Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

Intramolecular formal [4 + 2] cycloaddition of 3-ethoxycyclobutanones and alkenes

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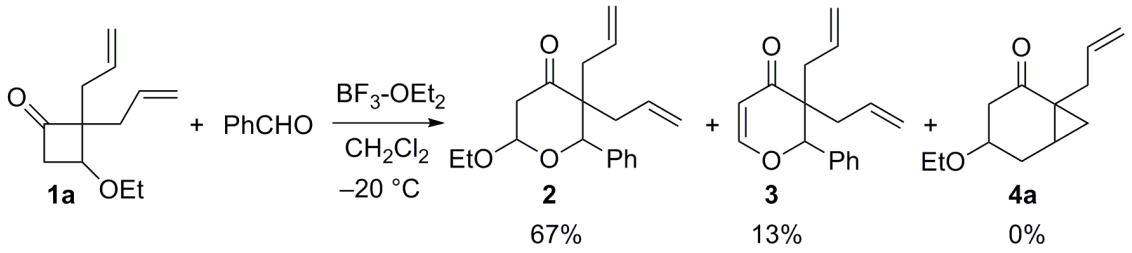
1. General

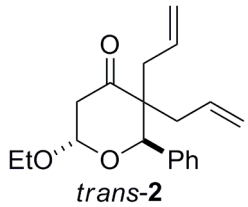
All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100. ^{1}H NMR spectra were recorded on a JEOL JNM EX270 (270 MHz) or a JEOL JNM GSX500 (500 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. ^{13}C NMR spectra were recorded on a JEOL JNM EX270 (270 MHz) or a JEOL JNM GSX500 (500 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard $CDCl_3$. High resolution mass spectra (HRMS) were recorded on a JEOL JMS-SX-102A mass spectrometer (EI). Elemental analyses were carried out on a Yanaco CHN Corder MT-5. Analytical TLC was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Silica-gel column chromatography was carried out on silica gel 60N (Kanto Kagaku Co., Ltd., spherical, neutral, 63–210 μm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Dichloromethane was distilled under argon from calcium hydride before use. All cycloaddition reactions were carried out under argon in dried glassware with magnetic stirring. A solution of $EtAlCl_2$ in hexane (1.04 M) was purchased from Aldrich. The reaction conditions for the preparation of 3-ethoxycyclobutanones were not optimized.

2. Typical experimental procedures and characterization data

2.1 Boron trifluoride etherate-catalyzed intermolecular formal [4 + 2] cycloaddition between 1a and benzaldehyde (Scheme 1)



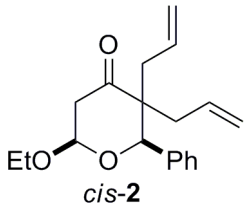
To a stirred solution of **1a** (77.4 mg, 0.398 mmol) and benzaldehyde (42.3 mg, 0.399 mmol) in dry dichloromethane (3 mL) was added at –45 °C boron trifluoride etherate (59 μL, 0.478 mmol), and the reaction mixture was stirred at –45 °C for 30 min and –20 °C for 3 h. The reaction was quenched by adding saturated aqueous ammonium chloride solution, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by preparative thin layer chromatography on silica gel (hexane / ethyl acetate = 5 : 1) to afford **2** (80.4 mg, 67%, *cis* / *trans* = 42 : 58) and **3** (13.5 mg, 13% yield).



trans-**2**

(±)-(2*R*,6*S*)-3,3-Diallyl-6-ethoxy-2,3,5,6-tetrahydro-2-phenyl-4*H*-pyran-4-one (*trans*-**2**, the major isomer)

Colorless needles: mp 64.5-65.0 °C (EtOH-H_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (t, *J* = 8.1 Hz, 3H), 1.77 (dd, *J* = 9.3, 15.4 Hz, 1H), 1.82 (dd, *J* = 7.1, 14.2 Hz, 1H), 2.54 (dd, *J* = 1.0, 15.1 Hz, 1H), 2.73 (dd, *J* = 7.6, 14.2 Hz, 1H), 2.76-2.80 (m, 1H), 2.84 (dd, *J* = 4.9, 15.1 Hz, 1H), 3.44 (qd, *J* = 7.1, 9.8 Hz, 1H), 3.64 (qd, *J* = 7.1, 10.0 Hz, 1H), 4.93-4.99 (m, 2H), 5.10-5.18 (m, 2H), 5.20 (s, 1H), 5.29-5.30 (m, 1H), 5.42-5.51 (m, 1H), 5.79-5.87 (m, 1H), 7.31-7.38 (m, 3H), 7.46-7.48 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 35.4, 37.2, 45.0, 56.8, 62.9, 73.5, 97.7, 118.0, 118.4, 127.8, 128.0, 128.1, 132.6, 135.1, 136.8, 207.0; IR (cm^{-1}, $CHCl_3$) 2915, 1713, 1294, 1125, 1053, 1022, 994, 922; Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.64; H, 8.17.

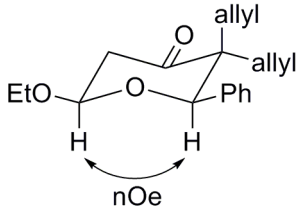


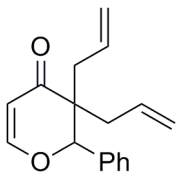
cis-**2**

(±)-(2*R*,6*R*)-3,3-Diallyl-6-ethoxy-2,3,5,6-tetrahydro-2-phenyl-4*H*-pyran-4-one (*cis*-**2**, the minor isomer)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H), 1.75-1.81 (m, 2H), 2.65-2.74 (m, 2H), 2.75-2.83 (m, 2H), 3.56 (qd, *J* = 7.1, 9.8 Hz, 1H), 3.98 (qd, *J* = 7.1, 9.8 Hz, 1H), 4.72 (s, 1H), 4.76 (dd, *J* = 4.2, 8.5 Hz, 1H), 4.94-5.00 (m, 2H), 5.12-5.18 (m, 2H), 5.41-5.49 (m, 1H), 5.71-5.79 (m, 1H), 7.31-7.38 (m, 3H), 7.47-7.49 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 35.2, 36.9, 46.9, 56.7, 64.9, 77.3, 100.0, 118.5, 118.6, 127.8, 127.9, 128.0, 132.3, 134.9, 136.5, 207.5; IR (cm^{-1}, $CHCl_3$) 2982, 1711, 1638, 1377, 1354, 1123, 1048, 922; HRMS (EI+) *m/z* calcd for $C_{19}H_{24}O_3$: 300.17255, found 300.17305.

The stereochemistry was determined by NOE experiments.



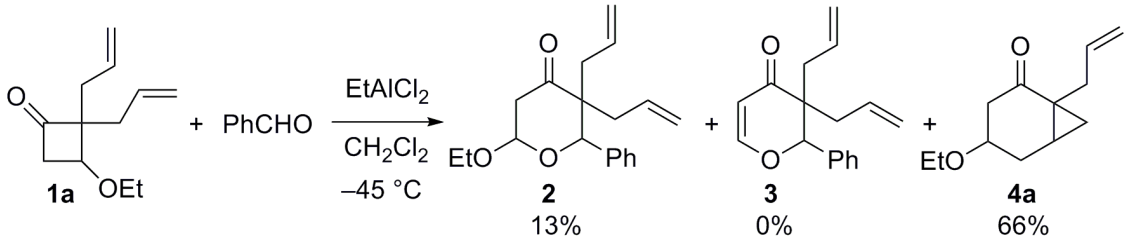


3

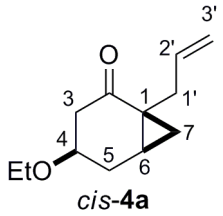
3,3-Diallyl-2,3-dihydro-2-phenyl-4*H*-pyran-4-one (3)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.77 (dd, *J* = 9.3, 15.1 Hz, 1H), 1.93-1.98 (m, 1H), 2.51-2.56 (m, 1H), 2.84 (tdd, *J* = 2.2, 4.6, 15.1 Hz, 1H), 4.90-4.95 (m, 1H), 5.00-5.03 (m, 1H), 5.11-5.16 (m, 1H), 5.17-5.20 (m, 1H), 5.45 (s, 1H), 5.52 (d, *J* = 5.9 Hz, 1H), 5.55-5.64 (m, 1H), 5.70-5.78 (m, 1H), 7.38-7.40 (m, 3H), 7.42 (dd, *J* = 0.5, 5.9 Hz, 1H), 7.47-7.49 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.2, 35.5, 51.9, 86.2, 107.0, 118.6, 119.1, 128.1, 128.1, 128.8, 132.5, 134.1, 134.8, 162.0, 195.2; IR (cm^{-1}, $CHCl_3$) 3013, 1669, 1605, 1406, 1254, 909; HRMS (EI+) *m/z* calcd for $C_{17}H_{18}O_2$: 254.13068, found 254.13048.

2.2 Ethylaluminum dichloride-catalyzed intramolecular formal [4 + 2] cycloaddition of 1a in the presence of benzaldehyde (Scheme 1)



To a stirred solution of **1a** (101.5 mg, 0.522 mmol) and benzaldehyde (55.4 mg, 0.522 mmol) in dry dichloromethane (3 mL) was added at –45 °C a solution of ethylaluminum dichloride (1.04 M in hexane, 0.60 mL, 0.624 mmol), and the mixture was stirred at –45 °C for 15 min. The reaction was quenched by adding water, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexane / ether = 20 : 1 → 5 : 1 and benzene / ethyl acetate = 40 : 1) to afford **4a** (66.7 mg, 66% yield, *cis* / *trans* = 79 : 21) and **2** (20.9 mg, 13% yield, *cis* / *trans* = 25 : 75) and **1a** (7% recovery).

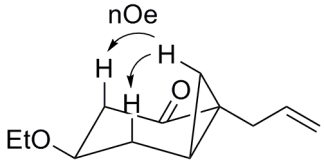


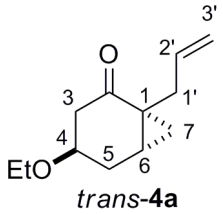
cis-**4a**

(±)-(1*R*,4*S*)-1-Allyl-4-ethoxybicyclo[4.1.0]heptan-2-one (*cis*-4a)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (dd, *J* = 4.9, 8.5 Hz, 1H, H7exo×1), 1.17 (t, *J* = 7.1 Hz, 3H, Me), 1.32 (dd, *J* = 5.1, 6.1 Hz, 1H, H7endo×1), 1.43-1.48 (m, 1H, H6), 1.84 (ddd, *J* = 2.0, 7.8, 13.9 Hz, 1H, H5ax), 1.94 (dd, *J* = 6.6, 14.6 Hz, 1H, H1'), 2.31 (dd, *J* = 9.0, 14.6 Hz, 1H, H3ax), 2.33-2.39 (m, 1H, H5eq), 2.48 (ddd, *J* = 1.7, 4.4, 15.4 Hz, 1H, H3eq), 2.67 (dd, *J* = 6.8, 14.6 Hz, 1H, H1'), 3.46 (q, *J* = 7.1 Hz, 2H, $OC\underline{H}_2$), 3.59-3.64 (m, 1H, H4), 4.96-5.01 (m, 2H, H3'), 5.72-5.80 (m, 1H, H2'); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4, 21.6, 22.8, 29.3, 33.7, 37.1, 43.4, 63.8, 75.4, 116.4, 135.3, 208.3; IR (cm^{-1}, $CHCl_3$) 3011, 1686, 1495, 1455, 1356, 1213, 1096, 1030; HRMS (EI+) *m/z* calcd for $C_{12}H_{18}O_2$:194.13068, found 194.13024.

The stereochemistry was determined by NOE experiments.



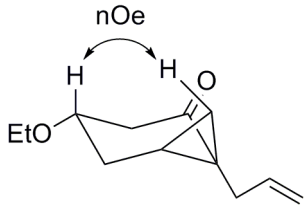


trans-**4a**

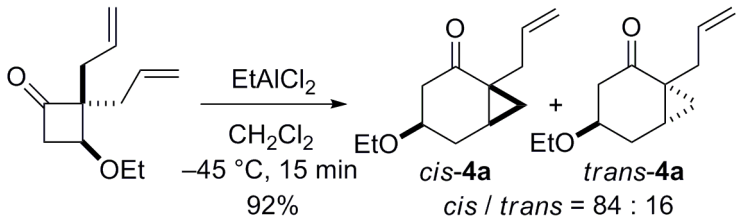
(±)-(1*R*,4*R*)-1-Allyl-4-ethoxybicyclo[4.1.0]heptan-2-one (*trans*-4a)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (dd, *J* = 5.6, 8.5 Hz, 1H, H7exo), 1.04 (dd, *J* = 5.6, 6.1 Hz, 1H, H7endo), 1.16 (t, *J* = 7.1 Hz, 3H, Me), 1.53-1.58 (m, 1H, H6), 1.97 (dd, *J* = 6.6, 14.8 Hz, 1H, H1'), 1.98-2.04 (m, 1H, H5ax), 2.16 (ddd, *J* = 2.4, 4.2, 13.8 Hz, 1H, H5eq), 2.25 (ddd, *J* = 1.0, 7.8, 15.1 Hz, 1H, H3ax), 2.55 (dd, *J* = 4.2, 16.6 Hz, 1H, H3eq), 2.72 (dd, *J* = 6.7, 14.8 Hz, 1H, H1'), 3.42 (qd, *J* = 7.1, 9.0 Hz, 1H, CH_2 of Et), 3.49 (qd, *J* = 7.1, 9.0 Hz, 1H, CH_2 of Et), 3.67-3.71 (m, 1H, H4ax), 4.97-5.03 (m, 2H, H3'), 5.74-5.82 (m, 1H, H2'); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4 (Me), 19.8 (C7), 22.0 (C6), 29.0 (C5), 33.0 (C1), 36.8 (C1'), 43.0 (C3), 63.4 ($O\underline{C}H_2$), 73.2 (C4), 116.2 (C3'), 135.2 (C2'), 207.6 (C2); IR (cm^{-1}, $CHCl_3$) 3011, 2928, 1686, 1642, 1364; HRMS (EI+) *m/z* calcd for $C_{12}H_{18}O_2$:194.13068, found 194.13075.

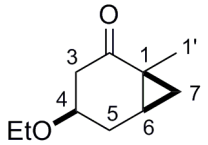
The stereochemistry was determined by NOE experiments.



2.3 A typical experimental procedure for $EtAlCl_2$-catalyzed intramolecular formal [4 + 2] cycloaddition of 2-alkenyl-3-ethoxycyclobutanones (Table 1, entry 1)



To a stirred solution of **1a** (129.9 mg, 0.669 mmol) in dry dichloromethane (2 mL) was added a 1.04 M solution of $EtAlCl_2$ in hexane (0.77 mL, 0.801 mmol) at –45 °C, and the reaction mixture was stirred for 15 min at –45 °C. The reaction was quenched by adding water, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated. The crude product was purified by column chromatography on silica gel (hexane / ethyl acetate = 50 : 1 + 1% triethylamine) to afford **4a** (119.1 mg, 92%) as a colorless oil. The ratio of *cis*-**4a** and *trans*-**4a** (*cis* / *trans* = 84 : 16) was determined by ^{1}H NMR analysis of the obtained **4a**. The *cis*-**4a** and *trans*-**4a** could be isolated by column chromatography on silica gel (hexane / ether). It should be noted that purification of the crude product by column chromatography on silica gel using an eluant without triethylamine caused the elimination of ethanol from **4a** to give the corresponding enone.

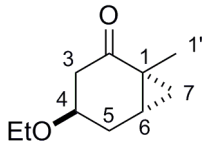


cis-**4c**

(±)-(1*R*,4*S*)-4-Ethoxy-1-methylbicyclo[4.1.0]heptan-2-one (*cis*-4c)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (dd, *J* = 4.6, 8.3 Hz, 1H, H7), 1.17 (t, *J* = 7.1 Hz, 3H, $CH_2C\underline{H}_3$), 1.20 (s, 3H, Me), 1.33 (t, *J* = 5.1 Hz, 1H, H7), 1.40-1.45 (m, 1H, H6), 1.80 (ddd, *J* = 2.2, 8.1, 13.9 Hz, 1H, H5), 2.29 (dd, *J* = 9.3, 15.4 Hz, 1H, H3ax), 2.35-2.41 (m, 1H, H5), 2.51 (ddd, *J* = 1.7, 4.4, 15.1 Hz, 1H, H3eq), 3.46 (q, J = 7.1 Hz, 2H, $OC\underline{H}_2$), 3.59-3.65 (m, 1H, H4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4, 19.3, 24.0, 24.8, 29.5, 29.9, 43.1, 63.8, 75.7, 209.5; IR (cm^{-1}, $CHCl_3$) 2978, 1682, 1458, 1375, 1352, 1219, 1098, 909; HRMS (EI+) *m/z* calcd for $C_{10}H_{16}O_2$: 168.11503, found 168.11520.

The stereochemistry was determined by the similarity in ^{1}H NMR spectra of *cis*-**4a**.



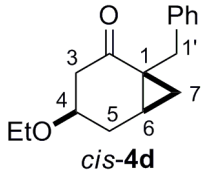
trans-**4c**

(±)-(1*R*,4*R*)-4-Ethoxy-1-methylbicyclo[4.1.0]heptan-2-one (*trans*-4c)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (dd, *J* = 5.1, 8.3 Hz, 1H, H7), 1.10 (t, *J* = 5.4 Hz, 1H, H7), 1.16 (t, *J* = 7.1 Hz, 3H, Me), 1.23 (s, 3H, Me), 1.51-1.55 (m, 1H, H6), 1.97-2.02 (m, 1H, H5), 2.15 (ddd, *J* = 2.4, 4.4, 13.7 Hz, 1H, H5), 2.26 (ddd, *J* = 1.0, 7.6, 16.8 Hz, 1H, H3), 2.55 (dd, *J*

= 4.2, 16.8 Hz, 1H, H3), 3.39-3.52 (m, 2H, OC$\underline{H}_2$), 3.67-3.72 (m, 1H, H4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5, 19.1, 21.4, 24.4, 29.1, 29.4, 42.6, 63.5, 73.4, 208.9; IR (cm^{-1}, $CHCl_3$) 2930, 1684, 1211, 1113; HRMS (EI+) *m/z* calcd for $C_{10}H_{16}O_2$: 168.11503, found 168.11460.

The stereochemistry was determined by the similarity in ^{1}H NMR spectra of *trans*-**4a**.

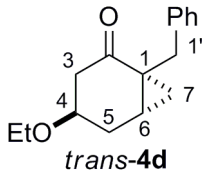


cis-**4d**

(±)-(1*R*,4*R*)-1-Benzyl-4-ethoxybicyclo[4.1.0]heptan-2-one (*cis*-4d)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (dd, *J* = 4.9, 8.5 Hz, 1H, H7), 1.14 (t, *J* = 7.1 Hz, 3H, Me), 1.37 (dd, *J* = 5.1, 6.1 Hz, 1H, H7), 1.48-1.53 (m, 1H, H6), 1.86 (ddd, *J* = 2.0, 7.1, 14.2 Hz, 1H, H5eq), 2.27-2.32 (m, 1H, H5ax), 2.33 (dd, *J* = 8.3, 16.1 Hz, 1H, H3ax), 2.41 (ddd, *J* = 1.5, 4.4, 15.6 Hz, 1H, H3eq), 2.51 (d, *J* = 14.6 Hz, 1H, H1'), 3.41 (d, *J* = 14.6Hz, 1H, H1'), 3.42 (q, *J* = 7.1 Hz, 2H), 3.54-3.59 (m, 1H, H4), 7.14-7.26 (m, 5H, Ph); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 15.3, 21.4, 22.4, 28.7, 34.6, 38.1, 43.4, 63.7, 74.9, 126.0, 128.1, 129.1, 139.3, 208.2; IR (cm^{-1}, $CHCl_3$) 3011, 1686, 1356, 1096; HRMS (EI+) *m/z* calcd for $C_{16}H_{20}O_2$: 244.14633, found 244.14640.

The stereochemistry was determined by the similarity in ^{1}H NMR spectra of *cis*-**4a**.

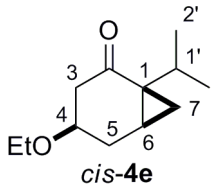


trans-**4d**

(±)-(1*R*,4*S*)-1-Benzyl-4-ethoxybicyclo[4.1.0]heptan-2-one (*trans*-4d)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (dd, *J* = 5.4, 8.5 Hz, 1H, H7), 1.07 (t, *J* = 5.7 Hz, 1H, H7), 1.11 (t, *J* = 7.1 Hz, 3H, Me), 1.57-1.61 (m, 1H), 1.98 (ddd, *J* = 5.6, 7.3, 13.7 Hz, 1H), 2.17 (ddd, *J* = 2.4, 4.2, 13.7 Hz, 1H), 2.21 (ddd, *J* = 0.7, 7.8, 16.8 Hz, 1H), 2.56 (d, *J* = 14.6 Hz, 1H, H1'), 2.58 (dd, *J* = 4.2, 16.8 Hz, 1H), 3.38 (qd, *J* = 7.1, 9.0 Hz, 1H, OC$\underline{H}_2$), 3.44 (qd, *J* = 7.1, 9.0 Hz, 1H, OC$\underline{H}_2$), 3.46 (d, *J* = 14.4 Hz, 1H, H1'), 3.64-3.69 (m, 1H, H4), 7.15-7.25 (m, 5H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4, 19.6, 22.0, 28.8, 33.9, 37.8, 43.3, 63.4, 72.9, 126.0, 128.1, 129.3, 139.1, 207.6; IR (cm^{-1}, $CHCl_3$) 3011, 1686, 1455, 1364, 1107, 1088; HRMS (EI+) *m/z* calcd for $C_{16}H_{20}O_2$: 244.14633, found 244.14620.

The stereochemistry was determined by the similarity in ^{1}H NMR spectra of *trans*-**4a**.

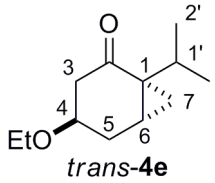


cis-**4e**

(±)-(1*R*,4*R*)-4-Ethoxy-1-isopropylbicyclo[4.1.0]heptan-2-one (*cis*-4e)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (d, *J* = 7.1 Hz, 3H, H2'), 0.98 (d, *J* = 6.8 Hz, 3H, H2'), 1.08 (dd, *J* = 5.1, 8.8 Hz, 1H, H7), 1.15 (dd, *J* = 5.1, 6.1 Hz, 1H, H7), 1.16 (t, *J* = 7.1, 3H, $CH_2C\underline{H}_3$), 1.33-1.38 (m, 1H), 1.81 (dd, *J* = 2.2, 8.1, 13.9 Hz, 1H), 1.85 (m, *J* = 6.8 Hz, 1H, H1'), 2.28 (ddd, *J* = 0.5, 9.0, 15.1 Hz, 1H), 2.31-2.37 (m, 1H), 2.44 (ddd, *J* = 1.7, 4.2, 15.1 Hz, 1H), 3.45 (qd, J = 0.7, 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 3.55-3.60 (m, 1H, H4); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 15.4, 18.2, 19.8, 20.0, 21.2, 29.4, 30.4, 38.6, 44.2, 63.7, 75.3; IR (cm^{-1}, $CHCl_3$) 3019, 1684, 1458, 1373, 1098; HRMS (EI+) *m/z* calcd for $C_{12}H_{20}O_2$: 196.14633, found 196.14647.

The stereochemistry was determined by the similarity in ^{1}H NMR spectra of *cis*-**4a**.

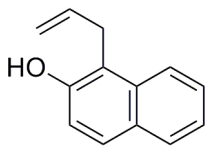


trans-**4e**

(±)-(1*R*,4*S*)-4-Ethoxy-1-isopropylbicyclo[4.1.0]heptan-2-one (*trans*-4e)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (d, *J* = 7.1 Hz, 3H, H2'), 0.89 (t, *J* = 5.6 Hz, 1H, H7), 1.00 (d, *J* = 6.8 Hz, 3H, H2'), 1.02 (dd, *J* = 5.6, 8.5 Hz, 1H, H2'), 1.15 (t, *J* = 7.1 Hz, 3H, $OCH_2C\underline{H}_3$), 1.43-1.47 (m, 1H, H6), 1.92 (m, 1H, H1'), 1.97-2.02 (m, 1H, H5), 2.10-2.14 (m, 1H, H5), 2.21-2.27 (m, 1H, H3), 2.51 (dd, *J* = 3.9, 16.6 Hz, 1H, H3), 3.39-3.51 (m, 2H, $OC\underline{H}_2$), 3.64-3.69 (m, 1H, H4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4, 18.0, 18.6, 20.1, 20.2, 29.2, 30.3, 37.9, 43.8, 63.3, 73.2, 208.3; IR (cm^{-1}, $CHCl_3$) 2979, 1686, 1456, 1383, 1109, 909; HRMS (EI+) *m/z* calcd for $C_{12}H_{20}O_2$: 196.14633, found 196.14601.

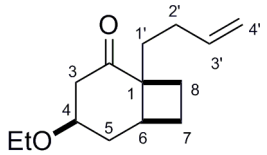
The stereochemistry was determined by the similarity in ^{1}H NMR spectra of *trans*-**4a**.



7

1-Allyl-2-naphthol (7)[1]

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (d, *J* = 5.6 Hz, C<u>H</u>$_2$CH=), 5.05-5.11 (m, 3H, O<u>H</u>, =C<u>H</u>$_2$), 6.03-6.10 (m, 1H, CH$_2$C<u>H</u>=), 7.08 (d, *J* = 8.8 Hz), 7.33 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.1 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.3, 116.0, 116.8, 117.9, 123.0, 123.2, 126.5, 128.3, 128.6, 129.4, 133.2, 135.7, 151.2; IR (cm^{-1}, $CHCl_3$) 3588, 1620, 1516, 1260, 814.

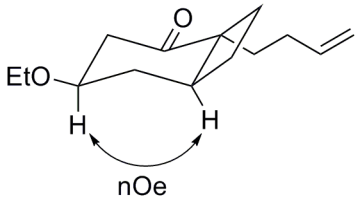


9a

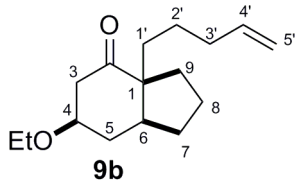
(±)-(1*R*,4*S*)-1-(3-Butenyl)-4-ethoxybicyclo[4.2.0]octan-2-one (9a)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (t, *J* = 7.1 Hz, 3H, Me), 1.67-1.73 (m, 2H, H5 and H1'), 1.77-1.87 (m, 3H, H7, H8, and H1'), 1.89-1.94 (m, 2H, H2'), 2.01-2.06 (m, 2H, H5 and H7), 2.32-2.37 (m, 1H, H8), 2.51 (ddd, *J* = 1.0, 6.8, 15.9 Hz, 1H, H3), 2.51-2.55 (m, 1H, H6), 2.63 (ddd, *J* = 1.0, 4.4, 15.9 Hz, 1H, H3), 3.47 (qd, *J* = 7.1, 9.0 Hz, 1H, OC<u>H</u>$_2$), 3.51 (qd, *J* = 7.1, 9.0 Hz, 1H, OC<u>H</u>$_2$), 3.84-3.88 (m, 1H, H4), 4.92-5.01 (m, 2H, H4') 5.71-5.79 (m, 1H, H3'); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4 (Me), 23.4 (C7), 28.8 (C8), 29.0 (C2'), 32.6 (C5), 37.6 (C1'), 39.2 (C6), 45.0 (C3), 52.4 (C1), 63.6 (O<u>C</u>H$_2$), 75.8 (C4), 114.7 (C4'), 138.1 (C3'), 215.2 (C2); IR (cm^{-1}, $CHCl_3$) 2930, 1701, 1642, 1451, 1354, 1210, 1084; HRMS (EI+) *m/z* calcd for $C_{14}H_{22}O_2$: 222.16198, found 222.16149.

The stereochemistry was determined by NOE experiments.



[1] (a) Tsang, K. Y.; Brimble, M. *Tetrahedron* **2007**, *63*, 6015. (b) Gozzo, F. C.; Fernandes, S. A.; Rodrigues, D. C.; Eberlin, M. N.; Marsaioli, A. J. *J. Org. Chem*. **2003**, *68*, 5493.

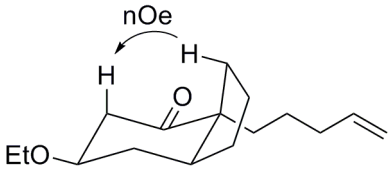


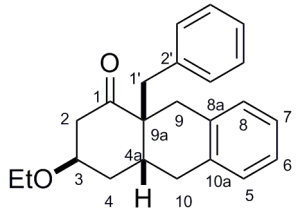
9b

(±)-(1*R*,4*S*)-4-Ethoxy-1-(4-pentenyl)bicyclo[4.3.0]nonan-2-one (9b)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (t, *J* = 7.1 Hz, 3H, Me), 1.14-1.20 (m, 1H, H2'), 1.21-1.30 (m, 1H, H2'), 1.36 (ddd, *J* = 5.4, 8.8, 12.9 Hz, 1H, H9×1), 1.43-1.70 (m, 6H, H5×1, H1' ×2, H8×2, and H7×1), 1.82-1.90 (m, 1H, H7×1), 1.94-2.12 (m, 4H, H3'×2, H5×1, and H6), 2.17 (ddd, *J* = 9.3, 10.2, 13.4 Hz, H9×1), 2.40 (dd, *J* = 8.1, 15.4 Hz, 1H, H3×1), 2.72 (ddd, *J* = 1.7, 5.1, 15.4 Hz, 1H, H3×1), 3.48 (qd, *J* = 7.1, 1.0 Hz, 2H, OC$\underline{H}_2$), 3.68-3.74 (m, 1H, H4), 4.93-5.01 (m, 2H, H5'×2), 5.72-5.80 (m, 1H, H4'); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (Me), 22.1 (C8), 24.7 (C2'), 32.0 (C7), 33.6 (C5), 34.2 (C9), 34.2 (C6), 36.6 (C1'), 43.4 (C3'), 44.4 (C3), 59.1 (C1), 63.5 (O$\underline{C}$H$_2$), 75.5 (C4), 114.7 (C5'), 138.5 (C4'), 213.4 (C2); IR (cm^{-1}, $CHCl_3$) 2939, 1698, 1640, 1458, 1375, 1356, 1235, 1102, 916; HRMS (EI+) *m/z* calcd for $C_{16}H_{26}O_2$: 250.19328, found 250.19373.

The stereochemistry was determined by NOE experiments.





9d

(±)-(3*R*,4a*R*,9a*R*)-9a-Benzyl-3-ethoxy-3,4,4a,9,9a-hexahydro-1-(2*H*)-anthracenone (**9d**, the major isomer)

Colorless crystals: mp 125.5-126.0 °C (hexane-ether); ^{1}H NMR (500 MHz, C_6D_6) δ 0.98 (t, *J* = 7.1 Hz, 3H, Me), 1.34 (ddd, *J* = 2.7, 12.5, 13.9 Hz, 1H, H4ax), 1.49-1.54 (m, 1H, H4eq), 2.09 (dd, *J* = 2.7, 17.6 Hz, 1H, H10), 2.31 (d, *J* = 16.4 Hz, 1H, H9), 2.32 (dd, *J* = 15.8, 4.2 Hz, 1H, H2), 2.45-2.50 (m, 1H, H4a), 2.54 (d, *J* = 14.4 Hz, 1H, Bn), 2.60 (ddd, *J* = 2.2, 3.7, 15.9 Hz, 1H, H2), 2.81 (d, *J* = 17.1 Hz, 1H, H9), 2.89 (dd, *J* = 6.3, 17.6 Hz, H10ax), 3.00 (qd, *J* = 6.8, 8.8 Hz, 1H, OC$\underline{H}_2$), 3.08 (qd,

J = 7.1, 8.8 Hz, 1H, OC<u>H</u>$_2$), 3.32-3.35 (m, 1H, H3), 3.67 (d, J = 14.4 Hz, 1H, Bn), 6.90-6.91 (m, 1H), 6.95-6.97 (m, 1H), 7.02-7.12 (m, 5H), 7.20-7.21 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 15.6 (Me), 30.2 (C4a), 31.4 (C10), 32.4 (C4), 34.7 (C9), 39.1 (Bn), 42.8 (C2), 52.7 (C9a), 63.0 (O<u>C</u>H$_2$), 74.1 (C3), 126.3, 126.3, 126.4, 127.9, 128.1, 128.4, 129.6, 129.6, 130.8, 133.3 (C8a), 134.2 (C10a), 138.7(C2'), 210.9; IR (cm^{-1}, $CHCl_3$) 3013, 1705, 1497, 1455, 1088, 702; HRMS (EI+) *m/z* calcd for $C_{23}H_{26}O_2$: 334.19328, found 334.19268.

The stereochemistry was determined by X-ray crystallographic analysis.

CCDC 735720 contains the supplementary crystallographic data of this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

$C_{23}H_{26}O_2$, M = 334.46, monoclinic, a = 10.286(3), b = 16.713(4), c = 11.099(3) Å, β = 112.789(2), U = 1759.0(7) Å^3, T = 123 K, space group P121/a1 (no. 14), Z = 4, 19979 reflections measured, 4596 unique (R_{int} = 0.136), 2609 reflections ($I > 3.0\sigma(I)$) were used in all calculations. The final $wR(F^2)$ was 0.0962 ($I > 3.0\sigma(I)$).

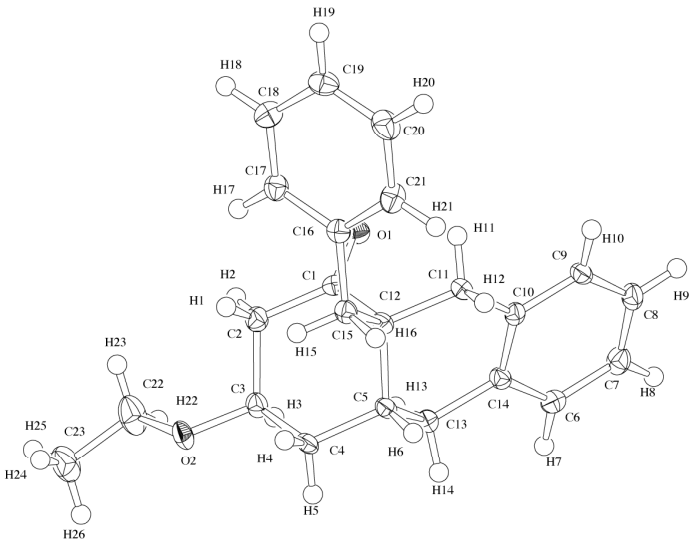
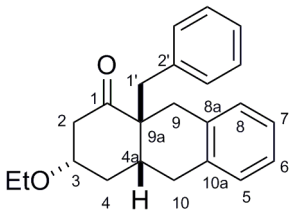


Figure S1. ORTEP figure of compound **9d**. Thermal ellipsoids of non-H atoms are drawn at the

50% probability. H atoms are indicated by small circles.



9d'

(±)-(3*R*,4a*S*,9a*S*)-9a-Benzyl-3-ethoxy-3,4,4a,9,9a-hexahydro-1-(2*H*)-anthracenone (**9d'**, the minor isomer)

Colorless crystals: mp 85.5-87.0 °C (EtOH); ^{1}H NMR (500 MHz, C_6D_6) δ 0.98 (t, *J* = 7.1 Hz, 3H, Me), 1.46 (ddd, *J* = 9.5, 12.9, 13.2 Hz, 1H, H4ax), 1.52-1.56 (m, 1H, H4eq), 1.71-1.74 (m, 1H, H4a), 2.19 (d, *J* = 16.6 Hz, 1H, H10eq), 2.34 (d, *J* = 17.1 Hz, 1H, H9), 2.44 (d, *J* = 13.9 Hz, 1H, H1'), 2.48 (dd, *J* = 9.8, 15.4 Hz, 1H, H2ax), 2.63 (ddd, *J* = 1.7, 5.4, 15.4 Hz, 1H, H2eq), 2.90 (d, *J* = 17.1 Hz, 1H, H9), 3.01-3.10 (m, 3H, H3, H10ax, OC$\underline{H}_2$), 3.60 (d, *J* = 14.2 Hz, 1H, H1'), 6.85 (d, *J* = 7.3 Hz, 1H, arom), 7.00-7.21 (m, 8H, arom); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.1 Hz, 3H, Me), 1.62-1.70 (m, 1H, H4), 1.95-2.00 (m, 2H, H4 and H4a), 2.52-2.64 (m, 4H), 2.73 (ddd, *J* = 1.7, 5.6, 15.9 Hz, 1H, H2), 3.14 (d, *J* = 17.1 Hz, 1H, H1' or H9), 3.21 (dd, *J* = 6.1, 17.3 Hz, 1H, H10), 3.43 (q, *J* = 7.1 Hz, 1H, OC$\underline{H}_2$), 3.43 (q, *J* = 7.1 Hz, 1H, OC$\underline{H}_2$), 3.47 (d, *J* = 14.4 Hz, 1H, H1' or H9), 3.50-3.56 (m, 1H, H3), 7.07-7.25 (m, 9H, arom); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (Me), 31.2 (C4a), 31.5 (C10), 34.4 (C4), 34.5 (C1' or C9), 38.9 (C1' or C9), 44.8 (C2), 52.1 (C9a), 63.5 (O$\underline{C}H_2$), 74.0 (C3), 126.1, 126.2, 126.3, 128.1, 129.2, 129.3, 130.4, 132.5, 133.5, 138.0, 212.6 (C1); ^{13}C NMR (125 MHz, C_6D_6) δ 15.7 (Me), 31.2 (C4a), 31.7 (C10), 34.4 (C4), 34.7 (C9), 39.0 (C1'), 44.9 (C2), 52.2 (C9a), 63.3 (O$\underline{C}H_2$), 74.3 (C3), 126.3, 126.4, 126.5, 128.4, 129.5, 129.8, 131.0, 133.0 (C8a or C10a), 133.7 (C8a or C10a), 138.8, 211.0 (C1); IR (cm^{-1}, $CHCl_3$) 3011, 1703, 1603, 1584, 1497, 1455, 1429, 1375, 1350, 1223, 1094, 740, 704; HRMS (EI+) *m/z* calcd for $C_{23}H_{26}O_2$: 334.19328, found 334.19341.

The stereochemistry was determined by X ray crystallographic analysis.

CCDC 735721 contains the supplementary crystallographic data of this compound. This compound contains two enantiomers. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

$C_{23}H_{26}O_2$, *M* = 334.46, orthorhombic, *a* = 7.3596(5), *b* = 19.161(1), *c* = 13.049(1) Å, *U* = 1840.1(2) Å^3, *T* = 123 K, space group Pna21 (no. 33), *Z* = 4, 21633 reflections measured, 2648 unique (R_{int} = 0.017), 4049 reflections (unaveraged Friedel pairs, $I > 3.0\sigma(I)$) were used in all calculations. The final $wR(F^2)$ was 0.0443 ($I > 3.0\sigma(I)$).

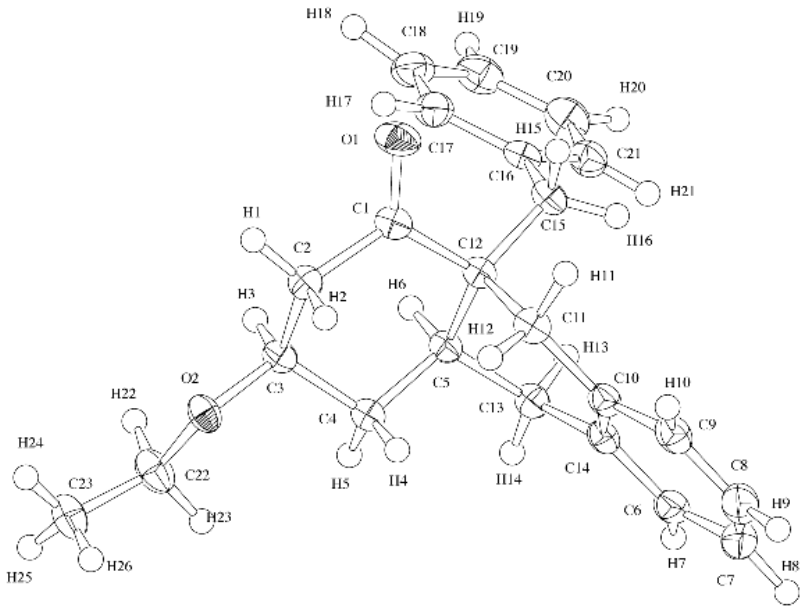
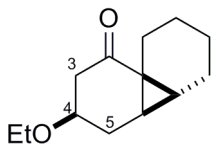


Figure S2. ORTEP figure of compound **9d'**. Thermal ellipsoids of non-H atoms are drawn at the 50% probability. H atoms are indicated by small circles.



cis-**9e**

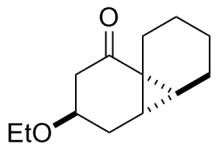
The reaction of employing a mixture of four diastereomers of **8e** (**8ea** : **8eb** : **8ec** : **8ed** = 33 : 29 : 24 : 14) was performed at –45 °C for 25 min and 0 °C for 5 min (Table 2, entry 5).

(±)-(1*R*,4*S*,4*S*,7*S*)-4-Ethoxytricyclo[5.4.0.0^{1,6}]undecan-2-one (***cis*-9e**, the major diastereomer)

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07-1.35 (m, 6H), 1.17 (t, J = 7.1 Hz, 3H, Me),

1.53-1.56 (m, 1H), 1.69 (ddd, *J* = 2.0, 8.8, 13.7 Hz, 1H, H5), 1.81-1.84 (m, 1H), 2.25 (dd, *J* = 10.5, 15.1 Hz, 1H, H3), 2.38-2.44 (m, 1H, H5), 2.52 (ddd, *J* = 2.0, 4.2, 14.9 Hz, 1H, H3), 2.69-2.74 (m, 1H), 3.43-3.49 (m, 2H), 3.53-3.59 (m, 1H, H4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4, 20.1, 21.0, 23.1, 23.2, 27.4, 30.0, 30.7, 33.8, 43.1, 63.7, 75.7, 208.9; IR (cm^{-1}, $CHCl_3$) 2932, 1674, 1451, 1375, 1354, 1096, 669; HRMS (EI+) *m/z* calcd for $C_{13}H_{20}O_2$: 208.14633, found 208.14599.

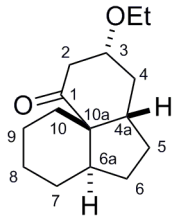
The stereochemistry was deduced by the similarity of ^{1}H NMR spectra of *cis*-**4a** (chemical shifts and coupling patters of H5).



trans-**9e**

(±)-(1*R*,4*S*,4*R*,7*S*)-4-Ethoxytricyclo[5.4.0.0^{1,6}]undecan-2-one (***trans*-9e**, the minor diastereomer) Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83-0.90 (m, 1H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.20-1.38 (m, 6H), 1.75-1.85 (m, 2H), 1.95-2.00 (m, 1H), 2.10-2.13 (m, 1H), 2.24-2.29 (m, 1H), 2.54 (dd, *J* = 4.2, 16.8 Hz, 1H), 2.67-2.73 (m, 1H), 3.38-3.52 (m, 2H), 3.68-3.72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5, 20.2, 20.9, 23.0, 23.1, 26.9, 27.7, 29.1, 30.3, 42.6, 63.4, 73.4, 208.4; IR (cm^{-1}, $CHCl_3$) 2930, 1676, 1449, 1119, 1094; HRMS (EI+) *m/z* calcd for $C_{13}H_{20}O_2$: 208.14633, found 208.14605.

The stereochemistry was deduced by the similarity of ^{1}H NMR spectra of *trans*-**4a**.



9f

(±)-(3*R*,4a*S*,6a*R*,10a*S*)-3-Ethoxy-dodecahydrobenzo[*c*]inden-1-one (**9f**)

The reaction of employing a mixture of four diastereomers of **8f** (33 : 23 : 23 : 21) was performed at –45 °C for 15 min and 0 °C for 15 min (Table 2, entry 6). Only one diastereomer was obtained. Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (t, *J* = 7.1 Hz, 3H), 1.24-1.30 (m, 1H), 1.37-1.65 (m, 10H), 1.79-1.86 (m, 1H), 1.97-2.07 (m, 3H), 2.53 (dd, *J* = 9.3, 13.9 Hz, 1H, H2ax), 2.54-2.59 (m, 1H), 2.69 (ddd, *J* = 1.2, 4.6, 13.9 Hz, 1H, H2eq), 3.43-3.53 (m, 2H), 3.55-3.61 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5, 20.8, 22.5, 25.8, 26.5, 29.6, 30.0, 34.7, 40.0, 44.5, 44.7, 56.9, 63.6, 76.2, 214.3; IR (cm^{-1}, $CHCl_3$) 2932, 1694, 1458, 1450, 1375, 1225, 1096; HRMS (EI+) *m/z* calcd for

$C_{15}H_{24}O_2$: 236.17763, found 236.17746.

The stereochemistry was determined by X-ray crystallography of a derivative of **9f** which was prepared by reduction with sodium borohydride followed by the reaction with 3,5-dinitrobenzoyl chloride.

CCDC 735722 contains the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

$C_{22}H_{28}N_2O_7$, M = 432.47, triclinic, a = 11.2136(2), b = 11.4312(3), c = 19.1419(7) Å, α = 85.877(4), β = 75.202(4), γ = 61.344(3), U = 2078.0(1) Å^3, T = 123 K, space group P-1 (no. 2), Z = 4, 24749 reflections measured, 10170 unique (R_{int} = 0.019), 7267 reflections ($I > 3.0\sigma(I)$) were used in all calculations. The final $wR(F^2)$ was 0.054 ($I > 3.0\sigma(I)$).

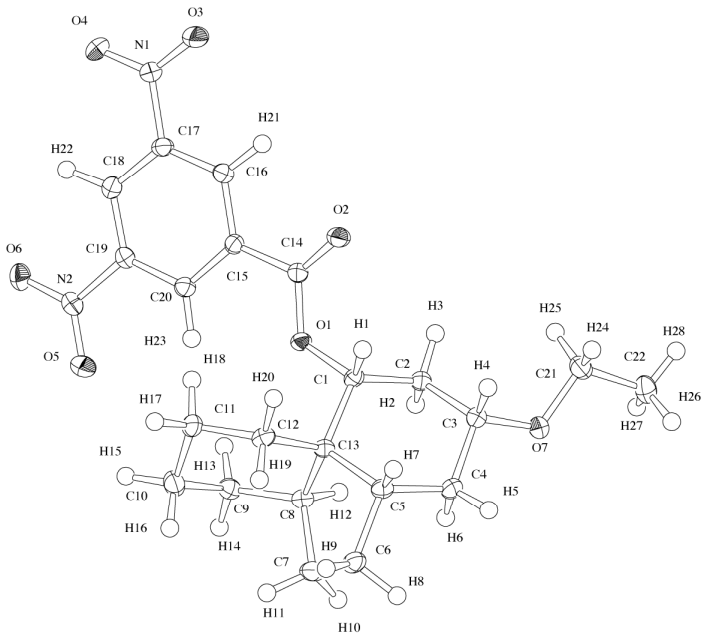
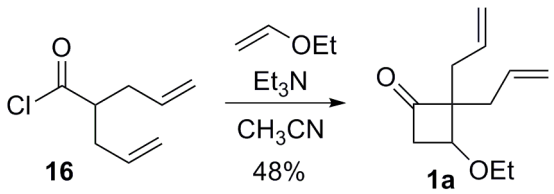


Figure S3. ORTEP figure of a derivative of **9f**. Thermal ellipsoids of non-H atoms are drawn at the 50% probability. H atoms are indicated by small circles.

2.4 Preparation of cyclobutanones

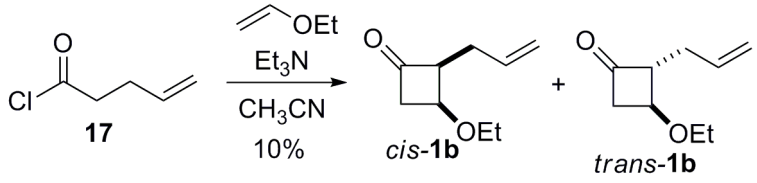
2.4.1 Preparation of 2,2-diallyl-3-ethocycyclobutanone (1a)



2,2-Diallyl-3-ethocycyclobutanone (1a)

To a stirred solution of 2-allylpent-4-enoyl chloride[2] **16** (10.3 g, 64.9 mmol) in acetonitrile (100 mL) was added slowly a solution of ethyl vinyl ether (11.2 mL, 117 mmol) and triethylamine (11.0 mL, 78.9 mmol) in acetonitrile (30 mL) for 40 min. The resulting yellow suspension was stirred at 90 for 2 h. The cooled reaction mixture was then filtered through Celite and volatiles were evaporated. The crude product was purified by column chromatography on silica gel (hexane / ethyl acetate = 19 : 1 → 15 : 1 → 5 : 1) followed by distillation (80–84 °C / 2.5 mmHg) to afford **1a** (6.11 g, 48%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.1 Hz, 3H), 2.29 (d, *J* = 7.3 Hz, 2H), 2.35 (dd, *J* = 8.1, 14.2 Hz, 1H), 2.53 (tdd, *J* = 1.2, 6.6, 14.4 Hz, 1H), 3.04 (dd, *J* = 5.9, 18.1 Hz, 1H), 3.13 (dd, *J* = 7.3, 18.1 Hz, 1H), 3.47-3.52 (m, 2H), 4.03 (dd, *J* = 5.6, 6.8 Hz, 1H), 5.06-5.14 (m, 4H), 5.68-5.77 (m, 1H), 5.82-5.90 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 33.4, 36.8, 50.8, 65.6, 69.4, 71.0, 118.1, 118.8, 132.8, 133.9, 211.2; IR (cm^{-1}, $CHCl_3$) 2980, 1775, 1640, 1439, 1345, 1188, 1123, 999, 922; HRMS (EI+) *m/z* calcd for $C_{12}H_{18}O_2$:194.13068, found 194.13012.

2.4.2 Preparation of 2-allyl-3-ethocycyclobutanone (1b)



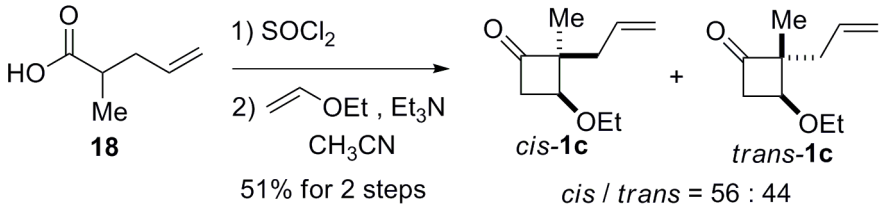
cis / *trans* = 30 : 70

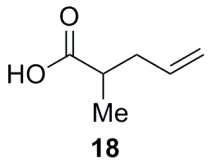
2-Allyl-3-ethoxycyclobutanone (**1b**) was obtained in 10% yield from pent-4-enoyl chloride (**17**) by the procedure described in the preparation of **1a**. The stereochemistry of **1b** was determined by H3 chemical shifts according to Huisgen's assignment.[3] Compound **1b**: ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 30 : 70) δ 1.21 (t, *J* = 6.8 Hz, 0.9H, *cis*-Me), 1.24 (t, *J* = 7.1 Hz, 2.1H, *trans*-Me),

[2] Bouhadir, K. H.; Zhou, J.-L.; Shevlin, P. B. *Synth. Commun*. **2005**, *35*, 1003-1010.
[3] Mayr, H.; Huisgen, R. *Tetrahedron Lett*. **1975**, 1349.

2.27-2.33 (m, 0.7H), 2.39-2.50 (m, 1.4H), 2.92 (ddd, *J* = 1.7, 3.7, 17.6 Hz, 0.3H), 3.02 (ddd, *J* = 4.4, 5.6, 17.6 Hz, 0.7H), 3.13 (ddd, *J* = 2.0, 6.8, 17.5 Hz, 0.7H), 3.20 (ddd, *J* = 5.1, 6.3, 17.6 Hz, 0.3H), 3.30-3.39 (m, 1H), 3.45-3.56 (m, 2H, OC$\underline{H}_2$), 3.96 (td, *J* = 5.1, 6.6 Hz, 0.7H, *trans*-H3), 4.30 (dt, *J* = 3.7, 6.6 Hz, 0.3H, *cis*-H3), 5.01-5.16 (m, 2H), 5.75-5.92 (m, 1H); ^{3}C NMR (125 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 30 : 70) δ 15.1 (*cis*), 15.2 (*trans*), 27.6 (*cis*), 31.7 (*trans*), 51.6 (*trans*), 52.3 (*cis*), 63.3 (*cis*), 65.2 (*trans*), 65.3 (*cis*), 65.9 (*trans*), 66.7 (*cis*), 69.1 (*trans*), 115.9 (*cis*), 117.1 (*trans*), 134.4 (*trans*), 135.9 (*cis*), 207.3 (*trans*), 209.0 (*cis*); IR (cm^{-1}, $CHCl_3$) 2980, 1781, 1642, 1341, 1123, 922; HRMS (EI+) *m/z* calcd for $C_9H_{14}O_2$:154.09938, found 154.09967.

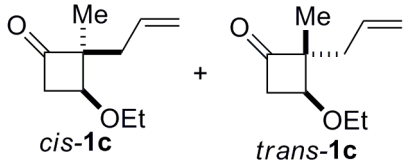
2.4.3 Preparation of 2-allyl-3-ethoxy-2-methylcyclobutanone (1c)





2-Methylpent-4-enoic acid (18)

2-Methylpent-4-enoic acid (**18**) was prepared by allylation of diethyl methylmalonate followed by hydrolysis and decarboxylation. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (d, *J* = 7.1 Hz, 3H), 2.18-2.24 (m, 1H), 2.42-2.48 (m, 1H), 2.53-2.60 (m, 1H), 5.05-5.12 (m, 2H), 5.73-5.82 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3, 37.5, 39.1, 117.2, 135.1, 182.3; IR (cm^{-1}, $CHCl_3$) 2980, 1709, 1649, 1496, 1244, 922; HRMS (EI+) *m/z* calcd for $C_6H_{10}O_2$: 114.06808, found 114.06836.

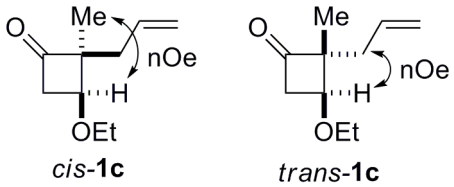


2-Allyl-3-ethoxy-2-methylcyclobutanone (1c)

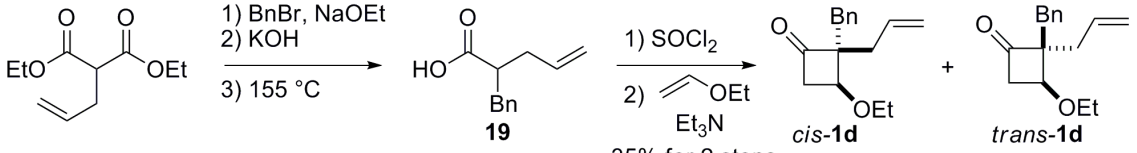
Compound **1c** was prepared from 2-methylpent-4-enoic acid (**18**) by formation of acid chloride with thionyl chloride, followed by [2 + 2] cycloaddition with ethyl vinyl ether using the method described in the preparation of **1a** (51% yield for 2 steps). Compound **1c**: ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 56 : 44) δ 1.16 (s, 1.68H, major Me), 1.18 (s, 1.32 H,

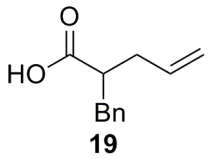
minor Me), 1.23 (t, *J* = 7.1 Hz, 1.32H, minor Me), 1.24 (t, *J* = 7.1 Hz, 1.68H, major Me), 2.25-2.30 (m, 0.88H, minor C$\underline{H_2}$CH=CH$_2$), 2.34 (dd, *J* = 8.1, 14.2 Hz, 0.56H, major C$\underline{H_2}$CH=CH$_2$), 2.48 (tdd, *J* = 1.2, 6.8, 14.2 Hz, 0.56H, major C$\underline{H_2}$CH=CH$_2$), 3.03 (dd, *J* = 5.6, 17.8 Hz, 0.44H, minor H2), 3.07 (dd, *J* = 5.6, 17.3 Hz, 0.56H, major H2), 3.16 (dd, *J* = 7.1, 15.6 Hz, 0.56H, major H2), 3.20 (dd, *J* = 7.1, 15.1 Hz, 0.44H, minor H2), 3.46-3.57 (m, 2H, OC$\underline{H_2}$), 3.88 (dd, *J* = 5.9, 6.8 Hz, 0.56H, major H3), 3.98 (dd, *J* = 5.6, 7.1 Hz, minor H3), 5.05-5.14 (m, 2H), 5.73-5.88 (m, 1H); ^{13}C NMR (67.5 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 56 : 44) δ 14.3, 15.1 (minor), 15.2 (major), 19.3, 35.4, 39.4, 50.2 (minor), 50.5 (major), 65.6 (minor), 65.6 (major), 65.9 (major), 66.3 (minor), 71.1, 73.9, 117.8 (major), 118.6 (minor), 133.0 (minor), 134.1 (major), 211.9 (major), 212.8 (minor); IR (cm^{-1}, $CHCl_3$) 1775, 1640, 1451, 1374, 1343, 1192, 1117, 922; HRMS (EI+) *m/z* calcd for $C_{10}H_{16}O_2$:168.11503, found 168.11496.

The stereochemistry was determined by NOE.



2.4.4 Preparation of 2-allyl-2-benzyl-3-ethoxycyclobutanone (1d)

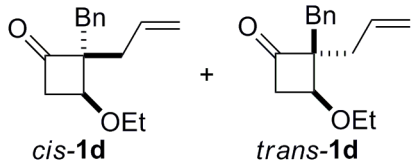




2-Benzylpent-4-enoic acid (19)[4]

2-Benzylpent-4-enoic acid (**19**) was prepared by benzylation of diethyl allylmalonate, followed by hydrolysis and decarboxylation. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27-2.32 (m, 1H), 2.36-2.42 (m, 1H), 2.75-2.81 (m, 2H), 2.96-3.01 (m, 1H), 5.06-5.11 (m, 2H), 5.74-5.82 (m, 1H), 7.17-7.22 (m, 3H), 7.26-7.30 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.6, 37.3, 46.9, 117.5, 126.5, 128.5, 128.9, 134.7, 138.8, 180.3; IR (cm^{-1}, $CHCl_3$) 3034, 1709, 1644, 1497, 1454, 922; HRMS (EI+) *m/z* calcd for $C_{12}H_{14}O_2$: 190.09938, found 190.09946.

[4] Curran, D. P.; Yu, H.; Liu, H. *Tetrahedron* **1994**, *50*, 7343.

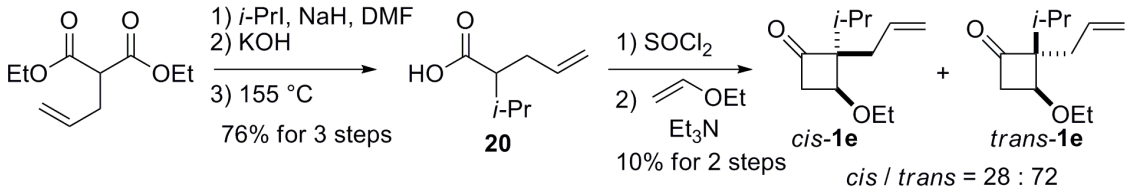


2-Allyl-2-benzyl-3-ethoxycyclobutanone (1d)

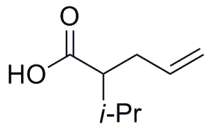
Compound **1d** was prepared as a colorless oil from 2-benzylpent-4-enoic acid (**19**) by formation of acid chloride with thionyl chloride, followed by [2 + 2] cycloaddition with ethyl vinyl ether using the method described in the preparation of **1a** (35% yield for 2 steps): ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 34 : 66) δ 1.16 (t, *J* = 7.1 Hz, 1.0H, minor Me), 1.29 (t, *J* = 7.1 Hz, 2.0H, major Me), 2.17 (dd, *J* = 7.6, 14.2 Hz, 0.66H, major), 2.22 (dd, *J* = 7.1, 14.6 Hz, 0.66H, major), 2.39 (dd, *J* = 8.1, 14.4 Hz, 0.34H, minor), 2.57 (dd, *J* = 6.3, 14.4 Hz, 0.34H, minor), 2.73 (d, *J* = 13.9 Hz, 0.34H, minor), 2.84 (dd, *J* = 7.3, 18.1 Hz, 0.34H, minor), 2.96-3.01 (m, 2H), 3.06-3.14 (m, 1.32H, major), 3.27 (qd, *J* = 7.1, 9.3 Hz, 0.34H, minor OC$\underline{H}_2$), 3.36 (qd, *J* = 7.1, 9.3 Hz, 0.34H, minor OC$\underline{H}_2$), 3.55 (q, *J* = 7.1 Hz, 1.34H, major OC$\underline{H}_2$), 4.02-4.07 (m, 1H, H3), 5.05-5.16 (m, 2H, =C$\underline{H}_2$), 5.68-5.76 (m, 0.67H, major C$\underline{H}$=CH$_2$), 5.91-6.00 (m, 0.34H, minor C$\underline{H}$=CH$_2$), 7.14-7.30 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 34 : 66) δ 15.1 (minor), 15.2 (major), 34.5 (minor), 34.6 (major), 36.9 (major), 38.5 (minor), 50.8 (minor), 50.9 (major), 65.4 (major), 65.4 (minor), 69.9, 70.5, 70.7 (minor), 70.7 (major), 118.3 (minor), 118.9 (major), 126.4 (major), 126.6 (minor), 128.0 (major), 128.4 (minor), 130.2 (minor), 130.4 (major), 133.1 (major), 134.1, 137.1, 210.8 (major), 211.5 (minor); IR (cm^{-1}, $CHCl_3$) 2930, 1773, 1640, 1603, 1497, 1455, 1441, 1374, 1345, 1186, 1123, 1078, 924; HRMS (EI+) *m/z* calcd for $C_{16}H_{20}O_2$:244.14633, found 244.14674.

The stereochemistry of **1d** was estimated by the fact that [2 + 2] cycloaddition between ketene and olefin gives cyclobutanones in which the bulkiest ketene and olefin substituents are in a 1,2-*cis* arrangement.[5]

2.4.5 Preparation of 2-allyl-3-ethoxy-2-isopropylcyclobutanone (1e)



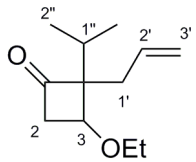
[5] Huisgen, R.; Mayr, H. *Tetrahedron Lett*. **1975**, 2969 and references cited therein.



