Supporting Information

Templated assembly of chiral medium-sized cyclic ethers via 8-*endo-trig* nucleophilic cyclization of cyclopropenes

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Complete References

Ref 2c: Kato, N.; Comer, E.; Sakata-Kato, T.; Sharma, A.; Sharma, M.; Maetani, M.; Bastien, J.; Brancucci, N. M.; Bittker, J. A.; Corey, V.; Clarke, D.; Derbyshire, E. R.; Dornan, G. L.; Duffy, S.; Eckley, S.; Itoe, M. A.; Koolen, K. M. J.; Lewis, T. A.; Lui, P. S.; Lukens, A. K.; Lund, E.; March, S.; Meibalan, E.; Meier, B. C.; McPhail, J. A.; Mitasev, B.; Moss, E. L.; Sayes, M.; Van Gessel, Y.; Wawer, M. J.; Yoshinaga, T.; Zeeman, A. M.; Avery, V. M.; Bhatia, S. N.; Burke, J. E.; Catteruccia, F.; Clardy, J. C.; Clemons, P. A.; Dechering, K. J.; Duvall, J. R.; Foley, M. A.; Gusovsky, F.; Kocken, C. H. M.; Marti, M.; Morningstar, M. L.; Munoz, B.; Neafsey, D. E.; Sharma, A.; Winzeler, E. A.; Wirth, D. F.; Scherer C. A.; Schreiber, S. L. *Nature* **2016**, *538*, 344-349.

Ref 2e: Dandapani, S.; Germain, A. R.; Jewett, I.; le Quement, S.; Marie, J.-C.; Muncipinto, G.; Duvall, J. R.; Carmody, L. C.; Perez, J. R.; Engel, J. C.; Gut, J.; Kellar, D.; Siqueira-Neto, J. L.; McKerrow, J. H.; Kaiser, M.; Rodriguez, A.; Palmer, M. A.; Foley, M.; Schreiber, S. L.; Munoz, B. *ACS Med. Chem. Lett.* **2014**, *5*, 149-153.

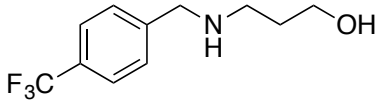
General Information

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, thus (+) correlates to CH_3 and CH groups, and (-) to CH_2 groups, respectively. 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 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 (S).

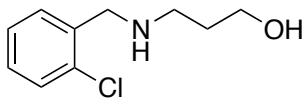
GC/MS analyses were performed on a Shimadzu GC-2010 gas chromatograph interfaced to a Shimadzu GCMS 2010S mass selective detector, and equipped with an AOC-20i auto-injector and an AOC-20S auto-sampler tray (150 vials). 30 m x 0.25 mm x 0.25 mm capillary column, SHR5XLB, polydimethylsiloxane, 5% Ph was 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. All commercially available reagents were purchased from Alfa Aesar, TCI America, Sigma-Aldrich or Acros Organics. 2-Bromo-1-methylcyclopropanecarbonyl chloride[1] and series of 1-bromo-2-alkyl-2-arylcyclopropane-1-carboxylic acids[2] were prepared according to the procedure published in our recent reports. Preparation of other non-commercially available starting materials is described below.

Experimental Procedures



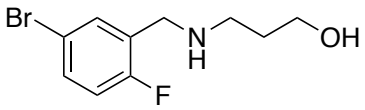
3-((4-(Trifluoromethyl)benzyl)amino)propan-1-ol (Typical procedure): To a stirring solution of 3-amino-1-propanol (1.00 g, 13.3 mmol, 1.00 equiv.) in methanol (9.5 mL), was added 4-(trifluoromethyl)benzaldehyde 1.82 mL (2.32 g, 13.3 mmol, 1.00 equiv.). The reaction mixture was stirred at room temperature for 1 h. Then, the mixture was cooled to 0 °C in a ice bath, and sodium borohydride (504 mg, 13.3 mmol) was added in little portions over a period of 15 min. The mixture was stirred at 0 °C for an additional 1 h, then quenched with water (50 mL). Most of the methanol was removed by evaporation under vacuum, and the resulting aqueous phase was extracted with dichloromethane (3 x 30 mL). The organic phase was washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated in vacuum to afford the titled product as colorless oil. Yield 2.98 g (12.8 mmol, 96%), as a white crystalline solid (m.p. 43.2-44.5 °C). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ ppm 7.57 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 3.84 (s, 2H), 3.80 – 3.78 (m, 2H), 2.95 (br. s, 2H), 2.89 – 2.85 (m, 2H), 1.73 (qd, *J* = 5.7, 4.8 Hz, 2H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ ppm 143.4, 129.4 (q, J_{CF} = 33.0 Hz), 128.3 (+, 2C), 125.4 (q, J_{CF} = 3.8 Hz, +, 2C), 124.1 (q, J_{CF} = 271.6 Hz), 64.1 (-), 53.4 (-), 49.3 (-), 30.8 (-); FT IR (NaCl, film, cm^{-1}) 3377, 3300, 2934, 1620 1454, 1327, 1163, 1123, 1067, 1019, 847, 820, 637; HRMS (TOF ES): found 234.1104, calculated for $C_{11}H_{15}F_3NO$ (M+H) 234.1106 (0.9 ppm).



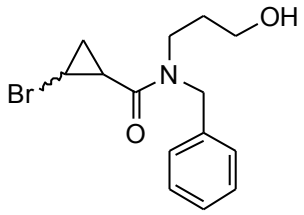
3-((2-Chlorobenzyl)amino)propan-1-ol: Obtained according to the typical procedure described above for the synthesis of 3-((4-(trifluoromethyl)benzyl)amino)propan-

(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) Edwards, A.; Ryabchuk, P.; Barkov, A.; Rubina, M.; Rubin, M. *Tetrahedron: Asymmetry* **2014**, *25*, 1537.

1-ol, employing 2-chlorobenzaldehyde (1.87 g, 13.3 mmol, 1.00 equiv.) instead of 4-(trifluoromethyl)benzaldehyde. Colorless oil, yield 2.47 g (12.4 mmol, 93%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ ppm 7.38-7.35 (m, 2H), 7.27-7.21 (m, 2H), 3.91 (s, 2H), 3.81 (t, *J* = 5.5 Hz, 2H), 2.90 (br. s, 2H) 2.88 (t, *J* = 5.9 Hz, 2H), 1.73 (quint, *J* = 5.8 Hz, 2H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ ppm 136.5, 133.8, 130.4 (+), 129.6 (+), 128.7 (+), 126.9 (+), 64.3 (-), 51.2 (-), 49.1 (-), 30.6 (-); FT IR (NaCl, film, cm^{-1}) 3310, 3067, 2934, 2853, 1472, 1443, 1102, 1051, 1038, 752, 679; HRMS (TOF ES): found 200.0844, calculated for $C_{10}H_{14}ClNO$ (M+H) 200.0842 (1.0 ppm).

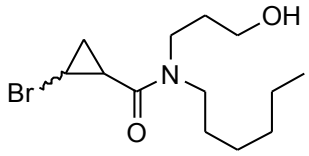


3-((5-Bromo-2-fluorobenzyl)amino)propan-1-ol: Obtained according to the typical procedure described above for the synthesis of 3-((4-(trifluoromethyl)-benzyl)amino)propan-1-ol, employing 5-bromo-2-fluorobenzaldehyde (2.70 g, 13.3 mmol, 1.00 equiv.) instead of 4-(trifluoromethyl)benzaldehyde. The crude material was additionally purified by preparative column chromatograph on Silica gel, eluting with mixture hexane/EtOAc 3:1 to afford the titled compound wa yellowish oil. Yield 3.14 g (12.0 mmol, 50%). ^{1}H NMR (500.13 MHz, $CDCl_3$) δ ppm 7.44 (dd, *J* = 6.5 Hz, 2.4 Hz, 1H), 7.35 (ddd, *J* = 8.7 Hz, 7.4 Hz, 2.4 Hz, 1H), 6.92 (dd, *J* = 9.5 Hz, 8.7 Hz, 1H), 3.81 (s, 2H), 3.80 (t, *J* = 5.3 Hz, 2H), 2.90 (br. s, 2H), 2.81 (t, *J* = 5.8 Hz, 2H), 1.73 (quint, *J* = 5.5 Hz, 2H); ^{13}C NMR (125.76 MHz, $CDCl_3$) δ ppm 160.2 (d, J_{CF} = 245.8 Hz), 133.1 (d, J_{CF} = 4.7 Hz, +), 131.8 (d, J_{CF} = 8.6 Hz, +), 128.5 (d, J_{CF} = 16.5 Hz), 117.2 (d, J_{CF} =23.5 Hz, +), 116.6 (d, J_{CF} = 3.6 Hz), 64.0 (-), 49.0 (-), 46.9 (d, J_{CF} = 2.7 Hz, -), 30.7 (-); FT IR (NaCl, film, cm^{-1}) 3318, 3106, 2932, 2850, 1483, 1454, 1402, 1234, 1172, 1098, 1071, 1030, 887, 813, 621; HRMS (TOF ES): found 262.0254, calculated for $C_{10}H_{13}BrFNO$ (M+H) 262.0254 (4.2 ppm);

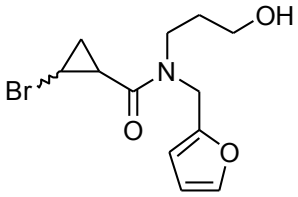


N-Benzyl-2-bromo-N-(3-hydroxypropyl)cyclopropane-carboxamide (**7b**): To a stirred solution of (3-benzyl-amino)propan-1-ol (550 mg, 3.3 mmol, 1.1 equiv) and triethylamine (610 mg, 6 mmol, 2 equiv) in dry THF (30 mL) was added 2-bromocyclopropanecarbonyl chloride (550 mg, 3.0 mmol). The mixture was stirred for 1 hr at room temperature, then the solvent was removed in vacuum. The residue was partitioned between 10% aqueous HCl (20 mL) and EtOAc (20 mL). The organic layer was separated and washed consecutively with 10% aqueous HCl (3 x 10 mL) and 4N aqueous NaOH (5 mL), dried with $MgSO_4$, filtered, and concentrated. The title compound was obtained as colorless oil, mixture of diastereomers, 2:1. This material was pure enough to be used for the following transformations without additional purification. Yield 690 mg (2.22 mmol, 74%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm [7.48-7.36 (m) & 7.36-7.27 (m) & 7.26-7.19 (m), S5H], [4.74 (d, *J* = 17.2 Hz) & 4.65 (d, *J* = 14.9 Hz), S1H], [4.66 (d, *J* = 17.4 Hz) & 4.54 (d, *J* = 14.9 Hz), S1H], 3.88 (br. s., 1 H), 3.71-3.42 (m, 4H), [3.30 (ddd, *J* = 7.6 Hz, 4.6 Hz, 3.0 Hz) & 3.27 (ddd, *J* = 7.8 Hz, 4.8 Hz, 3.0 Hz), S1H], [2.37 (ddd, *J* = 9.2 Hz, 5.9 Hz, 3.0 Hz) & 2.17 (ddd, *J* = 9.2 Hz, 5.9 Hz, 3.2 Hz), S1H], [1.83 (tt, *J* = 7.1 Hz, 6.1 Hz) & (1.78-1.64 (m), S3H], [1.37 (ddd, *J* = 9.4 Hz, 5.6 Hz, 4.8 Hz) & 1.33 (ddd, *J* = 9.1 Hz, 5.6 Hz, 4.8 Hz), S1H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) d major: 171.9, 136.0, 128.9 (+, 2C), 127.8

(+), 126.2 (+, 2C), 58.2 (-), 51.0 (-), 42.8 (-), 29.8 (-), 22.6 (+), 19.9 (+), 18.3 (-), minor: 170.4, 137.3, 128.4 (+, 2C), 127.9 (+, 2C), 127.3 (+), 58.9 (-), 49.0 (-), 43.9 (-), 31.5 (-), 22.3 (+), 20.2 (+), 18.1 (-); FTIR (NaCl, film, cm^1) 3387, 2930, 2874, 1620, 1450, 1215, 1055, 731, 698, 581; HRMS (TOF ES): found 334.0217, calculated for $C_{14}H_{18}NO_2BrNa$ (M+Na) 334.0419 (0.6 ppm);



2-Bromo-N-hexyl-N-(3-hydroxypropyl)cyclopropane-carboxamide (**7d**): mixture of diastereomers, 5:1. To a solution of (3-hexylamino)propan-1-ol[3] (350 mg, 2.2 mmol, 1.1 equiv) and triethylamine (410 g, 4.0 mmol, 2.0 equiv) in dry THF (15 mL) stirred at 0 °C was added a solution of 2-bromocyclopropanecarbonyl chloride (370 mg, 2.0 mmol, 1.0 equiv.) in dry THF (15 mL). The mixture was stirred for 5 hr at RT, then the solvent was removed in vacuum. The residue was partitioned between 10% aqueous HCl (20 mL) and EtOAc (20 mL). The organic layer was separated and washed consecutively with 10% aqueous HCl (3 x 10 mL) and 4N aqueous NaOH (5 mL), dried with $MgSO_4$, filtered, and concentrated. The title compound was obtained as colorless oil, mixture of diastereomers, 5:1. This material was pure enough to be used for the following transformations without additional purification. Yield 527 mg (1.72 mmol, 86%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm 3.90 (br. s., 2H), [3.68 (t, *J* = 5.7 Hz) & 3.56 (sxt, *J* = 6.8 Hz) & 3.49 (td, *J* = 6.1 Hz, 2.3 Hz) & 3.44 (t, *J* = 5.3 Hz) & 3.41-3.34 (m) & 3.34-3.23 (m) & 3.20 (ddd, *J* = 7.8 Hz, 4.7 Hz, 3.2 Hz), Σ7H], [2.26 (ddd, *J* = 9.2 Hz, 5.9 Hz, 3.0 Hz) & 2.12 (ddd, *J* = 9.2 Hz, 6.0 Hz, 3.0 Hz), Σ1H], [1.85 (quin, *J* = 6.3 Hz) & 1.77-1.56 (m) & 1.56-1.43 (m), Σ5H], 1.43-1.19 (m, 7H), [0.89 (t, *J* = 7.1 Hz) & 0.86 (t, *J* = 6.8 Hz), Σ3H]; ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm, major: 171.2, 58.0 (-), 48.2 (-), 42.6 (-), 31.3 (-), 30.2 (-), 29.4 (-), 26.4 (-), 22.5 (+), 22.4 (-), 19.9 (+), 18.1 (-), 13.9 (+); minor: 169.7, 59.0 (-), 46.7 (-), 44.7 (-), 32.0 (-), 31.5 (-), 27.6 (-), 26.5 (-), 22.4 (+), 22.3 (-), 20.2 (+), 17.8 (-), 13.9 (+); FT IR (NaCl, film, cm^1) 3408, 2955, 2930, 2858, 1620 1462, 1377, 1229, 1190, 1057, 725, 588; HRMS (TOF ES): found 328.0887, calculated for $C_{13}H_{24}BrNO_2Na$ (M+Na) 328.0888 (0.3 ppm);

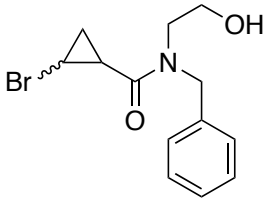


2-Bromo-N-(furan-2-ylmethyl)-N-(3-hydroxypropyl)cyclo-propanecarboxamide (**7e**): To a stirred solution of 3-((furan-2-ylmethyl)amino)propan-1-ol [4] (282 mg, 1.81 mmol, 1.10 equiv) and triethylamine (686 µL, 500 mg, 4.95 mmol, 3.00 equiv) in dry THF (5 mL) a solution of 2-bromo-1-methylcyclopropanecarbonyl chloride (300 mg, 1.65 mmol, 1.00 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). Combined organic solution was concentrated in vacuum. Preparative column

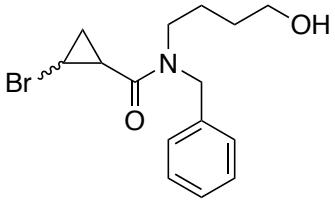
(3) Alnasleh, B. K.; Rubina, M.; Rubin, M. *Chem. Commun.* **2016**, *52*, 7494.

(4) Banning, J. E.; Prosser, A. R.; Alnasleh, B. K.; Smarker, J.; Rubina, M.; Rubin, M. *J. Org. Chem.* **2011**, *76*, 3968.

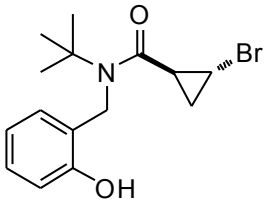
chromatography of a crude residue on silica gel afforded the title compound as a colorless oil, R_f 0.50 (DCM-EtOAc, 3:1). Yield 310 mg (1.02 mmol, 62%), mixture of two diastereomers, 2:1. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ [7.36 (s) & 7.29 (s), S1H], [6.35-6.28 (m) & 6.25 (d, *J* = 3.0 Hz) & 6.19 (d, *J* = 3.0 Hz), Σ2H], [4.59 (d, *J* = 16.9 Hz) & 4.53 (d, *J* = 15.4 Hz) & 4.53 (d, *J* = 16.9 Hz) & 4.48 (d, *J* = 15.4 Hz), Σ2H], [3.63-3.53 (m) & 3.54-3.44 (m) & 3.40 (t, *J* = 5.6 Hz) & 3.20 (ddd, *J* = 7.5 Hz, 4.7 Hz, 2.9 Hz), Σ4H], [2.35 (ddd, *J* = 9.1 Hz, 5.9 Hz, 3.2 Hz) & 2.28 (ddd, *J* = 9.1 Hz, 5.9 Hz, 3.2 Hz), Σ1H), [1.76 (quin, *J* = 6.5 Hz) & 1.69-1.55 (m), Σ3H], [1.34 (dt, *J* = 9.1 Hz, 5.6 Hz, 1H) & 1.29 (dt, *J* = 9.1 Hz, 5.3 Hz), Σ1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ major: 171.5, 149.5, 142.6 (+), 110.3 (+), 108.2 (+), 58.0 (-), 44.7 (-), 42.8 (-), 29.8 (-), 22.6 (+), 19.7 (+), 18.1 (-); minor: 170.1, 150.6, 141.9 (+), 110.2 (+), 108.4 (+), 58.6 (-), 44.3 (-), 42.1 (-), 31.4 (-), 22.1 (+), 20.1 (+), 18.0 (-); FT IR (NaCl, film, cm^1): 3414, 3117, 2932, 2876, 2341, 1626, 1504, 1477, 1454, 1373, 1356, 1229, 1188, 1072, 1055, 1013, 922, 741, 598, 586; HRMS (TOF ES): found 302.0391, calculated for $C_{12}H_{17}NO_3Br$ (M+H) 302.0392 (0.3 ppm);



N-benzyl-2-bromo-N-(2-hydroxyethyl)cyclopropane-1-carboxamide (**7a**): This material was prepared according to procedure described above for bromocyclopropane **7b**, employing (2-benzylamino)ethan-1-ol (500 mg, 3.3 mmol, 1.1 equiv.). After aqueous work up and extraction crude amide was used at the cyclization step as is without any purification.



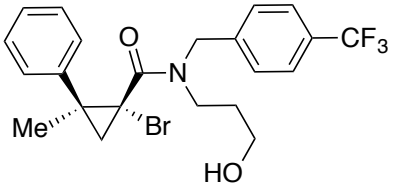
N-benzyl-2-bromo-N-(4-hydroxybutyl)cyclopropane-1-carboxamide (**7c**): This material was prepared according to procedure described above for bromocyclopropane **7b**, employing (4-benzylamino)butan-1-ol (590 mg, 3.3 mmol, 1.1 equiv.). After aqueous work up and extraction crude amide was used at the cyclization step as is without any purification.



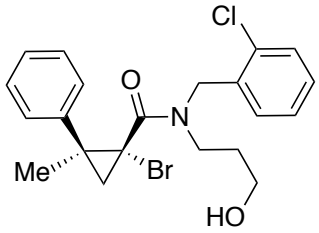
2-Bromo-N-(tert-butyl)-N-(2-hydroxybenzyl)cyclopropanecarboxamide (**11**) A solution of Me_3SiCl (261 mg, 2.40 mmol, 1.20 equiv), NEt_3 (708 mg, 975 mL, 7.00 mmol, 3.50 equiv), and 2-((*tert*-butylamino)methyl)phenol[5] (394 mg, 2.20 mmol, 1.10 equiv) was stirred in dry THF (30 mL) overnight under a nitrogen atmosphere. Then cyclopropylmonobromo acid chloride (367 mg, 2 mmol, 1 equiv) was added and allowed to stir for 3 hours. The solvent was removed by rotary evaporation and then partitioned between 10 mL 5% HCl & 10 mL EtOAc. The organic layer was washed with 5% HCl (3 x 15 mL) then dried with $MgSO_4$, filtered, and concentrated. The obtained crystalline material (mp 165-168 ^{o}C) was pure enough for the following transformation with no additional purification. Yield 583 mg (1.78 mmol, 89%). ^{1}H NMR (500.13 MHz, CD_3OD) δ ppm 7.04 (d, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.76 (t, *J* = 7.6 Hz, 1H),

(5) Modica, E.; Zanaletti, R.; Freccero, M.; Mella, M. *J. Org. Chem*. **2001**, *66*, 41.

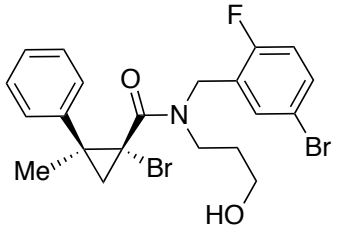
6.69 (d, *J* = 8.2 Hz, 1H), 4.67 (d, *J* = 19.2 Hz, 1H), 4.62 (d, *J* = 19.2 Hz, 1H), 3.04 (ddd, *J* = 7.6 Hz, 4.4 Hz, 3.2 Hz, 1H), 1.88 (ddd, *J* = 9.0 Hz, 6.0 Hz, 3.0 Hz, 1H), 1.41 (ddd, *J* = 7.6 Hz, 6.0 Hz, 5.0 Hz, 1H), 1.29 (s, 9H), 1.09 (dt, *J* = 9.5 Hz, 5.0 Hz, 1H); ^{13}C NMR (125.76 MHz, CD_3OD) δ ppm 174.0, 155.4, 129.2 (+), 127.7 (+), 126.6, 120.8 (+), 116.0 (+), 59.3, 45.4 (-), 28.8 (+, 3C), 26.6 (+), 20.4 (+), 18.6 (-); FT IR (NaCl, film, cm[1]): 3300, 2964, 2930, 1622, 1595, 1456, 1427, 1364, 1227, 1192, 754; HRMS (TOF ES): found 325.0670, calculated for $C_{15}H_{20}BrNO_2$ (M^+) 325.0677 (2.2 ppm).



(1R,2S)-1-Bromo-N-(3-hydroxypropyl)-2-methyl-2-phenyl-N-(4-(trifluoromethyl)benzyl)cyclopropane-1-carboxamide (**8t**): A fame-dried round bottom flask was charged with (-)-(1*R*,2*S*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (500 mg, 1.96 mmol, 1.00 equiv.), DMF (2 drops), and freshly distilled anhydrous dichloromethane (8.8 ml) under nitrogen atmosphere. Oxalyl chloride (336 µL, 498 mg, 3.92 mmol, 2 equiv.) was then added dropwise and the mixture was stirred at room temperature for 2h. The solution was concentrated under reduced pressure to provide the crude acyl chloride, which was then dissolved in anhydrous dichloromethane (2.5 mL) and added dropwise to a solution of the 3-((4-(trifluoromethyl)benzyl)amino)propan-1-ol 548 mg (2.35 mmol, 1.2 equiv.) and triethylamine (820 µL, 595 mg, 5.88 mmol, 3.00 equiv.) in andydrous dichloromethane (3.8 mL). The reaction mixture was stirred for 18 hours at RT and then partitioned between 1N HCl (10 mL) and dichloromethane (25 mL). The organic phase was then extracted with 1N HCl (3 x 10 mL). The combined aqueous layers were back-extracted once with dichloromethane (10 mL), which was combined with the other organic phases, washed with brine, dried with MgSO4, filtered, and concentrated under reduced pressure. The product was purified by column chromatography on silica gel eluting with mixture hexane-EtOAc (1:2) to afford the titled compound as colorless oil, R_f 0.44 (hexane-EtOAc, 1:2), yield 791 mg (1.68 mmol, 86%); $[\alpha]_D^{23}$ -41.5° (*c* 1.22, EtOH). NMR spectra show presence of two rotamers in a ratio of 1.5:1: ^{1}H NMR (500.13 MHz, $CDCl_3$) δ ppm [7.54 (d, *J* = 8.0 Hz) & 7.38-7.27 (m) & 7.12 (d, *J* = 8.0 Hz) & 6.64 (d, *J* = 7.9 Hz), Σ8H], [4.94 (d, *J* = 16.0 Hz) & 4.74 (d, *J* = 15.6 Hz), Σ1H], [4.04 (d, *J* = 15.6 Hz) & 3.93 (d, *J* = 16.0 Hz), Σ1H], [3.74-3.57 (m) & 3.37 (dt, *J* = 13.9, 6.8 Hz) & 3.12 (dt, *J* = 11.1, 5.4 Hz) & 2.93-2.63 (m) & 2.38 (br. s.) & 1.88 (s) & 1.86 (s), Σ10H], [1.50 (tq, *J* = 11.6, 5.4 Hz) & 1.23-1.03 (m), Σ3H]; ^{13}C NMR (125.79 MHz $CDCl_3$) δ ppm 168.7, 167.5, 125.8 (q, +, J_{CF} = 3.8 Hz), 125.6 (q, +, J_{CF} = 3.8 Hz), 60.9 (-), 58.3 (-), 51.8 (-), 47.4 (-), 45.5 (-), 42.5, 42.1, 40.8 (-), 32.3, 32.0, 30.3 (-), 29.2 (-), 27.4, 27.0, 25.1; The presence of rotomers and fluorine splitting renders the aromatic region too convoluted to accurately tabulate. A spectral chart and raw NMR data are available. FT IR (NaCl, film, cm^{-1}) 3428, 3061, 2953, 2932, 2874, 1636, 1499, 1447, 1418, 1325, 1165, 1125, 1067, 1018, 822, 770, 698; HRMS (TOF ES): found 492.0769, calculated for $C_{22}H_{23}BrF_3NO_2$ (M+Na) 492.0762 (1.4 ppm).

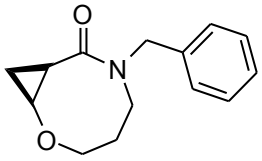


(1R,2S)-1-Bromo-N-(2-chlorobenzyl)-N-(3-hydroxypropyl)-2-methyl-2-phenylcyclopropane-1-carboxamide (**8u**): This material was synthesized according to procedure described above for compound **8t** employing 3-((2-chlorobenzyl)amino)propan-1-ol 469 mg (2.35 mmol, 1.2 equiv.) instead of (trifluoromethyl)benzyl)-amino)propan-1-ol. The titled compound was obtained as colorless oil, R_f 0.28 (Hexanes-EtOAc 1:1), yield 701 mg (1.6 mmol, 82%); $[\alpha]_D^{23}$ -58.7° (*c* 1.43, EtOH). NMR spectra show presence of two rotamers in a ratio of 1.8:1: ^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm [7.35-7.29 (m) & 7.28-7.23 (m) & 7.23-7.18 (m) & 7.18-7.19 (m) & 7.09-7.02 (m) & 6.99 (td, *J* = 7.7, 1.7 Hz) & 6.95-6.89 (m) & 6.82 (td, *J* = 7.6, 1.3 Hz) & 5.85 (dd, *J* = 7.2, 1.2 Hz), Σ8H], [4.82 (d, J = 17.2 Hz) & 4.52 (d, *J* = 16.4 Hz), Σ1H], [4.23 (d, *J* = 16.4 Hz) & 3.99 (d, *J* = 17.2 Hz), Σ1H], [3.67-3.47 (m) & 2.99 (dt, *J* = 11.6, 5.1 Hz) & 2.81 (ddd, *J* = 14.0, 11.7, 4.8) & 2.72-2.58 (m) & 2.51-2.37 (m) & 1.83 (s) & 1.78 (s), Σ10H], [1.44-1.35 (m) & 1.32 (d, *J* = 7.4 Hz) & 1.28 (d, *J* = 7.3 Hz) & 1.11-0.88 (m), Σ3H]; ^{13}C NMR (100.62 MHz $CDCl_3$) δ ppm 169.7, 168.9, 167.7, 60.8 (-), 58.4 (-), 49.4 (-), 46.2 (-), 45.5 (-), 42.6, 41.6 (-), 41.4, 40.8, 36.1, 32.3, 32.0, 30.4 (-), 29.1 (-), 28.3 (-), 28.0 (+), 27.0 (-), 26.8 (-), 25.1 (+); The presence of rotamers renders the aromatic region too convoluted to accurately tabulate. A spectral chart and raw NMR data are available. FT IR (NaCl, film, cm^{-1}) 3437, 3059, 3024, 2957, 2928, 2872, 1722, 1634, 1499, 1445, 1427, 1229, 1061, 770, 752, 737, 698; HRMS (TOF ES): found 458.0511, calculated for $C_{21}H_{23}BrClNO_2$ (M+Na) 458.0498 (2.8 ppm).

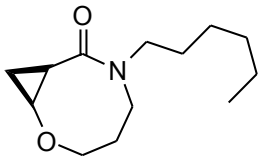


(1R,2S)-1-Bromo-N-(5-bromo-2-fluorobenzyl)-N-(3-hydroxypropyl)-2-methyl-2-phenylcyclopropane-1-carboxamide (**8v**): This material was synthesized according to procedure described above for compound **8t** employing 3-((5-bromo-2-fluorobenzyl)amino)propan-1-ol 616 mg (2.35 mmol, 1.2 equiv.) instead of (trifluoromethyl)benzyl)amino)propan-1-ol. The titled compound was obtained as colorless oil, R_f 0.24 (Hexanes-EtOAc 4:5), yield 860 mg (1.72 mmol, 88%); $[\alpha]_D^{23}$ -47.3° (*c* 1.54, EtOH). NMR spectra show presence of two rotamers in a ratio of 2.0:1: ^{1}H NMR (500.19 MHz, $CDCl_3$) δ ppm [7.38-7.24 (m) & 7.21-7.14 (m) & 7.12-7.06 (m) & 6.98-6.90 (m) & 6.79 (t, *J* = 9.1 Hz), Σ8H], [4.81 (d, *J* = 16.7 Hz) & 4.43 (dd, *J* = 15.2, 1.6 Hz), Σ1H], [4.16 (d, *J* = 15.2 Hz) & 4.02 (d, *J* = 16.7 Hz), Σ1H], [3.72-3.43 (m) & 3.11 (dt, *J* = 11.7, 5.2 Hz) & 2.82 (dt, *J* = 14.1, 6.0 Hz), Σ3H], [2.74 (d, *J* = 7.7 Hz) & 2.70 (d, *J* = 4.6 Hz), Σ1H], 2.68-2.56 (m, 1H), 2.06 (br. s., 1H), 1.85 (s, 3H), [1.47-1.35 (m) & 1.23-1.14 (m) & 1.13-1.03 (m), Σ3H]; ^{13}C NMR (125.79 MHz $CDCl_3$) δ ppm 168.8, 167.6, 61.0 (-), 58.4 (-), 46.0 (-), 44.8 (d, *J* = 5.7, -), 42.6, 41.7, 41.3 (-), 40.7 (d, *J* = 3.9 Hz, -), 32.4, 31.6, 30.4 (-), 29.2 (-), 27.3 (-), 27.1 (-), 25.1 (+), 24.6 (+); The presence of rotomers and fluorine splitting renders the aromatic region too convoluted to accurately tabulate. A spectral chart and raw NMR data are available. FT IR (NaCl, film, cm^{-1}) 3441, 3088, 3059, 2955, 2930, 1638, 1481, 1445, 1429, 1402, 1383, 1356, 1233, 1173, 1105, 1061, 814, 770, 737,

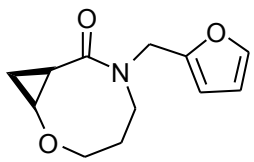
698, 619; HRMS (TOF ES): found 498.0074, calculated for $C_{21}H_{22}Br_2FNO_2$ (M+Na) 498.0080 (1.2 ppm).



(1S*,8R*)-6-Benzyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10b**): An oven-dried 50 mL round bottom flask was charged with bromocyclopropane **7a** (140 mg, 0.45 mmol, 1.0 equiv), 18-crown-6 (11.8 mg, 0.045 mmol, 10 mol%), KOH (88 mg, 1.57 mmol, 3.5 equiv) and anhydrous THF (10 mL). The mixture was stirred at RT for 2.25 hrs. The solvent was removed by rotary evaporation. The residue was purified by flash column chromatography on silica gel (R_f 0.28, eluent EtOAc) to obtain a title compound as a colorless crystalline solid, mp 51-55 ^oC. Yield 91 mg (0.40 mmol, 88%). ^1H NMR (500.13 MHz, $CDCl_3$) δ ppm 7.29-7.23 (m, 2H), 7.23-7.17 (m, 3H), 5.24 (d, *J* = 14.8 Hz, 1H), 3.85 (d, *J* = 15.1 Hz, 1H), 3.60 (td, *J* = 12.8 Hz, 3.2 Hz, 1H), 3.45 (ddd, *J* = 6.9 Hz, 6.1 Hz, 4.1 Hz, 1H), 3.17 (dd, *J* = 15.4 Hz, 6.9 Hz, 1H), 1.96 - 1.80 (m, 1H), 1.63 (dt, *J* = 10.2 Hz, 6.5 Hz, 1H), 1.53 (ddd, *J* = 15.2 Hz, 7.2 Hz, 3.2 Hz, 1H), 1.17 (td, *J* = 6.9 Hz, 3.9 Hz, 1H), 1.03 (dt, *J* = 10.2 Hz, 7.1 Hz, 1H); ^{13}C NMR (125.76 MHz, CD_3Cl) δ 169.7, 137.5, 128.5 (+, 2C), 128.1 (+, 2C), 127.3 (+), 72.8 (-), 61.0 (+), 48.6 (-), 46.0 (-), 30.1 (-), 22.7 (+), 10.5 (-); FTIR (NaCl, film, cm^1) 2928, 2870, 1634, 1481, 1439, 1229, 1080, 735, 698; HRMS (TOF ES): found 232.1332, calculated for $C_{14}H_{18}NO_2$ (M+H) 232.1338 (2.6 ppm).

