Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Supporting Information

A modular lead-oriented synthesis of diverse piperazine, 1,4-diazepane and 1,5-diazocane scaffolds

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General Experimental

All non-aqueous reactions were performed under an atmosphere of nitrogen unless otherwise stated. Water-sensitive reactions were performed in oven dried glassware, cooled under nitrogen before use, or flame dried, and cooled, under vacuum if stated. Solvents were removed *in vacuo* using a Büchi rotary evaporator and a Vacuubrand PC2001 Vario diaphragm pump. Tetrahydrofuran, dichloromethane, toluene, ethanol and acetonitrile were dried and purified by means of a Pure Solv MD solvent purification system (Innovative Technology Inc.). Anhydrous *N*,*N*-dimethylformamide and 1,4-dioxane was obtained in Oxford SureSeal™ bottles from Sigma–Aldrich. All other solvents used were of chromatography or analytical grade. Ether refers to diethyl ether and petrol refers to petroleum spirit (b.p. 40-60 °C). Commercially available starting materials were obtained from Sigma–Aldrich, Fluka, Lancaster or Alfa Aesar.

Thin layer chromatography was carried out on aluminium backed silica (Merck silica gel 60 F_{254}) plates supplied by Merck. Visualisation of the plates was achieved using an ultraviolet lamp (λ_{max} = 254 nm), phosphomolybdic acid, $KMnO_4$ or anisaldehyde. Flash chromatography was carried out using silica gel 60 (35-70 μm particles).

All optical rotations were carried out on a Schmidt & Haensch H532 instrument with a path length of 1 dm; concentrations are g/100 mL, the optical rotations are given in 10^{-1} degcm^{2}g^{-1} and units are omitted for clarity. Infrared spectra were recorded on a Perkin-Elmer One FT-IR spectrometer.

Proton and carbon NMR data were collected on an Advance 500, Bruker DPX500 and DPX300 spectrometer. All shifts were recorded against and internal standard of tetramethylsilane. Solvents ($CDCl_3$, DMSO-d_6 and MeOD-d_4) used for NMR experiments were obtained from SigmaAldrich. Splitting patterns are reported in an abbreviated manner: app. (apparent), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Signal assignments were generally made with the aid of COSY, DEPT 90 and 135, HMQC and HMBC.

Low resolution mass spectra data were recorded on an Aligent 1200 series LC system comprising a Bruker HCT Ultra ion trap mass spectrometer, a high vacuum degasser, a binary pump, a high performance autosampler, an autosampler thermostat, a thermostated column compartment and a diode array detector. The system used two solvent systems; MeCN/H_2O + 0.1% formic acid with a Phenomenex Luna C18 50 × 2 mm 5 micron column or MeCN/H_2O with a Phenomenex Luna C18 50 × 2 mm 5 micron column. Nominal and high resolution mass spectrometry, using electrospray ionisation, was recorded by Mrs Tanya Marinko-Covell on a Micromass LCT-KA11 or a Bruker Daltronics micrOTOF spectrometer.

Library Enumeration and Property Assessment

Virtual libraries were enumerated and manipulated using Accelrys Pipeline Pilot version 8.5 (Pipeline Pilot v8.5.0.200, Accelrys© Software Inc., 2011). A virtual library was enumerated based on the scaffolds shown in Figure S1 and the capping groups shown in Figure S2. The resulting compounds were virtually deprotected (i.e. PMB groups removed) if necessary and further derivatization was performed. Underivatised scaffolds were retained in both rounds of enumeration and included in the library. Molecular properties (AlogP, number of heavy atoms and number of aromatic rings) were calculated using the tools within Pipeline Pilot and filtered where necessary. The results were visualized and analysed using Dotmatics Vortex (Vortex v2012.11.15406, Dotmatics Limited, 2012).

Shape analysis – Principal Moments of Inertia Method

3D structures were generated from the 2D Pipeline Pilot output using Molecular Networks CORINA (CORINA v3.48.0026, Molecular Networks GmbH, 2010) and the lowest energy conformer selected. The 3D structures were used to generate the three Principal Moments of Inertia (I_1, I_2 and I_3) using Pipeline Pilot which were then normalised by dividing the two lower values by the largest (I_1/I_3 and I_2/I_3). These Normalised PMI plots generate a triangular plot with the corners defined by a perfect sphere, a perfect disk and a perfect rod shape.[1]

Shape Analysis – Rapid Overlay of Chemical Shape Method[2]

To define the shape diversity of lead-like space, 100,000 compounds within the heavy atom range 14-26 were randomly selected from the ZINC Database. These compounds were then merged with the enumerated library of compounds based on the scaffolds shown in Figure S1.

A set of reference shapes was generated. Initially, the first reference shape molecule was selected at random and all the other molecules scored against it using OpenEye ROCS (ROCS v3.1.2, OpenEye Scientific Software Inc., 2011).[3] Compounds with a shape Tanimoto score of 0.8 or above were regarded as matches and removed from the database. The compound with the lowest shape Tanimoto score was then taken as the next reference shape and the process repeated until all compounds in the database had been matched. This process generated 6244 reference shapes.

To assess their shape diversity, the shape of compounds was compared with those of the reference shapes. Compounds were considered to match the reference shapes if the shape Tanimoto score was 0.7 or above.

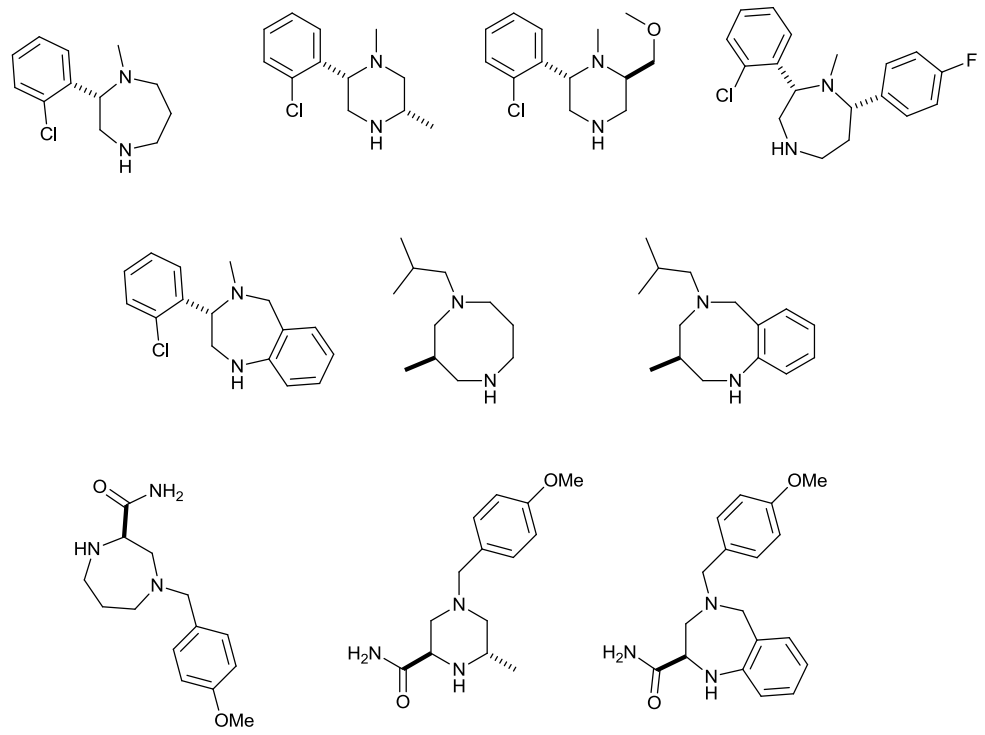


Figure S1 - Scaffold Structures

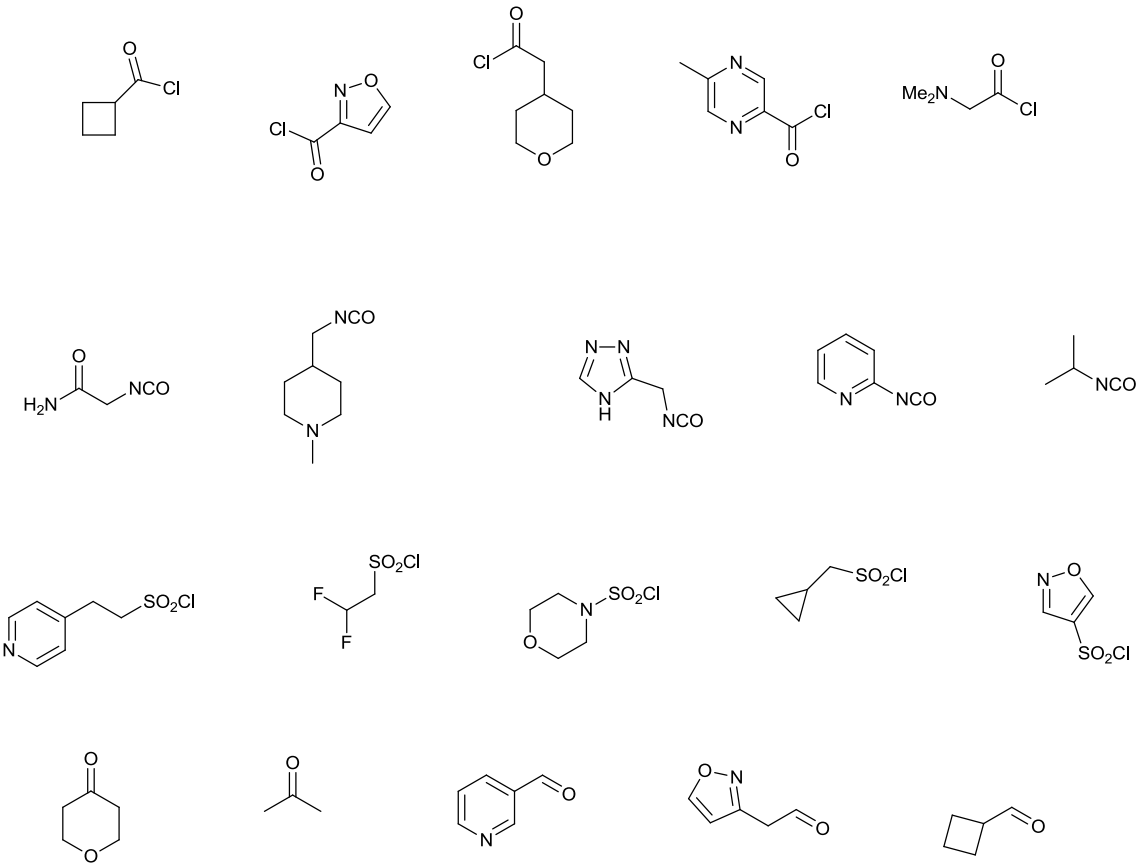


Figure S2 - Capping Groups

General Procedures

A. Reductive Amination

4-Methoxybenzaldehyde (1.2 eq.) was added to a suspension of amine (1.0 eq.) and molecular sieves (4Å) in methanol (1.0 M) and stirred at 50 °C until consumption of amine was complete (as indicated by TLC). The reaction mixture was filtered, cooled to 0 °C, $NaBH_4$ (2.0 eq.) added, reaction mixture warmed to rt and stirred until completion was observed. The reaction mixture was acidified (HCl, 5 M aq., to pH<2) concentrated to half volume *in vacuo* , extracted with EtOAc, aqueous phase basified (K_2CO_3, sat. aq. soln., to pH>12), extracted with EtOAc, organic phase washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

B1. Cyclic sulfamidate formation

The amino alcohol (1.0 eq.) in CH_2Cl_2 (0.4 M) was added dropwise to a stirred solution of $SOCl_2$ (1.1 eq.), NEt_3 (2.2 eq.) and imidazole (4 eq.) in CH_2Cl_2 (0.1 M) at −60 °C (CO_2 and $CHCl_3$) and the resulting solution was stirred at −60 °C until completion was indicated by TLC (typically < 3 h). The reaction mixture was warmed to room temperature, quenched by addition of water, phases separated, organic phase washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude cyclic sulfamidite. The crude cyclic sulfamidite was dissolved in MeCN (0.13 M), cooled to 0 °C (ice water bath), $NaIO_4$ (1.1 eq) $RuCl_3{\cdot}3H_2O$ (0.1 mol%) and water (0.16 M) were added sequentially and the resulting solution was stirred until completion was indicated by TLC. The cold reaction mixture was diluted with water (equal volume to that used in reaction), warmed to room temperature, extracted with Et_2O, washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

B2. Cyclic sulfamidate formation

A solution of aminoalcohol (1 equiv.) in DCM (0.8 M) was added dropwise to a solution of thionyl chloride (1.1 equiv.), imidazole (4 equiv.) and triethylamine (2.2 equiv.) in DCM (0.1 M) at -60 °C. The mixture was allowed to warm to room temperature with stirring until completion indicated by TLC. The mixture was washed with water and brine, dried ($MgSO_4$) and concentrated. The crude residue was dissolved in MeCN (0.17 M) and cooled to 0 °C. Sodium periodate (1.1 equiv.), ruthenium(III) chloride trihydrate (0.001 equiv.) and water (0.17 M) were added sequentially and the mixture stirred at 0 °C for 2 h. Water (0.35 M) was added and the mixture extracted with Et_2O, dried and concentrated.

C. Hydroxy sulfonamide formation

2-Nitrobenzenesulfonyl chloride (1.0 eq.) was added to a vigorously stirred solution of the amino alcohol (1.05 eq.), Na_2CO_3 (1.05 eq.) in 1:1 CH_2Cl_2–H_2O (0.8 M solution) and resulting mixture stirred at rt until completion was indicated by TLC (typically 24 h). The reaction mixture was acidified (HCl, 5 M aq., to pH<2), extracted with CH_2Cl_2, organic phase washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

D. Opening of cyclic sulfamidates with sulfonamides

NaH (60 % dispersion in oil, 1.1 eq.) was added to a solution of the sulfonamide (1.1 eq.) in DMF (0.2 M) and stirred for ten minutes, at which point the cyclic sulfamidate (1.0 eq.) was added and the resulting solution was stirred at room temperature (unless otherwise stated) until completion was indicated by TLC (typically 24 h). The reaction mixture was acidified (5 M HCl aq., 6 eq.), stirred for 1 h, basified (K_2CO_3 sat. aq. soln., to pH>12), extracted with EtOAc, washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product.

E. Cyclisation under Mitsunobu conditions

Diethylazodicarboxylate (1.3 eq.) was added dropwise to a solution of the alcohol (1.0 eq.), PPh_3 (1.4 eq.) in THF (0.05 M) at 0 °C, the resulting solution was warmed to room temperature and stirred until completion was indicated by TLC (typically 16 h). The resulting reaction mixture was concentrated *in vacuo* to give the crude product.

F. Heterocycle formation without purification of the intermediate

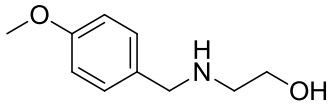
Sodium hydride (1.1 equiv.) was added to a solution of sulfonamidoalcohol (1 equiv.) in DMF (0.1 M) with stirring for 10 minutes. Cyclic sulfamidate (1.2 equiv.) was added and the mixture stirred for 20 h. Aqueous HCl (5 M) was added and the mixture stirred for 45 min. The mixture basified (>pH 12) with potassium carbonate, partitioned between diethyl ether and water, the phases separated, the organic fraction washed with water, dried ($MgSO_4$) and concentrated. The crude residue was purified by SCX chromatography (eluting with saturated NH_3 in MeOH). The intermediate was dissolved in THF (0.1 M). DEAD (1.1 equiv.) and triphenylphosphine (1.2 equiv.) were added and the mixture stirred for 18 h. The mixture was concentrated and the crude product was purified by SCX chromatography (eluting with saturated NH_3 in MeOH).

Purification by strong ion exchange (SCX) resin

Strong cation exchange resin (SCX, 5.0 g pre-packed cartridge, Supelco) was conditioned by washing with MeOH (>20 mL). The crude amine (<1 mmol) in MeOH (<5 mL) was added and non-basic compounds were eluted with MeOH. Basic compounds were eluted with NH_3 in MeOH (sat. soln.) and concentrated *in vacuo* to give the product. Resin was reconditioned by treatment with TfOH (1 M in MeOH, 20 mL) followed by washing with MeOH (10 mL).

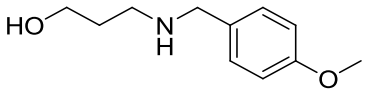
Synthesis of building blocks for the development of the synthetic approach

2-(4-Methoxybenzylamino)ethanol 6



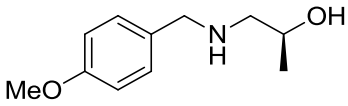
By general procedure **A**, 2-aminoethanol (4.10 g, 67.0 mmol) gave the *alcohol* **6** (10.0 g, 55.3 mmol, 82%) as a light brown oil which required no further purification; R_f 0.32 (50:8:1 CH_2Cl_2–EtOH–NH_4OH); ν_{max}/cm^{-1} (film) 3307, 2159, 2030, 1612, 1514, 1248; δ_H (500 MHz; $CDCl_3$) 7.25 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.88 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 3.8 (3H, s, OMe), 3.75 (2H, s, CH_2Ar), 3.65 (2H, t, *J* 5.2, 1-H), 2.79 (2H, t, *J* 5.1, 2-H), 2.24 (2H, s (broad), NH and OH); δ_C (75 MHz; $CDCl_3$) 159.1 (Ar 4-C), 132.6 (Ar 1-C), 129.7 (Ar 2-C and Ar 6-C), 114.2 (Ar 3-C and Ar 5-C), 61.3 (1-C), 55.7 (OMe), 53.3 (CH_2Ar), 50.8 (2-C); *m*/*z* (*ESI*) 182.1 (100%, MH^+); HRMS found MH^+, 182.1176. $C_{10}H_{15}NO_2$ requires *MH*, 182.1176.

3-(4-Methoxybenzylamino)propan-1-ol S1[5]



$Na(CN)BH_3$ (420 mg, 6.7 mmol) was added to a stirred solution of 3-aminopropanol (1.01 mL, 13.0 mmol) and 4-methoxybenzaldehyde (0.81 mL, 6.7 mmol) in methanol (50 mL) and stirred at rt for 16 h. Reaction was quenched by addition of HCl (5 M, to pH<2), concentrated *in vacuo*, taken up in water (20 mL) basified with K_2CO_3 (sat. aq. soln., to pH>11), extracted with CH_2Cl_2 (3 × 25 mL), dried ($MgSO_4$) and concentrated to give a crude product. Purification by column chromatography, eluting with 50:8:1 CH_2Cl_2–EtOH–NH_4OH, gave the *amino alcohol* **S1** (1.04 g, 5.30 mmol, 80%) as a light brown oil; R_f 0.22 (50:8:1 CH_2Cl_2–EtOH–NH_4OH); ν_{max} /cm^{-1} (film) 3295, 2526, 1613, 1514, 1248; δ_H (500 MHz; $CDCl_3$) 7.21 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.86 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 3.80 (5H, m, CH_2OH and OMe), 3.72 (2H, s, CH_2Ar), 3.05 (2H, s (broad), NH and OH), 2.88 (2H, t, *J* 5.7, CH_2NH), 1.71 (2H, pent, *J* 5.6, CH_2); δ_C (75 MHz; $CDCl_3$) 159.2 (Ar 4-C), 132.1 (Ar 1-C), 129.8 (Ar 2-C and Ar 6-C), 114.3 (Ar 3-C and Ar 5-C), 64.9 (CH_2OH), 55.7 (OMe), 53.8 (CH_2NH), 49.8 (CH_2Ar), 31.1 (CH_2); *m*/*z* (*ESI*) 196.1 (100%, MH^+); HRMS found MH^+, 196.1340. $C_{11}H_{17}NO_2$ requires *MH*, 196.1332.

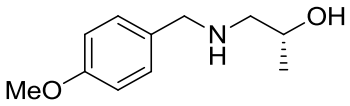
(*S*)-1-(4-Methoxybenzylamino)propan-2-ol S2[5]



By general procedure **A**, (*S*)-1-amino-2-propanol (1.00 g, 13.3 mmol) gave the *amino alcohol* **S2** (2.42 g, 12.4 mmol, 93%) as a light brown oil which required no further purification; R_f 0.34 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{26}$: 11.6 (c. 1.3, MeOH); ν_{max}/cm^{-1} (film) 3308, 2966, 1612, 1513; δ_H (500 MHz; $CDCl_3$) 7.24 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.87 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 3.75 (5H, m, OMe, 2-H and benzyl CH_a), 3.72 (1H, d, *J* 12.8, benzyl CH_b), 2.73 (1H, dd, *J* 12.0, 3.0, 1-H_a), 2.43 (1H, dd, *J* 12.0, 9.5, 1-H_b), 2.28 (2H, s (broad), NH and OH), 1.15 (3H, d, *J* 6.2, 3-H); δ_C (75 MHz; $CDCl_3$) 129.3 (Ar 2-C and Ar 6-C), 113.9 (Ar 3-

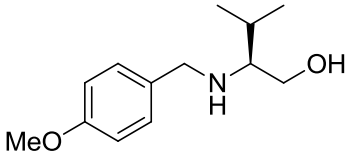
C and Ar 5-C), 65.6 (2-C), 56.1 (1-C), 55.3 (OMe), 53.0 (CH_2 benzyl), 20.4 (3-C); *m*/*z* (*ESI*) 196.1 (100%, MH^+); HRMS found MH^+, 196.1329. $C_{11}H_{17}NO_2$ requires *MH*, 196.1332.

(*R*)-1-(4-Methoxybenzylamino)propan-2-ol S3



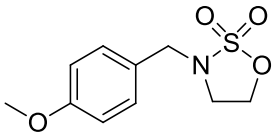
By general procedure **A**, (*R*)-1-amino-2-propanol (1.00 g, 13.3 mmol) gave the *amino alcohol* **S3** (2.57 g, 13.2 mmol, 98%) as a light brown oil which required no further purification, $[\alpha]_D^{26}$: −18.6 (c. 1.4, MeOH), spectroscopically identical to the enantiomer prepared previously.

(*S*)-2-(4-Methoxybenzylamino)-3-methylbutan-1-ol S4



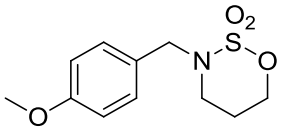
By general procedure **A**, (2*S*)-2-amino-3-methyl butanol (1.00 g, 6.1 mmol) gave the *amino alcohol* **S4** (1.78 g, 8.00 mmol, 80%) as a light brown oil which required no further purification; R_f 0.39 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{26}$: 0.5 (c. 1.1, MeOH); ν_{max}/cm^{-1} (film) 3367, 2957, 1612, 1513, 1248; δ_H (500 MHz; $CDCl_3$) 7.25 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.87 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 3.80 (3H, s, OMe), 3.77 (1H, d, *J* 12.7, benzyl CH_a), 2.70 (1H, d, *J* 12.7, benzyl CH_b), 3.63 (1H, dd, *J* 10.5, 4.2, 1-H_a), 3.35 (1H, dd, *J* 15.6, 7.0, 1-H_b), 2.47 (1H, m, 2-H), 1.86 (1H, app. sextet, *J* 6.7, 3-H), 0.97 (3H, d, *J* 6.9, 4-H), 0.91 (3H, d, *J* 6.9, methyl); δ_C (75 MHz; $CDCl_3$) 129.9 (Ar 2-C and Ar 6-C), 114.0 (Ar 3-C and Ar 5-C), 63.8 (1-C), 60.1 (2-C), 55.3 (OMe), 50.6 (CH_2 benzyl), 28.6 (3-C), 19.6 (4-C), 18.4 (methyl); *m*/*z* (*ESI*) 224.1 (100%, MH^+); HRMS found MH^+, 224.1645. $C_{13}H_{21}NO_2$ requires *MH*, 224.1645.

3-[(4-Methoxyphenyl)methyl]-1,2,3- oxathiazolidine-2,2-dione 7a[6]



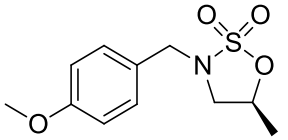
By general procedure **B1**, the amino alcohol **6** (5.93 g, 33.0 mmol) gave the *cyclic sulfamidate* **7a** (7.09 g, 29.2 mmol, 89%) as a light brown oil which solidified upon standing; R_f 0.56 (1:1, petrol–EtOAc); ν_{max}/cm^{-1} (film) 2962, 1612, 1584, 1455, 1301; δ_H (500 MHz; $CDCl_3$) 7.30 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.90 (2H, d, *J* 8.6, Ar 3-H and Ar 4-H), 4.50 (2H, t, *J* 6.5, 5-H), 4.18 (2H, s, CH_2 benzyl), 3.81 (3H, s, OMe), 3.39 (2H, t, *J* 6.5, 4-H); δ_C (75 MHz; $CDCl_3$) 160.2 (Ar4-C), 130.6 (Ar 2-C and Ar 6-C), 126.6 (Ar6-C), 114.7 (Ar 3-C and Ar 5-C), 67.2 (5-C), 55.8 (OMe), 51.4 (CH_2 benzyl), 47.4 (4-C); *m*/*z* (*ESI*) 266.0 (100%, MNa^+); HRMS found MNa^+, 266.0465. $C_{10}H_{13}NO_4S$ requires *MNa*, 266.0457.

3-[(4-Methoxyphenyl)methyl]-1,2,3- oxathiazinane-2,2-dione 7b



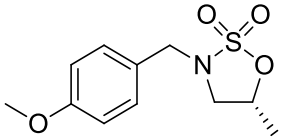
By general procedure **B1**, the amino alcohol **S1** (1.00 g, 5.1 mmol) gave the *cyclic sulfamidate* **7b** (1.08 g, 4.20 mmol, 83%) as a light brown oil which solidified upon standing; R_f 0.67 (1:1, petrol–EtOAc); ν_{max}/cm^{-1} (film) 2963, 1614, 1514, 1300, 1243; δ_H (500 MHz; $CDCl_3$) 7.26 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.89 (2H, d, *J* 8.6, Ar3-H and Ar 5-H), 4.65 (2H, t, *J* 5.6, 6-H), 4.28 (2H, s, CH_2 benzyl), 3.81 (3H, s, OMe), 3.39 (2H, t, *J* 5.7, 4-H), 1.81 (2H, app. pent, *J* 5.7, 5-H); δ_C (75 MHz; $CDCl_3$) 159.6 (Ar 4-C), 130.1 (Ar 3-C and Ar 5-C), 126.8 (Ar 1-C), 114.2 (Ar 2-C and Ar 6-C), 73.2 (6-C), 55.3 (OMe), 51.8 (CH_2 benzyl), 46.7 (4-C), 20.2 (5-C); *m*/*z* (*ESI*) 280.1 (100%, MNa^+); HRMS found MNa^+, 280.0630. $C_{11}H_{15}NO_4S$ requires *MNa*, 280.0614.

(5*S*)-3-[(4-Methoxyphenyl)methyl]-5-methyl- 1,2,3-oxathiazolidine-2,2-dione 7c



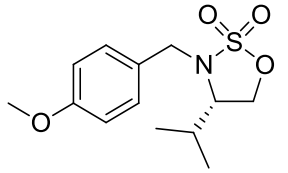
By general procedure **B1**, the alcohol **S2** (1.00 g, 5.1 mmol) gave the *cyclic sulfamidate* **7c** (1.25 g, 4.80 mmol, 95%) as a light brown oil which solidified upon standing; R_f 0.69 (1:1, petrol–EtOAc); $[\alpha]_D^{26}$: –21.8 (c. 1.0, MeOH); ν_{max}/cm^{-1} (film) 2986, 1611, 1515, 1333, 1253; δ_H (500 MHz; $CDCl_3$) 7.29 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.90 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.87 (1H, m, 5-H), 4.27 (1H, d, *J* 13.4, benzyl CH_a), 4.05 (1H, d, *J* 13.4, benzyl CH_b), 3.81 (3H, s, OMe), 3.40 (1H, dd, *J* 9.4, 6.1, 4-H_a), 3.03 (1H, dd, *J* 9.5, 8.0, 4-H_b), 1.49 (3H, d, *J* 6.3, CH_3); δ_C (75 MHz; $CDCl_3$) 159.7 (Ar 4-C), 130.1 (Ar 2-C and Ar 6-C), 126.3 (Ar 1-C), 114.2 (Ar 3-C and Ar 5-C), 76.6 (5-C), 55.3 (OMe), 53.6, 50.7, 19.4 (CH_3); *m*/*z* (*ESI*) 280.1 (100%, MNa^+); HRMS found MNa^+, 280.0621. $C_{11}H_{15}NO_4S$ requires *MNa*, 280.0614.

(5*R*)-3-[(4-Methoxyphenyl)methyl]-5-methyl- 1,2,3-oxathiazolidine-2,2-dione 7d



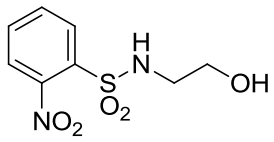
By general procedure **B1**, the amino alcohol **S3** (1.00 g, 5.1 mmol) gave the *cyclic sulfamidate* **7d** (1.15 g, 4.50 mmol, 88%) as a light brow oil which solidified upon standing, $[\alpha]_D^{26}$: 16.4 (c. 1.5, MeOH), spectroscopically identical to the enantiomer obtained previously.

(4*S*)-3-[(4-Methoxyphenyl)methyl]-4-(propan-2-yl)-1,2,3-oxathiazolidine-2,2-dione 7e



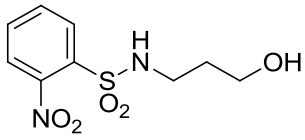
By general procedure **B1**, the amino alcohol **S4** (1.60 g, 7.20 mmol) gave the *cyclic sulfamidate* **7e** (1.81 g, 6.30 mmol, 89%) as a light brown oil which solidified upon standing; R_f 0.85 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{26}$: –7.6 (c. 2.2, MeOH); ν_{max}/cm^{-1} (film) 2965, 1613, 1515, 1346, 1185; δ_H (500 MHz; $CDCl_3$) 7.33 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.89 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.38 (1H, dd, *J* 8.9, 7.4, 5-H_a), 4.33 (1H, d, *J* 14.6, benzyl CH_a), 4.25 (1H, dd, *J* 8.9, 5.7, 5-H_b), 4.23 (1H, dd, *J* 14.6, benzyl CH_b), 3.81 (3H, s, OMe), 3.41 (1H, m, 4-H), 1.90 (1H, d sept., *J* 5.6, 1.2, propyl 2-H), 0.91 (3H, d, *J* 6.8, propyl 1-H), 0.87 (3H, d, *J* 7, propyl 3-H); δ_C (75 MHz; $CDCl_3$) 159.6 (Ar 4-C), 130.4 (Ar 2-C and Ar 6-C), 126.6 (Ar 1-C), 114.1 (Ar 3-C and Ar 5-C), 67.0 (5-C), 64.0 (4-C), 55.3 (OMe), 51.4 (CH_2 benzyl), 29.6 (2-C propyl), 18.2 (1-C propyl), 15.9 (3-C propyl); *m*/*z* (*ESI*) 308.1 (100%, MNa^+); HRMS found MNa^+, 308.0932. $C_{13}H_{19}NO_4S$ requires *MNa*, 308.0927.

_N_-(2-Hydroxyethyl)-2-nitrobenzenesulfonamide 8a[7]



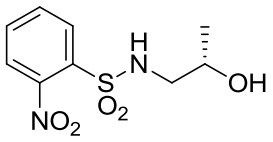
By general procedure **C**, 2-aminoethanol (1.22 g, 20.0 mmol) gave the *hydroxy sulfonamide* **8a** (3.99 g, 16.2 mmol, 81%) as a light yellow oil which solidified upon standing; R_f 0.57 (50:5:1 CH_2Cl_2–EtOH–NH_4OH); ν_{max}/cm^{-1} (film) 3257, 1540, 1439, 1360; δ_H (500 MHz; $CDCl_3$) 8.20 (1H, m, Ar 3-H), 7.93 (1H, m, Ar 6-H), 7.80 (2H, m, Ar 5-H and Ar 5-H), 5.81 (1H, t (broad), *J* 4.7, NH), 3.81 (2H, app. q, *J* 5, 2-H), 3.32 (2H, app. q, *J* 4.8, 1-H), 1.92 (1H, t, *J* 5.1, OH); δ_C (75 MHz; $CDCl_3$) 133.7 (Ar 3-C), 132.8 (Ar 6-C), 131.1 (Ar 4-C), 125.5 (Ar 5-C), 61.3 (2-C), 45.7 (1-C); *m*/*z* (*ESI*) 269.0 (100%, MNa^+); HRMS found MNa^+, 269.0211. $C_8H_{10}N_2O_5S$ requires *MNa*, 269.0203.

_N_-(3-Hydroxypropyl)-2-nitrobenzenesulfonamide, 8b[8]



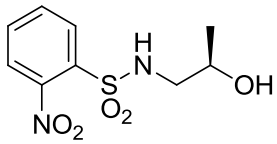
By general procedure **C**, 3-aminopropanol (1.58 g, 21.0 mmol) gave the *hydroxy sulfonamide* **8b** (5.38 g, 20.7 mmol, 98%) as a light yellow semi solid which required no further purification, R_f 0.14 (1:1 petrol–EtOAc); ν_{max} /cm^{-1} (film) 3328, 2965, 1537, 1414, 1362; δ_H (300 MHz, $CDCl_3$) 8.14 (1H, m, Ar 3-H), 7.56 (1H, m, Ar 6-H), 7.75 (2H, m, Ar 4-H and Ar 5-H), 5.87 (1H, s (broad), NH) 3.76 (2H, t, *J* 5.7, 3-H), 3.26 (2H, t, *J* 6.3, 1-H), 2.09 (1H, s (broad), OH), 1.78 (2H, app. pent., *J* 5.8, 2-H); δ_C (75 MHz; $CDCl_3$) 148.1 (Ar 2-C), 133.6 (Ar 5-C), 133.5 (Ar 1-C), 132.8 (Ar 4-C), 131.1 (Ar 6-C), 125.4 (Ar 3-C), 60.4 (3-C), 41.5 (1-C), 31.6 (2-C); *m*/*z* (*ESI*) 283.0 (100%, MNa^+); HRMS found MNa^+, 283.0360. $C_9H_{12}N_2O_5S$ requires *MNa*, 283.0359.

(*S*)-*N*-(2-Hydroxypropyl)-2-nitrobenzenesulfonamide 8c



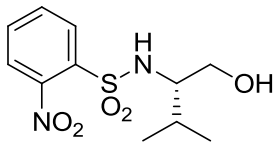
By general procedure **C**, (*S*)-1-amino-2-propanol (1.00 g, 13.3 mmol) gave the *hydroxy sulfonamide* **8c** (3.29 g, 12.5 mmol, 94%) as a light yellow amorphous solid which required no further purification, R_f 0.73 (50:8:1 CH_2Cl_2–EtOH–NH_4OH); $[\alpha]_D^{26}$: -20.5 (c. 1.3, MeOH); ν_{max}/cm^{-1} (film) 3340, 1538, 1361; δ_H (300 MHz; $CDCl_3$) 8.14 (1H, m, Ar 3-H), 7.88 (1H, m, Ar 6-H), 7.76 (2H, m, Ar 4-H and Ar 5-H), 5.78 (1H, t (broad), *J* 5.7, NH), 3.97 (1H, m, 2-H), 3.23 (1H, ddd, *J* 12.9, 7.1, 3.3, 1-H_a), 2.94 (1H, ddd, *J* 13.1, 8.0, 5.3, 1-H_b), 1.98 (1H, s (broad), OH), 1.20 (3H, d, *J* 6.3, 3-H); δ_C (75 MHz; $CDCl_3$) 134.1 (Ar 5-C), 133.3 (Ar 4-C), 131.5 (Ar 6-C), 125.9 (Ar 3-C), 66.94 (2-C), 50.9 (1-C), 21.1 (3-C); *m*/*z* (*ESI*) 283.0 (100%, MNa^+); HRMS found MNa^+, 283.0346. $C_9H_{12}N_2O_5S$ requires *MNa*, 283.0359.

(*R*)-*N*-(2-Hydroxypropyl)-2-nitrobenzenesulfonamide 8d



By general procedure **E**, (*R*)-1-amino-2-propanol (1.00 g, 13.3 mmol) gave the *hydroxy sulfonamide* **8d** (3.30 g, 12.7 mmol, 95%) as a light yellow amorphous solid which required no further purification, $[\alpha]_D^{26}$: 16.6 (c. 0.9, MeOH), spectroscopically identical to the enantiomer prepared previously.

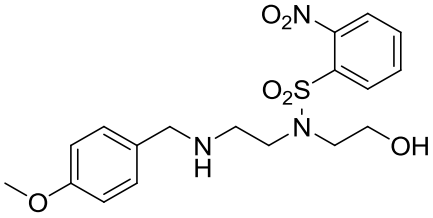
(*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-2-nitrobenzenesulfonamide, 8e



By general procedure **E**, (2*S*)-2-amino-3-methyl butanol (1.00 g, 9.7 mmol) gave the *hydroxy sulfonamide* **8e** (2.47 g, 12.7 mmol, 88%) as a light yellow amorphous solid which required no further purification; R_f 0.39 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{26}$: -29.6 (c. 1.1, MeOH); ν_{max}/cm^{-1} (film) 3327, 2963, 1538, 1360; δ_H (300 MHz; $CDCl_3$) 8.14 (1H, m, Ar 3-H), 7.87 (1H, m, Ar 6-H), 7.72 (2H, m, Ar 4-H and Ar 5-H), 5.52 (1H, d (broad), *J* 8.24, NH), 3.62 (2H, m, 1-H), 3.30 (1H, m, 2-H), 1.89 (1H, app. oct, *J* 6.7, 3-H), 1.76 (1H, t, *J* 5.7, OH), 0.88 (6H, t, *J* 6.8, 4-H and Me); δ_C (75 MHz; $CDCl_3$) 133.4 (Ar 5-C), 132.9 (Ar 4-C), 130.6 (Ar 6-C), 125.3 (Ar 3-C), 63.3 (1-C), 62.3 (2-C), 29.5 (3-C), 19.3 (4-C), 18.3 (Me); *m*/*z* (*ESI*) 311.1 (100%, MNa^+); HRMS found MNa^+, 311.0677. $C_{11}H_{16}N_2O_5S$ requires *MNa*, 311.0672.

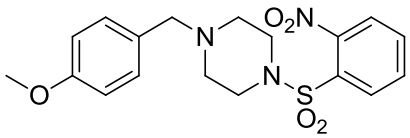
Development of the synthetic approach

***N*-(2'-Hydroxyethyl)-*N*-(2-(4-methoxybenzylamino)ethyl)-2'-nitrobenzenesulfonamide 9**



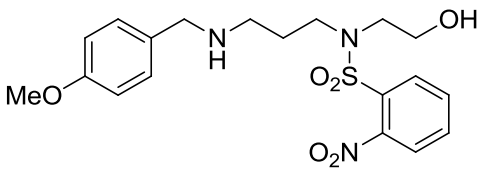
By general procedure **D**, the cyclic sulfamidate **7a** (1.00 g, 4.1 mmol) and sulfonamide **8a** gave the *amino alcohol* **9** (1.25 g, 3.00 mmol, 74%) as a colourless oil; R_f 0.58 (1:1, petrol–EtOAc); ν_{max}/cm^{-1} (film) 3320, 1611, 1543, 1345, 1249; δ_H (500 MHz; $CDCl_3$) 8.00 (1H, m, Ar 3'-H), 7.74 (2H, m, Ar 5'-H and Ar H-'6), 7.59 (1H, m, Ar 4'-H), 7.23 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.88 (2H, d, *J* 8.7, Ar 3-H and Ar 4-H), 3.87-3.85 (5H, m, OMe and 2-H), 3.80 (2H, s, CH_2 benzyl), 3.50 (2H, t, *J* 5.5, H1'), 3.47 (2H, t, *J* 4.7, 1-H), 2.95 (2H, t, *J* 6.5, 2'-H); δ_C (75 MHz; $CDCl_3$) 155.7 (Ar 4-C), 133.8 (Ar 4'-), 131.7 (Ar 5'-C), 130.8 (Ar 6'-C), 129.9 (Ar 2-C and Ar 6-C), 124.2 (Ar 3'-C), 114.1 (Ar 3-C and Ar 5-C), 62.4 (2-C), 55.3 (1'-C), 54.0 (OMe), 52.7 (CH_2 benzyl), 49.7 (1-C), 47.5 (2'-C); *m*/*z* (*ESI*) 410.1 (100%, MH^+).

1-(4-Methoxybenzyl)-4-(2'-nitrophenylsulfonyl)piperazine 10a[9]



By general procedure **E**, the amino alcohol **9** (0.40 g, 1.0 mmol), gave the *piperazine* **10a** (0.36 g, 0.90 mmol, 94%) as a light yellow oil; R_f 0.80 (9:1 CH_2Cl_2–MeOH); ν_{max}/cm^{-1} (film) 2937, 1612, 1546, 1513, 1373, 1249, 1174; δ_H (500 MHz; $CDCl_3$) 7.94 (1H, dd, *J* 7.5, 1.6, Ar 3'-H), 7.68 (2H, m, Ar 5'-H and Ar 6'-H), 7.60 (1H, dd, *J* 7.5, 1.7, Ar 4'-H), 7.18 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.84 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 3.79 (3H, s, OMe), 3.45 (2H, s, CH_2 benzyl), 3.30 (4H, t (broad), *J* 4.6, 3-H and 5-H), 2.50 (4H, t (broad), *J* 4.8, 2-H and 6-H); δ_C (75 MHz; $CDCl_3$) 133.7 (Ar 5'-C), 131.4 (Ar 4'-C), 130.9 (Ar 6'-C), 130.3 (Ar 2-C and Ar 6-C), 124.0 (Ar 4'-C), 113.7 (Ar 3-C and Ar 5-C), 62.0 (3-C and 5-C), 55.3 (OMe), 52.19 (CH_2 benzyl), 46.0 (2-C and 6-C); *m*/*z* (*ESI*) 392.1 (100%, MH^+); HRMS found MH^+, 392.1285. $C_{18}N_{21}N_3O_5S$ requires *MH*, 392.1275.

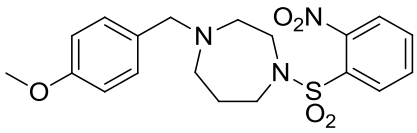
2-Hydroxy-*N*-(3'-{[(4-methoxyphenyl)methyl]amino}propyl)-*N*-(2'-nitrophenyl)ethane-1-sulfonamide S5



By general procedure **D** (heating at 80 °C), the cyclic sulfamidate **7b** (206 mg, 0.8 mmol) and the hydroxy sulfonamide **10a** gave the *amino alcohol* **S5** (165 mg, 0.4 mmol, 49%) as a light yellow oil; R_f 0.19 (9:1 CH_2Cl_2–MeOH); ν_{max}/cm^{-1} (film) 2963, 1612, 1544, 1515, 1341, 1249; δ_H (500 MHz; $CDCl_3$) 7.96 (1H, dd, *J*

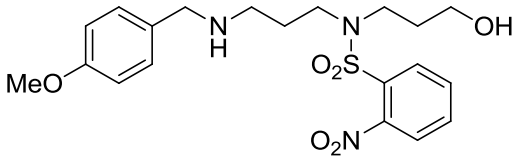
7.4, 1.4, Ar 3'-H), 7.68 (2H, app. d pent, *J* 7.3, 1.7, Ar 5'-H and Ar 6'-H), 7.60 (1H, dd, *J* 7.0, 1.8, Ar 4'-H), 7.22 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.86 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 3.79 (3H, s, OMe), 3.76 (2H, t, *J* 4.8, 2-H), 3.70 (2H, s, CH_2 benzyl), 3.43 (2H, t, *J* 6.6, 1'-H), 3.40 (2H, t, *J* 5, 1-H), 2.76 (2H, t, *J* 6.1, 3'-H), 1.88 (2H, pent, *J* 6.2, 2'-H); δ_C (75 MHz; $CDCl_3$) 158.8 (Ar 4-C), 148.4 (Ar 2'-C), 133.7 (Ar 1'-C), 132.0 (Ar 1-C), 131.6 (Ar 5'-C), 131.1 (Ar 4'-C), 130.8 (Ar 6'-C), 129.6 (Ar 2-C and Ar 6-C), 124.1 (Ar 3'-C), 113.9 (Ar 3-C and Ar 5-C), 61.5 (2-C), 55.3 (OMe), 53.4 (1-C), 52.6 (1'-C), 48.4 (CH_2 benzyl), 46.2 (3'-C), 28.5 (2'-C); *m*/*z* (*ESI*) 424.1 (100%, MH^+).

1-(4-Methoxybenzyl)-4-(2'-nitrophenylsulfonyl)-1,4-diazepane 10b[9]



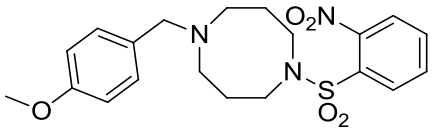
By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S5** (120 mg, 0.3 mmol) gave the *diazepane* **10b** (91 mg, 0.02 mmol, 80%) as a yellow oil; R_f 0.26 (1:1, petrol–EtOAc); ν_{max}/cm^{-1} (film); 3393, 1543, 1511, 1341, 1247, 1164; δ_H (500 MHz; $CDCl_3$) 7.99 (1H, m, Ar H-'3), 7.67 (2H, m, Ar 5'-H and Ar 6-H), 7.60 (1H, m, Ar 4'-H), 7.22 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.84 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 3.80 (3H, s, OMe), 3.58 (2H, s, CH_2 benzyl), 3.49 (4H, m, 3-H and 5-H), 2.71 (4H, m, 2-H and 7-H), 1.89 (2H, m, 6-H); δ_C (75 MHz; $CDCl_3$) 133.3, 131.5, 130.8, 129.9 (Ar 2-C and Ar 6-C), 124.0, 113.7 (Ar 3-C and Ar 5-C), 61.5, 55.9, 55.3, 54.4, 47.2; m/z (ES) 406.1 (MH^+); *m*/*z* (*ESI*) 406.1 (100%, MH^+); HRMS found MH^+, 406.1445. $C_{19}H_{23}N_3O_5S$ requires *MH,* 406.1431.

3-Hydroxy-*N*-(2'-{[(4-methoxyphenyl)methyl]amino}ethyl)-*N*-(2'-nitrophenyl)propane-1-sulfonamide S6



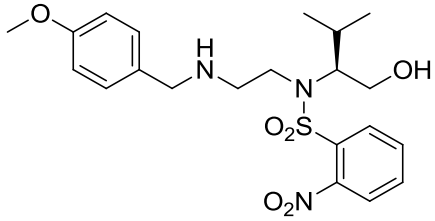
By general procedure **D** (heating at 80 °C), the cyclic sulfamidate **7b** (206 mg, 0.8 mmol) and the hydroxy sulfonamide **8b** gave the *amino alcohol* **S6** (209 mg, 0.5 mmol, 60%) as a light yellow oil; R_f 0.19 (9:1 CH_2Cl_2–MeOH); ν_{max}/cm^{-1} (film) 2963, 1612, 1544, 1515, 1341, 1249; δ_H (500 MHz; $CDCl_3$) 7.98 (1H, dd, *J* 7.4, 2.0, Ar 3'-H), 7.66 (2H, app. d pent, *J* 7.3, 1.7, Ar 5'-H and Ar H6'), 7.60 (1H, dd, *J* 7.7, 1.8, Ar 4'-H), 7.19 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.85 (2H, d, *J* 8.7, Ar 3-H and Ar 6-H), 3.79 (3H, s, OMe), 3.65 (2H, s, CH_2 benzyl), 3.64 (2H, t, *J* 5.9, 3-H), 3.43 (2H, t, *J* 6.9, 1'-H), 3.38 (2H, t, *J* 7.4, 1'-H), 2.60 (2H, t, *J* 6.8, 3'-H), 2.12 (2H, s (broad), NH and OH), 1.76 (4H, m, H2 and H2'); δ_C (75 MHz; $CDCl_3$) 158.7 (Ar 4-C), 148.1 (Ar 2'-C), 133.5 (Ar 5'-C), 133.2 (Ar 1'-C), 131.9 (Ar 1'-C), 131.7 (Ar 4'-C), 130.6 (Ar 6'-C), 129.4 (Ar 2-C and Ar 6-C), 124.2 (Ar 3'-C), 113.8 (Ar 3-C and Ar 5-C), 58.9 (3-C), 55.3 (OMe), 53.3 (1'-C), 46.0 (CH_2 benzyl), 44.7 (1'-C), 31.0 (3'-C), 28.5 (2-C); *m*/*z* (*ESI*) 438.2 (100%, MH^+).

1-(4-Methoxybenzyl)-5-(2'-nitrophenylsulfonyl)-1,5-diazocane 10c



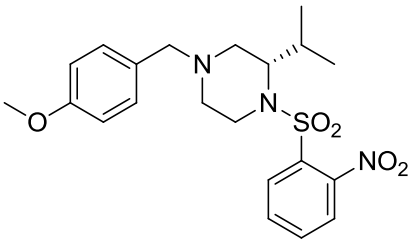
By general procedure **D**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S6** (282 mg, 0.6 mmol) gave the *diazocane* **10c** (256 mg, 0.6 mmol, 95%) as a yellow oil; R_f 0.21 (1:1, petrol–EtOAc); ν_{max}/cm^{-1} (film); 3399, 2933, 1611, 1543, 1371, 1246; δ_H (500 MHz; $CDCl_3$) 79.1 (1H, m, Ar 3'-H), 7.66 (2H, m, Ar 5'-H and Ar 6-H), 7.61 (1H, m, Ar 4'-H), 7.21 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.84 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 3.79 (3H, s, OMe), 3.60 (2H, s, CH_2 benzyl), 3.43 (4H, app. t, *J* 5.3), 2.66 (4H, t, *J* 6.3), 2.77 (4H, pent (broad), *J* 5.4); δ_C (75 MHz; $CDCl_3$) 158.6 (Ar 4-C), 113.1, 132.0, 131.4, 130.3, 130.1 (Ar 2-H and Ar 6-H), 124.1, 113.6 (Ar 3-H and Ar 5-H), 61.1 (OMe), 55.2 (CH_2 benzyl), 49.8, 49.5, 29.4; *m*/*z* (*ESI*) 420.2 (100%, MH^+); HRMS found MH^+, 420.1602. $C_{20}H_{25}N_3O_5S$ requires *MH,* 420.1588.

(2*S*)-1-Hydroxy-*N*-(2'-{[(4-methoxyphenyl)methyl]amino}ethyl)-3-methyl-*S*-(2'-nitrophenyl) butane-2-sulfonamide S7



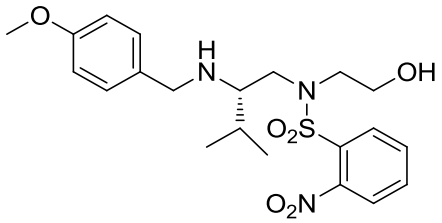
By general procedure **D**, the cyclic sulfamidate **7a** (219 mg, 0.9 mmol) and the hydroxy sulfonamide gave the *amino alcohol* **S7** (294 mg, 0.7 mmol, 72%) as a light yellow oil; R_f 0.50 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: 58.3 (c. 0.5, $CHCl_3$); ν_{max}/cm^{-1}; 2964, 1611, 1544, 1513, 1344, 1249; δ_H (500 MHz; $CDCl_3$) 7.95 (1H, dd, *J* 7.2, 2.0, Ar 3'-H), 7.69 (2H, app. d pentet, *J* 8.8, 2.2, Ar 5'-H and Ar 6'-H), 7.60 (1H, dd, *J* 7.2, 1.7, Ar 4'-H), 7.27 (2H, d, *J* 8.5, Ar 2-H and Ar 6-H), 6.88 (2H, d, *J* 8.4, Ar 3-H and Ar 5-H), 3.90 (1H, ddd, *J* 12.4, 8.2, 2.4, 1-H_a), 3.86 (1H, d, *J* 12.4, benzyl CH_a), 3.83-3.80 (4H, m, OMe and benzyl CH_b), 3.74 (1H0, ddd, *J* 12.6, 5.0, 2.4, 1-H_b), 3.67 (1H, ddd, *J* 14.4, 5.0, 2.4, 1'-H_a), 3.55 (1H, dd, *J* 14.1, 2.9, 1'-H_b), 3.16-3.10 (2H, m, 2-H), 3.07 (1H, app. dt, *J* 18.9, 3.1, 2'-H), 1.91 (1H, m, 3'-H), 1.60 (2H, s broad, NH and OH), 0.92 (3H, d, *J* 7.0, 4'-H), 0.89 (3H, d, *J* 6.9, methyl); *m*/*z* (*ESI*) 452.1 (100%, MH^+).

(*S*)-2-Isopropyl-4-(4-methoxybenzyl)-1-(2'-nitrophenylsulfonyl)piperazine 10d



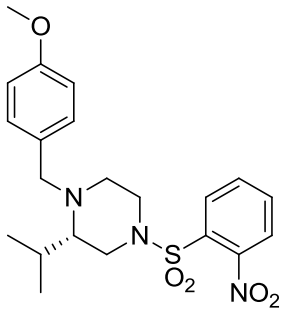
By general procedure **E**, the amino alcohol **S7** (282 mg, 0.6 mmol) gave the *piperazine* **10d** (256 mg, 0.6 mmol, 95%) as a yellow oil; R_f 0.70 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: 13.8 (c. 0.6, $CHCl_3$); ν_{max}/cm^{-1} (film) 2964, 1612, 1545, 1512, 1358, 1248; δ_H (500 MHz; $CDCl_3$) 8.03 (1H, m, Ar 3'-H), 7.66 (2H, m, Ar 5'-H and Ar 6'-H), 7.61 (1H, m, Ar 4'-H), 7.17 (2H, d, *J* 8.4, Ar 2-H and Ar 6-H), 6.83 (2H, d, *J* 8.5, Ar 3-H and Ar 5-H), 3.84 (1H, m, 2-H), 3.80 (3H, s, OMe), 3.44-3.40 (2H, m, benzyl CH_a and 6-H_a), 3.30 (1H, dt, *J* 15.5, 2.8, 6-H_b), 3.22 (1H, d, *J* 12.9, benzyl CH_b), 2.86 (1H, d, *J* 11.7, 3-H_a), 2.73 (1H, d, *J* 10.9, 5-H_a), 2.42 (1H, m, isopropyl CH), 2.00 (1H, dd, *J* 11.8, 3.4, 3-H_b), 1.95 (1H, dt, *J* 12.1, 3.3, 5-H_b), 0.76 (3H, d, *J* 6.5, methyl), 0.73 (3H, d, *J* 6.8, methyl); δ_C (75 MHz; $CDCl_3$) 158.8 (Ar 4-C), 147.6 (Ar 2-C′), 134.9 (Ar 1-C′), 133.2 9 (Ar 5-C′), 131.7 (Ar 6-C′), 130.0 (Ar 3-C and Ar 5-C), 124.1 (Ar 3-C′), 113.6 (Ar 2-C and Ar 6-C), 62.1, 61.4 (2-C), 55.3 (OMe), 53.2, 53.1, 42.1, 26.1 (isopropyl CH), 19.9 (Me), 19.5 (Me); *m*/*z* (*ESI*) 434.2 (100%, MH^+); HRMS found MH^+, 434.1765. $C_{21}H_{27}N_3O_5S$ requires *MH*, 434.1765.

