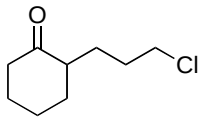
General Methods

All single-vessel reactions not utilizing water were carried out in oven- or flame-dried flasks under a positive pressure of argon. All chemicals were used as received from commercial sources. CH_2Cl_2 (DCM), tetrahydrofuran (THF), and acetonitrile (MeCN) were dried by passage through columns of neutral alumina with an Innovative Technology Pure-Solv 400 commercial solvent purification system prior to use. Thin-layer chromatography (TLC) was performed using commercial Analtech glass-backed silica plates (250 microns) with an organic binder. Visualization was accomplished using UV light or Seebach's stain. Flash chromatography was carried out using Sorbent Technologies standard grade silica gel (40-63 μm particle size, 230 × 400 mesh) with compressed nitrogen as a source of positive pressure, or using a Teledyne Isco CombiFlash R_f employing normal phase disposable columns. Melting points were performed in open capillary tubes using an SRS Optimelt automated melting point apparatus and are uncorrected. Infrared (IR) spectra were acquired as thin films or solids on a PerkinElmer Spectrum 100 FT-IR spectrometer, and the absorptions are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance spectrometer (400 MHz ^1H, 100 MHz ^{13}C). Chemical shifts are reported in parts per million (ppm), and referenced to the solvent: $CDCl_3$ with $\underline{CH}Cl_3$ as internal reference (7.27 ppm for ^1H and 77.23 ppm for ^{13}C). Coupling constants are reported in Hertz (Hz). High resolution mass spectra were obtained using a Waters LCT Premier instrument with a time of flight (TOF) mass analyzer and an electrospray ion source (ESI) or an Agilent 1200 RRLC system with UV detection (Agilent 1200 DAD SL) and mass detection (Agilent 6224 TOF) using a Waters Aquity BEH C18 column (2.1 × 50 mm, 1.7μm). Elution was done

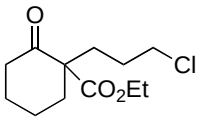
using a linear gradient of 5% CH_3CN in aqueous NH_4HCO_2 (pH set to 9.8) to 100% CH_3CN at a flow rate of 0.4 mL/min.

Known Starting Materials and Methods

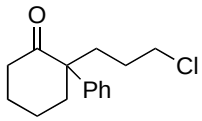
The following compounds were synthesized as described in the literature or purchased commercially.[1a-c]



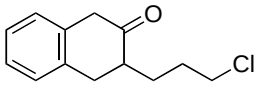
1a



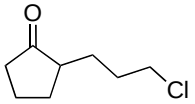
1b



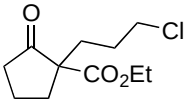
1c



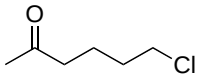
4a



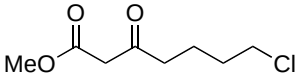
6a



6b



8a

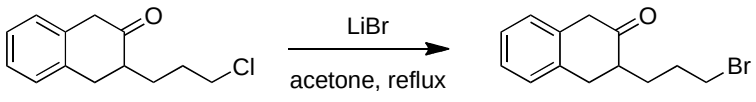


8b

Ethyl ester **6b** was synthesized using methods described in the cited literature, however spectral data was not available.

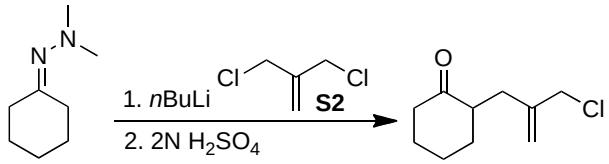
Ethyl 1-(3-chloropropyl)-2-oxocyclopentanecarboxylate 6b. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 4.15 (q, *J* = 7.1 Hz, 2H), 3.51 (m, 2H), 2.52 – 2.37 (m, 2H), 2.21 (m, 1H), 2.05 – 1.82 (m, 3H), 1.75 – 1.65 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 214.5, 170.8, 61.4, 59.7, 44.8, 37.8, 33.1, 31.1, 28.0, 19.5, 14.0; IR: 2965, 1749, 1718, 1447 cm^{-1}; HRMS (ESI) m/z calculated for (M+) $(C_{11}H_{17}ClO_3)^+$ 232.0866, found 232.0869.

Synthesis of New Starting Materials



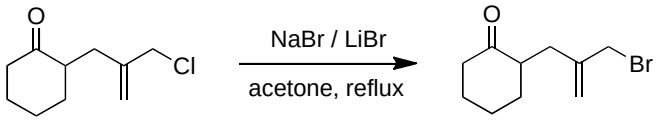
4a **4b**

3-(3-Bromopropyl)-3,4-dihydronaphthalen-2(1*H*)-one 4b. To a solution of **4a** (261 mg, 1.17 mmol) in acetone (5.9 ml) was added lithium bromide (1.52 g, 17.6 mmol). The mixture was heated to reflux for 48 h then diluted with dichloromethane and water. The layers were separated and the aqueous layer extracted into dichloromethane. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The crude oil was purified via silica gel column chromatography (0 to 5% ethyl acetate in hexanes) to afford **4b** (116 mg, 37%) as a brown oil. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.23 (m, 3H), 7.13 (m, 1H), 3.65 (d, *J* = 19.4 Hz, 1H), 3.59 (d, *J* = 19.4 Hz, 1H), 3.42 (m, 2H), 3.12 (dd, *J* = 15.4, 5.6 Hz, 1H), 2.88 (dd, *J* = 15.4, 10.0 Hz, 1H), 2.48 (m, 1H), 2.03 – 1.87 (m, 3H), 1.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 211.0, 135.6, 133.1, 128.0, 127.8, 126.9, 126.8, 46.6, 44.4, 34.4, 33.4, 30.3, 28.4; IR: 2930, 1710 cm^{-1}; HRMS (ESI) m/z calculated for $(M-Br)^+$ ($C_{13}H_{15}O$) 187.1123, found: 187.1122.



2-(2-(Chloromethyl)allyl)cyclohexanone 10a. To a solution of cyclohexanone dimethylhydrazone **S1** (1.54 g, 11.0 mmol) in THF (22 mL) at 0 °C was added *n*-butyllithium (4.91 mL of a 2.23 M solution in hexanes, 11 mmol). The reaction mixture was stirred for 30 min and then added dropwise via cannula over 5 – 6 min to a solution of dichloride **S2** (2.06 g, 16.4 mmol) in THF (17 mL) at 0 °C. After 15 min the reaction mixture was poured into a suspension of ether (60 mL) over 2 M H_2SO_4 (15 mL) and the mixture was stirred vigorously for 30 min. The layers were separated, the aqueous layer

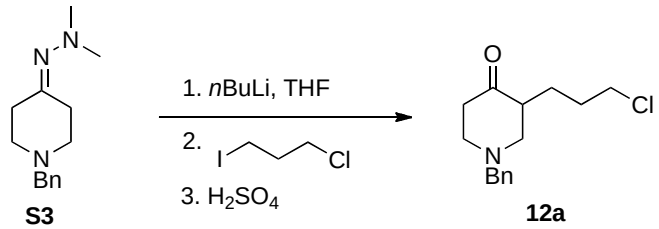
extracted (3x) into ether, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The crude residue was purified via silica gel column chromatography (0 to 5% ethylacetate in hexanes) to afford **10a** (1.64 g, 80%) as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ) δ 5.20 (s, 1H), 4.95 (q, *J* = 1.2 Hz, 1H), 4.05 (s, 2H), 2.75 (dd, *J* = 14.8, 5.6 Hz, 1H), 2.58 (m, 1H), 2.45 (m, 1H), 2.35 (m, 1H), 2.12 (m, 3H), 1.90 (m, 1H), 1.70 (m, 2H), 1.39 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.2, 143.0, 116.1, 48.8, 48.4, 42.1, 33.9, 33.2, 28.1, 25.0; IR: 2937, 1710 cm^{-1}; HRMS (ESI) m/z calculated for $(M+Na)^+$ $(C_{10}H_{15}ClONa)^+$ 209.0709, found: 209.0794.



10a **10b**

2-(2-(Bromomethyl)allyl)cyclohexanone 10b. A mixture of **10a** (508 mg, 2.72 mmol) and sodium bromide (2.8 g, 27.2 mmol) in acetone (14 mL) was heated to reflux for 15 h. After this time more sodium bromide (1.4 g, 13.6 mmol) was added and the mixture heated at reflux for an additional 40 h. Finally, lithium bromide (1.2 g, 13.6 mmol) and acetone (5 mL) were added and the mixture heated at reflux for 24 h. The reaction mixture was then diluted with ether, filtered through a pad of silica gel, and the filtrate concentrated under vacuum. The crude residue was purified via silica gel column chromatography to afford **10b** (379 mg, 60%) as a brown oil. Alternatively chloride **10a** (323 mg, 1.73 mmol) could be reacted with only lithium bromide (2.25 g, 26.0 mmol) in acetone (8.7 ml) in a similar fashion for 18 h at reflux to afford **10b** (167 mg), in 42% yield. While this procedure has the advantage of being faster, it is not as clean and provides a lower yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.23 (s, 1H), 4.95 (d, *J* = 1.2 Hz,

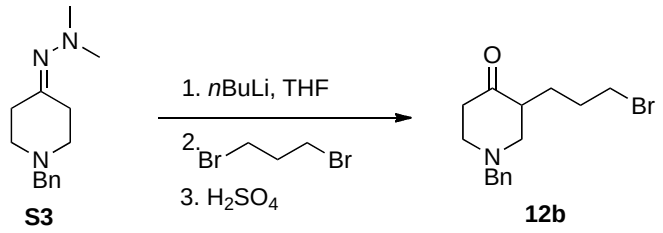
1H), 3.99 (d, *J* = 10.0 Hz, 1H), 3.95 (d, *J* = 10.0 Hz, 1H), 2.78 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.58 (m, 1H), 2.44 (m, 1H), 2.35 (m, 1H), 2.18 – 2.05 (m, 3H), 1.91 (m, 1H), 1.87 – 1.63 (m, 2H), 1.39 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.1, 143.2, 116.6, 48.7, 42.0, 36.7, 33.8, 33.4, 28.0, 24.9; IR: 2930, 1709 cm^{-1}; HRMS (ESI) m/z calculated for (M+) ($C_{10}H_{15}BrO$) 230.0306, found: 230.0309.



S3 **12a**

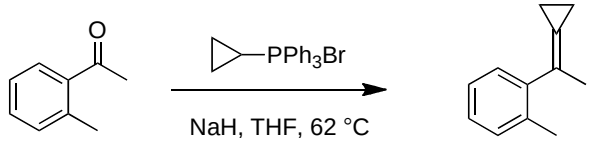
1-Benzyl-3-(3-chloropropyl)piperidin-4-one 12a. A solution of *n*-butyllithium (5.41 mL,of a 2.0 M solution in hexanes, 10.8 mmol) was added drop-wise to a solution of 1-benzyl-4-(2,2-dimethylhydrazono)piperidine **S3** (2.09 g, 9.02 mmol) in THF (30 mL) at -78 °C. The resulting solution was warmed to rt over 30 min. 1-Chloro-3-iodopropane (1.14 mL, 10.8 mmol) was added dropwise and the mixture was stirred for 1.5 h. H_2SO_4 (2 M, 30 mL) was added and the mixture was stirred for a further 30 min. The layers were separated, the aqueous layer extracted (3x) with ether, and the combined organic layers were washed with brine (20 mL) and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give a red oil that was purified via silica gel column chromatography (10 to 20% ethyl acetate in hexanes) to afford **12a** (1.17 g, 42%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 3H), 7.30 (m, 2H), 3.67 (d, *J* = 13.2 Hz, 1H), 3.58 (d, *J* = 13.2 Hz, 1H), 3.53 (m, 2H), 3.02 (m, 2H) 2.61—2.45 (m, 3H), 2.39 (m, 1H), 2.25 (t, *J* = 11.2 Hz, 1H), 1.96—1.60 (m, 3H), 1.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.7, 138.3, 129.1, 128.6, 127.6, 62.1, 59.1, 53.8, 49.4, 45.2, 41.2,

30.5, 25.2; IR: 2954, 2801, 1712 cm^{-1}. HRMS (ESI/APCI) *m/z* calculated $(M+H)^+$ for ($C_{15}H_{21}ClNO^+$): 266.1333, found: 266.1295.



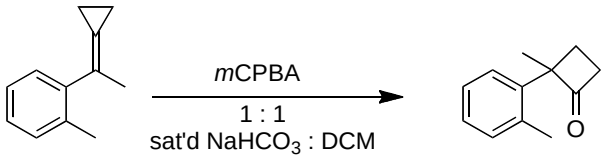
S3 **12b**

1-Benzyl-3-(3-bromopropyl)piperidin-4-one 12b. A solution of *n*-butylithium (5.40 mL, of a 2.0 M solution in hexanes, 10.8 mmol) was added drop-wise to a solution of 1-benzyl-4-(2,2-dimethylhydrazono)piperidine **12b** (2.09 g, 9.02 mmol) in THF (22.0 mL) at -78 °C. The resulting solution was warmed to rt over 30 min. The resulting orange solution was then added drop-wise via cannula to a solution of 1,3-dibromopropane (1.40 mL, 13.5 mmol) in THF (10.0 mL) at 0 °C, and the mixture was stirred for 1.5 h. H_2SO_4 (2 M, 30 ml) was added and the mixture was stirred for a further 15 min. The layers were separated, the aqueous layer was extracted with ether, and the combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give a red oil that was purified by silica gel column chromatography (0-20% ethyl acetate in hexanes) to give **12b** (1.050 g, 38%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (m, 3H), 7.29 (m, 2H), 3.65 (d, *J* = 14.0 Hz, 1H), 3.57 (d, *J* = 14.0 Hz, 1H), 3.38 (m, 2H), 3.00 (m, 2H) 2.60 - 2.45 (m, 3H), 2.38 (m, 1H), 2.24 (m, 1H), 1.88 (m, 2H), 1.79 (m, 1H), 1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 138.1, 128.9, 128.4, 127.4, 61.9, 58.9, 53.6, 49.1, 41.0, 33.6, 30.4, 26.3. IR: 3028, 2801, 1712, cm^{-1}; HRMS (ESI/APCI) *m/z* calculated $(M+H)^+$ for $C_{15}H_{21}BrNO^+$: 310.0807, found: 310.0791.



S4 **S5**

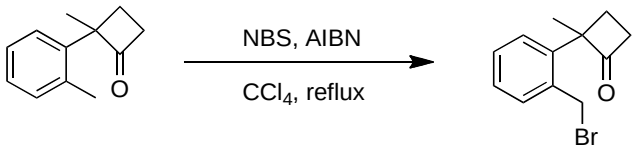
1-(1-Cyclopropylideneethyl)-2-methylbenzene S5. In a manner analogous to that of Fukumoto,[2] to a suspension of sodium hydride (805 mg, 20.1 mmol) in THF (13.4 ml) was added cyclopropyltriphenylphosphonium bromide (7.29 g, 19.0 mmol) via solid addition funnel over 5 min. The mixture was heated at 62 ºC for 20 h then a solution of 1-(*o*-tolyl)ethanone **S4** (1.5 g, 11.2 mmol) in THF (5.6 mL) was added via syringe. The mixture was stirred for 3 h and then water was added. The mixture was diluted with pentane and the layers separated. The aqueous layer was extracted into pentane (3x) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered through a plug of silica gel, and concentrated under vacuum. The crude oil was purified via silica gel column chromatography (0 to 5% ethyl acetate in hexanes) to afford **S5** (1.47 g, 83%) as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.22 – 7.16 (m, 4H), 2.26 (s, 3H), 2.15 (pent, *J* = 2.0 Hz, 3H), 1.16 (m, 2H), 1.06 (m, 2H); ^{13}C NMR (CDCl3, 100 MHz) δ 143.1, 135.2, 130.1, 128.0, 126.4, 125.4, 124.9, 120.7, 22.6, 19.9, 3.9, 2.2; IR: 2975, 1490 cm^{-1}. HRMS (EI) m/z calculated for (M+) ($C_{12}H_{14}$) 158.1096, found 158.1100.



S5 **S6**

2-Methyl-2-(*o*-tolyl)cyclobutanone S6. In a manner analogous to that of Fukumoto,[2] *meta*-chloroperbenzoic acid (*m*-CPBA, 3.39 g, 13.8 mmol) was added to a mixture of 1-

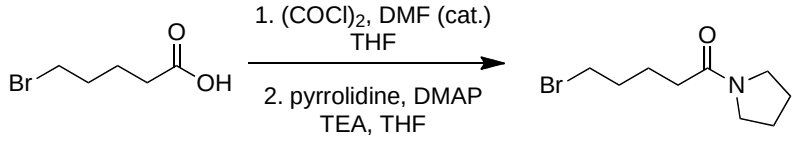
(1-cyclopropylideneethyl)-2-methylbenzene **S5** (1.36 g, 8.60 mmol) in 1 : 1 saturated $NaHCO_3$: DCM (22 mL). After 1 h the reaction mixture was diluted with water and DCM and the layers separated. The aqueous layer was extracted into DCM (3x) and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under vaccum. The crude oil was purified via silica gel column chromatography (0 to 10% ethyl acetate in hexanes) to afford **S6** (812 mg, 54%) as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.16 (m, 3H), 3.14 (ddd, *J* = 18.0, 10.8, 6.4 Hz, 1H), 3.06 (ddd, *J* = 18.0, 10.8, 6.4 Hz, 1H), 2.51 (dt, *J* = 10.8, 7.2 Hz, 1H), 2.39 (s, 3H), 2.29 (m, 1H), 1.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.4, 140.5, 134.8, 131.9, 126.7, 125.7, 125.6, 67.9, 42.3, 26.9, 24.3, 20.0; IR: 2961, 1770, 1490 cm^{-1}; HRMS (ESI) m/z calculated for (M+) ($C_{12}H_{14}O$) 174.1045, found: 174.1056.



S6 **14**

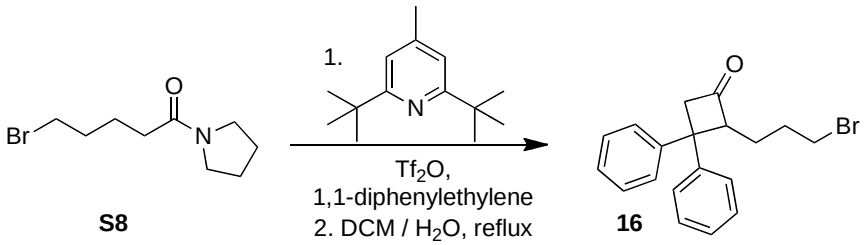
2-(2-Bromomethyl)phenyl)-2-methylcyclobutanone 14. A solution of 2-methyl-2-(*o*-tolyl)cyclobutanone **S6,** 747 mg, 4.29 mmol), *N*-bromosuccinamide (NBS, 840 mg, 4.72 mmol), and 2,2′-Azobis(2-methylpropionitrile) (AIBN, 141 mg, 0.86 mmol) in carbon tetrachloride (24 mL) was heated at reflux for 1 h. The reaction mixture was cooled to rt, diluted with pentane, filtered through filter paper, and concentrated under vacuum. The residue was purified via silica gel column chromatography (0 to 10% ethyl acetate in hexanes) to afford **14** (871 mg, 80%) as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55 (ddd, *J* = 7.2, 2.0, 0.8 Hz, 1H), 7.50 (ddd, *J* = 7.2, 2.0, 0.8 Hz, 1H), 7.25 (m, 2H),

4.65 (s, 2H), 3.21 (ddd, *J* = 18.0, 10.8, 6.4 Hz, 1H), 3.09 (ddd, *J* = 18.0, 10.8, 6.4 Hz, 1H), 2.69 (dt, *J* = 10.8, 7.2 Hz, 1H), 2.32 (m, 1H), 1.64 (s, 3H). ^{13}C NMR ($CDCl3_3$, 100 MHz) δ 211.0, 140.7, 134.8, 133.2, 128.5, 127.5, 126.2, 67.7, 42.6, 31.2, 26.9, 26.0; IR: 2961, 1770 cm^{-1}; HRMS (ESI) m/z calculated for $(M+Na)^+$ ($C_{12}H_{13}BrONa$) 275.0047, found: 275.0019.

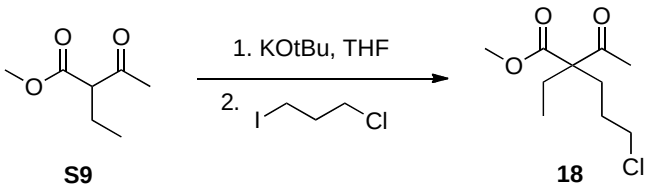


S7 **S8**

5-Bromo-1-(pyrrolidin-1-yl)pentan-1-one S8. This compound was previously reported by Dowd, however no spectral data was provided.[3a,b] To a solution of acid **S7** (3.00 g, 16.6 mmol) in THF (55 mL) was added oxalyl chloride (1.9 mL, 21.6 mmol) and a catalytic amount of DMF (~ 5 drops). The mixture was stirred at rt for 3.5 h, then concentrated under vacuum. The crude acid chloride was re-dissolved in THF (55 mL) and added to a solution of pyrrolidine (1.65 mL, 19.9 mmol), triethylamine (3.50 mL, 24.9 mmol), and *N*,*N*-dimethylaminopyridine (DMAP, 406 mg, 3.32 mmol) in THF (66 mL) via cannula. The resultant off-white suspension was stirred for 18 h then diluted with ether, filtered through a pad of celite, and the filtrate concentrated under vacuum. The crude residue was purified via silica gel column chromatography (40 to 70% ethyl acetate in hexanes) to afford **S8** (3.15 g, 81%) as a light-brown oil. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 3.38 (m, 6H), 2.25 (t, *J* = 8.0 Hz, 2H), 1.95 – 1.87 (m, 4H), 1.84 – 1.74 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 46.4, 45.5, 33.5, 33.4, 32.2, 26.0, 24.2, 23.3; IR: 2951, 1627 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $(M+H)^+$ ($C_9H_{17}BrNO$) 234.0494, found: 234.0519.

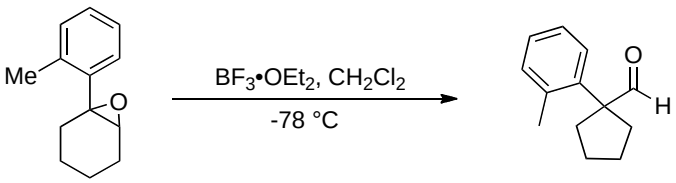


2-(3-Bromopropyl)-3,3-diphenylcyclobutanone 16. In a manner analogous to that of Fitjer,[4] to a solution of amide **S8** (786 mg, 3.36 mmol) in DCE (3.4 mL) at -15 °C was added trifluorosulfonic anhydride (0.68 mL, 4.03 mmol). After 20 min, a solution of 1,1-diphenylethylene (1.21 g, 6.72 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (828 mg, 4.03 mmol) in DCE (1 mL) was added dropwise. The reaction mixture was heated under reflux for 22 h and then concentrated under vacuum. The residue was extracted into ether (3x) and the remaining brown oil was dissolved in 1 : 1 DCM : H_2O (10 mL) and heated under reflux for 4 h. The reaction mixture was diluted with DCM, the layers separated and the aqueous layer extracted with DCM (3x) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified via silica gel column chromatography to afford the **16** (752 mg, 65%) as a red/brown oil that solidifies over time. MP = 58.4 – 59.8 ºC; ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.43 (m, 2H), 7.35 – 7.19 (m, 6H), 7.01 (m, 2H), 3.95 (m, 1H), 3.81 (dd, *J* = 16.8, 1.6 Hz, 1H), 3.62 (dd, *J* = 16.8, 2.8 Hz, 1H), 3.32 (m, 2H), 2.10 (sept, *J* = 7.2 Hz, 1H), 1.94 (m, 1H), 1.41 (d, *J* = 8.0 Hz, 1H), 1.37 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 207.8, 147.8, 143.0, 128.6, 128.3, 127.5, 127.3, 126.7, 126.6, 67.5, 58.2, 45.6, 33.6, 30.6, 26.0; IR: 2937, 1774 cm^{-1}; HRMS (ESI/APCI) m/z calculated for $(M+H)^+$ ($C_{19}H_{20}BrO$) 343.0698, found: 343.0683.



S9 **18**

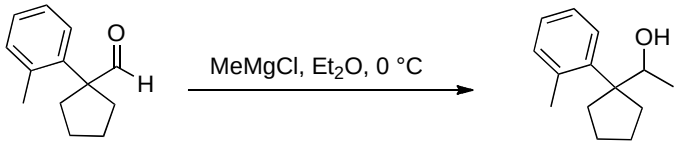
Methyl 2-acetyl-5-chloro-2-ethylpentanoate 18. Methyl 2-ethylacetoacetate (5.00 g, 34.7 mmol) was added to a suspension of potassium *tert*-butoxide (5.84 g, 52.0 mmol) in THF (100 mL) at 0 °C. The resulting solution was warmed to rt and stirred for 30 min. 1-Chloro-3-iodopropane (4.4 mL, 42 mmol) was added drop-wise and the mixture was stirred for 20 h whereupon it was quenched by the addition of saturated aqueous ammonium chloride (40 mL) and ether (100 mL) was then added. The layers were separated, the aqueous layer was extracted (3x) with ether and the combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a yellow oil that was purified via silica gel column chromatography to give **18** (3.98 g, 52%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (s, 3H), 3.51 (m, 2H), 2.13 (s, 3H), 1.94 (m, 4H), 1.59 (m, 2H), 0.78 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.1, 173.0, 63.6, 52.6, 45.0, 28.4, 27.5, 26.9, 24.6, 8.4; IR: 2970, 1741, 1710 cm^{-1}; MS: 221 (1), 178 (30), 115 (100).



S10 **S11**

1-(o-tolyl)cyclopentanecarbaldehyde S11. To a solution of 1-(o-tolyl)-7-oxabicyclo[4.1.0]heptane **S10**,[5] (1.0 g, 5.31 mmol) in DCM (40.0 mL) at -78 °C was added boron trifluoride diethyl etherate (4.0 mL, 32.4 mmol). The solution was stirred at this temperature for 3 h before it was warmed to rt and quenched with saturated aqueous sodium bicarbonate (100 mL). The layers were separated, the aqueous layer extracted

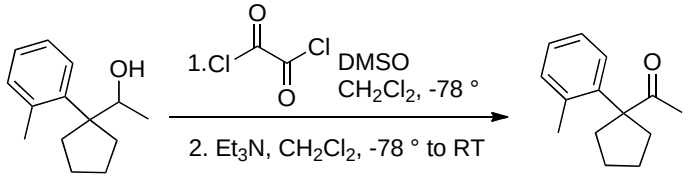
(3x) with DCM, and the combined organic layers were then washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Solvent evaporation afforded **S11** (940 mg, 94%) as a colorless oil that was used directly without purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.36 (s, 1H), 7.38 (s, 1H), 7.24 - 7.17 (m, 3H), 2.49 (m, 2H), 2.20 (m, 3H), 1.94 (m, 2H), 1.76 - 1.64 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.7, 138.9, 138.2, 132.2, 127.8, 127.3, 126.4, 63.7, 32.5, 24.7, 21.5; IR: 2953, 1719 cm^{-1}; HRMS (ESI) *m/z* calculated for $(M)^+$ ($C_{13}H_{16}O$) 188.1201, found: 188.1206.



