

**Cyclization by Intramolecular Carbolithiation of Alkyl- and
Vinylolithiums Prepared by the Action of Aromatic Radical-anions on
Phenyl Thioethers. High Stereoselectivity in the Cyclization
Accelerated by an Allylic Lithium Oxyanion**

Kai Deng, Ahlem Bensari-Bouguerra, Joseph Whetstone and Theodore Cohen*

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

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General Experimental Procedures.

All reactions were performed under an argon atmosphere in oven-dried (110 °C) flasks and standard precautions against moisture were taken. A dry ice/acetone bath was used to obtain a temperature of -78 °C. An ice/water bath was used to obtain 0 °C. A dry ice/acetonitrile bath was used to obtain -45 °C. Silica gel 60 (40-60 μm) was used for flash column chromatography. Thin-layer chromatography was performed on glass supported 250- μm silica GF plates. Visualization of TLC plates was accomplished with one or more of the following: 254 nm UV light; 7% phosphomolybdic acid in ethanol; 5% anisaldehyde in ethanol containing 5% sulfuric acid and a trace amount of acetic acid; and/or aqueous KMnO_4 (1%) with NaOH (0.1%) and K_2CO_3 (6%). Anhydrous magnesium sulfate was used as the drying reagent. Commercial solvents and reagents were used as received with the following exceptions. Tetrahydrofuran (THF) and diethyl ether were distilled over sodium benzophenone ketyl. CH_2Cl_2 and CH_3CN were distilled over CaH_2 . Benzene was dried over melting sodium. IR spectra were recorded on an FTIR spectrometer with peaks reported in cm^{-1} . Most ^1H and ^{13}C NMR spectra were recorded at 300 MHz for ^1H and 75 MHz for ^{13}C at 22 °C unless otherwise indicated. Chemical shift data are reported in unit of δ (ppm) using CHCl_3 as internal standard: $\delta = 7.27$ for ^1H NMR spectra and CDCl_3 as $\delta = 77.09$ for ^{13}C NMR spectra unless indicated otherwise. Multiplicities are given as s (singlet), d (double), t (triplet), q (quartet), m (multiplet), and br (broad). Coupling constants, J , are reported in Hz. Low and high-resolution mass spectra were recorded in EI mode.

Lithium 4, 4'-di-*t*-butylbiphenylide (LDBB)

To a flame-dried three-neck round-bottom flask, equipped with a glass-coated stirring bar, argon inlet and rubber septum was added 4,4'-di-*tert*-butylbiphenyl (DBB) (4.00 g, 15.0 mmol). Lithium ribbon was prepared by scraping the dark oxide coating off of the surface while it was immersed in mineral oil. The shiny metal was dipped in hexanes in order to remove the oil and then weighed (104 mg, 15.0 mmol) in a tared beaker containing mineral oil. The metal was sliced into small pieces while it was still immersed in mineral oil. The lithium pieces were dipped again in hexane prior to addition to the flask. THF (40 mL) was added to the DBB/lithium mixture via syringe. The reaction mixture was stirred at room temperature for about 5 min until a dark-blue color appeared on the lithium surface and it was then allowed to cool to 0 °C and stirred for 5 h. The resulting dark-blue solution of LDBB was ready for use in reductive lithiation (~ 7 mmol scale).

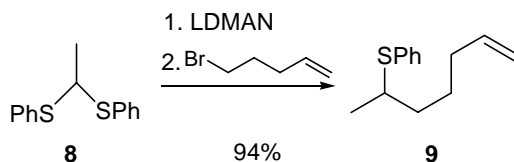
Lithium 1-(dimethylamino)naphthalenide (LDMAN)

To a flame-dried three-neck flask, equipped with a glass-coated stirring bar, rubber septum and argon inlet, was added 1-(dimethylamino)naphthalene (DMAN) (3.8 mL, 23 mmol) and 45 mL of THF. The solution was cooled to –55 °C. Lithium ribbon (161 mg, 23.0 mmol) was prepared and weighed by the method described for the preparation of LDBB. The lithium pieces were added while the flask was rapidly purged with argon. The reaction mixture was stirred at –55 °C for 5 h. The resulting dark-green solution of LDMAN was ready for use in reductive lithiation (~ 10 mmol scale).

Vynllithium

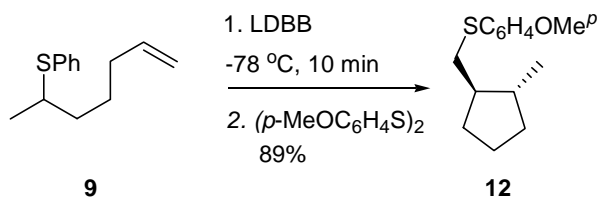
The following is a representative procedure for the preparation of vinyl lithium.

To a solution of vinyl bromide (0.74 mL, 10.2 mmol) in anhydrous ether (6 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-butyllithium (20.4 mmol, 12.0 mL). The resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h and then slowly warmed to $0\text{ }^{\circ}\text{C}$. After the mixture had been stirred at $0\text{ }^{\circ}\text{C}$ for 20 min, the vinyl lithium was ready to use.

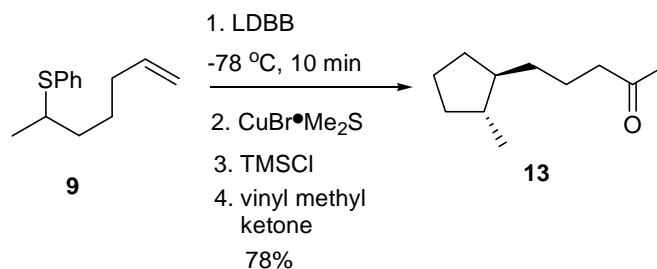


6-Phenylthio-1-heptene (9) A solution of LDMAN (54.5 mmol, prepared from 8.3 mL DMAN, and 378 mg Li in 60 mL THF) was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with 1,1-bis(phenylthio)ethane (6.46 g, 26.3 mmol). The dark green color of LDMAN turned to dark red. After 10 min of stirring, 1-bromo-4-pentene (3.11 mL, 26.3 mmol) was added. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h and then the temperature was raised to $-20\text{ }^{\circ}\text{C}$. After the solution had been stirred at $-20\text{ }^{\circ}\text{C}$ for 30 min, saturated NaHCO_3 solution (40 mL) was added. The reaction mixture was extracted with ether (70 mL \times 3). The combined organic layer, after being washed with 5% HCl (to remove DMAN) and then brine, was dried over anhydrous MgSO_4 , filtered and evaporated in vacuo. The resulting residue was purified by flash-column chromatography with hexane to give 5.04 g (93% yield) of **9** as a colorless oil. ^1H NMR: δ 7.36-7.20 (m, 5 H, aromatic), 5.77 (m, 1 H), 4.98 (d, 1 H, $J = 16.2\text{ Hz}$), 4.93 (d, 1 H, $J = 10.5\text{ Hz}$), 3.19 (m, 1 H), 2.07-2.00 (m, 2 H), 1.70-1.46 (m, 4 H), 1.26 (d, 3 H, $J = 6.9\text{ Hz}$). ^{13}C NMR: δ 138.6, 135.6, 132.0 (2 C), 128.9 (2 C), 126.7, 114.9, 43.3, 36.2, 33.7, 26.4, 21.3. IR ν_{max} (thin film): 3074, 2974, 2931, 2860, 1640, 1584, 1479, 1439, 912, 747, 692 cm^{-1} ; MS (EI) m/z (relative intensity):

206 (M^+ , 18), 137 (30), 110 (100), 96 (31), 81 (26), 55 (21); HRMS: exact mass calcd for $C_{13}H_{18}S$ (M^+): 206.1129, found 206.1137.

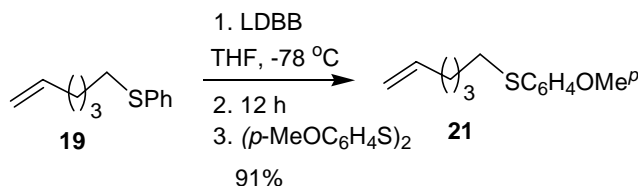


***trans*-2-Methylcyclopentylmethylthio)-4-methoxybenzene (12)** Freshly prepared LDBB (3.8 mmol in 10 mL of THF) at $-78\text{ }^{\circ}\text{C}$ was cannulated to a flask containing compound **9** (315 mg, 1.53 mmol) in 10 mL of THF at $-78\text{ }^{\circ}\text{C}$ under argon. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 10 min and then quenched with di-*p*-methoxyphenyl disulfide (640 mg, 2.30 mmol) in 5 mL of THF. The reaction mixture was extracted with ether (20 mL \times 3). The combined organic layer, after being washed with brine, was dried over anhydrous MgSO_4 , filtered and evaporated in vacuo. The resulting residue was purified by flash-column chromatography with 1% ethyl acetate in hexane to give 320 mg (89% yield) of **12** as a yellow oil. ^1H NMR: δ 7.40 (d, 2 H, $J = 9.6\text{ Hz}$), 6.85 (d, 2 H, $J = 9.6\text{ Hz}$), 3.80 (s, 3 H), 3.05 (dd, 1 H, $J = 12.3\text{ Hz}$, 4.6 Hz), 2.68 (dd, 1 H, $J = 12.3\text{ Hz}$, 8.6 Hz), 1.93 (m, 1 H), 1.83 (m, 1 H), 1.60-1.20 (m, 6 H), 0.98 (d, 3 H, $J = 6.3\text{ Hz}$). ^{13}C NMR: δ 158.6, 132.5 (2 C), 127.8, 114.6 (2 C), 55.3, 47.1, 41.1, 40.3, 34.9, 32.3, 23.7, 19.6. IR ν_{max} (thin film): 2951, 2867, 2835, 1593, 1494, 1462, 1284, 1244, 1180, 1034, 825 cm^{-1} ; MS (EI) m/z (relative intensity): 236 (M^+ , 74), 140 (100), 125 (20), 96 (9), 81 (8), 55 (17); HRMS: exact mass calcd for $C_{14}H_{20}OS$ (M^+): 236.1235, found 236.1234.

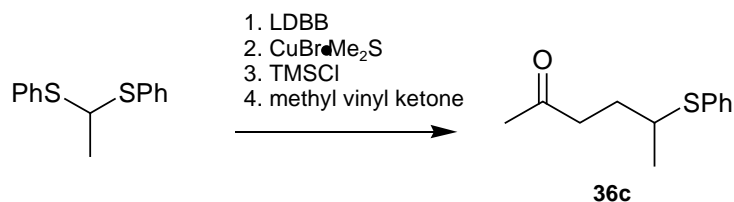


5-(*trans*-2-Methylcyclopentyl)pentan-2-one (13) Freshly prepared LDBB (3.4 mmol in 10 mL of THF) at $-78\text{ }^{\circ}\text{C}$ was cannulated to a flask containing compound **9** (278 mg, 1.35 mmol) in 10 mL THF at $-78\text{ }^{\circ}\text{C}$ under argon. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 15 min and then CuBr•Me₂S (417 mg, 2.02 mmol) was added. After the resulting mixture had been stirred for 3 h at $-78\text{ }^{\circ}\text{C}$, a solution of TMSCl (0.43 mL, 3.22 mmol) in 4 mL of THF was added followed by dropwise addition of a solution of methyl vinyl ketone (0.17 mL, 2.1 mmol) in 4 mL of THF. The resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 12 h. After the addition of 20 mL of 5% NaOH and 1 mL of 40% aqueous *n*-Bu₄NOH, the reaction mixture was allowed to warm to $0\text{ }^{\circ}\text{C}$. It was further stirred at room temperature for 1 h in order to hydrolyze all of the silyl enol ether to the corresponding ketone. Then the reaction mixture was filtered through Celite and extracted with ether (20 mL \times 3). The combined organic layer was dried over anhydrous MgSO₄, filtered through cotton and evaporated in vacuo. The residue was purified by flash-column chromatography (5% ethyl acetate) to give 176 mg (78% yield) of **13** as a yellow oil. IR ν_{max} (thin film): 2950, 2867, 1718, 1459, 1412, 1363, 1226, 1166 cm^{-1} . ¹H NMR: δ 2.46-2.41 (m, 2 H), 2.15 (s, 3 H), 1.90-1.70 (m, 2 H), 1.70-1.40 (m, 6 H), 1.30-1.0 (m, 4 H), 0.96 (d, 3 H, $J = 9.6\text{ Hz}$). ¹³C NMR: δ 209.1, 47.5, 44.1, 40.6, 34.8, 34.3, 32.3, 29.8, 23.5, 23.4, 19.4. MS (EI) m/z (relative intensity): 168 (M^+ , 4), 150 (4), 121

(6), 108 (36), 84 (50), 71 (34), 67 (24), 58 (100), 55 (43); HRMS: exact mass calcd for $C_{11}H_{20}O$ (M^+): 168.1514, found 168.1509.

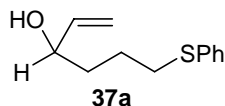


6-Lithio-1-hexene and its attempted cyclization in THF at $-78\text{ }^{\circ}\text{C}$ Freshly prepared LDBB (3.6 mmol in 10 mL of THF) at $-78\text{ }^{\circ}\text{C}$ was cannulated to a flask containing compound **19** (279 mg, 1.45 mmol) in 10 mL THF at $-78\text{ }^{\circ}\text{C}$ under argon. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 12 h before the addition of di-*p*-methoxyphenyl disulfide (650 mg, 2.3 mmol) in 5 mL of THF. After the mixture had been stirred for an additional 30 min, saturated NaHCO_3 solution (20 mL) was added and the mixture was allowed to warm to room temperature. The reaction mixture was extracted with ether (20 mL \times 3). The combined organic layer, after being washed with 5% NaOH (20 mL \times 3), was dried, filtered and evaporated in vacuo. The resulting residue was purified by flash-column chromatography (1% ethyl acetate in hexane) to give 294 mg (91% yield) of **21** as a colorless oil. ^1H NMR: δ 7.37 (d, 2 H, $J = 8.7$ Hz), 6.87 (d, 2 H, $J = 8.7$ Hz), 5.81 (m, 1 H), 5.05-4.95 (m, 2 H), 3.82 (s, 3 H), 2.85 (t, 3 H, $J = 6.9$ Hz), 2.09 (m, 2 H), 1.61 (m, 2 H), 1.53 (m, 2 H); ^{13}C NMR: δ 158.9, 138.6, 133.1 (2 C), 126.9, 114.8, 114.6 (2 C), 55.4, 35.8, 33.4, 28.9, 28.0.

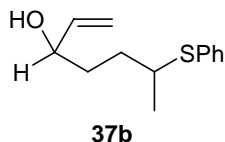


5-Phenylthiohexan-2-one (36c) To a THF solution (64 mL) of LDBB (25.6 mmol) at –78 °C was added 1,1-bis(phenylthio)ethane (2.78 g, 11.3 mmol) in 10 mL of THF. After the reaction mixture had been stirred at –78 °C for 10 min, CuBr•Me₂S (3.26 g, 15.8 mmol) was added. The formation of cuprate was insured by stirring the reaction mixture for 3 h at –78 °C. Then, a solution of TMSCl (3.0 mL, 23.5 mmol) in 7.5 mL of THF was added followed by dropwise addition of methyl vinyl ketone (1.21 mL, 14.6 mmol). After the resulting mixture was stirred for 12 h at –78 °C, aqueous 5% NaOH (40 mL) and 40% aqueous *n*-Bu₄NOH (1 mL) were added and the reaction mixture was allowed to warm to 0 °C. It was stirred at room temperature for 1 h in order to hydrolyze all of the silyl enol ether to ketone product. The mixture was filtered through Celite and extracted with ether (60 mL x 3). The combined organic layer was dried over anhydrous MgSO₄ and filtered through a plug of cotton and evaporated in vacuo. The residue was purified by flash-column chromatography to give 1.79 g (77%) of **36c** as a yellow oil. ¹H NMR (CDCl₃): δ 7.43-7.24 (m, 5 H, aromatic), 3.25 (m, 1 H), 2.68 (t, 2 H, J = 7.7 Hz), 2.15 (s, 3 H), 1.90-1.79 (m, 2 H), 1.30 (d, 3 H, J = 6.9 Hz); ¹³C NMR (CDCl₃): δ 208.4, 134.9, 132.2 (2C), 129.0 (2C), 127.1, 43.0, 40.9, 30.3, 30.2, 21.6; HRMS: exact mass calcd for C₁₂H₁₆OS (M⁺): 208.0922, found 208.0930.

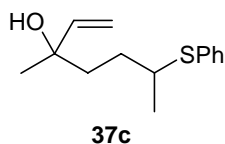
Compounds **37a**, **37b**, **37c**, **37d** and **37e** were prepared by vinyl lithium addition to the corresponding ketones or aldehydes, similar to the procedure described for the preparation of compound **23** in the Experimental Section of the paper.



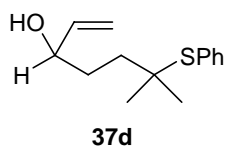
6-(Phenylthio)hex-1-en-3-ol (37a) ^1H NMR (CDCl_3): δ 7.34-7.16 (m, 5 H, aromatic), 5.83 (ddd, 1 H, $J = 16.6, 10.4, 6.2$ Hz), 5.20 (dd, 1 H, $J = 16.6, 2.6$ Hz), 5.09 (dd, 1 H, $J = 10.4, 2.6$ Hz), 4.09 (m, 1 H), 2.94 (t, 2 H, $J = 7.1$ Hz), 1.98 (br, 1 H, -OH), 1.82-1.60 (m, 4 H); ^{13}C NMR (CDCl_3): δ 141.0, 136.8, 129.1 (4 C), 125.9, 115.0, 72.7, 36.0, 33.6, 25.2; MS (EI) m/z (relative intensity): 208 (M^+ , 8), 190 (21), 149 (3), 136 (93), 110 (83), 98 (35), 77 (41), 70 (62), 65 (13), 57 (36); HRMS: exact mass calcd for $\text{C}_{12}\text{H}_{16}\text{OS}$ (M^+): 208.0922, found 208.0917.



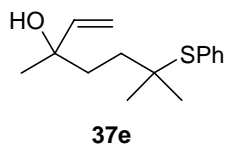
6-(Phenylthio)hept-1-en-3-ol (37b) Two diastereomers were obtained in an approximately 1:1 ratio. ^1H NMR: δ 7.46-7.25 (m, 5 H, aromatic), 5.87 (m, 1 H), 5.26 (d, 1 H, $J = 13.8$ Hz), 5.15 (d, 1 H, $J = 10.4$ Hz), 4.13 (m, 1 H), 3.27 (m, 1 H), 2.01 (s, 1 H, -OH), 1.80-1.60 (m, 4 H), 1.26 (d, 3 H, $J = 6.6$ Hz). diastereomer 1: ^{13}C NMR δ 141.0, 135.2, 132.1 (2 C), 129.0 (2 C), 126.8, 115.0, 73.1, 43.5, 34.4, 32.45, 21.42; diastereomer 2: ^{13}C NMR δ 141.0, 135.2, 132.1 (2 C), 129.0 (2 C), 126.8, 115.0, 73.0, 43.4, 34.2, 32.3, 21.36; MS m/z (relative intensity): 222 (M^+ , 19), 150 (63), 137 (42), 123 (23), 110 (100), 95 (35), 83 (24), 77 (28), 70 (54), 65 (30), 57 (51); HRMS: exact mass calcd for $\text{C}_{13}\text{H}_{18}\text{OS}$ (M^+): 222.1078, found 222.1081.



3-Methyl-6-(phenylthio)hept-1-en-3-ol (37c) Two diastereomers were obtained in an approximately 1:1 ratio. ^1H NMR: δ 7.42-7.20 (m, 5 H, aromatic), 5.86 (dd, $J = 17.6$, 10.9 Hz), 5.22 (d, $J = 17.6$ Hz), 5.07 (d, 1 H, $J = 10.9$ Hz), 3.20 (m, 1 H), 1.78-1.58 (m, 4 H), 1.46 (s, 1 H, -OH), 1.29 (s, 3 H), 1.28 (d, 3 H, $J = 6.7$ Hz). ^{13}C NMR diastereomer 1: δ 114.9, 135.3, 132.1 (2 C), 128.9 (2 C), 126.8, 112.1, 73.2, 43.85, 39.5, 30.91, 28.1, 21.5; diastereomer 2: δ 144.9, 135.3, 132.1 (2 C), 128.9 (2 C), 126.8, 112.1, 73.2, 43.78, 39.4, 30.85, 27.9, 21.4. MS m/z (relative intensity): 236 (M^+ , 47), 219 (22), 150 (35), 137 (38), 127 (21), 110 (70), 109 (100), 81 (24), 71 (72), 67 (46), 55 (32); HRMS: exact mass calcd for $\text{C}_{14}\text{H}_{20}\text{OS}$ (M^+): 236.1235, found 236.1235.

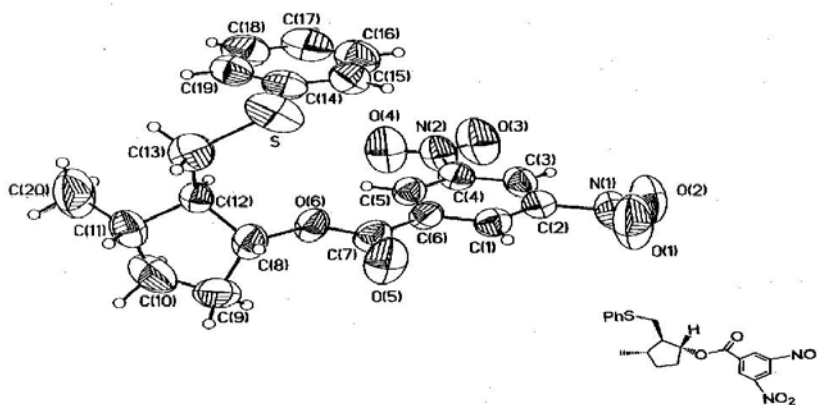
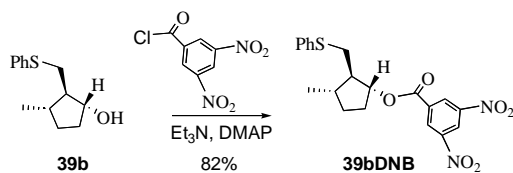


6-Methyl-6-(phenylthio)hept-1-en-3-ol (37d) ^1H NMR: δ 7.60-7.30 (m, 5 H, aromatic), 5.90 (m, 1 H), 5.25 (d, 1 H, $J = 17.1$ Hz), 5.13 (d, 1 H, $J = 10.4$ Hz), 4.10 (m, 1 H), 1.82-1.46 (m, 4 H), 1.26 (s, 6 H); ^{13}C NMR: δ 141.3, 137.6 (2 C), 132.2, 128.8, 128.6 (2 C), 114.8, 73.3, 49.1, 37.9, 32.4, 29.1, 28.9; IR ν_{max} (neat): 3377(br), 3074, 2959, 2862, 1474, 1438, 1364, 1025, 993, 923, 750, 705, 695 cm^{-1} ; MS (EI) m/z (relative intensity): 236 (M^+ , 2), 218 (10), 149 (62), 126 (61), 109 (100), 93 (29), 81 (39), 67 (96), 55 (65); HRMS: exact mass calcd for $\text{C}_{14}\text{H}_{20}\text{OS}$ (M^+): 236.1235, found 236.1230.



3,6-Dimethyl-6-phenylthiohept-1-en-3-ol (37e) ^1H NMR: δ 7.58-7.34 (m, 5 H, aromatic), 5.92 (dd, 1 H, $J = 17.5, 10.8$ Hz), 5.25 (d, 1 H, $J = 17.5$ Hz), 5.10 (d, 1 H, $J = 10.8$ Hz), 1.82 (m, 2 H), 1.58 (m, 2 H), 1.34 (s, 3 H), 1.26 (s, 6 H); ^{13}C NMR: δ 145.1, 137.6 (2 C), 132.3, 128.8, 128.6 (2 C), 112.0, 73.2, 49.1, 37.2, 36.3, 29.14, 29.07, 28.1; MS m/z (relative intensity): 250 (M^+ , 20), 233(7), 141(96), 123(45), 110(65), 95(36), 86(65), 81(57), 71(100), 55(61); HRMS: exact mass calcd for $\text{C}_{15}\text{H}_{22}\text{OS}$ (M^+): 250.1391, found 250.1387.

Stereochemistry determination of 39b by X-ray crystal structure analysis of the corresponding 3,5-dinitrobenzoate ester is shown below.

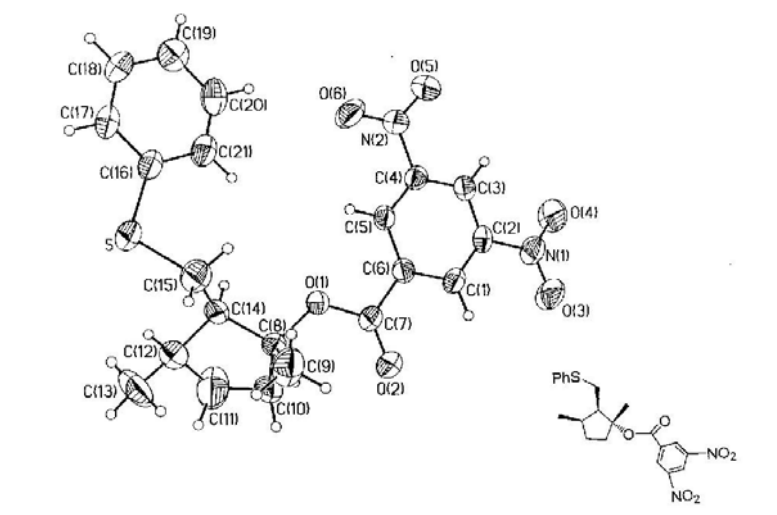
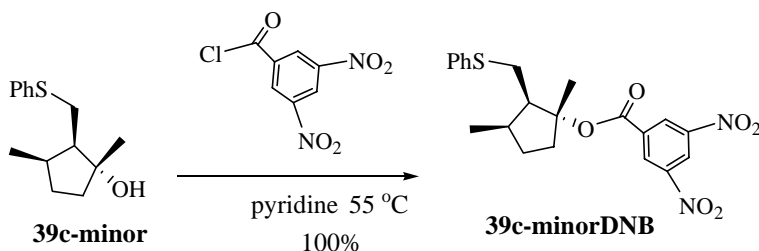


3,5-Dinitrobenzoic acid 3-methyl-2-phenylsulfanylmethyl-cyclopentyl ester

(39bDNB) To a solution of 3,5 dinitrobenzoyl chloride (208 mg, 0.90 mmol, 2.00

equiv.) in 4 mL of CH₂Cl₂, 4-(dimethylamino)pyridine (DMAP, 1.7 mg, 0.014 mmol, 0.03 equiv.) was added. The reaction mixture was stirred at rt for 5 min before the addition of the mixture of triethylamine (0.13 mL, 0.90 mmol) and alcohol **39b** (100 mg, 0.45 mmol). After the resulting mixture had been stirred at room temperature for 12 h, 10 mL of water was added. The reaction mixture was extracted with Et₂O (20 mL × 3). The combined organic layer, after being washed successively with 1 N H₂SO₄ (10 mL) and water (10 mL), was dried over MgSO₄, filtered through cotton and evaporated in vacuo. The resulting residue was purified by column chromatography (10% ethyl acetate in hexane) to give 166 mg of the title compound (82% yield) as a yellow solid. The product was crystallized from a mixed solvent of CH₂Cl₂ and hexane. IR (neat): 3101, 2955, 2871, 1728, 1544, 1344, 1277, 1169, 730, 721, 691. ¹H NMR: 9.20 (m, 1 H), 9.08 (m, 2 H), 7.28-7.12 (m, 5 H), 5.34 (m, 1 H), 3.25 (dd, J = 12.9, 5.1 Hz, 1 H), 3.01 (dd, J = 12.9, 8.0 Hz, 1 H), 2.18 – 1.80 (m, 5 H), 1.53 (m, 1 H), 1.16 (d, J = 6.4 Hz); ¹³C NMR: 162.3, 148.7, 136.6, 134.4, 129.5, 129.1, 128.9, 126.1, 122.3, 83.5, 52.1, 38.8, 35.9, 32.4, 31.5, 19.5; MS (EI) *m/z* (relative intensity): 416 (M⁺, 31), 195 (30), 149 (23), 123 (26), 110 (100), 95 (70); HRMS (EI) calcd for C₂₀H₂₀N₂O₆S (M⁺) 416.1042 found 416.1047.

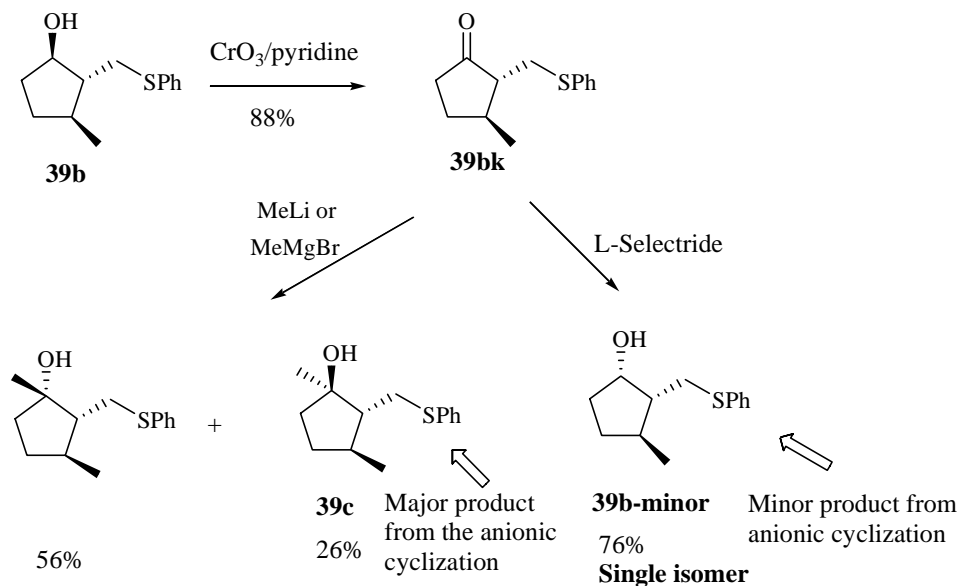
Stereochemistry determination of **39c-minor** by X-ray crystal structure analysis of the corresponding 3,5-dinitrobenzoate ester is shown below.



3,5-Dinitro-benzoic acid 1, 3-dimethyl-2-phenylsulfanylmethylcyclopentyl ester (39c-minorDNB) To a stirred solution of alcohol **39c-minor** (27 mg, 0.11 mmol) in 2 mL pyridine at room temperature was added 3,5 dinitrobenzoyl chloride (53 mg, 0.22 mmol, 2.0 equiv.), and the resulting mixture was heated at 55 °C for 12 h. After the reaction mixture had been cooled to room temperature, it was diluted with water (3 mL) and extracted with ether (5 mL \times 3). The combined organic layer was washed successively with 1 N H₂SO₄ (10 mL) and water (10 mL). After it was dried over MgSO₄ and filtered, the solvent was removed by rotary evaporation. The resulting residue was purified by column chromatography (10% ethyl acetate in hexane) to give 49 mg of the

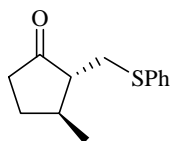
title compound (yield 100%) as a yellow solid. The product was crystallized from CH₂Cl₂ and hexane. IR (neat): 3100, 2959, 2923, 2874, 1724, 1544, 1344, 1285, 1168, 730, 720, 691; ¹H NMR: 9.20 (t, J = 1.8 Hz, 1 H), 9.12 (d, J = 1.8 Hz, 2 H), 7.54-7.17 (m, 5 H), 3.38 (dd, J = 12.3, 6.0 Hz, 1 H), 2.96 (dd, J = 12.2, 8.9 Hz, 1 H), 2.64 (m, 1 H), 2.52 (m, 1 H), 2.28 (m, 2 H), 2.08 (m, 1 H), 1.70 (s, 3 H), 1.44 (m, 1 H), 1.03 (d, J = 7.2 Hz). ¹³C NMR: 161.7, 148.7, 136.6, 135.5, 129.5, 129.2 (4 C), 126.3, 122.2, 93.6, 50.7, 38.3, 33.7, 31.1, 31.0, 21.9, 16.0. MS (EI) *m/z* (relative intensity) 430 (M⁺, 42), 347 (11), 245 (17), 218 (43), 123 (38), 109 (100), 93 (64), 67 (49); HRMS (EI) calcd for C₂₁H₂₂N₂O₆S (M⁺) 430.1199, found 430.1197.

Evidence for the stereochemistry of **39b-minor** and **39c**

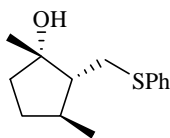


Compound **39b** (stereochemistry was known by X-ray analysis shown above) was oxidized to the corresponding ketone **39bk**. Reduction of the ketone **39bk** by L-Selectride gave a single compound, which was **39b-minor**. The addition of MeLi to the ketone gave two compounds as shown and the minor product was **39c**. The stereochemistry of these adducts was assigned on the basis that the addition is expected to

occur from the less hindered face, that is the opposite face of the ring from the phenylthiomethyl group.



***trans*-3-Methyl-2-phenylthiomethyl-cyclopentanone (39bk)** Using a literature ¹ procedure for the oxidation of **39b**, the ketone was isolated as an oil in 88% yield after column chromatography. IR (neat): 3058, 2955, 2925, 2870, 1740, 1582, 1480, 1439, 1155, 740, 691. ¹H NMR: 7.37-6.97 (m, 5 H), 3.33 (dd, J = 12.9, 4.0 Hz, 1 H), 3.07 (dd, J = 12.9, 5.8 Hz, 1 H), 2.48-1.94 (m, 6 H), 1.45 (s, 3 H), 1.21 (d, J = 8.4 Hz). ¹³C NMR: 218.7, 136.7, 129.5, 129.1, 126.3, 56.2, 38.2, 37.0, 32.4, 29.6, 19.8. HRMS (EI) calcd for C₁₃H₁₆OS (M⁺): 220.0922, found 220.0931.

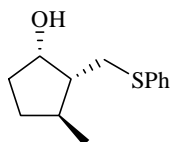


(1S*,2R*,3R*)-1,3-Dimethyl-2-phenylsulfanylmethyl-cyclopentanol² MeMgBr (3.0 M, 0.40 mL, 1.18 mmol) was added dropwise via syringe to a solution of *trans*-3-methyl-2-phenylthiomethyl-cyclopentanone **39bk** (65 mg, 0.295 mmol) in THF (5 mL) at -78 °C. The mixture was stirred at -78 °C for 1 h before it was warmed to 0 °C and quenched with saturated NaHCO₃ solution (10 mL). The resulting mixture was extracted with ether (10 mL × 3). The combined organic layer, after being washed with water (10 mL), was dried over MgSO₄, filtered through cotton and evaporated in vacuo. The residue was purified by column chromatography (10% ethyl acetate in hexanes) to give two products.

¹ Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000-4002.

² "*" Means that the compound is racemic and thus that these are relative configurations.

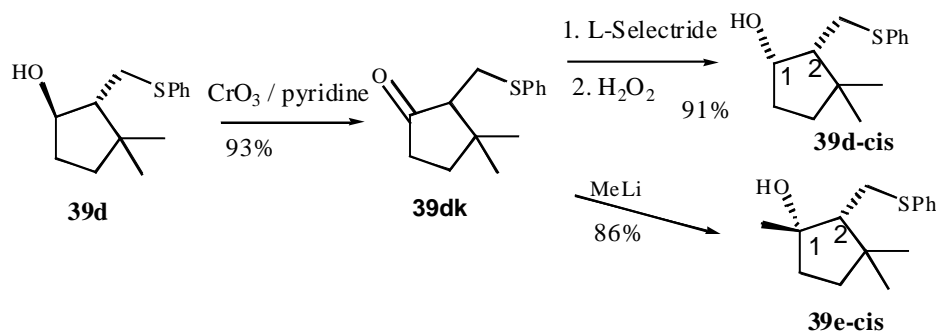
The major product (39 mg, 56%) has the following spectroscopic data: ^1H NMR: δ 7.35-7.04 (m, 5 H), 3.13 (dd, $J = 12.3, 8.8$ Hz, 1 H), 3.03 (dd, $J = 12.4, 5.3$ Hz, 1 H), 1.97-1.68 (m, 5 H), 1.37 (s, 3 H), 1.10 (m, 1 H); ^{13}C NMR: δ 137.3, 129.0, 128.7, 125.9, 80.8, 55.2, 41.3, 39.9, 33.1, 31.6, 29.6, 20.3; The minor product (18 mg, 26%) has completely identical spectra with the alcohol **39c** obtained from the cyclization.



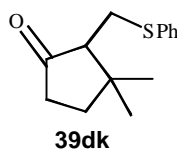
39b-minor

L-Selectride (lithium tri-*sec*-butylborohydride, 1.0 M in THF, 0.20 mL, 0.20 mmol) was added dropwise via syringe to a solution of *trans*-3-methyl-2-phenylthiomethylcyclopentanone **39bk** (22 mg, 0.10 mmol) dissolved in dry THF (10 mL) at $-78\text{ }^{\circ}\text{C}$. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 3 h before it was warmed to room temperature. A solution of NaOH (8 mg, 0.20 mmol) in 1 mL water was added followed by the addition of H_2O_2 (30% aqueous solution, 0.07 mL, 0.6 mmol). After the reaction mixture had been stirred at room temperature for 1 h, it was extracted with ether (10 mL \times 3). The combined organic layer was dried over MgSO_4 , filtered through cotton and evaporated in vacuo. The residue was purified by column chromatography (10% ethyl acetate in hexanes) to give an alcohol (17 mg, 76%) as a single diastereomer, which is completely identical in spectroscopic analysis with the minor product **39c-minor**.

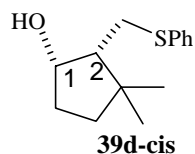
Evidence for the stereochemistry **39d** and **39e** is shown below.



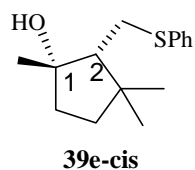
Compound **39d** was oxidized to the corresponding ketone. Reduction of the ketone by L-Selectride gave a single compound **39d-cis**, which was the diastereomer of **39d**. The addition of MeLi to the ketone gave a single compound, **39e-cis**, which was the diastereomer of **39e**. The stereochemistry of these adducts was assigned on the basis that the addition is expected to occur from the less hindered face, that is the opposite face of the ring from the phenylthiomethyl group.



3,3-Dimethyl-2-(phenylthiomethyl)cyclopentanone (39dk) Using a literature¹ procedure for the oxidation, the ketone was isolated as an oil in 93% yield from **39d** after column chromatography (5% ethyl acetate in hexanes). ^1H NMR: δ 7.41-7.08 (m, 5 H), 3.28 (dd, 1 H, $J = 13.3, 5.3$ Hz), 2.69 (dd, 1 H, $J = 13.3, 7.9$ Hz), 2.24-2.08 (m, 3 H), 1.71-1.65 (m, 2 H), 1.23 (s, 3 H), 0.84 (s, 3 H). ^{13}C NMR: δ 218.2, 136.75, 129.1 (2 C), 128.9 (2 C), 126.1, 59.3, 39.8, 35.9, 35.2, 29.3, 29.0, 21.6. HRMS (EI) calcd for $\text{C}_{14}\text{H}_{18}\text{OS}$ (M^+): 234.1078, found 234.1087.

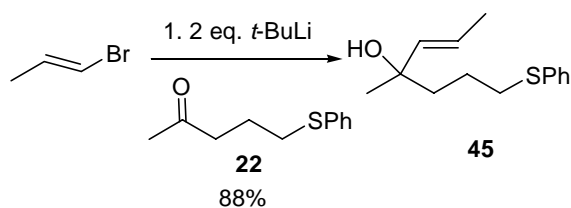


cis-3,3-Dimethyl-2-(phenylthiomethyl)cyclopentan-1-ol (39d-cis) L-Selectride (lithium tri-*sec*-butylborohydride, 1.0 M in THF, 0.60 mL, 0.60 mmol) was added dropwise via syringe to a solution of 3,3-dimethyl-2-(phenylthiomethyl)cyclopentanone **39dk** (71 mg, 0.30 mmol), dissolved in dry THF (10 mL) at -78 °C. The mixture was stirred at -78 °C for 3 h before it was warmed to room temperature. A solution of NaOH (24 mg, 0.60 mmol) in 1 mL water was added followed by the addition of H₂O₂ (30% aqueous solution, 0.20 mL, 1.8 mmol). After the reaction mixture had been stirred at room temperature for 1 h, it was extracted with ether (20 mL × 3). The combined organic extract was dried over MgSO₄, filtered through cotton and evaporated in vacuo. The resulting residue was purified by column chromatography to give 65 mg of **39d-cis** (91% yield) as an oil. ¹H NMR: 7.35-7.16 (m, 5 H), 4.41-4.39 (m, 1 H), 3.03-3.00 (m, 2 H), 1.96 (m, 2 H), 1.62 (m, 3 H), 1.36 (m, 1 H), 0.99 (s, 3 H), 0.96 (s, 3 H). ¹³C NMR: 136.6, 129.1 (4 C), 126.1, 74.0, 53.0, 40.7, 40.5, 32.6, 29.8, 29.3, 23.7.



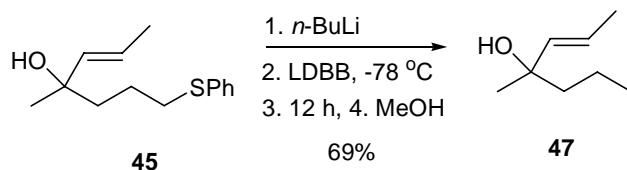
(1S*,2R*)-1,3,3-Trimethyl-2-(phenylthiomethyl)cyclopentan-1-ol (39e-cis) MeLi (1.4 M in ether, 0.73 mL, 1.0 mmol) was added dropwise via syringe to a solution of 3,3-dimethyl-2-(phenylthiomethyl)cyclopentanone **39dk** (48 mg, 0.21 mmol), dissolved in dry ether (5 mL) at -78 °C. The mixture was stirred at -78 °C for 1 h before it was warmed to 0 °C and quenched with water (10 mL). The reaction mixture was extracted

with ether (15 mL \times 3). The combined organic layer, after being washed with water (10 mL), was dried over MgSO₄, filtered and evaporated in vacuo. The resulting residue was purified by column chromatography (10% ethyl acetate in hexane) to give 44 mg of **39e-cis** (86% yield) as a pale yellow oil. ¹H NMR: δ 7.33-7.02 (m, 5 H), 3.00 (m, 2 H), 2.14-1.45 (m, 5 H), 1.40 (s, 3 H), 1.03 (s, 3 H), 0.97 (s, 3 H). ¹³C NMR: δ 137.0, 129.0 (2 C), 128.7 (2 C), 125.9, 80.9, 56.2, 42.2, 40.7, 39.8, 31.6, 30.3, 30.2, 23.2.

