

Controlling Factors for C—H Functionalization *versus* Cyclopropanation of Dihydronaphthalenes

Etienne Nadeau[†], Dominic L. Ventura[‡], Jonathan A. Brekan[‡] and Huw M. L. Davies^{†}*

[†] Department of Chemistry, Emory University, 1515 Dickey Drive, Atlanta, GA 30322, USA

[‡] Department of Chemistry, University at Buffalo, State University of New York, Buffalo, NY
14260-3000, USA

hmdavie@emory.edu

Supporting Information

General Considerations	S2
Experimental Procedures	S3
Copies of ¹ H and ¹³ C NMR spectra	S26

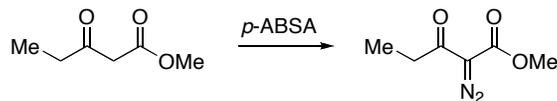
General Considerations

All reactions were conducted in flame-dried glassware under an inert atmosphere of dry argon. All reagents were used as received from commercial suppliers unless otherwise stated. Acetonitrile, dichloromethane, pentane, tetrahydrofuran and toluene were obtained through drying columns. 2,2-Dimethylbutane (2,2-DMB) was distilled from sodium metal. All solvents used for C–H functionalization reactions were degassed by bubbling argon through the solvent for 15 min prior to use. Flash chromatography was performed on silica gel (230-400 mesh) according to the method of W.C. Still.¹ Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.25 mm, 60 F₂₅₄) which were developed using standard visualizing agents: UV fluorescence (254 nm), phosphomolybdic acid / Δ or potassium permanganate / Δ . Melting points were determined using a melting point apparatus and are uncorrected. Optical rotations were measured on a polarimeter at 20 °C (589 nm). ¹H NMR spectra were recorded on a Nuclear Magnetic Resonance spectrometer at 600, 500 or 400 MHz. Residual protonated solvent served as internal standard (CHCl₃ δ = 7.26, C₆H₆ δ = 7.15) and data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad), and coupling constant in Hz. ¹³C NMR spectra were recorded at 150, 125 or 75 MHz. The solvent was used as internal standard (CDCl₃ δ = 77.0, C₆D₆ δ = 128.0) and spectra were obtained with complete proton decoupling. ¹⁹F NMR spectra were recorded at 375 MHz and CFCl₃ was used as internal standard (δ = 0). Infrared (IR) spectra were determined using a FTIR spectrometer and are reported in reciprocal centimeters (cm⁻¹). Diastereomeric ratios were determined by values derived from the ¹H NMR spectra of the crude reaction mixtures. Enantiomeric excess was determined by high performance liquid chromatography (HPLC) using chiral analytical columns with 2-propanol in hexane as eluant. **2a** and **12** were prepared according to literature procedures.²

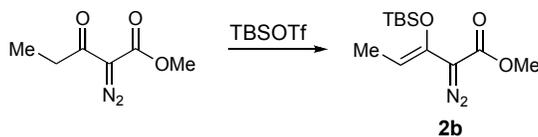
¹ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

² Davies, H. M. L.; Walji, A. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1733–1735.

Experimental Procedures



Methyl 2-diazo-3-oxopentanoate:³ Et₃N (11.7 mL, 84 mmol, 1.2 equiv.) was slowly added to a solution at 0 °C of methyl propionylacetate (8.8 mL, 70 mmol, 1 equiv.) and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) (18.5 g, 77 mmol, 1.1 equiv.) in 190 mL of acetonitrile. The cold bath was removed and the reaction was allowed to reach room temperature. The reaction was stopped after 2 h by filtering the mixture under vacuum. The white solid was washed with ethyl ether and the filtrate was concentrated under reduced pressure. The residue was triturated with hexanes and filtrated. The filtrate was concentrated under reduced pressure to give 8.99 g (82%) of the titled compound as a yellow oil. ¹H NMR (500 MHz, CDCl₃): δ = 3.83 (3H, s), 2.86 (2H, q, *J* = 7.3 Hz), 1.13 (3H, t, *J* = 7.3 Hz). The crude material was used in the next step without further purification.

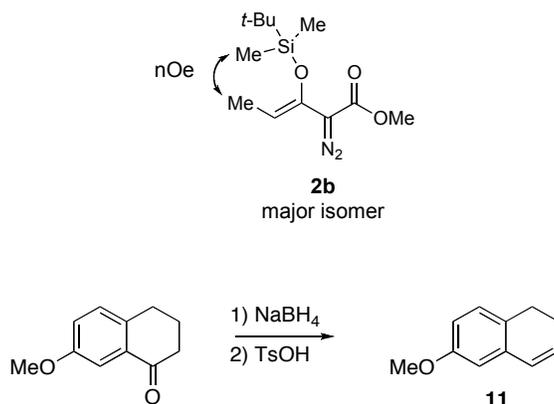


(Z)-Methyl 3-(tert-butyldimethylsilyloxy)-2-diazopent-3-enoate (2b**):** Et₃N (2.3 mL, 16.3 mmol, 1.4 equiv.) was added to a solution at 0 °C of methyl 2-diazo-3-oxopentanoate (1.82 g, 11.7 mmol, 1 equiv.) in 20 mL of anhydrous dichloromethane. TBSOTf (3.1 mL, 13.4 mmol, 1.15 equiv.) was then added over a 5 minutes period via syringe. The reaction was stopped after 1 h by adding 75 mL of hexanes. The organic layer was washed with 15 mL of sat. NaHCO₃ and 15 mL of sat. NaCl, dried over MgSO₄, filtered and evaporated under reduced pressure to give an orange oil which was purified on silica gel (hexanes then hexanes/ethyl acetate 95:5) to give 2.55 g (81 %) of **2b** (*Z/E* = 88:12) as an orange oil. *R*_f = 0.65 (hexane:ethyl acetate 80:20); IR (neat): ν = 2954, 2931, 2860, 2088, 1712, 1057, 838, 780; ¹H NMR (*Z* isomer) (400 MHz, CDCl₃): δ = 5.26 (1H, q, *J* = 7.2 Hz), 3.79 (3H, s), 1.68 (3H, d, *J* = 7.2 Hz), 0.98 (9H, s), 0.16 (6H, s); ¹³C

³ (a) Bagley, M. C.; Buck, R. T.; Hind, S. L.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 591–600. (b) Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709–1716.

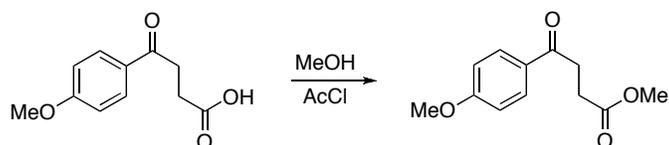
NMR (100 MHz, CDCl₃): δ = 165.2, 132.7, 107.8, 51.6, 25.4, 18.0, 11.6, -4.9, missing carbon attributed to C=N₂; HRMS (APCI): Calcd. for C₁₂H₂₃O₃N₂Si (MH⁺) 271.1473, found 271.1473.

Double bond geometry was assigned based on NMR studies. Key irradiation is shown bellow.

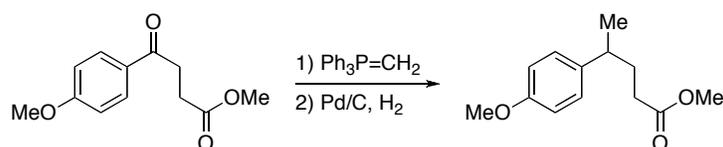


6-Methoxy-1,2-dihydronaphthalene (11):⁴ 7-Methoxy-1-tetralone (0.899 g, 5.1 mmol, 1.0 equiv) was dissolved in 40 mL of methanol and cooled to 0 °C in an ice/water bath. Then sodium borohydride (0.386 g, 10.2 mmol, 2.0 equiv) was added in one portion and the reaction was allowed to stir for 1 h. The reaction mixture was quenched with water and extracted with diethyl ether (5 x 20 mL). The combined ether extracts were dried with MgSO₄ and filtered. The solution was concentrated *in vacuo* to afford the crude alcohol. The latter was dissolved in 50 mL of dry toluene and *p*-toluenesulfonic acid (97 mg, 0.51 mmol, 0.10 equiv) was added. The solution was heated to 70 °C and stirred for 2 h. The solution was then cooled to rt and quenched with saturated NaHCO₃ and extracted with diethyl ether (3 x 20 mL). The combined ether extracts were dried with MgSO₄ and filtered. The resulting solution was concentrated *in vacuo* to give the crude residue. This residue was purified by flash chromatography on silica gel with pentane to give 737 mg (90% yield) of **11** as a colorless oil. R_f = 0.62 (pentane); IR (neat): ν = 1603, 1572, 1497, 1465, 1431, 1303, 1262, 1214, 1163, 1146, 1042, 878, 856, 816, 780, 694; ¹H NMR (500 MHz, CDCl₃): δ = 7.01 (1H, d, J = 8.0 Hz), 6.67 (1H, dd, J = 8.0, 2.5 Hz), 6.60 (1H, d, J = 2.5 Hz), 6.42 (1H, d, J = 9.5 Hz), 6.05 (1H, dt, J = 9.5, 4.0 Hz), 3.79 (3H, s), 2.73 (2H, t, J = 8.0 Hz), 2.36–2.27 (2H, m); ¹³C NMR (75 MHz, CDCl₃): δ = 158.2, 134.8, 129.0, 128.0, 127.7, 127.3, 111.6, 111.5, 54.9, 26.4, 23.4; HRMS (EI) Calcd. for C₁₁H₁₂O (M⁺) 160.0883, found 160.0878.

⁴ Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 3554–3572.



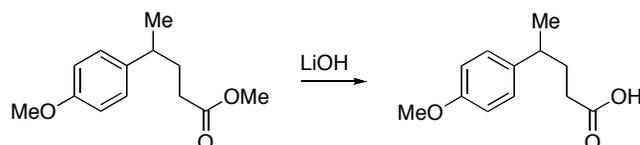
Methyl 4-(4-methoxyphenyl)-4-oxobutanoate:⁵ 3-(4-Methoxybenzoyl)propionic acid (25.0 g, 120 mmol, 1.0 equiv) was dissolved in 250 mL of methanol along with acetyl chloride (10.2 mL, 144 mmol, 1.2 equiv). The reaction mixture was then allowed to stir overnight at rt. The reaction mixture was quenched with saturated NaHCO₃ solution and then extracted with diethyl ether (4 x 20 mL). The combined organic extracts were washed with sat. NaCl and dried with MgSO₄. The resulting solution was filtered and concentrated *in vacuo* to give 22.70 g (85%) of the titled compound as a colorless oil. *R_f* = 0.30 (pentane:ether 80:20); IR (neat): ν = 1737, 1678, 1601, 1252, 1221, 1165, 1025, 834; ¹H NMR (400 MHz, CDCl₃): δ = 7.97 (2H, d, *J* = 8.8 Hz), 6.94 (2H, d, *J* = 8.8 Hz), 3.87 (3H, s), 3.70 (3H, s), 3.28 (2H, t, *J* = 6.4 Hz), 2.75 (2H, t, *J* = 6.4 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 196.5, 173.5, 163.6, 130.3, 129.7, 113.7, 55.5, 51.8, 33.0, 28.1; HRMS (EI) Calcd. for C₁₂H₁₄O₄ (M⁺) 222.0887, found 222.0894.



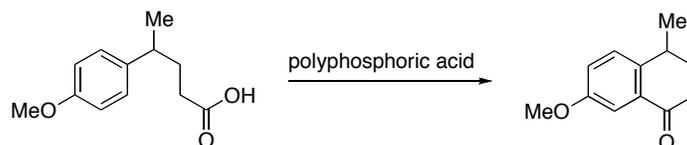
Methyl 4-(4-methoxyphenyl)pentanoate: Methyl triphenylphosphonium bromide (9.89 g, 27.7 mmol, 1.2 equiv) was dissolved in 60 mL of anhydrous THF and the reaction mixture was cooled to 0 °C. Then potassium *t*-butoxide (2.85 g, 25.4 mmol, 1.1 equiv) was added in one portion and the reaction was stirred for 0.5 h. Methyl 4-(4-methoxyphenyl)-4-oxobutanoate (5.13 g, 23.1 mmol, 1 equiv) was then added. After stirring for 1 h, the reaction mixture was quenched with 50 mL of dist. water. The aqueous layer was extracted with diethyl ether (3 x 50 mL). The combined organic extracts were washed with 20 mL of dist. water and 15 mL of sat. NaCl, dried with MgSO₄ and filtered. The solution was concentrated *in vacuo*, then triturated with hexanes. The mixture was filtered again and concentrated *in vacuo* to give the crude olefin. The latter was taken up in 100 mL of EtOAc and added to a 500 mL Parr hydrogenation bottle along with 5% Pd/C (4.9 g, 246 mg of Pd, 2.31 mmol). The bottle was purged with hydrogen gas at 40 psi and

⁵ Ruan, J.; Saidi, O.; Iggo, J. A.; Xiao, J. *J. Am. Chem. Soc.* **2008**, *130*, 10510–10511.

allowed to shake for 6 h. The mixture was filtered through a plug of silica gel, then concentrated *in vacuo* to give 3.79 g (74%) of the titled compound as a colorless oil. IR (neat): $\nu = 2958, 1737, 1510, 1242, 1175, 1165, 1036, 827$; $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 7.09$ (2H, d, $J = 8.4$ Hz), 6.84 (2H, d, $J = 8.4$ Hz), 3.79 (3H, s), 3.62 (3H, s), 2.62–2.71 (1H, m), 2.12–2.26 (2H, m), 1.78–1.98 (2H, m), 1.24 (3H, d, $J = 7.2$ Hz); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 174.1, 158.0, 138.3, 127.8, 113.8, 55.2, 51.4, 38.6, 33.4, 32.3, 22.3$; HRMS (EI) Calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_3$ (M^+) 222.1250, found 222.1255.



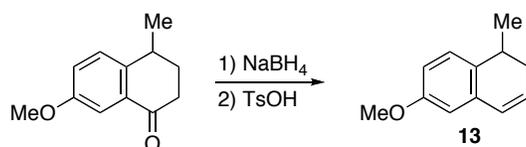
4-(4-Methoxyphenyl)pentanoic acid:⁶ Methyl 4-(4-methoxyphenyl)pentanoate (14.44 g, 65.0 mmol, 1 equiv) was dissolved in 200 mL of THF/MeOH/ H_2O 2:1:1. Then lithium hydroxide monohydrate (5.0 g, 122 mmol, 1.8 equiv) was added and the reaction mixture was heated to 50 °C for 1 h. The reaction mixture was cooled to rt and quenched with 10% HCl solution until pH of 2 was reached. The mixture was extracted with diethyl ether (4 x 25 mL) and the combined organic extracts were dried with MgSO_4 . The solution was filtered and concentrated *in vacuo* to give 13.37 g (98%) of the titled compound as a yellow oil. $R_f = 0.27$ (pentane:ether 80:20); IR (neat): $\nu = 2962, 2923, 1702, 1510, 1242, 1175, 1032, 834$; $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 7.09$ (2H, d, $J = 8.4$ Hz), 6.84 (2H, d, $J = 8.4$ Hz), 3.79 (3H, s), 2.64–2.76 (1H, m), 2.18–2.25 (2H, m), 1.78–1.98 (2H, m), 1.25 (3H, d, $J = 6.8$ Hz); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 179.0, 158.0, 138.1, 127.9, 113.9, 55.2, 38.5, 33.1, 32.1, 22.3$; HRMS (EI) Calcd. for $\text{C}_{12}\text{H}_{16}\text{O}_3$ (M^+) 208.1094, found 208.1096.



7-Methoxy-4-methyltetralone:⁶ A flask containing ~20 g of polyphosphoric acid was heated to 100 °C. Then 4-(4-methoxyphenyl)pentanoic acid (5.01 g, 24.0 mmol, 1 equiv) was added and the reaction mixture was allowed to stir for 2 h. The reaction mixture was quenched with ice-

⁶ Tanaka, J.; Miyake, T.; Iwasaki, N.; Adachi, K. *Bull. Chem. Soc. Jpn.* **1992**, 65, 2851–2853.

water (100 mL) and allowed to stir for 1 h. The mixture was extracted with DCM (3 x 30 mL) and the combined DCM extracts were washed with sat. NaCl and dried with MgSO₄. The mixture was filtered and concentrated *in vacuo* to give 3.60 g (79%) of the titled compound as a yellow oil. IR (neat): ν = 2961, 2937, 1681, 1607, 1492, 1283, 1234, 1042, 882, 823; ¹H NMR (400 MHz, CDCl₃): δ = 7.50 (1H, d, *J* = 2.8 Hz), 7.24 (1H, d, *J* = 8.8 Hz), 7.08 (1H, dd, *J* = 8.8, 2.8 Hz), 3.82 (3H, s), 2.98–3.08 (1H, m), 2.77 (1H, ddd, *J* = 17.4, 8.4, 4.6 Hz), 2.57 (1H, ddd, *J* = 17.4, 9.0, 4.8 Hz), 2.21 (1H, m), 1.86 (1H, m), 1.36 (3H, d, *J* = 6.8 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 198.3, 158.1, 141.6, 132.6, 128.6, 121.8, 109.1, 55.4, 36.3, 32.1, 30.8, 20.7; HRMS (EI) Calcd. for C₁₂H₁₄O₂ (M⁺) 190.0988, found 190.0996.



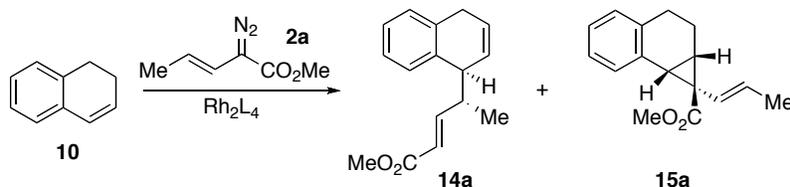
6-methoxy-1-methyl-1,2-dihydronaphthalene (13): 7-Methoxy-4-methyltetralone (2.76 g, 14.5 mmol, 1 equiv) was dissolved in 100 mL of methanol and cooled to 0 °C in an ice-water bath. Then sodium borohydride (1.10 g, 29.0 mmol, 2 equiv) was added portionwise over 20 min (4 equal portions). The reaction was allowed to stir for 1 h and was then quenched slowly with water and extracted with diethyl ether (5 x 20 mL). The combined organic extracts were dried with MgSO₄ and filtered. The resulting solution was concentrated under reduced pressure. The crude alcohol was dissolved in 70 mL of toluene along with *p*-toluenesulfonic acid (0.28 g, 1.5 mmol, 0.10 equiv). The reaction mixture was heated to 70 °C in an oil bath for 2 h, then cooled to rt and quenched with saturated NaHCO₃ solution. The mixture was extracted with diethyl ether (5 x 30 mL). The combined organic extracts were dried with MgSO₄ and filtered. The solution was concentrated *in vacuo* and purified by flash chromatography using pentane to give 1.72 g (68%) of the titled compound as a colorless oil. *R_f* = 0.27 (100% pentane); IR (neat): ν = 3031, 2951, 2920, 2829, 1604, 1570, 1493, 1259, 1161, 1039, 701; ¹H NMR (400 MHz, CDCl₃): δ = 7.09 (1H, d, *J* = 8.4 Hz), 6.72 (1H, dd, *J* = 8.4, 2.4 Hz), 6.63 (1H, d, *J* = 2.4 Hz), 6.42 (1H, d, *J* = 9.2 Hz), 5.99 (1H, dt, *J* = 9.2, 4.6 Hz), 3.80 (3H, s), 2.85–2.95 (1H, m), 2.42–2.50 (1H, m), 2.07–2.15 (1H, m), 1.23 (3H, d, *J* = 7.2 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 158.2, 134.4, 132.7, 128.0, 127.5, 126.8, 112.1, 111.8, 55.3, 31.6, 30.9, 20.3; HRMS (EI) Calcd. for C₁₂H₁₄O (M⁺) 174.1039, found 174.1045.

Procedures for reactions with (*E*)-methyl 2-diazopent-3-enoate (2a**) and 1,2-dihydronaphthalenes.**

(*R,E*)-methyl 4-((*S*)-1,4-dihydronaphthalen-1-yl)pent-2-enoate (14a**) and (1*R*,1*aS*,7*bS*)-methyl 1-((*E*)-prop-1-enyl)-1*a*,2,3,7*b*-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (**15a**):**

(Table 1, entry 1): **2a** (210 mg, 1.5 mmol, 3 equiv.) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **10** (65 mg, 0.5 mmol, 1 equiv.) and Rh₂(*S*-DOSP)₄ (19 mg, 0.01 mmol, 0.02 equiv.) in 5.5 mL of 2,2-DMB. After 0.5 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **14a** and **15a** (59 mg, 49% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% AgNO₃⁷ (hexane:ether).

(Table 1, entry 2): **2a** (140 mg, 1 mmol, 2 equiv.) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **10** (65 mg, 0.5 mmol, 1 equiv.) and Rh₂(*S*-PTAD)₄ (16 mg, 0.01 mmol, 0.02 equiv.) in 5.5 mL of 2,2-DMB. After 3 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **14a** and **15a** (81 mg, 67% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% AgNO₃ (hexane:ether).



14a: Colorless oil; *R_f* = 0.57 (hexane:ethyl acetate 80:20); IR (neat): ν = 3028, 2966, 2872, 1720; ¹H NMR (600 MHz, CDCl₃): δ = 7.15–7.21 (3H, m), 7.13 (1H, d, *J* = 7.1 Hz), 7.09 (1H, dd, *J* = 15.9, 6.9 Hz), 6.07–6.10 (1H, m), 5.82 (1H, d, *J* = 15.9 Hz), 5.74–5.78 (1H, m), 3.75 (3H, s), 3.62

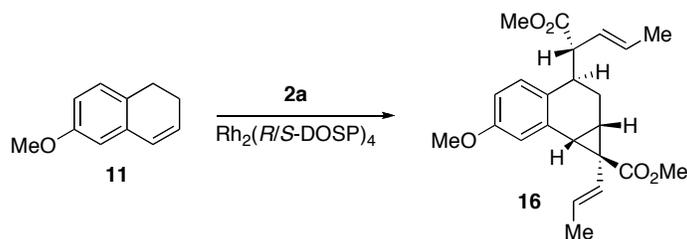
⁷ Li, T.-S.; Li, J.-T.; Li, H.-Z. *J. Chromatogr., A* **1995**, *715*, 372–375.

(1H, ddd, $J = 8.0, 3.9, 3.9$ Hz), 3.27–3.40 (2H, m), 2.77–2.84 (1H, m), 0.84 (3H, d, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 167.2, 152.7, 136.4, 135.4, 128.2, 128.0, 127.4, 126.1(2\text{C}), 125.4, 120.3, 51.5, 44.1, 43.8, 30.2, 13.2$; HRMS (APCI): Calcd. for $\text{C}_{16}\text{H}_{19}\text{O}_2$ (MH^+) 243.1380, found 243.1379; $[\alpha]_{\text{D}}^{20} -172.7$ (c 0.7, CHCl_3) for 99% ee; HPLC analysis: 99% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and -84% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.5% *i*-PrOH in hexane, 1 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 8.97$ min, 10.63 min).

15a: White solid; mp = 33–34 °C; $R_f = 0.57$ (hexane:ethyl acetate 80:20); IR (neat): $\nu = 3021, 2926, 1713, 1232$; ^1H NMR (400 MHz, CDCl_3): $\delta = 7.28\text{--}7.32$ (1H, m), 7.10–7.18 (2H, m), 6.98–7.02 (1H, m), 5.21–5.33 (2H, m), 3.70 (3H, s), 2.81 (1H, d, $J = 9.1$ Hz), 2.62 (1H, ddd, $J = 16.6, 7.0, 4.1$ Hz), 2.44 (1H, ddd, $J = 16.6, 9.8, 7.3$ Hz), 2.23 (1H, ddd, $J = 9.1, 5.7, 2.9$ Hz), 1.92–2.08 (2H, m), 1.48 (3H, d, $J = 4.8$ Hz); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 174.3, 135.7, 133.1, 132.2, 130.2, 128.3, 126.3, 125.9, 121.7, 52.3, 35.6, 29.9, 27.8, 26.6, 18.4, 17.9$; HRMS (APCI): Calcd. for $\text{C}_{16}\text{H}_{19}\text{O}_2$ (MH^+) 243.1380, found 243.1380; $[\alpha]_{\text{D}}^{20} +3.2$ (c 2.5, CHCl_3) for -74% ee; HPLC analysis: 48% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and -74% ee with $\text{Rh}_2(\text{S-PTAD})_4$ ((*S,S*)-Whelk-O 1, 0.5% *i*-PrOH in hexane, 1 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 13.24$ min, 14.47 min).

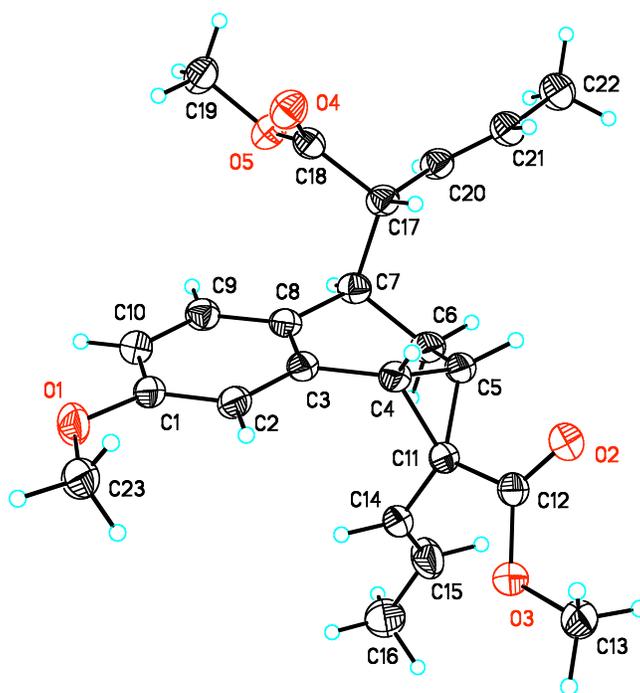
(1*R*,1*aS*,3*R*,7*bS*)-Methyl 6-methoxy-3-((*R,E*)-1-methoxy-1-oxopent-3-en-2-yl)-1-((*E*)-prop-1-enyl)-1*a*,2,3,7*b*-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (16**):**

(Scheme 3): **2a** (315 mg, 2.25 mmol, 3 equiv.) in 7 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **11** (120 mg, 0.75 mmol, 1 equiv.) and $\text{Rh}_2(\text{R/S-DOSP})_4$ (28 mg, 0.015 mmol, 0.02 equiv.) in 8 mL of 2,2-DMB. After 1 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2–80:20). **16** was further purified by recrystallization from hexane to afford 76 mg (26%) of **16**.



16: White solid; mp = 108–109 °C; R_f = 0.36 (hexane:ethyl acetate 80:20); IR (neat): ν = 2949, 1716, 1193, 1158; ^1H NMR (400 MHz, CDCl_3): δ = 6.87 (1H, d, J = 8.5 Hz), 6.78 (1H, d, J = 2.6 Hz), 6.61 (1H, dd, J = 8.5, 2.6 Hz), 5.69 (1H, dq, J = 15.2, 6.4 Hz), 5.51 (1H, ddq, J = 15.2, 9.5, 1.6 Hz), 5.44 (1H, dq, J = 15.9, 6.6 Hz), 4.86 (1H, dq, J = 15.9, 1.7 Hz), 3.76 (3H, s), 3.72 (3H, s), 3.43 (3H, s), 3.24 (1H, dd, J = 10.0, 10.0 Hz), 2.77–2.82 (1H, m), 2.77 (1H, d, J = 8.9 Hz), 2.22 (1H, ddd, J = 14.5, 9.1, 2.2 Hz), 2.08 (1H, ddd, J = 9.1, 9.1, 6.4 Hz), 1.73 (3H, dd, J = 6.4, 1.6 Hz), 1.56–1.62 (1H, m), 1.55 (3H, dd, J = 6.6, 1.7 Hz); ^{13}C NMR (100 MHz, CDCl_3): δ = 174.5, 174.1, 158.4, 133.7, 132.8, 131.8, 129.7, 129.2, 127.8, 121.9, 115.5, 112.6, 55.8, 55.1, 52.3, 51.3, 40.6, 35.8, 28.6, 23.2, 21.6, 18.8, 17.9; HRMS (APCI): Calcd. for $\text{C}_{23}\text{H}_{29}\text{O}_5$ (MH^+) 385.2010, found 385.2012.

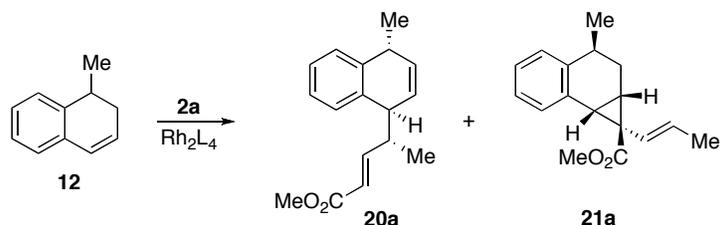
X-Ray crystal structure of **16**



(*R,E*)-Methyl 4-((1*S*,4*R*)-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (20a) and (1*R*,1*aS*,3*S*,7*bS*)-methyl 3-methyl-1-((*E*)-prop-1-enyl)-1*a*,2,3,7*b*-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (21a):

(Table 3, entry 1): **2a** (210 mg, 1.5 mmol, 3 equiv.) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **12** (72 mg, 0.5 mmol, 1 equiv.) and Rh₂(*S*-DOSP)₄ (19 mg, 0.01 mmol, 0.02 equiv.) in 5.5 mL of 2,2-DMB. After 2 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **20a** and **21a** (92 mg, 72% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% AgNO₃ (hexane:ether).

(Table 3, entry 2): **2a** (140 mg, 1 mmol, 2 equiv.) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **12** (72 mg, 0.5 mmol, 1 equiv.) and Rh₂(*S*-PTAD)₄ (16 mg, 0.01 mmol, 0.02 equiv.) in 5.5 mL of 2,2-DMB. After 15 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **20a** and **21a** (54 mg, 42% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% AgNO₃ (hexane:ether).

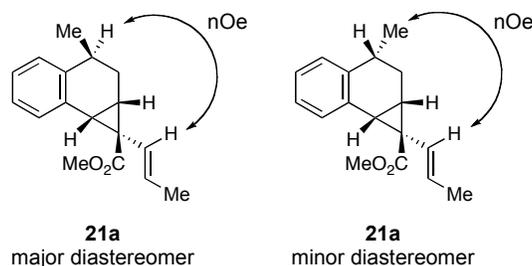


20a: Colorless oil; *R_f* = 0.63 (hexane:ethyl acetate 80:20); IR (neat): ν = 3024, 2966, 2872, 1721, 1271, 1173; ¹H NMR (400 MHz, CDCl₃): δ = 7.28–7.31 (1H, m), 7.19–7.24 (3H, m), 7.13 (1H, dd, *J* = 15.8, 6.5 Hz), 5.91 (1H, ddd, *J* = 10.2, 2.6, 1.3 Hz), 5.84 (1H, dd, *J* = 15.8, 1.6 Hz), 5.67 (1H, ddd, 10.2, 4.4, 2.5 Hz), 3.75 (3H, s), 3.61–3.65 (1H, m), 3.36–3.44 (1H, m), 2.81–2.89 (1H, m), 1.36 (3H, d, *J* = 7.3 Hz), 0.78 (3H, d, *J* = 7.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ = 167.4, 153.2, 140.8, 136.1, 134.4, 127.7, 127.2, 126.5, 126.3, 123.7, 120.5, 51.7, 43.9, 43.5, 32.8, 23.1, 13.0; HRMS (APCI): Calcd. for C₁₇H₂₁O₂ (MH⁺) 257.1536, found 257.1540; [α]_D²⁰ –189.2 (c 0.3, CHCl₃) for 91% ee; HPLC analysis: 91% ee with Rh₂(*S*-DOSP)₄ and –40% ee with Rh₂(*S*-

PTAD)₄ (Chiralcel OD-H, 0.5% *i*-PrOH in hexane, 1 mL/min, $\lambda = 254$ nm, $t_R = 7.57$ min, 8.37 min).

21a: Major/minor = 80:20; colorless oil; $R_f = 0.63$ (hexane:ethyl acetate 80:20); IR (neat): $\nu = 3021, 2954, 1715, 1233$; major: ¹H NMR (400 MHz, CDCl₃): $\delta = 7.23\text{--}7.29$ (1H, m), 7.09–7.19 (3H, m), 5.33 (1H, dq, $J = 15.9, 6.5$ Hz), 5.10 (1H, dq, $J = 15.9, 1.7$ Hz), 3.71 (3H, s), 2.82 (1H, d, $J = 9.5$ Hz), 2.58–2.67 (1H, m), 2.21 (1H, ddd, $J = 9.5, 7.3, 4.4$ Hz), 1.95 (1H, ddd, $J = 14.4, 5.8, 4.4$ Hz), 1.81 (1H, ddd, $J = 14.4, 7.3, 6.4$ Hz), 1.50 (3H, dd, $J = 6.5, 1.7$ Hz), 1.27 (3H, d, $J = 7$ Hz); ¹³C NMR (150 MHz, CDCl₃): $\delta = 174.6, 142.3, 132.8, 132.1, 130.6, 126.6, 126.0, 122.1, 52.3, 35.6, 31.6, 29.4, 26.6, 25.3, 22.2, 18.6$; HRMS (APCI): Calcd. for C₁₇H₂₁O₂ (MH⁺) 257.1536, found 257.1539; HPLC analysis: major diastereomer 74% ee with Rh₂(*S*-DOSP)₄ and –34% ee with Rh₂(*S*-PTAD)₄ ((*S,S*)-Whelk-O 1, 100% hexane, 0.5 mL/min, $\lambda = 254$ nm, $t_R = 13.55$ min, 14.93 min), minor diastereomer 50% ee with Rh₂(*S*-DOSP)₄ and –78% ee with Rh₂(*S*-PTAD)₄ (Chiralcel OD-H, 0.5% *i*-PrOH in hexane, 1 mL/min, $\lambda = 254$ nm, $t_R = 5.84$ min, 6.58 min).

