Supporting Information

Oxidative Carbocation Formation in Macrocycles: Synthesis of the Neopeltolide Macrocycle

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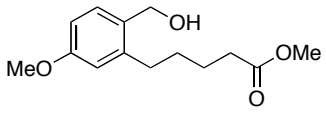
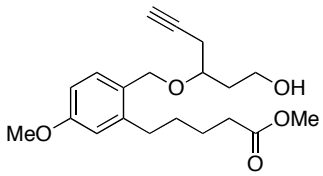
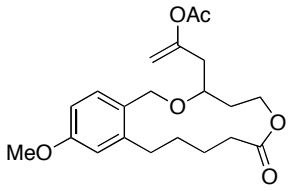
General Experimental Proton (^{1}H NMR) were recorded on Bruker Avance 300 spectrometer at 300 MHz or on a Brucker Avance 700 spectrometer at 700 MHz. Carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded on Bruker Avance 300 spectrometer at 75 MHz. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.26 ppm, for ^{13}C NMR: $CDCl_3$ = 77.23. Data are reported as follows: (s = singlet; d = doublet; t = triplet; q = quartet; dd = doublet of doublets; dt = doublet of triplets; br = broad). High resolution and low resolution mass spectra were recorded on a VG 7070 spectrometer. Infrared (IR) spectra were collected on a Mattson Cygnus 100 spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Samples for IR were prepared as a thin film on a NaCl plate by dissolving the compound in CH_2Cl_2 and then evaporating the CH_2Cl_2. Methylene chloride was distilled under N_2 from CaH_2. 1,2–dichloroethane was dried over 4Å molecular sieves. Analytical TLC was performed on E. Merck pre-coated (25 mm) silica gel 60F-254 plates. Visualization was done under UV (254 nm). Flash chromatography was done using ICN SiliTech 32-63 60 Å silica gel. Reagent grade ethyl acetate, diethyl ether, pentane and hexanes (commercial mixture) were purchased from EM Science and used as is for chromatography. All reactions were performed in oven or flame-dried glassware under a positive pressure of N_2 with magnetic stirring unless otherwise noted.



To a solution of **7**[1] (250 mg, 2.19 mmol) in 1.2 mL anhydrous THF at 0 °C was added 9-BBN (6.4 mL, 0.5 M in THF, 3.20 mmol). The reaction was warmed to RT after the addition and stirred for 4 hours, then was diluted with 12 mL anhydrous DMF and treated with $PdCl_2(dppf)\cdot CH_2Cl_2$ (49 mg, 0.060 mmol), **6** (428 mg, 2.00 mmol) and K_2CO_3 (550 mg, 4.0 mmol). The mixture was heated to 50 °C and stirred overnight. The reaction was quenched by pouring the crude mixture into H_2O, and the aqueous layer was then extracted with EtOAc and washed with H_2O three times. The combined organic layer was dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (20% EtOAc in hexane) to give desired coupled product for next step (354 mg, contaminated by borate derivatives). The crude coupled product was dissolved in 3 mL MeOH and cooled to 0 °C, followed by the addition of $NaBH_4$ (54 mg, 1.4 mmol). The reaction was stirred at 0 °C for 10 minutes, then was quenched with aq. $NaHCO_3$. The crude mixture was extracted with EtOAc, dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (30% EtOAc in hexane) to give **8** (244 mg, 49% over two steps).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.4 Hz, 1H), 6.75 (s, 1H), 6.73 (dd, J = 2.7, 7.8 Hz, 1H), 4.64 (d, J = 4.8 Hz, 2H), 3.81 (s, 3H), 3.68 (s, 3H), 2.70 (t, J = 7.8 Hz, 2H), 2.37 (t, J = 6.9 Hz, 2H), 1.79 - 1.60 (m, 4H); ^{13}C (75 MHz, $CDCl_3$) δ 174.1, 159.3, 142.1, 130.7, 130.1, 115.2, 110.9, 62.7, 55.1, 51.5, 33.8, 32.1, 30.6, 24.8; IR (neat) 3421, 2945, 2866, 1735, 1610, 1579, 1500, 1437, 1253, 1162, 1110, 1034, 1005 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{20}O_4$ (M^+) 252.1362, found 252.1351.



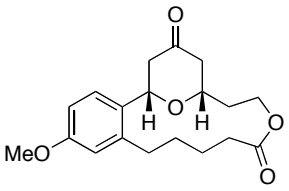
To a solution of **8** (800 mg, 3.17 mmol) in CH_2Cl_2 (6 mL) at 0 °C was added DBU (711 μL, 4.76 mmol) and Cl_3CCN (954 μL, 9.51 mmol). The reaction was warmed to RT and stirred for 1h. The mixture was directly concentrated to give a very viscous brown oil, and purified by neutralized silica gel flash chromatography (10% EtOAc and 1% Et_3N in hexane) to give the trichloroacetimidate of **8** (989 mg, 80%). The trichloroacetimidate and **9**[2] (356 mg, 1.56 mmol) were dissolved in toluene (30 mL) at RT. $La(OTf)_3$ (137 mg, 0.234 mmol) was added. The reaction was stirred at RT for 8 hours, then was filtered through a plug of silca gel using Et_2O as the eluent. The filtrate was concentrated and partially purified by flash chromatography (10% EtOAc in hexane) to give the desired homopropargylic ether (628 mg, containing some unreacted **9**). The crude ether was dissolved in MeOH (10 mL) and treated with a crystal of *p*-TsOH. The reaction was stirred at RT for 1.5 h, then was concentrated and purified by flash chromatography (45% EtOAc in hexane) to give **10** (339 mg, 63% over two steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.1 Hz, 1H), 6.72 (d, *J* = 2.7 Hz, 1H), 6.70 (dd, *J* = 2.7, 10.8 Hz, 1H), 4.66 (d, *J* = 10.8 Hz, 1H), 4.41 (d, *J* = 11.1 Hz, 1H), 3.78 (s, 3H), 3.81-3.69 (m, 3H); 3.66 (s, 3H), 2.68 (t, *J* = 8.1 Hz, 2H), 2.54 (ddd, *J* = 2.4, 4.8, 16.8 Hz, 1H), 2.46 (ddd, *J* = 2.7, 3.9, 14.1 Hz, 1H), 2.35 (t, *J* = 6.9 Hz, 2H), 2.30-2.19 (m, 1H), 2.04 (t, *J* = 2.4 Hz, 1H), 1.98-1.80 (m, 2H), 1.78-1.58 (m, 4H); ^{13}C (75 MHz, $CDCl_3$) δ 174.1, 159.5, 142.7, 131.2, 127.6, 115.1, 110.8, 80.8, 75.8, 70.4, 69.1, 60.1, 55.2, 51.5, 36.3, 33.9, 32.2, 30.6, 24.9, 23.6; IR (neat) 3447, 3288, 2947, 2869, 1734, 1610, 1579, 1502, 1437, 1349, 1260, 1164, 1063 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{28}O_5$ (M^+) 348.1925, found 348.1937.



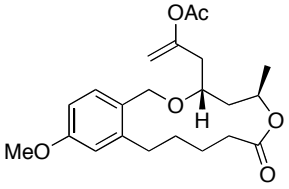
To a solution of **10** (339 mg, 0.974 mmol) of **10** in a mixture of THF, MeOH, and H_2O (3 mL, 1 mL, and 1 mL, respectively) at RT was added $LiOH{\cdot}H_2O$ (164 mg, 3.90 mmol). The reaction was stirred at RT for one hour, then was acidified with 0.5 M HCl until the pH was between 3 and 4. The aqueous solution was extracted with EtOAc three times, and the combined organic layer was dried with $MgSO_4$ and filtered. The filtrate was concentrated and was carried to the next step without purification. The crude acid (120 mg, 0.359 mmol) was dissolved in anhydrous THF (2.5 mL) followed by the addition of anhydrous Et_3N (250 μL, 1.80 mmol) at RT. The mixture was stirred for 20 min, then a solution of trichlorobenzoyl chloride (127 mg, 0.539 mmol) in THF (2.5 mL) was added. A precipitate formed after several minutes, and the stirring was continued for 2 h. The crude mixed acid anhydride was filtered through a pad of Celite and washed with toluene (160 mL total). The toluene solution of the mixd anhydride was added dropwise into a solution of DMAP (175 mg, 1.44 mmol) in toluene (50 mL) at 65 °C over a period of 5 hours. After the addition, the crude mixture was concentrated, re-dissolved in Et_2O and washed with aq. $NaHCO_3$. The organic layer was dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (15% EtOAc in hexane) to give the desired macrolactone (79 mg, 70% over two steps). To a suspension of $[(p\text{-cymene})RuCl_2]_2$ (6 mg, 0.01 mmol), Na_2CO_3 (4 mg, 0.04 mmol), tri(2-furyl)phosphine (5 mg, 0.02mmol), and acetic acid (29 μL, 0.50 mmol) in toluene (1.5 mL) was added 1-decyne (45 μL, 0.25 mmol). The mixture was heated to 80 °C and stirred for one hour. Another 29 μL portion of acetic acid and the macrolactone (79 mg, 0.25 mmol) were dissolved in toluene (1.5 mL) and added into the reaction through syringe. The reaction was stirred at the 80 °C overnight. Then crude mixture was loaded onto a small plug of silica gel and eluted with Et_2O. The residue was concentrated and purified by flash chromatography (15% Et_2O in hexane) to give **11** (65 mg, 70%).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.8 Hz, 1H), 6.71 (s, 1H), 6.69 (dd, *J* = 2.4, 7.8Hz, 1H), 4.85 (s, 1H), 4.84 (s, 1H), 4.58 (d, *J* = 9.6 Hz, 1H), 4.41 (ddd, *J* = 3.3, 7.2, 11.7 Hz, 1H), 4.32 (d, *J* = 9.6 Hz, 1H), 4.03 (ddd, *J* = 3.3, 7.5, 11.4 Hz, 1H), 3.78 (s, 3H), 3.81-3.70 (m, 1H), 2.75 (ddd, *J* = 3.9, 12.3, 12.3 Hz, 1H), 2.67 (dd, *J* = 5.4, 14.7 Hz, 1H), 2.54 (ddd, *J* = 4.8, 11.7, 11.7 Hz, 1H), 2.45 (dd, *J* = 6.6, 15.0 Hz, 1H), 2.50-2.34 (m, 2H), 2.09 (s, 3H), 2.05-1.84 (m, 3H), 1.84-1.73 (m, 2H), 1.70-1.59 (m, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 174.1, 169.1, 159.6, 153.0, 143.9, 132.5, 127.8, 115.4, 111.0, 104.2, 75.5, 69.6, 62.3, 55.2, 38.4, 33.4, 32.6, 32.3, 30.5, 25.5, 21.1; IR (neat) 2931, 2866, 1754, 1729, 1665, 1610,

1579, 1503, 1446, 1369, 1349, 1263, 1200, 1067, 1027 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{28}O_6Na$ $(M+Na)^+$ 399.1784, found 399.1790.

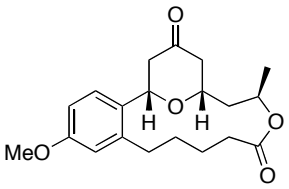
General procedure for the cyclization reactions: The substrate (1 eq.), 2,6-dichloropyridine (3 eq.) and 4 Å molecular sieves (2 mass eq.) were dissolved in anhydrous 1,2-dichloroethane to give an approximately 0.09 M solution. The mixture was stirred at room temperature for 15 minutes, then DDQ (1.5 eq or amount specified in the experiment detail) was added in one portion. The reaction was monitored by TLC at room temperature unless specified, and quenched by Et_3N when the starting material was consumed. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and Et_2O. The filtrate was concentrated and purified with flash chromatography to give the desired product.



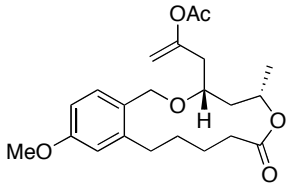
The general procedure for the cyclization reaction was followed with **11** (64 mg, 0.17 mmol), 2,6-dichloropyridine (76 mg, 0.51 mmol) and 4 Å molecular sieves (128 mg) in 1,2-dichloroethane (2 mL). DDQ (58 mg, 0.26 mmol) was initially added, and after 1.75 h another 7.7 mg DDQ was added. The reaction was stirred 15 more minutes then was quenched and purified by flash chromatography (35% EtOAc in hexane) to give the desired product **12** (41 mg, 73%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.1 Hz, 1H), 6.77 (dd, *J* = 2.7, 11.1 Hz, 1H), 6.75 (s, 1H), 4.73 (dd, *J* = 1.8, 12.3 Hz, 1H), 4.23-4.11 (m, 2H), 4.05 (ddd, *J* = 4.5, 8.7, 12.9 Hz, 1H), 3.00 (t, *J* = 15.0 Hz, 1H), 2.76 (tt, *J* = 3.0, 10.2 Hz, 1H), 2.65-2.55 (m, 1H), 2.55-2.40 (m, 4H), 2.39-2.28 (m, 1H), 1.96 (quintet, *J* = 4.8 Hz, 1H), 2.01-1.90 (m, 1H), 1.83-1.66 (m, 3H), 1.64-1.49 (m, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 207.0, 173.6, 159.6, 143.9, 128.3, 127.6, 115.9, 111.1, 75.4, 74.2, 60.6, 55.2, 48.1, 46.6, 34.1, 32.6, 30.4, 25.6; IR (neat) 2959, 2938, 2869, 1719, 1615, 1577, 1500, 1463, 1422, 1371, 1315, 1255, 1148, 1062, 1044, 1030, 803 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{24}O_5$ (M^+) 332.1624, found 332.1615.



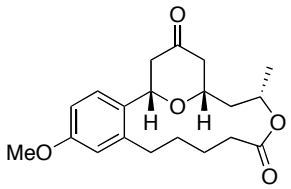
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.1 Hz, 1H), 6.70 (s, 1H), 6.68 (dd, *J* = 2.7, 8.4 Hz, 1H), 5.12 (ddq, *J* = 3.6, 6.3, 6.3 Hz, 1H), 4.82 (s, 2H), 4.60 (d, *J* = 9.9 Hz, 1H), 4.22 (d, *J* = 9.9 Hz, 1H), 3.84 (ddt, *J* = 3.0, 6.6, 6.6 Hz, 1H), 3.77 (s, 3H), 2.77 (dt, *J* = 3.9, 12.0 Hz, 1H), 2.66 (dd, *J* = 5.4, 15.0 Hz, 1H), 2.52-2.30 (m, 4H), 2.06 (s, 3H), 2.00-1.53 (m, 6H), 1.26 (d, *J* = 6.3 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 173.7, 169.0, 159.6, 153.1, 144.1, 132.5, 127.9, 115.4, 110.9, 104.1, 73.6, 70.0, 67.5, 55.2, 38.7, 38.3, 33.5, 32.4, 30.8, 25.4, 21.1, 20.3; IR (neat) 2933, 2866, 1755, 1726, 1665, 1610, 1579, 1504, 1446, 1369, 1263, 1199, 1117, 1084, 1028 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{30}O_6Na$ $(M+Na)^+$ 413.1940, found 413.1941.



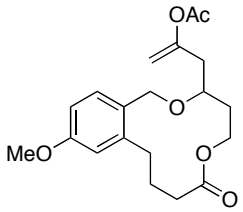
The general procedure for the cyclization reaction was followed with **13** (77 mg, 0.20 mmol), DDQ (67 mg, 0.30 mmol) 2,6-dichloropyridine (88 mg, 0.59 mmol), and 4 Å molecular sieves (154 mg) in 1,2-dichloroethane (2 mL). The mixture was stirred for 4 hours was purified by flash chromatography (30% EtOAc in hexane) to give the desired product **14** (51 mg, 74%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 1H), 6.75 (dd, *J* = 2.4, 8.1 Hz, 1H), 6.74 (s, 1H), 4.90 (ddq, *J* = 2.1, 6.0, 6.3 Hz, 1H), 4.72 (dd, *J* = 1.2, 12.1 Hz, 1H), 4.09 (ddt, *J* = 3.6, 3.6, 9.9 Hz, 1H), 3.79 (s, 3H), 3.00 (dd, *J* = 13.2, 13.2 Hz, 1H), 2.73-2.55 (m, 2H), 2.55-2.40 (m, 4H), 2.35-2.23 (m, 1H), 2.05-1.90 (m, 1H), 1.89-1.54 (m, 5H), 1.28 (d, *J* = 6.0 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 207.1, 173.3, 159.7, 144.2, 128.2, 127.4, 115.7, 111.2, 75.3, 73.3, 67.8, 55.2, 48.4, 46.5, 42.1, 34.5, 32.6, 30.5, 25.6, 20.3; IR (neat) 2931, 2869, 1722, 1610, 1578, 1504, 1461, 1370, 1256, 1153, 1123, 1059, 962 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{26}O_5$ (M^+) 346.1780, found 346.1783.



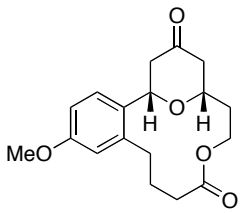
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 3.9, 9.3 Hz, 1H), 6.74-6.66 (m, 2H), 5.07 (ddq, *J* = 0.9, 5.5, 7.2 Hz, 1H), 4.83 (d, *J* = 1.5 Hz, 1H), 4.81 (s, 1H), 4.40 (d, *J* = 10.5 Hz, 1H), 4.35 (d, *J* = 10.5 Hz, 1H), 3.77 (s, 3H), 3.63 (ddt, *J* = 3.9, 3.9, 6.6 Hz, 1H), 2.75-2.56 (m, 3H), 2.49-2.35(m, 3H), 2.07 (s, 3H), 2.04-1.85 (m, 2H), 1.85-1.60 (m, 4H), 1.22 (d, *J* = 6.3 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 173.7, 169.1, 159.4, 152.8, 143.3, 132.5, 128.0, 115.1, 110.9, 104.2, 75.5, 70.6, 68.1, 55.1, 41.3, 38.9, 33.7, 31.9, 29.4, 24.4, 21.6, 21.0; IR (neat) 2933, 2869, 1755, 1724, 1665, 1610, 1579, 1503, 1449, 1369, 1262, 1205, 1084 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{30}O_6Na$ $(M+Na)^+$ 413.1940, found 413.1920.



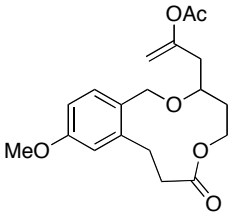
The general procedure for cyclization reaction was followed with **15** (88 mg, 0.22 mmol), DDQ (76 mg, 0.34 mmol) 2,6-dichloropyridine (100 mg, 0.67 mmol) and 4 Å molecular sieves (175 mg) in 1,2-dichloroethane (2.5 mL). The mixture was stirred for 4 hours then was purified by flash chromatography (30% EtOAc in hexane) to give the desired product **16** (53 mg, 69%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.7 Hz, 1H), 6.80 (dd, *J* = 3.0, 8.7 Hz, 1H), 6.71 (d, *J* = 2.7 Hz, 1H), 5.10 (ddq, *J* = 3.0, 6.3, 12.6 Hz, 1H), 4.68 (dd, *J* = 2.1, 12.0 Hz, 1H), 3.88-3.75 (m, 1H), 3.80 (s, 3H), 3.02 (dd, *J* = 3.0, 8.4 Hz, 1H), 2.96 (t, *J* = 12.3, 13.8 Hz, 1H), 2.55-2.40 (m, 4H), 2.38-2.29 (m, 2H), 2.10 (ddd, *J* = 6.6, 11.4, 15.6 Hz, 1H), 1.90-1.75 (m, 1H), 1.71-1.55 (m, 3H), 1.54-1.40 (m, 1H), 1.20 (d, *J* = 6.3 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 206.9, 173.5, 159.5, 142.2, 129.2, 127.6, 116.4, 111.3, 76.3, 74.3, 70.3, 55.2, 49.0, 46.3, 43.0, 35.0, 33.4, 28.3, 23.9, 20.9; IR (neat) 2922, 2856, 1721, 1611, 1579, 1504, 1456, 1423, 1371, 1309, 1266, 1151, 1095, 1068, 1045 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{26}O_5$ (M^+) 346.1780, found 346.1775.



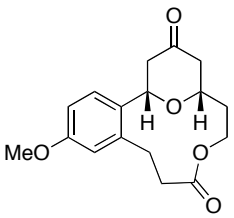
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.1 Hz, 1H), 6.71 (d, *J* = 2.7 Hz, 1H), 6.66 (dd, *J* = 2.4, 8.1 Hz, 1H), 4.82 (s, 2H), 4.65 (d, *J* = 9.9 Hz, 1H), 4.50-4.37 (m, 1H), 4.27 (d, *J* = 9.6 Hz, 1H), 4.18 (ddd, *J* = 2.7, 5.4, 11.1 Hz, 1H), 3.75 (s, 3H), 3.72-3.64 (m, 1H), 2.81-2.59 (m, 3H), 2.42 (dd, *J* = 7.2, 14.7 Hz, 1H), 2.36-2.25 (m, 2H), 2.06 (s, 3H), 2.02-1.80 (m, 4H); ^{13}C (75 MHz, $CDCl_3$) δ 173.2, 168.9, 159.5, 152.9, 143.1, 132.3, 127.8, 114.8, 110.7, 104.0, 76.6, 69.4, 62.2, 55.0, 37.7, 33.3, 32.2, 30.5, 26.6, 20.9; IR (neat) 3383 (br), 2953, 1754, 1728, 1665, 1611, 1578, 1504, 1457, 1432, 1369, 1258, 1197, 1116, 1070, 1041, 875, 803 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}O_6Na$ $(M+Na)^+$ 385.1627, found 385.1620.



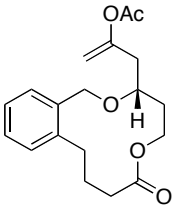
The general procedure for the cyclization reaction was followed with **17** (117 mg, 0.323 mmol), DDQ (110 mg, 0.48 mmol) 2,6-dichloropyridine (143 mg, 0.969 mmol) and 4 Å molecular sieves (234 mg) in 1,2-dichloroethane (3.5 mL). The mixture was stirred for 3.25 h then was purified by flash chromatography (35% EtOAc in hexane) to give the desired product **18** (78 mg, 76%).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 2.7 Hz, 1H), 6.68 (dd, *J* = 2.7, 8.7 Hz, 1H), 4.52 (ddd, *J* = 2.4, 11.1, 11.1 Hz, 1H), 4.45 (dd, *J* = 2.4, 12.0 Hz, 1H), 3.74 (ddd, *J* = 3.9, 3.9, 11.7 Hz, 1H), 3.56 (ddd, *J* = 3.6, 7.8, 10.8 Hz, 1H), 3.43 (s, 3H), 2.86 (ddd, *J* = 8.1, 8.1, 13.2 Hz, 1H), 2.63 (dd, *J* = 12.3, 12.3 Hz, 1H), 2.54 (ddd, *J* = 3.6, 8.1, 12.3 Hz, 1H), 2.36 (ddd, J = 1.8, 1.8, 13.8 Hz, 1H), 2.20-2.10 (m, 4H), 1.79-1.58 (m, 2H), 1.50-1.35 (m, 1H), 1.03 (ddd, *J* = 3.3, 3.3, 12.0 Hz, 1H); ^{13}C (75 MHz, C_6D_6) δ 205.1, 173.2, 160.5, 143.9, 115.9, 111.6, 77.2, 76.1, 61.3, 55.1, 48.2, 46.9, 36.1, 32.6, 29.9, 27.6; IR (neat) 2916, 2852, 1716, 1613, 1575, 1501, 1444, 1326, 1251, 1150, 1110, 1050 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{22}O_5$ (M^+) 318.1467, found 318.1464.



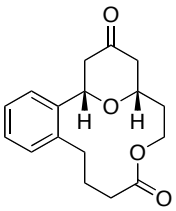
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 2.7 Hz, 1H), 6.69 (dd, *J* = 2.7, 8.4 Hz, 1H), 4.83 (d, *J* = 1.5 Hz, 1H), 4.81 (s, 1H), 4.53 (d, *J* = 10.8 Hz, 1H), 4.33 (d, *J* = 10.8 Hz, 1H), 4.35-4.24 (m, 1H), 4.05 (dt, *J* = 3.3, 11.1 Hz, 1H), 3.78 (s, 3H), 3.64 (ddt, *J* = 1.8, 5.1, 7.5 Hz, 1H), 3.12-2.94 (m, 2H), 2.77-2.64 (m, 2H), 2.56 (ddd, *J* = 3.0, 7.8, 14.1 Hz, 1H), 2.34 (dd, *J* = 7.5, 14.7 Hz, 1H), 2.13 (s, 3H), 2.08-1.92 (m, 1H), 1.75 (ddd, *J* = 3.3, 5.4, 15.3 Hz, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 172.3, 169.0, 159.8, 153.0, 142.4, 132.4, 128.0, 115.5, 111.4, 104.1, 73.5, 67.7, 62.4, 55.1, 38.0, 36.8, 31.9, 28.0, 21.1; IR (neat) 2922, 1753, 1732, 1665, 1611, 1505, 1454, 1429, 1370, 1318, 1198, 1147, 1068, 1043 cm^{-1}; HRMS(EI) calcd for $C_{20}H_{26}O_6Na$ (M+Na) 385.1627, found 385.1620.



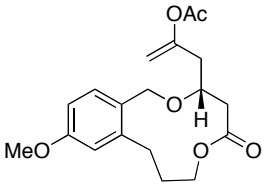
The general procedure for the cyclization reaction was followed with **19** (63 mg, 0.18 mmol), 2,6-dichloropyridine (81 mg, 0.55 mmol) and 4 Å molecular sieves (127 mg) were dissolved in 2 mL anhydrous 1,2-dichloroethane. DDQ (62 mg, 0.27 mmol) was initially added. After 4 h another 4 mg DDQ was added. The mixture was stirred two more hours then was purified by flash chromatography (40% EtOAc in hexane) to give the desired product **20** (41 mg, 73%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 2.7 Hz, 1H), 6.73 (dd, *J* = 2.4, 8.4 Hz, 1H), 4.72 (dd, *J* = 2.1, 12.0 Hz, 1H), 4.44 (dd, *J* = 5.4, 11.1 Hz, 1H), 4.18 (ddd, *J* = 5.1, 11.4, 11.4 Hz, 1H), 4.06 (dt, *J* = 5.1, 9.3 Hz, 1H), 3.79 (s, 3H), 3.16 (dd, *J* = 10.5, 12.6 Hz, 1H), 3.00-2.81 (m, 3H), 2.64 (d, *J* = 12.9 Hz, 1H), 2.49-2.25 (m, 4H), 1.62 (dd, *J* = 4.5, 15.0 Hz, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 206.7, 173.0, 159.9, 143.5, 128.8, 126.4, 116.8, 111.3, 75.1, 74.2, 61.6, 55.2, 48.1, 45.4, 37.5, 33.7, 28.7; IR (neat) 3016, 2950, 2898, 2857, 2817, 1724, 1613, 1575, 1508, 1456, 1427, 1387, 1352, 1310, 1288, 1267, 1150, 1118, 1061, 805 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{20}O_5Na$ $(M+Na)^+$ 327.1208, found 327.1202.



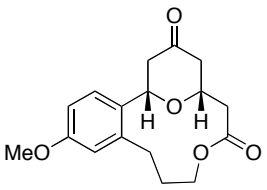
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.11 (m, 4H), 4.85 (s, 2H), 4.56 (d, *J* = 9.6 Hz, 1H), 4.45 (ddd, *J* = 3.3, 8.7, 11.7 Hz, 1H), 4.35 (d, *J* = 9.3 Hz, 1H), 4.21 (ddd, *J* = 3.0, 5.7, 11.4 Hz, 1H), 3.73 (ddt, *J* = 2.4, 5.4, 7.2 Hz, 1H), 2.86-2.65 (m, 3H), 2.46 (dd, *J* = 7.2, 15.0 Hz, 1H), 2.40-2.29 (m, 2H), 2.08 (s, 3H), 2.05-1.84 (m, 4H); ^{13}C (75 MHz, $CDCl_3$) δ 173.2, 169.0, 152.9, 141.6, 135.3, 131.1, 129.3, 128.5, 125.9, 104.2, 76.9, 70.1, 62.2, 37.8, 33.5, 32.2, 30.4, 26.7, 21.0; IR (neat) 2922, 1754, 1728, 1665, 1433, 1369, 1251, 1197, 1151, 1110, 1069, 879 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{24}O_5Na$ $(M+Na)^+$ 355.1521, found 355.1509.



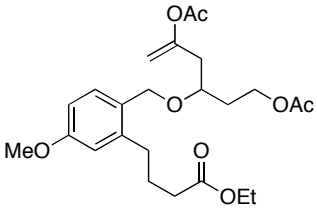
The general procedure for the cyclization reaction was followed except that the process was conducted at 40 °C with **21** (27 mg, 0.081 mmol), DDQ (55 mg, 0.24 mmol), 2,6-dichloropyridine (72 mg, 0.48 mmol) and 4 Å molecular sieves (54 mg) in 1,2-dichloroethane (1.2 mL). The reaction was stirred for 24 hours then was purified by flash chromatography (30% EtOAc in hexane) to give the desired product **22** (16 mg, 71%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.19 (m, 4H), 4.76 (dd, *J* = 2.4, 12.0 Hz, 1H), 4.69 (ddd, *J* = 2.1, 11.4, 11.4 Hz, 1H), 4.17 (ddd, *J* = 3.9, 3.9, 11.7 Hz, 1H), 4.02 (dddd, *J* = 1.5, 2.4, 7.8, 11.7 Hz, 1H), 2.97 (dd, *J* = 13.5, 13.5 Hz, 1H), 2.94-2.83 (m, 1H), 2.75 (ddd, *J* = 3.9, 9.0, 12.6 Hz, 1H), 2.58 (dd, *J* = 14.1, 14.1 Hz, 1H), 2.52 (dt, *J* = 2.1, 14.1 Hz, 1H), 2.39 (dt, *J* = 2.1, 14.1 Hz, 1H), 2.42-2.30 (m, 1H), 2.24 (dd, *J* = 2.1, 10.5 Hz, 1H), 2.20-2.03 (m, 2H), 1.96-1.77 (m, 2H); ^{13}C (75 MHz, $CDCl_3$) δ 206.6, 173.4, 141.4, 136.4, 130.1, 128.8, 126.5, 126.2, 77.2, 76.5, 60.9, 47.7, 46.3, 35.4, 32.4, 29.3, 26.9; IR (neat) 2959, 2918, 2857, 1723, 1326, 1257, 1153, 1071, 1048, 754 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{20}O_4$ (M^+) 288.1362, found 288.1369.