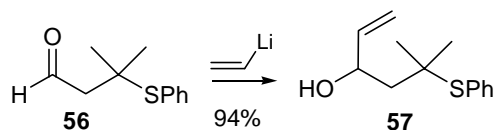


(E)-4-Methyl-7-(phenylthio)hept-2-en-4-ol (45) 1-Propenyllithium was prepared by a procedure similar to that for the preparation of vinylolithium from vinyl bromide. To 1-propenyllithium (8.26 mmol, freshly prepared from trans 1-bromopropene (1.00 g, 8.26 mmol) and *t*-BuLi (9.7 mL, 16.5 mmol) in 10 mL diethyl ether) at -78 °C, was added dropwise ketone **22** (890 mg, 4.60 mmol) in 5 mL of Et₂O via syringe. The reaction mixture was stirred for 2 h at -78 °C and then the temperature was raised to -20 °C and maintained there for 30 min before the addition of 20 mL of saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with ether (30 mL \times 3). The combined organic extract was dried over anhydrous MgSO₄, filtered through cotton and evaporated in vacuo. The residue was purified by flash-column chromatography (10% ethyl acetate in hexane) to give 954 mg (88% yield) of **45** as a yellow oil. ¹H NMR: δ 7.40-7.15 (m, 5 H, aromatic), 5.64-5.37 (m, 2 H), 2.93 (t, 2 H, *J* = 5.4 Hz), 1.70-1.65 (m, 7 H), 1.24 (s, 3 H); ¹³C NMR (CDCl₃) δ 137.9, 136.8, 129.1 (2 C), 129.0 (2 C), 125.9, 123.0, 72.7, 41.7,

34.2, 28.2, 23.9, 17.8. HRMS: exact mass calcd for C₁₄H₂₀OS (M⁺): 236.1235, found 236.1232.

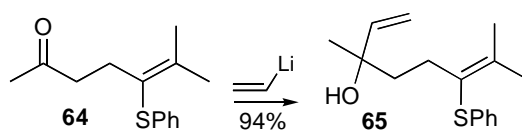


Attempted cyclization of reductive lithiation product 46 (R=H) of (E)-4-methyl-7-(phenylthio)hept-2-en-4-ol (45) in THF at –78 °C To a stirred solution of alcohol **45** (340 mg, 1.44 mmol) in 10 mL of THF at –78 °C under argon, was added *n*-BuLi (1.58 mmol, 1.0 mL of 1.6 M solution) via syringe. Freshly prepared LDBB (3.6 mmol in 10 mL THF) at –78 °C was cannulated to the reaction flask. The reaction mixture was stirred at –78 °C for 12 h before the addition of 15 mL of saturated aqueous NaHCO₃ solution. The reaction mixture was extracted with ether (20 mL × 3). The combined organic layer was dried over MgSO₄, filtered through cotton and evaporated in vacuo. The residue was purified by flash-column chromatography (10% ethyl acetate in hexane) to give 126 mg (69% yield) of the uncyclized protonated product **47** as a yellow oil. ¹H NMR: δ 5.70-5.50 (m, 2 H), 1.70 (d, 3 H, J = 5.2 Hz), 1.50-1.46 (m, 2 H), 1.36-1.30 (m, 2 H), 1.26 (s, 3 H), 0.92 (t, 3 H, J = 7.0 Hz).



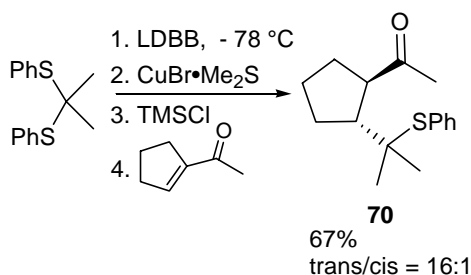
5-Methyl-5-(phenylthio)hex-1-en-3-ol (57) To a freshly prepared vinyl lithium solution (14.0 mmol, prepared from 1.00 mL (14.0 mmol) of vinyl bromide and 16.5 mL of 1.7 M *t*-BuLi in 9 mL anhydrous ether) at –78 °C, was added dropwise 3-methyl-2-butenal **56**

(1.97 g, 10.1 mmol) in 20 mL of THF via syringe. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2 h and then the temperature was raised to $-20\text{ }^{\circ}\text{C}$ and maintained there for 30 min before the addition of 10 mL of saturated aqueous NaHCO_3 . The resulting mixture was extracted with ether (20 mL \times 3). The combined organic layer was dried over anhydrous MgSO_4 , filtered through cotton and evaporated in vacuo. The residue was purified by flash-column chromatography (10 % ethyl acetate in hexane) to afford 2.12 g (94% yield) of **57** as a colorless oil. ^1H NMR: δ 7.60-7.30 (m, 5 H, aromatic), 5.90 (ddd, 1 H, $J = 17.1, 10.3, 5.7$ Hz), 5.31 (d, 1 H, $J = 17.1$ Hz), 5.10 (d, 1 H, $J = 10.3$ Hz), 4.56 (m, 1 H), 1.79 (dd, 1 H, $J = 15.0, 9.3$ Hz), 1.60 (dd, 1 H, $J = 15.0, 2.7$ Hz), 1.39 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR: δ 141.9, 137.6 (2 C), 131.6, 129.1, 128.8 (2 C), 114.1, 70.6, 48.7, 47.8, 30.0, 29.1; IR ν_{max} (neat): 3412 (br), 3074, 2967, 2927, 1473, 1438, 1365, 1127, 1025, 992, 923, 751, 695 cm^{-1} ; MS (EI) m/z (relative intensity): 222 (M^+ , 3), 204 (2), 149 (60), 110 (100), 95 (20), 57 (6); HRMS: exact mass calcd for $\text{C}_{13}\text{H}_{18}\text{OS}$ (M^+): 222.1078, found 222.1073.



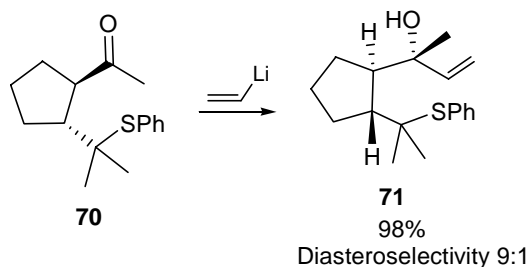
3,7-Dimethyl-6-(phenylthio)octa-1,6-dien-3-ol (65) To a freshly prepared vinyl lithium solution (6.8 mmol, prepared from 0.48 mL (6.8 mmol) of vinyl bromide and 8.0 mL of 1.7 M *t*-BuLi in 5 mL of anhydrous ether) at $-78\text{ }^{\circ}\text{C}$, was added ketone **64** (954 mg, 4.1 mmol) in 10 mL of THF via syringe. The reaction mixture was stirred for 2 h at $-78\text{ }^{\circ}\text{C}$ and then the temperature was raised to $-20\text{ }^{\circ}\text{C}$ and maintained there for 30 min before the addition of 20 mL of saturated aqueous NaHCO_3 solution. The resulting mixture was

extracted with ether (30 mL \times 3). The combined organic extract was dried over anhydrous MgSO_4 , filtered through cotton and evaporated in vacuo. The residue was purified by flash chromatography (10% ethyl acetate in hexane) to give 1.05 g (94% yield) of **65** as yellow oil. ^1H NMR: δ 7.30-7.10 (m, 5 H, aromatic), 5.83 (dd, 1 H, J = 17.4, 10.7 Hz), 5.15 (dd, 1 H, J = 17.4, 1.2 Hz), 4.99 (dd, 1 H, J = 10.7, 1.2 Hz), 2.33-2.25 (m, 2 H), 2.00 (s, 3 H), 1.90 (s, 3 H), 1.75-1.68 (m, 2 H), 1.34 (s, 1 H, -OH), 1.22 (s, 3 H); ^{13}C NMR (CDCl_3): δ 144.8, 140.4, 137.2, 129.0 (2 C), 128.0 (2 C), 125.8, 125.4, 112.0, 73.2, 41.0, 28.7, 27.8, 23.5, 21.1; MS m/z (relative intensity): 262 (M^+ , 64), 245 (26), 206 (37), 191 (100), 135 (49), 119 (88), 110 (52), 91 (55), 81 (51), 71 (85), 55 (43); HRMS: exact mass calcd for $\text{C}_{16}\text{H}_{22}\text{OS}$ (M^+): 262.1391, found 262.1385.



1-[trans-2-(1-Methyl-1-(phenylthio)ethyl)cyclopentyl]-ethan-1-one (70) To a solution of LDBB (15 mmol, in 40 mL of THF) at -78 $^\circ\text{C}$ was added 2,2-bis(phenylthio)propane (1.86 g, 7.14 mmol, in 8 mL of THF). After the mixture had been stirred at -78 $^\circ\text{C}$ for 10 min, $\text{CuBr}\cdot\text{Me}_2\text{S}$ (2.20 g, 10.7 mmol) was added with increased argon flow. After the mixture had been stirred for 3 h at -78 $^\circ\text{C}$ to insure the formation of the cuprate, a solution of TMSCl (1.48 mL, 11.6 mmol) in 4 mL of THF was added followed by dropwise addition of a solution of 1-acetylcyclopentene (0.74 mL, 6.43 mmol) in 3 mL of THF. The resulting mixture was stirred for 12 h at -78 $^\circ\text{C}$. Aqueous 5% NaOH (40 mL)

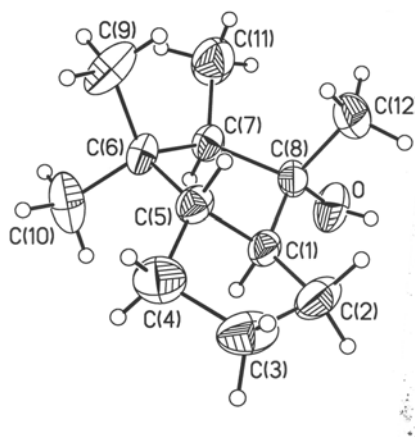
and 40% aqueous *n*-Bu₄NOH (1 mL) were added before the reaction mixture was allowed to warm to 0 °C. It was stirred at room temperature for about 1 h in order to hydrolyze all of the silyl enol ether to the ketone product. The mixture was filtered through Celite and extracted with ether (60 mL × 3). The combined organic layer was dried over MgSO₄, filtered through cotton and evaporated in vacuo. The resulting residue was purified by flash-column chromatography (5% ethyl acetate) to afford 1.18 g (63% yield) of **70** as a pale yellow oil. The corresponding *cis* product (78 mg, 4%) was also obtained. However, only the major *trans* product was fully characterized. ¹H NMR: δ 7.54-7.20 (m, 5 H, aromatic), 3.14 (m, 1 H), 2.77 (m, 1 H), 2.27 (s, 3 H), 2.19 (s, 1 H, -OH), 2.00-1.50 (m, 6 H), 1.19 (s, 3 H), 1.13 (s, 3 H). ¹³C NMR: δ 211.4, 137.8 (2 C), 128.8, 128.6 (2 C), 53.9, 52.5, 50.8, 32.4, 29.6, 29.4, 28.2, 27.2, 26.5. IR ν_{max} (thin film): 3058, 2958, 2868, 1709, 1473, 1439, 1365, 1157, 751, 695 cm⁻¹. MS *m/z* (relative intensity): 262 (M⁺, 13), 152 (100), 135 (20), 110 (95), 95 (52), 81 (26), 67 (79), 55 (39). HRMS: exact mass calcd C₁₆H₂₂OS (M⁺): 262.1391, found 262.1390.



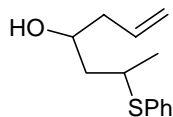
2-[2-(1-methyl-1-(phenylthio)ethyl)cyclopentyl]but-3-en-2-ol (71) To a freshly prepared vinyl lithium solution (5.7 mmol, prepared from 0.40 mL of vinyl bromide (5.7 mmol) and 8.0 mL of 1.7 M *tert*-BuLi in 5 mL anhydrous ether) at -78 °C, was added ketone **70** (0.87 g, 3.3 mmol) in 3 mL of Et₂O. The mixture was stirred for 2 h at -78 °C

and then the temperature was raised to $-20\text{ }^{\circ}\text{C}$ and maintained there for 30 min before the addition of 20 mL of saturated aqueous NaHCO_3 solution. The reaction mixture was extracted with ether ($30\text{ mL} \times 3$). The combined extract was dried over anhydrous MgSO_4 , filtered through cotton and evaporated in vacuo. The resulting residue was purified by flash-column chromatography (10% ethyl acetate in hexane) to give 844 mg (88% yield) of **71** as a colorless oil. Another diastereomer (78 mg, 8%) was also obtained, but only the major product was characterized. ^1H NMR: δ 7.56-7.25 (m, 5 H, aromatic), 5.88 (dd, 1 H, $J = 17.3, 10.7\text{ Hz}$), 5.28 (dd, 1 H, $J = 17.3, 1.5\text{ Hz}$), 5.05 (dd, 1 H, $J = 10.6, 1.5\text{ Hz}$), 2.38 (s, 1 H, -OH), 2.25-2.19 (m, 2 H), 1.95-1.58 (m, 6 H), 1.27 (s, 3 H), 1.18 (s, 3 H), 1.14 (s, 3 H); ^{13}C NMR: δ 143.6, 137.8 (2 C), 132.2, 128.8, 128.5 (2 C), 112.8, 75.5, 54.1, 51.5, 50.1, 30.1, 30.0, 28.1, 27.9, 27.7, 26.7; IR ν_{max} (thin film): 3455 (br), 3050, 2964, 2875, 1473, 1367, 1266, 1112, 1002, 921, 748, 695 cm^{-1} ; MS m/z (relative intensity): 290 (M^+ , 2.4), 272 (0.9), 219 (12), 181 (30), 163 (57), 151 (54), 121 (36), 110 (100), 95 (93), 81 (89), 67 (88), 55 (72); HRMS: exact mass calcd $\text{C}_{18}\text{H}_{26}\text{OS}$ (M^+): 290.1704, found 290.1691.

2,3,4,4-Tetramethylbicyclo[3.3.0]octan-2-ol (72)

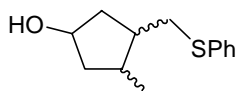


ORTEP drawing for trans-diquinane 72



75

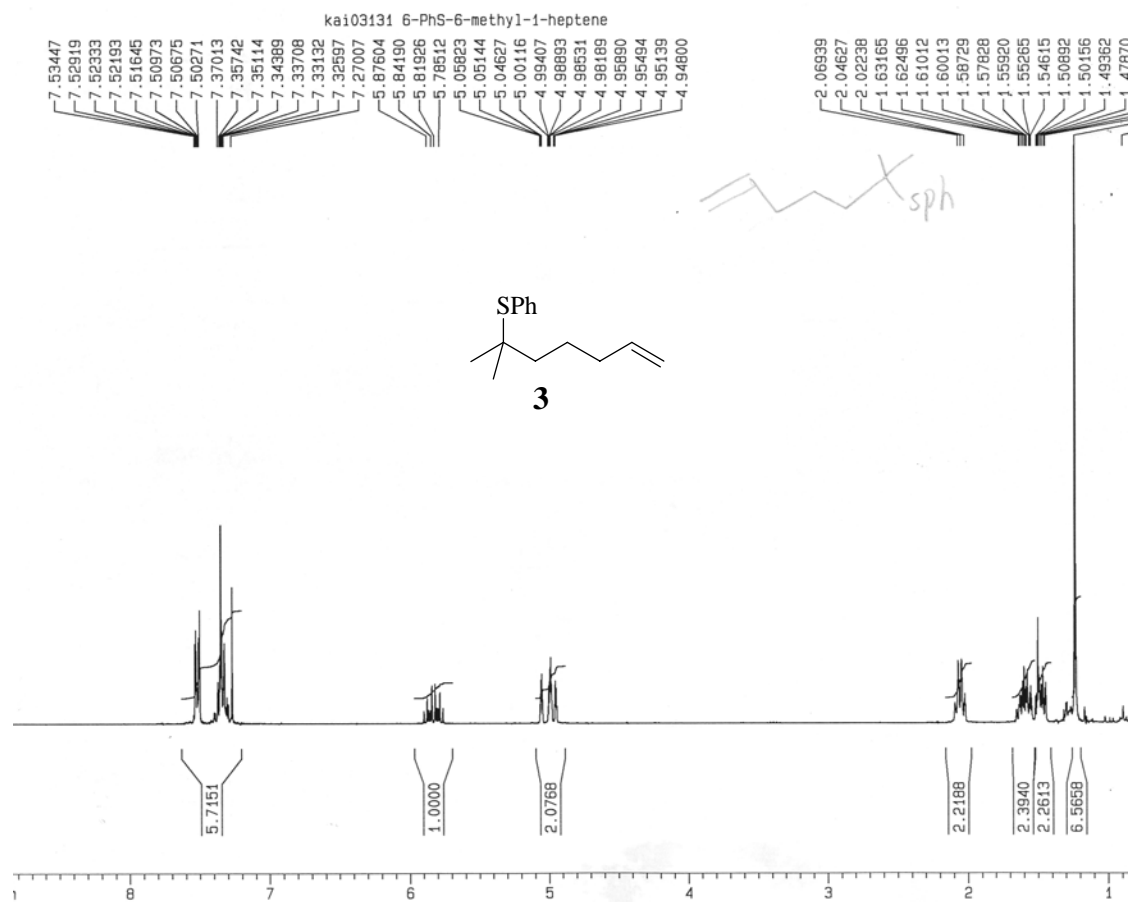
6-(Phenylthio)hept-1-en-4-ol (75) To a 1.80 g (10 mmol) solution of 3-(phenylthio)butyraldehyde (**74**) in 20 mL of THF was added 15 mL of commercial (Aldrich) allyl magnesium bromide solution (1M in ether) at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was then allowed to warm gradually to room temperature and stirred for 1 h (until total consumption of the starting aldehyde was shown by TLC). After being diluted with ether, the reaction mixture was poured into a saturated solution of NH_4Cl . The aqueous layer was extracted with ether twice. The combined extract was washed with water and brine, dried over anhydrous MgSO_4 and evaporated. Chromatography on silica gel afforded the corresponding homoallylic alcohol **75** in 68% yield as a 1:1 inseparable mixture of *syn* and *anti* isomers ^1H NMR: 7.23-7.45 (m, 10 H), 5.78-5.83 (m, 2 H), 5.11-5.16 (m, 4 H), 4.04 (m, 1 H), 3.85 (m, 1 H), 3.44-3.49 (m, 2 H), 2.20-2.29 (m, 4 H), 1.78-1.88 (m, 2 H), 1.56-1.67 (m, 4 H), 1.34 (d, 3H, $J = 4\text{ Hz}$), 1.32 (d, 3H, $J = 4\text{ Hz}$). ^{13}C NMR: 134.7, 134.6, 134.4, 134.3, 132.2, 131.9, 128.8, 126.8, 118.4, 118.2, 68.6, 68.1, 43.3, 43.30, 42.33, 42.2, 40.5, 40.0, 22.6, 20.8. MS (EI) m/z (relative intensity): 222 (M^+ , 28), 204 (20), 181 (15), 163 (10), 137 (100), 110 (63), 95 (15), 84 (18), 77 (24), 71 (37), 65 (25), 59 916). HRMS (EI) calculated for $\text{C}_{13}\text{H}_{18}\text{OS}$: 222.1078, found 222.1079.



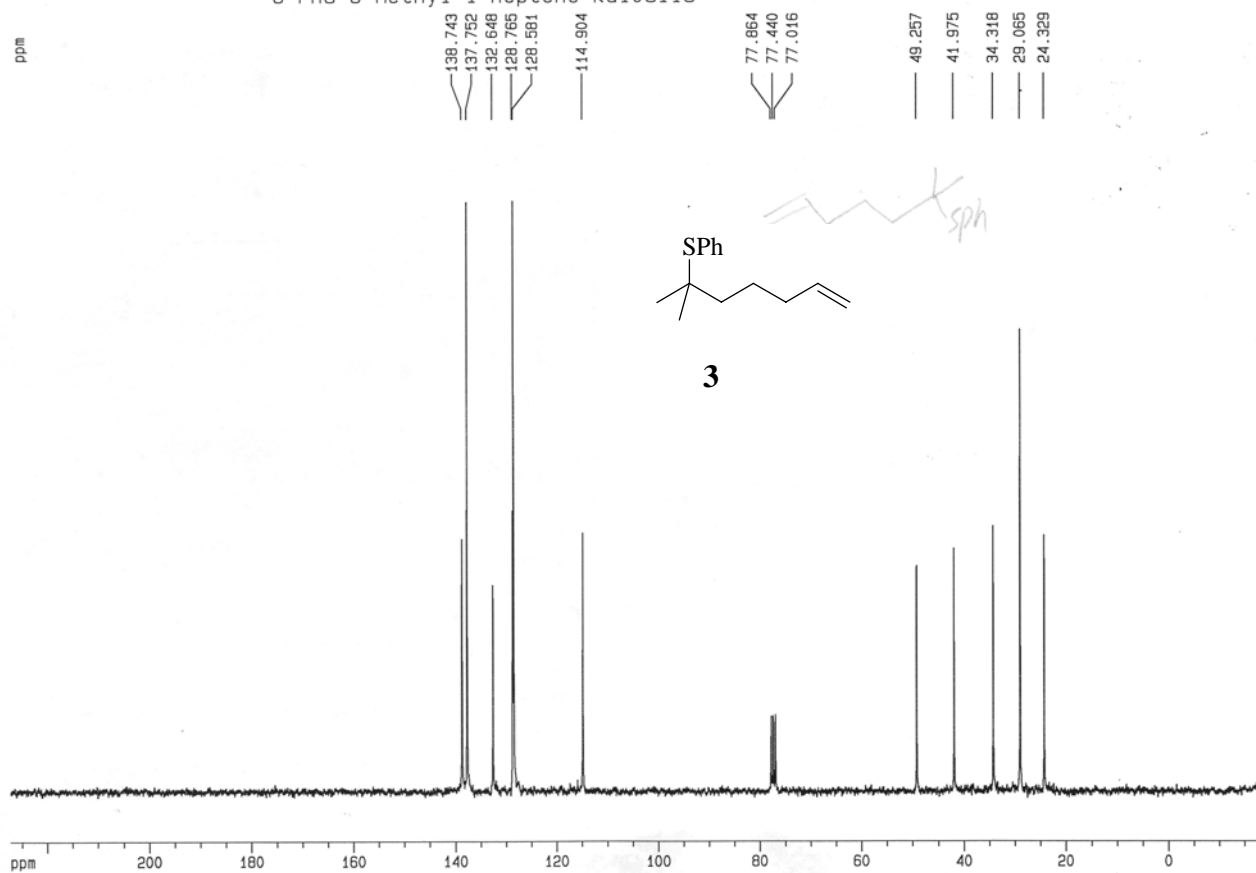
77

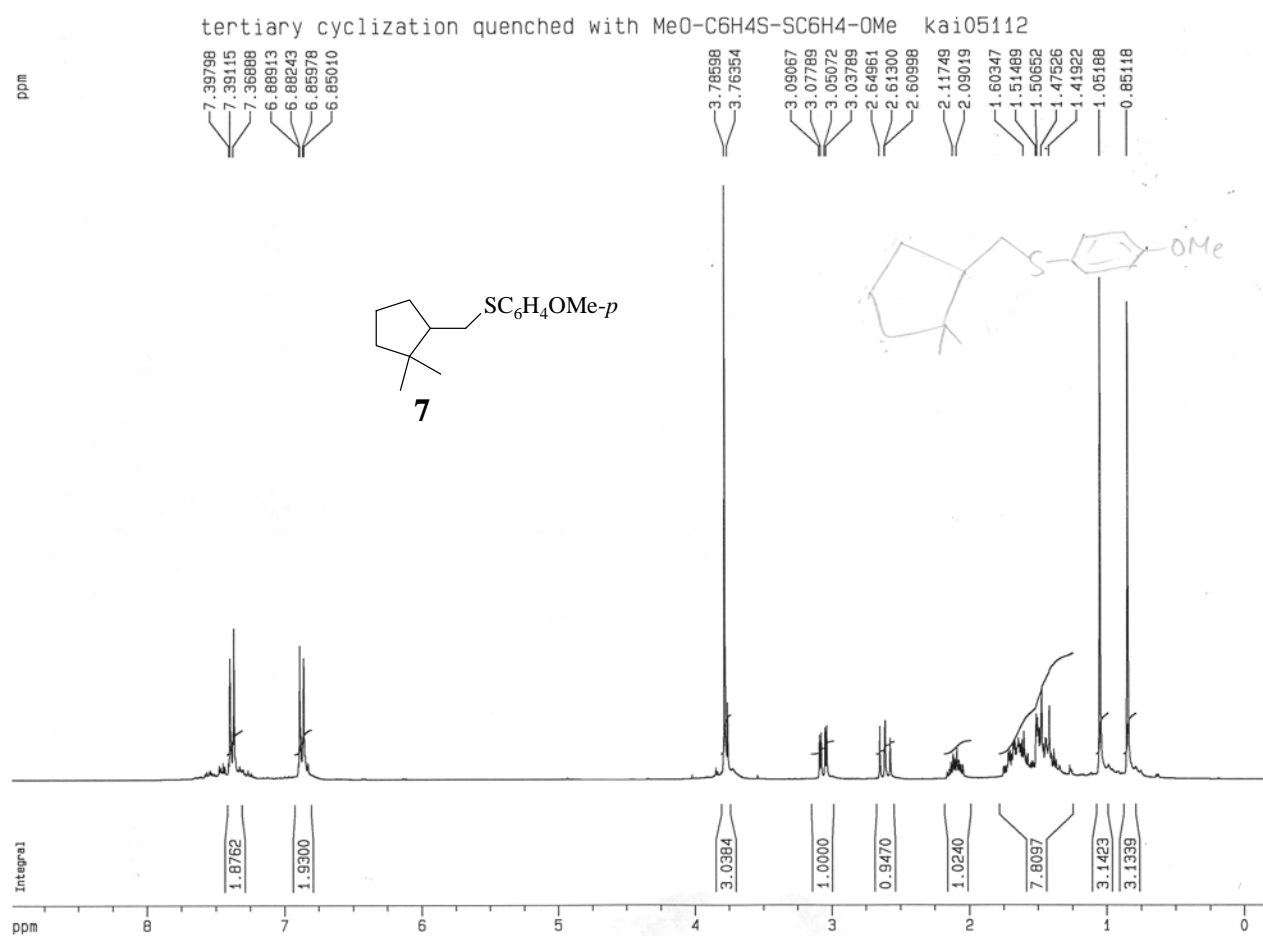
3-(Phenylthio)methyl-4-methylcyclopentanol (77) To a cooled solution ($-78\text{ }^{\circ}\text{C}$) of 445 mg (2.00 mmol) of homoallylic alcohol **75** in 5 mL of THF, was added dropwise

2.20 mmol of freshly titrated *n*-BuLi. After the mixture had been stirred for 15 min, it was transferred to a cooled (-78 °C) solution (17 mL) of 0.30 M LDBB. After the mixture had been stirred for 12 h at the same temperature, the reaction mixture was quenched with 654 mg (3.0 mmol) of PhSSPh and allowed to warm gradually to room temperature. Distilled water (20 mL) was added and the reaction was worked up in the usual way. The crude mixture was then subjected to silica gel chromatography using 8-10% EtOAc/hexane to afford a 58% yield of **77**. ¹H NMR: major isomer: 7.25-7.35 (m, 5 H), 4.32 (m, 1 H), 3.22 (dd, 1 H, J = 4.83, 12.3 Hz), 2.89 (dd, 1 H, J = 8.9, 12.3 Hz), 1.6-2.2 (m, 6 H), 1.04 (d, 3 H, J=6.5 Hz). ¹³C NMR: minor isomer 137.0, 128.7, 128.6, 125.6, 72.5, 43.3, 40.8, 40.4, 35.2, 34.8, 15.8; major isomer 137.1, 128.9, 128.7, 125.6, 72.2, 45.4, 44.7, 42.0, 38.9, 37.8, 19.1. MS (EI) *m/z* (relative intensity): 222 (M⁺, 100), 205 (22), 163 (26), 123 (34), 110 (65), 95 (40), 86 (30), 69 (24). HRMS (EI) calculated for C₁₃H₁₈OS: 222.1078, found 222.1079.

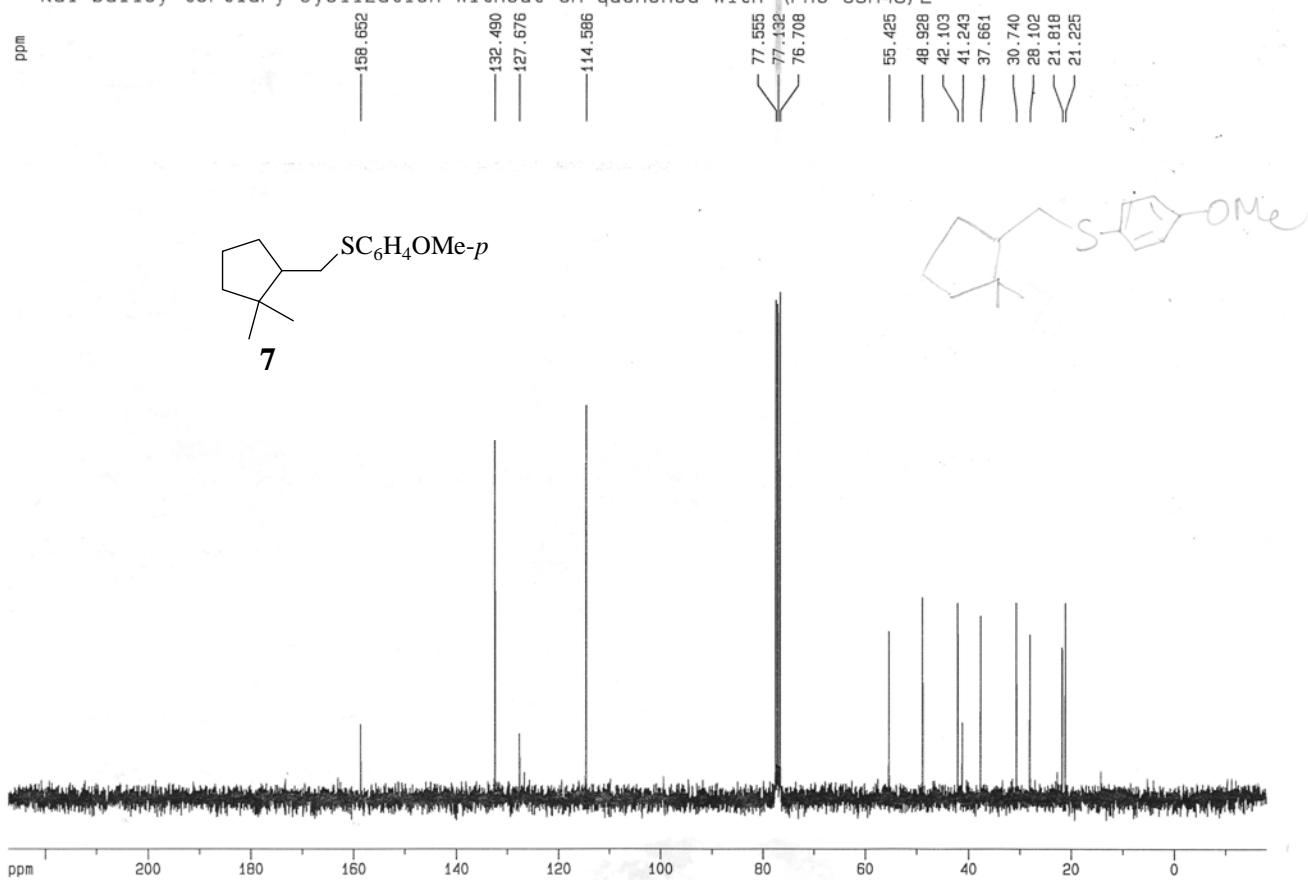


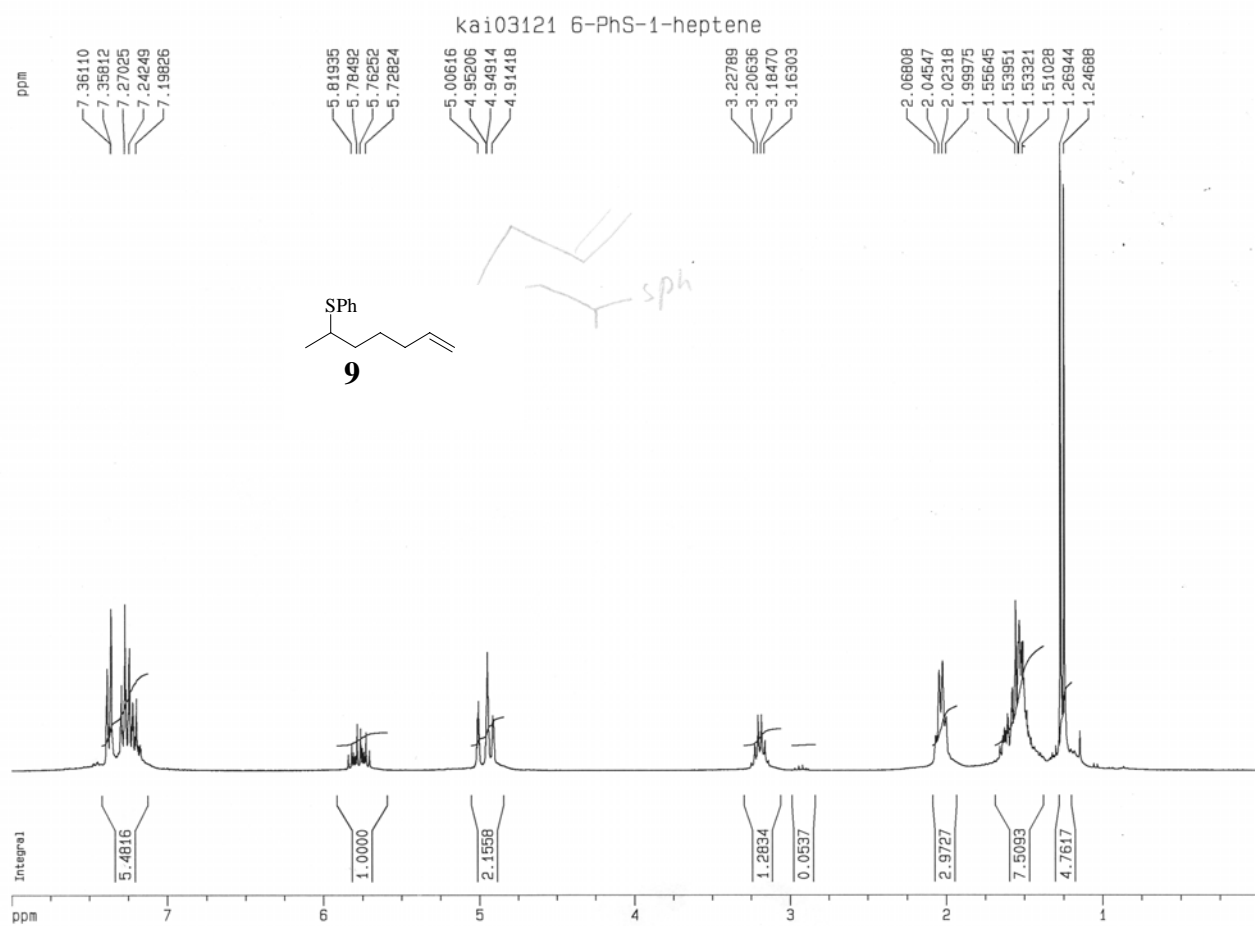
6-PhS-6-Methyl-1-heptene kai05115

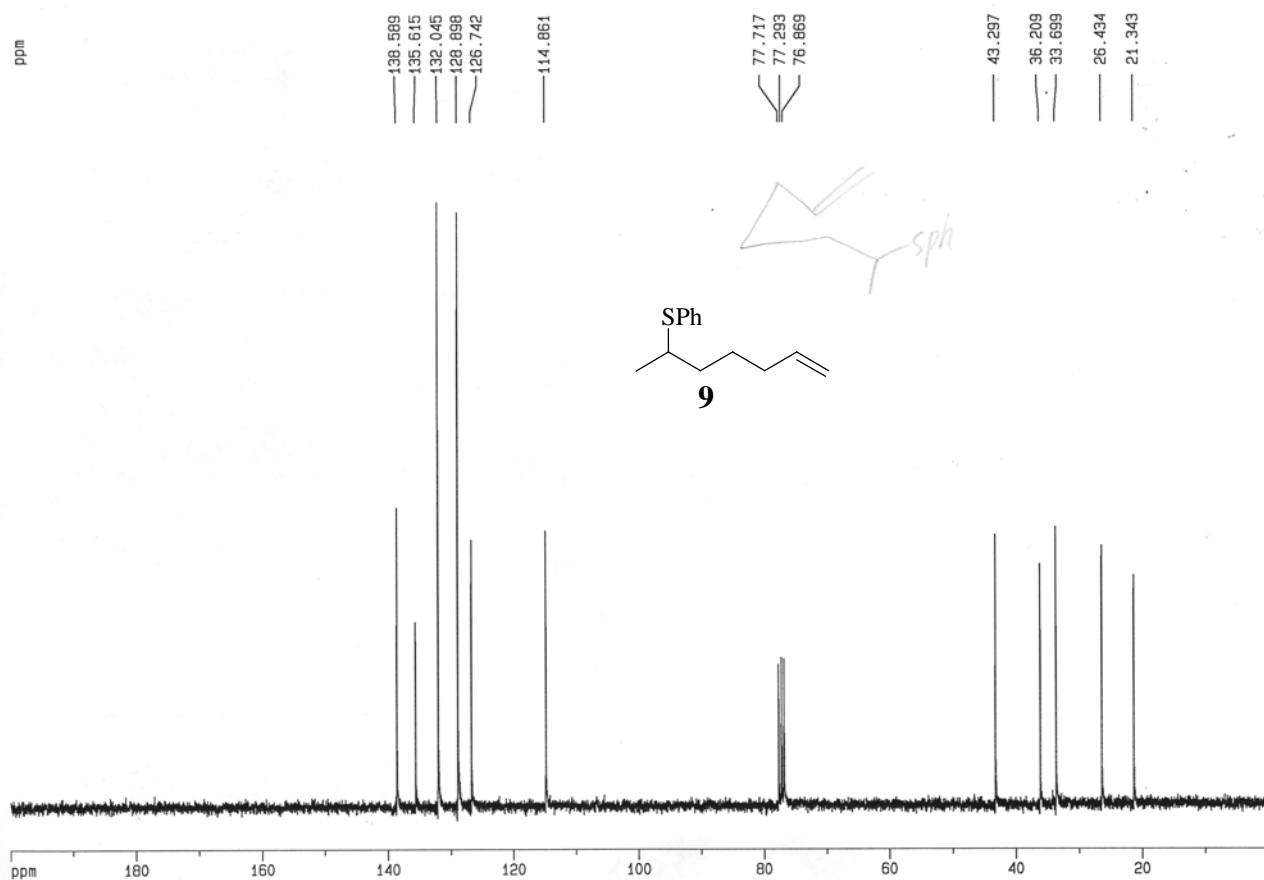


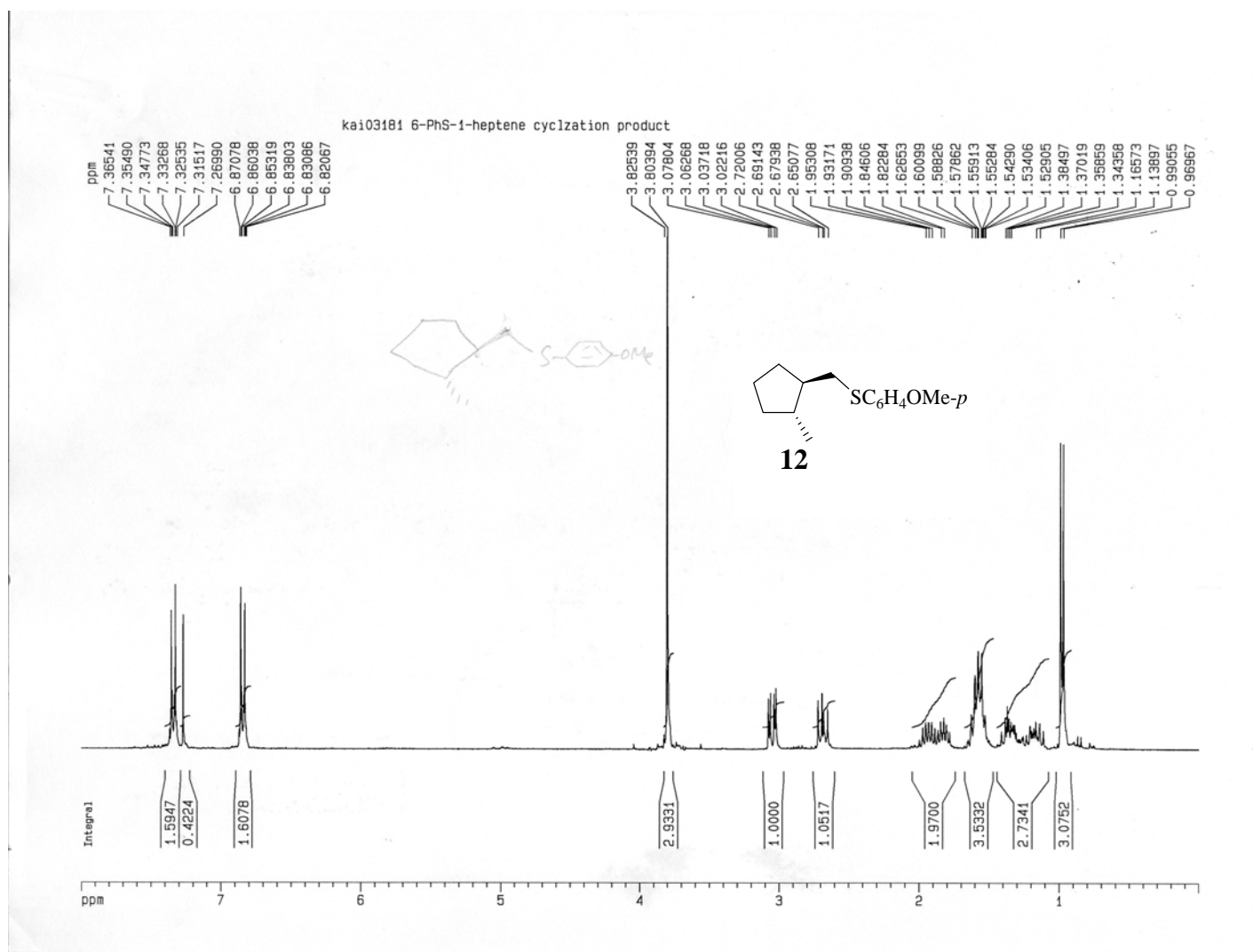


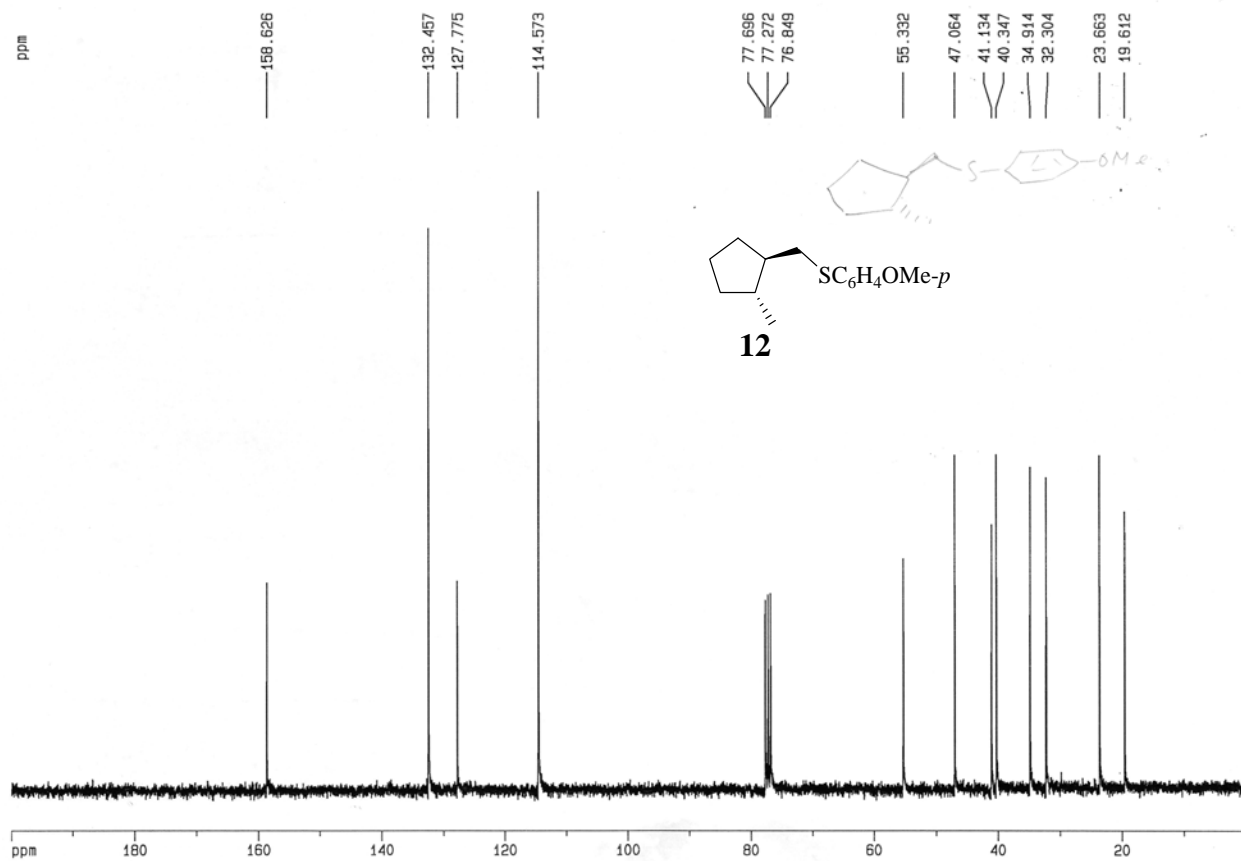
kai bailey tertiary cyclization without OH quenched with (PhO-C6H4S)2



