Supporting Information 1:

Enantioselective Hydroarylation of Bridged [3.2.1] Heterocycles: An Efficient Entry into the Homoepibatidine Skeleton

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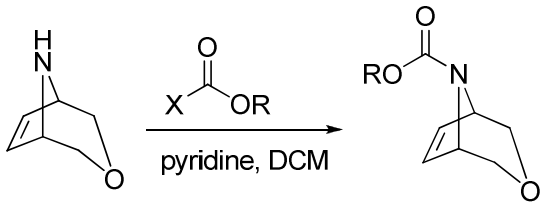
1. General:

The THF used in the hydroarylation reactions was thoroughly degassed with nitrogen before use, and special care was taken to keep the reactions oxygen free. All other chemicals and solvents were purchased from commercial vendors and used as received. $[Rh(cod)OH]_2$ and all Josiphos ligands were purchased from Strem or Aldrich. Proton (^1H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectroscopy were recorded on a 400 MHz Bruker NMR. Chemical shifts are recorded in parts per million using a standard of $CHCl_3$ at 7.27. The peak shapes are notated as follows: s, singlet; d, doublet; t, triplet, q, quartet; m, multiplet, br s, broad singlet. The hydroarylation products give a mix of rotational isomers in ^1H and ^{13}C NMR, the peak for the major isomer is reported. Mass spectrometry was performed using atmospheric pressure chemical ionization (APCI) or electron scatter (ES) ionization sources. High resolution mass spectroscopy (HRMS) was performed on an Agilent (6220) LC-MS TOF using a Xbridge C18 2.5 μm 3.0 X 5.0 mm at 60oC; ammonium formate: water as mobile phase A1 and 50:50 methanol:acetonitrile as mobile Phase B1. Silica gel chromatography was performed using a medium pressure Biotage or ISCO system using columns pre-packaged by various commercial vendors including Biotage and ISCO. Analtech pre-coated silica gel plates (250 μm) were used for analytical TLC. Infrared data were recorded on a Nicolet Avatar 360 FT-IR. Chiral HPLC was run on a Lux Cellulose or Lux Amylose 250 mm X 4.6 mm columns, 3.0 mL/min flowrate with a gradient of CO2/MeOH at a pressure of 120 bar, and detected at 210 or 254 nm. The terms “concentrated” and “evacuated” refer to the removal of solvent at reduced pressure on a rotary evaporator with a bath temperature less than 40 ºC.

2. Experimental procedures and compound characterization:

General Procedure A for the formation of carbamates:



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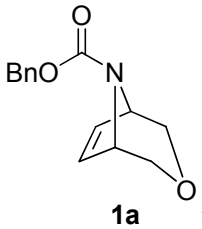
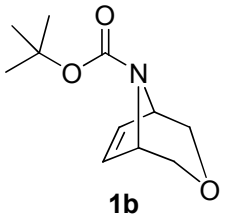
A solution of the amine (1.0 equivalent, as a TFA salt) in dichloromethane (0.5 M) and pyridine (3.0 equiv.) was chilled to 0 °C. The chloroformate (or Boc_2O in B, 2.0 equiv.) was added slowly and the reaction was warmed to room temperature and stirred for 16 hours. The reaction was quenched by addition of water (20 mL), and the product was extracted with DCM (3 X 20 mL). The combined organic layers were washed with water (20 mL), dried with MgSO4, filtered, and the solvents were removed under vacuum. Purification by column chromatography (Isco system, 40 g. Column, gradient elution, 0-50% EtOAc/heptanes) to yield the product.

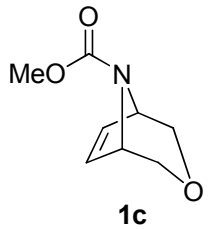


1a **Benzyl 3-oxa-8-azabicyclo[3.2.1]oct-6-ene-8-carboxylate (1a):** General procedure A using the secondary amine-TFA salt (1.30 g., 5.77 mmol) and benzyl chloroformate (1.70 mL, 11.5 mmol) yields **1a** (1.13 g., 4.60 mmol, 80%) as a clear oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.37 (s, 5 H) 6.28 (d, *J*=17.17 Hz, 2 H) 5.19 (s, 2 H) 4.58 (d, *J*=17.17 Hz, 2 H) 3.56 - 3.83 (m, 2 H) 3.43 (br. s., 2 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.10, 136.37, 131.04, 130.43, 128.40, 128.00, 127.84, 66.88, 64.56, 64.19, 59.78, 59.45. HRMS Calculated for $C_{14}H_{16}NO_3$ $(M+H)^+$246.1125; Found 246.1128. IR (cm^{-1}): 2956, 2854, 1696, 1413, 1360, 1277, 1088.



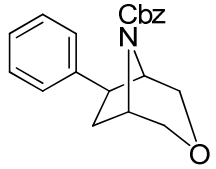
1b ***tert*-Butyl 3-oxa-8-azabicyclo[3.2.1]oct-6-ene-8-carboxylate (1b):** General procedure A using the secondary amine-TFA salt (1.34 g., 5.95 mmol) and di-tert-butyl dicarbonate (2.65 g., 11.9 mmol) yields **1b** (1.05 g., 4.97 mmol, 84%) as a white solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.26 (d, *J*=9.76 Hz, 2 H)

4.38 - 4.59 (m, 2 H) 3.71 (dd, *J*=18.73, 11.32 Hz, 2 H) 3.41 (d, *J*=10.93 Hz, 2 H) 1.43 - 1.55 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 152.93, 130.18, 129.58, 79.93, 65.59, 64.46, 61.11, 58.85, 28.29. HRMS Calculated for $C_{11}H_{17}NO_3Na$ $(M+Na)^+$ 234.1101; Found: 234.1100. IR (cm^{-1}): 2980, 2855, 1693, 1397, 1366, 1308, 1176, 1103, 1059.



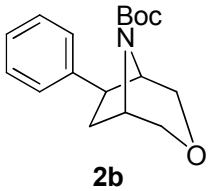
1c **Methyl 3-oxa-8-azabicyclo[3.2.1]oct-6-ene-8-carboxylate (1c):** General procedure A using the secondary amine-TFA salt (355 mg., 1.58 mmol) and methyl chloroformate (0.255 mL, 3.15 mmol) yields **1a** (178 mg., 1.05 mmol, 67%) as a clear oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.28 (d, *J*=8.20 Hz, 2 H) 4.45 - 4.69 (m, 2 H) 3.75 (s, 3 H) 3.71 (br. s., 2 H) 3.43 (d, *J*=10.54 Hz, 2 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.86, 131.15, 130.50, 64.56, 64.32, 59.77, 59.42, 52.44. HRMS Calculated for $C_8H_{12}NO_3$ $(M+H)^+$ 170.0812; Found 170.0815. IR (cm^{-1}): 2956, 2855, 1695, 1446, 1392, 1305, 1281, 1088.

Gereral Procedure B for the hydroarylation of Bridged Heterocycles:
Add Hydroxy(cyclooctadiene)rhodium dimer (5 mol %) and Josiphos SLJ002-1 (the *R,S*-diastereomer, 10 mol%) to a round bottom flask, flush with N2 and then dissolve in 1 mL sparged THF, stir 15 minutes. Add the catalyst solution to a mixture of boronic acid (1.5 equiv), triethylamine (2.0 equiv) and bridged heterocycle (1.0 equiv) in 1 mL sparged THF. Add 0.2 mL water, and stir 16 hours at room temperature. Filter the crude material through a plug of silica, wash with EtOAc (25 mL) and evaporate solvents. Purify by column chromatography (12 g. Isco column, gradient elution, 0-30% EtOAc/heptane) to yield the desired product.

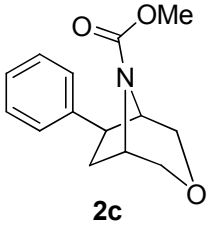


2a **(1*S*,5*R*,6*S*)-Benzyl 6-phenyl-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (2a):** General procedure B using bicycle **1a** (50 mg., 0.204 mmol.) and phenyl boronic acid (37 mg. 0.306 mmol) yields **2a** (53 mg., 0.163 mmol., 80 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.28 - 7.43 (m, 5 H) 7.13 - 7.26 (m, 5 H) 5.03 - 5.32 (m, 2 H) 4.32 - 4.52 (m, 1 H) 4.07 - 4.28 (m, 1 H) 3.63 - 3.89 (m, 4 H) 3.51 - 3.63 (m, 1 H) 2.44 - 2.65 (m, 1 H) 2.06 (td, *J*=11.81, 5.66 Hz, 1 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.48, 146.11, 136.54, 128.63, 128.44, 128.00, 127.86, 126.56, 126.41, 71.82, 71.27, 66.91, 62.78, 56.11, 46.54, 37.34. HRMS Calculated for $C_{20}H_{22}NO_3$ $(M+H)^+$ 324.1594; Found: 324.1593. IR (cm^{-1}): 3030, 2953,

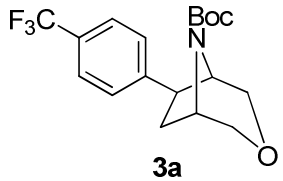
2852, 1695, 1414, 1312, 1213, 1101, 1086. $[\alpha]^{20}_{D}$ -103.6 (c 2.4, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 254 nm. detection) retention times: 5.19 min (minor), 5.38 min (major), 84% ee.



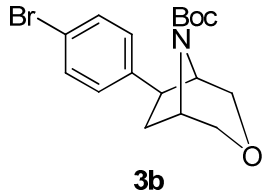
2b **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-phenyl-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (2b):** General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and phenyl boronic acid (37 mg. 0.30 mmol) yields **2b** (52 mg., 0.182 mmol., 76 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.29 (d, *J*=5.85 Hz, 2 H) 7.22 (d, *J*=6.63 Hz, 3 H) 4.20 - 4.43 (m, 1 H) 4.00 - 4.20 (m, 1 H) 3.61 - 3.85 (m, 4 H) 3.56 (dd, *J*=9.37, 5.07 Hz, 1 H) 2.45 - 2.60 (m, 1 H) 2.04 (dd, *J*=12.10, 6.24 Hz, 1 H) 1.42 - 1.57 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 166.90, 151.72, 129.92, 128.30, 126.68, 80.18, 71.67, 71.19, 62.65, 55.50, 51.99, 46.63, 37.36, 28.39. HRMS Calculated for $C_{17}H_{24}NO_3$ $(M+H)^+$ 290.1751; Found: 290.1744. IR (cm^{-1}): 2975, 2854, 1691, 1392, 1323, 1278, 1180, 1105, 1086. $[\alpha]^{20}_{D}$ -57.6 (c 2.1, $CHCl_3$). HPLC (Lux Amylose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 2.49 min (major), 2.86 min (minor), 95% ee.



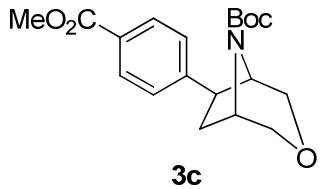
2c **(1*S*,5*R*,6*S*)-Methyl 6-phenyl-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (2c):** General procedure B using bicycle **1c** (50 mg., 0.20 mmol.) and phenyl boronic acid (37 mg. 0.30 mmol) yields **2c** (42 mg., 0.166 mmol., 83 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.27 - 7.33 (m, 2 H), 7.16 - 7.25 (m, 3 H), 4.27 - 4.48 (m, 1 H), 4.01 - 4.26 (m, 1 H), 3.70 - 3.87 (m, 5 H), 3.51 - 3.70 (m, 3 H), 2.55 (ddd, *J*=16.20, 12.68, 9.76 Hz, 1 H), 2.00 - 2.15 (m, 1 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 154.34, 146.20, 128.64, 126.56, 126.42, 71.75, 71.17, 62.81, 56.14, 52.44, 46.56, 37.38. HRMS Calculated for $C_{14}H_{18}NO_3$ $(M+H)^+$ 248.1281; Found: 248.1280. IR (cm^{-1}): 2954, 2854, 1700, 1449, 1394, 1322, 1106. $[\alpha]^{20}_{D}$ -100.9 (c 1.7, $CHCl_3$). HPLC (Lux Cellulose-3 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 2.29 min (minor), 2.74 min (major), 78% ee.



3a **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(4-(trifluoromethyl)phenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3a):** General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and para-trifluoromethylphenyl boronic acid (118 mg. 0.60 mmol) yields **3a** (75 mg., 0.214 mmol., 89 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.55 (d, *J*=8.20 Hz, 2 H) 7.33 (d, *J*=7.81 Hz, 2 H) 4.22 - 4.47 (m, 1 H) 3.96 - 4.20 (m, 1 H) 3.57 - 3.88 (m, 5 H) 2.46 - 2.67 (m, 1 H) 1.94 - 2.09 (m, 1 H) 1.40 - 1.56 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.08, 150.49, 127.75 - 129.16, 127.02, 125.58, 125.53, 80.24, 71.62, 71.15, 62.73, 55.59, 46.48, 37.45, 28.41. HRMS Calculated for $C_{18}H_{23}NO_3F_3$ $(M+H)^+$ 358.1625; Found: 358.1611. IR (cm^{-1}): 2980, 2857, 1692, 1393, 1324, 1162, 1113, 1086, 1069. $[\alpha]^{20}_D$ -72.0 (c 1.5, $CHCl_3$). HPLC (Lux Cellulose-4 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 2.15 min (minor), 2.29 min (major), 90% ee.

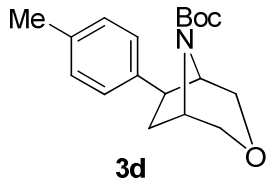


3b **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(4-bromophenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3b):** General procedure B using bicycle **1b** (250 mg., 1.18 mmol.) and para-bromophenyl boronic acid (301 mg. 1.50 mmol) yields **3b** (317 mg., 0.861 mmol., 73 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.35 - 7.51 (m, 2 H) 7.09 (d, *J*=7.81 Hz, 2 H) 4.19 - 4.42 (m, 1 H) 3.93 - 4.17 (m, 1 H) 3.60 - 3.84 (m, 4 H) 3.52 (dd, *J*=8.98, 5.07 Hz, 1 H) 2.47 - 2.59 (m, 1 H) 1.91 - 2.04 (m, 1 H) 1.43 - 1.54 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.09, 145.51, 131.58, 128.42, 120.05, 80.12, 71.61, 71.15, 62.81, 55.54, 46.10, 37.51, 28.41. HRMS Calculated for $C_{17}H_{23}NBrO_3$ $(M+H)^+$ 368.0856; Found: 368.0851. IR (cm^{-1}): 2974, 2854, 1688, 1489, 1391, 1323, 1160, 1103, 1084. $[\alpha]^{20}_D$ -55.0 (c 1.4, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 4.03 min (minor), 4.22 min (major), 92% ee.

