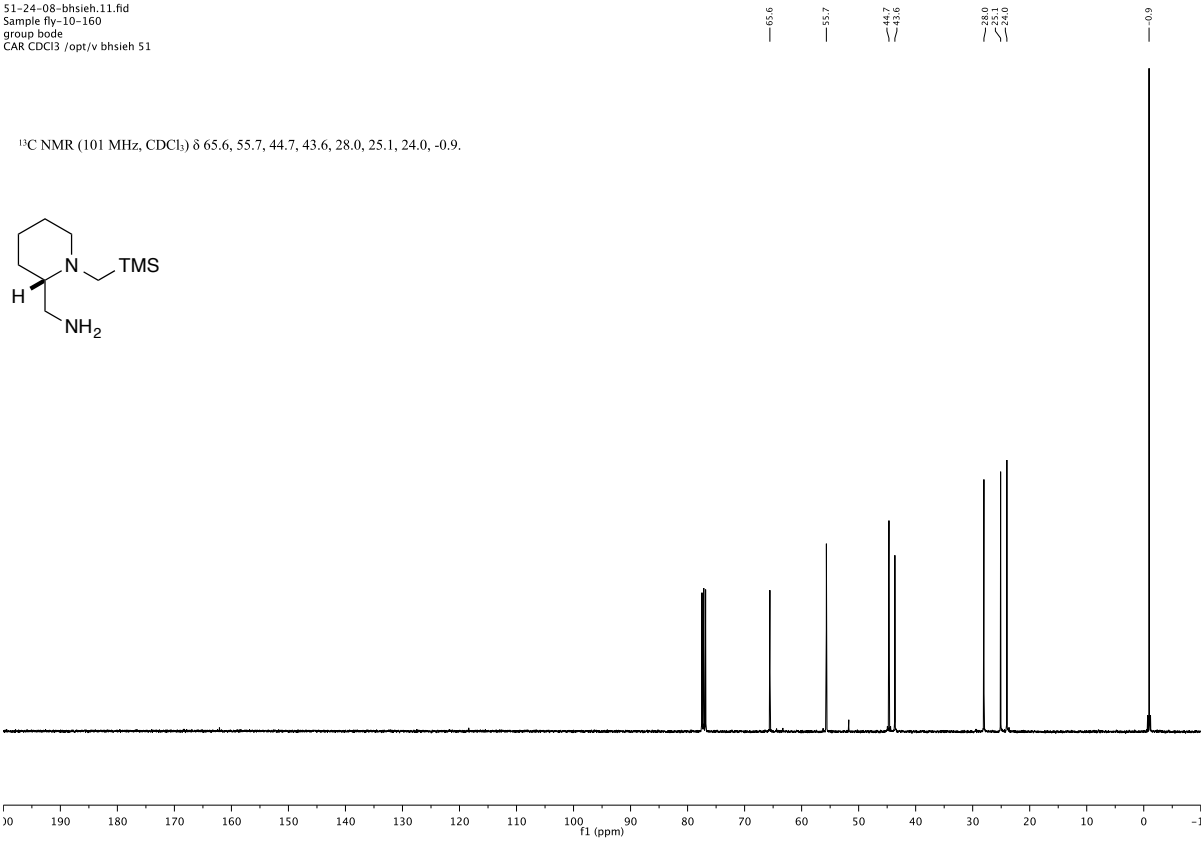
51-24-08-bhsieh.10.fid
Sample fly-10-160
group bode
PRO CDCl3 /opt/v bhsieh 51

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.93, 2.91, 2.90, 2.89, 2.89, 2.88, 2.63, 2.63, 2.62, 2.62, 2.60, 2.59, 2.59, 2.59, 2.34, 2.30, 2.12, 2.12, 2.11, 2.11, 2.09, 2.09, 2.09, 2.08, 2.06, 2.06, 2.06, 2.05, 2.02, 2.01, 2.00, 2.00, 1.99, 1.98, 1.98, 1.97, 1.97, 1.97, 1.96, 1.70, 1.69, 1.68, 1.67, 1.66, 1.65, 1.64, 1.64, 1.60, 1.56, 1.55, 1.54, 1.52, 1.51, 1.51, 1.51, 1.50, 1.50, 1.50, 1.49, 1.48, 1.48, 1.47, 1.47, 1.46, 1.45, 1.45, 1.44, 1.43, 1.43, 1.42, 1.42, 1.41, 1.32, 1.32, 1.31, 1.31, 1.30, 1.30, 1.29, 1.29, 1.28, 1.28, 1.27, 1.27, 1.27, 1.27, 1.26, 1.25, 1.25, 1.25, 1.24, 1.23, 1.22, 1.22, 1.21, 0.03.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.93–2.88 (m, 2 H), 2.61 (dd, *J* = 13.3, 3.4 Hz, 1 H), 2.32 (d, *J* = 14.4 Hz, 1 H), 2.09 (ddd, *J* = 12.1, 11.4, 3.3 Hz, 1 H), 2.09 (ddd, *J* = 11.7, 11.4, 3.1 Hz, 1 H), 2.02–1.96 (m, 3 H), 1.70–1.64 (m, 1 H), 1.62 (d, *J* = 14.4 Hz, 1 H), 1.56–1.43 (m, 4 H), 1.32–1.21 (m, 1 H), 0.03 (s, 9 H).

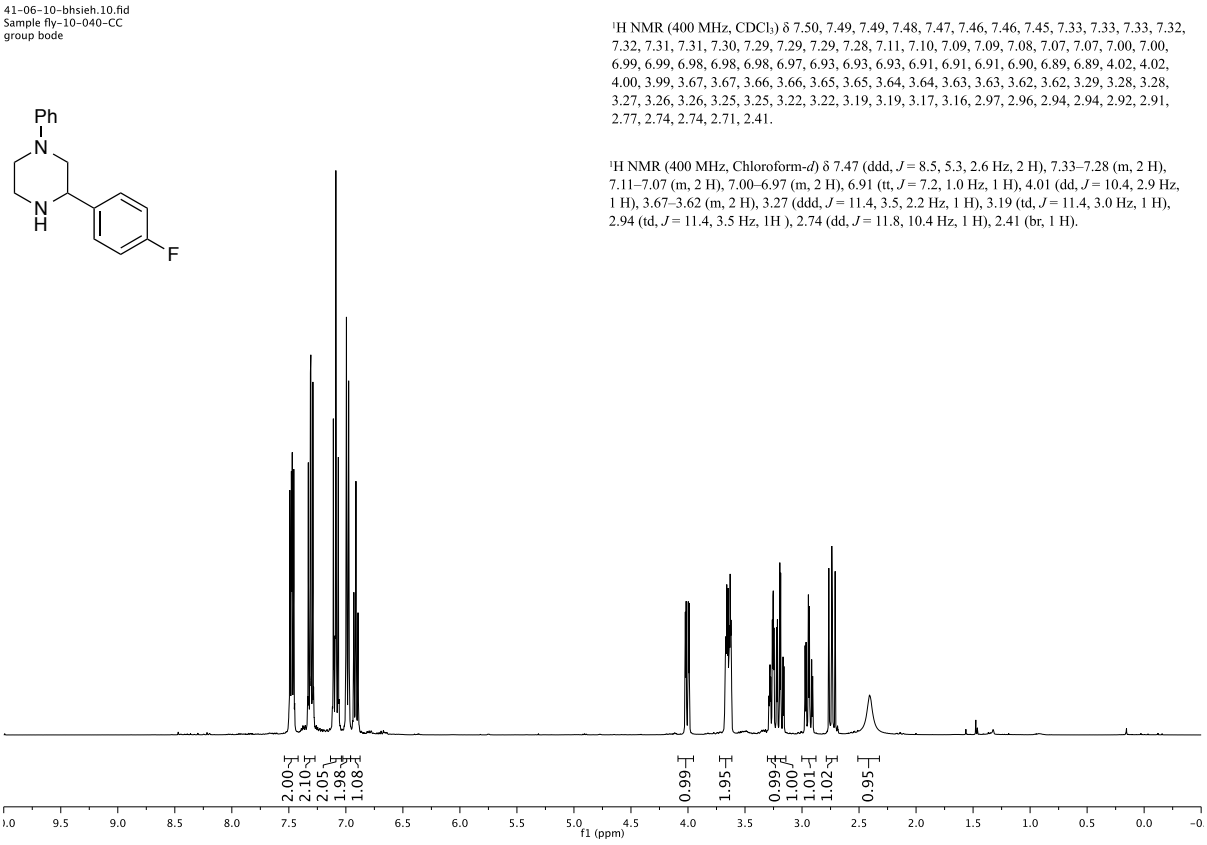


51-24-08-bhsieh.11.fid
Sample fly-10-160
group bode
CAR CDCl3 /opt/v bhsieh 51



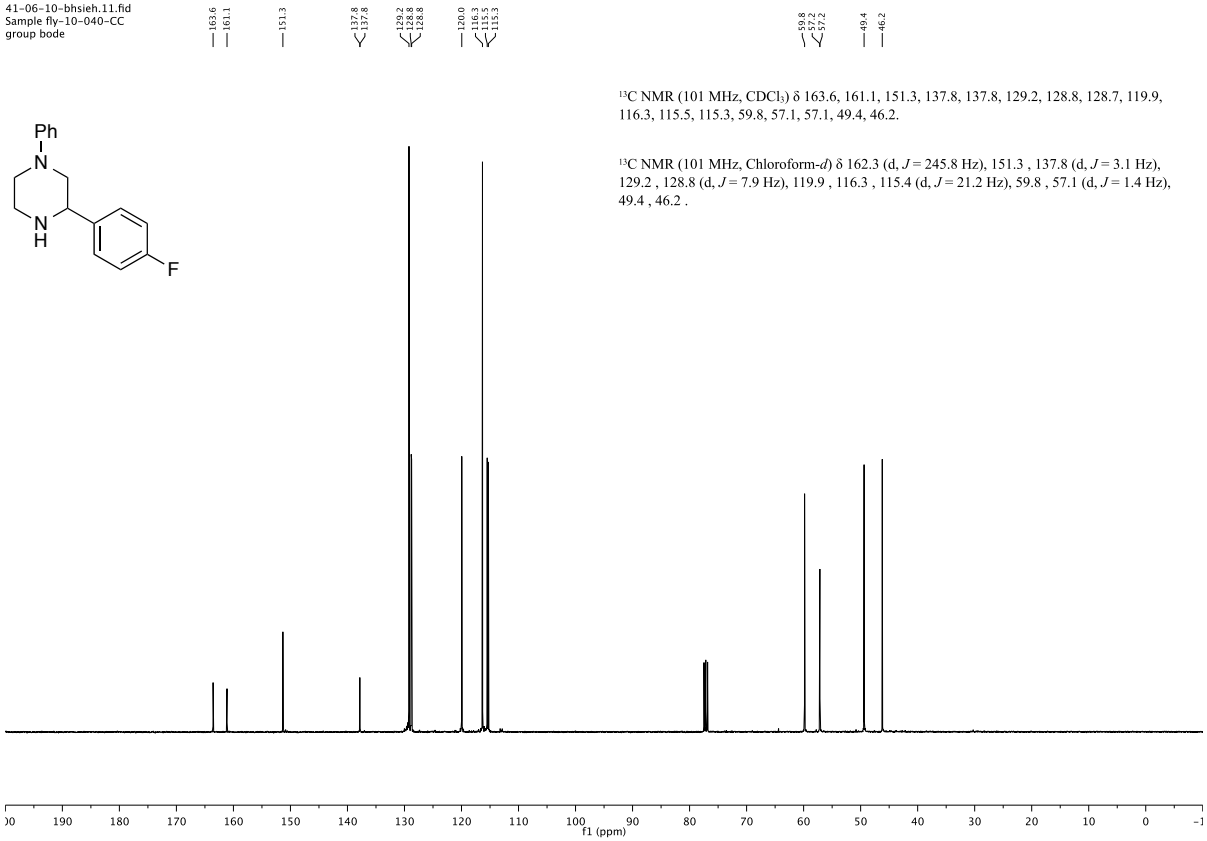
^{13}C NMR (101 MHz, $CDCl_3$) δ 65.6, 55.7, 44.7, 43.6, 28.0, 25.1, 24.0, -0.9.

3-(4-Fluorophenyl)-1-phenylpiperazine (8) (Table 1, entry 3)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50, 7.49, 7.49, 7.48, 7.47, 7.46, 7.46, 7.45, 7.33, 7.33, 7.33, 7.32, 7.32, 7.31, 7.31, 7.30, 7.29, 7.29, 7.29, 7.28, 7.11, 7.10, 7.09, 7.09, 7.08, 7.07, 7.07, 7.00, 7.00, 6.99, 6.99, 6.98, 6.98, 6.98, 6.97, 6.93, 6.93, 6.93, 6.91, 6.91, 6.91, 6.90, 6.89, 6.89, 4.02, 4.02, 4.00, 3.99, 3.67, 3.67, 3.66, 3.66, 3.65, 3.65, 3.64, 3.64, 3.63, 3.63, 3.62, 3.62, 3.29, 3.28, 3.28, 3.27, 3.26, 3.26, 3.25, 3.25, 3.22, 3.22, 3.19, 3.19, 3.17, 3.16, 2.97, 2.96, 2.94, 2.94, 2.92, 2.91, 2.77, 2.74, 2.74, 2.71, 2.41.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (ddd, *J* = 8.5, 5.3, 2.6 Hz, 2 H), 7.33–7.28 (m, 2 H), 7.11–7.07 (m, 2 H), 7.00–6.97 (m, 2 H), 6.91 (tt, *J* = 7.2, 1.0 Hz, 1 H), 4.01 (dd, *J* = 10.4, 2.9 Hz, 1 H), 3.67–3.62 (m, 2 H), 3.27 (ddd, *J* = 11.4, 3.5, 2.2 Hz, 1 H), 3.19 (td, *J* = 11.4, 3.0 Hz, 1 H), 2.94 (td, *J* = 11.4, 3.5 Hz, 1H), 2.74 (dd, *J* = 11.8, 10.4 Hz, 1 H), 2.41 (br, 1 H).

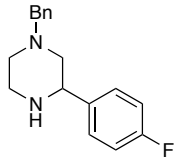


^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 161.1, 151.3, 137.8, 137.8, 129.2, 128.8, 128.7, 119.9, 116.3, 115.5, 115.3, 59.8, 57.1, 57.1, 49.4, 46.2.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.3 (d, *J* = 245.8 Hz), 151.3 , 137.8 (d, *J* = 3.1 Hz), 129.2 , 128.8 (d, *J* = 7.9 Hz), 119.9 , 116.3 , 115.4 (d, *J* = 21.2 Hz), 59.8 , 57.1 (d, *J* = 1.4 Hz), 49.4 , 46.2 .

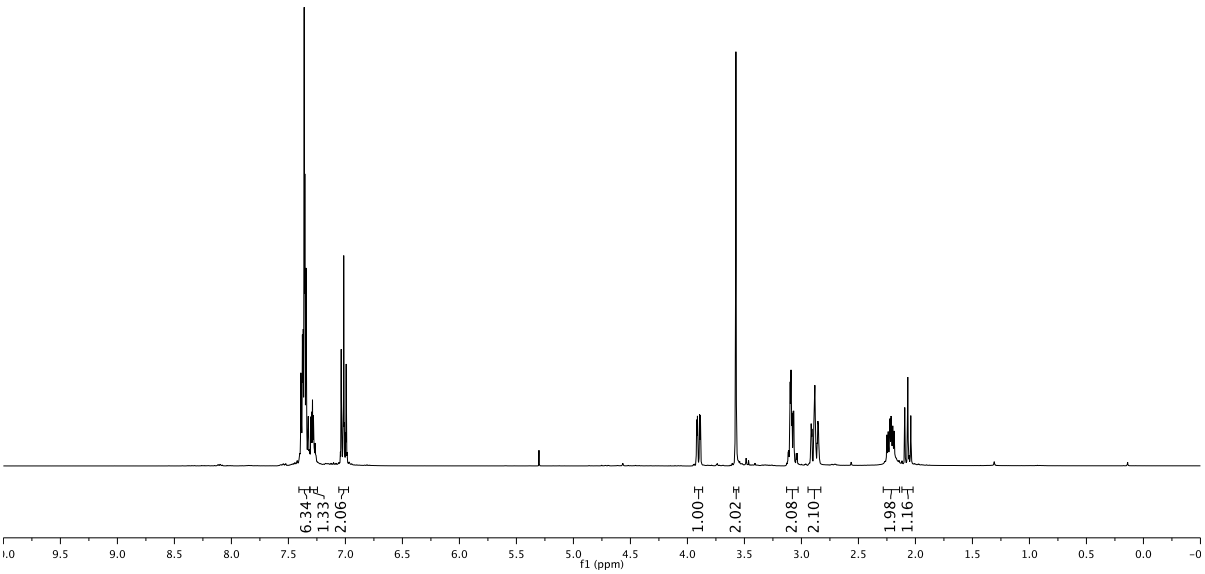
1-Benzyl-3-(4-fluorophenyl)piperazine (9a) (Table 1, entry 5–7 & Scheme 2)

42-06-10-bhsieh.10.fid
Sample fly-11-006-CC
group bode

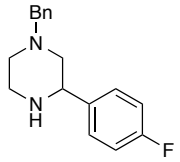


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39, 7.39, 7.38, 7.37, 7.36, 7.36, 7.35, 7.34, 7.34, 7.33, 7.33, 7.33, 7.30, 7.30, 7.29, 7.28, 7.28, 7.28, 7.27, 7.27, 7.04, 7.04, 7.03, 7.02, 7.01, 7.01, 7.00, 6.99, 6.99, 3.92, 3.91, 3.89, 3.89, 3.57, 3.12, 3.11, 3.10, 3.10, 3.09, 3.09, 3.09, 3.08, 3.07, 3.07, 3.04, 3.04, 2.92, 2.91, 2.91, 2.91, 2.89, 2.89, 2.88, 2.86, 2.85, 2.25, 2.24, 2.23, 2.22, 2.21, 2.21, 2.20, 2.19, 2.09, 2.07, 2.04.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39–7.33 (m, 6 H), 7.30–7.27 (m, 1 H), 7.04–6.99 (m, 2 H), 3.90 (dd, *J* = 10.2, 2.8 Hz, 1 H), 3.57 (s, 2 H), 3.12–3.04 (m, 2 H), 2.93–2.84 (m, 2 H), 2.22 (ddd, *J* = 11.0, 9.7, 4.8 Hz, 1 H), 2.21 (br, 1 H), 2.07 (t, *J* = 10.2 Hz, 1 H).



42-06-10-bhsieh.11.fid
Sample fly-11-006-CC
group bode

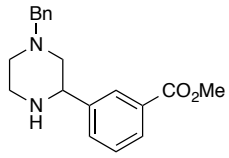


^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 160.9, 138.5, 138.4, 138.0, 129.3, 128.7, 128.6, 128.3, 127.1, 115.3, 115.1, 63.3, 61.4, 61.4, 59.7, 53.2, 46.2.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.1 (d, *J* = 245.2 Hz), 138.5 (d, *J* = 3.1 Hz), 138.0, 129.3, 128.6 (d, *J* = 7.9 Hz), 128.3, 127.1, 115.2 (d, *J* = 21.1 Hz), 63.3, 61.4 (d, *J* = 1.2 Hz), 59.7, 53.2, 46.2.

Methyl 3-(4-benzylpiperazin-2-yl)benzoate (9b) (Scheme 2)

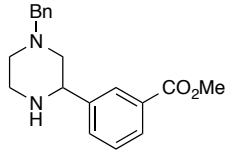
44-06-10-bhsieh.10.fid
Sample fly-11-015-CC
group bode



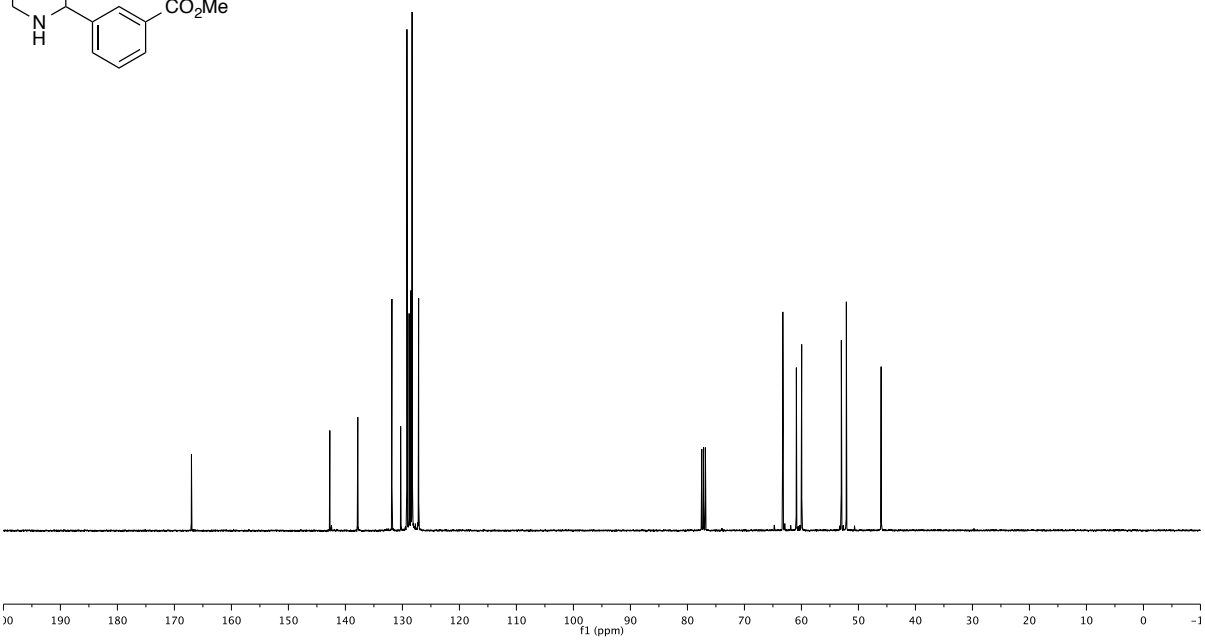
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09, 8.08, 8.08, 7.96, 7.96, 7.95, 7.94, 7.94, 7.93, 7.62, 7.61, 7.61, 7.60, 7.60, 7.59, 7.40, 7.39, 7.37, 7.36, 7.35, 7.34, 7.34, 7.33, 7.32, 7.32, 7.32, 7.31, 7.31, 7.30, 7.30, 7.29, 7.28, 7.28, 7.27, 7.26, 7.26, 7.25, 7.25, 7.24, 7.24, 3.99, 3.98, 3.97, 3.96, 3.91, 3.56, 3.13, 3.13, 3.12, 3.11, 3.10, 3.10, 3.09, 3.09, 3.09, 3.07, 3.06, 3.06, 3.04, 3.03, 2.93, 2.93, 2.93, 2.92, 2.91, 2.90, 2.90, 2.90, 2.87, 2.87, 2.84, 2.84, 2.69, 2.28, 2.27, 2.25, 2.24, 2.24, 2.24, 2.22, 2.21, 2.15, 2.12, 2.12, 2.09.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (t, *J* = 1.6 Hz, 1 H), 7.95 (dt, *J* = 7.8, 1.6 Hz, 1 H), 7.61 (dt, *J* = 7.7, 1.6 Hz, 1 H), 7.39 (apparent t, *J* = 7.8 Hz, 1 H), 7.36–7.24 (m, 5 H), 3.97 (dd, *J* = 10.2, 2.9 Hz, 1 H), 3.91 (s, 3 H), 3.56 (s, 2 H), 3.13–3.03 (m, 2 H), 2.93–2.84 (m, 2 H), 2.69 (br, 1 H), 2.25 (td, *J* = 10.7, 4.2 Hz, 1 H), 2.12 (dd, *J* = 11.0, 10.2 Hz, 1 H).

44-06-10-bhsieh.11.fid
Sample fly-11-015-CC
group bode



^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 142.7, 137.8, 131.8, 130.3, 129.2, 128.8, 128.5, 128.30, 128.27, 127.2, 77.2, 63.3, 60.9, 60.0, 53.0, 52.1, 46.0.