20

2-Isopropylpent-4-enoic acid (20)[6]

2-Isopropylpent-4-enoic acid (**20**) was prepared by isopropylation of diethyl allylmalonate, followed by hydrolysis and decarboxylation. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 1.89-1.96 (m, 1H), 2.23-2.38 (m, 3H), 5.01-5.04 (m, 1H), 5.07-5.11 (m,1H), 5.74-5.82 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.1, 20.2, 30.0, 33.6, 52.1, 116.7, 135.6, 180.6; IR (cm^{-1}, $CHCl_3$) 2967, 1705, 1644, 1441, 1231, 920; HRMS (EI+) *m/z* calcd for $C_8H_{14}O_2$:142.09938, found 142.09896.



1e

2-Allyl-3-ethoxy-2-isopropylcyclobutanone (1e)

Compound **1e** was prepared as a colorless oil from 2-isopropylpent-4-enoic acid (**20**) by chlorination of with thionyl chloride, followed by [2 + 2] cycloaddition with ethyl vinyl ether using the method described in the preparation of **1a** (10% yield for 2 steps). Compound **1e**: ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 28 : 72) δ 0.89 (d, *J* = 6.8 Hz, 0.84H, *cis*-H2''), 0.93 (d, *J* = 6.6 Hz, 0.84H, *cis*-H2''), 1.02 (d, *J* = 6.8 Hz, 2.16H, *trans*-H2''), 1.05 (d, *J* = 6.8 Hz, 2.16H, *trans*-H2''), 1.22 (t, *J* = 7.1 Hz, 2.16H, *trans*-Me), 1.24 (t, *J* = 7.1 Hz, 0.84H, *cis*-Me), 1.94 (m, 0.28H, *cis*-H1''), 2.23-2.36 (m, 2.44H, *trans*-H1'' + H1' + *trans*-H1'), 2.52-2.56 (m, 0.28H, *cis*-H1'), 2.94 (dd, *J* = 5.9, 18.1 Hz, 0.72H, *trans*-H2), 2.96 (dd, *J* = 5.9, 18.3 Hz, 0.28H, *cis*-H2), 3.03 (dd, *J* = 7.1, 17.6 Hz, 0.72H, *trans*-H2), 3.05 (dd, *J* = 7.3, 18.1 Hz, 0.28H, *cis*-H2), 3.41-3.54 (m, 2H, O$\underline{CH_2}$), 4.05 (dd, *J* = 5.9, 6.8 Hz, 0.72H, *trans*-H3), 4.09 (dd, *J* = 5.9, 7.3 Hz, 0.28H, *cis*-H3), 5.05-5.15 (m, 2H, H3'), 5.66-5.75 (m, 0.72H, *trans*-H2'), 5.86-5.94 (m, 0.28H, *cis*-H2'); ^{13}C NMR (125 MHz, $CDCl_3$, a mixture of diastereomers, *cis* / *trans* = 28 : 72) δ 15.2 (*cis* + *trans*), 16.7 (cis), 18.2 (cis), 18.5 (trans), 18.9 (trans), 28.1 (trans), 28.8 (cis), 29.7 (trans), 30.3 (cis), 32.0 (cis), 34.4 (trans), 51.1 (cis), 51.3 (trans), 65.4 (trans), 68.7 (cis), 71.6 (trans), 73.2 (cis), 117.5 (cis), 118.5 (trans), 134.0 (trans), 134.6 (cis), 212.7 (cis), 212.8 (trans); IR (cm^{-1}, $CHCl_3$) 2990, 1769, 1640, 1387, 1190, 1119, 922; HRMS (EI+) *m/z* calcd for $C_{12}H_{20}O_2$:196.14633, found 196.14704.

For determination of the stereochemistry of **1e**, see the determination of stereochemistry of **1d**.

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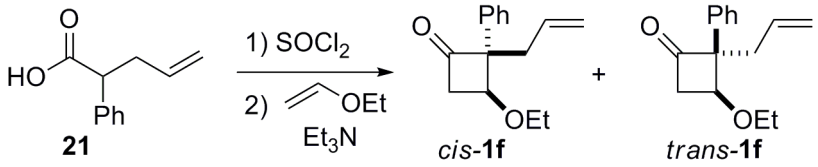
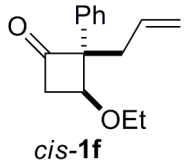
[6] Hanessian, S.; Claridge, S.; Johnstone, S. *J. Org. Chem.* **2002**, *67*, 4261.

2.4.6 Preparation of 2-allyl-3-ethoxy-2-phenylcyclobutanones (1f)



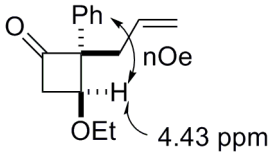
2-Phenylpent-4-enoic acid (**21**)[7] was prepared by allylation of diethyl phenymalonate followed by hydrolysis and decarboxylation. Compound **1f** was synthesized from 2-phenylpent-4-enoic acid (**21**) by chlorination of with thionyl chloride, followed by [2 + 2] cycloaddition with ethyl vinyl ether using the method of the synthesis of **1a** (19% yield for 2 steps).

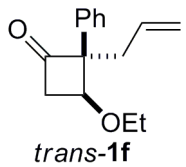


cis-**1f**

(±)-(2*R*,3*S*)-2-Allyl-3-ethoxy-2-phenylcyclobutanone (*cis*-1f): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (t, *J* = 7.1 Hz, 3H), 2.66-2.70 (m, 1H), 2.78 (tdd, *J* = 1.2, 7.1, 14.4 Hz, 1H), 3.15 (dd, *J* = 6.1, 17.8 Hz, 1H), 3.22 (dd, *J* = 7.3, 18.0 Hz, 1H), 3.63-3.69 (m, 2H), 4.43 (dd, *J* = 6.1, 7.3 Hz, 1H), 4.86-4.91 (m, 1H), 4.94-4.96 (m, 1H), 5.68-5.76 (m, 1H), 7.21-7.25 (m, 1H), 7.31-7.38 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3, 38.2, 50.7, 65.7, 73.6, 74.1, 118.0, 126.3, 126.8, 128.4, 133.5, 139.9, 208.5; IR (cm^{-1}, $CHCl_3$) 2982, 1775, 1640, 1601, 1493, 1447, 1379, 1345, 1209, 1121, 1080, 1049, 922; HRMS (EI+) *m/z* calcd for $C_{15}H_{18}O_2$: 230.13068, found 230.13072.

The stereochemistry was determined by NOE experiments.





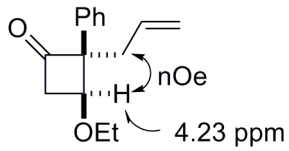
trans-**1f**

(±)-(2*R*,3*R*)-2-Allyl-3-ethoxy-2-phenylcyclobutanone (*trans*-1f): ^{1}H NMR (500 MHz, $CDCl_3$) δ

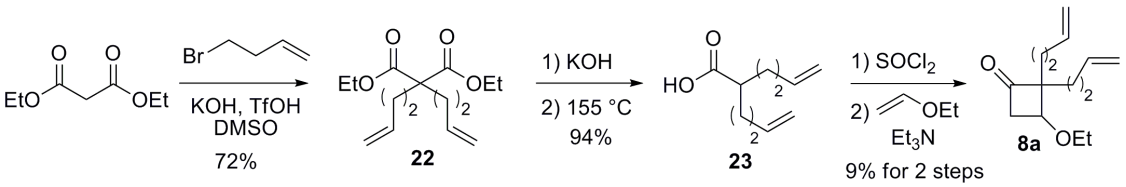
[7] Miller, R. D.; Goelitz, P. *J. Org. Chem.* **1981**, *46*, 1616.

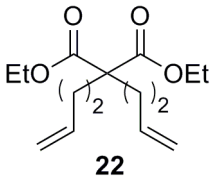
1.07 (t, *J* = 7.1 Hz, 3H), 2.62 (tdd, *J* = 1.2, 7.3, 14.2 Hz, 1H), 2.69 (tdd, *J* = 1.2, 7.1, 14.2 Hz, 1H), 3.01 (dd, *J* = 4.9, 18.1 Hz, 1H), 3.31 (dd, *J* = 6.8, 18.1 Hz, 1H), 3.36 (qd, *J* = 7.1, 9.3 Hz, 1H, OC$\underline{H}_2$), 3.47 (qd, *J* = 7.1, 9.3 Hz, 1H, OC$\underline{H}_2$), 4.23 (dd, *J* = 5.1, 6.8 Hz, 1H, H3), 5.05-5.10 (m, 2H), 5.65-5.73 (m, 1H), 7.22-7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 41.9, 51.1, 65.4, 72.6, 74.2, 118.9, 126.9, 127.9, 128.0, 132.8, 136.0, 209.7; IR (cm^{-1}, $CHCl_3$) 2980, 1777, 1640, 1601, 1495, 1447, 1375, 1347, 1190, 1121, 1065, 924; HRMS (EI+) *m/z* calcd for $C_{15}H_{18}O_2$: 230.13068, found 230.13021.

The stereochemistry was determined by NOE experiments. This assignment is consistent with Huisgen's assignment that the 3-H ring proton is more strongly deshielded by *cis*-vic- than *trans*-vic-alkyl group.



2.4.7 Preparation of 2,2-di(but-3-enyl)-3-ethoxycyclobutanone (8a)



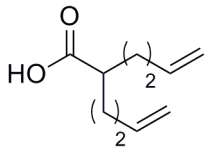


Diethyl dibut-3-enylmalonate (22)[8]

To a stirred mixture of potassium hydroxide (9.81 g, 175 mmol) in DMSO (50 mL) was added at 0 °C trifluoromethanesulfonic acid (6.7 mL, 75.7 mmol),[9] and the resulting mixture was stirred at room temperature for 15 min. 4-Bromo-1-butene (5.8 mL, 57.1 mmol) and diethyl malonate (4.0 g, 25.0 mmol) were added successively at room temperature, and the reaction mixture was stirred at 50 °C for 5.5 h. The reaction mixture was diluted with ether, and washed with 1 N hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and water (four times). The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was purified by column

[8] Conrad, J. C.; Eelman, M. D.; Duarte Silvia, J. A.; Monfette, S.; Parnas, H. H.; Snelgrove, J. L.; Fogg, D. E. *J. Am. Chem. Soc.* **2007**, *129*, 1024.
[9] Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, H. *Chirality* **2003**, *15*, 101.

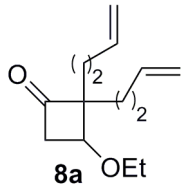
chromatography on silica gel (hexane / ether = 10 : 1) to afford **22** (4.81 g, 17.9 mmol, 72% yield) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.1 Hz, 6H), 1.93-2.02 (m, 8H), 4.19 (q, *J* = 7.1 Hz, 4H), 4.95-4.98 (m, 2H), 5.01-5.06 (m, 2H), 5.75-5.83 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 28.4, 31.6, 57.0, 61.1, 115.0, 137.6, 171.5; IR (cm^{-1}, $CHCl_3$) 2982, 1725, 1642, 1447, 1370, 1267, 1196, 1144, 1096, 1030, 918, 862; HRMS (EI+) *m/z* calcd for $C_{15}H_{24}O_4$: 268.16746, found 268.16698.



23

2-(But-3-enyl)hex-5-enoic acid (23)

To a stirred solution of diethyl dibut-3-enylmalonate **22** (4.80 g, 17.9 mmol) in ethanol (30 mL) was added a solution of potassium hydroxide (3.01 g, 53.6 mmol) in H_2O (13 mL), and the mixture was refluxed for 12 h. After evaporation of the solvent, the residue was acidified to pH 2 with 1 N hydrochloric acid, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. The obtained dibut-3-enylmalonic acid was heated at 155 °C for 4.5 h. The crude product was purified by column chromatography on silica gel (hexane / ether = 5 : 1) to afford 2-(but-3-enyl)hex-5-enoic acid **23** (2.82 g, 94% yield) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.55-1.62 (m, 2H), 1.73-1.81 (m, 2H), 2.04-2.17 (m, 4H), 2.41-2.47 (m, 1H), 4.97-5.00 (m, 2H), 5.02-5.06 (m, 2H), 5.75-5.83 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.1, 31.4, 44.0, 115.3, 137.6, 181.6; IR (cm^{-1}, $CHCl_3$) 2932, 1705, 1642, 1456, 1215, 995, 918; HRMS (EI+) *m/z* calcd for $C_{10}H_{16}O_2$: 168.11503, found 168.11510.



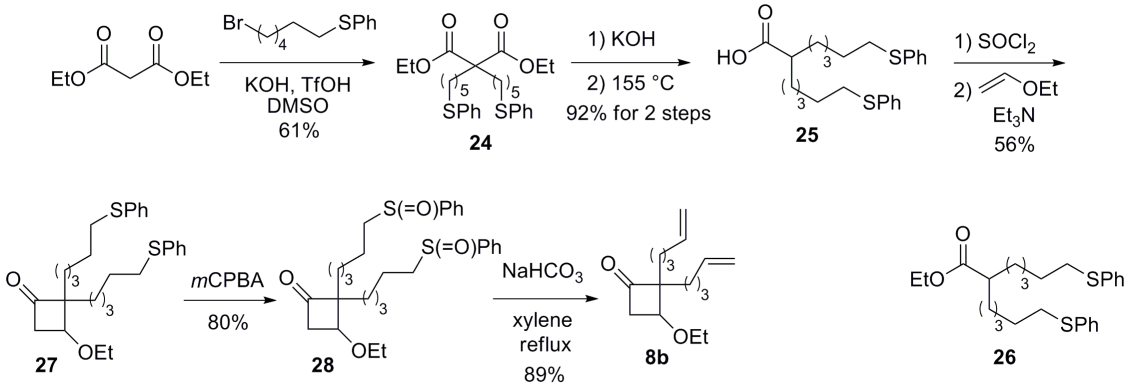
8a

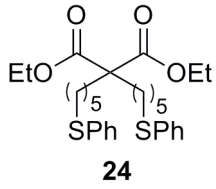
2,2-Di(but-3-enyl)-3-ethoxycyclobutanone (8a)

To a stirred solution of 2-(but-3-enyl)hex-5-enoic acid **23** (1.01 g, 6.00 mmol) in dry dichloromethane (10 mL) was added at 0 °C thionyl chloride (1.3 mL, 17.8 mmol) and DMF (0.05 mL, 0.64 mmol), and the reaction mixture was stirred at room temperature for 1 h. After evaporation of the solvent, the obtained 2-(but-3-enyl)hex-5-enoyl chloride was used without purification.

To a stirred solution of thus-obtained 2-(but-3-enyl)hex-5-enoyl chloride in acetonitrile (5 mL) was slowly added at room temperature a solution of ethyl vinyl ether (1.0 mL) and triethylamine (0.99 mL) in acetonitrile (7 mL). The reaction mixture was heated at 90 °C for 2 h, and cooled reaction mixture was filtered through Celite pad. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel (hexane / ether = 35 : 1) to afford 1-(but-3-enyl)bicyclo[2.1.1]hexan-5-one (191.4 mg, 22%) and **8a** (114.2 mg, 9%) as a colorless oil.
8a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.1 Hz, 3H), 1.57-1.73 (m, 3H), 1.82 (dd, *J* = 4.9, 12.0, 14.1 Hz, 1H), 1.98-2.20 (m, 4H), 3.03 (dd, *J* = 5.6, 17.8 Hz, 1H), 3.16 (dd, *J* = 7.1, 17.8 Hz, 1H), 3.45-3.55 (m, 2H), 3.96 (dd, *J* = 5.6, 7.1 Hz, 1H), 4.93-4.99 (m, 2H), 5.01-5.06 (m, 2H), 5.76-5.85 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 27.4, 28.2, 28.7, 31.2, 50.8, 65.5, 69.8, 72.1, 114.6, 115.0, 137.8, 138.5, 212.2; IR (cm^{-1}, $CHCl_3$) 2980, 1773, 1642, 1455, 1373, 1343, 1188, 1121, 995, 916; HRMS (EI+) *m/z* calcd for $C_{14}H_{22}O_2$: 222.16198, found 222.16246.

2.4.8 Preparation of 3-ethoxy-2,2-di(pent-4-enyl)cyclobutanone (8b)



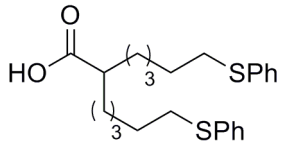


Diethyl 2,2-bis(5-phenylsulfanylpentyl)propanedioate (24)

Diethyl 2,2-bis(5-phenylsulfanylpentyl)propanedioate (**24**) was prepared from diethyl malonate and 5-bromo-1-phenylsulfanylpentane[10] by using the method described in the preparation of diethyl dibut-3-enylmalonate **22** (61% yield). Compound **24**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13-1.19 (m, 4H), 1.22 (t, *J* = 7.1 Hz, 6H), 1.39-1.45 (m, 4H), 1.60-1.67 (m, 4H), 1.82-1.86 (m, 4H), 2.89 (t, *J* =

[10] Ono, N.; Miyake, H.; Saito, T.; Kaji, A. *Synthesis* **1980**, 952.

7.3 Hz, 4H), 4.15 (q, *J* = 7.1 Hz, 4H), 7.13-7.17 (m, 2H), 7.25-7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 23.6, 28.8, 28.9, 32.1, 33.5, 57.4, 61.0, 125.7, 128.8, 128.9, 136.8, 171.7; IR (cm^{-1}, $CHCl_3$) 2934, 1723, 1586, 1482, 1439, 1228, 1157, 1094, 1026, 691; HRMS (EI+) *m/z* calcd for $C_{29}H_{40}S_2O_4$: 516.23681, found 516.23701.

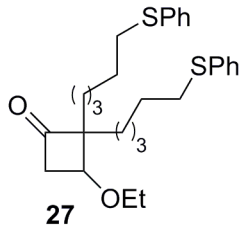


25

7-Phenylsulfanyl-2-(5-phenylsulfanylpentyl)heptanoic acid (25)

To a solution of diethyl 2,2-bis(5-phenylsulfanylpentyl)propanedioate **24** (5.78 g, 11 mmol) in ethanol (70 mL) was added a solution of potassium hydroxide (3.76 g, 67 mmol) in water (30 mL), and the mixture was refluxed for 9 h. After evaporation of solvents, 1 N hydrochloric acid was added (pH 2), and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried, and concentrated. Thus-obtained 2,2-bis(5-phenylsulfanylpentyl)propanedioic acid was heated at 155 °C for 5 h. The crude product was purified by column chromatography on silica gel (hexane / ethyl acetate) to afford ethyl 7-phenylsulfanyl-2-(5-phenylsulfanylpentyl)heptanoate **26** (2.37 g, 48%) and 7-phenylsulfanyl-2-(5-phenylsulfanylpentyl)heptanoic acid **25** (2.24 g, 48%). Ethyl ester **26** was hydrolyzed to **25** by using potassium hydroxide in ethanol-water in 92% yield (total 92% yield).

7-Phenylsulfanyl-2-(5-phenylsulfanylpentyl)heptanoic acid (**25**): colorless crystals: mp 55.0-56.0 °C (hexane-ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27-1.48 (m, 10H), 1.58-1.66 (m, 6H), 2.29-2.35 (m, 1H), 2.90 (t, *J* = 7.3 Hz, 4H), 7.14-7.17 (m, 2H), 7.25-7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.8, 28.6, 28.9, 31.9, 33.5, 45.2, 125.7, 128.8, 128.9, 136.8, 182.3; IR (cm^{-1}, $CHCl_3$) 2936, 1705, 1586, 1482, 1439, 1092, 1026, 909, 691, 669; Anal. Calcd. For $C_{24}H_{32}O_2S_2$: C, 69.19; H, 7.74. Found: C, 68.93; H, 7.81.

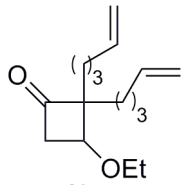


27

3-Ethoxy-2,2-bis(5-phenylsulfanylpentyl)cyclobutanone (27)

3-Ethoxy-2,2-bis(5-phenylsulfanylpentyl)cyclobutanone (**27**) was prepared from 7-phenylsulfanyl-2-(5-phenylsulfanylpentyl)heptanoic acid (**25**) by chlorination with thionyl

chloride, followed by [2 + 2] cycloaddition with ethyl vinyl ether by the method described in the preparation of **1a** (56% yield for 2 steps). Compound **27**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, *J* = 7.1 Hz, 3H), 1.24-1.70 (m, 16H), 2.90 (t, *J* = 6.8 Hz, 4H), 2.98 (dd, *J* = 5.6, 18.1 Hz, 1H), 3.11 (dd, *J* = 7.1, 17.8 Hz, 1H), 3.41-3.52 (m, 2H), 3.89 (dd, *J* = 5.9, 6.8 Hz, 1H), 7.14-7.18 (m, 2H), 7.25-7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 23.6, 24.0, 28.0, 28.9, 29.0, 29.2, 29.4, 32.0, 33.5, 50.7, 65.4, 70.2, 72.1, 125.7, 125.8, 128.8, 128.8, 128.9, 129.0, 136.8, 136.9, 212.8; IR (cm^{-1}, $CHCl_3$) 2936, 1771, 1586, 1482, 1439, 1120, 691; HRMS (EI+) *m/z* calcd for $C_{28}H_{38}S_2O_2$: 470.23133, found 470.23090.



8b

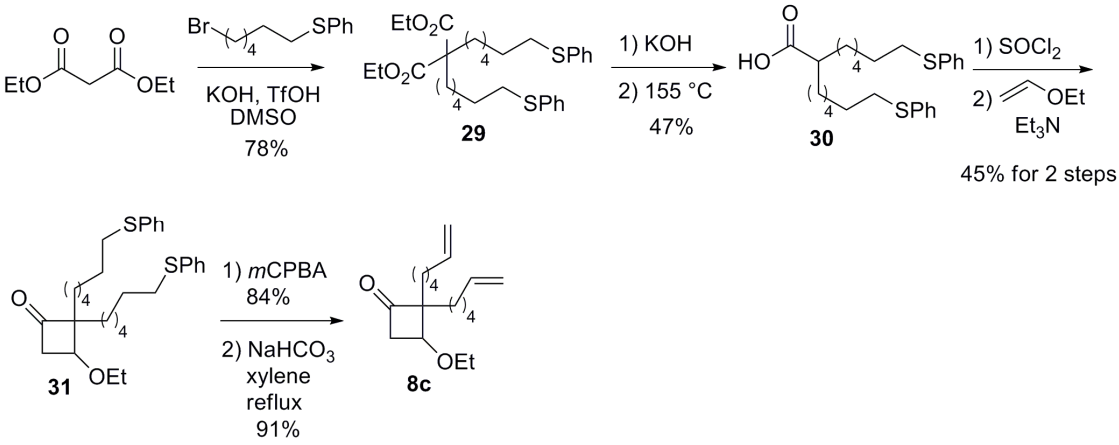
3-Ethoxy-2,2-di(pent-4-enyl)cyclobutanone (8b)

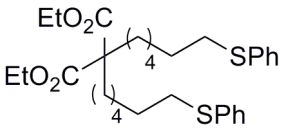
To a stirred solution of 3-ethoxy-2,2-bis(5-phenylsulfanylpentyl)cyclobutanone **27** (501 mg, 1.07 mmol) in dichloromethane (6 mL) was added at 0 °C a solution of *m*CPBA (65%, 563 mg, 2.12 mmol) in dichloromethane (4 mL), and the mixture was stirred at 0 °C for 15 min. The reaction was quenched with 10% aqueous $Na_2S_2O_3$ solution, and the mixture was extracted with dichloromethane. The combined organic extracts were washed with saturated aqueous sodium hydrogencarbonate solution, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel (hexane / ethyl acetate = 1 : 3 → ethyl acetate only) to afford 3-ethoxy-2,2-bis(5-phenylsulfinylpentyl)cyclobutanone **28** (430.5 mg, 80%).

A mixture of **28** (430.5 mg, 0.856 mmol) and sodium hydrogencarbonate (360 mg, 4.28 mmol) in xylene (7 mL) was refluxed for 14 h. Water was added to the cooled reaction mixture, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel (hexane / ethyl acetate = 30 / 1 → 15 / 1) to afford **8b** (191.3 mg, 89%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.1 Hz, 3H, Me), 1.30-1.74 (m, 8H), 2.02-2.07 (m, 4H), 3.00 (dd, *J* = 5.6, 17.8 Hz, 1H, H2), 3.13 (dd, *J* = 7.1, 18.1 Hz, 1H, H2), 3.44-3.54 (m, 2H, OC$\underline{H}_2$), 3.91 (dd, *J* = 5.6, 7.1 Hz, 1H, H3), 4.93-5.03 (m, 4H, CH=C$\underline{H}_2$), 5.74-5.83 (m, 2H, C$\underline{H}$=CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 23.3, 23.7, 27.6, 31.6, 34.0, 34.2, 50.7, 65.4, 70.3, 72.2, 114.6, 115.0, 138.2, 138.5, 212.7; IR (cm^{-1}, $CHCl_3$) 2940, 1771, 1640, 1458, 1373, 1343, 1215, 1186, 1121, 916; HRMS (EI+) *m/z* calcd for $C_{16}H_{26}O_2$: 250.19328, found 250.19399.

2.4.9 Preparation of 3-ethoxy-2,2-di(hex-5-enyl)cyclobutanone (8c)

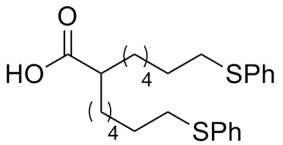
Compound **8c** was prepared by the method described in the synthesis of **8b**.





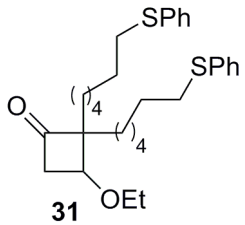
Diethyl 2,2-bis(6-phenylsulfanylhexyl)propanedioate (29)

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.10-1.17 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 6H), 1.27-1.33 (m, 4H), 1.39-1.45 (m, 4H), 1.60-1.66 (m, 4H), 1.82-1.85 (m, 4H), 2.90 (t, *J* = 7.3 Hz, 4H), 4.16 (q, *J* = 7.1 Hz, 4H), 7.14-7.17 (m, 2H), 7.25-7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 23.8, 28.5, 29.1, 29.4, 32.1, 33.5, 57.4, 61.0, 125.7, 128.8, 128.8, 136.9, 171.9; IR (cm^{-1}, $CHCl_3$) 2932, 1723, 1586, 1482, 1439, 1257, 1209, 1156, 1094, 1026, 691; HRMS (EI+) *m/z* calcd for $C_{31}H_{44}S_2O_4$: 544.26811, found 544.26786.



8-Phenylsulfanyl-2-(phenylsulfanylhexyl)octanoic acid (30)

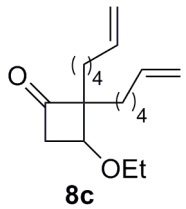
Colorless needles: mp 102.5-103.0 °C (hexane-ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25-1.35 (m, 8H), 1.38-1.48 (m, 6H), 1.60-1.66 (m, 6H), 2.29-2.35 (m, 1H), 2.90 (t, *J* = 7.3 Hz, 4H), 7.13-7.17 (m, 2H), 7.25-7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2, 28.6, 29.0, 29.0, 32.0, 33.5, 45.4, 125.6, 128.8, 128.9, 136.9, 182.5; IR (cm^{-1}, $CHCl_3$) 2934, 1705, 1586, 1482, 1439, 691; Anal. Calcd. For $C_{26}H_{36}O_2S_2$: C, 70.22; H, 8.16. Found: C, 69.98; H, 8.29.



31

3-Ethoxy-2,2-bis(6-phenylsulfanylhexyl)cyclobutanone (31)

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.1 Hz, 3H, Me), 1.26-1.70 (m, 20H), 2.90 (t, *J* = 7.3 Hz, 2H, SC<u>H</u>$_2$), 2.91 (t, *J* = 7.6 Hz, 2H, SC<u>H</u>$_2$), 2.99 (dd, *J* = 5.9, 17.8 Hz, 1H, H2), 3.12 (dd, *J* = 6.8, 17.8 Hz, 1H, H2), 3.42-3.52 (m, 2H, OC<u>H</u>$_2$), 3.89 (dd, *J* = 5.9, 6.8 Hz, 1H, H3), 7.14-7.18 (m, 2H), 7.26-7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 23.8, 24.2, 28.0, 28.6, 28.6, 29.0, 29.1, 29.5, 29.7, 32.0, 33.5, 50.6, 65.4, 70.3, 72.2, 77.2, 125.6, 125.7, 128.8, 128.8, 128.8, 128.9, 136.9, 137.0, 212.8; IR (cm^{-1}, $CHCl_3$) 2934, 1771, 1586, 1482, 1439, 1186, 1119, 752, 691, 669; HRMS (EI+) *m/z* calcd for $C_{30}H_{42}S_2O_2$: 498.26263, found 498.26196.

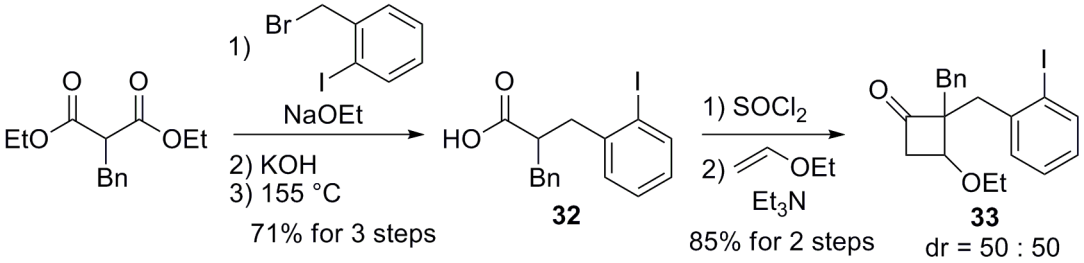


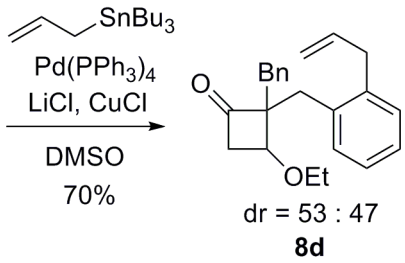
8c

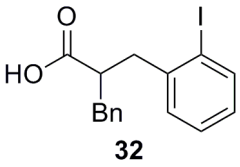
3-Ethoxy-2,2-di(hex-5-enyl)cyclobutanone (8c)

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, *J* = 6.8 Hz, 3H), 1.22-1.73 (m, 12H), 2.03-2.08 (m, 2H, C<u>H</u>$_2$CH=CH$_2$), 3.00 (dd, *J* = 5.6, 17.8 Hz, 1H, H2), 3.13 (dd, *J* = 7.1, 17.8 Hz, 1H, H2), 3.44-3.54 (m, 2H, OC<u>H</u>$_2$), 3.91 (dd, *J* = 5.6, 6.8 Hz, 1H, H3), 4.92-5.02 (m, 4H, CH=C<u>H</u>$_2$), 5.75-5.84 (m, 2H, C<u>H</u>=CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2, 23.4, 23.9, 27.9, 29.2, 29.5, 31.9, 33.5, 33.5, 50.7, 65.4, 70.4, 72.2, 114.3, 114.5, 138.6, 138.9, 212.9; IR (cm^{-1}, $CHCl_3$) 2936, 1771, 1640, 1462, 1372, 1343, 1186, 1121, 995, 914; HRMS (EI+) *m/z* calcd for $C_{18}H_{30}O_2$: 278.22458, found 278.22421.

2.4.10 Preparation of 2-(*o*-allylbenzyl)-2-benzyl-3-ethoxycyclobutanone (8d)



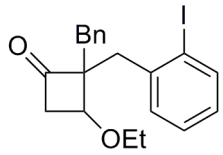




2-Benzyl-3-(*o*-iodophenyl)propanoic acid (32)

To a stirred solution of sodium ethoxide in ethanol which was prepared by using sodium (424 mg) and absolute ethanol (50 mL) was added at 70 °C diethyl benzylmalonate (3.33 mL, 14.2 mmol). 2-Iodobenzyl bromide (5.70 g, 19.2 mmol) in absolute ethanol (35 mL) was then added, and the mixture was stirred at 70 °C for 40 min. After evaporation of the solvent, water was added, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried, and concentrated. To a stirred solution of thus-obtained product in ethanol (40 mL) was added a solution of potassium hydroxide (4.77 g, 85.0 mmol) in water (30 mL), and the mixture was refluxed for 9 h. After evaporation of the solvent, the residue was washed with ether. The aqueous phase was acidified with1 N hydrochloric acid, and the mixture was extracted with ether. The concentrated product was purified by column chromatography on silica gel (hexane / ethyl aceate = 2 : 1) to afford 2-benzyl-3-(*o*-iodophenyl)propanoic acid **32** (3.70 g, 71% for 3 steps) as colorless crystals: mp 108.0-108.5 °C (hexane-ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.86 (dd, *J* = 5.9, 13.7 Hz, 1H), 2.93 (dd, *J* = 4.6, 13.2 Hz, 1H), 3.02-3.14 (m, 3H), 6.88-6.91 (m, 1H), 7.19-7.29 (m, 7H), 7.81 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.2, 42.4, 47.5, 100.6, 126.6, 128.3,

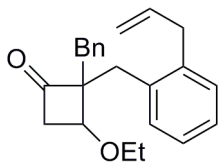
128.4, 128.9, 129.1, 130.3, 138.3, 139.7, 141.4, 179.7; IR (cm^{-1}, $CHCl_3$) 3021, 1709, 1223, 1210, 1013, 700, 699; Anal. Calcd. For $C_{16}H_{15}IO_2$: C, 52.48; H, 4.13. Found: C, 52.42; H, 4.09.



33

2-Benzyl-3-ethoxy-2-(*o*-iodobenzyl)cyclobutanone (33)

To a stirred solution of 2-benzyl-3-(*o*-iodophenyl)propanoic acid **32** (3.70 g, 10.1 mmol) in dichloromethane (40 mL) was added at 0 °C thionyl chloride (2.2 mL, 30.2 mmol) and DMF (0.08 mL, 1.03 mmol), and the mixture was stirred at room temperature for 2 h. After evaporation of volatiles, dry acetonitrile (30 mL) was added. To this solution was added a mixture of ethyl vinyl ether (3.5 mL, 36.5 mmol) and triethylamine (3.4 mL, 24.4 mmol) in acetonitrile (20 mL), and the reaction mixture was stirred at 90 °C for 3 h. Water was added, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexane / ethyl acetate) to afford **33** (3.61 g, 85% for 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of diastereomers, 50 : 50) δ 1.27 (t, *J* = 7.1 Hz, 1.5H, Me), 1.27 (t, *J* = 7.1 Hz, 1.5H, Me), 2.70 (dd, *J* = 7.1, 18.1 Hz, 0.5H, H2), 2.73 (dd, *J* = 7.1, 18.1 Hz, 0.5H, H2), 2.79 (d, *J* = 13.9 Hz, 0.5H), 2.89 (dd, *J* = 5.9, 17.8 Hz, 0.5H, H2), 2.93-2.99 (m, 1.5H), 3.06 (dd, *J* = 5.6, 17.8 Hz, 0.5H, H2), 3.14 (d, *J* = 14.4 Hz, 0.5H), 3.20 (d, *J* = 14.2 Hz, 0.5H), 3.30 (d, *J* = 15.1 Hz, 0.5H), 3.37 (d, *J* = 14.9 Hz, 0.5H), 3.49-3.56 (m, 2H, OC$\underline{H}_2$), 3.98 (t, *J* = 6.3 Hz, 0.5H, H3), 4.04 (dd, *J* = 5.9, 6.8 Hz, 0.5H, H3), 6.87 (dd, *J* = 1.5, 7.8 Hz, 0.5H), 6.91 (dd, *J* = 1.5, 7.8 Hz, 0.5H), 7.04-7.06 (m, 1H), 7.12 (dd, *J* = 1.2, 7.8 Hz, 0.5H), 7.17-7.33 (m, 5H), 7.49 (dd, *J* = 1.2, 7.8 Hz, 0.5H), 7.82 (d, *J* = 8.1 Hz, 0.5H), 7.84 (d, *J* = 8.1 Hz, 0.5H); ^{3}C NMR (125 MHz, $CDCl_3$, a mixture of diastereomers, 50 : 50) δ 15.2, 15.3, 36.5, 38.4, 39.6, 42.8, 51.2, 51.8, 65.6, 69.3, 69.5, 71.5, 71.5, 103.1, 103.2, 126.5, 126.6, 128.0, 128.2, 128.2, 128.3, 128.4, 130.2, 130.6, 130.8, 131.0, 137.0, 137.1, 139.6, 139.7, 140.5, 140.6, 210.5, 211.1; IR (cm^{-1}, $CHCl_3$) 3011, 1773, 1437, 1345, 1184, 1121, 1013, 702; HRMS (EI+) *m/z* calcd for $C_{20}H_{21}O_2I$: 420.05866, found 420.05848.

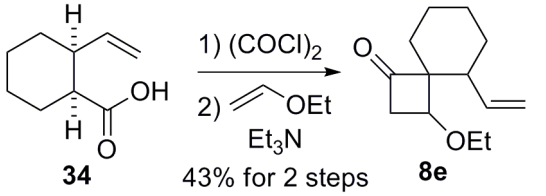


8d

2-(*o*-Allylbenzyl)-2-benzyl-3-ethoxycyclobutanone (8d)

To the mixture of LiCl (60.5 mg, 1.43 mmol), $Pd(PPh_3)_4$ (29 mg, 25 μmol), and CuCl[11] (124 mg, 1.25 mmol) was added a solution of **33** (98.7 mg, 0.235 mmol) in DMSO (4 mL). Allyltributylstannane (0.09 mL, 0.29 mmol) was then added, and the reaction mixture was stirred at room temperature for 1 h and at 60 °C for 10 h. The reaction mixture was cooled, and 5% aqueous NH_4OH and brine were added. The resulting mixture was extracted with ether, and the combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by column chromatography on 10% w/w KF and silica gel (hexane / ethyl acetate = 25 : 1) to afford **8d** (55.3 mg, 70%) as a mixture of two diastereomers (53 : 47): ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of diastereomers, 53 : 47) δ 1.26 (t, *J* = 6.8 Hz, 1.4H, minor Me), 1.28 (t, *J* = 7.1 Hz, 1.6H, major Me), 2.67-3.53 (m, 11H), 3.92 (t, *J* = 6.1 Hz, 0.53H, major H3), 4.05 (t, *J* = 6.1 Hz, 0.47H, minor H3), 4.80-5.05 (m, 2H), 5.77-5.94 (m, 1H), 7.05-7.44 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, a mixture of diastereomers, 53 : 47) δ 15.2, 15.2, 31.1, 34.7, 36.5, 37.3, 37.6, 39.3, 51.2, 51.3, 65.1, 65.3, 69.6, 70.1, 71.4, 71.8, 115.7, 115.8, 126.1, 126.4, 126.4, 126.5, 126.6, 126.8, 128.0, 128.4, 129.7, 129.7, 130.2, 130.6, 130.6, 131.1, 135.7, 135.8, 136.7, 137.1, 137.1, 137.3, 138.8, 138.9, 211.0, 211.2; IR (cm^{-1}, $CHCl_3$) 2980, 1773, 1219, 669; HRMS (EI+) *m/z* calcd for $C_{23}H_{26}O_2$: 334.19328, found 334.19294.

2.4.11 Preparation of 3-ethoxy-5-vinylspiro[3.5]nonan-1-one (8e)



34 **8e**

33 : 29 : 24 : 14

3-Ethoxy-5-vinylspiro[3.5]nonan-1-one (**8e**)

To a stirred solution of (±)-(1*R*,2*R*)-2-vinylcyclohexanecarboxylic acid[12] **34** (1.33 g, 8.60 mmol) in dry dichloromethane (15 mL) was added at 0 °C oxalyl chloride (1.1 mL, 13.0 mmol), and the mixture was stirred at room temperature for 1 h. After evaporation of volatiles, dry acetonitrile (13 mL) was added. To this solution was added a solution of ethyl vinyl ether (3.0 mL, 31.3 mmol) and triethylamine (2.9 mL, 20.8 mmol) in acetonitrile (7 mL) for 30 min. The resulting reaction mixture was stirred at 90 °C for 3 h. Water was added to the cooled reaction mixture, and the mixture was extracted with ether. The combined organic extracts were washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexane /

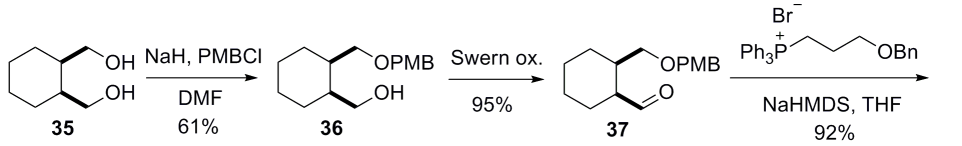
[11] Han, X.; Stoltz, B. M.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 7600.
[12] Moser, W. H.; Hegedus, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 7873.

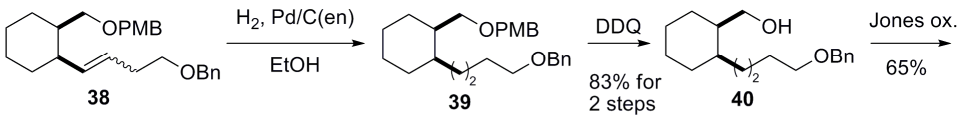
ether and hexane / dichloromethane) to afford **8e** (772 mg, 3.71 mmol, 43% combined yield for 2 steps) as a mixture of four diastereomers (**8ea** : **8eb** : **8ec** : **8ed** = 33 : 29 : 24 : 14). The ratio of diastereomer (**8ea-d**) was determined by ^{1}H NMR spectra.

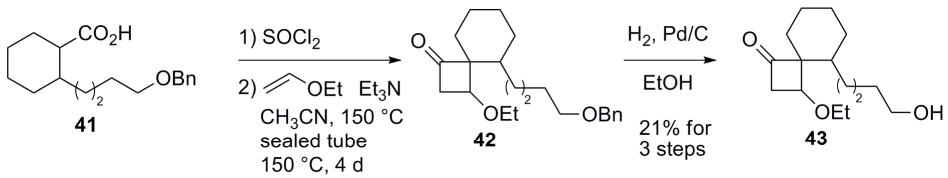
The major isomer **8ea**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H, Me), 1.27-1.34 (m, 1H), 1.43-1.75 (m, 6H), 1.81-1.86 (m, 1H), 2.58-2.62 (m, 1H), 2.92 (dd, *J* = 6.1, 17.6 Hz, 1H, H2), 3.12 (dd, *J* = 7.1, 17.8 Hz, 1H, H2), 3.54 (q, *J* = 7.1 Hz, 1H, OC<u>H</u>$_2$), 3.54 (q, *J* = 7.1 Hz, 1H, OC<u>H</u>$_2$), 3.83 (dd, *J* = 6.3, 7.1 Hz, 1H, H3), 5.03-5.07 (m, 2H, CH=C<u>H</u>$_2$), 6.14-6.21 (m, 1H, C<u>H</u>=CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3, 22.3, 23.4, 28.7, 31.5, 40.3, 50.9, 65.4, 70.7, 74.8, 114.9, 139.9, 212.0; IR (cm^{-1}, $CHCl_3$) 2936, 1767, 1636, 1449, 1192, 1123, 912; HRMS (EI+) *m/z* calcd for $C_{13}H_{20}O_2$: 208.14633, found 208.14695.

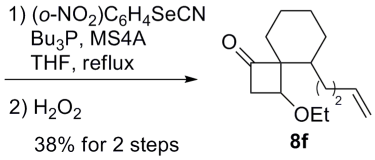
The relative stereochemistry of **8ea** was not determined.

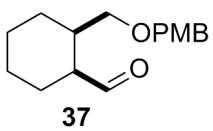
2.4.12 Preparation of 5-(but-3-enyl)-3-ethoxyspiro[3.5]nonan-1-one (8f)







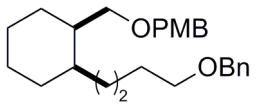




2-[(*p*-methoxybenzyl)methyl]cyclohexanecarboxaldehyde (37)

To a stirred suspension of NaH (1.51 g, 60%, 37.8 mmol, washed with hexane) in dry DMF (20 mL) was added a solution of *cis*-1,2-cyclohexanedimethanol **35** (5.43 g, 37.7 mmol) in dry DMF (15 mL) at room temperature, and the mixture was stirred at room temperature for 40 min. PMBCl (5.11 mL, 37.7 mmol) was added to the reaction mixture at 0 °C, and the mixture was stirred at room temperature for 1 h. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with water, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10 : 1 → 4 : 1 → 1 : 1) to afford {2-[(*p*-methoxybenzyloxy)methyl]cyclohexyl}methanol **36** (6.09 g, 61%) as a colorless oil.

To a stirred solution of oxalyl chloride (3.87 mL, 45.7 mmol) in dichloromethane (160 mL) was added a solution of DMSO (6.51 mL, 91.7 mmol) in dichloromethane (10 mL) at –78 °C. A solution of **36** (6.06 g, 22.9 mmol) in dichloromethane (10 mL) was then added to the mixture at –78 °C, and the reaction mixture was stirred at –78 °C for 15 min. Triethylamine (32 mL, 230 mmol) was added to the mixture, and the resulting mixture was stirred for at room temperature for 30 min. After addition of water, the mixture was extracted with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 6 : 1) to afford **37** (5.70 g, 95%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37-1.81 (m, 8H), 2.29-2.35 (m, 1H), 2.51-2.54 (m, 1H), 3.44 (dd, *J* = 5.9, 9.3 Hz, 1H), 3.54 (dd, *J* = 8.7, 9.0 Hz, 1H), 3.80 (s, 3H), 4.38 (s, 2H), 6.85-6.88 (m, 2H), 7.20-7.23 (m, 2H), 9.75 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.3, 23.5, 24.0, 27.3, 37.5, 50.3, 55.2, 70.7, 72.8, 113.7, 129.2, 130.3, 159.1, 204.5; IR (cm^{-1}, $CHCl_3$) 3019, 1717, 1613, 1514, 1248, 1084, 1036; HRMS (EI+) *m/z* calcd for $C_{16}H_{22}O_3$: 262.15690, found 262.15604.



39

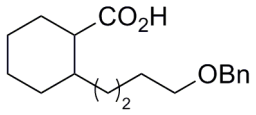
1-[4-(benzyloxy)butyl]-2-[(*p*-methoxybenzyloxy)methyl]cyclohexane (39)

To a stirred suspension of [3-(benxyloxy)propyl]triphenylphosphonium bromide[13] (10.8 g, 22.0 mmol) in dry THF (230 mL) was added a solution of sodium hexamethyldisilazide (1.90 N in THF, 10.5 mL, 20.0 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 15 min. A solution of **37** (5.23 g, 19.9 mmol) in THF (8 mL) was added at 0 °C, and the mixture was stirred

[13] (a) Ohtsuka, Y.; Niitsuma, S.; Tadokoro, H.; Hayashi, T.; Oishi, T. *J. Org. Chem*. **1984**, *49*, 2326. (b) Ziegler, F. E.; Klein, S. I.; Pati, U. K.; Wang, T.-F. *J. Am. Chem. Soc.* **1985**, *107*, 2731.

at 0 °C for 30 min. After evaporation of the solvent, the residue was filtered through Celite pad and the solid was washed with ether. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel (hexane only → hexane / ethyl acetate = 20 : 1 → 5 : 1) to afford 1-[4-(benzyloxy)but-1-enyl]-2-[(*p*-methoxybenzyloxy)methyl]cyclohexane **38** (7.26 g, 92%) as a pale yellow oil.

To the solution of **38** (7.26 g, 18.4 mmol) in EtOH (150 mL) was added Pd/C-ethylelediamine complex[14] (730. 4 mg). Under H_2 atmosphere (1 atm, balloon), the suspension was stirred at room temperature for 24 h. The reaction mixture was filtered through Celite pad, and the filtrate was concentrated to give **39** (7.10 g, 97%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$, two conformers) δ 1.01-1.86 (m, 16H), 3.20-3.40 (m, 4H), 3.72 (s, 3H), 4.28-4.38 (m, 2H), 4.42 (s, 2H), 6.78-6.81 (m, 2H), 7.16-7.27 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$, two conformers) δ 22.9, 24.2, 26.4, 28.7, 30.0, 33.3, 39.3, 42.2, 55.3, 70.5, 72.6, 72.7, 72.9, 113.7, 113.7, 127.4, 127.6, 128.3, 129.1, 129.1, 131.0, 138.7, 159.1; IR (cm^{-1}, $CHCl_3$) 2932, 1613, 1514, 1455, 1364, 1302, 1248, 1094, 1036; HRMS (EI+) *m/z* calcd for $C_{26}H_{36}O_3$: 396.26645, found 396.26611.



41

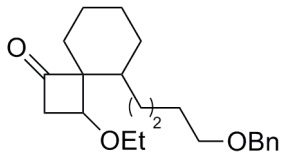
2-[4-(benzyloxy)butyl]cyclohexanecarboxylic acid (41)

To a stirred mixture of **39** (6.84 g, 17.2 mmol) in dichloromethane (150 mL) and water (70 mL) was added DDQ (4.8 g, 21.1 mmol) at room temperature, and the mixture was stirred at room temperature for 1 h. After addition of 10% aqueous $Na_2S_2O_3$ solution, the mixture was extracted with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel to afford 2-[4-(benzyloxy)butyl]cyclohexylmethanol **40** (4.22 g, 88%) as a pale yellow oil.

To a solution of **40** (4.06 g, 14.7 mmol) in acetone (120 mL) was added Jones reagent (8 mL, prepared by using CrO_3 (2 g), H_2SO_4 (1.8 mL), and H_2O (9mL)) at 0 °C, and the resulting mixture was stirred at 0 °C for 5.5 h. After addition of 10% aqueous $Na_2S_2O_3$ solution, the solvent was evaporated. The residue was extracted with ether, and the combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel (hexane / ether = 8 : 1 → 3 :1) to afford **41** (2.78 g, 65%) as a colorless oil. ^{1}H NMR analysis revealed that epimerization took place to give two diastereomers.

[14] Sajiki, H.; Hattori, K.; Hirota, K. *J. Org. Chem.* **1998**, *63*, 7990.

Compound **41**: ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of two diastereomers, 55 : 45) δ 0.87-0.90 (m, 0.55H), 1.13-2.08 (m, 15H), 2.59-2.62 (m, 0.45H), 3.45, 3.46 (t, *J* = 6.3 H, 2H), 4.49, 4.49 (s, 2H), 7.26-7.34 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, a mixture of two diastereomers, 55 : 45) δ 22.9, 23.8, 24.1, 25.4, 25.6, 28.0, 29.8, 29.9, 30.0, 30.5, 34.5, 37.1, 38.5, 45.1, 49.8, 70.3, 70.4, 72.9, 72.9, 127.4, 127.5, 127.6, 128.3, 138.6, 138.6, 180.8, 182.1; IR (cm^{-1}, $CHCl_3$) 2938, 1703, 1453, 1100; HRMS (EI+) *m/z* calcd for $C_{18}H_{26}O_3$: 290.18820, found 290.18865.

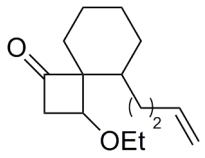


42

5-[4-(benzyloxy)butyl]-3-ethoxyspiro[3.5]nonan-1-one (42)

To a stirred solution of **41** (1.92 g, 6.61 mmol) in dichloromethane (15 mL) was added thionyl chloride (2.03 mL, 19.8 mmol) and DMF (51 μL, 0.66 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. After evaporation of volatiles, thus-formed acid chloride was dissolved in dry acetonitrile (10 mL). To this solution was added a solution of triethylamine (1.85 mL, 13.3 mmol) in ethyl vinyl ether (20 mL) and acetonitrile (40 mL) at room temperature. The mixture was heated in a sealed tube at 150 °C for 4 days. After cooling to room temperature, water was added and the solvent was evaporated. The residue was extracted with ether, and the combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated. Most of impurities was removed by column chromatography on silica gel (hexane/ether = 10 : 1 → 5 :1) to afford a mixture of **42** and some impurities (988 mg). This mixture was used in the next step. A part of this mixture was purified by preparative TLC (hexane/acetone) to give pure **42** as a mixture of four diastereomers (41 : 26 : 20 : 13).

Compound **42**: ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of four diastereomers, 41 : 26 : 20: 13) δ 1.18-1.96 (m, 18H), 2.74-3.57 (m, 6H), 3.80-4.16 (m, 1H), 4.49 (s, 2H), 7.25-7.34 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, a mixture of four diastereomers) δ 15.2, 15.3, 15.3, 22.1, 22.3, 22.7, 22.8, 24.2, 24.3, 24.3, 24.7, 24.8, 26.7, 27.1, 27.9, 29.5, 29.8, 29.9, 30.5, 30.9, 35.7, 38.8, 41.5, 49.8, 50.5, 50.8, 64.9, 65.2, 65.4, 65.4, 69.8, 70.3, 70.3, 70.5, 70.5, 71.0, 71.7, 71.7, 71.8, 72.8, 72.9, 72.9, 74.9, 75.2, 127.4, 127.5, 127.5, 127.6, 127.6, 128.3, 128.3, 138.6, 138.6, 138.7, 212.9, 213.3; IR (cm^{-1}, $CHCl_3$) 2936, 1765, 1455, 1210, 1115; HRMS (EI+) *m/z* calcd for $C_{22}H_{32}O_3$: 344.23515, found 344.23490.



8f

5-(but-3-enyl)-3-ethoxyspiro[3.5]nonan-1-one (8f)

A mixture of crude **42** (815 mg) and palladium on carbon (10%, 668 mg) in ethanol (40 mL) was stirred under hydrogen atmosphere (1 atm) for 3.5 h. The mixture was filtrated through Celite pad, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 3 : 1 → 1 : 1) to afford 3-ethoxy-5-(4-hydroxybutyl)spiro[3.5]nonan-1-one **43** (293 mg, 1.15 mmol, 21% yield for three steps) as a pale yellow oil.

To a refluxed suspension of **43** (293 mg, 1.15 mmol) , *o*-nitrophenyl selenocyanate (540 mg, 2.38 mmol), and molecular sieves 4A (121 mg) in dry THF (13 mL) was added a solution of tri-*n*-butyl phosphine (0.57 mL, 2.31 mmol) in THF (2 mL) for 10 min, and the reaction mixture was refluxed for 15 min.[15] After cooling to room temperature, the mixture was filtered through Celite pad, and the filtrate was concentrated. Some impurities were removed by column chromatography on silica gel (hexane/ethyl acetate = 3 : 1), and the crude product was used in the next step.

To the solution of the crude product in THF (15 mL) was added a solution of hydrogen peroxide (10%, 1.18 mL) at 0 °C, and the mixture was stirred at room temperature for 11 h.[16] Saturated aqueous $Na_2S_2O_3$ solution was added, and the mixture was extracted with ether. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 20 : 1 → 10 : 1 → 3 : 1) to afford **8f** (103.8 mg, 38% yield for two steps) as a mixture of four diastereomers (33 : 23 : 23 : 21).

Compound **8f**: ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of four diastereomers, 33 : 23 : 23: 21) δ 1.20-2.20 (m, 16H), 2.75-3.25 (m, 2H), 3.38-3.57 (m, 2H), 3.81-4.18 (m, 1H), 4.91-5.02 (m, 1H), 5.73-5.84 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, a mixture of four diastereomers) δ 15.2, 15.3, 15.3, 15.3, 22.1, 22.3, 22.5, 22.7, 22.8, 23.3, 24.7, 26.0, 26.1, 26.2, 26.8, 27.0, 27.7, 29.1, 29.2, 29.9, 31.1, 31.6, 31.7, 31.8, 31.9, 32.4, 35.3, 38.2, 40.8, 49.8, 50.4, 50.5, 50.9, 64.9, 65.2, 65.4, 65.4, 69.8, 70.3, 70.9, 71.6, 71.7, 71.8, 75.0, 75.2, 77.2, 114.2, 114.4, 114.8, 114.8, 138.5, 138.9, 139.2, 212.8, 213.2, 214.1, 214.2; IR (cm^{-1}, $CHCl_3$) 2936, 1767, 1640, 1447, 1374, 1347, 1188, 1123, 914; HRMS (EI+) *m/z* calcd for $C_{15}H_{24}O_2$: 236.17763, found 236.17757.

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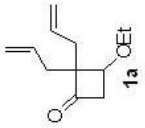
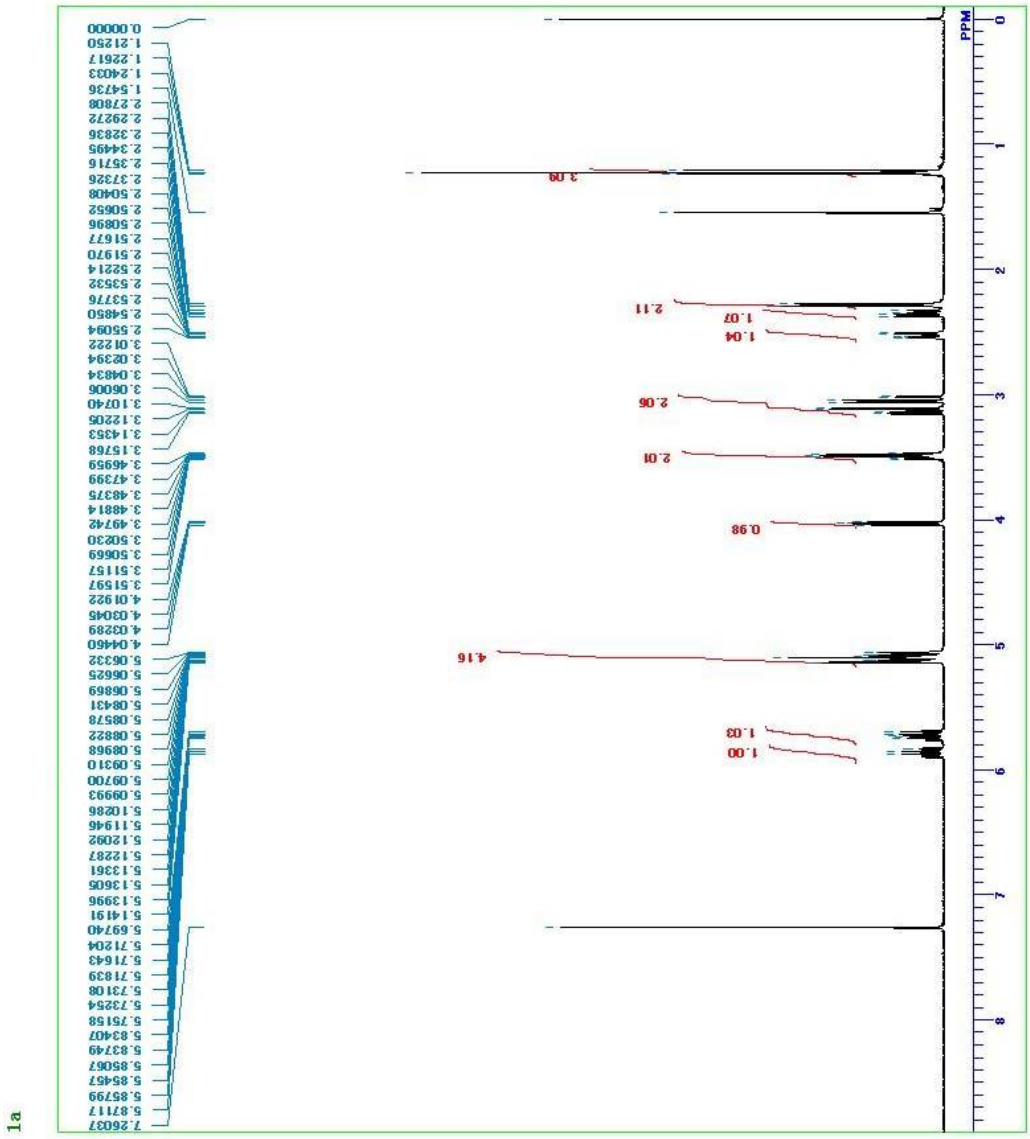
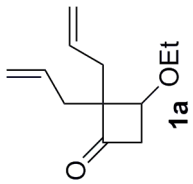
[15] (a) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem*. **1976**, *41*, 1485. (b) Torikai, K.; Watanabe, K.; Minato, H.; Imaizumi, T.; Murata, M.; Oishi, T. *Synlett* **2008**, *15*, 2368.
[16] Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947.