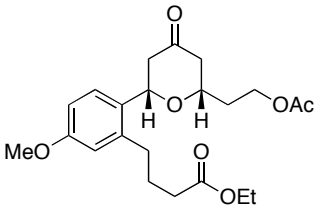
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.1 Hz, 1H), 6.73 (d, *J* = 2.7 Hz, 1H), 6.65 (dd, *J* = 2.7, 8.1 Hz, 1H), 4.87 (s, 2H), 4.62 (d, *J* = 10.8 Hz, 1H), 4.38 (d, *J* = 10.8 Hz, 1H), 4.40-4.30 (m, 1H), 4.10-3.99 (m, 1H), 3.97 (dt, *J* = 3.3, 10.5 Hz, 1H), 2.87-2.60 (m, 4H), 2.50-2.38 (m, 2H), 2.16 (s, 3H), 2.10-1.85 (m, 2H); ^{13}C (75 MHz, $CDCl_3$) δ 171.2, 169.0, 159.9, 152.3, 143.5, 132.3, 127.3, 115.1, 110.4, 104.6, 74.2, 70.7, 62.8, 55.1, 40.9, 38.0, 29.0, 26.6, 21.1; IR (neat) 2921, 1738, 1665, 1610, 1578, 1503, 1454, 1370, 1261, 1193, 1070, 1020 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{24}O_6$ (M^+) 348.1573, found 348.1561.



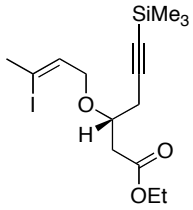
The general procedure for the cyclization reaction was followed with **23** (43 mg, 0.12 mmol), DDQ (42 mg, 0.19 mmol), 2,6-dichloropyridine (55 mg, 0.37 mmol) and 4 Å molecular sieves (86 mg) in 1,2-dichloroethane (1.5 mL). The mixture was stirred for 28 h then was purified by flash chromatography (35% EtOAc in hexane) to give the desired product **24** (24 mg, 65%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 2.7 Hz, 1H), 6.71 (dd, *J* = 2.7, 8.4 Hz, 1H), 4.88 (ddd, *J* = 2.7, 2.7, 10.8 Hz, 1H), 4.75 (dd, *J* = 1.8, 12.3 Hz, 1H), 4.33 (dddd, *J* = 2.7, 4.2, 11.4, 11.4 Hz, 1H), 3.79 (s, 3H), 3.73 (dd, *J* = 12.3, 12.3 Hz, 1H), 2.97 (dd, *J* = 12.9, 12.9 Hz, 1H), 2.82 (dd, *J* = 4.5, 14.7 Hz, 1H), 2.79-2.68 (m, 2H), 2.66-2.55 (m, 2H), 2.48 (dd, *J* = 11.4, 15.0 Hz, 1H), 2.36 (dd, *J* = 11.7, 14.4 Hz, 1H), 2.05-1.89 (m, 1H), 1.80-1.63 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.9, 170.2, 159.9, 145.1, 127.1, 126.2, 115.9, 110.3, 75.5, 74.3, 64.2, 55.2, 47.1, 45.0, 42.0, 30.9, 27.6; IR (neat) 2963, 2920, 1726, 1709, 1615, 1575, 1503, 1453, 1424, 1371, 1329, 1245, 1145, 1063, 1012, 814 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{20}O_5$ (M^+) 304.1311, found 304.1318.



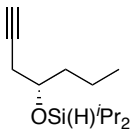
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.1 Hz, 1H), 6.72 (s, 1H), 6.71 (d, *J* = 9.6 Hz, 1H), 4.83 (s, 1H), 4.82 (s, 1H), 4.56 (d, *J* = 11.1 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 4.12 (q, *J* = 6.9 Hz, 4H), 3.78 (s, 3H), 3.70-3.58 (m, 1H), 2.68 (dt, *J* = 4.5, 7.5 Hz, 2H), 2.57 (dd, *J* = 6.0, 15.0 Hz, 1H), 2.45 (dd, *J* = 6.0, 14.7 Hz, 1H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.09 (s, 3H), 2.00 (s, 3H), , 2.00-1.75 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 173.4, 170.9, 169.0, 159.4, 152.9, 142.0, 131.3, 127.9, 115.1, 111.0, 104.1, 72.7, 68.7, 61.1, 60.3, 55.2, 38.2, 33.8, 33.1, 31.8, 26.2, 21.1, 20.9, 14.2; IR (neat) 2921, 1734, 1666, 1610, 1579, 1504, 1459, 1370, 1162, 1096, 1026 cm^{-1}; HRMS (EI) calcd for $C_{24}H_{34}O_8$ (M^+) 450.2254, found 450.2250.



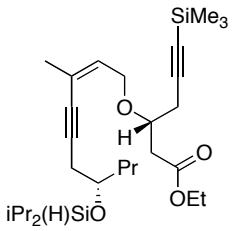
The general procedure for the cyclization reaction was followed with **25** (46 mg, 0.10 mmol), DDQ (35 mg, 0.15 mmol), 2,6-dichloropyridine (45 mg, 0.31 mmol), and 4 Å molecular sieves (92 mg) in 1,2-dichloroethane (1.2 mL). The mixture was stirred for 30 minutes then was purified by flash chromatography (30% EtOAc in hexane) to give the desired product **26** (32 mg, 76%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.7 Hz, 1H), 6.79 (dd, *J* = 2.7, 8.7 Hz, 1H), 6.72 (d, *J* = 2.4 Hz, 1H), 4.80 (dd, *J* = 2.4, 11.7 Hz, 1H), 4.30-4.15 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.95 (ddt, *J* = 3.6, 7.5, 7.5 Hz, 1H), 3.80 (s, 3H), 2.72-2.60 (m, 1H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.56-2.50 (m, 1H), 2.50-2.39 (m, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 2.01 (s, 3H), 2.08-1.83 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 206.6, 173.1, 170.9, 159.3, 140.4, 130.2, 127.2, 115.1, 111.9, 74.9, 74.2, 60.7, 60.4, 55.2, 48.6, 47.6, 35.3, 33.7, 31.8, 26.4, 20.9, 14.2; IR (neat) 2959, 2921, 1718, 1610, 1579, 1505, 1459, 1370, 1148, 1036 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{30}O_7$ (M^+) 406.1992, found 406.1986.



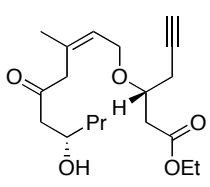
To a suspension of NaH (60% suspension in mineral oil, 10 mg, 0.25 mmol) in Et_2O (1.5 mL) at RT was added a solution of **32**[3] (500 mg, 2.53 mmol) in Et_2O (1 mL). After five minutes the mixture was cooled to 0 °C and Cl_3CCN (254 μL, 2.53 mmol) was added. After 10 minutes, the reaction was warmed to RT and concentrated. A mixture of 25 mL pentane and 0.1 mL methanol was added into the crude residue and the flask was shaken well to give a yellow suspension, which was filtrated through a plug of Celite with 10 mL pentane wash. The filtrate was concentrated without further purification for next step use (826 mg, 95%). To homopropargylic alcohol **33**[4] (115 mg, 0.504 mmol) in 2 mL anhydrous cyclohexane was added the trichloroacetimidate of iodobutenol (690 mg, 2.01 mmol). TfOH was added to the mixture at (8.7 μL, 0.075 mmol). A yellow precipitate formed within several minutes after the addition. The mixture was stirred at RT for 2 h, then was filtered through a small plug of Celite using hexane as the eluent. The filtrate was concentrated and purified by flash chromatography (4% → 5% Et_2O in hexane) to give the desired ether (159 mg, 77 %, *Z*/*E* = 7.3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (qt, *J* = 1.5, 5.7 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.10 (ddq, *J* = 1.5, 5.7, 11.4 Hz, 1H), 4.14-4.01 (m, 1H), 4.01-3.90 (m, 1H), 2.69 (dd, *J* = 4.5, 15.9 Hz, 1H), 2.65-1.38 (m, 3H), 2.53 (t, *J* = 1.5 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 0.15 (s, 9H); ^{13}C (75 MHz, $CDCl_3$) δ 171.1, 132.2, 102.5, 102.1, 87.2, 74.2, 74.1, 60.1, 39.5, 33.6, 25.2, 14.2, 0.0; IR (neat) 2959, 2176, 1737, 1250, 1208, 1159, 1100, 1046, 844, 760 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{22}O_3SiI$ $(M\text{-}CH_3)^+$ 393.0383, found 393.0386; $[\alpha]_D^{25} = -10.4$ ($CHCl_3$, *c* = 1.0).



34[5] (2.21 g, 19.7 mmol) and imidazole (2.68 g, 39.4 mmol) were dissolved in THF (120 mL). At solution of ^{i}Pr$_2$Si(H)Cl (3.56 g, 23.6 mmol) in THF (15 mL) was added dropwise into the reaction mixture, and a white precipitate formed immediately. The reaction was stirred at RT for 30 min, then was quenched with H_2O at 0 °C. The organic layer was extracted with Et_2O. The combined organic layer was washed with H_2O, dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (6% Et_2O in hexane) to give the desired product (3.31 g, 77%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.21 (s, 1H), 3.90-3.79 (m, 1H), 2.40 (ddd, *J* = 2.7, 5.4, 16.8 Hz, 1H), 2.34 (ddd, *J* = 2.7, 6.6, 16.8 Hz, 1H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.70-1.30 (m, 4H), 1.03 (s, 14H), 0.93 (t, *J* = 6.9 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 81.5, 72.8, 69.9, 38.5, 26.8, 18.4, 17.5, 17.4, 17.4, 14.1, 12.6, 12.5; IR (neat) 3314, 2957, 2941, 2867, 2092, 1463, 1366, 1243, 1111, 1091, 1040, 1002, 882, 841, 802 cm^{-1}; HRMS(EI) calcd for $C_{13}H_{25}OSi$ $(M\text{-}H)^+$ 225.1675, found 225.1676; $[\alpha]_D^{25} = -26.8$ ($CHCl_3$, *c* = 1.0).

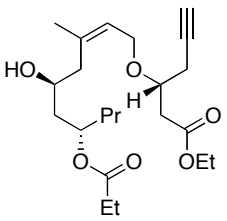


Vinyl iodide **35** (250 mg, 0.612 mmol) was dissolved in ^{i}Pr$_2$NH (4 mL), then $PdCl_2(PPh_3)_2$ (22 mg, 0.031 mmol) and CuI (18 mg, 0.092 mmol) were added sequentially. The mixture was purged with argon for 15 minutes, then the silylated alkyne (222 mg, 0.980 mmol) was added into the reaction via syringe. After 15 minutes the reaction mixture turned to a dark yellow/black slurry, which was filtered through a plug of silica gel using Et_2O as the eluent. The filtrate was concentrated and purified by flash chromatography (4% → 5% Et_2O in hexane) to give **36** (275 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69 (qt, *J* = 1.2, 6.3 Hz, 1H), 4.31-4.10 (m, 2H), 4.22 (s, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.93 (ddd, *J* = 4.8, 8.1, 12.6 Hz, 1H), 2.84 (ddt, *J* = 1.2, 5.1, 11.7 Hz, 1H), 2.71 (dd, *J* = 4.5, 15.6 Hz, 1H), 2.66-2.49 (m, 4H), 2.42 (dd, *J* = 7.5, 17.1 Hz, 1H), 1.84 (s, 3H), 1.68-1.50 (m, 2H), 1.50-1.32 (m, 2H), 1.27 (t, *J* = 6.9 Hz, 3H), 1.03 (s, 12H), 0.93 (t, J = 7.5 Hz, 3H), 0.14 (s, 9H); ^{13}C (75 MHz, $CDCl_3$) δ 171.3, 132.1, 121.8, 102.7, 92.4, 87.0, 80.4, 73.9, 73.0, 68.0, 60.4, 39.5, 38.8, 27.9, 25.0, 23.4, 18.4, 17.5, 17.4, 17.4, 14.2, 14.2, 12.6, 12.5, 0.0; IR (neat) 2957, 2866, 2177, 2091, 1739, 1462, 1375, 1250, 1205, 1158, 1091, 1038, 843, 760 cm^{-1}; HRMS (EI) calcd for $C_{28}H_{50}O_4Si$ (M^+) 506.3248, found 506.3236; $[\alpha]_D^{25} = -13.9$ ($CHCl_3$, *c* = 1.0).

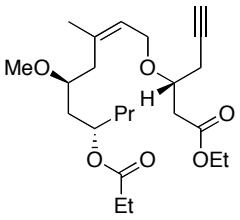


To **36** (100 mg, 0.194 mmol) in anhydrous THF (1 mL) was added Pt(DVDS) (7 μL, 2% Pt in xylene, 0.6 μmol). The reaction was stirred for one hour, then another 7 μL of the Pt(DVDS) solution was added. After 3 h, the crude mixture was filtered through a plug of silica gel using Et_2O as the eluent. The filtrate was concentrated and re-

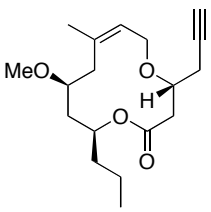
dissolved in THF (1.6 mL) followed by the addition of Bu_4NF (0.40 mL, 1M in THF, 0.40 mmol). The reaction was stirred for 15 minutes, after which DMF (2 mL) was added into the mixture, followed by an immediate and sequential addition of $KHCO_3$ (138 mg, 1.38 mmol), H_2O_2 (0.3 mL, 30% aqueous solution) and KF (80 mg, 1.4 mmol). The reaction mixture was then heated to 40 °C. After 30 minutes, another 0.2 mL H_2O_2 was added. After 1.5 h the mixture was cooled to then saturated aqueous Na_2SO_3 was slowly added into the flask. The crude mixture was stirred at 0 °C for 15 minutes, then was extracted with EtOAc three times. The combined organic layer was washed with brine three times, dried with $MgSO_4$, concentrated and purified by flash chromatography (25% EtOAc in hexane) to give **37** (38 mg, 57%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (qt, *J* = 0.9, 6.9 Hz, 1H), 4.15 (q, *J* = 6.9 Hz, 2H), 4.15-3.99 (m, 3H), 3.98-3.88 (m, 1H), 3.23 (s, 2H), 2.97 (d, *J* = 3.6 Hz, 1H), 2.68 (dd, *J* = 5.1, 16.2 Hz, 1H), 2.64-2.53 (m, 3H), 2.52-2.43 (m, 2H), 2.02 (t, *J* = 2.7 Hz, 1H), 1.76 (s, 3H), 1.55-1.32 (m, 4H), 1.27 (t, *J* = 7.2 Hz, 3H), 0.93 (t, *J* = 6.6 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 209.1, 171.2, 133.7, 125.1, 80.2, 73.8, 70.7, 67.4, 66.1, 60.6, 48.6, 47.4, 39.4, 38.6, 24.3, 23.8, 18.6, 14.2, 13.9; IR (neat) 3506, 3283, 2959, 2930, 2873, 1733, 1377, 1312, 1213, 1164, 1072, 1029 cm^{-1}; HRMS(EI) calcd for $C_{19}H_{30}O_5$ (M^+) 338.2093, found 338.2078; $[\alpha]_D^{25}$ = +12.0 ($CHCl_3$, *c* = 0.5).



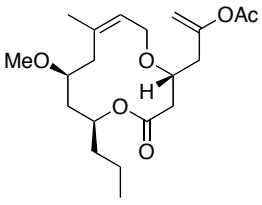
A solution of **37** (455 mg, 1.34 mmol) **37** and freshly distilled propionaldehyde (970 μL, 13.4 mmol) in THF (10 mL) was cooled to –10 °C. A freshly prepared SmI_2 solution (5.4 mL, 0.1 M in THF, 0.54 mmol) was added. The reaction was stirred under Ar for 4 hours, then was quenched with aq. $NaHCO_3$ at –10 °C. The crude mixture was extracted with EtOAc three times. The combined organic layer was dried with $MgSO_4$, concentrated and purified by flash chromatography (20% EtOAc in hexane) to give the desired product (411 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 (t, *J* = 6.6 Hz, 1H), 5.09 (ddd, *J* = 4.8, 8.4, 12.9 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.12-3.97 (m, 2H), 3.97-3.87 (m, 1H), 3.60 (dddd, *J* = 4.2, 4.2, 8.4, 12.6 Hz, 1H), 2.93 (d, 1H), 2.67 (dd, *J* = 5.1, 15.9 Hz, 1H), 2.57 (dd, *J* = 7.5, 15.3 Hz, 1H), 2.56-2.46 (m, 1H), 2.41 (ddd, *J* = 2.4, 6.6, 16.8 Hz, 1H), 2.32 (q, *J* = 7.5 Hz, 2H), 2.39-2.28 (m, 1H), 2.06 (dd, *J* = 4.8, 13.5 Hz, 1H), 2.01 (t, *J* = 2.7 Hz, 1H), 1.74 (s, 3H), 1.63-1.45 (m, 4H), 1.40-1.27 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.14 (dt, *J* = 0.6, 7.5 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 175.3, 171.2, 137.8, 124.0, 80.3, 73.7, 71.3, 70.6, 65.8, 65.5, 60.5, 42.7, 40.0, 39.4, 37.0, 27.8, 23.9, 23.8, 18.6, 14.2, 13.8, 9.3; IR (neat) 3507 (br), 3289, 2961, 2937, 2875, 1733, 1377, 1201, 1072, 1026 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{37}O_6$ (M^+) 397.2590, found 397.2571; $[\alpha]_D^{25}$ = –8.8 ($CHCl_3$, *c* = 1.0).



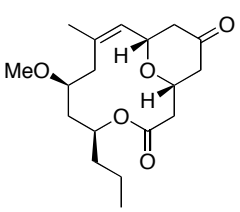
The reduction product (111 mg, 0.280 mmol) was dissolved in CH_2Cl_2 (3 mL) at 0 °C, followed by the addition of Proton Sponge (174 mg, 0.814 mmol) and Me_3OBF_4 (125 mg, 0.814 mmol). The mixture was stirred at 0 °C for 48 hours, then the reaction was quenched with aq. NH_4Cl. The crude mixture was extracted with EtOAc three times. The combined organic layer was dried with $MgSO_4$, concentrated and purified by flash chromatography (15% EtOAc in hexane) to give **38** (106 mg, 93%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.42 (t, *J* = 6.6 Hz, 1H), 5.10 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.07 (t, *J* = 7.2 Hz, 1H), 4.15-4.00 (m, 1H), 3.98-3.88 (m, 1H), 3.30 (s, 3H), 3.22 (dddd, *J* = 3.0, 3.0, 6.3, 12.3 Hz, 1H), 2.67 (dd, *J* = 5.1, 15.9 Hz, 1H), 2.57 (dd, *J* = 7.5, 15.6 Hz, 1H), 2.57-2.39 (m, 2H), 2.35 (dd, *J* = 7.8, 14.1 Hz, 1H), 2.29 (dd, *J* = 7.5, 15.0 Hz, 1H), 2.10 (dd, *J* = 7.2, 13.5 Hz, 1H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.74 (s, 3H), 1.62-1.38 (m, 4H), 1.36-1.25 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.8 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 174.0, 171.2, 136.8, 124.2, 80.2, 76.4, 73.7, 70.9, 70.6, 66.1, 60.5, 57.5, 39.6, 39.4, 37.3, 36.8, 27.9, 24.1, 23.8, 18.4, 14.2, 13.9, 9.4; IR (neat) 3275, 2962, 2935, 2876, 1734, 1462, 1376, 1263, 1194, 1094, 1029 cm^{-1}; HRMS (EI) calcd for $C_{23}H_{38}O_6$ (M^+) 410.2668, found 410.2665; $[\alpha]_D^{25}$ = –1.0 ($CHCl_3$, *c* = 1.0).



To a solution of **38** (173 mg, 0.421 mmol) in a mixture of THF, MeOH, and H_2O (1.5 mL/0.5 mL/0.5 mL), was added $LiOH{\cdot}H_2O$ (106 mg, 2.53 mmol). The reaction was stirred at 45 °C for 4 hours, then was cooled to 0 °C and treated with 0.5 M aq. HCl solution until the pH was 3 to 4. The crude mixture was extracted with EtOAc three times. The combined organic layer was dried with $MgSO_4$ and filtered. The residue was concentrated without purification for next step. To the crude acid in THF (2.5 mL) was added Et_3N (294 μL, 2.11 mmol). The mixture was stirred for 20 min, then a solution of trichlorobenzoyl chloride (154 mg, 0.632 mmol) taken THF (2.5 mL) was added into the reaction. A precipitate formed after several minutes, and the stirring was continued for 2 h. The crude mixed anhydride was filtered through a pad of Celite and washed with toluene (150 mL total). The resulting solution was then added dropwise into a solution of DMAP (206 mg, 1.69 mmol) in toluene (150 mL) at 65 °C over a period of 5 h. After the addition, the crude mixture was concentrated, re-dissolved in Et_2O and washed with aq. $NaHCO_3$. The organic layer was dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (10% EtOAc in hexane) to give **39** (92 mg, 71% over two steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (t, *J* = 7.8 Hz, 1H), 5.21 (dddd, *J* = 2.4, 5.1, 5.21, 12.9 Hz, 1H), 4.09-4.00 (m, 1H), 4.00-3.87 (m, 1H), 3.41 (dddd, *J* = 3.0, 5.4, 5.4, 11.1 Hz, 1H), 3.35 (s, 3H), 2.84 (dd, *J* = 3.6, 14.4 Hz, 1H), 2.64-2.52 (m, 2H), 2.43 (ddd, *J* = 2.7, 8.1, 16.8 Hz, 1H), 2.31 (dd, *J* = 7.8, 13.8 Hz, 1H), 2.18 (dd, *J* = 5.1, 13.5 Hz, 1H), 2.06 (t, *J* = 2.4 Hz, 1H), 1.87 (s, 3H), 1.71 (ddd, *J* = 2.4, 6.0, 14.7 Hz, 1H), 1.63 (dd, *J* = 3.3, 10.8 Hz, 1H), 1.59-1.41 (m, 2H), 1.41-1.23 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 170.3, 146.1, 120.3, 80.8, 80.0, 73.0, 72.6, 70.9, 63.8, 57.3, 40.8, 40.2, 38.4, 37.2, 26.4, 22.5, 18.6, 13.8; IR (neat) 3342, 2955, 2929, 2858, 1469, 1388, 1254, 1095, 1040, 837, 775 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{28}O_4$ (M^+) 308.1988, found 308.1991; $[\alpha]_D^{25}$ = –72.8 ($CHCl_3$, *c* = 1.0).

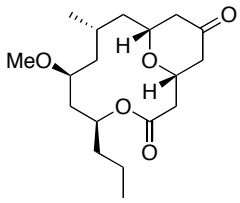


To a mixture of $[(p\text{-cymene})RuCl_2]_2$ (5 mg, 0.008 mmol), tri(2-furyl)phosphine (4 mg, 0.02 mmol), and Na_2CO_3 (3 mg, 0.03 mmol), in toluene (2 mL) were added acetic acid (24 μL, 0.41 mmol) and 1-decyne (37 μL, 0.20 mmol). The mixture was then heated to 80 °C and stirred for one hour. Another 24 μL portion of acetic acid and **39** (63 mg, 0.20 mmol) were dissolved in toluene (2 mL) and added into the reaction mixture. The reaction was stirred at 80 °C overnight. Then crude mixture was loaded onto a small plug of silica gel and eluted with Et_2O. The residue was concentrated and purified by flash chromatography (15% Et_2O in hexane) to give **40** (61 mg, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.50 (dt, *J* = 1.2, 7.8 Hz, 1H), 5.17 (dddd, *J* = 2.7, 5.7, 7.8, 10.5 Hz, 1H), 4.87 (s, 1H), 4.85 (d, *J* = 1.8 Hz, 1H), 4.01-3.83 (m, 3H), 3.40-3.31 (m, 1H), 3.34 (s, 3H), 2.76 (dd, *J* = 3.9, 14.4 Hz, 1H), 2.66 (dd, *J* = 4.8, 14.7 Hz, 1H), 2.52-2.41 (m, 2H), 2.28 (dd, *J* = 4.5, 13.5 Hz, 1H), 2.20 (dd, *J* = 7.8, 14.1 Hz, 1H), 2.15 (s, 3H), 1.86 (d, *J* = 1.5 Hz, 3H), 1.74 (ddd, *J* = 2.7, 5.4, 14.7 Hz, 1H), 1.68-1.44 (m, 3H), 1.30 (qt, *J* = 7.5, 7.5 Hz, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 170.4, 169.0, 152.5, 145.8, 120.5, 104.6, 81.2, 73.3, 72.4, 64.1, 57.2, 40.6, 39.7, 38.7, 37.3, 37.2, 26.3, 21.1, 18.6, 13.9; IR (neat) 2961, 2930, 2874, 1757, 1733, 1665, 1437, 1371, 1195, 1068, 1020 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{32}O_6$ (M^+) 368.2199, found 368.2188; $[\alpha]_D^{25}$ = –39.8 ($CHCl_3$, *c* = 0.25).



A mixture of **40** (30 mg, 0.081 mmol), 2,6-dichloropyridine (72 mg, 0.49 mmol), $LiClO_4$ (2 mg, 0.02 mmol), and 4 Å molecular sieves (60 mg) in 1,2-dichloroethane (1 mL) was stirred for 15 minutes, then DDQ (55 mg, 0.24 mmol) was added in one portion. The reaction stirred at RT for 18 hours, then was quenched by Et_3N. The crude mixture was filtered through a short plug of silica gel and eluted with CH_2Cl_2 and EtOAc. The filtrate was concentrated and purified by flash chromatography (20 % EtOAc in hexane) to give **41** (15 mg, 58 %) ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (dddd, *J* = 2.7, 5.7, 7.8, 11.7 Hz, 1H), 5.28 (d, *J* = 7.2 Hz, 1H), 4.23-4.11 (m, 2H), 3.53 (ddddd, *J* = 1.5, 1.5, 5.1, 5.1, 10.5 Hz, 1H), 3.37 (s, 3H), 2.69 (dd, *J* = 3.6, 15.0 Hz, 1H), 2.58 (dd, *J* = 10.8, 15.3 Hz, 1H), 2.52-2.31 (m, 4H), 2.67 (dd, *J* = 12.0, 14.7 Hz, 1H), 2.04 (dd, *J* = 10.2, 13.5 Hz, 1H), 1.89 (d, *J* = 0.6 Hz, 3H), 1.93-1.83 (m, 1H), 1.69 (ddd, *J* = 3.3, 11.7, 15.0 Hz, 1H), 1.57-1.47 (m, 1H), 1.41-1.23 (m, 3H),

0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 169.5, 148.3, 124.3, 81.7, 74.3, 73.4, 72.9, 57.9, 47.2, 46.8, 43.0, 42.4, 41.8, 37.3, 25.3, 18.6, 13.8; IR (neat) 2961, 2930, 2874, 1728, 1370, 1319, 1267, 1233, 1185, 1131, 1099, 1072, 807 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{28}O_5$ (M^+) 324.1937, found 324.1946; $[\alpha]_D^{25}$ = –92.3 ($CHCl_3$, c = 1.0); m.p. = 95-97 °C.



A mixture of **41** (46 mg, 0.14 mmol) and 10% Pd/C (15 mg, 0.014 mmol) in EtOH (3 mL) was evacuated and back-filled with H_2 three times. The mixture was stirred under an H_2 atmosphere for 6 hours, then was filtered through a plug of silica gel using EtOAc as the eluent. The filtrate was concentrated and the residue was purified by flash chromatography (6% → 8% Et_2O in CH_2Cl_2) to give **28** (34 mg, 74%). ^{1}H NMR (700 MHz, $CDCl_3$) δ 5.21 (dt, J = 4.9, 9.1 Hz, 1H), 4.04 (dddd, J = 2.8, 4.2, 10.5, 11.2 Hz, 1H), 3.58 (dddd, J = 2.1, 2.8, 9.1, 11.2 Hz, 1H), 3.50 (ddd, J = 2.8, 8.4, 9.8 Hz, 1H), 3.33 (s, 3H), 2.71 (dd, J = 3.5, 14.7 Hz, 1H), 2.51 (dd, J = 11.2, 14.7 Hz, 1H), 2.43 (ddd, J = 1.4, 2.8, 14.7 Hz, 1H), 2.33 (ddd, J = 1.4, 2.8, 14.0 Hz, 1H), 2.29 (dd, J = 11.2, 14.7 Hz, 1H), 2.24 (dd, J = 11.9, 14.7 Hz, 1H), 1.85 (ddd, J = 1.4, 10.5, 14.7 Hz, 1H), 1.71-1.59 (m, 3H), 1.54-1.47 (m, 2H), 1.41 (ddd, J = 1.4, 9.1, 15.4 Hz, 1H), 1.39-1.32 (m, 3H), 1.19 (ddd, J = 2.8, 11.2, 13.3 Hz, 1H), 1.01 (d, J = 7.0 Hz, 3H), 0.92 (t, J = 7.0 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 205.8, 169.9, 79.7, 75.7, 73.4, 73.4, 56.3, 48.8, 47.0, 44.3, 42.6, 41.9, 40.0, 37.0, 31.1, 25.4, 18.9, 13.9; IR (neat) 2958, 2923, 2872, 1726, 1459, 1368, 1257, 1091, 798 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{30}O_5$ (M^+) 326.2093, found 326.2096; $[\alpha]_D^{25}$ = –16.3 ($CHCl_3$, c = 0.16).