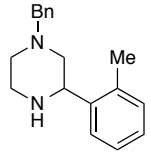


1-Benzyl-3-(*o*-tolyl)piperazine (9c) (Scheme 2)

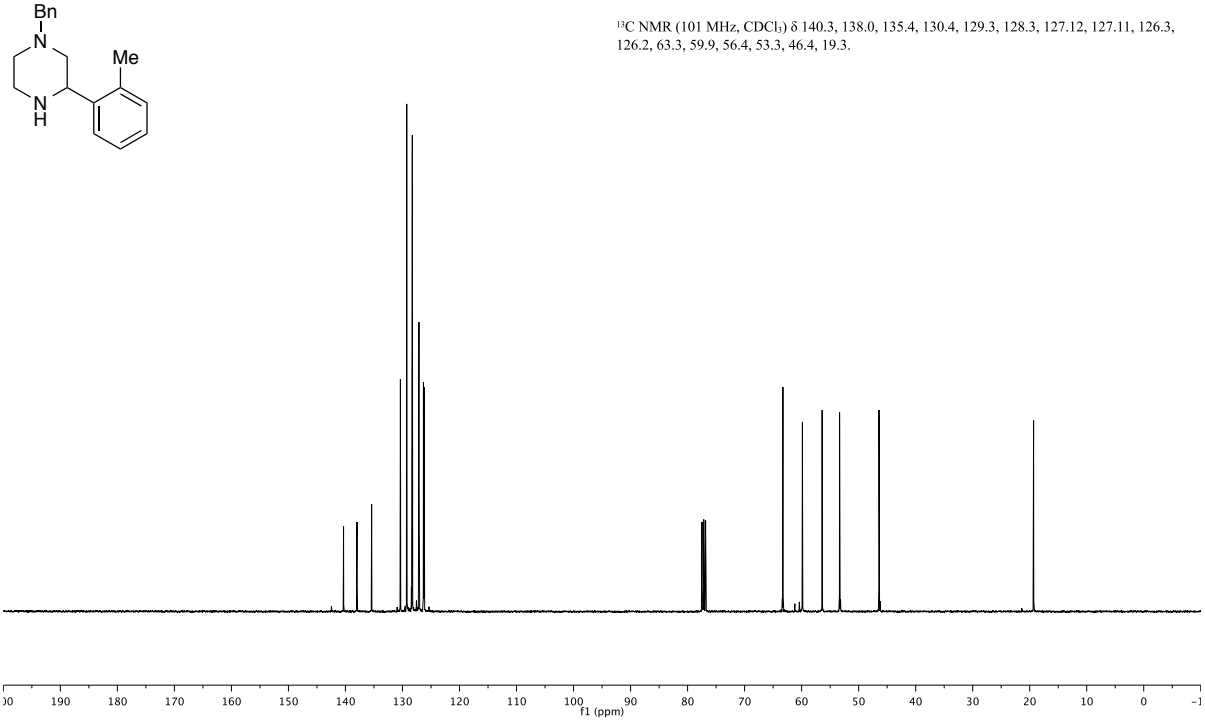
12-08-11-bhsieh.10.fid
Sample fly-11-012
group bode
PRO CDCl3 /opt/v bhsieh 12

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57, 7.55, 7.37, 7.37, 7.35, 7.35, 7.35, 7.33, 7.32, 7.31, 7.31, 7.28, 7.28, 7.27, 7.27, 7.26, 7.25, 7.25, 7.24, 7.24, 7.22, 7.22, 7.21, 7.20, 7.19, 7.18, 7.17, 7.16, 7.16, 7.14, 7.13, 7.12, 7.12, 4.14, 4.14, 4.12, 4.11, 3.62, 3.59, 3.57, 3.53, 3.13, 3.12, 3.11, 3.11, 3.10, 3.10, 2.91, 2.91, 2.90, 2.90, 2.89, 2.89, 2.88, 2.88, 2.87, 2.86, 2.48, 2.35, 2.29, 2.28, 2.27, 2.27, 2.26, 2.25, 2.24, 2.23, 2.06, 2.03, 2.03, 2.01.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.6 Hz, 1 H), 7.37–7.31 (m, 4 H), 7.28–7.24 (m, 1 H), 7.22–7.12 (m, 3 H), 4.13 (dd, *J* = 10.0, 2.6 Hz, 1 H), 3.60 (d, *J* = 13.1 Hz, 1 H), 3.55 (d, *J* = 13.1 Hz, 1 H), 3.13 –3.10 (m, 2 H), 2.91–2.86 (m, 2 H), 2.48 (br, 1 H), 2.35 (s, 3 H), 2.26 (ddd, *J* = 11.2, 9.2, 5.4 Hz, 1 H), 2.03 (dd, *J* = 11.2, 10.0 Hz, 1 H).

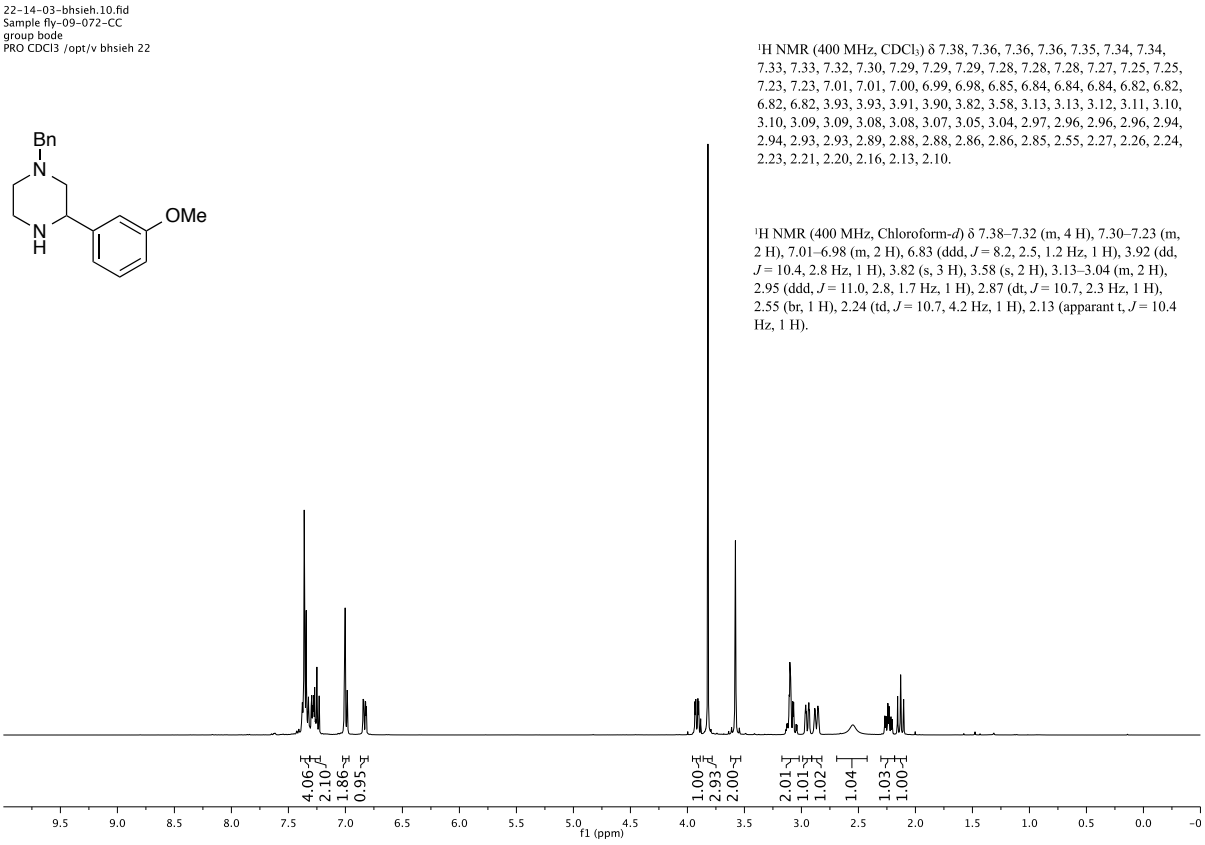


12-08-11-bhsieh.11.fid
Sample fly-11-012
group bode
CAR CDCl3 /opt/v bhsieh 12



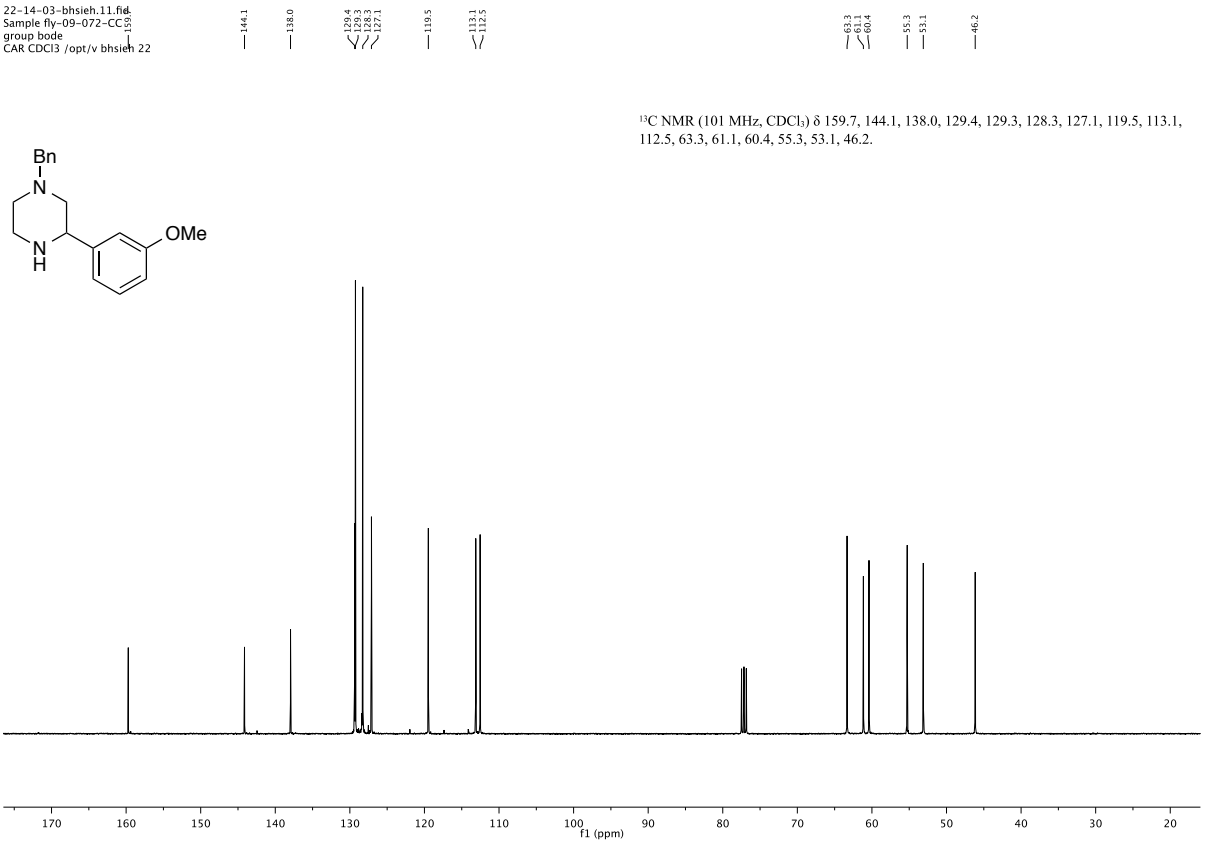
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 138.0, 135.4, 130.4, 129.3, 128.3, 127.12, 127.11, 126.3, 126.2, 63.3, 59.9, 56.4, 53.3, 46.4, 19.3.

1-Benzyl-3-(3-methoxyphenyl)piperazine (9d) (Scheme 2)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38, 7.36, 7.36, 7.36, 7.35, 7.34, 7.34, 7.33, 7.33, 7.32, 7.30, 7.29, 7.29, 7.29, 7.28, 7.28, 7.28, 7.27, 7.25, 7.25, 7.23, 7.23, 7.01, 7.01, 7.00, 6.99, 6.98, 6.85, 6.84, 6.84, 6.84, 6.82, 6.82, 6.82, 6.82, 3.93, 3.93, 3.91, 3.90, 3.82, 3.58, 3.13, 3.13, 3.12, 3.11, 3.10, 3.10, 3.09, 3.09, 3.08, 3.08, 3.07, 3.05, 3.04, 2.97, 2.96, 2.96, 2.96, 2.94, 2.94, 2.93, 2.93, 2.89, 2.88, 2.88, 2.86, 2.86, 2.85, 2.55, 2.27, 2.26, 2.24, 2.23, 2.21, 2.20, 2.16, 2.13, 2.10.

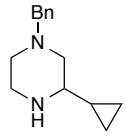
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38–7.32 (m, 4 H), 7.30–7.23 (m, 2 H), 7.01–6.98 (m, 2 H), 6.83 (ddd, *J* = 8.2, 2.5, 1.2 Hz, 1 H), 3.92 (dd, *J* = 10.4, 2.8 Hz, 1 H), 3.82 (s, 3 H), 3.58 (s, 2 H), 3.13–3.04 (m, 2 H), 2.95 (ddd, *J* = 11.0, 2.8, 1.7 Hz, 1 H), 2.87 (dt, *J* = 10.7, 2.3 Hz, 1 H), 2.55 (br, 1 H), 2.24 (td, *J* = 10.7, 4.2 Hz, 1 H), 2.13 (apparant t, *J* = 10.4 Hz, 1 H).



^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 144.1, 138.0, 129.4, 129.3, 128.3, 127.1, 119.5, 113.1, 112.5, 63.3, 61.1, 60.4, 55.3, 53.1, 46.2.

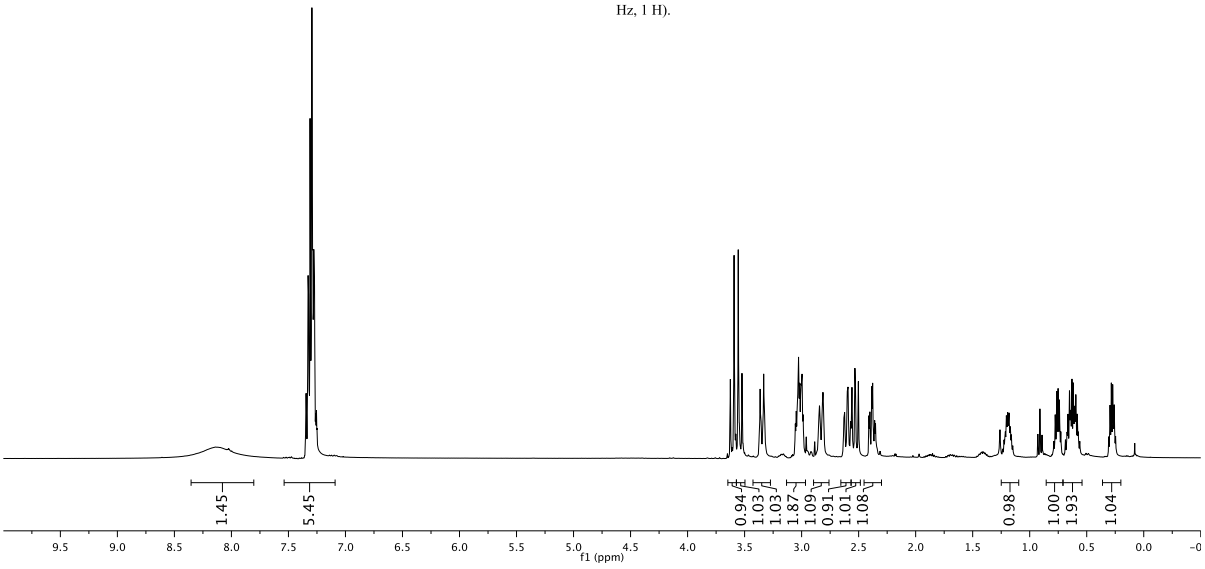
1-Benzyl-3-cyclopropylpiperazine (9e) (Scheme 2)

15-28-10-bhsieh.10.fid
Sample fly-11-008
group bode
PRO CDCl3 /opt/v bhsieh 15

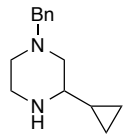


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13, 7.35, 7.35, 7.34, 7.33, 7.33, 7.32, 7.32, 7.31, 7.29, 7.29, 7.29, 7.28, 7.28, 7.27, 7.26, 7.26, 7.25, 7.25, 3.63, 3.59, 3.56, 3.52, 3.37, 3.36, 3.36, 3.34, 3.33, 3.33, 3.06, 3.05, 3.04, 3.04, 3.03, 3.03, 3.02, 3.01, 3.01, 3.00, 3.00, 2.99, 2.85, 2.84, 2.82, 2.81, 2.63, 2.62, 2.60, 2.59, 2.57, 2.56, 2.56, 2.53, 2.53, 2.50, 2.41, 2.40, 2.38, 2.38, 2.36, 2.35, 1.24, 1.23, 1.22, 1.21, 1.21, 1.20, 1.19, 1.18, 1.18, 1.17, 1.17, 1.16, 1.15, 0.79, 0.78, 0.76, 0.75, 0.74, 0.73, 0.69, 0.67, 0.66, 0.65, 0.64, 0.64, 0.63, 0.62, 0.62, 0.61, 0.60, 0.60, 0.58, 0.58, 0.57, 0.56, 0.31, 0.30, 0.28, 0.27, 0.26, 0.25.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (br, 1 H), 7.35–7.25 (m, 5 H), 3.61 (d, *J* = 13.1 Hz, 1 H), 3.54 (d, *J* = 13.1 Hz, 1 H), 3.35 (ddd, *J* = 12.4, 2.9, 2.9 Hz, 1 H), 3.06–2.99 (m, 2 H), 2.83 (dd, *J* = 12.4, 1.9 Hz, 1 H), 2.60 (ddd, *J* = 11.9, 11.8, 2.9 Hz, 1 H), 2.53 (dd, *J* = 12.1, 10.0 Hz, 1 H), 2.38 (ddd, *J* = 10.0, 9.7, 3.1 Hz, 1 H), 1.19 (apparent dddd, *J* = 12.9, 9.7, 8.1, 4.8 Hz, 1 H), 0.76 (dddd, *J* = 9.6, 5.1, 5.1, 4.9 Hz, 1 H), 0.69–0.56 (m, 2 H), 0.28 (dddd, *J* = 10.2, 4.9, 4.7, 4.7 Hz, 1 H).



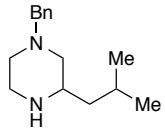
15-28-10-bhsieh.11.fid
Sample fly-11-008
group bode
CAR CDCl3 /opt/v bhsieh 15



^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 129.0, 128.5, 127.5, 62.4, 61.0, 55.7, 49.4, 43.9, 11.8, 4.1, 3.9.

1-Benzyl-3-isobutylpiperazine (9f) (Scheme 2)

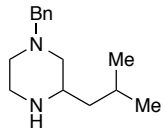
4-07-04-bhsieh.10.fid
Sample fly-09-094-CC
group bode
PRO CDCl3 /opt/v bhsieh 4



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30, 7.30, 7.30, 7.29, 7.28, 7.27, 7.25, 7.24, 7.24, 7.24, 7.23, 7.23, 7.22, 7.22, 7.21, 4.43, 3.54, 3.50, 3.47, 3.44, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.94, 2.94, 2.93, 2.92, 2.92, 2.92, 2.91, 2.91, 2.91, 2.90, 2.89, 2.89, 2.88, 2.88, 2.88, 2.87, 2.81, 2.81, 2.81, 2.80, 2.79, 2.78, 2.77, 2.77, 2.76, 2.76, 2.76, 2.75, 2.74, 2.73, 2.73, 2.18, 2.17, 2.15, 2.14, 2.12, 2.11, 1.87, 1.85, 1.85, 1.82, 1.71, 1.69, 1.69, 1.67, 1.67, 1.66, 1.66, 1.64, 1.64, 1.63, 1.62, 1.61, 1.39, 1.37, 1.36, 1.34, 1.32, 1.27, 1.25, 1.25, 1.23, 1.22, 1.21, 1.20, 0.88, 0.87, 0.86, 0.86.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30–7.27 (m, 4 H), 7.25–7.21 (m, 1 H), 4.43 (br, 1 H), 3.49 (apparent q, *J* = 13.0 Hz, 2 H), 3.03 (dt, *J* = 12.1, 2.9 Hz, 1 H), 2.94– 2.87 (m, 2 H), 2.81–2.73 (m, 2 H), 2.15 (apparent td, *J* = 11.3, 3.2 Hz, 1 H), 1.85 (dd, *J* = 11.3, 9.9 Hz, 1 H), 1.66 (apparent dh, *J* = 7.8, 6.6 Hz, 1 H), 1.36 (apparent dt, *J* = 14.0, 7.1 Hz, 1 H), 1.23 (ddd, *J* = 14.0, 7.8, 6.3 Hz, 1 H), 0.88 (d, *J* = 2.6 Hz, 3 H), 0.86 (d, *J* = 2.6 Hz, 3 H).

4-07-04-bhsieh.11.fid
Sample fly-09-094-CC
group bode
CAR CDCl3 /opt/v bhsieh 4



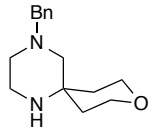
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.9, 129.2, 128.3, 127.2, 63.3, 59.2, 53.2, 52.8, 45.3, 42.7, 24.3, 23.0, 22.6.

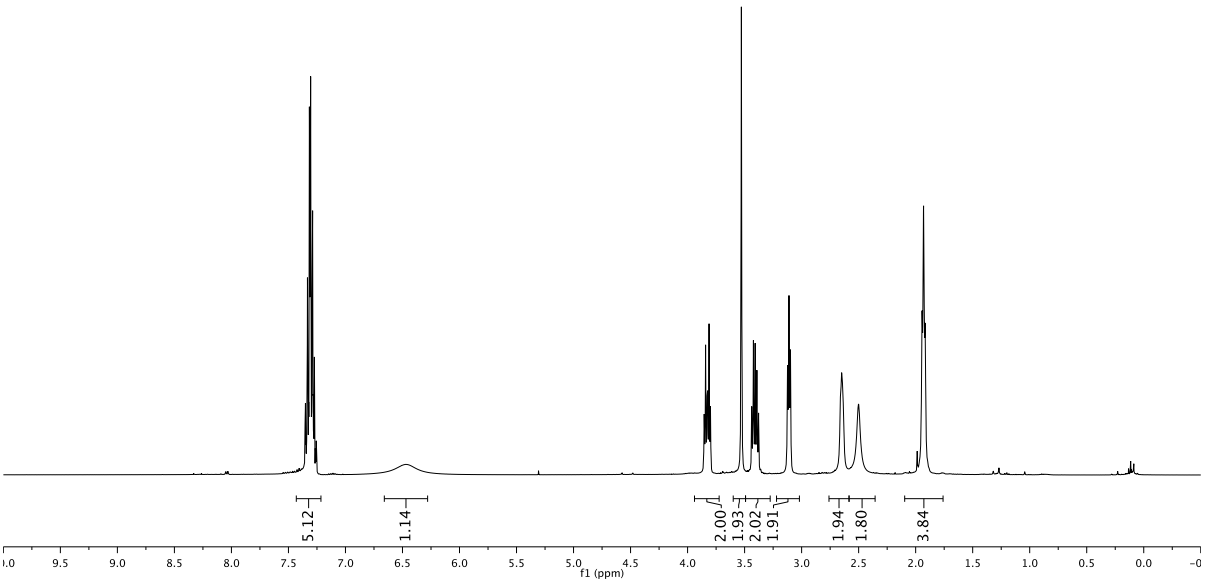
4-Benzyl-9-oxa-1,4-diazaspiro[5.5]undecane (9g) (Scheme 2)

41-08-10-bhsieh.10.fid
Sample fly-10-145-cyoxo-CC
group bode

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35, 7.35, 7.35, 7.34, 7.33, 7.33, 7.32, 7.32, 7.31, 7.31, 7.31, 7.29, 7.29, 7.28, 7.28, 7.28, 7.27, 7.26, 7.26, 6.47, 3.85, 3.84, 3.83, 3.82, 3.81, 3.80, 3.53, 3.44, 3.42, 3.41, 3.39, 3.38, 3.12, 3.11, 3.10, 2.66, 2.65, 2.64, 2.63, 2.50, 1.94, 1.93, 1.92.

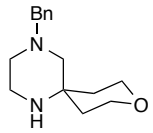
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35–7.26 (m, 5 H), 6.47 (br, 1 H), 3.83 (dt, *J* = 12.0, 4.9 Hz, 2 H), 3.53 (s, 2 H), 3.41 (dt, *J* = 12.0, 6.0 Hz, 2 H), 3.11 (apparent t, *J* = 5.2 Hz, 2 H), 2.65 (dd, *J* = 6.8, 3.8 Hz, 2 H), 2.50 (br, 2 H), 1.93 (apparent t, *J* = 5.5 Hz, 4 H).





41-08-10-bhsieh.11.fid
Sample fly-10-145-cyoxo-CC
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.9, 128.8, 128.5, 127.4, 63.3, 62.6, 58.9, 52.7, 52.5, 39.9, 33.6.