Relative stereochemistry was assigned based on literature precedents² and confirmed by NMR studies. Key irradiations are shown bellow.

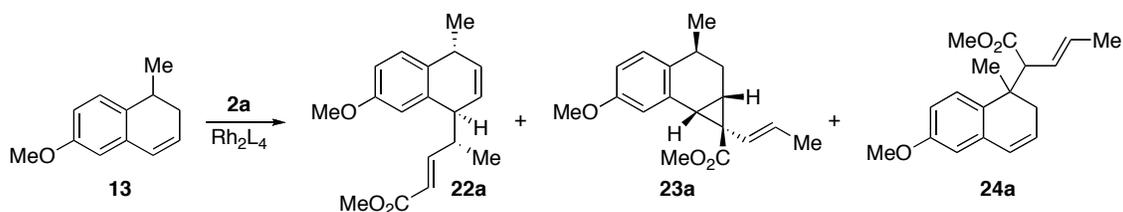


(*R,E*)-methyl 4-((1*S*,4*R*)-7-methoxy-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (22a) and (1*R*,1*aS*,3*S*,7*bS*)-methyl 6-methoxy-3-methyl-1-((*E*)-prop-1-enyl)-1*a*,2,3,7*b*-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (23a):

(Table 4, entry 1): **2a** (4.80 g, 34.4 mmol, 2 equiv.) in 20 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **13** (3.00 g, 17.2 mmol, 1 equiv.) and

Rh₂(*R*-DOSP)₄ (650 mg, 0.344 mmol, 0.02 equiv.) in 60 mL of 2,2-DMB. After 0.5 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ethyl acetate 90:10) to afford **22a**, **23a** and **24a** (4.14 g, 84% combined yield).

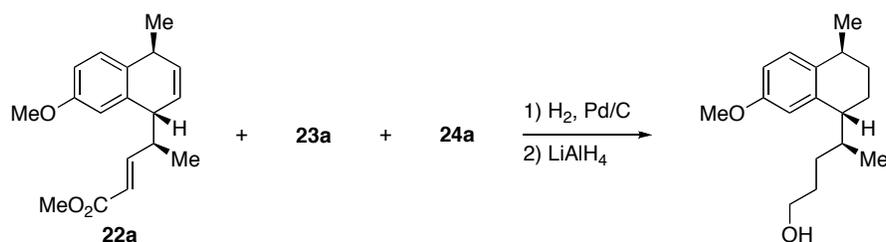
(Table 4, entry 2): **2a** (168 mg, 1.2 mmol, 2 equiv.) in 5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **13** (105 mg, 0.6 mmol, 1 equiv.) and Rh₂(*S*-PTAD)₄ (19 mg, 0.012 mmol, 0.02 equiv.) in 7 mL of 2,2-DMB. After 1 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 95:5–80:20) to afford **22a**, **23a** and *epi*-**24a** (129 mg, 75% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% AgNO₃ (hexane:ether).



22a: Colorless oil; R_f = 0.53 (hexane:ethyl acetate 80:20); IR (neat): ν = 3024, 2963, 2871, 2836, 1720; ¹H NMR (400 MHz, CDCl₃): δ = 7.21 (1H, d, J = 8.6 Hz), 7.13 (1H, dd, J = 15.7, 6.5 Hz), 6.80 (1H, dd, J = 8.6, 2.5 Hz), 6.72 (1H, d, J = 2.5 Hz), 5.89 (1H, ddd, J = 10.2, 2.7, 1.1 Hz), 5.85 (1H, dd, J = 15.7, 1.7 Hz), 5.64 (1H, ddd, J = 10.2, 4.1, 2.5 Hz), 3.81 (3H, s), 3.75 (3H, s), 3.56–3.62 (1H, m), 3.30–3.38 (1H, m), 2.80–2.88 (1H, m), 1.33 (3H, d, J = 7.3 Hz), 0.78 (3H, d, J = 6.7 Hz); ¹³C NMR (100 MHz, CDCl₃): δ = 167.4, 158.0, 153.1, 137.4, 134.7, 133.2, 128.2, 123.3, 120.5, 112.6, 112.5, 55.4, 51.7, 44.3, 43.6, 32.2, 23.2, 12.9; HRMS (APCI): Calcd. for C₁₈H₂₃O₃ (MH⁺) 287.1647, found 287.1643; HPLC analysis: –36% with Rh₂(*S*-PTAD)₄ ((*S,S*)-Whelk-O 1, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 22.52 min, 26.51 min).

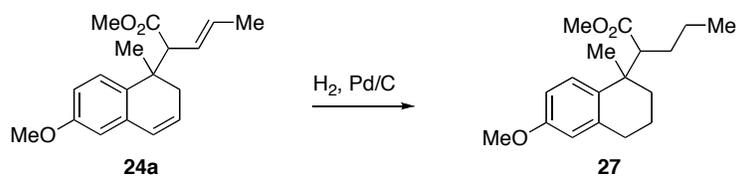
23a: Major/minor = 90:10; colorless oil; R_f = 0.53 (hexane:ethyl acetate 80:20); IR (neat): ν = 3021, 2952, 1713, 1230; major: ¹H NMR (400 MHz, CDCl₃): δ = 7.03 (1H, d, J = 8.3 Hz), 6.83 (1H, d, J = 2.9 Hz), 6.71 (1H, dd, J = 8.3, 2.9 Hz), 5.35 (1H, dq, J = 15.7, 6.5 Hz), 5.11 (1H, dq, 15.7, 1.6 Hz), 3.79 (3H, s), 3.71 (3H, s), 2.79 (1H, d, J = 9.2 Hz), 2.52–2.61 (1H, m), 2.19 (1H,

ddd, $J = 9.2, 7.0, 4.3$ Hz), 1.94 (1H, ddd, $J = 14.4, 6.0, 4.3$ Hz), 1.78 (1H, ddd, $J = 14.4, 7.0, 7.0$ Hz), 1.51 (3H, dd, $J = 6.7, 1.6$ Hz), 1.24 (3H, d, $J = 6.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 174.5, 157.7, 134.4, 133.3, 132.7, 127.5, 122.0, 115.1, 112.8, 55.2, 52.3, 35.6, 30.7, 29.8, 26.9, 25.6, 22.3, 18.6$; HRMS (APCI): Calcd. for $\text{C}_{18}\text{H}_{23}\text{O}_3$ (MH^+) 287.1642, found 287.1643.



(S)-4-((1R,4S)-7-Methoxy-4-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)pentan-1-ol:² The purified mixture of **22a**, **23a** and **24a** (4.14 g, from the $\text{Rh}_2(\text{R-DOSP})_4$ -catalyzed reaction, Table 4, entry 1) was taken up in 100 mL of ethyl acetate and transferred to a Parr hydrogenation bottle containing 5% Pd/C (1.80 g, 90 mg of Pd, 0.85 mmol). The vessel was purged with H_2 . The reaction was shaken under H_2 atmosphere (35 psi) for 12 h at rt, then filtrated on a short plug of silica gel. The plug was washed with ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane:ethyl acetate 95:5) to yield 1.38 g (28% over 2 steps from **13**) of the C–H activation/Cope rearrangement product. The latter (200 mg, 0.7 mmol) was dissolved in 5 mL of THF and cooled to 0°C . The reaction vessel was purged with argon and LiAlH_4 (50 mg, 1.4 mmol) was added portionwise to the stirring solution against positive argon pressure. The reaction was stirred for 0.5 h, quenched slowly with H_2O (10 mL), followed by 10% HCl (5 mL). The aqueous layer was extracted with ether (3 x 10 mL). The organic extracts were combined and dried with MgSO_4 , filtered and evaporated under reduced pressure. The crude product was purified on silica gel (hexane:ethyl acetate 60:40) to give 160 mg (87%) of the titled compound. Colorless oil; IR (neat): $\nu = 2927, 1607, 1491, 1279, 1237, 1051, 804$; ^1H NMR (500 MHz, CDCl_3): $\delta = 7.17$ (1H, d, $J = 8.5$ Hz), 6.77 (1H, d, $J = 2.5$ Hz), 6.71 (1H, dd, $J = 8.5, 2.5$ Hz), 3.79 (3H, s), 3.69 (2H, t, $J = 6.5$ Hz), 2.86–2.92 (1H, m), 2.65–2.74 (1H, m), 2.08–2.16 (1H, m), 1.89–1.95 (1H, m), 1.78–1.84 (1H, m), 1.60–1.73 (2H, m), 1.44–1.58 (3H, m), 1.28–1.41 (2H, m), 1.26 (3H, d, $J = 6.5$ Hz), 0.66 (3H, d, $J = 6.5$ Hz); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 157.5, 141.2, 135.9, 127.5, 112.9, 110.8, 63.3, 55.2, 42.1, 37.3, 32.5, 31.8, 31.2(2\text{C}), 21.9, 21.6, 14.5$; HRMS (EI): Calcd. for $\text{C}_{17}\text{H}_{26}\text{O}_2$ (M^+) 262.1927, found

262.1937; $[\alpha]_D^{20} +76.7$ (c 1.1, CHCl_3); HPLC analysis: 81% ee (Chiralcel OJ, 0.5% *i*-PrOH in hexane, 0.8 mL/min, $\lambda = 254$ nm, $t_R = 29.9$ min, 47.9 min).



Methyl 2-(6-methoxy-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)pentanoate (**27**):

Typical experimental procedure for hydrogenation of 24a epimers: In a Parr hydrogenation bottle was added *epi*-**24a** (Table 4, entry 2) (29 mg, 0.1 mmol), 30 mL of ethyl acetate and 5% Pd/C (32 mg, 1.6 mg of Pd, 0.015 mmol). The vessel is purged with H_2 . The reaction mixture was shaken under H_2 atmosphere (40 psi) for 18 h, then filtrated on a short plug of silica gel. The plug was washed with ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane:ether 98:2–96:4) to yield 18 mg (62%) of the titled compound.

epi-**27** (Table 4, entry 2): 62% yield (18 mg); colorless oil; $R_f = 0.58$ (hexane:ethyl acetate 80:20); IR (neat): $\nu = 2956, 2933, 2871, 1730$; ^1H NMR (400 MHz, CDCl_3): $\delta = 7.24$ (1H, d, $J = 8.7$ Hz), 6.69 (1H, dd, $J = 8.7, 2.9$ Hz), 6.54 (1H, d, $J = 2.9$ Hz), 3.76 (3H, s), 3.37 (3H, s), 2.77 (1H, dd, $J = 12.1, 2.9$ Hz), 2.62–2.74 (2H, m), 2.19 (1H, ddd, $J = 13.5, 10.8, 3.0$ Hz), 1.88–1.96 (1H, m), 1.62–1.77 (2H, m), 1.54–1.61 (1H, m), 1.43–1.52 (1H, m), 1.31 (3H, s), 1.14–1.30 (2H, m), 0.90 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 175.9, 157.3, 138.8, 135.2, 129.1, 113.3, 111.7, 55.6, 55.3, 50.9, 39.1, 33.2, 30.8, 30.1, 28.4, 22.0, 19.6, 14.3$; HRMS (APCI): Calcd. for $\text{C}_{18}\text{H}_{27}\text{O}_3$ (MH^+) 291.1955, found 291.1956.

27 (Table 4, entry 1): 5% yield (250 mg) (yield over 2 steps from **13**); colorless oil; $R_f = 0.57$ (hexane:ethyl acetate 80:20); IR (neat): $\nu = 2957, 2871, 2837, 1732, 1501$; ^1H NMR (500 MHz, CDCl_3): $\delta = 7.13$ (1H, d, $J = 8.9$ Hz), 6.71 (1H, dd, $J = 8.9, 2.4$ Hz), 6.58 (1H, d, $J = 2.4$ Hz), 3.77 (3H, s), 3.65 (3H, s), 2.85 (1H, dd, $J = 11.8, 2.3$ Hz), 2.65–2.76 (2H, m), 2.00 (1H, ddd, $J = 13.6, 10.9, 2.9$ Hz), 1.80–1.87 (1H, m), 1.64–1.74 (2H, m), 1.58 (1H, ddd, $J = 13.6, 6.6, 2.6$ Hz), 1.28 (3H, s), 1.15–1.24 (1H, m), 1.04–1.14 (1H, m), 0.93–1.02 (1H, m), 0.79 (3H, t, $J = 7.3$ Hz);

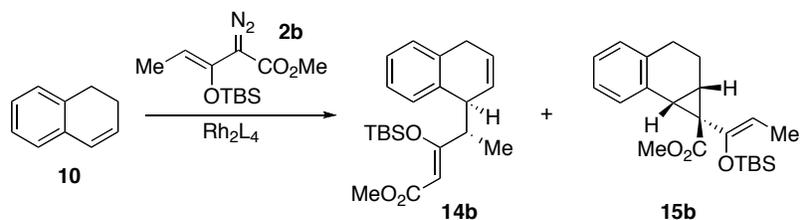
^{13}C NMR (125 MHz, CDCl_3): $\delta = 175.7, 157.1, 138.9, 135.1, 127.3, 113.3, 112.3, 55.7, 55.0, 51.0, 39.2, 32.3, 30.9, 30.1, 29.3, 21.6, 19.5, 13.8$; HRMS (EI): Calcd. for $\text{C}_{18}\text{H}_{26}\text{O}_3$ (M^+) 290.1876, found 290.1880; $[\alpha]_{\text{D}}^{20} -14.8$ (c 3.09, CHCl_3); HPLC analysis: 98% ee (Chiralcel OJ, 0.4% *i*-PrOH in hexane, 0.4 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 15.10$ min, 17.12 min).

Procedures for reactions with (*Z*)-methyl 3-(*tert*-butyldimethylsilyloxy)-2-diazopent-3-enoate (2b**) and 1,2-dihydronaphthalenes.**

(*S,Z*)-Methyl 3-(*tert*-butyldimethylsilyloxy)-4-((*S*)-1,4-dihydronaphthalen-1-yl)pent-2-enoate (14b**) and (1*R*,1*aS*,7*bS*)-methyl 1-((*Z*)-1-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-1*a*,2,3,7*b*-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (**15b**):**

(Table 1, entry 3): **2b** (270 mg, 1 mmol, 1 equiv.) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **10** (390 mg, 3 mmol, 3 equiv.) and $\text{Rh}_2(\text{S-DOSP})_4$ (19 mg, 0.01 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **14b** and **15b** (272 mg, 73% combined yield).

(Table 1, entry 4): **2b** (270 mg, 1 mmol, 1 equiv.) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **10** (390 mg, 3 mmol, 3 equiv.) and $\text{Rh}_2(\text{S-PTAD})_4$ (16 mg, 0.01 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **14b** and **15b** (291 mg, 78% combined yield).



14b: Colorless oil; $R_f = 0.56$ (pentane:ether 80:20); IR (neat): $\nu = 1723, 1626, 1201, 1161, 1080, 839, 825, 782, 747$; ^1H NMR (500 MHz, C_6D_6): $\delta = 7.31$ (1H, d, $J = 7.5$ Hz), 7.10 (1H, t, $J = 7.5$

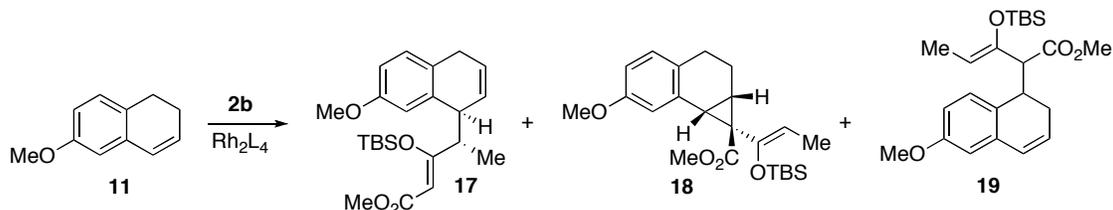
Hz), 7.04 (1H, t, $J = 7.0$ Hz), 6.91 (1H, d, $J = 7.5$ Hz), 5.80 (2H, s), 5.33 (1H, s), 4.12–4.18 (1H, m), 3.44 (3H, s), 2.98–3.13 (2H, m), 2.71–2.73 (1H, m), 1.08 (9H, s), 0.64 (3H, d, $J = 7.0$ Hz), 0.45 (3H, s), 0.30 (3H, s); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 169.1, 164.9, 136.8, 135.0, 128.0, 126.8, 126.7, 125.9, 125.6, 124.1, 98.3, 49.4, 48.4, 40.6, 29.5, 25.5, 18.3, 10.8, -4.2, -4.4$; HRMS (ESI) Calcd. for $\text{C}_{22}\text{H}_{33}\text{O}_3\text{Si}$ (MH^+) 373.2193, found 373.2196; $[\alpha]_{\text{D}}^{20} -92.1$ (c 1.12, CHCl_3) for 88 % ee; HPLC analysis: 88% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 45% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.2% *i*-PrOH in hexane, 0.5 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 10.3$ min (major), 12.2 min (minor)).

15b: Colorless oil; $R_f = 0.52$ (pentane:ether 80:20); IR (neat): $\nu = 1721, 1675, 1494, 1472, 1462, 1435, 1334, 1305, 1239, 1203, 1160, 1076, 874, 837, 799, 779, 753$; ^1H NMR (500 MHz, CDCl_3): $\delta = 7.21\text{--}7.23$ (1H, m), $7.07\text{--}7.12$ (2H, m), $6.95\text{--}6.97$ (1H, m), 3.98 (1H, br s), 3.70 (3H, s), 2.78 (1H, d, $J = 9.0$ Hz), $2.57\text{--}2.64$ (1H, m), 2.50 (1H, dd, $J = 16.5, 7.0$ Hz), $2.25\text{--}2.31$ (2H, m), $1.88\text{--}1.95$ (1H, m), 1.25 (3H, d, $J = 6.0$ Hz), 0.91 (9H, br s), 0.14 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 173.9, 143.1, 136.4, 133.1, 129.9, 128.0, 126.2, 125.6, 110.7, 52.0, 38.9, 33.4, 28.3, 25.8, 25.6, 18.5, 18.4, 11.1, -4.3, -4.8$; HRMS (EI) Calcd. for $\text{C}_{22}\text{H}_{32}\text{O}_3\text{Si}$ (M^+) 372.2115, found 372.2113; $[\alpha]_{\text{D}}^{20} -22.6$ (c 0.72, CHCl_3) for 93% ee; HPLC analysis: 40% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 93% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 100% hexane, 0.8 mL/min, $\lambda = 230$ nm, $t_{\text{R}} = 11.8$ min (major), 14.3 min (minor)).

(*S,Z*)-Methyl 3-(*tert*-butyldimethylsilyloxy)-4-((*S*)-7-methoxy-1,4-dihydronaphthalen-1-yl)pent-2-enoate (17), (1*R*,1*aS*,7*bS*)-methyl 1-((*Z*)-1-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-6-methoxy-1*a*,2,3,7*b*-tetrahydro-1*H* cyclopropa[*a*]naphthalene-1-carboxylate (18) and (*Z*)-methyl 3-(*tert*-butyldimethylsilyloxy)-2-(6-methoxy-1,2-dihydronaphthalen-1-yl)pent-3-enoate (19):

(Table 2, entry 1): **2b** (270 mg, 1 mmol, 1 equiv.) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **11** (480 mg, 3 mmol, 3 equiv.) and $\text{Rh}_2(\text{S-DOSP})_4$ (19 mg, 0.01 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **17**, **18** and **19** (362 mg, 90% combined yield).

(Table 2, entry 2): **2b** (270 mg, 1 mmol, 1 equiv.) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **11** (480 mg, 3 mmol, 3 equiv.) and $\text{Rh}_2(\text{S-PTAD})_4$ (16 mg, 0.01 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **17**, **18** and **19** (330 mg, 82% combined yield).



17: Colorless oil; $R_f = 0.57$ (pentane:ether 80:20); IR (neat): $\nu = 1722, 1624, 1503, 1464, 1434, 1370, 1277, 1254, 1239, 1201, 1160, 1081, 1042, 968, 895, 837, 810, 782$; $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.03$ (1H, d, $J = 8.0$ Hz), 6.74–6.76 (2H, m), 6.07–6.09 (1H, m), 5.70–5.72 (1H, m), 5.11 (1H, s), 3.92–3.96 (1H, m), 3.78 (3H, s), 3.67 (3H, s), 3.23–3.34 (2H, m), 2.64–2.70 (1H, m), 1.05 (9H, s), 0.72 (3H, d, $J = 7.0$ Hz), 0.32 (3H, s), 0.28 (3H, s); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 169.6, 166.0, 158.0, 138.1, 129.2, 127.6, 127.5, 124.0, 112.6, 111.6, 98.7, 55.1, 50.5, 48.8, 41.1, 29.3, 26.0, 18.7, 11.4, -3.8, -4.0$; HRMS (EI) Calcd. for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{Si}$ (M^+) 402.2221, found 402.2219; $[\alpha]_D^{20} -53.2$ (c 0.54, CHCl_3) for 33% ee; HPLC analysis: 90% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 33% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.4% *i*-PrOH in hexane, 0.5 mL/min, $\lambda = 254$ nm, $t_R = 10.6$ min (major), 12.1 min (minor)).

18: Colorless oil; $R_f = 0.51$ (pentane:ether 80:20); IR (neat): $\nu = 1720, 1676, 1610, 1505, 1463, 1435, 1334, 1304, 1238, 1193, 1167, 1113, 1076, 1040, 866, 837, 779$; $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 6.87$ (1H, d, $J = 8.0$ Hz), 6.79 (1H, d, $J = 2.5$ Hz), 6.65 (1H, dd, $J = 8.0, 2.5$ Hz), 4.02 (1H, br s), 3.79 (3H, s), 3.70 (3H, s), 2.72 (1H, d, $J = 9.0$ Hz), 2.40–2.55 (2H, m), 2.24–2.30 (2H, m), 1.85–1.92 (1H, m), 1.26 (3H, br s), 0.91 (9H, br), 0.14 (3H, s), 0.08 (3H, s); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 173.9, 157.5, 143.1, 134.1, 128.8, 128.6, 115.0, 112.2, 110.4, 55.2, 52.0, 38.9, 33.6, 28.3, 25.7, 24.7, 18.8, 18.5, 11.1, -4.3, -4.7$; HRMS (EI) Calcd. for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{Si}$ (M^+) 402.2221, found 402.2228; $[\alpha]_D^{20} +26.0$ (c 0.64, CHCl_3) for 95% ee; HPLC analysis: 95% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.2% *i*-PrOH in hexane, 0.5 mL/min, $\lambda = 230$ nm, $t_R =$

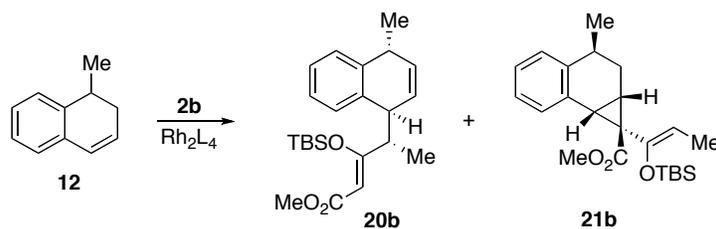
18.6 min (major), 21.2 min (minor)).

19: Colorless oil; $R_f = 0.56$ (pentane:ether 80:20); IR (neat): $\nu = 1738, 1668, 1603, 1572, 1496, 1432, 1344, 1261, 1204, 1186, 1146, 1091, 1048, 880, 837, 778, 704$; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.05$ (1H, d, $J = 8.6$ Hz), 6.59–6.64 (2H, m), 6.44 (1H, dd, $J = 9.3, 2.9$ Hz), 5.93 (1H, ddd, $J = 9.3, 6.4, 2.5$ Hz), 4.93 (1H, q, $J = 6.7$ Hz), 3.77 (3H, s), 3.43 (3H, s), 3.14–3.19 (2H, m), 2.52 (1H, dd, $J = 16.9, 6.4$ Hz), 2.35–2.41 (1H, m), 1.59 (3H, d, $J = 6.7$ Hz), 0.96 (9H, s), 0.13 (3H, s), 0.12 (3H, s); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 173.0, 158.7, 147.4, 134.4, 129.6, 128.3, 127.6, 127.3, 111.74, 111.71, 104.6, 55.2, 54.6, 51.4, 38.8, 26.2, 25.9, 18.3, 11.1, -3.9, -4.2$; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{SiNa}$ (MNa^+) 425.2119, found 425.2122; $[\alpha]_{\text{D}}^{20} +16.9$ (c 0.10, CHCl_3) for 90% ee; HPLC analysis: 90% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 45% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.1 % *i*-PrOH in hexane, 0.5 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 48.4$ min (major), 65.6 min (minor)).

(*S,Z*)-Methyl 3-(*tert*-butyldimethylsilyloxy)-4-((1*S*,4*R*)-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (20b) and (1*R*,1*aS*,3*S*,7*bS*)-methyl 1-((*Z*)-1-(*tert*-butyldimethylsilyloxy)-prop-1-enyl)-3-methyl-1*a*,2,3,7*b*-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (21b):

(Table 3, entry 3): **2b** (540 mg, 2 mmol, 4 equiv.) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **12** (73 mg, 0.5 mmol, 1 equiv.) and $\text{Rh}_2(\text{S-DOSP})_4$ (9 mg, 0.005 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **20b** and **21b** (112 mg, 58% combined yield).

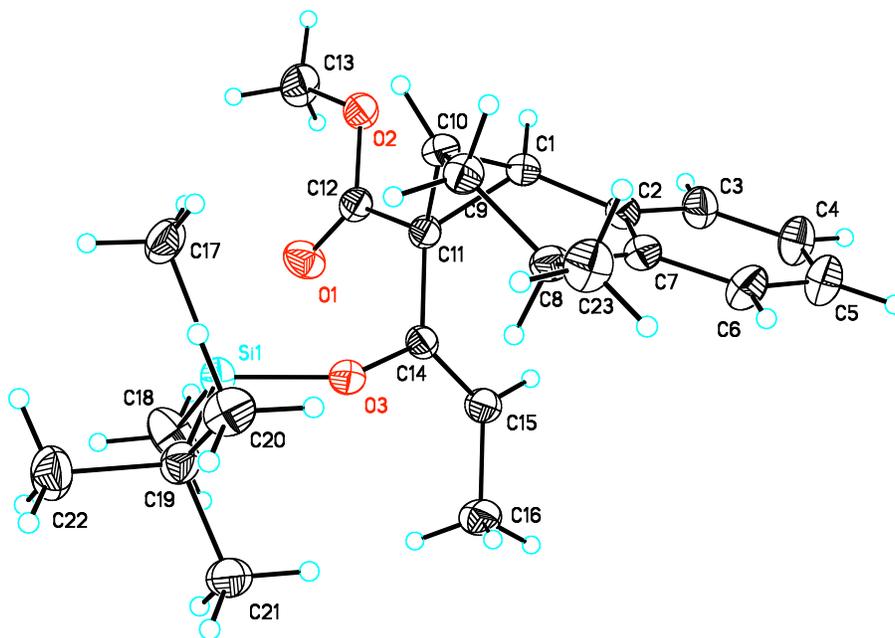
(Table 3, entry 4): **2b** (540 mg, 2 mmol, 4 equiv.) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **12** (73 mg, 0.5 mmol, 1 equiv.) and $\text{Rh}_2(\text{S-PTAD})_4$ (8 mg, 0.005 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **20b** and **21b** (174 mg, 90% combined yield).



20b: Colorless oil; $R_f = 0.67$ (pentane:ether 80:20); IR (neat): $\nu = 1721, 1624, 1250, 1202, 838, 778$; $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 7.27\text{--}7.31$ (1H, m), $7.18\text{--}7.24$ (3H, m), 5.91 (1H, ddd, $J = 10.2, 2.9, 1.6$ Hz), 5.67 (1H, ddd, $J = 10.2, 4.0, 2.4$ Hz), 5.12 (1H, s), $3.95\text{--}3.99$ (1H, m), 3.68 (3H, s), $3.37\text{--}3.45$ (1H, m), 2.72 (1H, dq, $J = 7.0, 4.1$ Hz), 1.35 (3H, d, $J = 7.3$ Hz), 1.04 (9H, s), 0.66 (3H, d, $J = 7.0$ Hz), 0.31 (3H, s), 0.29 (3H, s); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 169.7, 166.0, 140.8, 136.4, 133.8, 127.3, 126.7, 126.3, 126.2, 122.7, 98.9, 50.6, 48.2, 40.2, 32.7, 26.0, 23.2, 18.7, 11.4, -3.7, -3.8$; HRMS (EI) Calcd. for $\text{C}_{23}\text{H}_{34}\text{O}_3\text{Si}$ (M^+) 386.2272, found 386.2283; $[\alpha]_D^{20} +70.8$ (c 0.68, CHCl_3) for 88% ee; HPLC analysis: 86% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 88% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 100% hexane, 0.25 mL/min, $\lambda = 254$ nm, $t_R = 27.7$ min (major), 33.0 min (minor)).

21b: White solid; mp = 100–102 °C; $R_f = 0.63$ (pentane:ether 80:20); IR (neat): $\nu = 1721, 1675, 1462, 1434, 1332, 1305, 1239, 1165, 1124, 1076, 837, 777, 755$; $^1\text{H NMR}$ (600 MHz, CDCl_3): $\delta = 7.23$ (1H, d, $J = 7.1$ Hz), $7.10\text{--}7.19$ (3H, m), 4.06 (1H, br s), 3.71 (3H, s), 2.79 (1H, d, $J = 9.1$ Hz), $2.64\text{--}2.72$ (1H, m), $2.24\text{--}2.28$ (2H, m), 1.66 (1H, ddd, $J = 14.6, 10.4, 4.6$ Hz), 1.26 (3H, d, $J = 6.7$ Hz), 1.24 (3H, d, $J = 6.7$ Hz), 0.91 (9H, s), 0.14 (3H, s), 0.08 (3H, s); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 174.0, 143.1, 141.3, 132.8, 130.2, 126.5, 125.5, 125.3, 110.8, 52.0, 39.2, 33.8, 28.7, 28.2, 27.3, 25.7, 20.1, 18.4, 11.0, -4.3, -4.7$; HRMS (EI) Calcd. for $\text{C}_{23}\text{H}_{34}\text{O}_3\text{Si}$ (M^+) 386.2272, found 386.2266; $[\alpha]_D^{20} -12.1$ (c 0.32, CHCl_3) for 96% ee; HPLC analysis: 53% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 96% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 100% hexane, 0.25 mL/min, $\lambda = 254$ nm, $t_R = 39.5$ min (major), 44.0 min (minor)).

X-Ray crystal structure of **21b**

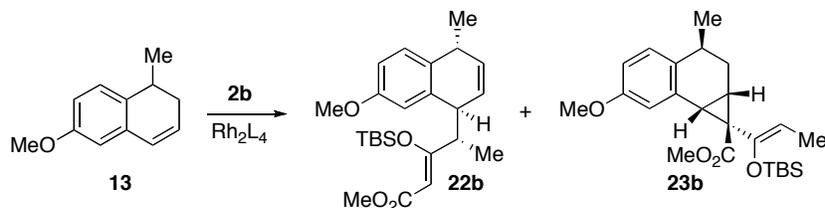


(*S,Z*)-Methyl 3-(*tert*-butyldimethylsilyloxy)-4-((1*S*,4*R*)-7-methoxy-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (**22b**) and (1*R*,1*aS*,6*S*,7*aS,Z*)-methyl 1-(1-(*tert*-butyldimethylsilyloxy)prop-1-enyl)-3-methoxy-6-methyl-1*a*,6,7,7*a*-tetrahydro-1*H* cyclopropa[*a*]naphthalene-1-carboxylate (**23b**):

(Table 4, entry 3): **2b** (811 mg, 3 mmol, 3 equiv.) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **13** (174 mg, 1 mmol, 1 equiv.) and Rh₂(*S*-DOSP)₄ (19 mg, 0.01 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **22b** and **23b** (229 mg, 55% combined yield).

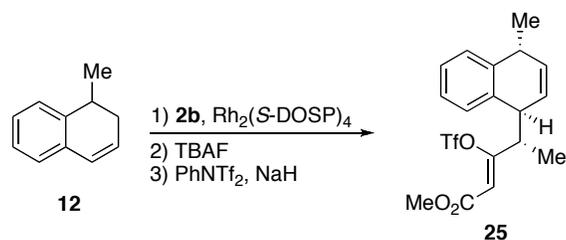
(Table 4, entry 4): **2b** (811 mg, 3 mmol, 3 equiv.) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **13** (174 mg, 1 mmol, 1 equiv.) and Rh₂(*S*-PTAD)₄ (16 mg, 0.01 mmol, 0.01 equiv.) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of

additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **22b** and **23b** (375 mg, 90% combined yield).