2-Hydroxy-*N*-[(2'*S*)-2'-{[(4-methoxyphenyl)methyl]amino}-3-methylbutyl]-*S*-(2'-nitrophenyl) ethane-1-sulfonamide S8



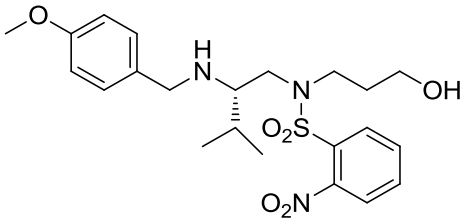
By general procedure **D**, the cyclic sulfamidate **7e** (257 mg, 0.9 mmol) and the hydroxy sulfonamide **8a** gave the *amino alcohol* **S8** (306 mg, 0.7 mmol, 75%) as a light yellow oil; R_f 0.50 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: 58.3 (c. 0.6, $CHCl_3$); ν_{max}/cm^{-1} (film) 2965, 1606, 1543, 1513, 1346, 1250; δ_H (500 MHz; $CDCl_3$) 7.95 (1H, dd, *J* 7.2, 2.0, Ar 3'-H), 7.69 (2H, app. d pentet, *J* 8.8, 2.2, Ar 5'-H and Ar 6'-H), 7.60 (1H, dd, *J* 7.2, 1.7, Ar 4'-H), 7.27 (2H, d, *J* 8.5, Ar 2-H and Ar 6-H), 6.88 (2H, d, *J* 8.4, Ar 3-H and Ar 5-H), 3.90 (1H, ddd, *J* 12.4, 8.2, 2.4, 1-H_a), 3.86 (1H, d, *J* 12.4, benzyl CH_a), 3.83-3.80 (4H, m, OMe and benzyl CH_b), 3.74 (1H, ddd, *J* 12.6, 5.0, 2.4, 1-H_b), 3.67 (1H, ddd, *J* 14.4, 5.0, 2.4, 1'-H_a), 3.55 (1H, dd, *J* 14.1, 2.9, 1'-H_b), 3.16-3.10 (2H, m, 2-H), 3.07 (1H, app. dt, *J* 18.9, 3.1, 2'-H), 1.91 (1H, m, 3'-H), 1.60 (2H, s broad, NH and OH), 0.92 (3H, d, *J* 7, 4'-H), 0.89 (3H, d, *J* 6.9, methyl); δ_C (75 MHz; $CDCl_3$) 133.7 (Ar 5'-C), 131.6 (Ar 6'-C), 130.7 (Ar 4'-C), 129.9 (Ar 2-C and Ar 6-C), 124.2 (Ar 2'-C), 114.1 (Ar 3-C and Ar 5-C), 62.4 (2-C), 61.7 (2'-C), 55.3 (1-C), 54.8 (OMe), 52.7 (CH_2 benzyl), 52.0 (1'-C), 29.1 (3'-C), 18.5 (4'-C), 17.8 (methyl); m/z (ES) 452.1 (MH^+).

(*S*)-2-Isopropyl-1-(4-methoxybenzyl)-4-(2'-nitrophenylsulfonyl)piperazine 10e



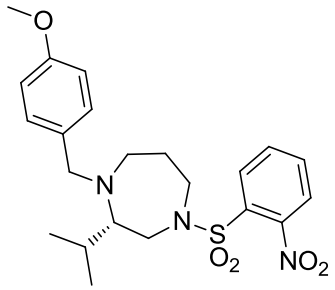
By general procedure **E**, the amino alcohol **S8** (289 mg, 1.0 mmol) gave the *piperazine* **10d** (260 mg, 0.6 mmol, 96%) as a yellow oil; R_f 0.63 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: 94.9 (c. 0.4, $CHCl_3$); ν_{max}/cm^{-1} (film) 2964, 1611, 1546, 1373, 1173; δ_H (500 MHz; $CDCl_3$) 7.93 (1H, m, Ar 3'-H), 7.69 (2H, m, Ar 5'-H and Ar 6'-H), 7.61 (1H, m, Ar 4-H), 7.18 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.83 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 4.03 (1H, d, *J* 13.0, benzyl CH_a), 3.79 (3H, s, OMe), 3.61 (1H, dt, *J* 12.2, 2.7, 5-H_a), 3.47 (1H, m, 3-H_a), 3.06 (1H, d, *J* 13.0, benzyl CH_b), 2.86-2.79 (3H, m, 5-H_b, 3-H_b and 2-H), 2.36 (1H, sept, *J* 5.4, isopropyl CH), 2.25-2.23 (1H, m, 6-H_a), 2.17 (1H, m, 6-H_b), 1.03 (3H, d, *J* 6.8, methyl), 0.95 (3H, d, *J* 6.8, methyl); δ_C (75 MHz, $CDCl_3$) 158.7 (Ar 4-C), 148.6, 133.7 (Ar 5-C′), 131.4 (Ar 3-C′), 130.9 (Ar 6-C′), 130.8, 130.5, 129.9 (Ar 3-C and Ar 5-C), 124.0 (Ar 3-C′), 113.7 (Ar 2-C and Ar 6-C), 64.3 (2-C), 55.4, 55.3 (OMe), 49.7, 44.7, 44.4, 26.5 (isopropyl CH), 19.7 (Me), 16.2 (Me); *m*/*z* (*ESI*) 434.2 (100%, MH^+); HRMS found MH^+, 434.1764. $C_{21}H_{27}N_3O_5S$ requires *MH*, 434.1744.

3-Hydroxy-*N*-[(2'*S*)-2'-{[(4-methoxyphenyl)methyl]amino}-3-methylbutyl]-*S*-(2'-nitrophenyl) propane-1-sulfonamide S9



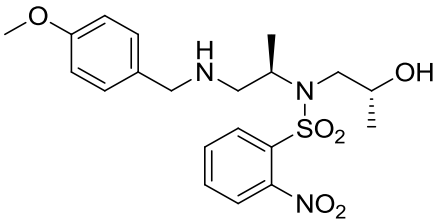
By general procedure **D**, the cyclic sulfamidate **7e** (228 mg, 0.8 mmol) and the hydroxy sulfonamide **8b** gave the *amino alcohol* **S9** (290 mg, 0.6 mmol, 78%) as a light yellow oil; R_f 10.4 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: 10.4 (c. 0.3, $CHCl_3$); ν_{max}/cm^{-1} (film) 3363, 2960, 1606, 1543, 1250; δ_H (500 MHz; $CDCl_3$) 8.02 (1H, m, Ar 3'-H), 7.62 (2H, m, Ar 5'-H and Ar 6'-H), 7.53 (1H, m, Ar 4'-H), 7.14 (2H, d, *J* 8.5, Ar 2-H and Ar 6-H), 6.82 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 3.80 (3H, s, OMe), 3.71 (1H, d, *J* 12.7, benzyl CH_a), 3.63 (2H, app. t, *J* 5.8, 3-H), 3.57 (1H, d, *J* 12.8, benzyl CH_b), 3.55 (1H, m, 1-H_a), 3.34-3.26 (3H, m, 1-H_b and 1'-H), 2.66 (1H, m, 2'-H), 1.97 (1H, m, 3'-H), 1.72 (4H, m broad, 2-H, NH and OH), 0.90 (3H, d, *J* 4.1, 4-H), 0.89 (3H, d, *J* 4.1, methyl); δ_C (75 MHz, $CDCl_3$) 131.6 (Ar 4'-C), 131.0 (Ar 5'-C), 129.7 (Ar 2-C and Ar 6-C), 124.2 (Ar 3'-C), 113.8 (Ar 3-C and Ar 5-C), 59.2 (3-C), 55.3 (OMe), 48.5 (1-C), 30.7 (C1'), 27.9, 18.3 (4'-C), 17.1 (methyl); *m*/*z* (*ESI*) 466.2 (100%, MH^+).

(*S*)-2-Isopropyl-1-(4-methoxybenzyl)-4-(2'-nitrophenylsulfonyl)-1,4-diazepane, 10f



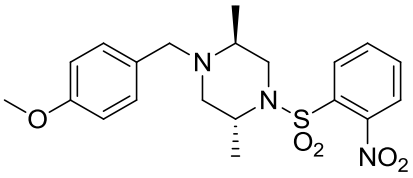
By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S9** (270 mg, 0.6 mmol) gave the *diazepane* **10f** (145 mg, 0.3 mmol, 56%) as a yellow oil; R_f 0.46 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: 15.4 (c. 1 $CHCl_3$); ν_{max}/cm^{-1} (film) 3374, 2960, 1711, 1544, 1511, 1373, 1249; δ_H (500 MHz; $CDCl_3$) 7.99 (1H, m, Ar 2'-H), 7.69 (2H, m, Ar 5'-H and Ar 6-H), 7.62 (1H, m, Ar 4'-H), 7.27 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.85 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 3.93 (1H, d, *J* 13.8, benzyl CH_a), 3.80 (3H, s, OMe), 3.78 (1H, d, *J* 14.1 benzyl CH_b), 3.66 (1H, dd, *J* 14.3, 4.9, 3-H_a), 3.56 (1H, m, 5-H_a), 30 (1H, dd, *J* 14.2, 10.4, 3-H_b), 3.23 (1H, m, 5-H_b), 2.93 (1H, ddd, *J* 15.3, 8.7, 3.3, 7-H_a), 2.78 (1H, ddd, *J* 15.7, 7.9, 3.4, 7-H_b), 2.70 (1H, m, H2), 1.92 (1H, m, 6-H_a), 1.76 (1H, sept, *J* 7.3, CH isopropyl), 1.65 (1H, m, 6-H_b), 1.02 (3H, d, *J* 6.7, methyl), 0.92 (3H, d, *J* 6.7, methyl); δ_C (75 MHz, $CDCl_3$) 158.5,133.3, 131.6, 130.6, 129.7 (Ar 2-C and Ar 6-C), 124.1, 113.5 (Ar 3-C and Ar 5-C), 68.13, 55.3, 53.9, 51.6, 49.4, 47.6, 31.0, 26.2 (CH isopropyl), 20.5 (Me), 19.8 (Me); *m*/*z* (*ESI*) 448.2 (100%, MH^+); HRMS found MH^+, 448.1912. $C_{22}H_{29}N_3O_5S$ requires *MH*, 448.1901.

(2*R*)-2-Hydroxy-*N*-[(2'*R*)-1'-{[(4-methoxyphenyl)methyl]amino}propan-2-yl]-*S*-(2'-nitrophenyl) propane-1-sulfonamide S10



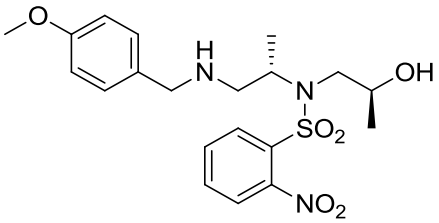
By general procedure **D**, the cyclic sulfamidate **7c** (206 mg, 0.8 mmol) and the hydroxy sulfonamide **8d** gave the *amino alcohol* **S10** (238 mg, 0.5 mmol, 68%) as a light yellow oil; R_f 0.45 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: -48.5 (c. 3.1 $CHCl_3$); R_f 0.45 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: -48.5 (c. 3.1 $CHCl_3$); ν_{max}/cm^{-1} (film); 3313, 2973, 1612, 1545, 1347, 1249; δ_H (500 MHz; $CDCl_3$) 8.02 (1H, m, Ar 3'-H), 7.65 (2H, m, Ar 5'-H and Ar 6'-H), 7.53 (1H, m, Ar 4'-H), 7.16 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.86 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.23 (1H, m, 2-H), 4.08 (1H, m, 2'-H), 3.80 (4H, m, OMe and 1-H_a), 3.75 (1H, d, *J* 13.0, benzyl CH_a), 3.57 (1H, d, *J* 13.0, benzyl CH_b), 3.55 (1H, dd, *J* 15.2, 1.7, 1-H_b), 2.76 (1H, dd, *J* 15.2, 9.9, 1'-H_a), 2.65 (2H, m, 1'-H_b and OH), 1.17 (3H, d, *J* 6.3, 3-H), 0.93 (3H, d, *J* 6.6, 3'-H); δ_C (75 MHz; $CDCl_3$) 158.9 (Ar 4-C), 133.7 (Ar 5'-C), 133.3 (Ar 2'-C), 131.6 (Ar 4'-C), 130.8 (Ar 6'-C), 130.5 (Ar 1'-C), 129.5 (Ar 2-C and Ar 6-C), 123.8 (Ar 3'-C), 114.0 (Ar 3-C and Ar 5-C), 66.9 (2-C), 55.3 (OMe), 52.8 (CH_2 benzyl), 52.0 (1-C), 51.7 (2-C), 51.3 (2'-C), 20.1 (3-C), 15.9 (3'-C); *m*/*z* (*ESI*) 438.1 (100%, MH^+).

(2*S*,5*R*)-1-(4-Methoxybenzyl)-2,5-dimethyl-4-(2'-nitrophenylsulfonyl)piperazine, *ent*-10h



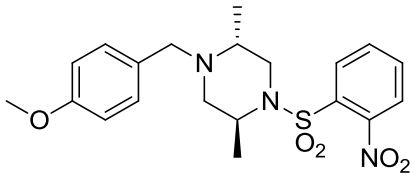
By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S10** (219 mg, 0.5 mmol) gave the *piperazine ent*-**10h** (100 mg, 0.2 mmol, 48%) as a yellow oil; R_f 0.70 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: -82.7 (c. 1.9, $CHCl_3$); ν_{max}/cm^{-1} (film) 3383, 2974, 1612, 1544, 1372, 1248; (500 MHz; $CDCl_3$) 8.03 (1H, m, Ar 3'-H), 7.69-7.62 (3H, m, Ar 4'-H, Ar 5'-H and Ar 6'-H), 7.23 (2H, d, *J* 8.4, Ar 2-H and Ar 6-H), 6.84 (2H, d, *J* 8.6, Ar 3-H and Ar 5-H), 4.05 (1H, s (broad), 5-H), 3.79 (3H, s, OMe), 3.60 (1H, d, *J* 13.1, 3-H_a), 3.52 (1H, d, *J* 13.3, benzyl CH_a), 3.43 (1H, d, *J* 13.2, benzyl CH_b), 3.37 (1H, d, *J* 13.4, 3-H_b), 2.96 (1H, s (broad), 2-H), 2.84 (1H, dd, *J* 11.8, 3.8, 6-H_a), 2.20 (1H, d, *J* 11.7, 6-H_b), 1.18 (3H, d, *J* 6.7, methyl 5-C), 0.91 (3H, d, *J* 6.4, methyl 2-C); δ_C (75 MHz; $CDCl_3$) 158.7 (Ar 4-C), 147.8 (Ar 2'-C), 134.2 (Ar 1'-C), 133.3 (Ar 5'-C), 132.0 (Ar 1-C), 131.6 (Ar 4'-C), 130.8 (Ar 6'-C), 129.6 (Ar 2-C and Ar 6-C), 124.2 (Ar 3'-C), 113.6 (Ar 3-C and Ar 4-C), 58.0 (3-C), 55.2 (5-C), 51.9 (OMe), 50.1 (6-C), 49.6 (CH_2 benzyl), 47.1 (C1), 15.9 (methyl), 7.5 (methyl); *m*/*z* (*ESI*) 420.2 (100%, MH^+); HRMS found MH^+, 420.1601. $C_{20}H_{25}N_3O_5S$ requires *MH*, 420.1588.

(2*S*)-2-Hydroxy-*N*-[(2'*S*)-1'-{[(4-methoxyphenyl)methyl]amino}propan-2-yl]-*S*-(2'-nitrophenyl) propane-1-sulfonamide S11



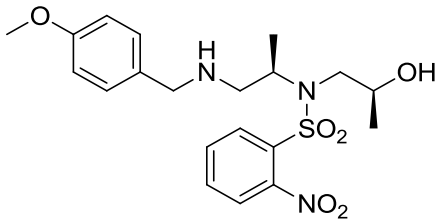
By general procedure **D**, the cyclic sulfamidate **7d** (206 mg, 0.8 mmol) and the hydroxy sulfonamide **8c** gave the *amino alcohol* **S11** (257 mg, 0.6 mmol, 74%) as a light yellow oil; R_f 0.63 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: 47.6 (c. 4.1 $CHCl_3$); ν_{max}/cm^{-1} (film) 2973, 1612, 1545, 1513, 1371, 1249; δ_H (500 MHz; $CDCl_3$) 8.01 (1H, m, Ar 3'-H), 7.64 (2H, m, Ar 5'-H and Ar 6'-H), 7.52 (1H, m, Ar 4'-H), 7.17 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.86 (2H, d, *J* 8.7, Ar 3-H and Ar 6-H), 4.23 (1H, m, 2-H), 4.09 (1H, m, 2'-H), 3.80 (4H, m (broad), OMe and 1-H_a), 3.74 (1H, d, *J* 13.0, benzyl CH_a), 3.58 (1H, d, *J* 13.0, benzyl CH_b), 3.55 (1H, dd, *J* 15.4, 1.7, 1-H_b), 2.76 (1H, dd, *J* 15.2, 9.9, H1'-H_a), 2.65 (1H, m, 1'-H_b), 1.17 (3H, d, *J* 6.3, 3-H), 0.92 (3H, d, *J* 6.6, 3'-H); δ_C (75 MHz; $CDCl_3$) 158.9 (Ar 1-C), 148.2 (Ar 2'-C), 133.7 (Ar 5'-C), 133.3 (Ar 1'-C), 131.6 (Ar 6'-C), 130.8 (Ar 4'-C), 130.6 (Ar 1-C), 129.6 (Ar 2-C and Ar 6-C), 123.9 (Ar 3'-C), 114.0 (Ar 3-C and Ar 5-C), 66.9 (2-C), 55.3 (OMe), 52.8 (2'-C), 52.1 (CH_2 benzyl), 51.6 (1-C), 51.3 (C1-1'), 20.0 (3'-C), 15.9 (3'-C); m/z (ES) 438.2 (MH^+).

(2*R*,5*S*)-1-(4-Methoxybenzyl)-2,5-dimethyl-4-(2'-nitrophenylsulfonyl)piperazine 10h



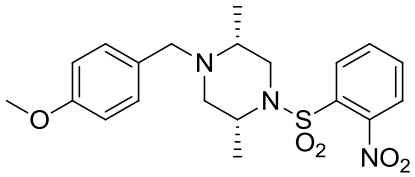
By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S11** (223 mg, 0.5 mmol) gave the *piperazine* **10h** (118 mg, 0.3 mmol, 55%) as a yellow oil, $[\alpha]_D^{24}$: 94.9 (c. 0.4, $CHCl_3$), spectroscopically identical to the enantiomer obtained previously.

(2*S*)-2-Hydroxy-*N*-[(2'*R*)-1'-{[(4-methoxyphenyl)methyl]amino}propan-2-yl]-*S*-(2'-nitrophenyl) propane-1-sulfonamide S12



By general procedure **D**, the cyclic sulfamidate **9c** (206 mg, 0.8 mmol) and the hydroxy sulfonamide **8c** gave the *amino alcohol* **S12** (247 mg, 0.6 mmol, 71%) as a light yellow oil; R_f 0.50 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: -11.5 (c. 3.2, $CHCl_3$); ν_{max}/cm^{-1} (film) 3316, 2935, 1611, 1544, 1249; δ_H (500 MHz; $CDCl_3$) 8.02 (1H, m, Ar 3'-H), 7.65 (2H, m, Ar 5'-H and Ar 6'-H), 7.56 (1H, m, Ar 3'-H), 7.20 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.85 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.17 (1H, m, 2-H), 3.90 (1H, m, 2'-H), 3.81-3.75 (4H, m (broad), OMe, benzyl CH_a), 3.70 (1H, d, *J* 13.0, benzyl CH_b), 3.44 (1H, dd, *J* 14.8, 10.3, 1-H_a), 3.25 (1H, dd, *J* 14.8, 3.0, 1-H_b), 2.76 (1H, app. t, *J* 12.2, 1'-H_a), 2.68 (1H, dd, *J* 12.3, 5.9, 1'-H_b), 1.18 (3H, d, *J* 6.2, 3-H), 1.05 (3H, d, *J* 6.8, 3'-H); δ_C (75 MHz; $CDCl_3$) 158.9 (Ar 4-C), 134.1 (Ar 2'-C), 133.4 (Ar 5'-C), 131.5 (Ar 4'-C), 140.0 (Ar 6'-C), 130.7 (Ar 1'-C), 130.0 (Ar 1'-C), 129.5 (Ar 2-C and Ar 6-C), 124.0 (Ar 3'-C), 113.9 (Ar 3-C and Ar 5-C), 65.7 (2-C), 55.3 (OMe), 54.0 (CH_2 benzyl), 53.5 (1-C), 53.3 (1'-C), 52.8 (2'-C), 20.4 (3-C), 15.9 (3'-C); *m*/*z* (*ESI*) 438.1 (100%, MH^+).

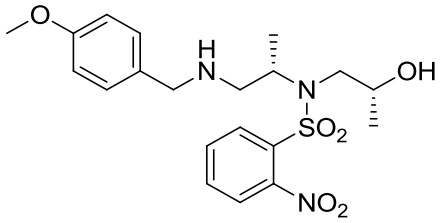
(2*R*,5*R*)-1-(4-Methoxybenzyl)-2,5-dimethyl-4-(2'-nitrophenylsulfonyl)piperazine *ent*-10i



By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S12** (208 mg, 0.5 mmol) gave the *piperazine ent*-**10i** (82 mg, 0.2 mmol, 41%) as a yellow oil; R_f 0.78 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: -65.3 (c. 0.4, $CHCl_3$); ν_{max}/cm^{-1} (film) 2937, 1611, 1544, 1512, 1373, 1249; δ_H (500 MHz; $CDCl_3$) 8.05 (1H, m, Ar 3'-H), 7.68-7.62 (3H, m, Ar 4'-H, Ar 5'-H and Ar 6'-H), 7.18 (2H, d, *J* 8.5, Ar 2-H and Ar 6-H), 6.83 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.06 (1H, d, *J* 13.3, benzyl CH_a), 3.99 (1H, s (broad), 5-H), 3.79 (3H, s, OMe), 3.50 (1H, dd, *J* 12.3, 3.5, 3-H_a), 3.05 (1H,

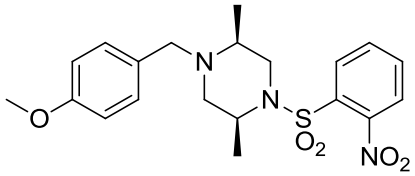
dd, *J* 13.3, 11.0, 3-H_b), 2.88 (1H, d, *J* 13.3, benzyl CH_b), 2.51 (1H, dd, *J* 11.7, 1.9, 6-H_a), 2.32 (1H, m, 2-H), 2.14 (1H, dd, *J* 11.6, 3.3, 6-H_b), 1.21 (3H, d, *J* 6.7, methyl), 1.16 (3H, d, *J* 6.1, methyl); δ_C (75 MHz; $CDCl_3$) 158.6 (Ar 4-C), 133.9 (Ar 2'-C), 133.3, , 131.7, 130.9, 130.8, 129.7 (Ar 2-C and Ar 6-C), 124.3, 113.7 (Ar 3-C and Ar 5-C), 56.4, 56.3, 56.2, 55.2, 50.2, 47.3, 17.5 (methyl), 15.8 (methyl); *m/z* (*ESI*) 420.2 (100%, MH^+); HRMS found MH^+, 420.1607. $C_{20}H_{25}N_3O_5S$ requires *MH*, 420.1593.

(2*R*)-2-Hydroxy-*N*-[(2'*S*)-1'-{[(4-methoxyphenyl)methyl]amino}propan-2-yl]-*S*-(2'-nitrophenyl) propane-1-sulfonamide S13



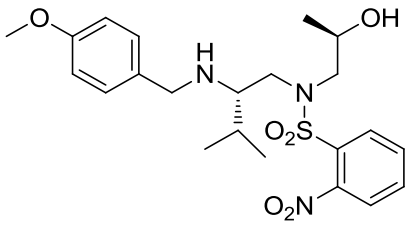
By general procedure **D**, the cyclic sulfamidate **7d** (206 mg, 0.8 mmol) and the hydroxy sulfonamide **8d** gave the *amino alcohol* **S13** (265 mg, 0.6 mmol, 76%) as a light yellow oil, $[\alpha]_D^{24}$: 16.3 (c. 4.1 $CHCl_3$), spectroscopically identical to the enantiomer obtained previously.

(2*S*,5*S*)-1-(4-Methoxybenzyl)-2,5-dimethyl-4-(2'-nitrophenylsulfonyl)piperazine 10i



By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S13** (240 mg, 0.6 mmol) gave the *piperazine* **10i** (112 mg, 0.3 mmol, 48%), $[\alpha]_D^{24}$: 84.8 (c. 0.3, $CHCl_3$), spectroscopically identical to the enantiomer obtained previously.

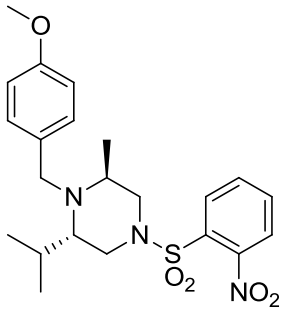
(2*R*)-2-Hydroxy-*N*-[(2'*S*)-2-{[(4-methoxyphenyl)methyl]amino}-3-methylbutyl]-*S*-(2'-nitrophenyl)propane-1-sulfonamide S14



By general procedure **D**, the cyclic sulfamidate **9e** (228 mg, 0.8 mmol) and the hydroxy sulfonamide **8d** gave the *amino alcohol* **S14** (323 mg, 0.7 mmol, 87%) as a light yellow oil; R_f 0.63 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: 32.9 (c. 6.8, $CHCl_3$); ν_{max}/cm^{-1} (film) 3385, 2965, 1611, 1546, 1373, 1249; δ_H (500 MHz; $CDCl_3$) 7.96 (1H, m, Ar 3'-H), 7.68 (2H, m, Ar 5'-H and Ar 6'-H), 7.56 (1H, m, Ar 4'-H), 7.25 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.86 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.04 (1H, m, 2-H), 3.79 (3H, s, OMe), 3.79 (1H, d, *J* 12.2, benzyl CH_a), 3.65 (1H, d, *J* 12.2, benzyl CH_b), 3.28-3.20 (3H, m, 1-H and 1'-H_a), 3.13 (1H, dd, *J* 14.3, 8.4, 1'-H_b),

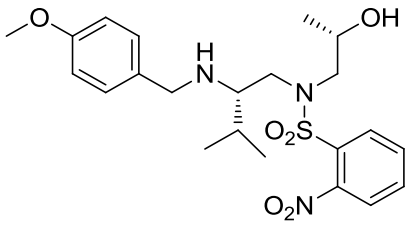
2.96 (1H, m, 2'-H), 2.04 (1H, m, H3'), 1.18 (3H, d, *J* 6.3, 3-H), 0.95 (3H, d, *J* 7, 4'-H), 0.90 (3H, d, *J* 6.9, methyl); δ_C (75 MHz, $CDCl_3$) 158.8 (Ar 4-C), 148.6 (Ar 2'-C), 133.7 (Ar 5'-C), 131.6 (Ar 1'-C), 131.5 (Ar 1'-C), 131.4 (Ar 6'-C), 130.8 (Ar 4'-C), 129.7 (Ar 2-C and Ar 6-C), 124.0 (Ar 3'-C), 114.0 (Ar 3-C and Ar 5-C), 63.3 (2-C), 59.7 (2'-C), 57.8 (CH_2 benzyl), 55.3 (OMe), 50.4 (1-C), 50.1 (1'-C), 28.4 (3'-C), 20.1 (3-C), 19.0 (4'-C), 16.9 (methyl); m/z (ES) 466.2 (MH^+).

(2*S*,6*S*)-2-*iso*Propyl-1-(4-methoxybenzyl)-6-methyl-4-(2'-nitrophenylsulfonyl)piperazine, 10j



By general procedure **E**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S14** (280 mg, 0.6 mmol) gave the *piperazine* **10j** (123 mg, 0.3 mmol, 46%) as a yellow oil; R_f 0.78 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: –251.3 (c. 0.5, $CHCl_3$); ν_{max}/cm^{-1} (film) 2966, 1611, 1546, 1511, 1373, 1248; δ_H (500 MHZ; $CDCl_3$) 7.93 (1H, m, Ar 3'-H), 7.70 (2H, m, Ar 5'-H and Ar 6'-H), 7.60 (1H, m, Ar 4'-H), 7.20 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.83 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 3.78 (3H, s, OMe), 3.67 (1H, d, *J* 13.6, benzyl CH_a), 3.53 (1H, d, *J* 13.6, benzyl CH_b), 3.44 (1H, dd, *J* 12.1, 3.0, 3-H_a), 3.14-3.05 (3H, m, 3-H_b and 5-H), 3.00 (1H, dd, *J* 12.0, 7.1, 2-H), 2.54 (1H, dt, *J* 7.2, 3.1, 6-H), 2.14 (1H, sept, *J* 7.1, isopropyl CH), 1.07 (3H, d, *J* 6.6, Methyl), 0.95 (3H, d, *J* 6.8, Methyl), 0.87 (3H, d, *J* 6.7, Methyl); δ_C (75 MHz, $CDCl_3$) 158.6 (Ar 4-C), 133.5, 131.4, 130.9, 129.4 (Ar 2-C and Ar 6-C), 124.0, 113.7 (Ar 3-C and Ar 5-C), 58.9, 55.3, 49.1, 48.3, 47.7, 42.3, 26.3, 19.8, 18.0, 13.2; *m*/*z* (*ESI*) 448.1 (100%, MH^+); HRMS found MH^+, 448.1922. $C_{22}H_{29}N_3O_5S$ requires *MH*, 448.1901.

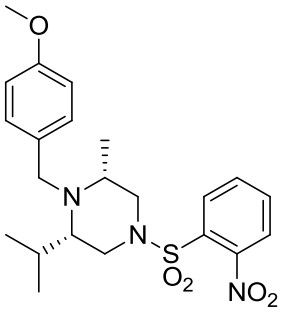
(2*S*)-2-Hydroxy-*N*-[(2'*S*)-2'-{[(4-methoxyphenyl)methyl]amino}-3-methylbutyl]-*S*-(2'-nitrophenyl)propane-1-sulfonamide S15



By general procedure **D**, the cyclic sulfamidate **7e** (228 mg, 0.8 mmol) and the hydroxy sulfonamide **8c** gave the *amino alcohol* **S15** (319 mg, 0.7 mmol, 86%) as a light yellow oil R_f 0.65 (9:1 CH_2Cl_2–MeOH); $[\alpha]_D^{24}$: 27.2 (c. 5.2, $CHCl_3$); ν_{max}/cm^{-1} (film) 3096, 2964, 1611, 1546, 1373, 1249; δ_H (500 MHz; $CDCl_3$) 7.96 (1H, m, Ar 3'-H), 7.68 (2H, m, Ar 5'-H and Ar 6'-H), 7.56 (1H, m, Ar 4'-H), 7.25 (2H, d, *J* 8.7, Ar 2-H and Ar 6-H), 6.86 (2H, d, *J* 8.7, Ar 3-H and Ar 5-H), 4.04 (1H, m, 2-H), 3.79 (3H, s, OMe), 3.79 (1H, d, *J* 12.2, benzyl CH_a), 3.65 (1H, d, *J* 12.2, benzyl CH_b), 3.28-3.20 (3H, m, 1-H and 1'-H_a), 3.13 (1H, dd, *J* 14.3, 8.4,

1'-H_b), 2.96 (1H, m, 2'-H), 2.04 (1H, m, 3'-H), 1.18 (3H, d, *J* 6.3, 3-H), 0.95 (3H, d, *J* 7, 4'-H), 0.90 (3H, d, *J* 6.9, methyl); δ_C (75 MHz, $CDCl_3$) 158.8 (Ar 4-C), 148.6 (Ar 2'-C), 133.7 (Ar 5'-C), 131.6 (Ar 1'-C), 131.5 (Ar 1'-C), 131.4 (Ar 6'-C), 130.8 (Ar 4'-C), 129.7 (Ar 2-C and Ar 6-C), 124.0 (Ar 3'-C), 114.0 (Ar 3-C and Ar 5-C), 63.3 (2-C), 59.7 (2'-C), 57.8 (CH_2 benzyl), 55.3 (OMe), 50.4 (1-C), 50.1 (1'-C), 28.4 (3'-C), 20.1 (3-C), 19.0 (4'-C), 16.9 (methyl); *m*/*z* (*ESI*) 466.2 (100%, MH^+).

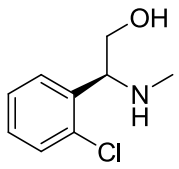
(2*S*,6*R*)-2-*iso*Propyl-1-(4-methoxybenzyl)-6-methyl-4-(2'-nitrophenylsulfonyl)piperazine 10k



By general procedure **C**, followed by purification by column chromatography, eluting with 50:1 CH_2Cl_2–MeOH, the amino alcohol **S15** (280 mg, 0.6 mmol) gave the *piperazine* **10k** (126 mg, 0.3 mmol, 47%) as a yellow oil; R_f 0.72 (1:1, petrol–EtOAc); $[\alpha]_D^{24}$: 1.5 (c. 4, $CHCl_3$); ν_{max}/cm^{-1} (film) 2965, 1610, 1546, 1511, 1373, 1246; δ_H (500 MHz; $CDCl_3$) 7.95 (1H, m,Ar 3-H), 7.70 (2H, m, Ar 4-H and Ar 6-H), 7.60 (1H, m, Ar 5-H), 7.20 (2H, d, *J* 8.6, Ar 2-H and Ar 6-H), 6.81 (2H, d, *J* 8.7 Ar 3-H and Ar 5-H), 3.78 (3H, s, OMe), 3.74 (1H, d, *J* 16.4 benzyl CH_a), 3.60 (1H, d, *J* 16.5, benzyl CH_b), 3.61 (1H, dt, *J* 11.9, 2.5, 5-H_a), 3.54 (1H, dt, *J* 11.9, 2.2, 3-H_a), 2.77 (1H, m, 6-H), 2.73 (1H, dd, *J* 12.0, 10.0, 5-H_b), 2.62 (1H, dd, *J* 12.0, 10.1, 3-H_b), 2.48 (1H, m, 1-H), 2.11 (1H, m, CH isopropyl), 1.10 (3H, d, *J* 6.3, Me), 0.94 (3H, d, *J* 6.9, Me (isopropyl)), 0.76 (3H, d, *J* 6.8, Me (isopropyl)); δ_C (75 MHz, $CDCl_3$) 133.7, 132.3, 132.0, 131.5, 130.9, 128.9 (Ar 2-C and Ar 6-C), 124.0, 113.5 (Ar 3-C and Ar 5-C), 65.2, 55.3, 55.2, 52.7, 50.8, 44.8, 27.9 (CH isopropyl), 20.2 (Me), 19.0 (Me (isopropyl)), 16.6 (Me (isopropyl)); *m*/*z* (*ESI*) 448.2 (100%, MH^+); HRMS found MH^+, 448.1922. $C_{22}H_{29}N_3O_5S$ requires *MH*, 448.1901.

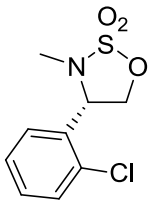
Synthesis of building blocks for exemplification of the synthetic approach

(2*S*)-2-(2-chlorophenyl)-2-(methylamino)ethan-1-ol 12



Ethyl chloroformate (2.86 ml, 30.0 mmol) was added to a solution of (2*S*)-amino(2-chlorophenyl)ethanoic acid (5.204 g, 28 mmol) and sodium carbonate (6 g, 56.6 mmol) in water (60 ml) and dioxane (50 ml) at 0 °C. The mixture was warmed to rt and stirred for 15 h. Aqueous HCl (150 ml, 1 M) was added with care, followed by EtOAc (150 ml) and the phases separated. The aqueous phase was extracted with EtOAc (3 × 100 ml), the combined organics were dried ($MgSO_4$) and concentrated. The crude residue was taken up in THF (100 ml) and cooled to 0 °C. $LiAlH_4$ (1.539 g, 40.5 mmol) was added with care. The mixture was warmed 70 °C and stirred for 4 days. The reaction was cooled to 0 °C, water (1.6 ml) and aqueous sodium hydroxide (1.6 ml, 15% w/w) were added with care, and the mixture stirred for 45 min. Water (4.8 ml) was added with stirring for a further 1 h. The white slurry was filtered through Celite and the precipitate washed with EtOAc (100 ml). The filtrate was dried ($MgSO_4$), concentrated, and the crude product purified by flash column chromatography (eluting with 97:3 DCM—MeOH) to give the *title compound* as a brown oil (2.391 g, 46%), R_F: 0.32 (95:5, DCM—MeOH); $[\alpha]_D^{24}$: +67.7 (c. 1, MeOH); ν_{max}/cm^{-1} (film) 3253, 1472, 1442; ∂_H (500 MHz; $CDCl_3$) 7.40 (1H, dd, *J* 7.7, 1.7, Ar3-H or Ar6-H), 7.37 (1H, dd, *J* 7.8, 1.3, Ar3-H or Ar6-H), 7.28 (1H, dt, *J* 7.4, 1.2, Ar4-H or Ar5-H), 7.21 (1H, dt, *J* 7.4, 1.7, Ar4-H or Ar5-H), 4.20 (1H, dd, *J* 8.0, 4.0, 2-H), 3.80 (1H, dd, *J* 10.8, 4.0, 1-H_A), 3.52 (1H, dd, *J* 10.8, 8.0, 1-H_B), 2.35 (3H, s, Nme); ∂_C (125 MHz; $CDCl_3$) 137.5, 134.0, 129.9, 128.5, 127.9, 127.1, 64.6, 62.4, 34.0; *m/z* (ES) [M+H^+] 186 (100%, M+H^+); HRMS Found: 186.0685, M+H^+ requires 186.068.

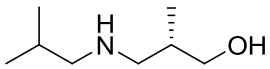
(4*S*)-4-(2-chlorophenyl)-3-methyl-1,2,3- oxathiazolidine-2,2-dione 7f



General procedure B2 was followed using aminoalcohol **12** (2.076 g, 11.2 mmol), thionyl chloride (0.90 ml, 12.3 mmol), triethylamine (3.42 ml, 24.6 mmol), imidazole (3.043 g, 44.8 mmol), sodium periodate (2.634 g, 12.3 mmol) and ruthenium(III) chloride trihydrate (2.9 mg, 0.01 mmol). The crude product was purified by flash column chromatography (eluting with 90:10 petrol—EtOAc) to give the *title compound* as a white amorphous solid (1.362 g, 49%), R_F: 0.27 (90:10, Petrol—EtOAc); $[\alpha]_D^{24}$: +116.1 (c. 0.9, $CHCl_3$); ν_{max}/cm^{-1} (film) 1352, 1180; ∂_H (500 MHz; $CDCl_3$) 7.62-7.60 (1H, m, Ar), 7.44-7.33 (3H, m, Ar), 5.06 (1H, t, *J* 7.6, 5-

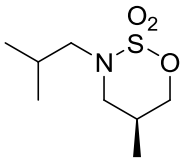
H_A), 4.86 (1H, dd, *J* 7.6, 8.5, 4-H), 4.21 (1H, t, *J* 8.5, 5-H_B), 2.76 (3H, s, NMe); ∂_C (125 MHz; $CDCl_3$) 133.4, 132.7, 130.4, 130.2, 128.1, 127.6, 71.4, 61.5, 32.4; *m/z* (ES) [M+Na^+] 270 (100%, M+Na^+), 248 (55%, M+H^+); HRMS Found: 269.9958, M+Na^+ requires 269.9962.

(2*S*)-2-Methyl-3-[(2-methylpropyl)amino]propan-1-ol 15



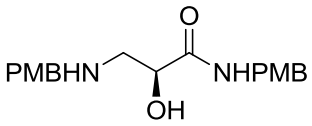
(*R*)-3-bromo-2-methyl-1-propanol (5.00 g, 32.7 mmol) was dissolved in isobutylamine (25 ml) and stirred for 3 h. The solvent was removed, water (50 ml) and potassium carbonate (5 g) added with stirring. The solvent was removed The residue was triturated with EtOAc, filtered, and the organic filtrate was concentrated to give the *title compound* as a yellow oil (1.997 g, 42%), $[\alpha]_D^{24}$: +4.9 (c. 0.3, MeOH); ν_{max}/cm^{-1} (film) 3250; ∂_H (500 MHz; $CDCl_3$) 3.73-3.71 (1H, m, 1-H_A), 3.55-3.51 (1H, m, 1-H_B), 2.91-2.88 (1H, m, 3-H or N-2-methylpropyl 1-H), 2.59-2.57 (1H, m, 3-H or N-2-methylpropyl 1-H), 2.52-2.48 (1H, m, 3-H or N-2-methylpropyl 1-H), 2.39-2.35 (1H, m, 3-H or N-2-methylpropyl 1-H), 2.02-1.96 (1H, m, 2-H or N-2-methylpropyl 1-H), 1.76-1.71 (1H, m, 2-H or N-2-methylpropyl 1-H), 0.91 (6H, d, *J* 6.7, N-2-methylpropyl 3-H), 0.80 (3H, d, *J* 6.7, 2-Me); ∂_C (125 MHz; $CDCl_3$) 70.9, 57.9, 53.4, 33.8, 28.0, 20.5, 14.9; *m/z* (EI) [M-H+] 144 (100%, M-H+); HRMS Found: 144.1433, M-H+ requires 144.1388.

(5*S*)-5-Methyl-3-(2-methylpropyl)-1,2,3-oxathiazinane-2,2-dione 7g



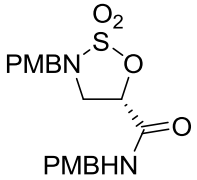
General procedure B2 was followed using the amino alcohol **15** (1.997 g, 13.8 mmol), thionyl chloride (1.11 ml, 15.2 mmol), imidazole (3.754 g, 55.2 mmol), triethylamine (4.22 ml, 30.4 mmol), sodium periodate (3.249 g, 15.2 mmol) and ruthenium(III) chloride trihydrate (3.6 mg, 0.014 mmol). The crude product was purified by flash column chromatography (eluting with 89:11 petrol—EtOAc) to give the *title compound* as a colourless oil (1.760 g, 61%), R_F: 0.26 (89:11, Petrol—EtOAc); $[\alpha]_D^{24}$: +26.1 (c. 0.9, $CHCl_3$); ν_{max}/cm^{-1} (film) 1368, 1188; ∂_H (500 MHz; $CDCl_3$) 4.37 (2H, d, *J* 7, isobutyl 1-H), 3.47 (1H, dd, *J* 11.1, 13.9, 6-H_A or 6-H_B), 3.22-3.18 (1H, m, 6-H_A or 6-H_B), 3.10 (1H, ddd, *J* 13.5, 7.9, 0.8, 4-H_A or 4-H_B), 2.81 (1H, dd, *J* 13.5, 6.8, 4-H_A or 4-H_B), 2.31 (1H, dddd, *J* 9.9, 6.9, 5.5, 3.6, 5-H), 1.89-1.80 (1H, dsept, *J* 7.0, 1.1, isobutyl 2-H), 0.95-0.91 (9H, m, isobutyl 3-H and Me); ∂_C (125 MHz; $CDCl_3$) 57.2, 55.9, 27.5, 25.2, 19.9, 19.8, 12.8; *m/z* (ES) [M+Na^+] 230 (100%, M+Na^+); HRMS Found: 230.0813, M+Na^+ requires 230.1821.

(2*S*)-2-Hydroxy-3-[(4-methoxyphenyl)amino]-*N*-[(4-methoxyphenyl)methyl]propanamide 17



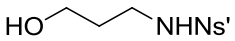
Prepared by the method of Breuning *et al*.[4] to give the title compound[4] as a white amorphous solid (12.768 g, 85%), $[\alpha]_D^{24}$: −3.7 (c. 1, $CHCl_3$); ν_{max}/cm^{-1} (film) 1644; ∂_H (500 MHz; $CDCl_3$) 7.49 (1H, br s, 1-NH), 7.19 (2H, d, *J* 8.7, Ar_A), 7.13 (2H, d, *J* 8.7, Ar_B), 6.85 (2H, d, *J* 8.7, Ar), 6.83 (2H, d, *J* 8.7, Ar), 4.83 (2H, d, *J* 5.7, amidobenzyl-H), 4.02 (1H, t, *J* 6, 2-H), 3.79 (3H, s, $OMe_{A\ or\ B}$), 3.79 (3H, s, $OMe_{A\ or\ B}$), 3.69 (2H, d, *J* 5.1, aminobenzyl-H), 3.03 (1H, dd, *J* 12.3, 6.0, 3-H_A), 2.95 (1H, dd, *J* 12.3, 6.0, 3-H_B), 1.53 (2H, br s, 3-NH and OH); ∂_C (125 MHz; $CDCl_3$) 172.8, 159.1, 158.9, 131.5, 130.2, 129.3, 129.1, 114.1, 114.0, 69.1, 55.3, 55.3, 52.9, 51.1, 42.7; *m/z* (ES) [M+H^+] 345 (100%, M+H^+); HRMS Found: 345.1807, M+H^+ requires 345.1809.

(5*S*)-3-(4-Methoxyphenyl)-*N*-[(4-methoxyphenyl)methyl]-2,2-dioxo-1,3-oxazolidine-5-carboxamide 7h



General procedure B2 was followed using the amino alcohol **17** (1.000 g, 2.7 mmol), thionyl chloride (0.22 ml, 2.9 mmol), imidazole (727 mg, 10.7 mmol), triethylamine (0.82 ml, 5.9 mmol), sodium periodate (572 mg, 2.7 mmol) and ruthenium(III) chloride trihydrate (0.7 mg, 0.003 mmol). The crude product was purified by flash column chromatography (eluting with 67:33 petrol—EtOAc) to give the *title compound* as a colourless amorphous solid (601 mg, 51%), $[\alpha]_D^{24}$: +83.5 (c. 1, $CHCl_3$); ν_{max}/cm^{-1} (film) 1674, 1354, 1187; ∂_H (500 MHz; $CDCl_3$) 7.21 (2H, d, *J* 8.7, Ar), 7.20 (2H, d, *J* 8.7, Ar), 6.88 (2H, d, *J* 8.7, Ar), 6.88 (2H, d, *J* 8.7, Ar), 6.76 (1H, br s, NH), 4.92 (1H, dd, *J* 7.6, 5.3, 5-H), 4.42 (1H, dd, *J* 5.9, 3.0, 3-benzyl H), 4.15 (2H, s, amidobenzyl H), 3.81 (3H, s, OMe_A), 3.80 (3H, s, OMe_B), 3.69 (1H, dd, *J* 10.6, 7.6, 4-H_A), 3.56 (1H, dd, *J* 10.6, 5.3, 4-H_B); ∂_C (125 MHz; $CDCl_3$) 166.5, 160.0, 159.3, 130.2, 129.1, 128.9, 125.3, 114.4, 114.3, 75.5, 55.3, 51.4, 49.7, 43.0; *m/z* (ES) [M+Na^+] 429 (100%, M+Na^+); HRMS Found: 429.1089, M+Na^+ requires 429.1091.

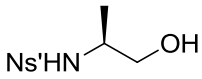
Propan-1-ol-3-(4-nitrophenyl)sulfonamide 8b'



4-Nitrobenzenesulfonyl chloride (11.26 g, 50.8 mmol) was added to a solution of 3-aminopropan-1-ol (4.05 ml, 53.3 mmol) and sodium carbonate (5.65 g, 53.3 mmol) in DCM (30 ml) and water (30 ml). The mixture was stirred vigorously for 2 h. Aqueous HCl (50 ml, 5 M) was added and the DCM removed under vacuum. EtOAc (80 ml) was added, the phases separated, the aqueous phase extracted with EtOAc (3 × 50 ml), the combined organics dried ($MgSO_4$), concentrated, and the crude product purified by flash column chromatography (eluting with 90:10 DCM—MeOH) to give the *title compound* as an amorphous colourless solid (13.134 g, quant.), R_F: 0.35 (95:5, DCM—MeOH); ν_{max}/cm^{-1} (film) 1530, 1351, 1336, 1162; ∂_H (500 MHz; CD_3CN) 8.41 (2H, d, *J* 8.9, Ar3-H), 8.03 (2H, d, *J* 8.9, Ar2-H), 7.91 (1H, br s, NH), 4.40 (1H, br s,

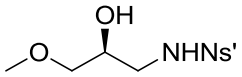
OH), 3.34-3.32 (2H, m, propyl 3-H), 2.84 (2H, t, *J* 7.2, propyl 1-H), 3.49-3.48 (2H, m, propyl 2-H); ∂_C (125 MHz; $CDCl_3$) 149.5, 146.1, 128.0, 124.6, 57.8, 39.9, 32.3; *m/z* (ES) [M+Na^+] 283 (100%, M+Na^+); HRMS Found: 283.0355, M+Na^+ requires 283.0359.

(2*S*)-1-Hydroxy-*S*-(4-nitrophenyl)propane-2-sulfonamide 8f



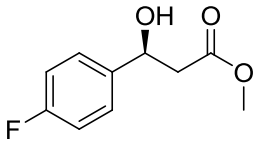
4-Nitrobenzenesulfonyl chloride (8.442 g, 38.1 mmol) was added to a solution of (*S*)-2-aminopropan-1-ol (3.11 ml, 40.0 mmol) and sodium carbonate (4.24 g, 40.0 mmol) in DCM (50 ml) and water (50 ml) at 0 °C. The mixture was warmed to rt and stirred vigorously for 16 h. Aqueous HCl (50 ml, 5 M) was added and the DCM removed under vacuum. EtOAc (80 ml) was added, the phases separated, the aqueous phase extracted with EtOAc (3 × 80 ml), the combined organics dried ($MgSO_4$), concentrated, and the crude product purified by flash column chromatography (eluting with 95:5 DCM—MeOH) to give the *title compound* as a yellow amorphous solid (8.430 g, 85%), R_F: 0.47 (95:5, DCM—MeOH); $[\alpha]_D^{24}$: −4.8 (c. 1.3, MeOH); ν_{max}/cm^{-1} (film) 1531, 1352, 1166; ∂_H (500 MHz; DMSO) 8.41 (2H, d, *J* 8.9, Ar3-H), 8.07 (2H, d, *J* 8.9, Ar2-H), 3.30-3.27 (1H, m, 2-H), 3.22-3.13 (2H, m, 1-H), 0.92 (3H, d, *J* 6.4, 3-H); ∂_C (125 MHz; $CDCl_3$) 149.3, 147.9, 127.9, 124.4, 64.9, 51.3, 17.8; *m/z* (ES) [M+Na^+] 283 (100%, M+Na^+); HRMS Found: 283.0346, M+Na^+ requires 283.0359.

(2*S*)-2-Hydroxy-3-methoxy-S-(4-nitrophenyl)propane-1-sulfonamide 8g



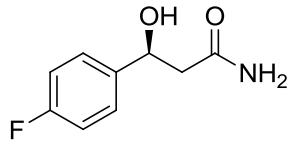
(*S*)-Glycidyl methyl ether (0.38 ml, 4.2 mmol) was added to a saturated solution of ammonia in MeOH (50 ml) and stirred for 3 days. The solvent was removed. The residue was taken up in DCM (20 ml) and 4-nitrobenzenesulfonyl chloride (1.019 g, 4.6 mmol) and triethylamine (1.16 ml, 8.4 mmol) were added. The mixture was stirred for 18 h. DCM (40 ml) and aqueous HCl (40 ml, 1 M) were added and the phases separated. The aqueous phase was extracted with DCM (3 × 40 ml) and the combined organic fractions washed with brine (60 ml), dried ($MgSO_4$) and concentrated. The crude residue was purified by flash column chromatography (eluting with 98:2 DCM—MeOH) to give the *title compound* as a white amorphous solid (653 mg, 54%), $[\alpha]_D^{24}$: −2.2 (c. 0.6, MeOH); ν_{max}/cm^{-1} (film) 1531, 1351, 1164; ∂_H (500 MHz; CD_3CN) 8.36 (2H, d, *J* 9, Ar3-H), 8.05 (2H, d, *J* 9, Ar4-H), 3.70-3.68 (1H, m, 2-H), 3.27 (2H, d, *J* 5.4, 3-H), 3.27 (3H, s, OMe), 3.12 (1H, d, *J* 5.2, OH), 3.06-3.03 (1H, m, 1-H_A), 2.90-2.85 (1H, m, 1-H_B); ∂_C (125 MHz; CD_3CN) 149.9, 145.8, 127.9, 124.1, 73.7, 68.1, 58.0, 45.7; *m/z* (ES) [M+Na^+] 313 (100%, M+Na^+); HRMS Found: 313.0467, M+Na^+ requires 313.0465.

