Concise Synthesis of Triasteranones from Barbaralones

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Supplementary Information

Contents

1. General Information

Reactions. All air-sensitive reactions were carried out under an inert atmosphere using oven-dried apparatus.

Chromatography. Thin layer chromatography (TLC) was performed on Merck DF-Alufoilien 60F254 0.2 mm precoated plates. Column chromatography was carried out using a Teledyne NextGen100 with disposable silica gel columns.

Melting Points. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. The solvent of recrystallization is reported in parentheses.

IR Spectra. Infrared (IR) spectra were recorded on Bruker platinum alpha FTIR spectrometer on the neat compound using the attenuated total refraction technique.

NMR Spectra. NMR spectra were acquired on Bruker Ascend 400 or Ascend 500 spectrometers. ^{1}H and ^{13}C NMR spectra were referenced to external tetramethylsilane via the residual protonated solvent (^{1}H) or the solvent itself (^{13}C). ^{19}F NMR spectra were referenced through the solvent lock (^{2}H) signal according to the IUPAC-recommended secondary referencing method following Bruker protocols. All chemical shifts are reported in parts per million (ppm). For $CDCl_3$, the shifts are referenced to 7.26 ppm for ^{1}H NMR spectroscopy and 77.16 ppm for ^{13}C NMR spectroscopy. ^{13}C NMR Assignments were made using the DEPT sequence with secondary pulses at 90° and 135° or using 2D NMR spectroscopy techniques including HSQC and HMBC. Coupling constants (*J*) are quoted to the nearest 0.1 Hz.

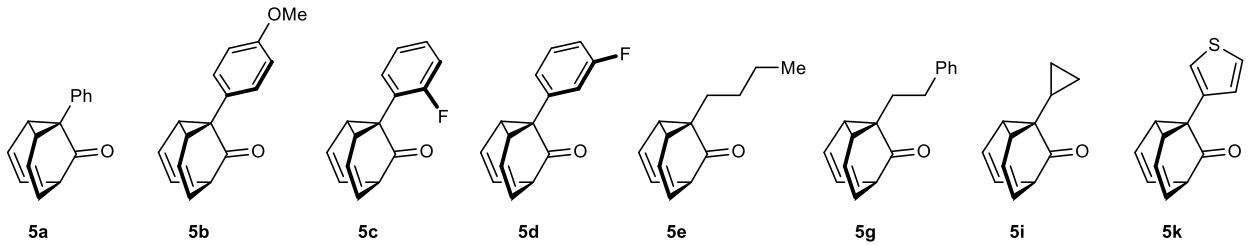
Mass Spectra. Electrospray ionisation (ESI) high-resolution mass spectrometry (HRMS) analyses were performed on a Bruker micrOTOFII mass spectrometer (Bruker Daltonik, Bremen, Germany), interfaced to an Agilent 1200 HPLC (Agilent Technologies, Santa Clara, USA). Samples were presented in solution for analysis by Flow Injection, 1 μL of solution being injected into the ion source of the instrument along with a flow of 0.2 mL min^{-1} of 70% MeOH/H_2O eluent. The mass spectrometer was operated in electrospray ionisation (ESI) mode at a typical resolving power of 8000. Control of the analysis was performed through Bruker's Compass Open Access QC automated data acquisition and reporting software (v1.3; Bruker Daltonik, Bremen, Germany).

X-ray Crystallography. Single crystal X-ray diffraction data for compounds **6b** and **13a'** were collected on an Oxford Diffraction GV1000 diffractometer (TitanS2 CCD area detector, mirror-monochromated Cu-Kα radiation source; λ = 1.54184 Å, ω scans). Data for compounds **14a** and **14g** were collected on an Oxford Diffraction GV1000 diffractomer (AtlasS2 CCD area detector, mirror-monochromated Cu-Kα radiation source; λ = 1.54184 Å, ω scans). Data for compound **14ka** were

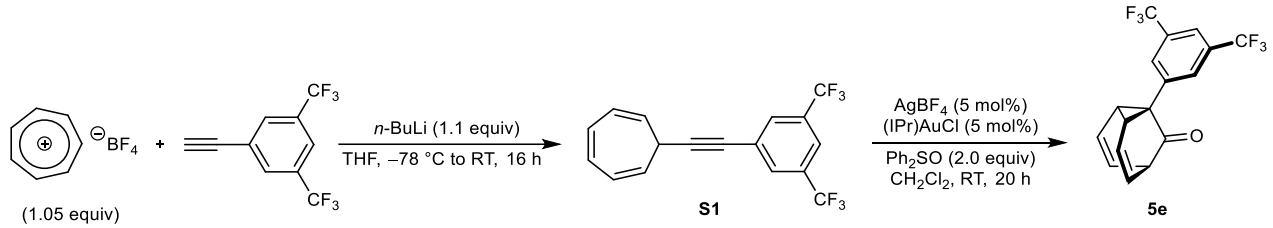
collected on an XtaLAB PRO MM007 diffractomer (PILATUS3 R 200K Hybrid Pixel Array detector, mirror-monochromated Cu-Kα radiation source; λ = 1.54184 Å, ω scans). Single crystals were selected, mounted using Fomblin® (YR-1800 perfluoropolyether oil) on a polymer-tipped MiTeGen MicroMount™, and cooled rapidly to 120 K in a stream of cold N_2 using an Oxford Cryosystems open flow cryostat.[1] Cell parameters were refined from the observed positions of all strong reflections and absorption corrections were applied using a Gaussian numerical method with beam profile correction (CrysAlisPro).[2] Structures were solved within Olex2[3] by dual space iterative methods (SHELXT)[4] and all non-hydrogen atoms refined by full-matrix least-squares on all unique F2 values with anisotropic displacement parameters (SHELXL).[5] Hydrogen atoms were refined both freely and with constrained riding geometries and thermal parameters linked to Uiso of their parent atoms. Structures were checked with checkCIF (http://checkcif.iucr.org). CCDC 2522306–2522310 contain the supplementary data for these compounds. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

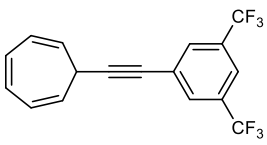
2. Synthesis of Barbaralones

The following known barbaralones were prepared according to known procedures.[6]

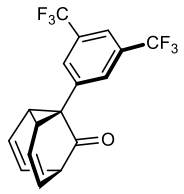


Preparation of Barbaralone 5e



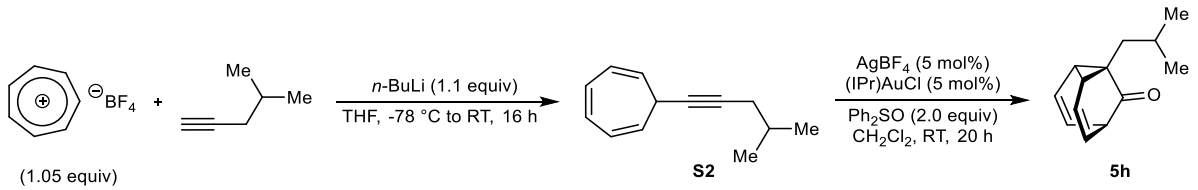


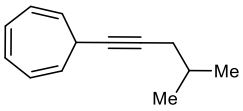
7-{[3,5-Bis(trifluoromethyl)phenyl]ethynyl}cyclohepta-1,3,5-triene (S1). Following a literature procedure,[7] in an oven-dried, two-neck round bottom flask under an argon atmosphere, a solution of 1-ethynyl-3,5-bis(trifluoromethyl)benzene (0.30 mL, 1.70 mmol) in anhydrous THF (10 mL) was cooled to –78 °C. *n*-BuLi (2.5 M in THF, 0.75 mL, 1.87 mmol) was added and the mixture was stirred at –78 °C for 40 min. Tropylium tetrafluoroborate (332 mg, 1.87 mmol) was added in one portion and the mixture was stirred for 16 h while being allowed to warm slowly to room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (× 3). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane) gave *7-alkynylcyclohepta-1,3,5-triene* **S1** as a pale yellow oil (466 mg, 84%). R_f = 0.88 (100% *n*-pentane); IR 3032, 2238 (C≡C), 1381, 1279, 1174, 1133, 897, 847, 744, 701, 683 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (2H, s, Ar**H**), 7.79 (1H, s, Ar**H**), 6.76–6.66 (2H, m, HC=CHC**H**=C**H**CH=CH), 6.30–6.21 (2H, m, HC=C**H**CH=CHC**H**=CH), 5.41 (2H, dd, *J* = 9.1, 5.6 Hz, **H**C=CHCH=CHCH=C**H**), 2.77 (1H, tt, *J* = 2.8, 1.5 Hz, C**H**C≡C); ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.1 (q, J_{CF} = 33.5 Hz, 2 × C), 131.8 (m, 2 × CH), 131.3 (2 × CH), 125.9 (C), 125.5 (2 × CH), 122.61 (q, J_{CF} = 272.8 Hz, 2 × C), 121.9 (2 × CH), 121.5 (q, J_{CF} = 3.8 Hz, CH), 95.1 (C), 78.2 (C), 32.2 (CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1; HRMS (EI) Exact mass calculated for: $[C_{17}H_{10}F_6]^+$ $[M]^+$: 328.0681, found: 328.0674.



1-[3,5-Bis(trifluoromethyl)phenyl]tricyclo[3.3.1.0^{2,8}]nona-3,6-dien-9-one (5f). A round bottom flask was charged with $AgBF_4$ (7.0 mg, 0.040 mmo1), chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) (22 mg, 35.4 μmol), and CH_2Cl_2 (3 mL), and the resulting suspension was stirred at room temperature for 10 min. Diphenyl sulfoxide (284 mg, 1.40 mmol) was added, followed by 7-alkynyl cyclohepta-1,3,5-triene **S1** (230 mg, 0.701 mmol) *via* pipette using CH_2Cl_2 (0.5 mL) as a rinse. The resulting mixture was stirred at room temperature for 20 h. The reaction was filtered through a silica plug using EtOAc as eluent and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane to 15% EtOAc/*n*-pentane) gave *barbaralone* **1e** as a white amorphous solid (175 mg, 73%). R_f = 0.50 (6% EtOAc/*n*-pentane); IR 3054, 1705 (C=O), 1621, 1473, 1359, 1277, 1172, 1128, 1015, 778, 661 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (1H, s, Ar**H**), 7.68 (2H, s, Ar**H**), 5.97–5.86 (4H, m, 2 × C**H**=C**H**), 3.28 (1H, tt, *J* = 6.1, 1.4 Hz, O=CC**H**), 3.22–3.15 (2H, m, 2 × O=CCC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.8 (C), 139.5 (C), 132.0 (q, J_{CF} = 33.2 Hz, 2 × C), 130.0 (q, J_{CF} = 3.9 Hz, 2 × CH), 124.2 (2 × CH), 123.4 (J_{CF} = 272.9 Hz, 2 × C), 122.1–121.7 (m, CH), 121.0 (2 × CH), 48.4 (CH), 42.9 (2 × CH), 39.4 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –62.7; HRMS (ESI) Exact mass calculated for $[C_{17}H_{10}F_6ONa]^+$ $[M+Na]^+$: 367.0528, found 367.0526.

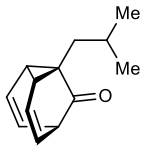
Preparation of Barbaralone 5h





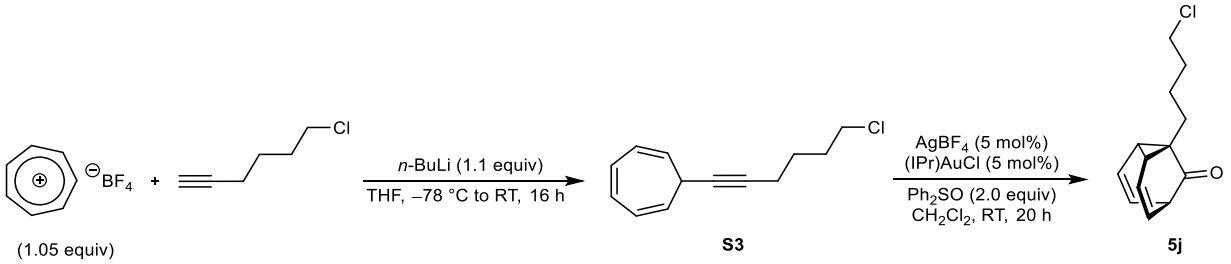
7-(4-Methylpent-1-yn-1-yl)cyclohepta-1,3,5-triene (S2). Following a literature procedure,[6] in an oven-dried, two-neck round bottom flask under an argon atmosphere, 4-methylpent-1-yne (1.65 mL, 14.0 mmol) was dissolved in anhydrous THF (82 mL) and cooled to –78 °C. *n*-BuLi (2.5 M in THF, 1.1 equiv) was added and the resulting solution was stirred at –78 °C for 40 min. Tropylium tetrafluoroborate (2.49 g, 14.0 mmol) was added in one portion and the mixture was stirred for 16 h while being allowed to warm slowly to room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (×3). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane) gave *7-alkynylcyclohepta-1,3,5-triene* **S2** as a pale yellow oil (2.00 g, 83%). R_f = 0.90 (100% *n*-pentane); IR 3027, 3018, 2957, 2906, 2869, 2833, 1699, 1463, 1463, 1385, 1385, 1283, 1167, 744, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69–6.60 (2H, m, HC=CHC**H**=C**H**CH=CH), 6.20–6.10 (2H, m,

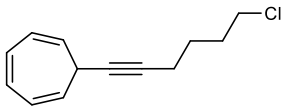
HC=C**H**CH=CHC**H**=CH), 5.33 (2H, dd, *J* = 9.1, 5.5 Hz, **H**C=CHCH=CHCH=C**H**), 2.50–2.41 (1H, m, C**H**C≡C), 2.12 (2H, dd, *J* = 6.6, 2.3 Hz, C≡CC**H**$_2$), 1.89–1.75 (1H, m, C**H**(CH$_3$)$_2$), 1.00 (6H, d, *J* = 6.6 Hz, CH(C**H**$_3$)$_2$); ^{13}C NMR (126 MHz, CDCl$_3$) δ 131.1 (2 × CH), 124.6 (2 × CH), 124.5 (2 × CH), 82.5 (C), 79.6 (C), 32.0 (CH), 28.3 (CH), 28.1 (CH$_2$), 22.1 (2 × CH$_3$); HRMS (EI) Exact Mass calculated for [C$_{13}$H$_{16}$]$^+$ [M]$^+$: 172.1247, found: 172.1239.



1-Isobutyltricyclo[3.3.1.0^{2,8}]nona-3,6-dien-9-one (5h). A round bottom flask was charged with AgBF$_4$ (29 mg, 0.15 mmo1), chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) (93 mg, 0.15 mmo1), and CH$_2$Cl$_2$ (15 mL), and the resulting suspension was stirred at room temperature for 10 min. Diphenyl sulfoxide (1.21 g, 6.00 mmol) was added, followed by a solution of the 7-alkynyl cyclohepta-1,3,5-triene **S2** (517 mg, 3.00 mmol) in CH$_2$Cl$_2$ (3 mL) and the mixture was stirred at room temperature for 20 h. The reaction was filtered through a silica plug using EtOAc as eluent and concentrated *in vacuo*. Purification of the residue by column chromatography gave *barbaralone* **5h** as a yellow oil (150 mg, 27%). R$_f$ = 0.54 (2% EtOAc/*n*-pentane); IR 3046, 2955, 2868, 1702 (C=O), 1620, 1467, 1244, 1167, 1102, 1027, 766, 738, 717 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.91–5.83 (2H, m, 2 × C**H**=CH), 5.75–5.68 (2H, m, 2 × CH=C**H**), 3.13–3.06 (1H, m, O=CC**H**), 2.58–2.51 (2H, m, 2 × O=CCC**H**), 2.05–1.90 (1H, m, C**H**(CH$_3$)$_2$), 1.52 (2H, d, *J* = 7.5 Hz, C**H**$_2$), 0.86 (6H, d, *J* = 6.6 Hz, CH(C**H**$_3$)$_2$); ^{13}C NMR (126 MHz, CDCl$_3$) δ 210.5 (C), 126.6 (2 × CH), 121.5 (2 × CH), 50.0 (CH), 40.6 (2 × CH), 40.0 (CH$_2$), 32.8 (C), 26.4 (CH), 23.1 (2 × CH$_3$); HRMS (ESI) Exact mass calculated for [C$_{13}$H$_{16}$ONa]$^+$ [M+Na]$^+$: 211.1093, found 211.1093.

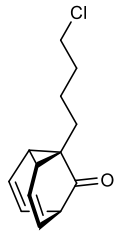
Preparation of Barbaralone 5j





7-(6-Chlorohex-1-yn-1-yl)cyclohepta-1,3,5-triene (S3). Following a literature procedure,[6] in an oven-dried, two-neck round bottom flask under an atmosphere of argon, a solution of 6-chlorohex-1-yne (1.00 g, 8.57 mmol) in anhydrous THF (54 mL) was cooled to –78 °C. *n*-BuLi (2.5 M in hexanes, 3.8 mL, 9.5 mmol) was added and the mixture was stirred at –78 ºC for 40 min. Tropylium tetrafluroborate (1.60 g, 9.01 mmol) was added in one portion and the mixture was stirred for 16 h while being allowed to warm

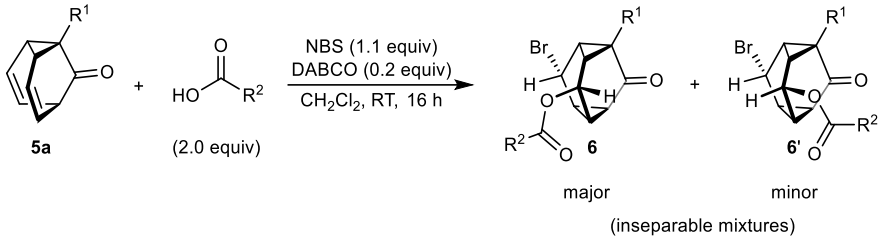
slowly to room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (× 3). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane) gave *7-alkynylcyclohepta-1,3,5-triene* **S3** as a brown oil (1.77 g, 68%). R_f = 0.33 (100% *n*-pentane); IR 3055, 3026, 2953, 2867, 1454, 1435, 1279, 745, 703, 652 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.69–6.59 (2H, m, HC=CHC**H**=C**H**CH=CH), 6.21–6.10 (2H, m, HC=C**H**CH=CHC**H**=CH), 5.34–5.26 (2H, m, **H**C=CHCH=CHCH=C**H**), 3.61–3.56 (2H, m, C$\mathbf{H}_2$Cl), 2.49–2.39 (1H, m, C**H**C≡C), 2.31–2.26 (2H, m, C≡CC$\mathbf{H}_2$), 1.99–1.88 (2H, m, C$\mathbf{H}_2CH_2$Cl), 1.74–1.64 (2H, m, C$\mathbf{H}_2CH_2CH_2$Cl); ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.1 (2 × CH), 124.7 (2 × CH), 124.2 (2 × CH), 82.4 (C), 79.7 (C), 44.8 (CH_2), 31.9 (CH), 31.7 (CH_2), 26.2 (CH_2), 18.2 (CH_2); HRMS (EI) Exact mass calculated for $[C_{13}H_{15}{}^{35}Cl]^+$ $[M]^+$: 206.0857, found: 206.0805.



1-(4-Chlorobutyl)tricyclo[3.3.1.0^{2,8}]nona-3,6-dien-9-one (5j). A round bottom flask was charged with (1,3-bis(2,6-diisopropylphenyl)-2,3-dihydro-1*H*-imidazol-2-yl)gold(II) chloride (75 mg, 0.12 mmol), $AgBF_4$ (24 mg, 0.12 mmol), and CH_2Cl_2 (10 mL), and the resulting suspension was stirred at room temperature for 10 min. Diphenyl sulfoxide (489 mg, 2.42 mmol) was added, followed by 7-alkynyl cyclohepta-1,3,5,-triene **S3** (500 mg, 2.42 mmol) *via* pipette using CH_2Cl_2 (2 mL) as a rinse. The reaction mixture was stirred at room temperature for 16 h. The reaction was filtered through a silica plug using EtOAc as an eluent and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane to 10% EtOAc/*n*-pentane) gave *barbaralone* **5j** as a brown oil (280 mg, 52%). R_f = 0.67 (10% EtOAc/*n*-pentane); IR 3047, 2952, 2938, 2919, 2865, 2846, 1701 (C=O), 1620, 1456, 1310, 767, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.75–5.67 (2H, m, 2 × C**H**=CH), 5.66–5.58 (2H, m, 2 × CH=C**H**), 3.53 (2H, t, *J* = 6.7 Hz, C$\mathbf{H}_2$Cl), 3.06 (1H, tt, *J* = 6.4, 0.9 Hz, O=CC**H**), 2.85–2.77 (2H, m, 2 × O=CC**H**), 1.82–1.73 (2H, m, C$\mathbf{H}_2CH_2$Cl), 1.66–1.58 (2H, m, C$\mathbf{H}_2CH_2CH_2CH_2$Cl), 1.55–1.45 (2H, m, C$\mathbf{H}_2CH_2CH_2$Cl); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.3 (C), 121.5 (4 × CH), 47.9 (CH), 45.1 (CH_2), 32.8 (CH_2), 30.7 (CH_2), 23.5 (CH_2), 2 signals were not observed; HRMS (EI) Exact mass calculated for $[C_{13}H_{15}{}^{35}ClO]^+$ $[M]^+$: 222.0806, found: 222.0813.

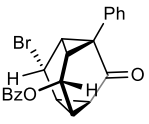
3. Synthesis of Triasteranones by the Bromoesterification of Barbaralones

General Procedure A



A reaction vial was charged with barbaralone **5a** (62 mg, 0.30 mmol), the carboxylic acid (0.59–0.60 mmol) and CH_2Cl_2 (1.5 mL). NBS (58 mg, 0.33 mmol) and DABCO (6.7 mg, 0.06 mmol) were added sequentially, each in one portion, and the reaction was stirred at room temperature for 16 h. Saturated aqueous $NaHCO_3$ solution (3 mL) was added, and the aqueous layer was separated and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. An ^{1}H NMR spectrum of the residue was used to determine the diastereomeric ratio. Purification of the residue by column chromatography (100% *n*-pentane to 70% EtOAc/*n*-pentane) gave the diastereomeric triasteranones **6** and **6'** as an inseparable mixture.

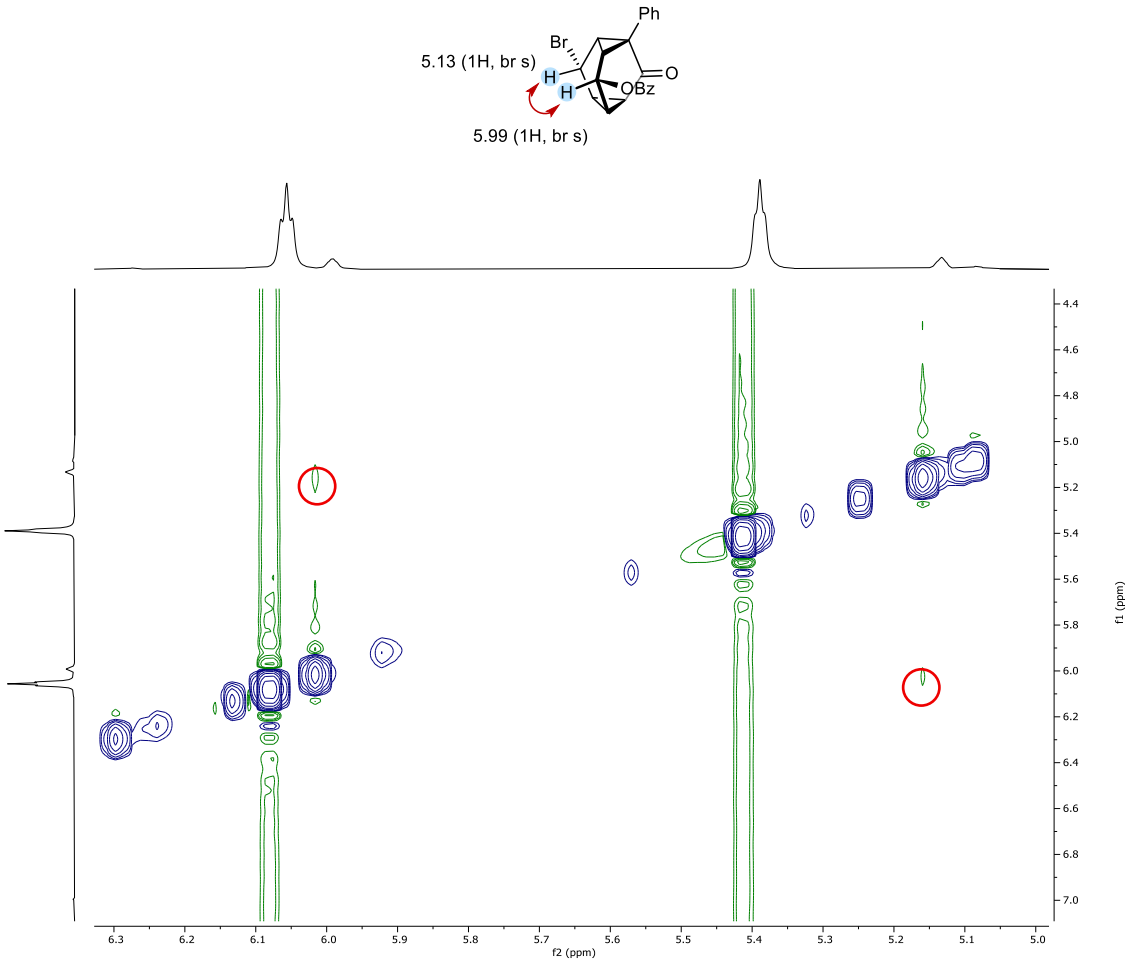
NOTE: The following section focuses on structures and characterization data of the major diastereomers **6**, with ^{1}H NMR and ^{19}F NMR (where relevant) signals attributable to the minor diastereomers also provided.

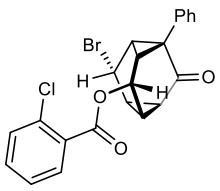


(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl benzoate (6a). General Procedure A was followed using benzoic acid (73 mg, 0.60 mmol) to give a 7.3:1 mixture of crude triasteranones **6a** and **6a'**, respectively. Purification by column chromatography (100% *n*-pentane to 40% EtOAc/*n*-pentane) gave a 6.8:1 inseparable mixture of **6a** and **6a'** as a colorless oil (98 mg, 80%). R_f = 0.58 (26% EtOAc/*n*-pentane); IR 3059, 3028, 1713 (C=O), 1685 (C=O), 1326, 1266, 1112, 1093, 1068, 1025, 960, 944 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (2H, d, *J* = 7.3 Hz, Ar**H**), 7.62 (1H, t, *J* = 7.4 Hz, Ar**H**), 7.49 (2H, t, *J* = 7.7 Hz, Ar**H**), 7.39–7.28 (5H, m, Ar**H**), 6.06 (1H, t, *J* = 3.5 Hz, OC**H**), 5.39 (1H, t, *J* = 3.0 Hz, C**H**Br), 2.81–2.74 (1H, m, PhCC**H**), 2.73–2.66 (1H, m, PhCC**H**), 2.62–2.54 (1H, m, O=CCHC**H**), 2.54–2.46 (1H, m, O=CCHC**H**), 2.37 (1H, t, *J* = 8.3 Hz, O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.1 (C), 166.2 (C), 136.6 (C), 133.7 (CH), 130.2 (2 × CH), 129.9 (2 × CH), 129.8 (C), 128.7 (2 × CH), 128.7 (2 × CH), 128.2 (CH), 64.2 (CH), 44.2 (CH), 43.3 (C), 39.8 (CH), 37.1 (CH), 32.7 (CH), 31.2 (CH), 28.9 (CH); HRMS (ESI) Exact mass calculated for $[C_{22}H_{18}{}^{79}BrO_3]^+$ $[M+H]^+$: 405.0597, found 405.0597.

Characteristic ^{1}H NMR signals of the minor diastereomer **6a'** were observed at: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.99 (1H, br s, OC**H**), 5.13 (1H, br s, C**H**Br).

The relative configuration of **6a'** was assigned based on the the NOESY spectrum. A through-space interaction was observed between the two hydrogen atoms shown below.

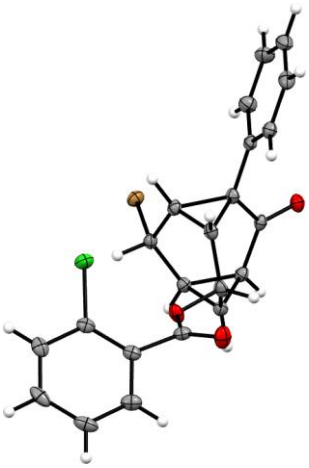


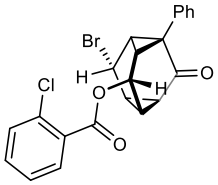


(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 2-chlorobenzoate (6b). General Procedure A was followed using 2-chlorobenzoic acid (93 mg, 0.59 mmol) to give a 5.8:1 mixture of crude triasteranones **6b** and **6b'**. Purification by column chromatography (100% *n*-pentane to 60% EtOAc/*n*-pentane) gave a 6.3:1 inseparable mixture of **6b** and **6b'** as a colorless oil (91 mg, 69%). R_f = 0.54 (26% EtOAc/*n*-pentane); IR 3061, 2980, 1729 (C=O), 1685 (C=O), 1247, 1123, 1087, 960, 910, 749, 728, 699, 650 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (1H, d, *J* = 8.1 Hz, Ar**H**), 7.53–7.43 (2H, m, Ar**H**), 7.41–7.27 (6H, m, Ar**H**), 6.08 (1H, t, *J* = 3.5 Hz, OC**H**), 5.37 (1H, t, *J* = 3.0 Hz, C**H**Br), 2.81–2.75 (1H, m, PhCC**H**), 2.73–2.68, (1H, m, PhCC**H**), 2.61–2.55 (1H, m, O=CCHC**H**), 2.54–2.48 (1H, m, O=CCHC**H**), 2.37 (1H, t, *J* = 8.2 Hz, O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.1 (C), 165.6 (C), 136.5 (C), 133.8 (C), 133.2 (CH), 131.6 (CH), 131.4 (CH), 130.2 (2 × CH), 129.9 (C), 128.7 (2 × CH), 128.2 (CH), 127.0 (CH), 65.0 (CH), 44.1 (CH), 43.3 (C), 39.8 (CH), 36.9 (CH), 32.7 (CH), 31.1 (CH), 28.9 (CH); HRMS (ESI) Exact mass calculated for $[C_{22}H_{16}{}^{79}Br^{35}ClNaO_3]^+$ $[M+Na]^+$: 464.9864, found 464.9854.

Characteristic ^{1}H NMR signals of the minor diastereomer **6b'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (1H, br s, OC**H**), 5.13 (1H, br s, C**H**Br).

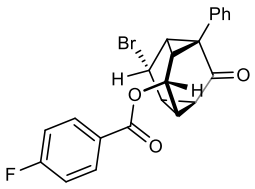
Slow vapour diffusion of *n*-heptane into a solution of **6b** in CH_2Cl_2 gave crystals suitable for X-ray crystallography.





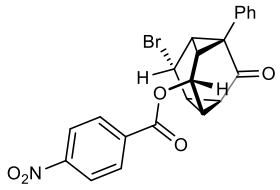
6b
CCDC 2522306

ORTEP with ellipsoid probabilities at 50%



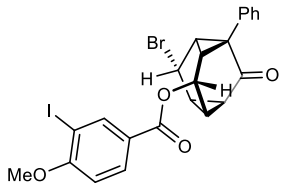
(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 4-fluorobenzoate (6c). General Procedure A was followed using 4-fluorobenzoic acid (83 mg, 0.59 mmol) to give a 6:1 mixture of crude triasteranones **6c** and **6c'**, respectively. Purification by column chromatography (100% *n*-pentane to 40% EtOAc/*n*-pentane) gave a 5.4:1 inseparable mixture of **6c** and **6c'** as a colorless oil (102 mg, 79%). R_f = 0.31 (20% EtOAc/*n*-pentane); IR 3060, 1717 (C=O), 1686 (C=O), 1602, 1506, 1265, 1154, 1114, 1088, 961, 768 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (2H, dd, J =8.7, 5.5 Hz, Ar**H**), 7.41–7.28 (5H, m, Ar**H**), 7.16 (2H, t, J = 8.6 Hz, Ar**H**), 6.04 (1H, t, J = 3.5 Hz, OC**H**), 5.37 (1H, t, J = 3.0 Hz, C**H**Br), 2.80–2.73 (1H, m, PhCC**H**), 2.73–2.65 (1H, m, PhCC**H**), 2.62–2.54 (1H, m, O=CCHC**H**), 2.53–2.44 (1H, m, O=CCHC**H**), 2.37 (1H, t, J = 8.2 Hz, O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0 (C), 166.2 (d, J_{CF} = 255.1 Hz, C), 165.2 (C), 136.5 (C), 132.5 (d, J_{CF} = 9.4 Hz, 2 × CH), 130.2 (2 × CH), 128.7 (2 × CH), 128.2 (CH), 126.0 (d, J_{CF} = 3.0 Hz, C), 115.9 (d, J_{CF} = 22.1 Hz, 2 × CH), 64.4 (CH), 44.1 (CH), 43.3 (C), 39.7 (CH), 37.0 (CH), 32.6 (CH), 31.1 (CH), 28.9 (CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ –104.36; HRMS (ESI) Exact mass calculated for $[C_{22}H_{16}{}^{79}BrFO_3Na]^+$ $[M+H]^+$: 449.0159, found 449.0154.

Characteristic NMR signals of the minor diastereomer **6c'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (1H, br s, OC**H**), 5.12 (1H, br s, C**H**Br); ^{19}F NMR (376 MHz, $CDCl_3$) δ –104.29.



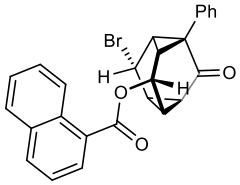
(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 4-nitrobenzoate (6d). General Procedure A was followed using 4-nitrobenzoic acid (100 mg, 0.60 mmol) to give a 5.8:1 mixture of crude triasteranones **6d** and **6d'**, respectively. Purification by column chromatography (100% *n*-pentane to 40% EtOAc/*n*-pentane) gave a 4.8:1 inseparable mixture of **6d** and **6d'** as a colorless oil (29 mg, 21%). R_f = 0.30 (30% EtOAc/*n*-pentane); IR 1722 (C=O), 1686 (C=O), 1526, 1529, 1347, 1326, 1266, 1118, 1101, 959, 910, 850, 720 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37–8.30 (2H, m, Ar**H**), 8.30–8.21 (2H, m, Ar**H**), 7.42–7.29 (5H, m, Ar**H**), 6.10 (1H, t, *J* = 3.4 Hz, OC**H**), 5.37 (1H, t, *J* = 3.0 Hz, C**H**Br), 2.81–2.75 (1H, m, PhCC**H**), 2.74–2.68 (1H, m, O=CCC**H**), 2.65–2.57 (1H, m, O=CCHC**H**), 2.55–2.47 (1H, m, O=CCHC**H**), 2.40 (1H, t, *J* = 8.2 Hz, O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.7 (C), 164.4 (C), 151.0 (C), 136.3 (C), 135.1 (C), 131.0 (2 × CH), 130.1 (2 × CH), 128.7 (2 × CH), 128.3 (CH), 123.9 (2 × CH), 65.6 (CH), 43.6 (C), 43.3 (CH), 39.6 (CH), 36.7 (CH), 32.5 (CH), 30.9 (CH), 28.9 (CH); HRMS (ESI) Exact mass calculated for $[C_{22}H_{16}{}^{79}BrNO_5Na]^+$ [M+Na]$^+$: 476.0104, found 476.0104.

Characteristic ^{1}H NMR signals of the minor diastereomer **6d'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (1H, br s, OC**H**), 5.24 (1H, br s, C**H**Br).



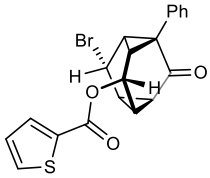
(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 3-iodo-4-methoxybenzoate (6e). General Procedure A was followed using 3-iodo-4-methoxybenzoic acid (166 mg, 0.60 mmol) to give a mixture of crude triasteranones **6e** and **6e'**, the ratio of which could not be determined by ^{1}H NMR spectroscopy because of the complexity of the NMR spectrum. Purification by column chromatography (100% *n*-pentane to 40% EtOAc/*n*-pentane) gave a 7.3:1 inseparable mixture of **6e** and **6e'** as a colorless oil (40 mg, 24%). R_f = 0.38 (26% EtOAc/*n*-pentane); IR 2941, 1711 (C=O), 1682 (C=O), 1592, 1490, 1327, 1305, 1264, 1232, 1114, 1043, 960, 909, 764, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (1H, d, *J* = 2.1 Hz, Ar**H**), 8.06 (1H, dd, *J* = 8.7, 2.1 Hz, Ar**H**), 7.41–7.28 (5H, m, Ar**H**), 6.86 (1H, dd, *J* = 8.4, 5.8 Hz, Ar**H**), 6.02 (1H, t, *J* = 3.4, 3.4 Hz, OC**H**), 5.39 (1H, t, *J* = 3.0, 3.0 Hz, C**H**Br), 3.96 (3H, d, *J* = 3.4 Hz, C**H**$_3$), 2.79–2.72 (1H, m, PhCC**H**), 2.72–2.63 (1H, m, PhCC**H**), 2.63–2.53 (1H, m, O=CCHC**H**), 2.53–2.42 (1H, m, O=CCHC**H**), 2.37 (1H, t, *J* = 8.2 Hz, O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.1 (C), 164.6 (C), 162.3 (C), 141.1 (CH), 136.6 (C), 132.1 (CH), 130.2 (2 × CH), 128.7 (2 × CH), 128.2 (CH), 123.8 (C), 110.2 (CH), 85.7 (C), 64.3 (CH), 56.8 (CH_3), 44.2 (CH), 43.3 (C), 39.8 (CH), 37.0 (CH), 32.7 (CH), 31.2 (CH), 28.9 (CH); HRMS (ESI) Exact mass calculated for $[C_{23}H_{18}{}^{79}BrIO_4Na]^+$ [M+Na]$^+$: 586.9325, found 586.9318.

Characteristic ^{1}H NMR signals of the minor diastereomer **6e'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (1H, br s, OC**H**), 5.30 (1H, br s, C**H**Br).



(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 1-naphthoate (6f). General Procedure A was followed using 1-naphthoic acid (103 mg, 0.60 mmol) to give a 9.5:1 mixture of crude triasteranones **6f** and **6f'**, respectively. Purification by column chromatography (100% *n*-pentane to 40% EtOAc/*n*-pentane) gave an 8.2:1 inseparable mixture of **6f** and **6f'** as a colorless oil (101 mg, 77%). R_f = 0.40 (20% EtOAc/*n*-pentane); IR 3060, 2173, 1713, 1685, 1510, 1276, 1238, 1195, 1132, 1006 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (1H, d, *J* = 8.6 Hz, Ar**H**), 8.23 (1H, dd, *J* = 7.2, 1.4 Hz, Ar**H**), 8.08 (1H, d, *J* = 8.1 Hz, Ar**H**), 7.92 (1H, d, *J* = 8.1 Hz, Ar**H**), 7.65 (1H, ddd, *J* = 8.6, 6.8, 1.5 Hz, Ar**H**), 7.60–7.52 (2H, m, Ar**H**), 7.42–7.36 (4H, m, Ar**H**), 7.35–7.30 (1H, m, Ar**H**), 6.16 (1H, t, *J* = 3.4 Hz, OC**H**), 5.41 (1H, t, *J* = 2.9 Hz, C**H**Br), 2.87 (1H, dt, *J* = 8.1, 3.2 Hz, PhCC**H**), 2.73 (1H, dt, *J* = 8.3, 2.9 Hz, PhCC**H**), 2.67–2.54 (2H, m, 2 × O=CCHC**H**), 2.41 (1H, t, *J* = 8.2, 8.2 Hz, O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2 (C), 167.0 (C), 136.6 (C), 134.2 (CH), 134.1 (C), 131.5 (C), 130.6 (CH), 130.2 (2 × CH), 128.9 (CH), 128.7 (2 × CH), 128.3 (CH), 128.2 (CH), 126.6 (CH), 126.5 (C), 125.6 (CH), 124.6 (CH), 64.2 (CH), 44.2 (CH), 43.3 (C), 39.8 (CH), 37.2 (CH), 32.7 (CH), 31.3 (CH), 29.0 (CH); HRMS (ESI) Exact mass calculated for $[C_{26}H_{19}{}^{79}BrO_3Na]^+$ $[M+Na]^+$: 481.0410, found 481.0417.

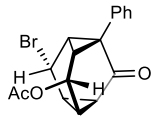
Characteristic ^{1}H NMR signals of the minor diastereomer **6f'** were observed at: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01 (1H, t, *J* = 3.3 Hz, OC**H**).



(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl thiophene-2-carboxylate (6g). General Procedure A was followed using thiophene-2-carboxylic acid (76 mg, 0.59 mmol) to give a 6.3:1 mixture of crude triasteranones **6g** and **6g'**, respectively. Purification by column chromatography (100% *n*-pentane to 30% EtOAc/*n*-pentane) gave an 8.2:1 inseparable mixture of **6g** and **6g'** as a colorless oil (89 mg, 72%). R_f = 0.27 (20% EtOAc/pentane); IR 3060, 1708 (C=O), 1684 (C=O), 1524, 1416, 1359, 1327, 1255, 1093, 1070, 960, 944, 718 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (1H, dd, *J* = 3.8, 1.3 Hz, Ar**H**), 7.63 (1H, dd, *J* = 5.0, 1.3 Hz, Ar**H**), 7.42–7.28 (5H, m, Ar**H**), 7.15 (1H, dd, *J* = 5.0, 3.8 Hz, Ar**H**), 6.01 (1H, t, *J* = 3.5 Hz, OC**H**), 5.37 (1H, t, *J* = 3.0 Hz, C**H**Br), 2.83–2.74 (1H, m, PhCC**H**), 2.74–2.65 (1H, m, PhCC**H**), 2.62–2.52 (1H, m, O=CCHC**H**), 2.52–2.44 (1H, m, O=CCHC**H**), 2.36 (1H, t, *J* = 8.2 Hz, O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0 (C), 161.8 (C), 136.5 (C), 134.3 (CH), 133.3 (CH), 133.1 (C), 130.2 (2 × CH), 128.7 (2 × CH), 128.2 (2 × CH),

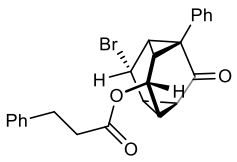
64.5 (CH), 44.1 (CH), 43.3 (C), 39.8 (CH), 37.0 (CH), 32.7 (CH), 31.1 (CH), 28.9 (CH); HRMS (ESI) Exact mass calculated for $[C_{20}H_{15}{}^{79}BrO_3SNa]^+$ $[M+Na]^+$: 436.9818, found 436.9822.

Characteristic ^{1}H NMR signals of the minor diastereomer **6g'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (1H, t, *J* = 2.8 Hz, OC**H**), 5.11 (1H, t, *J* = 2.6 Hz, C**H**Br).