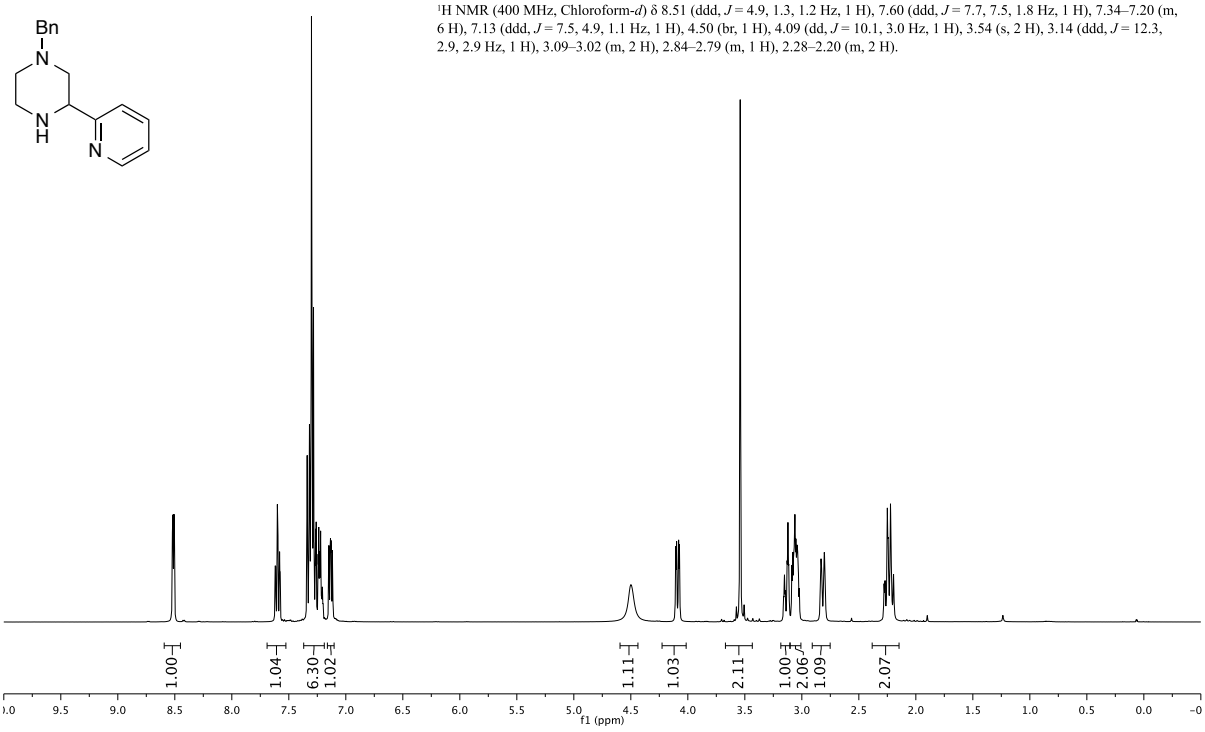


1-Benzyl-3-(pyridin-2-yl)piperazine (9h) (Scheme 2)

11-08-11-bhsieh.10.fid
Sample fly-11-009
group bode
PRO CDCl3 /opt/v bhsieh 11

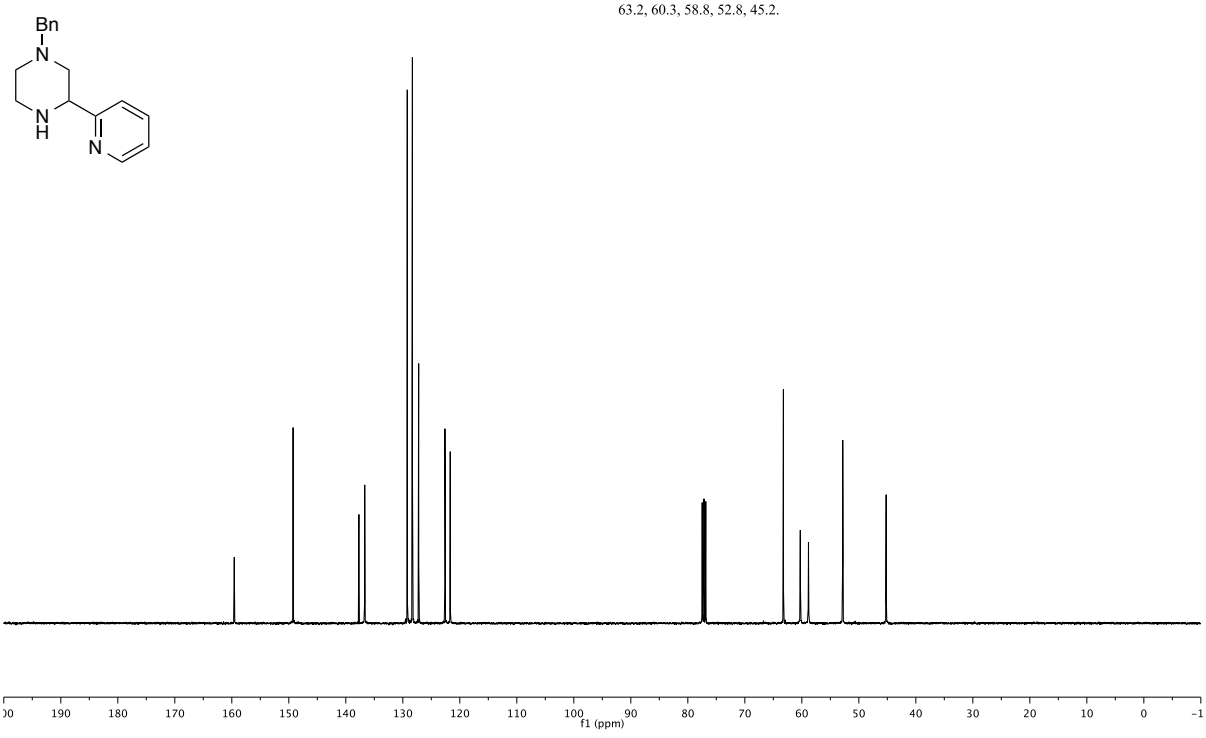
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52, 8.52, 8.51, 8.51, 8.51, 8.50, 7.62, 7.61, 7.60, 7.60, 7.58, 7.58, 7.34, 7.34, 7.34, 7.32, 7.32, 7.32, 7.30, 7.30, 7.29, 7.28, 7.28, 7.27, 7.26, 7.26, 7.24, 7.24, 7.23, 7.22, 7.22, 7.21, 7.21, 7.20, 7.15, 7.15, 7.14, 7.13, 7.13, 7.13, 7.12, 7.12, 4.50, 4.11, 4.10, 4.08, 4.07, 3.54, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.09, 3.08, 3.07, 3.07, 3.07, 3.06, 3.05, 3.05, 3.04, 3.04, 3.03, 3.03, 3.02, 2.84, 2.83, 2.83, 2.82, 2.81, 2.80, 2.80, 2.79, 2.28, 2.27, 2.25, 2.24, 2.22, 2.21, 2.20.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.51 (ddd, *J* = 4.9, 1.3, 1.2 Hz, 1 H), 7.60 (ddd, *J* = 7.7, 7.5, 1.8 Hz, 1 H), 7.34–7.20 (m, 6 H), 7.13 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1 H), 4.50 (br, 1 H), 4.09 (dd, *J* = 10.1, 3.0 Hz, 1 H), 3.54 (s, 2 H), 3.14 (ddd, *J* = 12.3, 2.9, 2.9 Hz, 1 H), 3.09–3.02 (m, 2 H), 2.84–2.79 (m, 1 H), 2.28–2.20 (m, 2 H).



11-08-11-bhsieh.11.fid
Sample fly-11-009
group bode
CAR CDCl3 /opt/v bhsieh 11

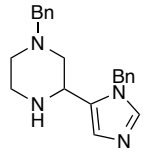
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 149.2, 137.7, 136.7, 129.2, 128.3, 127.2, 122.6, 121.7, 63.2, 60.3, 58.8, 52.8, 45.2.



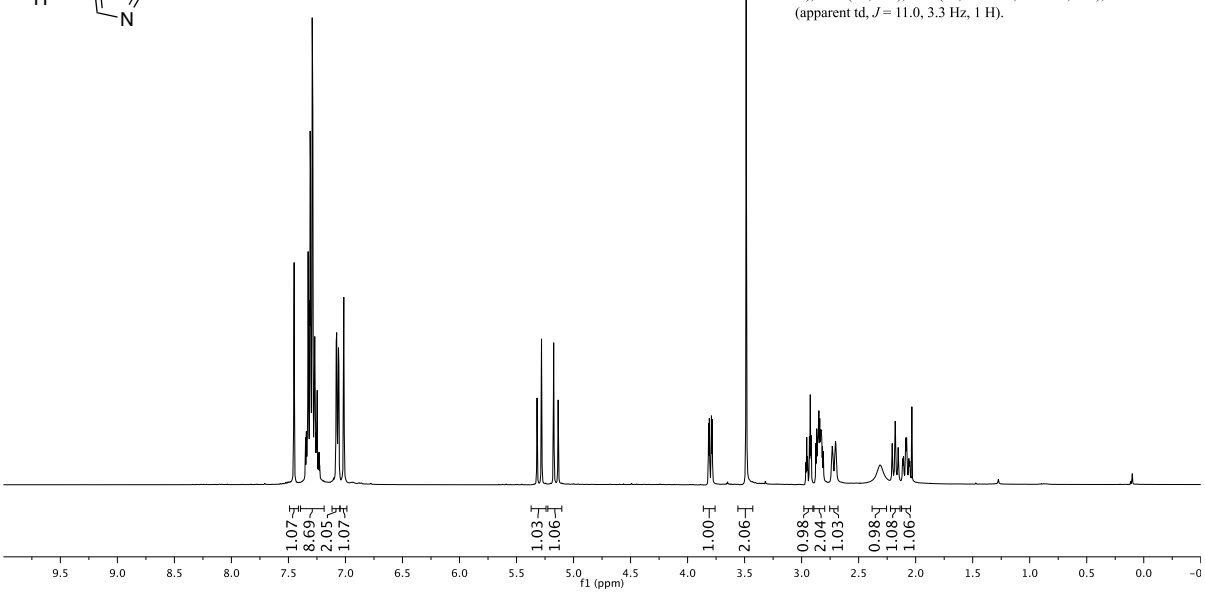
1-Benzyl-3-(1-benzyl-1*H*-imidazol-5-yl)piperazine (9i) (Scheme 2)

60-01-09-bhsieh.10.fid
Sample fly-11-013-CC
group bode
PRO CDCl3 /opt/v bhsieh 60

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45, 7.45, 7.35, 7.35, 7.34, 7.34, 7.33, 7.33, 7.32, 7.32, 7.31, 7.31, 7.31, 7.30, 7.29, 7.29, 7.28, 7.27, 7.27, 7.27, 7.26, 7.26, 7.25, 7.24, 7.23, 7.23, 7.08, 7.08, 7.08, 7.07, 7.07, 7.06, 7.06, 7.06, 7.02, 7.01, 7.01, 5.32, 5.28, 5.17, 5.14, 3.82, 3.82, 3.81, 3.81, 3.79, 3.79, 3.79, 3.78, 3.49, 2.96, 2.96, 2.95, 2.93, 2.92, 2.92, 2.88, 2.87, 2.86, 2.86, 2.85, 2.85, 2.84, 2.84, 2.84, 2.83, 2.83, 2.83, 2.82, 2.82, 2.81, 2.74, 2.73, 2.73, 2.72, 2.71, 2.70, 2.70, 2.69, 2.31, 2.21, 2.18, 2.15, 2.11, 2.11, 2.09, 2.08, 2.06, 2.05.

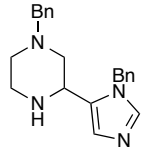


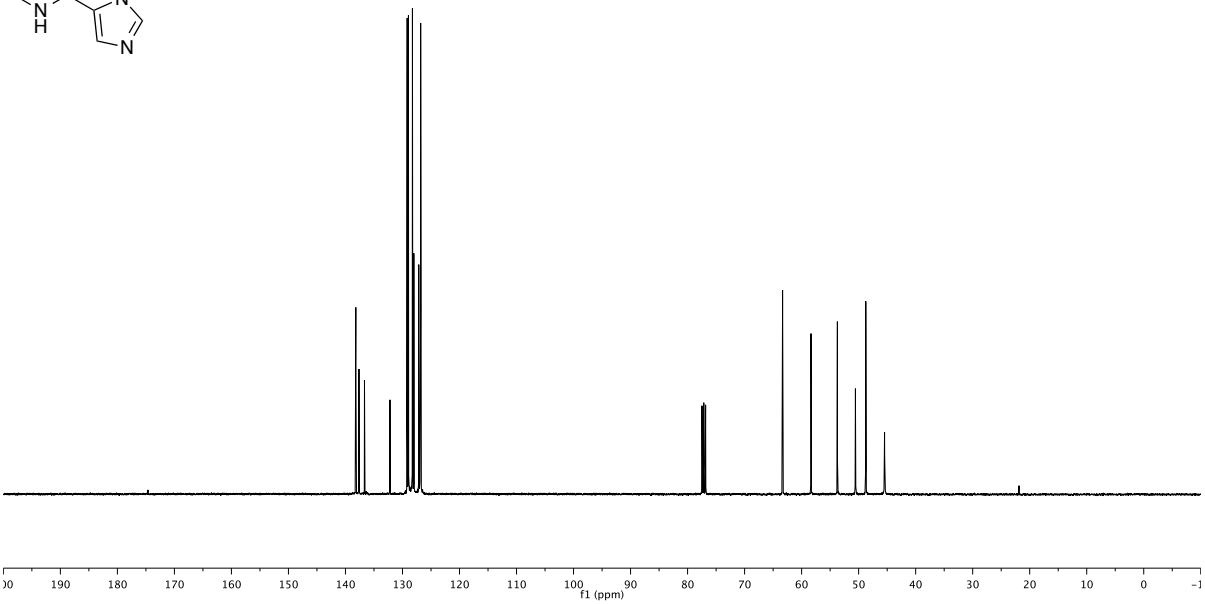
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 1.0 Hz, 1 H), 7.35–7.23 (m, 8 H), 7.08–7.06 (m, 2 H), 7.01 (apparent br, 1 H), 5.30 (d, *J* = 15.7 Hz, 1 H), 5.15 (d, *J* = 15.7 Hz, 1 H), 3.80 (ddd, *J* = 10.0, 2.8, 0.7 Hz, 1 H), 3.49 (s, 2 H), 2.94 (dt, *J* = 12.6, 3.0 Hz, 1 H), 2.88–2.81 (m, 2 H), 2.72 (apparent dq, *J* = 11.0, 2.5 Hz, 1 H), 2.31 (br , 1 H), 2.18 (dd, *J* = 10.0, 10.0 Hz, 1 H), 2.08 (apparent td, *J* = 11.0, 3.3 Hz, 1 H).



60-01-09-bhsieh.11.fid
Sample fly-11-013-CC
group bode
CAR CDCl3 /opt/v bhsieh 60

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 137.6, 136.7, 132.2, 129.2, 129.0, 128.3, 128.0, 127.1, 126.9, 126.8, 63.3, 58.4, 53.7, 50.6, 48.7, 45.5.



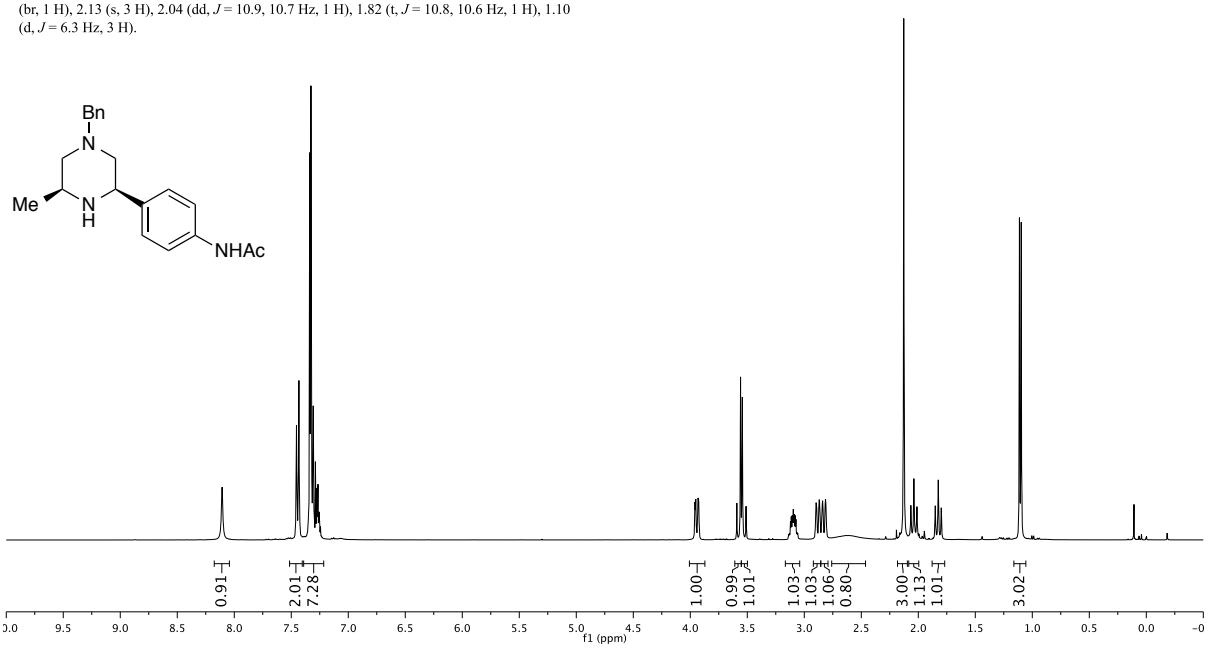


N-(4-((2*R*,6*S*)-4-Benzyl-6-methylpiperazin-2-yl)phenyl)acetamide (16a) (Scheme 3)

44-08-10-bhsieh.10.fid
Sample fly-11-039-CC
group bode

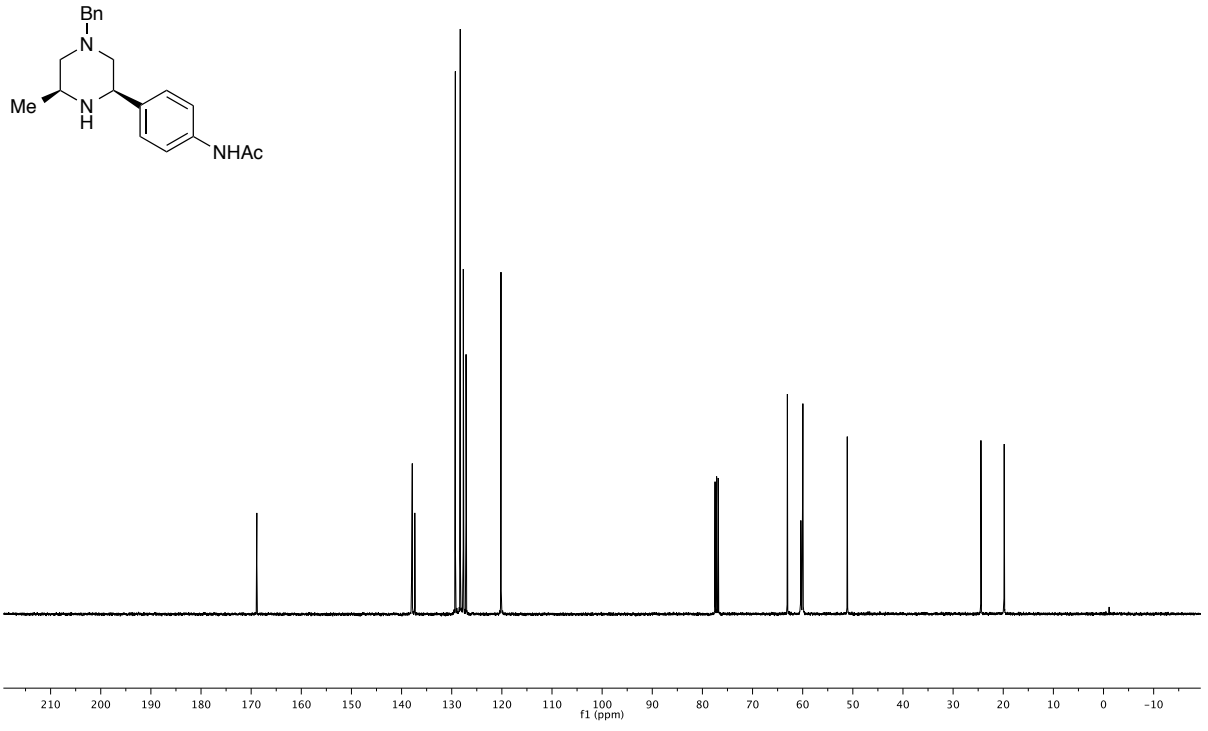
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11, 7.46, 7.45, 7.45, 7.44, 7.43, 7.43, 7.35, 7.34, 7.33, 7.33, 7.31, 7.31, 7.30, 7.29, 7.29, 7.28, 7.28, 7.27, 7.27, 7.26, 7.25, 7.25, 3.96, 3.95, 3.93, 3.93, 3.59, 3.56, 3.54, 3.51, 3.14, 3.13, 3.12, 3.11, 3.10, 3.10, 3.10, 3.09, 3.08, 3.07, 3.06, 3.06, 2.90, 2.87, 2.84, 2.81, 2.62, 2.13, 2.07, 2.04, 2.01, 1.85, 1.82, 1.80, 1.11, 1.10.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (s, 1 H), 7.46–7.43 (m, 2 H), 7.35–7.25 (m, 7 H), 3.94 (dd, *J* = 10.7, 2.8 Hz, 1 H), 3.58 (d, *J* = 13.1 Hz, 1 H), 3.53 (d, *J* = 13.1 Hz, 1 H), 3.10 (dqd, *J* = 10.6, 6.3, 2.8 Hz, 1 H), 2.88 (d, *J* = 10.9 Hz, 1 H), 2.82 (d, *J* = 10.8 Hz, 1 H), 2.62 (br, 1 H), 2.13 (s, 3 H), 2.04 (dd, *J* = 10.9, 10.7 Hz, 1 H), 1.82 (t, *J* = 10.8, 10.6 Hz, 1 H), 1.10 (d, *J* = 6.3 Hz, 3 H).

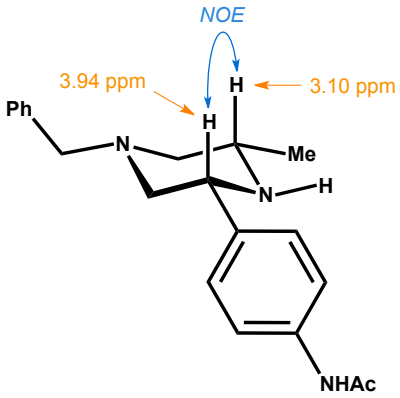


44-08-10-bhsieh.11.fid
Sample fly-11-039-CC
group bode

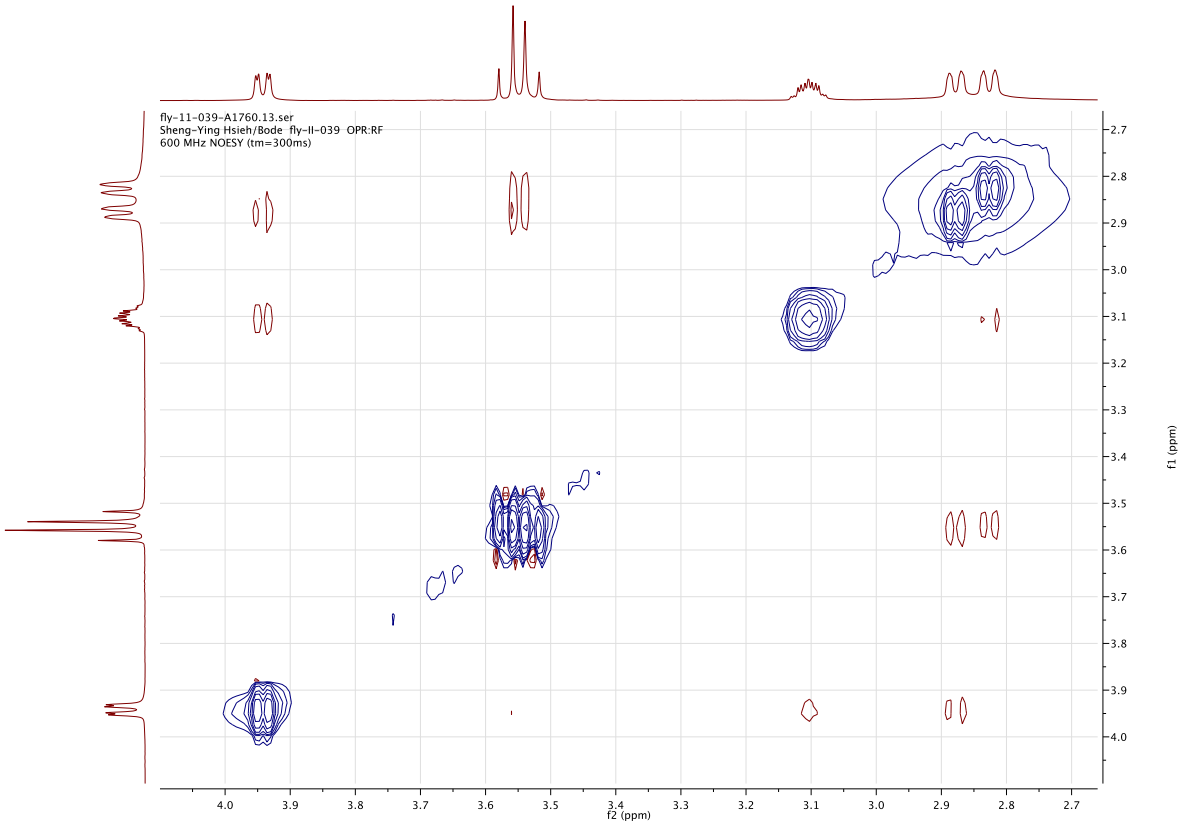
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 138.0, 137.9, 137.4, 129.3, 128.3, 127.7, 127.1, 120.2, 63.1, 60.4, 60.0, 60.0, 51.1, 24.4, 19.8.