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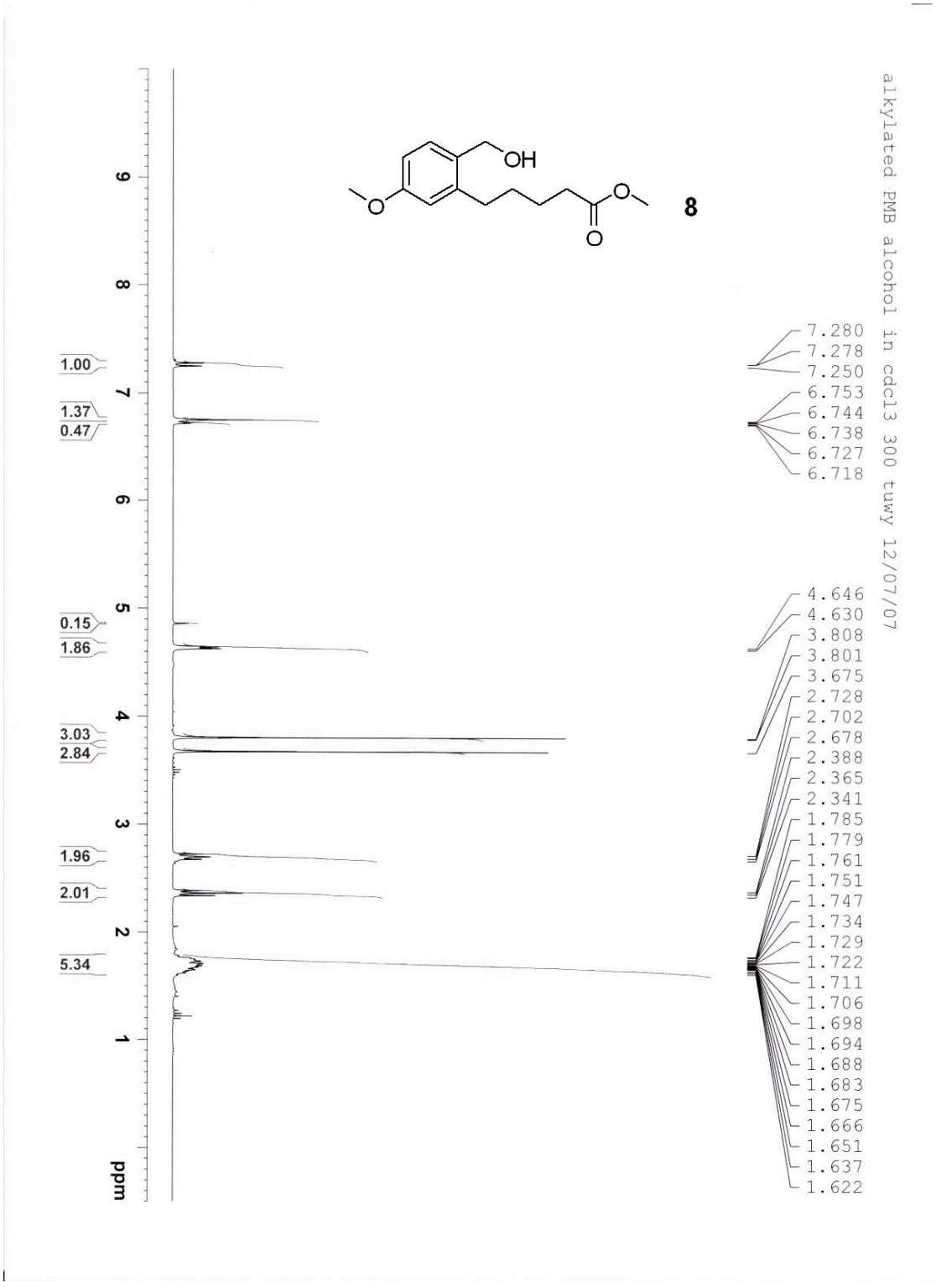
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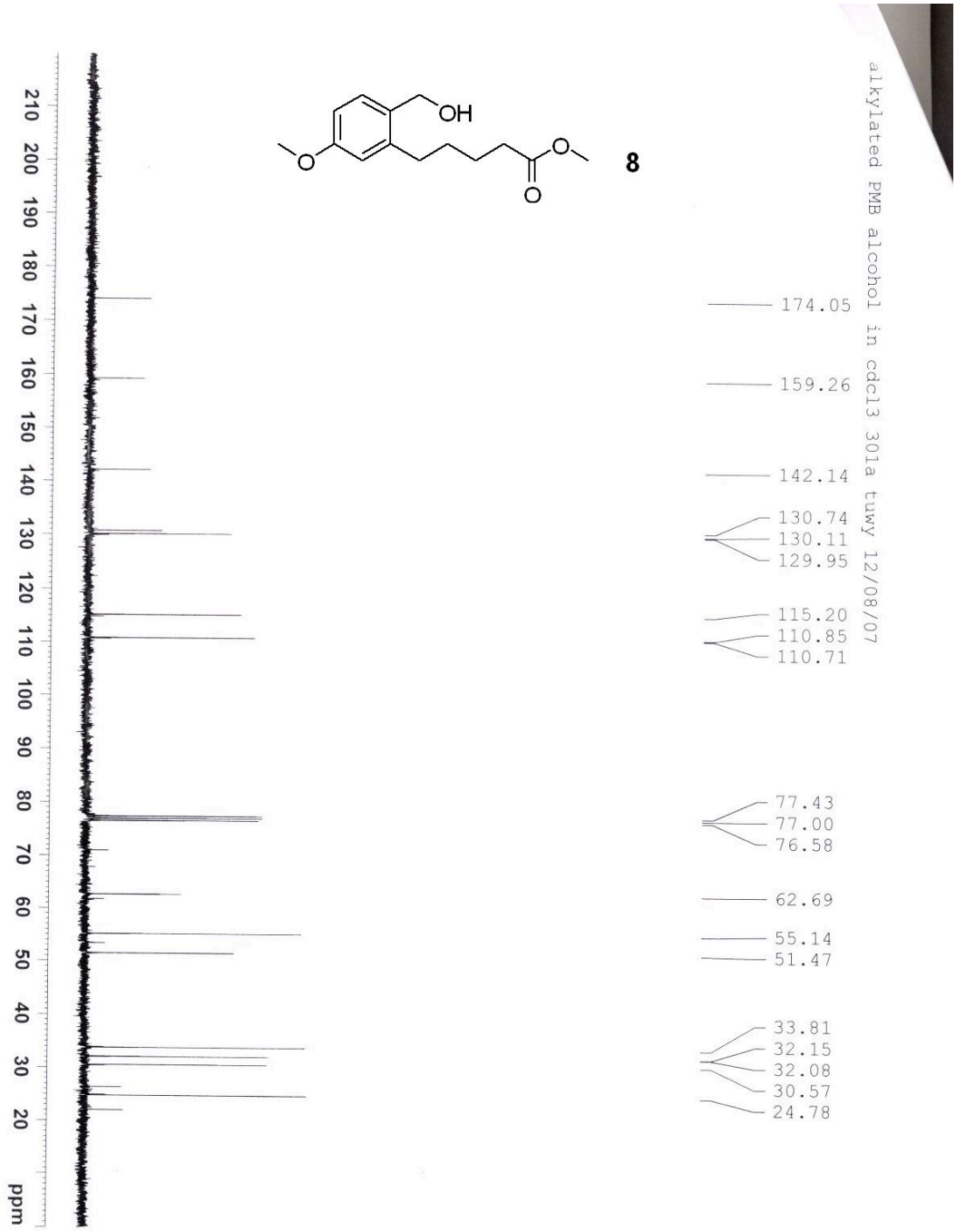
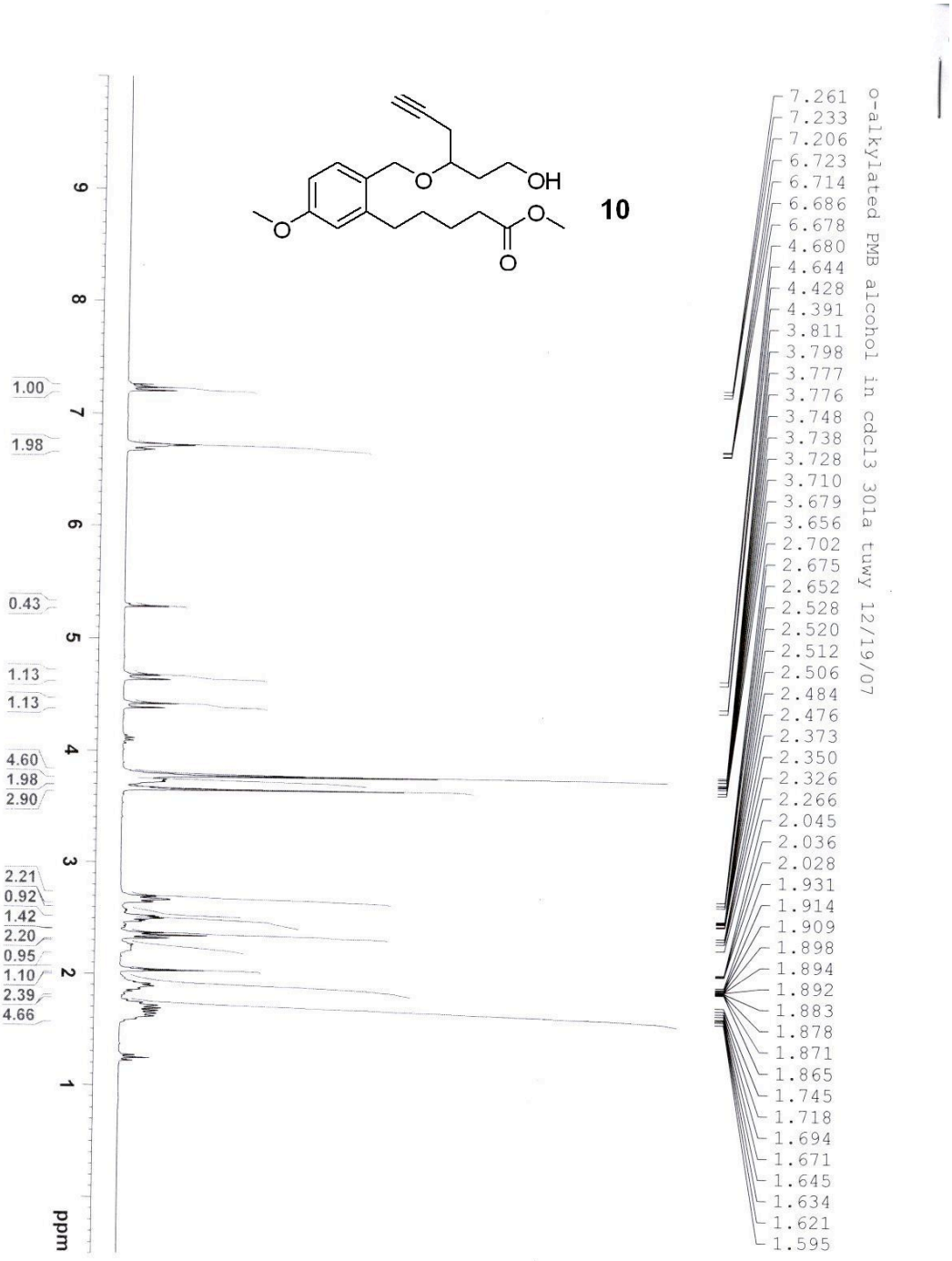
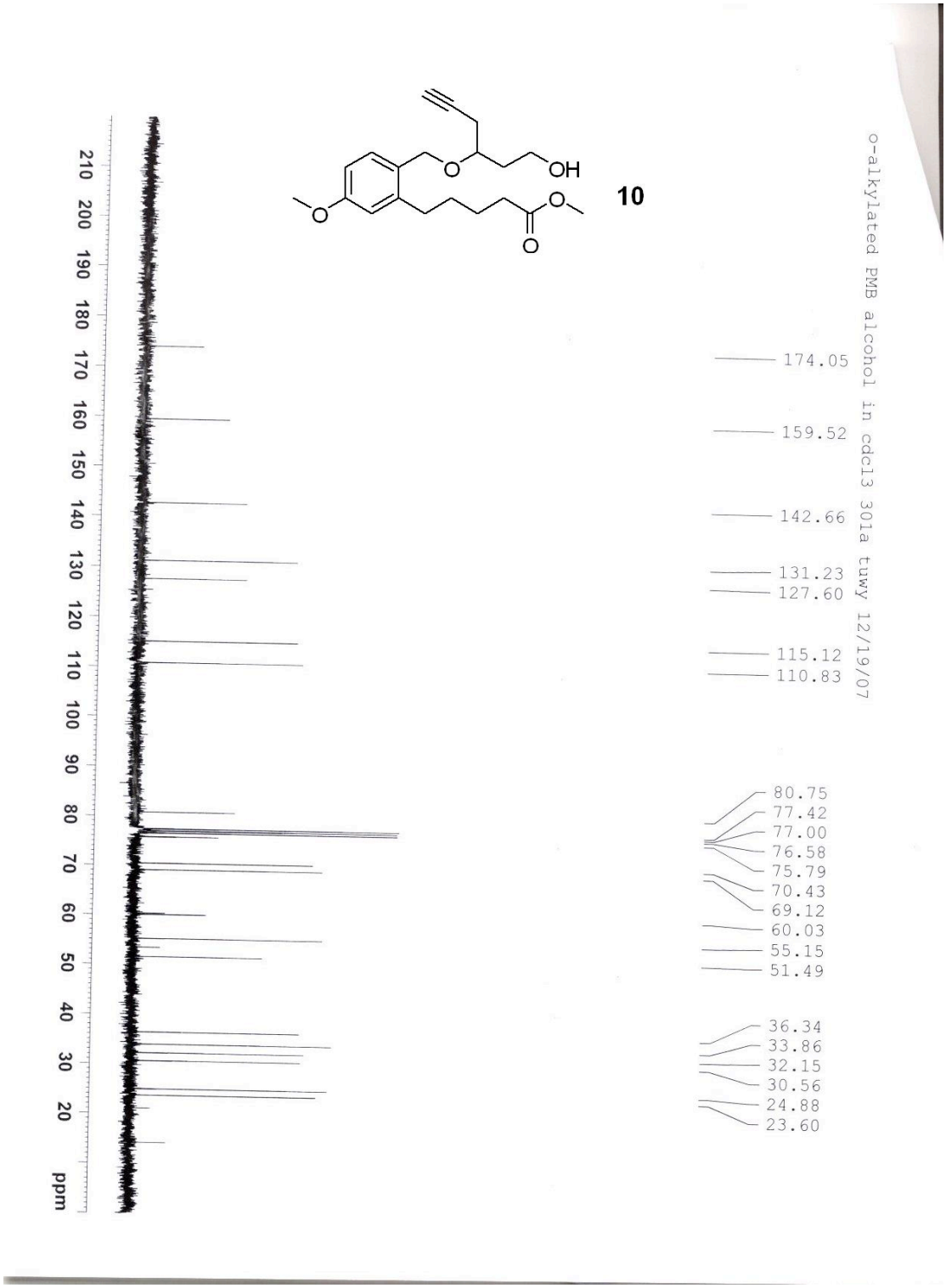
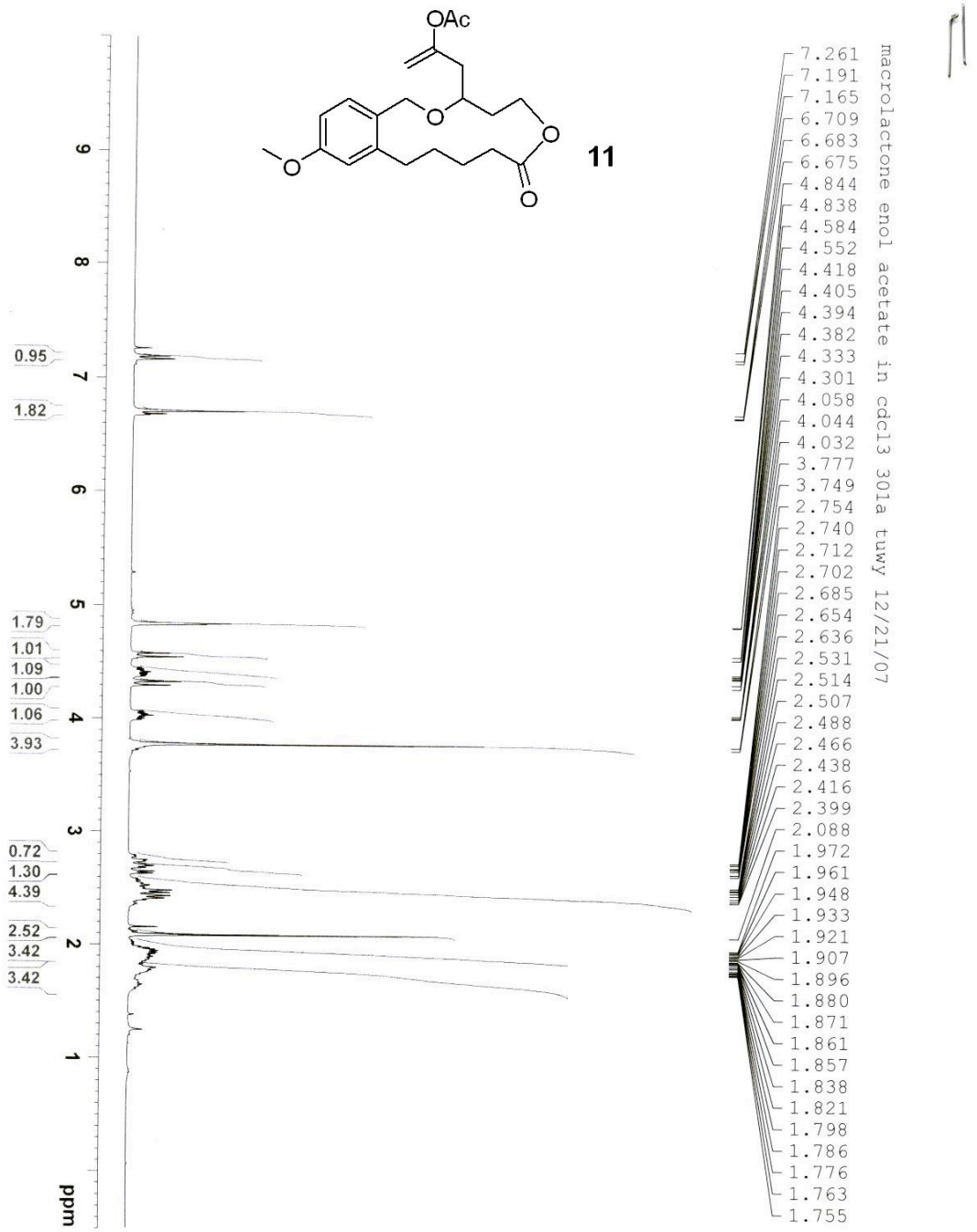
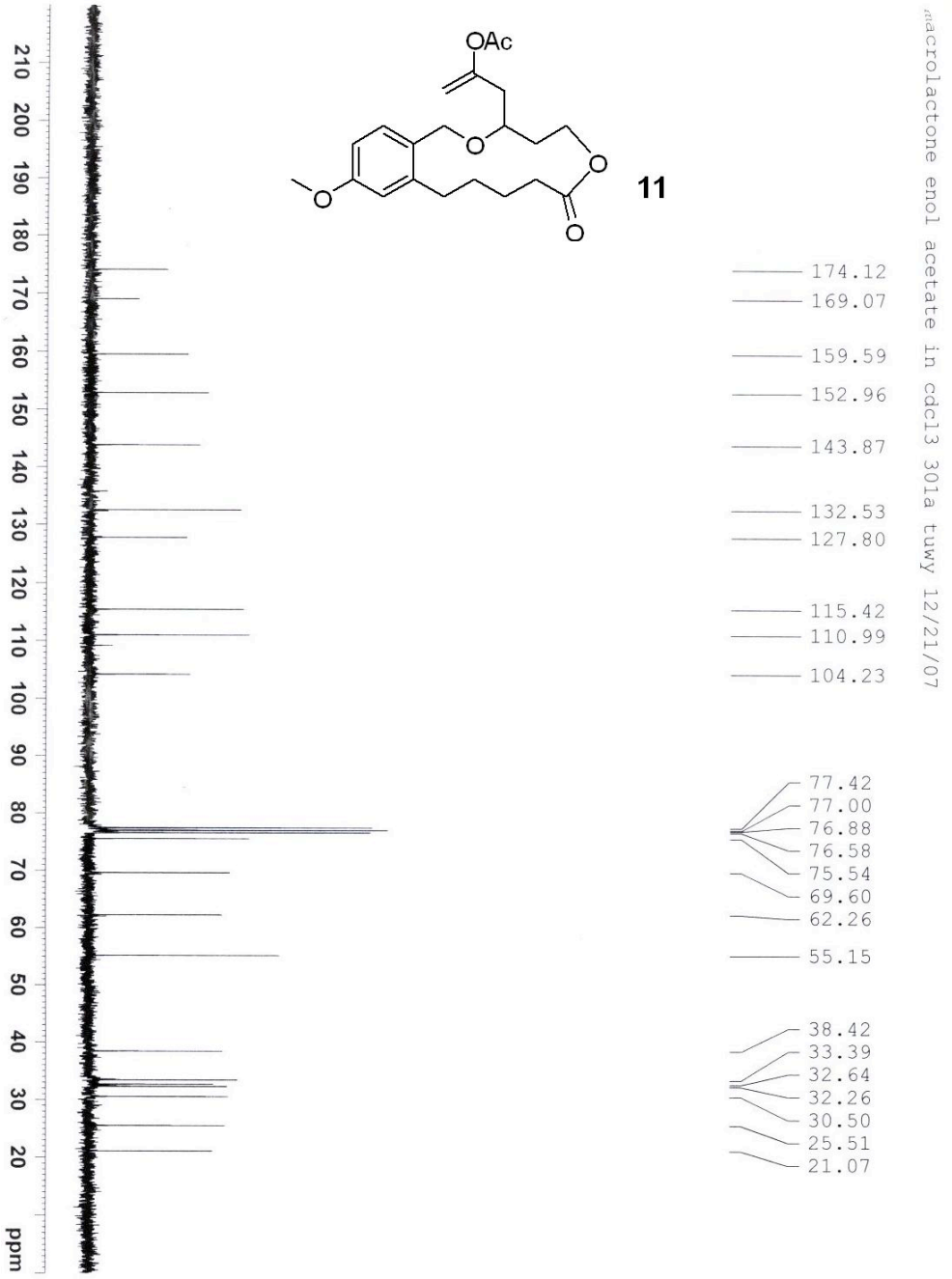
1.00
1.37
0.47
0.15
1.86
3.03
2.84
1.96
2.01
5.34
ppm

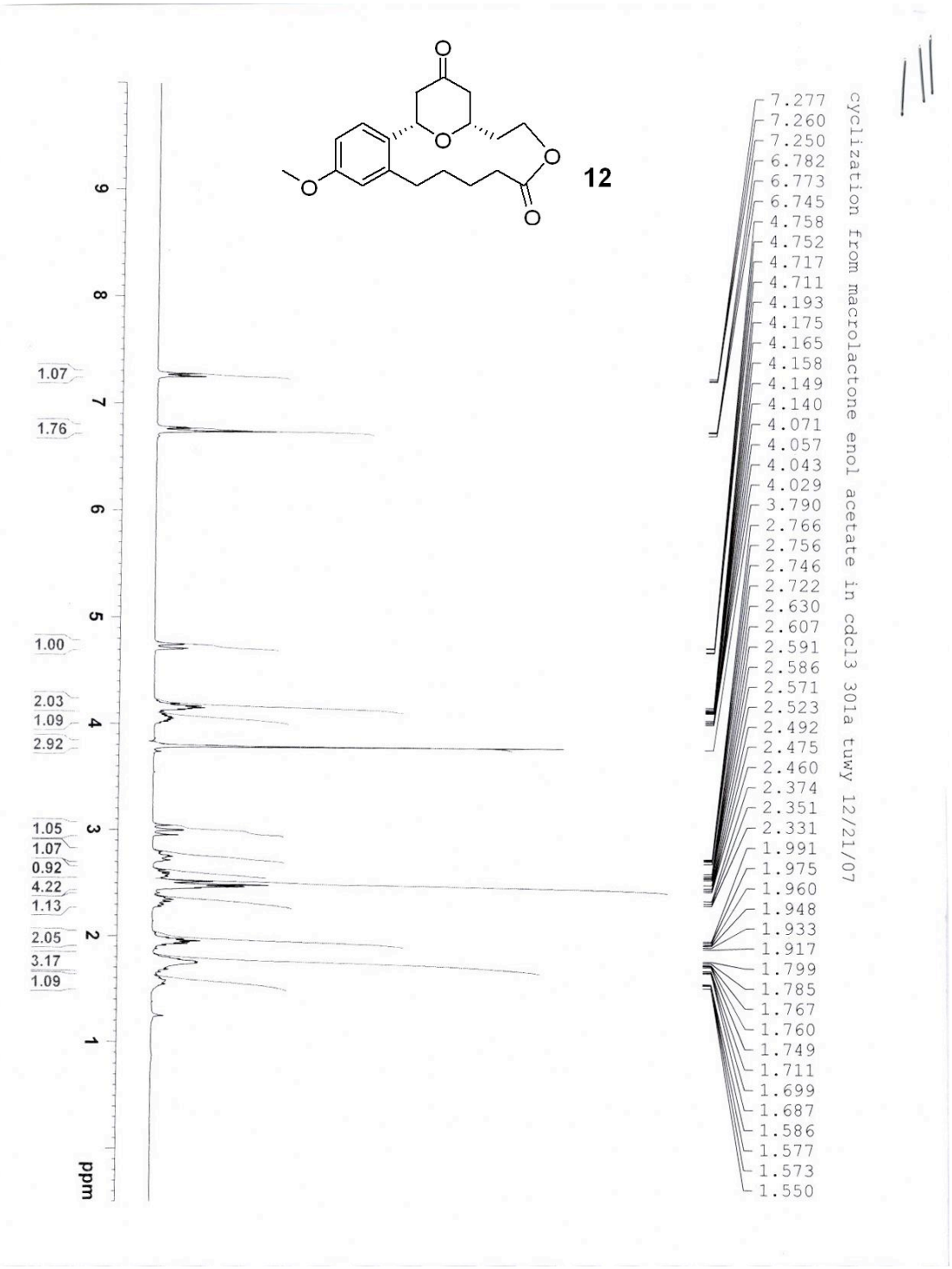

alkylated PMB alcohol in cdcl3 301a tuwy 12/08/07
OH
O
O
O
8
174.05
159.26
142.14
130.74
130.11
129.95
115.20
110.85
110.71
77.43
77.00
76.58
62.69
55.14
51.47
33.81
32.15
32.08
30.57
24.78
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

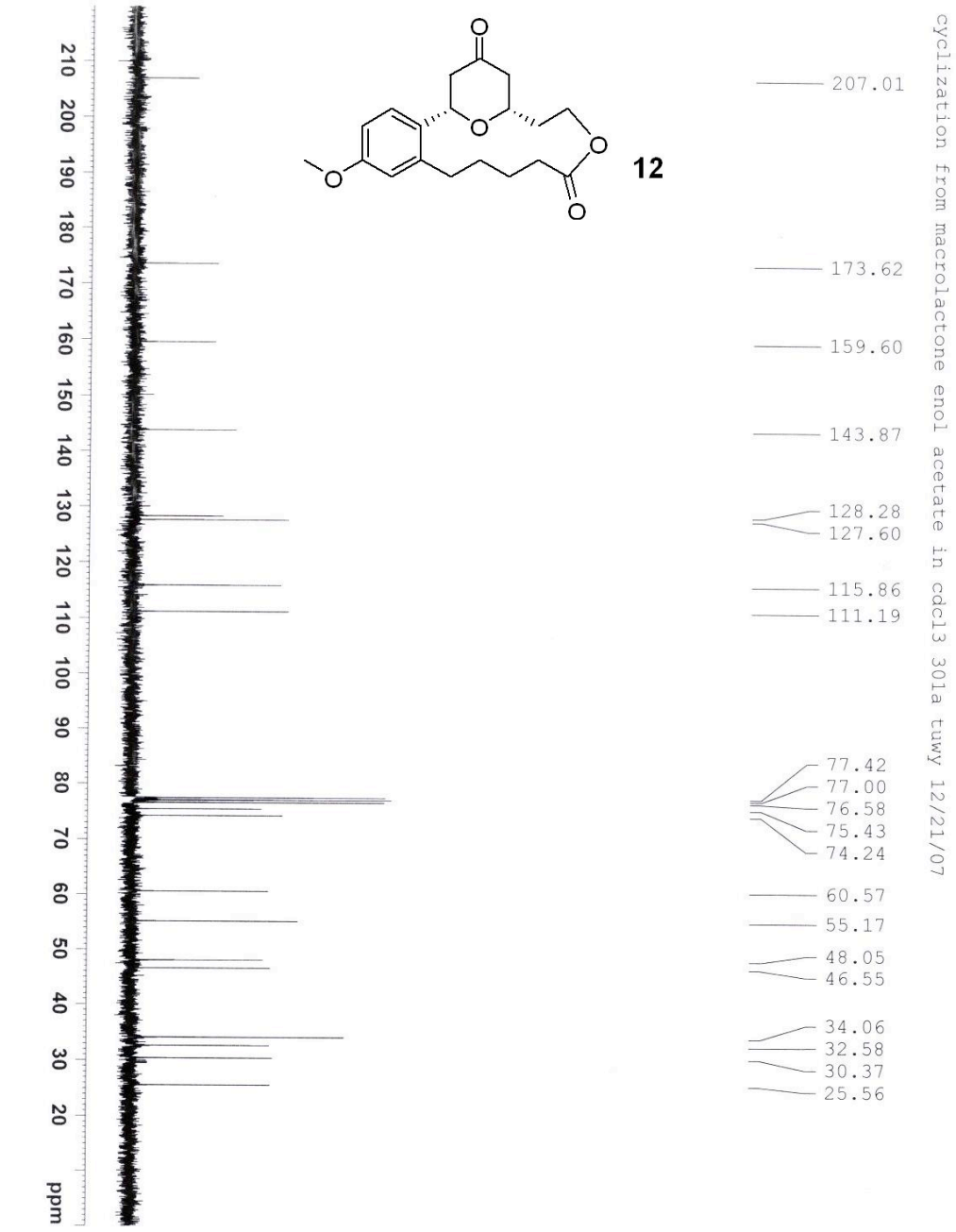

10
OH
O
O
O
1.00
1.98
0.43
1.13
1.13
4.60
1.98
2.90
2.21
0.92
1.42
2.20
0.95
1.10
2.39
4.66
ppm
o-alkylated PMB alcohol in cdcl3 301a tuwy 12/19/07
7.261
7.233
7.206
6.723
6.714
6.686
6.678
4.680
4.644
4.428
4.391
3.811
3.798
3.777
3.776
3.748
3.738
3.728
3.710
3.679
3.656
2.702
2.675
2.652
2.528
2.520
2.512
2.506
2.484
2.476
2.373
2.350
2.326
2.266
2.045
2.036
2.028
1.931
1.914
1.909
1.898
1.894
1.892
1.883
1.878
1.871
1.865
1.745
1.718
1.694
1.671
1.645
1.634
1.621
1.595


o-alkylated PMB alcohol in cdcl3 301a tuwy 12/19/07
174.05
159.52
142.66
131.23
127.60
115.12
110.83
80.75
77.42
77.00
76.58
75.79
70.43
69.12
60.03
55.15
51.49
36.34
33.86
32.15
30.56
24.88
23.60
OH
O
O
O
O
10
ppm