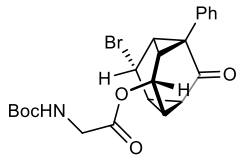
(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl acetate (6h). General Procedure A was followed using acetic acid (34 μL, 0.595 mmol) to give a 5:1 mixture of crude triasteranones **6h** and **6h'**, respectively. Purification by column chromatography (100% *n*-pentane to 50% EtOAc/*n*-pentane) gave a 7.5:1 inseparable mixture of **6h** and **6h'** as a colorless oil (78 mg, 75%). R_f = 0.27 (2% EtOAc/*n*-pentane); IR 1737 (C=O), 1683 (C=O), 1367, 1232, 1091, 1023, 962, 898, 719, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.28 (5H, m, Ar**H**), 5.82–5.76 (1H, m, OC**H**), 5.35–5.29 (1H, m, C**H**Br), 2.62 (2H, app br s, 2 × PhCC**H**), 2.51 (1H, t, *J* = 8.1 Hz, O=CCHC**H**), 2.38–2.26 (2H, m, O=CCHC**H** and O=CC**H**), 2.14 (3H, s, C**H**$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.1 (C), 170.7 (C), 136.6 (C), 130.2 (2 × CH), 128.7 (2 × CH), 128.1 (CH), 63.5 (CH), 44.2 (CH), 43.2 (C), 39.7 (CH), 37.0 (CH), 32.6 (CH), 31.1 (CH), 28.8 (CH), 21.4 (CH_3); HRMS (ESI) Exact mass calculated for $[C_{17}H_{15}{}^{79}BrO_3Na]^+$ $[M+Na]^+$: 369.0096, found 369.0094.

Characteristic ^{1}H NMR signals of the minor diastereomer **6h'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 (1H, t, *J* = 3.5 Hz, OC**H**), 5.06 (1H, t, *J* = 2.4 Hz, C**H**Br).



(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 3-phenylpropanoate (6i). General Procedure A was followed using 3-phenylpropanoic acid (89 mg, 0.595 mmol) to give a 5.1:1 mixture of crude triasteranones **6i** and **6i'**, respectively. Purification by column chromatography (100% *n*-pentane to 30% EtOAc/*n*-pentane) gave a 6:1 inseparable mixture of **6i** and **6i'** as a colorless oil (76 mg, 58%). R_f = 0.25 (20% EtOAc/*n*-pentane); IR 3027, 1732 (C=O), 1685 (C=O), 1496, 1369, 1245, 1170, 1154, 961, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.26 (7H, m, Ar**H**), 7.27–7.18 (3H, m, Ar**H**), 5.78–5.71 (1H, m, OC**H**), 5.12 (1H, t, *J* = 2.0 Hz, C**H**Br), 3.00 (2H, t, *J* = 7.4 Hz, PhC**H**$_2$), 2.73 (2H, t, *J* = 7.6 Hz, O=CC**H**$_2$), 2.58–2.46 (2H, m, 2 × PhCC**H**), 2.46–2.37 (1H, m, O=CCHC**H**), 2.33–2.19 (2H, m, O=CCHC**H** and O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2 (C), 172.6 (C), 140.1 (C), 136.6 (C), 130.1 (2 × CH), 128.7 (2 × CH), 128.6 (2 × CH), 128.4 (2 × CH), 128.1 (CH), 126.6 (CH), 63.6 (CH), 44.2 (C), 43.1 (CH), 39.6 (CH), 36.9 (CH), 36.0 (CH_2), 32.6 (CH), 31.2 (CH_2), 31.0 (CH), 28.8 (CH); HRMS (ESI) Exact mass calculated for $[C_{24}H_{21}{}^{79}BrO_3Na]^+$ $[M+Na]^+$: 459.0566, found 459.0566.

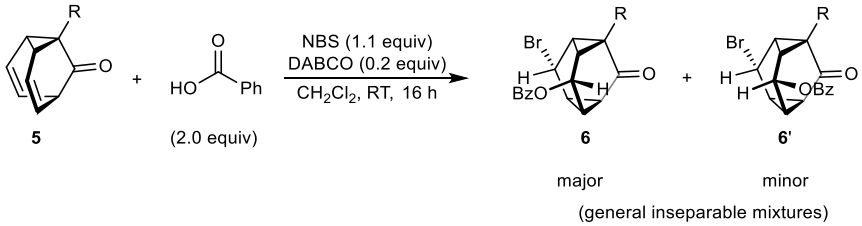
Characteristic ^{1}H NMR signals of the minor diastereomer **6i'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (1H, t, *J* = 3.4 Hz, OC**H**), 5.01 (1H, t, *J* = 3.2 Hz, C**H**Br).



(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl (*tert*-butoxycarbonyl)glycinate (6j). General Procedure A was followed using (*tert*-butoxycarbonyl)glycine (104 mg, 0.595 mmol) to give a 12.6:1 mixture of crude triasteranones **6j** and **6j'**, respectively. Purification by column chromatography (100% *n*-pentane to 60% EtOAc/*n*-pentane) gave a 10.2:1 inseparable mixture of **6j** and **6j'** as a colorless oil (101 mg, 73%). R_f = 0.56 (50% EtOAc/*n*-pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.28 (5H, m, Ar**H**), 5.87 (1H, s, OC**H**), 5.28 (1H, s, C**H**Br), 5.01 (1H, br s, N**H**), 3.97 (2H, d, *J* = 5.9 Hz, NC**H**$_2$), 2.65–2.61 (2H, m, 2 × PhCC**H**), 2.55–2.47 (1H, m, O=CCHC**H**), 2.39–2.27 (2H, m, O=CCHC**H** and O=CC**H**), 1.46 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9 (C), 170.3 (C), 155.9 (C), 136.4 (C), 130.1 (2 × CH), 128.7 (2 × CH), 128.2 (CH), 80.5 (C), 64.8 (CH), 43.8 (CH), 43.2 (C), 42.7(CH_2), 39.6 (CH), 36.7 (CH), 32.6 (CH), 30.9 (CH), 28.8 (CH), 28.5 (3 × CH_3); HRMS (ESI) Exact mass calculated for $[C_{22}H_{24}{}^{79}BrNO_5Na]^+$ $[M+Na]^+$: 484.0730, found 484.0727.

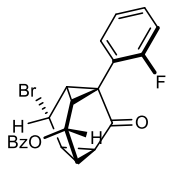
Characteristic ^{1}H NMR signals of the minor diastereomer **6j'** were observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (1H, br s, OC**H**), 5.15 (1H, br s, C**H**Br).

General Procedure B

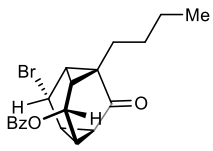


A reaction vial was charged with the barbaralone **5** (0.20 mmol), benzoic acid (49 mg, 0.40 mmol) and CH_2Cl_2 (1 mL). NBS (39 mg, 0.22 mmol) and DABCO (4.5 mg, 0.04 mmol) were added sequentially, each in one portion, and the reaction was stirred at room temperature for 16 h. Saturated aqueous $NaHCO_3$ solution (3 mL) was added, and the aqueous layer was separated and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. An ^{1}H NMR spectrum of the residue was used to determine the diastereomeric ratio. Purification of the residue by column chromatography (100% *n*-pentane to 70% EtOAc/*n*-pentane) gave the diastereomeric triasteranones **6** and **6'** as an inseparable mixture.

NOTE: The following section focuses on structures and characterization data of the major diastereomers **6**, with ^{1}H NMR signals attributable to the minor diastereomers also provided.

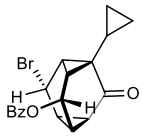


(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-(2-fluorophenyl)tetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl benzoate (6k). General Procedure B was followed using barbaralone **5d** (45 mg, 0.20 mmol) to give a 9.1:1 mixture of crude triasteranones **6k** and **6k'**, respectively. Purification by column chromatography (100% *n*-pentane to 30% EtOAc/*n*-pentane) gave **6k** as a colorless oil (67 mg, 78%). R_f = 47% (20% EtOAc/*n*-pentane); IR 3065, 1716 (C=O), 1687 (C=O), 1498, 1452, 1265, 1109, 961, 912, 761, 712 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (2H, dd, *J* = 8.3, 1.4 Hz, Ar**H**), 7.61 (1H, tt, *J* = 7.4, 1.3 Hz, Ar**H**), 7.48 (2H, t, *J* = 7.8 Hz, Ar**H**), 7.36–7.27 (2H, m, Ar**H**), 7.14 (1H, td, *J* = 7.6, 1.2 Hz, Ar**H**), 7.07 (1H, ddd, *J* = 9.8, 8.6, 1.2 Hz, Ar**H**), 6.08 (1H, app t, *J* = 3.5, Hz, OC**H**), 5.40 (1H, app t, *J* = 3.0 Hz, C**H**Br), 2.79 (1H, app dt, *J* = 8.3, 2.9 Hz, ArCC**H**), 2.65 (1H, app, dt, *J* = 8.3, 3.3 Hz, ArCC**H**), 2.62–2.49 (2H, m, 2 × O=CCHC**H**), 2.37 (1H, app t, *J* = 8.2 Hz, O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7 (C), 166.1 (C), 162.1 (d, J_{CF} = 249.2 Hz, C), 133.7 (CH), 131.6 (d, J_{CF} = 3.3 Hz, CH), 130.3 (d, J_{CF} = 8.2 Hz, CH), 129.9 (2 × CH), 129.8 (C), 128.7 (2 × CH), 124.3 (d, J_{CF} = 3.6 Hz, CH), 124.1 (d, J_{CF} = 14.6 Hz, C), 115.8 (d, J_{CF} = 21.0 Hz, CH), 64.0 (CH), 43.7 (CH), 39.1 (CH), 38.3 (C), 37.5 (CH), 32.7 (CH), 31.1 (CH), 28.8 (CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.2; HRMS (ESI) Exact mass calculated for $[C_{22}H_{17}{}^{79}BrFO_3]^+$ $[M+H]^+$: 427.0340, found 427.0329.



(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-butyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl benzoate (6l). General Procedure A was followed using barbaralone **5f** (38 mg, 0.20 mmol) to give a 5.4:1 mixture of crude triasteranones **6l** and **6l'**, respectively. Purification by column chromatography (100% *n*-pentane to 30% EtOAc/*n*-pentane) gave a 4.1:1 inseparable mixture of **6l** and **6l'** as a colorless oil (55 mg, 71%). R_f = 0.30 (4% EtOAc/*n*-pentane); IR 2955, 2931, 2869, 2859, 1716 (C=O), 1685 (C=O), 1267, 1069, 1026, 962, 712 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (2H, dd, *J* = 8.3, 1.4 Hz, Ar**H**), 7.61 (1H, td, *J* = 7.3, 1.4 Hz, Ar**H**), 7.48 (2H, app t, *J* = 7.8 Hz, Ar**H**), 5.82 (1H, app t, *J* = 3.5 Hz, OC**H**), 5.26 (1H, app t, *J* = 3.0 Hz, C**H**Br), 2.49–2.43 (1H, m, CH_2CC**H**), 2.39–2.32 (1H, m, CH_2CC**H**), 2.32–2.20 (3H, m, 2 × O=CCHC**H** and O=CC**H**), 1.72–1.61 (1H, m, C**H**$_a$H$_b$CH$_2$CH$_2$CH$_3$), 1.48–1.26 (5H, m, CH$_a$C**H**$_b$C**H**$_2$C**H**$_2$CH$_3$), 1.48–1.26 (6H, m, C**H**$_2$C**H**$_2$C**H**$_2$CH$_3$), 0.89 (3H, t, *J* = 7.3 Hz, C**H**$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.7 (C), 166.2 (C), 133.6 (CH), 129.9 (C), 129.8 (2 × CH), 128.7 (2 × CH), 64.6 (CH), 44.5 (CH), 38.7 (CH), 38.0 (C), 37.5 (CH), 32.8 (CH), 32.2 (CH_2), 31.1 (CH), 29.1 (CH), 28.9 (CH_2), 23.0 (CH_2), 14.1 (CH_3); HRMS (ESI) Exact mass calculated for $[C_{20}H_{22}{}^{79}BrO_3]^+$ $[M+H]^+$: 389.0747, found 389.0745.

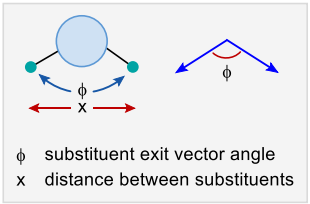
Characteristic ^{1}H NMR signals of the minor diastereomer **6l'** were observed at: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90–5.85 (1H, br s, OC**H**), 5.05–5.00 (1H, br s, C**H**Br).

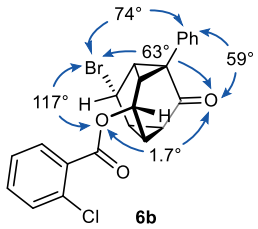


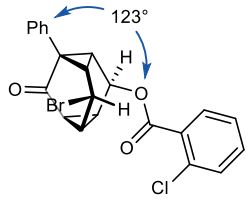
(±)-(3*S*,7*S*)-7-Bromo-9-oxo-1-cyclopropyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl benzoate (6m). General Procedure A was followed using barbaralone **5i** (34 mg, 0.20 mmol) to give a 2.7:1 mixture of crude triasteranones **6m** and **6m'**, respectively. Purification by column chromatography (100% *n*-pentane to 30% EtOAc/*n*-pentane) gave a 2.9:1 inseparable mixture of **6m** and **6m'** as a colorless oil (34 mg, 46%). R_f = (10% EtOAc/*n*-pentane); IR 1715 (C=O), 1685 (C=O), 1267, 1106, 1069, 1027, 964, 713, 635, 417 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (2H, d, *J* = 6.8 Hz, Ar**H**), 7.65–7.54 (1H, m, Ar**H**), 7.52–7.42 (2H, m, Ar**H**), 5.79 (1H, app t, *J* = 3.5 Hz, OC**H**), 5.22 (1H, app t, *J* = 3.0 Hz, C**H**Br), 2.51–2.42 (1H, m, O=CCHC**H**), 2.42–2.34 (1H, m, O=CCHC**H**), 2.30 (1H, app t, *J* = 8.1 Hz, O=CC**H**), 2.13–2.05 (1H, m, CH_2CHCC**H**), 2.05–1.97 (1H, m, CH_2CHCC**H**), 0.67–0.40 (3H, m, C**H**$_a$H$_b$C**H**$_a$H$_b$ and CH_2C**H**), 0.17–0.03 (1H, m, $CH_aH_bCH_a$**H**$_b$), –0.01 to –0.15 (1H, m, CH_a**H**$_b$$CH_aH_b$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.0 (C), 166.2 (C), 133.6 (CH), 130.2 (C), 129.8 (2 × CH), 128.7 (2 × CH), 64.4 (CH), 44.1 (CH), 38.5 (C), 35.2 (CH), 35.1 (CH), 32.4 (CH), 30.9 (CH), 29.0 (CH), 9.9 (CH), 2.6 (CH_2), 1.1 (CH_2); HRMS (ESI) Exact mass calculated for [$C_{19}H_{18}{}^{79}BrO_3$]$^+$ [M+H]$^+$: 373.0434, found 373.0432.

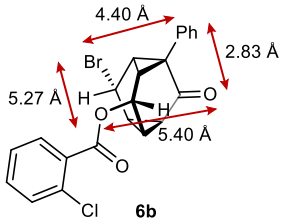
A characteristic ^{1}H NMR signal of the minor diastereomer **6m'** was observed at: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.96 (1H, br s, C**H**Br).

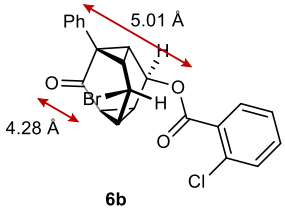
4. Structural Analysis of 6b: Substituent Exit Vector Angles and Distances Between Substituents







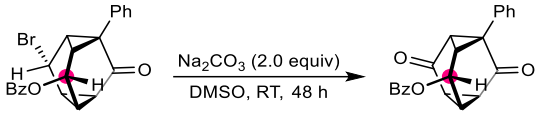




From the X-ray structure of **6b** (see page 10), the exit vector angles between substituents and distances between substituents were measured, and the values are shown in the diagrams above.

5. Further Functionalizations

7,9-Dioxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl benzoate (7)

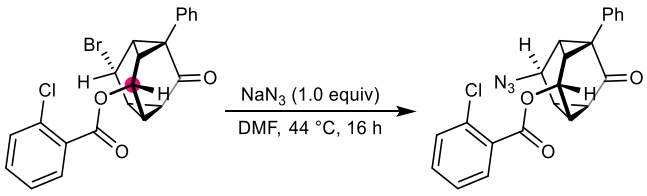


6a (6.8:1 mixture) **7** 55% (7.2:1 mixture)

To a solution of triasteranone **6a** (60 mg, 0.15 mmol, 6.8:1 mixture of diastereomers) in DMSO (0.73 mL) was added Na_2CO_3 (31 mg, 0.29 mmol) and the reaction was stirred at room temperature for 48 h. The reaction was diluted with H_2O (10 mL) and the aqueous layer was separated and extracted with EtOAc (3 × 3 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane to 50% EtOAc/*n*-pentane) gave *triasteranedione* **7** as a 7.2:1 inseparable mixture of diastereomers as a colorless oil (28 mg, 55%). R_f = 0.53 (30% EtOAc/*n*-pentane); IR 3063, 1717 (C=O), 1692 (C=O), 1450, 1319, 1265, 1177, 1112, 1070, 973, 714, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (2H, dd, *J* = 7.1, 1.2 Hz, Ar**H**), 7.62 (1H, tt, *J* = 7.5, 1.4 Hz, Ar**H**), 7.49 (2H, t, *J* = 7.9 Hz, Ar**H**), 7.38–7.33 (3H, m, Ar**H**), 7.25–7.18 (2H, m, Ar**H**), 6.18 (1H, app t, *J* = 3.2 Hz, OC**H**), 3.06 (1H, app dt, *J* = 8.2, 3.5 Hz, PhCC**H**), 2.86–2.78 (1H, m, O=CC**H**), 2.71 (1H, dd, *J* = 8.3, 2.9 Hz, O=CC**H**), 2.65–2.53 (2H, m, 2 × O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0 (C), 196.9 (C), 166.2 (C), 134.8 (C), 133.9 (CH), 130.0 (4 × CH), 129.3 (C), 129.0 (CH), 128.9 (2 × CH), 128.8 (2 × CH), 62.8 (CH), 46.7 (C), 39.1 (CH), 38.8 (CH), 33.1 (CH), 32.7 (CH), 31.7 (CH); HRMS (ESI) Exact mass calculated for $[C_{22}H_{16}O_4Na]^+$ [M+Na]$^+$: 367.0941, found 367.0932.

A characteristic ^{1}H NMR signal of the minor diastereomer was observed at: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (1H, t, *J* = 3.5 Hz, OC**H**).

(±)-(3*S*,7*R*)-7-Azido-9-oxo-1-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-yl 2-chlorobenzoate (8)



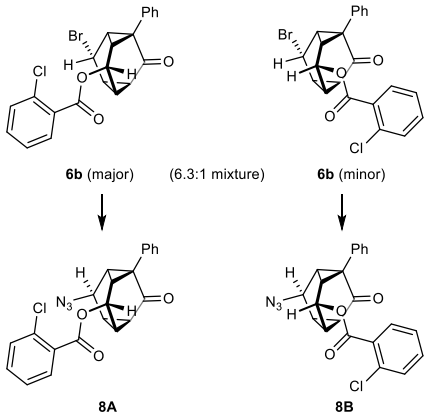
6b (6.3:1 mixture) **8** 64% (76:14:10 mixture)

To a solution of triasteranone **6b** (44 mg, 0.10 mmol, 6.3:1 mixture of diastereomers) in DMF (1.0 mL) was added NaN_3 (6.5 mg, 0.10 mmol) and the mixture was stirred at 44 °C for 16 h. The reaction was cooled to room temperature and concentrated *in vacuo*. Purification of the residue by column chromatography (100 % cyclohexane to 30% EtOAc/cyclohexane) gave *azide* **8** as a 76:14:10

inseparable mixture of diastereomers as a colorless oil (26 mg, 64%). R_f = 0.29 (20% EtOAc/cyclohexane); IR 3060, 2095 (N=N=N), 1683 (C=O), 1286, 1245, 1118, 1047, 964, 939, 749, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.06 (1H, dd, *J* = 7.8, 1.7 Hz, Ar**H**), 7.54–7.43 (2H, m, Ar**H**), 7.41–7.29 (4H, m, Ar**H**), 7.24–7.20 (2H, m, Ar**H**), 6.05 (1H, app t, *J* = 3.4, Hz, OC**H**), 4.69 (1H, app t, *J* = 3.2 Hz, C**H**N), 2.61 (1H, app dt, *J* = 7.9, 3.2 Hz, O=CCHC**H**), 2.41–2.36 (2H, m, O=CCHC**H** and PhCC**H**), 2.26–2.17 (2H, m, PhCC**H** and O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.6 (C), 165.4 (C), 136.4 (C), 134.4 (C), 133.2 (CH), 132.0 (CH), 131.4 (CH), 129.9 (2 × CH), 129.4 (C), 128.7 (2 × CH), 128.3 (CH), 126.9 (CH), 64.7 (CH), 51.1 (CH), 41.5 (C), 32.7 (CH), 31.4 (CH), 27.2 (CH), 26.0 (CH), 24.9 (CH); Exact mass calculated for $[C_{22}H_{17}{}^{35}ClN_3O_3]^+$ $[M+H]^+$: 406.0953, found 406.0968.

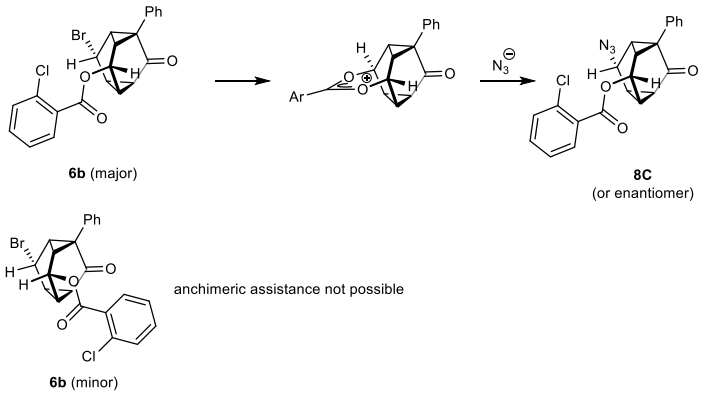
Discussion of Stereochemical Outcome in the Formation of **8**:

- An S_N2 mechanism would be expected to give only two diastereomers of **8**, one from each diastereomer of the starting material.

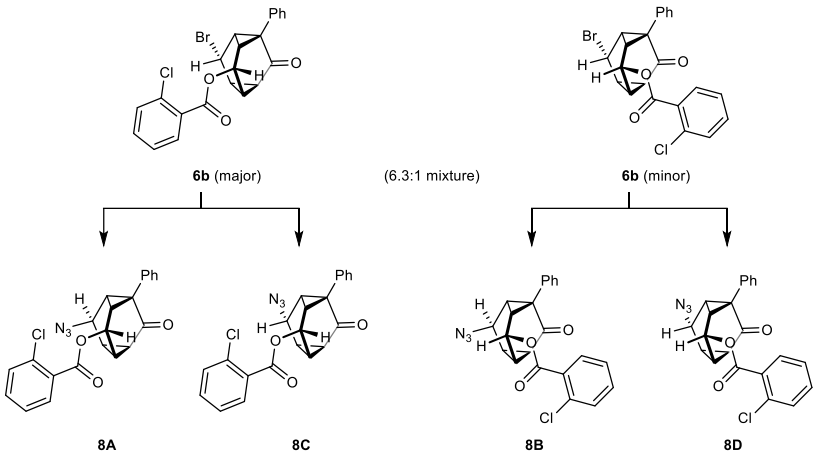


In the experiment, we see **8A** as the major isomer, but because it was isolated as 76:14:10 mixture along with two minor diastereomers, it appears unlikely that an S_N2 pathway is the only mechanism operating.

- A mechanism involving anchimeric assistance of the 2-chlorobenzoate ester would give a third diastereomer **8C**, which can only occur from the major diastereomer of the starting material **6b**.



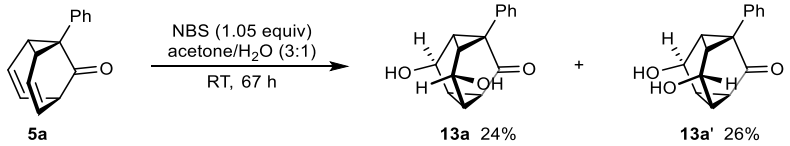
- An S_N1 mechanism would be expected to give up to four diastereomers of **8**.



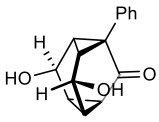
However, one of these diastereomers (possibly **8D**) would have to arise from formation of an intermediate carbocation from the minor diastereomer of bromide **6b**, followed by the attack of the azide nucleophile from the more hindered face of that carbocation (both faces are not equally accessible). The combination of these factors may mean that too little of the fourth diastereomer is formed for us to detect and isolate. Therefore, we cannot conclusively rule out an S_N1 mechanism taking place alongside other mechanisms.

6. Preparation of Triasteranediols 13a and 13a'

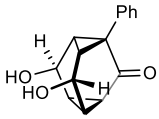
(±)-(7*R*,9*R*)-7,9-Dihydroxy-2-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-one (12a) and (±)-(7*R*,9*S*)-7,9-Dihydroxy-2-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-one (13a')



A round bottom flask was charged with barbaralone **5a** (40 mg, 0.19 mmol) and a 3:1 mixture of acetone:H_2O (4 mL). NBS (36 mg, 0.20 mmol) was added in one portion, the resulting solution was stirred at room temperature for 16 h, and the reaction was concentrated *in vacuo*. CH_2Cl_2 (5 mL) and 2 M aqueous NaOH solution (15 mL) was added, and the mixture was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo.* Purification of the residue by column chromatography (100% CH_2Cl_2 to 10% of *solution A* in CH_2Cl_2, where *solution A* was made up by adding MeOH to aqueous NH_3 solution (30%) give a 2 M solution of NH_3) to give *diol* **13a** as an amorphous white solid (11 mg, 24%) followed by *diol* **13a'** as a white solid (12 mg, 26%).

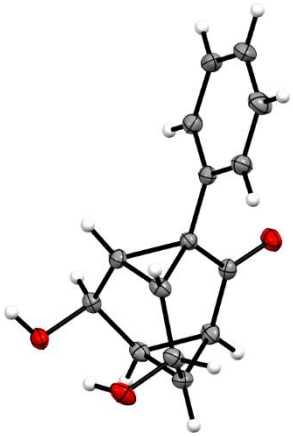


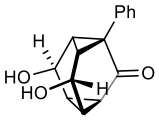
(±)-(7*R*,9*R*)-7,9-Dihydroxy-2-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-one (13a). R_f = 0.50 (10% of *solution A* in CH_2Cl_2, where solution A was made up by adding MeOH to aqueous NH_3 solution (30%) give a 2 M solution of NH_3); IR 3365 (OH), 1655 (C=O), 1363, 1044, 1031, 977, 907, 727, 699, 563 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.26 (3H, m, Ar**H**), 7.25–7.19 (2H, m, Ar**H**), 4.88 (1H, s, C**H**OH), 4.70 (1H, s, C**H**OH), 2.61(1H, br s, O**H**), 2.45–2.42 (1H, m, PhCC**H**), 2.39–2.36 (1H, m, PhCC**H**), 2.34 (1H, br s, O**H**), 2.25–2.21 (1H, m, O=CCHC**H**), 2.18–2.14 (1H, m, O=CCHC**H**), 2.09–2.04 (1H, m, O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.0 (C), 137.7 (C), 130.3 (2 × CH), 128.6 (2 × CH), 127.8 (CH), 60.9 (CH), 60.7 (CH), 41.9 (C), 39.1 (CH), 37.5 (CH), 32.0 (CH), 30.9 (CH), 27.4 (CH); HRMS (ESI) Exact mass calculated for $[C_{15}H_{14}O_3Na]^+$ $[M+Na]^+$: 265.0835, found 265.0835.



(±)-(7*R*,9*S*)-7,9-Dihydroxy-2-phenyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonan-3-one (13a'). R_f = 0.31 (10% of *solution A* in CH_2Cl_2, where solution A was made up by adding MeOH to aqueous NH_3 solution (30%) give a 2 M solution of NH_3); m.p. 186–187 °C (*n*-heptane/CH_2Cl_2); IR 3399 (OH), 1671 (C=O), 1446, 1045, 1010, 983, 932, 701, 663, 542 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (3H, m, Ar**H**), 7.20–7.15 (2H, m, Ar**H**), 4.89–4.82 (2H, m, 2 × C**H**OH), 2.87 (2H, d, *J* = 7.3 Hz, 2 × O**H**), 2.37–2.31 (2H, m, 2 × PhCC**H**), 2.18–2.11 (2H, m, 2 × O=CCHC**H**), 2.08–2.01 (1H, m, O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.1 (C), 137.3 (C), 130.0 (2 × CH), 128.7 (2 × CH), 127.9 (CH), 61.3 (2 × CH), 41.8 (C), 35.9 (2 × CH), 29.1 (2 × CH), 27.8 (CH); HRMS (ESI) Exact mass calculated for $[C_{15}H_{14}O_3Na]^+$ $[M+Na]^+$: 265.0835, found 265.0835.

Slow vapour diffusion of *n*-heptane into a solution of **13a'** in CH_2Cl_2 gave crystals suitable for X-ray crystallography. Note: **13a'** crystallized with a molecule of CH_2Cl_2 in the unit cell, which is not shown for clarity.



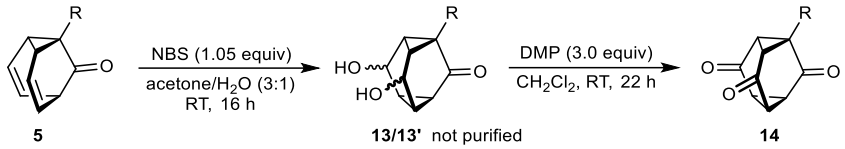


13a'
CCDC 2522307

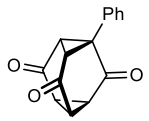
ORTEP with ellipsoid probabilities at 50%

7. Synthesis of Triasteranetriones from Barbaralones

General Procedure C

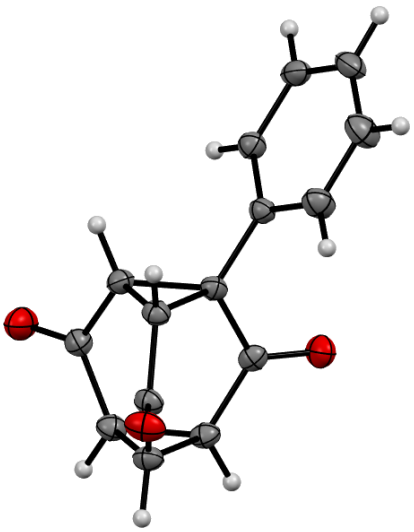


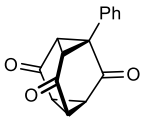
A round bottom flask was charged with the 1-substituted barbaralone (0.50 mmol) and a 3:1 mixture of acetone:H_2O (4 mL). NBS (93 mg, 0.52 mmol) was added in one portion, and the resulting solution was stirred at room temperature for 16 h. The reaction was concentrated *in vacuo* and H_2O (5 mL) was added. The aqueous layer was saturated with NaCl and extracted with CH_2Cl_2 (5 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to leave the diols **13/13'**, which were used immediately in the next step without purification. The crude diols **13/13'** were dissolved in CH_2Cl_2 (2.5 mL) and Dess-Martin periodinane (DMP) (636 mg, 1.50 mmol) was added in one portion. The mixture was stirred at room temperature for 16 h. 2 M Aqueous NaOH solution (30 mL) was added, and the resulting mixture was stirred vigorously for 1 h. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (EtOAc/*n*-pentane) gave the triasteranetrione **14**.



1-Phenyltetracyclo[3.3.1.$0^{2,8}$.$0^{4,6}$]nonane-3,7,9-trione (14a). General Procedure C was followed using barbaralone **5a** (104 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 90% EtOAc/*n*-pentane) gave **14a** as a white solid (58 mg, 48% over two steps from **5a**). R_f = 0.48 (40% EtOAc/*n*-pentane); m.p. 241–247 °C (CH_2Cl_2/*n*-pentane); IR 2956, 2917, 2849, 2316, 1697 (C=O), 1463 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.34 (3H, m, Ar**H**), 7.25–7.19 (2H, m, Ar**H**), 2.99–2.93 (2H, m, 2 × O=CC**H**), 2.90–2.83 (1H, m, O=CC**H**), 2.82–2.75 (2H, m, 2 × O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.6 (C), 193.2 (2 × C), 133.2 (C), 130.0 (2 × CH), 129.5 (CH), 129.1 (2 × CH), 49.4 (C), 40.7 (2 × CH), 35.1 (2 × CH), 33.7 (CH); HRMS (ESI) Exact mass calculated for $[C_{15}H_9O_3]^-$ $[M–H]^-$: 237.0557, found 237.0557.

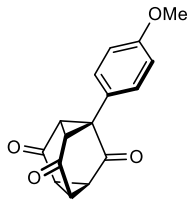
Slow vapour diffusion of *n*-pentane into a solution of **14a** in CH_2Cl_2 gave crystals suitable for X-ray crystallography.



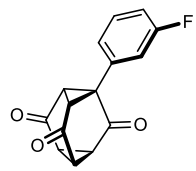


14a
CCDC 2522308

ORTEP with ellipsoid probabilities at 50%

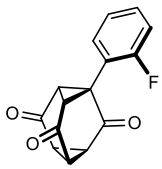


1-(4-Methoxyphenyl)tetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14b). General Procedure C was followed using barbaralone **5b** (119 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 60% EtOAc/*n*-pentane) gave **14b** as a white solid (87 mg, 65% over two steps from **5b**). R_f = 0.57 (50% EtOAc/*n*-pentane); m.p. 214–215 °C (CH_2Cl_2/heptane); IR 3575, 3003, 2944, 2293, 2253, 1633 (C=O), 1442, 1375, 1039, 919 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18–7.14 (2H, m, Ar**H**), 6.93–6.89 (2H, m, Ar**H**), 3.83 (3H, s, OC**H**$_3$), 2.96–2.92 (2H, m, 2 × O=CC**H**), 2.90–2.84 (1H, m, O=CC**H**), 2.83–2.77 (2H, m, 2 × O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.0 (C), 193.4 (2 × C), 160.3 (C), 131.2 (2 × CH), 125.3 (C), 114.5 (2 × CH), 55.5 (CH_3), 48.9 (C), 41.0 (2 × CH), 35.1 (2 × CH), 33.5 (CH); HRMS (ESI) Exact mass calculated for $[C_{16}H_{12}O_4Na]^+$ [M+Na]$^+$: 291.0628, found 291.0630.

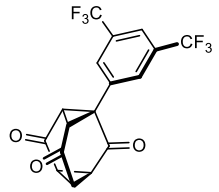


1-(3-Fluorophenyl)tetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14c). General Procedure C was followed using barbaralone **5c** (113 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 60% EtOAc/*n*-pentane) gave **14c** as a white solid (82 mg, 62% over two steps from **5c**). R_f = 0.40 (40% EtOAc/*n*-pentane); m.p.194–195 °C (CH_2Cl_2/heptane) IR 3070, 1699 (C=O), 1615, 1591, 1493, 1444, 1310, 1177, 1080, 916, 728, 691, 530, 409 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (1H, app td, J = 8.1, 5.8 Hz, Ar**H**), 7.08 (1H, app tdd, J = 8.5, 2.5, 1.0 Hz, Ar**H**), 7.01 (1H, app dt, J = 7.7, 1.3 Hz, Ar**H**), 6.95 (1H, ddd, J = 9.2, 2.5, 1.7 Hz, Ar**H**), 2.97–2.92 (2H, m, 2 × O=CC**H**), 2.90–2.84 (1H, m, O=CC**H**), 2.83–2.76 (2H, m, 2 × O=CC**H**); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0 (C), 192.7 (2 × C), 162.8 (d, J_{CF} = 248.7 Hz, C), 135.3 (d, J_{CF} = 7.7 Hz, C), 130.7 (d, J_{CF} = 8.4 Hz, CH), 125.7 (d, J_{CF} = 2.9 Hz, CH), 117.3 (d, J_{CF} = 22.7 Hz, CH), 116.7 (d, J_{CF} = 21.3 Hz, CH), 48.6 (C), 40.5 (2 × CH),

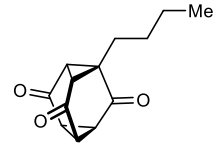
35.0 (2 × CH), 33.6 (CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ –111.5; HRMS (ESI) Exact mass calculated for $[C_{15}H_8FO_3]^-$ $[M–H]^-$: 255.0463, found 255.0463.



1-(2-Fluorophenyl)tetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14d). General Procedure C was followed using barbaralone **5d** (113 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 60% EtOAc/*n*-pentane) gave **14d** as an amorphous white solid (70 mg, 55% over two steps from **5d**). R_f = 0.35 (30% EtOAc/*n*-pentane); m.p. 246–248 °C (CH_2Cl_2/*n*-heptane); IR 3068, 1700 (C=O), 1618, 1585, 1498, 1455, 1308, 1239, 1203, 1110, 1081, 763, 735, 409 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.36 (1H, m, Ar**H**), 7.18–7.06 (3H, m, Ar**H**), 2.95–2.91 (2H, m, 2 × O=CC**H**), 2.91–2.84 (1H, m, O=CC**H**), 2.83–2.77 (2H, m, 2 × O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.7 (C), 192.0 (2 × C), 161.8 (d, J_{CF} = 250.4 Hz, C), 131.7 (d, J_{CF} = 8.3 Hz, CH), 130.7 (d, J_{CF} = 2.7 Hz, CH), 124.7 (d, J_{CF} = 3.7 Hz, CH), 121.0 (d, J_{CF} = 14.2 Hz, C), 116.2 (d, J_{CF} = 20.9 Hz, CH), 44.1 (C), 40.2 (2 × CH), 35.1 (2 × CH), 33.6 (CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ –113.5; HRMS (ESI) Exact mass calculated for $[C_{15}H_8FO_3]^-$ $[M–H]^-$: 255.0463, found 255.0464.

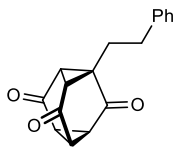


1-(3,5-Bis(trifluoromethyl)phenyl)tetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14e). General Procedure C was followed using barbaralone **5e** (172 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 60% EtOAc/*n*-pentane) gave **14e** as a white solid (112 mg, 60% over two steps from **1e**). R_f = 0.57 (40% EtOAc/*n*-pentane); m.p. 215–216 °C (CH_2Cl_2/*n*-heptane); IR 3070, 1700 (C=O), 1625, 1473, 1358, 1279, 1178, 1131, 1081, 1060, 950, 908, 731, 705, 682 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (1H, s, Ar**H**), 7.71–7.66 (2H, m, Ar**H**), 3.03–2.98 (2H, m, 2 × O=CC**H**), 2.96–2.91 (1H, m, O=CC**H**), 2.89–2.83 (2H, m, 2 × O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.2 (C), 191.8 (2 × C), 135.3 (C), 132.7 (q, J_{CF} = 33.9 Hz, 2 × C), 130.4 (m, 2 × CH), 123.6 (hept, J_{CF} = 3.8 Hz, CH), 122.9 (q, J_{CF} = 272.1 Hz, 2 × C), 47.9 (C), 39.9 (2 × CH), 35.1 (2 × CH), 33.7 (CH); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –62.9; HRMS (ESI) Exact mass calculated for $[C_{17}H_7F_6O_3]^-$ $[M–H]^-$: 373.0305, found 373.0304.



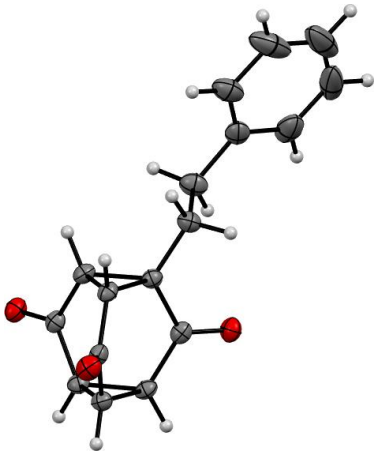
1-Butyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14f). General Procedure C was followed using barbaralone **5f** (94 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 55% EtOAc/*n*-pentane) gave **14f** as a white solid (52 mg, 48% over two steps from **5f**). R_f = 0.55 (40% EtOAc/*n*-pentane); m.p. 96–97 °C (CH_2Cl_2/*n*-heptane); IR 3064, 2959, 2930, 2861, 1683 (C=O), 1466, 1327, 1300, 1072, 910, 873, 534 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72 (1H, dd, *J* = 8.6, 7.4 Hz, O=CC**H**), 2.66–2.60 (2H, m, 2 ×

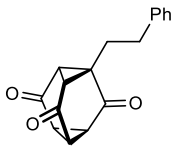
O=CC**H**), 2.52–2.47 (2H, m, 2 × O=CC**H**), 1.59–1.53 (2H, m, C**H**$_2$CH$_2$CH$_2$CH$_3$), 1.37–1.21 (4H, m, C**H**$_2$C**H**$_2$CH$_3$), 0.86 (3H, t, J = 7.1 Hz, C**H**$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.7 (C), 193.8 (2 × C), 44.8 (C), 40.6 (2 × CH), 34.7 (2 × CH), 34.1 (CH), 31.5 (CH_2), 28.7 (CH_2), 22.6 (CH_2), 13.9 (CH_3); HRMS (ESI) Exact mass calculated for $[C_{13}H_{13}O_3]^-$ $[M–H]^-$: 217.0870, found 217.0872.



1-Phenethyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14g). General Procedure C was employed but with one modification in that barbaralone **5g** (100 mg, 0.42 mmol) was employed (the quantities of all other reagents and solvents remained unchanged). Purification by column chromatography (100% *n*-pentane to 70% EtOAc/*n*-pentane) gave **14g** as a white solid (58 mg, 51% over two steps from **5g**). R_f = 0.49 (30% EtOAc/*n*-pentane); m.p. 138–139 °C (MeOH/*n*-hexane); IR 3060, 1686 (C=O),1492, 1453, 1327, 1296,1070, 911, 730, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.27 (2H, m, Ar**H**), 7.26–7.18 (1H, m, Ar**H**), 7.16–7.02 (2H, m, Ar**H**), 2.86–2.72 (3H, m, O=CC**H** and C**H**$_2$Ph), 2.71–2.58 (2H, m, 2 × O=CC**H**), 2.51–2.36 (2H, m, 2 × O=CC**H**), 1.95–1.79 (2H, m, C**H**$_2$CH$_2$Ph); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5 (C), 193.2 (2 × C), 139.0 (C), 128.8 (2 × CH), 128.4 (2 × CH), 126.5 (CH), 44.1 (C), 40.2 (2 × CH), 34.7 (2 × CH), 34.2 (CH_2), 34.1 (CH), 32.9 (CH_2); HRMS (ESI) Exact mass calculated gfor $[C_{17}H_{14}O_3Na]^+$ $[M+Na]^+$: 289.0835, found: 289.0833.

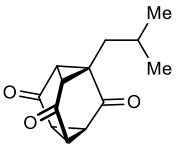
Slow vapour diffusion of *n*-hexane into a solution of **14g** in MeOH gave crystals suitable for X-ray crystallography. Note: there are two distinct molecules in the unit cell, only one of which is shown for clarity.