4. ^{1}H and ^{13}C NMR spectra of new compounds



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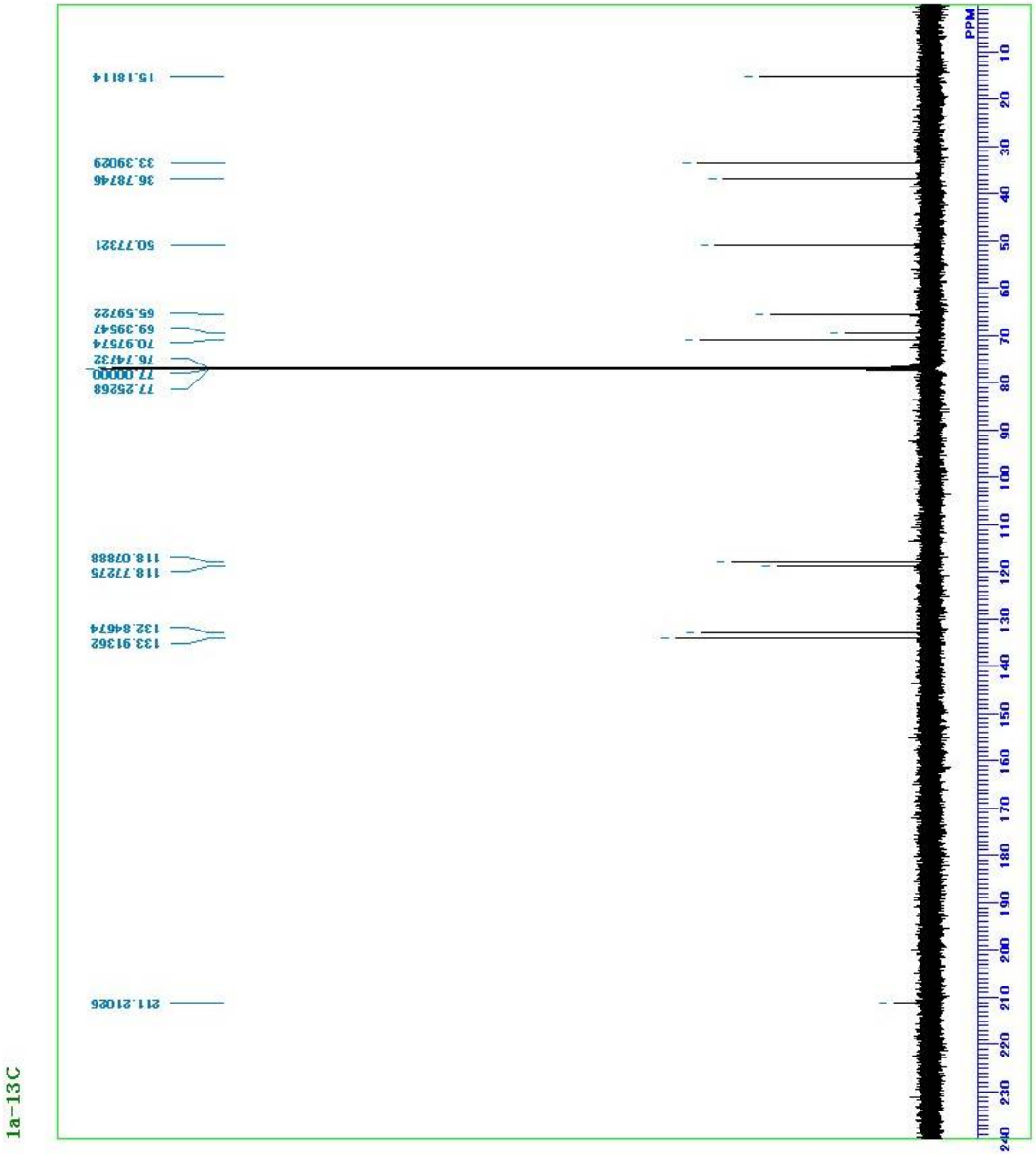
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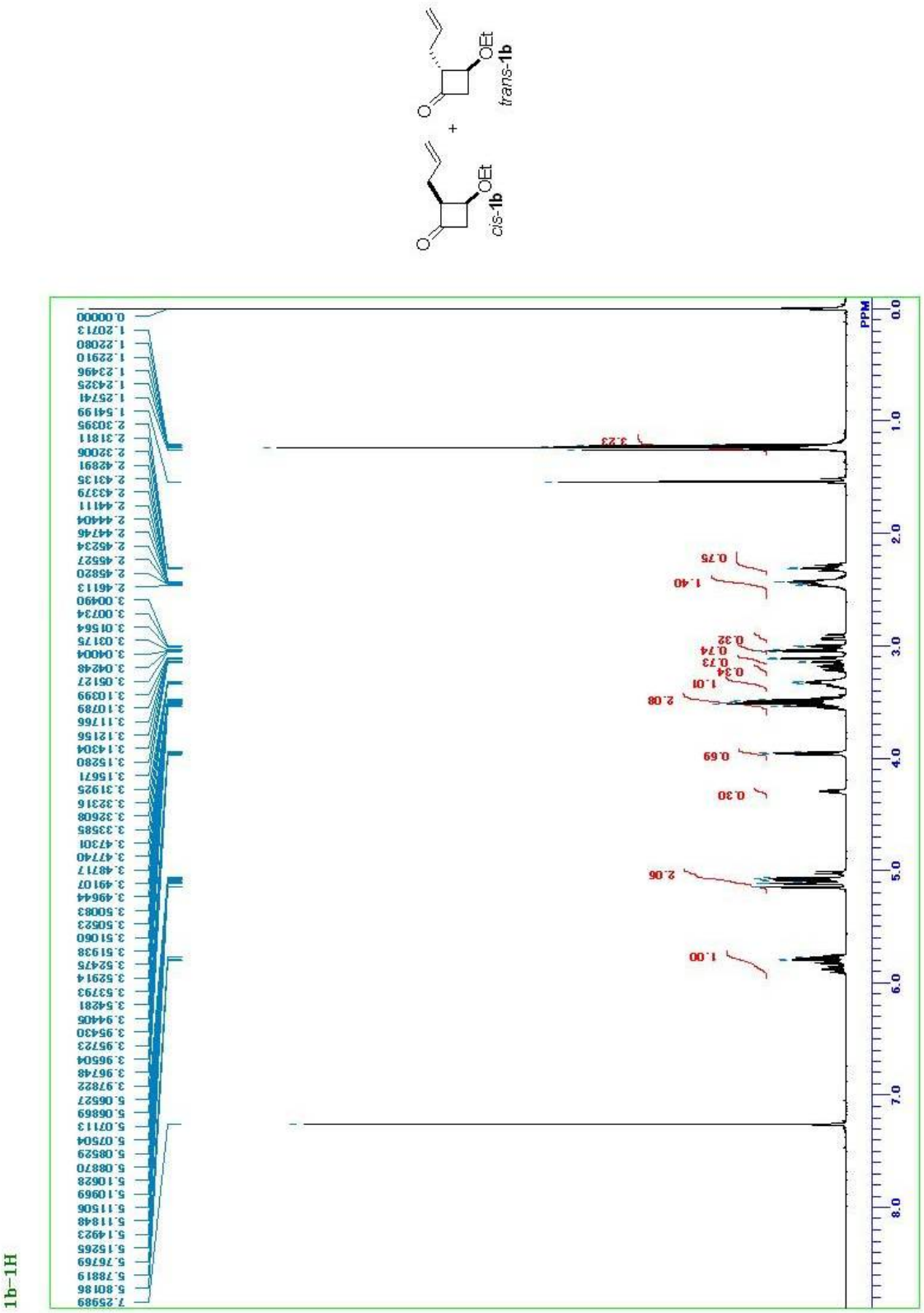
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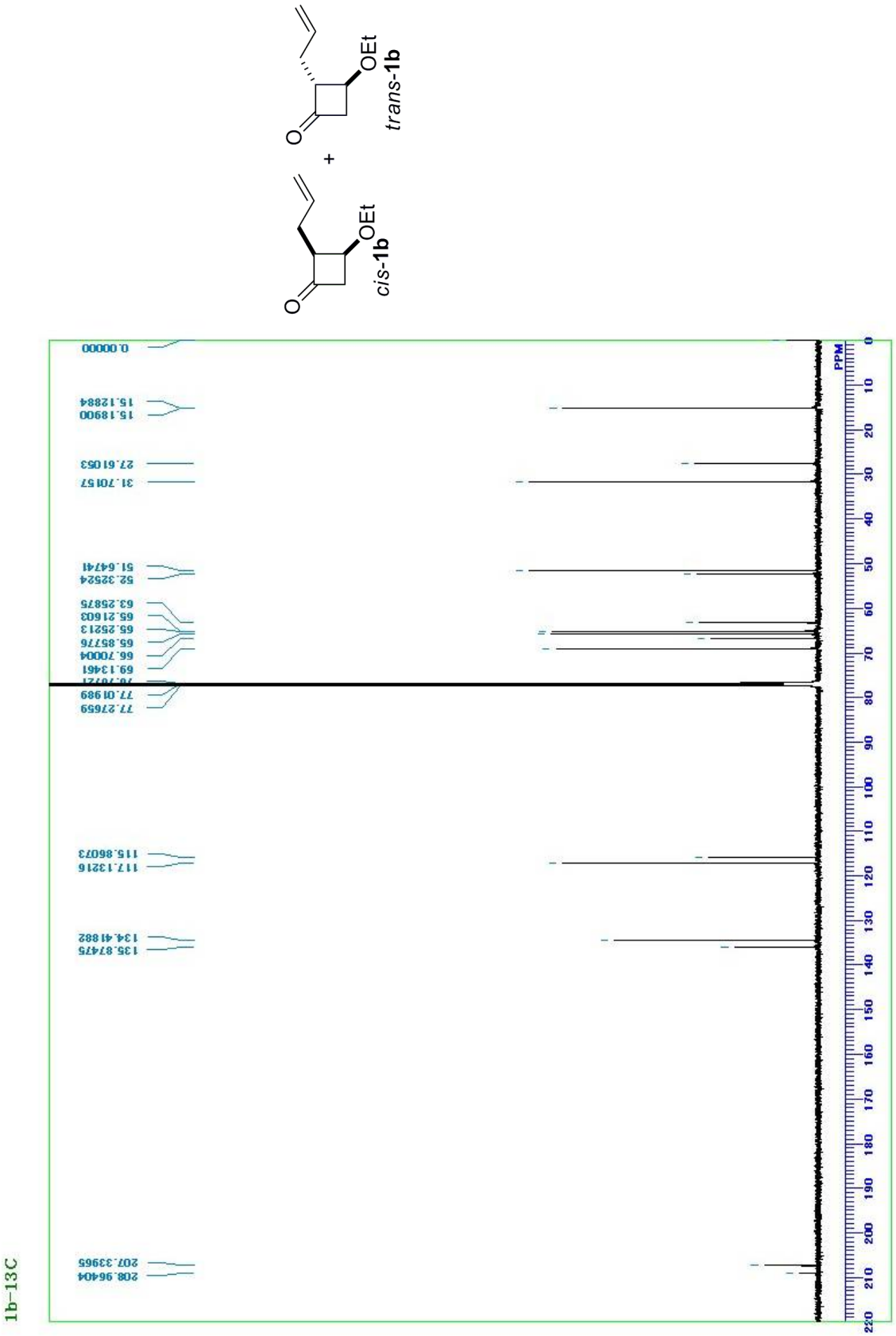
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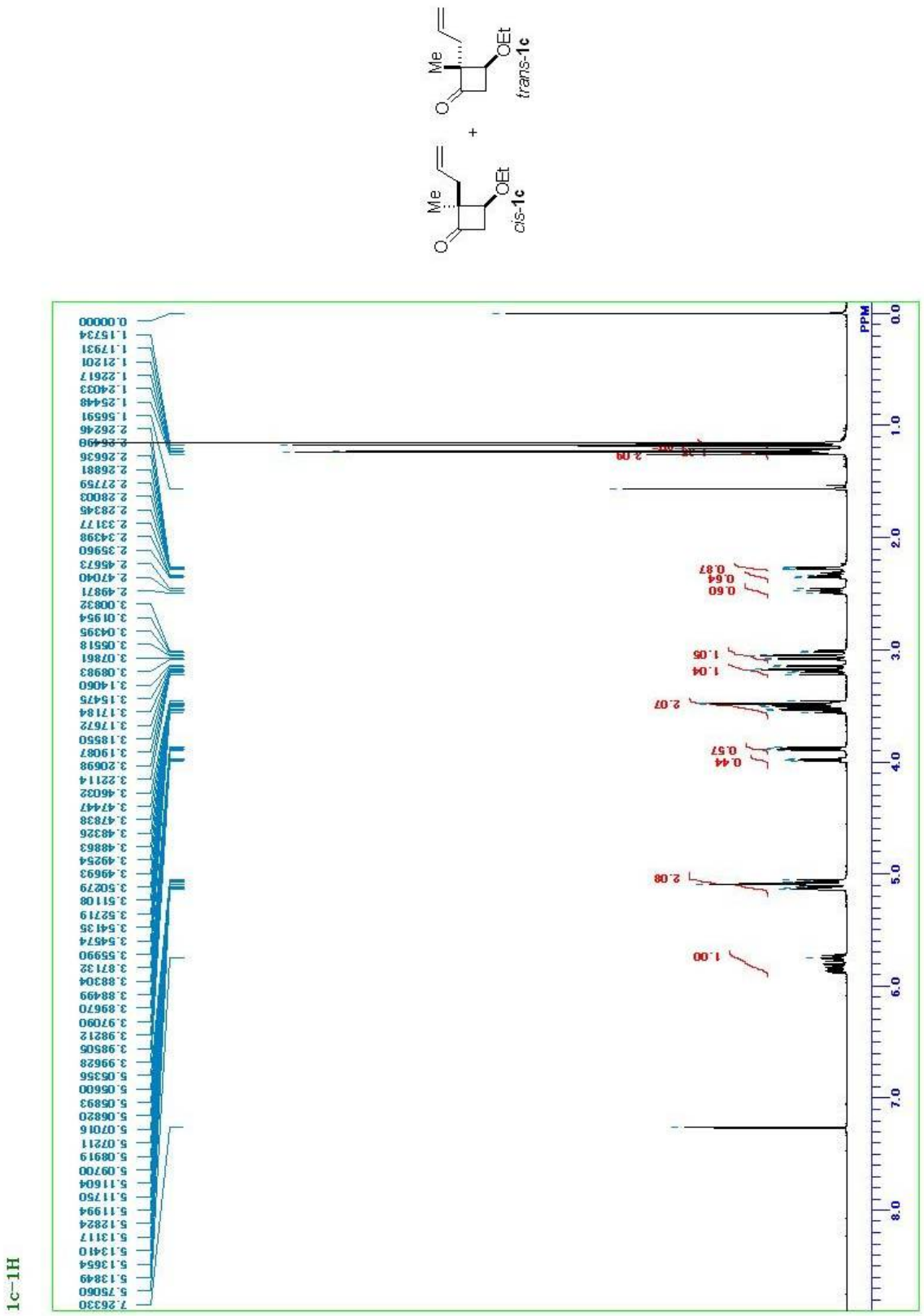
OEt
cis-1b
1b-13C
PPM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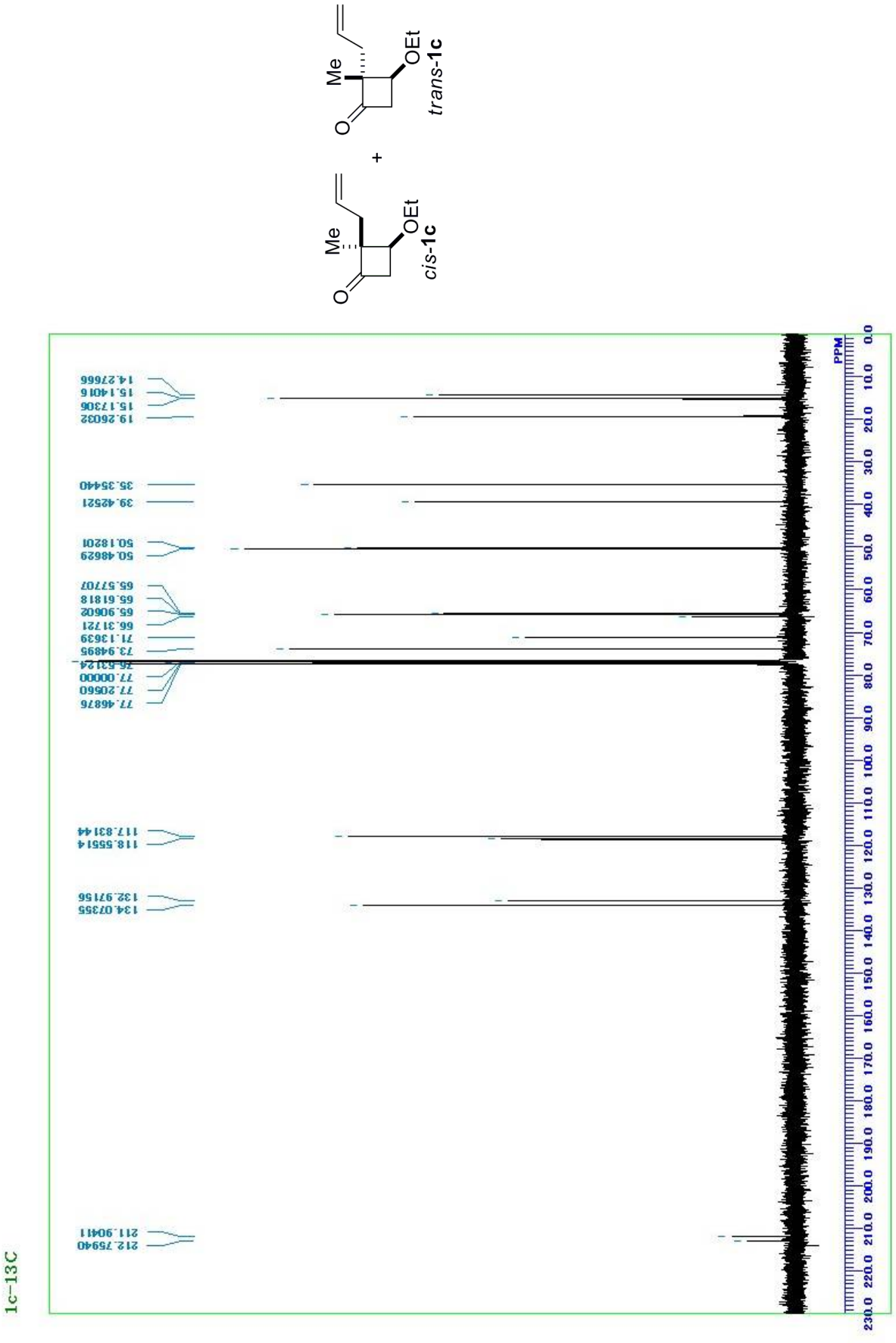
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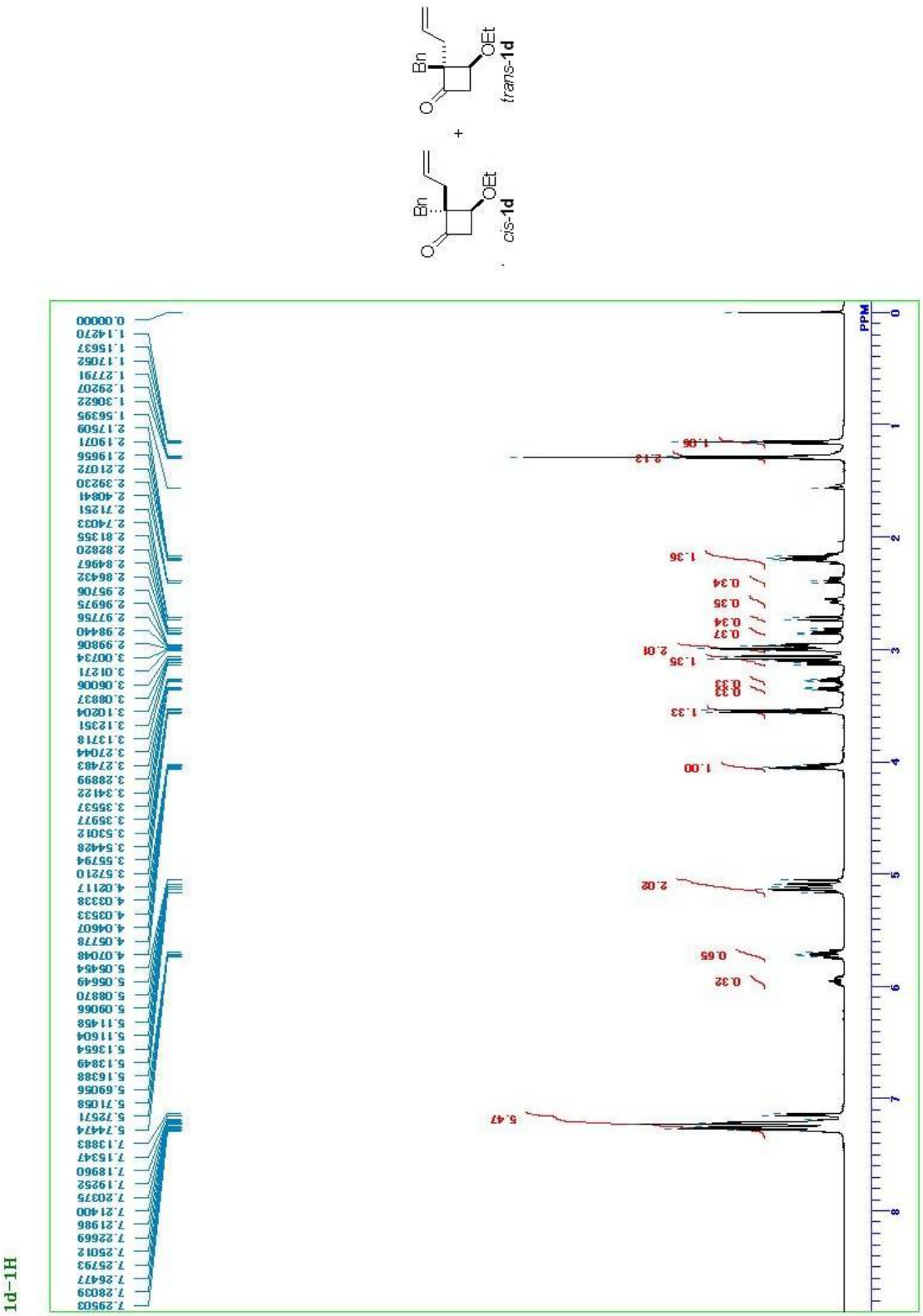
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6
7
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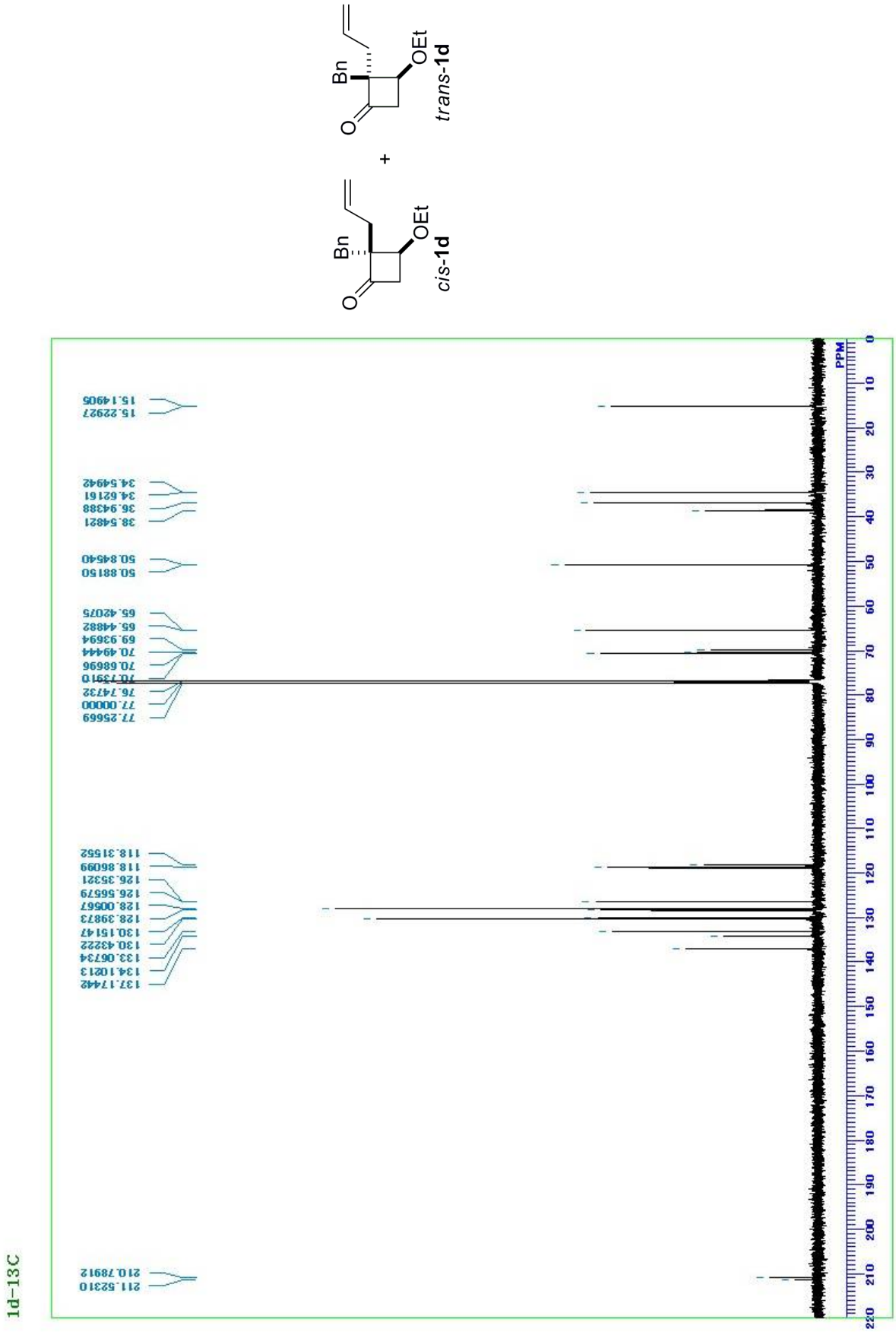
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cis-1d
1d-13C
PPM


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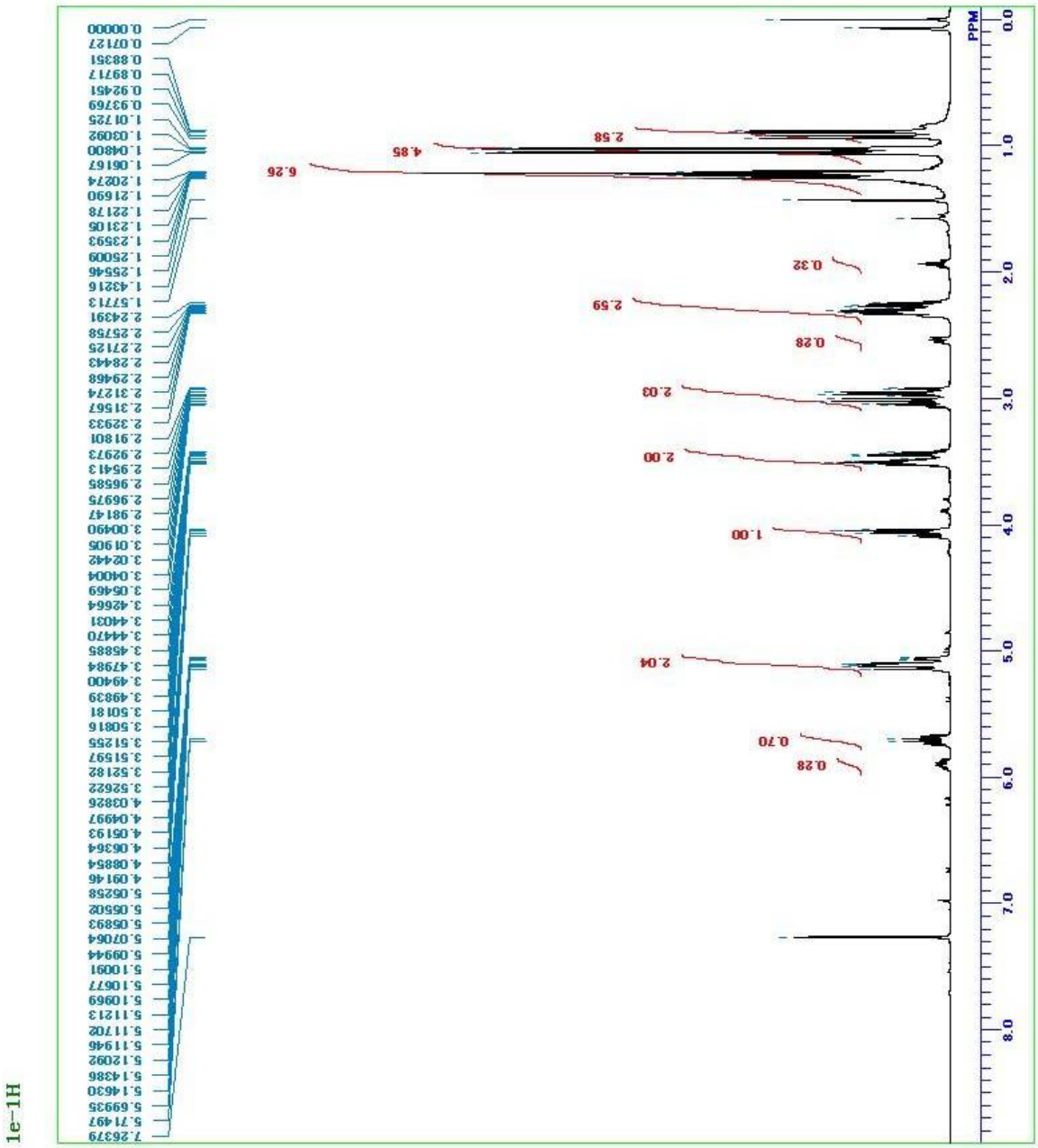
+
i-Pr
OEt
cis-1e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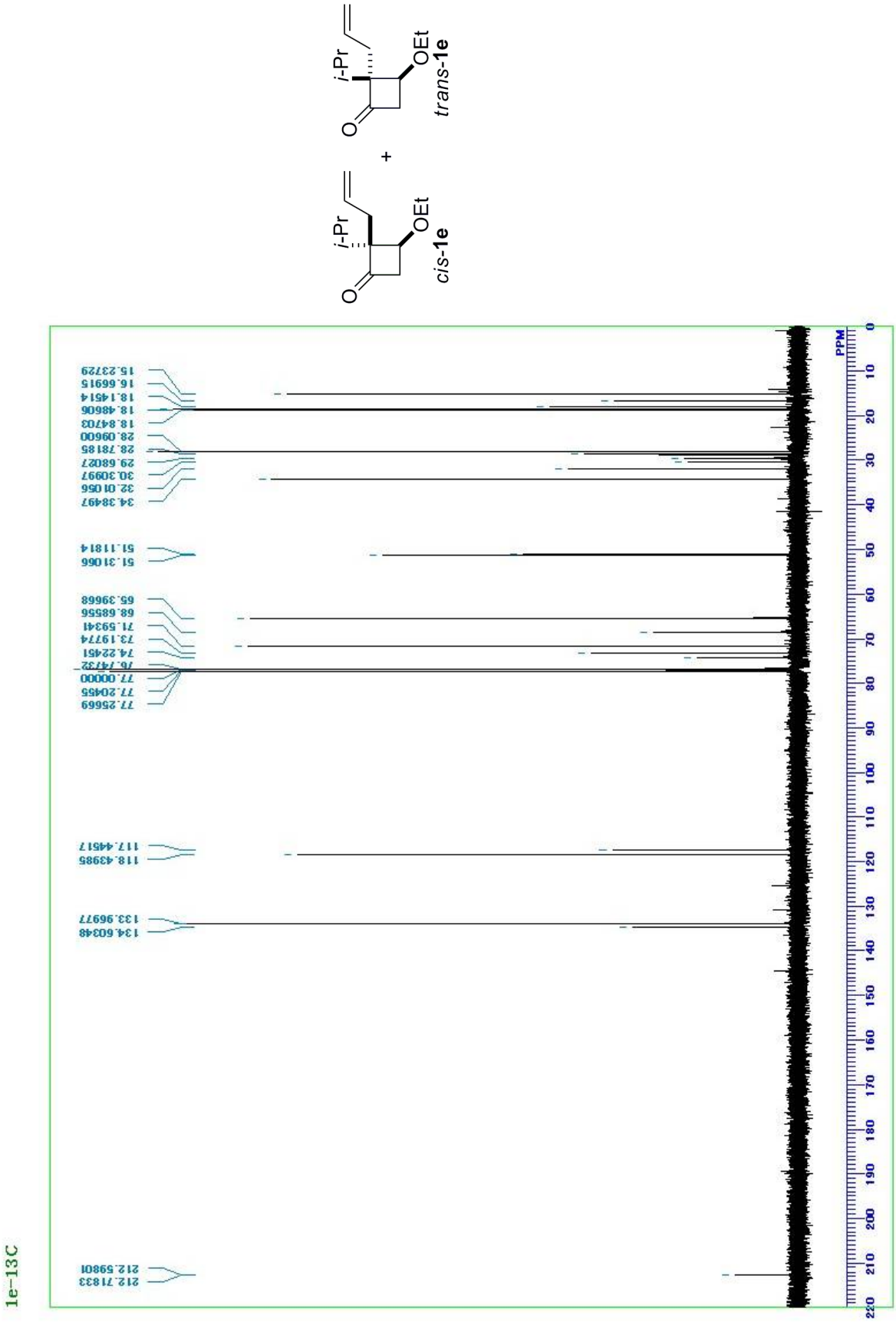
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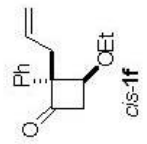

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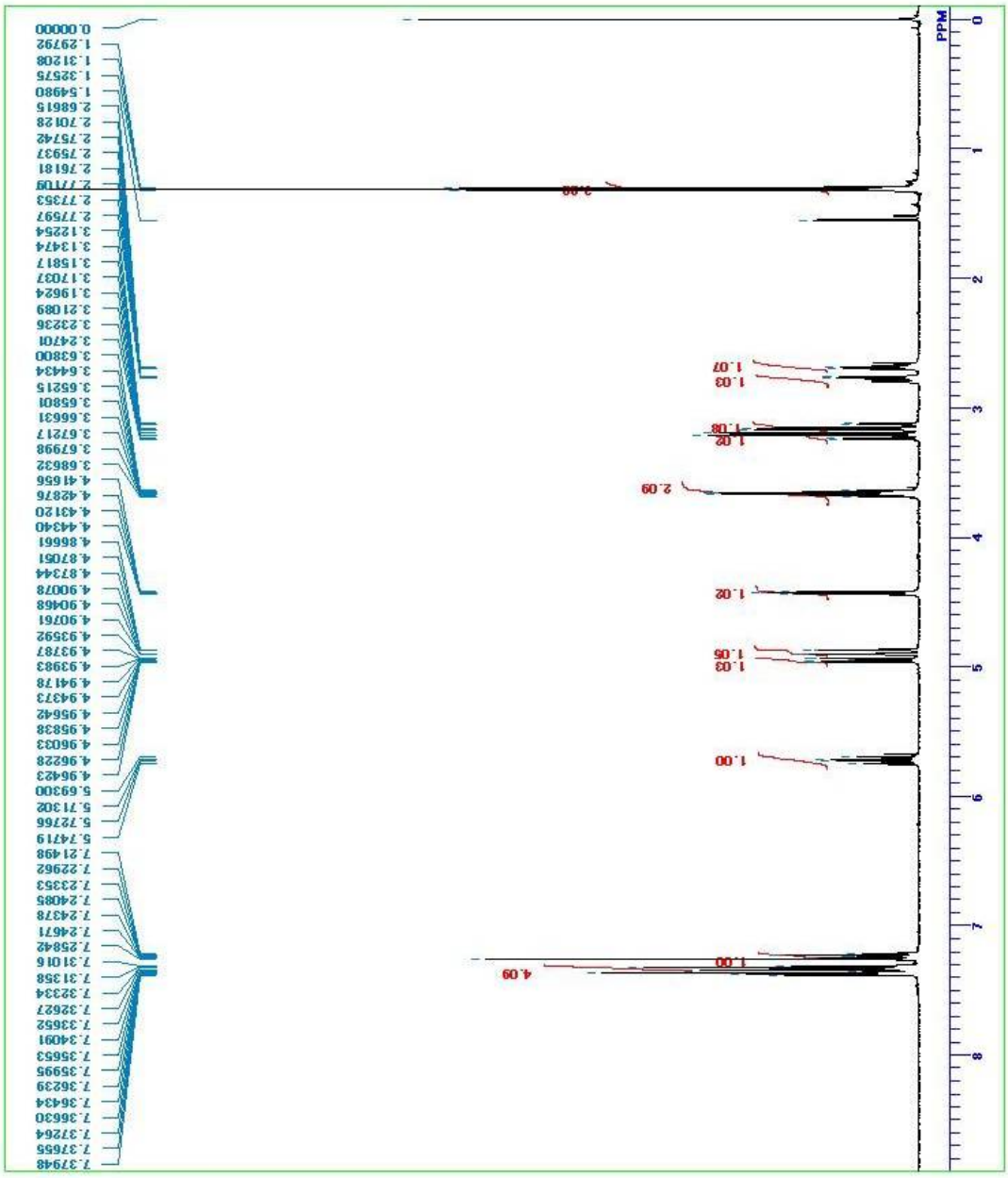

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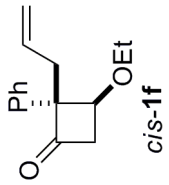
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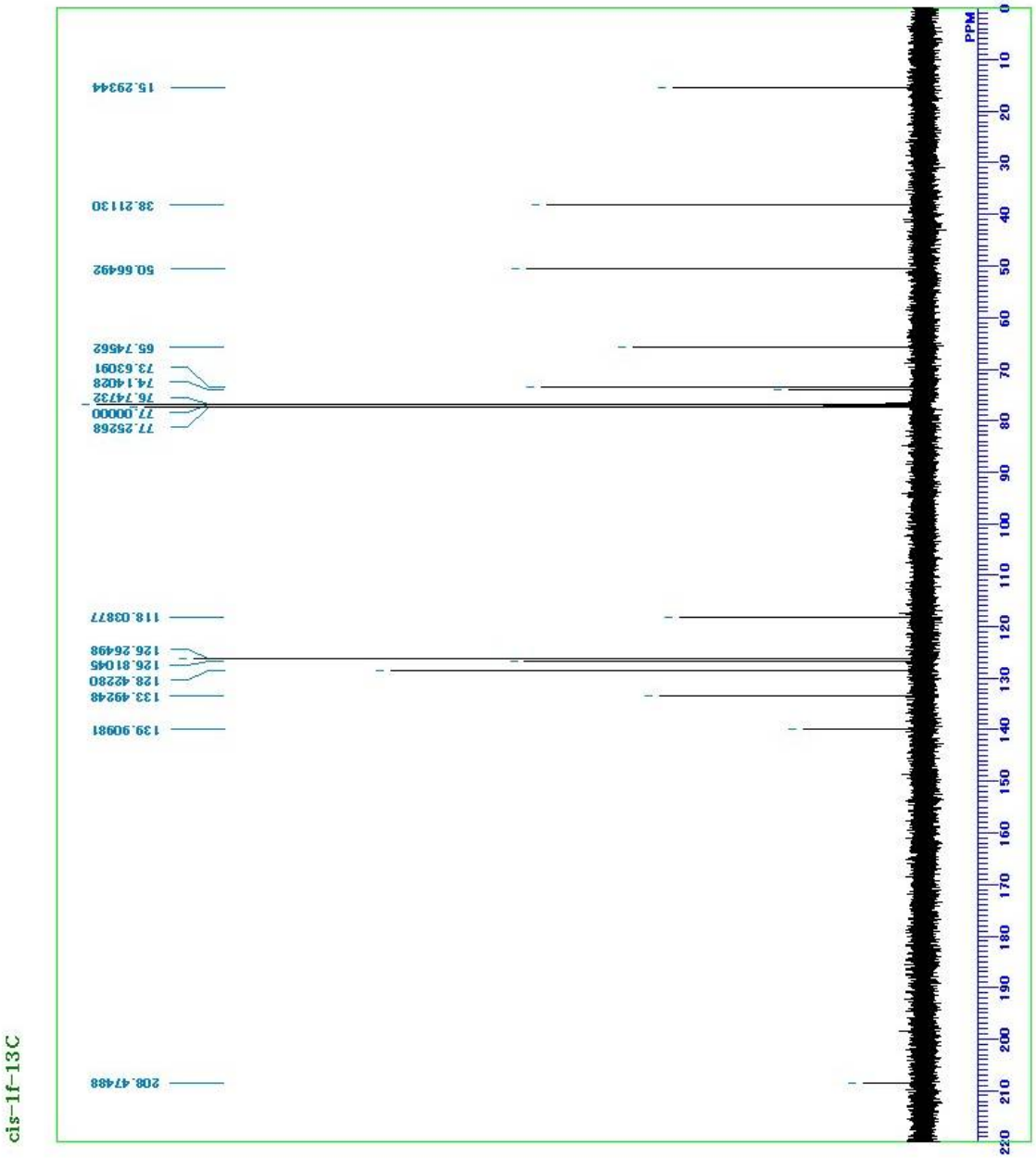
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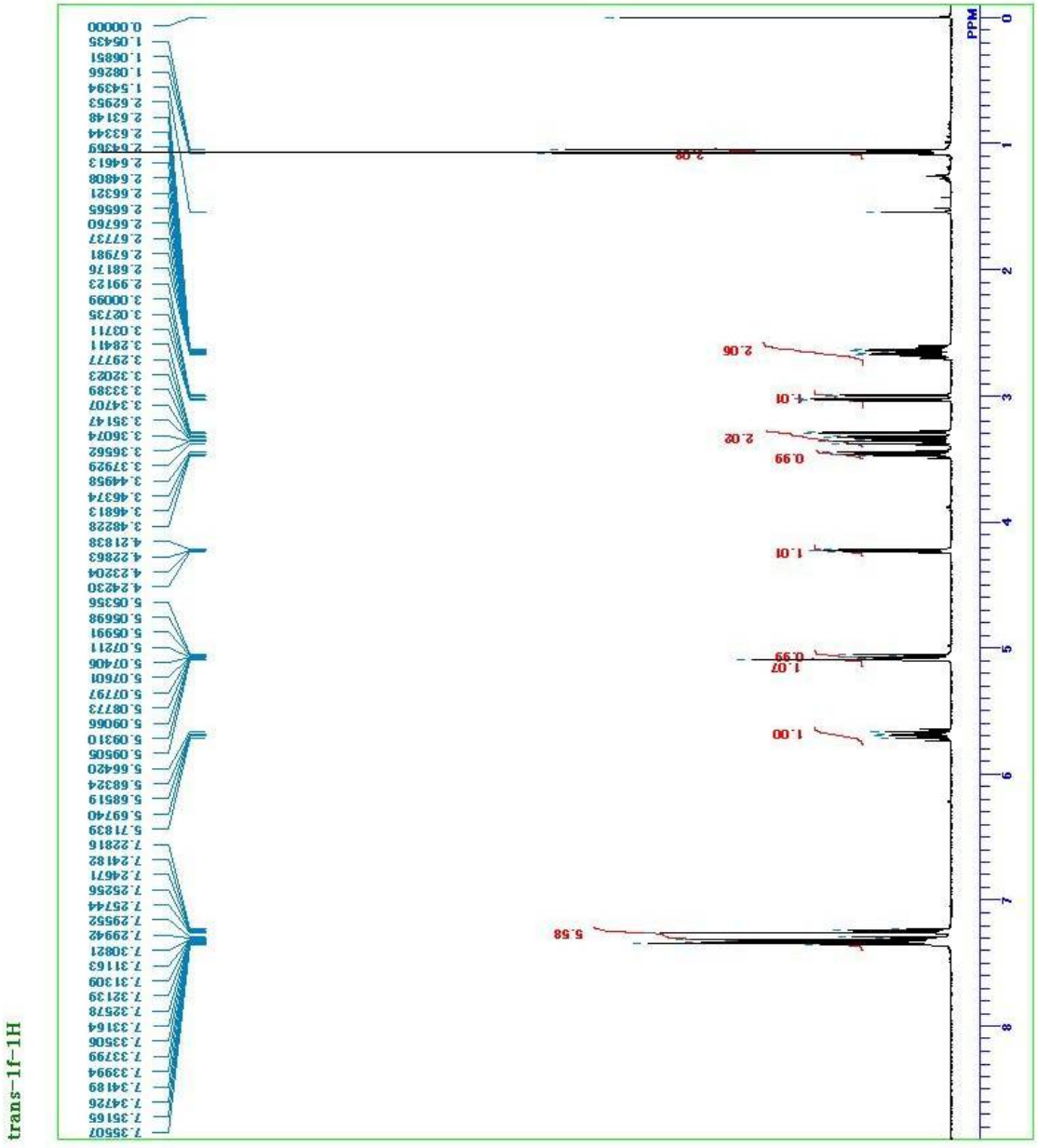
PPM


Ph
OEt
O
trans-1f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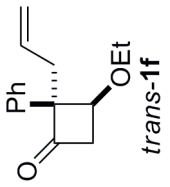
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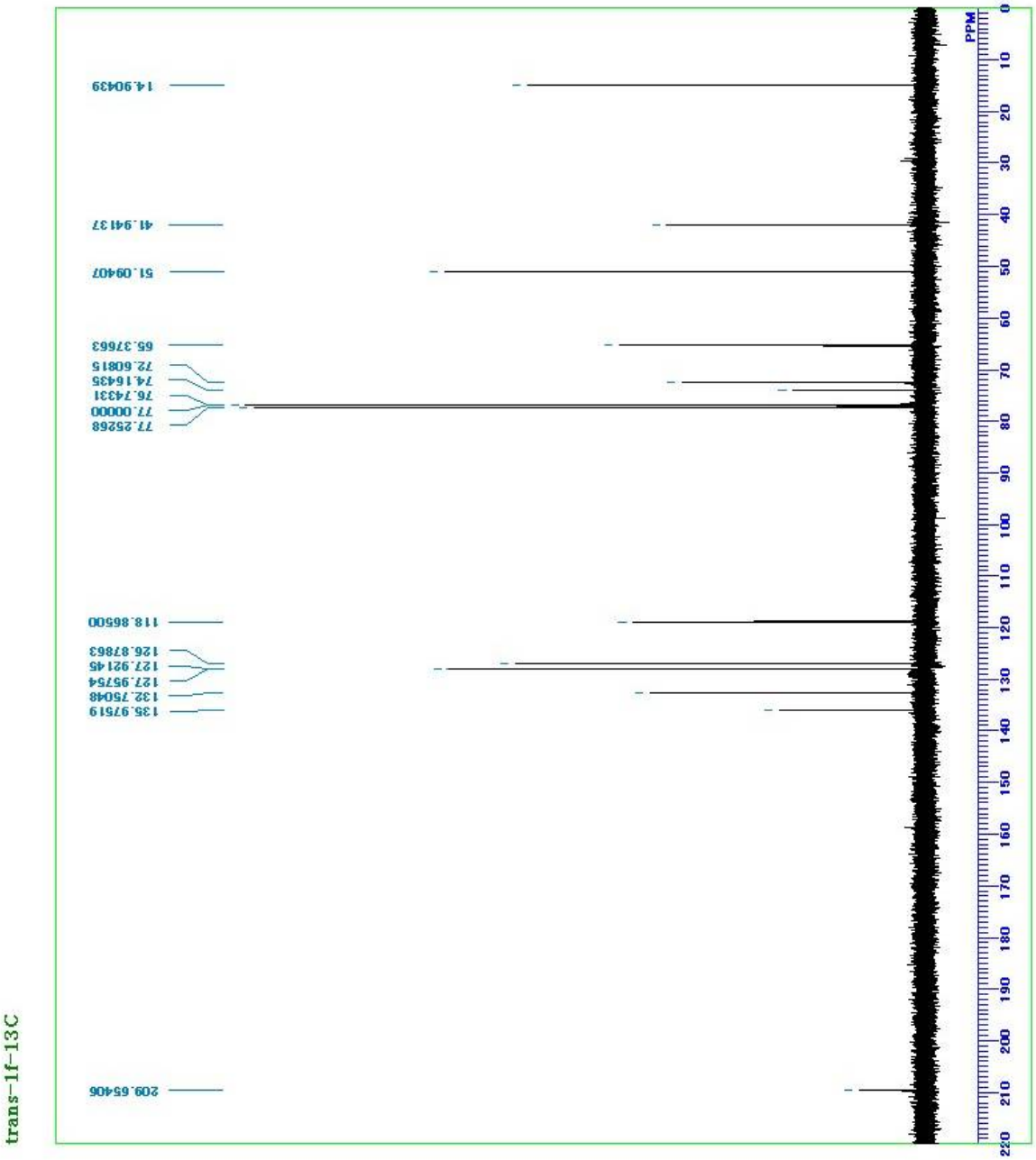
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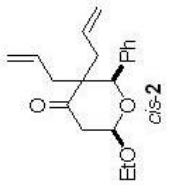
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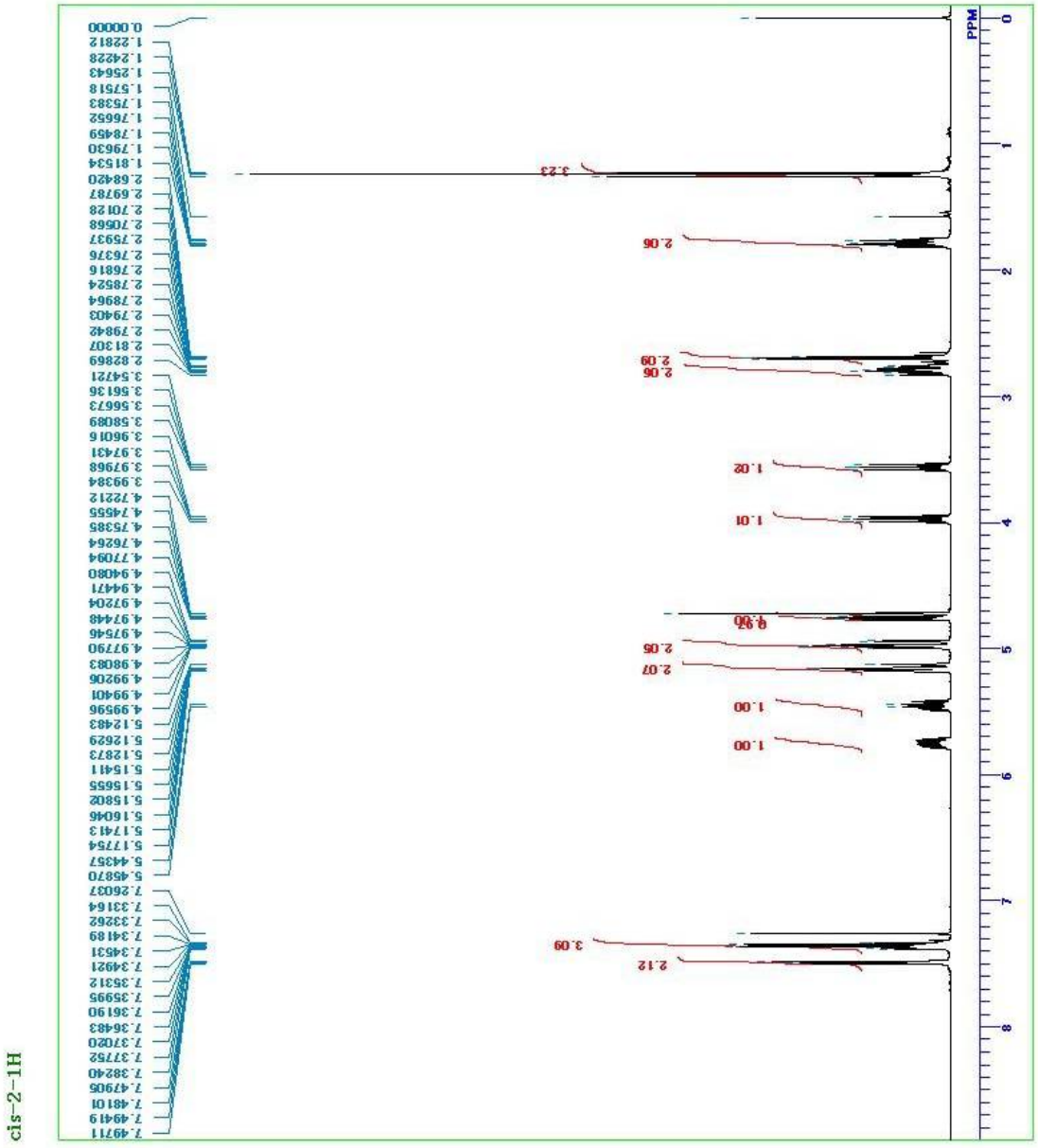
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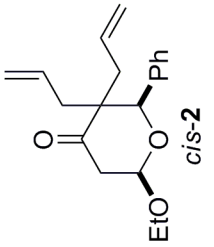

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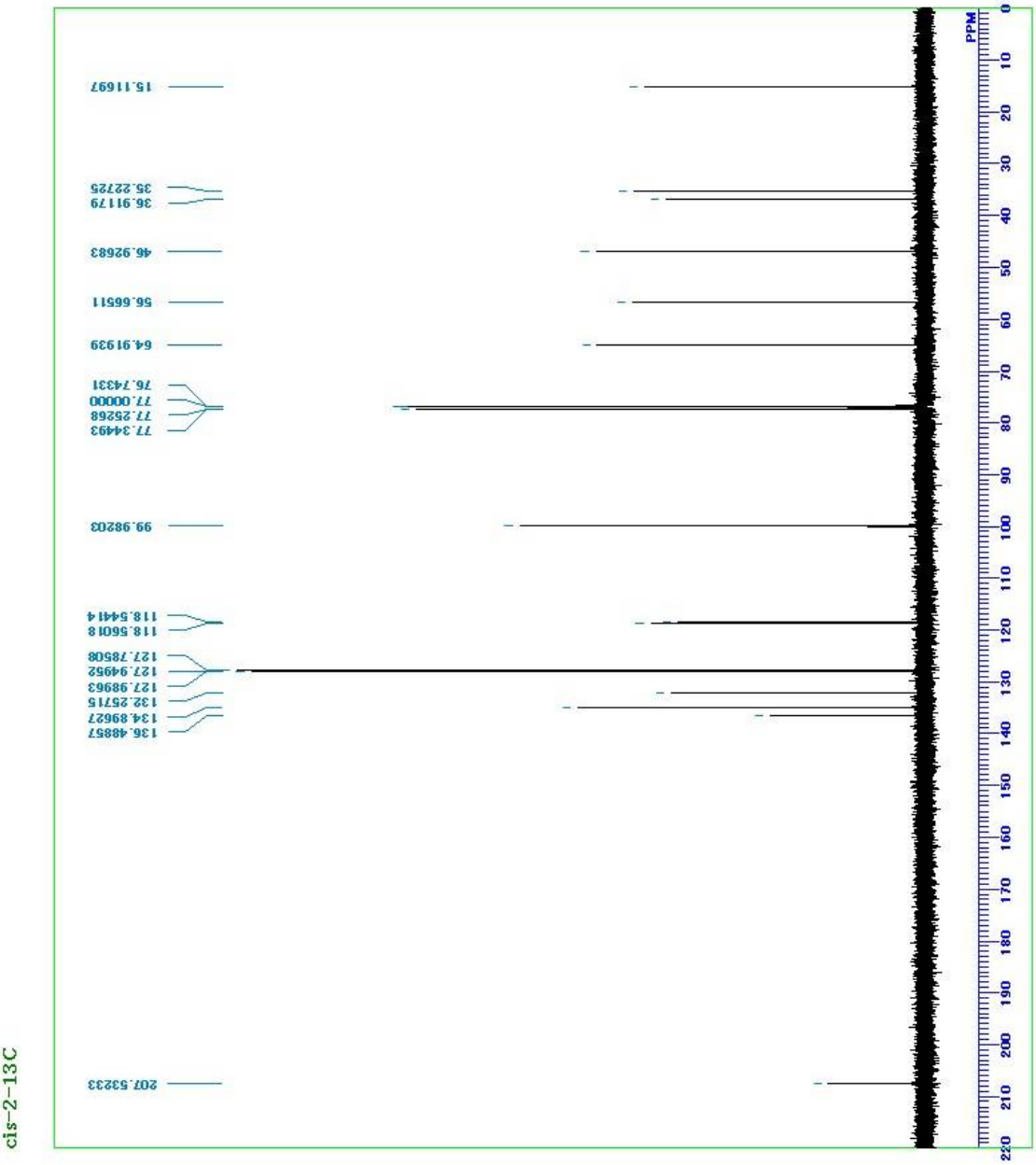