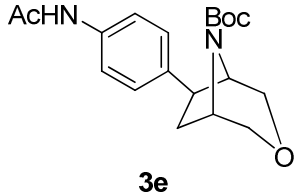


3c **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(4-(methoxycarbonyl)phenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3c):**General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and para-methoxycarbonylphenyl boronic acid (109 mg. 0.30 mmol) yields **3c** (70 mg., 0.204 mmol., 85%) as a white powder. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.96 (d, *J*=7.80 Hz, 1 H) 7.25 - 7.31 (m, 2 H) 4.21 - 4.46 (m, 1 H) 3.98 - 4.19 (m, 1 H) 3.91 (d, *J*=3.90 Hz, 3 H) 3.55 - 3.85 (m, 5 H) 2.47 - 2.62 (m, 1

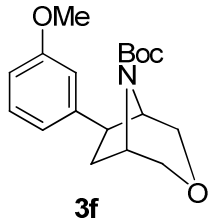
H) 2.02 (dd, *J*=11.71, 6.24 Hz, 1 H) 1.42 - 1.55 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 166.91, 153.02, 151.75, 129.93, 128.32, 126.69, 80.17, 71.69, 71.21, 62.66, 55.52, 52.01, 46.66, 37.39, 28.41. HRMS Calculated for $C_{19}H_{26}NO_5$ $(M+H)^+$ 348.1805; Found: 348.1811. IR (cm^{-1}): 2975, 2854, 1721, 1692, 1392, 1323, 1278, 1180, 1106, 1086. $[\alpha]^{20}_D$ -126.0 (c 1.0, $CHCl_3$). HPLC (Lux Cellulose-3 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 2.25 min (minor), 2.84 min (major), 90% ee.



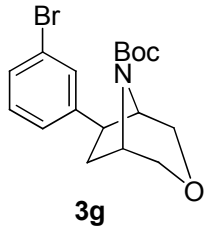
3d **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-*p*-tolyl-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3d):**General procedure B using bicycle **1b** (50 mg.,0.24 mmol.) and para-tolyl boronic acid (41 mg. 0.30 mmol) yields **3d** (58 mg., 0.194 mmol., 81%) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.11 (s, 4 H) 4.18 - 4.41 (m, 1 H) 3.97 - 4.17 (m, 1 H) 3.49 - 3.84 (m, 5 H) 2.45 - 2.57 (m, 1 H) 2.29 - 2.36 (m, 3 H) 2.00 (dt, *J*=12.39, 6.10 Hz, 1 H) 1.43 - 1.56 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.18, 143.55, 135.84, 129.20, 126.55, 79.90, 71.78, 71.25, 62.96, 61.63, 55.59, 46.21, 37.71, 28.43, 20.92. HRMS Calculated for $C_{18}H_{26}NO_3$ $(M+H)^+$ 304.1907; Found: 304.1902. IR (cm^{-1}): 2974, 2854, 1690, 1454, 1391, 1323, 1102, 1085. $[\alpha]^{20}_D$ -65.3 (c 1.5, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.31 min (minor), 3.40 min (major), 89% ee.



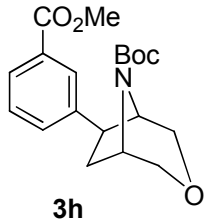
3e **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(4-acetamidophenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3e):** General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and para-(acetylamino)phenyl boronic acid (54 mg. 0.30 mmol) yields **3e** (67 mg., 0.197 mmol., 82 %) as a white powder. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.41 (d, *J*=7.80 Hz, 2 H) 7.23 (br. s., 1 H) 7.16 (d, *J*=7.81 Hz, 2 H) 4.18 - 4.41 (m, 1 H) 3.94 - 4.16 (m, 1 H) 3.59 - 3.84 (m, 4 H) 3.53 (dd, *J*=8.78, 4.88 Hz, 1 H) 2.44 - 2.57 (m, 1 H) 2.18 (s, 3 H) 1.98 (dt, *J*=12.39, 6.10 Hz, 1 H) 1.42 - 1.56 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 168.46, 153.23, 142.46, 136.25, 127.12, 120.19, 80.09, 71.68, 71.19, 61.68, 55.58, 46.03, 37.52, 28.43, 24.43. HRMS Calculated for $C_{19}H_{27}N_2O_4$ $(M+H)^+$ 347.1965; Found: 347.1952. IR (cm^{-1}): 3310, 2976, 2854, 1667, 1602, 1535, 1516, 1414, 1368, 1321, 1162, 1105, 1087. $[\alpha]^{20}_D$ -39.4 (c 1.6, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.76 min (major), 6.00 min (minor), 93% ee.



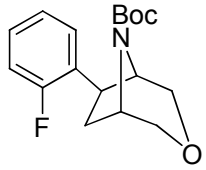
3f **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(3-methoxyphenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3f):** General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and meta-methoxyphenyl boronic acid (48 mg., 0.30 mmol) yields **3f** (66 mg., 0.209 mmol., 87 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.89 (s, 2 H) 7.40 (dd, *J*=12.88, 7.81 Hz, 2 H) 4.21 - 4.47 (m, 1 H) 3.99 - 4.17 (m, 1 H) 3.91 (br. s., 3 H) 3.55 - 3.85 (m, 5 H) 2.46 - 2.64 (m, 1 H) 2.04 (dd, *J*=12.29, 5.66 Hz, 1 H) 1.39 - 1.57 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 159.80, 153.10, 148.11, 129.53, 118.99, 112.45, 111.55, 79.93, 71.74, 71.39, 62.77, 55.55, 55.11, 46.57, 37.46, 28.41. HRMS Calculated for $C_{18}H_{26}NO_4$ $(M+H)^+$ 320.1856; Found: 320.1850. IR (cm^{-1}): 2973, 2853, 1690, 1601, 1393, 1324, 1256, 1162, 1106, 1086. $[\alpha]^{20}_D$ -83.1 (c 1.3, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.41 min (major), 3.52 min (minor), 96% ee.



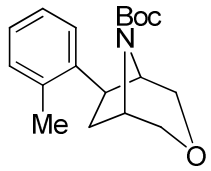
3g **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(3-bromophenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3g):**General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and meta-bromophenyl boronic acid (60 mg. 0.30 mmol) yields **3g** (72 mg., 0.173 mmol., 82%) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.30 - 7.42 (m, 2 H) 7.15 (d, *J*=6.63 Hz, 2 H) 4.20 - 4.44 (m, 1 H) 3.99 - 4.17 (m, 1 H) 3.58 - 3.85 (m, 4 H) 3.47 - 3.56 (m, 1 H) 2.45 - 2.60 (m, 1 H) 2.00 (dd, *J*=12.29, 5.66 Hz, 1 H) 1.44 - 1.55 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 152.88, 148.73, 130.10, 129.83, 129.45, 125.48, 122.71, 80.23, 71.67, 71.21, 62.52, 55.40, 46.31, 37.51, 28.43. HRMS Calculated for $C_{17}H_{22}NBrNaO_3$ $(M+Na)^+$ 390.0675; Found: 390.0679. IR (cm^{-1}): 2974, 2855, 1692, 1476, 1392, 1324, 1162, 1106, 1086. $[\alpha]^{20}_D$ -49.8 (c 2.2, $CHCl_3$). HPLC (Lux Cellulose-4 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.94 min (minor), 4.02 min (major), 86% ee.



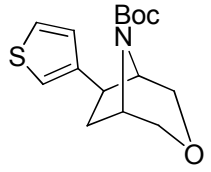
3h **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(3-(methoxycarbonyl)phenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3h):**General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and meta-methoxycarbonylphenyl boronic acid (110 mg. 0.60 mmol) yields **3h** (57 mg., 0.17 mmol., 69%) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.21 (t, *J*=7.80 Hz, 1 H) 6.69 - 6.86 (m, 3 H) 4.21 - 4.40 (m, 1 H) 4.02 - 4.20 (m, 1 H) 3.80 (s, 3 H) 3.58 - 3.77 (m, 4 H) 3.54 (dd, *J*=9.17, 4.88 Hz, 1 H) 2.42 - 2.58 (m, 1 H) 1.95 - 2.09 (m, 1 H) 1.41 - 1.55 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 166.98, 152.98, 146.72, 131.19, 130.43, 128.69, 127.95, 127.69, 80.07, 71.67, 71.15, 62.65, 55.50, 52.02, 46.35, 37.39, 28.36. HRMS Calculated for $C_{19}H_{26}NO_5$ $(M+H)^+$ 348.1805; Found: 348.1804. IR (cm^{-1}): 2975, 2853, 1722, 1691, 1393, 1287, 1200, 1104, 1087. $[\alpha]^{20}_D$ -87.3 (c 1.1, $CHCl_3$). HPLC (Lux Amylose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.68 min (major), 4.27 min (minor), 94% ee.



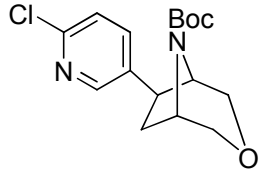
3i **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(2-fluorophenyl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3i):**General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and ortho-fluorophenyl boronic acid (86 mg. 0.60 mmol) yields **3i** (26 mg., 0.086 mmol., 36 %) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.14 - 7.26 (m, 2 H) 6.97 - 7.13 (m, 2 H) 4.01 - 4.44 (m, 2 H) 3.86 - 3.98 (m, 1 H) 3.58 - 3.83 (m, 4 H) 2.42 - 2.61 (m, 1 H) 1.92 - 2.11 (m, 1 H) 1.40 - 1.56 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.20, 132.74, 127.66, 127.02, 124.45, 124.25, 115.21, 79.98, 71.61, 71.35, 62.11, 55.36, 38.27, 35.41, 28.38. HRMS Calculated for $C_{17}H_{23}NFO_3$ $(M+H)^+$ 308.1656; Found: 308.1661. IR (cm^{-1}): 2976, 2856, 1692, 1492, 1393, 1325, 1163, 1107, 1087. $[\alpha]^{20}_D$ +28.0 (c 1.3, $CHCl_3$). HPLC (Lux Cellulose-4 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 2.88 min (major), 2.97 min (minor), 42% ee.



3j **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-*o*-tolyl-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3j):**General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and ortho-tolyl boronic acid (85 mg. 0.60 mmol) yields **3j** (12 mg., 0.041 mmol., 17%) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.05 - 7.26 (m, 4 H) 4.05 - 4.44 (m, 2 H) 3.68 - 3.91 (m, 4 H) 3.60 - 3.68 (m, 1 H) 2.48 - 2.64 (m, 1 H) 2.37 (s, 3 H) 1.83 - 2.00 (m, 1 H) 1.50 (d, *J*=17.17 Hz, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 152.99, 144.34, 135.02, 130.13, 126.45, 126.05, 124.92, 79.96, 72.00, 71.38, 61.88, 55.52, 42.01, 36.44, 28.47, 20.06. HRMS Calculated for $C_{18}H_{26}NO_3$ $(M+H)^+$ 304.1907; Found: 304.1906. IR (cm^{-1}): 2974, 2854, 1692, 1393, 1324, 1162, 1104, 1086. $[\alpha]^{20}_D$ +71.6 (c 1.6, $CHCl_3$). HPLC (Lux Amylose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 2.88 min (minor), 3.15 min (major), 77% ee.

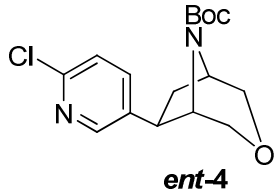


3k **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(thiophen-3-yl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (3k):**General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and 3-thiophene boronic acid (39 mg. 0.30 mmol) yields **3k** (58 mg., 0.20 mmol., 83%) as a yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.27 (s, 1 H) 6.89 - 7.11 (m, 2 H) 4.21 - 4.41 (m, 1 H) 3.97 - 4.21 (m, 1 H) 3.50 - 3.87 (m, 5 H) 2.38 - 2.58 (m, 1 H) 2.00 (td, *J*=13.27, 6.63 Hz, 1 H) 1.33 - 1.56 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.40, 146.70, 126.69, 126.02, 119.17, 79.92, 71.50, 71.37, 62.52, 55.29, 42.02, 36.51, 28.37. HRMS Calculated for $C_{15}H_{21}NNaSO_3$ $(M+Na)^+$ 318.1134; Found: 318.1130. IR (cm^{-1}): 2974, 2854, 1687, 1391, 1366, 1323, 1160, 1103, 1085. $[\alpha]^{20}_D$ -50.0 (c 1.6, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.53 min (minor), 3.58 min (major), 77% ee.

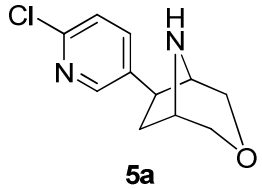


4 **(1*S*,5*R*,6*S*)-*tert*-Butyl 6-(6-chloropyridin-3-yl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (4):** General procedure B using bicycle **1b** (50 mg., 0.24 mmol.) and 4-chloro-3-pyridine boronic acid (94 mg. 0.60 mmol) and running the reaction at 50 °C yields **4** (43 mg., 0.127 mmol., 53 %) as a yellow oil. ^{1}H NMR (400

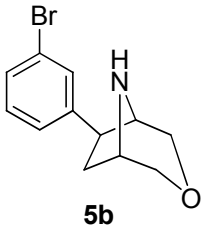
MHz, CHLOROFORM-*d*) δ ppm 8.26 (br. s., 1 H) 7.43 - 7.59 (m, 1 H) 7.19 - 7.31 (m, 1 H) 4.20 - 4.48 (m, 1 H) 3.92 - 4.15 (m, 1 H) 3.50 - 3.87 (m, 5 H) 2.47 - 2.66 (m, 1 H) 1.95 (dt, *J*=12.10, 6.05 Hz, 1 H) 1.41 - 1.60 (m, 9 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 153.10, 149.53, 148.23, 140.80, 136.87, 124.30, 80.49, 71.40, 70.99, 62.68, 55.58, 43.43, 37.48, 28.41. HRMS Calculated for $C_{16}H_{22}N_2ClO_3$ $(M+H)^+$ 325.1313; Found: 325.1314. IR (cm^{-1}): 2976, 2856, 1691, 1458, 1393, 1326, 1162, 1106, 1086. $[\alpha]^{20}_D$ -64.0 (c 1.8, $CHCl_3$). HPLC (Lux Cellulose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 3.91 min (major), 6.69 min (minor), 78% ee.



