Supporting Information

Templated Assembly of Medium Cyclic Ethers via *exo-trig* Nucleophilic Cyclization to Cyclopropenes

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General Information

NMR spectra were recorded on a Bruker Avance DPX-400 instrument, equipped with a quadruple-band gradient probe (H/C/P/F QNP) or a Bruker Avance DRX-500 with a dual carbon/proton cryoprobe (CPDUL). ^{13}C NMR spectra were registered with broad-band decoupling. The (+) and (-) designations represent positive and negative intensities of signals in ^{13}C DEPT-135 experiments. The following notation are used to discribe multiplets: (s) – singlet, (br. s) – broad singlet, (d) – doublet, (t) – triplet, (app. t) – apparent triplet, i.e. doublet of doublets with nearly identical values of two coupling constants, (q) – quartet, (quin) – quintet, (m) – multiplet or massive of overlapping multiplets. ^{1}H NMR spectra for diastereomeric bromocyclopropanes recorded for mixtures are not listed separately, in all cases combined integrations of the related signals are provided after summation signs (Σ).

GC/MS analyses were performed on a Shimadzu GC-2010 gas chromatograph interfaced to a Shimadzu GCMS 2010S mass selective detector, and equipped with an AOC-20i auto-injector and an AOC-20S auto-sampler tray (150 vials). 30 m x 0.25 mm x 0.25 μm capillary column, SHR5XLB, polydimethylsiloxane, 5% Ph was employed. Helium (99.96%), additionally purified by passing consecutively through a CRS oxygen/ moisture/hydrocarbon trap (#202839) and VICI oxygen/moisture trap (P100-1), was used as a carrier gas. High resolution mass-spectra were obtained using a LCT Premier (Micromass Technologies) instrument using electrospray ionization and time of flight detection techniques. IR spectra were recorded on a Shimadzu FT-IR 8400S instrument.

Glassware employed in moisture-free syntheses was flame-dried in vacuum prior to use. Water was purified by dual stage deionization, followed by dual stage reverse osmosis. Anhydrous tetrahydrofuran was obtained by passing degassed commercially available HPLC-grade inhibitor-free solvent consecutively through two columns filled with activated alumina (Innovative Technology). Anhydrous triethylamine was obtained by distillation of ACS-grade commercially available materials over calcium hydride in a nitrogen atmosphere. 3-Benzylamino-1-propanol, 4-benzylamino-1-butanol, 5-benzyl-amino-1-pentanol, and 2-cyclohexylamino-1-ethanol were purchased from TCI America and used as received. All other commercially available reagents were purchased from Sigma-Aldrich or Acros Organics. 2-Bromo-1-methylcyclopropanecarbonyl chloride was prepared according to the procedure published in our previous report.[1] Preparation of other non-commercially available starting materials is described below.

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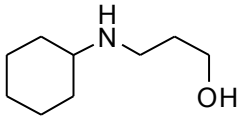
(1) (a) Banning, J. E.; Prosser, A. R.; Rubin, M. *Org. Lett.* **2010**, *12*, 1488. (b) Sherrill, W. M.; Kim, R.; Rubin, M. *Synthesis* **2009**, 1477.
(2) Wagner, B. J.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1990**, *55*, 4156.

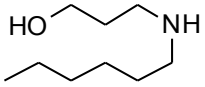
Preparation of Starting Materials

Syntheses of Amino Alcohols



3-Cyclohexylamino-1-propanol[2]: Three neck round bottom flask (250 mL) equipped with a reflux condenser, a thermometer, and addition funnel (100 mL) was charged with $LiAlH_4$ (1.30 g, 38.4 mmol, 1.50 eq) and anhydrous THF (30 mL). The resulting suspension was stirred at 0 ^oC and a solution of methyl 3-(cyclohexylamino)propanoate[3] (4.40 g, 23.2 mmol, 1.00 equiv) in dry THF (50 mL) was added drop wise over 30 min. Once addition was complete the mixture was stirred at reflux overnight, then quenched at 0 ^oC consecutively with water (20 mL) and a concentrated aqueous solution of NaOH (5.0 g in 5 mL of water). The resulting suspension was diluted with water (30 mL) and THF (50 mL) and filtered through a fritted funnel. The filter cake was washed with THF (3 x 20 ml), and the washing liquids were combined with the filtrate. The resulting solution was saturated with NaCl and extracted with THF (3 x 20 ml). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The crude product was purified by vacuum distillation (bp 60 ^oC at 15 torr) to afford the titled compound as colorless oil, solidifying upon standing. Yield 2.4 g (15.1 mmol, 65%).

^1H NMR (400.13 MHz, $CDCl_3$) δ 3.80 (t, J = 5.2 Hz, 2H), 2.89 (t, J = 5.7 Hz, 2H), 2.41 (tt, J = 10.3 Hz, 3.6 Hz, 1H), 2.05 (br. s, 2H), 1.97-1.79 (m, 2 H), 1.77-1.52 (m, 5H), 1.31-1.13 (m, 3H), 1.11-0.99 (m, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 64.5 (-), 56.6 (+), 46.9 (-), 33.4 (-, 2C), 31.2 (-), 26.0 (-), 24.9 (-, 2C);



3-(Hexylamino)propan-1-ol[4]: Three neck round bottom flask (250 mL) equipped with a reflux condenser, a thermometer, and addition funnel (100 ml) was charged with $LiAlH_4$ (1.50 g, 38.4 mmol, 1.5 equiv) and anhydrous THF (30 mL). The resulting suspension was stirred at 0 ^oC, a solution of methyl 3-(hexylamino)propanoate[5] (4.80 g, 25.6 mmol, 1.00 equiv) in dry THF (50 mL) and was added dropwise over 30 min. Once addition was complete the mixture was stirred at reflux overnight, and then quenched consecutively with water (20 mL) and a concentrated solution of NaOH (5.00 g in 5 ml of water) at 0 ^oC. The mixture was diluted with THF (50 mL) and of water (30 mL) and the resulting suspension was filtered through a fritted funnel. The filter cake was washed with THF (3 x 20 mL), and the washing liquid was combined with the filtrate. The resulting filtrate was saturated with NaCl and extracted with THF (3 x 20 mL). The combined organic phases were dried with Na_2SO_4, filtered and concentrated. The resulting yellowish oil was purified by

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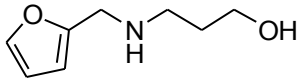
(2) Wagner, B. J.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1990**, *55*, 4156.
(3) Polshettiwar, V.; Varma, R. S. *Tetrahedron* **2010**, *66*, 1091.
(4) Schade, W.; Beger, J.; Jacobi, R.; Neumann, R. *J. Prakt. Chem.* **1983**, *325*, 364.
(5) Yadav, J. S.; Reddy, B. V. S.; Basak, A. K.; Narsaiah, A. V. *Chem. Lett.* **2003**, *32*, 988.

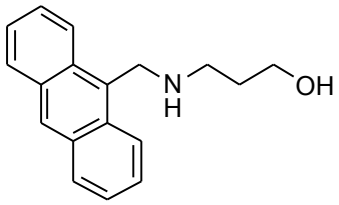
vacuum distillation to afford the titled compound as colorless oil. Yield 2.80 g (15.9 mmol, 62%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.77 (t, *J* = 5.6 Hz, 2H), 2.84 (t, *J* = 5.8 Hz, 2H), 2.57 (t, *J* = 7.1 Hz, 2H), 1.67 (quin, *J* = 5.6 Hz, 2H), 1.44 (quin, *J* = 7.1 Hz, 2H), 1.35-1.19 (m, 6H), 0.86 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 64.1 (-), 49.9 (-), 49.8 (-), 31.6 (-), 30.7 (-), 29.8 (-), 26.9 (-), 22.5 (-), 13.9 (+);



3-((Furan-2-ylmethyl)amino)propan-1-ol[6]: To a stirred solution of furfural (5.00 g, 52.0 mmol, 1.00 equiv) in MeOH (30 mL) was added 3-aminopropan-1-ol (4.00 g, 53.3 mmol, 1.00 equiv), and the mixture was stirred for 30 min at room temperature, then cooled to 0 ^{o}C and $NaBH_4$ (2.90 g, 76.6 mmol, 1.50 equiv) was added by small portions over 10 min. The suspension was stirred for 4 hrs at room temperature and the solvent was removed in vacuum. An aqueous solution of KOH (5.00 g, 47.8 mmol, 1.7 equiv in 20 mL of water) was added and the solution was partitioned between EtOAC and brine. The aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The resulting crude oil was distilled (130 ^{o}C) to afford the title compound as a colorless viscous oil. Yield 7.50 g (48.4 mmol, 93%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 1.8 Hz, 0.8 Hz, 1H), 6.27 (dd, *J* = 3.2 Hz, 1.9 Hz, 1H), 6.14 (d, *J* = 3.0 Hz, 1H), 3.74 (s, 2H), 3.71 (t, *J* = 5.6 Hz, 2H), 2.78 (t, *J* = 6.1 Hz, 2H), 1.66 (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 153.2, 141.7 (+), 110.0 (+), 106.9 (+), 63.0 (-), 48.0 (-), 45.7 (-), 30.9 (-);



3-((Anthracen-9-ylmethyl)amino)propan-1-ol[7]: To a stirred solution of anthracene-9-carbaldehyde (2.0 g, 9.6 mmol) in methanol (200 mL) was added 3-aminopropanol (800 mg, 10.7 mmol, 1.1 equiv.). The mixture was stirred for 30 min at room temperature, then cooled to 0 ^{o}C, and $NaBH_4$ (547 mg, 14.4 mmol, 1.50 equiv) was added by small portions over 5 min. The formed suspension was stirred for 3 hrs, then most of the solvent was removed in vacuum, and the residue was quenched with 2% aqueous KOH and extracted with dichloromethane (4 x 20 mL). Combined organic phases were dried with MgSO4, filtered and concentrated. The obtained yellow solid was recrystallized from hexane-EtOAc 10:1 mixture to afford the title compound as yellow needles, mp 82-83 ^{o}C, yield 1.8 g (6.78 mmol, 71%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.31 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.3 Hz, 2H), 7.59-7.54 (m, 2H), 7.50-7.47 (m, 2H), 4.76 (s, 2H), 3.84 (app. t, *J* = 5.2 Hz, 2H), 3.15 (app. t, *J* = 5.7 Hz, 2H), 2.05 (br. s, 2H), 1.79 (quin, *J* = 5.6 Hz, 2H); ^{13}C NMR

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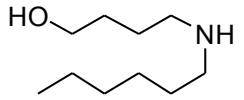
(6) (a) Artyushin, O. I.; Petrovskii, P. V.; Mastryukova, T. A.; Kabachnik, M. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1991**, 2154. (b) Yur'ev, Yu. K.; Novitskii, K. Yu.; Bolesov, I. G. *Zh. Obshch. Khim.* **1959**, *29*, 2951.

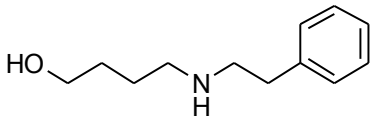
(7) Tachibana, Y.; Kawasaki, H.; Kihara, N.; Takata, T. *J. Org. Chem.* **2006**, *71*, 5093.

(100.67 MHz, $CDCl_3$) δ 131.4 (2C), 130.7, 130.2 (2C), 129.2 (+, 2C), 127.4 (+), 126.2 (+, 2C), 124.9 (+, 2C), 123.8 (+, 2C), 64.2 (-), 50.4 (-), 45.7 (-), 30.8 (-); Chemical Formula: C18H19NO Molecular Weight: 265.350



4-Hexylamino-1-butanol[8]: Two neck round bottom flask equipped with a reflux condenser was charged with neat *n*-hexylamine (5.60 g, 55.2 mmol, 3.00 equiv), and a solution of 4-chlorobutan-1-ol (2.00 g, 18.4 mmol 1.00 equiv) and MeOH (20 mL) was added dropwise over 30 min. Once addition was complete the mixture was heated at reflux for 12 hr. The solvent was removed in vacuum and the resulting salt was washed with hexane (3 x 10 ml) and dissolved in a solution of KOH (3.10 g, 55.2 mmol, 3.00 equiv) in water (20 mL). Then the mixture was partitioned between THF (20 ml) and brine (20 ml) and the aqueous phase was extracted with THF (3 x 20 ml). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The resulting crude material was purified by vacuum distillation (100 ^oC at 1 torr) to afford the titled compound as colorless oil. Yield 1.6 g (9.2 mmol, 50 %).

^1H NMR (400.13 MHz, $CDCl_3$) δ 3.75 (br.s, 2H), 3.55 (t, J = 6.0 Hz, 2H), 2.64 (t, J = 5.8 Hz, 2H), 2.59 (t, J = 7.3 Hz, 2H), 1.88-1.80 (m, 2H), 1.67-1.59 (m, 4H), 1.48 (quin, J = 7.3 Hz, 2H), 1.31-1.24 (m, 4H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 62.5 (-), 49.6 (-), 49.5 (-), 32.6 (-), 31.7 (-), 29.6 (-), 28.8 (-), 26.9 (-), 22.5 (-), 14.0 (+);



4-(Phenethylamino)butan-1-ol[9]: Two neck round bottom flask equipped with a reflux condenser was charged with neat 2-phenylethanamine (13.4 g, 110 mmol, 3.00 equiv), and a solution of 4-chlorobutan-1-ol (4.00 g, 36.8 mmol, 1.00 equiv) in MeOH (30 mL) was added dropwise over 30 min. Once addition was complete the mixture was heated at reflux for 12 hr. The solvent was removed in vacuum, the resulting salt was washed with hexane (3 x 10 mL) and dissolved in a solution of KOH (6.2 g, 110.4 mmol, 3 equiv) in water (30 mL). The resulting mixture was partitioned between THF (20 ml) and brine (20 ml) and extracted with THF (3 x 20 ml). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The resulting greenish oil was purified by vacuum distillation (110 ^oC at 1 torr) to afford the titled compound as colorless oil. Yield 6.00 g (31.1 mmol, 85 %).

^1H NMR (400.13 MHz, $CDCl_3$) δ 7.33-7.25 (m, 2H), 7.24-7.07 (m, 3H), 3.57 (t, J = 5.3 Hz, 2H), 2.90-2.84 (m, 2H), 2.84-2.77 (m, 2H), 2.64 (t, J = 5.8 Hz, 2H), 1.72-1.52 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 139.4, 128.5 (+, 2C), 128.3 (+, 2C), 126.1 (+), 62.2 (-), 50.3 (-), 49.3 (-), 35.7 (-), 32.1 (-), 28.2 (-);

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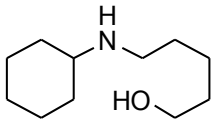
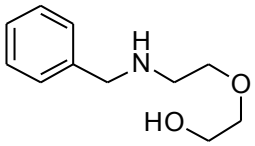
(8) Suzuki, K.; Tobe, A.; Adachi, S.; Daikoku, S.; Hasegawa, Y.; Shioiri, Y.; Kobayashi, M.; Kanie, O. *Org. Biomol. Chem.* **2009**, *7*, 4726.

(9) Paden, J. H.; Adkins, H. *J. Am. Chem. Soc.* **1936**, *58*, 2487.



5-(Cyclohexylamino)pentan-1-ol[10]: A two neck round bottom flak equipped with a reflux condenser was charged with neat cyclohexylamine (3.00 g, 33.7 mmol, 3.00 equiv), and a solution 5-chloropentan-1-ol (1.53 g, 12.5 mmol, 1.00 equiv) in MeOH (10 ml) was added dropwise over 10 min. Once addition was complete the mixture was heated at reflux for 18 hrs. The solvent was removed in vacuum; the resulting salt was washed with hexane (3 x 10 ml) and dissolved in a solution of KOH (1.89 g, 33.7 mmol) in water 10 (mL). The resulting mixture was partitioned between THF (10 mL) and brine (10 mL) and extracted with THF (3 x 20 mL). The combined organic phases were dried with Na_2SO_4, filtered, and concentrated. The resulting oil was distilled (bp 115 ^oC at 1 torr) to afford the title compound as colorless oil. Yield 1.39 g (20.2 mmol, 60%).

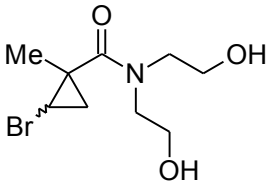
^1H NMR (400.13 MHz, $CDCl_3$) δ 3.64 (t, J = 6.4 Hz, 2H), 2.65 (t, J = 7.1 Hz, 2H), 2.42 (tt, J = 10.6 Hz, 3.7 Hz, 1H), 2.05 (br. s., 2H), 1.97-1.83 (m, 2H), 1.80-1.68 (m, 2H), 1.68-1.48 (m, 4H), 1.48-1.38 (m, 4H), 1.32-1.02 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 62.4 (-), 56.9 (+), 46.6 (-), 33.4 (-, 2C), 32.4 (-), 29.7 (-), 26.1 (-), 25.1 (-, 2C), 23.5 (-);



2-(2-(Benzylamino)ethoxy)ethanol[11]: A solution of 2-(2-chloroethoxy)ethanol (5.0 g, 40.1 mmol) in methanol (30 mL) was added to stirred neat benzylamine (12.9 g, 120.4 mmol, 3.0 equiv). The mixture was heated at reflux (bath temperature 100 ^oC) for 24 hr, then solvent was removed in vacuum. The obtained crystalline residue was washed with hexane (3 x 50 mL) and dissolved in water (50 mL), basified with solid KOH (6.5 g), and extracted with EtOAc (3 x 80 mL). Combined organic phases were dried with Na_2SO_4, filtered, and concentrated in vacuum. The residue was distilled in vacuum, bp 110 oC (0.5 torr). Yield 4.23 g (21.7 mmol, 54%).

^1H NMR (400.13 MHz, $CDCl_3$) δ 7.37-7.21 (m, 5H), 3.79 (s, 2H), 3.68 (app. t, J = 4.6 Hz, 2H), 3.59 (app. t, J = 5.2 Hz, 2H), 3.54 (app. t, J = 4.6 Hz, 2H), 2.80 (app. t, J = 5.2 Hz, 2H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 139.6, 128.3 (+, 2C), 128.1 (+, 2C), 126.9 (+), 72.4 (-), 70.0 (-), 61.3 (-), 53.6 (-), 48.4 (-).

Syntheses of Bromocyclopropanes

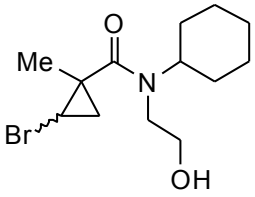


2-Bromo-N,N-bis(2-hydroxyethyl)-1-methylcyclopropanecarboxamide (**4a**): To a stirred solution of 2,2-diethanolamine (1.17 g, 11.2 mmol, 2.2 equiv) in dry THF (4 mL) was added dropwise a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (1.00 g, 5.1 mmol, 1.0 equiv) in dry THF (4 mL). The mixture was stirred for 1 hr, then quenched with brine and extracted with EtOAc (3 x 25 mL).

(10) Sassaman, M. B. *Tetrahedron* **1996**, *52*, 10835.
(11) Vinter, A.; Avdagic, A.; Stimac, V.; Palej, I.; Cikos, A.; Sunjic, V.; Alihodzic, S. *Synthesis* **2010**, 255.

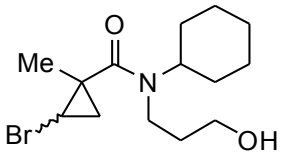
Combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuum. Crude residue was purified by preparative column chromatography on silica gel (eluting with EtOAc) to afford the title compound. Yield 1.09 g (4.08 mmol, 80%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 4.32 (br.s, 2H), 4.06-3.28 (m, 8H), [3.37 (dd, *J* = 8.2 Hz, 5.1 Hz) & 2.99 (dd, *J* = 6.9 HZ, 4.7 Hz), Σ1H], [1.66 (ps.-t, *J* = 8.2 Hz, 6.9 Hz) & 1.54 (dd, *J* = 6.0 Hz, 4.7 Hz), Σ1H], [1.47 (s) & 1.43 (s), Σ3H], [1.19 (ps.-t, *J* = 6.9 Hz, 6.0 Hz) & 0.89 (app. t, *J* = 6.9 Hz, 5.1 Hz), Σ1H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ major: 174.0, 60.0 (-), 59.2 (-), 51.1 (-), 48.6 (-), 27.9, 25.9 (+), 21.5 (-), 19.6 (+); minor: 172.5, 60.1 (-), 59.7 (-), 51.5 (-), 48.9 (-), 27.9 (+), 25.7, 22.2 (-), 21.8 (+); FT IR (cm^{-1}, film): 3421, 2988, 2941, 2908, 2876, 2837, 2658, 2621, 2442, 2363, 2332, 2230, 1757, 1610, 1290, 1232, 1213, 1132, 1088, 1020, 928, 862, 831, 712, 685, 650, 604, 523, 473; HRMS (TOF ES): found 266.0388, calculated for $C_9H_{17}NO_3Br$ (M+H) 266.0392 (1.5 ppm).



2-Bromo-N-cyclohexyl-N-(2-hydroxyethyl)-1-methylcyclopropanecarboxamide (**4b**): To a stirred solution of 2-(cyclohexylamino)ethanol (158 mg, 1.10 mmol, 1.10 equiv) and triethylamine (422 μL, 308 mg, 3.00 mmol, 3.00 equiv) in dry THF (10 mL) was added (dropwise over 10 min) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (200 mg, 1.01 mmol, 1.0 equiv) in dry THF (10 mL). The resulting suspension was stirred for 30 min at room temperature and then filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 mL). The combined organic solution was concentrated in vacuum. Preparative column chromatography of a crude residual oil on silica gel afforded the title compound as a clear oil, R_f 0.30 (hexane-EtOAc, 1:2). Yield 196 mg (0.65 mmol, 65 %).

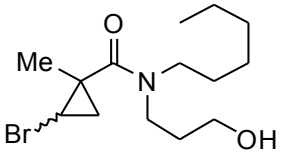
^{1}H NMR (400.13 MHz, $CDCl_3$) δ [3.99 (br. s.) & 3.83-3.68 (m) & 3.67-3.43 (m) & 3.39-3.25 (m), Σ5H], [3.11 (dd, *J* = 8.2 Hz, 4.9 Hz) & 2.99 (dd, *J* = 7.5 Hz, 4.7 Hz), Σ1H], [2.05 (d, *J* = 11.4 Hz) & 1.81 (br. s.) & 1.73-1.58 (m) & 1.58-1.50 (m) & 1.49-1.27 (m), Σ11H], [1.38 (s) & 1.31 (s), Σ3H], [1.22-1.00 (m) & 0.86 (dd, *J* = 6.8 Hz, 5.1 Hz, 1H), Σ2H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 173.4, 171.6, 62.6 (-), 62.5 (-), 57.4 (+), 57.2 (+), 45.5 (-), 44.8 (-), 32.6 (-), 31.9 (-), 31.6 (-), 31.4 (-), 28.1, 27.0 (+), 25.8, 25.7 (-), 25.6 (-), 25.52 (-), 25.47 (-), 25.3 (+), 25.04 (-), 25.02 (-), 23.0 (-), 21.6 (+), 21.2 (-), 19.5 (+); FT IR (cm^{-1}, film): 3402, 2932, 2856, 1618, 1470, 1454, 1423, 1375, 1319, 1298, 1197, 1163, 1144, 1074, 1053, 894, 731, 623, 509; HRMS (TOF ES): found 304.0913, calculated for $C_{13}H_{23}NOBr$ (M+H) 304.0912 (0.3 ppm).



2-Bromo-N-cyclohexyl-N-(3-hydroxypropyl)-1-methylcyclopropanecarboxamide (**4c**): To a stirred solution of 3-(cyclohexylamino)propan-1-ol (580 mg, 3.80 mmol, 1.10 equiv) and triethylamine (1.45 mL, 1.06 g, 10.5 mmol, 3.00 equiv) in dry THF (25 mL) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (620 mg, 3.14 mmol, 0.90 equiv) in THF (20 mL) was added dropwise over 10 min. The resulting suspension was stirred for 30 min at room temperature and then filtered through a fritted funnel. The filter cake was washed with

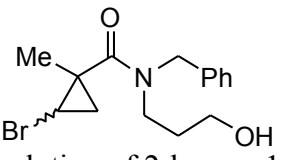
EtOAc (3 x 10 ml). The combined filtrates were concentrated in vacuum. Preparative column chromatography of the residual crude oil on silica gel afforded the title compound as a yellowish crystalline solid, R_f 0.45 (hexane-EtOAc 1:1). Yield 946 mg (2.90 mmol, 85 %).

^{1}H NMR (500.13 MHz, $CDCl_3$) δ 3.96-3.76 (m, 2H), 3.61-3.38 (m, 3H), 3.34-3.22 (m, 1H), [3.13 (dd, *J* = 8.2 Hz, 4.7 Hz) & 3.02 (dd, *J* = 7.6 Hz, 4.7 Hz), Σ1H], 1.94-1.79 (m, 2H), 1.79-1.64 (m, 4H), 1.64-1.48 (m, 4H), [1.43 (s) & 1.35 (s), Σ3H], 1.48-1.42 (m, 1H), 1.41-1.33 (m, 1H), 1.13 (tt, *J* = 13.0 Hz, 3.7 Hz, 1H), 0.90 (dd, *J* = 6.6 Hz, 5.4 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ major 172.8, 59.0 (-), 57.6 (+), 37.9 (-), 33.2 (-), 32.1 (-), 31.8 (-), 27.2 (+), 26.1, 26.0 (-), 25.8 (-), 25.3 (-), 21.4 (-), 19.8 (+); minor: 170.9, 59.0 (-), 58.0 (+), 38.4 (-), 33.4 (-), 33.2 (-), 32.4 (s, 1 C), 28.5 (+), 26.0, 25.3 (-), 24.4 (-), 23.6 (-), 22.0 (-), 19.8 (+); FT IR (cm^{-1}, film): 3400, 2932, 2856, 1616, 1472, 1454, 1425, 1369, 1350, 1325, 1298, 1269, 1240, 1197, 1157, 1144, 1059, 986, 933, 897, 870, 756, 733, 623, 509; HRMS (TOF ES): found 340.0886, calculated for $C_{14}H_{24}NO_2BrNa$ (M+Na) 340.0888 (0.6 ppm);



2-Bromo-N-hexyl-N-(3-hydroxypropyl)-1-methylcyclopropane-carboxamide (**4d**): To a stirred solution of 3-(hexylamino)-propan-1-ol (500 mg, 3.15 mmol, 1.00 equiv) and triethylamine (1.30 mL, 950 mg, 9.50 mmol, 3.00 equiv) in dry THF (25 ml) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (620 mg, 3.14 mmol, 0.90 equiv) in dry THF (20 mL was added dropwise over 10 min. The resulting suspension was stirred for 30 min at room temperature and then filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 ml), and the combined filtrates were concentrated in vacuum. Preparative column chromatography of the residual crude oil on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane-EtOAc, 1:1). Yield 736 mg (2.30 mmol, 73%).

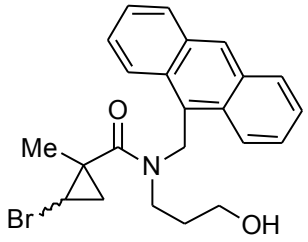
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 3.66 (br. s., 1H), 3.63-3.52 (m, 1H), 3.52-3.31 (m, 4H), 3.19 (dd, *J* = 8.2 Hz, 4.9 Hz, 1H), 1.75-1.67 (m, 3H), 1.66-1.57 (m, 2H), 1.49 (s, 3H), 1.36 (m, 7H), 0.99-0.84 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 173.2, 58.2 (-), 47.5 (-), 40.3 (-), 31.5 (-), 30.2 (-), 28.4 (-), 27.4, 26.6 (+), 26.0 (-), 22.5 (-), 21.6 (-), 19.8 (+), 13.9 (+); FT IR (cm^{-1}, film): 3410, 2934, 2874, 1614, 1497, 1472, 1454, 1427, 1379, 1358, 1325, 1298, 1271, 1236, 1184, 1078, 1057, 1030, 1001, 933, 870, 825, 739, 698, 625, 573, 544, 490, 463; HRMS (TOF ES): found 342.1043, calculated for $C_{14}H_{26}NO_2BrNa$ (M+Na) 342.1045 (0.6 ppm);



N-Benzyl-2-bromo-N-(3-hydroxypropyl)-1-methylcyclopropane-carboxamide (**4e**): To a stirred solution of 3-(benzylamino)-propan-1-ol (850 mg, 5.10 mmol, 1.02 equiv) and triethylamine (2.06 mL, 1.50 g, 15.0 mmol, 3.00 equiv) in dry THF (25 mL) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (1.0 g, 5.0 mmol, 1.0 equiv) in dry THF (20 mL) was added dropwise over 10 min. The resulting suspension was stirred for 30 min at room temperature and filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 mL). The combined organic filtrates were

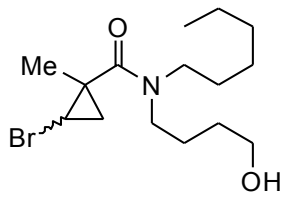
concentrated in vacuum. Preparative column chromatography of a resulting crude oil on silica gel afforded the title compound as a colorless oil, R_f 0.30 (hexane-EtOAc, 1:3). Yield 1.30 g (4.00 mmol, 80%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.39-7.15 (m, 5H), [5.12 (d, *J* = 16.9 Hz) & 4.71 (d, *J* = 16.4 Hz), Σ1H], [4.66 (d, *J* = 16.4 Hz) & 4.45 (d, *J* = 16.9 Hz), Σ1H], 4.00-2.90 (m, 5H), 1.75-1.57 (m, 3H), [1.49 (s) & 1.33 (s), Σ3H], [1.21 (ps.-t, *J* = 7.3 Hz, 6.8 Hz) & 0.92 (dd, *J* = 6.8 Hz, 5.1 Hz), Σ1H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 173.5, 172.1, 135.7, 135.6, 128.9 (+, 2C), 128.8 (+, 2C), 127.7 (+), 127.5 (+), 126.6 (+, 2C), 126.5 (+, 2C), 58.3 (-), 58.2 (-), 50.4 (-, 2C), 40.9 (-), 40.7 (-), 29.3 (-), 29.2 (-), 28.0, 27.0 (+), 25.9 (+), 25.8 (+), 22.4, 21.7 (+), 21.6 (-), 19.8 (-); FT IR (cm^{-1}, film): 3400 (br), 3075, 2985, 1624, 1421, 1265, 1186, 894, 739, 704; HRMS (TOF ES): found 246.1501, calculated for $C_{15}H_{20}NO_2$ (M-Br) 246.1494 (2.8 ppm).



N-(Anthracen-9-ylmethyl)-2-bromo-N-(3-hydroxypropyl)-1-methylcyclopropanecarboxamide (**4f**): To a stirred solution of 3-((anthracen-9-ylmethyl)amino)propan-1-ol (295 mg, 1.11 mmol, 1.11 equiv) and triethylamine (420 μL, 307 mg, 3.03 mmol, 3 equiv.) in dry THF (20 mL) was added dropwise a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (200 mg, 1.01 mmol, 1 equiv) in dry THF (10 mL). The mixture was stirred overnight, then concentrated in vacuum. The residue was quenched with brine and extracted with EtOAc (3 x 15 mL). Combined organic phases were dried with $MgSO_4$, filtered and concentrated. Preparative column chromatography of the residual crude oil on silica gel afforded the title compound as yellowish solid, R_f 0.15 and 0.35 (hexane-EtOAc 1:1). Yield 276 mg (0.65 mmol, 64%).