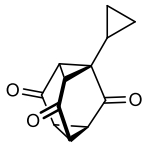
14g
CCDC 2522309

ORTEP with ellipsoid probabilities at 50%

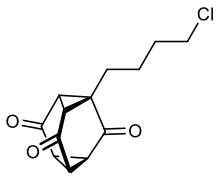


1-Isobutyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14h). General Procedure C was followed using barbaralone **5h** (94 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 55% EtOAc/*n*-pentane) gave **14h** as a white solid (52 mg, 47% over two steps from **5h**). R_f = 0.57 (40% EtOAc/*n*-pentane); m.p. 122–124 °C

(CH_2Cl_2/*n*-heptane); IR 3074, 2956, 2869, 1684 (C=O), 1466, 1329, 1299, 1112, 1071, 987, 914, 875 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.77–2.70 (1H, m, O=CC**H**), 2.67–2.59 (2H, m, 2 × O=CC**H**), 2.53–2.48 (2H, m, 2 × O=CC**H**), 2.03–1.91 (1H, m, C**H**$(CH_3)_2$), 1.47 (2H, d, *J* = 7.4 Hz, C$\mathbf{H}_2$), 0.87 (6H, d, *J* = 6.7 Hz, CH(C$\mathbf{H}_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8 (C), 193.8 (2 × C), 43.6 (C), 40.9 (2 × CH), 40.6 (CH_2), 34.6 (2 × CH), 34.2 (CH), 26.2 (CH_2), 22.8 (2 × CH_3); HRMS (ESI) Exact mass calculated for $[C_{13}H_{13}O_3]^-$ $[M–H]^-$: 217.0870, found 217.0866.

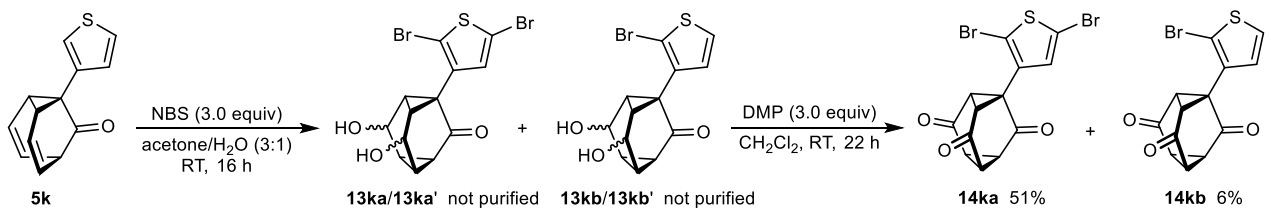


1-Cyclopropyltetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14i). General Procedure C was followed using barbaralone **5i** (86 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 55% EtOAc/*n*-pentane) gave **14i** as a white solid (12 mg, 12% over two steps from **5i**). R_f = 0.48 (40% EtOAc/*n*-pentane); m.p. 156–157 °C (CH_2Cl_2/*n*-heptane); IR 3070, 1695 (C=O), 1319, 1302, 1088, 965, 917, 873, 790, 536 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.82–2.75 (1H, m, O=CC**H**), 2.68–2.62 (2H, m, 2 × O=CC**H**), 2.33–2.29 (2H, m, 2 × O=CC**H**), 1.63–1.54 (1H, m, C**H**$(CH_2)_2$), 0.66–0.56 (2H, m, C$\mathbf{H}_a$H$_b$C**H**H$_b$), 0.05–(–0.09) (2H, m, CH$_a$**H**$_b$CH**H**$_b$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.9 (C), 193.6 (2 × C), 45.7 (C), 38.2 (2 × CH), 34.6 (2 × CH), 34.0 (CH), 10.0 (CH), 2.2 (2 × CH_2); HRMS (ESI) Exact mass calculated for $[C_{12}H_9O_3]^-$ $[M–H]^-$: 201.0557, found 201.0554.

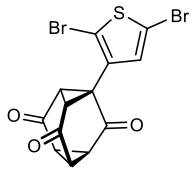


1-(4-Chlorobutyl)tetracyclo[3.3.1.02,8.0^{4,6}]nonane-3,7,9-trione (14j). General Procedure C was followed using barbaralone **5j** (111 mg, 0.50 mmol). Purification by column chromatography (100% *n*-pentane to 65% EtOAc/*n*-pentane) gave **14j** as a white solid (58 mg, 45% over two steps from **5j**). R_f = 0.28 (30% EtOAc/*n*-pentane); IR 3063, 2963, 1696 (C=O), 1300, 1089, 981, 917, 873, 536 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.52 (2H, t, *J* = 6.5 Hz, C$\mathbf{H}_2$Cl), 2.78–2.72 (1H, m, O=CC**H**), 2.69–2.64 (2H, m, 2 × O=CC**H**), 2.57–2.52 (2H, m, 2 × O=CC**H**), 1.76 (2H, p, *J* = 6.8 Hz, C$\mathbf{H}_2$CH$_2$Cl), 1.64–1.51 (4H, m, C$\mathbf{H}_2$C$\mathbf{H}_2$CH$_2$CH$_2$Cl); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6 (C), 193.5 (2 × C), 44.49 (C), 44.47 (CH_2), 40.5 (2 × CH), 34.7 (2 × CH), 34.1 (CH_2), 32.2 (CH), 24.1 (CH_2); HRMS (EI) Exact mass calculated for $[C_{13}H_{13}{}^{35}ClO_3]^+$ $[M]^+$: 252.0548, found: 252.0521.

Preparation of Triasteranetriones 14ka and 14kb

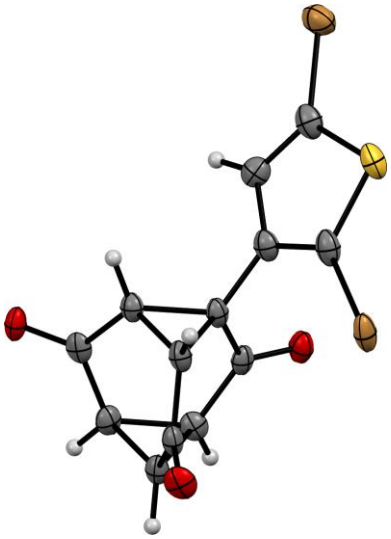


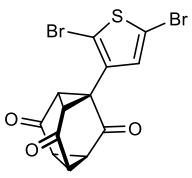
A round bottom flask was charged with barbaralone **5k** (107 mg, 0.50 mmol) and a 3:1 mixture of acetone:H_2O (4 mL). NBS (267 mg, 1.50 mmol) was added in one portion, and the resulting solution was stirred at room temperature for 96 h. The reaction was concentrated *in vacuo* and H_2O (5 mL) was added. The aqueous layer was saturated with NaCl and extracted with CH_2Cl_2 (5 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to leave the diols **13ka**/**13ka'** and **13kb**/**13kb'**, which were used immediately in the next step without purification. The crude diols **13ka**/**13ka'** and **13kb**/**143b'** were dissolved in CH_2Cl_2 (2.5 mL) and Dess-Martin periodinane (DMP) (636 mg, 1.50 mmol) was added in one portion. The mixture was stirred at room temperature for 16 h. 2 M Aqueous NaOH solution (30 mL) was added, and the resulting mixture was stirred vigorously for 1 h. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (100% *n*-pentane to 50% EtOAc/*n*-pentane) gave triasteranetrione **14ka** as a white solid (103 mg, 51%) followed by triasteranetrione **14kb** as a white solid (10 mg, 6%).



1-(2,5-Dibromothiophen-3-yl)tetracyclo[3.3.1.$0^{2,8}$.$0^{4,6}$]nonane-3,7,9-trione (14ka). R_f = 0.40 (30% EtOAc/*n*-pentane); m.p. 250–252 °C (CH_2Cl_2/*n*-heptane); IR 3067, 1700 (C=O), 1541, 1432, 1309, 1098, 1077, 1005, 950, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (1H, s, Ar**H**), 2.90–2.87 (2H, m, 2 × O=CC**H**), 2.87–2.83 (1H, m, O=CC**H**), 2.82–2.77 (2H, m, 2 × O=CC**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.2 (2 × C), 191.0 (C), 133.7 (C), 131.1 (CH), 115.7 (C), 112.4 (C), 43.3 (C), 40.9 (2 × CH), 35.0 (2 × CH), 33.6 (CH); HRMS (ESI) Exact mass calculated for $[C_{13}H_5Br_2O_3S]^-$ $[M–H]^-$: 398.8332, found 398.8333.

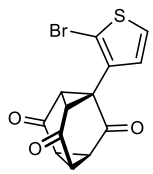
Slow vapour diffusion of *n*-heptane into a solution of **14ka** in CH_2Cl_2 gave crystals suitable for X-ray crystallography.





14ka
CCDC 2522310

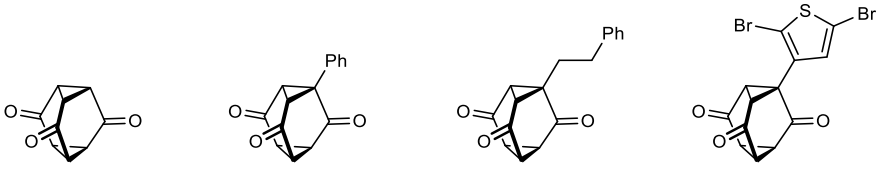
ORTEP with ellipsoid probabilities at 50%



1-(2-Bromothiophen-3-yl)tetracyclo[3.3.1.0^{2,8}.0^{4,6}]nonane-3,7,9-trione (14kb). R_f = 0.27 (30% EtOAc/*n*-pentane); m.p. 233–234 °C (CH_2Cl_2/*n*-heptane); IR 3074, 2922, 1702 (C=O), 1343, 1307, 1079, 1002, 963, 940, 913, 735, 710, 631 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (1H, d, *J* = 5.7 Hz, Ar**H**), 6.77 (1H, d, *J* = 5.6 Hz, Ar**H**), 2.93–2.89 (2H, m), 2.89–2.84 (1H, m), 2.82–2.76 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.6 (2 × C), 191.4 (C), 133.0 (C), 128.5 (CH), 127.1 (CH), 116.5 (C), 43.7 (C), 41.1 (2 × CH), 35.0 (2 x CH), 33.6 (CH); HRMS (ESI) Exact mass calculated for $[C_{13}H_6BrO_3S]^-$ $[M–H]^-$: 320.9227, found 320.9218.

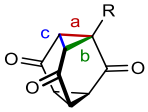
8. Structural Analysis of Triasteranetriones

The lengths of the C–C bonds in the cyclopropanes of unsubstituted triasteranetrione[8] and triasteranetriones **14a**, **14g**, and **14ka** were measured from their X-ray structures. Because of crystal packing effects, the bond lengths in the X-ray structures differ from "idealized" values, i.e., what may be expected from the symmetries of the compounds. **Note**: triasteranetrione **14g** has two distinct molecules in the unit cell, and the bond lengths are quoted for each molecule in the tables below.



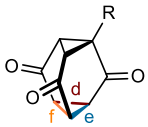
triasteranetrione CCDC 1282156 | **14a** CCDC 2522308 | **14g** CCDC 2522308 | **14ka** CCDC 2522310

Table S1. Bond Lengths (Å) in the Substituted Cyclopropane Ring



Compound	a	b	c	(a + b)/2	(a + b + c)/3
triasteranetrione[8]	1.514	1.514	1.521	1.514	1.516
14a	1.530	1.529	1.516	1.5295	1.525
14g (molecule 1)	1.529	1.528	1.526	1.5285	1.528
14g (molecule 2)	1.527	1.527	1.529	1.527	1.528
14ka	1.526	1.532	1.519	1.529	1.526

Table S2. Bond Lengths (Å) in the Unsubstituted Cyclopropane Ring

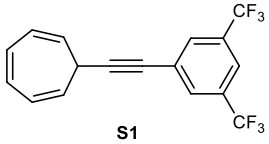


Compound	d	e	f	(d + e)/2	(d + e + f)/3
triasteranetrione[8]	1.514	1.514	1.521	1.514	1.516
14a	1.529	1.529	1.519	1.529	1.526
14g (molecule 1)	1.527	1.516	1.525	1.5215	1.523
14g (molecule 2)	1.524	1.520	1.525	1.522	1.523
14ka	1.526	1.544	1.532	1.535	1.534

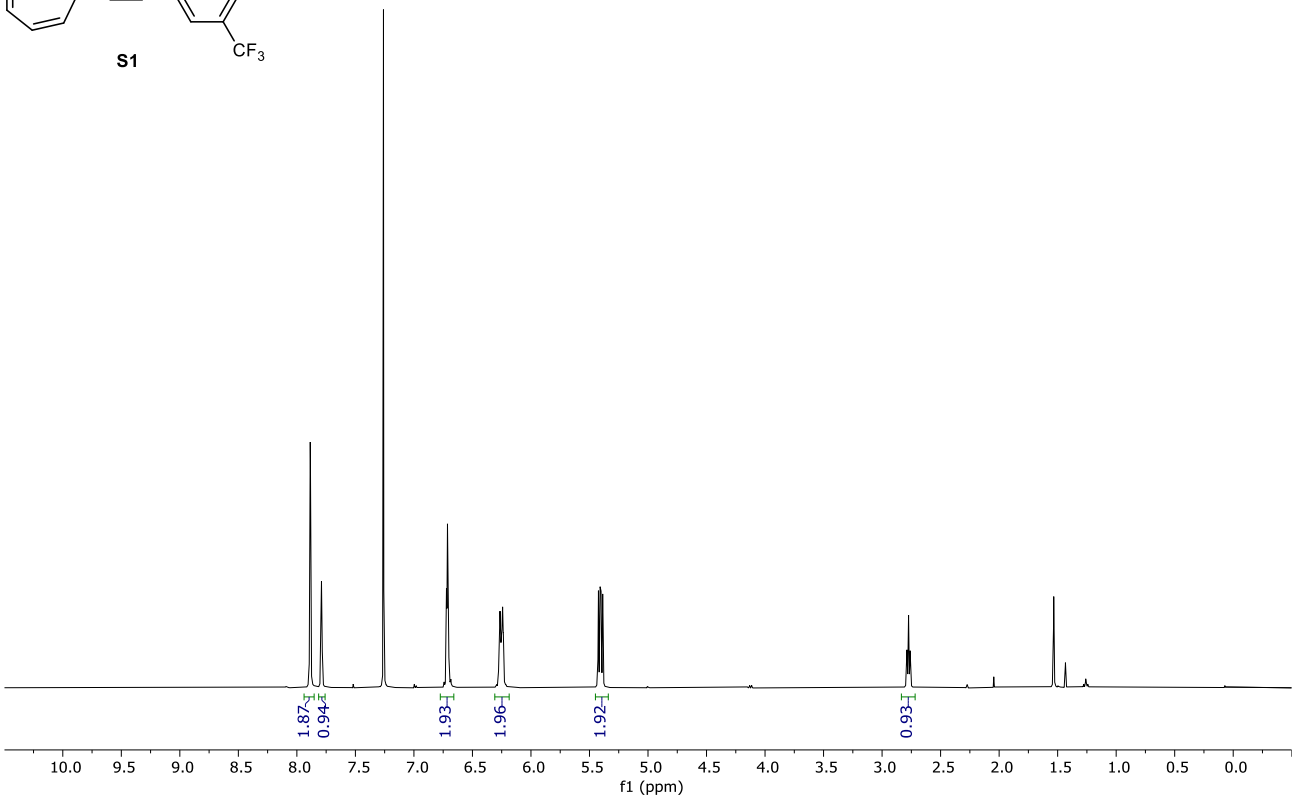
Table S3. Overall Average Bond Length (Å) of the Six Cyclopropane C–C Bonds

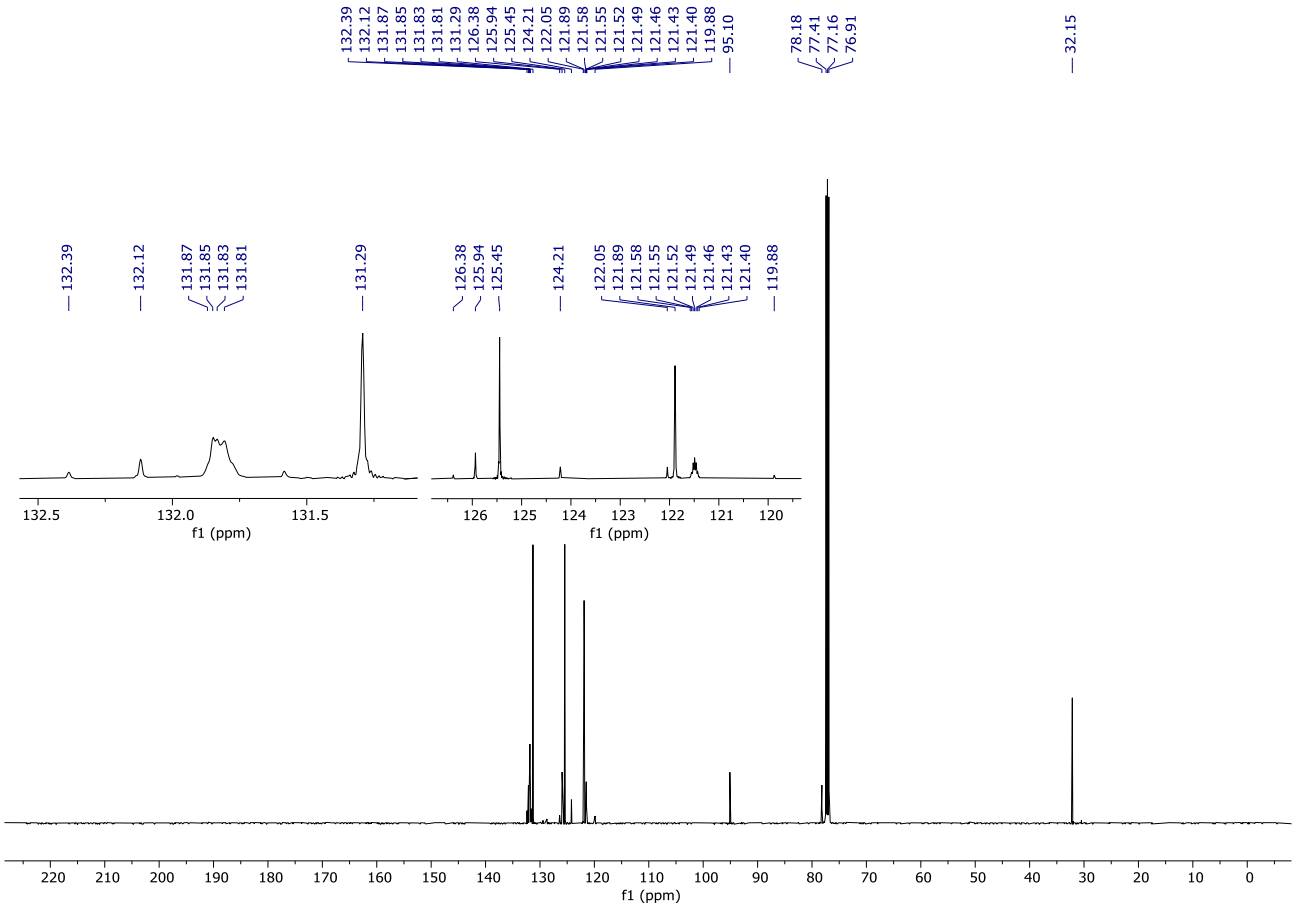
Compound	(a + b + c + d + e + f)/6
triasteranetrione[8]	1.156
14a	1.525
14g (molecule 1)	1.525
14g (molecule 2)	1.525
14ka	1.530

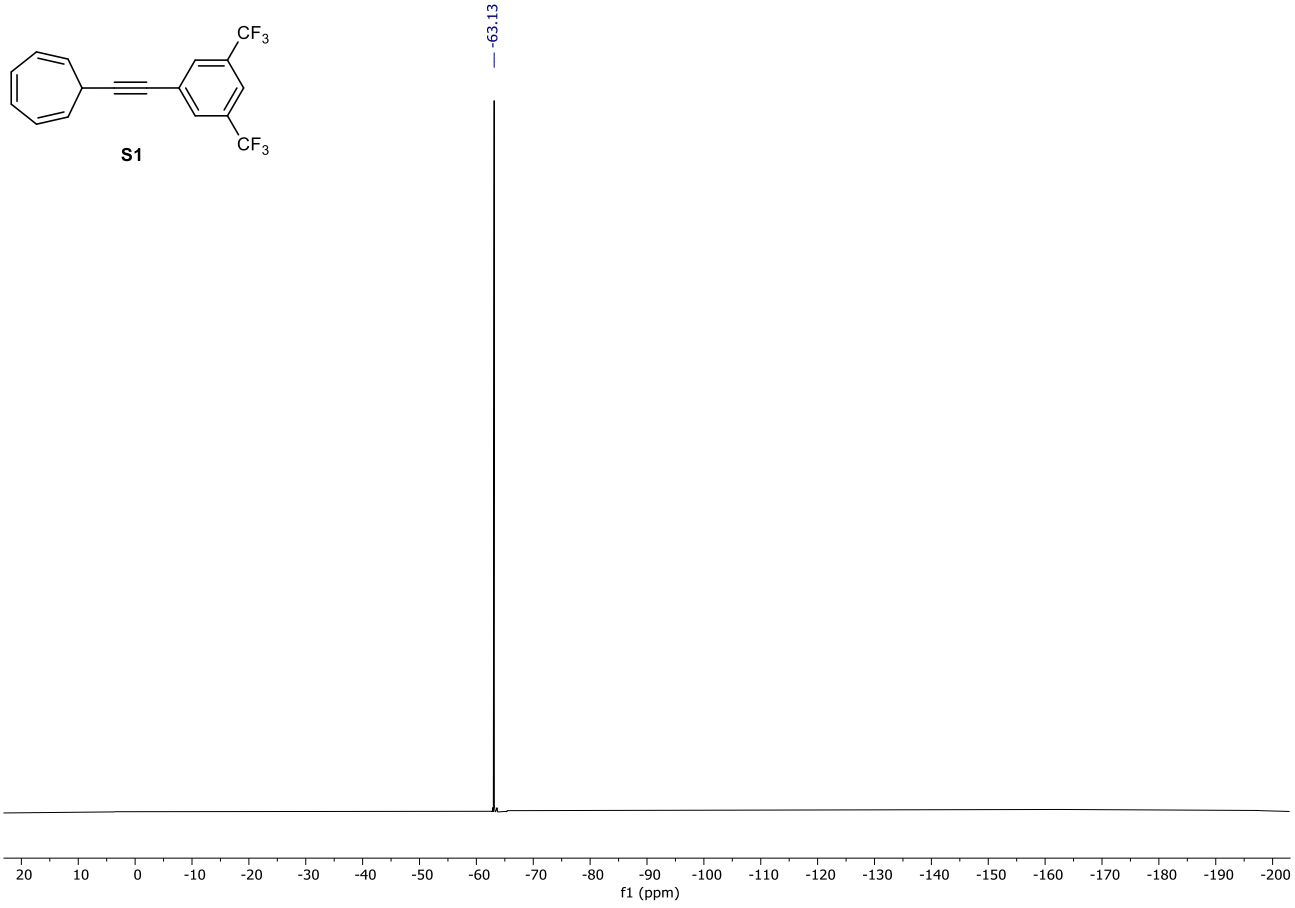
9. NMR Spectra



S1






CF3
CF3
S1
-63.13
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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-100
-110
-120
-130
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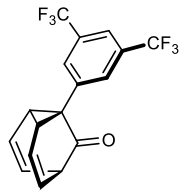
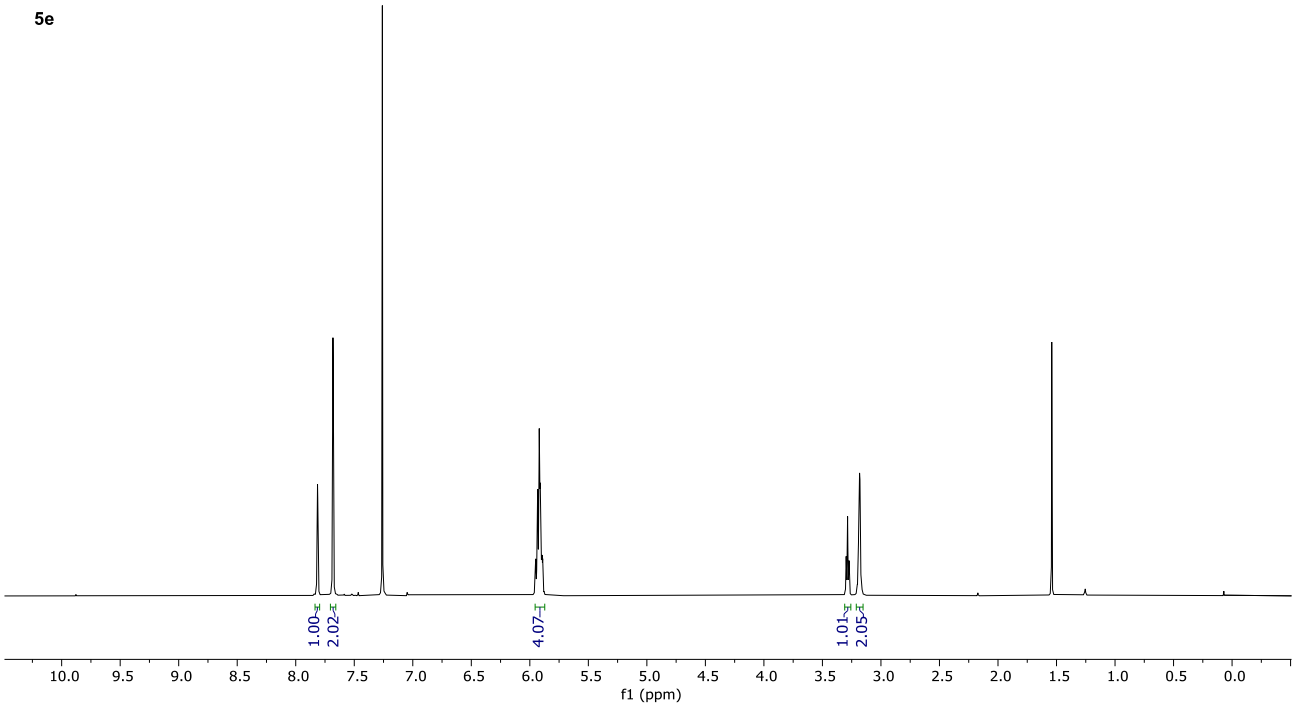
-150
-160
-170
-180
-190
-200
f1 (ppm)


F3C
CF3
O

5e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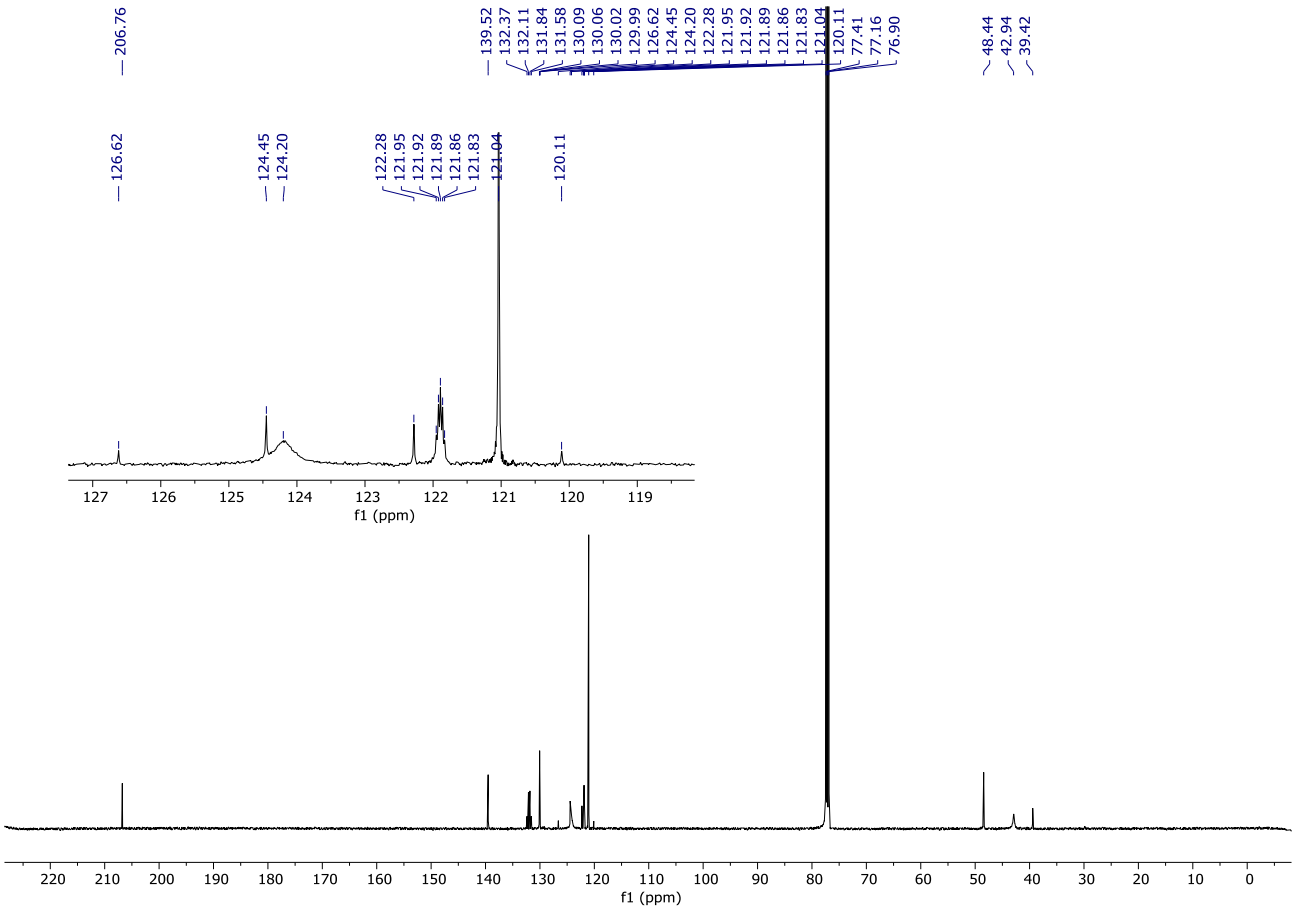
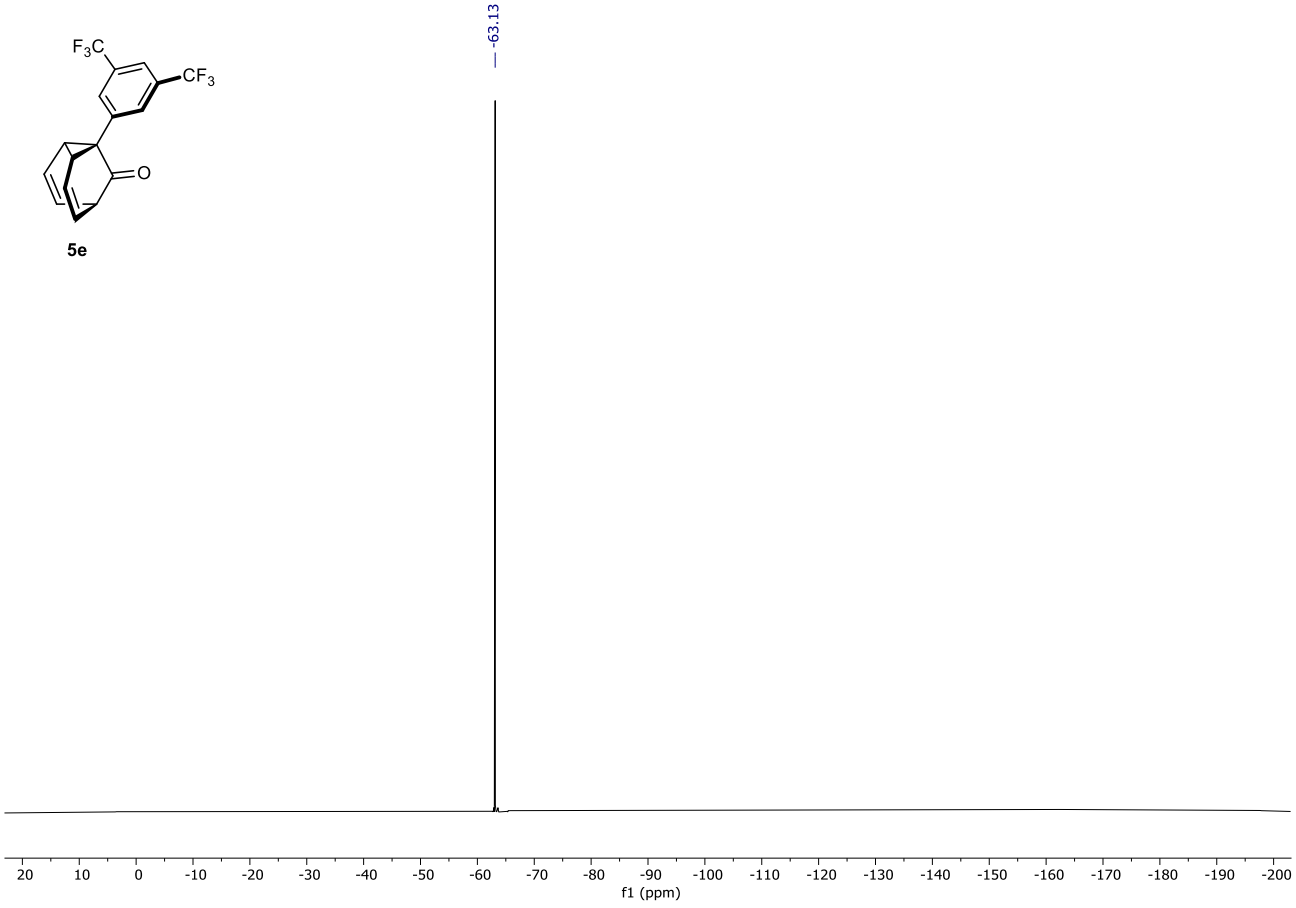
2.02
4.07
1.01
2.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


206.76
139.52
132.37
132.11
131.84
131.58
130.09
130.06
130.02
129.99
126.62
124.45
124.20
122.28
121.95
121.92
121.89
121.86
121.83
121.04
120.11
77.41
77.16
76.90
48.44
42.94
39.42
126.62
124.45
124.20
122.28
121.95
121.92
121.89
121.86
121.83
121.04
120.11
127 126 125 124 123 122 121 120 119
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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CF3
O
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20
10
0
-10
-20
-30
-40
-50
-60
-70
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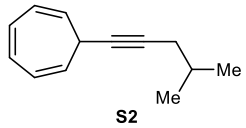
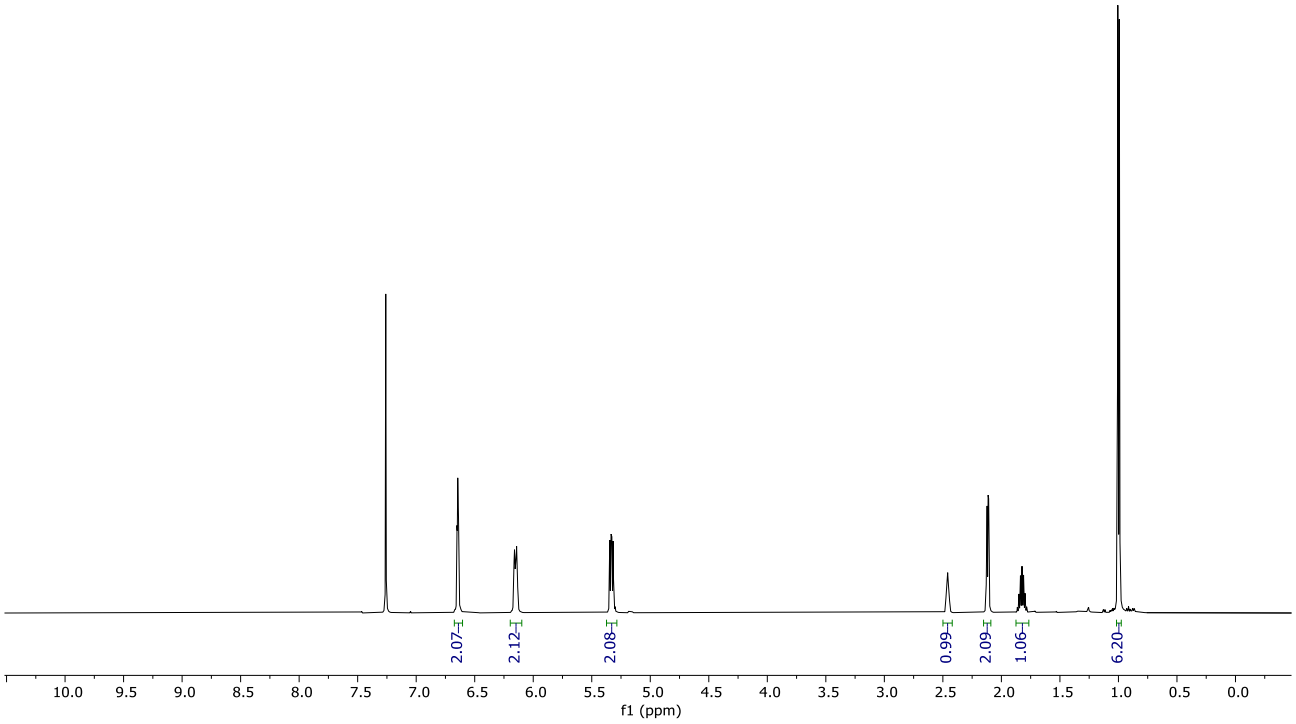
-160
-170
-180
-190
-200
f1 (ppm)


Me
Me

S2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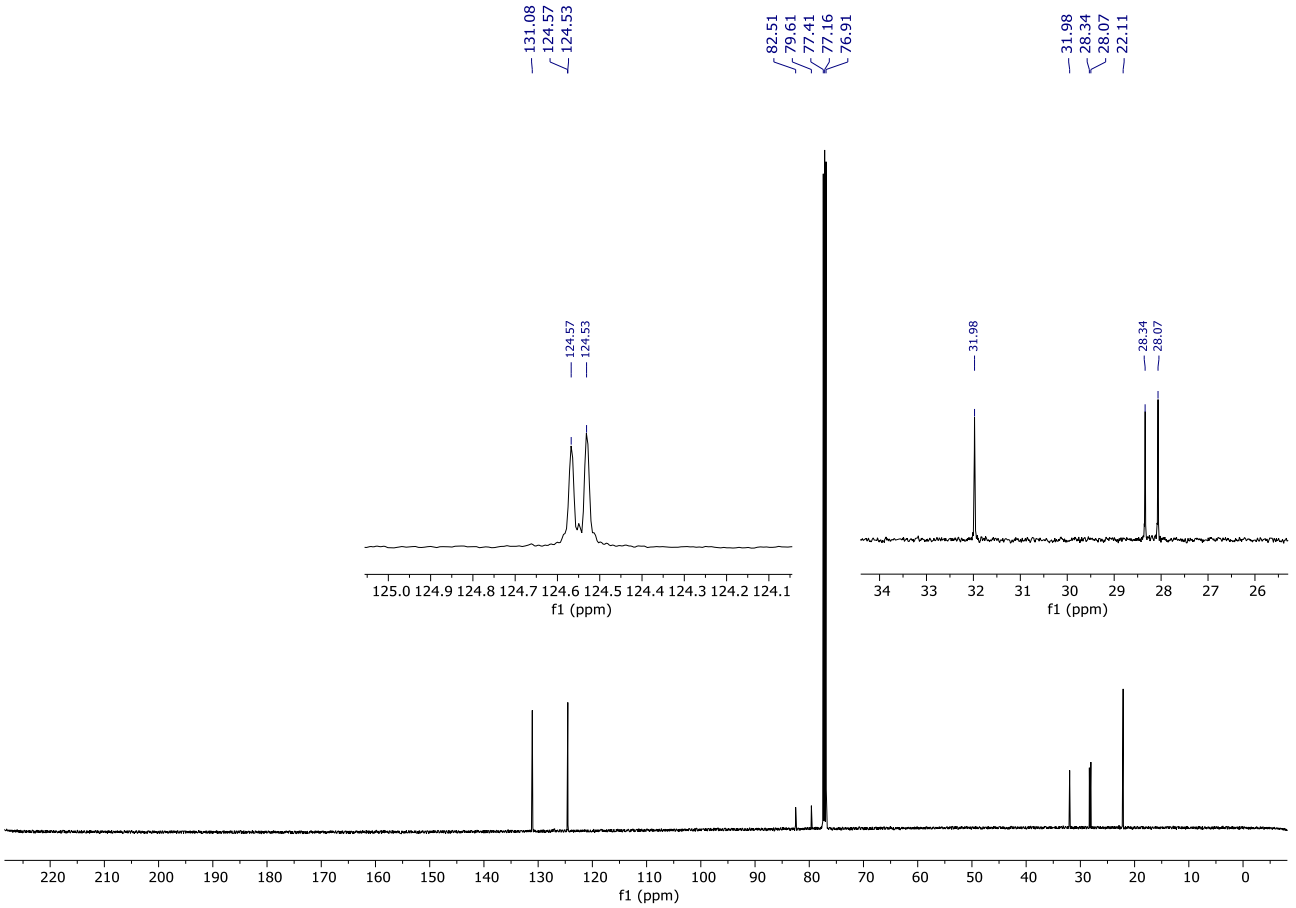
2.08
0.99
2.09
1.06
6.20
f1 (ppm)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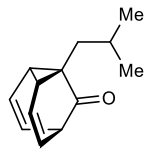
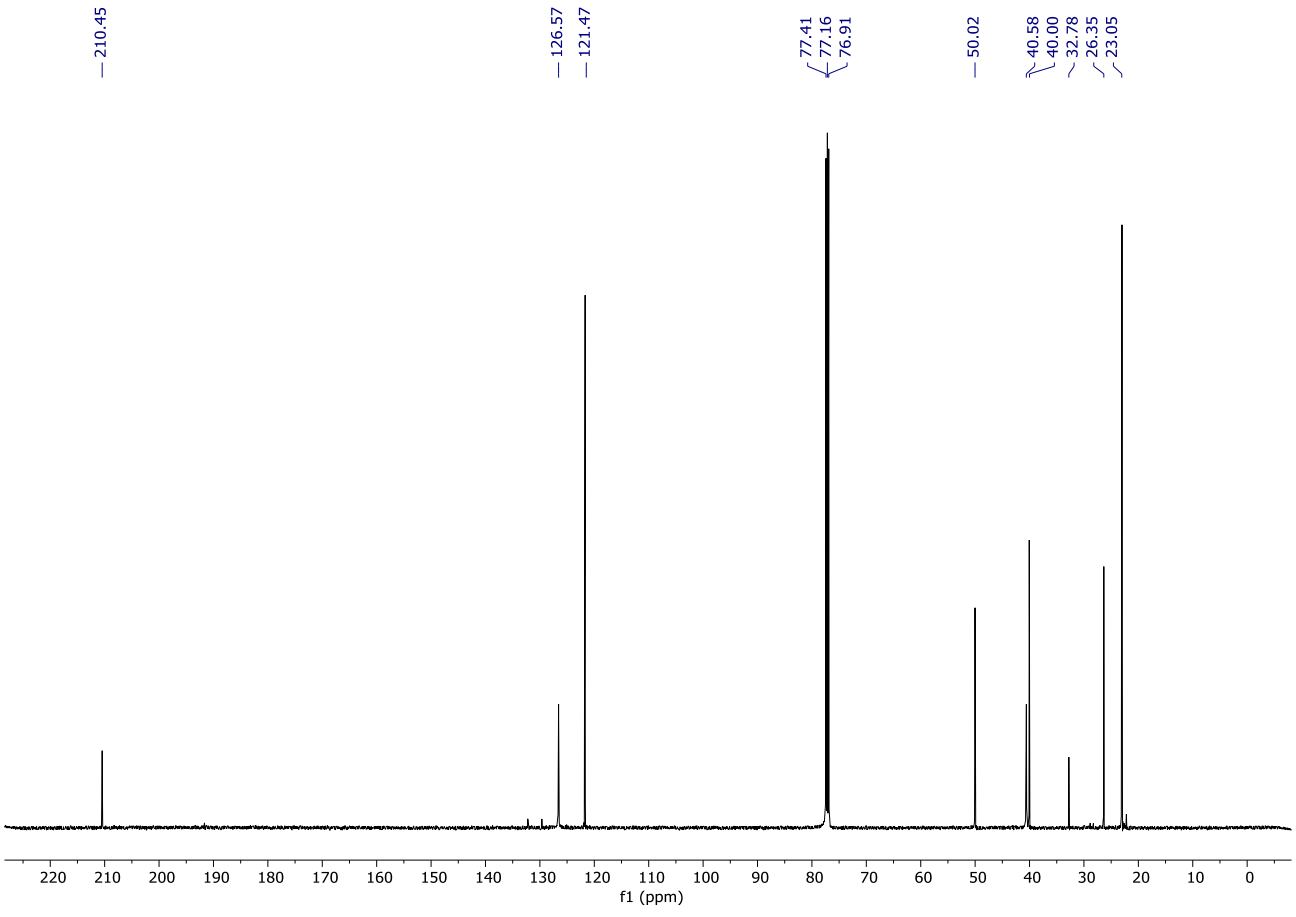
124.57
124.53
82.51
79.61
77.41
77.16
76.91
31.98
28.34
28.07
22.11
f1 (ppm)