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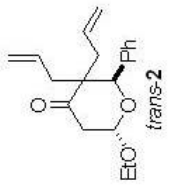
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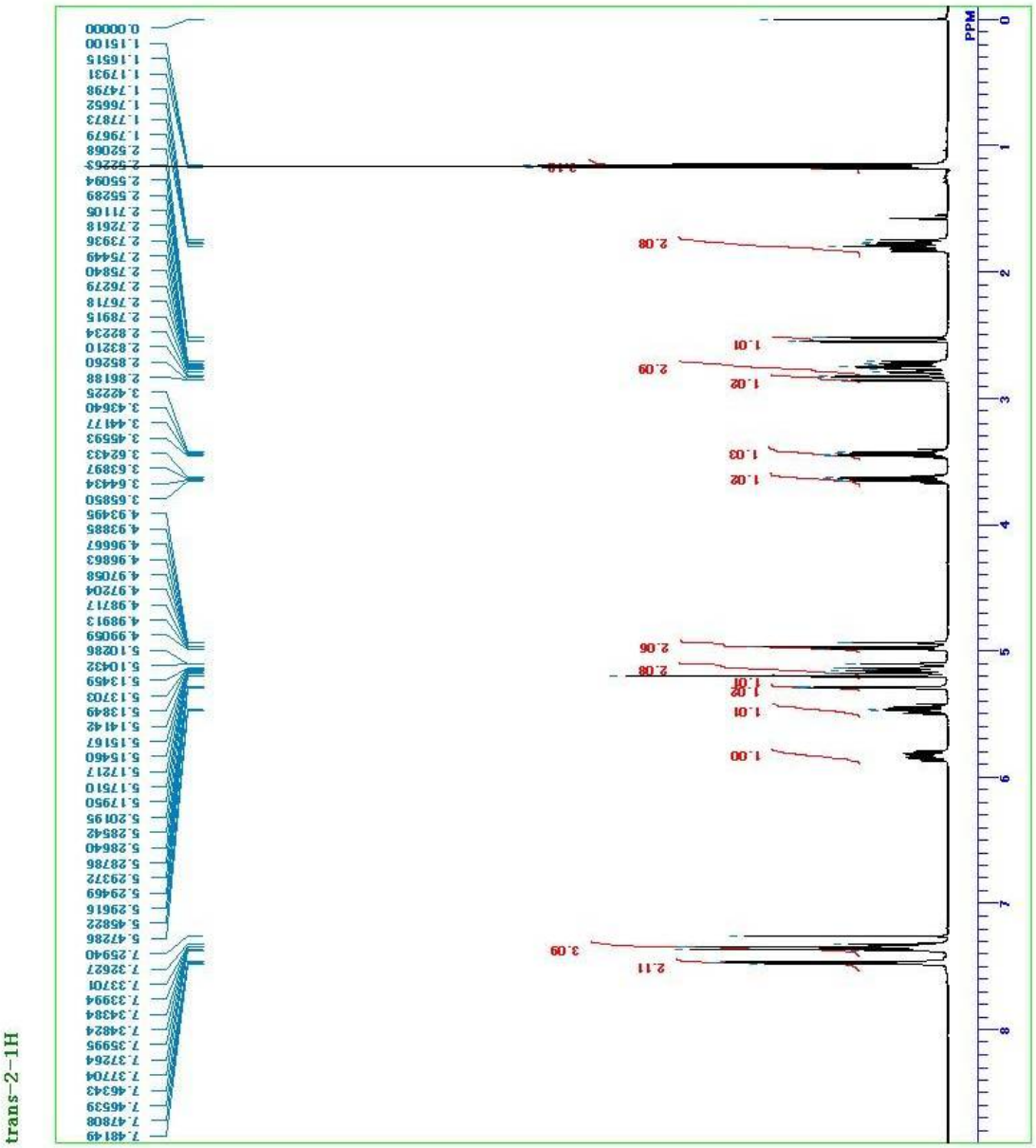
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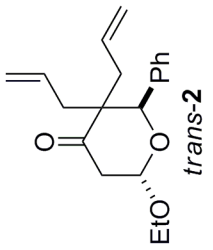
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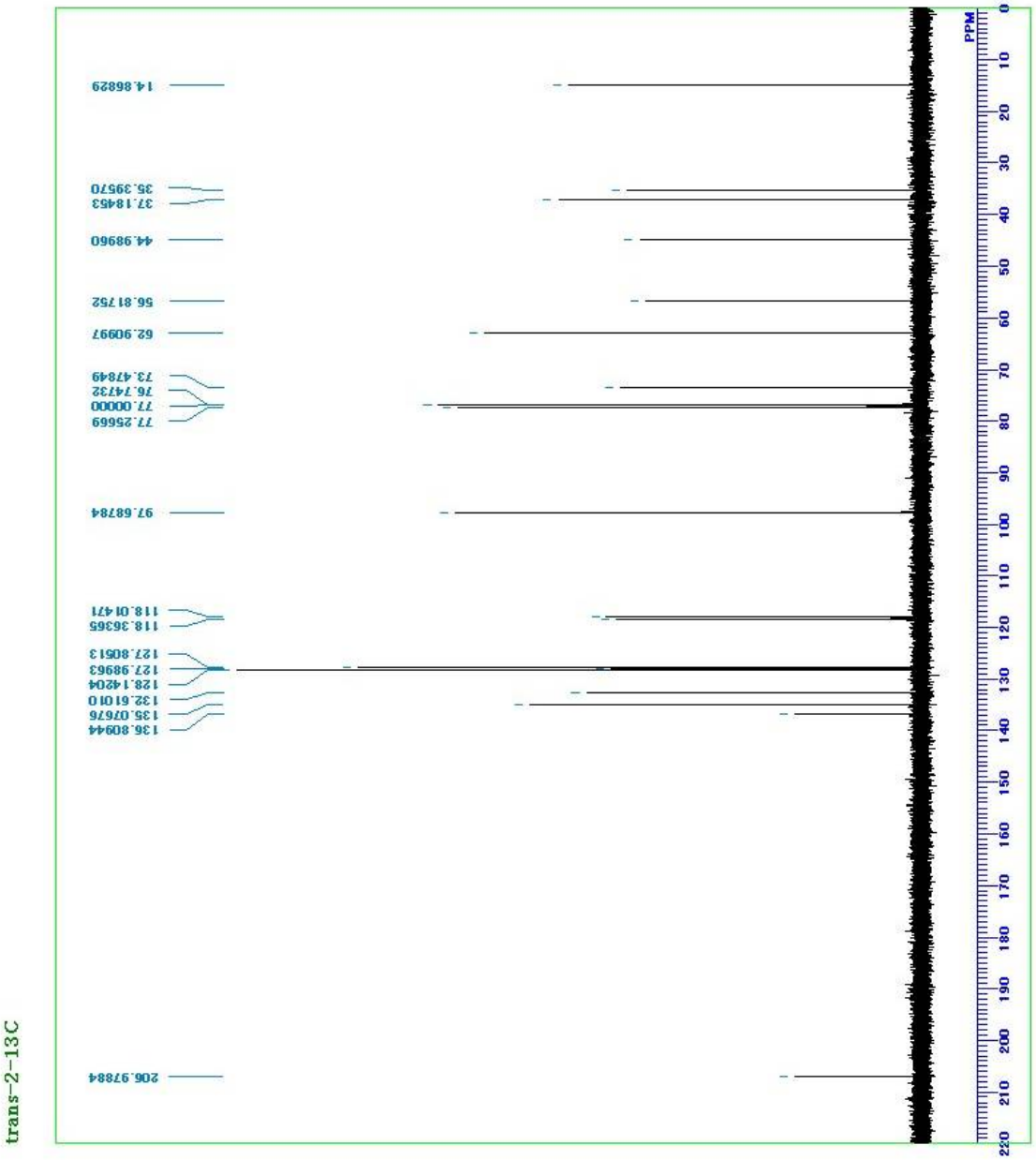
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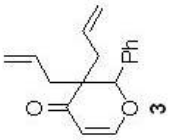
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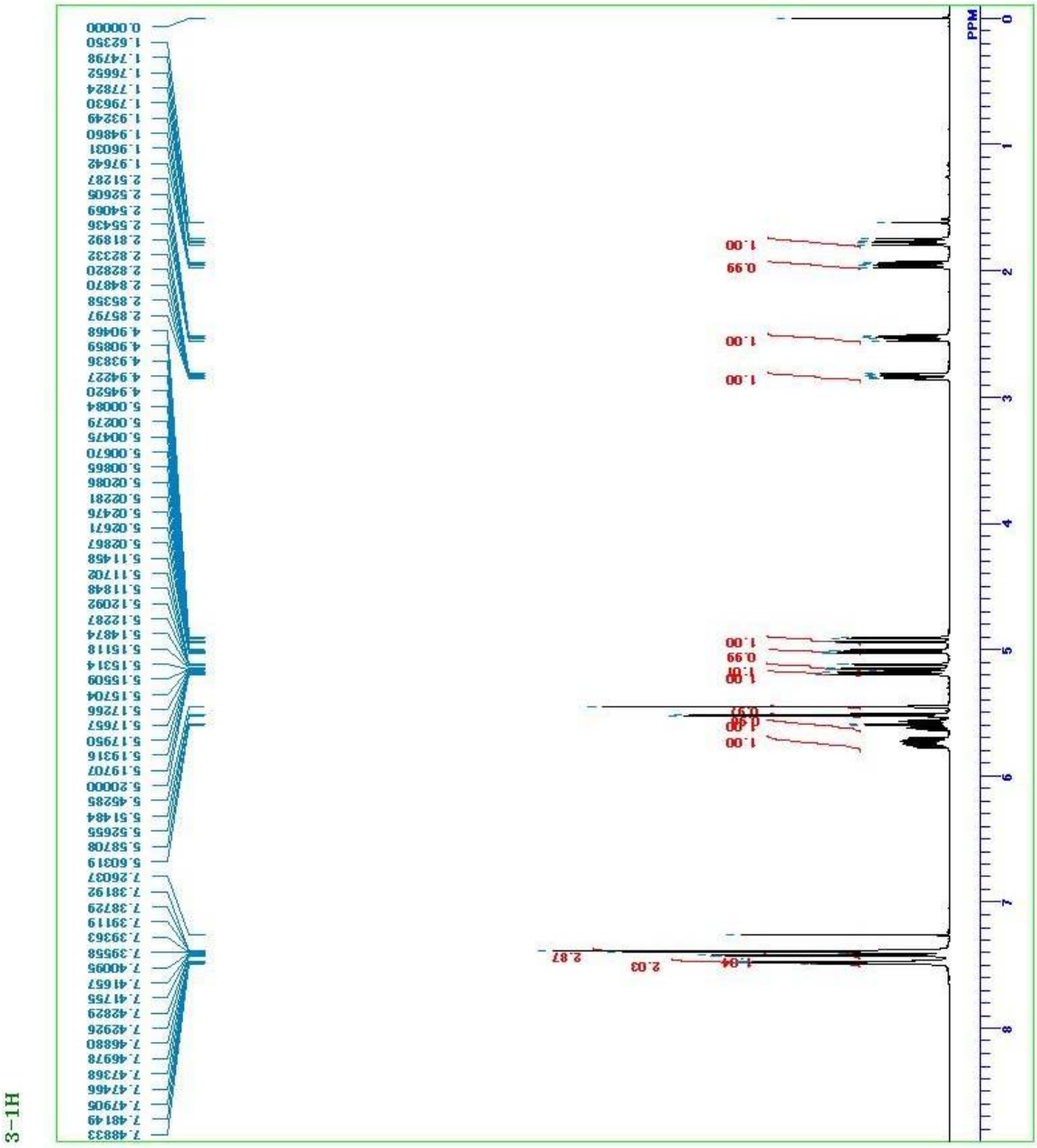
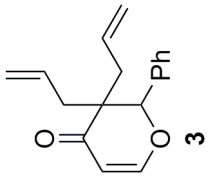
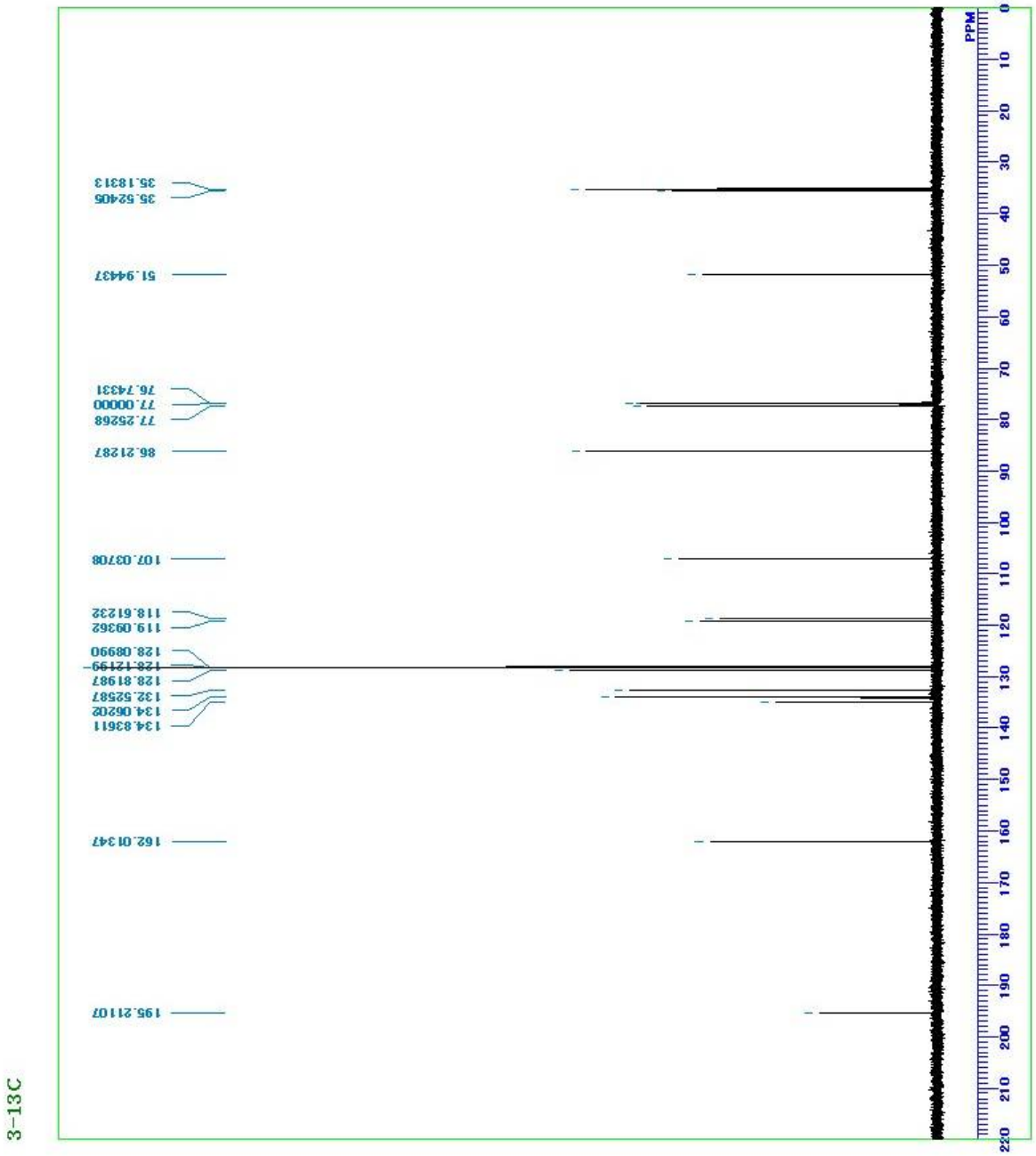
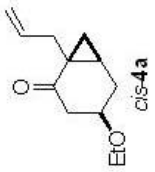
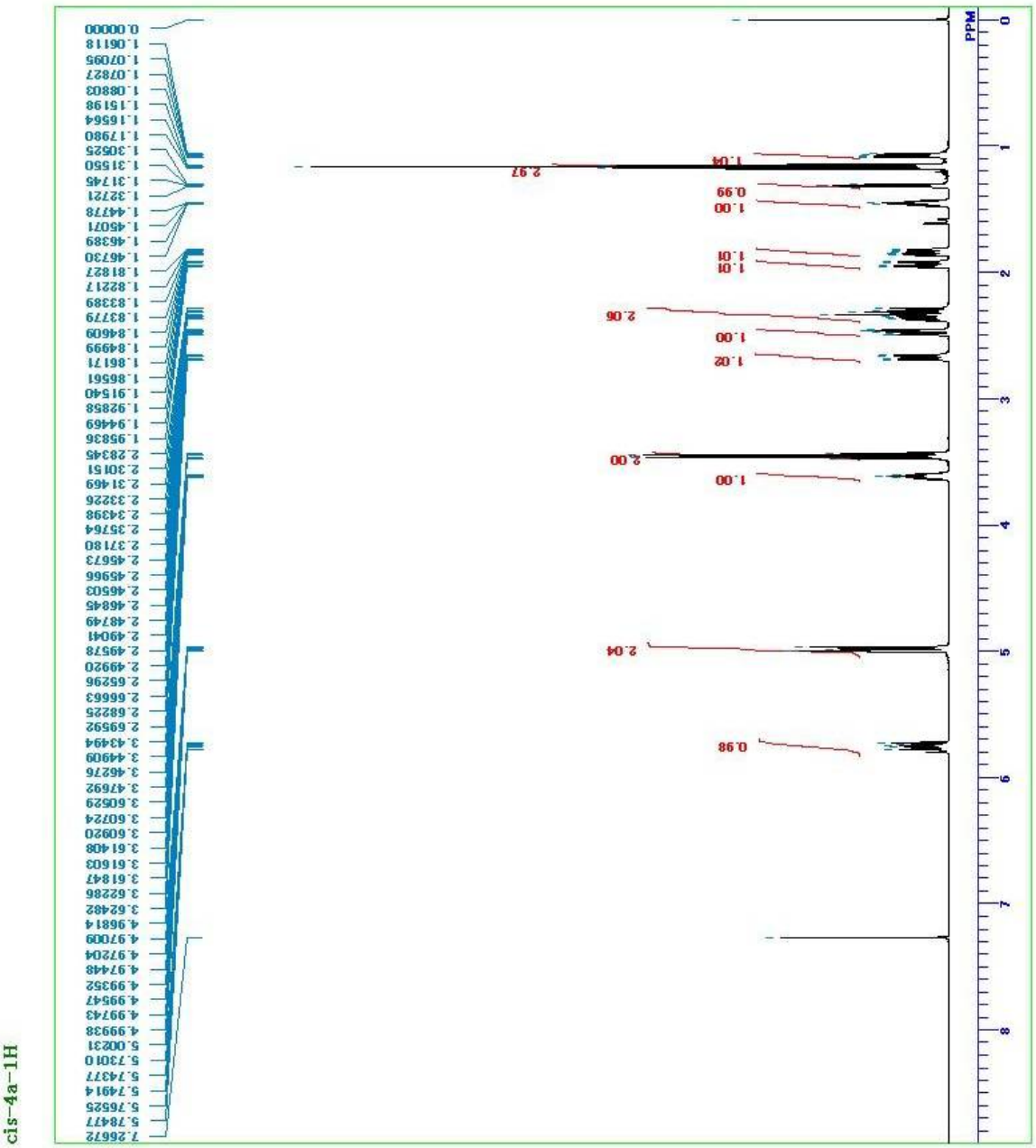
O
3

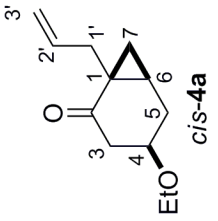

3-1H
PPM
0
1
2
3
4
5
6
7
8
1.00
0.99
1.00
1.00
1.00
0.99
1.00
1.00
2.87
2.03
1.84


Ph
O
O
3

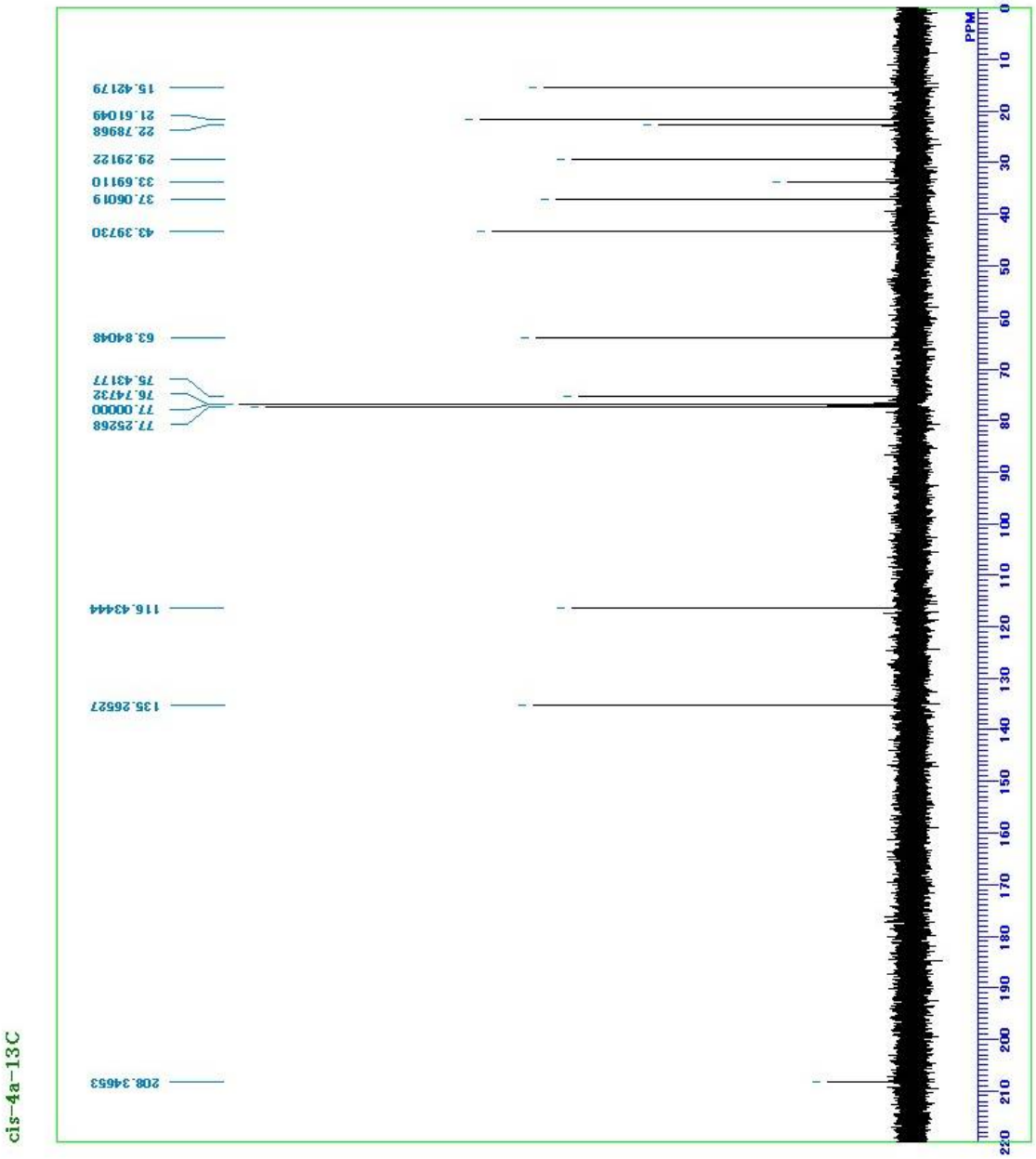

3-13C
PPM
195.21107
162.01347
134.83611
134.06202
132.52587
128.81987
128.12199
128.08990
119.09362
118.61232
107.03708
86.21287
77.25268
77.00000
76.74331
51.94437
35.52405
35.18313

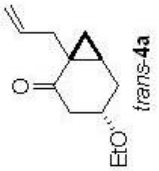

O
EtO
cis-4a

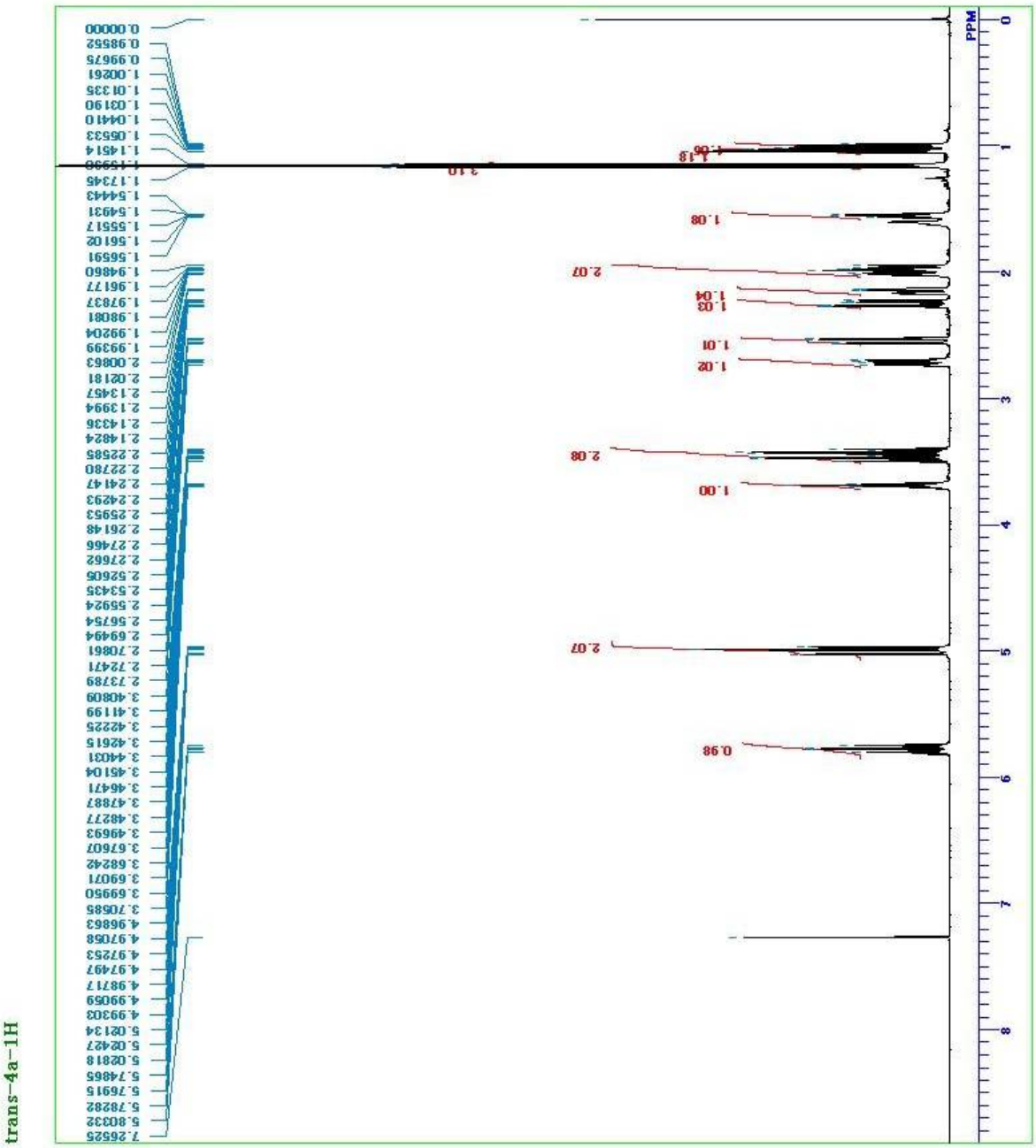

cis-4a-1H
PPM
2.97
1.04
0.99
1.00
1.01
1.01
2.06
1.00
1.02
2.00
1.00
2.04
0.98

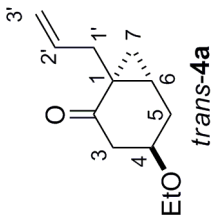

3'
2'
1'
7
1
6
O
5
3
4
EtO

cis-**4a**

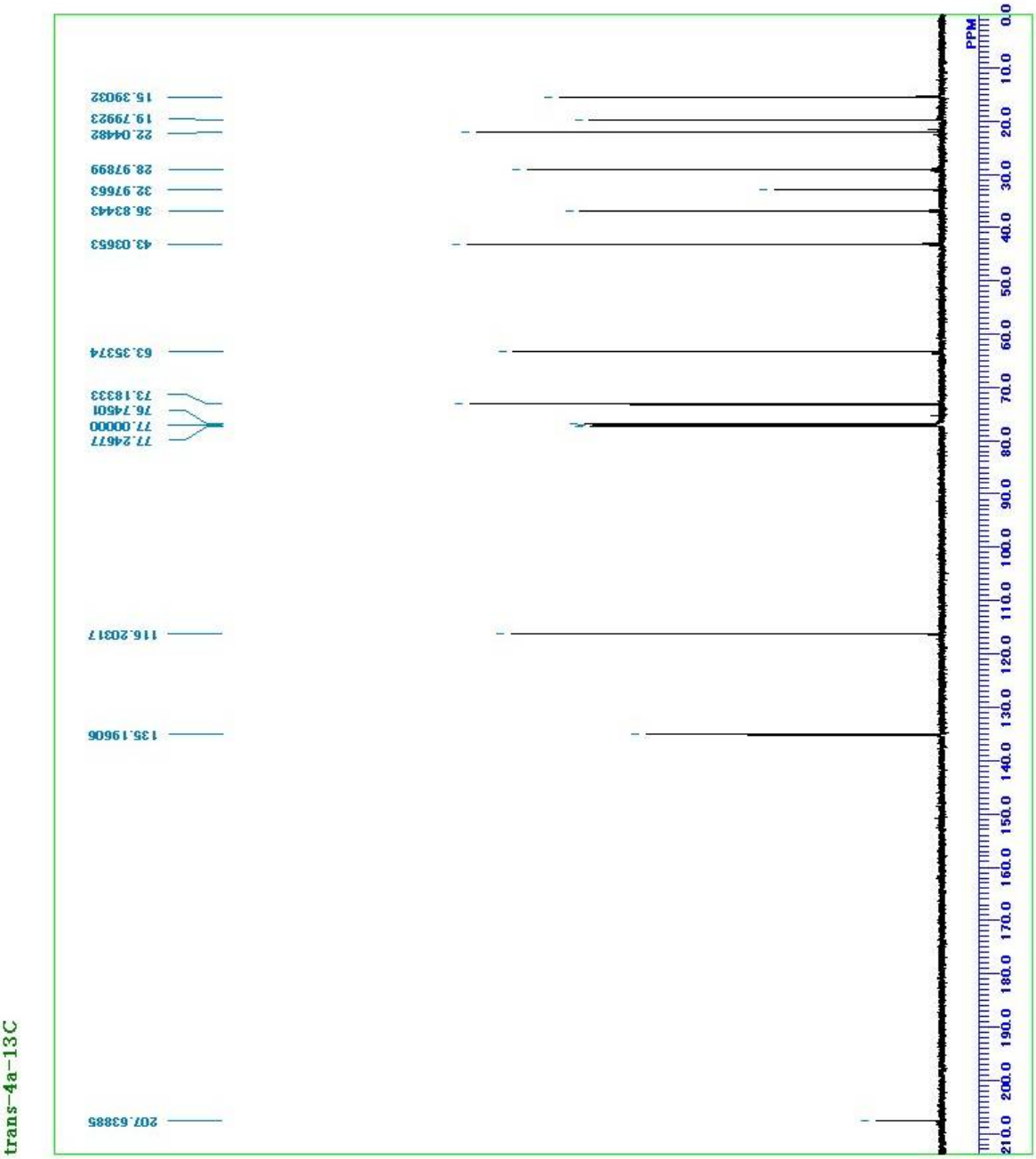

15.42179
21.61049
22.78968
29.29122
33.69110
37.06019
43.39730
63.84048
75.43177
76.74732
77.00000
77.25268
116.43444
135.26527
208.34653
PPM
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
cis-4a-13C

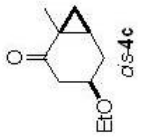

trans-4a
EtO

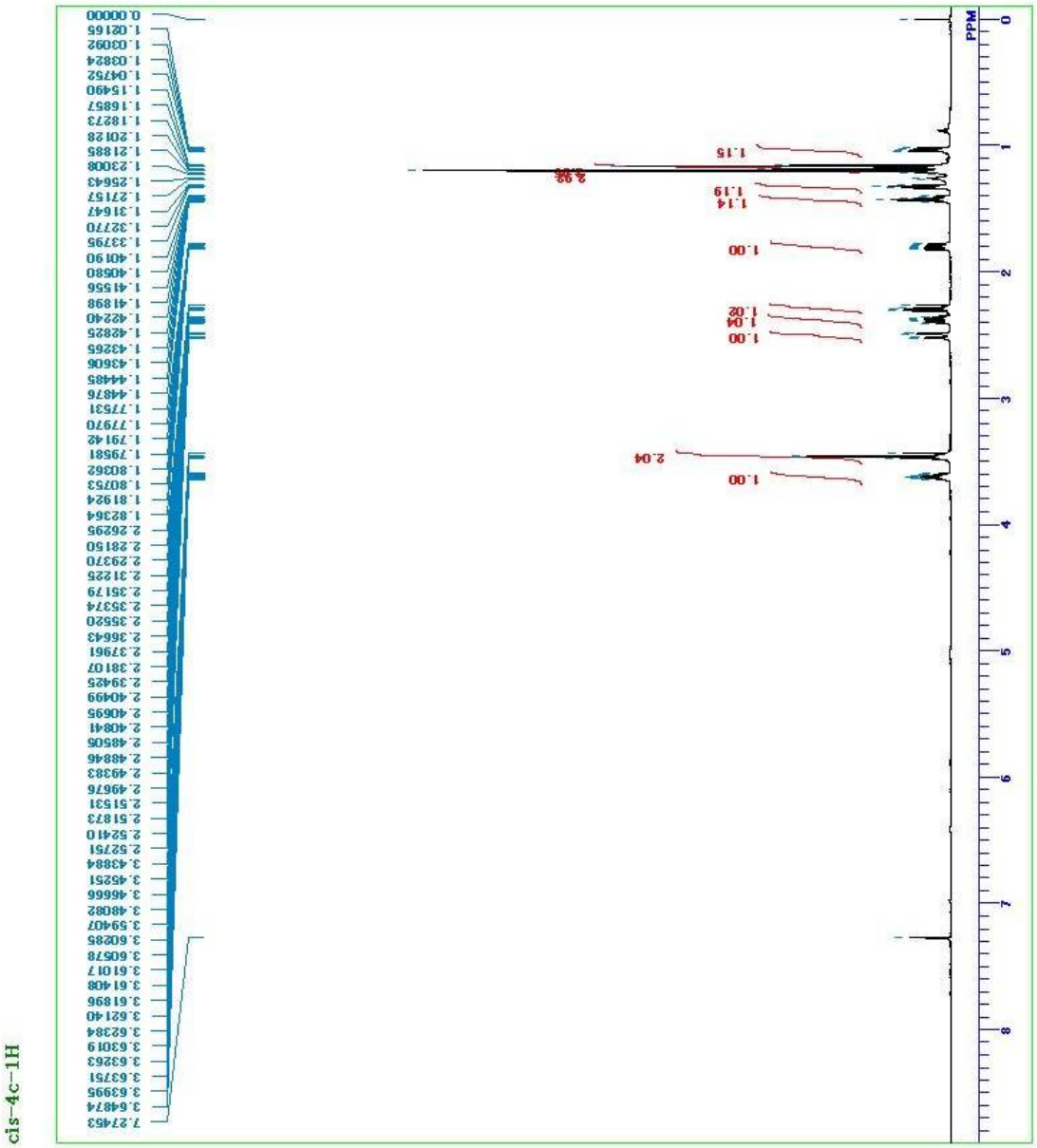

trans-4a-1H
PPM
3.10
1.08
2.07
1.03
1.04
1.01
1.02
2.08
1.00
2.07
0.98

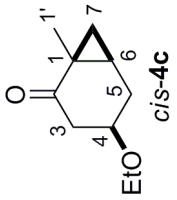

3'
2'
1'
7
1
6
5
4
3
O
EtO

trans-**4a**

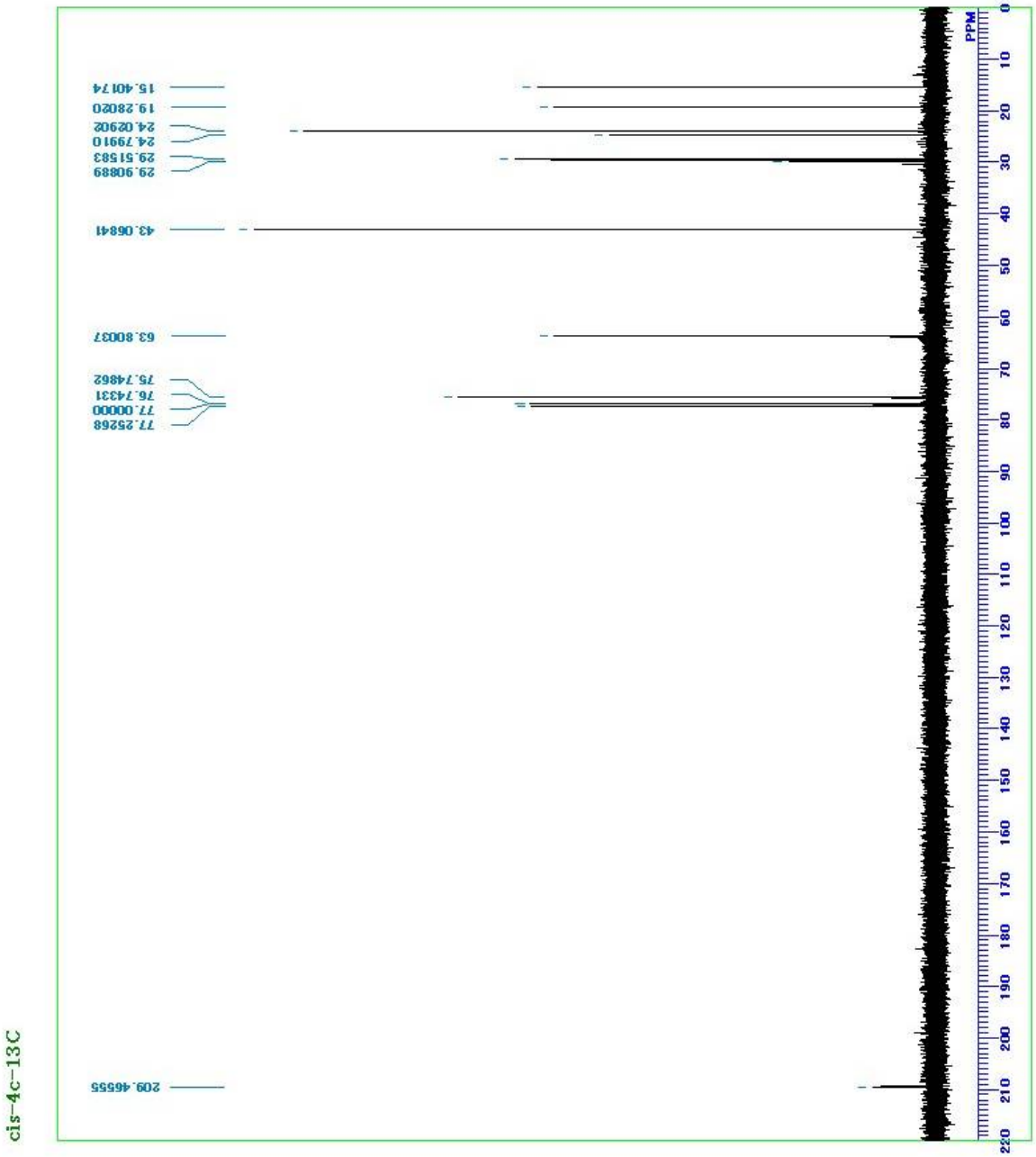

trans-4a-13C
207.63885
135.19606
116.20317
77.24677
77.00000
76.74501
73.18333
63.35374
43.03653
36.83443
32.97663
28.97899
22.04482
19.79923
15.39032
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0

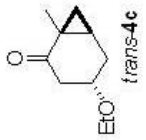

O
EtO
cis-4c

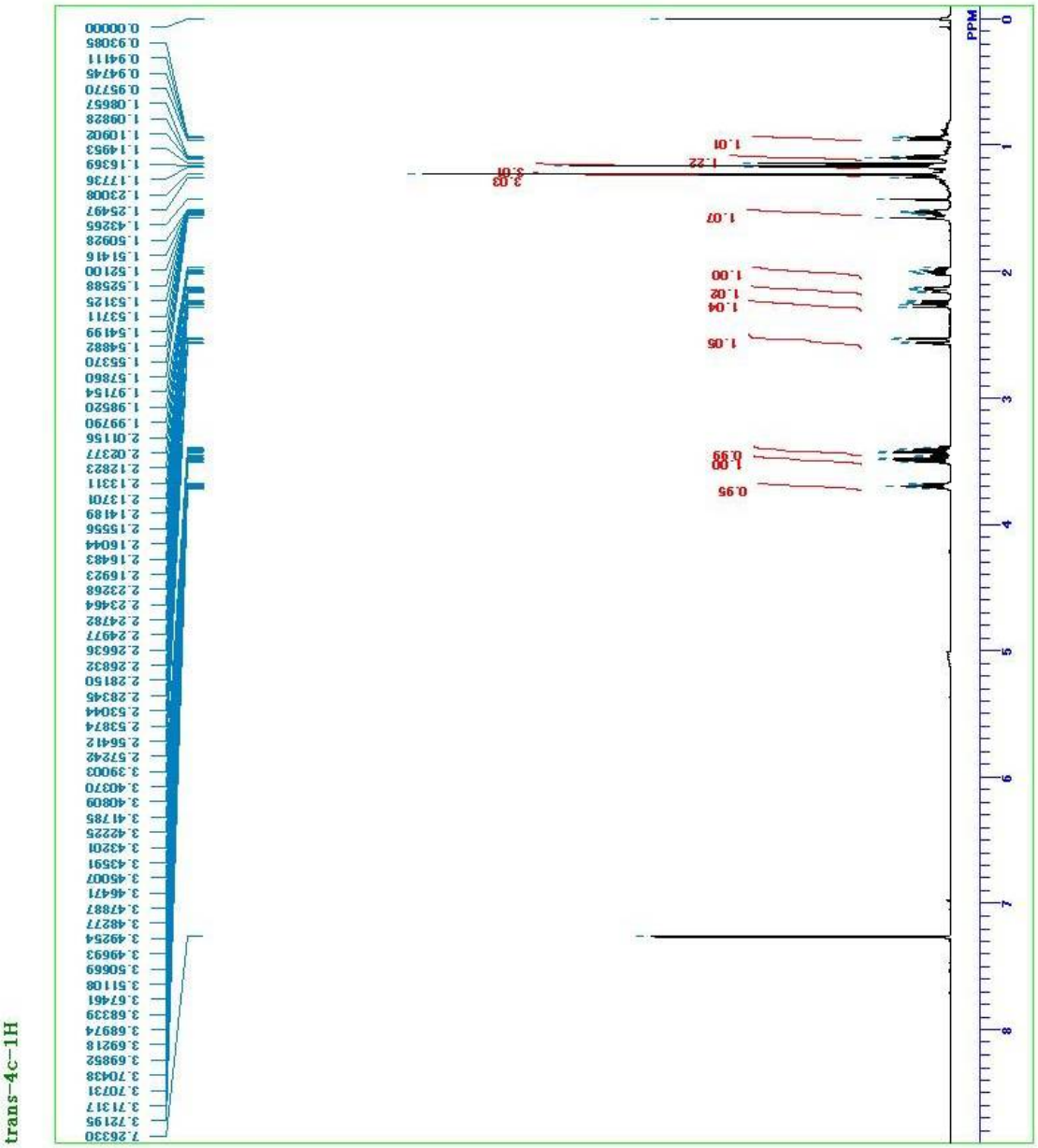

cis-4c-1H
PPM
1.15
3.98
1.19
1.14
1.00
1.00
1.04
1.02
2.04
1.00

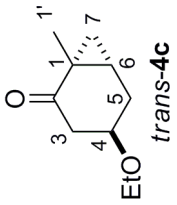

O
EtO
1
1'
3
4
5
6
7

cis-**4c**

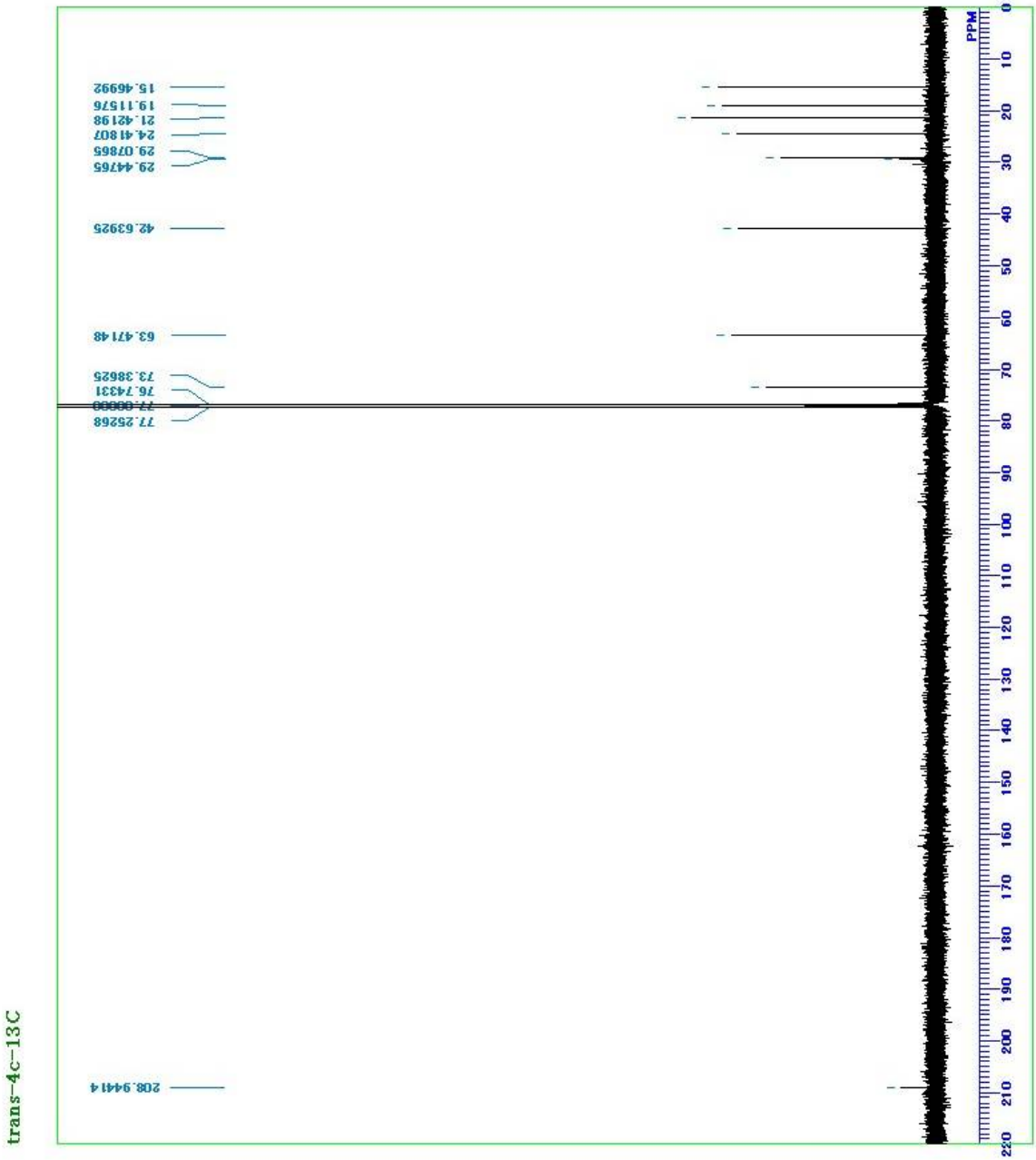

cis-4c-13C
209.46555
77.25268
77.00000
76.74331
75.74862
63.80037
43.06841
29.90889
29.51583
24.79910
24.02902
19.28020
15.40174
PPM

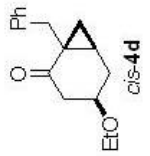

EtO
trans-4c

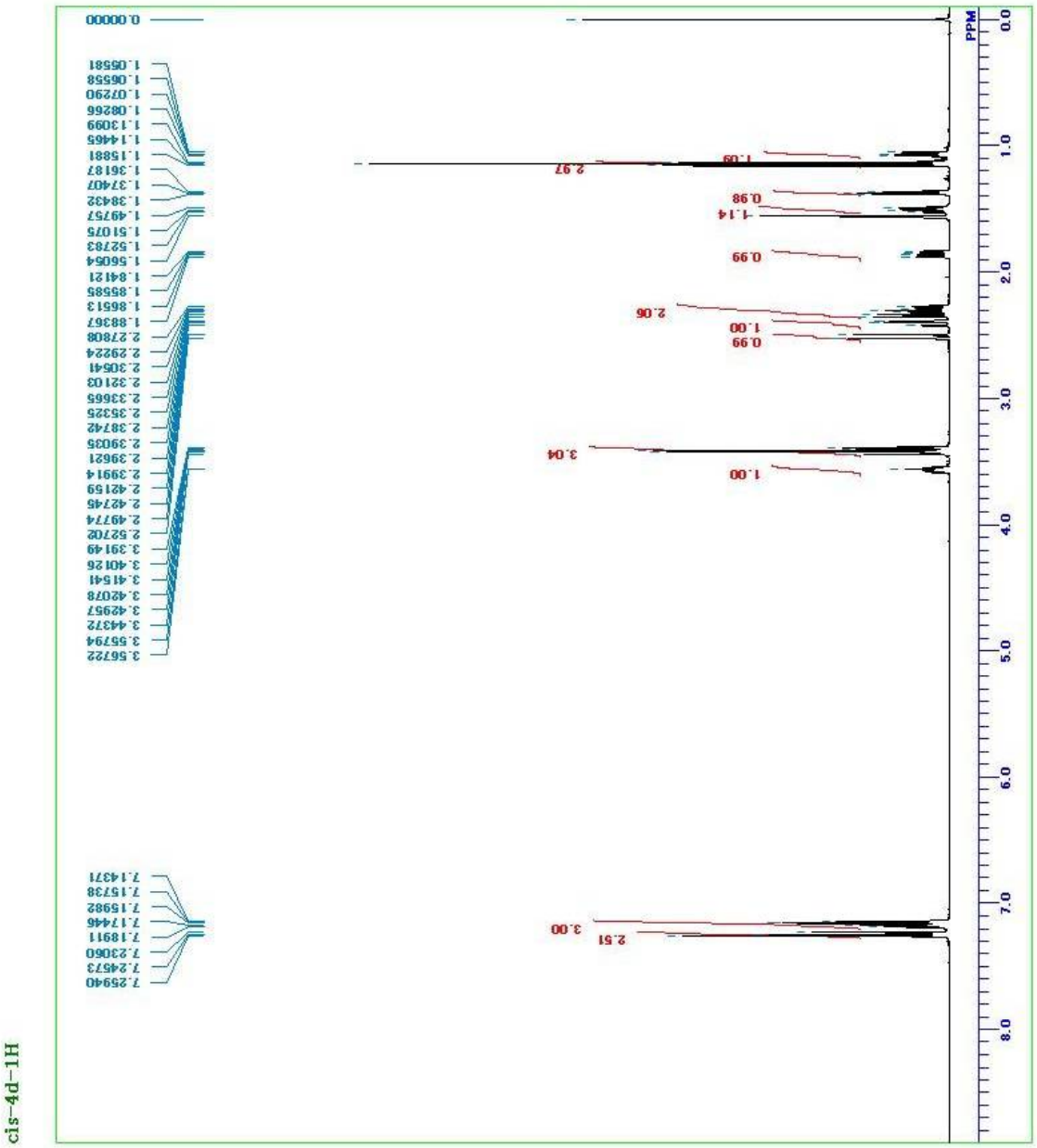

trans-4c-1H
PPM
1.01
1.22
3.01
3.03
1.07
1.00
1.02
1.04
1.05
0.99
1.00
0.95

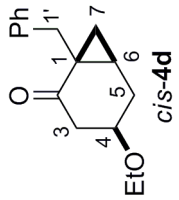

O
EtO
1
1'
3
4
5
6
7

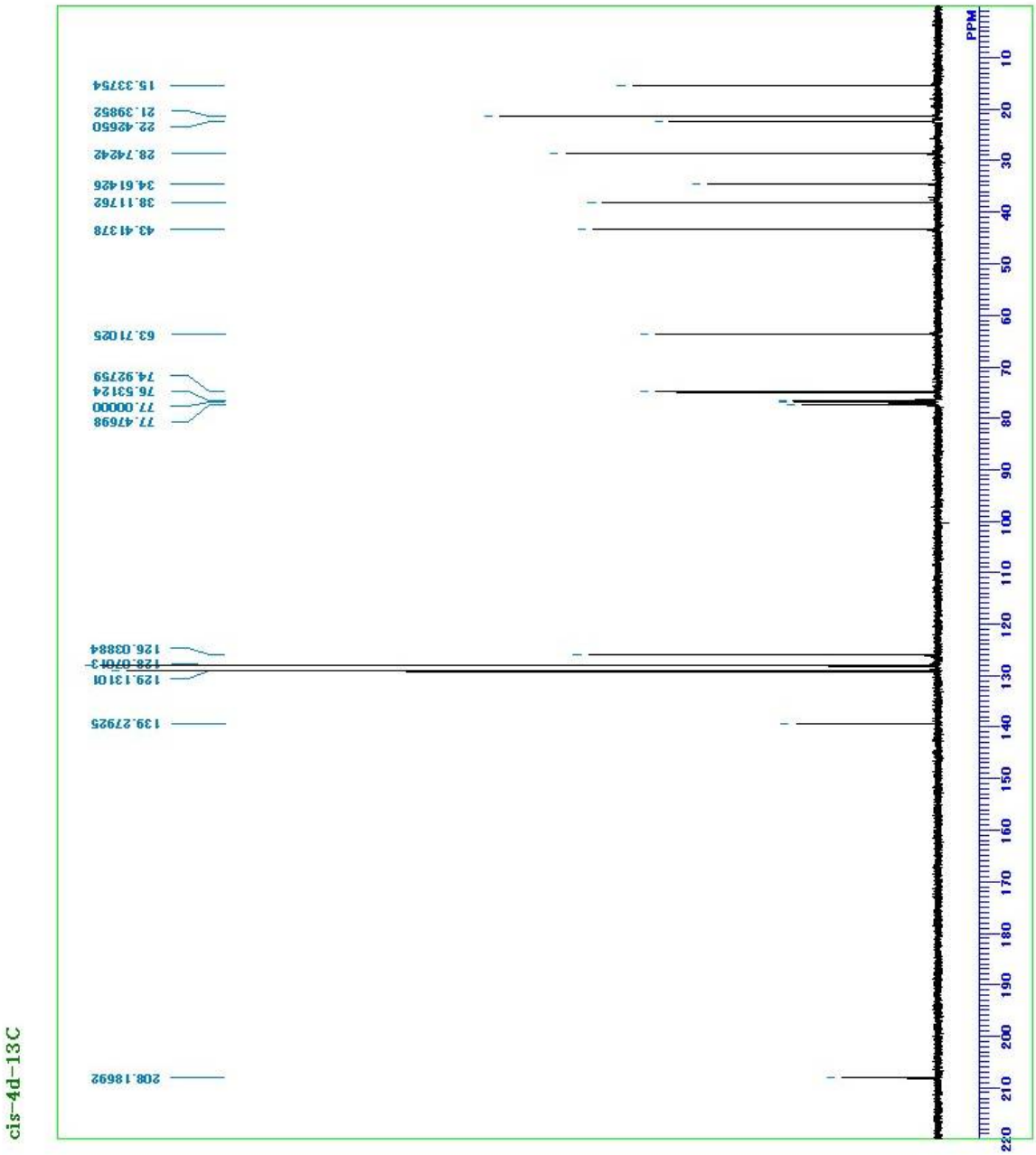
trans-**4c**

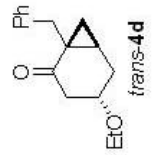

trans-4c-13C
208.94414
77.25268
76.74331
73.38625
63.47148
42.63925
29.44765
29.07865
24.41807
21.42198
19.11576
15.46992
PPM

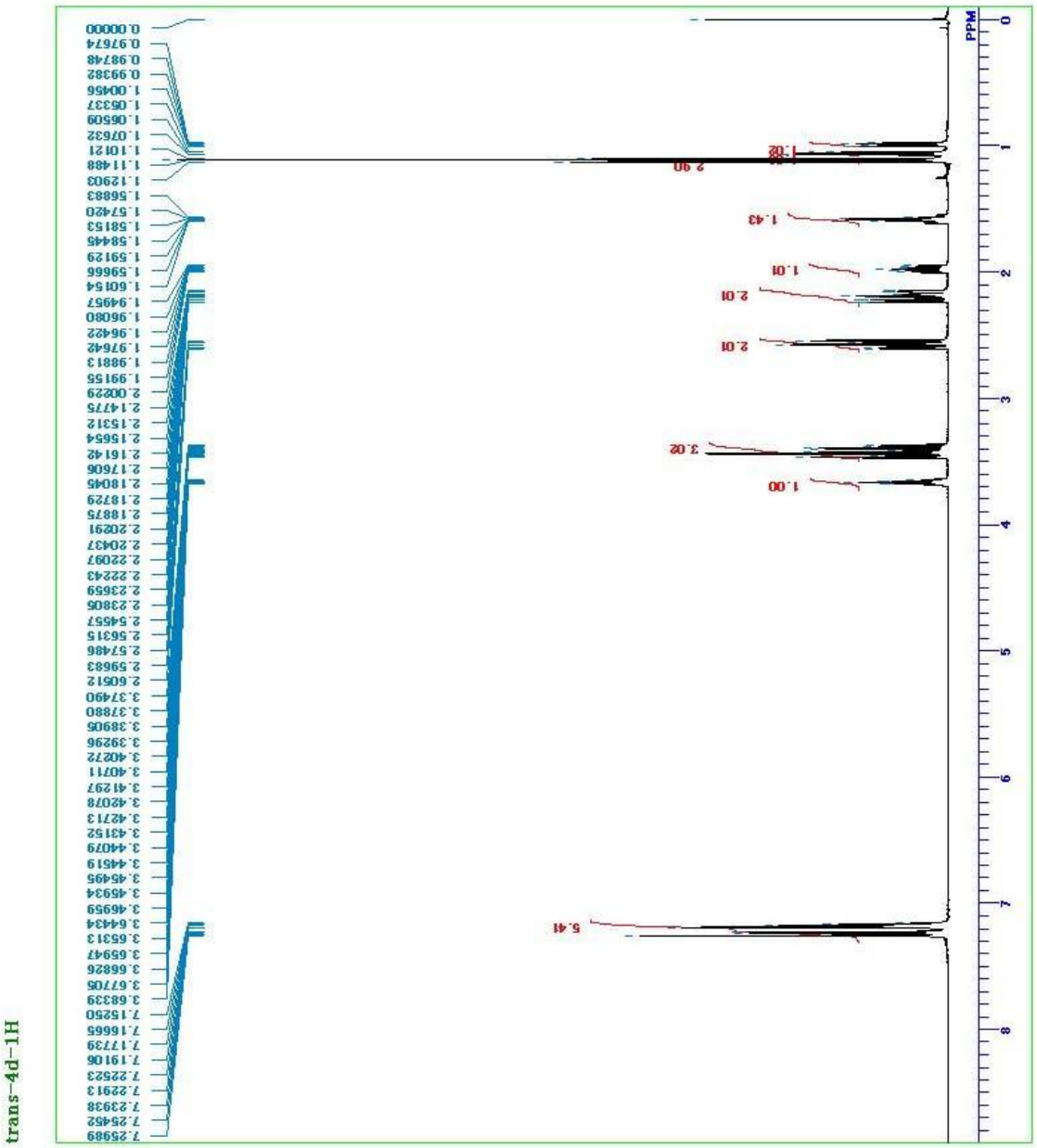

Ph
O
EtO
cis-4d


cis-4d-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
2.97
1.09
0.98
1.14
0.99
2.06
1.00
0.99
3.04
1.00
3.00
2.51


Ph
1'
7
1
6
O
5
3
4
EtO
cis-**4d**

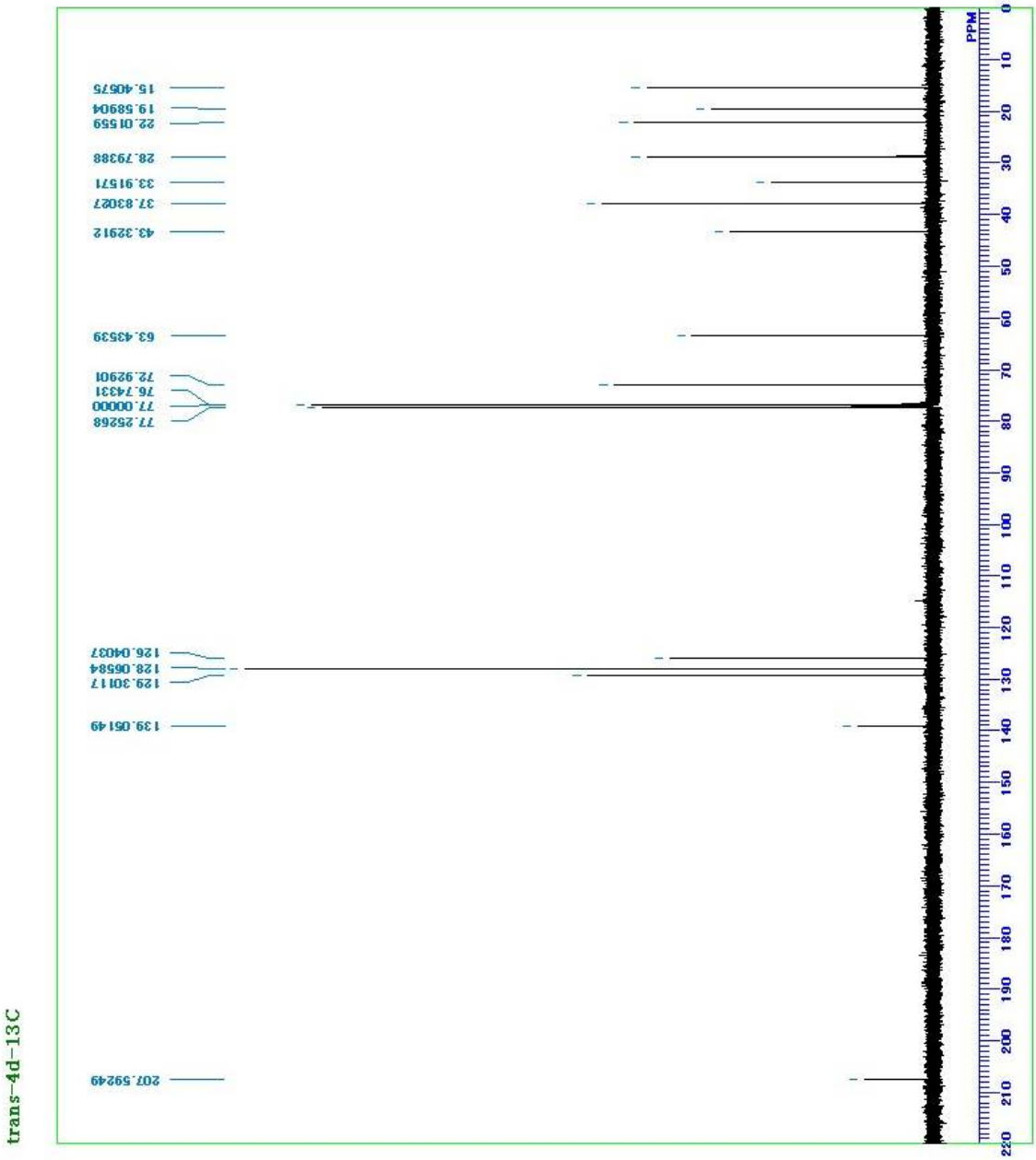

cis-4d-13C
15.33754
21.39852
22.42650
28.74242
34.61426
38.11762
43.41378
63.71025
74.92759
76.53124
77.00000
77.47698
126.03884
128.07013
129.13101
139.27925
208.18692
PPM

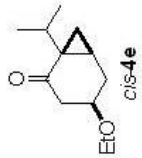

Ph
O
EtO
trans-4d

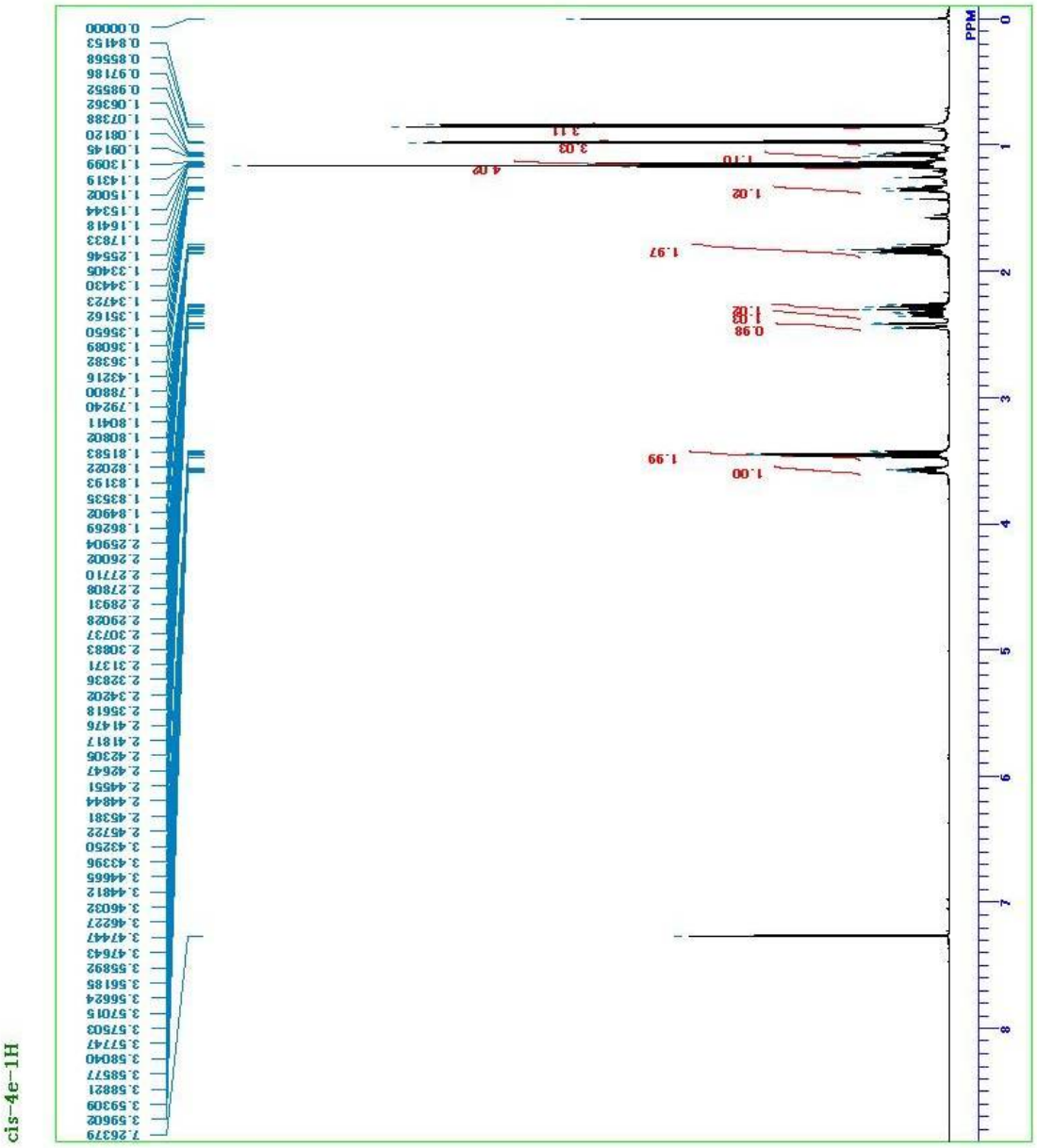

trans-4d-1H
PPM
0
1
2
3
4
5
6
7
8
2.90
1.43
1.01
2.01
2.01
3.02
1.00
5.41

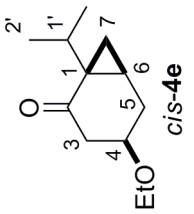

Ph
1'
7
1
6
O
5
3
4
EtO

trans-**4d**

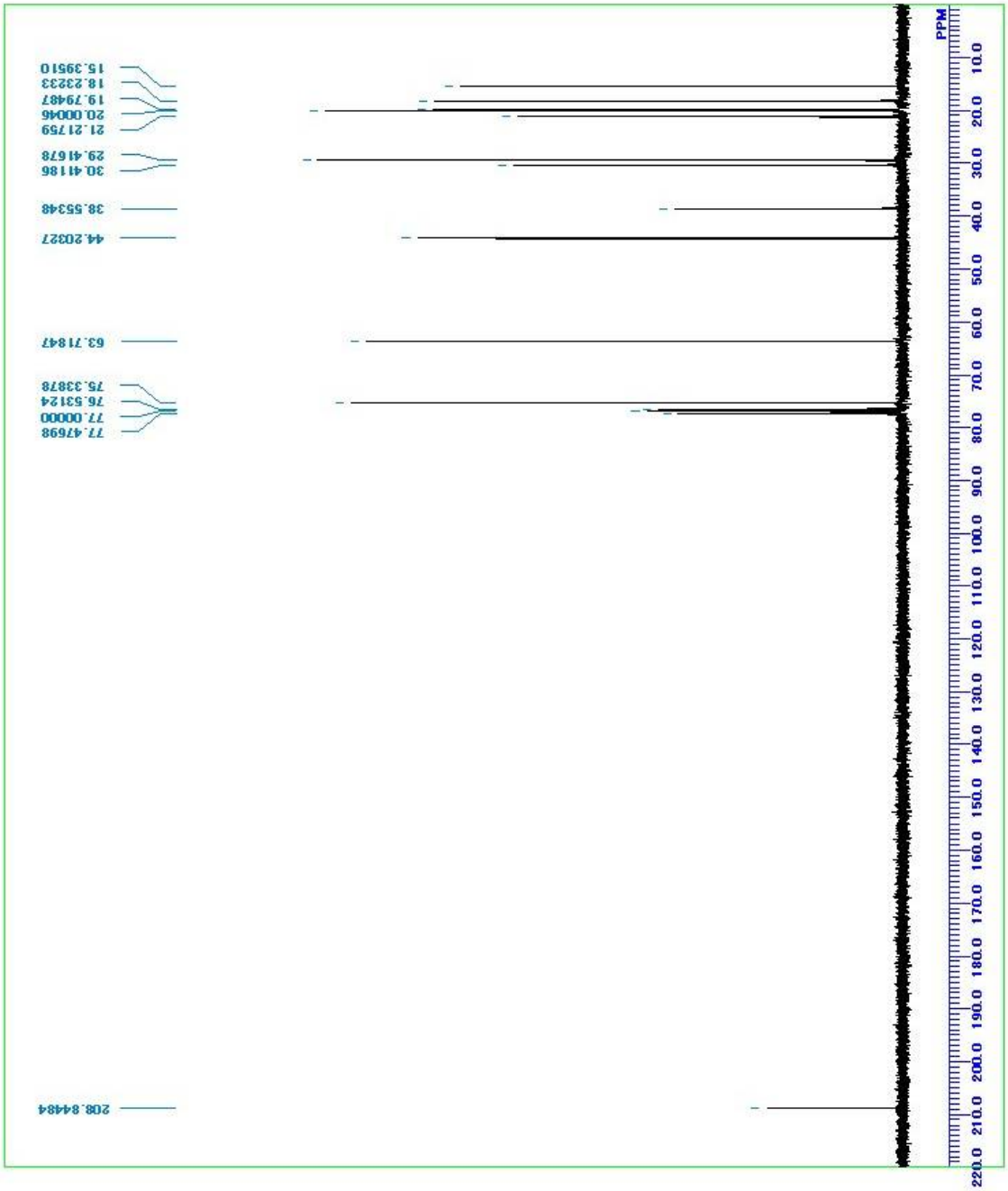

trans-4d-13C
15.40575
19.58904
22.01559
28.79388
33.91571
37.83027
43.32912
63.43539
72.92901
76.74331
77.00000
77.25268
126.04037
128.06584
129.30117
139.06149
207.59249
PPM