22b: Colorless oil; $R_f = 0.61$ (pentane:ether 80:20); IR (neat): $\nu = 1723, 1625, 1253, 1202, 1163, 826, 781$; $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.20$ (1H, d, $J = 8.5$ Hz), 6.79 (1H, dd, $J = 8.5, 2.5$ Hz), 6.74 (1H, d, $J = 2.5$ Hz), 5.90 (1H, d, $J = 10.0$ Hz), 5.65 – 5.63 (1H, m), 5.11 (1H, s), 3.92 – 3.94 (1H, m), 3.79 (3H, s), 3.68 (3H, s), 3.30 – 3.40 (1H, m), 2.68 – 2.72 (1H, m), 1.32 (3H, d, $J = 7.0$ Hz), 1.05 (9H, s), 0.67 (3H, d, $J = 6.5$ Hz), 0.32 (3H, s), 0.28 (3H, s); $^{13}\text{C NMR}$ (75 MHz, C_6D_6): $\delta = 169.8, 165.6, 158.6, 137.9, 134.5, 133.2, 128.6, 122.7, 113.1, 111.7, 99.0, 54.7, 50.2, 48.9, 41.2, 32.5, 26.3, 23.5, 19.0, 11.4, -3.4, -3.9$; HRMS (EI) Calcd. for $\text{C}_{24}\text{H}_{36}\text{O}_4\text{Si}$ (M^+) 416.2377, found 416.2379; $[\alpha]_{\text{D}}^{20} -18.0$ (c 1.2, CHCl_3) for 88% ee; HPLC analysis: 85% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 88% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.2% *i*-PrOH in hexane, 0.5 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 11.7$ min (major), 16.5 min (minor)).

23b: Colorless oil; $R_f = 0.47$ (pentane:ether 80:20); IR (neat): $\nu = 1720, 1500, 1464, 1434, 1332, 1306, 1237, 1218, 1168, 1070, 1048, 860, 837, 800$; $^1\text{H NMR}$ (500 MHz, CDCl_3): $\delta = 7.10$ (1H, d, $J = 8.5$ Hz), 6.82 (1H, d, $J = 2.5$ Hz), 6.72 (1H, dd, $J = 8.5, 2.5$ Hz), 4.12 (1H, br s), 3.79 (3H, s), 3.72 (3H, s), 2.77 (1H, d, $J = 9.0$ Hz), 2.60 – 2.67 (1H, m), 2.24 – 2.30 (2H, m), 1.63 (1H, ddd, $J = 14.2, 10.7, 5.2$ Hz), 1.27 (3H, d, $J = 6.5$ Hz), 1.24 (3H, d, $J = 7.0$ Hz), 0.93 (9H, s), 0.17 (3H, s), 0.10 (3H, s); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): $\delta = 173.9, 157.2, 143.0, 134.0, 133.4, 126.1, 115.1, 112.1, 110.5, 55.0, 51.9, 39.1, 34.0, 28.5, 27.8, 27.5, 25.6, 20.1, 18.3, 11.0, -4.3, -4.8$; HRMS (EI) Calcd. for $\text{C}_{24}\text{H}_{36}\text{O}_4\text{Si}$ (M^+) 416.2377, found 416.2382; $[\alpha]_{\text{D}}^{20} +22.8$ (c 1.3, CHCl_3) for 96% ee; HPLC analysis: 59% ee with $\text{Rh}_2(\text{S-DOSP})_4$ and 96% ee with $\text{Rh}_2(\text{S-PTAD})_4$ (Chiralcel OD-H, 0.1% *i*-PrOH in hexane, 0.8 mL/min, $\lambda = 235$ nm, $t_{\text{R}} = 24.1$ min (minor), 34.8 min (major)).



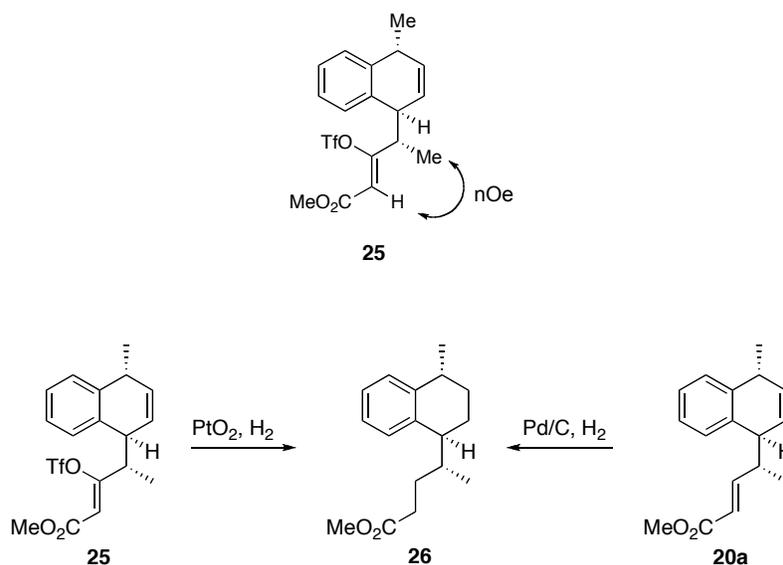
(S,Z)-Methyl 4-((1S,4R)-4-methyl-1,4-dihydronaphthalen-1-yl)-3-(trifluoromethylsulfonyl)pent-2-enoate (25):⁸ Diazo compound **2b** (1.08 g, 4 mmol, 4 equiv) in 10 mL of 2,2-DMB was added dropwise by syringe pump over 2 h to a solution of 1-methyl-1,2-dihydronaphthalene **12** (0.144g, 1 mmol, 1 equiv) and Rh₂(S-DOSP)₄ (0.038 g, 0.02 mmol, 0.02 equiv) in 10 mL of 2,2-DMB. The reaction mixture was stirred for an additional 14 h, then concentrated *in vacuo*. The crude was quickly purified by flash chromatography (hexane:ether 99:1 to 98:2) to yield 217 mg of a mixture of **20b** and **21b**. This mixture was dissolved in 10 mL of THF and cooled to 0 °C. TBAF (211 mg, 0.67 mmol, 1.2 equiv.) was added to the solution in one portion. After 0.7 h, the reaction was diluted with 30 mL of ether and 10 mL of distilled water. The aqueous layer was extracted with ether (3 x 30 mL). The organic extracts were combined and washed with 10 mL of distilled water and 10 mL of saturated aqueous NaCl, dried over MgSO₄, filtered and concentrated under vacuum. The crude was quickly purified by flash chromatography (hexane:ether 95:5 to 93:7) to yield 88 mg of a mixture of C–H activation/Cope rearrangement product and cyclopropane. The mixture was dissolved in 3 mL of dry THF and cooled to 0 °C. NaH (23 mg, 0.96 mmol) was added to the solution, followed 5 minutes later by PhNTf₂ (229 mg, 0.64 mmol). After 1 h, the cold bath was removed and the reaction allowed to reach rt. After 6 h, the reaction was diluted with 30 mL of ether and 10 mL of distilled water. The aqueous layer was extracted with ether (2 x 30 mL). The organic extracts were combined and washed with 5 mL of distilled water and 5 mL of saturated aqueous NaCl, dried over MgSO₄, filtered and concentrated under vacuum. The crude was purified by flash chromatography (hexane:ether 95:5 to 90:10) to yield 25 mg (12%, theoretical yield from *R*-**12**) of vinyl triflate **25**.

White solid; mp = 83–85 °C; *R*_f = 0.60 (hexane:ethyl acetate 80:20); IR (neat): ν = 3027, 2977, 2959, 2932, 1739, 1430, 1207; ¹H NMR (400 MHz, CDCl₃): δ = 7.29–7.32 (1H, m), 7.20–7.25 (2H, m), 7.14–7.17 (1H, m), 6.00 (1H, ddd, *J* = 10.3, 2.9, 1.4 Hz), 5.75 (1H, d, *J* = 1.3 Hz), 5.57

⁸ (a) Jigajinni, V. B.; Wightman, R. H. *Tetrahedron Lett.* **1982**, *23*, 117–120. (b) Martínez, A. G.; Alvarez, R. M.; Casado, M. M.; Subramanian, L. R.; Hanack, M. *Tetrahedron* **1987**, *43*, 275–279. (c) Comins, D. L.; Benjelloun, N. R. *Tetrahedron Lett.* **1994**, *35*, 829–832.

(1H, ddd, $J = 10.3, 4.1, 2.4$ Hz), 3.94–3.98 (1H, m), 3.82 (3H, s), 3.38–3.46 (1H, m), 3.02–3.08 (1H, m), 1.37 (3H, d, $J = 7.3$ Hz), 0.75 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 163.0, 161.3, 140.5, 135.5, 134.5, 127.4, 126.8, 126.7(2\text{C}), 120.8, 118.5$ (q, $J = 320$ Hz), 111.6, 52.1, 45.7, 39.6, 32.6, 23.1, 11.2; ^{19}F NMR (375 MHz, CDCl_3): $\delta = -74.6$; HRMS (APCI): Calcd. for $\text{C}_{18}\text{H}_{20}\text{O}_5\text{F}_3\text{S}$ (MH^+) 405.0978, found 405.0979.

Double bond geometry was assigned based on NMR studies. Key irradiation is shown bellow.



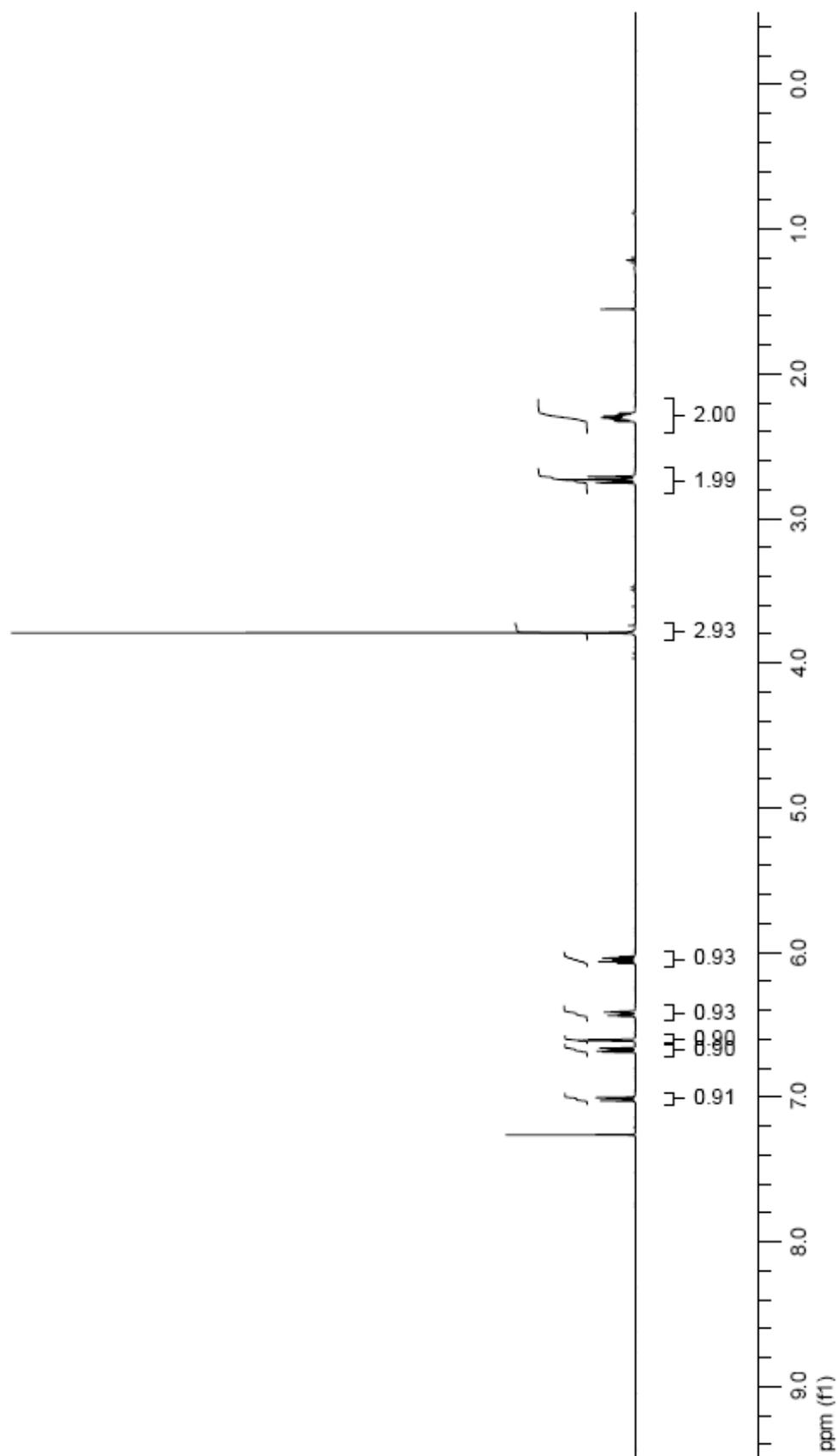
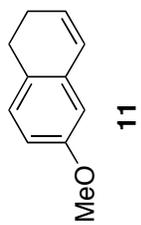
(*R*)-Methyl 4-((1*S*,4*R*)-4-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)pentanoate (26):⁸

From vinyl triflate **25**: In a Parr hydrogenation bottle was added vinyl triflate **25** (7 mg, 0.017 mmol), 20 mL of MeOH, PtO_2 (1.2 mg, 0.0051 mmol) and Li_2CO_3 (2.5 mg, 0.034 mmol). The vessel was purged with H_2 . The mixture was shaken under H_2 atmosphere (30 psi) for 14 h at rt, then diluted with 40 mL of ether and 20 mL of distilled water. The aqueous layer was extracted with ether (3 x 40 mL). The combined organic extracts were washed with 10 mL of distilled water and 10 mL saturated aqueous NaCl, dried over MgSO_4 , filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane:ether 99:1) to yield 4 mg (90%) of **26**.

From **20a**:⁸ In a Parr hydrogenation bottle was added **20a** (14 mg, 0.055 mmol), 30 mL of ethyl acetate, and 5% Pd/C (24 mg, 1.2 mg of Pd, 0.011 mmol). The vessel was purged with H_2 . The mixture was shaken under H_2 atmosphere (30 psi) for 13 h at rt, then filtrated on a short plug of

silica gel. The plug was washed with ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane:ether 99:1) to yield 12.5 mg (89%) of **26**.

Colorless oil; $R_f = 0.62$ (hexane:ethyl acetate 80:20); IR (neat): $\nu = 3022, 2954, 2930, 2869, 1738, 1168$; $^1\text{H NMR}$ (600 MHz, CDCl_3): $\delta = 7.23\text{--}7.26$ (1H, m), $7.17\text{--}7.21$ (1H, m), $7.11\text{--}7.15$ (2H, m), 3.70 (3H, s), $2.90\text{--}2.94$ (1H, m), $2.74\text{--}2.81$ (1H, m), $2.34\text{--}2.46$ (2H, m), $2.10\text{--}2.18$ (1H, m), $1.92\text{--}1.98$ (1H, m), $1.75\text{--}1.87$ (2H, m), $1.62\text{--}1.69$ (1H, m), $1.52\text{--}1.59$ (1H, m), $1.32\text{--}1.39$ (1H, m), 1.29 (3H, d, $J = 6.7$ Hz), 0.66 (3H, d, $J = 6.7$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 174.4, 143.3, 139.4, 127.4, 126.7, 125.5, 125.3, 51.6, 41.6, 36.9, 33.1, 32.6, 31.4, 30.2, 21.8, 21.5, 14.2$; HRMS (APCI): Calcd. for $\text{C}_{17}\text{H}_{25}\text{O}_2$ (MH^+) 261.1849, found 261.1849; $[\alpha]_{\text{D}}^{20} -36.5$ (c 0.97, CHCl_3); HPLC analysis: 93% ee ((S,S)-Whelk-O 1, 0.5% *i*-PrOH in hexane, 1 mL/min, $\lambda = 254$ nm, $t_{\text{R}} = 11.04$ min, 12.56 min).



DLV-17d6c13

Pulse Sequence: s2pu1

Solvent: CDCl3

Ambient temperature

CEMINT-300 "roesy.chem.buffalo.edu"

Relax. delay 5.000 sec

Pulse 90.0 degrees

Acq. time 1.706 sec

Width 18761.7 Hz

24 repetitions

OBSERVE C13, 75.4536899 MHZ

DECOUPLE H1, 300.0754431 MHZ

Power 1023 dB

continuously on

WALTZ-16 modulated

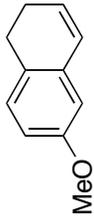
DATA PROCESSING

Line broadening 1.0 Hz

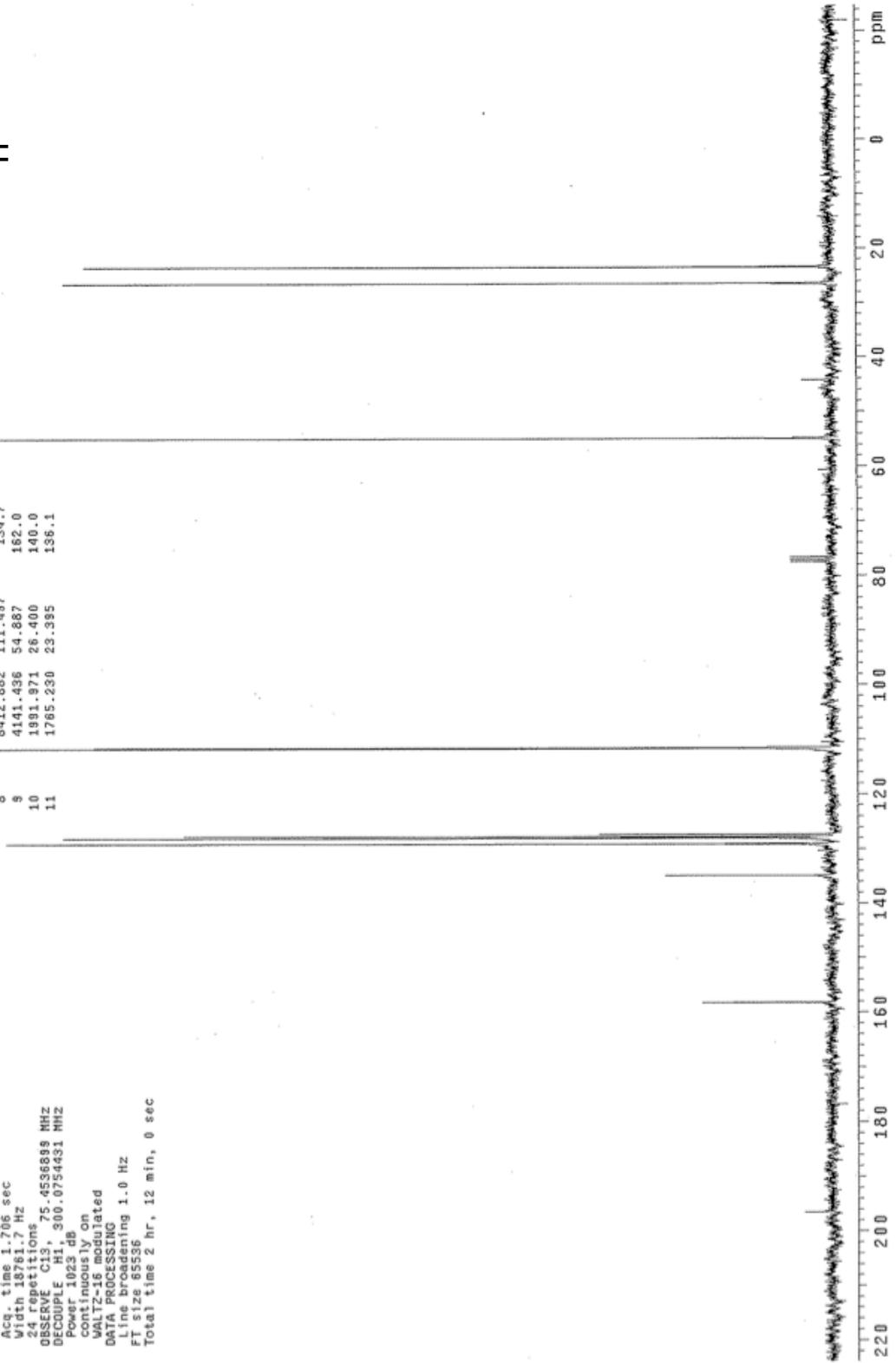
FT size 65536

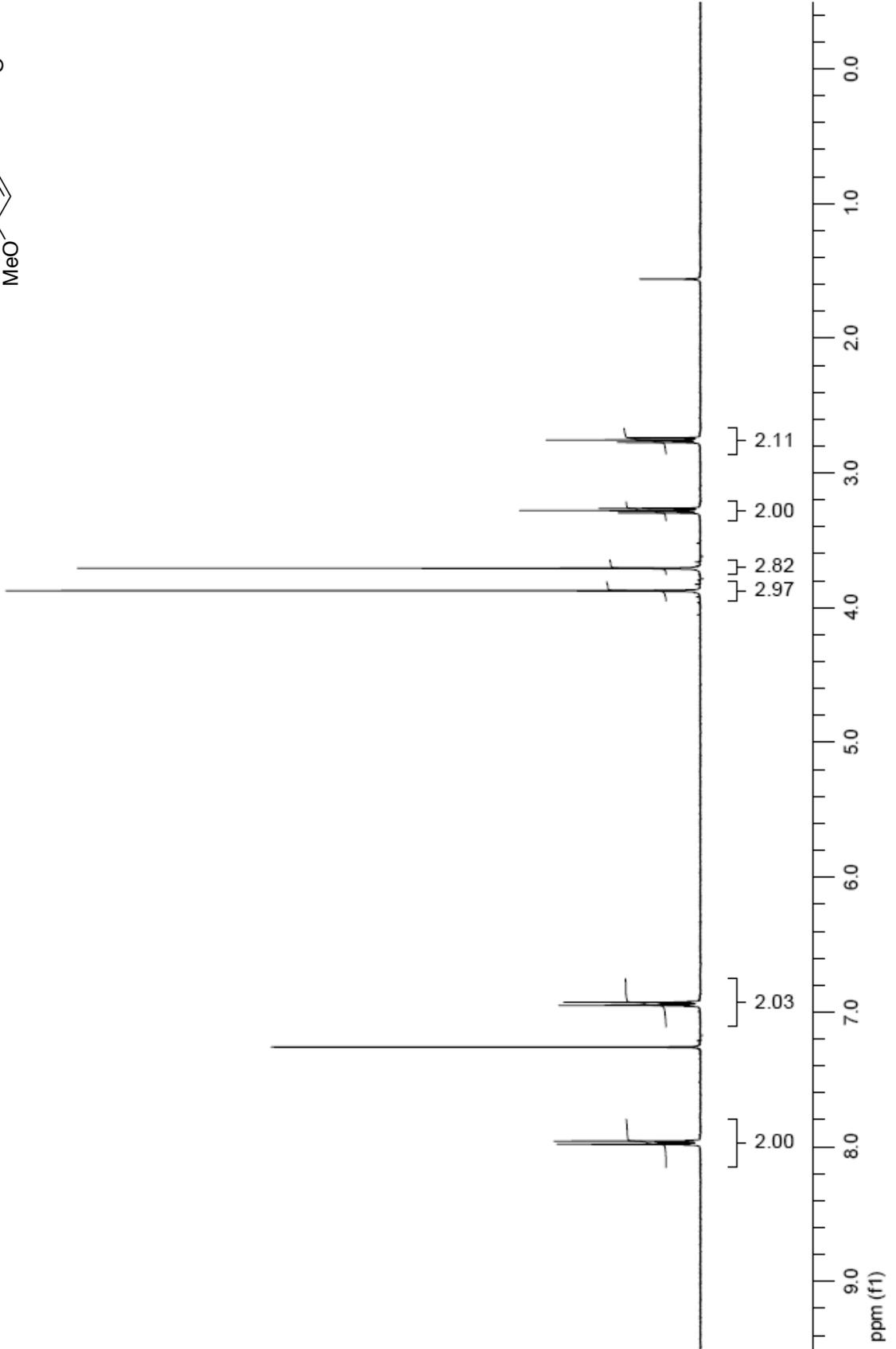
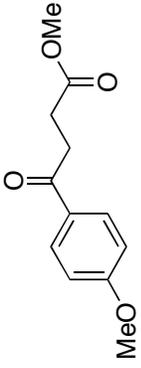
Total time 2 hr, 12 min, 0 sec

INDEX	FREQUENCY	PPM	HEIGHT
1	1194.248	158.167	23.4
2	10173.566	134.832	30.0
3	8733.824	129.004	150.6
4	8655.853	127.972	140.3
5	8634.195	127.684	118.4
6	8603.848	127.281	42.1
7	8422.044	111.619	154.1
8	8412.882	111.497	134.7
9	4141.436	54.887	162.0
10	1991.971	26.400	140.0
11	1785.230	23.395	136.1



11

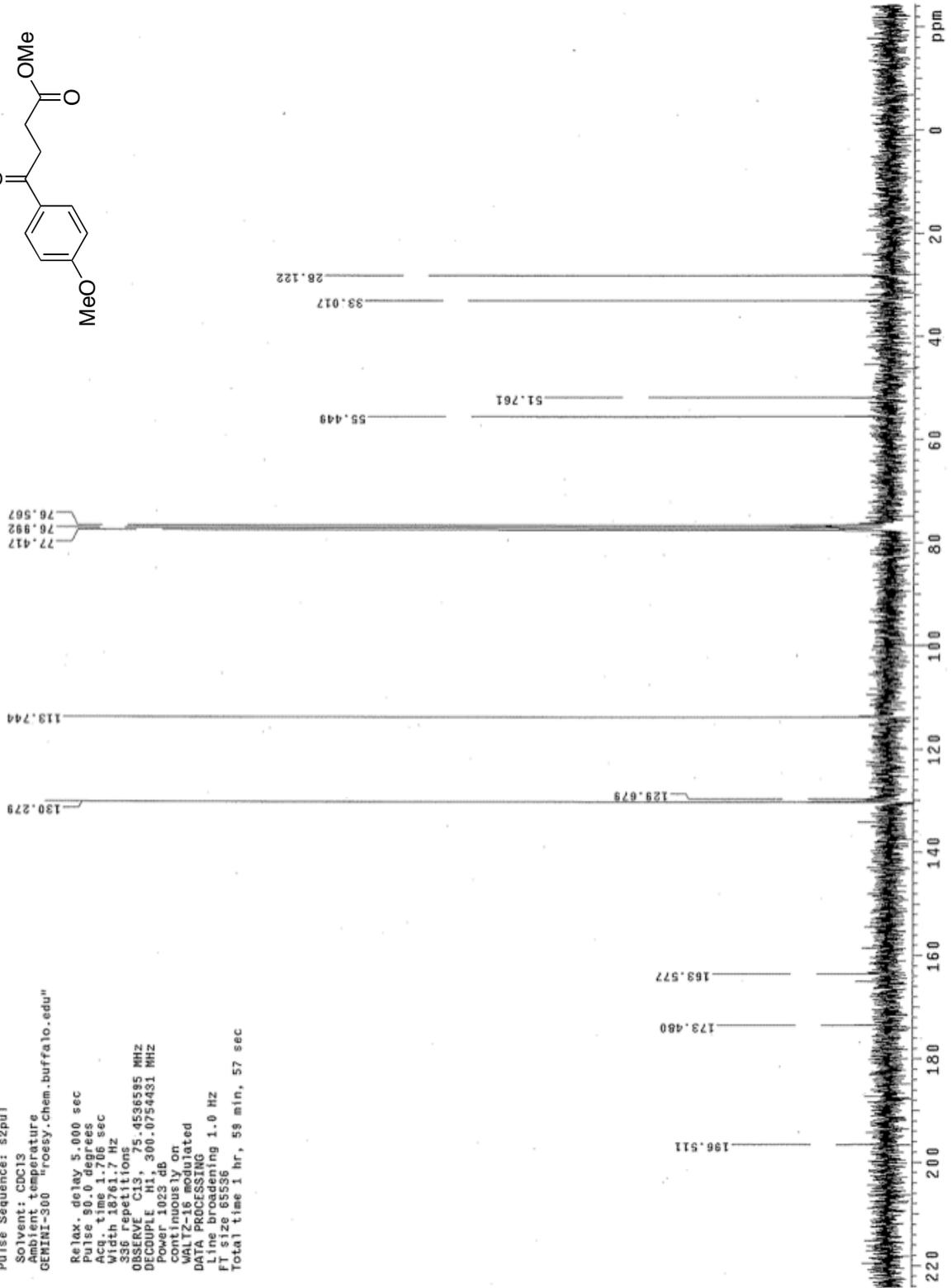
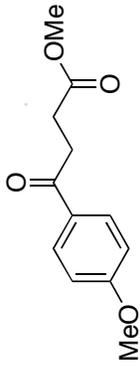




1JBOw4, c. 12
EST-10

Pulse Sequence: s2pu1
Solvent: CDCl3
Ambient temperature
GEMINI-300 "rossy.Chem.buffalo.edu"

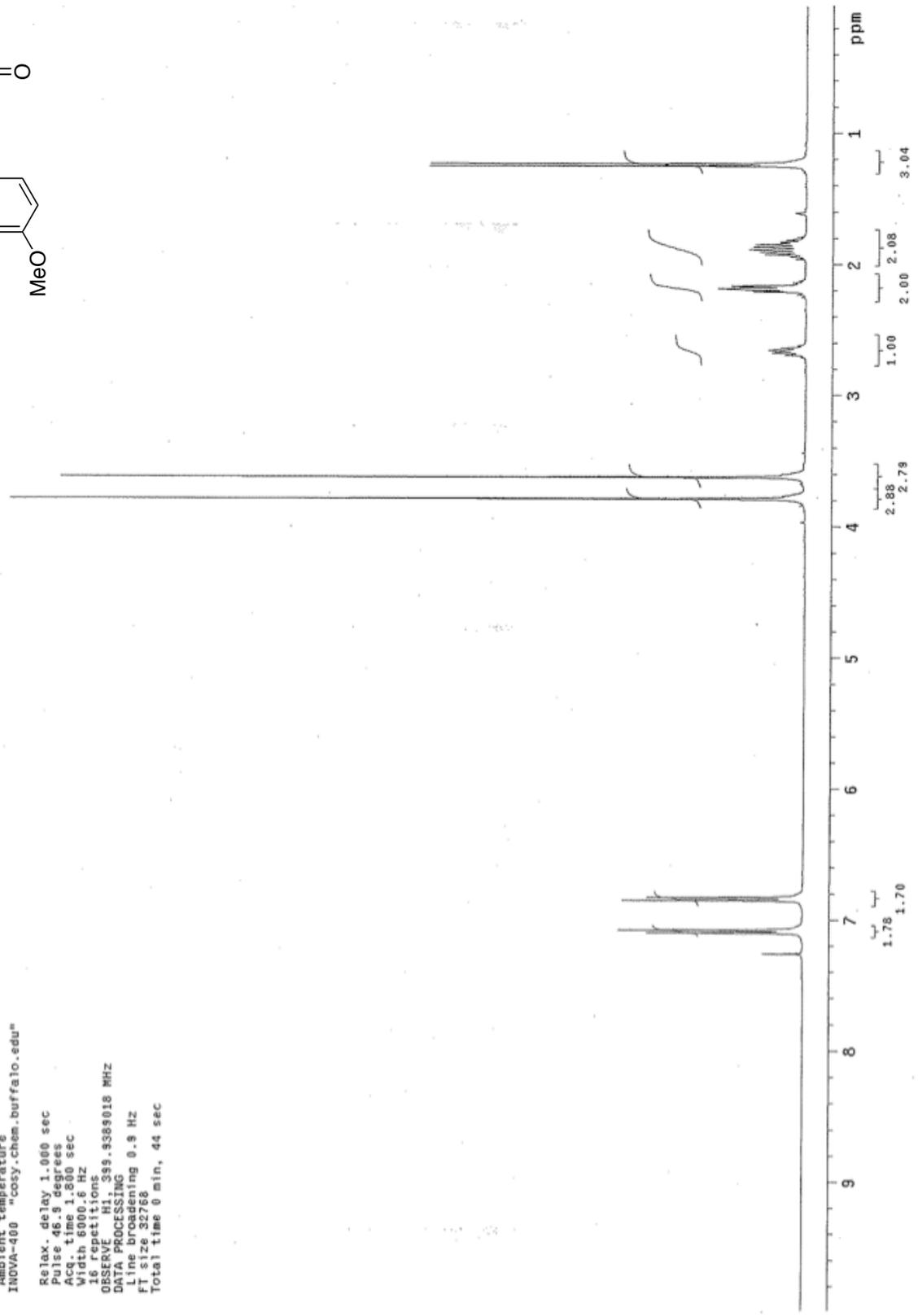
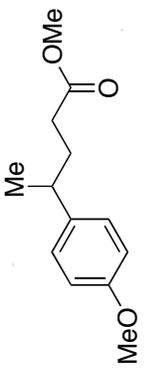
Relax. delay 5.000 sec
Pulse 90.0 degrees
Acq. time 1.766 sec
Width 18761.7 Hz
336 repetitions
OBSERVE C13, 75.4536595 MHz
DECOUPLE H1, 300.0754431 MHz
Power 1023 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
F1 size 65536
Total time 1 hr, 59 min, 57 sec



9jb066

Pulse Sequence: s2pu1
Solvent: CDCl3
Ambient temperature
INOVA-400 "cosy.chem.buffalo.edu"

