

**Cyclization by Intramolecular Carbolithiation of Alkyl- and
Vinyllithiums 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 KMnO₄ (1%) with NaOH (0.1%) and K₂CO₃ (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. CH₂Cl₂ and CH₃CN were distilled over CaH₂. Benzene was dried over melting sodium. IR spectra were recorded on an FTIR spectrometer with peaks reported in cm⁻¹. Most ¹H and ¹³C NMR spectra were recorded at 300 MHz for ¹H and 75 MHz for ¹³C at 22 °C unless otherwise indicated. Chemical shift data are reported in unit of δ (ppm) using CHCl₃ as internal standard: δ = 7.27 for ¹H NMR spectra and CDCl₃ as δ = 77.09 for ¹³C 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).

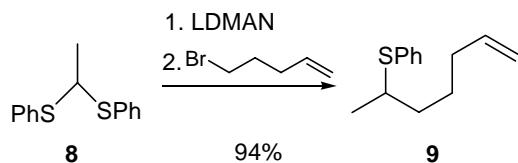
Lithium 1-(dimethylamino)naphthalenide (LDMAN)

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).

Vinyllithium

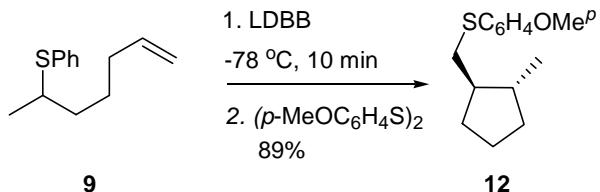
The following is a representative procedure for the preparation of vinyl lithium.

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

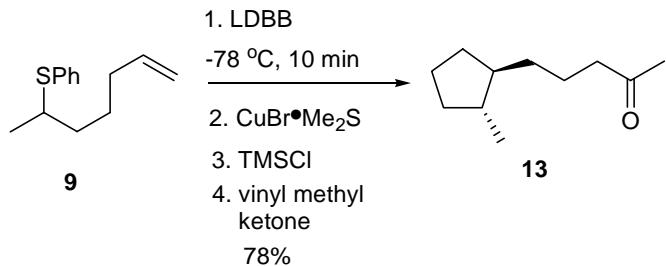


6-Phenylthio-1-heptene (9) A solution of LDMAN (54.5 mmol, prepared from 8.3 mL DMAN, and 378 mg Li in 60 mL THF) was cooled to -78°C and treated with 1,1-bis(phenylthio)ethane (6.46 g, 26.3 mmol). The dark green color of LDMAN turned to dark red. After 10 min of stirring, 1-bromo-4-pentene (3.11 mL, 26.3 mmol) was added. The reaction mixture was stirred at -78°C for 2 h and then the temperature was raised to -20°C . After the solution had been stirred at -20°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 Hz), 4.93 (d, 1 H, J = 10.5 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 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.

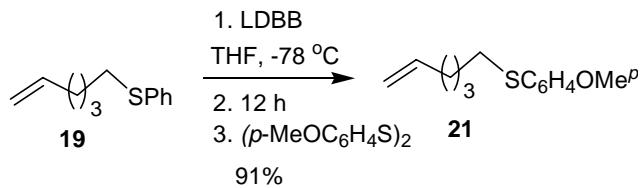


trans-2-Methylcyclopentylmethylthio)-4-methoxybenzene (12) Freshly prepared LDBB (3.8 mmol in 10 mL of THF) at -78 $^{\circ}\text{C}$ was cannulated to a flask containing compound **9** (315 mg, 1.53 mmol) in 10 mL of THF at -78 $^{\circ}\text{C}$ under argon. The reaction mixture was stirred at -78 $^{\circ}\text{C}$ 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 Hz), 6.85 (d, 2 H, J = 9.6 Hz), 3.80 (s, 3 H), 3.05 (dd, 1 H, J = 12.3 Hz, 4.6 Hz), 2.68 (dd, 1 H, J = 12.3 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 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.

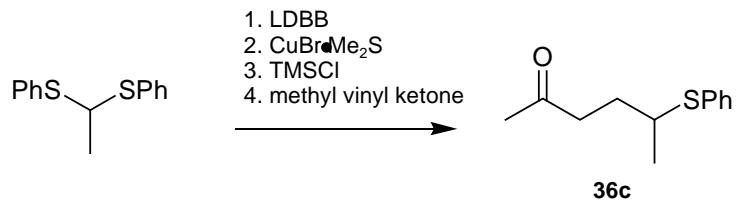


5-(*trans*-2-Methylcyclopentyl)pentan-2-one (13) Freshly prepared LDBB (3.4 mmol in 10 mL of THF) at -78°C was cannulated to a flask containing compound **9** (278 mg, 1.35 mmol) in 10 mL THF at -78°C under argon. The reaction mixture was stirred at -78°C for 15 min and then CuBr•Me₂S (417 mg, 2.02 mmol) was added. After the resulting mixture had been stirred for 3 h at -78°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°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 °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 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 C₁₁H₂₀O (M⁺): 168.1514, found 168.1509.

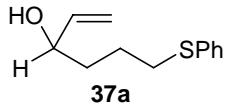


6-Lithio-1-hexene and its attempted cyclization in THF at -78 °C Freshly prepared LDBB (3.6 mmol in 10 mL of THF) at -78 °C was cannulated to a flask containing compound **19** (279 mg, 1.45 mmol) in 10 mL THF at -78 °C under argon. The reaction mixture was stirred at -78 °C for 12 h before the addition 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 NaHCO₃ solution (20 mL) was added and the mixture was allowed to warm to room temperature. The reaction mixture was extracted with ether (20 mL × 3). The combined organic layer, after being washed with 5% NaOH (20 mL × 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); ¹³C 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.

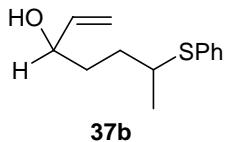


5-Phenylthiohexan-2-one (36c) To a THF solution (64 mL) of LDBB (25.6 mmol) at -78°C was added 1,1-bis(phenylthio)ethane (2.78 g, 11.3 mmol) in 10 mL of THF. After the reaction mixture had been stirred at -78°C for 10 min, CuBr•Me₂S (3.26 g, 15.8 mmol) was added. The formation of cuprate was insured 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.

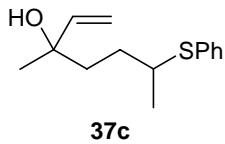
Compounds **37a**, **37b**, **37c**, **37d** and **37e** were prepared by vinyl lithium addition to the corresponding ketones or aldehydes, similar to the procedure described for the preparation of compound **23** in the Experimental Section of the paper.



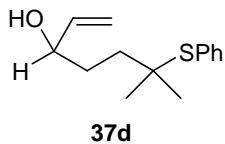
6-(Phenylthio)hex-1-en-3-ol (37a) ^1H NMR (CDCl_3): δ 7.34-7.16 (m, 5 H, aromatic), 5.83 (ddd, 1 H, J = 16.6, 10.4, 6.2 Hz), 5.20 (dd, 1 H, J = 16.6, 2.6 Hz), 5.09 (dd, 1 H, J = 10.4, 2.6 Hz), 4.09 (m, 1 H), 2.94 (t, 2 H, J = 7.1 Hz), 1.98 (br, 1 H, -OH), 1.82-1.60 (m, 4 H); ^{13}C NMR (CDCl_3): δ 141.0, 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.



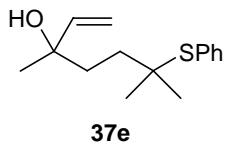
6-(Phenylthio)hept-1-en-3-ol (37b) Two diastereomers were obtained in an approximately 1:1 ratio. ^1H NMR: δ 7.46-7.25 (m, 5 H, aromatic), 5.87 (m, 1 H), 5.26 (d, 1 H, J = 13.8 Hz), 5.15 (d, 1 H, J = 10.4 Hz), 4.13 (m, 1 H), 3.27 (m, 1 H), 2.01 (s, 1 H, -OH), 1.80-1.60 (m, 4 H), 1.26 (d, 3 H, J = 6.6 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.

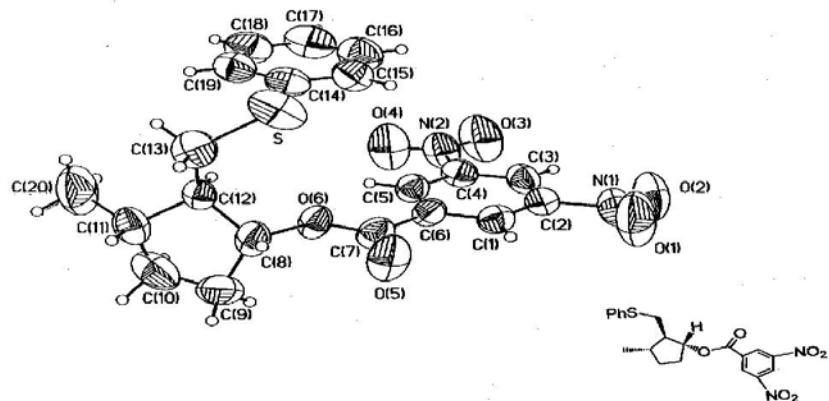
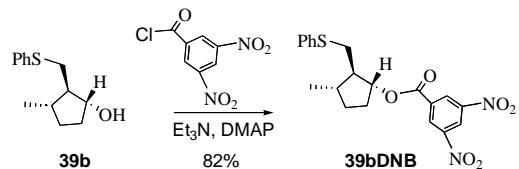


6-Methyl-6-(phenylthio)hept-1-en-3-ol (37d) ^1H NMR: δ 7.60-7.30 (m, 5 H, aromatic), 5.90 (m, 1 H), 5.25 (d, 1 H, J = 17.1 Hz), 5.13 (d, 1 H, J = 10.4 Hz), 4.10 (m, 1 H), 1.82-1.46 (m, 4 H), 1.26 (s, 6 H); ^{13}C NMR: δ 141.3, 137.6 (2 C), 132.2, 128.8, 128.6 (2 C), 114.8, 73.3, 49.1, 37.9, 32.4, 29.1, 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.

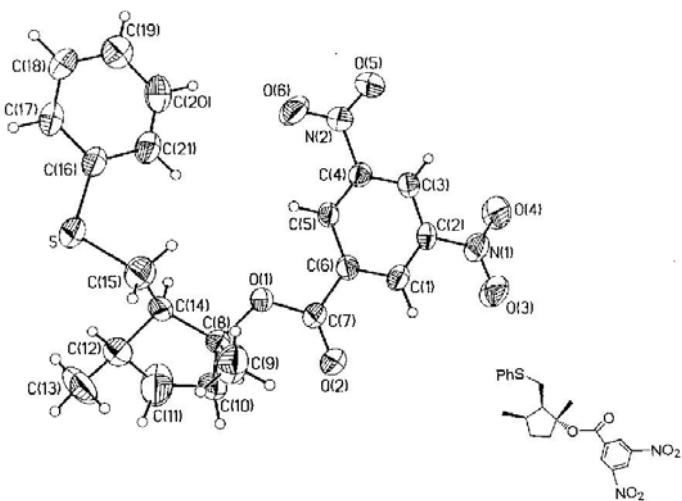
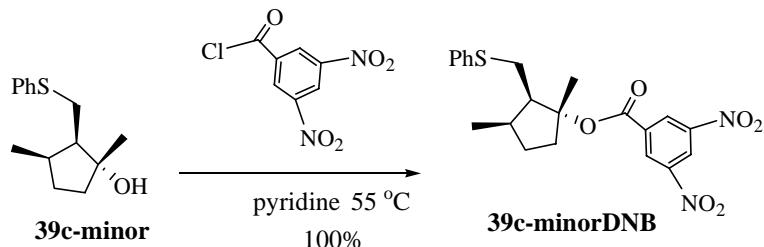


3,5-Dinitrobenzoic acid 3-methyl-2-phenylsulfanyl-methyl-cyclopentyl ester

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

equiv.) in 4 mL of CH_2Cl_2 , 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 Et_2O (20 mL \times 3). The combined organic layer, after being washed successively with 1 N H_2SO_4 (10 mL) and water (10 mL), was dried over MgSO_4 , 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 CH_2Cl_2 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); ^{13}C 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 $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_6\text{S}$ (M^+) 416.1042 found 416.1047.

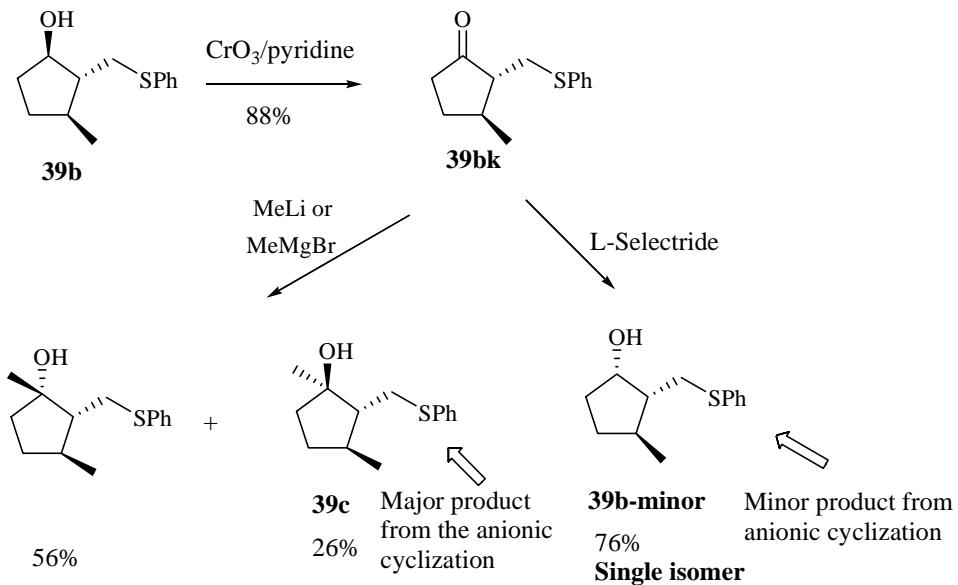
Stereochemistry determination of **39c-minor** by X-ray crystal structure analysis of the corresponding 3,5-dinitrobenzoate ester is shown below.



3,5-Dinitro-benzoic acid 1, 3-dimethyl-2-phenylsulfanyl methylcyclopentyl 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 × 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

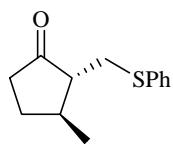
title compound (yield 100%) as a yellow solid. The product was crystallized from CH_2Cl_2 and hexane. IR (neat): 3100, 2959, 2923, 2874, 1724, 1544, 1344, 1285, 1168, 730, 720, 691; ^1H NMR: 9.20 (t, J = 1.8 Hz, 1 H), 9.12 (d, J = 1.8 Hz, 2 H), 7.54-7.17 (m, 5 H), 3.38 (dd, J = 12.3, 6.0 Hz, 1 H), 2.96 (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). ^{13}C 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 $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_6\text{S}$ (M^+) 430.1199, found 430.1197.

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

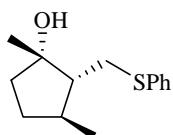


Compound **39b** (stereochemistry was known by X-ray analysis shown above) was oxidized to the corresponding ketone **39bk**. Reduction of the ketone **39bk** by L-Selectride gave a single compound, which was **39b-minor**. The addition of MeLi to the ketone gave two compounds as shown and the minor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

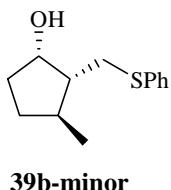


(1S*,2R*,3R*)-1,3-Dimethyl-2-phenylsulfanylmethyl-cyclopentanol² MeMgBr (3.0 M, 0.40 mL, 1.18 mmol) was added dropwise via syringe to a solution of *trans*-3-methyl-2-phenylthiomethyl-cyclopentanone **39bk** (65 mg, 0.295 mmol) in THF (5 mL) at -78 °C. The mixture was stirred at -78 °C for 1 h before 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.

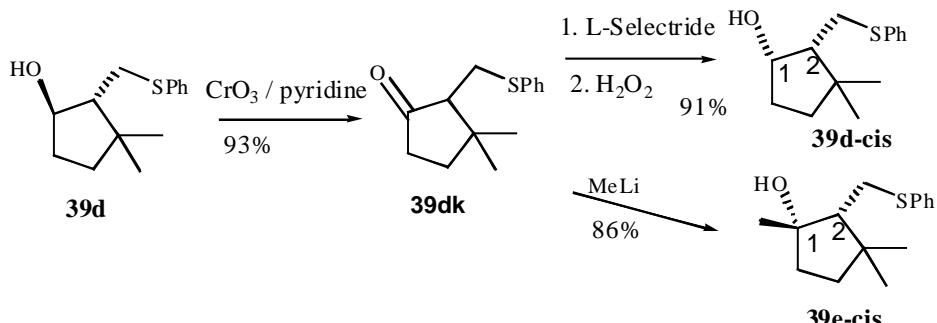
² "*" Means that the compound is racemic and thus that these are relative configurations.

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.

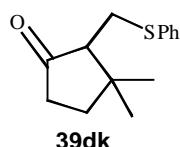


L-Selectride (lithium tri-*sec*-butylborohydride, 1.0 M in THF, 0.20 mL, 0.20 mmol) was added dropwise via syringe to a solution of *trans*-3-methyl-2-phenylthiomethyl-cyclopentanone **39bk** (22 mg, 0.10 mmol) dissolved in dry THF (10 mL) at -78 °C. The mixture was stirred at -78 °C for 3 h before it was warmed to room temperature. A solution of NaOH (8 mg, 0.20 mmol) in 1 mL water was added followed by the addition of H₂O₂ (30% aqueous solution, 0.07 mL, 0.6 mmol). After the reaction mixture had been stirred at room temperature for 1 h, it was exacted with ether (10 mL \times 3). The combined organic layer 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 an alcohol (17 mg, 76%) as a single diastereomer, which is completely identical in spectroscopic analysis with the minor product **39c-minor**.

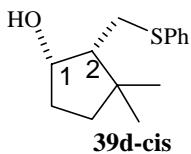
Evidence for the stereochemistry **39d** and **39e** is shown below.



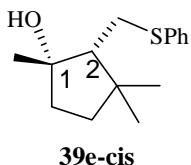
Compound **39d** was oxidized to the corresponding ketone. Reduction of the ketone by L-Selectride gave a single compound **39d-cis**, which was the diastereomer of **39d**. The addition of MeLi to the ketone gave a single compound, **39e-cis**, which was the diastereomer of **39e**. The stereochemistry 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). ¹³C 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 C₁₄H₁₈OS (M⁺): 234.1078, found 234.1087.

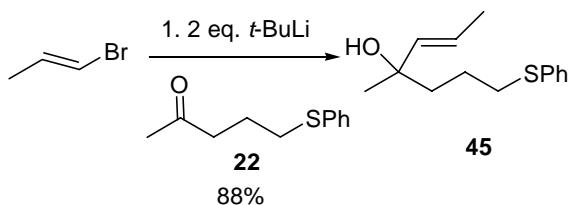


cis-3,3-Dimethyl-2-(phenylthiomethyl)cyclopentan-1-ol (39d-cis) L-Selectride (lithium tri-*sec*-butylborohydride, 1.0 M in THF, 0.60 mL, 0.60 mmol) was added dropwise via syringe to a solution of 3,3-dimethyl-2-(phenylthiomethyl)cyclopentanone **39dk** (71 mg, 0.30 mmol), dissolved in dry THF (10 mL) 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 exacted 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 ($15\text{ mL} \times 3$). The combined organic layer, after being washed with water (10 mL), was dried over MgSO_4 , 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). ^{13}C 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.

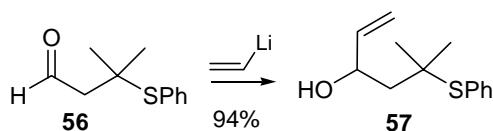


(E)-4-Methyl-7-(phenylthio)hept-2-en-4-ol (45) 1-Propenyllithium was prepared by a procedure similar to that for the preparation of vinyl lithium from vinyl bromide. To 1-propenyllithium (8.26 mmol, freshly prepared from trans 1-bromopropene (1.00 g, 8.26 mmol) and *t*-BuLi (9.7 mL, 16.5 mmol) in 10 mL diethyl ether) at $-78\text{ }^\circ\text{C}$, was added dropwise ketone **22** (890 mg, 4.60 mmol) in 5 mL of Et_2O 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 reaction mixture was extracted with ether ($30\text{ mL} \times 3$). The combined organic extract was dried over anhydrous MgSO_4 , filtered through cotton and evaporated in vacuo. The residue was purified by flash-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, $J = 5.4\text{ Hz}$), 1.70-1.65 (m, 7 H), 1.24 (s, 3 H); ^{13}C NMR (CDCl_3) 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 $C_{14}H_{20}OS$ (M^+): 236.1235, found 236.1232.

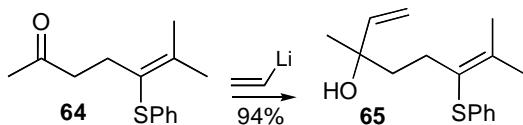


Attempted cyclization of reductive lithiation product **46 (R=H) of (*E*)-4-methyl-7-(phenylthio)hept-2-en-4-ol (**45**) in THF at -78 °C** To a stirred solution of alcohol **45** (340 mg, 1.44 mmol) in 10 mL of THF at -78 °C under argon, was added *n*-BuLi (1.58 mmol, 1.0 mL of 1.6 M solution) via syringe. 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).



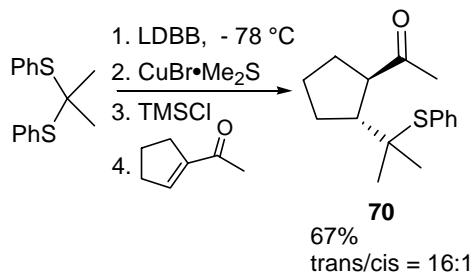
5-Methyl-5-(phenylthio)hex-1-en-3-ol (57) To a freshly prepared vinyl lithium solution (14.0 mmol, prepared from 1.00 mL (14.0 mmol) of vinyl bromide and 16.5 mL of 1.7 M *t*-BuLi in 9 mL anhydrous ether) at -78 °C, was added dropwise 3-methyl-2-butenal **56**

(1.97 g, 10.1 mmol) in 20 mL of THF via syringe. The reaction mixture was stirred at -78°C for 2 h and then the temperature was raised to -20°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 $\text{C}_{13}\text{H}_{18}\text{OS} (\text{M}^+)$: 222.1078, found 222.1073.



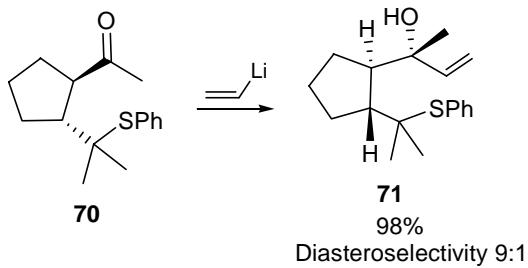
3,7-Dimethyl-6-(phenylthio)octa-1,6-dien-3-ol (65) To a freshly prepared vinyl lithium solution (6.8 mmol, prepared from 0.48 mL (6.8 mmol) of vinyl bromide and 8.0 mL of 1.7 M *t*-BuLi in 5 mL of anhydrous ether) at -78°C , was added ketone **64** (954 mg, 4.1 mmol) in 10 mL of THF via syringe. The reaction mixture was stirred for 2 h at -78°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 NaHCO_3 solution. The resulting 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 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); ¹³C NMR (CDCl₃): 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 C₁₆H₂₂OS (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 °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 °C for 10 min, CuBr•Me₂S (2.20 g, 10.7 mmol) was added with increased argon flow. After the mixture had been stirred for 3 h at -78 °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 °C. Aqueous 5% NaOH (40 mL)

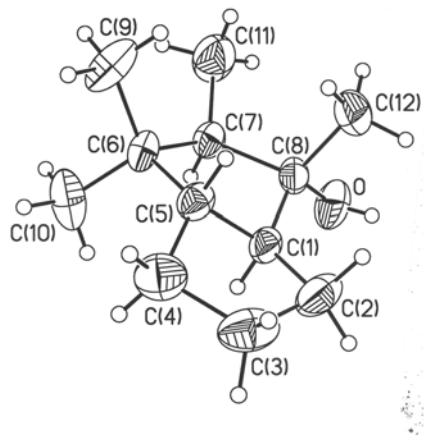
and 40% aqueous *n*-Bu₄NOH (1 mL) were added before the reaction mixture was allowed to warm to 0 °C. It was stirred at room temperature for about 1 h in order to hydrolyze all of the silyl enol ether to the ketone product. The mixture was filtered through Celite and extracted with ether (60 mL × 3). 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.



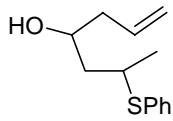
2-[2-(1-methyl-1-(phenylthio)ethyl)cyclopentyl]but-3-en-2-ol (71) To a freshly prepared vinyl lithium solution (5.7 mmol, prepared from 0.40 mL of vinyl bromide (5.7 mmol) and 8.0 mL of 1.7 M *tert*-BuLi in 5 mL anhydrous ether) at -78 °C, was added ketone **70** (0.87 g, 3.3 mmol) in 3 mL of Et₂O. The 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 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 Hz), 5.28 (dd, 1 H, J = 17.3, 1.5 Hz), 5.05 (dd, 1 H, J = 10.6, 1.5 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)

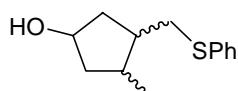


ORTEP drawing for *trans*-diquinane **72**



75

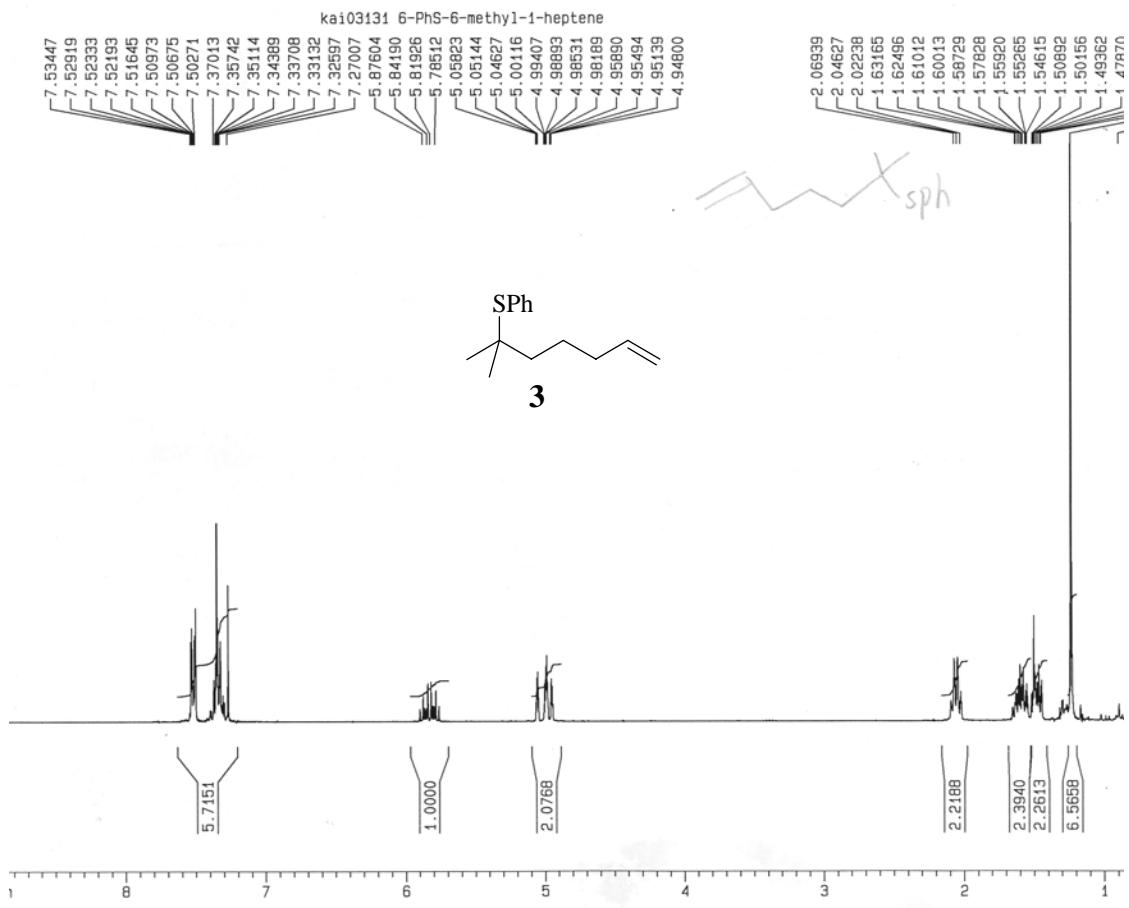
6-(Phenylthio)hept-1-en-4-ol (75) To a 1.80 g (10 mmol) solution of 3-(phenylthio)butyraldehyde (74) in 20 mL of THF was added 15 mL of commercial (Aldrich) allyl magnesium bromide solution (1M in ether) at -78 °C. The reaction mixture was then allowed to warm gradually to room temperature and stirred 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 NH₄Cl. The aqueous layer was extracted with ether twice. The combined extract was washed with water and brine, dried over anhydrous MgSO₄ 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 Hz), 1.32 (d, 3H, J = 4 Hz). ¹³C 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 (16). HRMS (EI) calculated for C₁₃H₁₈OS: 222.1078, found 222.1079.



77

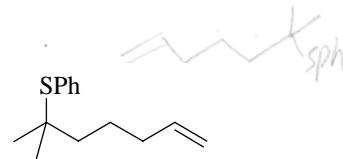
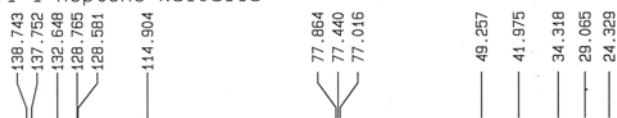
3-(Phenylthio)methyl-4-methylcyclopentanol (77) To a cooled solution (-78 °C) of 445 mg (2.00 mmol) of homoallylic alcohol 75 in 5 mL of THF, was added dropwise

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

ppm

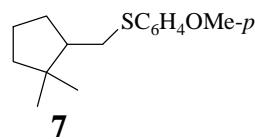
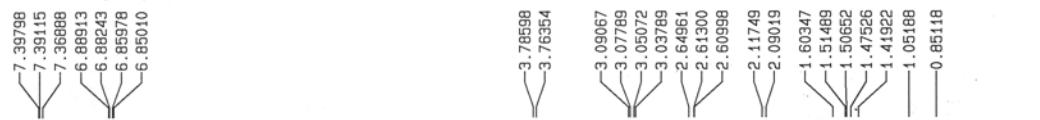