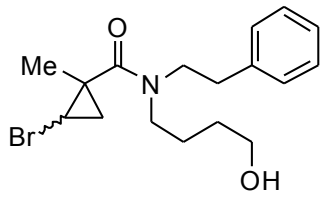
^{1}H NMR (400.13 MHz, $CDCl_3$) δ [8.51 (s) & 8.41 (s), Σ1H], 8.26 (d, *J* = 8.8 Hz, 2H), [8.06 (d, *J* = 8.8 Hz) & 7.98 (d, *J* = 8.1 Hz), Σ2H], 7.60-7.43 (m, 4H), [5.93 (d, *J* = 14.4 Hz) & 5.88 (d, *J* = 15.4 Hz), Σ1H], [5.72 (d, *J* = 14.4 Hz) & 5.65 (d, *J* = 15.4 Hz), Σ1H], 3.43-2.96 (m, 5H), [1.86-1.82 (m) & 1.71-1.57 (m), Σ3H], [1.82 (s) & 1.37 (s), Σ3H], [1.44 (app. t, *J* = 7.1 Hz) & 1.28 (app. t, *J* = 7.1 Hz), Σ1H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ major: 170.5, 131.2 (2C), 130.9 (2C), 129.1 (+, 2C), 128.2 (+), 127.3, 126.3 (+, 2C), 125.0 (+, 2C), 124.3 (+, 2C), 59.9 (-), 43.1 (-), 40.3 (-), 32.1 (-), 28.3, 25.9 (+), 23.3 (s, 1 C), 21.9 (+); minor: 172.2, 131.6 (2C), 131.2 (2C), 129.5 (+, 2C), 129.2 (+), 127.0 (+, 2C), 125.1 (+, 2C), 124.4, 123.4 (+, 2C), 58.1 (-), 44.5 (-), 40.3 (-), 31.6 (-), 28.5, 25.9 (+), 23.9 (-), 21.7 (+); FT IR (cm^{-1}, film): 3397, 3053, 2957, 2932, 2876, 1718, 1672, 1626, 1614, 1429, 1377, 1285, 1229, 1173, 1159, 1095, 1055, 932, 854, 735, 700; HRMS (TOF ES): found 448.0894, calculated for $C_{23}H_{24}NO_2BrNa$ (M+Na) 448.0888 (1.3 ppm);



2-Bromo-N-hexyl-N-(4-hydroxybutyl)-1-methylcyclopropane-carboxamide (**4g**): A 25 ml round-bottomed flask was charged with 4-(hexylamino)butan-1-ol (88 mg, 0.56 mmol, 1.1 equiv), triethylamine (212 μL, 154 mg, 1.53 mmol, 3.00 equiv), and dry THF (5 mL). The mixture was stirred, and a solution of 2-

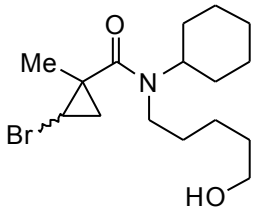
bromo-1-methylcyclopropanecarbonyl chloride (100 mg, 0.51 mmol, 1.00 equiv) in THF (5 mL) was added dropwise over 5 min. The resulting suspension was stirred for 30 min at room temperature, then filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 ml). The combined filtrates were concentrated in vacuum. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.2 (Hexane-EtOAc 1:1). Yield 128 mg (0.38 mmol, 75%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm 3.77-3.61 (m, 2H), 3.48-3.29 (m, 3H), 3.28-3.11 (m, 2H), 2.42 (br. s, 1H), 1.71-1.43 (m, 8H), 1.45 (s, 3H), 1.41-1.31 (m, 3H), 1.28 (br. s., 2H), 0.98-0.81 (m, 4H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ major: 171.7, 62.1 (-), 47.5 (-), 44.2 (-), 31.5 (-), 29.5 (-), 28.5 (-), 27.5 (+), 26.6 (-), 26.0, 23.6 (-), 22.5 (-, 2C), 21.4 (-), 14.0 (+); minor: 171.4, 62.1 (-), 47.0 (-), 44.4 (-), 31.5 (-), 29.9 (-), 28.5 (-), 27.7 (+), 27.0 (-), 26.0, 24.9 (-), 22.5 (-, 2C), 21.4 (-), 19.7 (+); FT IR (cm^{-1}, film): 3418, 3404, 2932, 2860, 1622, 1462, 1429, 1377, 1325, 1178, 1130, 1082, 1068, 1034, 615; HRMS (TOF ES): found 334.1388, calculated for $C_{15}H_{29}NO_2Br$ (M+H) 334.1382 (1.8 ppm);



2-Bromo-N-(4-hydroxybutyl)-1-methyl-N-phenethylcyclopropanecarboxamide (**4h**): To a stirred solution of 4-(phenethylamino)butan-1-ol (250 mg, 1.29 mmol, 1.00 equiv) and triethylamine (550 μL, 400 mg, 3.96 mmol, 3.0 equiv) in dry THF (10 ml) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (260 mg, 1.29 mmol, 1.00 equiv) in dry THF (10 mL) was added dropwise over 10 min. The resulting suspension was stirred for 30 min at room temperature and filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 mL). The combined filtrates were concentrated in vacuum. Preparative column chromatography o f the crude residual oil on silica gel afforded the title compound as a colorles oil, R_f 0.20 (hexane-EtOAc, 1:1). Yield 300 mg (0.85 mmol, 66%), mixture of diastereomers 1:1).

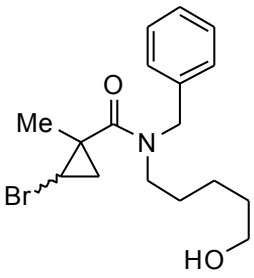
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.37-7.21 (m, 5H), 3.72-3.58 (m, 4H), 3.45-3.11 (m, 2H), 2.90-2.85 (m, 2H), 1.84 (br. s, 1H), 1.73-1.55 (m, 6H), [1.44 (s) & 1.42 (s), Σ3H], 0.90-0.84 (m, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 171.9, 171.6, 138.8, 137.6, 128.7 (+, 4C), 128.6 (+, 2C), 128.3 (+, 2C), 126.8 (+),126.3 (+), 61.9 (-), 61.8 (-), 48.8 (-), 47.5 (-), 46.1 (-), 44.1 (-), 34.5 (-), 33.2 (-), 29.7 (+), 29.4 (+), 27.4, 27.2, 25.9 (-), 25.8 (-), 24.7 (-), 23.4 (-), 21.3 (-), 21.2 (-), 19.6 (+, 2C); FT IR (cm^{-1}, film): 3416, 2935, 2870, 2361, 2341, 1622, 1454, 1427, 1171, 1068, 1032, 750, 700; HRMS (TOF ES): found 354.1060, calculated for $C_{17}H_{25}NO_2Br$ (M+H) 354.1069 (2.5 ppm);



2-Bromo-N-cyclohexyl-N-(5-hydroxypentyl)-1-methylcyclopropanecarboxamide (**4i**), mixture of diastereomers, 1.1:1. 25 ml round-bottomed flask was charged with 5-(cyclohexylamino)-pentan-1-ol (122 mg, 0.66 mmol, 1.10 equiv) and triethylamine (246 μL, 179 mg, 1.77 mmol, 3.00 equiv), and dry THF (5 mL). A solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (116.5 mg, 0.59 mmol, 1.00 equiv) in THF (5 mL) was added dropwise over 5 min. The resulting suspension was stirred for 30 min at room temperature, and then filtered through

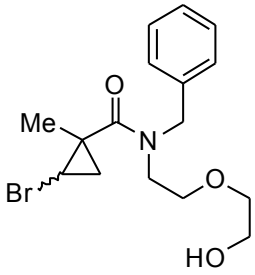
a fritted funnel. The filter cake was washed with EtOAc (3 x 10 mL). The combined filtrates were concentrated in vacuum. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.30 (Hexane-EtOAc 1:2). Yield 143 mg (0.41 mmol, 70%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ [3.85-3.70 (m) & 3.62 (t, *J* = 6.4 Hz), 3.28-3.09 (m) & 3.09-2.97 (m), Σ7H], [2.11 (d, *J* = 13.1 Hz) & 1.93-1.78 (m) & 1.78-1.66 (m) & 1.62-1.53 (m), Σ10H], [1.42 (s) & 1.34 (s), Σ3H], [1.52-1.41 (m) & 1.39-1.33 (m) & 1.27-1.23 (m) & 1.21-1.09 (m) & 0.91-0.81 (m), Σ8H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.2, 169.4, 62.0 (-), 61.9 (-), 57.3 (+), 57.0 (+), 42.7 (-), 42.2 (-), 32.6 (-), 32.1 (-), 31.98 (-), 31.96 (-), 31.7 (-), 31.5 (-), 28.5 (-), 28.4, 28.3 (-), 28.2 (+), 27.2 (+), 25.9 (-), 25.8 (-), 25.7 (-), 25.6 (-), 25.4, 25.2 (-), 25.1 (-), 23.3 (-), 23.3 (-), 23.0 (-), 21.8 (+), 21.1 (-), 19.5 (+); FT IR (cm^{-1}, film): 3434, 2978, 2934, 2860, 2797, 2642, 2621, 2492, 1732, 1614, 1568, 1553, 1539, 1454, 1423, 1385, 1306, 1188, 1161, 1084, 764, 613, 579, 519, 471; HRMS (TOF ES): found 368.1209, calculated for $C_{16}H_{28}BrNO_2Na$ (M+Na) 368.1201 (2.2 ppm).



N-Benzyl-2-bromo-N-(5-hydroxypentyl)-1-methylcyclopropane-carboxamide (**4j**): To a stirred solution of 5-(benzylamino)pentan-1-ol (700 mg, 3.60 mmol, 1.10 equiv) and triethylamine (1.47 mL, 1.07 g, 10.6 mmol, 3.00 equiv) in dry THF (25 mL) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (640 mg, 3.20 mmol, 1.00 equiv) in dry THF (20 mL) was added dropwise over 10 min. The resulting suspension was stirred for 30 min at room temperature and filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 ml). The combined filtrates were concentrated in vacuum. Preparative column chromatography of the residual crude oil on silica gel afforded the title compound as a colorless oil, R_f 0.20 (hexane-EtOAc, 1:3). Yield 882 mg (2.50 mmol, 78%).

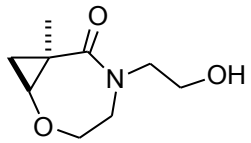
^{1}H NMR (400.13 MHz, $CDCl_3$) δ [7.47-7.34 (m) & 7.34-7.19 (m), Σ5H], [5.09 (d, *J* = 17.2 Hz) & 4.86 (d, *J* = 15.2 Hz), Σ1H], [4.50 (d, *J* = 16.9 Hz) & 4.48 (d, *J* = 15.2 Hz), Σ1H], [3.80 (dddd, *J* = 13.9 Hz, 9.6 Hz, 5.8 Hz, 1.2 Hz) & 3.57-3.51 (m), Σ1H], 3.61 (t, *J* = 6.6 Hz) & 3.57 (t, *J* = 6.6 Hz), Σ2H], [3.25 (ddd, *J* = 14.1 Hz, 11.4 Hz, 4.8 Hz) & 2.77 (ddd, *J* = 13.5 Hz, 9.8 Hz, 5.3 Hz), Σ1H], 2.95 - 3.10 (m, 1H), 2.18 (br. s., 2H), 1.87-1.72 (m, 1H), 1.72-1.46 (m, 4H), [1.41 (s) & 1.31 (s), Σ3H], 1.37-1.26 (m, 1H), 1.26-1.11 (m, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ major: 170.7, 136.5, 128.7 (+, 2C), 127.4 (+), 126.6 (+, 2C), 62.4 (-), 50.6 (-), 45.3 (-), 32.2 (-), 27.9, 26.0 (-), 25.9 (+), 23.1 (-), 22.4 (-), 21.7 (+); minor: 170.6, 137.1, 128.3 (+, 2C), 128.0 (+, 2C), 127.1 (+), 62.3 (-), 47.5 (-), 46.7 (-), 32.2 (-), 28.0 (-), 27.9, 25.9 (+), 23.3 (-), 22.5 (-), 21.8 (+); FT IR (cm^{-1}, film): 3412, 2934, 2849, 1628, 1495, 1452, 1427, 1373, 1358, 1323, 1300, 1236, 1205, 1184, 1076, 1041, 1030, 1003, 957, 939, 735, 698, 609, 461; HRMS (TOF ES): found 376.0888, calculated for $C_{17}H_{24}NO_2BrNa$ (M+Na) 376.0888 (0.0 ppm);



N-Benzyl-2-bromo-N-(2-(2-hydroxyethoxy)ethyl)-1-methylcyclopropanecarboxamide (**4k**): mixture of diastereomers 1.1:1. 25 mL round bottomed flask was charged with 2-(2-(benzylamino)-ethoxy)ethanol (110 mg, 0.56 mmol, 1.1 equiv), triethylamine (152 mg, 1.50 mmol, 3.0 equiv) and anhydrous THF (5 mL). A solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (100 mg, 0.51 mmol, 1.0 equiv) in dry THF (5 mL) was added dropwise over 10 min. The resulting suspension was stirred for 30 min at room temperature, and then filtered through a fritted funnel. The filter cake was washed with EtOAc (3 x 10 mL). The combined filtrates were concentrated in vacuum. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.25 (Hexane-EtOAc 1:1). Yield 89 mg (0.25 mmol, 50%).

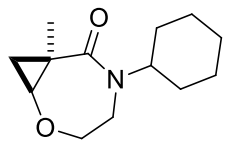
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.40-7.27 (m, 3H), 7.20-7.16 (m, 2H), [4.86-4.76 (m) & 4.52-4.45 (m), Σ2H], 3.72-3.67 (m, 2H), 3.63-3.57 (m, 2H), 3.54-3.45 (m, 4H), 3.26-3.20 (m, 1H), 2.27-2.18 (m, 1H), 1.80-1.73 (m, 1H), 1.51 (m, 3H), 0.96-0.91 (m, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 172.8 (2C), 137.2, 136.3, 128.9 (+, 2C), 128.6 (+, 2C), 127.6 (+, 4C), 126.6 (+, 2C), 72.4 (-), 72.2 (-), 68.3 (-), 67.9 (-), 61.7 (-, 2C), 51.6 (-), 47.6 (-), 46.5 (-), 44.3 (-), 28.5 (+), 27.2 (+), 26.0, 25.8, 21.6 (-, 2C), 19.7 (+, 2C); FT IR (cm^{-1}, film): 3435, 2926, 1634, 1452, 1423, 1188, 1124, 1070, 1030, 737, 698, 625, 604, 571; HRMS (TOF ES): found 356.0862, calculated for $C_{16}H_{23}BrNO_3$ (M+H) 356.0861 (0.3 ppm).

Medium Size Ring Cyclizations



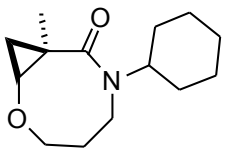
(1S*,7R*)-5-(2-Hydroxyethyl)-7-methyl-2-oxa-5-azabicyclo-[5.1.0]octan-6-one (**6a**): To a mixture of *t*-BuOK (155 mg, 1.38 mmol, 2.00 equiv), 18-crown-6 ether (18.2 mg, 0.70 mmol, 10 mol%) in THF (5 mL) was added bromocyclopropane **4a** (186 mg, 0.70 mmol, 1.00 equiv). The mixture was stirred for 1 hr at 40 ^{o}C. Then the mixture was partitioned between water (10ml) and EtOAc (10ml), and extracted with EtOAc (3 x 10 ml). The combined organic phases were dried with Na_2SO_4, filtered and concentrated. No further purification was necessary. Yield 93 mg (0.50 mmol, 72%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 4.16 (ddd, *J* = 15.4 Hz, 12.6 Hz, 5.1 Hz, 1H), 3.75-3.73 (m, 2H), 3.67 (dd, *J* = 11.1 Hz, 5.1 Hz, 1H), 3.56 (dt, *J* = 14.2 Hz, 5.8 Hz, 1H), 3.48 (dt, *J* = 14.4 Hz, 4.8 Hz, 1H), 3.22 (dd, *J* = 15.2 Hz, 4.6 Hz, 1H), 2.97 (dd, *J* = 5.8 Hz, 2.8 Hz, 1H), 1.24 (s, 3H), 1.06 (dd, *J* = 6.8 Hz, 2.8 Hz, 1H), 0.82 (ps.-t, *J* = 6.8 Hz, 5.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 174.3, 64.2 (+), 61.7 (+), 56.5 (-), 50.3 (+), 47.1 (+), 26.3, 18.1 (+), 17.8 (-); FT IR (cm^{-1}, film): 3389, 2955, 2920, 2866, 1626, 1481, 1439, 1371, 1209, 1153, 1097, 1056, 1040, 789, 700, 660; HRMS (TOF ES): found 229.1677, calculated for $C_{12}H_{23}NO_3$ (M^+) 229.1678 (0.4 ppm);



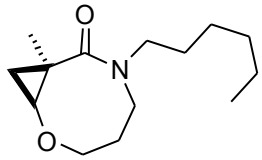
(1S*,7R*)-5-Cyclohexyl-7-methyl-2-oxa-5-azabicyclo[5.1.0]octan-6-one (**6b**): To a mixture of *t*-BuOK (82 mg, 0.73 mmol, 2.4 equiv), 18-crown-6 ether (13.2 mg, 0.03 mmol, 10 mol%) in THF (3 mL) was added bromocyclopropane **4b** (92 mg, 0.3 mmol, 1.0 equiv). The mixture was stirred for 4 hrs at 80 ^{o}C. The KBr precipitate was filtered off on a fritted funnel and the solvent was removed in vacuum. Flash column chromatography of the residue through a silica plug in EtOAc afforded the title compound as a yellowish oil, Yield 60 mg (0.27 mmol, 91%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm 4.38 (tt, *J* = 12.0 Hz, 3.6 Hz, 1H), 3.80 (ddd, *J* = 15.4 Hz, 12.6 Hz, 4.8 Hz, 1H), 3.71 (dd, *J* = 11.0 Hz, 4.9 Hz, 1H), 3.56 (ddd, *J* = 12.4 Hz, 11.1 Hz, 4.5 Hz, 1H), 3.21 (dd, *J* = 15.3 Hz, 4.7 Hz, 1H), 2.92 (dd, *J* = 6.1 Hz, 2.8 Hz, 1H), 1.83-1.60 (m, 4H), 1.44-1.22 (m, 6H), 1.20 (s, 3H), 1.09-1.02 (m, 1H), 0.80 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 172.1, 66.4 (-), 56.5 (+), 51.6 (+), 39.7 (-), 30.5 (-), 26.6, 25.5 (-), 25.32 (-), 25.29 (+), 17.8 (-); FT IR (cm^{-1}, film): 2930, 2856, 1645, 1472, 1423, 1379, 1366, 1329, 1263, 1236, 1211, 1196, 1157, 1140, 1092, 1040, 789, 665; HRMS (TOF ES): found 246.1441, calculated for $C_{13}H_{21}NO_2Na$ (M+Na) 246.1470 (2.4 ppm).



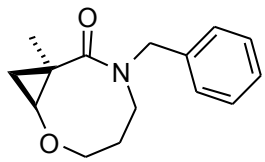
(1S*,8R*)-6-Cyclohexyl-8-methyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**6c**): To a mixture of *t*-BuOK (139 mg, 1.25 mmol, 2.5 equiv), 18-crown-6 ether (13 mg, 0.05 mmol, 10 mol%) in dry THF (5 mL) was added bromocyclopropane **4c** (160 mg, 0.5 mmol, 1.0 equiv). The mixture was stirred for 12 hrs at 80 ^{o}C. The KBr precipitate was filtered and the solvent was removed in vacuum. Preparative column chromatography on silica gel afforded the title compound as a colorless oil, R_f 0.30 (hexane-EtOAc 2:1). Yield 105 mg (0.45 mmol, 89%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 4.38 (ddt, *J* = 15.1 Hz, 7.7 Hz, 3.6 Hz, 1H), 4.09 (dd, *J* = 12.5 Hz, 5.2 Hz, 1H), 3.80 (dd, *J* = 15.7 Hz, 9.9 Hz, 1H), 3.61 (td, *J* = 12.7 Hz, 3.2 Hz, 1H), 3.42 (dd, *J* = 15.7 Hz, 7.3 Hz, 1H), 3.18 (dd, *J* = 7.2 Hz, 3.9 Hz, 1H), 2.02-1.84 (m, 3H), 1.84-1.54 (m, 5H), 1.51-1.28 (m, 4H), 1.18 (s, 3H), 1.12 (dd, *J* = 6.4 Hz, 3.9 Hz, 1H), 0.75 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 172.1, 72.8 (-), 67.7 (+), 53.8 (+), 41.8 (-), 33.4 (-), 31.5 (-), 30.3 (-), 27.9, 26.0 (-), 25.7 (-), 25.6 (-), 20.1 (+), 16.8 (-); FT IR (cm^{-1}, film): 2932, 2856, 2360, 2351, 1612, 1458, 1421, 1325, 1198, 1057, 986; HRMS (TOF ES): found 238.1804, calculated for $C_{14}H_{24}NO_2$ (M+H) 238.1807 (1.3 ppm);



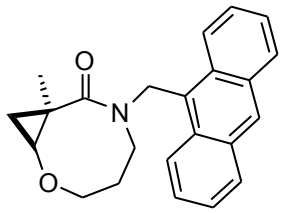
(1S*,8R*)-6-Hexyl-8-methyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**6d**): To a mixture of *t*-BuOK (72.9 mg, 0.65 mmol, 2.0 equiv), 18-crown-6 ether (8.6 mg, 0.033 mmol, 10 mol%) in THF (3 mL) was added bromocyclopropane **4d** (103 mg, 0.33 mmol, 1.0 equiv). The mixture was stirred for 12 hrs at 80 ^{o}C. The KBr precipitate was filtered off on a fritted funnel and the solvent was removed in vacuum. Preparative column chromatography on silica gel afforded the title compound as a clear oil, R_f 0.35 (hexane-EtOAc 1:1). Yield 65.3 mg (0.27 mmol, 84%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ 4.08 (dd, *J* = 12.6 Hz, 5.3 Hz, 1H), 3.97 (dd, *J* = 15.3 Hz, 10.5 Hz, 1H), 3.93-3.78 (m, 1H), 3.61 (td, *J* = 12.7 Hz, 3.2 Hz, 1H), 3.27 (dd, *J* = 15.2 Hz, 7.1 Hz, 1H), 3.15 (dd, *J* = 7.3 Hz, 3.8 Hz, 1H), 2.73 (ddd, *J* = 13.6 Hz, 8.2 Hz, 5.9 Hz, 1H), 1.92 (dddd, *J* = 15.1 Hz, 12.7 Hz, 10.1 Hz, 5.3 Hz, 1H), 1.62 (ddd, *J* = 15.2 Hz, 7.1 Hz, 3.0 Hz, 1H), 1.58-1.46 (m, 2H), 1.26 (br. s., 6H), 1.19 (s, 3H), 1.09 (dd, *J* = 6.6 Hz, 3.8 Hz, 1H), 0.90-0.79 (m, 3H), 0.68 (t, *J* = 6.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 171.9, 72.6 (-), 67.5 (+), 46.1 (-), 45.7 (-), 31.5 (-), 30.5 (-), 27.4 (-), 27.3, 26.4 (-), 22.4 (-), 19.7 (+), 16.7 (-), 13.9 (+); FT IR (cm^{-1}, film): 2955, 2930, 2858, 1637, 1481, 1464, 1441, 1423, 1364, 1325, 1250, 1203, 1150, 1132, 1103, 1070, 1045, 1009, 733, 559, 500, 424; HRMS (TOF ES): found 262.1785, calculated for $C_{14}H_{25}NO_2Na$ (M+Na) 262.1783 (0.8 ppm);



(1S*,8R*)-6-benzyl-8-methyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**6e**): To a mixture of *t*-BuOK (112 mg, 1.00 mmol, 2.00 equiv), 18-crown-6 ether (13.2 mg, 0.05 mmol, 10 mol%) in THF (5 mL) was added bromocyclopropane **4e** (163 mg, 0.50 mmol, 1.00 equiv). The mixture was stirred for 2 hrs at 80 °C. The KBr precipitate was filtered off on a fritted funnel and the solvent was removed in vacuum. Filtration of the residue through a silica plug in EtOAc afforded the title compound as a crystalline solid, Yield 93 mg (0.38 mmol, 76%).

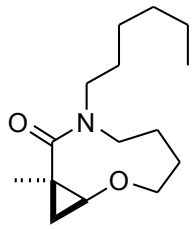
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.37-7.20 (m, 5H), 5.32 (d, *J* = 14.9 Hz, 1H), 4.13 (dd, *J* = 12.8 Hz, 5.4 Hz, 1H), 3.96 (dd, *J* = 15.7 Hz, 10.9 Hz, 1H), 3.90 (d, *J* = 14.9 Hz, 1H), 3.64 (td, *J* = 12.7 Hz, 3.2 Hz, 1H), 3.28-3.18 (m, 2H), 2.07-1.86 (m, 1H), 1.59 (ddd, *J* = 15.2 Hz, 7.1 Hz, 3.0 Hz, 1H), 1.29 (s, 3H), 1.21 (dd, *J* = 6.8 Hz, 3.8 Hz, 1H), 0.79 (t, *J* = 6.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 172.6, 137.5, 128.5 (+, 2C), 127.7 (+, 2C), 127.2 (+), 72.6 (-), 67.5 (+), 48.3 (-), 45.3 (-), 29.9 (-), 27.1, 19.7 (+), 16.8 (-); FT IR (cm^{-1}, film): 2982, 2962, 2943, 2908, 2874, 1738, 1697, 1636, 1479, 1423, 1393, 1373, 1300, 1244, 1103, 1047, 1001, 916, 849, 733, 700, 648, 635, 608, 461; HRMS (TOF ES): found 246.1490, calculated for $C_{15}H_{20}NO_2$ (M+H) 246.1494 (1.6 ppm).



(1S*,8R*)-6-(Anthracen-9-ylmethyl)-8-methyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**6f**): To a stirred suspension of *t*-BuOK (62 mg, 0.55 mmol, 2.5 equiv), 18-crown-6 (6.0 mg, 22 μmol, 10 mol%) in anhydrous THF (3 mL) was added bromocyclopropane **4f** (94 mg, 0.22 mmol, 1.0 equiv). The resulting dark-brown mixture was stirred for 6 hrs at 60 °C. The KBr precipitate was filtered off and the filtrate was concentrated in vacuum. Preparative column chromatography of a residue on silica gel afforded the title compound as an orange solid, R_f 0.20 (hexane-EtOAc 1:1). Yield 70.0 mg (0.20 mmol, 92%).

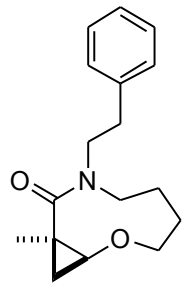
^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm 8.48 (s, 1H), 8.33 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.3 Hz, 2H), 7.55 (ddd, *J* = 8.4 Hz, 6.6 Hz, 1.5 Hz, 2H), 7.49 (dd, *J* = 7.3 Hz, 6.8 Hz, 2H), 6.33 (d, *J* = 15.2 Hz, 1H), 5.10 (d, *J* = 15.2 Hz, 1H), 4.12 (dd, *J* = 12.6 Hz, 5.1 Hz, 1H), 3.64 (dd, *J* = 15.5 Hz, 10.0 Hz, 1H), 3.56 (td, *J* = 12.9 Hz, 3.0 Hz, 1H), 3.20 (dd, *J* =

7.2 Hz, 3.7 Hz, 1H), 2.91 (dd, *J* = 15.7 Hz, 7.3 Hz, 1H), 2.23-2.09 (m, 1H), 1.48 (dd, *J* = 16.5 Hz, 6.9 Hz, 1H), 1.37 (dd, *J* = 6.6 Hz, 3.8 Hz, 1H), 1.14 (s, 3H), 0.83 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ 172.6, 131.5 (2C), 131.4 (2C), 129.2 (+, 2C), 128.24 (+), 128.17, 126.5 (+, 2C), 125.1 (+, 2C), 124.0 (+, 2C), 72.7 (-), 67.7 (+), 43.3 (-), 39.1 (-), 30.5 (-), 27.9, 19.5 (+), 16.8 (-); FT IR (cm^{-1}, film): 2957, 2928, 2868, 1634, 1445, 1423, 1362, 1312, 1244, 1202, 1188, 1146, 1109, 1070, 966, 928, 891, 854, 762, 737; HRMS (TOF ES): found 346.1806, calculated for $C_{23}H_{24}NO_2$ (M+H) 346.1807 (0.3 ppm).



(1S*,9R*)-7-Hexyl-9-methyl-2-oxa-7-azabicyclo[7.1.0]decan-8-one (**6g**): To a mixture of *t*-BuOK (65.1 mg, 0.56 mmol, 2.00 equiv), 18-crown-6 ether (8 mg, 0.03 mmol, 10 mol%) in THF (3 mL) was added bromocyclopropane **4g** (92.2 mg, 0.29 mmol, 1.00 equiv). The mixture was stirred for 3 hrs at 80 °C. The KBr precipitate was filtered off on a fritted funnel and the solvent was removed in vacuum. Preparative column chromatography on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane-EtOAc 1:1). Yield 97.0 mg (0.24 mmol, 84%).

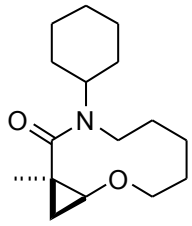
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 4.19 (dd, *J* = 12.8 Hz, 7.2 Hz, 1H), 4.11 (td, *J* = 13.9 Hz, 2.8 Hz, 1H), 3.86 (m, *J* = 14.0 Hz, 8.2 Hz, 7.8 Hz, 0.8 Hz, 1H), 3.35 (dd, *J* = 14.1 Hz, 4.3 Hz, 1H), 3.28 (dd, *J* = 12.8 Hz, 6.7 Hz, 1H), 3.11 (dd, *J* = 7.1 Hz, 3.5 Hz, 1H), 2.77 (ddd, *J* = 13.7 Hz, 8.8 Hz, 5.3 Hz, 1H), 2.01-1.90 (m, 1H), 1.84-1.70 (m, 2H), 1.66-1.38 (m, 4H), 1.35-1.26 (m, 6H), 1.21 (s, 3H), 1.23 (dd, *J* = 6.4 Hz, 3.7 Hz, 1H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.72 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.6, 71.6 (-), 65.7 (+), 43.5 (-), 42.5 (-), 31.5 (-), 27.7, 27.3 (-), 26.8 (-), 26.5 (-), 25.4 (-), 22.6 (-), 20.3 (+), 17.0 (-), 14.0 (+); FT IR (cm^{-1}, film): 2953, 2930, 2870, 1636, 1468, 1427, 1194, 1159, 1099; HRMS (TOF ES): found 276.1937, calculated for $C_{15}H_{27}NO_2Na$ (M+Na) 276.1939 (0.7 ppm).



(1S,9R)-9-methyl-7-phenethyl-2-oxa-7-azabicyclo[7.1.0]decan-8-one (**6h**): To a mixture of *t*-BuOK (62.7 mg, 0.56 mmol, 2.00 equiv), 18-crown-6 ether (7.4 mg, 0.028 mmol, 10 mol%) in THF (3 mL) was added bromocyclopropane **4h** (100 mg, 0.28 mmol, 1.00 equiv). The mixture was stirred for 6 hrs at 60 °C. The KBr precipitate was filtered off on a fritted funnel and the filtrate was concentrated in vacuum. Preparative column chromatography on silica gel afforded the title compound as a colorless oil, R_f 0.36 (hexane-EtOAc 1:1). Yield 65.0 mg (0.24 mmol, 86%).

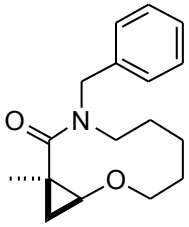
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.33-7.18 (m, 5H), 4.17 (dd, *J* = 12.8 Hz, 6.9 Hz, 1H), 4.13-4.05 (m, 1H), 4.00 (td, *J* = 14.0 Hz, 2.9 Hz, 1H), 3.24 (dd, *J* = 12.8 Hz, 6.9 Hz, 1H), 3.09 (dd, *J* = 6.8 Hz, 3.3 Hz, 1H), 3.12-3.04 (m, 1H), 3.04-2.94 (m, 2H), 2.90-2.81 (m, 1H), 2.01-1.86 (m, 1H), 1.81-1.71 (m, 1H), 1.49-1.31 (m, 2H), 1.24 (dd, *J* = 6.6 Hz, 3.5 Hz, 1H), 1.13 (s, 3H), 0.71 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 171.7, 139.3, 128.8 (+, 2C), 128.3 (+, 2C), 126.2 (+), 71.5 (-), 65.6 (+), 44.3 (-), 44.2 (-), 33.2 (-), 27.6, 27.3 (-), 25.3 (-), 20.1 (+), 16.8 (-); FT IR (cm^{-1}, film): 3084, 3024, 2932, 2870,

2359, 1637, 1468, 1441, 1425, 1362, 1280, 1192, 1167, 1099, 1047, 983, 748, 702, 505; HRMS (TOF ES): found 296.1618, calculated for $C_{17}H_{23}NO_2Na$ (M+Na) 296.1626 (2.7 ppm);



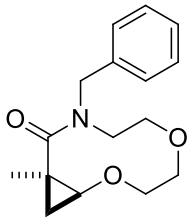
(1S*,10R*)-8-cyclohexyl-10-methyl-2-oxa-8-azabicyclo[8.1.0]undecan-9-one (**6i**): To a mixture of *t*-BuOK (67.3 mg, 0.60 mmol, 2.00 equiv), 18-crown-6 ether (8 mg, 0.03 mmol, 10 mol%) in THF (3 mL) was added bromocyclopropane **4i** (104 mg, 0.30 mmol, 1.00 equiv). The mixture was stirred overnight at 80 ^{o}C. The KBr precipitate was filtered off on a fritted funnel and the filtrate was concentrated in vacuum. Preparative column chromatography on silica gel afforded the title compound as a colorless oil, R_f 0.25 (hexane-EtOAc 1:1). Yield 69.3 mg (0.42 mmol, 87%).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm 3.94 (ddd, *J* = 14.4 Hz, 11.4 Hz, 4.9 Hz, 1H), 3.85 (ddd, *J* = 11.2 Hz, 7.6 Hz, 3.7 Hz, 1H), 3.70-3.60 (m, 2H), 3.26 (ddd, *J* = 14.2 Hz, 4.9 Hz, 3.4 Hz, 1H), 3.06 (dd, *J* = 7.6 Hz, 4.3 Hz, 1H), 1.97-1.79 (m, 4H), 1.78-1.54 (m, 6H), 1.40 (dd, *J* = 6.6 Hz, 4.6 Hz, 1H), 1.47-1.23 (m, 5H), 1.20 (s, 3H), 1.22-1.07 (m, 1H), 0.68 (t, *J* = 6.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 172.1, 70.4 (-), 65.6 (+), 57.4 (+), 43.7 (-), 30.9 (-), 30.0 (-), 28.6, 27.9 (-), 26.9 (-), 26.4 (-), 26.3 (-), 25.8 (-), 21.4 (+), 17.7 (-), 17.2 (-); FT IR (cm^{-1}, film): 2930, 2854, 1630, 1448, 1420, 1367, 1360, 1327, 1306, 1259, 1192, 1173, 1148, 1136, 1105, 1051, 1020, 785, 710, 503; HRMS (TOF ES): found 288.1944, calculated for $C_{16}H_{27}NO_2Na$ (M+Na) 288.1939 (1.7 ppm);



(1S*,10R*)-8-Benzyl-10-methyl-2-oxa-8-azabicyclo[8.1.0]undecan-9-one (**6j**): To a mixture of *t*-BuOK (140 mg, 1.25 mmol, 2.50 equiv), 18-crown-6 ether (13.2 mg, 0.05 mmol, 10 mol%) in THF (3 mL) was added bromocyclopropane **4j** (177 mg, 0.50 mmol, 1.00 equiv). The mixture was stirred for 4 hrs at 80 ^{o}C. The KBr precipitate was filtered off on a fritted funnel and the solvent was removed in vacuum. Preparative column chromatography on silica gel afforded the title compound as a colorless oil, R_f 0.40 (hexane-EtOAc 1:3). Yield 97 mg (0.35 mmol, 70%).