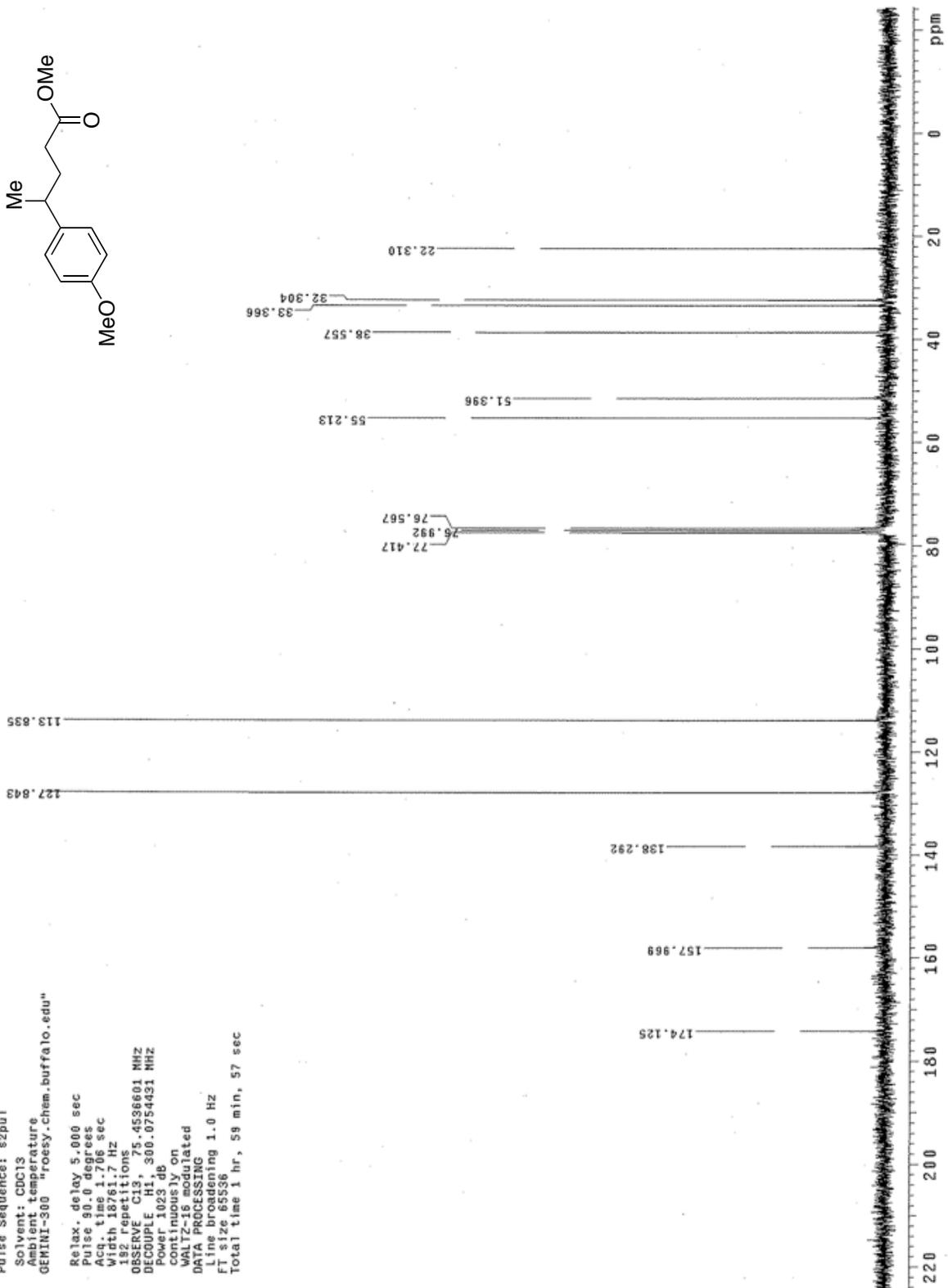
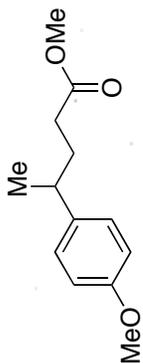
Relax. delay 1.000 sec
Pulse 46.9 degrees
Acq. time 1.800 sec
Width 6000.6 Hz
Observations
OPERATIONS
DATA PROCESSING 99.9389018 MHz
File processing 0.9 Hz
FT size 32768
Total time 0 min, 44 sec

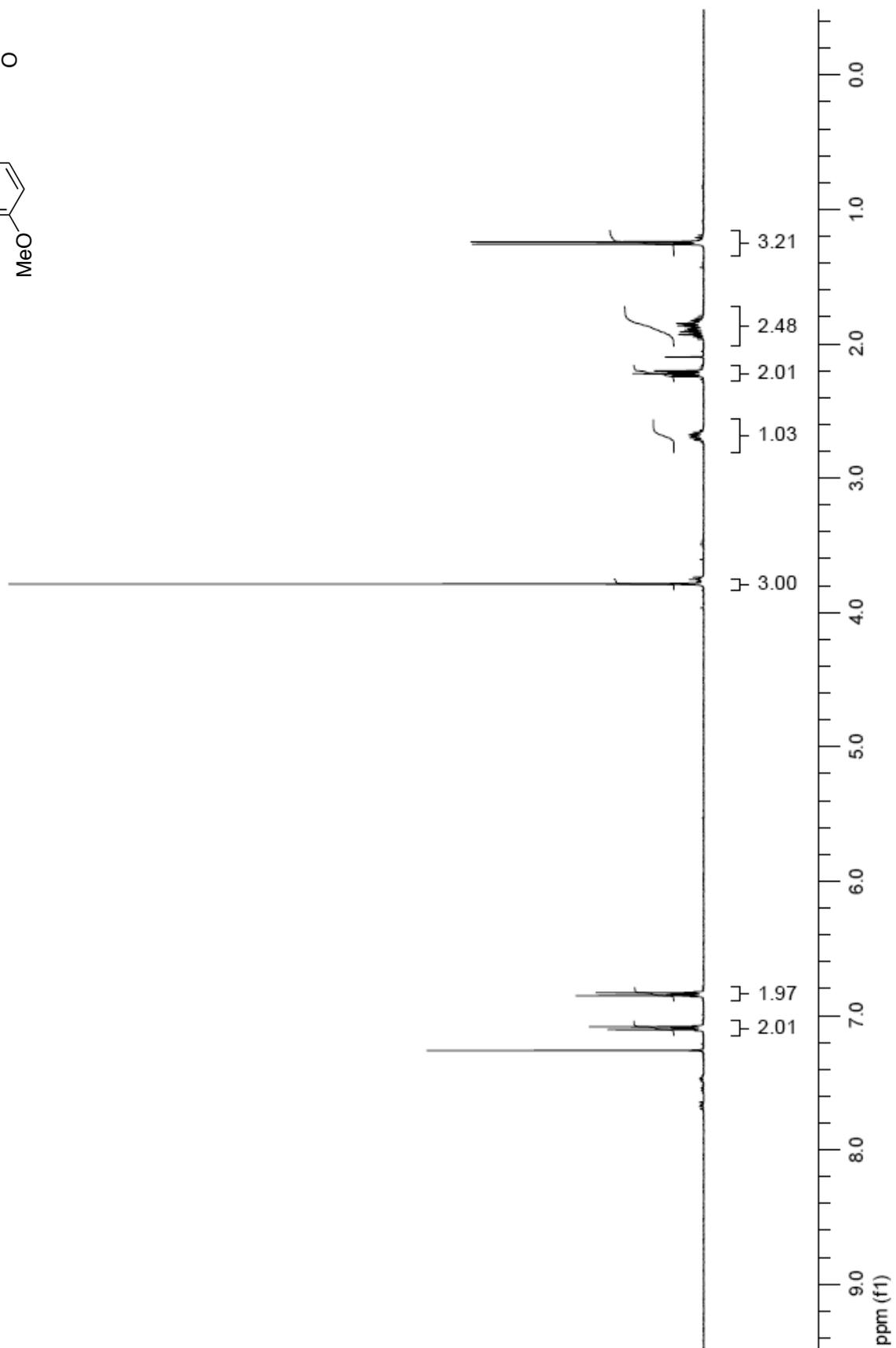
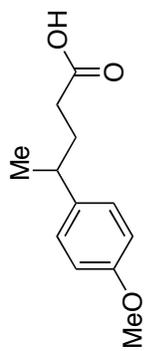


9Jb086.c13

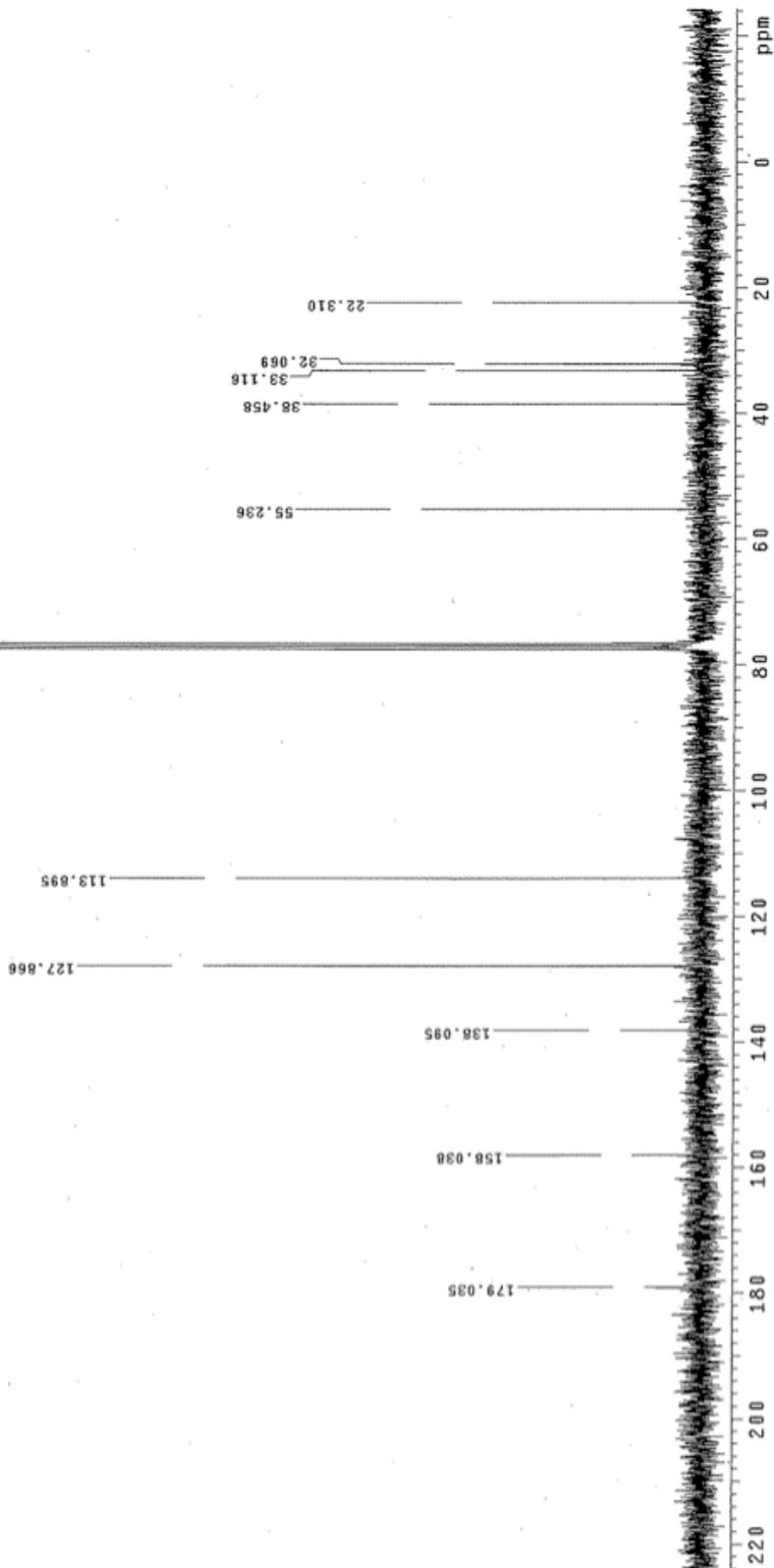
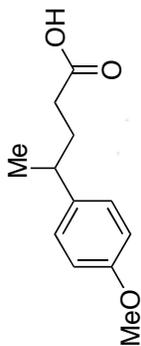
Pulse Sequence: s2pu1
Solvent: CDCl3
Acq. temperature
GENIUI-300 "roesy.Chem.buff@io.edu"

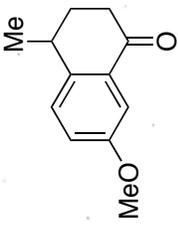
Relax. delay 5.000 sec
Pulse 90.0 degrees
Acq. time 1.706 sec
Width 18761.7 Hz
OBSERVED F1 F2 5.4586601 MHz
DECOUPLE F1, 300.0754431 MHz
Power 1023.48
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 59 min, 57 sec



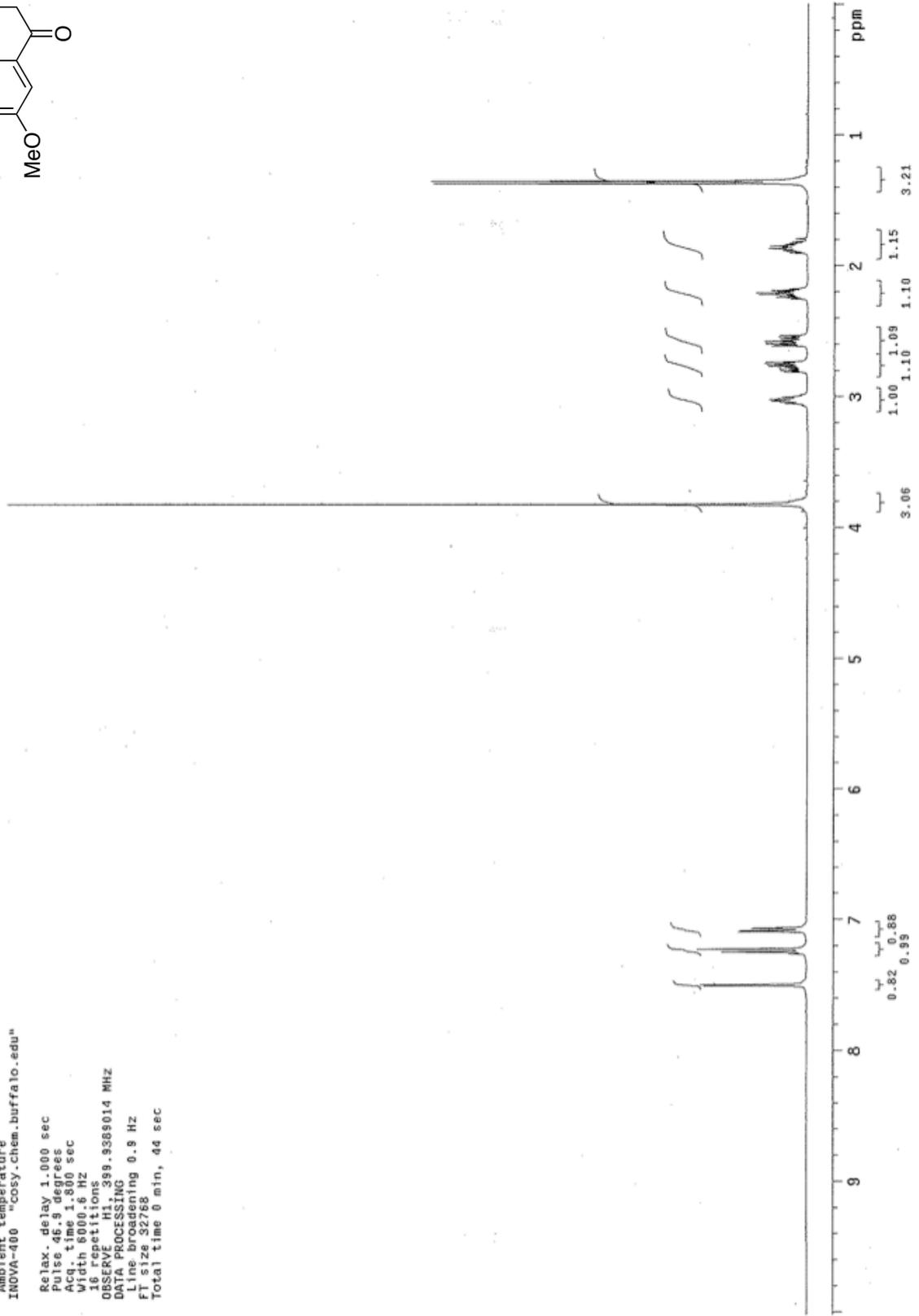


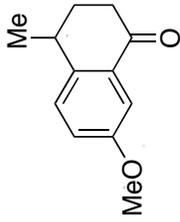
9jb067.c13
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 GEMINI-300 "roesy.chem.buffalo.edu"
 Relax_delay 5.000 sec
 Pulse_prog 2dhsqc
 Acq_time 1.295 sec
 Width 18761.7 Hz
 240 repetitions
 OBSERVE C13 75.4536589 MHz
 DECOUPLE H1 300.0754431 MHz
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 1 hr, 59 min, 57 sec



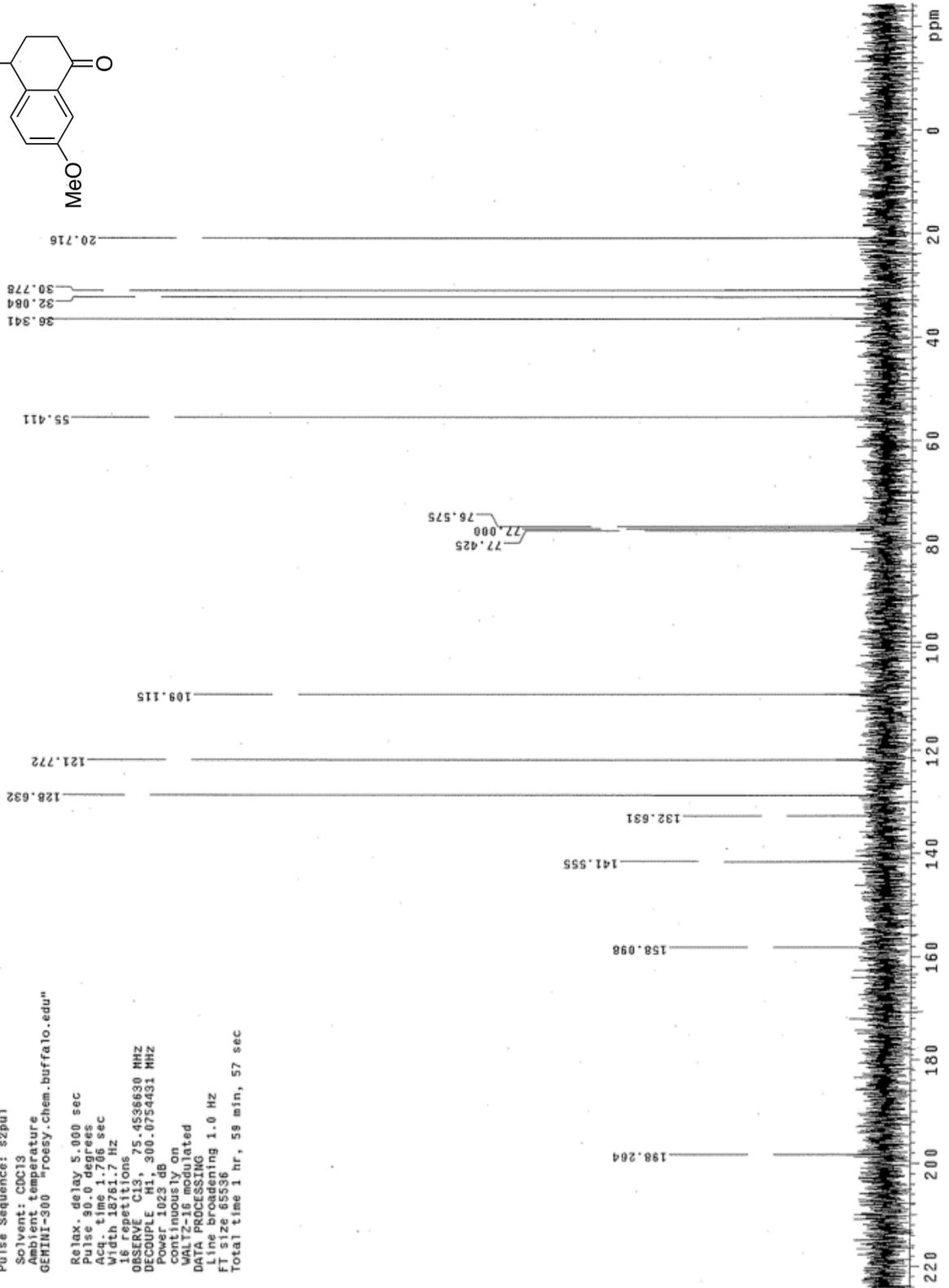


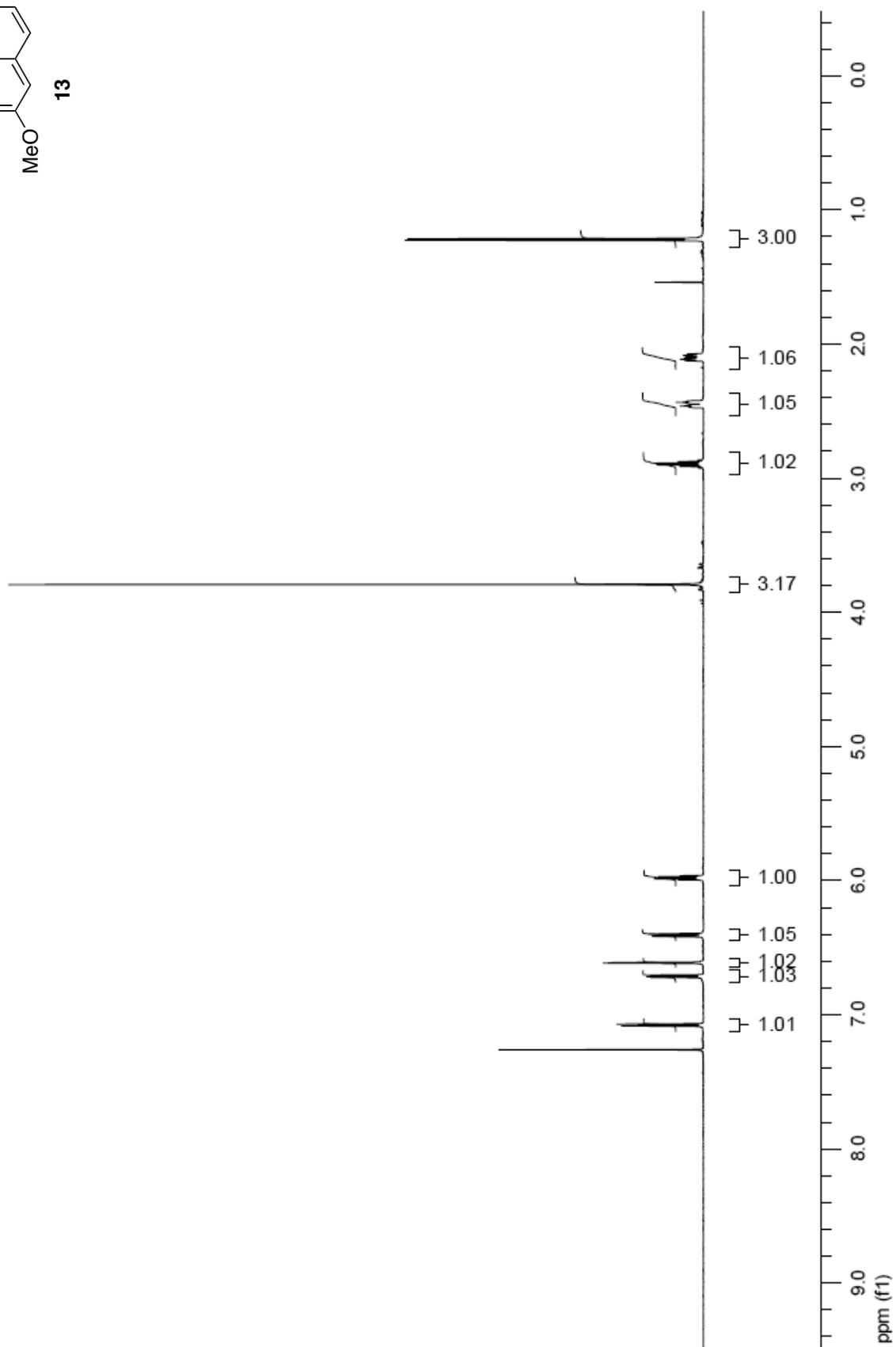
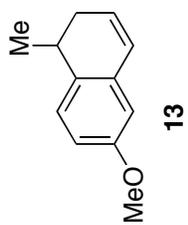
9Jb060
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 INOVA-400 "cosy.chem.buffalo.edu"
 Relax. delay 1.000 sec
 Pulse 46.9 degrees
 Acq. time 1.800 sec
 Width 6000.6 Hz
 16 repetitions
 OBSERVE H1, 399.9389014 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 32768
 Total time 0 min, 44 sec





9jb060.c13
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 GEMINI-300 "roesy.chem.buffalo.edu"
 Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.786 sec
 Width 18761.7 Hz
 16 repetitions
 OBSERVE C13 75.4536630 MHz
 DECOUPLE H1 300.0754431 MHz
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 1 hr, 59 min, 57 sec

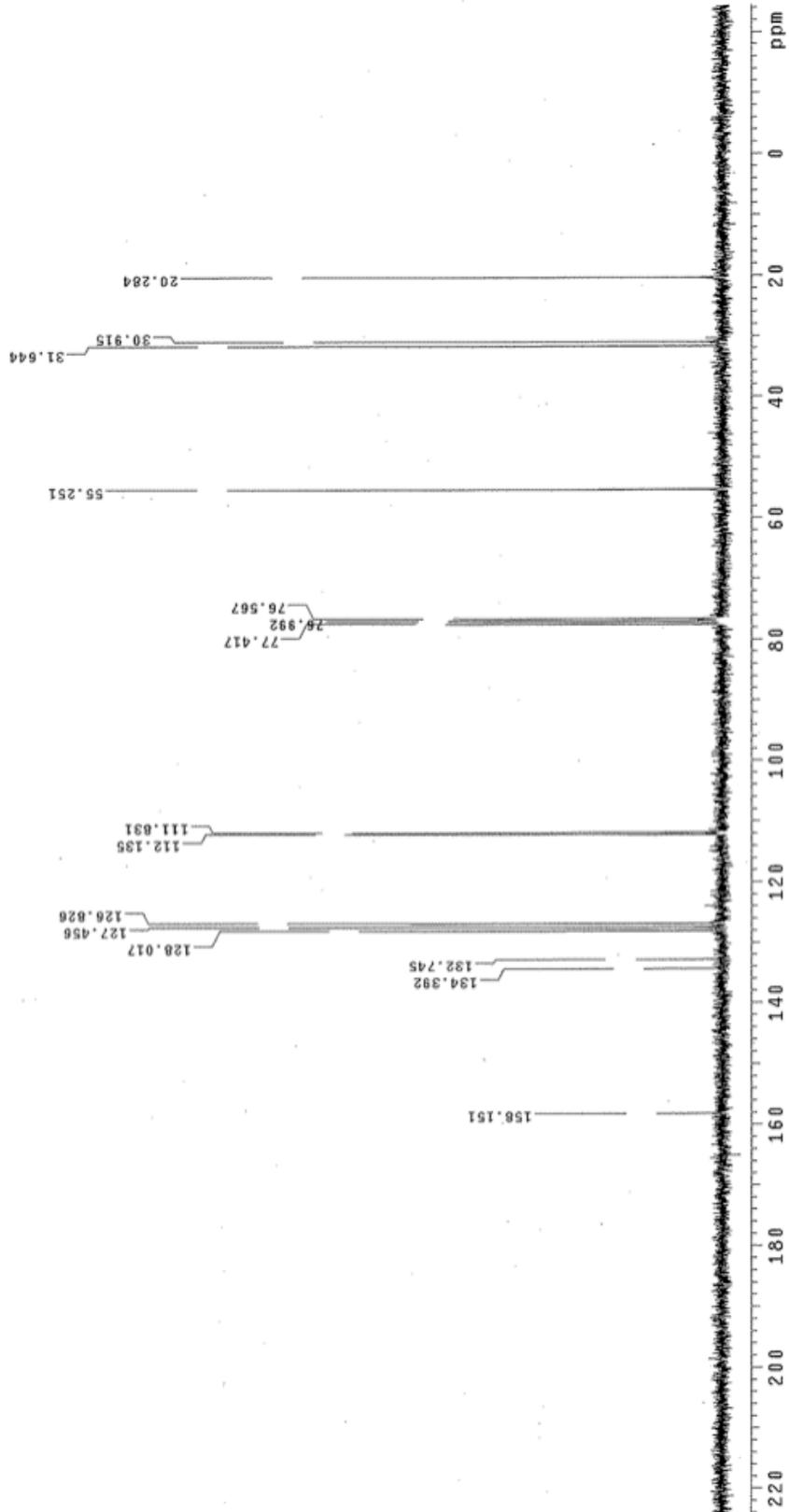
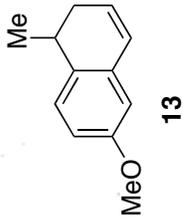


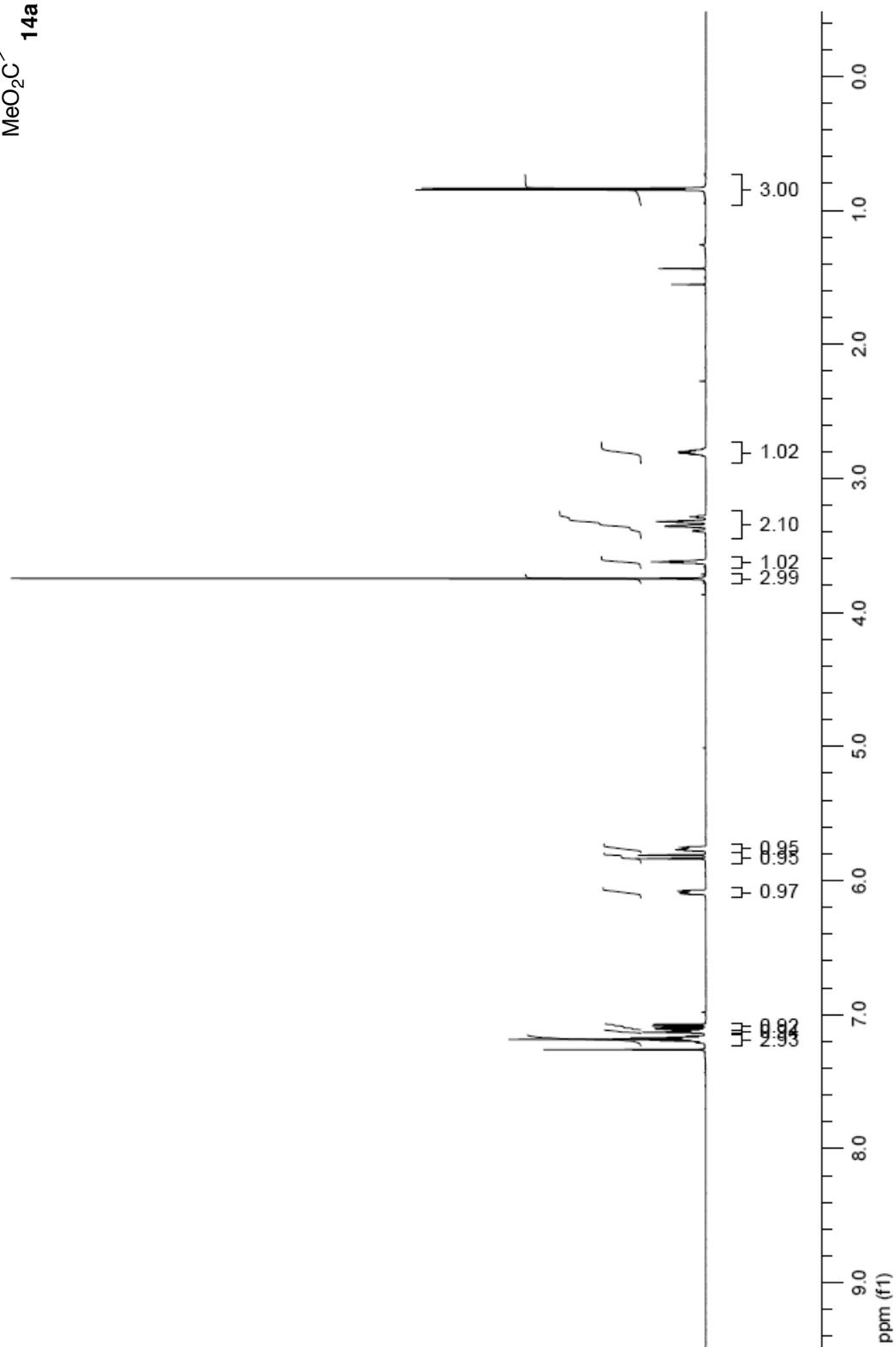
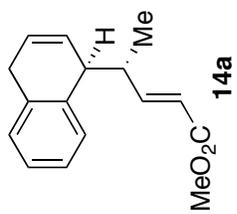


93b061.c13

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
GEMINI-300 "roesy.chem.buffalo.edu"