3

200 180 160 140 120 100 80 60 40 20 0

tertiary cyclization quenched with MeO-C₆H₄S-SC₆H₄-OMe kai05112

ppm

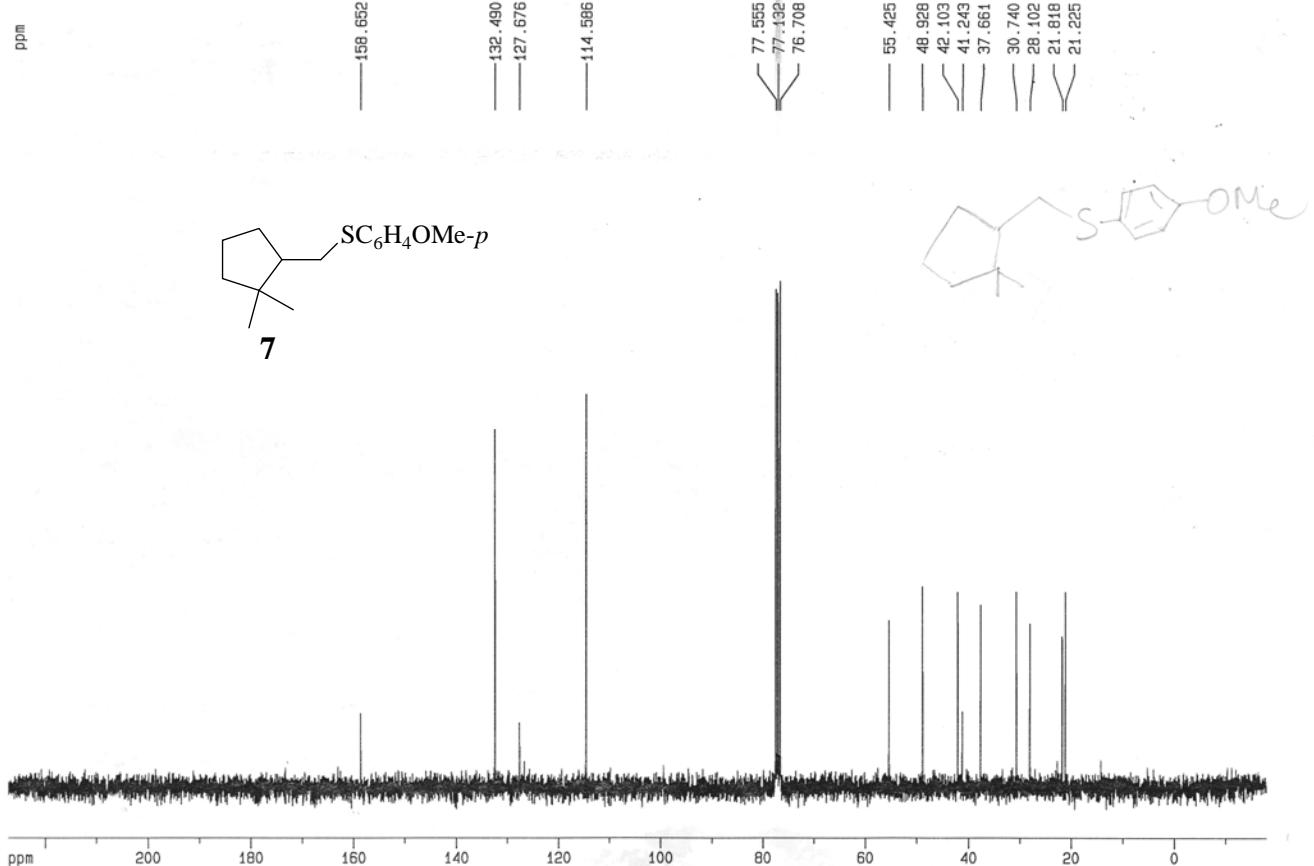


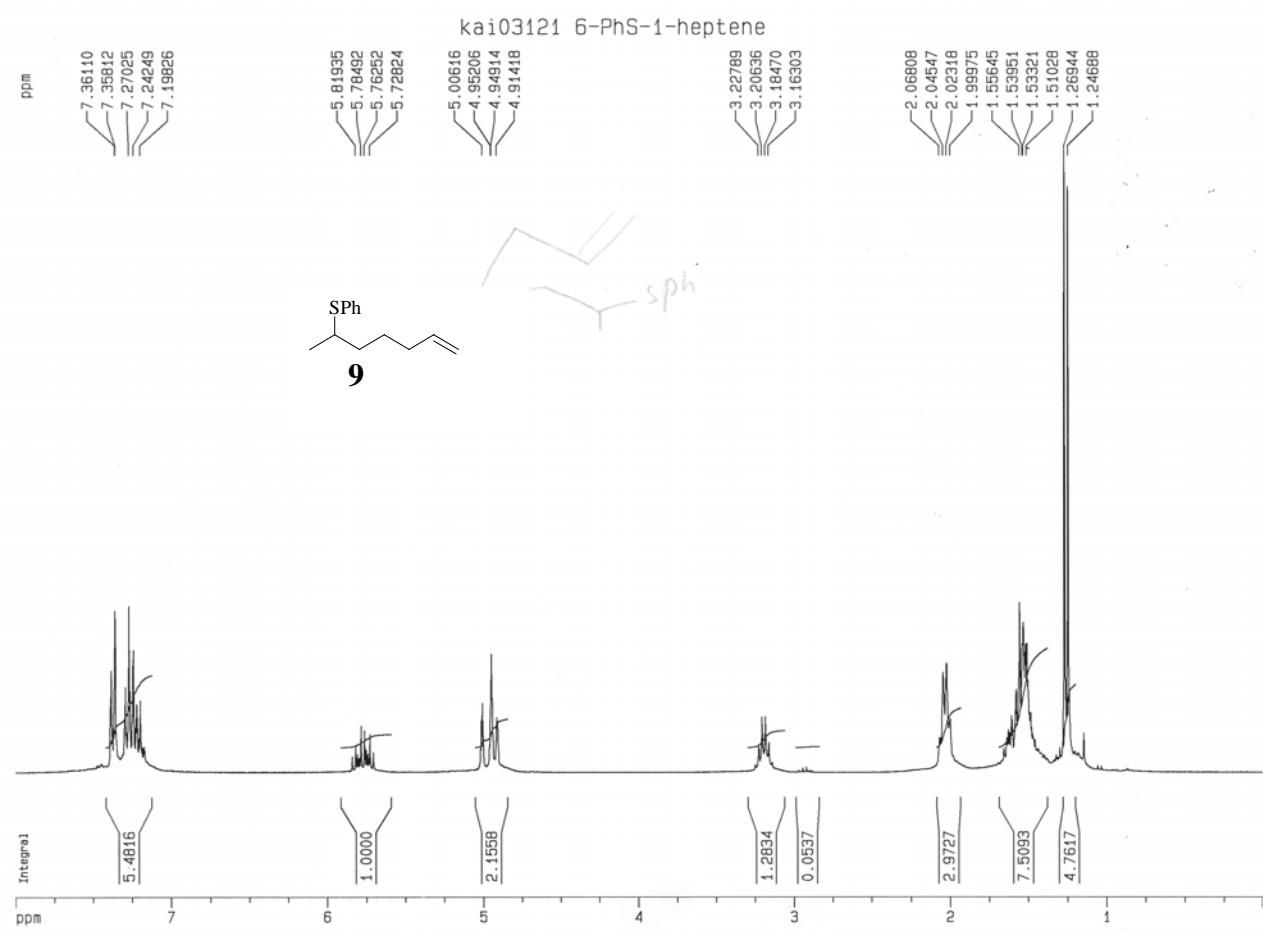
Integral

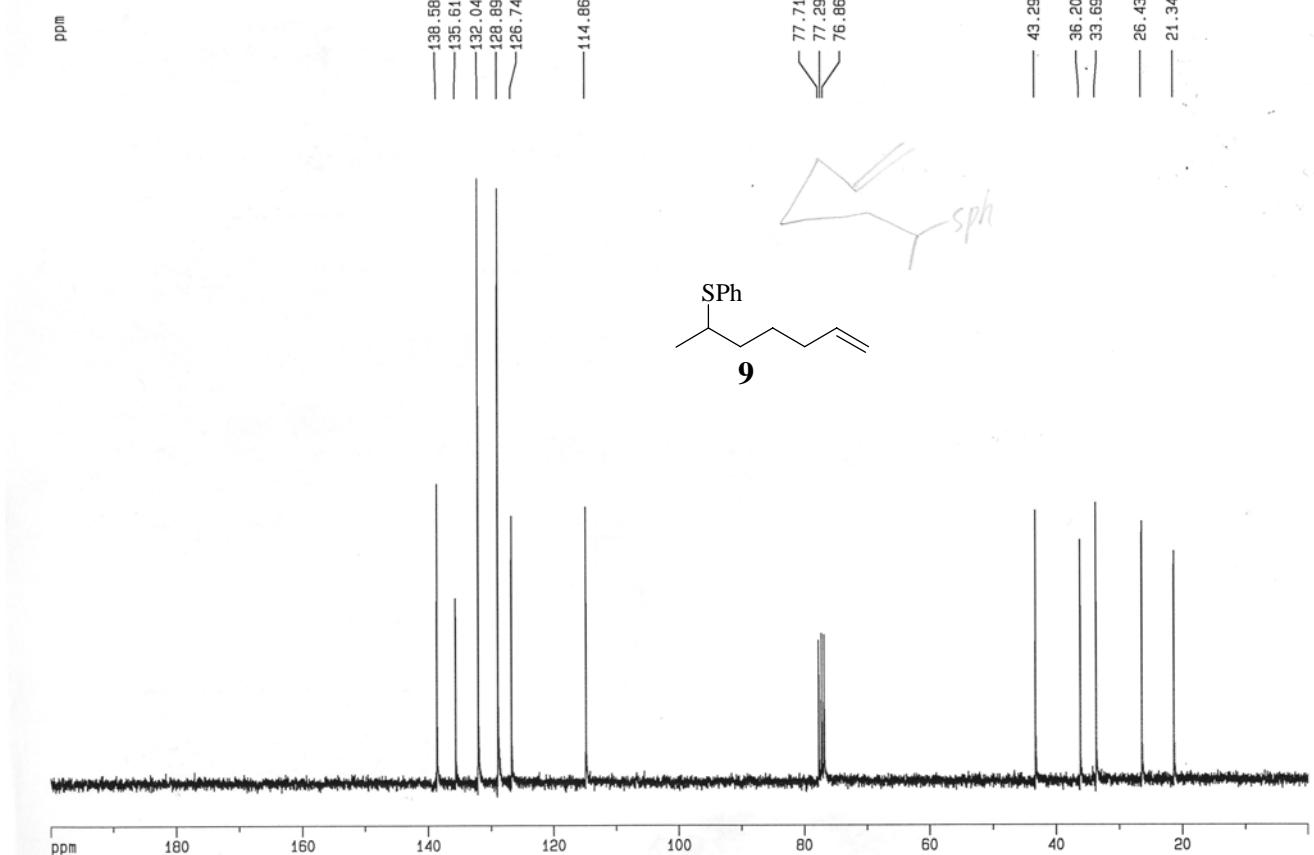
ppm 8 7 6 5 4 3 2 1 0

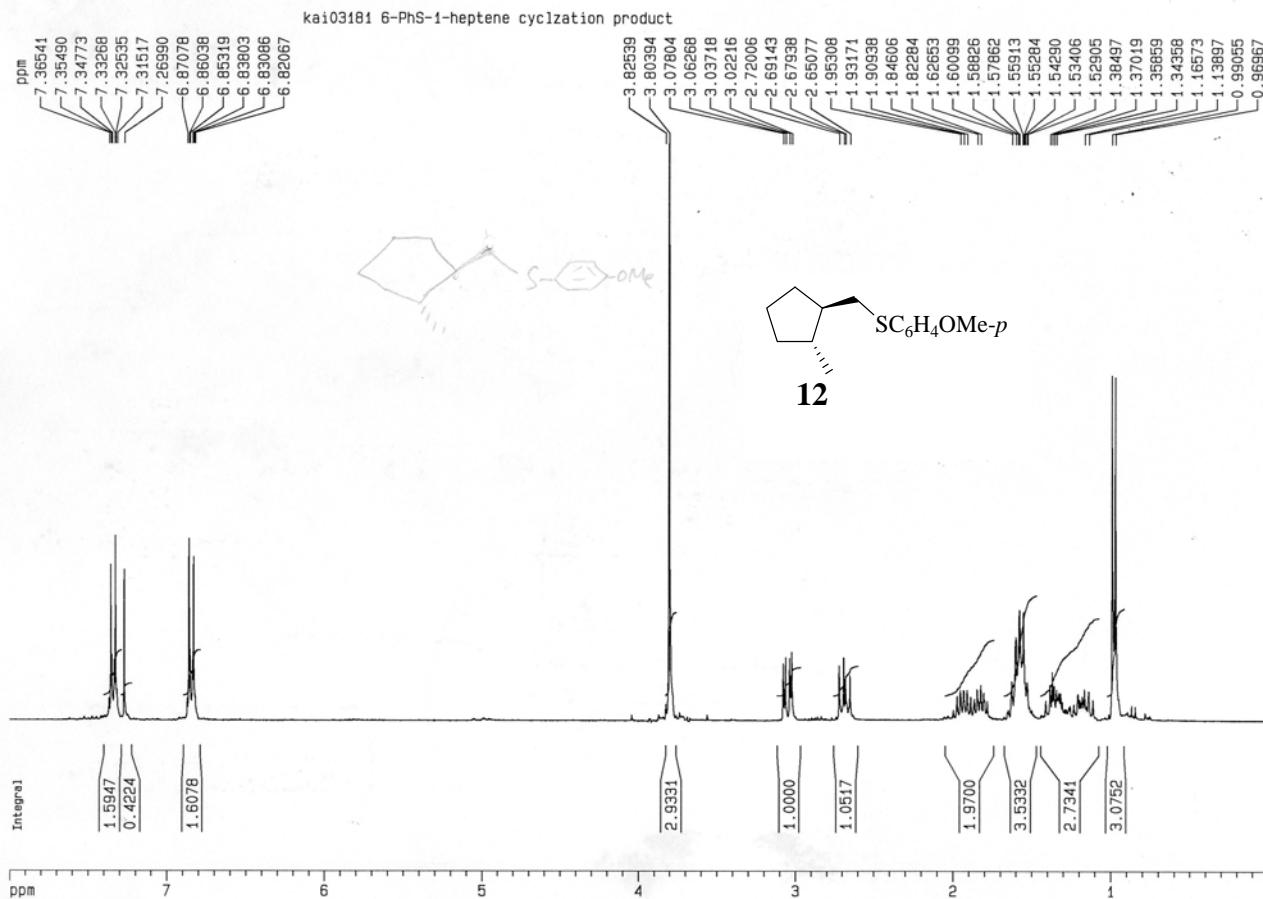
1.8762 1.9300 3.0384 1.0000 0.9470 1.0240 7.8097 3.1423 3.1339 0.85118

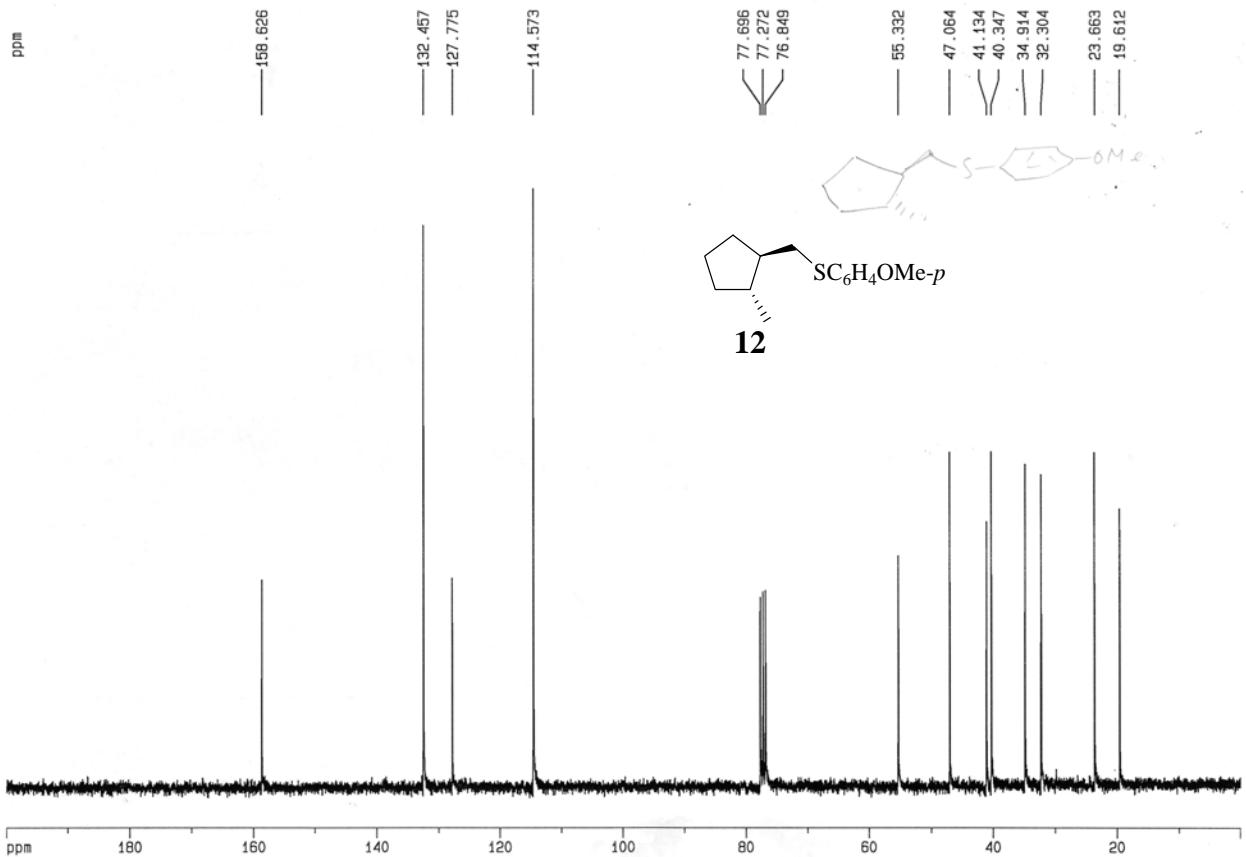
kai bailey tertiary cyclization without OH quenched with (PhO-C₆H₄S) 2



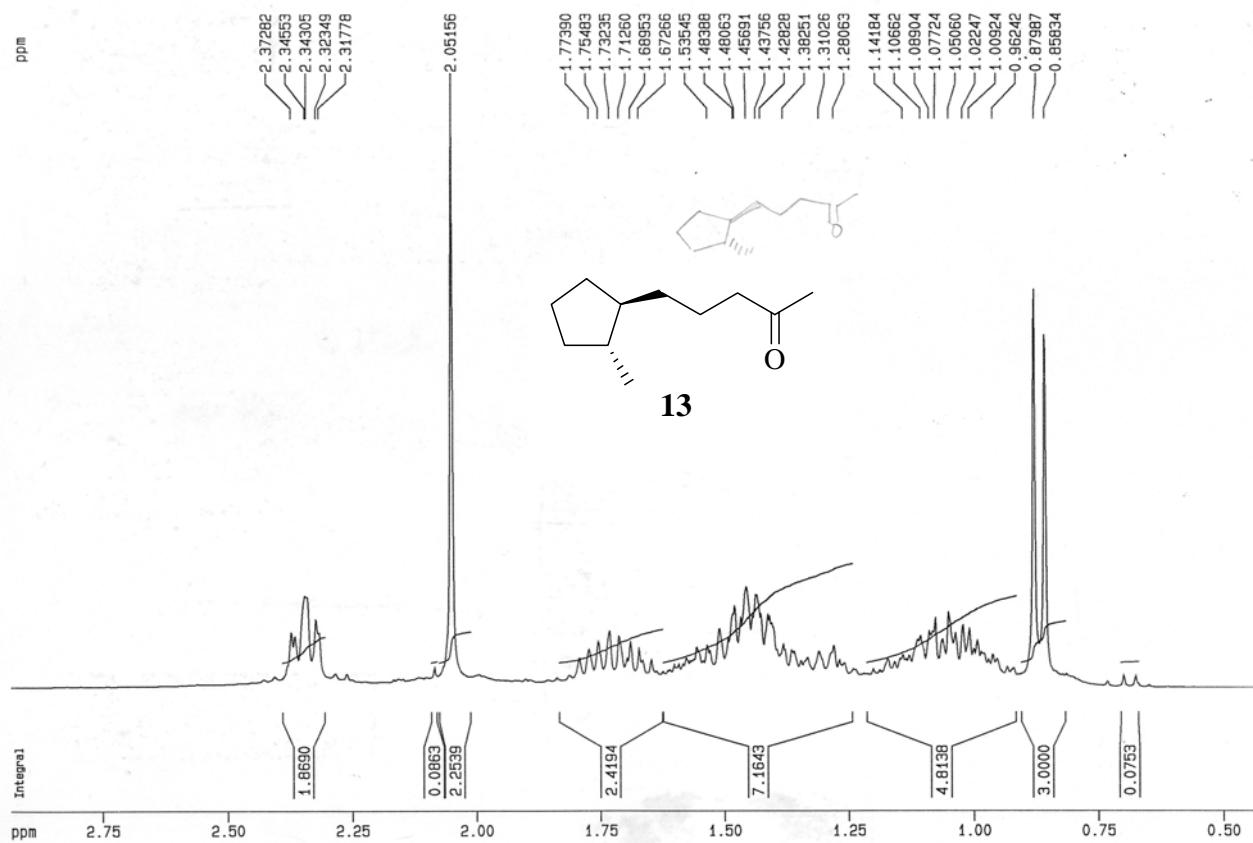


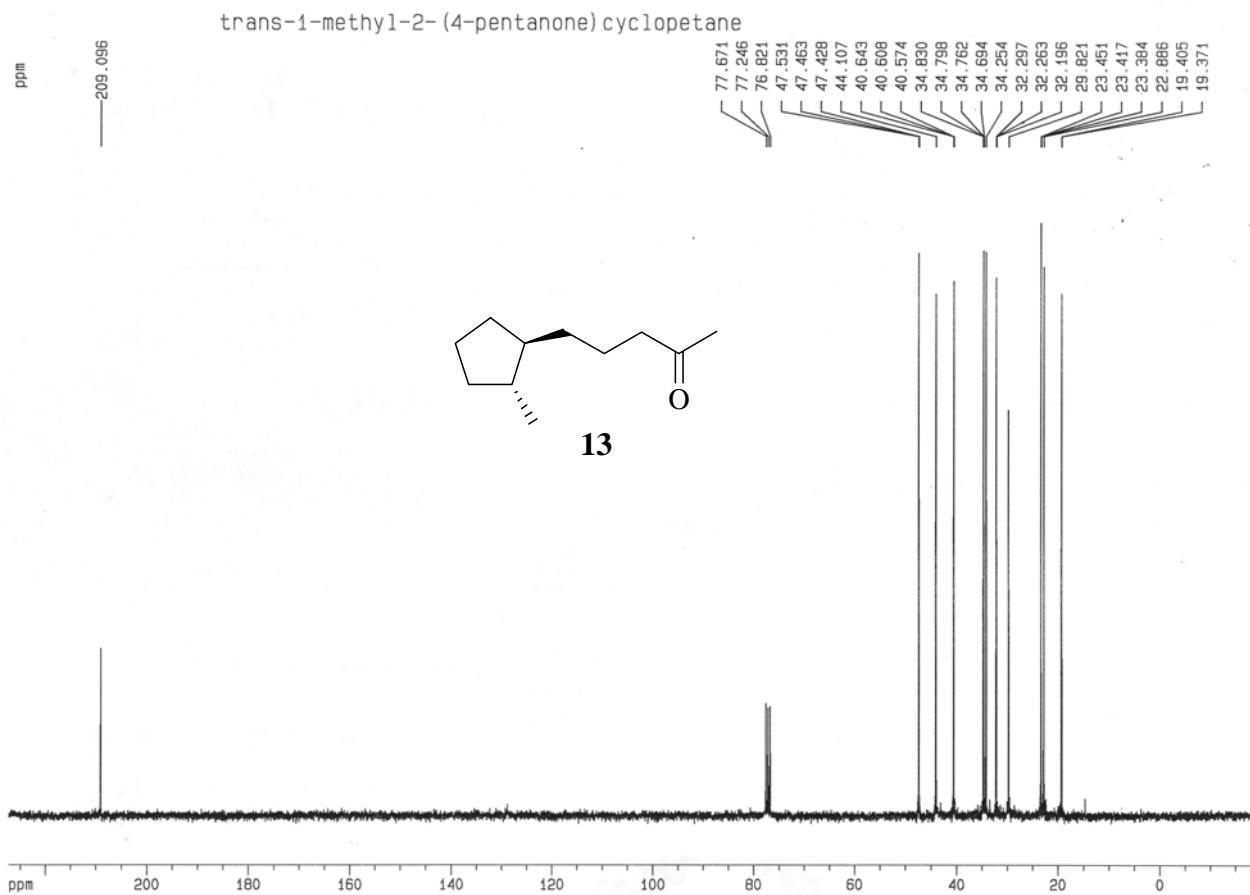






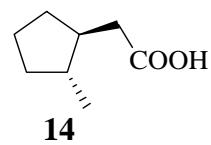
trans-1-methyl-2-(4-pentanone)cyclopentane





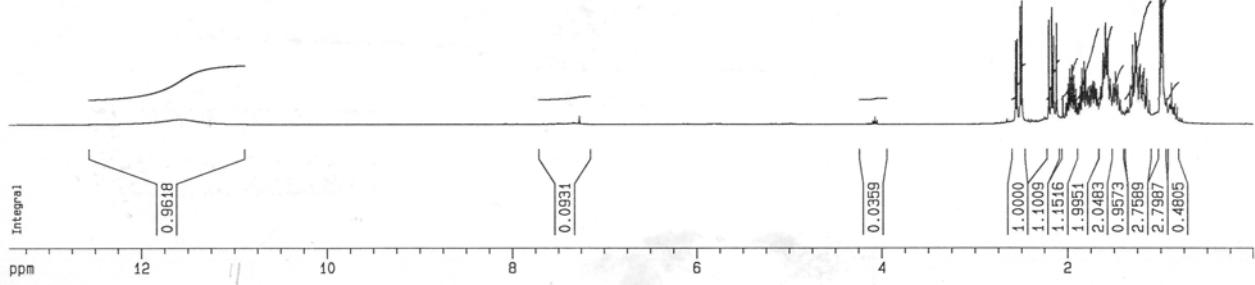
kai0711 acid

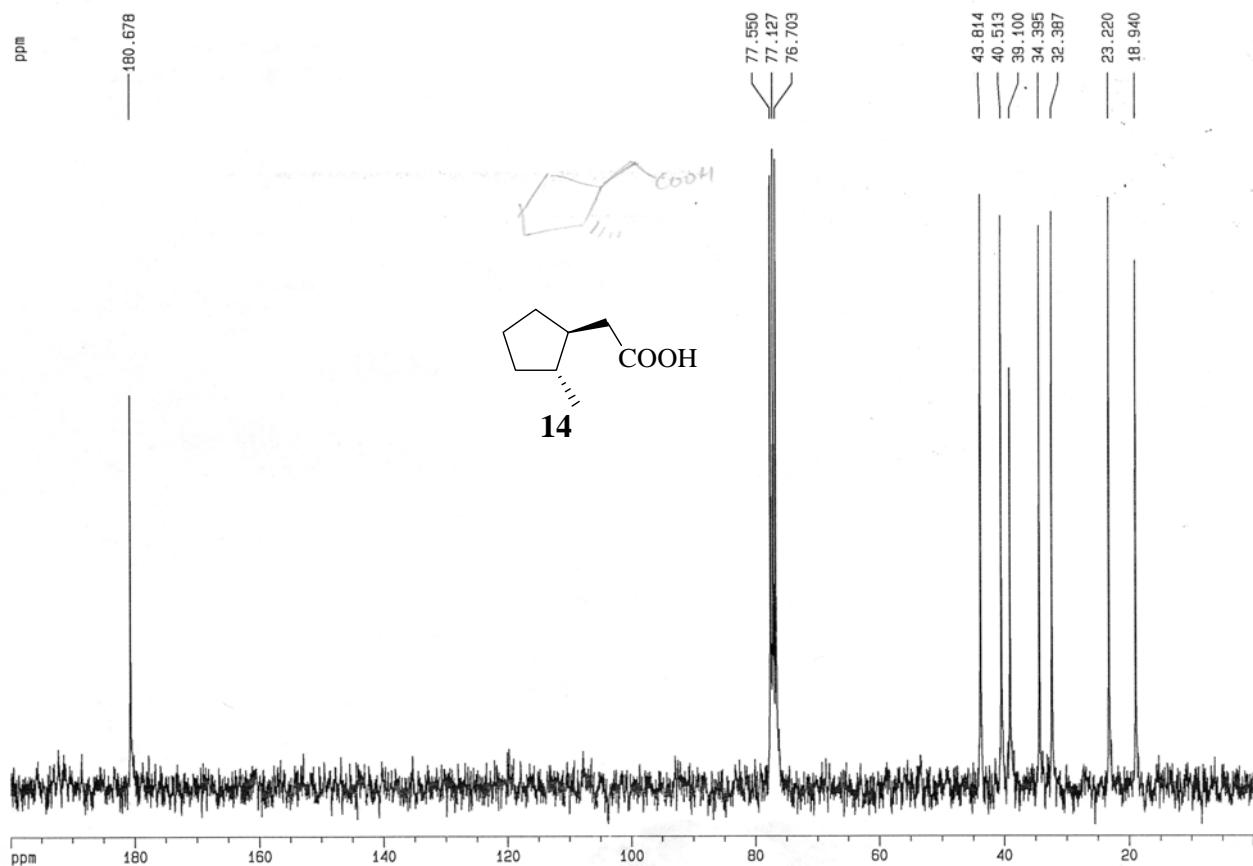
ppm



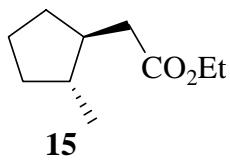
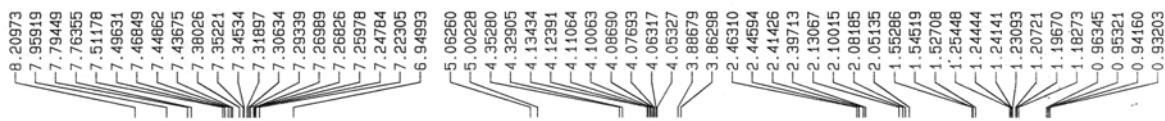
14

2.51074
2.49432
2.20228
2.17106
2.12109
1.59255
1.56639
1.27166
1.27166
0.98266
0.98437
0.88458