***ent*-4** **(1*R*,5*S*,6*R*)-*tert*-Butyl 6-(6-chloropyridin-3-yl)-3-oxa-8-azabicyclo[3.2.1]octane-8-carboxylate (4):** Identical procedure to **4** using Josiphos SLJ002-2 (the *S,R*-diastereomer, 10 mol%) yields **ent-4**, which has identical NMR, IR and HRMS spectra to **4**. $[\alpha]^{20}_D$ +73.6 (c 2.8, $CHCl_3$). HPLC (Lux Amylose-2 250 mm X 4.6 mm column, 3.0 mL/min CO_2/MeOH, 120 bar, 210 nm. detection) retention times: 4.27 min (minor), 4.64 min (major), 85% ee.



5a **(1*S*,5*R*,6*S*)-6-(6-chloropyridin-3-yl)-3-oxa-8-azabicyclo[3.2.1]octane (5a):** Hydrochloric acid (4.0 M in dioxane, 0.416 mL, 1.66 mmol) was added slowly to a solution of **4** (108 mg., 0.33 mmol) in chloroform (1.0 mL). The resulting solution was stirred for 4 hours and then solvents were removed under vacuum. Direct purification by reverse phase chromatography yielded **5a** (46 mg., 0.201 mmol., 61% yield) as a white powder. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.33 (d, *J*=2.73 Hz, 1 H) 7.70 (dd, *J*=8.39, 2.54 Hz, 1 H) 7.19 - 7.30 (m, 1 H) 3.60 - 3.86 (m, 4 H) 3.44 - 3.58 (m, 2 H) 3.19 (s, 1 H) 2.53 (dd, *J*=12.68, 9.17 Hz, 1 H) 1.87 (dt, *J*=12.39, 6.10 Hz, 111 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 149.09, 148.26, 141.72, 137.12, 124.09, 73.73, 73.42, 62.72, 56.24, 43.19, 38.46. HRMS Calculated for $C_{11}H_{14}N_2ClO$ $(M+H)^+$ 225.0789; Found: 225.0787. IR (cm^{-1}): 2945, 2851, 1563, 1454, 1386, 1099, 1081. $[\alpha]^{20}_D$ -38.0 (c 1.0, $CHCl_3$).



5b **(1*S*,5*R*,6*S*)-6-(3-bromophenyl)-3-oxa-8-azabicyclo[3.2.1]octane (5b):** Hydrochloric acid (4.0 M in dioxane, 0.10 mL, 0.41 mmol) was added slowly to a solution of **3g** (50 mg., 0.14 mmol) in chloroform (1.0 mL). The resulting solution was stirred for 4 hours and then solvents were removed under vacuum. Direct purification by column chromatography (12 g. column, gradient elution, 0-30% EtOH/DCM) yielded **5b** (25 mg., 0.084 mmol., 60% yield as the HCl salt) as a white powder. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.52 (s, 1 H) 7.37 (t, *J*=6.83 Hz, 2 H) 7.16 - 7.24 (m, 1 H) 3.93 - 4.12 (m, 2 H) 3.82 (d, *J*=6.24 Hz, 1 H) 3.66 - 3.78 (m, 2 H) 3.63 (dd, *J*=8.78, 6.05 Hz, 1 H) 3.53 (s, 1 H) 2.48 - 2.70 (m, 1 H) 2.06 - 2.22 (m, 1 H). ^{13}C NMR (101 MHz, CHLOROFORM-*d*) δ ppm 146.76, 130.47, 130.37, 129.88, 125.59, 122.81, 71.52, 70.93, 62.87, 56.84, 45.31, 36.88. HRMS Calculated for $C_{12}H_{15}NBrO$ $(M+H)^+$ 268.0332; Found: 268.0331. IR (cm^{-1}): 2944, 2857, 2711, 2539, 1596, 1565, 1477, 1091. $[\alpha]^{20}_D$ -13.8 (c 1.5, $CHCl_3$).

3. Computational Details

Energy calculations for the transition state (TS) searches employed the B3LYP exchange-correlation energy functional[1,2] and the LACV3P* basis set due to the presence of Rhodium (effective core potentials are needed). The LACV3P basis set is a triple-zeta contraction of the LACVP basis set[3] developed and tested at Schrödinger.[4] The standard search option along the lowest Hessian eigenvector was used.[4] Frequency calculations for the TS structures were performed at 298K, following the experimental conditions. Only one imaginary frequency corresponding to the reaction coordinate was obtained for both TS structures. The identification of stationary points on the potential energy surface was performed in the gas-phase followed by single-point solvation calculations through the application of the Poisson-Boltzmann solver using THF as the solvent.[5,6] These calculations employed the LACV3P**+ basis set. All calculations were performed within the Jaguar program.[4]

(1) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(2) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*,11623.

(3) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(4) *Jaguar*, version 7.7; Schrödinger, LLC: New York, NY, 2010.

(5) Tannor, D. J.; Marten, B.; Murphy, R.; Friesner, R. A.; Sitkoff, D.; Nicholls, A.; Ringnalda, M.; Goddard, W. A., III; Honig, B. *J. Am. Chem. Soc.* **1994,** *116,* 11875.

(6) Marten, B.; Kim, K.; Cortis, C.; Friesner, R. A.; Murphy, R. B.; Ringnalda, M. N.; Sitkoff, D.; Honig, B. *J. Phys. Chem.* **1996,** *100,* 11775.

4. Biological Assay Data

Target	IC_{50} (uM)
Nicotinic acetylcholine receptor	0.17
Sodium-dependent seratonin transporter (5HTT)	>10
Seratonin 5-HT2b	>10
Beta-2 adrenergic receptor	>10
Cyclooxygenase 2	>10
D1 dopamine receptor (non-specific)	>10
Sodium-dependent dopamine transporter (DAT)	>10
Glucocorticoid receptor	>10
Histamine H1 receptor	>10
Muscarinic acetylcholine receptor M1	>10
Mu-type opioid receptor (MOR-1)	>10
Sodium-dependent noradrenaline transporter (NAT)	>10
Rat N-Type calcium channel (non-specific)	>10
Rat L-Type calcium channel (non-specific)	>10
Rat alpha 1 adrenergic receptor (non-specific)	>10
Rat sodium channel (non-specific)	>10
Peroxisome proliferator activated receptor gamma (PPAR-gamma)	>10
cGMP-inhibited cAMP phosphodiesterase 3B (PDE3B)	>10

5. X-RAY CRYSTALLOGRAPHY REPORT: compound 4

SUMMARY:

- The structure was solved in the $P2_12_12_1$ space group
- The asymmetric unit is comprised of one molecule of 00705549-1230-001

- R value 6%
- Absolute configuration

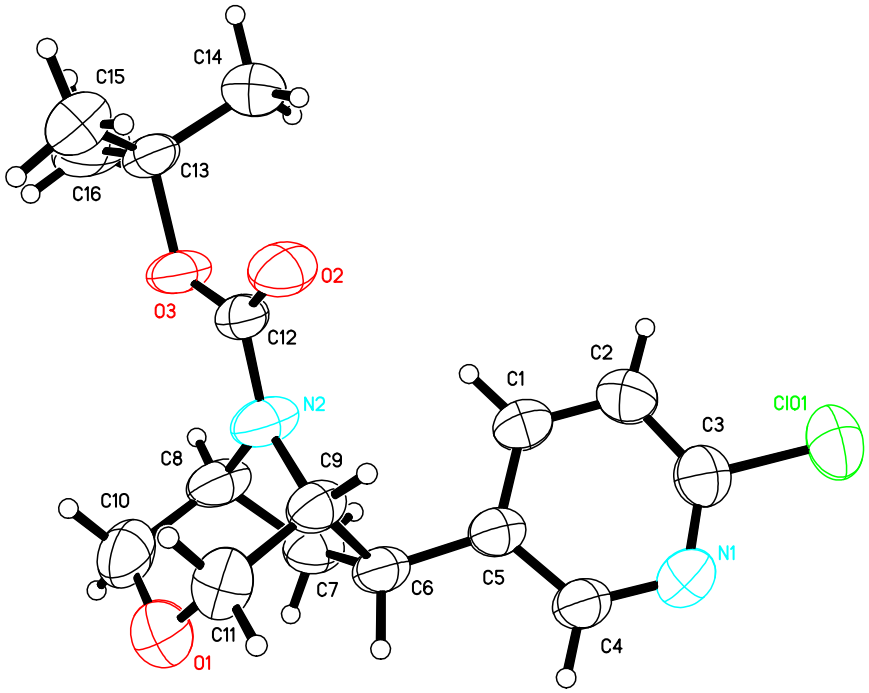


Figure 1. ORTEP with ellipsoids drawn at 50% confidence level.

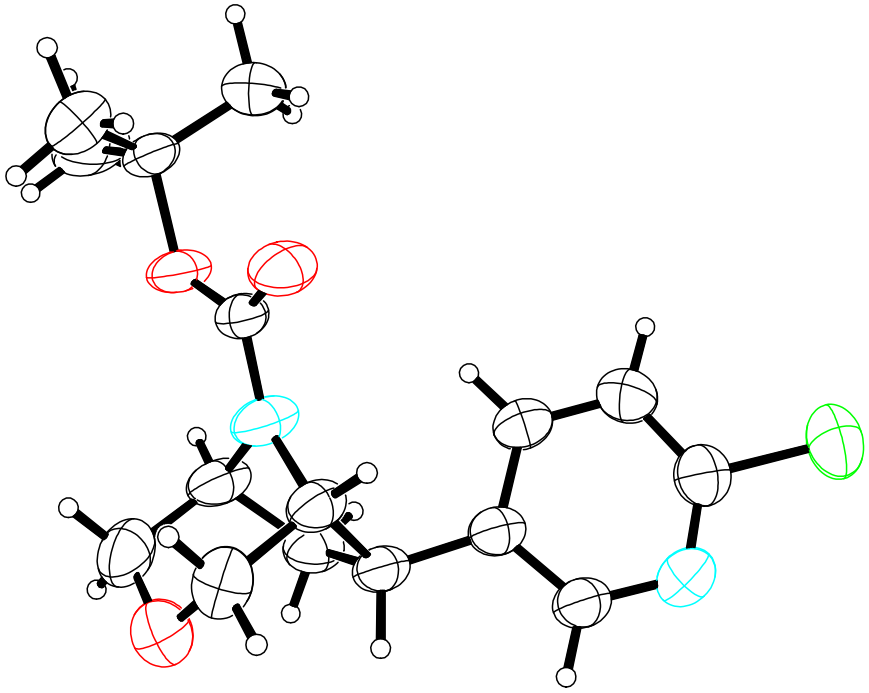


Figure 2. ORTEP with ellipsoids drawn at 50% confidence level.

EXPERIMENTAL:

Data collection was performed on a Bruker APEX diffractometer at room temperature. Data collection consisted of omega and phi scans.

The structure was solved by direct methods using SHELX software suite in the space group $P2_12_12_1$. The structure was subsequently refined by the full-matrix least squares method. All non-hydrogen atoms were found and refined using anisotropic displacement parameters.

All hydrogen atoms were placed in calculated positions and were allowed to ride on their carrier atoms. The final refinement included isotropic displacement parameters for all hydrogen atoms.

Absolute configuration was determined by examination of the Flack parameter. In this case, the parameter = 0.0383 with esd of 0.0240; within range for absolute configuration determination.

The final R-index was 6%. A final difference Fourier revealed no missing or misplaced electron density.

Pertinent crystal, data collection and refinement are summarized in table 1. Atomic coordinates, bond lengths, bond angles, Torsion angles and displacement parameters are listed in tables 2 –6.

Software and References

SHELXTL, Version 5.1, Bruker AXS, 1997

PLATON, A.L. Spek, J. Appl. Cryst. 2003, 36, 7-13.

MERCURY, C.F. Macrae, P.R. Edington, P. McCabe, E. Pidcock, G.P. Shields, R. Taylor, M. Towler and J. van de Streek, *J. Appl. Cryst.* **39**, 453-457, 2006.

R.W.W. Hooft et al. *J. Appl. Cryst.* (2008). 41. 96-103.

H.D. Flack, *Acta Cryst.* 1983, **A**39, 867-881.

Table 1. Crystal data and structure refinement for 00705549-1230-001.

Identification code	z238g	
Empirical formula	C16 H21 Cl N2 O3	
Formula weight	324.80	
Temperature	298(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.9446(8) Å	□= 90°.
	b = 10.3967(9) Å	□= 90°.
	c = 16.1629(13) Å	□ = 90°.
Volume	1671.1(2) $Å^3$	
Z	4	
Density (calculated)	1.291 Mg/m^3	
Absorption coefficient	2.142 mm^{-1}	
F(000)	688	
Crystal size	0.68 x 0.60 x 0.55 mm^3	
Theta range for data collection	5.06 to 68.63°.	
Index ranges	-11<=h<=11, -12<=k<=12, -19<=l<=18	
Reflections collected	17235	
Independent reflections	3047 [R(int) = 0.0905]	
Completeness to theta = 68.63°	99.5 %	
Absorption correction	None	
Max. and min. transmission	0.3854 and 0.3236	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3047 / 0 / 202	

Goodness-of-fit on F^2	1.069
Final R indices [I>2sigma(I)]	R1 = 0.0613, wR2 = 0.1649
R indices (all data)	R1 = 0.0625, wR2 = 0.1671
Absolute structure parameter	0.04(2)
Largest diff. peak and hole	0.367 and -0.211 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)

for 00705549-1230-001. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	-788(3)	5403(3)	702(2)	65(1)
C(2)	-756(4)	6560(3)	295(2)	68(1)
C(3)	-1908(4)	6926(3)	-102(2)	56(1)
C(4)	-3020(3)	5157(3)	268(2)	52(1)
C(5)	-1957(3)	4668(3)	698(1)	47(1)
C(6)	-2052(3)	3381(2)	1126(1)	47(1)
C(7)	-1848(3)	3460(3)	2078(2)	53(1)
C(8)	-691(2)	2538(3)	2264(2)	56(1)
C(9)	-951(2)	2432(3)	852(2)	48(1)
C(10)	-1193(4)	1171(4)	2356(2)	72(1)
C(11)	-1460(4)	1065(3)	912(2)	64(1)
C(12)	1394(2)	2548(3)	1372(2)	44(1)
C(13)	3524(2)	2556(3)	2126(2)	55(1)
C(14)	4039(3)	3780(3)	1726(2)	67(1)

C(15)	4087(4)	1354(4)	1722(3)	80(1)
C(16)	3779(3)	2582(6)	3048(2)	91(1)
Cl(01)	-1908(1)	8414(1)	-618(1)	80(1)
N(1)	-3027(3)	6282(2)	-136(2)	58(1)
N(2)	60(2)	2634(3)	1491(1)	57(1)
O(1)	-2058(3)	834(2)	1695(2)	72(1)
O(2)	1899(2)	2552(2)	688(1)	57(1)
O(3)	2042(2)	2527(2)	2094(1)	57(1)

Table 3. Bond lengths [Å] and angles [°] for 00705549-1230-001.