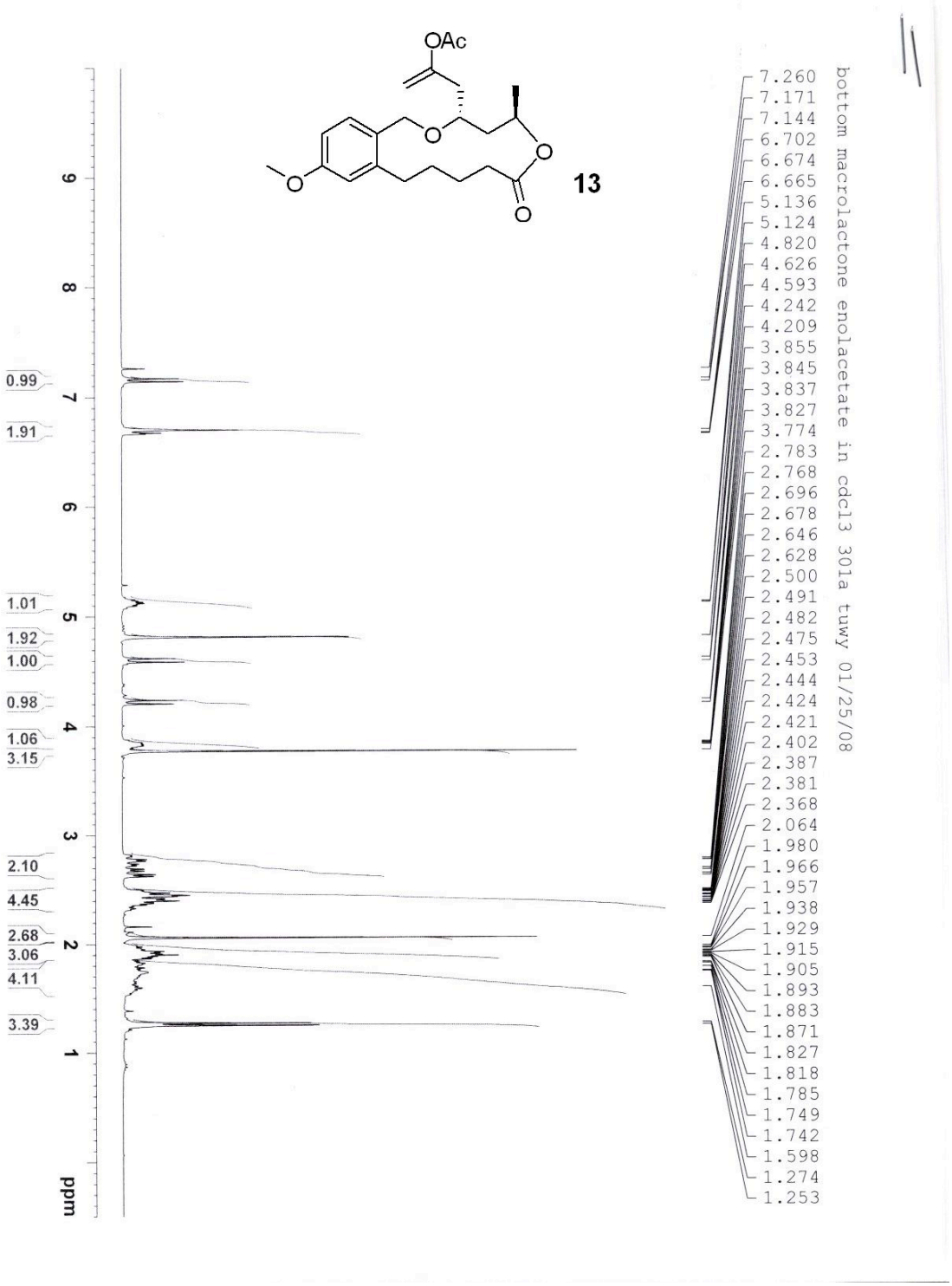

OAc
O
O
O
O
11
macrolactone enol acetate in cdcl3 301a tuwy 12/21/07
7.261
7.191
7.165
6.709
6.683
6.675
4.844
4.838
4.584
4.552
4.418
4.405
4.394
4.382
4.333
4.301
4.058
4.044
4.032
3.777
3.749
2.754
2.740
2.712
2.702
2.685
2.654
2.636
2.531
2.514
2.507
2.488
2.466
2.438
2.416
2.399
2.088
1.972
1.961
1.948
1.933
1.921
1.907
1.896
1.880
1.871
1.861
1.857
1.838
1.821
1.798
1.786
1.776
1.763
1.755
0.95
1.82
1.79
1.01
1.09
1.00
1.06
3.93
0.72
1.30
4.39
2.52
3.42
3.42
ppm

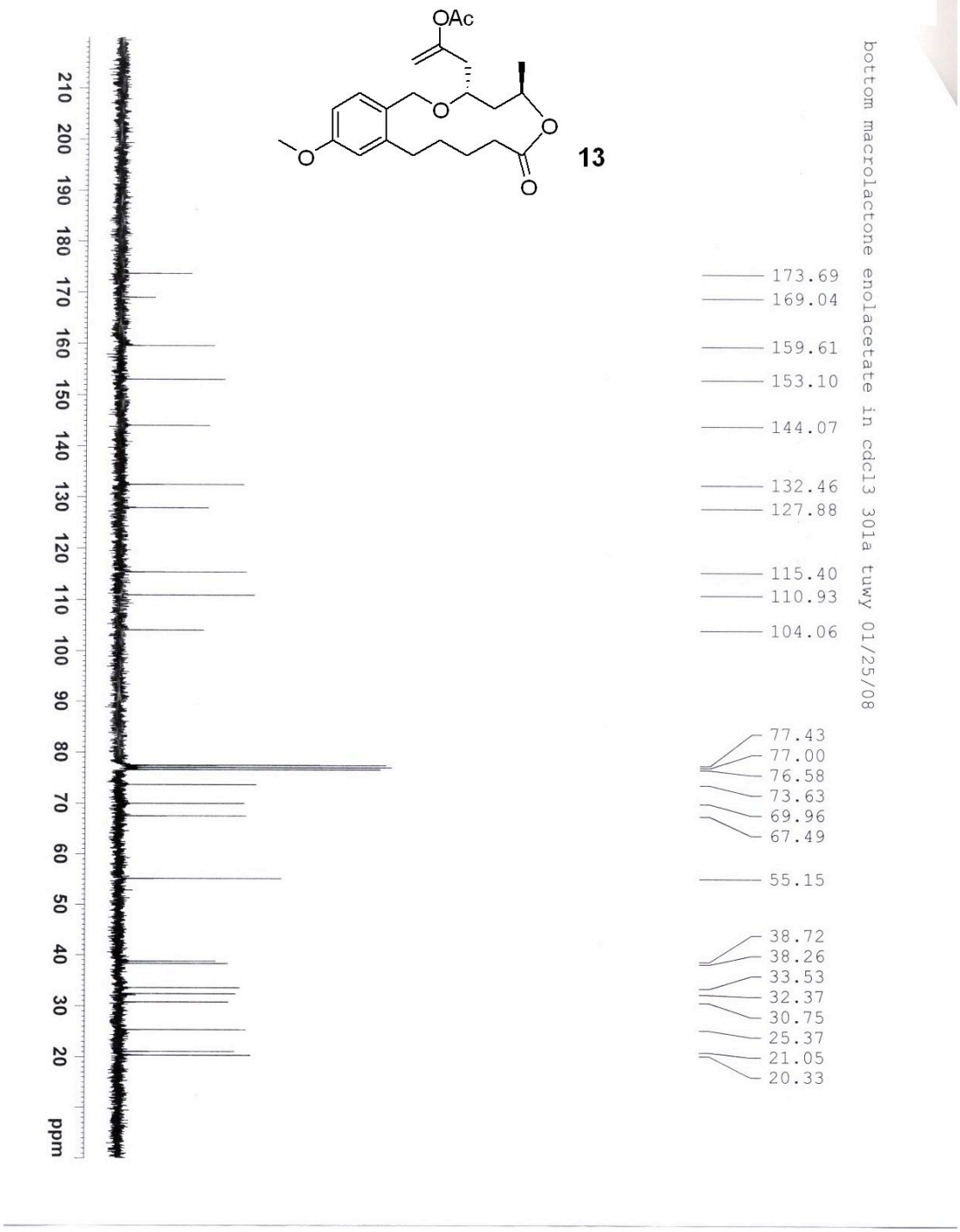

OAc
O
O
O
O
11
macrolactone enol acetate in cdcl3 301a tuwy 12/21/07
174.12
169.07
159.59
152.96
143.87
132.53
127.80
115.42
110.99
104.23
77.42
77.00
76.88
76.58
75.54
69.60
62.26
55.15
38.42
33.39
32.64
32.26
30.50
25.51
21.07
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

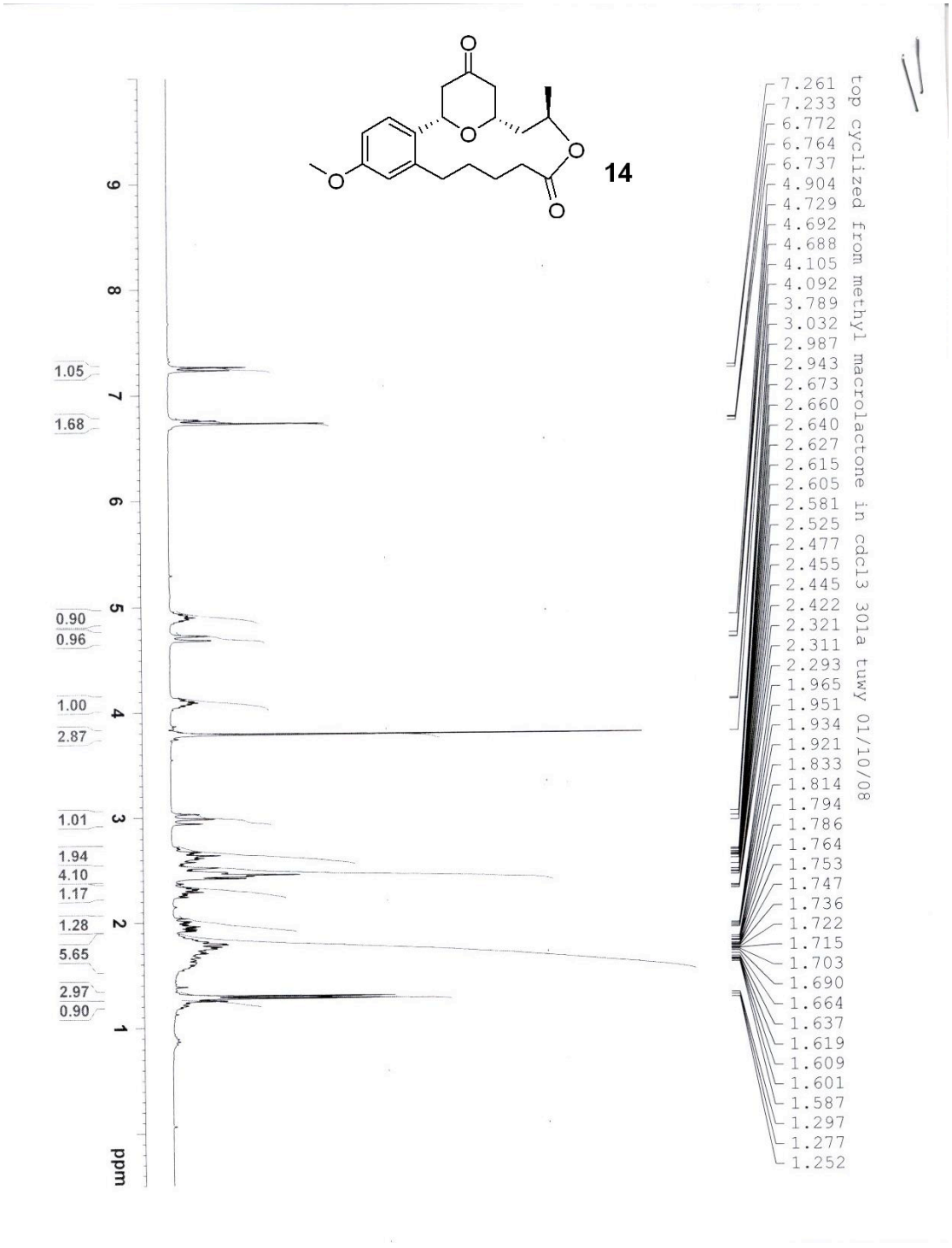

12
cyclization from macrolactone enol acetate in cdcl3 301a tuwy 12/21/07
7.277
7.260
7.250
6.782
6.773
6.745
4.758
4.752
4.717
4.711
4.193
4.175
4.165
4.158
4.149
4.140
4.071
4.057
4.043
4.029
3.790
2.766
2.756
2.746
2.722
2.630
2.607
2.591
2.586
2.571
2.523
2.492
2.475
2.460
2.374
2.351
2.331
1.991
1.975
1.960
1.948
1.933
1.917
1.799
1.785
1.767
1.760
1.749
1.711
1.699
1.687
1.586
1.577
1.573
1.550
1.07
1.76
1.00
2.03
1.09
2.92
1.05
1.07
0.92
4.22
1.13
2.05
3.17
1.09
ppm

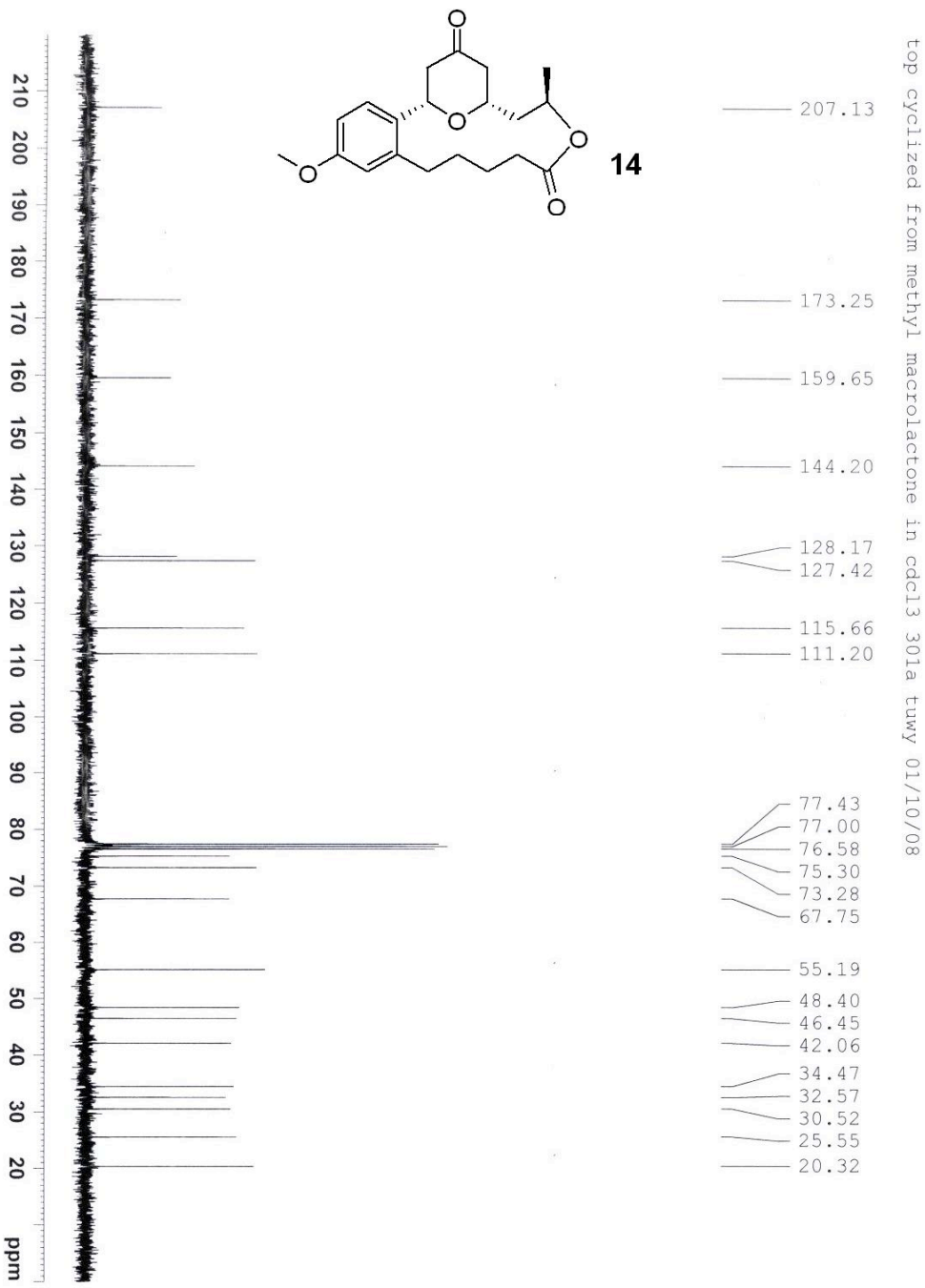

cyclization from macrolactone enol acetate in cdcl3 301a tuwy 12/21/07
207.01
173.62
159.60
143.87
128.28
127.60
115.86
111.19
77.42
77.00
76.58
75.43
74.24
60.57
55.17
48.05
46.55
34.06
32.58
30.37
25.56
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

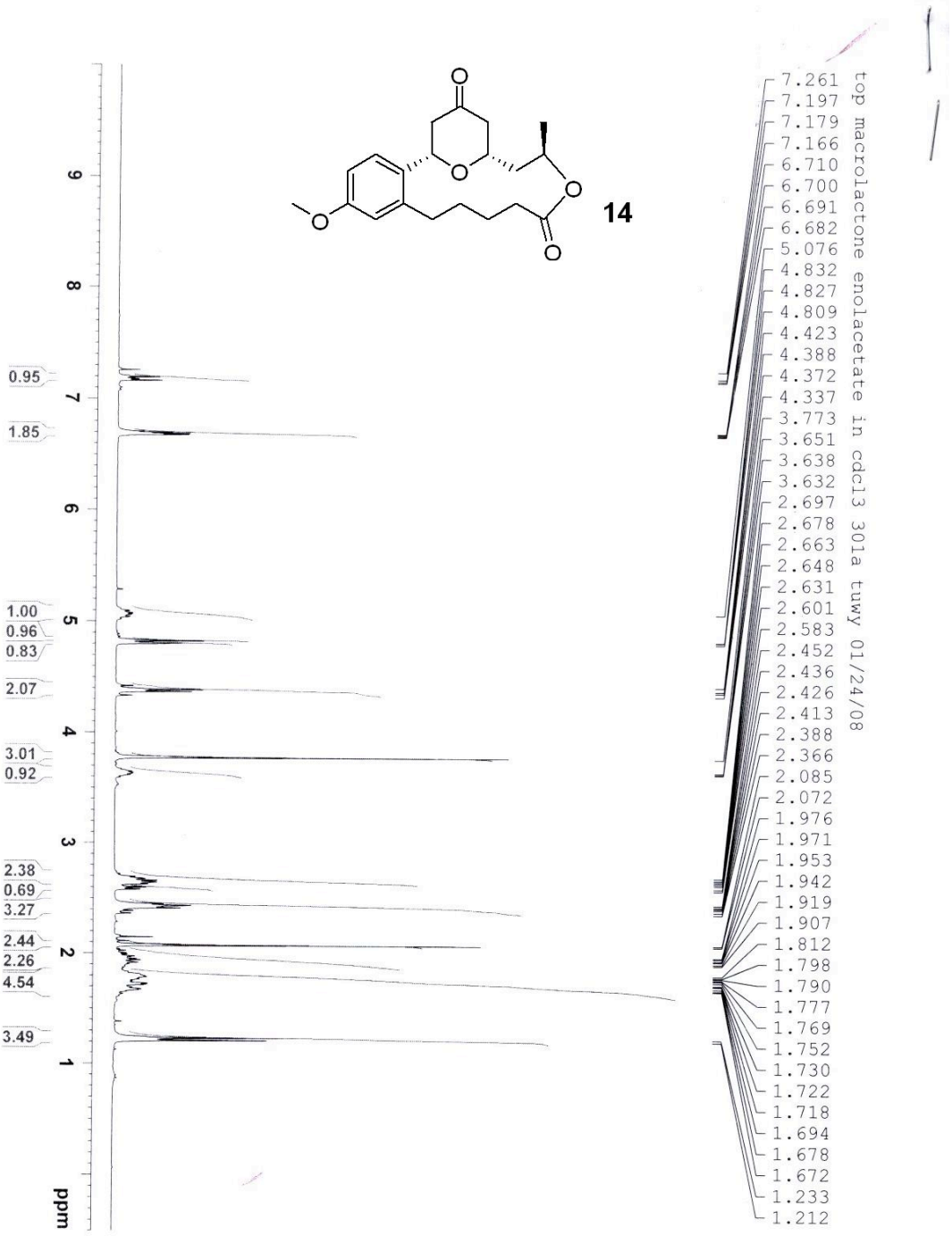
12

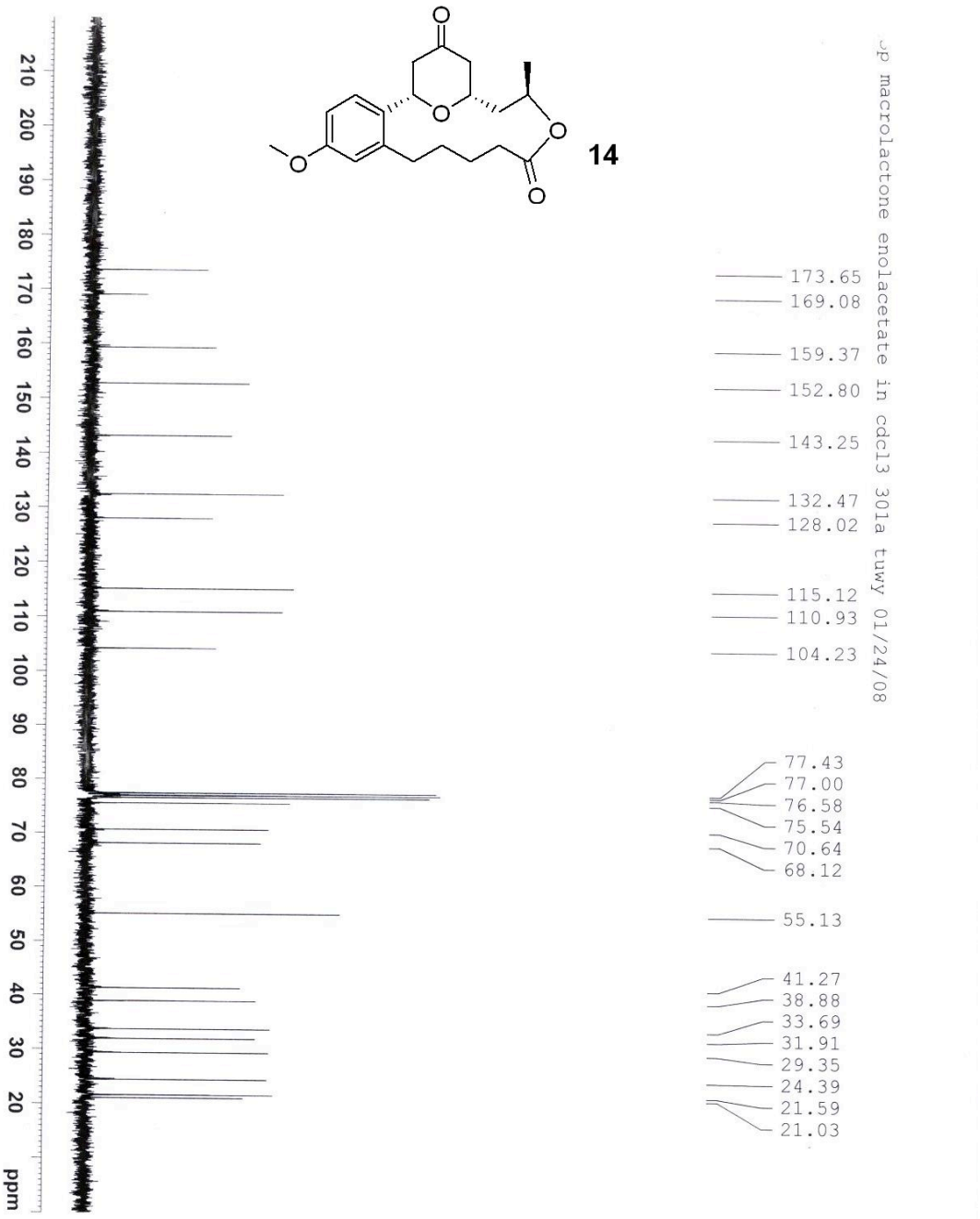

OAc
O
O
O
O
13
bottom macrolactone enolacetate in cdcl3 301a tuwy 01/25/08
7.260
7.171
7.144
6.702
6.674
6.665
5.136
5.124
4.820
4.626
4.593
4.242
4.209
3.855
3.845
3.837
3.827
3.774
2.783
2.768
2.696
2.678
2.646
2.628
2.500
2.491
2.482
2.475
2.453
2.444
2.424
2.421
2.402
2.387
2.381
2.368
2.064
1.980
1.966
1.957
1.938
1.929
1.915
1.905
1.893
1.883
1.871
1.827
1.818
1.785
1.749
1.742
1.598
1.274
1.253
0.99
1.91
1.01
1.92
1.00
0.98
1.06
3.15
2.10
4.45
2.68
3.06
4.11
3.39
ppm

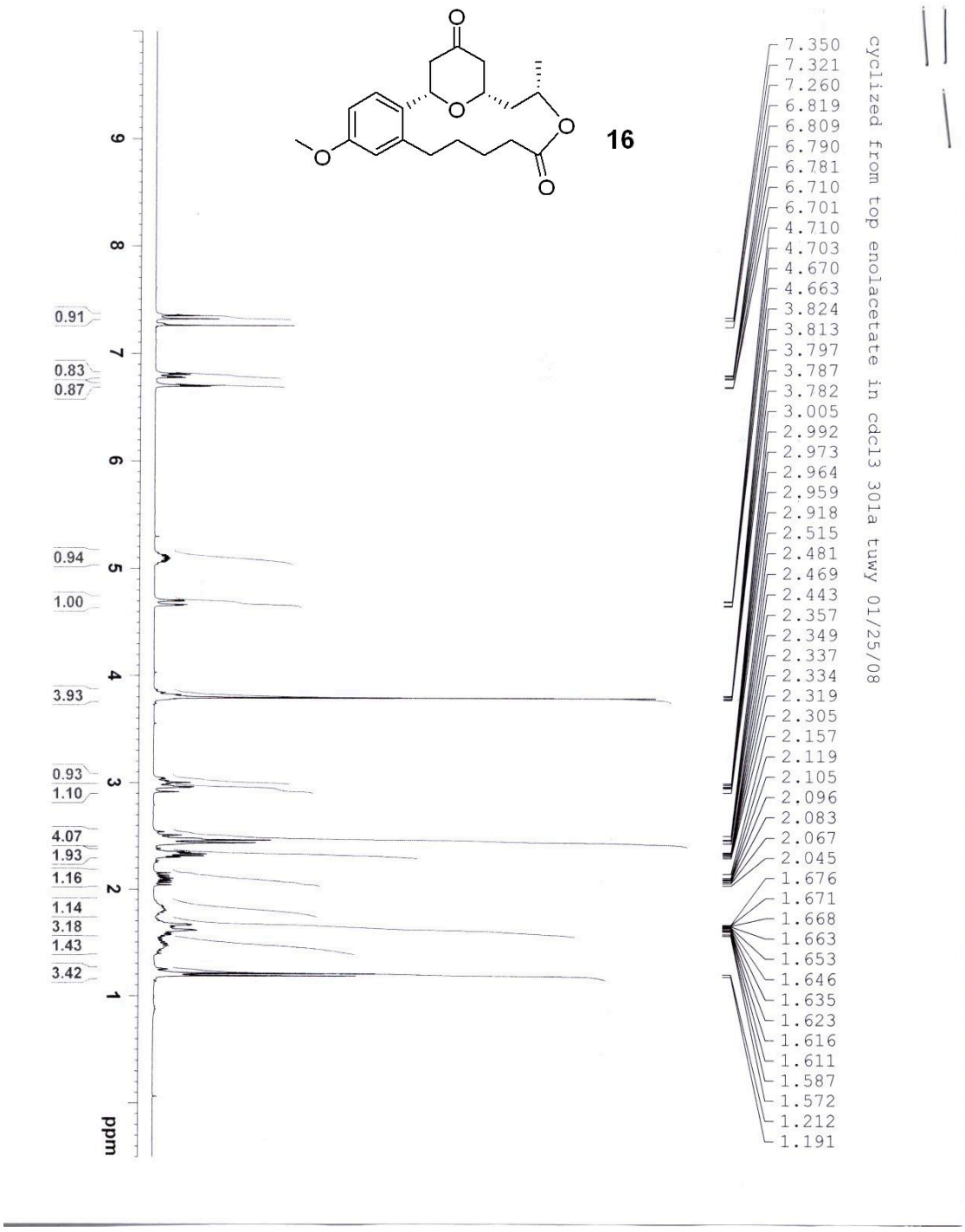

OAc
O
O
O
O
13
bottom macrolactone enolacetate in cdcl3 301a tuwy 01/25/08
173.69
169.04
159.61
153.10
144.07
132.46
127.88
115.40
110.93
104.06
77.43
77.00
76.58
73.63
69.96
67.49
55.15
38.72
38.26
33.53
32.37
30.75
25.37
21.05
20.33
ppm

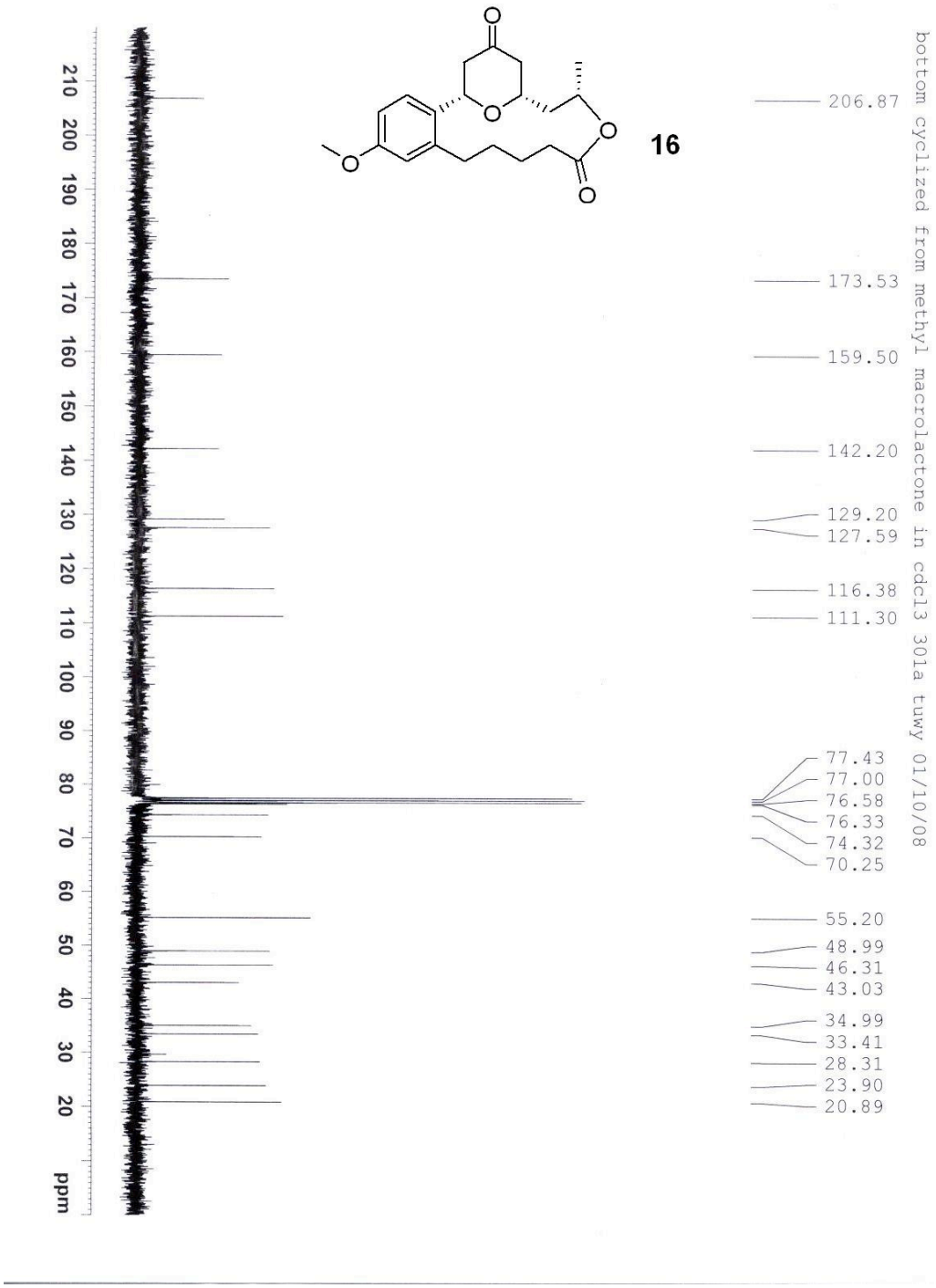

14
1.05
1.68
0.90
0.96
1.00
2.87
1.01
1.94
4.10
1.17
1.28
5.65
2.97
0.90
ppm
top cyclized from methyl macrolactone in cdcl3 301a tuwy 01/10/08
7.261
7.233
6.772
6.764
6.737
4.904
4.729
4.692
4.688
4.105
4.092
3.789
3.032
2.987
2.943
2.673
2.660
2.640
2.627
2.615
2.605
2.581
2.525
2.477
2.455
2.445
2.422
2.321
2.311
2.293
1.965
1.951
1.934
1.921
1.833
1.814
1.794
1.786
1.764
1.753
1.747
1.736
1.722
1.715
1.703
1.690
1.664
1.637
1.619
1.609
1.601
1.587
1.297
1.277
1.252