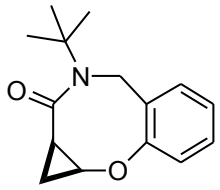


(1S*,8R*)-6-Hexyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10d**): An oven-dried 50 mL round bottom flask was charged with bromocyclopropane **7b** (165 mg, 0.53 mmol, 1.0 equiv), 18-crown-6 (14 mg, 0.053 mmol, 10 mol%), KOH (74 mg, 1.33 mmol, 2.5 equiv.) and anhydrous THF (10 mL). The mixture was stirred at RT for 2.25 hrs. The solvent was removed by rotary evaporation. The residue was purified by flash column chromatography on silica gel, eluting first with mixture EtOAc/hexane 3:1, and then with mixture EtOAc/MeOH 3:1, to obtain a title compound as a colorless amorphous solid, R_f 0.83 EtOAc/MeOH 3:1. Yield 107 mg (90%, 0.48 mmol). ^1H NMR (400.13 MHz, $CDCl_3$) δ ppm 4.22-4.06 (m, 2H), 3.88 (dddd, *J* = 13.4 Hz, 8.1 Hz, 6.6 Hz, 1.0 Hz, 1H), 3.66 (td, *J* = 12.7 Hz, 3.2 Hz, 1H), 3.48 (td, *J* = 6.7 Hz, 4.0 Hz, 1H), 3.28 (dd, *J* = 15.3 Hz, 6.9 Hz, 1H), 2.76 (ddd, *J* = 13.9 Hz, 8.8 Hz, 5.6 Hz, 1H), 2.02-1.86 (m, 1H), 1.71-1.43 (m, 4H), 1.13-1.21 (m, 6H), 1.15 (td, *J* = 6.8 Hz, 3.8 Hz, 1H), 1.03 (dt, *J* = 10.2 Hz, 7.0 Hz, 1H), 0.88 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ 169.1, 72.8 (-), 61.0 (+), 46.8 (-), 45.9 (-), 31.6 (-), 30.7 (-), 27.6 (-), 26.6 (-), 22.9 (+), 22.6 (-), 14.0 (+), 10.3 (-); FTIR (NaCl, film, cm^1) 2955, 2930, 2858, 1626, 1485, 1462, 1373, 1225, 1095, 725; HRMS (TOF ES): found 226.1807, calculated for $C_{13}H_{24}NO_2$ (M+H) 226.1807 (0.0 ppm).

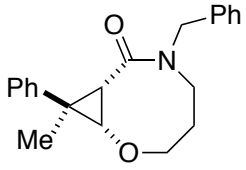


(1S*,8R*)-6-(Furan-2-ylmethyl)-2-oxa-6-azabicyclo[6.1.0]-nonan-7-one (**10e**): To a stirred suspension of powdered KOH (46 mg, 0.83 mmol, 2.5 equiv) and 18-crown-6 ether (8.7 mg, 0.033 mmol, 10 mol%) in dry THF (3 mL) was added bromocyclopropane **7c** (100 mg, 0.33 mmol, 1.0 equiv). The

mixture was vigorously stirred at 25 °C for 3 hrs. The KBr precipitate was filtered off on a fritted funnel and the filtrate wa concentrated in vacuum. Preparative column chromatography of a residual oil on silica gel afforded the title compound as a crystalline solid, R_f 0.30 (CH_2Cl_2-EtOAc, 3:1). Yield 69 mg (0.31 mmol, 95%). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ ppm 7.37 (d, *J* = 1.0 Hz, 1H), 6.37-6.31 (m, 1H), 6.29 (d, *J* = 3.3 Hz, 1H), 5.06 (d, *J* = 15.4 Hz, 1H), 4.22-4.08 (m, 2H), 3.68 (td, *J* = 12.6 Hz, 3.3 Hz, 1H), 3.55-3.48 (m, 1H), 3.41 (dd, *J* = 15.4 Hz, 6.8 Hz, 1H), 1.95-1.80 (m, 1H), 1.74-1.59 (m, 3H), 1.22 (td, *J* = 6.9 Hz, 3.9 Hz, 1H), 1.08 (dt, *J* = 10.2 Hz, 6.9 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 169.5, 151.0, 142.1 (+), 110.5 (+), 108.6 (+), 72.8 (-), 60.9 (+), 46.4 (-), 41.7 (-), 30.2 (-), 22.7 (+), 10.4 (-); FT IR (NaCl, film, cm^1): 3115, 2959, 2932, 2872, 1728, 1634, 1504, 1479, 1464, 1423, 1393, 1362, 1337, 1281, 1248, 1225, 1200, 1165, 1148, 1121, 1107, 1080, 1041, 1011, 982, 964, 932, 885, 833, 762, 743, 600, 540, 417; HRMS (TOF ES): found 222.1129, calculated for $C_{12}H_{16}NO_3$ (M+H) 222.1130 (0.5 ppm).



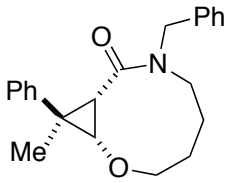
(1aR*,9aS*)-3-(tert-Butyl)-1,3,4,9a-tetrahydrobenzo[b]cyclopropa[g][1,5]oxazocin-2(1aH)-one (**12**): An oven-dried 50 mL round bottom flask was charged with bromocyclopropane **11** (184mg, 0.56 mmol, 1 equiv), 18-crown-6 (14.9 mg, 0.056 mmol, 10 mol%), KOH (78.6 mg, 1.4 mmol, 2.5 equiv.) and anhydrous THF (15 mL). The mixture was stirred at 50 °C for 12 hrs. The solvent was removed by rotary evaporation. The residue was absorbed onto silica gel and then purified by flash column chromatography on silica gel being flushed (eluent EtOAc/hexane 1:2 R_f: 0.30 product). Yield 129 mg (93%, 0.52 mmol) clear crystalline solid, mp 115-116 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 7.24 (td, *J* = 7.6 Hz, 1.8 Hz, 1H), 7.15 (dd, *J* = 7.6 Hz, 1.5 Hz, 1H), 7.09-7.03 (m, 2H), 5.59 (d, *J* = 17.2 Hz, 1H), 4.35 (d, *J* = 16.9 Hz, 1H), 3.79 (td, *J* = 6.2 Hz, 3.0 Hz, 1H), 2.22 (dt, *J* = 10.1 Hz, 6.3 Hz, 1H), 1.41 (td, *J* = 6.9 Hz, 3.2 Hz, 1H), 1.35 (s, 9H), 1.15 (dt, *J* = 10.1 Hz, 6.7 Hz, 1H); ^{13}C NMR (100.67 MHz, $CDCl_3$) δ ppm 169.9, 157.5, 130.8 (+), 128.9 (+), 128.7, 123.6 (+), 121.8 (+), 57.7, 56.9 (+), 48.9 (-), 28.5 (+, 3C), 26.6 (+), 10.4 (-); FT IR (NaCl, film, cm^1): 3456, 2993, 2966, 2924, 1651, 1489, 1408, 1358, 1225, 1194, 1111, 754; HRMS (TOF ES): found 268.1311, calculated for $C_{15}H_{19}NO_2Na$ (M+Na) 268.1313 (0.7 ppm).



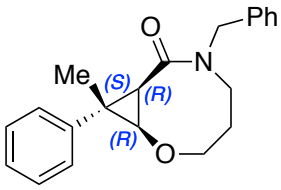
(1S*,8S*,9R*)-6-Benzyl-9-methyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (*rac*-**10g**, Typical procedure): A flame dried 25 mL round-bottom flask equipped with a drying tube and magnetic stir bar was charged with (*rac*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (127.5 mg, 0.50 mmol, 1.00 equiv), DMF (3 drops) and 10 mL of CH_2Cl_2. The mixture was then treated with oxalyl chloride (65 μL, 0.75 mmol, 1.5 equiv) at 0°C, stirred for 15 min, then warmed to room temperature and additionally stirred for 2 hours. The solvent was then removed in vacuum and the crude acyl chloride was dissolved in 10 mL of dry THF and added dropwise to a solution of 3-(benzylamino)propan-1-ol (99 mg, 0.6 mmol, 1.20 equiv) and triethyl amine (209 μL, 1.50 mmol, 3.00 equiv.) in 10 mL of THF. The reaction mixture was stirred overnight. After the reaction was complete,

the solvent was removed in vacuum and the resulting residue was partitioned between 10 mL of EtOAc and 10 mL of water. The organic phase was separated; the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. The residue was filtered through a short plug of Silica gel, eluting with EtOAc to afford *rac*-*N*-benzyl-1-bromo-*N*-(3-hydroxy-propyl)-2-methyl-2-phenylcyclopropane-1-carboxamide (*rac*-**8g**) as a colorless oil. Yield 110 mg (0.27 mmol, 54%), R_f 0.28 (hexanes/EtOAc 2:1). This material was used for the cyclization step as is without additional purification.

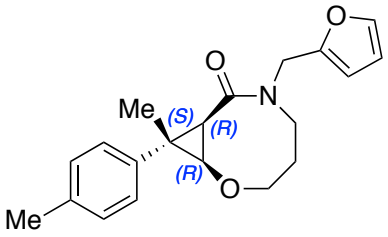
An oven-dried 10 mL Weaton vial was charged with obtained bromocyclopropane *rac*-**8g** (110 mg, 0.27 mmol, 1.0 equiv.), *t*-BuOK (183 mg, 1.62 mmol, 6.00 equiv), and anhydrous DMSO (7.0 mL). The reaction mixture was stirred overnight at 40 °C, and then the reaction mixture was poured into a separatory funnel and was partitioned between 10 mL of water and 100 mL of ethyl acetate. Organic layers were washed with water (3 x 10 mL) and brine (10 mL). Organic extract was dried over $MgSO_4$, filtered and evaporated. Residual oil was dissolved in mixture hexane-EtOAc 3:1 to make c.a. 20% solution, which was loaded on a top of Silica gel column (15 mm ID, 60 mm hight). Flash column chromatography afforded the title compound as a colorless oil. R_f 0.34 (hexanes/EtOAc 3:1). Yield 74 mg (0.229 mmol 85%), dr 100:0. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.07 (m, 10H), 5.16 (d, *J* = 14.7 Hz, 1H), 4.15 (dd, *J* = 12.6, 5.3 Hz, 1H), 3.97 (d, *J* = 14.7 Hz, 1H), 3.98–3.89 (m, 1H), 3.67 (td, *J* = 12.7, 3.1 Hz, 1H), 3.58 (d, *J* = 6.3 Hz, 1H), 3.19 (dd, *J* = 15.5, 7.2 Hz, 1H), 1.99–1.89 (m, 1H), 1.87 (d, *J* = 6.3 Hz, 1H), 1.57 (ddd, *J* = 9.2, 6.6, 2.0 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 146.0, 137.8, 128.7 (+, 2C), 128.6 (+, 2C), 128.4 (+, 2C), 127.9 (+, 2C), 127.5 (+), 126.5 (+), 72.7 (-), 68.5 (+), 48.9 (-), 46.4 (-), 31.4 (+), 30.6 (-), 30.1, 17.9 (+); FT IR (KBr, cm^{-1}): 3031, 1635, 1477, 1419, 1263, 1147, 1110, 1091, 1014, 933, 916, 883, 761, 730, 700, 617; HRMS (TOF ES): found 321.1720, calculated for $C_{21}H_{23}NO_2$ (M^+) 321.1729 (2.8 ppm).



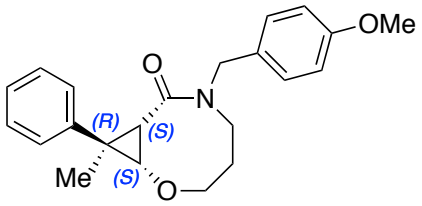
(1S*,9S*,10R*)-7-benzyl-10-methyl-10-phenyl-2-oxa-7-azabi-cyclo[7.1.0]decan-8-one (**10h**): This material was obtained according to the typical procedure described above employing *rac*-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (127.5 mg, 0.50 mmol, 1.00 equiv) and 4-(benzylamino)butan-1-ol (107 mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8h** was 155 mg (0.37 mmol, 74%), R_f 0.37 (hexanes/EtOAc 1:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 26 mg (0.077 mmol 21%), dr 100:0. R_f 0.36 (hexanes/EtOAc 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 6.94 (m, 10H), 5.35 (d, *J* = 14.7 Hz, 1H), 4.29 (dd, *J* = 12.8, 7.5 Hz, 1H), 4.23–4.11 (m, 1H), 3.86 (d, *J* = 14.7 Hz, 1H), 3.52 (d, *J* = 6.4 Hz, 1H), 3.42 (ddd, *J* = 12.8, 7.8, 1.0 Hz, 1H), 3.17 (ddd, *J* = 14.8, 4.9, 1.7 Hz, 1H), 1.96 (d, *J* = 6.4 Hz, 1H), 2.00–1.87 (m, 1H), 1.81 (ddd, *J* = 15.0, 7.3, 3.6 Hz, 1H), 1.61 (s, 3H), 1.59–1.49 (m, 1H), 1.46–1.33 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 146.6, 137.7, 128.7 (+, 2C), 128.6 (+, 2C), 128.5 (+, 2C), 127.9 (+, 2C), 127.4 (+), 126.5 (+), 72.2 (-), 66.7 (+), 45.8 (-), 43.5 (-), 31.4 (+), 29.9, 27.6 (-), 25.0 (-), 17.3 (+); FT IR (KBr, cm^{-1}): 2927, 1643, 1633, 1444, 1429, 1151, 1091, 810, 763, 734, 700, 648, 599, 559; HRMS (TOF ES): found 334.1807, calculated for $C_{22}H_{24}NO_2$ (M-H) 334.1807 (1.5 ppm).



(-)-(1R,8R,9S)-6-benzyl-9-methyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10g**): This material was obtained according to the procedure described above for *rac*-**10g**, employing (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid instead of racemic starting material. Physical appearance, chromatographic and spectral properties of this compound were identical to those described above for the racemic sample. Yield 74 mg (0.229 mmol 85%), dr 100:0. $[\alpha]_D$= -88.2° (c 0.660, CH_2Cl_2).



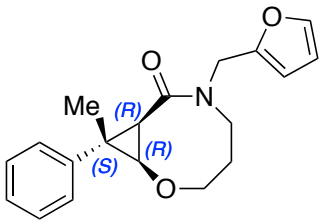
(-)-(1R,8R,9S)-6-(furan-2-ylmethyl)-9-methyl-9-(p-tolyl)-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10j**): This material was obtained according to the typical procedure described above employing (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (134.5 mg, 0.50 mmol, 1.00 equiv) and 3-((furan-2-ylmethyl)amino)propan-1-ol[4] (93 mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8j** was 82 mg (0.20 mmol, 40%), R_f 0.25 (hexanes/EtOAc 2:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 54 mg (0.166 mmol 83%), dr 100:0. R_f 0.40 (hexanes/EtOAc 2:1). $[\alpha]_D$= -26.8° (c 0.340, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23–7.12 (m, 3H), 7.01 (d, *J* = 7.8 Hz, 2H), 6.33–5.89 (m, 2H), 4.85 (d, *J* = 15.2 Hz, 1H), 4.12 (d, *J* = 15.3 Hz, 1H), 4.10 (dd, *J* = 12.6, 5.3 Hz, 1H), 3.93 (dd, *J* = 15.5, 10.4 Hz, 1H), 3.62 (td, *J* = 12.7, 3.1 Hz, 1H), 3.50 (d, *J* = 6.2 Hz, 1H), 3.32 (dd, *J* = 15.5, 7.1 Hz, 1H), 2.21 (s, 3H), 1.82 (ddd, *J* = 11.7, 4.8, 2.2 Hz, 1H), 1.75 (d, *J* = 6.2 Hz, 1H), 1.63–1.44 (m, H), 1.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 151.4, 143.2, 142.2(+), 136.2, 129.3 (+, 2C), 127.8 (+, 2C), 110.6 (+), 108.8 (+), 72.8 (-), 68.6 (+), 46.9 (-), 42.0 (-), 31.3 (+), 30.7 (-), 21.1 (+), 18.0 (+); FT IR (KBr, cm^{-1}): 3386, 1639, 1477, 1421, 1380, 929, 883, 817, 779, 723, 703, 665, 648, 626, 599; HRMS (TOF ES): found 326.1762, calculated for $C_{20}H_{24}NO_3$ (M+H) 326.1756 (1.8 ppm).



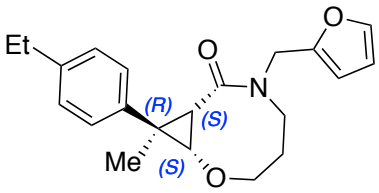
(-)-(1S,8S,9R)-6-(4-methoxybenzyl)-9-methyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10k**): This material was obtained according to the typical procedure described above employing (-)-(1*R*,2*S*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (127.5 mg, 0.50 mmol, 1.00 equiv) and 3-((4-methoxybenzyl)amino)propan-1-ol[6] (117mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8k** was 113 mg (0.260 mmol, 52%), R_f 0.23 (hexanes/EtOAc 1:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 59 mg (0.169 mmol 65%), dr 100:0. R_f 0.33 (hexanes/EtOAc 2:1). $[\alpha]_D$= -28.5° (c 0.280, CH_2Cl_2). ^{1}H NMR (500

(6) James, T.; MacLellan, P.; Burslem, G. M.; Simpson, I.; Grant, J. A.; Warriner, S.; Sridharan, V.; Nelson, A. *Org. Biomol. Chem.* **2014**, *12*, 2584.

MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.34–7.24 (m, 4H), 7.20 (t, *J* = 7.3 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.14 (d, *J* = 14.5 Hz, 1H), 4.21 (dd, *J* = 12.6, 5.2 Hz, 1H), 3.98 (d, *J* = 14.5 Hz, 1H), 4.00–3.90 (m, 1H), 3.80 (s, 3H), 3.72 (td, *J* = 12.7, 3.0 Hz, 1H), 3.63 (d, *J* = 6.3 Hz, 1H), 3.25 (dd, *J* = 15.4, 7.1 Hz, 1H), 1.98 (dd, *J* = 7.6, 5.1 Hz, 1H), 1.91 (d, *J* = 6.3 Hz, 1H), 1.70–1.57 (m, 1H), 1.52 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 159.1, 146.1, 129.9, 129.8 (+, 2C), 128.6 (+, 2C), 127.9 (+, 2C), 126.5 (+), 114.1 (+, 2C), 72.8 (-), 68.5 (+), 55.4 (+), 48.3 (-), 46.2 (-), 31.5 (+), 30.6 (-), 30.1 (+), 17.9 (+); FT IR (KBr, cm^{-1}): 3406, 1631, 1512, 1477, 1440, 1245, 1222, 927, 883, 815, 802, 761,702, 630, 609; HRMS (TOF ES): found 350.1759, calculated for $C_{19}H_{21}NO_3$ (M^+) 350.1756 (0.3 ppm).

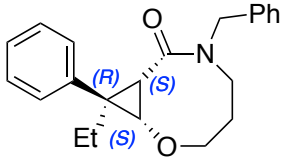


(-)-(1R,8R,9S)-6-(furan-2-ylmethyl)-9-methyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10l**): This material was obtained according to the typical procedure described above employing (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (134.5 mg, 0.50 mmol, 1.00 equiv) and 3-((furan-2-ylmethyl)amino)-propan-1-ol[4] (93 mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8l** was 82 mg (0.20 mmol, 40%), R_f 0.25 (hexanes/EtOAc 2:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 54 mg (0.166 mmol 83%), dr 100:0. R_f 0.4 (hexanes/EtOAc 2:1). $[\alpha]_D$= -26.8° (c 0.340, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23–7.12 (m, 3H), 7.01 (d, *J* = 7.8 Hz, 2H), 6.33–5.89 (m, 2H), 4.85 (d, *J* = 15.2 Hz, 1H), 4.12 (d, *J* = 15.3 Hz, 1H), 4.10 (dd, *J* = 12.6, 5.3 Hz, 1H), 3.93 (dd, *J* = 15.5, 10.4 Hz, 1H), 3.62 (td, *J* = 12.7, 3.1 Hz, 1H), 3.50 (d, *J* = 6.2 Hz, 1H), 3.32 (dd, *J* = 15.5, 7.1 Hz, 1H), 2.21 (s, 3H), 1.82 (ddd, *J* = 11.7, 4.8, 2.2 Hz, 1H), 1.75 (d, *J* = 6.2 Hz, 1H), 1.63–1.44 (m, H), 1.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 151.4, 143.2, 142.2(+), 136.2, 129.3 (+, 2C), 127.8 (+, 2C), 110.6 (+), 108.8 (+), 72.8 (-), 68.6 (+), 46.9 (-), 42.0 (-), 31.3 (+), 30.7 (-), 21.1 (+), 18.0 (+); FT IR (KBr, cm^{-1}): 3386, 1639, 1477, 1421, 1380, 929, 883, 817, 779, 723, 703, 665, 648, 626, 599; HRMS (TOF ES): found 326.1762, calculated for $C_{20}H_{24}NO_3$ (M+H) 326.1756 (1.8 ppm).

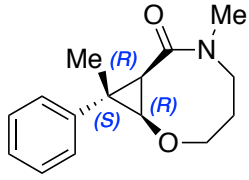


(+)-(1S,8S,9R)-9-(4-ethylphenyl)-6-(furan-2-ylmethyl)-9-methyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10m**): This material was obtained according to the typical procedure described above employing (-)-(1*R*,2*S*)-1-bromo-2-methyl-2-(4-ethylphenyl)-cyclopropanecarboxylic acid (141.5 mg, 0.50 mmol, 1.00 equiv) and 3-((furan-2-ylmethyl)amino)propan-1-ol[4] (93 mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8m** was 138 mg (0.33 mmol, 65%), R_f 0.36 (hexanes/EtOAc 2:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 106 mg (0.310 mmol 94%), dr 100:0. R_f 0.48 (hexanes/EtOAc 2:1). $[\alpha]_D$= +30.0° (c 0.400, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.39–6.26 (m, 2H), 4.95 (d, *J* = 15.2 Hz, 1H), 4.23 (d, *J* = 15.3 Hz, 1H), 4.20 (dd, *J* = 13.6, 4.1 Hz, 1H), 4.03 (dd, *J* = 15.5, 10.4 Hz, 1H), 3.72 (td, *J* = 12.7, 3.1 Hz, 1H), 3.60

(d, *J* = 6.2 Hz, 1H), 3.42 (dd, *J* = 15.5, 7.1 Hz, 1H), 2.61 (q, *J* = 7.6 Hz, 2H), 2.00–1.87 (m, 1H), 1.87 (d, *J* = 6.2 Hz, 1H), 1.71–1.60 (m, 1H), 1.46 (s, 3H), 1.22 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 151.4, 143.3 (+), 142.5, 142.2, 128.1 (+, 2C), 127.9 (+, 2C), 110.6 (+), 108.7 (+), 72.8 (-), 68.6 (+), 46.9 (-), 42.0 (-), 31.3 (+), 30.7 (-), 29.8, 28.5 (-), 18.0 (+), 15.7 (+); FT IR (KBr, cm^{-1}): 2962, 2931, 2871, 2079, 1992, 1643, 1633, 1514, 1477, 1421, 1380, 1353, 1336, 1301, 1263, 1242, 1211, 1147, 1108, 1089, 1012, 931, 883, 831, 813, 779, 732, 702, 665, 646, 624, 599; HRMS (TOF ES): found 339.1835, calculated for $C_{21}H_{25}NO_3$ (M^+) 339.1834 (0.3 ppm).

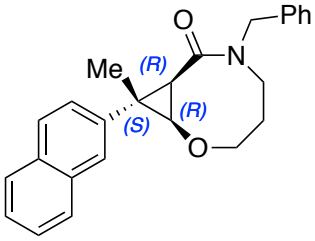


(+)-(1S,8S,9R)-6-benzyl-9-ethyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10n**): This material was obtained according to the typical procedure described above employing (-)-(1*R*,2*S*)-1-bromo-2-ethyl-2-phenylcyclopropanecarboxylic acid (134.5 mg, 0.50 mmol, 1.00 equiv) and 3-(benzylamino)propan-1-ol (99 mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8n** was 200 mg (0.48 mmol, 96%), R_f 0.30 (hexanes/EtOAc 2:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 127 mg (0.379 mmol 79%), dr 100:0. R_f 0.38 (hexanes/EtOAc 3:1 $[\alpha]_D$= +9.1° (c 0.780, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60–7.04 (m, 10H), 5.28 (d, *J* = 14.7 Hz, 1H), 4.23 (dd, *J* = 12.6, 5.3 Hz, 1H), 3.99 (d, *J* = 14.8 Hz, 1H), 3.99–3.92 (m, 1H), 3.77–3.62 (m, 2H), 3.23 (dd, *J* = 15.5, 7.2 Hz, 1H), 2.12–1.93 (m, 2H), 1.88 (d, *J* = 6.2 Hz, 1H), 1.77 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.64 (ddd, *J* = 15.0, 6.6, 1.9 Hz, 1H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 143.9, 137.8, 129.4 (+, 2C), 128.7 (+, 2C), 128.4 (+, 2C), 128.4 (+, 2C), 127.5 (+), 126.6 (+), 72.9 (-), 68.3 (+), 48.8 (-), 46.3 (-), 35.2, 32.4 (+), 30.6 (-), 24.9 (-), 11.4 (+); FT IR (KBr, cm^{-1}): 3056, 2966, 2935, 1633, 1477, 1421, 1357, 1265, 1247, 1357, 1265, 1247, 1220, 114, 1105, 1014, 935, 887, 763, 736, 702, 682, 659, 617, 595; HRMS (TOF ES): found 335.1891, calculated for $C_{22}H_{25}NO_2$ (M+) 335.1885 (1.8 ppm).

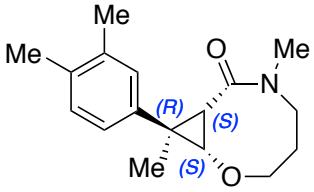


(+)-(1R,8R,9S)-6,9-dimethyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10o**): This material was obtained according to the typical procedure described above employing (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (127.5 mg, 0.50 mmol, 1.00 equiv) and 3-methylamino-1-propanol (57 µL, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8o** was 90 mg (0.27 mmol, 52%), R_f 0.22 (hexanes/EtOAc 1:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 41 mg (0.165 mmol 61%), dr 100:0. R_f 0.44 (CH_2Cl_2/MeOH 10:1). $[\alpha]_D$= +3.2° (c 0.380, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.34 (m, 2H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.22–7.10 (m, 1H), 4.35–4.07 (m, 2H), 3.74 (td, *J* = 12.7, 3.2 Hz, 1H), 3.61 (d, *J* = 6.3 Hz, 1H), 3.19 (dd, *J* = 15.3, 7.2 Hz, 1H), 2.99 (s, 3H), 2.12–1.98 (m, 1H), 1.87 (d, *J* = 6.2 Hz, 1H), 1.76–1.63 (m, 1H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.8, 146.1, 128.6 (+, 2C), 127.8 (+, 2C), 126.5 (+), 72.7 (-), 68.5 (+), 49.5(-), 33.7 (+), 31.3 (+), 30.4 (-), 30.0, 17.8 (+); FT IR (KBr, cm^{-1}): 2958, 2929, 1633, 1494, 1456, 1444, 1400, 1380, 1352, 1294, 1263, 1218, 1151, 1130, 1091, 1064,

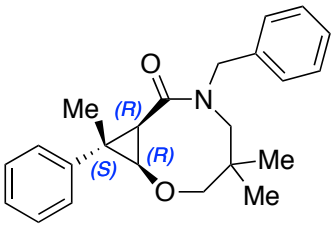
1024, 1010, 931, 763, 702, 684.; HRMS (TOF ES): found 244.1340, calculated for $C_{15}H_{18}NO_2$ (M-H) 244.1338 (0.8 ppm).



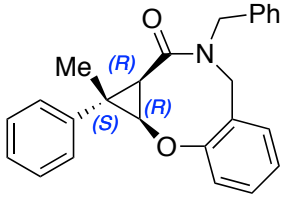
(+)-(1R,8R,9S)-6-benzyl-9-methyl-9-(naphthalen-2-yl)-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10p**): This material was obtained according to the typical procedure described above employing (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-(naphthalen-2-yl)cyclopropanecarboxylic acid (88 mg, 0.20 mmol, 1.00 equiv) and 3-(benzylamino)-propan-1-ol (40 mg, 0.24 mmol, 1.20 equiv) as starting materials. Yield of **8p** was 70 mg (0.155 mmol, 78%), R_f 0.28 (hexanes/EtOAc 3:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 28 mg (0.076 mmol 49%), dr 100:0. $[\alpha]_D$= +25.8° (c 0.60, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (ddd, *J* = 7.8, 7.1, 2.0 Hz, 4H), 7.57 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.51–7.41 (m, 2H), 7.35 (d, *J* = 4.4 Hz, 4H), 7.32–7.27 (m, 1H), 5.27 (dd, *J* = 14.7, 0.7 Hz, 1H), 4.25 (dd, *J* = 12.6, 5.2 Hz, 1H), 4.05 (d, *J* = 14.8 Hz, 1H), 4.06–3.98 (m, 1H), 3.78 (dd, *J* = 12.7, 3.1 Hz, 1H), 3.74 (d, *J* = 6.3 Hz, 1H), 3.27 (dd, *J* = 15.5, 7.2 Hz, 1H), 2.05 (d, *J* = 6.2 Hz, 1H), 2.04 (dd, *J* = 10.4, 7.6 Hz, 1H), 1.66 (ddd, *J* = 13.2, 5.6, 1.8 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 143.4, 137.8, 133.6, 132.3, 128.7 (+, 2C), 128.5 (+, 2C), 127.8 (+), 127.7 (+), 127.5 (+), 126.6 (+), 126.2 (+), 125.8 (+), 72.8 (-), 68.5 (+), 49.0 (-), 46.5 (-), 31.5 , 30.6 (+), 30.4 (-), 17.9 (+); FT IR (KBr, cm^{-1}): 3058, 1633, 1475, 1421, 1261, 858, 819, 748, 734, 702, 676, 659, 648, 609; HRMS (TOF ES): found 372.1966, calculated for $C_{25}H_{26}NO_2$ (M+H) 372.1964 (0.5 ppm).



(+)-(1S,8S,9R)-9-(3,4-dimethylphenyl)-6,9-dimethyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10q**): This material was obtained according to the typical procedure described above employing (-)-(1*R*,2*S*)-1-bromo-2-methyl-2-(3,4-dimethylphenyl)cyclopropanecarboxylic acid (141.5 mg, 0.50 mmol, 1.00 equiv) and 3-methylamino-1-propanol (57 μL, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8q** was 92 mg (0.26 mmol, 52%), R_f 0.33 (hexanes/EtOAc 1:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 48 mg (0.174 mmol 67%), dr 100:0. R_f 0.40 (CH_2Cl_2/MeOH 10:1). $[\alpha]_D$= +7.5° (c 0.320, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1H), 7.10 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 4.41–4.06 (m, 2H), 3.73 (td, *J* = 12.7, 3.2 Hz, 1H), 3.58 (d, *J* = 6.2 Hz, 1H), 3.19 (dd, *J* = 15.3, 7.2 Hz, 1H), 2.99 (s, 3H), 2.23 (s, 3H), 2.22 (s, 3H), 2.10–1.99 (m, 1H), 1.84 (d, *J* = 6.3 Hz, 1H), 1.74–1.63 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 143.7, 136.8, 134.8, 129.9 (+), 129.3 (+), 125.2 (+), 72.7 (-), 68.6 (+), 49.5 (-), 33.7 (+), 31.2 (+), 30.4 (-), 29.7, 19.8 (+), 19.4 (+), 17.9 (+) ;FT IR (KBr, cm^{-1}): 2960, 2933, 2869, 2071, 1633, 1502, 1487, 1454, 1434, 1398, 1382, 1292, 1261, 1222, 1124, 1089, 1022 , 929, 873, 819, 783, 717, 705, 634, 595; HRMS (TOF ES): found 273.1730, calculated for $C_{17}H_{23}NO_2$ (M^+) 273. 1730 (0.4 ppm).



(-)-(1R,8R,9S)-6-benzyl-4,4,9-trimethyl-9-phenyl-2-oxa-6-azabicyclo[6.1.0]nonan-7-one (**10r**): This material was obtained according to the typical procedure described above employing (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (127.5 mg, 0.50 mmol, 1.00 equiv) and 3-(benzylamino)-2,2-dimethylpropan-1-ol[7] (116 mg, 0.6 mmol, 1.20 equiv) as starting materials. Yield of **8r** was 90 mg (0.209 mmol, 54%), R_f 0.26 (hexanes/EtOAc 5:1). This crude material was subjected to elimination step to afford the title compound as a colorless oil. Yield 27 mg (0.077 mmol 37%), dr 100:0. R_f 0.36 (hexanes/EtOAc 5:1). $[\alpha]_D$= -150.8° (c 0.240, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–6.98 (m, 10H), 5.58 (d, *J* = 14.9 Hz, 1H), 3.88 (d, *J* = 15.6 Hz, 1H), 3.64 (dd, *J* = 19.1, 8.0 Hz, 2H), 3.59–3.48 (m, 1H), 3.41 (d, *J* = 12.3 Hz, 1H), 2.83 (d, *J* = 15.6 Hz, 1H), 1.99–1.69 (m, 1H), 1.44 (s, 3H), 1.14 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 145.8, 137.6, 128.7 (+, 2C), 128.6 (+, 2C), 128.2 (+, 2C), 127.8 (+, 2C), 127.5 (+), 126.5 (+), 84.6 (-), 68.6 (+), 56.1 (-), 51.6 (-), 38.2, 31.6 (+), 29.3, 25.3(+), 23.0(+), 17.9 (+); FT IR (KBr, cm^{-1}): 3388, 2088, 1643, 1633, 1556, 1519, 1473, 1421, 1394, 1355, 1282, 1265, 1249, 1228, 1207, 1143, 1093, 1081, 1062, 1027, 993, 700; HRMS (TOF ES): found 348.1963, calculated for $C_{23}H_{26}NO_2$ (M-H) 348.1964 (0.3 ppm).