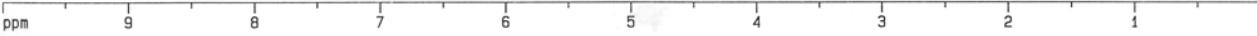




ppm



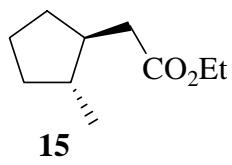
Integral



ppm

kai0929 trans-ester

173.779



77.544
77.121
76.698

60.215

44.102
40.558
39.403
34.481
32.409
23.259
19.005
14.377



ppm

200

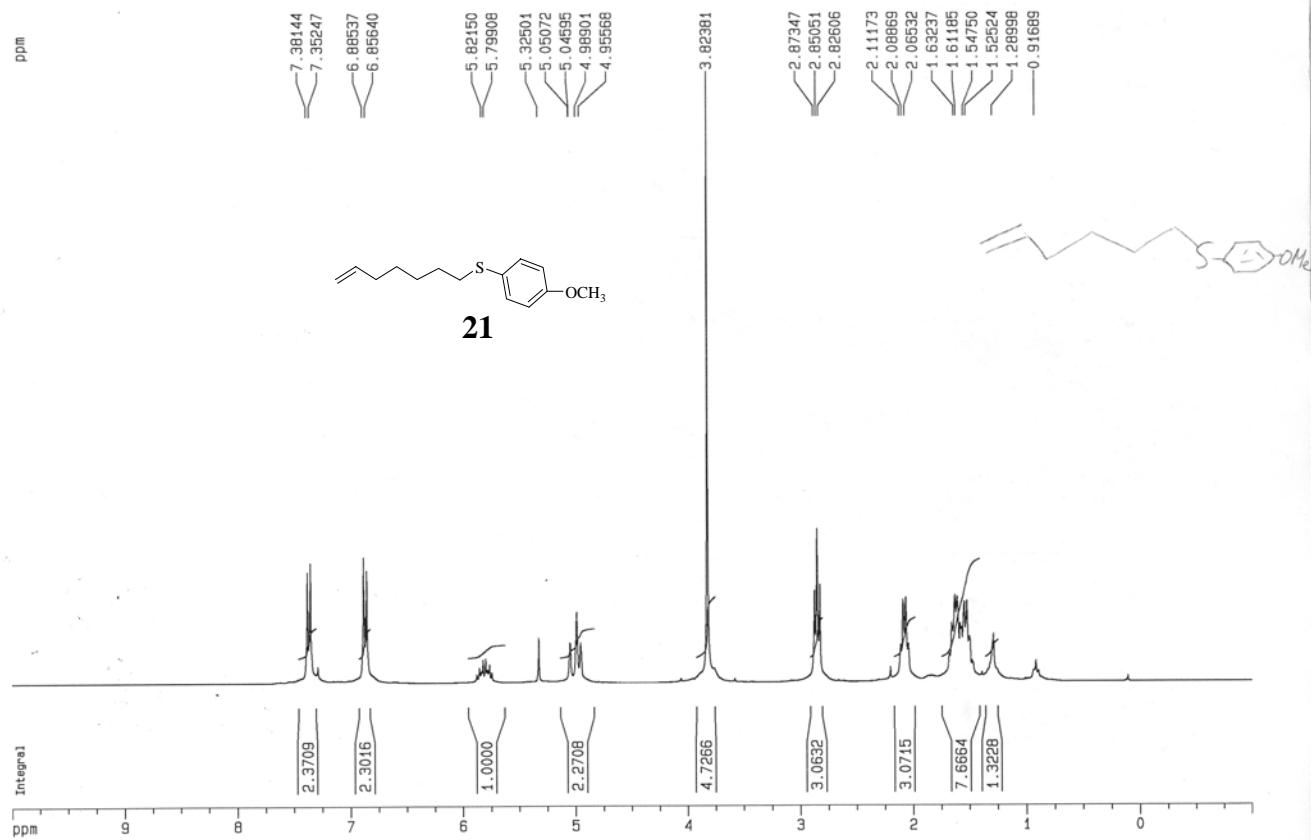
150

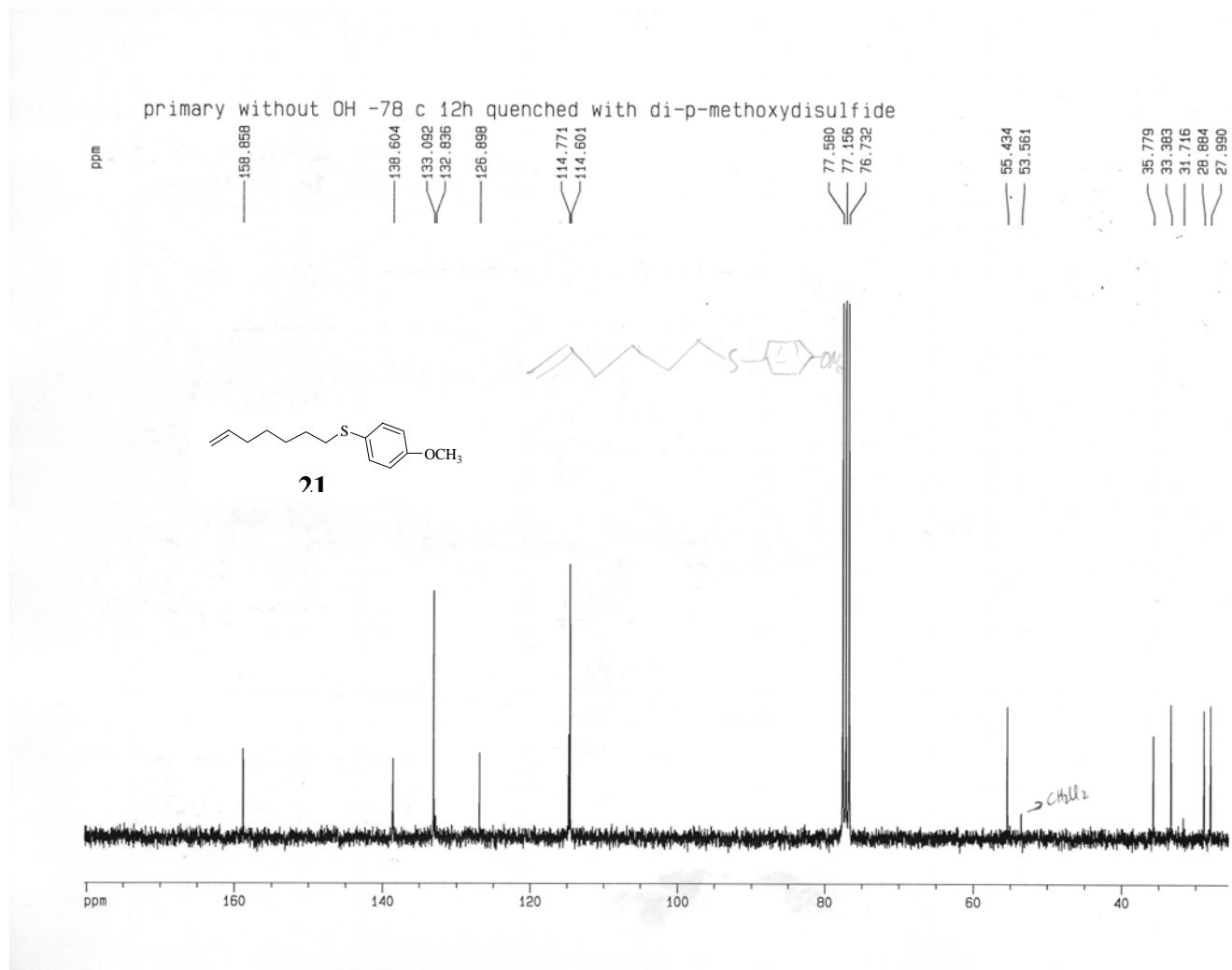
100

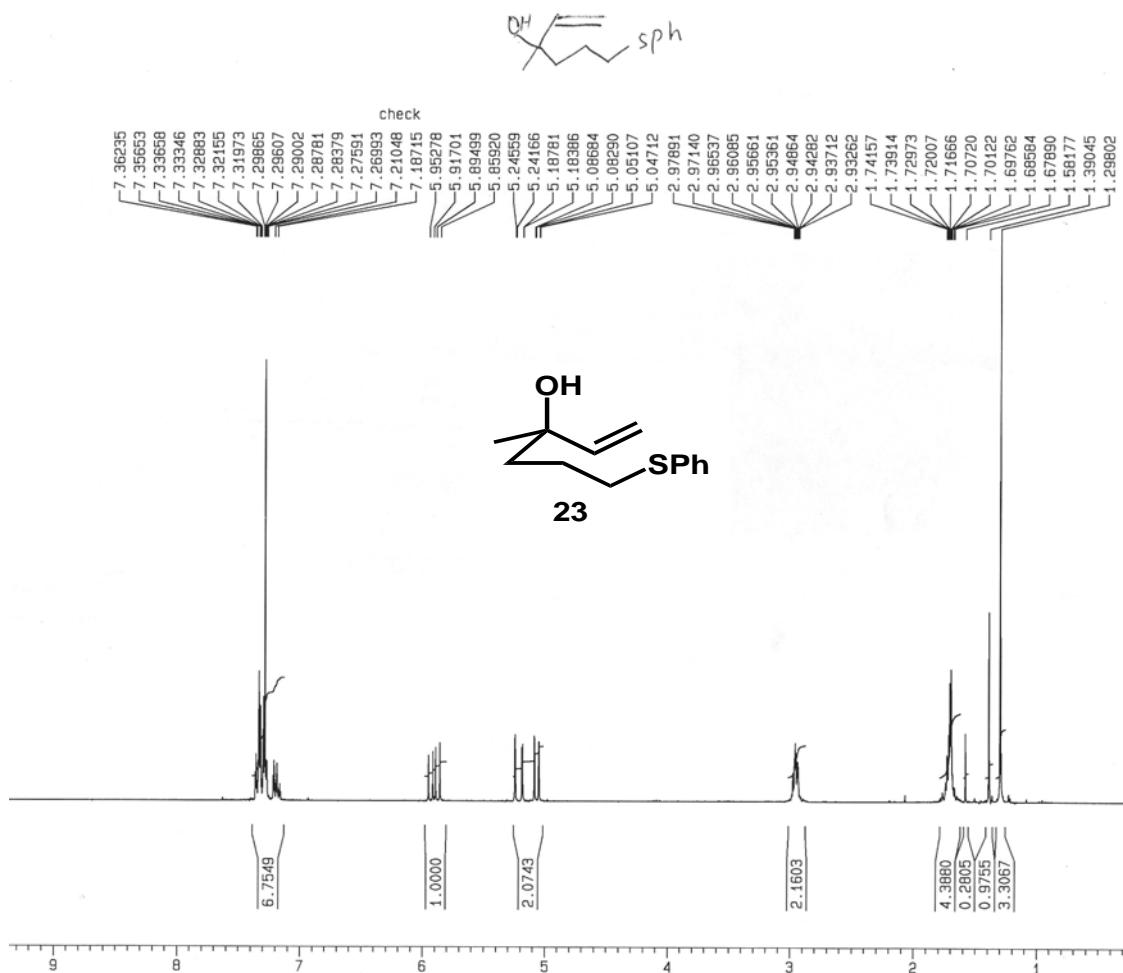
50

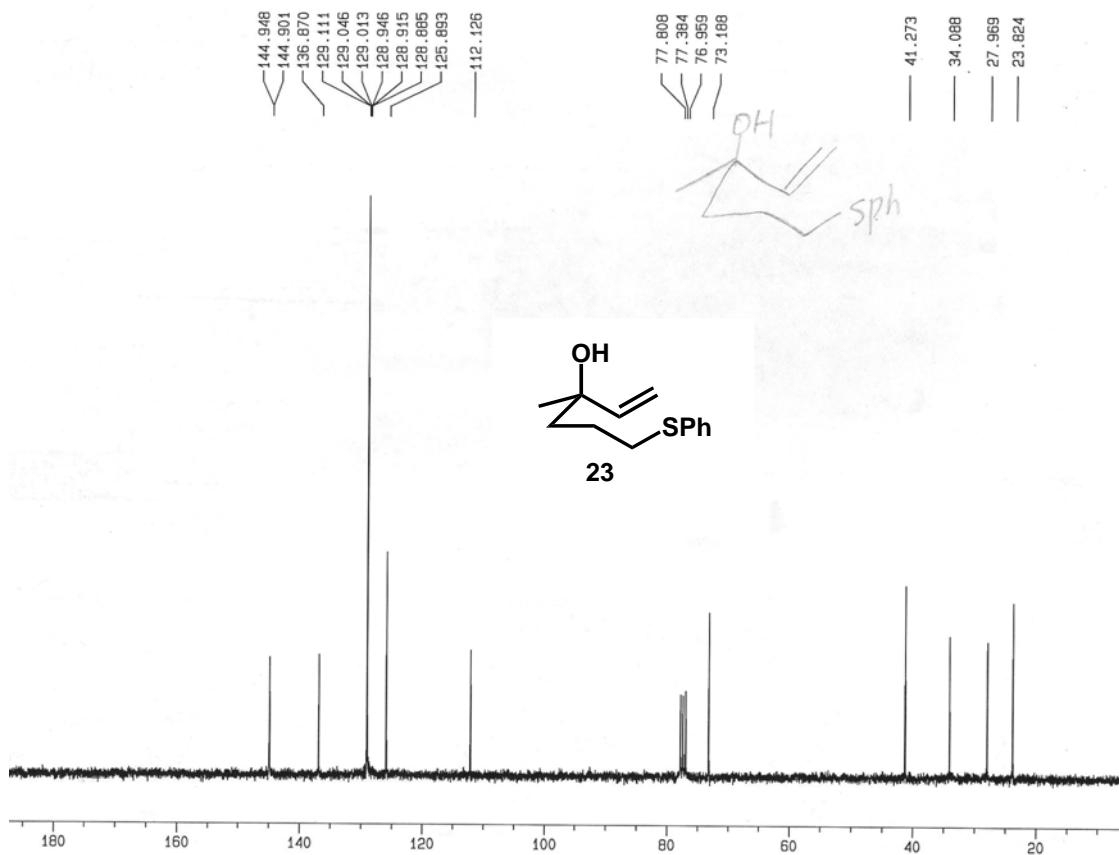
0

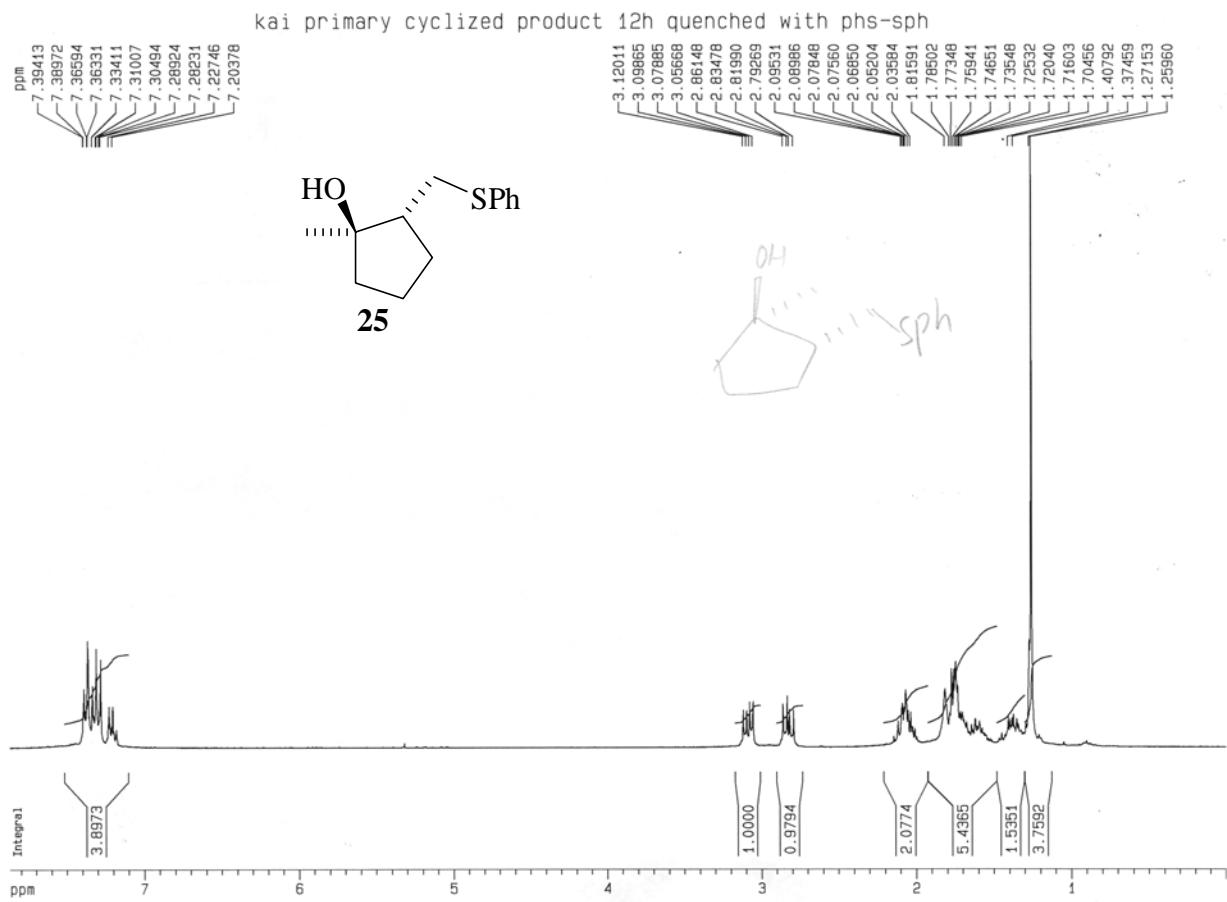
primary without OH -78 °C 12h quenched with di-p-methoxydisulfide



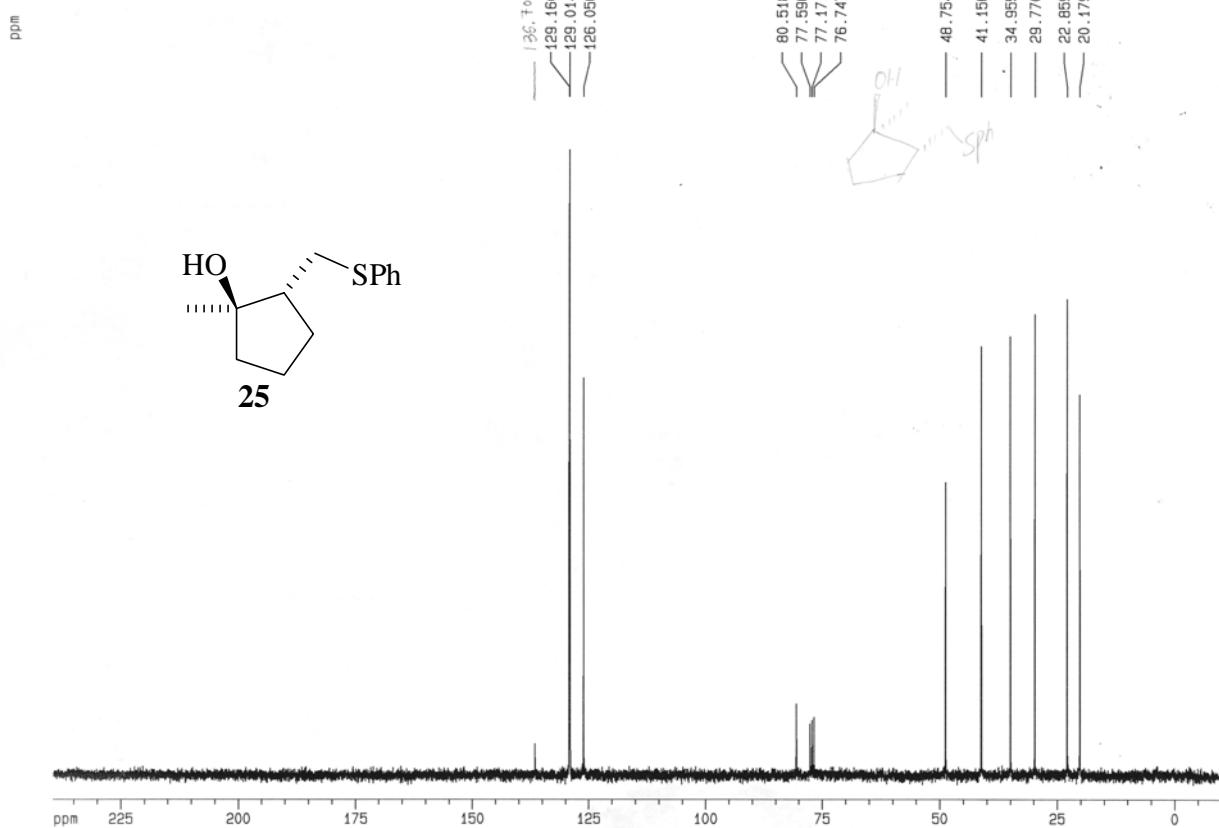




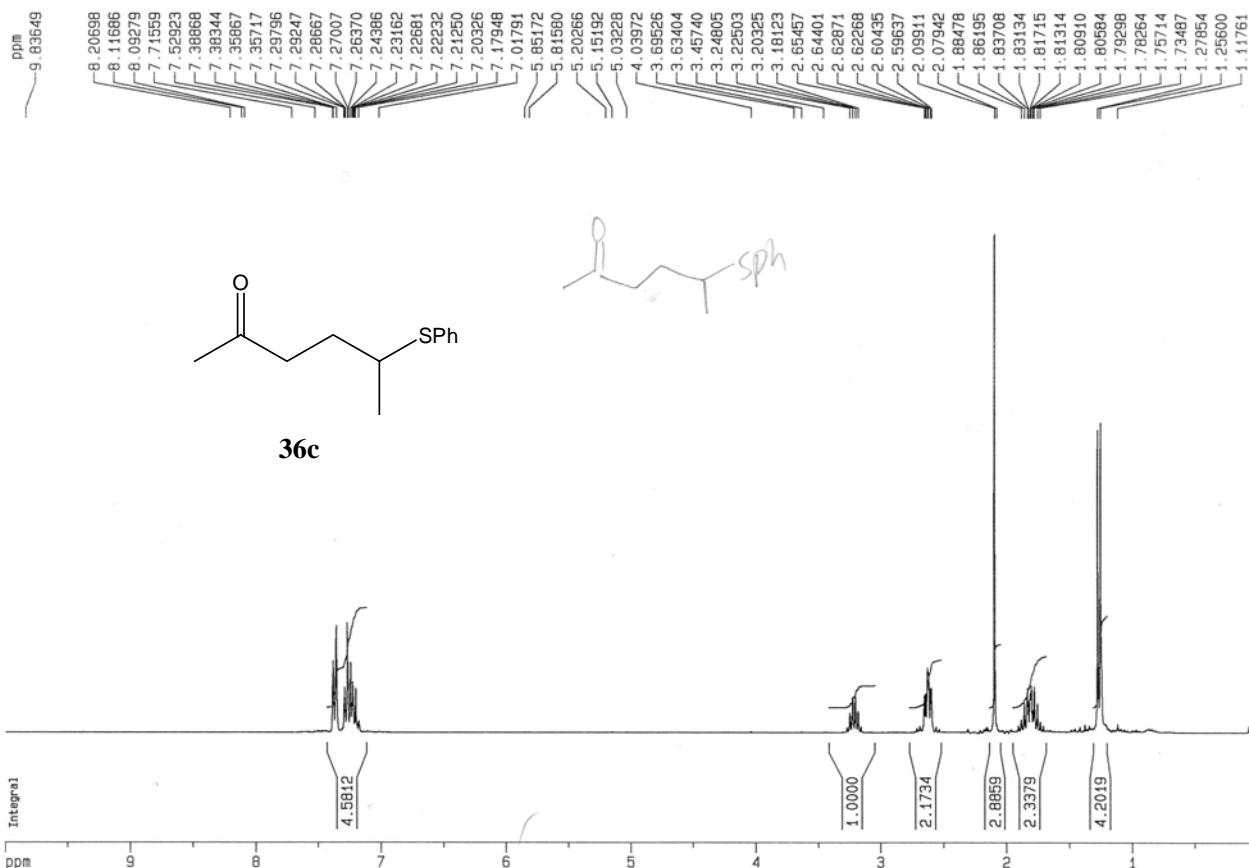


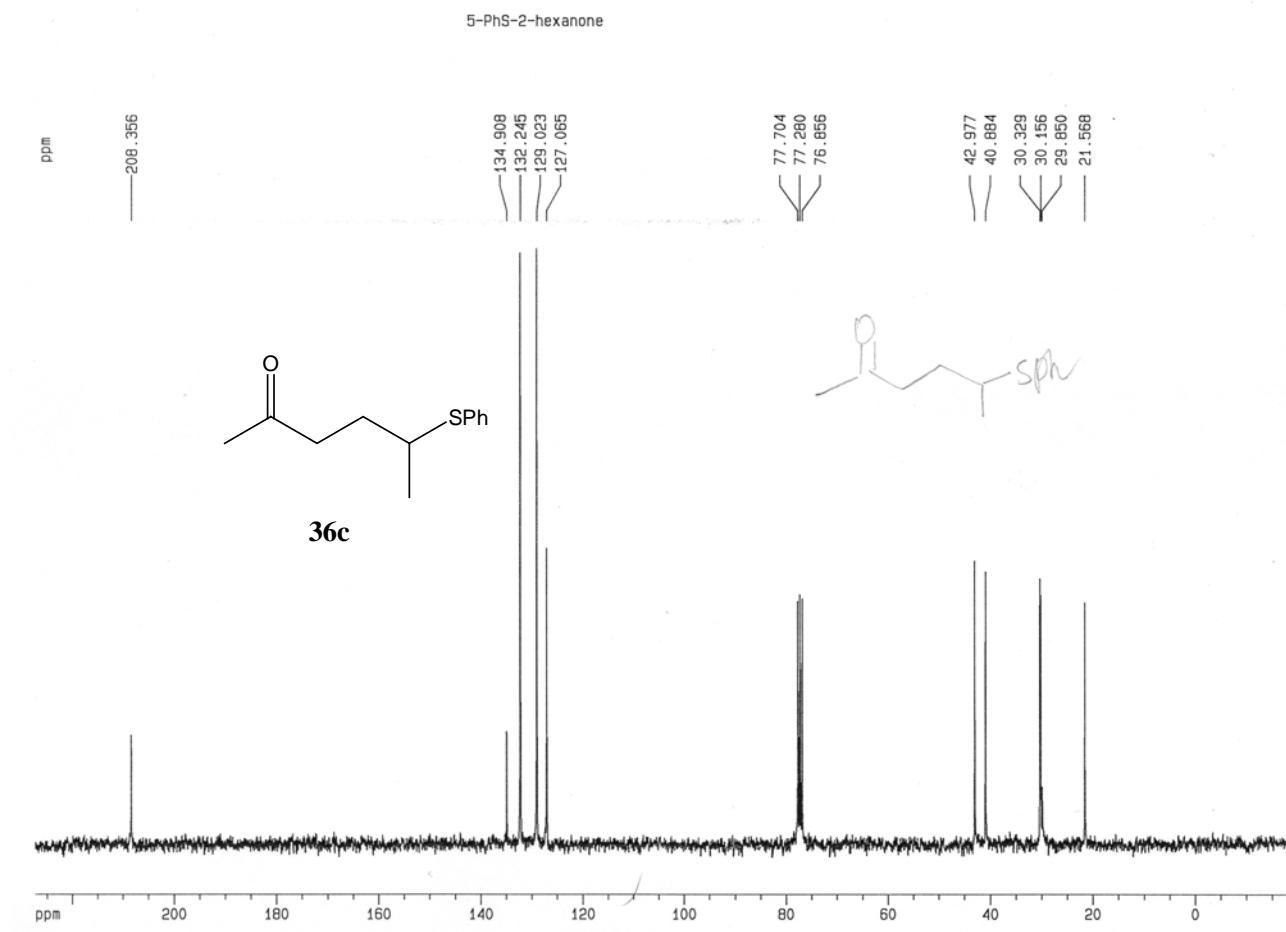


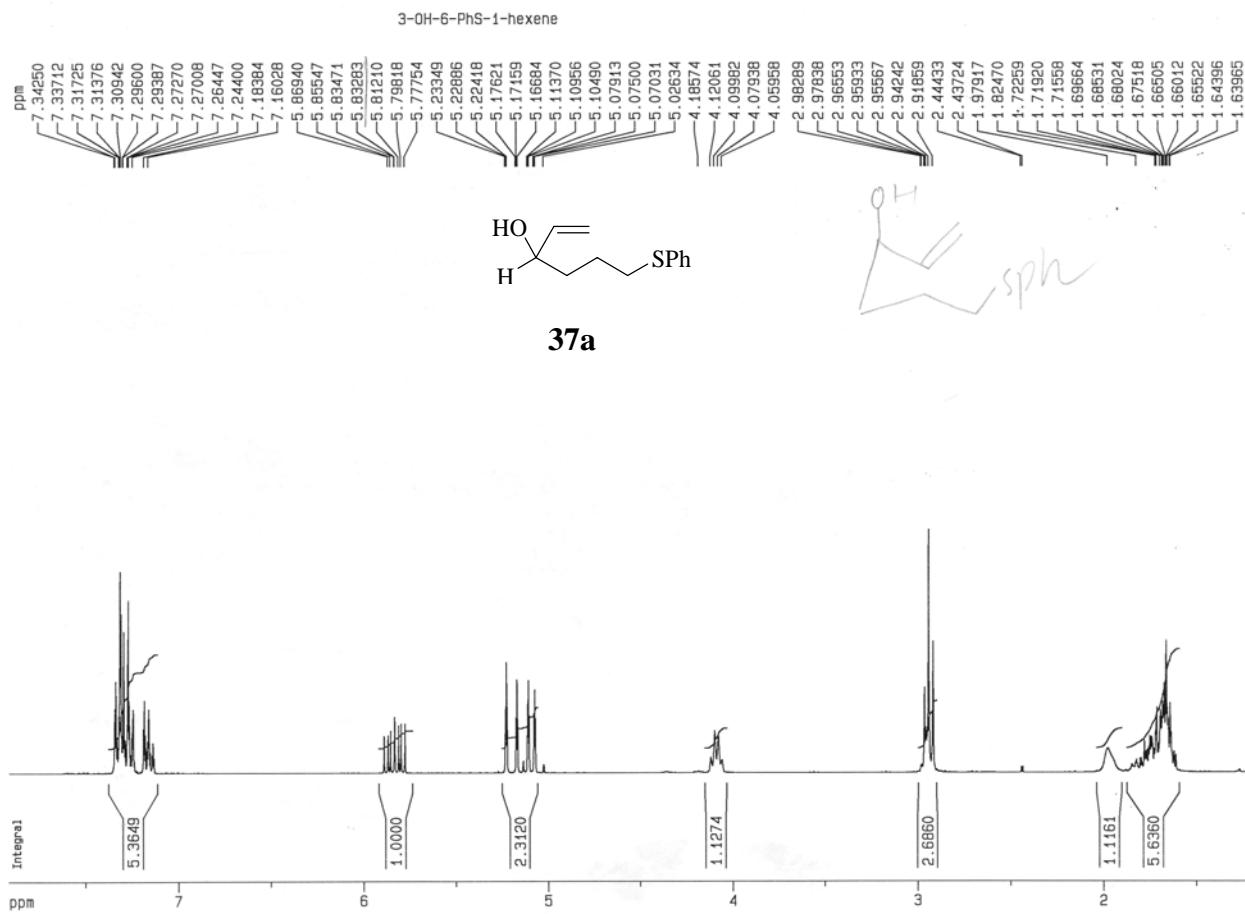
kai primary cyclized product quenched with disulfide 08/16/00