S11 **S12**

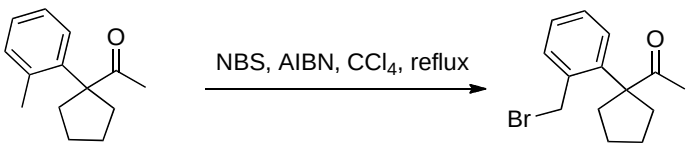
1-(1-(o-tolyl)cyclopentyl)ethanol S12. To a solution of methylmagnesium chloride (3.0 mL, of a 2.9 M solution in ether, 8.7 mmol) in Et_2O (20.0 ml) was added a solution of **S11** (919 mg, 4.88 mmol) in ether (10 mL) at 0 °C. The resulting suspension was stirred for 30 min at which time TLC analysis indicated complete consumption of **S11**. The reaction was quenched by slow addition of saturated aqueous ammonium chloride (20 mL) and the layers were separated. The aqueous layer was extracted with ether (3x) and the combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. Solvent evaporation afforded an oily residue that was purified via silica gel column chromatography (0 to 15% ethylacetate in hexanes) to afford **S12** (472 mg, 47%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 1H), 7.16 - 7.10 (m, 3H), 4.07 (pent, *J* = 6.0 Hz, 1H,), 2.50 (s, 3H), 2.28 (m, 2H), 2.02 (m, 2H), 1.76 (m, 1H), 1.67 (m, 3H), 1.25 (d, *J* = 6.0 Hz, 1H), 1.04 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

144.5, 137.2, 133.0, 129.4, 126.4, 125.6, 71.9, 57.6, 35.7, 34.3, 25.2, 24.6, 23.6, 19.4; IR: 3407, 2953 cm^{-1}; MS: 160 (8), 159 (57), 105 (100).



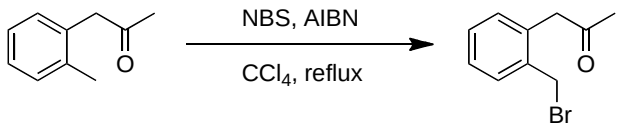
S12 **S13**

1-(1-(o-tolyl)cyclopentyl)ethanone S13. To a solution of oxalyl chloride (0.97 mL, 11 mmol) in DCM (20 mL) at -78 °C was added dimethylsulfoxide (1.56 mL, 22 mmol) drop-wise over 5 min the resulting solution was stirred for 10 min. A solution of **S12** (452 mg, 2.21 mmol) in DCM (6 mL) was then added and the mixture was maintained at -78 ° for 1 hour. Triethylamine (4.6 ml, 33 mmol) was then added and the mixture was allowed to warm slowly to rt over 20 min. The suspension was diluted with saturated aqueous sodium bicarbonate (20 mL) and the layers were separated. The aqueous layer was extracted with DCM (3x) and the combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. Solvent evaporation afforded a yellow oil that was purified by silica gel column chromatography (0 to 10% ethyl acetate in hexanes) to afford **S13 (**301 mg, 68%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (m, 1H); 7.24 - 7.13 (m, 3H), 2.44 (m, 2H), 2.17 (s, 3H), 1.95 (m, 2H), 1.87 (s, 3H), 1.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 142.5, 137.3, 132.2, 127.2, 126.3, 126.3, 65.3, 34.9, 26.3, 24.8, 21.0; IR: 2953, 1702 cm^{-1}; MS: 160 (32), 159 (34), 145 (30), 115 (100).



S13 **20**

1-(1-(2-(Bromomethyl)phenyl)cyclopentyl)ethanone 20. To a solution of **20** (275 mg, 1.36 mmol) in carbon tetrachloride (13 mL) was added *N*-bromosuccinimide (265 mg, 1.49 mmol) followed by azobisisobutyronitrile (45 mg, 0.27 mmol). The resulting suspension was heated under reflux for 2.5 h at which time the mixture was cooled to rt, diluted with hexanes (100 mL), and the white precipitate was removed by filtration. Solvent evaporation afforded a yellow oil that was purified via silica gel column chromatography (0 to 10% ethylacetate in hexanes) to give **20** (276 mg, 72%) as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (m, 2H), 7.31 (m, 2H), 4.45 (s, 2H), 2.51 (m, 2H), 2.01 (m, 2H), 1.93 (s, 3H), 1.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0, 141.7, 137.4, 133.8, 129.0, 128.1, 126.9, 65.4, 35.4, 31.5, 26.4, 24.5; IR: 2955, 1702 cm^{-1}; HRMS (EI) *m/z* calculated for $(M\text{-}Br)^+$ ($C_{14}H_{17}O$) 201.1279 found: 201.1274.



S14 **22**

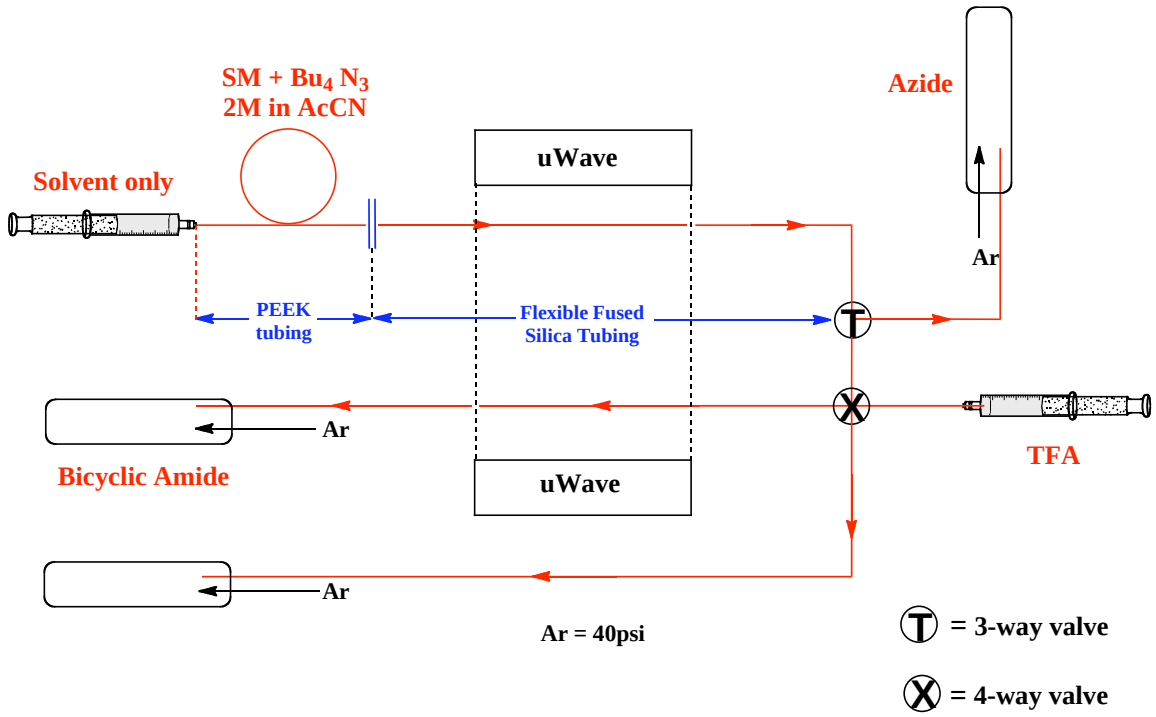
1-(2-(Bromomethyl)phenyl)propan-2-one 22. The preparation of **22** was achieved using the method described for **14** affording 1.0 g of **22** (60%) as a brown oil. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.39 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.28 (m, 2H), 7.18 (dd, *J* = 7.2, 1.6 Hz, 1H), 4.50 (s, 2H), 3.92 (s, 2H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 205.6, 136.2, 133.5, 131.3, 130.7, 129.2, 127.8, 47.8, 31.9, 29.7; IR ν = 3023, 1709 cm^{-1}; HRMS (ESI) m/z calculated for $(M\text{-}Br)^+$ ($C_{10}H_{11}O$) 147.0810, found: 147.0812.

Construction of the MACOS Apparatus

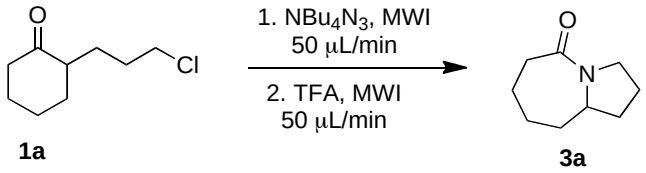
All connections were made using PEEK™ connectors and/or union bodies. The 2 mL sample loop was constructed from PEEK™ tubing (Upchurch part # 1531L). The loop is connected to the apparatus after loading and just prior to the reaction as described below

via a union body. The flexible fused silica tubing (Polymicro part # 1068150029) is connected to the other end of this union body. This initial flexible fused silica flow path ends in a 3-way valve (Upchruch part # V-100L), which connects to a PEEK™ tubing exit channel into a sealed Biotage microwave vial and another PEEK™ tube that connects to the 4-way valve (Upchurch part # V-100T) for continuing flow. The 4-way valve is connected to two PEEK™ tubes; one is an inlet for flowing in a second reagent while the other is a collection tube for performing the second step of a flow experiment outside of the microwave channel. The final connection to the 4-way valve is a flexible fused silica tube that proceeds through the microwave cavity to another collection vial. The syringe pumps are from Harvard Apparatus (Part #PY8 55-3333). The microwave used is a standard Biotage Initiator system that has been modified so as to allow for operation while the microwave chamber is open; it is operated in service mode.

General Schematic:



Representative Procedure for MACOS Azide displacement / Schmidt Sequence

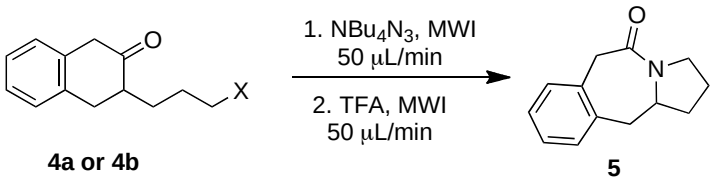


1a **3a**

Hexahydro-1*H*-pyrrolo[1,2-*a*]azepin-5(6*H*)-one 3a. The MACOS apparatus was constructed as shown above in the general schematic. A solution of chloride **1a** (312 mg, 1.78 mmol, 1 equiv.) and *N*,*N*,*N*,*N*-tetrabutylammonium azide (558 mg, 1.96 mmol, 1.1 equiv.) in acetonitrile (0.89 mL, 2M with respect to the halide) was added into a 2 mL sample loop. (A 4 ± 2% material remainder due to syringe handling was typical for this procedure. Yields are uncorrected). The loop was connected to the apparatus and a luer-lock syringe containing 3 mL of acetonitrile connected to the other end and placed in the syringe pump. A second luer-lock syringe was loaded with trifluoracetic acid (3 mL, excess), connected to the second valve, and placed into the second syringe pump. Back-pressure tubes were connected to the collection vessels (crimp-sealed microwave vials) and then the microwave was turned on to 125 W (or 300 W as indicated in the text) and both pumps were set to infuse at 50 μl/min. The back-pressure was then immediately set to 40 psi and the reaction flowed over 1h. The collected material was flushed with toluene three times under vacuum and the mixture dissolved in toluene and filtered through a plug of basic alumina, further eluting with ethylacetate. The filtrate was concentrated under vacuum to afford a crude mixture of product and tetrabutylammonium salts. The crude mixture was purified via silica gel column chromatography (0.5% aqueous ammonium hydroxide, 2.5% methanol in dichloromethane) to afford **3a** (189 mg, 69%) as a pale-yellow oil. The chromatography conditions described above are absolutely necessary to remove the tetrabutylammonium

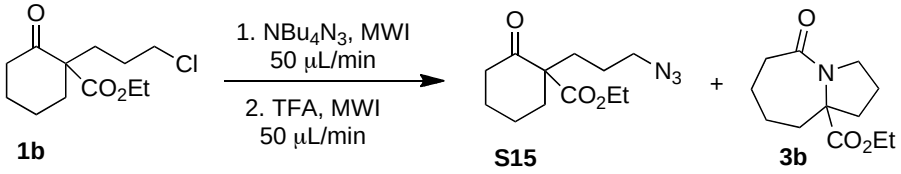
salts. Other conditions caused co-elution of the salts with the amide product. Data for the product is consistent with literature values.[1b]

MACOS Reactions



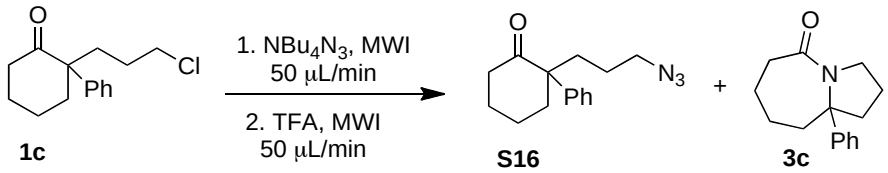
4a or 4b **5**

2,3,11,11a-Tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]azepin-5(6*H*)-one 5. Reaction of **4a** (261 mg, 1.17 mmol) performed at 125 W under the representative MACOS conditions described above afforded **5** (142 mg, 60%) as a brown solid and recovered starting material (61 mg, 23%). Similarly, reaction of **4b** (106 mg, 0.40 mmol) under the MACOS conditions described above afforded **5** (49 mg, 61%) as brown solid with no recovered starting material. Product data is consistent with literature data in both cases.[1b]



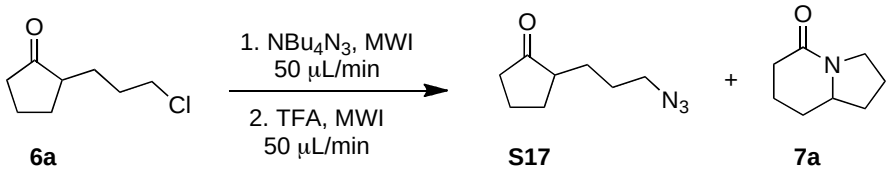
1b **S15** **3b**

Ethyl 5-oxooctahydro-1H-pyrrolo[1,2-*a*]azepine-9*a*-carboxylate 3b. Reaction of **1b** (300 mg, 1.22 mmol) performed at 125 W under the representative MACOS conditions described above afforded **3b** (187 mg, 68%) as a yellow oil and recovered starting material **1b** (16 mg, 5%) and **S15** (18 mg, 6%). Data for the products was consistent with those reported in the literature.[1b,6]



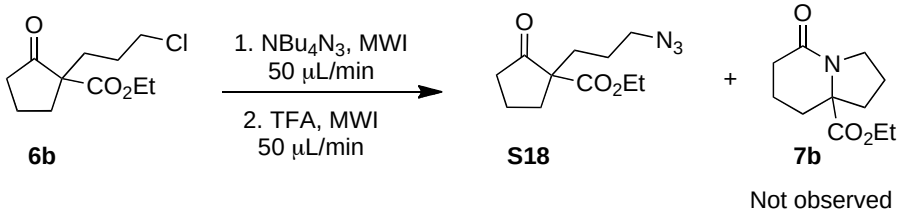
1c **S16** **3c**

9a-Phenylhexahydro-1*H*-pyrrolo[1,2-*a*]azepin-5(6*H*)-one 3c. Reaction of **1c** (300 mg, 1.19 mmol) performed at 125 W under the representative MACOS conditions described above afforded azide **S16** (182 mg, 60%), amide **3c** (15 mg, 5%) and recovered starting material (46 mg, 15% uncorrected). The azide and chloride were isolated as a mixture and masses determined through ^{1}H NMR ratios. Product data is consistent with literature data.[1c]



6a **S17** **7a**

Hexahydroindolizin-5(1*H*)-one 7. Reaction of **6a** (223 mg, 1.39 mmol) performed at 125 W under the representative MACOS conditions described above afforded **7a** (16 mg, 8%), azide **S17** (86 mg, 37%) and recovered starting material (43 mg, 19%). The azide and chloride were isolated as a mixture and masses determined by GC-MS ratios. Product data is consistent with literature data.[1b]

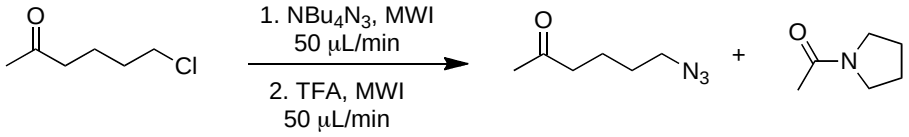


6b **S18** **7b**

Not observed

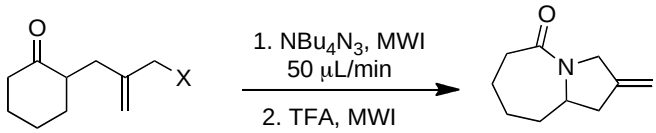
Ethyl 1-(3-azidopropyl)-2-oxocyclopentanecarboxylate 7b. Reaction of **6b** (346 mg, 1.48 mmol) performed at 125 W under the representative MACOS conditions described above afforded azide **S18** (233 mg, 66%) and recovered starting material (56 mg, 16%). The azide and chloride were isolated as a mixture and masses determined by GC-MS ratios. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 4.15 (q, *J* = 7.1 Hz, 2H), 3.27 (m, 2H), 2.52 – 2.38 (m, 2H), 2.22 (m, 1H), 2.05 – 1.83 (m, 4H), 1.69 – 1.57 (m, 2H), 1.52 (m, 1H), 1.23 (t, *J*

= 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 214.5, 170.8, 61.4, 59,8, 51.4, 37.8, 33.1, 30.8, 24.3, 19.5, 14.0; IR: 2967, 2093, 1749, 1718 cm^{-1}; HRMS (ESI) m/z calculated for $(M+Na)^+$ ($C_{11}H_{17}N_3O_3Na$) 262.1168, found: 262.1190.



8a **S19** **9a**

1-(Pyrrolidin-1-yl)ethanone 9a. Reaction of **8a** (279 mg, 2.07 mmol) performed at 125 W under the representative MACOS conditions described above afforded **9a** (58 mg, 25%), azide **S19** (106 mg, 36%) and recovered starting material (39 mg, 14%). The azide and chloride were isolated as a mixture and masses determined by GC-MS ratios. Product data is consistent with literature data.[1b]

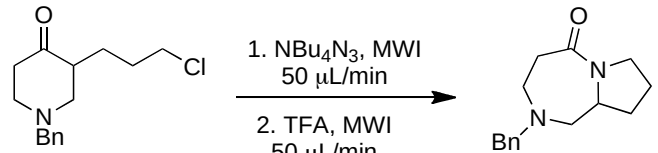


10a, X = Cl
10b, X= Br

11

2-Methylenehexahydro-1*H*-pyrrolo[1,2-*a*]azepin-5(6*H*)-one 11. Reaction of **10a** (286 mg, 1.53 mmol) performed at 300 W under the representative MACOS conditions described above afforded **11** (130 mg, 51%) as brown oil and recovered **10a** (39 mg, 14%, contains impurity). Similarly, reaction of **10b** (257 mg, 1.11 mmol) performed at 300 W under the representative MACOS conditions described above afforded **11** (98 mg, 53%) as brown oil. The impurity seen in the previous reaction with the recovered chloride was also collected (18 mg, 7%) and found to contain no starting material.^{1}H NMR ($CDCl_3$, 400 MHZ) δ 4.96 (q, *J* = 1.6 Hz, 2H), 4.14 (d, *J* = 16.0 Hz, 1H), 4.05 (d, *J* = 16.0 Hz, 1H), 3.88 (m, 1H), 2.93 (dd, 14.4, 8.8 Hz, 1H), 2.54 (dd, *J* = 14.0, 6.8 Hz,

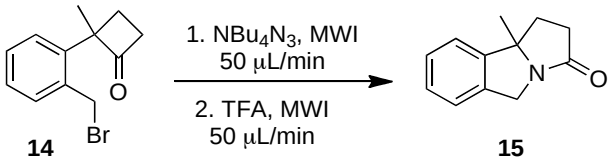
1H), 2.43 (m, 1H), 2.35 (dd, *J* = 15.6, 3.6 Hz, 1H), 1.97 – 1.76 (m, 3H), 1.58 – 1.45 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.2, 143.0, 107.1, 59.0, 51.5, 40.8, 37.8, 35.9, 29.6, 23.2; IR: 2930, 2857, 1626 cm^{-1}; HRMS (ESI) m/z calculated for $(M+H)^+$ ($C_{10}H_{16}NO^+$) 166.1232, found: 166.1227.



12a, X = Cl
12b, X = Br

13

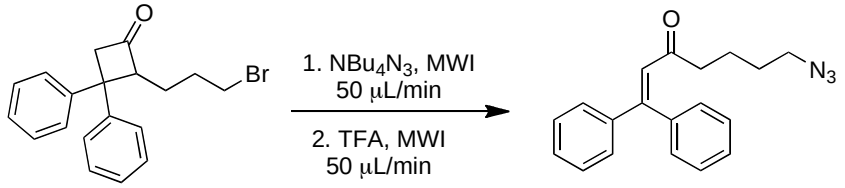
2-Benzylhexahydro-1H-pyrrolo[1,2-a][1,4]diazepin-5(2H)-one 13. Reaction of **12a** (266 mg, 1.00 mmol) performed at 125 W under the representative MACOS conditions described above afforded **13** (188 mg, 77%) as a pale-yellow oil and recovered **12a** (30 mg, 11%). Similarly, reaction of **12b** (233 mg, 0.75 mmol) performed at 125 W under the representative MACOS conditions described above afforded **13** (112 mg, 61%) as a pale-yellow oil and no recovered starting material. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 - 7.24 (m, 5H), 3.87 (q, *J* = 8.4 Hz, 1H), 3.75 (m, 1H), 3.58 (s, 2H), 3.30 (ddd, *J* = 11.6, 9.2, 6.4 Hz, 1H), 2.92 (m, 2H), 2.74 (m, 1H), 2.53 (dd, *J* = 14.4, 6.8 Hz, 1H,), 2.32 (t, *J* = 12.4 Hz, 1H,), 2.15 (m, 1H), 2.09 (dd, *J* = 12.8, 9.2 Hz, 1H,), 1.82 (m, 1H), 1.70 (m, 1H), 1.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 138.6, 129.4, 128.9, 127.7, 63.5, 62.3, 58.6, 51.2, 47.4, 39.4, 32.8, 23.8; IR: 2921, 1636 cm^{-1}. HRMS (ESI/APCI): *m/z* calculated for $(M)^+$ ($C_{15}H_{21}ClNO^+$) 245.1576, found: 245.1456.



14

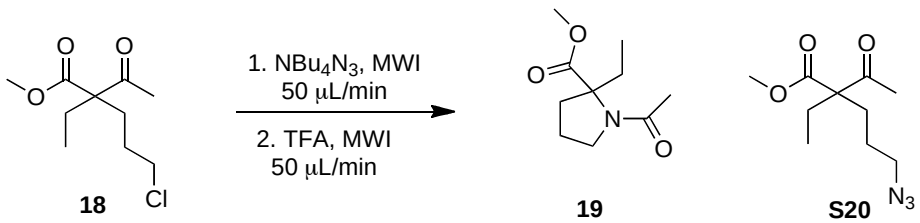
15

9b-Methyl-5,9b-dihydro-1*H*-pyrrolo[2,1-*a*]isoindol-3(2*H*)-one 15. Reaction of **14** (166 mg, 0.65 mmol) performed at 300 W under the representative MACOS conditions described above afforded **15** (66 mg, 54%) as a brown solid. MP = 83.4 – 96.9 ºC; ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.27 (m, 4H), 4.90 (d, *J* = 15.2 Hz, 1H), 4.24 (d, *J* = 15.2 Hz, 1H), 2.92 (m, 1H), 2.40 (m, 2H), 2.28 (dt, *J* = 12.0, 9.2 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.8, 146.7, 137.7, 127.7, 127.6, 123.0, 120.9, 72.1, 47.0, 35.3, 32.7, 26.8; IR: 2963, 1682 cm^{-1}; HRMS (ESI) m/z calculated for $(M+H)^+$ ($C_{12}H_{14}NO$) 188.1075, found 188.1107.



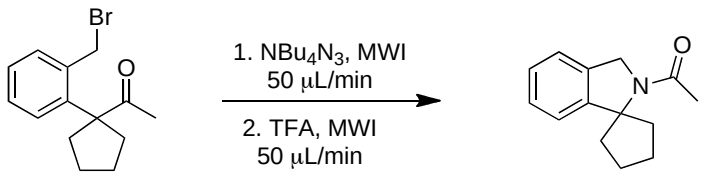
16 **17**

7-azido-1,1-diphenylhept-1-en-3-one 17. Reaction of **16** (364 mg, 1.06 mmol) performed at 300 W under the representative MACOS conditions described above afforded **17** (270 mg, 83%) as an orange oil. ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.41 – 7.29 (m, 8H), 7.22 – 7.19 (m, 2H), 6.59 (s, 1H), 3.17 (t, *J* = 6.8 Hz, 2H), 2.26 (t, *J* = 6.8 Hz, 2H), 1.53 (m, 2H), 1.44 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.4, 153.5, 140.7, 138.9, 129.4, 129.3, 128.5, 128.3, 128.3, 128.2, 126.3, 51.0, 42.1, 28.1, 21.2; IR: 3058, 2934, 2091, 1689, 1655 cm^{-1}; HRMS (ESI) m/z calculated for $(M+H)^+$ ($C_{19}H_{20}N_3O$) 306.1606, found 306.1611. (2D data included with spectra).



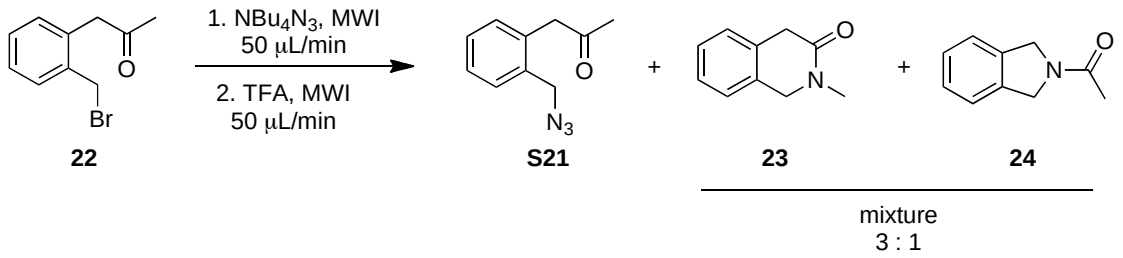
18 **19** **S20**

Methyl 1-acetyl-2-ethylpyrrolidine-2-carboxylate 19. Reaction of **18** (264 mg, 1.28 mmol) performed at 200 W under the representative MACOS conditions described above afforded **S20** (180 mg, 66%) as a yellow oil and recovered **19** (12 mg, < 5% contains impurity). For azide **S20**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.75 (s, 3H), 3.30 (m, 2H), 2.14 (s, 3H), 1.92 (m, 4H), 1.40 (m, 2H), 0.79 (t, *J* = 7.6 Hz, 3H,); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.1, 173.0, 63.7, 52.6, 51.7, 28.2, 26.9, 24.7, 23.8, 8.4; IR: 2955, 2094, 1741, 1710 cm^{-1}; MS: 199 (1), 178 (35), 115 (100). Data for amide **19**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (m, 1H), 3.70 (s, 3H), 3.51 (m, 1H), 2.42 (m, 1H), 2.08 (s, 3H), 2.04 (m, 3H), 1.92 (m, 2H), 0.83 (t, *J* = 7.2 Hz, 3H,); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 169.2, 69.1, 52.4, 50.0, 35.4, 26.3, 24.04, 23.3, 8.2; IR: 2969, 1735, 1645 cm^{-1}; HRMS (ESI) *m/z* calculated for $(M+H)^+$ $(C_{10}H_{18}NO_3)^+$ 200.1308 found: 200.1321.