(-)-(1S,1aR,9aR)-3-benzyl-1-methyl-1-phenyl-1a,3,4,9a-tetrahydrobenzo[b]cyclopropa[g][1,5]oxazocin-2(1H)-one (**10s**): A solution of Me_3SiCl (76.5 µL, 0.6 mmol, 1.20 equiv), NEt_3 (244 µL, 1.75 mmol, 3.5 equiv), and 2-((benzylamino)-methyl)phenol[8] (98 mg, 0.55 mmol, 1.10 equiv) was stirred in dry THF (10 mL) overnight under a nitrogen atmosphere. Then 2-bromocyclopropanecarbonyl chloride obtained according to a typical protocol from (+)-(1*S*,2*R*)-1-bromo-2-methyl-2-phenylcyclopropanecarboxylic acid (127.5 mg, 0.50 mmol, 1.00 equiv), was added and allowed to stir for 3 hours. The solvent was removed by rotary evaporation and then partitioned between 10 mL 5% HCl & 10 mL EtOAc. The organic layer was washed with 5% HCl (3 x 15 mL) then dried with $MgSO_4$, filtered, and concentrated which afforded (1*S*,2*R*)-N-benzyl-1-bromo-N-(2-hydroxybenzyl)-2-methyl-2-phenylcyclopropane-1-carboxamide **8s** as a viscous oil R_f 0.5 (hexanes/EtOAc 5:1). This crude material was subjected directly to elimination step to afford the title compound as a colorless oil. Yield 88 mg (0.244 mmol 31%), dr 100:0. R_f 0.28 (hexanes/EtOAc 5:1). $[\alpha]_D$= -229.7° (c 0.40, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.39–7.20 (m, 9H), 7.12 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.05–6.93 (m, 2H), 5.45 (d, *J* = 16.4 Hz, 1H), 5.17 (d, *J* = 14.7 Hz, 1H), 4.00 (d, *J* = 6.0 Hz, 1H), 3.81 (dd, *J* = 29.3, 15.6 Hz, 2H), 2.44 (d, *J* = 5.9 Hz, 1H), 1.71 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 157.1, 145.3, 137.4, 131.3 (+), 129.5 (+), 128.8 (+, 2C), 128.7 (+, 2C), 128.6 (+, 2C), 128.0 (+, 2C), 127.6 (+),

(7) Posakony, J. J.; Tewson, T. J. *Synthesis* **2002**, 859.
(8) Shaikh, A. K.; Cobb, A. J. A.; Varvounis, G. *Org. Lett.* **2012**, *14*, 584.

126.9 (+), 125.9, 123.3 (+), 121.7 (+), 63.7 (+), 50.0 (-), 47.9 (-), 32.0 (+), 30.7, 16.9 (+); FT IR (KBr, cm^{-1}): 2972, 1649, 1604, 1488, 1429, 1269, 1224, 1209, 858, 823, 796, 761, 736, 700, 648, 617; HRMS (TOF ES): found 369.1731, calculated for $C_{25}H_{23}NO_2$ (M^+) 369.1729 (0.5 ppm).

NOE Data for 10s

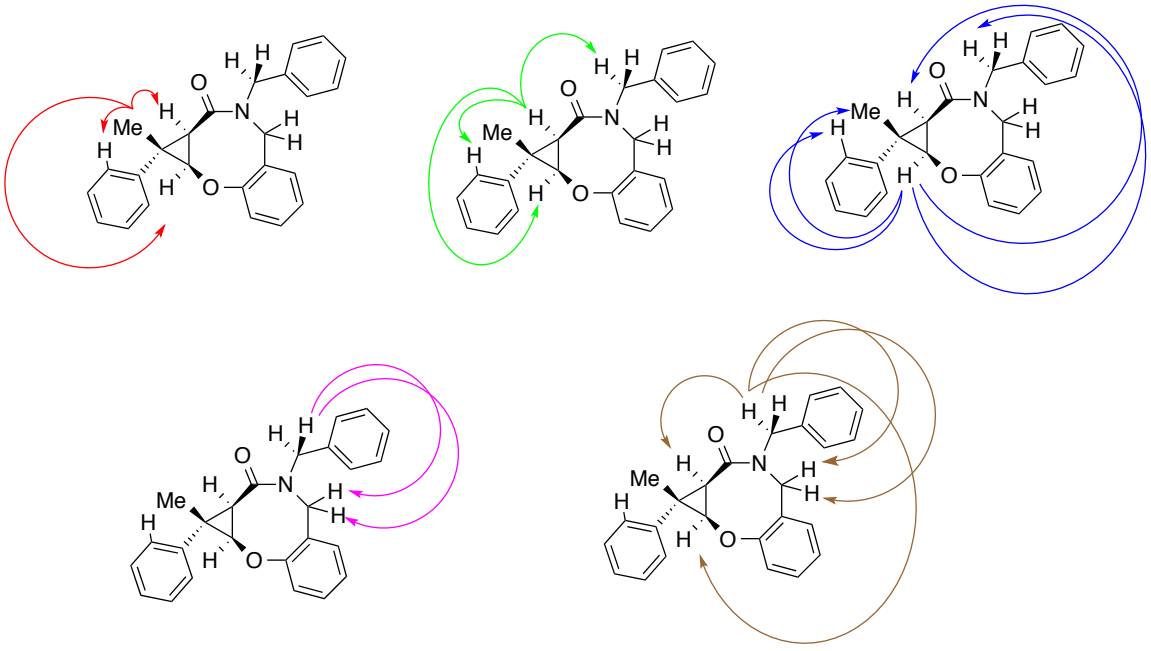


Figure 1. Observed NOEs upon irradiation at 1.71 ppm (red), 2.44 ppm (green), 4.00 ppm (blue), 5.17 ppm (purple), 5.45 ppm (brown) for compound **10s**. For color-coded spectral charts corresponding to these experiments, see Figure 2.

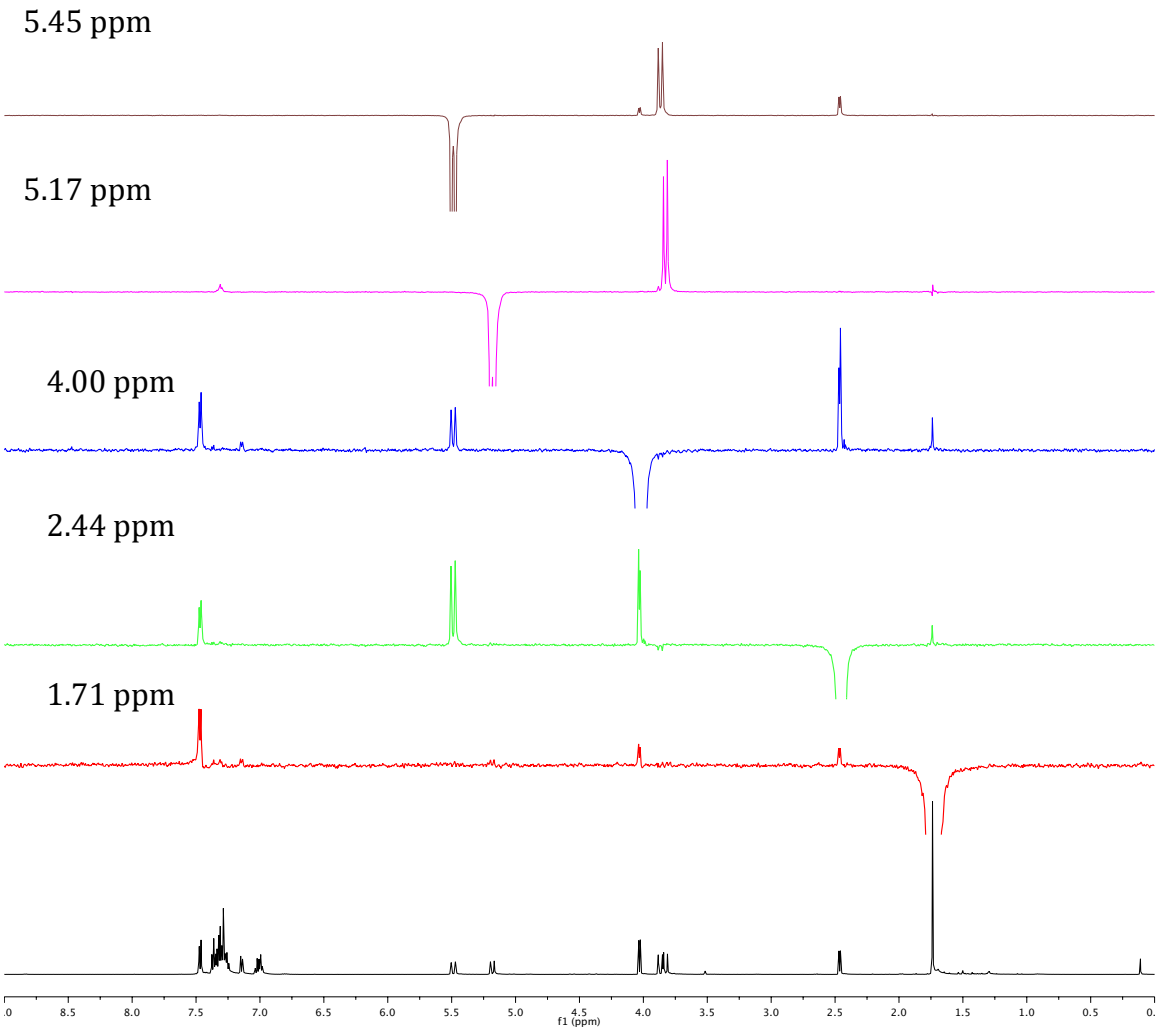
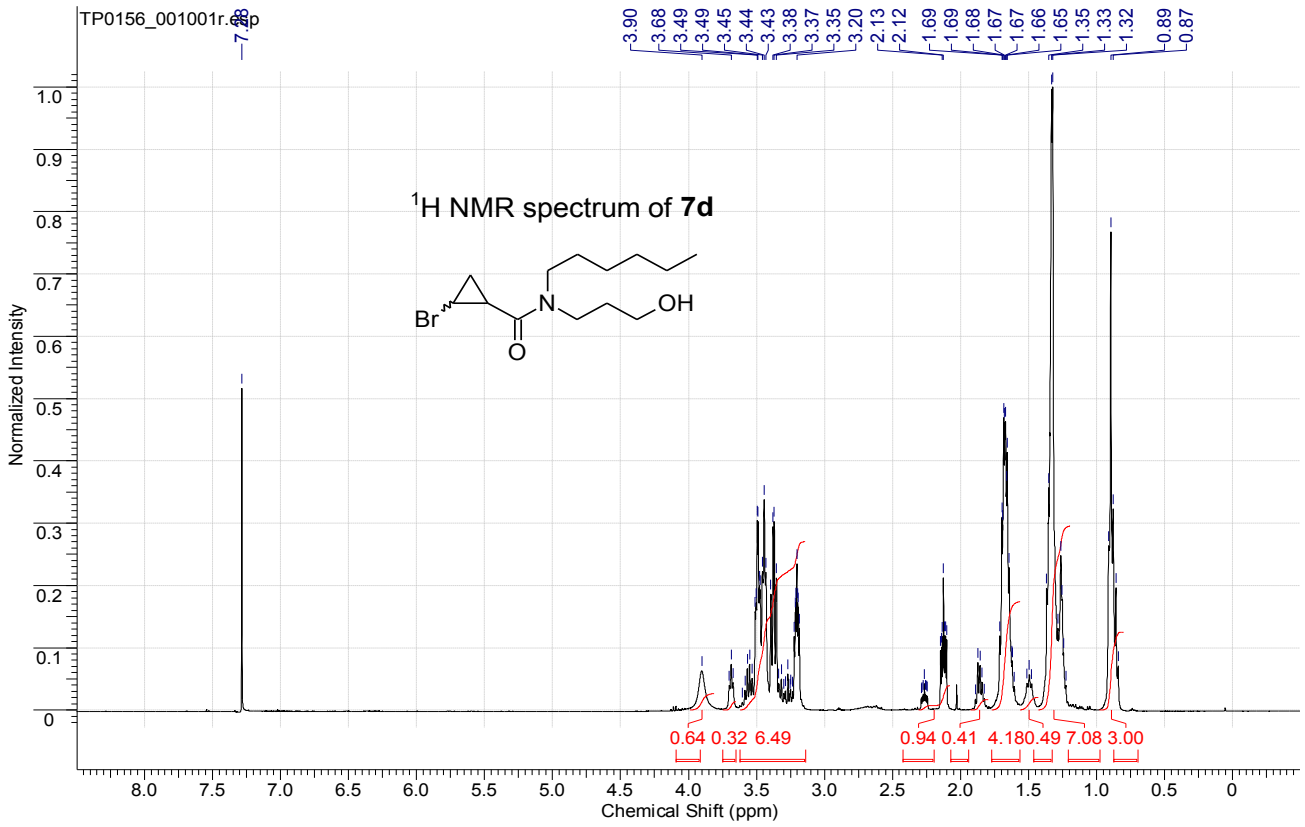
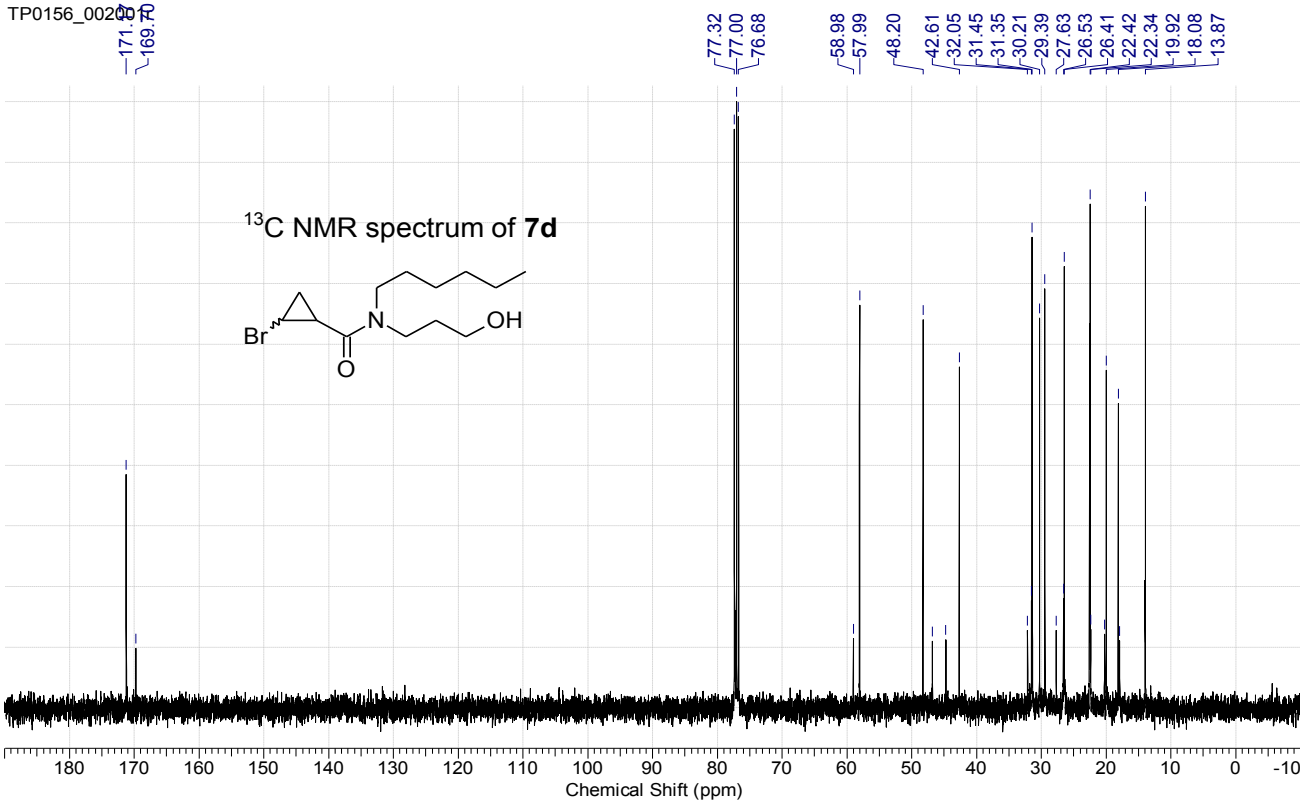
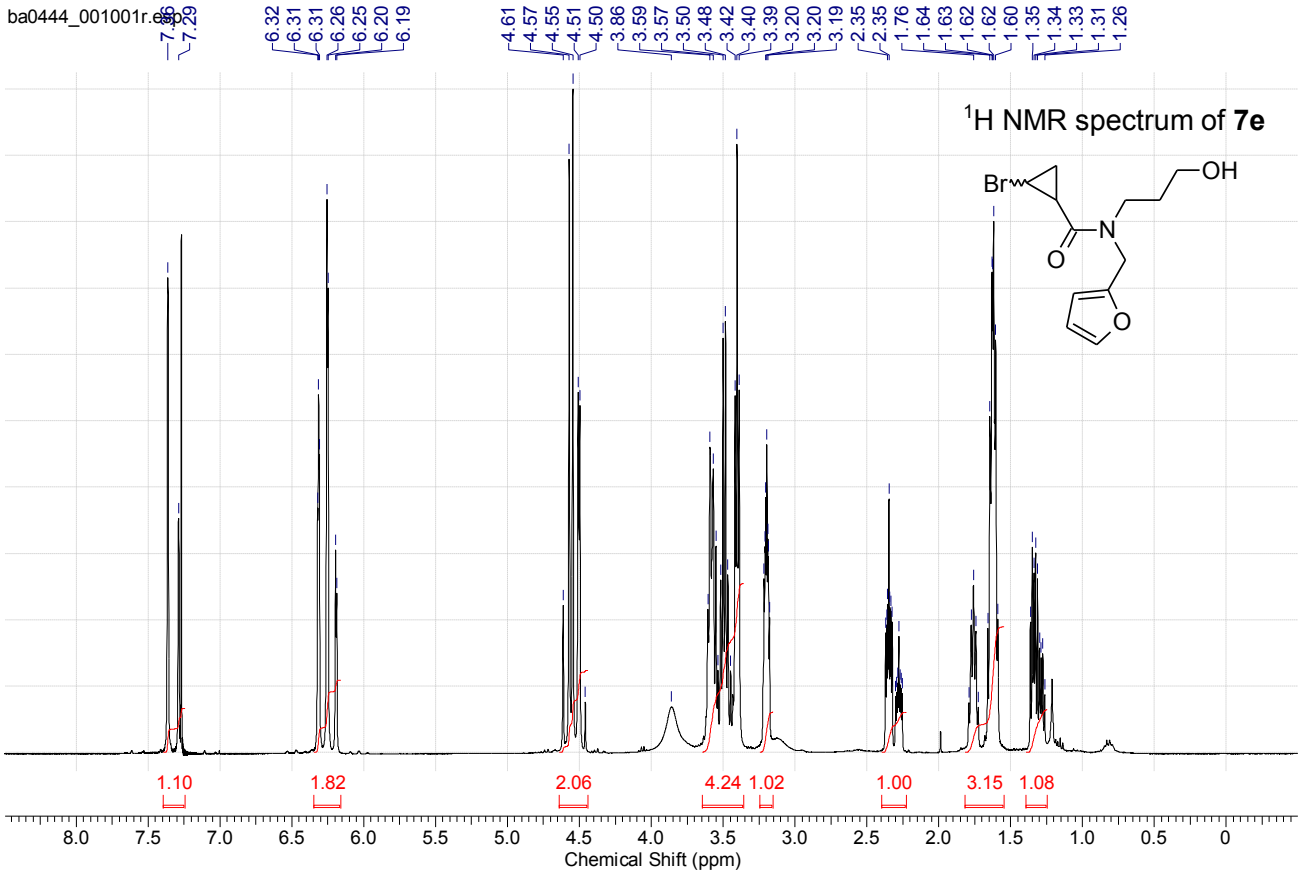
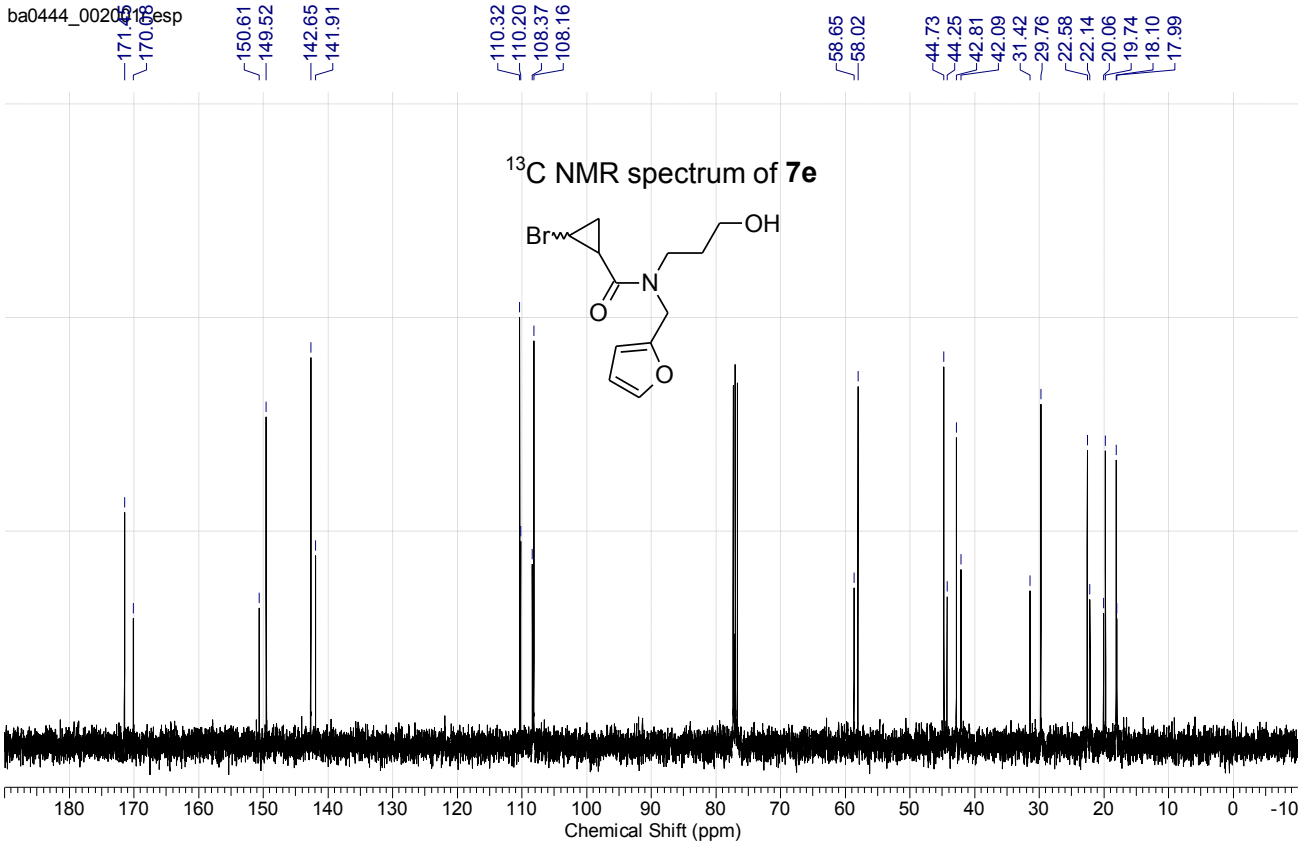


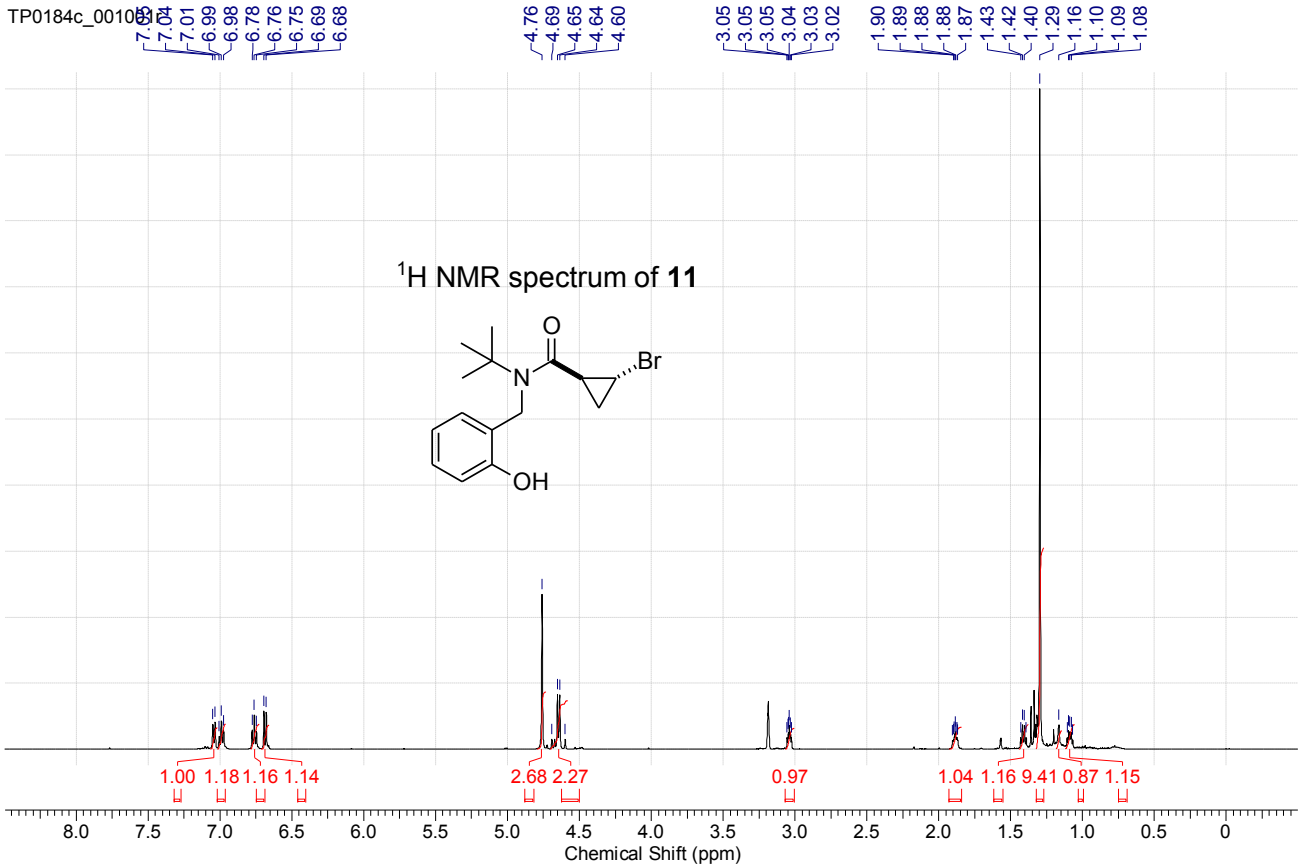
Figure 2. 1D NOEDIFF spectra of **10s**. Chemical shifts of the irradiated multiplets are listed at the left side of each chart.


TP0156_001001r.esp
^{1}H NMR spectrum of **7d**
Br
N
OH
O
Normalized Intensity
Chemical Shift (ppm)
0.64 0.32 6.49
0.94 0.41 4.18 0.49 7.08 3.00


TP0156_002001r.esp
^{13}C NMR spectrum of **7d**
Br
N
OH
O
Chemical Shift (ppm)


ba0444_001001r.esp
7.29
6.32
6.31
6.31
6.26
6.25
6.20
6.19
4.61
4.57
4.55
4.51
4.50
3.86
3.59
3.57
3.50
3.48
3.42
3.40
3.39
3.20
3.20
3.19
2.35
2.35
1.76
1.64
1.63
1.62
1.62
1.60
1.35
1.34
1.33
1.31
1.26
1H NMR spectrum of 7e
Br
OH
N
O
O
1.10
1.82
2.06
4.24
1.02
1.00
3.15
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)


ba0444_002001r.esp
171.48
170.18
150.61
149.52
142.65
141.91
110.32
110.20
108.37
108.16
58.65
58.02
44.73
44.25
42.81
42.09
31.42
29.76
22.58
22.14
20.06
19.74
18.10
17.99
13C NMR spectrum of 7e
Br
OH
N
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical Shift (ppm)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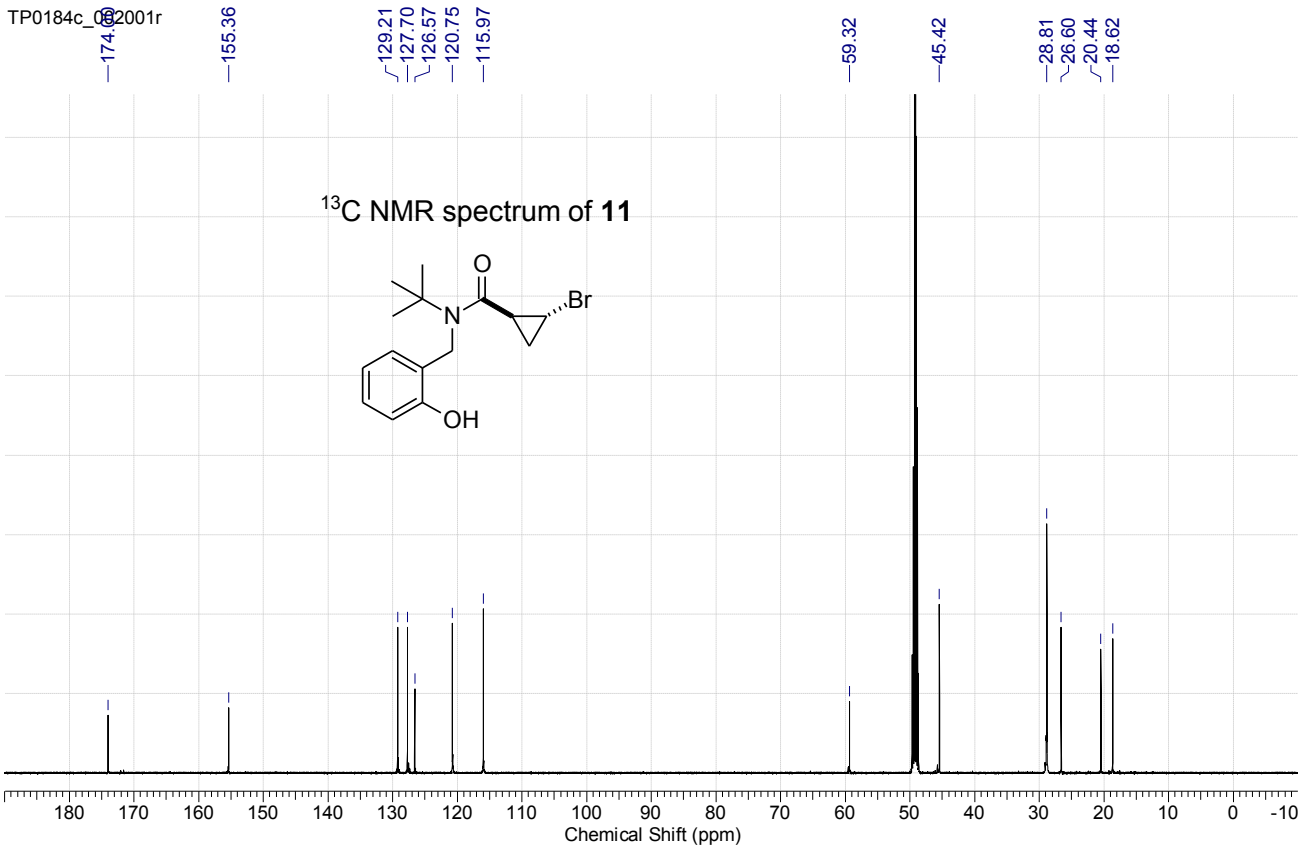
7.04
7.01
6.99
6.98
6.78
6.76
6.75
6.69
6.68
4.76
4.69
4.65
4.64
4.60
3.05
3.05
3.05
3.04
3.03
3.02
1.90
1.89
1.88
1.88
1.87
1.43
1.42
1.40
1.29
1.16
1.10
1.09
1.08
1H NMR spectrum of 11
O
N
Br
OH
1.00 1.18 1.16 1.14
2.68 2.27
0.97
1.04 1.16 9.41 0.87 1.15
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