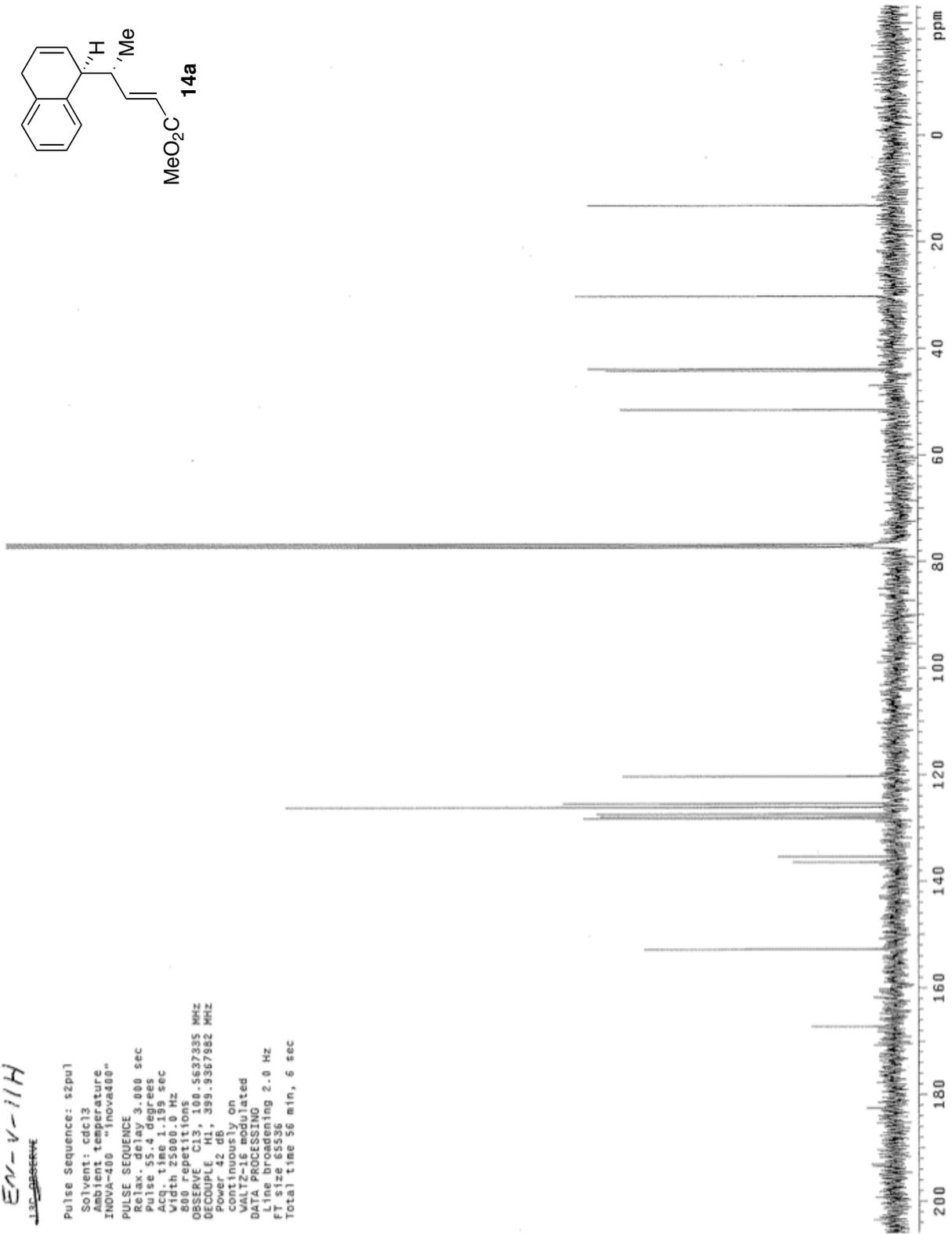
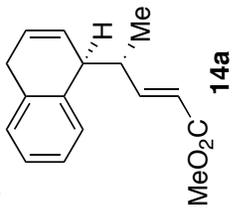
Relax. delay 5.000 sec
Pulse 90.0 degrees
Acq. time 1.706 sec
Width 18761.7 Hz
of repetitions 8
OBSERVE GAS, 75.4526607 MHz
DECOUPLE GAS, 800.0754431 MHz
Power 1823.1 dB
Channel 100 MHz
MAG2, 16 channels
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65556
Total time 1 hr, 59 min, 57 sec

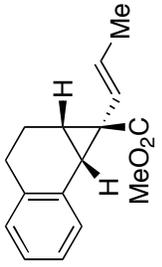




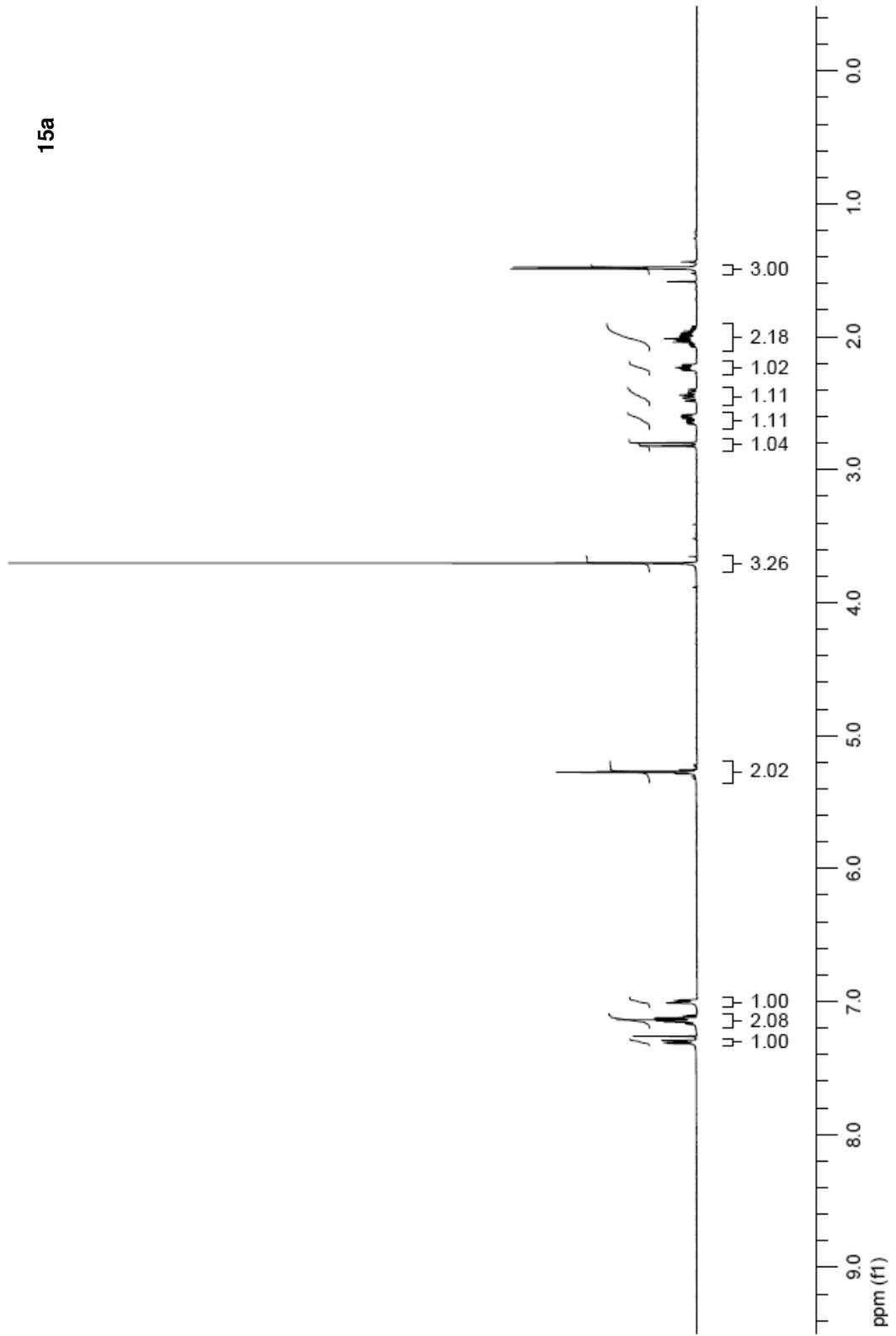
EN-V-11H
JSC OBSERVE

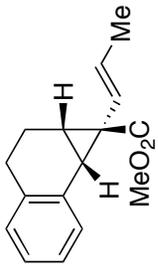
Pulse Sequence: s2pu1
Solvent: cdcl3
Ambient temperature
INOVA-400 "Inova400"
PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 55.4 degrees
Acq. time 1.195 sec
Width 25000.0 Hz
800 repetitions
OBSERVE CH3, 100.5627235 MHz
DECUPLE CH2, 399.3567982 MHz
acquire 42 dt
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 56 min, 6 sec



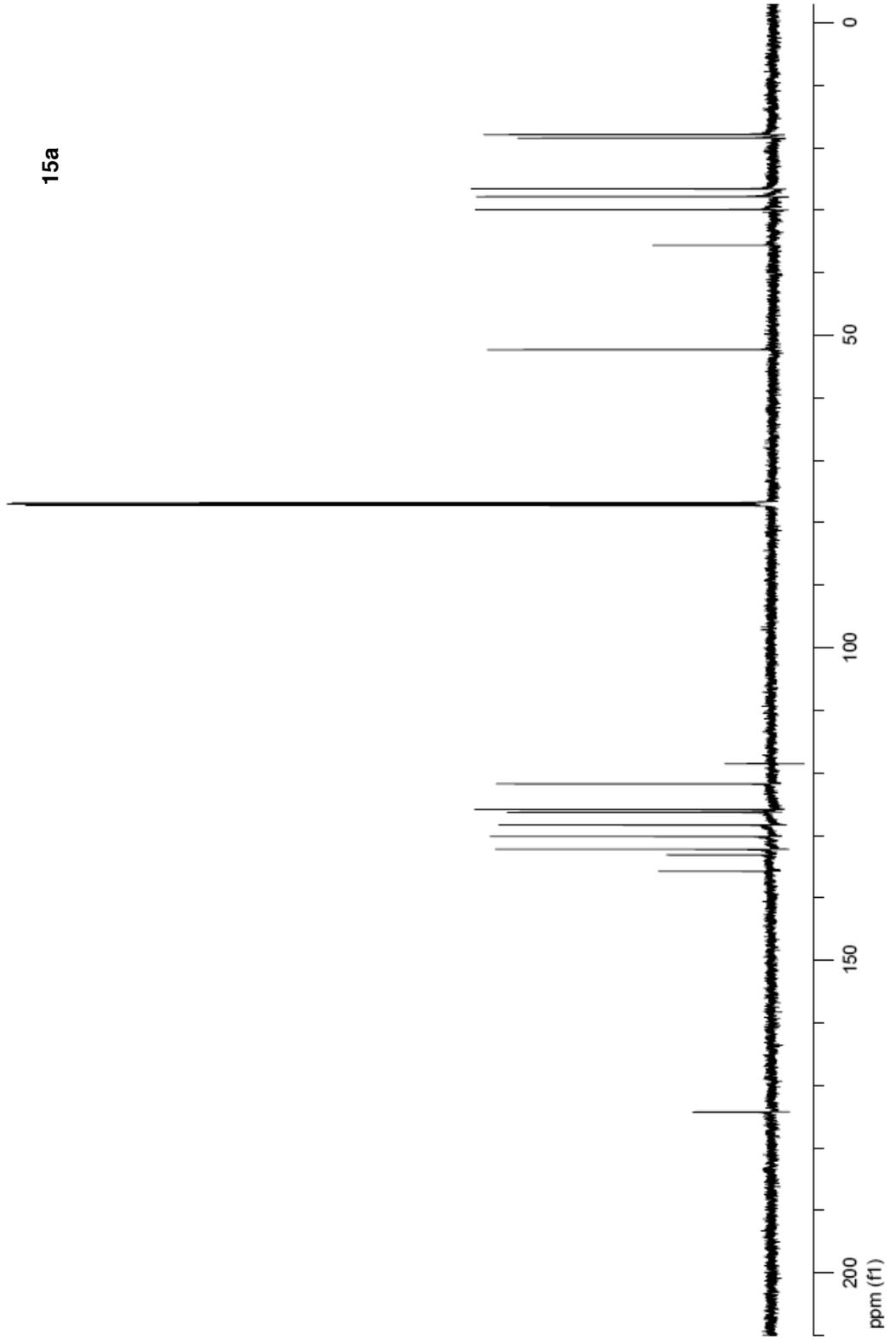


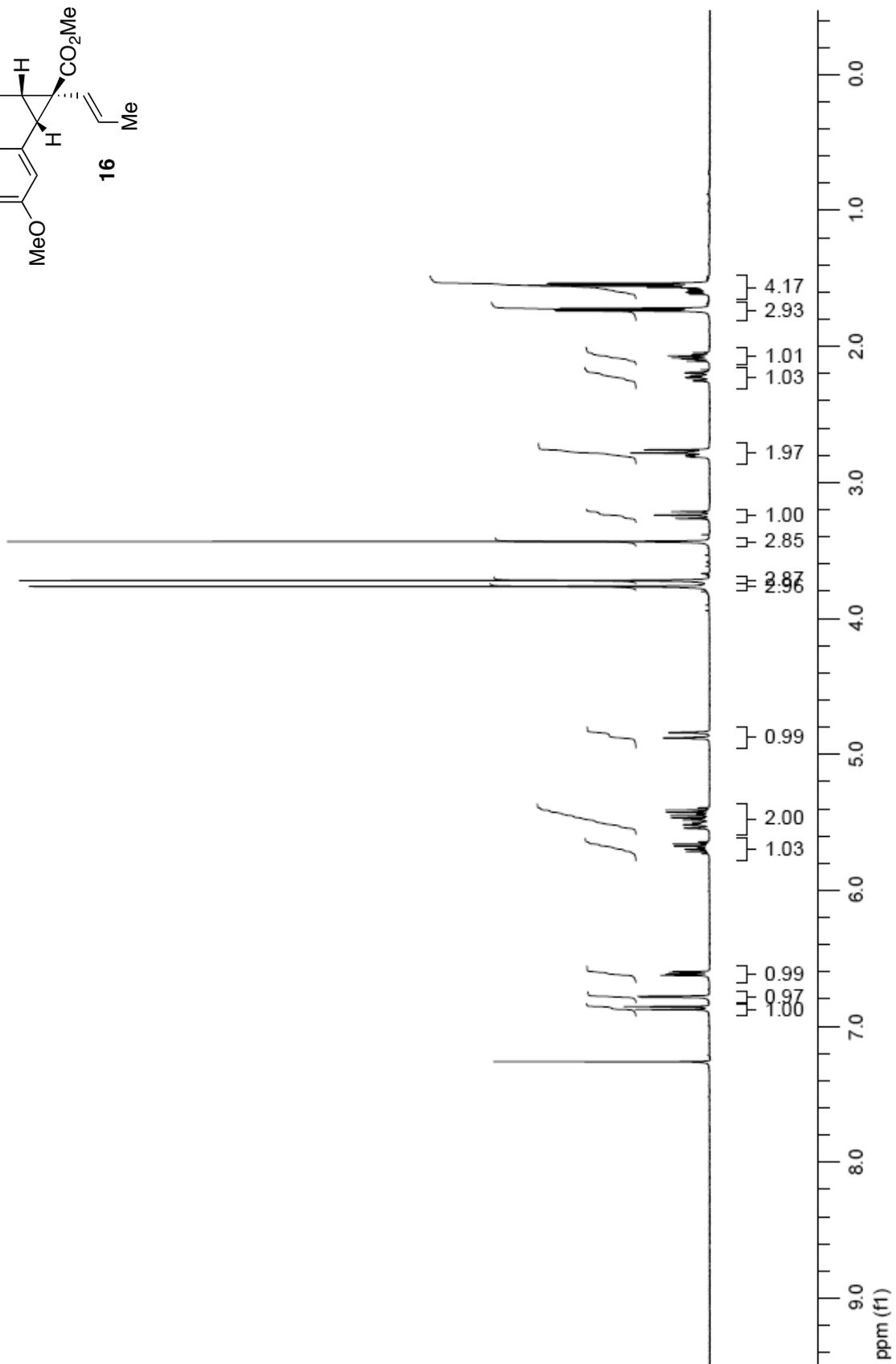
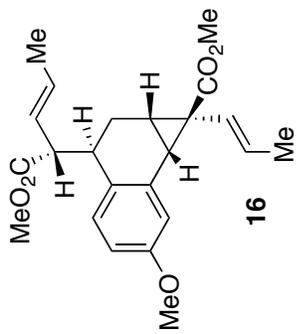
15a

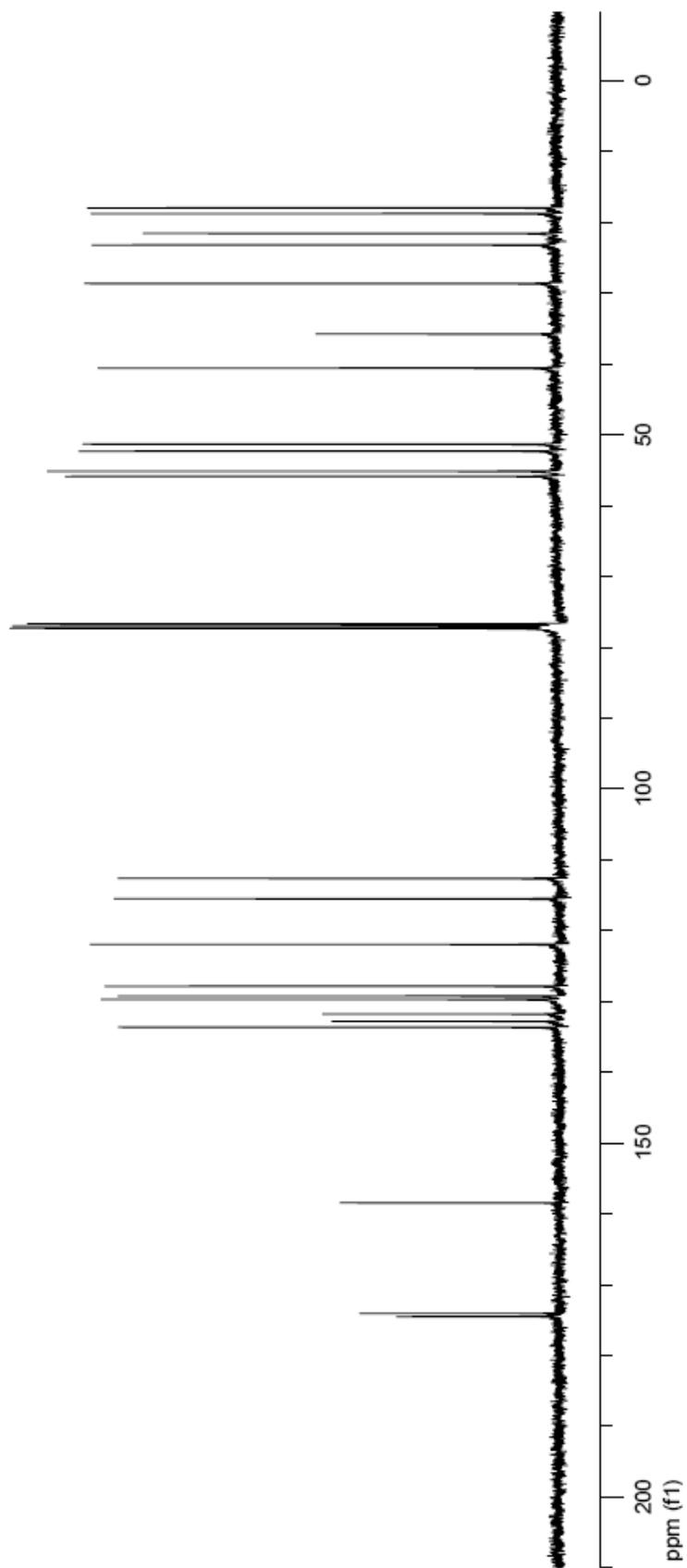
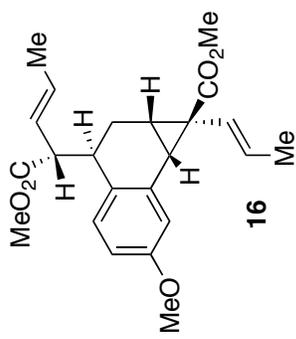


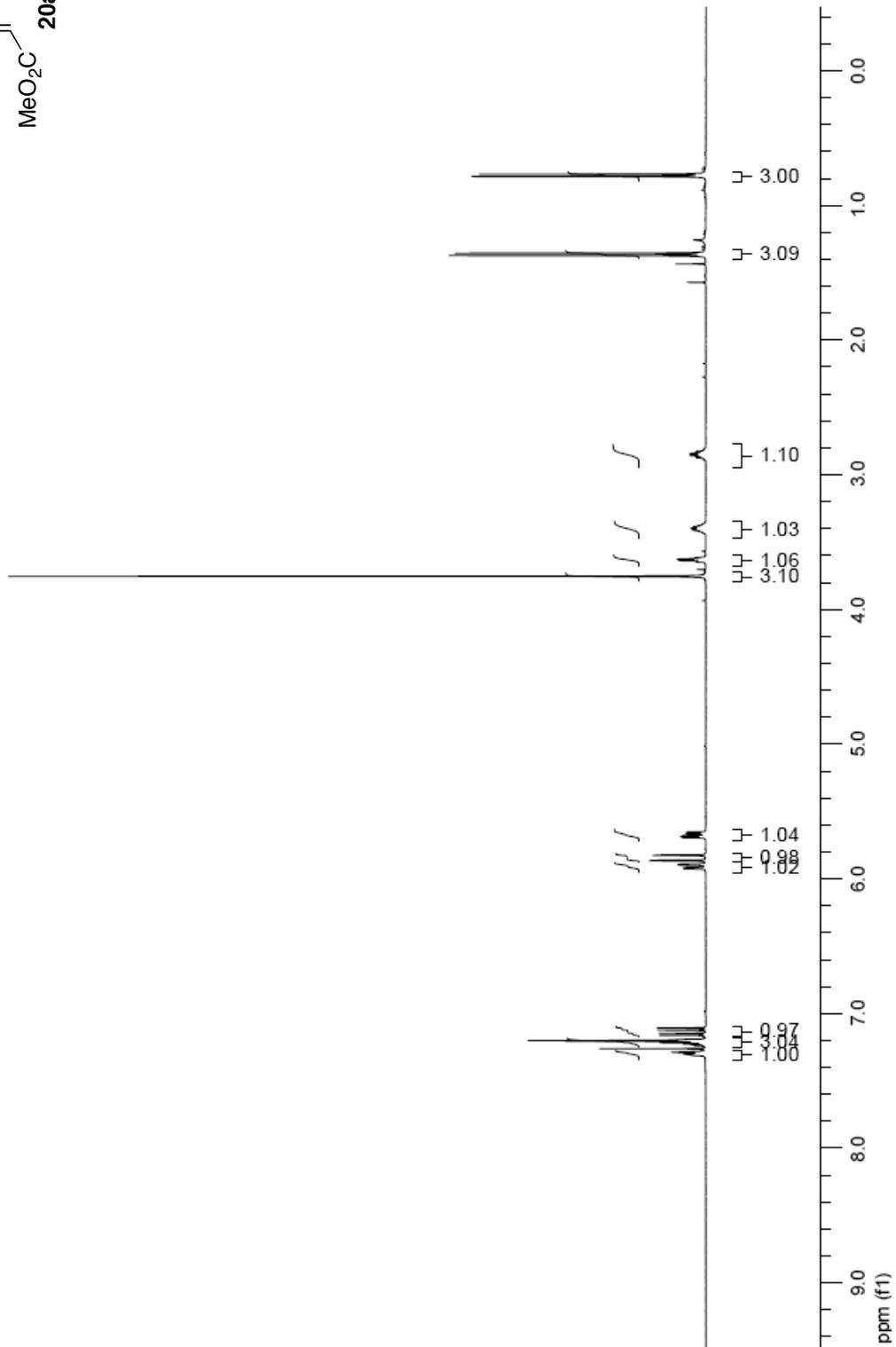
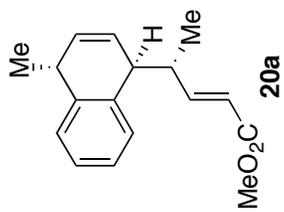


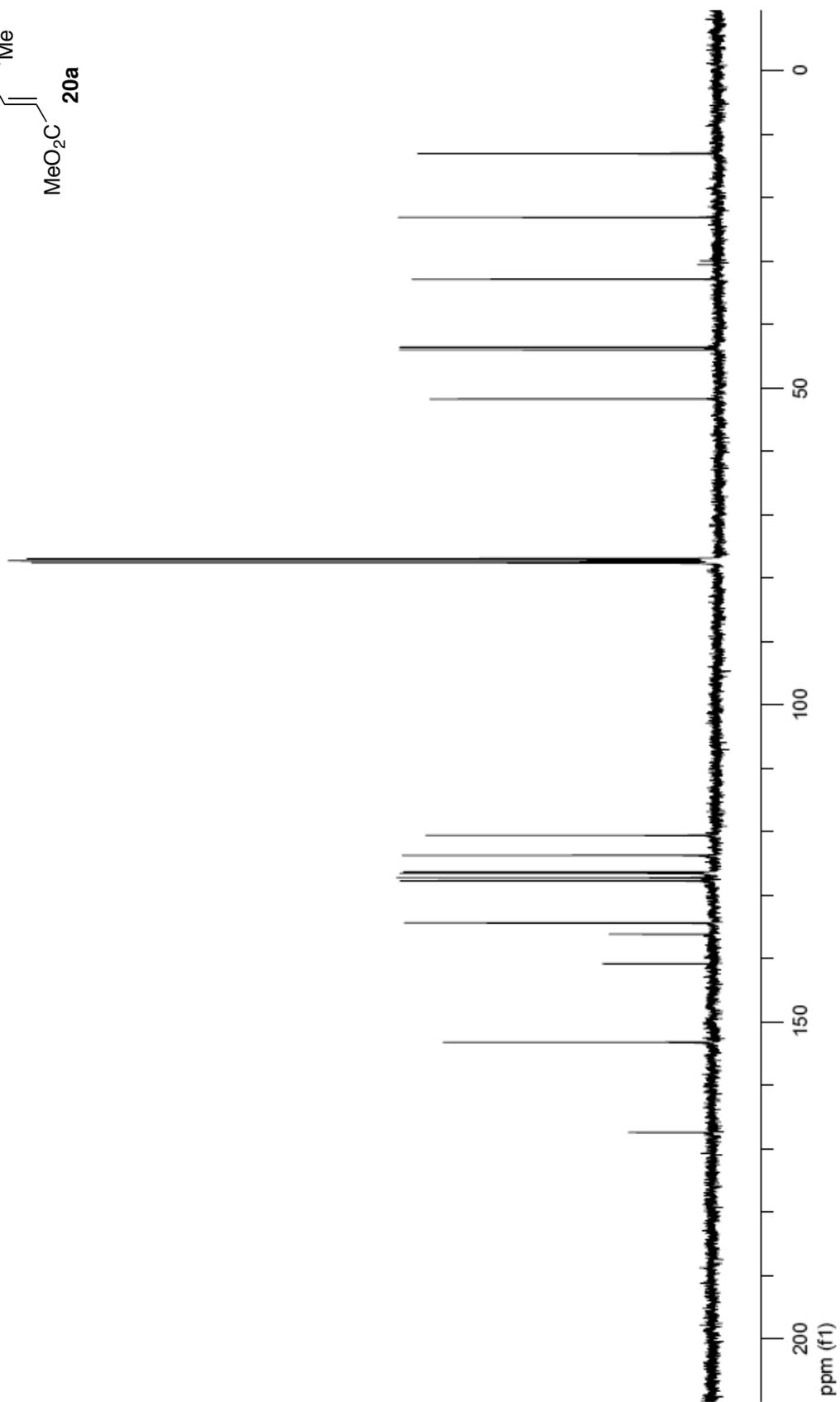
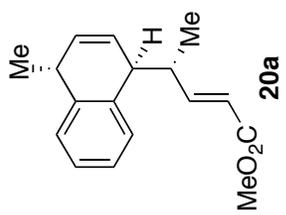
15a