Methyl (3*S*)-3-(4-fluorophenyl)-3-hydroxypropanoate 21



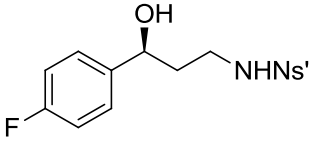
Triethylamine (8.52 ml, 61.2 mmol) and formic acid (5.77 ml, 153.1 mmol) were stirred together at 0 °C. The mixture was warmed to rt, methyl-4-fluorobenzoylacetate (4.07 ml, 25.5 mmol) and RuCl(*p*-cymene)[(*R*,*R*)-Ts-DPEN) (81.1 mg, 0.13 mmol) were added, and the mixture was stirred for 7 days. Water (50 ml) and EtOAc (50 ml) were added and the phases separated. The aqueous phase was extracted with EtOAc (3 × 50 ml). the combined organics were washed with saturated aqueous sodium bicarbonate (100 ml) and brine (100 ml), dried ($MgSO_4$), and concentrated. The crude residue was purified by flash column chromatography (eluting with 80:20 petrol—EtOAc) to give the *title compound* (4.809 g, 95%; 96% ee) as a brown oil, R_F: 0.35 (80:20, Petrol—EtOAc); $[\alpha]_D^{24}$: +40.3 (c. 0.8, $CHCl_3$); ν_{max}/cm^{-1} (film) 1732, 1222; ∂_H (500 MHz; $CDCl_3$) 7.36-7.33 (2H, m, Ar3-H), 7.06-7.02 (2H, m, Ar2-H), 5.13-5.11 (1H, m, 3-H), 3.73 (3H, s, OMe), 3.28 (1H, br s, OH), 2.77-2.67 (2H, m, 2-H); ∂_C (125 MHz; $CDCl_3$) 172.7, 163.3, 161.4, 138.3, 138.3, 127.4, 127.4, 115.5, 115.3, 69.7, 51.9, 43.2; *m/z* (ES) [M+Na^+] 221 (100%, M+Na^+); HRMS Found: 221.059, M+Na^+ requires 221.0584. The enantiomeric excess of the product was determined by chiral analytical HPLC: OD:H column eluting with 5% IPA in hexane (12.1 min, minor; 13.3 min, major).

(3*S*)-3-(4-Fluorophenyl)-3-hydroxypropanamide 22



Alcohol **21** (3.994 g, 20.2 mmol) was added to a saturated solution of ammonia in MeOH (400 ml) and stirred for 3 days. The solvent was removed and the crude residue was purified by flash column chromatography (eluting with 90:10 DCM—MeOH) to give the *title compound* as a colourless oil (2.886 g, 78%), $[\alpha]_D^{24}$: +27 (c. 0.8, MeOH); ν_{max}/cm^{-1} (film) 1654, 1223; ∂_H (500 MHz; CD_3CN) 7.39-7.36 (2H, m, Ar), 7.09-7.06 (2H, m, Ar), 4.99 (1H, m, 3-H), 2.48-2.45 (2H, m, 2-H (exchanges with solvent)); ∂_C (125 MHz; CD_3CN) 173.5, sort coupling, 140.2, sort coupling, sort coupling, 69.1, 43.5; *m/z* (ES) [M+Na^+] 206 (100%, M+Na^+); HRMS Found: 206.0591, M+Na^+ requires 206.0588.

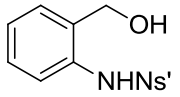
(3*S*)-3-(4-Fluorophenyl)-3-hydroxy-S-(4-nitrophenyl)propane-1-sulfonamide 8h



$LiAlH_4$ (0.934 g, 24.6 mmol) was added to a solution of amidoalcohol **22** (1.493 g, 8.2 mmol) in THF (150 ml) at 0 °C. The mixture was warmed to rt and stirred for 19 h. The mixture was cooled to 0 °C and water (0.95 ml) and aqueous sodium hydroxide (0.95 ml, 15% w/w) were added with care. The slurry was stirred for 45 min and then water (2.8 ml) was added with stirring for a further 1 h. The slurry was filtered and the

precipitate washed with EtOAc (100 ml). The filtrate was concentrated and dried ($MgSO_4$). The crude residue was taken up in DCM (200 ml), to which 4-nitrobenzenesulfonyl chloride (2.184 g, 9.8 mmol) and triethylamine (1.71 ml, 12.3 mmol) were added. The mixture was stirred for 15 h. Water (150 ml) was added, the phases separated, and the aqueous fraction extracted with DCM (3 × 100 ml). The combined organic fractions were dried ($MgSO_4$), concentrated, and the crude residue purified by flash column chromatography (eluting with 67:33 petrol—EtOAc) to give the *title compound* as a yellow oil (1.242 g, 43%), R_F: 0.18 (67:33, Petrol—EtOAc); $[\alpha]_D^{24}$: +28.7 (c. 0.9, $CHCl_3$); ν_{max}/cm^{-1} (film) 1530, 1350, 1222, 1162; ∂_H (500 MHz; $CDCl_3$) 8.37 (2H, d, *J* 8.9, Ar3-H), 8.06 (2H, d, *J* 8.9, Ar2-H), 5.51 (1H, br s, NH), 4.83 (1H, t, *J* 6.2, 3-H), 3.28-3.23 (1H, m, 2-H_A), 3.15-3.12 (1H, m, 2-H_B), 2.15 (1H, br s, OH), 1.88 (2H, q, *J* 6, 1-H); ∂_C (125 MHz; $CDCl_3$) 163.4, 161.4, 150.1, 146.0, 139.2, 128.3, 127.2, 127.1, 124.4, 115.7, 115.6; *m/z* (ES) [M+Na^+] 377 (100%, M+Na^+); HRMS Found: 377.0579, M+Na^+ requires 377.0578.

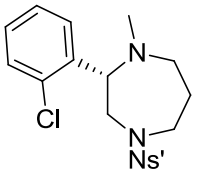
_N_-[2-(Hydroxymethyl)phenyl]-4-nitrobenzene-1-sulfonamide 8i



Pyridine (4.58 ml, 56.8 mmol) was added to a solution of 2-aminobenzyl alcohol (5.00 g, 40.6 mmol) and 4-nitrobenzenesulfonyl chloride (10.79 g, 48.7 mmol) in DCM (150 ml) and stirred for 1.5 h. Aqueous HCl (100 ml, 1 M) was added and the phases separated. The aqueous phase was extracted with EtOAc (3 × 70 ml). The combined organics were dried ($MgSO_4$), concentrated, and the crude residue was purified by flash column chromatography (eluting with 67:33 petrol—EtOAc) to give the *title compound* as a pink amorphous solid (8.765 g, 70%), R_F: 0.29 (67:33, Petrol—EtOAc); ν_{max}/cm^{-1} (film) 1531, 1350, 1166; ∂_H (500 MHz; CD_3CN) 8.47 (1H, br s, NH), 8.28 (2H, d, *J* 9, Ns3-H), 7.95 (2H, d, *J* 9, Ns2-H), 7.31-7.16 (4H, m, Ar), 4.38 (2H, d, *J* 5.1, CH2), 3.57 (1H, t, *J* 5.1, OH); ∂_C (125 MHz; CD_3CN) 150.2, 145.0, 134.6, 133.6, 128.4, 128.1, 128.1, 125.8, 124.3, 123.2, 61.6; *m/z* (ES) [M+Na^+] 331 (80%, M+Na^+); HRMS Found: 331.0348, M+Na^+ requires 331.0359.

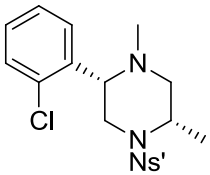
Exemplification of the synthetic approach

(2*S*)-2-(2-chlorophenyl)-1-methyl-4-[(4-nitrobenzene)sulfonyl]-1,4-diazepane 10l



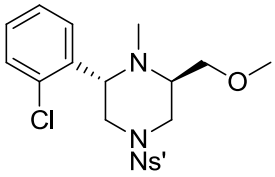
General procedure F was followed using the hydroxy sulfonamide **8b** (312 mg, 1.2 mmol) and sulfamidate **7f** (248 mg, 1.0 mmol). The aminoalcohol intermediate was isolated (374 mg), 271 mg was taken on to ring closing. The *title compound* was isolated as a yellow oil (258 mg, 87%), $[\alpha]_D^{24}$: +81.3 (c. 1.1, MeOH); ν_{max}/cm^{-1} (film) 1539, 1348, 1162; ∂_H (500 MHz; $CDCl_3$) 8.32 (2H, d, *J* 8.9, Ns3-H), 7.96 (2H, d, *J* 8.9, Ns2-H), 7.53 (1H, br d, *J* 6.9, Ar3-H or Ar6-H), 7.38 (1H, dd, *J* 7.8, 1.5, Ar3-H or Ar6-H), 7.25-7.19 (2H, m, Ar3-H and Ar5-H), 3.99 (1H, d, *J* 8.2, 2-H), 3.68-3.61 (2H, m, 3-H_A and 5-H_A), 3.12-3.00 (3H, m, 3-H_B, 5-H_B and 7-H_A), 2.79 (1H, dd, *J* 9.7, 13.1, 7-H_B), 2.14 (4H, m, NMe and 6-H_A), 2.06-2.01 (1H, br m, 6-H_B); ∂_C (125 MHz; $CDCl_3$) 150.0, 144.8, 133.5, 129.8, 128.8, 128.7, 128.6, 128.3, 127.2, 124.4, 67.3, 54.0, 51.3, 47.4, 44.5, 27.8; *m/z* (ES) [M+H^+] 410 (100%, M+H^+); HRMS Found: 410.0937, M+H^+ requires 410.0936.

(2*R*,5*S*)-2-(2-chlorophenyl)-1,5-dimethyl-4-[(4-nitrobenzene)sulfonyl]piperazine 10m



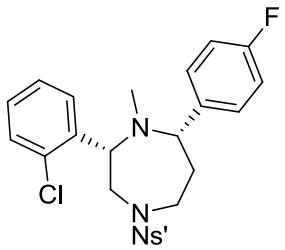
General procedure F was followed using the hydroxy sulonamide **8f** (312 mg, 1.2 mmol) and the cyclic sulfamidate **7f** (248 mg, 1.0 mmol). The aminoalcohol intermediate was isolated (183 mg), 128 mg was taken on to ring closing. The product required further purification by flash column chromatography (eluting with 80:20 petrol—EtOAc) to give the *title compound* as a yellow oil (125 mg, 44%), R_F: 0.86 (50:50, Petrol—EtOAc); $[\alpha]_D^{24}$: +63.6 (c. 0.8, $CHCl_3$); ν_{max}/cm^{-1} (film) 1531, 1350, 1164; ∂_H (500 MHz; CD_3CN) 8.36 (2H, d, *J* 9, Ns3-H), 8.04 (2H, d, *J* 9, Ns2-H), 7.54 (1H, dd, *J* 7.7, 1.7, Ar3-H or Ar6-H), 7.36 (1H, dd, *J* 8.0, 1.7, Ar3-H or Ar6-H), 7.28 (1H, td, *J* 7.7, 1.7, Ar4-H or Ar5-H), 7.22 (1H, ddd, *J* 8.0, 7.7, 1.7, Ar4-H or Ar5-H), 4.28-4.25 (1H, m, 5-H), 3.73 (1H, dd, *J* 12.8, 3.7, 2-H or 3-H_A), 3.41 (1H, dd, *J* 11.6, 3.7, 2-H or 3-H_A), 2.99 (1H, dd, *J* 12.8, 11.6, 3-H_B), 2.75 (1H, dd, *J* 11.7, 1.8, 6-H_A), 2.31 (1H, dd, *J* 11.7, 3.8, 6-H_B), 1.34 (3H, s, NMe), 1.34 (3H, d, *J* 6.8, 5-Me); ∂_C (125 MHz; $CDCl_3$) 149.9, 147.0, 136.6, 133.5, 129.8, 128.9, 128.9, 128.3, 127.4, 124.5, 63.6, 59.9, 49.6, 45.5, 43.3, 16.0; *m/z* (ES) [M+H^+] 410 (100%, M+H^+); HRMS Found: 410.0938, M+H^+ requires 410.0936.

(2*S*,6*R*)-2-(2-Chlorophenyl)-6-(methoxymethyl)-1-methyl-4-[(4-nitrobenzene)sulfonyl] piperazine 10n



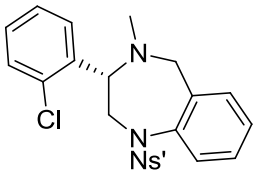
General procedure F was followed using the hydroxy sulfonamide **8g** (200 mg, 0.7 mmol) and the cyclic sulfamidate **7f** (155 mg, 0.6 mmol). The *title compound* was isolated as a yellow oil (153 mg, 55%), $[\alpha]_D^{24}$: +99.8 º (c. 1, $CHCl_3$); ν_{max}/cm^{-1} (film) 1531, 1351, 1173; ∂_H (500 MHz; $CDCl_3$) 8.36 (2H, d, *J* 8.9, Ns3-H), 7.92 (2H, d, *J* 8.9, Ns2-H), 7.38-7.35 (2H, m, Ar), 7.23-7.21 (2H, m, Ar), 4.30 (1H, dd, *J* 10.3, 3.7, 2-H), 3.96 (1H, dt, *J* 11.2, 2.7, 5-H_A), 3.79-3.71 (3H, m, 3-H_A and 6-CH_2), 3.43 (3H, s, OMe), 3.12 (1H, dd, *J* 8.2, 3.7, 3-H_B), 2.63 (1H, dd, *J* 10.5, 2.7, 5-H_B), 2.22 (1H, dd, *J* 11.2, 10.5, 6-H), 2.15 (3H, s, 4-Me); ∂_C (125 MHz; $CDCl_3$) 150.2, 142.2, 136.3, 133.9, 129.9, 129.0, 128.9, 128.8, 127.3, 124.4, 65.7, 59.3, 58.9, 56.9, 51.2, 47.9, 39.5; *m/z* (ES) $[M+H^+]$ 440 (100%, $M+H^+$); HRMS Found: 440.1046, $M+H^+$ requires 440.1041.

(2*S*,7*R*)-2-(2-chlorophenyl)-7-(4-fluorophenyl)-1-methyl-4-[(4-nitrobenzene)sulfonyl]-1,4-diazepane 10o



General procedure F was followed using the hydroxy sulfonamide **8h** (389 mg, 1.1 mmol) and the cyclic sulfamidate **7f** (248 mg, 1.0 mmol). The aminoalcohol intermediate was isolated (415 mg), 326 mg was taken on to ring closing. The *title compound* was isolated as a yellow oil (314 mg, 80%), $[\alpha]_D^{24}$: +32.5 (c. 1.2, $CHCl_3$); ν_{max}/cm^{-1} (film) 1531, 1349, 1222, 1163; ∂_H (500 MHz; $CDCl_3$) 8.35 (2H, d, *J* 8.9, Ns3-H), 8.00 (2H, d, *J* 8.9, Ns2-H), 7.56 (1H, dd, *J* 7.6, 1,8, Ar), 7.42 (1H, dd, *J* 7.8, 1.5, Ar), 7.36-7.34 (2H, m, Ar), 7.29-7.22 (2H, m, Ar), 7.00 (2H, t, *J* 8.7, Ar), 4.42 (1H, dd, *J* 10.0, 4.2, 2-H), 3.88 (1H, dd, *J* 10.1, 1.7, 7-H), 3.65-3.57 (3H, m, 3-H and 5-H_A), 3.41-3.37 (1H, m, 5-H_B), 2.45-2.37 (1H, m, 6-H_A), 2.14 (1H, dtd, *J* 8.2, 4.3, 2.1, 6-H_B), 1.83 (3H, s, NMe); ∂_C (125 MHz; $CDCl_3$) 162.8, 160.9, 150.1, 144.5, 138.6, 134.1, 130.2, 128.8, 128.5, 128.5, 128.3, 128.1, 127.0, 124.7, 115.5, 115.3, 67.1, 65.9, 49.6, 46.2, 37.2, 34.9; *m/z* (ES) $[M+H^+]$ 504 (100%, $M+H^+$); HRMS Found: 504.1172, $M+H^+$ requires 504.1155.

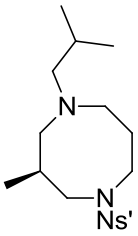
(3*S*)-3-(2-chlorophenyl)-4-methyl-1-[(4-nitrobenzene)sulfonyl]-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine 10p



General procedure F was followed using the hydroxy sulfonamide **8i** (370 mg, 1.2 mmol) and the cyclic sulfamidate **7f** (248 mg, 1.0 mmol). The *title compound* was isolated as a yellow oil (50 mg, 11%), $[\alpha]_D^{24}$: +34 (c. 0.1, $CHCl_3$); ν_{max}/cm^{-1} (film) 1531, 1349, 1167; ∂_H (500 MHz; $CDCl_3$) 8.33 (2H, d, *J* 8.9, Ns3-H), 7.92 (2H, d, *J* 8.9, Ns2-H), 7.50 (1H, d, *J* 7.8, Ar), 7.38-7.32 (4H, m, Ar), 7.23-7.20 (3H, m, Ar), 4.21-4.16 (1H, m, 2-H_A), 3.97 (1H, d, *J* 10.1, 2-H_B), 3.43 (1H, d, *J* 14, 5-H_A), 3.34 (1H, dd, *J* 10.1, 14.5, 3-H), 3.13

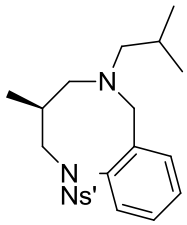
(1H, d, *J* 14, 5-H_B), 1.97 (3H, s, NMe); ∂_C (125 MHz; $CDCl_3$) 150.1, 146.4, 138.6, 137.7, 133.6, 130.9, 129.9, 128.9, 128.8, 128.7, 128.5, 128.4, 127.3, 124.4, 54.5, 42.7; *m/z* (ES) [$M+H^+$] 458 (100%, $M+H^+$); HRMS Found: 458.093, $M+H^+$ requires 458.0936.

(3*S*)-3-Methyl-1-(2-methylpropyl)-5-[(4-nitrobenzene)sulfonyl]-1,5-diazocane 10q



General procedure F was followed using the hydroxy sulfonamide **8b** (312 mg, 1.2 mmol) and the cyclic sulfamidate **7g** (207 mg, 1.0 mmol). The product required further purification by flash column chromatography (eluting with 80:20 petrol—EtOAc) to give the *title compound* as a yellow oil (47 mg, 13%), R_F: 0.69 (95:5, DCM—MeOH); $[\alpha]_D^{24}$: −12.3 (c. 0.8, $CHCl_3$); ν_{max}/cm^{-1} (film) 1530, 1349, 1161; ∂_H (500 MHz; $CDCl_3$) 8.35 (2H, d, *J* 8.9, Ns3-H), 7.99 (2H, d, *J* 8.9, Ns2-H), 3.45 (1H, ddd, *J* 14.1, 5.7, 3.8, 6-H_A), 3.39 (1H, dd, *J* 14.1, 3.0, 4-H_A), 3.24 (1H, ddd, *J* 14.0, 9.1, 3.3, 6-H_B), 2.94 (1H, dd, *J* 14.1, 8.4, 4-H_B), 2.72 (1H, ddd, *J* 14.4, 9.6, 5.2, 8-H_A), 2.60 (1H, dd, *J* 13.3, 5.1, 2-H_A), 2.49 (1H, td, *J* 13.4, 5.1, 8-H_B), 2.30-2.20 (3H, m, 2-H_B and 2-methylpropyl 1-H), 2.16-2.07 (1H, m, 3-H), 1.88-1.66 (3H, m, 7-H and 2-methylpropyl 2-H), 0.91-0.83 (9H, m, 3-Me, 2-methylpropyl 2-Me and 2-methylpropyl 3-H); ∂_C (125 MHz; $CDCl_3$) 149.8, 145.8, 128.0, 124.3, 67.2, 58.8, 56.0, 53.4, 51.0, 50.0, 35.3, 29.6, 26.8, 20.9, 20.8, 18.0; *m/z* (ES) [$M+H^+$] 370 (100%, $M+H^+$); HRMS Found: 370.1804, $M+H^+$ requires 370.1795.

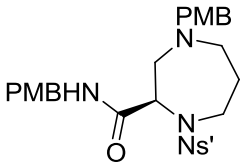
(3*S*)-3-Methyl-1-(2-methylpropyl)-5-[(4-nitrobenzene)sulfonyl]-1,5-diazocane 10r



General procedure F was followed using the hydroxy sulfonamide **8i** (370 mg, 1.2 mmol) and the cyclic sulfamidate **7g** (207 mg, 1.0 mmol). The product required further purification by flash column chromatography (eluting with 80:20 petrol—EtOAc) to give the *title compound* as a yellow oil (58 mg, 14%), R_F: 0.69 (95:5, DCM—MeOH); $[\alpha]_D^{24}$: −12.3 (c. 0.8, $CHCl_3$); ν_{max}/cm^{-1} (film) 1530, 1349, 1161; ∂_H (500 MHz; $CDCl_3$) 8.35 (2H, d, *J* 8.9, Ns3-H), 7.99 (2H, d, *J* 8.9, Ns2-H), 3.45 (1H, ddd, *J* 14.1, 5.7, 3.8, 6-H_A), 3.39 (1H, dd, *J* 14.1, 3.0, 4-H_A), 3.24 (1H, ddd, *J* 14.0, 9.1, 3.3, 6-H_B), 2.94 (1H, dd, *J* 14.1, 8.4, 4-H_B), 2.72 (1H, ddd, *J* 14.4, 9.6, 5.2, 8-H_A), 2.60 (1H, dd, *J* 13.3, 5.1, 2-H_A), 2.49 (1H, td, *J* 13.4, 5.1, 8-H_B), 2.30-2.20 (3H, m, 2-H_B and 2-methylpropyl 1-H), 2.16-2.07 (1H, m, 3-H), 1.88-1.66 (3H, m, 7-H and 2-methylpropyl 2-H), 0.91-0.83 (9H, m, 3-Me, 2-methylpropyl 2-Me and 2-methylpropyl 3-H); ∂_C (125 MHz;

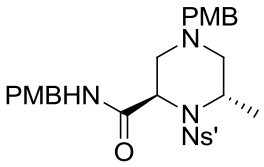
$CDCl_3$) 149.8, 145.8, 128.0, 124.3, 67.2, 58.8, 56.0, 53.4, 51.0, 50.0, 35.3, 29.6, 26.8, 20.9, 20.8, 18.0; *m/z* (ES) [M+H$^+$] 370 (100%, M+H$^+$); HRMS Found: 370.1804, M+H$^+$ requires 370.1795.

(2*R*)-*N*,4-Bis[(4-methoxyphenyl)methyl]-1-[(4-nitrobenzene)sulfonyl]-1,4-diazepane-2-carboxamide 10s



General procedure F was followed using the hydroxy sulfonamide **8h** (256 mg, 0.6 mmol) and the cyclic sulfamidate **7h** (203 mg, 0.5 mmol). The product required further purification by flash column chromatography (eluting with 67:33 petrol—EtOAc) to give the *title compound* as a colourless oil (106 mg, 38%), R_F: 0.29 (50:50, petrol—EtOAc); $[\alpha]_D^{24}$: +25.1 (c. 0.9, $CHCl_3$); ν_{max}/cm^{-1} (film) 1673, 1531, 1348, 1159; ∂_H (500 MHz; $CDCl_3$) 8.31 (2H, d, *J* 8.8, Ns3-H), 8.05 (2H, d, *J* 8.8, Ns2-H), 7.15 (2H, d, *J* 8.6, Ar), 6.99 (3H, m, Ar and NH), 6.86 (2H, d, *J* 8.6, Ar), 6.76 (2H, d, *J* 8.6, Ar), 4.55 (1H, dd, *J* 6.9, 3.8, 2-H), 4.29 (1H, dd, *J* 5.6, 2.8, amidobenzyl-H), 3.81 (3H, s, OMe_A), 3.78 (3H, s, OMe_B), 3.74-3.65 (1H, m, 7-H_A), 3.56 (2H, s, 4-CH_2), 3.35 (1H, ddd, *J* 14.0, 8.4, 3.6, 7-H_B), 3.14 (1H, dd, *J* 14.3, 6.9, 3- or 5-H), 2.88 (1H, dd, *J* 14.2, 3.7, 3- or 5-H), 2.71-2.61 (1H, m, 3- or 5-H), 2.61-2.52 (1H, m, 3- or 5-H), 1.90-1.78 (1H, m, 6-H_A), 1.70-1.58 (1H, m, 6-H_B); ∂_C (125 MHz; $CDCl_3$) 169.0, 159.2, 159.0, 150.0, 145.3, 130.0, 129.6, 129.2, 128.9, 124.2, 114.2, 113.8, 105.0, 61.8, 60.7, 57.0, 55.3, 55.2, 55.0, 45.0, 43.1, 28.4; *m/z* (ES) [M+H$^+$] 569 (100%, M+H$^+$); HRMS Found: 569.2073, M+H$^+$ requires 569.2064.

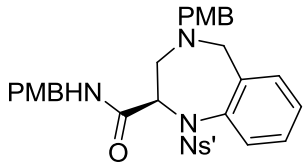
(2*R*,6*S*)-*N*,4-Bis[(4-methoxyphenyl)methyl]-6-methyl-1-[(4-nitrobenzene)sulfonyl]piperazine-2-carboxamide 10t



General procedure F was followed using the hydroxy sulfonamide **8f** (256 mg, 0.6 mmol) and the cyclic sulfamidate **7h** (203 mg, 0.5 mmol). The product required further purification by flash column chromatography (eluting with 67:33 petrol—EtOAc) to give the *title compound* as a yellow oil (22 mg, 8%), R_F: 0.18 (67:33, petrol—EtOAc); $[\alpha]_D^{24}$: +31.1 (c. 0.7, $CHCl_3$); ν_{max}/cm^{-1} (film) 1671, 1513, 1349, 1169; ∂_H (500 MHz; $CDCl_3$) 8.31 (2H, d, *J* 8.9, Ns3-H), 8.21 (2H, d, *J* 8.9, Ns2-H), 7.33 (1H, br s, NH), 7.17 (2H, d, *J* 8.6, (4-methoxyphenyl)-H), 6.97 (2H, d, *J* 8.6, (4-methoxyphenyl)-H), 6.88 (2H, d, *J* 8.6, (4-methoxyphenyl)-H), 6.72 (2H, d, *J* 8.6, (4-methoxyphenyl)-H), 4.83 (1H, t, *J* 3.4, 2-H), 4.36 (2H, d, *J* 5.4, amidobenzyl-H), 3.82 (3H, s, OMe_A), 3.78 (3H, s, OMe_B), 3.65 (1H, dqd, *J* 9.6, 6.8, 2.5, 6-H), 3.46 (1H, d, *J* 12.7, 4-CH_{2A}), 3.32 (1H, d, *J* 12.7, 4-CH_{2B}), 3.12 (1H, ddd, *J* 12.3, 3.4, 3-H_A), 2.65 (1H, d, *J* 10.3, 5-H_A), 2.45 (1H, dd, *J* 12.3, 3.4, 3-H_B), 2.18 (1H, dd, *J* 11.2, 10.0, 5-H_B), 1.24 (3H, d, *J* 6.9, 6-Me); ∂_C (125 MHz; $CDCl_3$) 168.6, 159.2, 159.1, 149.8, 148.8, 130.1, 129.7, 129.36, 128.7, 128.5, 124.1, 114.2, 113.9, 61.7, 60.0,

58.8, 55.3, 55.2, 53.9, 52.6, 43.3, 17.1; *m/z* (ES) [M+H$^+$] 569 (100%, M+H$^+$); HRMS Found: 569.2091, M+H$^+$ requires 569.2064.

(2*R*)-*N*,4-Bis[(4-methoxyphenyl)methyl]-1-[(4-nitrobenzene)sulfonyl]-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine-2-carboxamide 10u



General procedure F was followed using the hydroxy sulfonamide **8i** (185 mg, 0.6 mmol) and the cyclic sulfamidate **7h** (203 mg, 0.5 mmol). The product required further purification by flash column chromatography (eluting with 67:33 petrol—EtOAc) to give the *title compound* as a yellow oil (106 mg, 38%), R_F: 0.21 (67:33, petrol—EtOAc); $[\alpha]_D^{24}$: +103.9 (c. 0.8, $CHCl_3$); ν_{max}/cm^{-1} (film) 1670, 1530, 1349, 1167; ∂_H (500 MHz; $CDCl_3$) 8.39 (2H, d, *J* 8.7, Ns), 8.31 (2H, br s, Ns), 7.26 (1H, t, *J* 7.4, Ar), 7.15 (1H, t, *J* 7.5, Ar), 7.01 (1H, dd, *J* 7.5, 1.4, Ar), 6.80-6.76 (2H, m, Ar), 6.74-6.67 (5H, m, Ar), 6.54 (2H, br s, Ar), 5.00 (1H, s, 2-H), 4.16-4.05 (1H, m, 5-H_A), 3.81-3.72 (7H, m, $OMe_{A\ and\ B}$ and 5-H_B), 3.62-3.55 (4H, m, 4-CH_2 and amidobenzyl-H), 3.26 (1H, br s, 3-H_A), 3.06 (1H, dd, *J* 13.2, 3.0, 3-H_B); ∂_C (125 MHz; $CDCl_3$) 167.3, 159.1, 159.0, 150.2, 147.4, 136.8, 130.6, 130.0, 129.1, 129.1, 129.0, 128.9, 128.8, 124.4, 114.1, 114.0, 113.9, 105.0, 62.8, 61.5, 59.1, 55.3, 55.2, 53.4, 51.8; *m/z* (ES) [M+H$^+$] 617 (100%, M+H$^+$); HRMS Found: 617.2076, M+H$^+$ requires 617.2064.

References

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5. W. F. McCalmont, J. R. Patterson, M. A. Lindenmuth, T. N. Heady, D. M. Haverstick, L. S. Gray and T. L. Macdonald, *Bioorg. Med. Chem.*, 2005, **13,** 3821.
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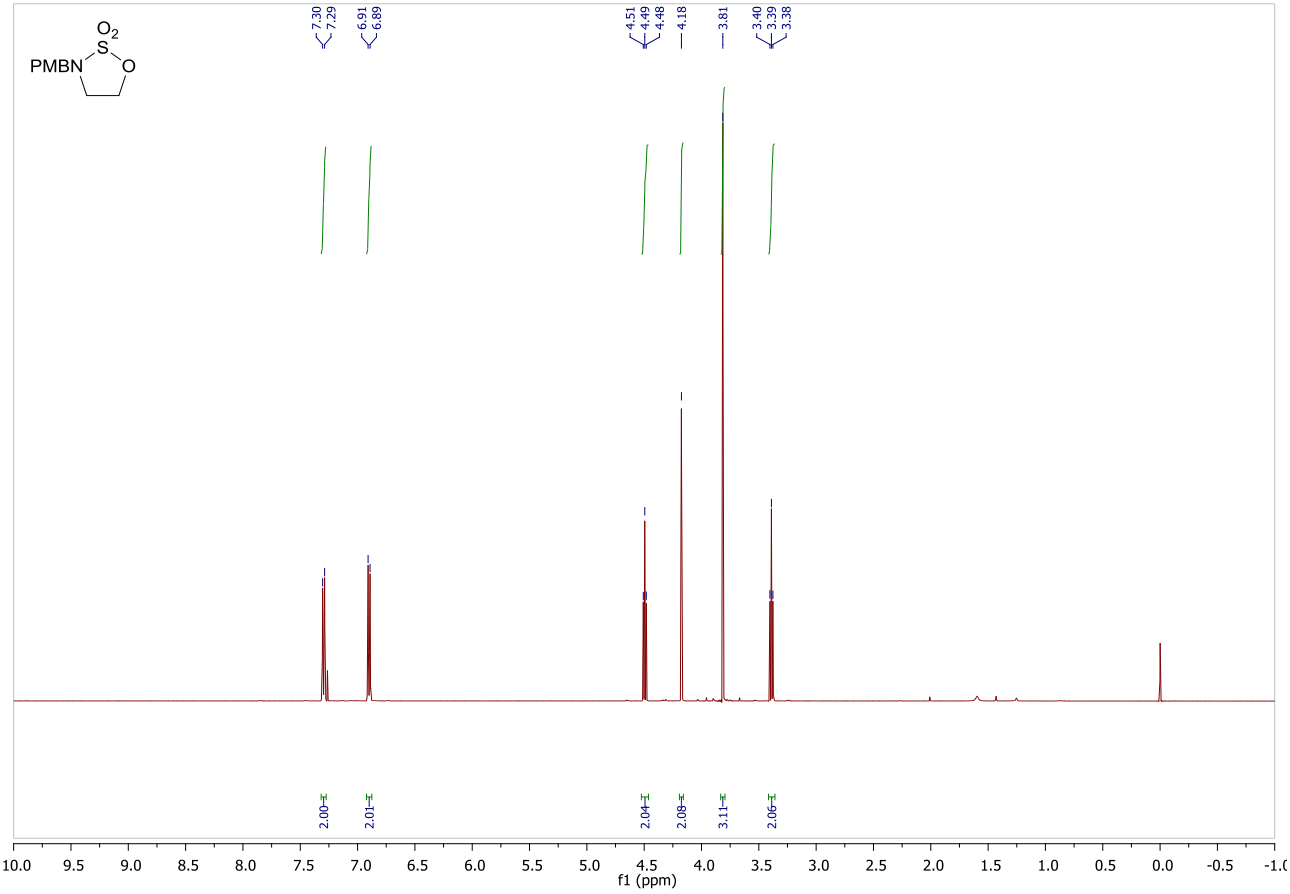
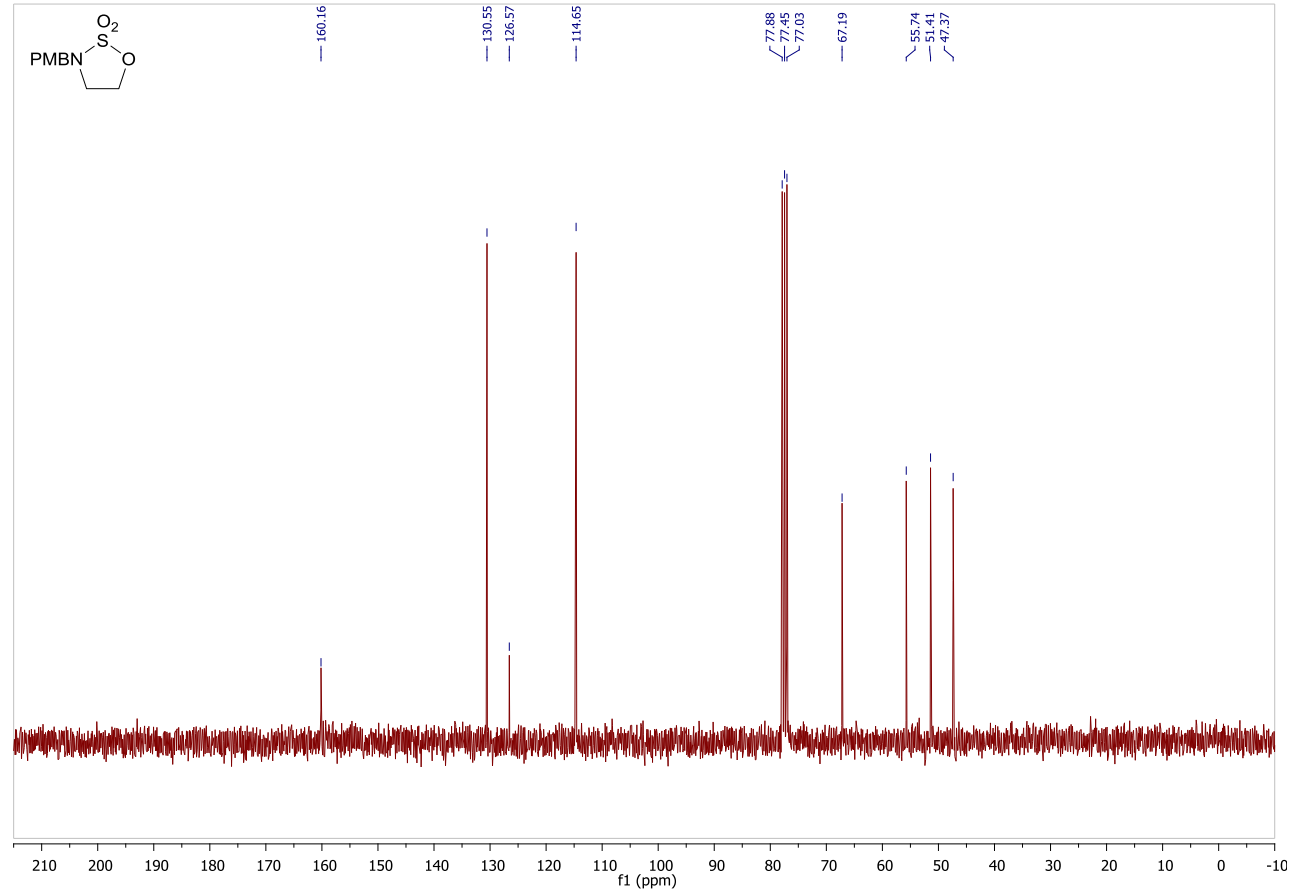
8. W. Kurosawa, T. Kan, and T. Fukuyama, *J. Am. Chem. Soc.*, 2003, **125**, 8112.
9. The piperazine **10a** and the diazepane **10b** are commercially available.

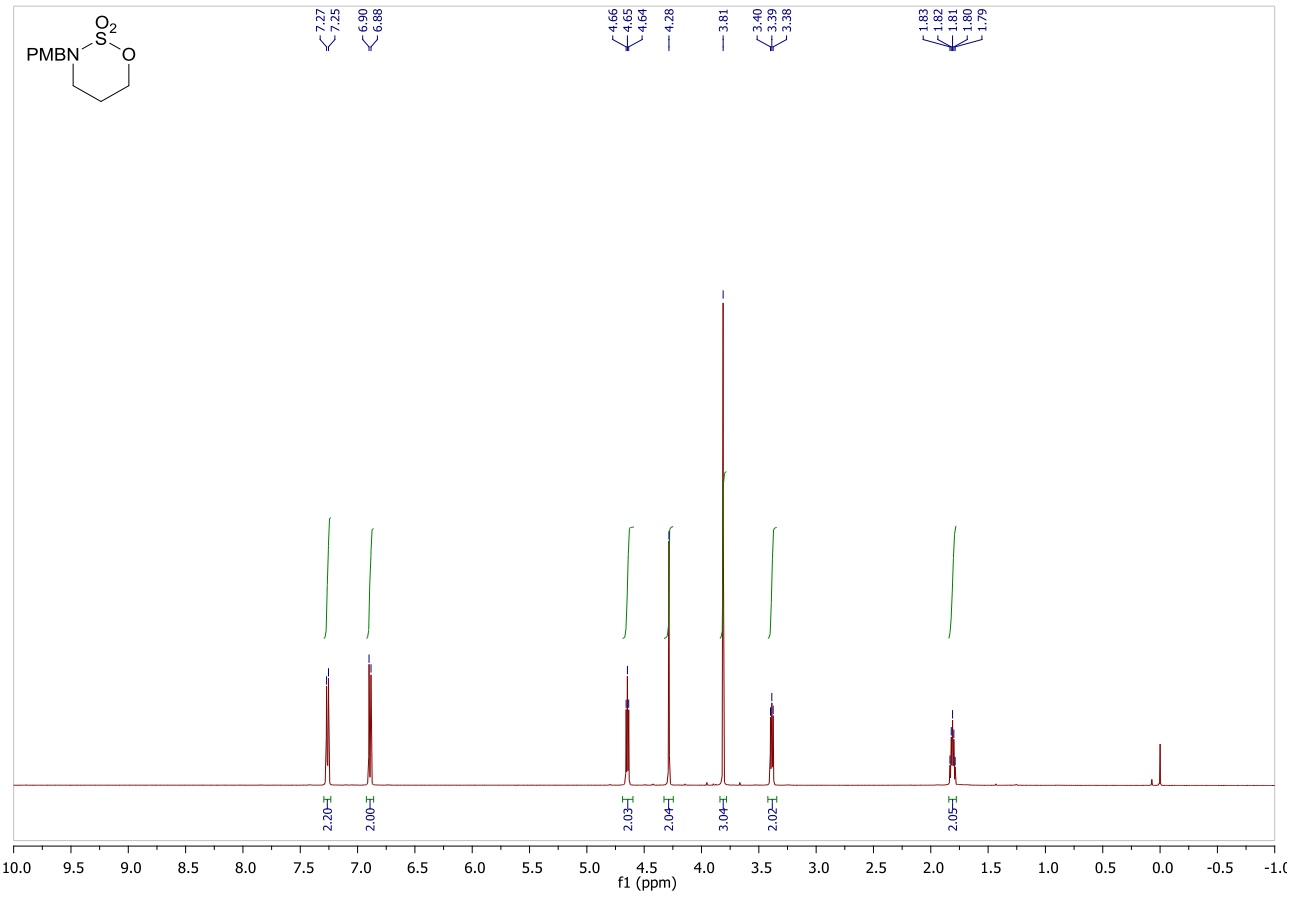
Spectra of products of key transformations

7a





7b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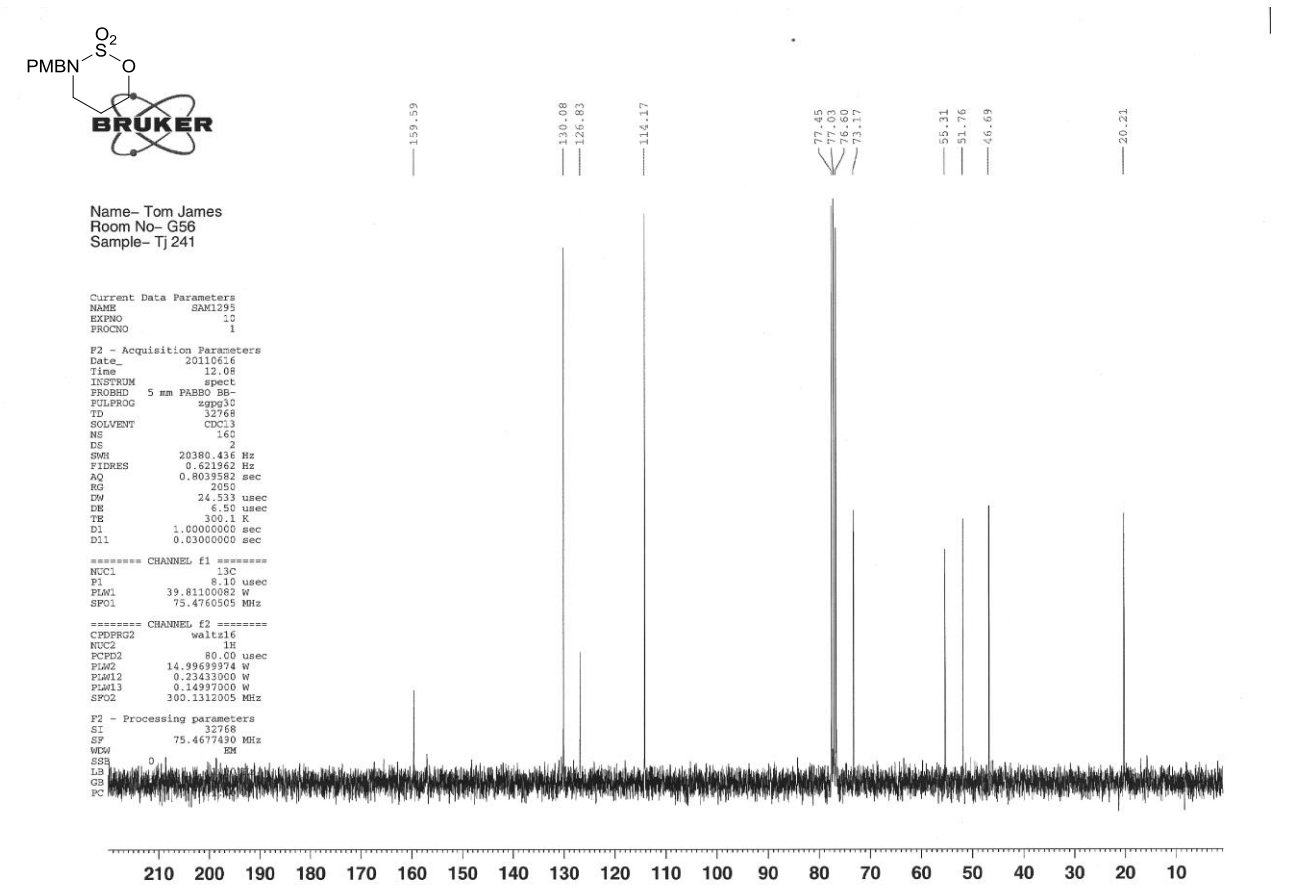
3.04
2.02
2.05
f1 (ppm)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Sample- Tj 241
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PROCNO 1
F2 - Acquisition Parameters
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Time 12.08
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FIDRES 0.621962 Hz
AQ 0.8039582 sec
RG 2050
DW 24.533 usec
DE 6.50 usec
TE 300.1 K
D1 1.00000000 sec
D11 0.03000000 sec
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NUC1 13C
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SFO1 75.4760505 MHz
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PCPD2 80.00 usec
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F2 - Processing parameters
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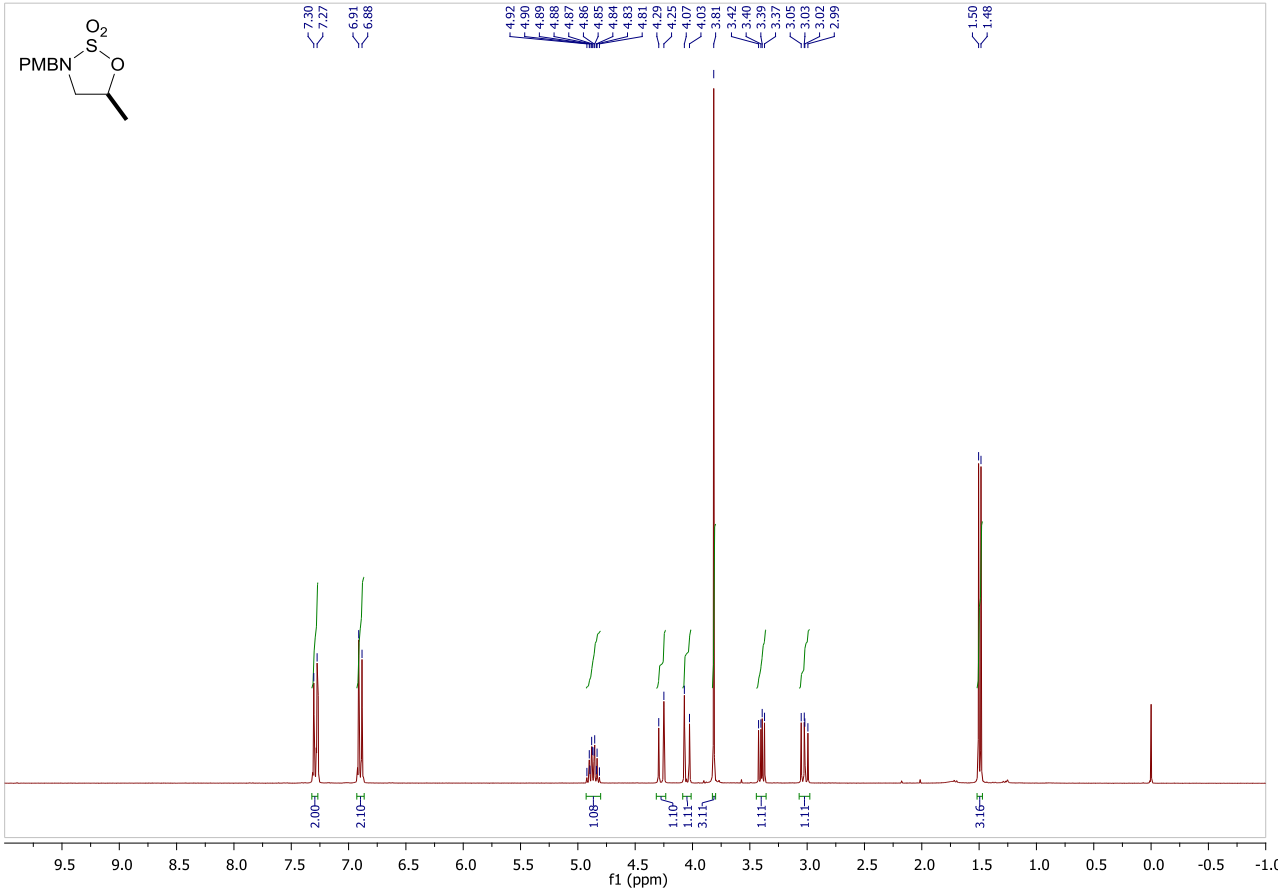
7c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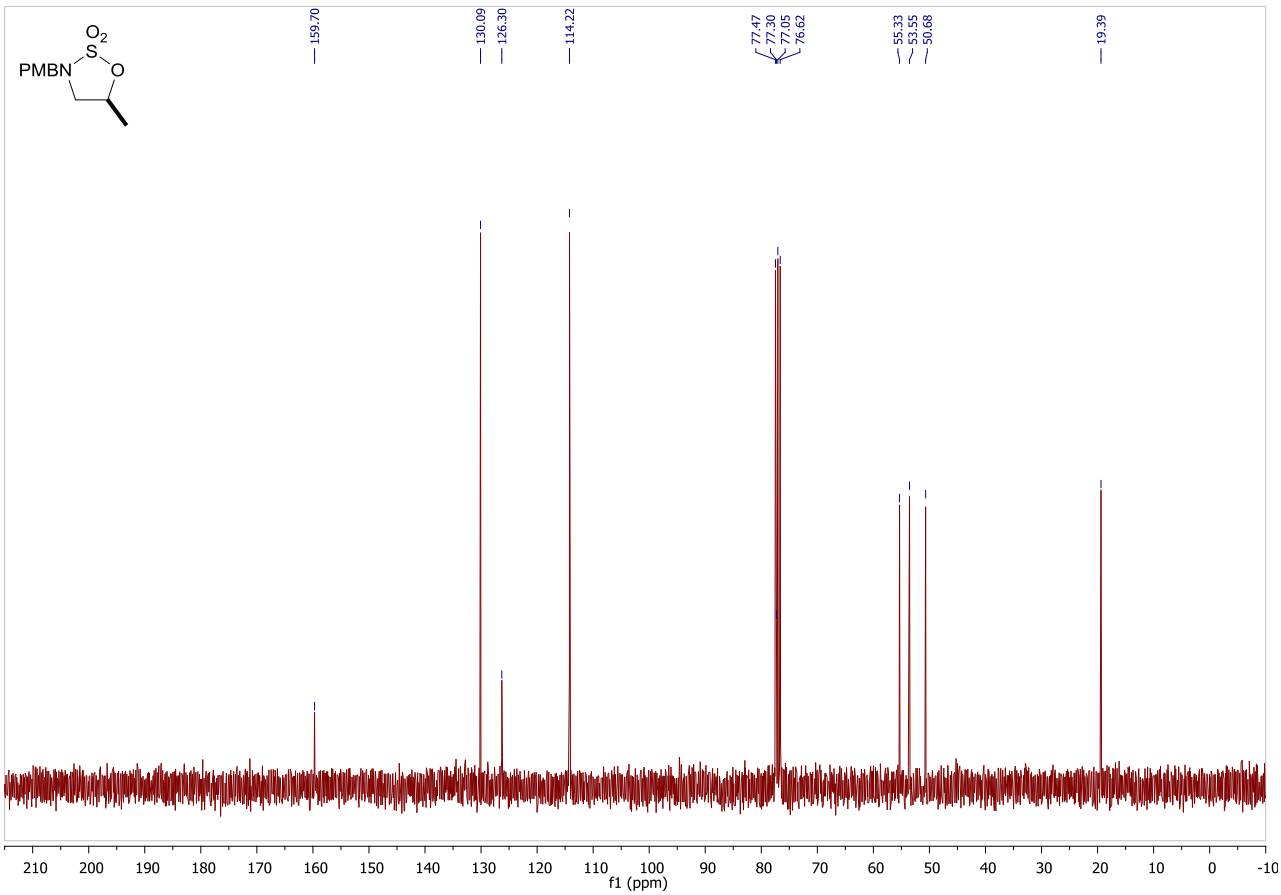
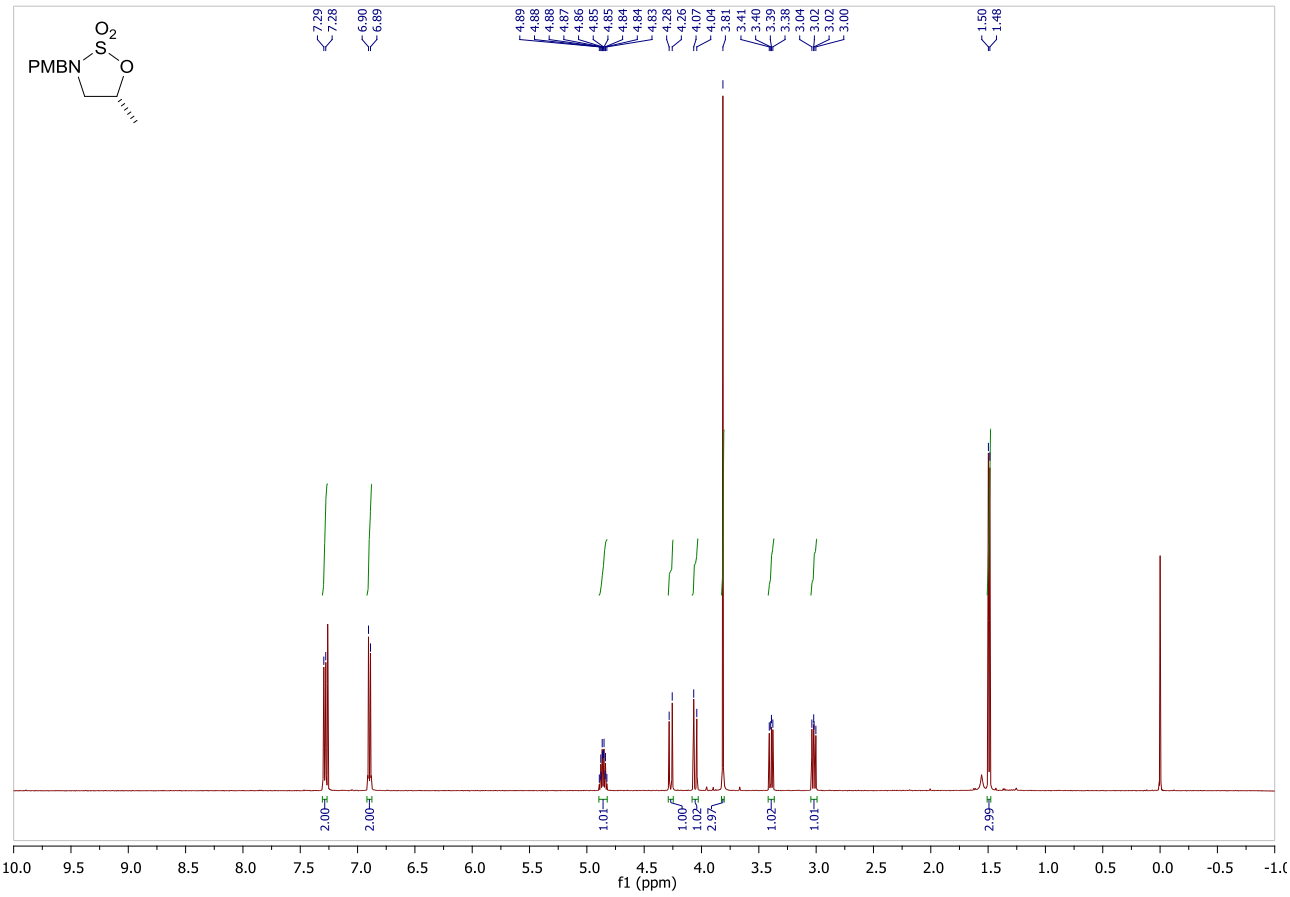
1.11
3.11
1.11
1.11
3.16
f1 (ppm)