C(1)-C(2)	1.372(5)	C(11)-O(1)	1.420(4)
C(1)-C(5)	1.391(4)	C(12)-O(2)	1.215(3)
C(2)-C(3)	1.367(5)	C(12)-O(3)	1.333(3)
C(3)-N(1)	1.299(5)	C(12)-N(2)	1.344(3)
C(3)-Cl(01)	1.758(3)	C(13)-O(3)	1.475(3)
C(4)-N(1)	1.339(4)	C(13)-C(16)	1.511(4)
C(4)-C(5)	1.364(4)	C(13)-C(14)	1.516(4)
C(5)-C(6)	1.509(4)	C(13)-C(15)	1.518(5)
C(6)-C(9)	1.540(4)		
C(6)-C(7)	1.554(3)	C(2)-C(1)-C(5)	119.9(3)
C(7)-C(8)	1.528(4)	C(3)-C(2)-C(1)	116.7(3)
C(8)-N(2)	1.459(3)	N(1)-C(3)-C(2)	126.5(3)
C(8)-C(10)	1.514(5)	N(1)-C(3)-Cl(01)	115.7(2)
C(9)-N(2)	1.456(3)	C(2)-C(3)-Cl(01)	117.8(3)
C(9)-C(11)	1.511(4)	N(1)-C(4)-C(5)	125.3(3)
C(10)-O(1)	1.416(5)	C(4)-C(5)-C(1)	116.5(2)

C(4)-C(5)-C(6)	121.0(2)	C(10)-O(1)-C(11)	112.1(3)
C(1)-C(5)-C(6)	122.5(2)	C(12)-O(3)-C(13)	120.93(19)
C(5)-C(6)-C(9)	113.0(2)		
C(5)-C(6)-C(7)	113.5(2)		
C(9)-C(6)-C(7)	103.1(2)		
C(8)-C(7)-C(6)	105.1(2)		
N(2)-C(8)-C(10)	108.4(3)		
N(2)-C(8)-C(7)	100.0(2)		
C(10)-C(8)-C(7)	111.1(2)		
N(2)-C(9)-C(11)	108.8(2)		
N(2)-C(9)-C(6)	101.2(2)		
C(11)-C(9)-C(6)	110.2(2)		
O(1)-C(10)-C(8)	111.0(2)		
O(1)-C(11)-C(9)	110.9(3)		
O(2)-C(12)-O(3)	126.6(2)		
O(2)-C(12)-N(2)	122.6(2)		
O(3)-C(12)-N(2)	110.7(2)		
O(3)-C(13)-C(16)	101.7(2)		
O(3)-C(13)-C(14)	109.9(2)		
C(16)-C(13)-C(14)	110.4(3)		
O(3)-C(13)-C(15)	109.7(3)		
C(16)-C(13)-C(15)	112.1(3)		
C(14)-C(13)-C(15)	112.5(3)		
C(3)-N(1)-C(4)	115.1(3)		
C(12)-N(2)-C(9)	124.8(2)		
C(12)-N(2)-C(8)	128.5(2)		
C(9)-N(2)-C(8)	104.16(19)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 00705549-1230-001. The anisotropic

displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	48(2)	72(2)	77(2)	13(2)	-21(1)	-13(1)
C(2)	58(2)	70(2)	77(2)	14(2)	-11(2)	-19(2)
C(3)	62(2)	57(1)	49(1)	-1(1)	3(1)	1(1)
C(4)	41(1)	55(1)	60(1)	0(1)	-7(1)	-2(1)
C(5)	39(1)	56(1)	46(1)	-2(1)	-3(1)	-2(1)
C(6)	33(1)	57(1)	49(1)	0(1)	-5(1)	-3(1)
C(7)	40(1)	72(2)	47(1)	0(1)	6(1)	-2(1)
C(8)	34(1)	95(2)	38(1)	7(1)	-2(1)	1(1)
C(9)	38(1)	66(2)	41(1)	3(1)	-3(1)	2(1)
C(10)	63(2)	91(2)	61(2)	28(2)	7(1)	18(2)
C(11)	70(2)	60(2)	61(2)	3(1)	-7(1)	9(1)
C(12)	29(1)	54(1)	47(1)	8(1)	2(1)	1(1)
C(13)	28(1)	75(2)	61(1)	18(1)	-3(1)	3(1)
C(14)	48(2)	73(2)	79(2)	10(2)	-2(2)	-9(1)
C(15)	53(2)	77(2)	112(3)	18(2)	-2(2)	13(2)
C(16)	47(2)	161(4)	66(2)	32(2)	-18(1)	-2(2)
Cl(01)	96(1)	63(1)	80(1)	19(1)	3(1)	2(1)
N(1)	52(1)	61(1)	62(1)	1(1)	-8(1)	8(1)

N(2)	34(1)	99(2)	38(1)	5(1)	0(1)	3(1)
O(1)	69(1)	70(1)	77(1)	17(1)	3(1)	-2(1)
O(2)	41(1)	84(1)	45(1)	3(1)	10(1)	4(1)
O(3)	28(1)	96(1)	47(1)	14(1)	1(1)	-2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 00705549-1230-001.

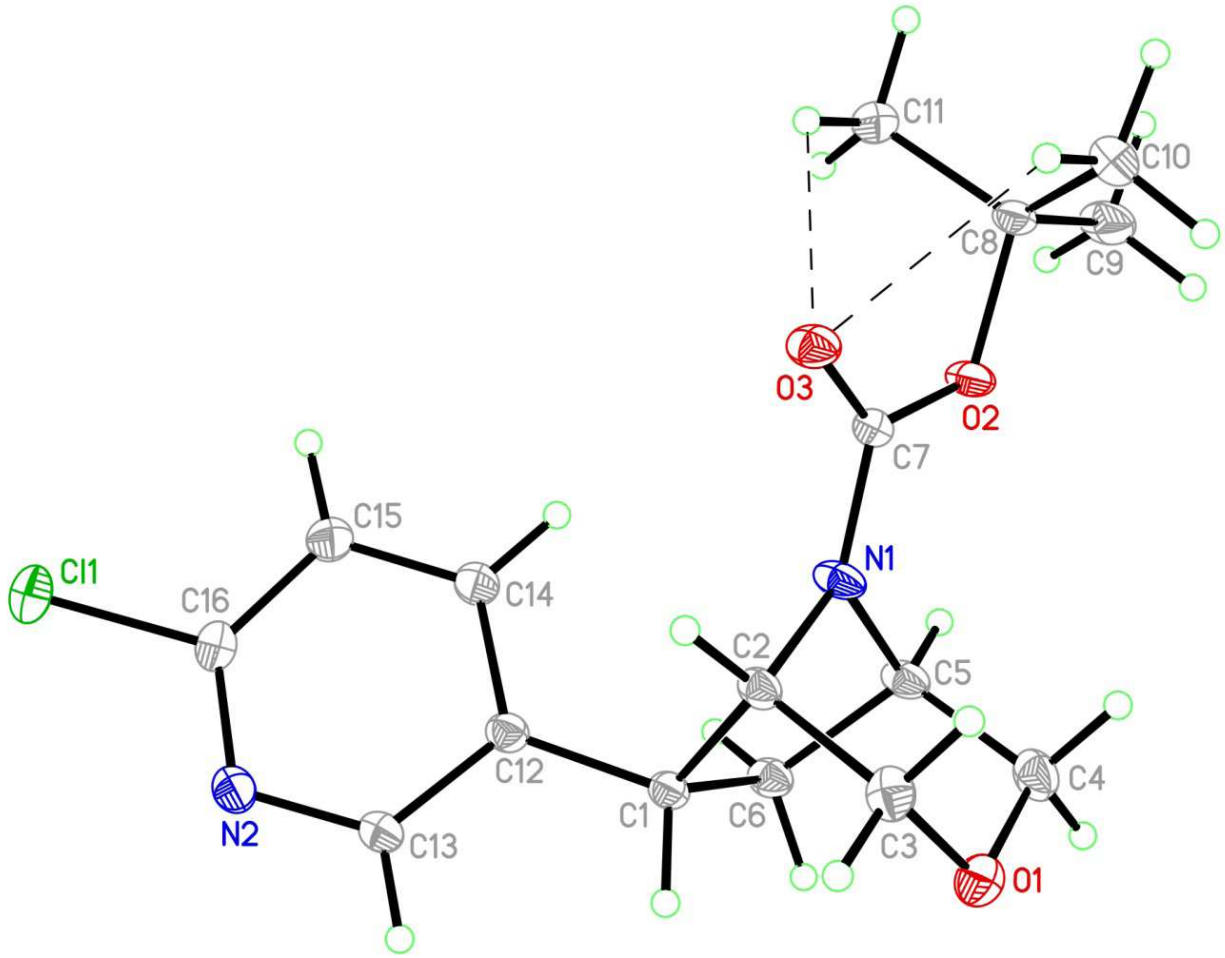
	x	y	z	U(eq)
H(016)	-30	5110	981	79
H(018)	12	7071	289	82
H(013)	-3804	4670	253	62
H(010)	-2936	3003	1012	56
H(01A)	-1620	4330	2245	63
H(01B)	-2657	3198	2368	63
H(009)	-157	2816	2742	67
H(007)	-606	2632	299	58
H(02C)	-432	586	2367	86
H(02D)	-1671	1085	2876	86
H(02A)	-2117	913	479	76
H(02B)	-719	473	829	76
H(01C)	3816	3776	1148	100
H(01D)	4998	3828	1790	100
H(01E)	3629	4511	1987	100
H(01F)	3635	611	1938	120

H(01G)	5032	1292	1836	120
H(01H)	3950	1399	1134	120
H(02E)	3380	3339	3282	137
H(02F)	4731	2590	3149	137
H(02G)	3390	1832	3298	137

Structure Report for *ent*-4

Sample Preparation

Figure 1: Thermal ellipsoid representation at the 50% probability level of SFY_015 with atomic labeling scheme. The two weak intramolecular C—H···O hydrogen bonds are drawn as dashed lines. Chiralities: C1 (R), C2 (S) and C5 (R).



The sample consisted of a few dry colorless blocks and a larger amount of white fluffy amorphous material. The crystals had been obtained from a mixture of dichloromethane and heptanes. The crystal chosen for data collection was a fragment of one of the colorless blocks with the dimensions 0.28 x 0.30 x 0.36 mm3.

Data Collection and Data Reduction

Pfizer had indicated that low-temperature data collection was acceptable and the crystal was mounted on a MiTeGen™ mount with mineral oil. Diffraction data (φ- and ω-scans) were collected at 100K on a Bruker-AXS X8 Kappa Duo diffractometer coupled to a Smart Apex2 CCD detector with graphite-monochromated Mo $K\alpha$ radiation (= 0.71073 Å) from a fine-focus sealed tube. Data reduction was carried out with the program SAINT[1] and semi-empirical absorption correction based on equivalents was performed with the program SADABS[2]. A summary of crystal properties and data/refinement statistics is given in Table 1.

Structure Solution and Refinement

The structure was solved with direct methods using the program SHELXS[3] and refined against *F*2 on all data with SHELXL[4] using established refinement techniques[5]. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed in geometrically calculated positions and refined using a riding model while constraining their *Uiso* to 1.2 times the *Ueq* of the atoms to which they bind (1.5 times for methyl groups). The three methyl groups were treated as rigid, however the torsion angles were refined. The diffraction data show significant anomalous signal and the absolute structure could be established with confidence. The configurations of the compound's three chiral carbon atoms are as follows: Chirality at C1 is R, at C2 is S and at C5 is R. More details below.

Crystal Structure

The submitted compound crystallizes in the orthorhombic chiral space group *P*212121 with one molecule per asymmetric unit. Two weak intramolecular C—H···O hydrogen bonds fixate the torsion angles of two of the three methyl groups in the *t*Bu group. In addition, there are two crystallographically independent intermolecular very weak hydrogen bonds, C4—H4A···Cl1*i* and C15—H15···N2*ii* (symmetry codes *i*: 3/2-*x*, 1-*y*, -1/2+*z*; *ii*: 1/2+*x*, 3/2-*y*, 1-*z*), however the respective hydrogen-acceptor distances are 0.78 and 0.75 Å longer than the sum of van-der-Waals radii, which makes those interactions too weak to consider. All four independent C—H···A (A = acceptor) interactions are listed in Table 2. Figure 1 shows the molecule of SFY_015 with the two weak intramolecular C—H···O hydrogen bonds. It may be worth noting that the plane of the chloropyridine ring (as defined by atoms C12, C13, C14, C15, C16 and N2) forms an 85.81(5)° angle with atoms C2, C1, C6 of the core moiety, while the COO*t*Bu ester substituent (as defined by atoms O2, O3, C7 and C8) is just 10.77(4)° out of the plane defined by atoms C2, N1, C5. The two substituents mentioned form an angle of 58.90(4)°. Figure 2 shows packing plots corresponding to views along the three crystallographic axes. The absolute structure could be determined based on anomalous signal from chlorine: The Flack-*x* parameter[6] refined to 0.01(3). Analysis of the anomalous signal by the method introduced by Hooft & Spek[7] calculates the probability of the absolute structure to be correct to 1.0, the probability of the structure to be a racemic twin to 0.0 and the probability of the absolute structure to be incorrect to 0.0. It can therefore be determined with high confidence that the configuration of the molecule is C1 (R), C2 (S) and C5 (R).