NOESY of *N*-(4-((2*R*,6*S*)-4-benzyl-6-methylpiperazin-2-yl)phenyl)acetamide (16a)

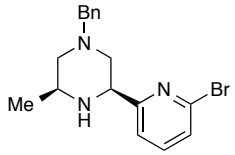


16a



(3*S*,5*S*)-1-Benzyl-3-(6-bromopyridin-2-yl)-5-methylpiperazine (16b) (Scheme 3)

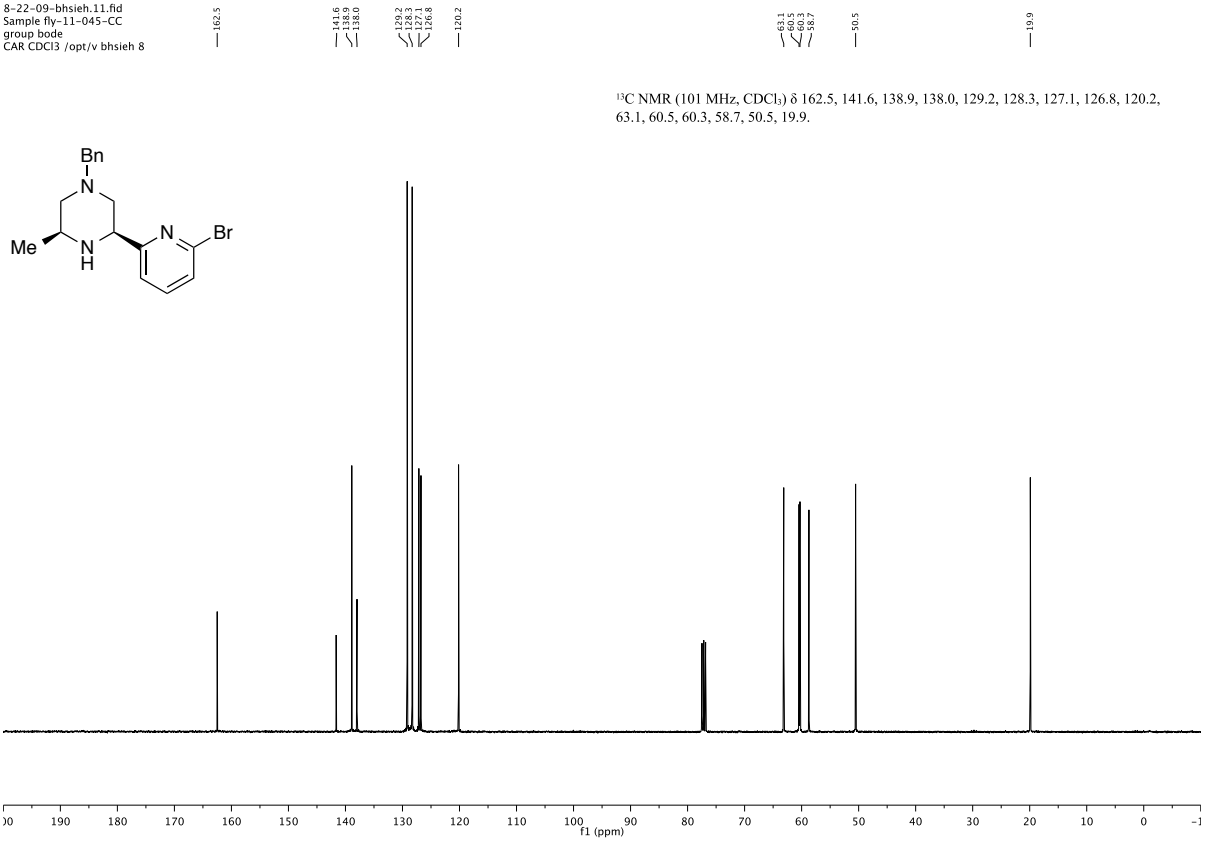
8-22-09-bhsieh.10.fid
Sample fly-11-045-CC
group bode
PRO CDCl3 /opt/v bhsieh 8



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50, 7.48, 7.46, 7.36, 7.36, 7.35, 7.34, 7.33, 7.33, 7.32, 7.32, 7.31, 7.31, 7.29, 7.29, 7.29, 7.28, 7.27, 7.27, 7.26, 7.26, 7.25, 7.25, 7.24, 7.24, 4.09, 4.08, 4.07, 4.06, 3.60, 3.57, 3.55, 3.52, 3.12, 3.11, 3.10, 3.10, 3.09, 3.09, 3.08, 3.08, 3.08, 3.07, 3.07, 3.06, 3.06, 3.06, 3.05, 3.04, 2.85, 2.85, 2.83, 2.82, 2.20, 2.05, 2.02, 1.99, 1.77, 1.75, 1.72, 1.12, 1.10.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (t, *J* = 7.7 Hz, 1 H), 7.36–7.24 (m, 7 H), 4.07 (dd, *J* = 10.5, 3.0 Hz, 1 H), 3.58 (d, *J* = 13.1 Hz, 1 H), 3.54 (d, *J* = 13.1 Hz, 1 H), 3.12–3.04 (m, 2 H), 2.84 (dd, *J* = 10.8, 2.9 Hz, 1 H), 2.20 (br, 1 H), 2.02 (t, *J* = 10.5 Hz, 1 H), 1.75 (t, *J* = 10.8 Hz, 1 H), 1.11 (d, *J* = 6.4 Hz, 3 H).

8-22-09-bhsieh.11.fid
Sample fly-11-045-CC
group bode
CAR CDCl3 /opt/v bhsieh 8



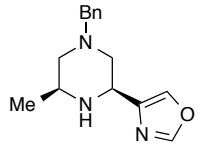
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 141.6, 138.9, 138.0, 129.2, 128.3, 127.1, 126.8, 120.2, 63.1, 60.5, 60.3, 58.7, 50.5, 19.9.

4-((2*S*,6*S*)-4-Benzyl-6-methylpiperazin-2-yl)oxazole (16c) (Scheme 3)

43-08-10-bhsieh.10.fid
Sample fly-11-020-CC
group bode

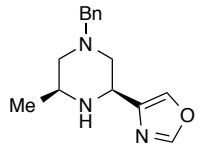
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82, 7.82, 7.56, 7.55, 7.55, 7.36, 7.35, 7.35, 7.34, 7.33, 7.32, 7.32, 7.32, 7.31, 7.30, 7.30, 7.29, 7.28, 7.27, 7.27, 7.27, 7.26, 7.26, 7.25, 7.25, 7.25, 7.24, 7.24, 4.05, 4.05, 4.03, 4.02, 3.56, 3.12, 3.11, 3.10, 3.10, 3.10, 3.09, 3.09, 3.09, 3.08, 3.08, 3.07, 3.07, 3.07, 3.06, 3.05, 3.04, 3.04, 2.85, 2.85, 2.83, 2.82, 2.20, 2.10, 2.08, 2.05, 1.80, 1.77, 1.77, 1.75, 1.09, 1.08.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 1.0 Hz, 1 H), 7.55 (t, *J* = 1.0 Hz, 1 H), 7.36–7.24 (m, 5 H), 4.04 (dd, *J* = 10.6, 3.0 Hz, 1 H), 3.56 (s, 2 H), 3.12–3.04 (m, 2 H), 2.84 (dd, *J* = 10.9, 2.9 Hz, 1 H), 2.20 (br, 1 H), 2.08 (dd, *J* = 10.6 Hz, 1 H), 1.77 (dd, *J* = 10.9, 10.1 Hz, 1 H), 1.08 (d, *J* = 6.4 Hz, 3 H).

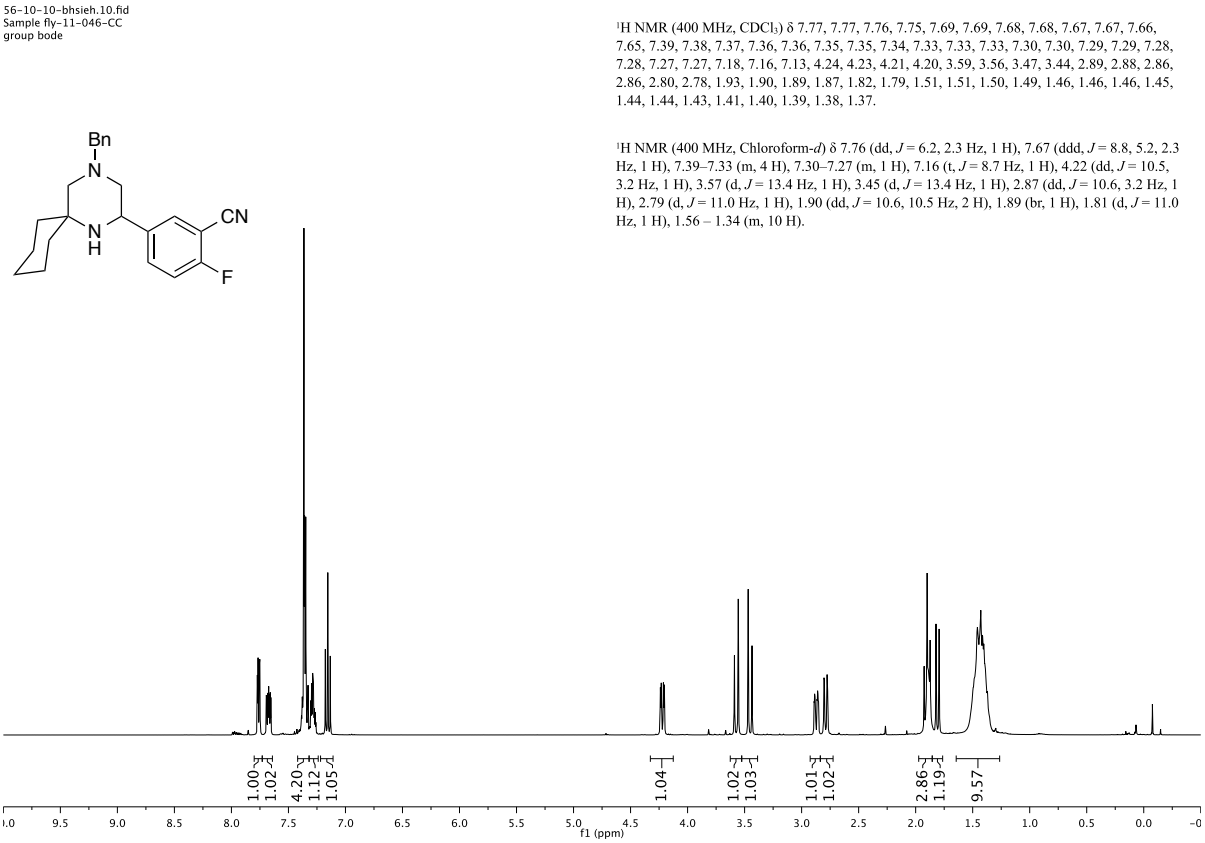


43-08-10-bhsieh.11.fid
Sample fly-11-020-CC
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 141.2, 137.9, 134.5, 129.2, 128.3, 127.2, 63.1, 60.5, 57.7, 52.5, 50.7, 19.8.

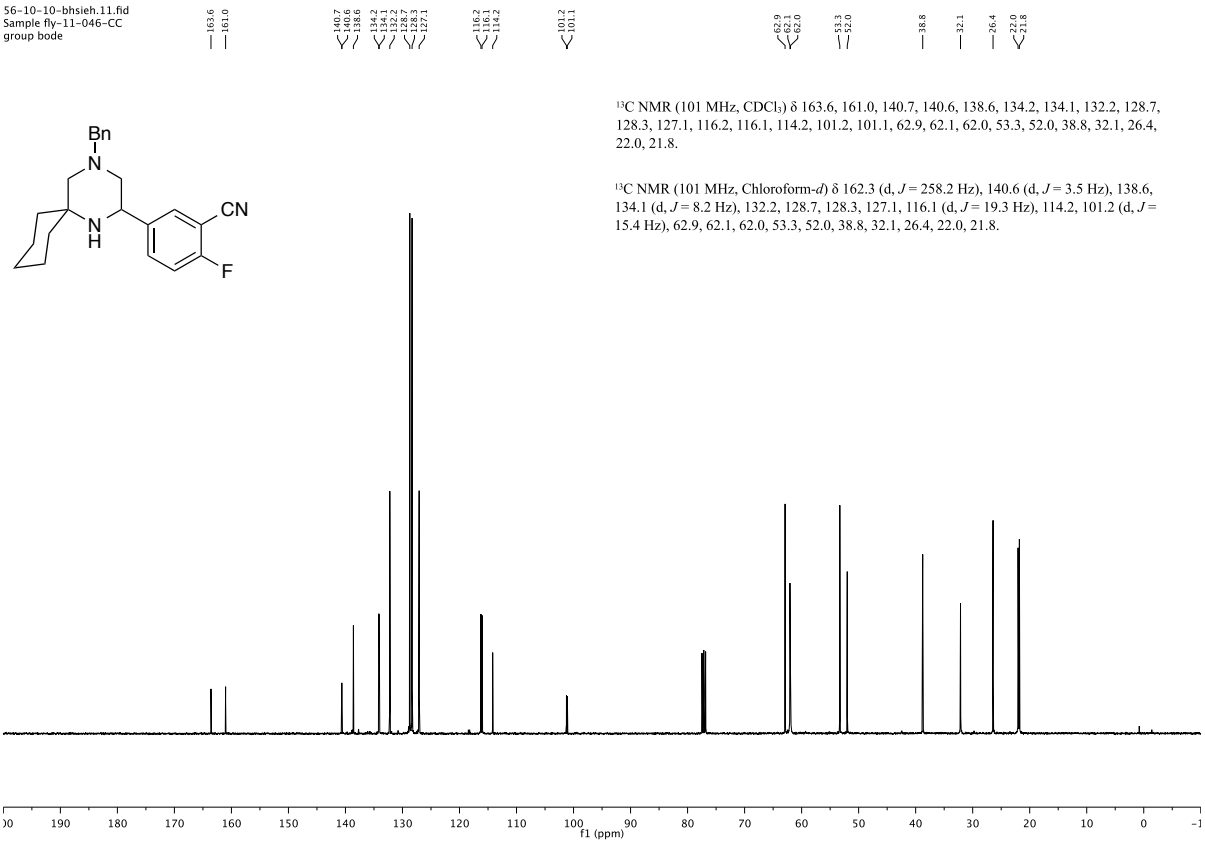


5-(4-Benzyl-1,4-diazaspiro[5.5]undecan-2-yl)-2-fluorobenzonitrile (17a) (Scheme 3)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77, 7.77, 7.76, 7.75, 7.69, 7.69, 7.68, 7.68, 7.67, 7.67, 7.66, 7.65, 7.39, 7.38, 7.37, 7.36, 7.36, 7.35, 7.35, 7.34, 7.33, 7.33, 7.33, 7.30, 7.30, 7.29, 7.29, 7.28, 7.28, 7.27, 7.27, 7.18, 7.16, 7.13, 4.24, 4.23, 4.21, 4.20, 3.59, 3.56, 3.47, 3.44, 2.89, 2.88, 2.86, 2.86, 2.80, 2.78, 1.93, 1.90, 1.89, 1.87, 1.82, 1.79, 1.51, 1.51, 1.50, 1.49, 1.46, 1.46, 1.46, 1.45, 1.44, 1.44, 1.43, 1.41, 1.40, 1.39, 1.38, 1.37.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 6.2, 2.3 Hz, 1 H), 7.67 (ddd, *J* = 8.8, 5.2, 2.3 Hz, 1 H), 7.39–7.33 (m, 4 H), 7.30–7.27 (m, 1 H), 7.16 (t, *J* = 8.7 Hz, 1 H), 4.22 (dd, *J* = 10.5, 3.2 Hz, 1 H), 3.57 (d, *J* = 13.4 Hz, 1 H), 3.45 (d, *J* = 13.4 Hz, 1 H), 2.87 (dd, *J* = 10.6, 3.2 Hz, 1 H), 2.79 (d, *J* = 11.0 Hz, 1 H), 1.90 (dd, *J* = 10.6, 10.5 Hz, 2 H), 1.89 (br, 1 H), 1.81 (d, *J* = 11.0 Hz, 1 H), 1.56 – 1.34 (m, 10 H).



^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 161.0, 140.7, 140.6, 138.6, 134.2, 134.1, 132.2, 128.7, 128.3, 127.1, 116.2, 116.1, 114.2, 101.2, 101.1, 62.9, 62.1, 62.0, 53.3, 52.0, 38.8, 32.1, 26.4, 22.0, 21.8.

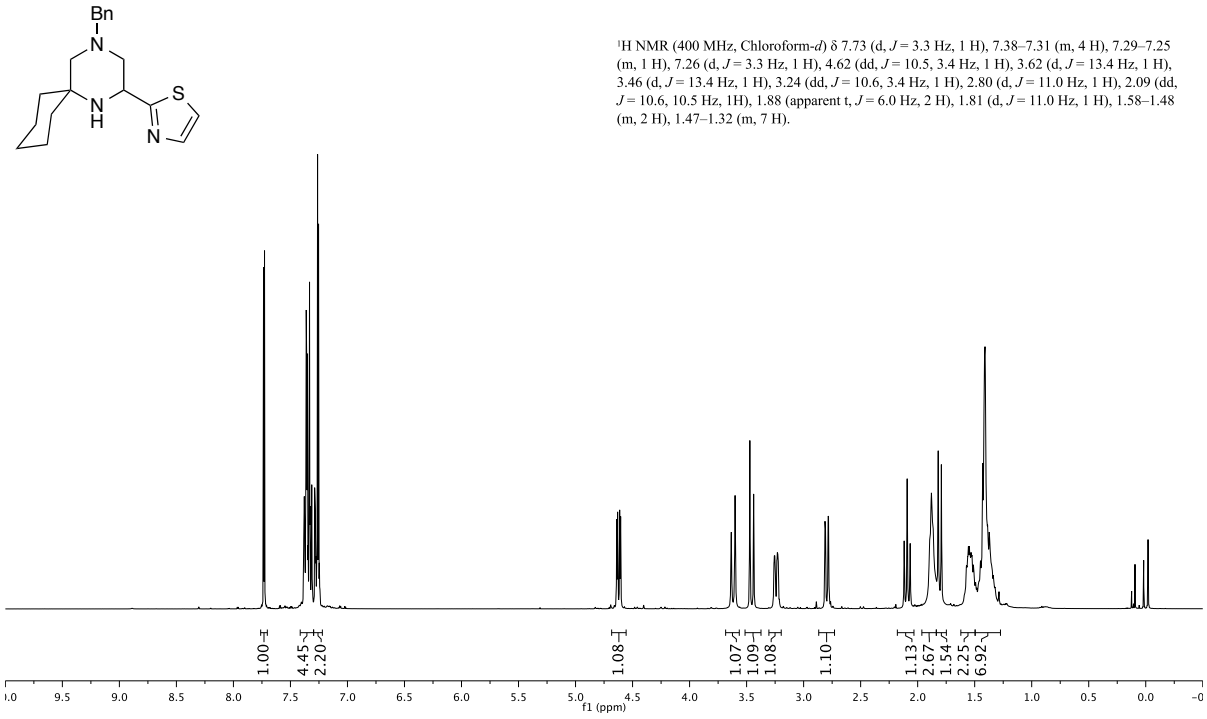
^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.3 (d, *J* = 258.2 Hz), 140.6 (d, *J* = 3.5 Hz), 138.6, 134.1 (d, *J* = 8.2 Hz), 132.2, 128.7, 128.3, 127.1, 116.1 (d, *J* = 19.3 Hz), 114.2, 101.2 (d, *J* = 15.4 Hz), 62.9, 62.1, 62.0, 53.3, 52.0, 38.8, 32.1, 26.4, 22.0, 21.8.

2-(4-Benzyl-1,4-diazaspiro[5.5]undecan-2-yl)thiazole (17b) (Scheme 3)

54-10-10-bhsieh.10.fid
Sample fly-11-024-CC
group bode

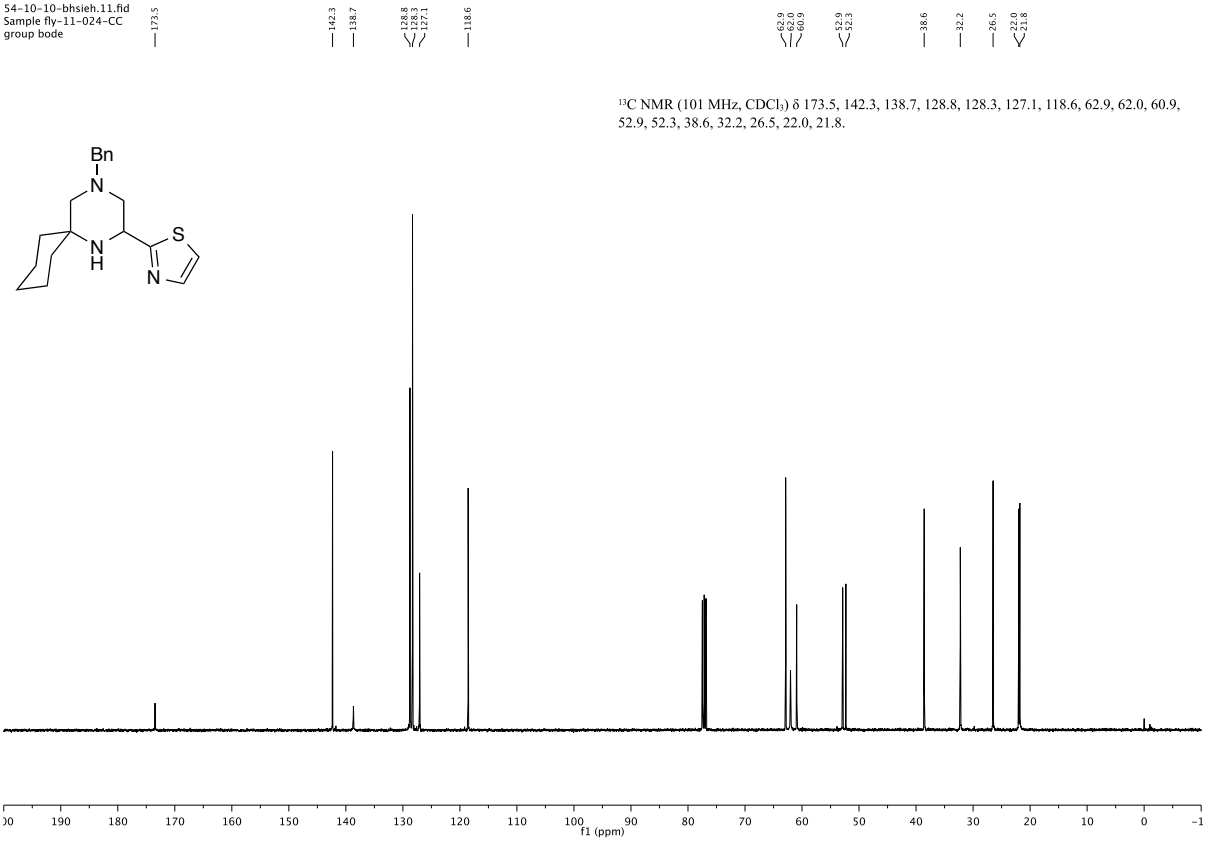
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74, 7.73, 7.38, 7.38, 7.37, 7.36, 7.36, 7.35, 7.35, 7.35, 7.34, 7.34, 7.33, 7.33, 7.32, 7.32, 7.31, 7.29, 7.29, 7.28, 7.28, 7.27, 7.27, 7.26, 7.26, 7.25, 7.25, 7.25, 4.64, 4.63, 4.61, 4.60, 3.63, 3.60, 3.47, 3.44, 3.26, 3.25, 3.23, 3.22, 2.81, 2.78, 2.12, 2.09, 2.07, 1.89, 1.88, 1.86, 1.82, 1.79, 1.58, 1.58, 1.57, 1.57, 1.56, 1.56, 1.56, 1.55, 1.54, 1.53, 1.53, 1.52, 1.51, 1.51, 1.49, 1.49, 1.48, 1.47, 1.47, 1.46, 1.46, 1.45, 1.45, 1.43, 1.42, 1.41, 1.41, 1.40, 1.39, 1.39, 1.39, 1.37, 1.37, 1.36, 1.35, 1.35, 1.34, 1.33, 1.32.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 3.3 Hz, 1 H), 7.38–7.31 (m, 4 H), 7.29–7.25 (m, 1 H), 7.26 (d, *J* = 3.3 Hz, 1 H), 4.62 (dd, *J* = 10.5, 3.4 Hz, 1 H), 3.62 (d, *J* = 13.4 Hz, 1 H), 3.46 (d, *J* = 13.4 Hz, 1 H), 3.24 (dd, *J* = 10.6, 3.4 Hz, 1 H), 2.80 (d, *J* = 11.0 Hz, 1 H), 2.09 (dd, *J* = 10.6, 10.5 Hz, 1H), 1.88 (apparent t, *J* = 6.0 Hz, 2 H), 1.81 (d, *J* = 11.0 Hz, 1 H), 1.58–1.48 (m, 2 H), 1.47–1.32 (m, 7 H).



54-10-10-bhsieh.11.fid
Sample fly-11-024-CC
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 142.3, 138.7, 128.8, 128.3, 127.1, 118.6, 62.9, 62.0, 60.9, 52.9, 52.3, 38.6, 32.2, 26.5, 22.0, 21.8.