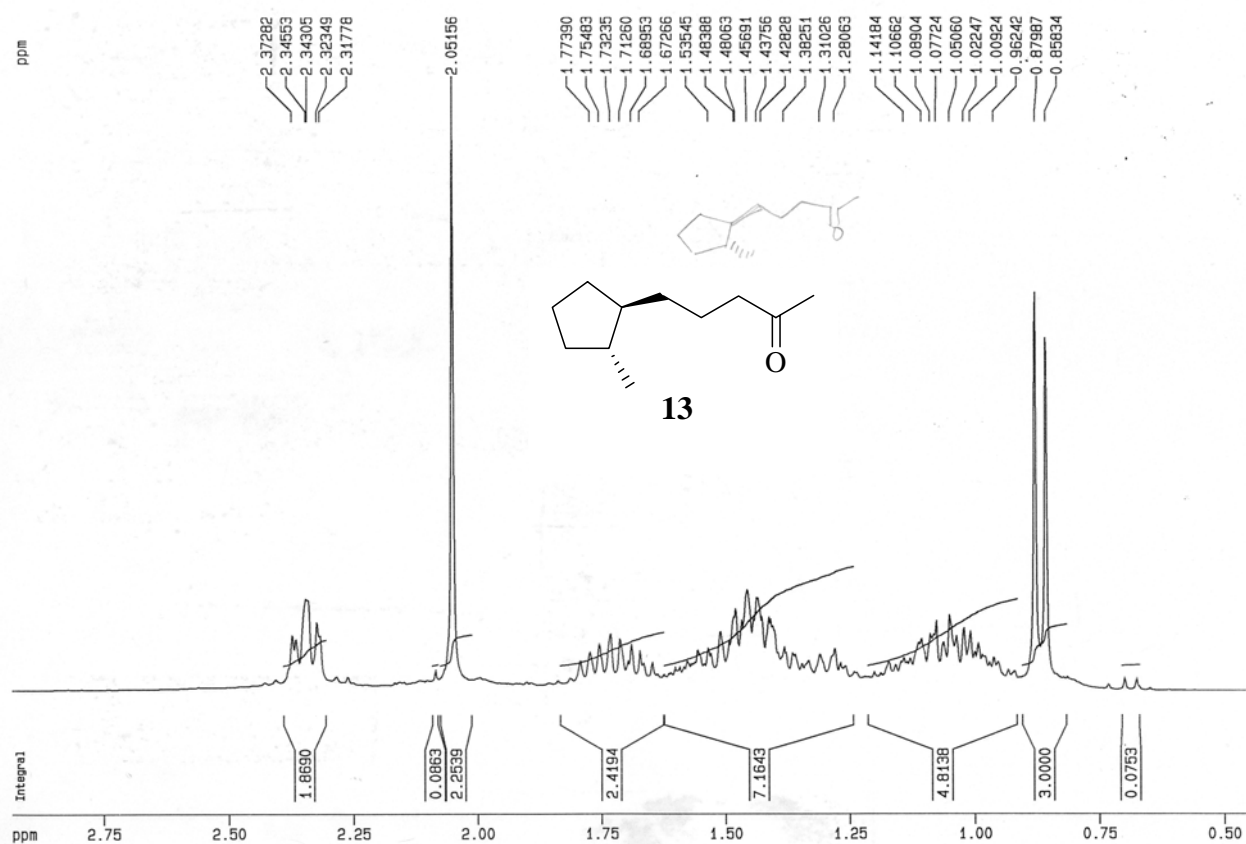


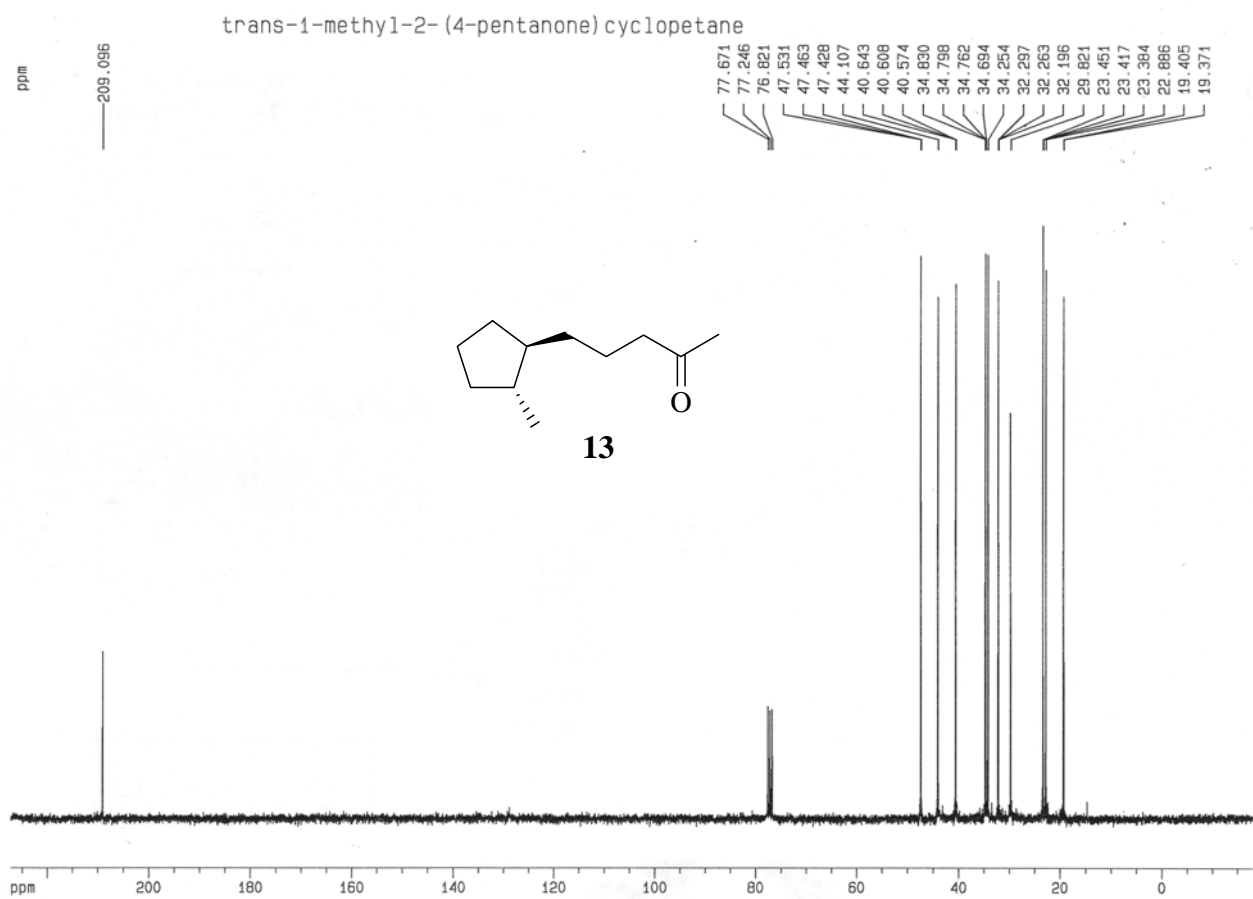




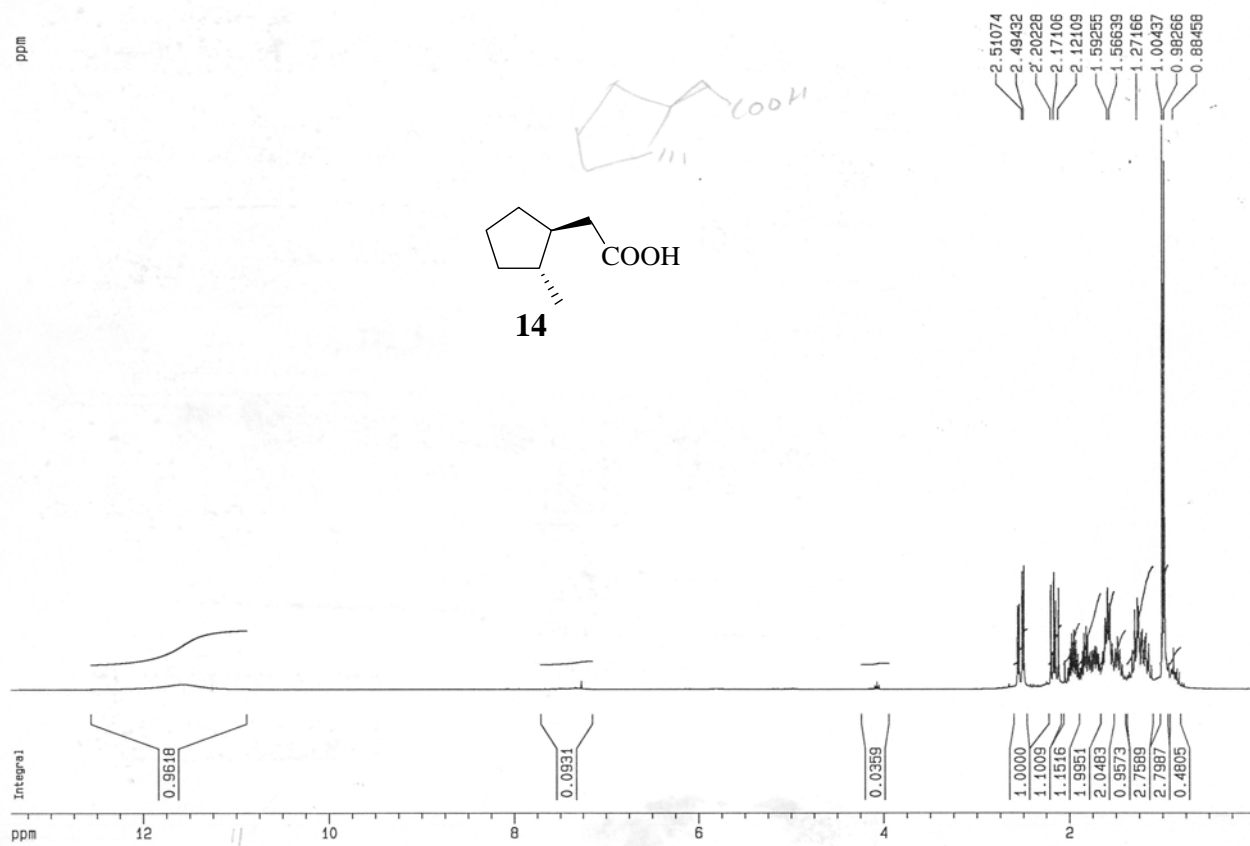


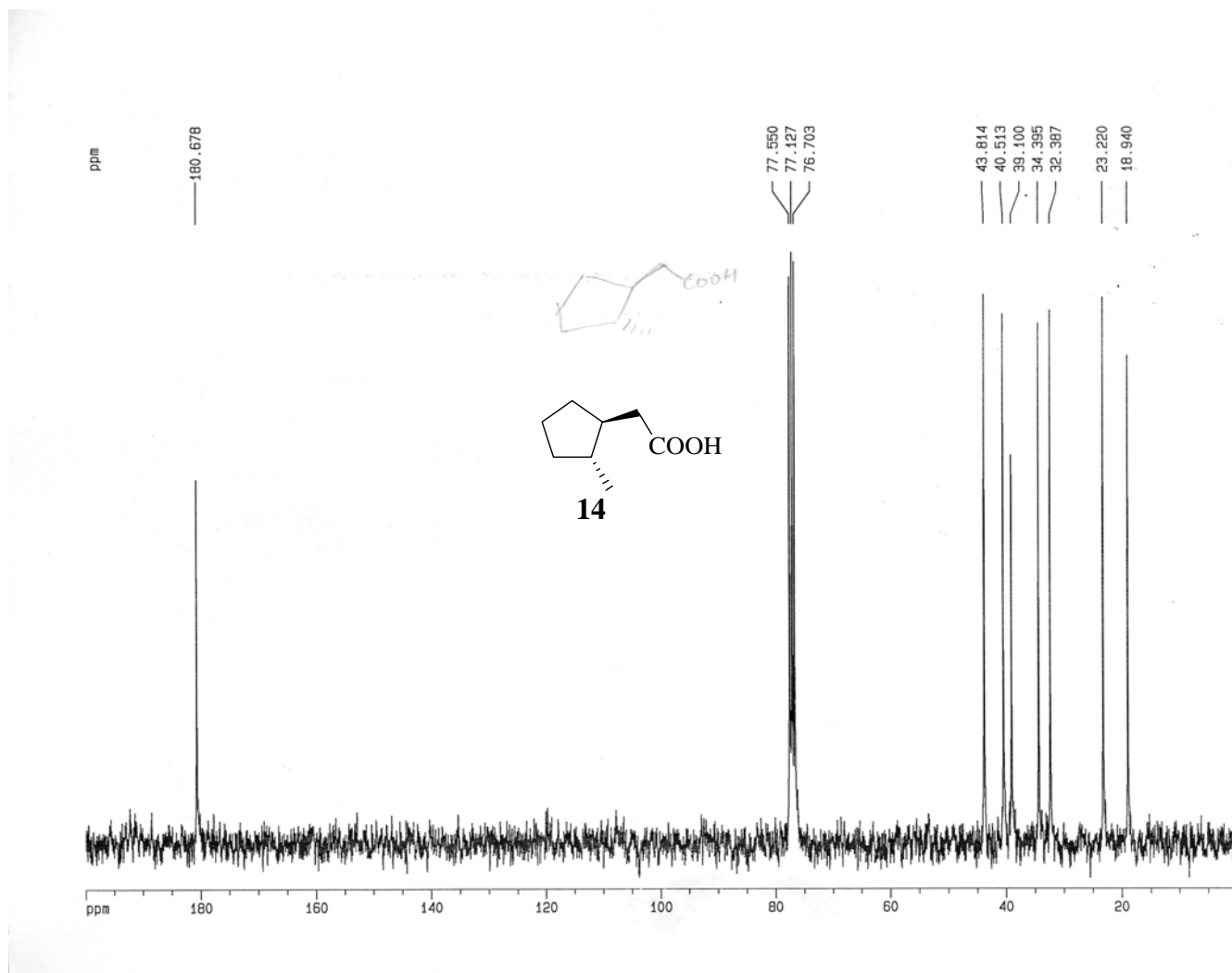
trans-1-methyl-2-(4-pentanone)cyclopentane

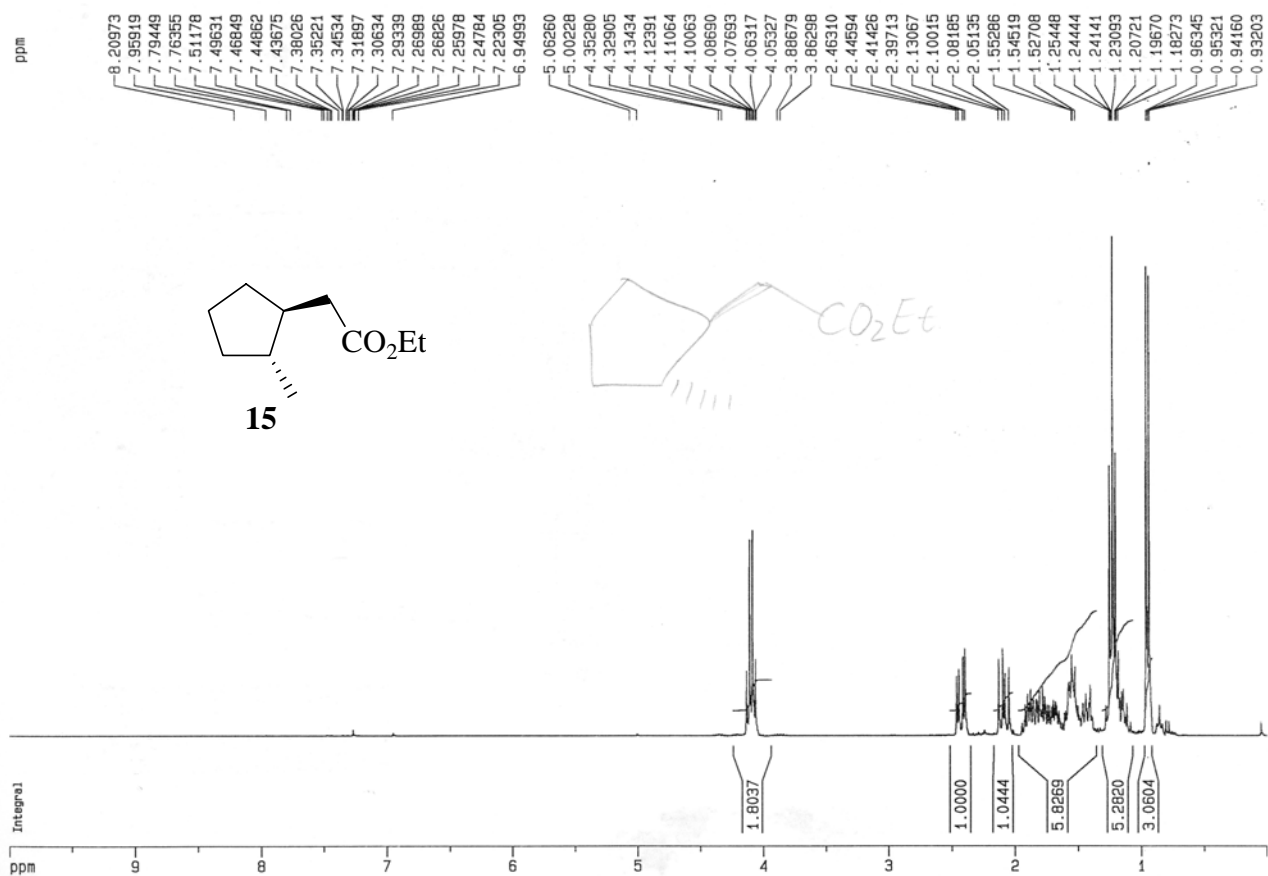


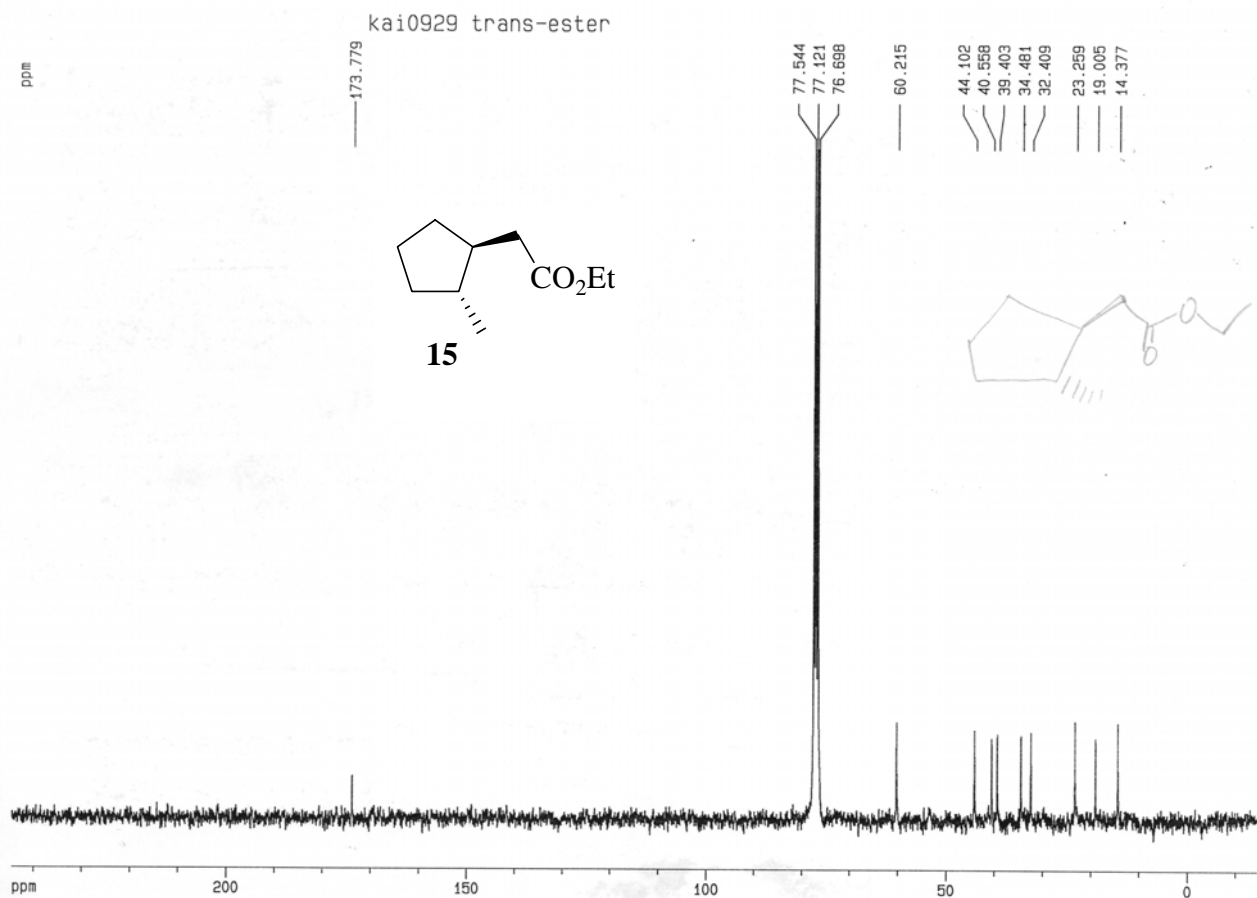


kai0711 acid

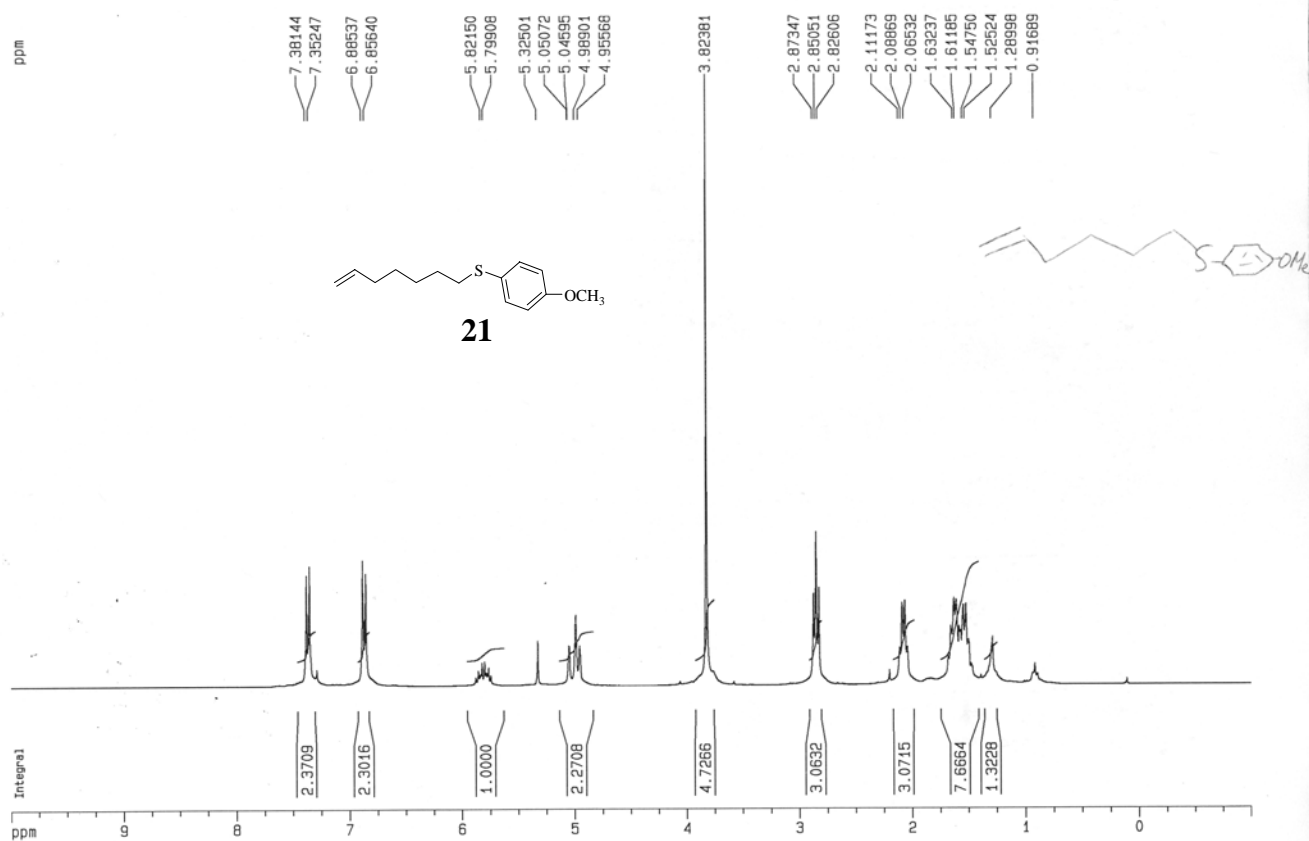




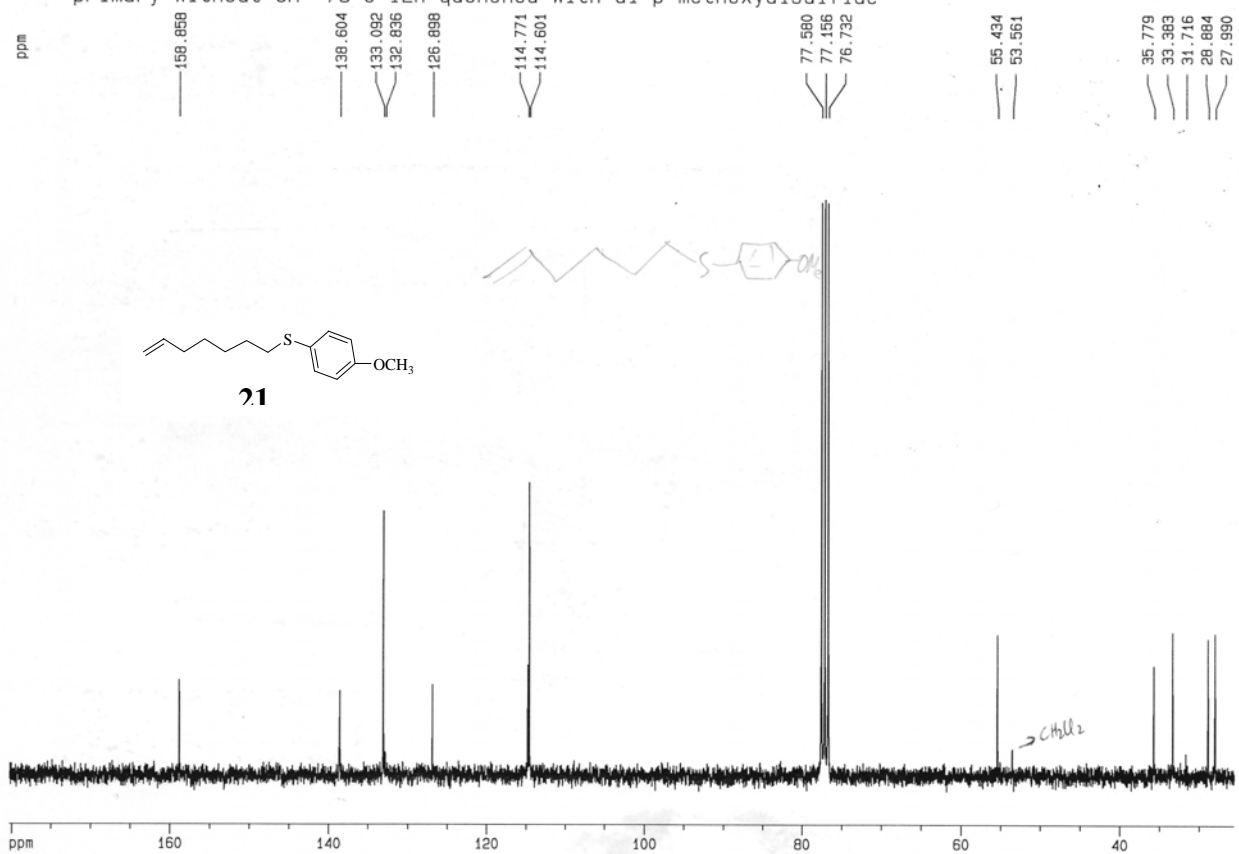


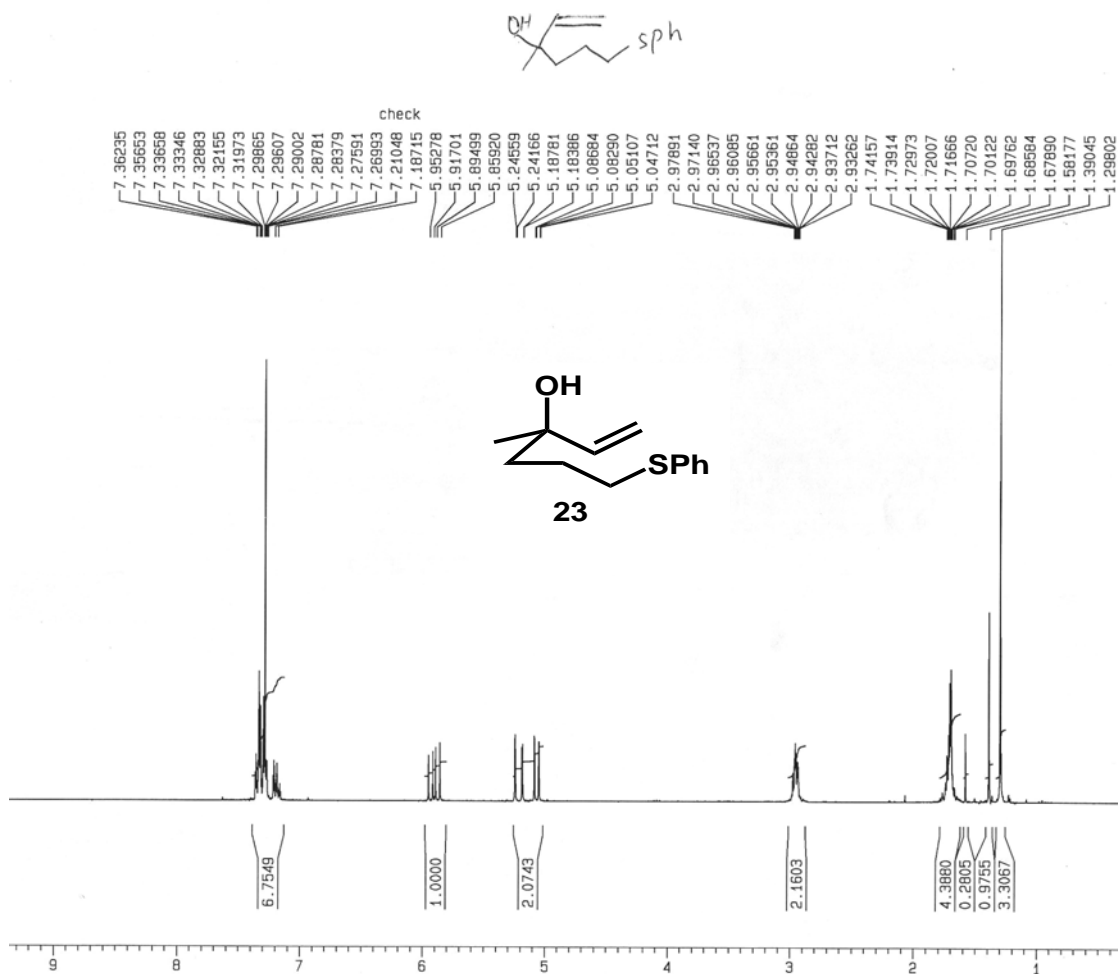


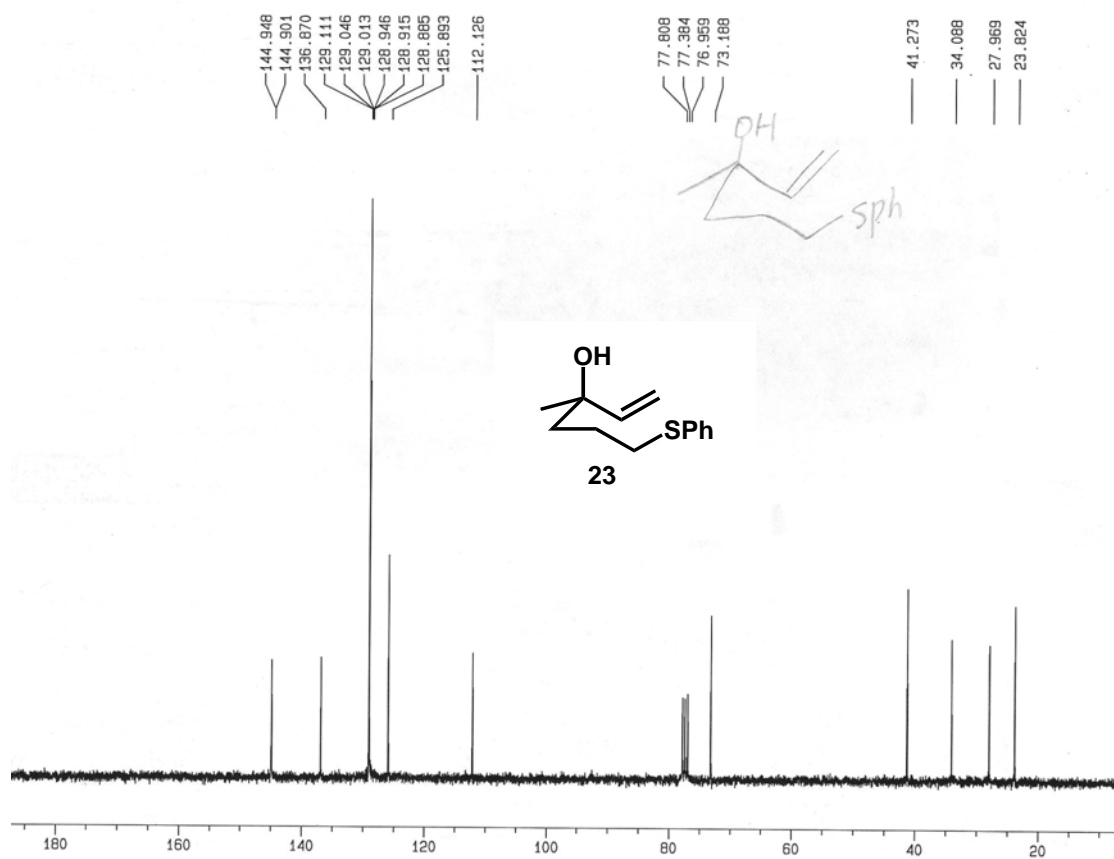
primary without OH -7B c 12h quenched with di-p-methoxydisulfide