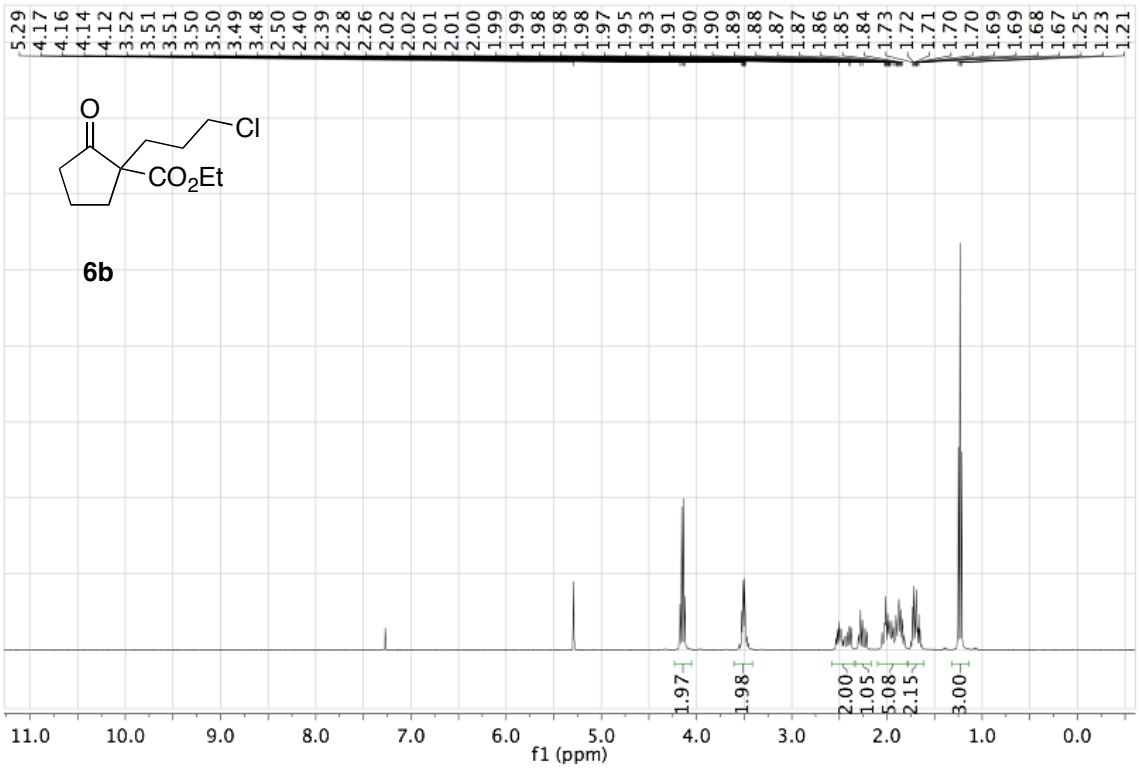


20 **21**

1-(Spiro[cyclopentane-1,1'-isoindolin]-2'-yl)ethanone 21. Reaction of **20** (242 mg, 0.861 mmol) performed at 300 W under the representative MACOS conditions described above afforded **21** (125 mg, 67%) as white solid and an uncharacterized impurity (37 mg). MP = 145.0 – 146.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33—7.17 (m, 4H), 4.78 (s, 2H), 2.68 (m, 2H), 2.22 (m, 2H), 2.15 (s, 3H), 1.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 150.2, 133.2, 128.6, 127.3, 121.9, 121.8, 76.7, 54.2, 40.1, 27.5, 24.6; IR: 2939, 1650 cm^{-1}; HRMS (ESI) *m/z* calculated for $(M+H)^+$ $(C_{14}H_{18}NO^+)$ 216.1410, found: 216.1412.



2-methyl-1,2-dihydroisoquinolin-3(4*H*)-one 23, and **1-(isoindolin-2-yl)ethanone 24.** Reaction of **22** (163 mg, 0.72 mmol) performed at 300 W under the representative MACOS conditions described above afforded azide **S21** (55 mg, 40%) as a light-brown oil and amides **23** and **24** (39 mg, 33%) as a 3 : 1 mixture as determined by ^{1}H NMR spectroscopy. Analytical amounts of amides **23** and **24** were separated via silica gel column chromatography (40 to 100% ethyl acetate in hexanes). Data for each amide is consistent with data found in the literature.[7] Data for azide **S21**: ^{1}H NMR ($CDCl_3$, 400 MHZ) δ 7.36 – 7.31 (m, 3H), 7.20 (m, 1H), 4.32 (s, 2H), 3.83 (s, 2H), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 205.6, 134.0, 133.4, 131.3, 130.0, 128.9, 127.7, 52.9, 48.0, 29.2; IR: 3026, 2097, 1719 cm^{-1}; HRMS (ESI) m/z calculated for $(M+Na)^+$ $(C_{10}H_{11}N_3ONa)^+$ 212.0800, found: 212.0799.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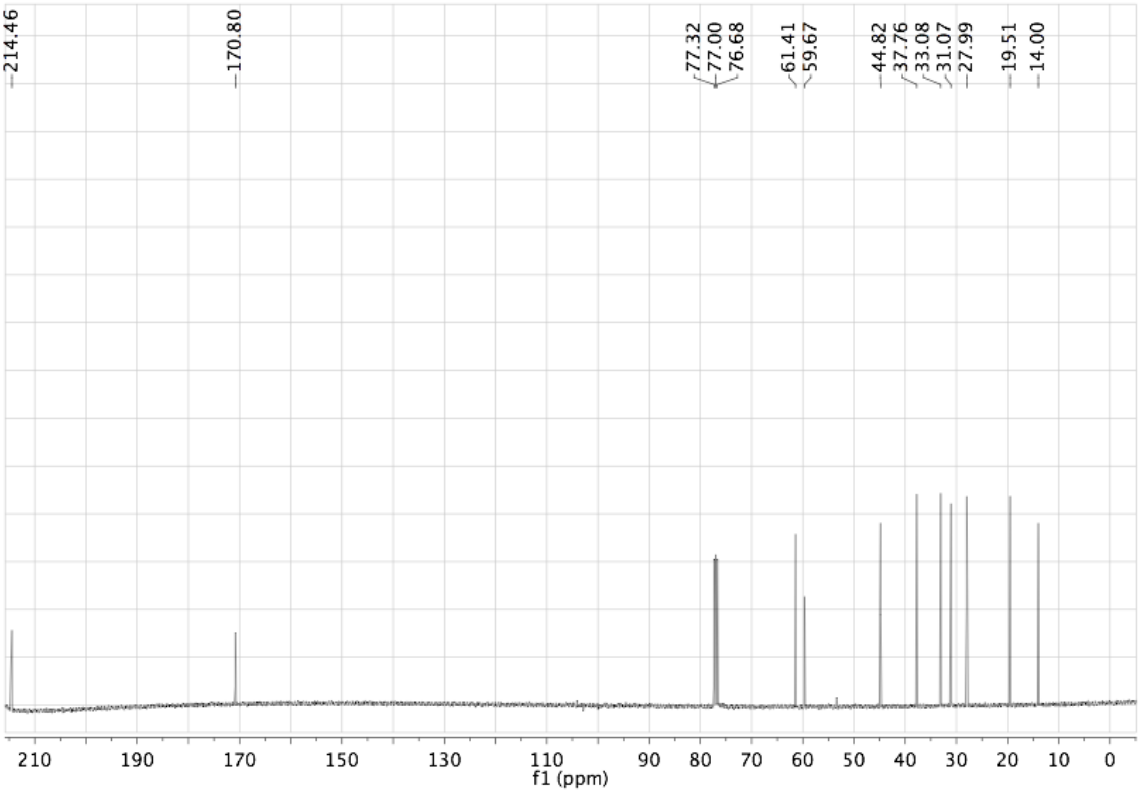
O
Cl
CO2Et
6b
1.97 1.98 2.00 1.05 5.08 2.15 3.00
11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
f1 (ppm)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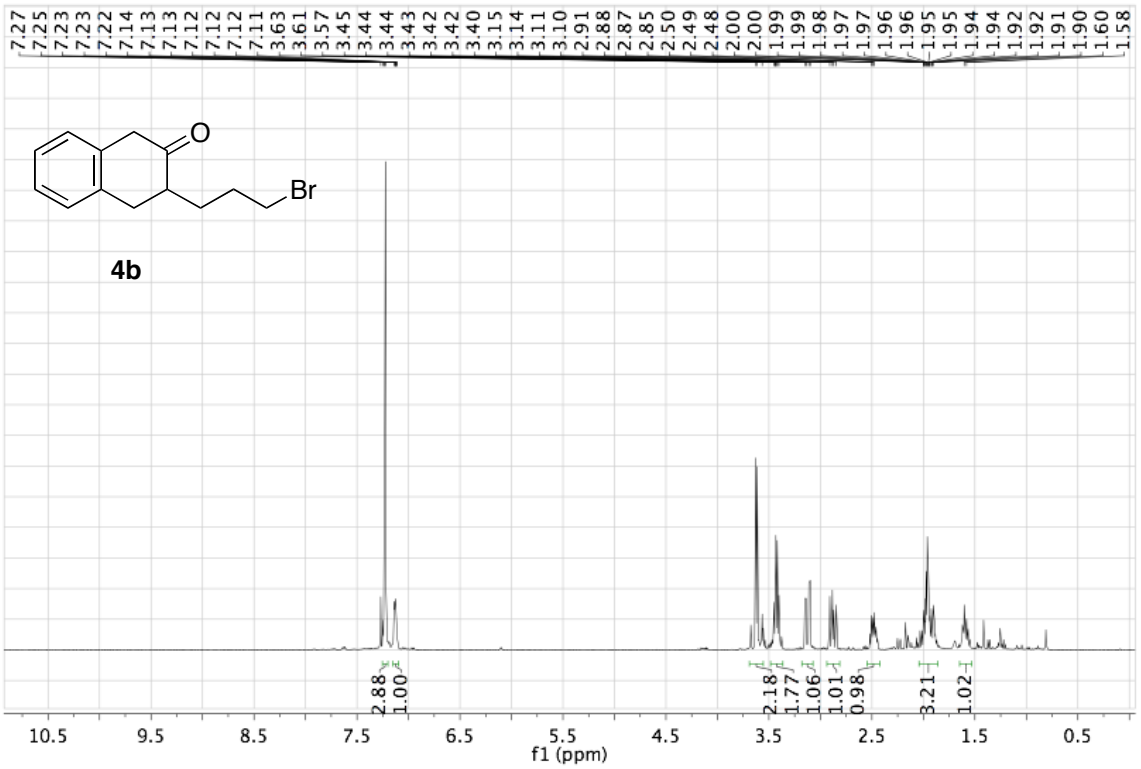
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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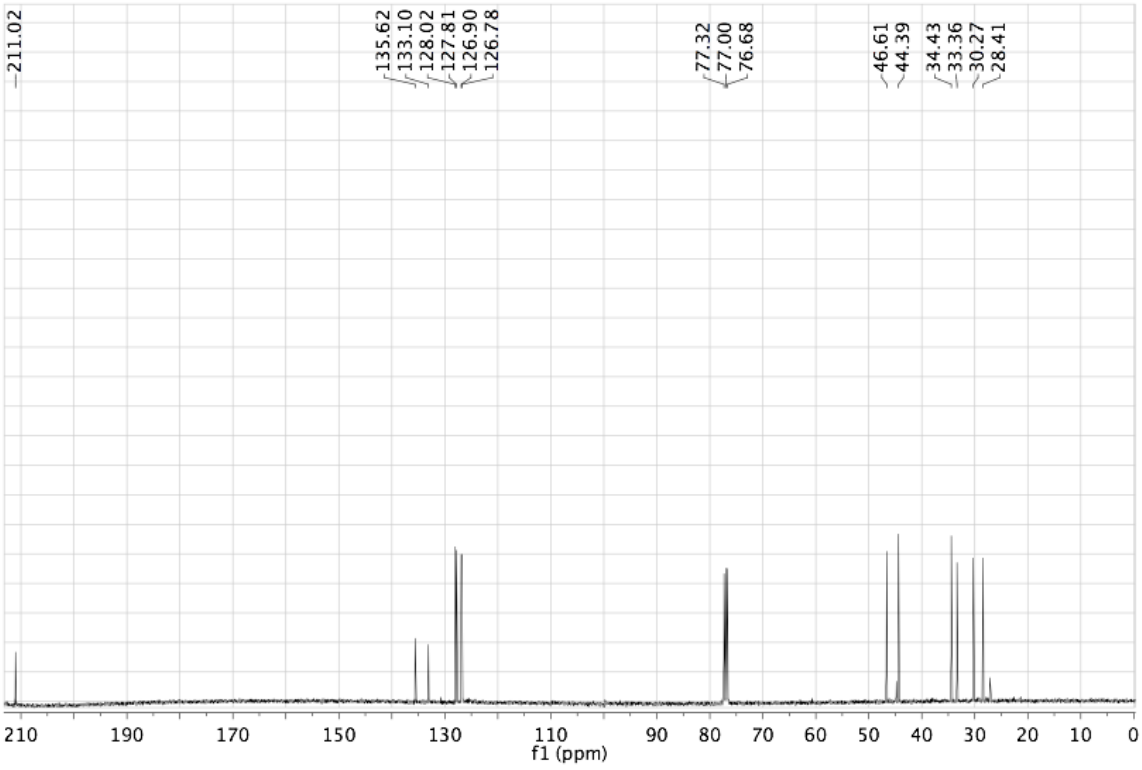
O
Br
4b
2.88 1.00 2.18 1.77 1.06 1.01 0.98 3.21 1.02
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)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135.62 133.10 128.02 127.81 126.90 126.78
77.32 77.00 76.68
46.61 44.39 34.43 33.36 30.27 28.41
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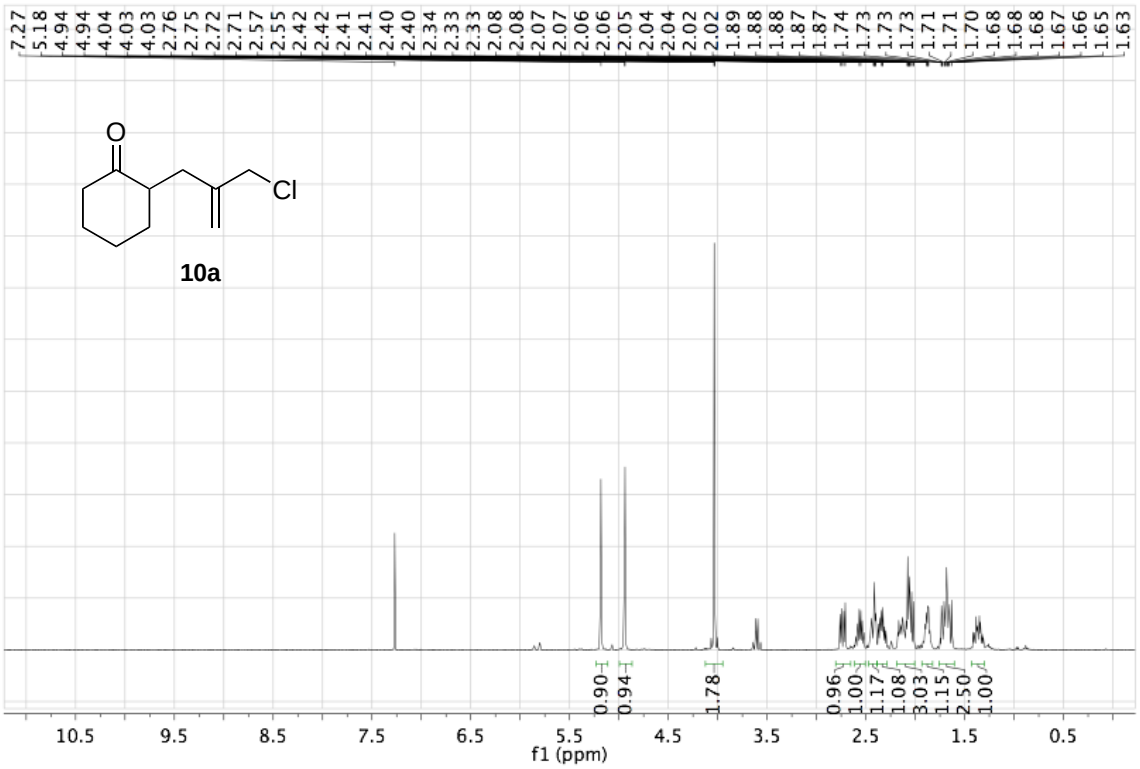
f1 (ppm)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2.41
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2.08
2.08
2.07
2.07
2.06
2.06
2.05
2.04
2.04
2.02
2.02
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1.68
1.67
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1.63
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1.08
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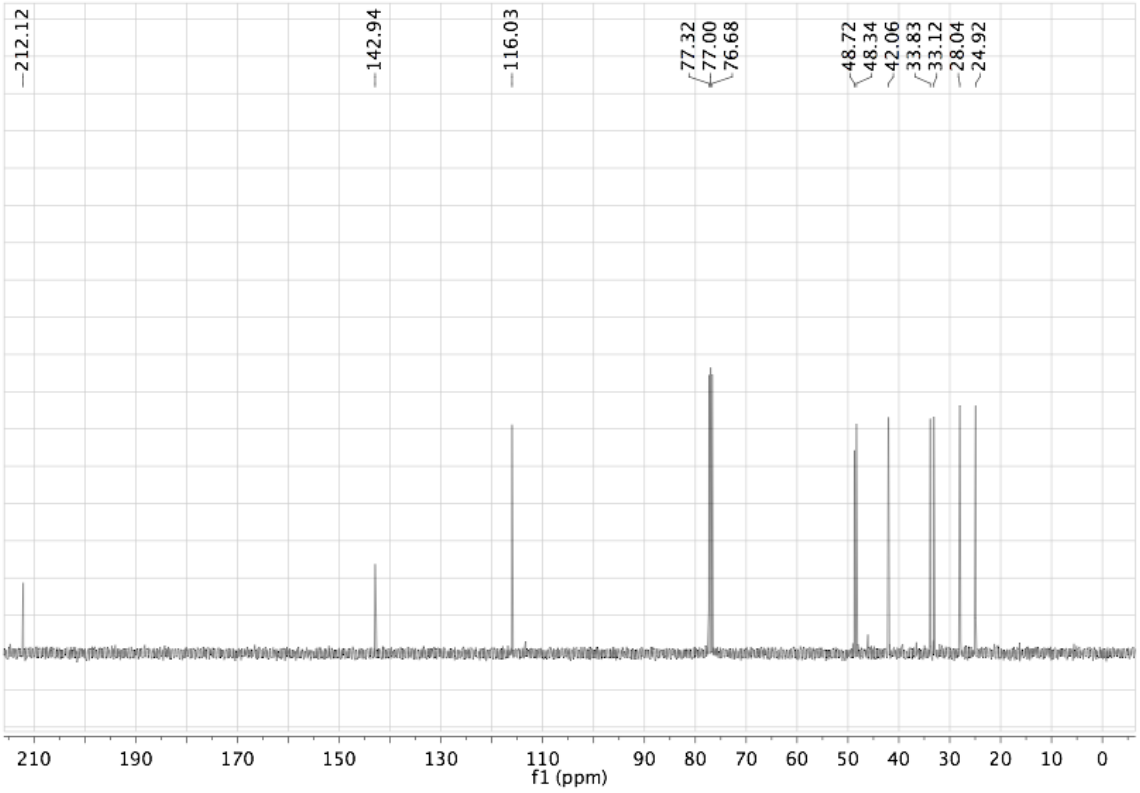
f1 (ppm)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76.68
48.72
48.34
42.06
33.83
33.12
28.04
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90
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50
40
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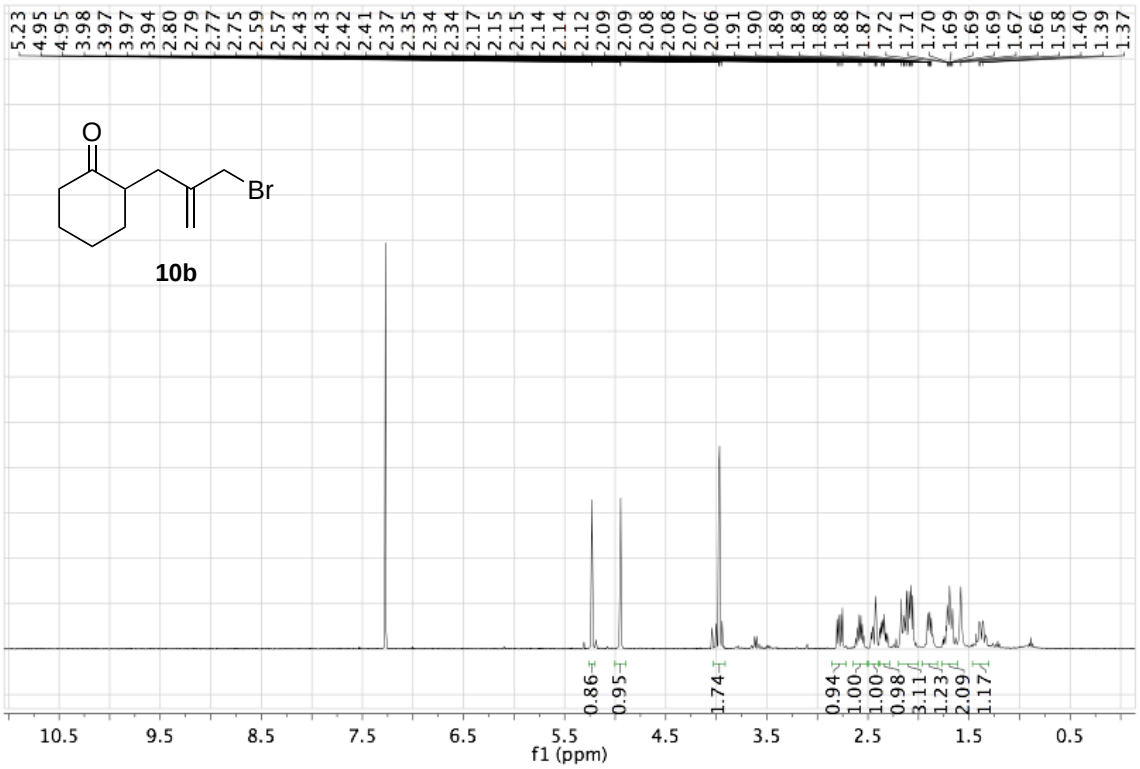
10
0
f1 (ppm)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Br
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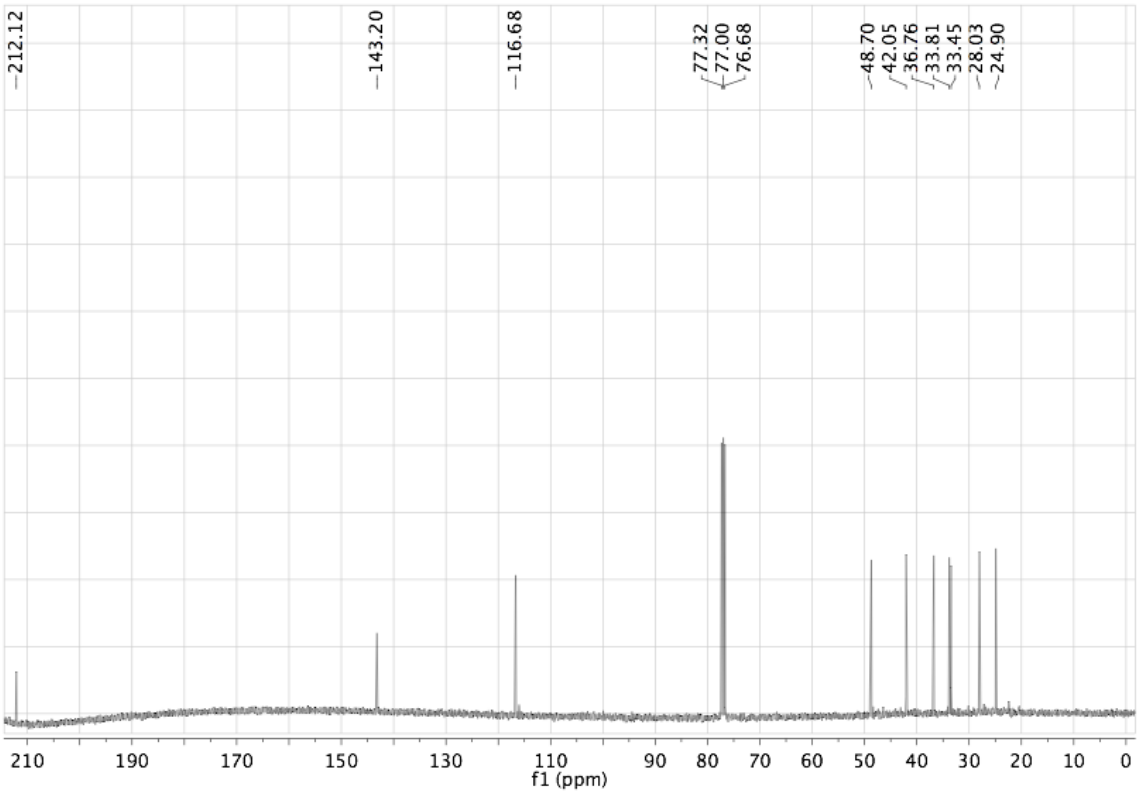
f1 (ppm)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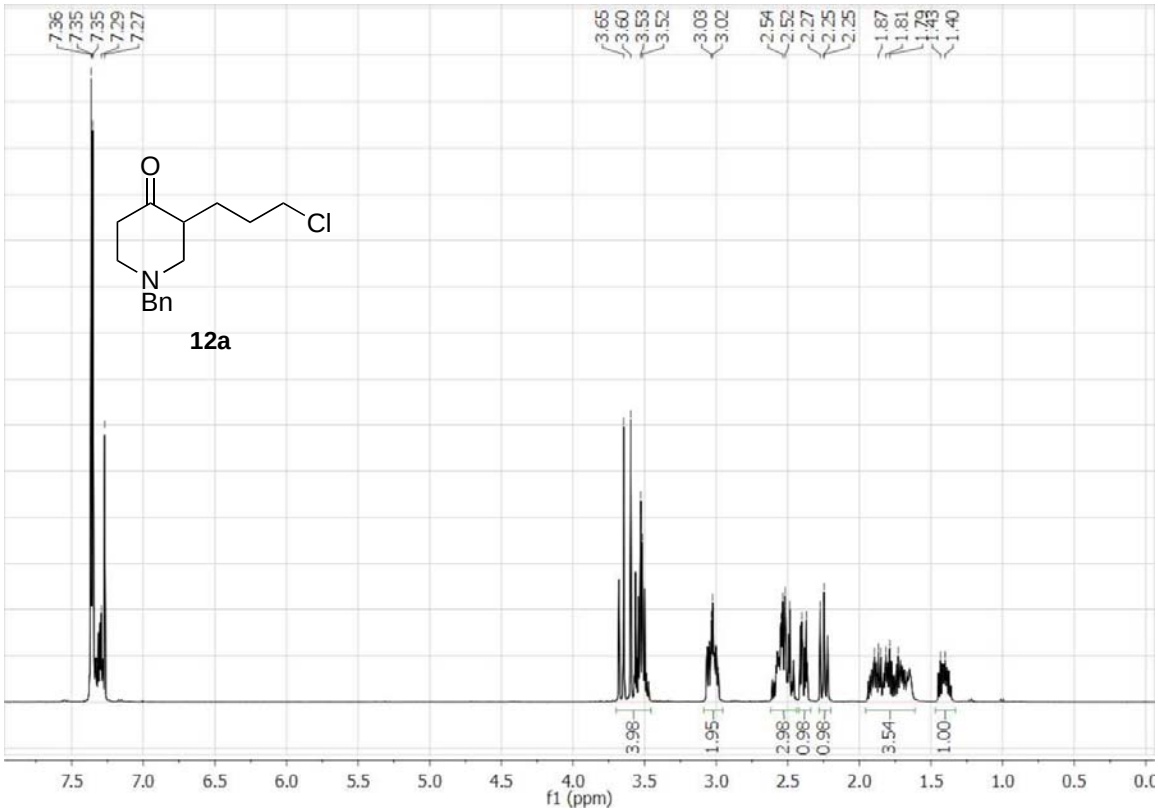
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1.79
1.43
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Cl
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Bn
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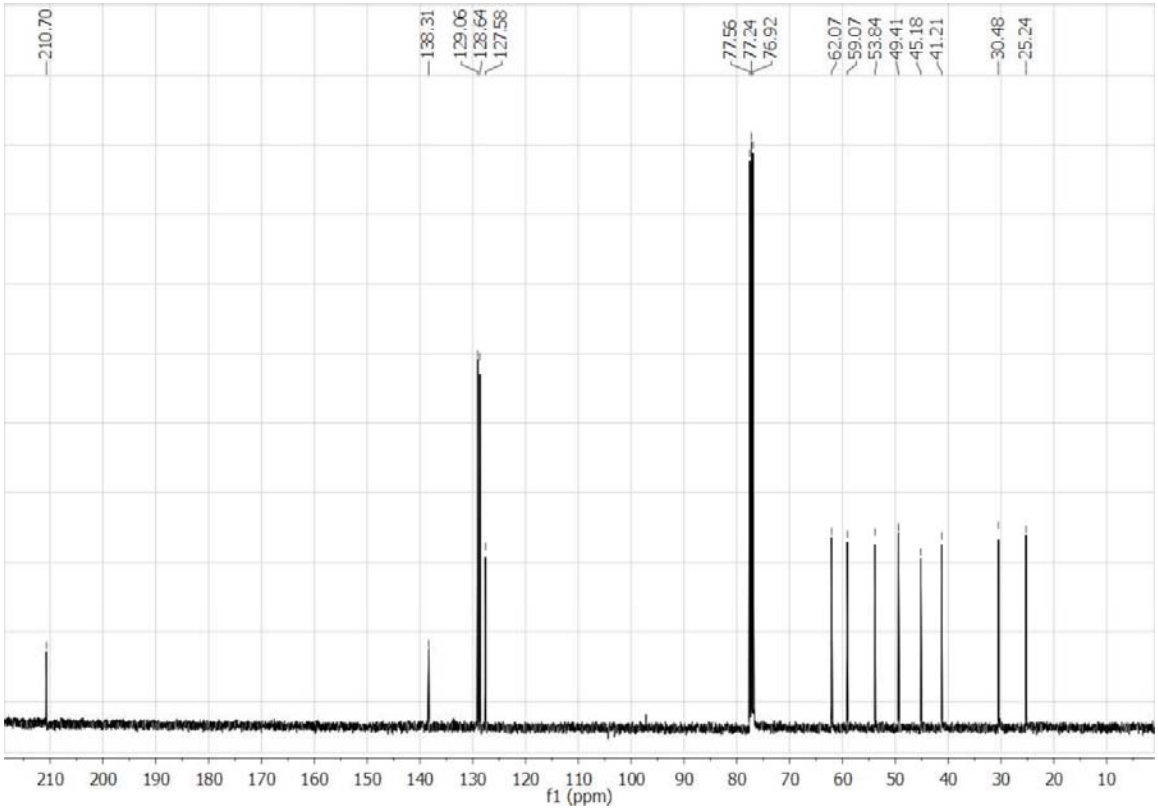
3.54
1.00
f1 (ppm)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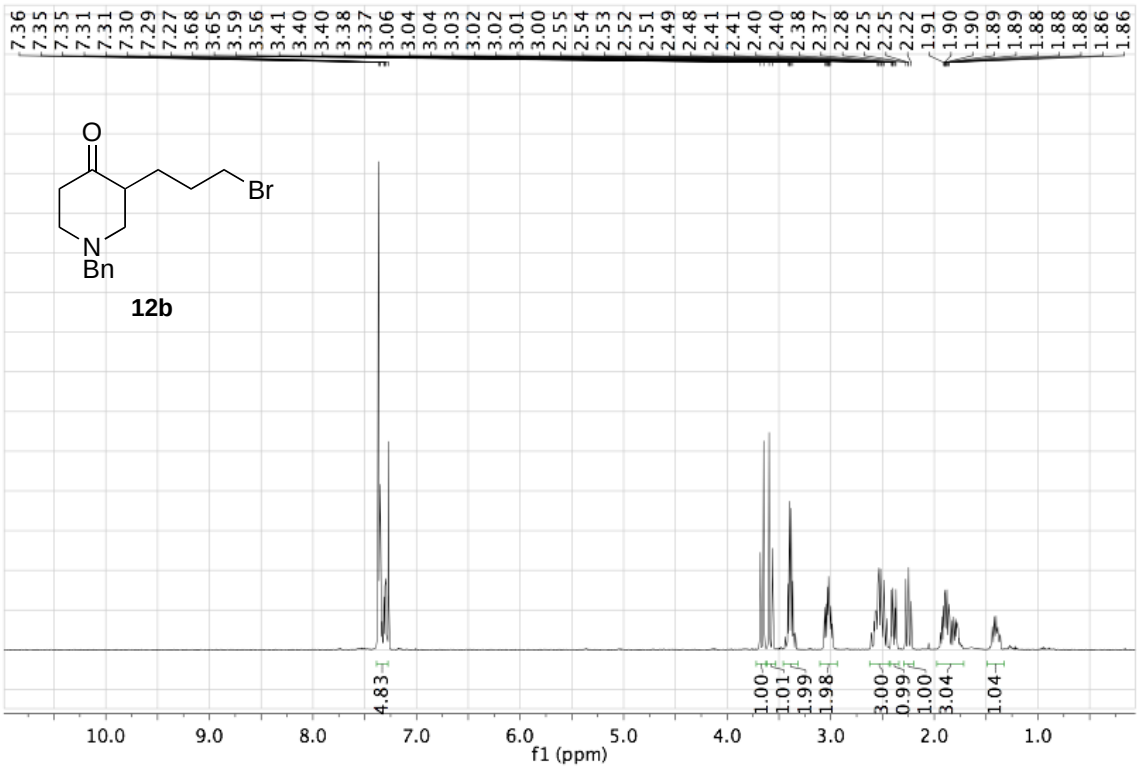
25.24
f1 (ppm)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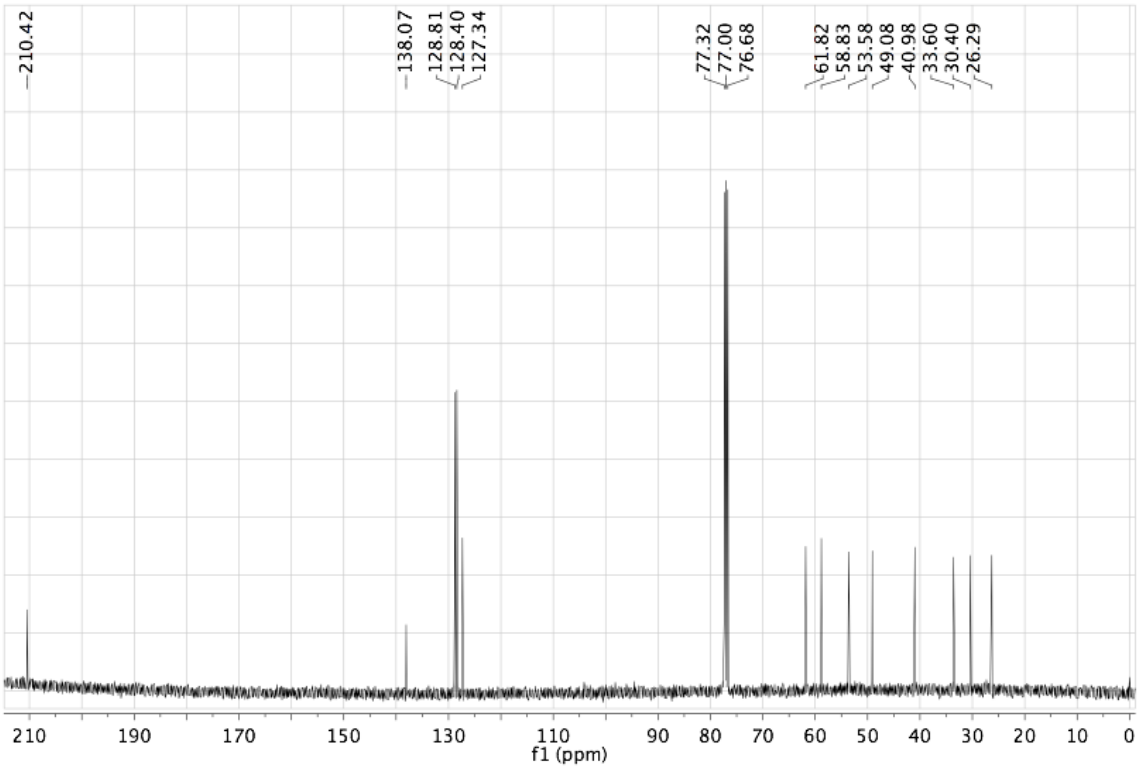
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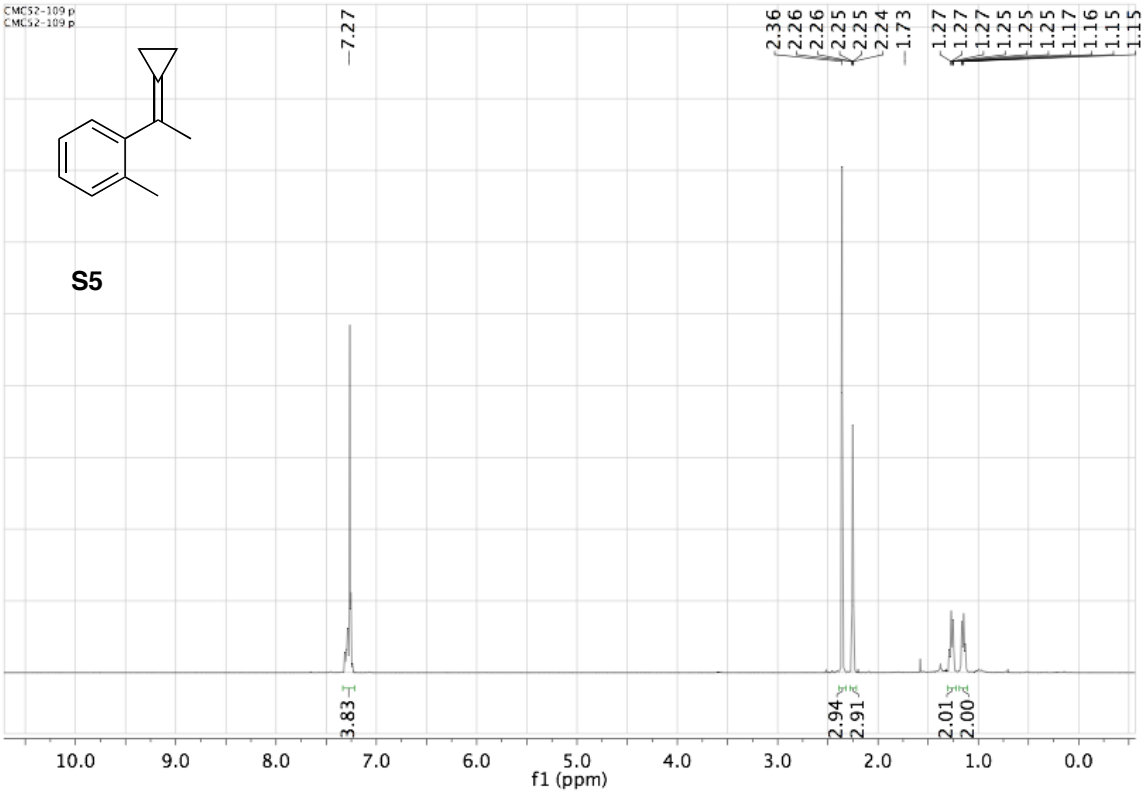
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CMCS2-109 p
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2.01
2.00
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8.0
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3.0
2.0
1.0
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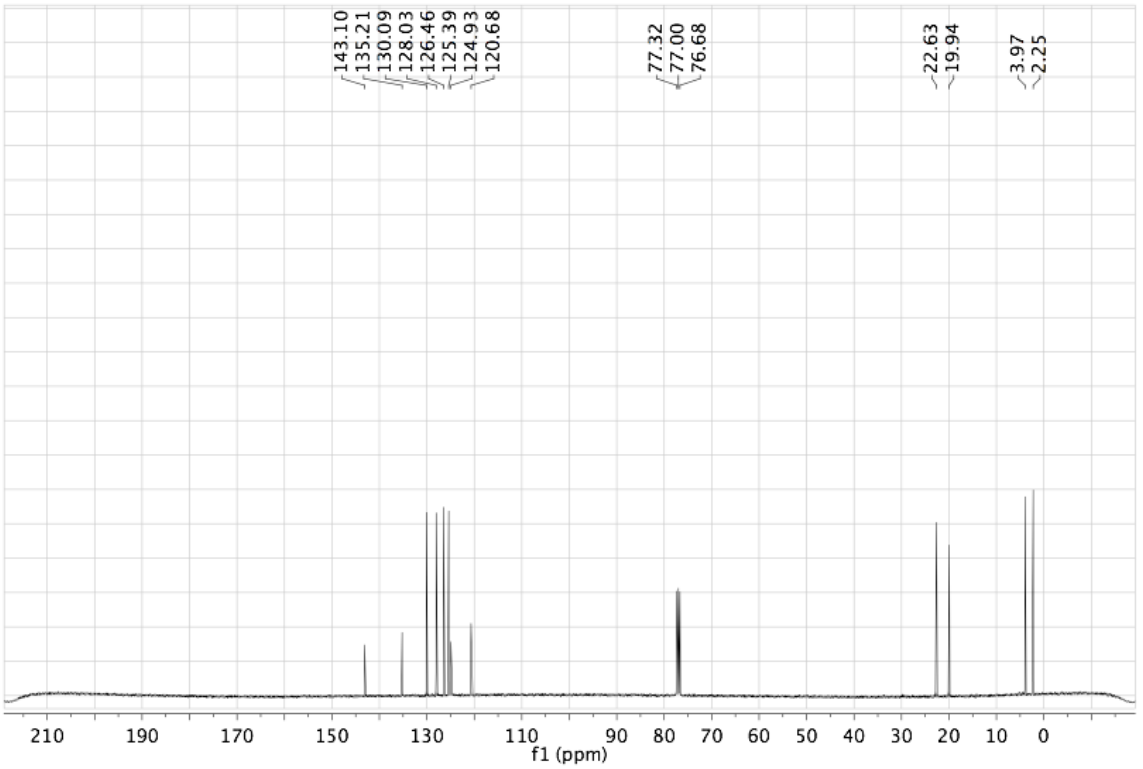
f1 (ppm)