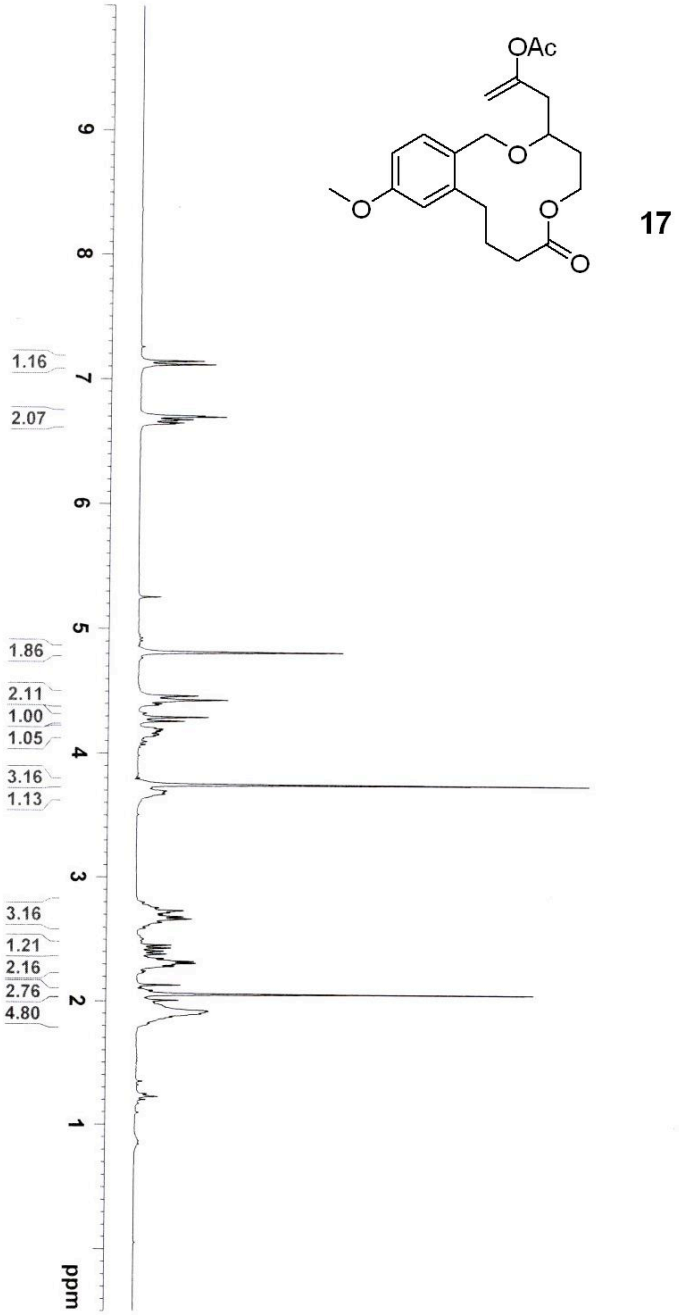

14
207.13
173.25
159.65
144.20
128.17
127.42
115.66
111.20
77.43
77.00
76.58
75.30
73.28
67.75
55.19
48.40
46.45
42.06
34.47
32.57
30.52
25.55
20.32
top cyclized from methyl macrolactone in cdcl3 301a tuwy 01/10/08
ppm

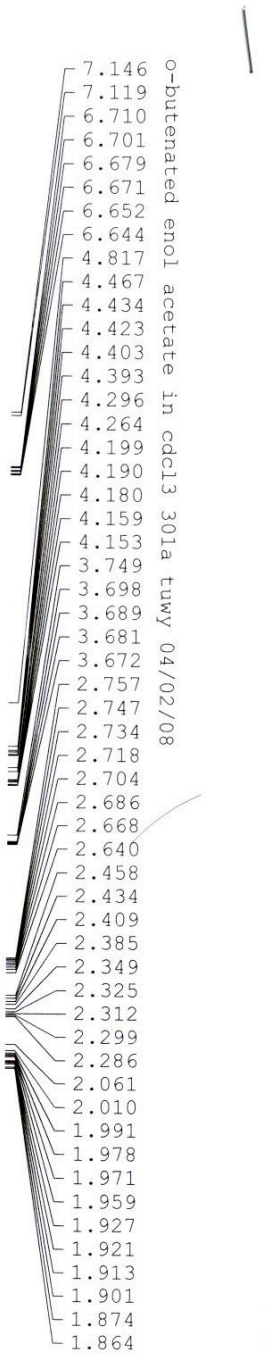

14
top macrolactone enolacetate in cdcl3 301a tuwy 01/24/08
7.261
7.197
7.179
7.166
6.710
6.700
6.691
6.682
5.076
4.832
4.827
4.809
4.423
4.388
4.372
4.337
3.773
3.651
3.638
3.632
2.697
2.678
2.663
2.648
2.631
2.601
2.583
2.452
2.436
2.426
2.413
2.388
2.366
2.085
2.072
1.976
1.971
1.953
1.942
1.919
1.907
1.812
1.798
1.790
1.777
1.769
1.752
1.730
1.722
1.718
1.694
1.678
1.672
1.233
1.212
0.95
1.85
1.00
0.96
0.83
2.07
3.01
0.92
2.38
0.69
3.27
2.44
2.26
4.54
3.49
ppm

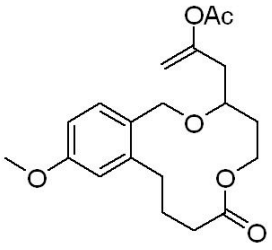

14
cp macrolactone enolacetate in cdcl3 301a tuwy 01/24/08
173.65
169.08
159.37
152.80
143.25
132.47
128.02
115.12
110.93
104.23
77.43
77.00
76.58
75.54
70.64
68.12
55.13
41.27
38.88
33.69
31.91
29.35
24.39
21.59
21.03
ppm


16
cyclized from top enolacetate in cdcl3 301a tuwy 01/25/08
7.350
7.321
7.260
6.819
6.809
6.790
6.781
6.710
6.701
4.710
4.703
4.670
4.663
3.824
3.813
3.797
3.787
3.782
3.005
2.992
2.973
2.964
2.959
2.918
2.515
2.481
2.469
2.443
2.357
2.349
2.337
2.334
2.319
2.305
2.157
2.119
2.105
2.096
2.083
2.067
2.045
1.676
1.671
1.668
1.663
1.653
1.646
1.635
1.623
1.616
1.611
1.587
1.572
1.212
1.191
0.91
0.83
0.87
0.94
1.00
3.93
0.93
1.10
4.07
1.93
1.16
1.14
3.18
1.43
3.42
ppm


16
bottom cyclized from methyl macrolactone in cdcl3 301a tuwy 01/10/08
206.87
173.53
159.50
142.20
129.20
127.59
116.38
111.30
77.43
77.00
76.58
76.33
74.32
70.25
55.20
48.99
46.31
43.03
34.99
33.41
28.31
23.90
20.89
ppm


OAc
O
O
O
O
17
1.16
2.07
1.86
2.11
1.00
1.05
3.16
1.13
3.16
1.21
2.16
2.76
4.80
9
8
7
6
5
4
3
2
1
ppm

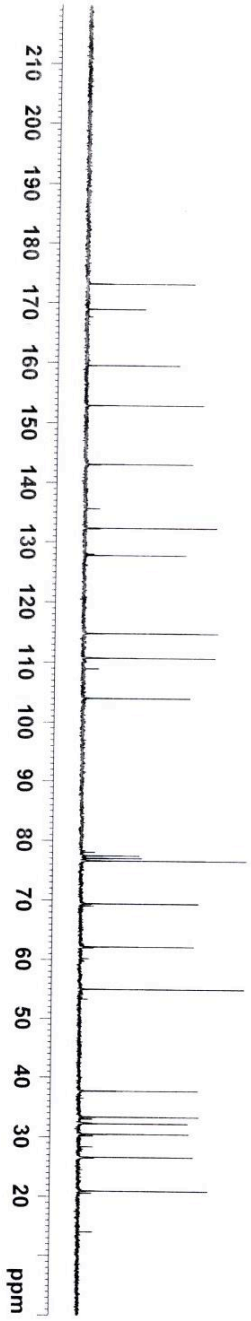

o-butenated enol acetate in cdcl3 301a tuwy 04/02/08
7.146
7.119
6.710
6.701
6.679
6.671
6.652
6.644
4.817
4.467
4.434
4.423
4.403
4.393
4.296
4.264
4.199
4.190
4.180
4.159
4.153
3.749
3.698
3.689
3.681
3.672
2.757
2.747
2.734
2.718
2.704
2.686
2.668
2.640
2.458
2.434
2.409
2.385
2.349
2.325
2.312
2.299
2.286
2.061
2.010
1.991
1.978
1.971
1.959
1.927
1.921
1.913
1.901
1.874
1.864

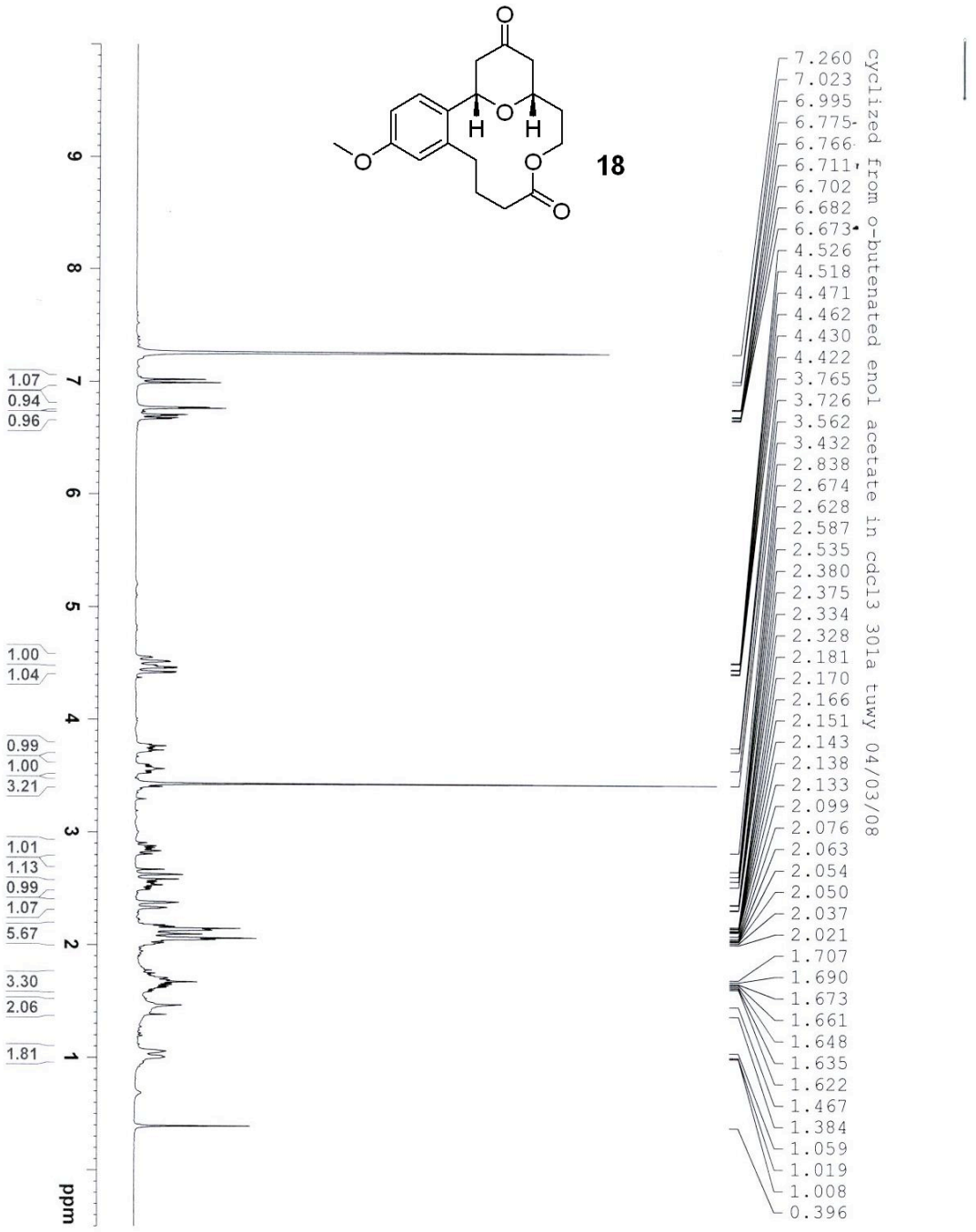


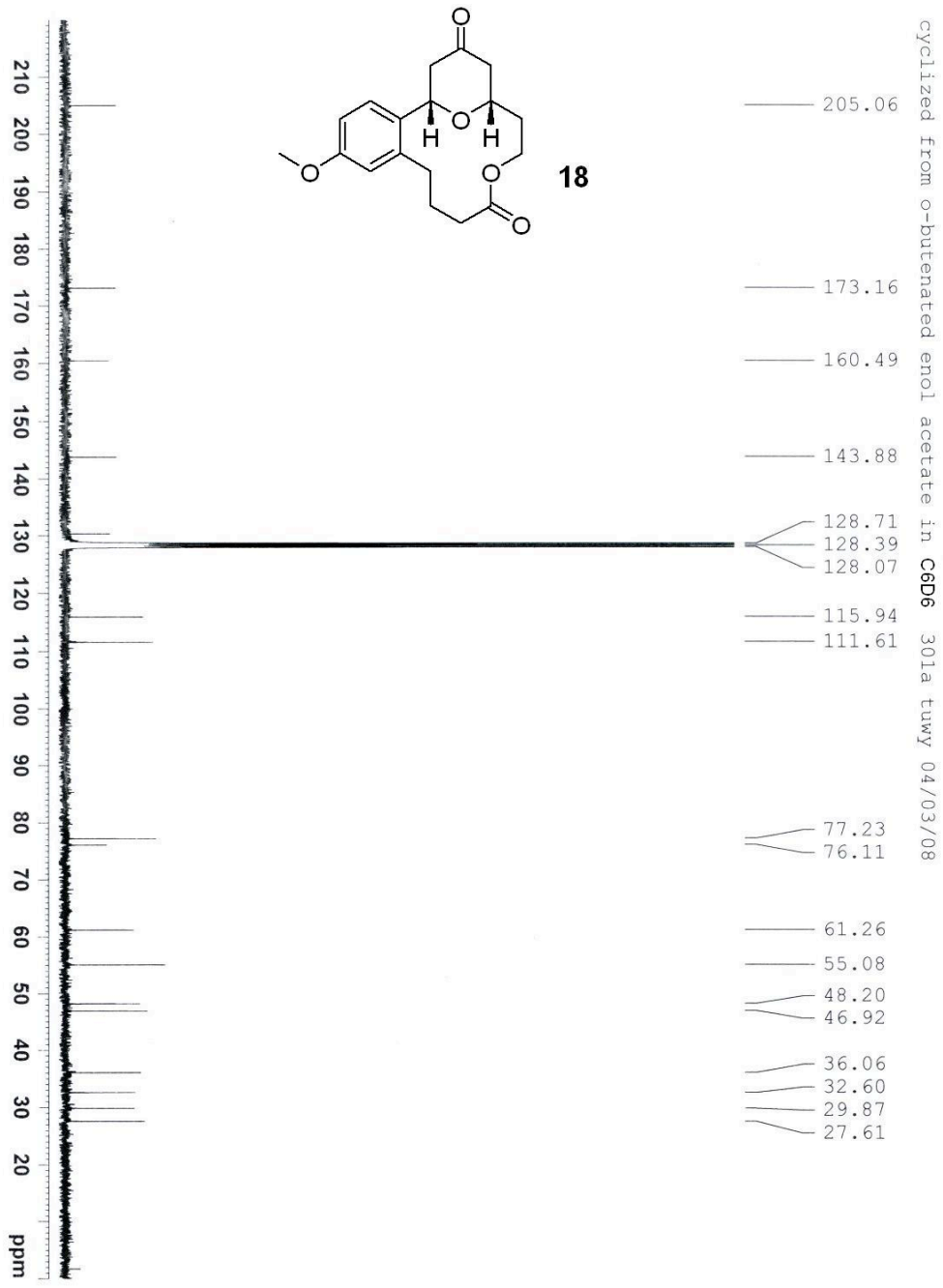
17

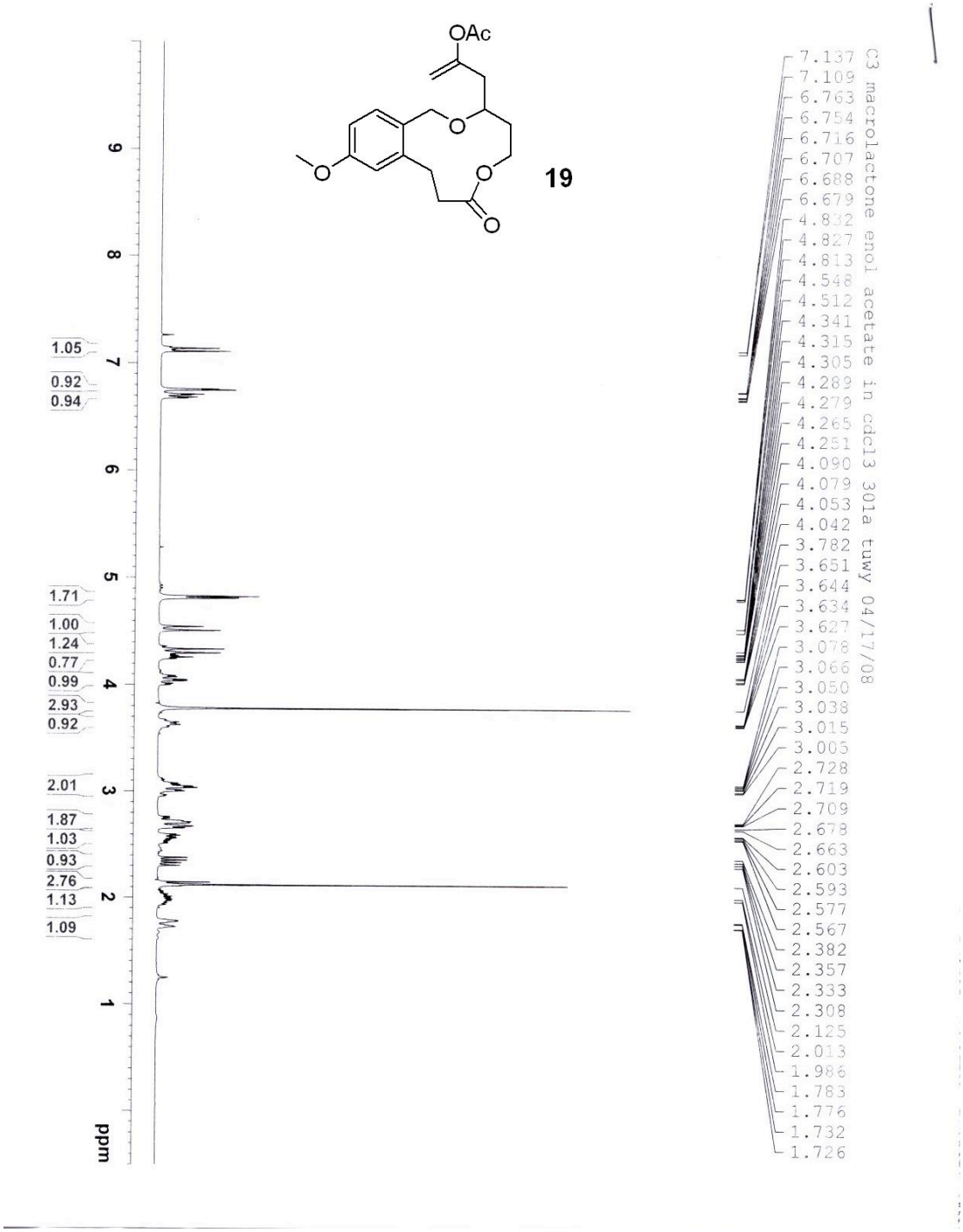
o-butenated enol acetate in cdcl3 301a tuwy 04/02/08

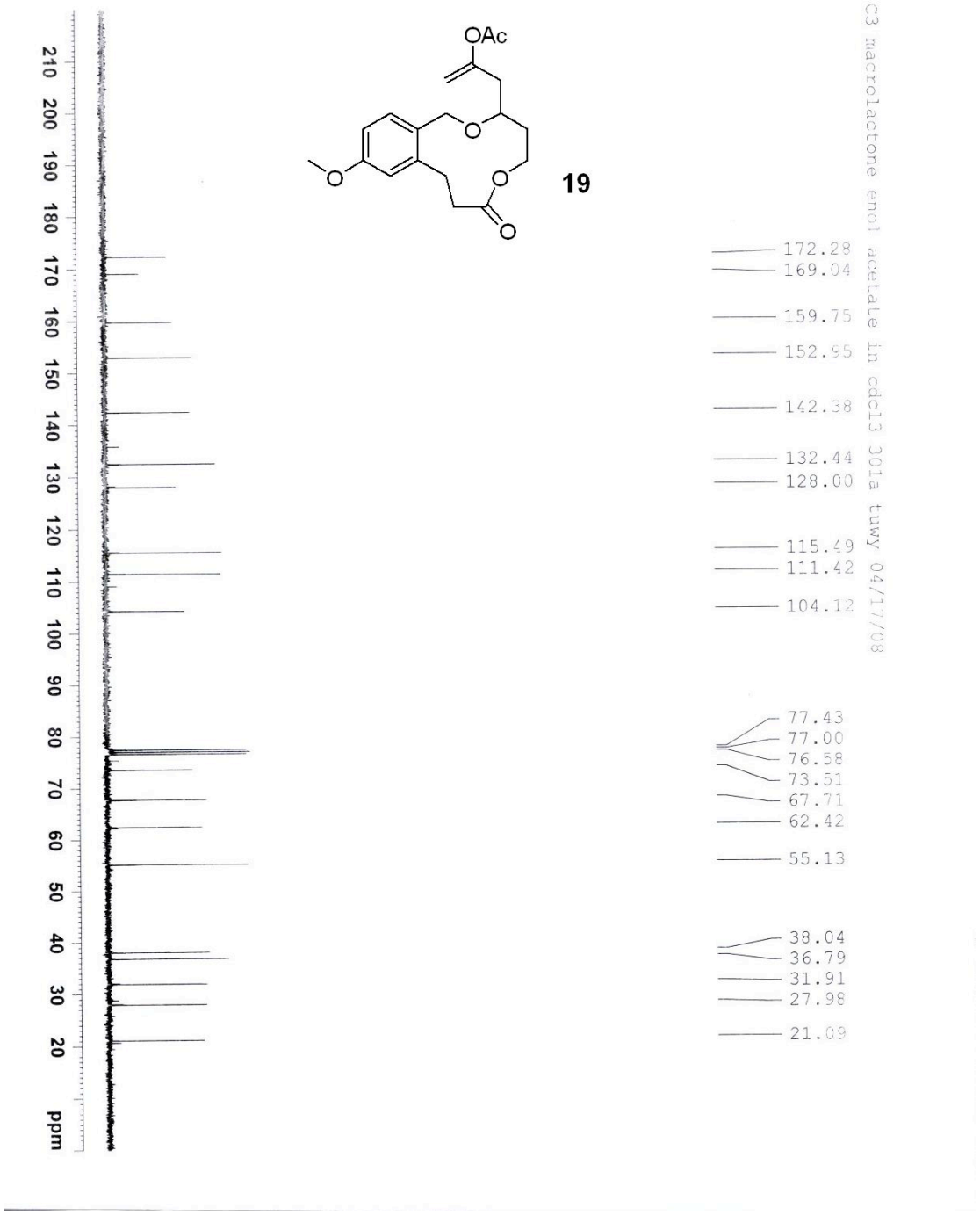
173.16
168.93
159.54
152.93
143.12
132.33
127.79
114.81
110.72
104.03
77.43
77.00
76.56
69.40
62.21
54.98
37.66
33.30
32.20
30.46
26.61
20.93

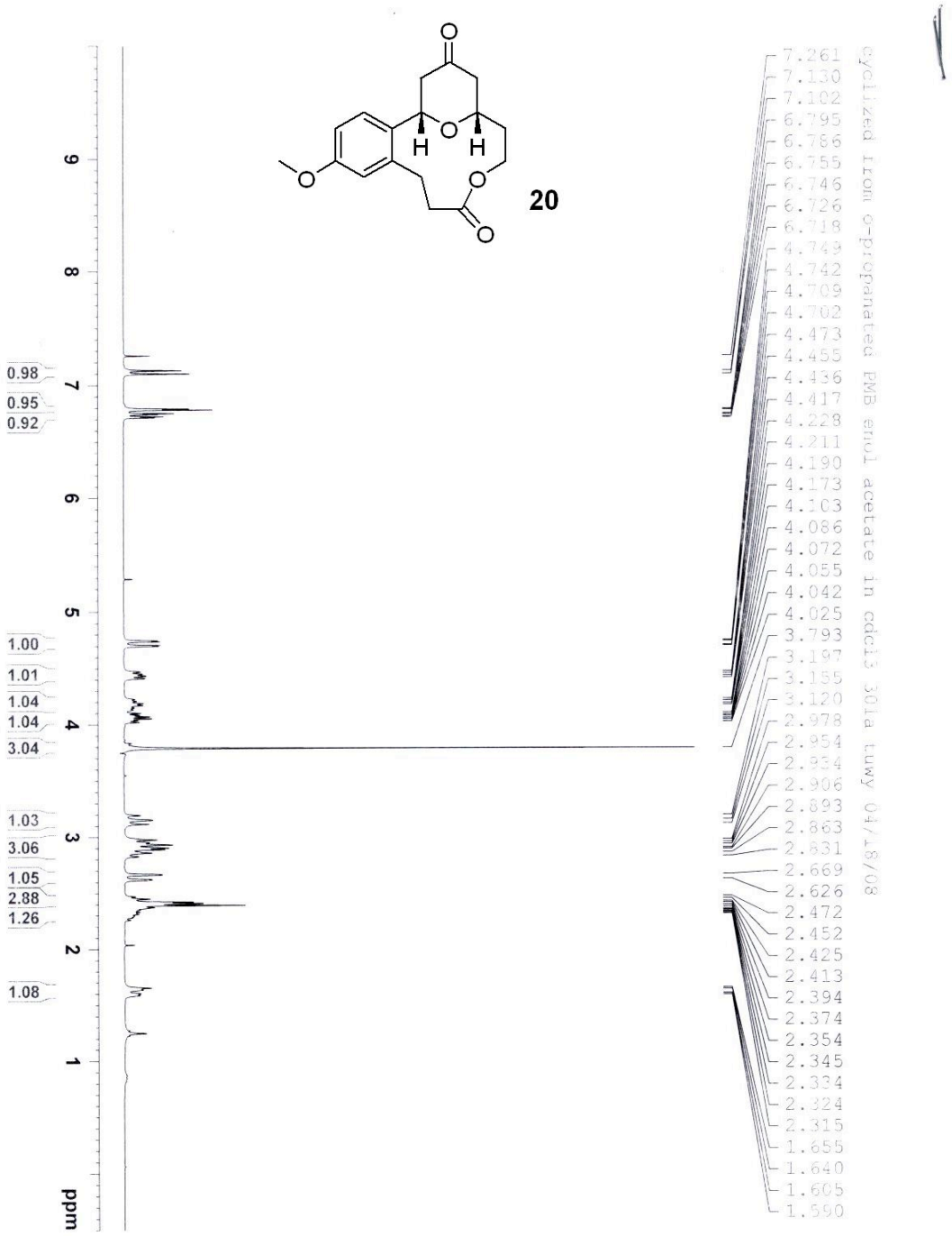


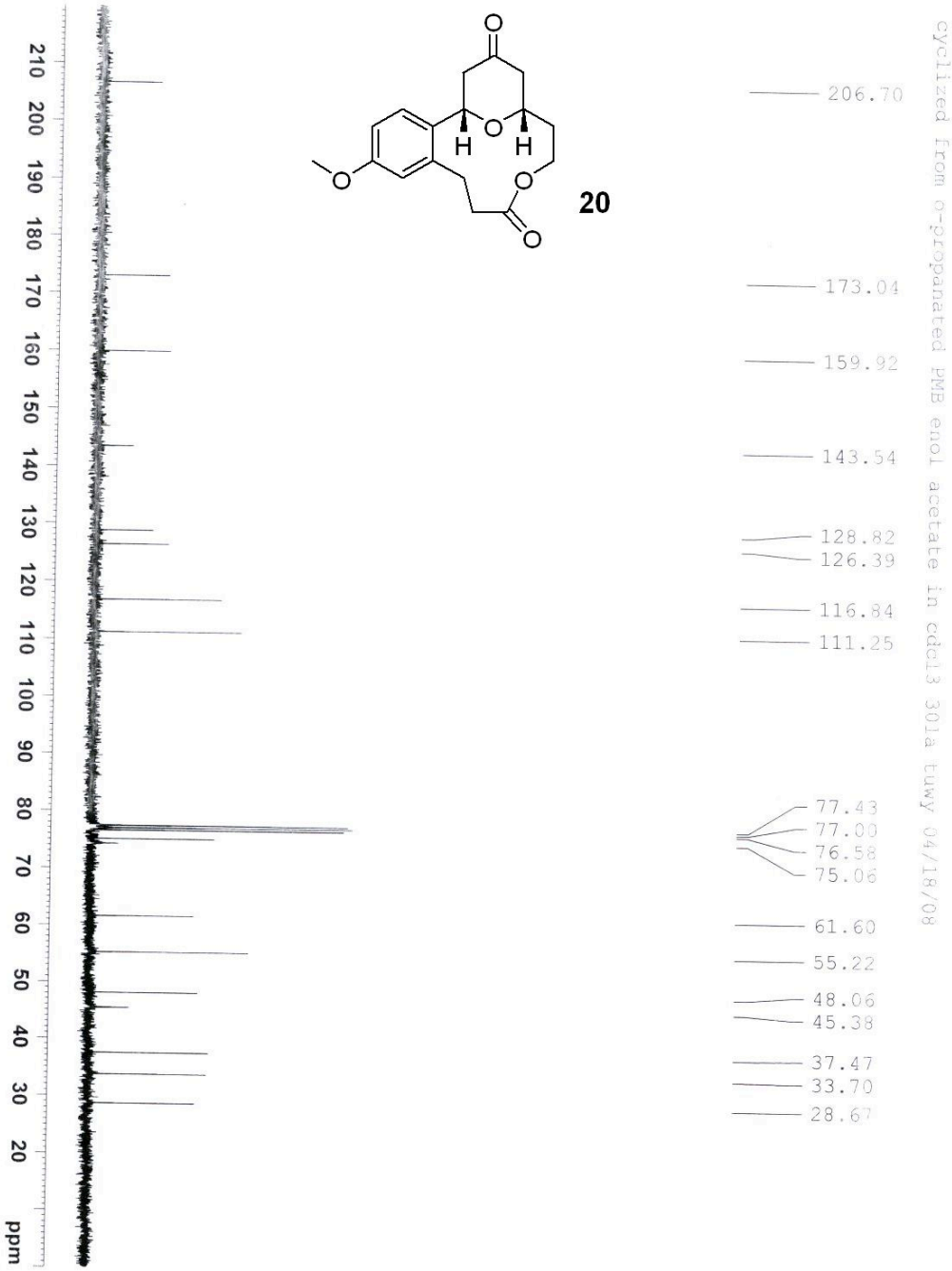

18
cyclized from o-butenated enol acetate in cdcl3 301a tuwy 04/03/08
7.260
7.023
6.995
6.775
6.766
6.711
6.702
6.682
6.673
4.526
4.518
4.471
4.462
4.430
4.422
3.765
3.726
3.562
3.432
2.838
2.674
2.628
2.587
2.535
2.380
2.375
2.334
2.328
2.181
2.170
2.166
2.151
2.143
2.138
2.133
2.099
2.076
2.063
2.054
2.050
2.037
2.021
1.707
1.690
1.673
1.661
1.648
1.635
1.622
1.467
1.384
1.059
1.019
1.008
0.396
1.07
0.94
0.96
1.00
1.04
0.99
1.00
3.21
1.01
1.13
0.99
1.07
5.67
3.30
2.06
1.81
ppm