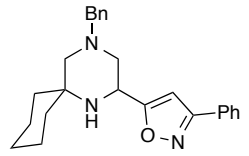


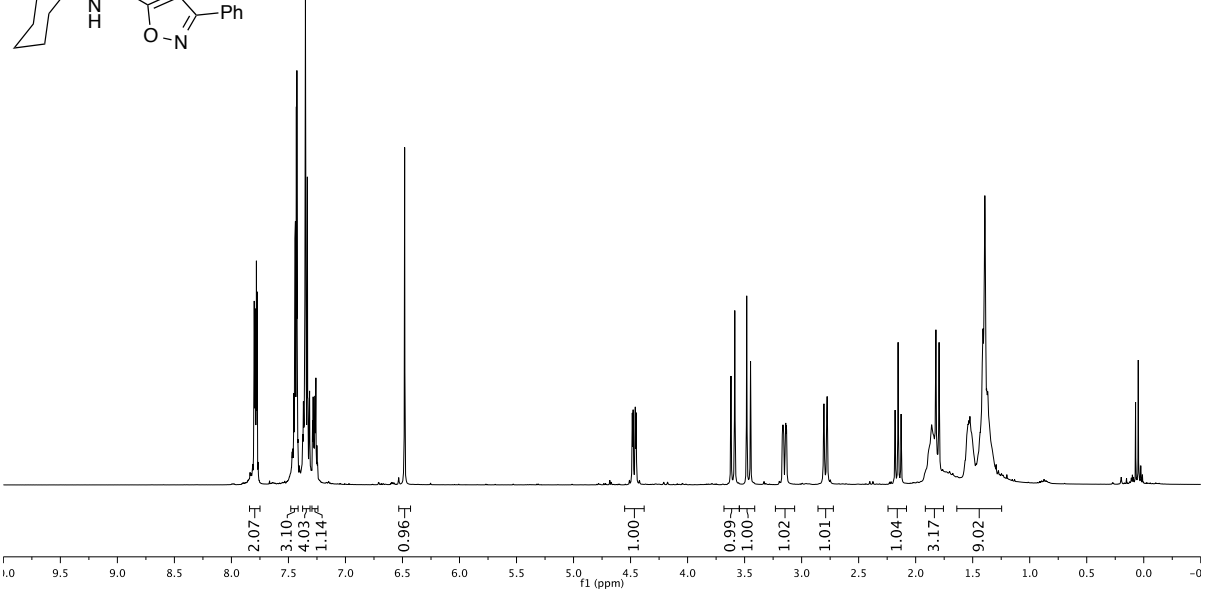
5-(4-Benzyl-1,4-diazaspiro[5.5]undecan-2-yl)-3-phenylisoxazole (17c) (Scheme 3)

38-05-11-bhsieh.10.fid
Sample fly-11-087-CC
group bode
PRO CDCl3 /opt/v bhsieh 38

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80, 7.80, 7.79, 7.79, 7.79, 7.78, 7.78, 7.78, 7.45, 7.45, 7.45, 7.44, 7.44, 7.43, 7.43, 7.42, 7.42, 7.37, 7.36, 7.35, 7.35, 7.35, 7.35, 7.34, 7.33, 7.33, 7.32, 7.32, 7.31, 7.29, 7.28, 7.28, 7.27, 7.27, 7.27, 7.26, 7.26, 7.25, 6.48, 4.49, 4.48, 4.46, 4.45, 3.62, 3.59, 3.48, 3.45, 3.17, 3.16, 3.14, 3.13, 2.81, 2.80, 2.78, 2.78, 2.18, 2.15, 2.13, 1.90, 1.88, 1.86, 1.84, 1.84, 1.82, 1.79, 1.56, 1.55, 1.55, 1.54, 1.53, 1.52, 1.51, 1.50, 1.49, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.39, 1.39, 1.38, 1.37, 1.35, 1.33.

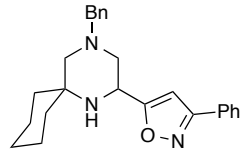
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80–7.78 (m, 2 H), 7.45–7.42 (m, 3 H), 7.37–7.31 (m, 4 H), 7.29–7.25 (m, 1 H), 6.48 (s, 1 H), 4.47 (dd, *J* = 10.6, 2.6 Hz, 1 H), 3.60 (d, *J* = 13.3 Hz, 1 H), 3.46 (d, *J* = 13.3 Hz, 1 H), 3.15 (dd, *J* = 10.5, 2.6 Hz, 1 H), 2.79 (d, *J* = 11.1 Hz, 1 H), 2.15 (dd, *J* = 10.6, 10.5 Hz, 1 H), 1.90–1.81 (m, 2 H), 1.81 (d, *J* = 11.1 Hz, 1 H), 1.56–1.49 (m, 2 H), 1.45–1.33 (m, 7 H).





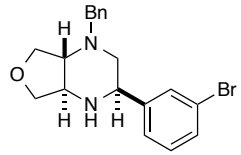
38-05-11-bhsieh.11.fid
Sample fly-11-087-CC
group bode
CAR CDCl3 /opt/v bhsieh 38

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 162.3, 138.5, 130.0, 129.2, 128.9, 128.8, 128.4, 127.2, 126.9, 98.7, 62.9, 62.0, 58.5, 52.1, 47.9, 38.5, 32.0, 26.4, 21.9, 21.8.



(*trans*,*cis*)-1-Benzyl-3-(3-bromophenyl)octahydrofuro[3,4-*b*]pyrazine (18a) (Scheme 3)

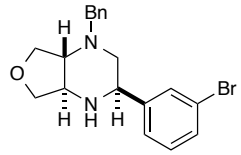
53-10-10-bhsieh.10.fid
Sample fly-11-022-CC
group bode



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59, 7.59, 7.58, 7.42, 7.42, 7.42, 7.42, 7.40, 7.40, 7.40, 7.40, 7.34, 7.33, 7.33, 7.33, 7.32, 7.32, 7.31, 7.31, 7.30, 7.30, 7.30, 7.29, 7.29, 7.29, 7.29, 7.28, 7.28, 7.28, 7.27, 7.27, 7.27, 7.27, 7.26, 7.20, 7.18, 7.16, 4.06, 4.05, 4.03, 4.03, 4.02, 4.02, 4.00, 3.99, 3.73, 3.71, 3.70, 3.68, 3.66, 3.63, 3.62, 3.60, 3.59, 3.57, 3.38, 3.35, 3.31, 3.29, 3.28, 3.28, 3.27, 3.26, 3.26, 3.24, 2.94, 2.93, 2.91, 2.90, 2.54, 2.53, 2.52, 2.52, 2.50, 2.50, 2.49, 2.48, 2.07, 2.05, 2.05, 2.04, 2.02.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (t, *J* = 2.0 Hz, 1 H), 7.41 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1 H), 7.34–7.26 (m, 6 H), 7.18 (t, *J* = 7.9 Hz, 1 H), 4.06 – 3.99 (m, 2 H), 4.01 (dd, *J* = 10.6, 3.1 Hz, 1 H), 3.71 (dd, *J* = 10.6, 7.2 Hz, 1 H), 3.65 (d, *J* = 13.1 Hz, 1 H), 3.59 (dd, *J* = 10.5, 7.0 Hz, 1 H), 3.36 (d, *J* = 13.1 Hz, 1 H), 3.27 (ddd, *J* = 10.6, 9.2, 7.2 Hz, 1 H), 2.92 (dd, *J* = 11.4, 3.1 Hz, 1 H), 2.51 (ddd, *J* = 10.5, 9.2, 7.0 Hz, 1 H), 2.05 (dd, *J* = 11.4, 10.6 Hz, 1 H), 2.04 (br, 1 H).

53-10-10-bhsieh.11.fid
Sample fly-11-022-CC
group bode



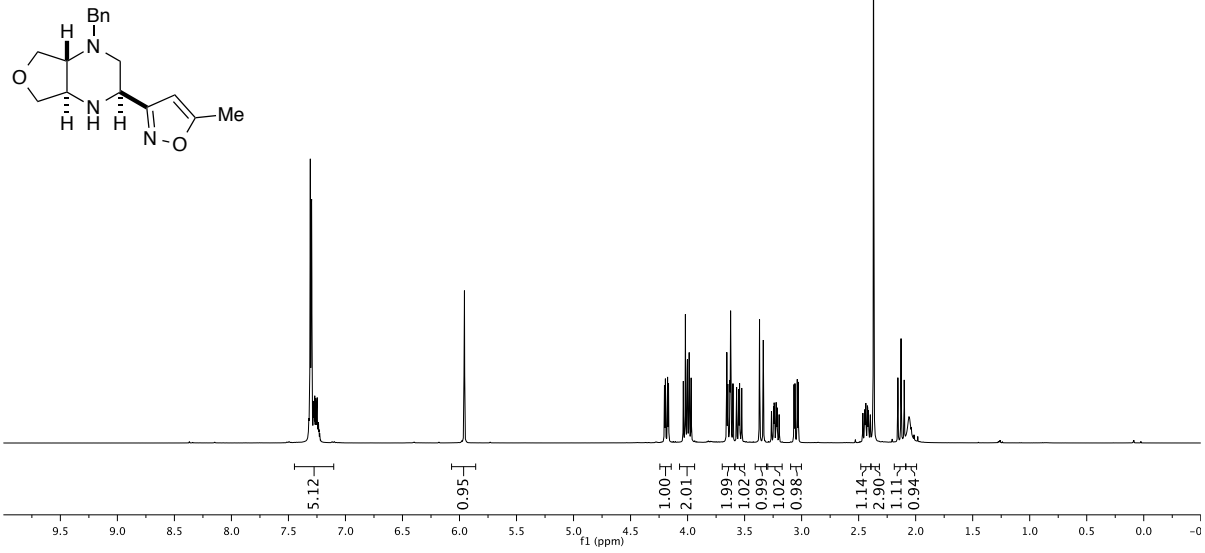
^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 137.5, 130.9, 130.4, 130.1, 129.2, 128.4, 127.5, 126.1, 122.6, 69.9, 69.8, 68.2, 62.0, 61.8, 61.0, 60.9.

(*trans*,*cis*)-1-Benzyl-3-(5-methylisoxazol-3-yl)octahydrofuro[3,4-*b*]pyrazine (18b) (Scheme 3)

53-23-09-bhsieh.10.fid
Sample fly-11-048-CC
group bode
PRO CDCl3 /opt/v bhsieh 53

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33, 7.32, 7.32, 7.31, 7.31, 7.30, 7.30, 7.30, 7.29, 7.28, 7.28, 7.28, 7.28, 7.27, 7.27, 7.26, 7.26, 7.25, 7.25, 7.24, 7.24, 7.23, 7.23, 5.96, 5.96, 4.20, 4.19, 4.18, 4.17, 4.04, 4.02, 4.00, 4.00, 3.99, 3.99, 3.97, 3.66, 3.65, 3.63, 3.62, 3.62, 3.60, 3.57, 3.55, 3.54, 3.53, 3.37, 3.34, 3.26, 3.25, 3.24, 3.24, 3.22, 3.22, 3.21, 3.20, 3.07, 3.06, 3.04, 3.03, 2.46, 2.45, 2.44, 2.44, 2.42, 2.42, 2.41, 2.40, 2.37, 2.37, 2.16, 2.13, 2.10, 2.06.

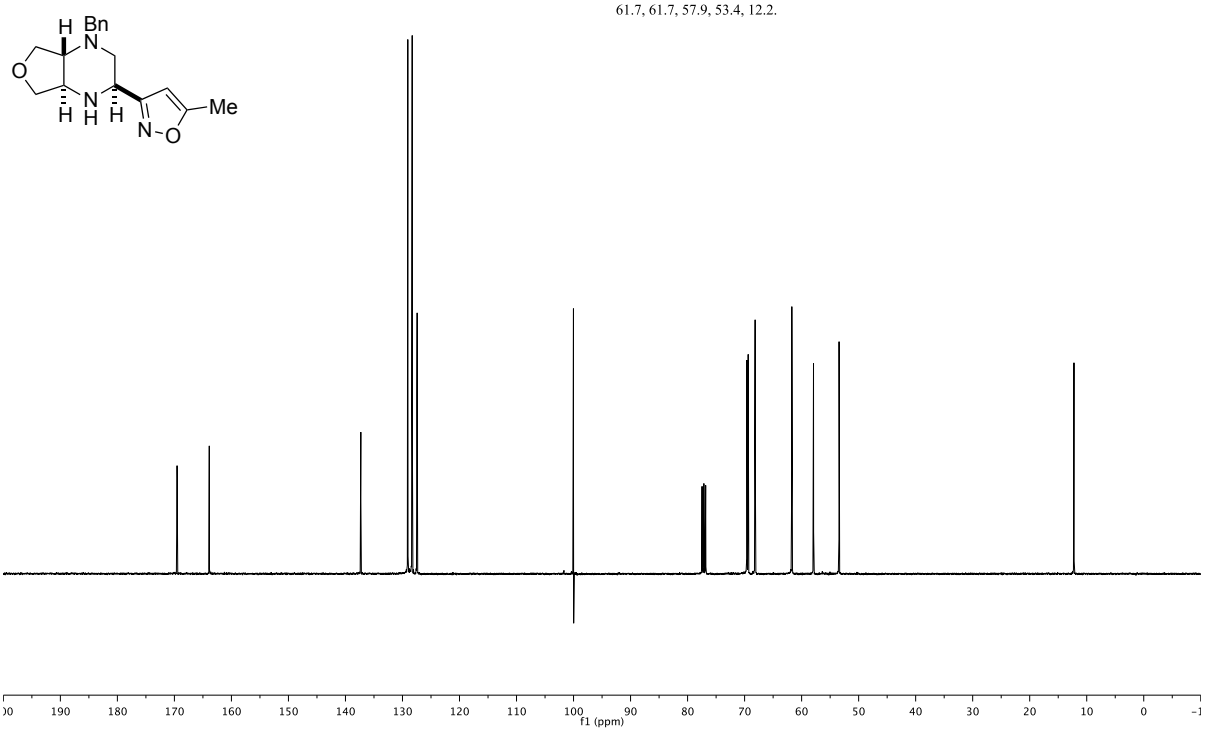
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33–7.23 (m, 5 H), 5.96 (d, *J* = 1.0 Hz, 1 H), 4.19 (dd, *J* = 11.0, 3.2 Hz, 1 H), 4.02 (dd, *J* = 7.3, 7.3 Hz, 1 H), 3.99 (dd, *J* = 7.5, 6.7 Hz, 1 H), 3.64 (d, *J* = 13.2 Hz, 1 H), 3.62 (dd, *J* = 10.7, 7.3 Hz, 1 H), 3.55 (dd, *J* = 10.5, 7.5 Hz, 1 H), 3.35 (d, *J* = 13.2 Hz, 1 H), 3.23 (ddd, *J* = 10.7, 9.1, 7.3 Hz, 1 H), 3.05 (dd, *J* = 11.2, 3.2 Hz, 1 H), 2.43 (ddd, *J* = 10.5, 9.1, 6.7 Hz, 1H), 2.37 (d, *J* = 1.0 Hz, 3 H), 2.13 (dd, *J* = 11.2, 11.0 Hz, 1 H), 2.06 (br, 1 H).



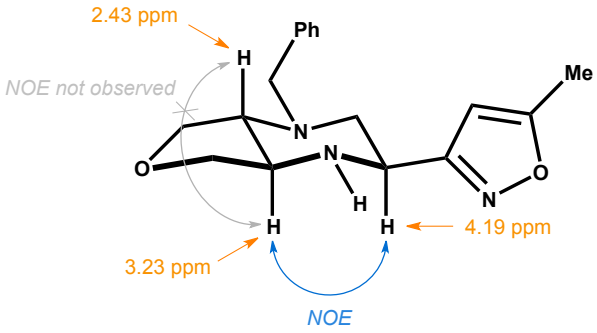
53-23-09-bhsieh.11.fid
Sample fly-11-048-CC
group bode
CAR CDCl3 /opt/v bhsieh 53

169.5 163.9 137.3 129.1 128.3 127.4 100.0 69.6 69.4 68.2 61.7 61.7 57.9 53.4 12.2

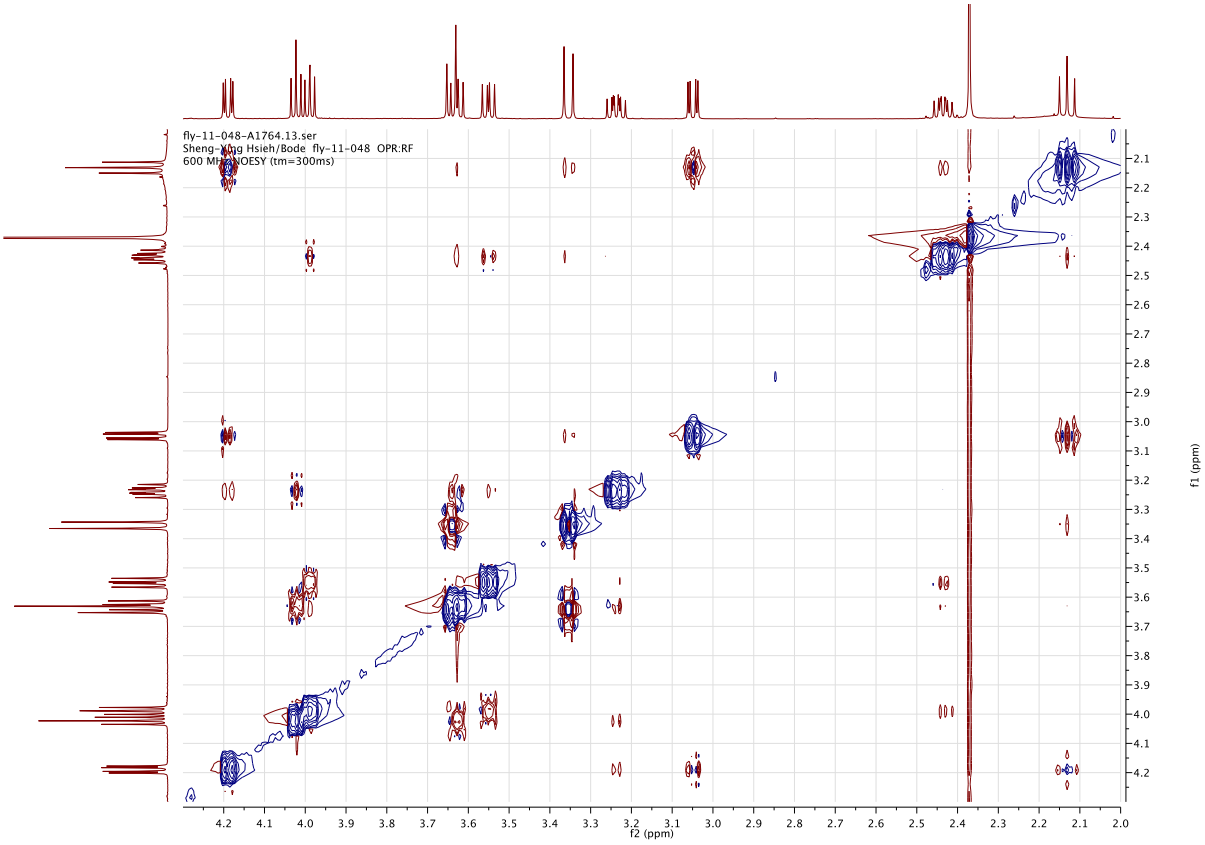
^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 163.9, 137.3, 129.1, 128.3, 127.4, 100.0, 69.6, 69.4, 68.2, 61.7, 61.7, 57.9, 53.4, 12.2.



NOESY of (*trans*,*cis*)-1-benzyl-3-(5-methylisoxazol-3-yl)octahydrofuro[3,4-*b*]pyrazine (18b)



18b

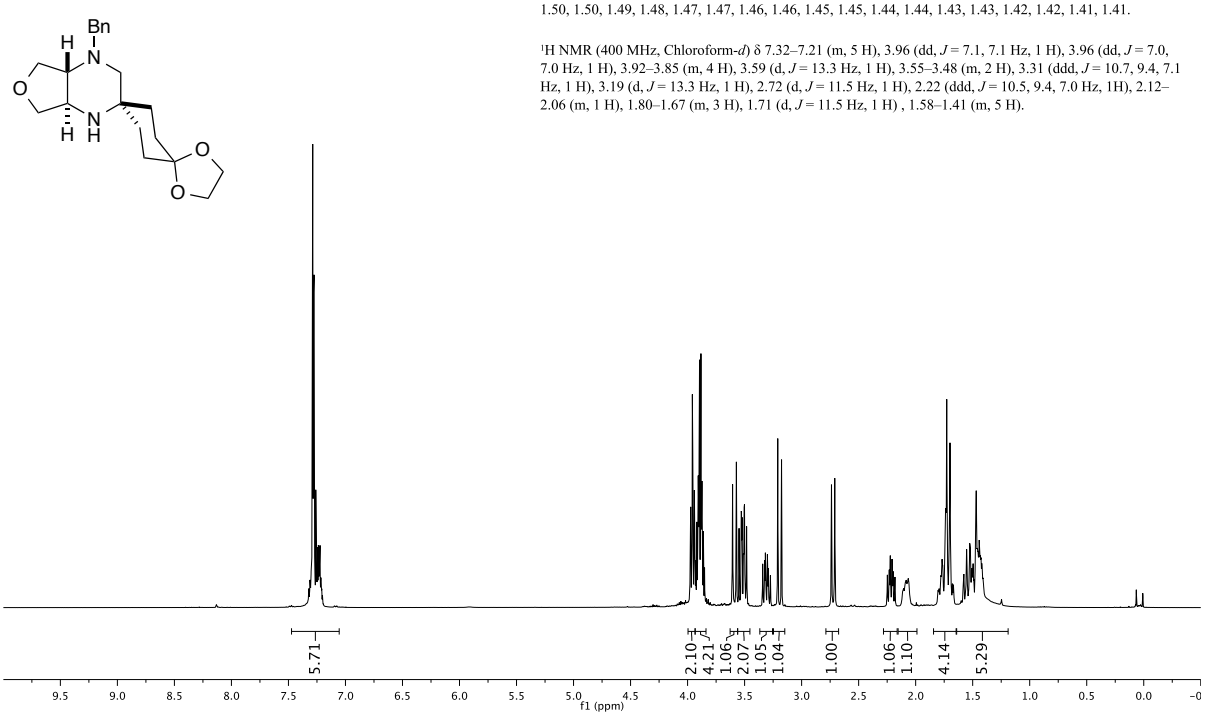


(*trans*)-4'-Benzylhexahydro-1'*H*-spiro[cyclohexane-1,2'-furo[3,4-*b*]pyrazin]-4-one ethylene ketal (18c) (Scheme 3)

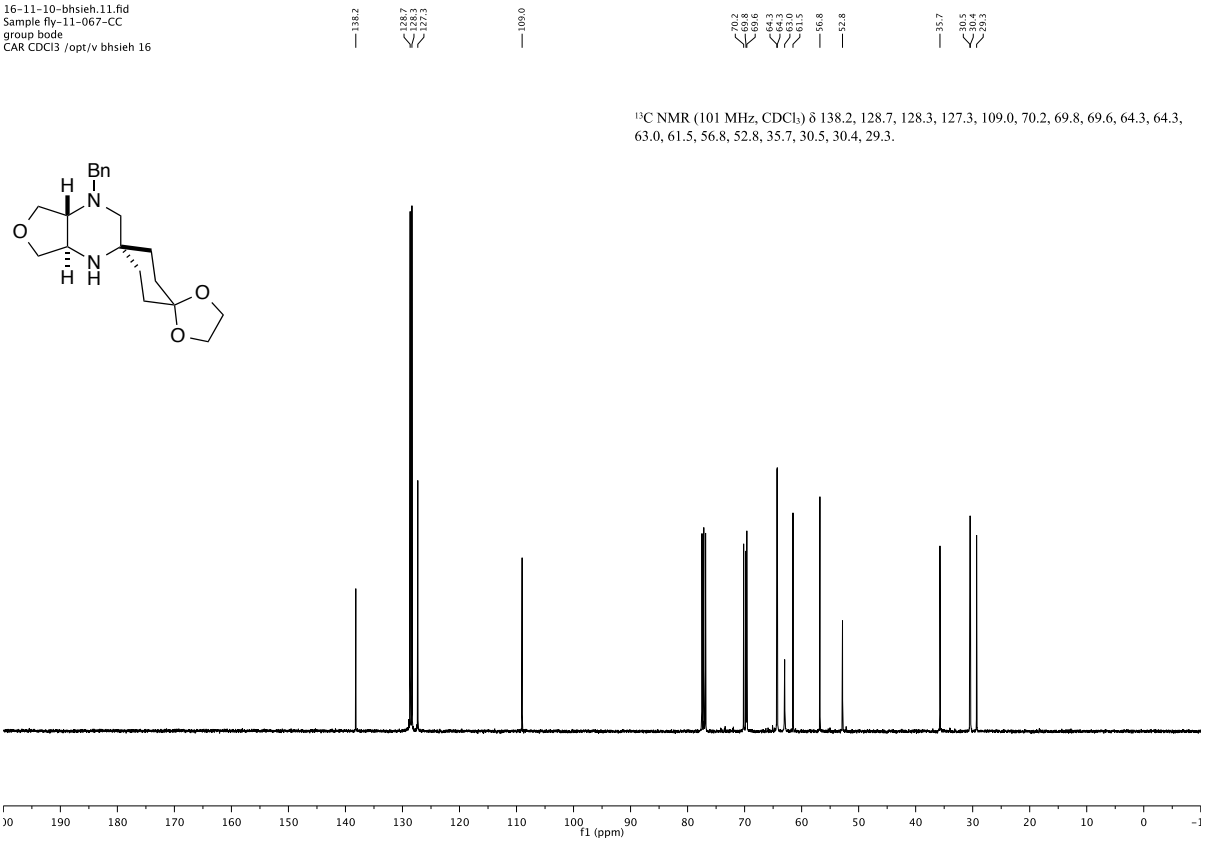
16-11-10-bhsieh.10.fid
Sample fly-11-067-CC
group bode
PRO CDCl3 /opt/v bhsieh 16

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32, 7.31, 7.30, 7.29, 7.28, 7.27, 7.27, 7.26, 7.26, 7.25, 7.25, 7.24, 7.23, 7.23, 7.22, 7.22, 7.21, 7.21, 3.98, 3.97, 3.96, 3.96, 3.94, 3.94, 3.93, 3.92, 3.91, 3.91, 3.90, 3.90, 3.90, 3.89, 3.88, 3.88, 3.87, 3.87, 3.86, 3.85, 3.61, 3.57, 3.55, 3.53, 3.53, 3.53, 3.52, 3.51, 3.50, 3.50, 3.48, 3.34, 3.32, 3.32, 3.31, 3.30, 3.30, 3.29, 3.27, 3.21, 3.18, 2.74, 2.71, 2.25, 2.23, 2.22, 2.22, 2.21, 2.21, 2.20, 2.19, 2.18, 2.12, 2.11, 2.11, 2.10, 2.09, 2.08, 2.08, 2.07, 2.06, 1.80, 1.79, 1.78, 1.77, 1.76, 1.76, 1.75, 1.74, 1.74, 1.73, 1.73, 1.72, 1.71, 1.70, 1.70, 1.69, 1.68, 1.68, 1.67, 1.67, 1.58, 1.58, 1.56, 1.55, 1.55, 1.53, 1.52, 1.52, 1.51, 1.51, 1.50, 1.50, 1.49, 1.48, 1.47, 1.47, 1.46, 1.46, 1.45, 1.45, 1.44, 1.44, 1.43, 1.43, 1.42, 1.42, 1.41, 1.41.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32–7.21 (m, 5 H), 3.96 (dd, *J* = 7.1, 7.1 Hz, 1 H), 3.96 (dd, *J* = 7.0, 7.0 Hz, 1 H), 3.92–3.85 (m, 4 H), 3.59 (d, *J* = 13.3 Hz, 1 H), 3.55–3.48 (m, 2 H), 3.31 (ddd, *J* = 10.7, 9.4, 7.1 Hz, 1 H), 3.19 (d, *J* = 13.3 Hz, 1 H), 2.72 (d, *J* = 11.5 Hz, 1 H), 2.22 (ddd, *J* = 10.5, 9.4, 7.0 Hz, 1H), 2.12–2.06 (m, 1 H), 1.80–1.67 (m, 3 H), 1.71 (d, *J* = 11.5 Hz, 1 H) , 1.58–1.41 (m, 5 H).