S5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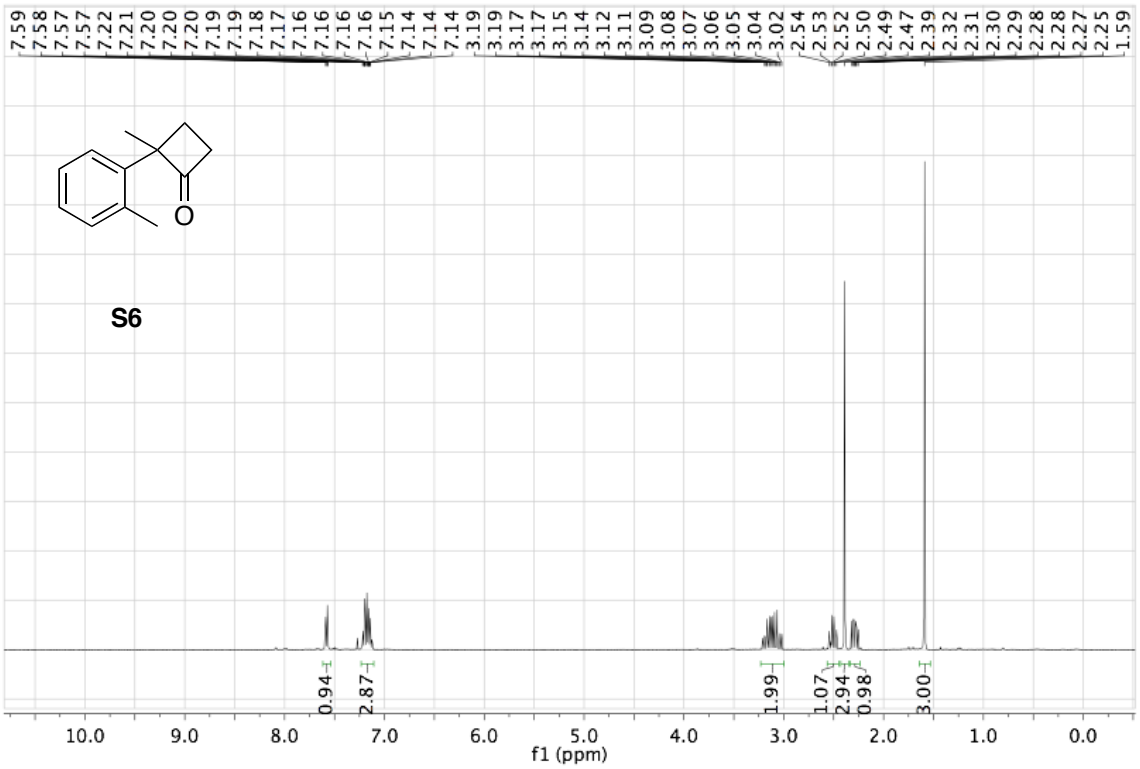
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O
S6
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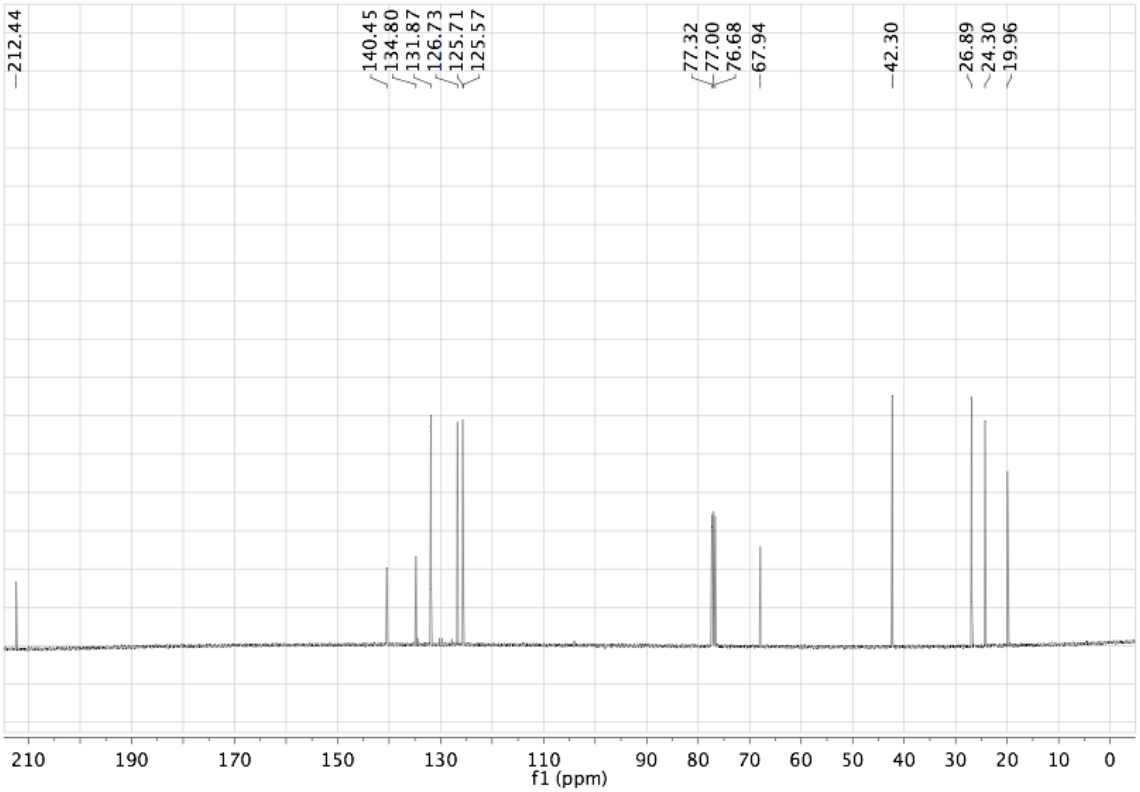
f1 (ppm)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26.89 24.30 19.96
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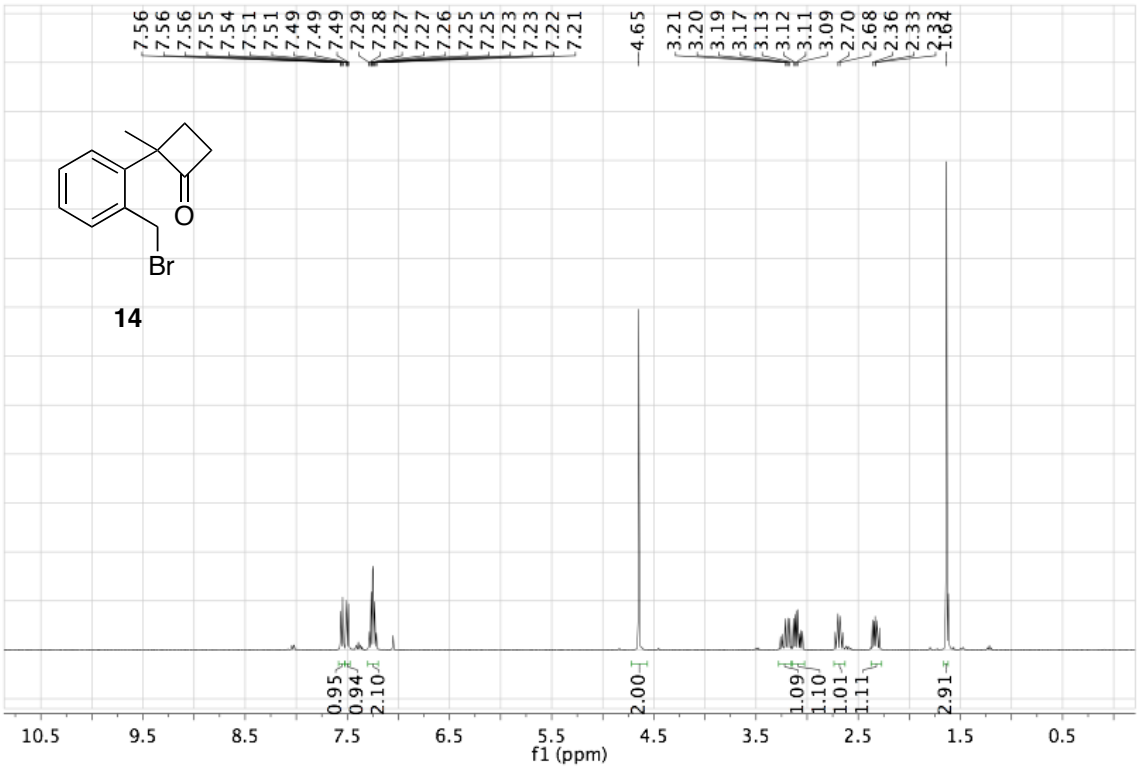
f1 (ppm)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3.17
3.13
3.12
3.11
3.09
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Br
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0.94
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2.00
1.09
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1.01
1.11
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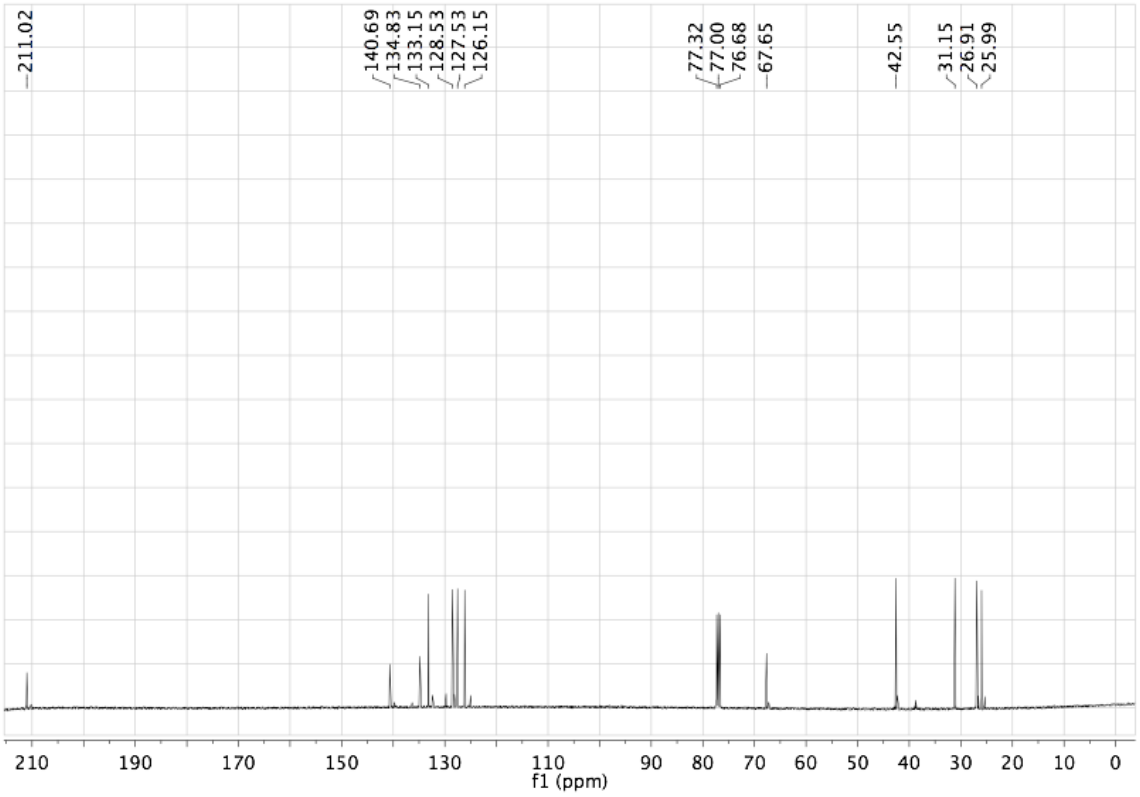
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26.91
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150
130
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90
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50
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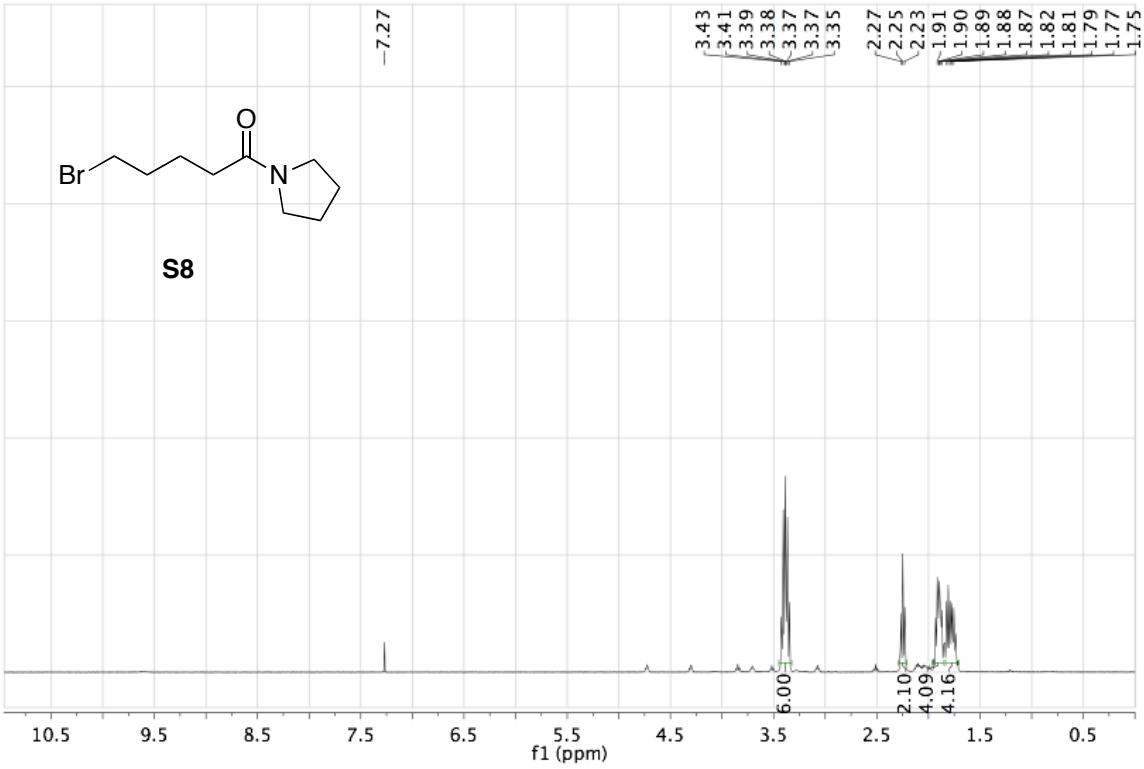
0
f1 (ppm)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1.77
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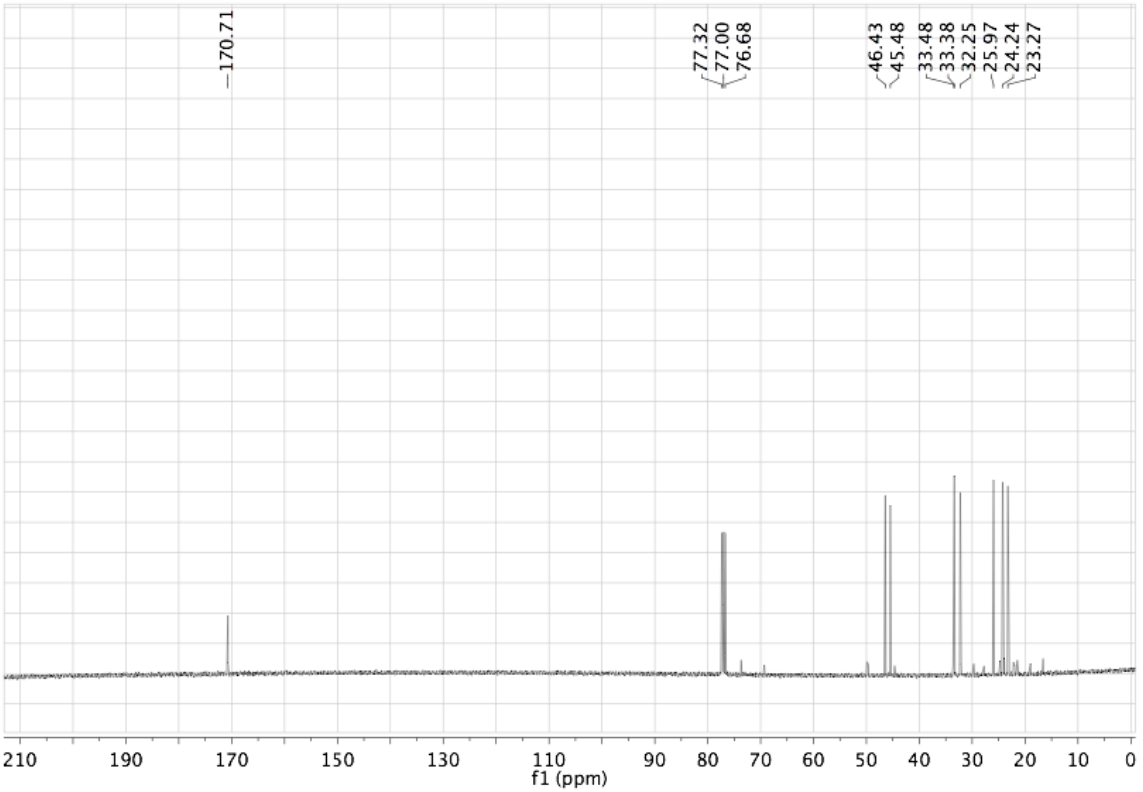
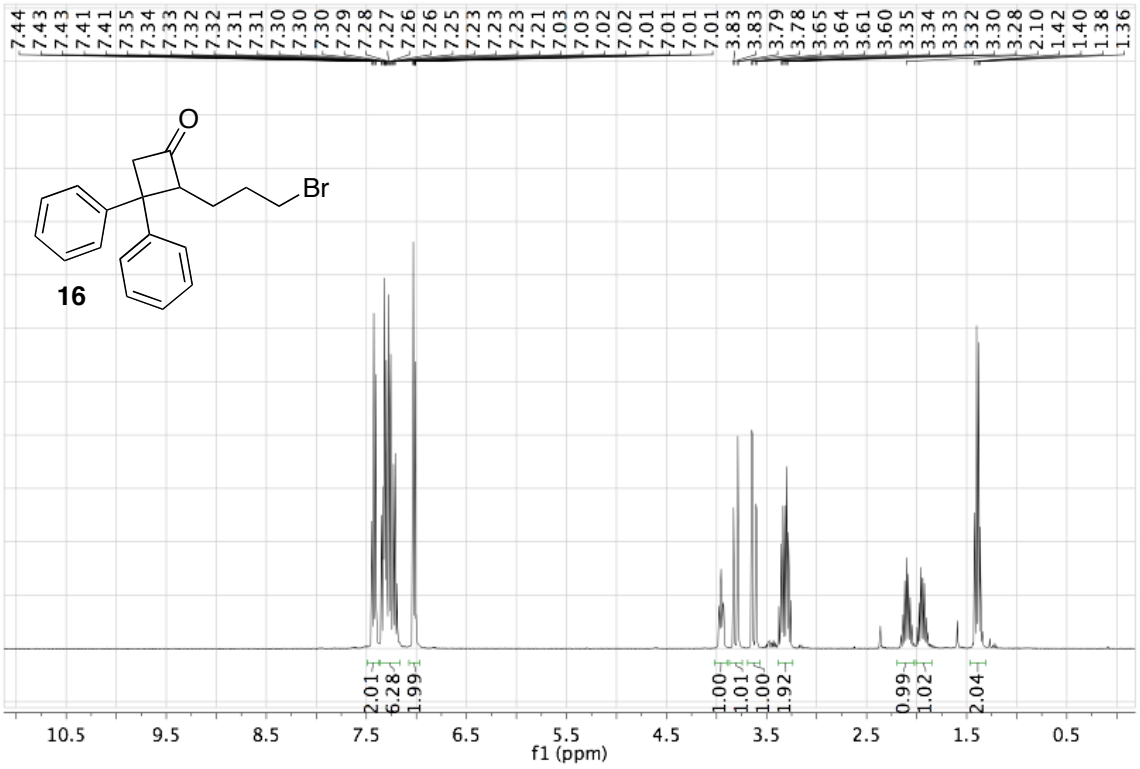
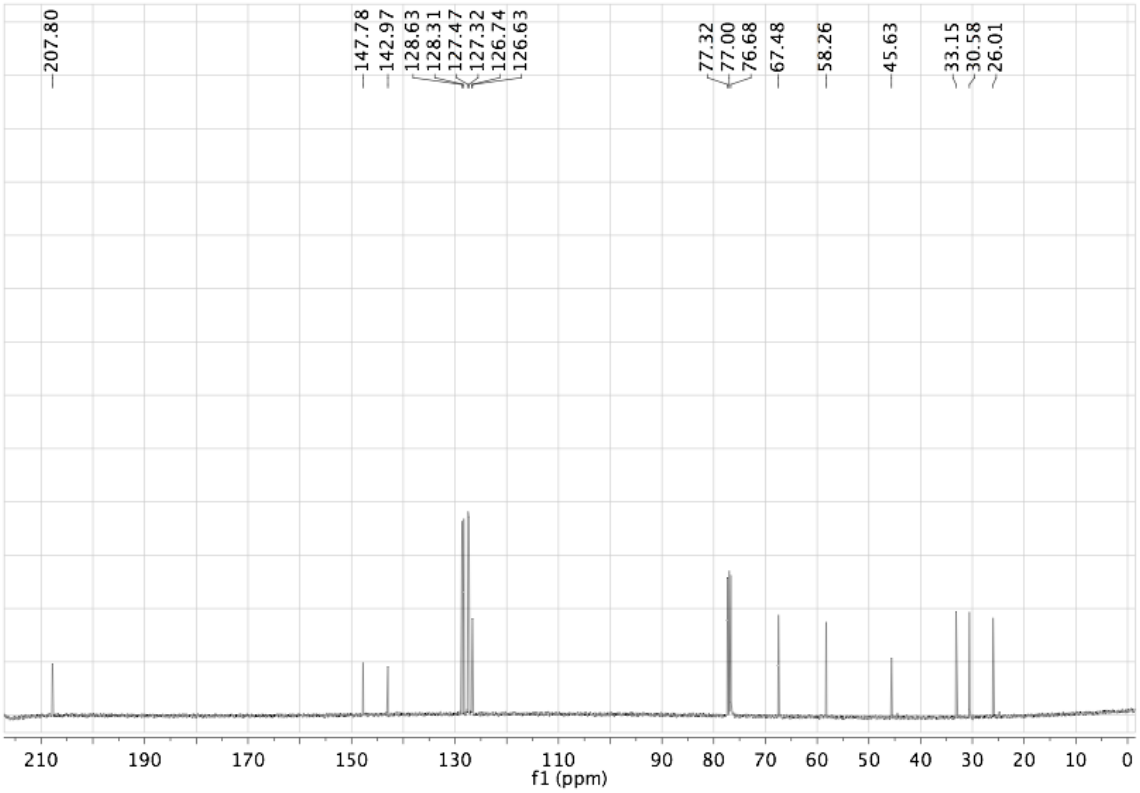
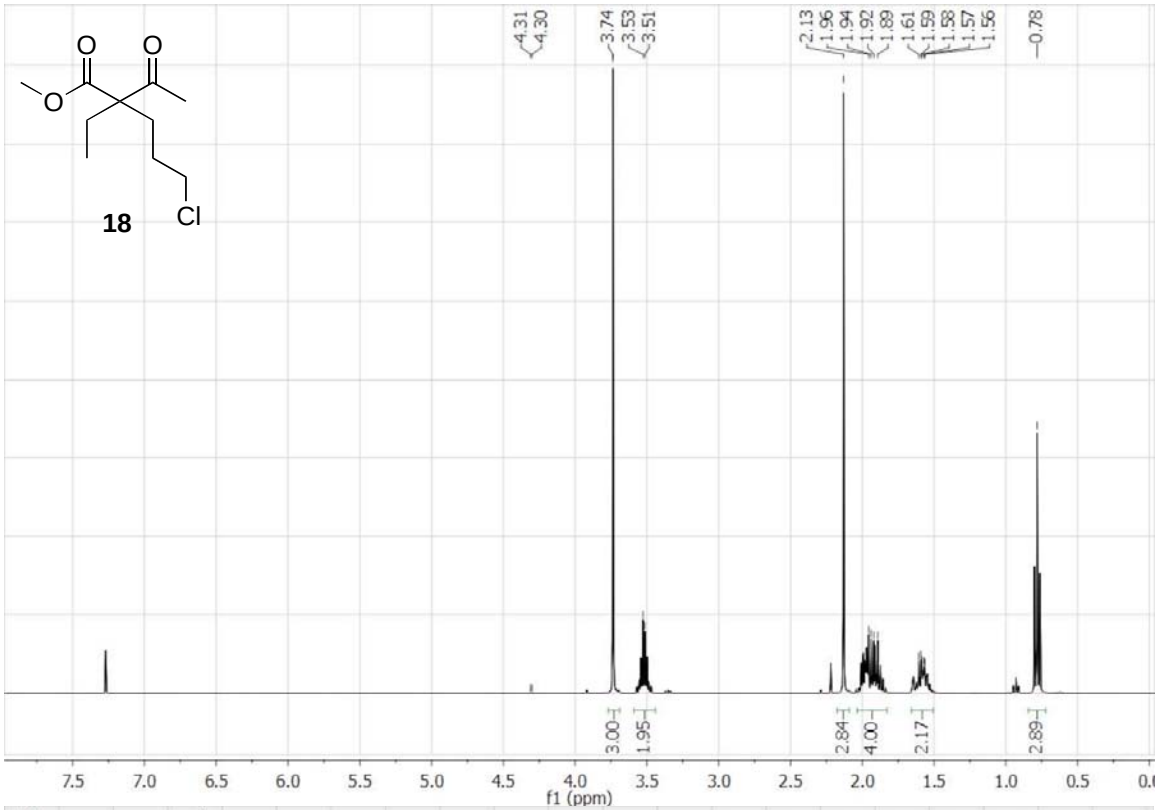
4.09
4.16
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