PMBN
O2
S
O
159.70
130.09
126.30
114.22
77.47
77.30
77.05
76.62
55.33
53.55
50.68
19.39
f1 (ppm)

7d


PMBN
O2
S
O
7.29
7.28
6.90
6.89
4.89
4.88
4.88
4.88
4.87
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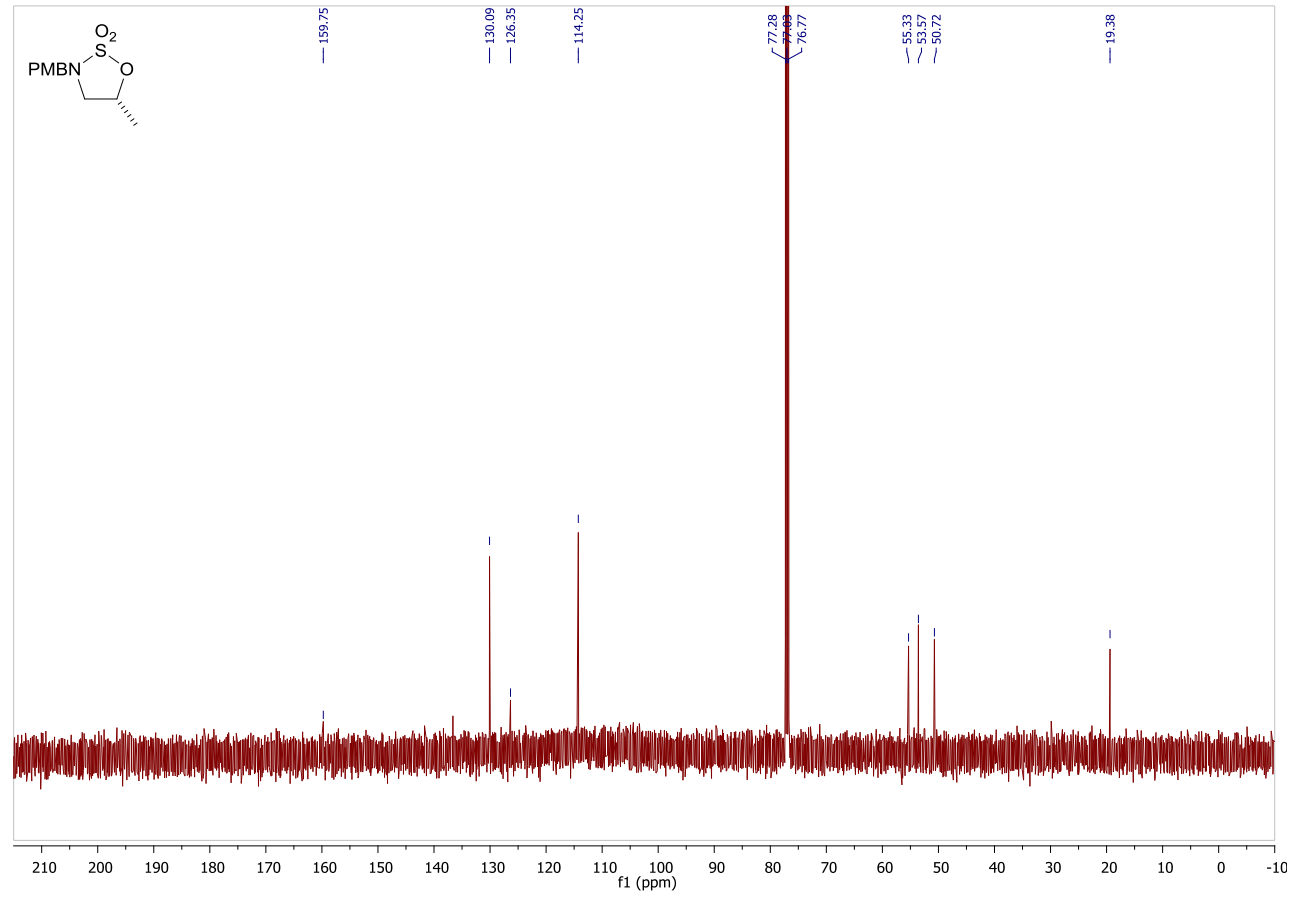
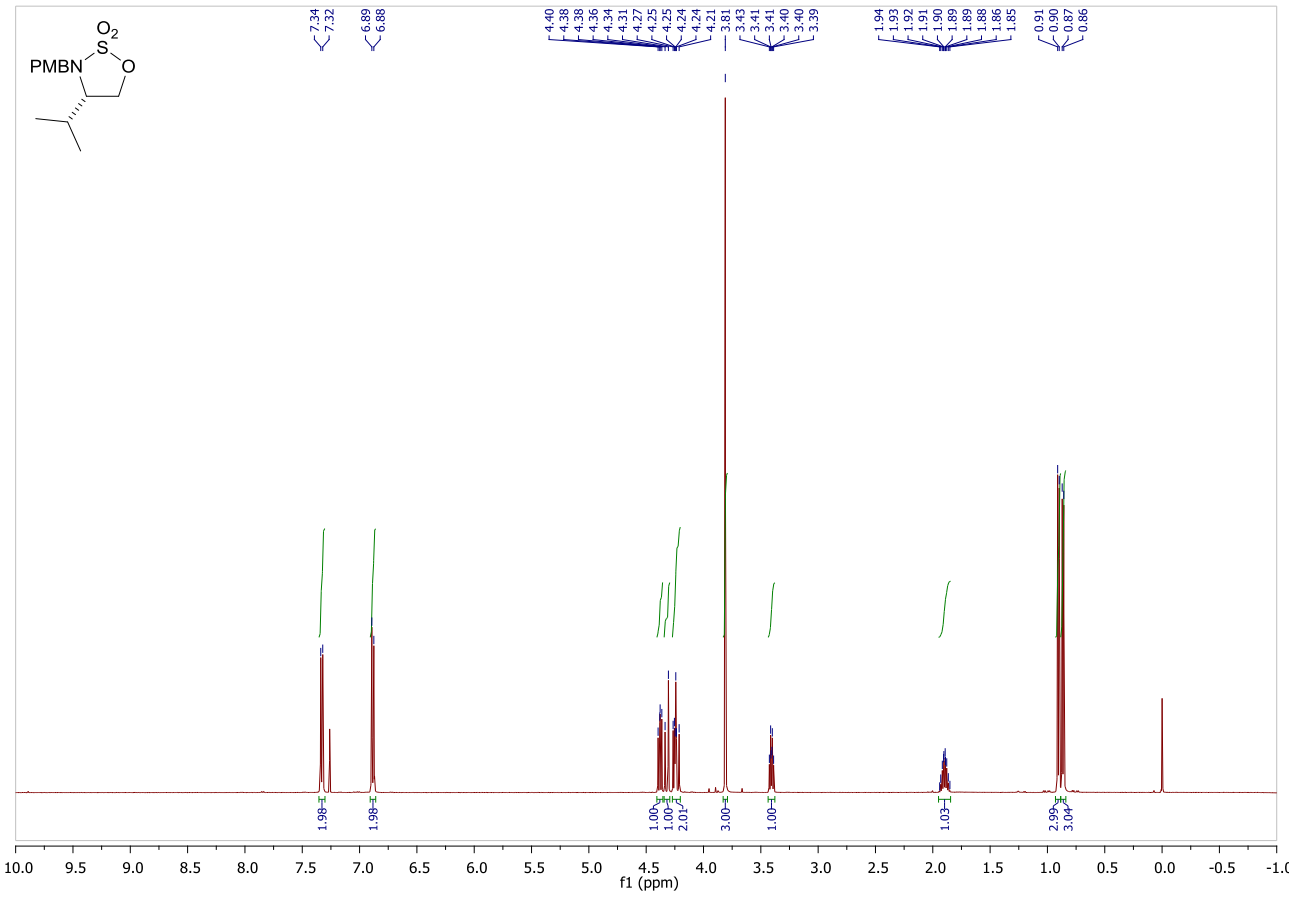
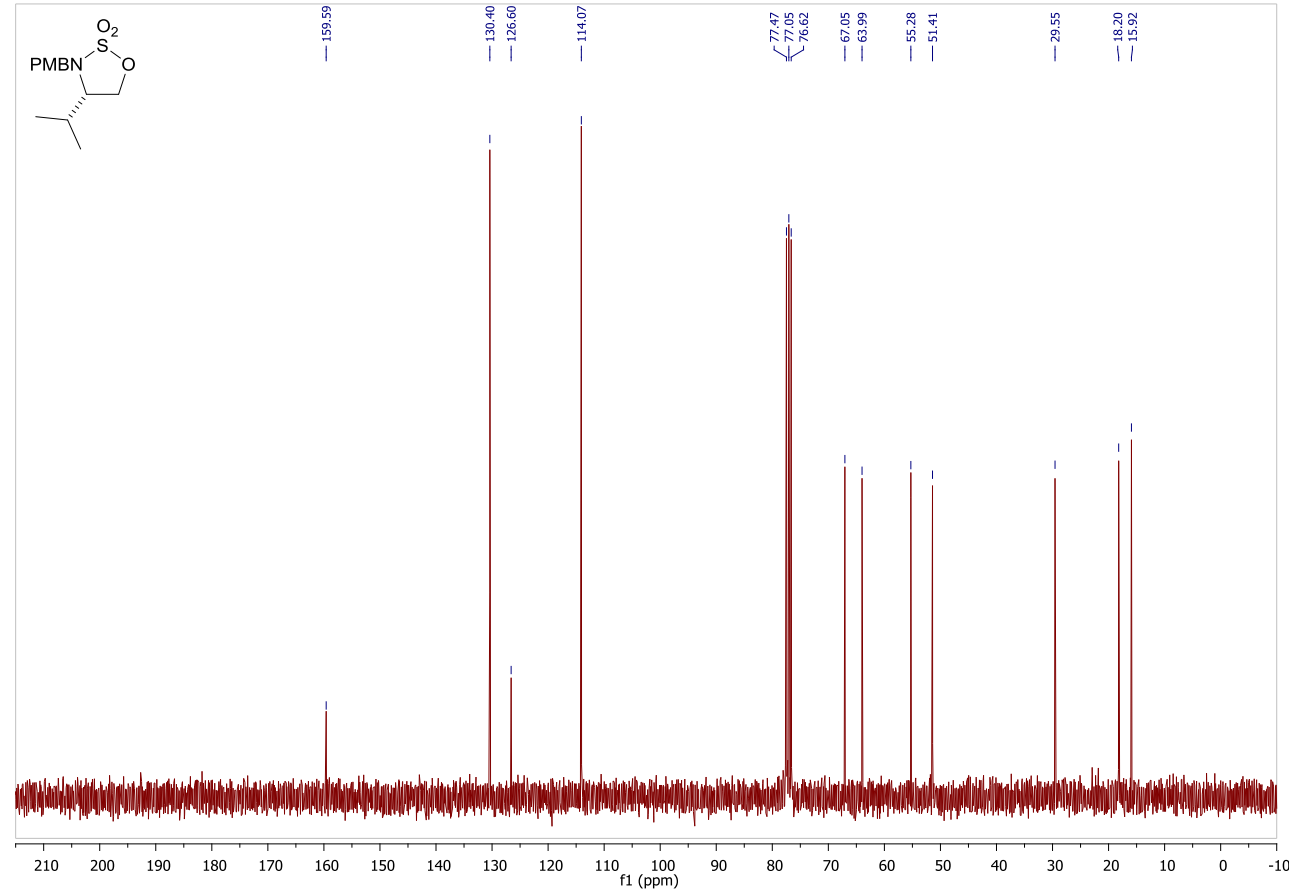
4.85
4.85
4.84
4.84
4.84
4.83
4.28
4.26
4.07
4.04
3.81
3.41
3.40
3.39
3.38
3.04
3.02
3.02
3.00
1.50
1.48
2.00
2.00
1.01
1.00
1.02
2.97
1.02
1.01
2.99
f1 (ppm)

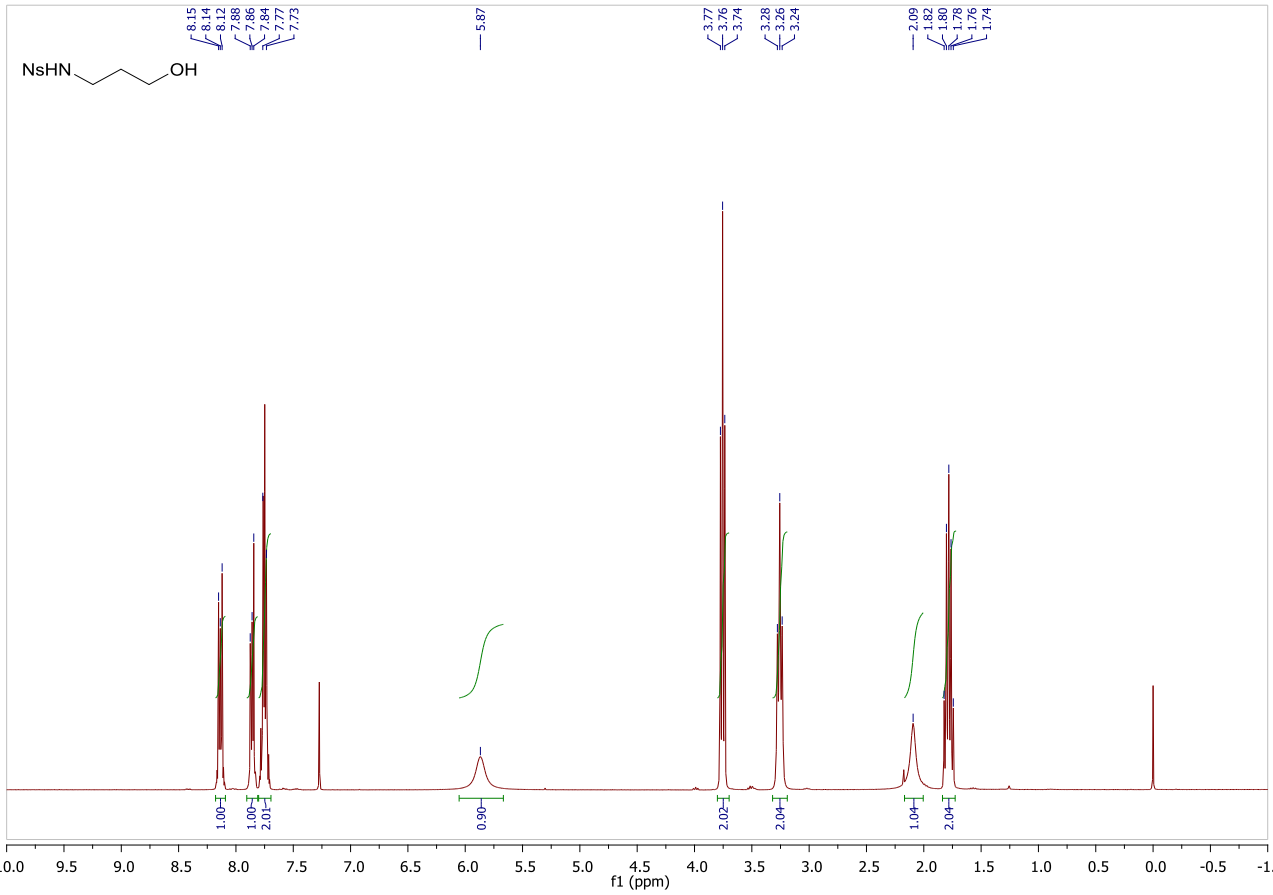

PMBN
O2
S
O
159.75
130.09
126.35
114.25
77.28
77.03
76.77
55.33
53.57
50.72
19.38
f1 (ppm)

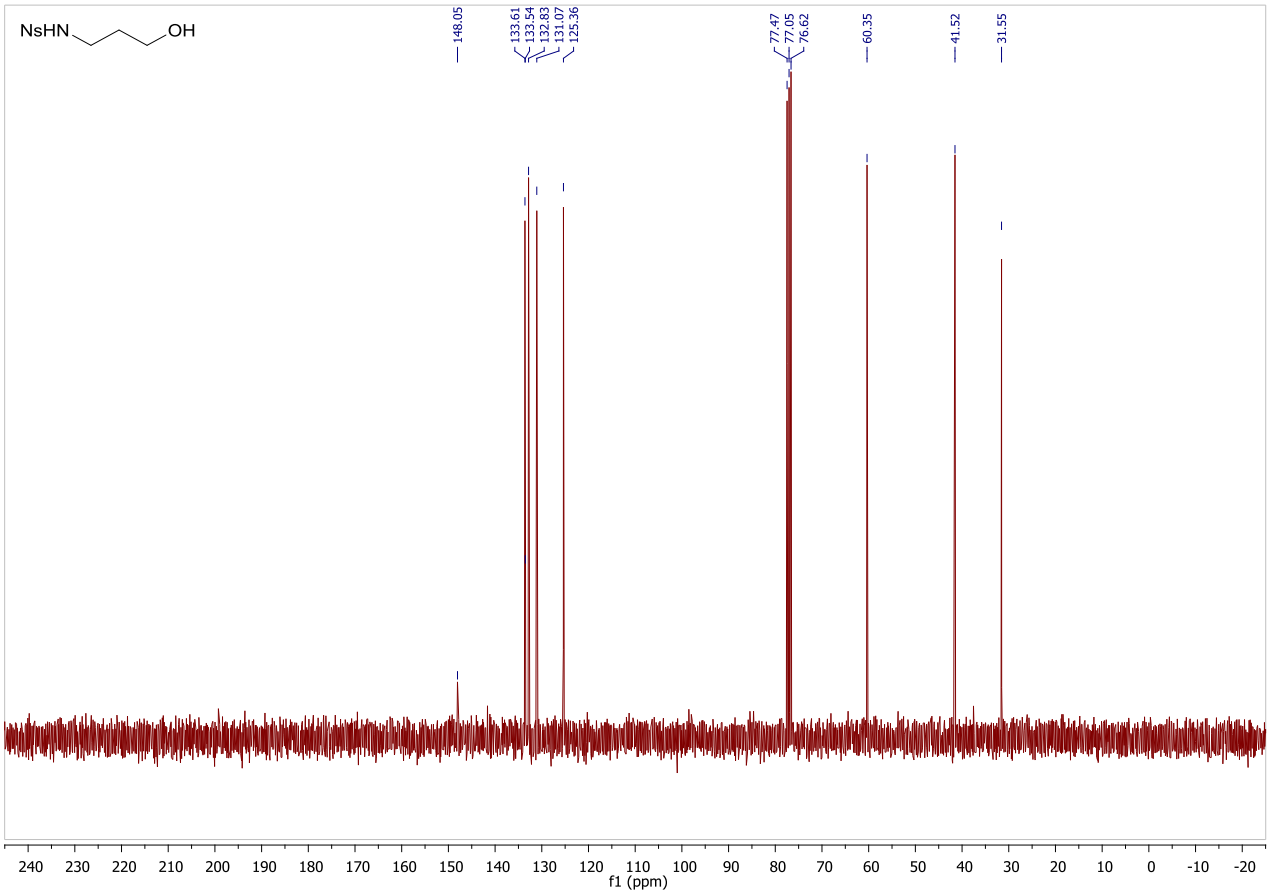
7e


PMBN
O2
S
O
7.34
7.32
6.89
6.88
4.40
4.38
4.38
4.36
4.34
4.31
4.27
4.25
4.25
4.24
4.24
4.21
3.81
3.43
3.41
3.41
3.40
3.40
3.39
1.94
1.93
1.92
1.91
1.90
1.89
1.89
1.88
1.86
1.85
0.91
0.90
0.87
0.86
1.98
1.98
1.00
1.00
2.01
3.00
1.00
1.03
2.99
3.04
f1 (ppm)

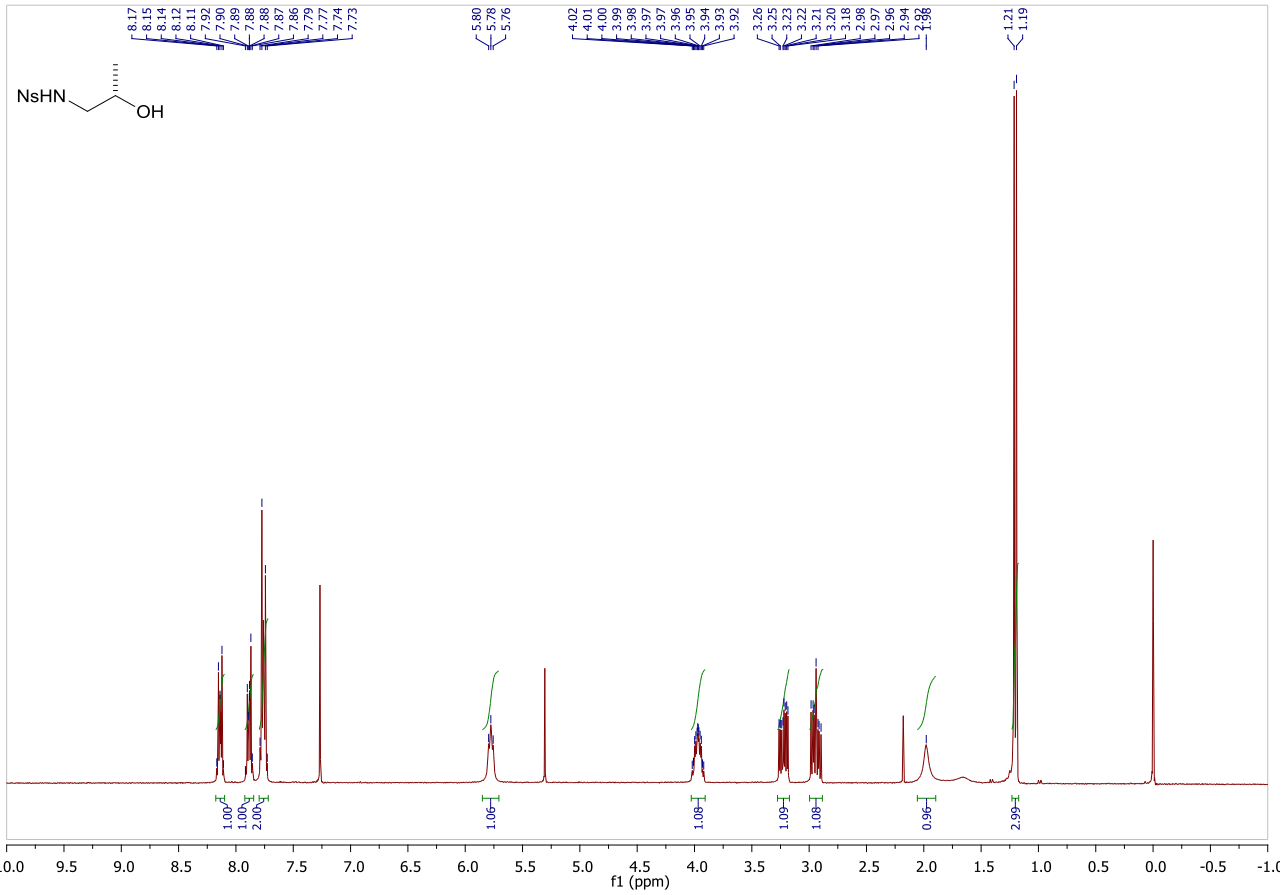

PMBN
O2
S
O
159.59
130.40
126.60
114.07
77.47
77.05
76.62
67.05
63.99
55.28
51.41
29.55
18.20
15.92
f1 (ppm)

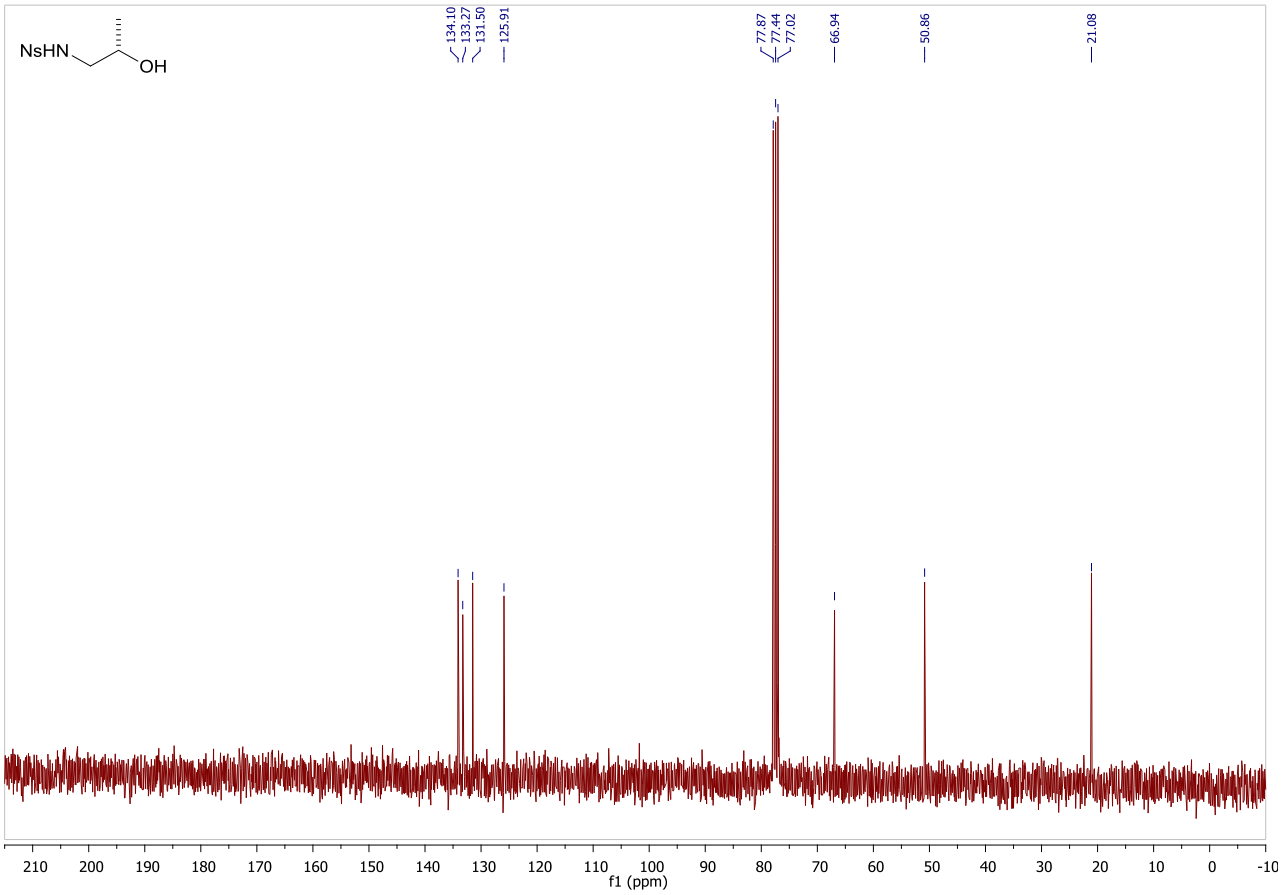
8b


NsHN
OH
8.15
8.14
8.12
7.88
7.86
7.84
7.77
7.73
5.87
3.77
3.76
3.74
3.28
3.26
3.24
2.09
1.82
1.80
1.78
1.76
1.74
1.00
1.00
2.01
0.90
2.02
2.04
1.04
2.04
f1 (ppm)

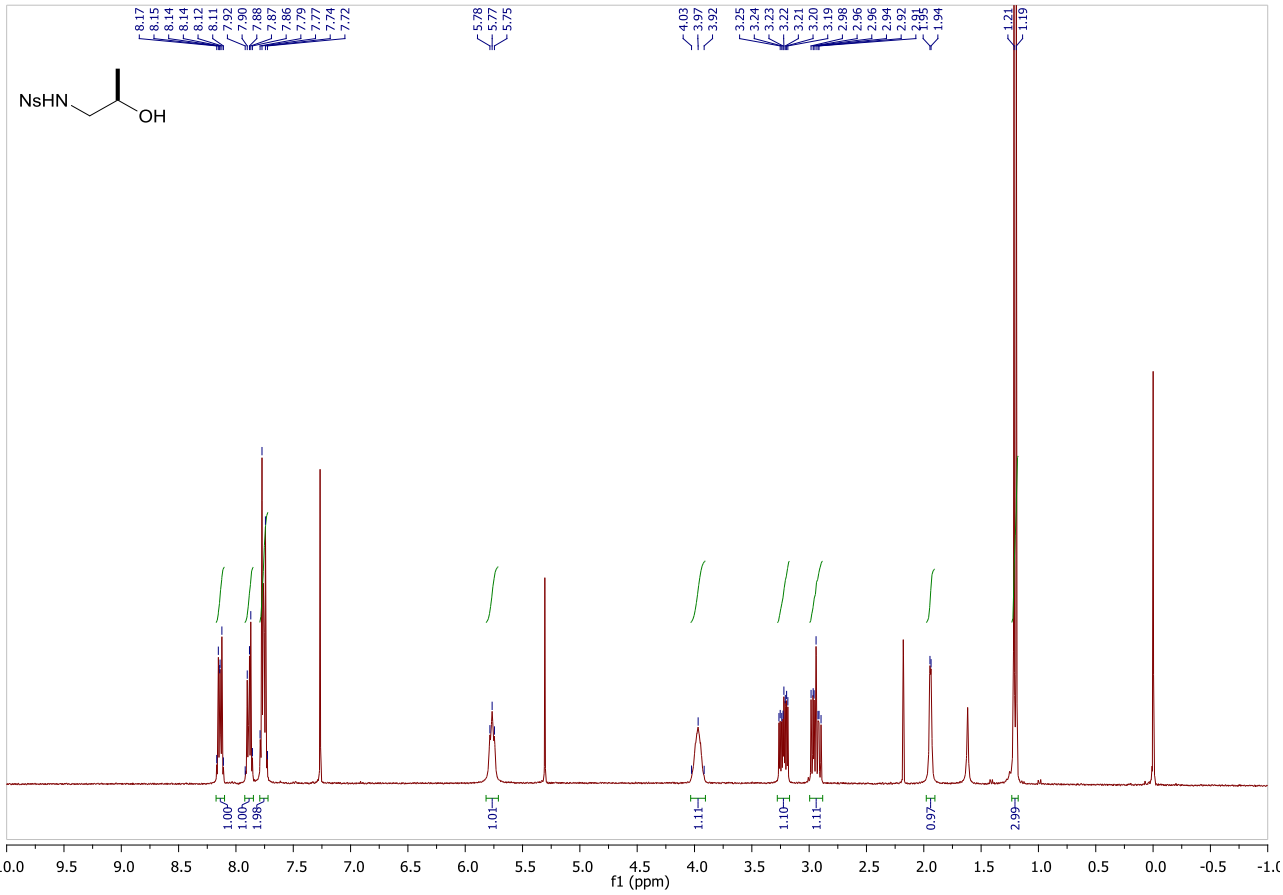

NsHN
OH
148.05
133.61
133.54
132.83
131.07
125.36
77.47
77.05
76.62
60.35
41.52
31.55
f1 (ppm)

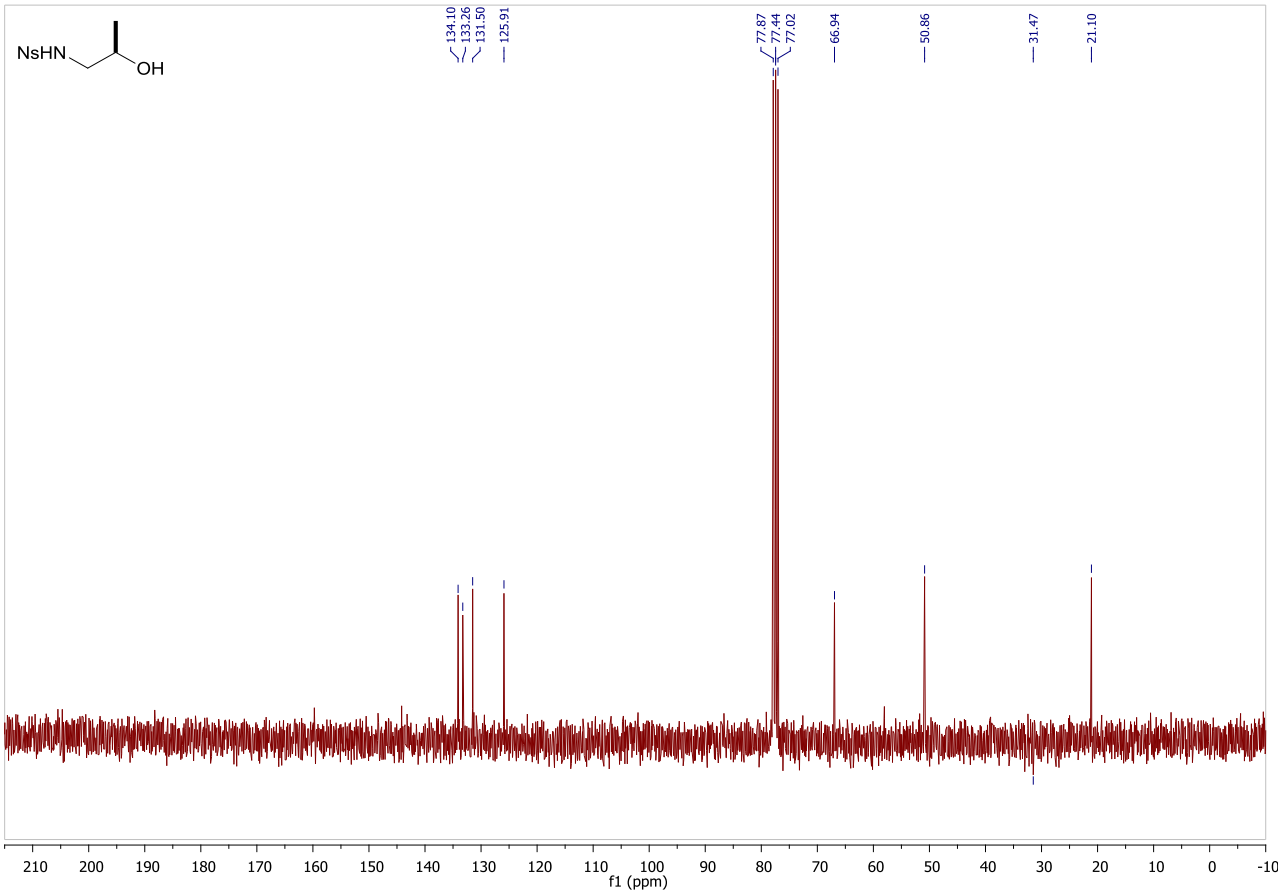
8c


NsHN
OH
8.17
8.15
8.14
8.12
8.11
7.92
7.90
7.89
7.88
7.88
7.87
7.86
7.79
7.77
7.74
7.73
5.80
5.78
5.76
4.02
4.01
4.00
3.99
3.98
3.97
3.97
3.96
3.95
3.94
3.93
3.92
3.26
3.25
3.23
3.22
3.21
3.20
3.18
2.98
2.97
2.96
2.94
1.98
1.21
1.19
1.00
1.00
2.00
1.06
1.08
1.09
1.08
0.96
2.99
f1 (ppm)

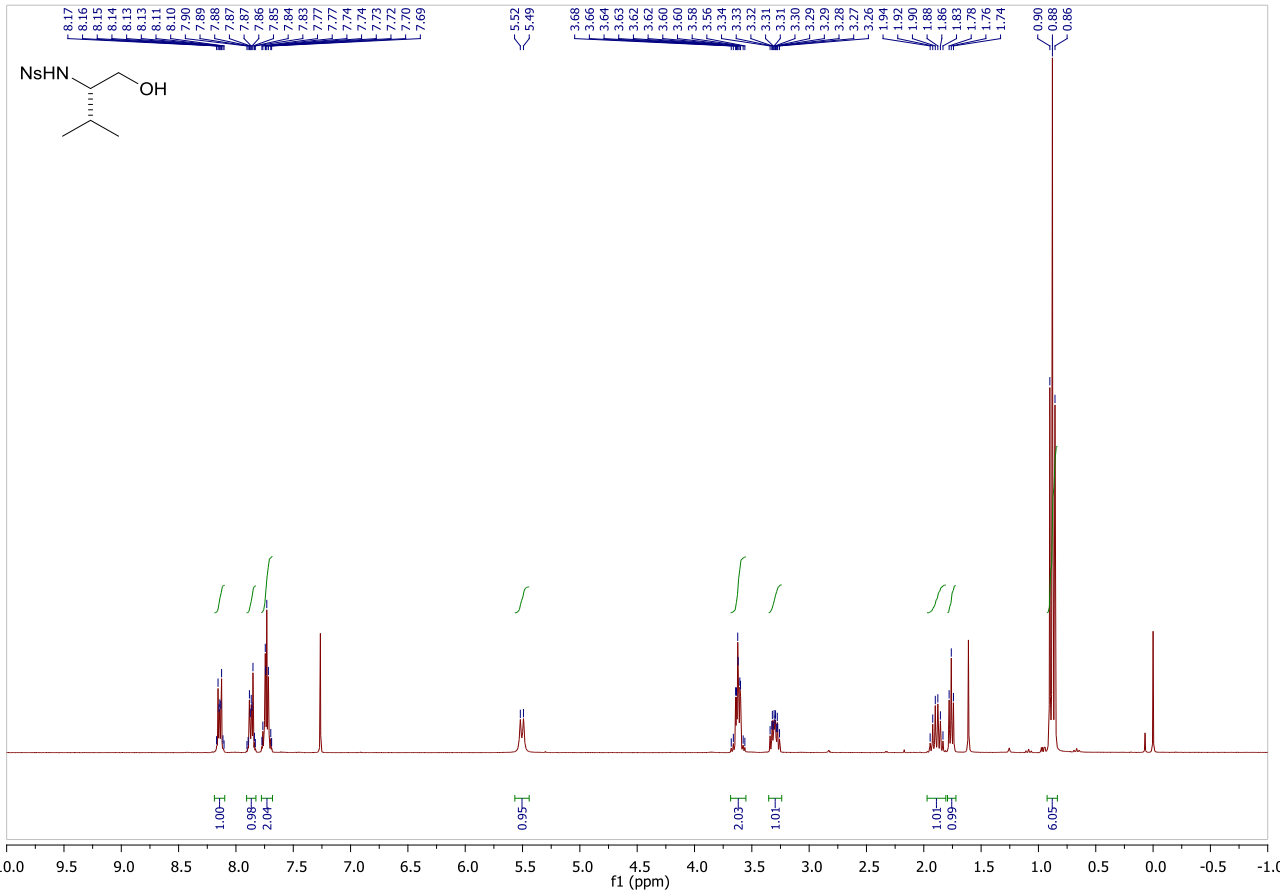

NsHN
OH
134.10
133.27
131.50
125.91
77.87
77.44
77.02
66.94
50.86
21.08
f1 (ppm)

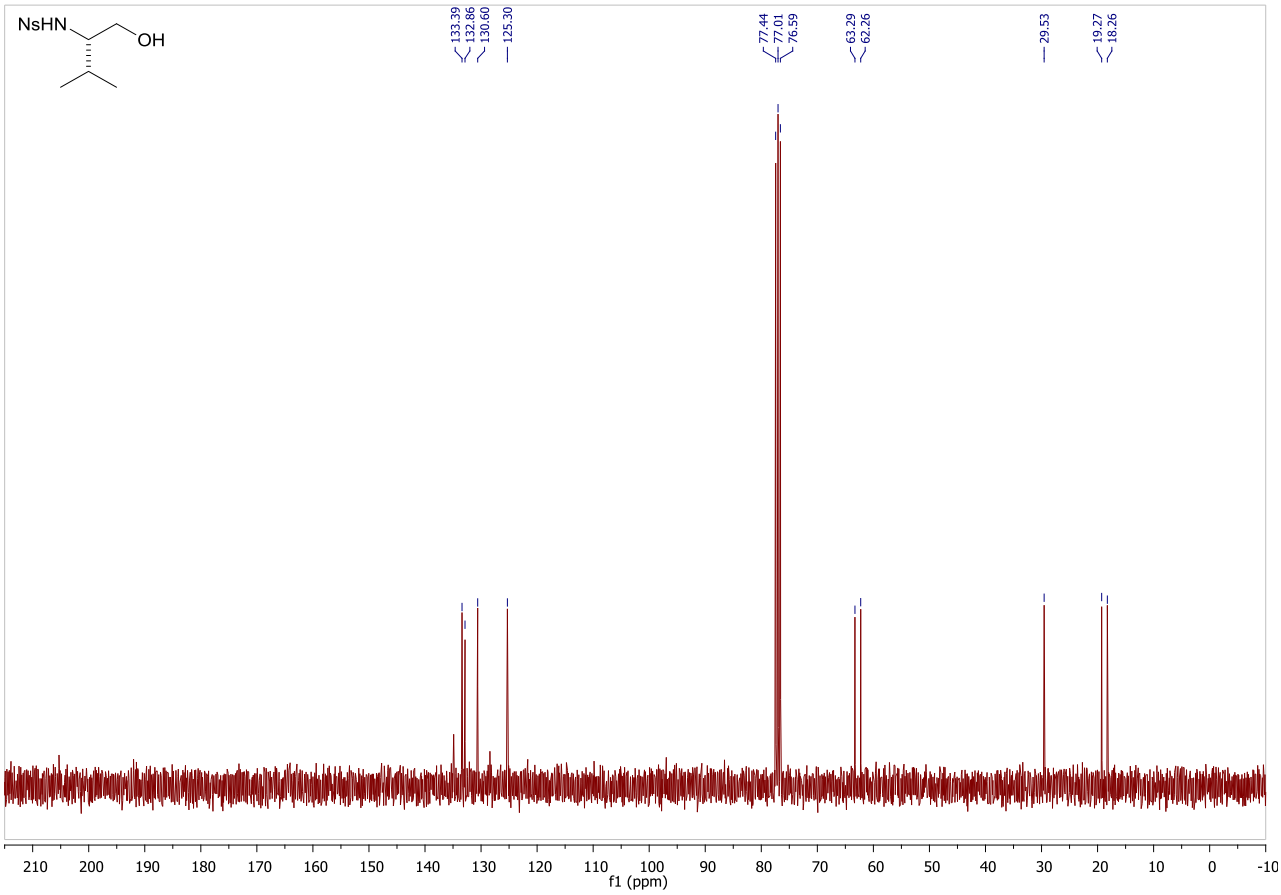
8d


NsHN
OH
8.17
8.15
8.14
8.14
8.12
8.11
7.92
7.90
7.88
7.87
7.86
7.79
7.77
7.74
7.72
5.78
5.77
5.75
4.03
3.97
3.92
3.25
3.24
3.23
3.22
3.21
3.20
3.19
2.98
2.96
2.96
2.94
2.92
1.95
1.94
1.21
1.19
1.00
1.00
1.98
1.01
1.11
1.10
1.11
0.97
2.99
f1 (ppm)

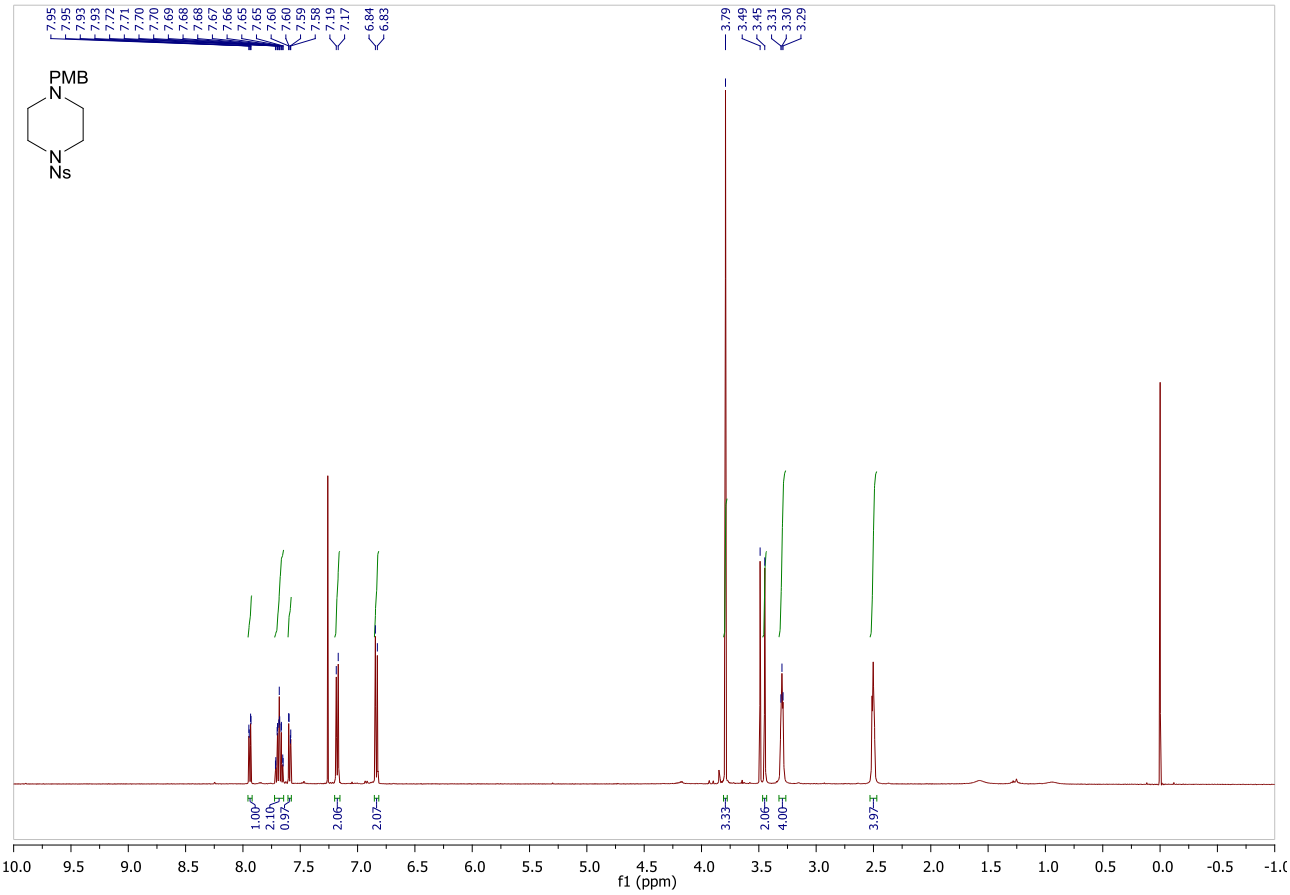

NsHN
OH
134.10
133.26
131.50
125.91
77.87
77.44
77.02
66.94
50.86
31.47
21.10
f1 (ppm)