18
205.06
173.16
160.49
143.88
128.71
128.39
128.07
115.94
111.61
77.23
76.11
61.26
55.08
48.20
46.92
36.06
32.60
29.87
27.61
cyclized from o-butenated enol acetate in C6D6 301a tuwy 04/03/08
ppm

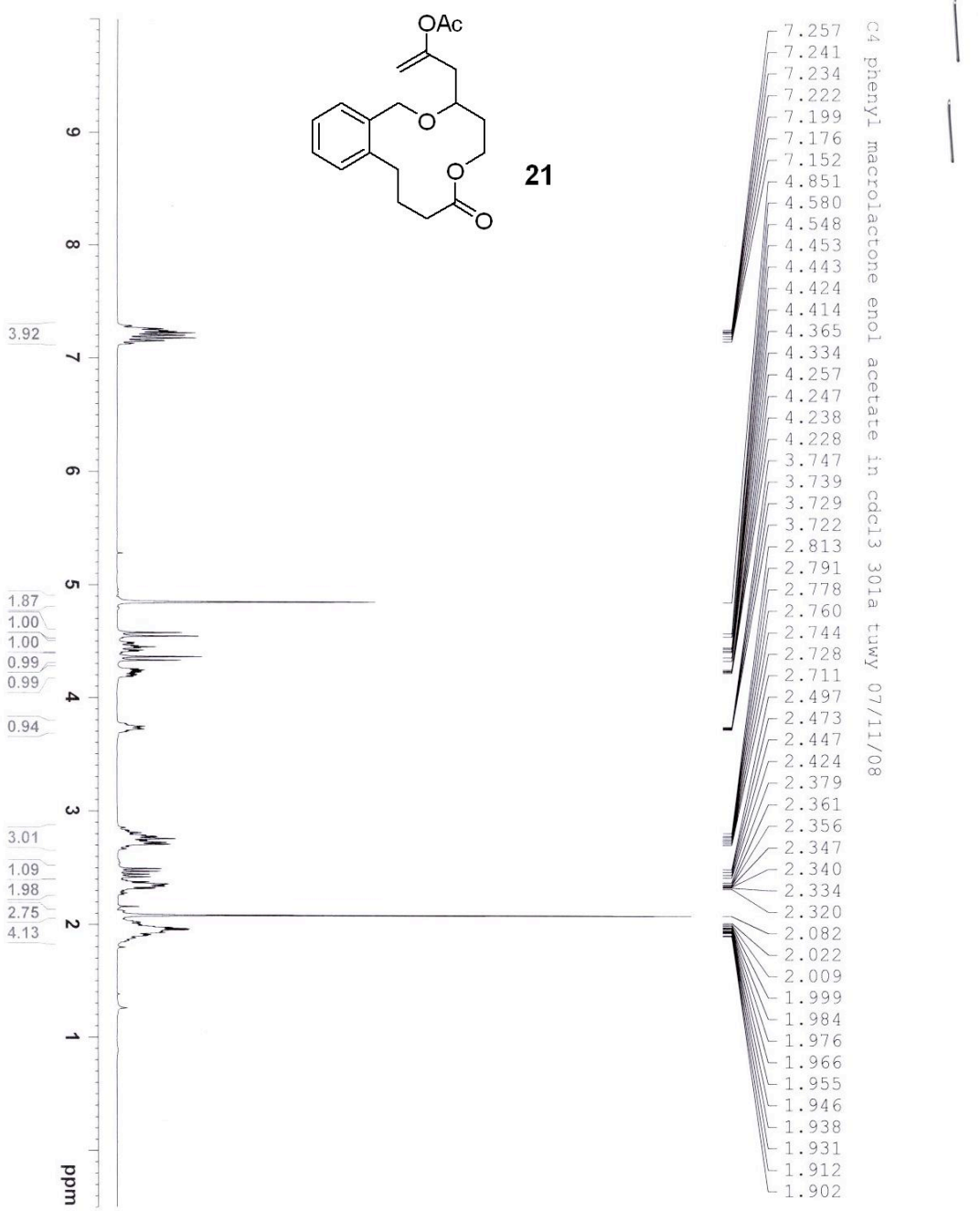

OAc
O
O
O
O
19
1.05
0.92
0.94
1.71
1.00
1.24
0.77
0.99
2.93
0.92
2.01
1.87
1.03
0.93
2.76
1.13
1.09
9
8
7
6
5
4
3
2
1
ppm
C3 macrolactone enol acetate in cdcl3 301a tuwy 04/17/08
7.137
7.109
6.763
6.754
6.716
6.707
6.688
6.679
4.832
4.827
4.813
4.548
4.512
4.341
4.315
4.305
4.289
4.279
4.265
4.251
4.090
4.079
4.053
4.042
3.782
3.651
3.644
3.634
3.627
3.078
3.066
3.050
3.038
3.015
3.005
2.728
2.719
2.709
2.678
2.663
2.603
2.593
2.577
2.567
2.382
2.357
2.333
2.308
2.125
2.013
1.986
1.783
1.776
1.732
1.726

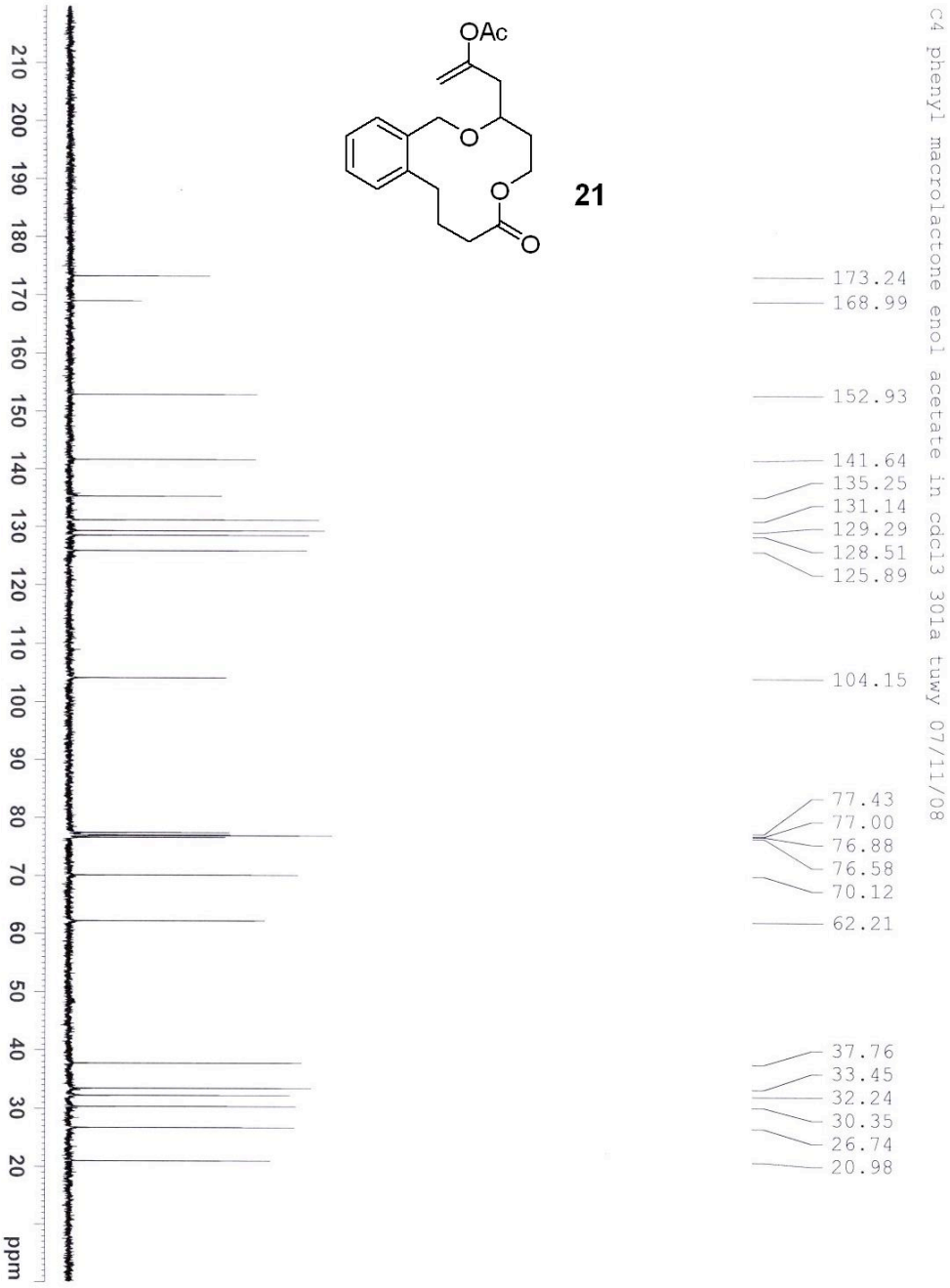

OAc
O
O
O
O
19
C3 macrolactone enol acetate in cdcl3 301a tuwy 04/17/08
172.28
169.04
159.75
152.95
142.38
132.44
128.00
115.49
111.42
104.12
77.43
77.00
76.58
73.51
67.71
62.42
55.13
38.04
36.79
31.91
27.98
21.09
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

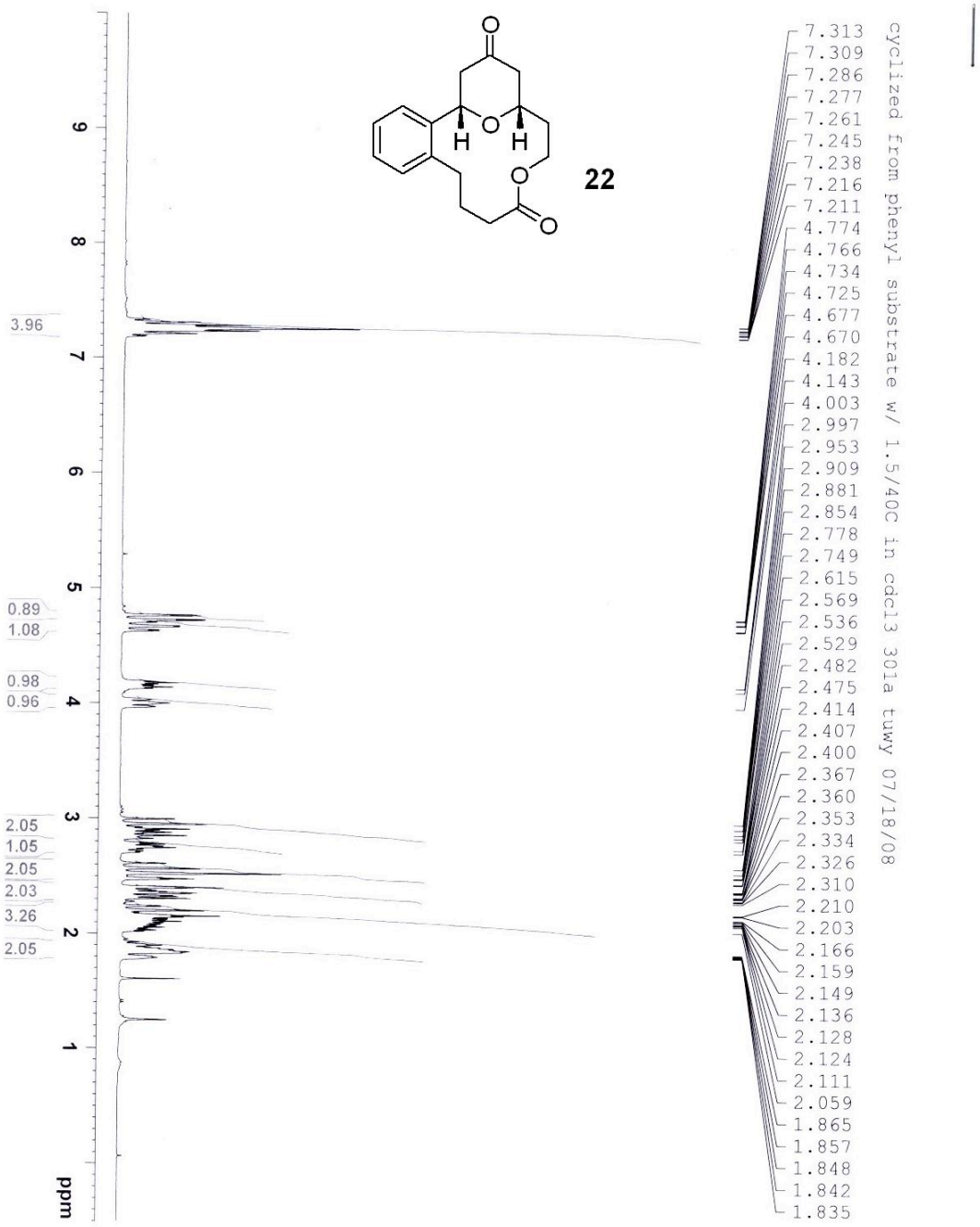

20
cyclized from o-propanated PMB enol acetate in cdcl3 30la tuny 04/18/08
7.261
7.130
7.102
6.795
6.786
6.755
6.746
6.726
6.718
4.749
4.742
4.709
4.702
4.473
4.455
4.436
4.417
4.228
4.211
4.190
4.173
4.103
4.086
4.072
4.055
4.042
4.025
3.793
3.197
3.155
3.120
2.978
2.954
2.934
2.906
2.893
2.863
2.831
2.669
2.626
2.472
2.452
2.425
2.413
2.394
2.374
2.354
2.345
2.334
2.324
2.315
1.655
1.640
1.605
1.590
0.98
0.95
0.92
1.00
1.01
1.04
1.04
3.04
1.03
3.06
1.05
2.88
1.26
1.08
ppm

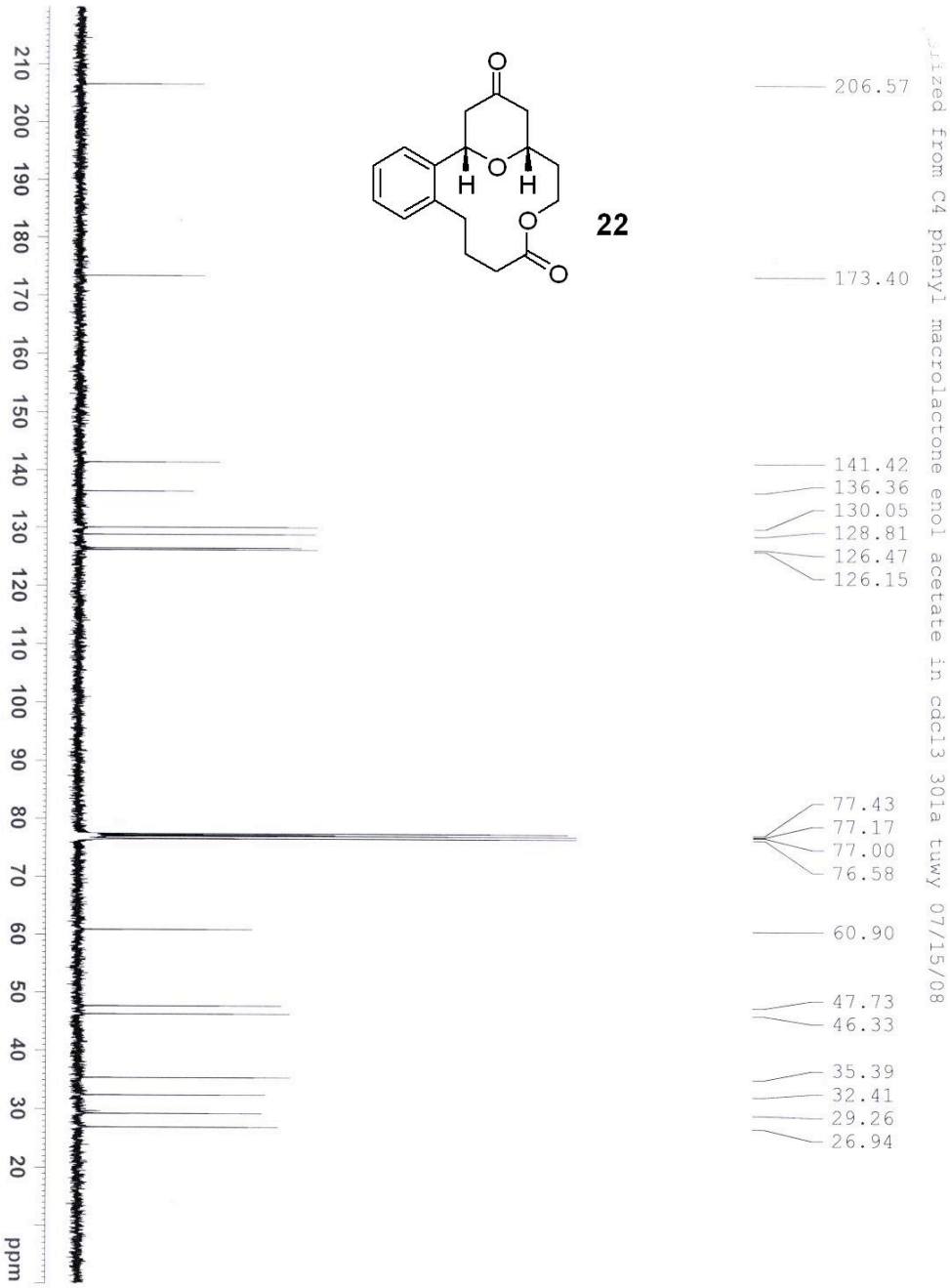

cyclized from o-propanated PMB enol acetate in cdcl3 301a tuwy 04/18/08
206.70
173.04
159.92
143.54
128.82
126.39
116.84
111.25
77.43
77.00
76.58
75.06
61.60
55.22
48.06
45.38
37.47
33.70
28.67
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm
O
H
O
H
O
O
O

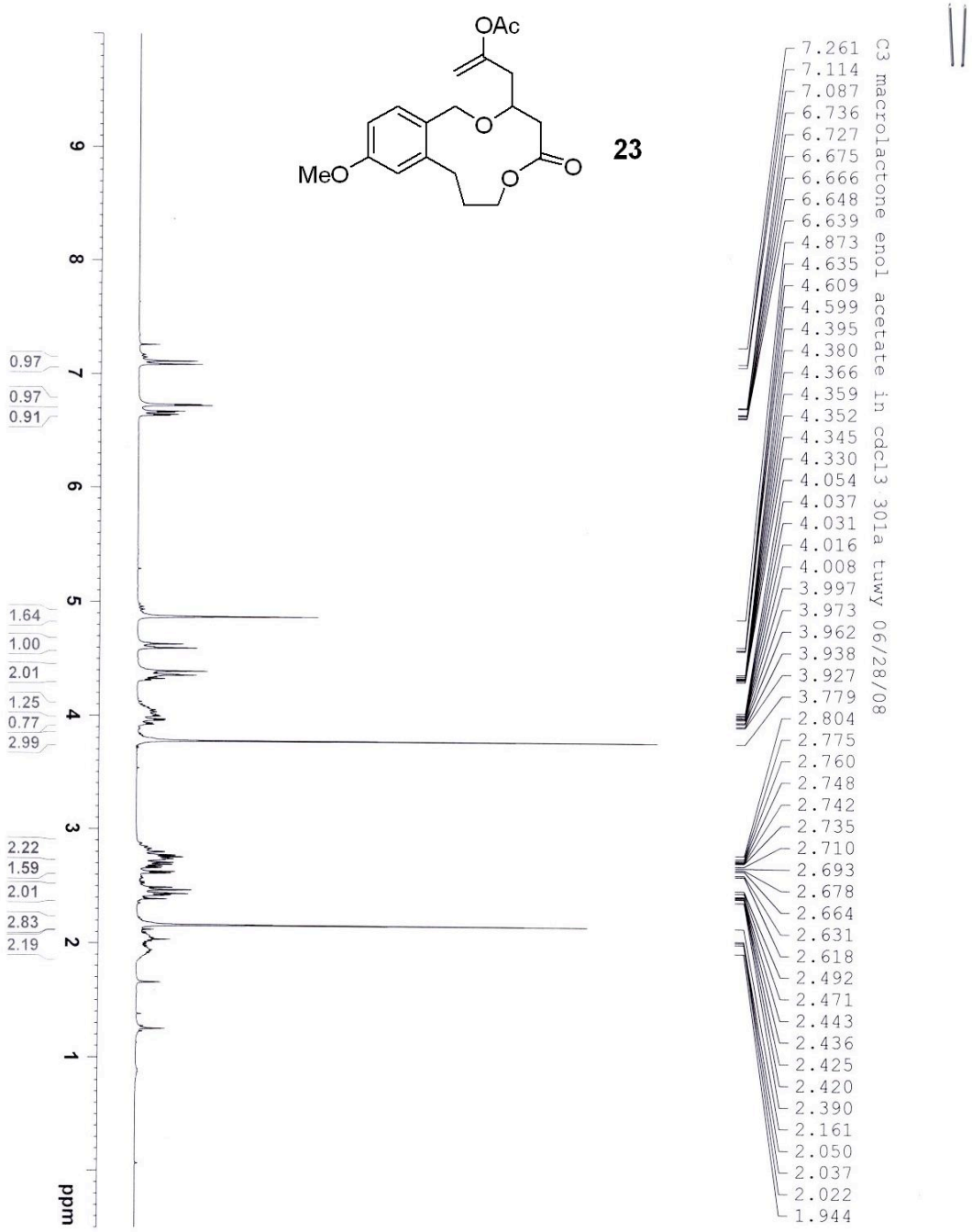
20

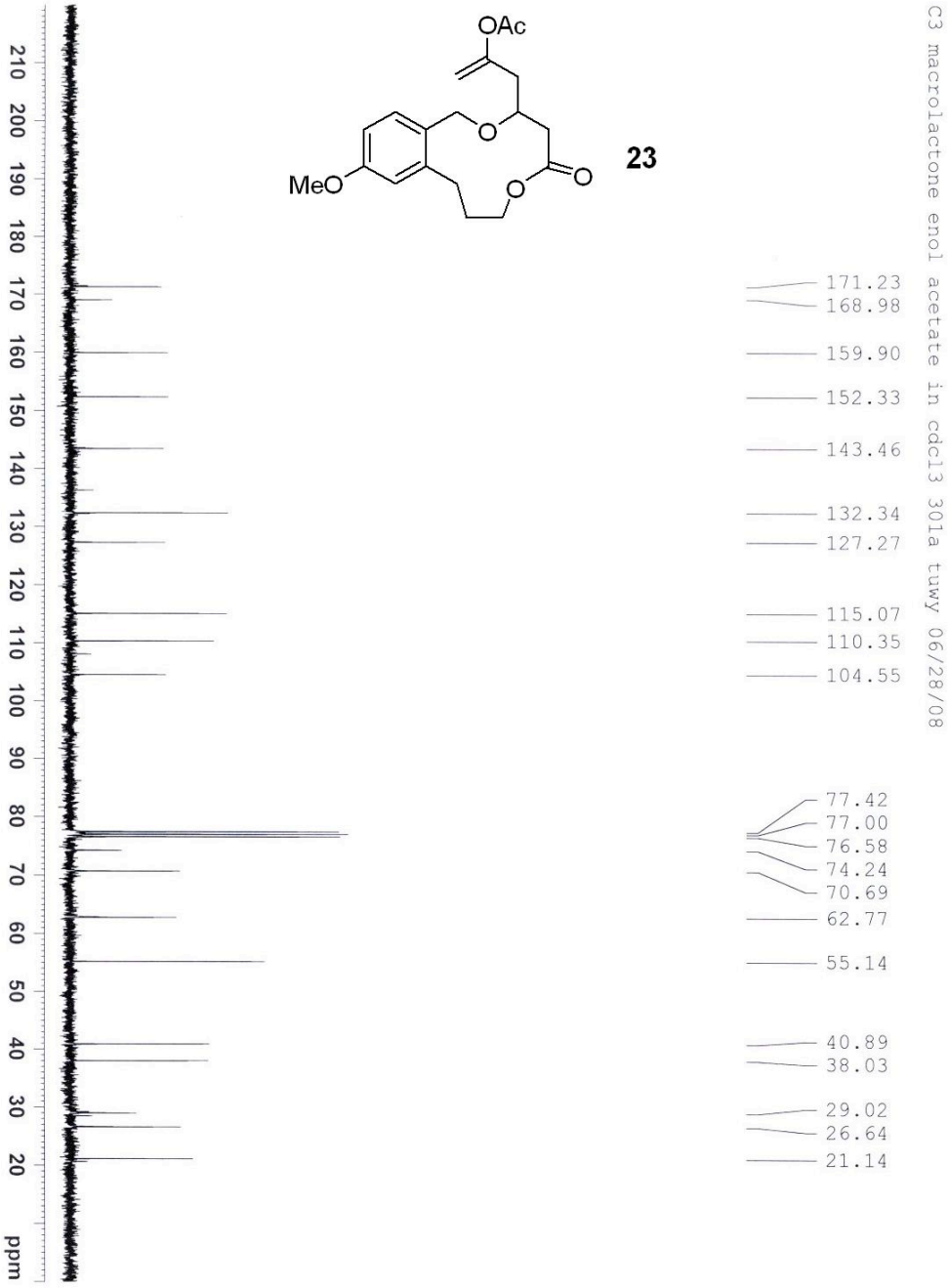

OAc
O
O
O
21
3.92
1.87
1.00
1.00
0.99
0.99
0.94
3.01
1.09
1.98
2.75
4.13
ppm
C4 phenyl macrolactone enol acetate in cdcl3 301a tuwy 07/11/08
7.257
7.241
7.234
7.222
7.199
7.176
7.152
4.851
4.580
4.548
4.453
4.443
4.424
4.414
4.365
4.334
4.257
4.247
4.238
4.228
3.747
3.739
3.729
3.722
2.813
2.791
2.778
2.760
2.744
2.728
2.711
2.497
2.473
2.447
2.424
2.379
2.361
2.356
2.347
2.340
2.334
2.320
2.082
2.022
2.009
1.999
1.984
1.976
1.966
1.955
1.946
1.938
1.931
1.912
1.902

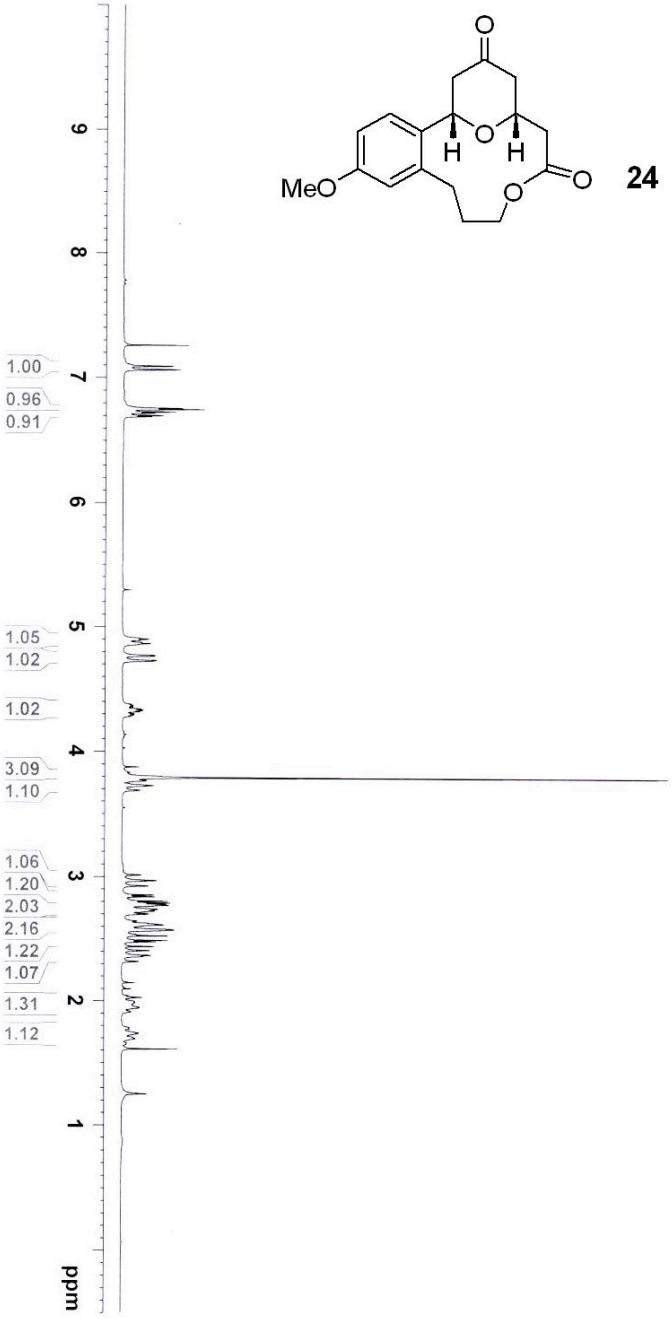

OAc
O
O
O
21
c4 phenyl macrolactone enol acetate in cdcl3 301a tuwy 07/11/08
173.24
168.99
152.93
141.64
135.25
131.14
129.29
128.51
125.89
104.15
77.43
77.00
76.88
76.58
70.12
62.21
37.76
33.45
32.24
30.35
26.74
20.98
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