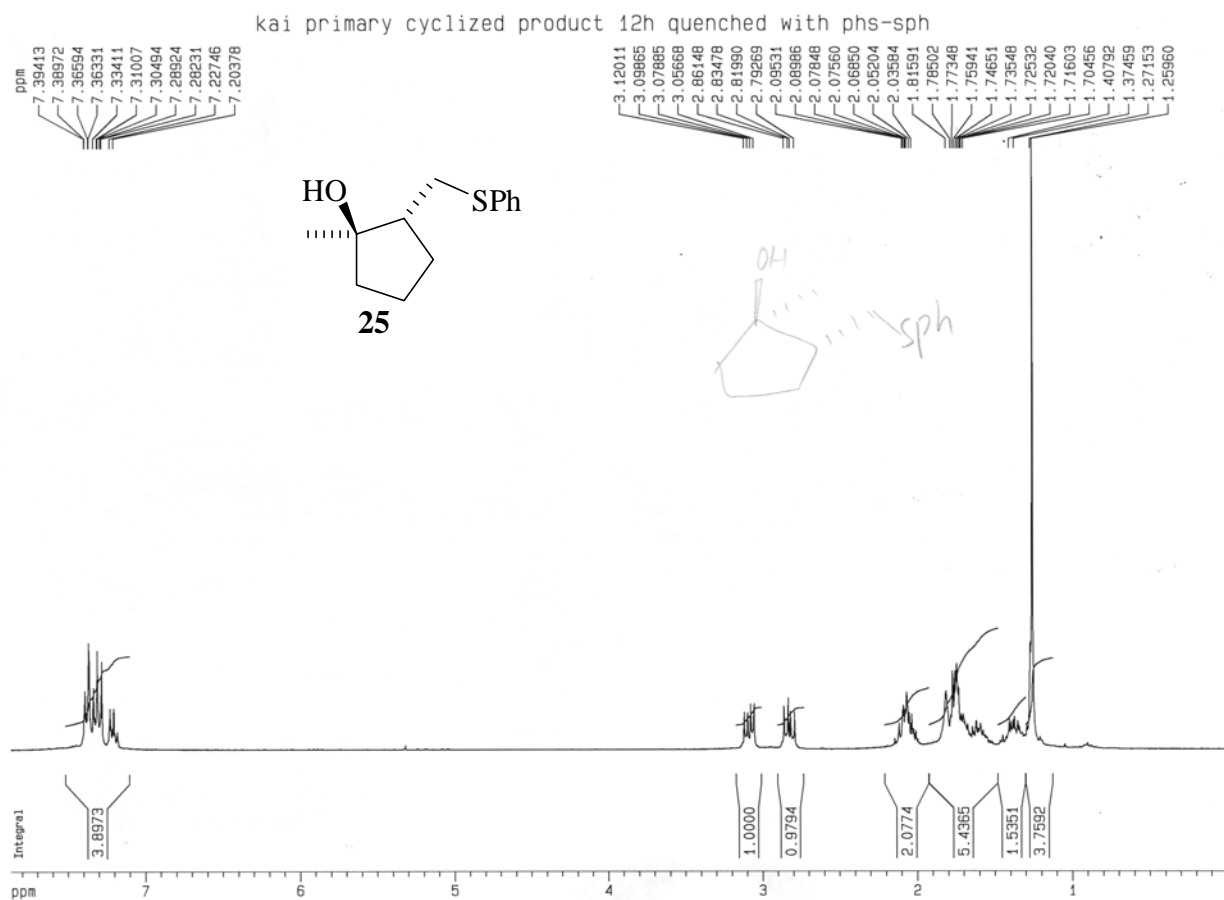


primary without OH -78 c 12h quenched with di-p-methoxydisulfide

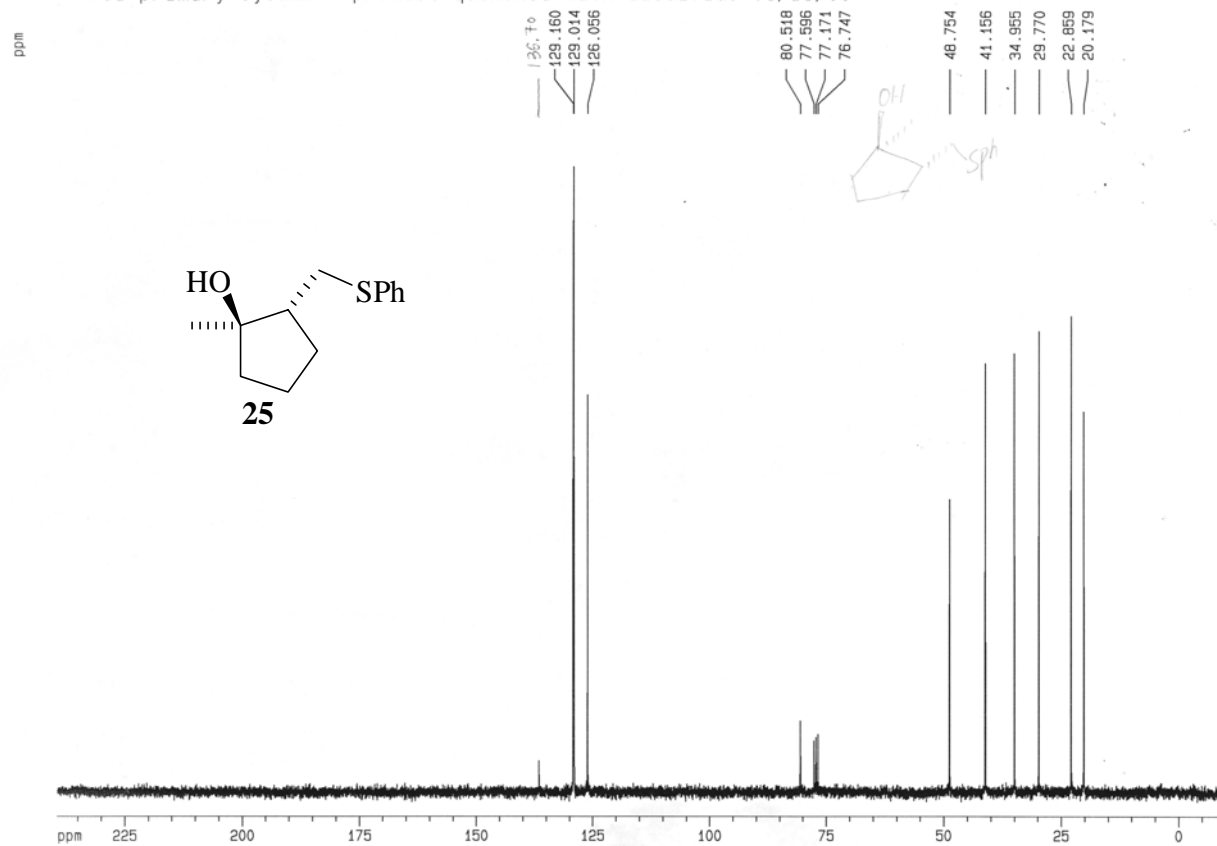


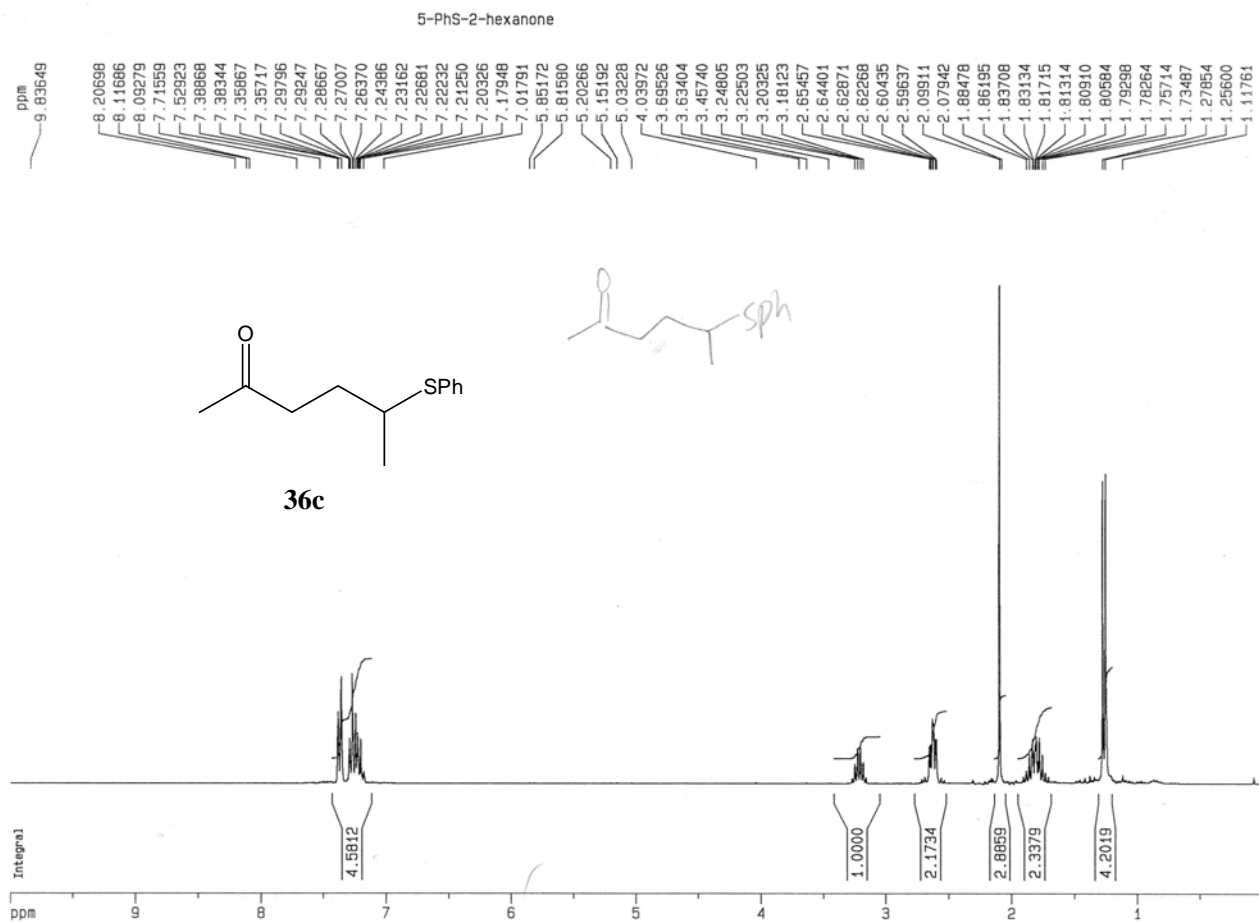




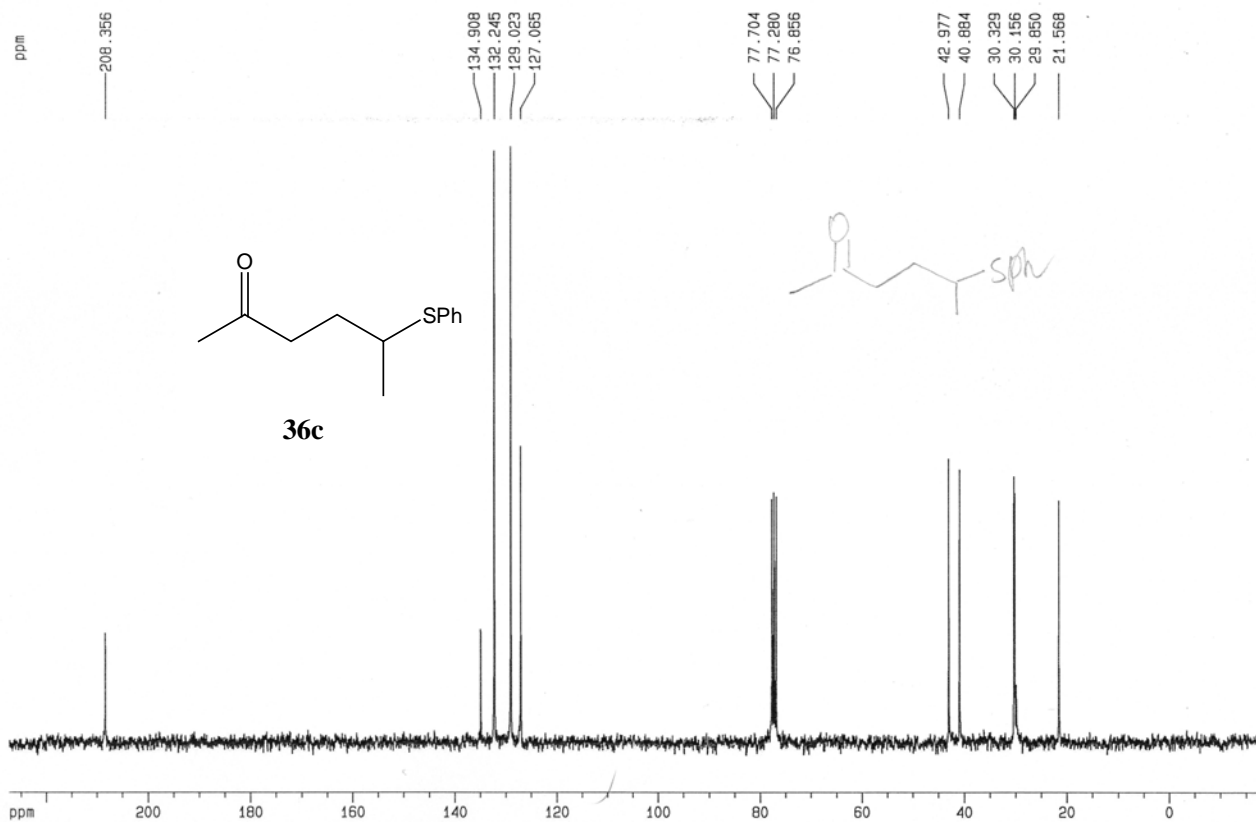


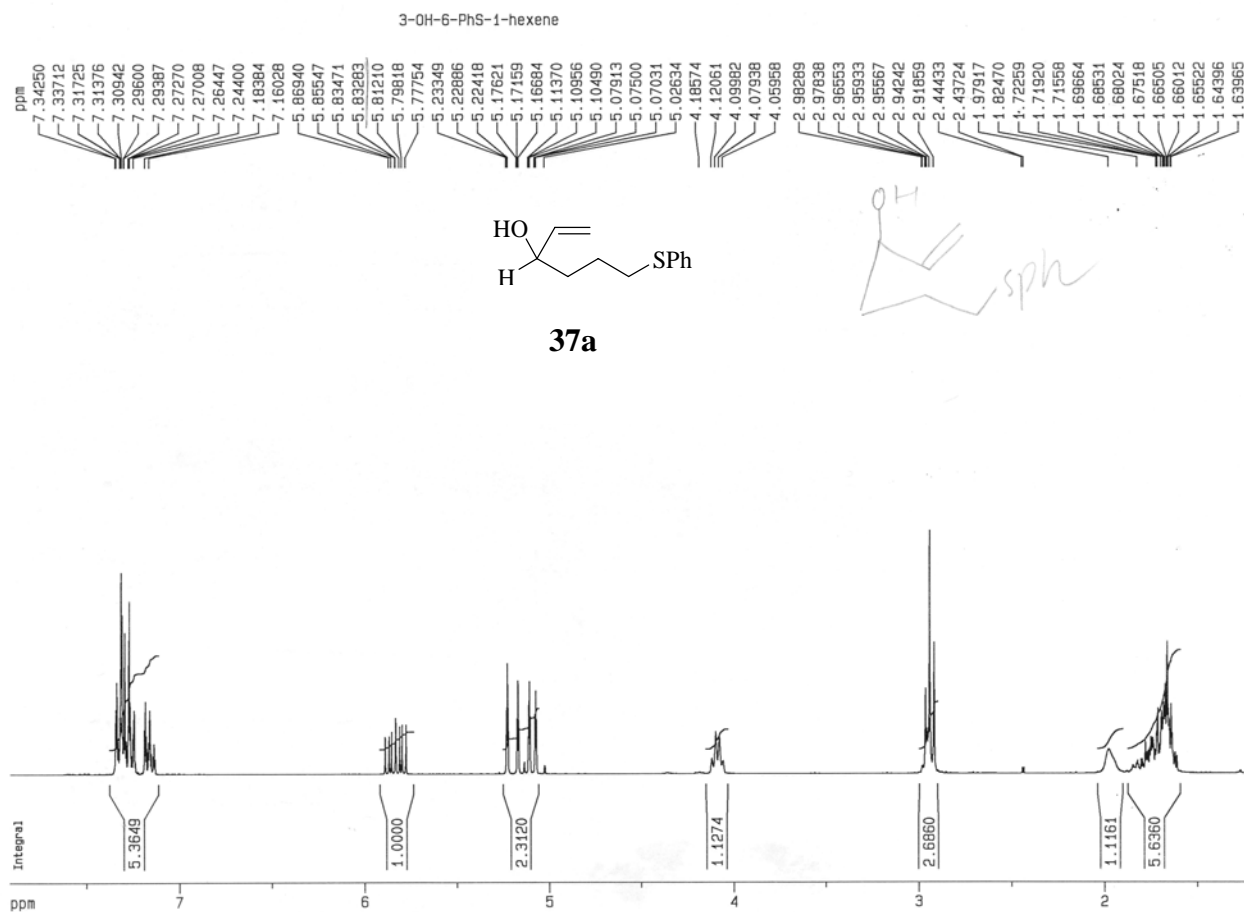
kai primary cyclized product quenched with disulfide 08/16/00

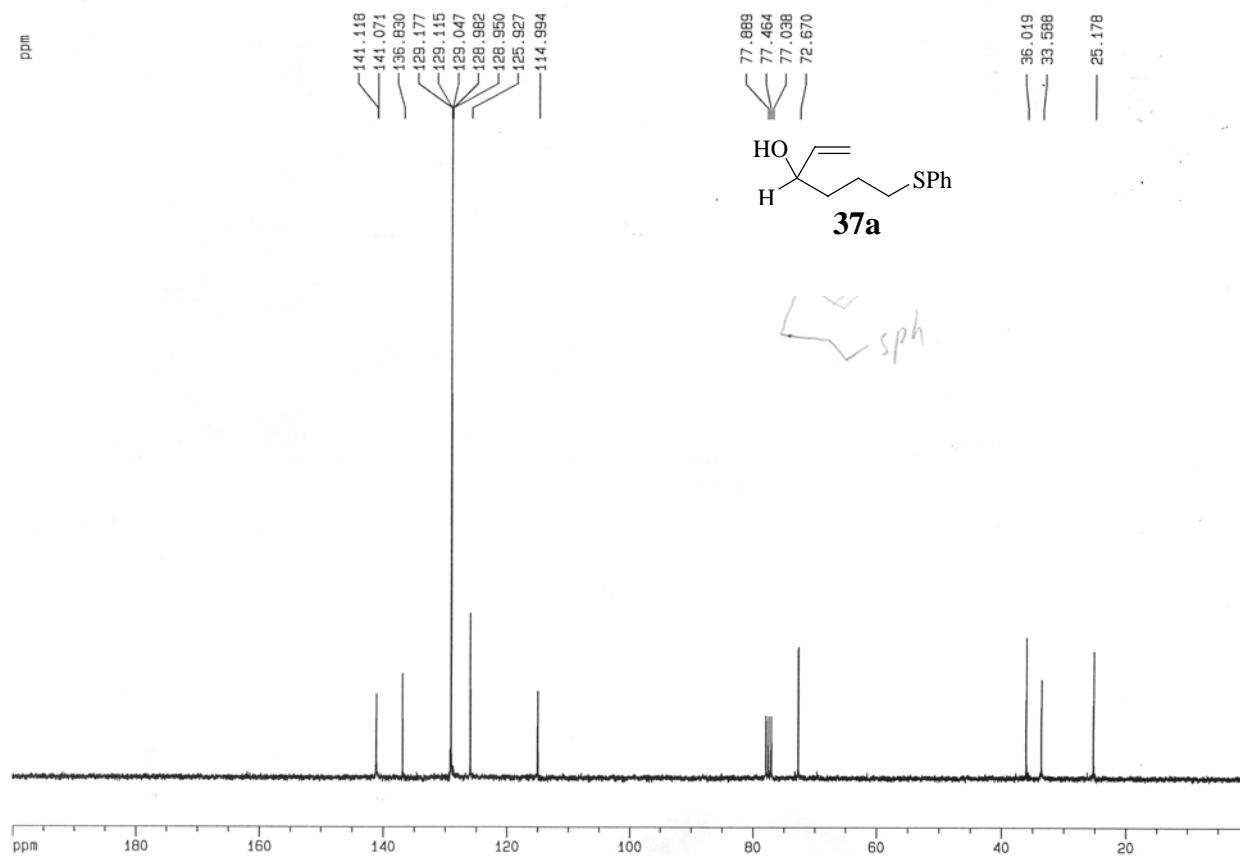


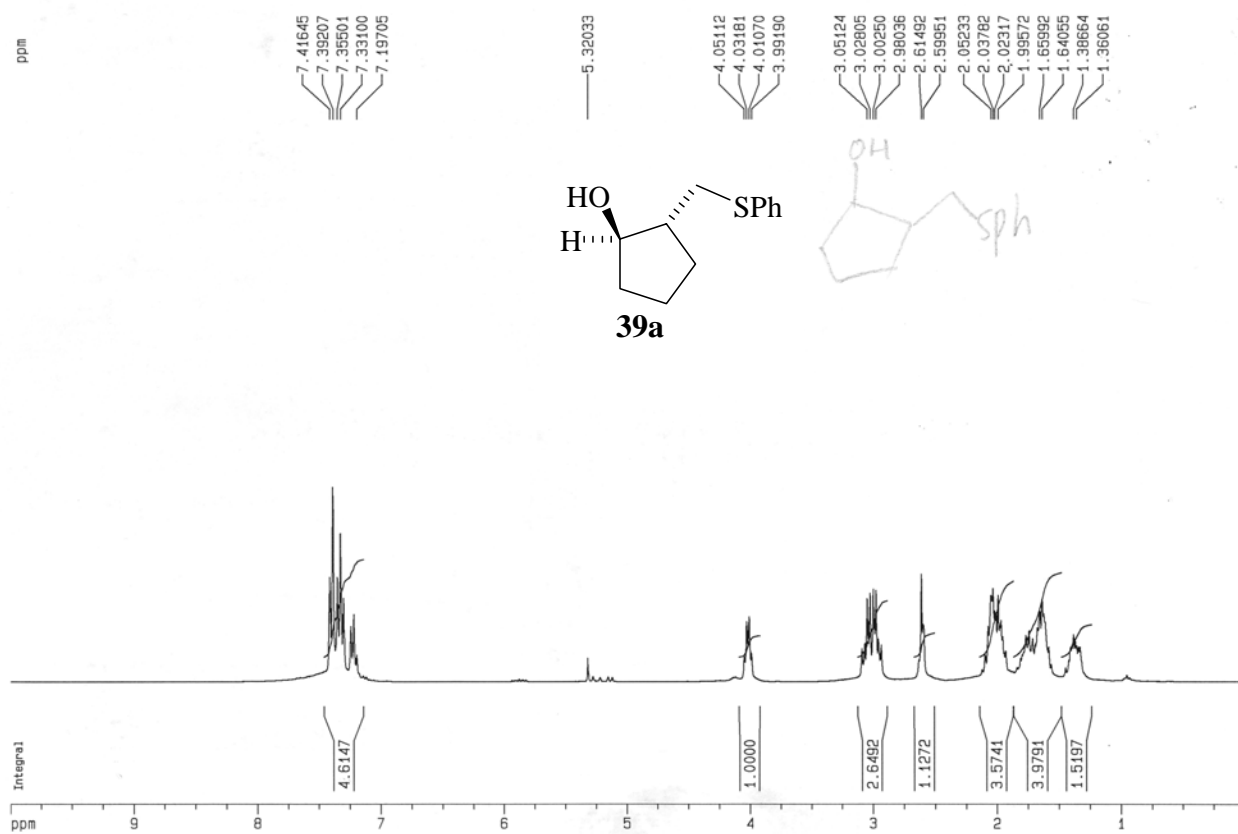


5-PhS-2-hexanone

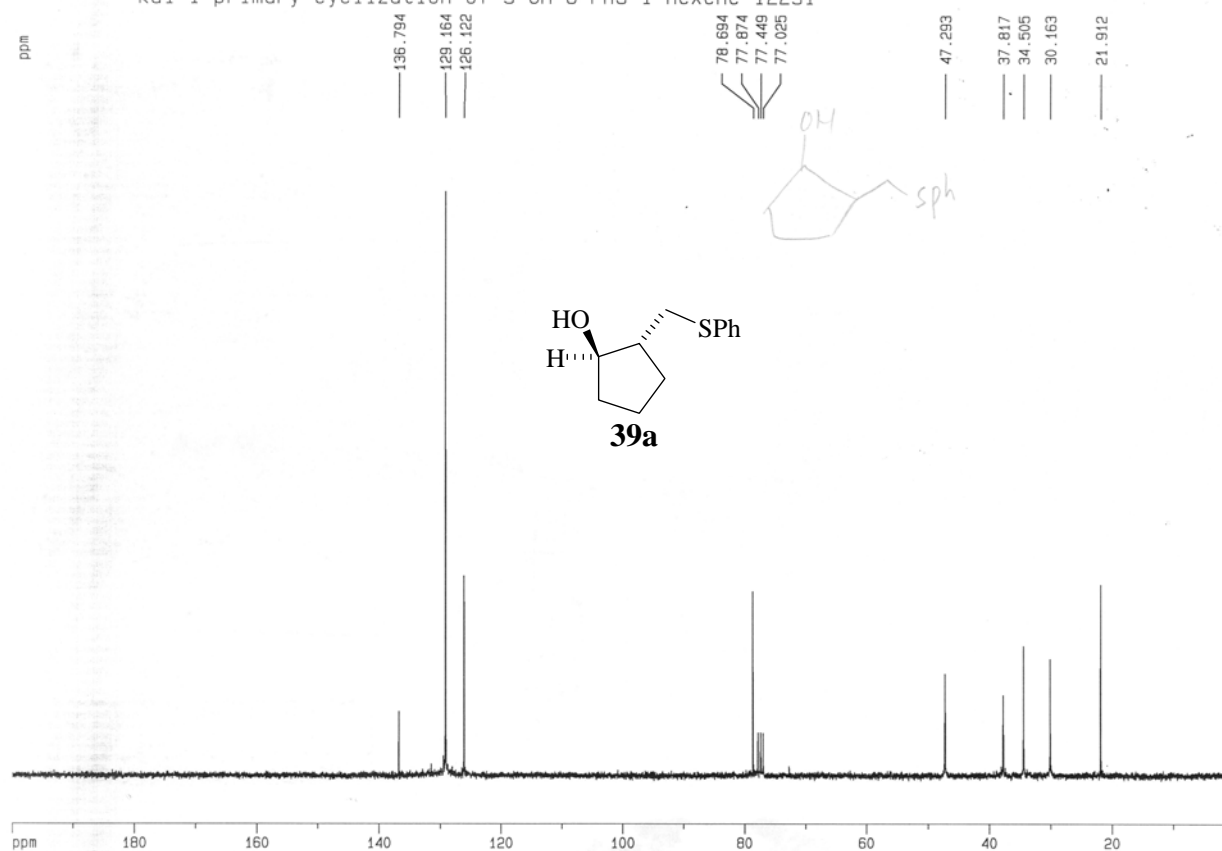




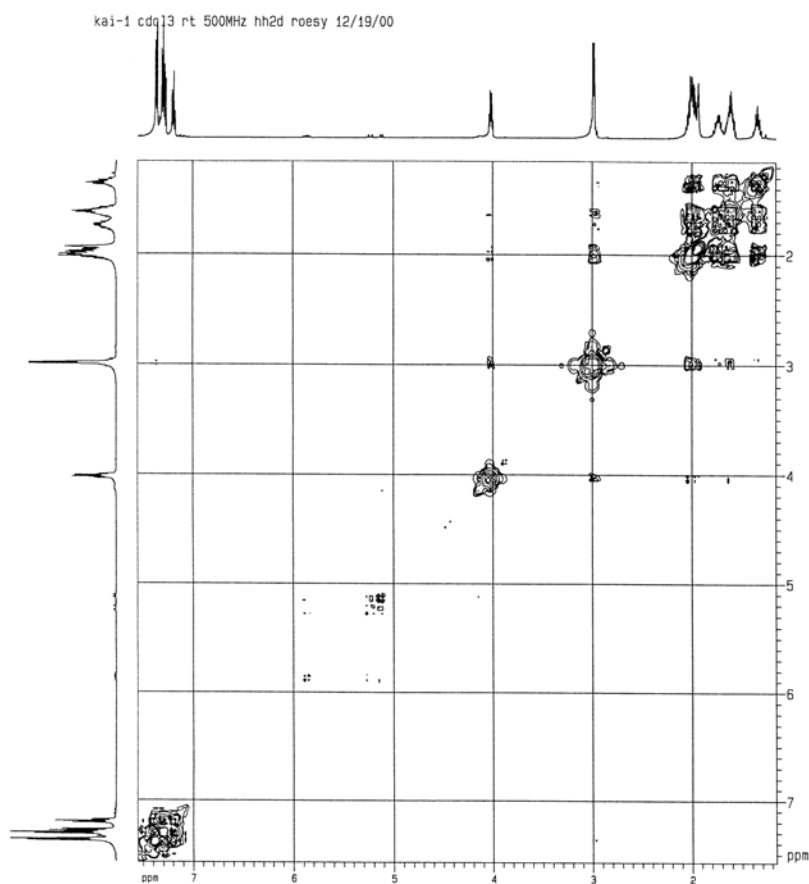
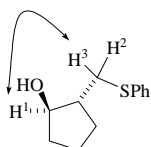




kai-1 primary cyclization of 3-OH-6-PhS-1-hexene 12231



The COSY spectrum of compound 39a



Current Data Parameters

NAME	kai-1
EXPNO	11110
PROCNO	1

F2 - Acquisition Parameters

Date_	000000
Time	12.11
INSTRUM	spcrt
PROBHD	5 mm TXI 13C
PULPROG	roesytp
TD	1324
SOLVENT	CDCl3
NS	60
DS	16
SWH	4496.403 Hz
FIDRES	4.351218 Hz
AQ	0.1119198 sec
RG	96.5
QW	111.200 usec
DE	6.00 usec
TE	290.0 K
dt	0.000030 sec
d12	0.000200 sec
D1	1.0000000 sec
PL1	0.00 dB
P1	9.70 usec
PL11	6.00 dB
P15	20000.00 usec
DE	6.00 usec
SFO1	500.132506 MHz
NAC1	31
RG	0.0011120 sec

F1 - Acquisition parameters

NO	2
TD	256
SFO1	500.1323 MHz
FIDRES	17.564345 Hz
SW	8.390 ppm

F2 - Processing parameters

SI	512
SF	500.130002 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

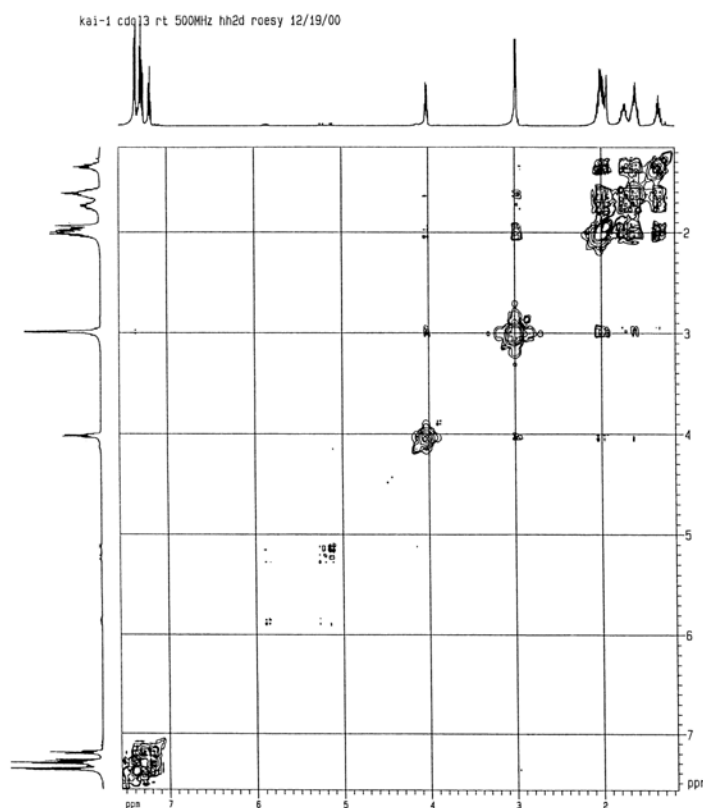
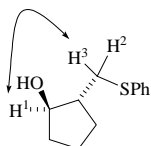
F1 - Processing parameters

SI	512
MC2	1091
SF	500.1299996 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

CU2	15.00 cm
CU1	15.00 cm
FOPLD	7.395 ppm
FOLD	3778.44 Hz
FOPH	1.163 ppm
FPH	561.76 Hz
FOPD	7.574 ppm
FOLD	3787.82 Hz
FPH	1.147 ppm
FPH	573.60 Hz
F2PHCN	0.42611 ppm/cm
F2DCN	213.11075 Hz/cm
F1PHCN	0.42645 ppm/cm
F1DCN	214.28136 Hz/cm

The ROESY spectrum of compound 39a



Current Data Parameters

NAME	kai-1
EXPNO	11110
PROCNO	1

F2 - Acquisition Parameters

Date_	200000
Time	12.11
INSTRUM	gpcpt1
PROBHD	5 mm TAI 13C
PULPROG	zgpg30
TD	1624
SOLVENT	CDCl3
NS	60
DS	16
SWH	4496.463 Hz
FIDRES	4.361218 Hz
AQ	0.1129108 sec
RG	96.5
DM	111.200 umec
DE	8.00 umec
TE	290.2 K
QT	0.0000030 sec
QZ	0.0000000 sec
D1	1.0000000 sec
PL1	0.00 dB
PL2	0.10 umec
PL11	0.00 dB
PL15	200000.00 umec
DE	8.00 umec
SFO1	500.1325006 MHz
RG1	31
RG2	0.00011320 sec

F1 - Acquisition parameters

NS	2
TD	256
SFO1	500.1323333 MHz
FIDRES	17.564545 Hz
DM	8.900 umec

F2 - Processing parameters

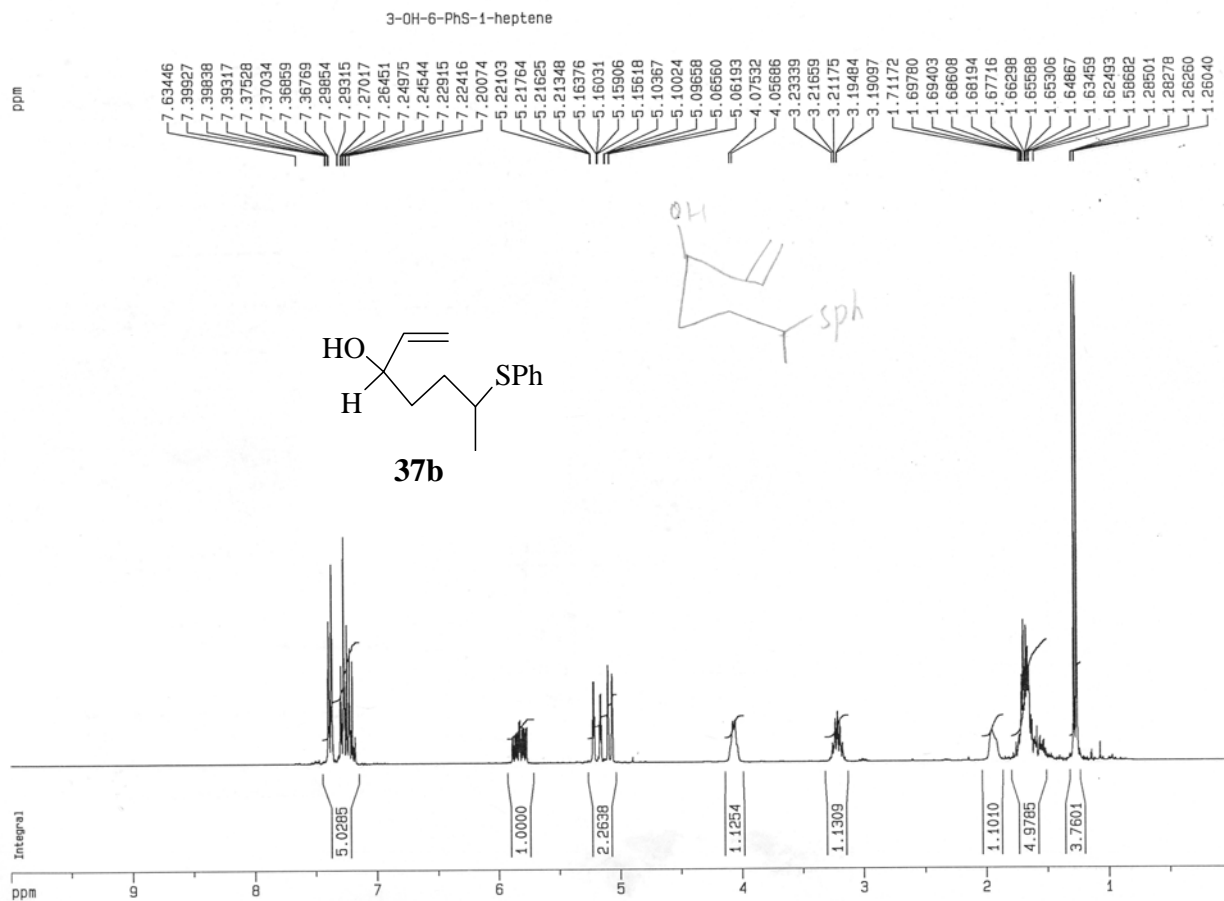
SF	500.1300000 MHz
WDW	SINE
SGB	0
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GB	0
PC	1.00

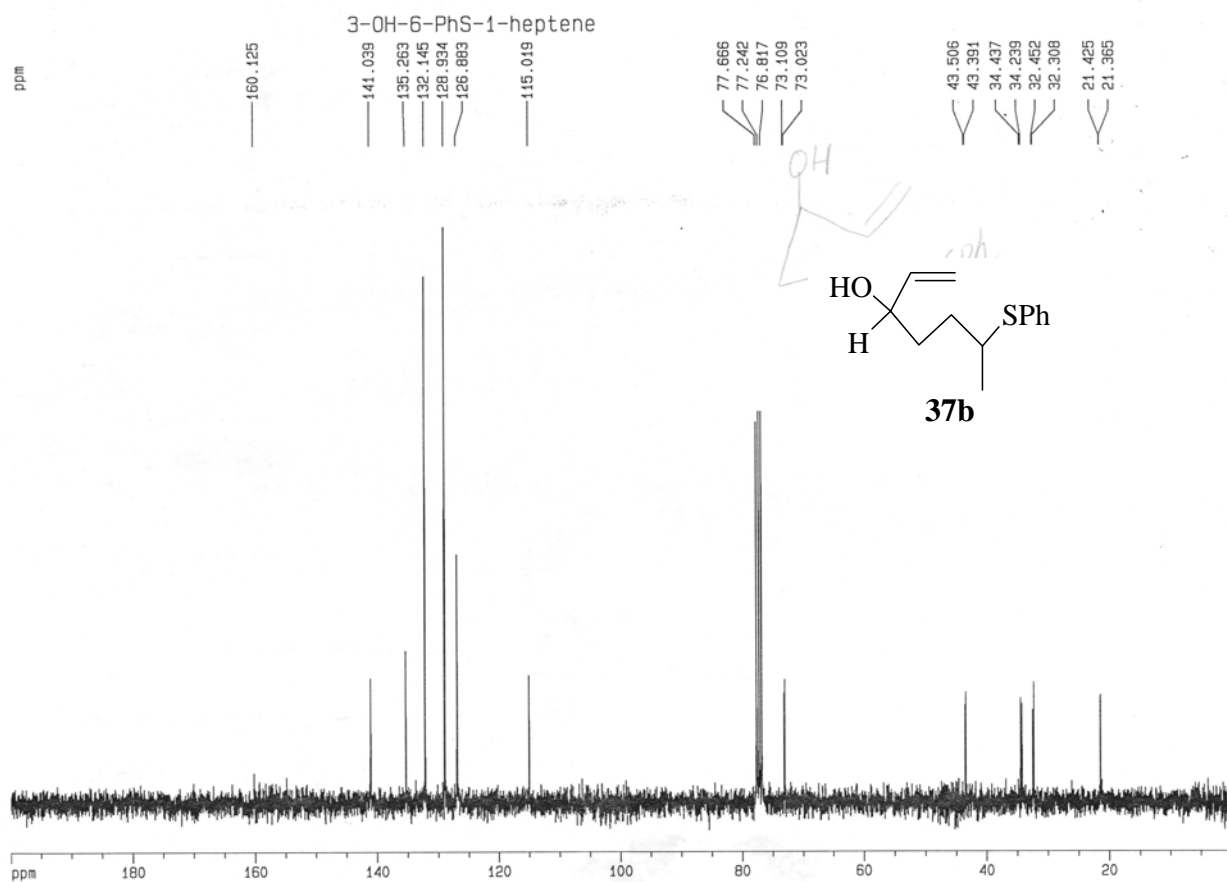
F1 - Processing parameters

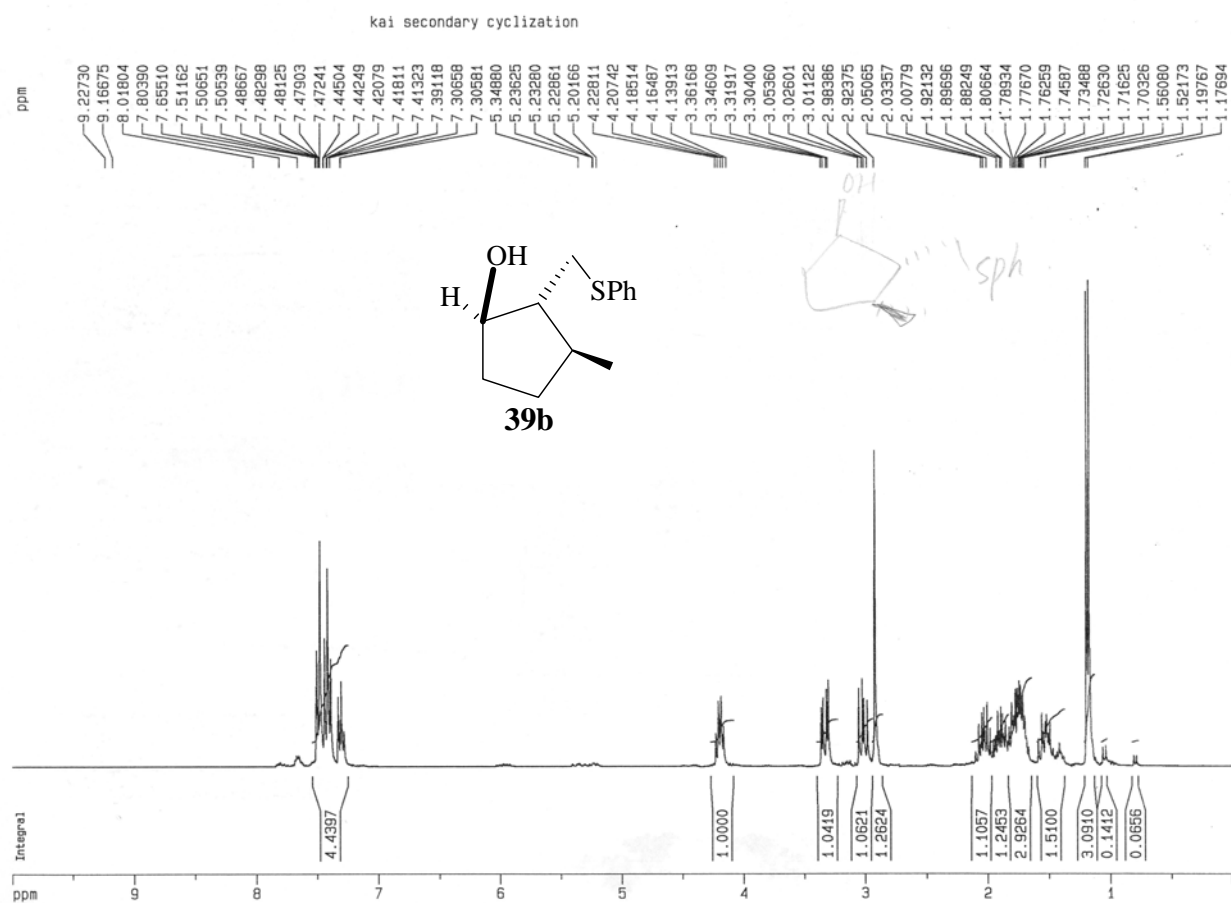
SF	500.1299996 MHz
WDW	SINE
SGB	0
LB	0.00 Hz
GB	0