O
EtO
cis-4e

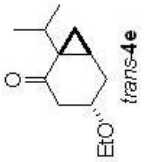

cis-4e-1H
PPM
4.02
3.11
3.03
1.10
1.02
1.97
0.98
1.03
1.00
1.99

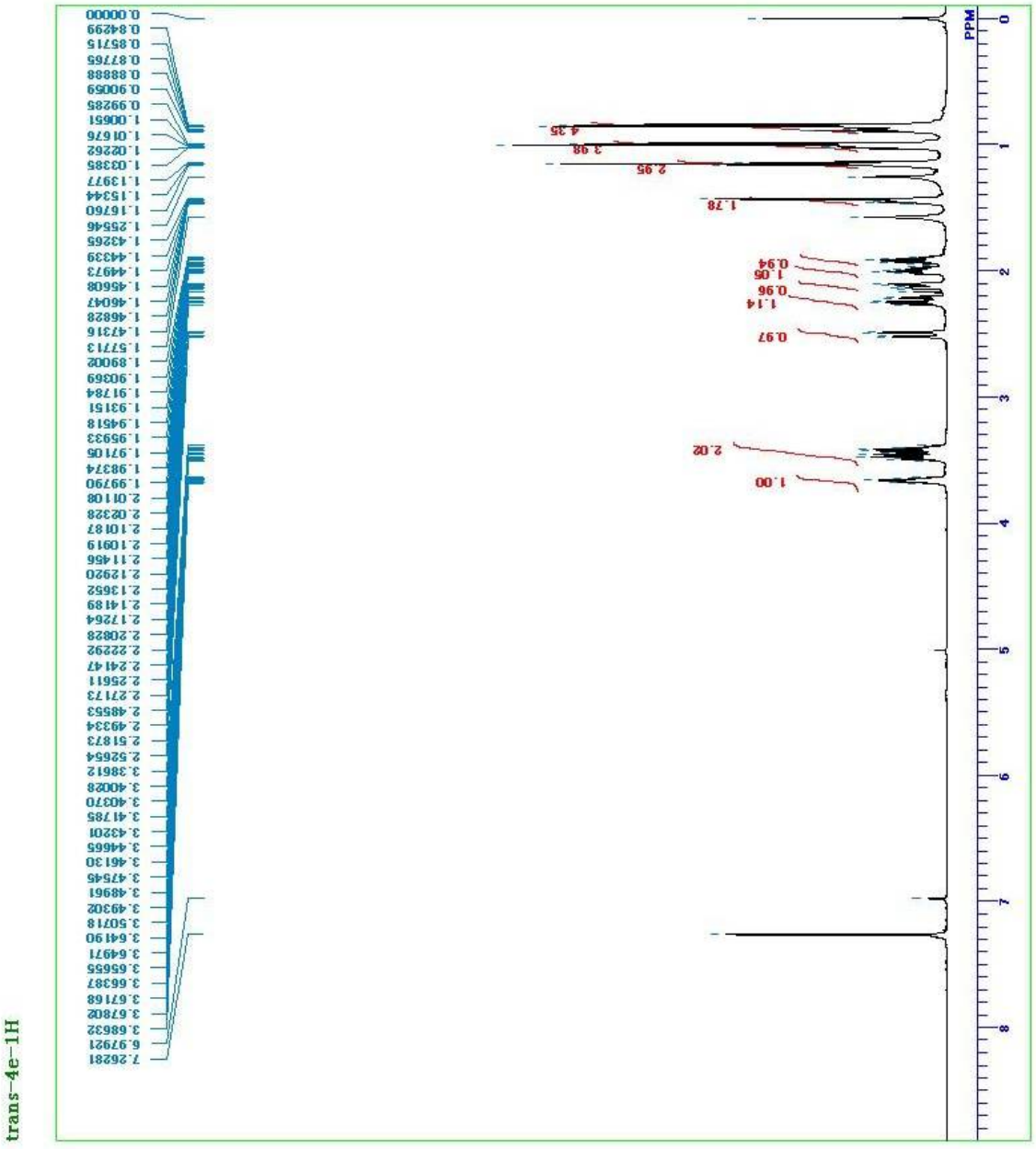


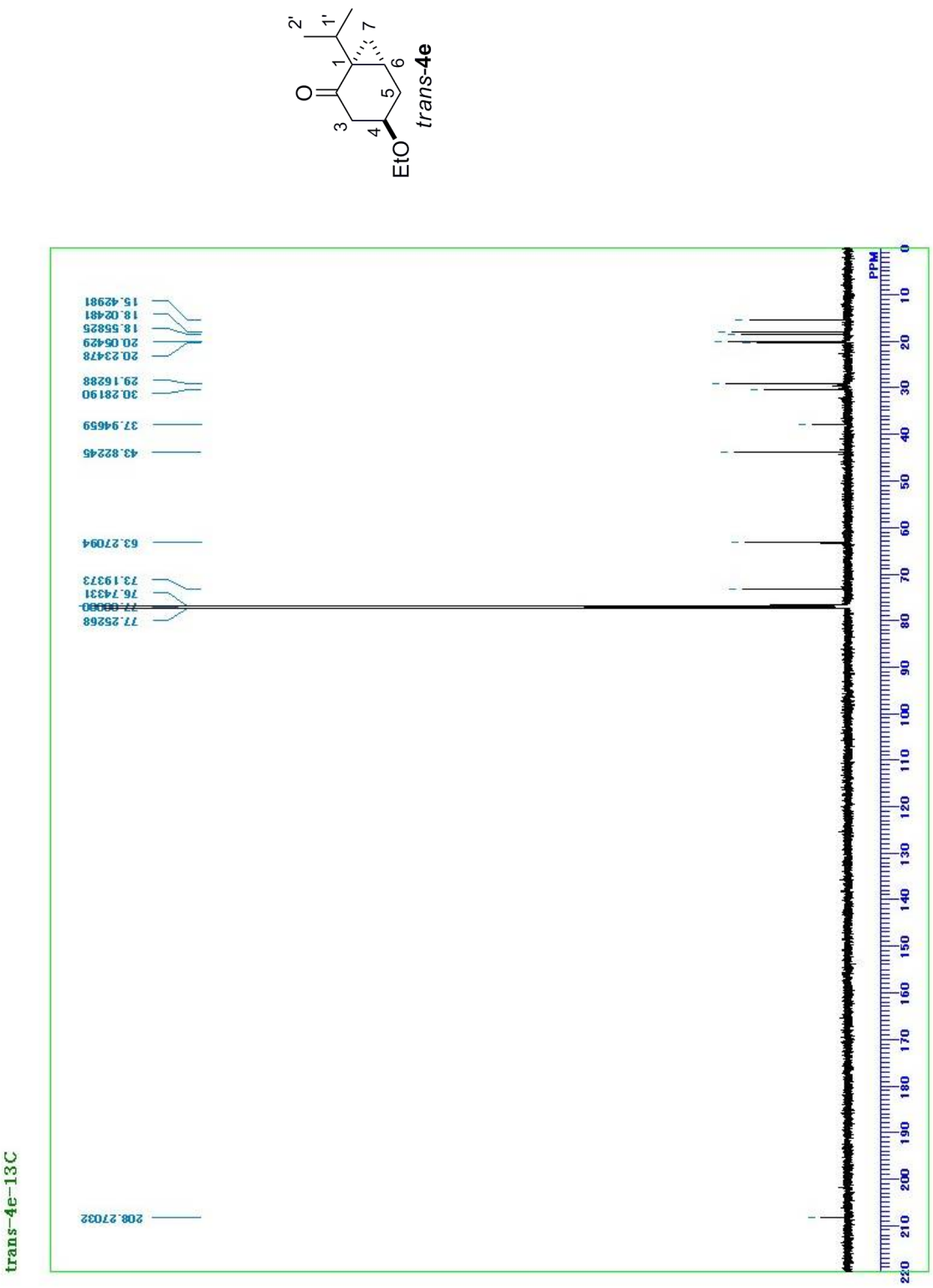
cis-**4e**

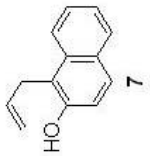


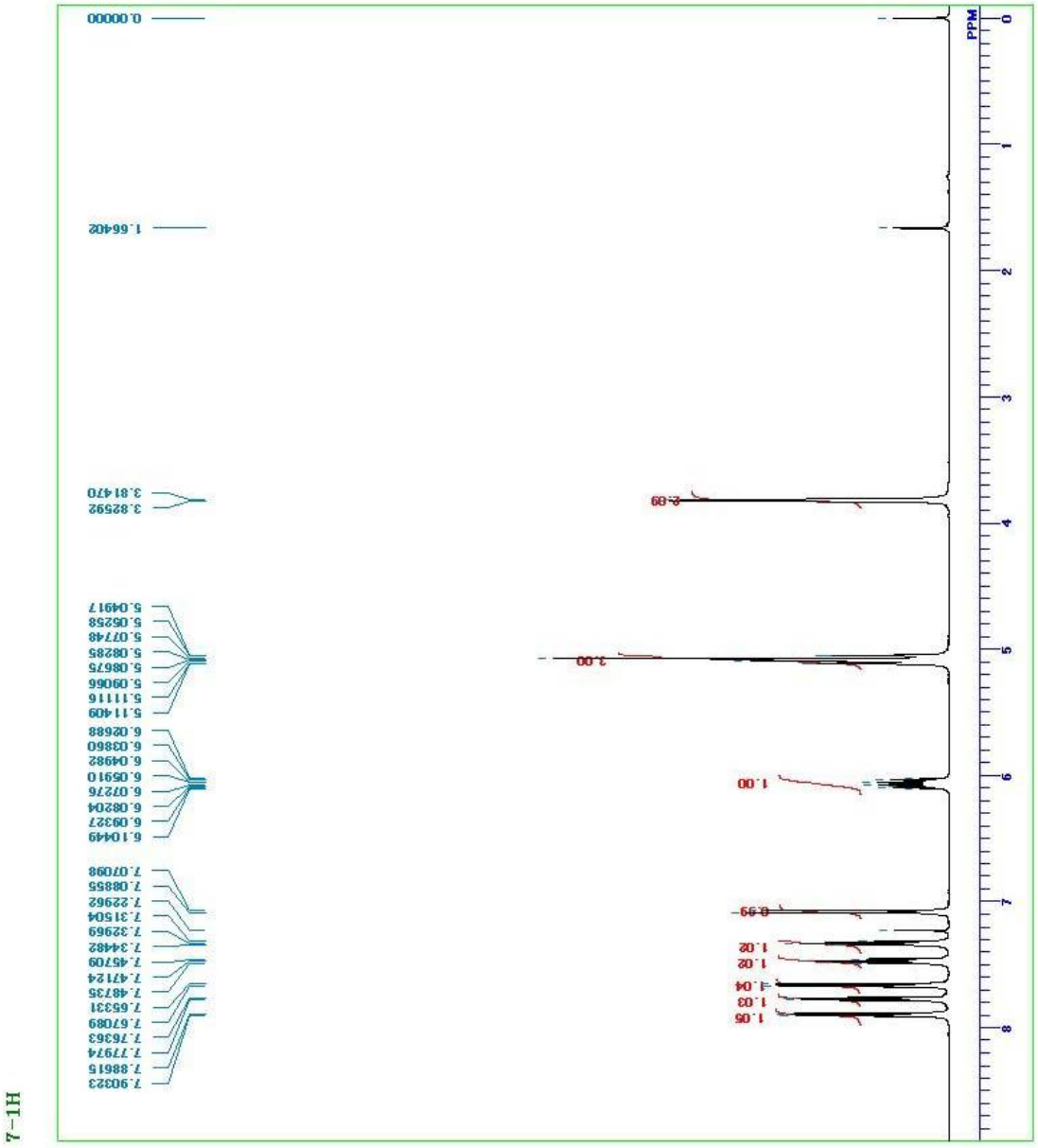
cis-4e-13C

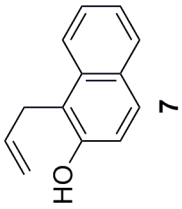

trans-4e
EtO

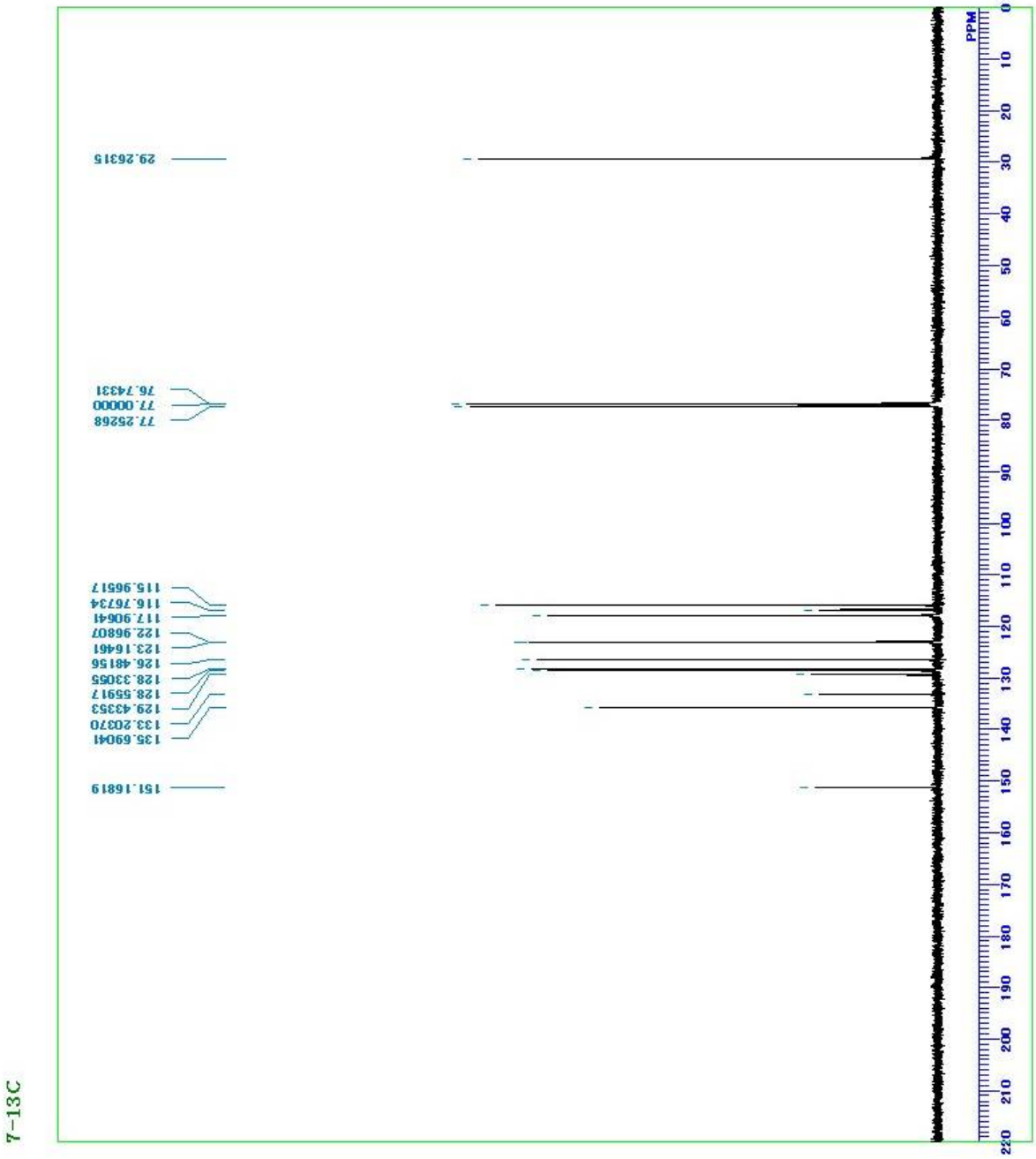

trans-4e-1H
PPM
4.35
3.98
2.95
1.78
0.94
1.05
0.96
1.14
0.97
2.02
1.00

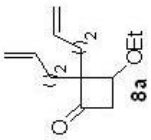

trans-4e
EtO
trans-4e-13C
PPM
15.42981
18.02481
18.55825
20.05429
20.23478
29.16288
30.28190
37.94659
43.82245
63.27094
73.19373
76.74331
77.00000
77.25268
208.27032

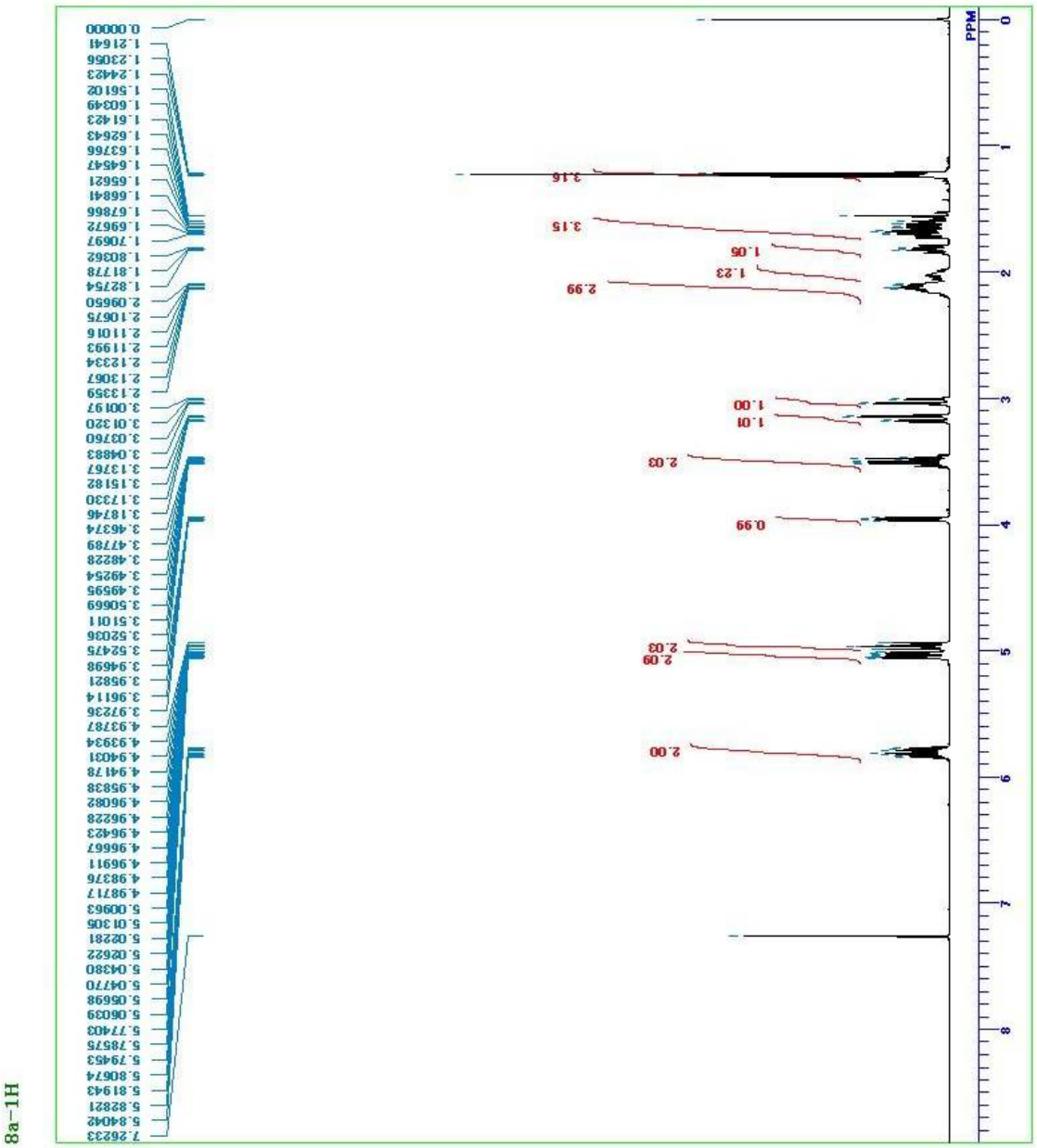

HO
7

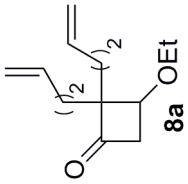

7-1H
PPM
0.00000
1.66402
3.81470
3.82592
5.04917
5.06258
5.07748
5.08285
5.08675
5.09066
5.11116
5.11409
6.02688
6.03860
6.04982
6.05910
6.07276
6.08204
6.09327
6.10449
7.07098
7.08855
7.22962
7.31504
7.32969
7.34482
7.45709
7.47124
7.48735
7.65331
7.67089
7.76363
7.77974
7.88615
7.90323
2.89
3.00
1.00
0.99
1.02
1.02
1.04
1.03
1.06


HO
7

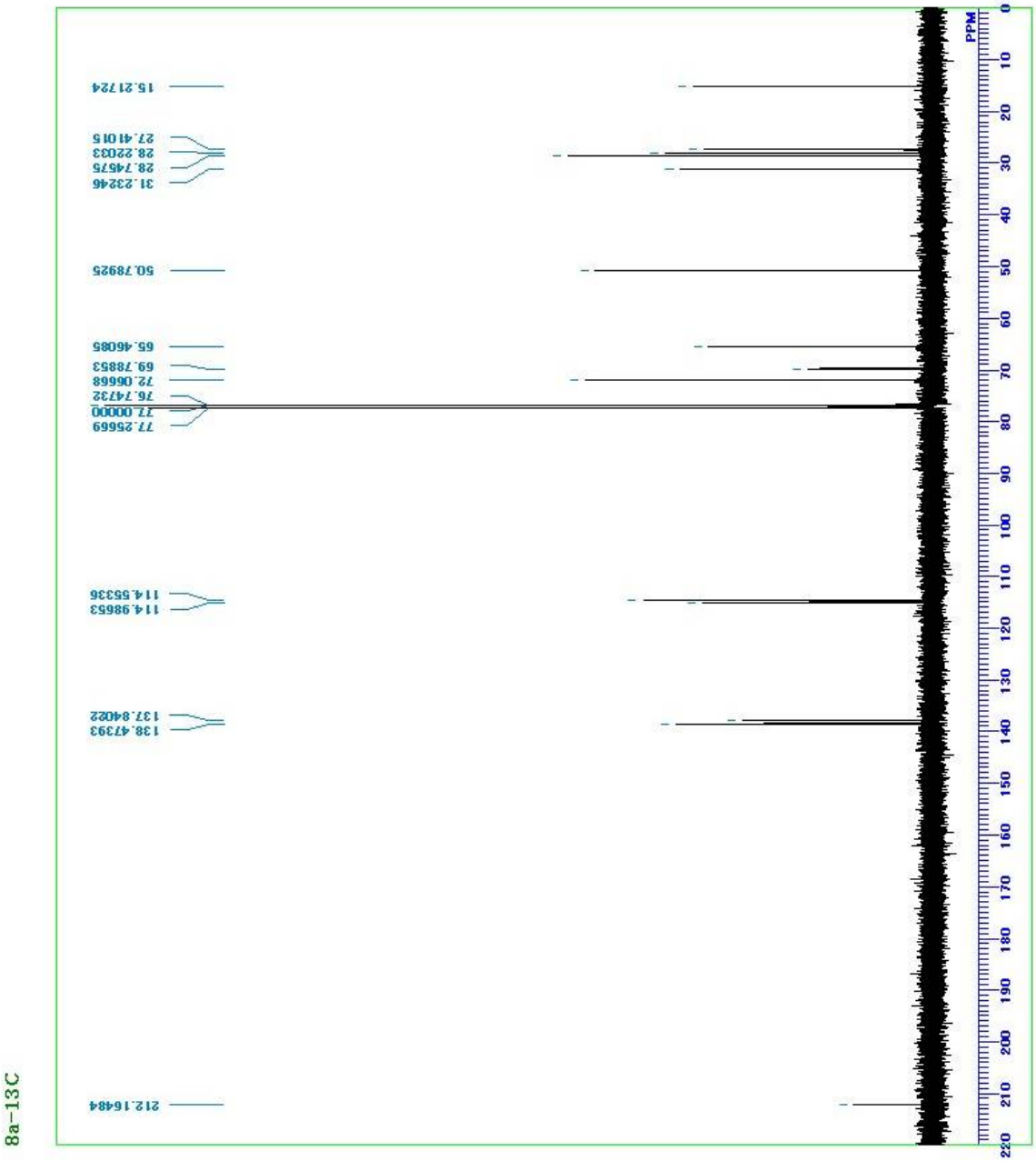

7-13C
PPM
29.26315
77.25268
77.00000
76.74331
151.16819
135.69041
133.20370
129.43353
128.55917
128.33055
126.48156
123.16461
122.96807
117.90641
116.76734
115.96517

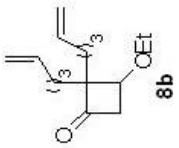

OEt
8a

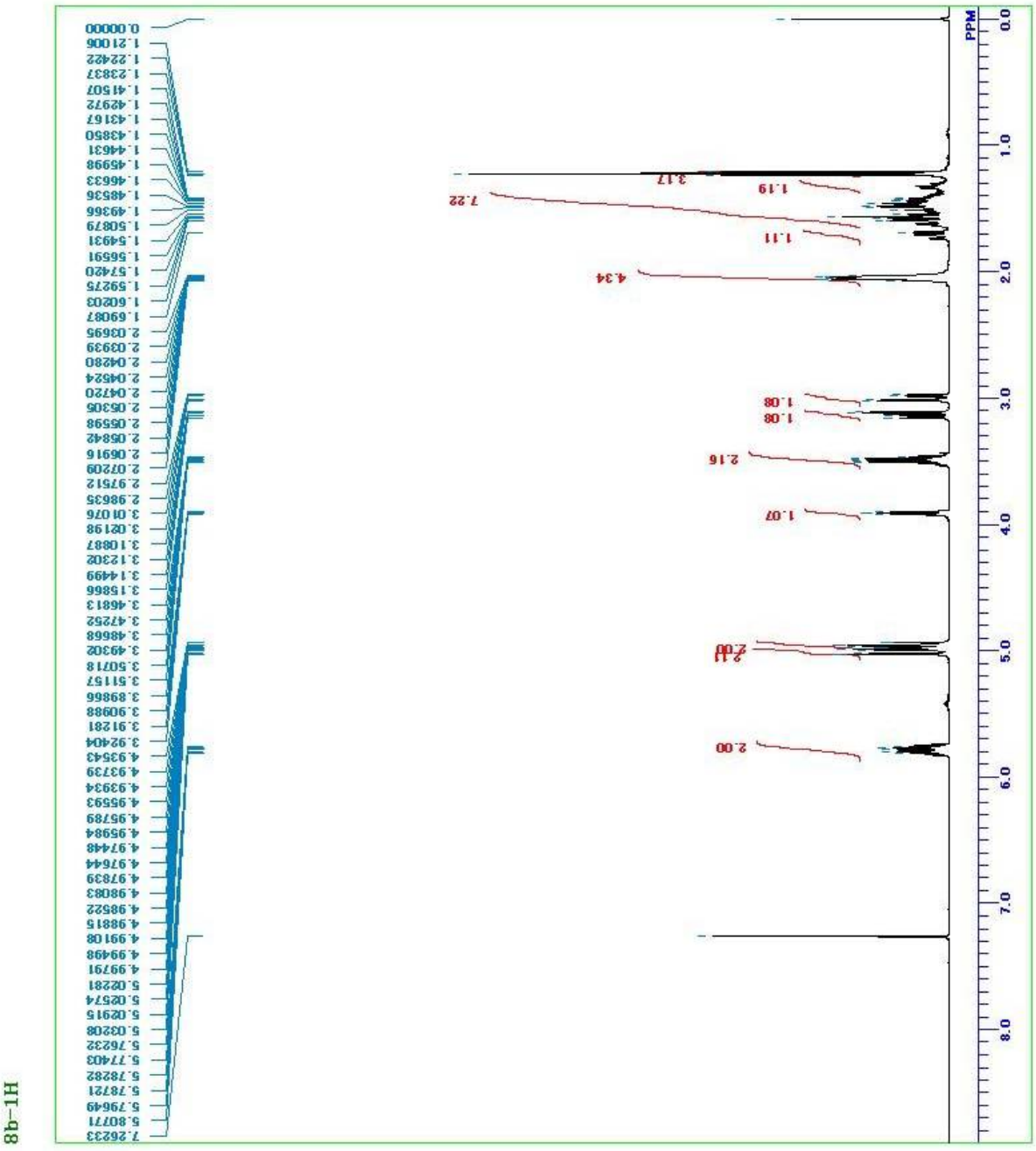

8a-1H
PPM
3.16
3.15
1.06
1.23
2.99
1.00
1.01
2.03
0.99
2.09
2.03
2.00

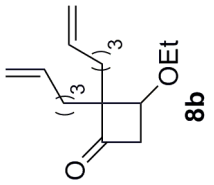

OEt
O

8a

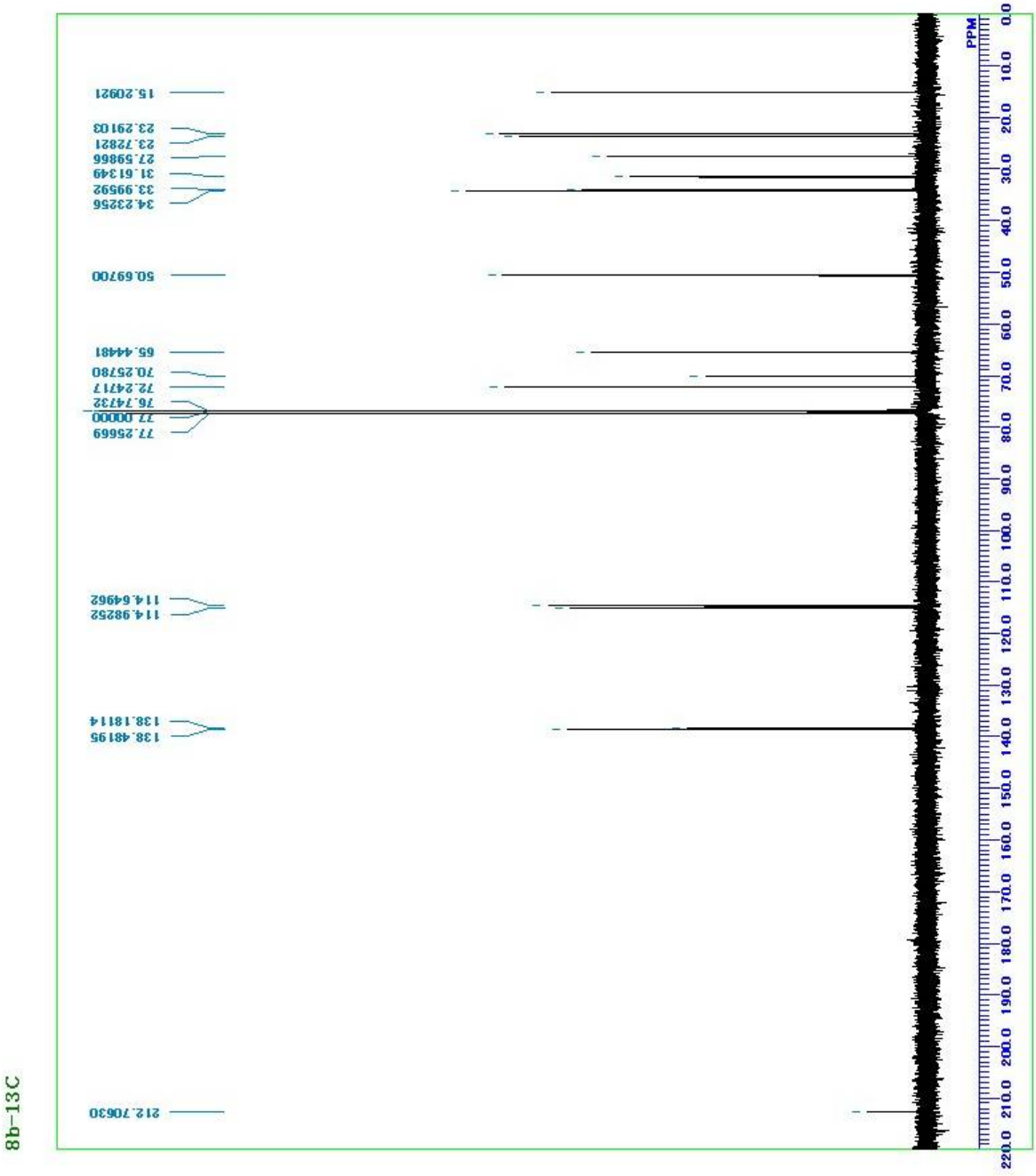

8a-13C
15.21724
27.41015
28.22033
28.74575
31.23246
50.78925
65.46085
69.78853
72.06668
76.74732
77.00000
77.25669
114.55336
114.98653
137.84022
138.47393
212.16484
PPM

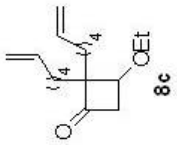

OEt
8b

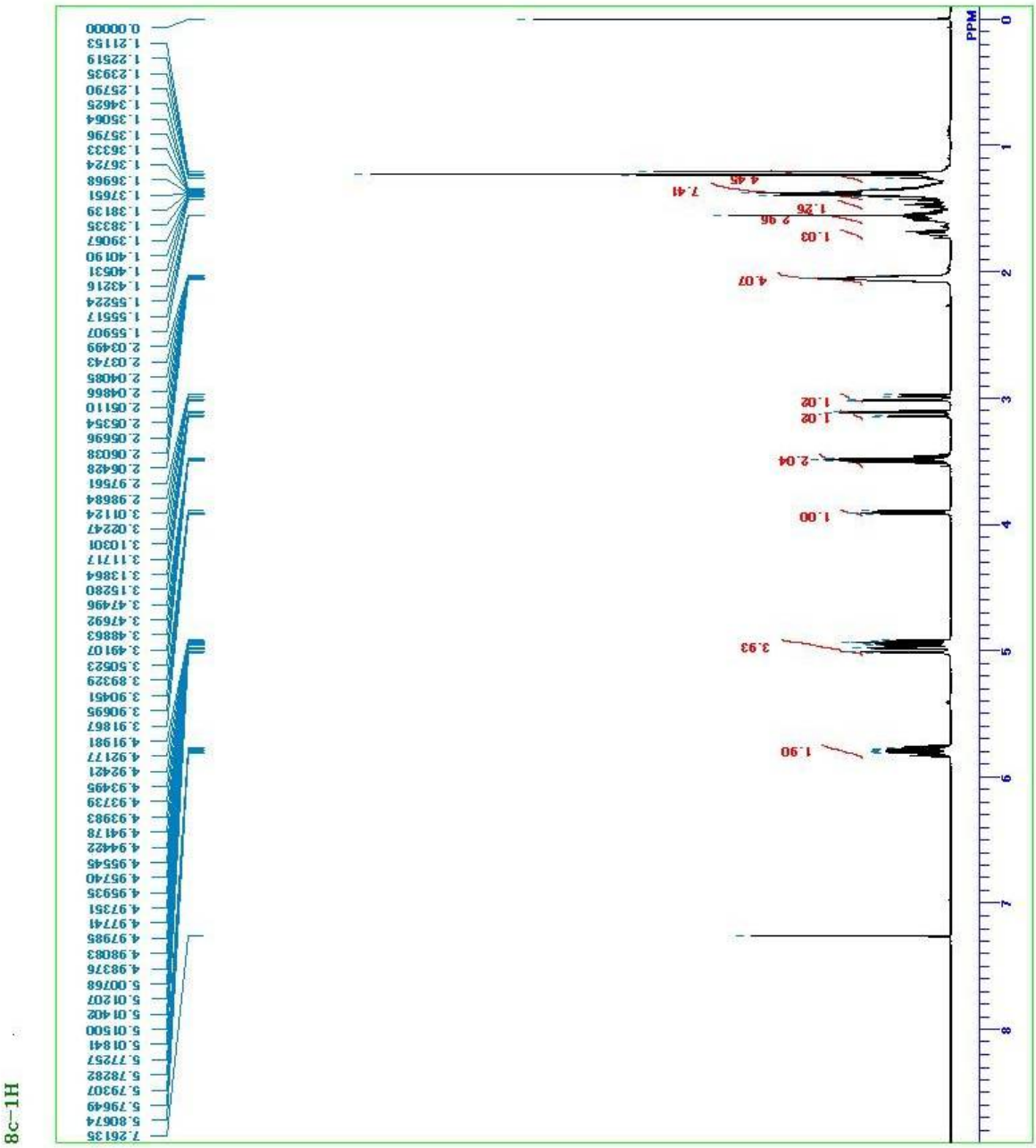

8b-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
3.17
1.19
7.22
1.11
4.34
1.08
1.08
2.16
1.07
2.00
2.00


OEt
O
3
3

8b


8b-13C
PPM
15.20921
23.29103
23.72821
27.59866
31.61349
33.99592
34.23256
50.69700
65.44481
70.25780
72.24717
76.74732
77.00000
77.25669
114.64962
114.98252
138.48195
138.18114
212.70630


OEt
O
8c


8c-1H
PPM
0
1
2
3
4
5
6
7
8
7.41
4.45
1.26
2.96
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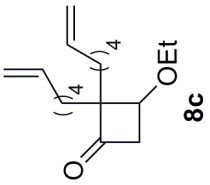
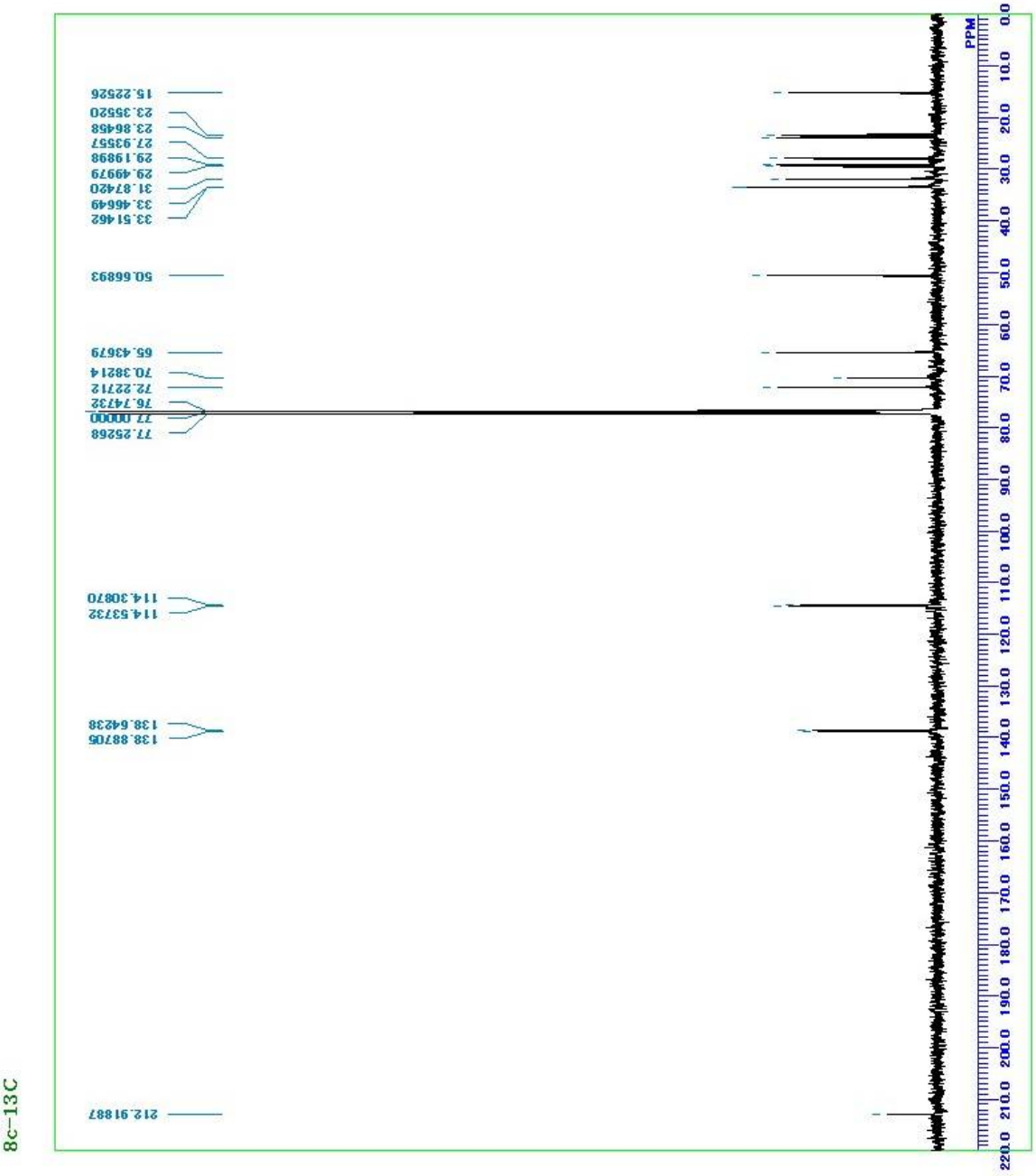
1.02
1.02
2.04
1.00
3.93
1.90


OEt
4
4
O

8c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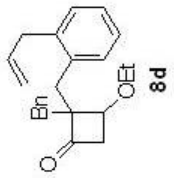
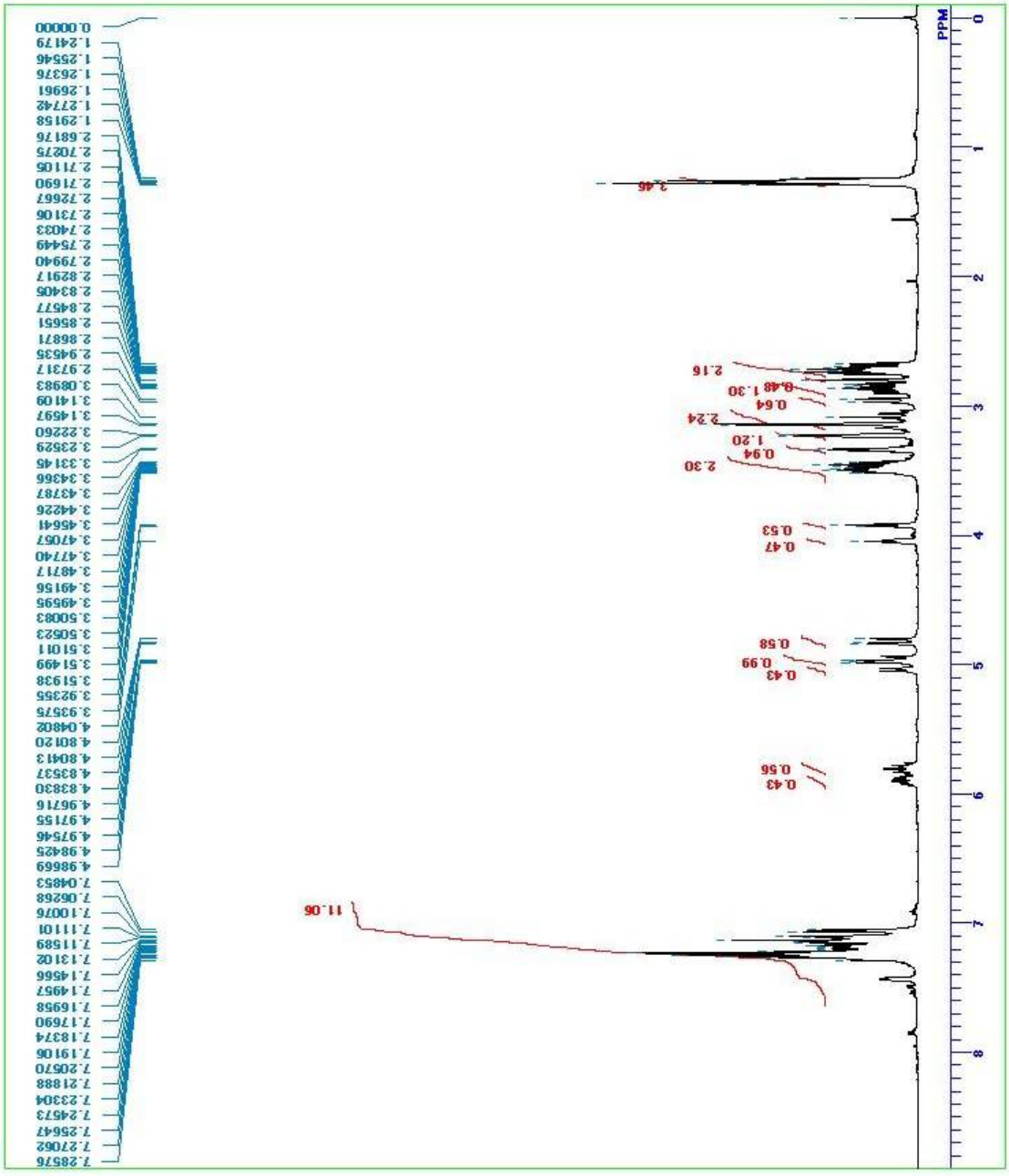
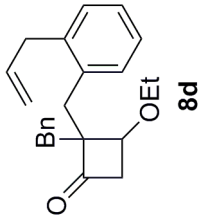
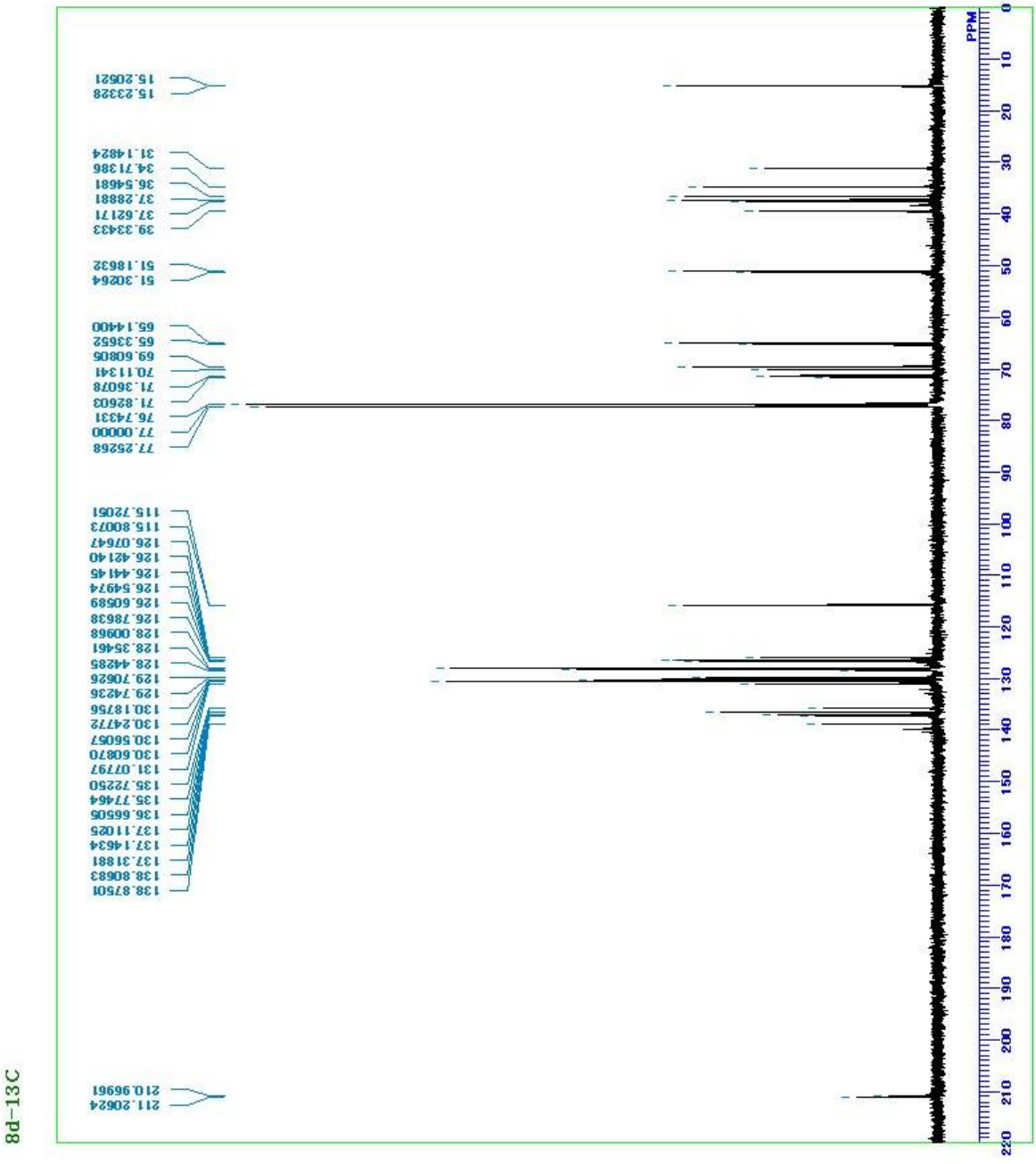
212.91887
138.88706
138.64238
114.53732
114.30870
77.25268
77.00000
76.74732
72.22712
70.38214
65.43679
50.66893
33.51462
33.46649
31.87420
29.49979
29.19898
27.93557
23.86458
23.35520
15.22526

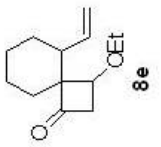

Bn
OEt
O
8d

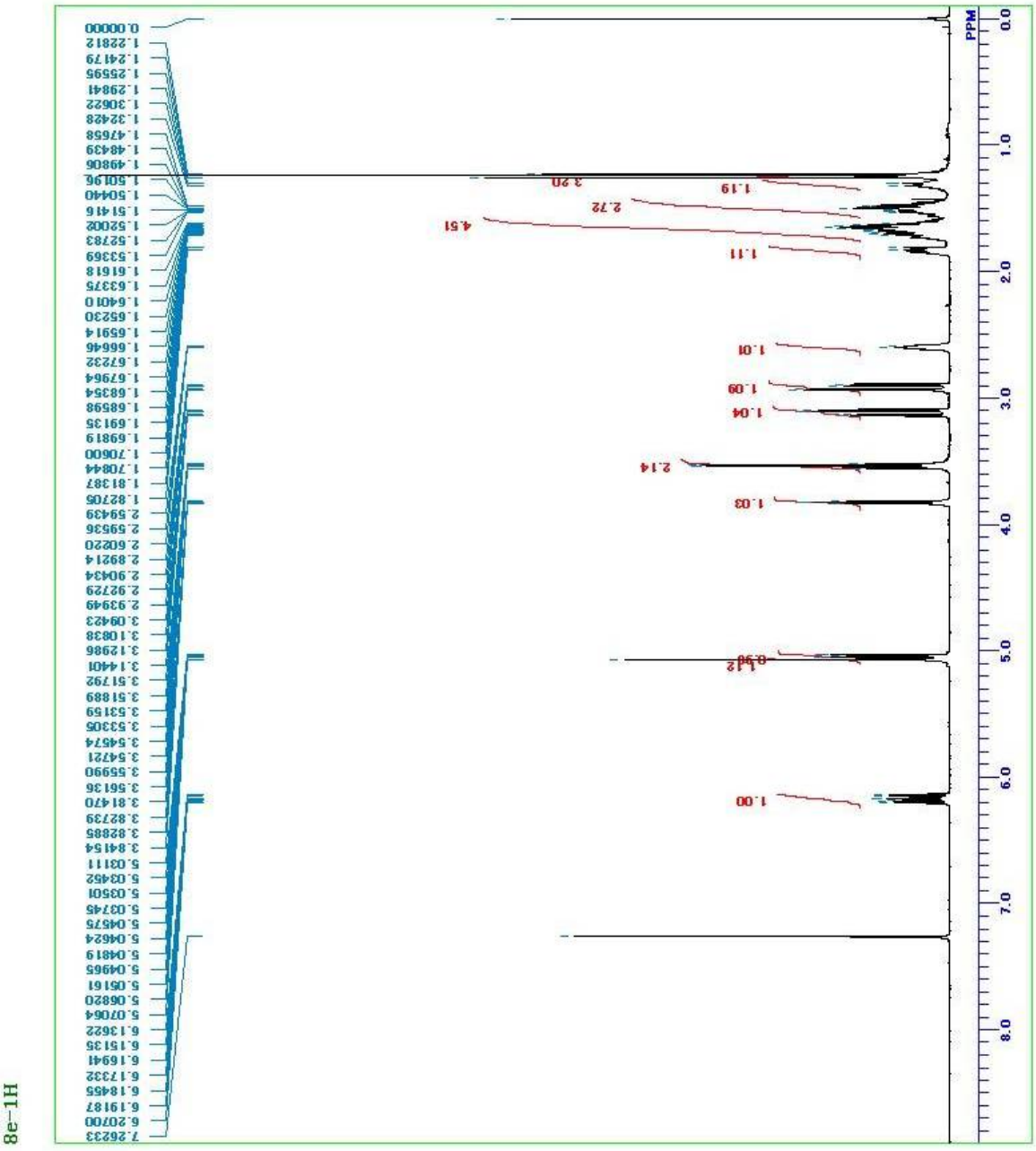

8d-1H
PPM
11.06
3.46
2.16
2.30
2.24
1.30
1.20
0.94
0.64
0.58
0.56
0.53
0.48
0.47
0.43
0.99

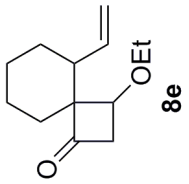


8d

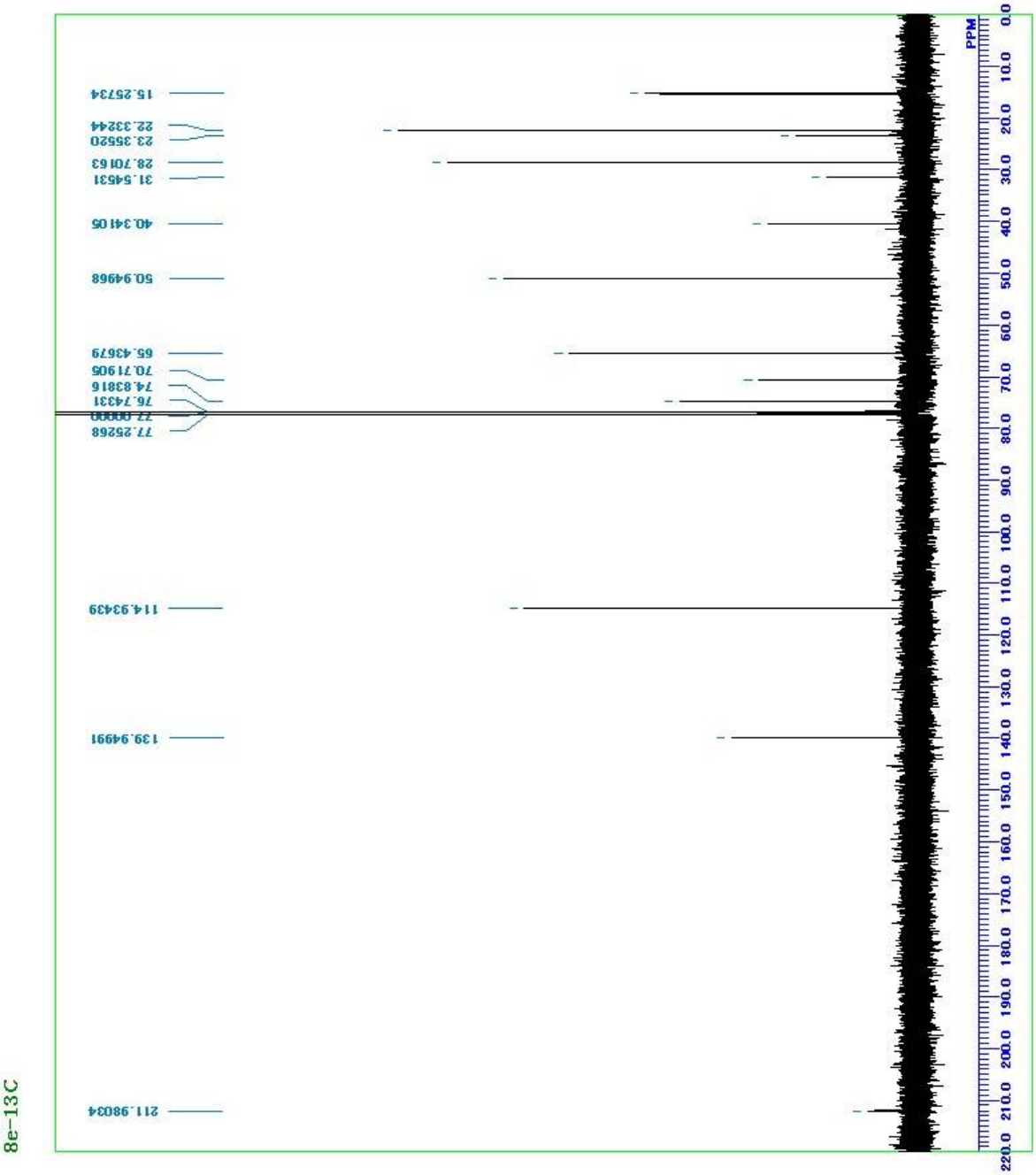



OEt
8e


8e-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
3.20
1.19
2.72
4.51
1.11
1.01
1.09
1.04
2.14
1.03
0.94
1.00