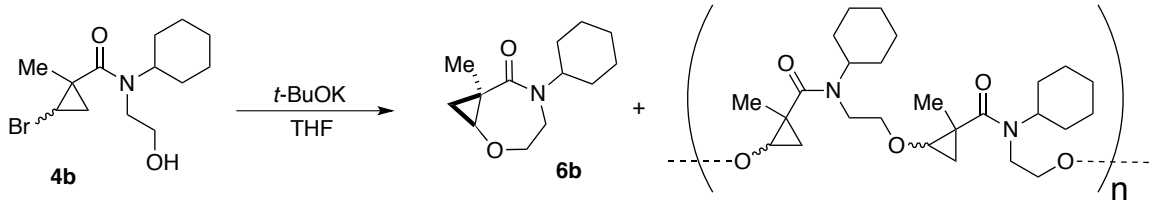
^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.37-7.30 (m, 2H), 7.30-7.22 (m, 3H), 5.53 (d, *J* = 14.9 Hz, 1H), 3.98 (td, *J* = 13.1 Hz, 4.6 Hz, 1H), 3.92 (td, *J* = 6.3 Hz, 4.3 Hz, 1H), 3.72 (d, *J* = 14.9 Hz, 1H), 3.66 (ddd, *J* = 11.3 Hz, 8.8 Hz, 2.8 Hz, 1H), 3.12 (dd, *J* = 7.6 Hz, 4.3 Hz, 1H), 3.10 (ddd, *J* = 13.9 Hz, 5.2 Hz, 2.1 Hz, 1H), 2.07-1.93 (m, 1H), 1.82-1.70 (m, 1H), 1.49 (dd, *J* = 6.6 Hz, 4.3 Hz, 1H), 1.58-1.38 (m, 3H), 1.27 (s, 3H), 1.34 - 1.22 (m, 1H), 0.78 (dd, *J* = 7.3 Hz, 6.6 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 172.5, 137.3, 128.5 (+, 2C), 127.9 (+, 2C), 127.1 (+), 70.2 (-), 65.3 (+), 45.4 (-), 43.5 (-), 27.8, 27.4 (-), 24.7 (-), 20.7 (+), 17.3 (-), 16.3 (-); FT IR (cm^{-1}, film): 3026, 2930, 2874, 1630, 1441, 1425, 1356, 1236, 1192, 1150, 1105, 1051, 1032, 739, 700; HRMS (TOF ES): found 296.1621, calculated for $C_{17}H_{23}NO_2Na$ (M+Na) 296.1626 (1.7 ppm).



(1S*,10R*)-8-Benzyl-10-methyl-2,5-dioxa-8-azabicyclo[8.1.0]undecan-9-one (**6k**): To a mixture of *t*-BuOK (37 mg, 0.33 mmol, 2.5 equiv), 18-crown-6 (3.5 mg, 13 μmol, 10 mol%) in THF (2 mL) was added bromocyclopropane **4k** (49 mg, 0.13 mmol, 1.0 equiv). The resulting mixture was stirred at 50 ^{o}C for 12 hrs. The KBr precipitate was filtered off and the filtrate was concentrated in vacuum. Preparative column chromatography of a residue on silica gel afforded the title compound as a colorless oil, R_f 0.20 (hexane-EtOAc 1:1). Yield 29 mg (0.10 mmol, 80%).

^{1}H NMR (500.13 MHz, $CDCl_3$) δ ppm 7.35-7.30 (m, 2H), 7.29-7.23 (m, 3H), 5.44 (d, *J* = 15.4 Hz, 1H), 4.35-4.21 (m, 1H), 4.04-3.90 (m, 3H), 3.76-3.62 (m, 3H), 3.29 (d, *J* = 12.3 Hz, 1H), 3.15 (dd, *J* = 7.3 Hz, 4.1 Hz, 1H), 2.98 (br. s., 1H), 1.73 (dd, *J* = 6.6 Hz, 4.1 Hz, 1H), 1.34 (s, 3H), 0.76 (dd, *J* = 7.3 Hz, 6.6 Hz, 1H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ ppm 172.0, 137.5, 128.6 (+, 2C), 127.8 (+), 127.2 (+, 2C), 70.0 (-), 66.8 (-), 65.3 (+), 64.7 (-), 47.1 (-), 44.4 (-), 27.5, 21.2 (+), 18.4 (-); FT IR (cm^{-1}, film): 2957, 2922, 2860, 2359, 2339, 2330, 1634, 1448, 1425, 1263, 1146, 1115, 741, 698; HRMS (TOF ES): found 298.1422, calculated for $C_{16}H_{21}NO_3Na$ (M+Na) 298.1422 (1.0 ppm).

Investigation on Concentration Effects



mixture of linear oligo- and polymers

To a mixture of *t*-BuOK (27 mg, 0.24 mmol, 2.4 equiv), 18-crown-6 ether (4.4 mg, 0.01 mmol, 10 mol%) in THF (variable volume) was added bromocyclopropane **4b** (31 mg, 0.1 mmol, 1.0 equiv) and *n*-tetradecane (15 mg) as internal standard for GC analysis. The mixture was stirred for 4 hrs at 80 ^{o}C. The KBr precipitate was filtered off on a fritted funnel and the solvent was removed in vacuum to control the mass balance. Cyclic monomer **6b** was separated by filtration of the crude product through a short plug of Silica gel (about 1 g, measured with accuracy of 0.1 mg) eluting with ethyl acetate. The yield of **6b** was estimated by quantitative GC analysis (instrument was calibrated to determine concentration of 6b versus *n*-tetradecane). The Silica gel plug was dried in high vacuum and weighed to estimate the mass of the polar fraction of oligo- and polymers absorbed. The results are shown in the Table 1.

Table 1. Influence of concentration on efficiency of 7-exo-trig cyclization of **4b**

#	Volume of THF, mL (Concentration of **4b**)	Mass of polymeric fraction (yield, %)	Yield of cyclic monomer **6b**	Material balance
1	100 μL (1.0 M)	11.8 mg (53%)	44%	97%
2	200 μL (0.5 M)	5.6 mg (25%)	73%	98%
3	400 μL (0.25 M)	3.3 mg (15%)	81%	96%
4	670 μL (0.15 M)	1.8 mg (8%)	90%	98%
5	1 mL (0.1 M)	0.9 mg (4%)	95%	99%
6	2 mL (0.05 M)	0.4 mg (2%)*	93%	95%
7	5 mL (0.02 M)	0.2 mg (1%)*	90%	91%

* Determination of chemical yields of polymers in these experiments is associated with measurement of rather little mass differences and, unavoidably, performed with significant error, which also might be responsible for the observed imperfect material balance.

Assignment of Relative Configurations

^{1}H NOE DIFF experiments unambiguously confirmed *cis*-configurations of cyclopropane moiety in representative products, obtained in 8-*exo-trig* (**6f**), 9-*exo-trig* (**6h**), and 10-*exo-trig* (**6j**) cyclizations. The corresponding spectral charts and 3D molecular structures showcasing the significant NOE responses are shown below. In each case NOE responses have been detected between the corresponding methyl group and a set of two hydrogen atoms in cyclopropane, one of them being a deshielded proton next to ethereal oxygen. Relative configurations of the products obtained in *exo-trig* cyclizations were assigned by analogy.

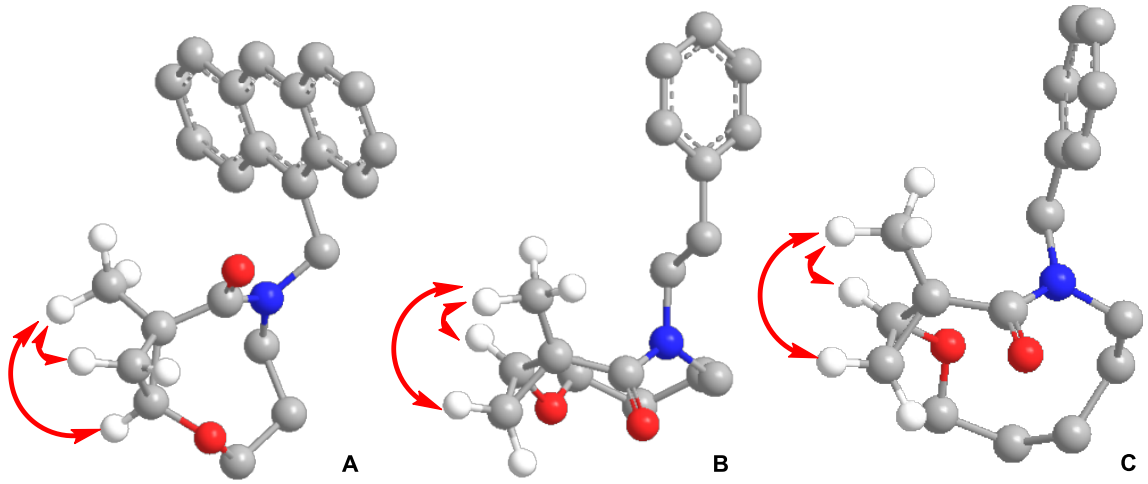


Figure 1. MM2-Optimized 3D molecular structures of three cyclization products: **6f** (A), **6h** (B), and **6j** (C). NOE responses, imperative for the assignment of the relative configuration are shown as red arrows connecting the corresponding hydrogen atoms.

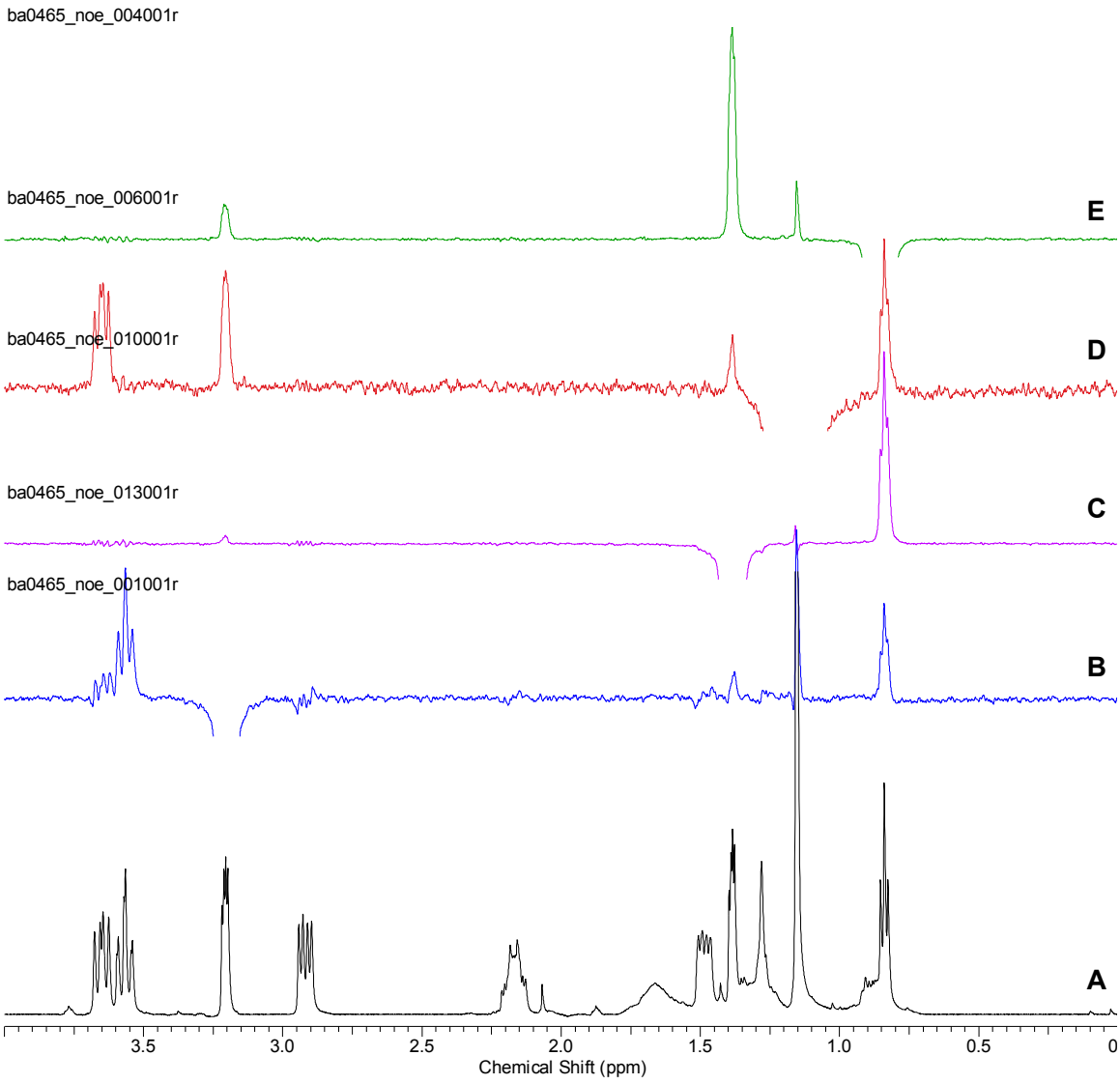


Figure 2. NOE experiments performed for compound **6f**. All spectra were registered at 500.13 MHz. The charts represent: (A) – reference ^{1}H NMR spectrum; (B) – NOE DIFF experiment with excitation at 3.21 ppm and mixing time 100 ms; (C) - NOE DIFF experiment with excitation at 1.39 ppm and mixing time 1.0 s; (D) - NOE DIFF experiment with excitation at 1.16 ppm and mixing time 500 ms; (E) - NOE DIFF experiment with excitation at 0.84 ppm and mixing time 1 s.

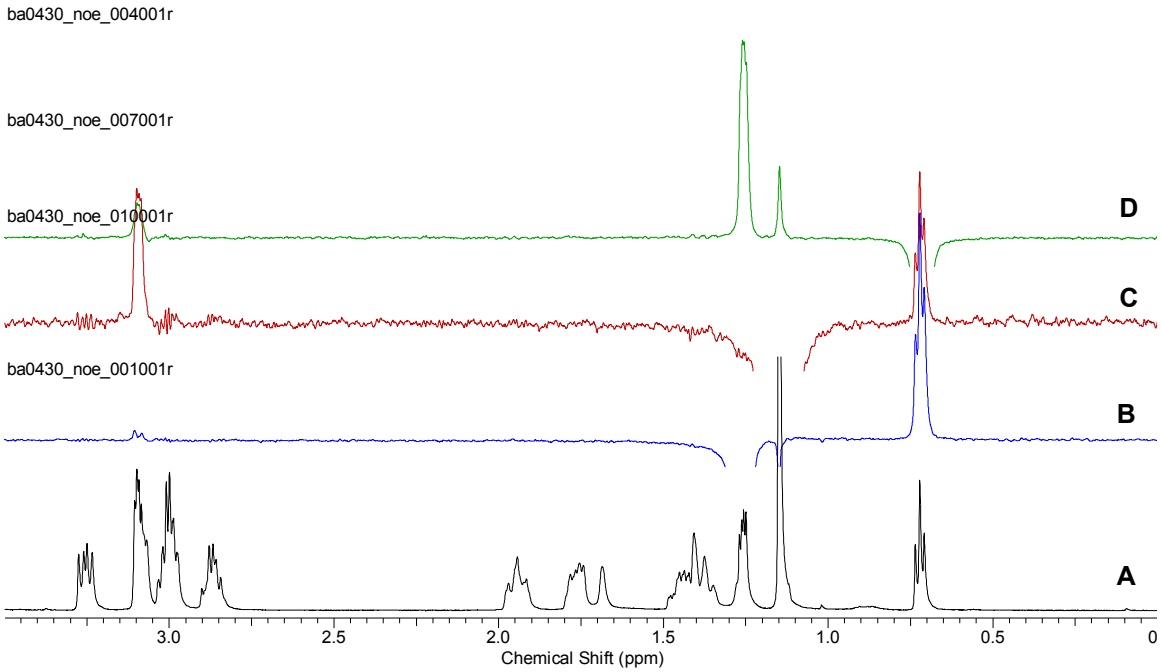


Figure 3. NOE experiments performed for compound **6h**. All spectra were registered at 500.13 MHz. The charts represent: (A) – reference ^{1}H NMR spectrum; (B) – NOE DIFF experiment with excitation at 1.26 ppm and mixing time 1 s; (C) - NOE DIFF experiment with excitation at 1.15 ppm and mixing time 1.0 s; (D) - NOE DIFF experiment with excitation at 0.72 ppm and mixing time 1 s.

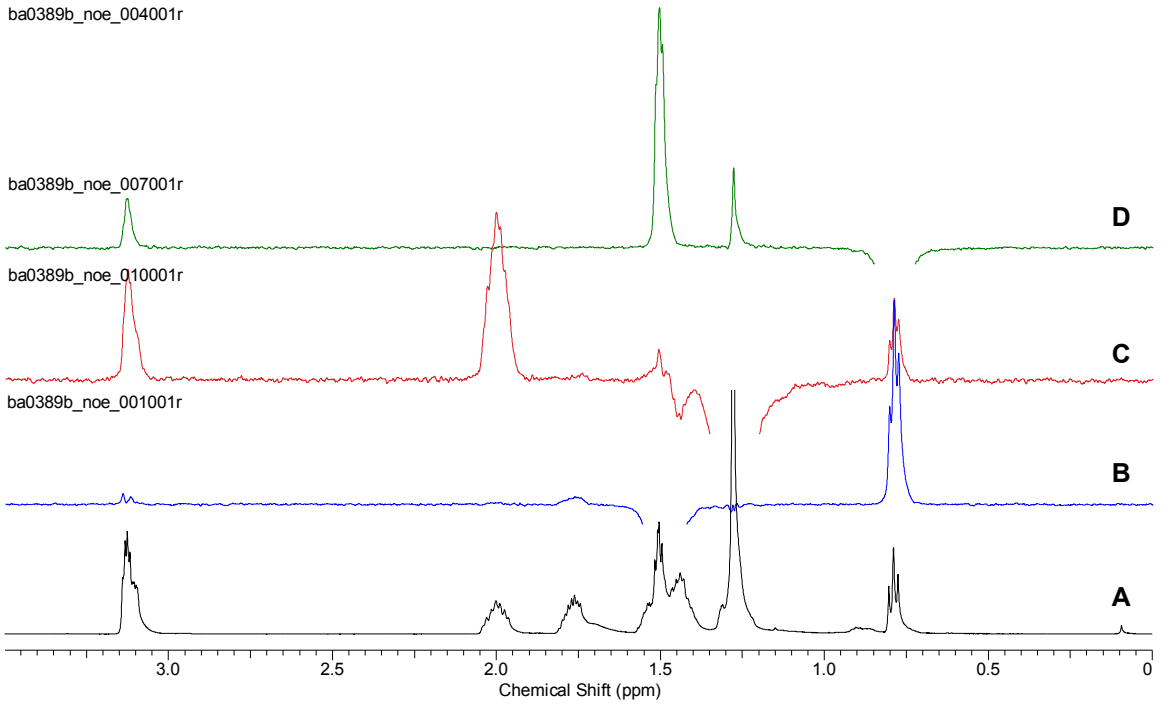
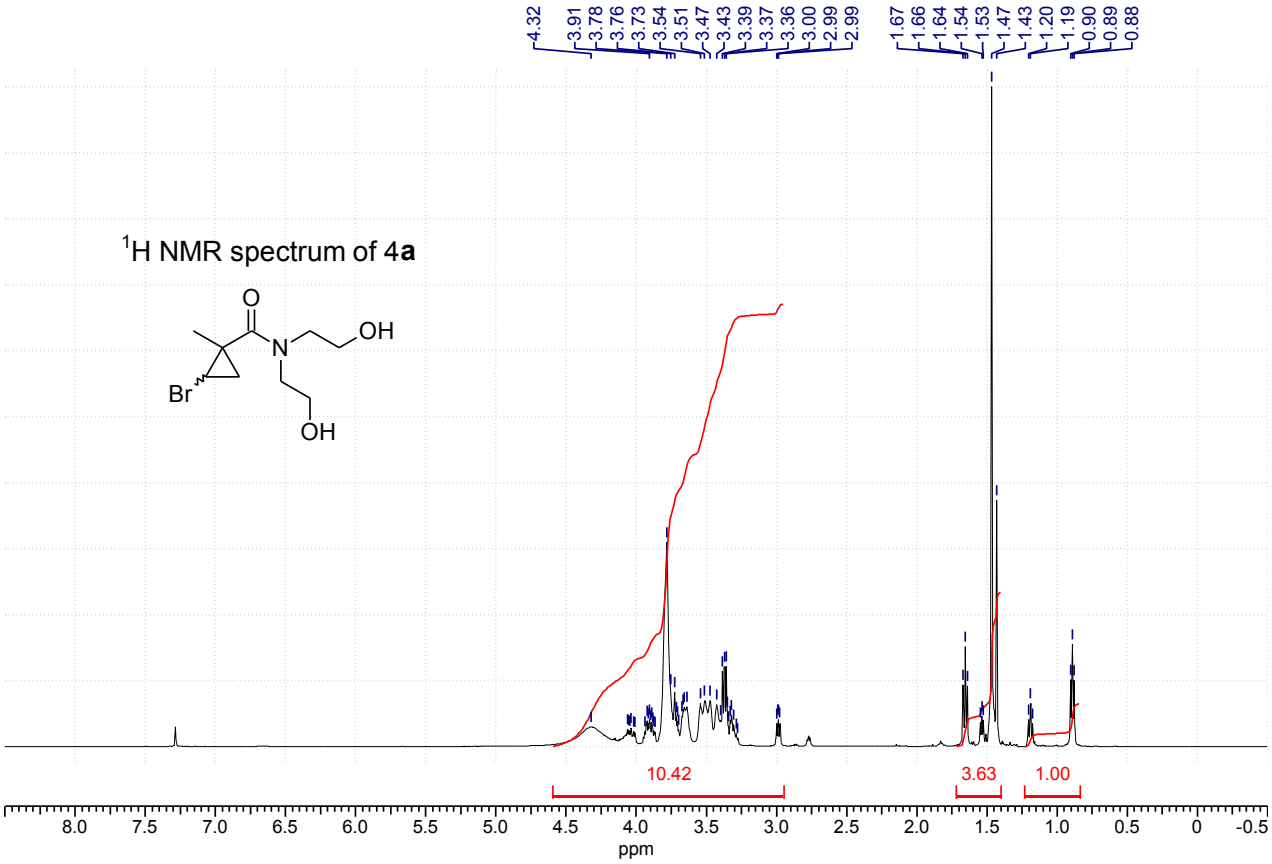


Figure 4. NOE experiments performed for compound **6j**. All spectra were registered at 500.13 MHz. The charts represent: (A) – reference ^{1}H NMR spectrum; (B) – NOE DIFF experiment with excitation at 1.51 ppm and mixing time 1 s; (C) - NOE DIFF experiment with excitation at 1.28 ppm and mixing time 1.0 s; (D) - NOE DIFF experiment with excitation at 0.79 ppm and mixing time 1 s.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3.51
3.47
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3.37
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3.00
2.99
2.99
1.67
1.66
1.64
1.54
1.53
1.47
1.43
1.20
1.19
0.90
0.89
0.88
1H NMR spectrum of 4a
O
N
OH
Br
OH
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3.63
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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0
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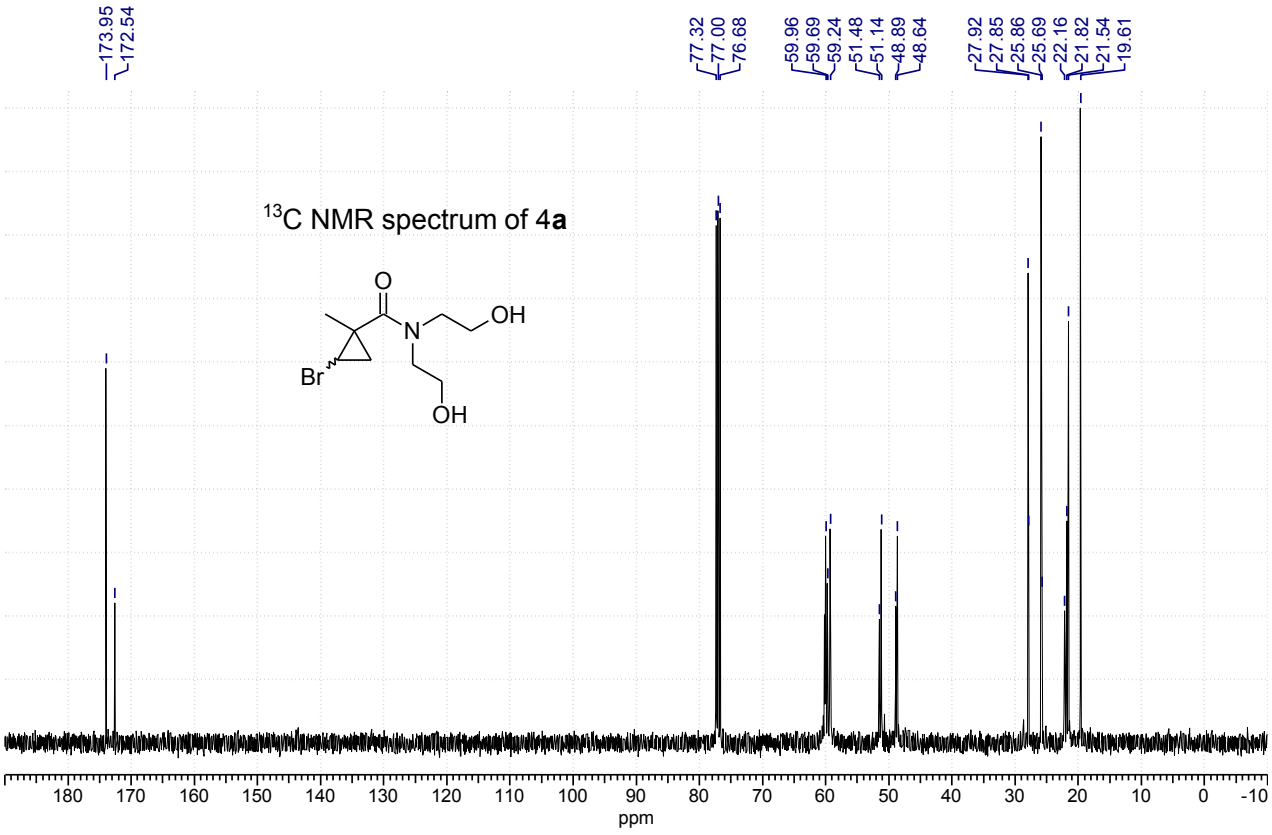
ppm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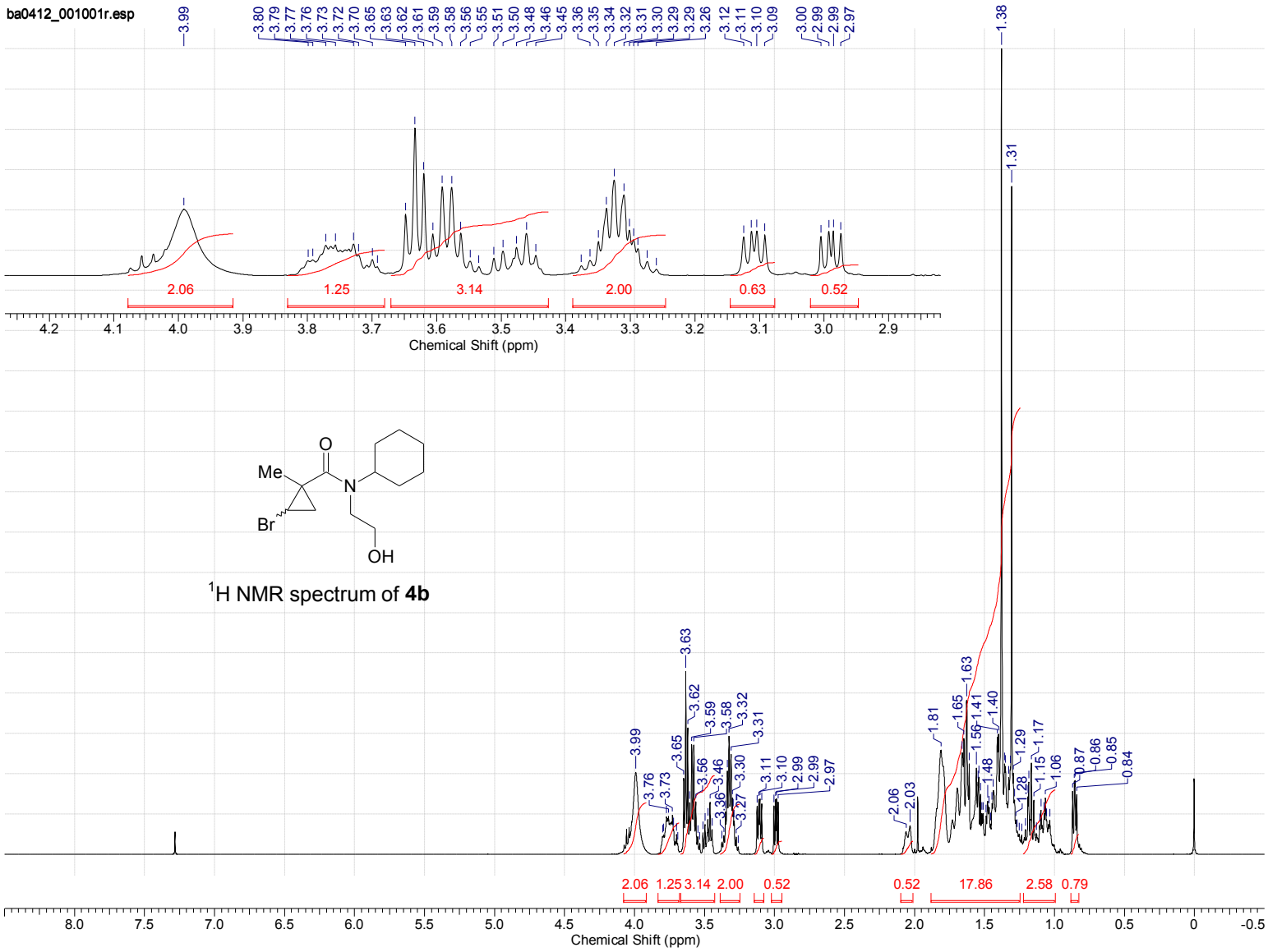
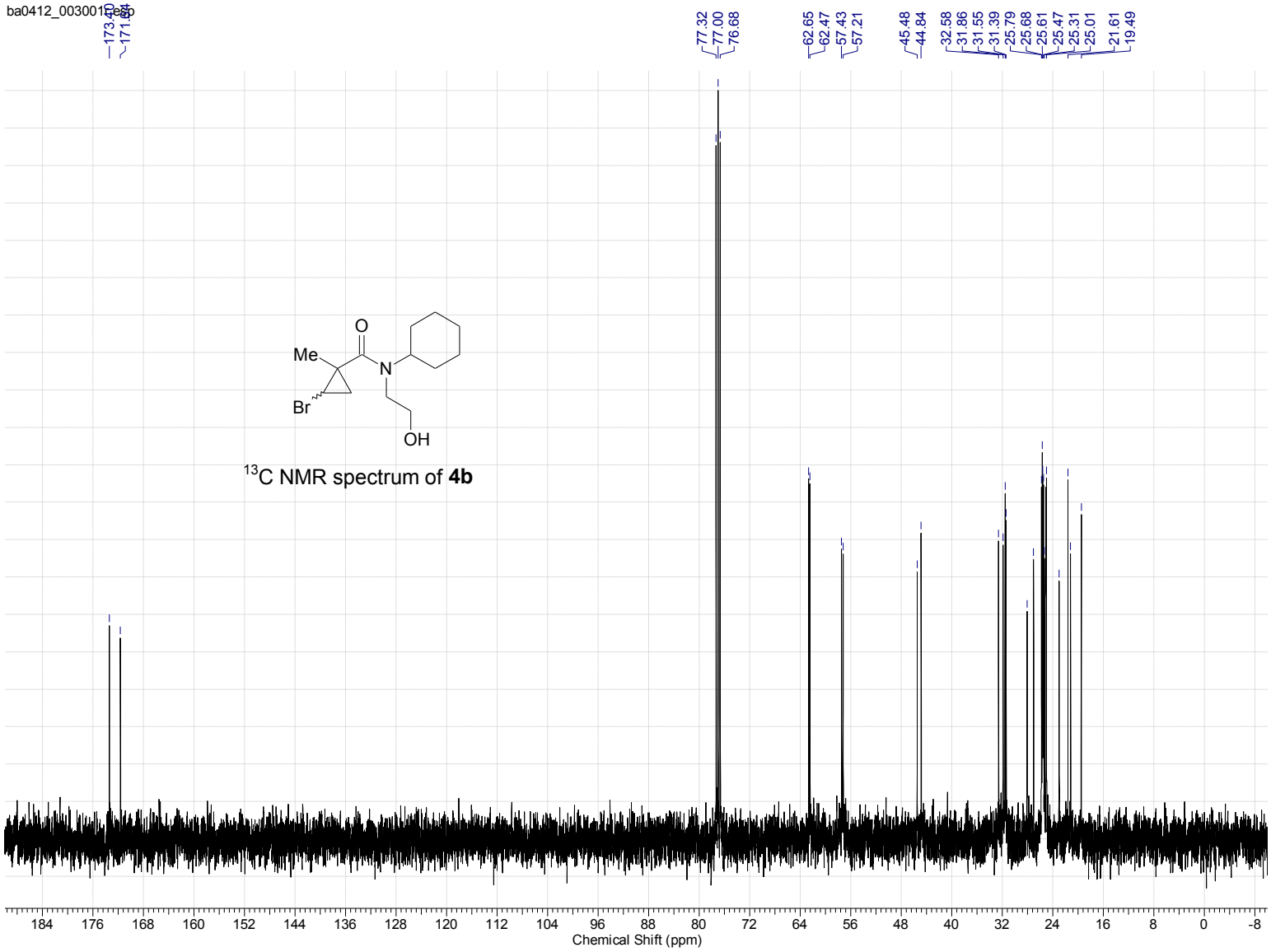
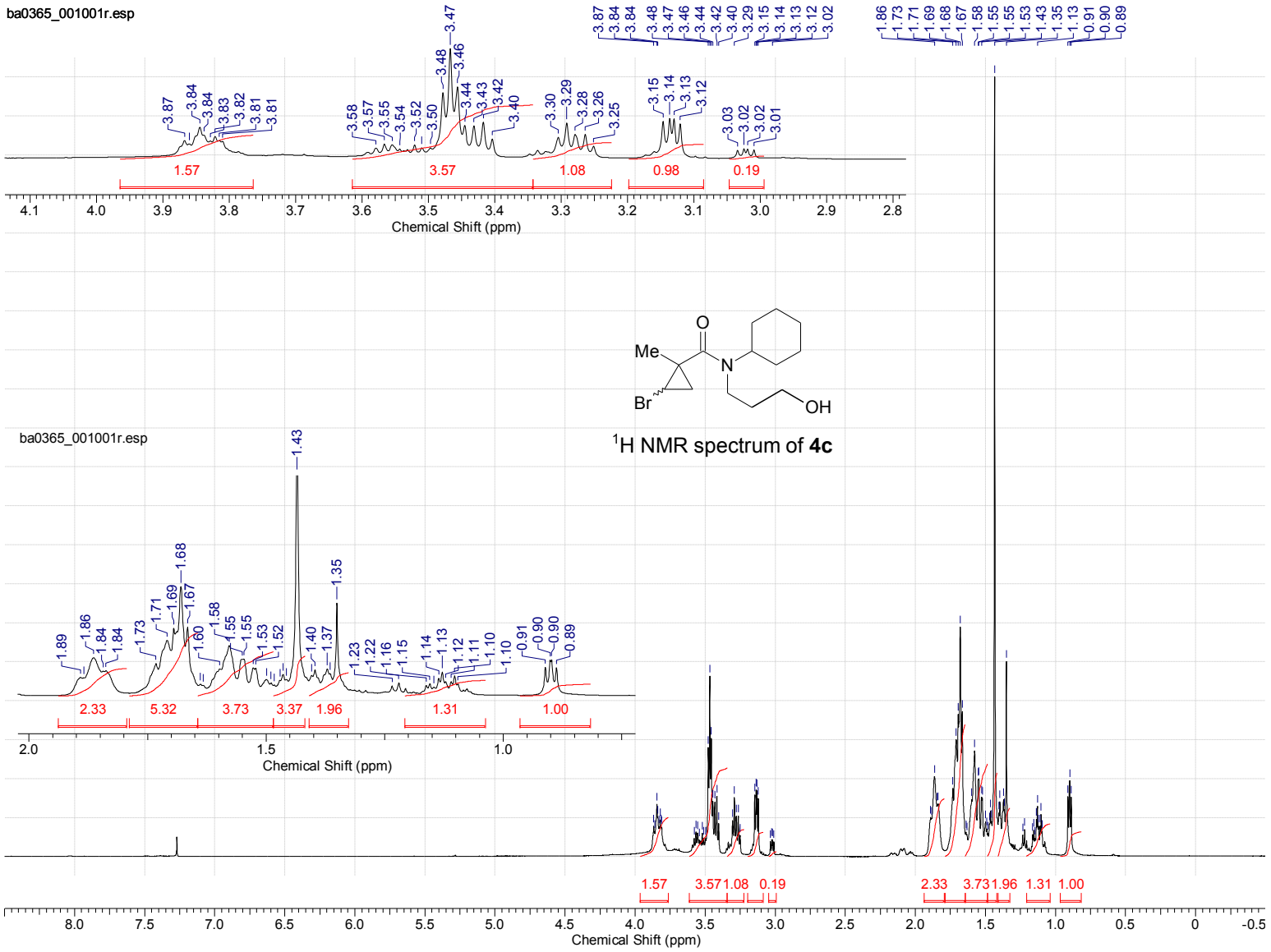
77.00
76.68
59.96
59.69
59.24
51.48
51.14
48.89
48.64
27.92
27.85
25.86
25.69
22.16
21.82
21.54
19.61
13C NMR spectrum of 4a
O
N
OH
Br
OH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm