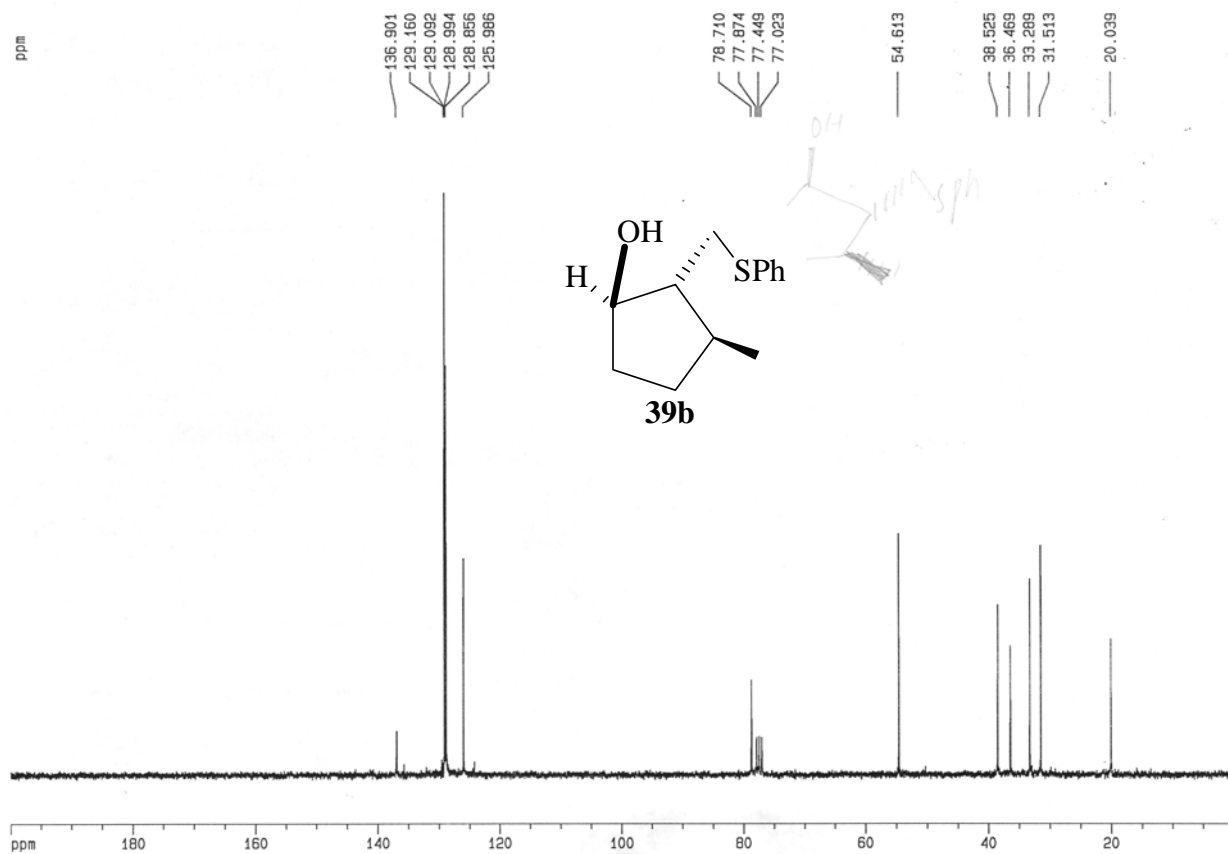
2D NMR plot parameters

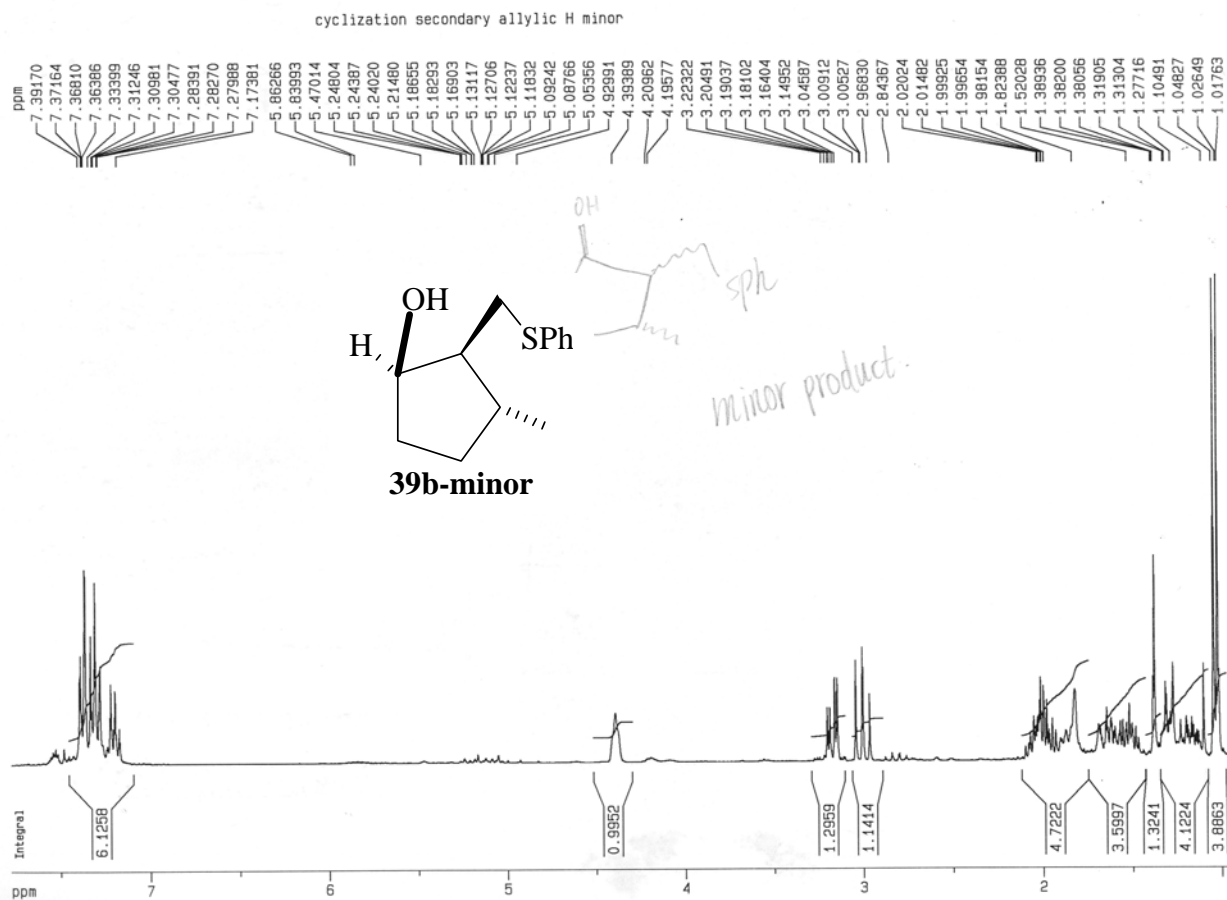
CH2	15.00 cm
CH1	15.00 cm
F2PLD	7.355 ppm
F2D	3778.44 Hz
F2H1	1.163 ppm
F2H2	581.78 Hz
F2PLD	7.314 ppm
F2D	3787.82 Hz
F2H1	1.147 ppm
F2H2	573.80 Hz
F2PMDH	0.42611 ppm/cm
F2MDH	213.11575 Hz/cm
F2PMDH	0.42615 ppm/cm
F2MDH	214.28136 Hz/cm

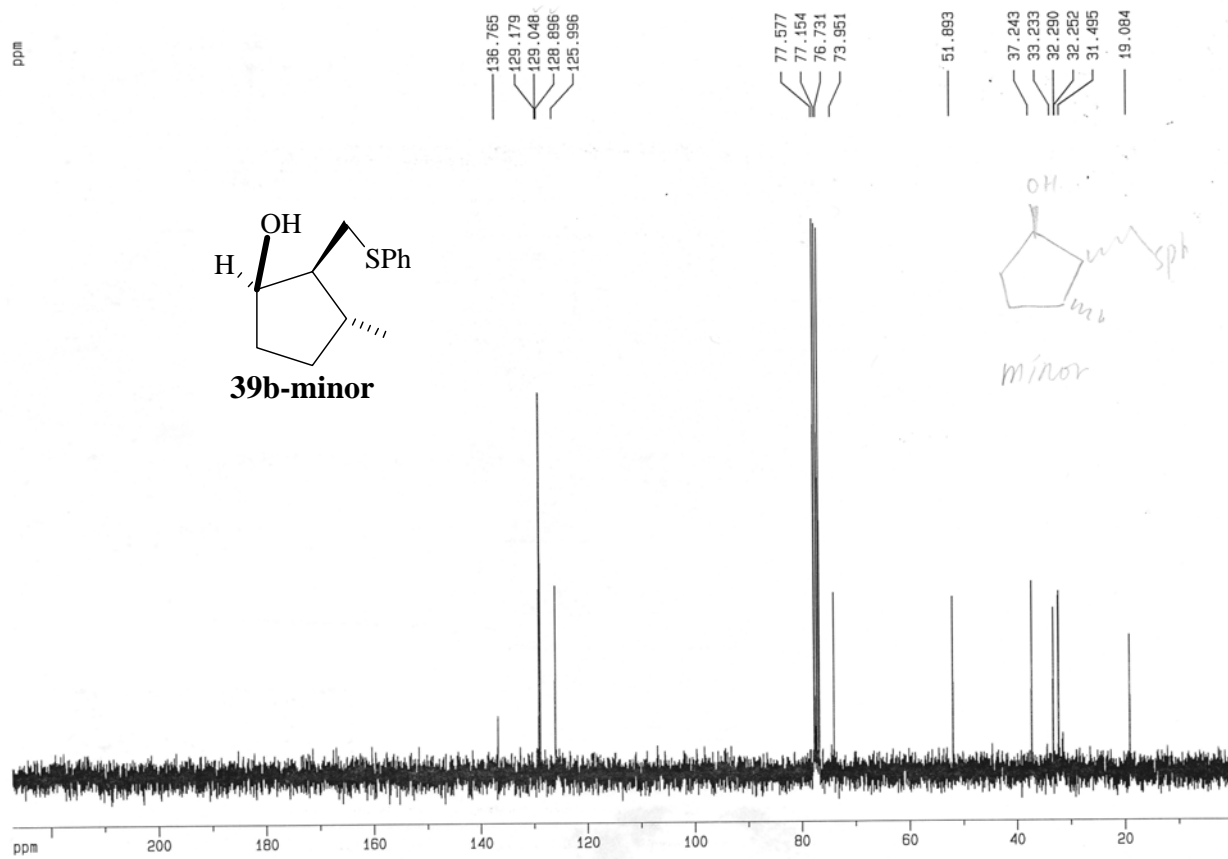


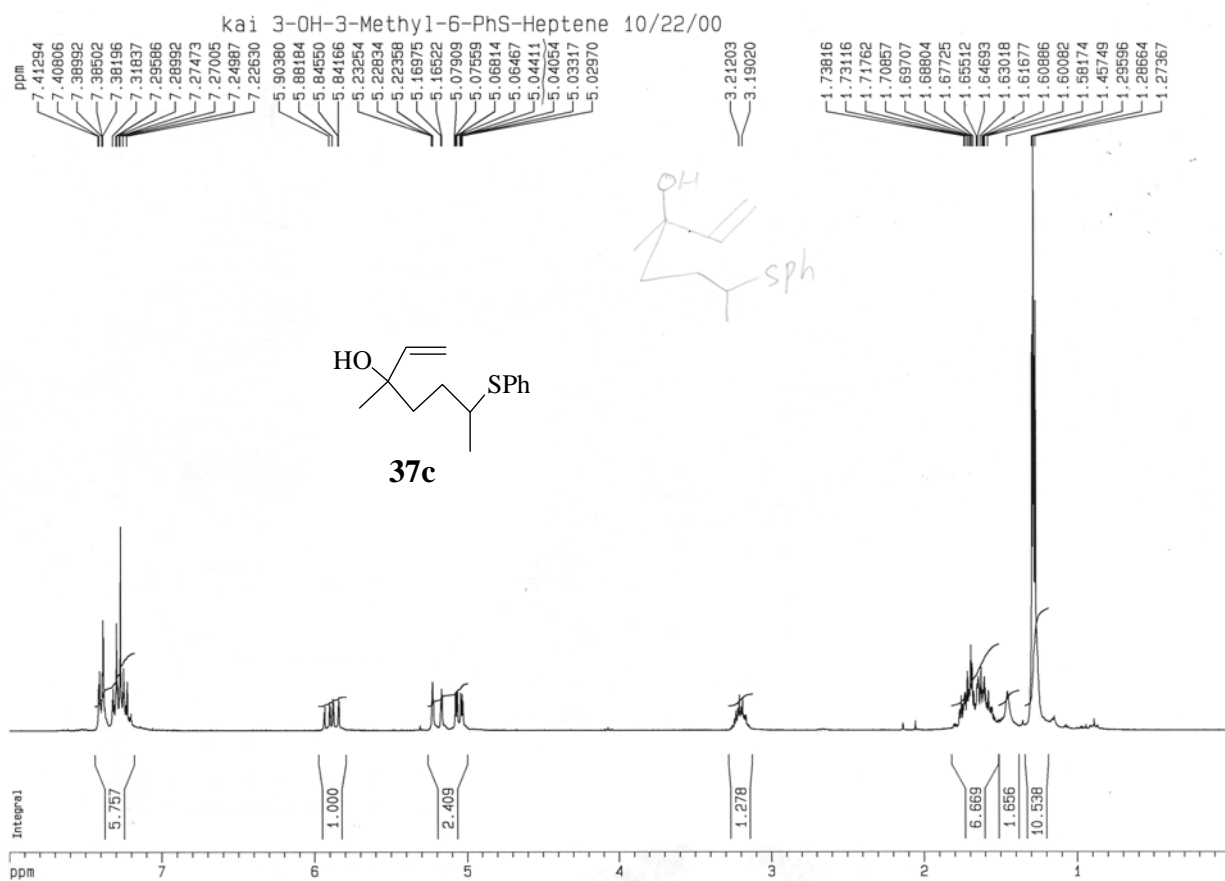


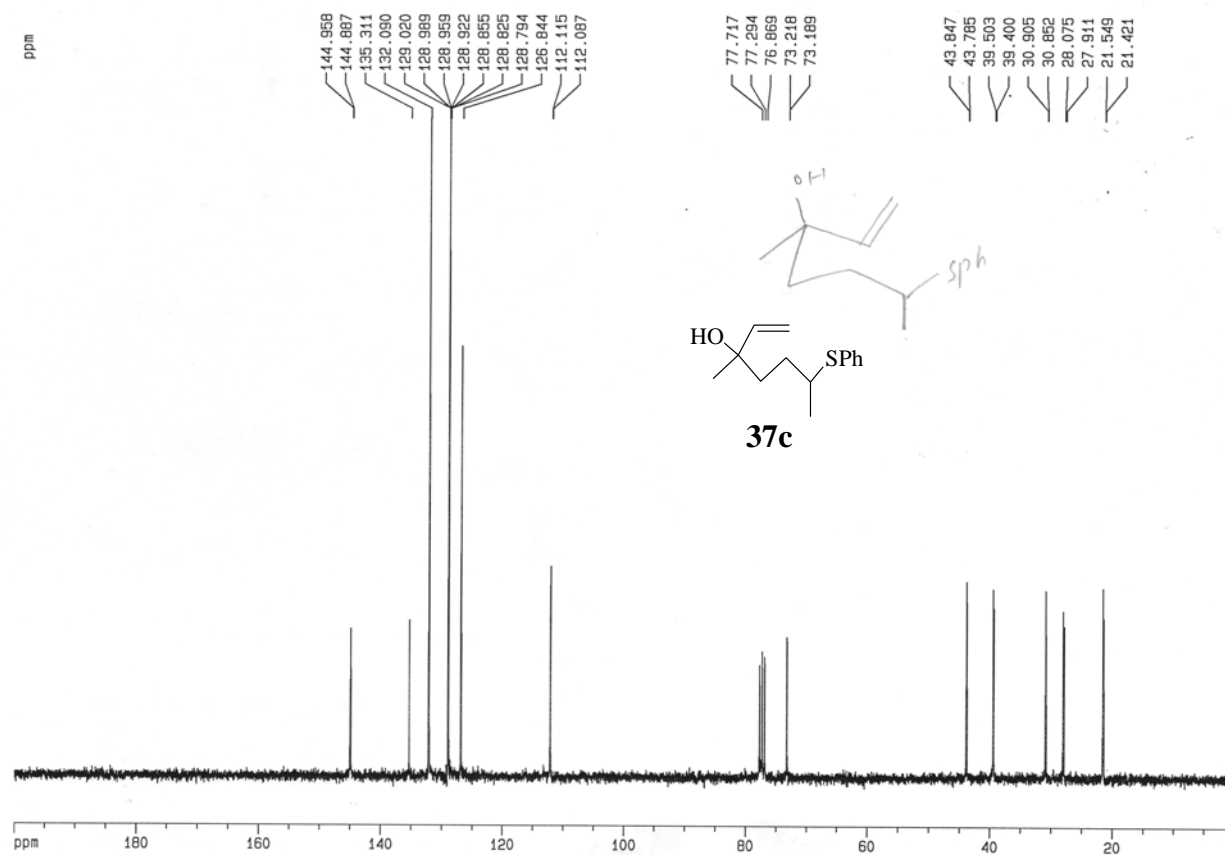




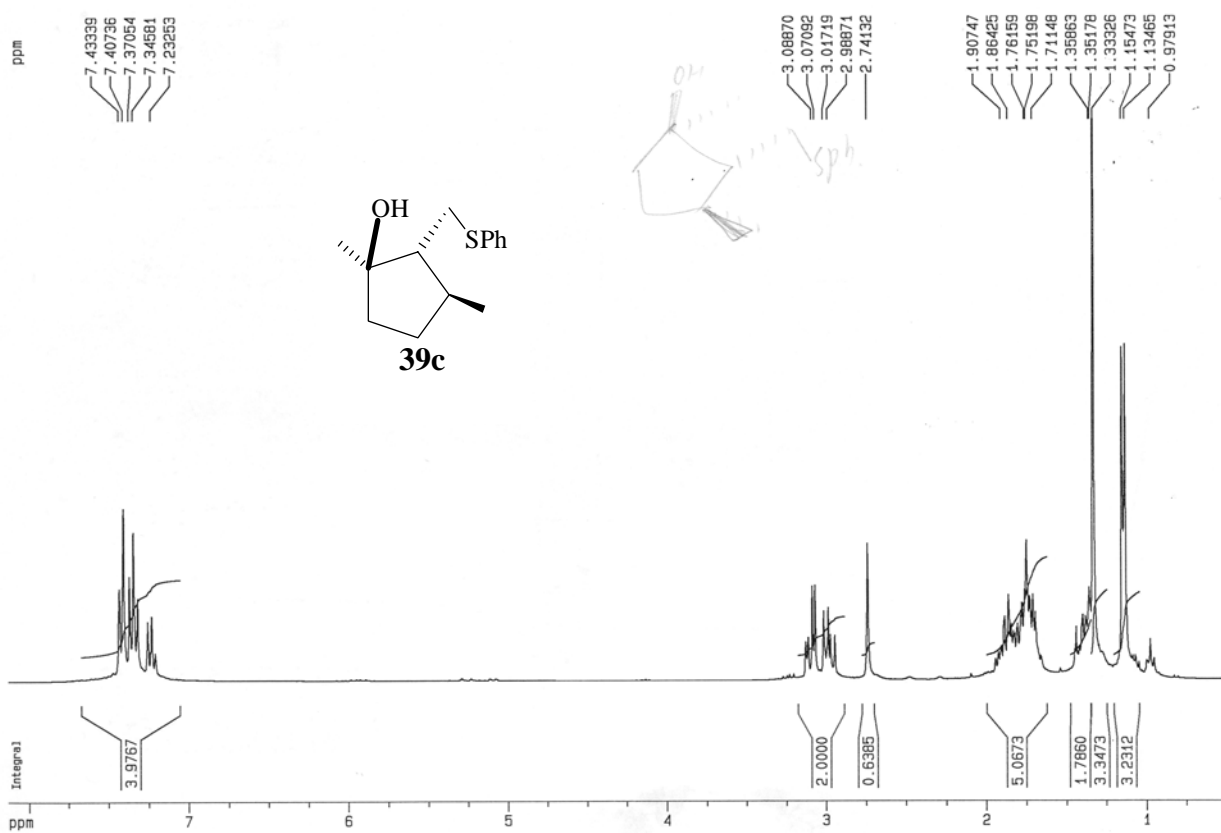


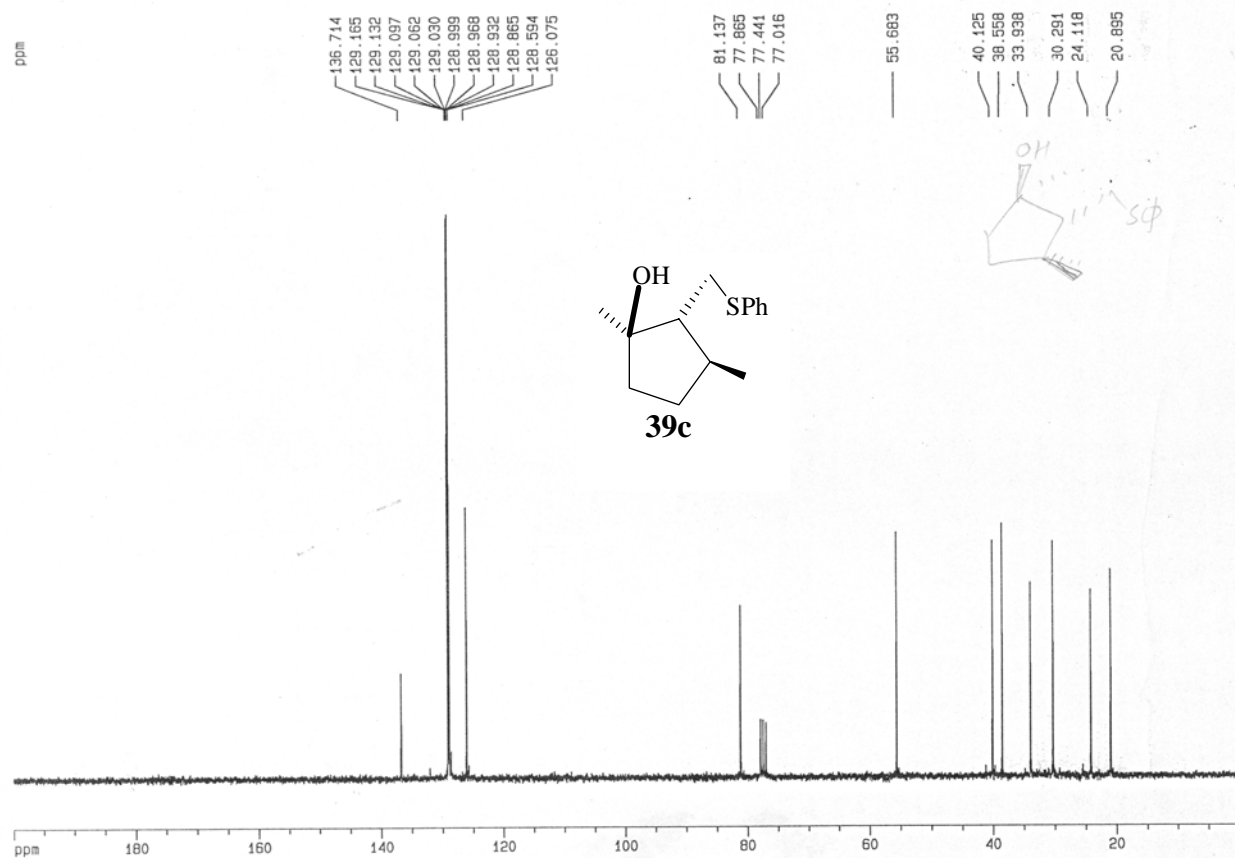




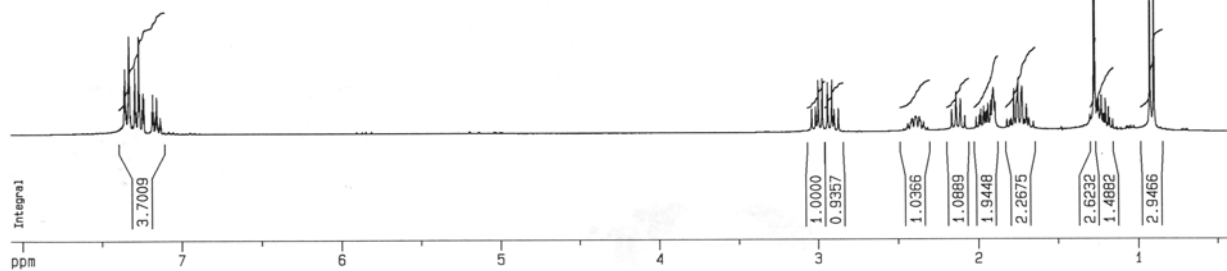
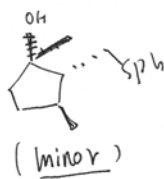
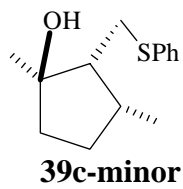
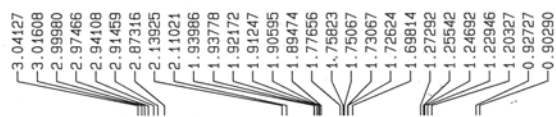
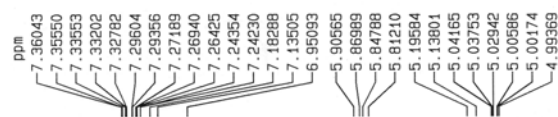


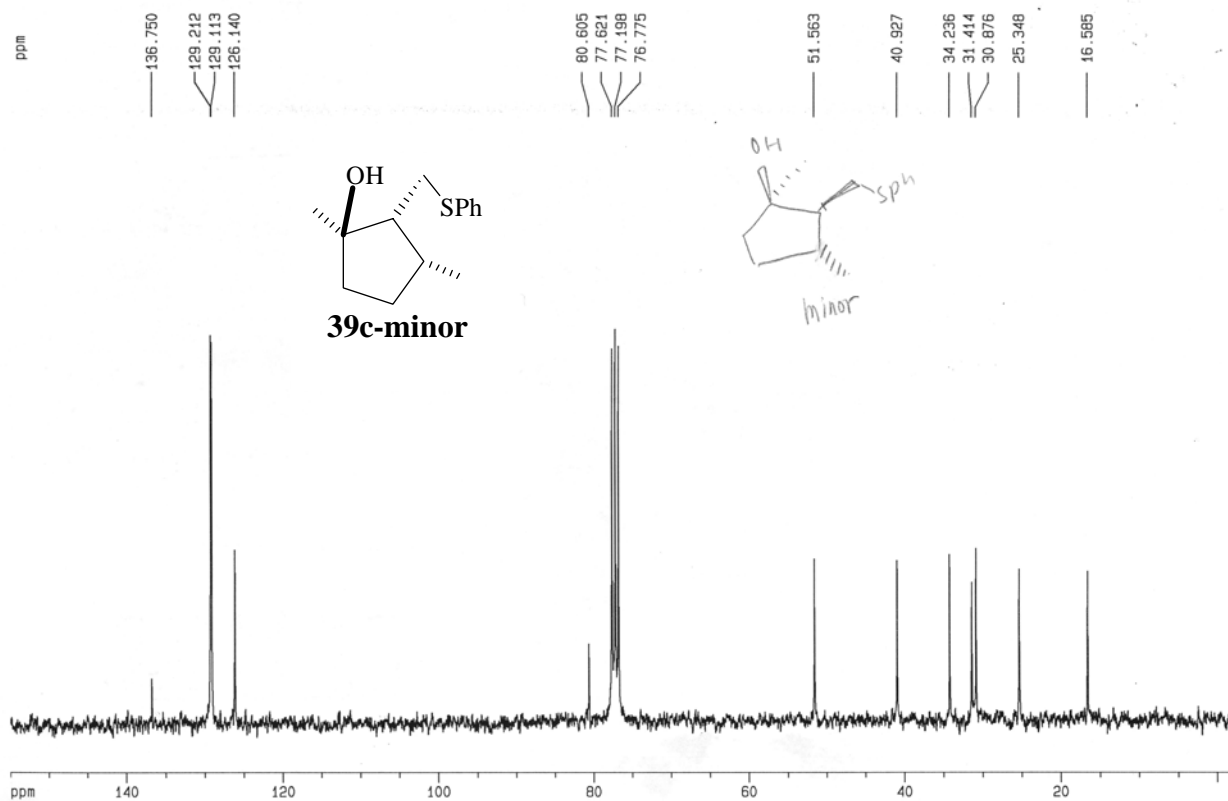
k 3-OH-3-methyl-6-PhS-1-heptene cyclization product major