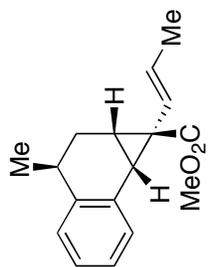




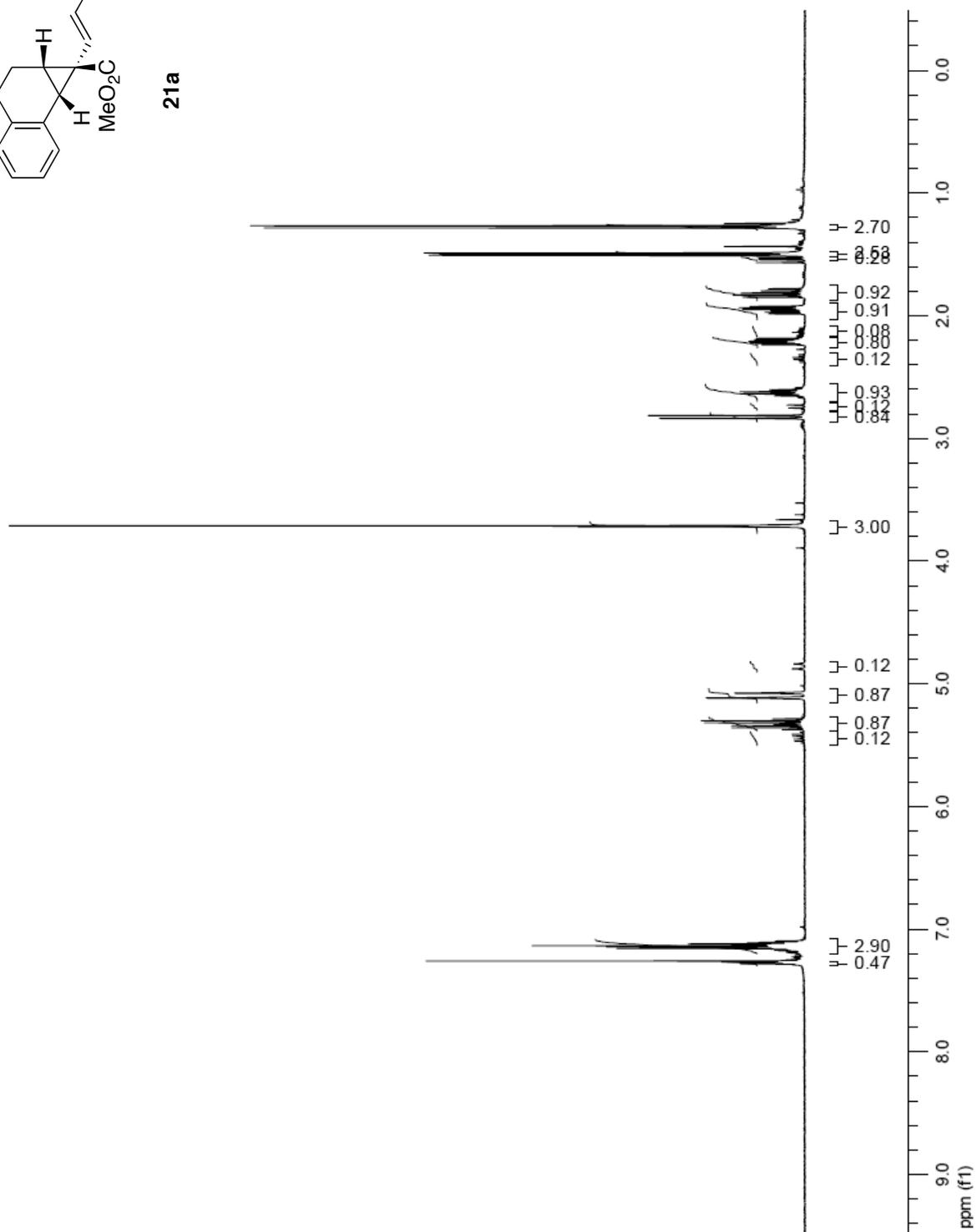


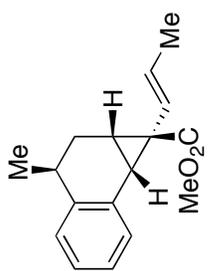




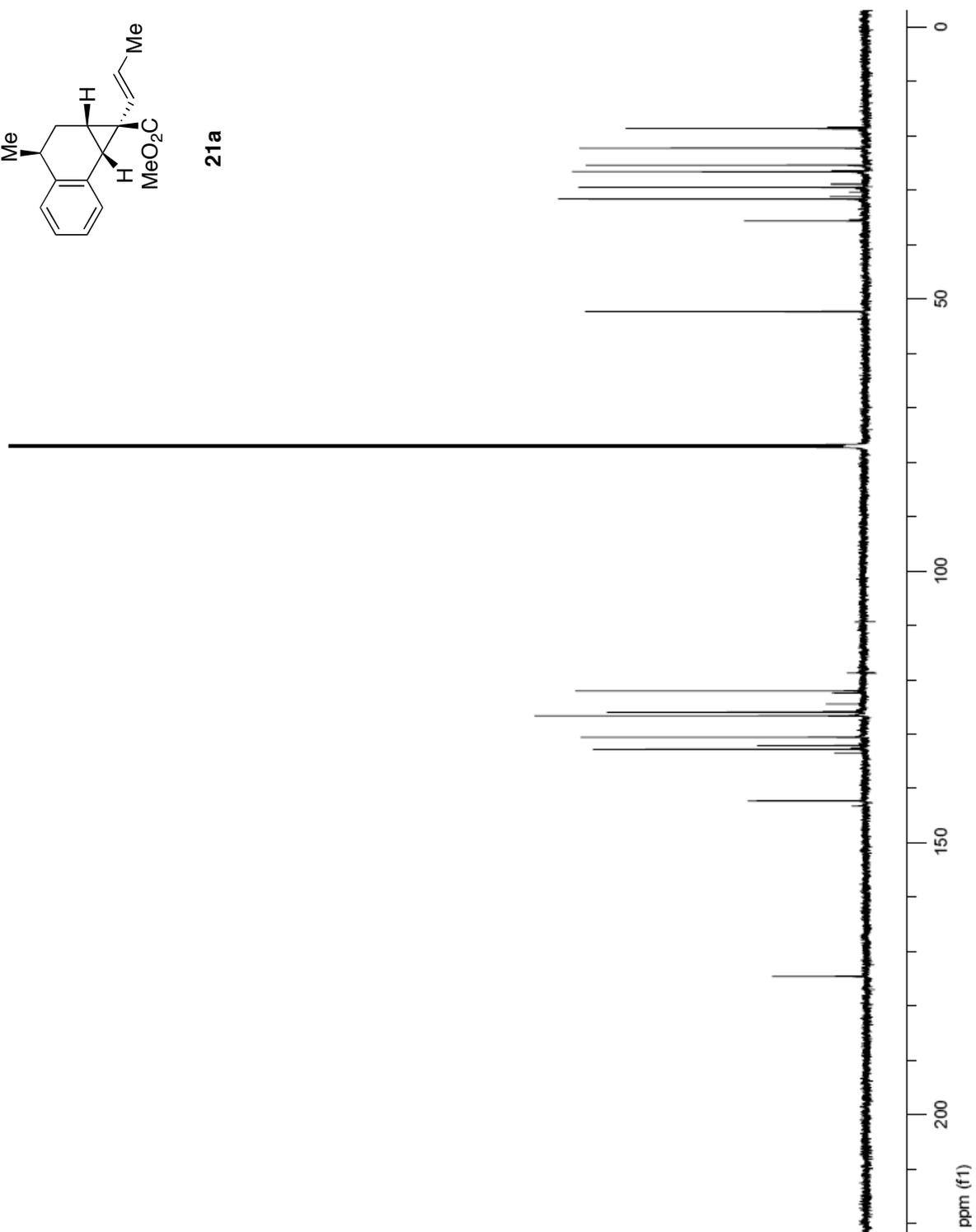


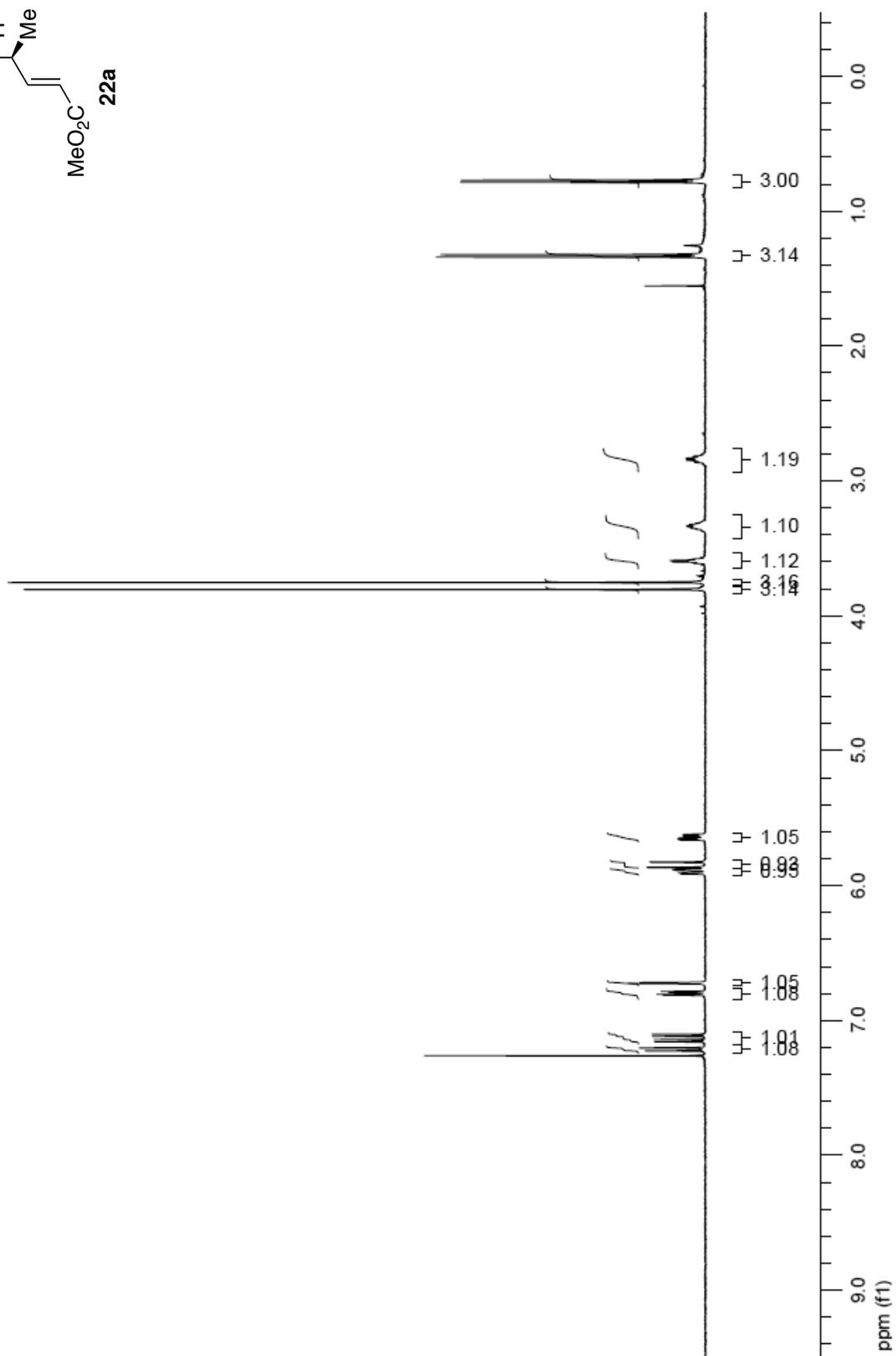
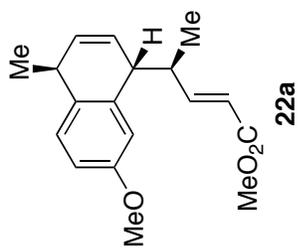
21a

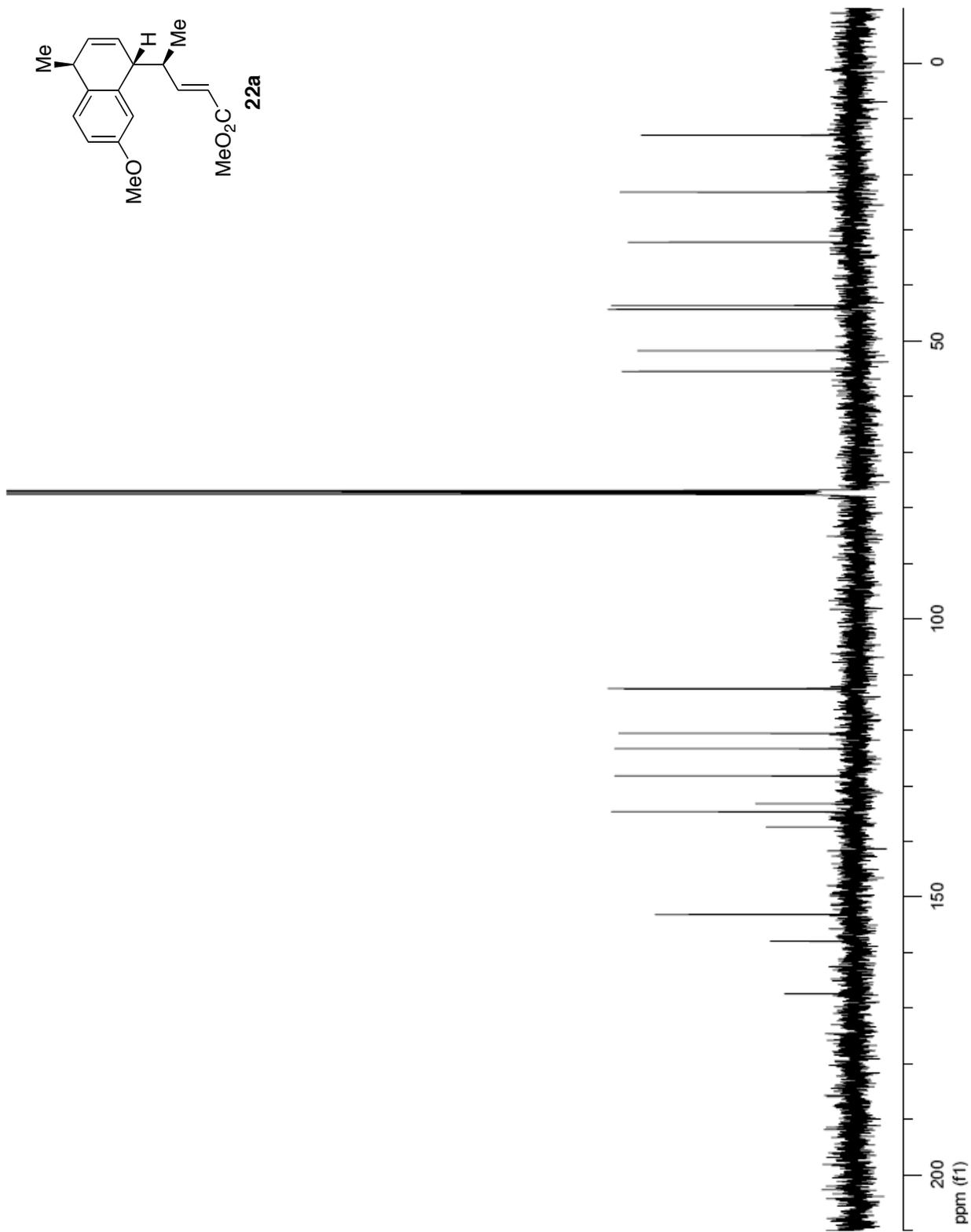


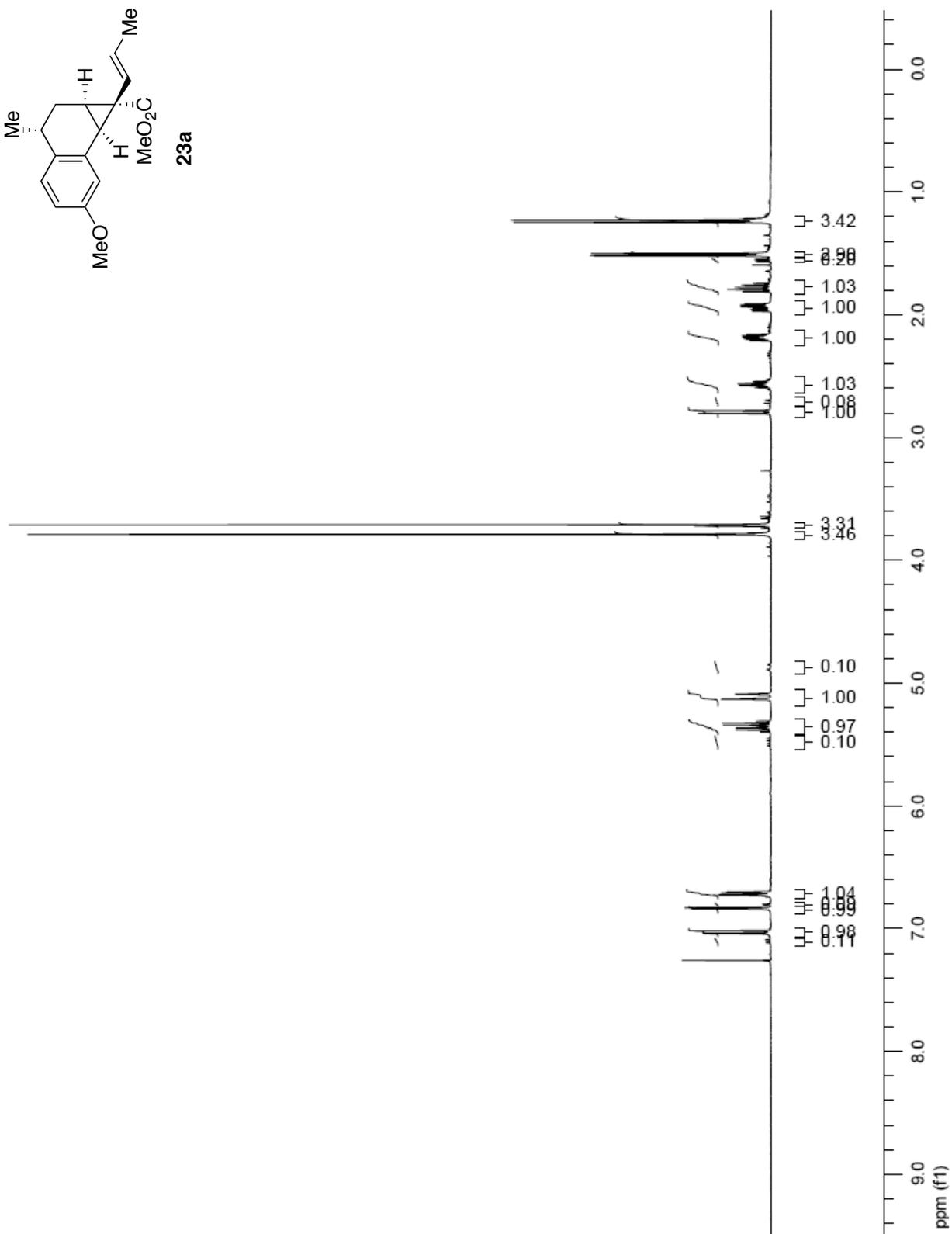
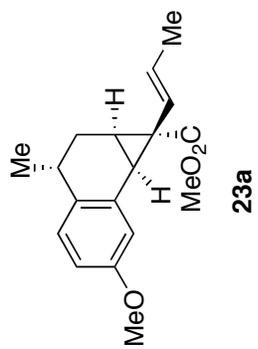


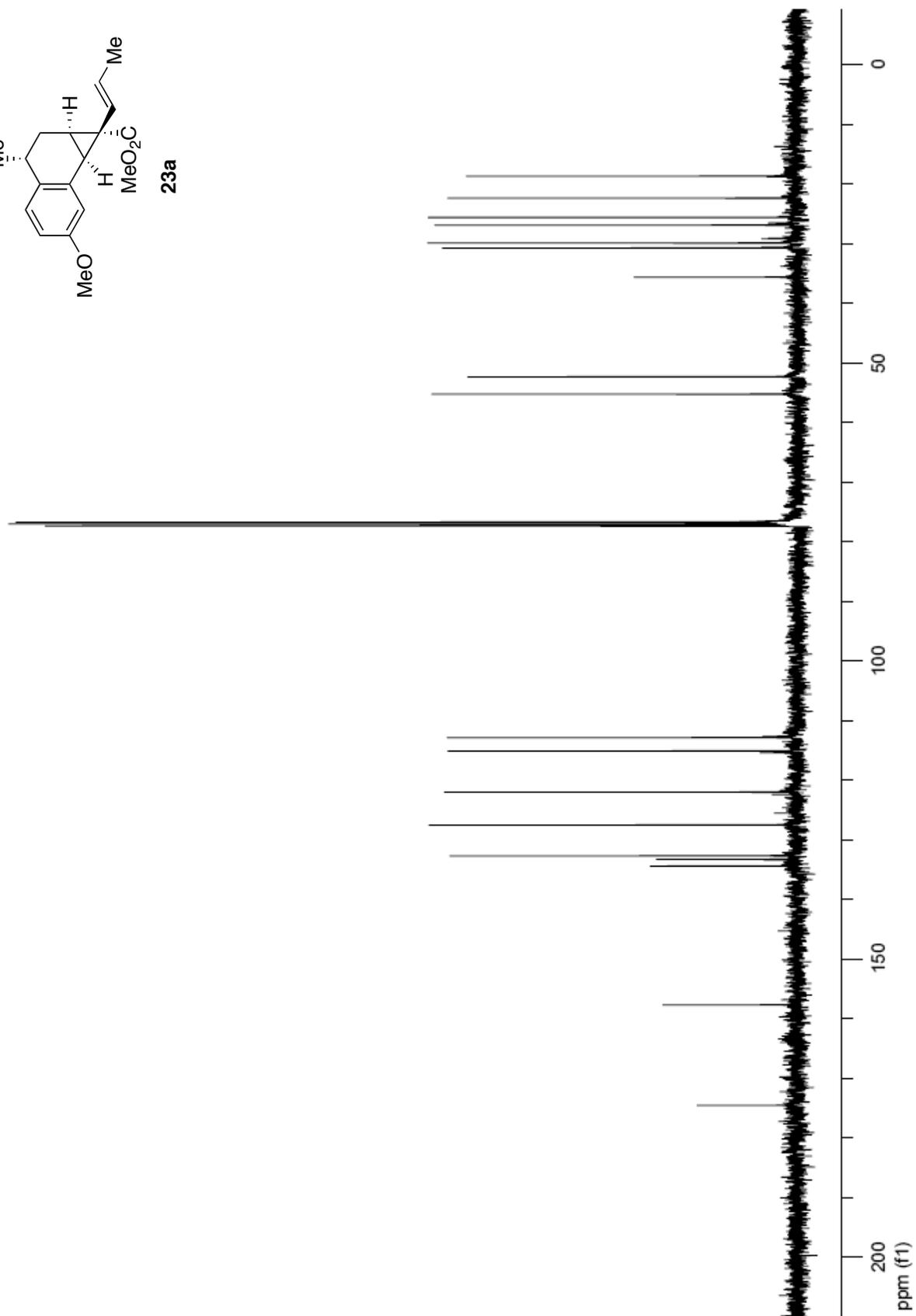
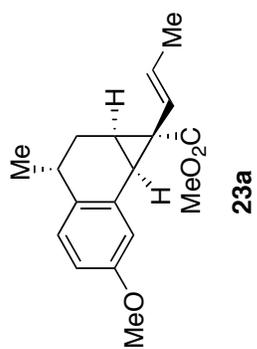
21a



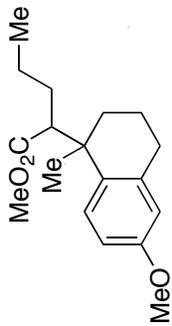




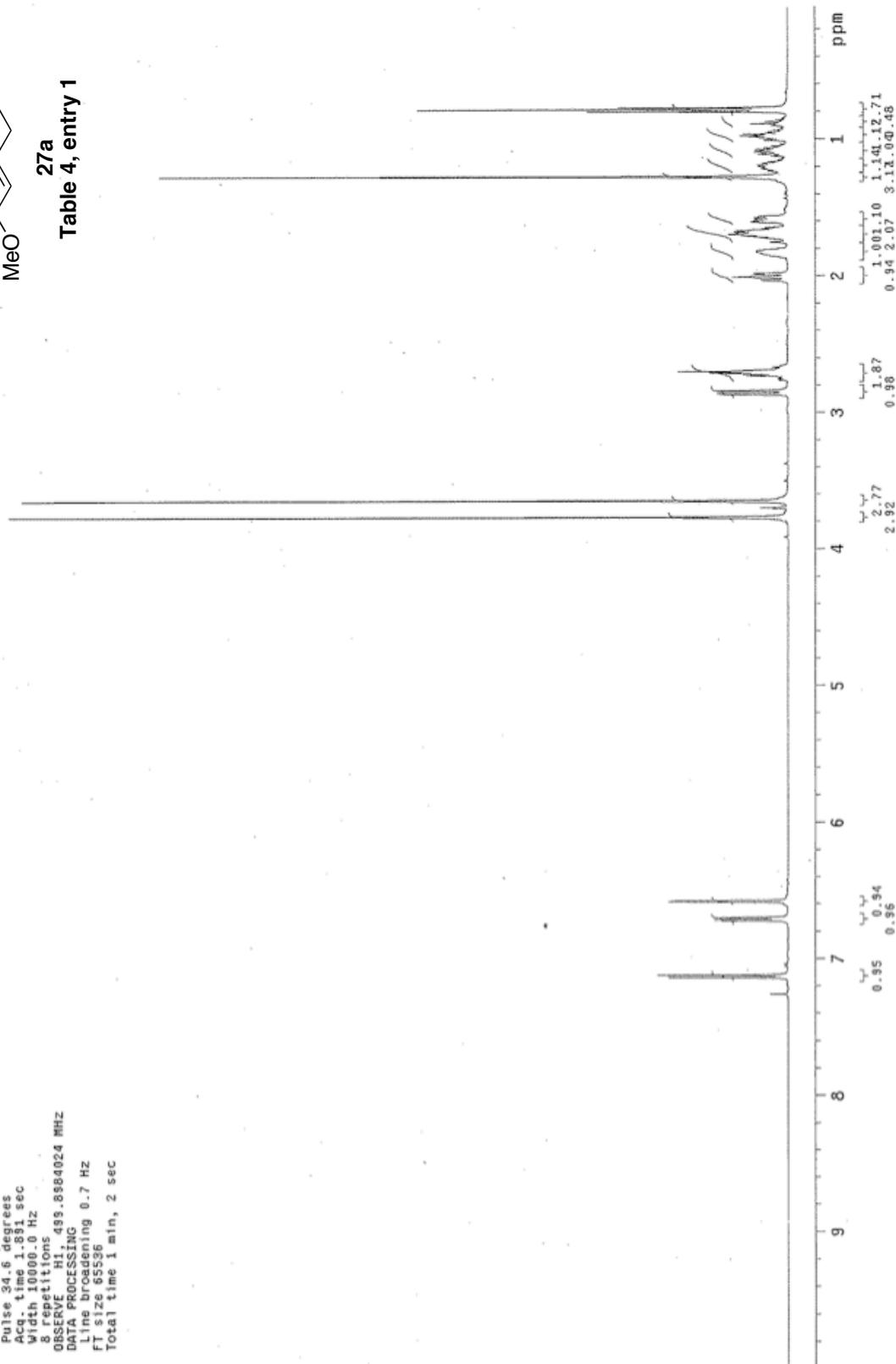




12jb023-H2.f6.7
Pulse Sequence: s2pu1
Solvent: CDCl3
Ambient temperature
INOVA-500 "tocsy.chem.buffalo.edu"
Relax. delay 2.000 sec
Pulse 34.6 degrees
Acq. time 1.891 sec
Width 10000.0 Hz
epitlions
OBSERVED FID 489.8880024 MHz
DATA PROCESSING 0.7 Hz
FT size 65596
Total time 1 min, 2 sec



27a
Table 4, entry 1



12jb023.h2.retro.c13

Pulse Sequence: s2pul

Solvent: CDCl3

Ambient temperature

User: 1-14-87

INOVA-500 "tocsy.chem.buffalo.edu"

Relax. delay 10.000 sec

Pulse 91.8 degrees

Acq. time 3.00 sec

Width 3187.0 Hz

24 divisions

OBSERVE C13, 125.6995567 MHz

DECUPLE H1, 499.9008303 MHz

Power 40 dB,

continuously on

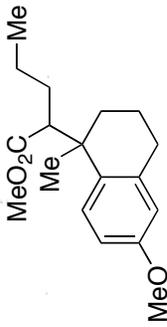
WALTZ-16 modulated

DATA PROCESSING

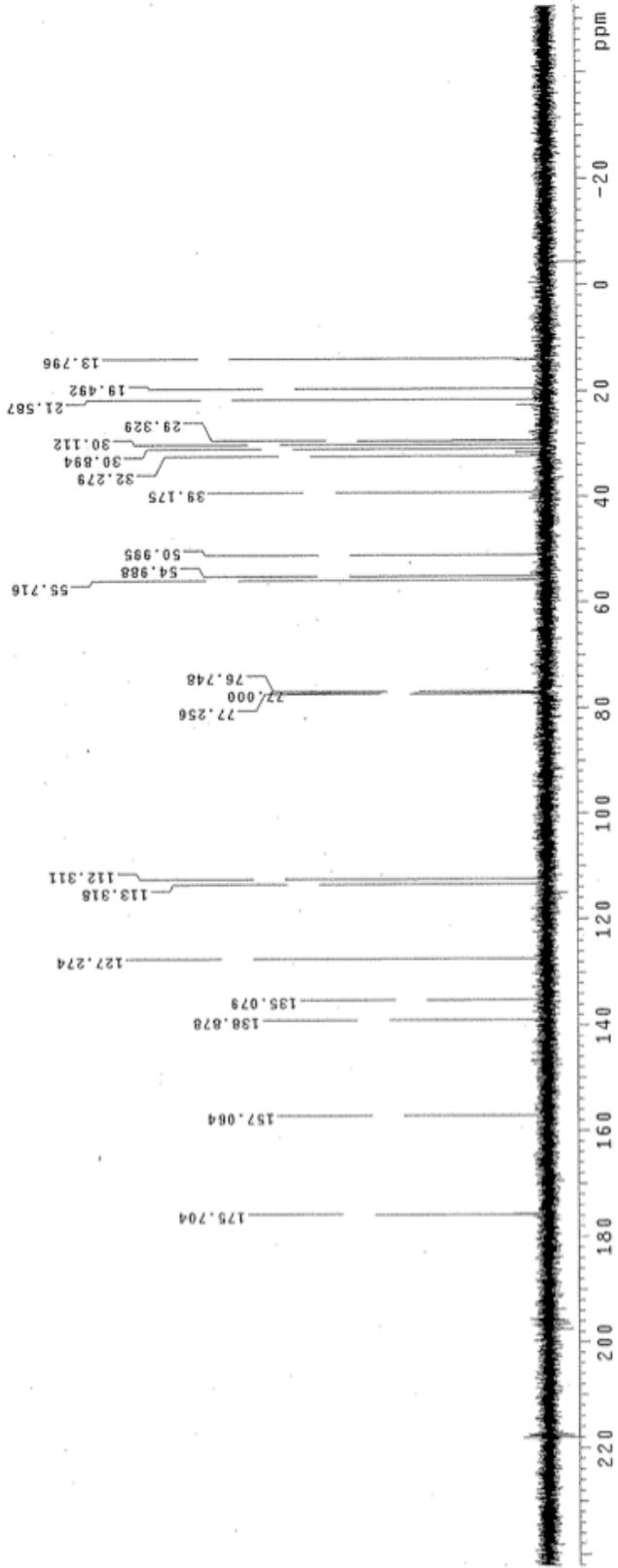
Line broadening 0.5 Hz

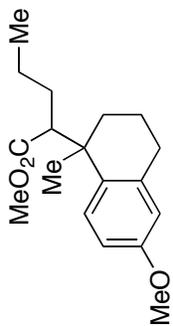
FT size 131072

Total time 1 hr, 36 min, 30 sec



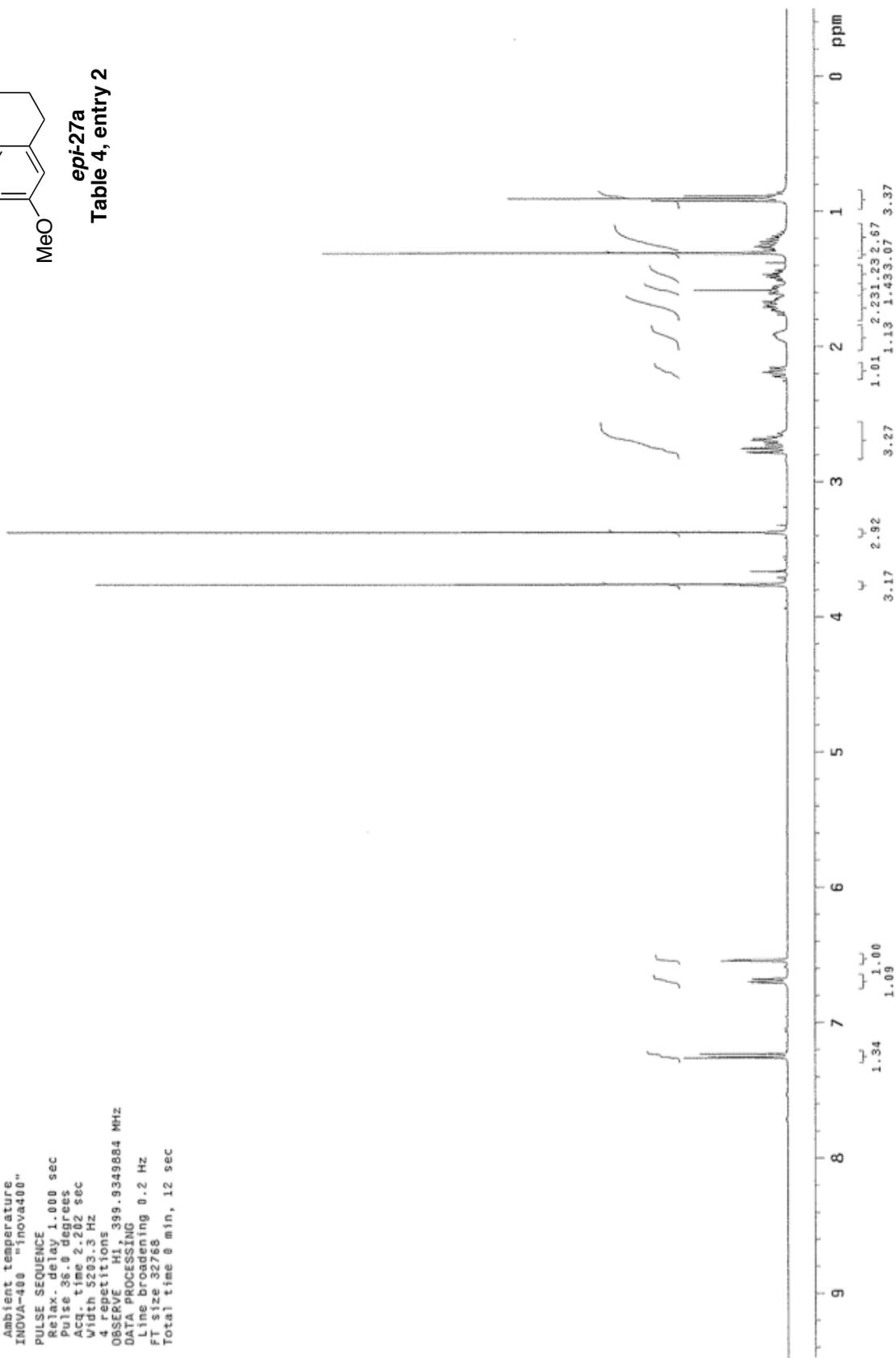
27a
Table 4, entry 1

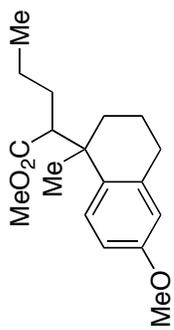




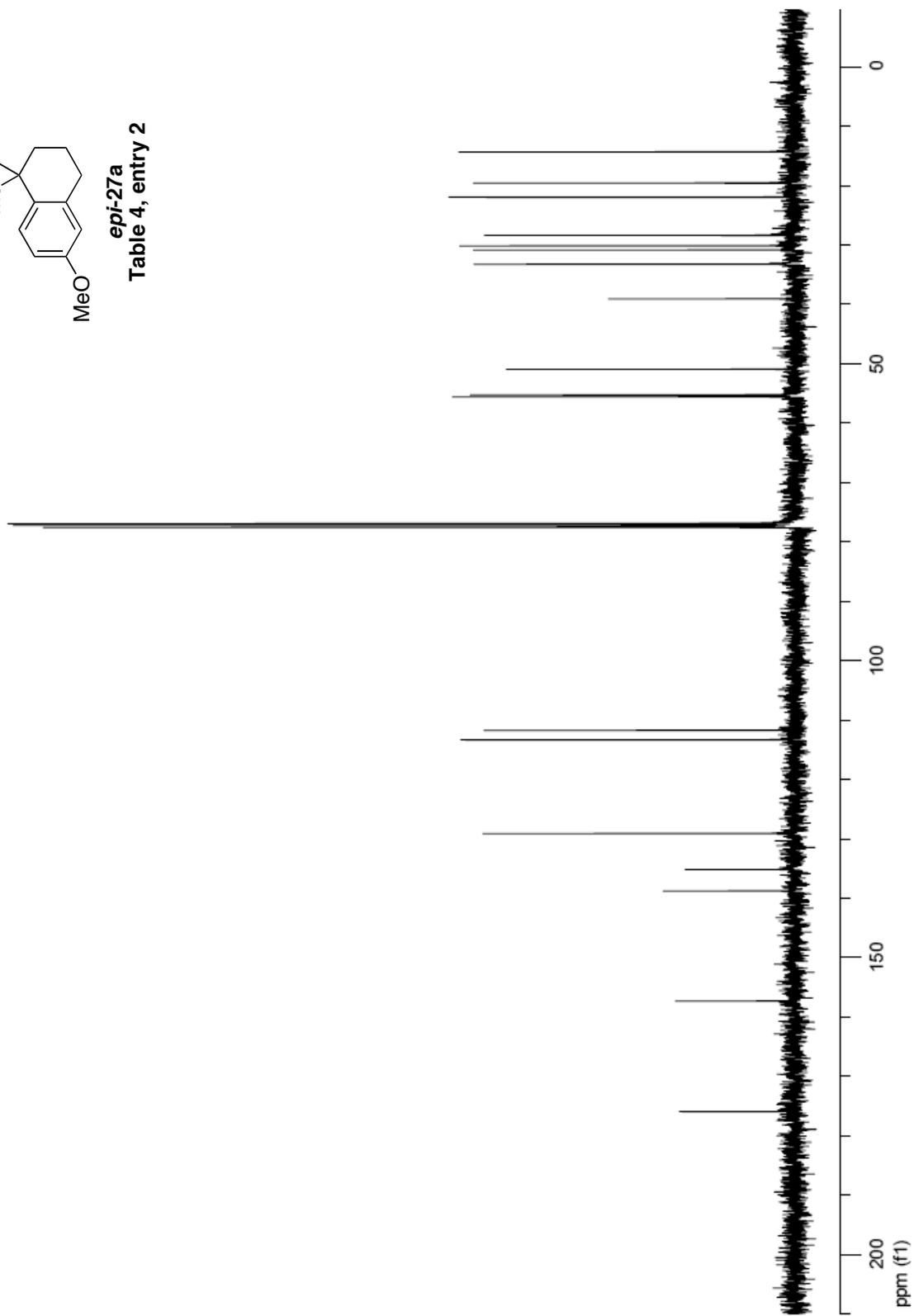
epi-27a
Table 4, entry 2

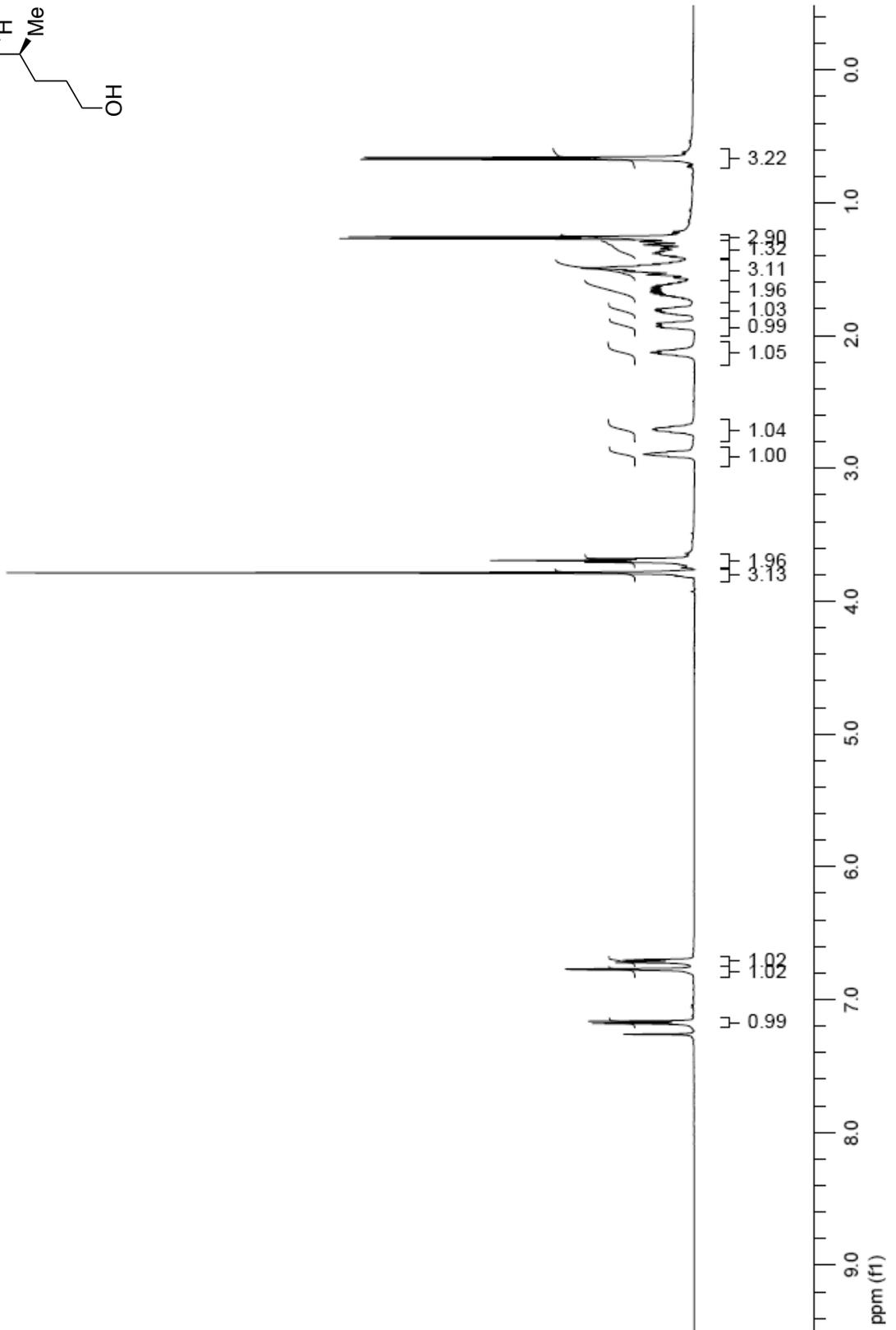
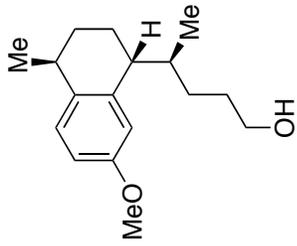
EN-V-796
Pulse Sequence: s2pu1
Solvent: cdcl3
Ambient temperature
INOVA-400 "inova400"
PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 36.9 degrees
Acq. time 2.202 sec
Width 5203.3 Hz
4 repetitions
OBSERVE F1 399.9349884 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FI size 32768
Total time 8 min, 12 sec