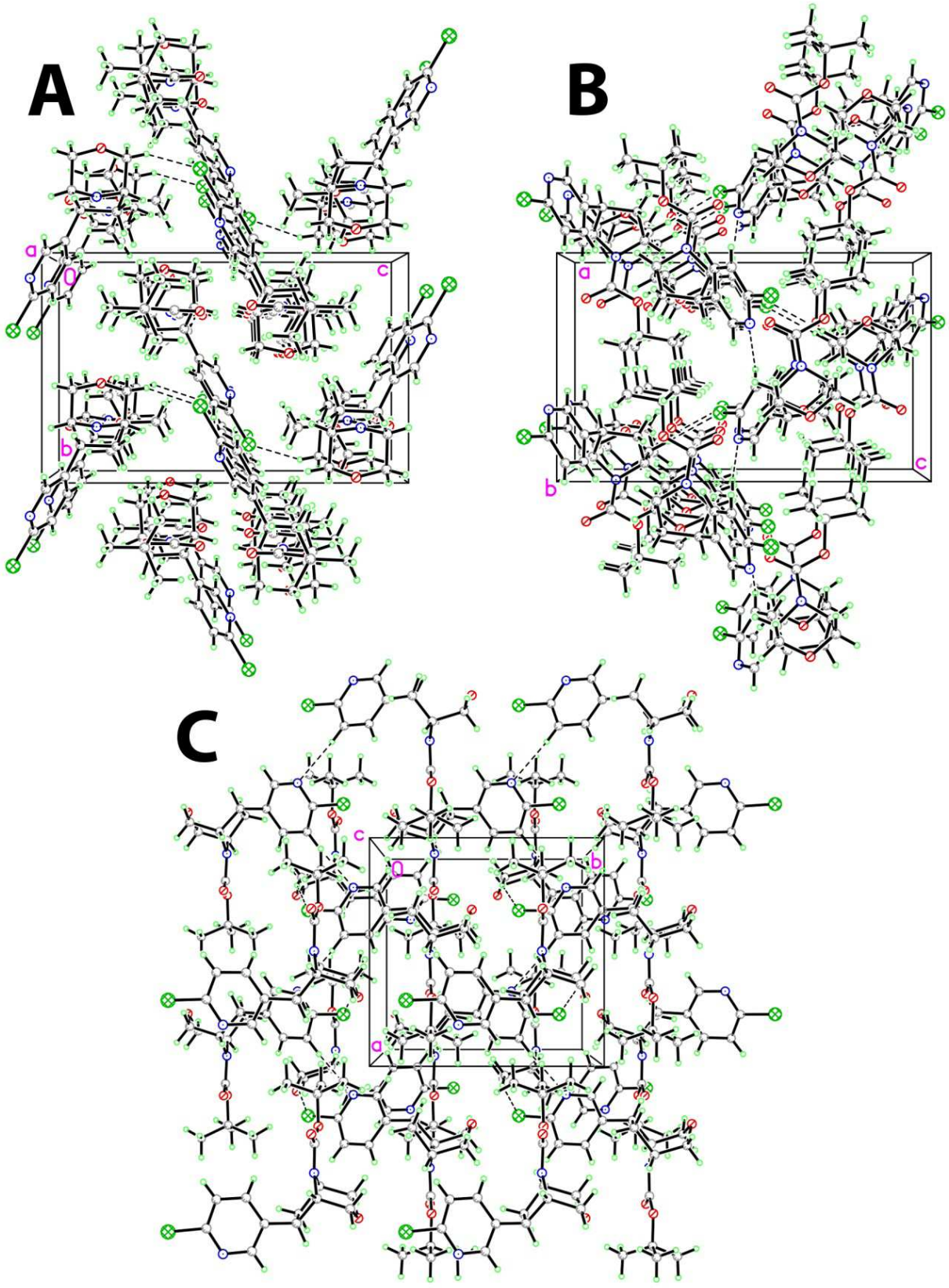

A
B
C
a
b
c
0

Figure 2: Packing plots of SFY_015. Panels **A**, **B** and **C** show projections along the crystallographic *a*-, *b*-, and *c*-axis, respectively. The very weak intermolecular C—H···Cl and C—H···N hydrogen bonds mentioned above and listed in Table 2 are drawn as thin dashed lines.

Table 1: Crystal data and structure refinement for **SFY_015**.

Identification code	sfy15
Empirical formula	C16 H21 Cl N2 O3
Formula weight	324.80
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	*P*212121
Unit cell dimensions	*a* = 9.8721(7) Å □ = 90°.
	b = 10.1397(7) Å □ = 90°.
	c = 16.1579(12) Å □ = 90°.
Volume	1617.4(2) Å3
Z	4
Density (calculated)	1.334 Mg/m3
Absorption coefficient	0.250 mm-1
F(000)	688
Crystal size	0.33 x 0.31 x 0.28 mm3
Theta range for data collection	2.37 to 31.50°.
Index ranges	-14<=*h*<=14, -14<=*k*<=14, -23<=*l*<=23
Reflections collected	46801
Independent reflections	5389 [*Rint* = 0.0275]
Completeness to theta = 31.50°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9332 and 0.9220
Refinement method	Full-matrix least-squares on *F*2
Data / restraints / parameters	5389 / 0 / 202
Goodness-of-fit on *F*2	1.093
Final *R* indices [*I*>2σ(*I*)]	*R*1 = 0.0268, *wR*2 = 0.0735
R indices (all data)	*R*1 = 0.0276, *wR*2 = 0.0742
Absolute structure parameter	0.01(3)
Largest diff. peak and hole	0.379 and -0.181 e.Å-3

Table 2: Hydrogen bond parameters for **SFY_015** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(4)-H(4A)...Cl(1)#1	0.99	2.80	3.7253(11)	156.3
C(10)-H(10A)...O(3)	0.98	2.45	3.0263(13)	117.3
C(11)-H(11C)...O(3)	0.98	2.41	3.0000(13)	118.3
C(15)-H(15)...N(2)#2	0.95	2.55	3.4954(13)	172.4

Symmetry transformations used to generate equivalent atoms:
#1 -x+3/2,-y+1,z-1/2 #2 x+1/2,-y+3/2,-z+1

References

[1] Bruker (**2011**). SAINT, Bruker-AXS Inc., Madison, Wisconsin, USA.

[2] Sheldrick, G. M., (**2009**). SADABS, University of Göttingen, Germany.
[3] Sheldrick, G. M., *Acta Cryst.* **1990**, *A46*, 467-473.
[4] Sheldrick, G. M., *Acta Cryst.* **2008**, *A64*, 112-122.
[5] Müller, P., *Crystallography Reviews* **2009**, *15*, 57-83.
[6] Flack H. D., *Acta Cryst.* **1983**, *A39*, 876-881.
[7] Hooft, R. W. W., Straver, L. H. Spek, A. L., *J. Appl. Cryst.* **2008**, *41*, 96-103.

6. HPLC Traces

CHIRAL PURIFICATION GROUP

ANALYTICAL REPORT

Sample Information

705549-1054-001B

Chemists Ryan Brawn
Zone CVMD

Project Code: OTHER
Action EE Determined
Scale-Up Amt 10mg
Date Rec. 11/19/2012
Date Comp. 11/21/2012
DAG Contact Qi Yan

Method Information

Instrument aurora SFC
Column Chiralcel AS-H
Reference No. 112612-4
Dimensions 4.6mm x 25cm
Mobile Phase 5-60% CO2/Methanol
Flow 3.0ml/min
Modifier None

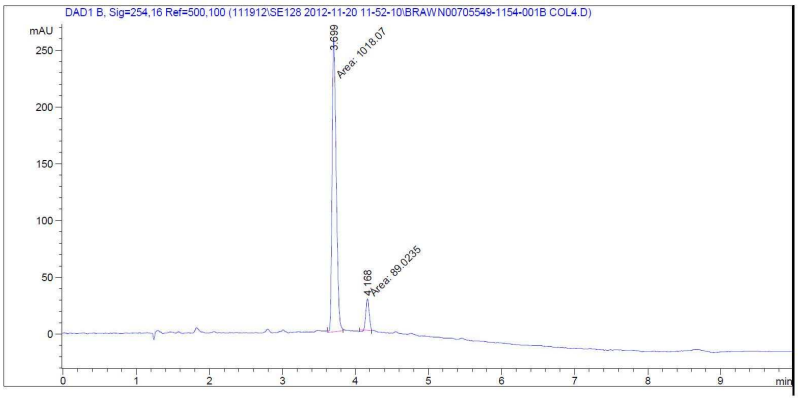
Results

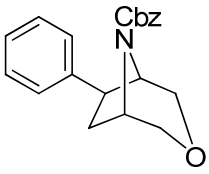
Alpha 1.13

			Area %
RT 1	3.699	**Area 1** 101.80	91.96
RT 2	4.168	**Area 2** 8.90	8.04
RT 3		**Area 3**	0.00
RT 4		**Area 4**	0.00

UV **UV Max.**

Notes





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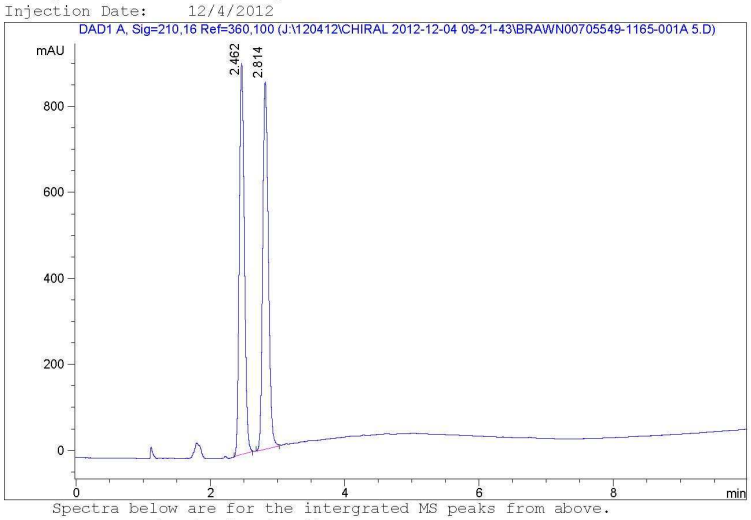
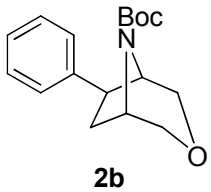
on: 12/4/2012
location: Vial 3
Injection Vol: Actual Injection Volume not ->
Injection Date: 12/4/2012



Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.462	4.762e3	48.965	DAD1 A, Sig=210
2	2.814	4.963e3	51.035	



2b

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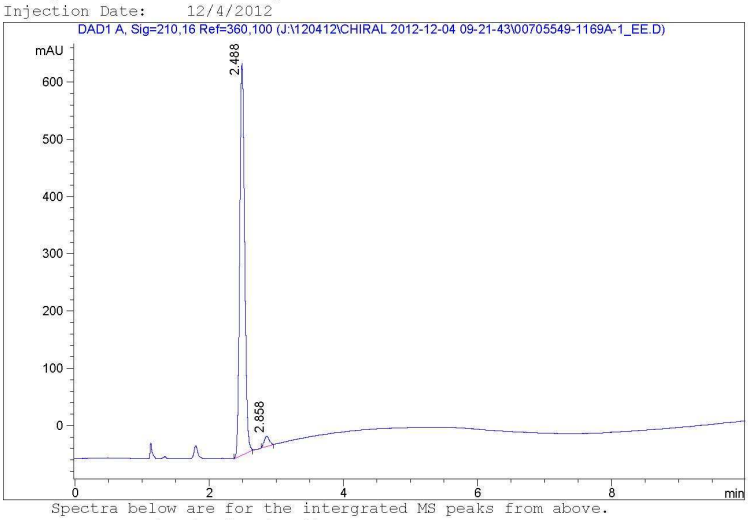
data acquired by:
on: 12/4/2012
location: Vial 22
Injection Vol: Actual Injection Volume not ->
Injection Date: 12/4/2012



Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.488	3.468e3	97.285	DAD1 A, Sig=210
2	2.858	96.803	2.715	

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data acquired by:
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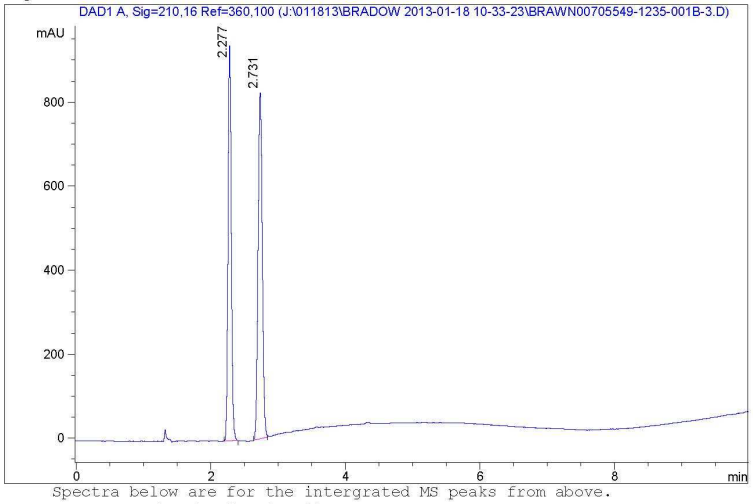

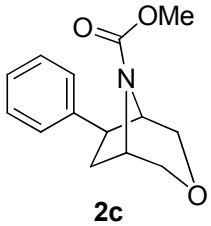

2c

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.277	3.181e3	47.044	DAD1 A, Sig=210
2	2.731	3.581e3	52.956	

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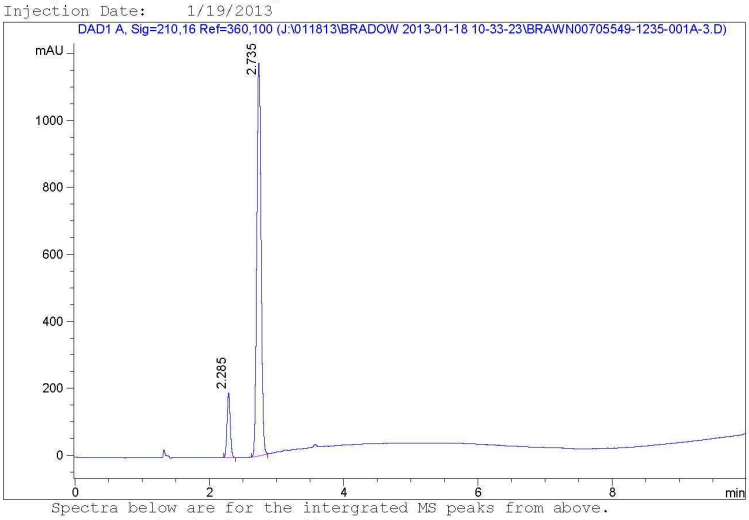

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.285	634.011	10.855	DAD1 A, Sig=210
2	2.735	5.207e3	89.145	