TP0184c_002001r
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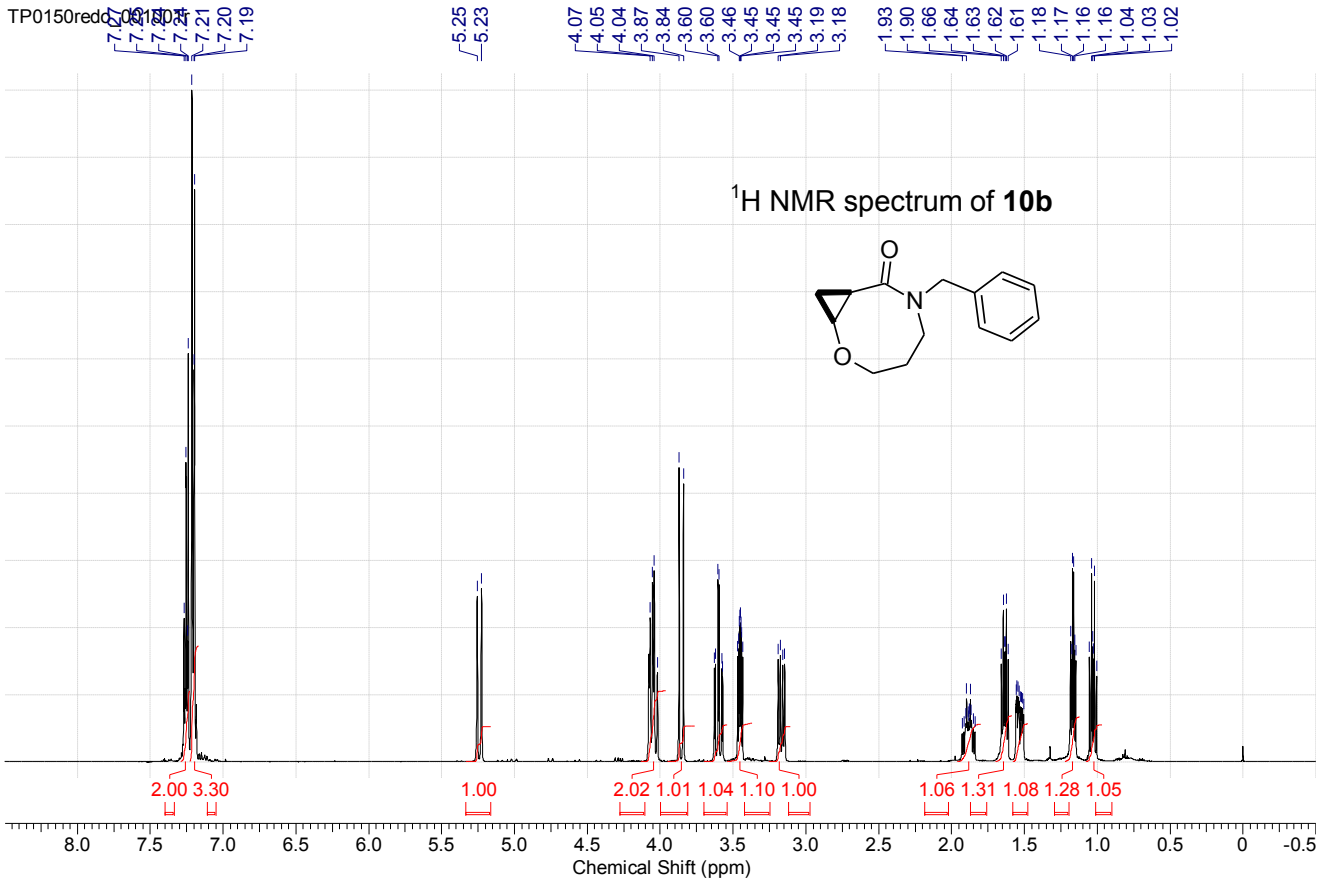
155.36
129.21
127.70
126.57
120.75
115.97
59.32
45.42
28.81
26.60
20.44
18.62
13C NMR spectrum of 11
O
N
Br
OH
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical Shift (ppm)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7.20
7.19
5.25
5.23
4.07
4.05
4.04
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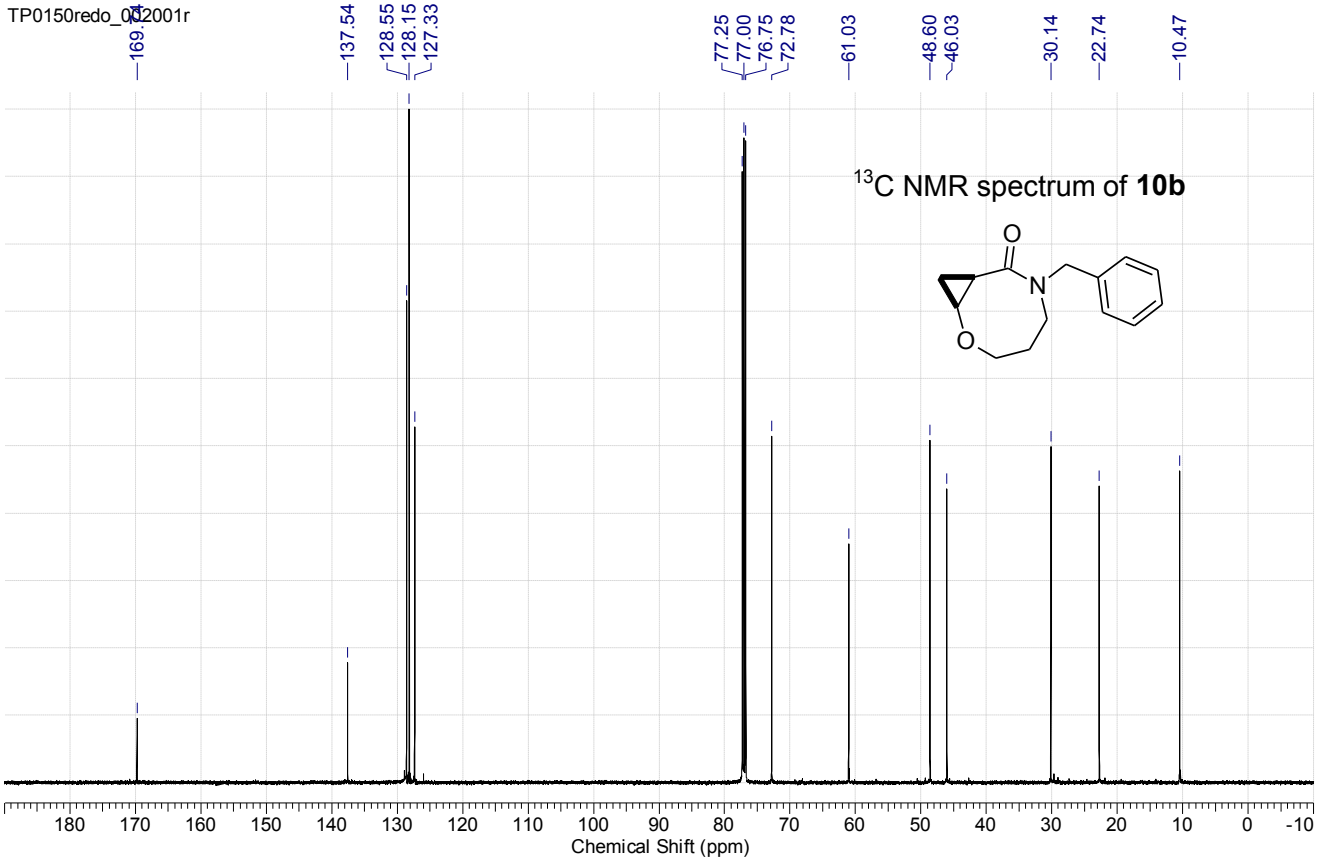
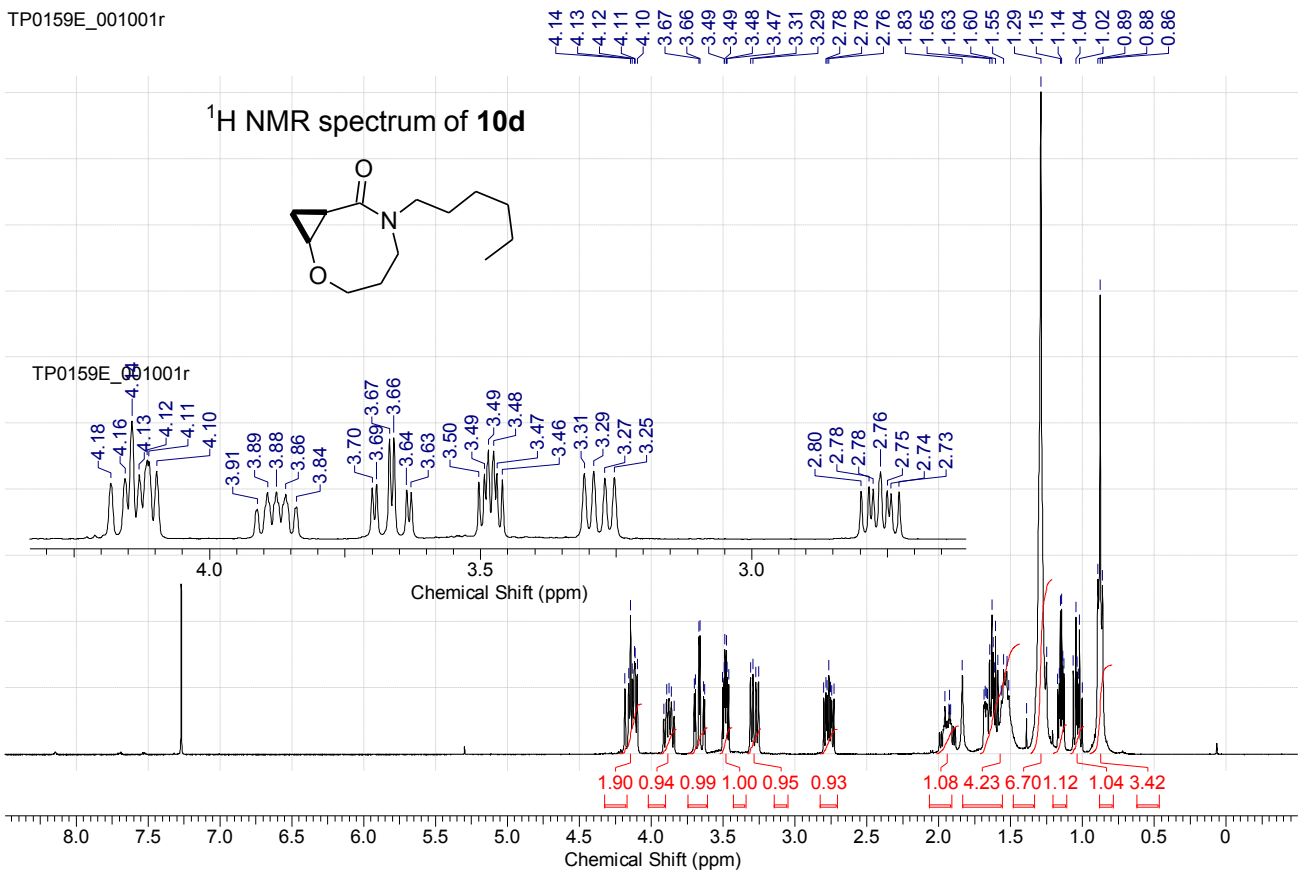
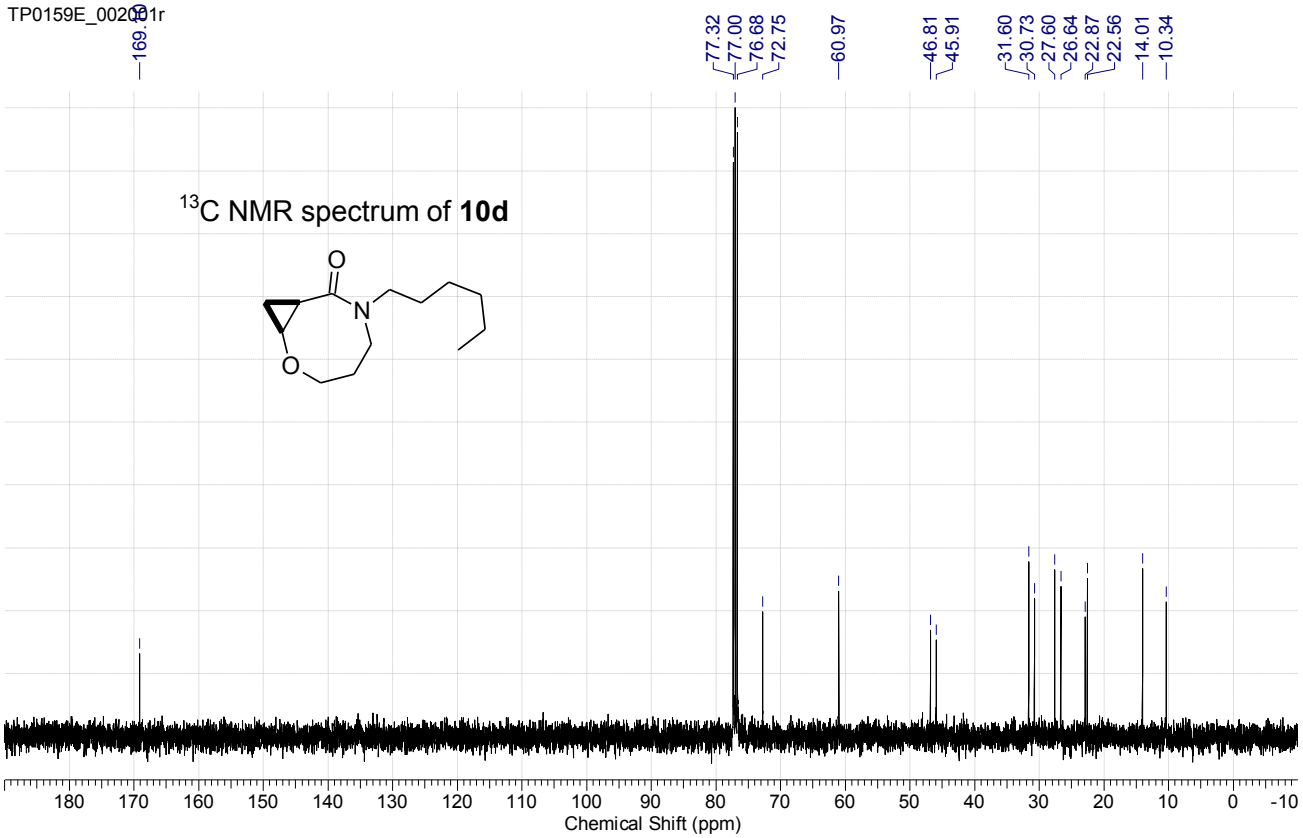
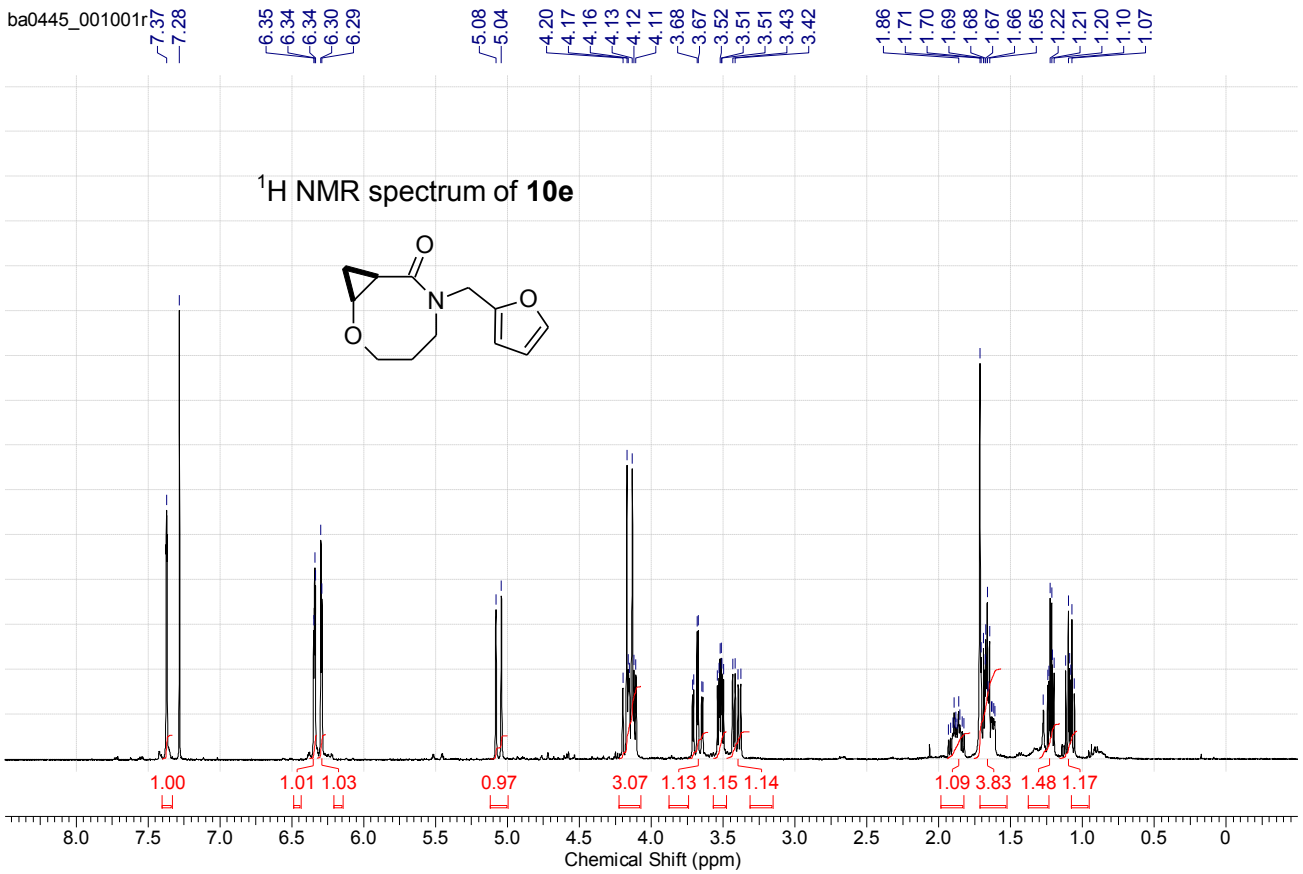
3.60
3.60
3.46
3.45
3.45
3.19
3.18
1.93
1.90
1.66
1.64
1.63
1.62
1.61
1.18
1.17
1.16
1.16
1.04
1.03
1.02
^{1}H NMR spectrum of **10b**
O
N
O
2.00 3.30
1.00
2.02 1.01 1.04 1.10 1.00
1.06 1.31 1.08 1.28 1.05
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0 -0.5
Chemical Shift (ppm)


TP0150redo_0[illegible]2001r
169.71
137.54
128.55
128.15
127.33
77.25
77.00
76.75
72.78
61.03
48.60
46.03
30.14
22.74
10.47
^{13}C NMR spectrum of **10b**
O
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical Shift (ppm)


TP0159E_001001r
^{1}H NMR spectrum of **10d**
Chemical Shift (ppm)
1.90 0.94 0.99 1.00 0.95 0.93
1.08 4.23 6.70 1.12 1.04 3.42


TP0159E_002001r
^{13}C NMR spectrum of **10d**
Chemical Shift (ppm)


ba0445_001001r
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6.34
6.34
6.30
6.29
5.08
5.04
4.20
4.17
4.16
4.13
4.12
4.11
3.68
3.67
3.52
3.51
3.51
3.43
3.42
1.86
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.22
1.21
1.20
1.10
1.07
1H NMR spectrum of 10e
O
N
O
O
1.00
1.01
1.03
0.97
3.07
1.13
1.15
1.14
1.09
3.83
1.48
1.17
8.0
7.5
7.0
6.5
6.0
5.5
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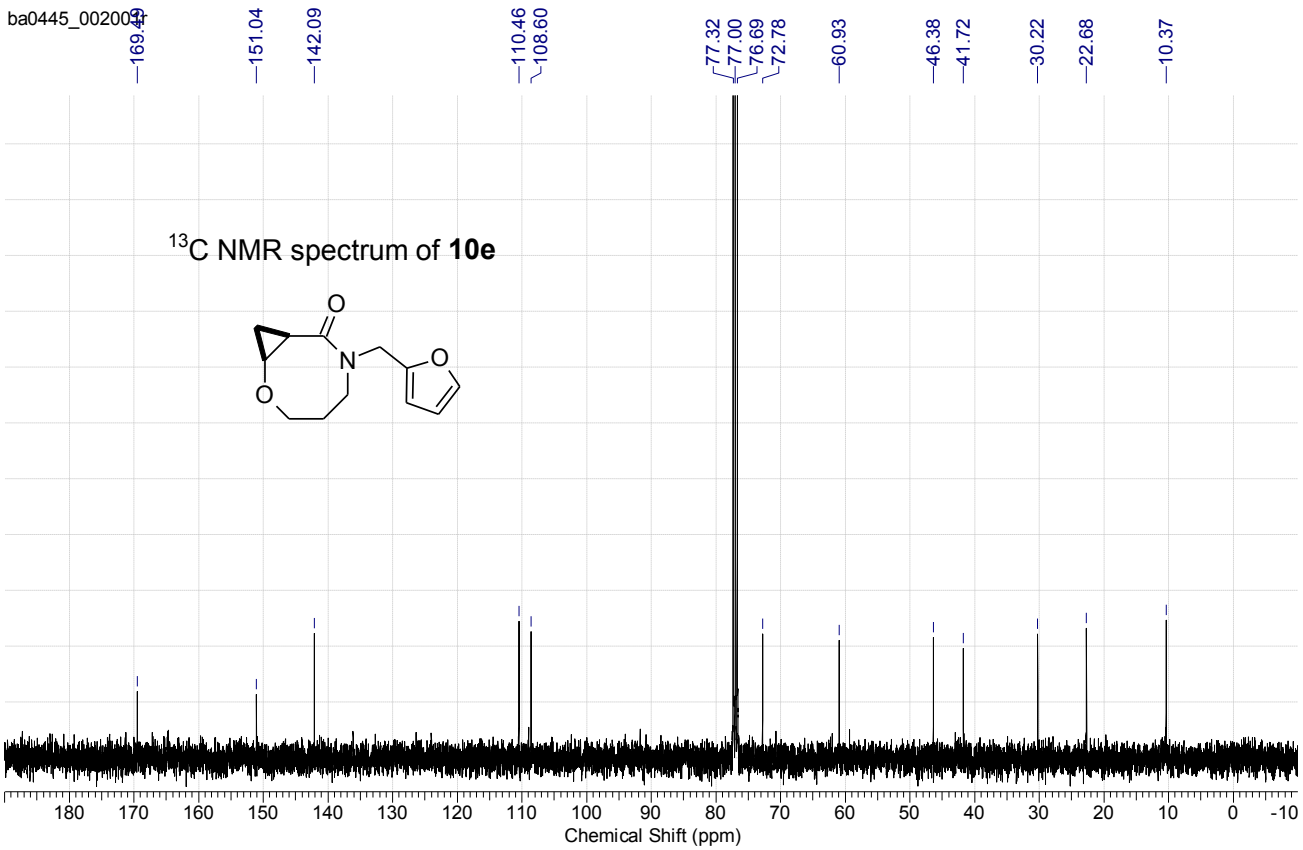
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


ba0445_002001r
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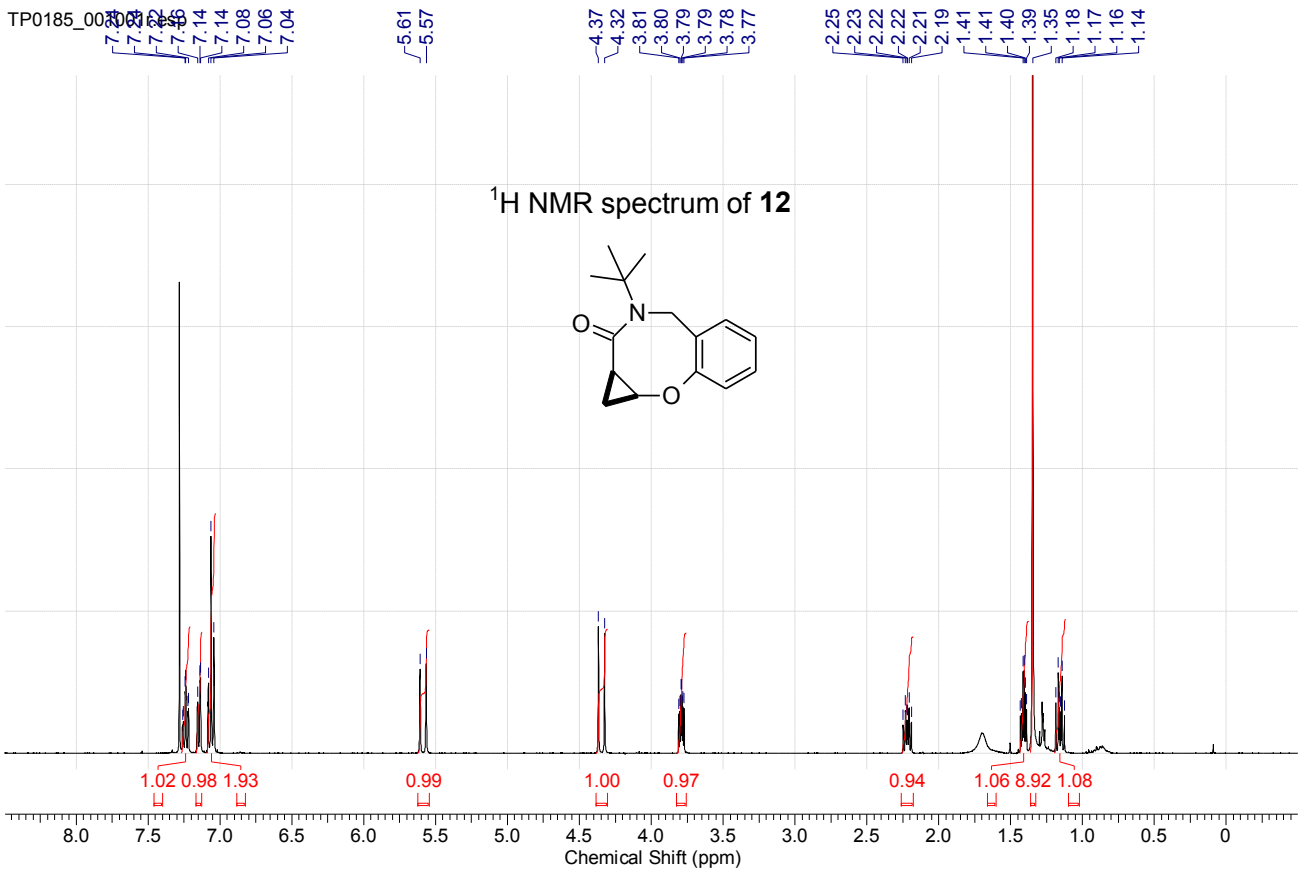
142.09
110.46
108.60
77.32
77.00
76.69
72.78
60.93
46.38
41.72
30.22
22.68
10.37
13C NMR spectrum of 10e
O
N
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical Shift (ppm)


TP0185_002001r.esp
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7.06
7.04
5.61
5.57
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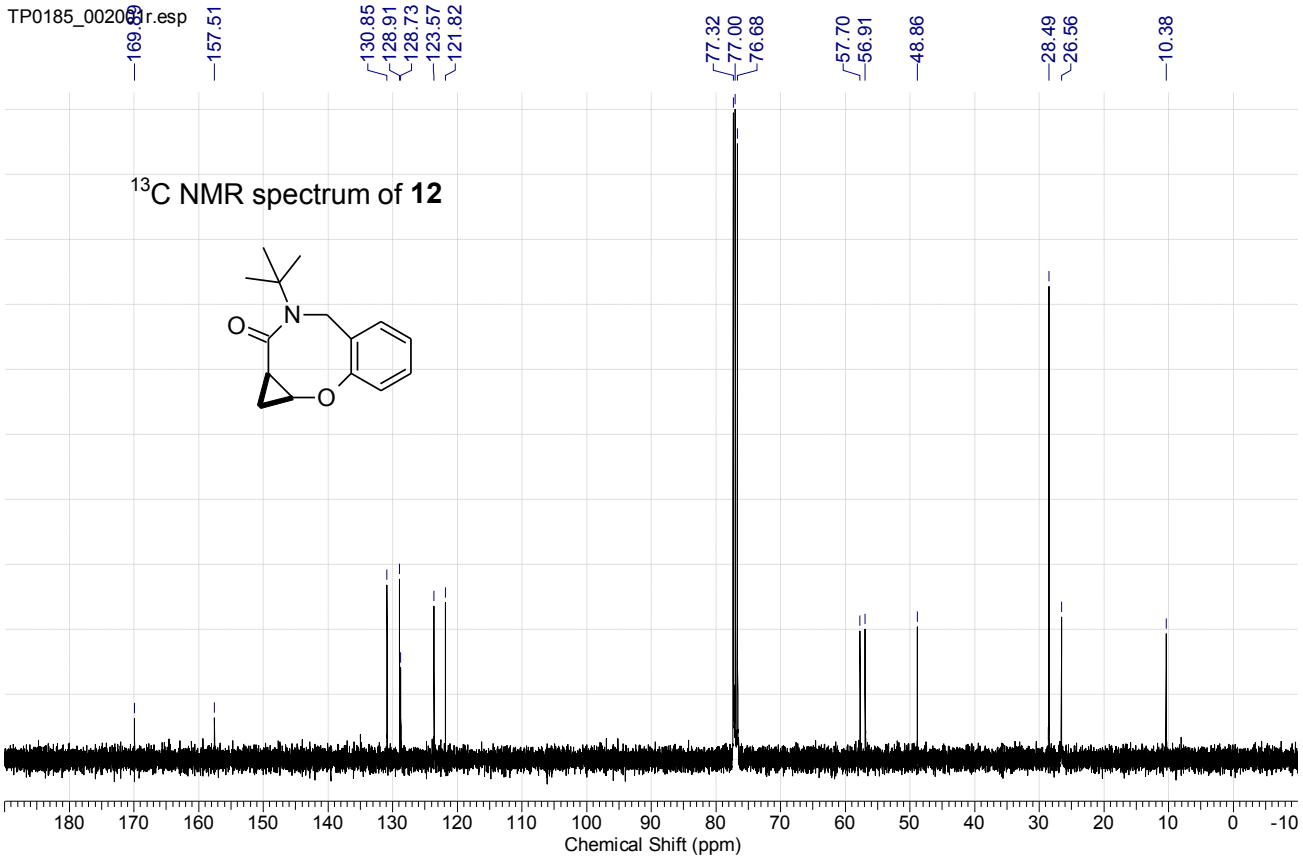
3.79
3.78
3.77
2.25
2.23
2.22
2.22
2.21
2.19
1.41
1.41
1.40
1.39
1.35
1.18
1.17
1.16
1.14
1H NMR spectrum of 12
N
O
O
1.02 0.98 1.93
0.99
1.00
0.97
0.94
1.06 8.92 1.08
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)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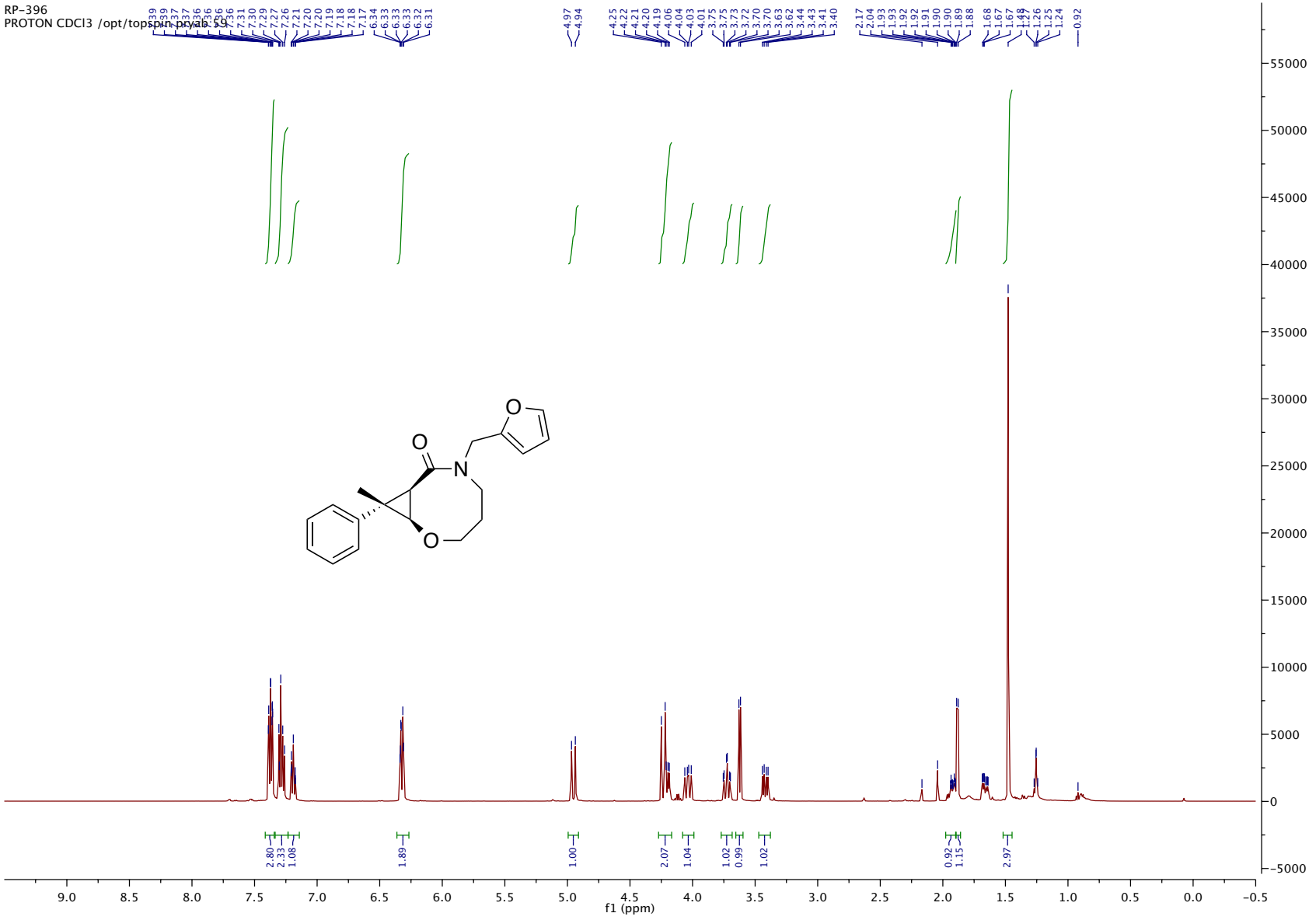
128.73
123.57
121.82
77.32
77.00
76.68
57.70
56.91
48.86
28.49
26.56
10.38
13C NMR spectrum of 12
N
O
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical Shift (ppm)