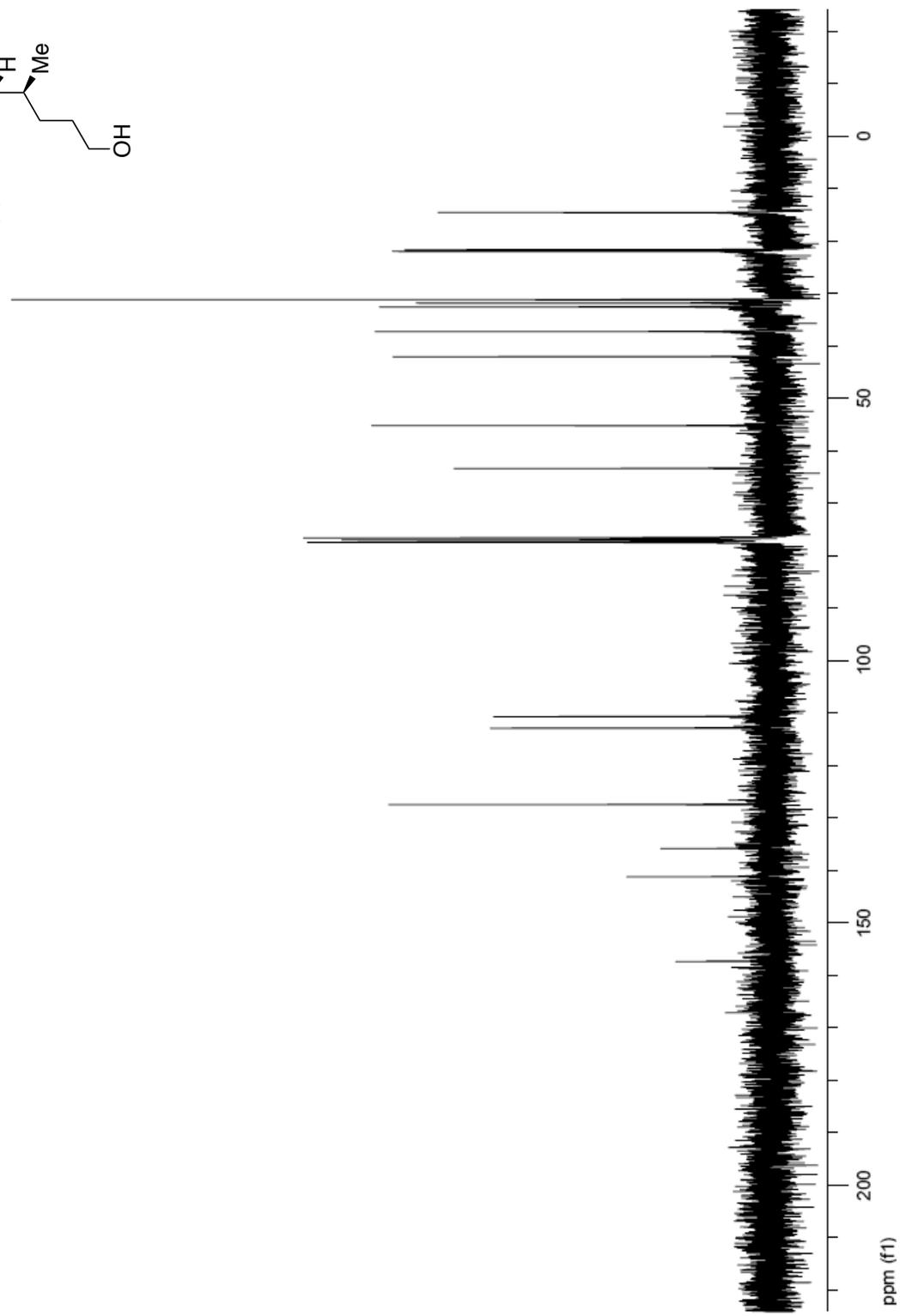
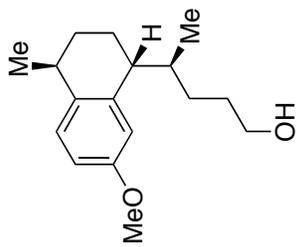




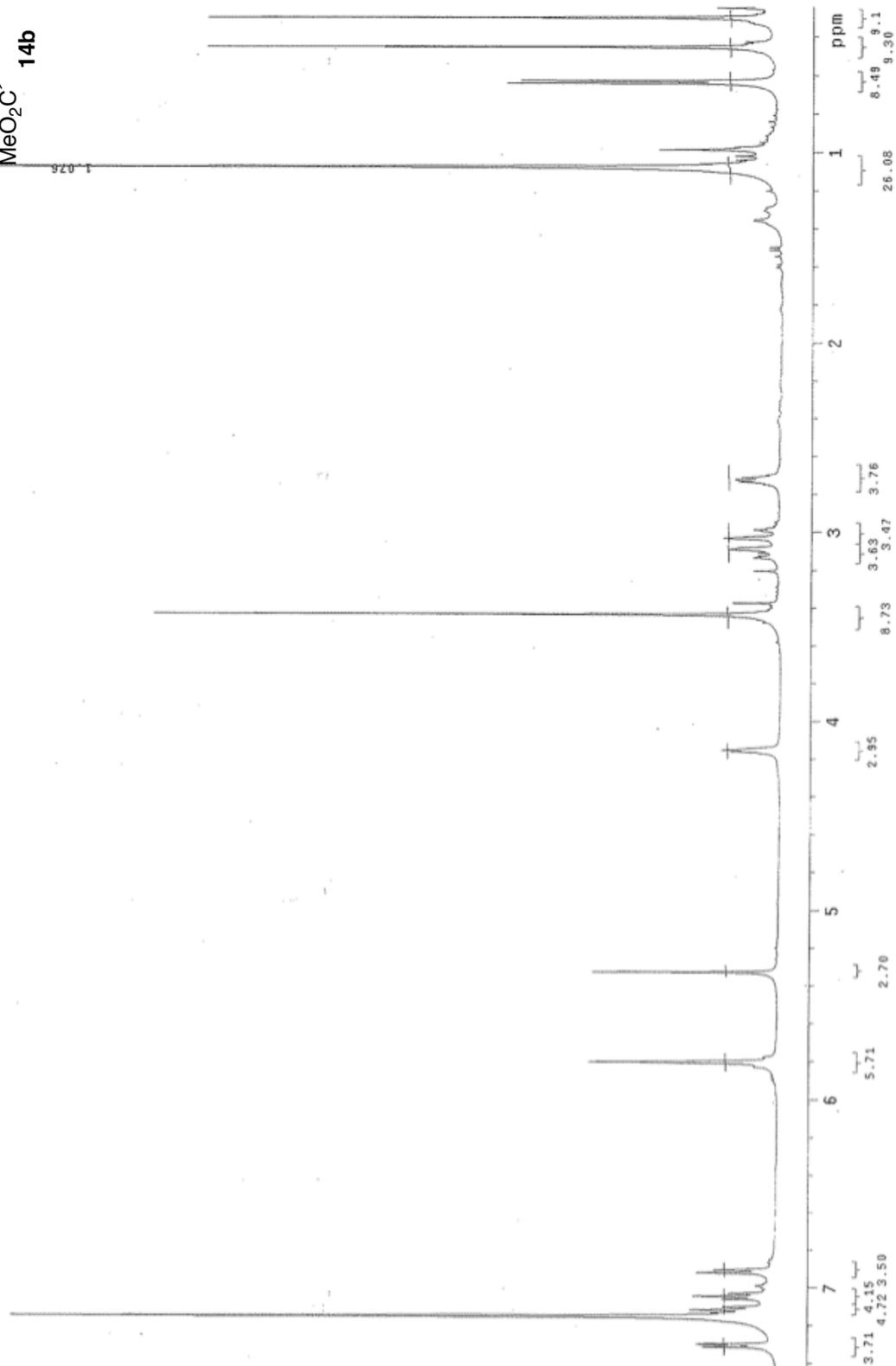
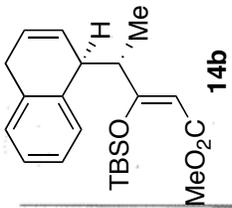
epi-27a
Table 4, entry 2







DLV-1484fr22-30
Pulse Sequence: s2pu1

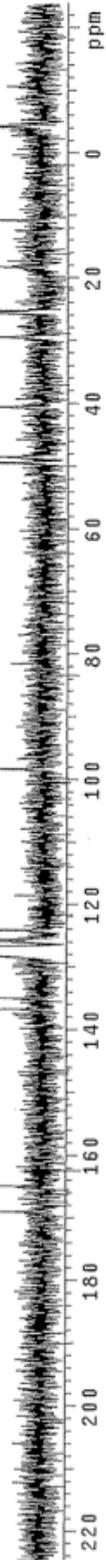
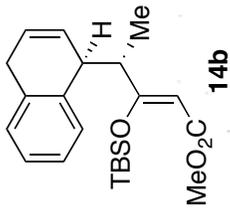


DLV-1484c13

Pulse Sequence: s2pul
Solvent: Benzene
Ambient temperature
GEMINI-300 "roesy.chem.buffalo.edu"

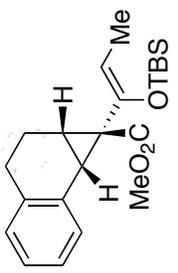
Relax. delay 5.000 sec
Pulse width 10.000 degrees
Acquisition time 1.700 sec
Width 18761.7 MHz
372 repetitions
OBSERVE C13, 75.4536263 MHz
DECOUPLE H1, 300.0754701 MHz
Power 1023 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 0 min, 0 sec

INDEX	FREQUENCY PPM	HEIGHT
1	12756.369	169.062
2	12445.459	164.942
3	10318.324	136.751
4	10186.056	134.986
5	9655.277	127.963
6	9626.648	127.584
7	9602.599	127.265
8	9578.551	126.948
9	9565.954	126.779
10	9558.511	126.681
11	9501.825	125.929
12	9476.059	125.586
13	9363.261	124.093
14	7415.917	88.284
15	3727.929	49.407
16	3654.639	48.436
17	3060.301	40.559
18	2229.488	29.548
19	2220.889	28.434
20	1926.593	29.533
21	1905.960	29.260
22	1379.207	18.279
23	819.498	10.781
24	-313.912	-4.160
25	-330.517	-4.580

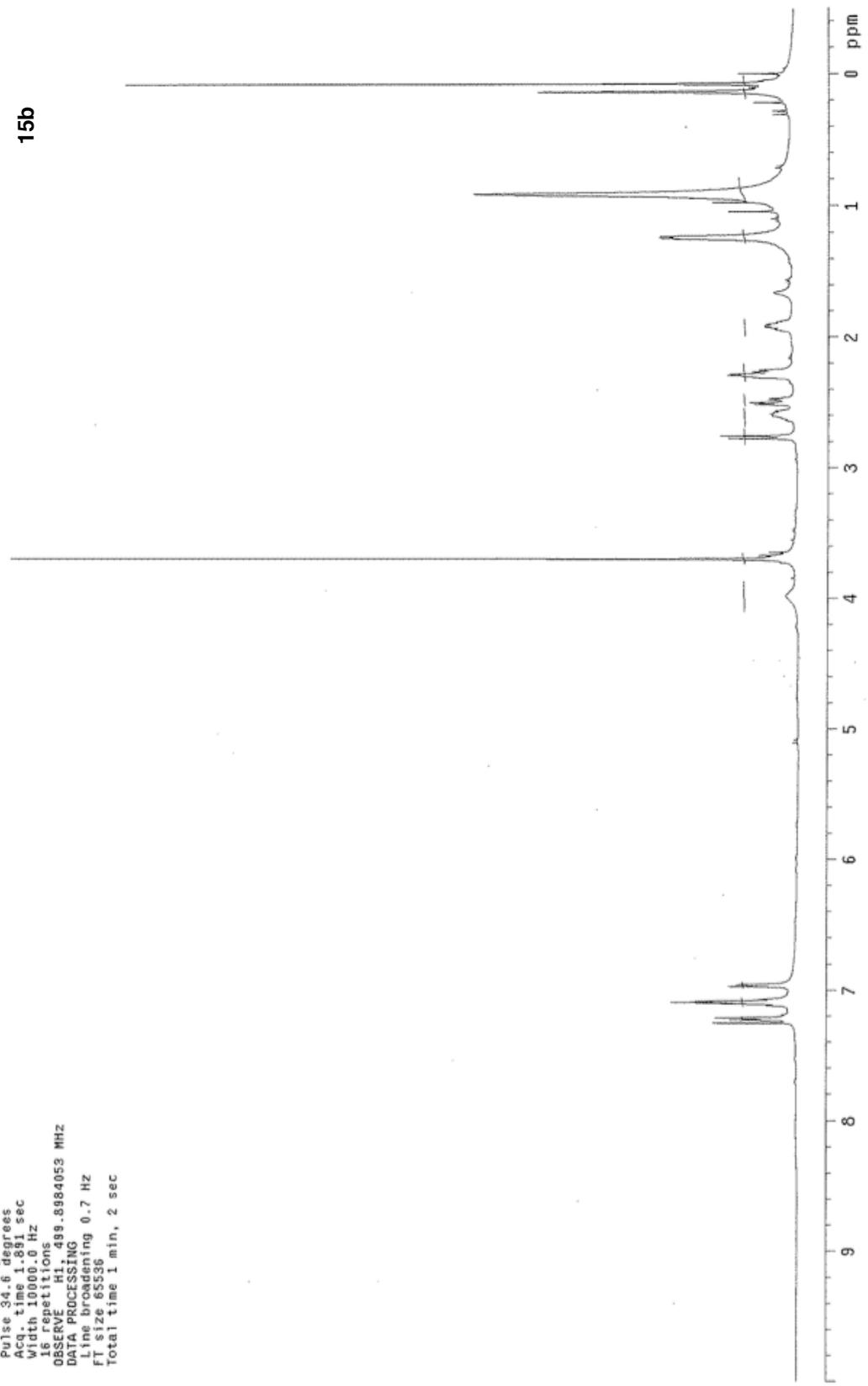


DLV-1977r22-26
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 INOVA-500 "tocsy.chem.buffalo.edu"
 Relax. delay 2.000 sec
 Pulse 34.6 degrees
 Acq. time 1.891 sec
 Width 10000.0 Hz
 16 repetitions
 OBSERVE HI 499.8984053 MHz
 DATA PROCESSING
 Line broadening 0.7 Hz
 FT size 65536
 Total time 1 min, 2 sec

INDEX	FREQUENCY	PPM	HEIGHT
1	1850.891	3.703	140.9
2	39.673	0.079	120.6



15b

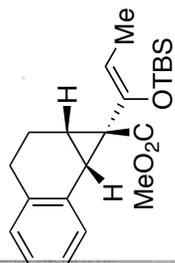


DLV-1977c13

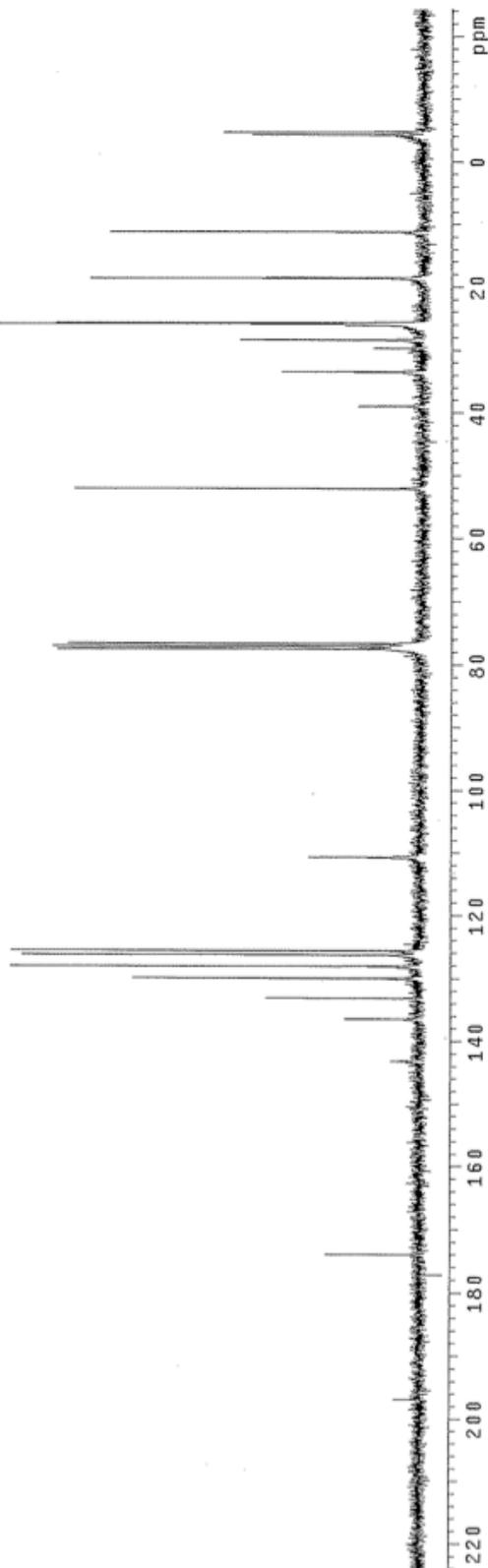
Pulse Sequence: s2pul
Solvent: CDCl3
Acquisition temperature:
GEMINI-300 "fosy.Chem.buffalo.edu"

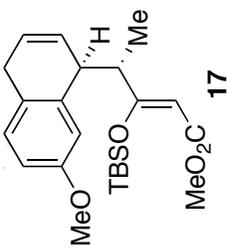
Relax. delay 5.000 sec
Pulse 30.0 degrees
Acq. time 1.706 sec
Width 18761.7 Hz
788 repetitions
OBSERVE CH, 75.4536601 MHz
DECOUPLE CH, 300.0734431 MHz
Power 1023 dB on
WALTZ-16 on
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 64 hr, 27 min, 22 sec

INDEX	FREQUENCY PPM	HEIGHT
1	13123.495	173.928
2	10294.950	136.441
3	10044.160	135.117
4	9804.249	129.837
5	9660.532	128.033
6	9524.258	126.227
7	9474.443	125.566
8	8349.696	110.863
9	5841.996	77.425
10	5825.391	77.205
11	5809.932	77.000
12	5777.867	76.575
13	3324.426	52.011
14	2935.008	38.888
15	2522.751	33.434
16	2137.977	28.335
17	1861.050	25.990
18	1843.300	25.755
19	1832.421	25.611
20	1899.349	18.548
21	1891.905	18.447
22	838.793	11.117
23	-327.552	-4.341
24	-360.189	-4.774



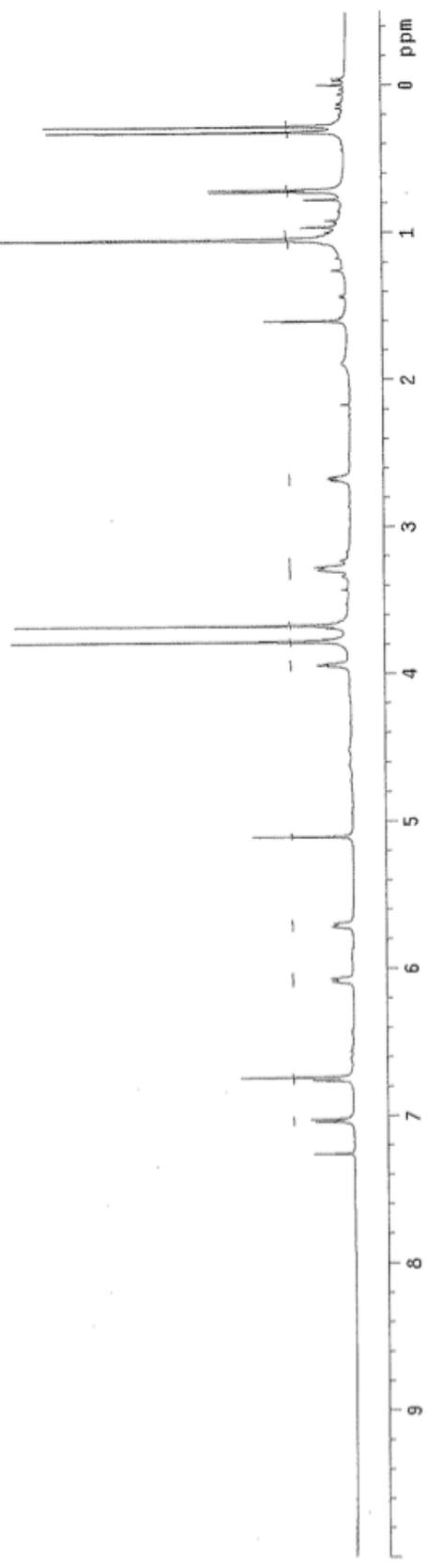
15b





DLV-1972fr39-44
 Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 INOVA-500 "tocsy.Chem.buffalo.edu"
 Relax. delay 2.000 sec
 Pulse 34.5 degrees
 Acq. time 1.891 sec
 Width 10000.0 Hz
 16 repetitions
 OBSERVE H1, 499.8984034 MHZ
 DATA PROCESSING
 Line broadening 0.7 Hz
 FT size 65536
 Total time 1 min, 2 sec

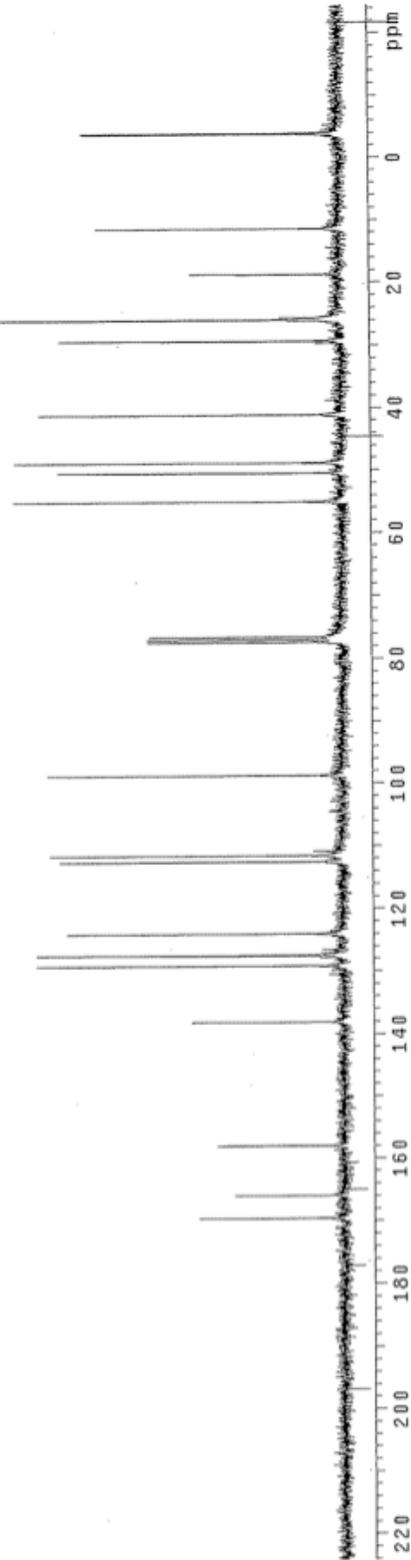
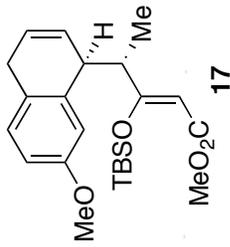
INDEX	FREQUENCY PPM	HEIGHT
1	3511.963	7.3
2	3370.361	18.4
3	2552.185	16.3
4	1891.174	54.4
5	1836.548	53.8
6	800.781	14.0
7	524.292	140.9
8	481.567	7.8
9	388.489	7.5
10	362.244	22.5
11	355.225	22.6
12	160.217	48.2
13	140.686	48.8



DLV-1972c13 (C₁₃/cpic)
 Pulse Sequence: e2pu1
 Solvent: CDCl₃
 Ambient temperature
 GEMINI-300 "roesy.chem.buffalo.edu"

Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Acq. time 1.706 sec
 Width 18761.7 Hz
 356 repetitions
 OBSERVE C13, 75.4536630 MHz
 DECOUPLE H1, 300.0754431 MHz
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 2 hr, 12 min, 0 sec

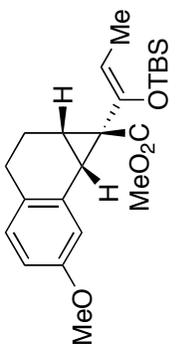
INDEX	FREQUENCY PPM	HEIGHT
1	12794.894	169.572
2	12521.714	165.952
3	11921.850	158.000
4	10422.063	138.125
5	9747.584	129.186
6	9627.322	127.593
7	9619.879	127.494
8	9359.355	124.041
9	8492.489	112.552
10	8418.034	111.566
11	7449.801	98.733
12	5640.279	52.402
13	5808.214	46.927
14	5776.150	38.537
15	4156.321	55.054
16	3809.338	50.486
17	3685.661	48.847
18	3104.432	41.144
19	2212.412	29.321
20	1958.760	25.860
21	1410.801	18.698
22	861.124	11.413
23	-284.056	-3.764
24	-298.350	-3.954



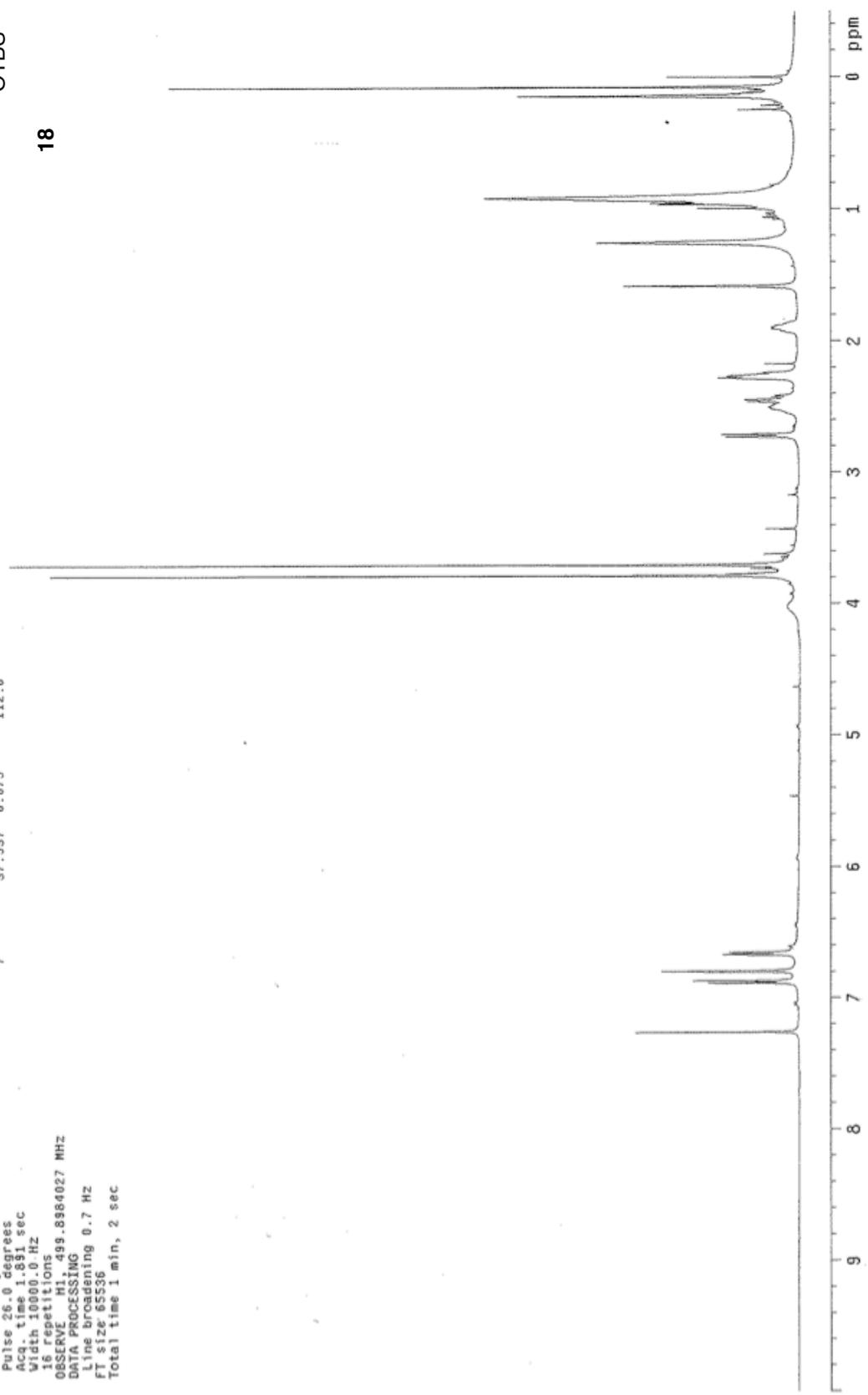
DLV-2024-61-65

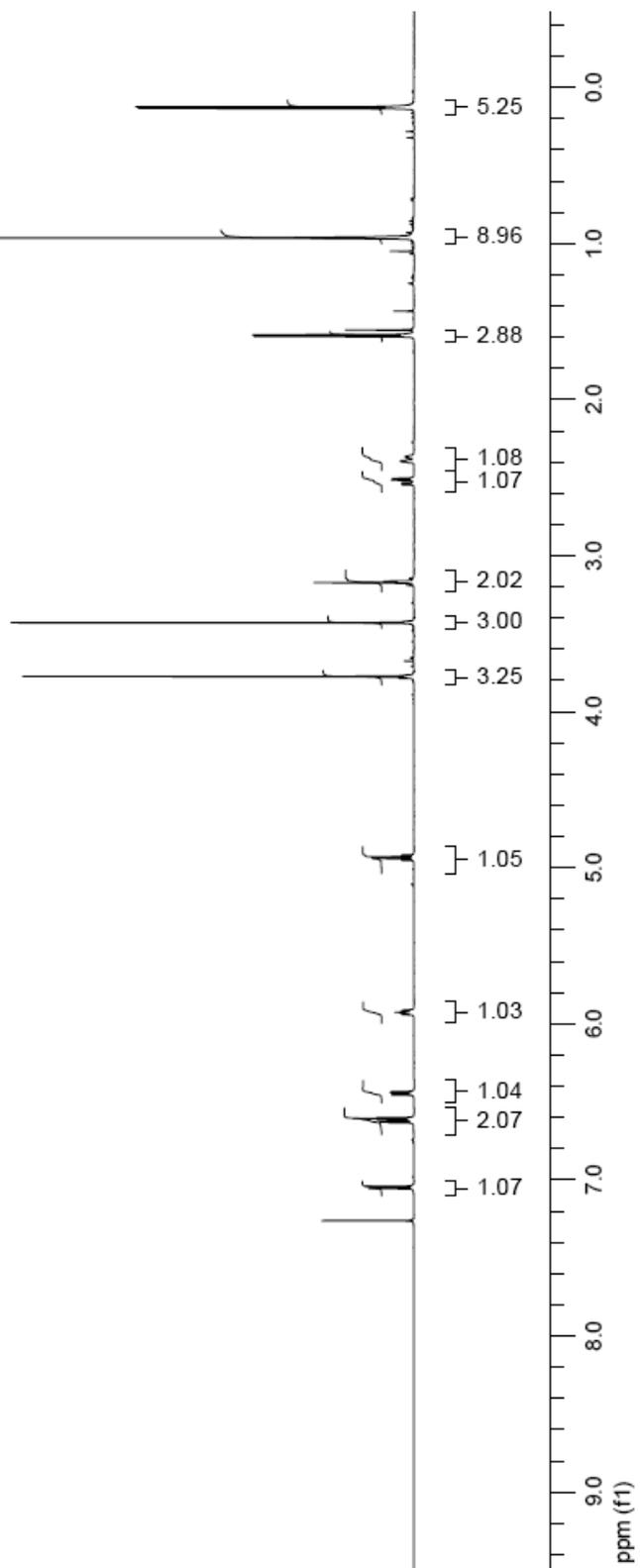
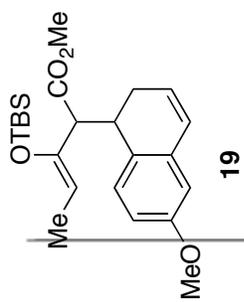
Pulse Sequence: s2pul
Solvent: D2O
Acq. temperature
INDVA-500 "locsy.chem.buffalo.edu"
Relax. delay 2.000 sec
Pulse 26.0 degrees
Acq. time 1.891 sec
Width 10000.0 Hz
16 repetitions
OBSERVE H1, 499.8984027 MHz
DATA PROCESSING
Line broadening 0.7 Hz
FT size 65536
Total time 1 min, 2 sec