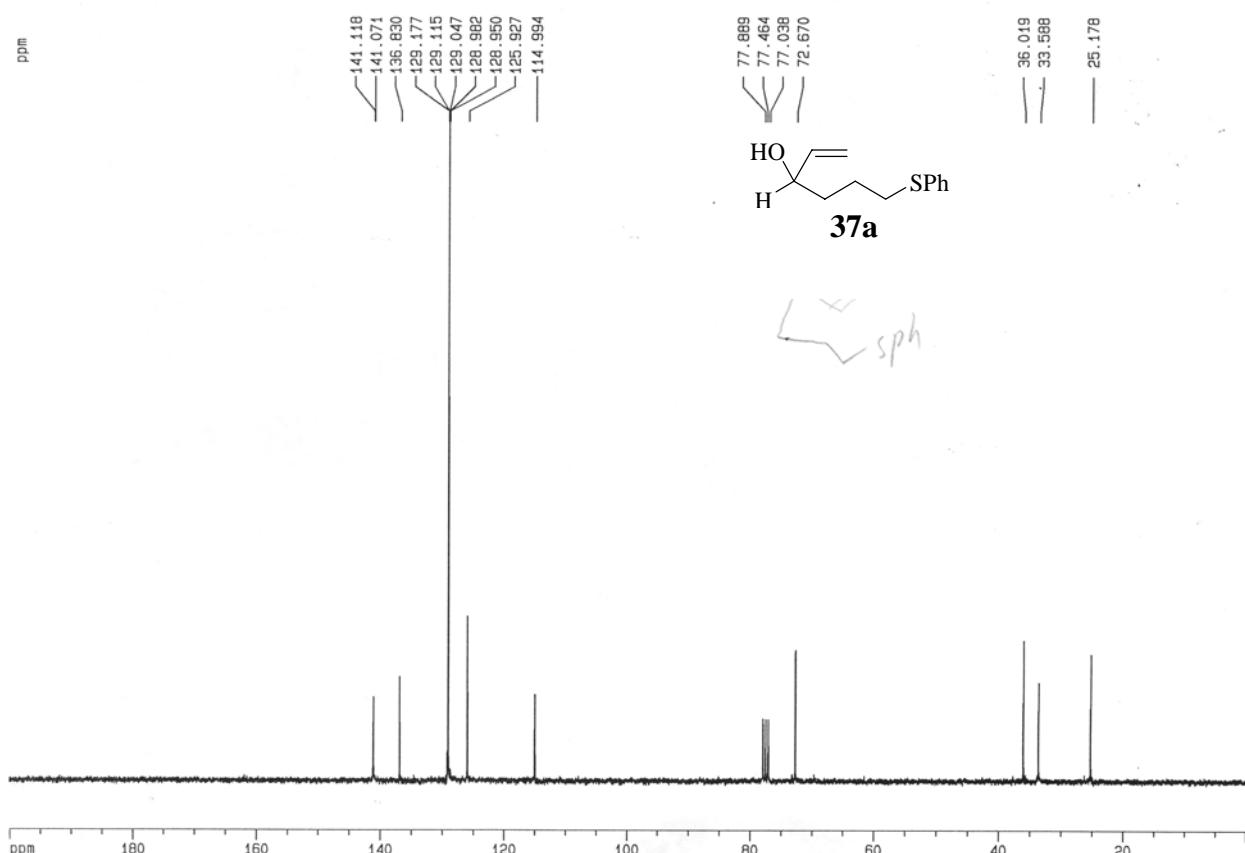
5-PhS-2-hexanone

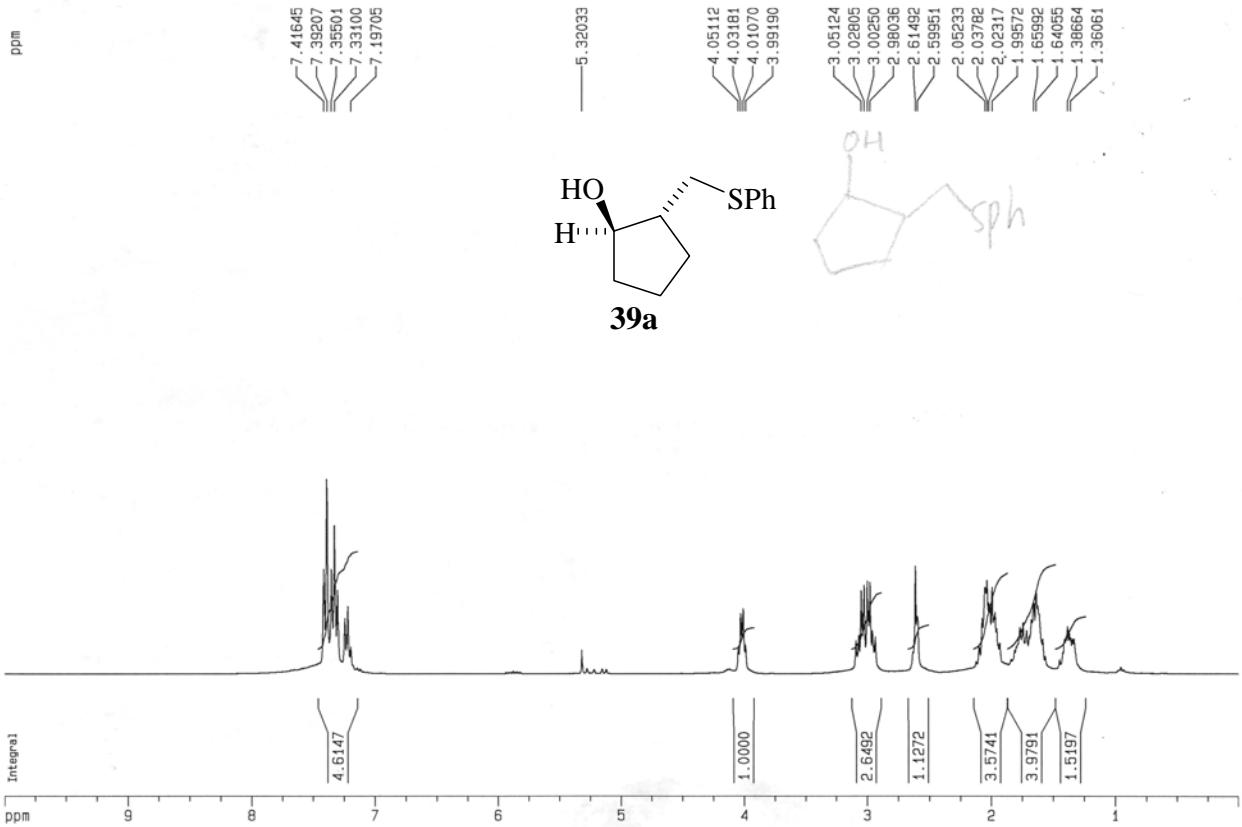


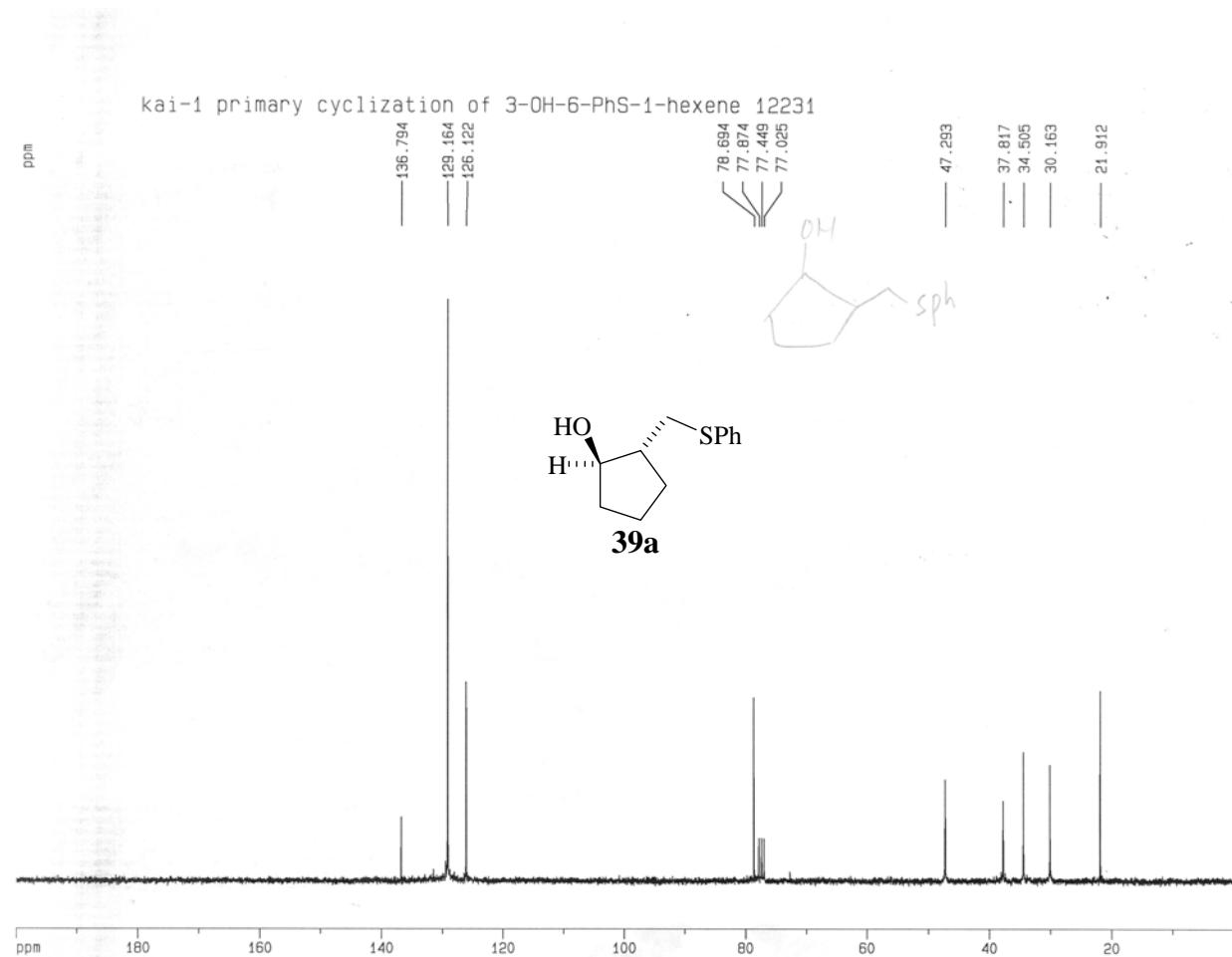




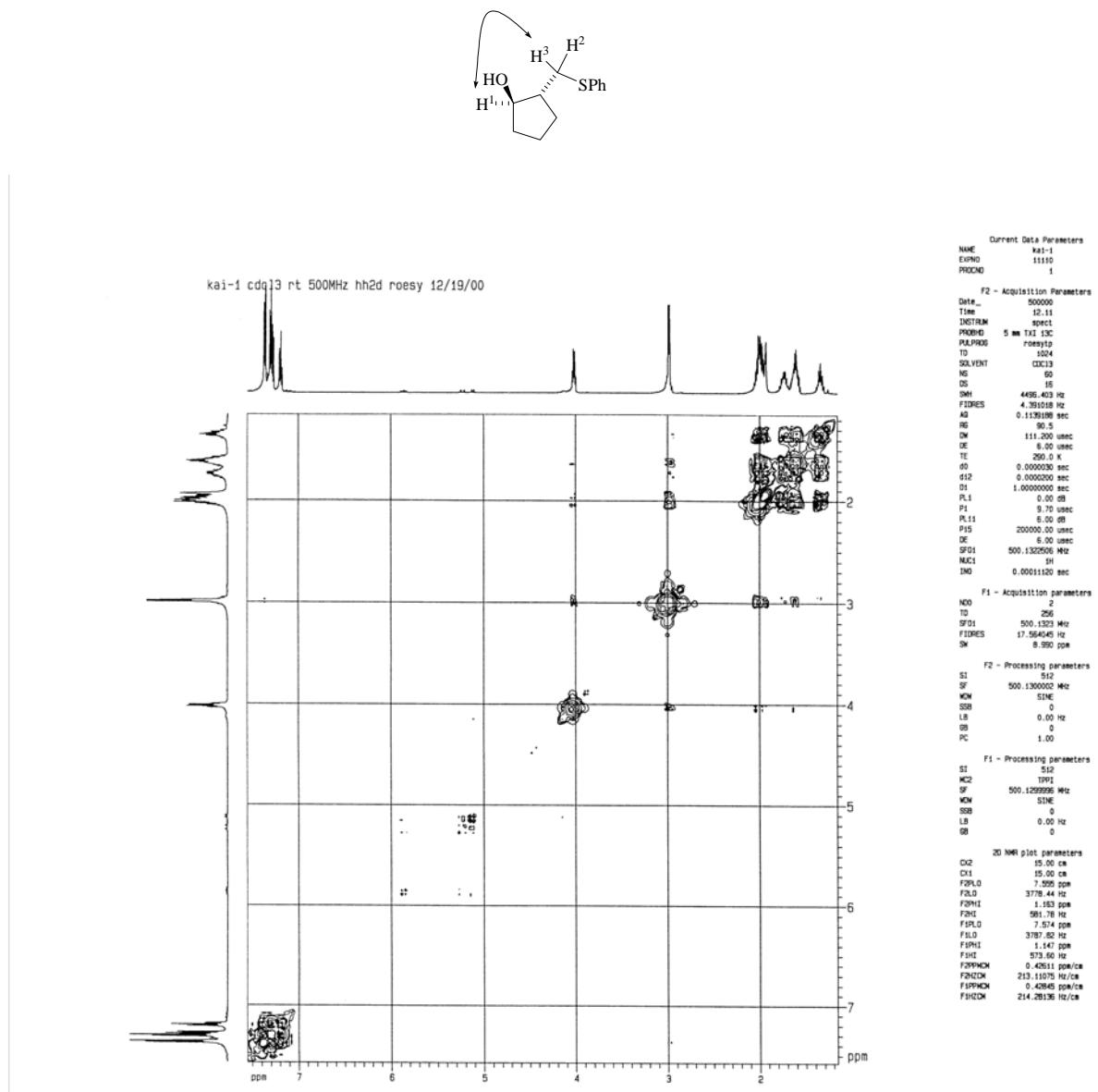
ppm



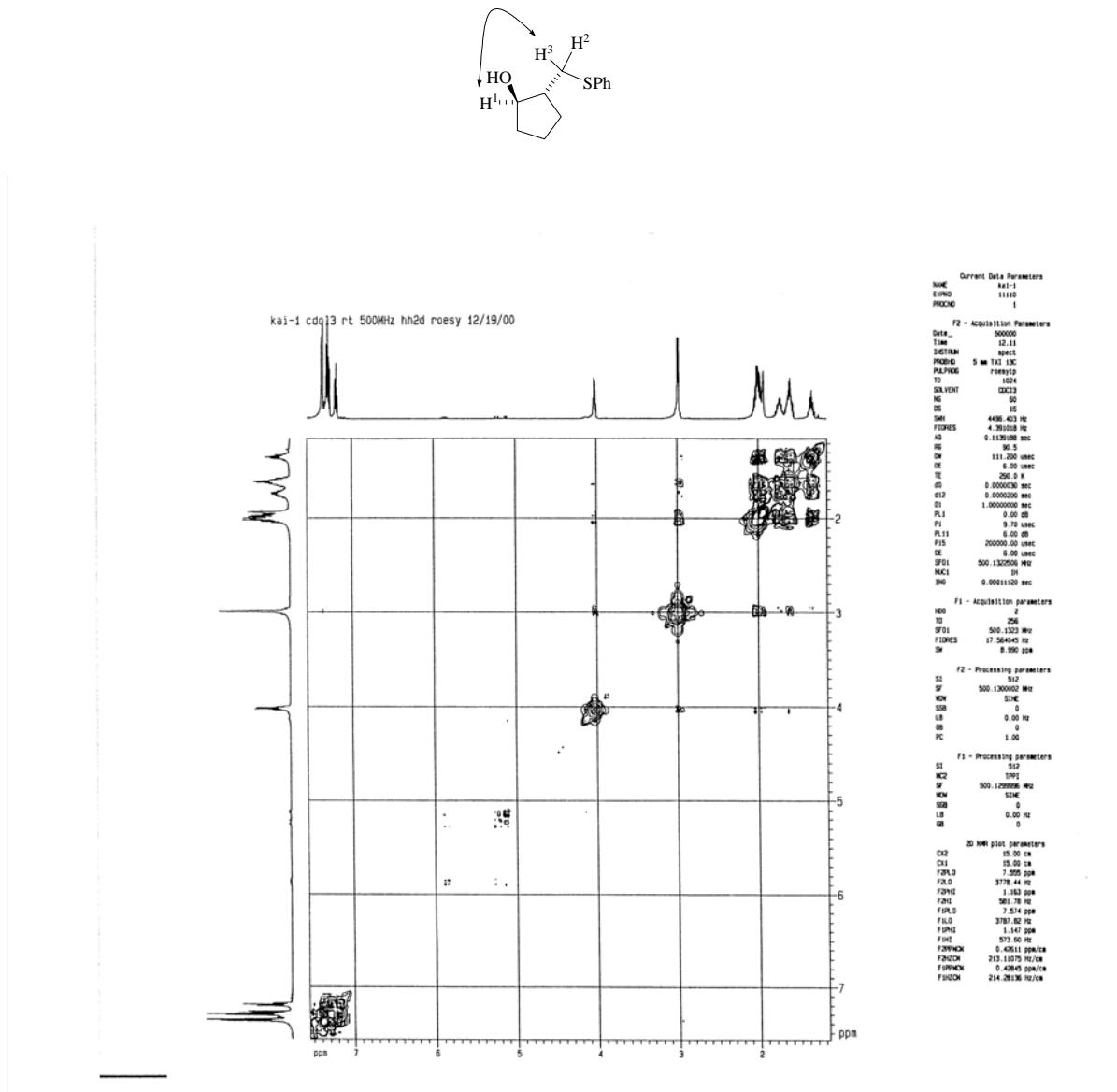


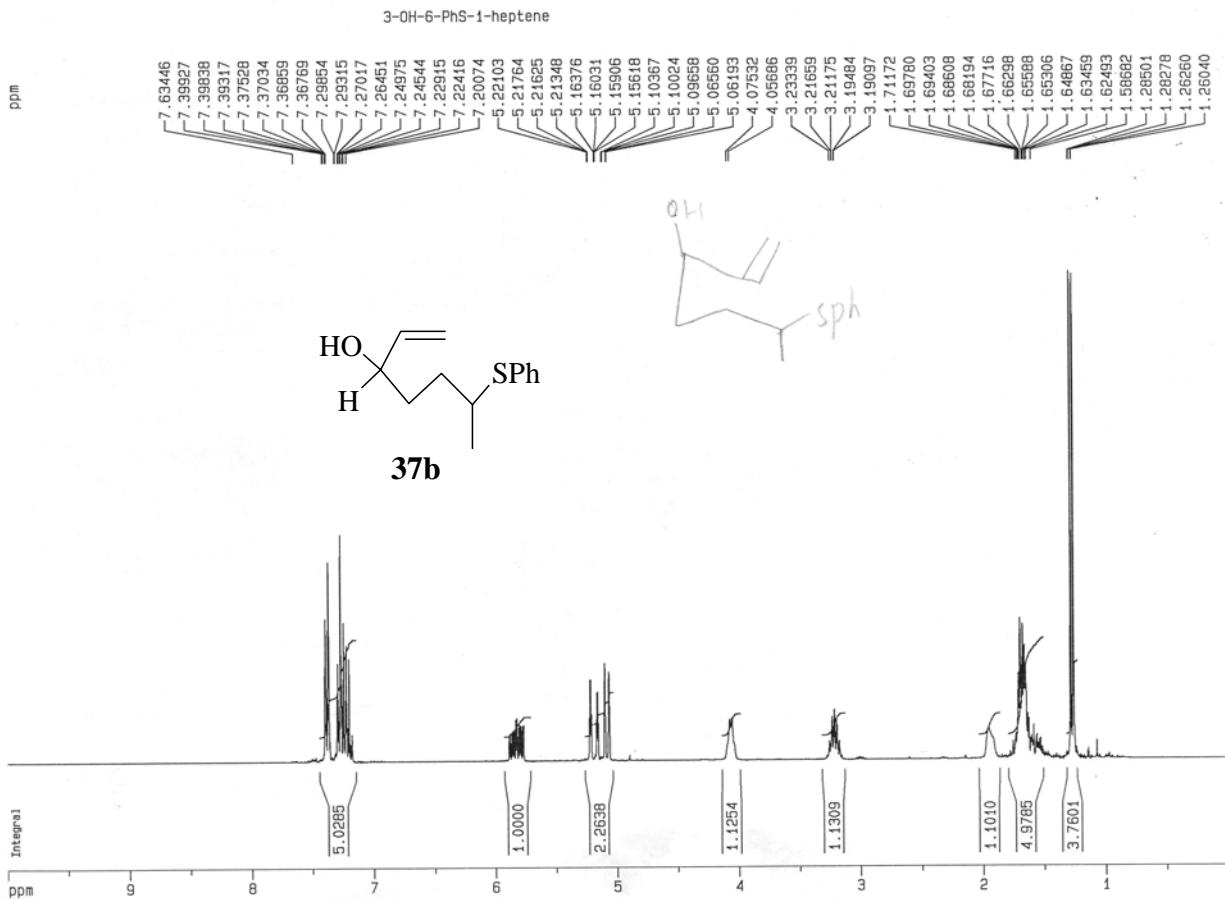


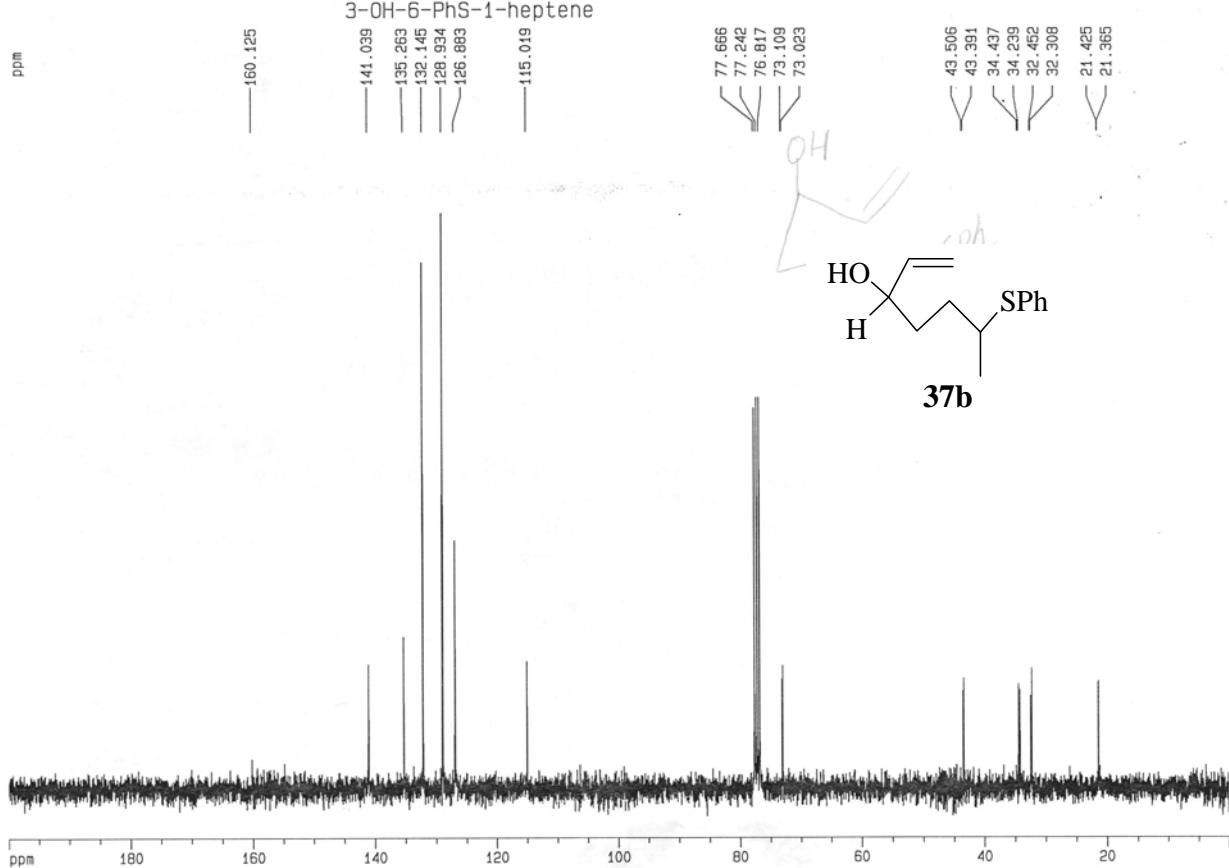
The COSY spectrum of compound 39a

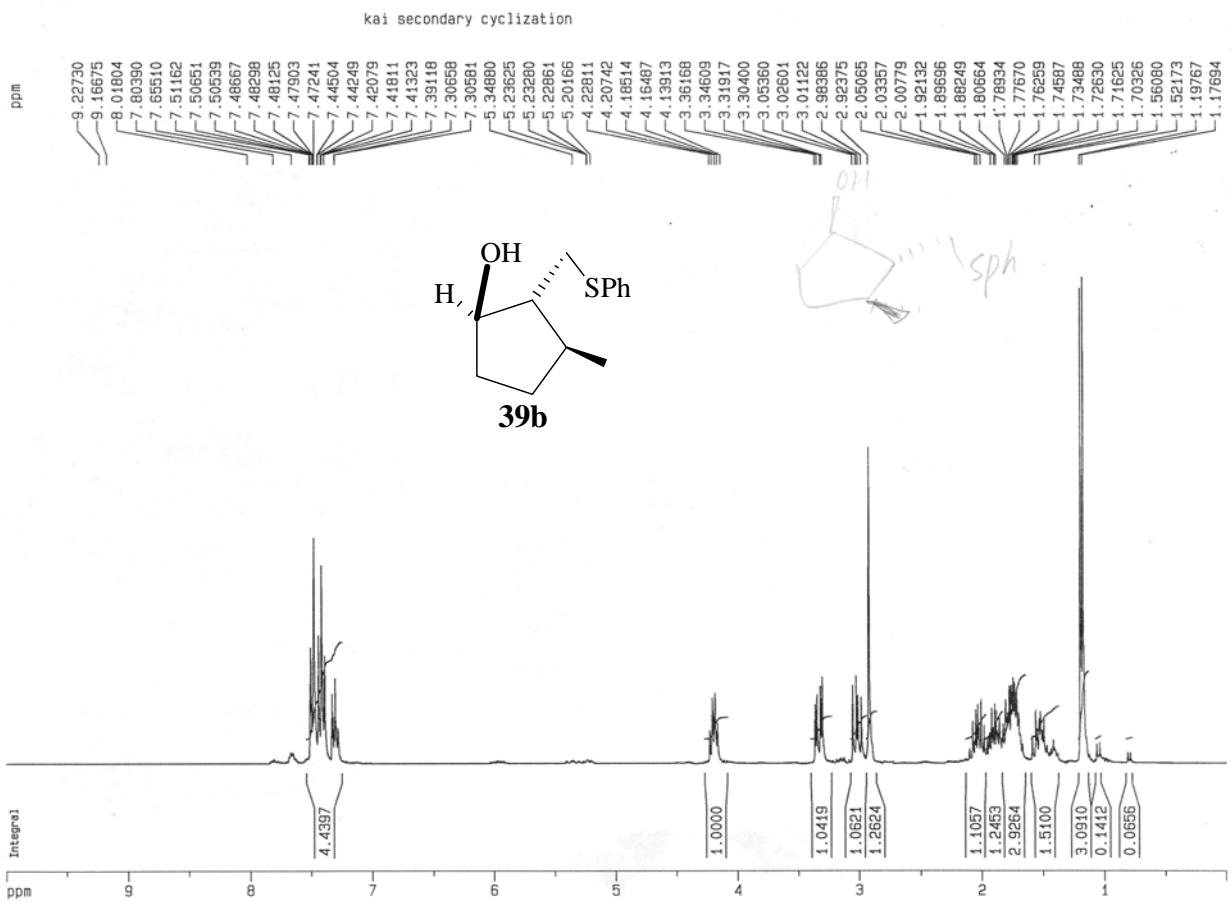


The ROESY spectrum of compound 39a

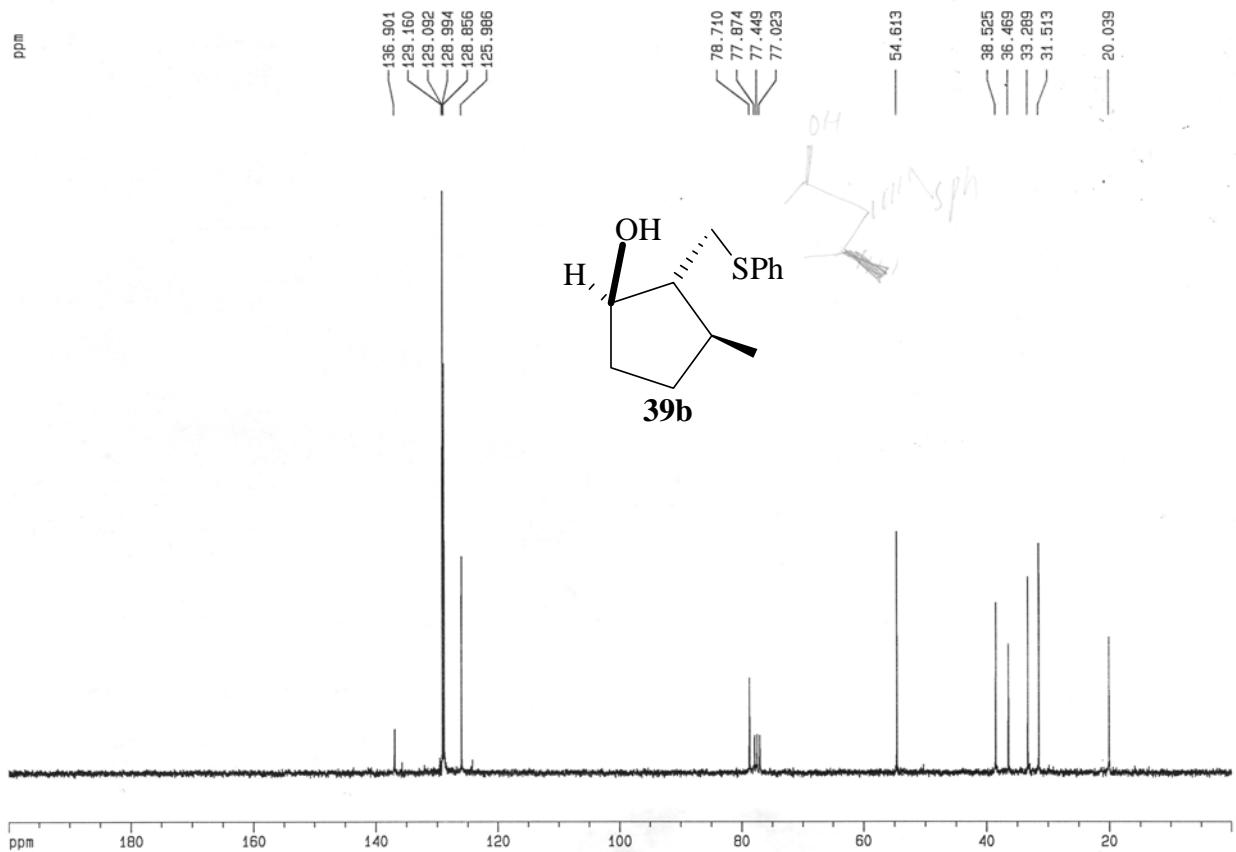


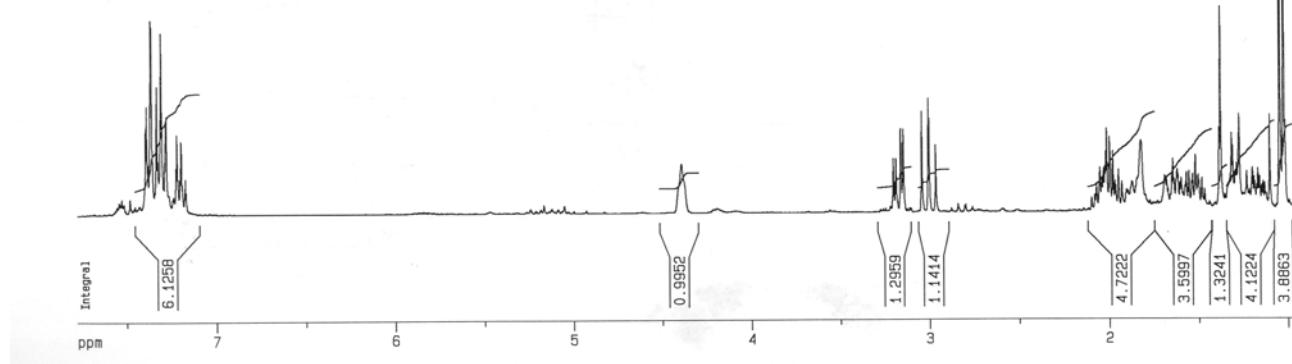
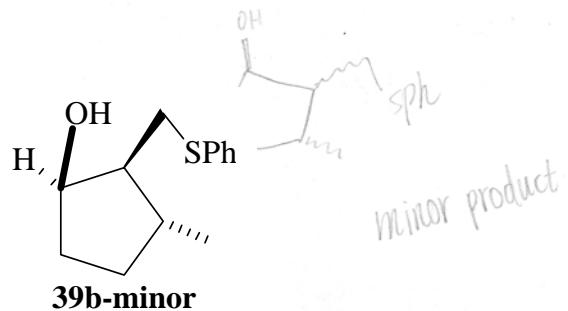
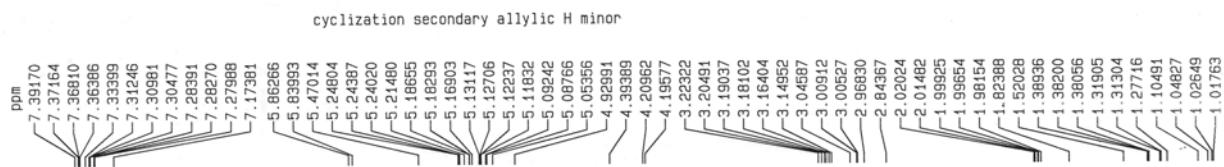




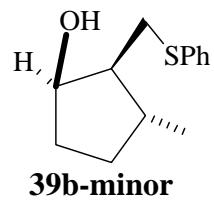


ppm





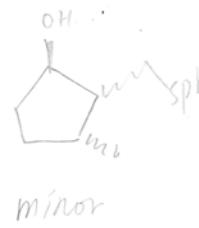
ppm



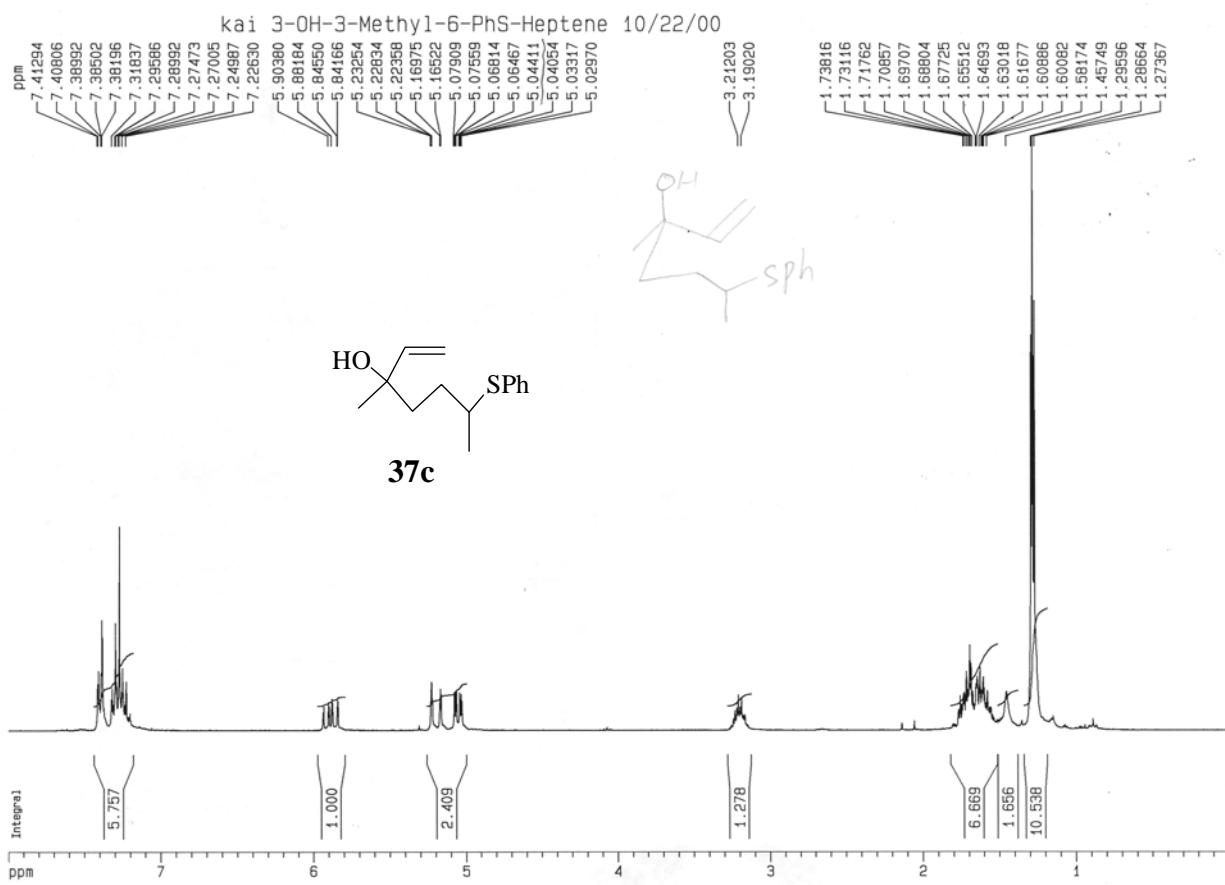
136.765
129.179
129.048
128.896
125.996

77.577
77.154
76.731
73.951

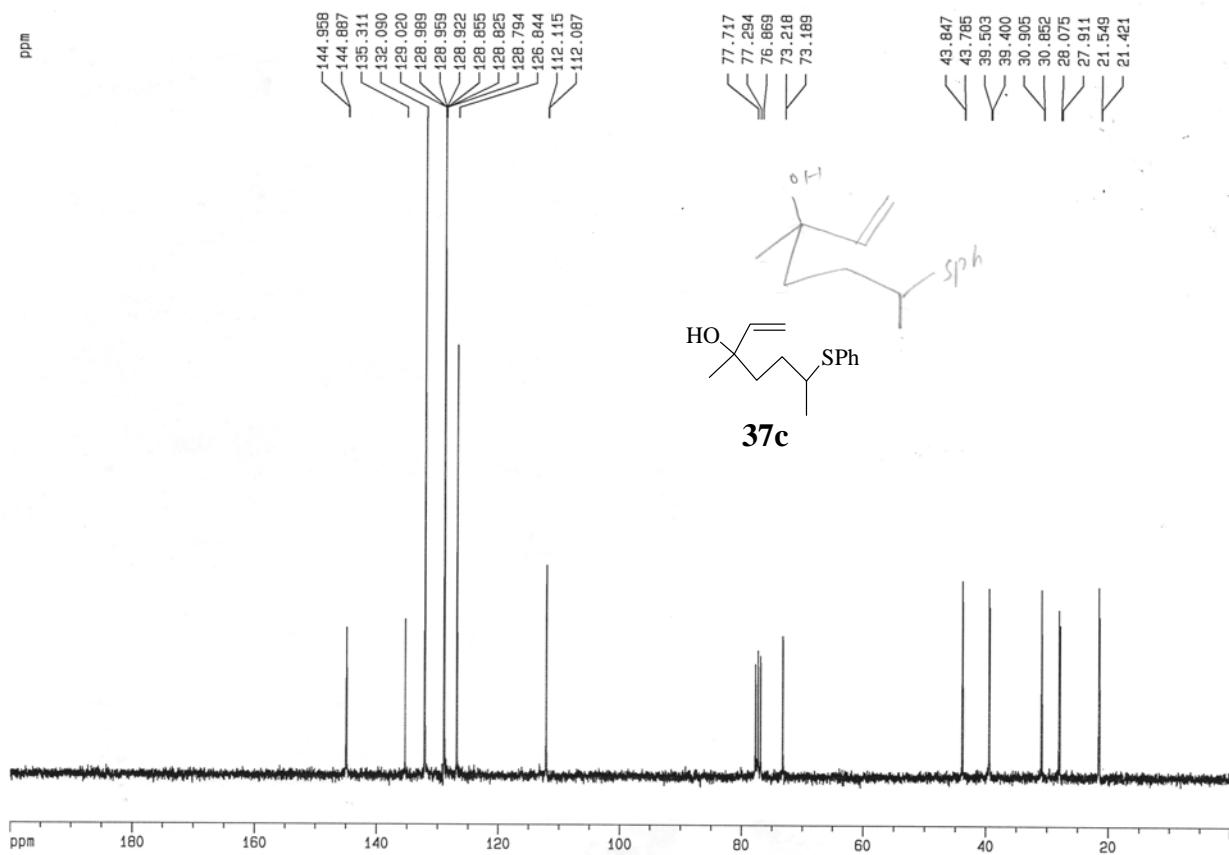
54.893
37.243
33.233
32.290
32.292
31.495
19.084



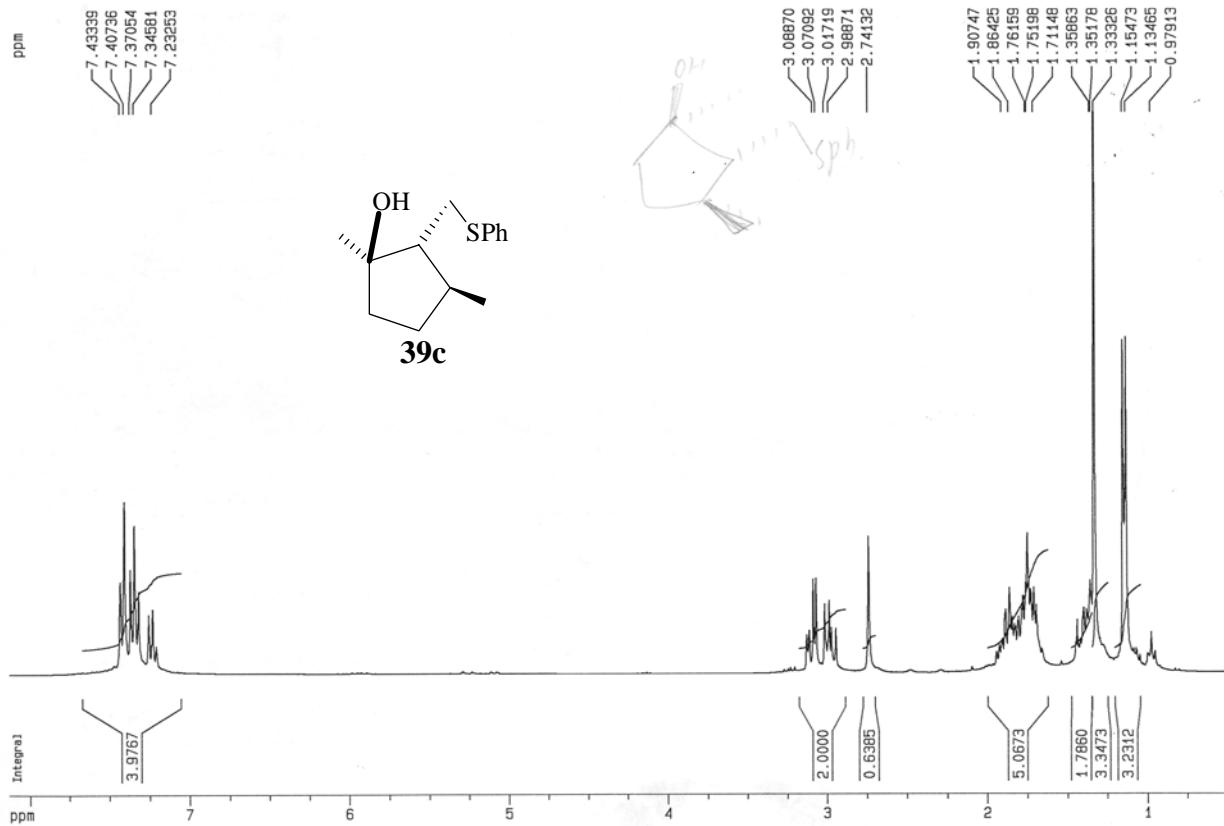
ppm 200 180 160 140 120 100 80 60 40 20



ppm



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

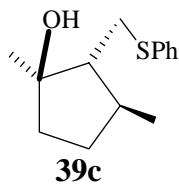


ppm

136.714
129.165
129.132
129.097
129.052
129.030
128.999
128.968
128.932
128.885
128.854
126.075

81.137
77.865
77.441
77.016

55.683
40.125
38.558
33.938
30.291
24.118
20.895

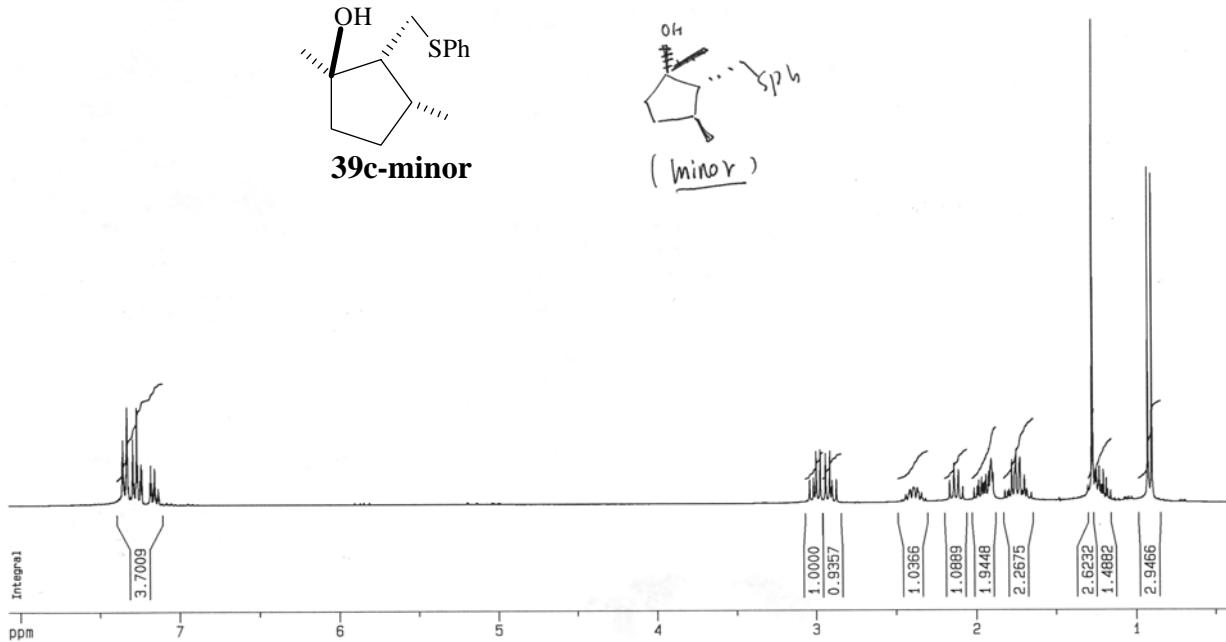
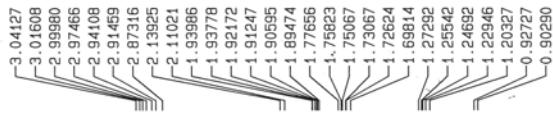
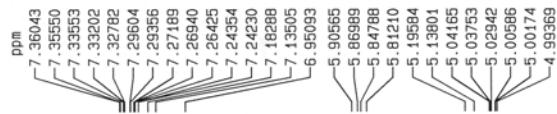


39c

ppm

180 160 140 120 100 80 60 40 20

2nd cyclization



ppm

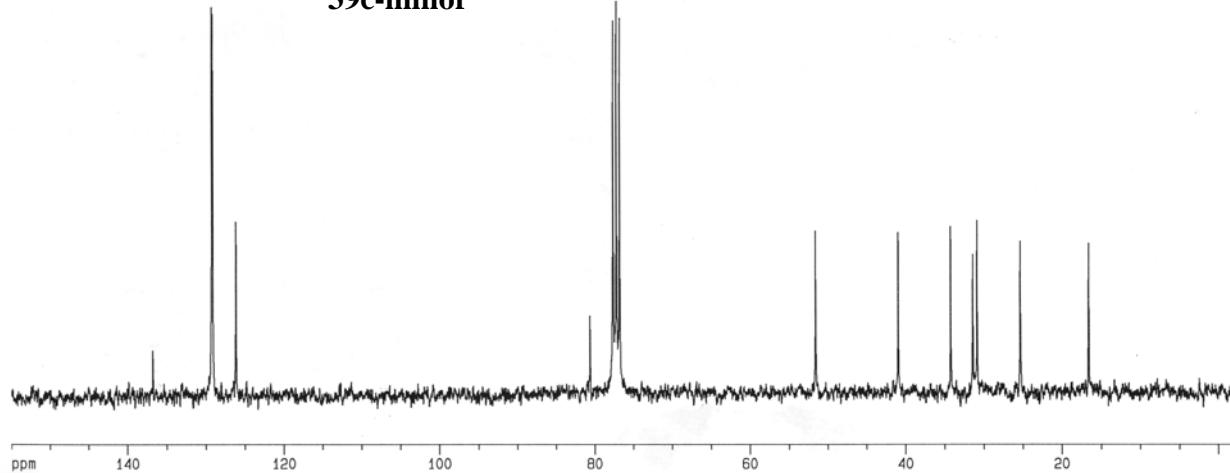
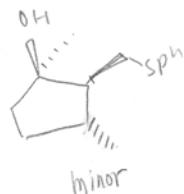
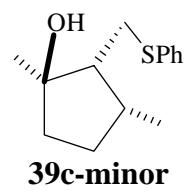
-136.750
-129.212
-128.113
-126.140