8e

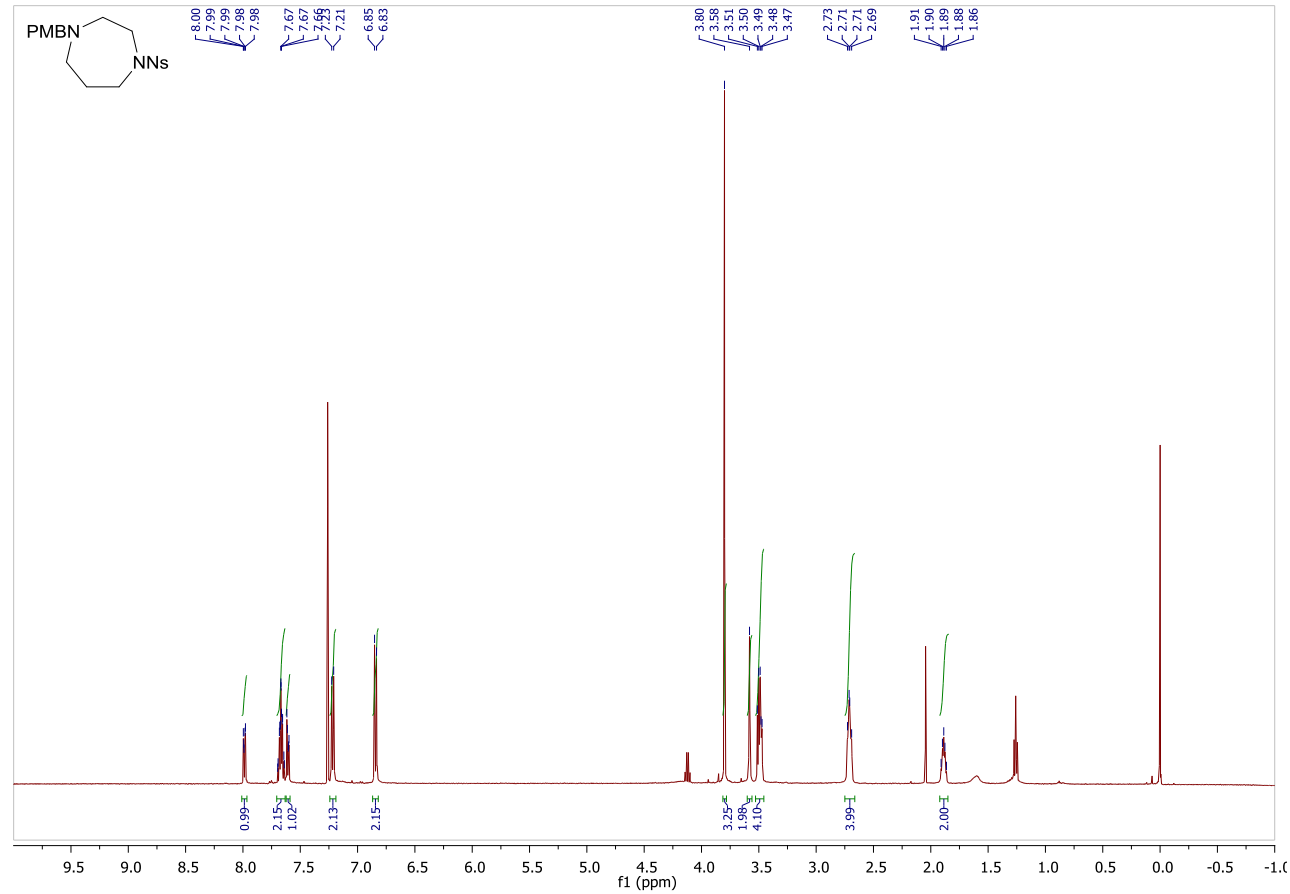




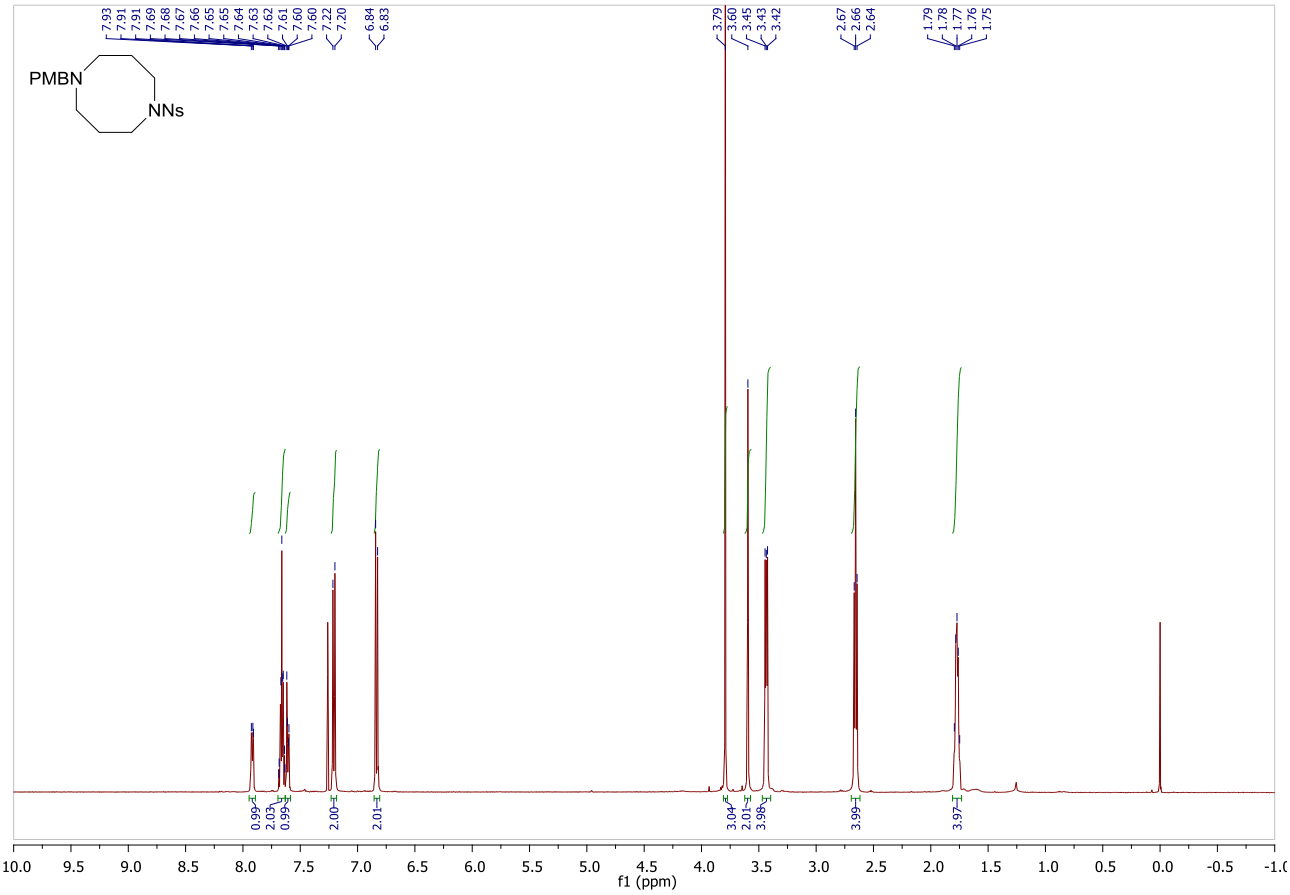
10a

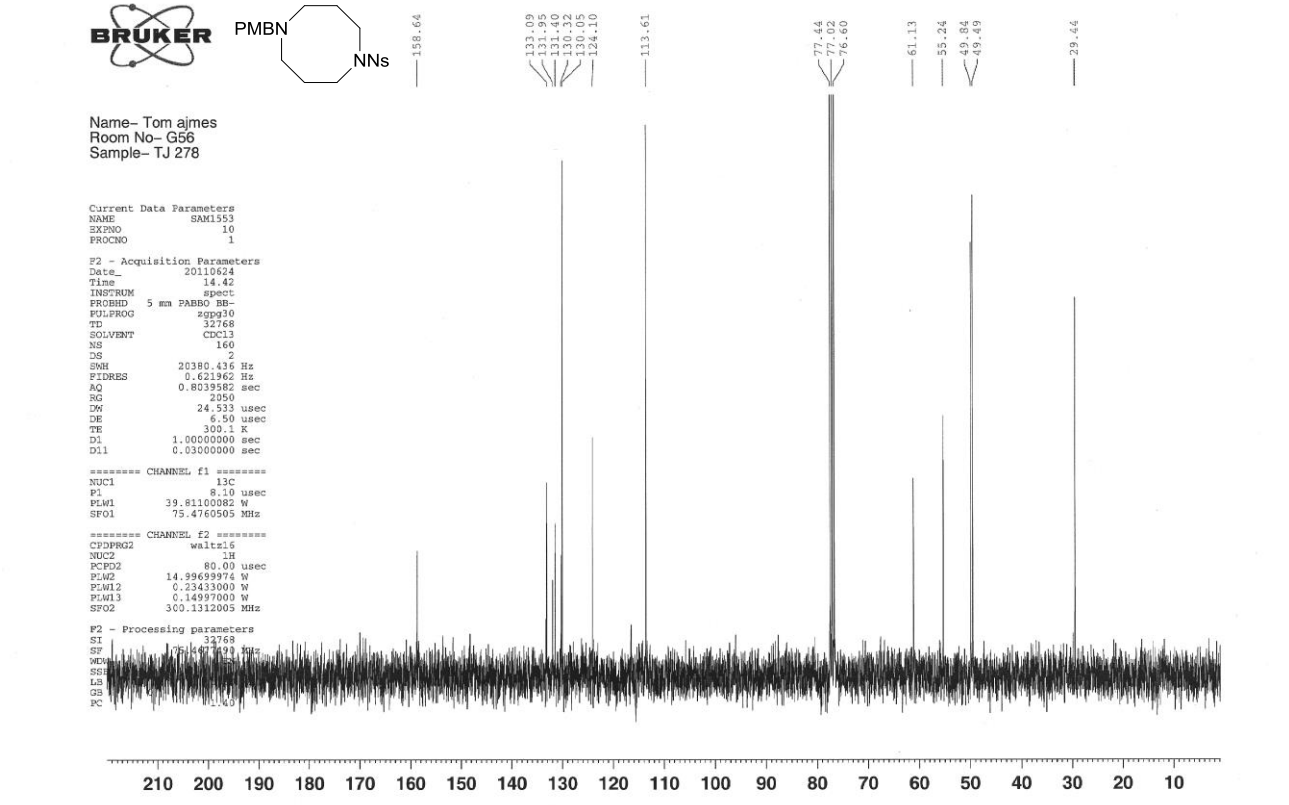


10b

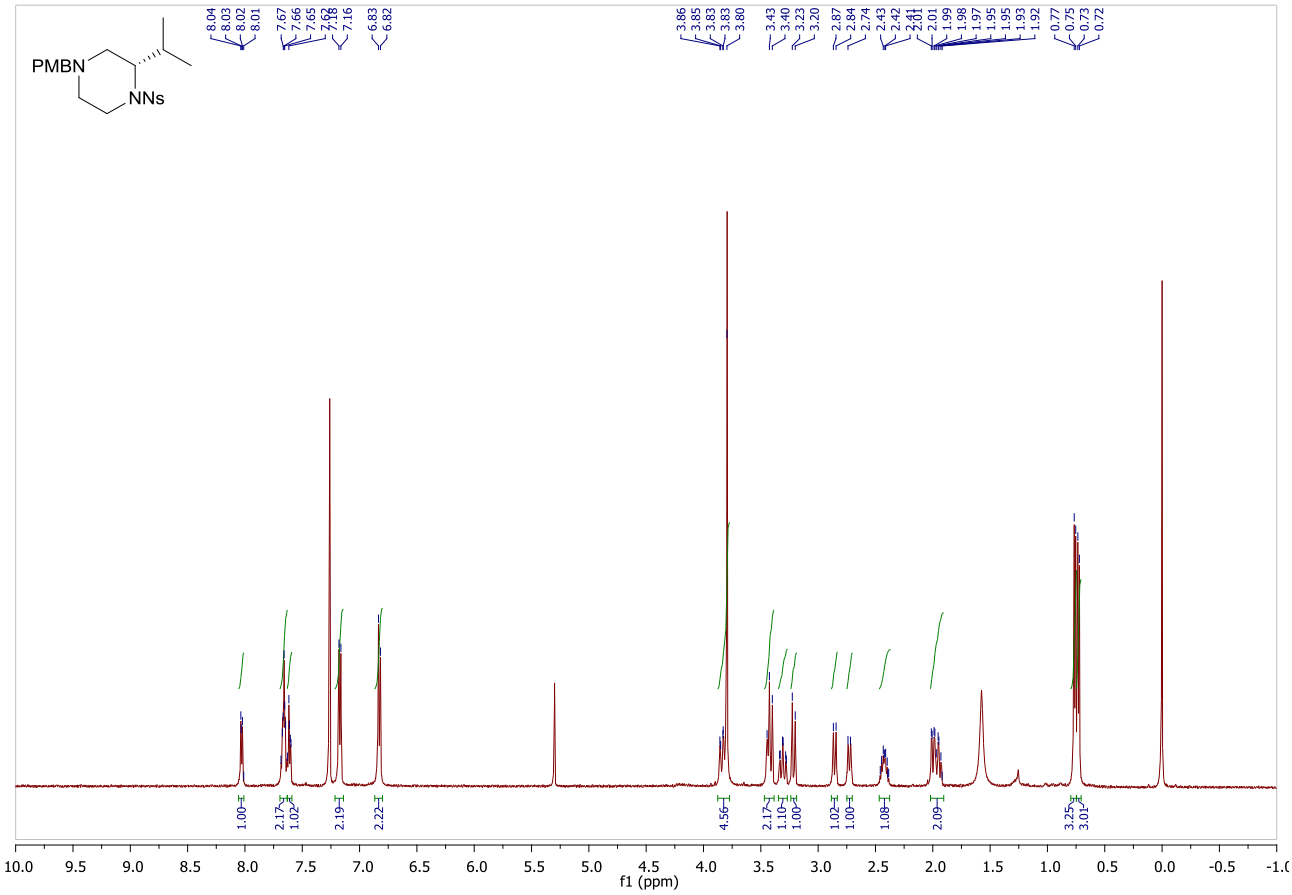


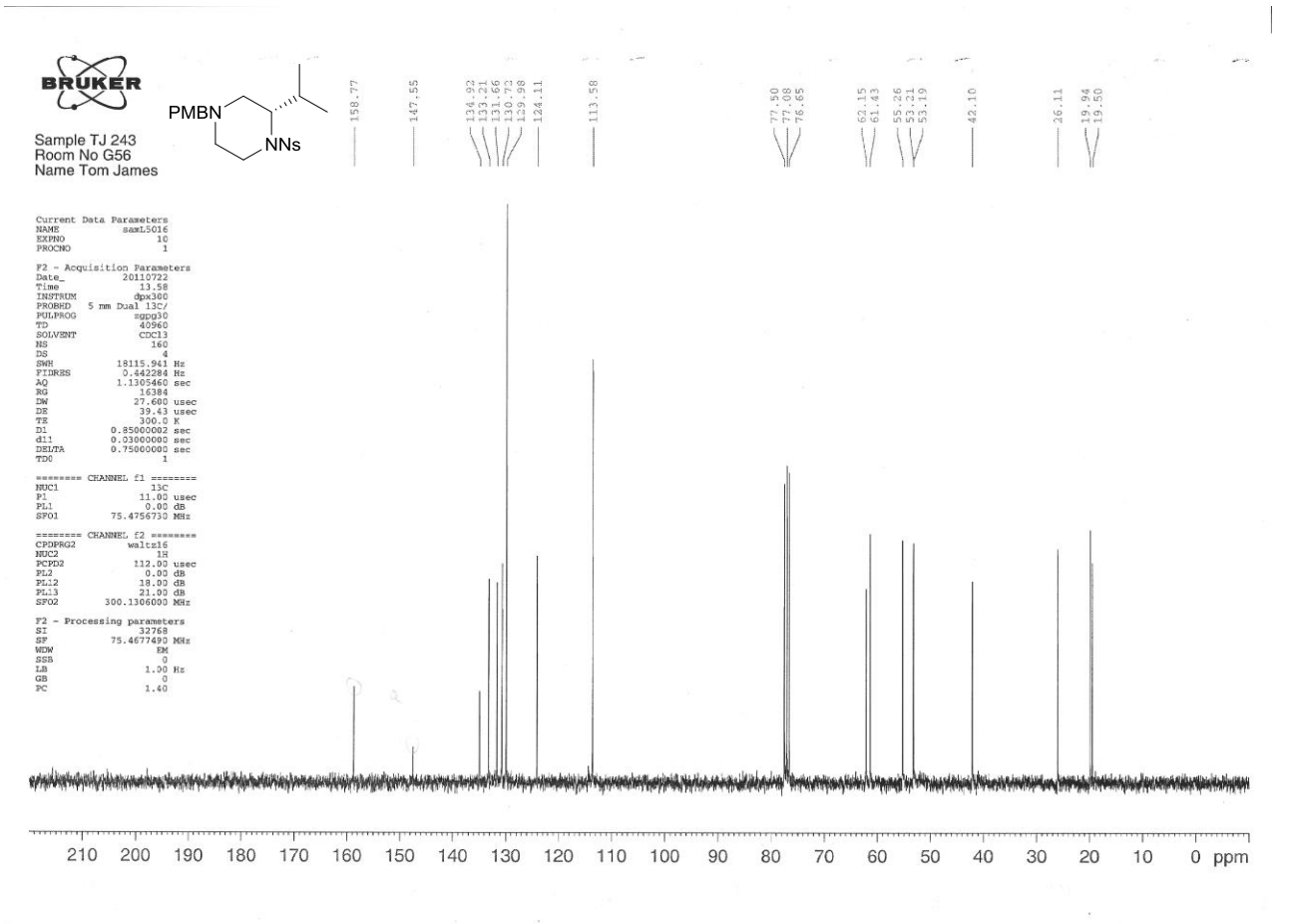
10c


PMBN
NNs
f1 (ppm)

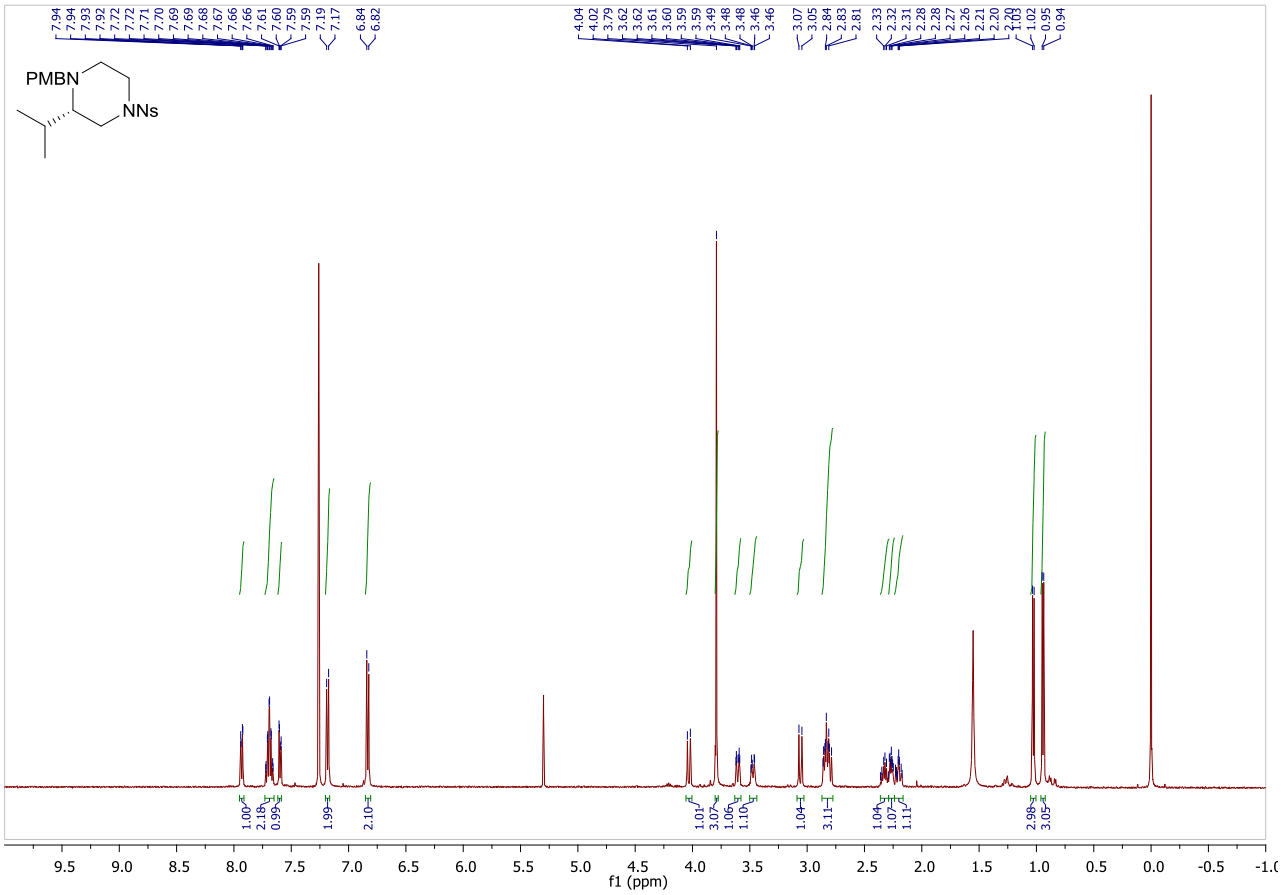

BRUKER
PMBN
NNs
Name- Tom ajmes
Room No- G56
Sample- TJ 278
f1 (ppm)

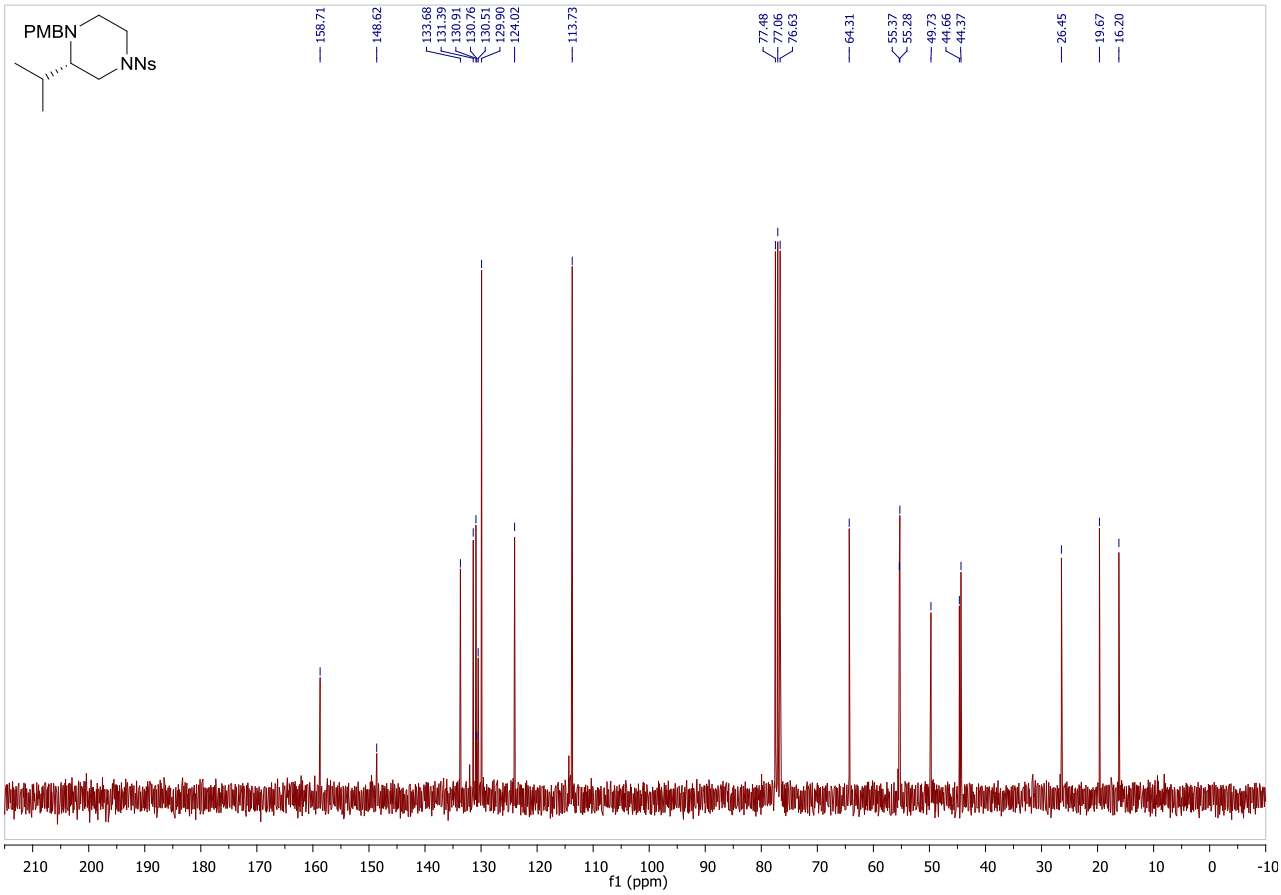
10d


PMBN
NNs
f1 (ppm)

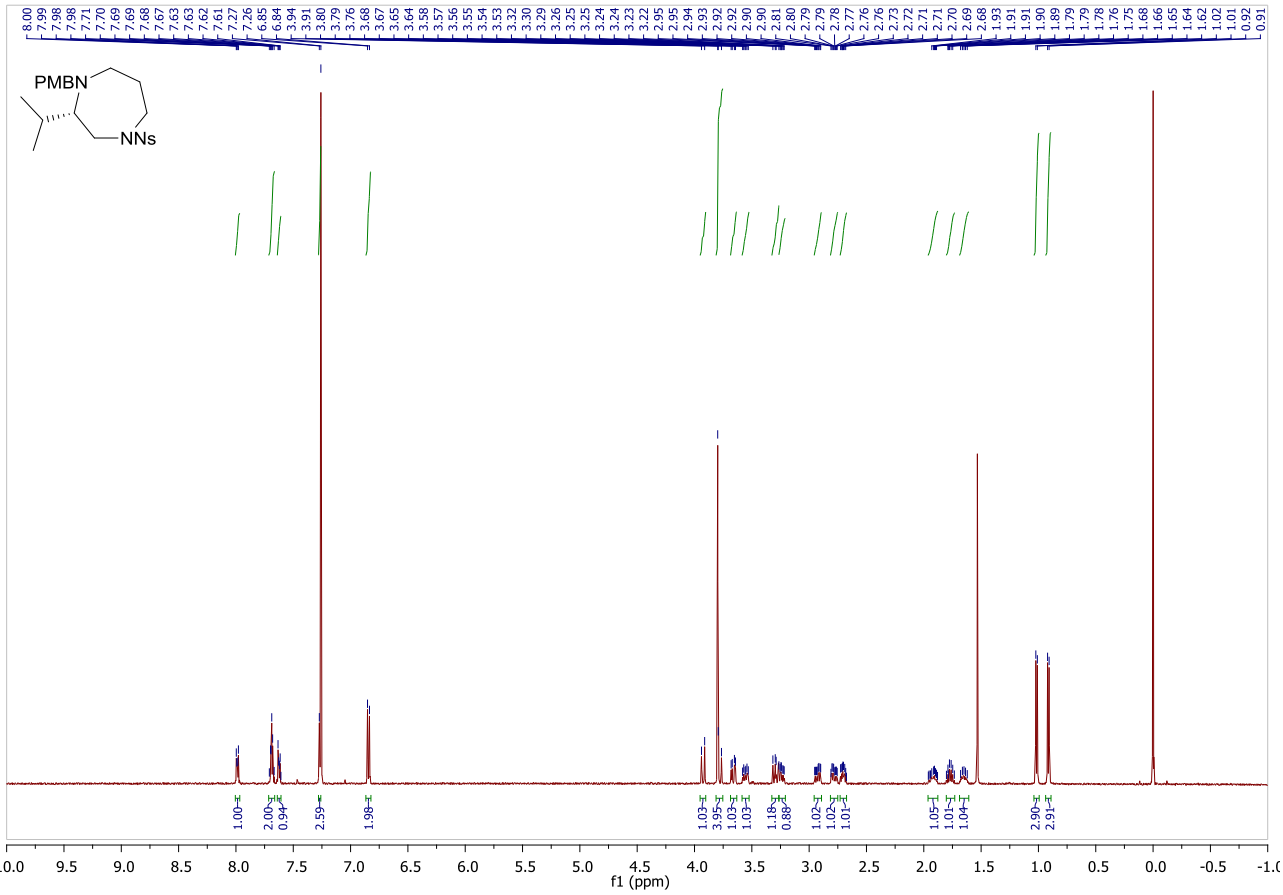

BRUKER
PMBN
NNs
Sample TJ 243
Room No G56
Name Tom James
ppm

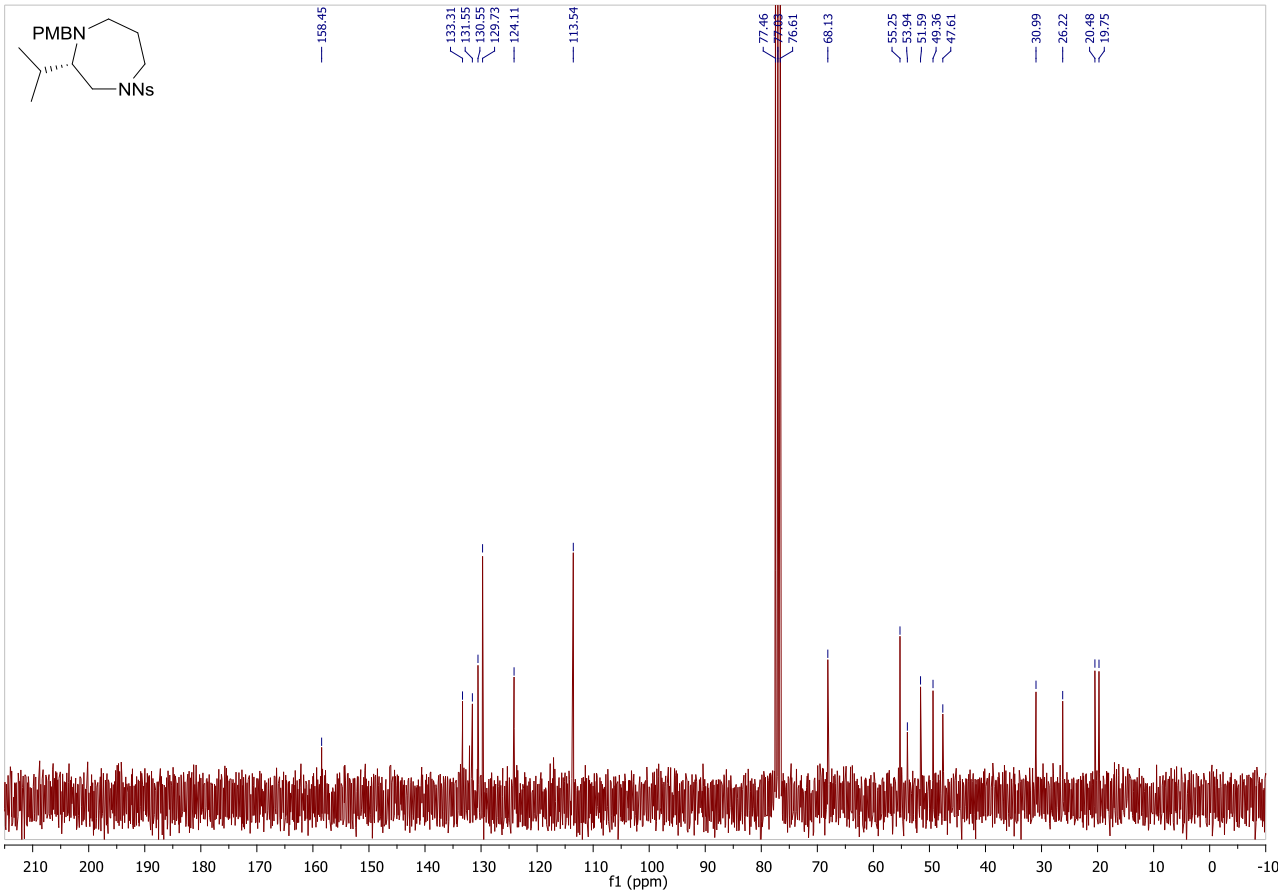
10e



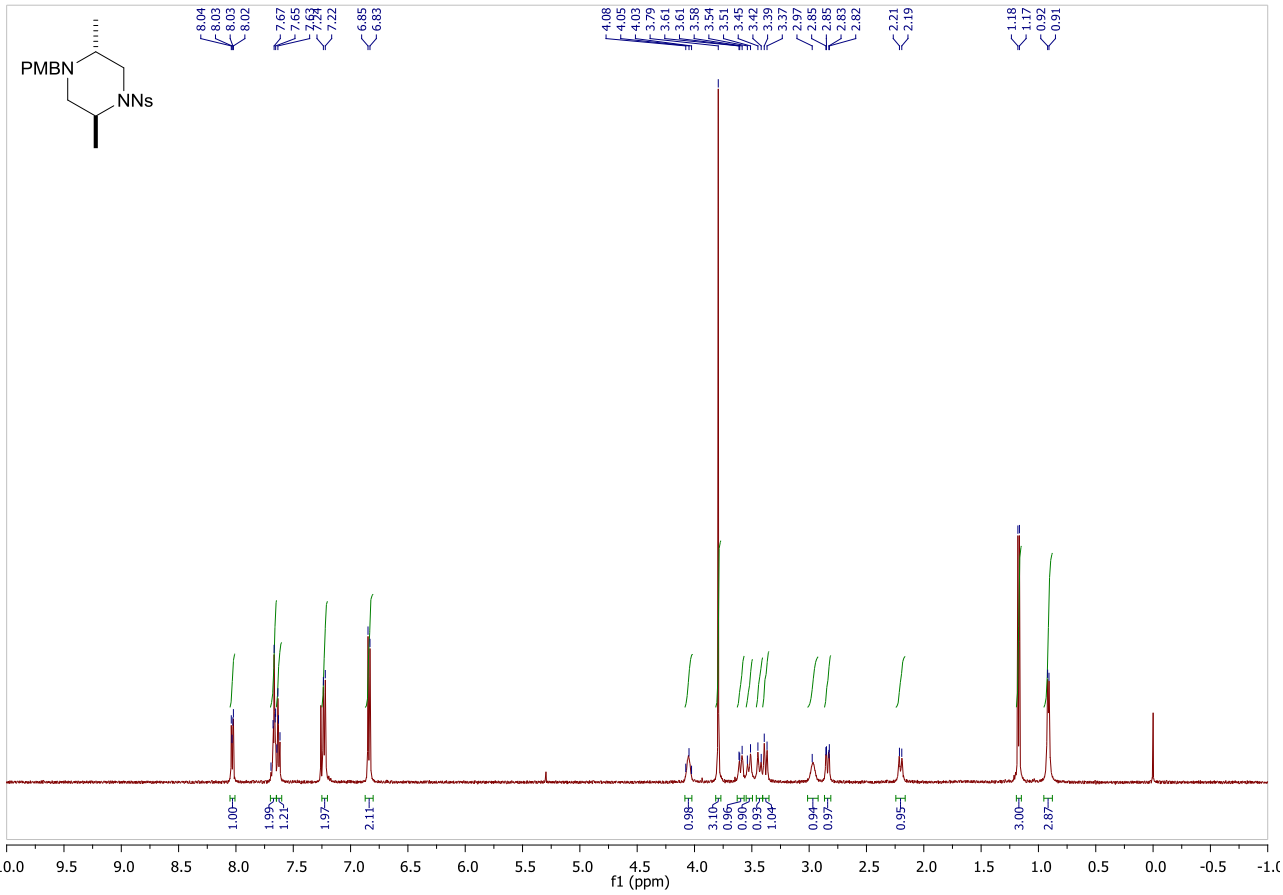


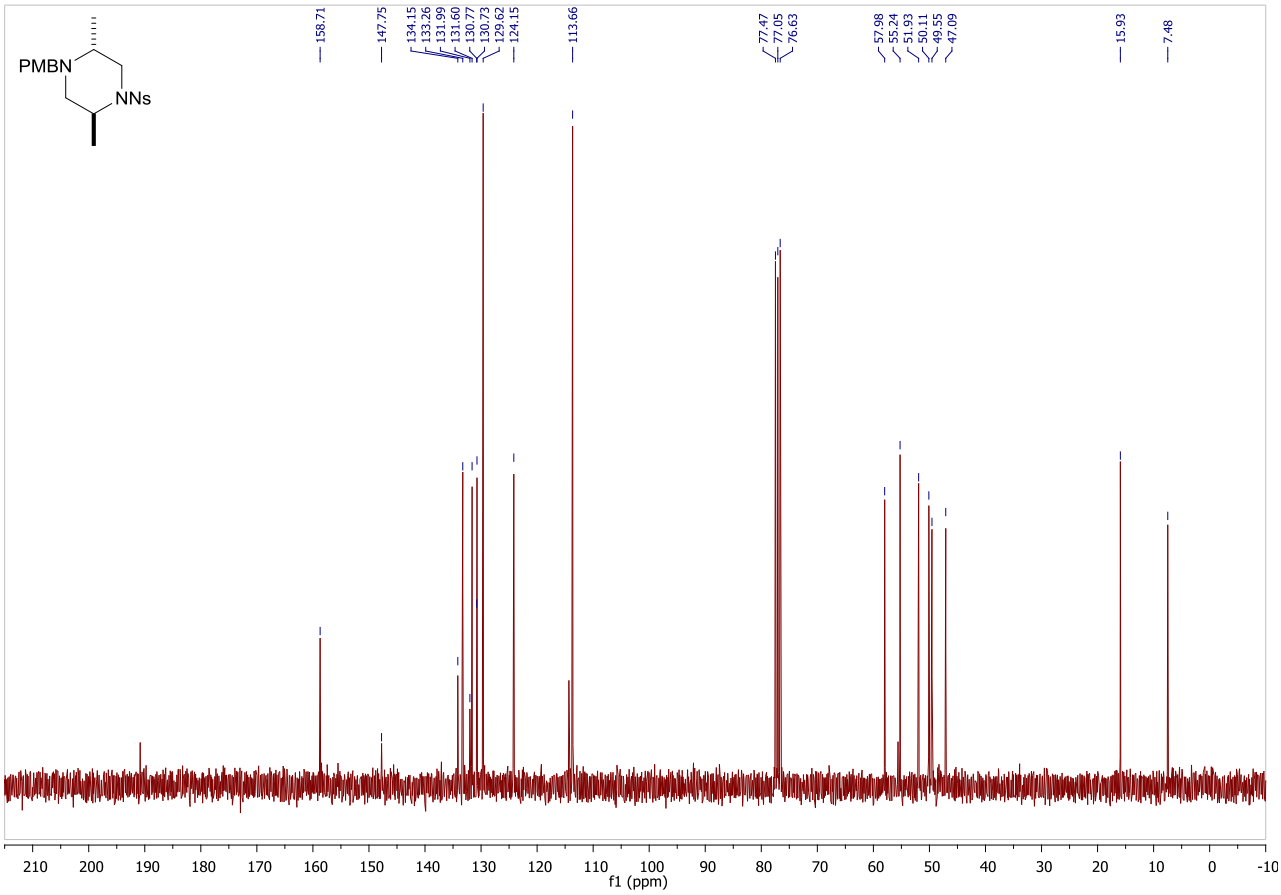
10f


PMBN
NNs
f1 (ppm)

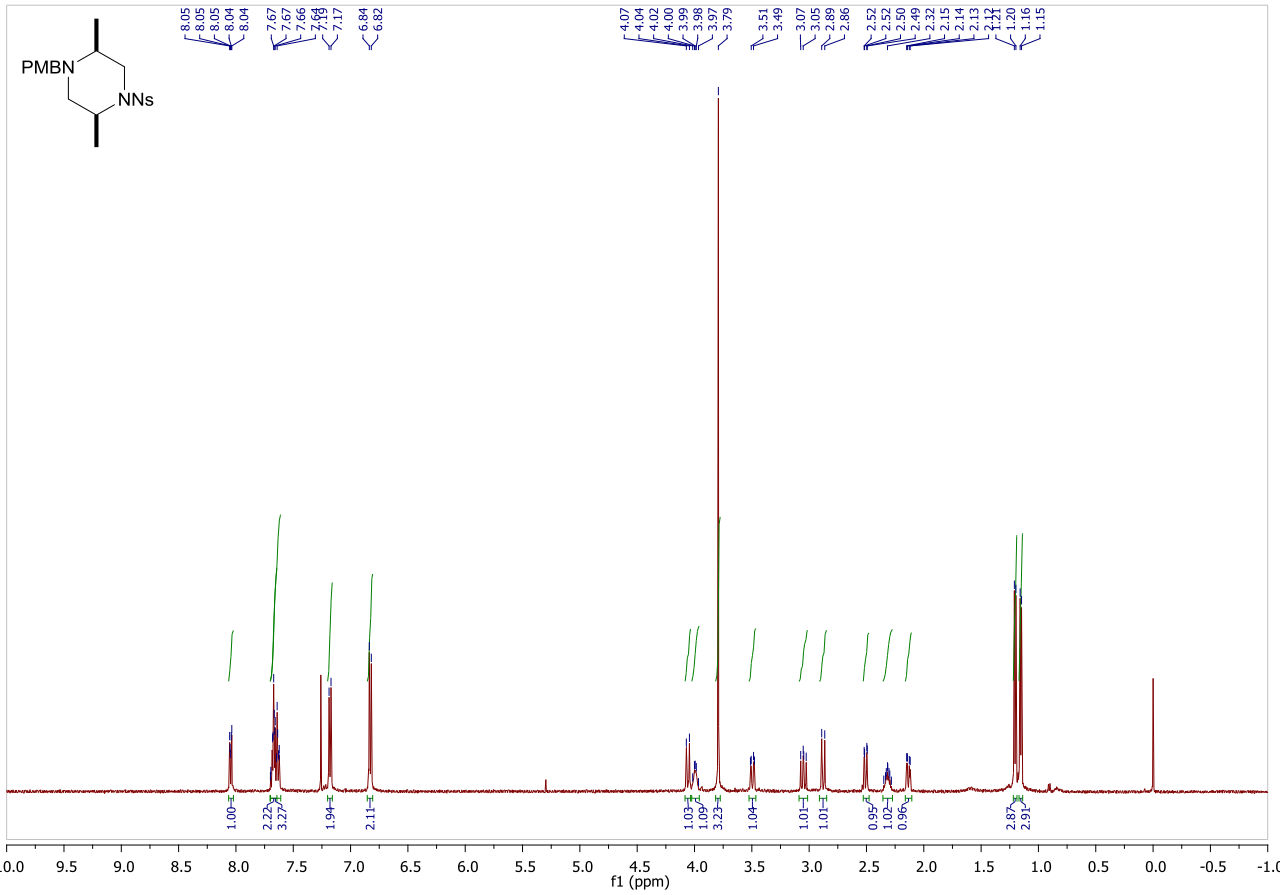

PMBN
NNs
158.45
133.31
131.55
130.55
129.73
124.11
113.54
77.46
77.03
76.61
68.13
55.25
53.94
51.59
49.36
47.61
30.99
26.22
20.48
19.75
f1 (ppm)