OEt
O

8e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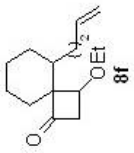
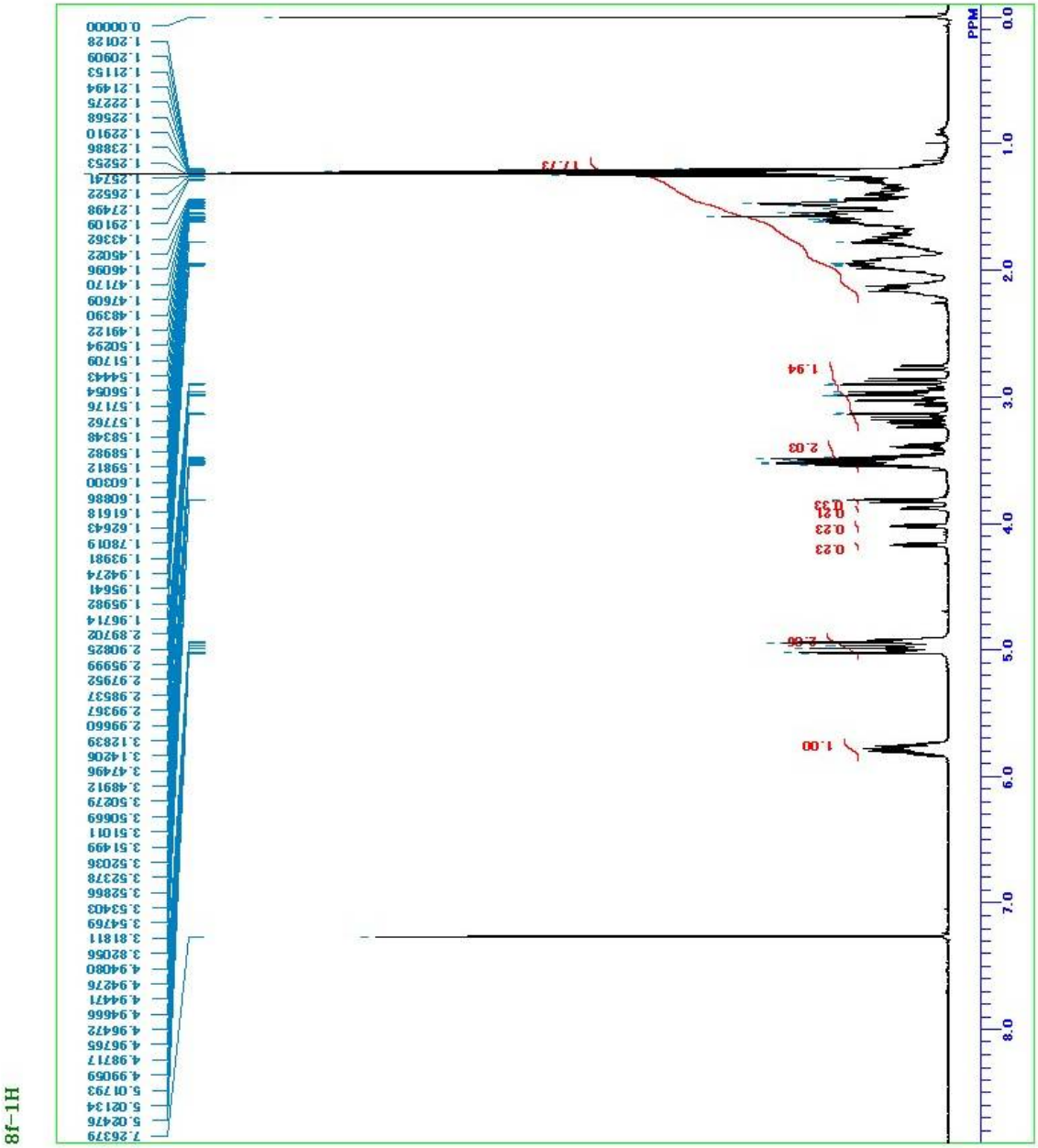
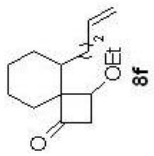
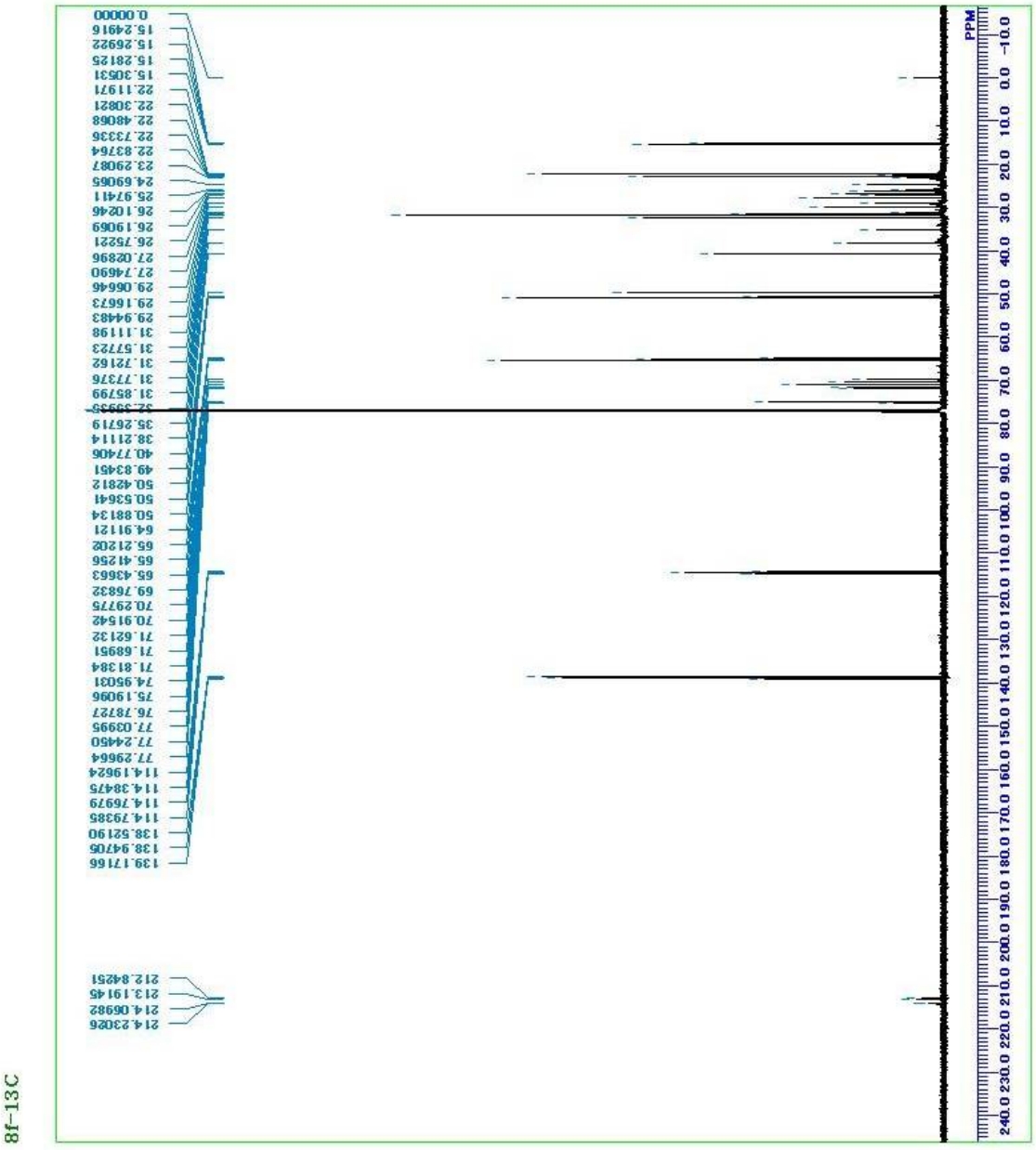
22.33244
23.35520
28.70163
31.54531
40.34105
50.94968
65.43679
70.71905
74.83816
76.74331
77.00000
77.25268
114.93439
139.94991
211.98034
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
220.0

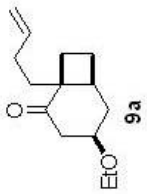
8e-13C

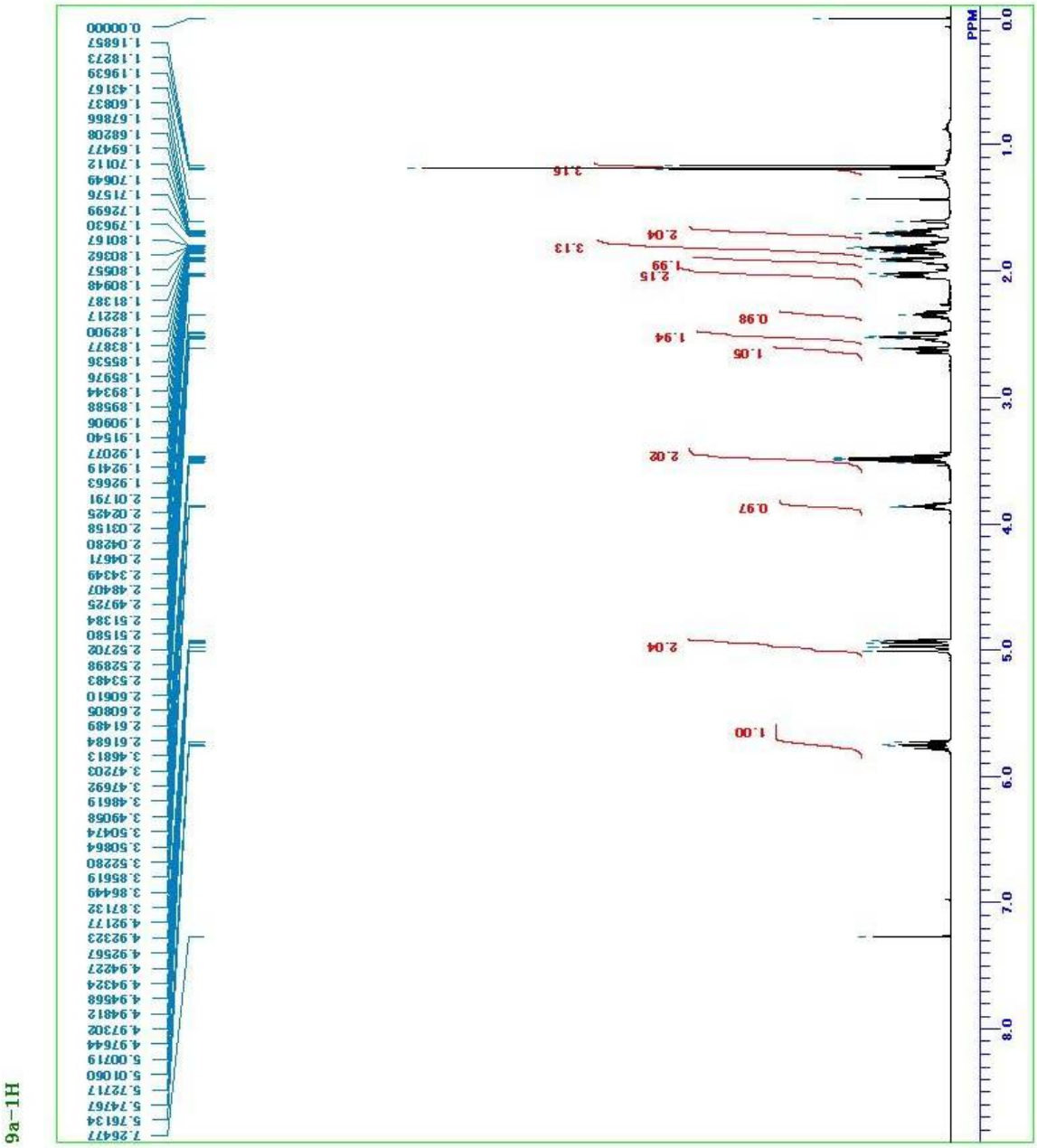

OEt
8f
O

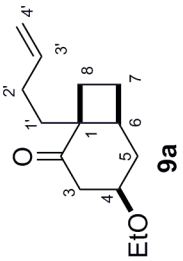

8f-1H
PPM
17.73
1.94
2.03
0.33
0.21
0.23
0.23
2.66
1.00

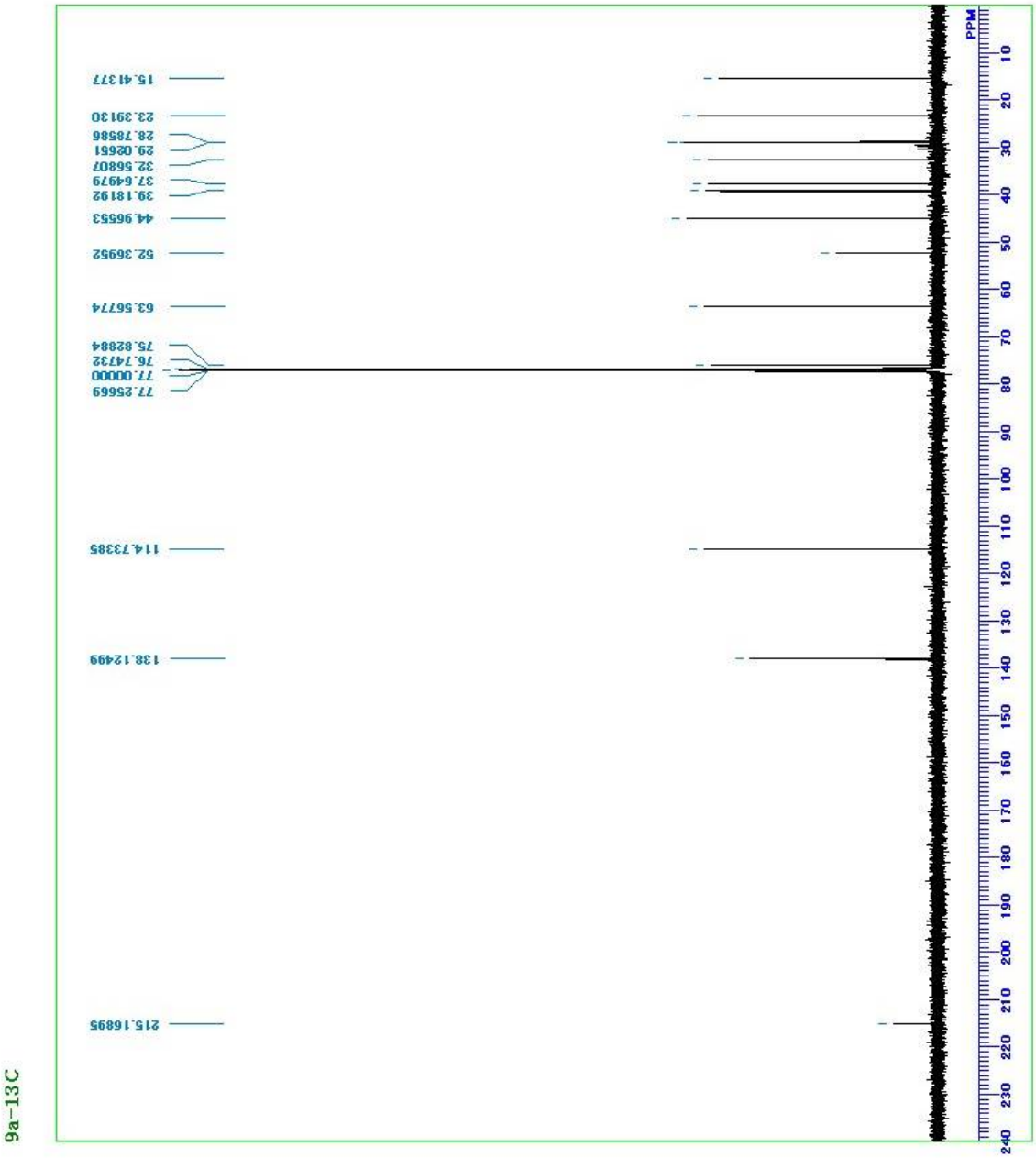

OEt
8f


8f-13C
PPM


O
EtO
9a


9a-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
3.16
2.04
3.13
2.15
1.99
0.98
1.94
1.05
2.02
0.97
2.04
1.00


4'
3'
2'
1'
8
7
6
5
4
3
1
O
EtO
9a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28.78586
29.02651
32.56807
37.64979
39.18192
44.96553
52.36952
63.56774
75.82884
76.74732
77.00000
77.25669
114.73385
138.12499
215.16895
PPM
10
20
30
40
50
60
70
80
90
100
110
120
130
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150
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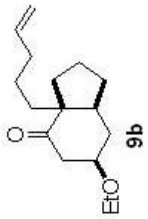
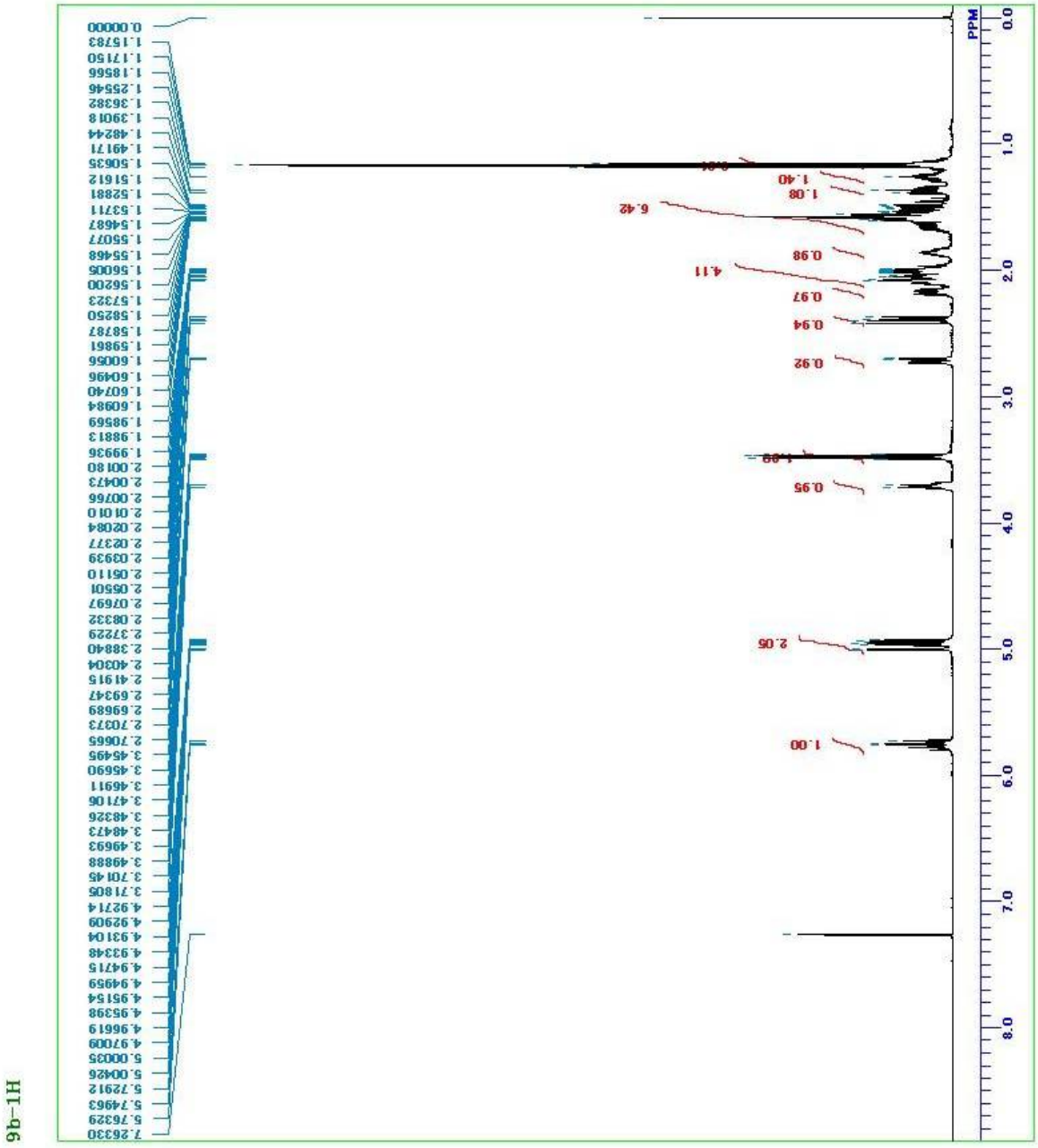
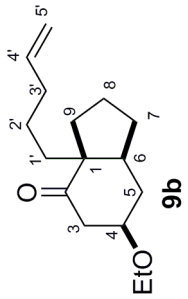
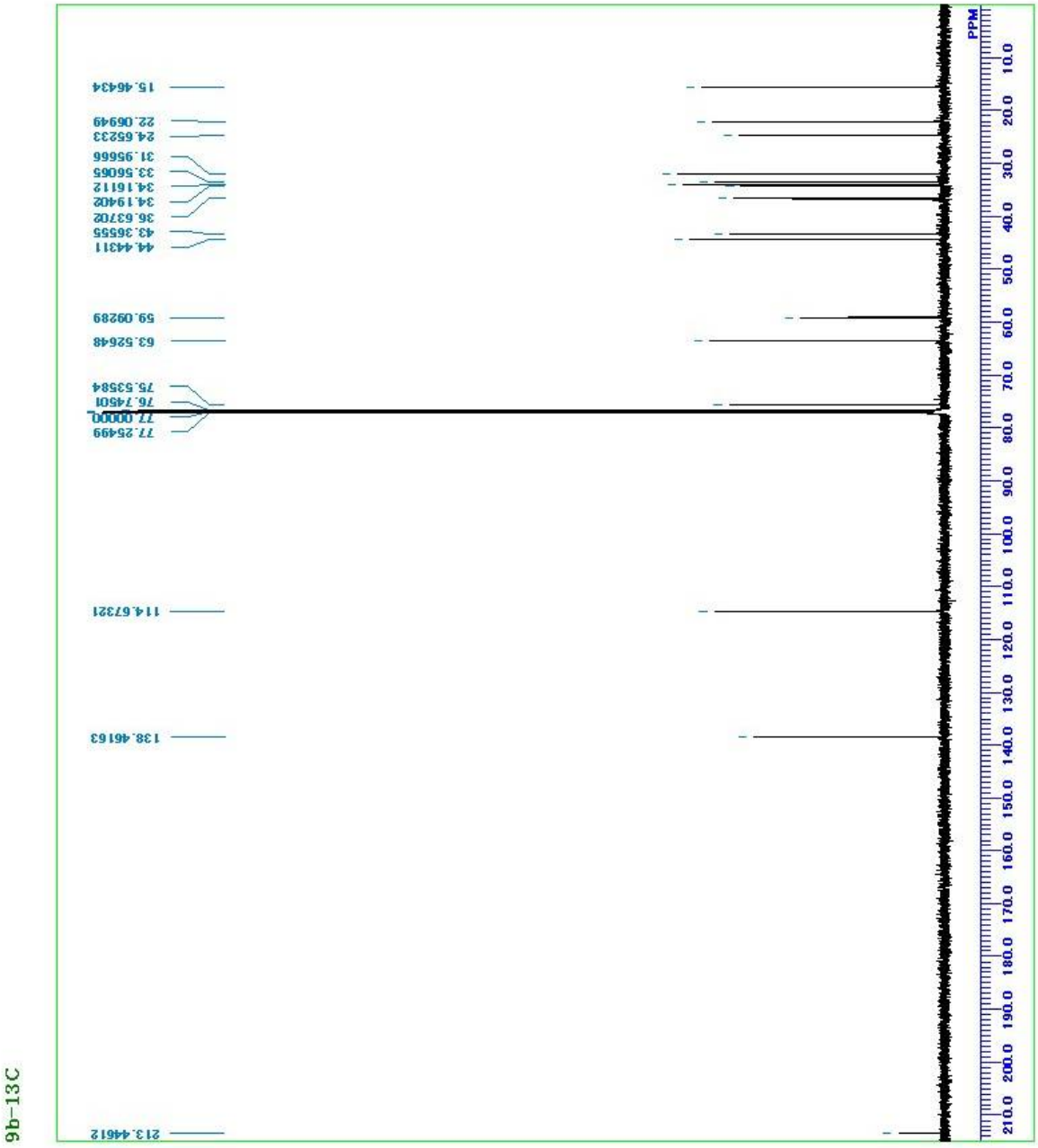
170
180
190
200
210
220
230
240

9a-13C


9b
EtO


9b-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
6.42
4.11
2.05
1.00
1.40
1.08
0.98
0.97
0.94
0.92
0.95


5'
4'
3'
2'
1'
8
9
7
6
1
5
O
3
4
EtO
9b


9b-13C
PPM
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114.67321
77.25499
77.00000
76.74501
75.53584
63.52648
59.09289
44.44311
43.36555
36.63702
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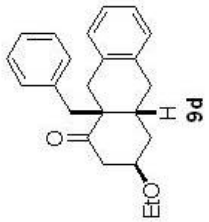
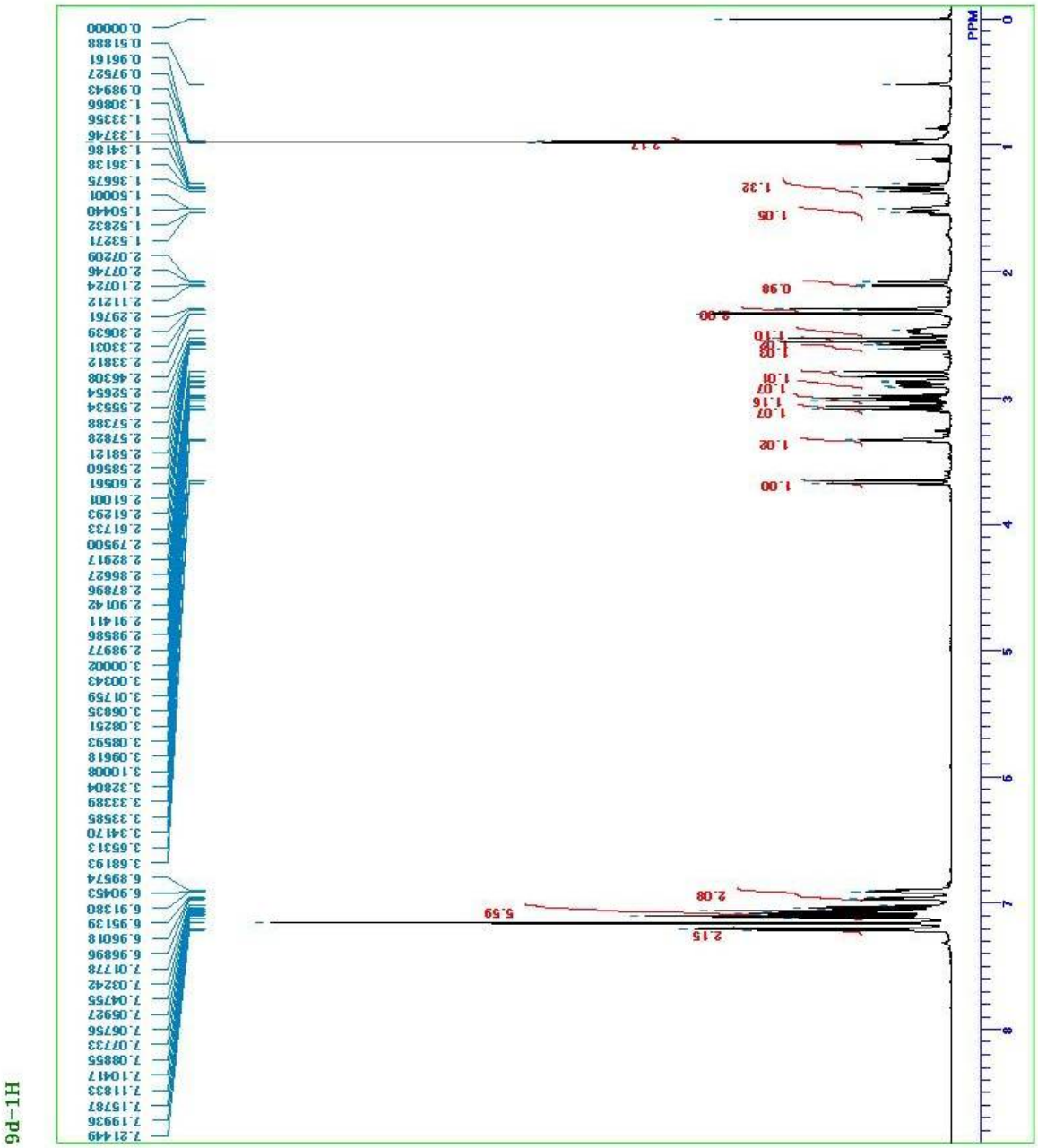
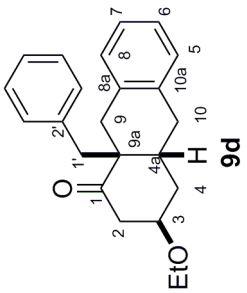
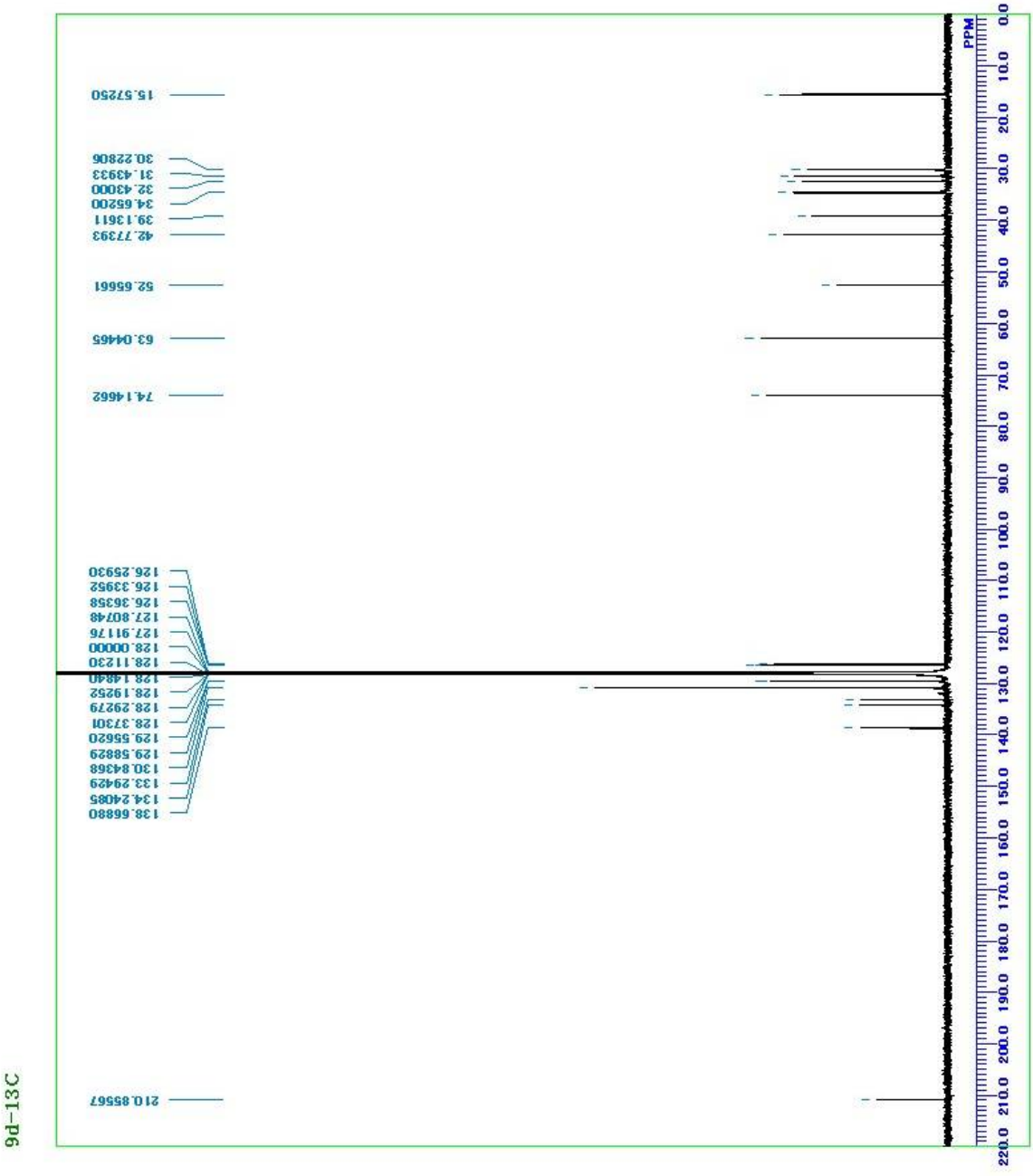
34.16112
33.56065
31.95666
24.65233
22.06949
15.46434


9d
H
O
EtO


9d-1H-p6
PPM
0
1
2
3
4
5
6
7
8
2.12
1.32
1.06
0.98
2.00
1.10
1.03
1.01
1.07
1.07
1.16
1.01
1.02
1.00
2.08
5.59
2.15


O
H
EtO
9d


9d-13C
PPM
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31.43933
32.43000
34.65200
39.13611
42.77393
52.65661
63.04465
74.14662
126.25930
126.33952
126.36358
127.80748
127.91176
128.00000
128.11230
128.14840
128.19252
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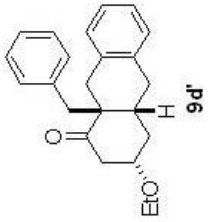
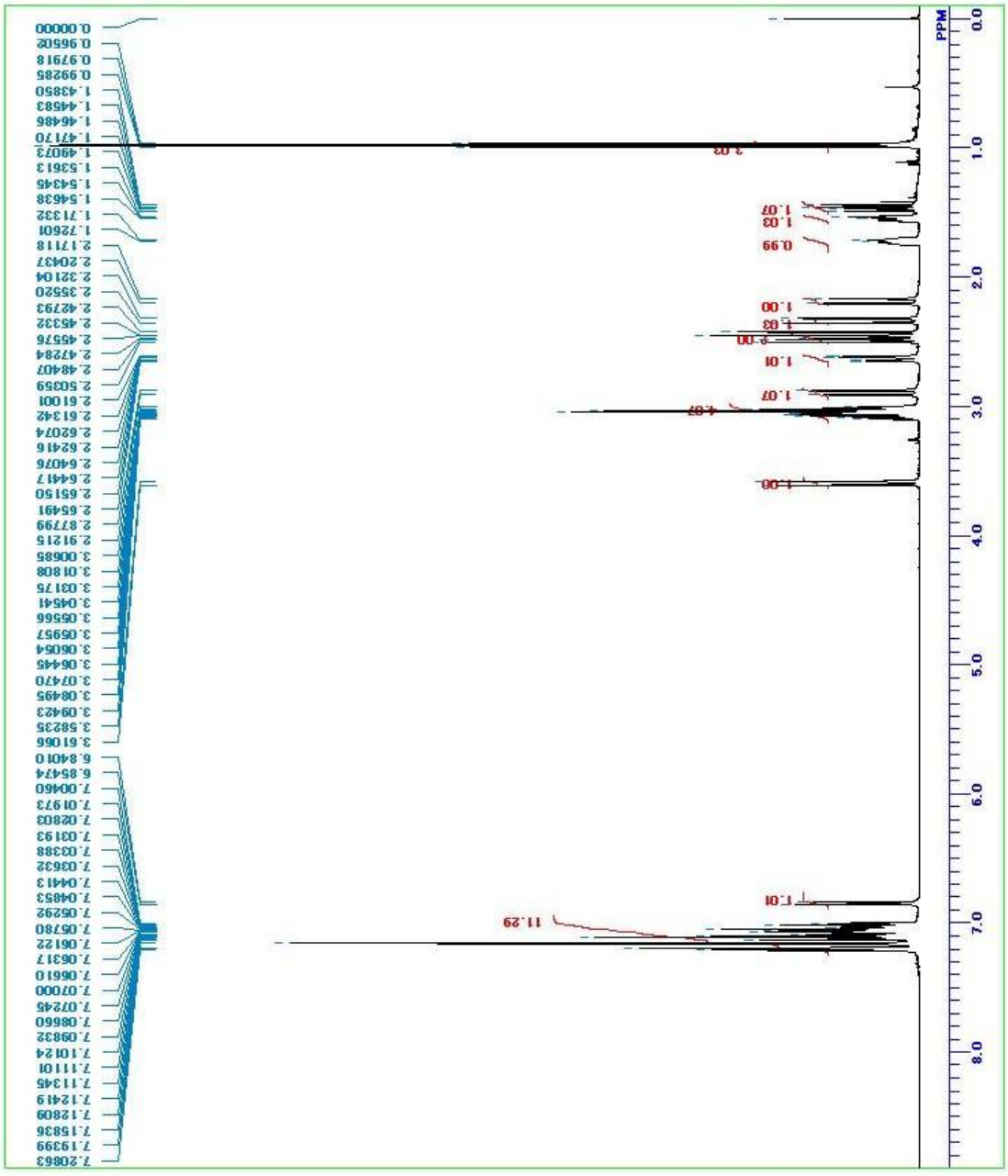
134.24085
138.66880
210.85567


9d'
H
O
EtO


PPM
0.0
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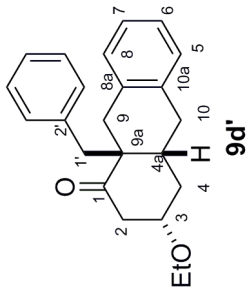
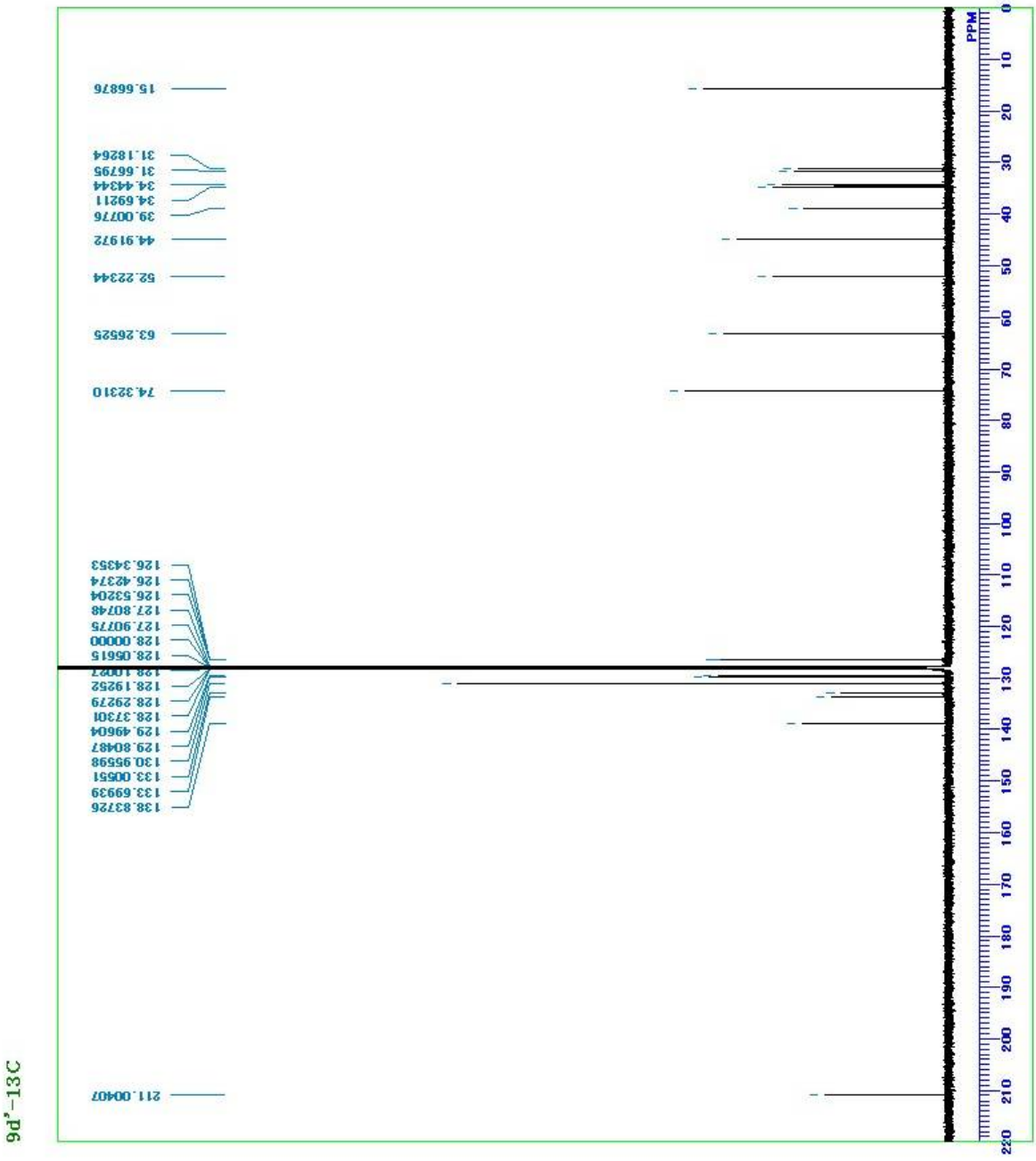
2.0
3.0
4.0
5.0
6.0
7.0
8.0
11.29
4.07
3.02
2.00
1.07
1.03
0.99
1.00
1.03
2.00
1.01
1.07
1.00
1.01

1H-'9d


9d'
EtO
O
H


9d'-13C
PPM
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31.66795
34.44344
34.69211
39.00776
44.91972
52.22344
63.26525
74.32310
126.34353
126.42374
126.53204
127.80748
127.90775
128.00000
128.05615
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128.37301
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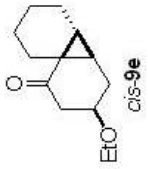
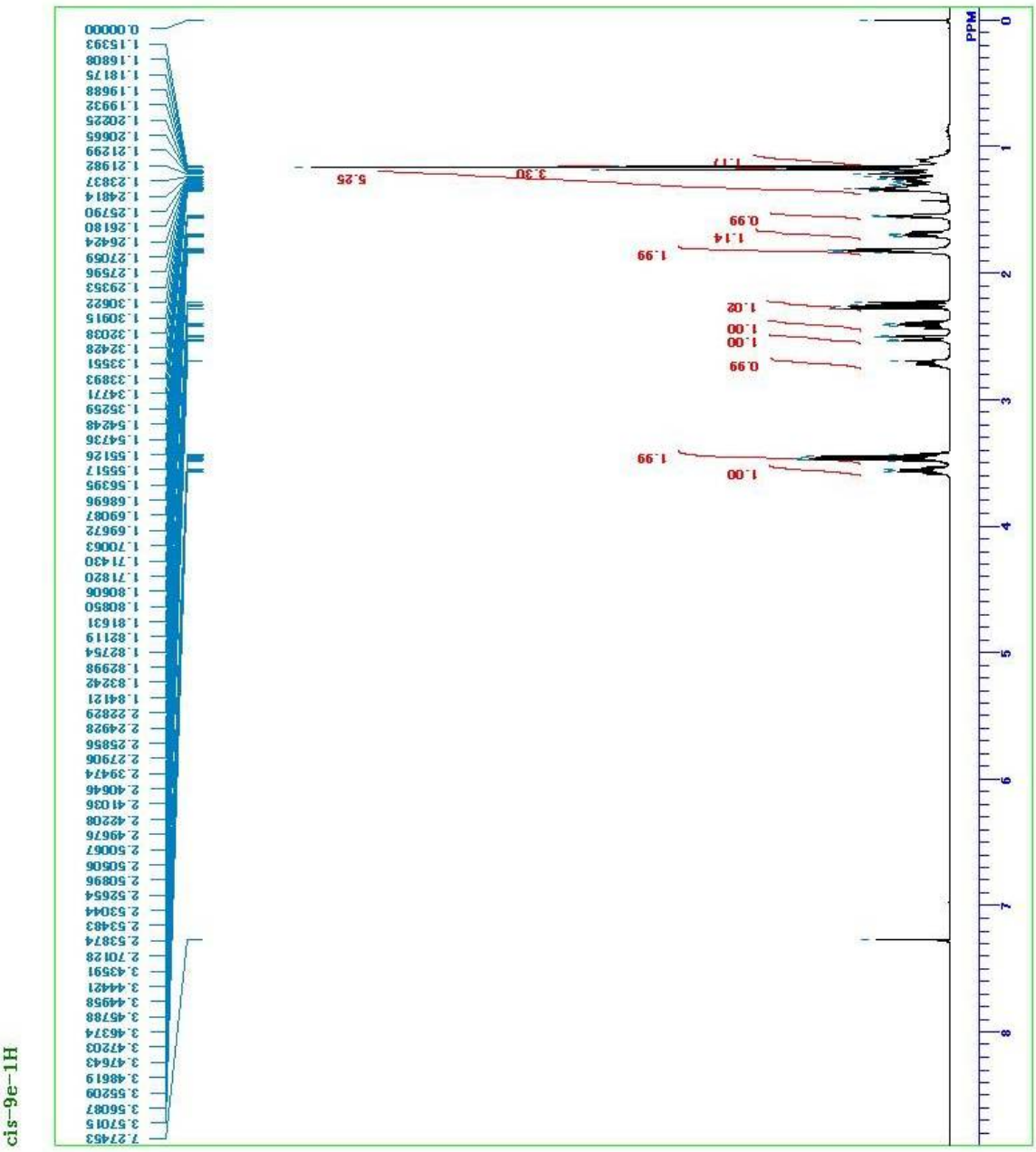
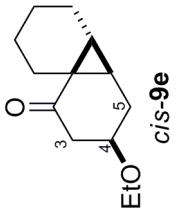
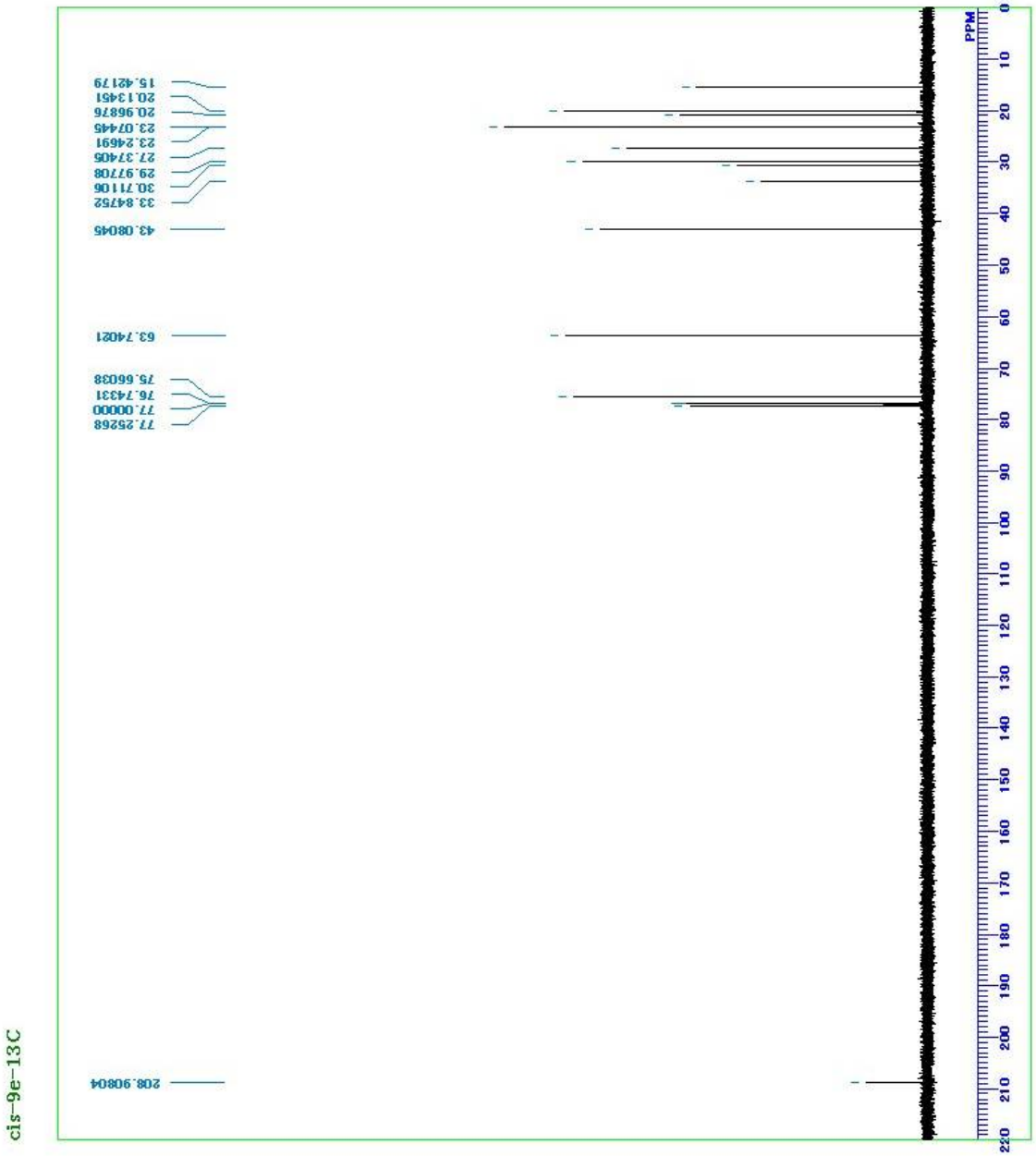
129.80487
130.95598
133.00651
133.69939
138.83726
211.00407


O
EtO
cis-9e


cis-9e-1H
PPM
5.25
3.30
1.17
0.99
1.14
1.99
1.02
1.00
1.00
0.99
1.99
1.00


O
3
4
5
EtO

cis-**9e**


cis-9e-13C
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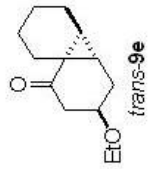
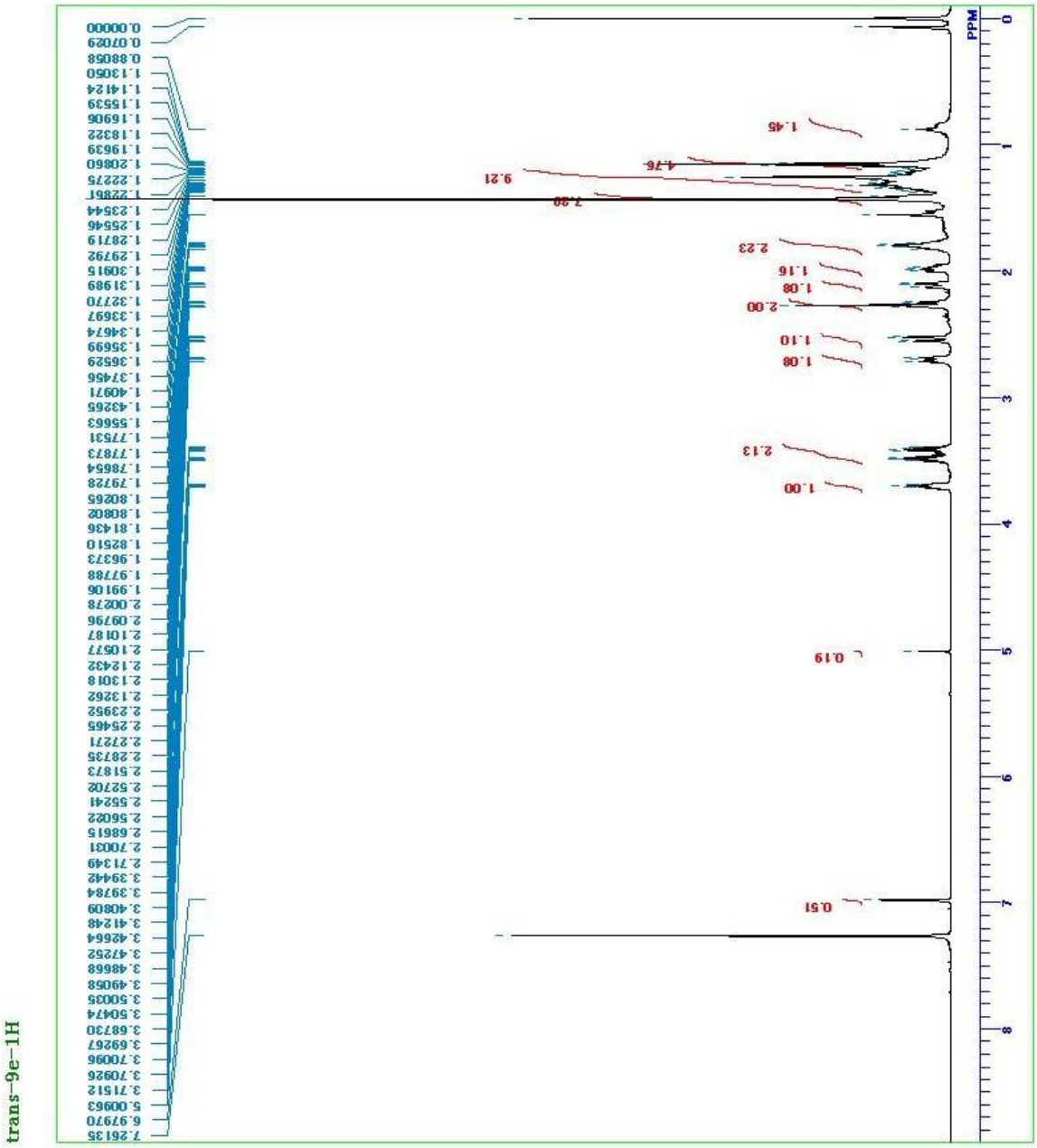
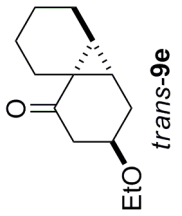
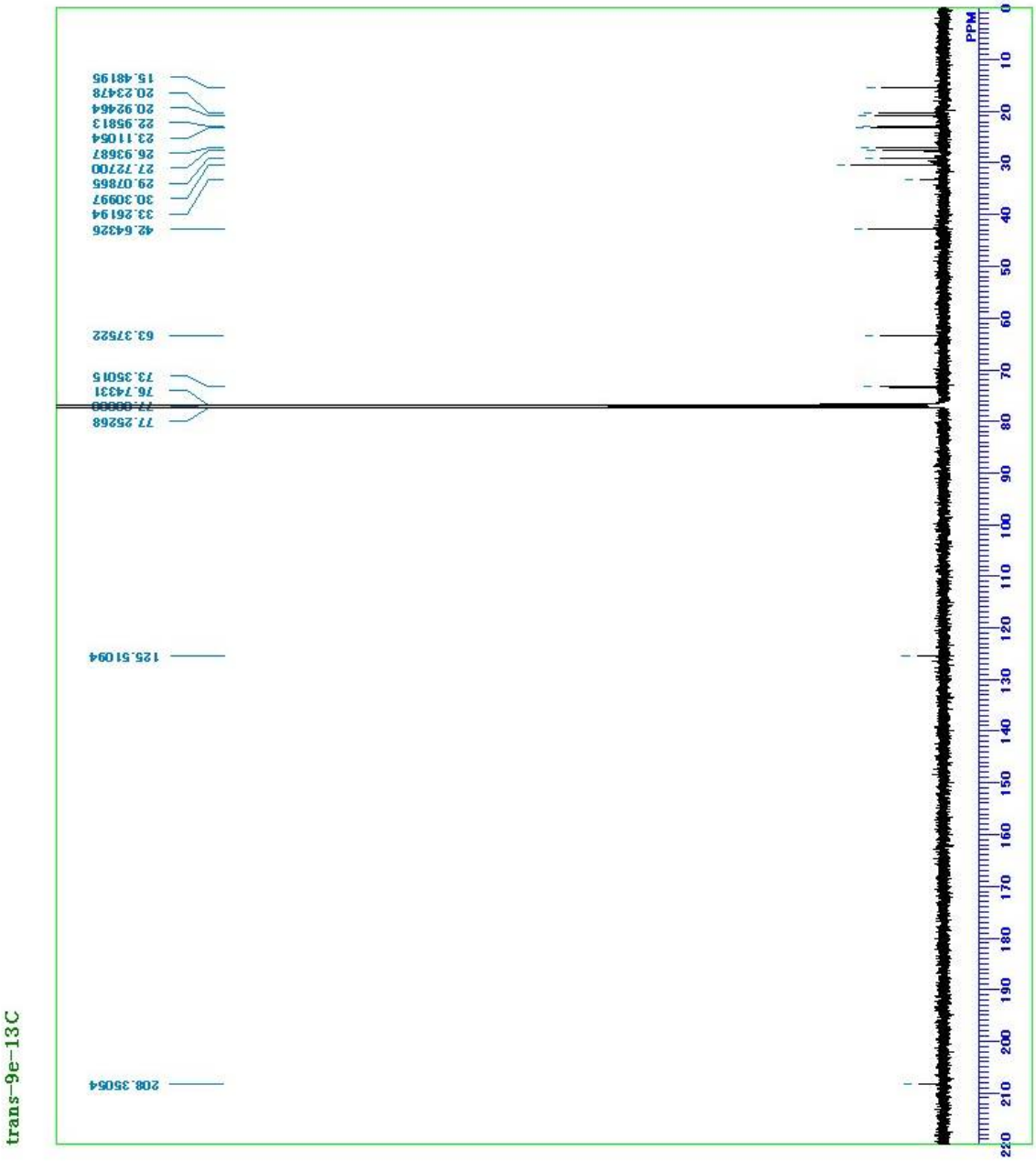
77.00000
76.74331
75.66038
63.74021
43.08045
33.84752
30.71106
29.97708
27.37405
23.24691
23.07445
20.96876
20.13451
15.42179
PPM

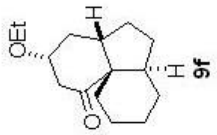

O
EtO
trans-9e

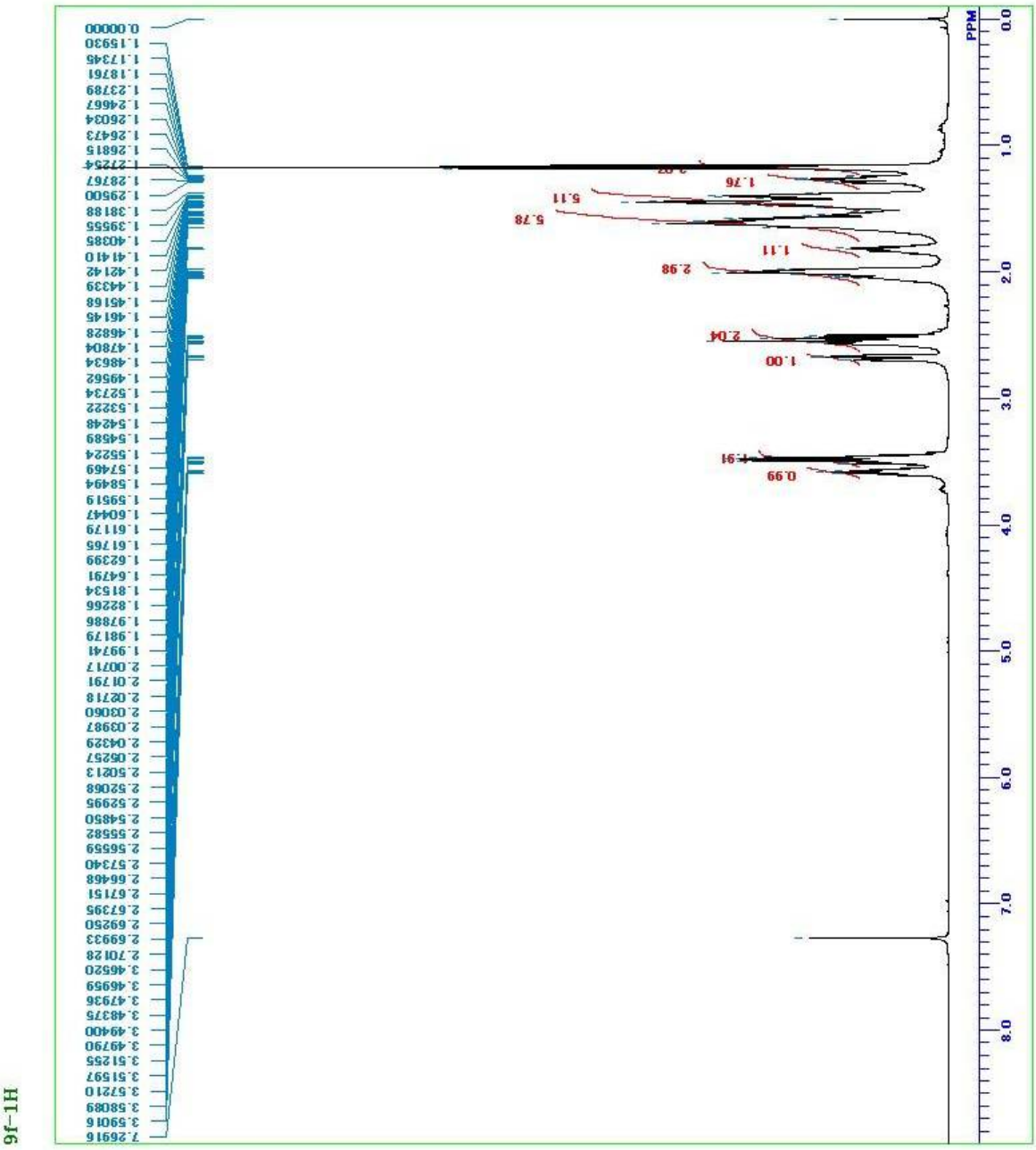

trans-9e-1H
PPM
0
1
2
3
4
5
6
7
8
1.45
4.76
9.21
7.30
2.23
1.16
1.08
2.00
1.10
1.08
2.13
1.00
0.19
0.51

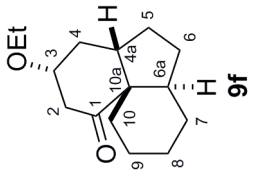

O
EtO

trans-**9e**

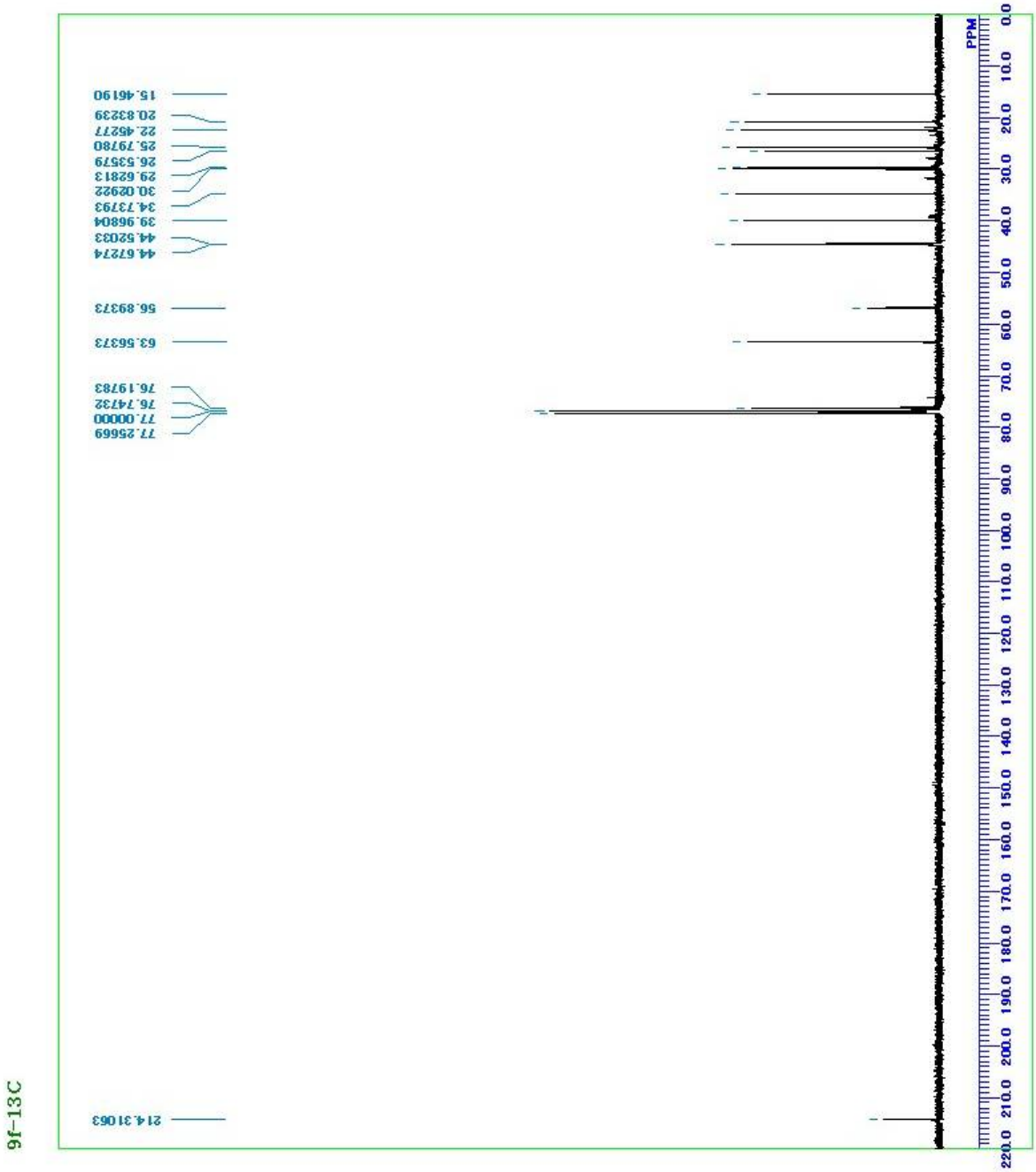

trans-9e-13C
PPM
15.48195
20.23478
20.92464
22.95813
23.11054
26.93687
27.72700
29.07865
30.30997
33.26194
42.64326
63.37522
73.35015
76.74331
77.00000
77.25268
125.51094
208.35064