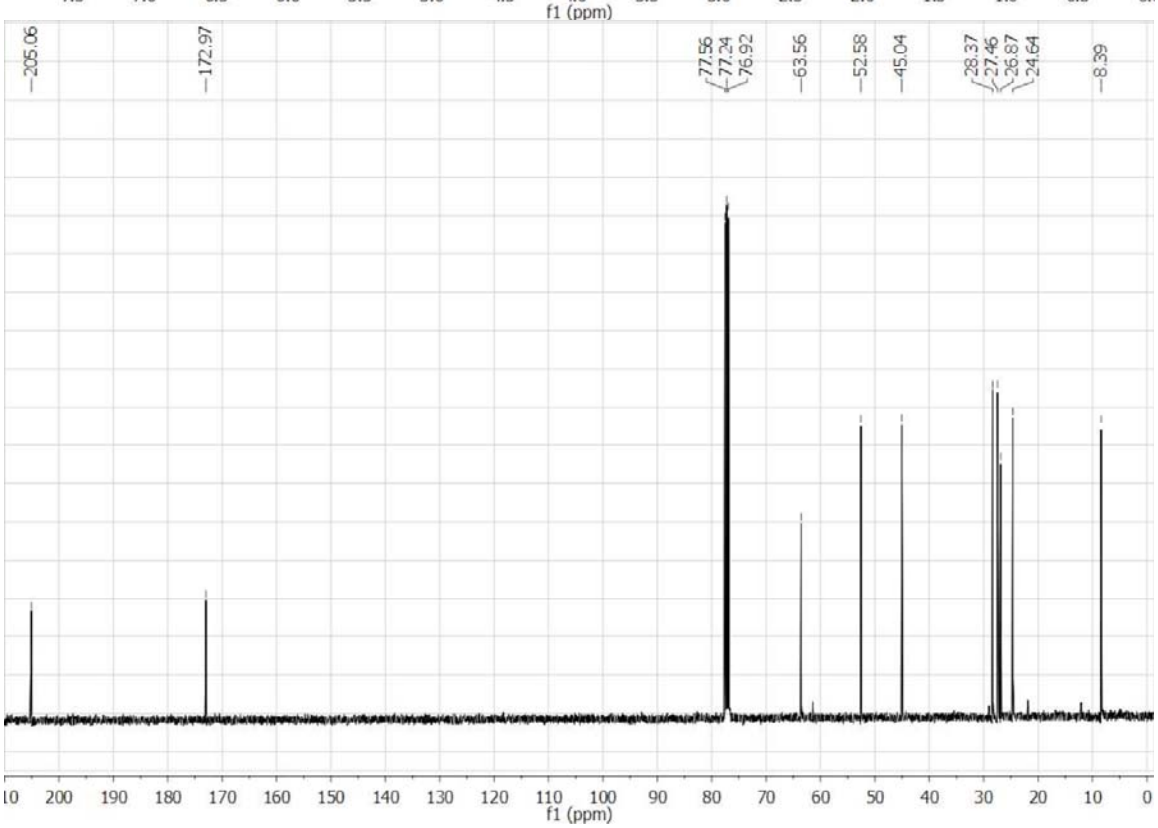
S8

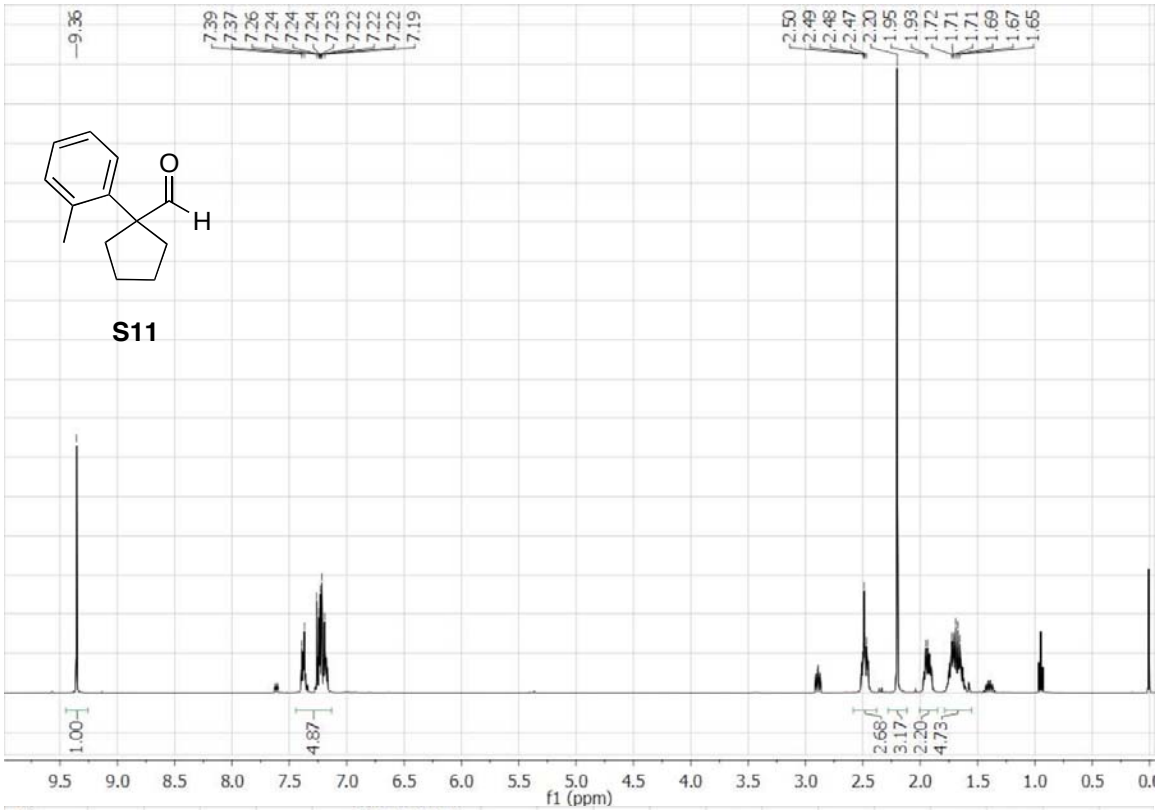

170.71
77.32
77.00
76.68
46.43
45.48
33.48
33.38
32.25
25.97
24.24
23.27
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
Br
16
7.44 7.43 7.43 7.41 7.41 7.35 7.34 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.30 7.29 7.28 7.27 7.26 7.26 7.25 7.23 7.23 7.23 7.21 7.03 7.03 7.02 7.02 7.01 7.01 7.01 7.01 3.83 3.83 3.79 3.78 3.65 3.64 3.61 3.60 3.35 3.34 3.33 3.32 3.30 3.28 2.10 1.42 1.40 1.38 1.36
2.01 6.28 1.99 1.00 1.01 1.00 1.92 0.99 1.02 2.04
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)

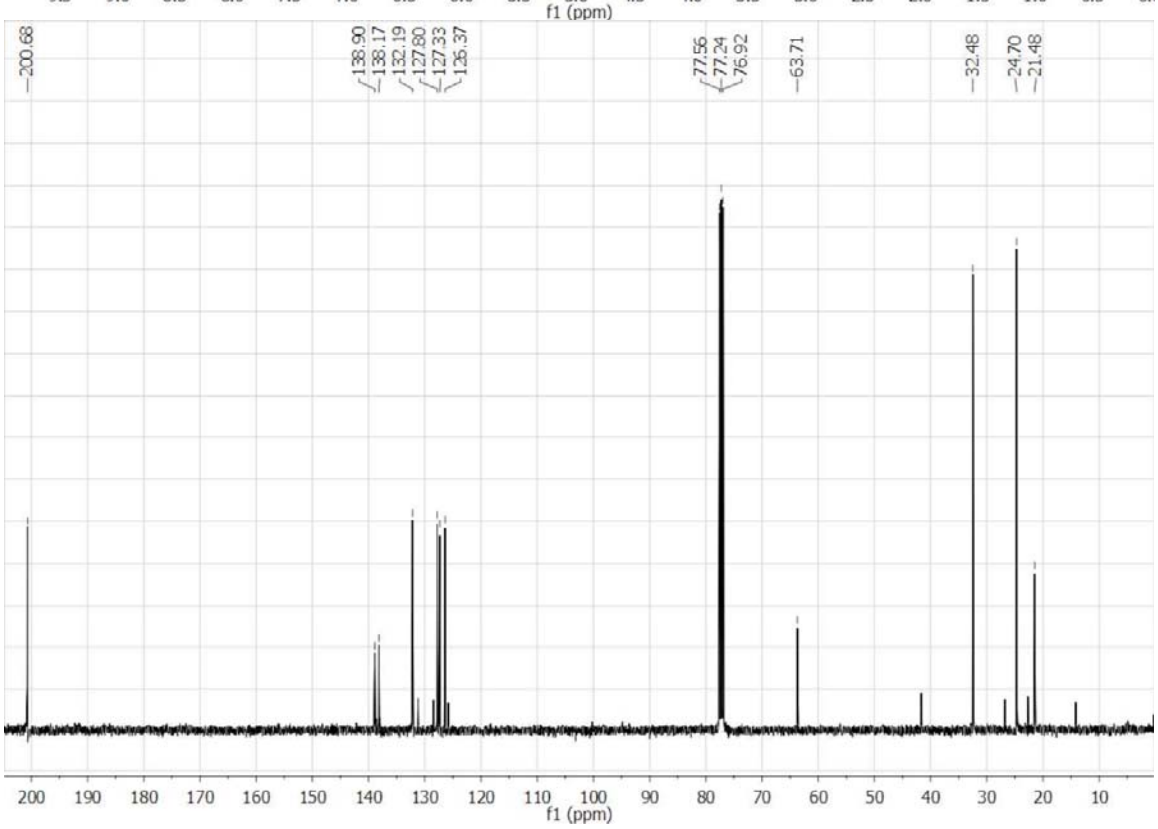

207.80
147.78 142.97 128.63 128.31 127.47 127.32 126.74 126.63
77.32 77.00 76.68 67.48 58.26 45.63 33.15 30.58 26.01
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

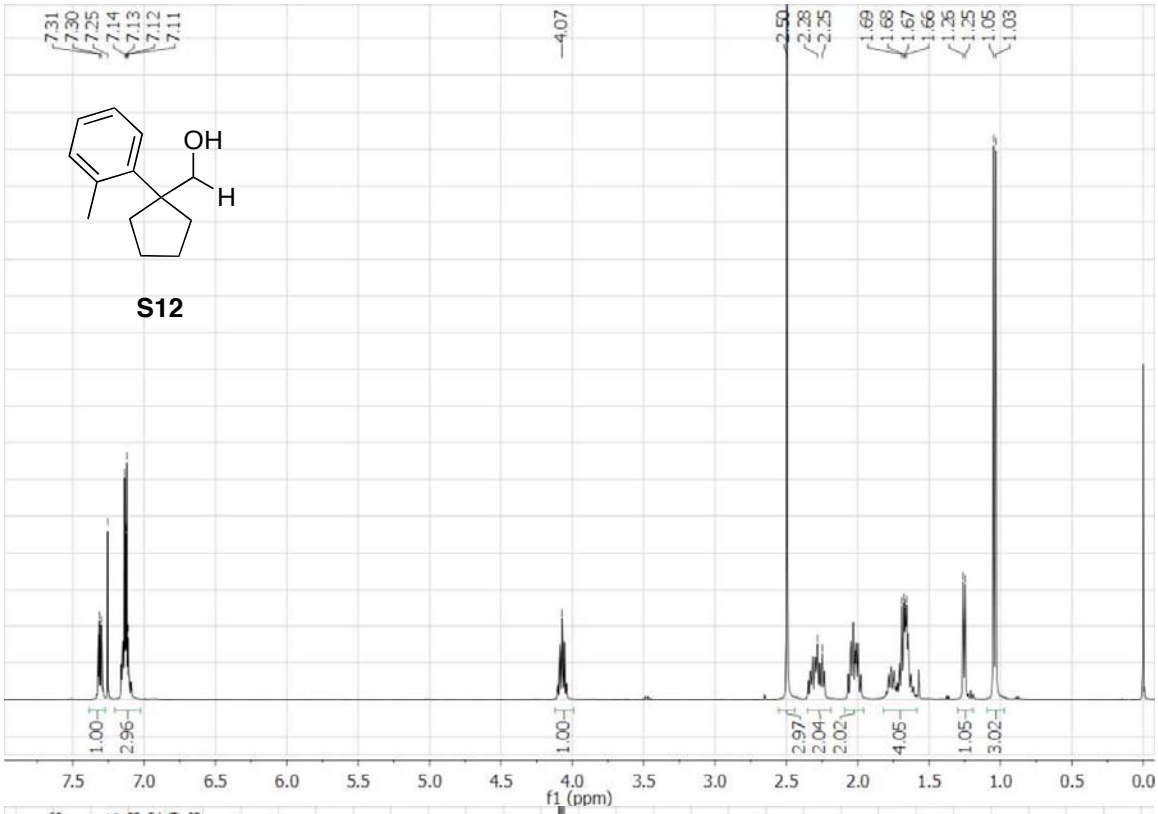

O
O
O
Cl
18
4.31
4.30
3.74
3.53
3.51
2.13
1.96
1.94
1.92
1.89
1.61
1.59
1.58
1.57
1.56
0.78
3.00
1.95
2.84
4.00
2.17
2.89
f1 (ppm)


205.06
172.97
77.56
77.24
76.92
63.56
52.58
45.04
28.37
27.46
26.87
24.64
8.39
f1 (ppm)