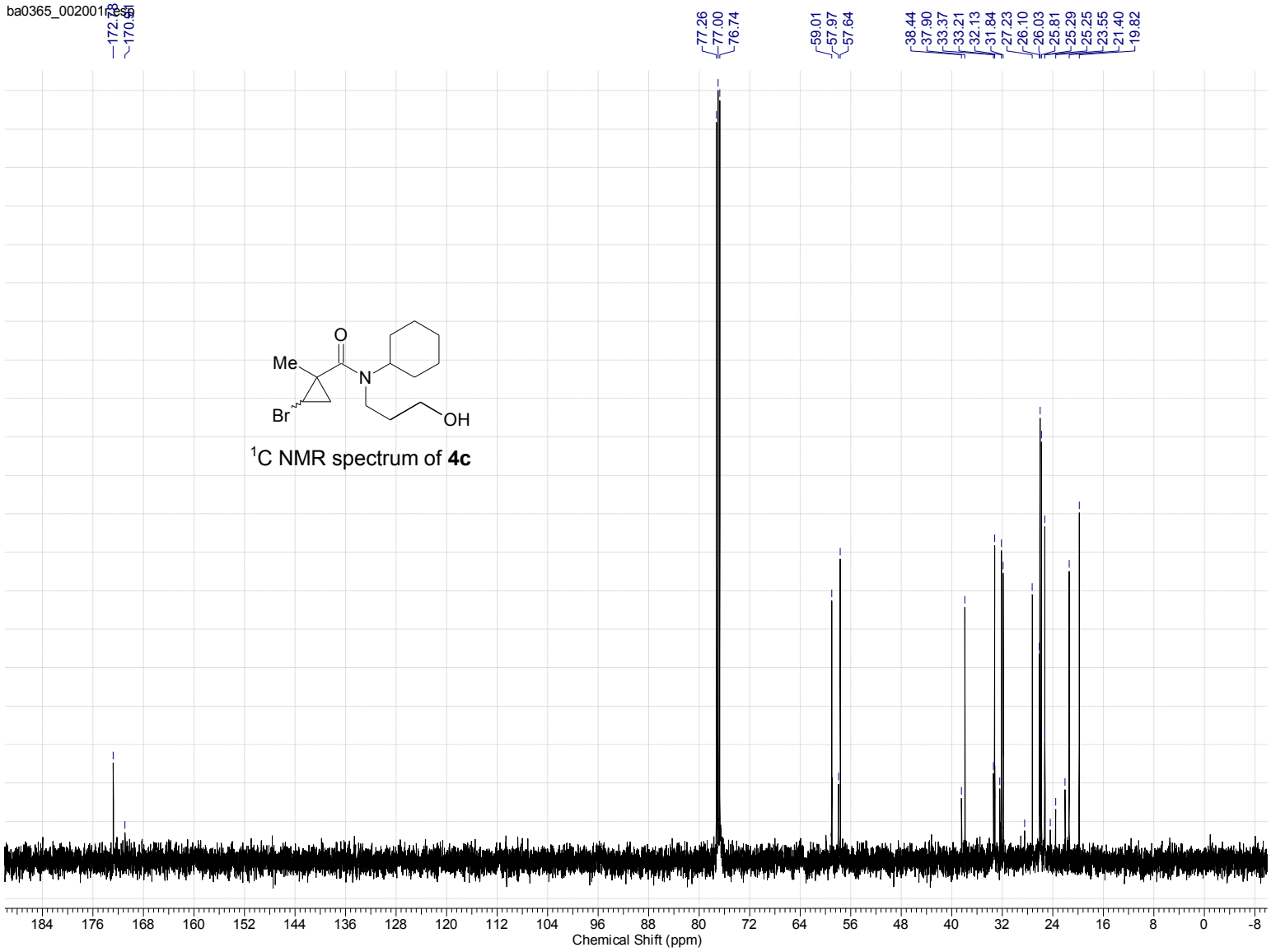
^{1}H NMR spectrum of **4b**



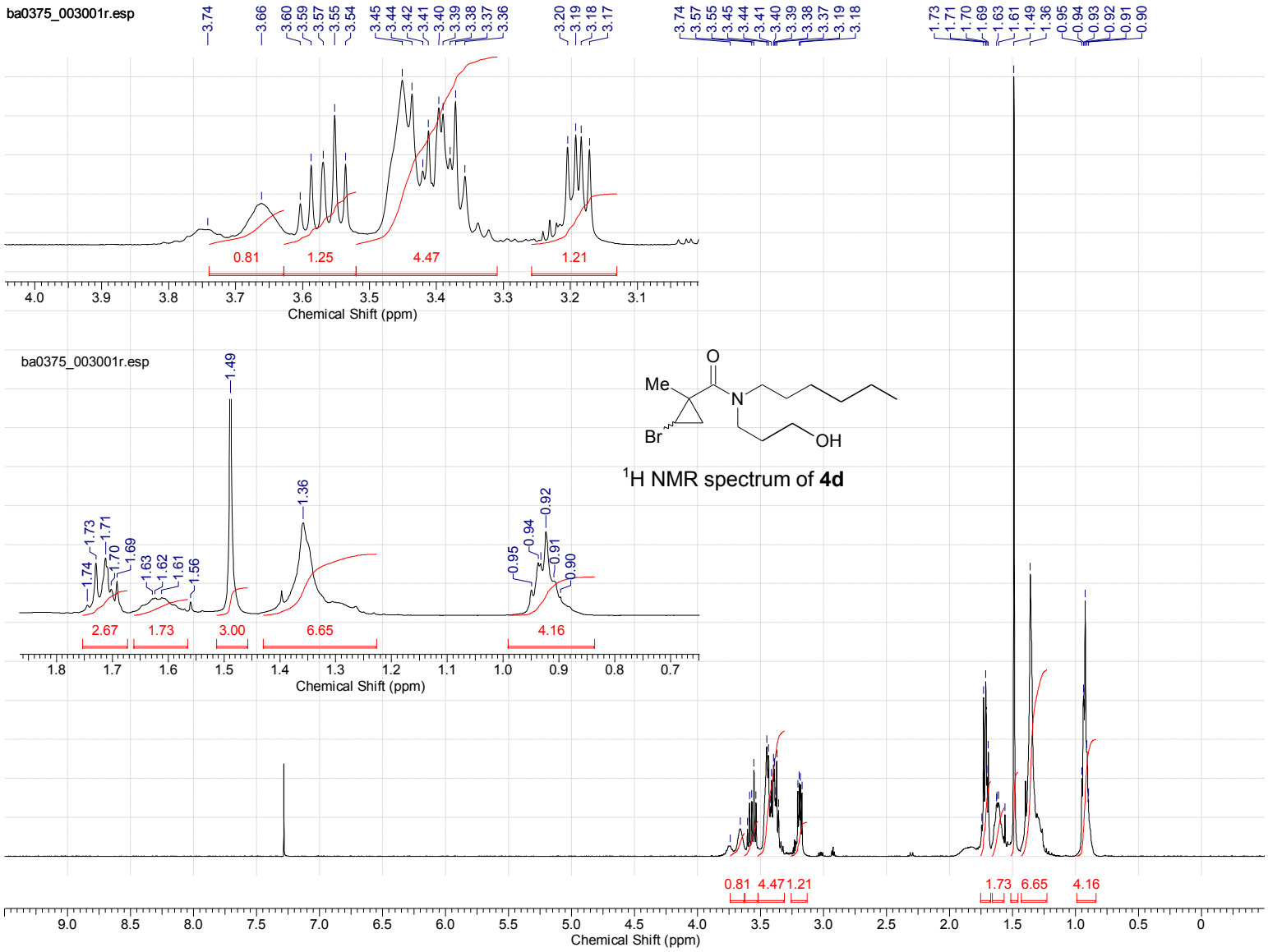
^{13}C NMR spectrum of **4b**



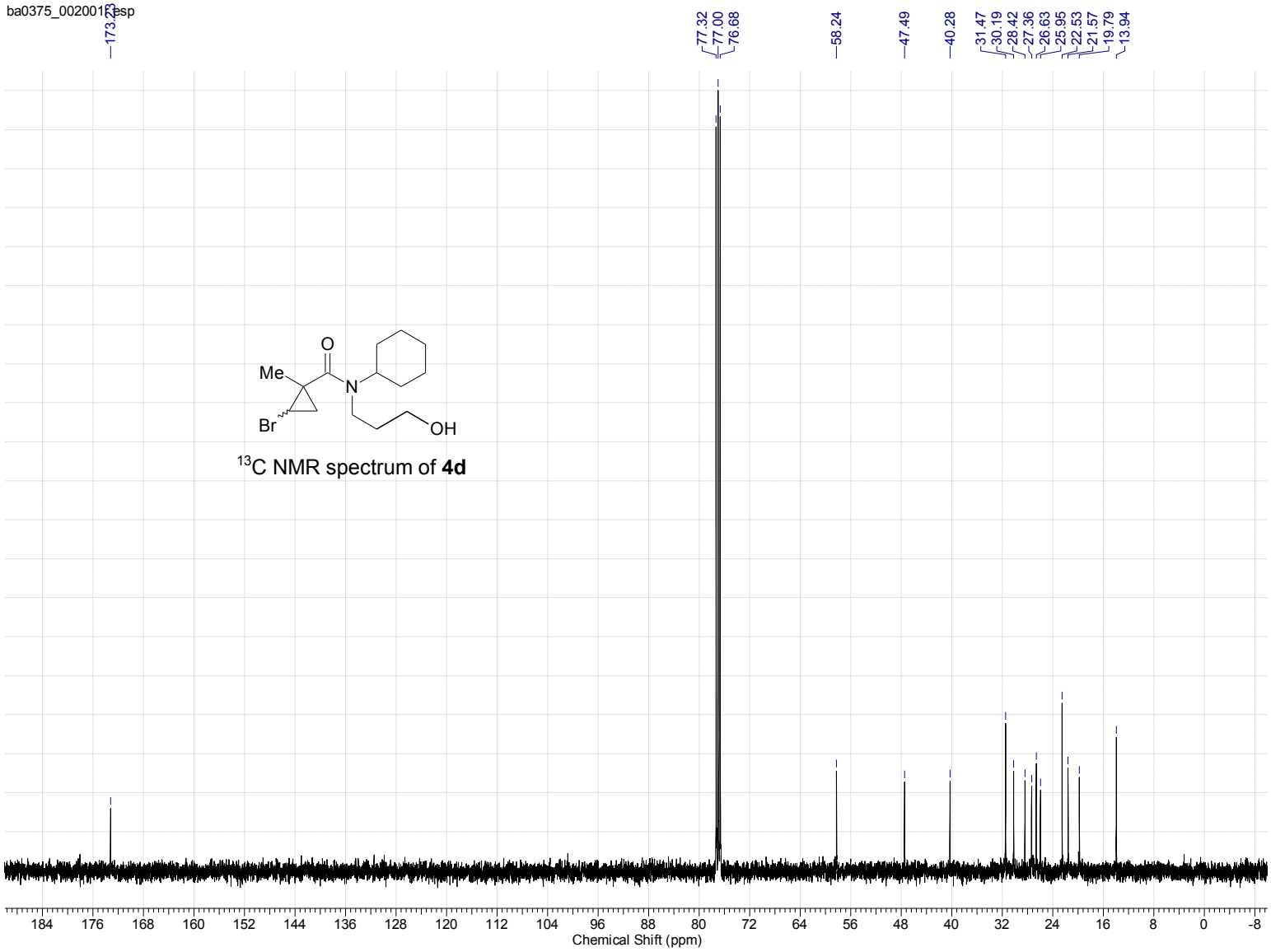
^{1}H NMR spectrum of **4c**



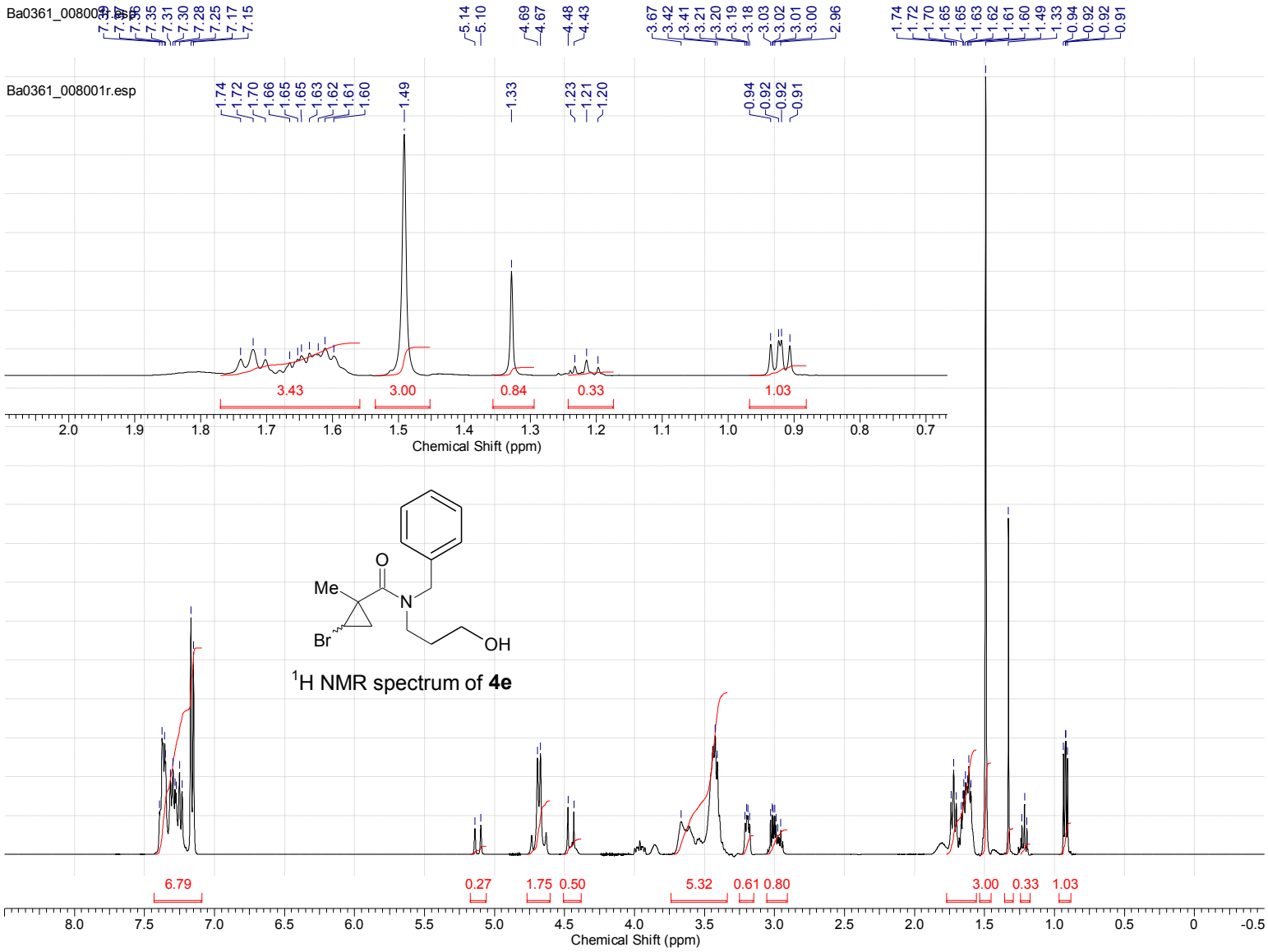
^{1}C NMR spectrum of **4c**



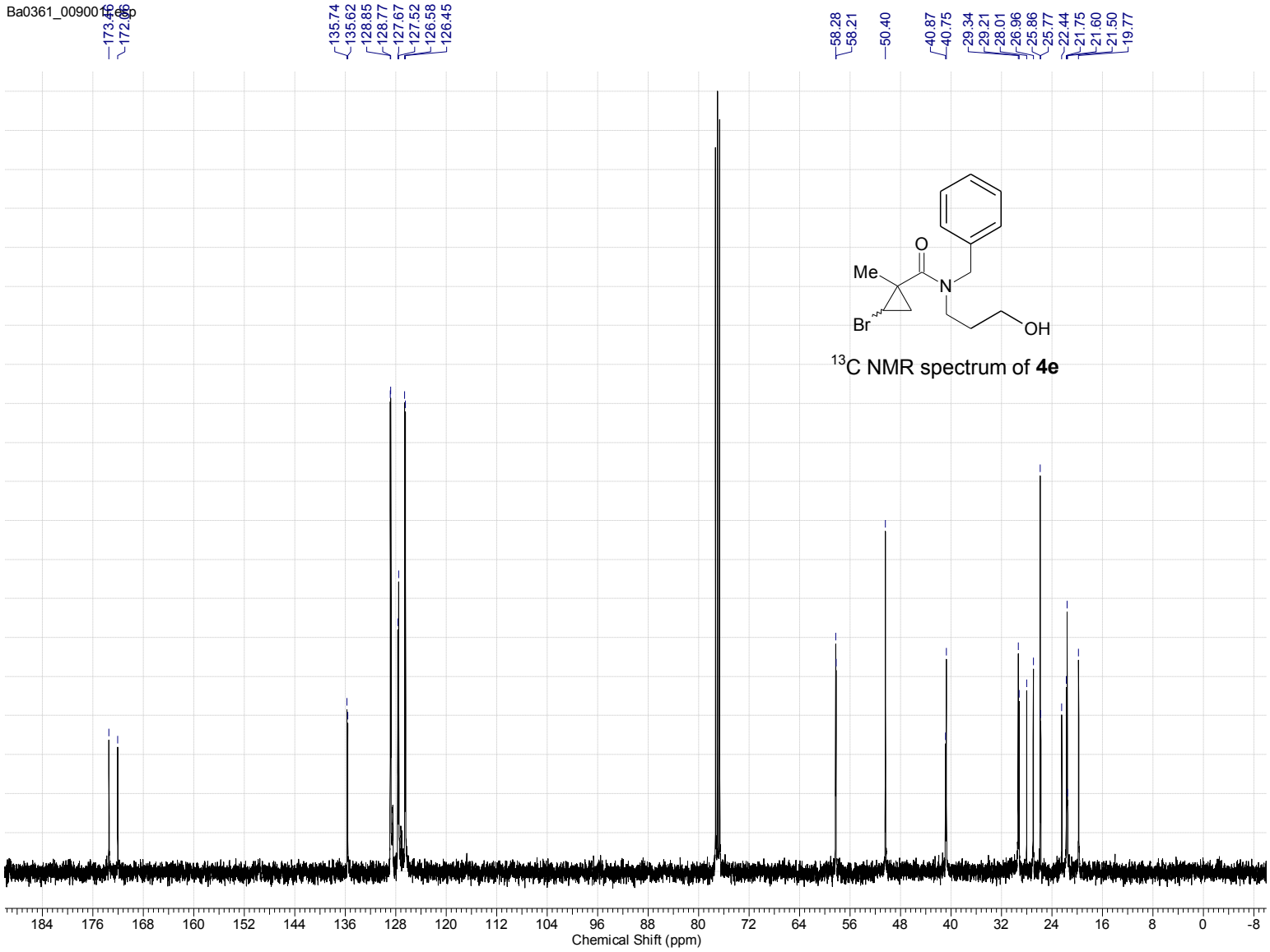
^{1}H NMR spectrum of **4d**



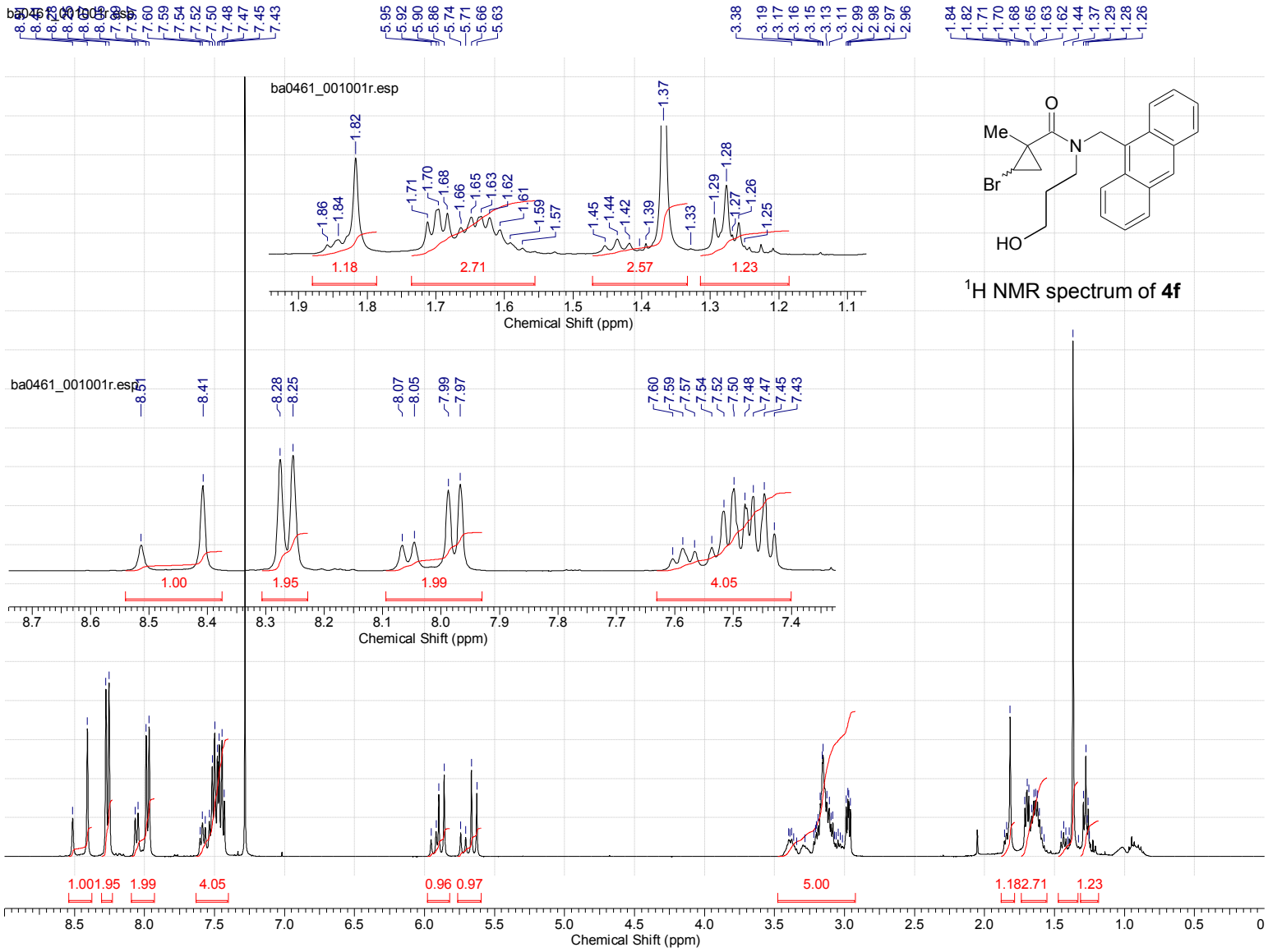
^{13}C NMR spectrum of **4d**



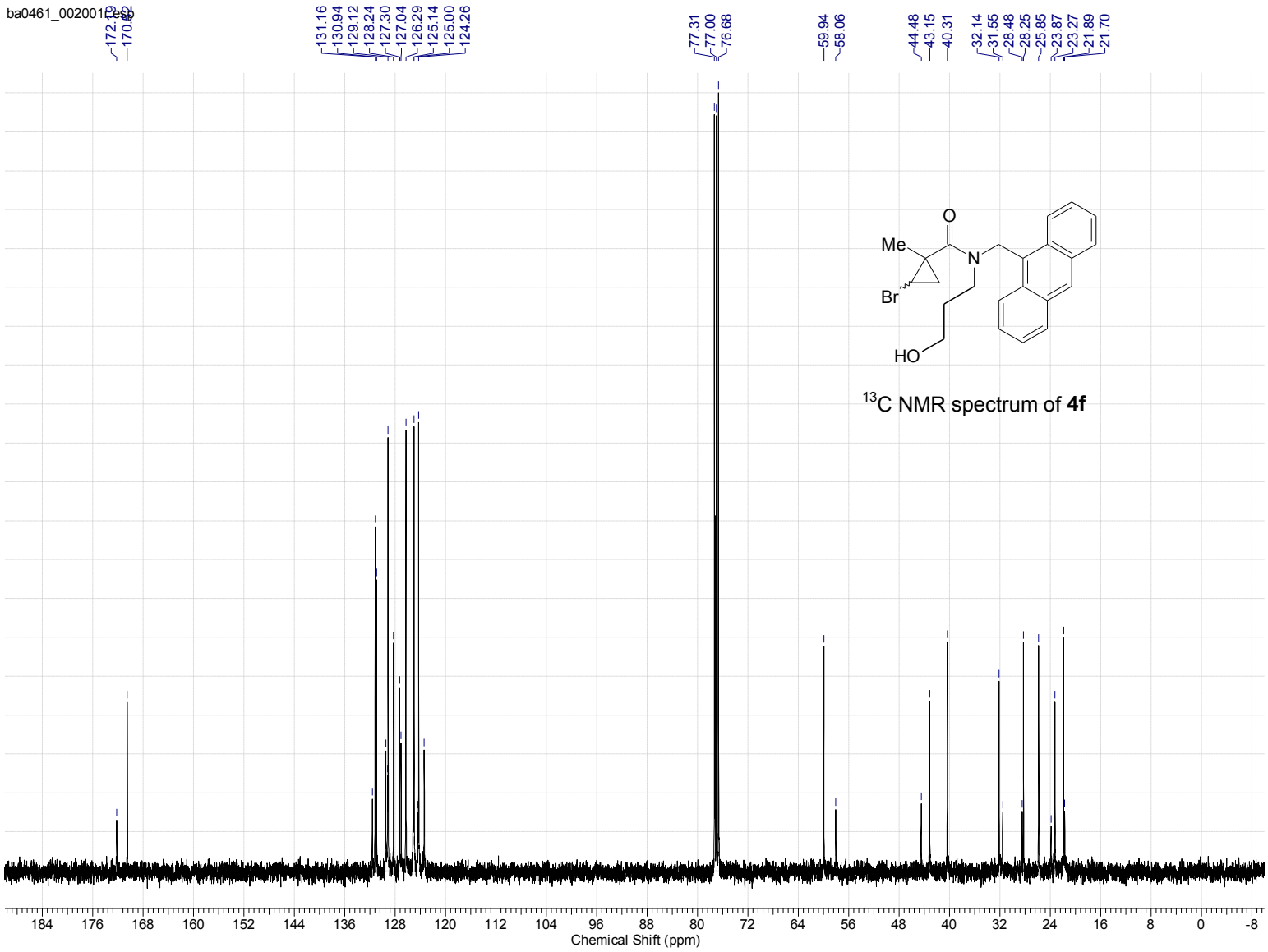
^{1}H NMR spectrum of **4e**



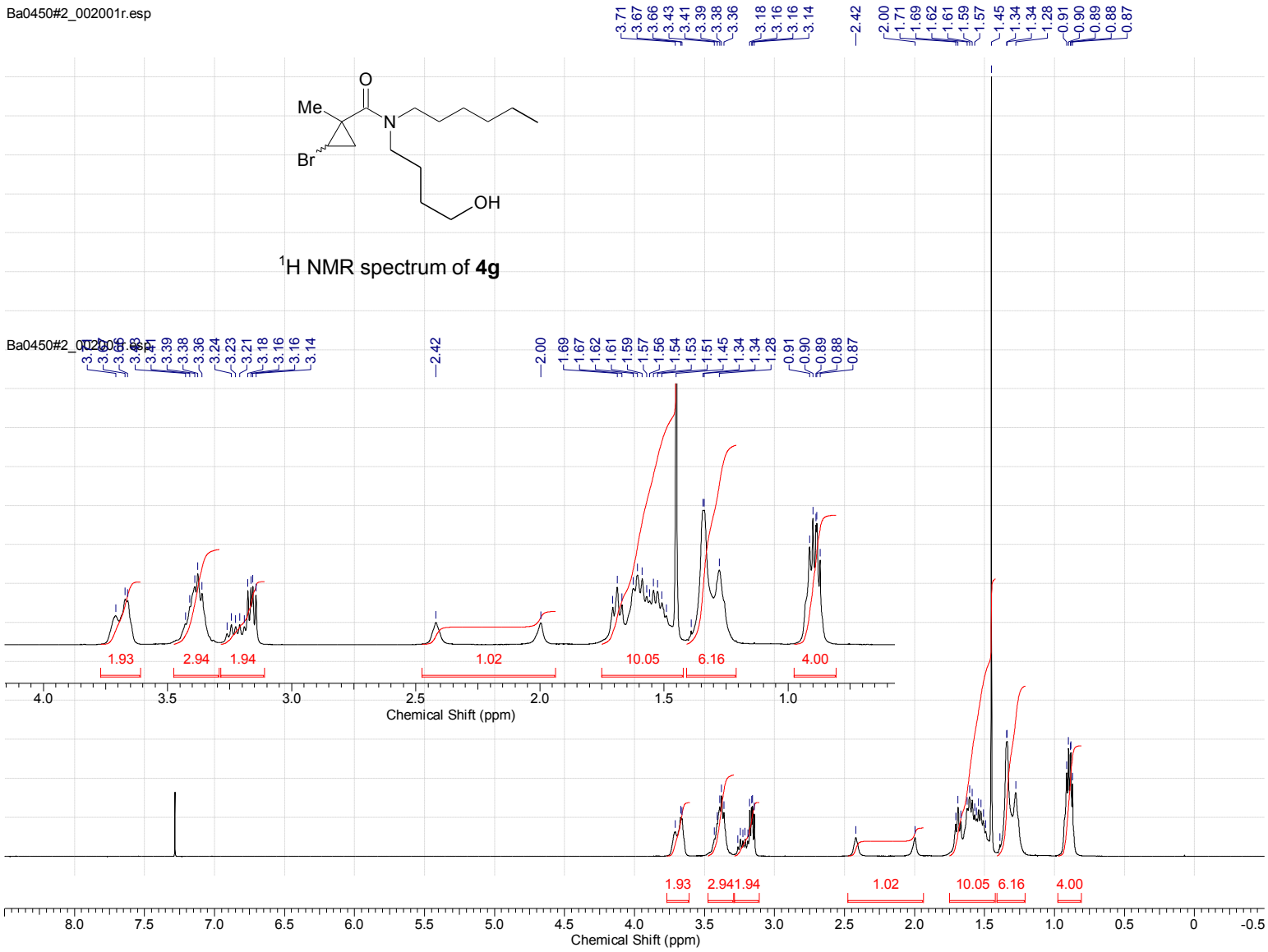
^{13}C NMR spectrum of **4e**



^{1}H NMR spectrum of **4f**



^{13}C NMR spectrum of **4f**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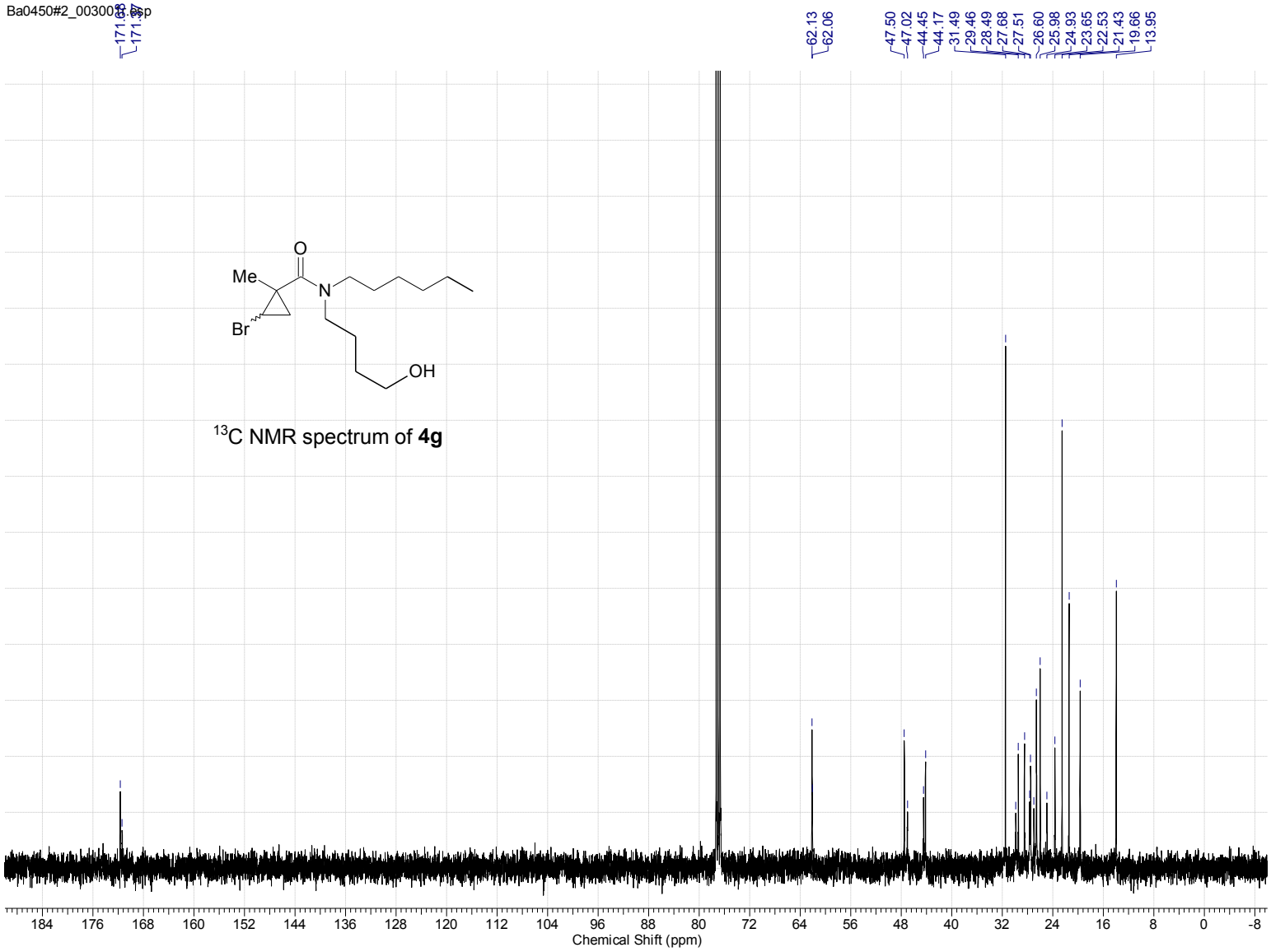
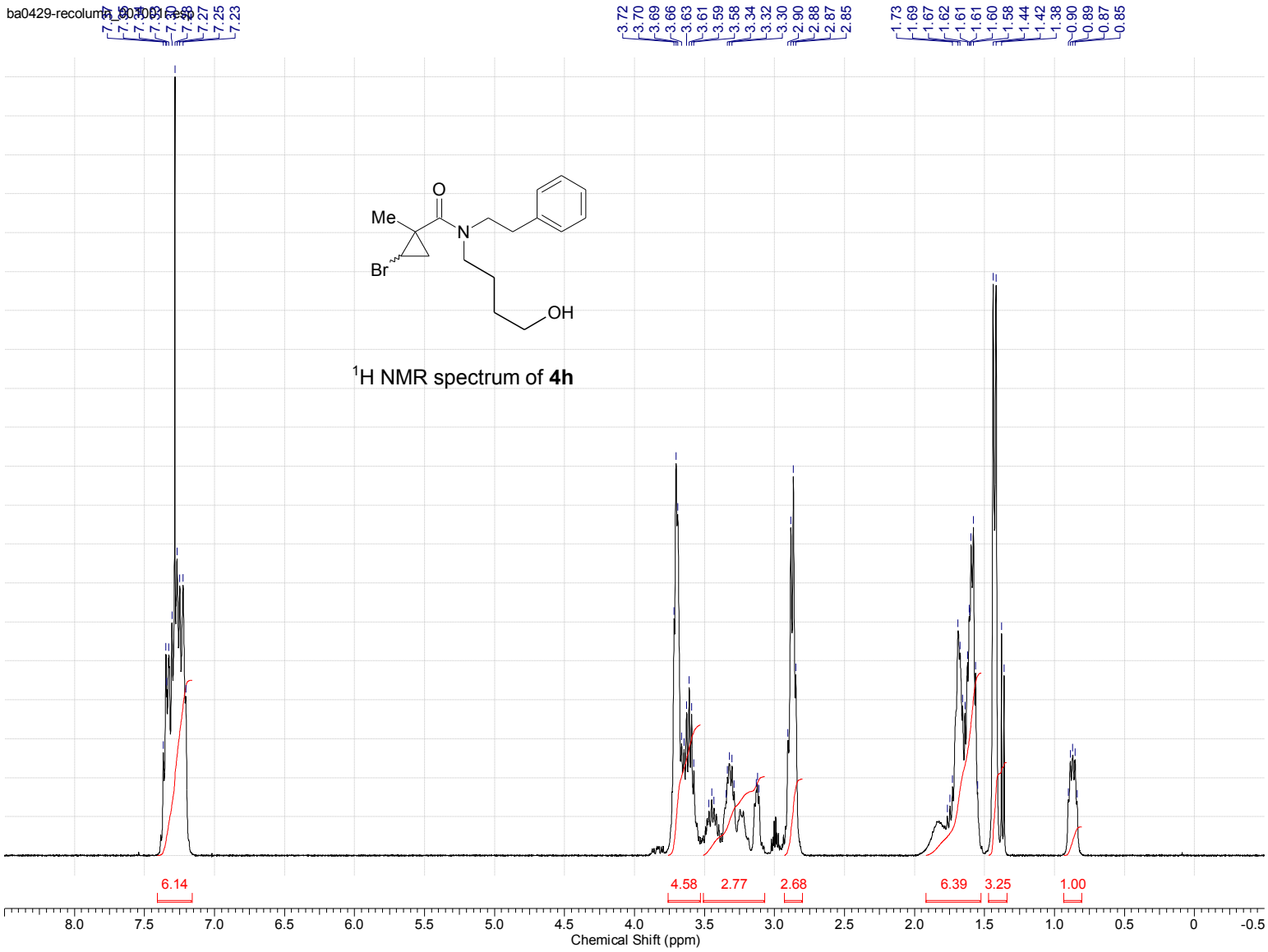