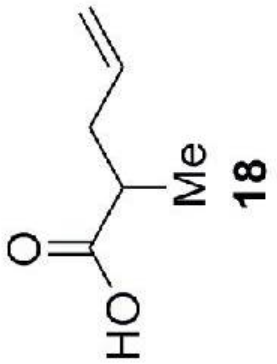

OEt
H
H
O
9f


9f-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
5.78
5.11
1.76
2.98
1.11
2.04
1.00
0.99
1.91

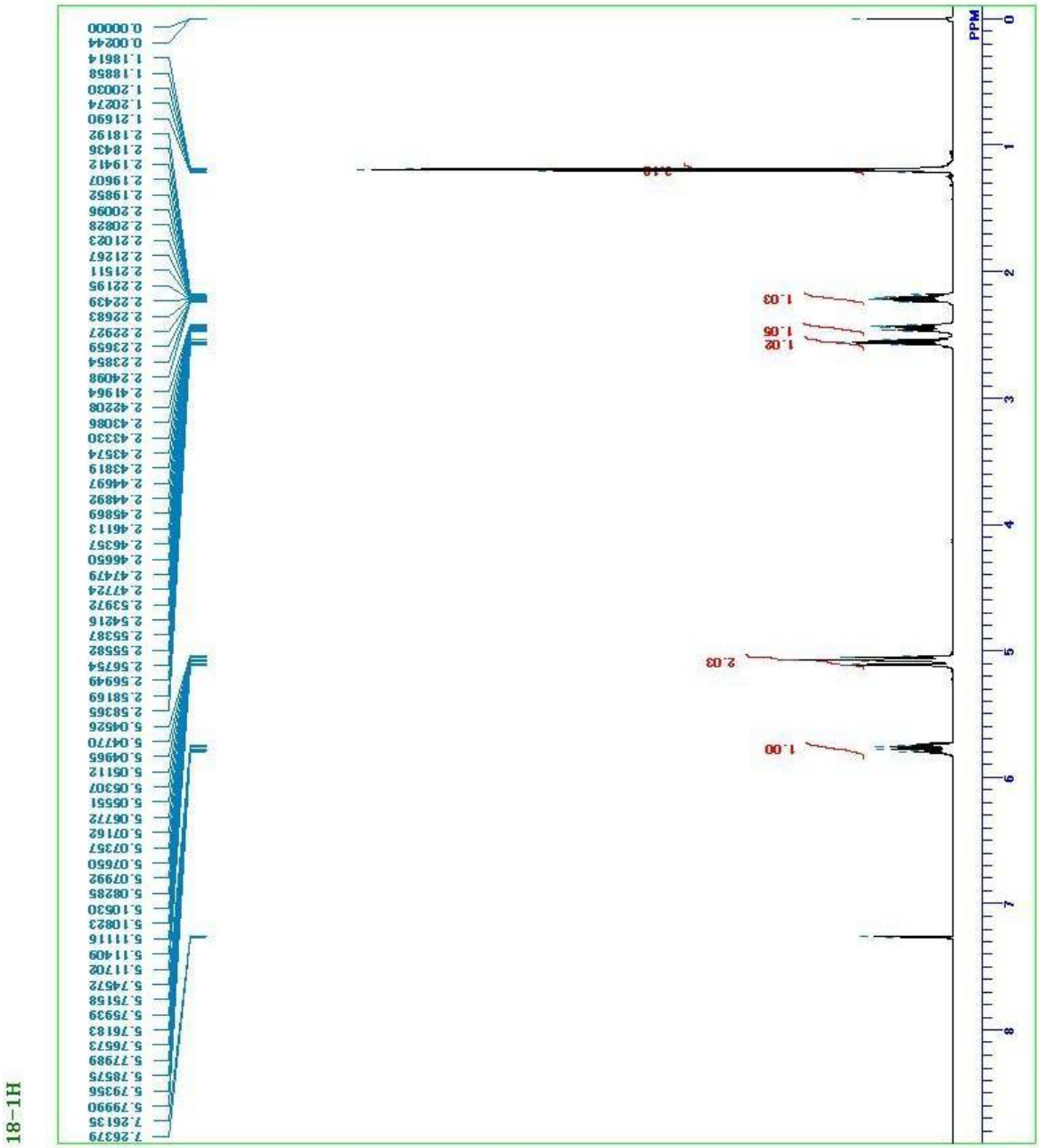

OEt
H
H
O
1
2
3
4
5
6
7
8
9
10
10a
4a
6a

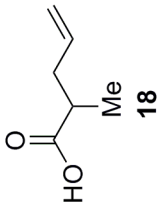
9f


9f-13C
214.31063
77.25669
77.00000
76.74732
76.19783
63.56373
56.89373
44.67274
44.52033
39.96804
34.73793
30.02922
29.62813
26.53579
25.79780
22.46277
20.83239
15.46190
PPM

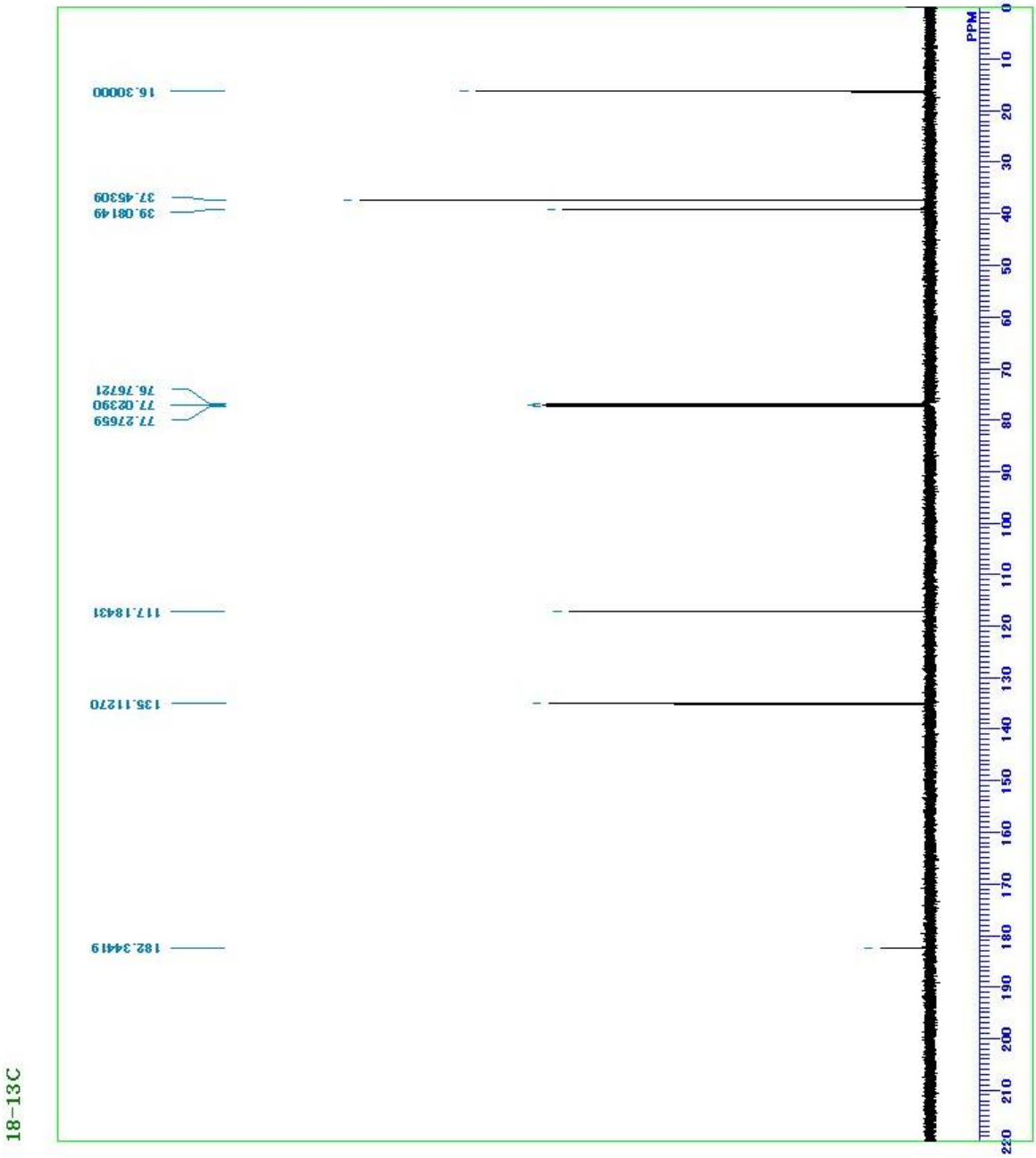


18




Me
O
HO

18


18-13C
182.34419
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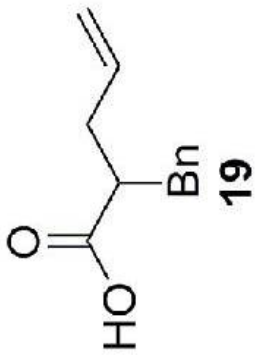
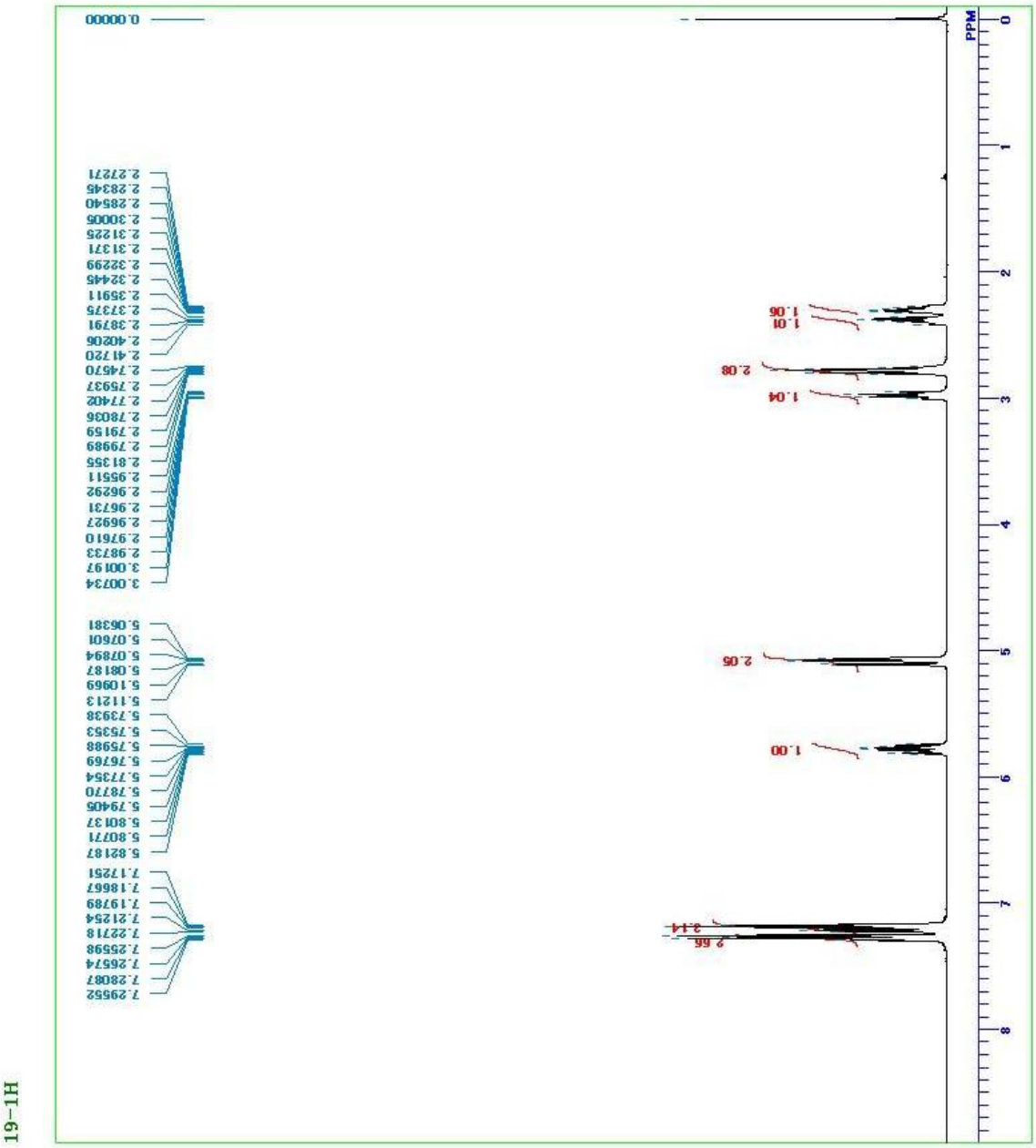
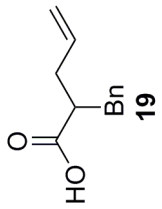
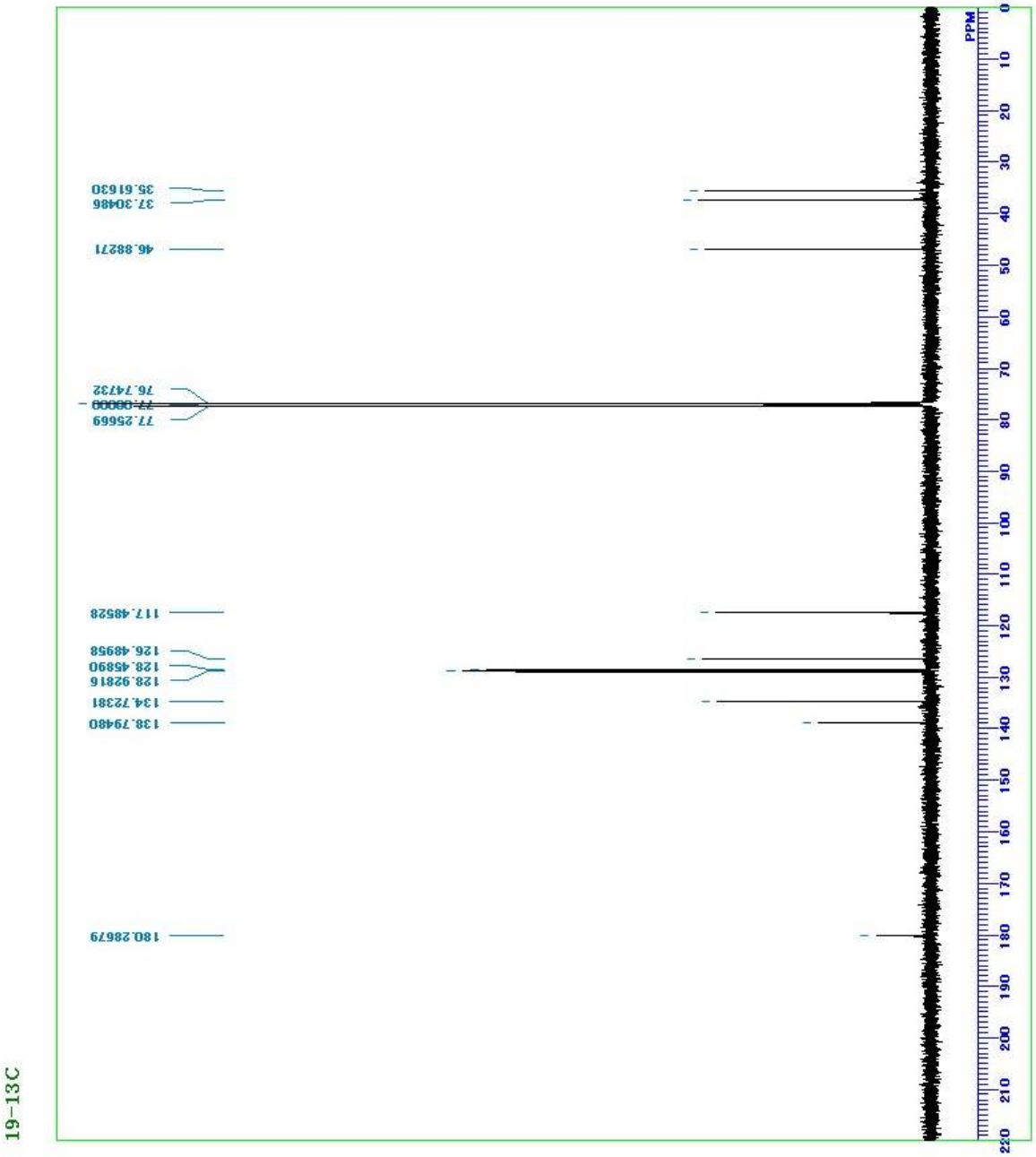
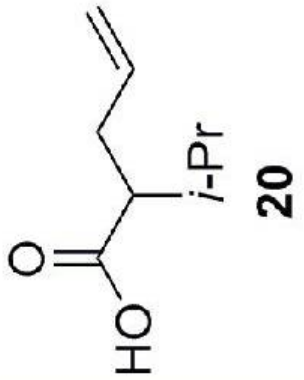
117.18431
77.27659
77.02390
76.76721
39.08149
37.46309
16.30000
PPM


Bn
19
O
HO

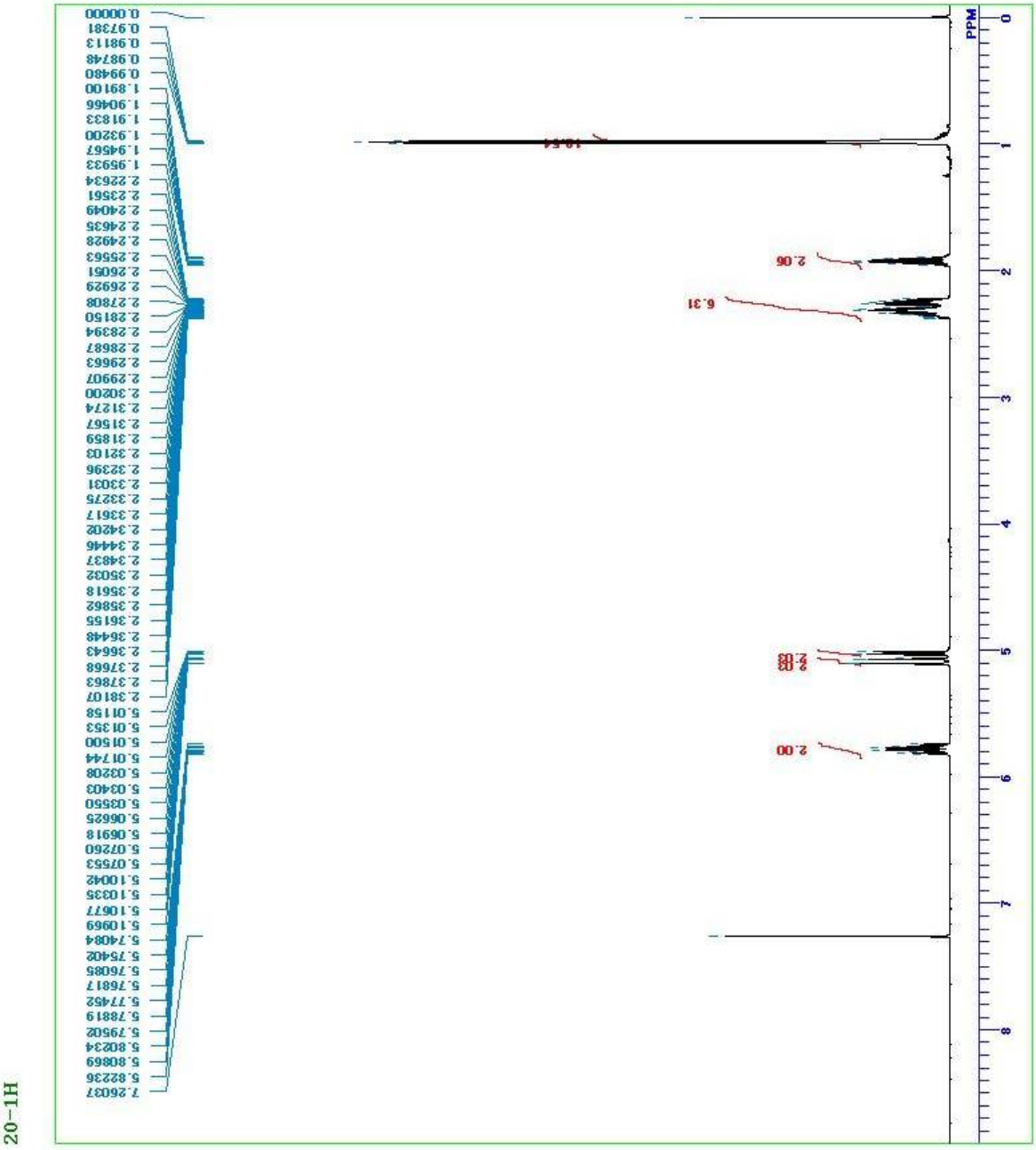

19-1H
PPM
0
1
2
3
4
5
6
7
8
1.06
1.01
2.08
1.04
2.06
1.00
2.66
3.14

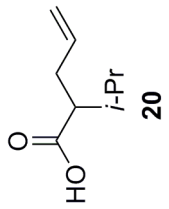

Bn
19
O
HO


PPM
35.61630
37.30486
46.88271
76.74732
77.25669
117.48528
126.48958
128.45890
128.92816
134.72381
138.79480
180.28679
19-13C



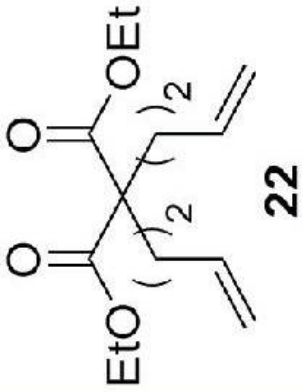
20



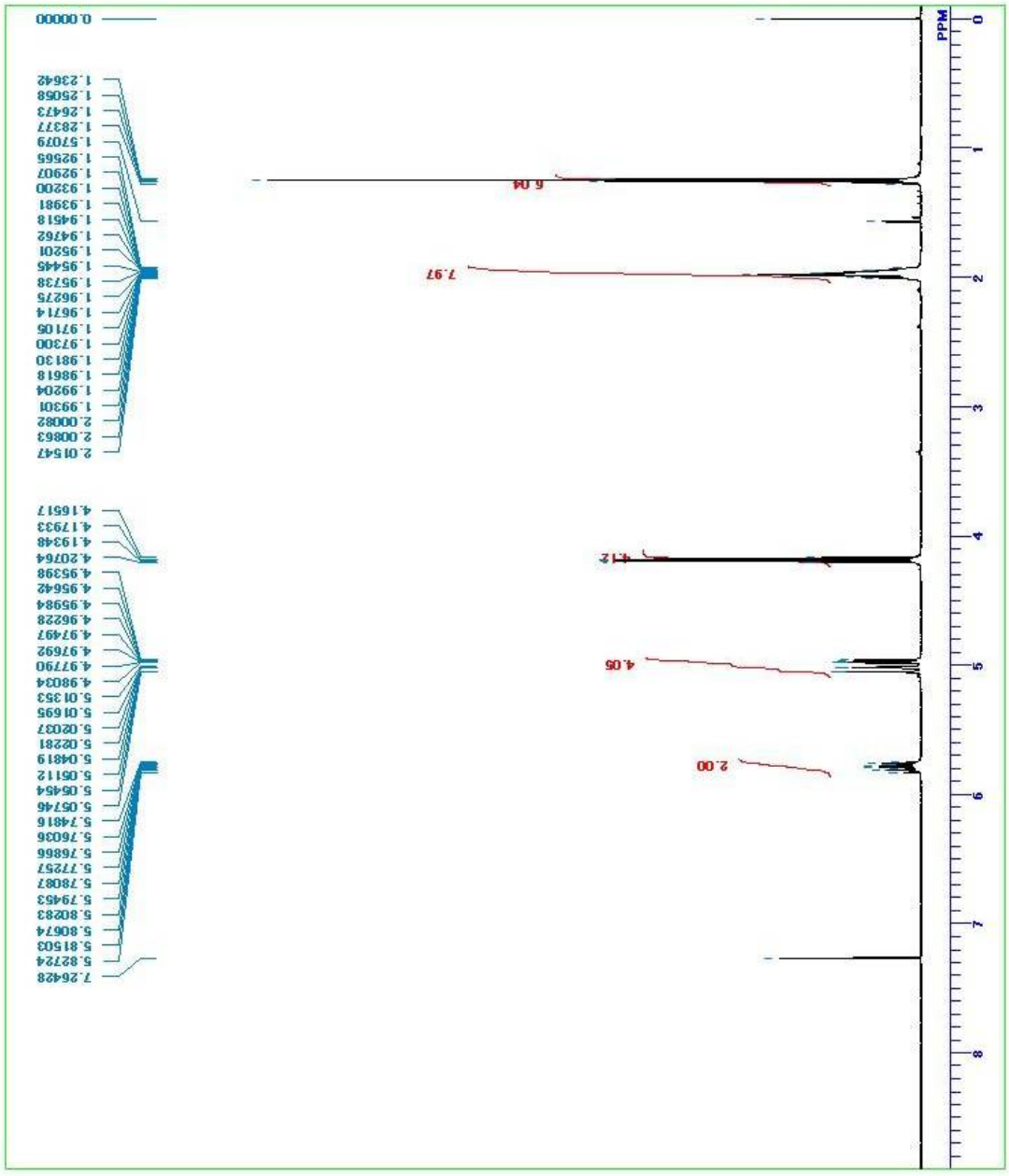

HO
O
i-Pr

20

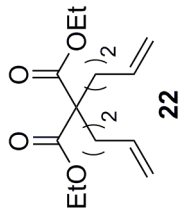

20-13C
180.59964
135.60218
116.66707
77.25669
76.74732
52.12486
33.57880
30.03323
20.21874
20.06231
PPM



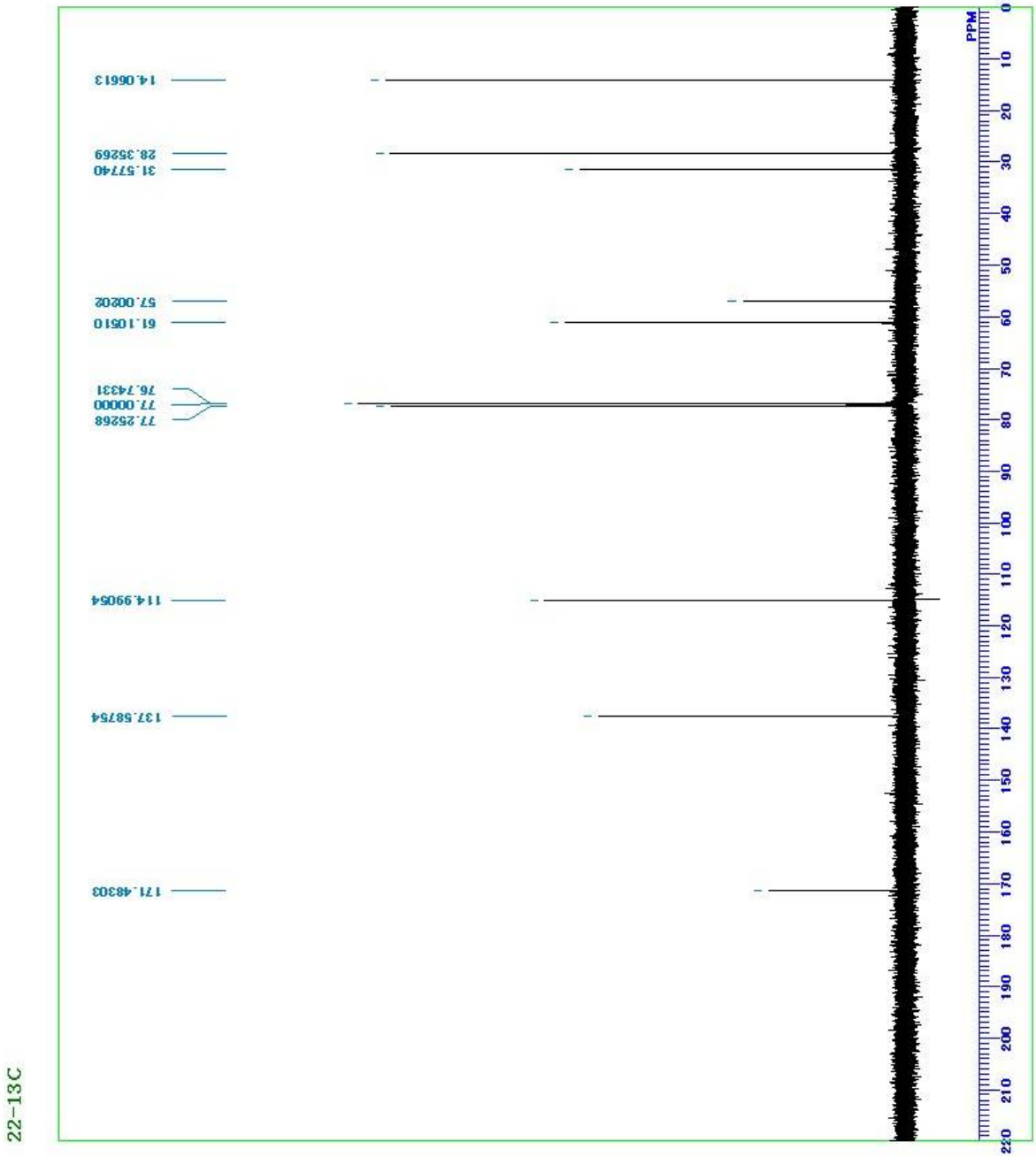
22



22-1H


OEt
O
O
EtO
2
2

22


22-13C
PPM
14.06613
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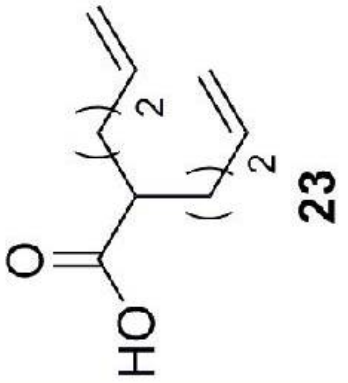
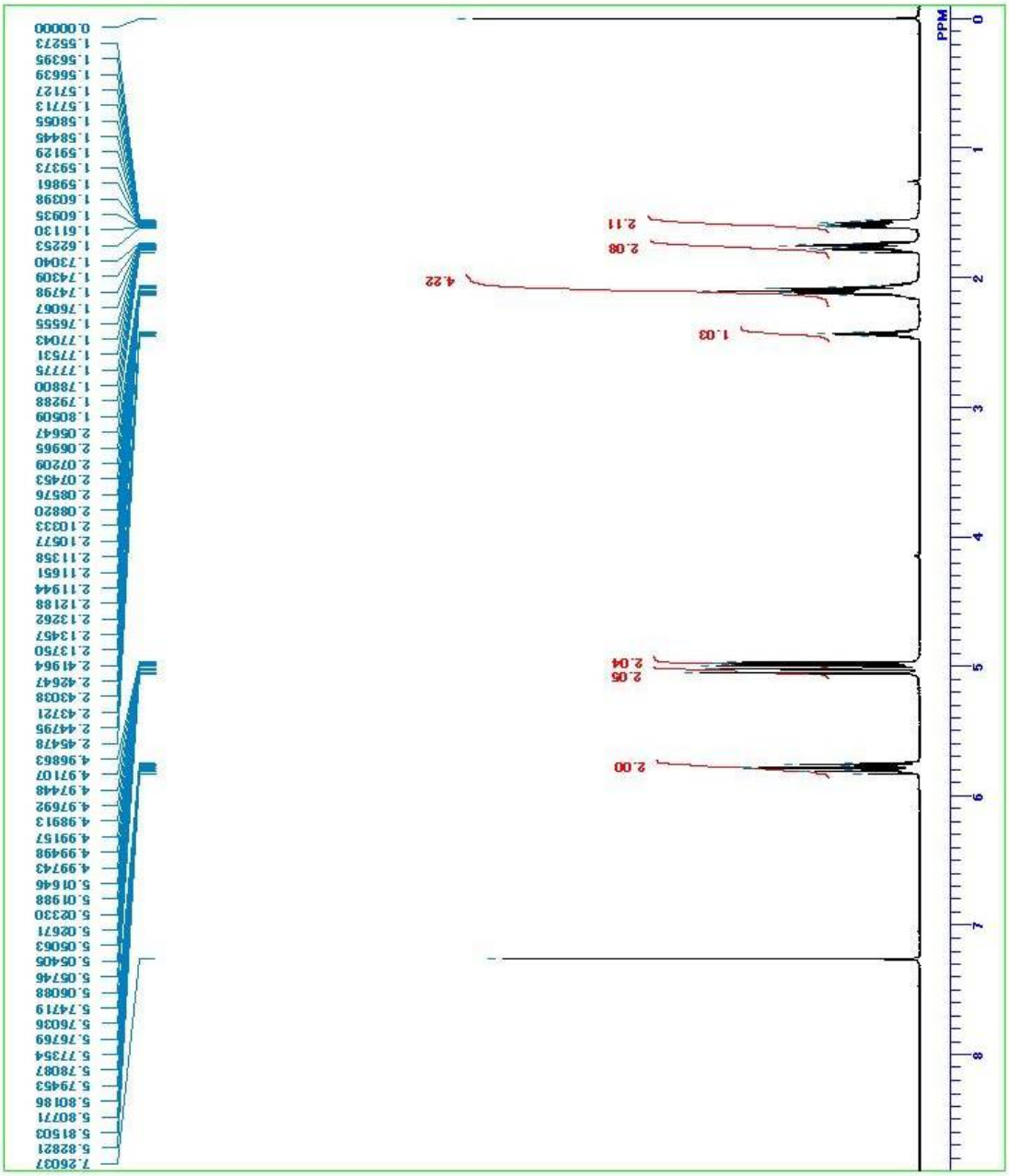
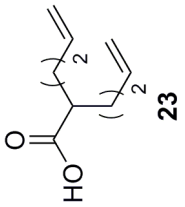
31.57740
57.00202
61.10510
76.74331
77.00000
77.25268
114.99054
137.58754
171.48303

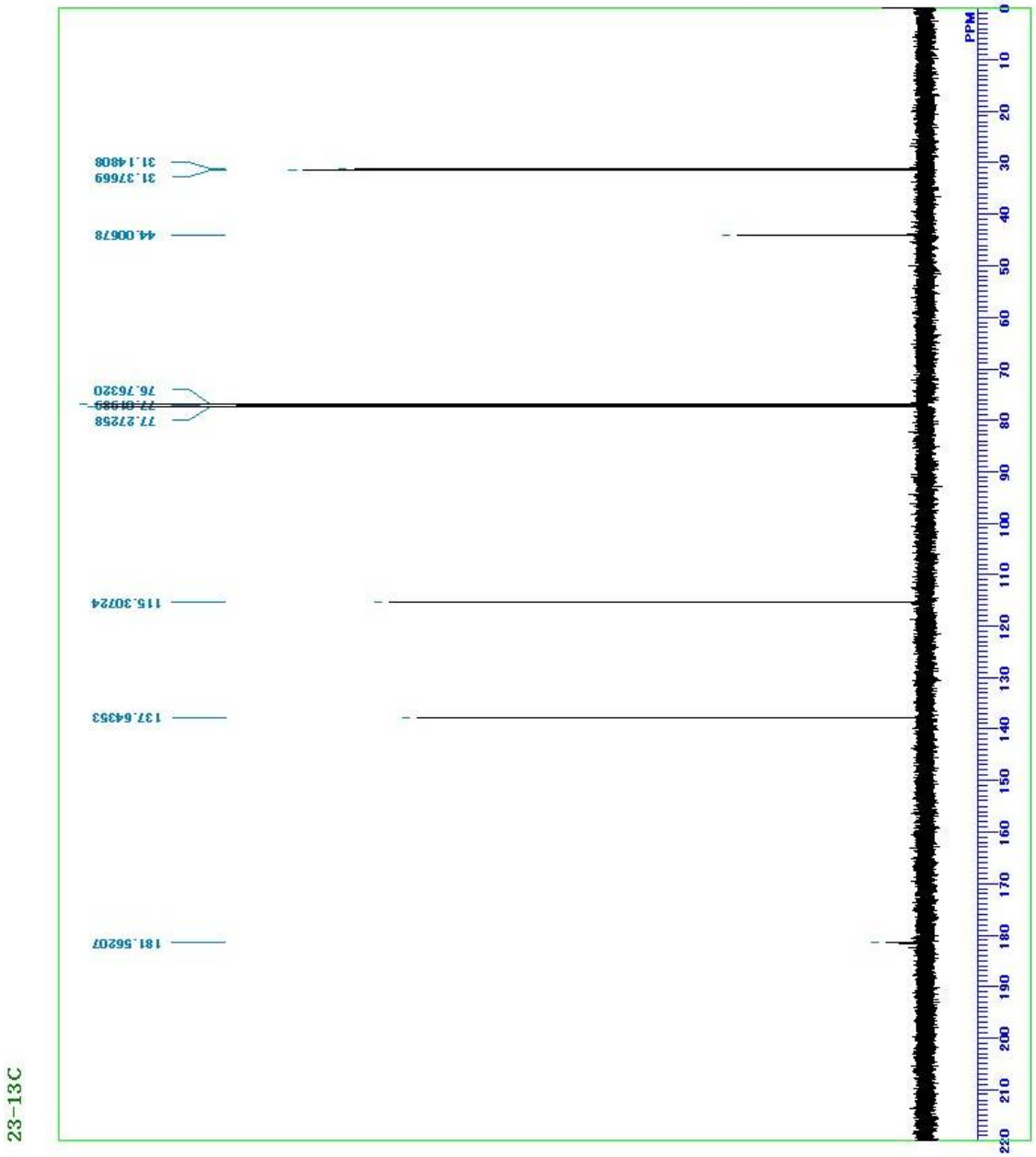


23




O
HO
2
2

23


23-13C
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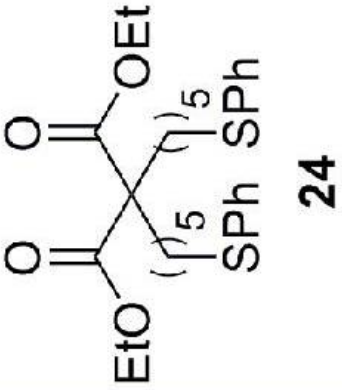
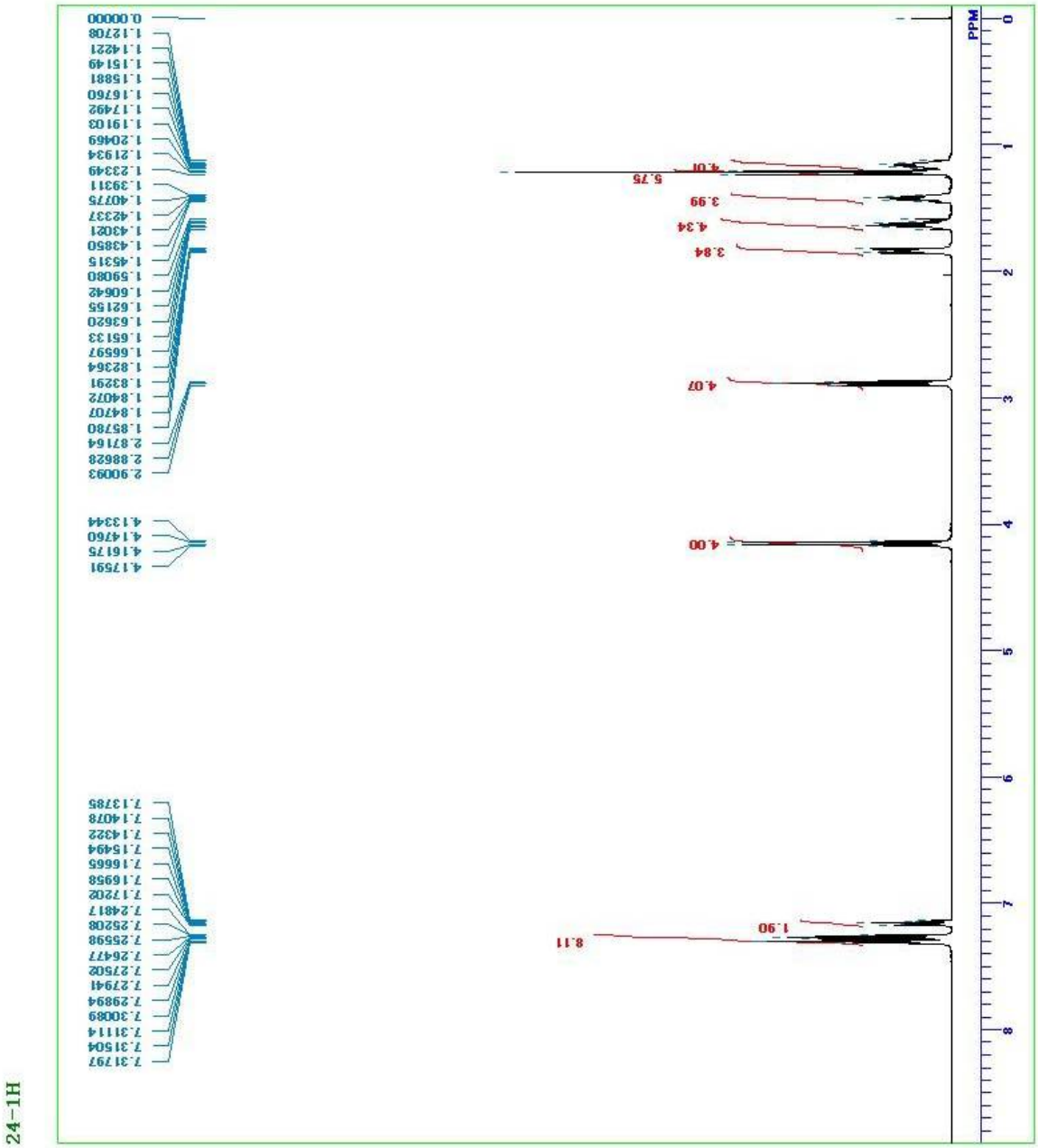
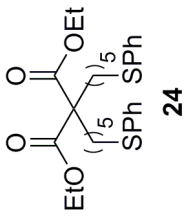
115.30724
77.27258
76.76320
44.00678
31.14808
31.37669
PPM

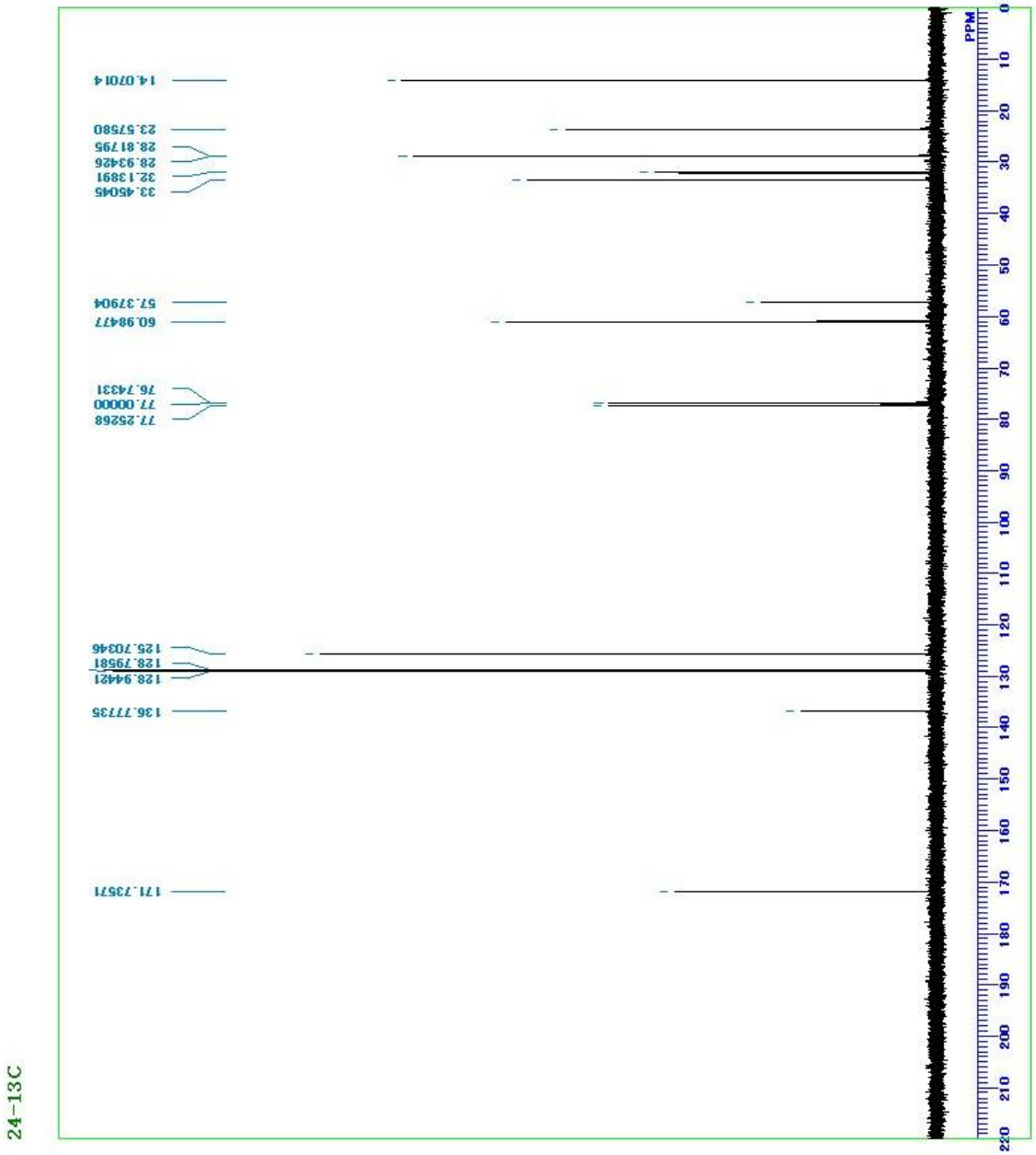

O
OEt
5
SPh
SPh
5
O
EtO

24

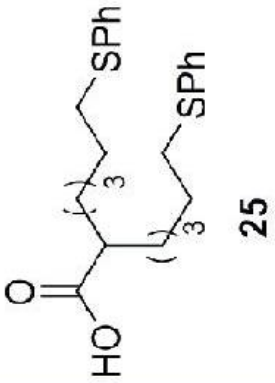

24-1H
PPM
0
1
2
3
4
5
6
7
8
8.11
1.90
5.75
4.01
3.99
4.34
3.84
4.07
4.00


O
OEt
5
SPh
O
EtO
5
SPh

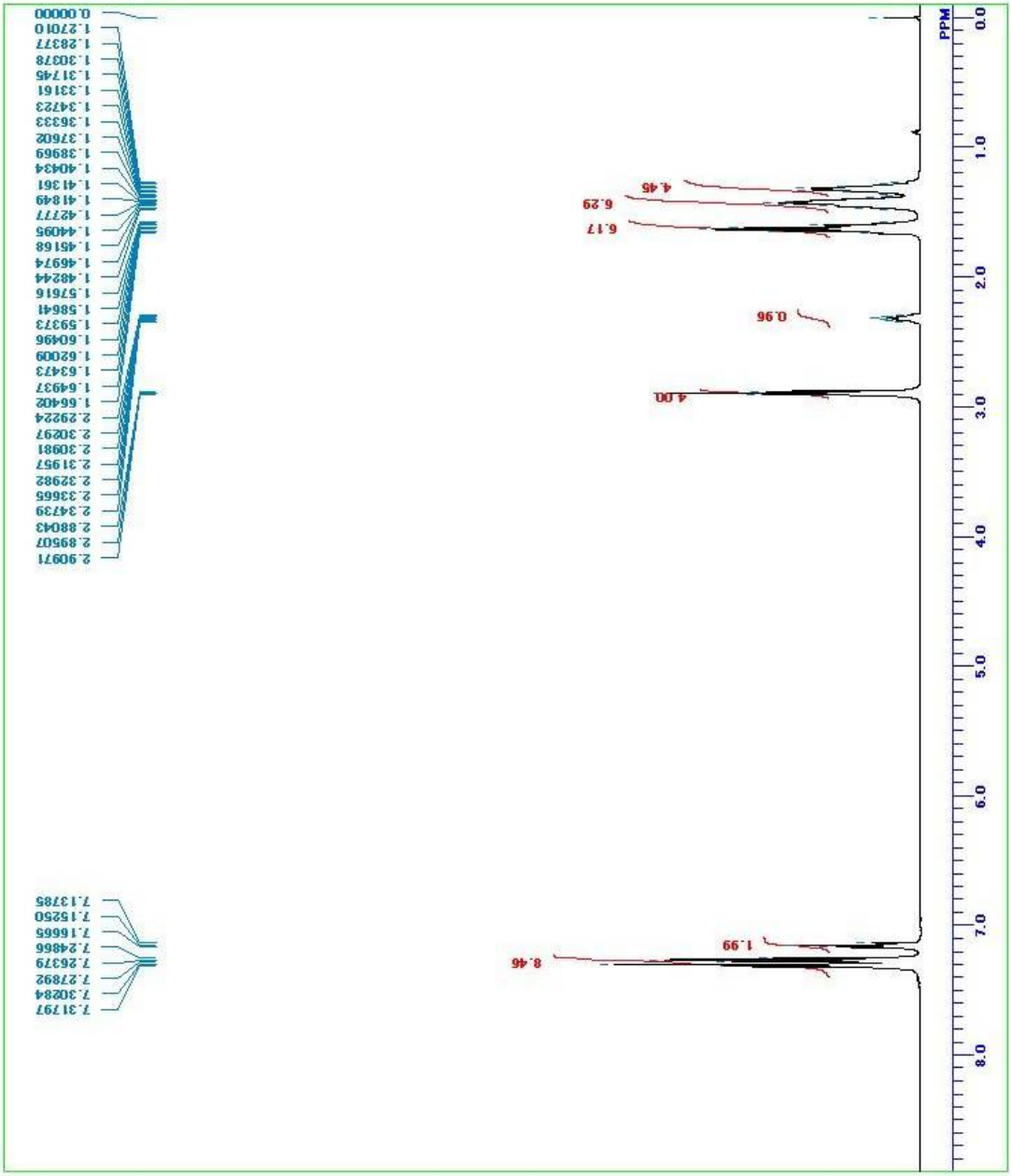
24

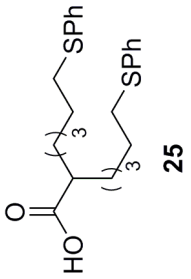

14.07014
23.57580
28.81795
28.93426
32.13891
33.45045
57.37904
60.98477
76.74331
77.00000
77.25268
125.70346
128.79581
128.94421
136.77735
171.73571
PPM
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220

24-13C

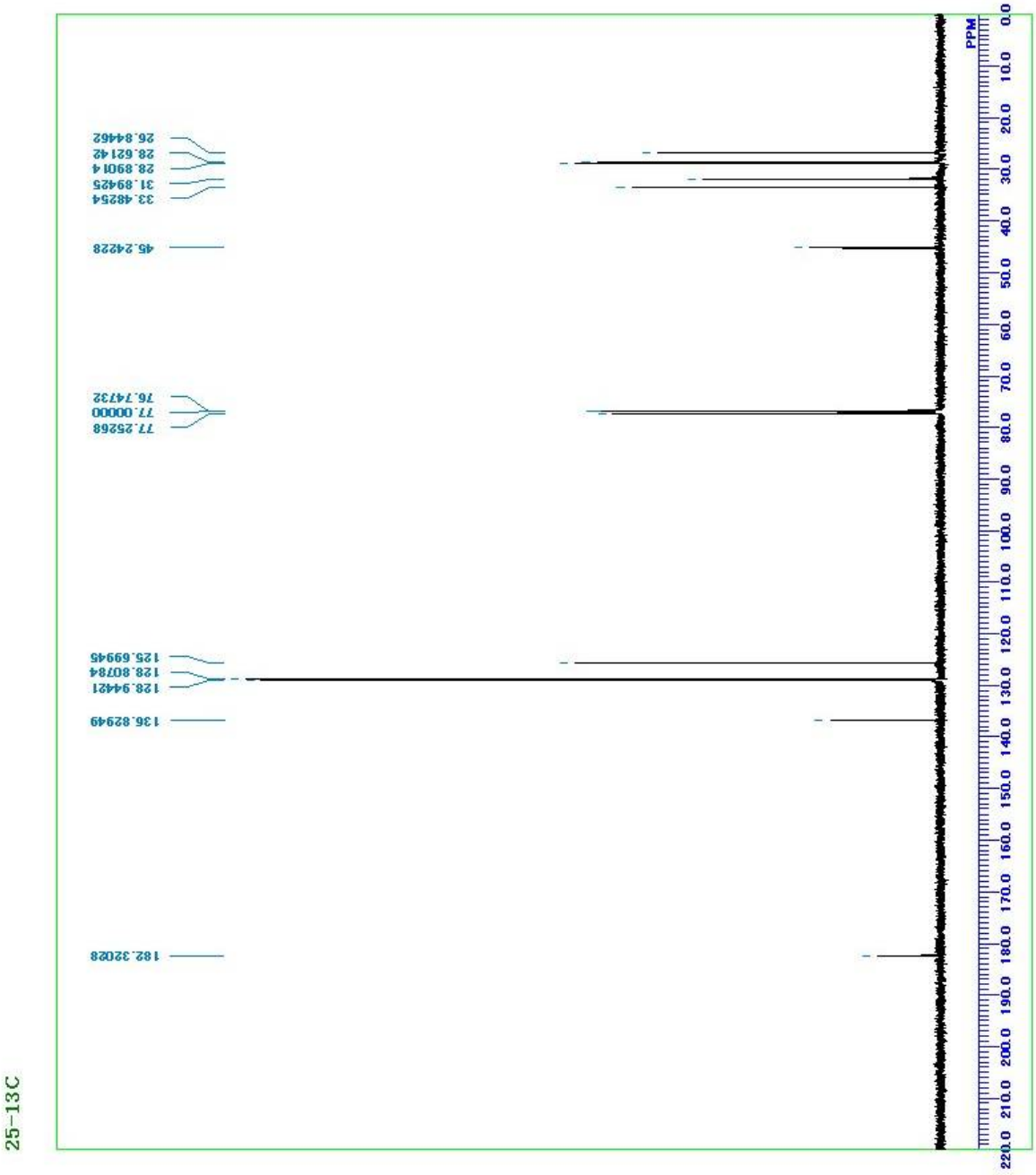


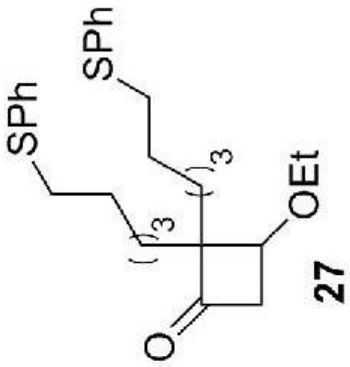
25



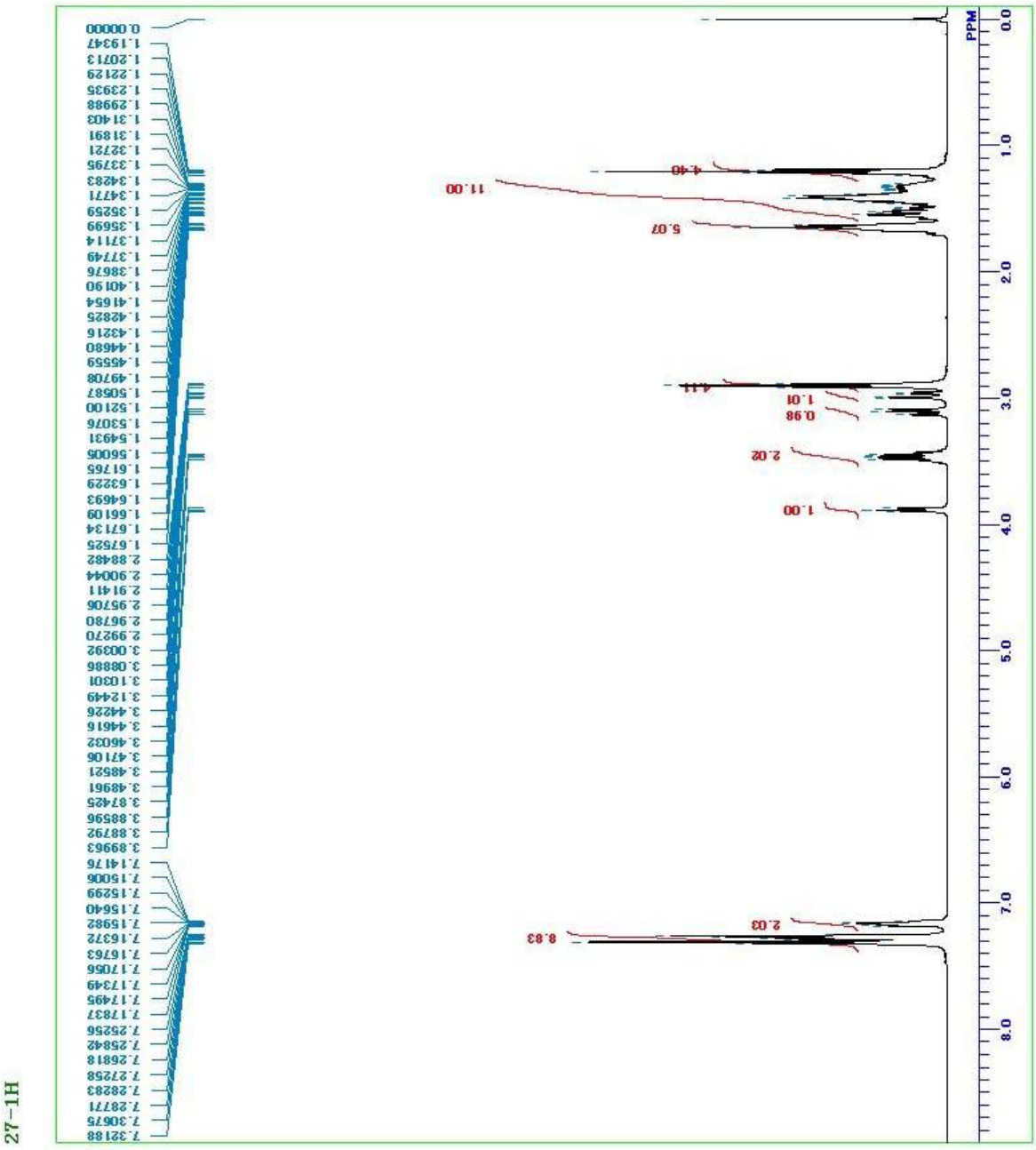

SPh
SPh
3
3
O
HO

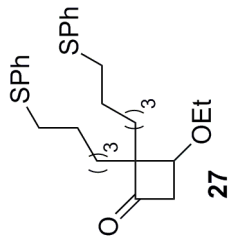
25


25-13C
182.32028
136.82949
128.94421
128.80784
125.69945
77.25268
77.00000
76.74732
45.24228
33.48254
31.89425
28.89014
28.62142
26.84462
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
220.0