Me
Me
O

5h

1.80
1.83
0.91
1.93
0.99
1.96
5.91
10.0 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)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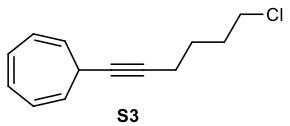
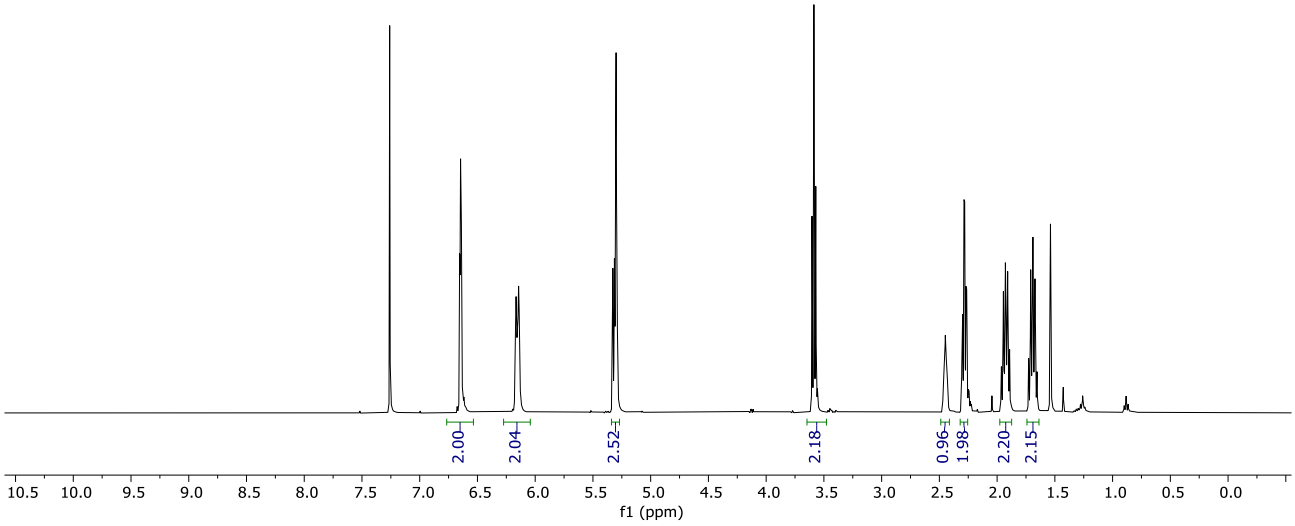
77.41
77.16
76.91
50.02
40.58
40.00
32.78
26.35
23.05
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Cl

S3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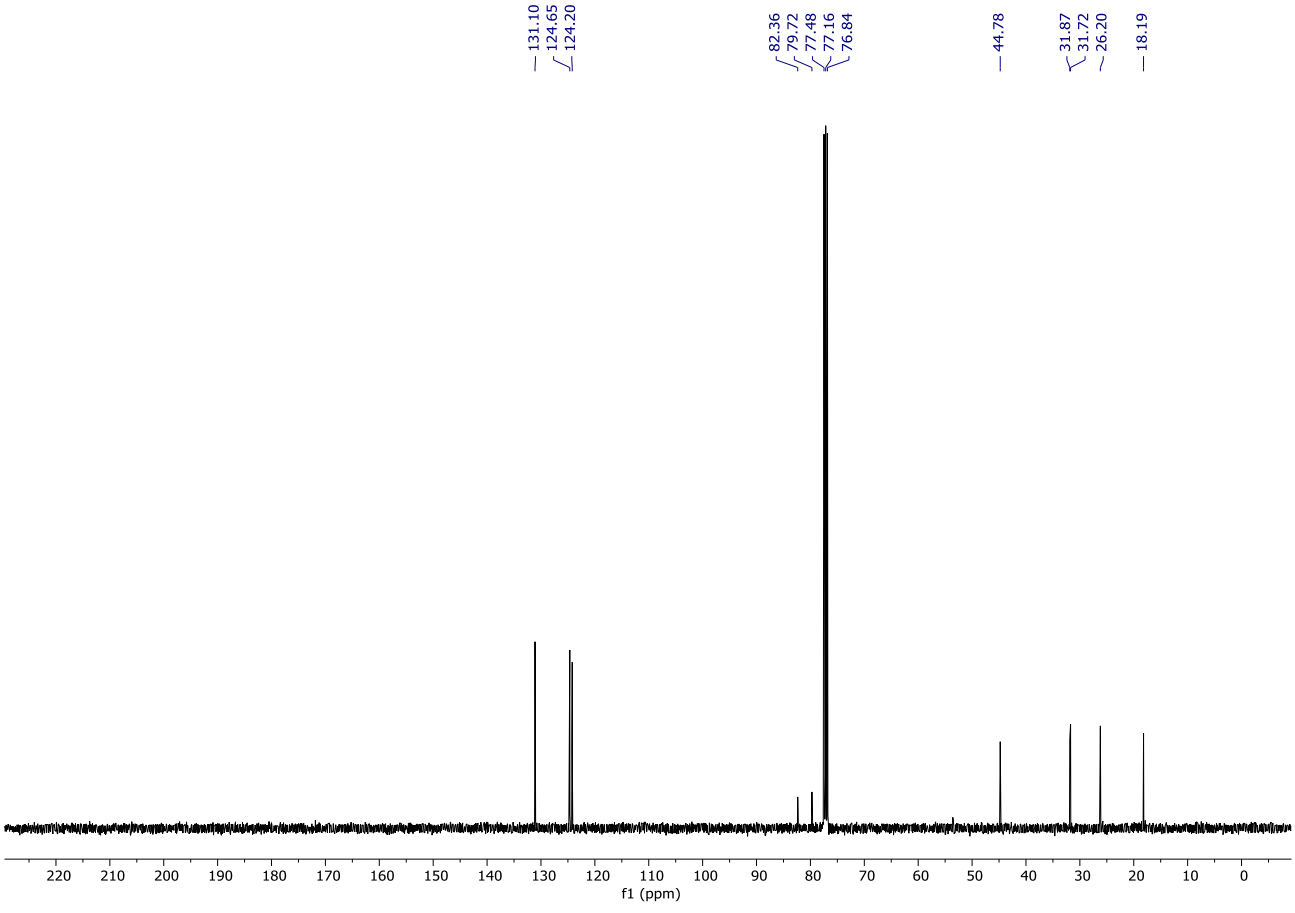
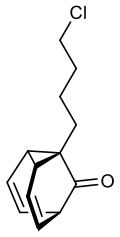
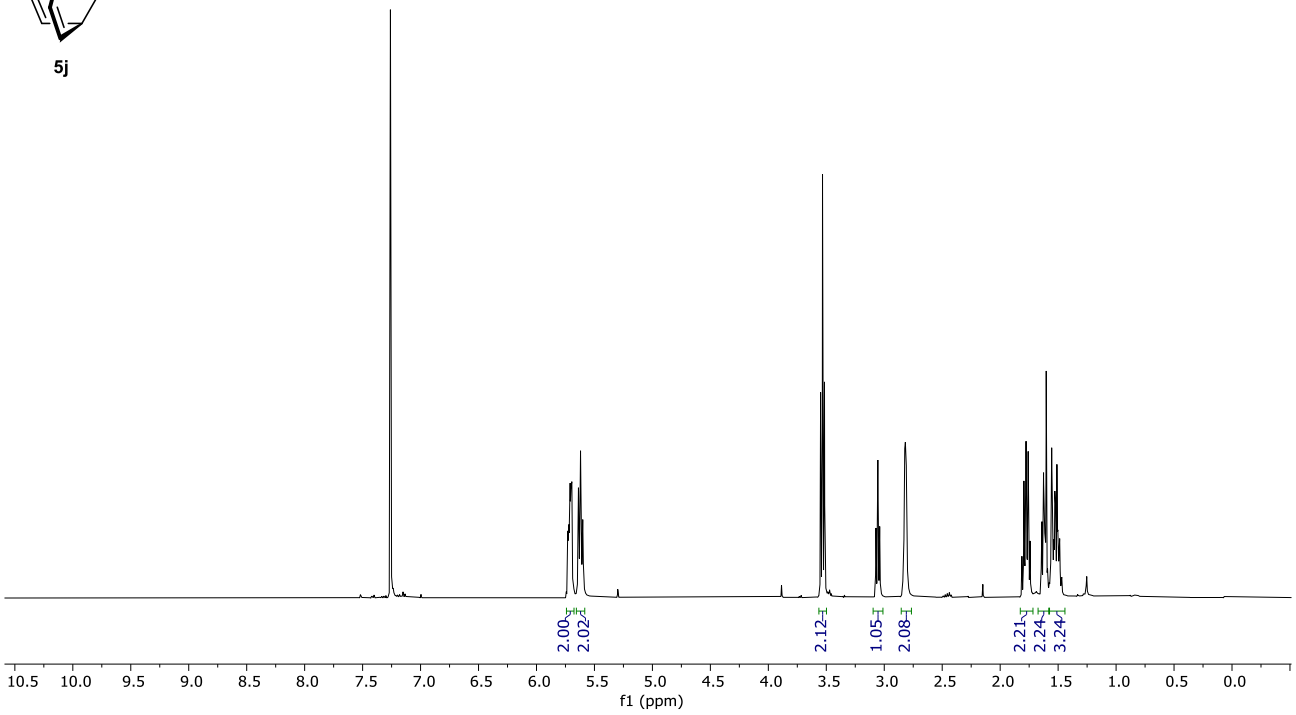
2.18
0.96
1.98
2.20
2.15
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


131.10
124.65
124.20
82.36
79.72
77.48
77.16
76.84
44.78
31.87
31.72
26.20
18.19
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Cl
O

5j


2.00
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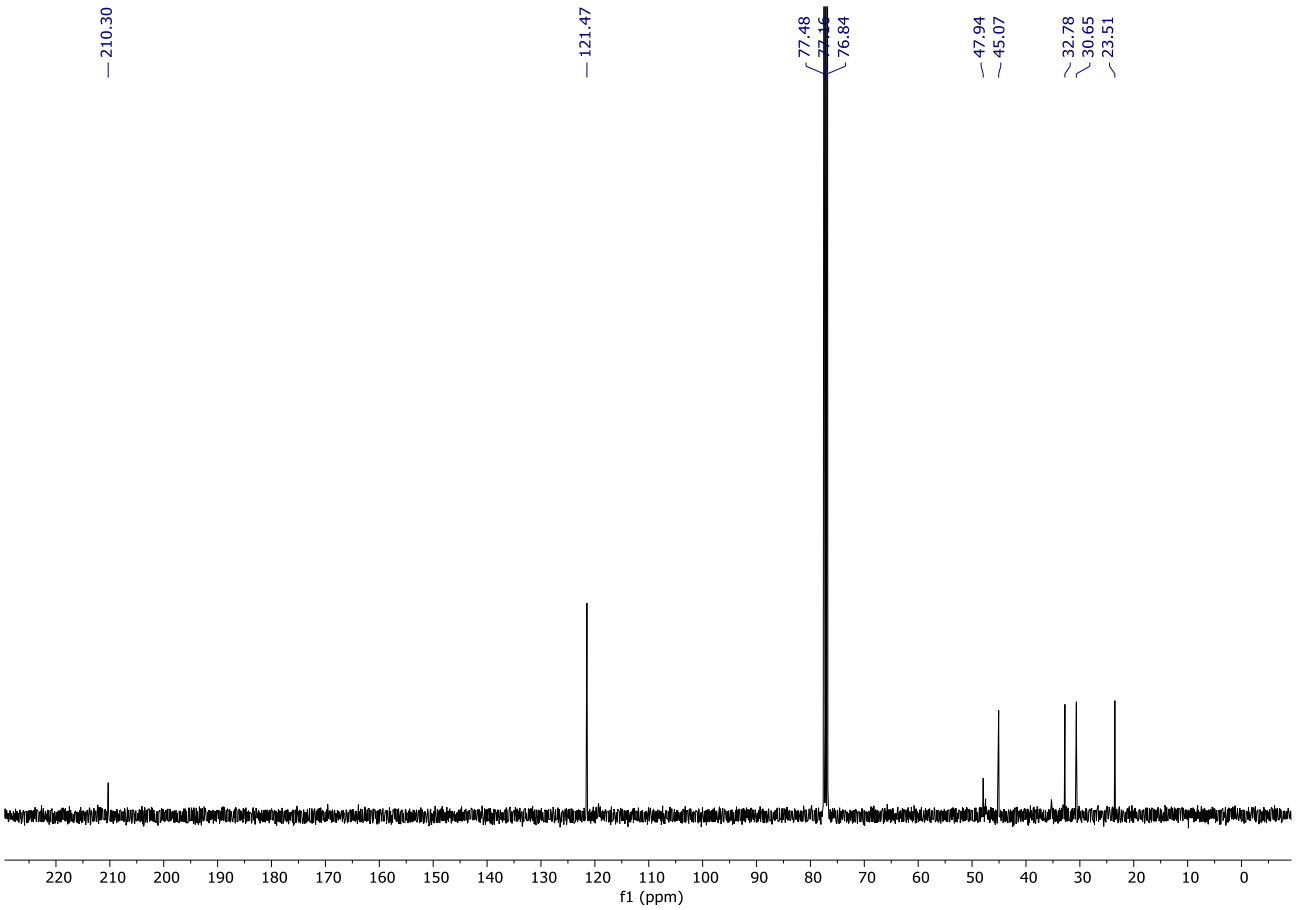
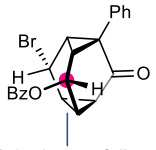
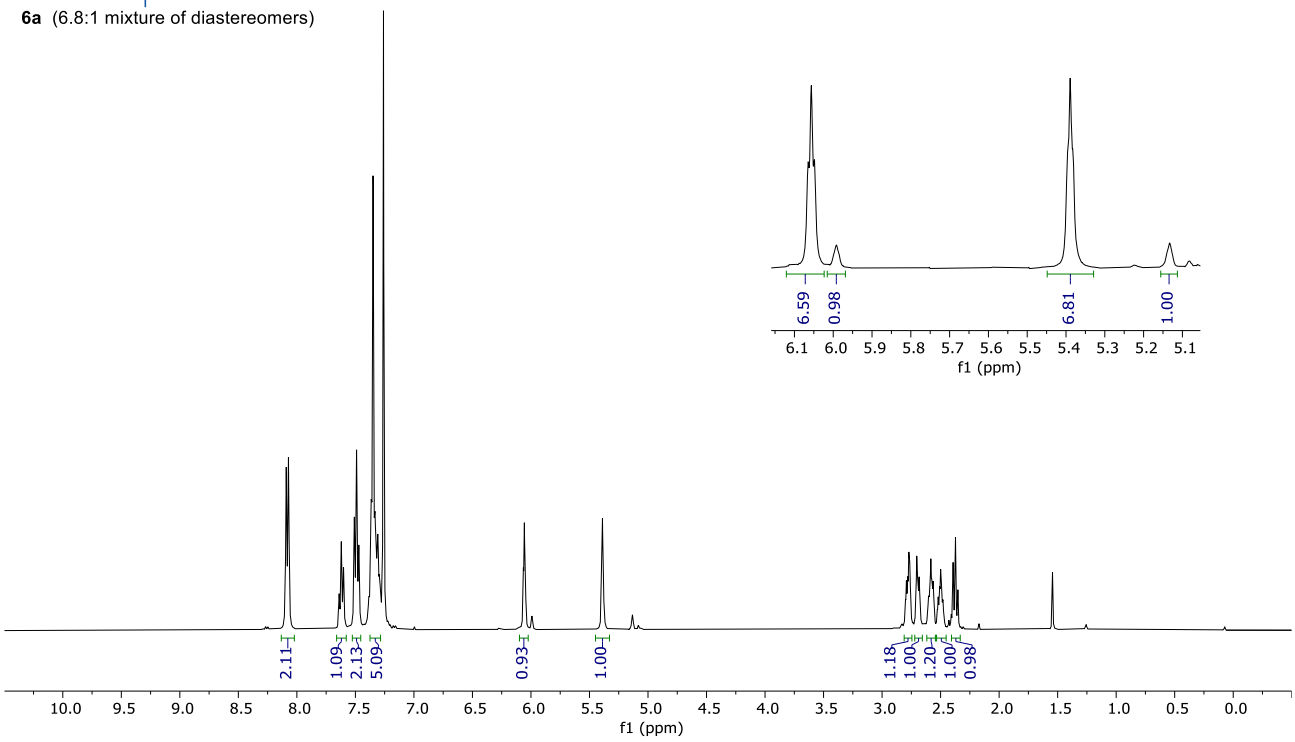
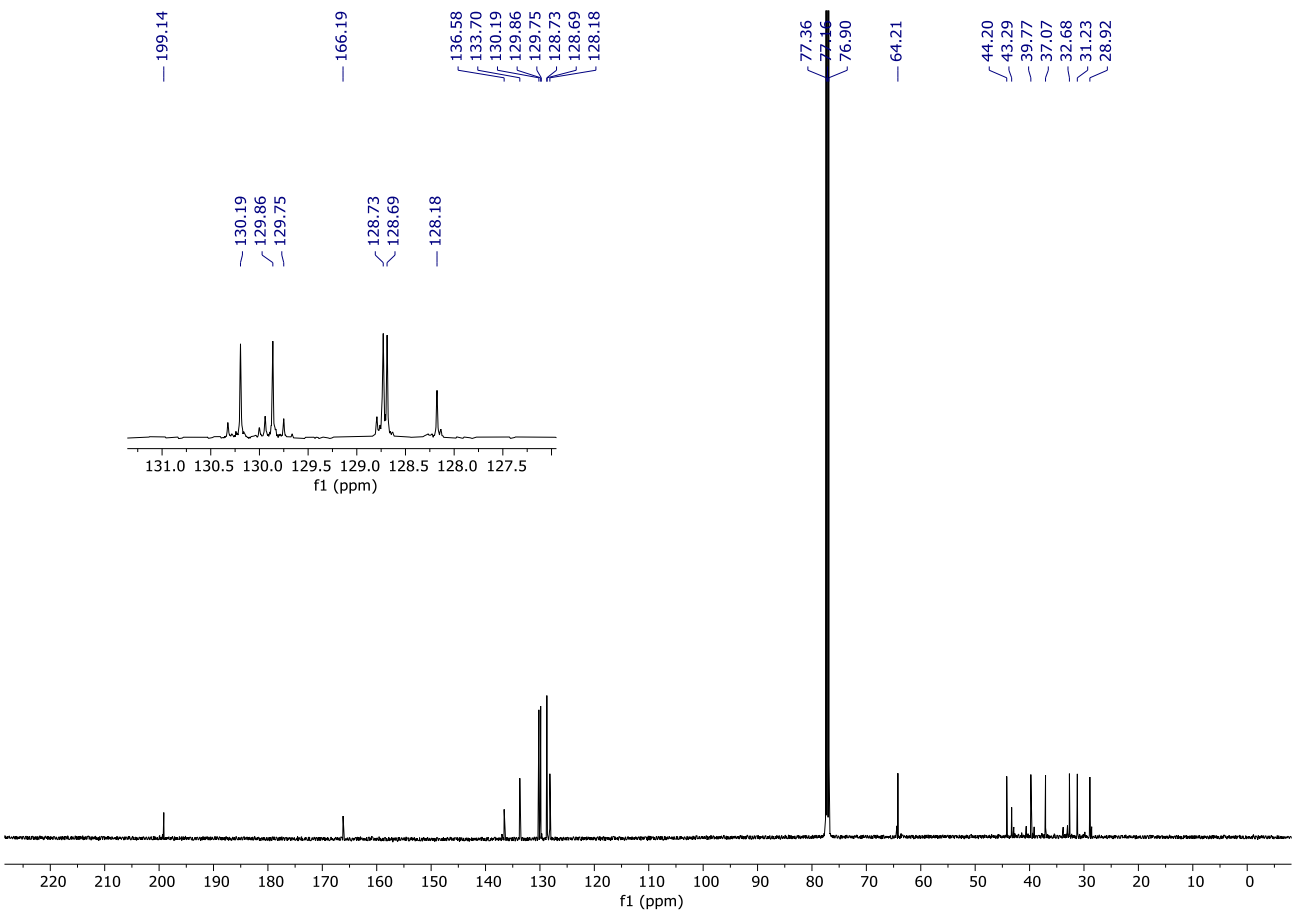
2.12
1.05
2.08
2.21
2.24
3.24
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

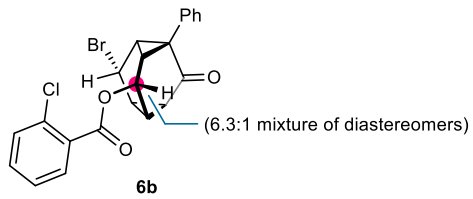

210.30
121.47
77.48
77.16
76.84
47.94
45.07
32.78
30.65
23.51
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



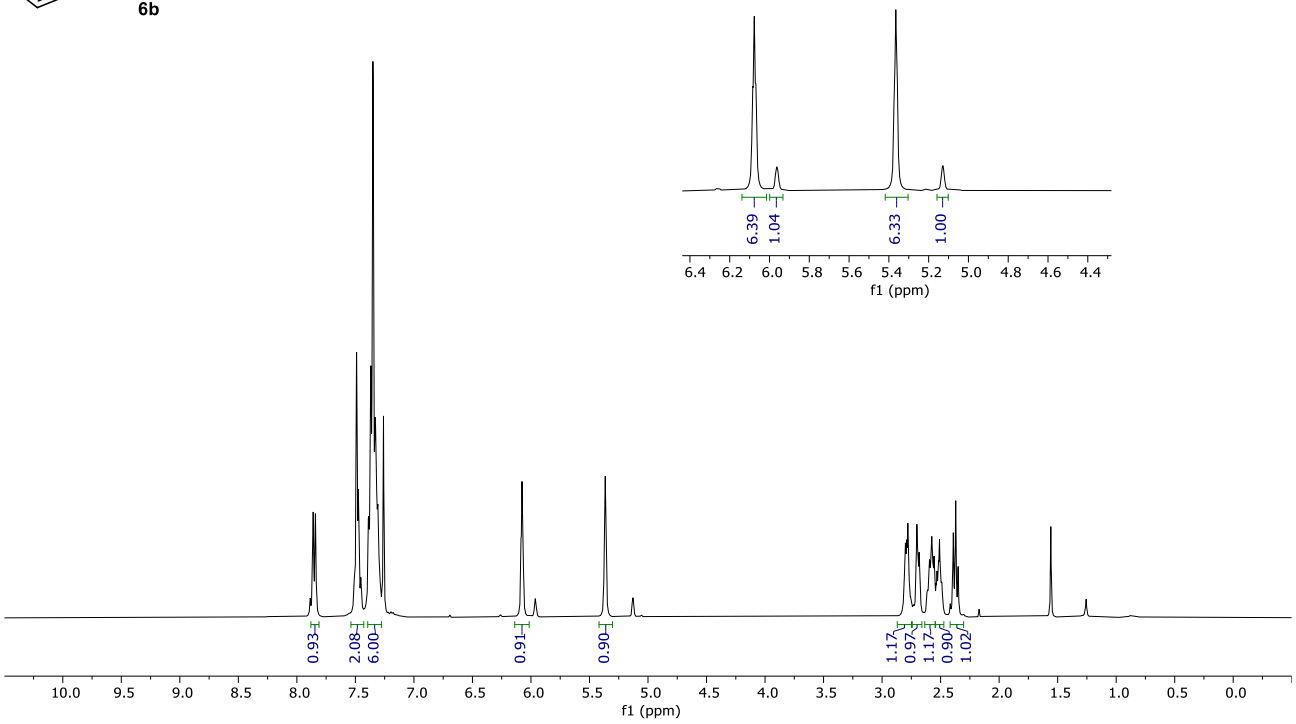
6a (6.8:1 mixture of diastereomers)

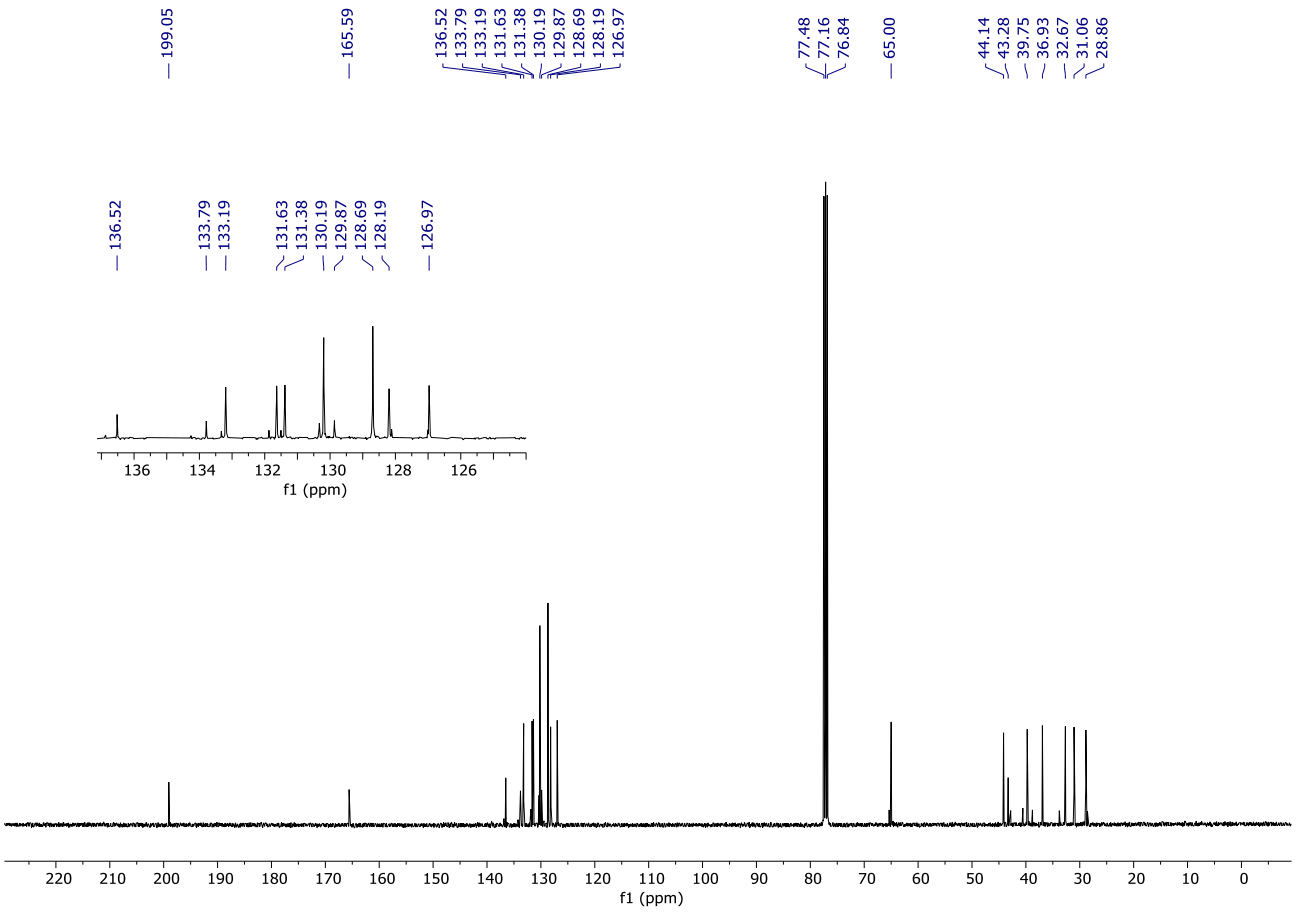


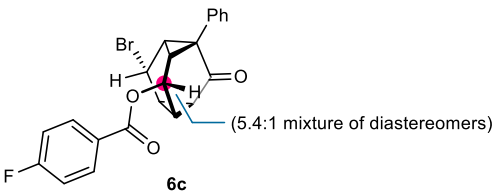



Ph
Br
H
O
O
H
Cl
O
O
(6.3:1 mixture of diastereomers)

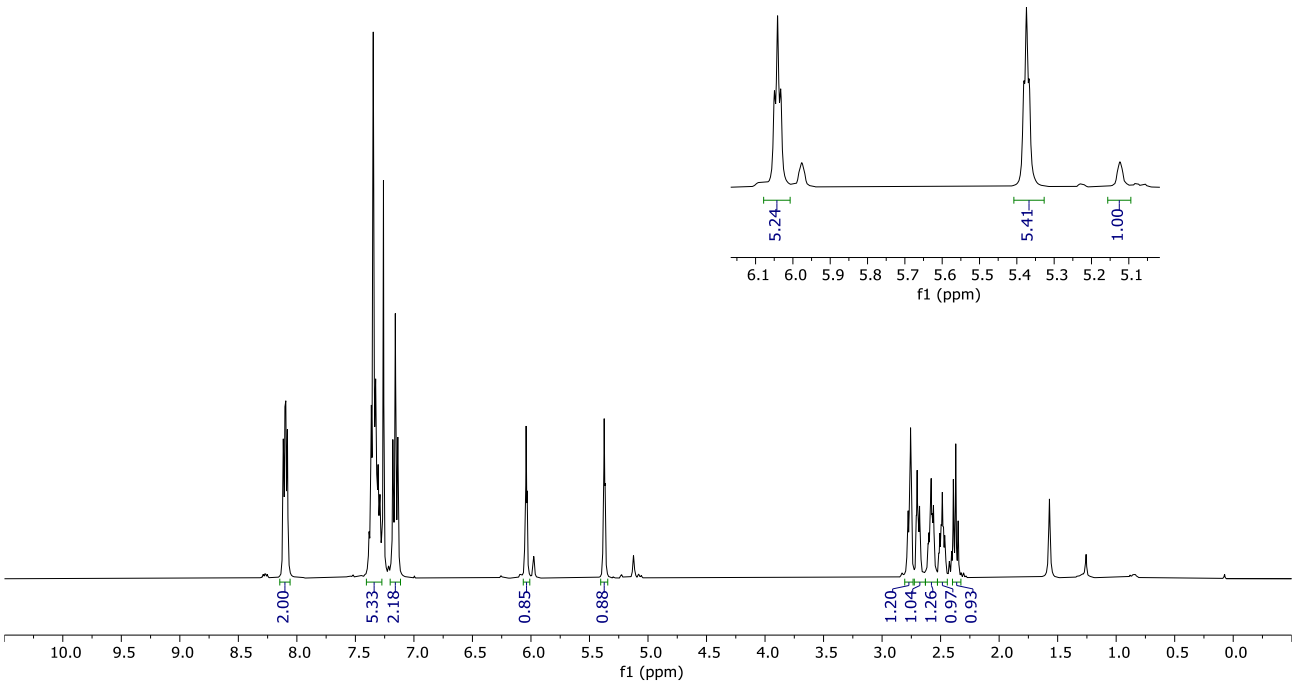
6b

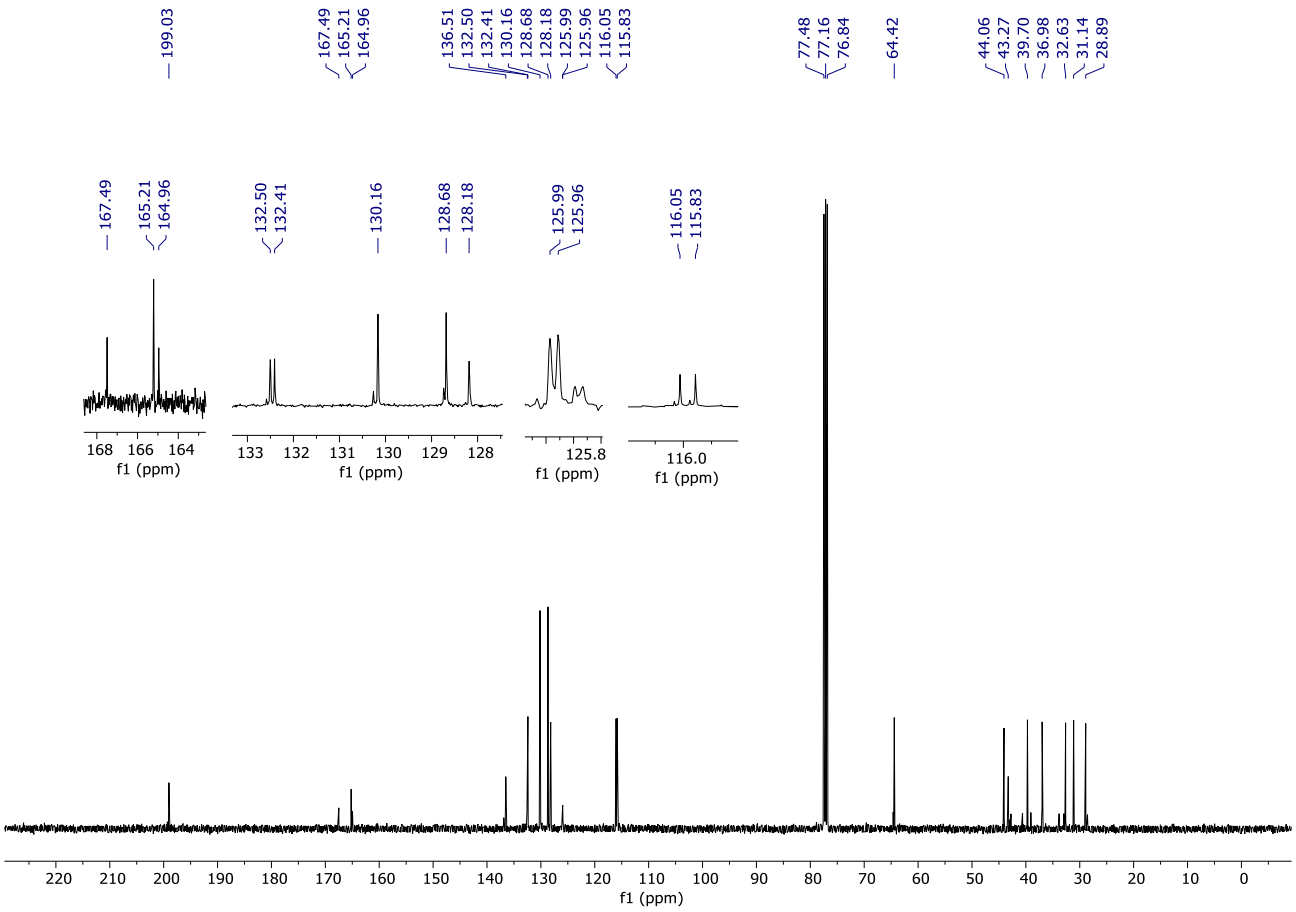

6.39
1.04
6.33
1.00
f1 (ppm)
0.93
2.08
6.00
0.91
0.90
1.17
0.97
1.17
0.90
1.02
f1 (ppm)

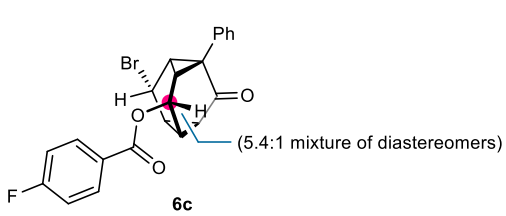

199.05
165.59
136.52
133.79
133.19
131.63
131.38
130.19
129.87
128.69
128.19
126.97
77.48
77.16
76.84
65.00
44.14
43.28
39.75
36.93
32.67
31.06
28.86
f1 (ppm)
f1 (ppm)


Ph
Br
H
O
H
O
O
F
(5.4:1 mixture of diastereomers)

6c

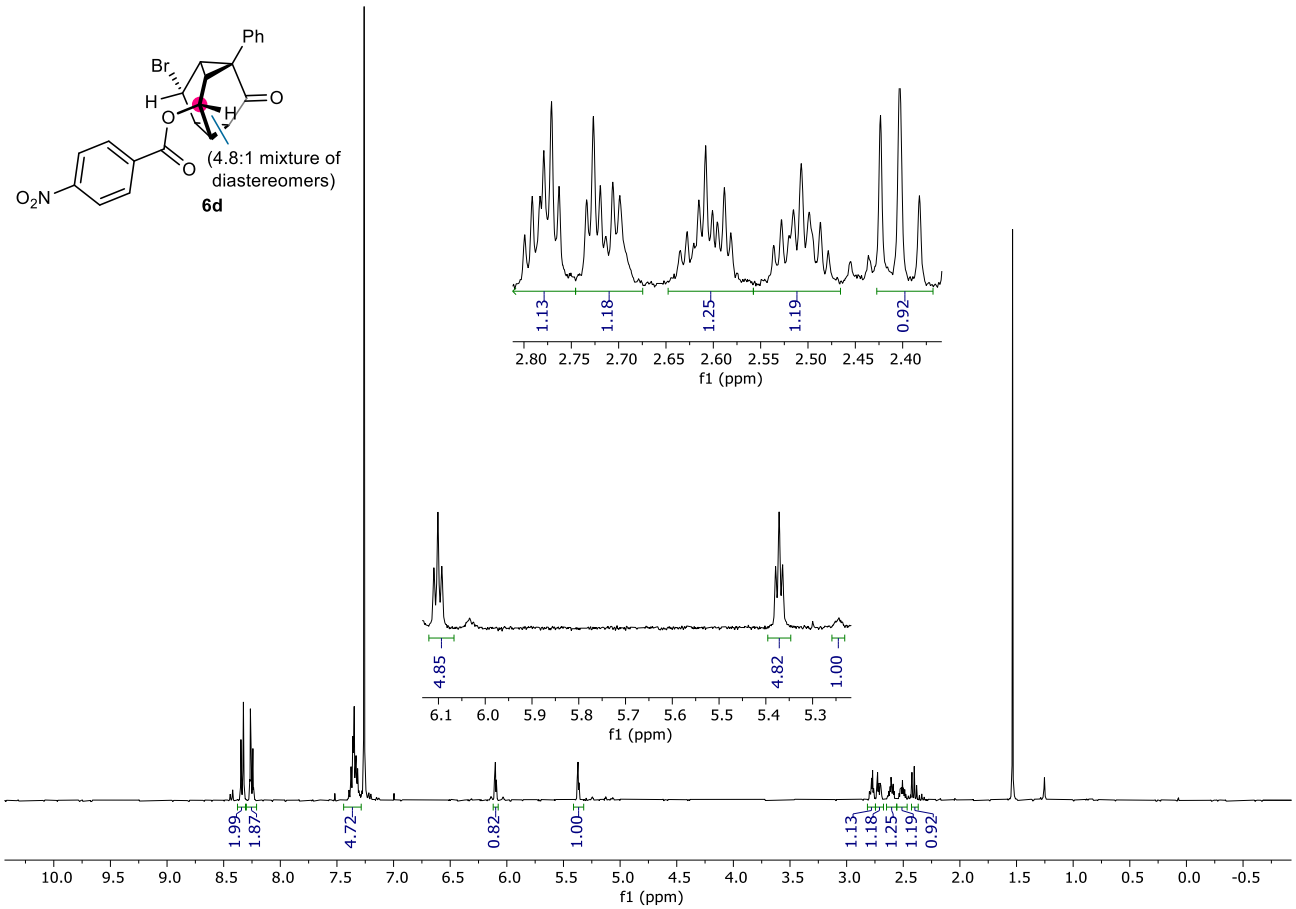

5.24
5.41
1.00
f1 (ppm)
2.00
5.33
2.18
0.85
0.88
1.20
1.04
1.26
0.97
0.93
f1 (ppm)

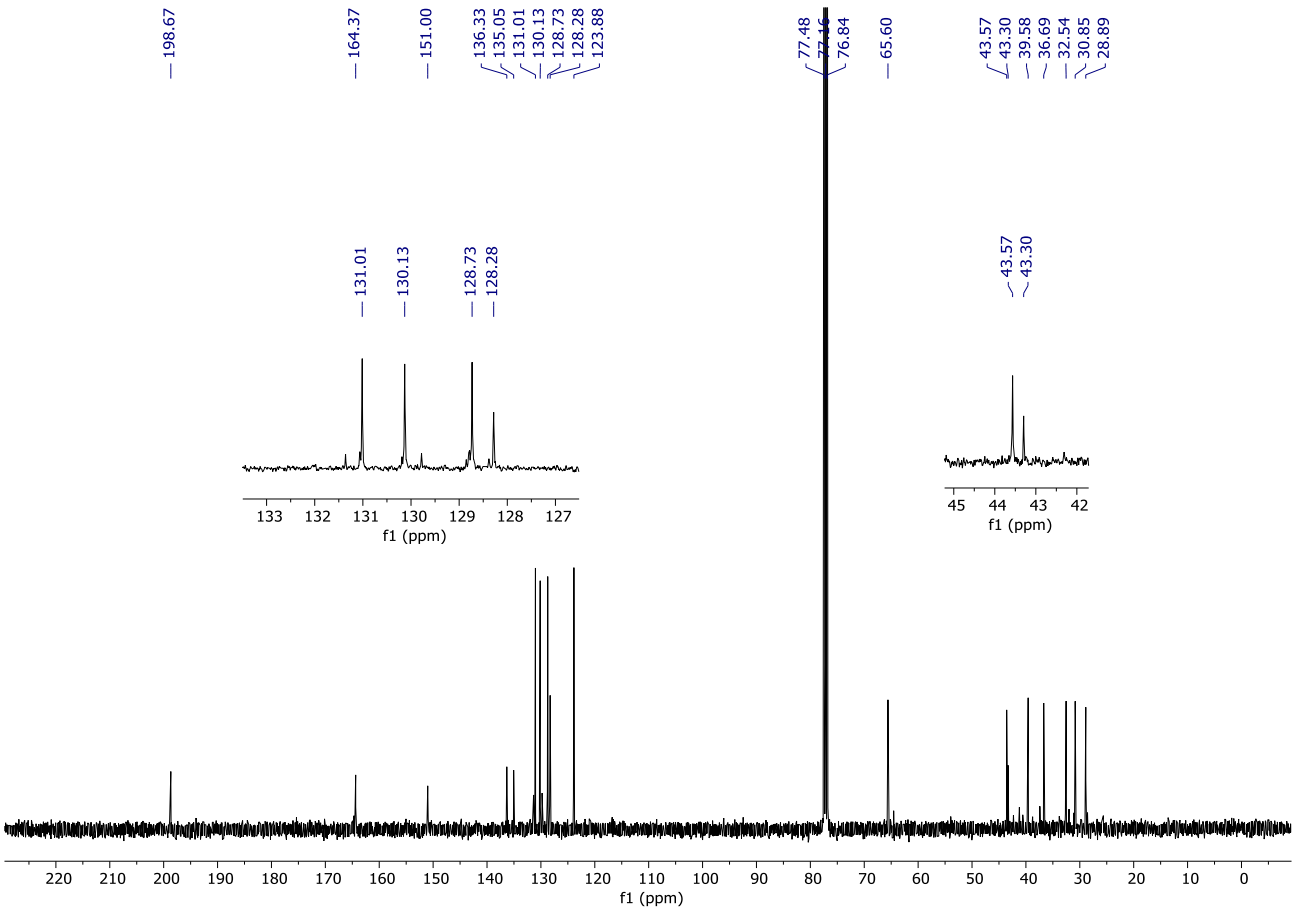

199.03
167.49
165.21
164.96
136.51
132.50
132.41
130.16
128.68
128.18
125.99
125.96
116.05
115.83
77.48
77.16
76.84
64.42
44.06
43.27
39.70
36.98
32.63
31.14
28.89
f1 (ppm)