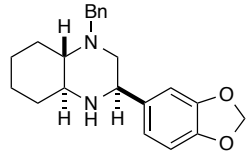
16-11-10-bhsieh.11.fid
Sample fly-11-067-CC
group bode
CAR CDCl3 /opt/v bhsieh 16



^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 128.7, 128.3, 127.3, 109.0, 70.2, 69.8, 69.6, 64.3, 64.3, 63.0, 61.5, 56.8, 52.8, 35.7, 30.5, 30.4, 29.3.

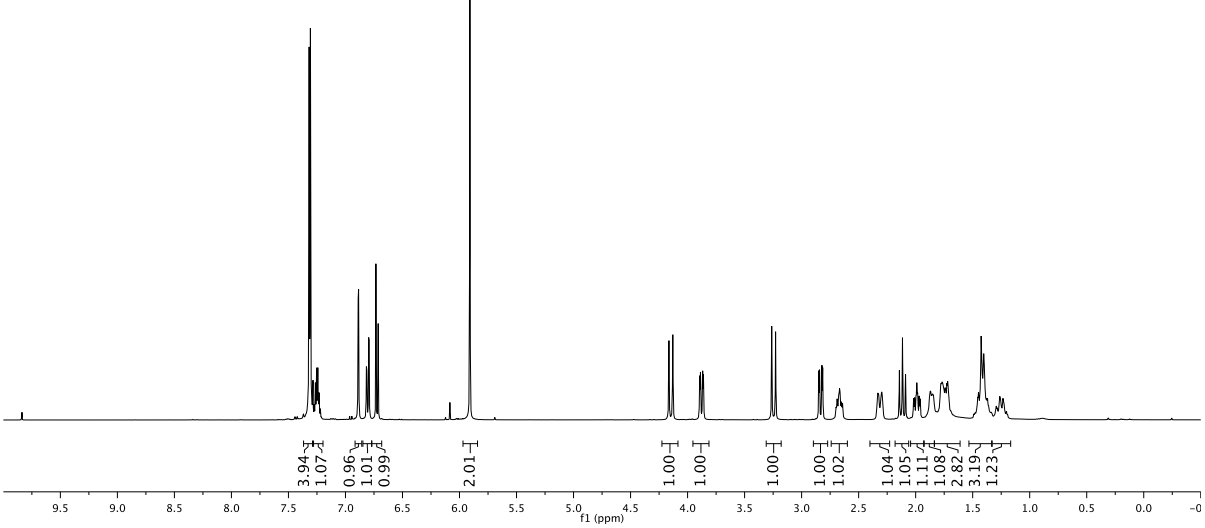
(*trans*,*cis*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-1-benzyldecahydroquinoxaline (19a) (Scheme 3)

14-11-10-bhsieh.10.fid
Sample fly-11-028-CC
group bode
PRO CDCl3 /opt/v bhsieh 14



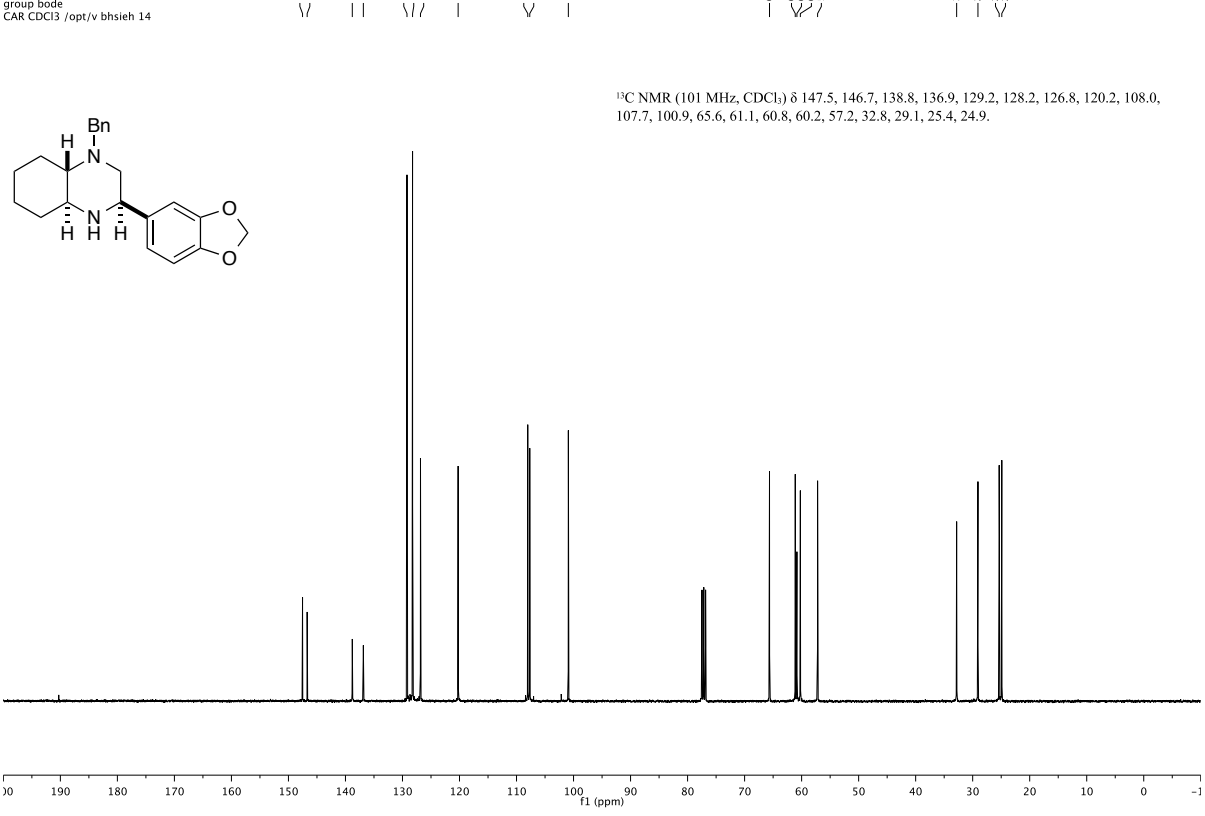
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34, 7.33, 7.32, 7.31, 7.29, 7.29, 7.29, 7.27, 7.26, 7.25, 7.25, 7.24, 7.24, 7.23, 7.23, 7.22, 6.89, 6.89, 6.82, 6.81, 6.80, 6.79, 6.73, 6.71, 5.91, 4.16, 4.13, 3.89, 3.89, 3.87, 3.86, 3.26, 3.23, 2.85, 2.84, 2.82, 2.82, 2.70, 2.69, 2.68, 2.67, 2.67, 2.66, 2.65, 2.64, 2.33, 2.32, 2.31, 2.30, 2.30, 2.29, 2.14, 2.12, 2.09, 2.02, 2.01, 2.00, 1.99, 1.99, 1.98, 1.97, 1.96, 1.88, 1.88, 1.87, 1.86, 1.85, 1.84, 1.78, 1.78, 1.77, 1.77, 1.77, 1.76, 1.75, 1.75, 1.74, 1.74, 1.73, 1.72, 1.71, 1.49, 1.48, 1.46, 1.46, 1.45, 1.43, 1.41, 1.40, 1.40, 1.39, 1.38, 1.38, 1.37, 1.36, 1.35, 1.34, 1.33, 1.30, 1.29, 1.28, 1.27, 1.26, 1.26, 1.25, 1.24, 1.23, 1.23, 1.22, 1.20, 1.19.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 4.4 Hz, 4 H), 7.29–7.21 (m, 1 H), 6.89 (d, *J* = 1.6 Hz, 1 H), 6.80 (dd, *J* = 8.0, 1.6 Hz, 1 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 5.91 (s, 2 H), 4.15 (d, *J* = 13.6 Hz, 1 H), 3.88 (dd, *J* = 10.9, 2.8 Hz, 1 H), 3.25 (d, *J* = 13.6 Hz, 1 H), 2.83 (dd, *J* = 10.9, 2.8 Hz, 1 H), 2.67 (ddd, *J* = 10.6, 8.7, 3.9 Hz, 1 H), 2.33–2.29 (m, 1 H), 2.12 (dd, *J* = 10.9, 10.9 Hz, 1 H), 1.99 (ddd, *J* = 10.6, 8.6, 3.6 Hz, 1H), 1.88–1.84 (m, 1 H), 1.78–1.71 (m, 3 H), 1.49–1.33 (m, 3 H), 1.30–1.19 (m, 1 H).

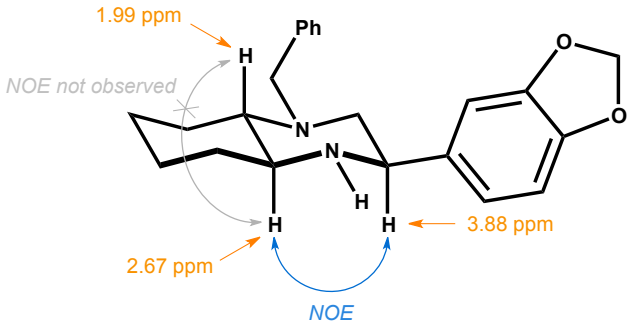


14-11-10-bhsieh.11.fid
Sample fly-11-028-CC
group bode
CAR CDCl3 /opt/v bhsieh 14

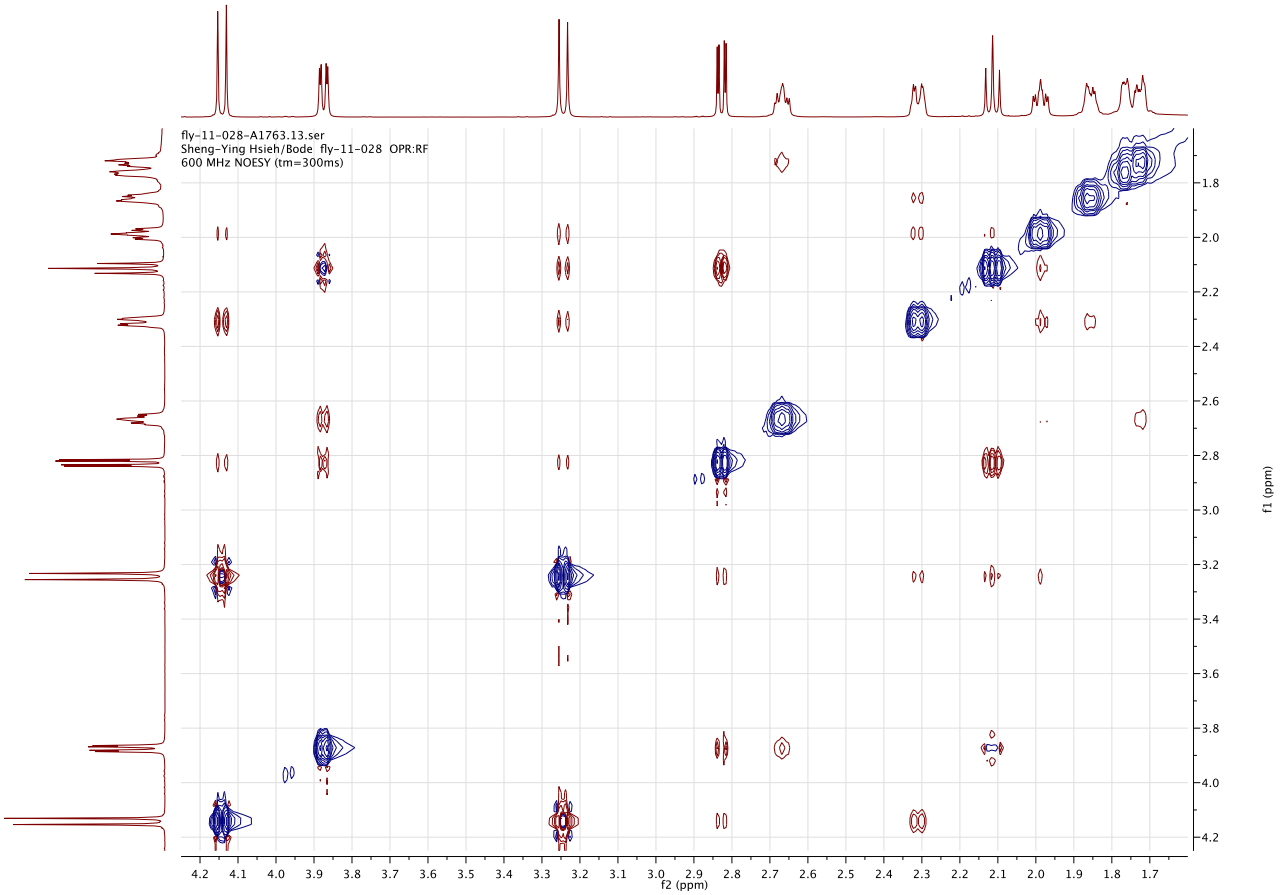
^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 146.7, 138.8, 136.9, 129.2, 128.2, 126.8, 120.2, 108.0, 107.7, 100.9, 65.6, 61.1, 60.8, 60.2, 57.2, 32.8, 29.1, 25.4, 24.9.



NOESY of (*trans*,*cis*)-3-(benzo[*d*][1,3]dioxol-5-yl)-1-benzyldecahydroquinoxaline (19a)



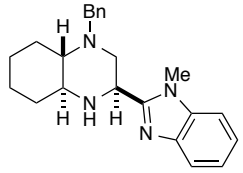
19a



(*trans*,*cis*)-1-Benzyl-3-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)decahydroquinoxaline (19b) (Scheme 3)

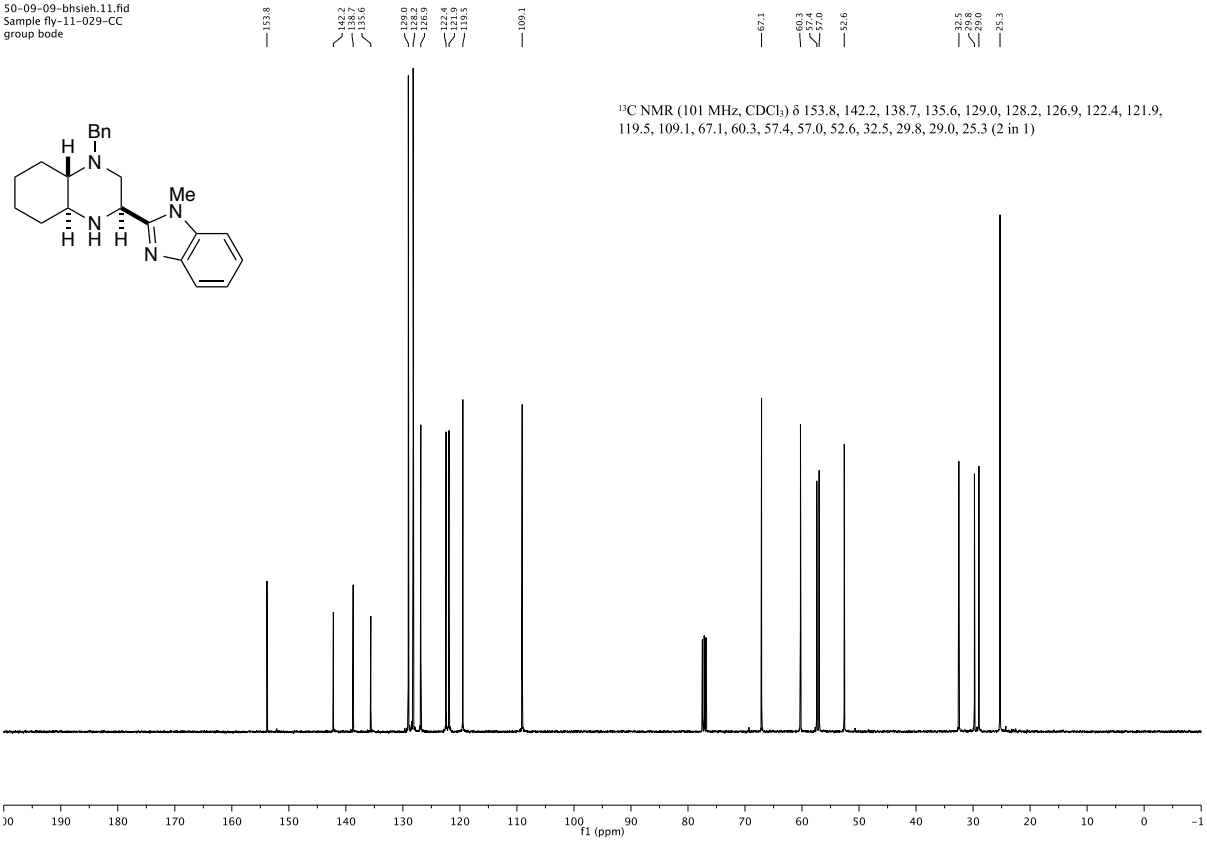
50-09-09-bhsieh.10.fid
Sample fly-11-029-CC
group bode

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75, 7.74, 7.74, 7.74, 7.73, 7.73, 7.72, 7.72, 7.71, 7.35, 7.34, 7.34, 7.33, 7.32, 7.32, 7.31, 7.31, 7.30, 7.30, 7.29, 7.29, 7.29, 7.28, 7.28, 7.27, 7.27, 7.27, 7.25, 7.25, 7.24, 7.24, 7.24, 7.24, 7.23, 7.23, 7.22, 7.22, 7.21, 7.21, 7.20, 7.20, 7.20, 7.20, 4.33, 4.33, 4.31, 4.30, 4.23, 4.20, 3.67, 3.22, 3.19, 3.05, 3.04, 3.02, 3.01, 2.72, 2.71, 2.70, 2.69, 2.69, 2.68, 2.67, 2.66, 2.47, 2.44, 2.44, 2.42, 2.35, 2.35, 2.34, 2.34, 2.32, 2.32, 2.31, 2.31, 2.18, 2.01, 2.01, 2.00, 1.99, 1.98, 1.98, 1.97, 1.96, 1.95, 1.94, 1.91, 1.90, 1.90, 1.89, 1.89, 1.87, 1.87, 1.86, 1.85, 1.85, 1.84, 1.83, 1.81, 1.80, 1.80, 1.80, 1.79, 1.79, 1.78, 1.78, 1.77, 1.77, 1.45, 1.44, 1.43, 1.41, 1.41, 1.40, 1.39, 1.38, 1.37, 1.36, 1.36, 1.35, 1.35, 1.34, 1.33, 1.32, 1.29, 1.28, 1.28, 1.27, 1.26, 1.25, 1.25, 1.24, 1.23, 1.22, 1.22, 1.21, 1.19.



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75–7.71 (m, 1 H), 7.35–7.27 (m, 4 H), 7.25–7.20 (m, 4 H), 4.32 (dd, *J* = 10.7, 2.9 Hz, 1 H), 4.22 (d, *J* = 13.4 Hz, 1 H), 3.67 (s, 3 H), 3.21 (d, *J* = 13.4 Hz, 1 H), 3.03 (dd, *J* = 11.6, 2.9 Hz, 1 H), 2.69 (ddd, *J* = 10.8, 8.7, 3.4 Hz, 1 H), 2.44 (dd, *J* = 11.6, 10.7 Hz, 1 H), 2.35–2.31 (m, 1 H), 2.18 (br, 1 H), 1.98 (ddd, *J* = 10.8, 8.7, 3.5 Hz, 1 H), 1.91–1.83 (m, 2 H), 1.81–1.77 (m, 1 H), 1.45–1.32 (m, 3 H), 1.29–1.19 (m, 1 H).

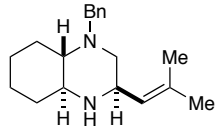
50-09-09-bhsieh.11.fid
Sample fly-11-029-CC
group bode



^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8, 142.2, 138.7, 135.6, 129.0, 128.2, 126.9, 122.4, 121.9, 119.5, 109.1, 67.1, 60.3, 57.4, 57.0, 52.6, 32.5, 29.8, 29.0, 25.3 (2 in 1)

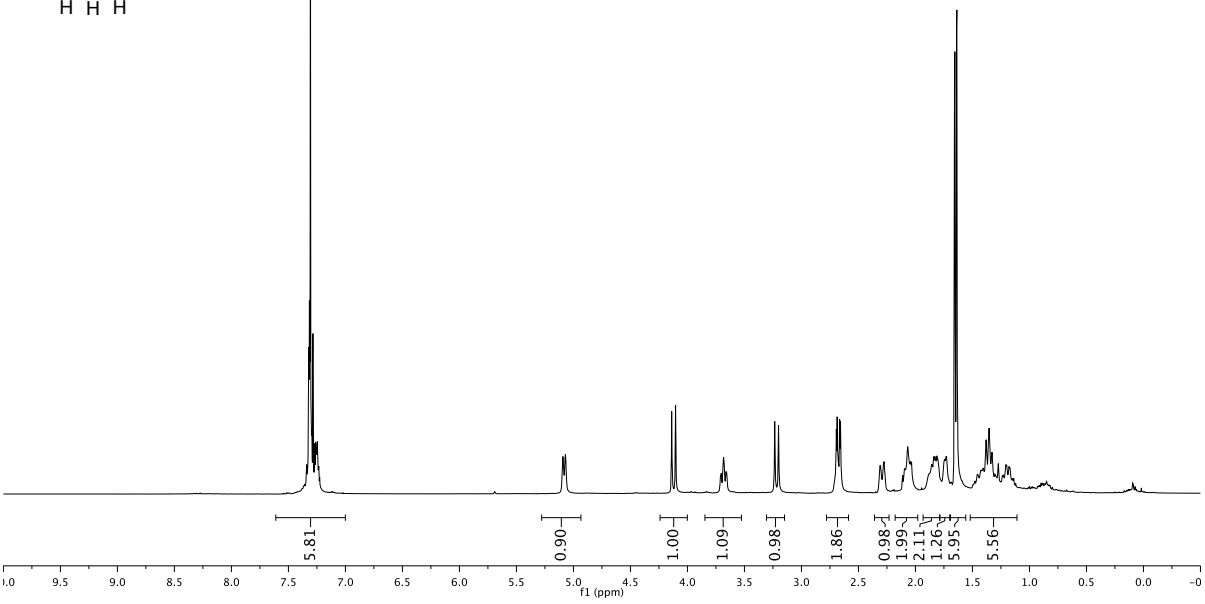
(*trans*,*cis*)-1-Benzyl-3-(2-methylprop-1-en-1-yl)decahydroquinoxaline (19c) (Scheme 3)

11-10-10-bhsieh.10.fid
Sample fly-11-041-CC
group bode



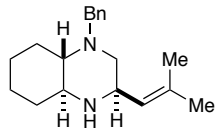
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31, 7.30, 7.30, 7.29, 7.29, 7.28, 7.27, 7.27, 7.26, 7.25, 7.24, 7.24, 7.23, 7.23, 7.23, 7.22, 7.22, 7.21, 7.21, 7.20, 5.07, 5.04, 4.11, 4.08, 3.69, 3.68, 3.66, 3.66, 3.66, 3.65, 3.64, 3.63, 3.21, 3.18, 2.67, 2.66, 2.64, 2.63, 2.29, 2.29, 2.28, 2.28, 2.26, 2.25, 2.24, 2.09, 2.09, 2.07, 2.04, 2.02, 2.01, 1.86, 1.83, 1.83, 1.83, 1.82, 1.81, 1.81, 1.80, 1.80, 1.79, 1.78, 1.78, 1.78, 1.77, 1.77, 1.76, 1.73, 1.72, 1.72, 1.72, 1.71, 1.70, 1.68, 1.68, 1.63, 1.63, 1.61, 1.61, 1.47, 1.47, 1.46, 1.46, 1.45, 1.43, 1.40, 1.40, 1.39, 1.38, 1.36, 1.35, 1.35, 1.33, 1.33, 1.31, 1.30, 1.30, 1.28, 1.27, 1.26, 1.25, 1.21, 1.20, 1.18, 1.17, 1.15, 1.15, 1.14, 1.12, 1.11, 1.11, 1.10.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31–7.20 (m, 5 H), 5.06 (d, *J* = 8.8 Hz, 1 H), 4.10 (d, *J* = 13.5 Hz, 1 H), 3.69–3.63 (m, 1 H), 3.19 (d, *J* = 13.5 Hz, 1 H), 2.58–2.65 (m, 1 H), 2.65 (dd, *J* = 11.7, 3.1 Hz, 1 H), 2.29–2.24 (m, 1 H), 2.09–2.01 (m, 2 H), 1.86–1.76 (m, 2 H), 1.73–1.68 (m, 1 H), 1.63 (d, *J* = 1.4 Hz, 3 H), 1.61 (d, *J* = 1.4 Hz, 3 H), 1.47– 1.10 (m, 5 H).