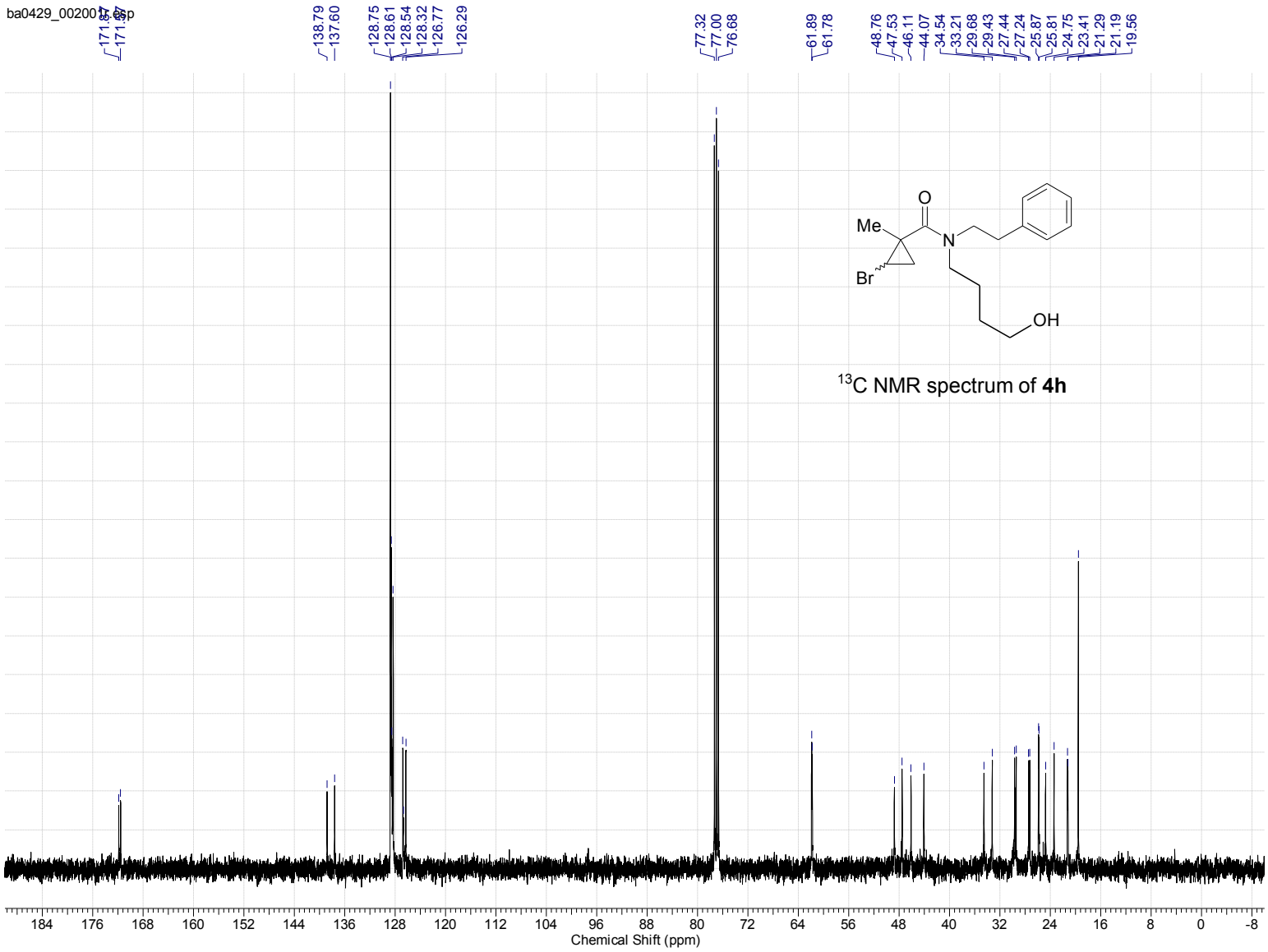
O
N
OH
1H NMR spectrum of 4g
Chemical Shift (ppm)



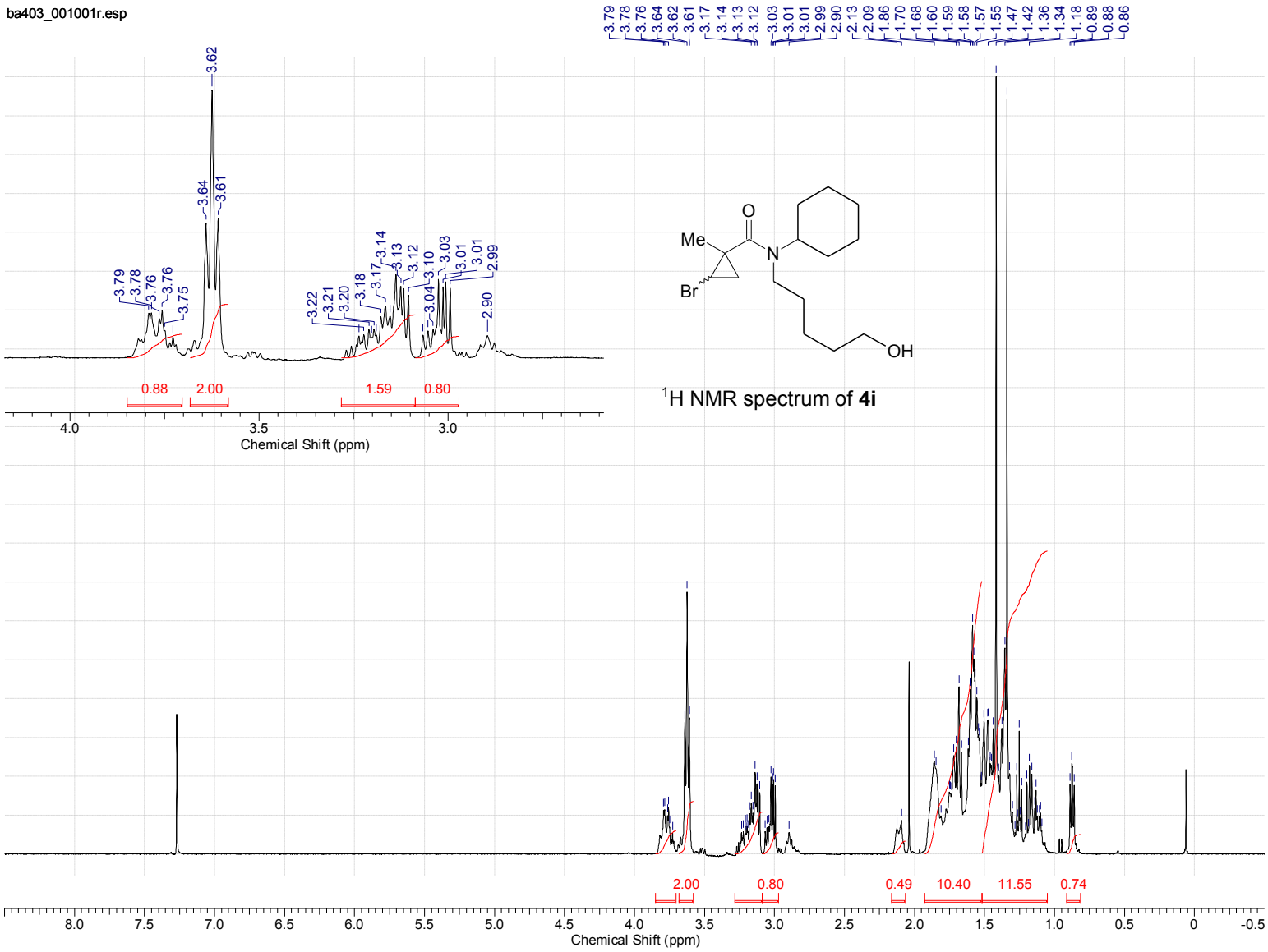
^{13}C NMR spectrum of **4g**



^{1}H NMR spectrum of **4h**



^{13}C NMR spectrum of **4h**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3.5
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Chemical Shift (ppm)
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Me
N
Br
OH
1H NMR spectrum of 4i
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7.0
6.5
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5.0
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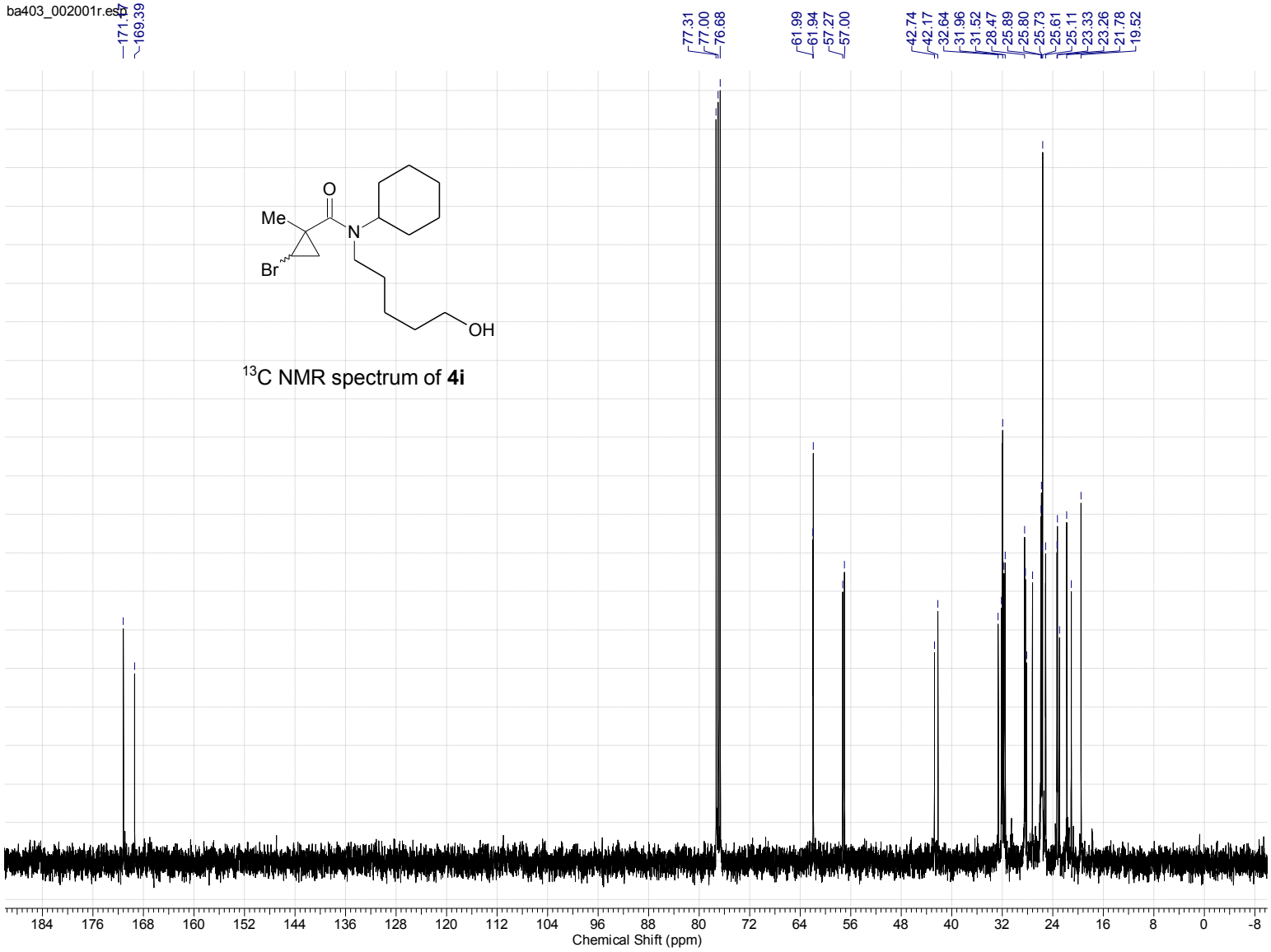
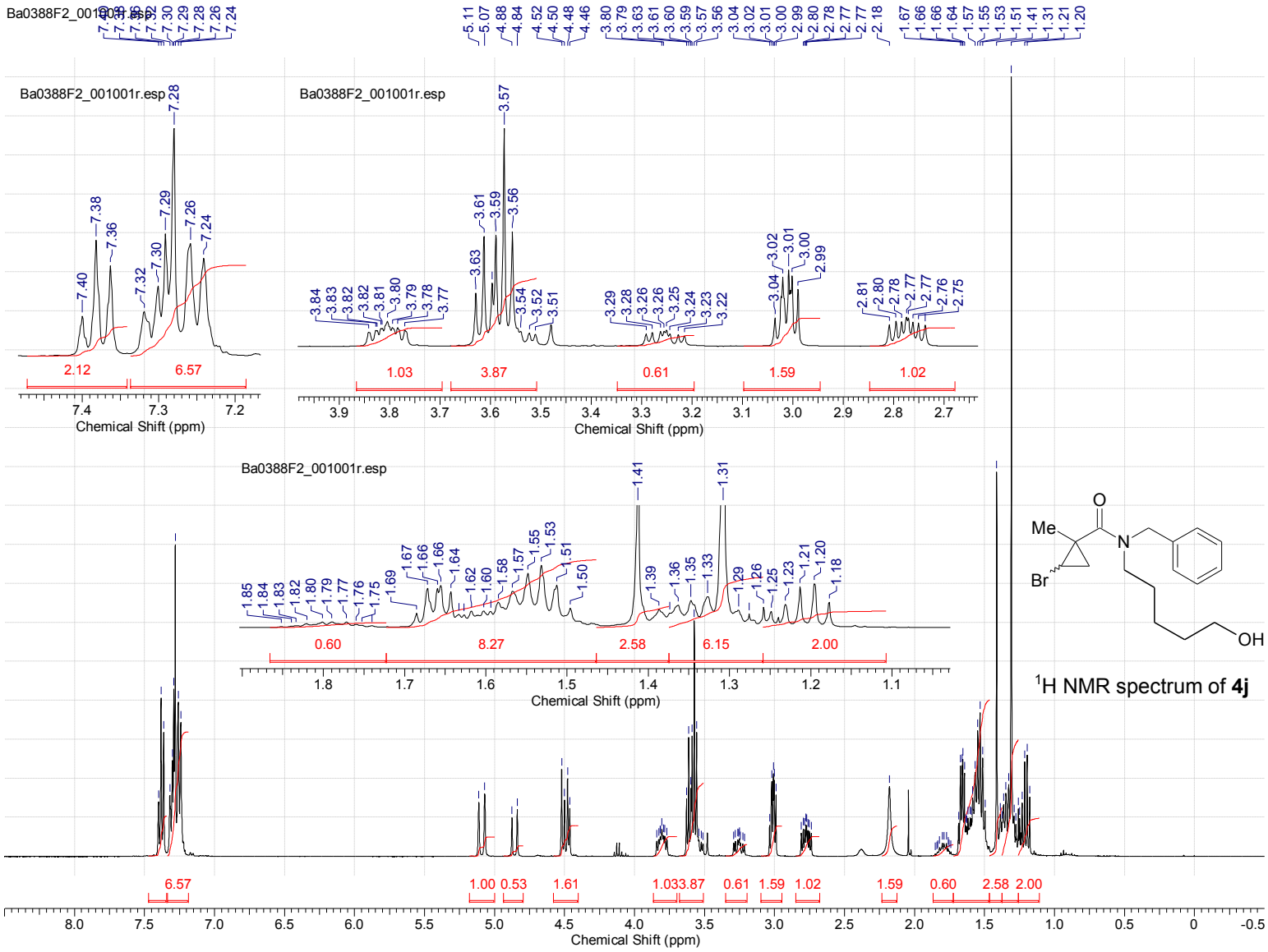
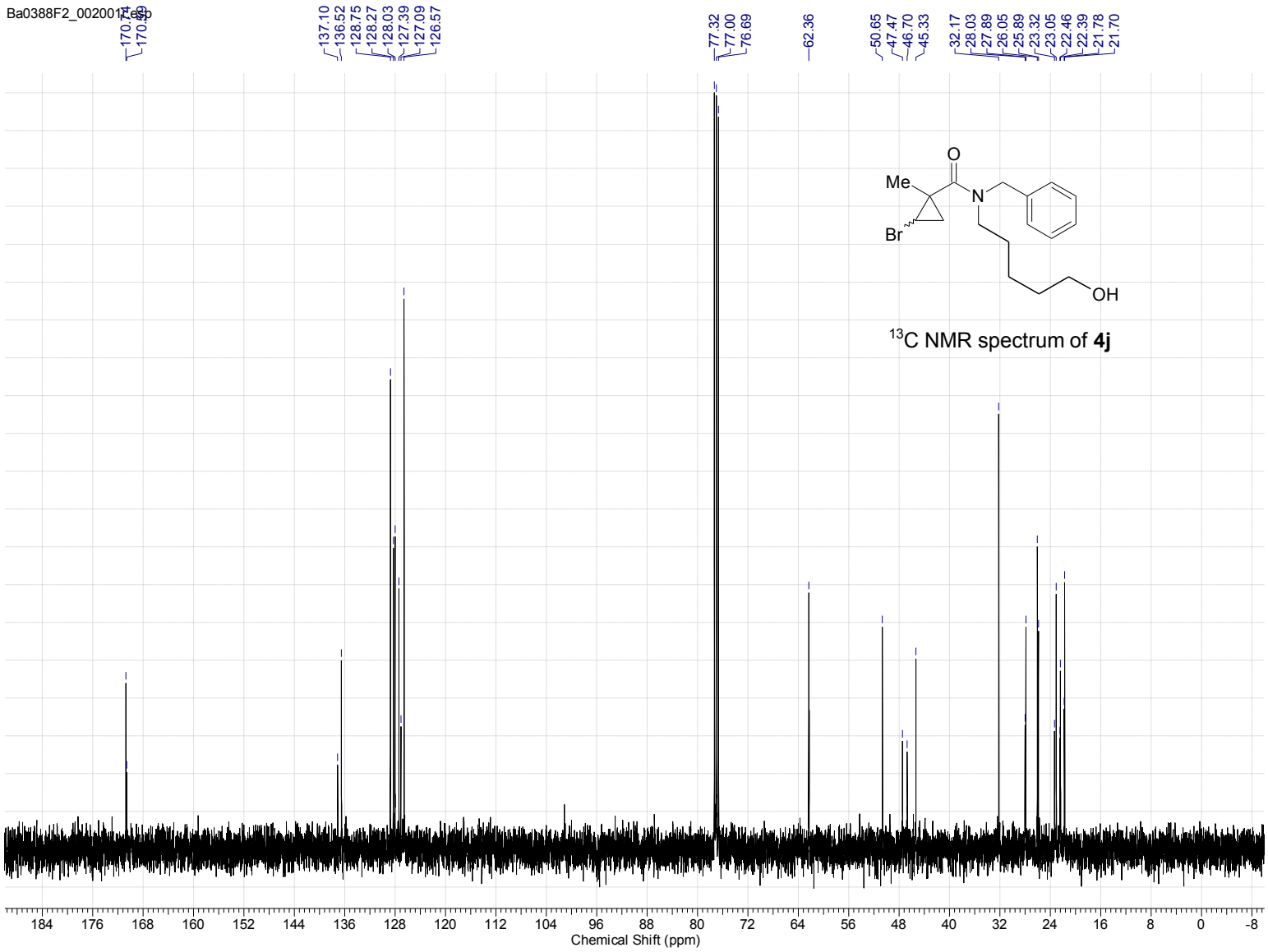
Chemical Shift (ppm)