80.605
77.621
77.198
76.775

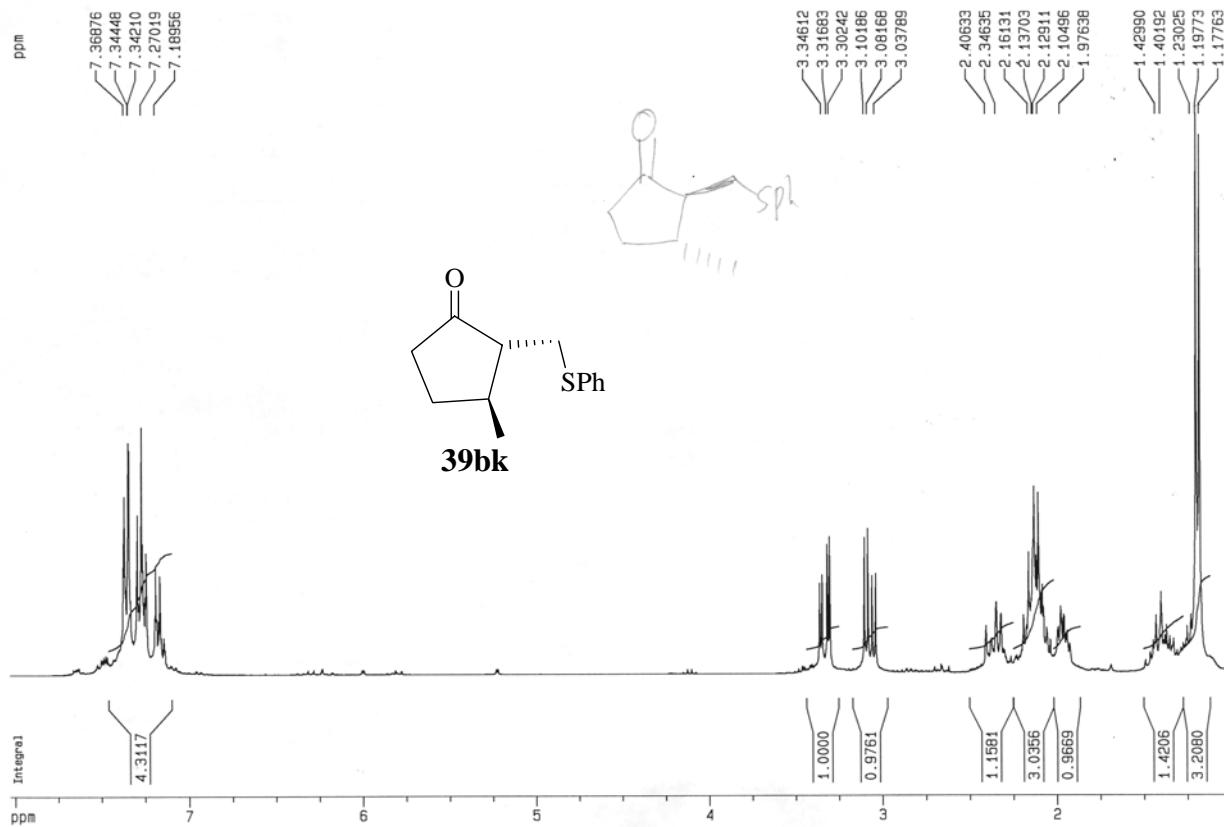
51.563

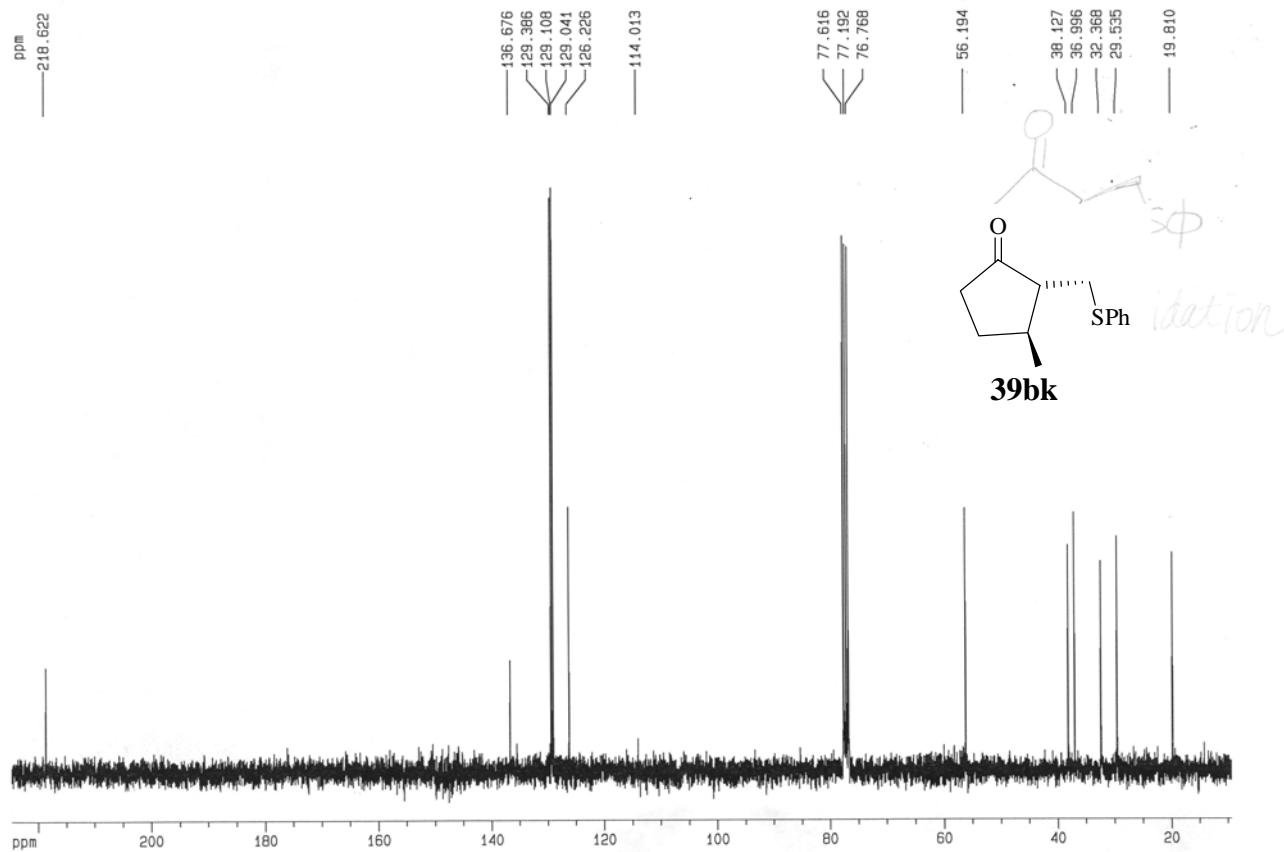
40.927
34.236
31.414
30.876
25.348

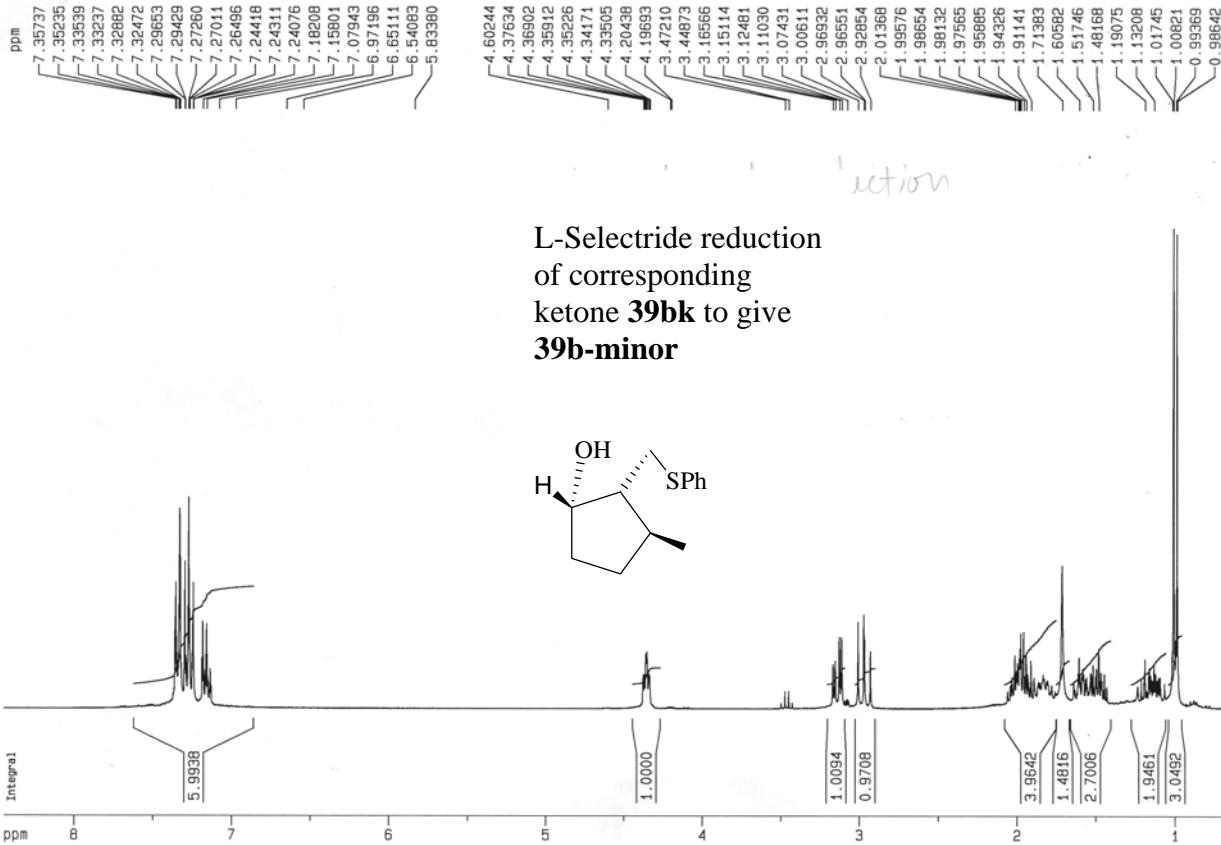
16.585

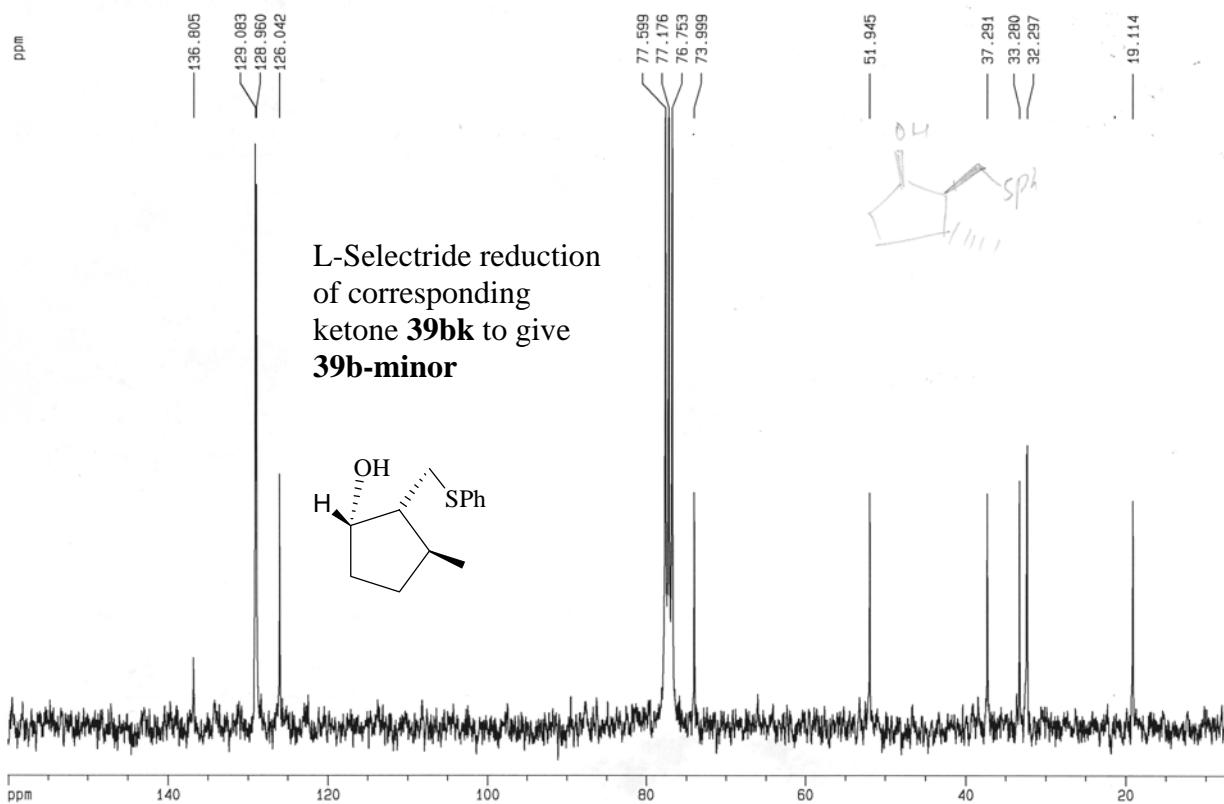


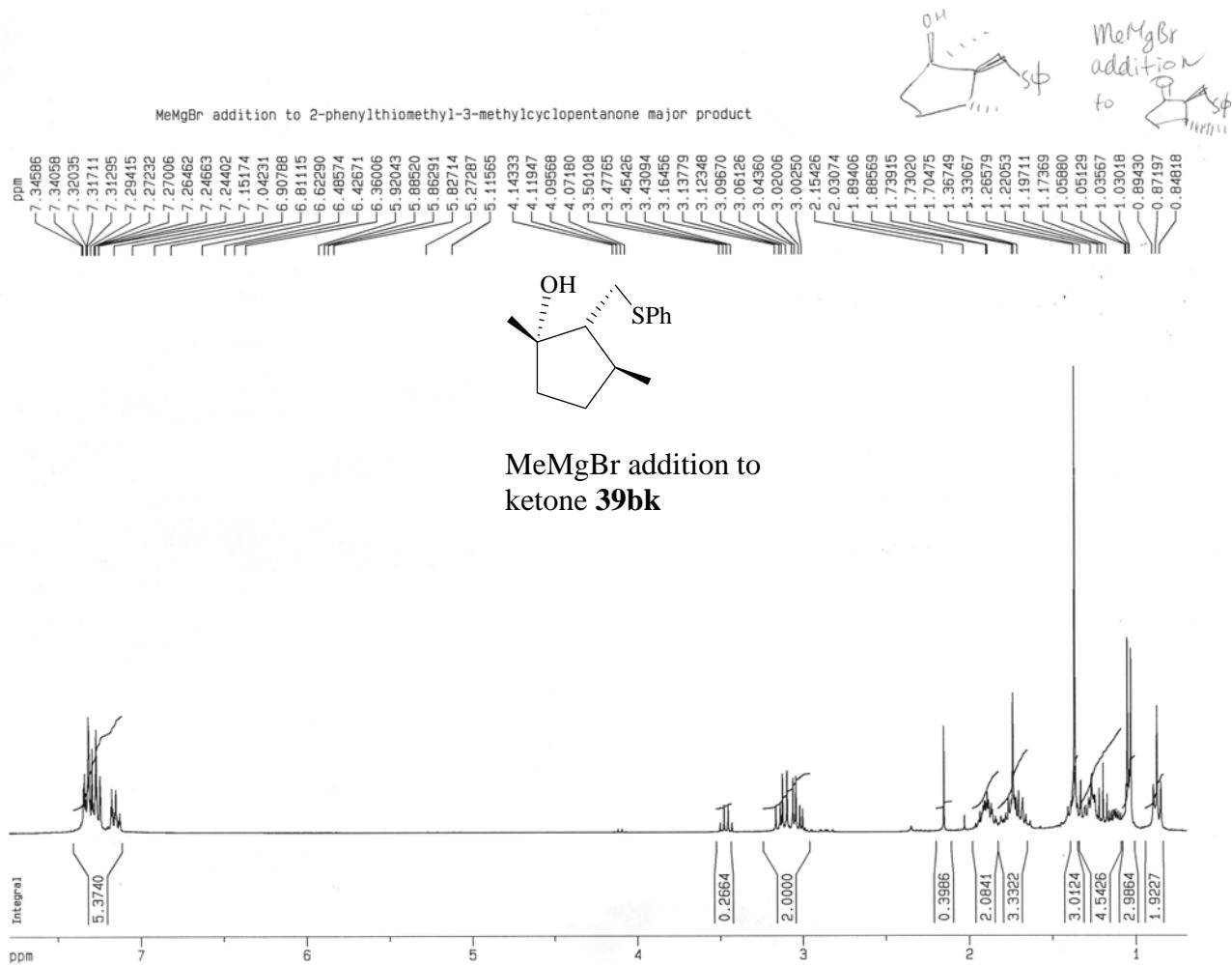
2-phenylthio-3-methylcyclopentanone

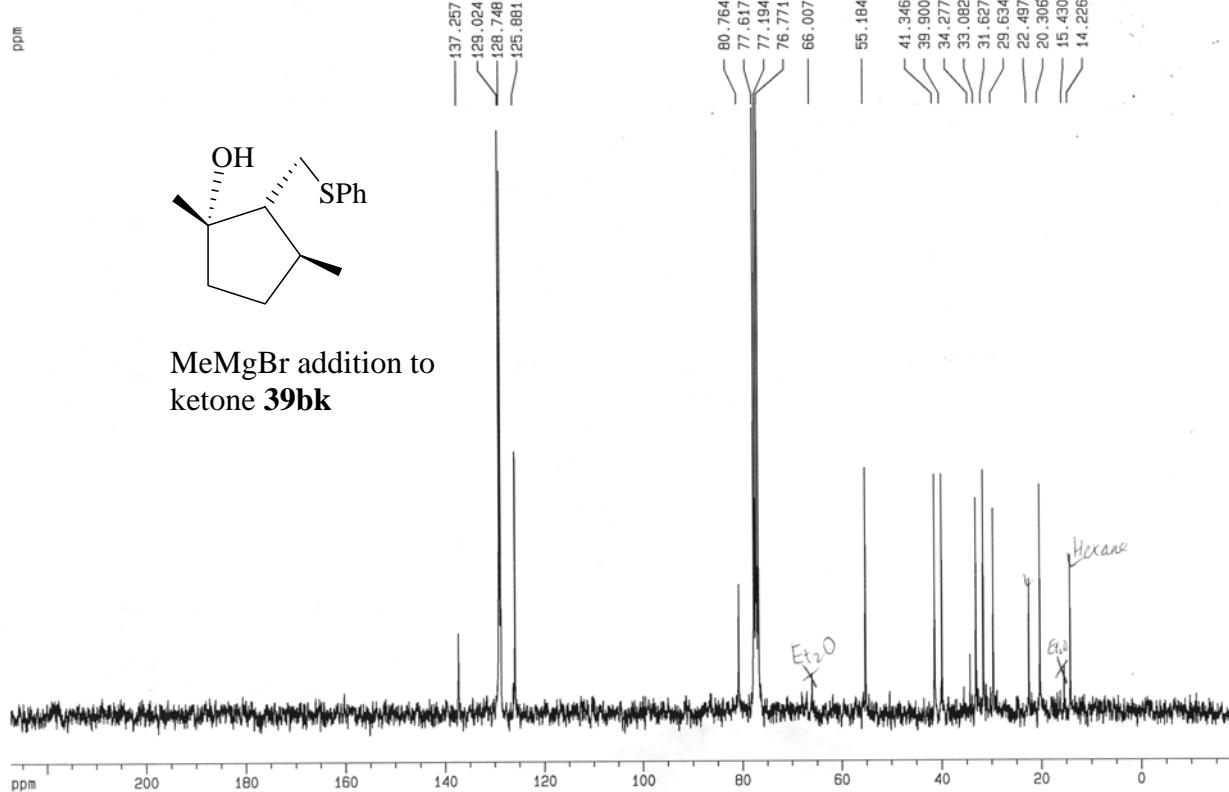


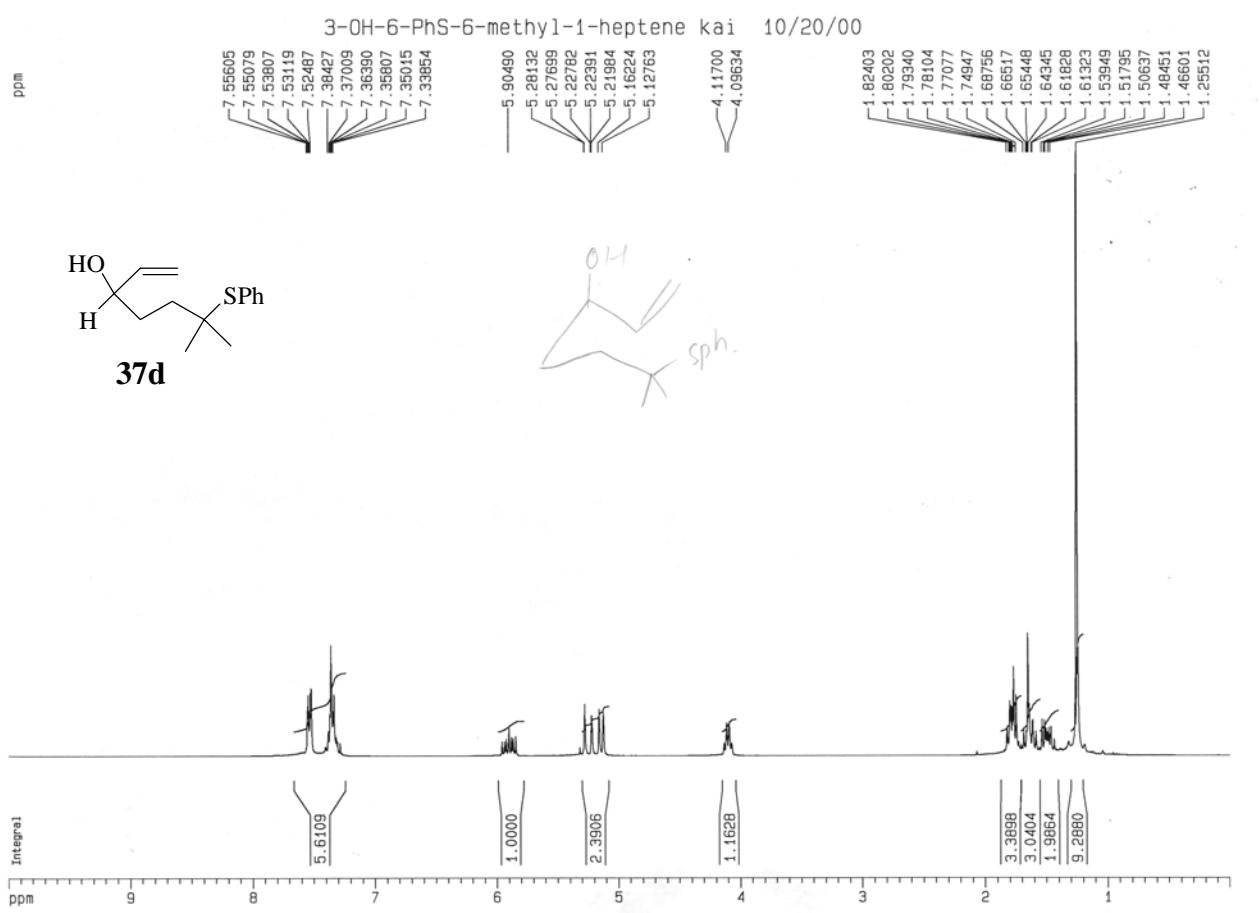




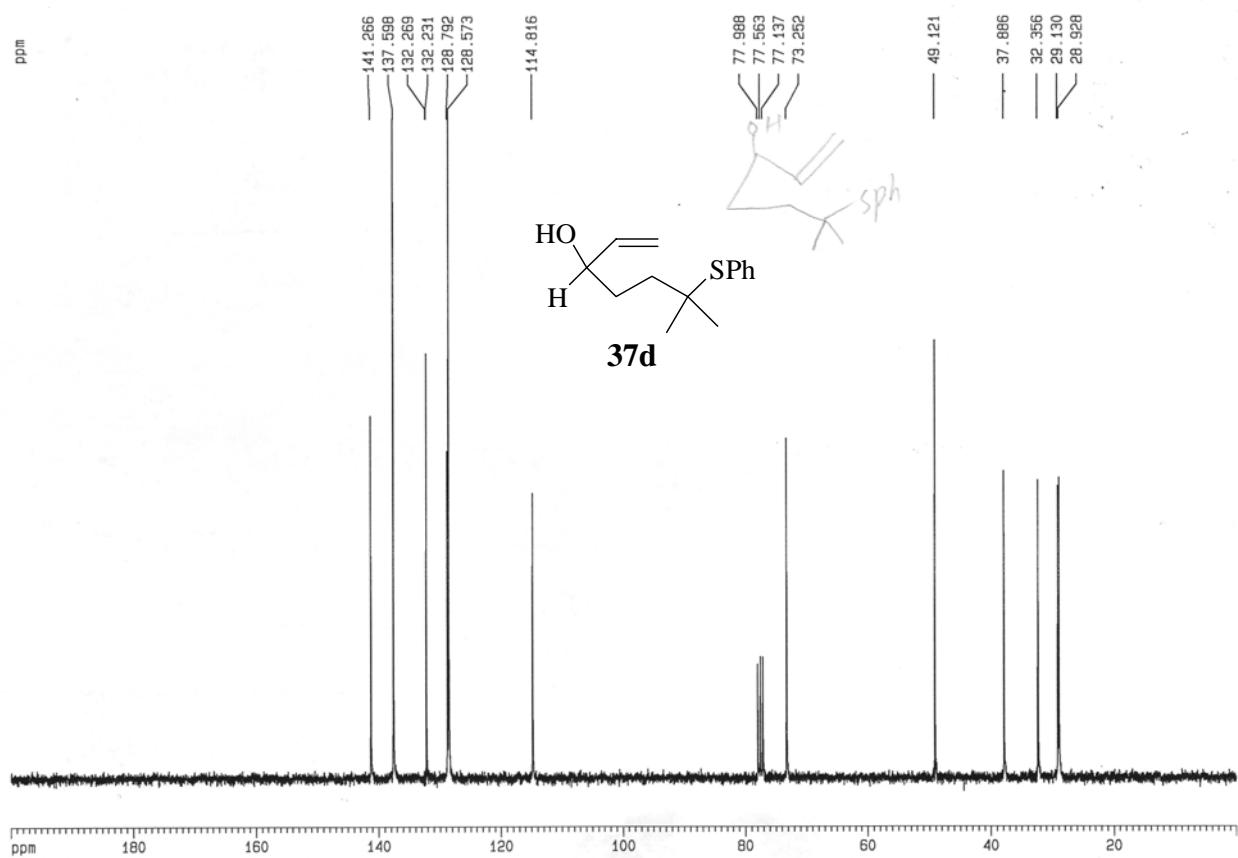


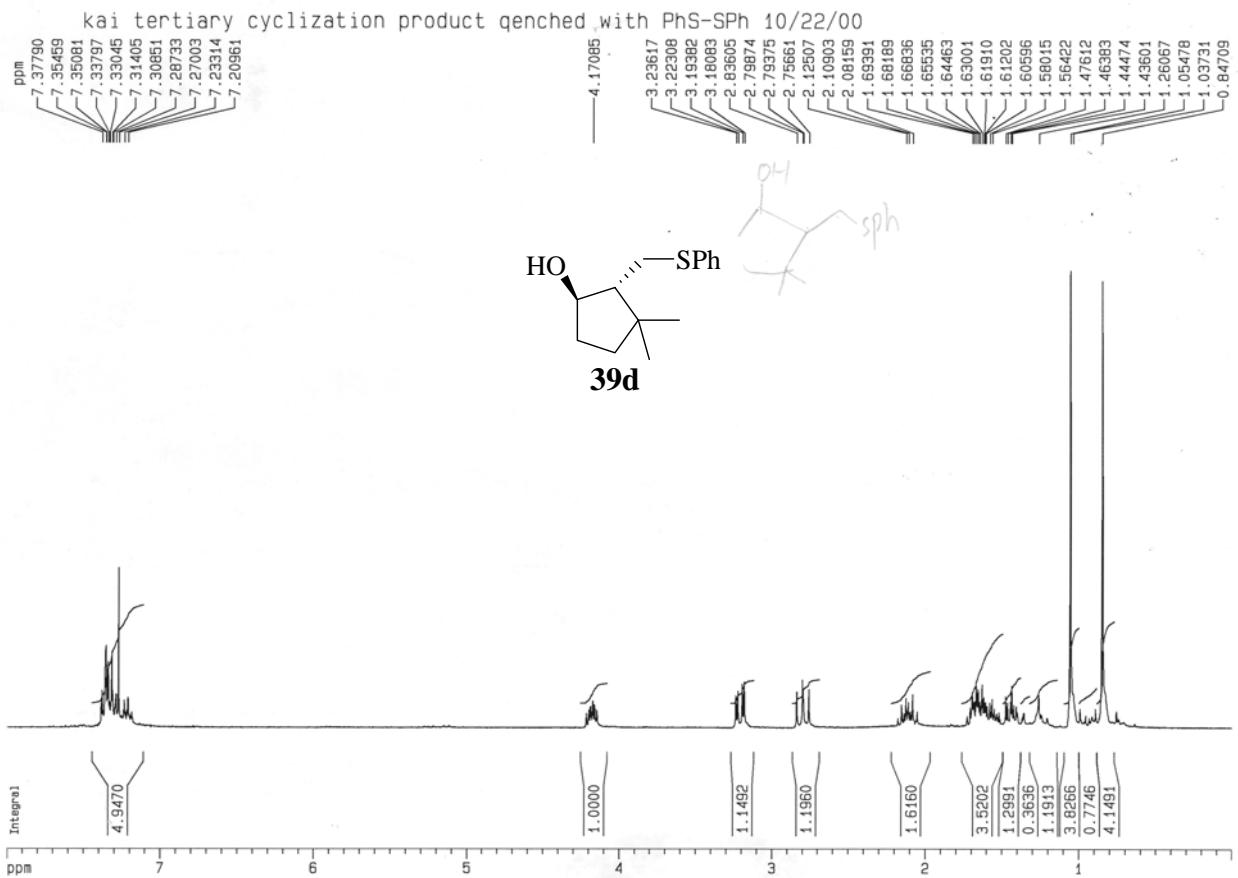






ppm





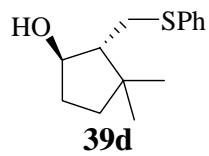
kai-3 3-OH-6-methyl-6-PhS heptene cyclization product 12233

ppm

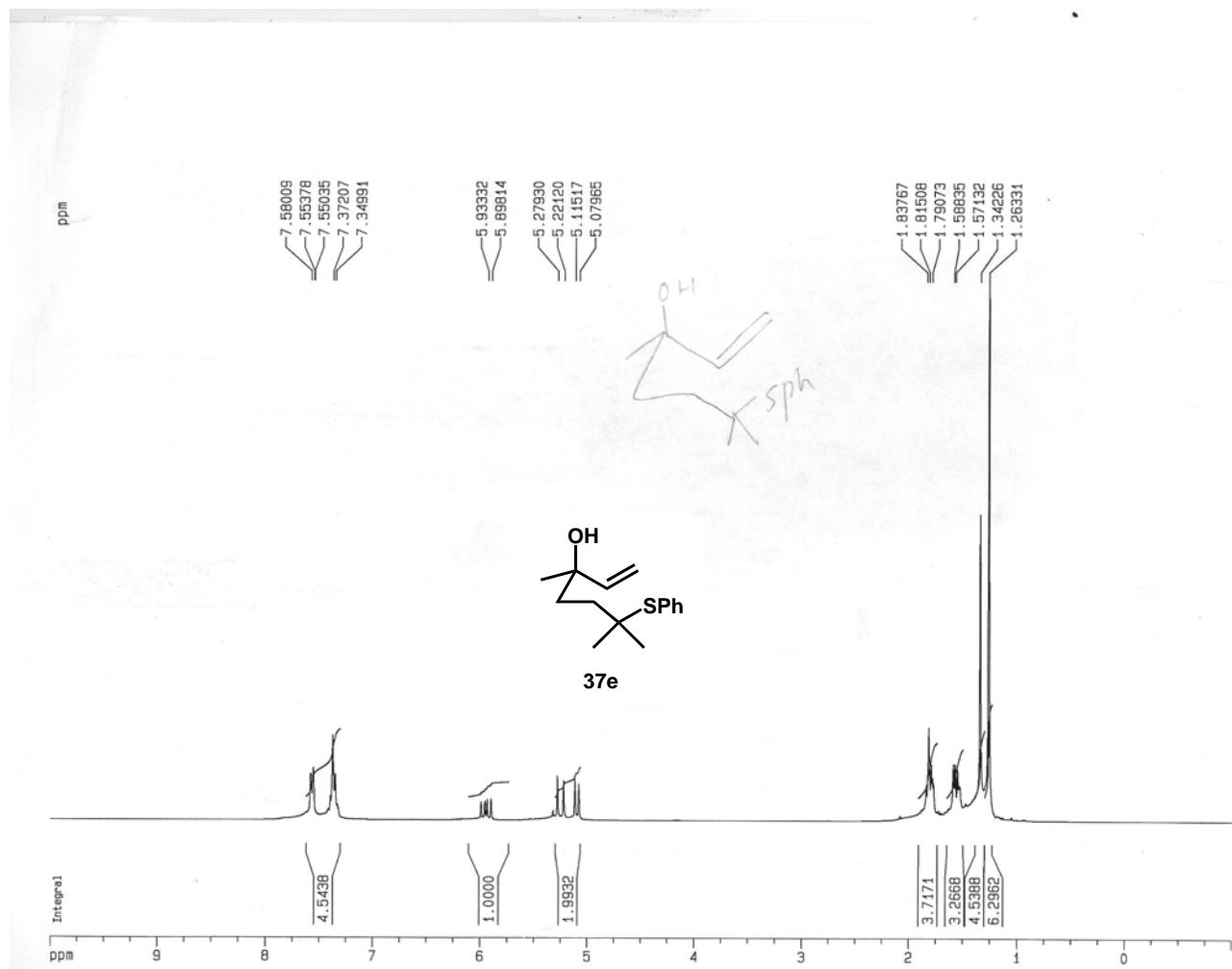
— 136.101
— 129.232
— 126.383

— 79.859
— 77.716
— 77.291
— 76.866

— 56.178
— 41.621
— 39.287
— 34.019
— 31.603
— 29.041
— 28.968
— 23.106



180 160 140 120 100 80 60 40 20



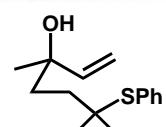
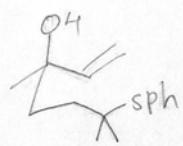
ppm