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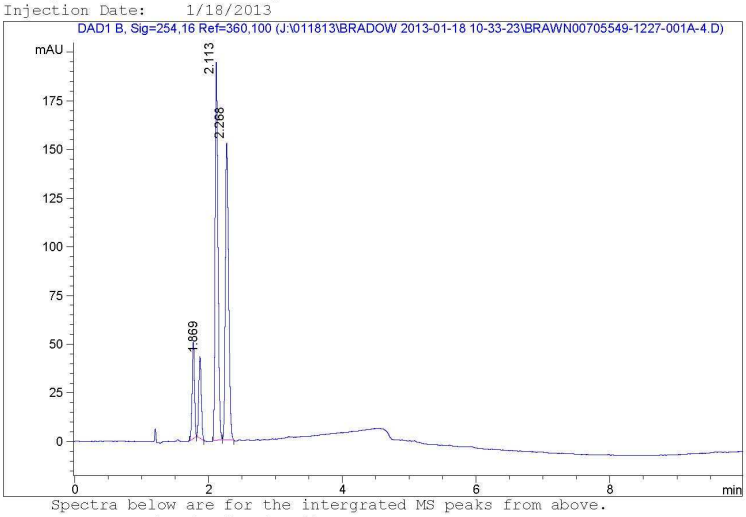
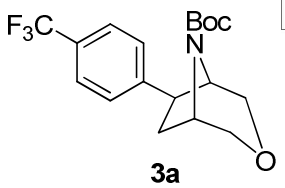


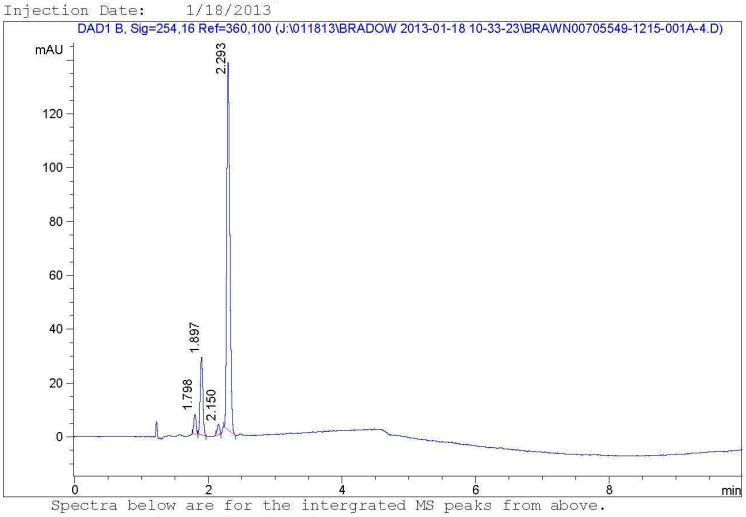


3a

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	1.769	121.593	9.194	DAD1 B, Sig=254
2	1.869	111.170	8.406	
3	2.113	569.943	43.097	
4	2.268	519.750	39.302	

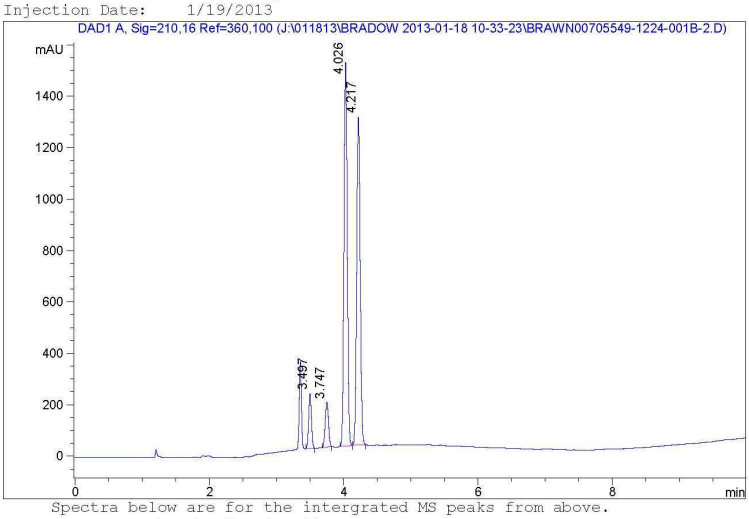
Sample:Brawn00705549-1215-001A
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1215-001A-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/18/2013
location: Vial 2
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/18/2013



Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

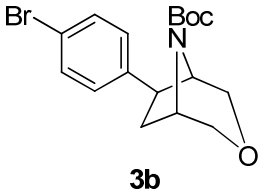
#	Meas. R	Area	Area %	Signal Desc.
1	1.798	17.132	3.150	DAD1 B, Sig=254
2	1.897	77.046	14.167	
3	2.150	9.486	1.744	
4	2.293	440.189	80.939	

Sample:Brawn00705549-1224-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1224-001B-2.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN2.M
data acquired by:
on: 1/19/2013
location: Vial 20
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



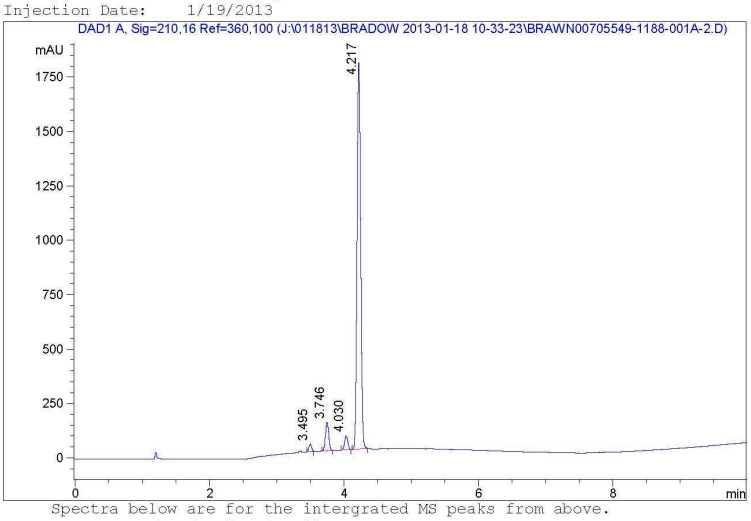
Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	3.497	614.946	5.647	DAD1 A, Sig=210
2	3.747	586.862	5.389	
3	4.026	5.050e3	46.372	
4	4.217	4.638e3	42.592	



3b

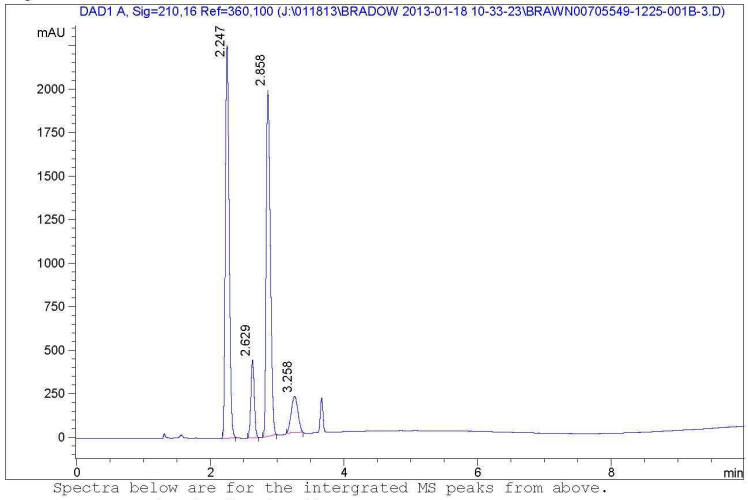
Sample:Brawn00705549-1188-001A-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1188-001A-2.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN2.M
data acquired by:
on: 1/19/2013
location: Vial 21
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

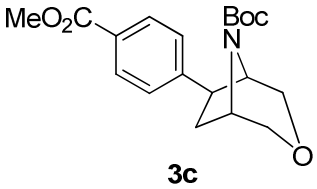
#	Meas. R	Area	Area %	Signal Desc.
1	3.495	98.354	1.329	DAD1 A, Sig=210
2	3.746	444.811	6.009	
3	4.030	214.166	2.893	
4	4.217	6.645e3	89.769	

Sample:Brawn00705549-1225-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1225-001B-3.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN3.M
data acquired by:
on: 1/19/2013
location: Vial 16
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



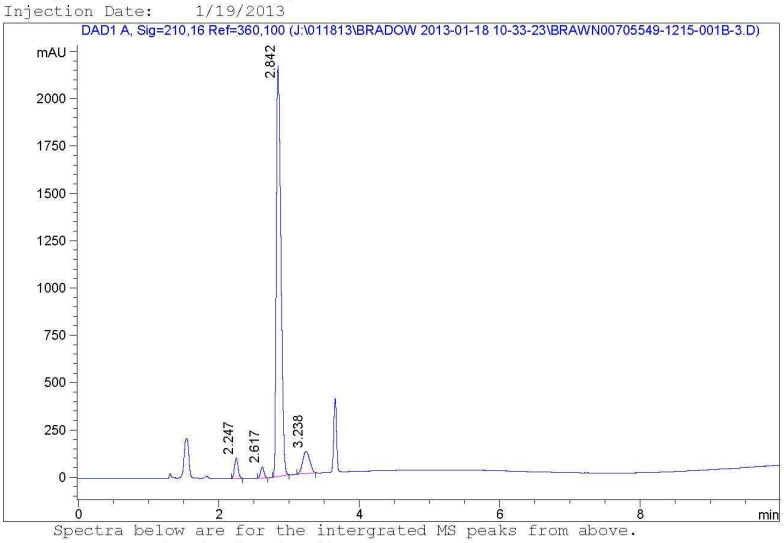
Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.247	8.941e3	43.632	DAD1 A, Sig=210
2	2.629	1.562e3	7.623	
3	2.858	8.546e3	41.707	
4	3.258	1.442e3	7.039	



3c

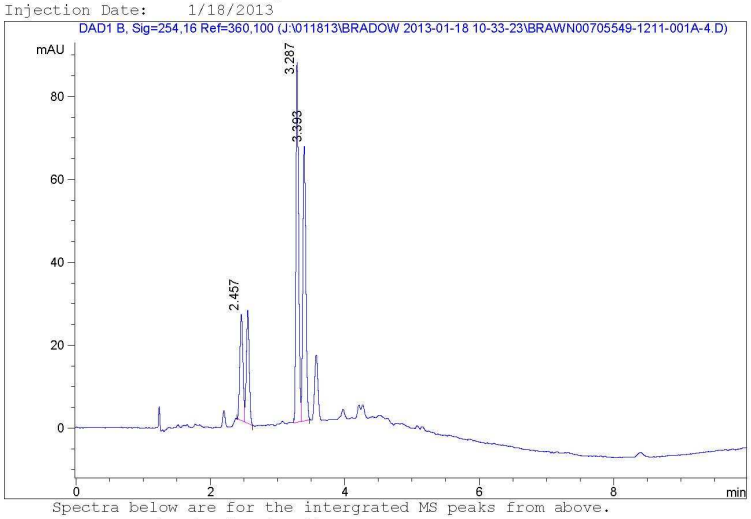
Sample:Brawn00705549-1215-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1215-001B-3.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN3.M
data acquired by:
on: 1/19/2013
location: Vial 17
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013

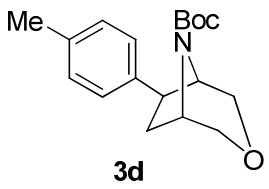


Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.247	376.795	3.370	DAD1 A, Sig=210
2	2.617	205.883	1.841	
3	2.842	9.773e3	87.416	
4	3.238	824.218	7.372	

Sample:Brawn00705549-1211-001A-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1211-001A-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/18/2013
location: Vial 3
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/18/2013



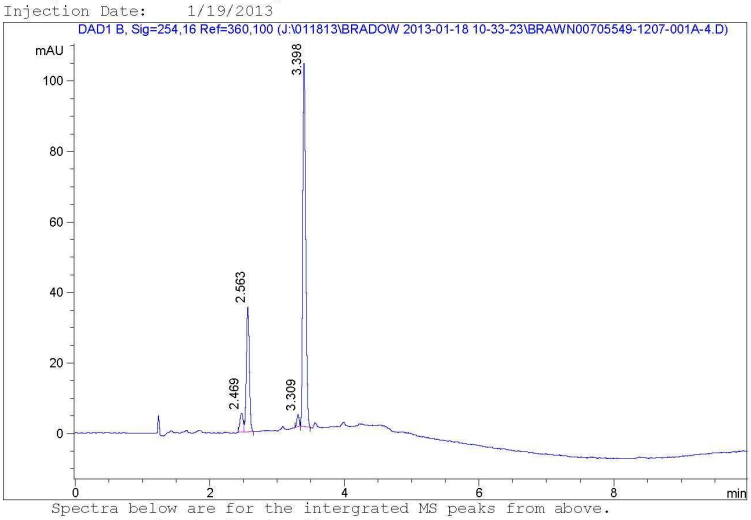


3d

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.457	83.344	13.747	DAD1 B, Sig=254
2	2.553	79.880	13.176	
3	3.287	236.450	39.002	
4	3.393	206.581	34.075	

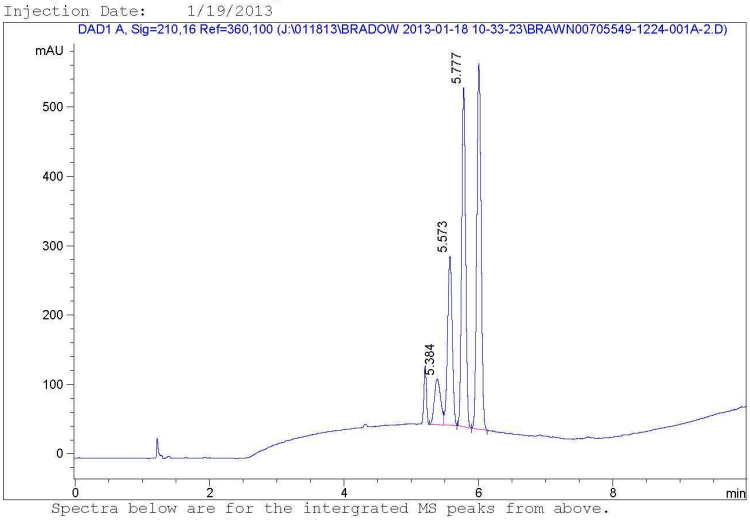
Sample:Brawn00705549-1207-001A-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1207-001A-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 4
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

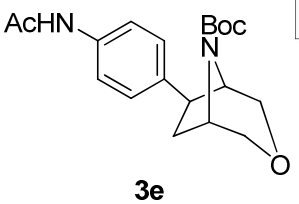
#	Meas. R	Area	Area %	Signal Desc.
1	2.469	17.902	3.990	DAD1 B, Sig=254
2	2.563	107.267	23.910	
3	3.309	7.818	1.743	
4	3.398	315.646	70.357	