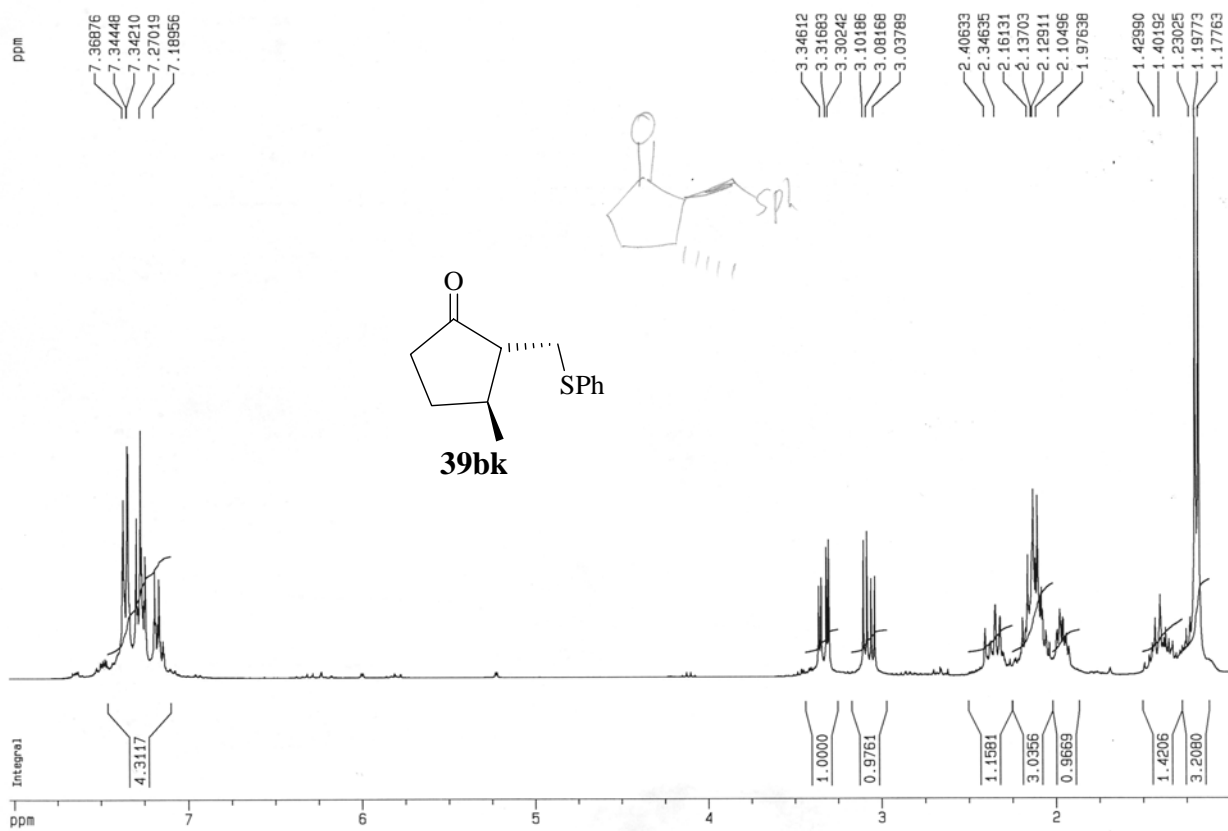


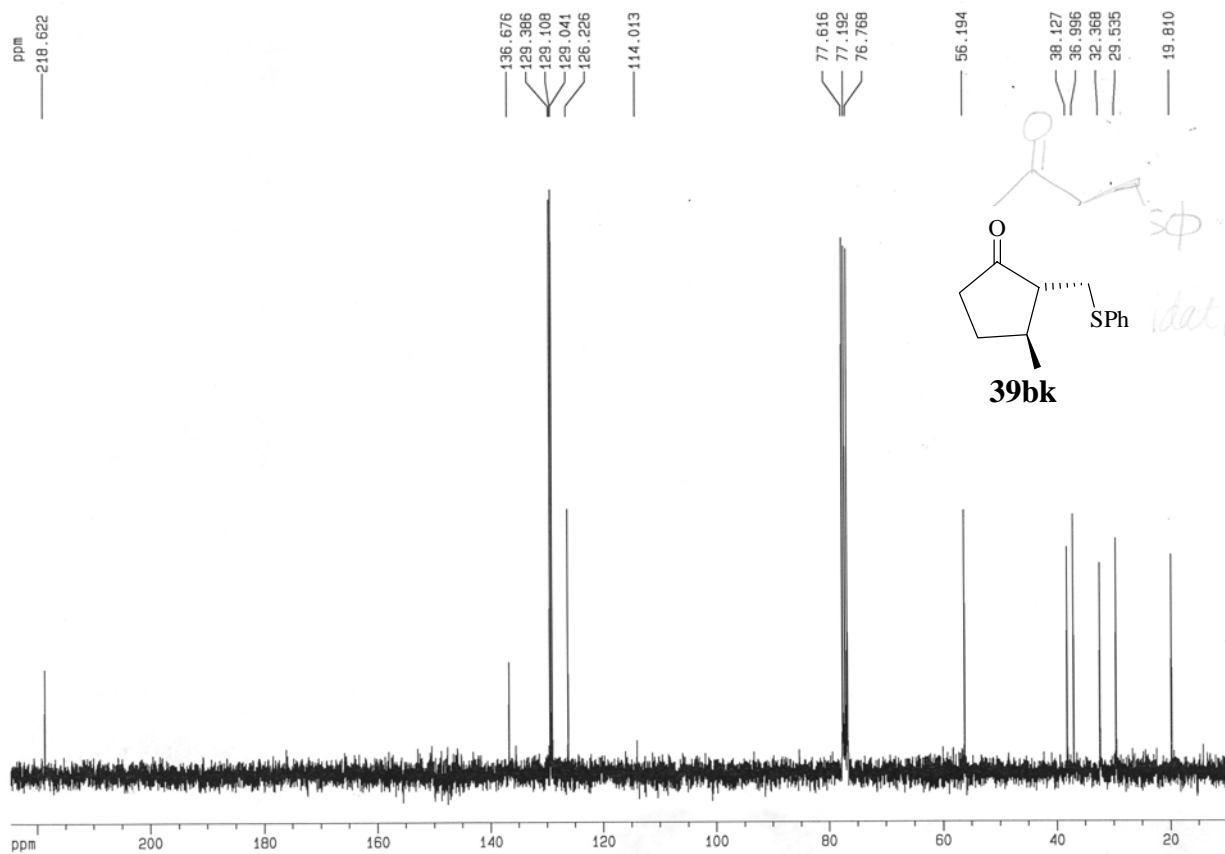
2nd cyclization

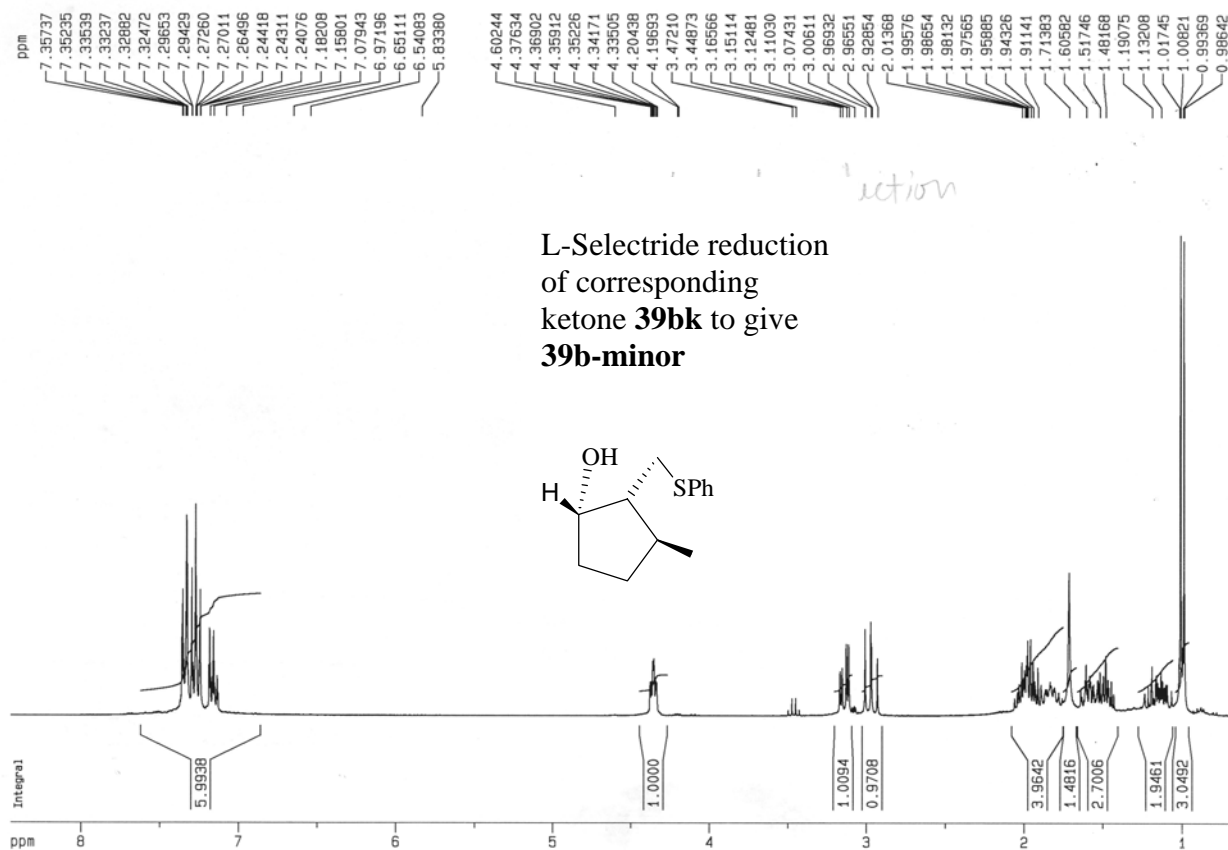


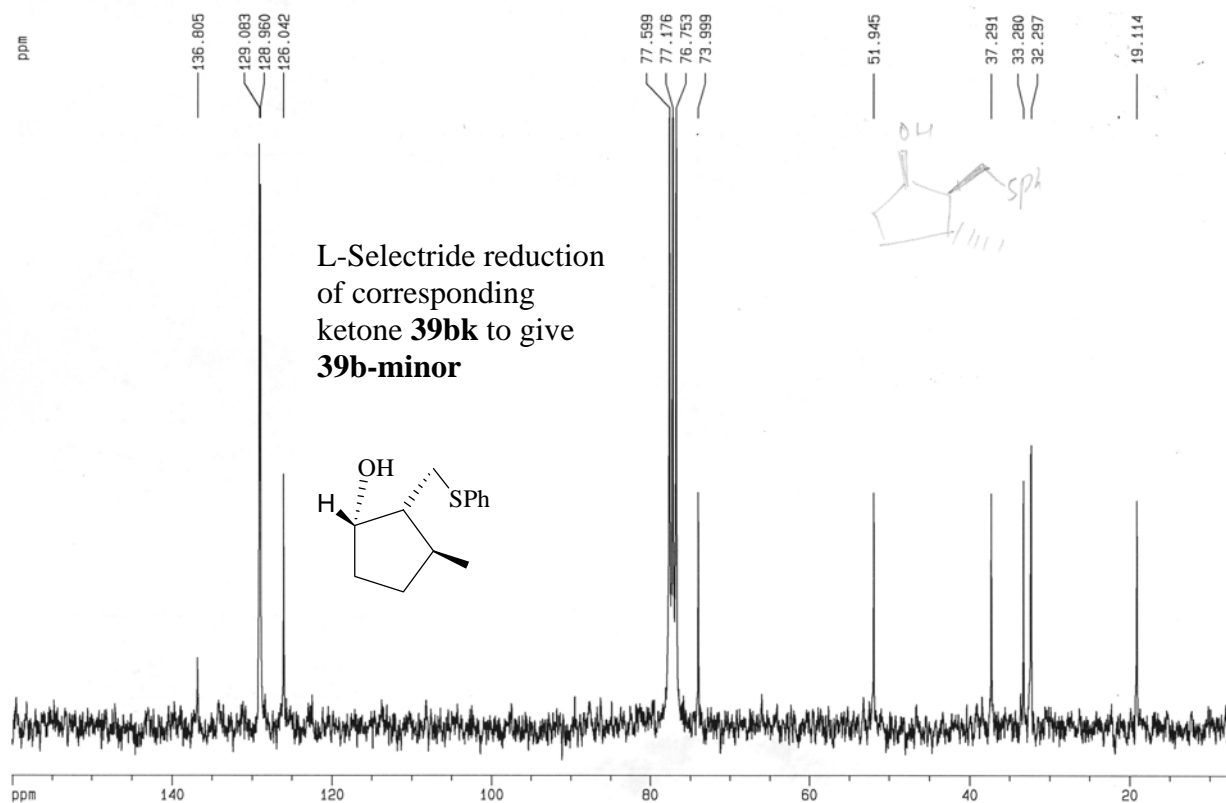


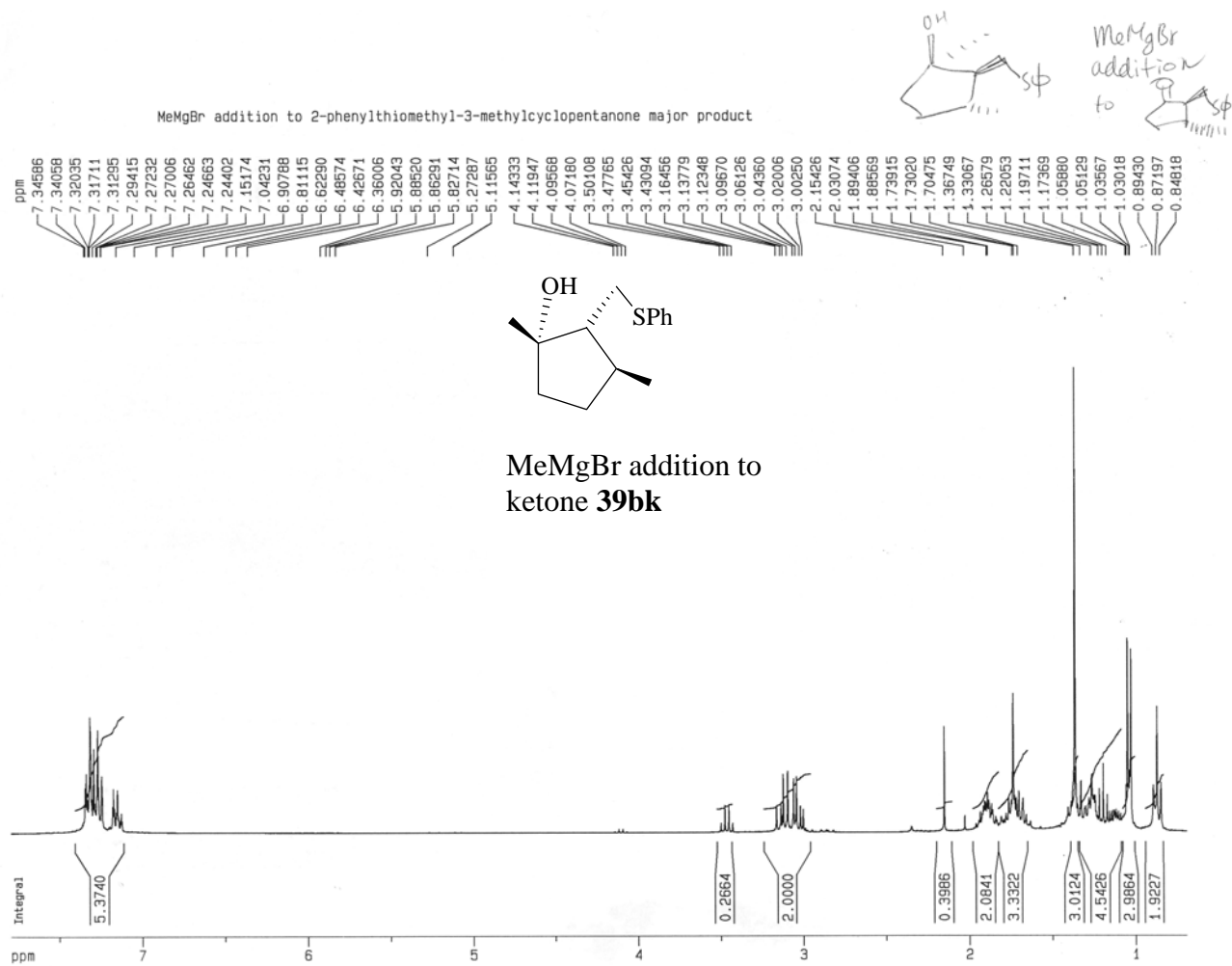
2-phenylthio-3-methylcyclopentanone

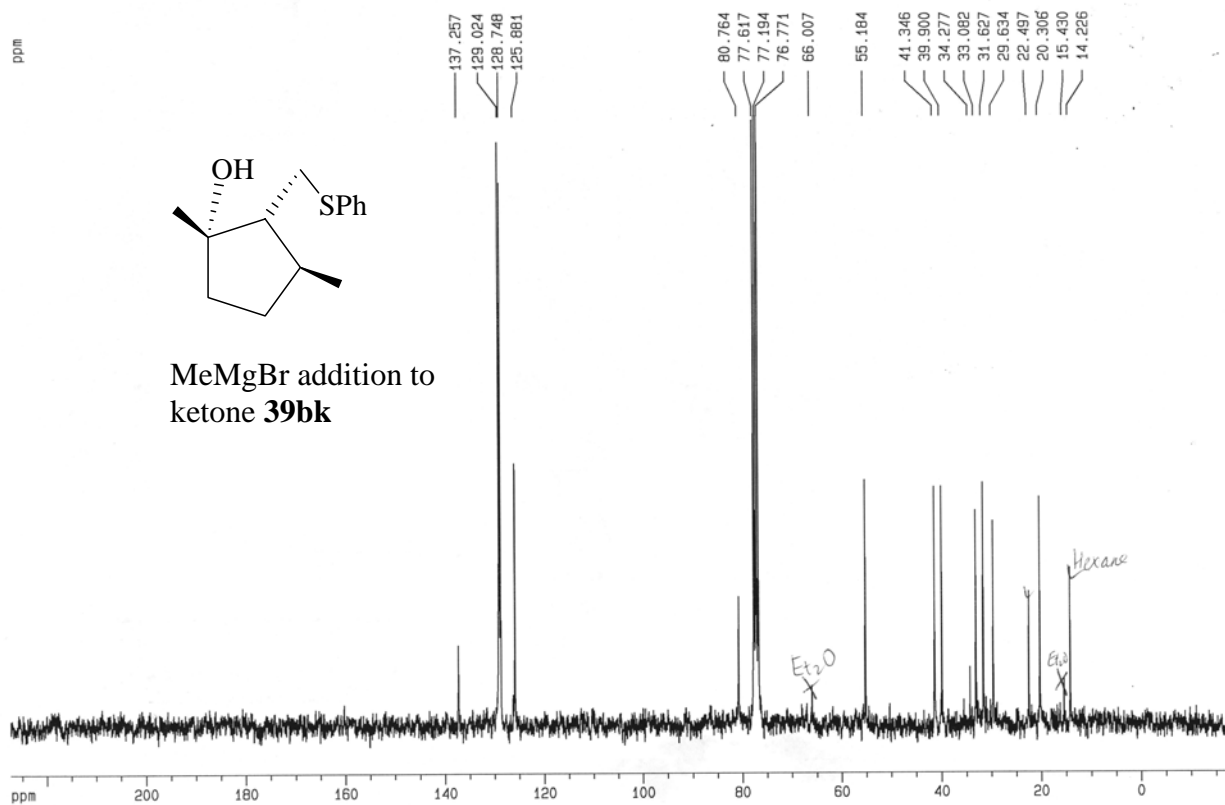


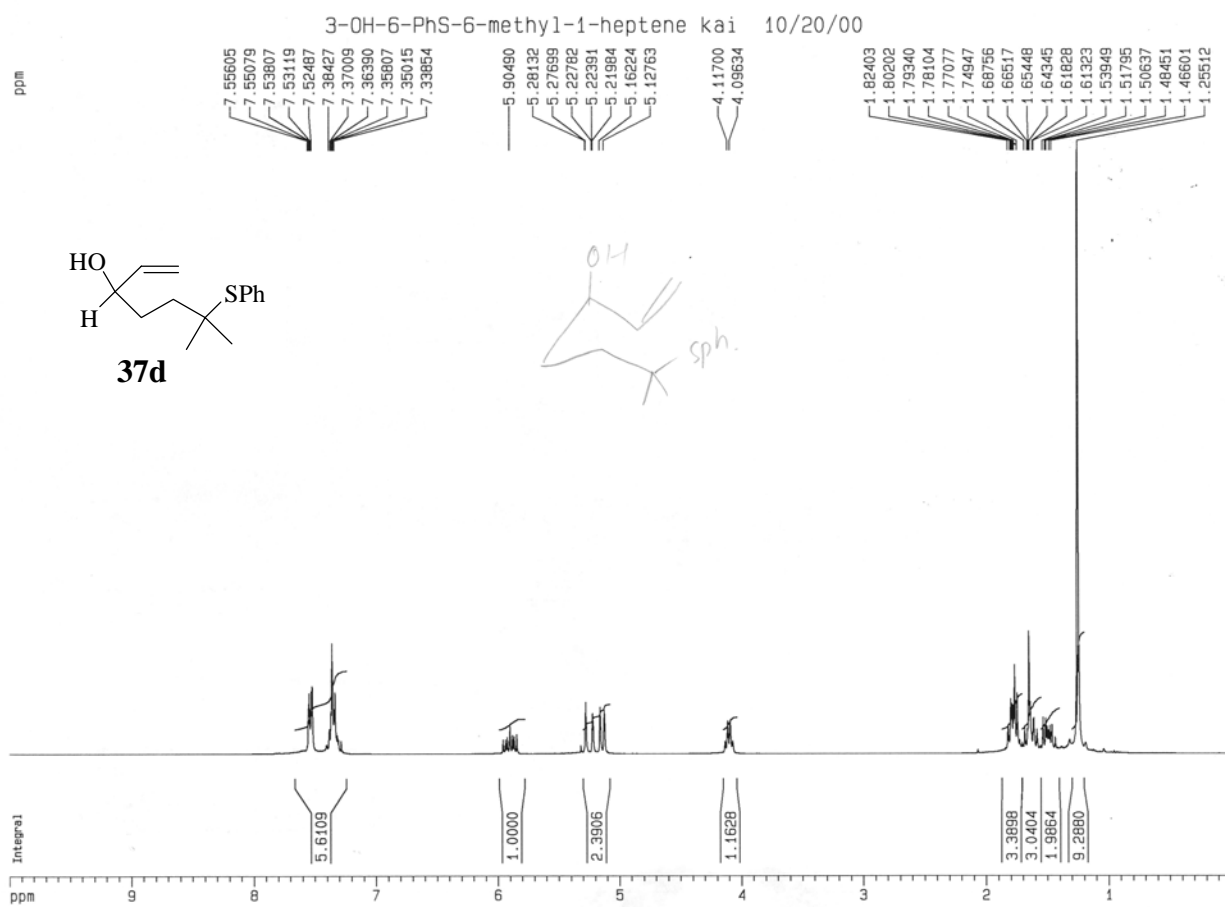


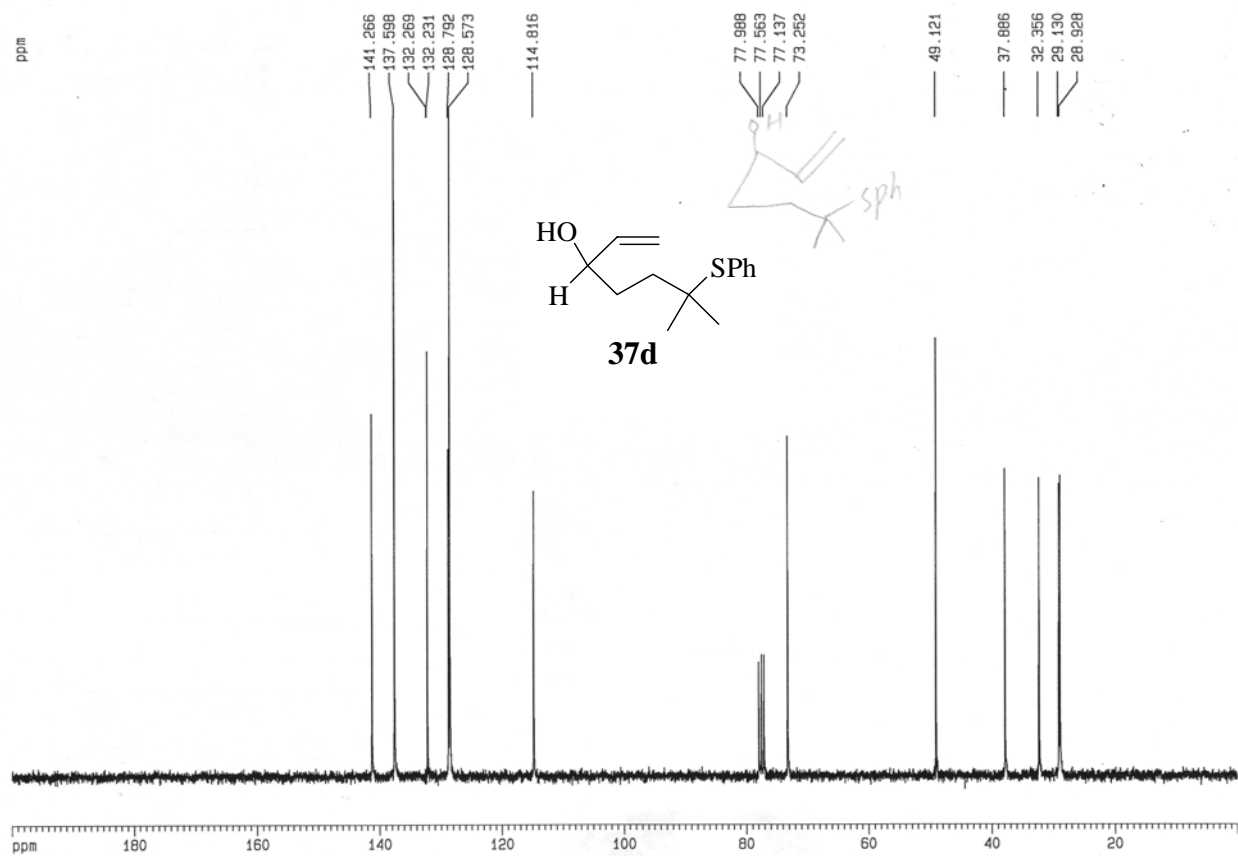


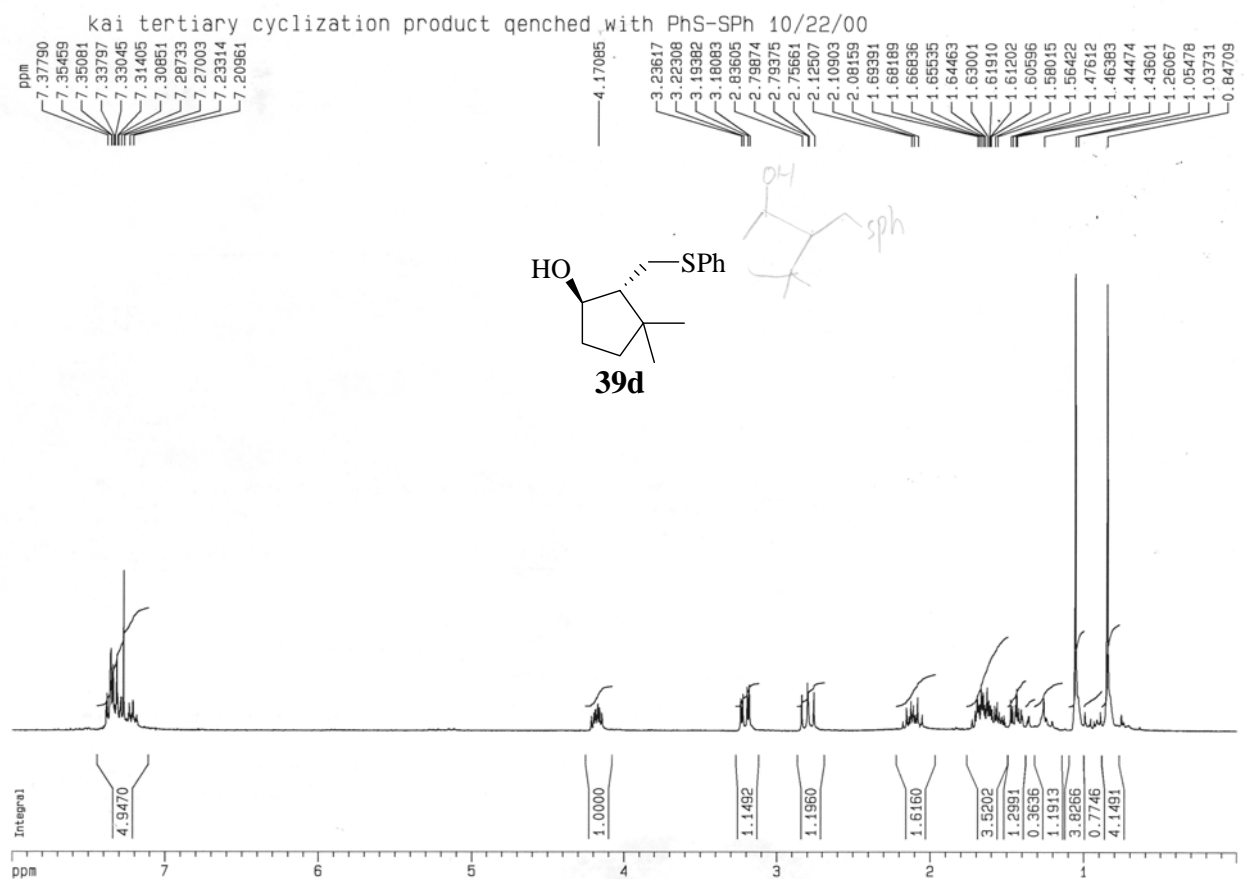


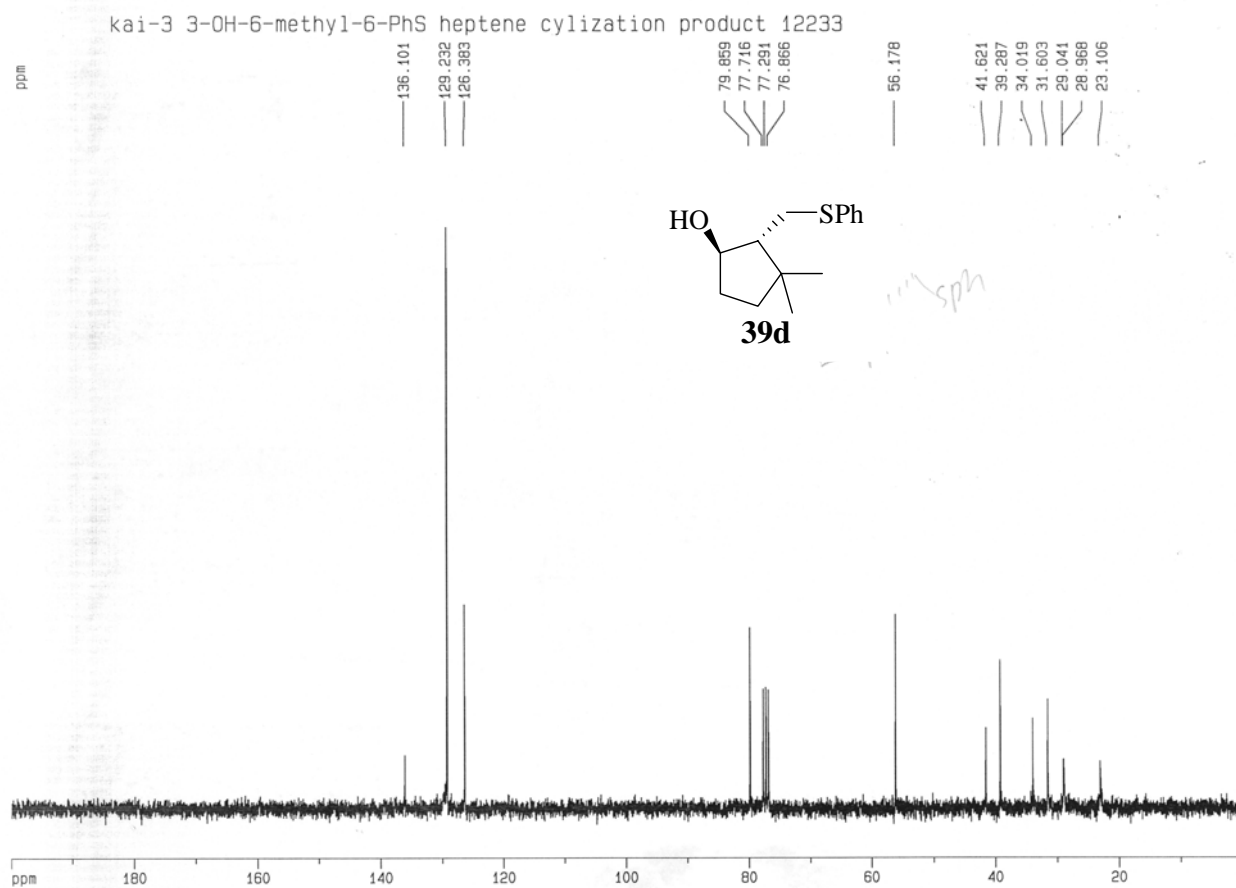


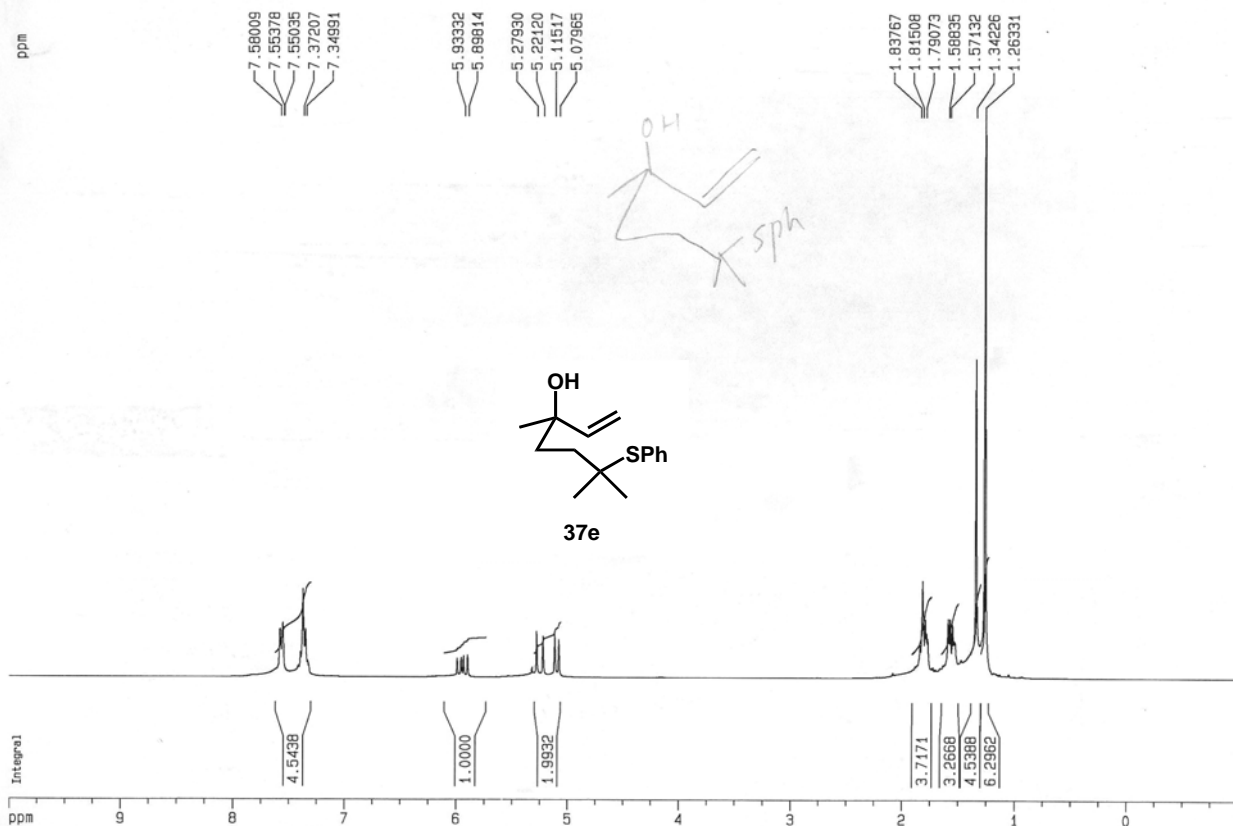


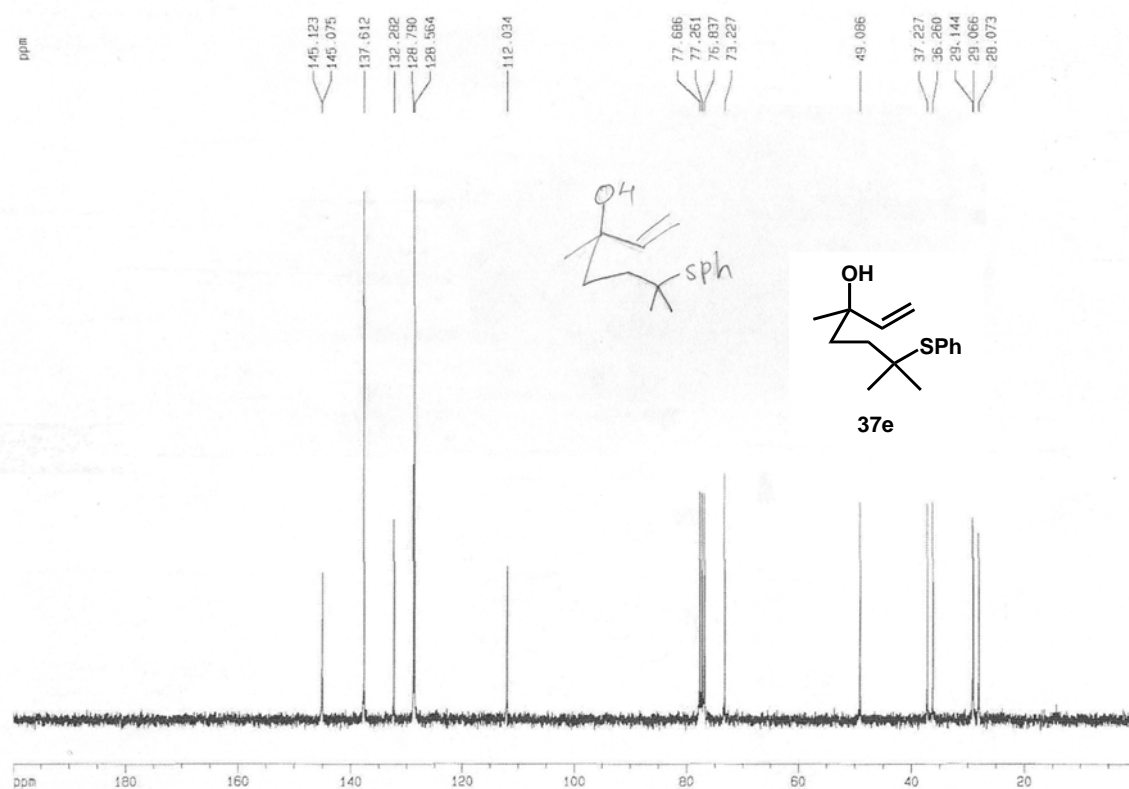


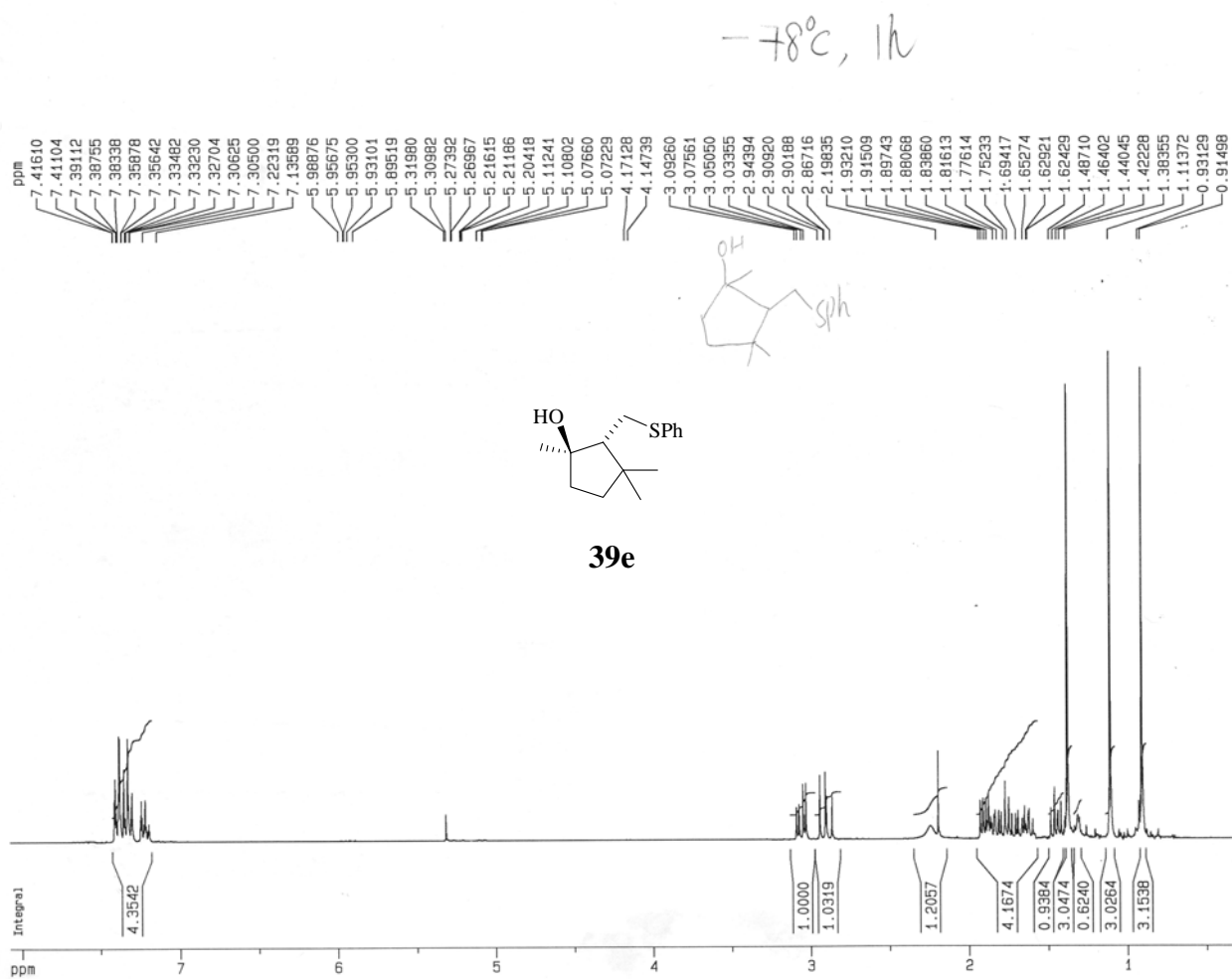


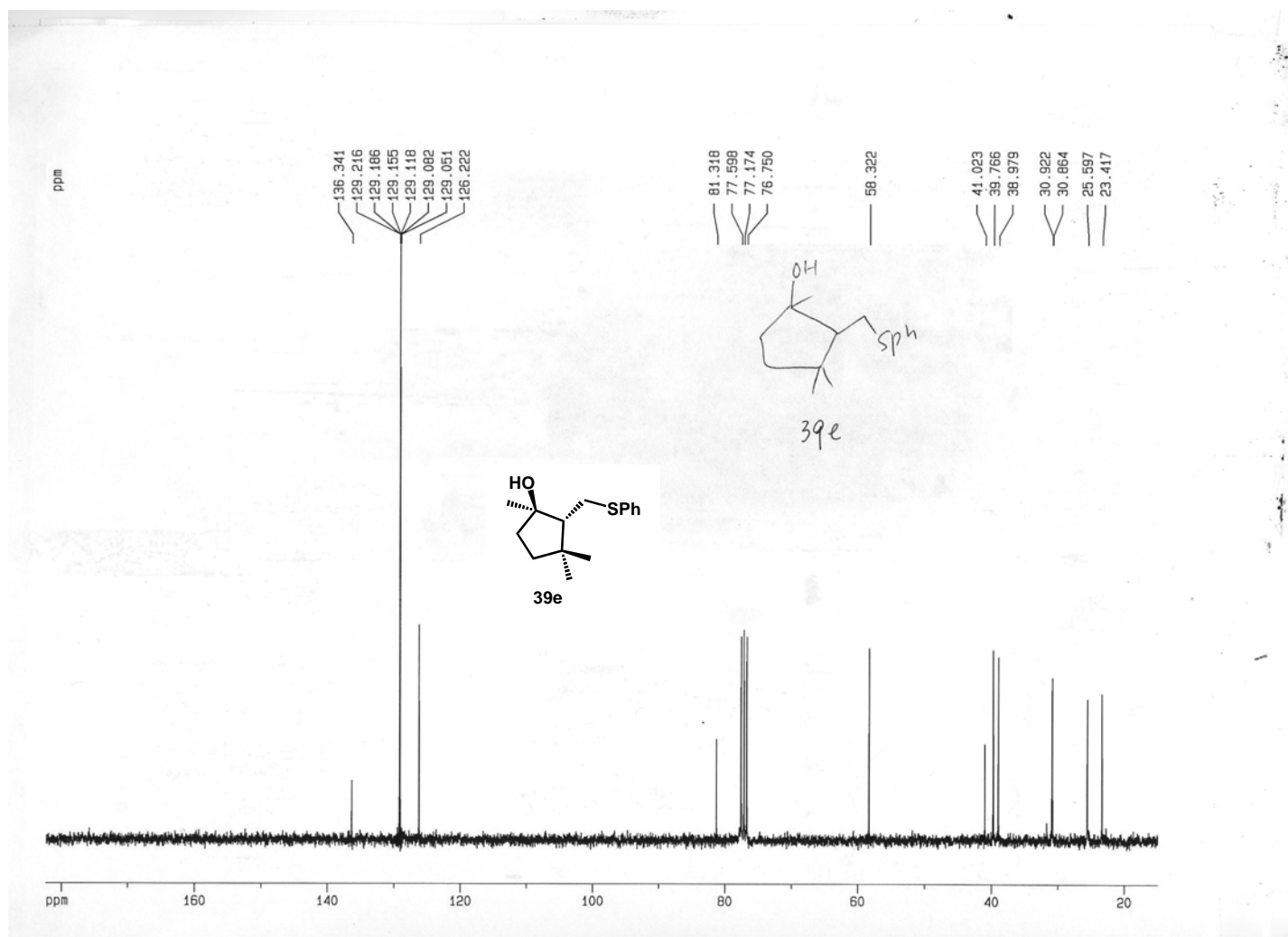


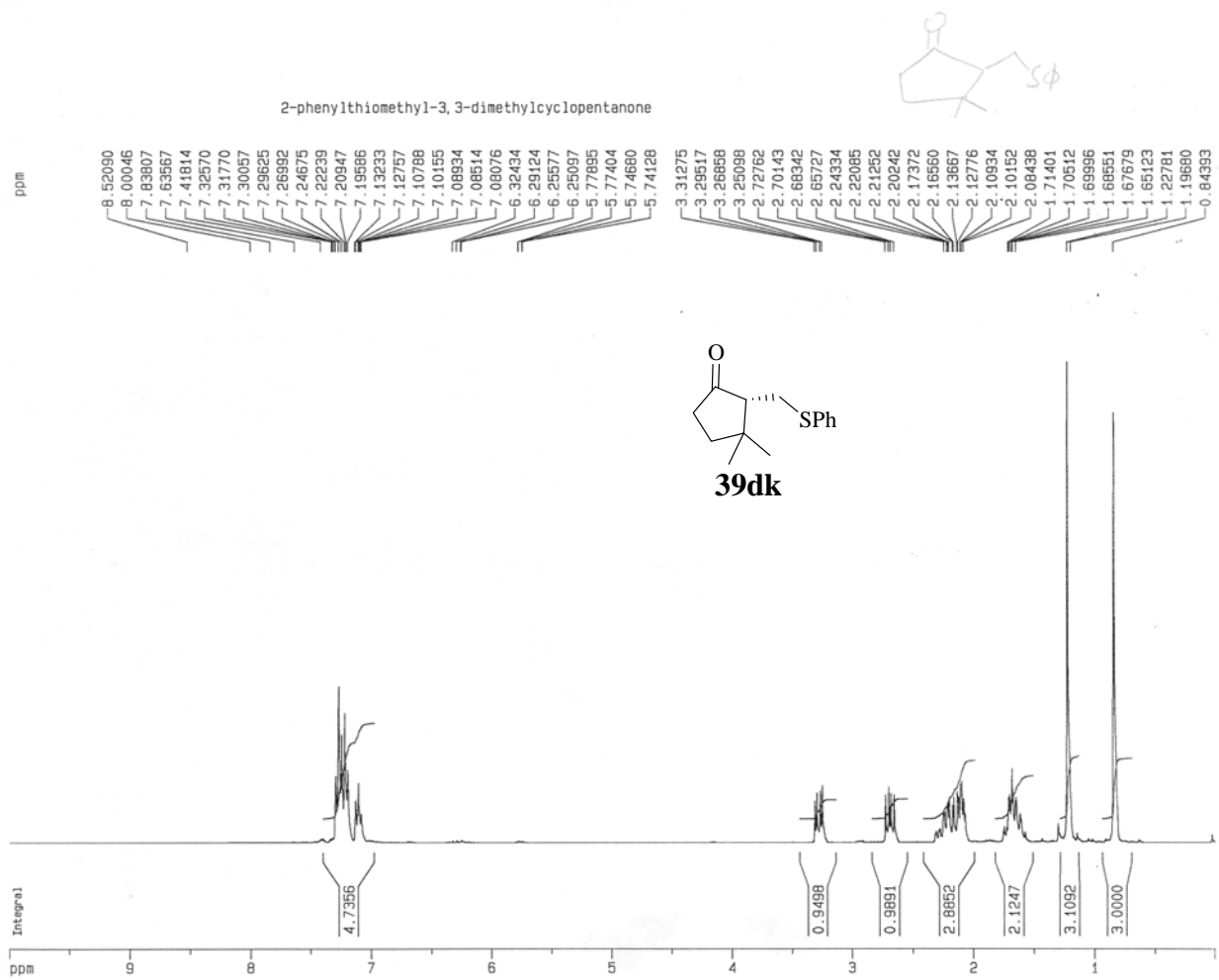




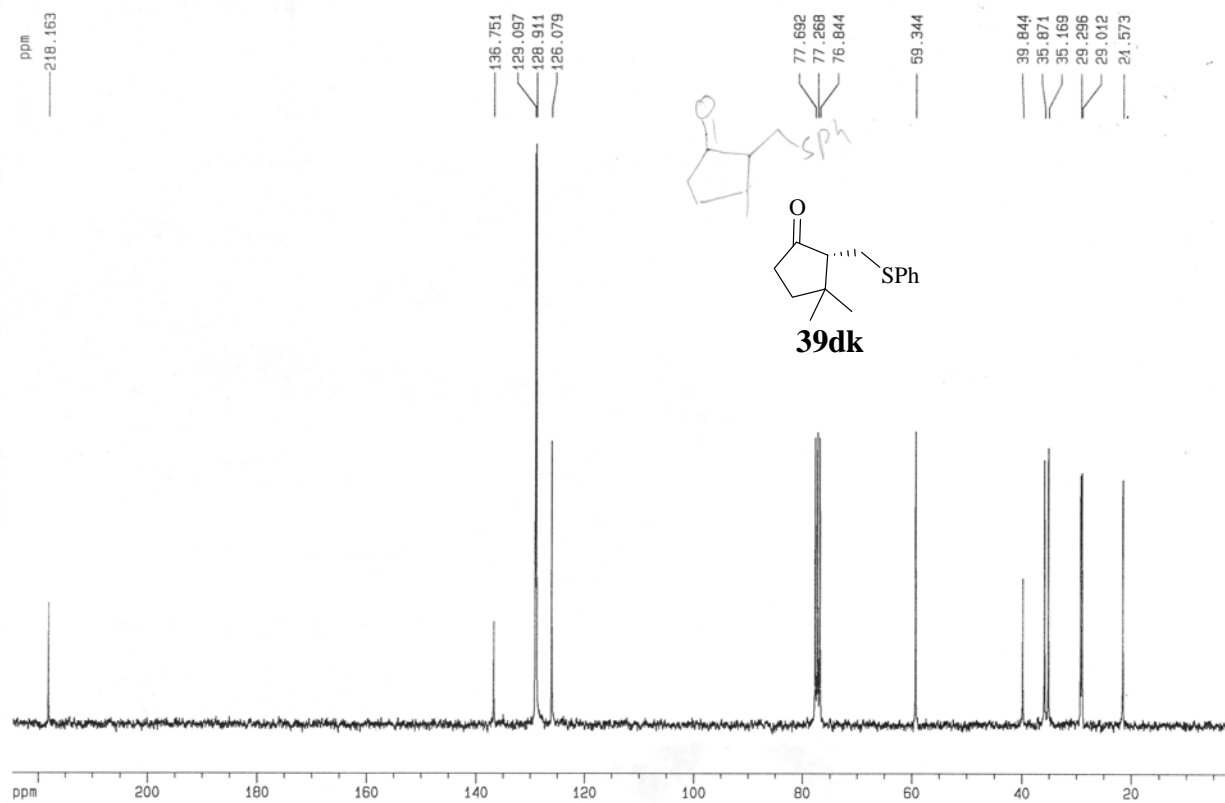




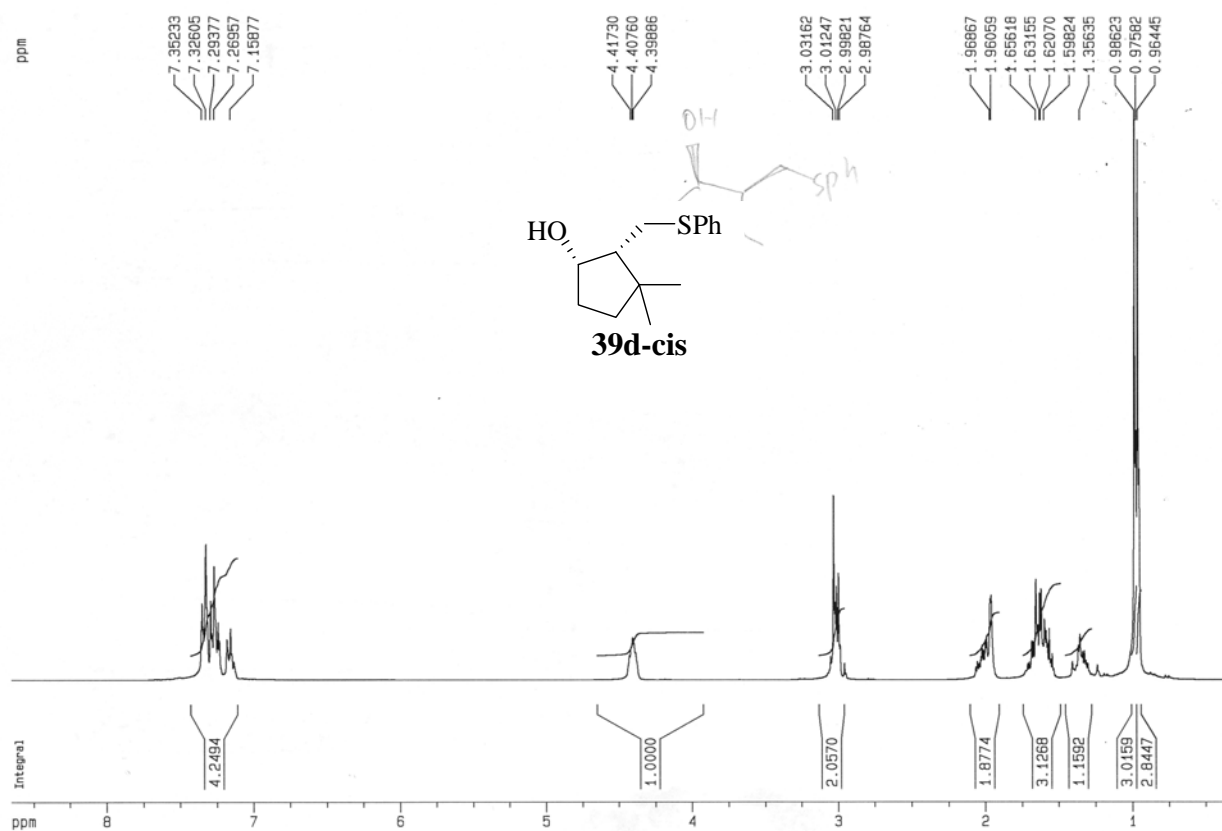




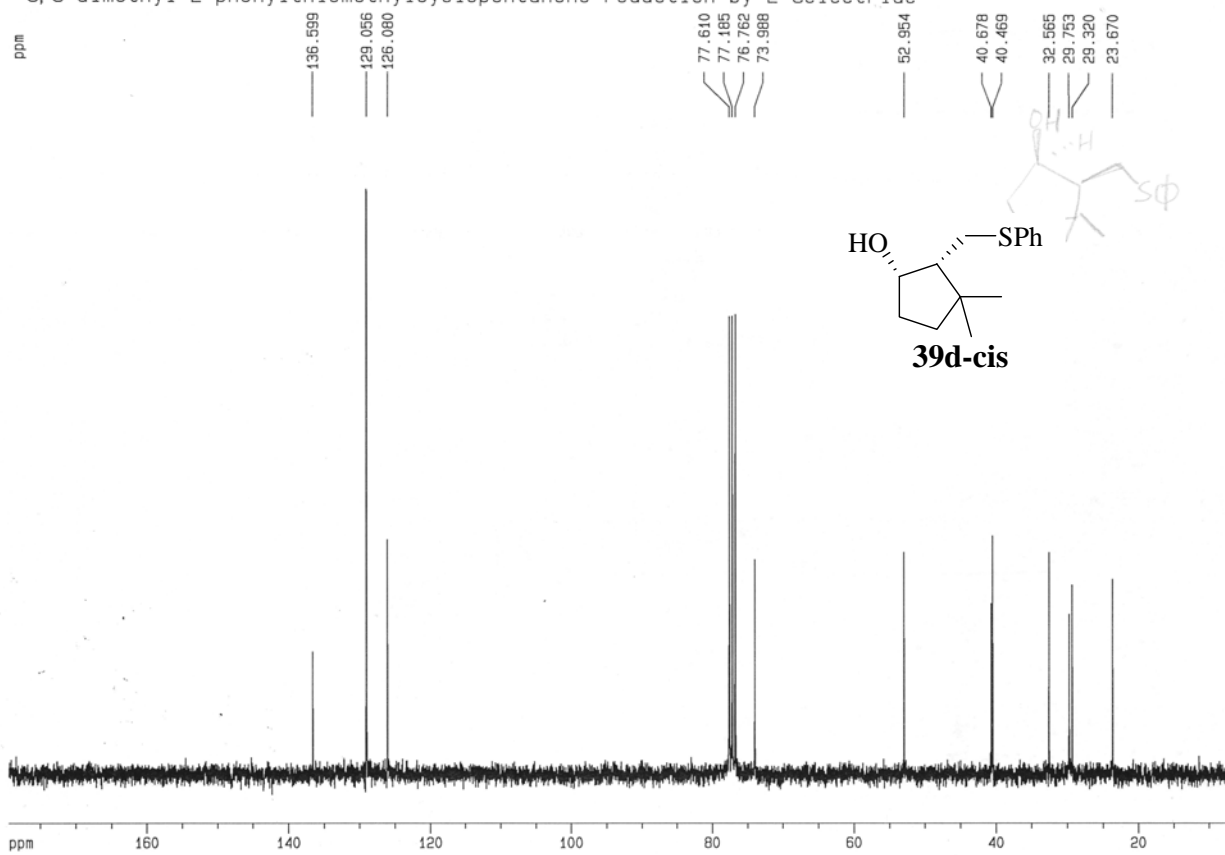
2-phenylthiomethyl-3,3-dimethylcyclopentanone