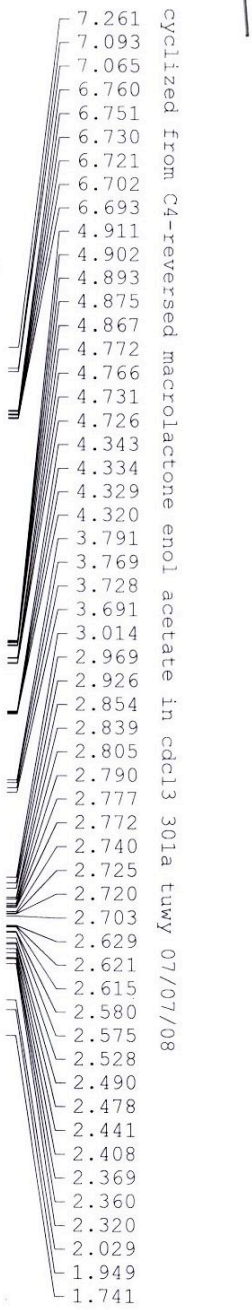

22
cyclized from phenyl substrate w/ 1.5/40C in cdcl3 301a tuwy 07/18/08
7.313
7.309
7.286
7.277
7.261
7.245
7.238
7.216
7.211
4.774
4.766
4.734
4.725
4.677
4.670
4.182
4.143
4.003
2.997
2.953
2.909
2.881
2.854
2.778
2.749
2.615
2.569
2.536
2.529
2.482
2.475
2.414
2.407
2.400
2.367
2.360
2.353
2.334
2.326
2.310
2.210
2.203
2.166
2.159
2.149
2.136
2.128
2.124
2.111
2.059
1.865
1.857
1.848
1.842
1.835
3.96
0.89
1.08
0.98
0.96
2.05
1.05
2.05
2.03
3.26
2.05
ppm

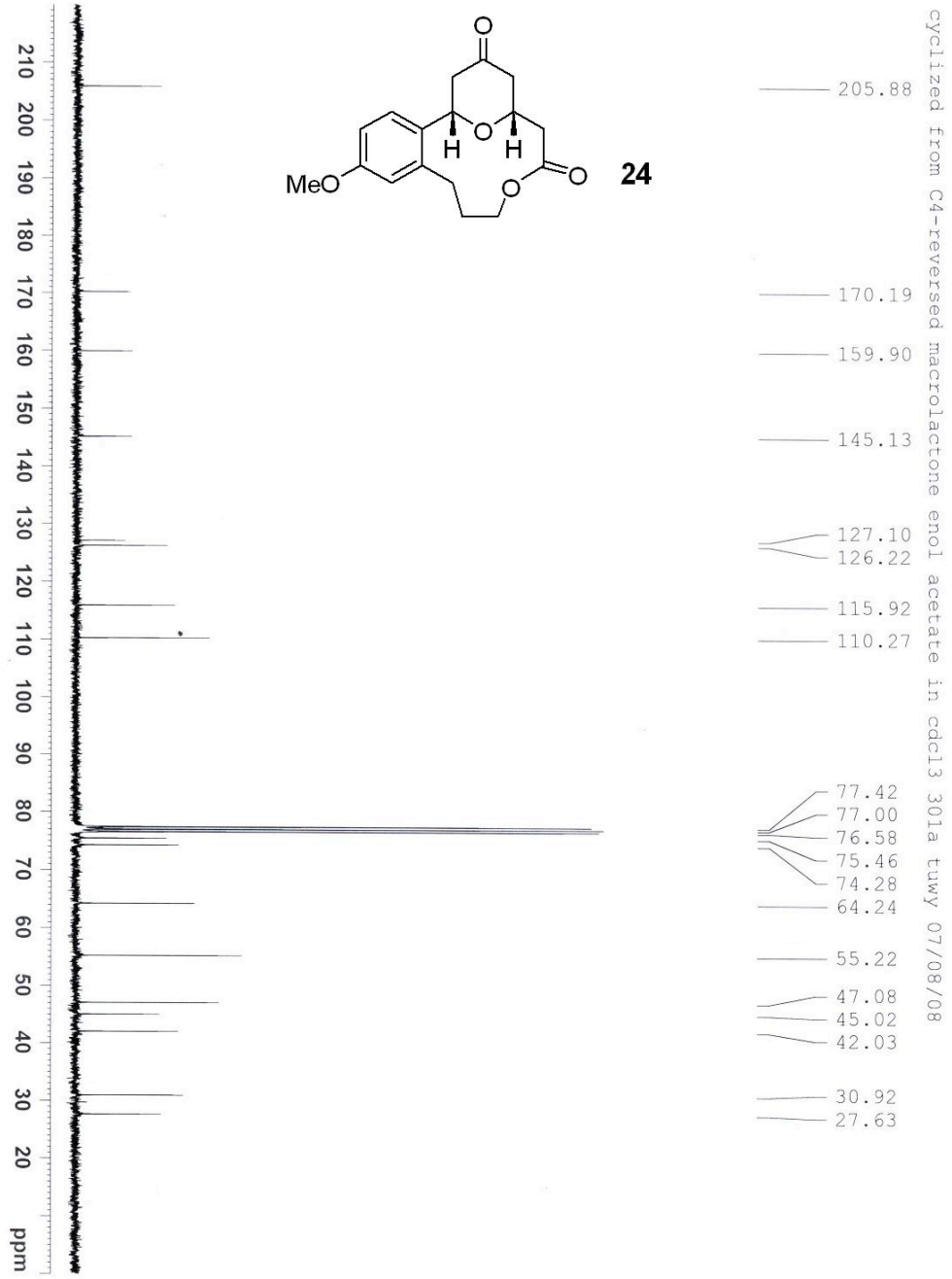

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm
206.57
173.40
141.42
136.36
130.05
128.81
126.47
126.15
77.43
77.17
77.00
76.58
60.90
47.73
46.33
35.39
32.41
29.26
26.94
O
H
O
H
O
O
22
ized from C4 phenyl macrolactone enol acetate in cdcl3 301a tuwy 07/15/08


OAc
MeO
O
O
O
23
0.97
0.97
0.91
1.64
1.00
2.01
1.25
0.77
2.99
2.22
1.59
2.01
2.83
2.19
ppm
C3 macrolactone enol acetate in cdcl3 301a tuwy 06/28/08
7.261
7.114
7.087
6.736
6.727
6.675
6.666
6.648
6.639
4.873
4.635
4.609
4.599
4.395
4.380
4.366
4.359
4.352
4.345
4.330
4.054
4.037
4.031
4.016
4.008
3.997
3.973
3.962
3.938
3.927
3.779
2.804
2.775
2.760
2.748
2.742
2.735
2.710
2.693
2.678
2.664
2.631
2.618
2.492
2.471
2.443
2.436
2.425
2.420
2.390
2.161
2.050
2.037
2.022
1.944


OAc
MeO
O
O
O
23
C3 macrolactone enol acetate in cdcl3 301a tuwy 06/28/08
171.23
168.98
159.90
152.33
143.46
132.34
127.27
115.07
110.35
104.55
77.42
77.00
76.58
74.24
70.69
62.77
55.14
40.89
38.03
29.02
26.64
21.14
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

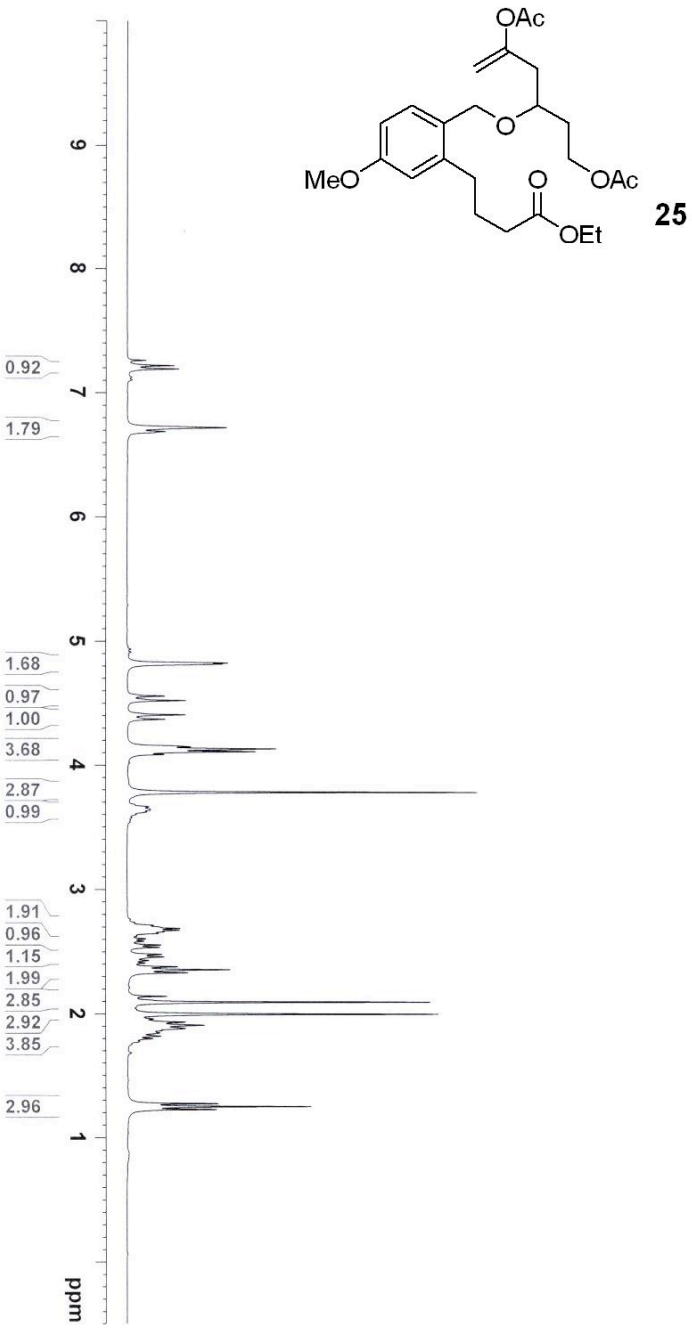

MeO
H
O
H
O
O
O
24
1.00
0.96
0.91
1.05
1.02
1.02
3.09
1.10
1.06
1.20
2.03
2.16
1.22
1.07
1.31
1.12
9
8
7
6
5
4
3
2
1
ppm


cyclized from C4-reversed macrolactone enol acetate in cdcl3 301a tuwy 07/07/08
7.261
7.093
7.065
6.760
6.751
6.730
6.721
6.702
6.693
4.911
4.902
4.893
4.875
4.867
4.772
4.766
4.731
4.726
4.343
4.334
4.329
4.320
3.791
3.769
3.728
3.691
3.014
2.969
2.926
2.854
2.839
2.805
2.790
2.777
2.772
2.740
2.725
2.720
2.703
2.629
2.621
2.615
2.580
2.575
2.528
2.490
2.478
2.441
2.408
2.369
2.360
2.320
2.029
1.949
1.741

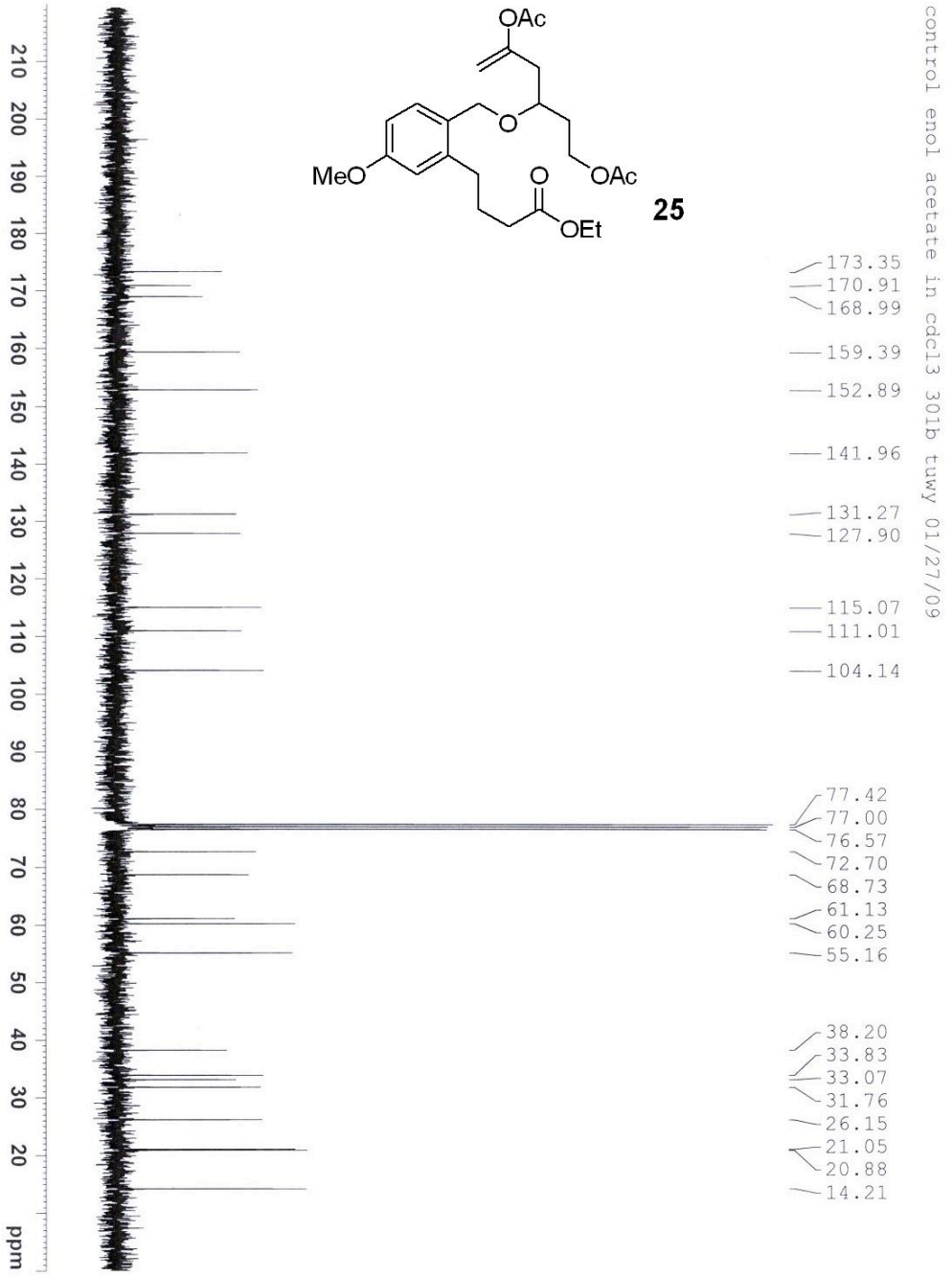

cyclized from C4-reversed macrolactone enol acetate in cdcl3 301a tuwy 07/08/08
205.88
170.19
159.90
145.13
127.10
126.22
115.92
110.27
77.42
77.00
76.58
75.46
74.28
64.24
55.22
47.08
45.02
42.03
30.92
27.63
ppm

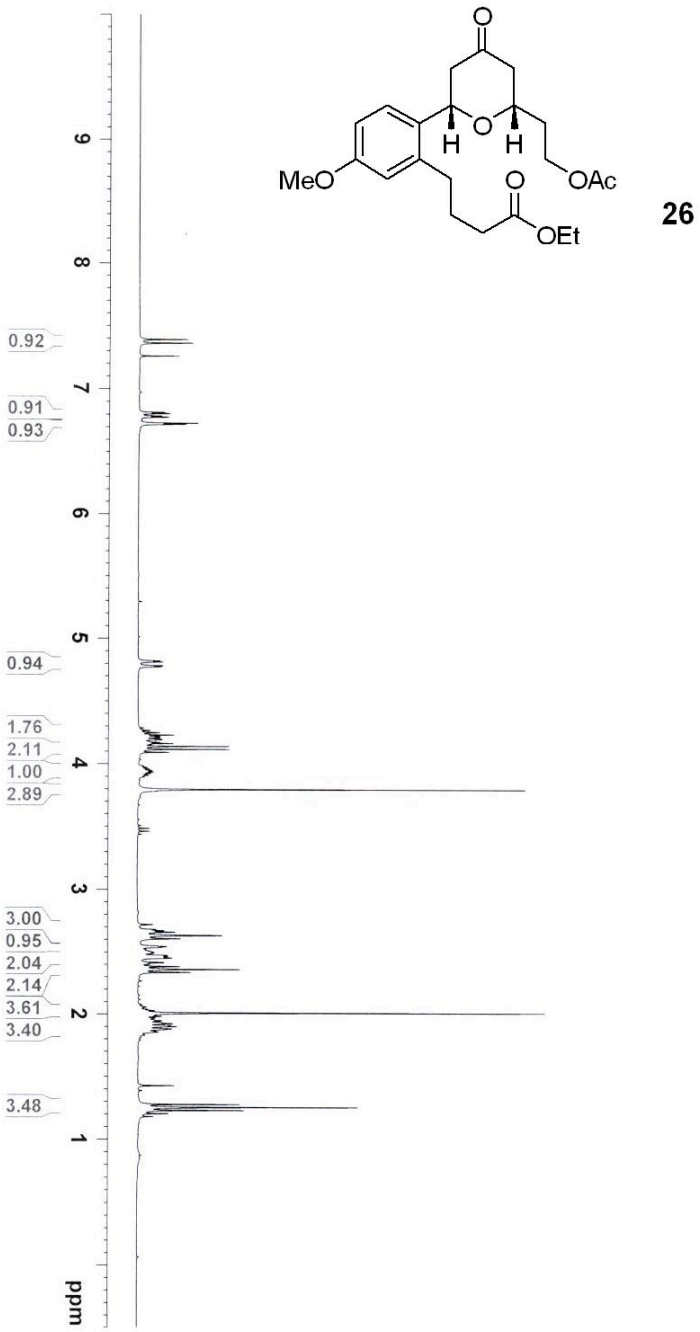
MeO
H
O
H
O
O

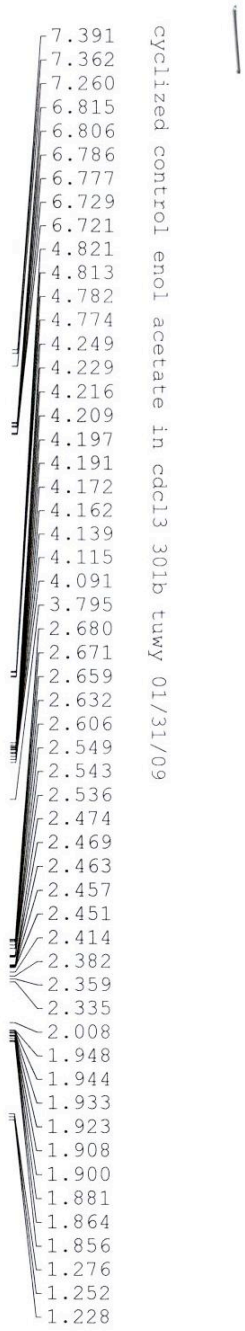
24


OAc
MeO
O
OAc
O
OEt
25
0.92
1.79
1.68
0.97
1.00
3.68
2.87
0.99
1.91
0.96
1.15
1.99
2.85
2.92
3.85
2.96
ppm

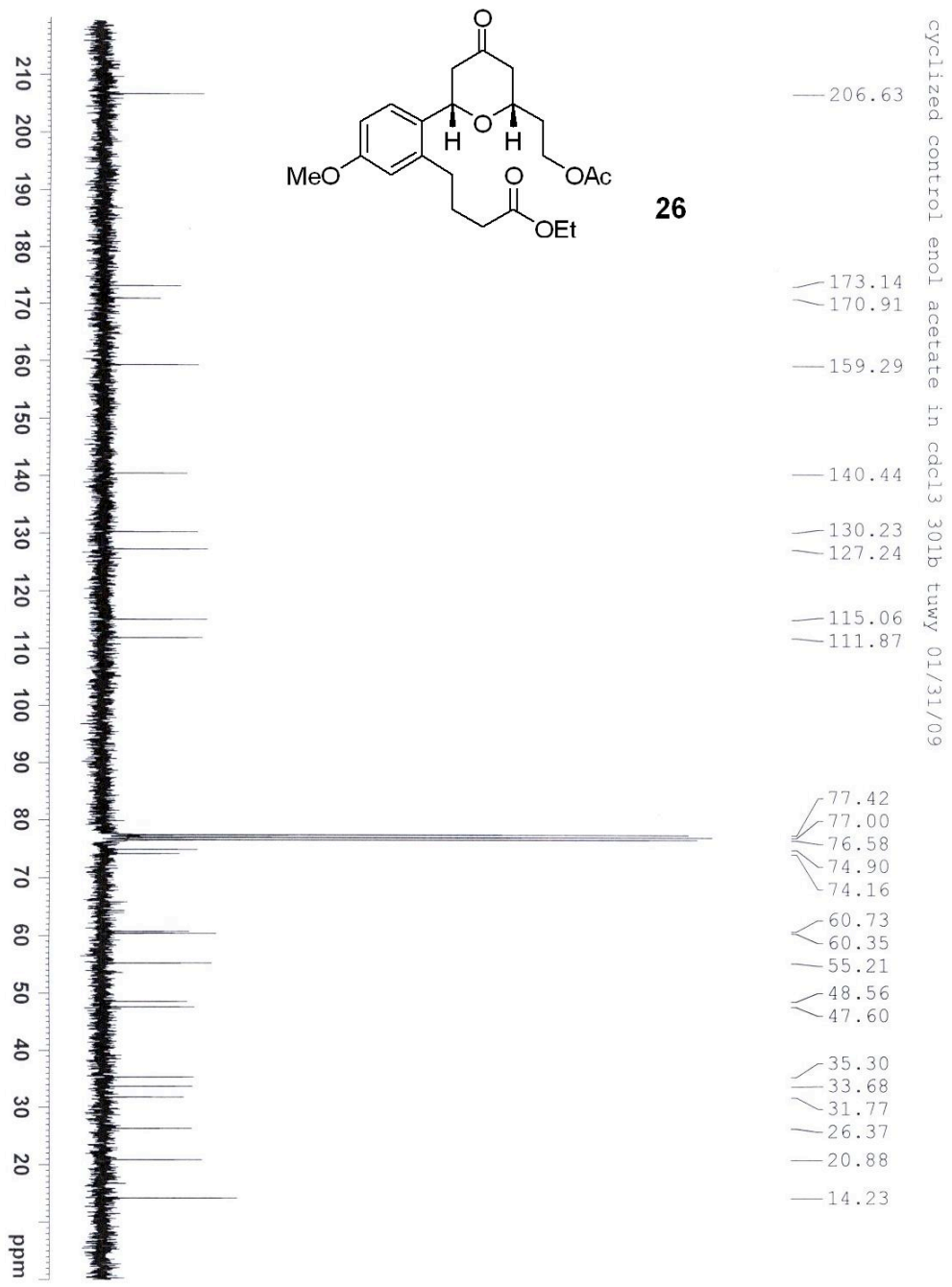

control enol acetate in cdcl3 301b tuwy 01/27/09
7.260
7.218
7.191
6.723
6.691
4.824
4.816
4.559
4.522
4.407
4.370
4.148
4.132
4.109
4.086
3.780
3.662
3.644
3.637
3.621
3.600
2.714
2.699
2.689
2.674
2.663
2.650
2.628
2.606
2.587
2.557
2.537
2.480
2.460
2.431
2.410
2.380
2.355
2.331
2.141
2.093
2.035
1.996
1.959
1.933
1.908
1.882
1.866
1.845
1.819
1.799
1.778
1.272
1.248
1.225


OAc
O
MeO
O
OAc
OEt
25
control enol acetate in cdcl3 301b tuwy 01/27/09
173.35
170.91
168.99
159.39
152.89
141.96
131.27
127.90
115.07
111.01
104.14
77.42
77.00
76.57
72.70
68.73
61.13
60.25
55.16
38.20
33.83
33.07
31.76
26.15
21.05
20.88
14.21
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

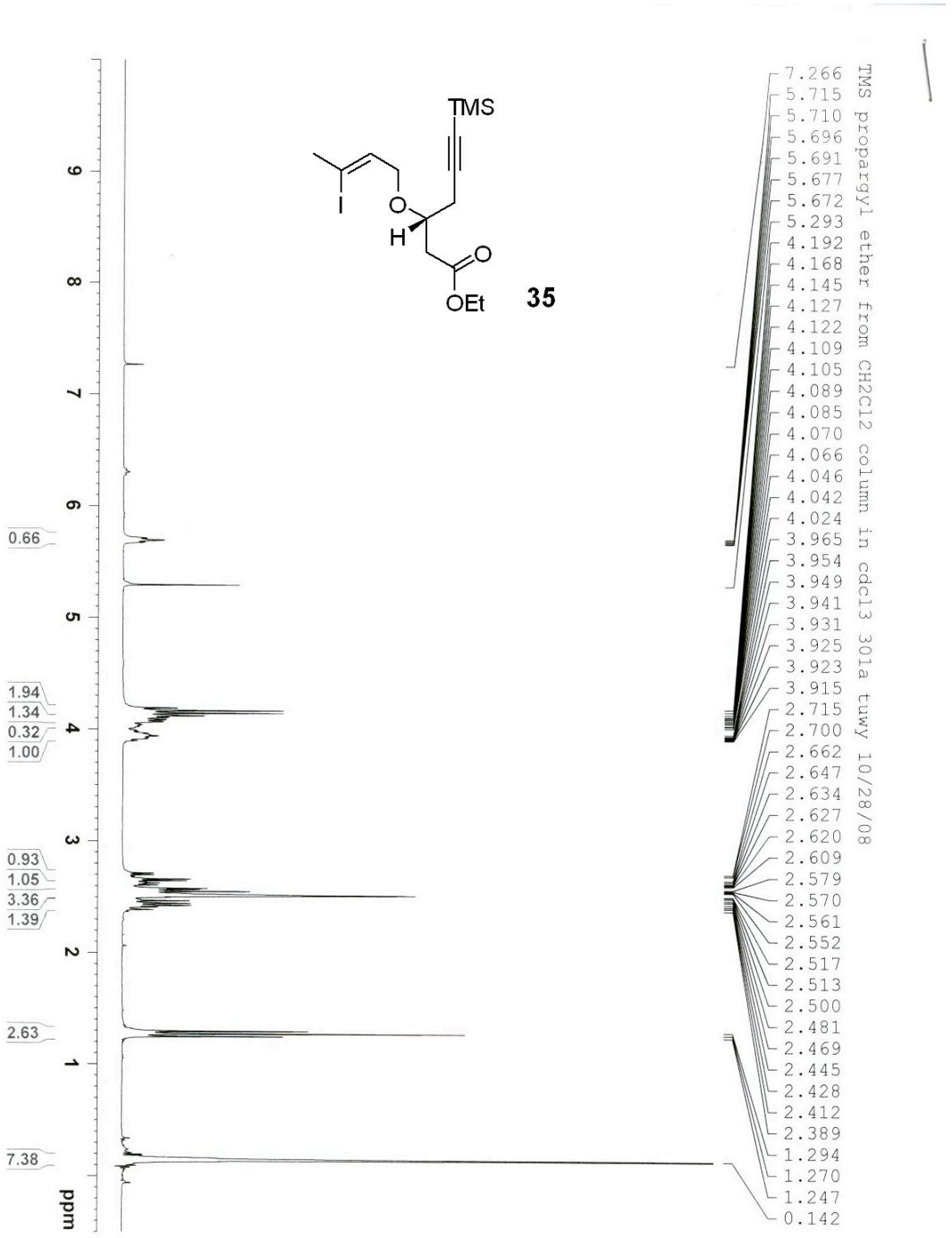


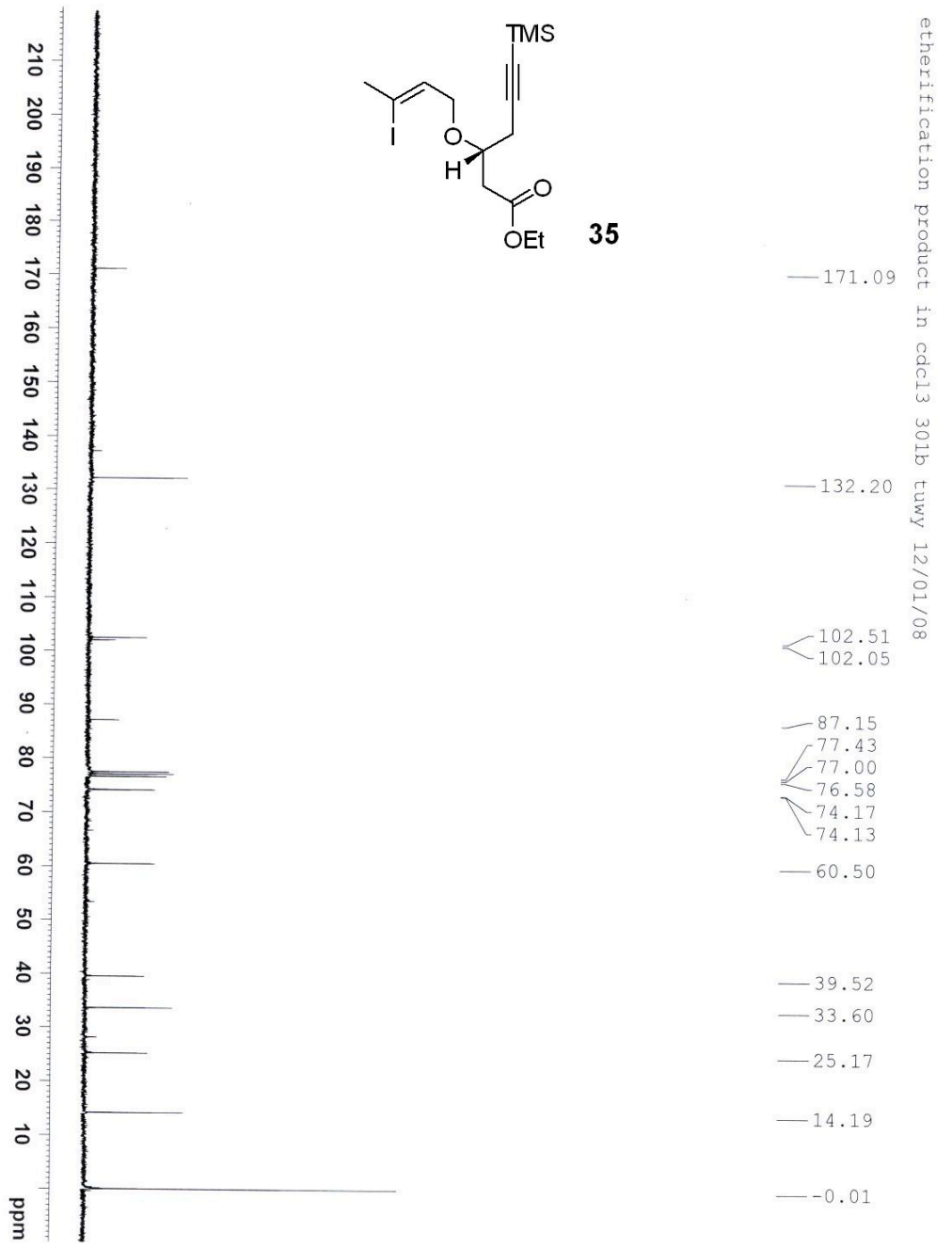


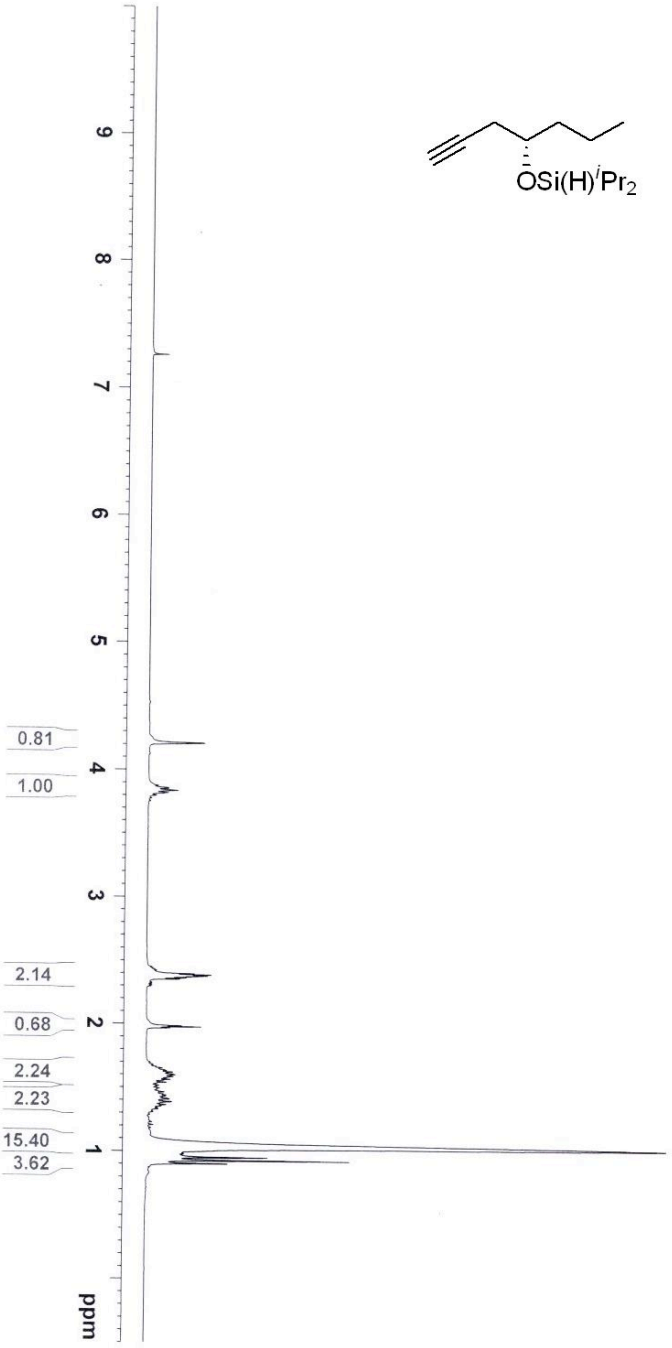
cyclized control enol acetate in cdcl3 301b tuwy 01/31/09