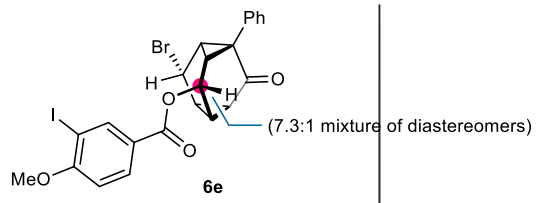

Ph
Br
H
O
H
O
O
F
(5.4:1 mixture of diastereomers)

6c

-104.29
-104.36
-104.29
-104.36
-104.20
-104.30
-104.40
f1 (ppm)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

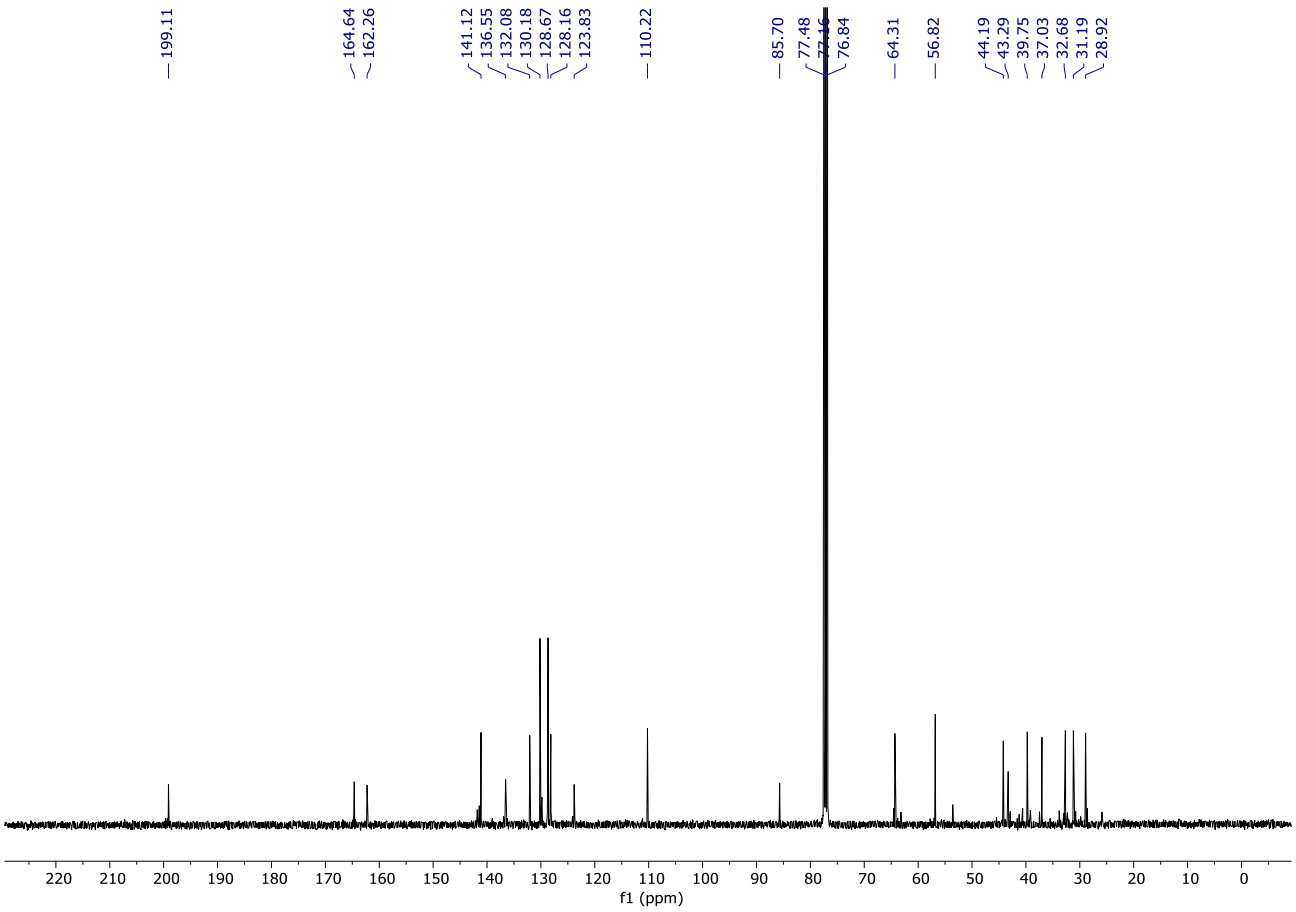

Ph
Br
H
O
O
H
O
O2N
(4.8:1 mixture of diastereomers)
6d
1.13
1.18
1.25
1.19
0.92
2.80 2.75 2.70 2.65 2.60 2.55 2.50 2.45 2.40
f1 (ppm)
4.85
4.82
1.00
6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3
f1 (ppm)
1.99
1.87
4.72
0.82
1.00
1.13
1.18
1.25
1.19
0.92
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

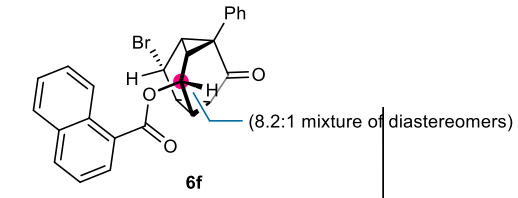

198.67
164.37
151.00
136.33
135.05
131.01
130.13
128.73
128.28
123.88
77.48
77.16
76.84
65.60
43.57
43.30
39.58
36.69
32.54
30.85
28.89
131.01
130.13
128.73
128.28
133 132 131 130 129 128 127
f1 (ppm)
43.57
43.30
45 44 43 42
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
Br
H
O
O
H
I
O
MeO
(7.3:1 mixture of diastereomers)

6e

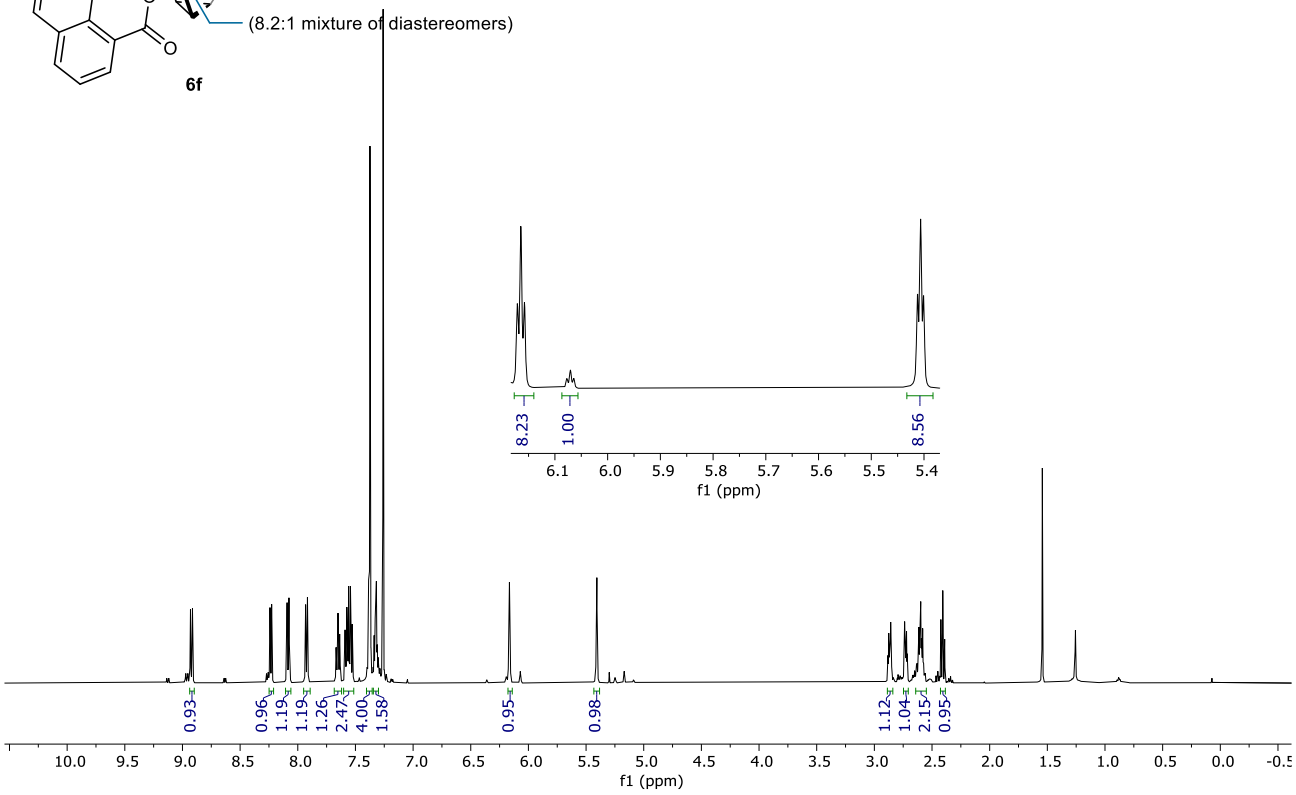
7.39
1.10
7.30
1.00
f1 (ppm)
0.83
0.92
4.94
0.95
0.68
0.71
3.00
0.95
0.99
1.05
0.83
0.94
f1 (ppm)

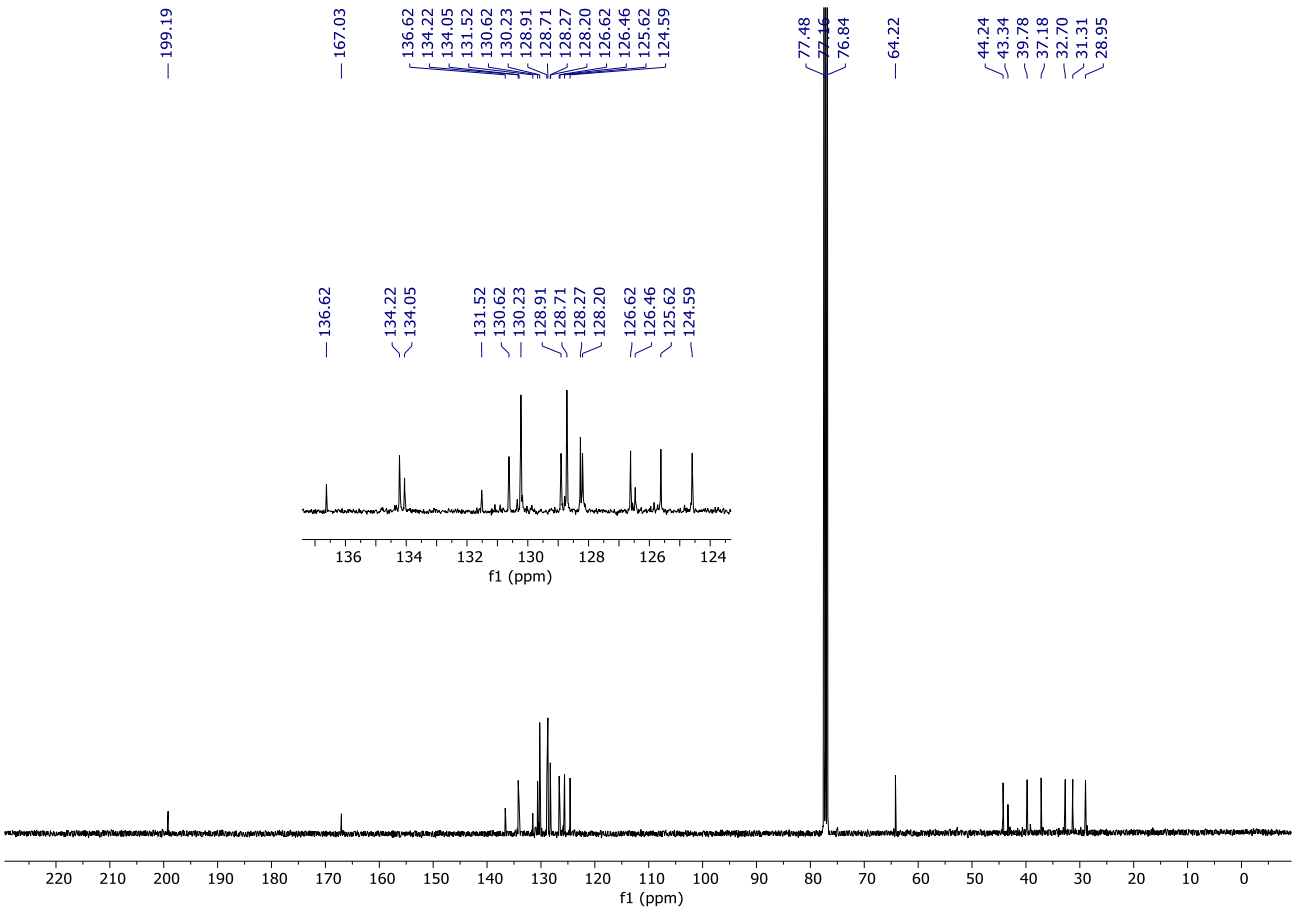

199.11
164.64
162.26
141.12
136.55
132.08
130.18
128.67
128.16
123.83
110.22
85.70
77.48
77.16
76.84
64.31
56.82
44.19
43.29
39.75
37.03
32.68
31.19
28.92
f1 (ppm)

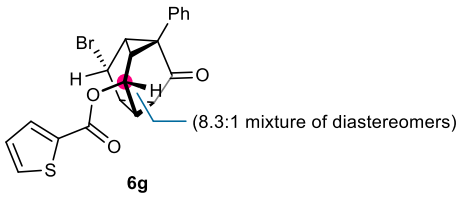


(8.2:1 mixture of diastereomers)

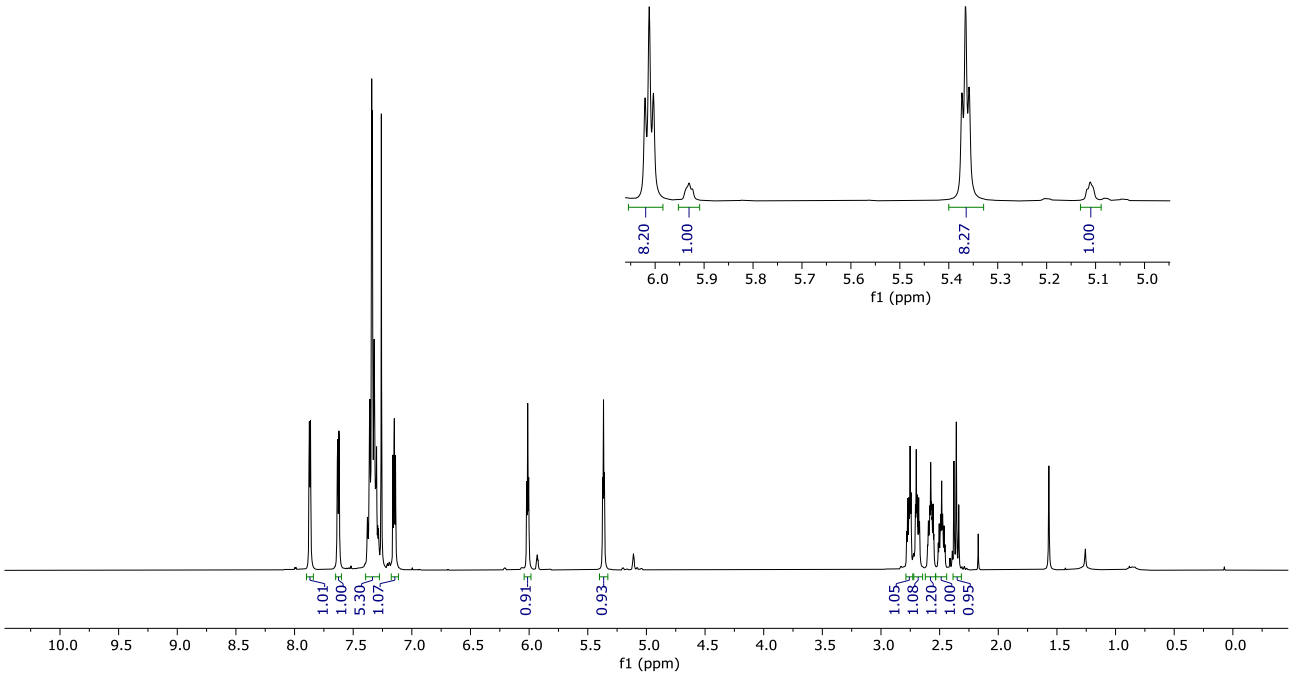
6f

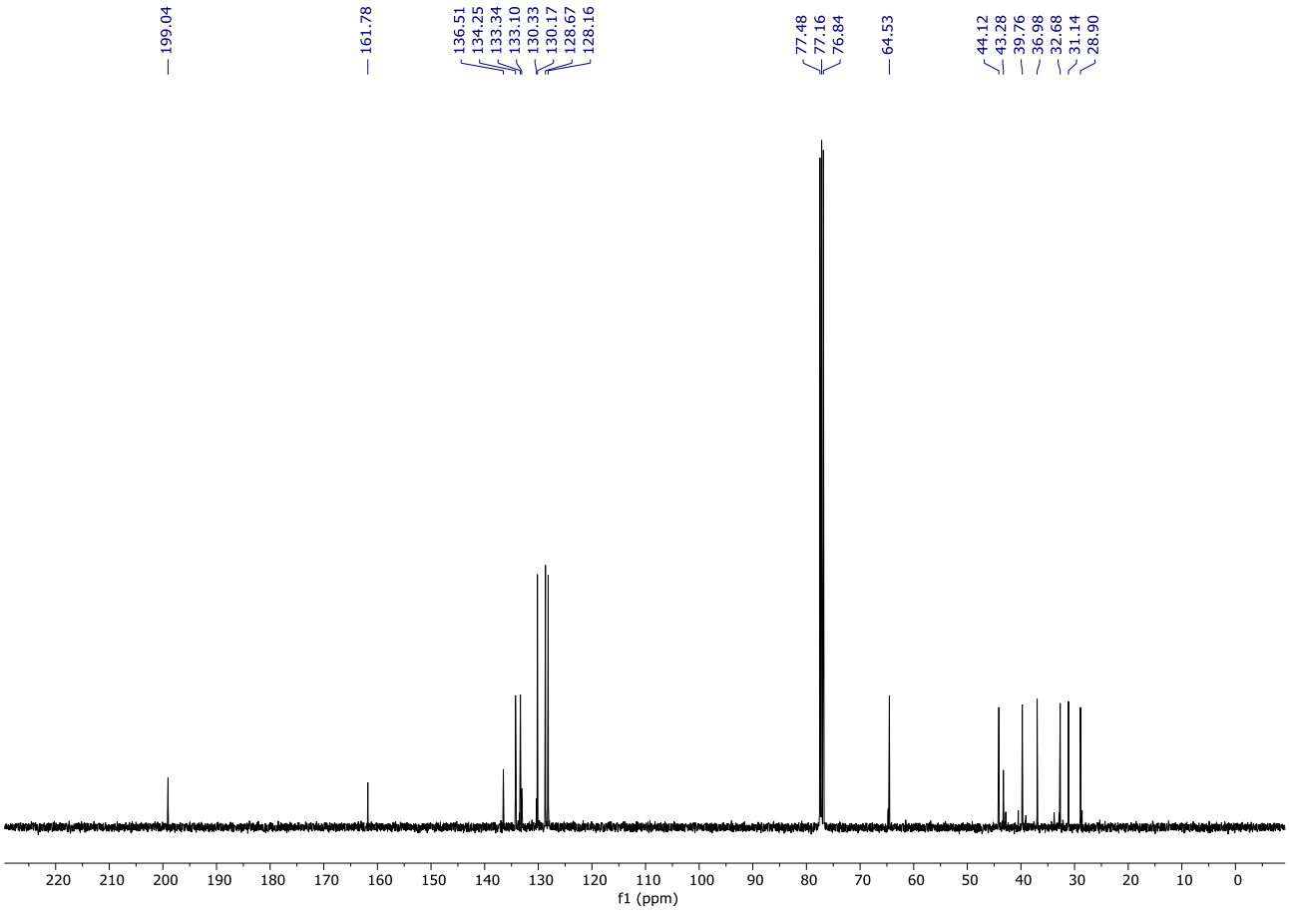


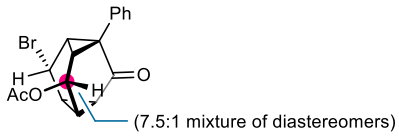



Ph
Br
H
O
O
H
O
S
(8.3:1 mixture of diastereomers)

6g

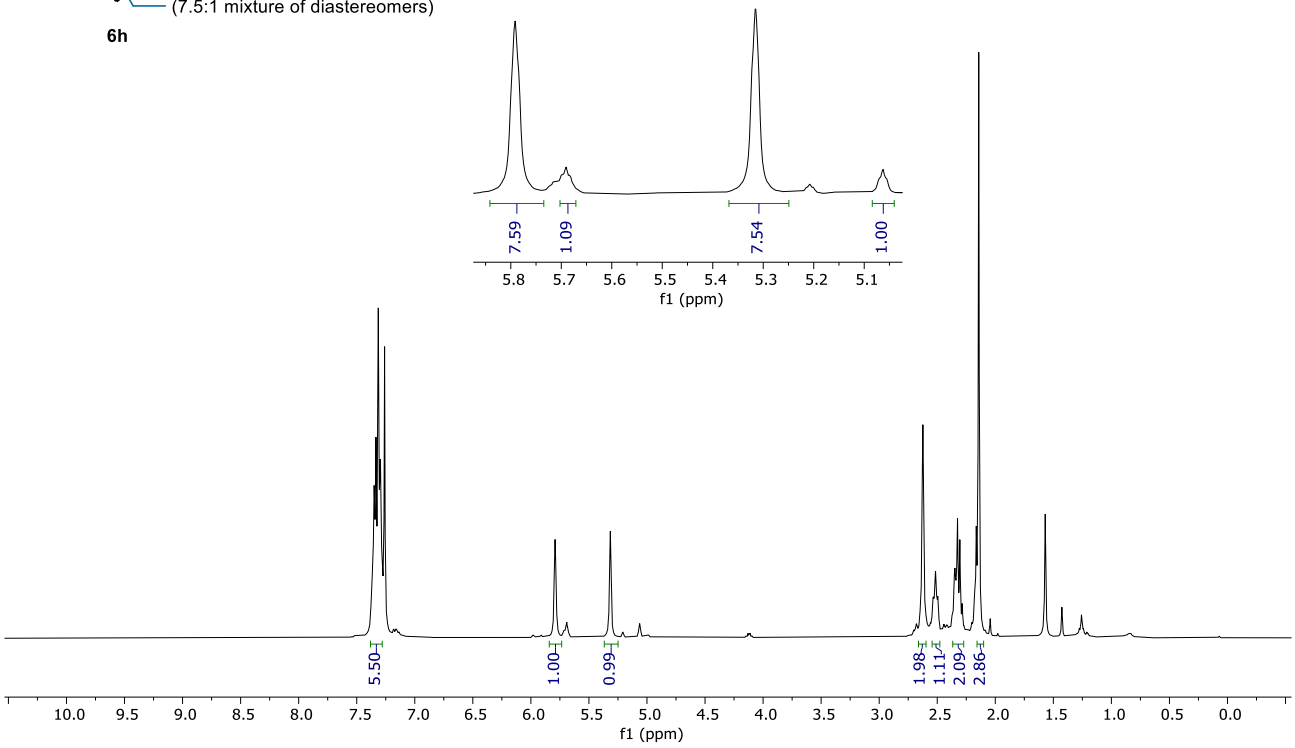

8.20
1.00
8.27
1.00
f1 (ppm)
1.01
1.00
5.30
1.07
0.91
0.93
1.05
1.08
1.20
1.00
0.95
f1 (ppm)

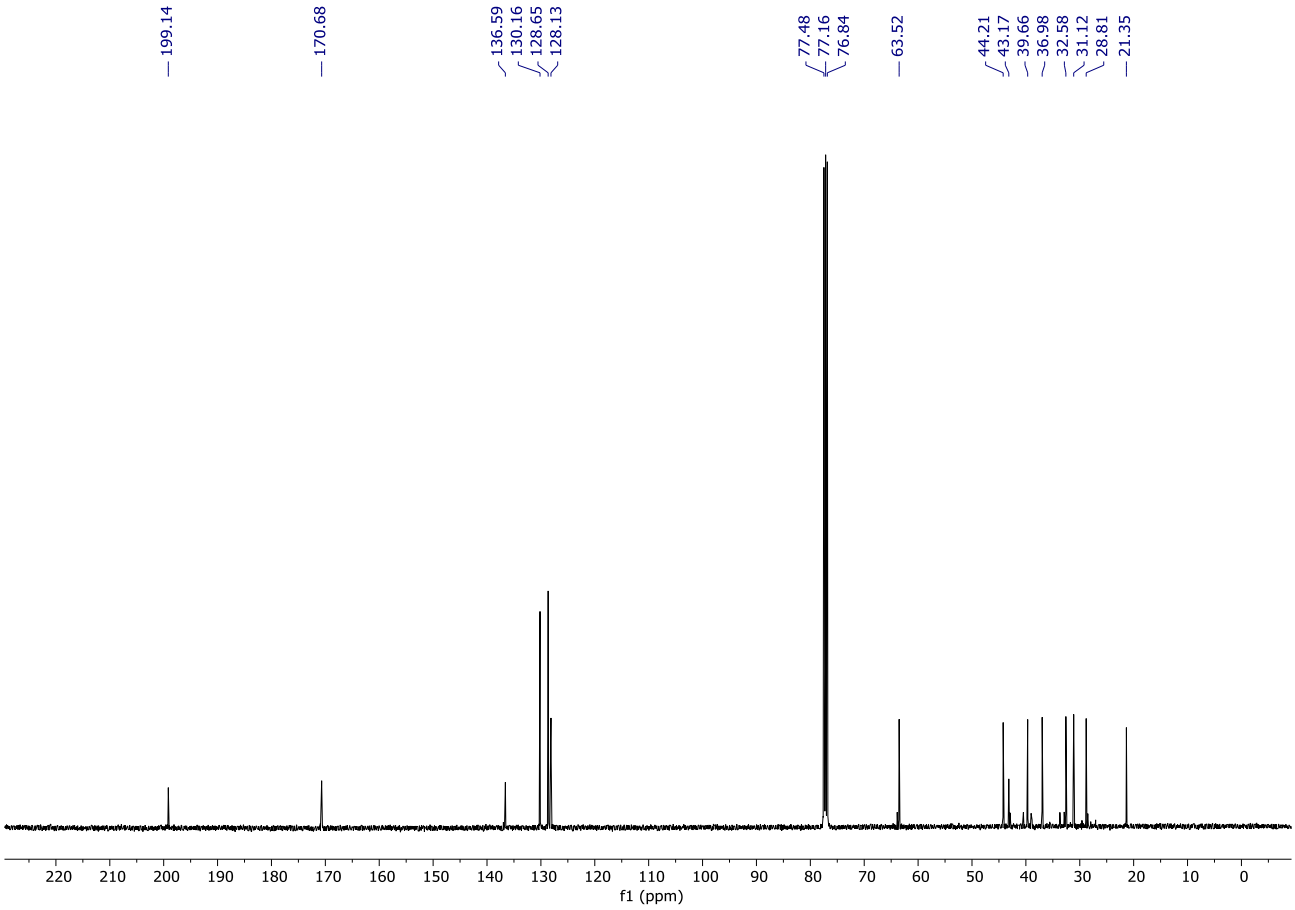

199.04
161.78
136.51
134.25
133.34
133.10
130.33
130.17
128.67
128.16
77.48
77.16
76.84
64.53
44.12
43.28
39.76
36.98
32.68
31.14
28.90
f1 (ppm)

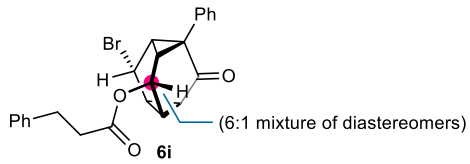


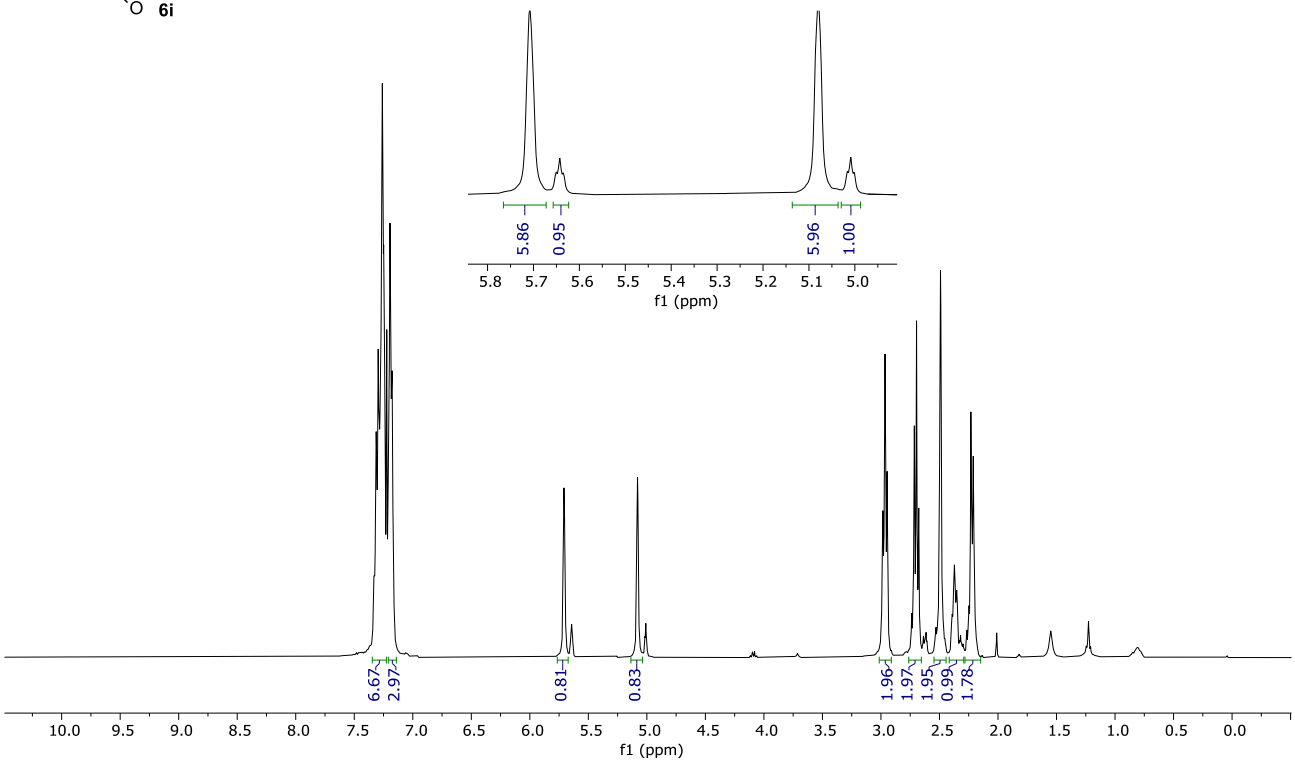
(7.5:1 mixture of diastereomers)

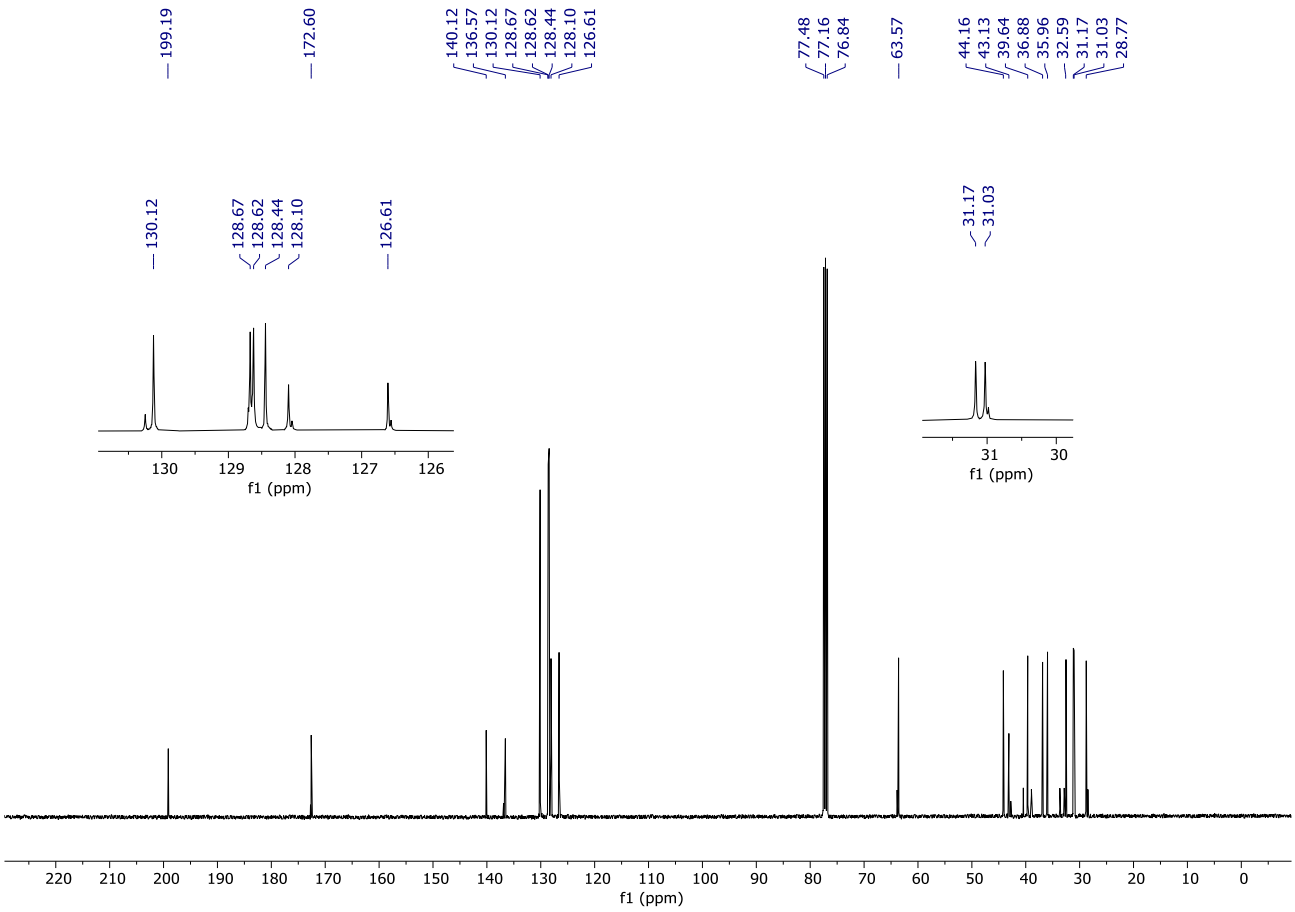
6h

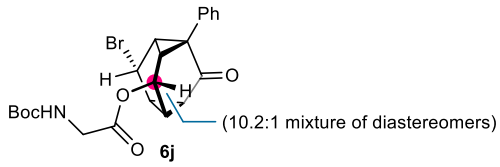




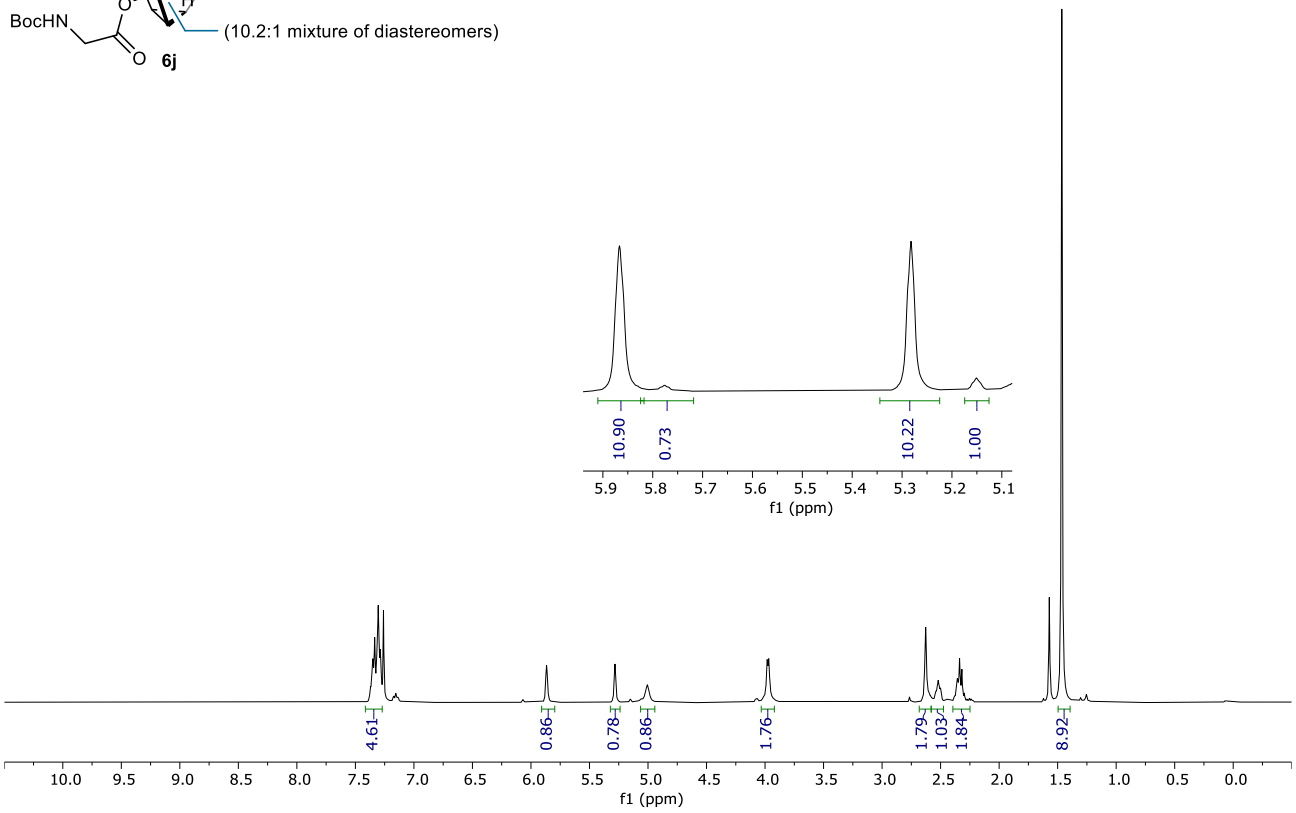

Ph
Br
H
O
O
H
Ph
O
(6:1 mixture of diastereomers)
6i

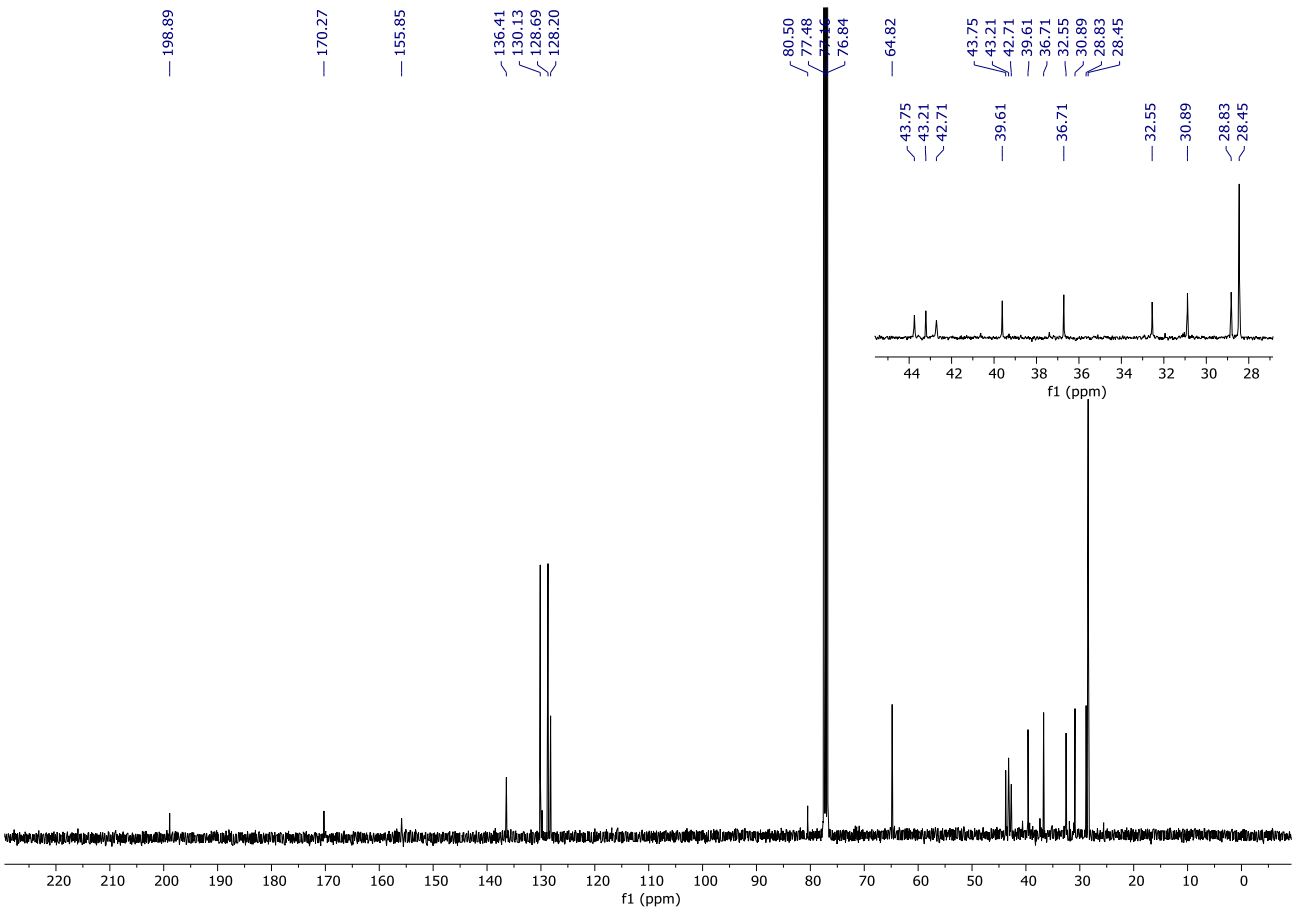

5.86
0.95
5.96
1.00
f1 (ppm)
6.67
2.97
0.81
0.83
1.96
1.97
1.95
0.99
1.78
f1 (ppm)

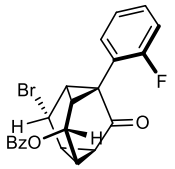

199.19
172.60
140.12
136.57
130.12
128.67
128.62
128.44
128.10
126.61
77.48
77.16
76.84
63.57
44.16
43.13
39.64
36.88
35.96
32.59
31.17
31.03
28.77
130.12
128.67
128.62
128.44
128.10
126.61
f1 (ppm)
31.17
31.03
f1 (ppm)
f1 (ppm)


Ph
Br
H
O
O
H
BocHN
O
(10.2:1 mixture of diastereomers)