145.123
145.075
137.612
132.262
128.790
128.564

112.034

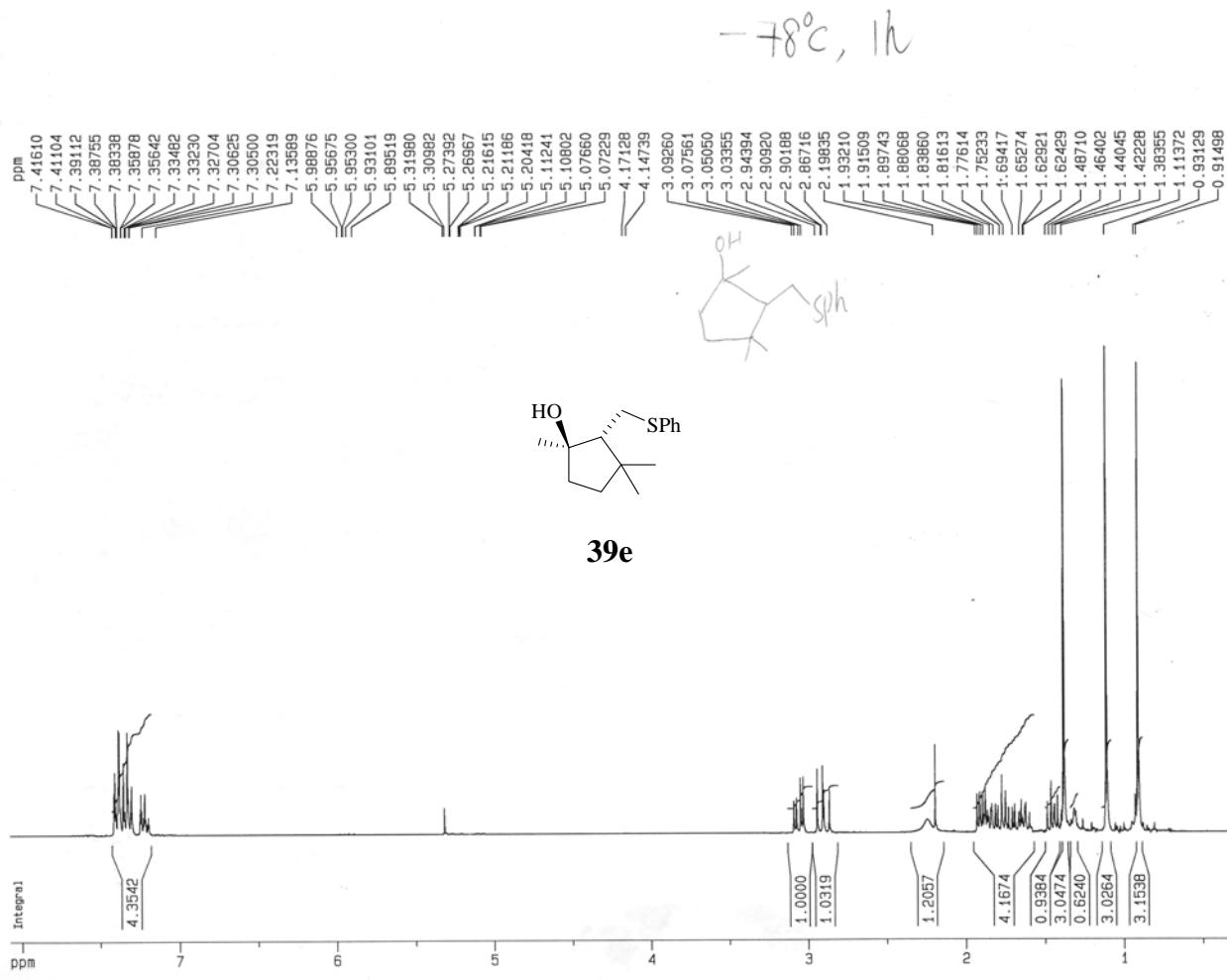
77.686
77.261
76.837
73.227

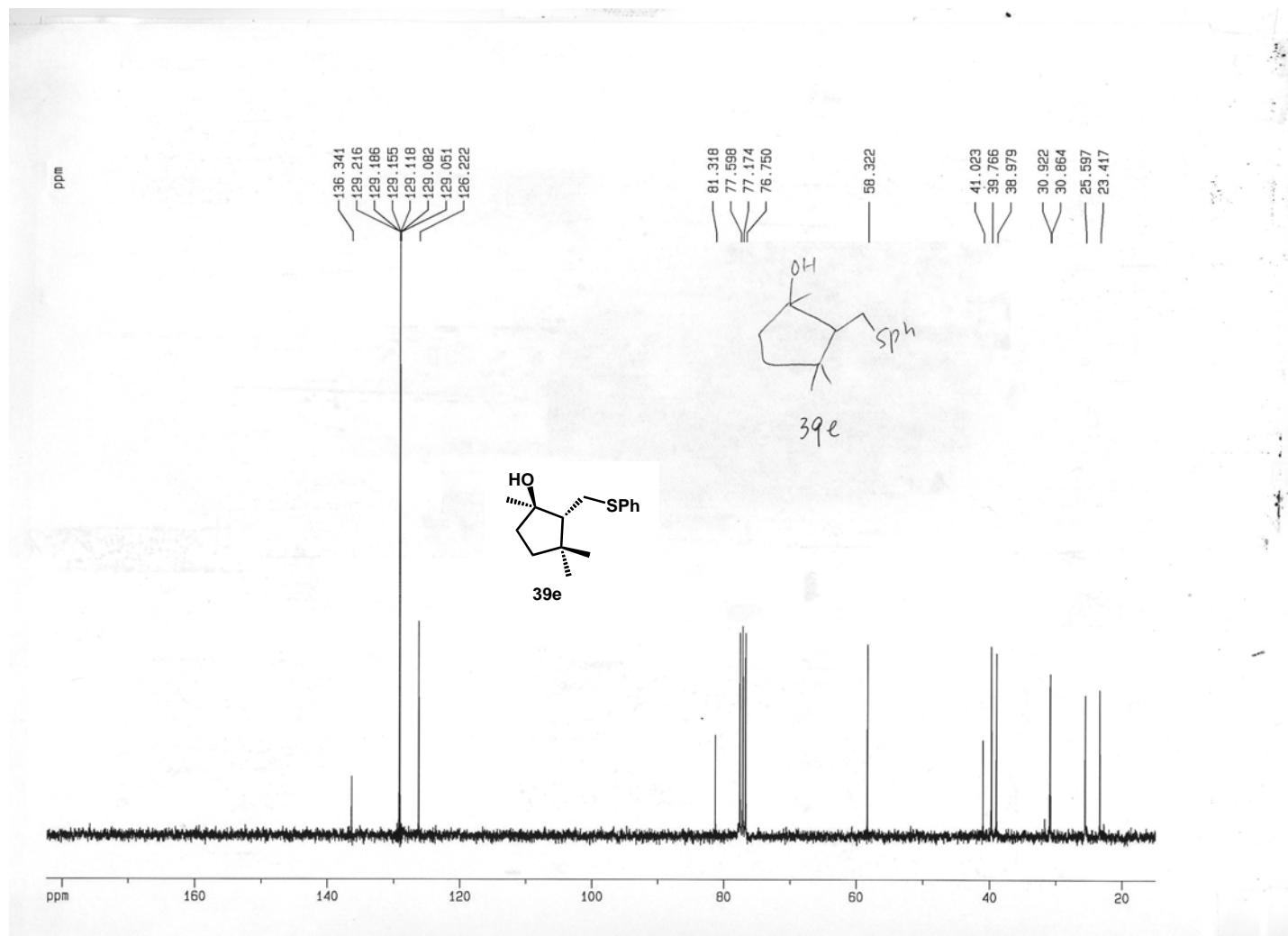
49.086
37.227
36.260
29.144
29.066
28.073

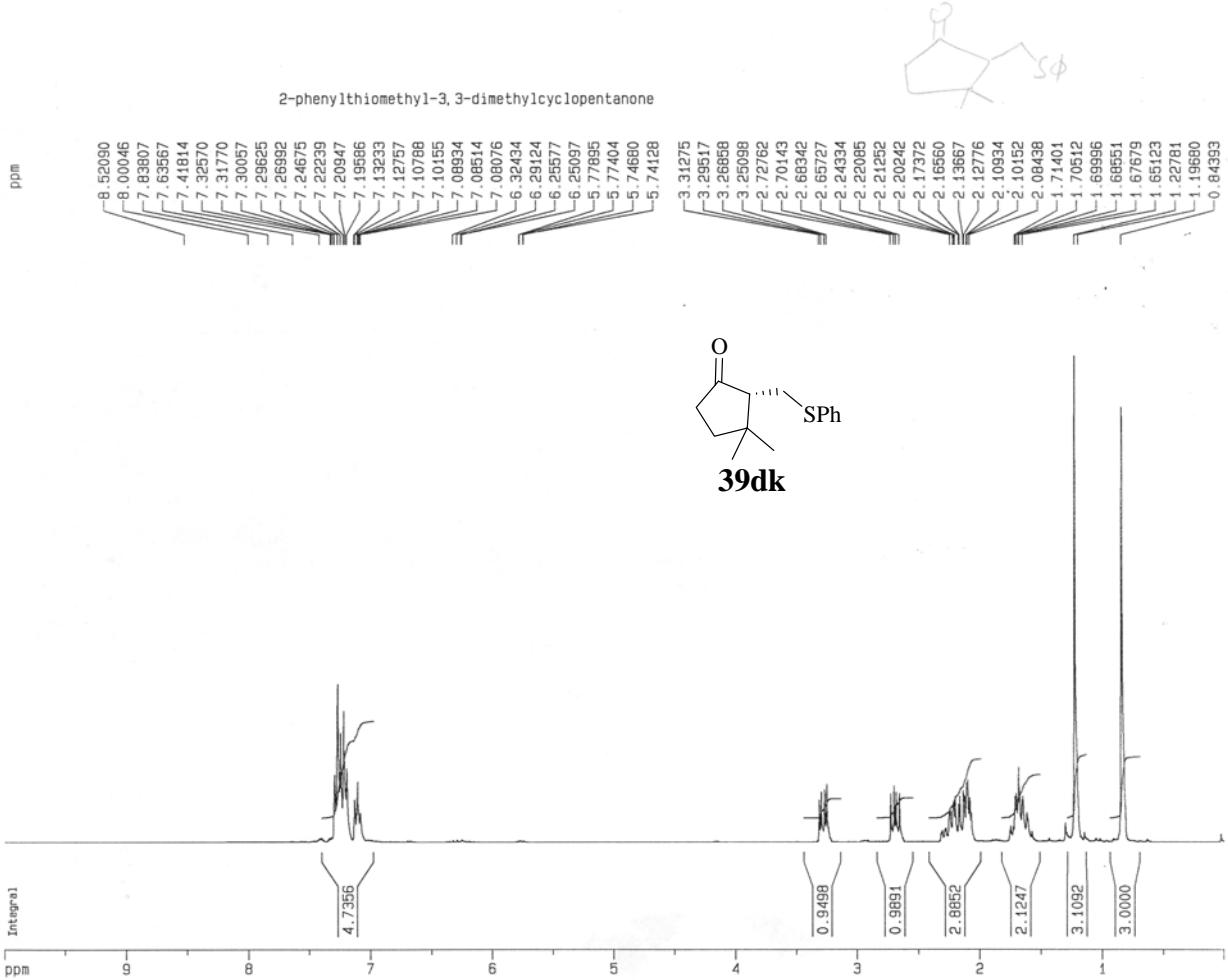


37e

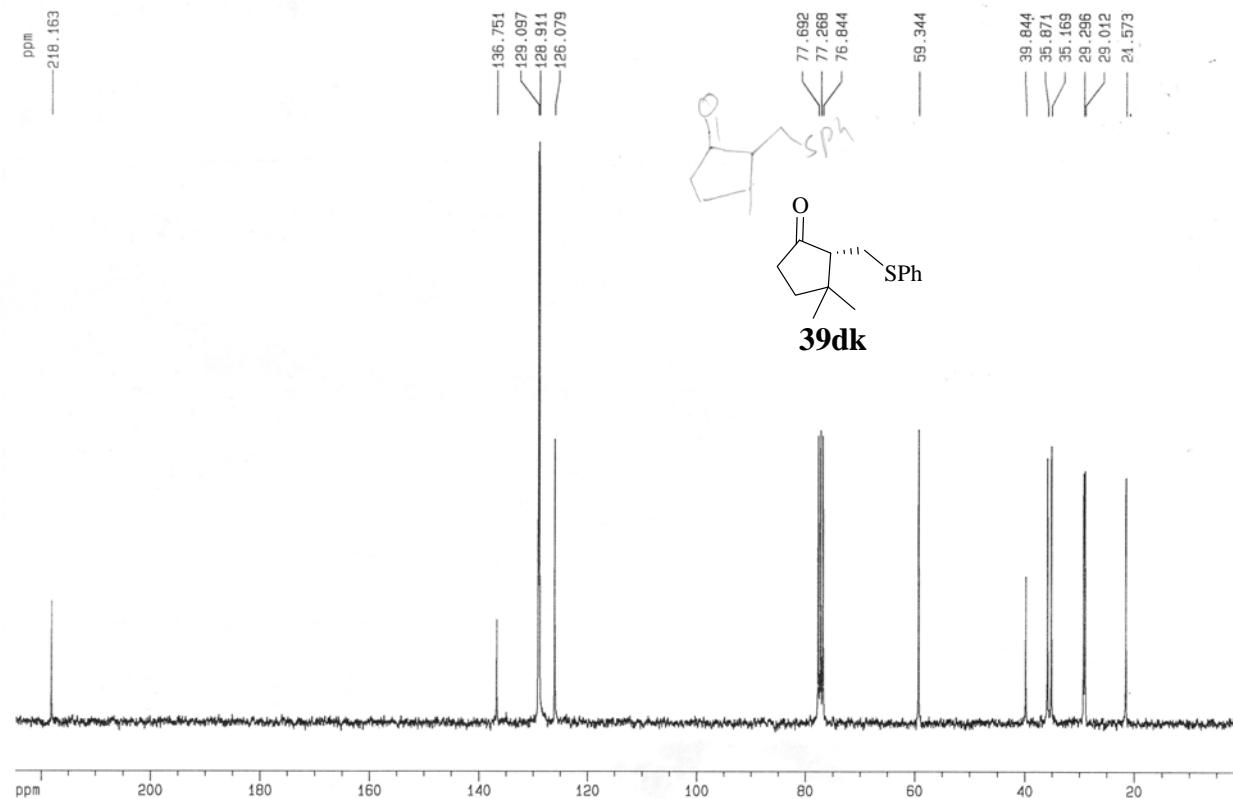
180 160 140 120 100 80 60 40 20



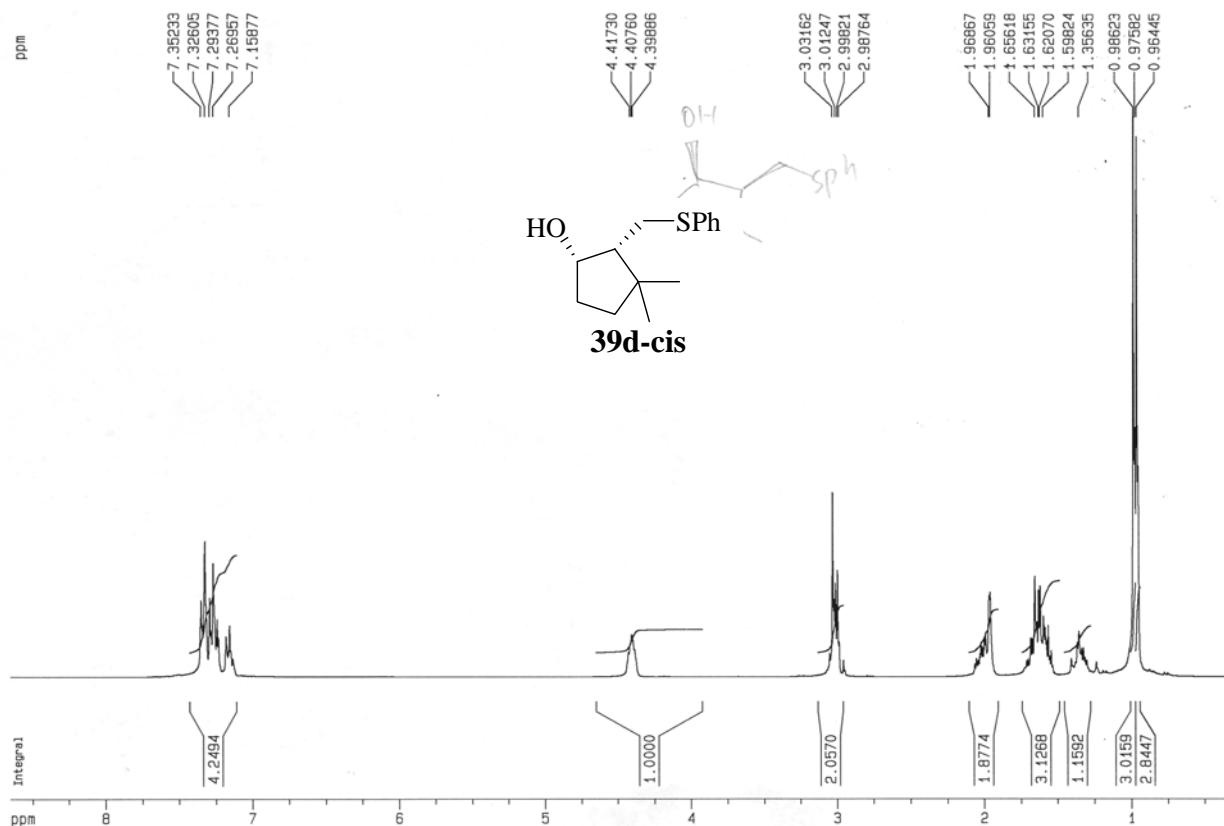


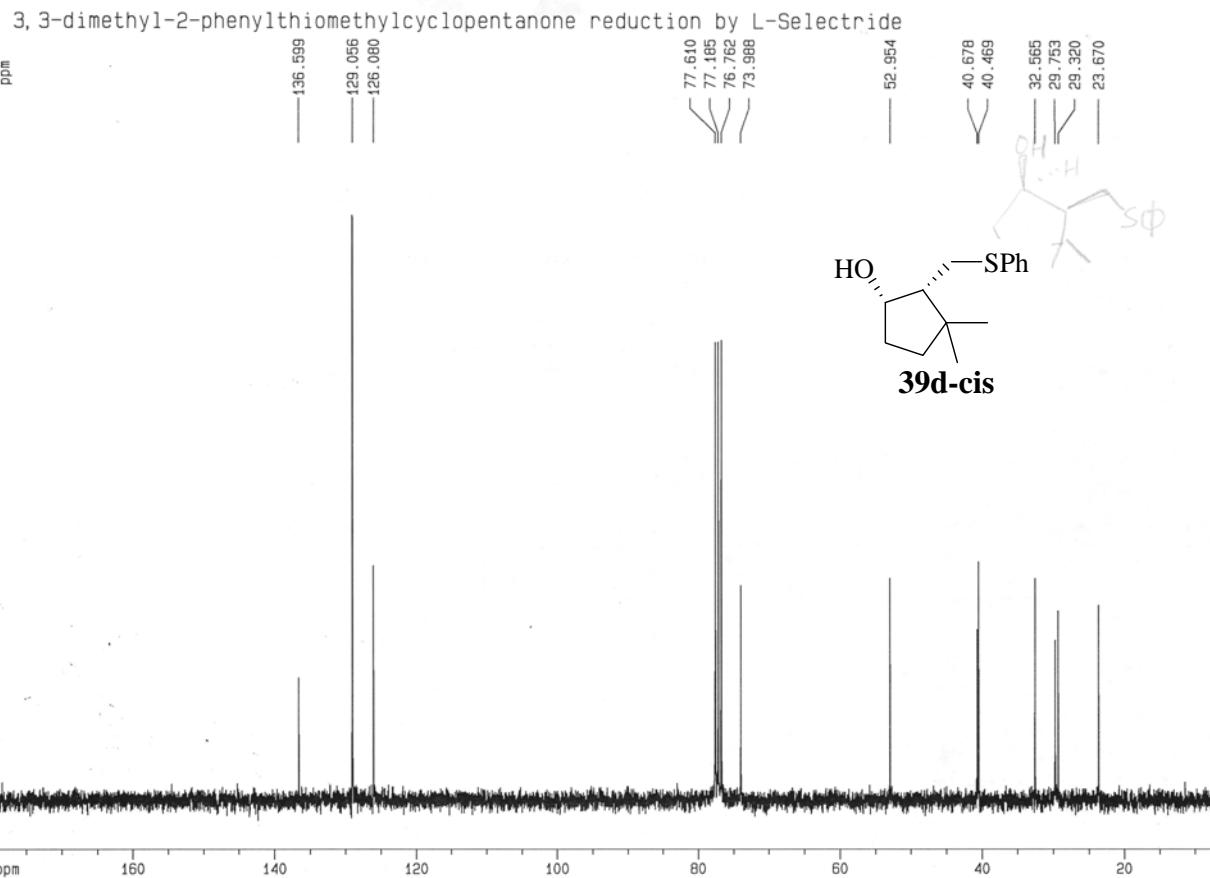


2-phenylthiomethyl-3,3-dimethylcyclopentanone

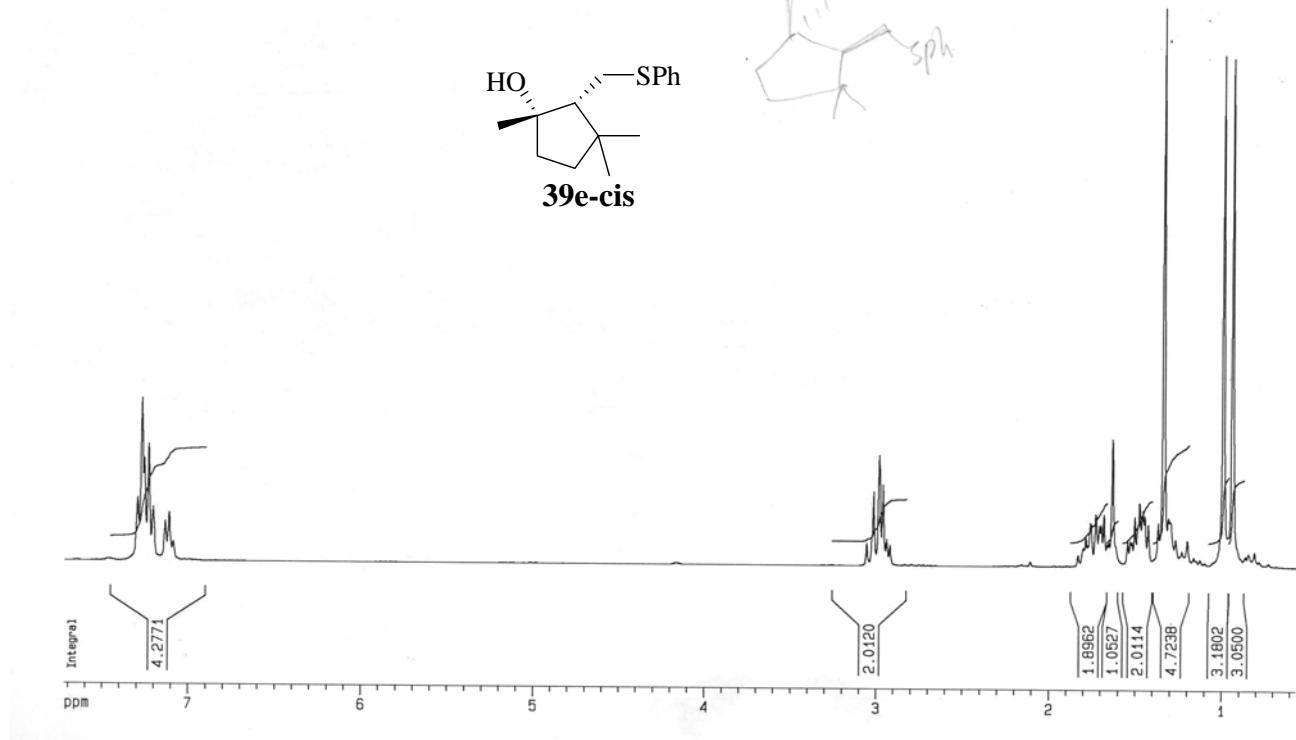
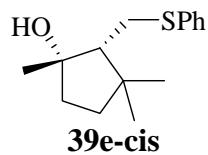


3, 3-dimethyl-2-phenylthiomethylcyclopentanone reduction by L-Selectride



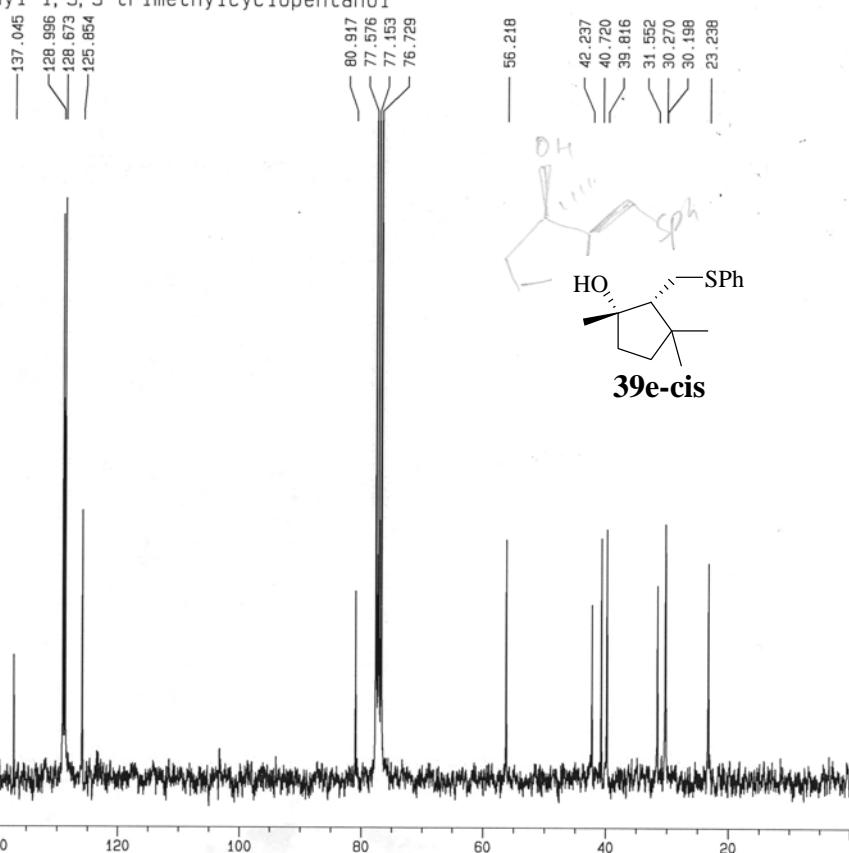


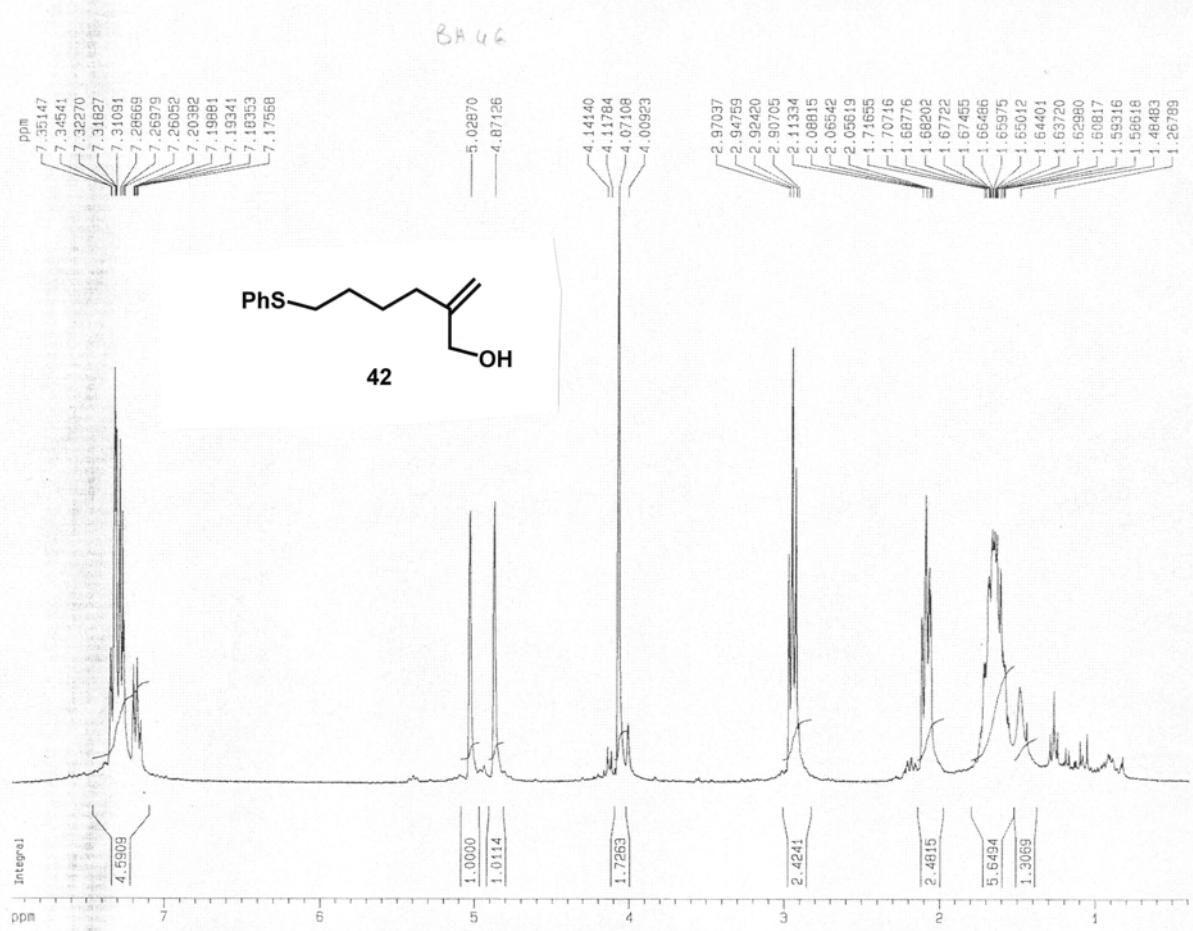
2-phenylthiomethyl-1, 3, 3-trimethylcyclopentanol

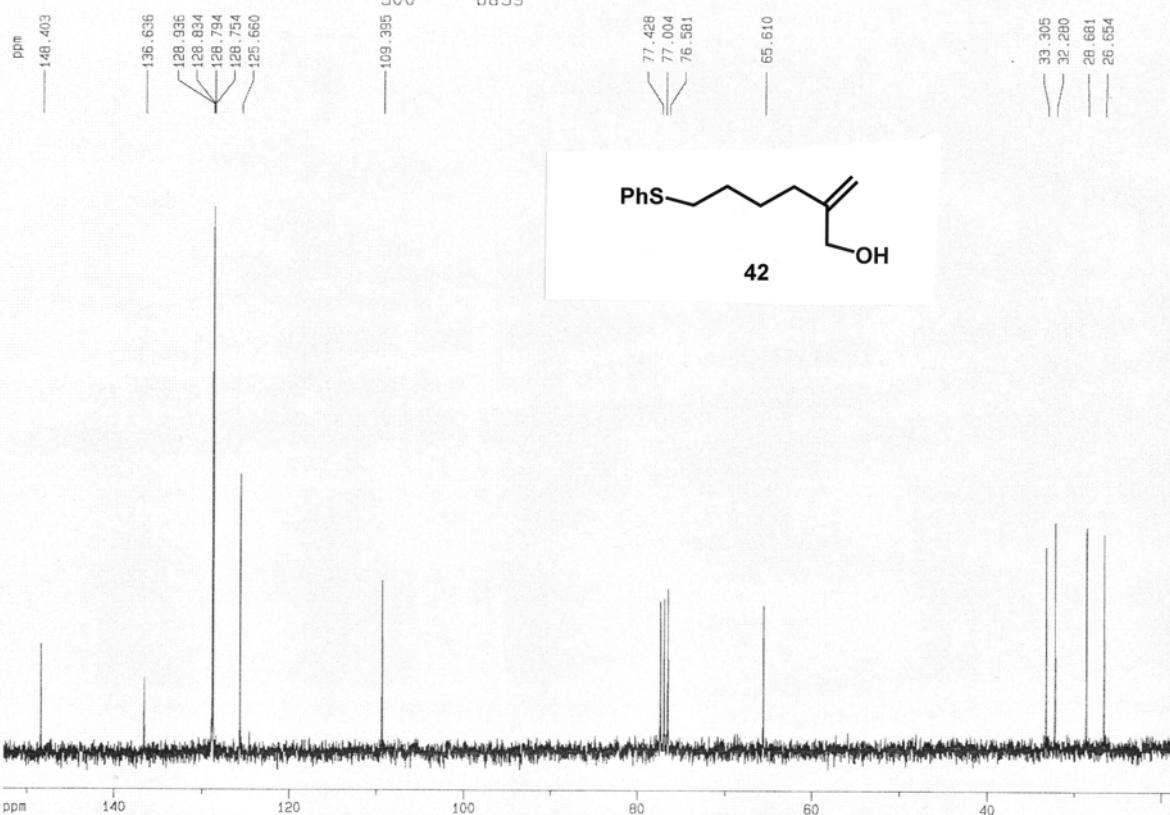


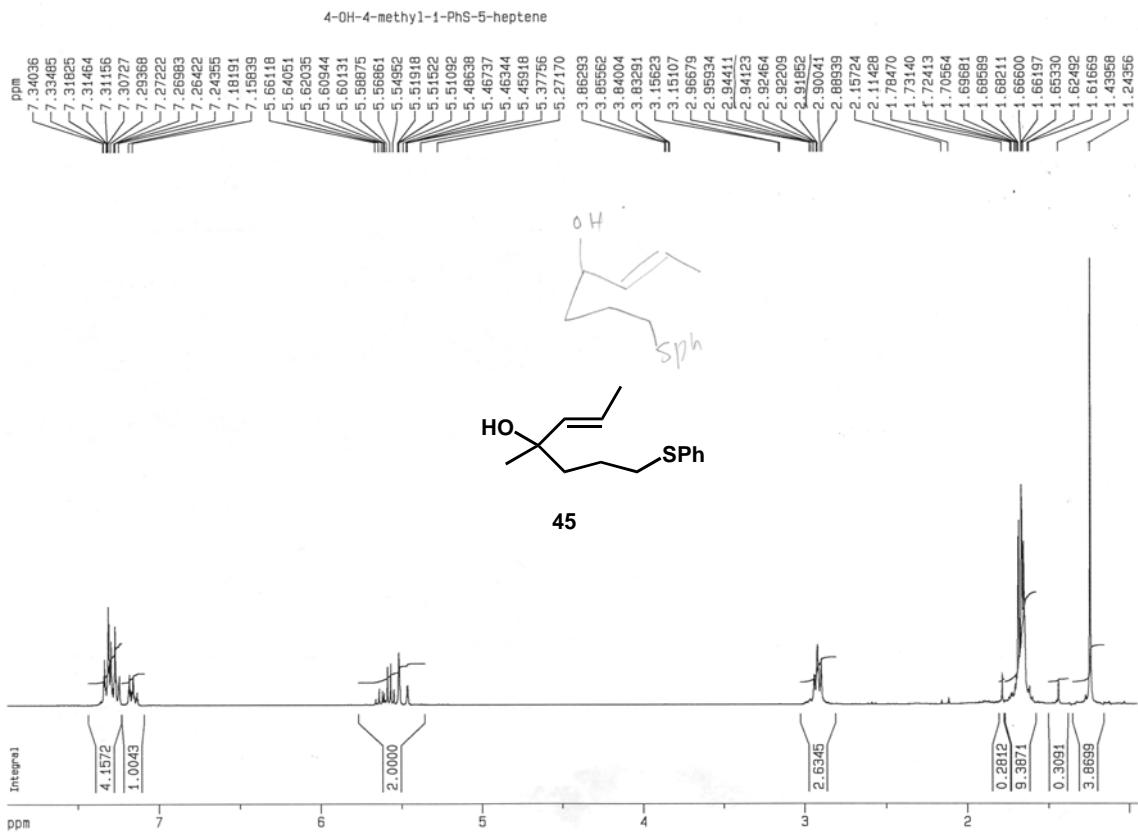
2-phenylthiomethyl-1, 3, 3-trimethylcyclopentanol