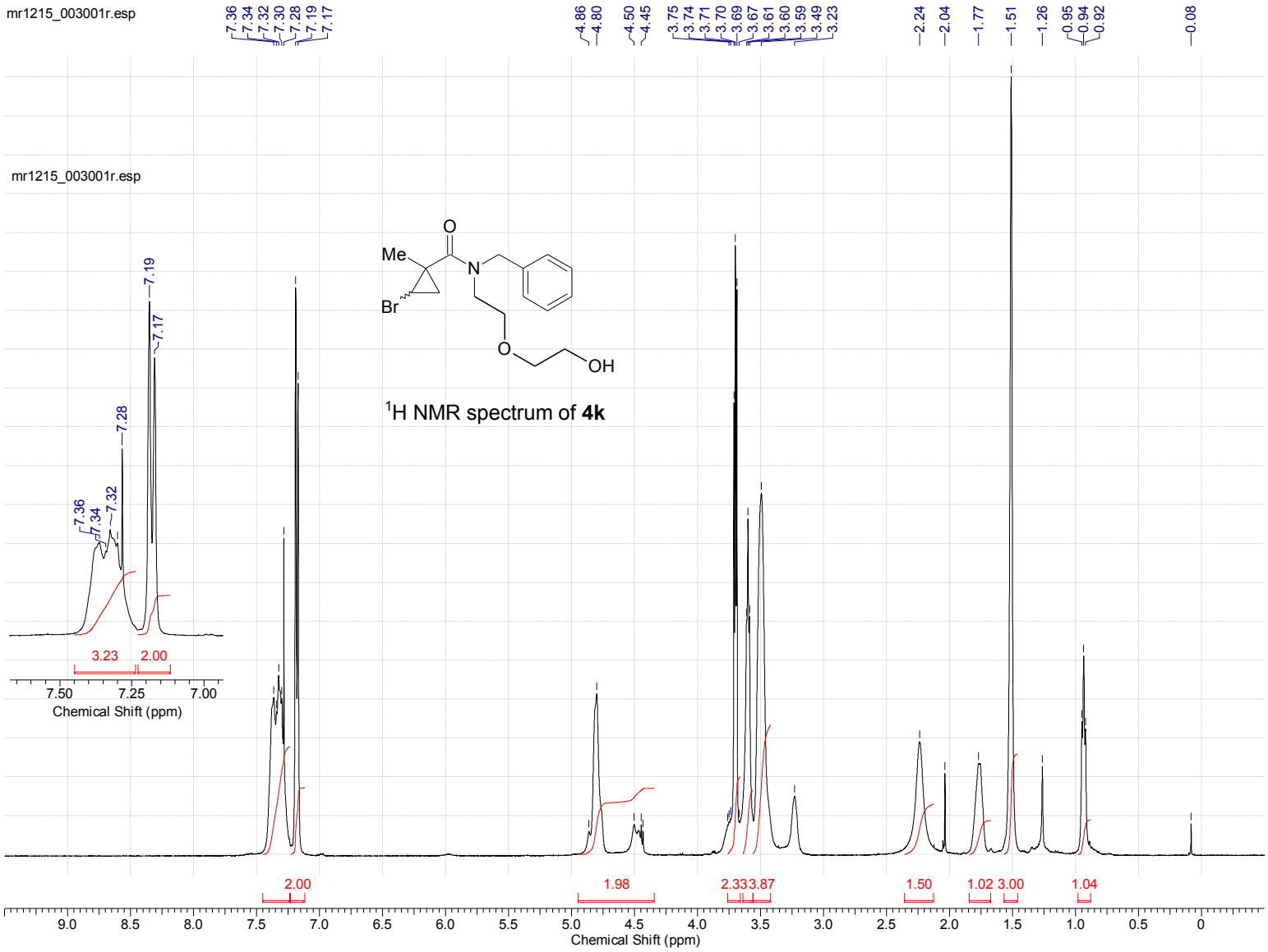
^{13}C NMR spectrum of **4i**



^{1}H NMR spectrum of **4j**



^{13}C NMR spectrum of **4j**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Br
N
O
O
OH
1H NMR spectrum of 4k
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Chemical Shift (ppm)
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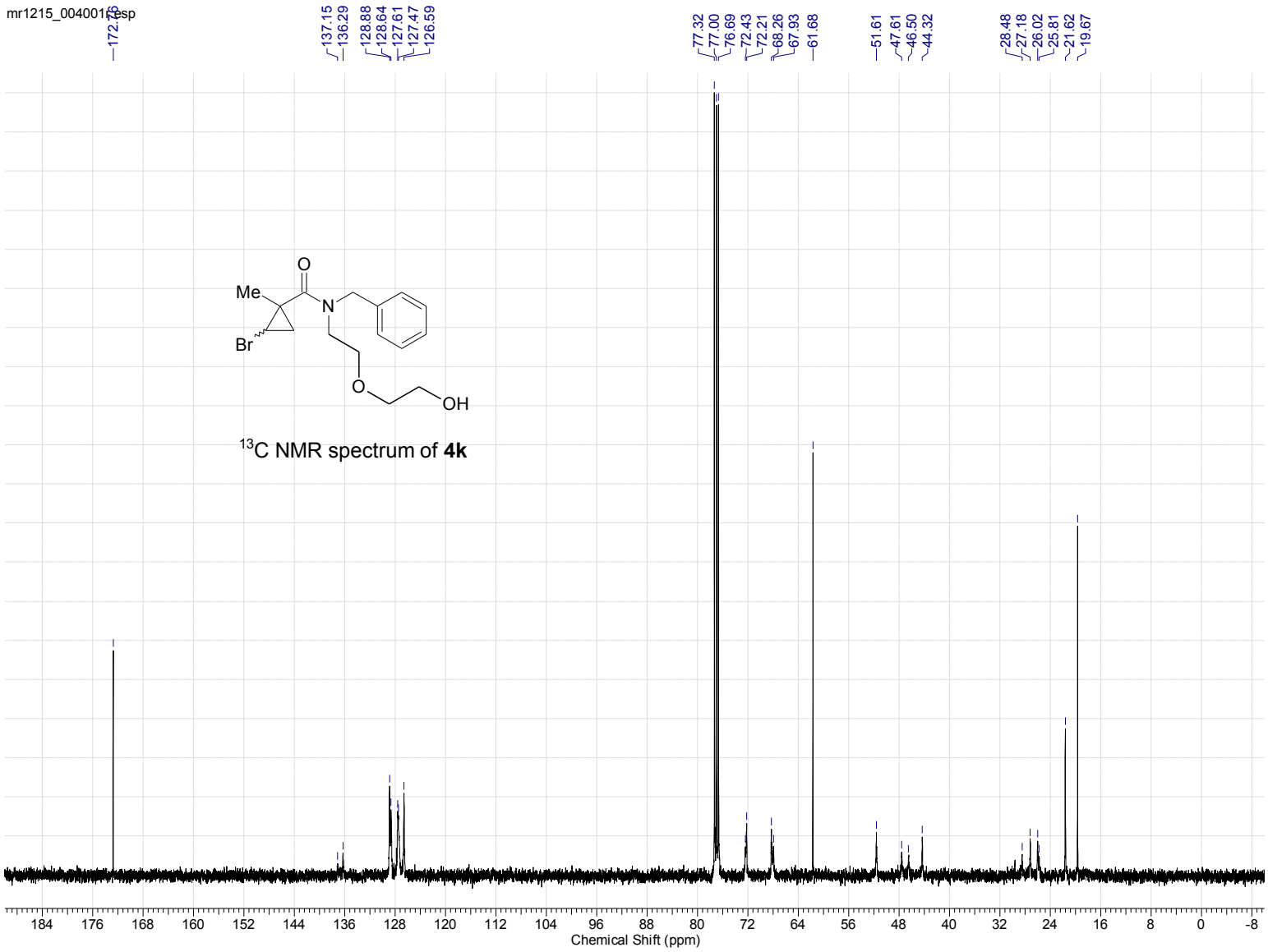
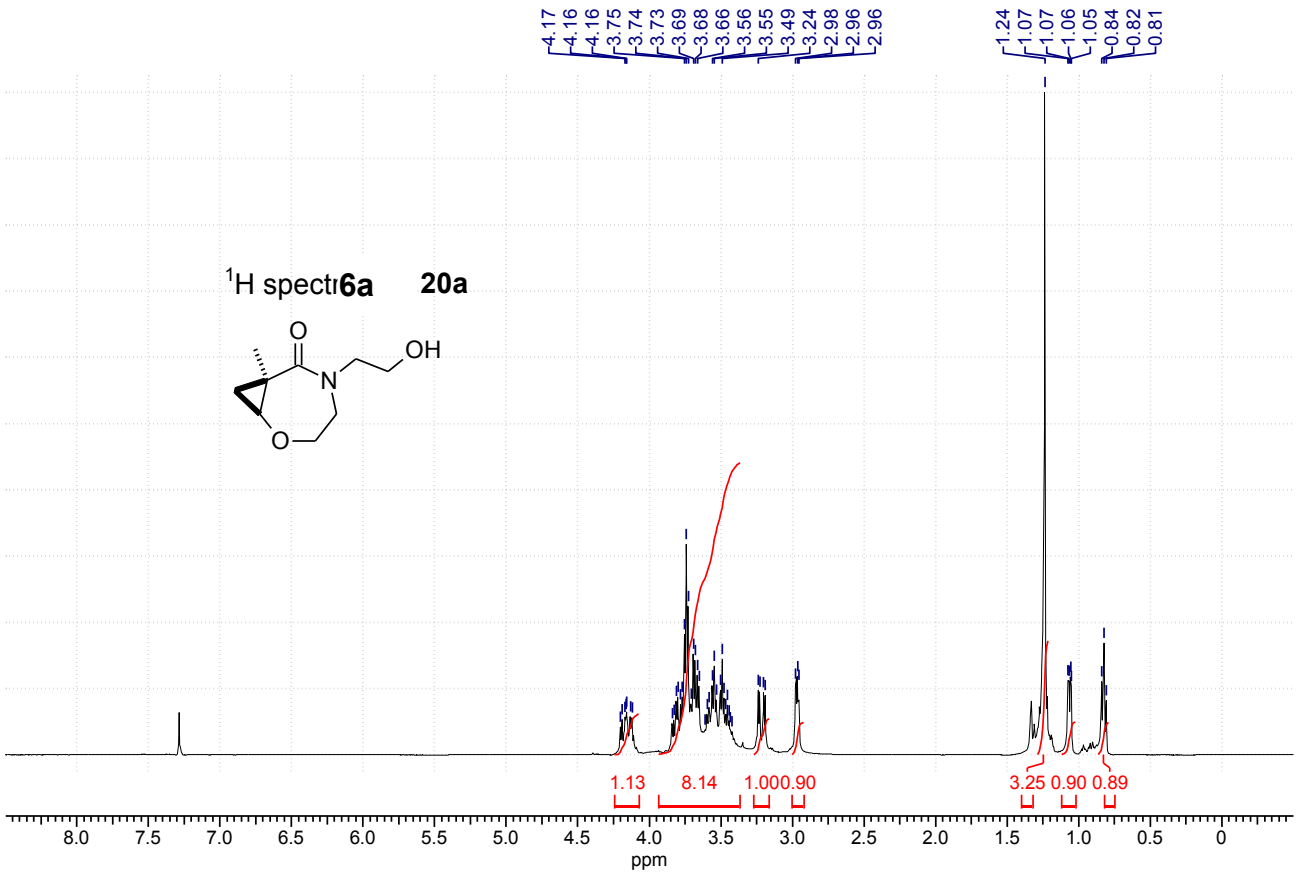
1.02
3.00
1.04
Chemical Shift (ppm)



^{13}C NMR spectrum of **4k**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3.24
2.98
2.96
2.96
1.24
1.07
1.07
1.06
1.05
0.84
0.82
0.81
1H spectr 6a 20a
O
OH
N
O
1.13
8.14
1.00
0.90
3.25
0.90
0.89
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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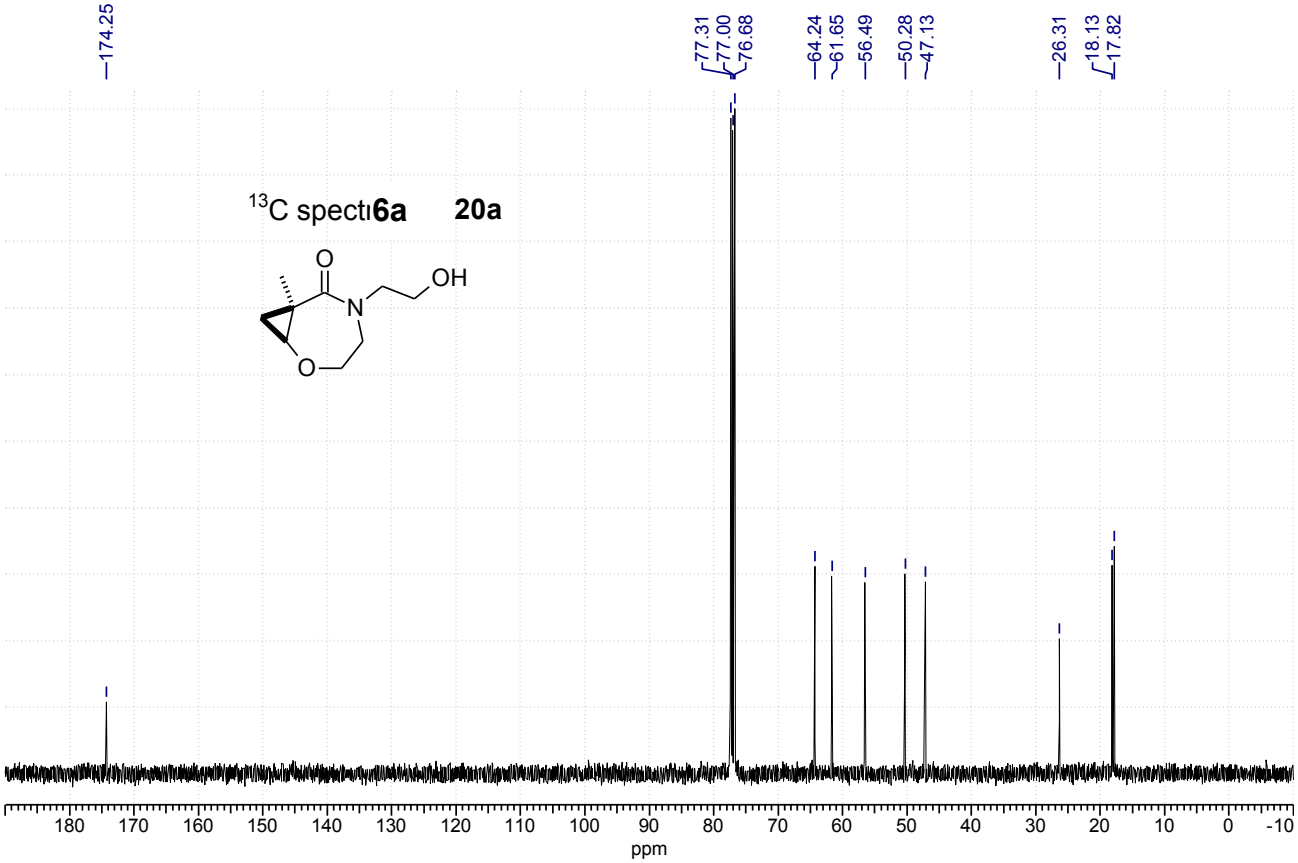
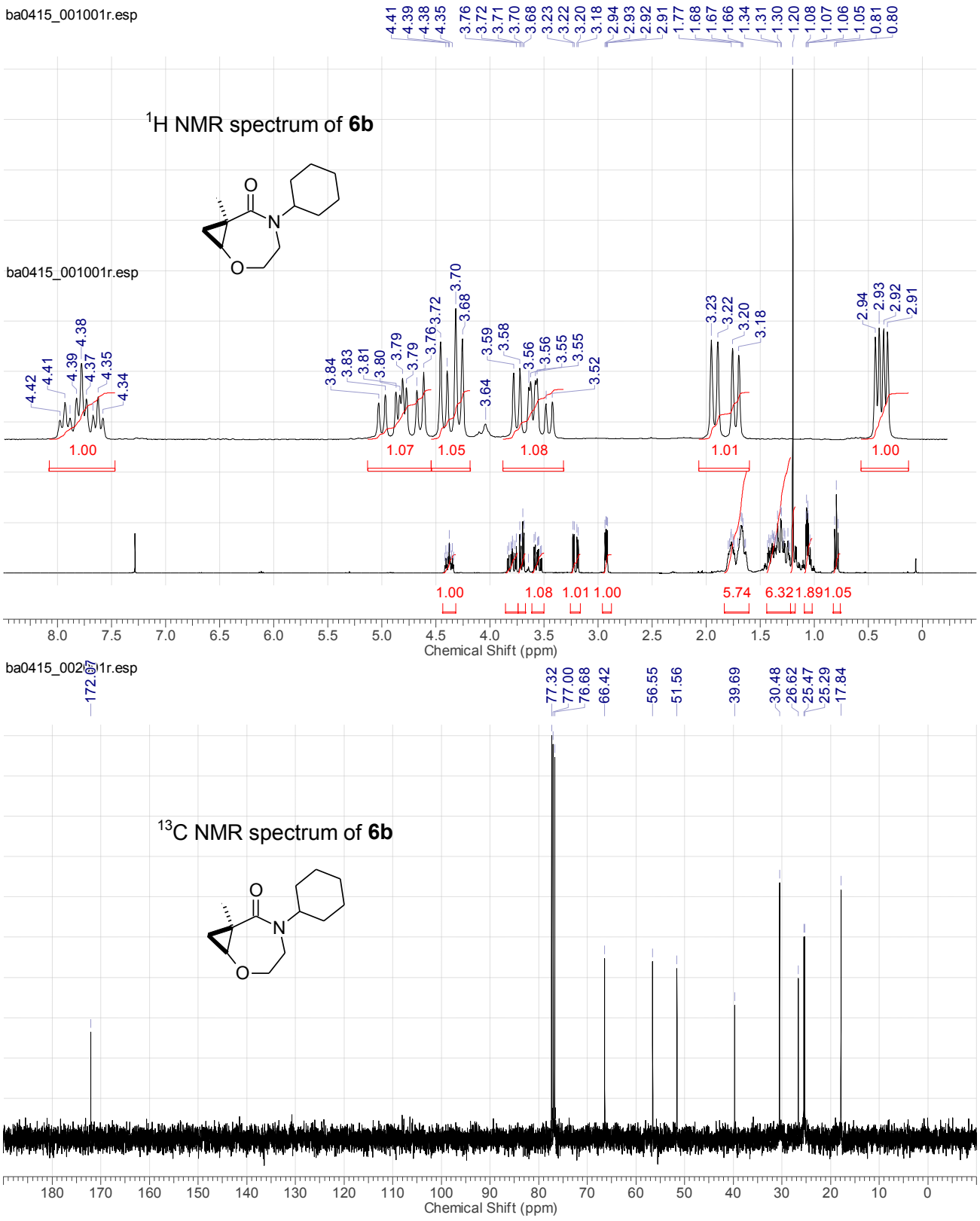
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm


174.25
77.31
77.00
76.68
64.24
61.65
56.49
50.28
47.13
26.31
18.13
17.82
13C spectr 6a 20a
O
OH
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm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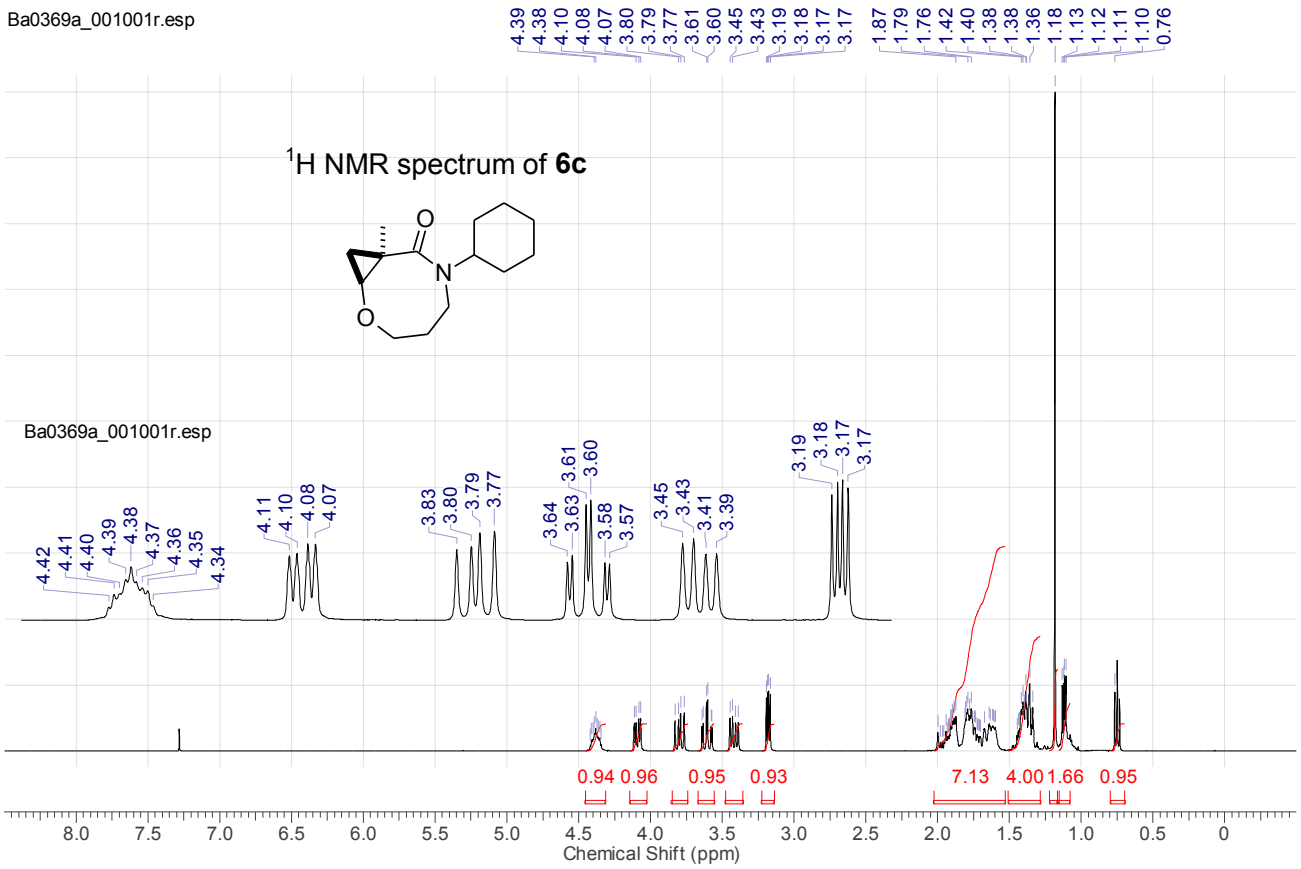
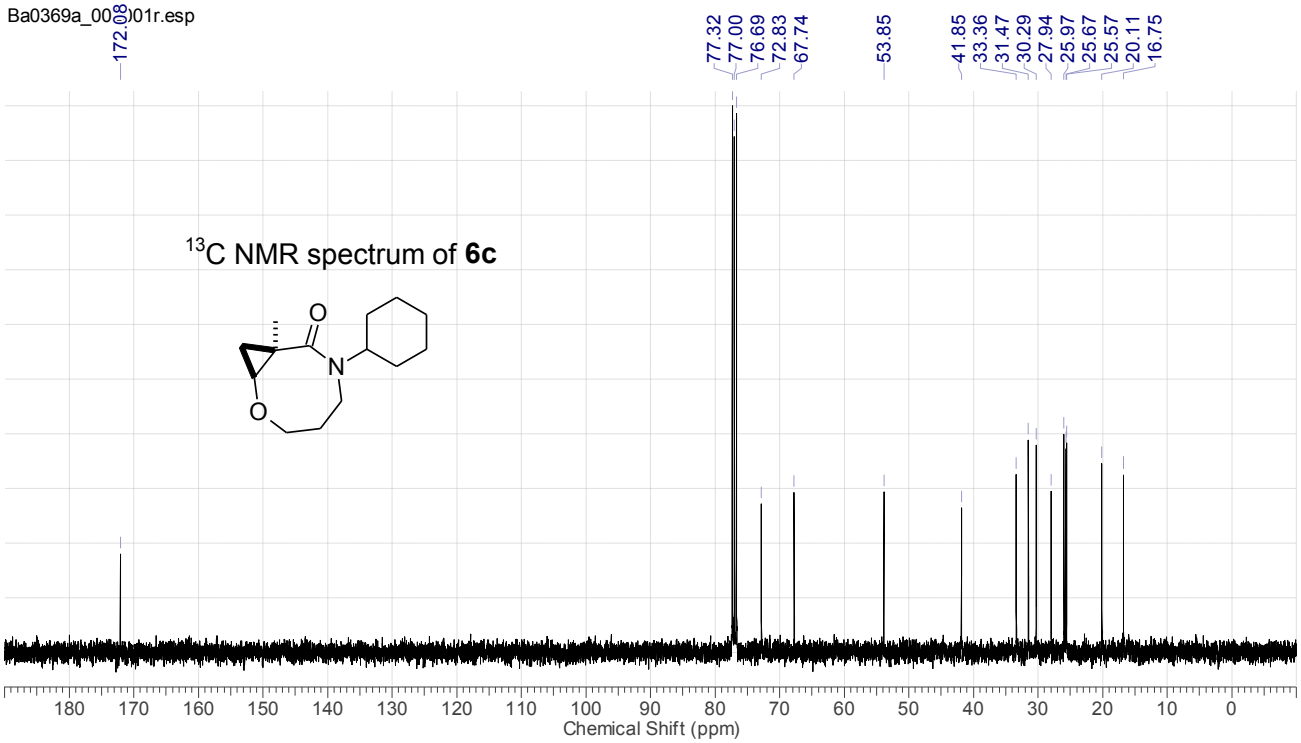
4.41 4.39 4.38 4.35 3.76 3.72 3.71 3.70 3.68 3.23 3.22 3.20 3.18 2.94 2.93 2.92 2.91 1.77 1.68 1.67 1.66 1.34 1.31 1.30 1.20 1.08 1.07 1.06 1.05 0.81 0.80
^{1}H NMR spectrum of **6b**
O
N
O
ba0415_001001r.esp
4.42 4.41 4.39 4.38 4.37 4.35 4.34
3.84 3.83 3.81 3.80 3.79 3.79 3.76 3.72 3.70 3.68 3.64 3.59 3.58 3.56 3.55 3.55 3.52
3.23 3.22 3.20 3.18
2.94 2.93 2.92 2.91
1.00 1.07 1.05 1.08 1.01 1.00
1.00 1.08 1.01 1.00 5.74 6.32 1.89 1.05
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)
ba0415_002[illegible]1r.esp
172.07
77.32 77.00 76.68 66.42 56.55 51.56 39.69 30.48 26.62 25.47 25.29 17.84
^{13}C NMR spectrum of **6b**
O
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


Ba0369a_001001r.esp
4.39 4.38 4.10 4.08 4.07 3.80 3.79 3.77 3.61 3.60 3.45 3.43 3.19 3.18 3.17 3.17 1.87 1.79 1.76 1.42 1.40 1.38 1.38 1.36 1.18 1.13 1.12 1.11 1.10 0.76
1H NMR spectrum of 6c
O
N
O
Ba0369a_001001r.esp
4.42 4.41 4.40 4.39 4.38 4.37 4.36 4.35 4.34 4.11 4.10 4.08 4.07 3.83 3.80 3.79 3.77 3.64 3.63 3.61 3.60 3.58 3.57 3.45 3.43 3.41 3.39 3.19 3.18 3.17 3.17
0.94 0.96 0.95 0.93 7.13 4.00 1.66 0.95
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)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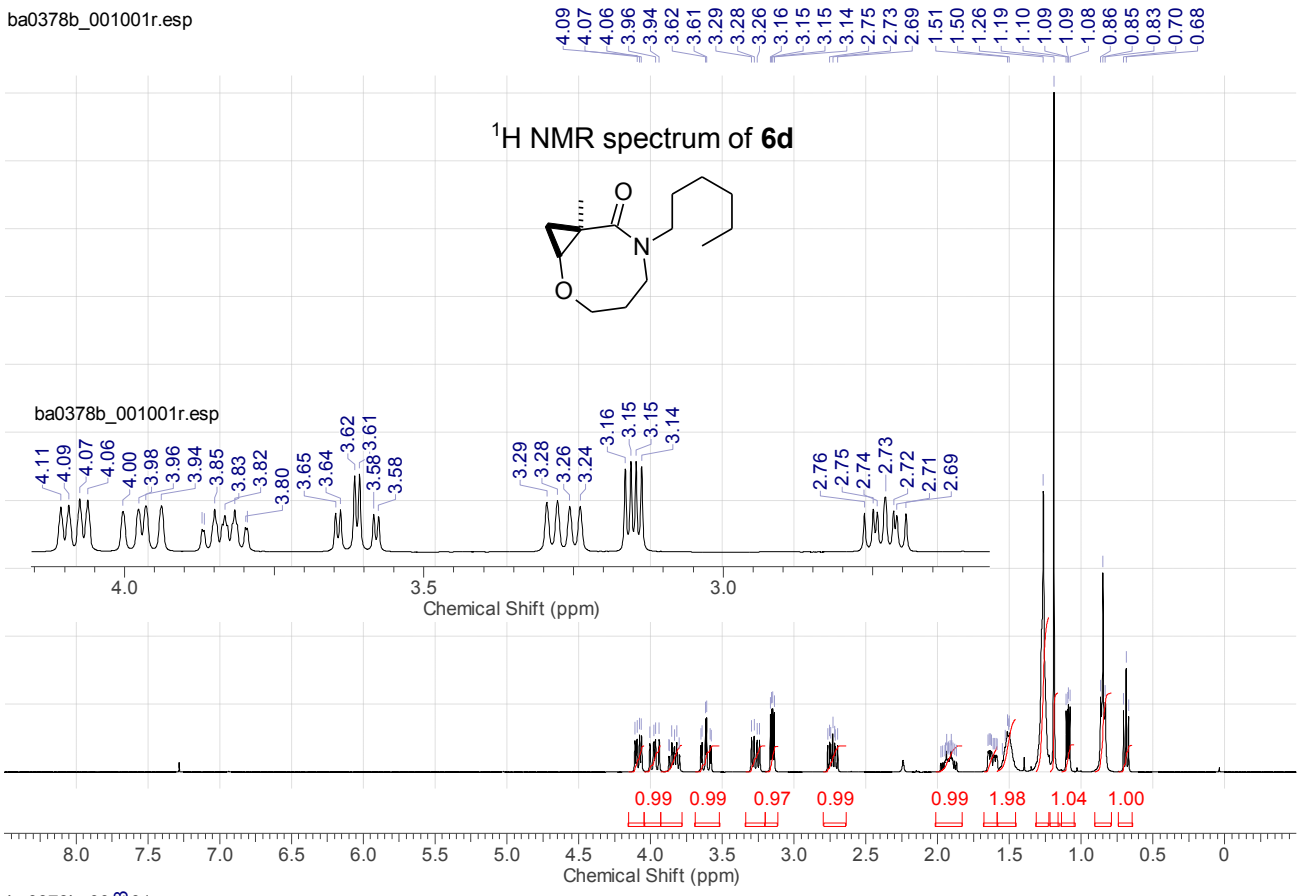
172.08
77.32 77.00 76.69 72.83 67.74 53.85 41.85 33.36 31.47 30.29 27.94 25.97 25.67 25.57 20.11 16.75
13C NMR spectrum of 6c
O
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)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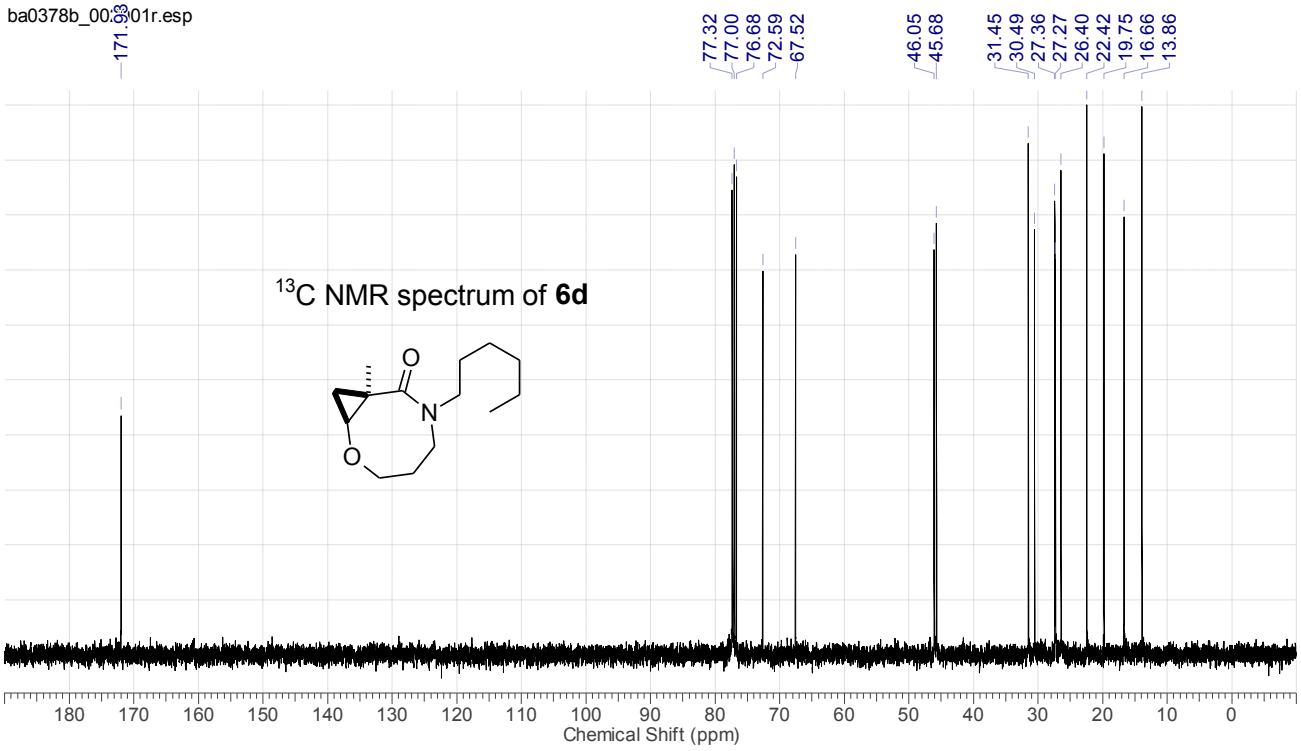
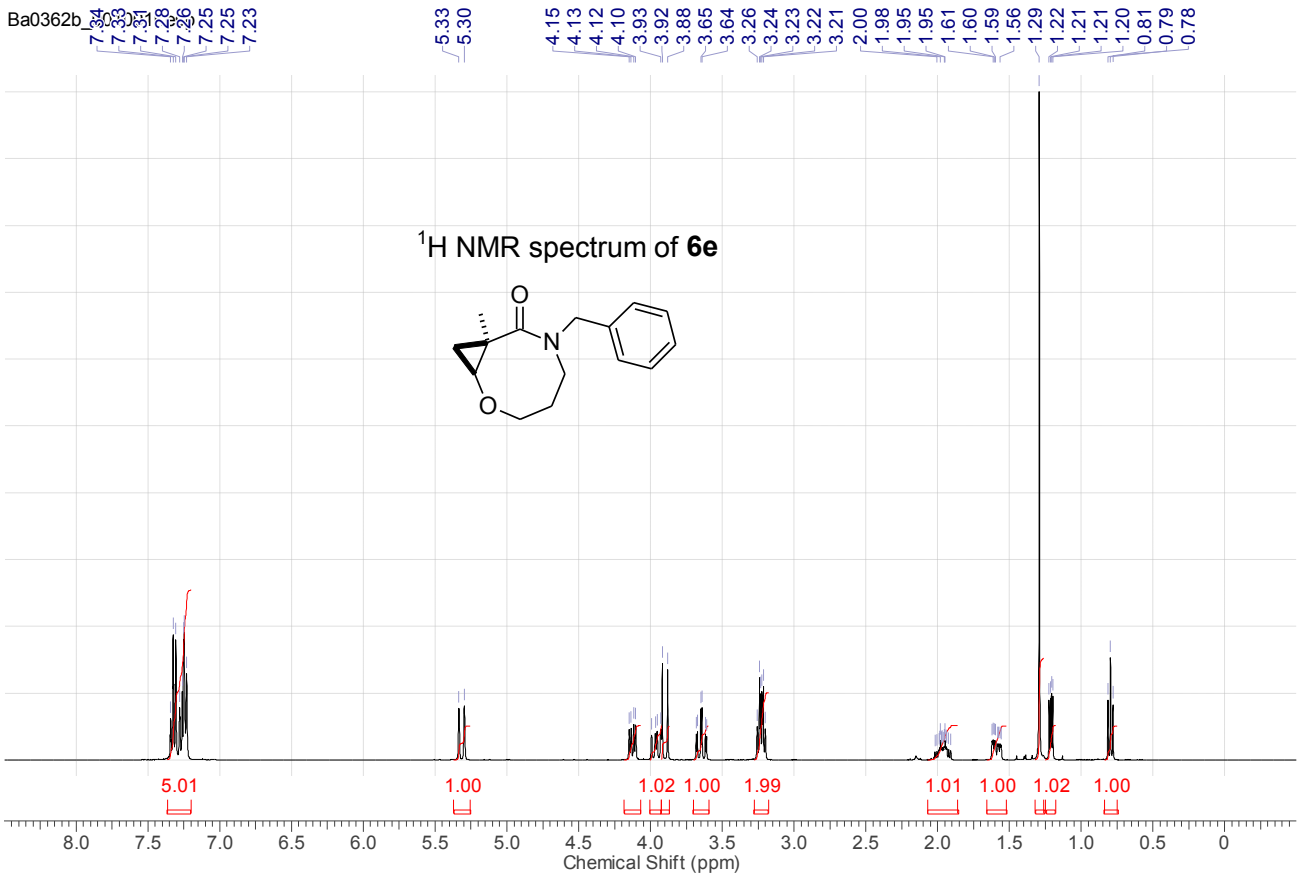
^{1}H NMR spectrum of **6d**
O
N
O
ba0378b_001001r.esp
4.11 4.09 4.07 4.06 4.00 3.98 3.96 3.94 3.85 3.83 3.82 3.80 3.65 3.64 3.62 3.61 3.58 3.58
3.29 3.28 3.26 3.24 3.16 3.15 3.15 3.14
2.76 2.75 2.74 2.73 2.72 2.71 2.69
4.0 3.5 3.0
Chemical Shift (ppm)
0.99 0.99 0.97 0.99 0.99 1.98 1.04 1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


ba0378b_001001r.esp
171.93
77.32 77.00 76.68 72.59 67.52
46.05 45.68
31.45 30.49 27.36 27.27 26.40 22.42 19.75 16.66 13.86
^{13}C NMR spectrum of **6d**
O
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)