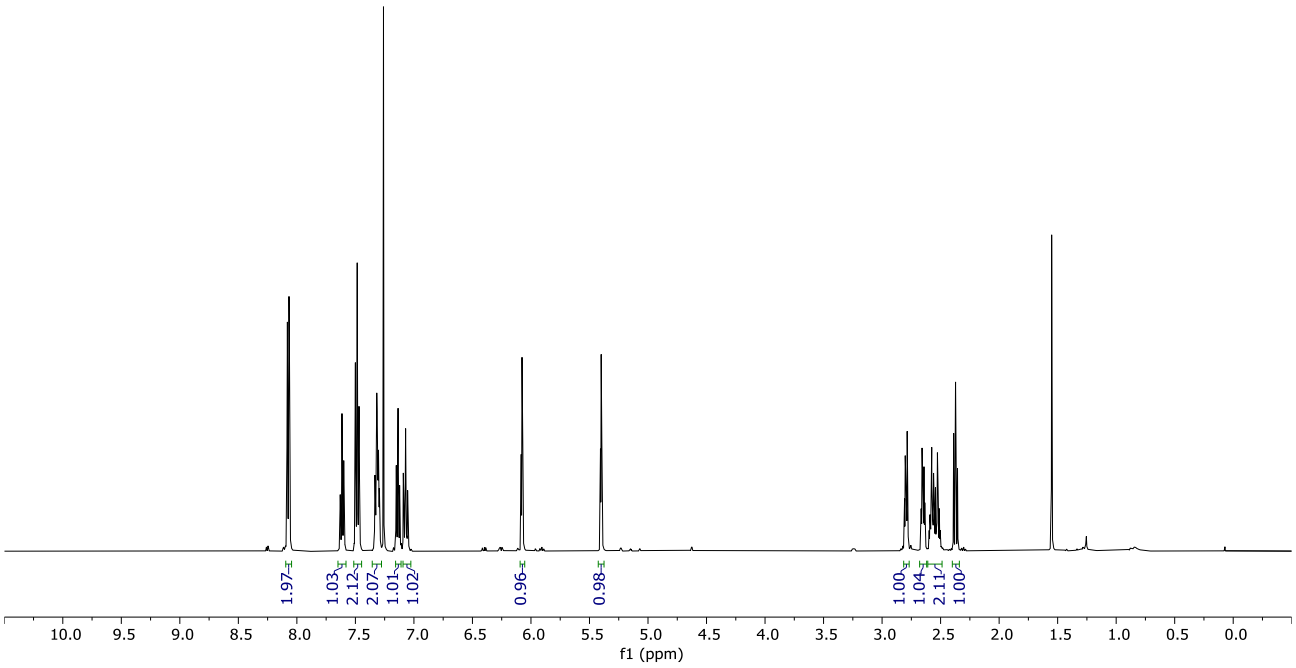
6j

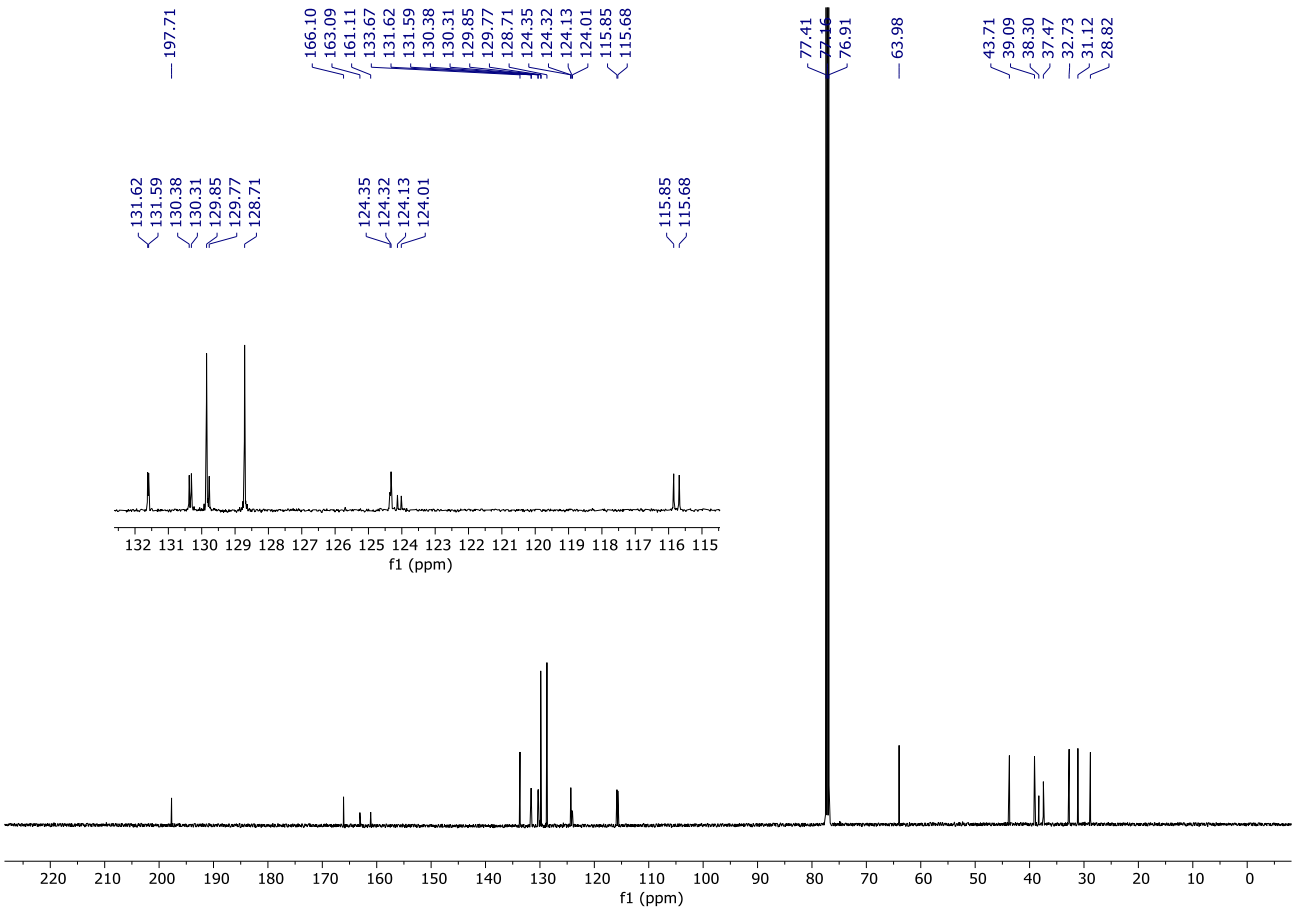

10.90
0.73
10.22
1.00
f1 (ppm)
4.61
0.86
0.78
0.86
1.76
1.79
1.03
1.84
8.92
f1 (ppm)

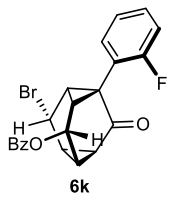

198.89
170.27
155.85
136.41
130.13
128.69
128.20
80.50
77.48
77.16
76.84
64.82
43.75
43.21
42.71
39.61
36.71
32.55
30.89
28.83
28.45
f1 (ppm)
f1 (ppm)


Br
F
H
O
BzO
H

6k

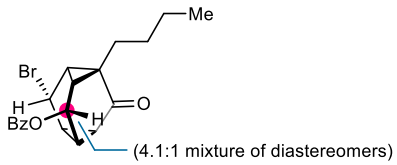

1.97
1.03
2.12
2.07
1.01
1.02
0.96
0.98
1.00
1.04
2.11
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


197.71
166.10
163.09
161.11
133.67
131.62
131.59
130.38
130.31
129.85
129.77
128.71
124.35
124.32
124.13
124.01
115.85
115.68
77.41
77.16
76.91
63.98
43.71
39.09
38.30
37.47
32.73
31.12
28.82
132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Br
H
BzO
H
O
F

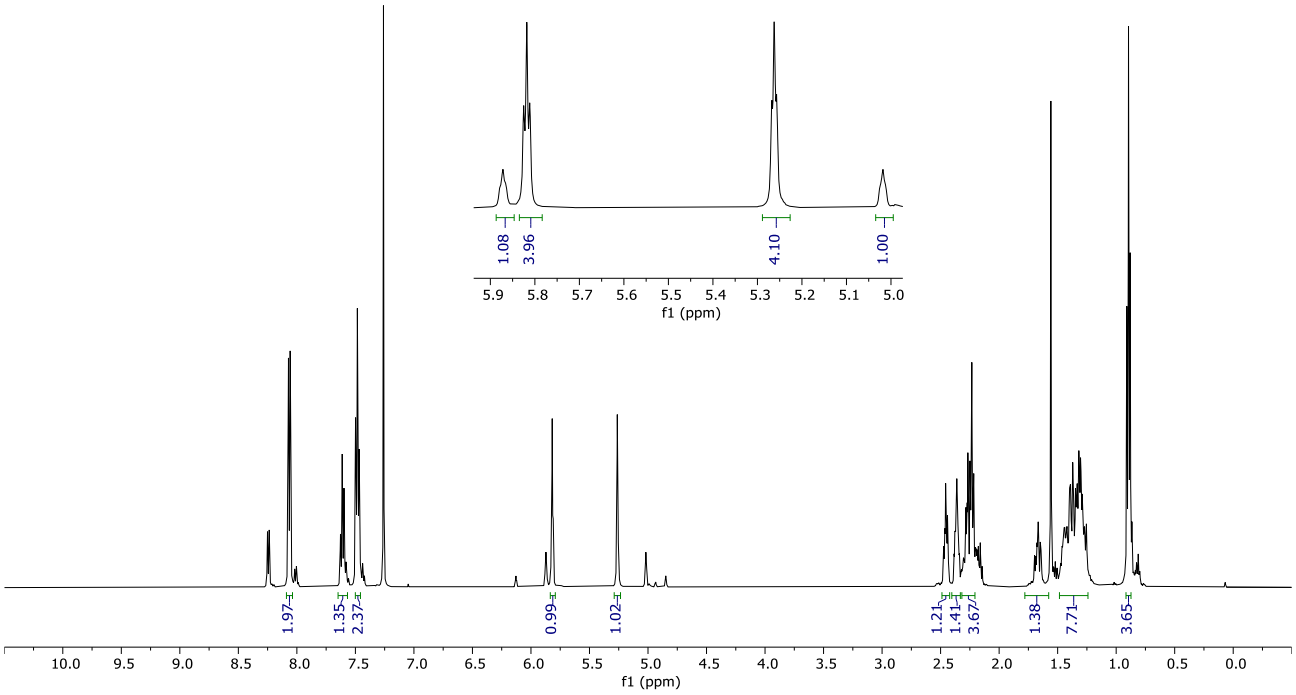
6k

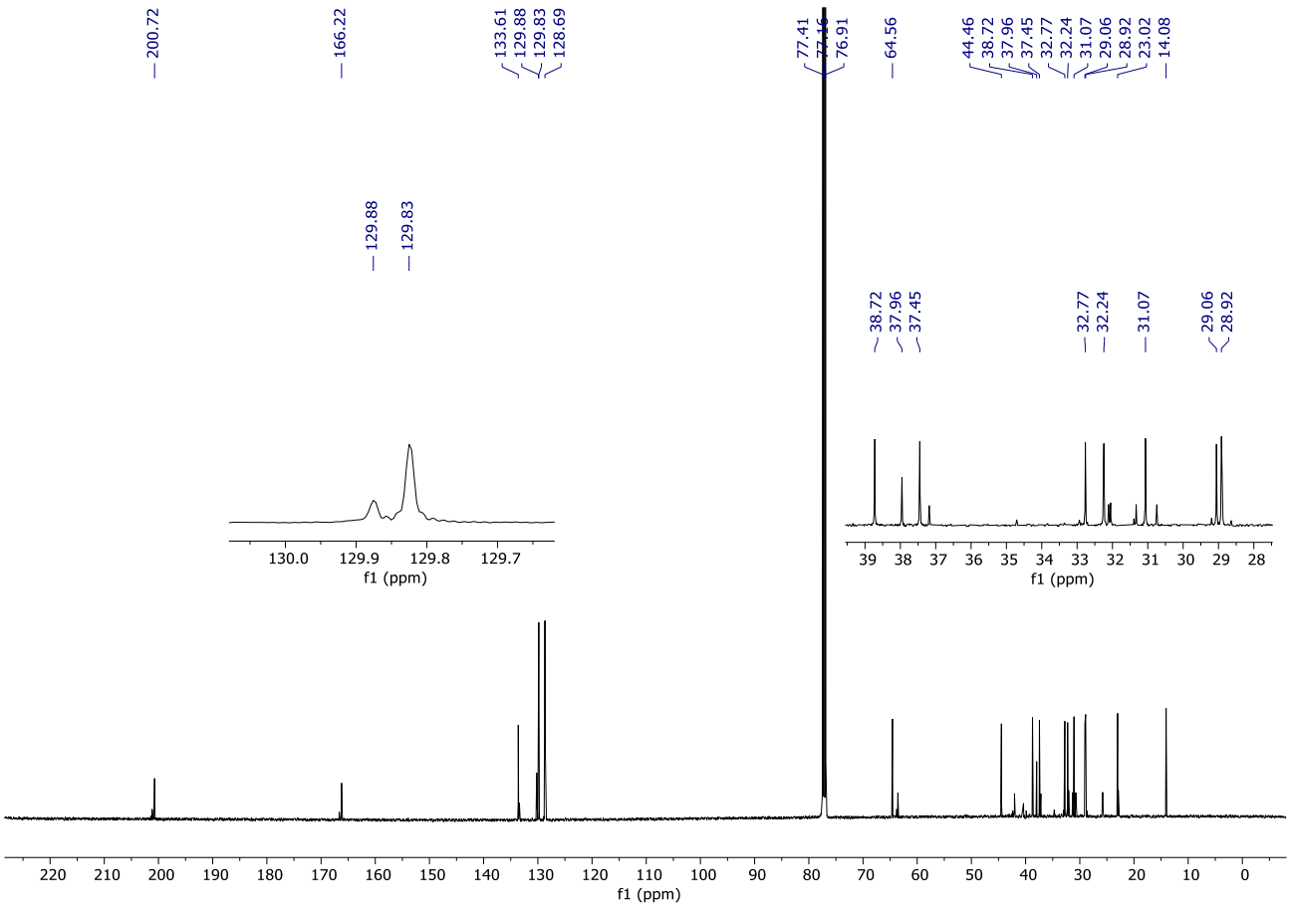
-114.18
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

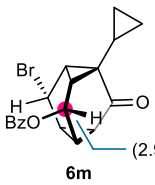


(4.1:1 mixture of diastereomers)

6l

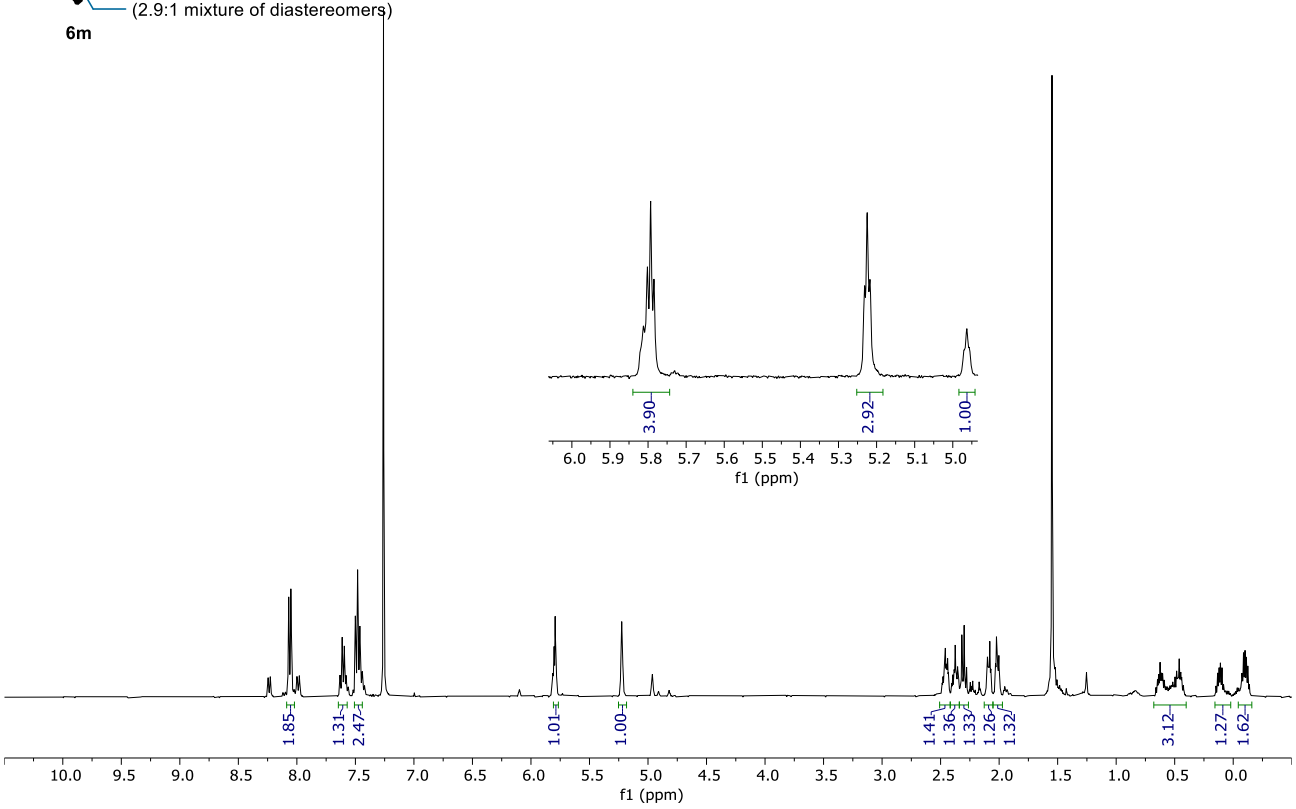


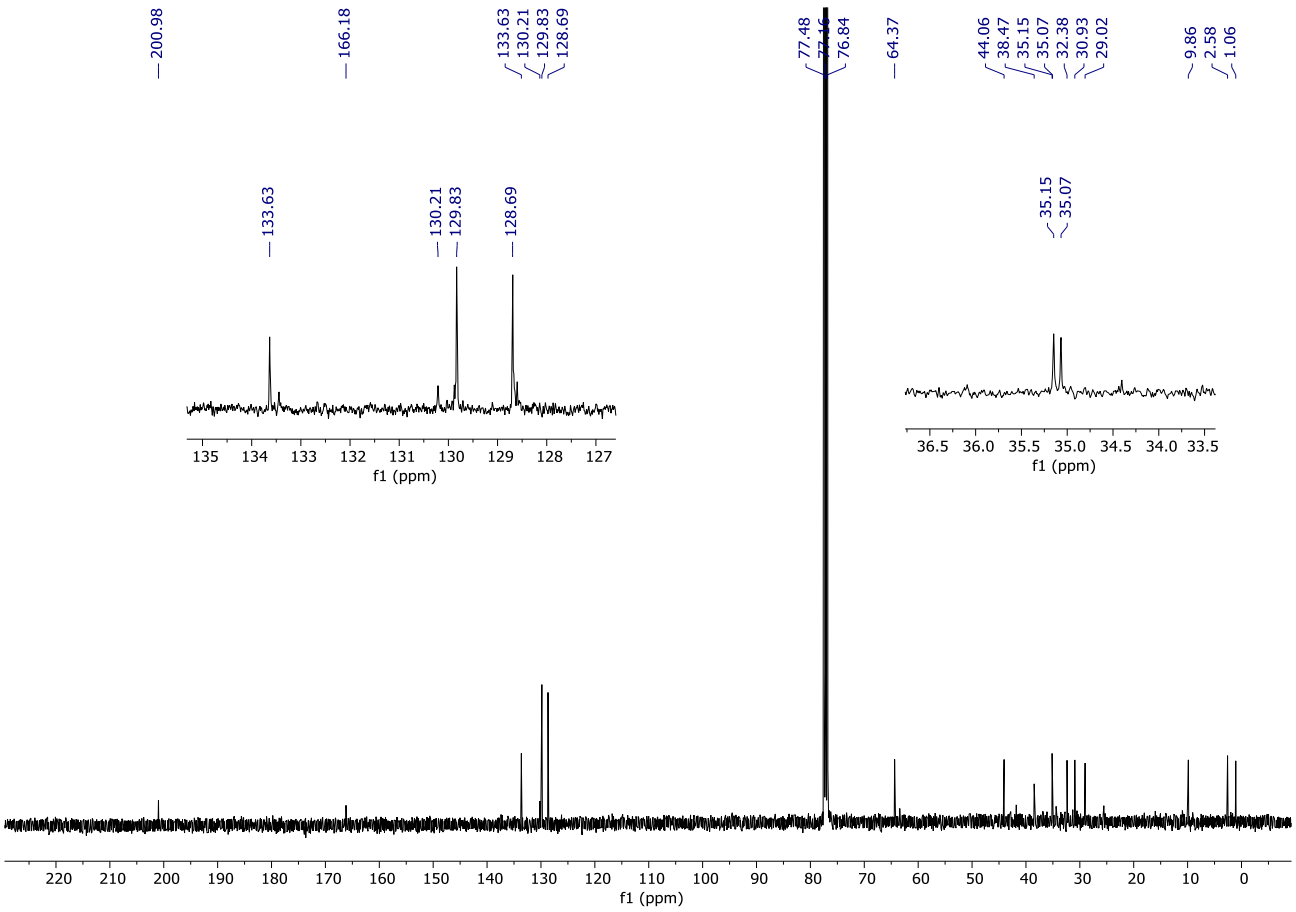


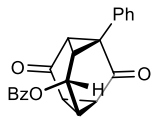


(2.9:1 mixture of diastereomers)

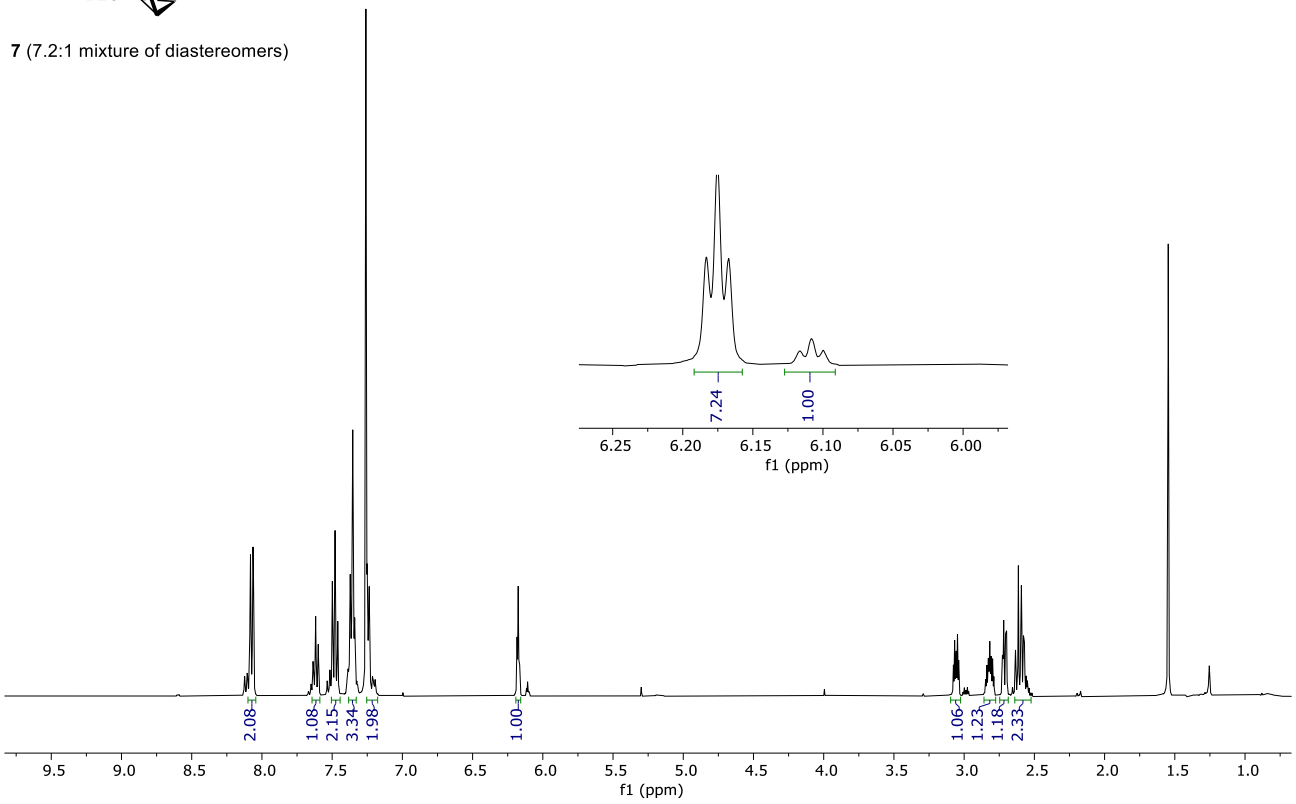
6m

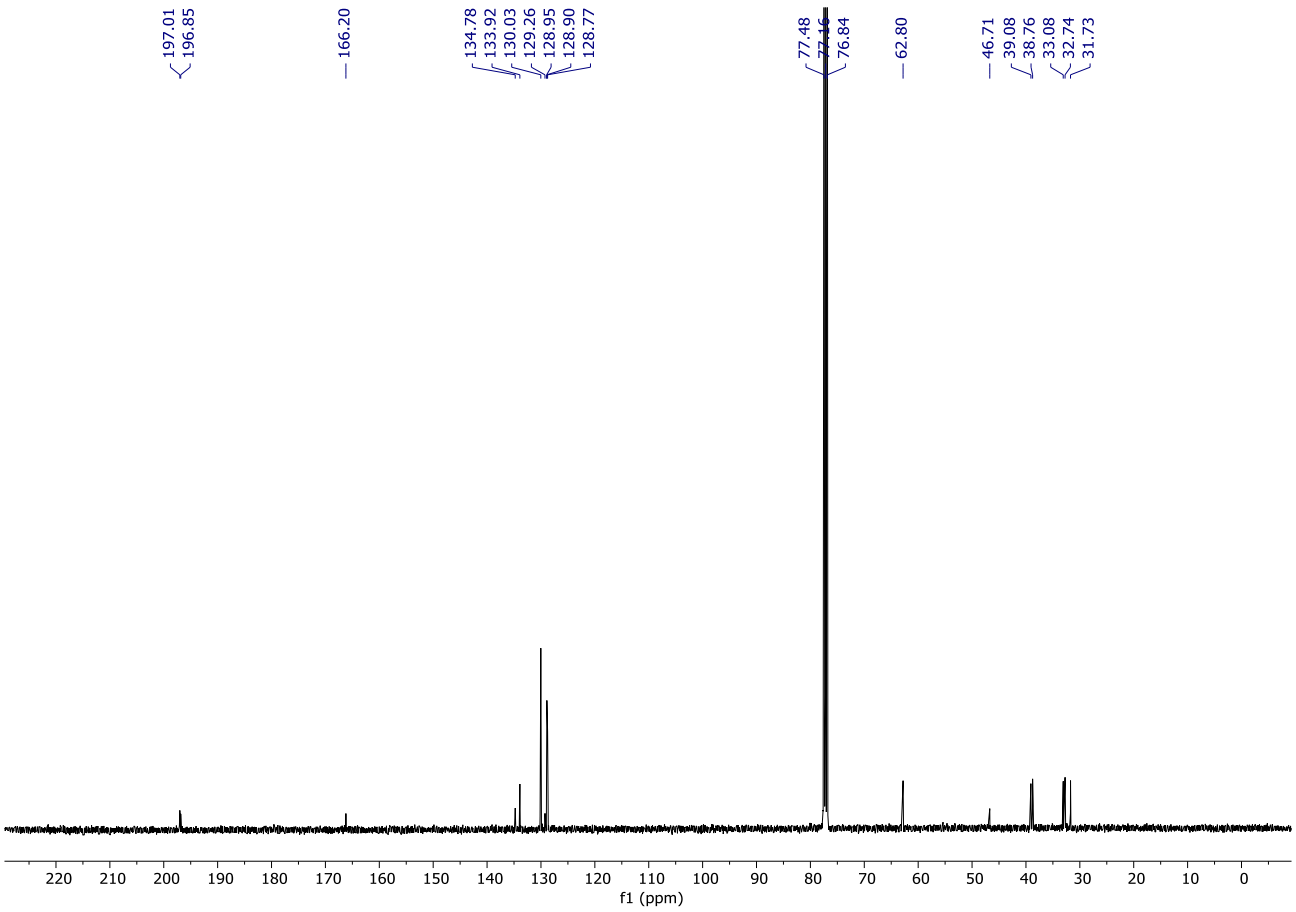


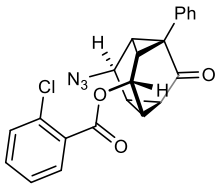




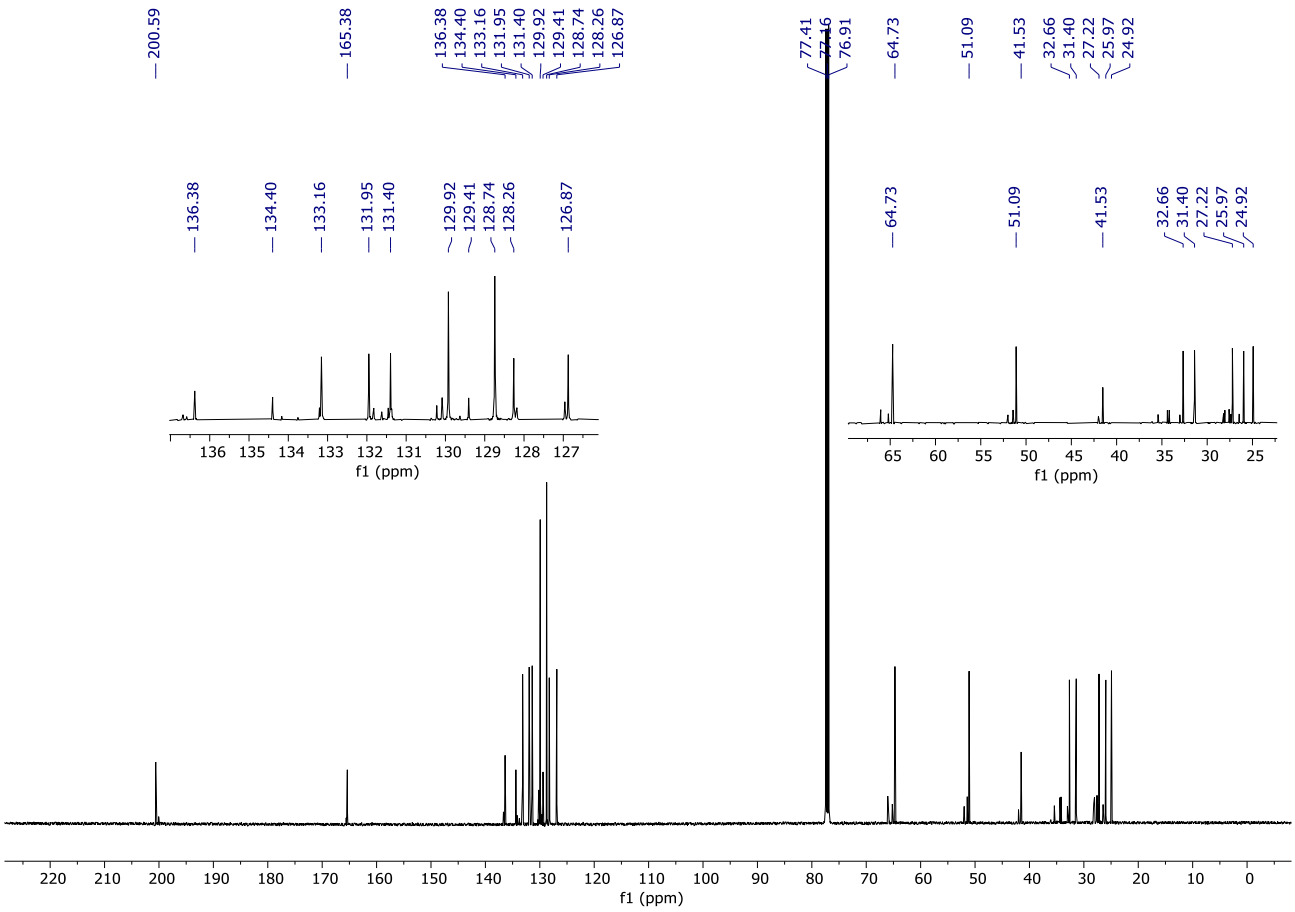
7 (7.2:1 mixture of diastereomers)

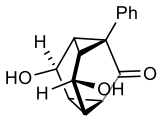




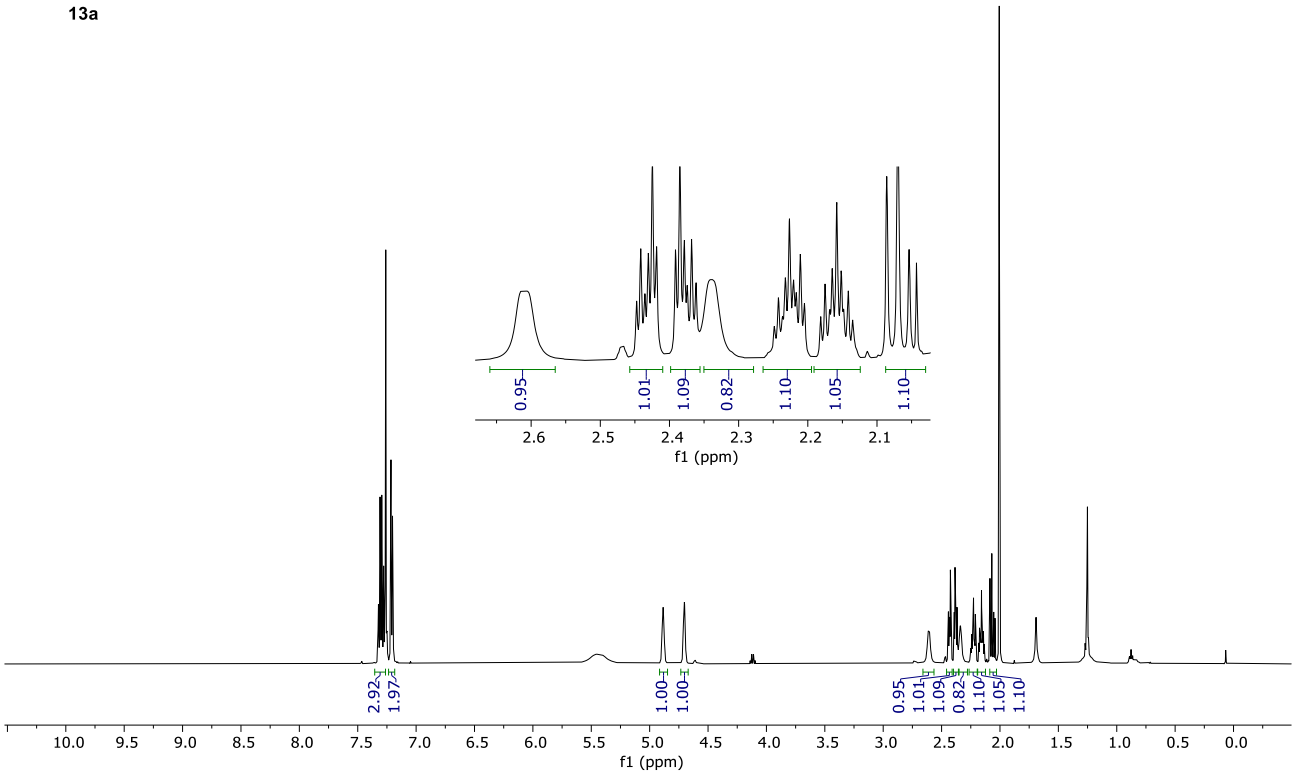


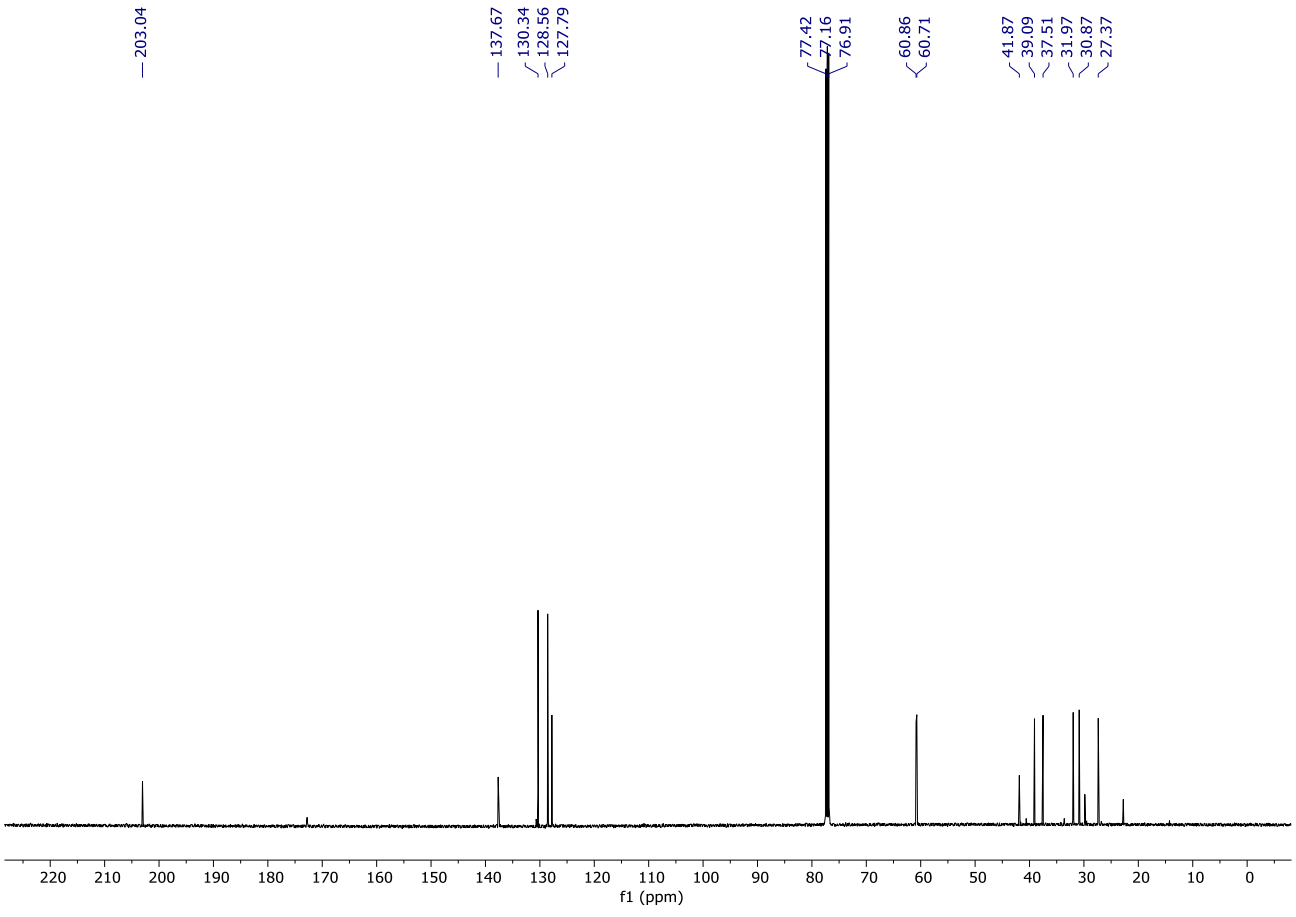
8 (74:16:10 mixture of diastereomers)

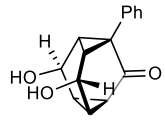



Ph
H
HO
H
OH
O

13a

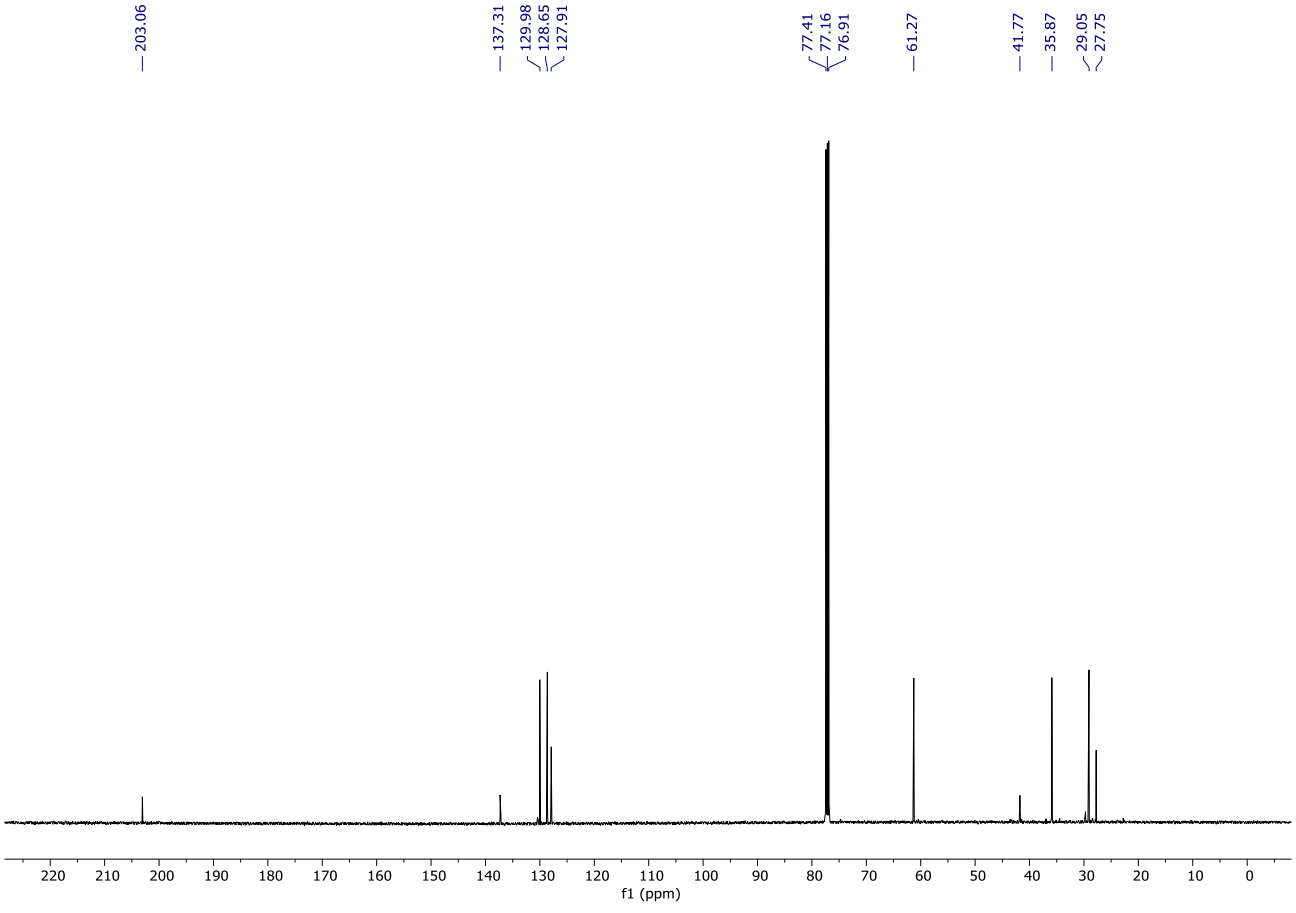

0.95
1.01
1.09
0.82
1.10
1.05
1.10
f1 (ppm)
2.92
1.97
1.00
1.00
0.95
1.01
1.09
0.82
1.10
1.05
1.10
f1 (ppm)