ppm

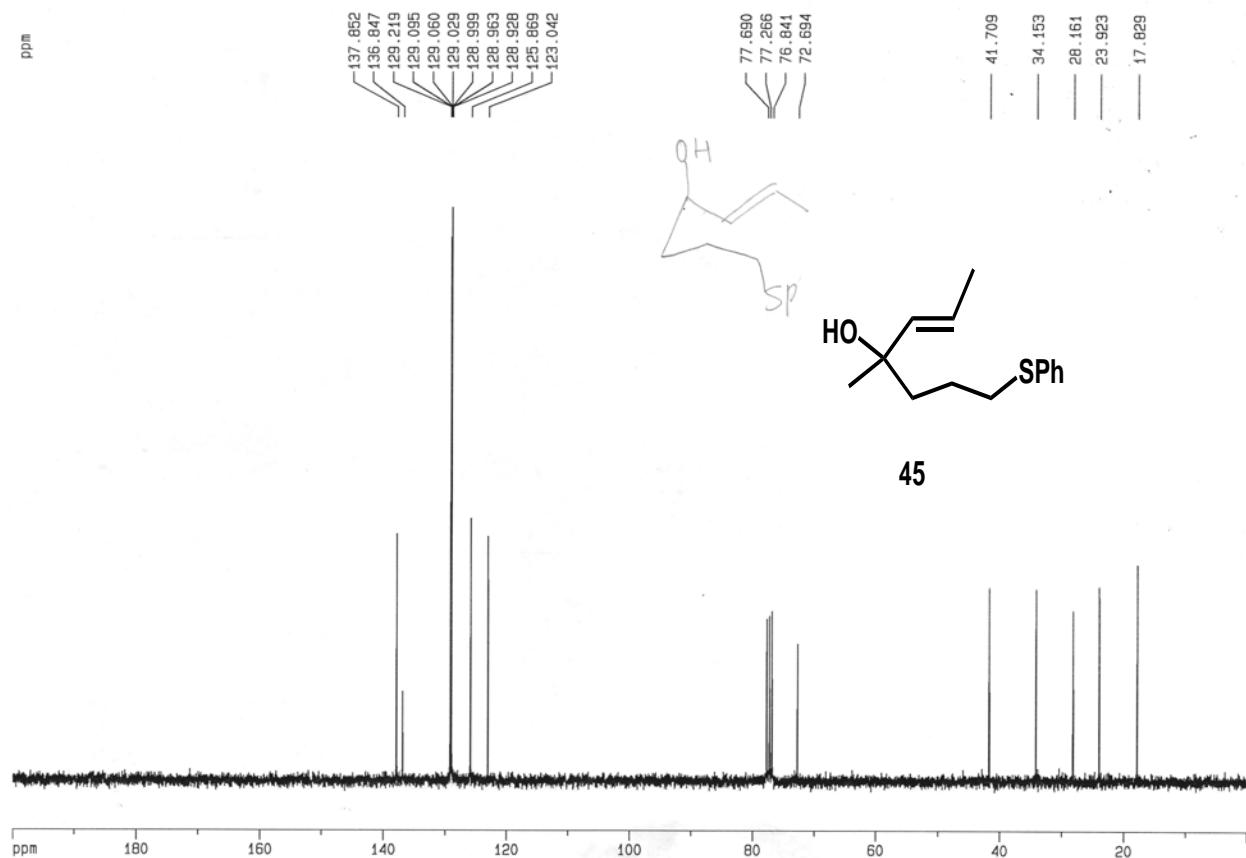




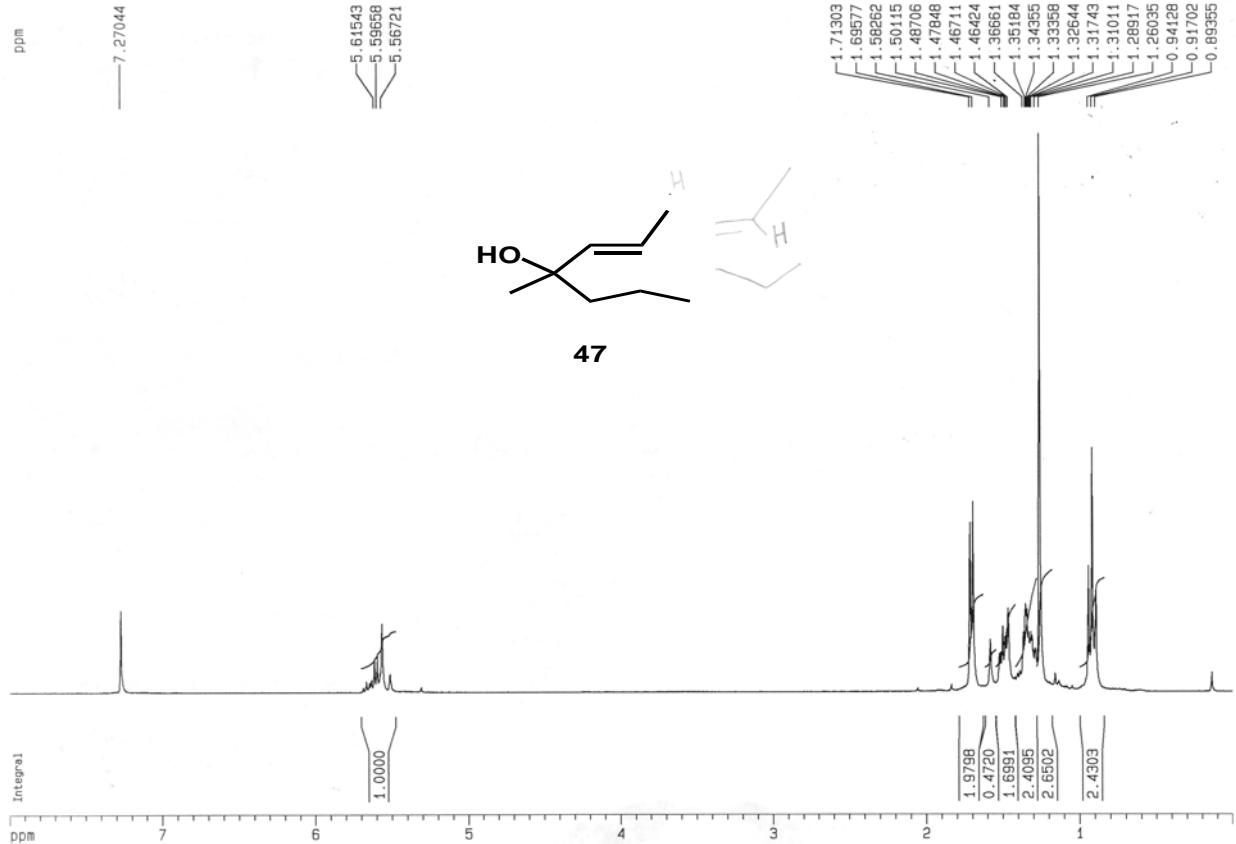


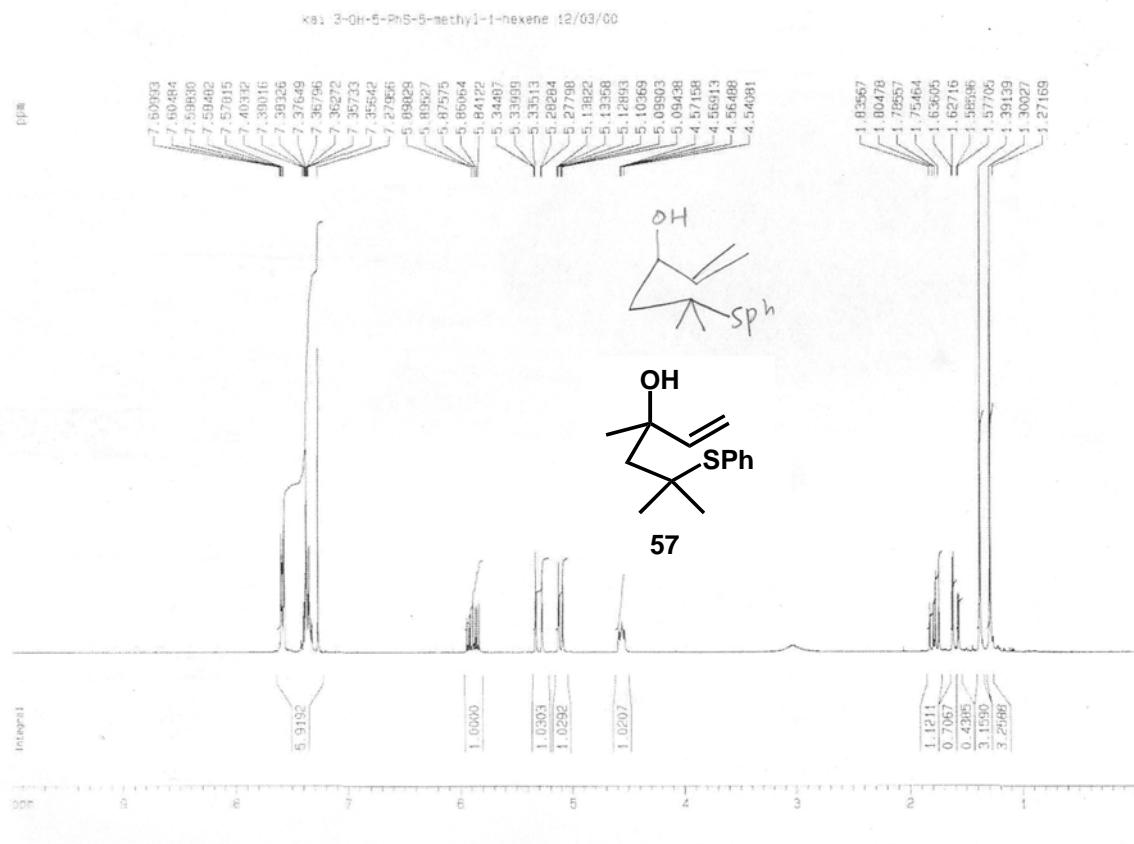


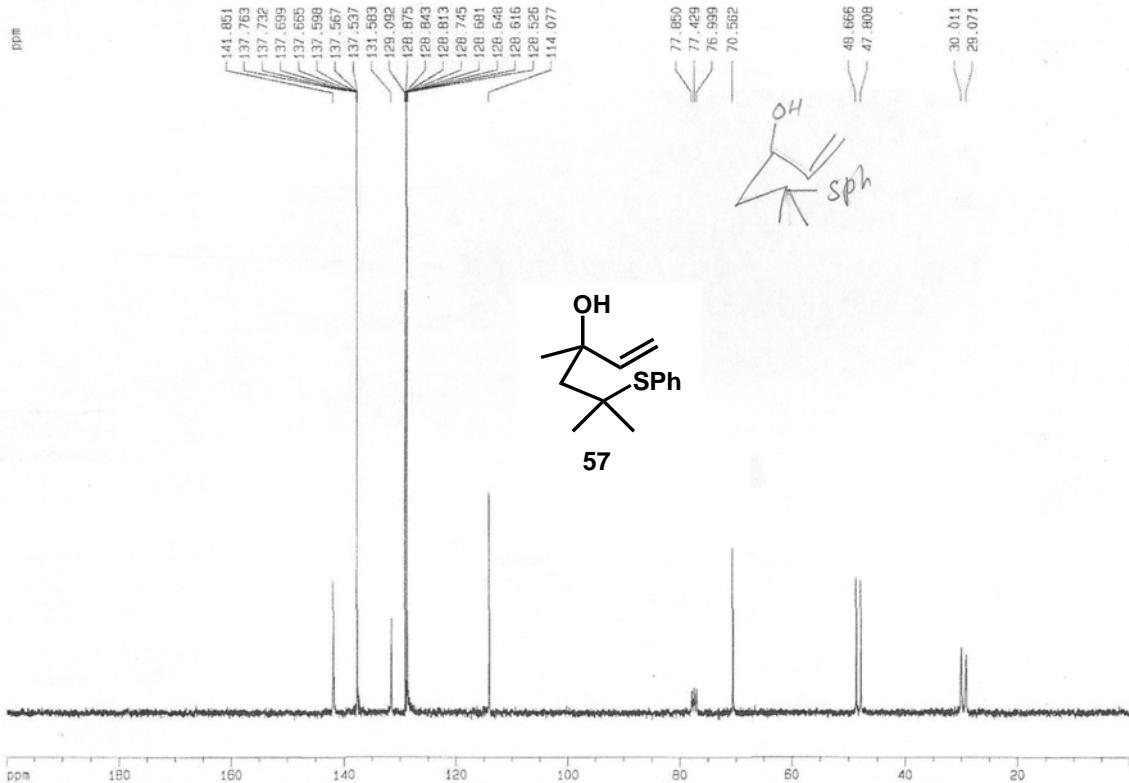
ppm

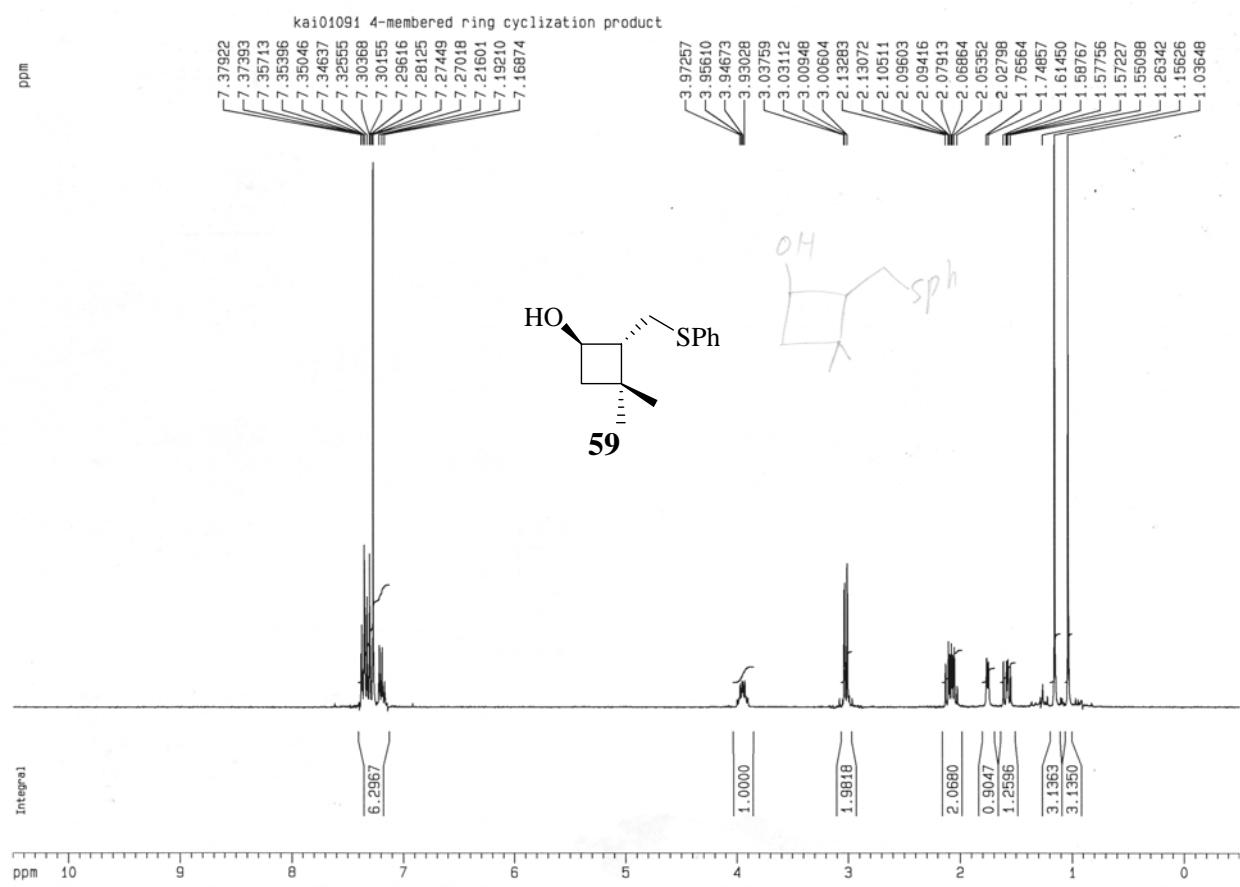


Kai 08/15/00 terminal cyclized product quenched with water

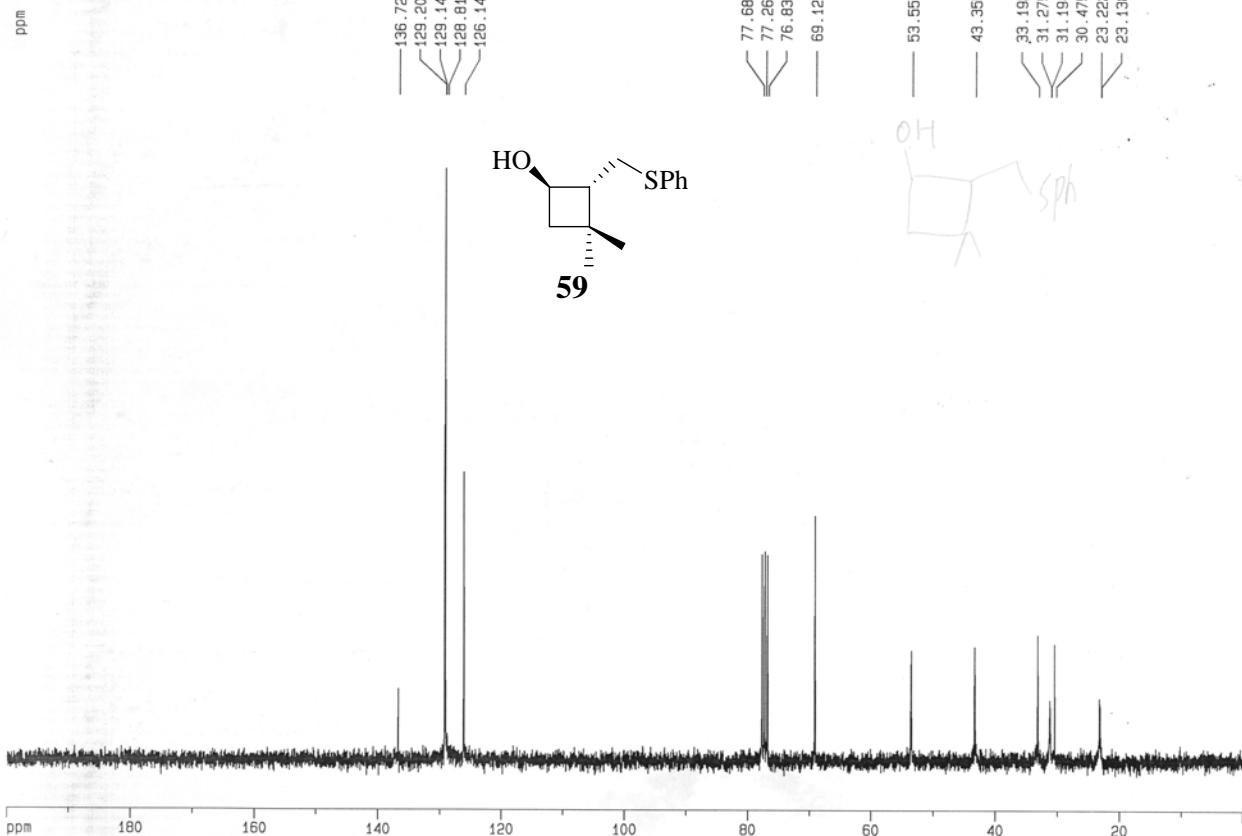




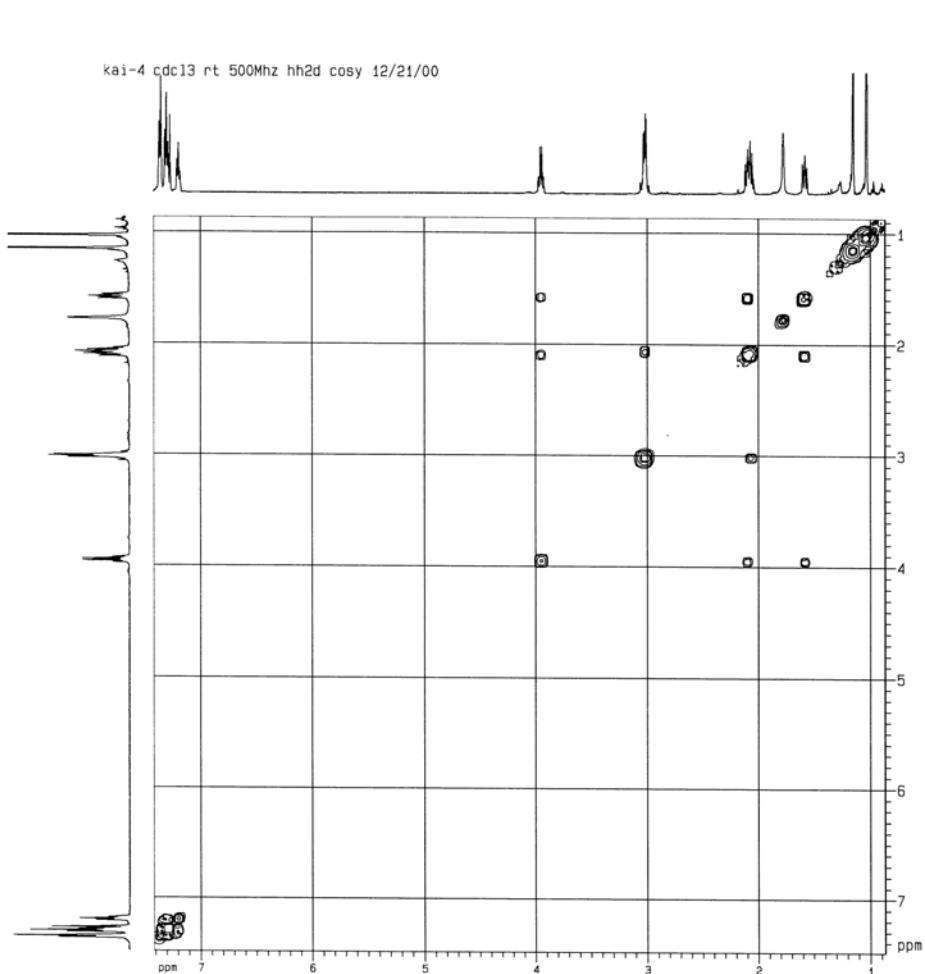
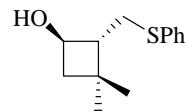




kai-4 3-OH-5-PhS-5-methyl-1-hexene cyclization 12234



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
 PROBODIM 5 mm T1/T2
 PULPROG cosy
 TD 1024
 SOLVENT CDCl3
 NS 8
 DS 16
 SWH 4496.403 Hz
 FIDRES 4.361019 Hz
 AQ 0.1136169 sec
 R6 90.5
 DW 111.200 usec
 DE 4.00 usec
 T6 200
 D6 0.0000030 sec
 D1 1.0000000 sec
 P1 9.70 usec
 P0 9.70 usec
 D2 6.00 usec
 SF01 500.1320000 MHz
 NUC1 1H
 PL1 0.00 dB
 INO 0.00022240 sec

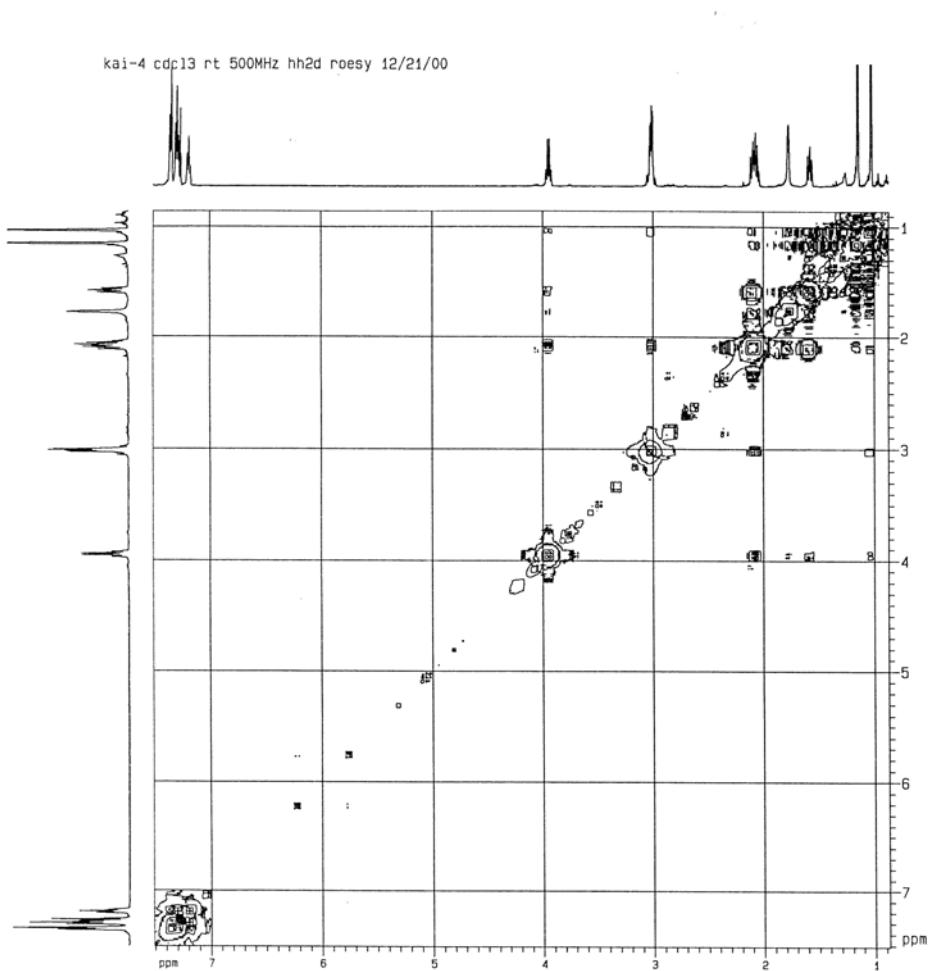
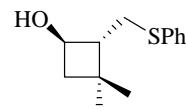
F1 - Acquisition parameters
 N00 TD 114
 SF01 500.1320000 MHz
 FIDRES 39.442065 Hz
 SW 8.990 ppm

F2 - Processing parameters
 S1 512
 SF 500.1300074 MHz
 MW SINE
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 S1 512
 MC2 64
 SF 500.1300072 MHz
 MW SINE
 SSB 0
 LB 0.00 Hz
 GB 0

2D NMR plot parameters
 CX2 15.00 sec
 CX1 15.00 sec
 F2R0 7.418 ppm
 F2L0 3709.78 Hz
 F2R1 0.868 ppm
 F2L1 434.08 Hz
 F2R2 7.400 ppm
 F2L2 3745.14 Hz
 F1R0 0.868 ppm
 F1R1 434.31 Hz
 F2P0CH 0.43665 ppm/ca
 F2Z0CH 218.37998 Hz/ca
 F1P0CH 0.44133 ppm/ca
 F1Z0CH 220.72151 Hz/ca

The ROESY spectrum of 59



Current Data Parameters

NAME	Kai-4
EXPNO	11110
PROCNO	1

F2 - Acquisition Parameters

TD	500000
Time	8.45
INSTRUM	spec
PROBOD	5 mm TXI 13C
POLPROB	1024
TD	1024
SOLVENT	CDCl3
NS	80
DS	16
SWH	4000.00 Hz
ETRATES	4.300108 Hz
AR	0.115918 sec
RG	90.5
DM	111.200 usec
DE	6.00 usec
TE	299.0 sec
DD	0.000000 sec
dt2	0.0000200 sec
DI	1.0000000 sec
PL1	0.00 dB
P1	9.70 usec
PL11	6.00 dB
P15	2000.00 usec
DE	6.00 usec
SF01	500.132295 MHz
NUC1	1H
IN0	0.0001120 sec

F1 - Acquisition parameters

TD	225
SF01	500.1323 MHz
ETRATES	19.98399 Hz
SW	8.998 ppm

F2 - Processing parameters

SI	1024
SF	500.1300043 MHz
NOM	SINE
SSB	0
LB	0.00 Hz
BB	0
PC	0.10

F1 - Processing parameters

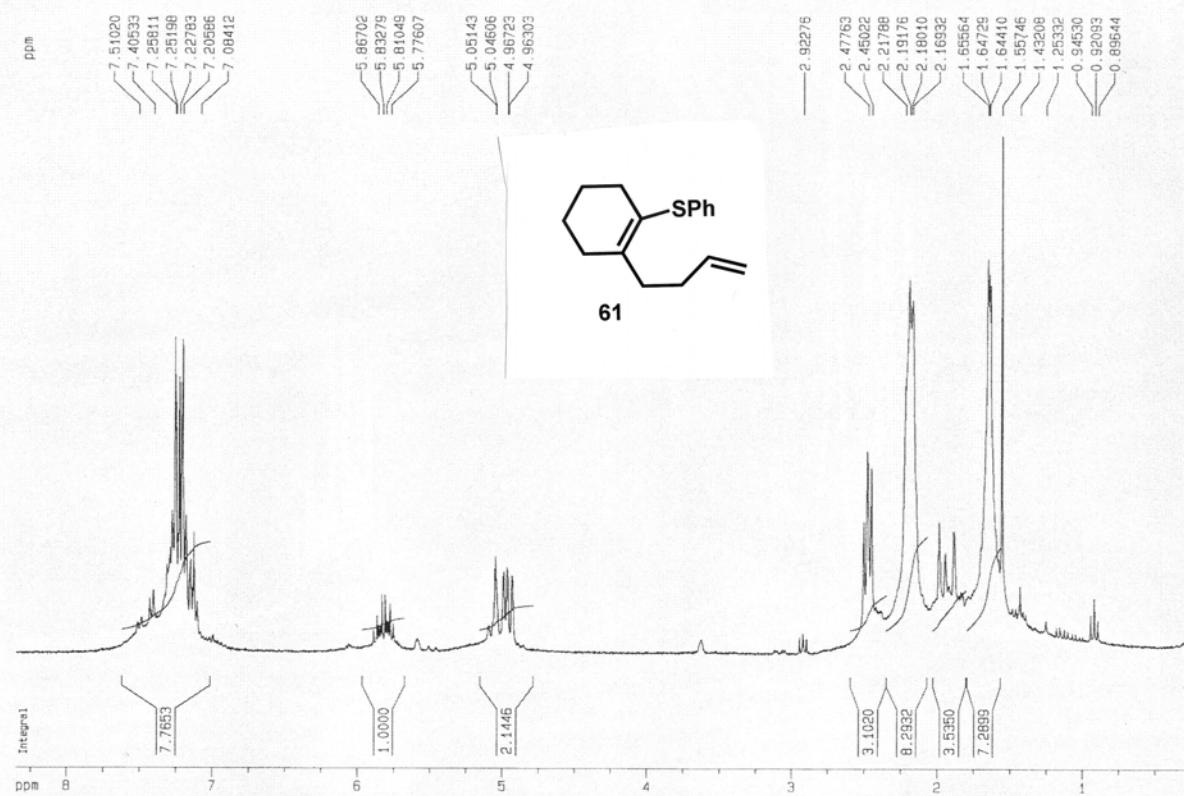
SI	1024
MC2	1024
SF	500.1300042 MHz
NOM	SINE
SSB	0
LB	0.00 Hz
BB	0

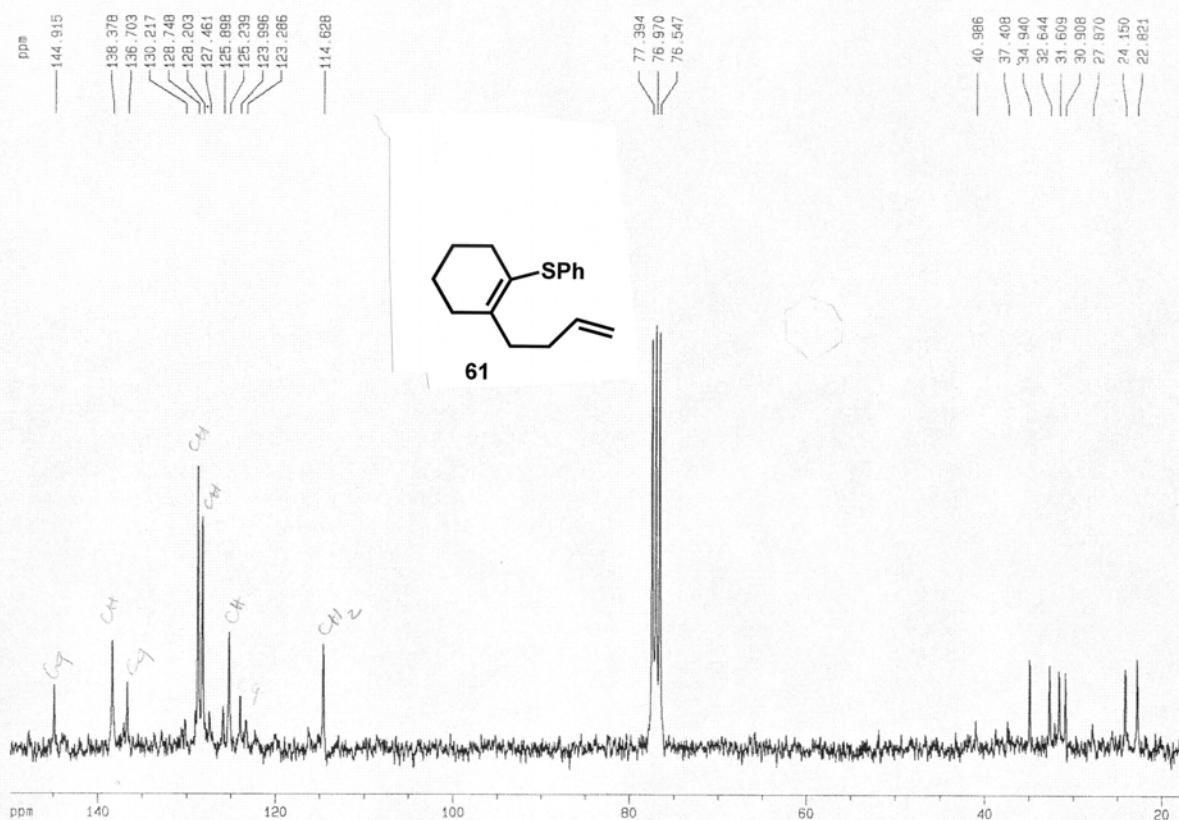
2D NMR plot parameters

CX2	45.00 cm
CX1	15.00 cm
F2PL0	7.512 ppm
F2LO	375.64 Hz
F2PHI	0.874 ppm
F2HI	437.42 Hz
F1PL0	7.512 ppm
F1LO	3755.85 Hz
F1PHI	0.857 ppm
F1HI	428.50 Hz
F2PPHIC	0.44250 ppm/cm
F2CHC	221.44231 Hz/cm
F1PPHIC	0.44267 ppm/cm
F1CHC	221.09246 Hz/cm