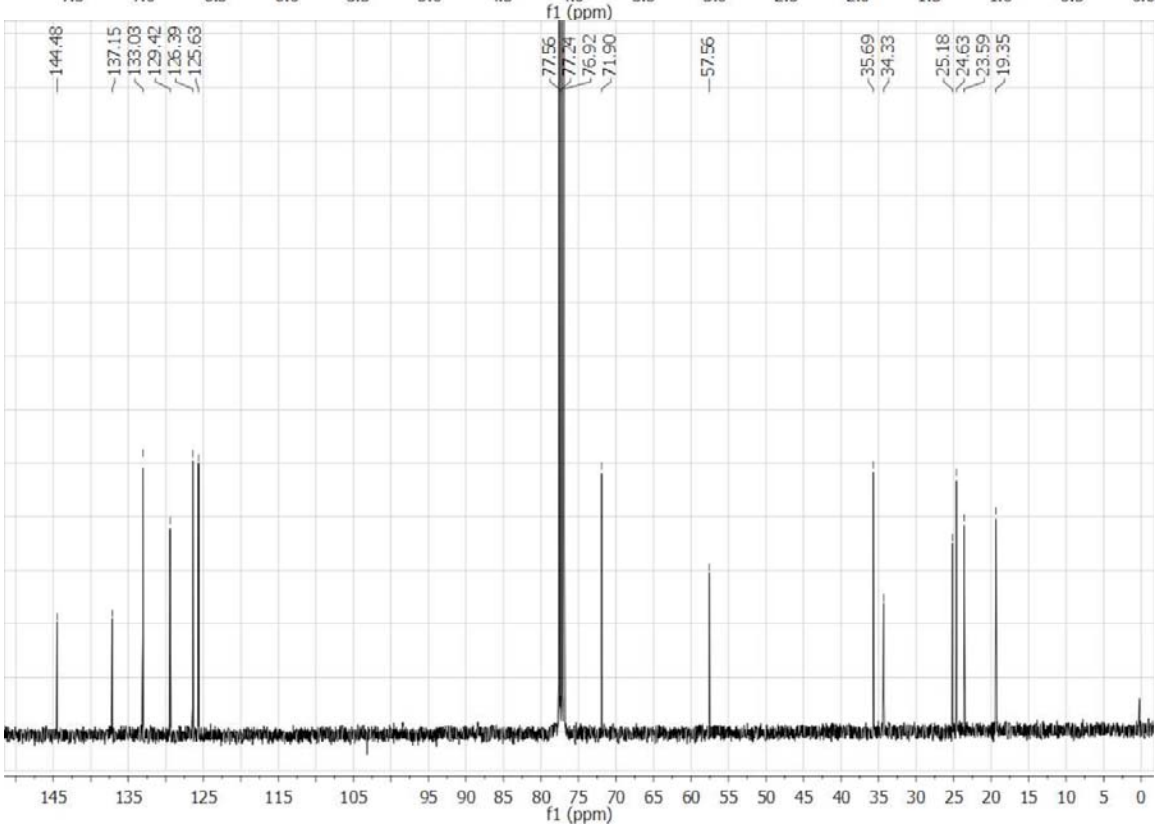

9.36
7.39
7.37
7.26
7.24
7.24
7.24
7.23
7.22
7.22
7.22
7.19
2.50
2.49
2.48
2.47
2.20
1.95
1.93
1.72
1.71
1.71
1.69
1.67
1.65
O
H
1.00
4.87
2.68
3.17
2.20
4.73
f1 (ppm)

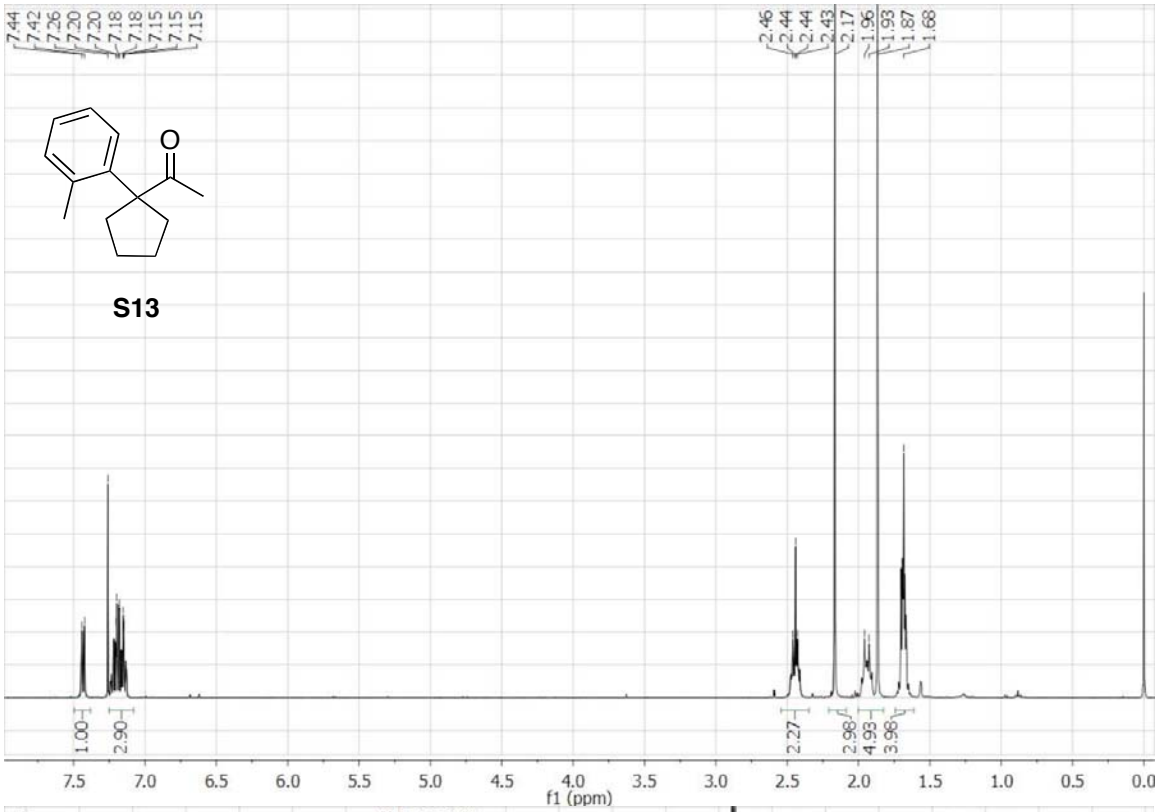
S11


200.68
138.90
138.17
132.19
127.80
127.33
126.37
77.56
77.24
76.92
63.71
32.48
24.70
21.48
f1 (ppm)

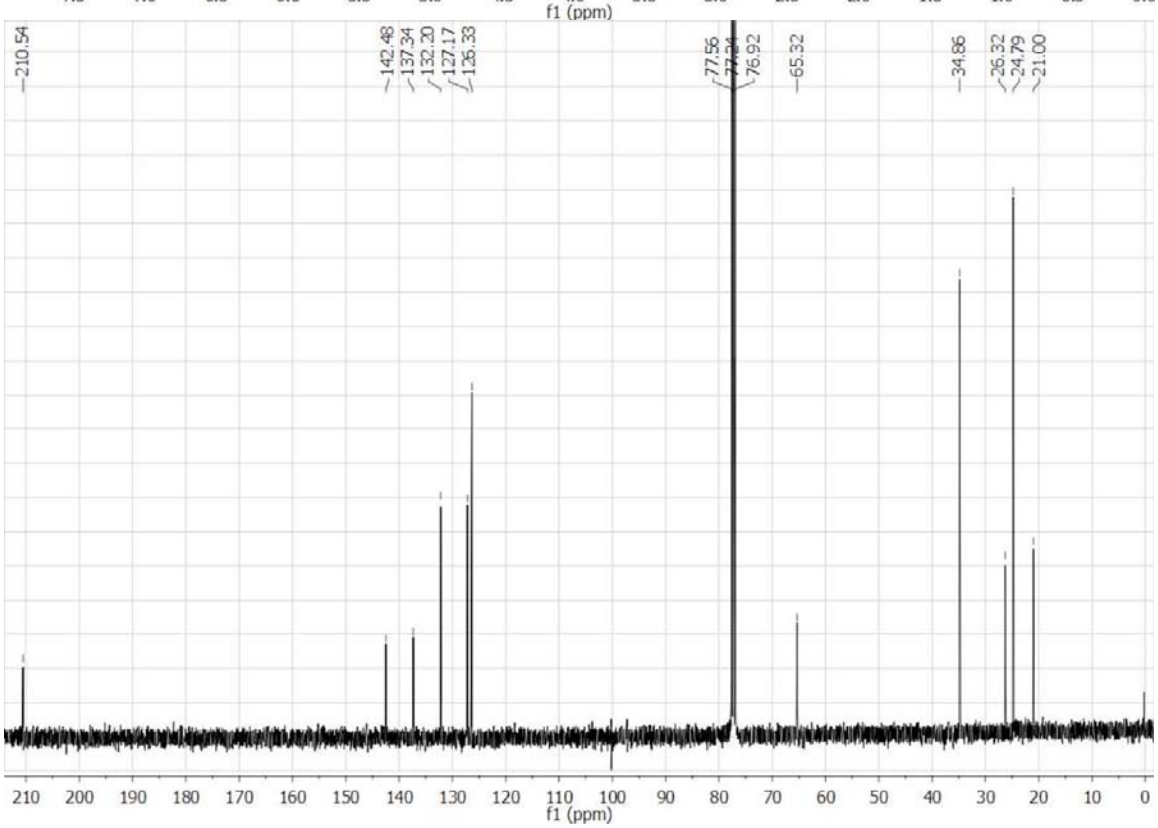

7.31
7.30
7.25
7.14
7.13
7.12
7.11
4.07
2.50
2.28
2.25
1.69
1.68
1.67
1.66
1.26
1.25
1.05
1.03
OH
H
1.00
2.96
1.00
2.97
2.04
2.02
4.05
1.05
3.02
f1 (ppm)

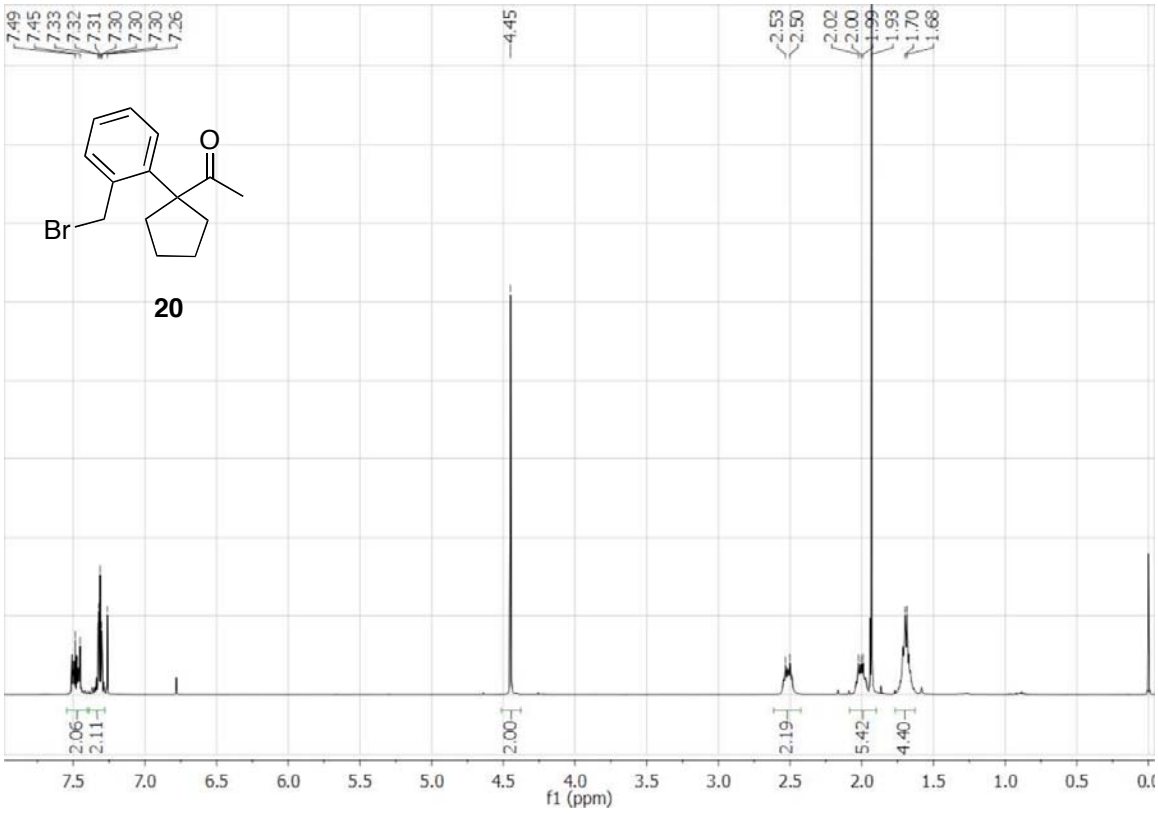
S12


144.48
137.15
133.03
129.42
126.39
125.63
77.56
77.24
76.92
71.90
57.56
35.69
34.33
25.18
24.63
23.59
19.35
f1 (ppm)

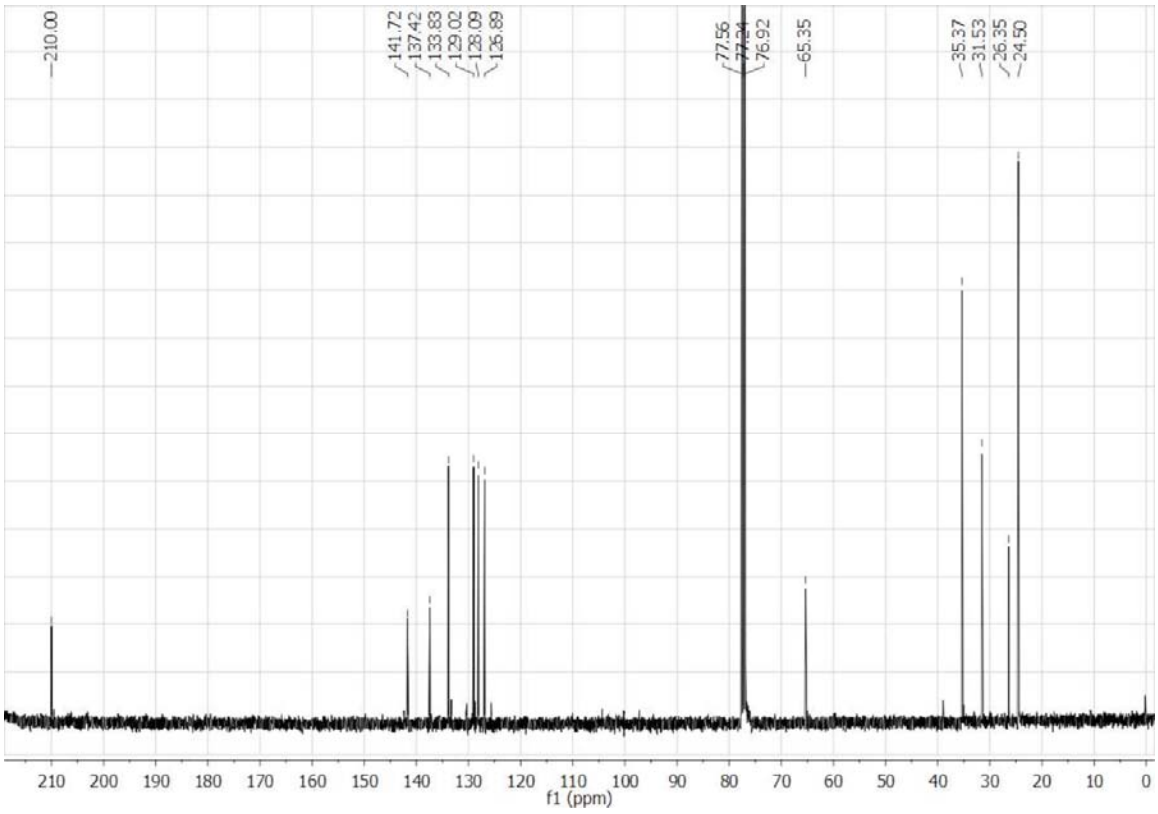

7.44
7.42
7.26
7.20
7.20
7.18
7.18
7.15
7.15
7.15
2.46
2.44
2.44
2.43
2.17
1.96
1.93
1.87
1.68
O
1.00
2.90
2.27
2.98
4.93
3.96
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

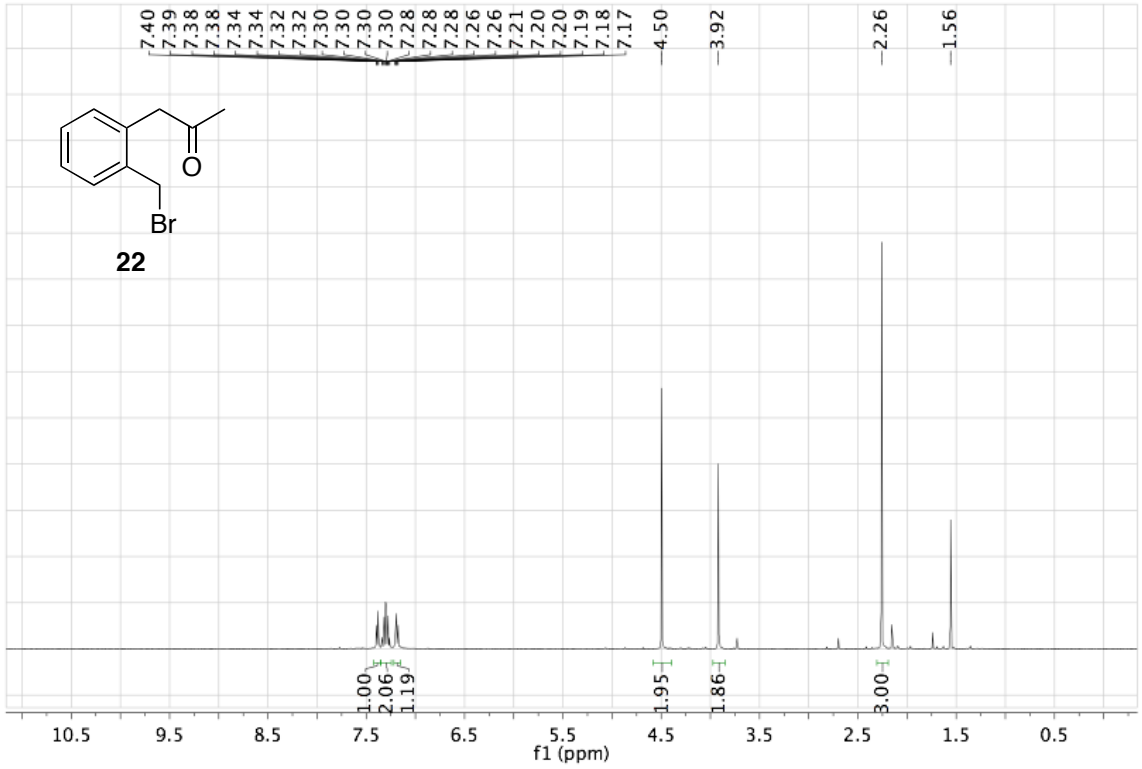
S13

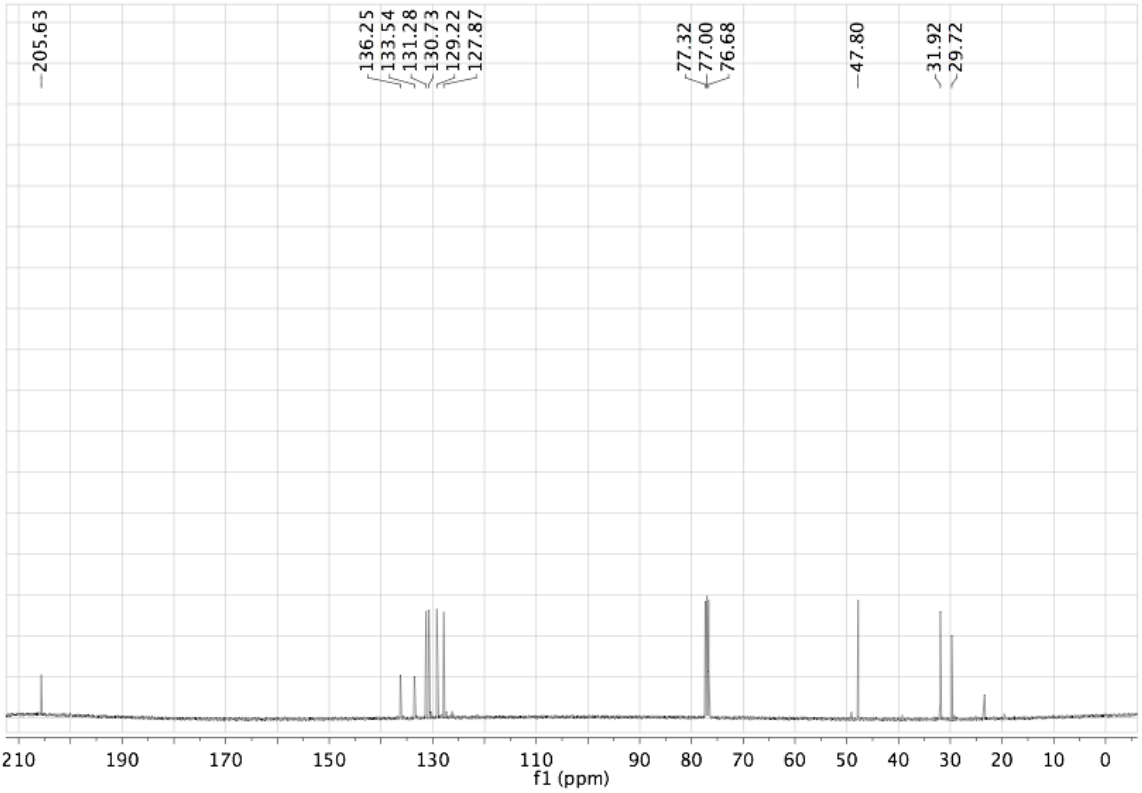

210.54
142.48
137.34
132.20
127.17
126.33
77.56
77.24
76.92
65.32
34.86
26.32
24.79
21.00
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

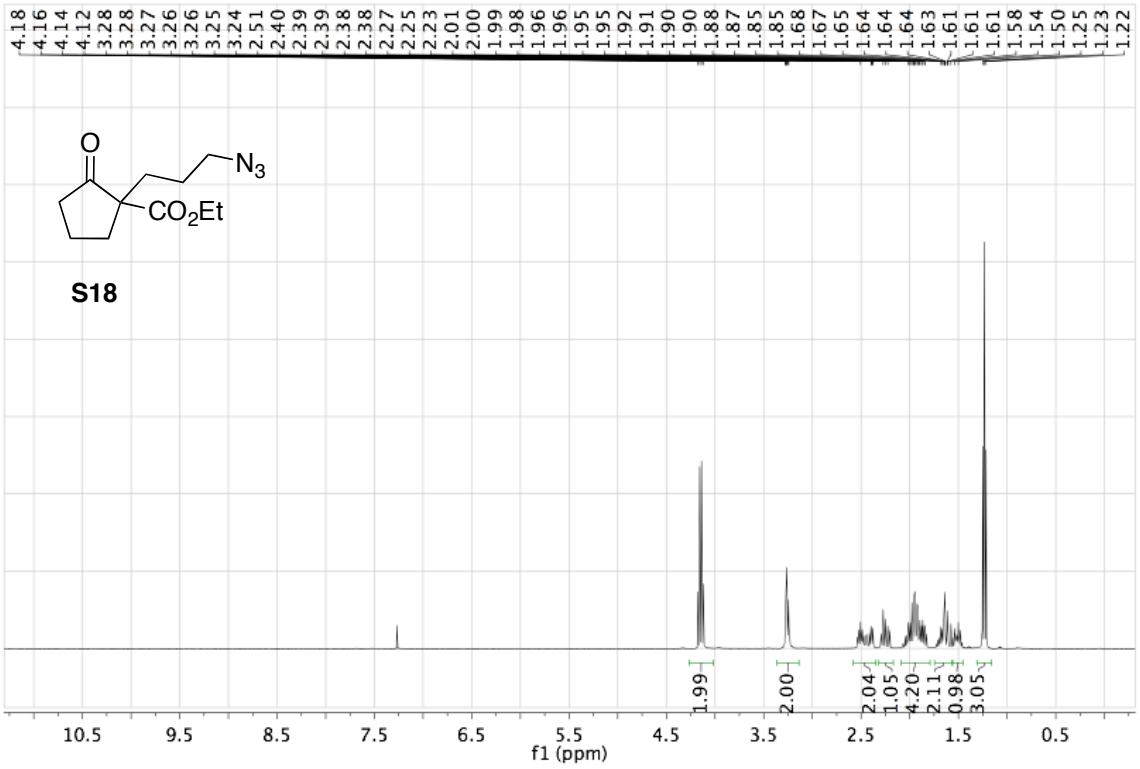

7.49
7.45
7.33
7.32
7.31
7.30
7.30
7.30
7.26
4.45
2.53
2.50
2.02
2.00
1.99
1.93
1.70
1.68
O
Br
2.06
2.11
2.00
2.19
5.42
4.40
f1 (ppm)

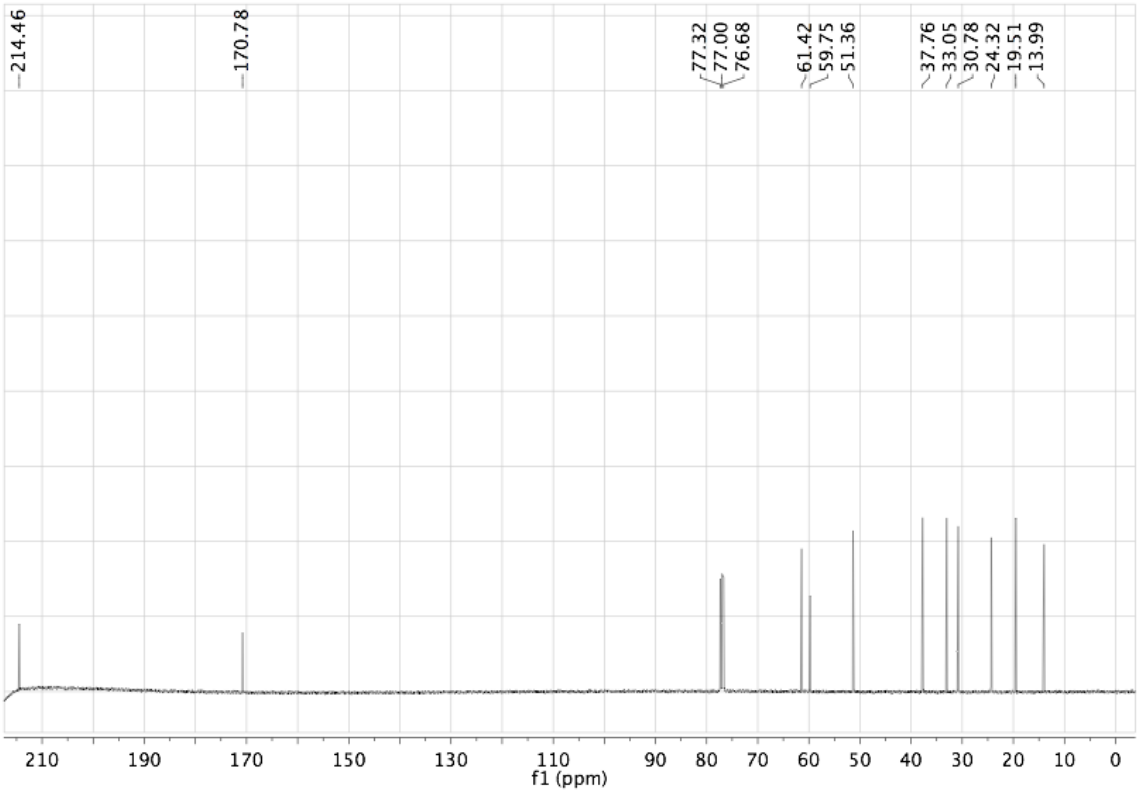
20

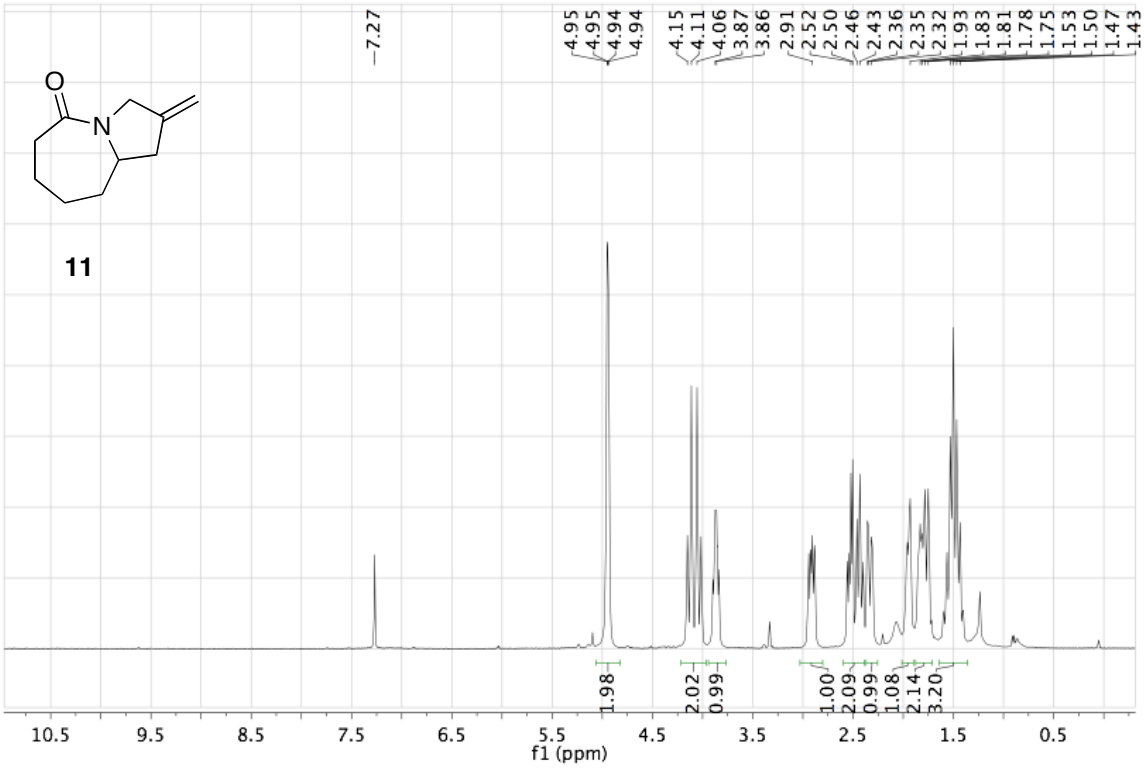

210.00
141.72
137.42
133.83
129.02
128.09
126.89
77.56
77.24
76.92
65.35
35.37
31.53
26.35
24.50
f1 (ppm)