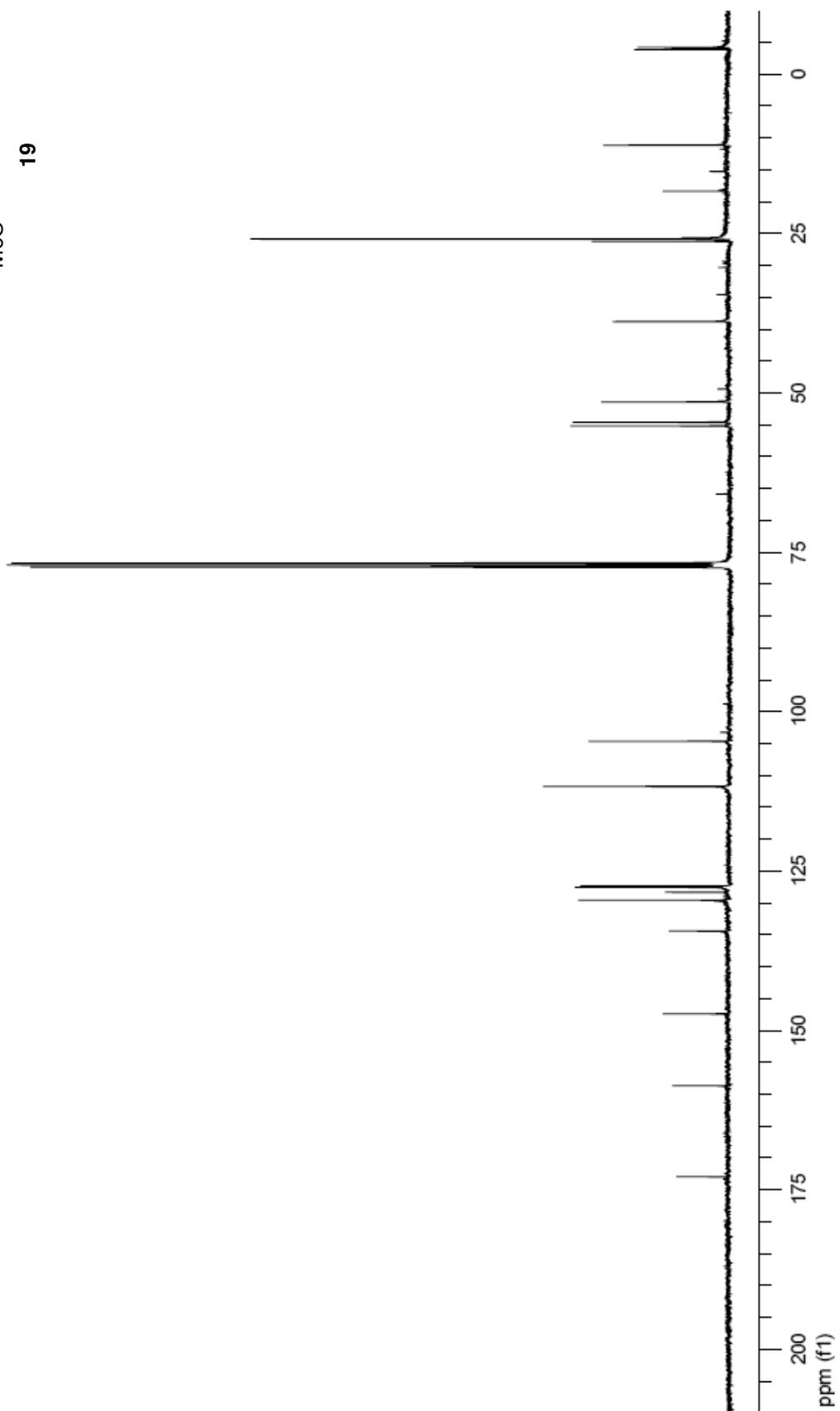
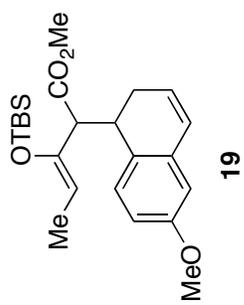
INDEX	FREQUENCY PPM	HEIGHT
1	1893.005	3.787
2	1852.112	3.705
3	627.136	1.255
4	466.308	0.933
5	457.458	0.915
6	70.801	0.142
7	37.537	0.075

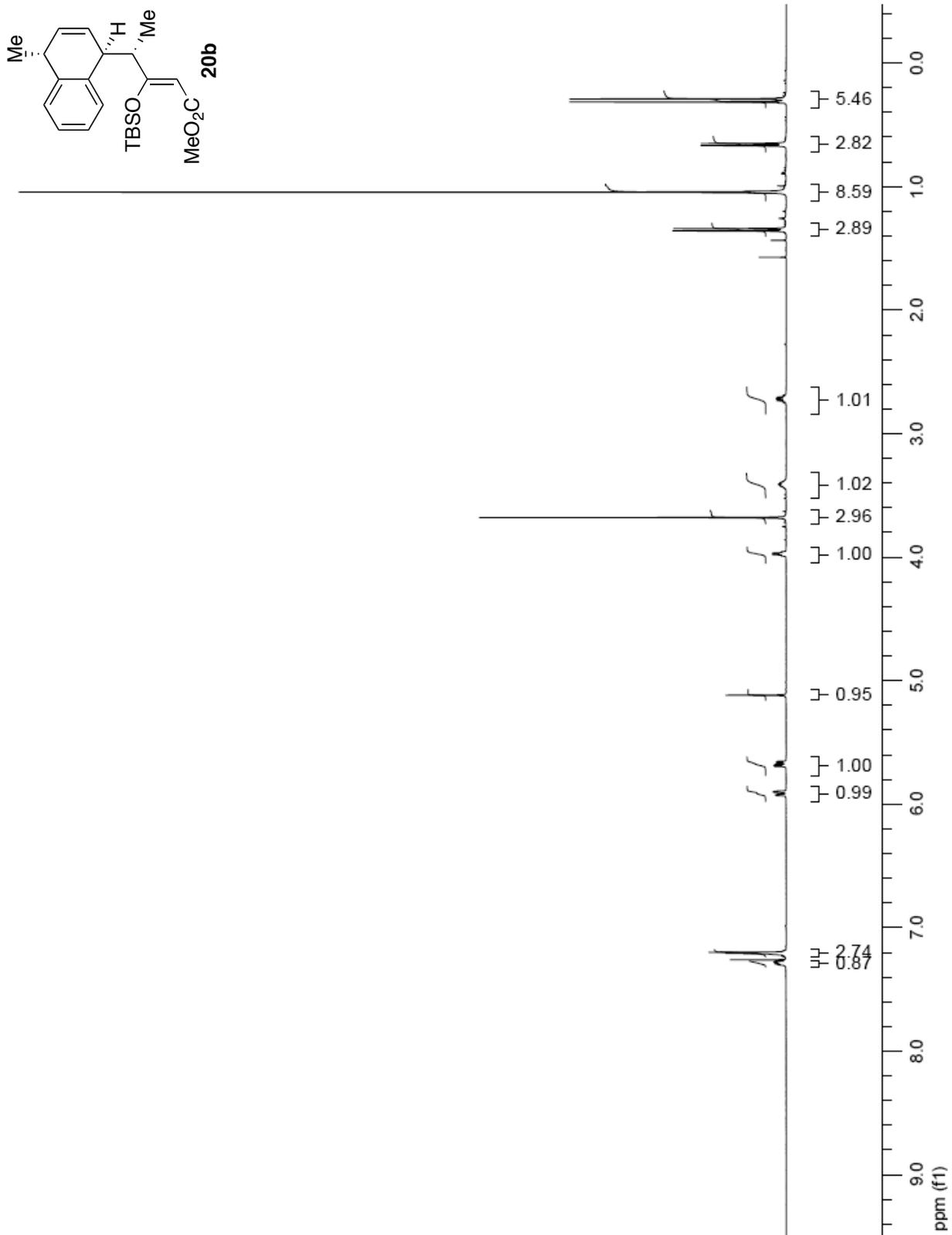


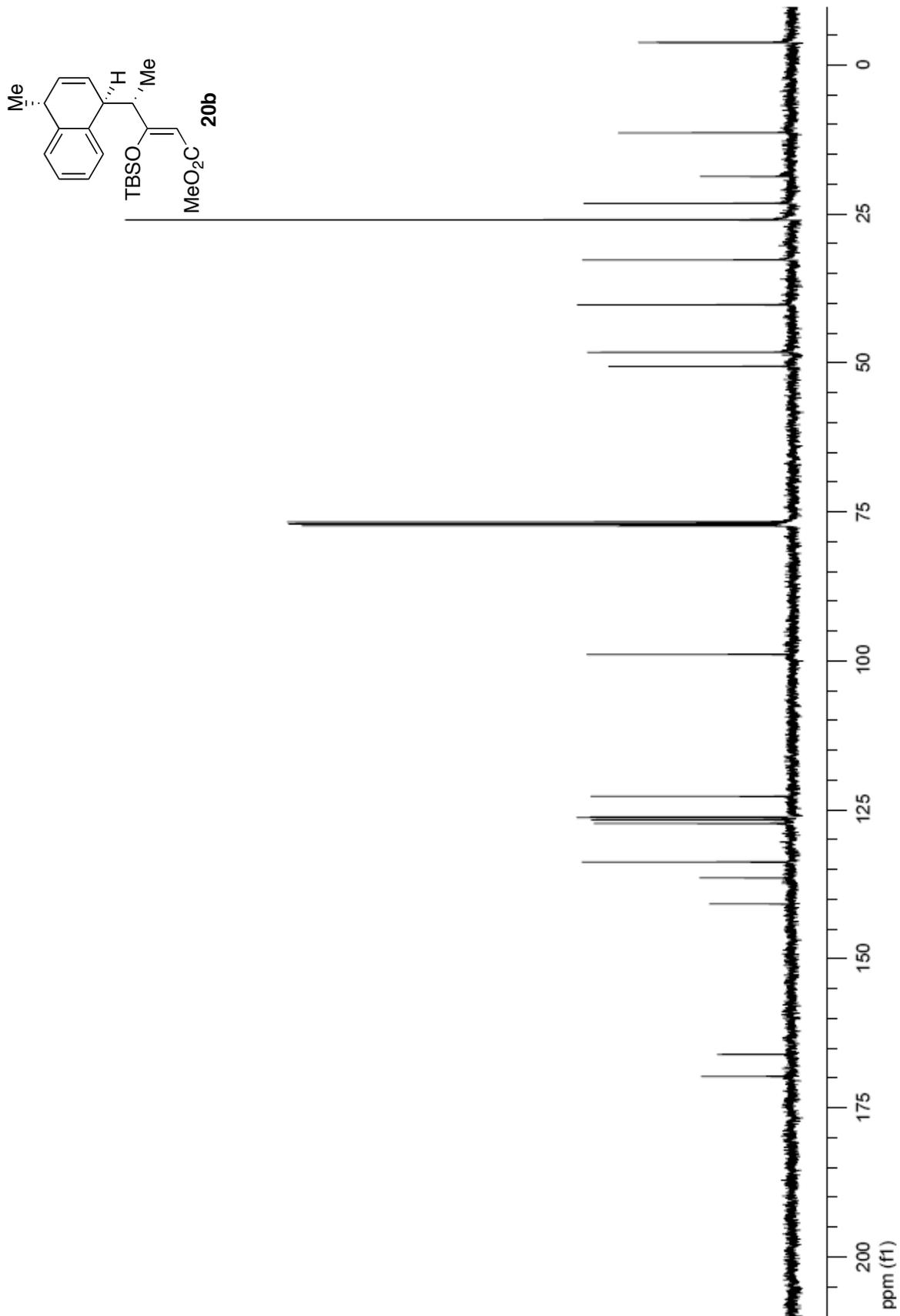
18

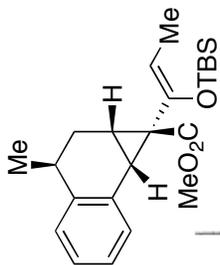










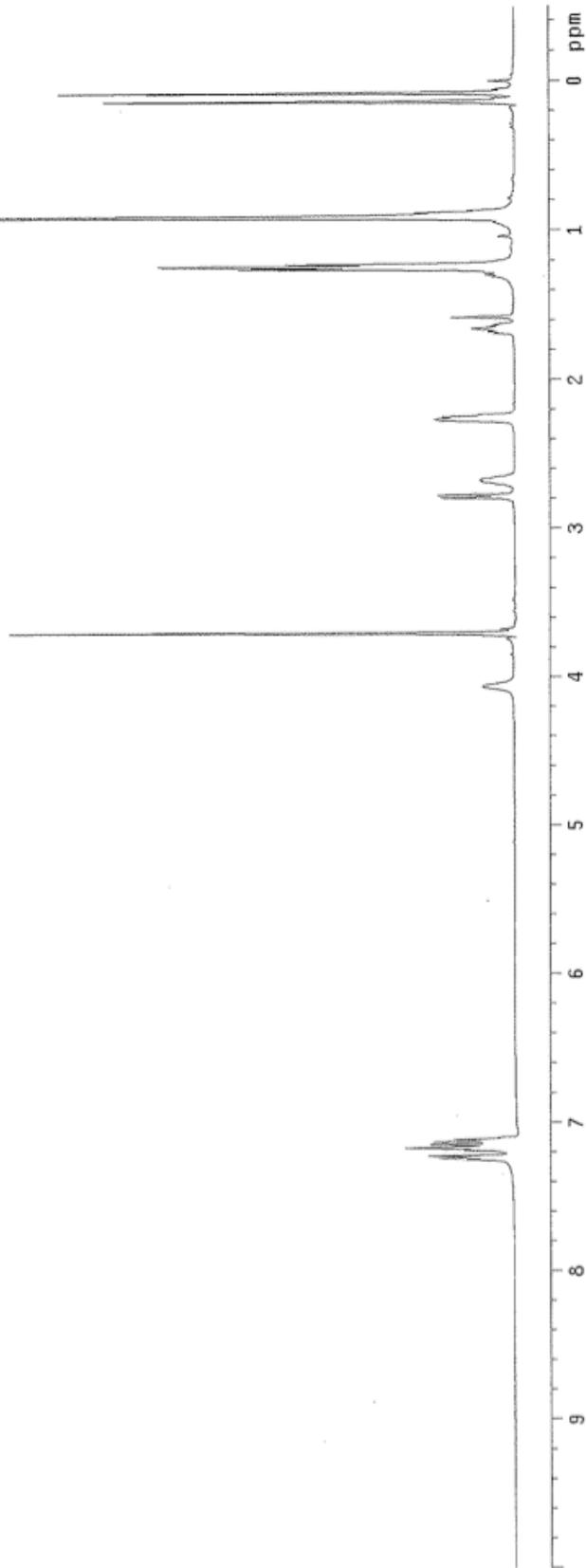


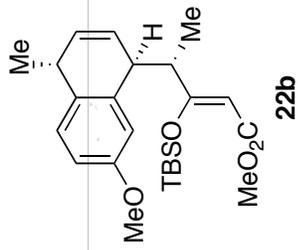
21b

INDEX 1 FREQUENCY PPM HEIGHT
 -2517.395 -5.036 0.0

DLV-1988fr49-54
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 INOVA-500 "tocsy.Chem.buffalo.edu"

Relax. delay 2.000 sec
 Pulse 34.6 degrees
 Acq. time 1.891 sec
 Width 10000.0 Hz
 16 repetitions
 OBSERVE H1, 499.8984077 MHZ
 DATA PROCESSING
 Line broadening 0.7 Hz
 FT size 65536
 Total time 1 min, 2 sec





DLV-1978fr47-60

Pulse Sequence: s2pu1

Solvent: CDCl3

Temperature

INOVA-500 "Eocsy.Chem.buffalo.edu"

Relax. delay 2.000 sec

Pulse 34.6 degrees

Acq. time 1.891 sec

Width 10000.0 Hz

16 repetitions

OBSERVE F1 499.8964022 MHz

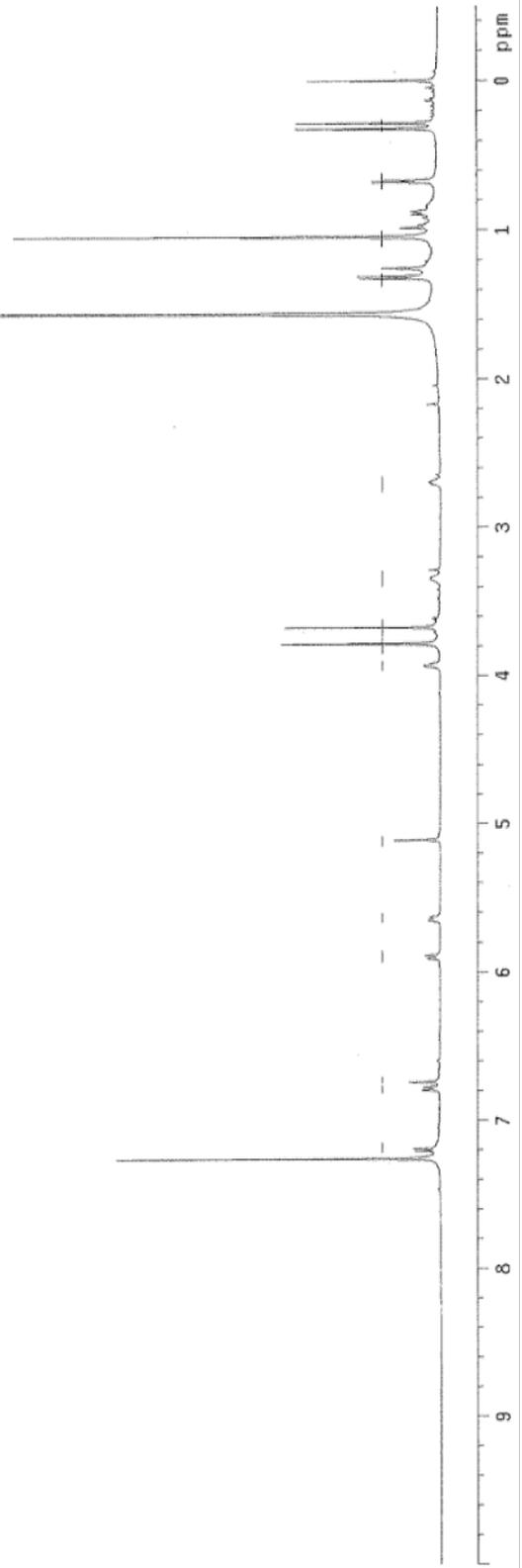
DATA PROCESSING

Line broadening 0.7 Hz

File size 85536

Total time 1 min, 2 sec

INDEX	FREQUENCY PPM	HEIGHT
1	3629.761	7.261
2	2554.626	5.110
3	1892.700	3.788
4	1837.483	3.676
5	783.081	1.566
6	662.231	1.325
7	655.212	1.311
8	627.136	1.255
9	523.071	1.046
10	491.943	0.984
11	339.050	0.678
12	332.336	0.665
13	160.217	0.320
14	141.602	0.283
15	-0.000	-0.000



DLV-1387fr24-40c13 in benzene

Pulse Sequence: s2pu

Solvent: Benzene

Acquisition Temperature

GENIWI-300 "roesy.Chem.buffalo.edu"

Relax. delay 5.000 sec

Pulse 90.0 degrees

Acq. time 1.706 sec

Width 18761.7 Hz

25 repetitions

DESERVING 75.453669 MHz

DECOUPLE C13, 90.0754701 MHz

PCOUNT 1023, 8B

continuously on

WALTZ-16 modulated

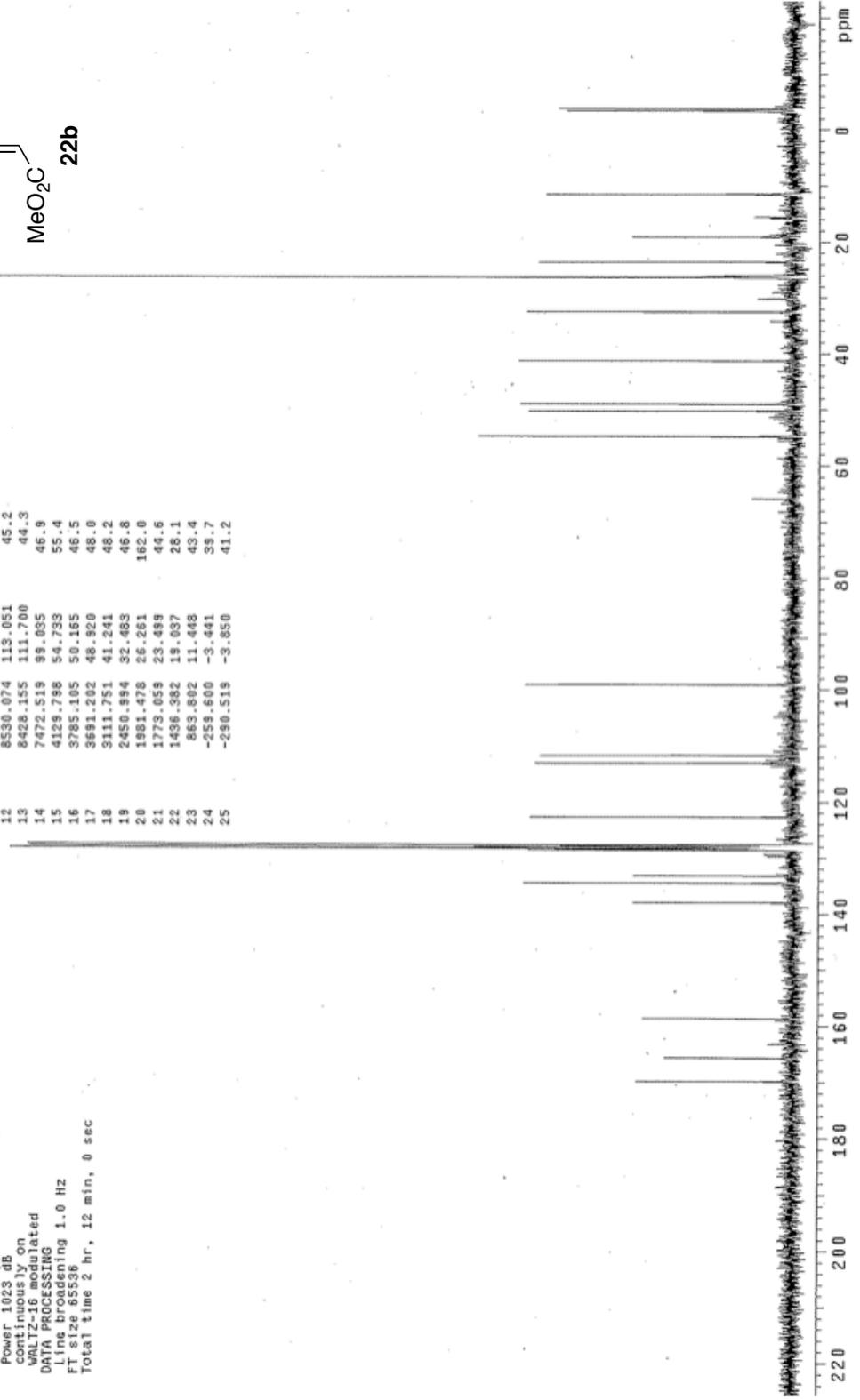
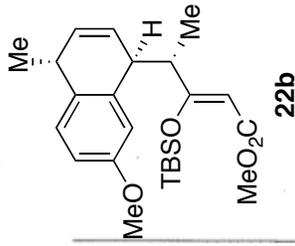
DATA PROCESSING

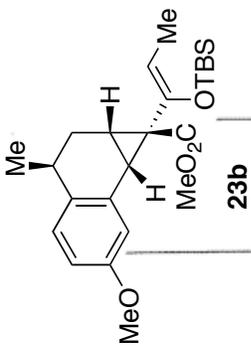
Line broadening 1.0 Hz

FT size 65536

Total time 2 hr, 12 min, 0 sec

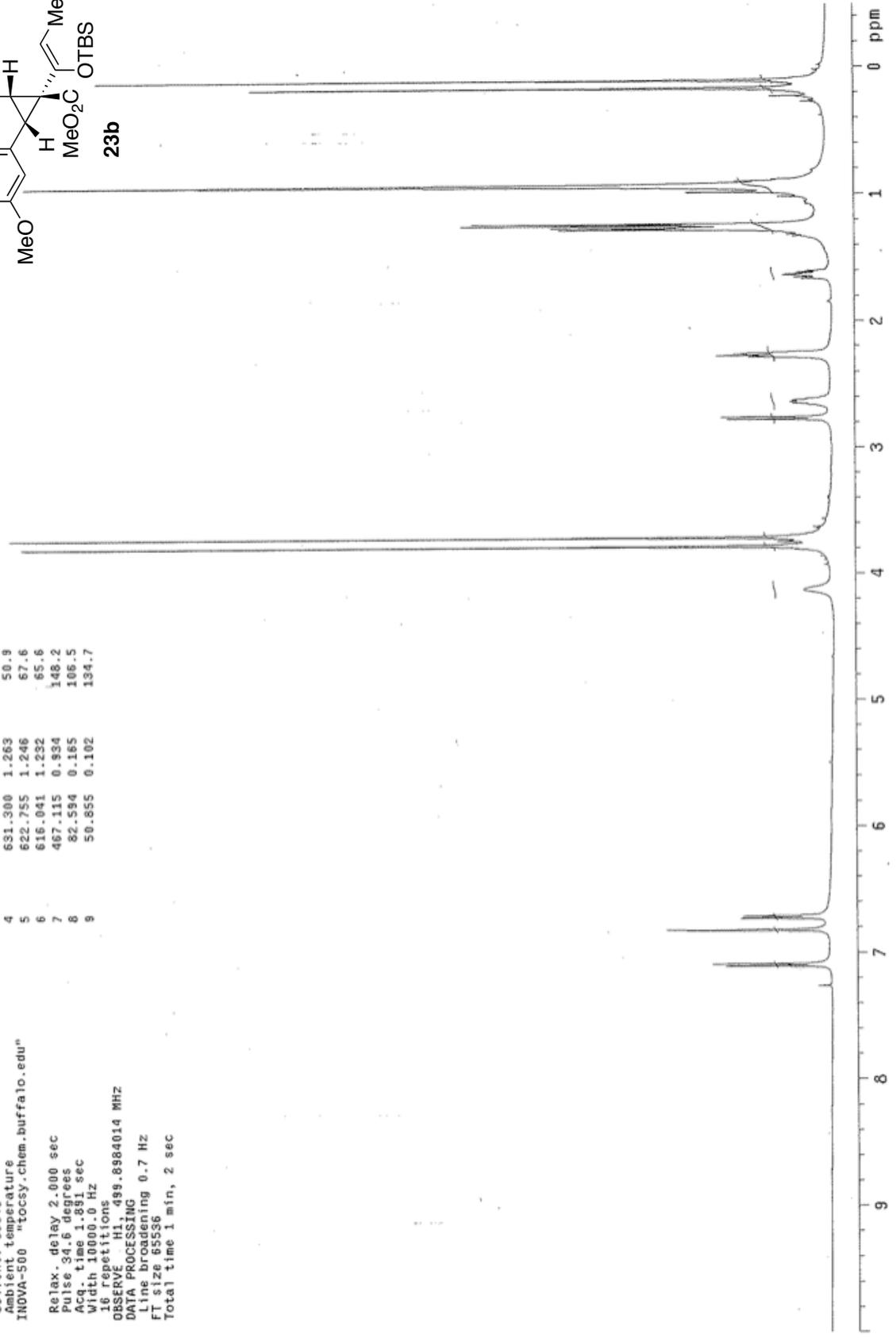
INDEX	FREQUENCY	PPM	HEIGHT
1	12812.972	169.813	27.2
2	12486.908	165.624	22.2
3	11988.417	159.620	26.1
4	10407.564	137.833	27.8
5	10147.613	134.488	47.2
6	10046.838	133.153	27.8
7	9701.000	128.568	46.4
8	9682.105	128.319	138.9
9	9658.057	128.000	135.4
10	9653.436	127.674	135.8
11	9257.251	122.688	46.1
12	8530.074	118.051	45.2
13	8428.155	111.700	44.3
14	7472.519	99.035	46.9
15	4129.788	54.733	55.4
16	3795.105	50.165	46.5
17	3691.202	48.520	48.0
18	3111.751	41.241	48.2
19	2450.894	32.483	46.8
20	1981.478	26.261	162.0
21	1773.059	23.489	44.6
22	1496.382	19.037	28.1
23	863.802	11.468	43.4
24	-259.600	-3.441	39.7
25	-259.519	-3.850	41.2





INDEX	FREQUENCY	PPH	HEIGHT
1	1892.591	3.786	149.0
2	1856.886	3.715	151.2
3	638.014	1.276	49.7
4	631.300	1.263	50.9
5	622.755	1.246	67.6
6	616.041	1.232	65.6
7	467.115	0.934	148.2
8	82.594	0.165	106.5
9	50.855	0.102	134.7

DLV-1771fr20-28
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 INOVA-500 "tocsy.chem.buffalo.edu"
 Relax. delay 2.000 sec
 Pulse 34.6 degrees
 Acq. time 1.891 sec
 Width 10000.0 Hz
 16 repetitions
 OBSERVE H1, 499.8984014 MHZ
 DATA PROCESSING
 Line broadening 0.7 Hz
 FT size 65536
 Total time 1 min, 2 sec



DLV-1771r20-28c13
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 GEMINI-300 "roesy.Chem.buffalo.edu"

Relax. delay 5.000 sec
 Pulse 90.0 degrees
 Width 18741.700 sec
 24 repetitions
 OBSERVE C13 75.4538675 MHZ
 DECOUPLE H1 300.0754431 MHZ
 Power 1023 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 2 hr, 12 min, 0 sec

INDEX	FREQUENCY PPM	HEIGHT
1	13120.060	173.882
2	11864.865	157.248
3	10780.805	143.012
4	10107.717	133.959
5	10065.819	133.405
6	8517.387	126.136
7	8687.146	115.132
8	8461.550	112.142
9	8337.873	110.503
10	5841.997	77.425
11	5809.932	77.000
12	5777.868	76.575
13	4150.923	55.001
14	3816.983	51.812
15	2948.178	39.073
16	2567.412	34.026
17	2148.856	28.479
18	2095.606	27.773
19	2071.558	27.455
20	1934.712	25.641
21	1519.019	20.132
22	1383.890	18.341
23	890.205	11.003
24	-328.124	-4.348
25	-363.052	-4.812