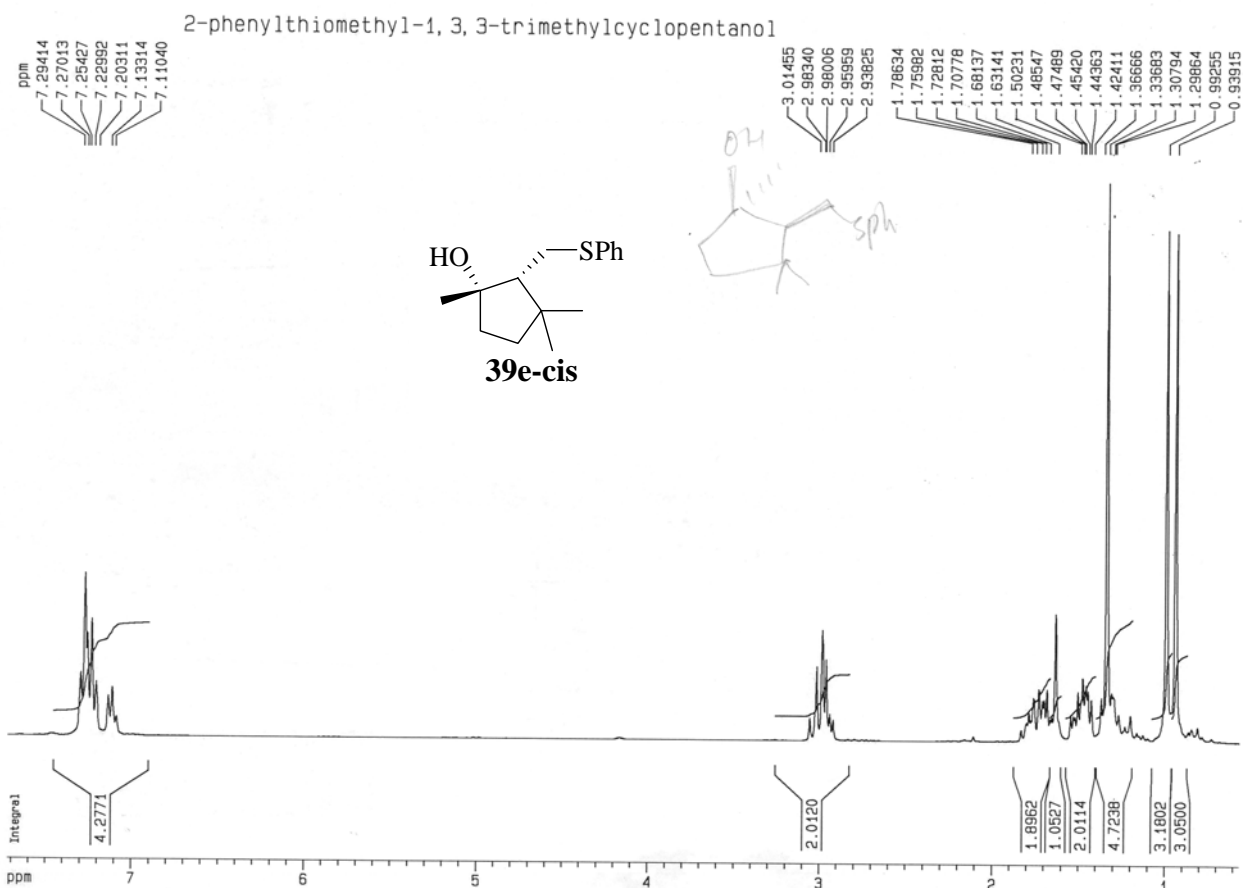


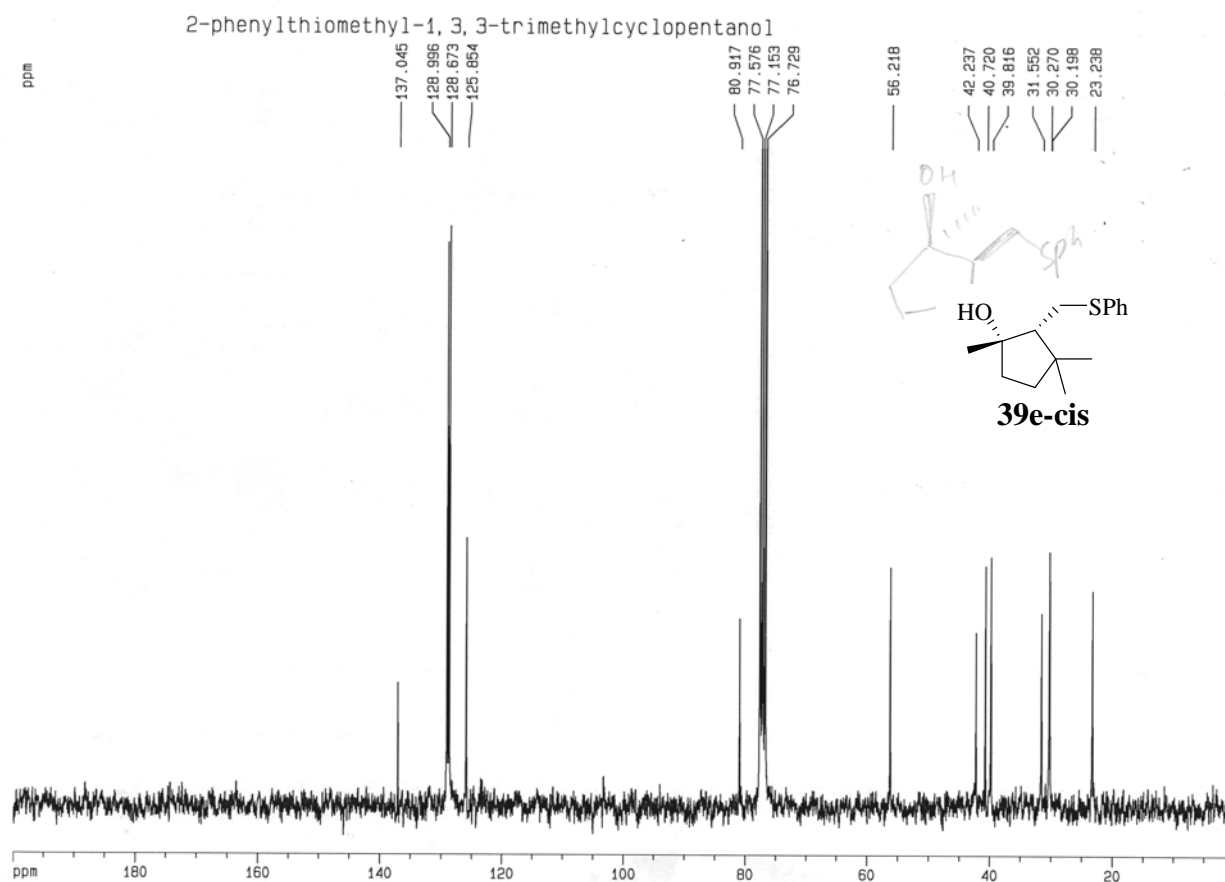
3,3-dimethyl-2-phenylthiomethylcyclopentanone reduction by L-Selectride



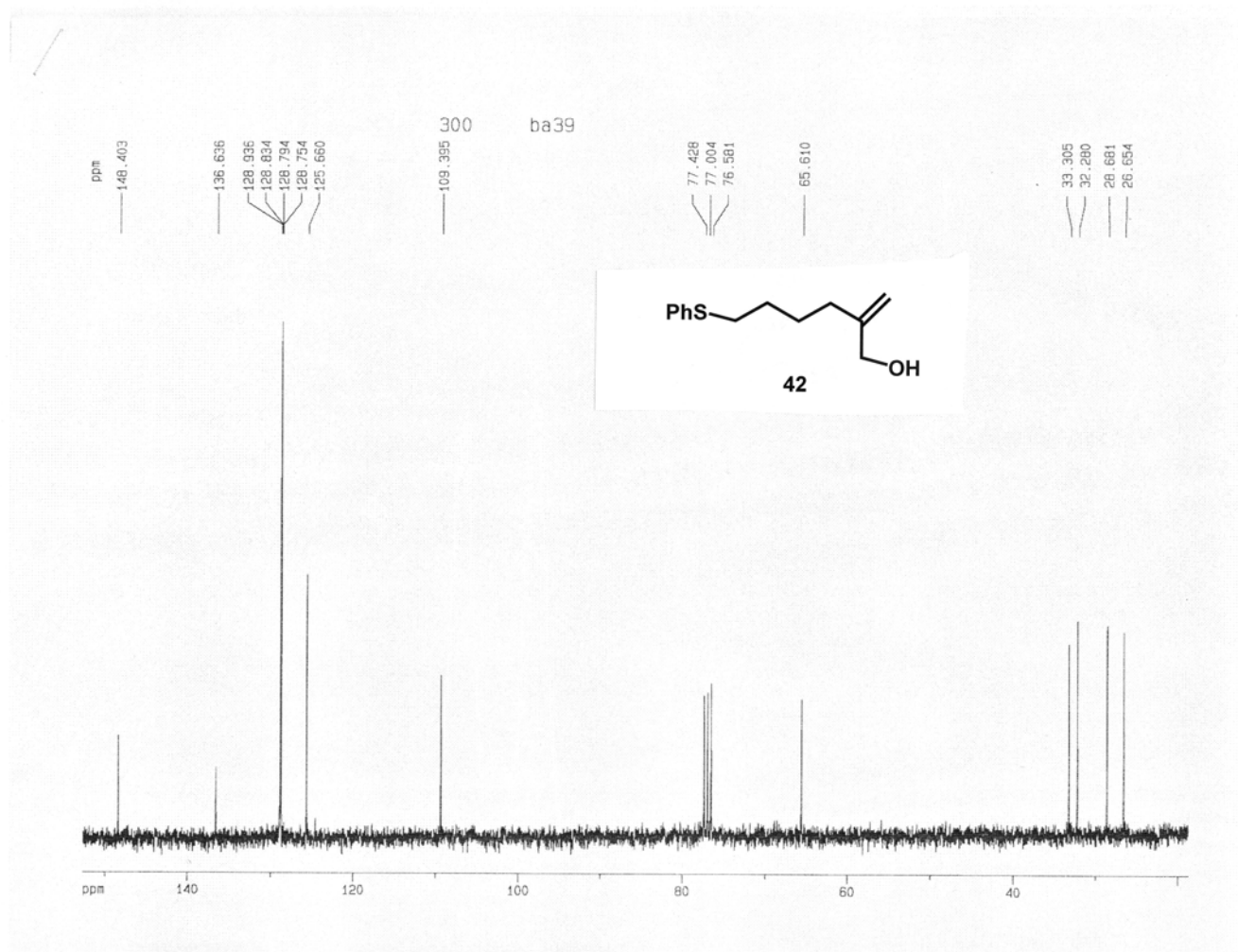
3,3-dimethyl-2-phenylthiomethylcyclopentanone reduction by L-Selectride

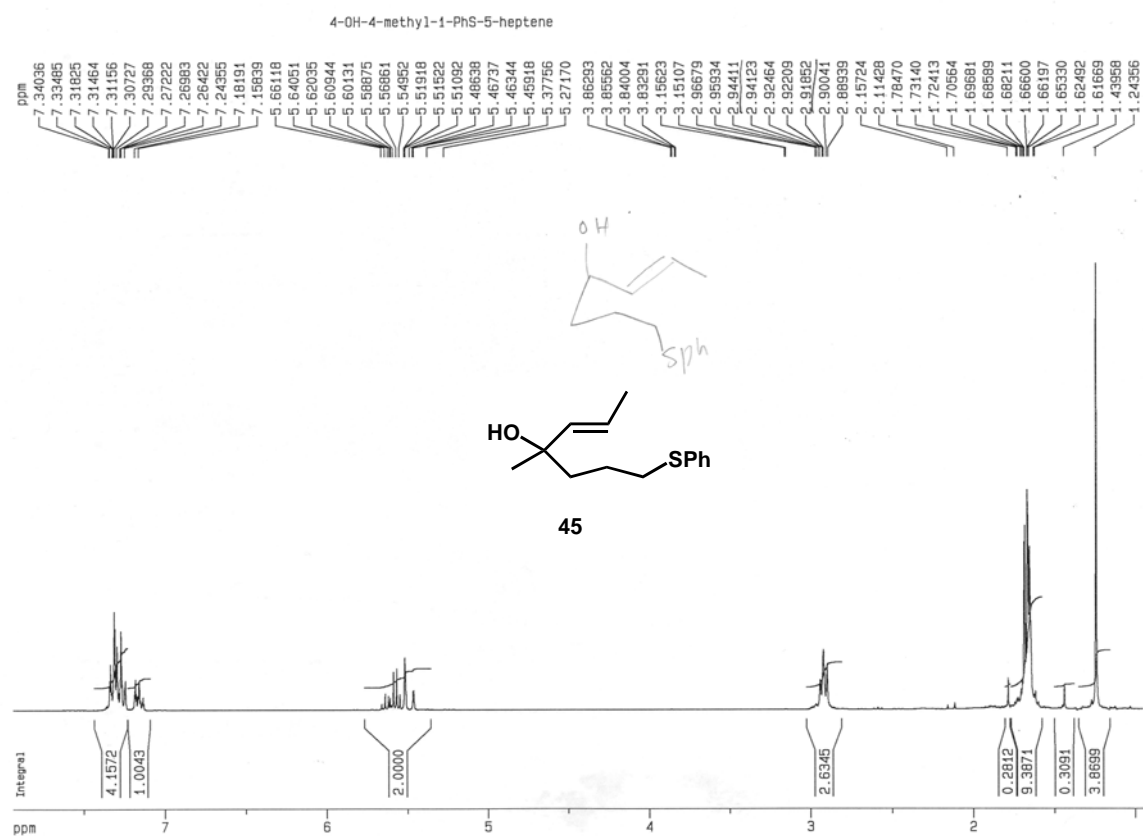


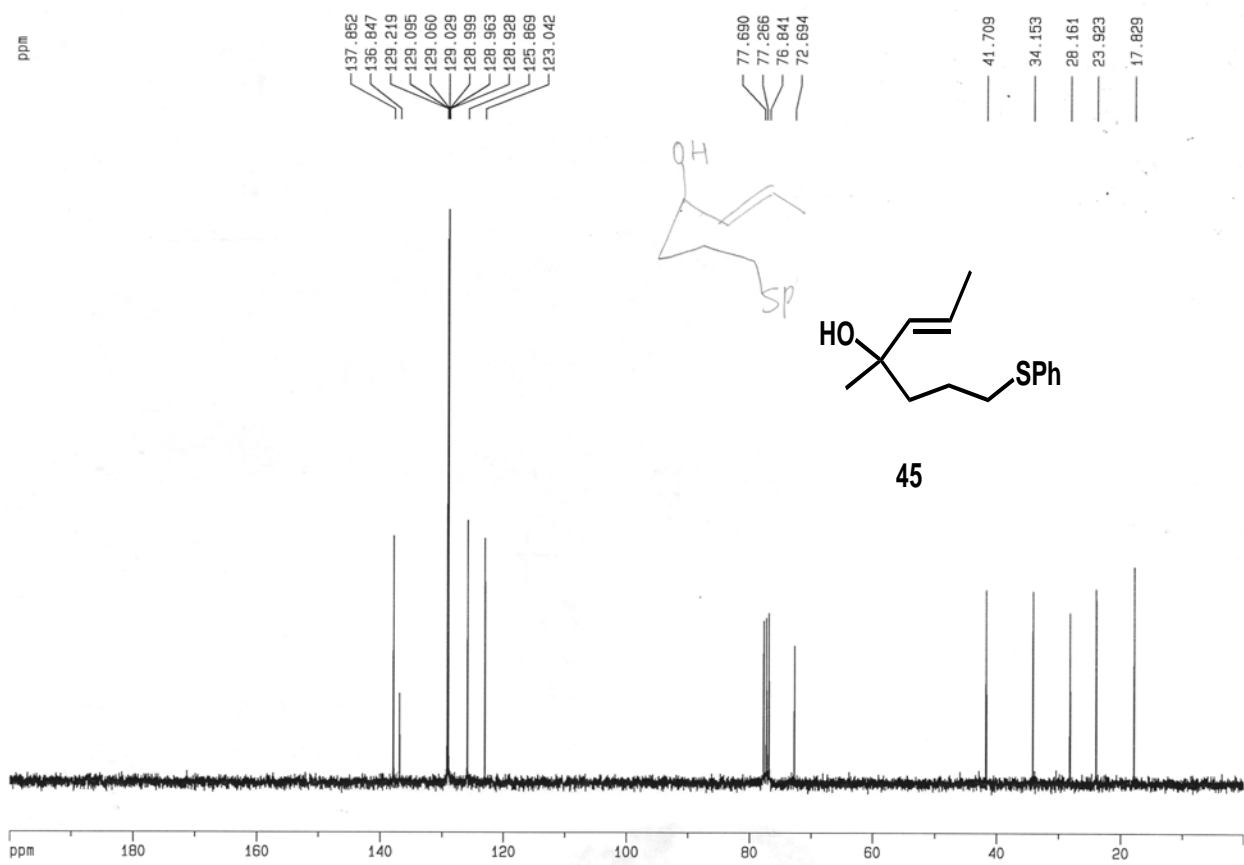


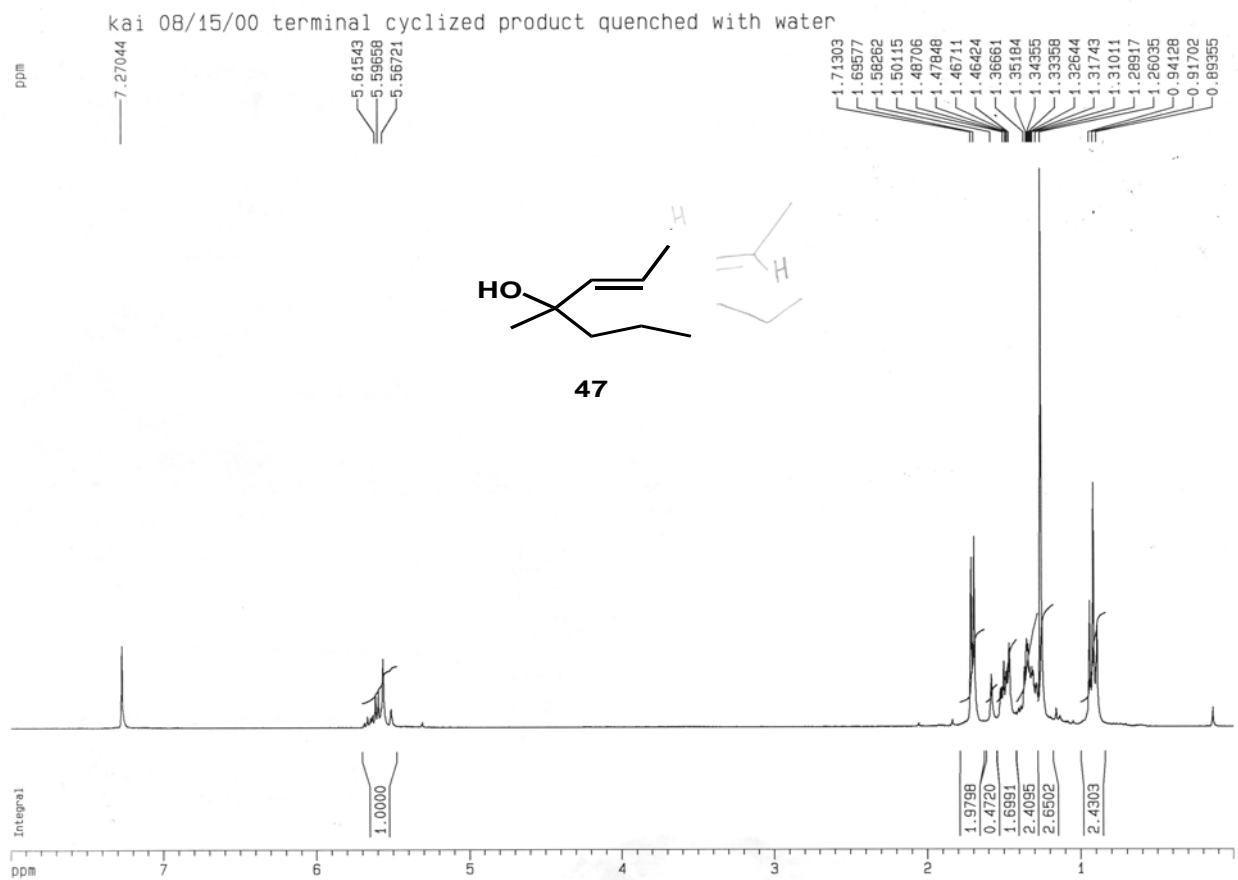




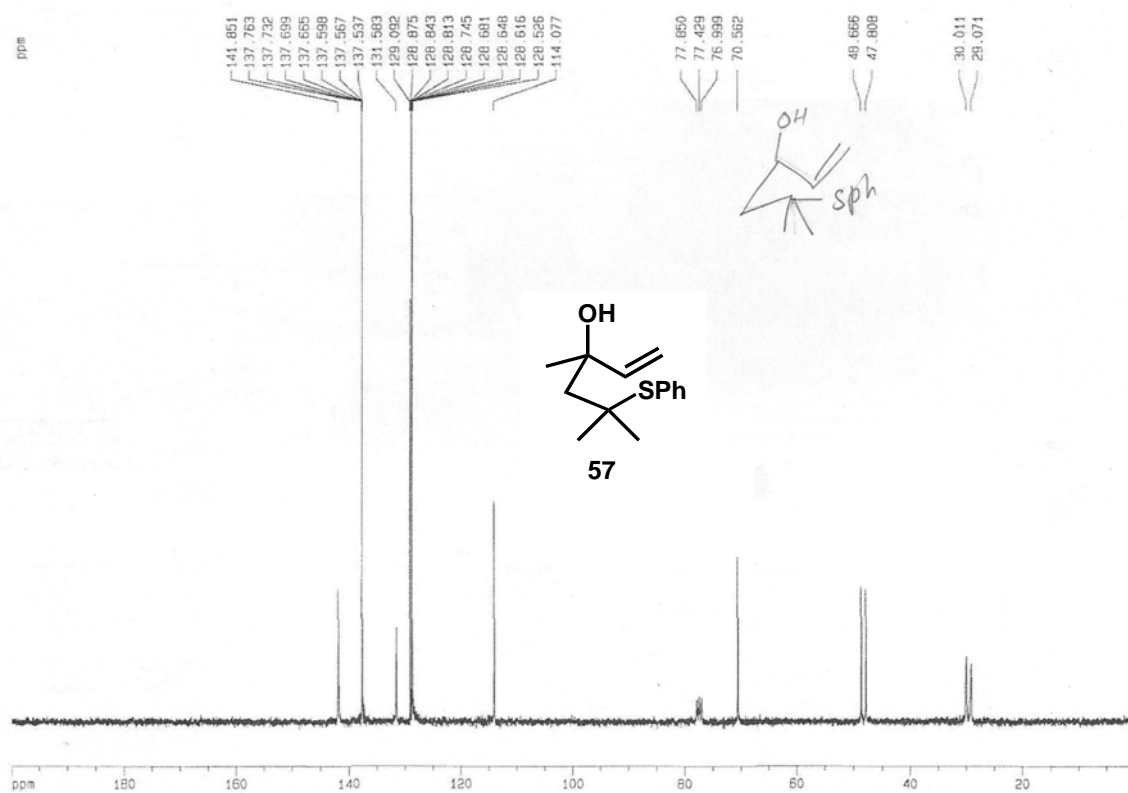


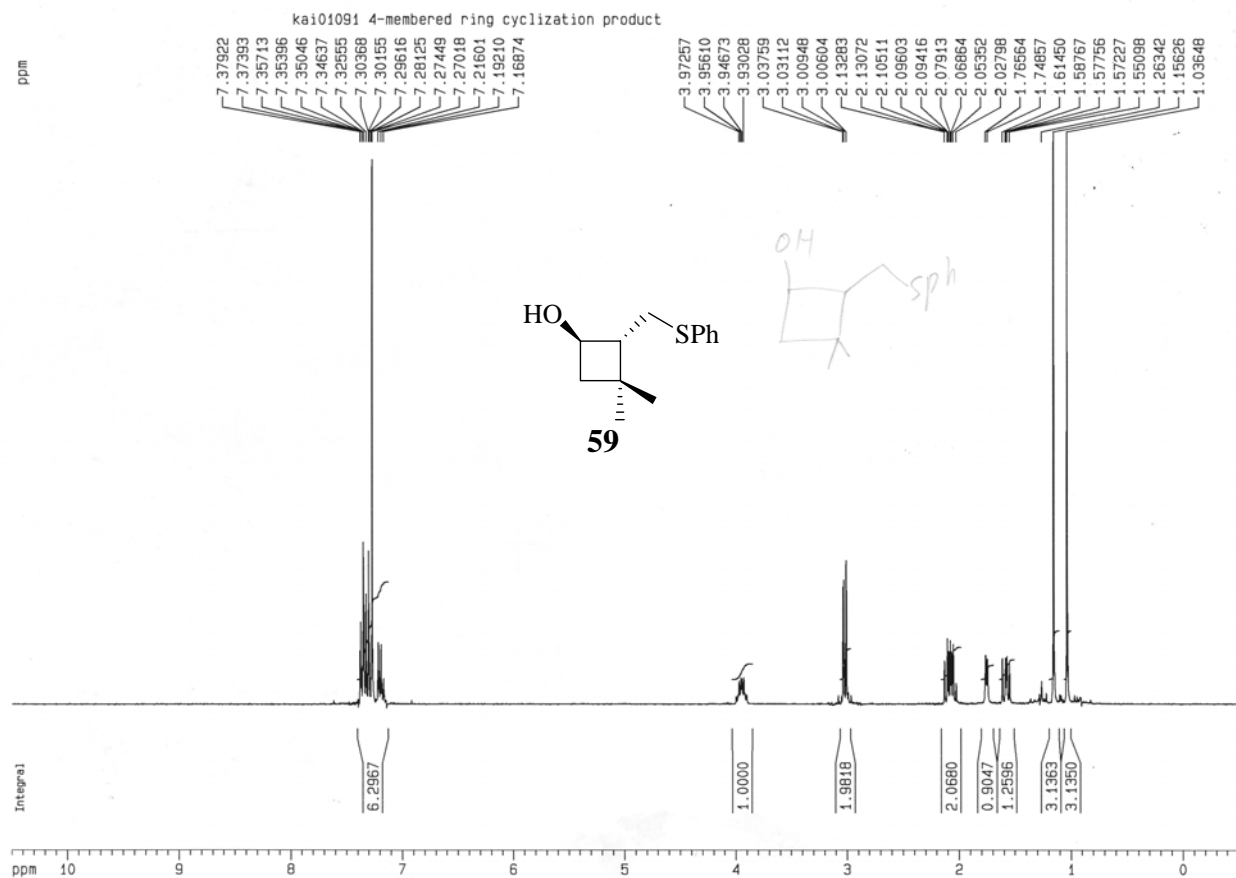




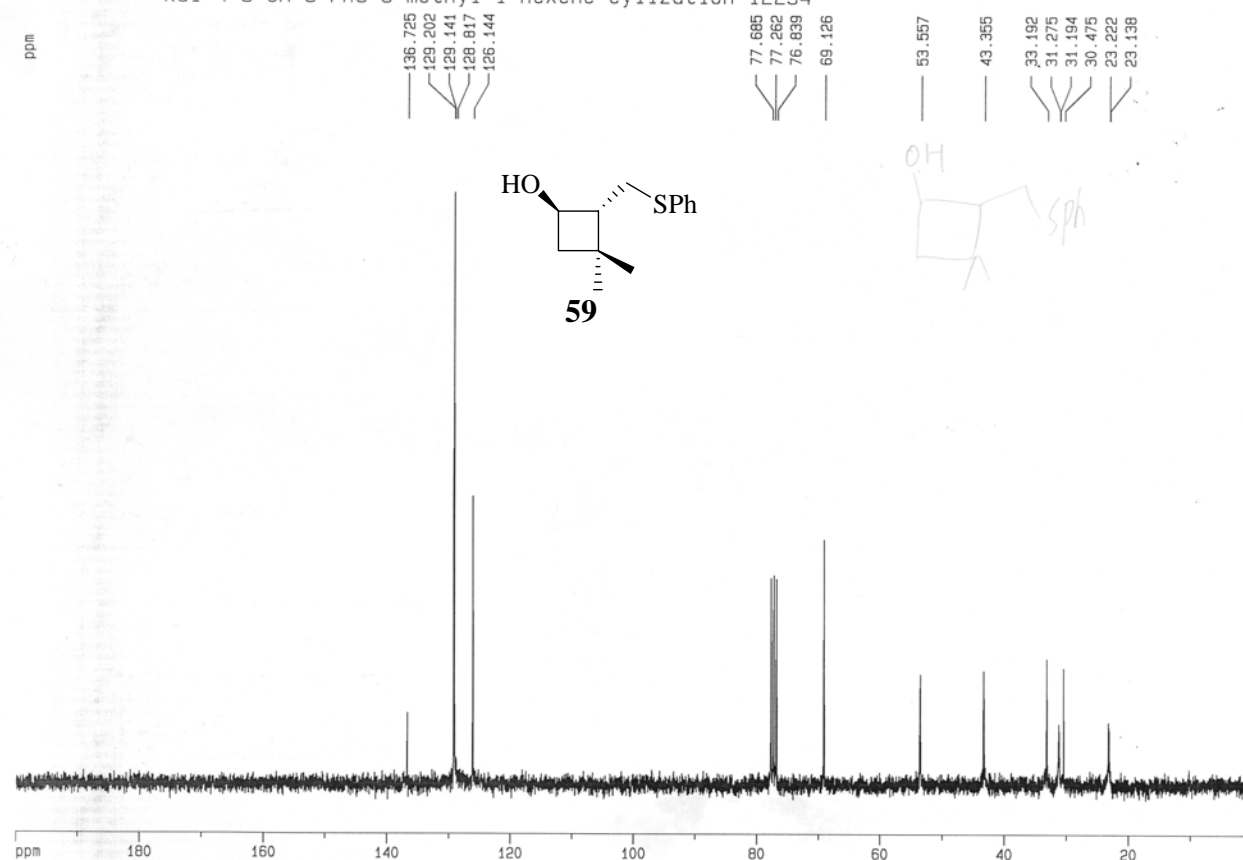




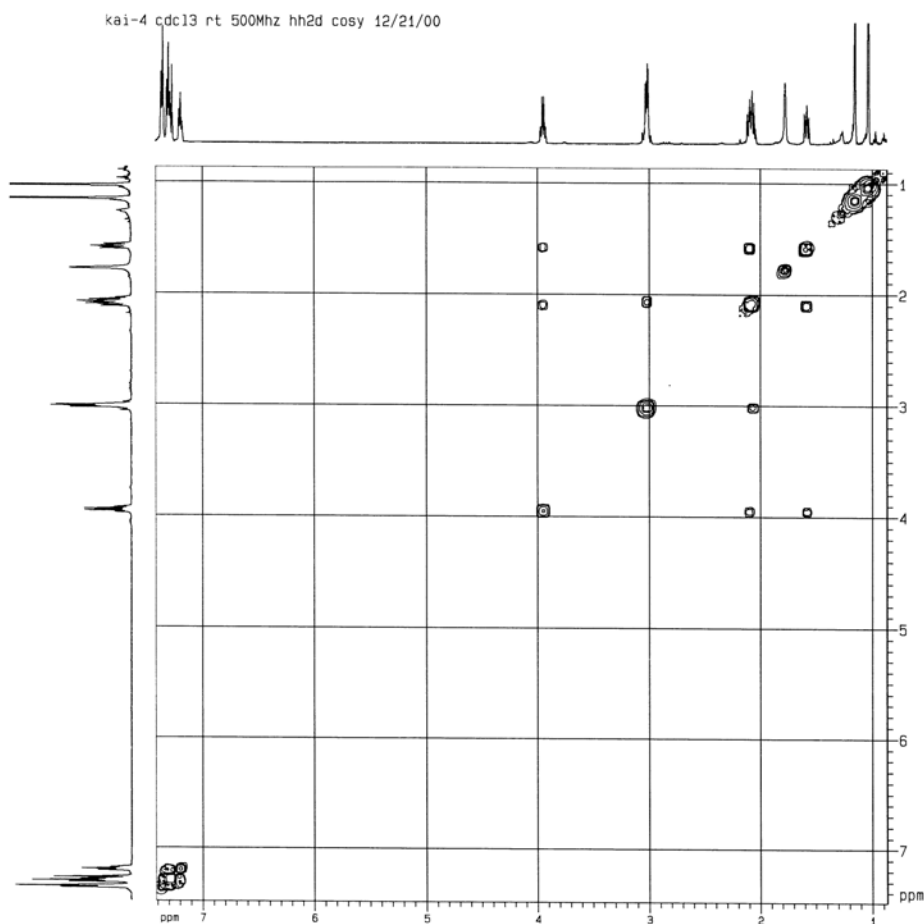
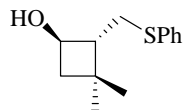




kai-4 3-OH-5-PhS-5-methyl-1-hexene cyclization 12234



The COSY spectrum of 59



Current Data Parameters

NAME	kai-4
EXPNO	11
PROCNO	1

F2 - Acquisition Parameters

Date_	500000
Time	8.26
INSTRUM	spect
PROBHD	5 mm Txi 13c
PULPROG	cosy
TD	1024
SOLVENT	CDCl3
NS	8
DS	16
SWH	4496.403 Hz
FIDRES	4.391018 Hz
AQ	0.1139188 sec
RG	90.5
DM	111.200 usec
DE	6.00 usec
TE	290.0 K
DO	0.0000030 sec
D1	1.00000000 sec
P1	9.70 usec
PO	9.70 usec
DE	6.00 usec
SFO1	500.1322906 MHz
NUC1	1H
PL1	0.00 dB
IN0	0.0002240 sec

F1 - Acquisition parameters

NO	1
TD	114
SFO1	500.1323 MHz
FIDRES	39.442065 Hz
SW	8.990 ppm

F2 - Processing parameters

SI	512
SF	500.130074 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

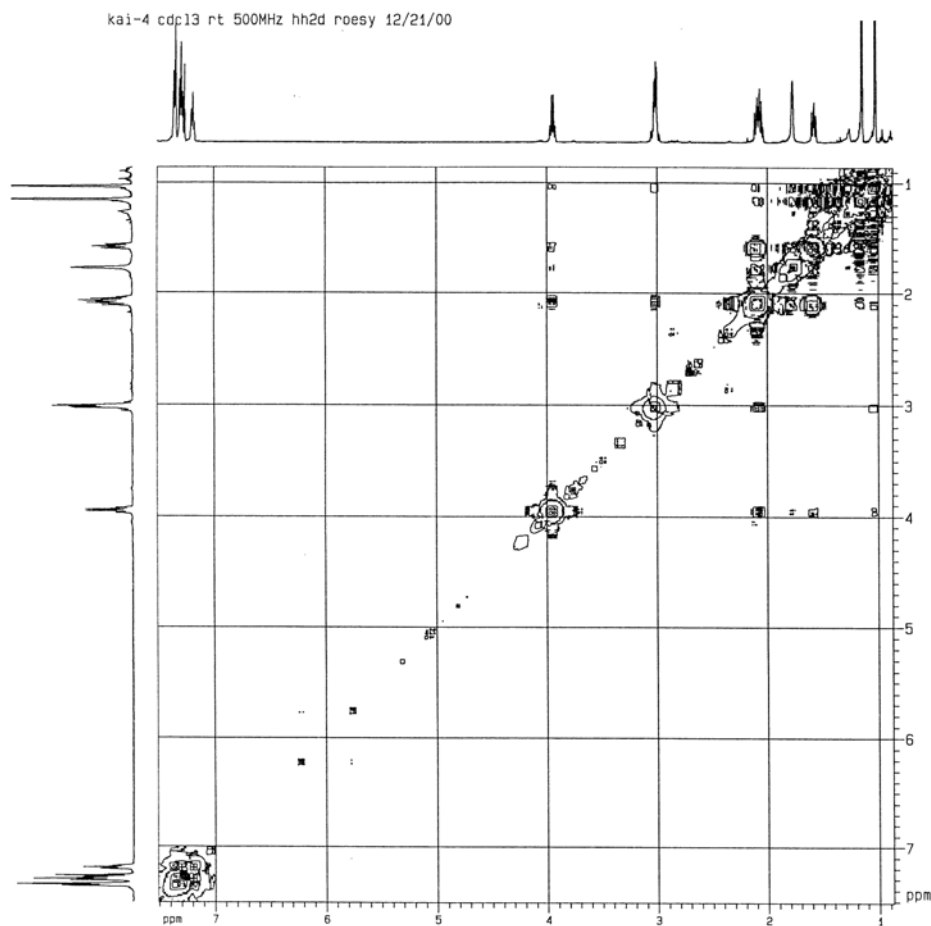
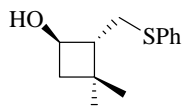
F1 - Processing parameters

SI	512
MC2	0
SF	500.130072 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

CX2	15.00 cm
CX1	15.00 cm
F2PL0	7.418 ppm
F2L0	3709.78 Hz
F2PH1	0.868 ppm
F2H1	434.08 Hz
F1PL0	7.488 ppm
F1L0	3745.14 Hz
F1PH1	0.868 ppm
F1H1	434.31 Hz
F2PPMCM	0.43655 ppm/cm
F2HZCM	218.37999 Hz/cm
F1PPMCM	0.44133 ppm/cm
F1HZCM	220.72151 Hz/cm

The ROESY spectrum of 59



Current Data Parameters

NAME	kai-4
EXPNO	11110
PROCNO	1

F2 - Acquisition Parameters

Date_	500000
Time	6.45
INSTRUM	spect
PROBHD	5 mm TXI 13C
PULPROG	roesytp
TD	1024
SOLVENT	CDCl3
NS	80
DS	16
SWH	4496.403 Hz
FIDRES	4.391018 Hz
AQ	0.1138188 sec
RG	90.0
CK	111.200 usec
DE	6.00 usec
TE	290.0 K
EC	0.0000030 sec
EL2	0.0000030 sec
OL	1.00000000 sec
PL1	0.00 dB
PL1	9.70 usec
PL11	6.00 dB
PL15	200000.00 usec
DE	6.00 usec
SFO1	500.1322508 MHz
NUC1	1H
INQ	0.00011120 sec