11-10-10-bhsieh.11.fid
Sample fly-11-041-CC
group bode

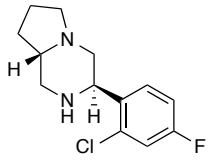
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 136.5,* 129.2, 128.3, 127.0, 123.6,* 64.8, 60.3, 57.5, 57.0, 54.0, 31.7, 29.1, 25.9, 25.1, 24.9, 18.5.



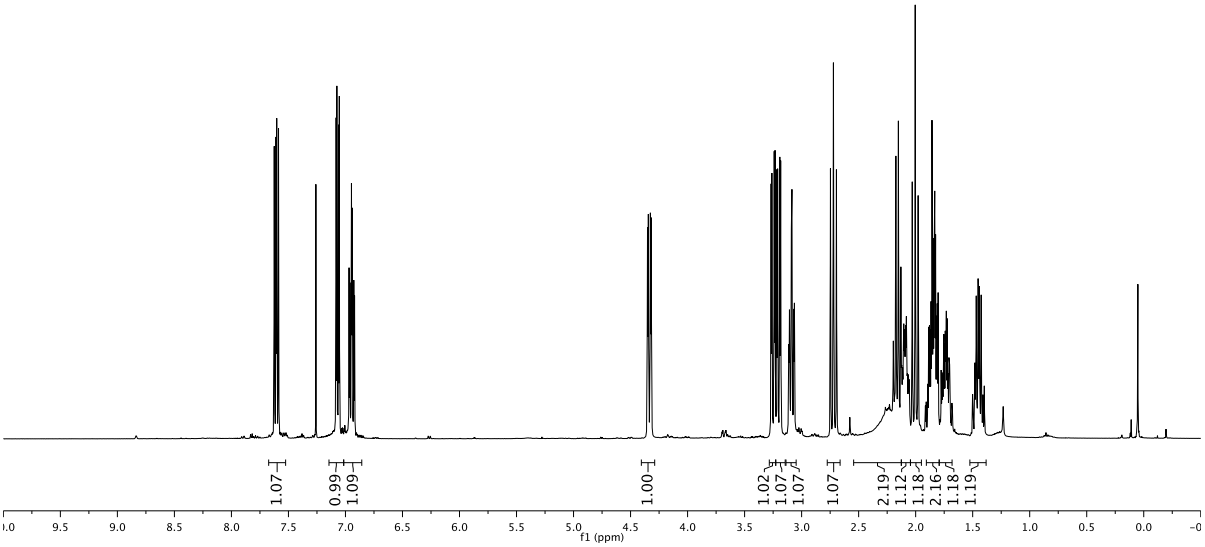
(3*R*,8a*S*)-3-(2-Chloro-4-fluorophenyl)octahydropyrrolo[1,2-*a*]pyrazine (20a) (Scheme 3)

55-10-10-bhsieh.10.fid
Sample fly-11-027-CC
group bode

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62, 7.61, 7.60, 7.59, 7.08, 7.08, 7.06, 7.05, 6.97, 6.96, 6.95, 6.94, 6.93, 6.92, 4.35, 4.34, 4.33, 4.32, 3.27, 3.26, 3.24, 3.23, 3.22, 3.21, 3.19, 3.18, 3.11, 3.11, 3.09, 3.08, 3.07, 3.06, 2.75, 2.72, 2.72, 2.69, 2.24, 2.20, 2.17, 2.15, 2.13, 2.12, 2.12, 2.10, 2.10, 2.09, 2.08, 2.07, 2.06, 2.06, 2.03, 2.00, 1.98, 1.89, 1.89, 1.88, 1.87, 1.87, 1.86, 1.85, 1.85, 1.84, 1.83, 1.83, 1.82, 1.81, 1.80, 1.78, 1.77, 1.76, 1.76, 1.75, 1.75, 1.74, 1.74, 1.73, 1.72, 1.72, 1.72, 1.71, 1.70, 1.70, 1.50, 1.48, 1.47, 1.47, 1.46, 1.46, 1.45, 1.45, 1.44, 1.44, 1.43, 1.41, 1.40.

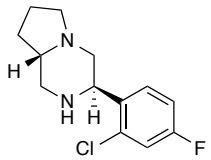


^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (dd, *J* = 8.7, 6.3 Hz, 1 H), 7.07 (dd, *J* = 8.6, 2.7 Hz, 1 H), 6.94 (ddd, *J* = 8.7, 8.3, 2.7 Hz, 1 H), 4.34 (dd, *J* = 10.1, 2.9 Hz, 1 H), 3.25 (dd, *J* = 11.0, 2.9 Hz, 1 H), 3.20 (dd, *J* = 10.6, 2.9 Hz, 1 H), 3.09 (ddd, *J* = 8.7, 8.6, 2.3 Hz, 1 H), 2.72 (dd, *J* = 11.0, 10.0 Hz, 1 H), 2.24 (br, 1 H), 2.16 (ddd, *J* = 8.8, 8.8, 8.7 Hz, 1H), 2.09 (dddd, *J* = 10.0, 6.5, 6.0, 2.9 Hz, 1 H), 2.00 (dd, *J* = 10.6, 10.1 Hz, 1 H), 1.89–1.80 (m, 2 H), 1.78–1.70 (m, 1 H), 1.50–1.40 (m, 1 H).



55-10-10-bhsieh.11.fid
Sample fly-11-027-CC
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 160.3, 135.6, 135.6, 133.8, 133.7, 129.4, 129.3, 116.9, 116.7, 114.3, 114.1, 62.8, 58.3, 55.4, 53.5, 51.0, 27.4, 21.3.



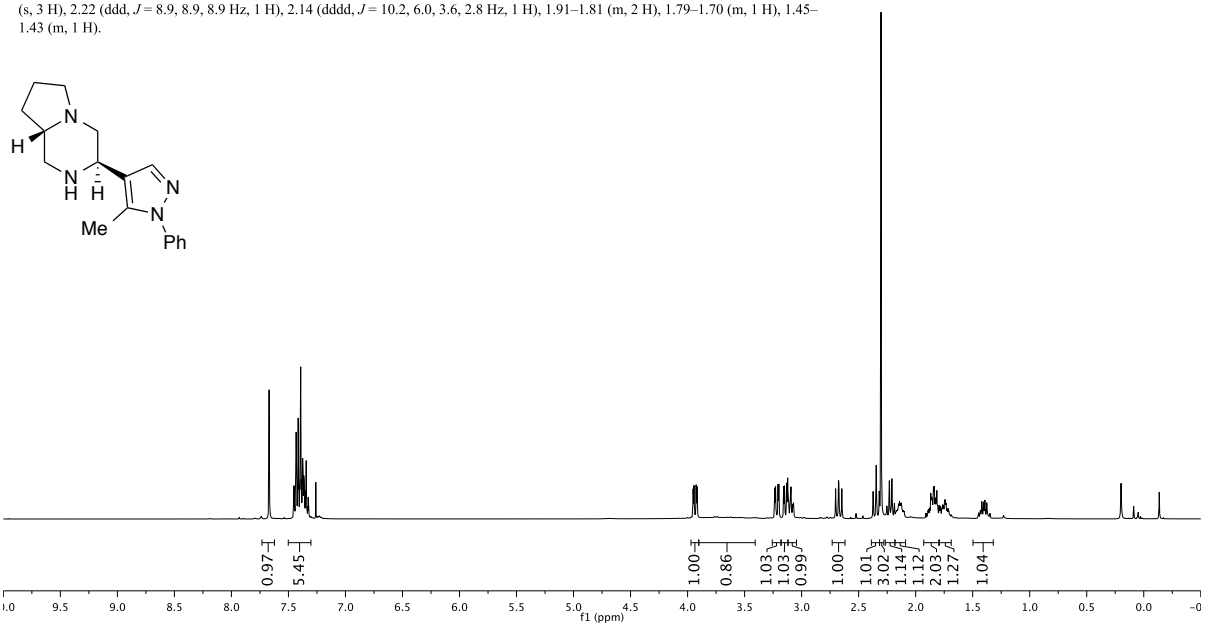
^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.6 (d, *J* = 249.0 Hz), 135.6 (d, *J* = 3.5 Hz), 133.8 (d, *J* = 10.1 Hz), 129.4 (d, *J* = 8.6 Hz), 116.8 (d, *J* = 24.5 Hz), 114.2 (d, *J* = 20.6 Hz), 62.8, 58.3, 55.4, 53.5, 51.0, 27.4, 21.3.

(3*R*,8a*S*)-3-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)octahydropyrrolo[1,2-*a*]pyrazine (20b) (Scheme 3)

17-11-10-bhsieh.10.fid
Sample fly-11-070-CC
group bode
PRO CDCl3 /opt/v bhsieh 17

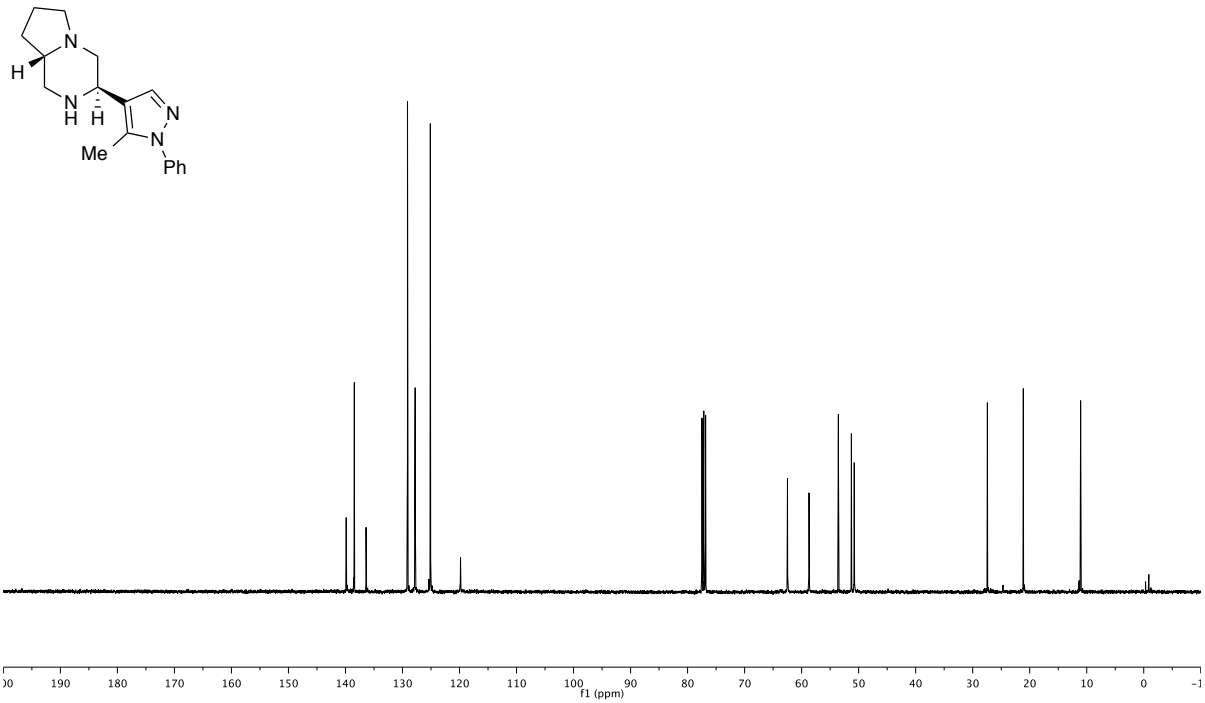
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67, 7.45, 7.45, 7.45, 7.44, 7.44, 7.43, 7.43, 7.43, 7.42, 7.42, 7.41, 7.41, 7.40, 7.39, 7.39, 7.38, 7.38, 7.37, 7.37, 7.37, 7.36, 7.36, 7.35, 7.35, 7.34, 7.34, 7.33, 7.33, 7.32, 3.95, 3.94, 3.93, 3.92, 3.74, 3.24, 3.23, 3.21, 3.20, 3.16, 3.15, 3.13, 3.12, 3.12, 3.10, 3.09, 3.08, 3.07, 2.70, 2.68, 2.67, 2.65, 2.37, 2.35, 2.32, 2.30, 2.25, 2.23, 2.21, 2.19, 2.17, 2.17, 2.16, 2.15, 2.14, 2.13, 2.13, 2.12, 2.12, 2.11, 2.10, 1.91, 1.90, 1.89, 1.89, 1.88, 1.88, 1.87, 1.86, 1.86, 1.85, 1.85, 1.84, 1.84, 1.83, 1.82, 1.81, 1.81, 1.79, 1.78, 1.77, 1.76, 1.76, 1.76, 1.75, 1.74, 1.74, 1.73, 1.73, 1.72, 1.72, 1.71, 1.70, 1.45, 1.43, 1.42, 1.41, 1.40, 1.39, 1.38, 1.36, 1.36, 1.35.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (s, 1 H), 7.45–7.32 (m, 5 H), 3.93 (dd, *J* = 10.5, 3.1 Hz, 1 H), 3.74 (br, 1 H), 3.22 (dd, *J* = 11.6, 2.8 Hz, 1 H), 3.14 (dd, *J* = 10.8, 3.1 Hz, 1 H), 3.12–3.07 (m, 1 H), 2.67 (dd, *J* = 11.6, 10.1 Hz, 1 H), 2.35 (dd, *J* = 10.8, 10.5 Hz, 1 H), 2.30 (s, 3 H), 2.22 (ddd, *J* = 8.9, 8.9, 8.9 Hz, 1 H), 2.14 (dddd, *J* = 10.2, 6.0, 3.6, 2.8 Hz, 1 H), 1.91–1.81 (m, 2 H), 1.79–1.70 (m, 1 H), 1.45–1.43 (m, 1 H).



17-11-10-bhsieh.11.fid
Sample fly-11-070-CC
group bode
CAR CDCl3 /opt/v bhsieh 17

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 138.5, 136.4, 129.1, 127.8, 125.1, 119.8, 62.5, 58.7, 53.6, 51.3, 50.8, 27.4, 21.1, 11.1.

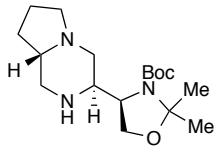


(*R*)-*tert*-Butyl 2,2-dimethyl-4-((3*S*,8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-3-yl)oxazolidine-3-carboxylate (20c) (Scheme 3)

12-11-10-bhsieh.10.fid
Sample fly-11-030-CC
group bode

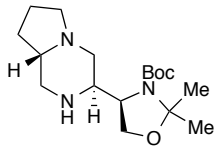
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15, 4.07, 3.95, 3.89, 3.87, 3.86, 3.85, 3.30, 3.27, 3.20, 3.17, 3.14, 3.12, 3.12, 3.10, 3.09, 2.68, 2.65, 2.62, 2.29, 2.27, 2.25, 2.23, 2.17, 2.14, 2.11, 1.89, 1.88, 1.87, 1.87, 1.86, 1.85, 1.84, 1.83, 1.83, 1.82, 1.81, 1.80, 1.80, 1.79, 1.78, 1.77, 1.76, 1.76, 1.75, 1.74, 1.73, 1.73, 1.72, 1.72, 1.71, 1.70, 1.54, 1.45, 1.44, 1.44, 1.43, 1.42, 1.39.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.15 (br, 1 H), 4.07 (br, 1 H), 3.95 (br, 1 H), 3.87 (dd, *J* = 9.4, 6.4 Hz, 1 H), 3.28 (d, *J* = 10.6 Hz, 1 H), 3.18 (d, *J* = 10.6 Hz, 1 H), 3.14–3.09 (m, 2 H), 2.65 (dd, *J* = 10.9, 10.9 Hz, 1 H), 2.26 (ddd, *J* = 8.8, 8.2, 8.2 Hz, 1 H), 2.17–2.13 (m, 2 H), 1.87–1.71 (m, 3 H), 1.54 (s, 3 H), 1.45–1.39 (m, 13 H).



12-11-10-bhsieh.11.fid
Sample fly-11-030-CC
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0*, 152.3, 94.3, 93.9*, 80.6*, 64.2*, 62.8*, 59.3*, 58.9, 56.0*, 53.5*, 53.2*, 52.8, 49.9*, 28.5*, 27.0*, 26.9*, 26.1, 23.9*, 22.4, 21.0*.

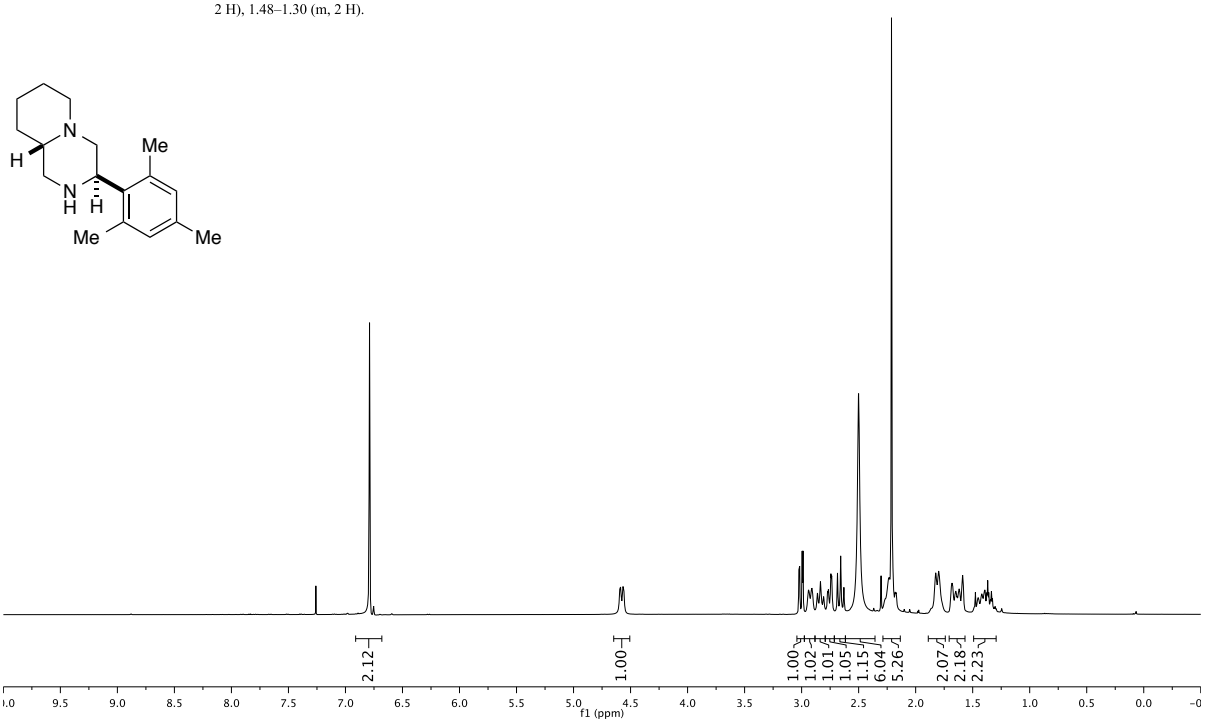


cis-3-Mesityloctahydro-1*H*-pyrido[1,2-*a*]pyrazine (21a) (Scheme 3)

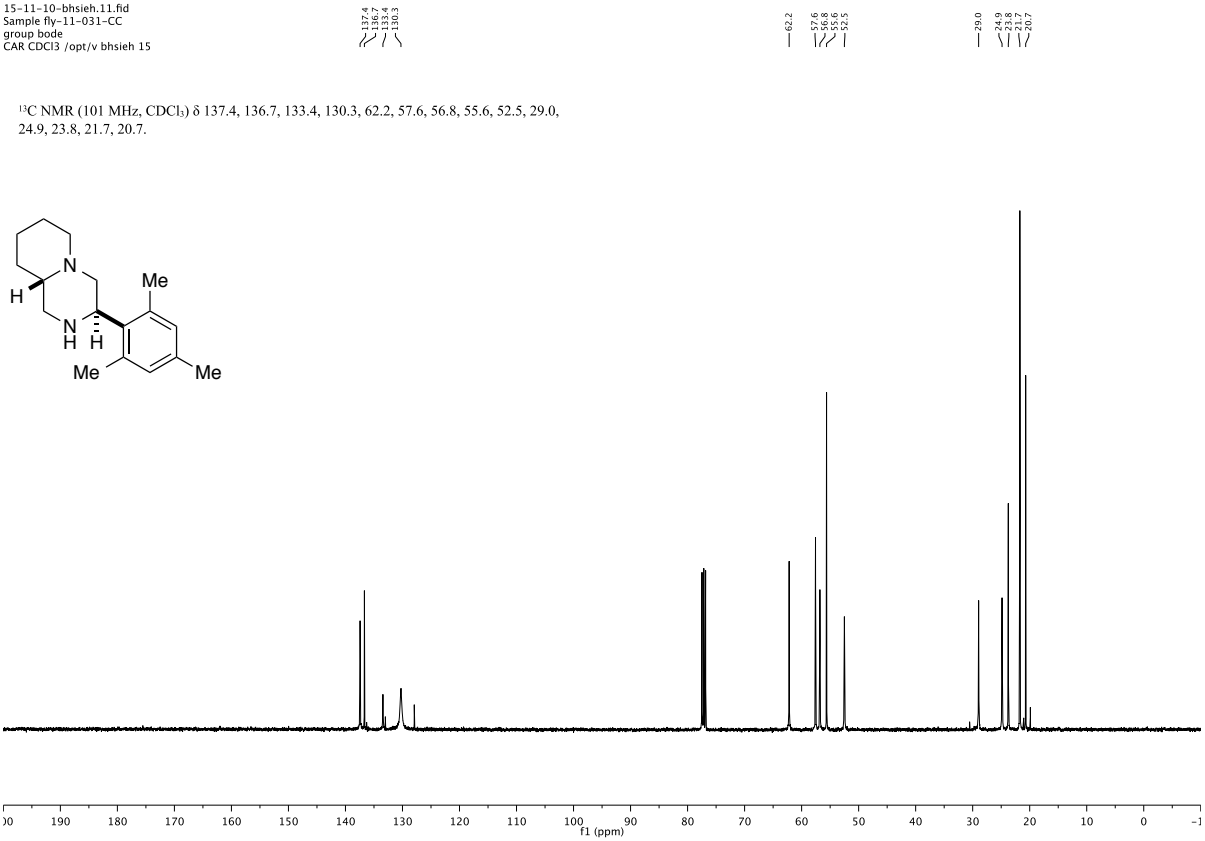
15-11-10-bhsieh.10.fid
Sample fly-11-031-CC
group bode
PRO CDCl3 /opt/v bhsieh 15

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79, 4.59, 4.59, 4.57, 4.56, 3.02, 3.02, 3.00, 2.99, 2.94, 2.91, 2.86, 2.83, 2.81, 2.77, 2.76, 2.74, 2.74, 2.69, 2.66, 2.63, 2.50, 2.27, 2.27, 2.25, 2.24, 2.23, 2.21, 2.20, 2.18, 2.17, 1.83, 1.83, 1.82, 1.82, 1.81, 1.81, 1.81, 1.80, 1.79, 1.69, 1.69, 1.68, 1.68, 1.67, 1.65, 1.65, 1.64, 1.62, 1.62, 1.61, 1.60, 1.59, 1.59, 1.58, 1.48, 1.48, 1.45, 1.45, 1.42, 1.40, 1.39, 1.38, 1.37, 1.36, 1.34, 1.34, 1.33, 1.30.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.79 (s, 2 H), 4.58 (dd, *J* = 11.2, 3.2 Hz, 1 H), 3.01 (dd, *J* = 11.6, 2.9 Hz, 1 H), 2.92 (d, *J* = 11.6 Hz, 1 H), 2.83 ddt, *J* = 11.6, 10.9 Hz, 1 H), 2.75 (dd, *J* = 11.5, 3.2 Hz, 1 H), 2.66 (dd, *J* = 11.5, 11.2 Hz, 1 H), 2.50 (s, 6 H), 2.21 (s, 3 H), 2.27–2.17 (m, 2 H), 1.83–1.79 (m, 2 H), 1.69–1.58 (m, 2 H), 1.48–1.30 (m, 2 H).