RP-396
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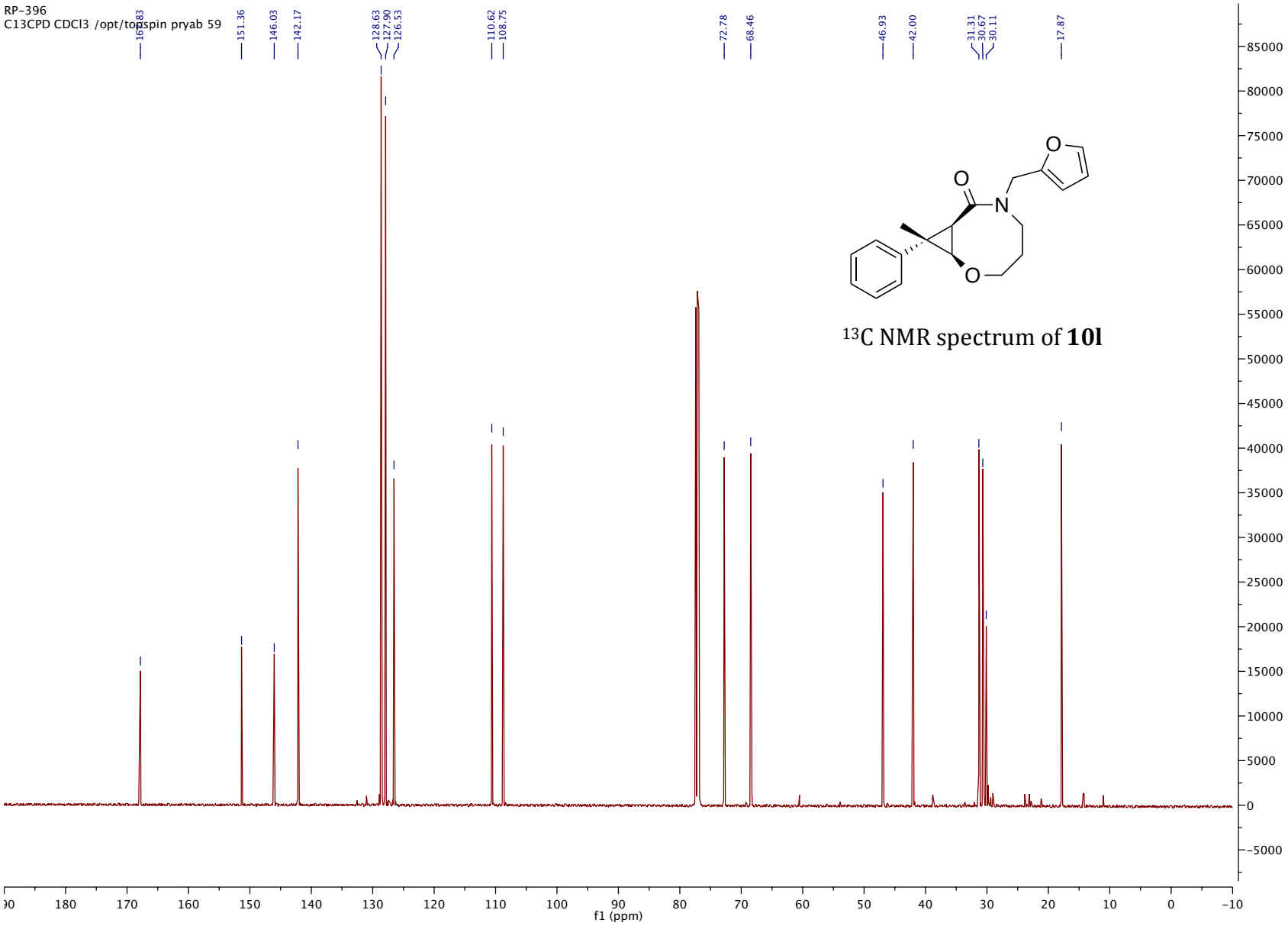
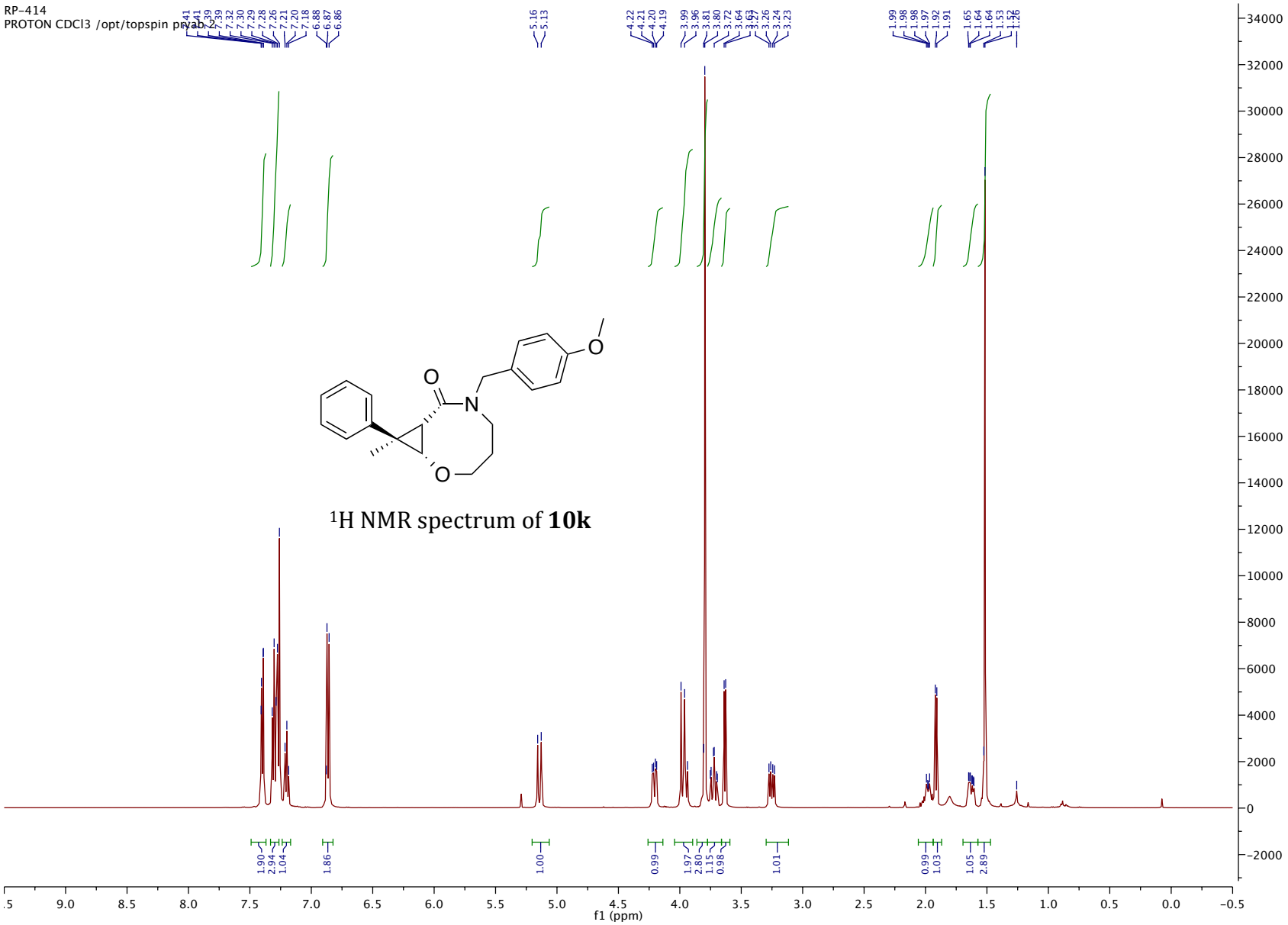
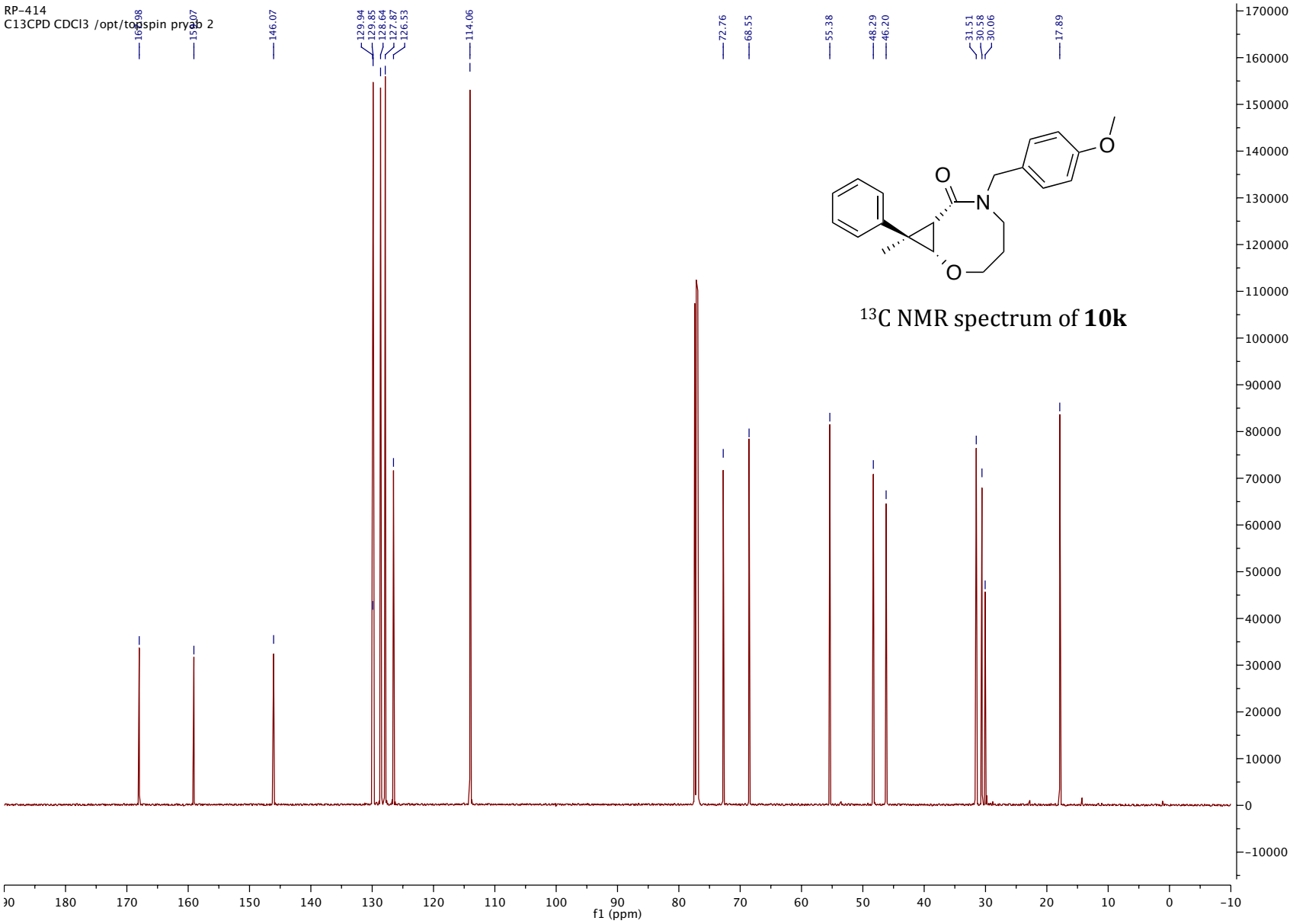
4.97 4.94
4.25 4.22 4.21 4.20 4.19 4.06 4.04 4.03 4.01 3.75 3.75 3.73 3.72 3.70 3.70 3.63 3.62 3.44 3.43 3.41 3.40
2.17 2.04 1.93 1.93 1.92 1.92 1.91 1.90 1.90 1.89 1.88 1.68 1.67 1.67
1.26 1.25 1.24 0.92
O
O
N
O
2.80 2.33 1.08 1.89 1.00 2.07 1.04 1.02 0.99 1.02 0.92 1.15 2.97
f1 (ppm)