Ba0362b_
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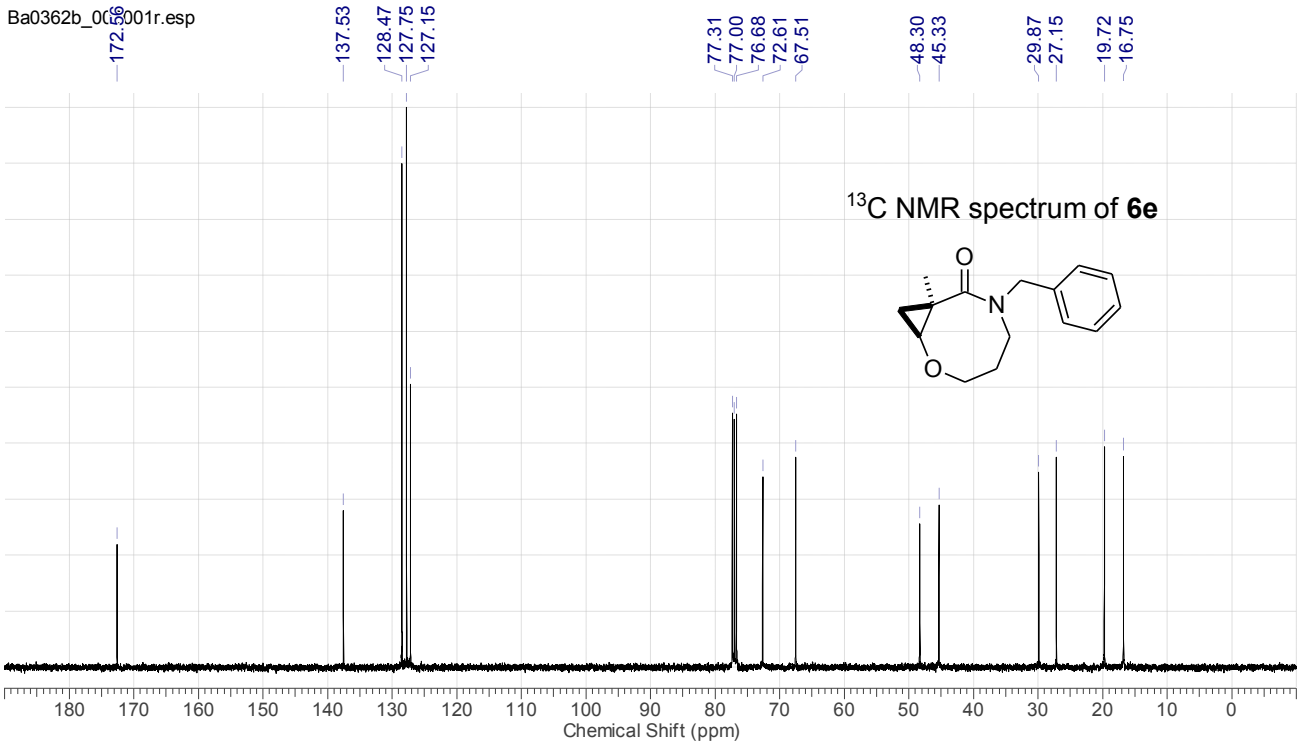
7.33
7.31
7.28
7.26
7.25
7.25
7.23
5.33
5.30
4.15
4.13
4.12
4.10
3.93
3.92
3.88
3.65
3.64
3.26
3.24
3.23
3.22
3.21
2.00
1.98
1.95
1.95
1.61
1.60
1.59
1.56
1.29
1.22
1.21
1.21
1.20
0.81
0.79
0.78
1H NMR spectrum of 6e
O
N
O
5.01
1.00
1.02
1.00
1.99
1.01
1.00
1.02
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Ba0362b_001r.esp
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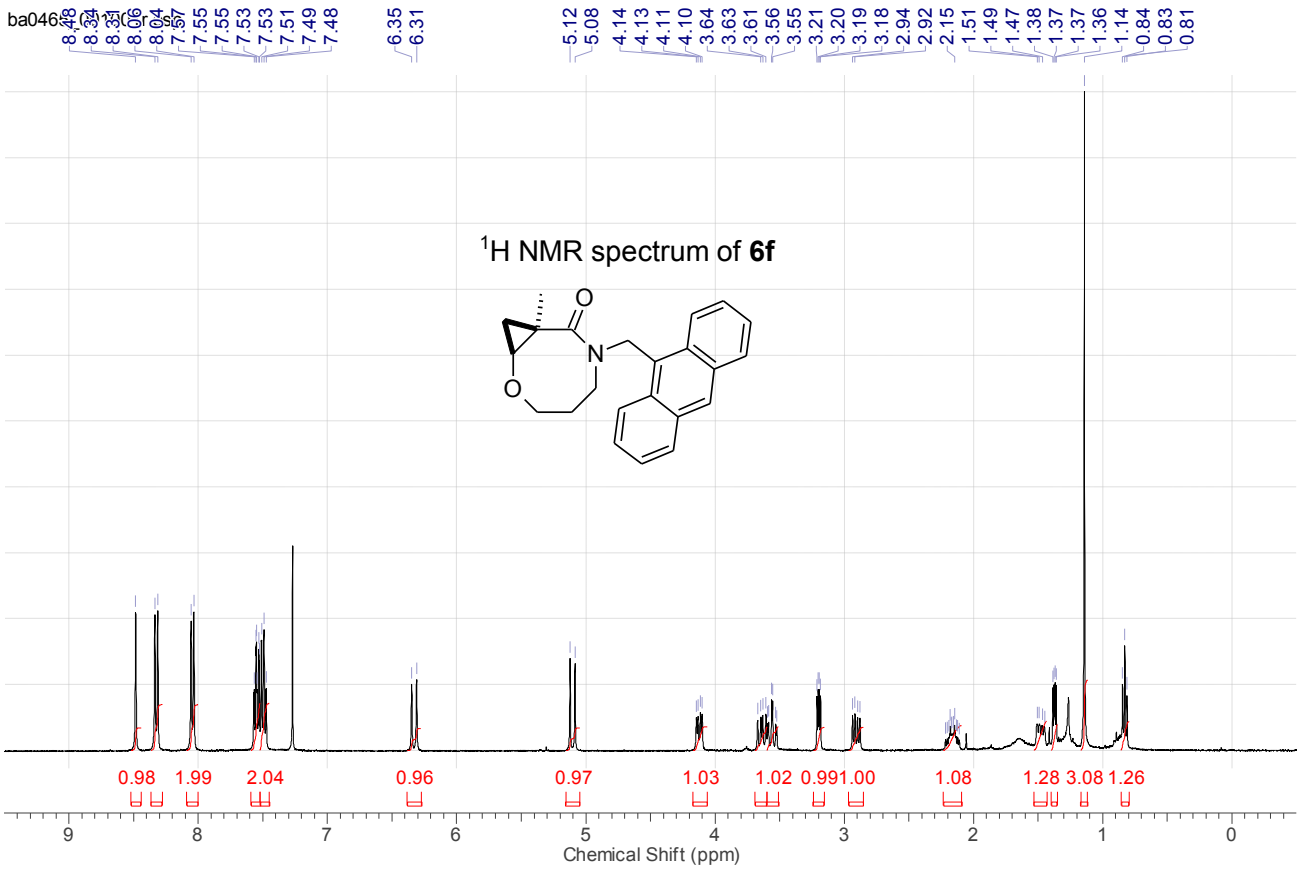
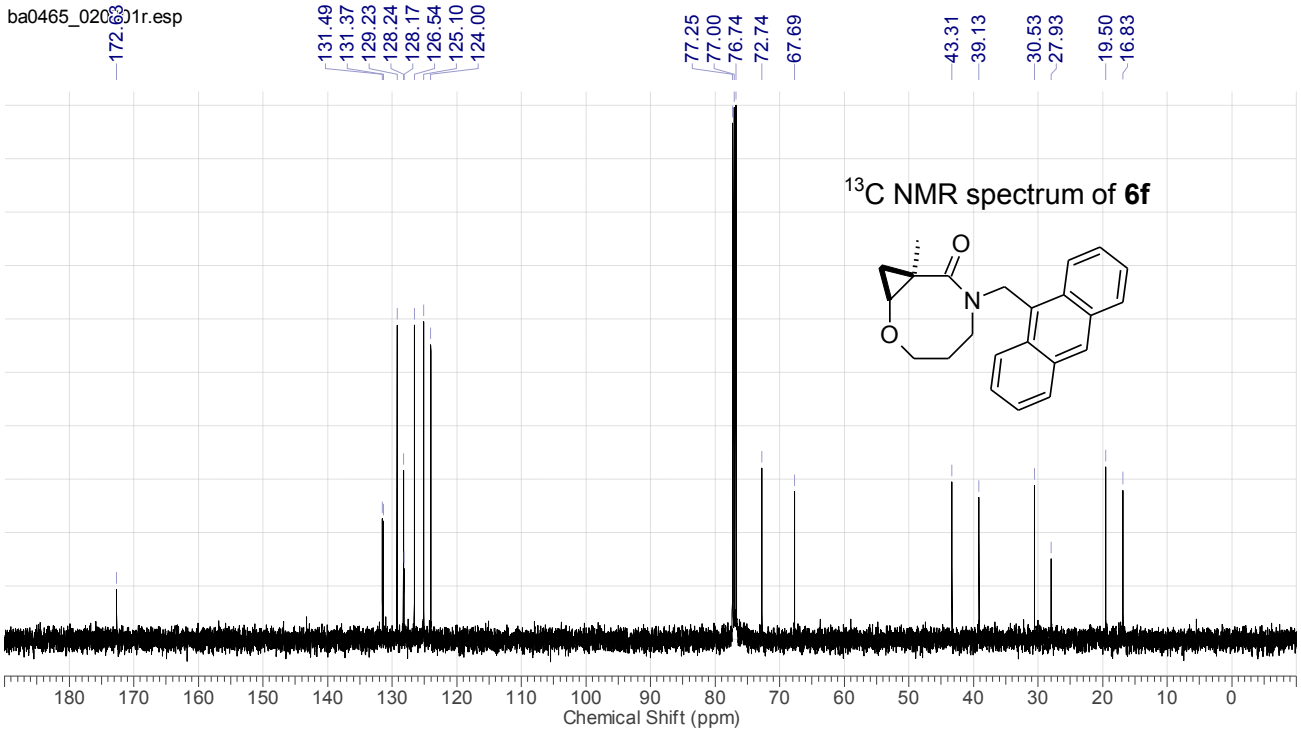
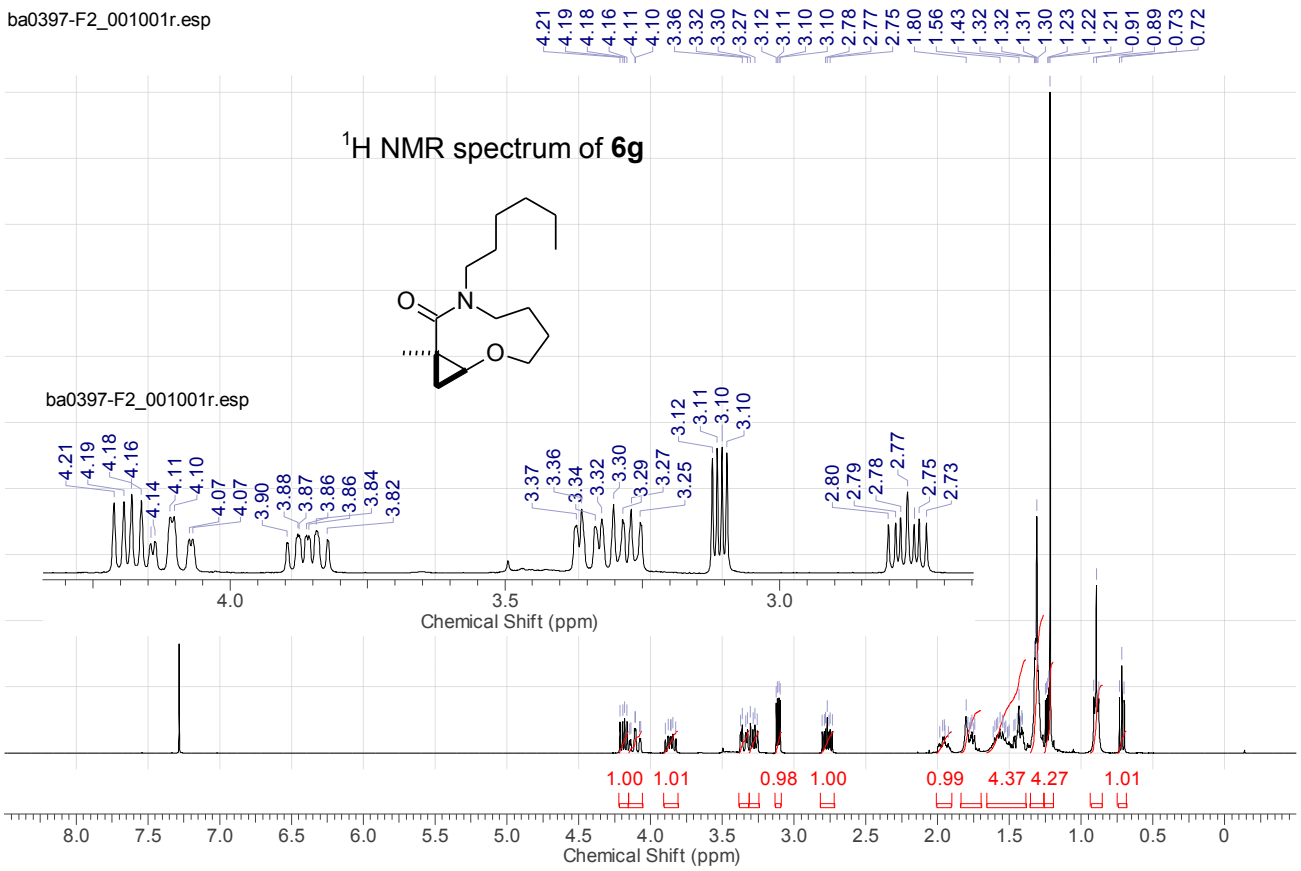
128.47
127.75
127.15
77.31
77.00
76.68
72.61
67.51
48.30
45.33
29.87
27.15
19.72
16.75
13C NMR spectrum of 6e
O
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

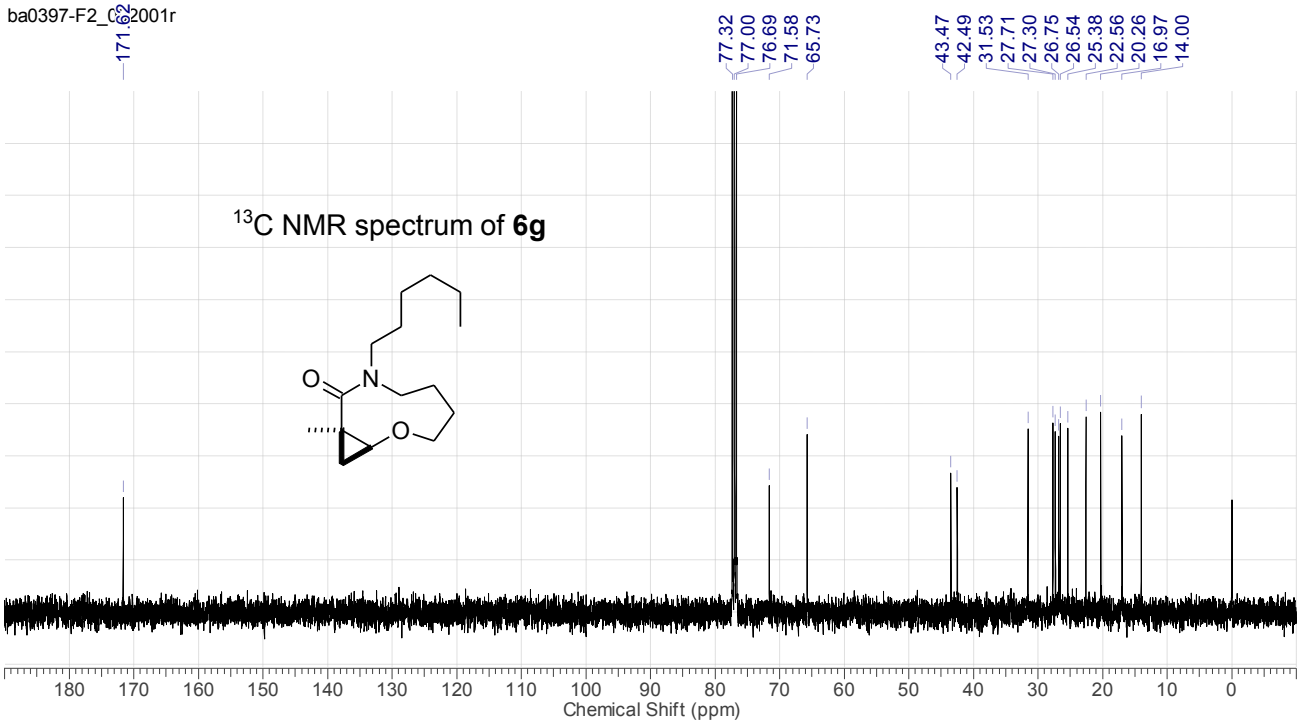


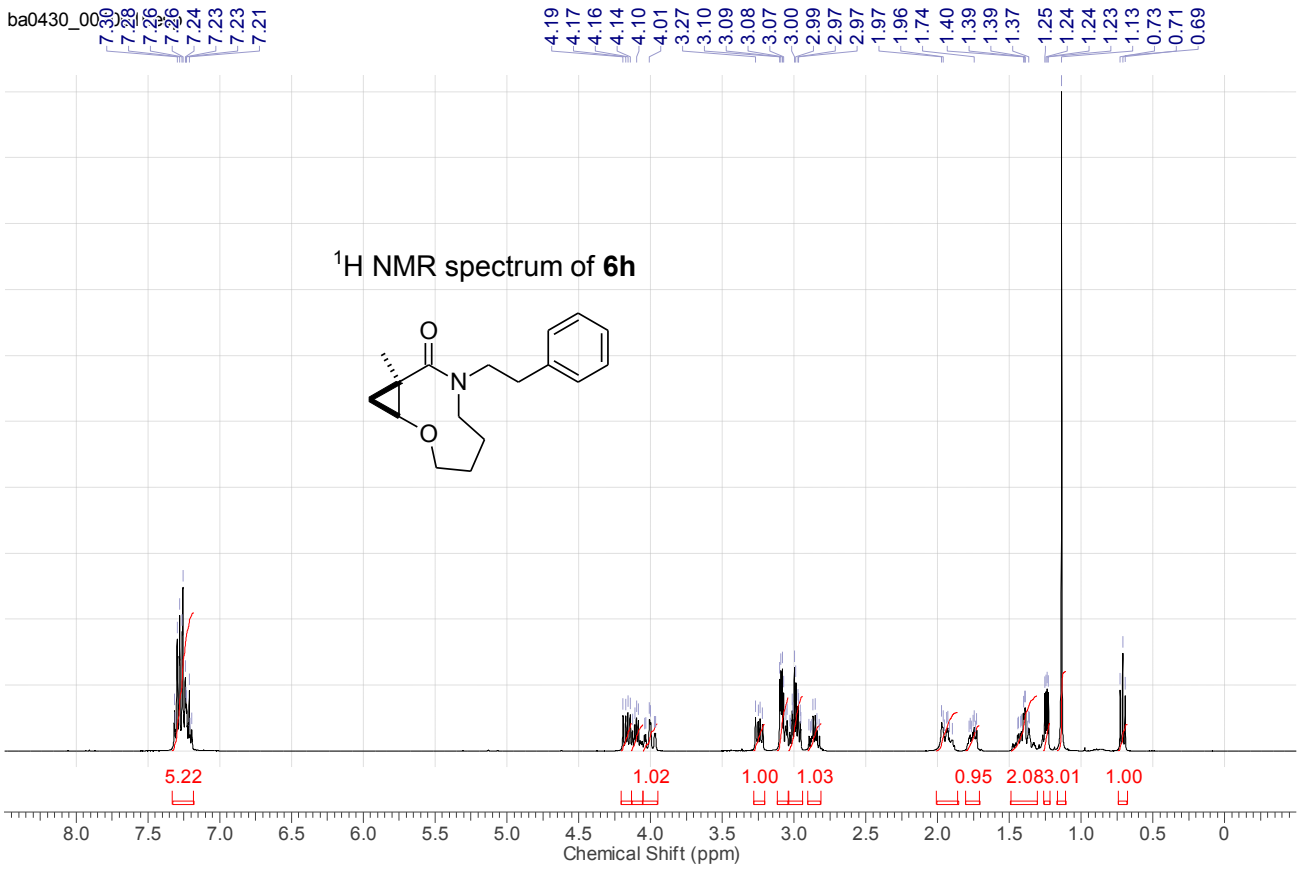
^{1}H NMR spectrum of **6f**



^{13}C NMR spectrum of **6f**


ba0397-F2_001001r.esp
4.21 4.19 4.18 4.16 4.11 4.10 3.36 3.32 3.30 3.27 3.12 3.11 3.10 3.10 2.78 2.77 2.75 1.80 1.56 1.43 1.32 1.32 1.31 1.30 1.23 1.22 1.21 0.91 0.89 0.73 0.72
^{1}H NMR spectrum of **6g**
O
N
O
ba0397-F2_001001r.esp
4.21 4.19 4.18 4.16 4.14 4.11 4.10 4.07 4.07 3.90 3.88 3.87 3.86 3.86 3.84 3.82
3.37 3.36 3.34 3.32 3.30 3.29 3.27 3.25
3.12 3.11 3.10 3.10
2.80 2.79 2.78 2.77 2.75 2.73
4.0 3.5 3.0
Chemical Shift (ppm)
1.00 1.01 0.98 1.00 0.99 4.37 4.27 1.01
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


ba0397-F2_002001r
171.62
77.32 77.00 76.69 71.58 65.73
43.47 42.49 31.53 27.71 27.30 26.75 26.54 25.38 22.56 20.26 16.97 14.00
^{13}C NMR spectrum of **6g**
O
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)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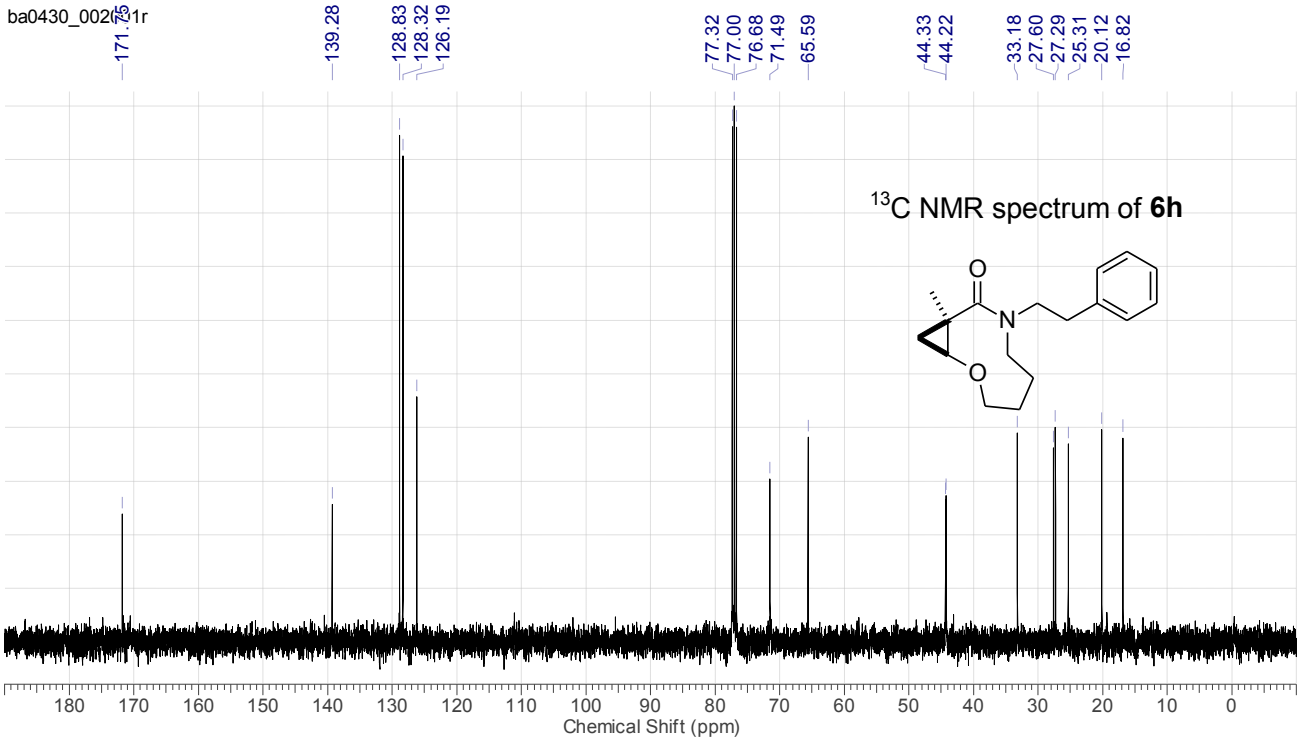
7.28
7.26
7.26
7.24
7.23
7.21
4.19
4.17
4.16
4.14
4.10
4.01
3.27
3.10
3.09
3.08
3.07
3.00
2.99
2.97
2.97
1.97
1.96
1.74
1.40
1.39
1.39
1.37
1.25
1.24
1.24
1.23
1.13
0.73
0.71
0.69
^{1}H NMR spectrum of **6h**
O
N
O
5.22
1.02
1.00
1.03
0.95
2.08
3.01
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)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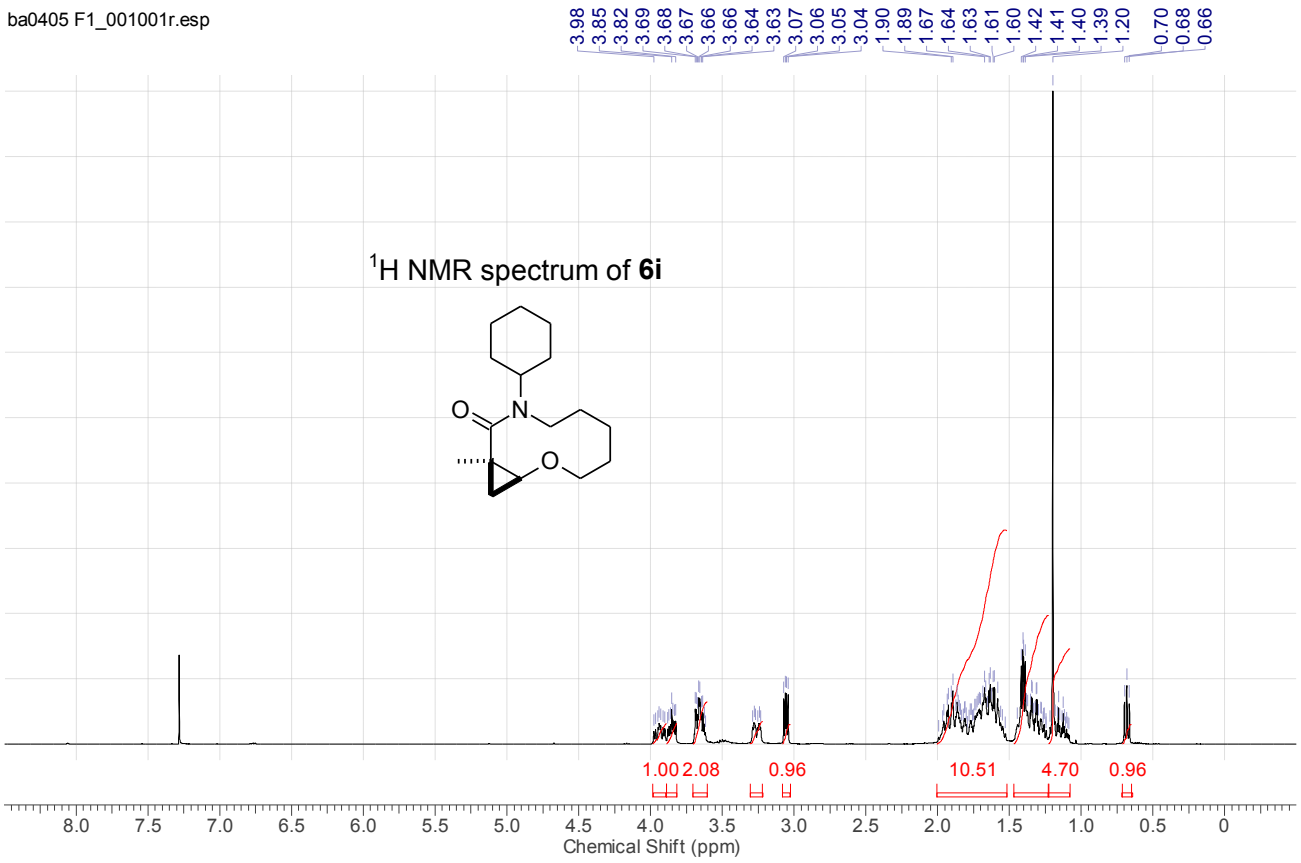
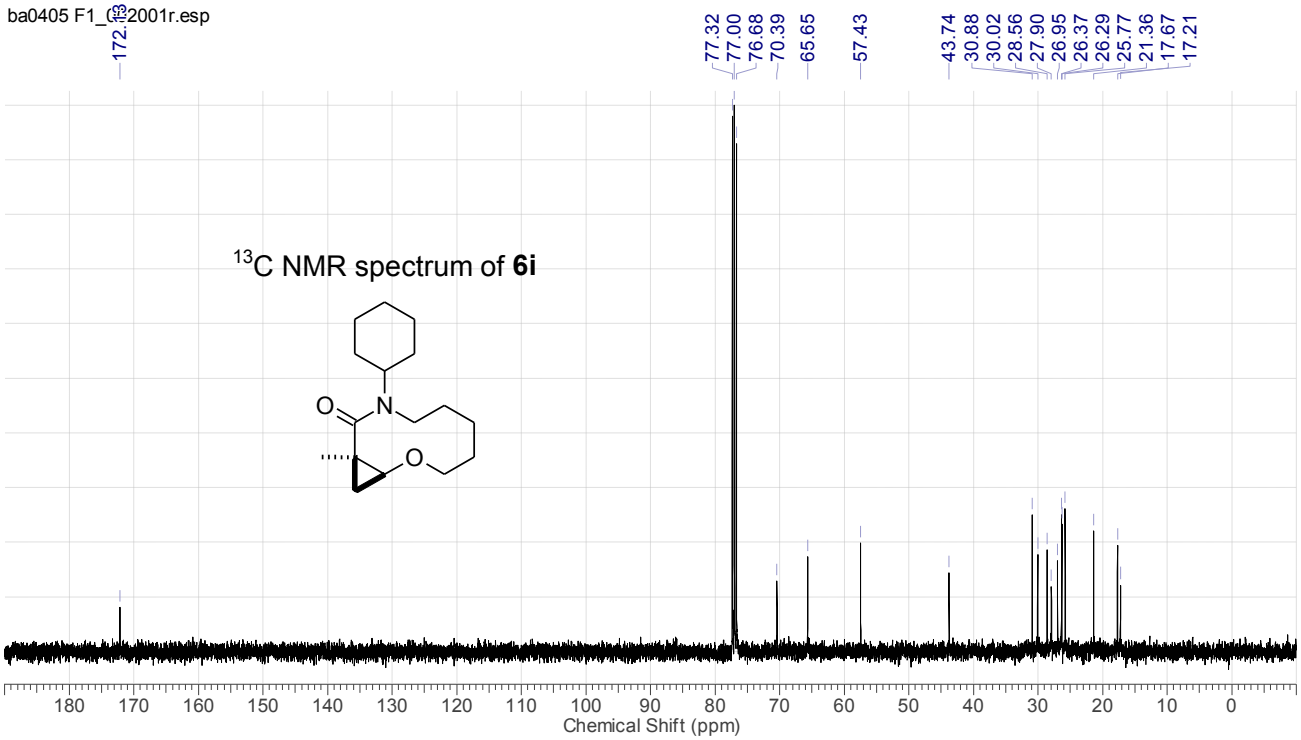
139.28
128.83
128.32
126.19
77.32
77.00
76.68
71.49
65.59
44.33
44.22
33.18
27.60
27.29
25.31
20.12
16.82
^{13}C NMR spectrum of **6h**
O
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)