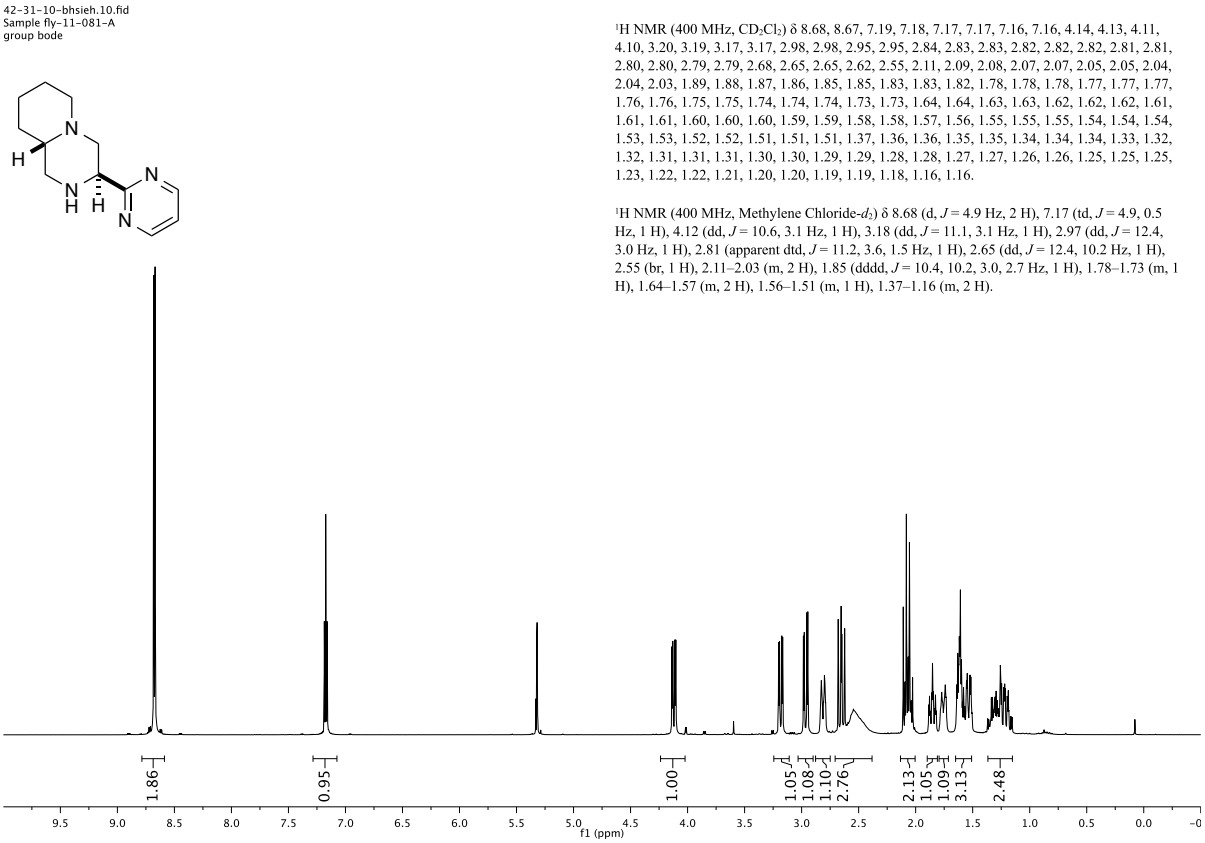


15-11-10-bhsieh.11.fid
Sample fly-11-031-CC
group bode
CAR CDCl3 /opt/v bhsieh 15



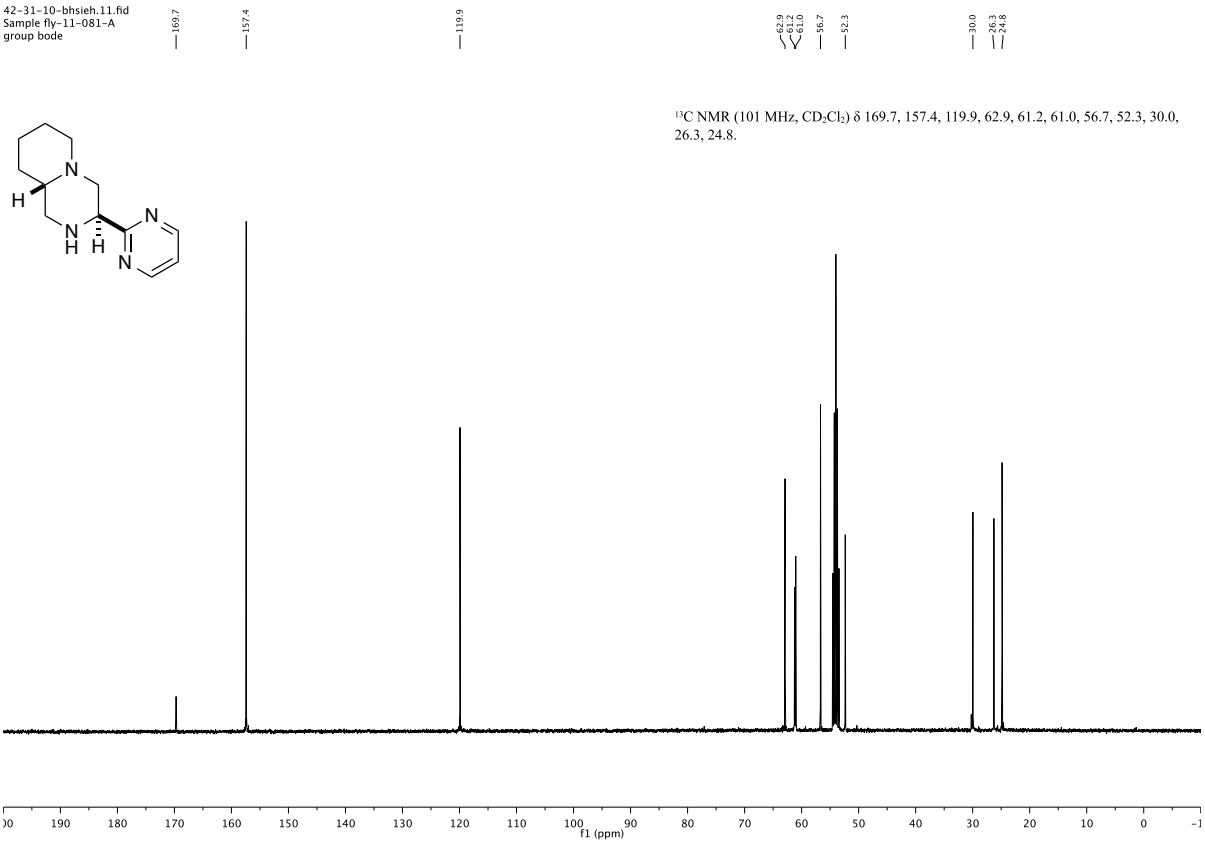
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4, 136.7, 133.4, 130.3, 62.2, 57.6, 56.8, 55.6, 52.5, 29.0, 24.9, 23.8, 21.7, 20.7.

cis-3-(Pyrimidin-2-yl)octahydro-1*H*-pyrido[1,2-*a*]pyrazine (21b) (Scheme 3)



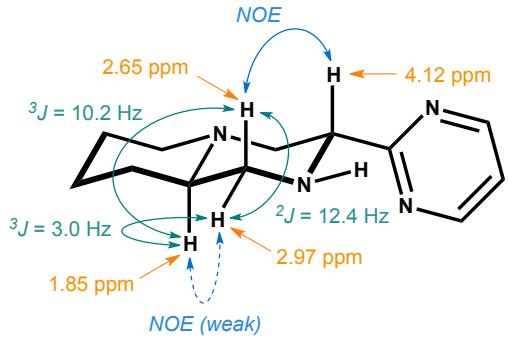
^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.68, 8.67, 7.19, 7.18, 7.17, 7.17, 7.16, 7.16, 4.14, 4.13, 4.11, 4.10, 3.20, 3.19, 3.17, 3.17, 2.98, 2.98, 2.95, 2.95, 2.84, 2.83, 2.83, 2.82, 2.82, 2.82, 2.81, 2.81, 2.80, 2.80, 2.79, 2.79, 2.68, 2.65, 2.65, 2.62, 2.55, 2.11, 2.09, 2.08, 2.07, 2.07, 2.05, 2.05, 2.04, 2.04, 2.03, 1.89, 1.88, 1.87, 1.86, 1.85, 1.85, 1.83, 1.83, 1.82, 1.78, 1.78, 1.78, 1.77, 1.77, 1.77, 1.76, 1.76, 1.75, 1.75, 1.74, 1.74, 1.74, 1.73, 1.73, 1.64, 1.64, 1.63, 1.63, 1.62, 1.62, 1.62, 1.61, 1.61, 1.61, 1.60, 1.60, 1.60, 1.59, 1.59, 1.58, 1.58, 1.57, 1.56, 1.55, 1.55, 1.55, 1.54, 1.54, 1.54, 1.53, 1.53, 1.52, 1.52, 1.51, 1.51, 1.51, 1.37, 1.36, 1.36, 1.35, 1.35, 1.34, 1.34, 1.34, 1.33, 1.32, 1.32, 1.31, 1.31, 1.31, 1.30, 1.30, 1.29, 1.29, 1.28, 1.28, 1.27, 1.27, 1.26, 1.26, 1.25, 1.25, 1.25, 1.23, 1.22, 1.22, 1.21, 1.20, 1.20, 1.19, 1.19, 1.18, 1.16, 1.16.

^{1}H NMR (400 MHz, Methylene Chloride-d_2) δ 8.68 (d, J = 4.9 Hz, 2 H), 7.17 (td, J = 4.9, 0.5 Hz, 1 H), 4.12 (dd, J = 10.6, 3.1 Hz, 1 H), 3.18 (dd, J = 11.1, 3.1 Hz, 1 H), 2.97 (dd, J = 12.4, 3.0 Hz, 1 H), 2.81 (apparent dtd, J = 11.2, 3.6, 1.5 Hz, 1 H), 2.65 (dd, J = 12.4, 10.2 Hz, 1 H), 2.55 (br, 1 H), 2.11–2.03 (m, 2 H), 1.85 (dddd, J = 10.4, 10.2, 3.0, 2.7 Hz, 1 H), 1.78–1.73 (m, 1 H), 1.64–1.57 (m, 2 H), 1.56–1.51 (m, 1 H), 1.37–1.16 (m, 2 H).

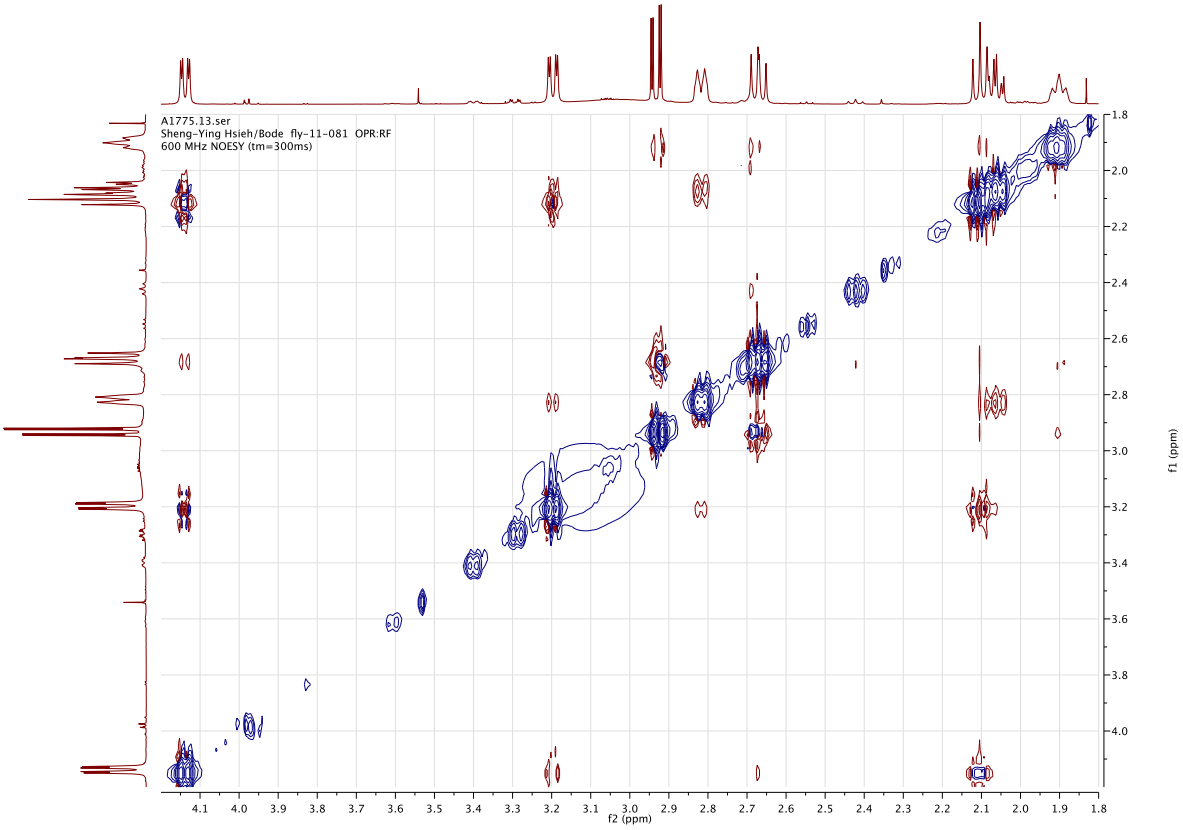


^{13}C NMR (101 MHz, CD_2Cl_2) δ 169.7, 157.4, 119.9, 62.9, 61.2, 61.0, 56.7, 52.3, 30.0, 26.3, 24.8.

NOESY of *cis*-3-(pyrimidin-2-yl)octahydro-1*H*-pyrido[1,2-*a*]pyrazine (21b)



21b

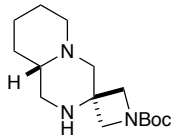


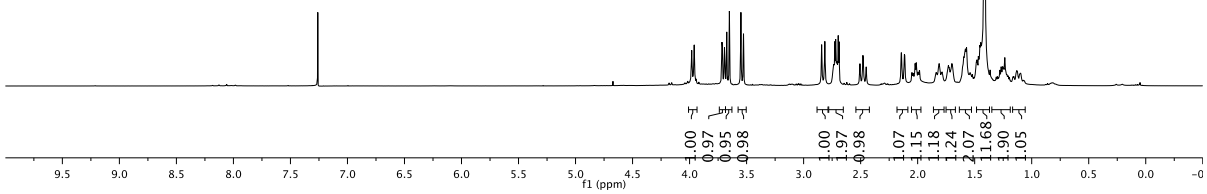
tert-Butyl octahydrospiro[azetidine-3,3'-pyrido[1,2-*a*]pyrazine]-1-carboxylate (21c) (Scheme 3)

43-31-10-bhsieh.10.fid
Sample fly-11-071-B
group bode

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.98, 3.96, 3.72, 3.70, 3.67, 3.65, 3.55, 3.53, 2.84, 2.81, 2.74, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.51, 2.48, 2.45, 2.14, 2.12, 2.05, 2.04, 2.02, 2.01, 2.00, 2.00, 1.99, 1.98, 1.84, 1.81, 1.79, 1.75, 1.74, 1.74, 1.73, 1.73, 1.72, 1.72, 1.71, 1.70, 1.69, 1.61, 1.60, 1.59, 1.58, 1.57, 1.57, 1.56, 1.55, 1.54, 1.53, 1.52, 1.51, 1.49, 1.48, 1.48, 1.47, 1.47, 1.46, 1.45, 1.45, 1.44, 1.44, 1.43, 1.42, 1.41, 1.41, 1.39, 1.38, 1.36, 1.36, 1.31, 1.31, 1.30, 1.28, 1.27, 1.27, 1.25, 1.25, 1.25, 1.24, 1.23, 1.22, 1.22, 1.21, 1.21, 1.20, 1.20, 1.16, 1.16, 1.13, 1.12, 1.11, 1.10.

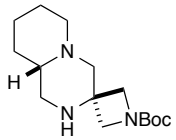
^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.97 (d, *J* = 8.9 Hz, 1 H), 3.71 (d, *J* = 8.9 Hz, 1 H), 3.66 (d, *J* = 9.2 Hz, 1 H), 3.54 (d, *J* = 9.2 Hz, 1 H), 2.83 (d, *J* = 11.1 Hz, 1H), 2.74–2.69 (m, 2 H), 2.48 (t, *J* = 11.0, 11.0 Hz, 1 H), 2.13 (d, *J* = 11.1 Hz, 1 H), 2.02 (ddd, *J* = 11.2, 11.1, 4.3 Hz, 1 H), 1.81 (apparent t, *J* = 10.5 Hz, 1 H), 1.75–1.69 (m, 1 H), 1.61–1.51 (m, 2 H), 1.49–1.42 (m, 1 H), 1.41 (s, 9 H), 1.31–1.20 (m, 2 H), 1.16–1.10 (m, 1 H).





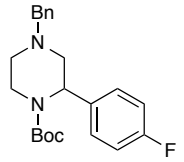
43-31-10-bhsieh.11.fid
Sample fly-11-071-B
group bode

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 79.5, 63.0, 61.4, 60.8, 58.8, 56.0, 52.4, 48.6, 29.4, 28.5, 25.6, 24.1.



tert-Butyl 4-benzyl-2-(4-fluorophenyl)piperazine-1-carboxylate (22)

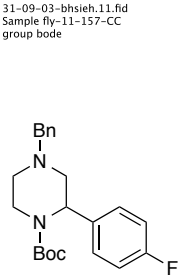
31-09-03-bhsieh.10.fid
Sample fly-11-157-CC
group bode



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43, 7.43, 7.42, 7.41, 7.41, 7.40, 7.39, 7.35, 7.35, 7.34, 7.33, 7.33, 7.32, 7.31, 7.30, 7.29, 7.29, 7.28, 7.28, 7.27, 7.26, 7.25, 7.25, 7.01, 7.01, 7.00, 6.99, 6.99, 6.98, 6.98, 6.98, 6.97, 6.96, 6.95, 5.21, 3.92, 3.89, 3.60, 3.57, 3.46, 3.43, 3.23, 3.20, 3.04, 3.01, 3.01, 2.98, 2.97, 2.84, 2.81, 2.44, 2.43, 2.41, 2.40, 2.20, 2.18, 2.17, 2.15, 1.48.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43–7.39 (m, 2 H), 7.35–7.25 (m, 5 H), 7.01–6.95 (m, 2 H), 5.21 (apparent s, 1 H), 3.90 (apparent d, *J* = 13.5 Hz, 1 H), 3.58 (d, *J* = 13.0 Hz, 1 H), 3.45 (d, *J* = 13.0 Hz, 1 H), 3.22 (apparent d, *J* = 12.0, 1 H), 3.00 (dt, *J* = 13.5, 7.1 Hz, 1 H), 2.83 (apparent d, *J* = 11.2 Hz, 1 H), 2.42 (dd, *J* = 12.0, 4.2 Hz, 1 H), 2.18 (apparent t, *J* = 11.2 Hz, 1 H), 1.48 (s, 9 H).

31-09-03-bhsieh.11.fid
Sample fly-11-157-CC
group bode

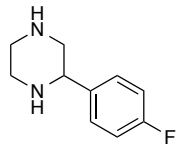


^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 160.6, 155.0, 137.9, 136.4, 129.6, 129.5, 129.3, 128.4, 127.4, 115.0, 114.8, 80.2, 63.2, 55.2, 53.4, 52.8, 39.9, 28.6.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.9 (d, *J* = 245.0 Hz), 155.0, 137.9 (apparent s), 136.4, 129.6 (d, *J* = 7.8 Hz), 129.3, 128.4, 127.4, 114.9 (d, *J* = 21.0 Hz), 80.2, 63.2, 55.2, 53.4, 52.8, 39.9, 28.6.

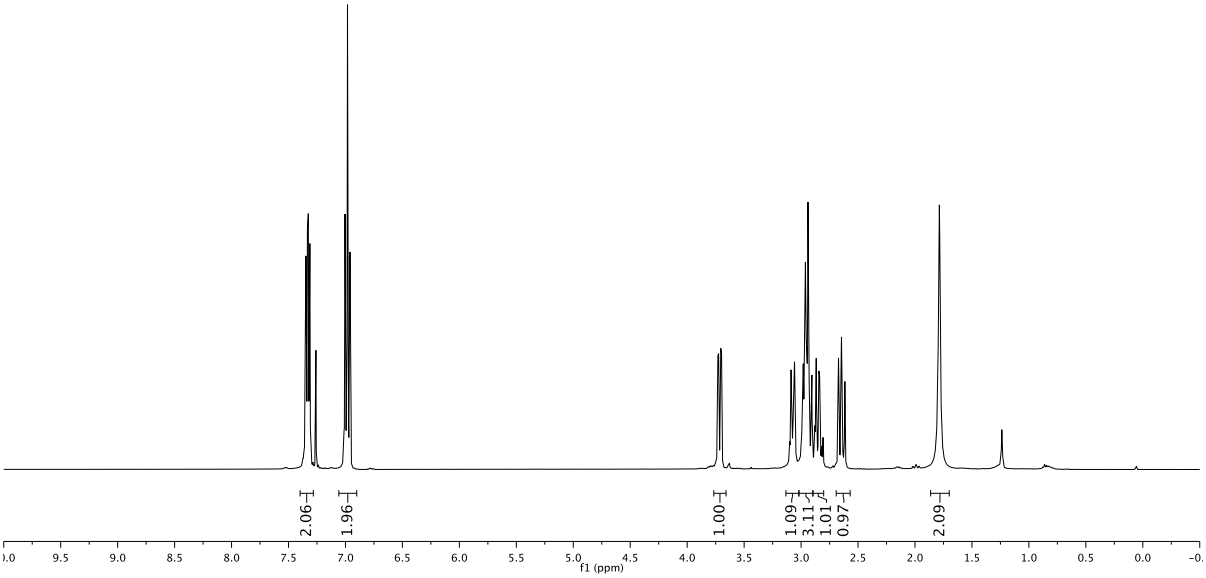
2-(4-Fluorophenyl)piperazine (23)

2-11-03-bhsieh.10.fid
Sample fly-11-158-final-2
group bode
PRO CDCl3 /opt/v bhsieh 2

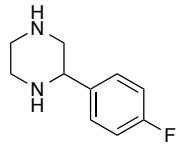


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36, 7.35, 7.34, 7.33, 7.33, 7.32, 7.31, 7.30, 7.01, 7.00, 7.00, 6.99, 6.98, 6.98, 6.97, 6.96, 6.95, 3.73, 3.72, 3.71, 3.70, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 2.99, 2.98, 2.97, 2.96, 2.96, 2.95, 2.94, 2.94, 2.93, 2.91, 2.91, 2.88, 2.87, 2.84, 2.84, 2.82, 2.81, 2.67, 2.65, 2.64, 2.62, 1.79.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (ddd, *J* = 8.6, 5.4, 2.6 Hz, 2 H), 7.01–6.95 (m, 2 H), 3.71 (dd, *J* = 10.2, 2.8 Hz, 1 H), 3.10–3.05 (m, 1 H), 2.99–2.91 (m, 3 H), 2.88–2.81 (m, 1 H), 2.64 (dd, *J* = 12.1, 10.2 Hz, 1 H), 1.79 (br, 2 H).



2-11-03-bhsieh.11.fid
Sample fly-11-158-final-2
group bode
CAR CDCl3 /opt/v bhsieh 2



^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 161.0, 138.7, 138.7, 128.5, 128.5, 115.4, 115.2, 61.4, 54.5, 47.9, 46.1.

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.2 (d, *J* = 245.1 Hz), 138.7 (d, *J* = 3.1 Hz), 128.5 (d, *J* = 7.9 Hz), 115.3 (d, *J* = 21.2 Hz), 61.4, 54.5, 47.9, 46.1.