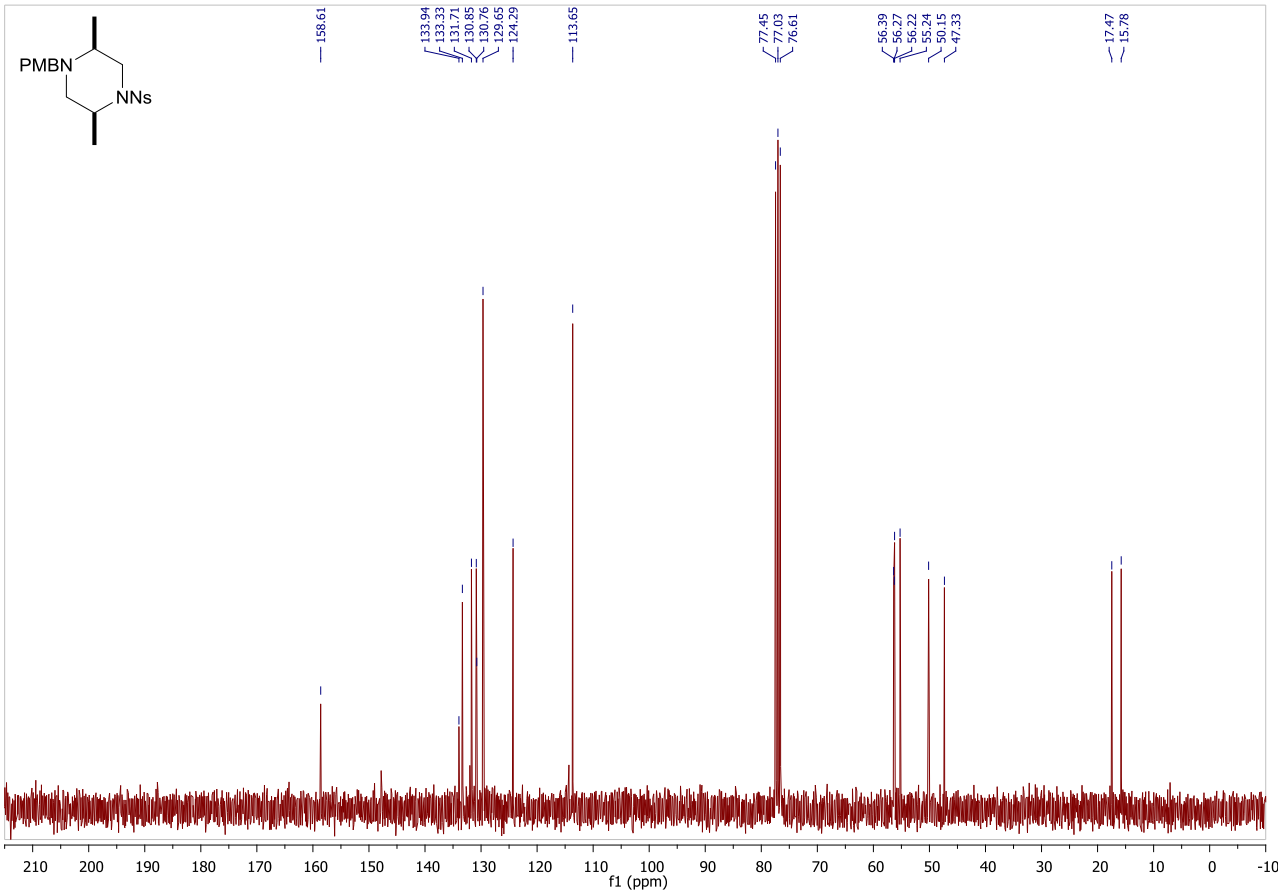
10h



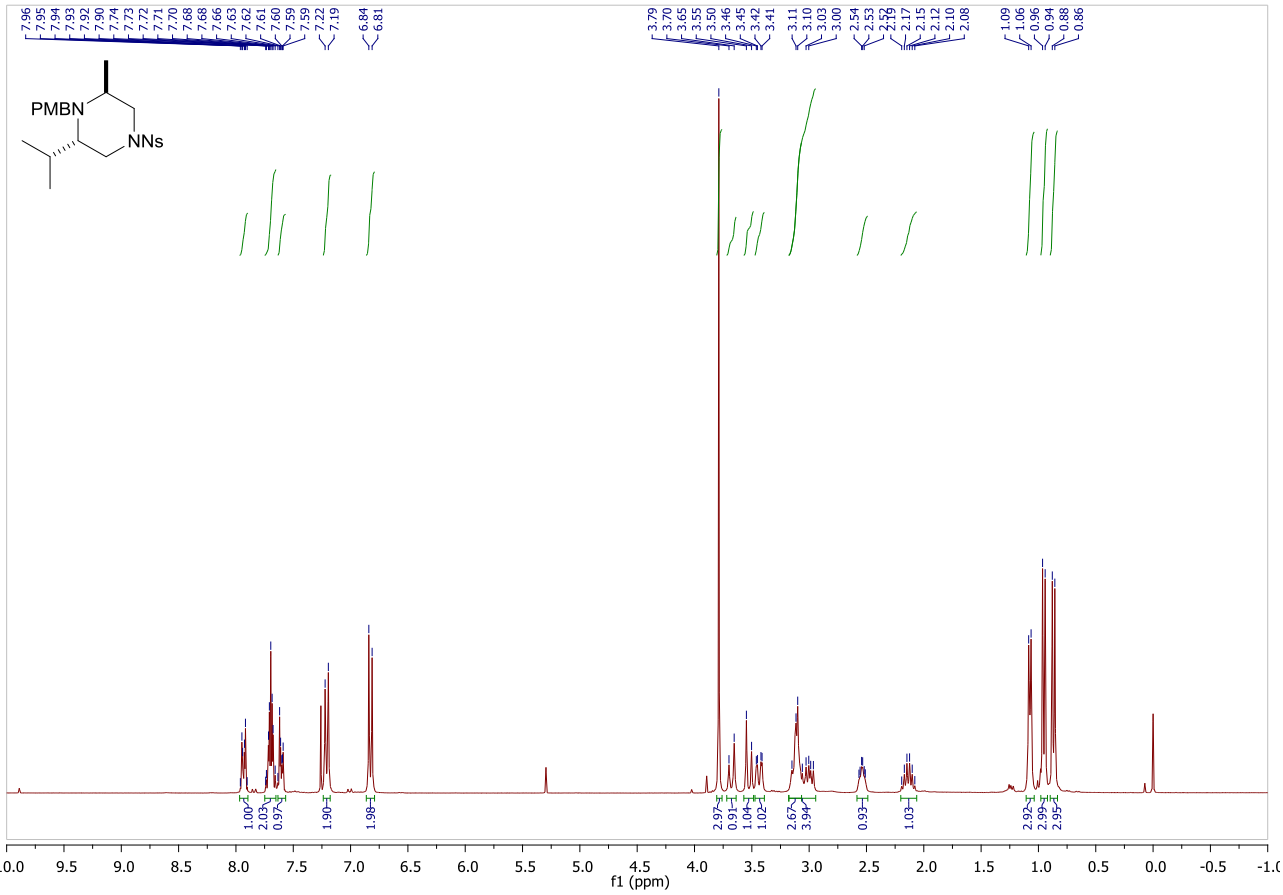


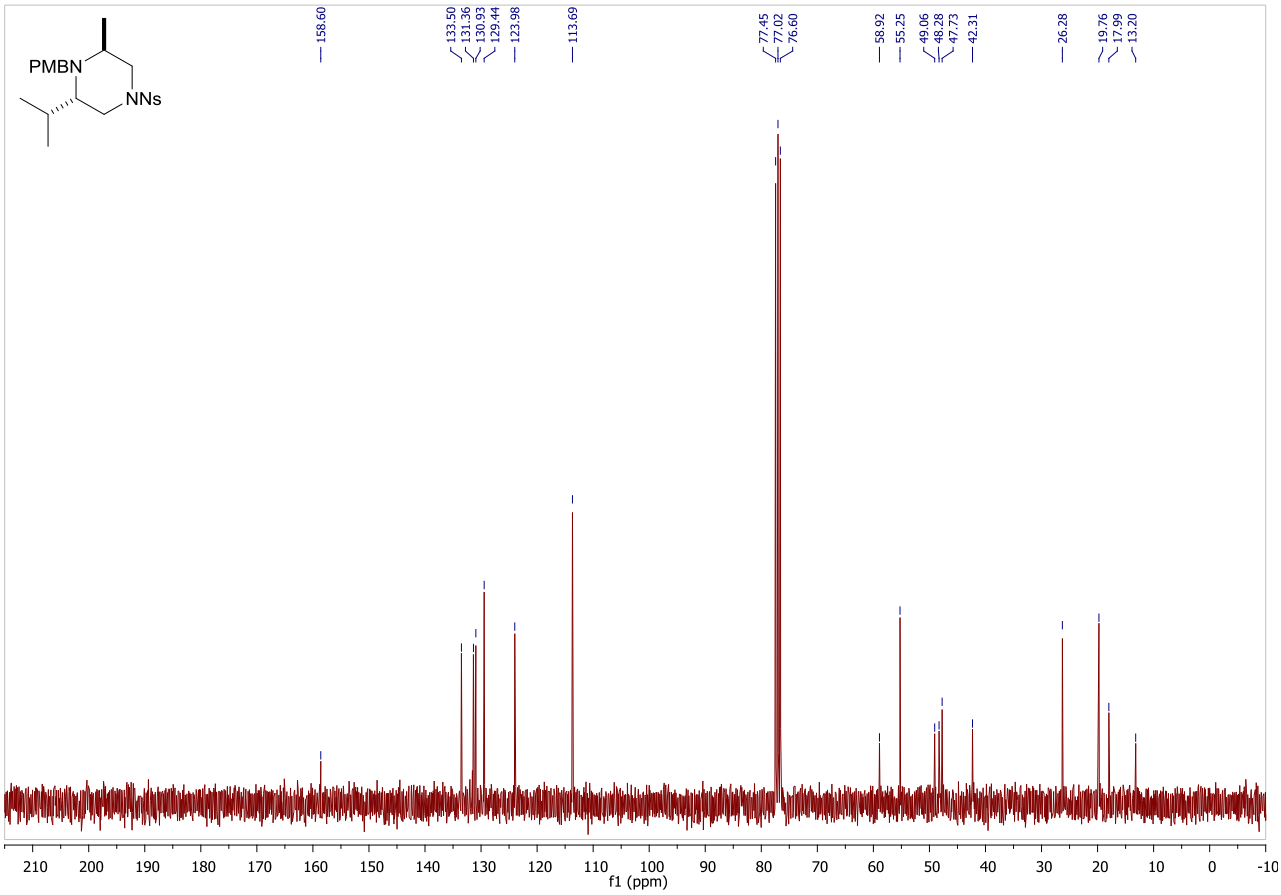
10i



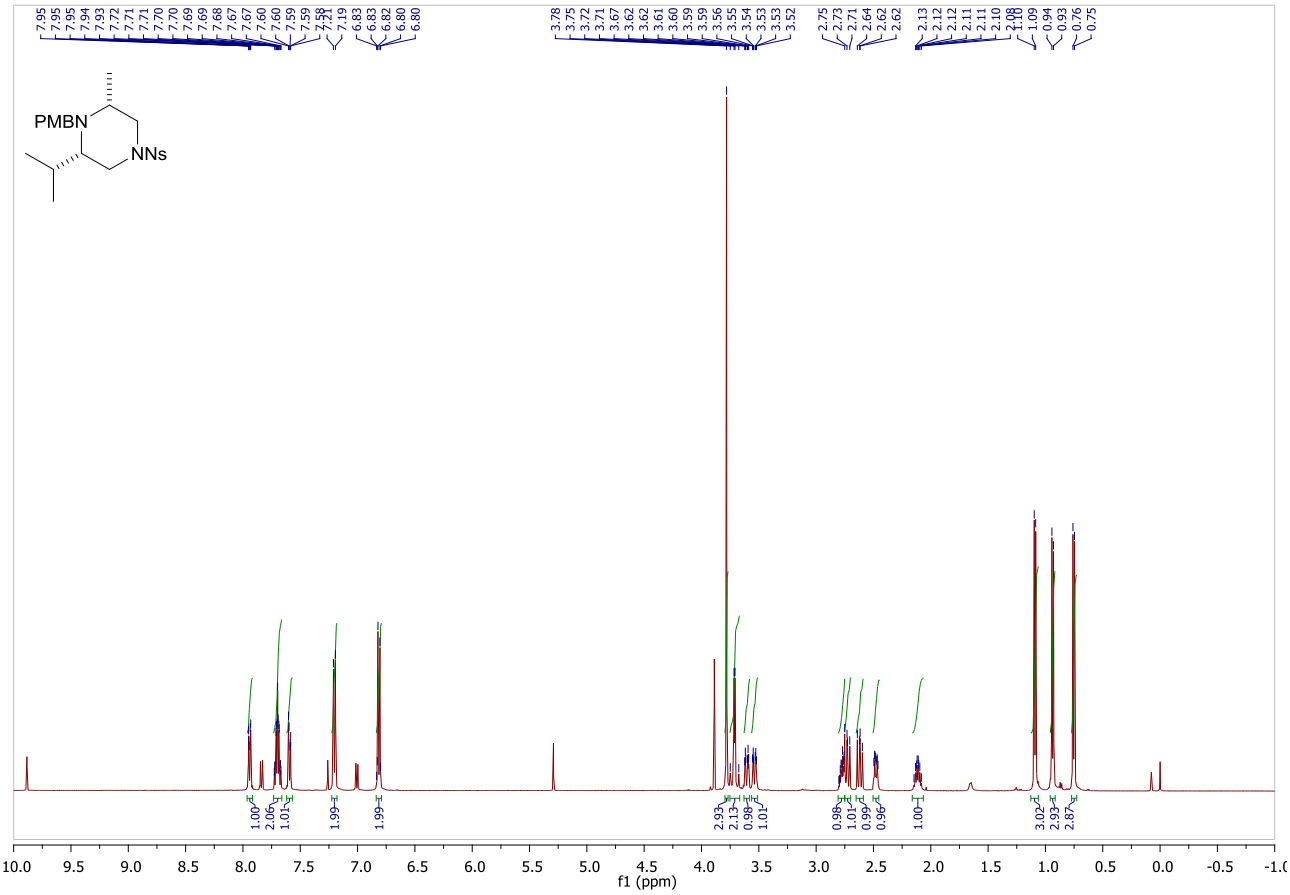


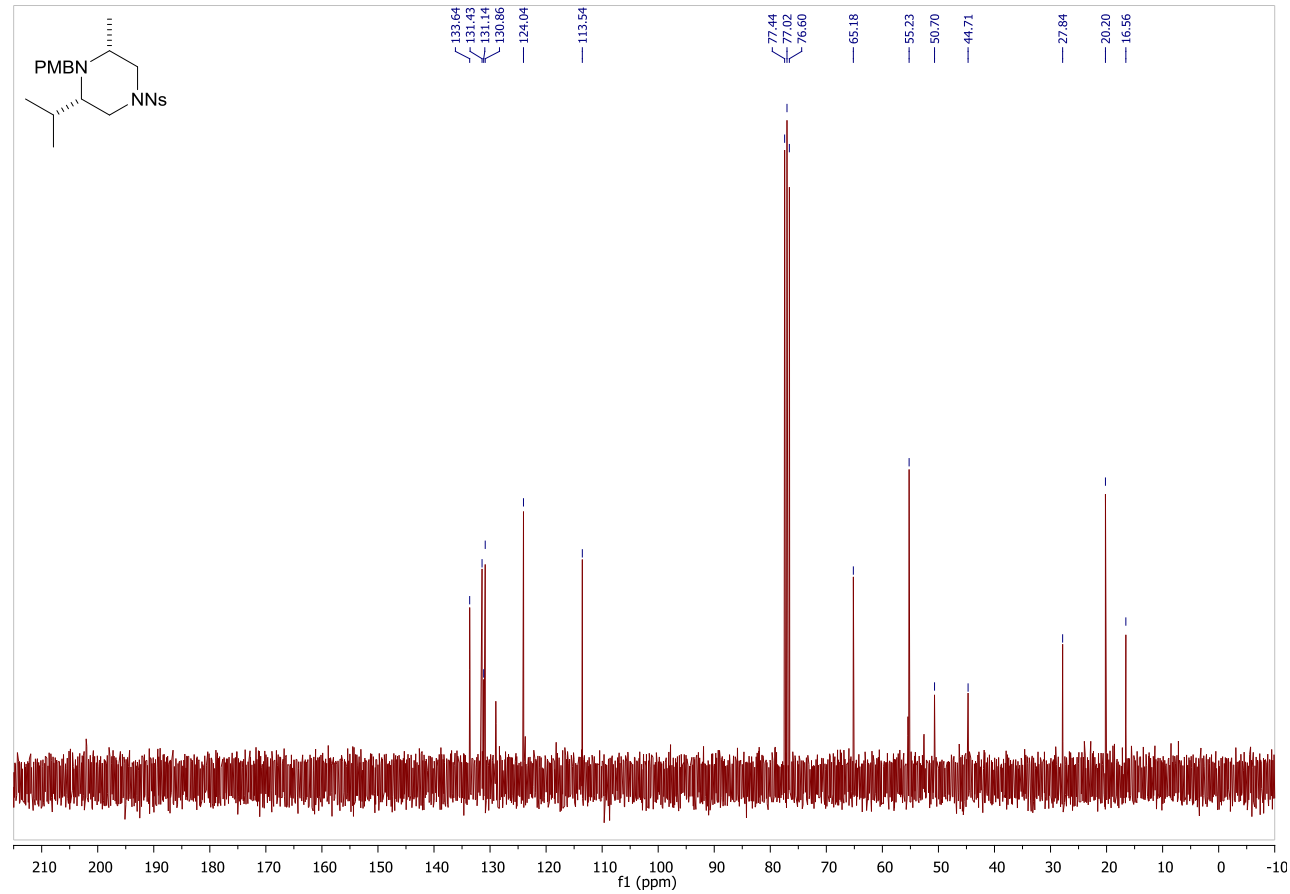
10j



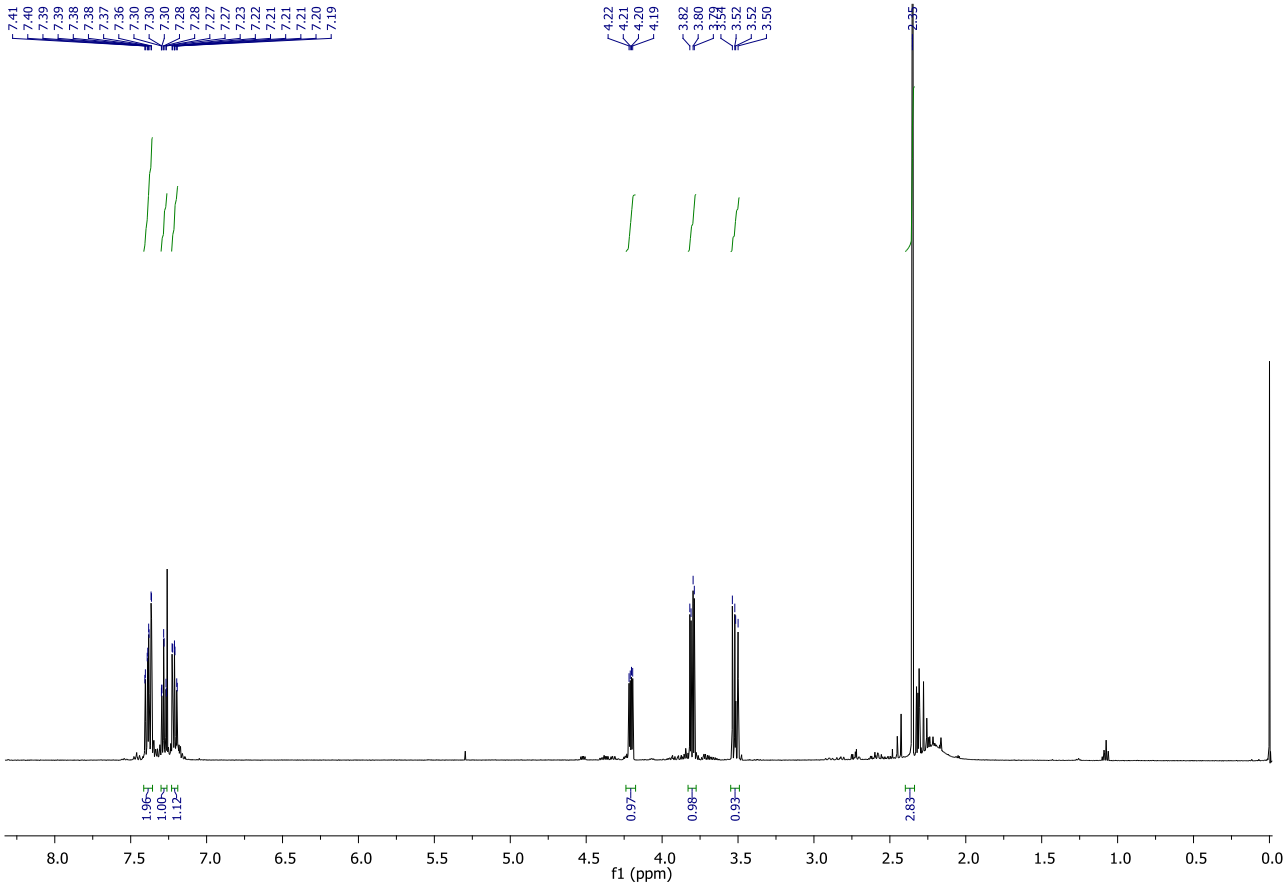


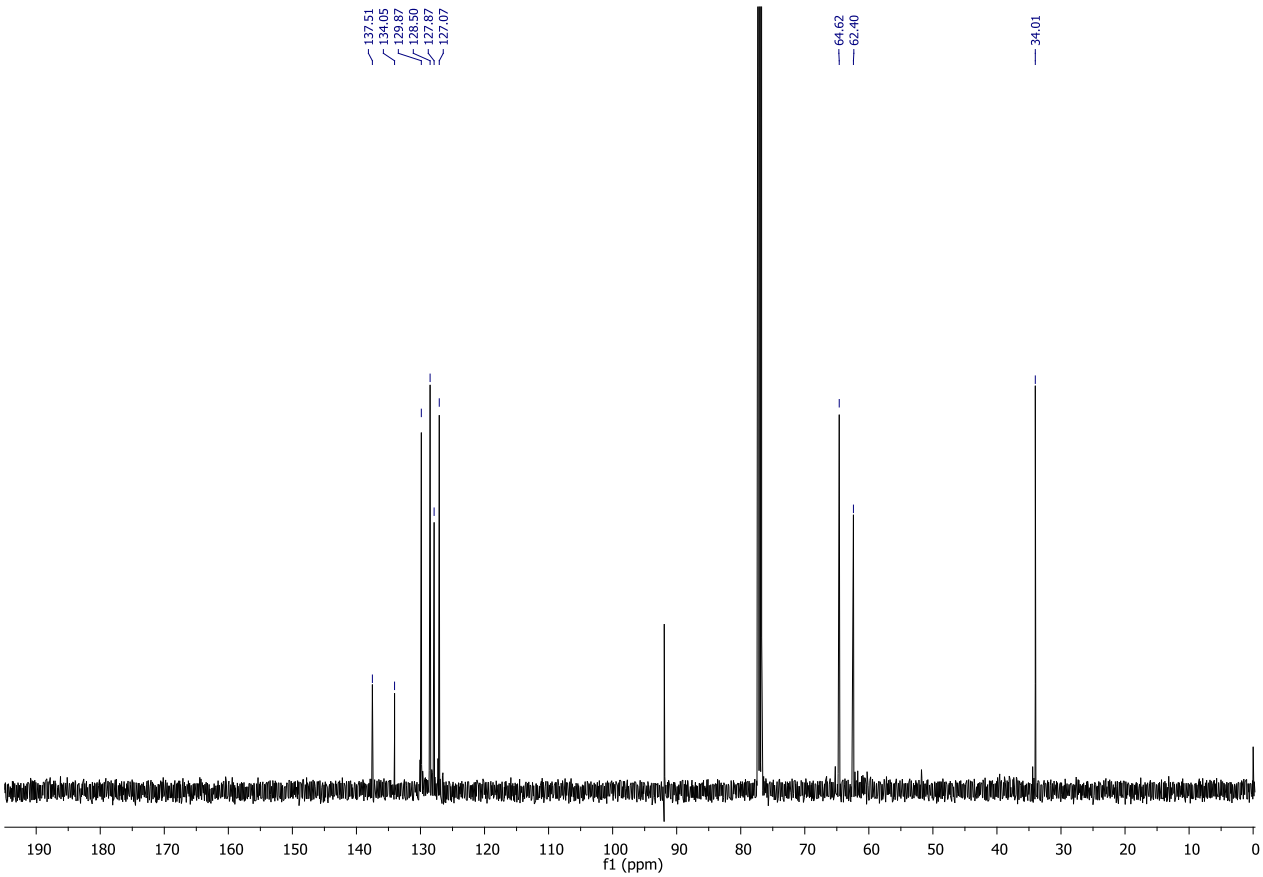
10k



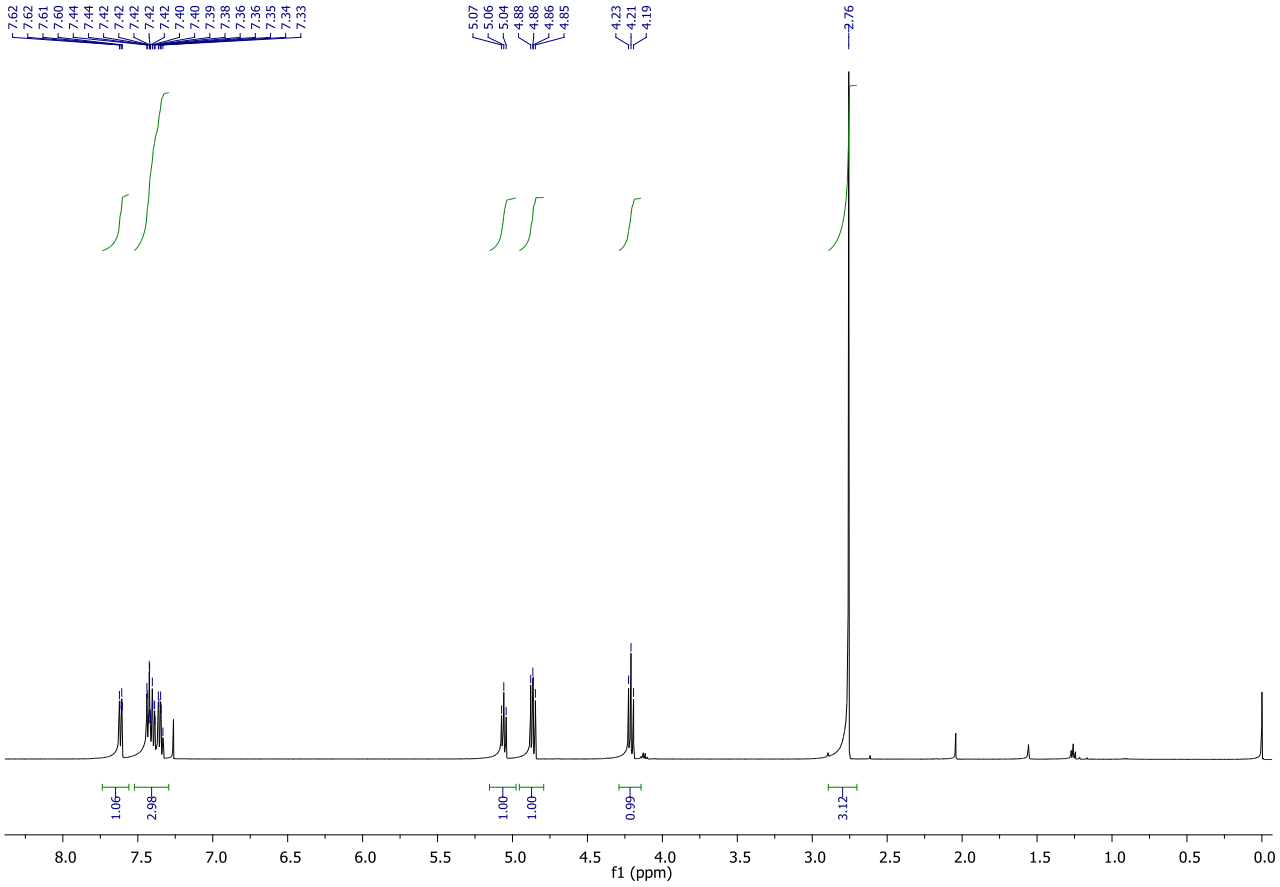


12


7.41
7.40
7.39
7.39
7.38
7.38
7.37
7.36
7.30
7.30
7.30
7.28
7.28
7.27
7.27
7.23
7.22
7.21
7.21
7.21
7.20
7.19
4.22
4.21
4.20
4.19
3.82
3.80
3.54
3.52
3.52
3.50
2.35
1.96
1.00
1.12
0.97
0.98
0.93
2.83
f1 (ppm)


137.51
134.05
129.87
128.50
127.87
127.07
64.62
62.40
34.01
f1 (ppm)

7f


7.62
7.62
7.61
7.60
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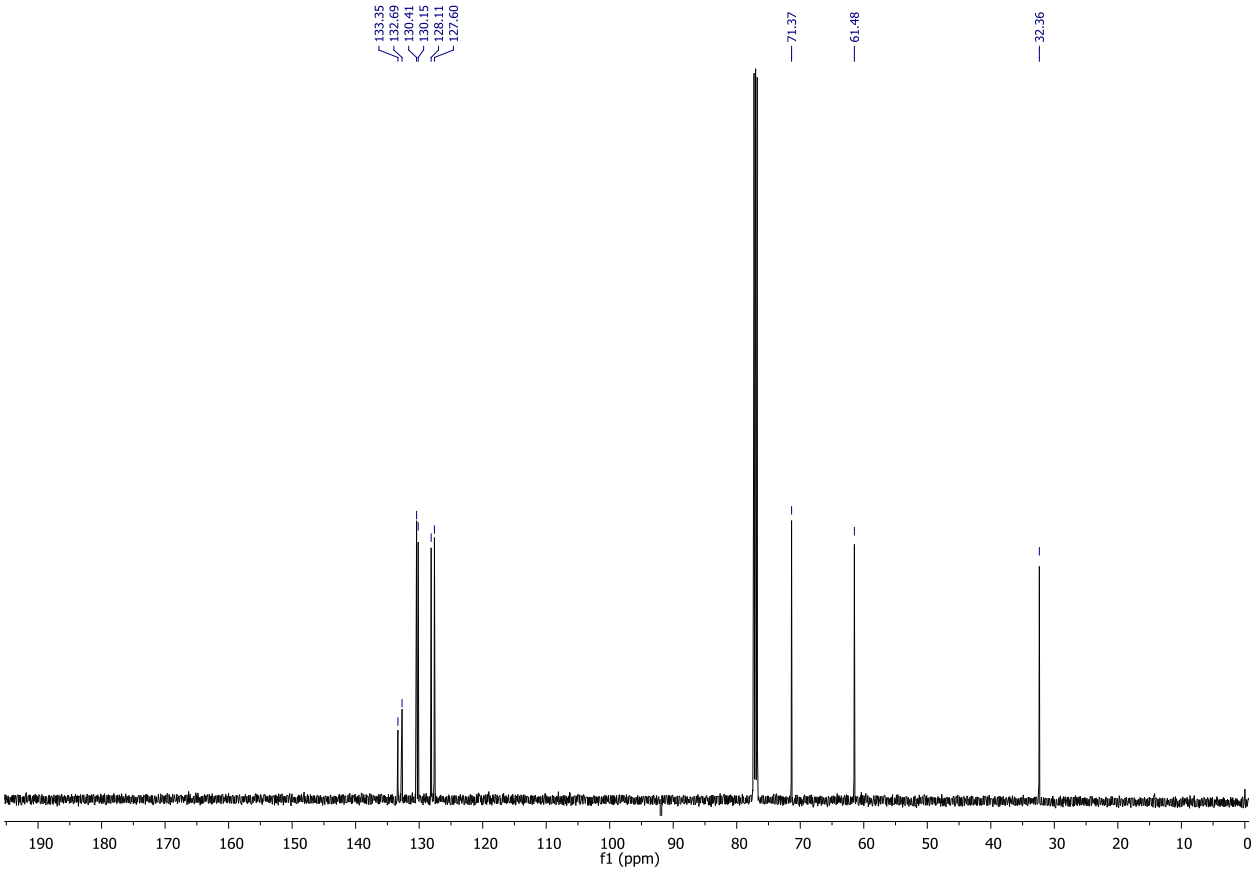
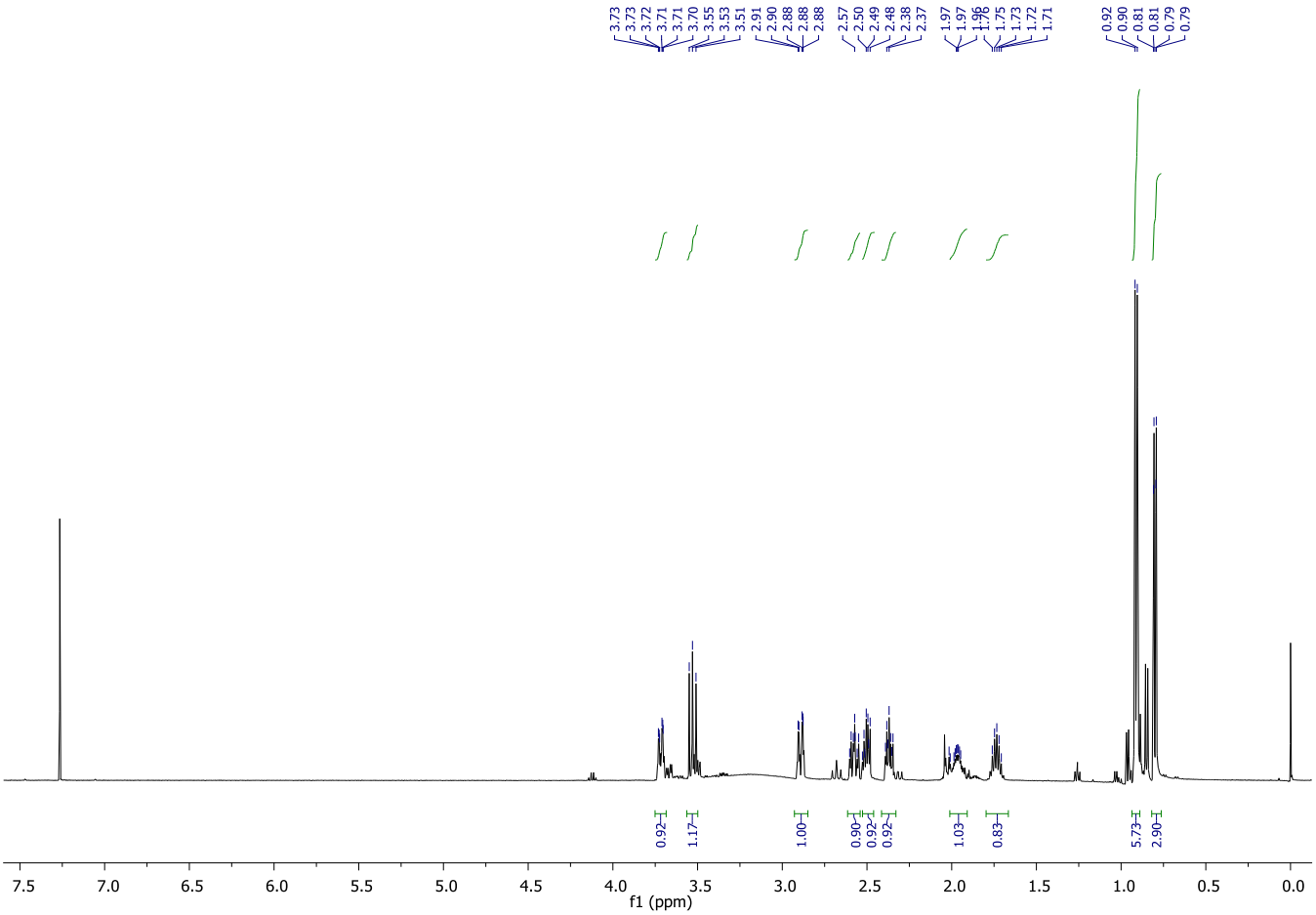
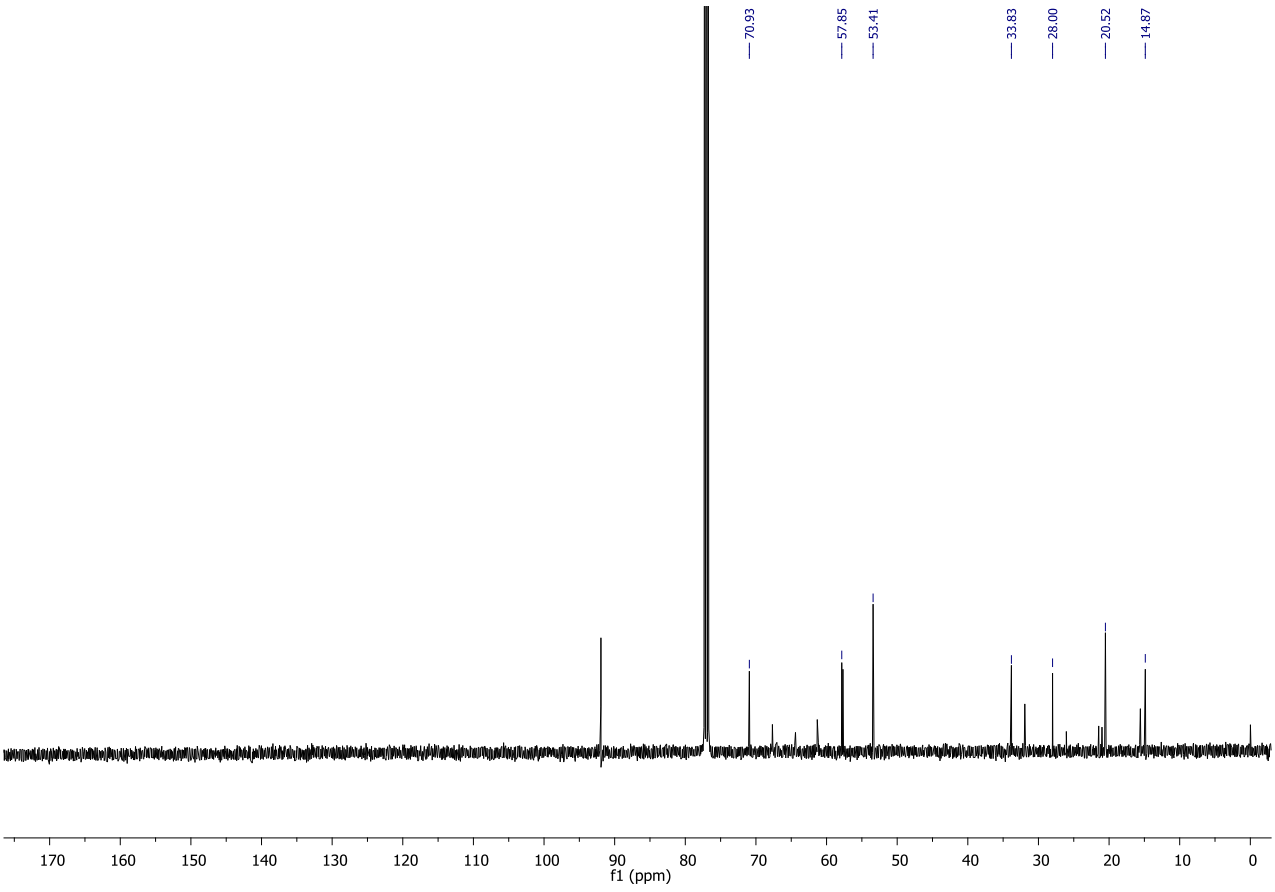
7.44
7.42
7.42
7.42
7.42
7.40
7.40
7.39
7.38
7.36
7.36
7.35
7.34
7.33
5.07
5.06
5.04
4.88
4.86
4.86
4.85
4.23
4.21
4.19
2.76
1.06
2.98
1.00
1.00
0.99
3.12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

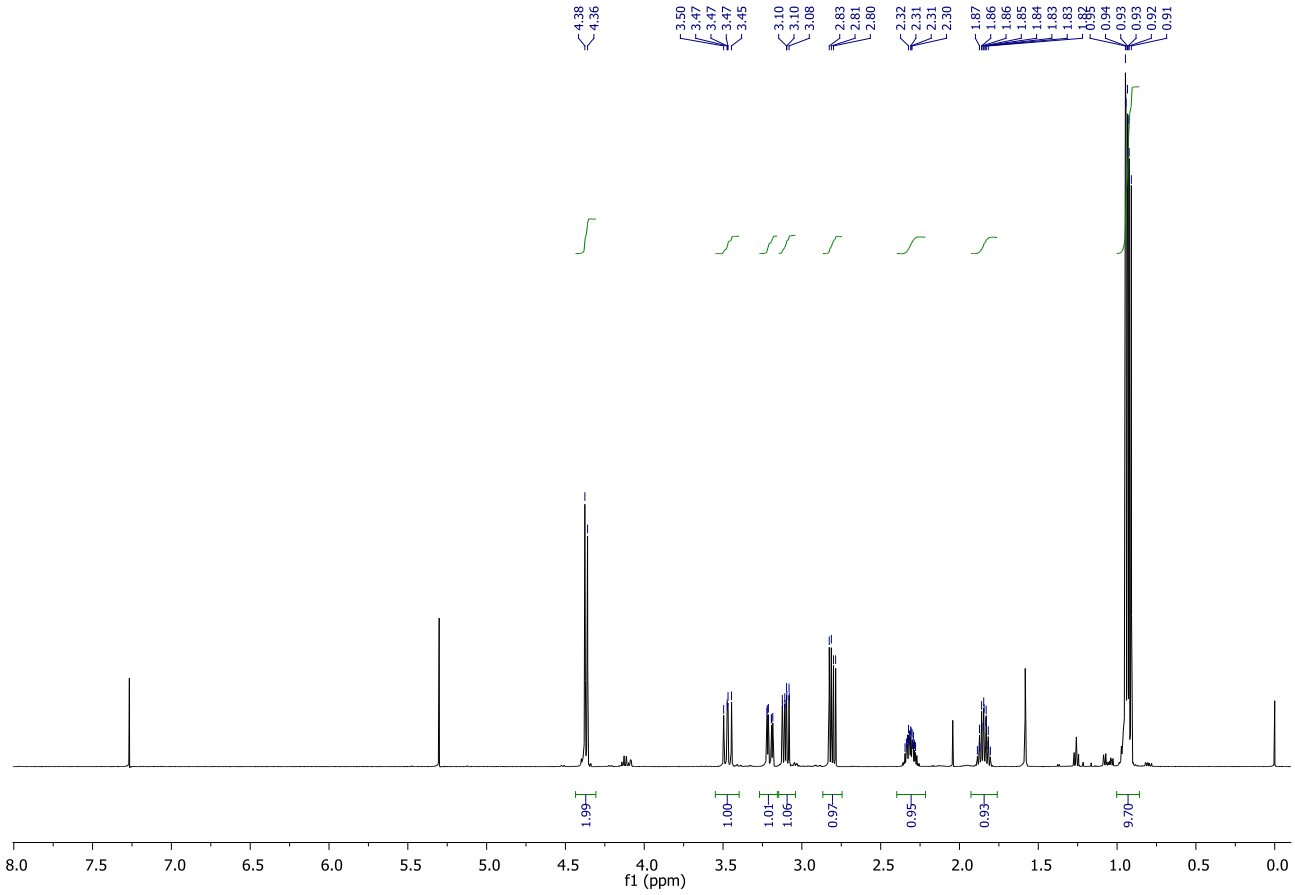

133.35
132.69
130.41
130.15
128.11
127.60
71.37
61.48
32.36
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

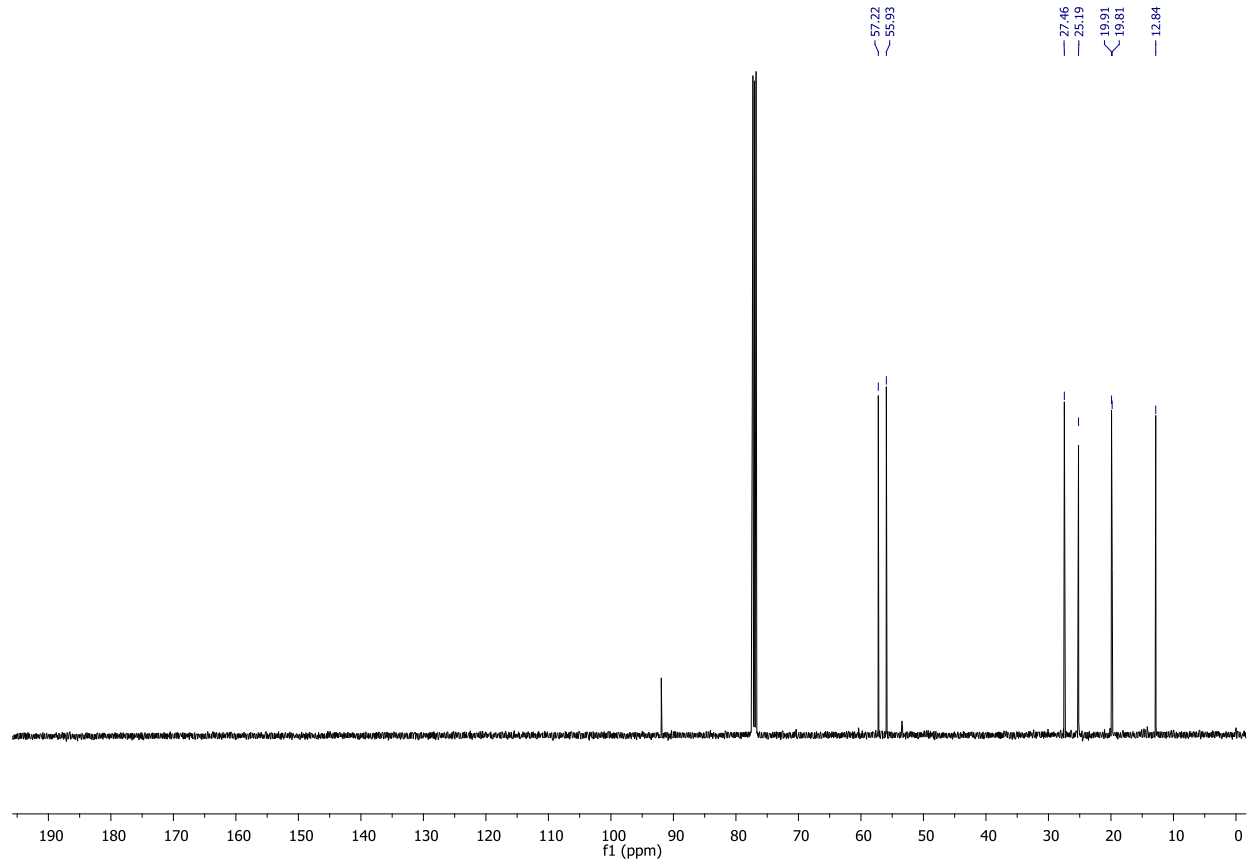
15


3.73
3.73
3.72
3.71
3.71
3.70
3.55
3.53
3.51
2.91
2.90
2.88
2.88
2.88
2.57
2.50
2.49
2.48
2.38
2.37
1.97
1.97
1.96
1.75
1.73
1.72
1.71
0.92
0.90
0.81
0.81
0.79
0.79
0.92
1.17
1.00
0.90
0.92
0.92
1.03
0.83
5.73
2.90
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
f1 (ppm)


70.93
57.85
53.41
33.83
28.00
20.52
14.87
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

7g


4.38
4.36
3.50
3.47
3.47
3.47
3.45
3.10
3.10
3.08
2.83
2.81
2.80
2.32
2.31
2.31
2.30
1.87
1.86
1.86
1.85
1.84
1.83
1.83
0.94
0.93
0.93
0.92
0.91
1.99
1.00
1.01
1.06
0.97
0.95
0.93
9.70
f1 (ppm)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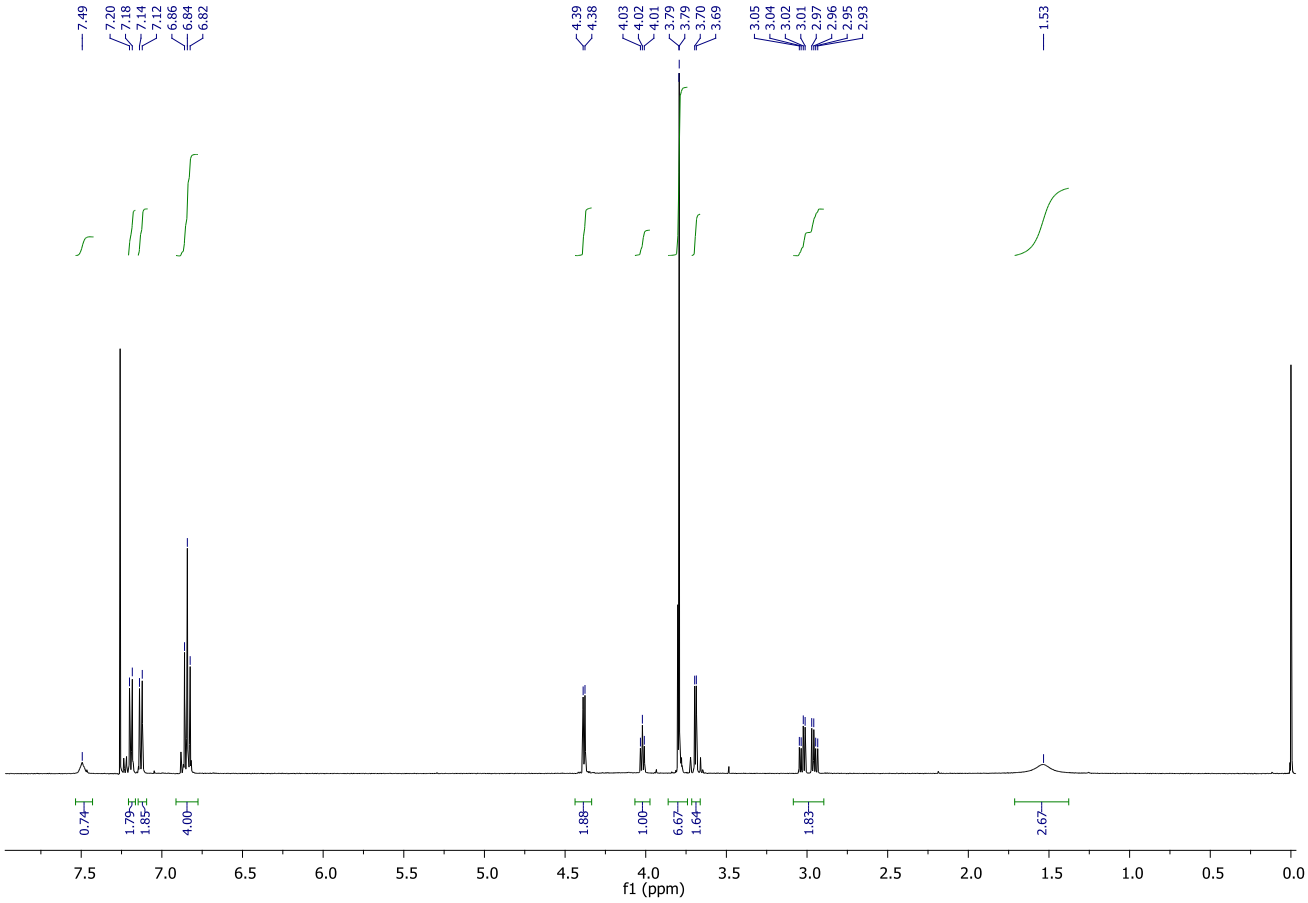
55.93
27.46
25.19
19.91
19.81
12.84
f1 (ppm)

17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7.18
7.14
7.12
6.86
6.84
6.82
4.39
4.38
4.03
4.02
4.01
3.79
3.79
3.70
3.69
3.05
3.04
3.02
3.01
2.97
2.96
2.95
2.93
1.53
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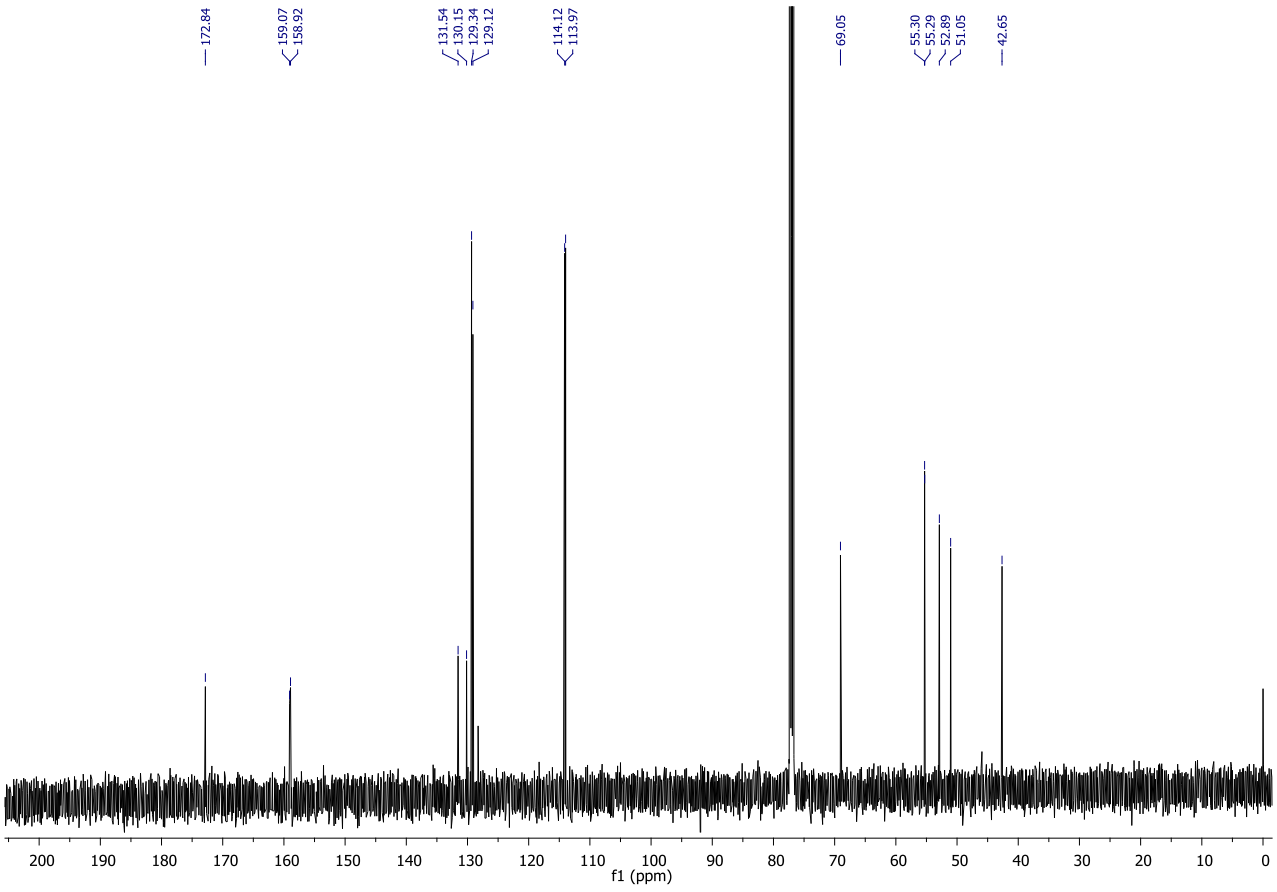
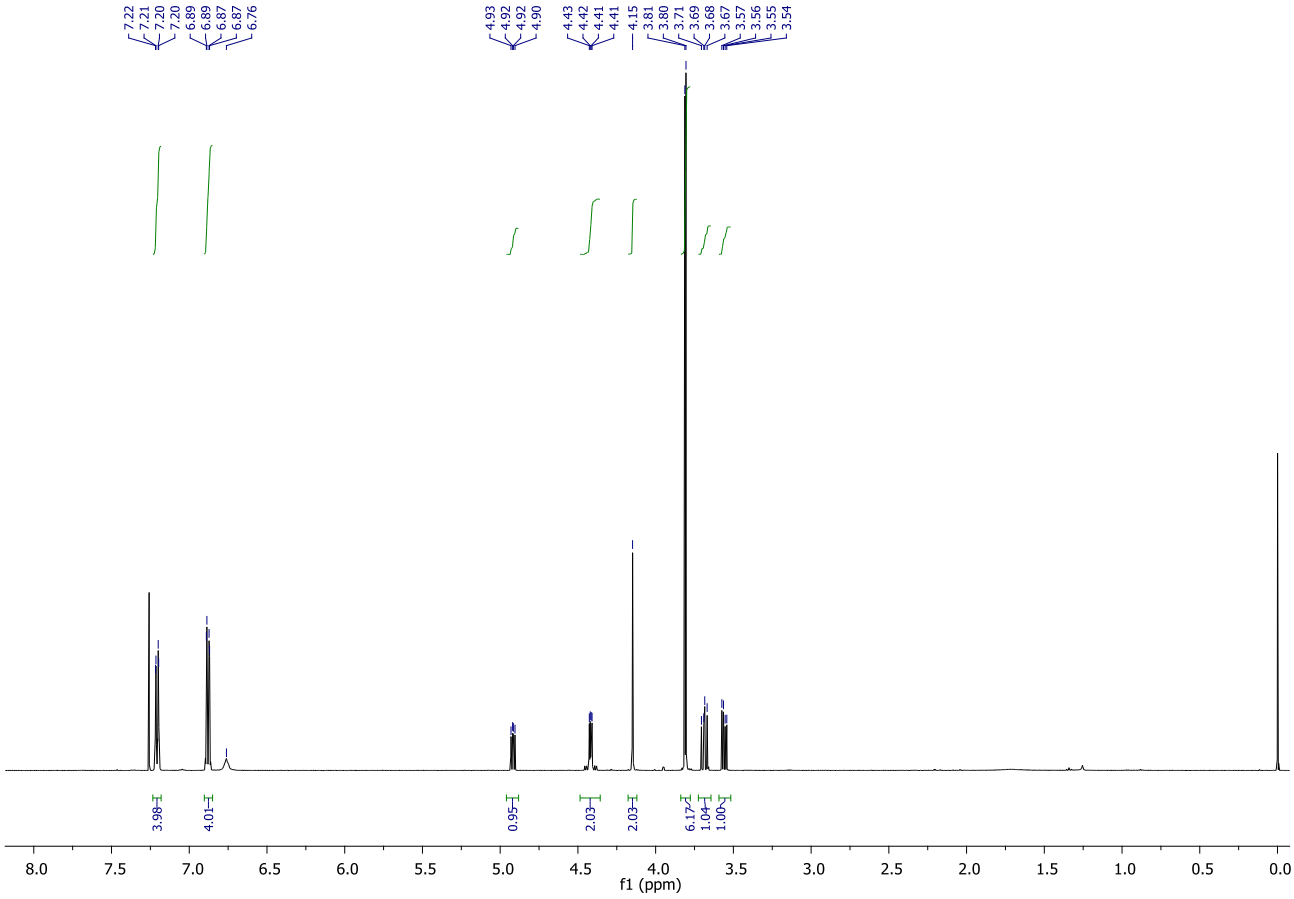
1.79
1.85
4.00
1.88
1.00
6.67
1.64
1.83
2.67
f1 (ppm)


172.84
159.07
158.92
131.54
130.15
129.34
129.12
114.12
113.97
69.05
55.30
55.29
52.89
51.05
42.65
f1 (ppm)

7h


7.22
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7.20
7.20
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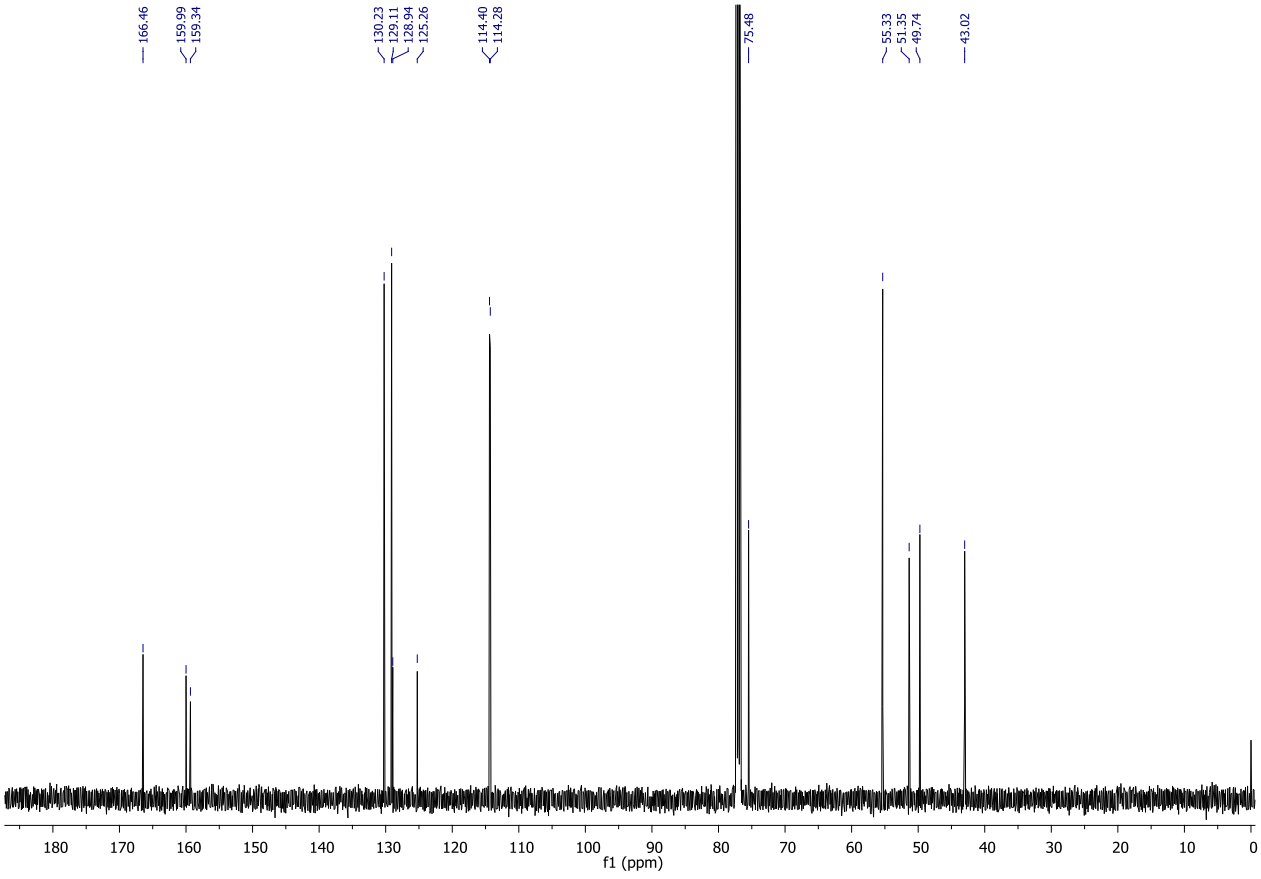
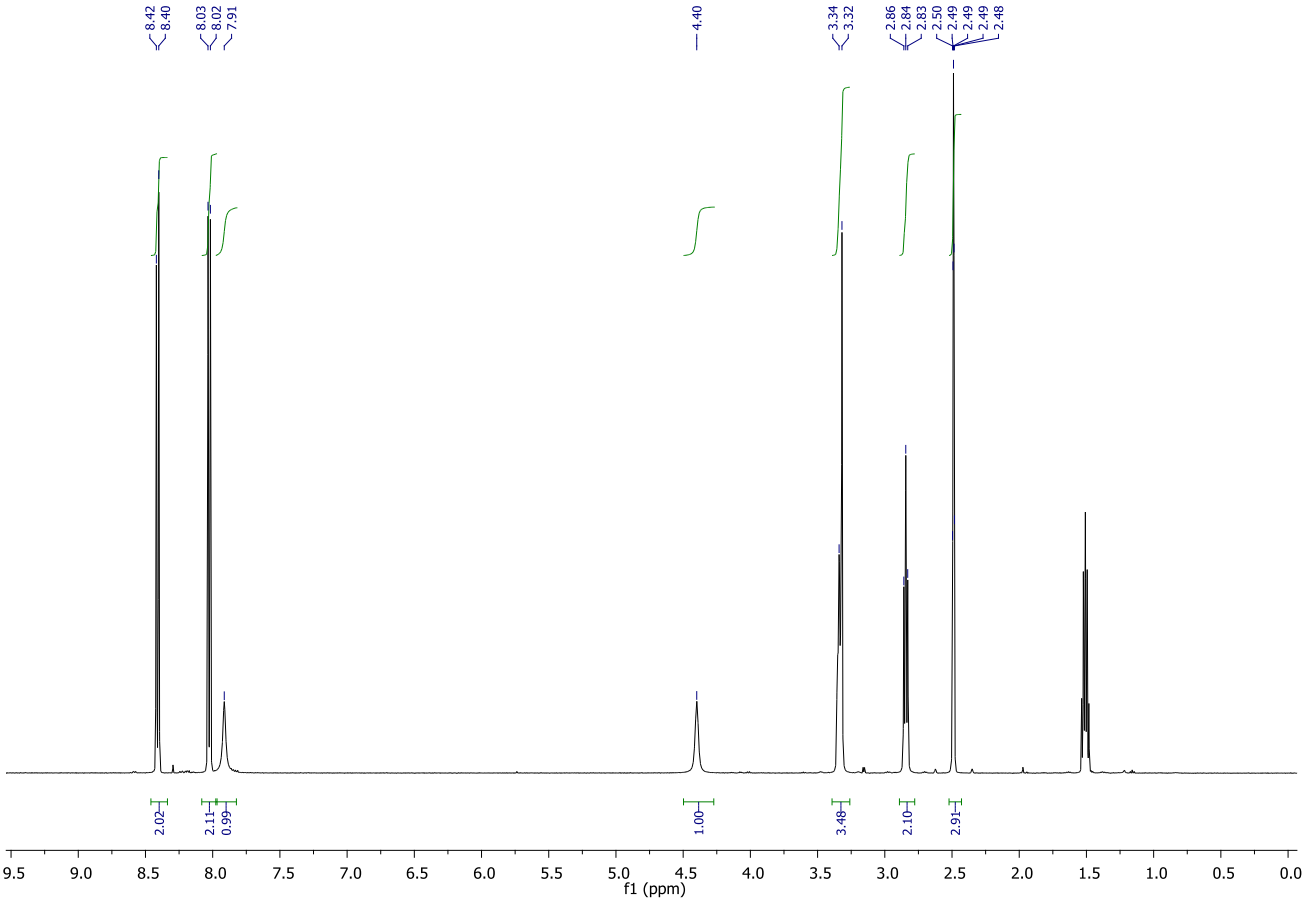
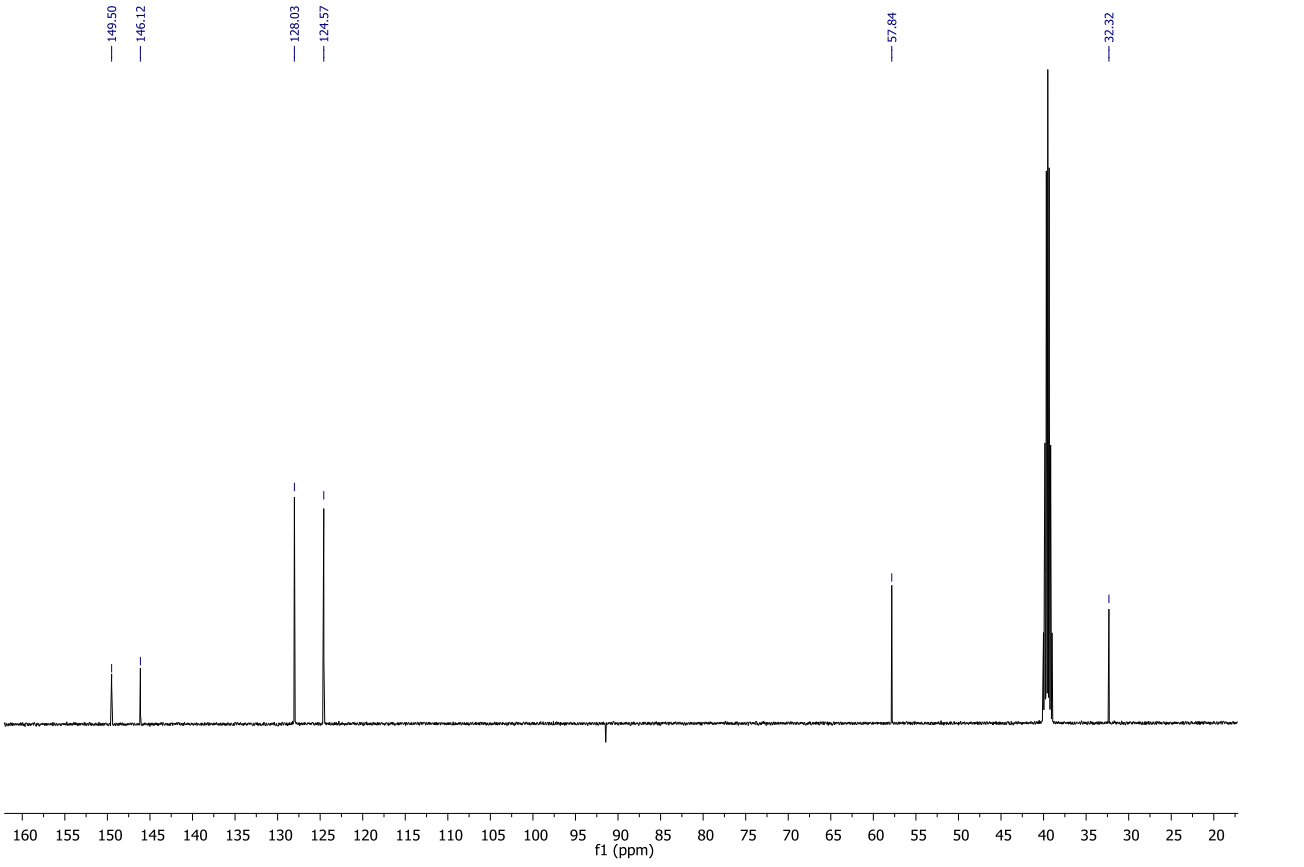
6.89
6.87
6.87
6.76
4.93
4.92
4.92
4.90
4.43
4.42
4.41
4.41
4.15
3.81
3.80
3.71
3.69
3.68
3.67
3.57
3.56
3.55
3.54
3.98
4.01
0.95
2.03
2.03
6.17
1.04
1.00
f1 (ppm)