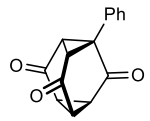

203.04
137.67
130.34
128.56
127.79
77.42
77.16
76.91
60.86
60.71
41.87
39.09
37.51
31.97
30.87
27.37
f1 (ppm)


Ph
H
HO
HO
H
O

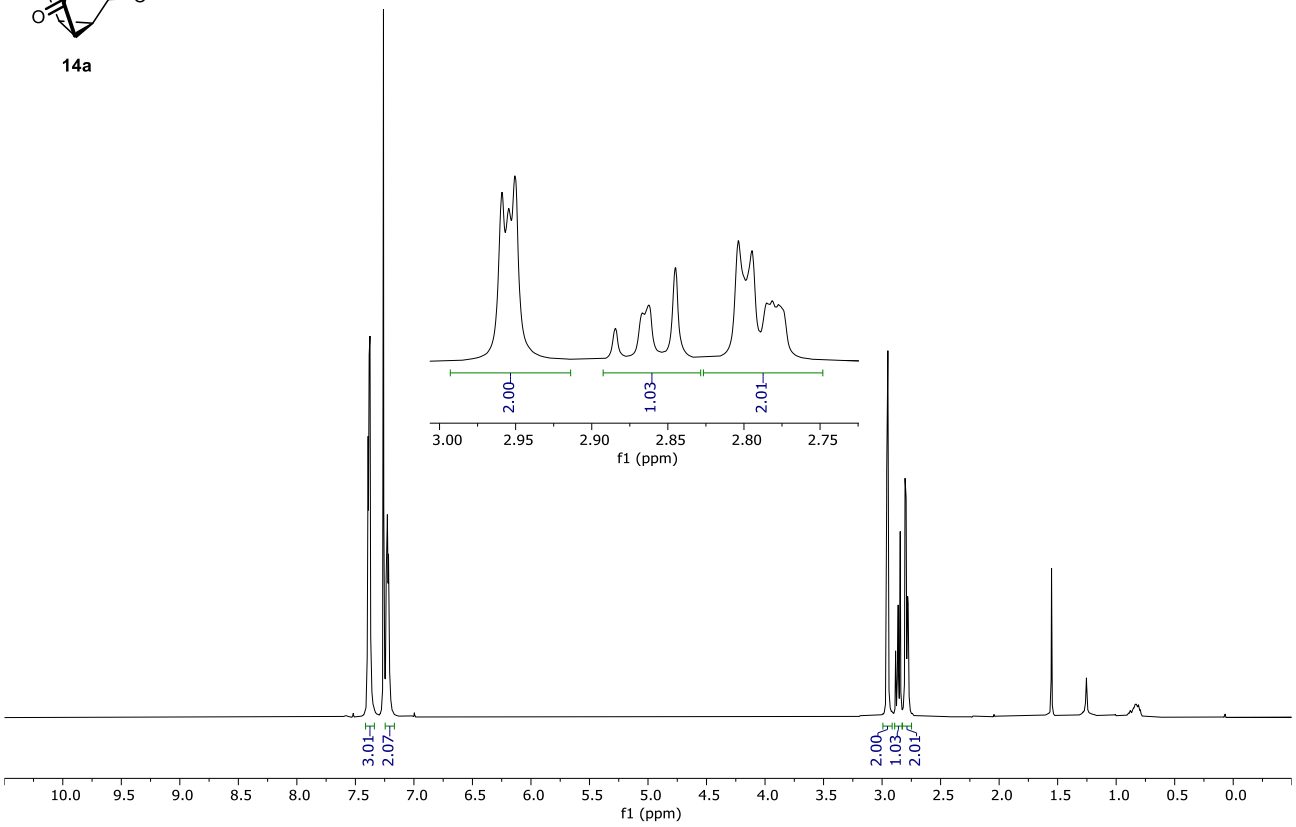
13a'

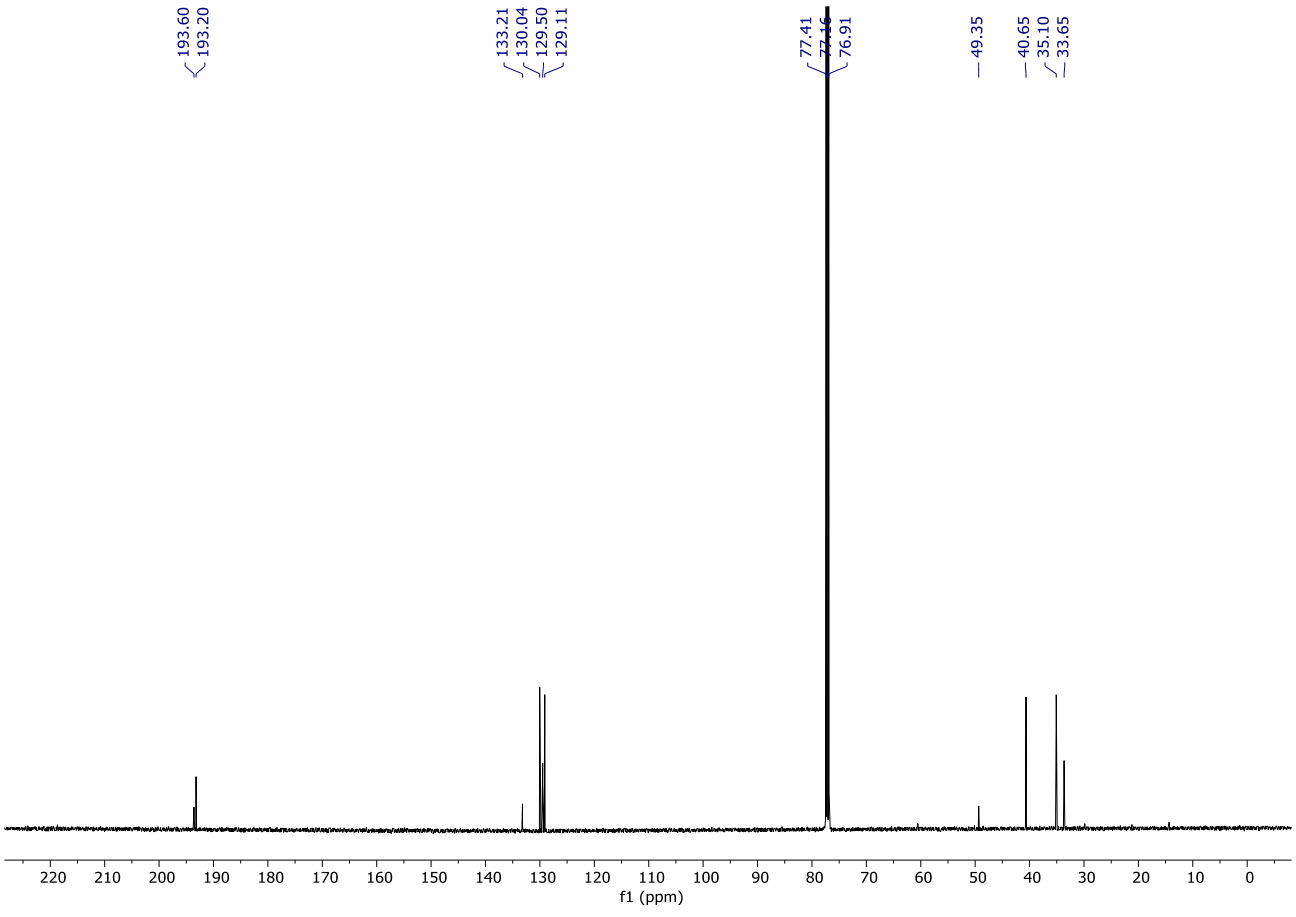
3.10
1.96
1.96
1.91
2.02
1.97
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

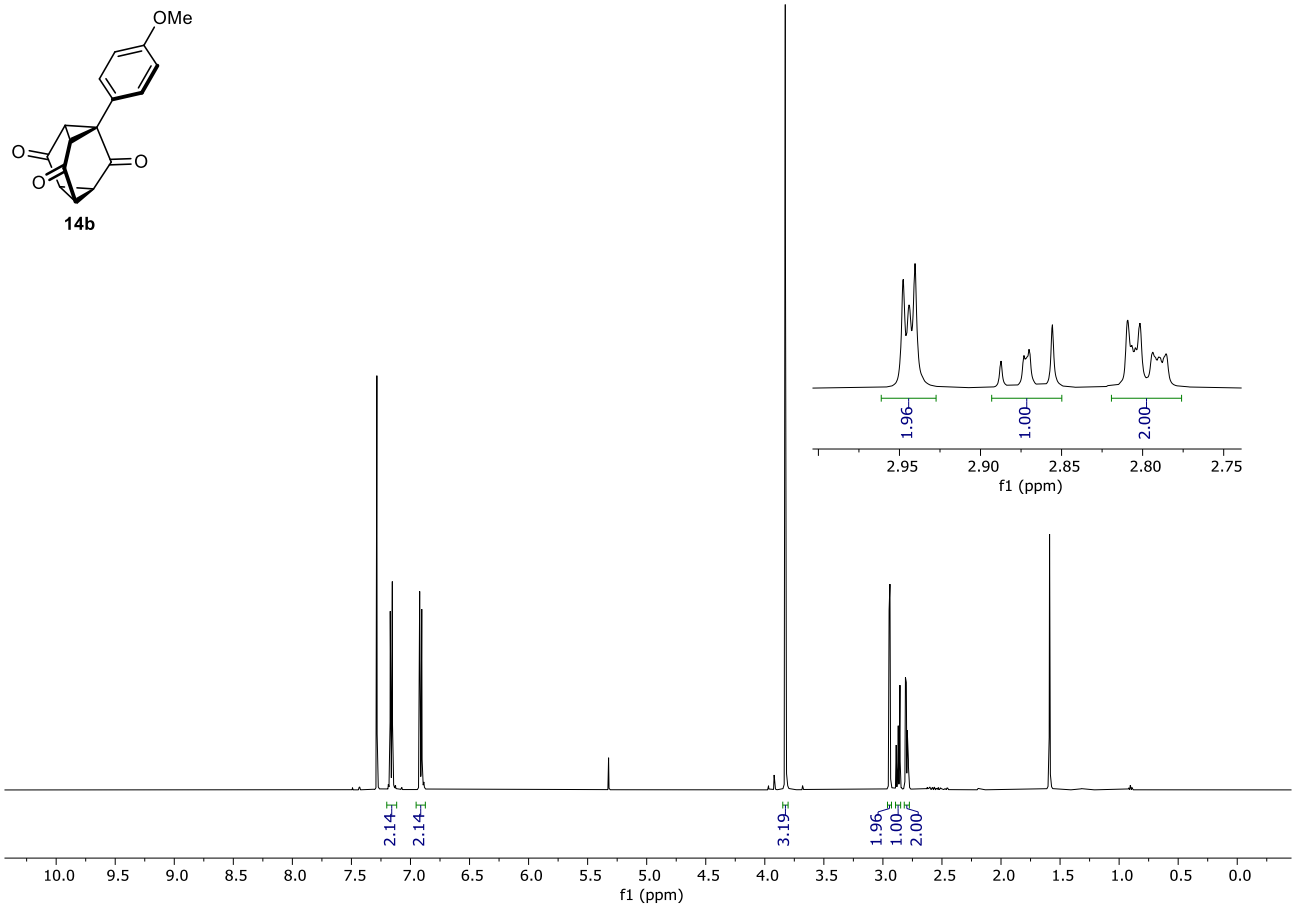

203.06
137.31
129.98
128.65
127.91
77.41
77.16
76.91
61.27
41.77
35.87
29.05
27.75
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

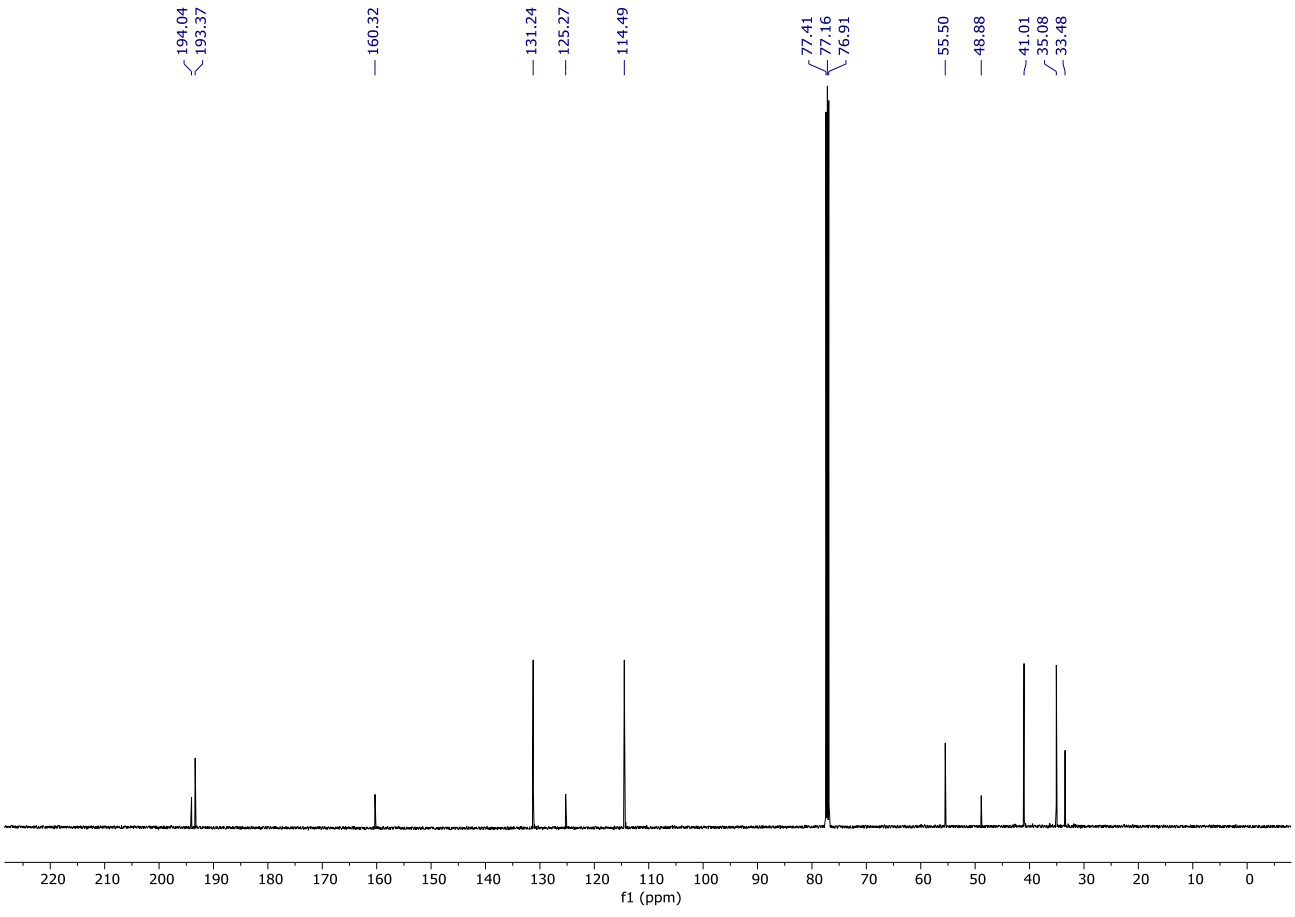

Ph
O
O
O

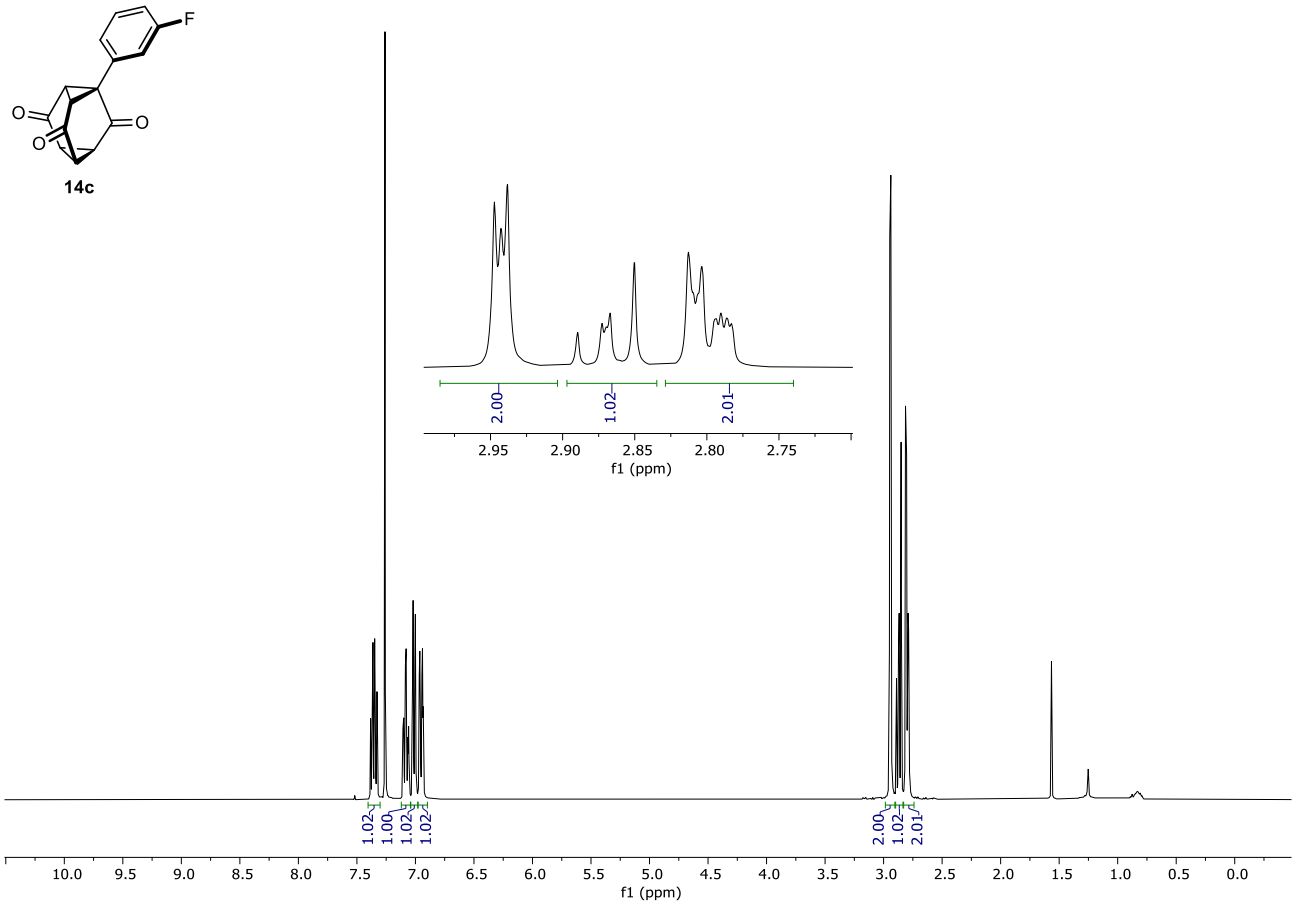
14a

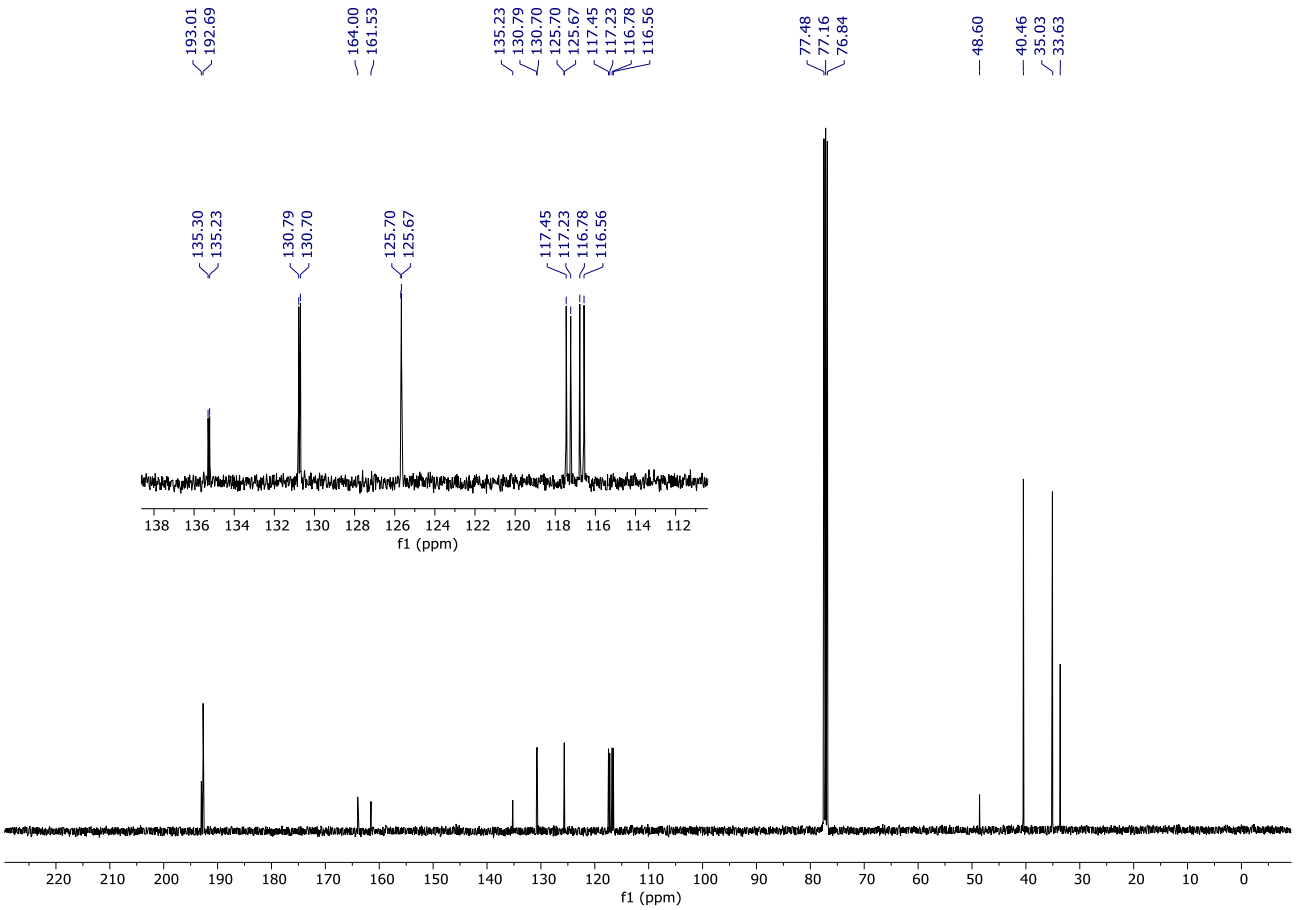

2.00
1.03
2.01
3.00 2.95 2.90 2.85 2.80 2.75
f1 (ppm)
3.01
2.07
2.00
1.03
2.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

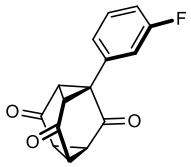

193.60
193.20
133.21
130.04
129.50
129.11
77.41
77.16
76.91
49.35
40.65
35.10
33.65
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OMe
O
O
O
14b
1.96
1.00
2.00
2.95
2.90
2.85
2.80
2.75
f1 (ppm)
2.14
2.14
3.19
1.96
1.00
2.00
10.0
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)


194.04
193.37
160.32
131.24
125.27
114.49
77.41
77.16
76.91
55.50
48.88
41.01
35.08
33.48
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

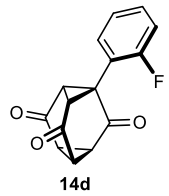

F
O
O
O
14c
2.00
1.02
2.01
2.95 2.90 2.85 2.80 2.75
f1 (ppm)
1.02
1.00
1.02
1.02
2.00
1.02
2.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


193.01
192.69
164.00
161.53
135.23
130.79
130.70
125.70
125.67
117.45
117.23
116.78
116.56
77.48
77.16
76.84
48.60
40.46
35.03
33.63
135.30
135.23
130.79
130.70
125.70
125.67
117.45
117.23
116.78
116.56
138 136 134 132 130 128 126 124 122 120 118 116 114 112
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

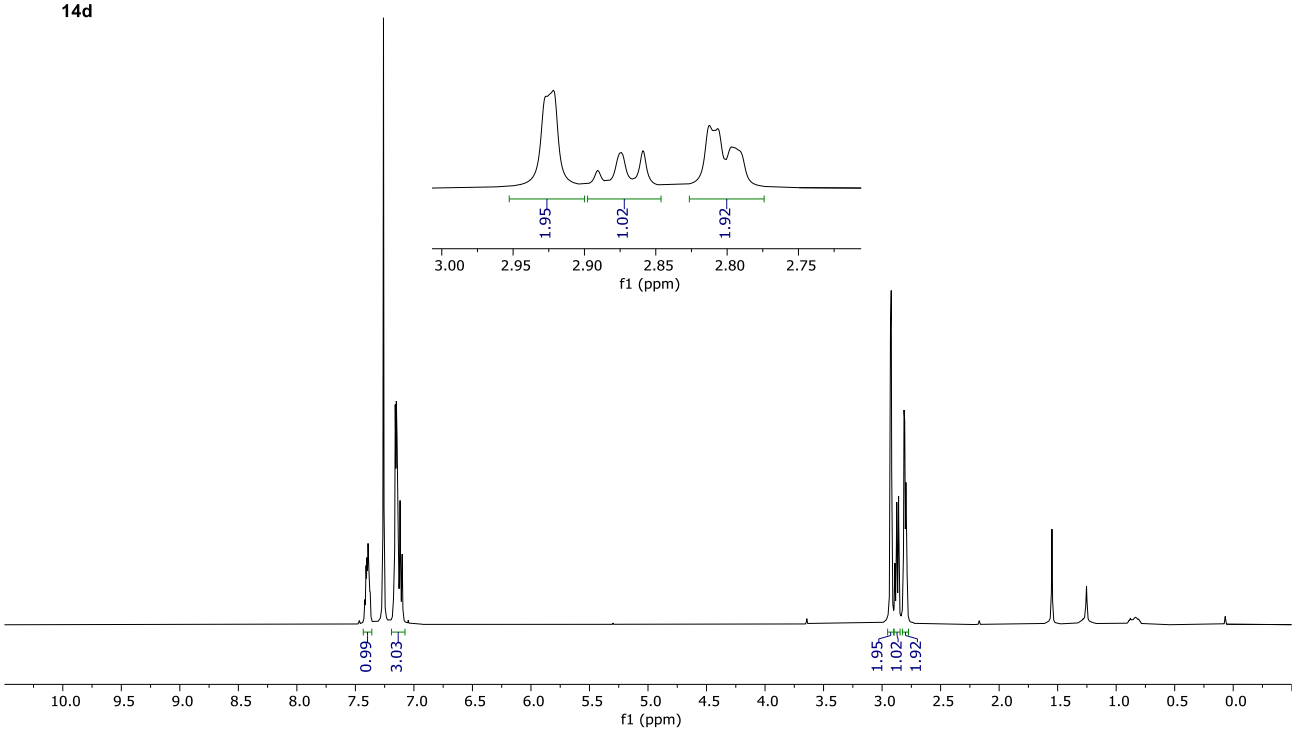

F
O
O
O

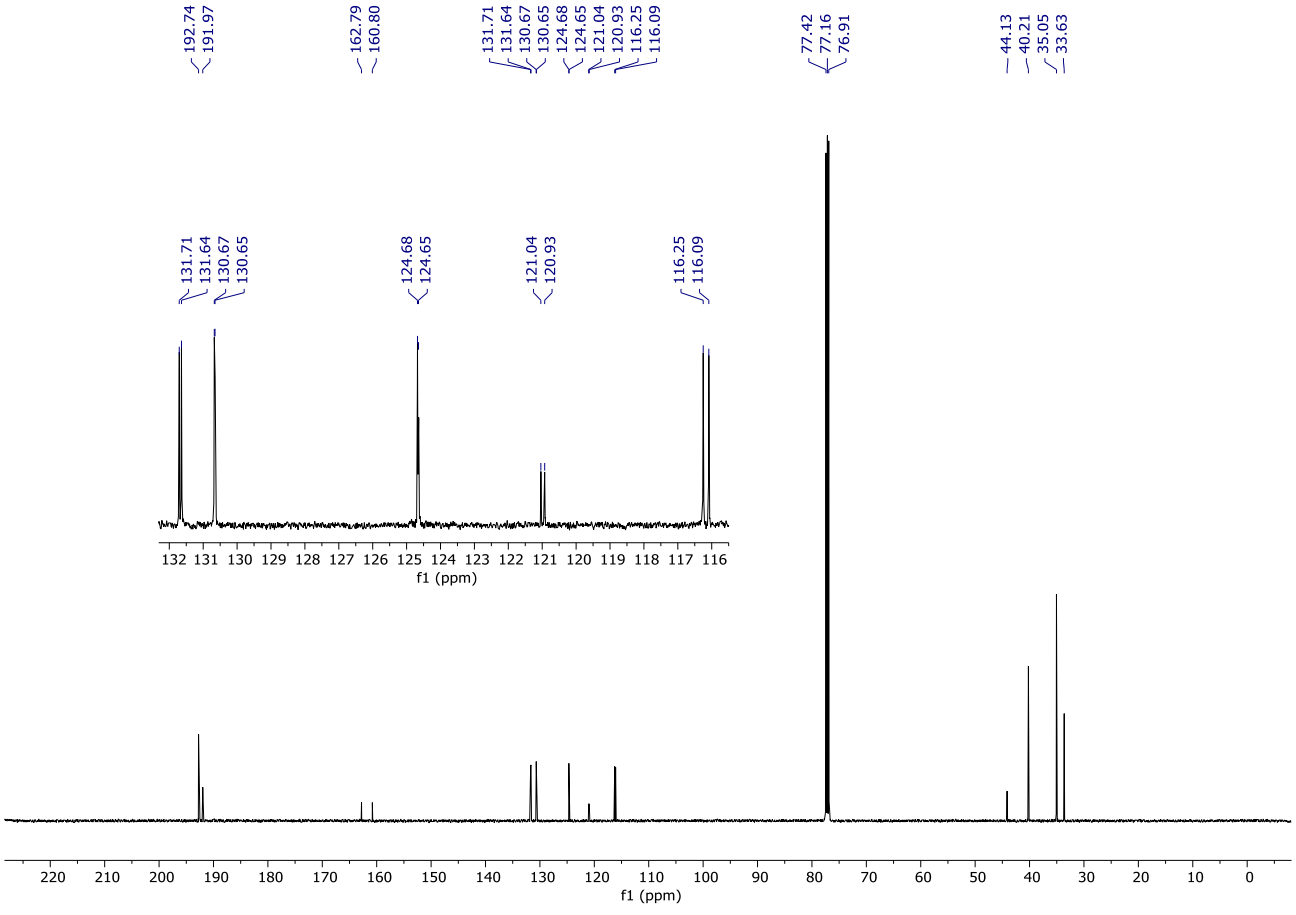
14c

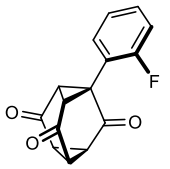
-111.45
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


F
O
O
O

14d

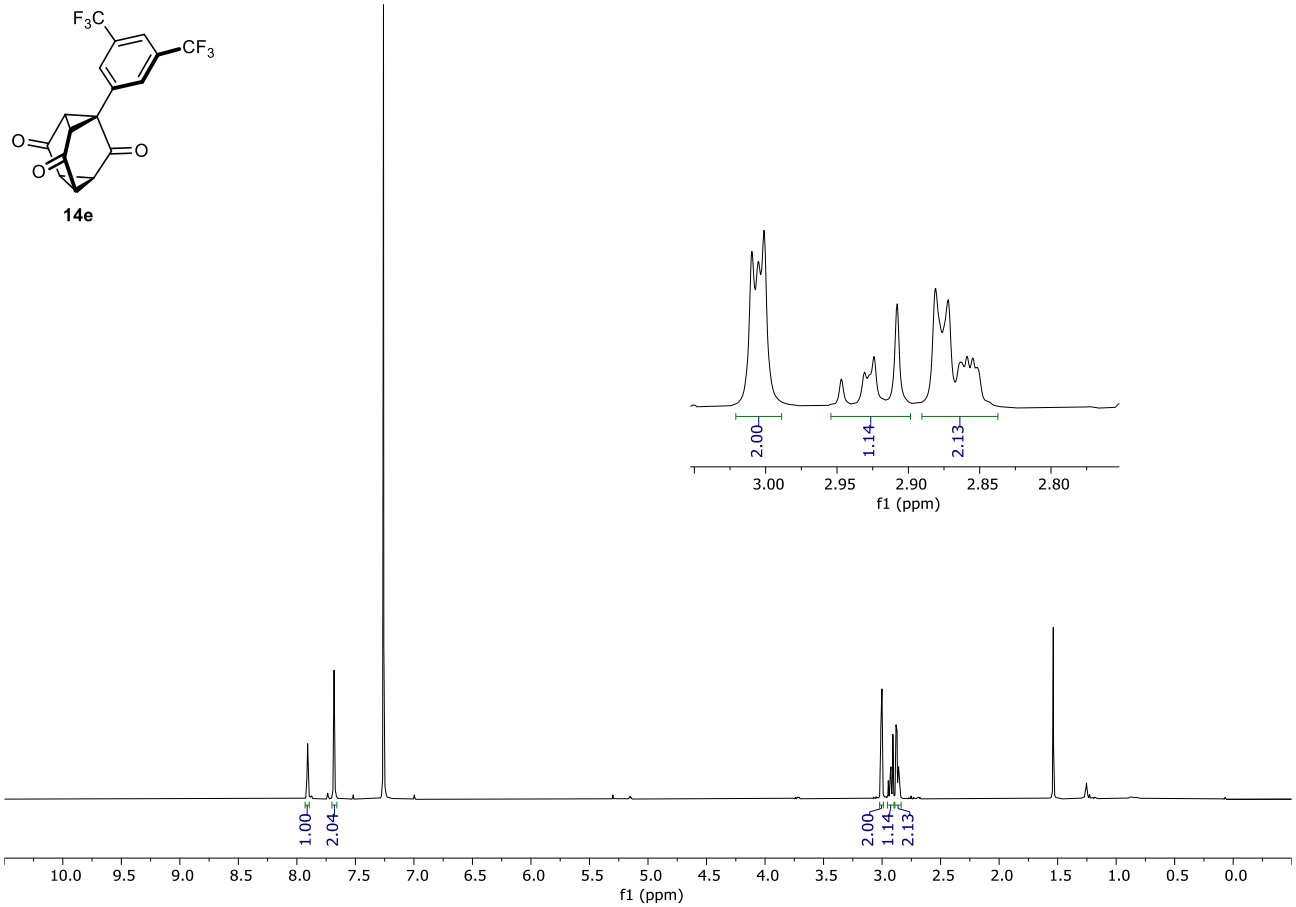

1.95
1.02
1.92
3.00 2.95 2.90 2.85 2.80 2.75
f1 (ppm)
0.99
3.03
1.95
1.02
1.92
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

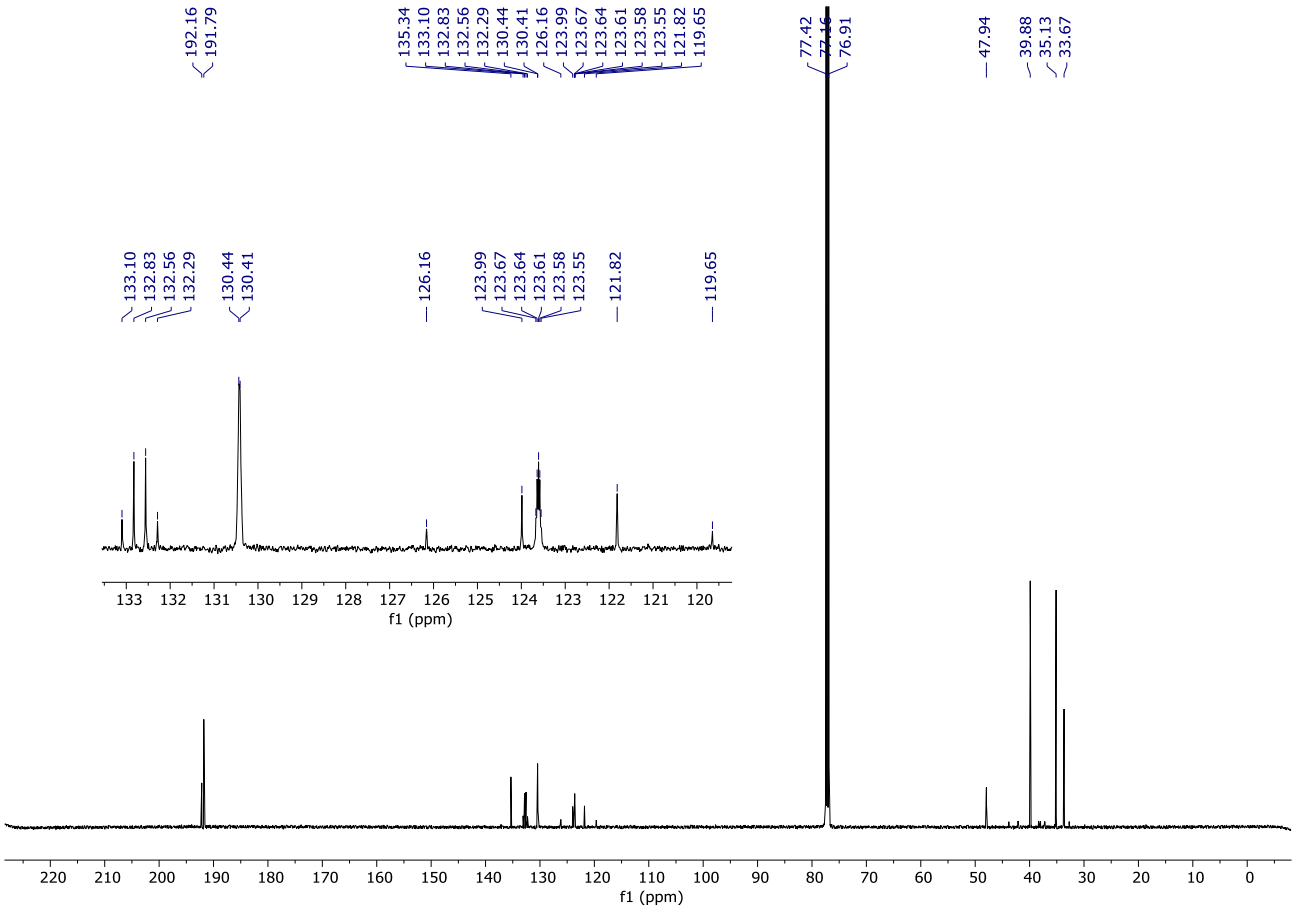

192.74
191.97
162.79
160.80
131.71
131.64
130.67
130.65
124.68
124.65
121.04
120.93
116.25
116.09
77.42
77.16
76.91
44.13
40.21
35.05
33.63
131.71
131.64
130.67
130.65
124.68
124.65
121.04
120.93
116.25
116.09
132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

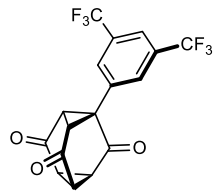

F
O
O
O

14d

-113.51
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

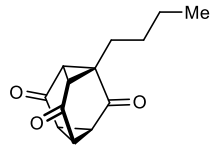

F3C
CF3
O
O
O
14e
2.00
1.14
2.13
3.00 2.95 2.90 2.85 2.80
f1 (ppm)
1.00
2.04
2.00
1.14
2.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


192.16
191.79
135.34
133.10
132.83
132.56
132.29
130.44
130.41
126.16
123.99
123.67
123.64
123.61
123.58
123.55
121.82
119.65
77.42
77.16
76.91
47.94
39.88
35.13
33.67
133 132 131 130 129 128 127 126 125 124 123 122 121 120
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

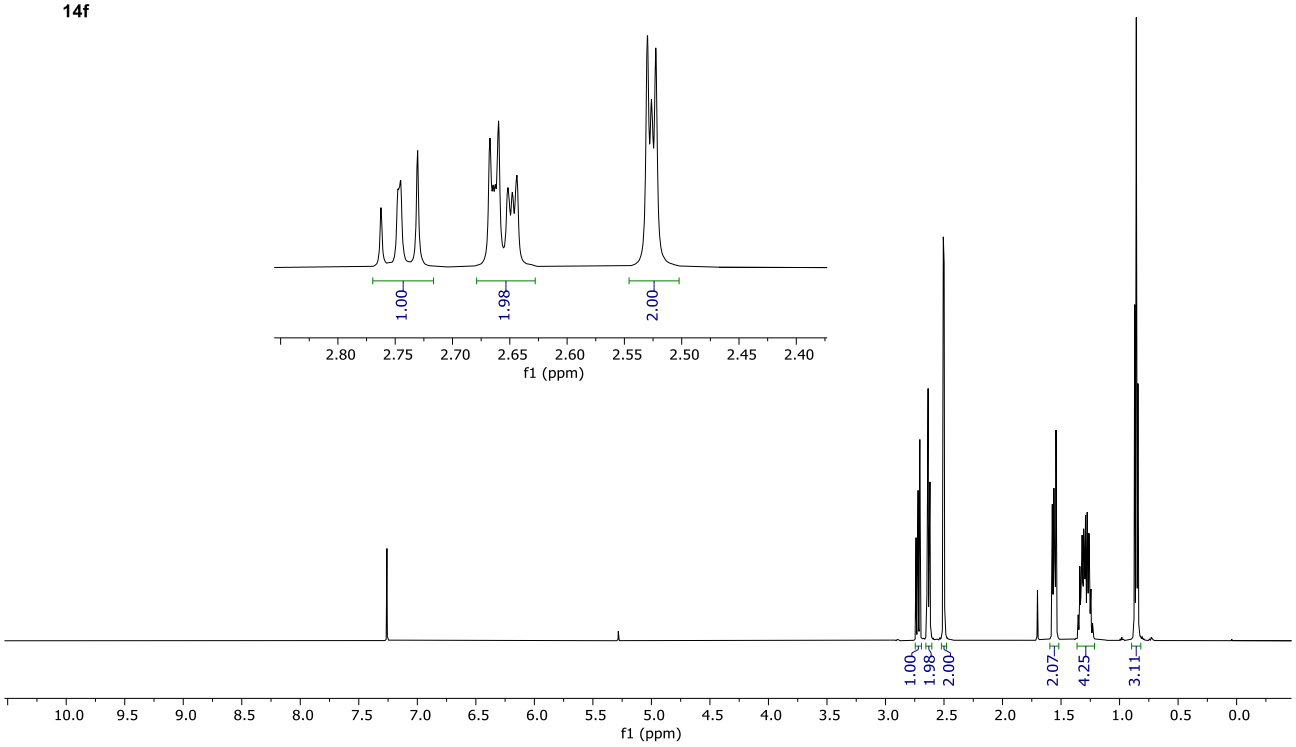

F3C
CF3
O
O
O

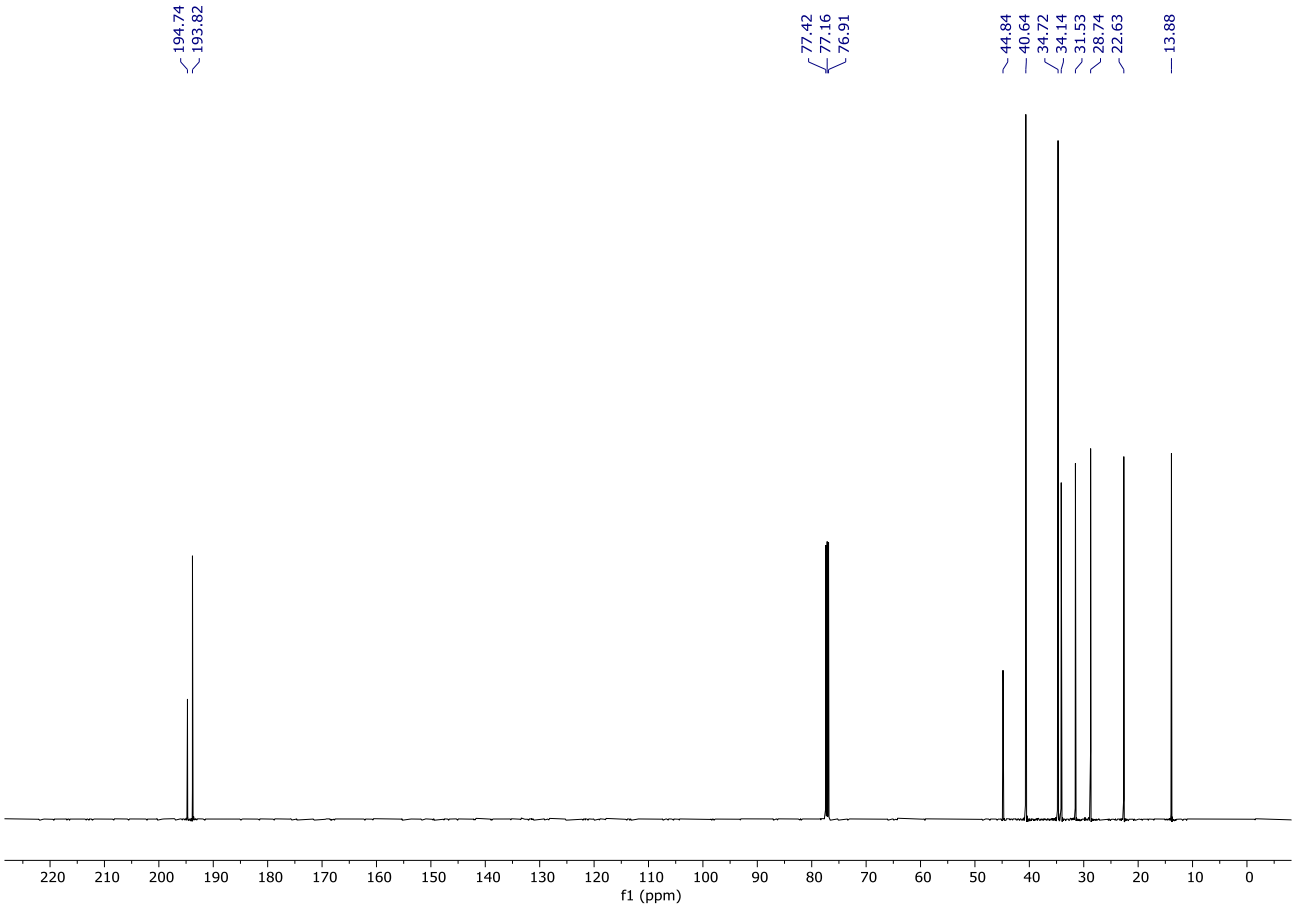
14e

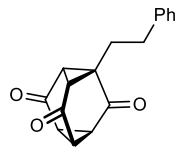
-62.86
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