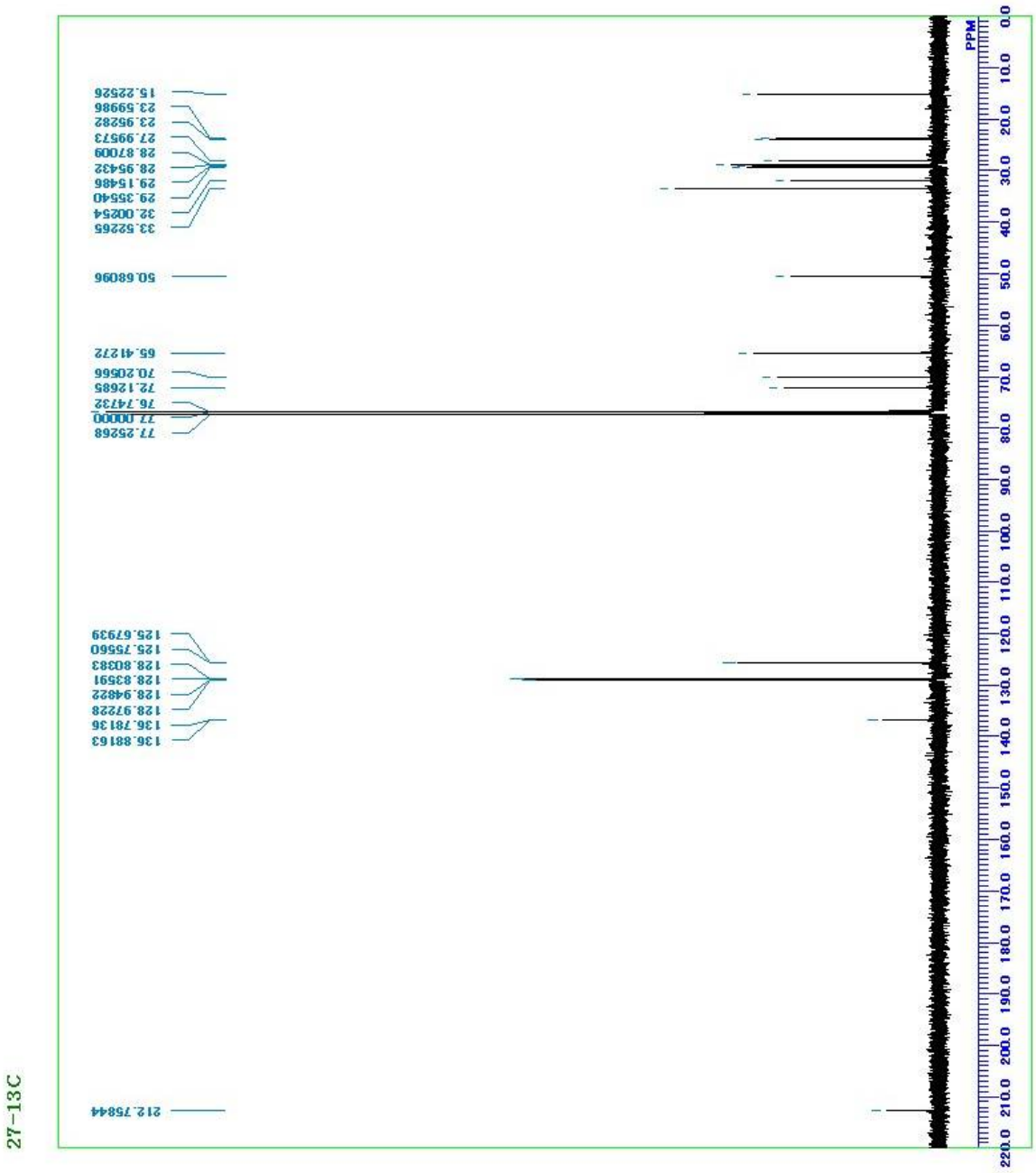

SPh
SPh
3
3
OEt
O

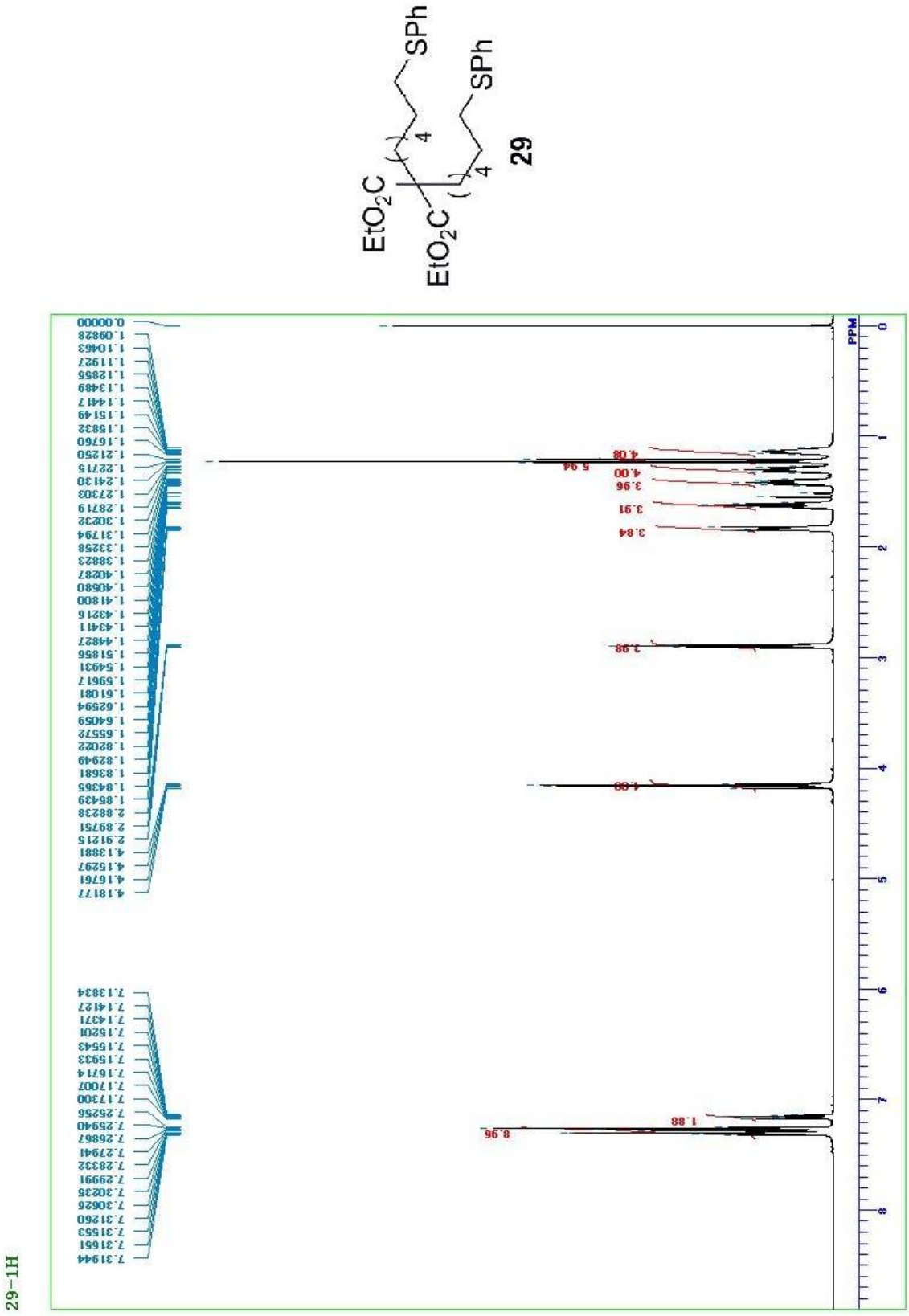
27

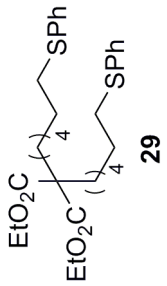

27-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
4.40
11.00
5.07
4.11
1.01
0.98
2.02
1.00
2.03
8.83



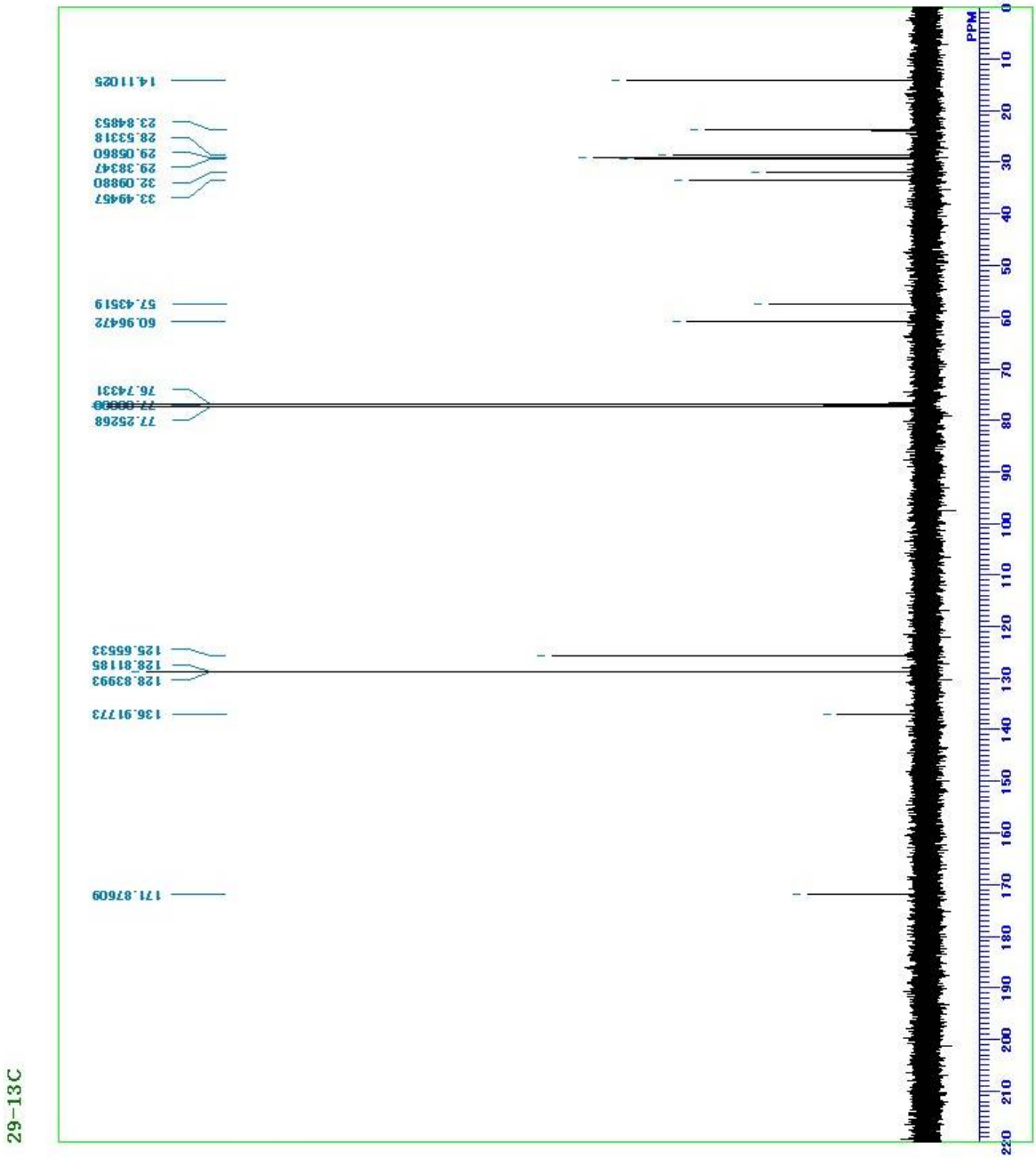
27

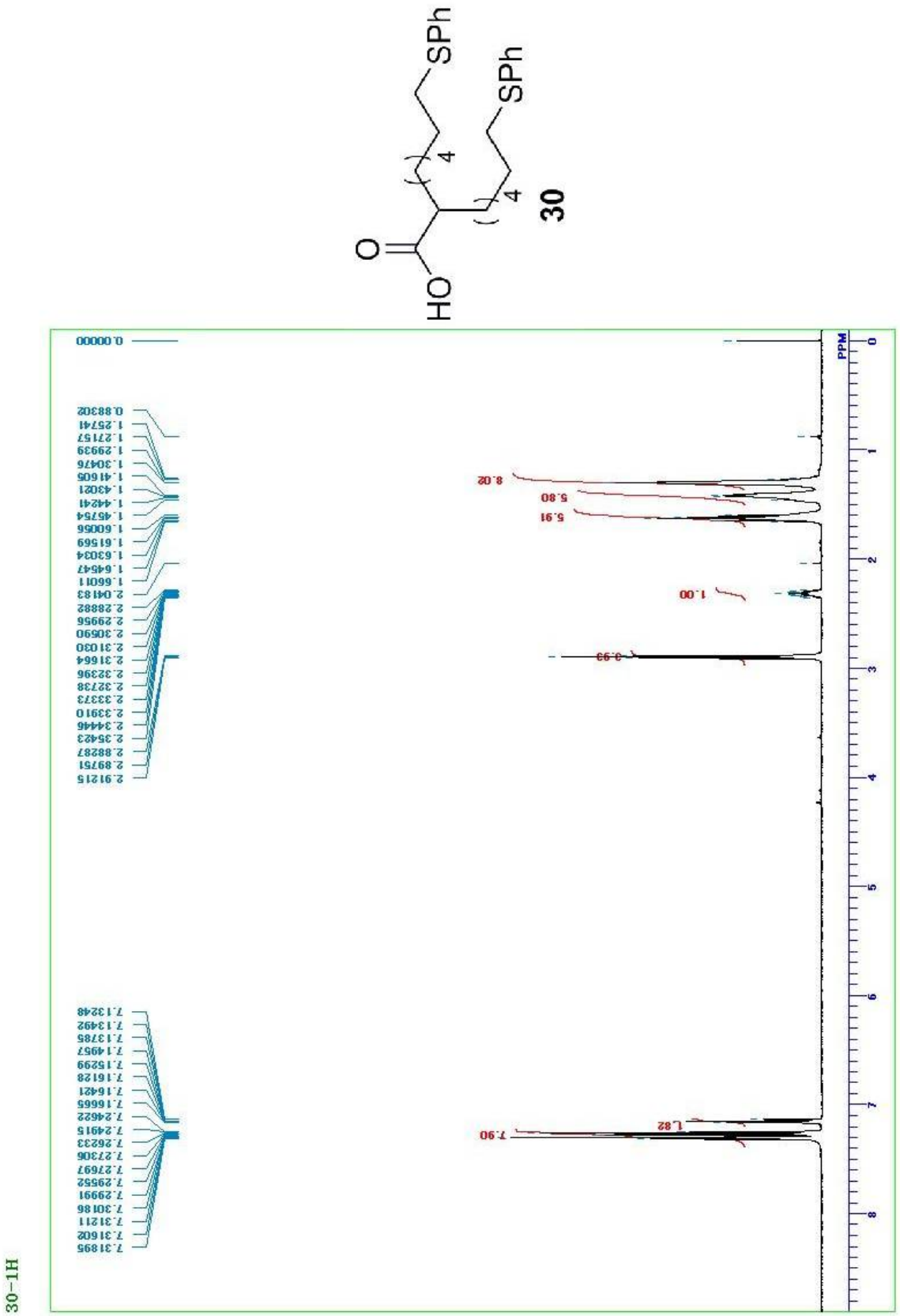


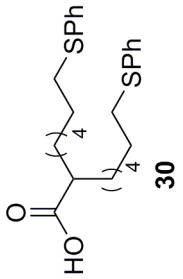

SPh
SPh
4
4
EtO2C
EtO2C
29
29-1H
PPM
0
1
2
3
4
5
6
7
8
5.94
4.08
4.00
3.96
3.91
3.84
3.98
4.88
8.96
1.88


SPh
SPh
4
4
EtO2C
EtO2C

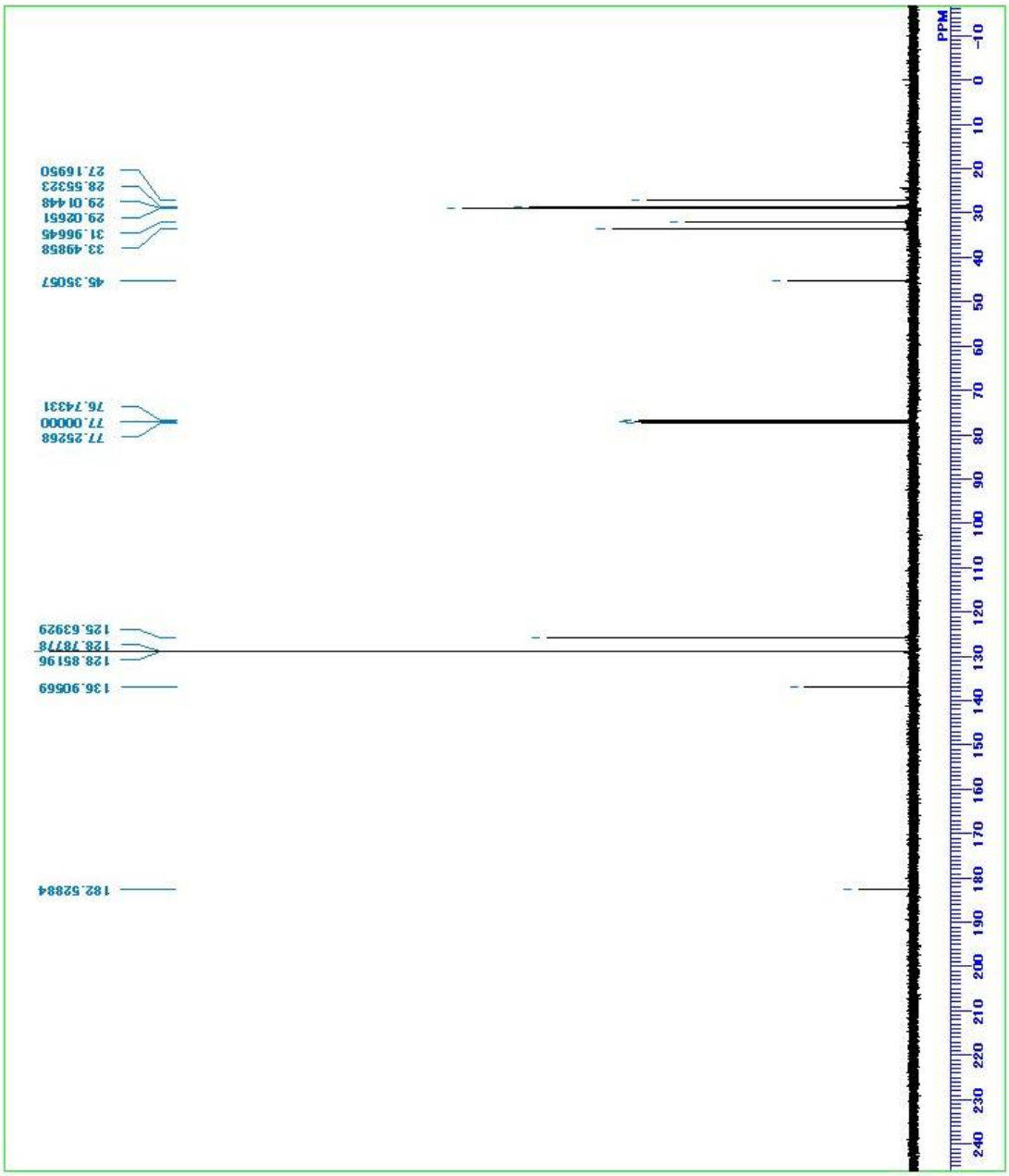
29


29-13C
PPM
14.11025
23.84853
28.53318
29.05860
29.38347
32.09880
33.49457
57.43519
60.96472
76.74331
77.25268
125.65533
128.81185
128.83993
136.91773
171.87609

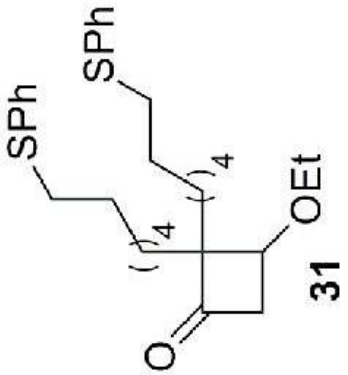

SPh
SPh
4
4
O
HO
30
30-1H
PPM
8.02
5.80
5.91
1.00
3.93
7.90
1.82


SPh
SPh
4
4
O
HO

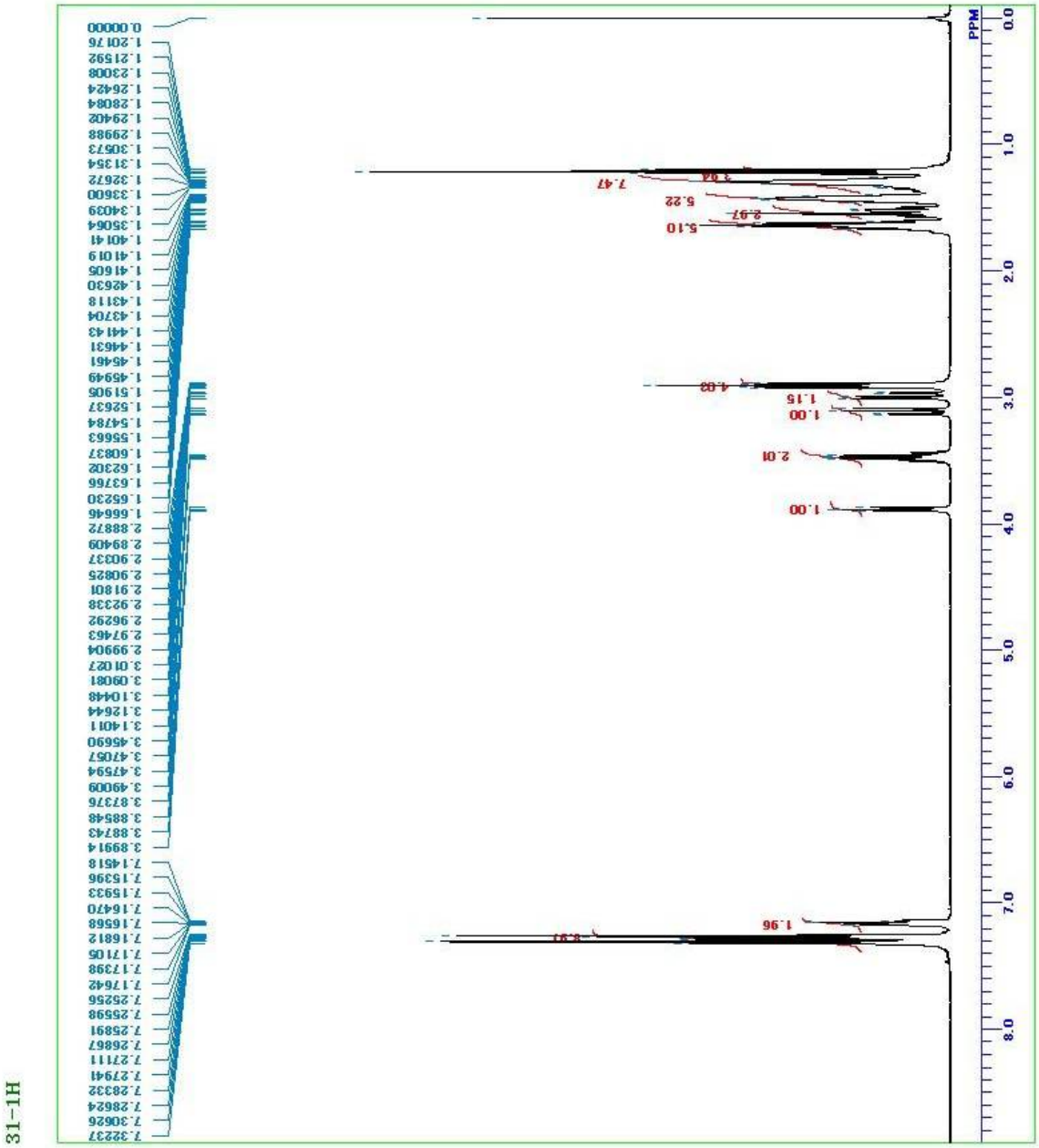
30

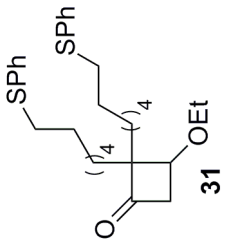

PPM
182.52884
136.90569
128.85196
128.78778
125.63929
77.25268
77.00000
76.74331
45.35057
33.49858
31.96645
29.02651
29.01448
28.55323
27.16950

30-13C

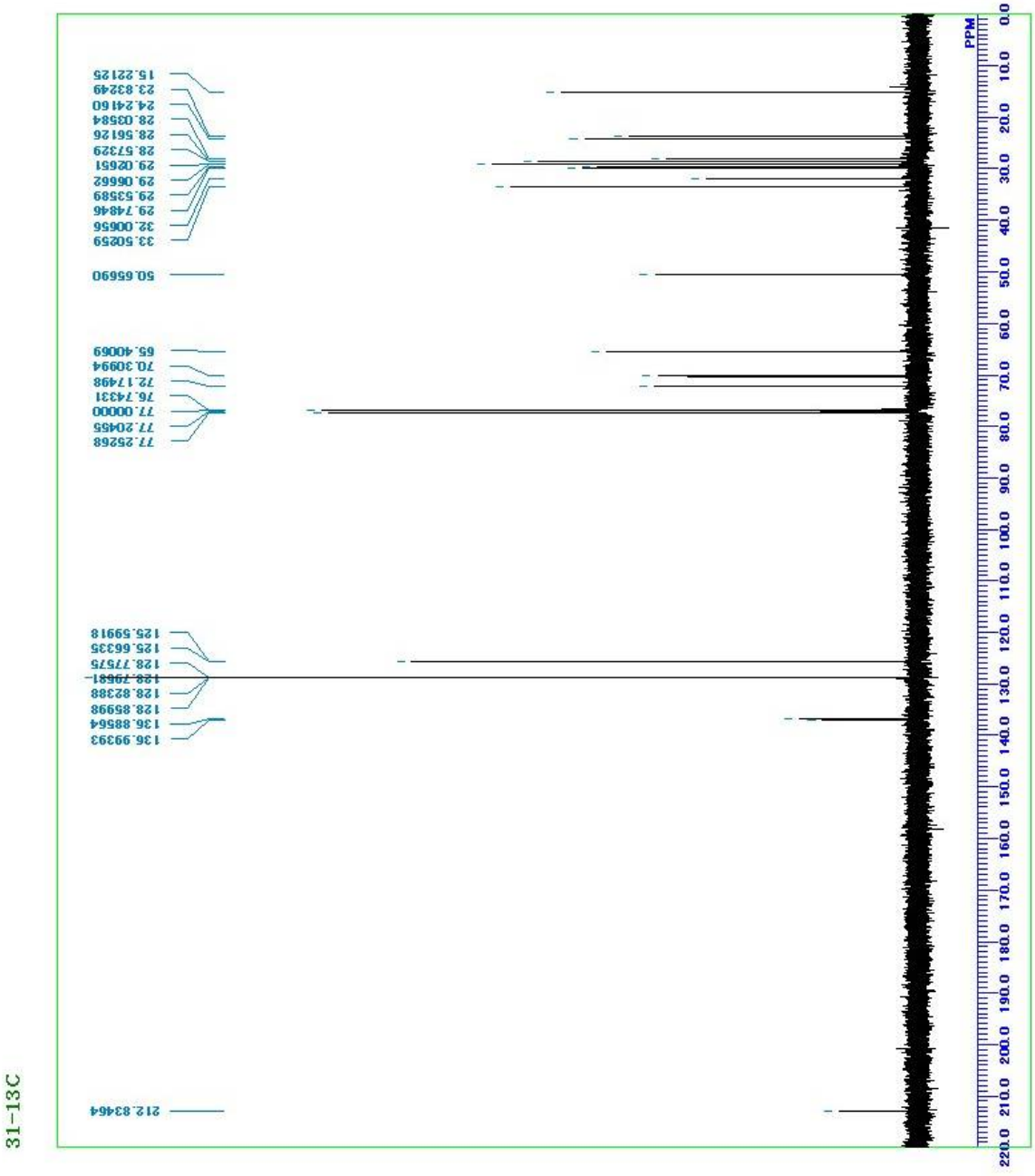

SPh
SPh
4
4
OEt
O

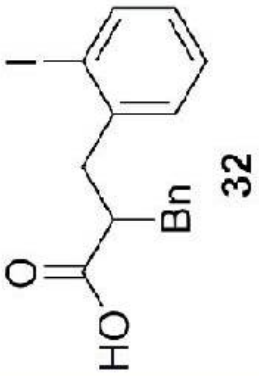
31


31-1H
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
7.47
5.22
2.97
5.10
4.08
1.15
1.00
2.01
1.00
1.96
8.31

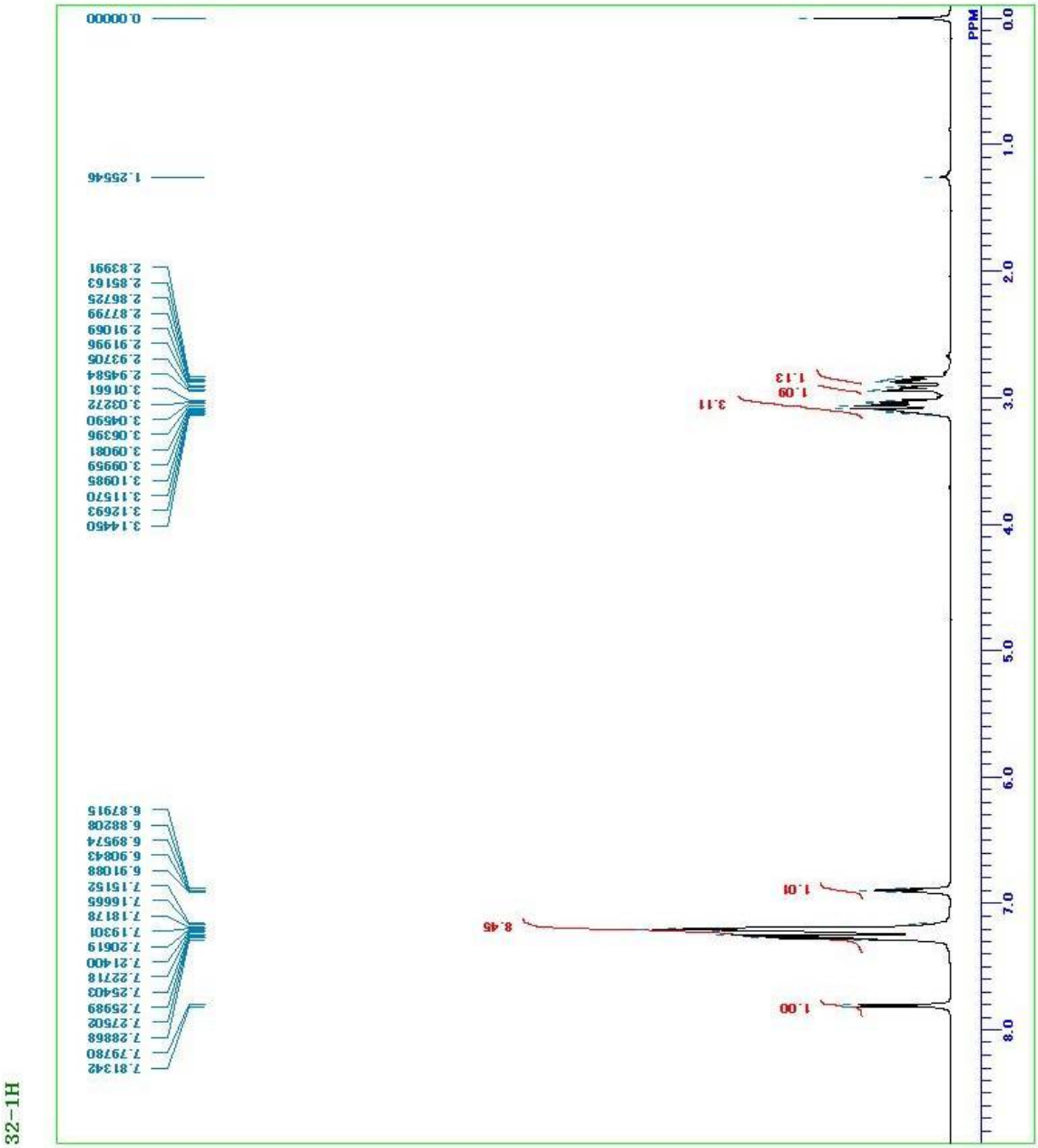


31

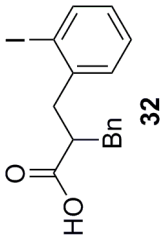



I
Bn
O
HO

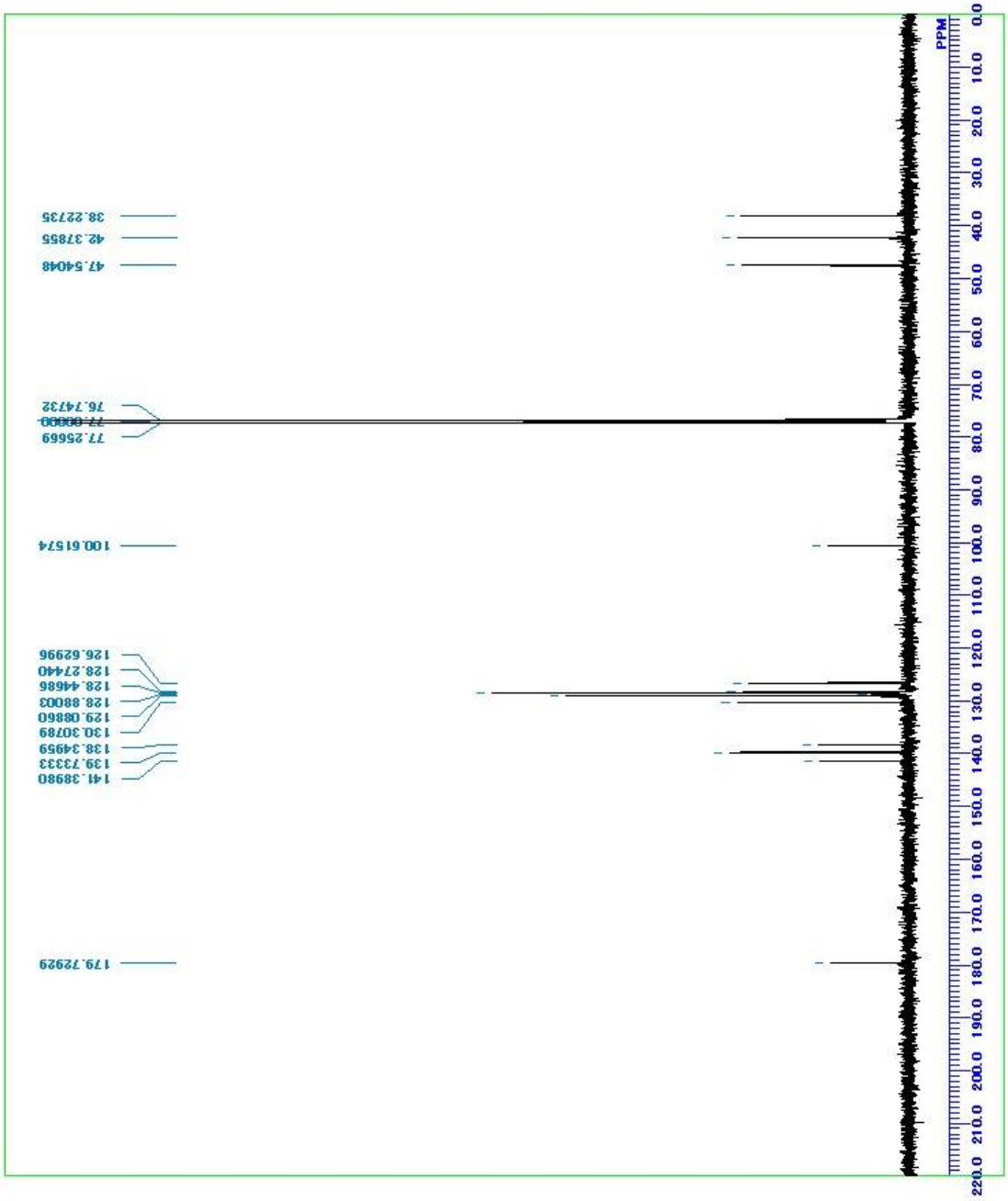
32

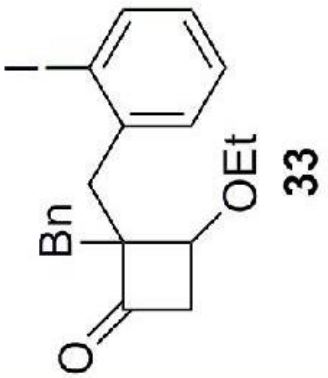

0.00000
1.25546
2.83991
2.85163
2.86725
2.87799
2.91069
2.91996
2.93705
2.94584
3.01661
3.03272
3.04590
3.06396
3.09081
3.09959
3.10985
3.11570
3.12693
3.14450
6.87915
6.88208
6.89574
6.90843
6.91088
7.15152
7.16665
7.18178
7.19301
7.20619
7.21400
7.22718
7.25403
7.25989
7.27502
7.28868
7.79780
7.81342
8.45
1.00
1.01
3.11
1.09
1.13
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0

32-1H

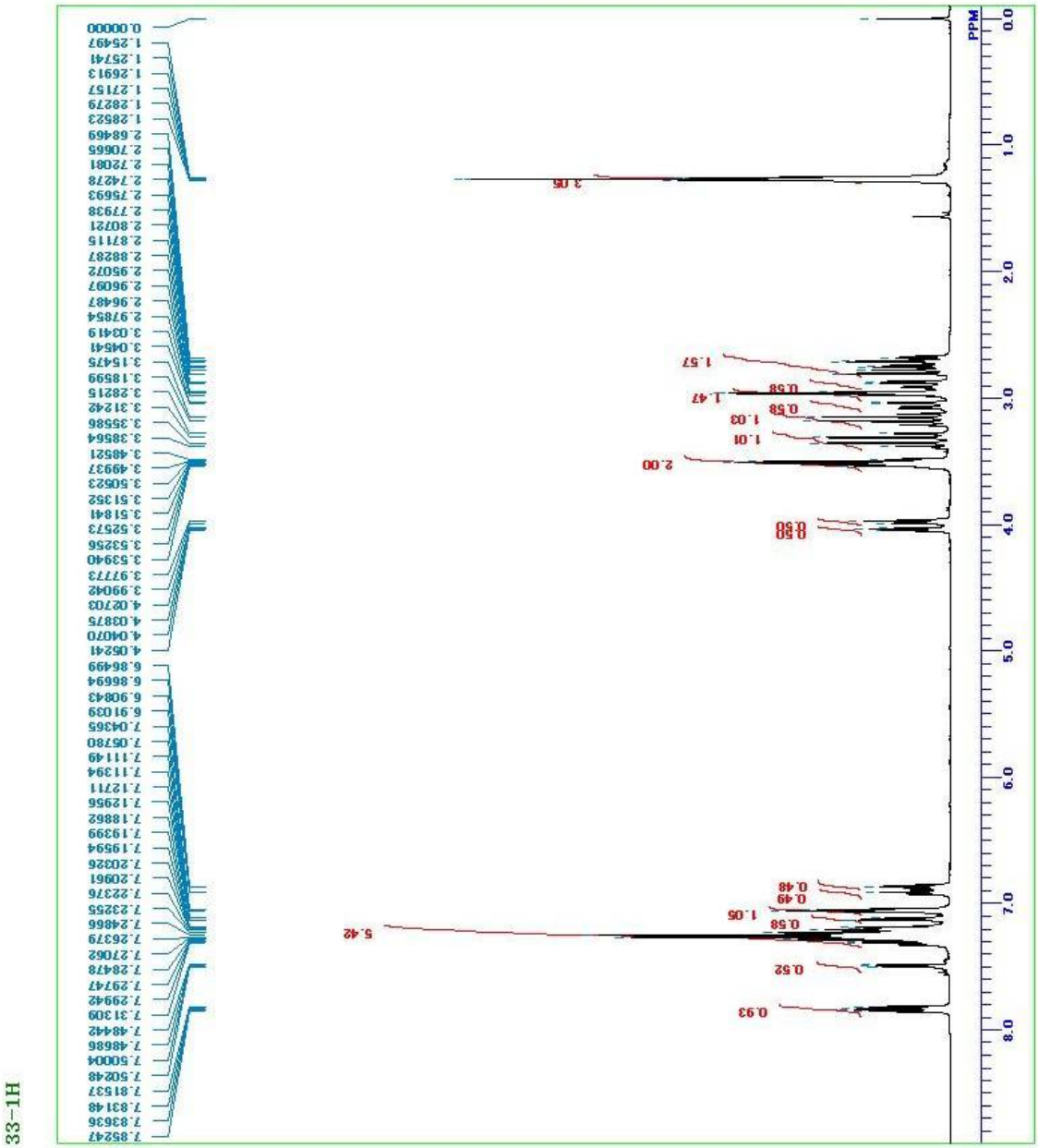

I
Bn
O
HO

32

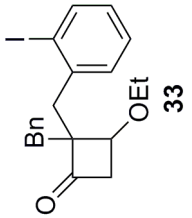

32-13C
PPM
38.22735
42.37855
47.54048
76.74732
77.25669
100.61574
126.62996
128.27440
128.44686
128.88003
129.08860
130.30789
138.34959
139.73333
141.38980
179.72929


I
OEt
Bn
O

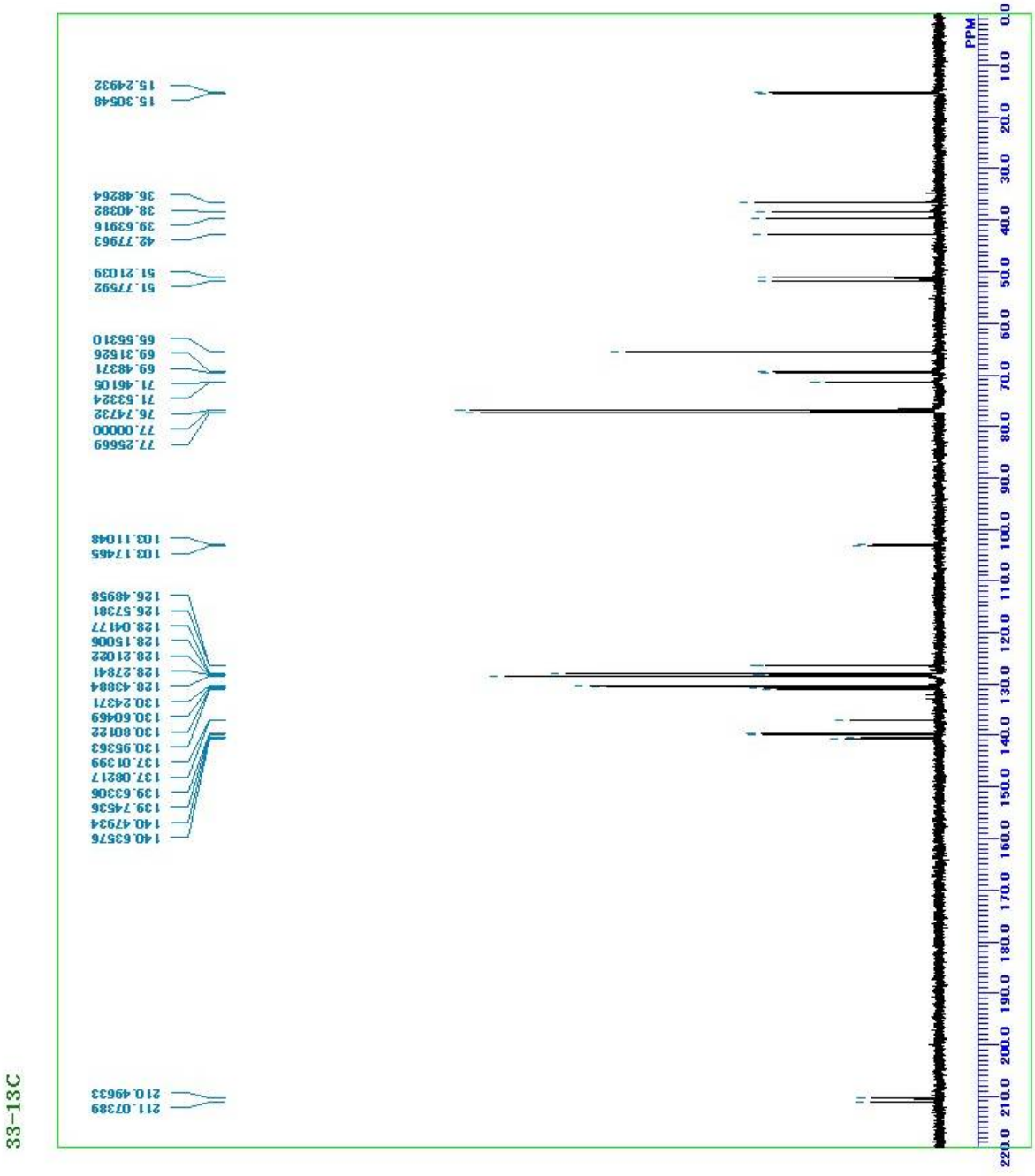
33


PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
3.06
1.57
1.47
0.58
1.03
1.01
2.00
0.58
5.42
1.05
0.58
0.49
0.48
0.52
0.93

33-1H

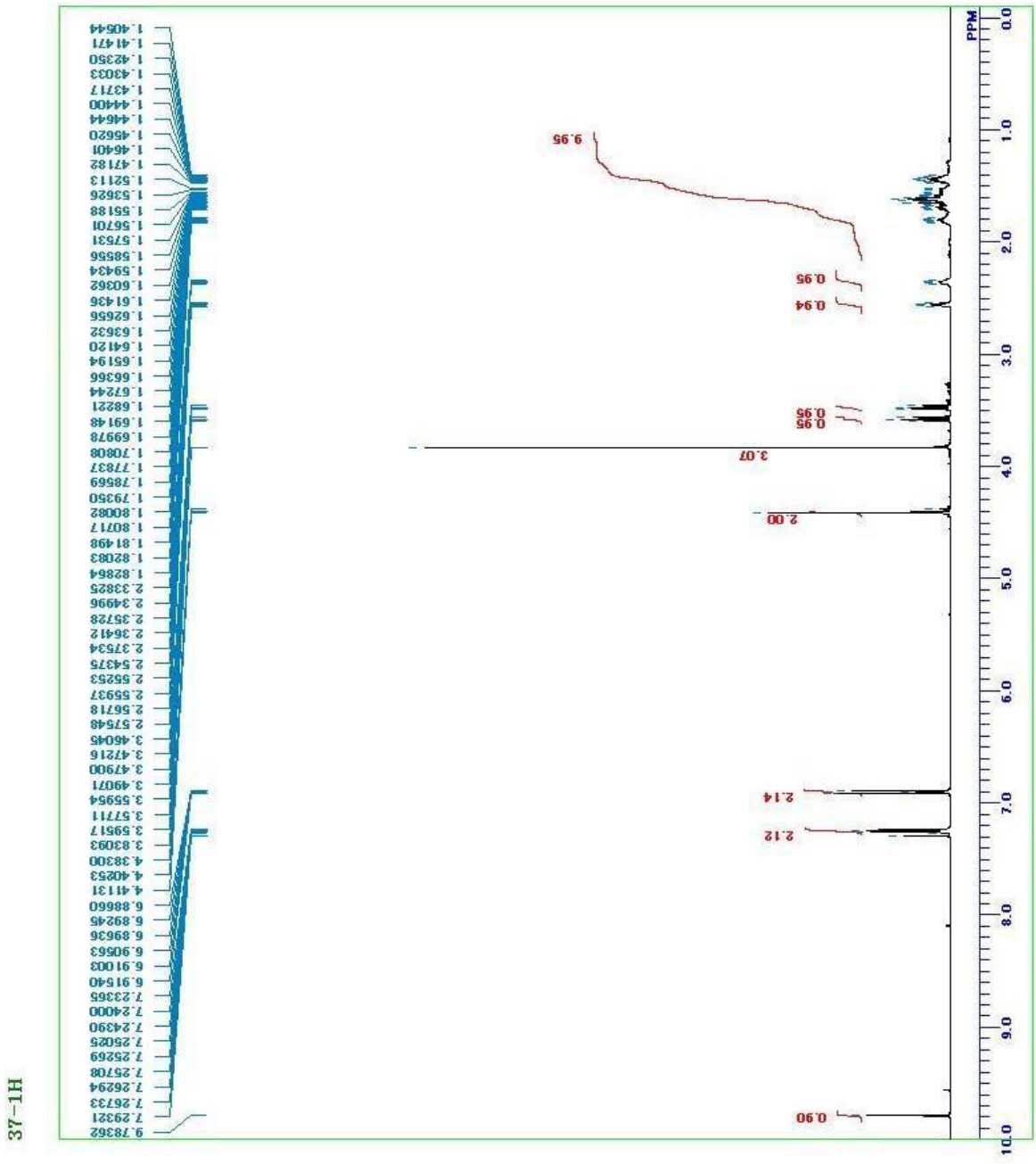

I
OEt
Bn
O

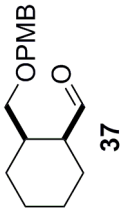
33


15.24932
15.30548
36.48264
38.40382
39.63916
42.77963
51.21039
51.77592
65.55310
69.31526
69.48371
71.46105
71.53324
76.74732
77.00000
77.25669
103.11048
103.17465
126.48958
126.57381
128.04177
128.15006
128.21022
128.27841
128.43884
130.24371
130.60469
130.80122
130.95363
137.01399
137.08217
139.63306
139.74536
140.47934
140.63576
211.07389
210.49633
PPM

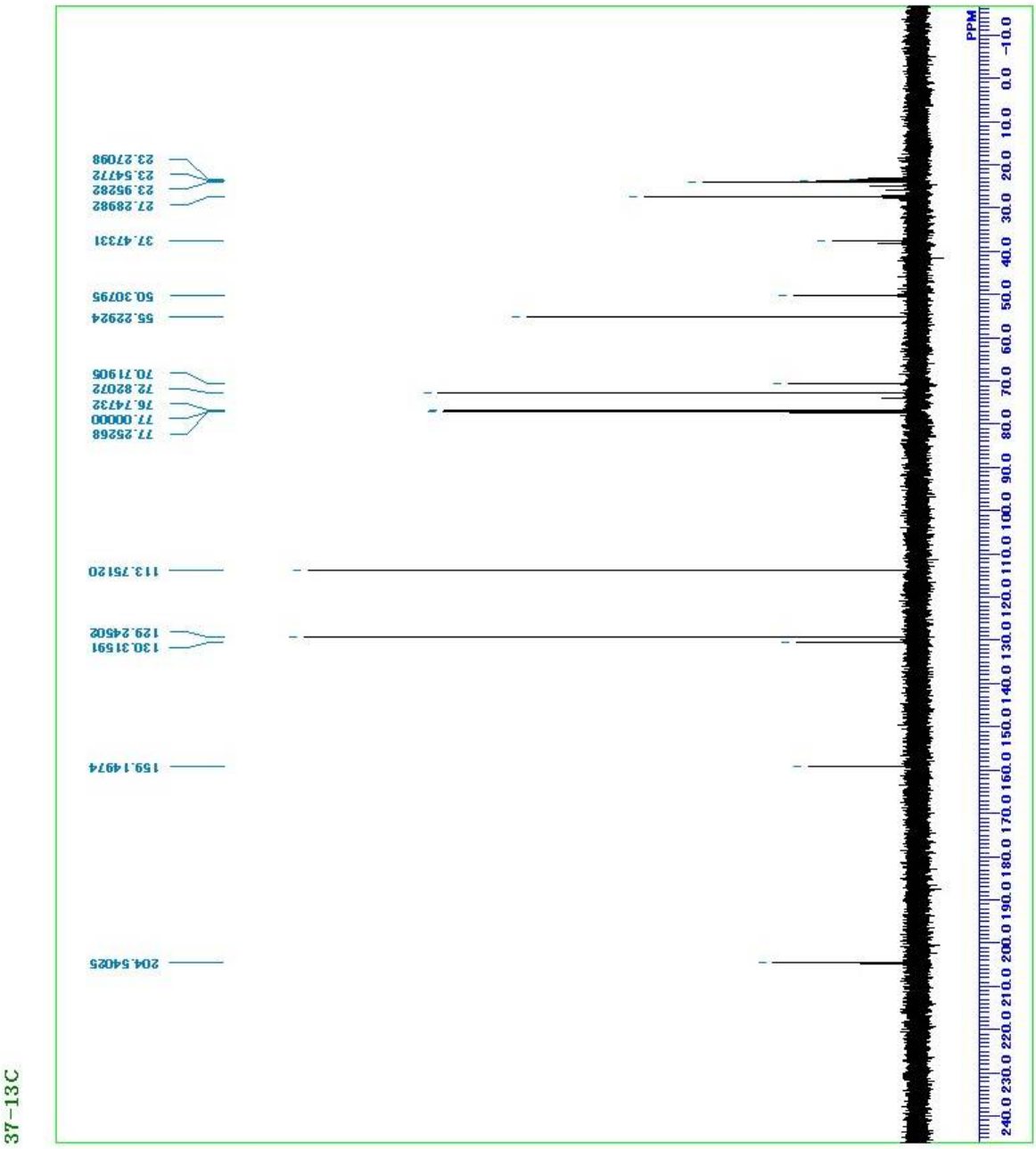
33-13C


OPMB
O
37

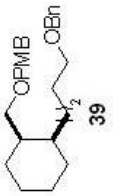

37-1H
PPM
9.95
0.95
0.94
0.95
0.95
3.07
2.00
2.14
2.12
0.90

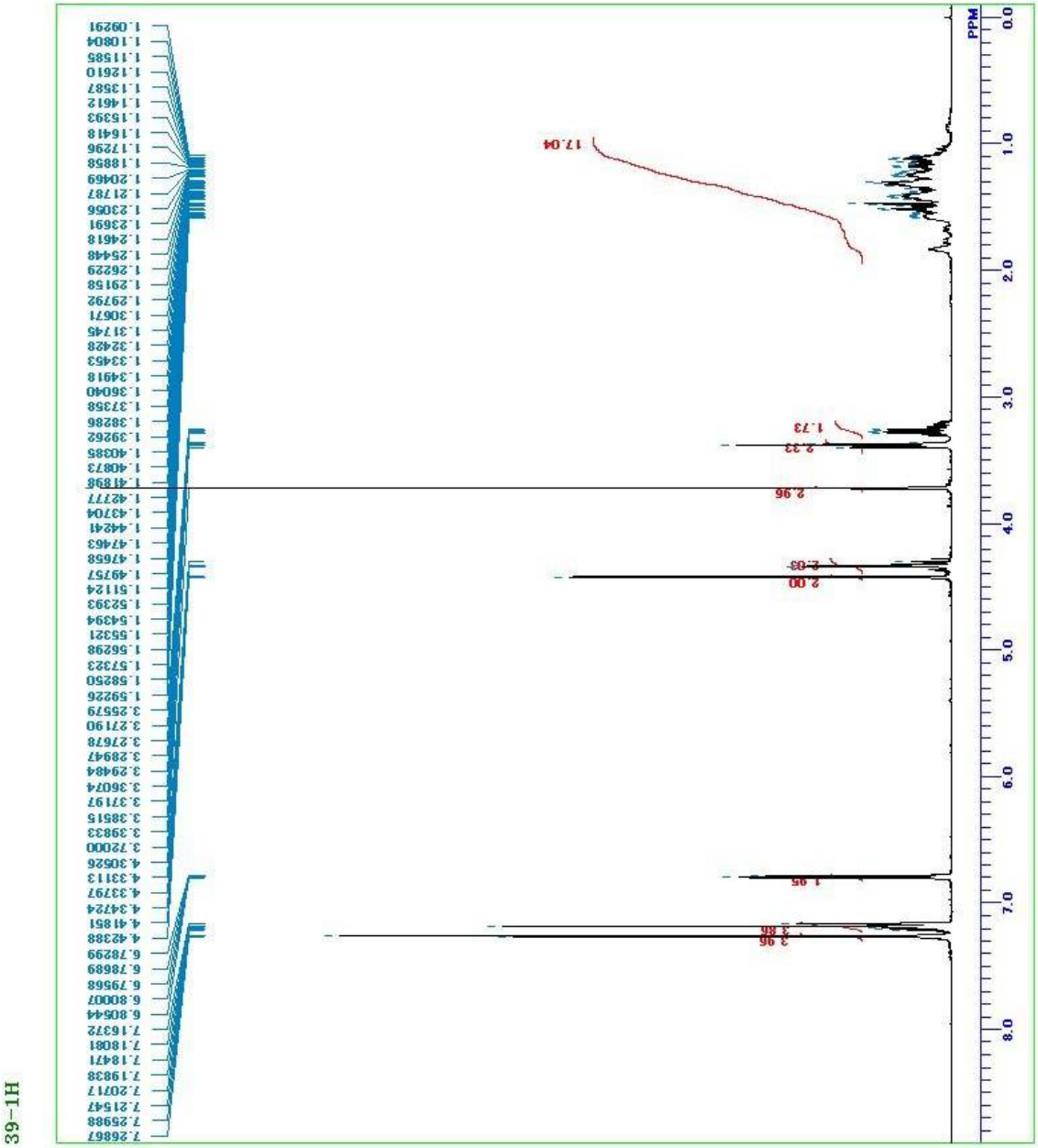

OPMB
O

37


23.27098
23.54772
23.95282
27.28982
37.47331
50.30795
55.22924
70.71905
72.82072
76.74732
77.00000
77.25268
113.75120
129.24502
130.31591
159.14974
204.54025
PPM

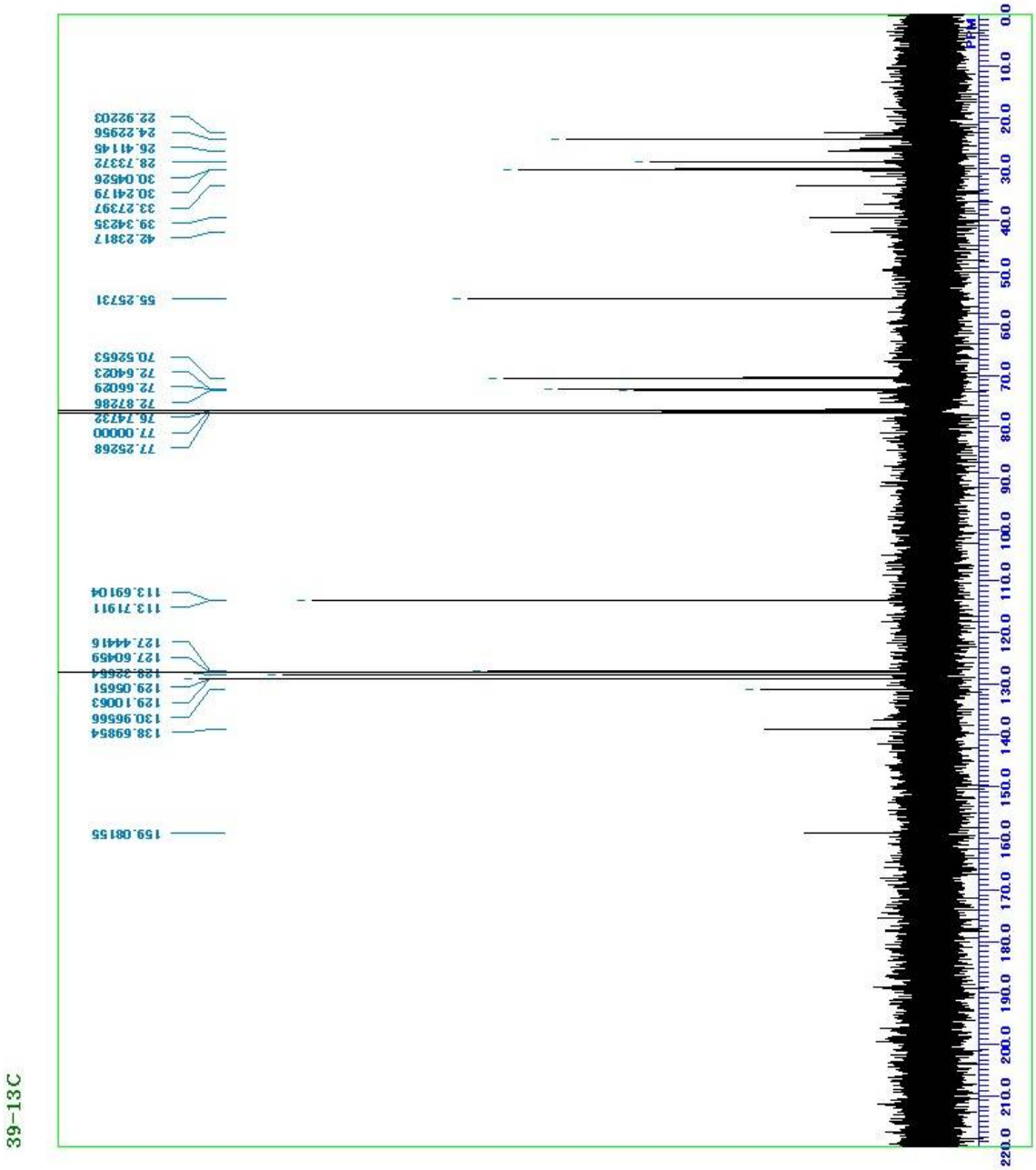
37-13C


OPMB
OBn
39

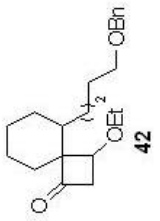

39-1H
PPM
17.04
1.73
2.33
2.96
2.03
2.00
1.95
3.86
3.96

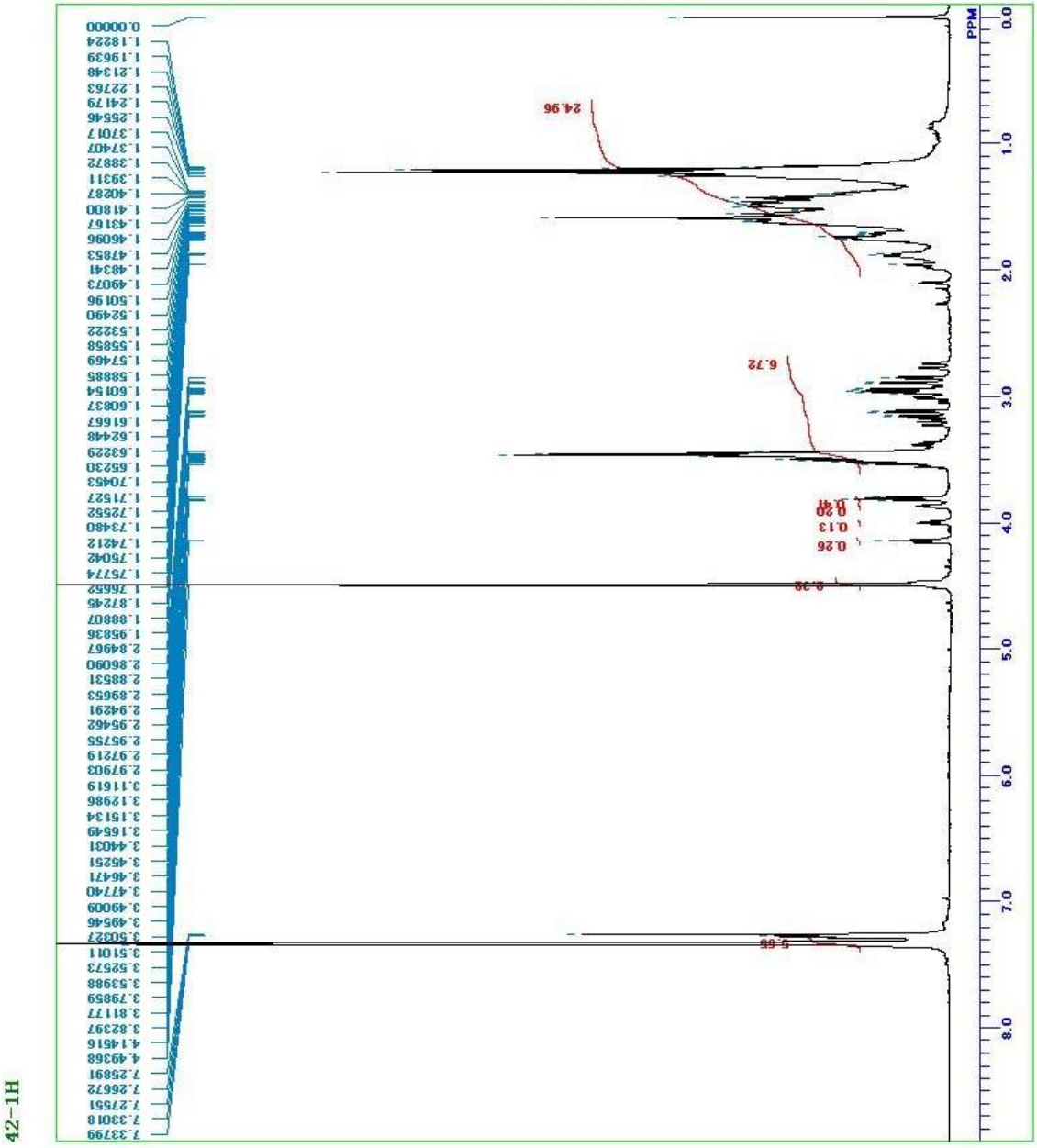

OPMB
OBn
2

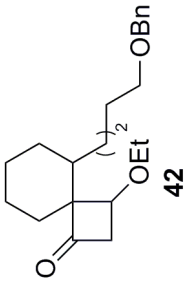
39


22.92203
24.22956
26.41146
28.73372
30.04526
30.24179
33.27397
39.34235
42.23817
55.25731
70.52653
72.64023
72.66029
72.87286
76.74732
77.00000
77.25268
113.69104
113.71911
127.44416
127.60459
128.22664
129.05651
129.10063
130.96566
138.69854
159.08155
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
220.0

39-13C


OBn
OEt
42


42-1H
PPM
24.96
6.72
0.26
0.13
0.20
0.41
0.38
5.66



42