Sample:Brawn00705549-1224-001A-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1224-001A-2.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN2.M
data acquired by:
on: 1/19/2013
location: Vial 7
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



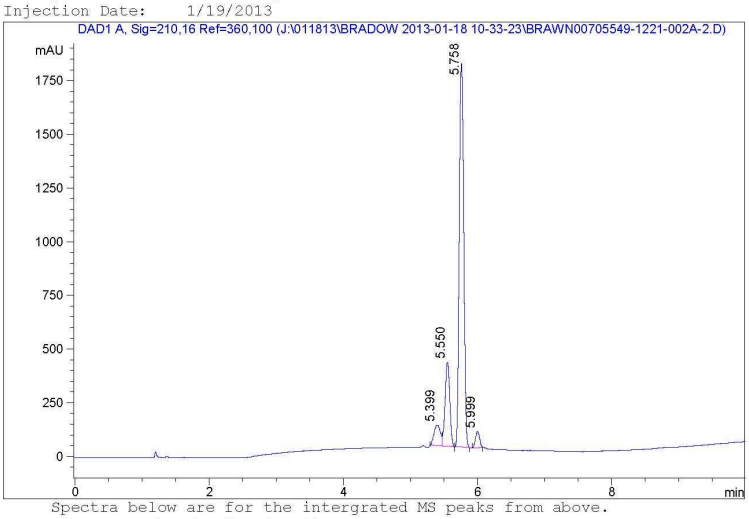
Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	5.384	427.304	7.201	DAD1 A, Sig=210
2	5.573	1.160e3	19.553	
3	5.777	1.989e3	33.514	
4	6.004	2.358e3	39.732	



3e

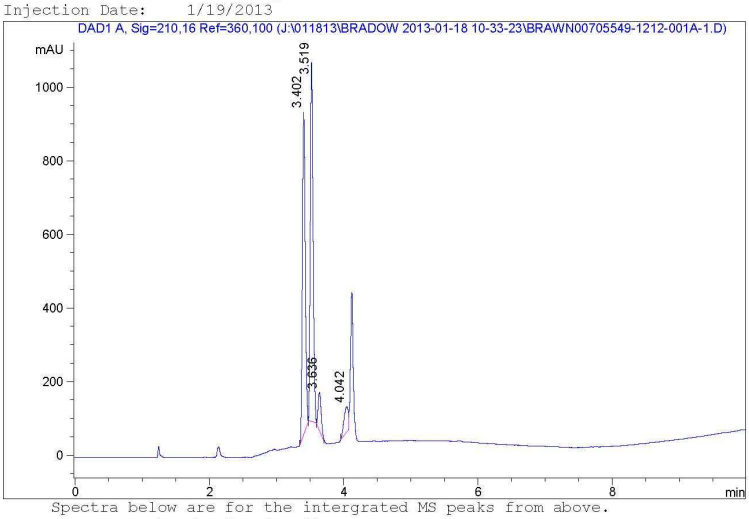
Sample:Brawn00705549-1221-002A-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1221-002A-2.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN2.M
data acquired by:
on: 1/19/2013
location: Vial 22
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013

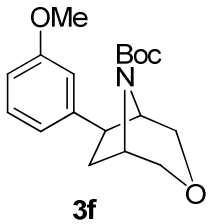


Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	5.399	626.259	5.616	DAD1 A, Sig=210
2	5.550	1.900e3	17.042	
3	5.758	8.303e3	74.464	
4	5.999	320.978	2.878	

Sample:Brawn00705549-1212-001A-
  Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1212-001A-1.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN1.M
data acquired by:
            on: 1/19/2013
      location: Vial 5
   Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



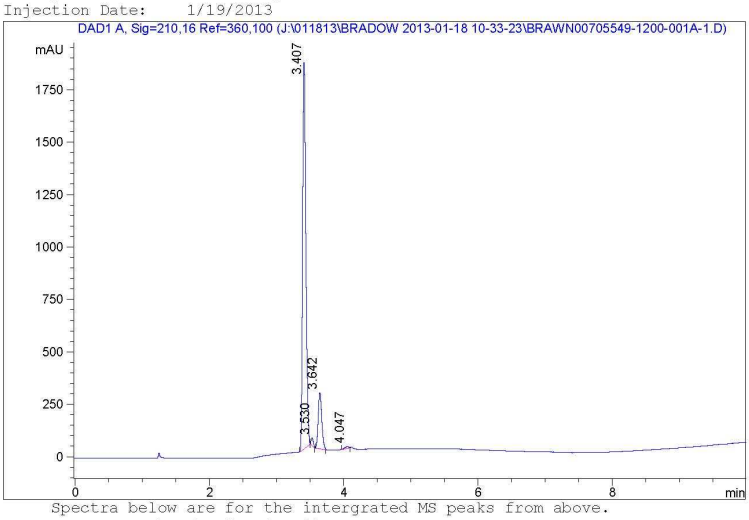


3f

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	3.402	2.560e3	42.622	DAD1 A, Sig=210
2	3.519	2.813e3	46.834	
3	3.636	323.123	5.379	
4	4.042	310.316	5.166	

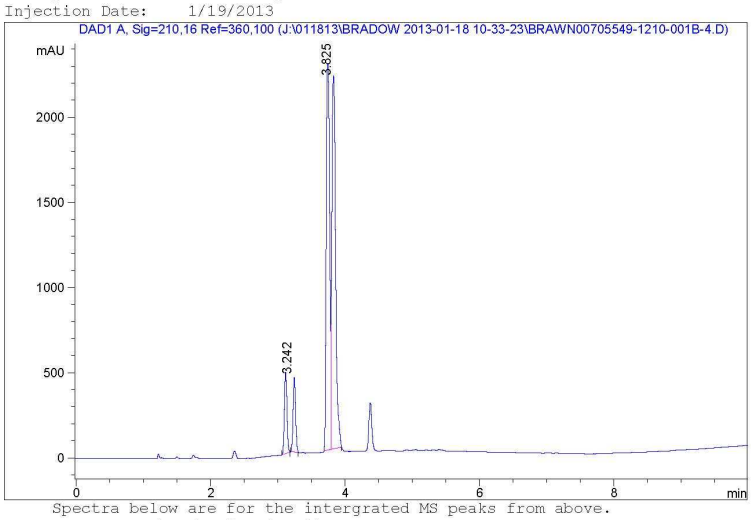
Sample:Brawn00705549-1200-001A
  Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1200-001A-1.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN1.M
data acquired by:
            on: 1/19/2013
      location: Vial 6
   Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013

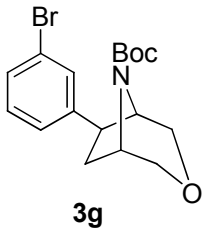


Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	3.407	6.099e3	84.716	DAD1 A, Sig=210
2	3.530	78.798	1.095	
3	3.642	982.854	13.652	
4	4.047	38.632	0.537	

Sample:Brawn00705549-1210-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1210-001B-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 18
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



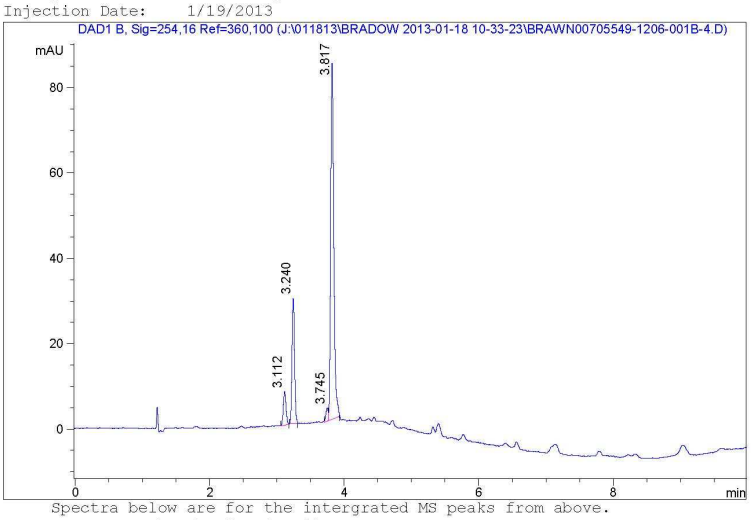


3g

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	3.113	1.247e3	6.590	DAD1 A, Sig=210
2	3.242	1.126e3	5.948	
3	3.740	8.111e3	42.861	
4	3.825	8.440e3	44.602	

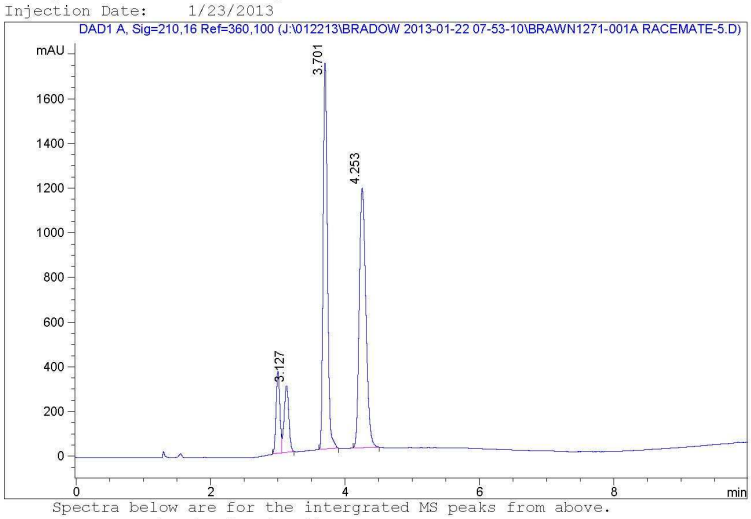
Sample:Brawn00705549-1206-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1206-001B-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 19
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

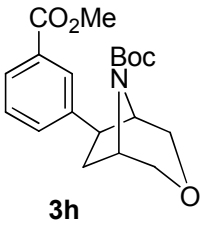
#	Meas. R	Area	Area %	Signal Desc.
1	3.112	22.122	5.911	DAD1 B, Sig=254
2	3.240	77.806	20.790	
3	3.745	7.510	2.007	
4	3.817	266.818	71.293	

Sample:Brawn1271-001A racemate-
  Data:J:\012213\BRADOW 2013-01-22 07-53-10\BRAWN1271-001A RACEMATE-5.D
Method:C:\Chem32\1\DATA\012213\BRADOW 2013-01-22 07-53-10\METHANOL_COLUMN5.M
data acquired by:
            on: 1/23/2013
      location: Vial 10
   Injection Vol: Actual Injection Volume not ->
Injection Date: 1/23/2013



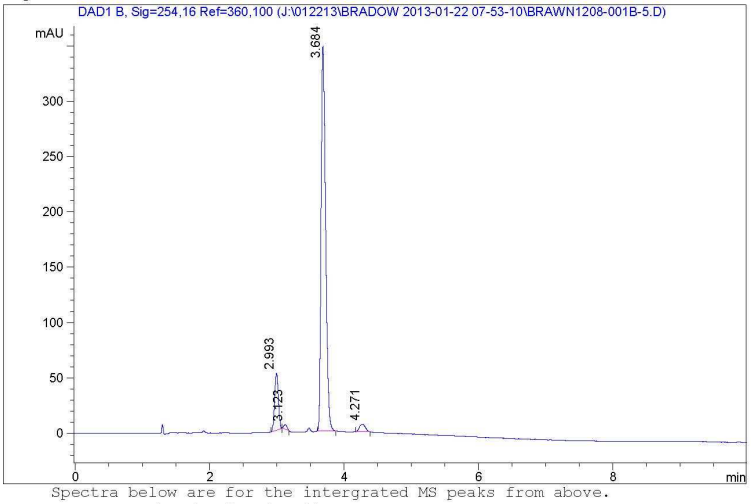
Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	3.000	1.441e3	7.785	DAD1 A, Sig=210
2	3.127	1.429e3	7.718	
3	3.701	7.716e3	41.674	
4	4.253	7.929e3	42.823	



3h

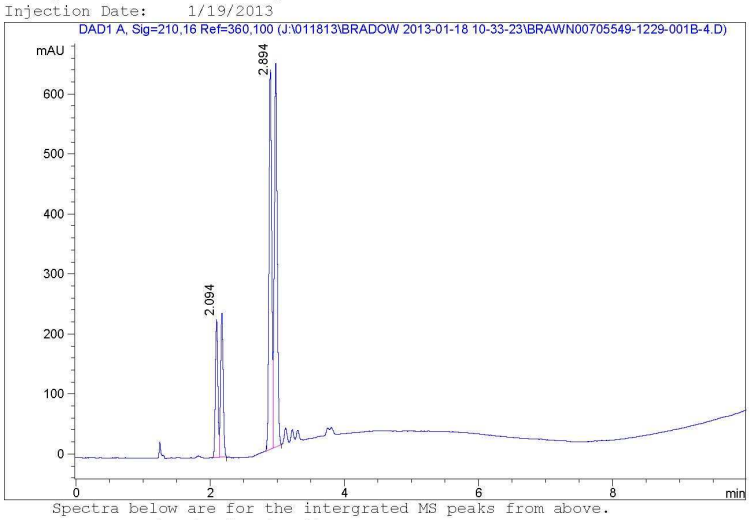
Sample:Brawn1208-001B-
  Data:J:\012213\BRADOW 2013-01-22 07-53-10\BRAWN1208-001B-5.D
Method:C:\Chem32\1\DATA\012213\BRADOW 2013-01-22 07-53-10\METHANOL_COLUMN5.M
data acquired by:
            on: 1/23/2013
      location: Vial 13
   Injection Vol: Actual Injection Volume not ->
Injection Date: 1/23/2013

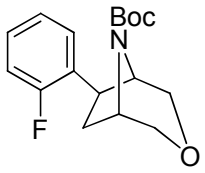


Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.993	198.087	10.563	DAD1 B, Sig=254
2	3.123	14.203	0.757	
3	3.684	1.622e3	86.512	
4	4.271	40.664	2.168	

Sample:Brawn00705549-1229-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1229-001B-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 8
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