F1 - Acquisition parameters

NO	2
TD	225
SFO1	500.13031 MHz
FIDRES	19.983899 Hz
SW	8.990 ppm

F2 - Processing parameters

SI	1024
SF	500.1300043 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	0.10

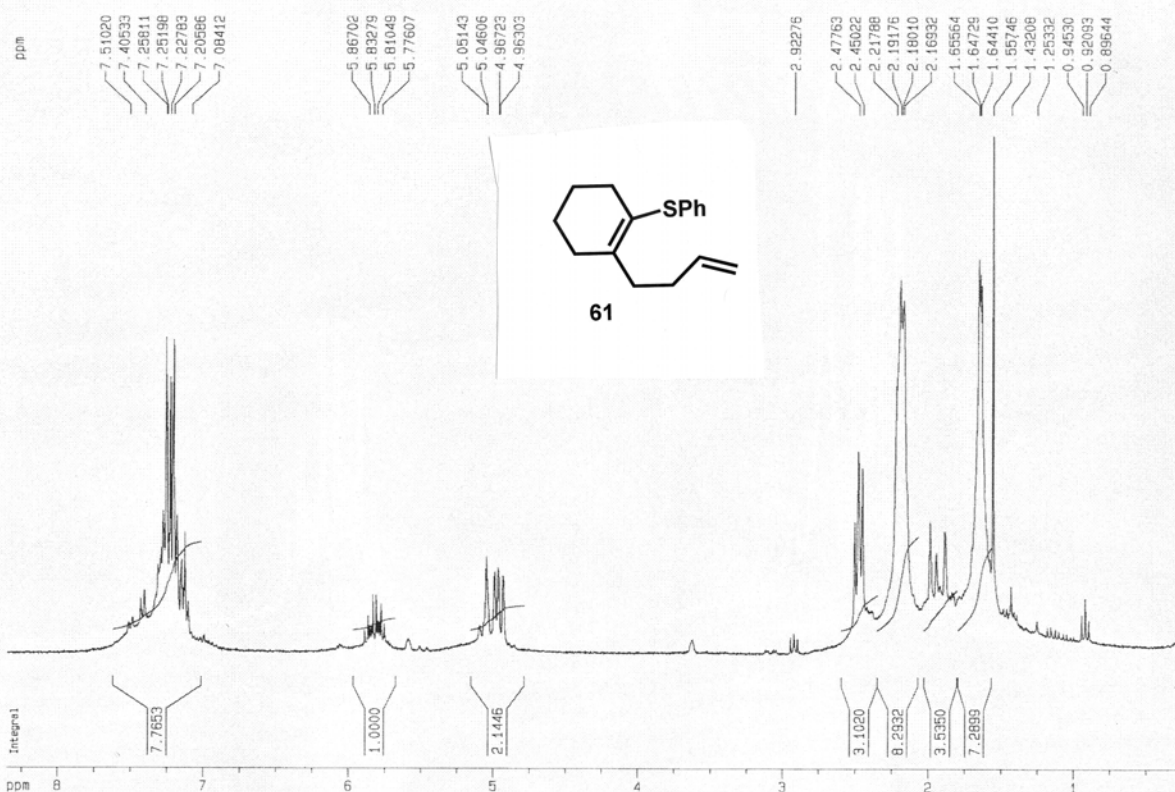
F1 - Processing parameters

SI	1024
MC2	TPP1
SF	500.1300042 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

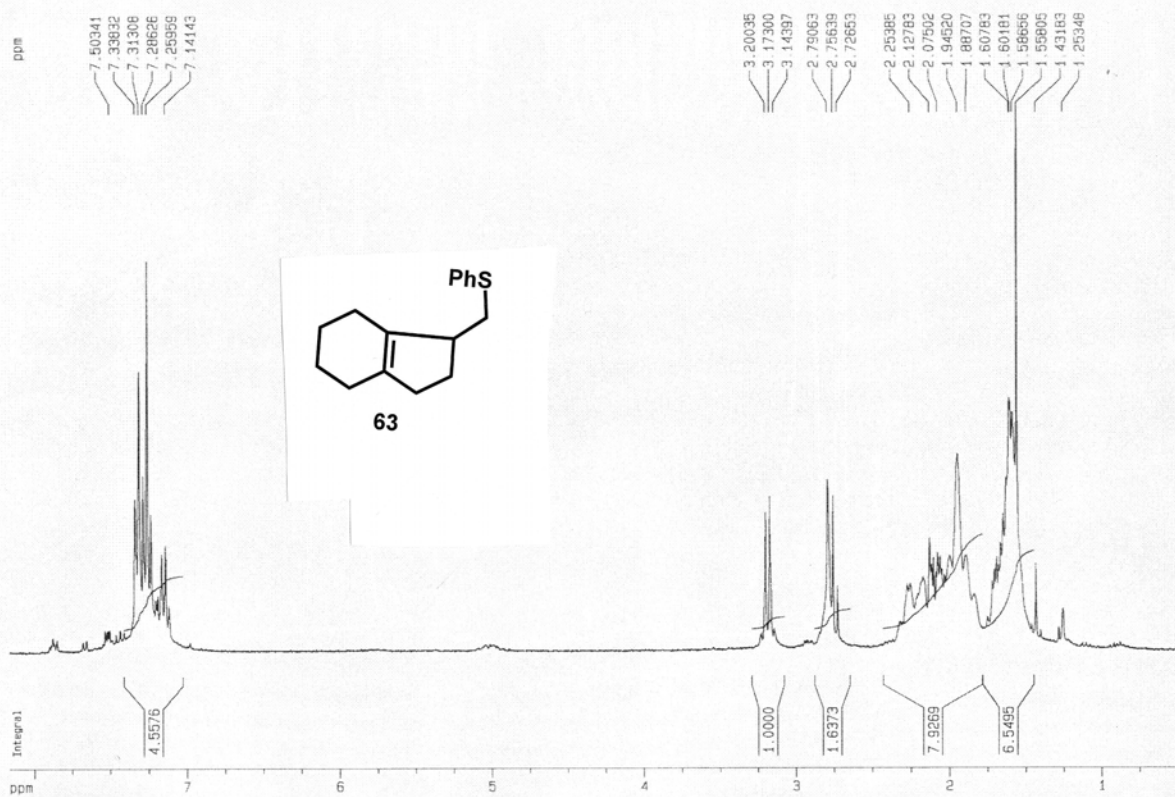
2D NMR plot parameters

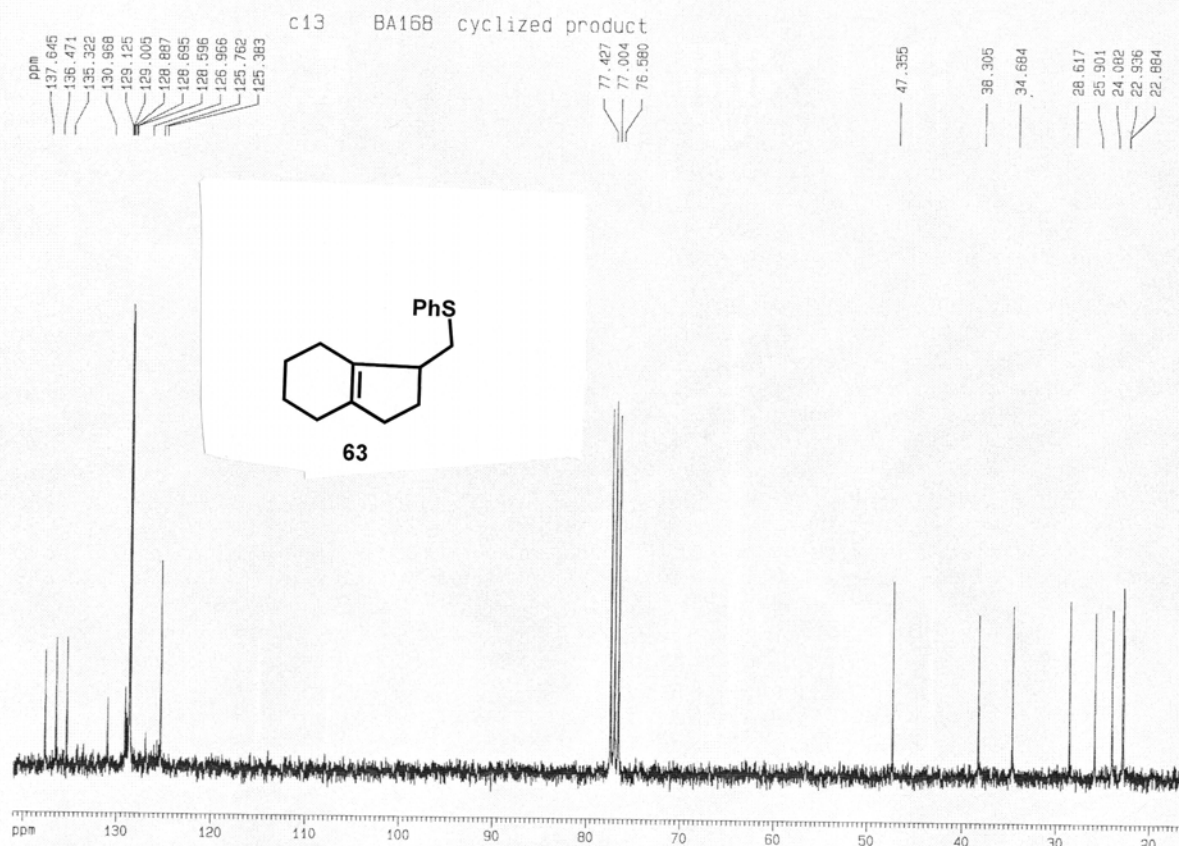
CX2	15.00 cm
CX1	15.00 cm
F2P10	7.512 ppm
F2L0	3756.84 Hz
F2P11	0.874 ppm
F2H1	437.23 Hz
F1P10	7.512 ppm
F1L0	3756.89 Hz
F1P11	0.857 ppm
F1H1	428.50 Hz
F2PPHCK	0.44250 ppm/cm
F2HCK	221.30731 Hz/cm
F1PPHCK	0.44367 ppm/cm
F1HCK	221.85246 Hz/cm

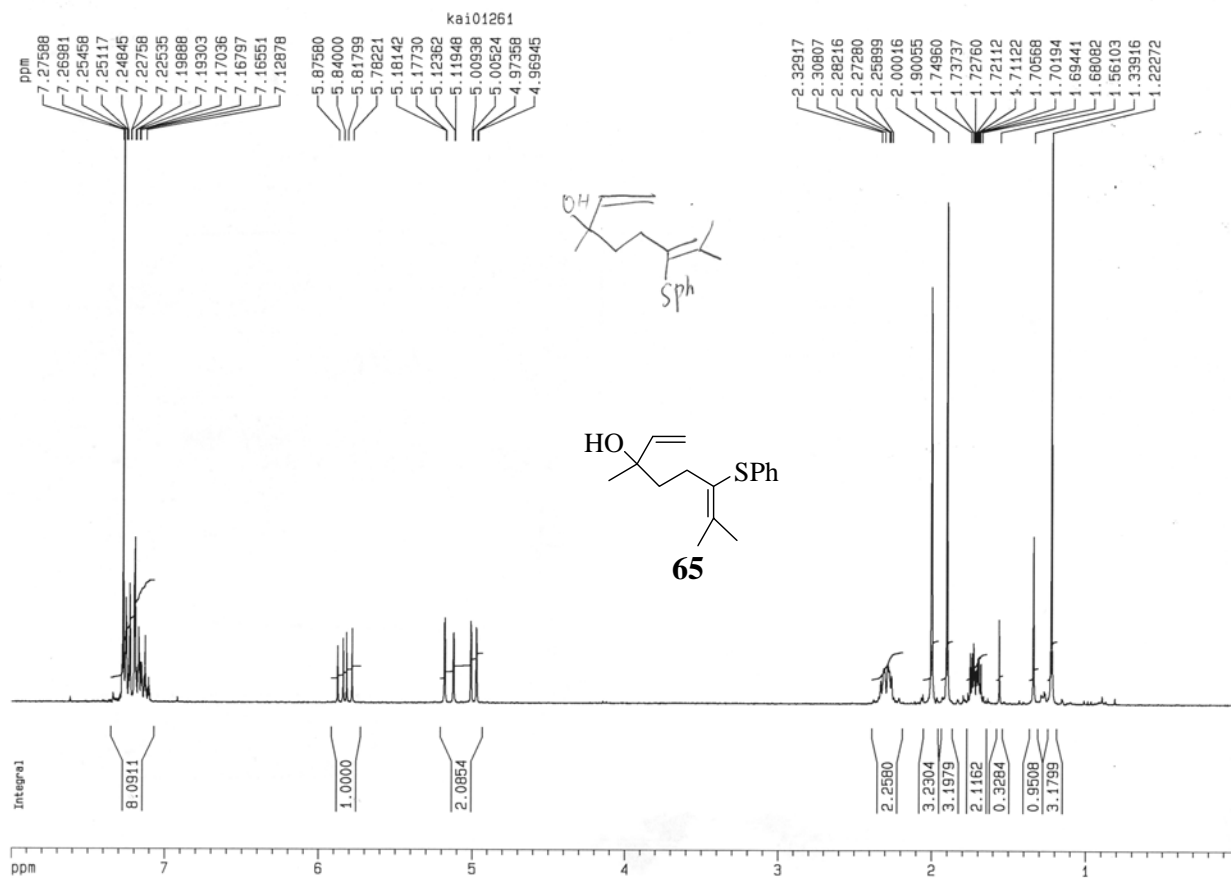
BA 121

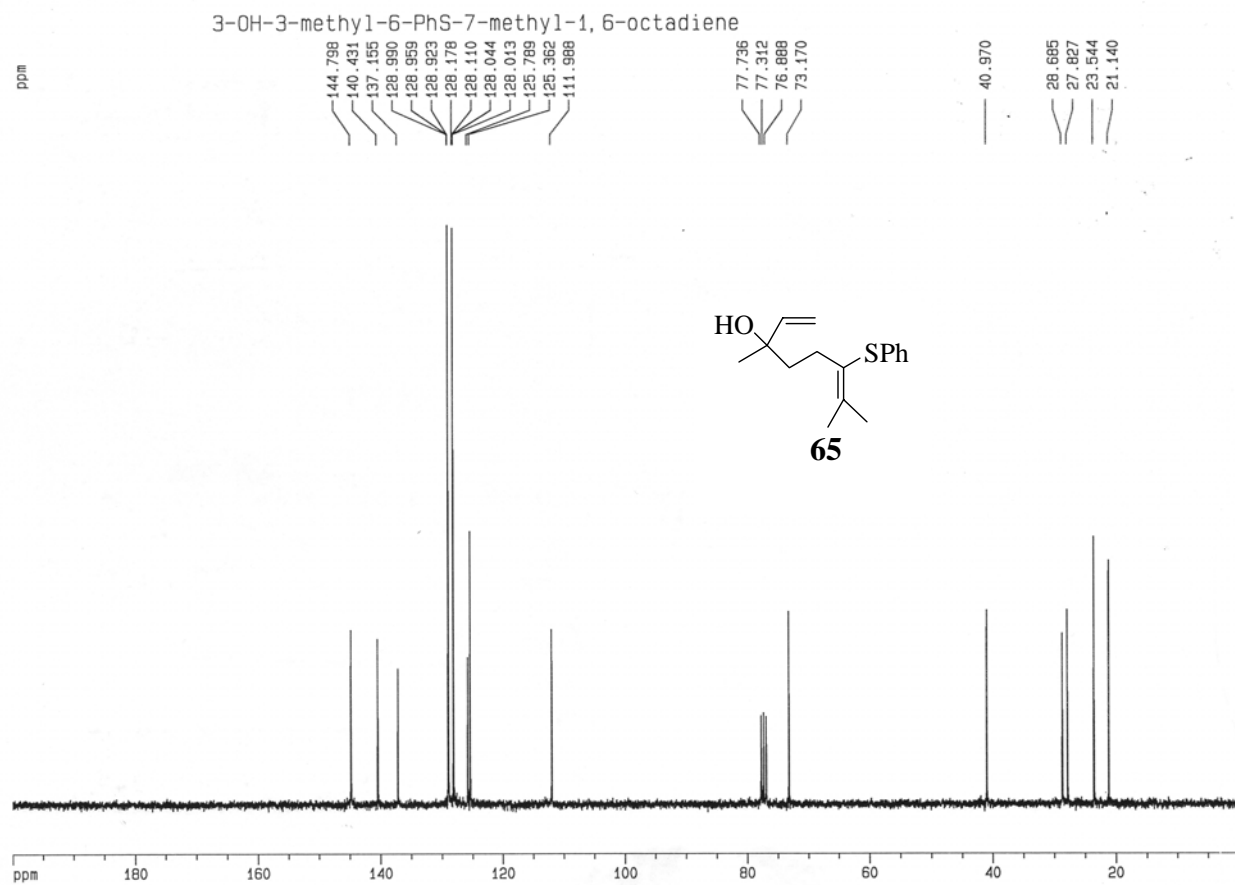


300 ba168

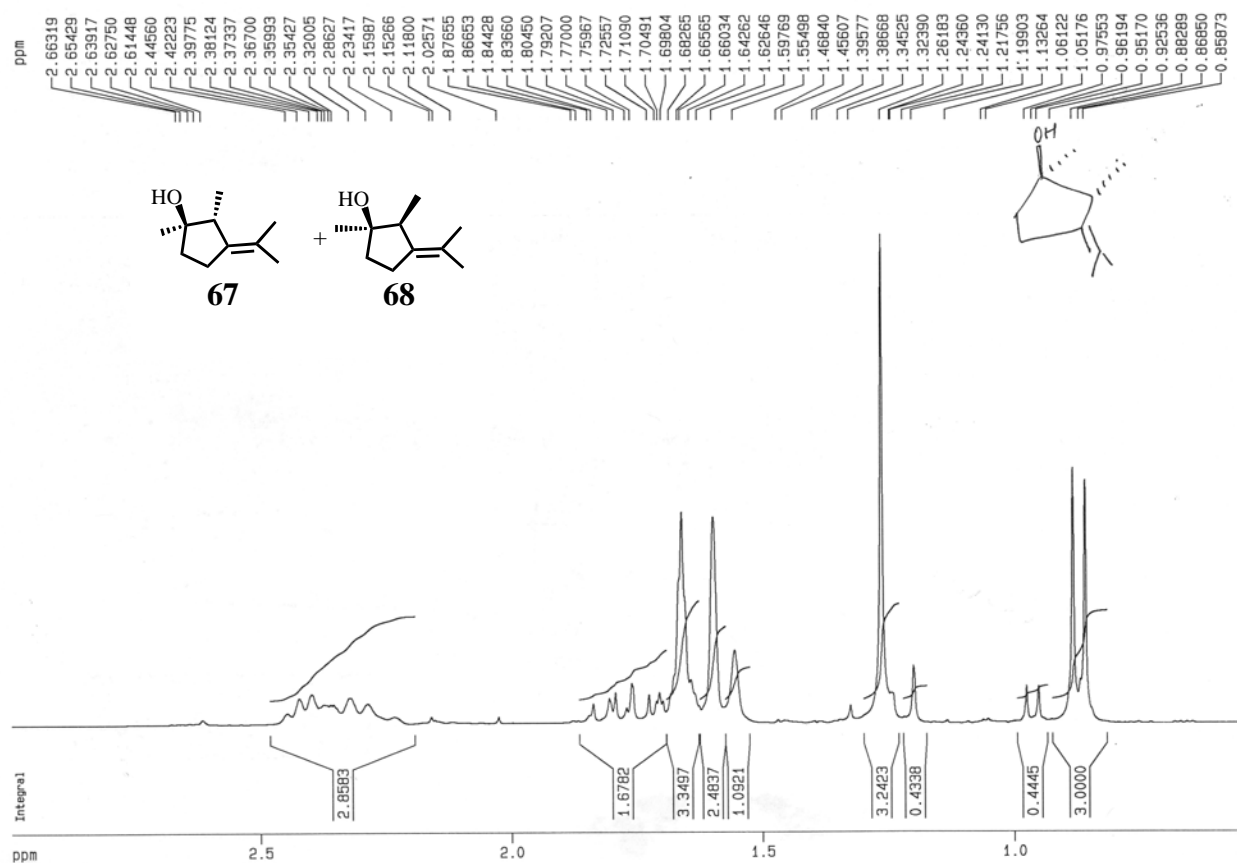




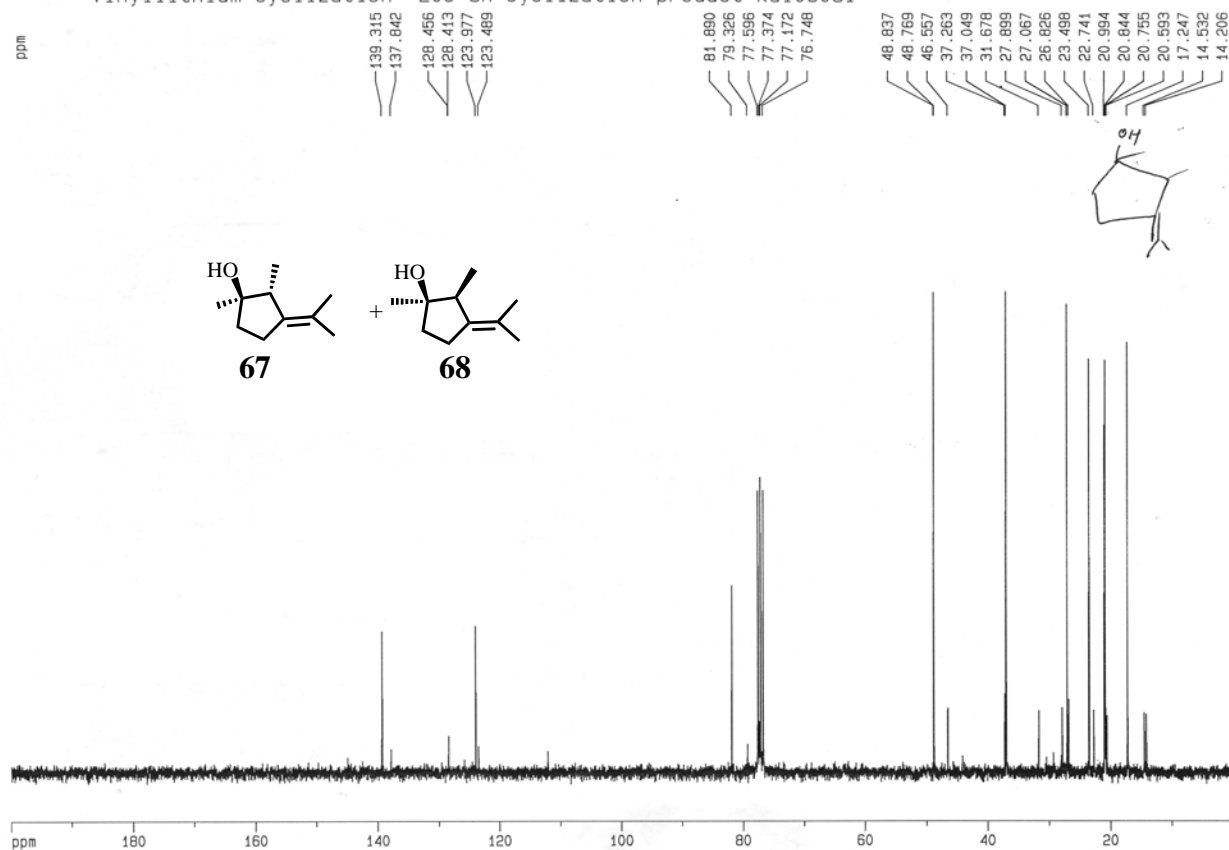


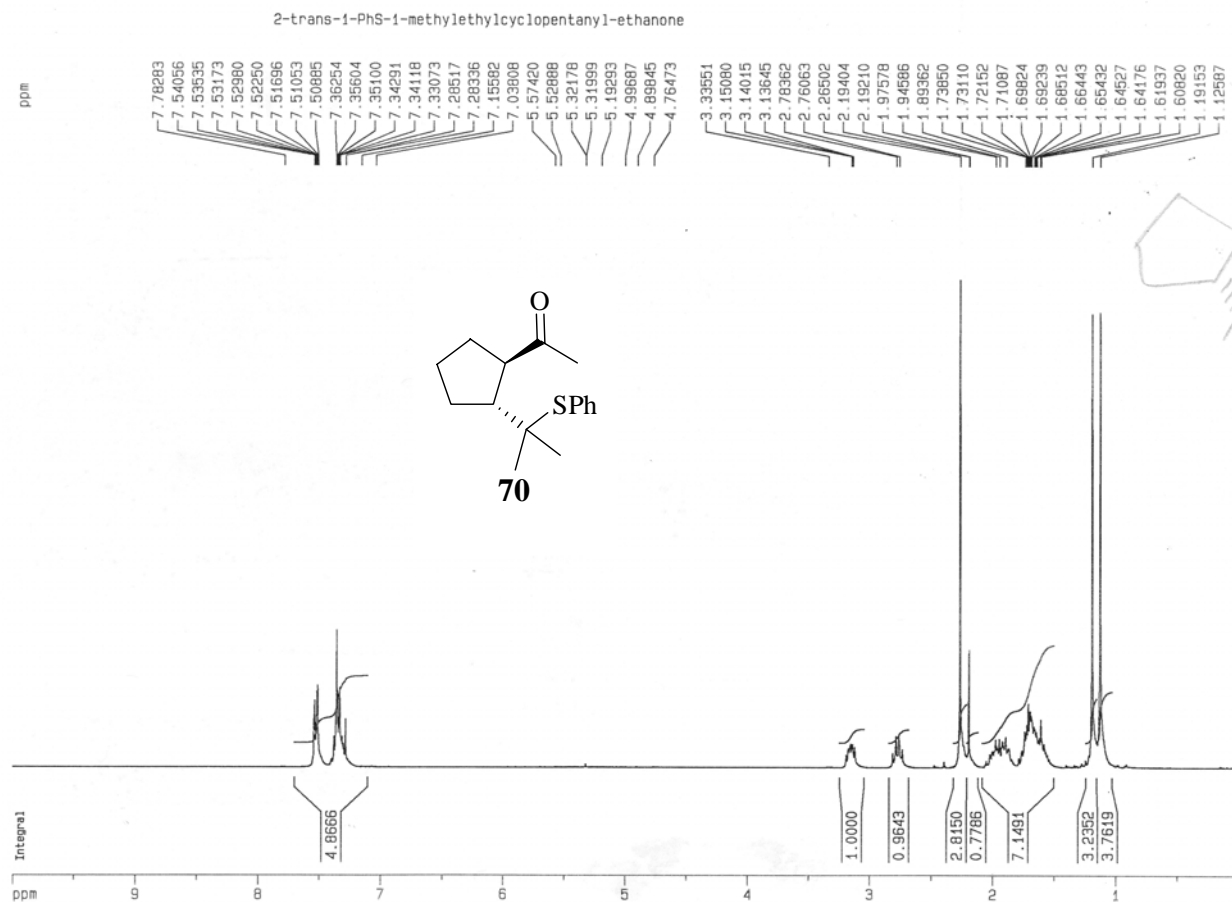


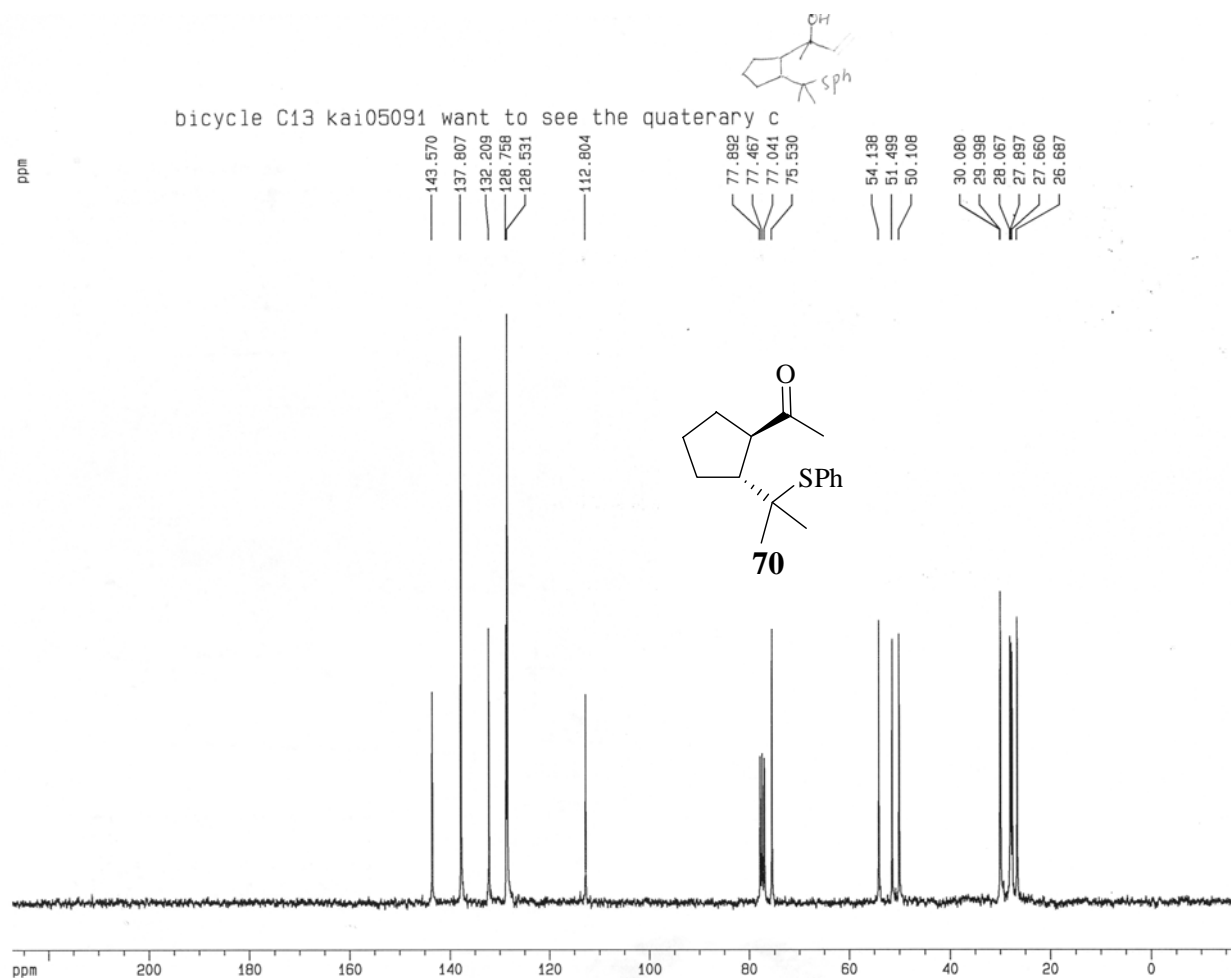
vinyl lithium cyclization -20c 5h cyclization product kai09051

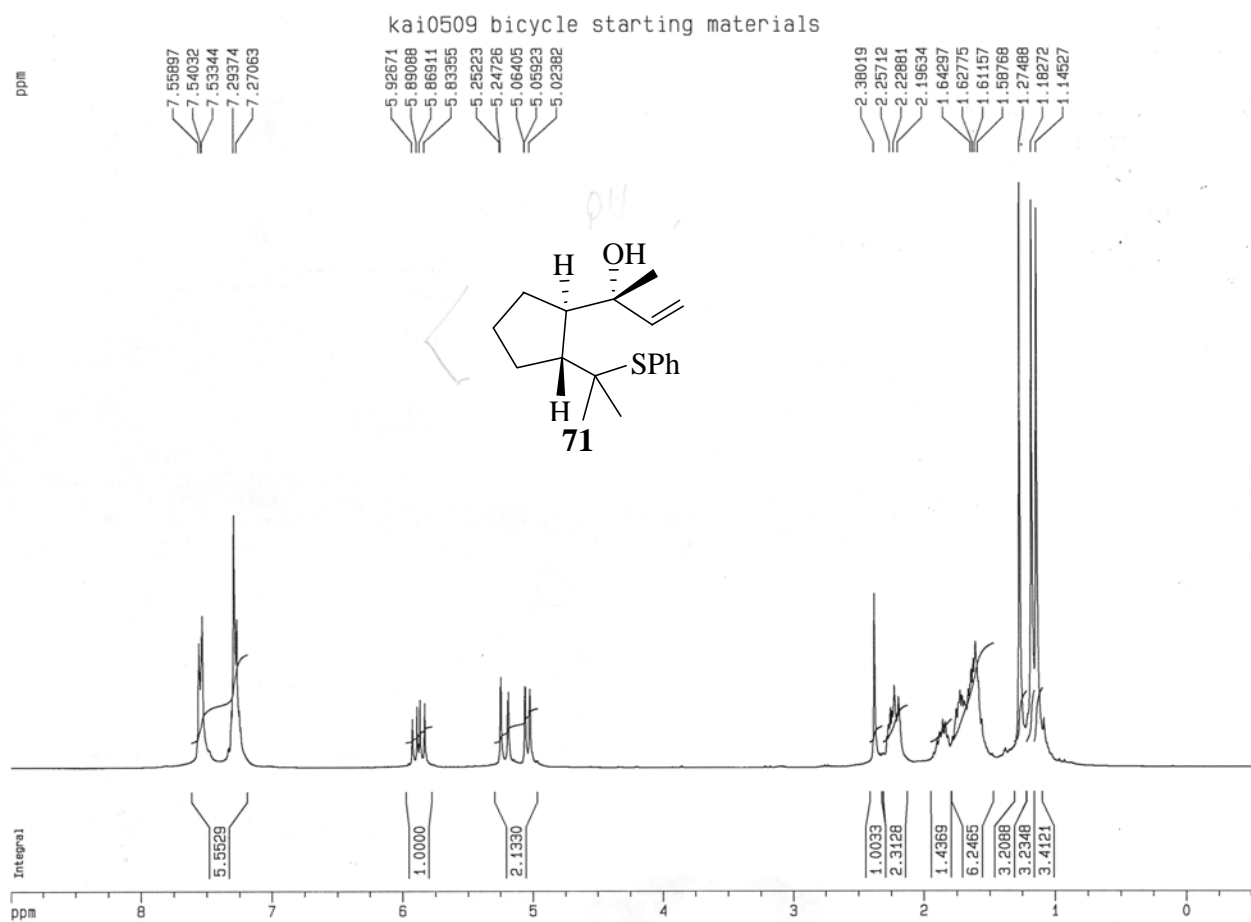


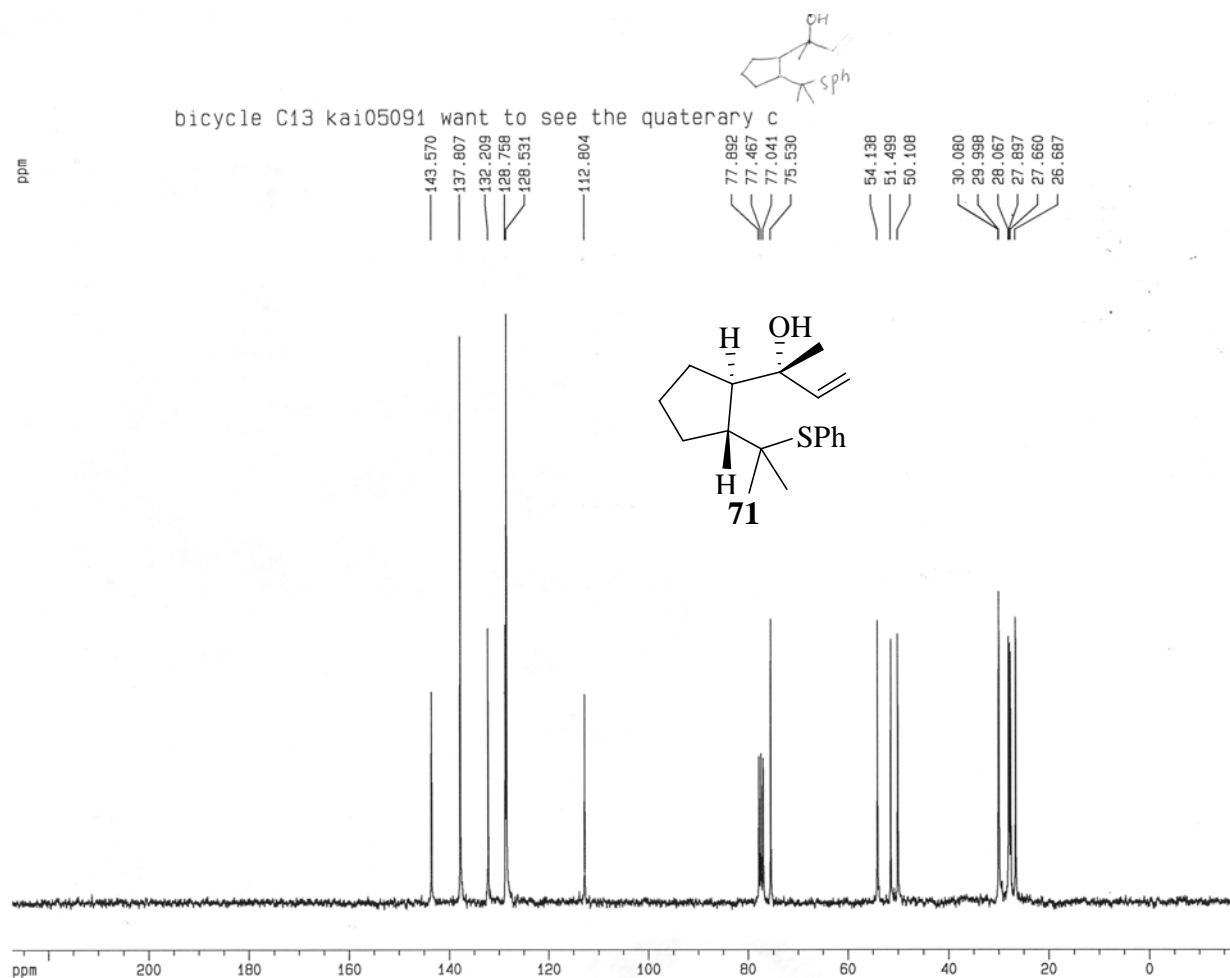
vinyl lithium cyclization -20c 5h cyclization product kai09051

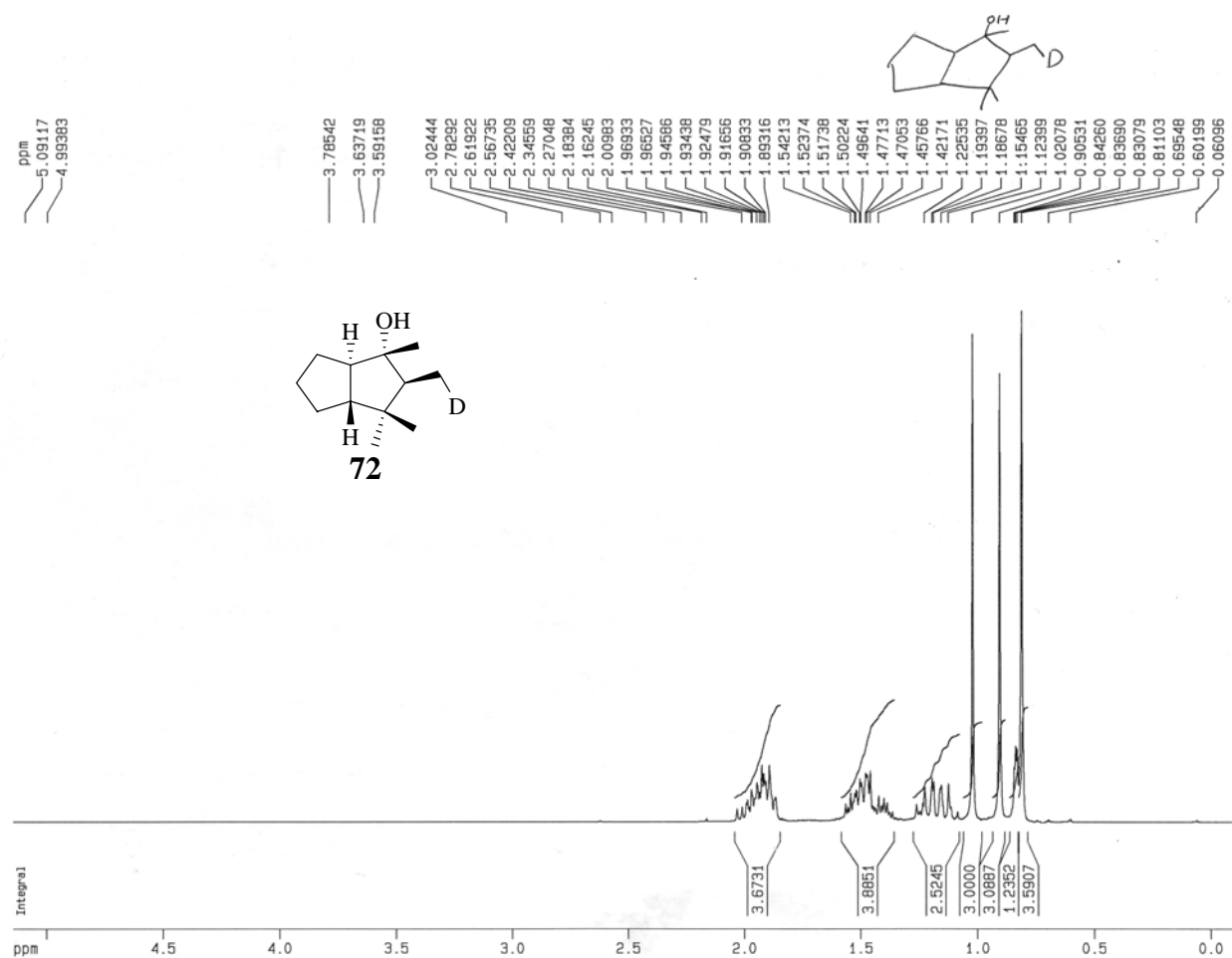




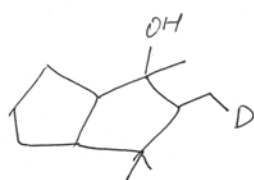








ppm



-78°C, 1h