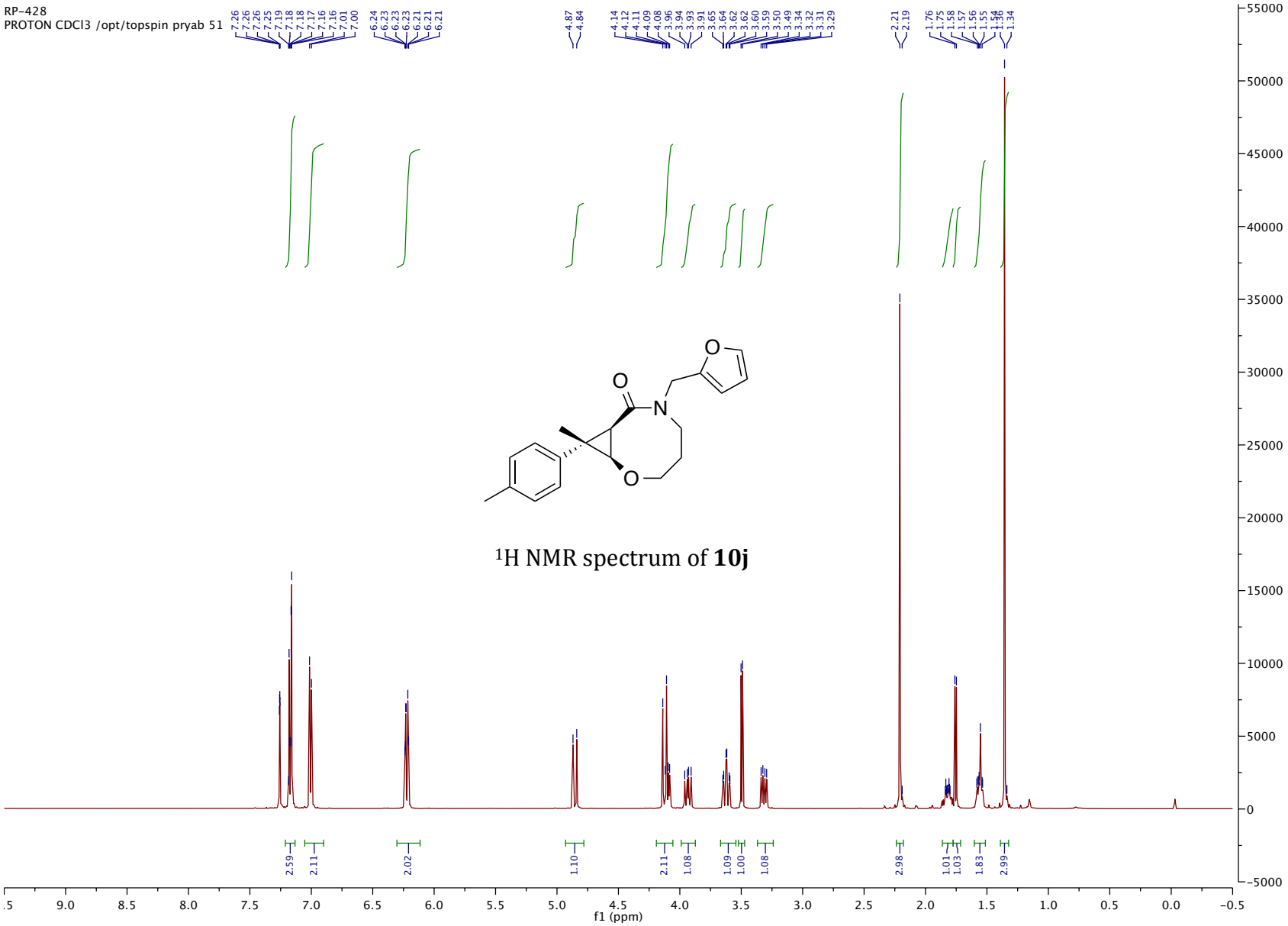
^{13}C NMR spectrum of **10l**



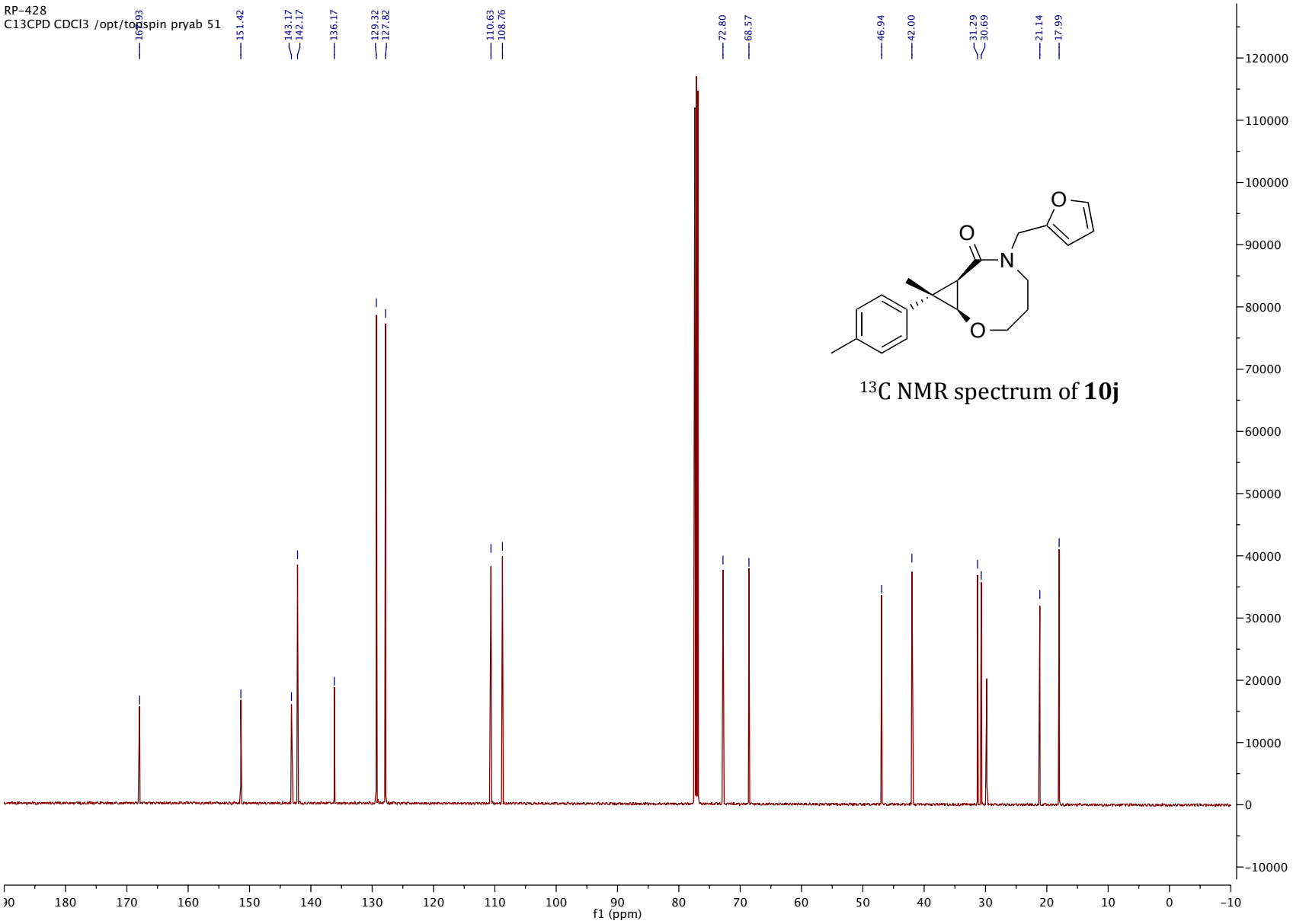
^{1}H NMR spectrum of **10k**



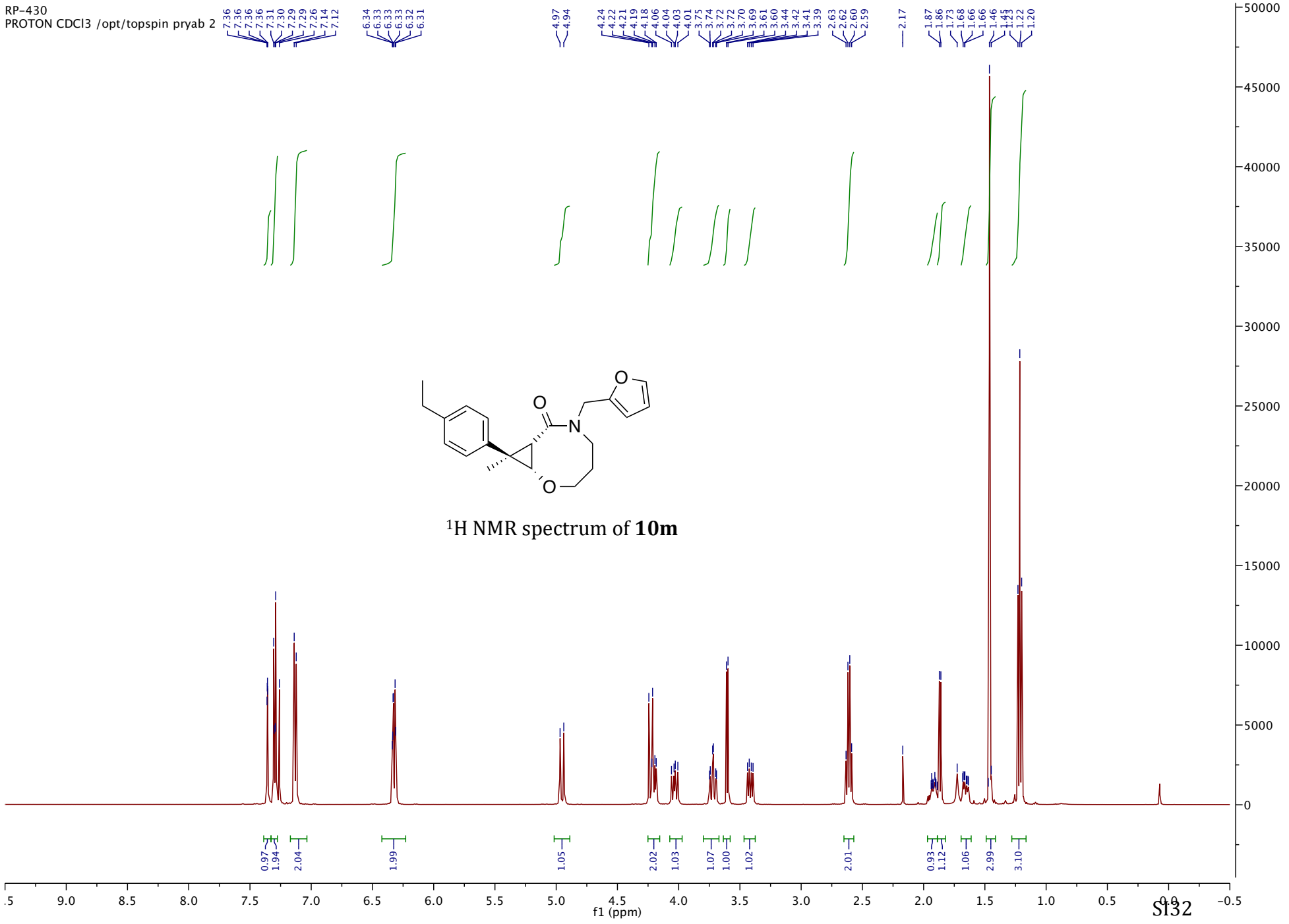
^{13}C NMR spectrum of **10k**



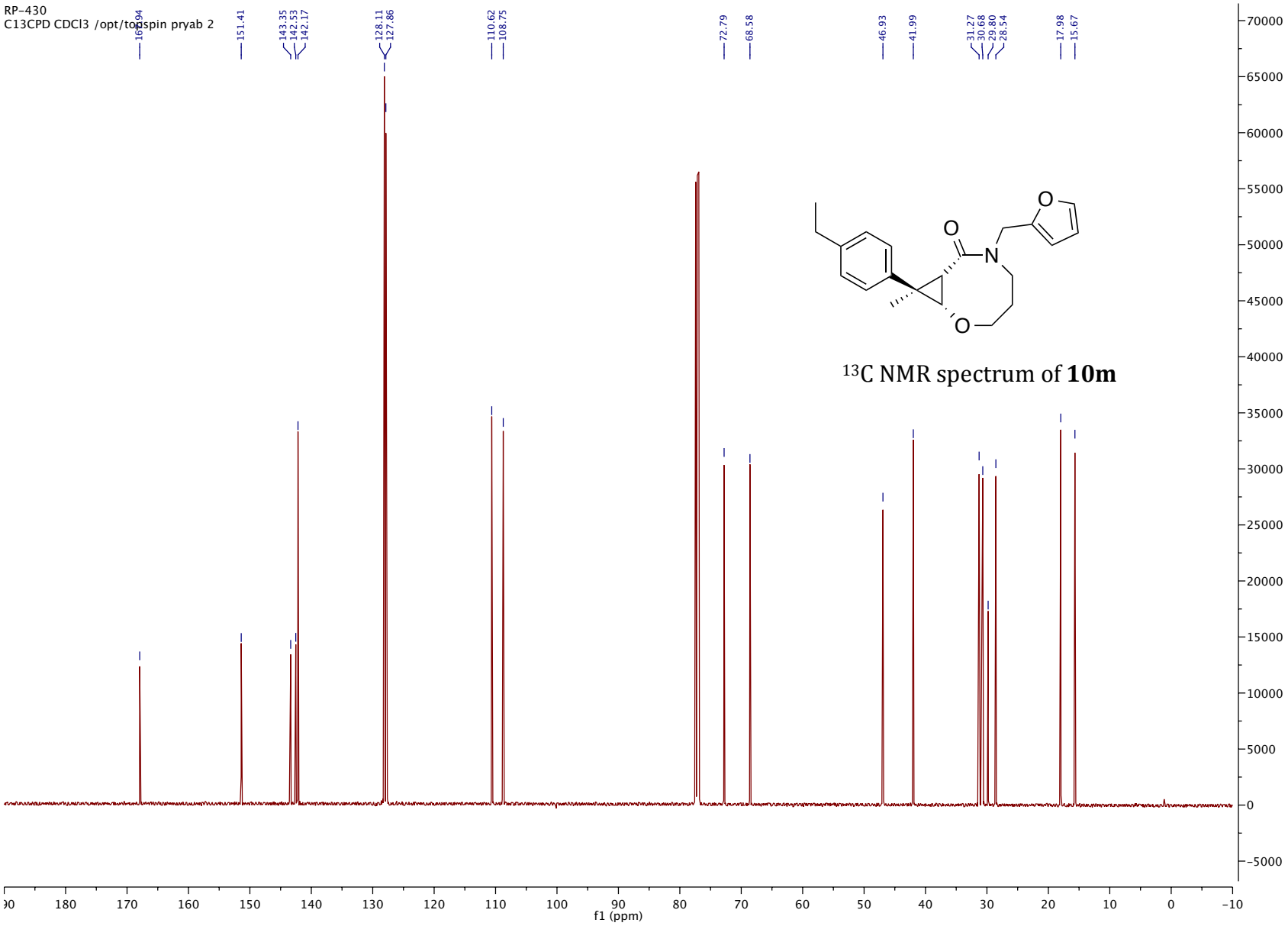
^{1}H NMR spectrum of **10j**



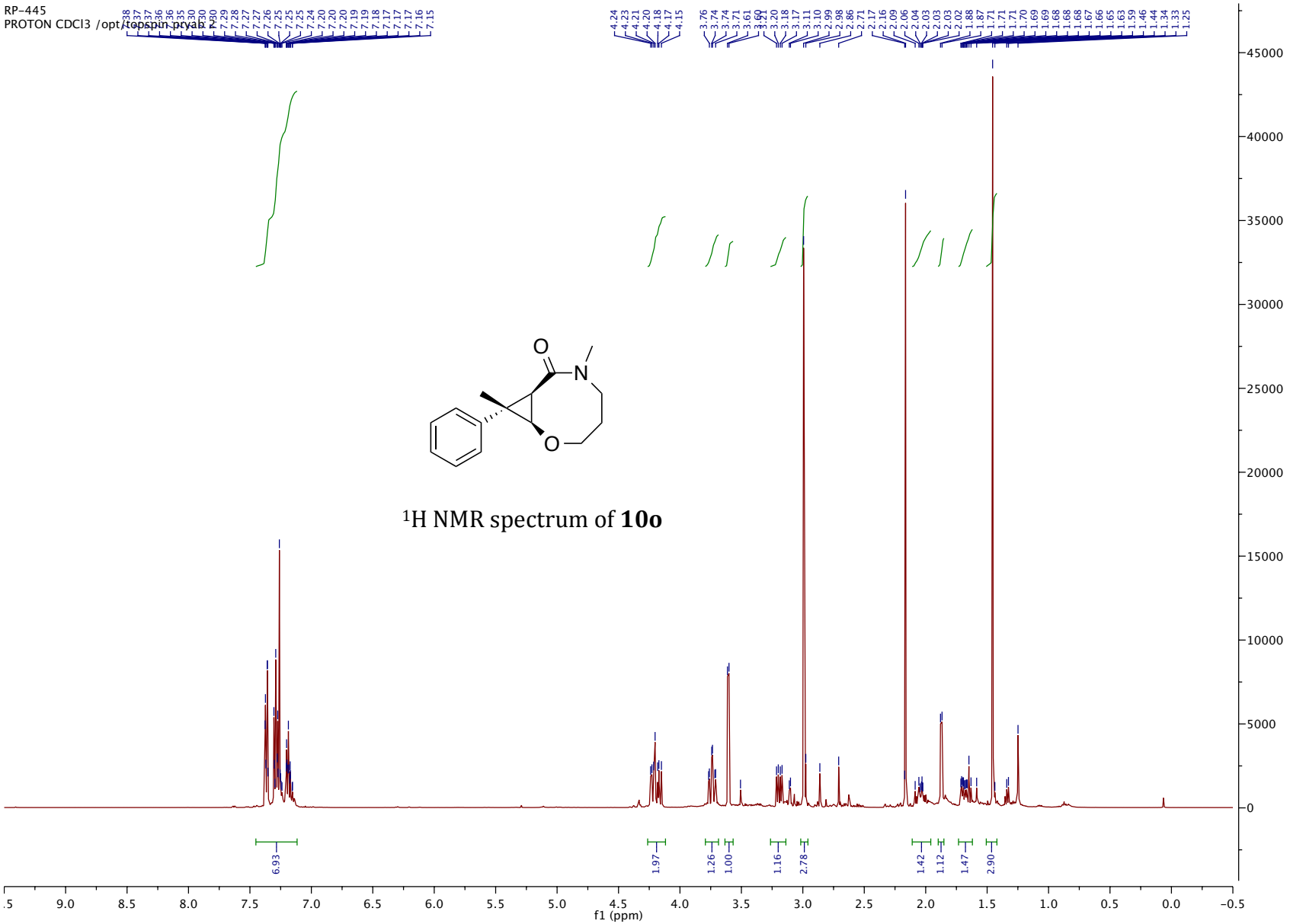
^{13}C NMR spectrum of **10j**



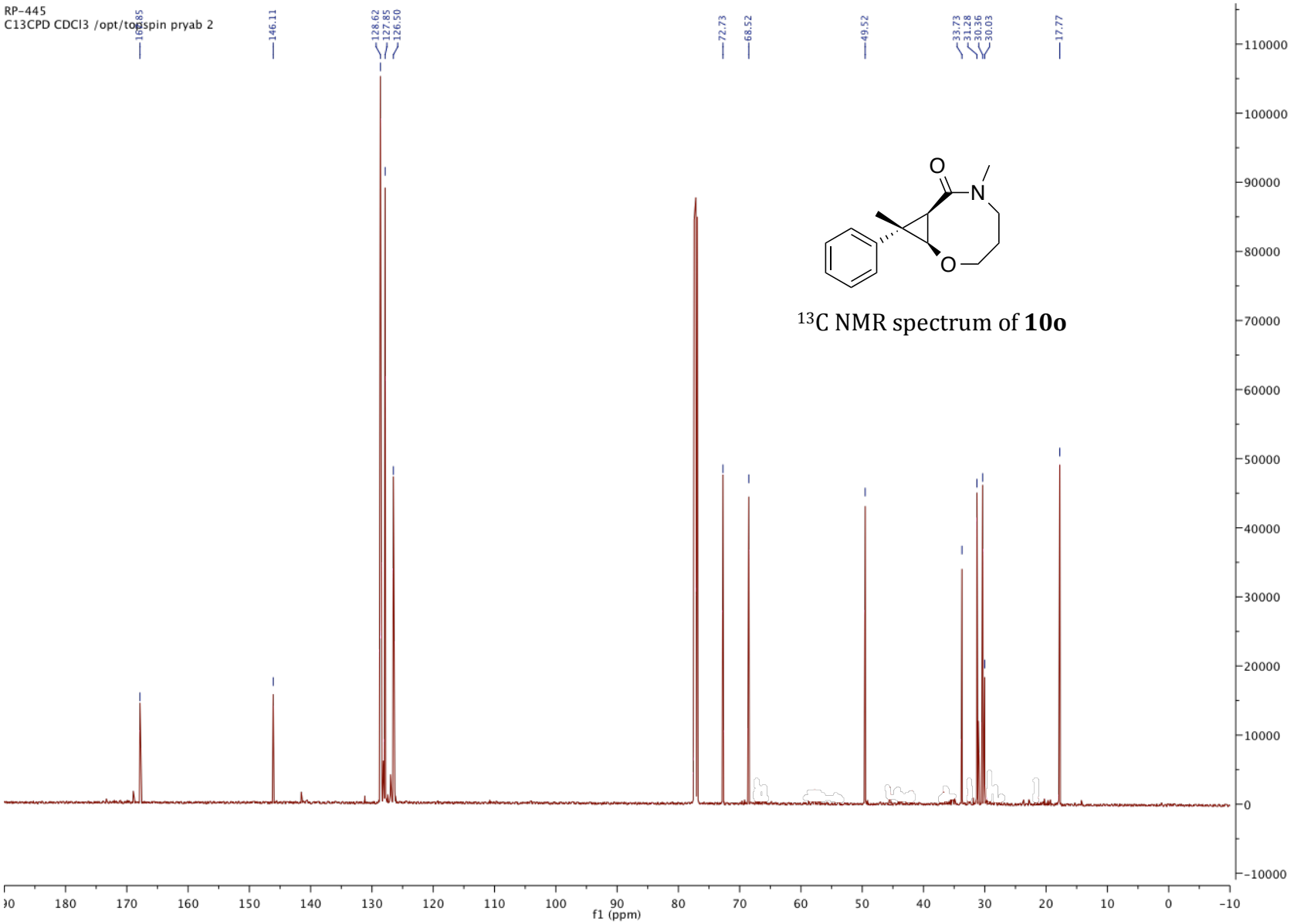
^{1}H NMR spectrum of **10m**



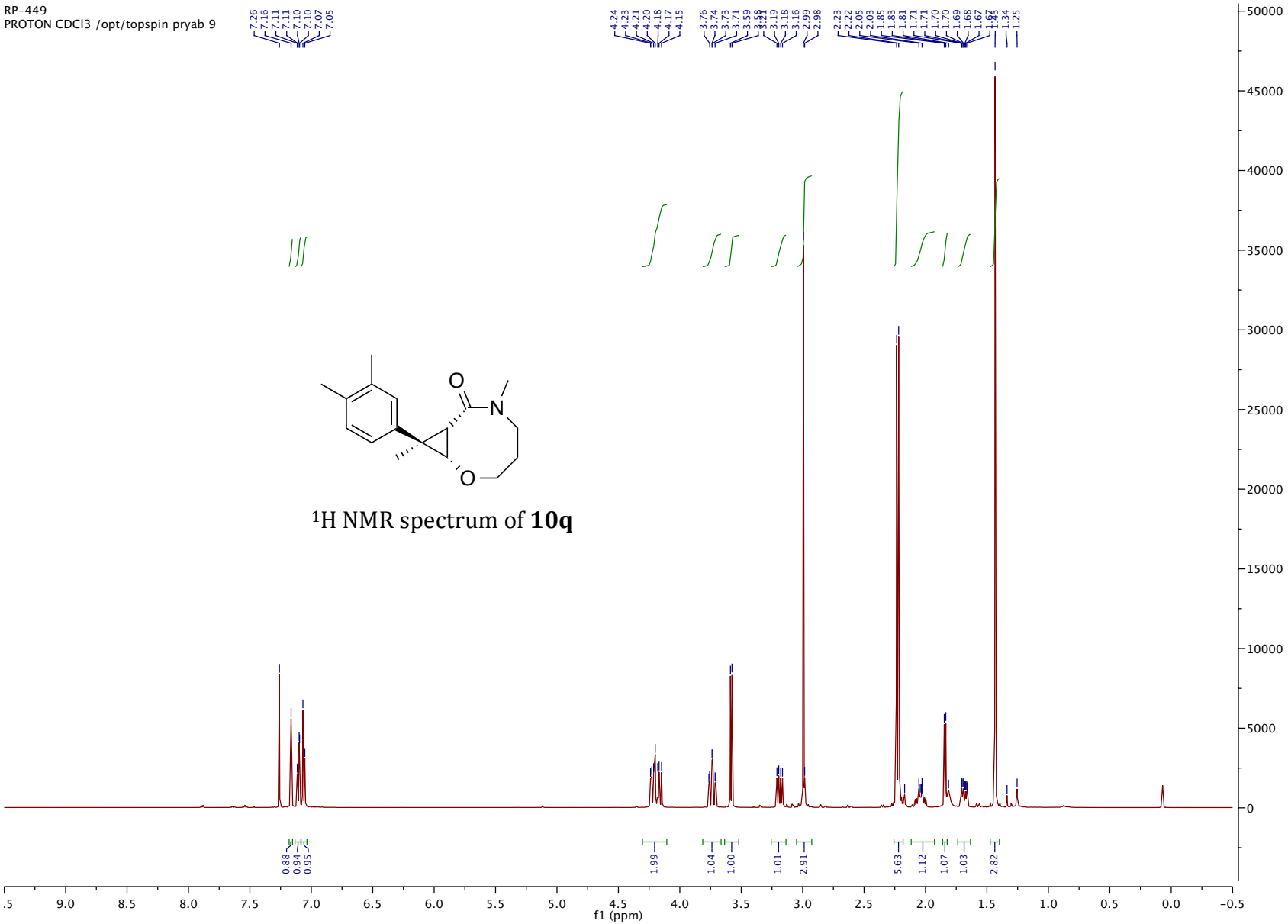
^{13}C NMR spectrum of **10m**



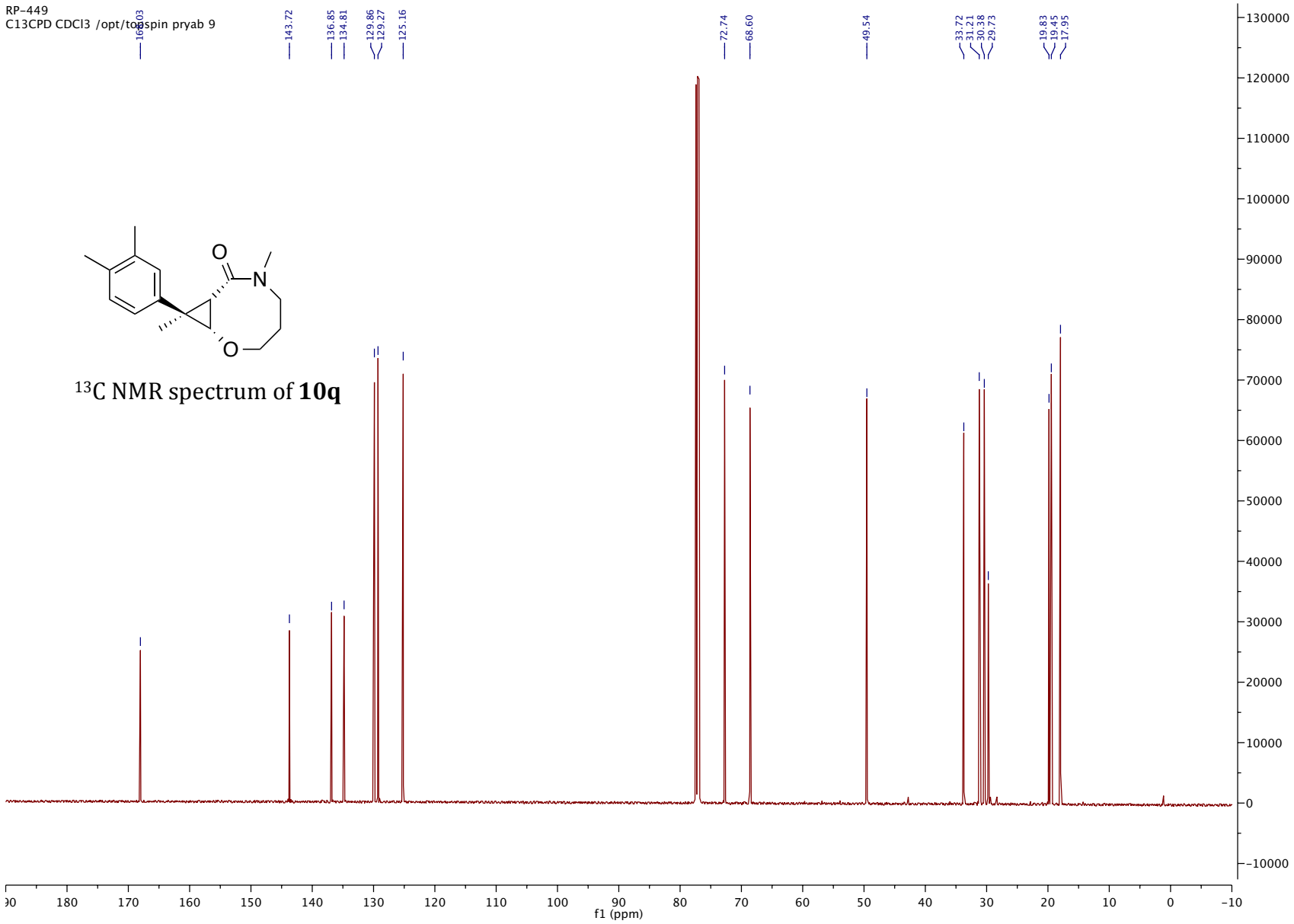
^{1}H NMR spectrum of **10o**



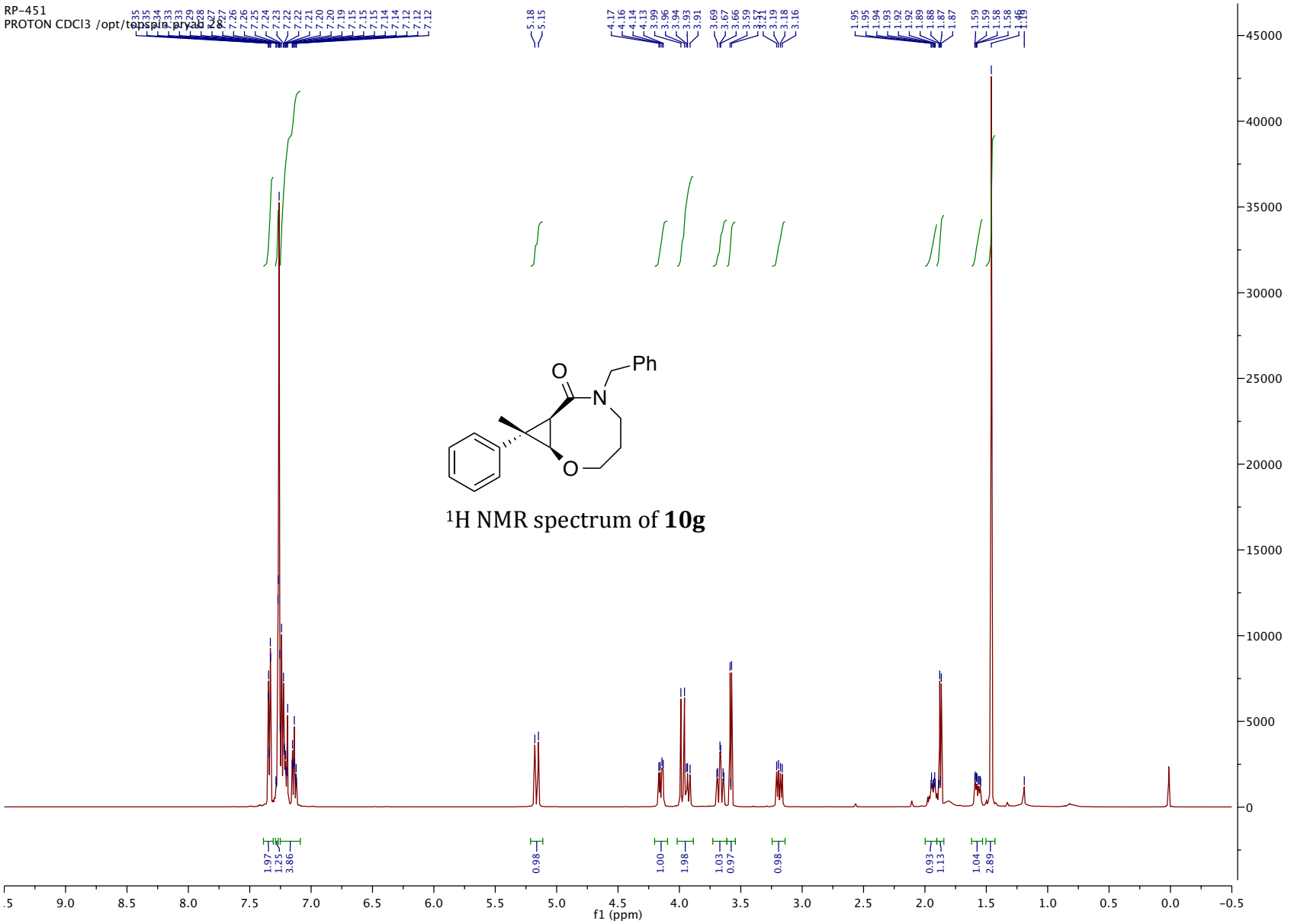
^{13}C NMR spectrum of **10o**



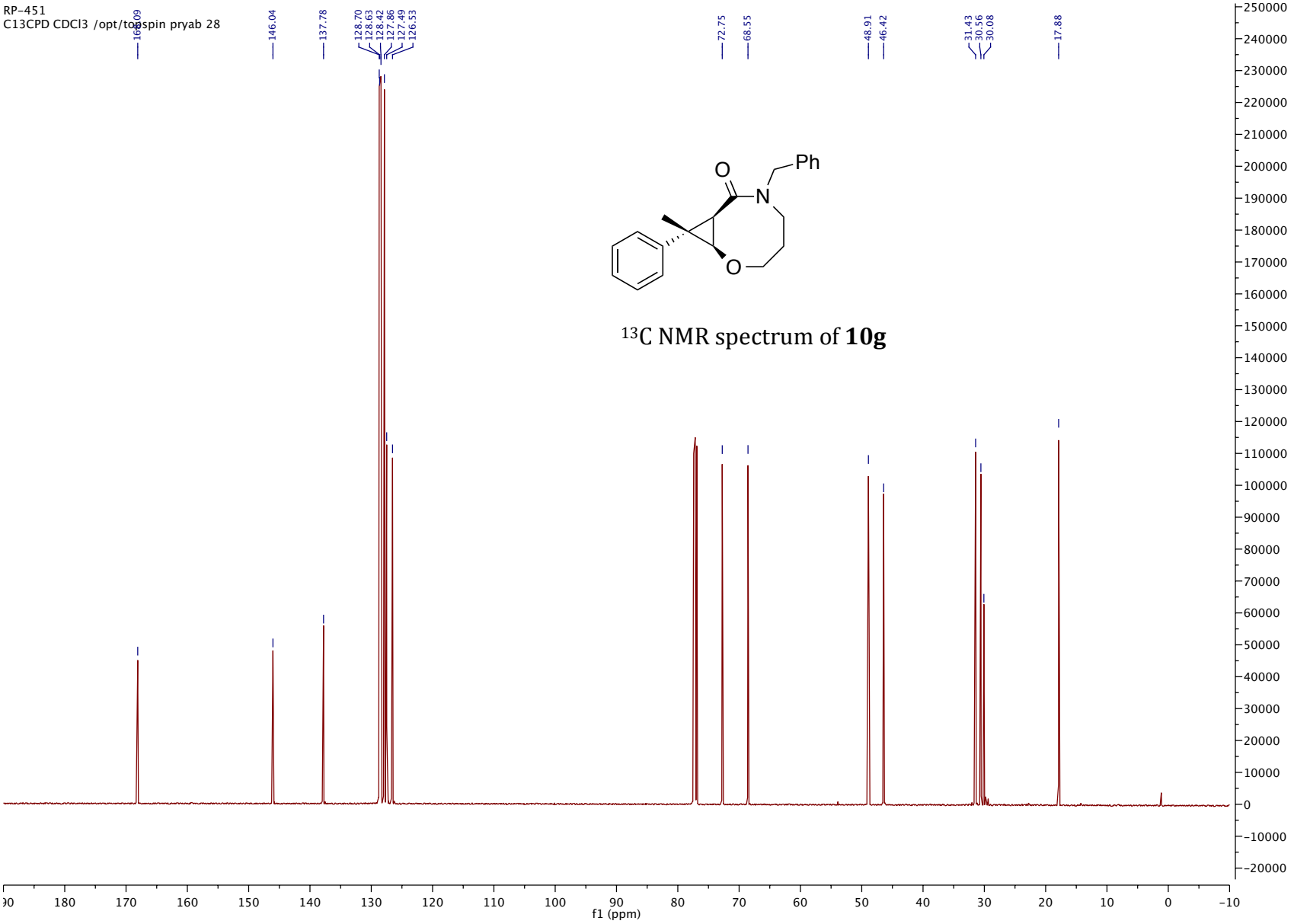
^{1}H NMR spectrum of **10q**



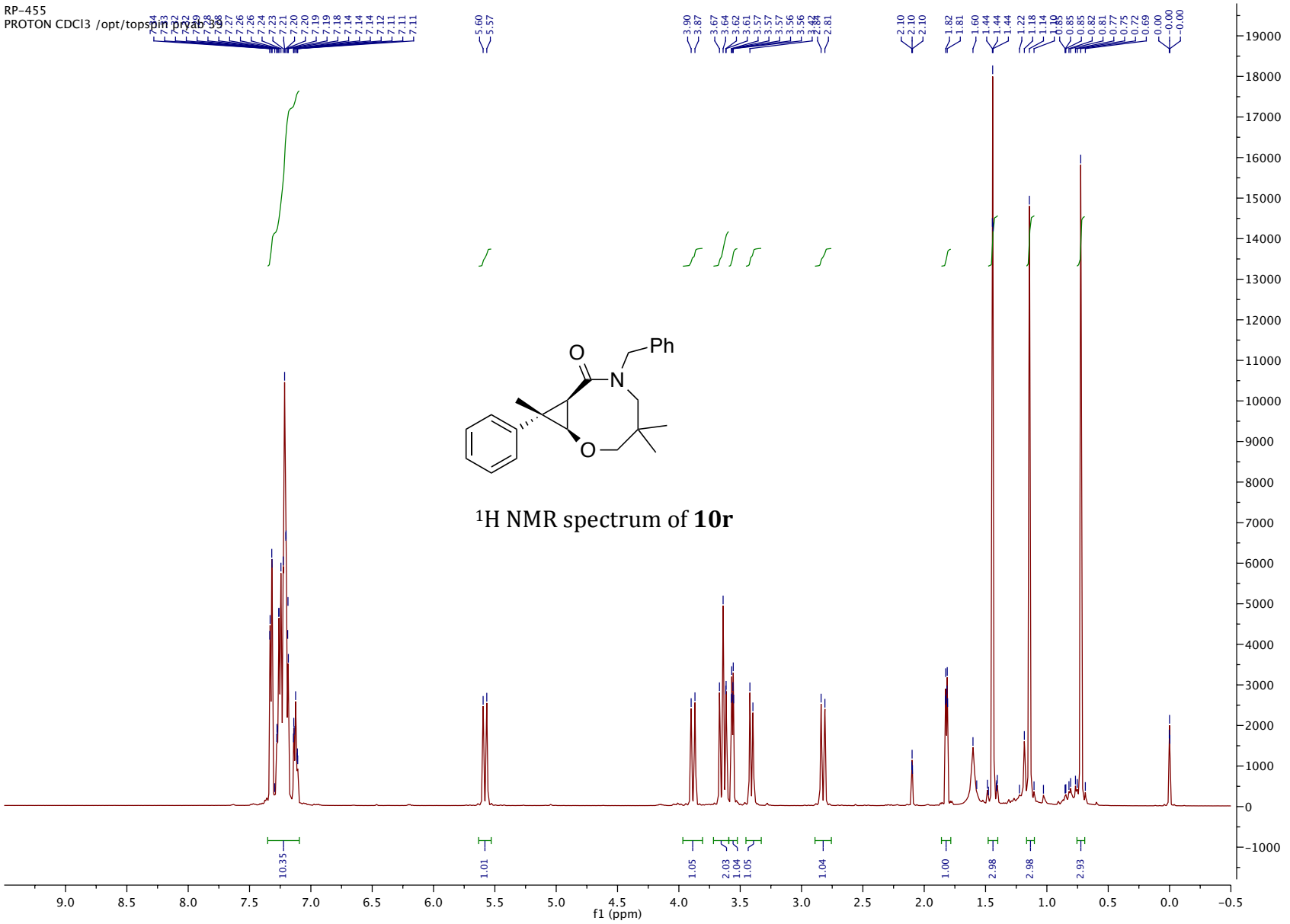
^{13}C NMR spectrum of **10q**



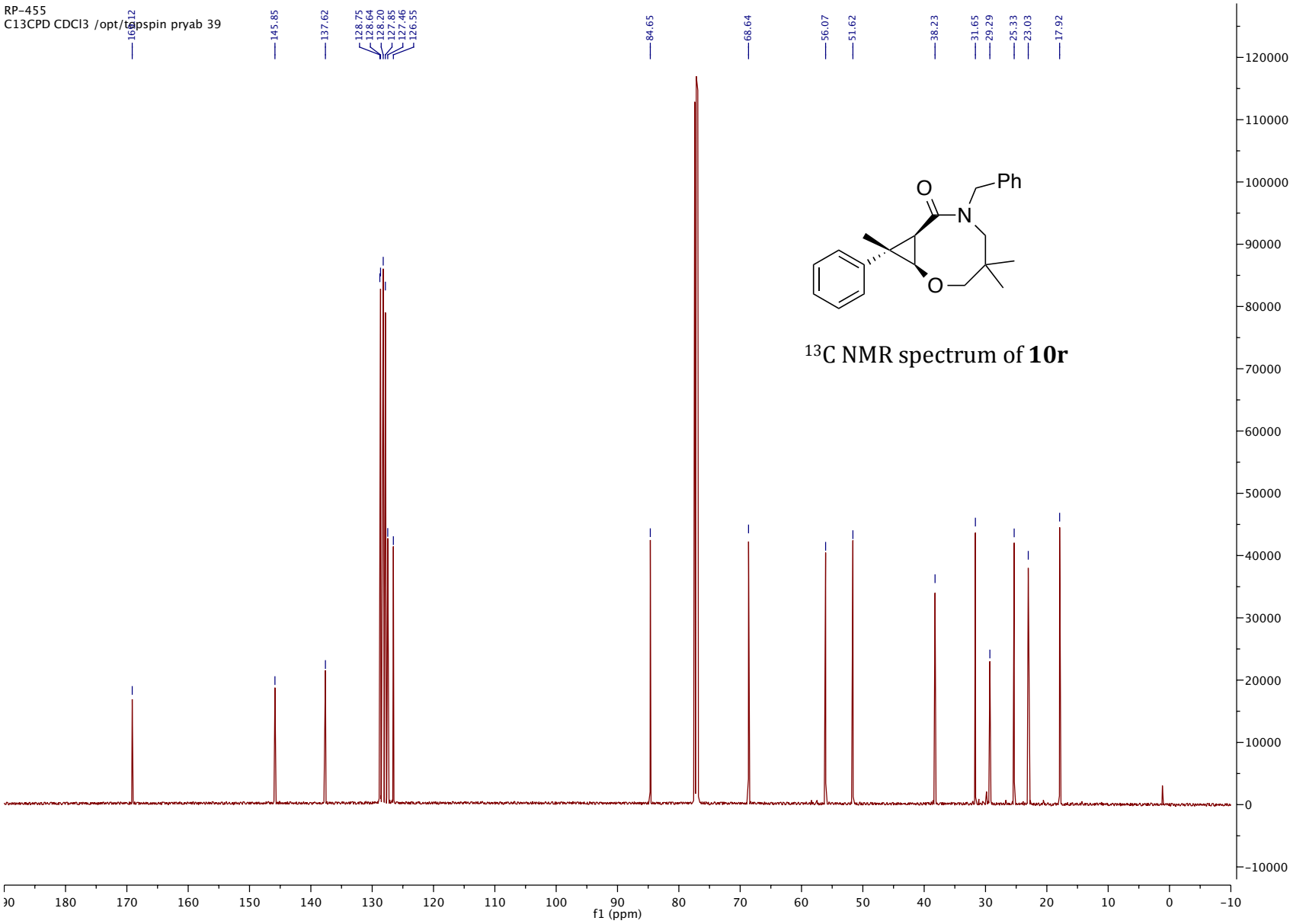
^{1}H NMR spectrum of **10g**



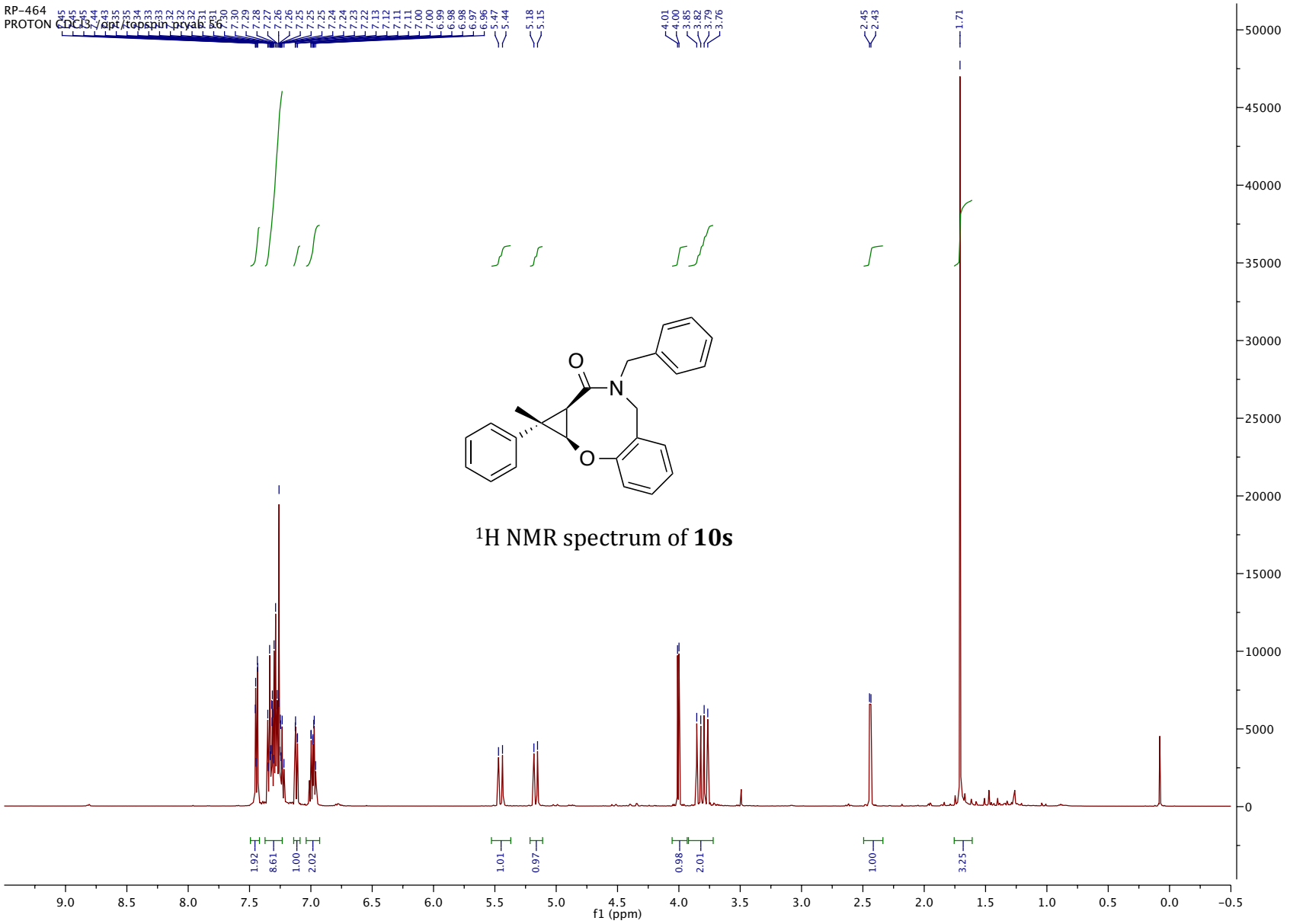
^{13}C NMR spectrum of **10g**



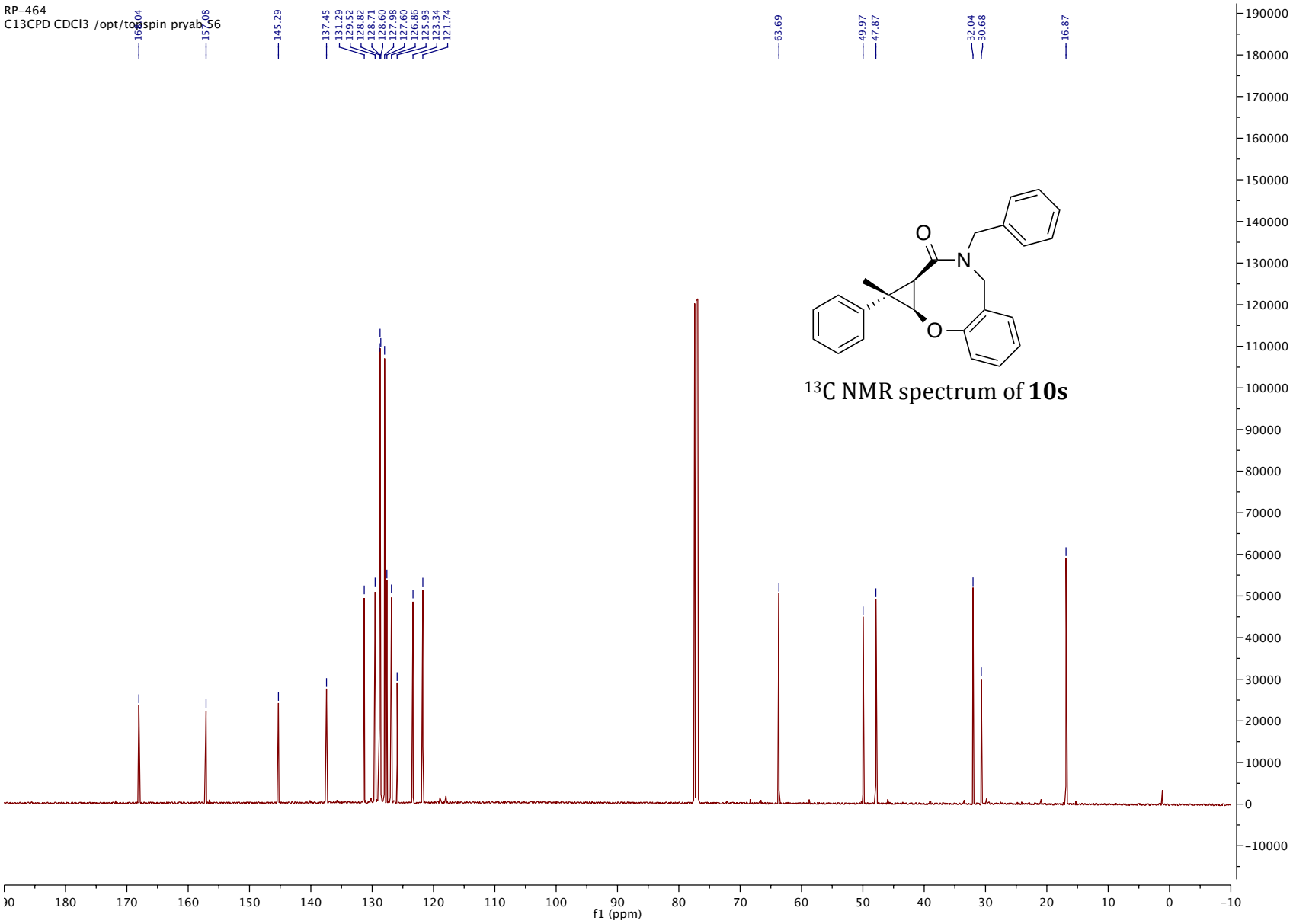
^{1}H NMR spectrum of **10r**