Me
O
O
O

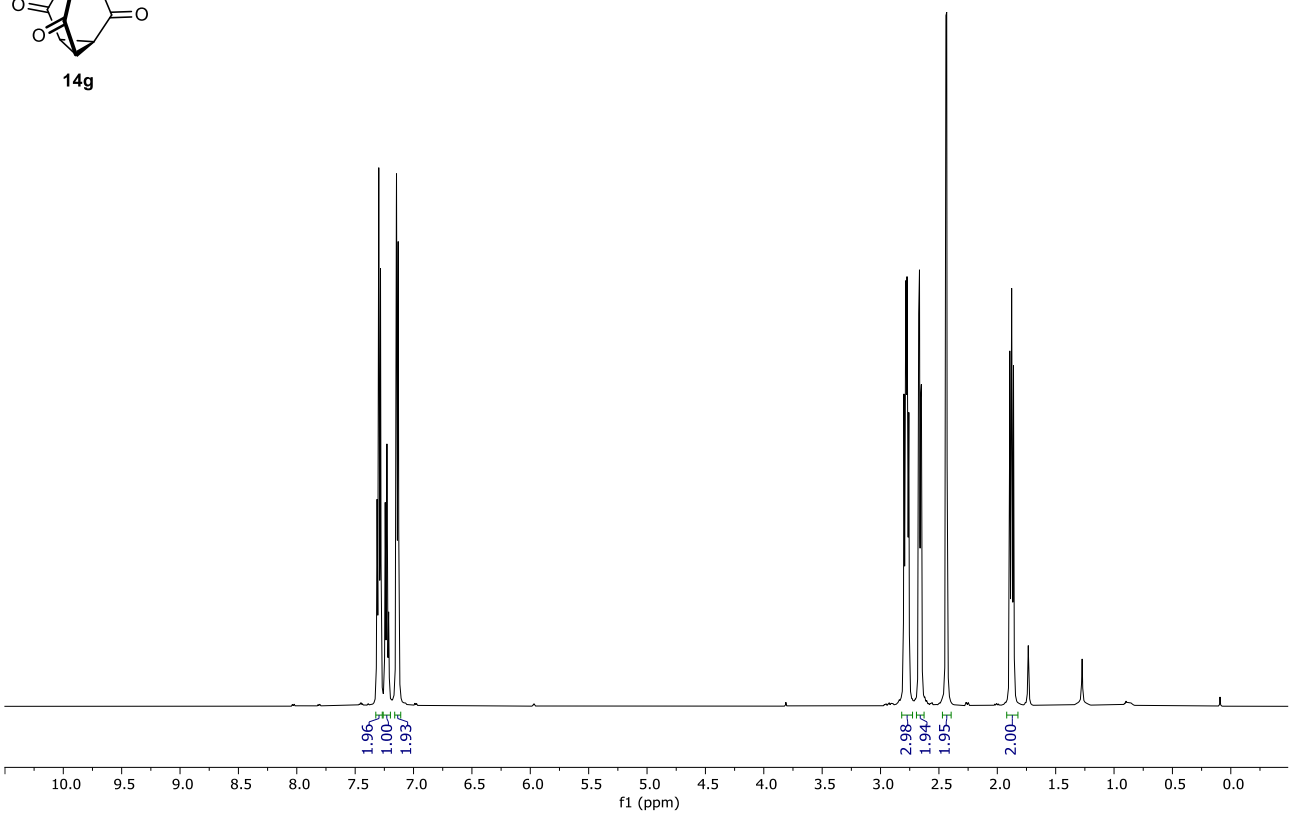
14f

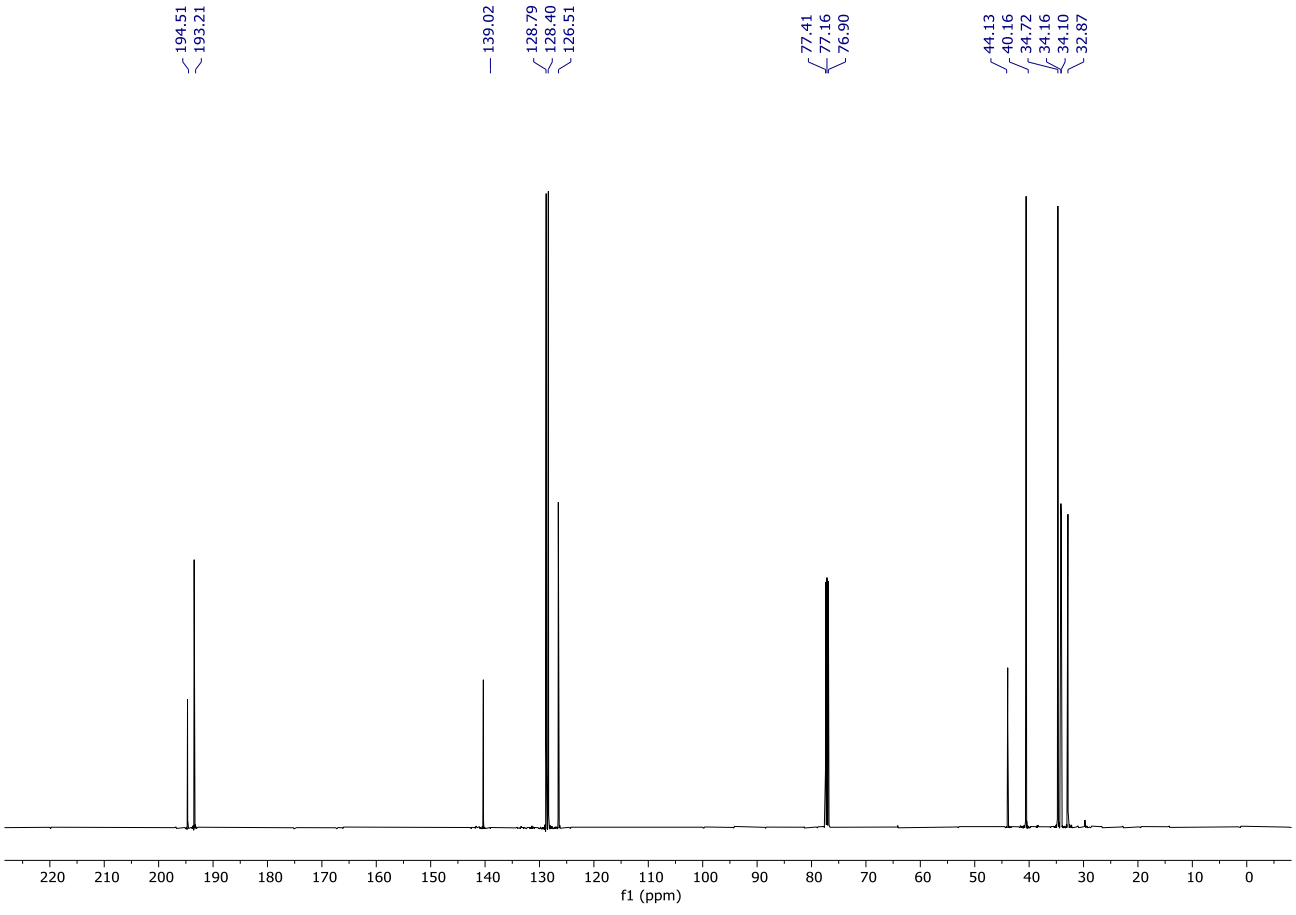

1.00
1.98
2.00
2.80 2.75 2.70 2.65 2.60 2.55 2.50 2.45 2.40
f1 (ppm)
1.00
1.98
2.00
2.07
4.25
3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

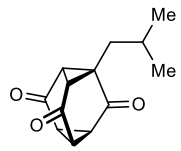

194.74
193.82
77.42
77.16
76.91
44.84
40.64
34.72
34.14
31.53
28.74
22.63
13.88
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
O
O
O

14g

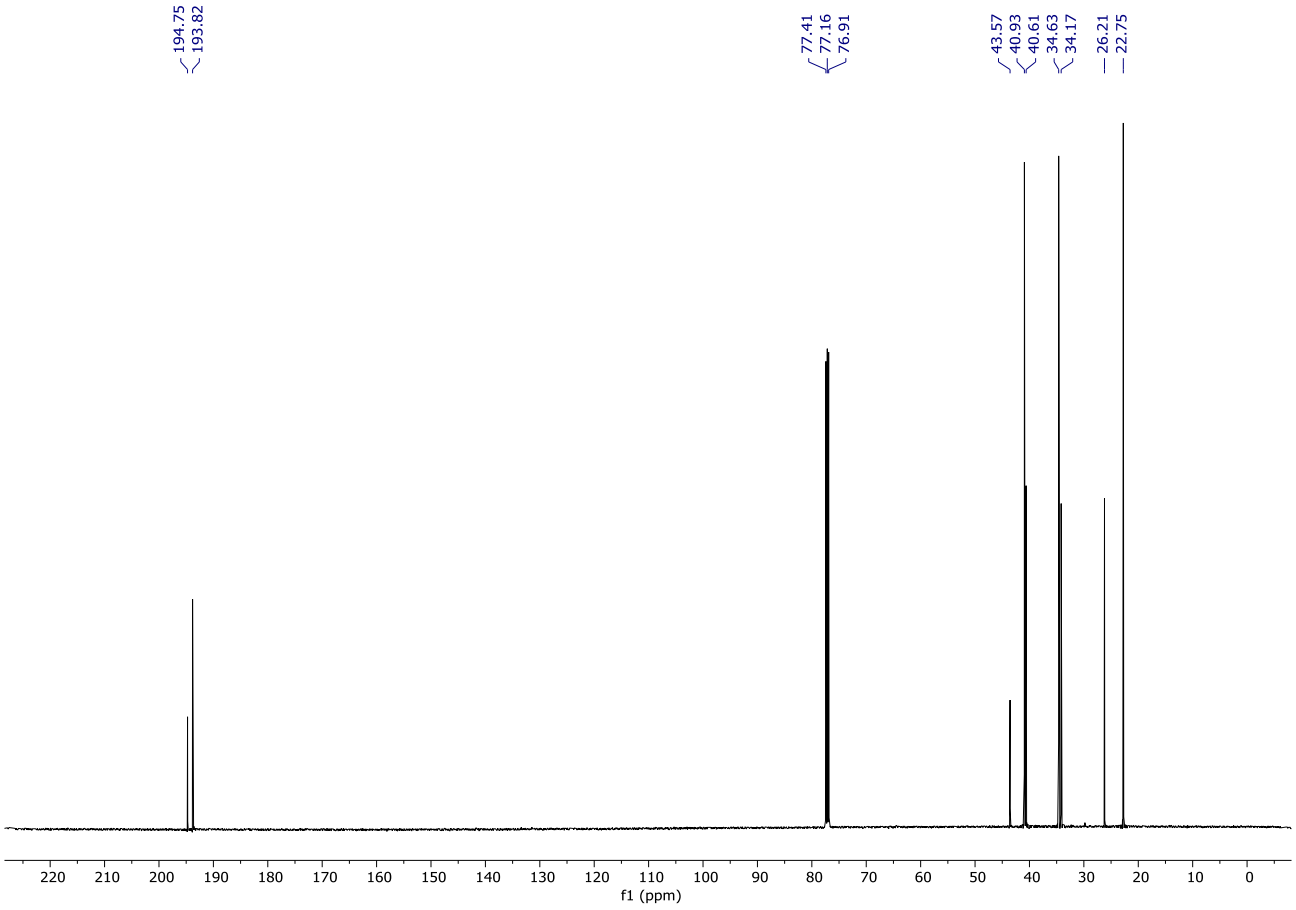

1.96
1.00
1.93
2.98
1.94
1.95
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

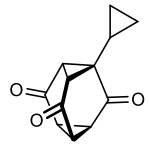

194.51
193.21
139.02
128.79
128.40
126.51
77.41
77.16
76.90
44.13
40.16
34.72
34.16
34.10
32.87
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Me
Me
O
O
O

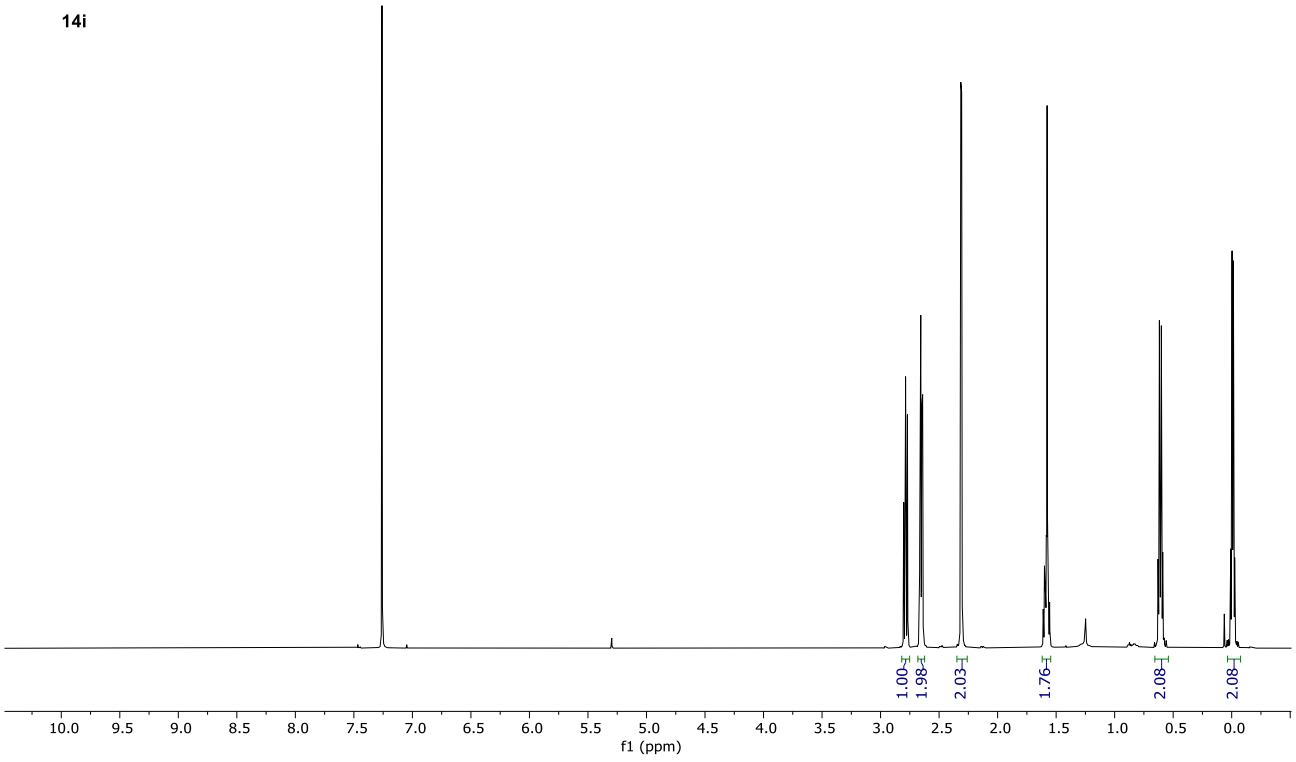
14h

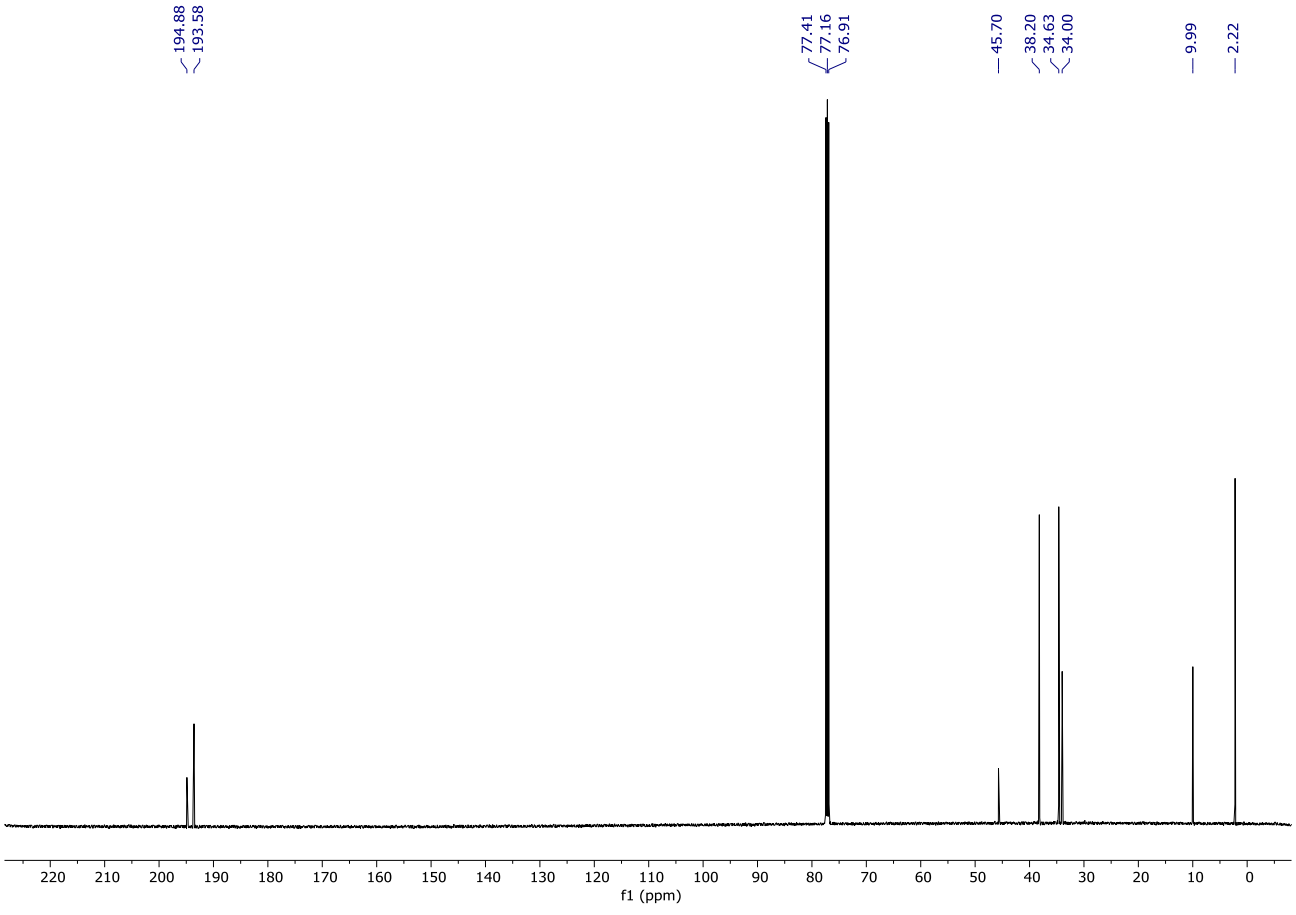
1.00
2.00
2.04
1.03
2.09
6.42
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

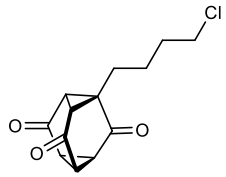

194.75
193.82
77.41
77.16
76.91
43.57
40.93
40.61
34.63
34.17
26.21
22.75
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



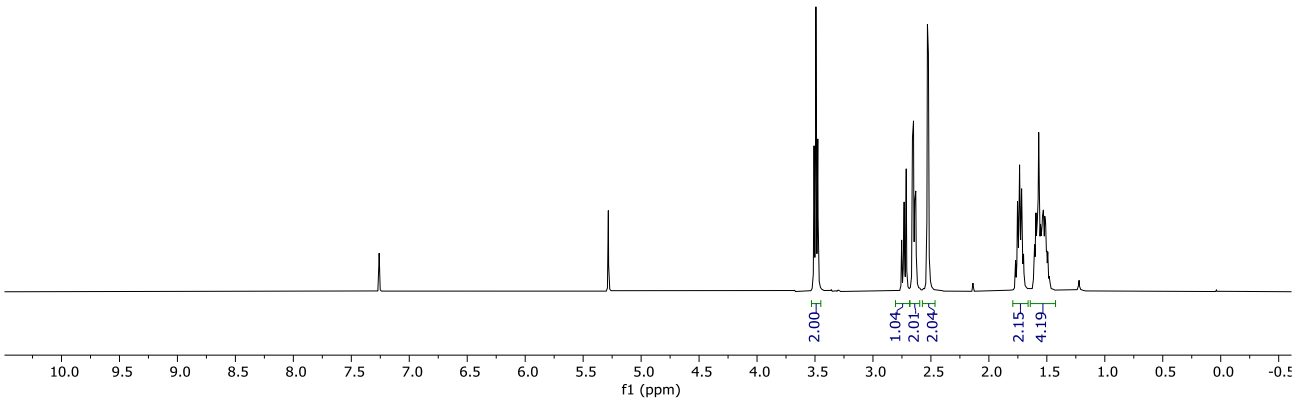
14i

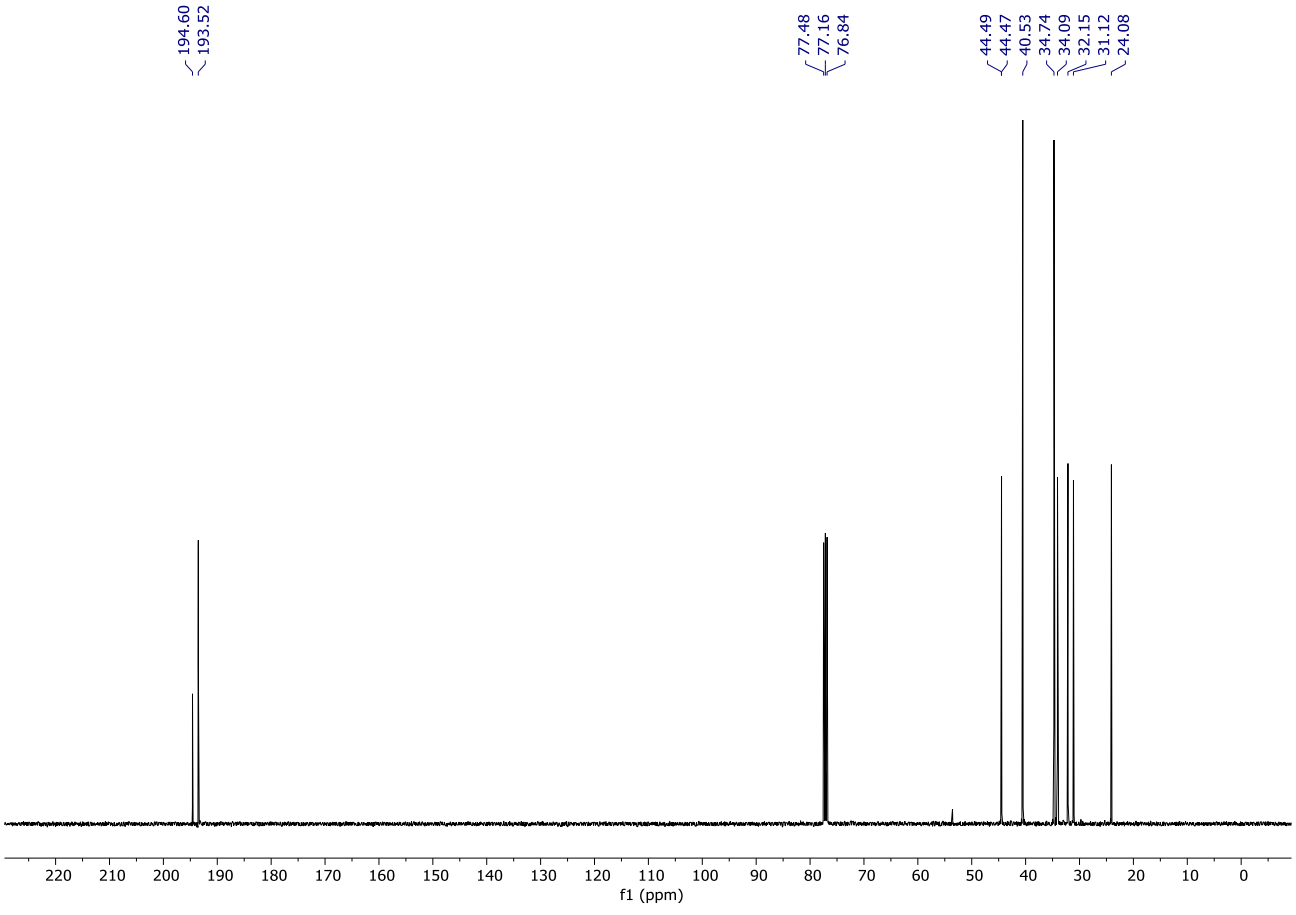

1.00
1.98
2.03
1.76
2.08
2.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

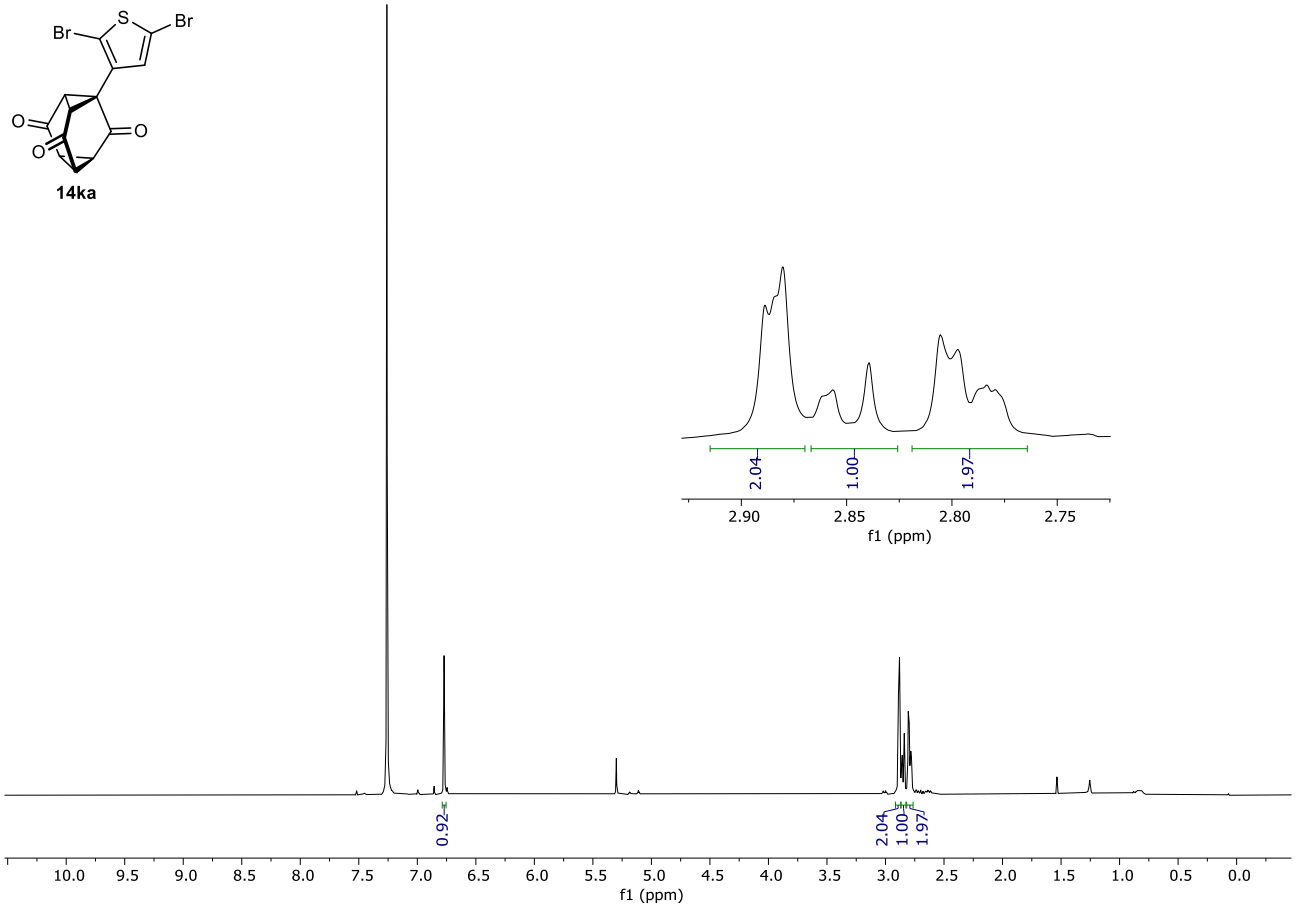

194.88
193.58
77.41
77.16
76.91
45.70
38.20
34.63
34.00
9.99
2.22
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

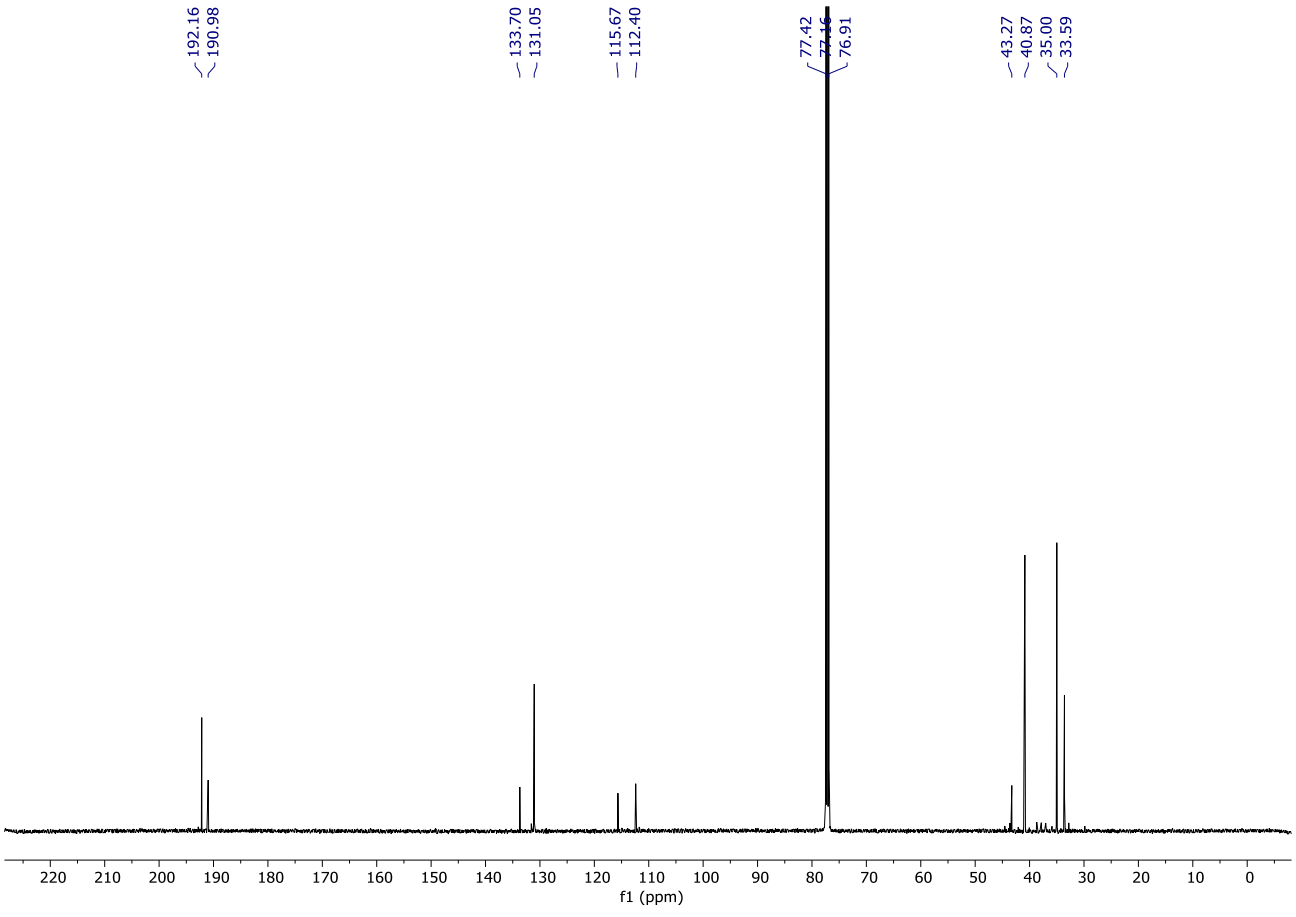

Cl
O
O
O

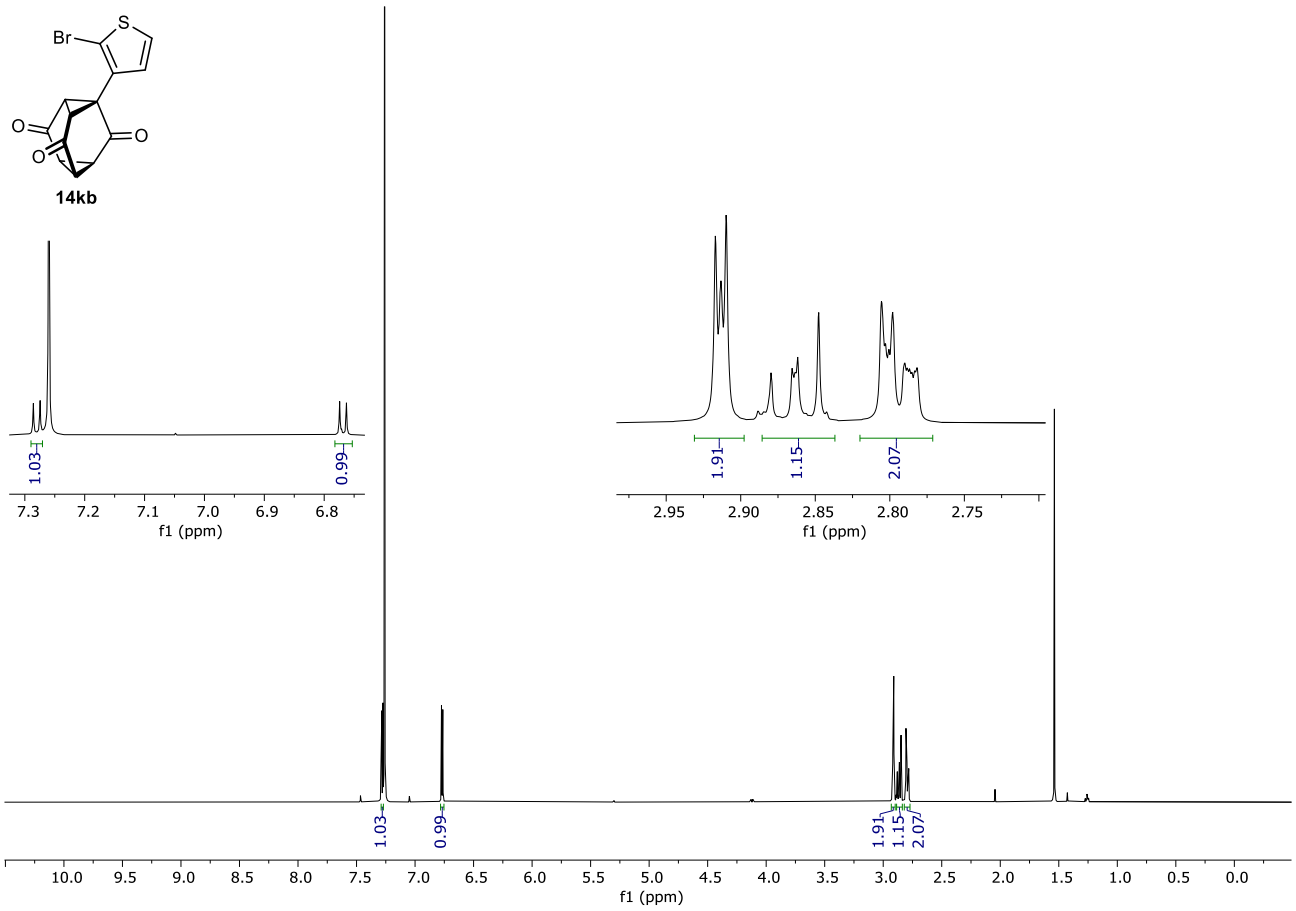
14j

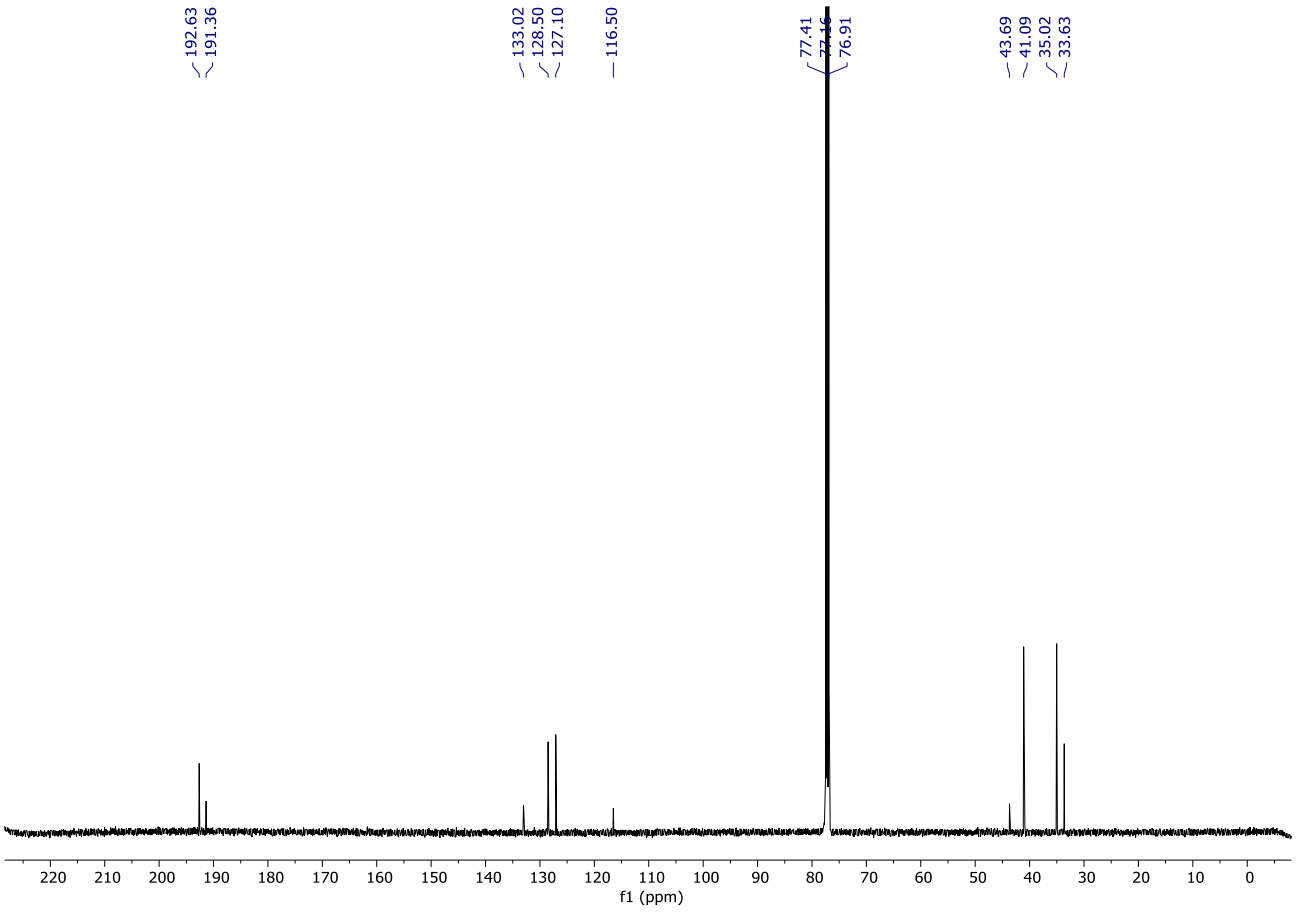

2.00
1.04
2.01
2.04
2.15
4.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


194.60
193.52
77.48
77.16
76.84
44.49
44.47
40.53
34.74
34.09
32.15
31.12
24.08
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Br
S
Br
O
O
O
14ka
2.04
1.00
1.97
2.90
2.85
2.80
2.75
f1 (ppm)
0.92
2.04
1.00
1.97
10.0
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)


192.16
190.98
133.70
131.05
115.67
112.40
77.42
77.16
76.91
43.27
40.87
35.00
33.59
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Br
S
O
O
O
14kb
1.03
0.99
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
1.91
1.15
2.07
2.95
2.90
2.85
2.80
2.75
f1 (ppm)
1.03
0.99
1.91
1.15
2.07
10.0
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)


192.63
191.36
133.02
128.50
127.10
116.50
77.41
77.16
76.91
43.69
41.09
35.02
33.63
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

10. References

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