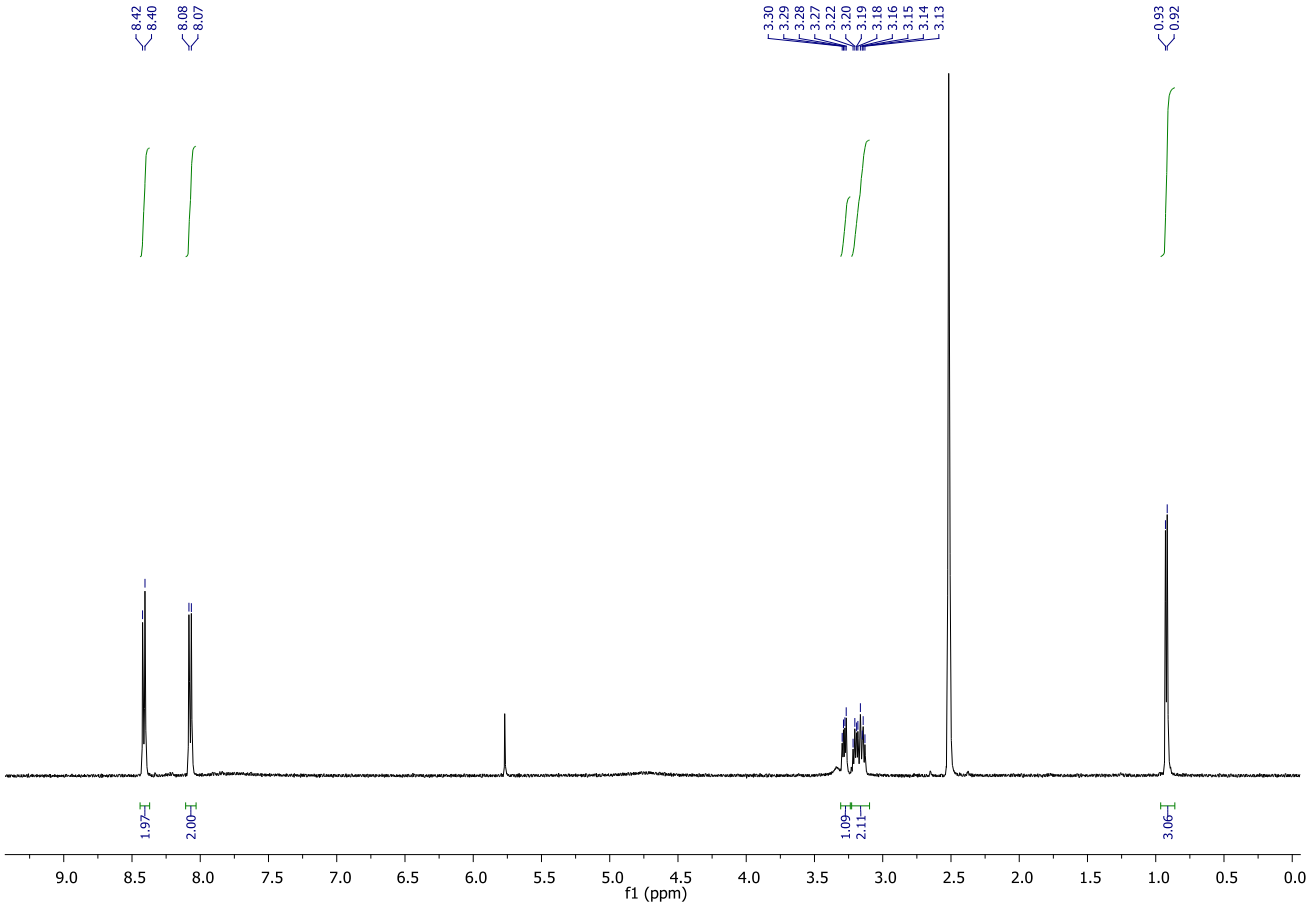

166.46
159.99
159.34
130.23
129.11
128.94
125.26
114.40
114.28
75.48
55.33
51.35
49.74
43.02
f1 (ppm)

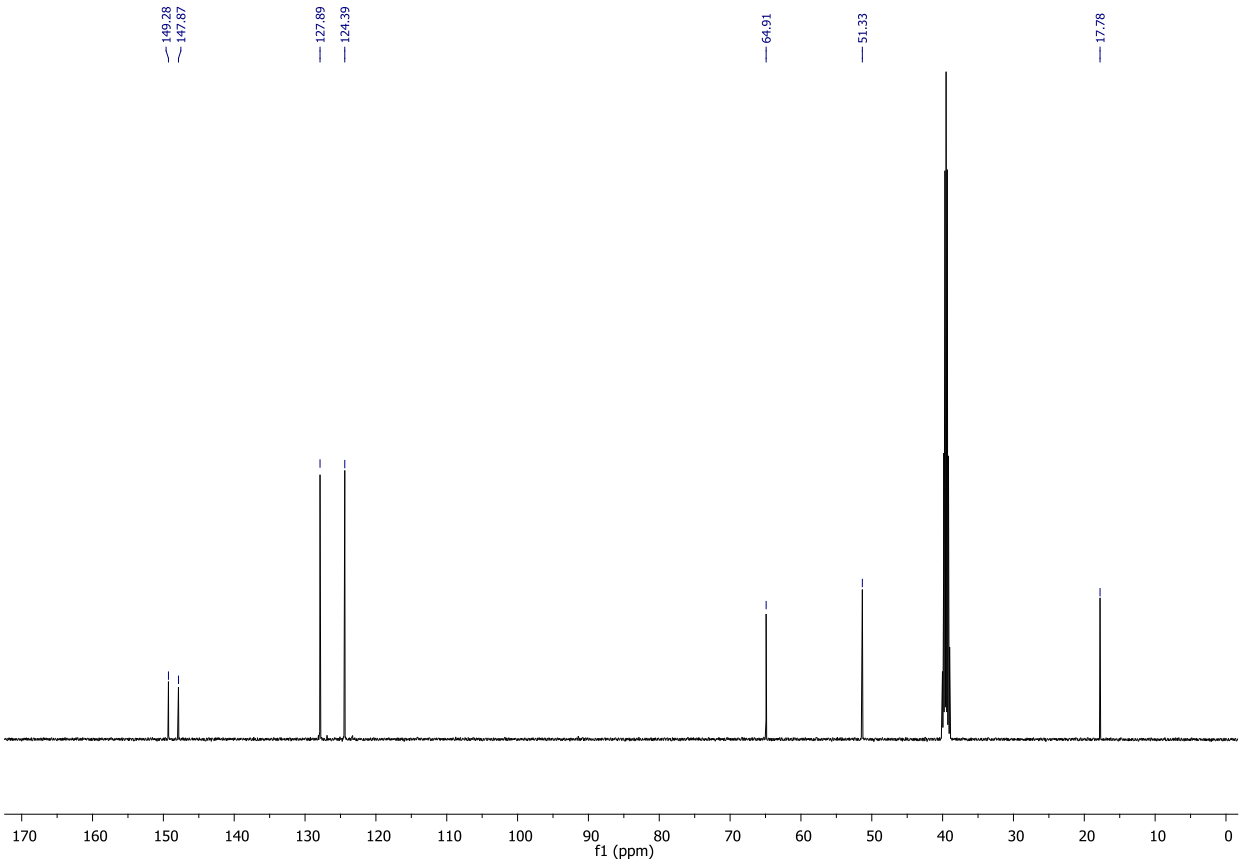
8b’


8.42
8.40
8.03
8.02
7.91
4.40
3.34
3.32
2.86
2.84
2.83
2.50
2.49
2.49
2.49
2.48
2.02
2.11
0.99
1.00
3.48
2.10
2.91
f1 (ppm)


149.50
146.12
128.03
124.57
57.84
32.32
f1 (ppm)

8f


8.42
8.40
8.08
8.07
3.30
3.29
3.28
3.27
3.22
3.20
3.19
3.18
3.16
3.15
3.14
3.13
0.93
0.92
1.97
2.00
1.09
2.11
3.06
f1 (ppm)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127.89
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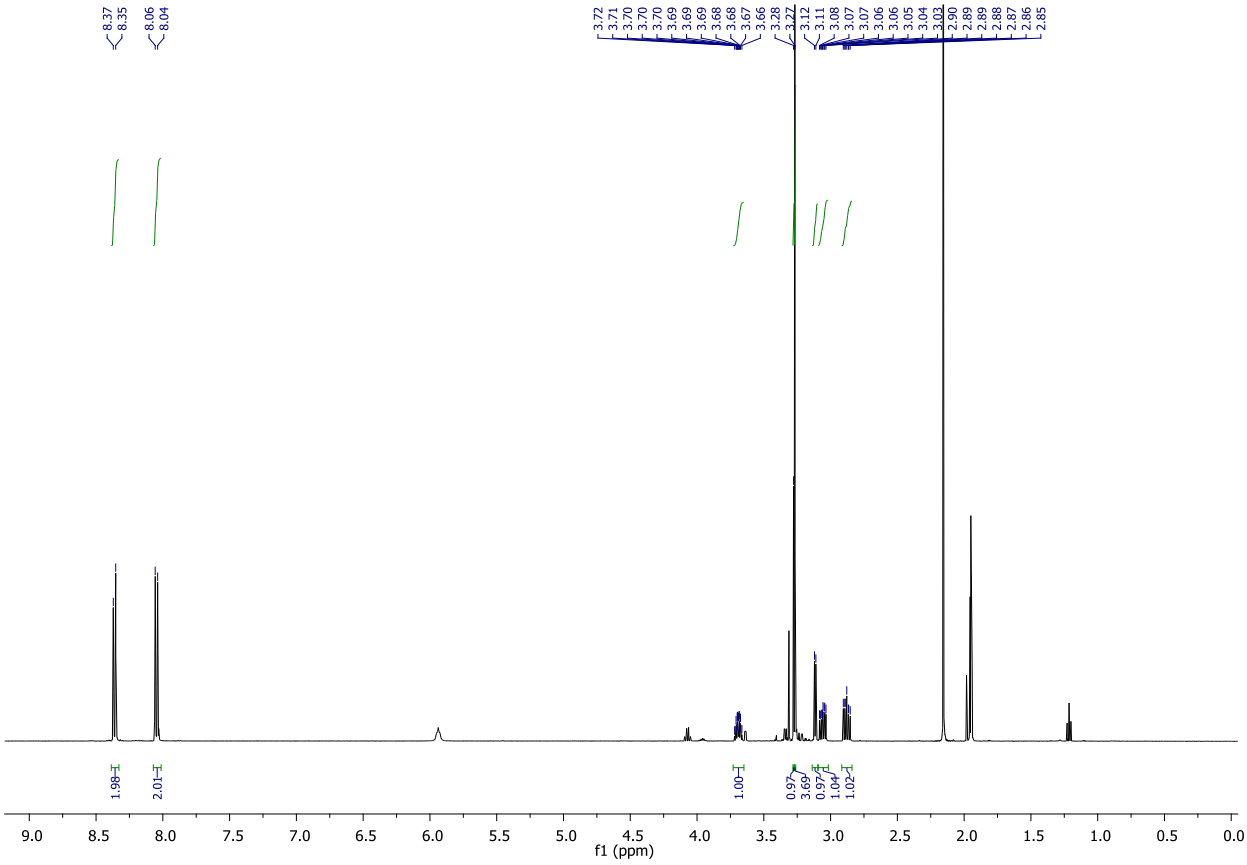
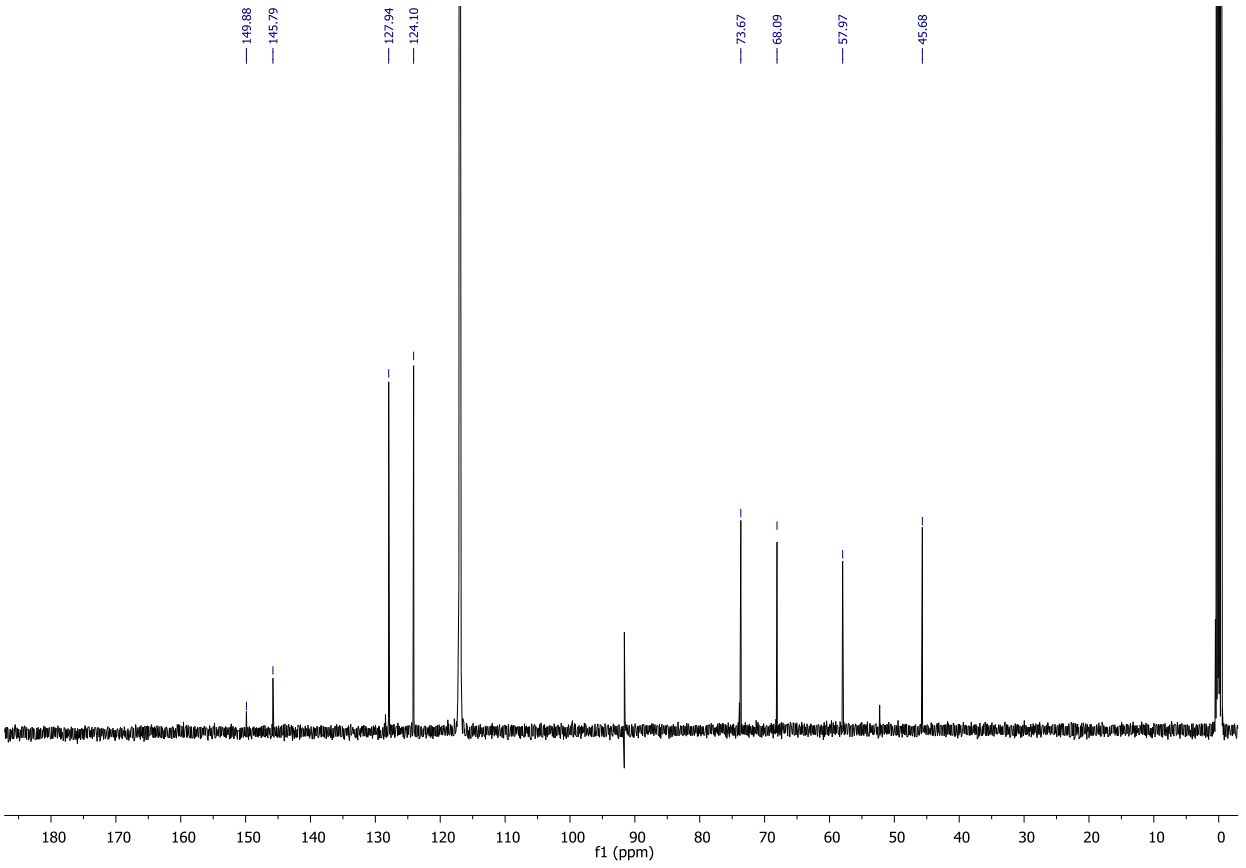
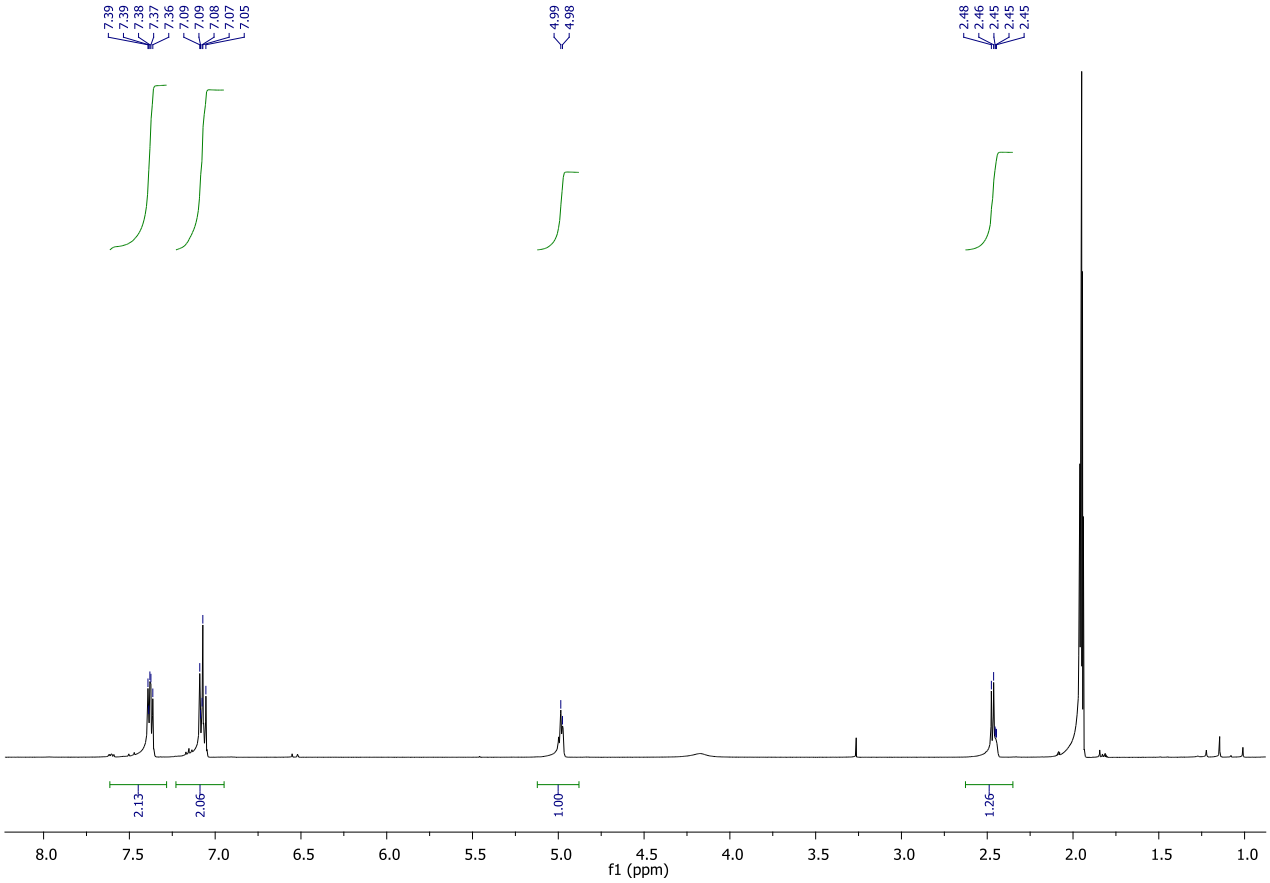
51.33
17.78
f1 (ppm)

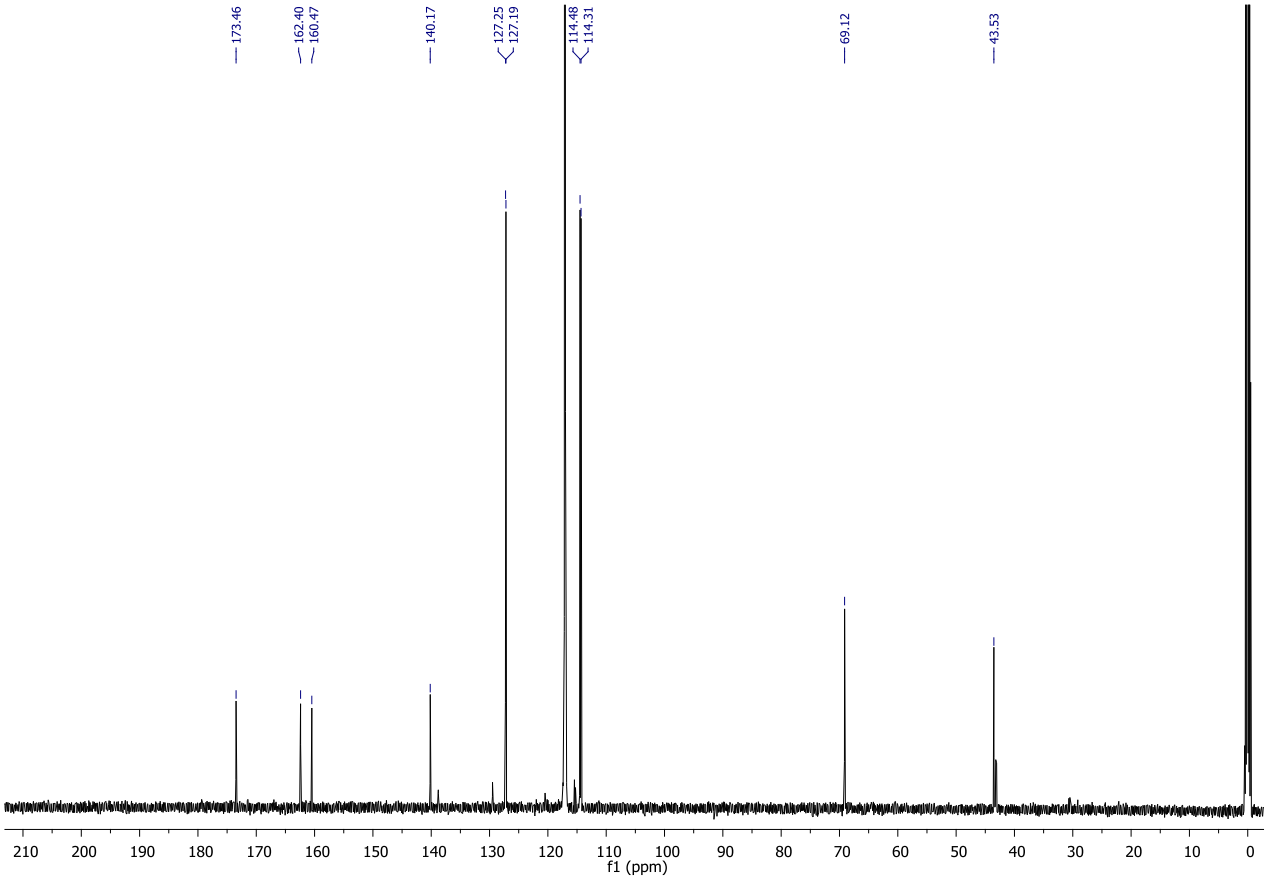
8g


8.37
8.35
8.06
8.04
3.72
3.71
3.70
3.70
3.70
3.69
3.69
3.69
3.68
3.68
3.67
3.66
3.28
3.22
3.12
3.11
3.08
3.07
3.07
3.06
3.06
3.05
3.04
3.03
2.90
2.89
2.89
2.88
2.87
2.86
2.85
1.98
2.01
1.00
0.97
3.69
0.97
1.04
1.02
f1 (ppm)

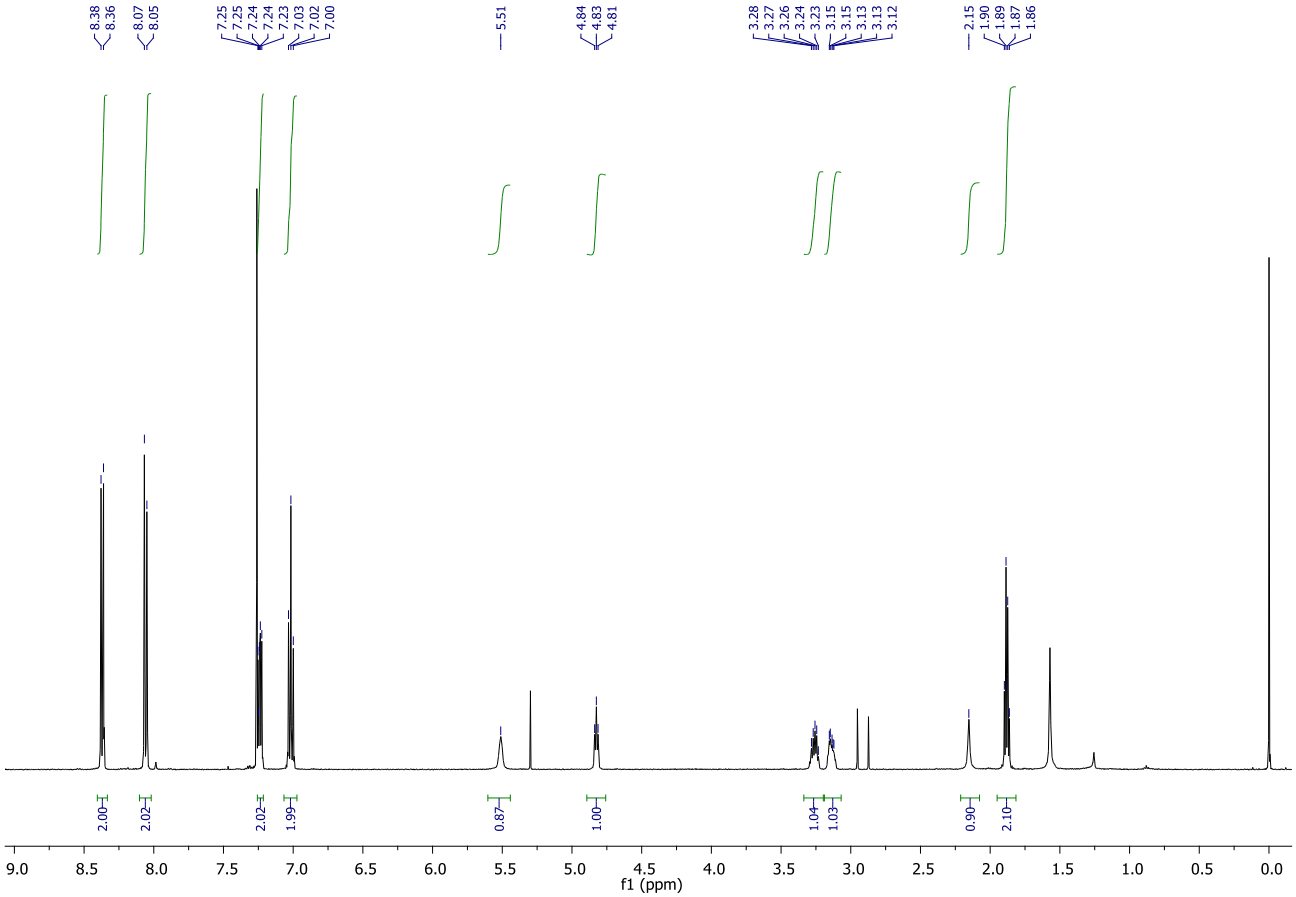

149.88
145.79
127.94
124.10
73.67
68.09
57.97
45.68
f1 (ppm)

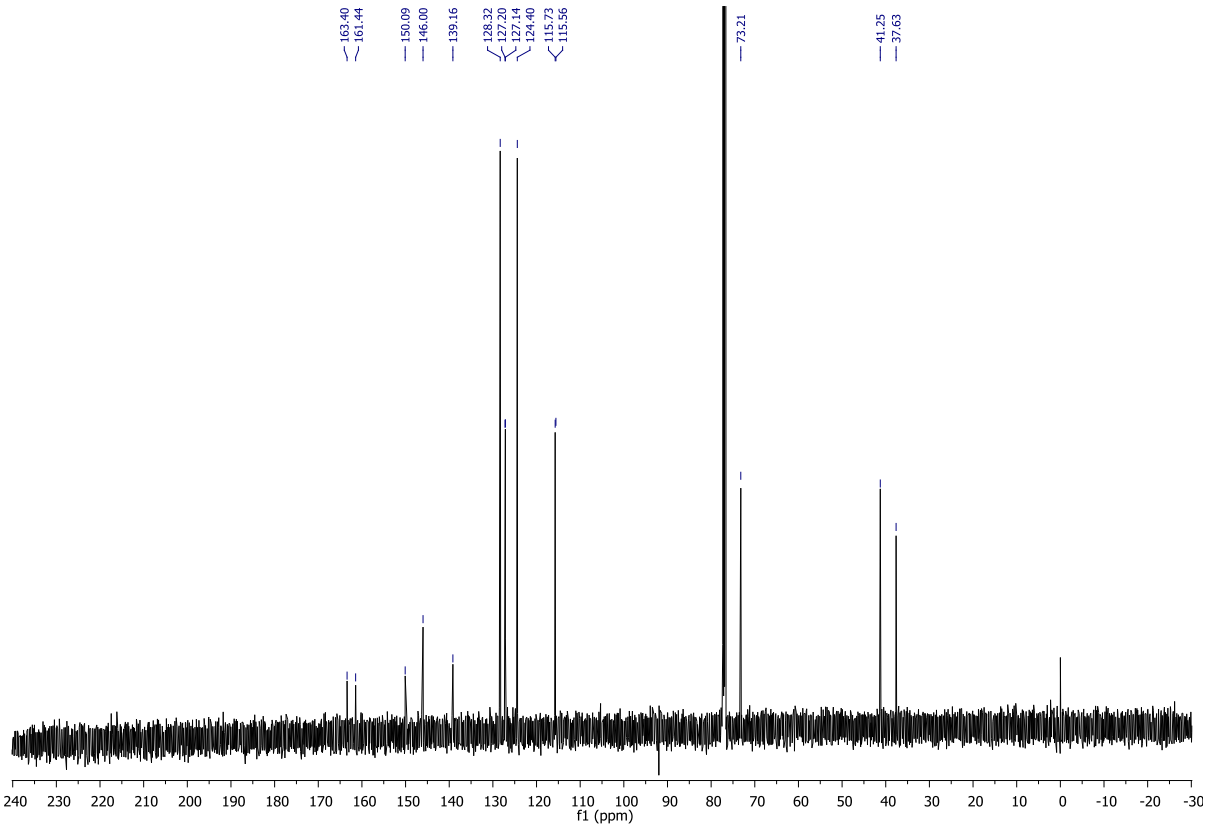
22


7.39
7.39
7.38
7.37
7.36
7.09
7.09
7.08
7.07
7.05
4.99
4.98
2.48
2.46
2.45
2.45
2.45
2.13
2.06
1.00
1.26
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
f1 (ppm)


173.46
162.40
160.47
140.17
127.25
127.19
114.48
114.31
69.12
43.53
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

8h


8.38
8.36
8.07
8.05
7.25
7.25
7.24
7.24
7.23
7.03
7.02
7.00
5.51
4.84
4.83
4.81
3.28
3.27
3.26
3.24
3.23
3.15
3.15
3.13
3.13
3.12
2.15
1.90
1.89
1.87
1.86
2.00
2.02
2.02
1.99
0.87
1.00
1.04
1.03
0.90
2.10
f1 (ppm)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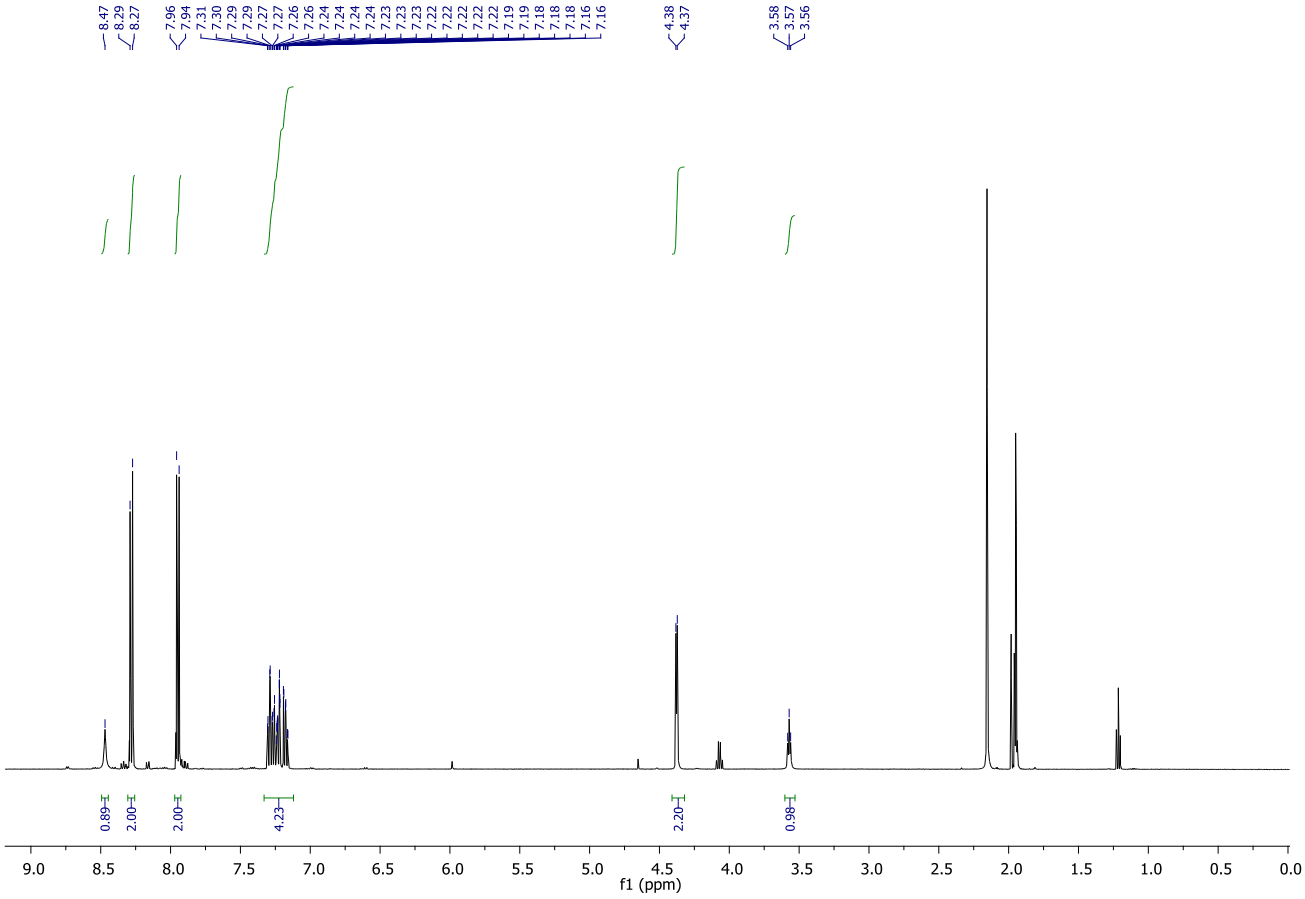
127.14
124.40
115.73
115.56
73.21
41.25
37.63
f1 (ppm)

8i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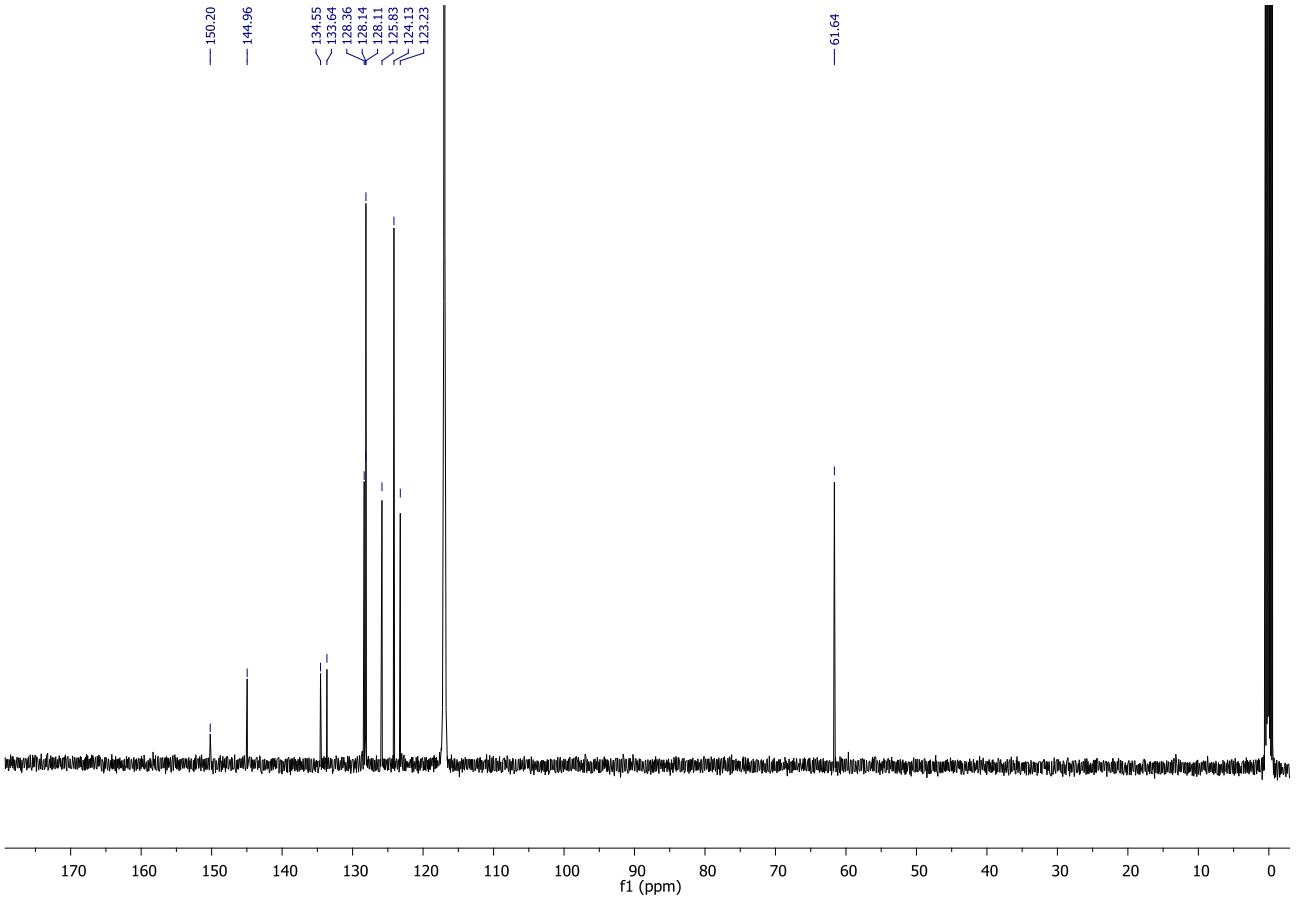
7.94
7.31
7.30
7.29
7.29
7.27
7.27
7.26
7.26
7.24
7.24
7.24
7.24
7.23
7.23
7.23
7.22
7.22
7.22
7.22
7.22
7.19
7.19
7.18
7.18
7.18
7.16
7.16
4.38
4.37
3.58
3.57
3.56
0.89
2.00
2.00
4.23
2.20
0.98
f1 (ppm)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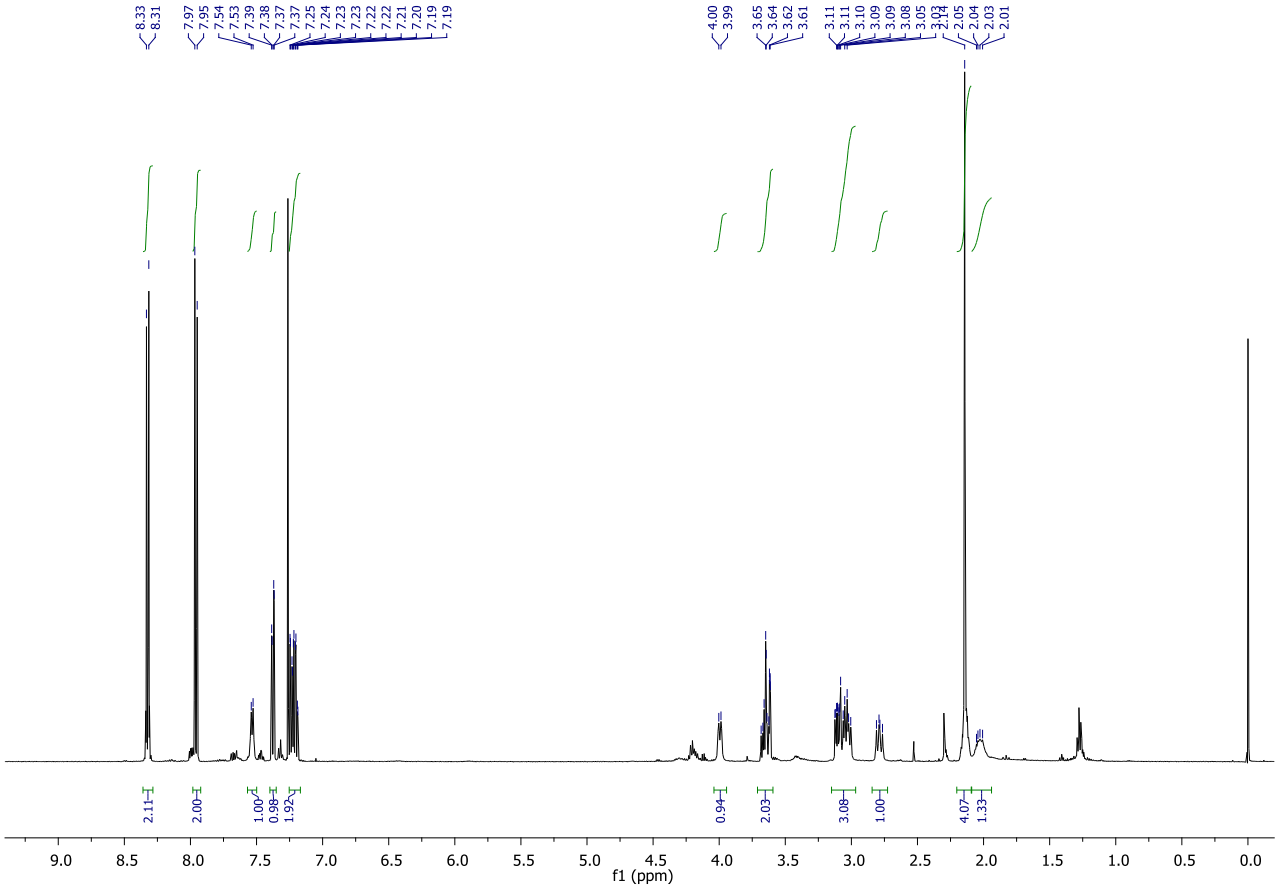
133.64
128.36
128.14
128.11
125.83
124.13
123.23
61.64
f1 (ppm)

10l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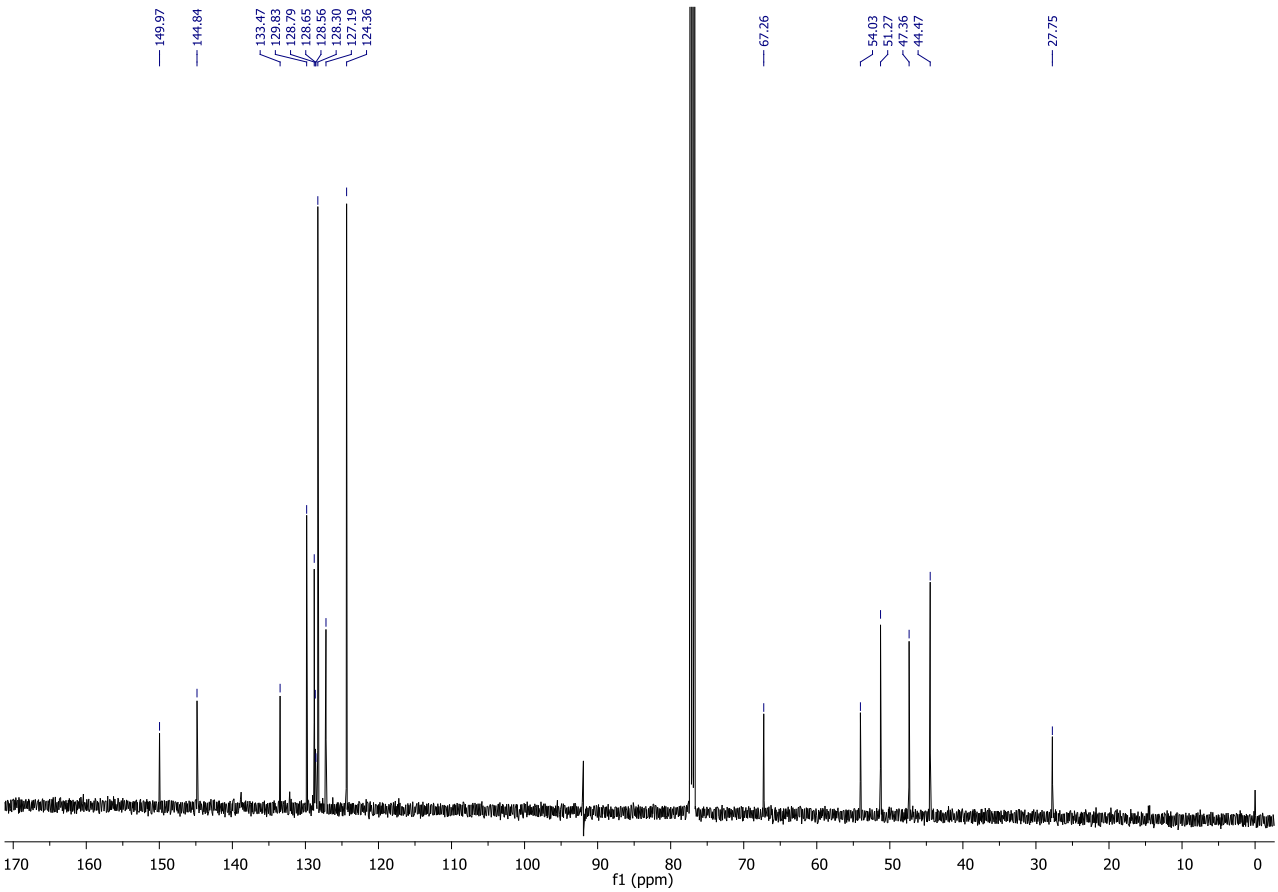
7.54
7.53
7.39
7.38
7.37
7.37
7.25
7.24
7.23
7.23
7.22
7.22
7.21
7.20
7.19
7.19
4.00
3.99
3.65
3.64
3.62
3.61
3.11
3.11
3.10
3.09
3.09
3.08
3.05
2.05
2.04
2.03
2.01
2.11
2.00
1.00
0.98
1.92
0.94
2.03
3.08
1.00
4.07
1.33
f1 (ppm)


149.97
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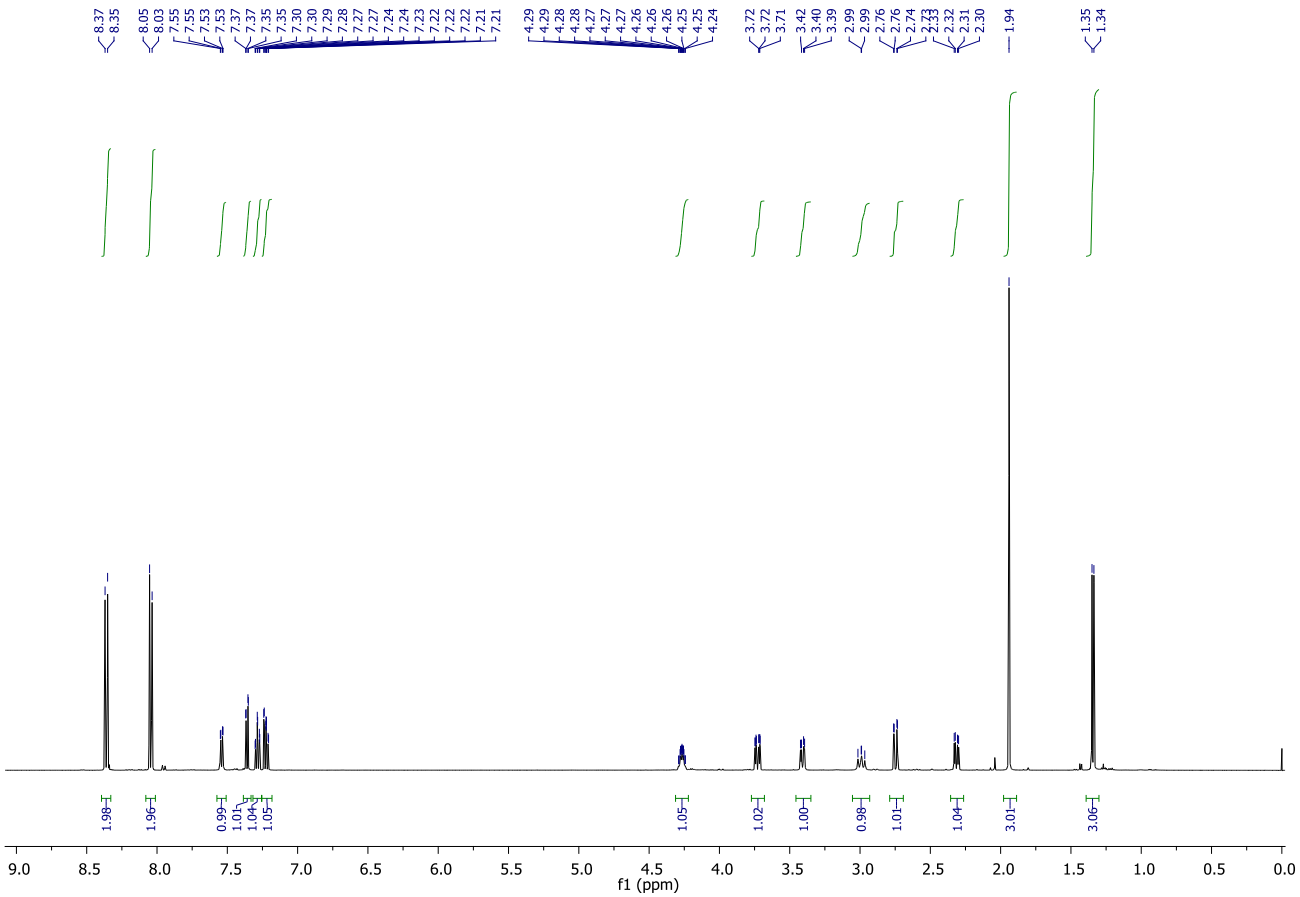
133.47
129.83
128.79
128.65
128.56
128.30
127.19
124.36
67.26
54.03
51.27
47.36
44.47
27.75
f1 (ppm)

10m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8.03
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7.55
7.53
7.53
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7.37
7.35
7.35
7.30
7.30
7.29
7.28
7.27
7.27
7.24
7.24
7.23
7.22
7.22
7.22
7.21
7.21
7.21
4.29
4.29
4.28
4.28
4.27
4.27
4.27
4.26
4.26
4.26
4.25
4.25
4.24
3.72
3.72
3.71
3.42
3.40
3.39
2.99
2.99
2.76
2.76
2.74
2.33
2.32
2.31
2.30
1.94
1.35
1.34
1.98
1.96
0.99
1.01
1.04
1.05
1.05
1.02
1.00
0.98
1.01
1.04
3.01
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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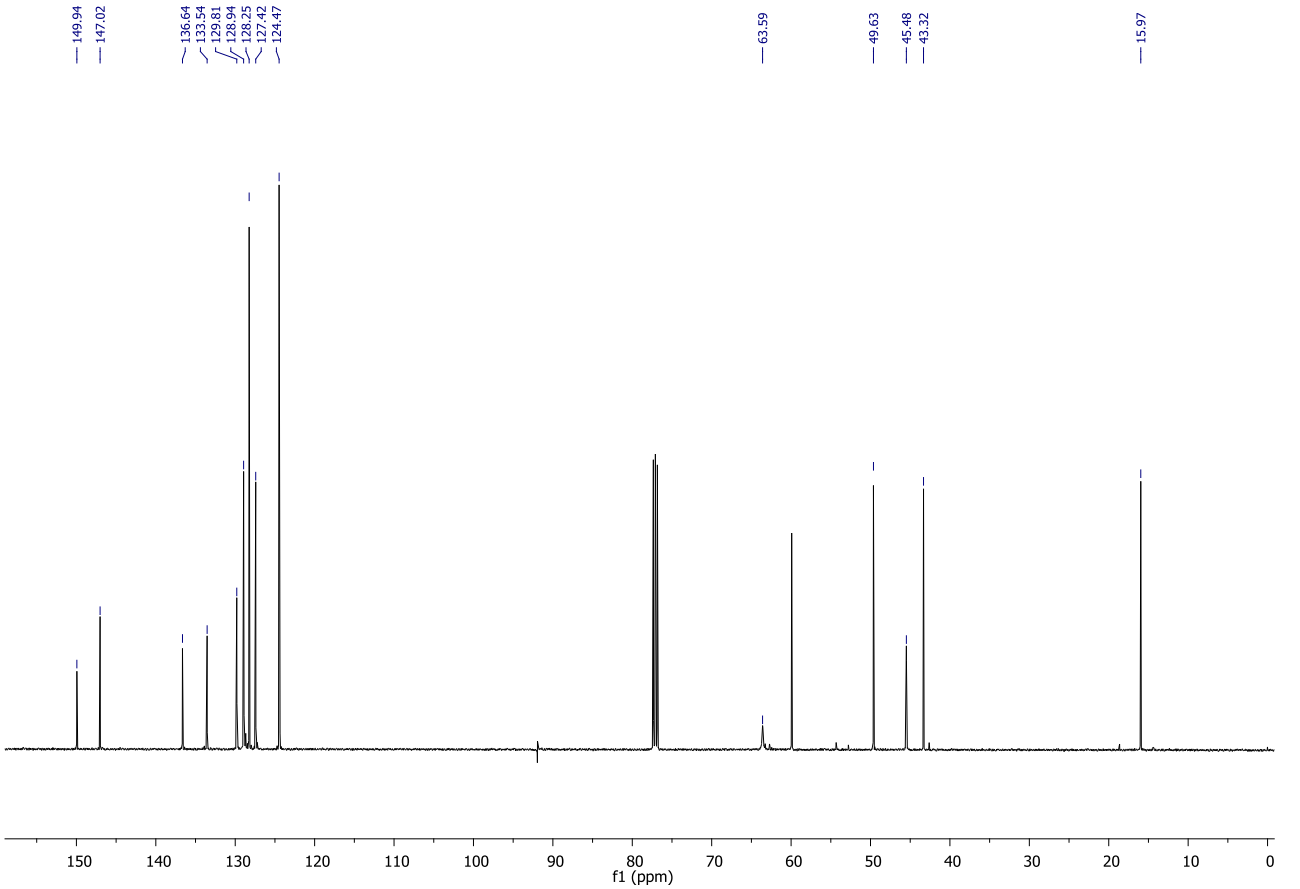
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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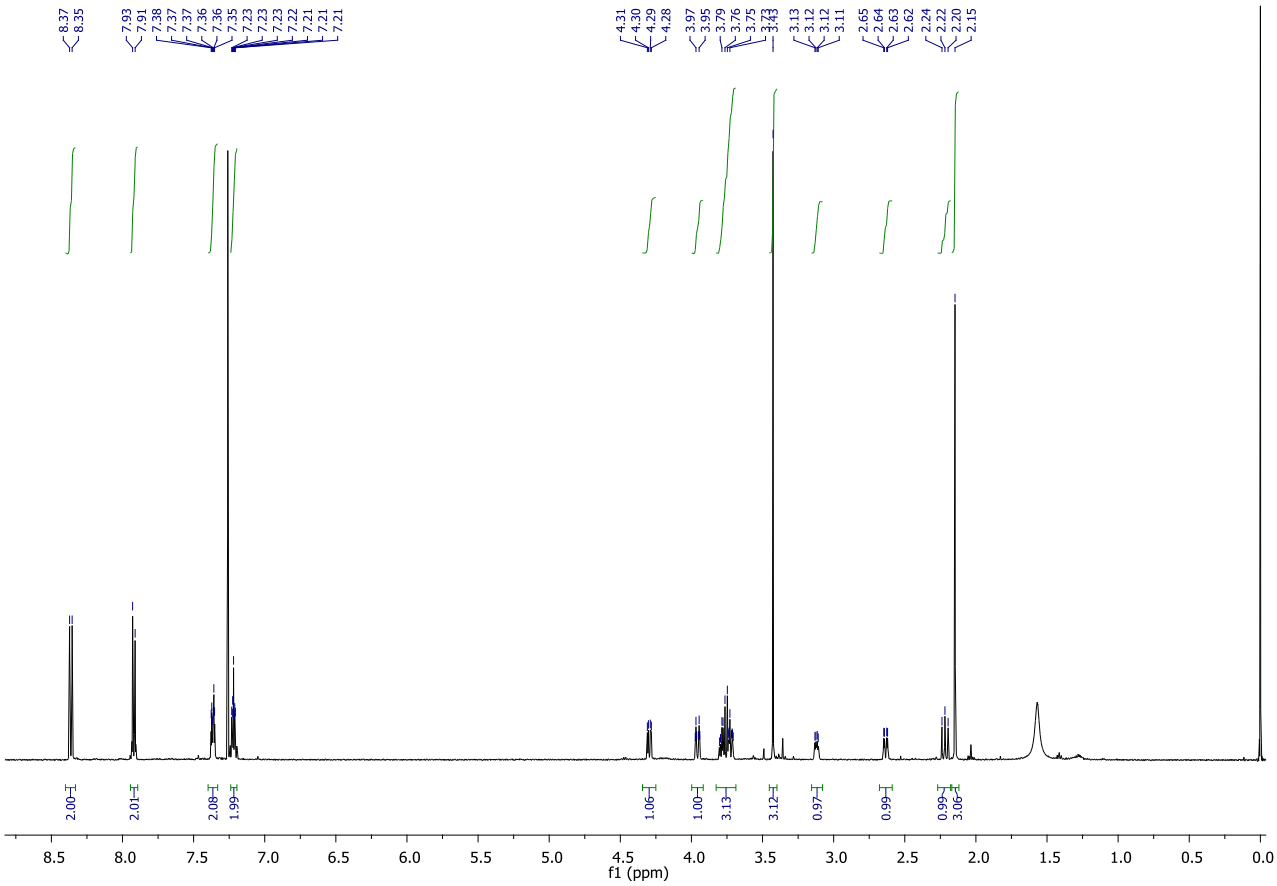
133.54
129.81
128.94
128.25
127.42
124.47
63.59
49.63
45.48
43.32
15.97
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