ba0405 F1_001001r.esp
3.98
3.85
3.82
3.69
3.68
3.67
3.66
3.66
3.64
3.63
3.07
3.06
3.05
3.04
1.90
1.89
1.67
1.64
1.63
1.61
1.60
1.42
1.41
1.40
1.39
1.20
0.70
0.68
0.66
1H NMR spectrum of 6i
O
N
O
1.00
2.08
0.96
10.51
4.70
0.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)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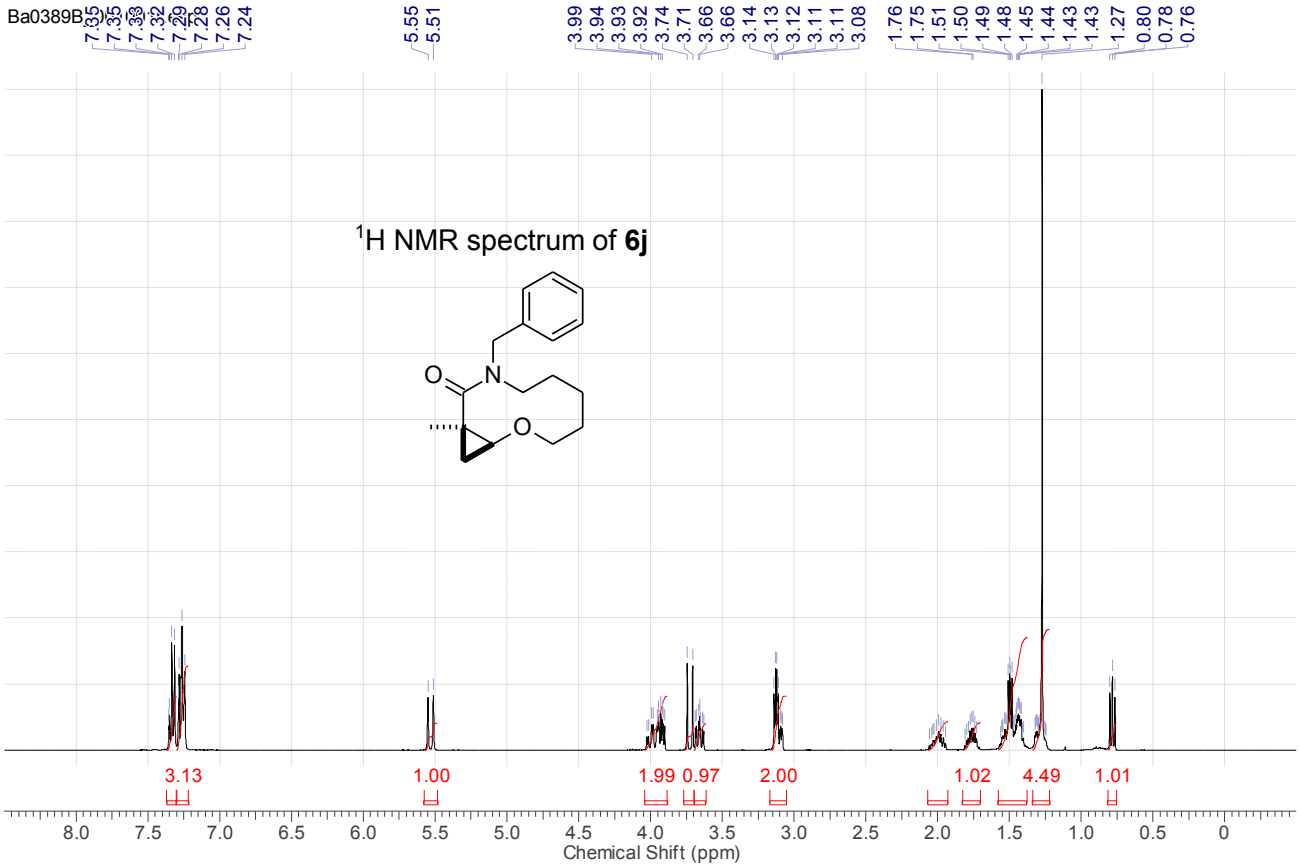
77.00
76.68
70.39
65.65
57.43
43.74
30.88
30.02
28.56
27.90
26.95
26.37
26.29
25.77
21.36
17.67
17.21
13C NMR spectrum of 6i
O
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)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7.28
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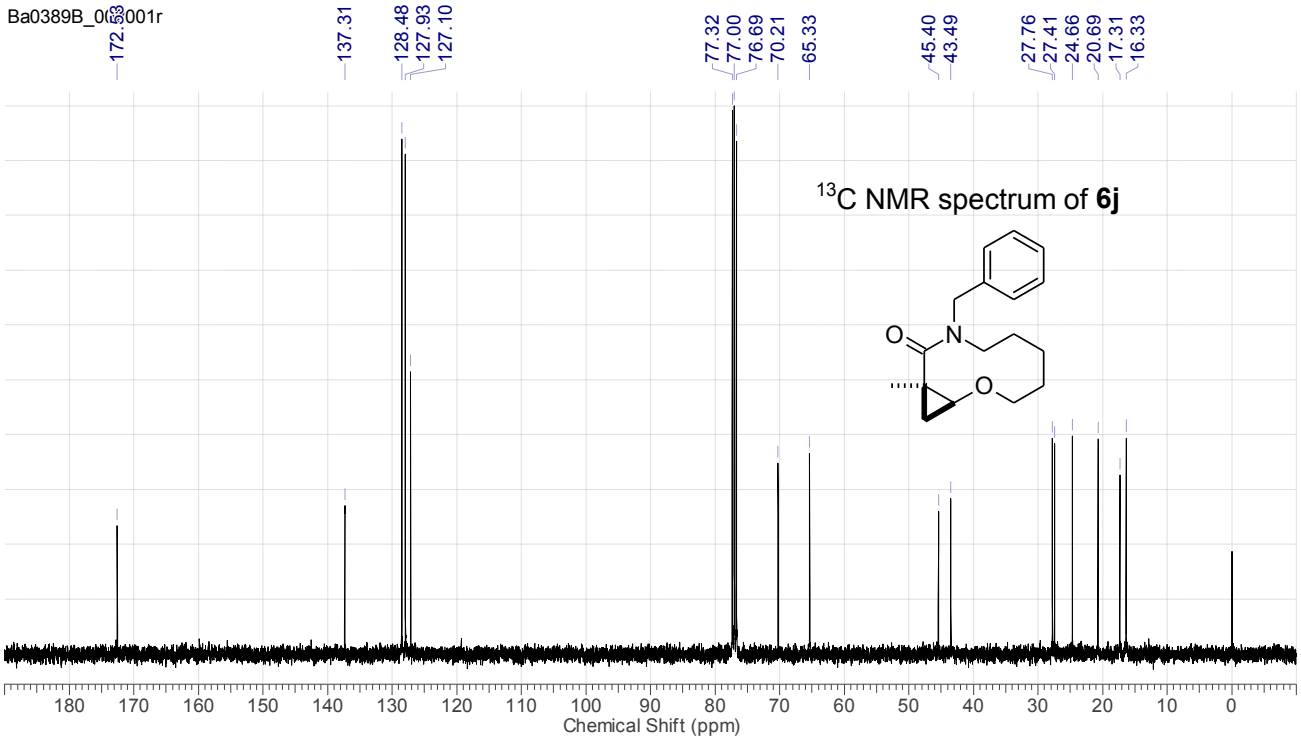
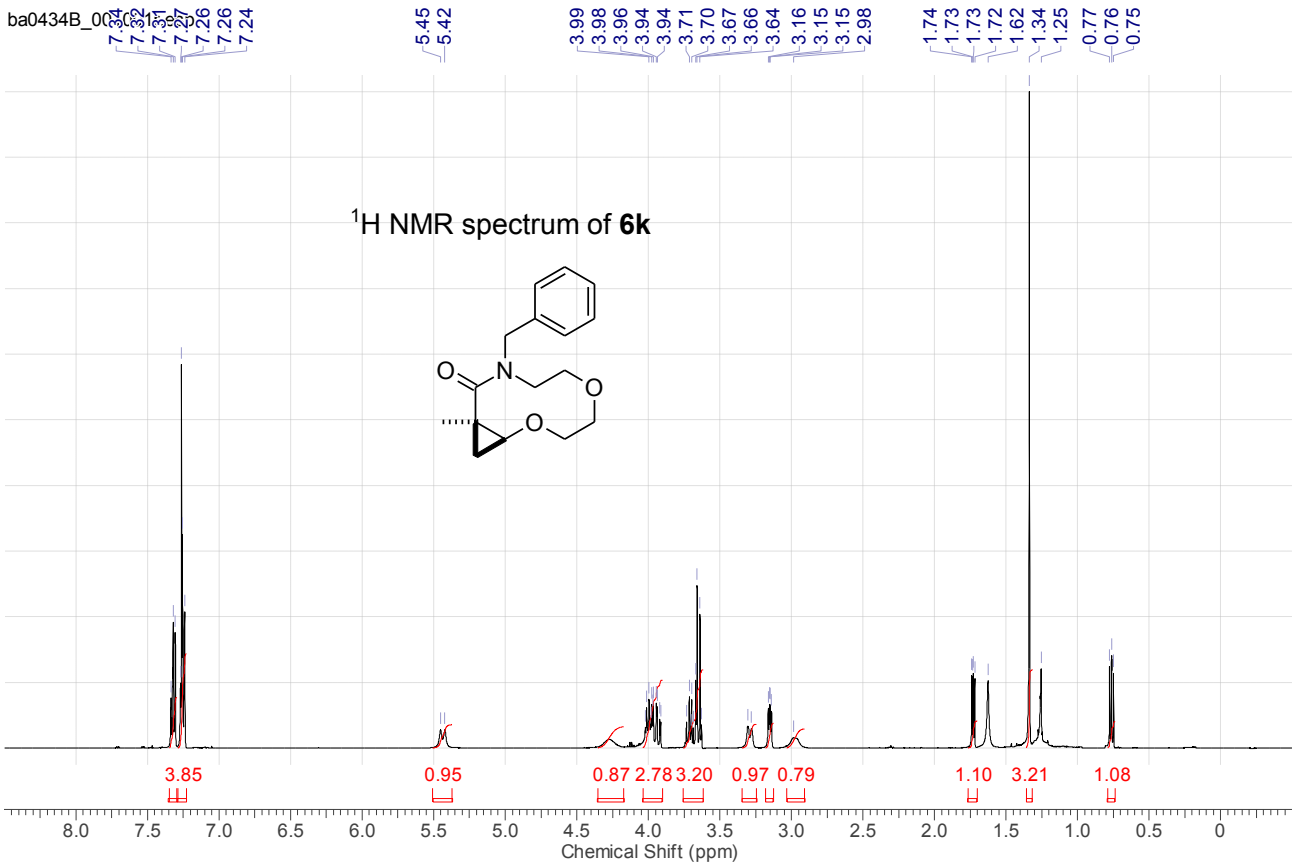
7.24
5.55
5.51
3.99
3.94
3.93
3.92
3.74
3.71
3.66
3.66
3.14
3.13
3.12
3.11
3.11
3.08
1.76
1.75
1.51
1.50
1.49
1.48
1.45
1.44
1.43
1.43
1.27
0.80
0.78
0.76
1H NMR spectrum of 6j
O
N
O
3.13
1.00
1.99
0.97
2.00
1.02
4.49
1.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Ba0389B_0
001r
172.53
137.31
128.48
127.93
127.10
77.32
77.00
76.69
70.21
65.33
45.40
43.49
27.76
27.41
24.66
20.69
17.31
16.33
13C NMR spectrum of 6j
O
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)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7.26
7.26
7.24
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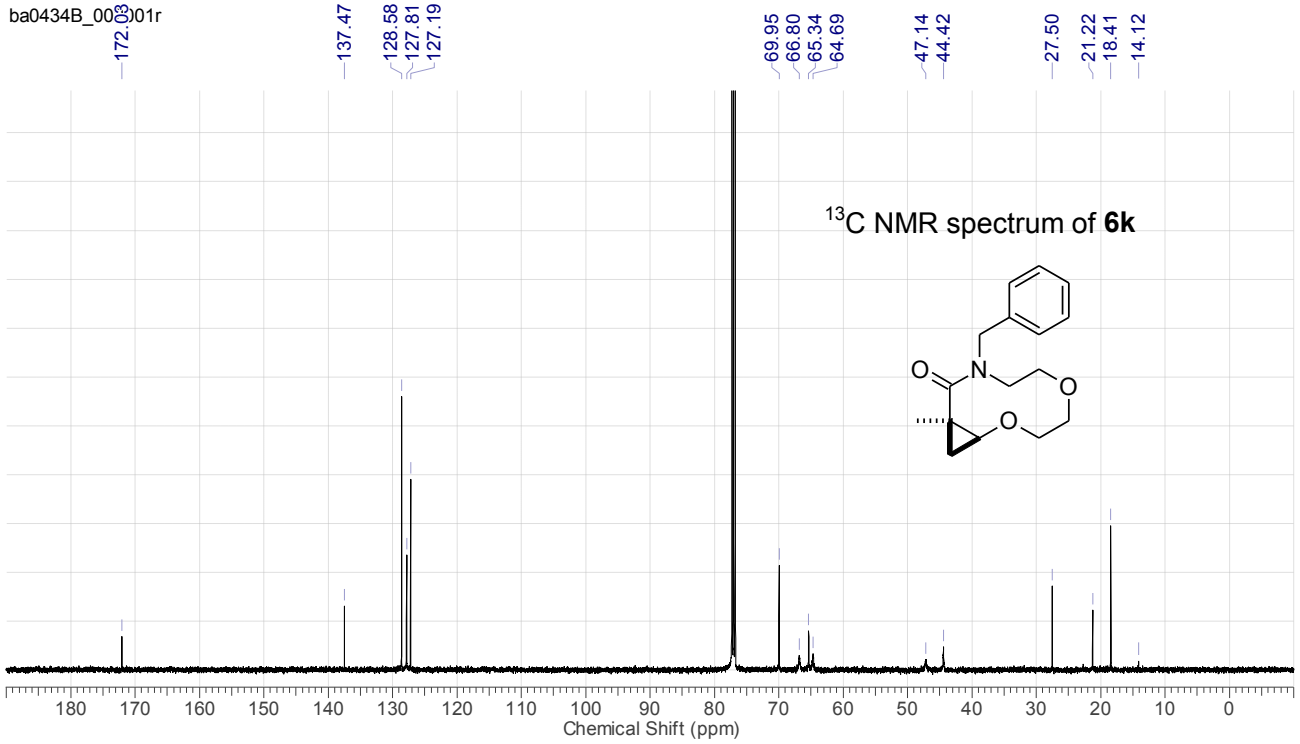
5.42
3.99
3.98
3.96
3.94
3.94
3.71
3.70
3.67
3.66
3.64
3.16
3.15
3.15
2.98
1.74
1.73
1.73
1.72
1.62
1.34
1.25
0.77
0.76
0.75
^{1}H NMR spectrum of **6k**
O
N
O
O
3.85
0.95
0.87
2.78
3.20
0.97
0.79
1.10
3.21
1.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


ba0434B_0003_01r
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137.47
128.58
127.81
127.19
69.95
66.80
65.34
64.69
47.14
44.42
27.50
21.22
18.41
14.12
^{13}C NMR spectrum of **6k**
O
N
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

Computational Structures: Optimized Geometries.

DFT studies were performed using b3lyp functional in 6-311++G** basis.[12] Geometries of starting materials **9**, **12** and products **10**, **13** were optimized to locate the corresponding minima. Transition states **TS1**-**TS3** (see below) were found using Sinchronous Transit Guided Quasi-Newton (STQN) algorithm[13] (QST2 option using the geometries of the corresponding starting materials and products, or QST3 option, also taking into account estimated geometry of the transition state – used to locate **TS2**) assessing the force constants before each iteration (Tables 1-3). To verify location of the saddle point and assess the thermochemistry, analysis of vibrational spectra were performed in all cases showing only one imaginary frequency, corresponding to the stretching vibration of the newly forming C-O bond. Tables of atomic XYZ-coordinates and molecular graphs for all optimized structures are provided on the following pages.

(12) Spartan'10, version 1.1.0, Wavefunction Inc.

(13) (a) Peng, C.; Ayala, P. Y.; Schlegel, H. B.; Frisch, M. J. *J. Comp. Chem.* **1996**, *17*, 49. (b) Peng, C.; Schlegel, H. B. *Israel J. Chem.* **1994**, *33*, 449.

Coordinated complex 12

Atom	X	Y	Z
C	-0.669617	1.094007	-0.233850
C	-0.336850	1.937718	0.963363
C	0.672280	1.307294	0.450077
H	-0.723861	2.621915	1.701751
H	1.736842	0.991601	0.388189
O	3.298052	0.098521	0.140035
C	4.338284	0.989070	0.314623
H	5.022930	0.706296	1.140935
H	4.978650	1.094475	-0.585499
H	3.992626	2.019603	0.554294
C	-1.309179	-0.276225	-0.032058
C	-3.309325	-1.642509	0.315785
H	-4.123422	-1.727530	-0.411369
H	-2.581389	-2.430176	0.142877
H	-3.730019	-1.753679	1.321173
C	-3.526055	0.807458	0.333450
H	-4.062061	0.740558	1.286314
H	-2.950659	1.727329	0.325259
H	-4.267275	0.841872	-0.472793
N	-2.652481	-0.347407	0.178874
C	-0.934769	1.692233	-1.616974
H	-0.633076	0.998241	-2.409285
H	-1.989269	1.939558	-1.782972
H	-0.352452	2.608410	-1.736499
O	-0.618838	-1.307666	-0.080554
K	1.961446	-1.775144	-0.218781

E	-1114.47981 au	C_v	231.60 J/mol°
ZPE	540.21 kJ/mol	S°	477.47 J/mol°
H°	-1114.25967 au	G°	-1114.31387 au

Dipole moment 7.72 D

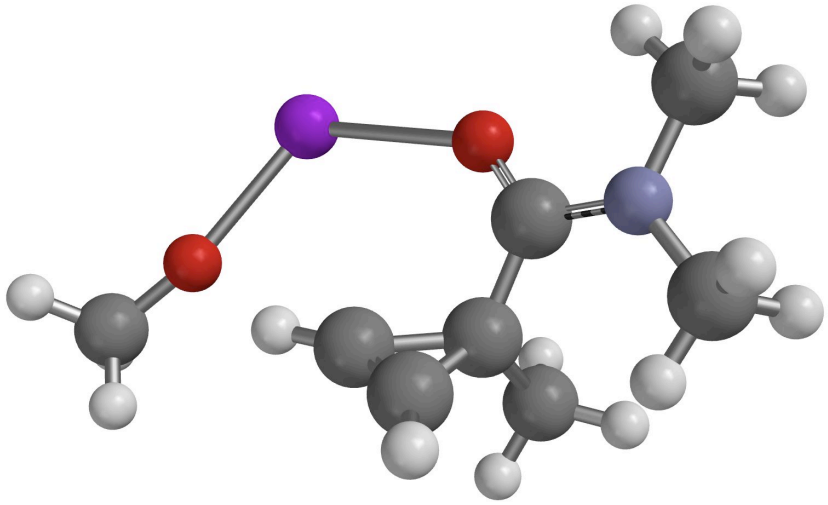

Figure 5. Optimized Geometry of **12** – pre-reactive complex in the reaction of cyclopropene 3-carboxamide with methoxide anion templated with K^+.

Coordinated complex 13

Atom	X	Y	Z
C	0.316249	-0.820092	-0.815586
C	0.122412	-2.079381	0.000879
C	-1.051810	-1.308405	-0.381154
H	0.270610	-3.017502	-0.538406
H	-1.754623	-1.595178	-1.173626
O	-1.833066	-0.594028	0.654267
C	-2.203409	-1.442577	1.738751
H	-2.548080	-0.806886	2.558881
H	-3.015296	-2.123613	1.447267
H	-1.332683	-2.027370	2.050124
C	0.911581	0.425361	-0.182460
C	2.719982	1.566367	0.989078
H	3.711331	1.711200	0.546500
H	2.092711	2.422803	0.758435
H	2.838175	1.479851	2.075080
C	2.892217	-0.865739	0.586872
H	2.217471	-1.722014	0.568738
H	3.642990	-0.938767	-0.209294
H	3.412518	-0.840571	1.548538
N	2.105690	0.358011	0.452079
C	0.628083	-0.850809	-2.318882
H	0.434518	0.103669	-2.825529
H	1.681407	-1.104500	-2.487741
H	0.029628	-1.628155	-2.801731
O	0.328734	1.532901	-0.296582
K	-2.126193	1.701138	-0.276224

E	-1114.45627 au	C_v	221.79 J/mol°
ZPE	549.28 kJ/mol	S°	462.57 J/mol°
H°	-1114.23333 au	G°	-1114.28586 au

Dipole moment 8.60 D

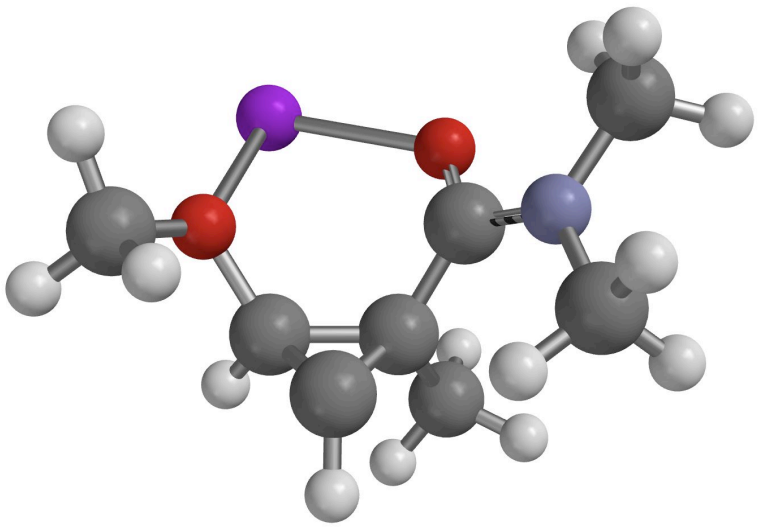

Figure 6. Optimized Geometry of **13** – product the reaction of cyclopropene 3-carboxamide with methoxide anion templated with K^+.

TS3

Atom	X	Y	Z
C	-0.433974	0.997765	-0.788388
C	-0.330044	2.083820	0.233591
C	0.842163	1.571437	-0.209650
H	-0.745315	3.077975	0.316235
H	1.710997	1.945002	-0.740845
O	1.885234	0.564847	0.967479
C	1.515713	0.791551	2.291993
H	1.361724	-0.150522	2.846383
H	2.271209	1.381652	2.836306
H	0.559207	1.349289	2.325697
C	-0.829851	-0.426547	-0.408976
C	-2.302383	-1.987853	0.754503
H	-3.290672	-2.274182	0.378875
H	-1.560055	-2.686799	0.379531
H	-2.325977	-2.027198	1.849636
C	-2.890290	0.399256	0.733166
H	-2.771457	0.618051	1.799580
H	-2.723550	1.314908	0.178759
H	-3.913386	0.051288	0.556326
N	-1.962727	-0.642868	0.307270
C	-0.772323	1.272772	-2.262245
H	-0.441157	0.465283	-2.924877
H	-1.854134	1.389223	-2.403185
H	-0.299890	2.205378	-2.581894
O	-0.131443	-1.392844	-0.785878
K	2.365113	-1.249921	-0.551799

E	-1114.44194 au	C_v	228.80 J/mol°
ZPE	544.36 kJ/mol	S°	469.49 J/mol°
H°	-1114.22040 au	G°	-1114.27372 au
Dipole moment 5.77 D			

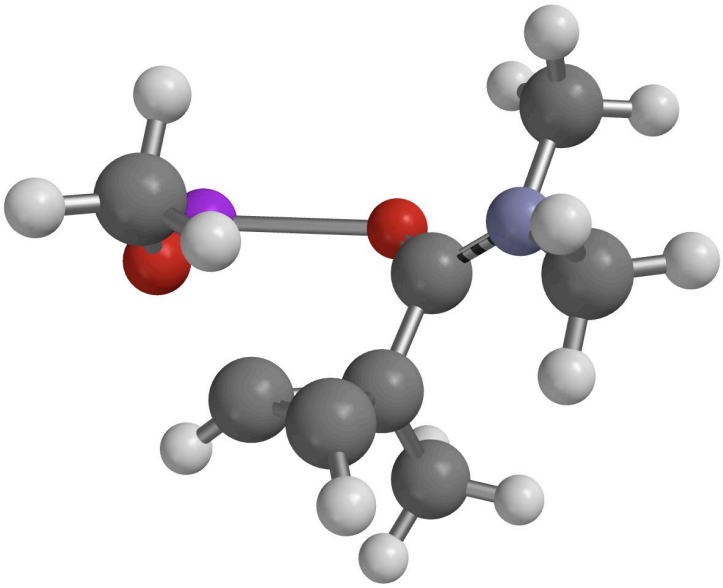

Figure 7. Optimized Geometry of **TS3** – transition state in the reaction of of cyclopropene 3-carboxamide with methoxide anion. Obtained as a saddle point between complexes **12** and **13** using QTS2 algorithm.

Coordinated complex 9

Atom	X	Y	Z
C	-1.645144	-0.481400	-0.048677
C	-1.245030	-1.351859	-1.210521
O	1.406858	0.100266	-1.282976
C	1.181499	1.423496	-1.516015
H	2.005273	2.076890	-1.149959
H	1.069736	1.680188	-2.592483
C	-0.535633	0.152691	0.789315
C	0.738914	2.075883	1.473559
H	1.770611	1.766789	1.269923
H	0.671971	3.159932	1.363078
H	0.490888	1.797001	2.496289
C	-0.137890	1.920702	-0.837351
H	-0.990068	1.519977	-1.382324
H	-0.210084	3.014096	-0.848263
N	-0.211384	1.454857	0.555302
C	-1.605955	-1.985502	-0.139402
H	-1.783290	-2.902378	0.396568
H	-0.859521	-1.322910	-2.214669
K	1.875026	-1.636566	0.231312
O	-0.021572	-0.502857	1.714422
C	-2.983753	0.252767	-0.019311
H	-3.734526	-0.325091	-0.563747
H	-3.332451	0.378044	1.011114
H	-2.928673	1.248274	-0.468714

E	-1113.31181 au	C_v	208.41 J/mol°
ZPE	492.29 kJ/mol	S°	444.12 J/mol°
H°	-1113.11142 au	G°	-1113.16186 au
Dipole moment 4.42 D			

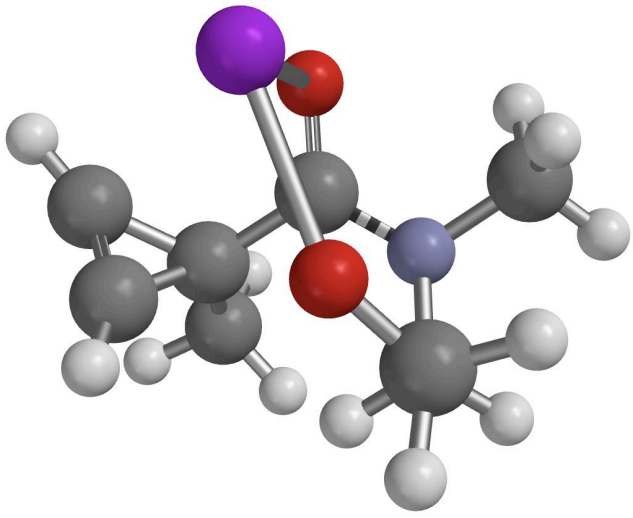

Figure 8. Optimized Geometry of **9** – pre-reactive complex in the K^+-templated 7-*exo-trig* cyclization of cyclopropene 3-carboxamide tethered to alkoxide.

Coordinated complex 10

Atom	X	Y	Z
C	0.110429	0.943695	-0.787646
C	-0.162861	1.689429	0.491941
O	-0.612908	0.900054	1.608711
C	-1.975990	0.536416	1.501077
H	-2.156141	-0.189230	2.299650
H	-2.638389	1.399625	1.675382
C	-0.072670	-0.560692	-0.704286
C	-1.575078	-2.426927	-0.189677
H	-1.650332	-2.689528	0.872689
H	-2.511103	-2.702647	-0.683873
H	-0.754628	-2.985900	-0.632994
C	-2.332539	-0.065092	0.124323
H	-2.481373	0.727483	-0.609039
H	-3.280290	-0.604002	0.204883
N	-1.320058	-1.002726	-0.365404
C	1.245356	1.529449	0.069643
H	1.634206	2.451658	-0.372561
H	-0.703099	2.639432	0.438433
K	2.804042	-0.599439	0.588684
O	0.847723	-1.368207	-0.927119
C	-0.280325	1.527634	-2.138180
H	-0.250649	2.619617	-2.089531
H	0.424232	1.213729	-2.916564
H	-1.285286	1.229940	-2.469560

E	-1113.32505 au	C_v	195.41 J/mol°
ZPE	501.08 kJ/mol	S°	429.08 J/mol°
H°	-1113.12219 au	G°	-1113.17092 au

Dipole moment 4.44 D

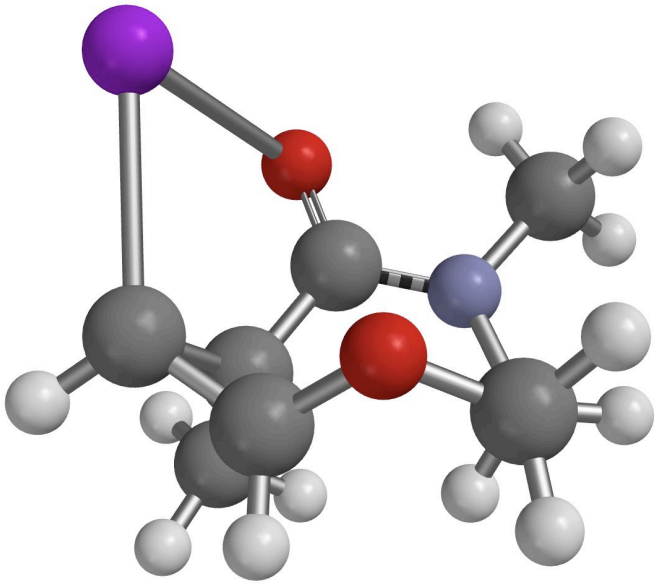

Figure 9. Optimized Geometry of **10** – product the K^+-templated 7-*exo-trig* cyclization of cyclopropene 1-carboxamide tethered to alkoxide.

TS1 (pseudo-boat)

Atom	X	Y	Z
C	-0.021608	1.469323	-0.266056
C	0.585867	1.326882	1.089363
O	0.474227	-0.551995	1.515455
C	-0.823928	-0.847491	1.913055
H	-0.947161	-1.940463	1.992426
H	-1.064841	-0.439726	2.913385
C	-0.411944	0.154852	-0.951724
C	-1.878326	-1.769966	-1.069936
H	-1.292164	-2.600805	-0.653554
H	-2.937145	-1.966958	-0.889575
H	-1.692708	-1.728995	-2.141145
C	-1.900931	-0.287899	0.933183
H	-2.055425	0.774991	1.108079
H	-2.860131	-0.784631	1.103431
N	-1.521109	-0.489408	-0.468780
C	1.434337	1.643532	0.081216
H	2.172087	2.414188	-0.079180
H	0.307629	1.666150	2.078153
K	2.238205	-1.044267	-0.203493
O	0.243205	-0.317473	-1.891329
C	-0.940437	2.641171	-0.597717
H	-0.655042	3.516195	-0.007917
H	-0.854156	2.909422	-1.655887
H	-1.996706	2.420868	-0.401697

E	-1113.28400 au	C_v	204.42 J/mol°
ZPE	494.71 kJ/mol	S°	437.54 J/mol°
H°	-1113.08301 au	G°	-1113.13270 au

Dipole moment 3.72 D

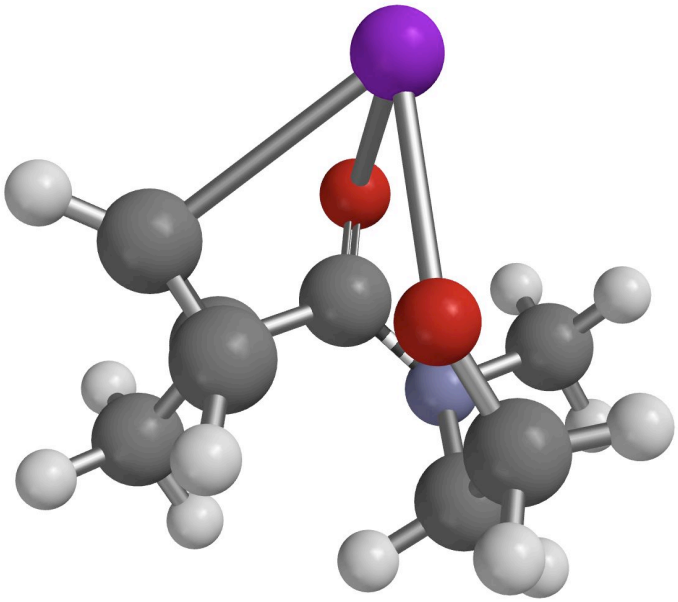

Figure 10. Optimized Geometry of **TS5**– transition state in product the K^+-templated 7-*exo-trig* cyclization of cyclopropene 1-carboxamide tethered to alkoxide. Obtained as a saddle point between **SM5** and **PDT5** using QTS2 algorithm.

TS2 (pseudo-chair)

Atom	X	Y	Z
C	-0.582696	1.371492	0.019387
C	0.044454	0.940958	1.317014
O	0.777331	-0.801053	1.200525
C	-0.124126	-1.868766	1.143792
H	0.372256	-2.800124	1.466634
H	-0.965070	-1.720756	1.844538
C	-0.482399	0.191382	-0.955705
C	-2.663385	-0.648921	-0.108012
H	-3.218665	0.126628	-0.632584
H	-3.241392	-1.572870	-0.183561
H	-2.593855	-0.376647	0.951755
C	-0.685200	-2.091961	-0.282251
H	-1.393526	-2.927370	-0.302553
N	-1.374326	-0.874200	-0.758483
C	0.728385	1.863639	0.573461
H	1.046798	2.868815	0.813688
H	-0.353743	0.829906	2.317051
K	2.620366	0.009241	-0.309388
O	0.461631	0.049085	-1.731097
C	-1.815472	2.283009	-0.008367
H	-1.506455	3.305700	0.222144
H	-2.279739	2.300543	-0.999439
H	-2.585314	2.001822	0.716763
H	0.122980	-2.321080	-0.978027

E	-1113.26202 au	C_v	203.44 J/mol°
ZPE	494.78 kJ/mol	S°	433.44 J/mol°
H°	-1113.06108 au	G°	-1113.11030 au

Dipole moment 2.98 D

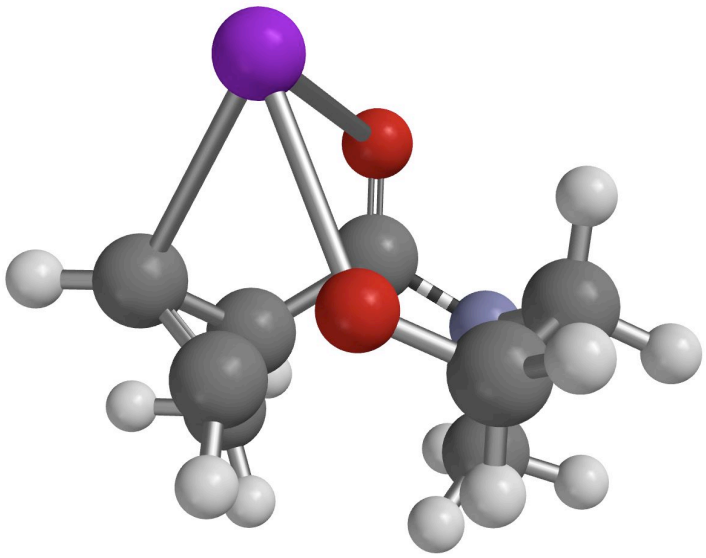

Figure 11. Optimized Geometry of chair-like **TS5'**– transition state in product the K^+-templated 7-*exo-trig* cyclization of cyclopropene 1-carboxamide tethered to alkoxide. Obtained by editing structure of **TS1** and optimizing it a saddle point between **SM5** and **PDT5** using QTS3 algorithm.