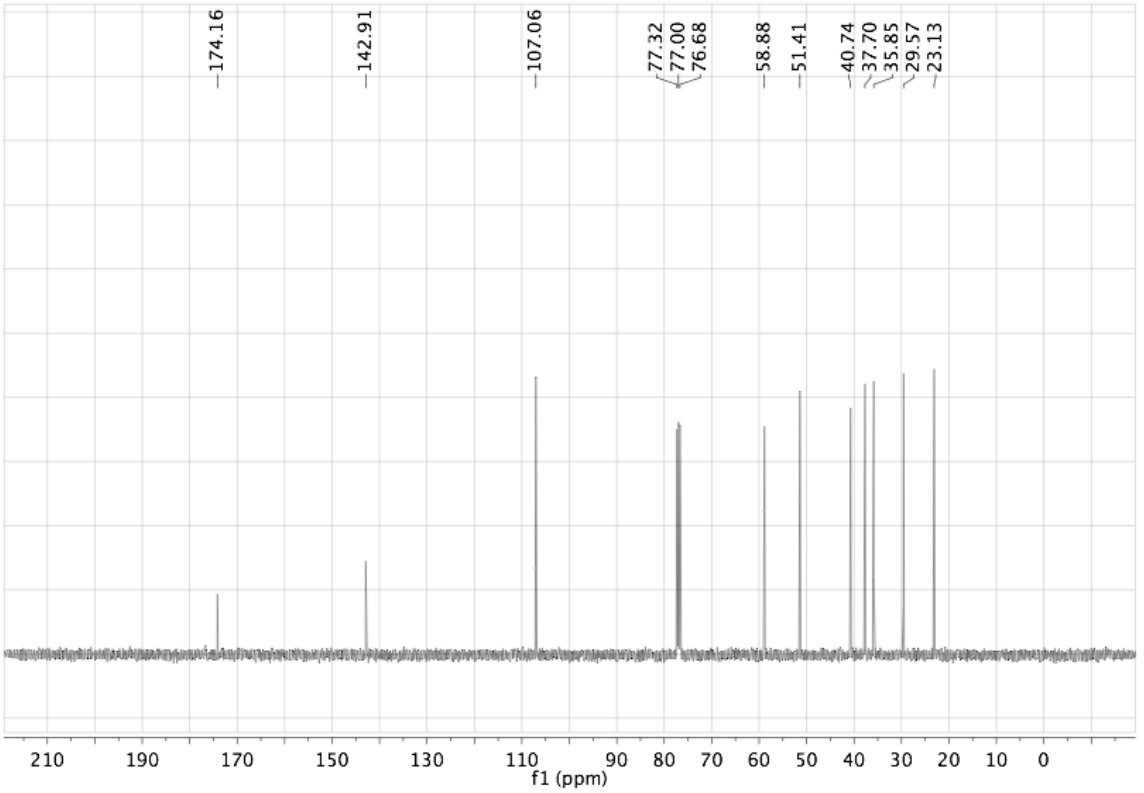

7.40
7.39
7.38
7.38
7.34
7.34
7.32
7.32
7.30
7.30
7.30
7.30
7.28
7.28
7.28
7.26
7.26
7.21
7.20
7.20
7.19
7.18
7.17
4.50
3.92
2.26
1.56
O
Br
22
1.00
2.06
1.19
1.95
1.86
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

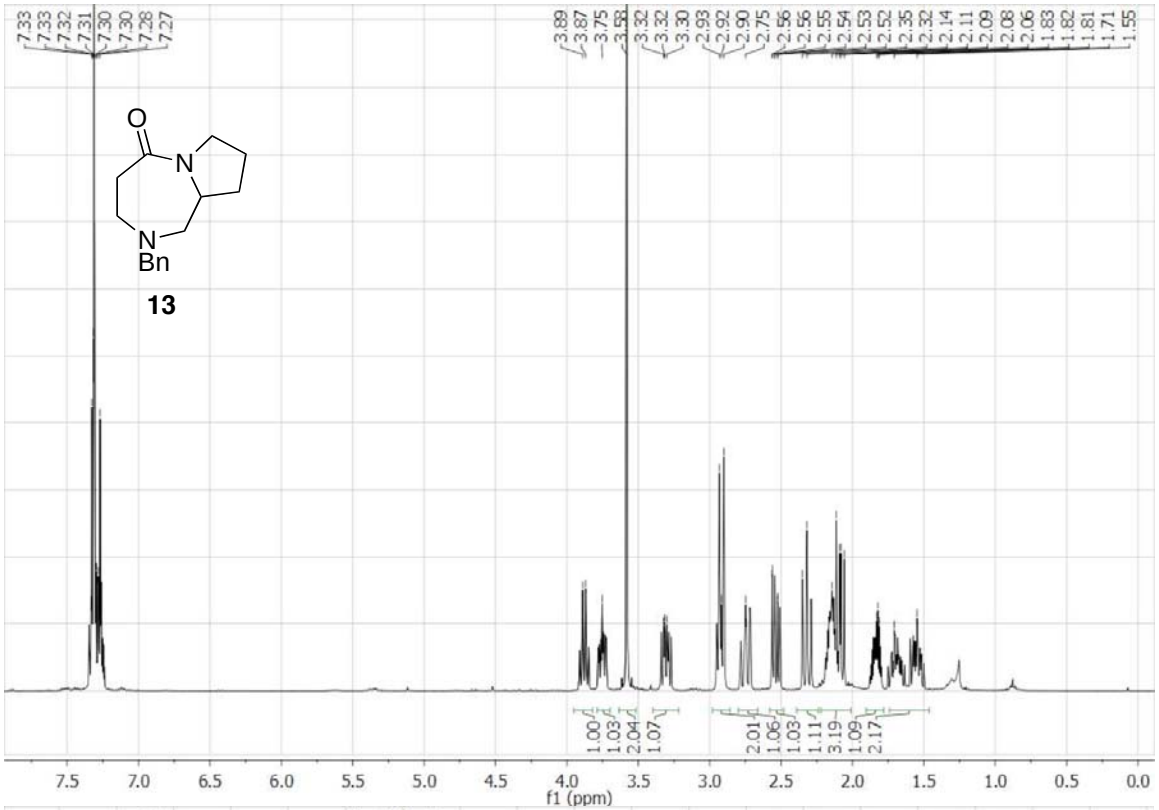

205.63
136.25
133.54
131.28
130.73
129.22
127.87
77.32
77.00
76.68
47.80
31.92
29.72
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

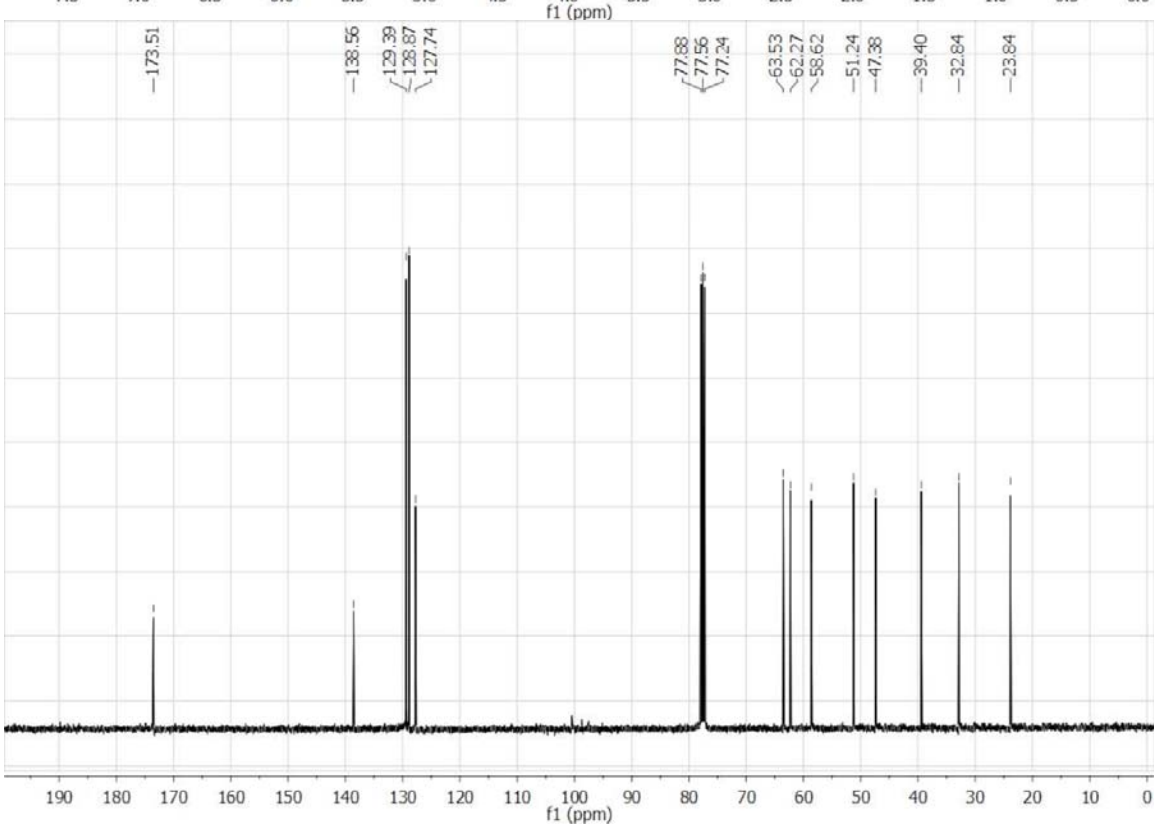

4.18 4.16 4.14 4.12 3.28 3.28 3.27 3.26 3.26 3.25 3.24 2.51 2.40 2.39 2.39 2.38 2.38 2.27 2.25 2.23 2.01 2.00 1.99 1.98 1.96 1.96 1.95 1.95 1.92 1.91 1.90 1.90 1.88 1.87 1.85 1.85 1.68 1.67 1.65 1.64 1.64 1.64 1.63 1.61 1.61 1.61 1.58 1.54 1.50 1.25 1.23 1.22
O
N3
CO2Et
S18
1.99
2.00
2.04
1.05
4.20
2.11
0.98
3.05
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)

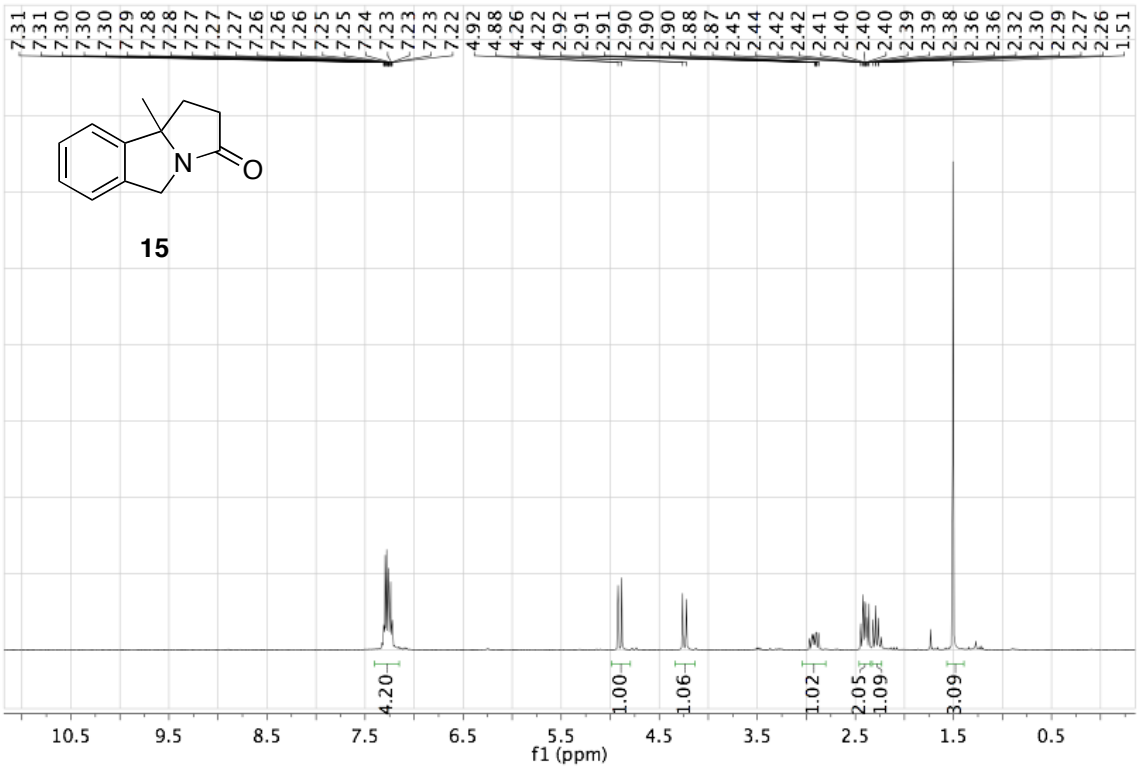

214.46
170.78
77.32
77.00
76.68
61.42
59.75
51.36
37.76
33.05
30.78
24.32
19.51
13.99
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

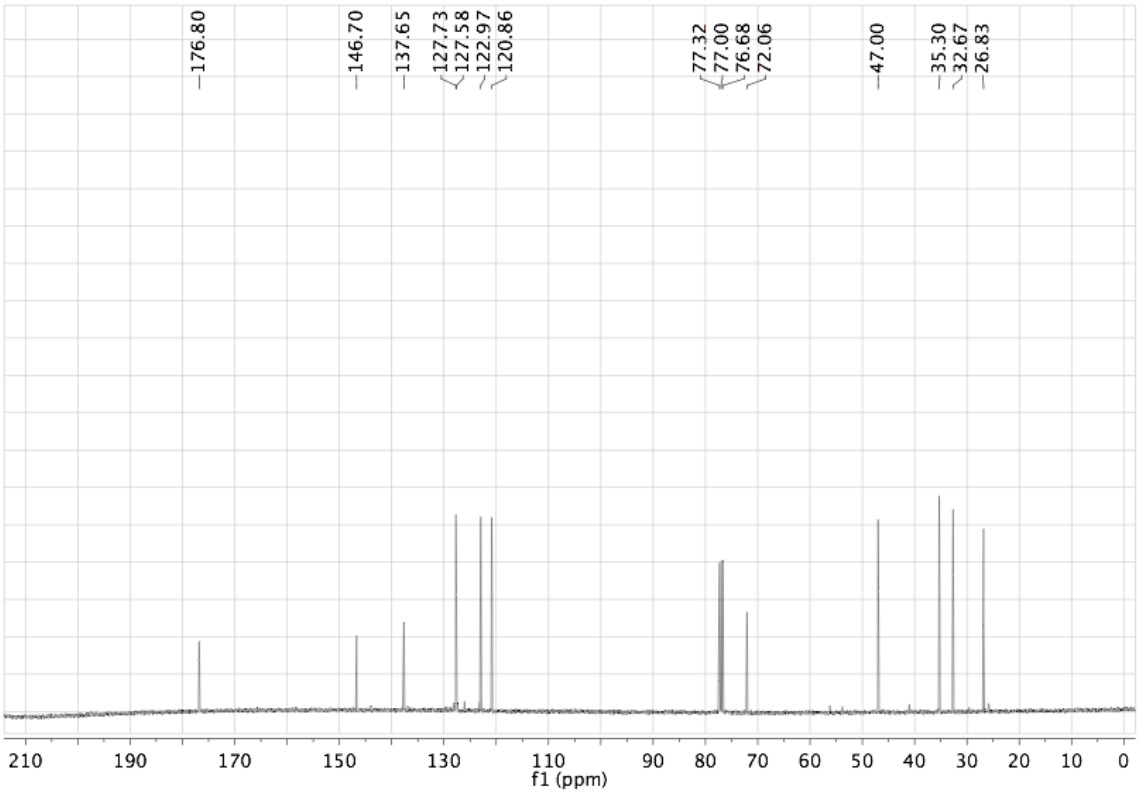

O
N
11
7.27
4.95
4.95
4.94
4.94
4.15
4.11
4.06
3.87
3.86
2.91
2.52
2.50
2.46
2.43
2.36
2.35
2.32
1.93
1.83
1.81
1.78
1.75
1.53
1.50
1.47
1.43
1.98
2.02
0.99
1.00
2.09
0.99
1.08
2.14
3.20
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

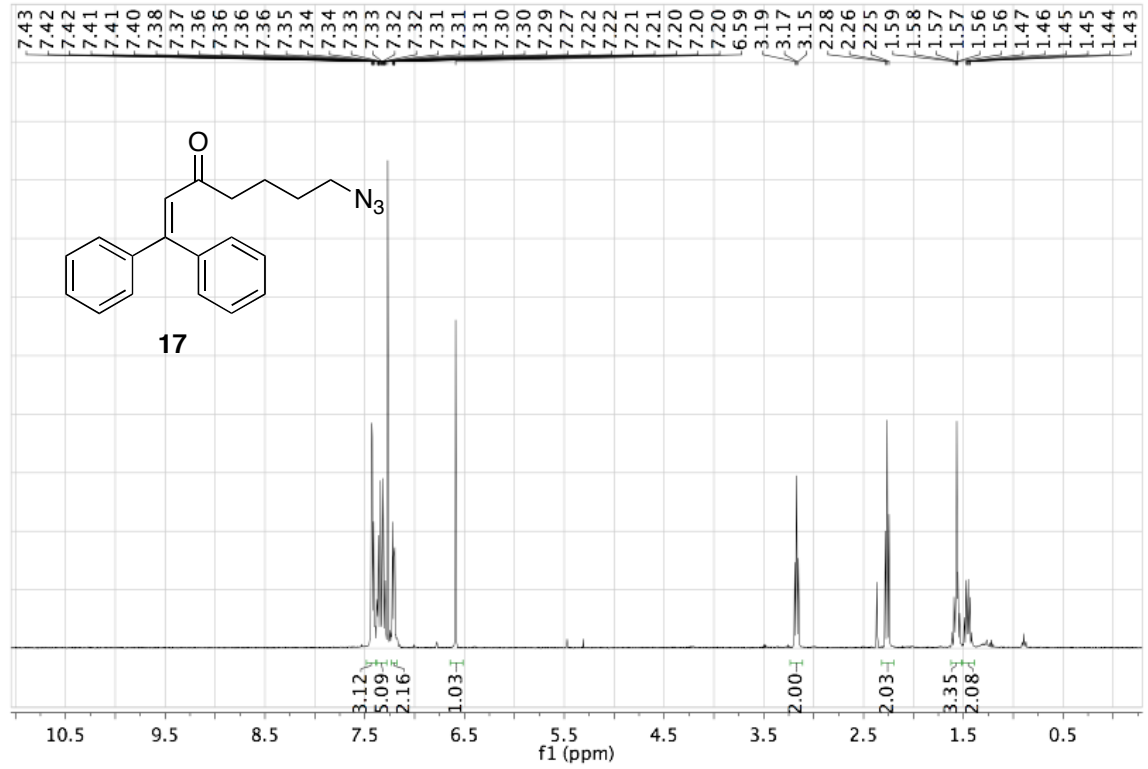

174.16
142.91
107.06
77.32
77.00
76.68
58.88
51.41
40.74
37.70
35.85
29.57
23.13
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

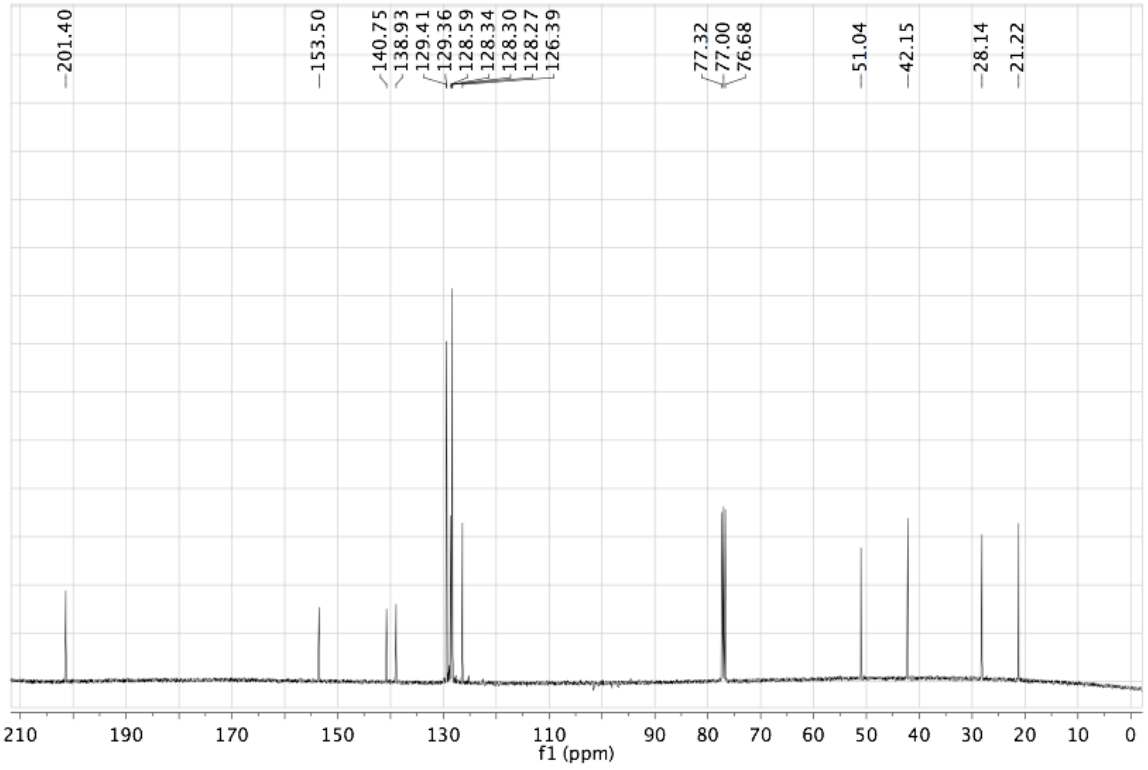

O
N
N
Bn
13
f1 (ppm)


f1 (ppm)

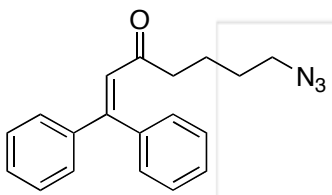

7.31 7.31 7.30 7.30 7.30 7.29 7.28 7.28 7.27 7.27 7.27 7.26 7.26 7.26 7.25 7.25 7.24 7.23 7.23 7.23 7.22
4.92 4.88 4.26 4.22 2.92 2.91 2.91 2.90 2.90 2.90 2.88 2.87 2.45 2.44 2.42 2.42 2.41 2.40 2.40 2.40 2.40 2.39 2.39 2.38 2.36 2.36 2.32 2.30 2.29 2.27 2.26 1.51
N
O
15
4.20
1.00
1.06
1.02
2.05
1.09
3.09
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)


176.80
146.70
137.65
127.73
127.58
122.97
120.86
77.32
77.00
76.68
72.06
47.00
35.30
32.67
26.83
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
N3
17
f1 (ppm)

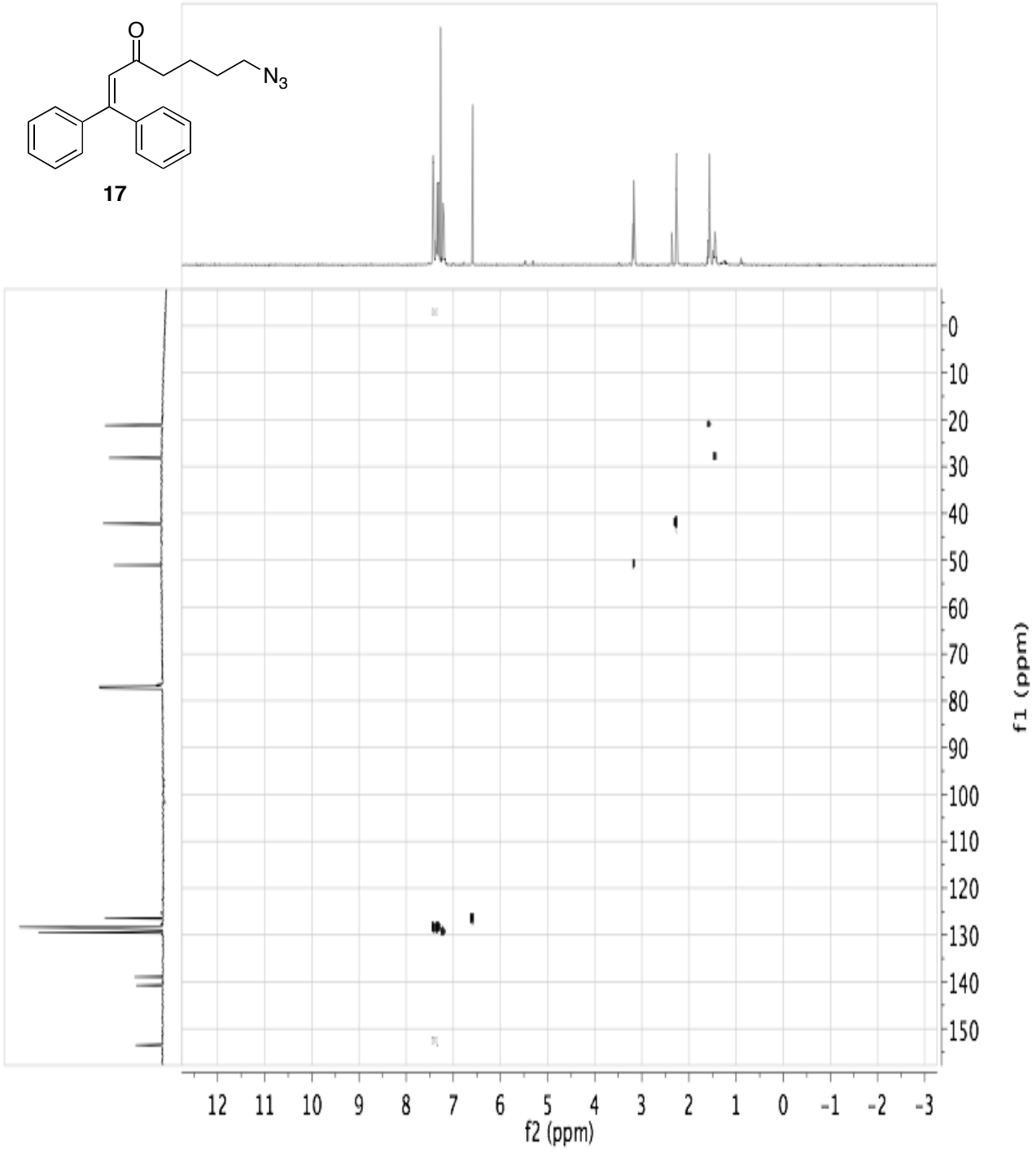

f1 (ppm)