10n


8.37
8.35
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7.91
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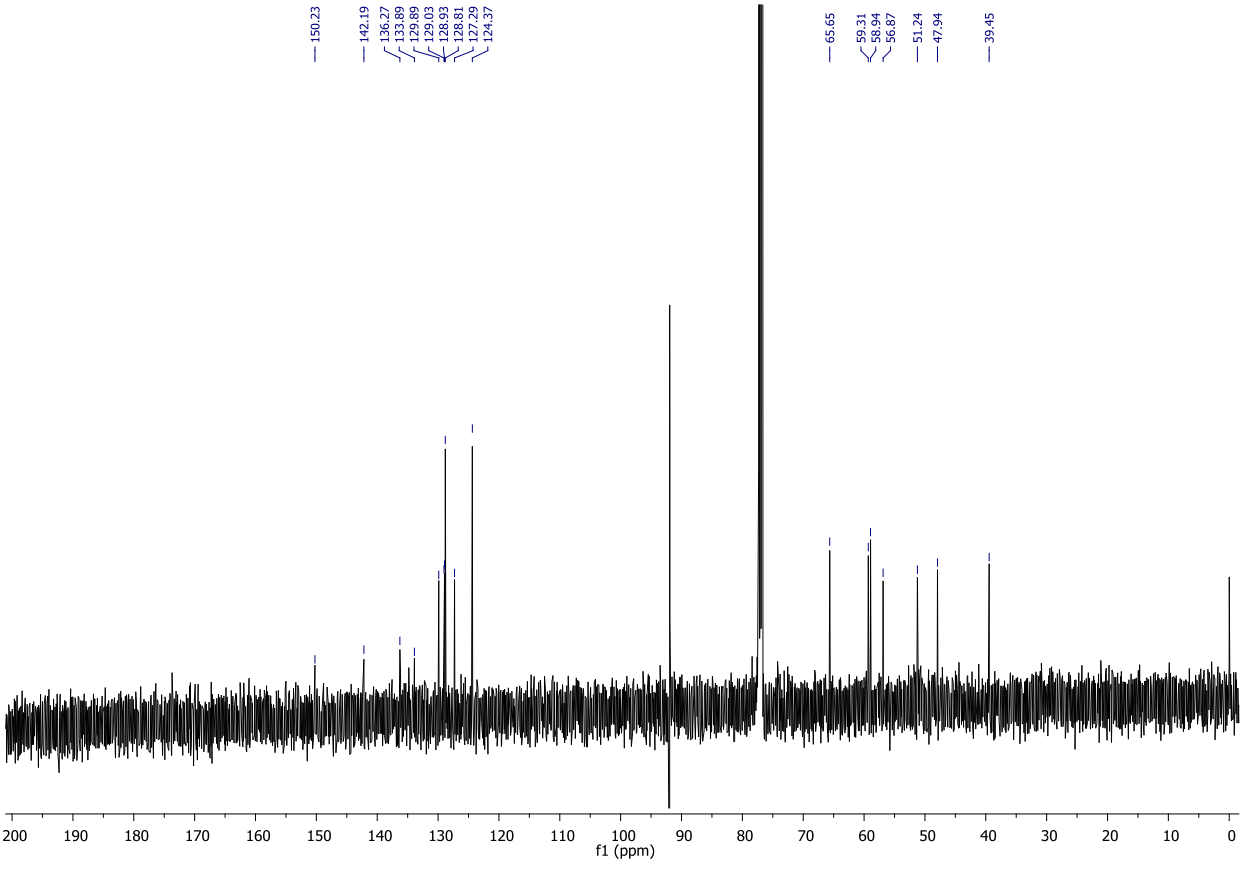
7.37
7.37
7.36
7.36
7.35
7.23
7.23
7.22
7.21
7.21
7.21
4.31
4.30
4.29
4.28
3.97
3.95
3.79
3.76
3.75
3.73
3.13
3.12
3.12
3.11
2.65
2.64
2.63
2.62
2.24
2.22
2.20
2.15
2.00
2.01
2.08
1.99
1.06
1.00
3.13
3.12
0.97
0.99
0.99
3.06
f1 (ppm)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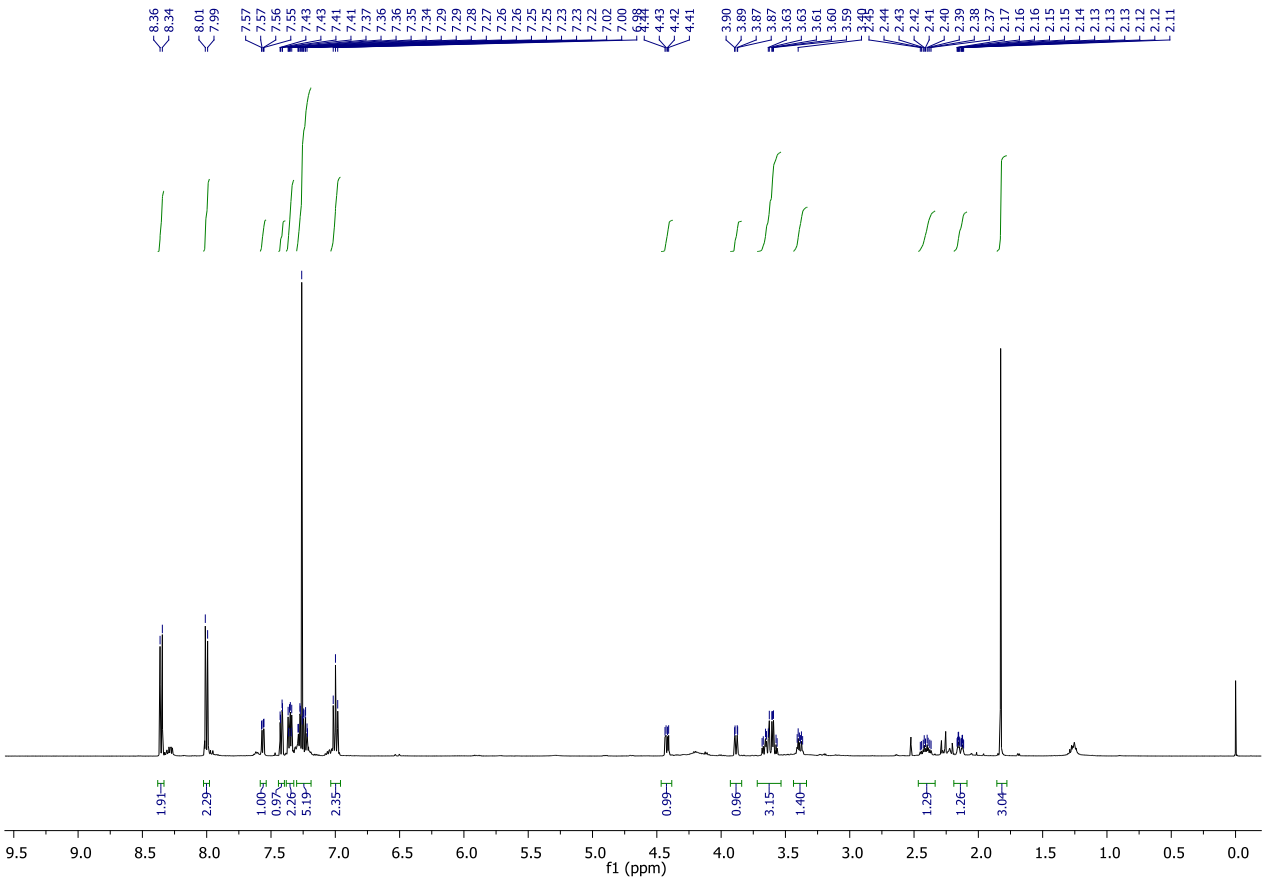
142.19
136.27
133.89
129.89
129.03
128.93
128.81
127.29
124.37
65.65
59.31
58.94
56.87
51.24
47.94
39.45
f1 (ppm)

10o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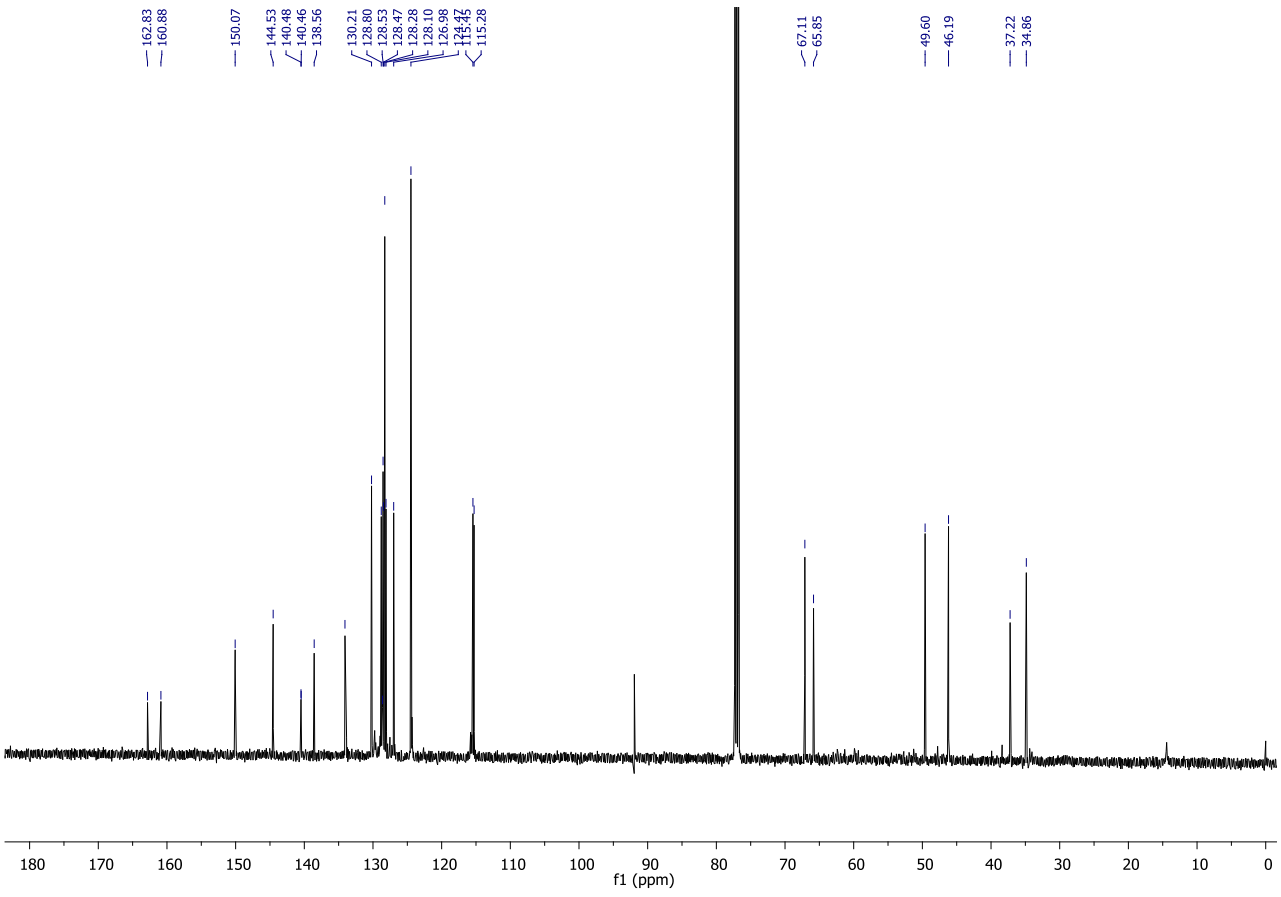
7.55
7.43
7.41
7.41
7.37
7.36
7.36
7.35
7.34
7.29
7.29
7.28
7.27
7.26
7.26
7.25
7.25
7.23
7.22
7.02
7.00
6.98
4.44
4.43
4.42
4.41
3.90
3.89
3.87
3.87
3.63
3.63
3.61
3.60
3.59
3.40
2.45
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.17
2.16
2.16
2.15
2.15
2.14
2.13
2.13
2.13
2.12
2.12
2.11
1.91
2.29
1.00
0.97
2.26
5.19
2.35
0.99
0.96
3.15
1.40
1.29
1.26
3.04
9.5
9.0
8.5
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
f1 (ppm)


162.83
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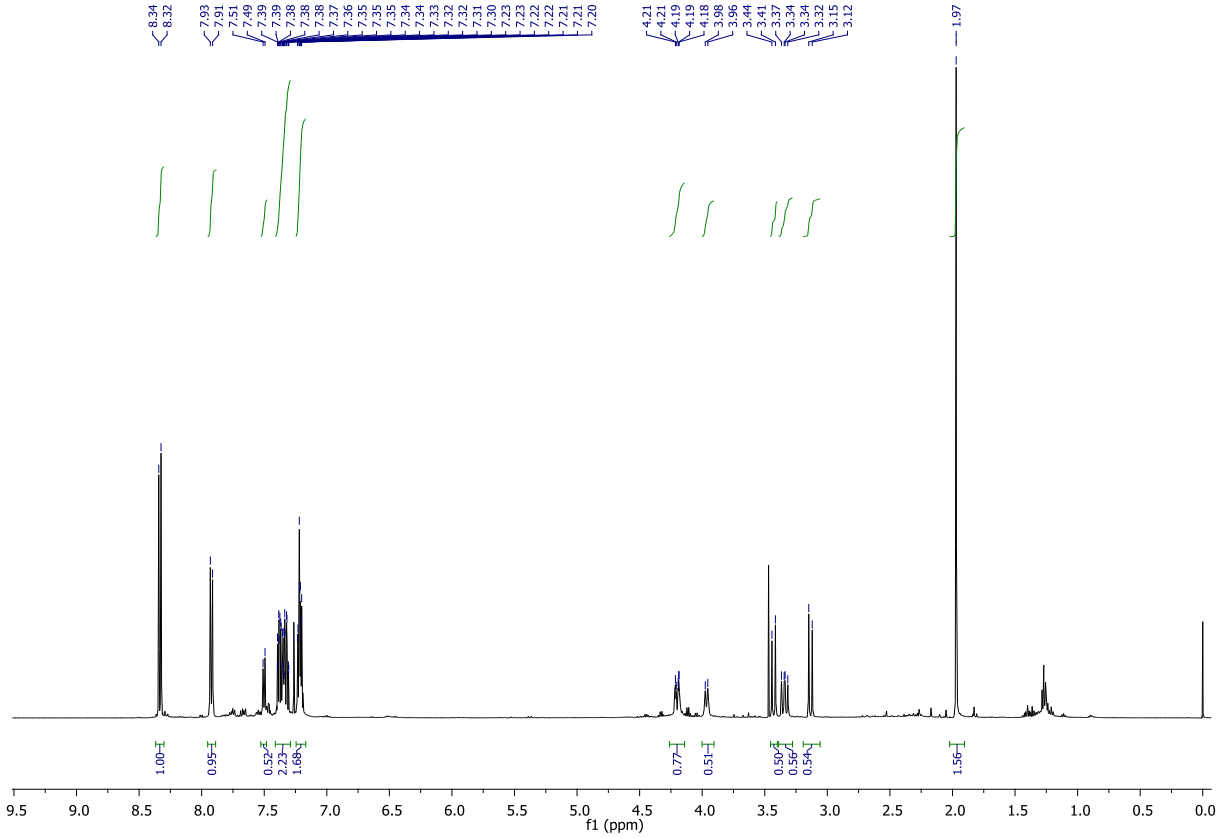
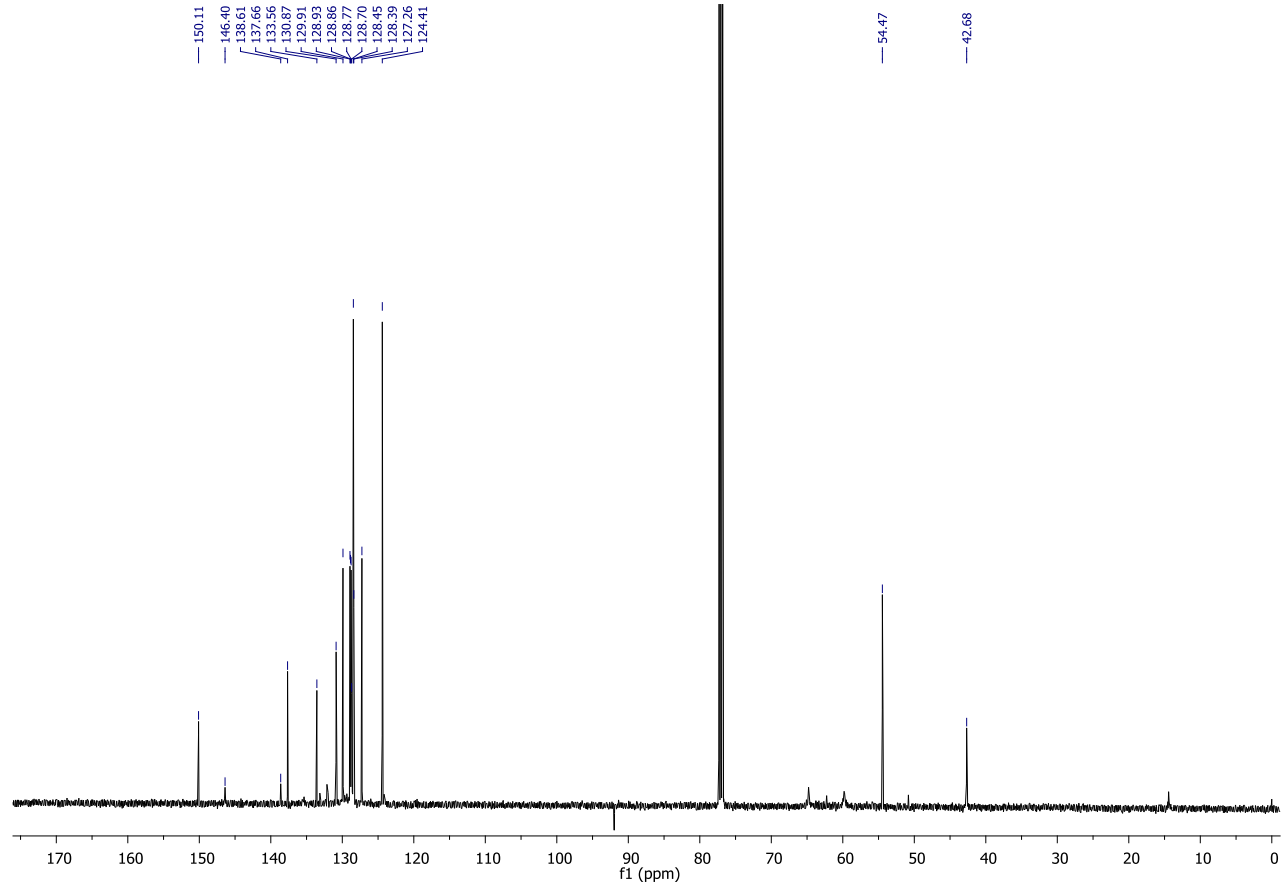
144.53
140.48
140.46
138.56
130.21
128.80
128.53
128.47
128.28
128.10
126.98
120.47
115.42
115.28
67.11
65.85
49.60
46.19
37.22
34.86
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

10p


8.34
8.32
7.93
7.91
7.51
7.49
7.39
7.39
7.38
7.38
7.38
7.37
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.32
7.32
7.31
7.30
7.23
7.23
7.22
7.22
7.21
7.21
7.20
4.21
4.21
4.19
4.19
4.18
3.98
3.96
3.44
3.41
3.37
3.34
3.34
3.32
3.15
3.12
1.97
1.00
0.95
0.52
2.23
1.68
0.77
0.51
0.50
0.56
0.54
1.56
f1 (ppm)


150.11
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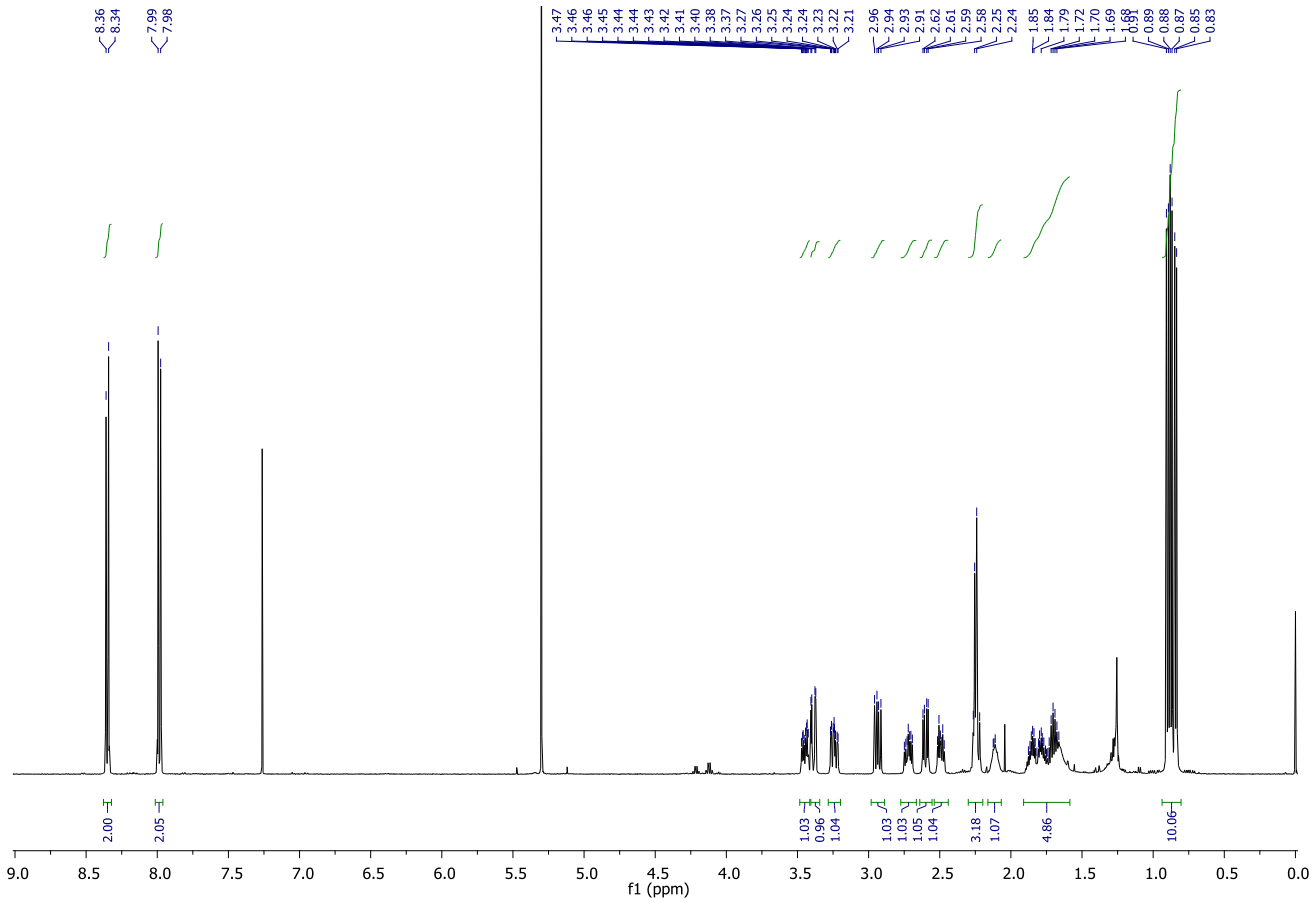
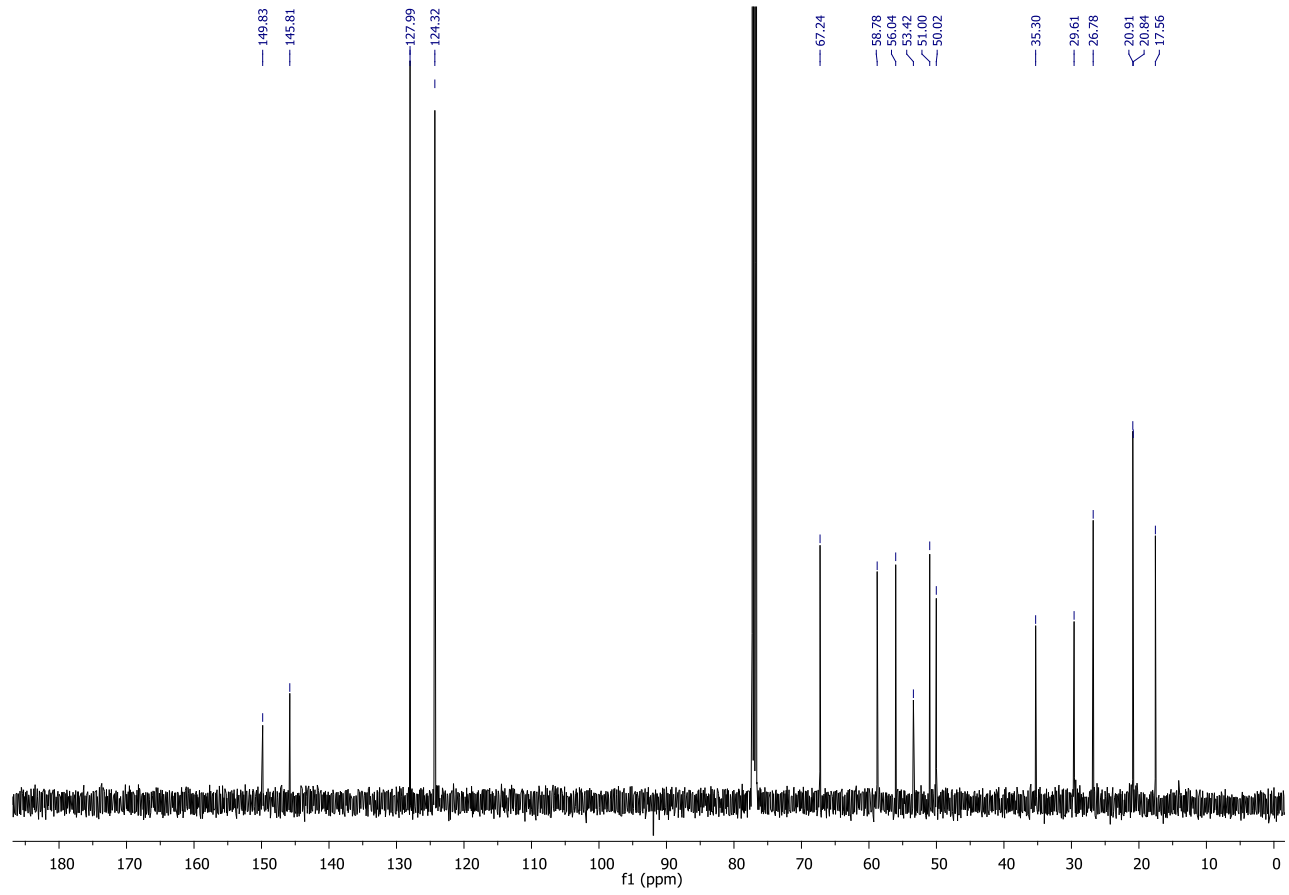
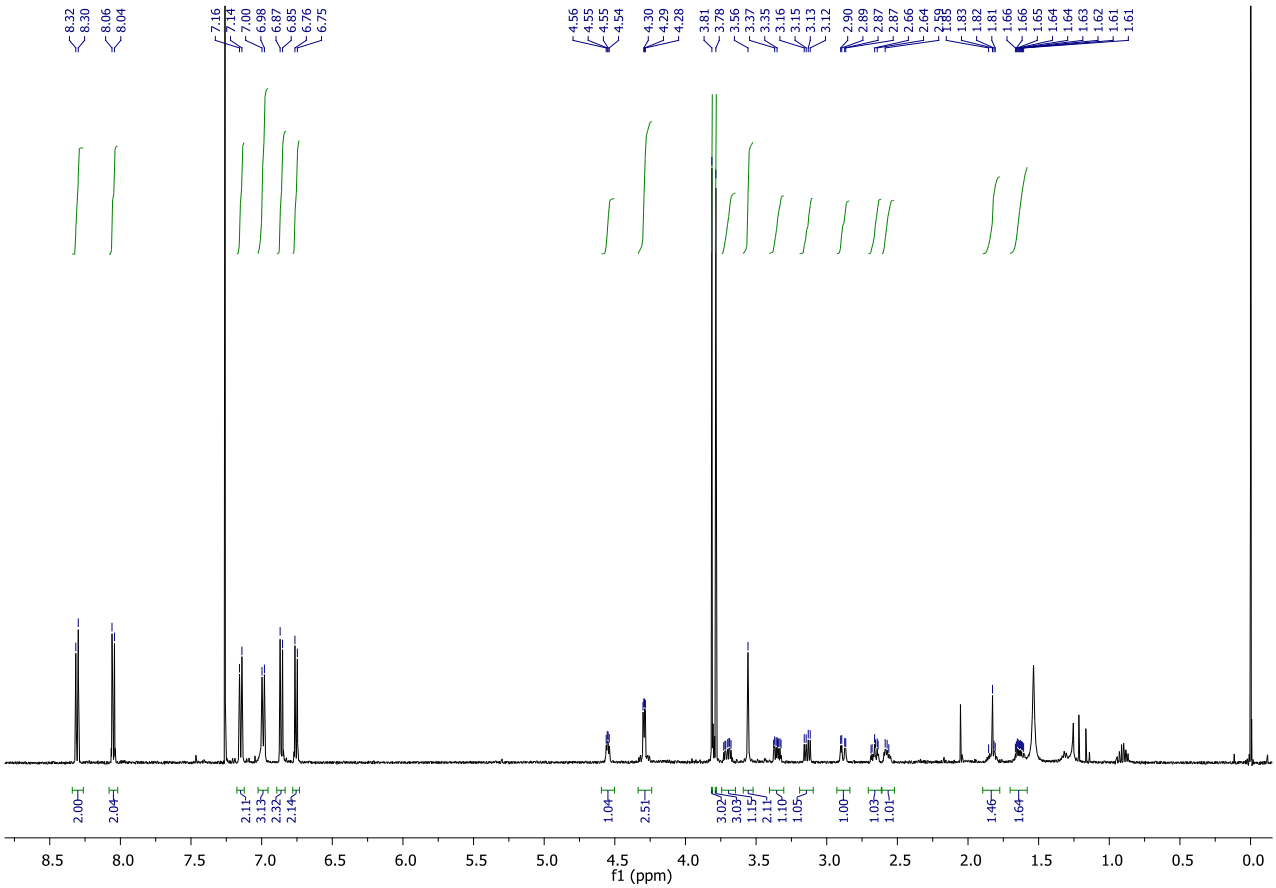
138.61
137.66
133.56
130.87
129.91
128.93
128.86
128.77
128.70
128.45
128.39
127.26
124.41
54.47
42.68
f1 (ppm)

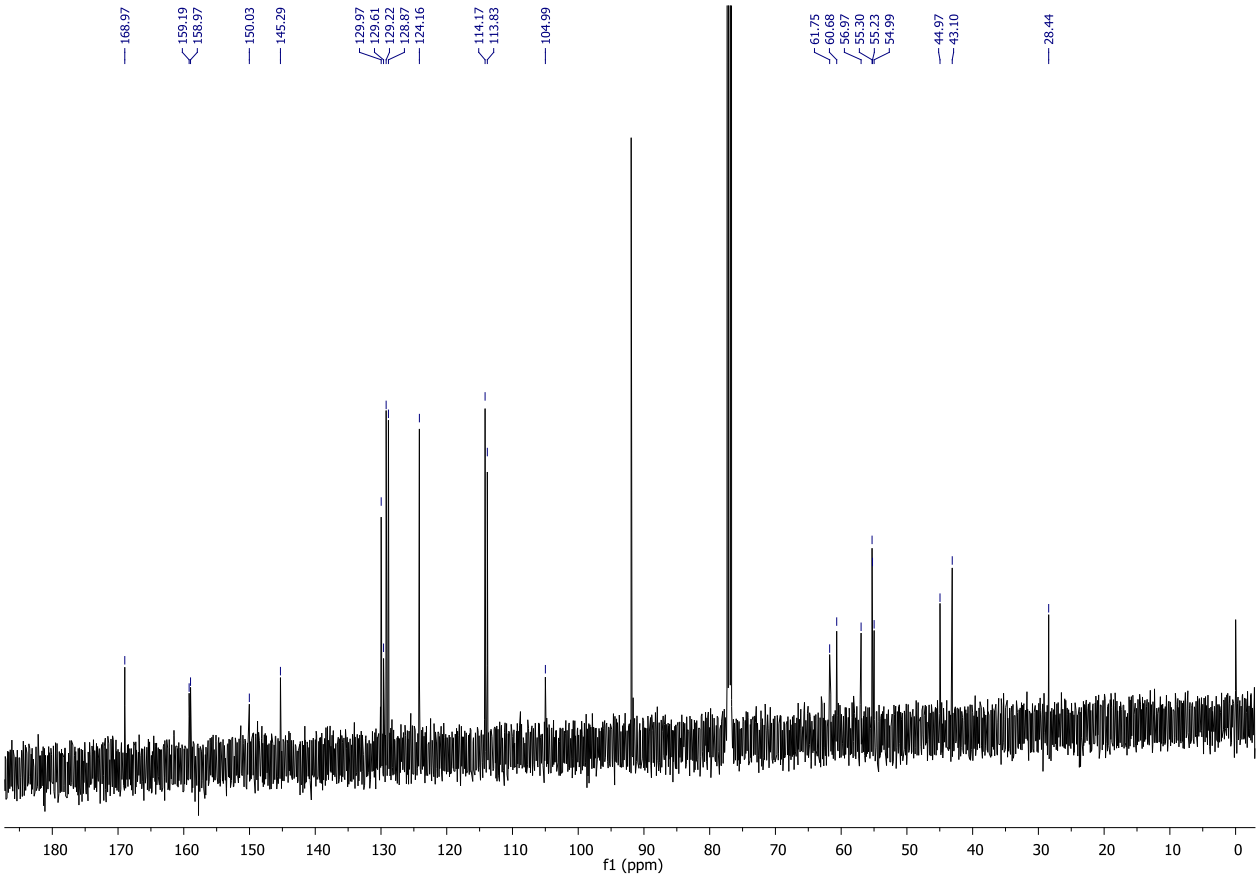
10q


8.36
8.34
7.99
7.98
3.47
3.46
3.45
3.44
3.43
3.42
3.41
3.40
3.38
3.37
3.27
3.26
3.25
3.24
3.23
3.22
3.21
2.96
2.94
2.93
2.91
2.62
2.61
2.59
2.58
2.25
2.24
1.85
1.84
1.79
1.72
1.70
1.69
0.89
0.88
0.87
0.85
0.83
2.00
2.05
1.03
0.96
1.04
1.03
1.03
1.05
1.04
3.18
1.07
4.86
10.06
f1 (ppm)

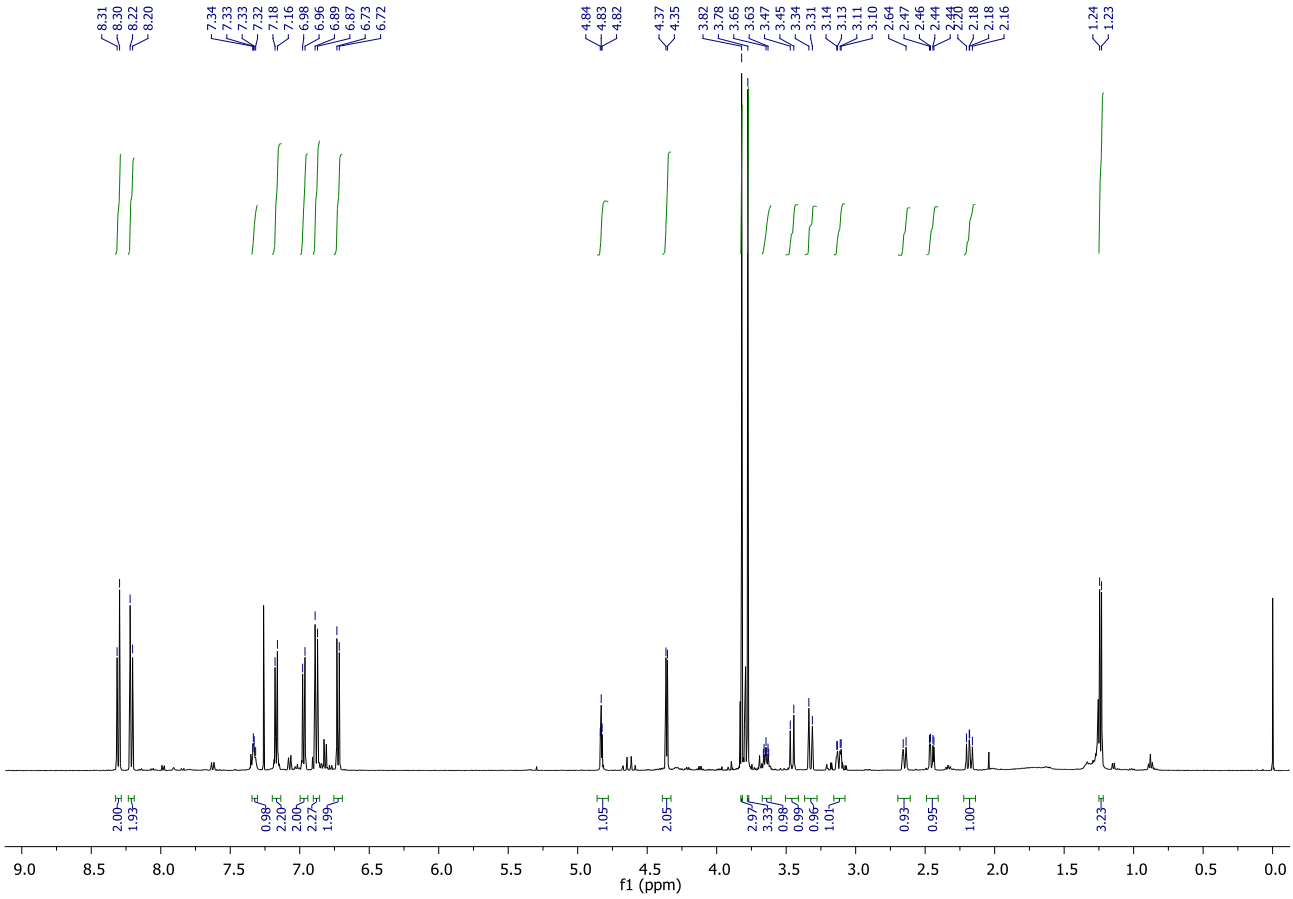

149.83
145.81
127.99
124.32
67.24
58.78
56.04
53.42
51.00
50.02
35.30
29.61
26.78
20.91
20.84
17.56
f1 (ppm)

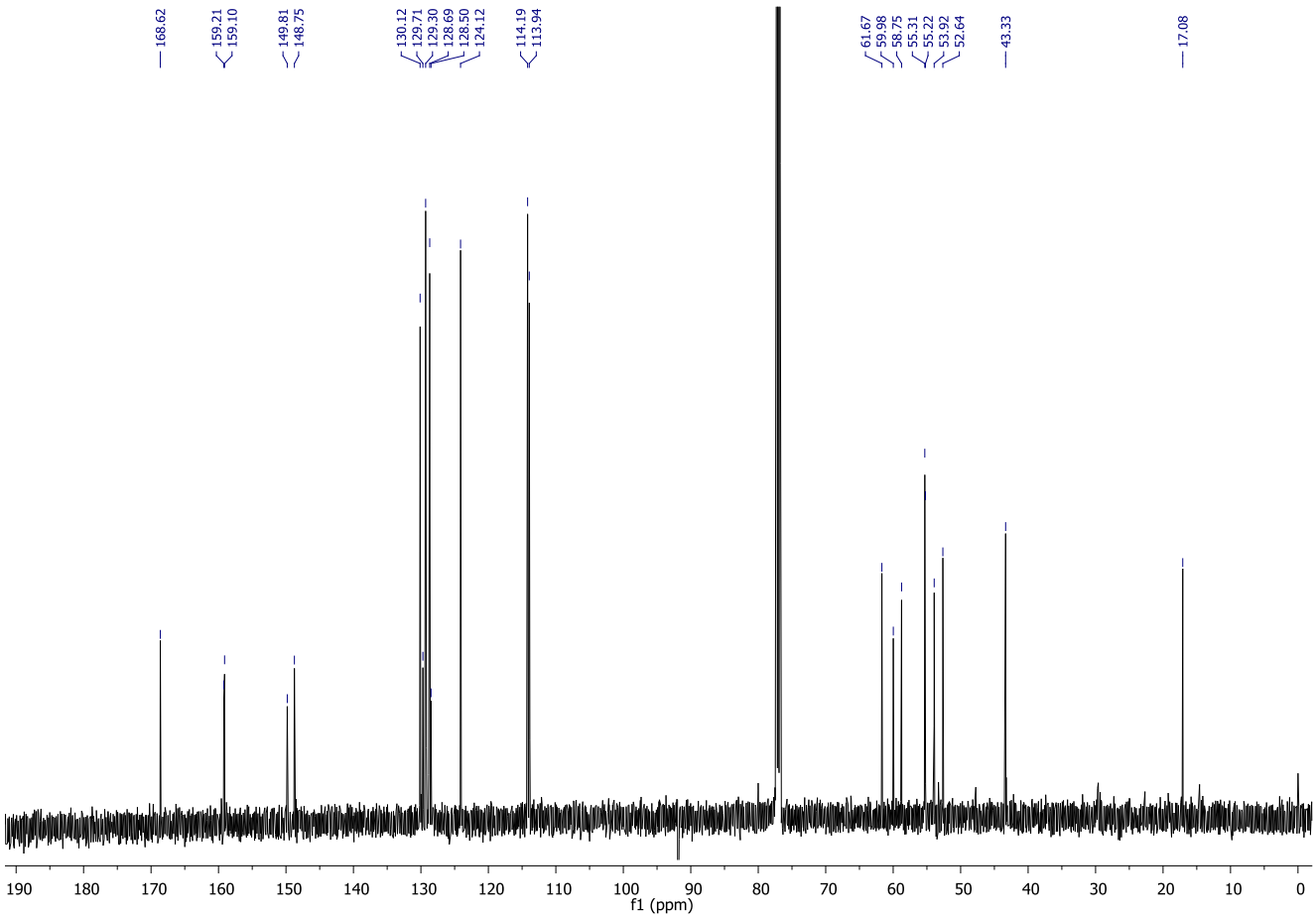
10s


8.32
8.30
8.06
8.04
7.16
7.14
7.00
6.98
6.87
6.85
6.76
6.75
4.56
4.55
4.55
4.54
4.30
4.29
4.28
3.81
3.78
3.56
3.37
3.35
3.16
3.15
3.13
3.12
2.90
2.89
2.87
2.87
2.66
2.64
1.85
1.83
1.82
1.81
1.66
1.66
1.65
1.64
1.64
1.63
1.62
1.61
1.61
2.00
2.04
2.11
3.13
2.32
2.14
1.04
2.51
3.02
3.03
1.15
2.11
1.10
1.05
1.00
1.03
1.01
1.46
1.64
f1 (ppm)

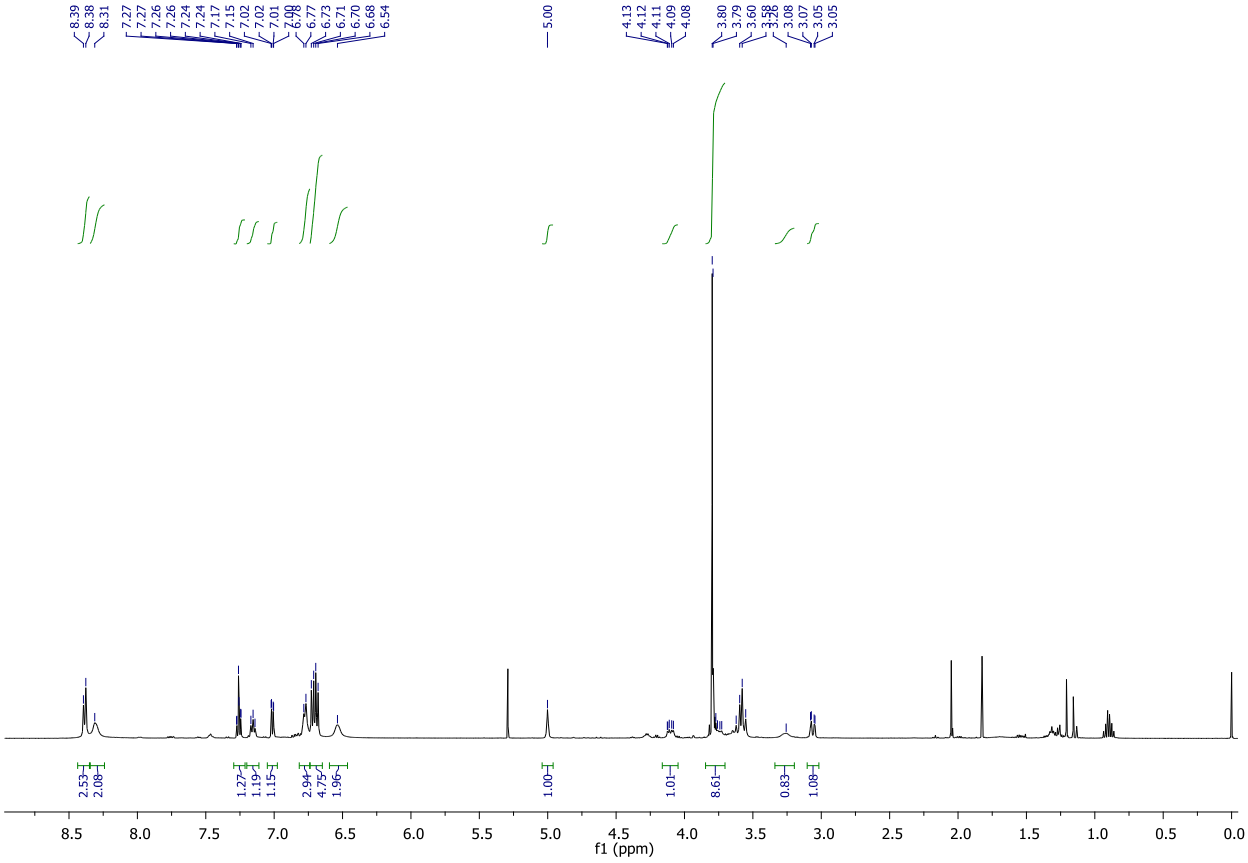

168.97
159.19
158.97
150.03
145.29
129.97
129.61
129.22
128.87
124.16
114.17
113.83
104.99
61.75
60.68
56.97
55.30
55.23
54.99
44.97
43.10
28.44
f1 (ppm)

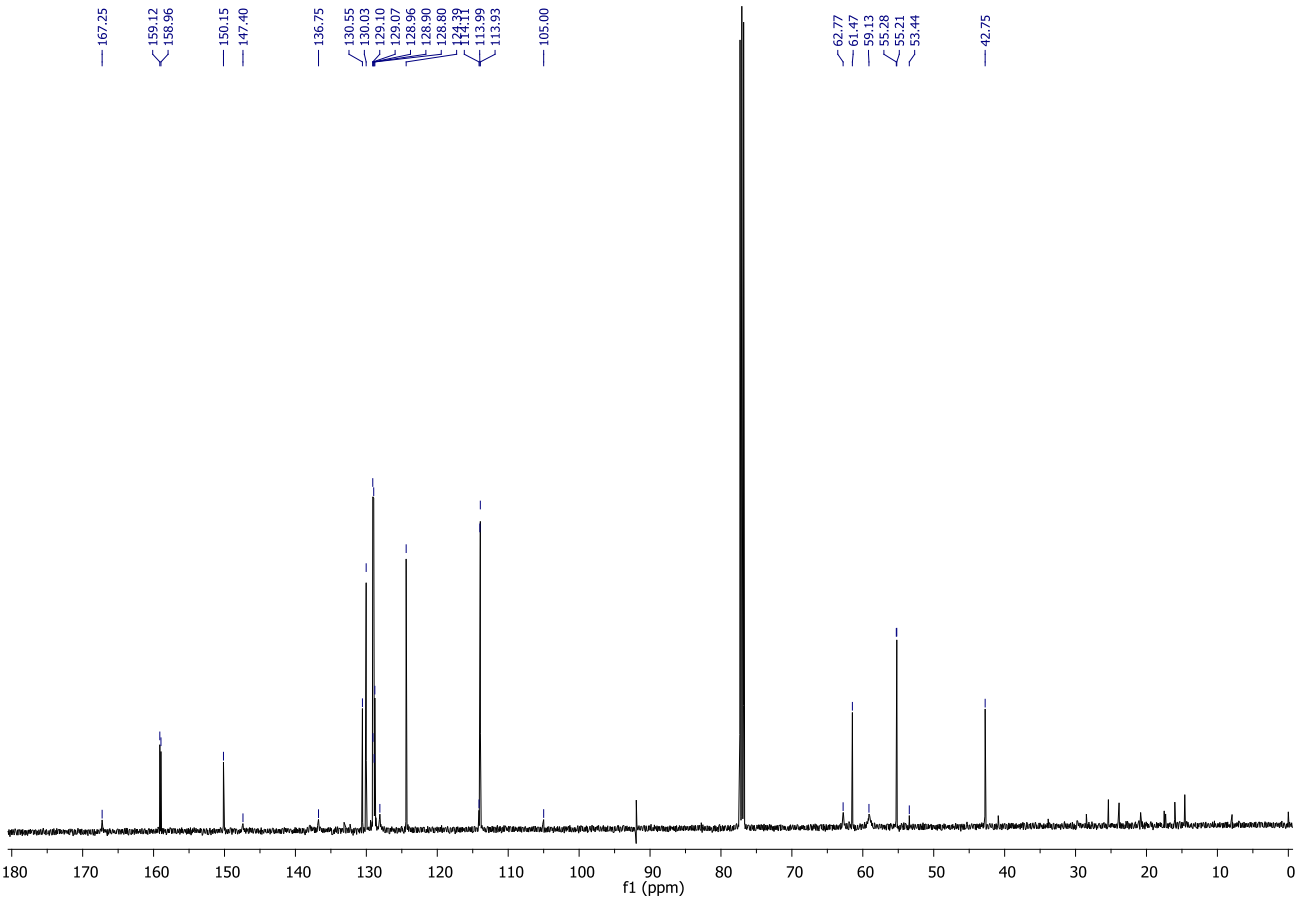
10t


8.31
8.30
8.22
8.20
7.34
7.33
7.33
7.32
7.18
7.16
6.98
6.96
6.89
6.87
6.73
6.72
4.84
4.83
4.82
4.37
4.35
3.82
3.78
3.65
3.63
3.47
3.45
3.34
3.31
3.14
3.13
3.11
3.10
2.64
2.47
2.46
2.44
2.18
2.18
2.16
1.24
1.23
2.00
1.93
0.98
2.20
2.06
2.27
1.99
1.05
2.05
2.97
3.33
0.98
0.99
0.96
1.01
0.93
0.95
1.00
3.23
f1 (ppm)


168.62
159.21
159.10
149.81
148.75
130.12
129.71
129.30
128.69
128.50
124.12
114.19
113.94
61.67
59.98
58.75
55.31
55.22
53.92
52.64
43.33
17.08
f1 (ppm)

10u


8.39
8.38
8.31
7.27
7.27
7.26
7.26
7.24
7.24
7.17
7.15
7.02
7.02
7.01
7.00
6.78
6.77
6.73
6.71
6.70
6.68
6.54
5.00
4.13
4.12
4.11
4.09
4.08
3.80
3.79
3.60
3.58
3.08
3.07
3.05
3.05
2.53
2.08
1.27
1.19
1.15
2.94
4.75
1.96
1.00
1.01
8.61
0.83
1.08
f1 (ppm)


167.25
159.12
158.96
150.15
147.40
136.75
130.55
130.03
129.10
129.07
128.96
128.90
128.80
124.39
114.11
113.99
113.93
105.00
62.77
61.47
59.13
55.28
55.21
53.44
42.75
f1 (ppm)