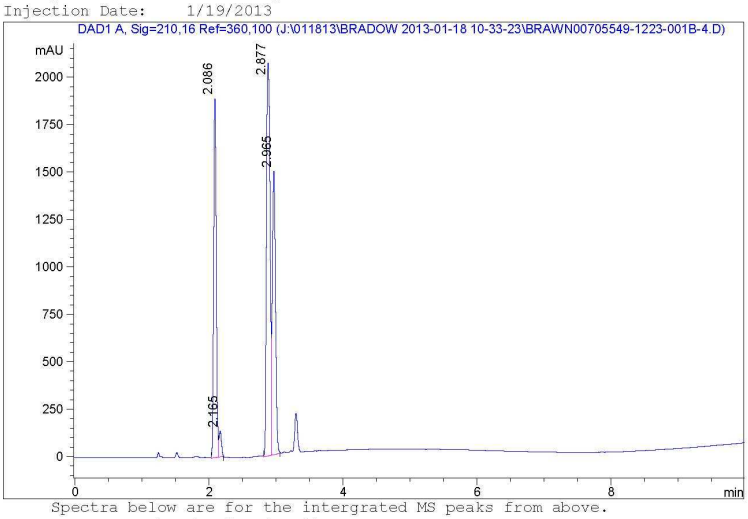


3i

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.094	580.935	11.780	DAD1 A, Sig=210
2	2.172	636.561	12.908	
3	2.894	1.811e3	36.714	
4	2.975	1.903e3	38.597	

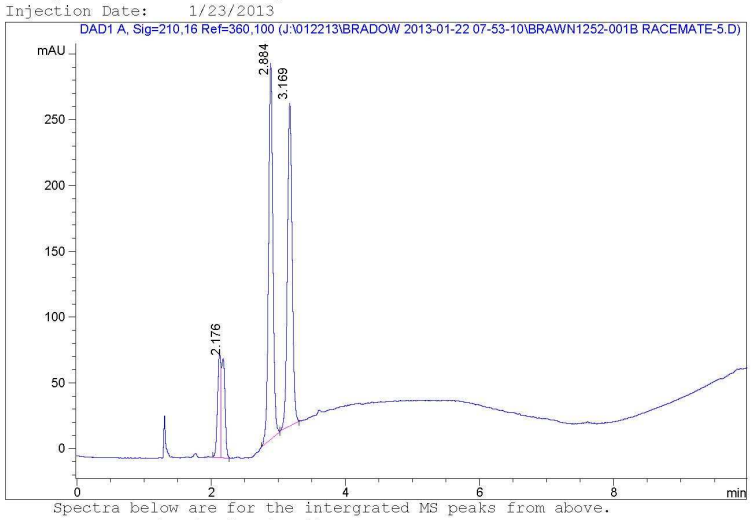
Sample:Brawn00705549-1223-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1223-001B-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 9
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013

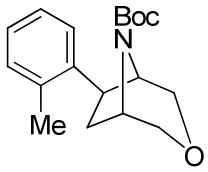


Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.086	5.135e3	28.240	DAD1 A, Sig=210
2	2.165	330.669	1.818	
3	2.877	7.803e3	42.914	
4	2.965	4.915e3	27.028	

Sample:Brawn1252-001B racemate-
Data:J:\012213\BRADOW 2013-01-22 07-53-10\BRAWN1252-001B RACEMATE-5.D
Method:C:\Chem32\1\DATA\012213\BRADOW 2013-01-22 07-53-10\METHANOL_COLUMN5.M
data acquired by:
on: 1/23/2013
location: Vial 11
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/23/2013



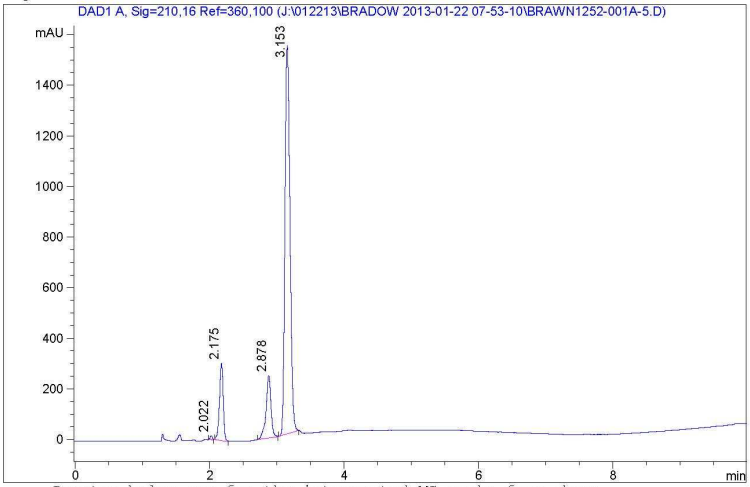


3j

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.123	283.210	9.345	DAD1 A, Sig=210
2	2.176	266.149	8.782	
3	2.884	1.280e3	42.242	
4	3.169	1.201e3	39.631	

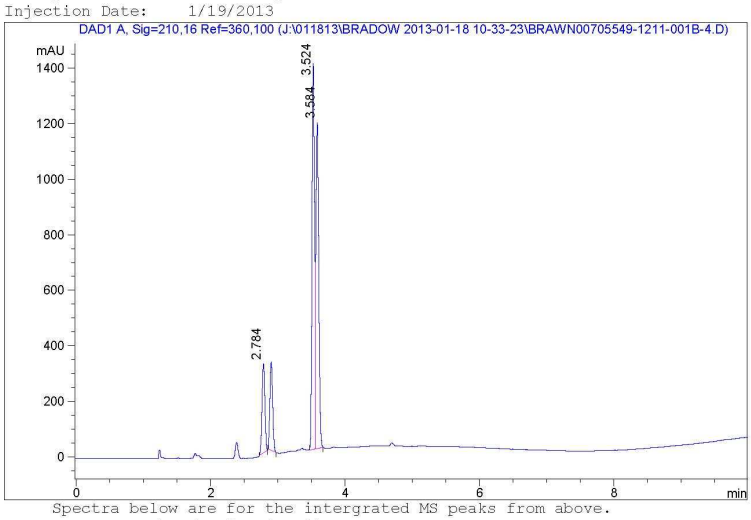
Sample:Brawn1252-001A-
Data:J:\012213\BRADOW 2013-01-22 07-53-10\BRAWN1252-001A-5.D
Method:C:\Chem32\1\DATA\012213\BRADOW 2013-01-22 07-53-10\METHANOL_COLUMN5.M
data acquired by:
on: 1/23/2013
location: Vial 12
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/23/2013

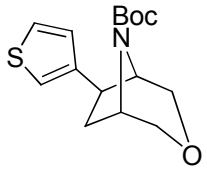


Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.022	38.126	0.364	DAD1 A, Sig=210
2	2.175	1.194e3	11.405	
3	2.878	1.248e3	11.920	
4	3.153	7.988e3	76.311	

Sample:Brawn00705549-1211-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1211-001B-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 12
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



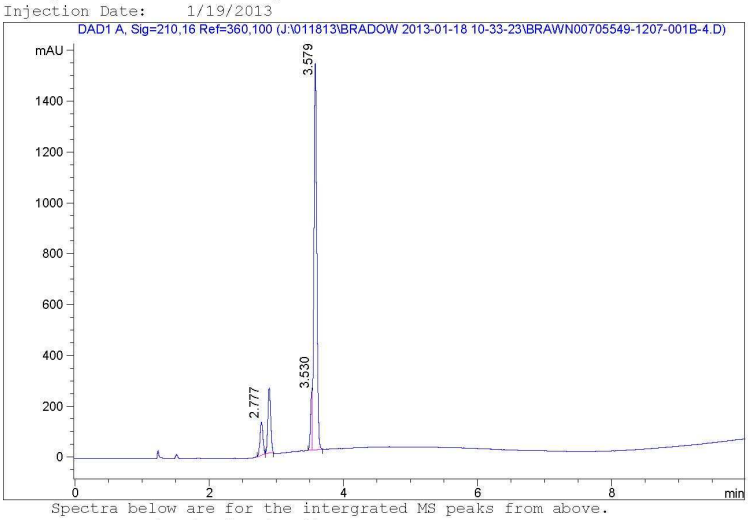


3k

Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.784	952.450	10.666	DAD1 A, Sig=210
2	2.899	914.562	10.241	
3	3.524	3.633e3	40.686	
4	3.584	3.430e3	38.407	

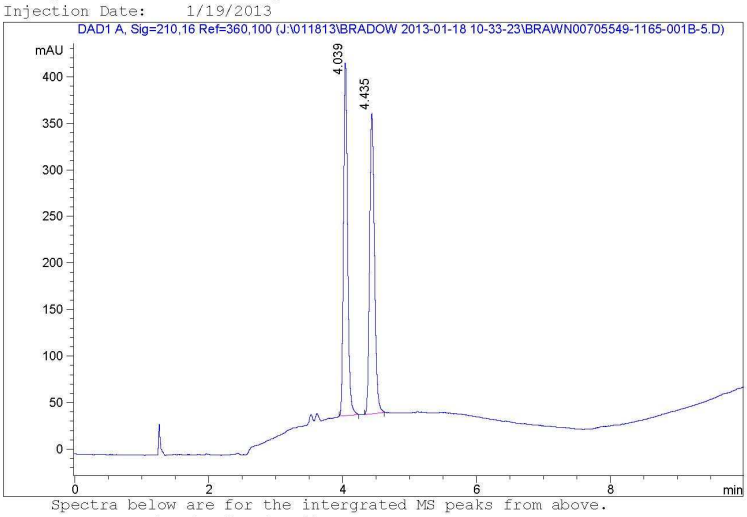
Sample:Brawn00705549-1207-001B-
Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1207-001B-4.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN4.M
data acquired by:
on: 1/19/2013
location: Vial 13
Injection Vol: Actual Injection Volume not ->
Injection Date: 1/19/2013



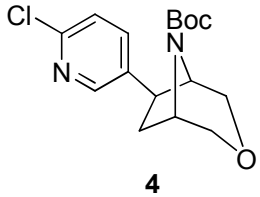
Spectra below are for the intergrated MS peaks from above.
See Spetra header for details.

#	Meas. R	Area	Area %	Signal Desc.
1	2.777	393.705	6.455	DAD1 A, Sig=210
2	2.893	752.182	12.332	
3	3.530	400.752	6.570	
4	3.579	4.553e3	74.643	

```
Sample:Brawn00705549-1165-001B-
  Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1165-001B-5.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN5.M
data acquired by:
              on:  1/19/2013
        location:  Vial 14
   Injection Vol:  Actual Injection Volume not  ->
Injection Date:    1/19/2013
```

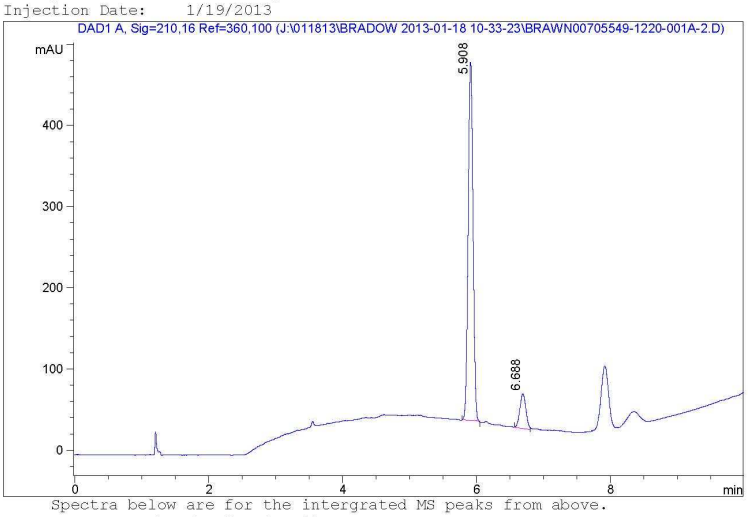



```
   Spectra below are for the intergrated MS peaks from above.
   See Spetra header for details.
  #  Meas. R  Area   Area %   Signal Desc.
 ------------------------------------------
   1   4.039 1.613e3  49.865 DAD1 A, Sig=210
   2   4.435 1.622e3  50.135
 ------------------------------------------
```



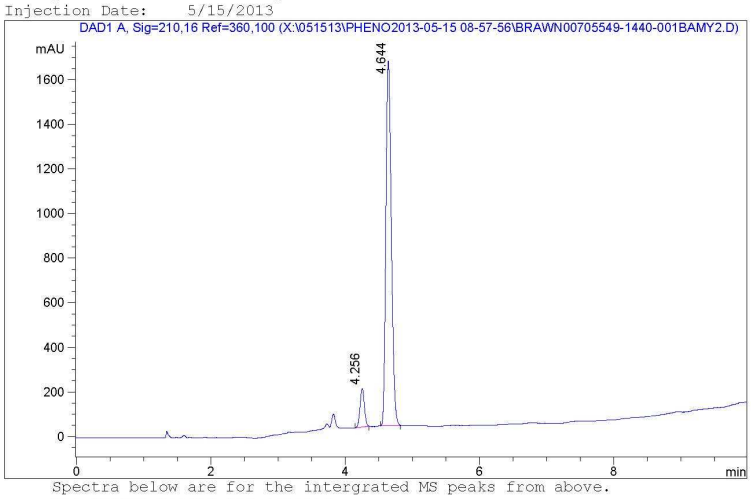
4

```
Sample:Brawn00705549-1220-001A-
  Data:J:\011813\BRADOW 2013-01-18 10-33-23\BRAWN00705549-1220-001A-2.D
Method:C:\Chem32\1\DATA\011813\BRADOW 2013-01-18 10-33-23\METHANOL_COLUMN2.M
data acquired by:
              on:  1/19/2013
        location:  Vial 15
   Injection Vol:  Actual Injection Volume not  ->
Injection Date:    1/19/2013
```

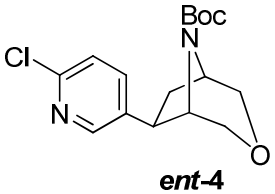



```
   Spectra below are for the intergrated MS peaks from above.
   See Spetra header for details.
  #  Meas. R  Area   Area %   Signal Desc.
 ------------------------------------------
   1   5.908 2.228e3  89.268 DAD1 A, Sig=210
   2   6.688 267.819  10.732
 ------------------------------------------
```

```
Sample:Brawn00705549-1440-001B
  Data:X:\051513\PHENO2013-05-15 08-57-56\BRAWN00705549-1440-001BAMY2.D
Method:C:\Chem32\1\DATA\051513\Pheno2013-05-15 08-57-56\METHANOL_COLUMN5.M
data acquired by:
             on:  5/15/2013
       location:  Vial 3
   Injection Vol:  Actual Injection Volume not  ->
Injection Date:    5/15/2013
```




```
  Spectra below are for the intergrated MS peaks from above.
  See Spetra header for details.
 #  Meas. R  Area    Area %   Signal Desc.
-------------------------------------------
  1   4.256 757.400   7.582 DAD1 A, Sig=210
  2   4.644 9.232e3  92.418
-------------------------------------------
```



***ent*-4**