COSY

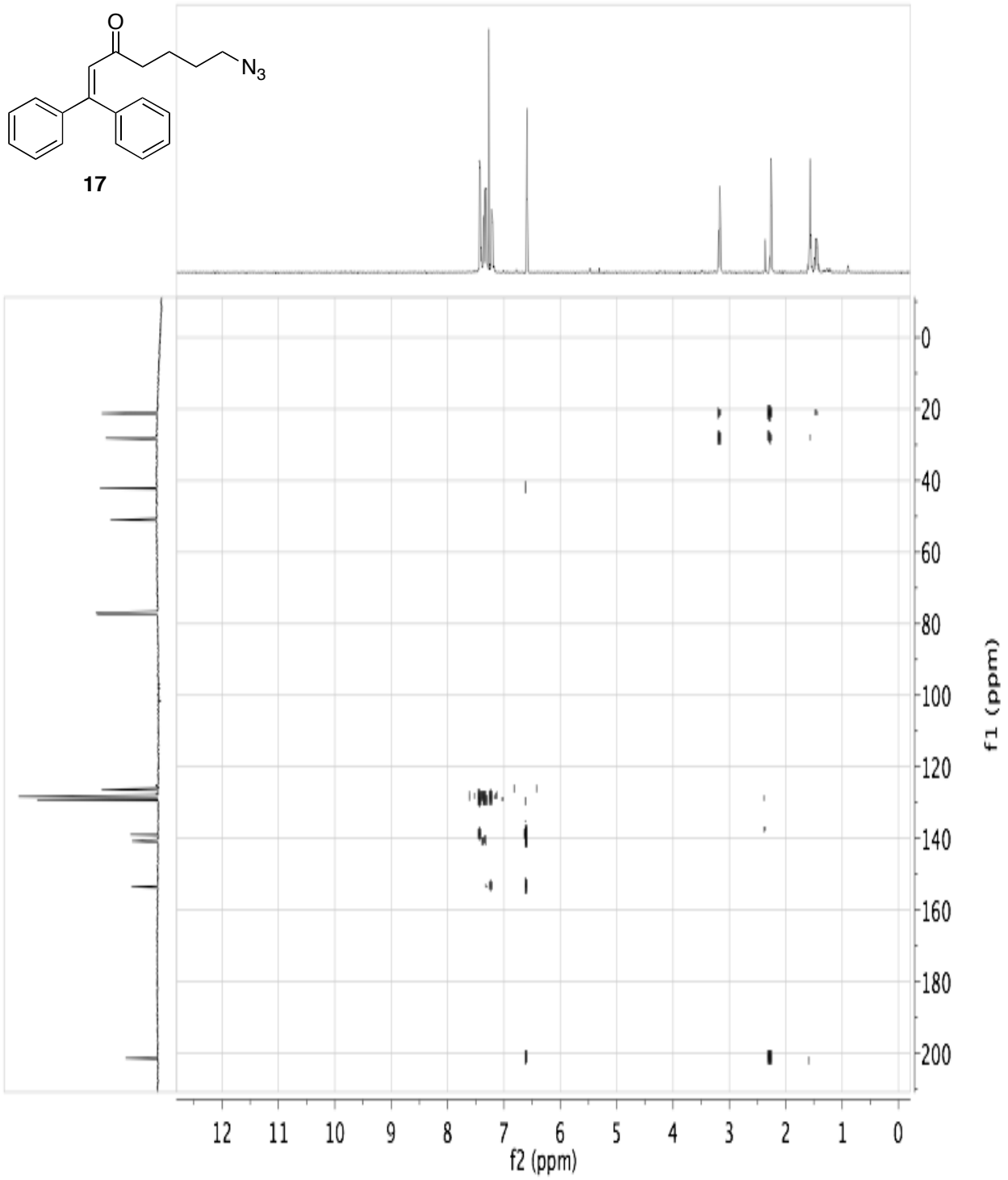


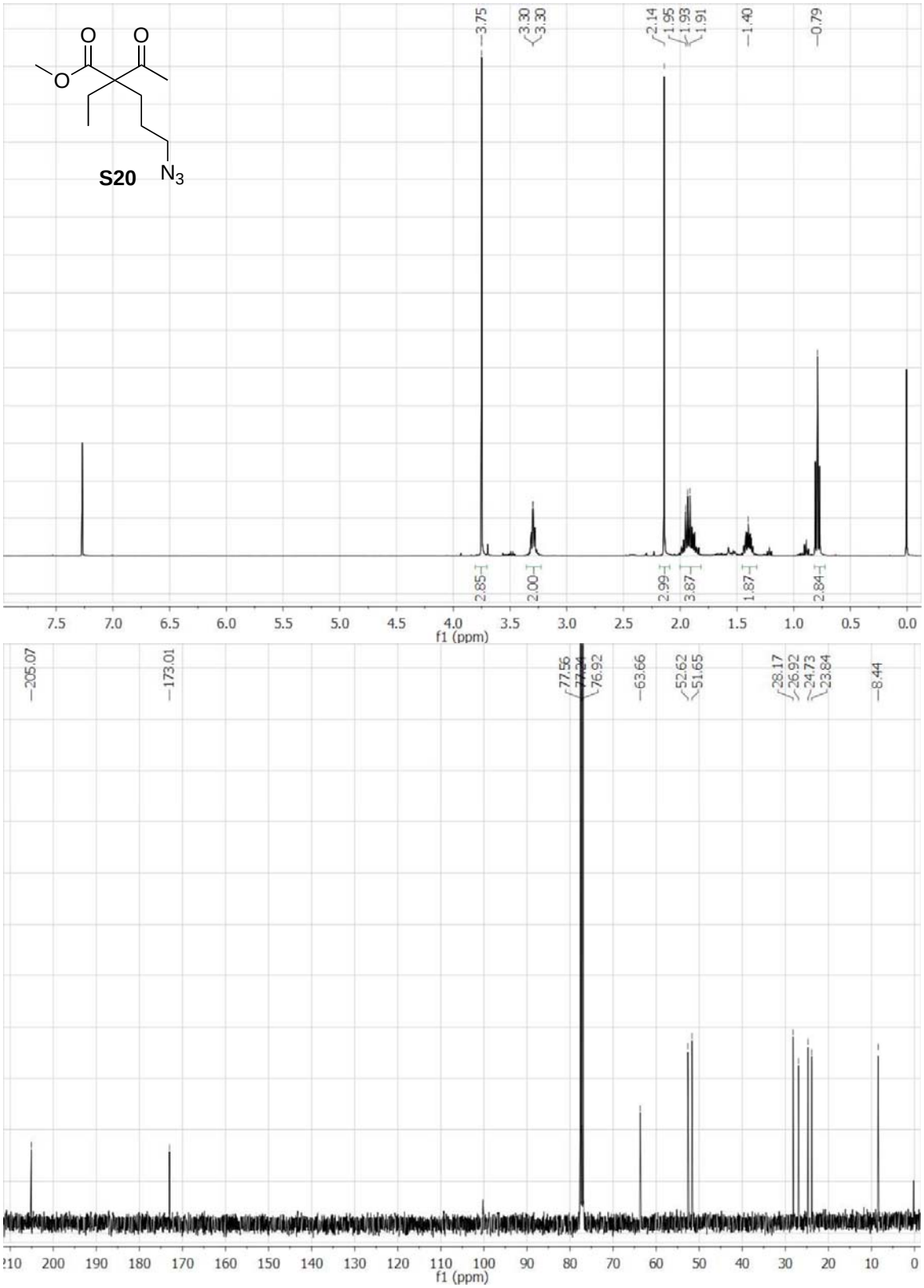
17

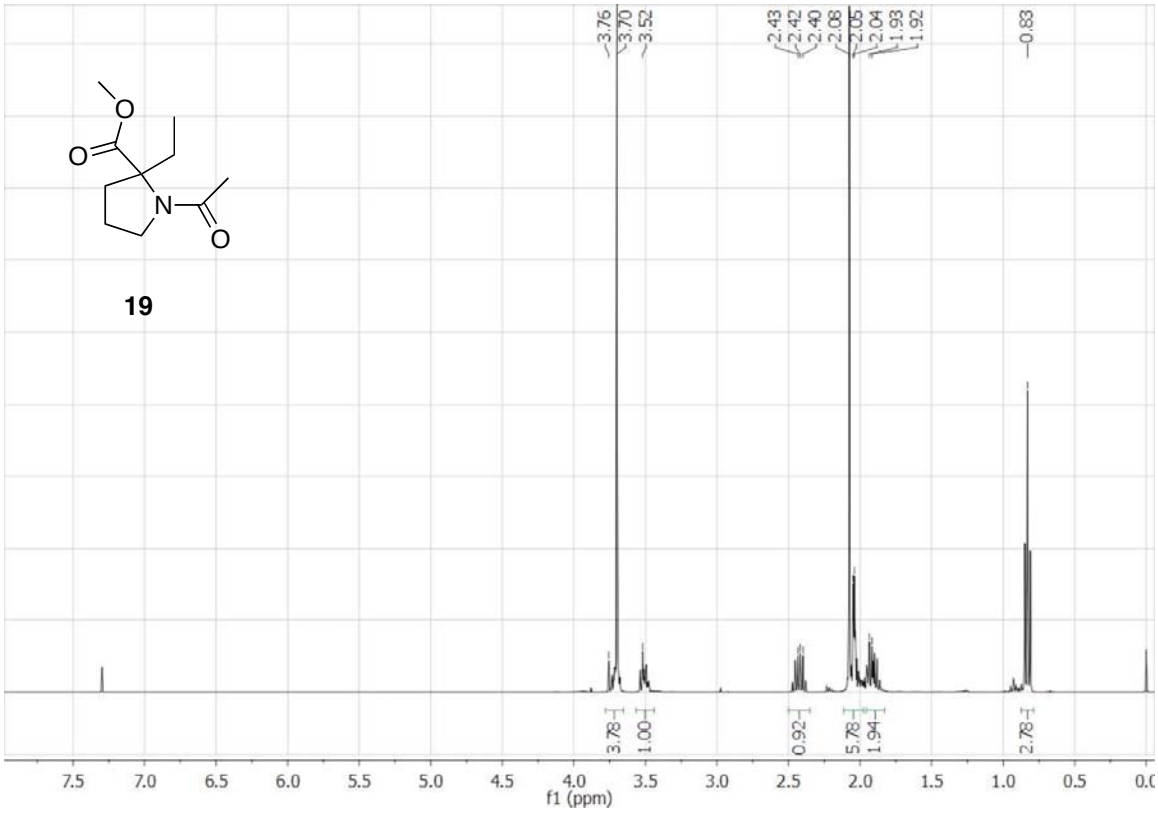
HSQC


O
N3
17
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f2 (ppm)

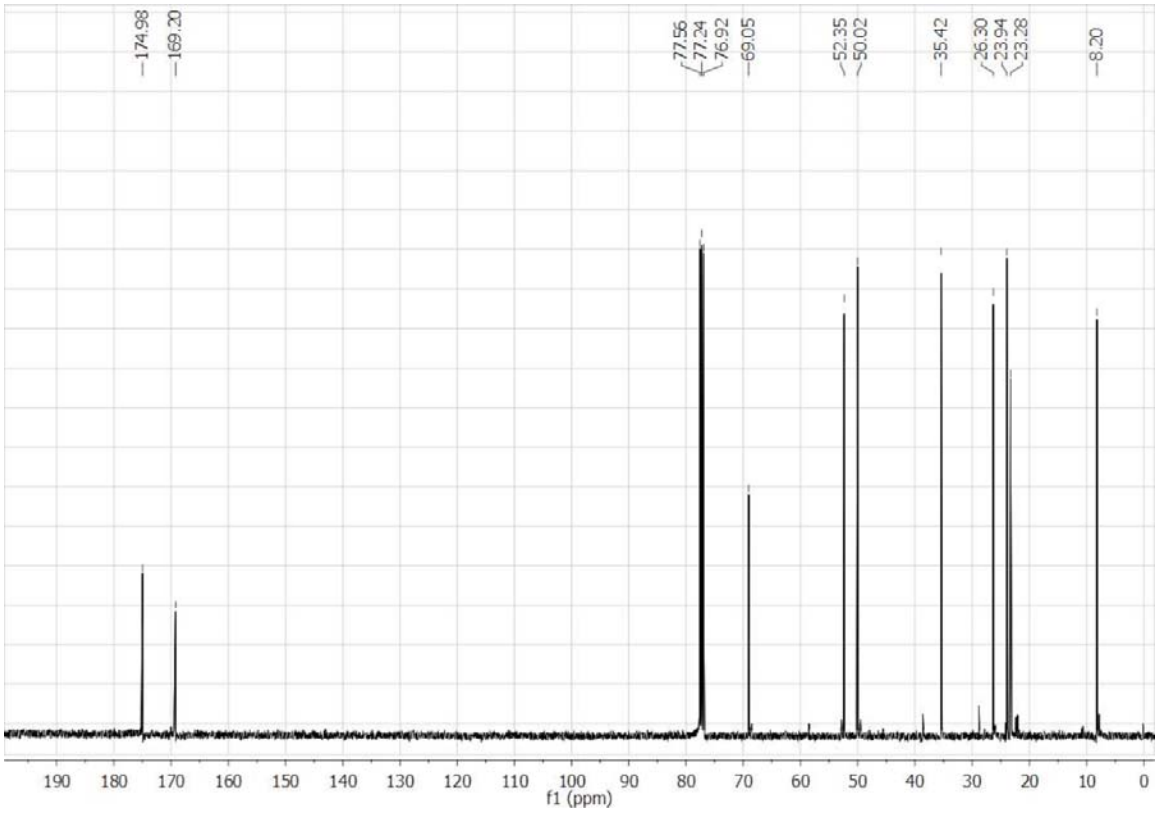
HMBC

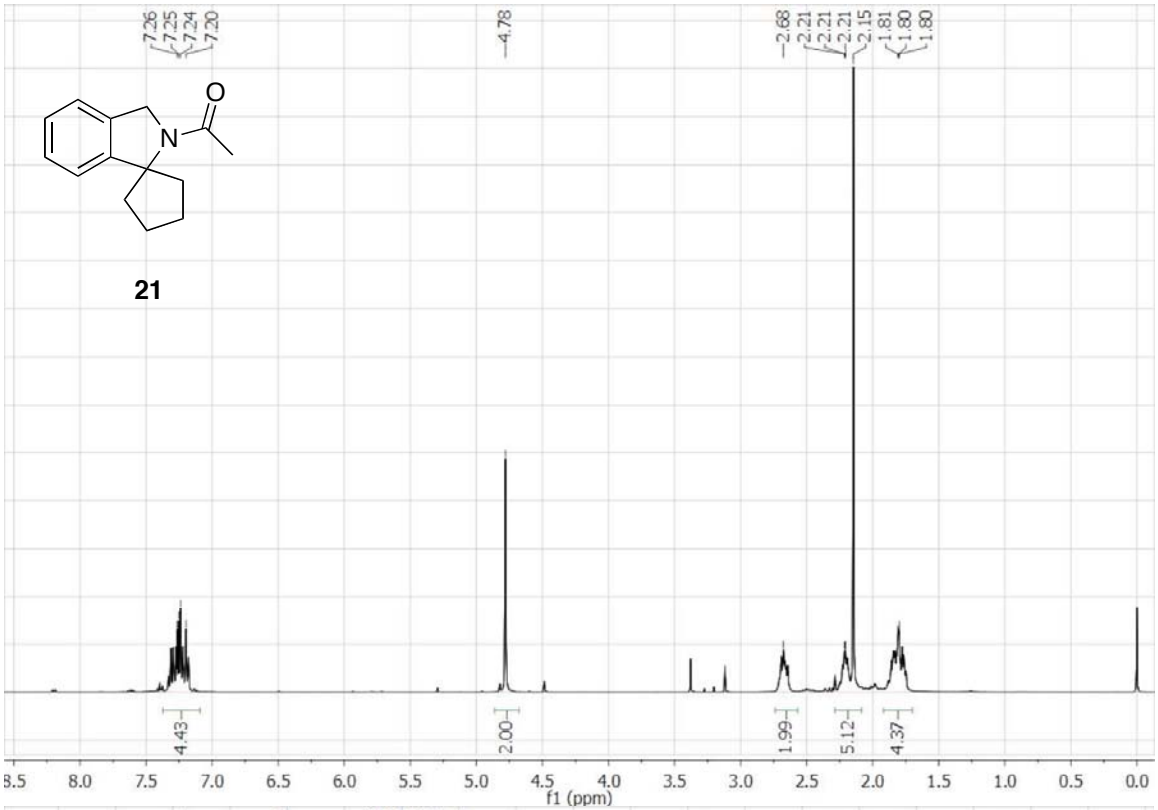

O
N3
17
0
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
12
11
10
9
8
7
6
5
4
3
2
1
0
f2 (ppm)


S20
N3
3.75
3.30
3.30
2.14
1.95
1.93
1.91
1.40
0.79
2.85
2.00
2.99
3.87
1.87
2.84
f1 (ppm)
205.07
173.01
77.56
76.92
63.66
52.62
51.65
28.17
26.92
24.73
23.84
8.44
f1 (ppm)

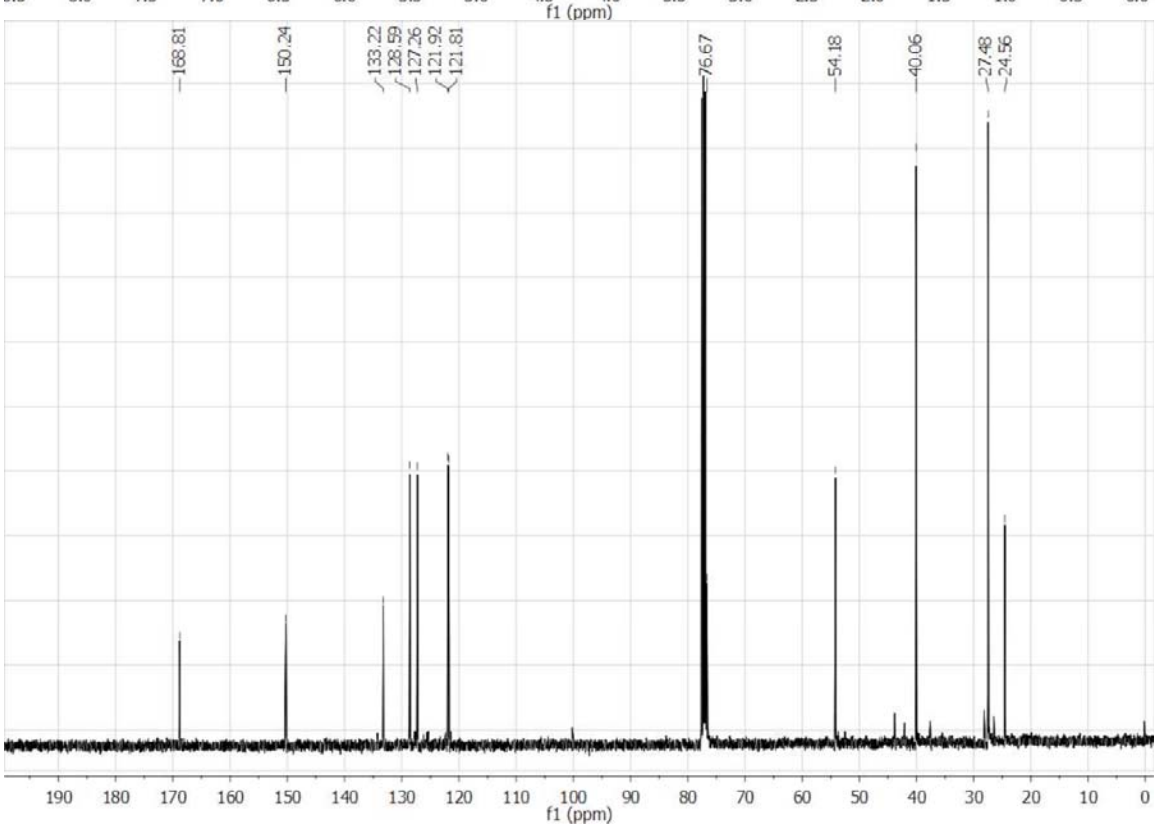

3.76
3.70
3.52
2.43
2.42
2.40
2.08
2.05
2.04
1.93
1.92
0.83
3.78
1.00
0.92
5.78
1.94
2.78
f1 (ppm)

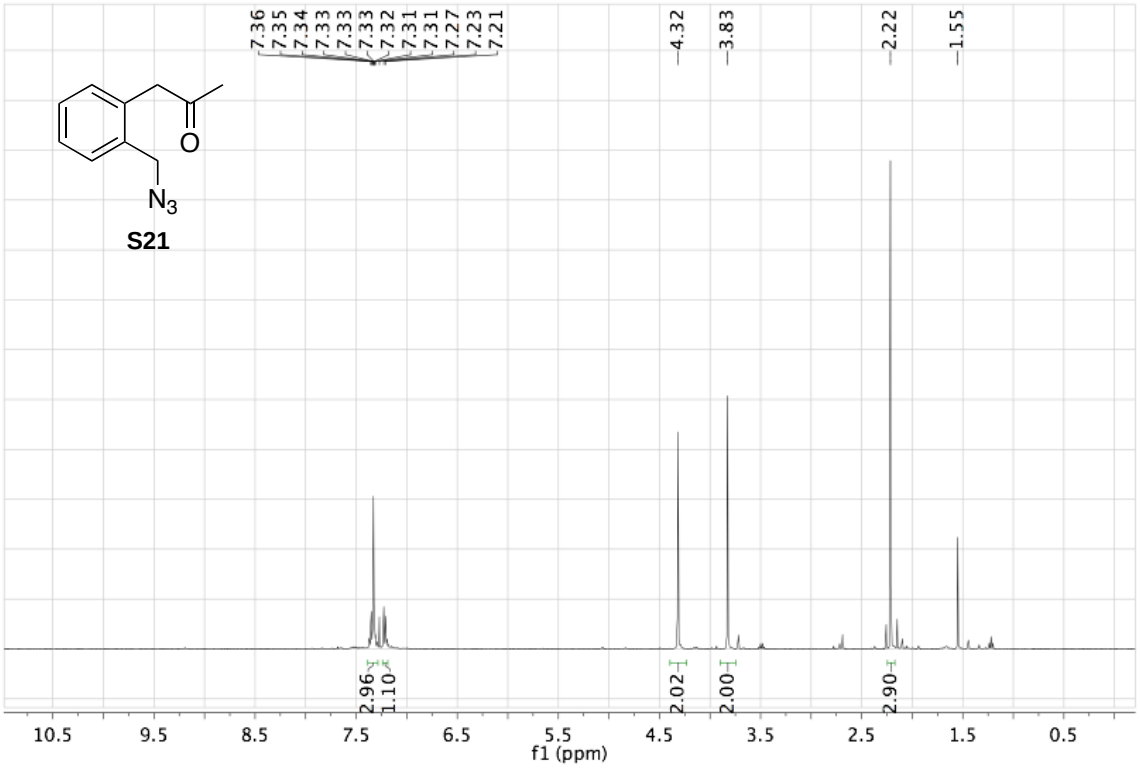
19


174.98
169.20
77.56
77.24
76.92
69.05
52.35
50.02
35.42
26.30
23.94
23.28
8.20
f1 (ppm)

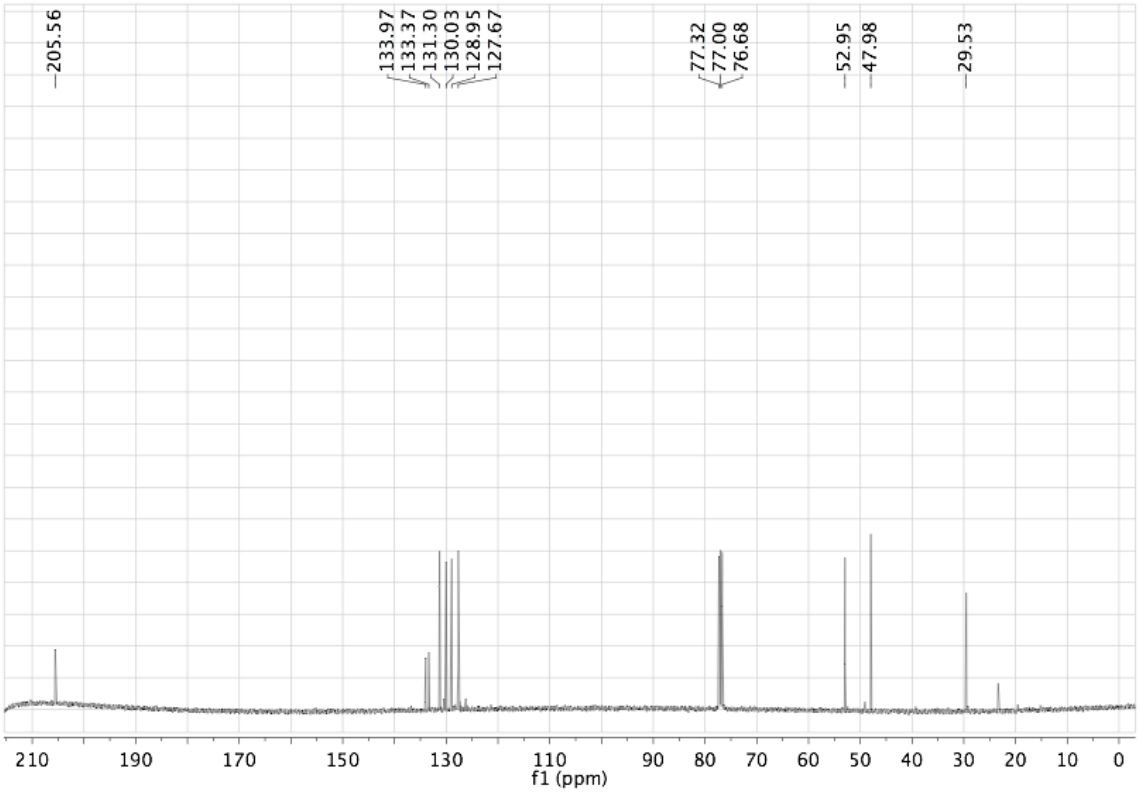

7.26
7.25
7.24
7.20
4.78
2.68
2.21
2.21
2.21
2.15
1.81
1.80
1.80
O
N
4.43
2.00
1.99
5.12
4.37
f1 (ppm)

21


168.81
150.24
133.22
128.59
127.26
121.92
121.81
76.67
54.18
40.06
27.48
24.56
f1 (ppm)


7.36
7.35
7.34
7.33
7.33
7.33
7.32
7.31
7.31
7.27
7.23
7.21
4.32
3.83
2.22
1.55
O
N3
2.96
1.10
2.02
2.00
2.90
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

S21


205.56
133.97
133.37
131.30
130.03
128.95
127.67
77.32
77.00
76.68
52.95
47.98
29.53
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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