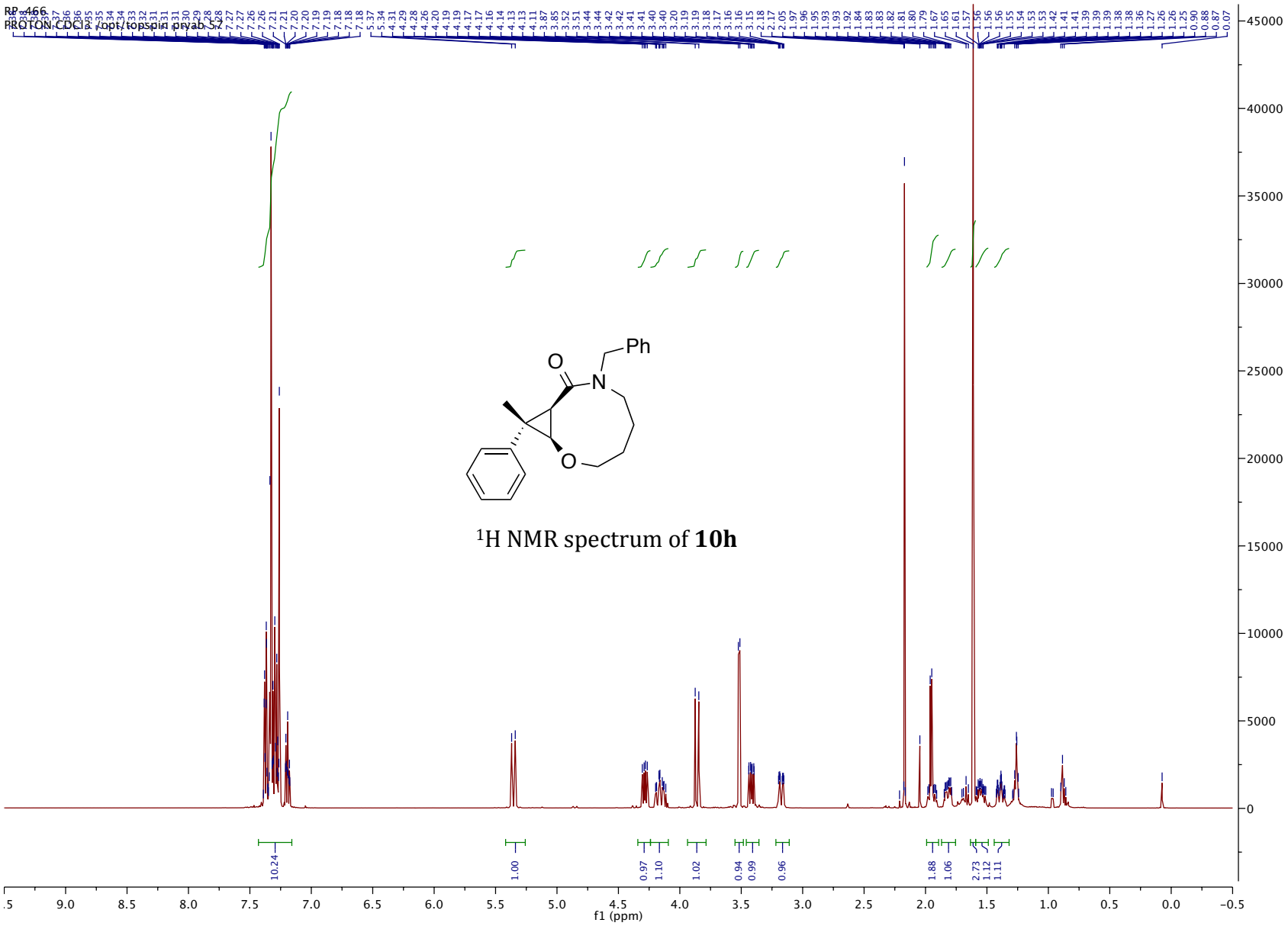
^{13}C NMR spectrum of **10r**



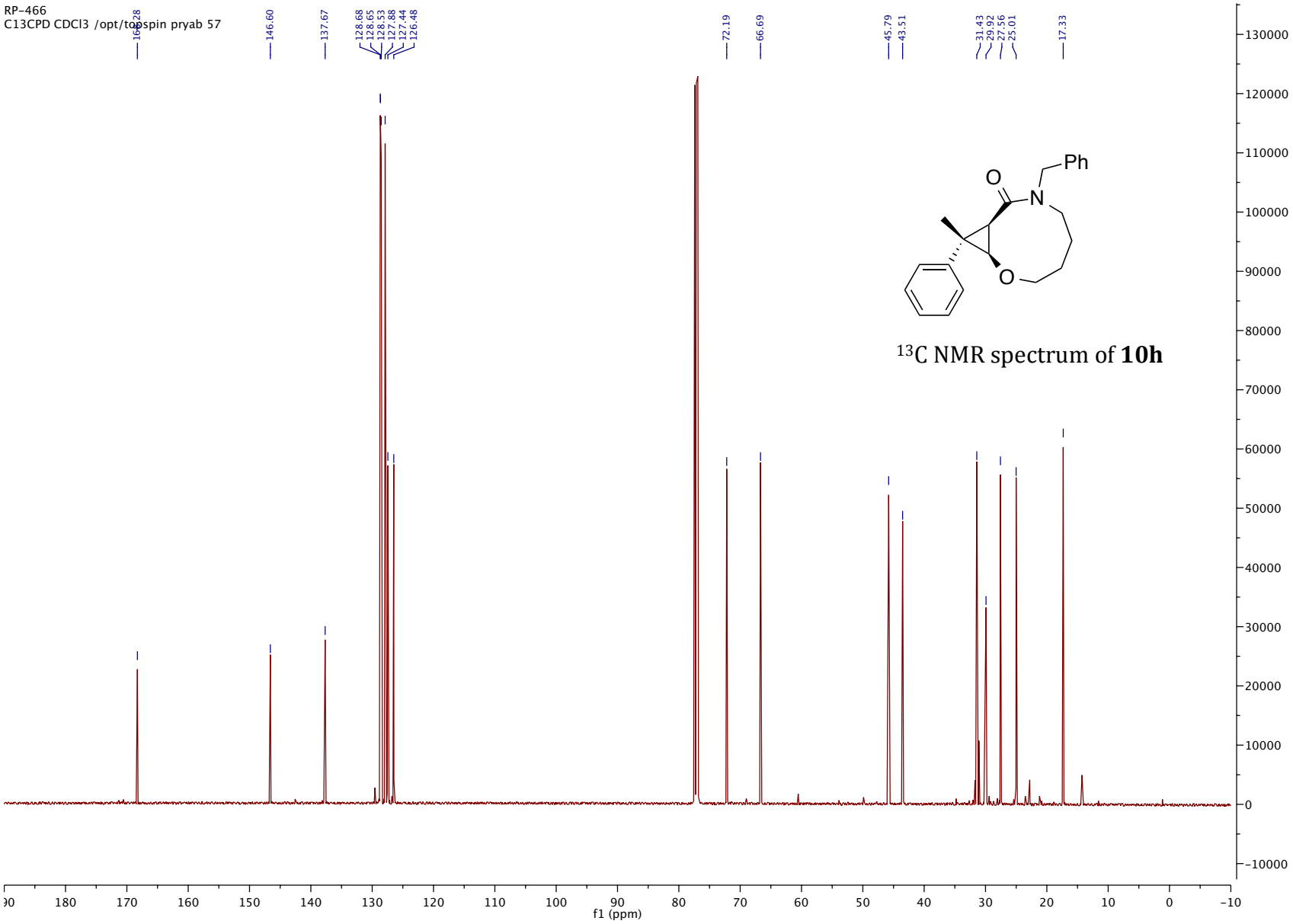
^{1}H NMR spectrum of **10s**



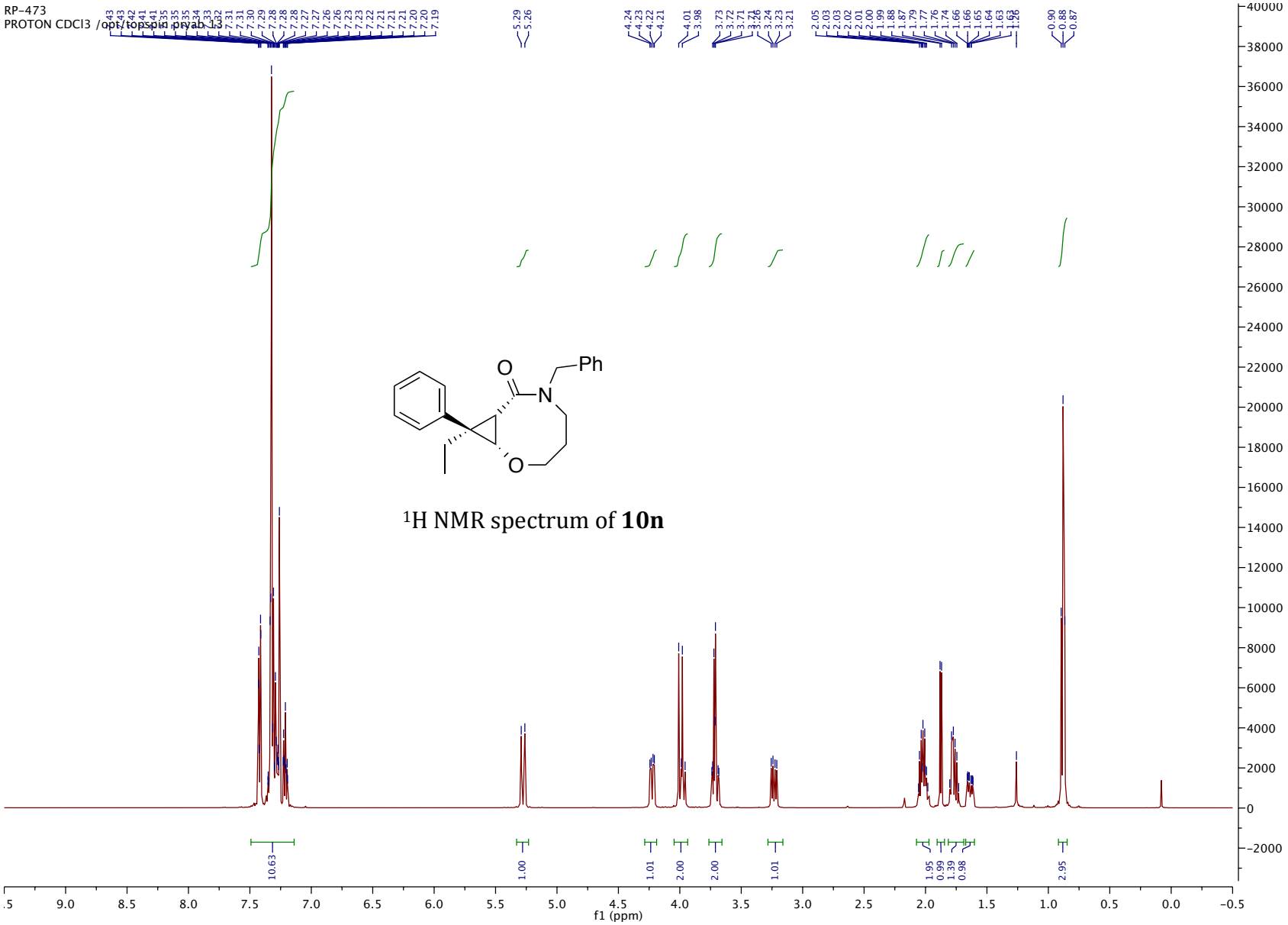
^{13}C NMR spectrum of **10s**



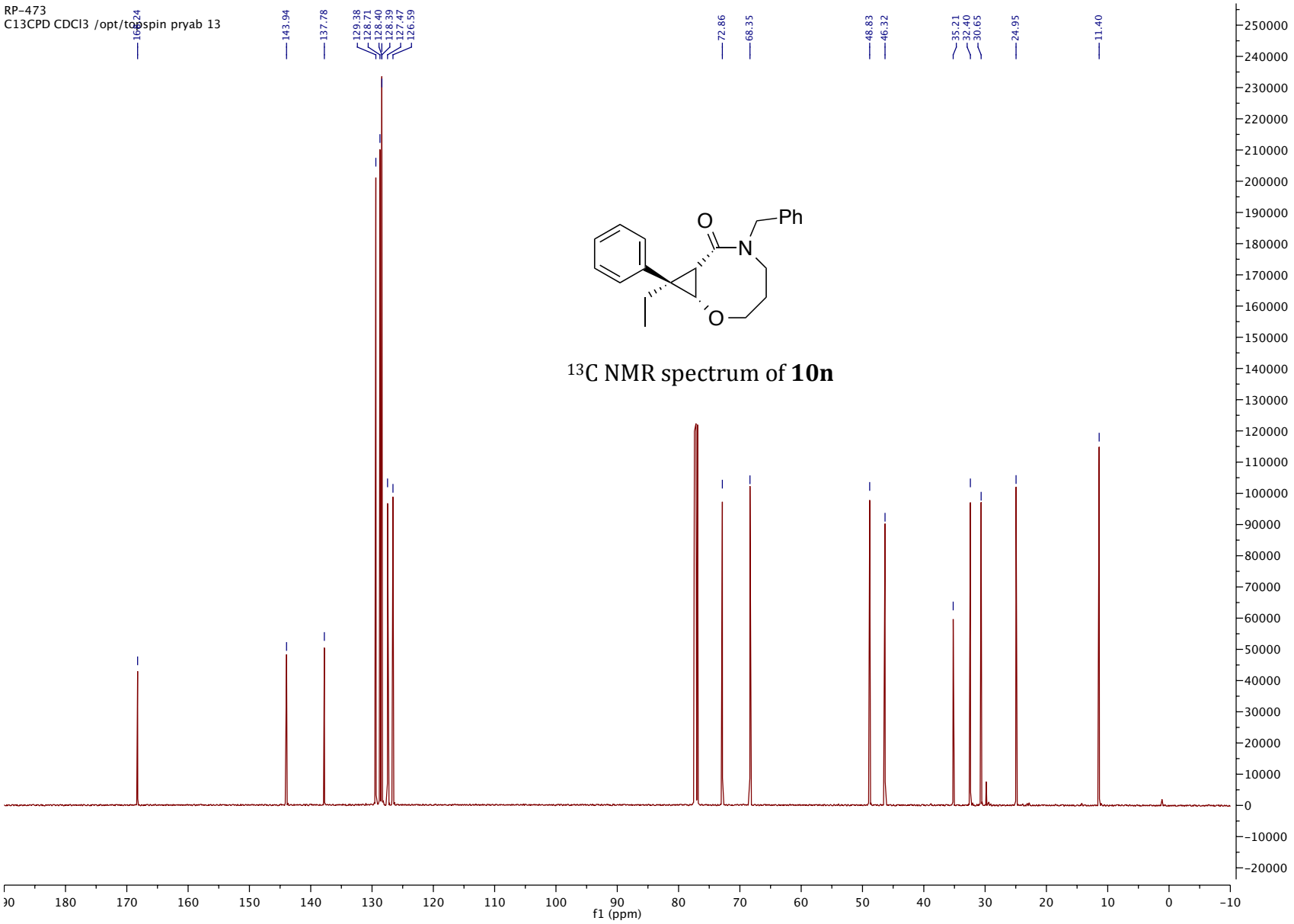
^{1}H NMR spectrum of **10h**



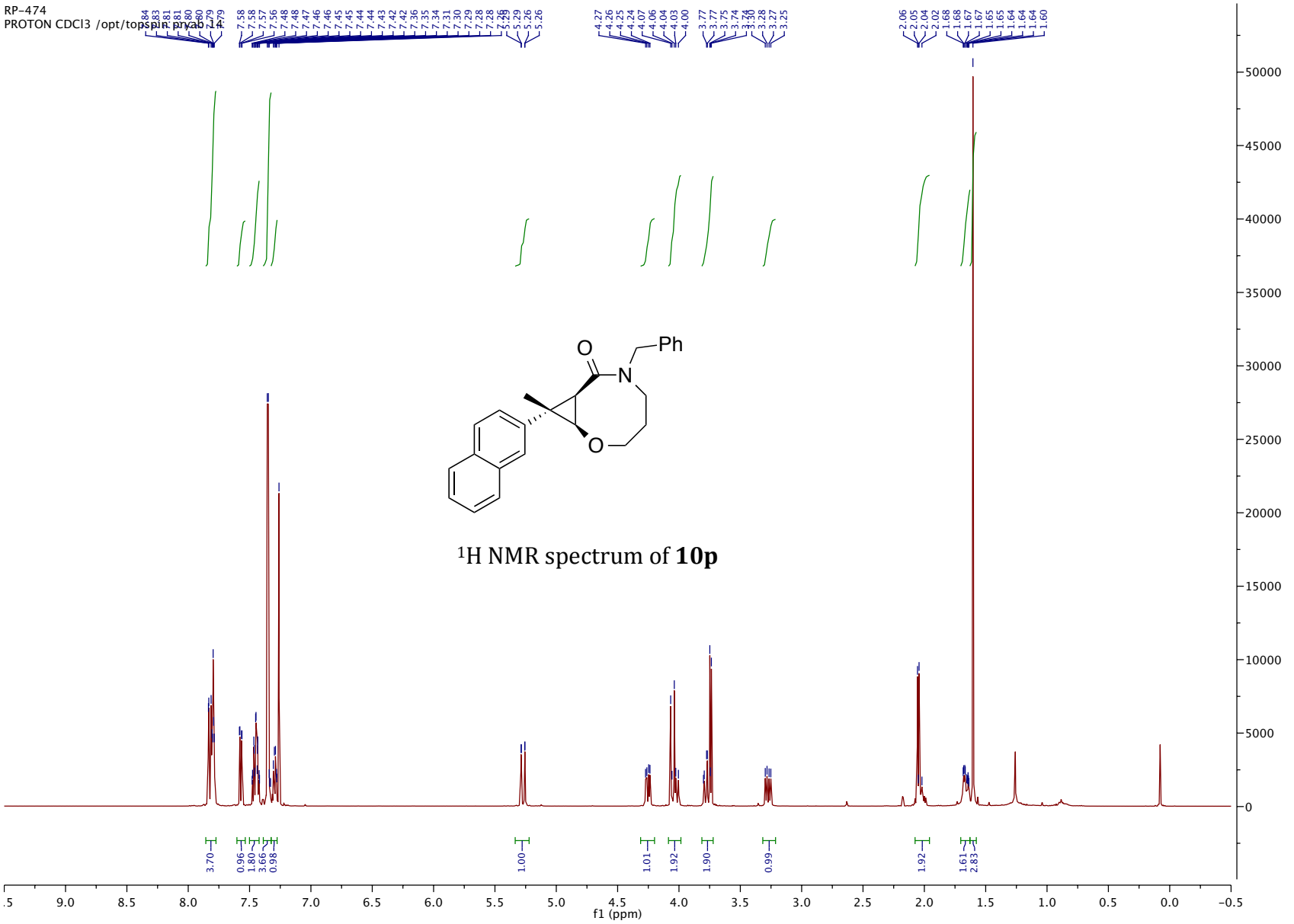
^{13}C NMR spectrum of **10h**



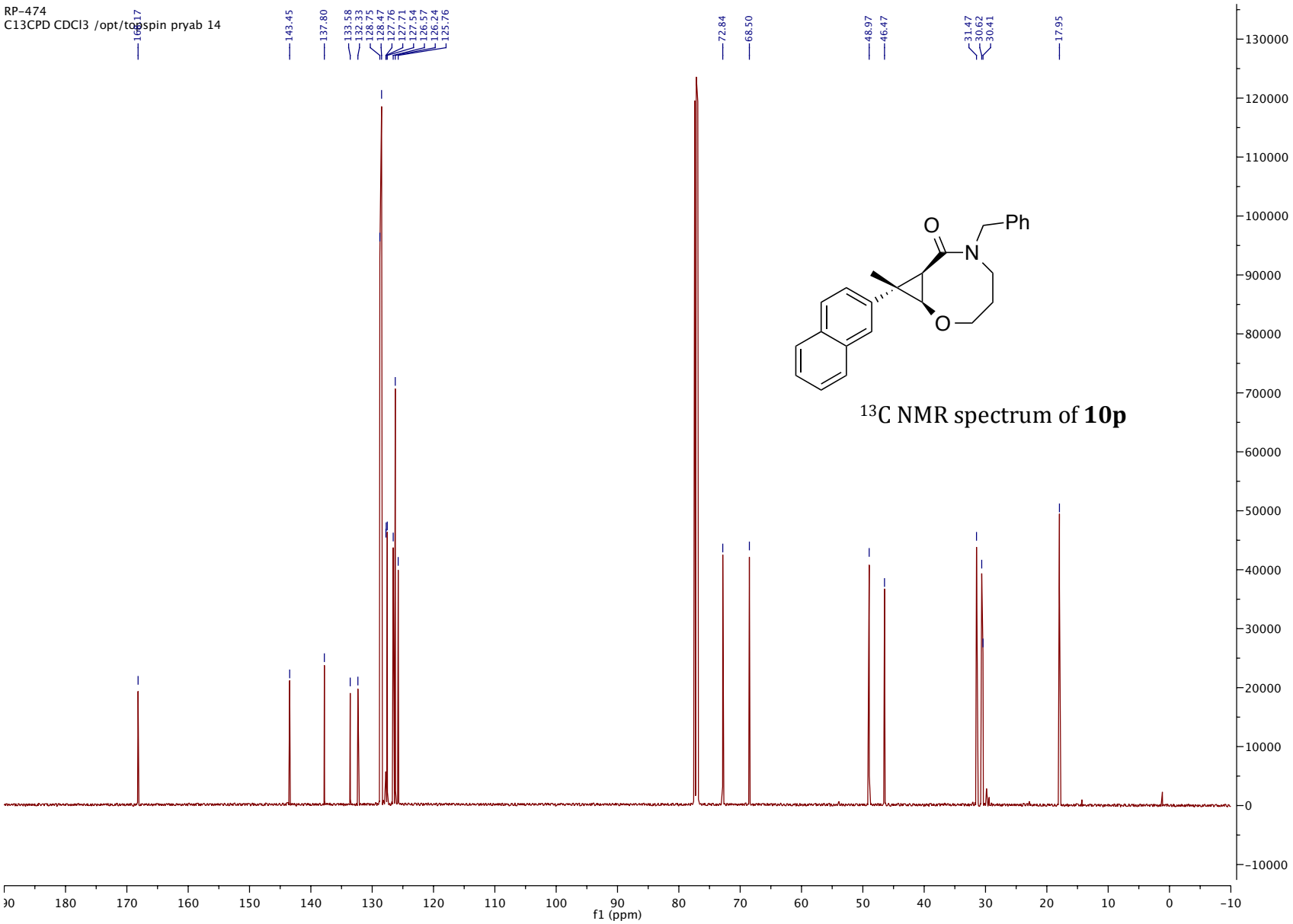
^{1}H NMR spectrum of **10n**



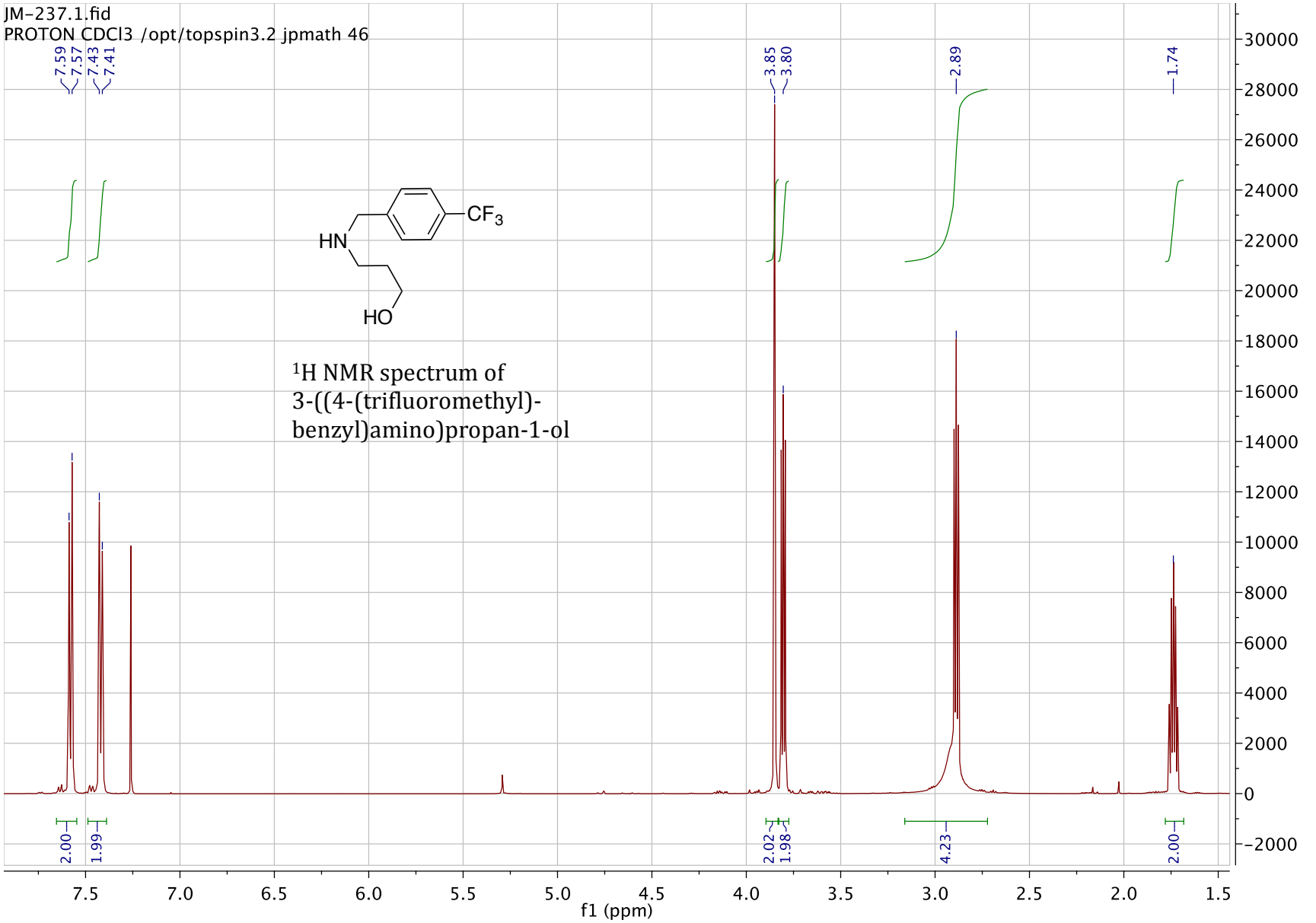
^{13}C NMR spectrum of **10n**



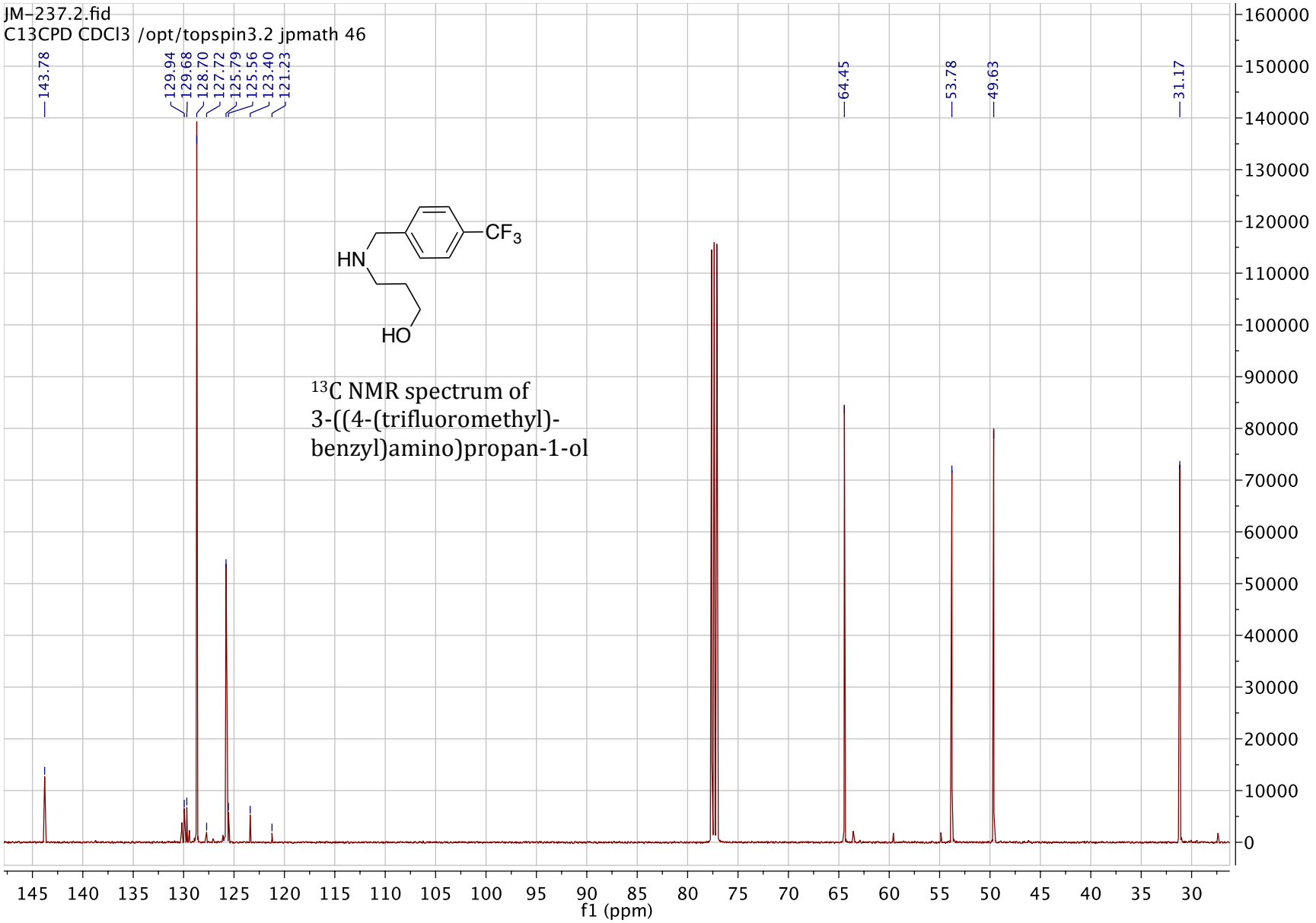
^{1}H NMR spectrum of **10p**



^{13}C NMR spectrum of **10p**



^{1}H NMR spectrum of 3-((4-(trifluoromethyl)-benzyl)amino)propan-1-ol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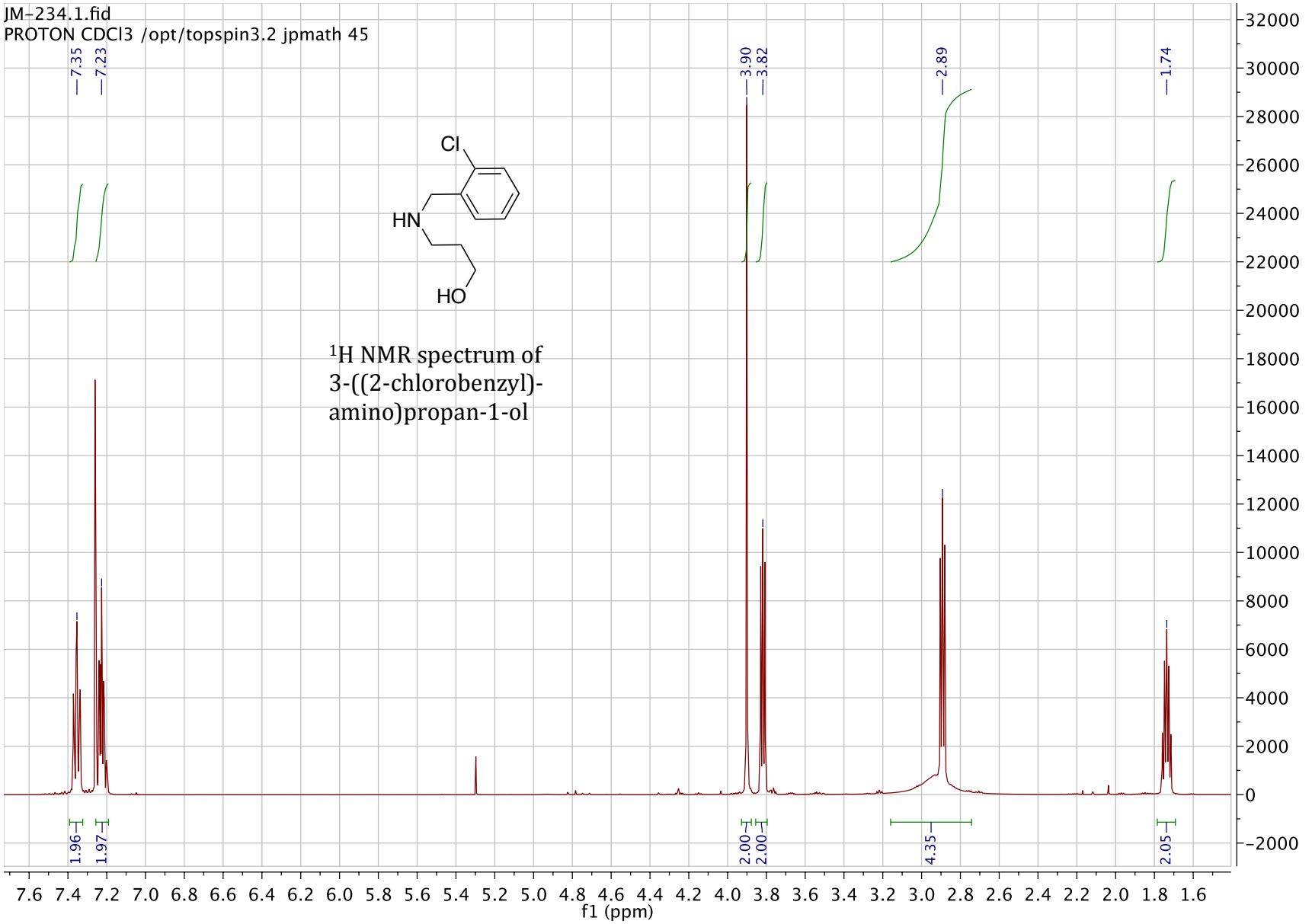
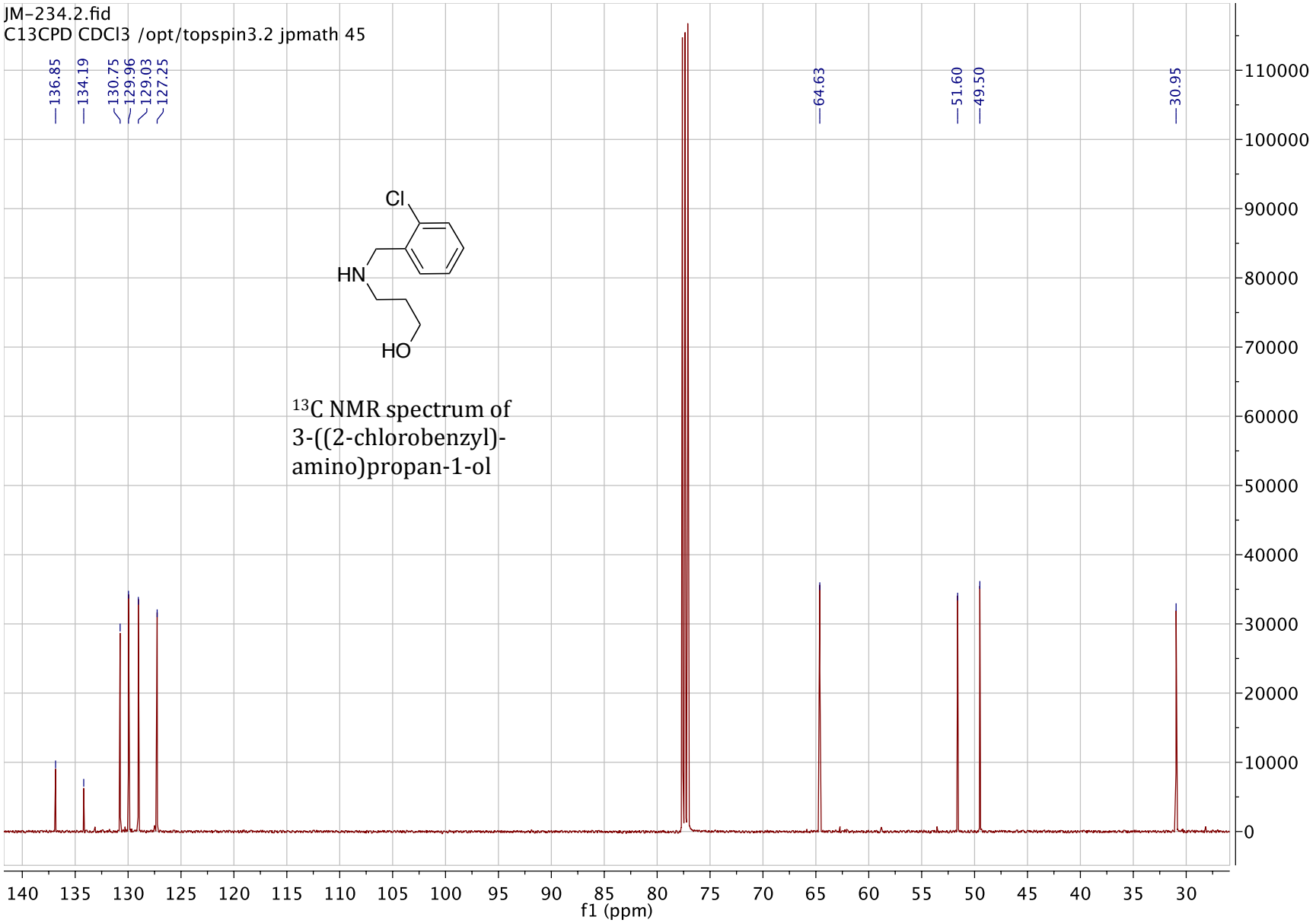
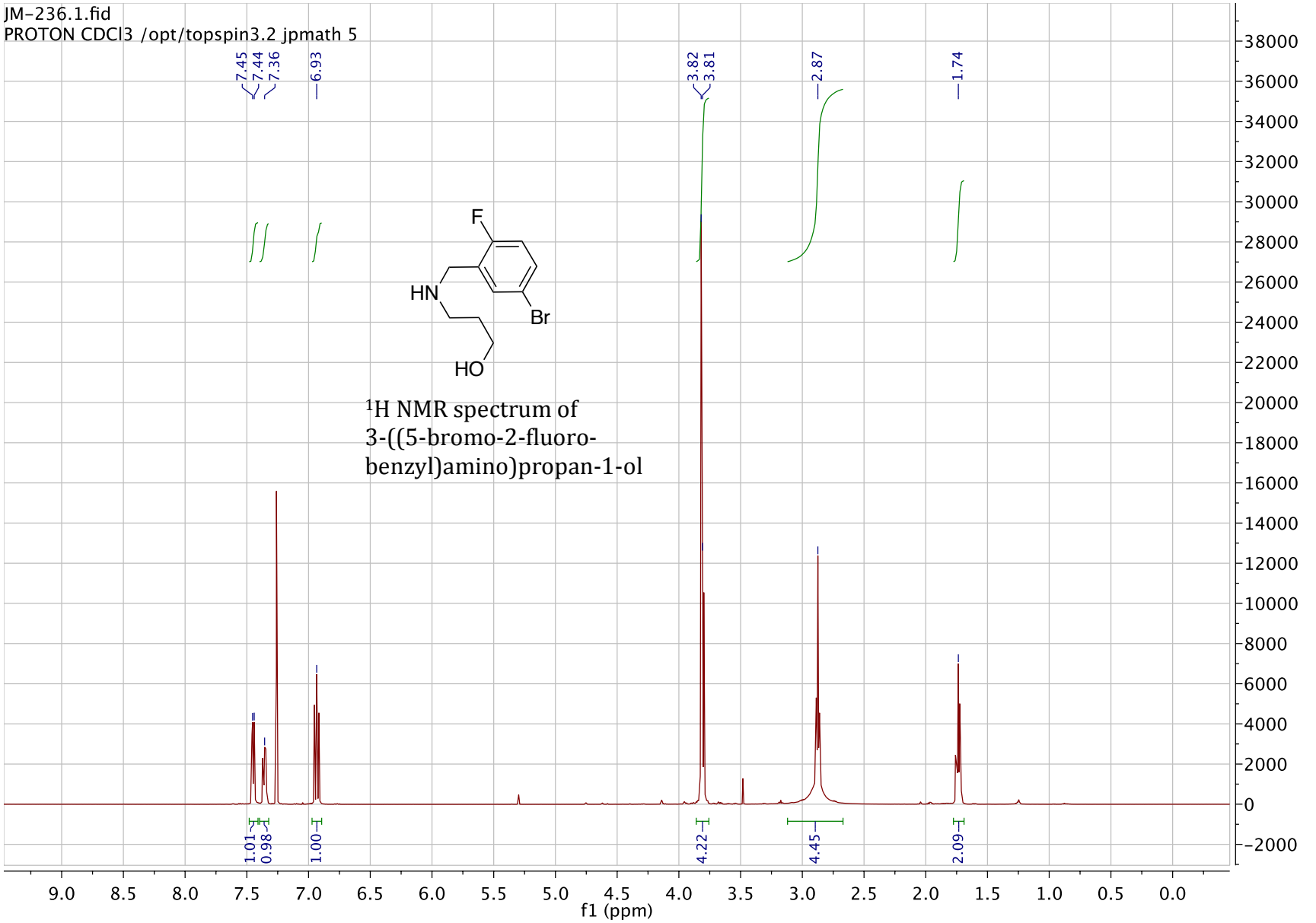
143.78
129.94
129.68
128.70
127.72
125.79
125.56
123.40
121.23
64.45
53.78
49.63
31.17
CF3
HN
HO
13C NMR spectrum of
3-((4-(trifluoromethyl)-
benzyl)amino)propan-1-ol
f1 (ppm)