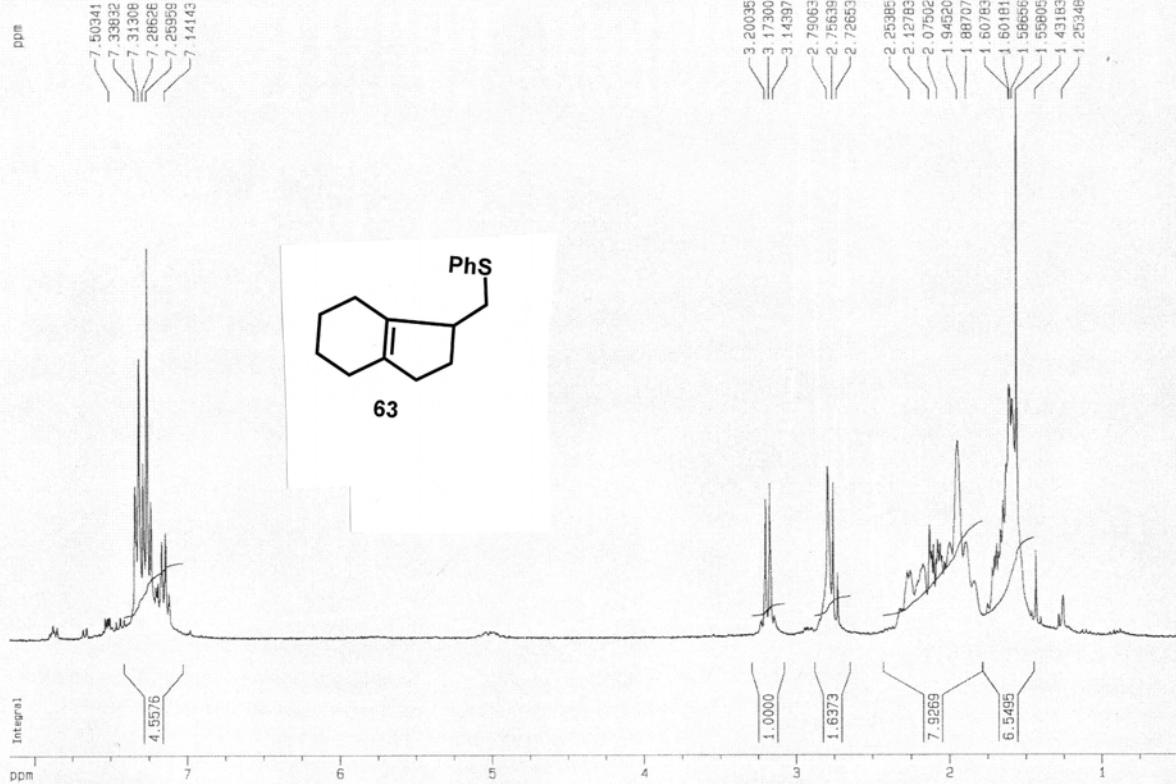
ppm

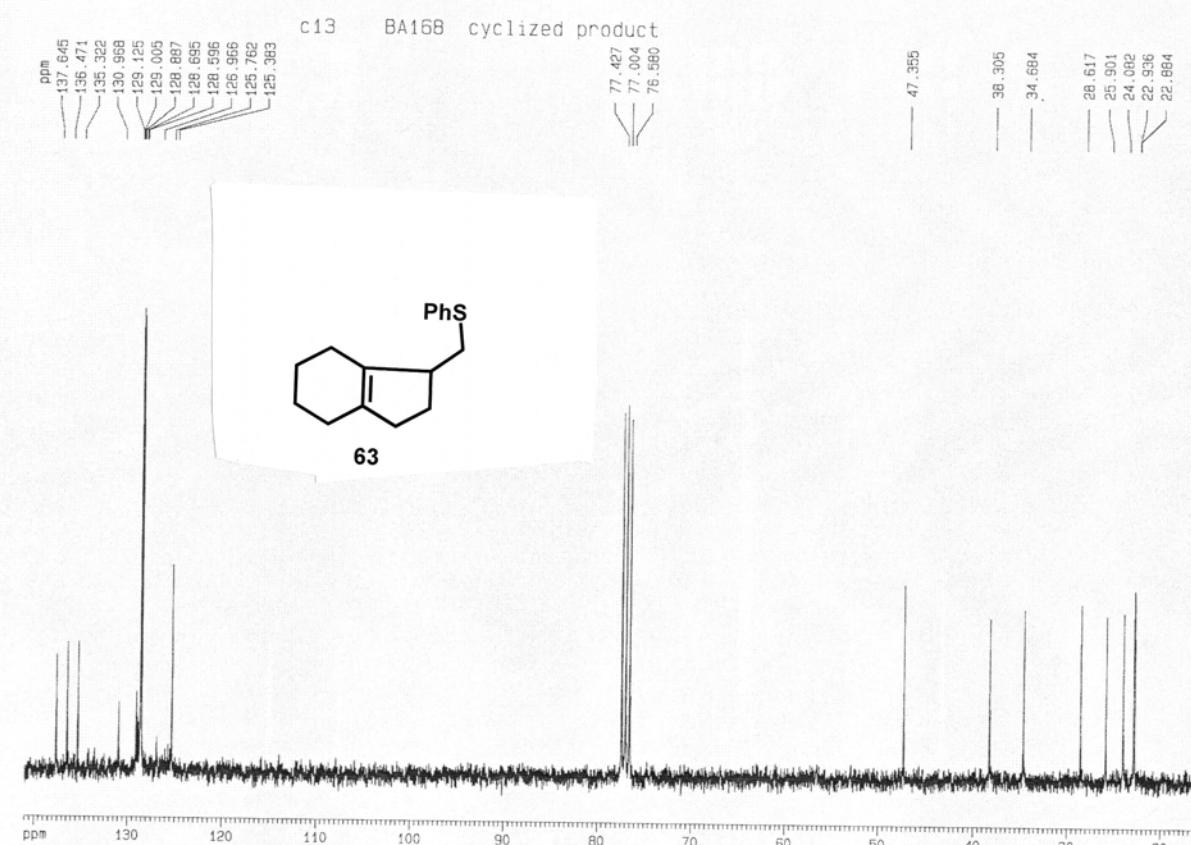
PA 121

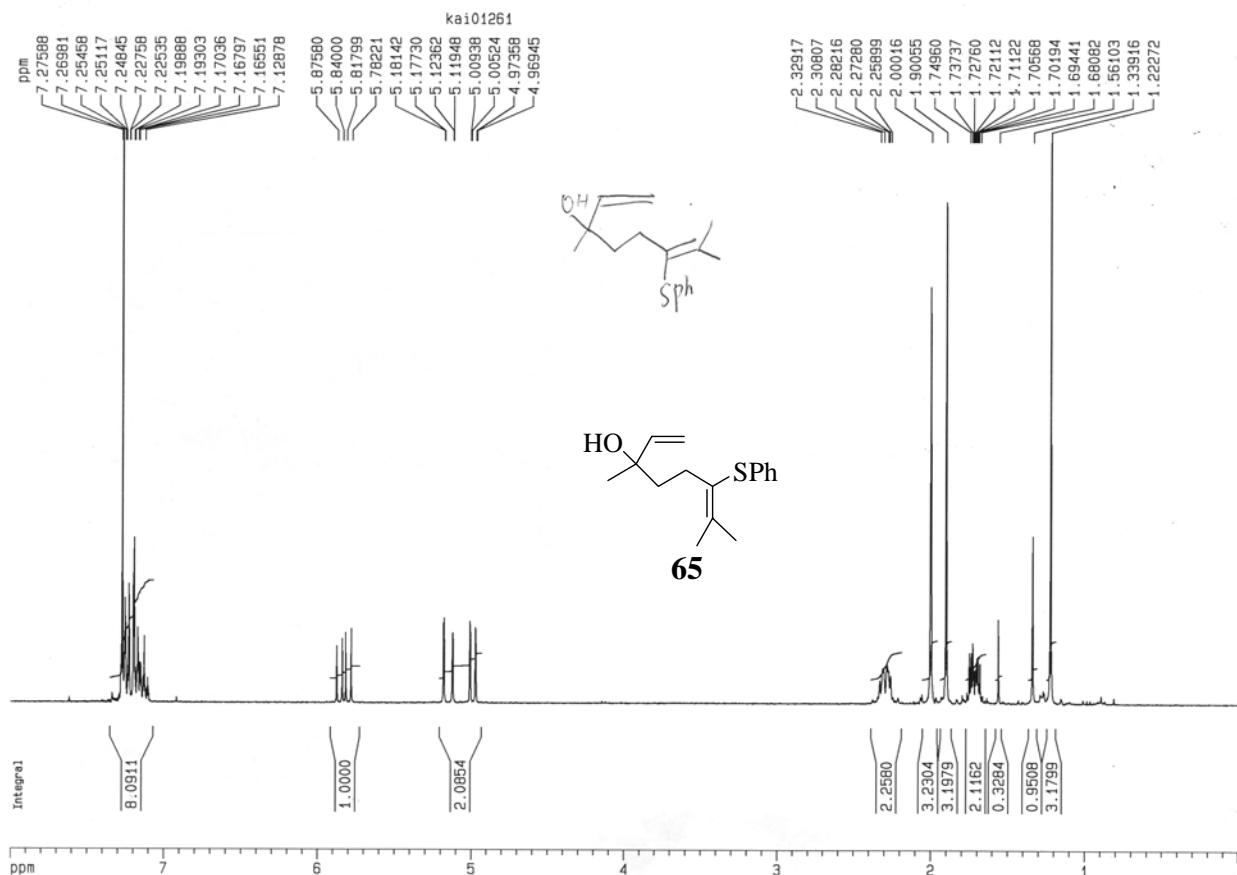


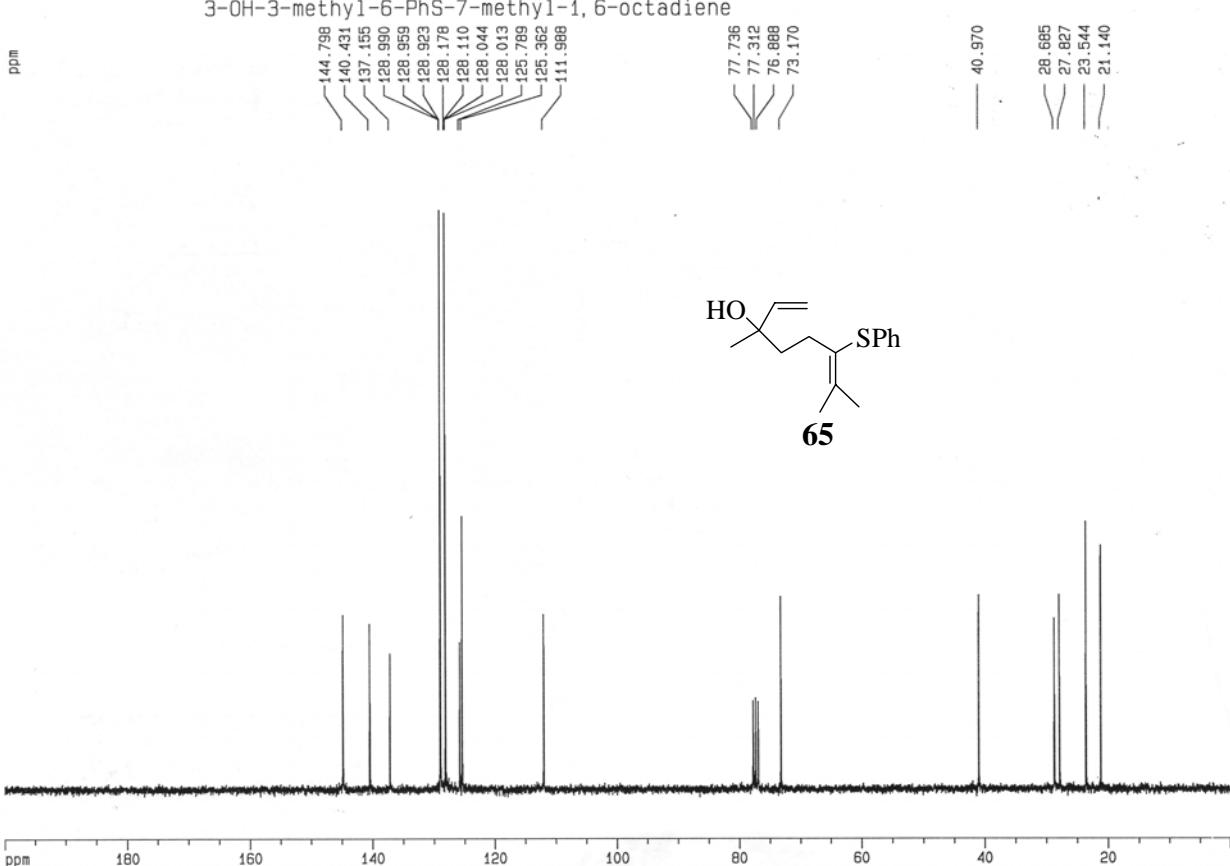


300 ba168

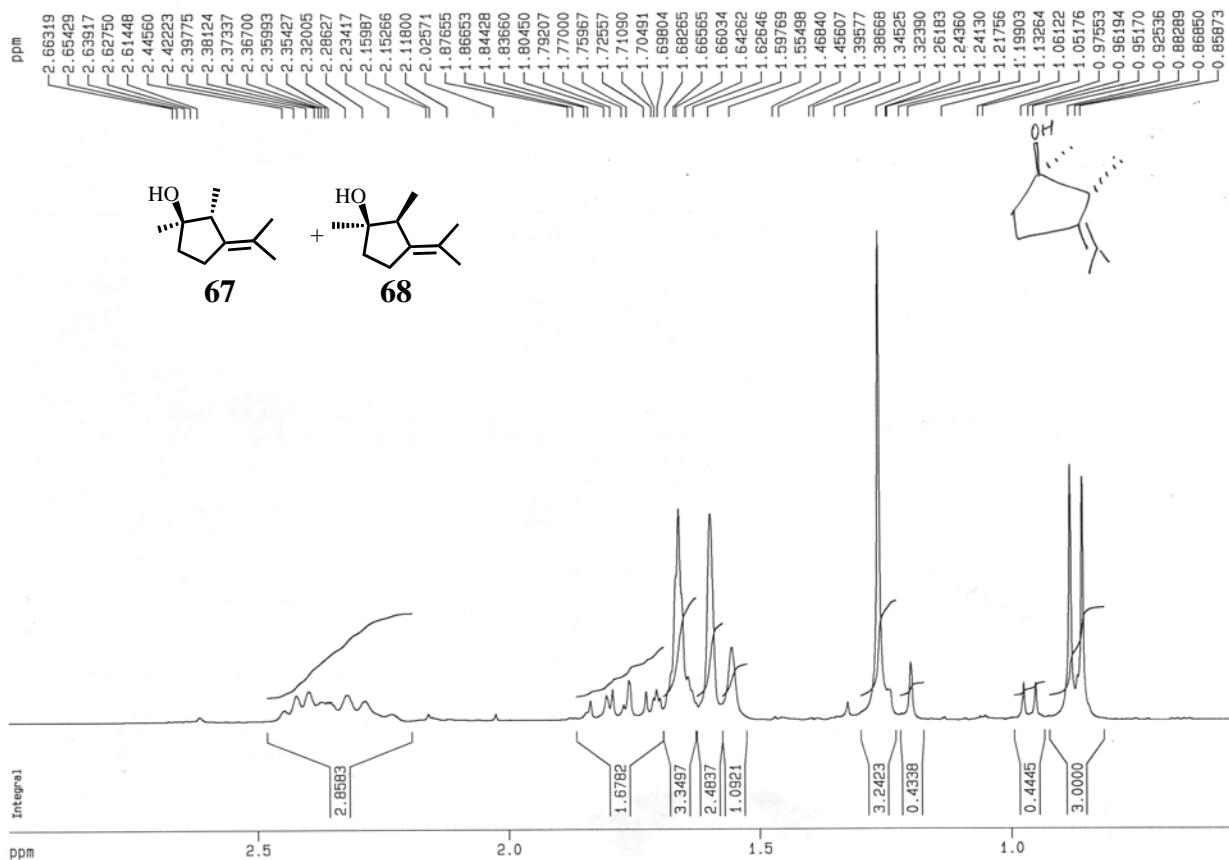


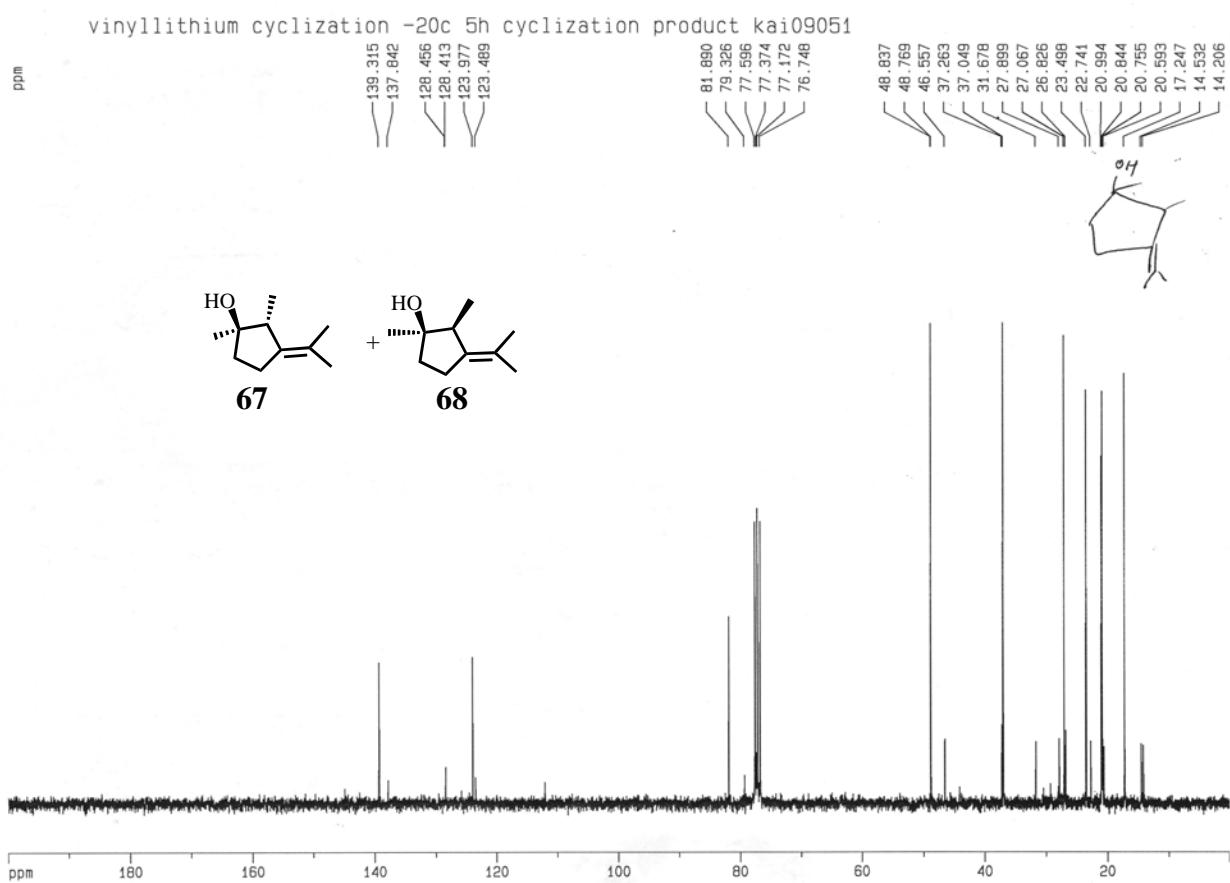


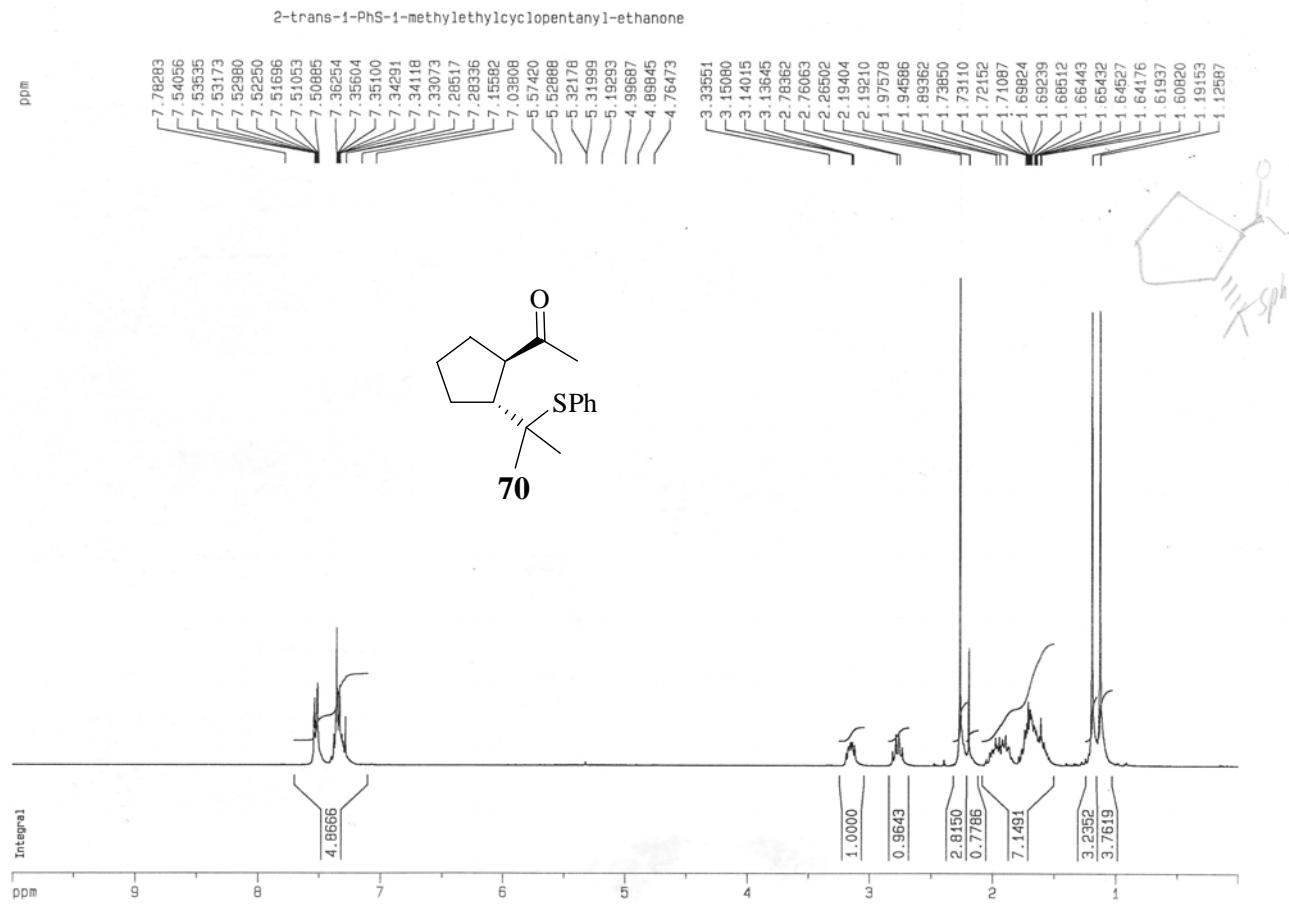




vinyllithium cyclization -20c 5h cyclization product kai09051

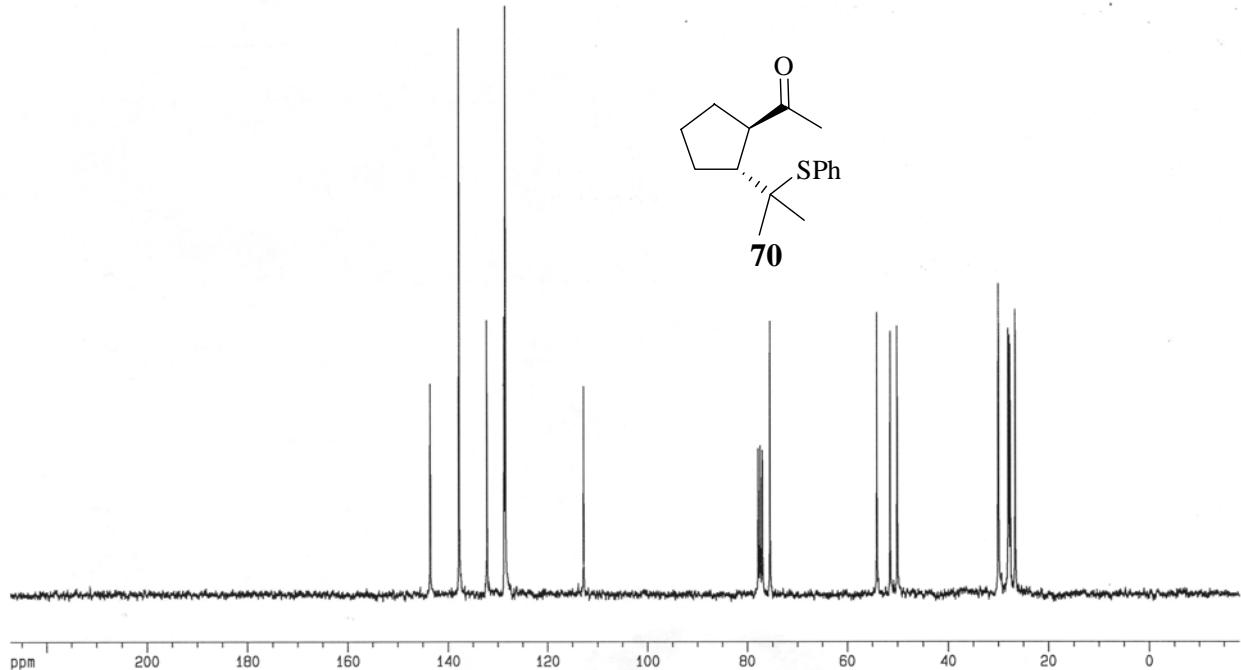
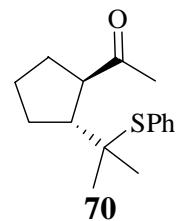
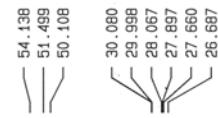
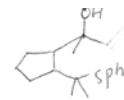
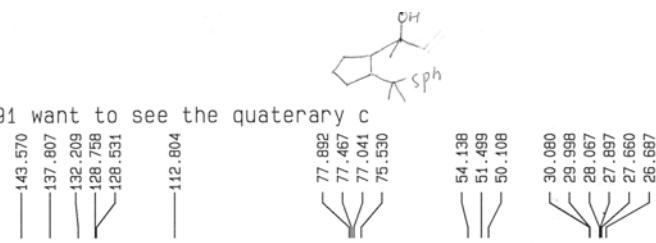


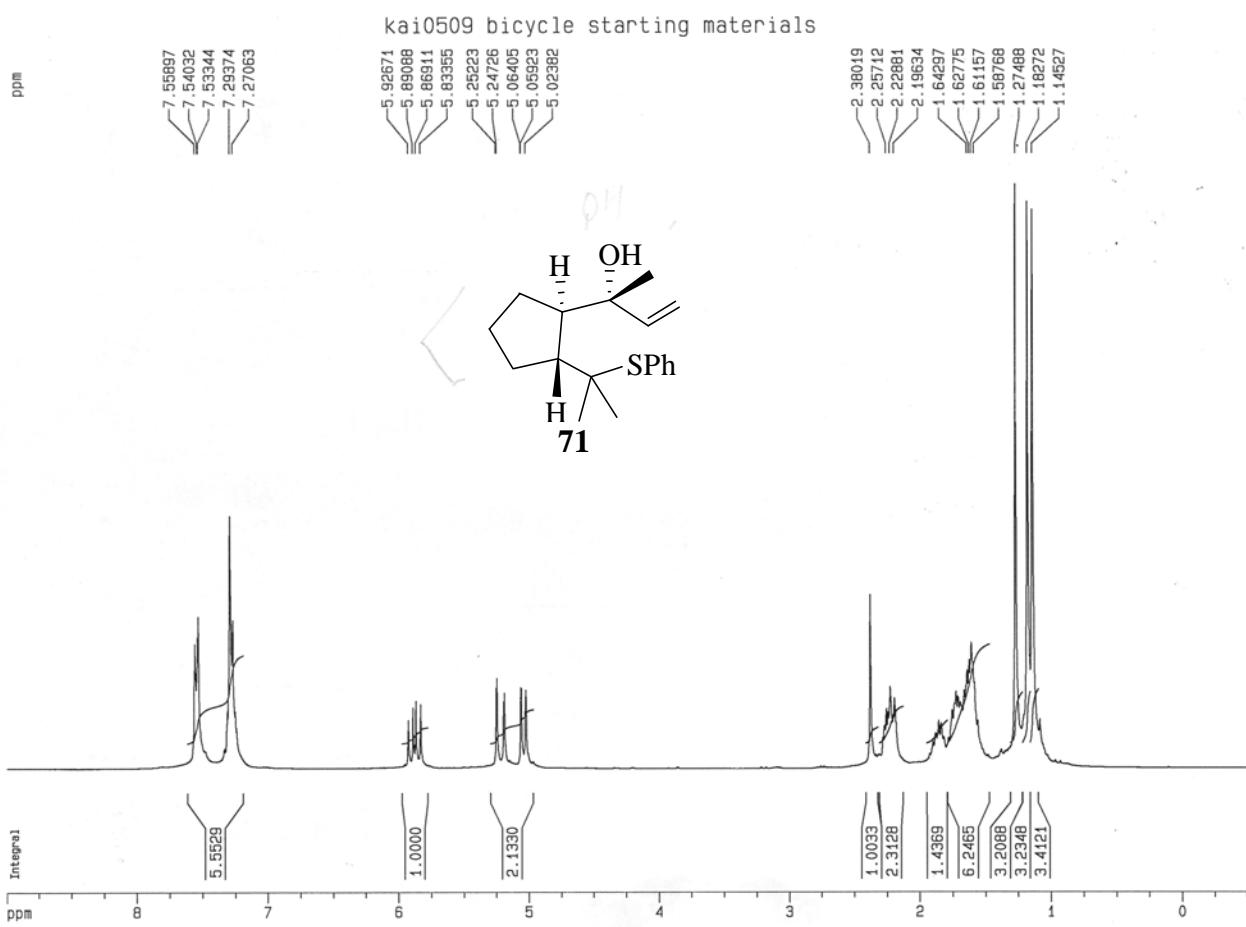




ppm

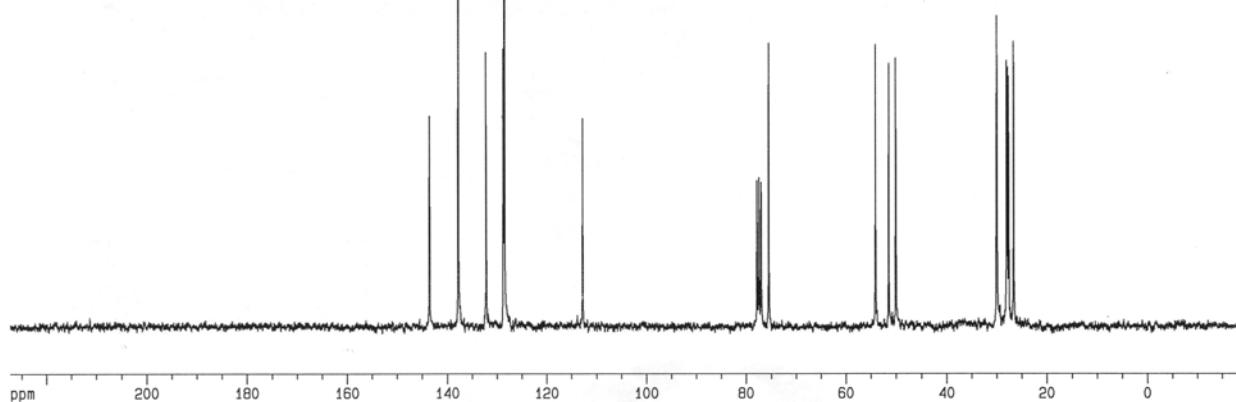
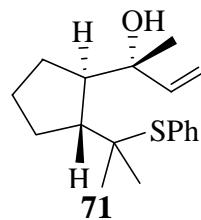
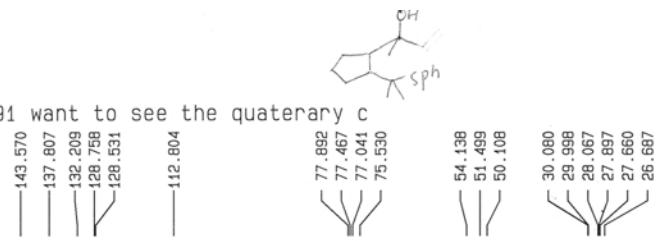
bicycle C13 kai05091 want to see the quaternary c

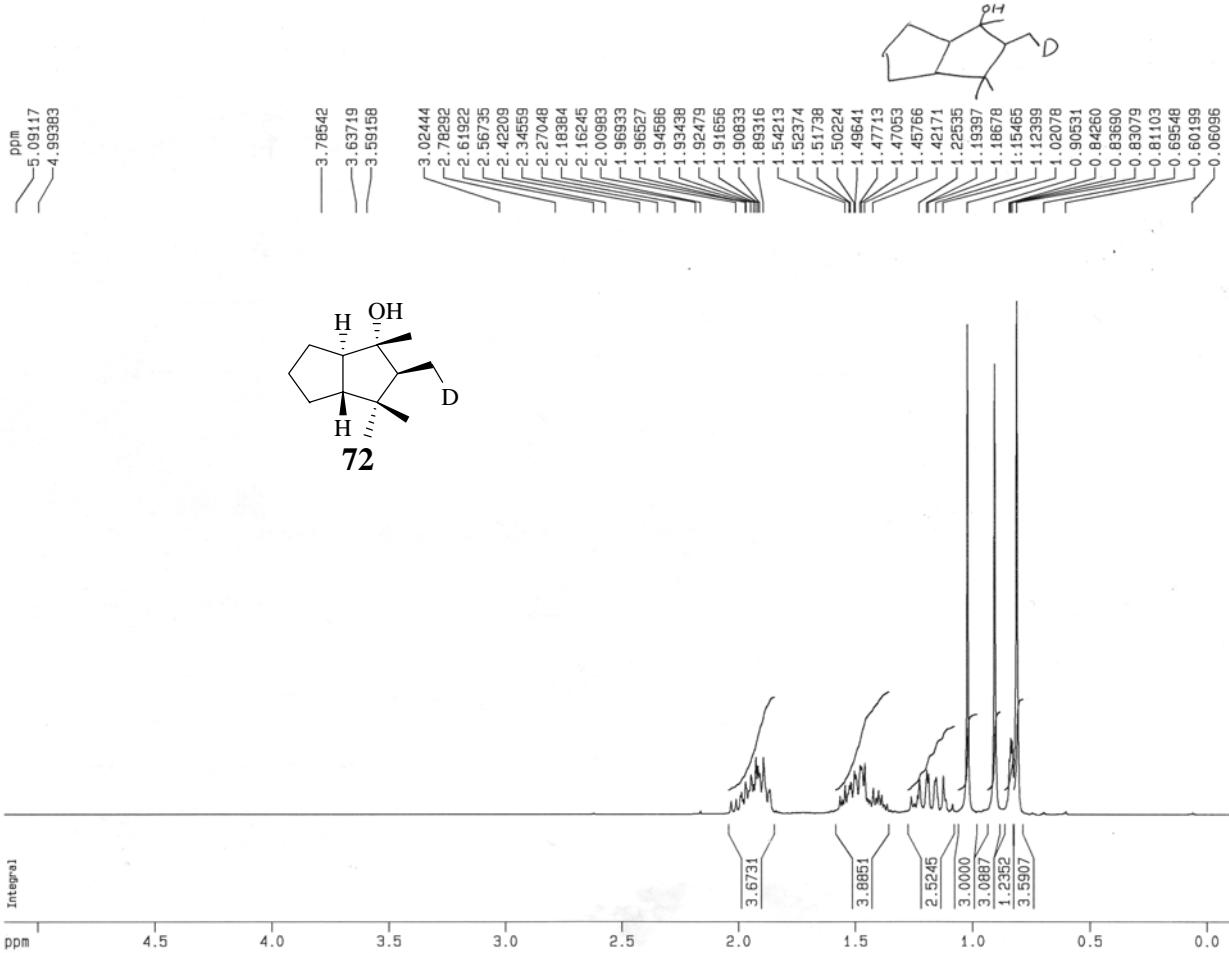




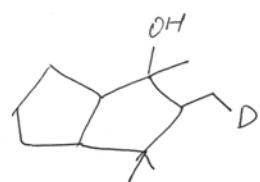
ppm

bicycle C13 kai05091 want to see the quaternary c





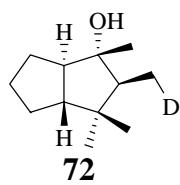
ppm



-78°C, 1h

77.5694
77.1478
76.7222
61.3121
59.0755
58.1226

34.5102
26.9888
26.8840
26.1733
21.7664
21.5729
20.4647
17.3190
9.5662
9.3317
9.0774



180 160 140 120 100 80 60 40 20