^{1}H NMR spectrum of 3-((2-chlorobenzyl)-amino)propan-1-ol



^{13}C NMR spectrum of 3-((2-chlorobenzyl)-amino)propan-1-ol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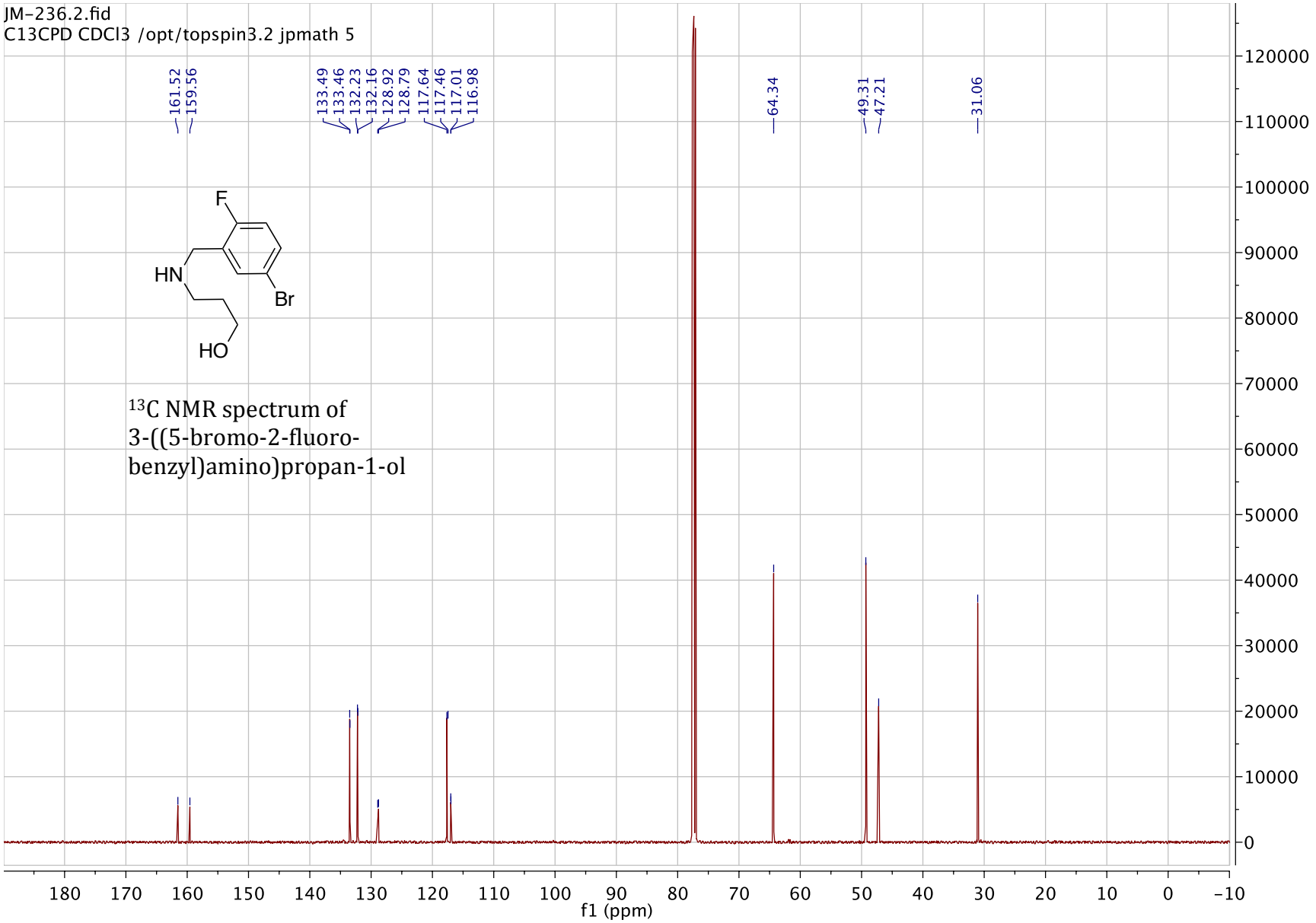
7.45
7.44
7.36
6.93
3.82
3.81
2.87
1.74
F
HN
Br
HO
1H NMR spectrum of
3-((5-bromo-2-fluoro-
benzyl)amino)propan-1-ol
1.01
0.98
1.00
4.22
4.45
2.09
f1 (ppm)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133.46
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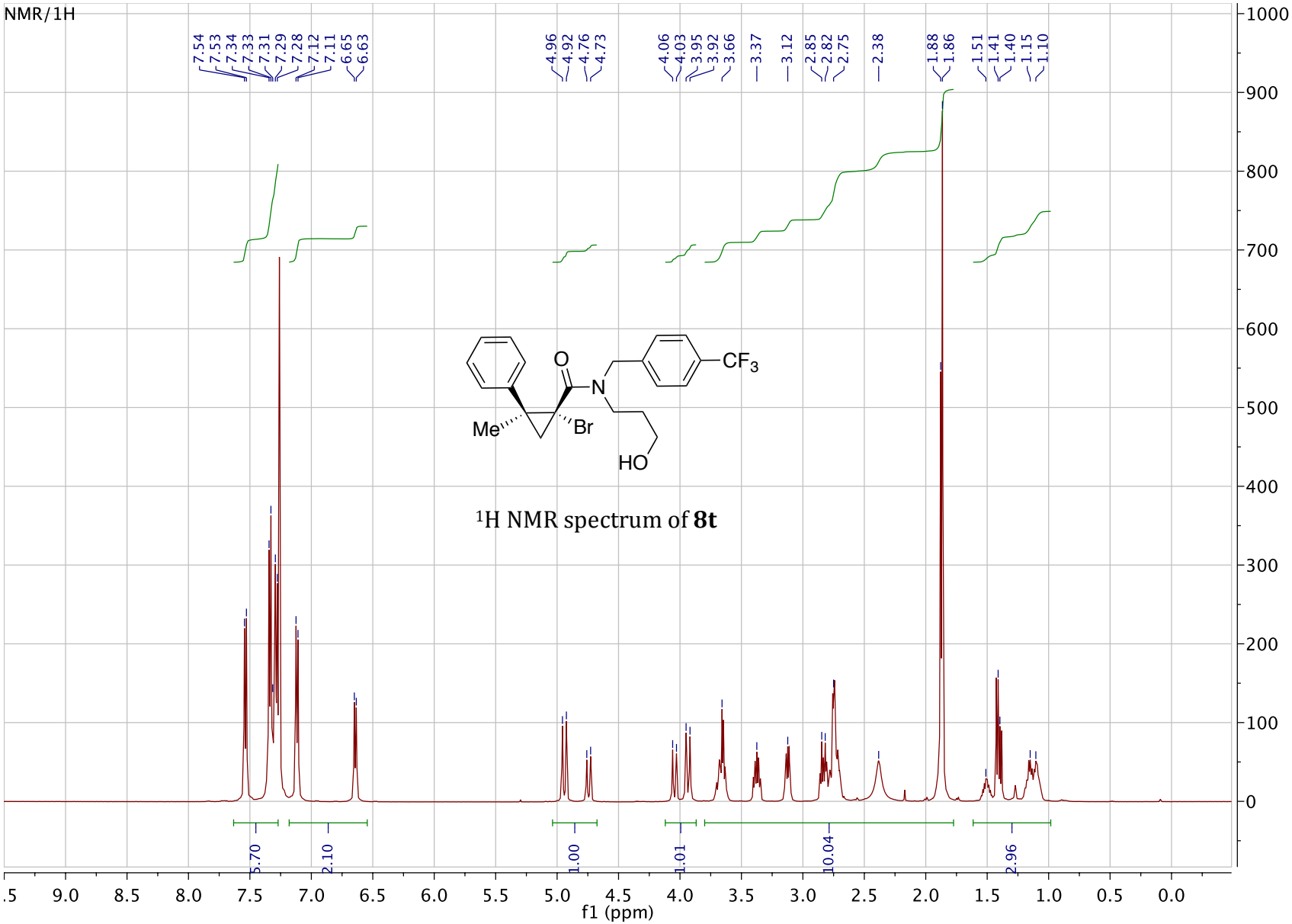
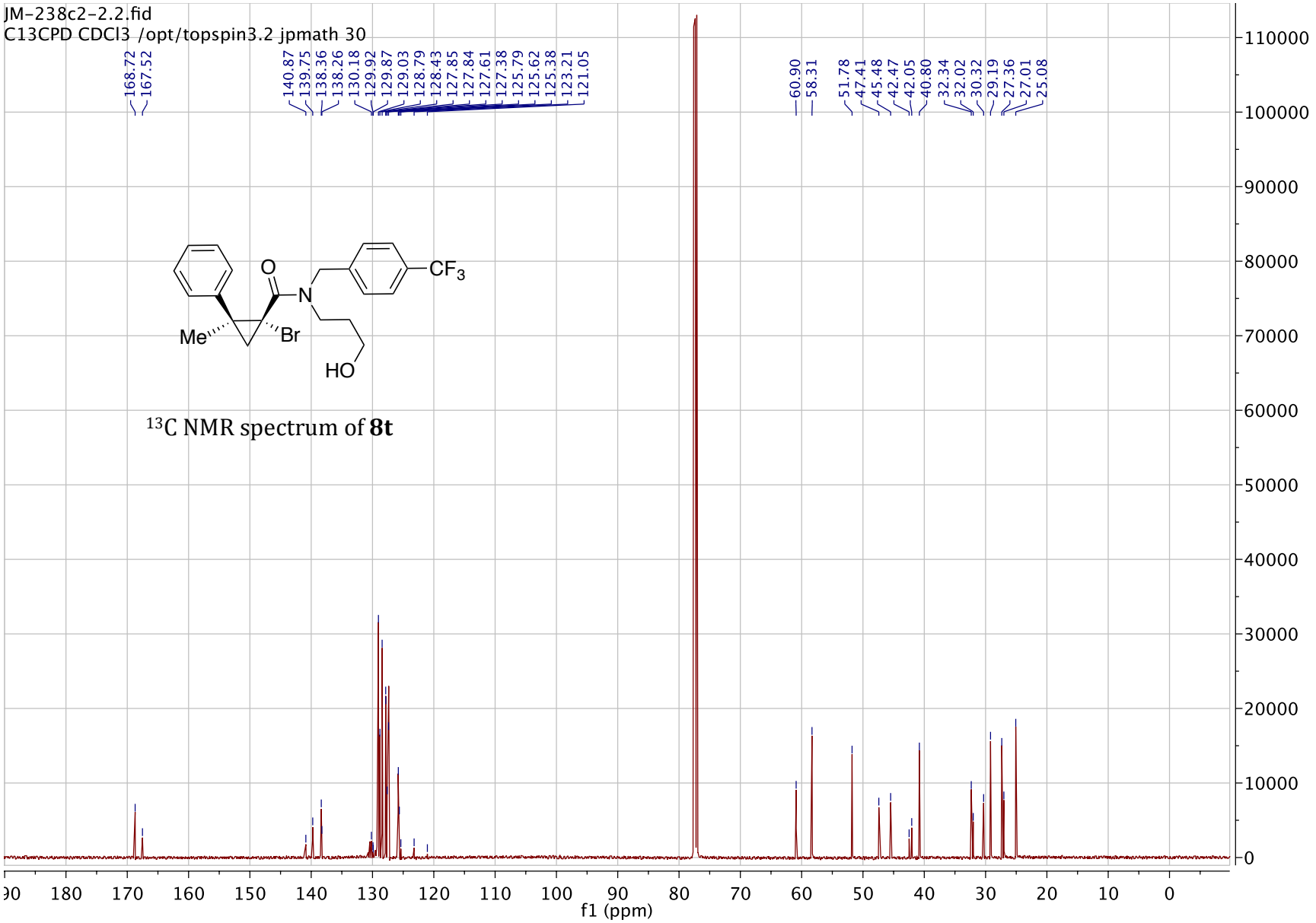
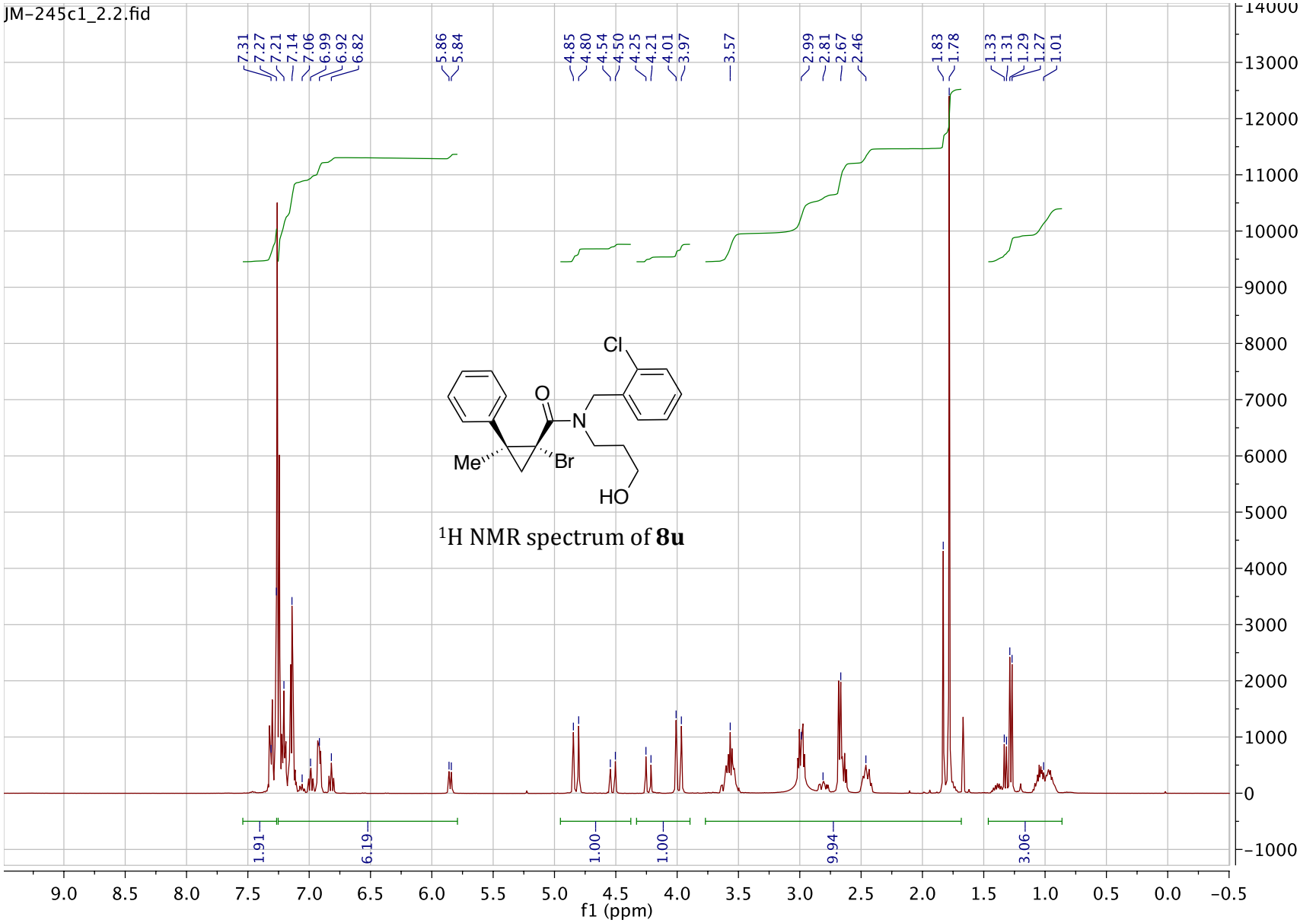
128.79
117.64
117.46
117.01
116.98
64.34
49.31
47.21
31.06
F
HN
Br
HO
13C NMR spectrum of
3-((5-bromo-2-fluoro-
benzyl)amino)propan-1-ol
f1 (ppm)



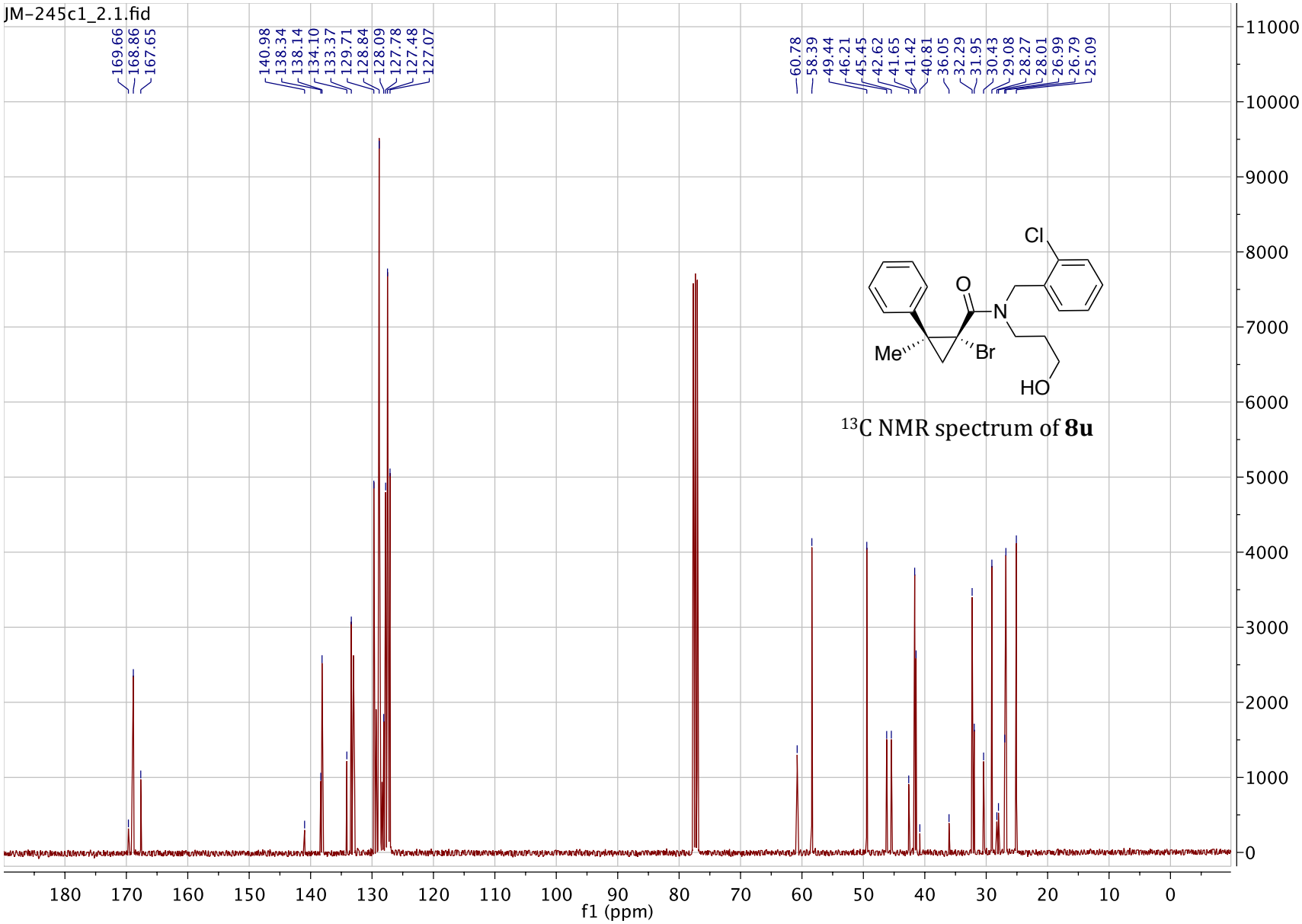
^{1}H NMR spectrum of **8t**



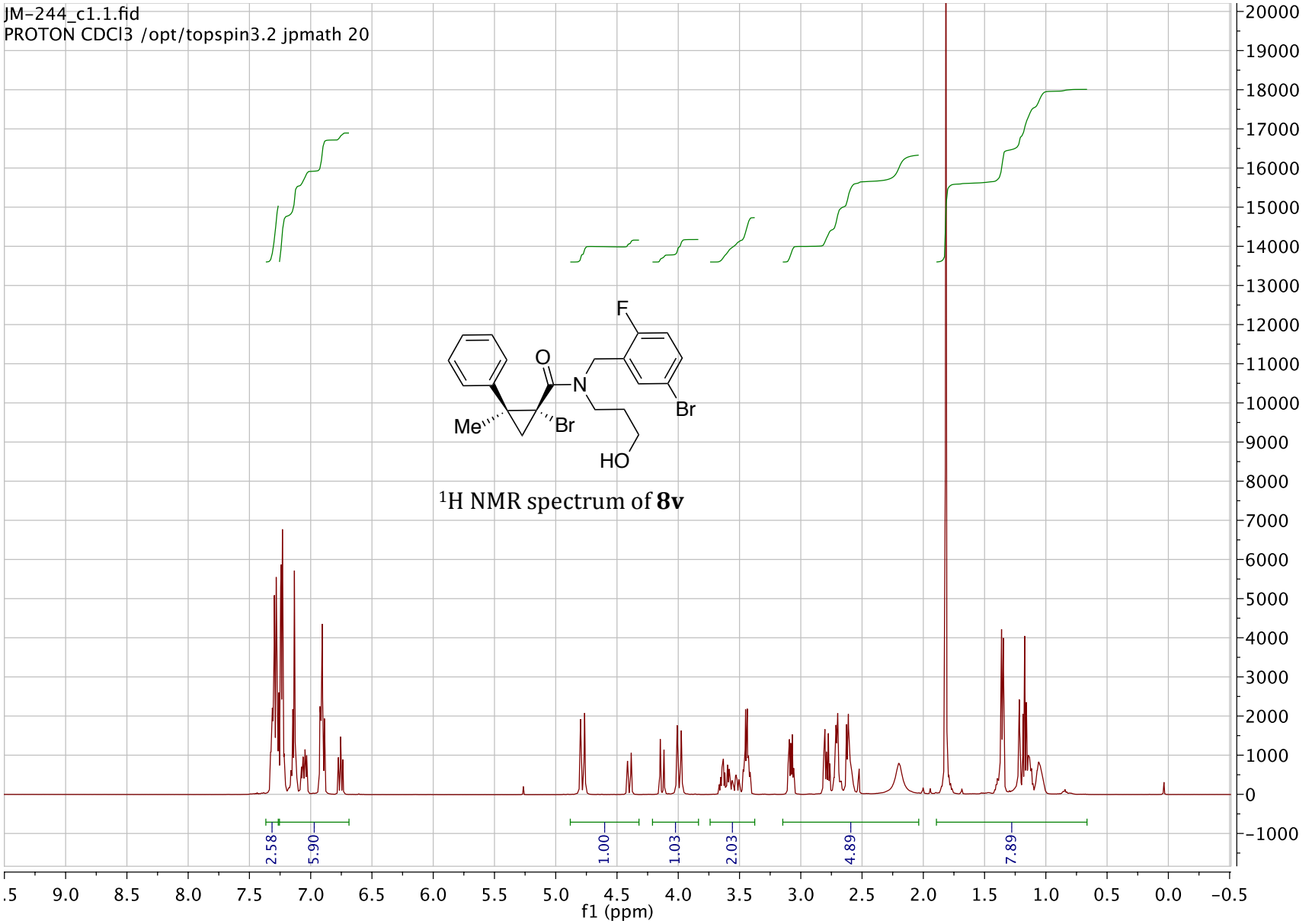
^{13}C NMR spectrum of **8t**



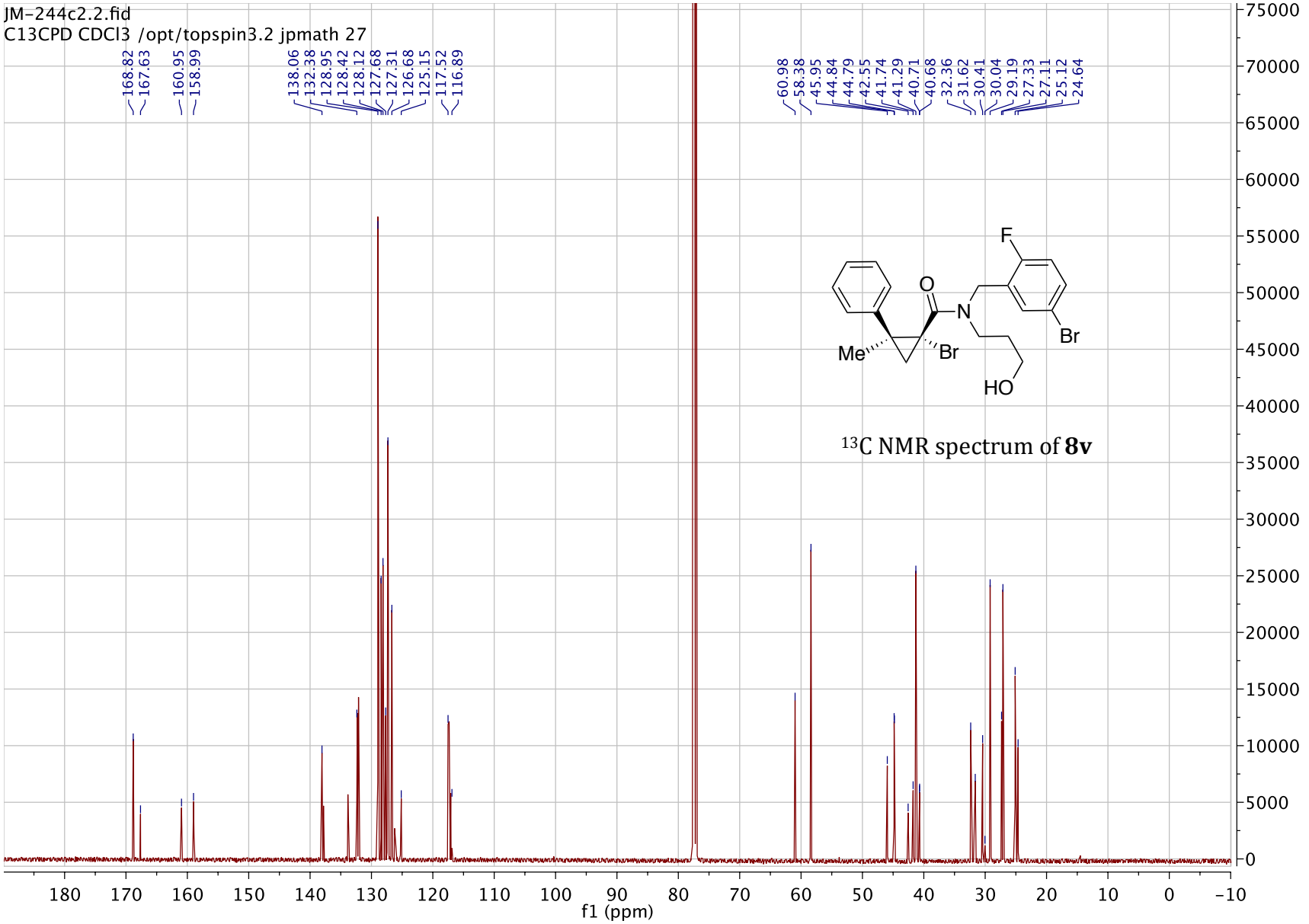
^{1}H NMR spectrum of **8u**



^{13}C NMR spectrum of **8u**



^{1}H NMR spectrum of **8v**



^{13}C NMR spectrum of **8v**