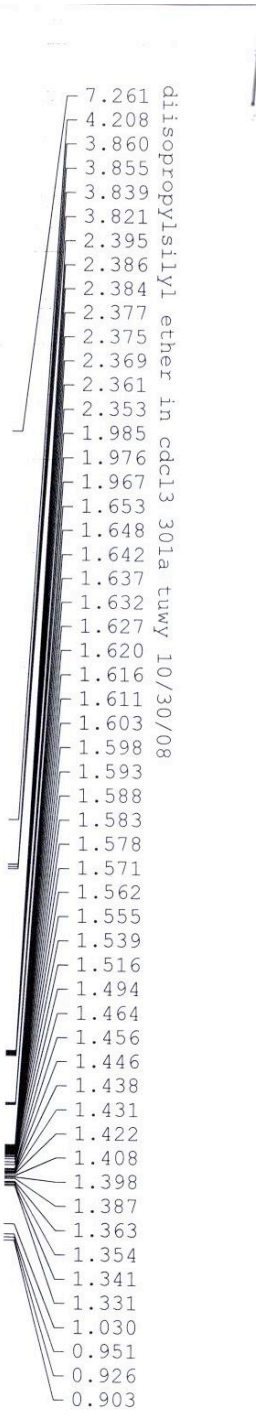

cyclized control enol acetate in cdcl3 301b tuwy 01/31/09
206.63
173.14
170.91
159.29
140.44
130.23
127.24
115.06
111.87
77.42
77.00
76.58
74.90
74.16
60.73
60.35
55.21
48.56
47.60
35.30
33.68
31.77
26.37
20.88
14.23
ppm
MeO
OAc
OEt
H
H
O
O
O

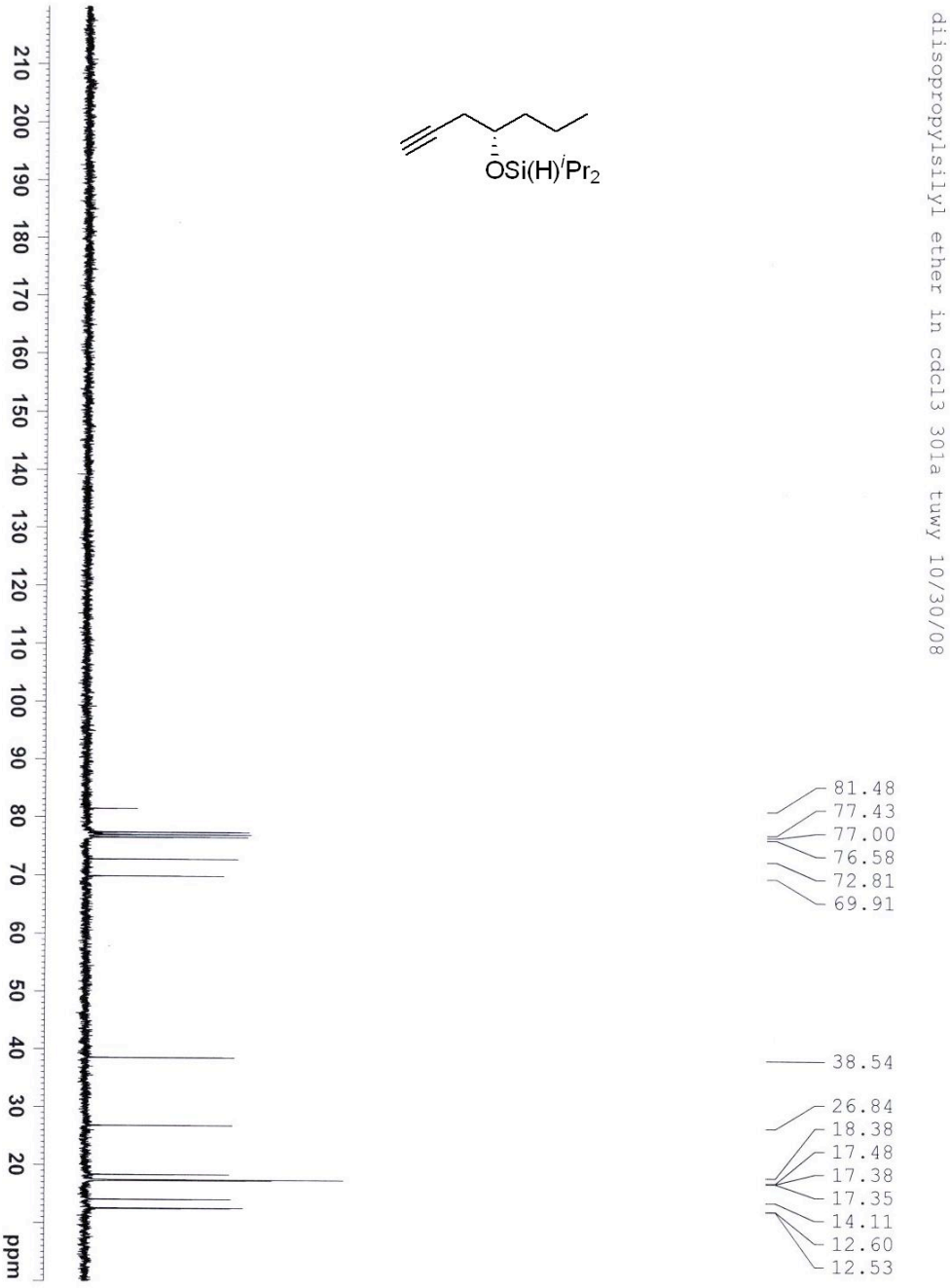
26

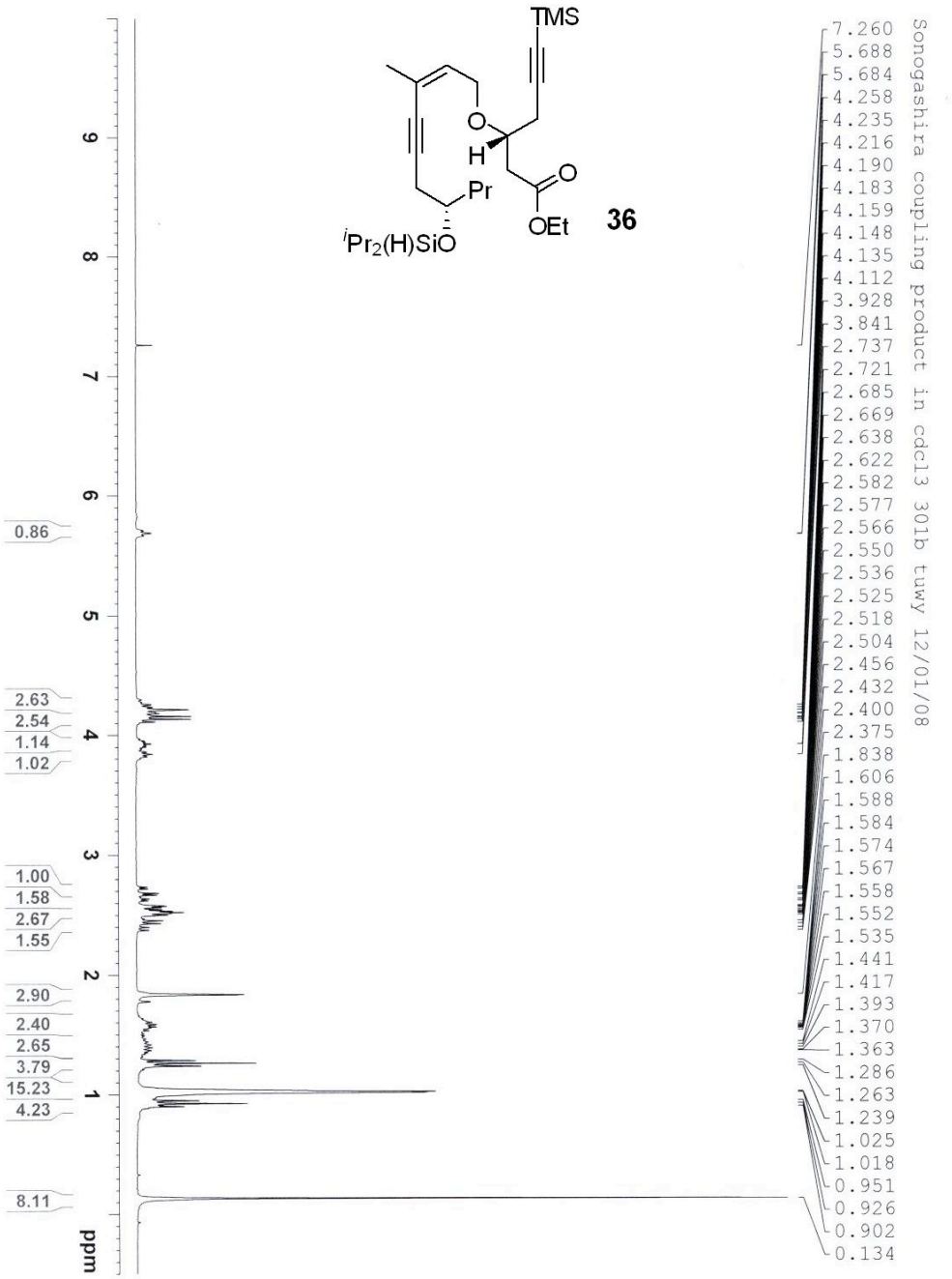

TMS
I
O
H
O
OEt
35
TMS propargyl ether from CH2Cl2 column in cdcl3 301a tuwy 10/28/08
7.266
5.715
5.710
5.696
5.691
5.677
5.672
5.293
4.192
4.168
4.145
4.127
4.122
4.109
4.105
4.089
4.085
4.070
4.066
4.046
4.042
4.024
3.965
3.954
3.949
3.941
3.931
3.925
3.923
3.915
2.715
2.700
2.662
2.647
2.634
2.627
2.620
2.609
2.579
2.570
2.561
2.552
2.517
2.513
2.500
2.481
2.469
2.445
2.428
2.412
2.389
1.294
1.270
1.247
0.142
0.66
1.94
1.34
0.32
1.00
0.93
1.05
3.36
1.39
2.63
7.38
ppm

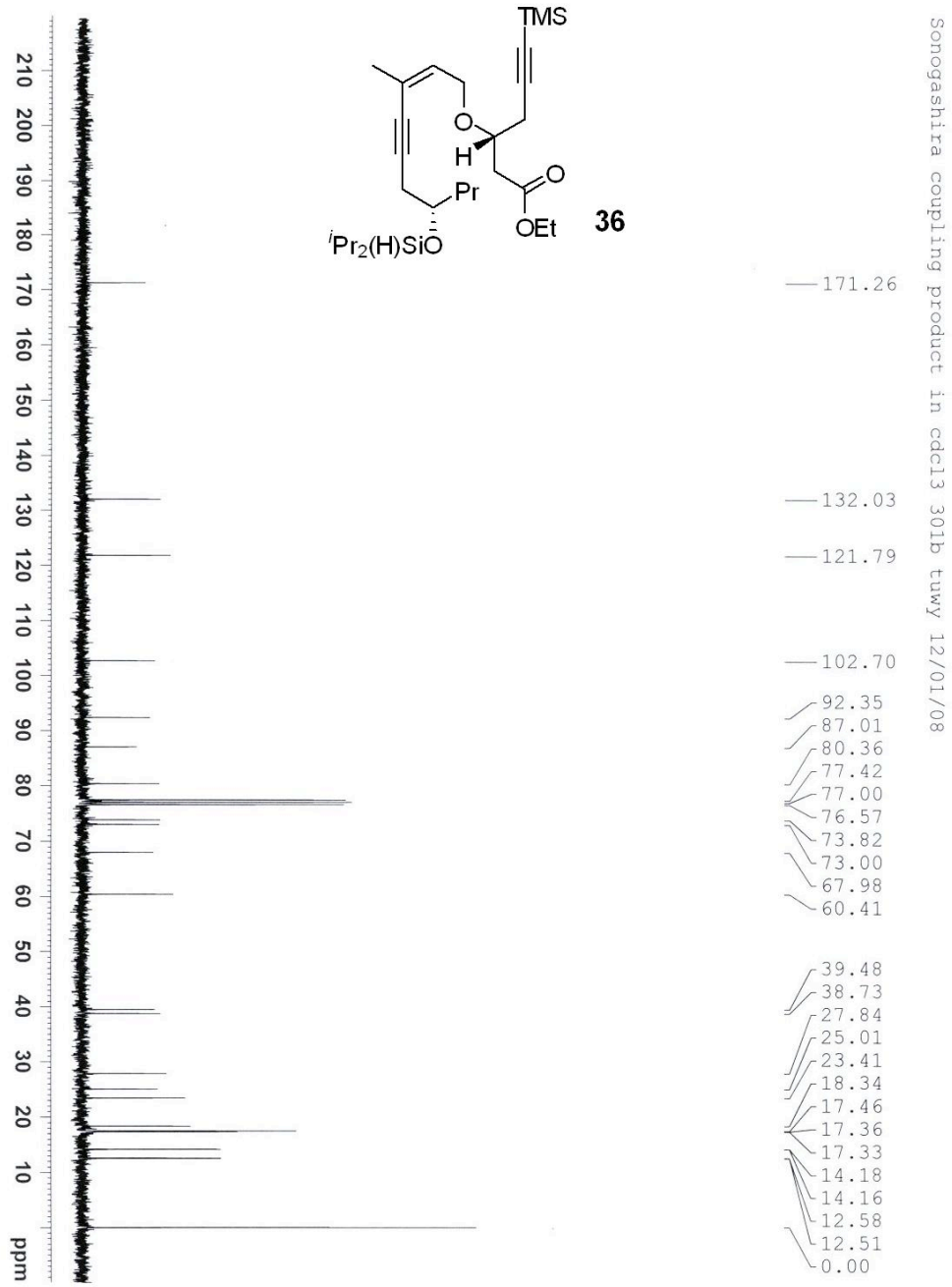

TMS
I
O
H
O
OEt
35
etherification product in cdcl3 301b tuwy 12/01/08
171.09
132.20
102.51
102.05
87.15
77.43
77.00
76.58
74.17
74.13
60.50
39.52
33.60
25.17
14.19
-0.01
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

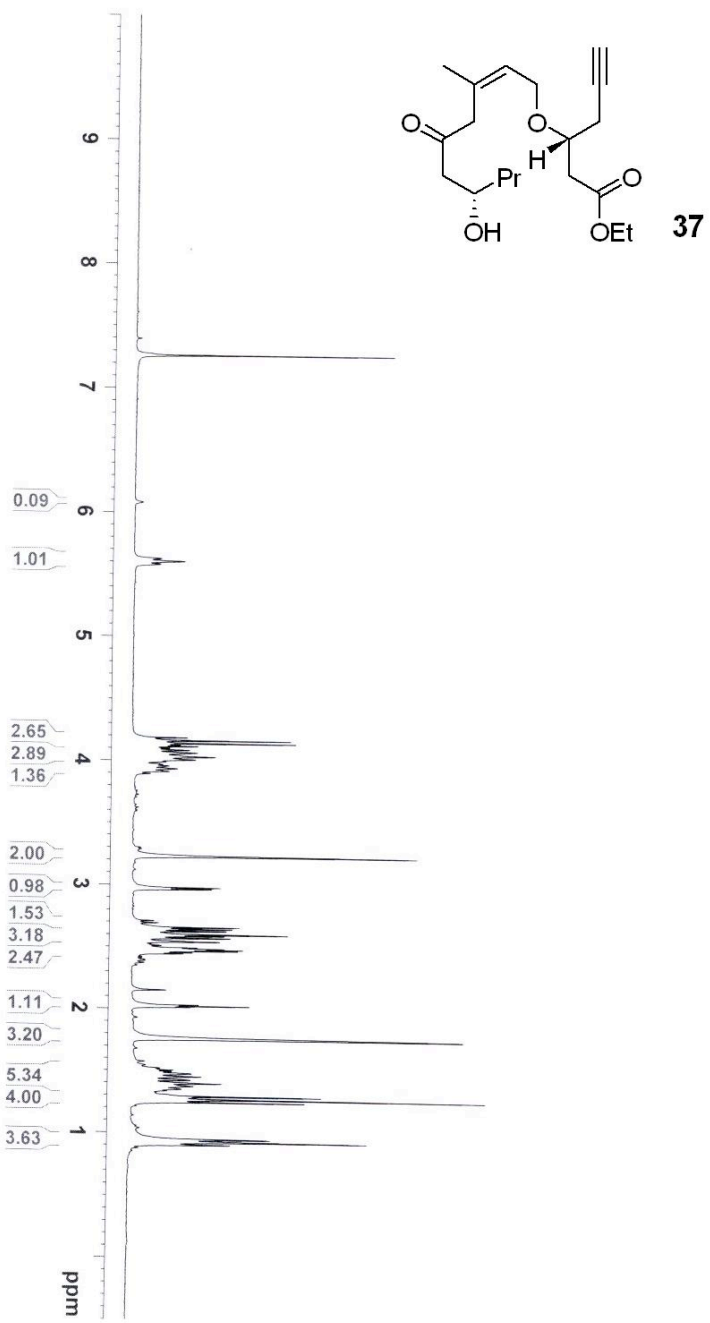

OSi(H)iPr2
0.81
1.00
2.14
0.68
2.24
2.23
15.40
3.62
ppm


diisopropylsilyl ether in cdcl3 301a tuwy 10/30/08
7.261
4.208
3.860
3.855
3.839
3.821
2.395
2.386
2.384
2.377
2.375
2.369
2.361
2.353
1.985
1.976
1.967
1.653
1.648
1.642
1.637
1.632
1.627
1.620
1.616
1.611
1.603
1.598
1.593
1.588
1.583
1.578
1.571
1.562
1.555
1.539
1.516
1.494
1.464
1.456
1.446
1.438
1.431
1.422
1.408
1.398
1.387
1.363
1.354
1.341
1.331
1.030
0.951
0.926
0.903


diisopropylsilyl ether in cdcl3 301a tuwy 10/30/08
OSi(H)iPr2
81.48
77.43
77.00
76.58
72.81
69.91
38.54
26.84
18.38
17.48
17.38
17.35
14.11
12.60
12.53
ppm

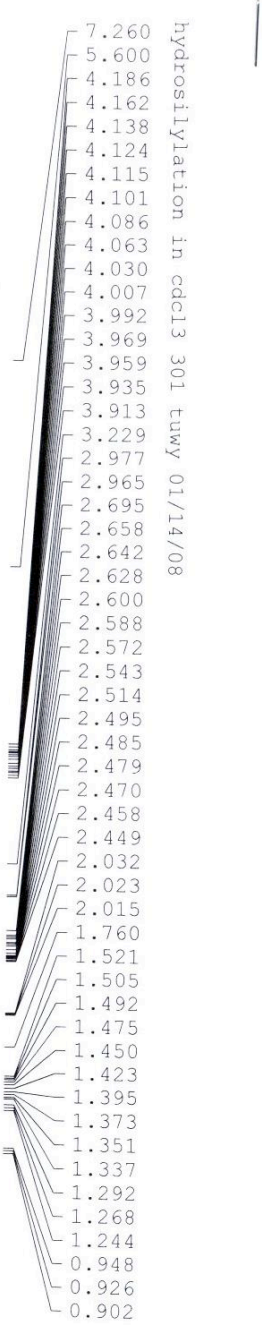

TMS
O
H
Pr
O
OEt
$^{i}Pr_2(H)SiO$
36
Sonogashira coupling product in cdcl3 301b tuwy 12/01/08
7.260
5.688
5.684
4.258
4.235
4.216
4.190
4.183
4.159
4.148
4.135
4.112
3.928
3.841
2.737
2.721
2.685
2.669
2.638
2.622
2.582
2.577
2.566
2.550
2.536
2.525
2.518
2.504
2.456
2.432
2.400
2.375
1.838
1.606
1.588
1.584
1.574
1.567
1.558
1.552
1.535
1.441
1.417
1.393
1.370
1.363
1.286
1.263
1.239
1.025
1.018
0.951
0.926
0.902
0.134
0.86
2.63
2.54
1.14
1.02
1.00
1.58
2.67
1.55
2.90
2.40
2.65
3.79
15.23
4.23
8.11
ppm

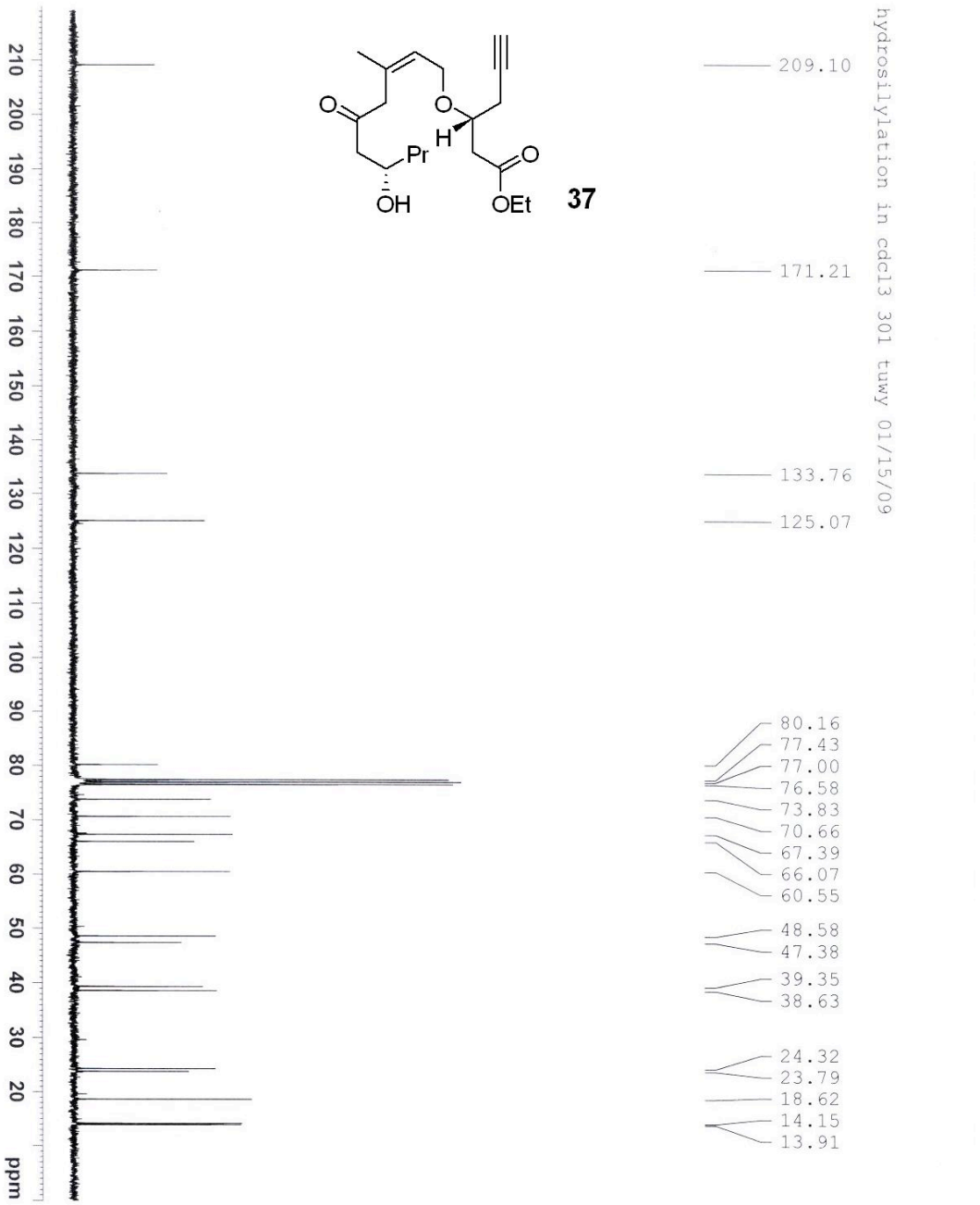

TMS
O
H
Pr
O
OEt
$^{i}Pr_2(H)SiO$
36
Sonogashira coupling product in cdcl3 301b tuwy 12/01/08
171.26
132.03
121.79
102.70
92.35
87.01
80.36
77.42
77.00
76.57
73.82
73.00
67.98
60.41
39.48
38.73
27.84
25.01
23.41
18.34
17.46
17.36
17.33
14.18
14.16
12.58
12.51
0.00
ppm


0.09
1.01
2.65
2.89
1.36
2.00
0.98
1.53
3.18
2.47
1.11
3.20
5.34
4.00
3.63
ppm

O
O
H
Pr
O
OH
OEt

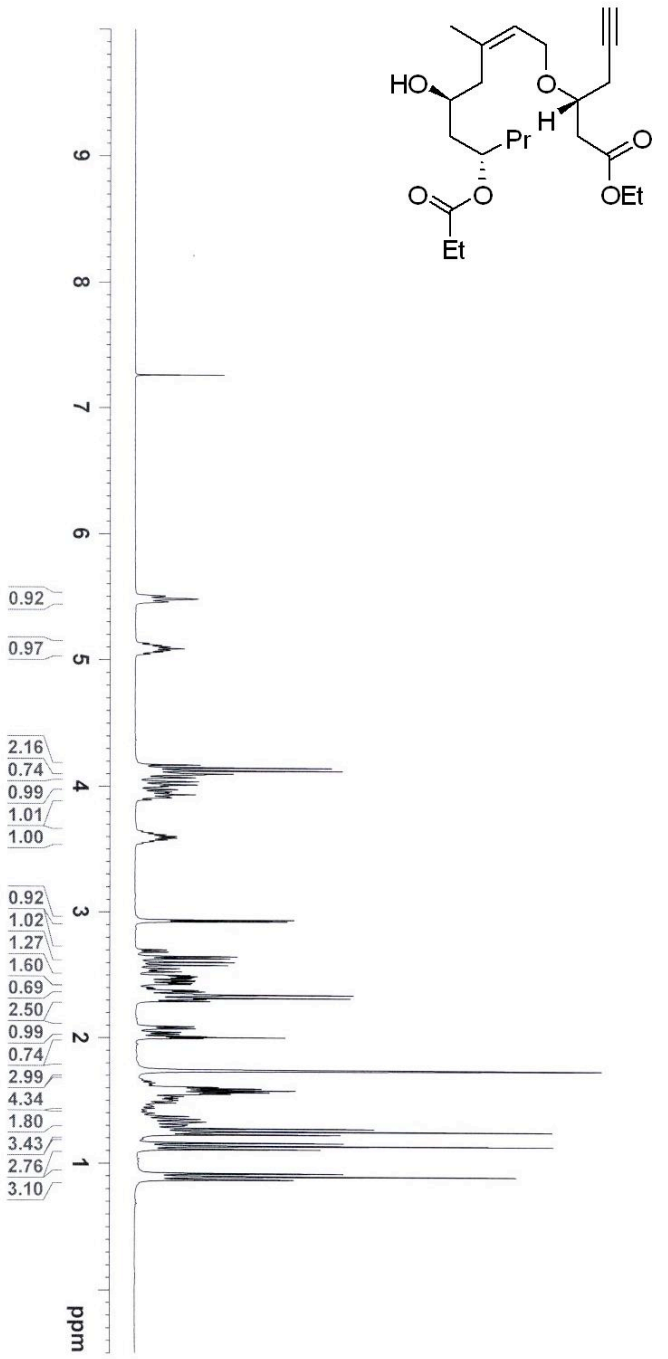
37

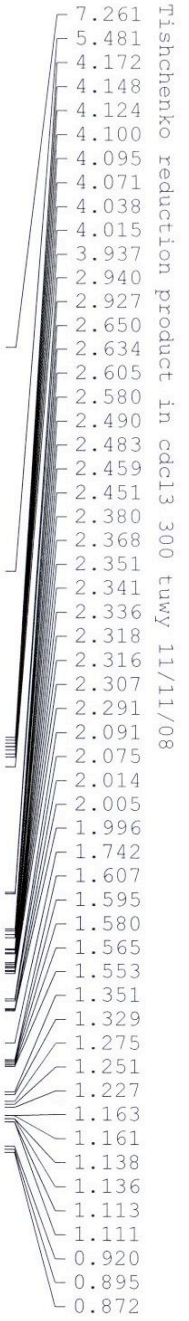

hydrosilylation in cdcl3 301 tuwy 01/14/08
7.260
5.600
4.186
4.162
4.138
4.124
4.115
4.101
4.086
4.063
4.030
4.007
3.992
3.969
3.959
3.935
3.913
3.229
2.977
2.965
2.695
2.658
2.642
2.628
2.600
2.588
2.572
2.543
2.514
2.495
2.485
2.479
2.470
2.458
2.449
2.032
2.023
2.015
1.760
1.521
1.505
1.492
1.475
1.450
1.423
1.395
1.373
1.351
1.337
1.292
1.268
1.244
0.948
0.926
0.902

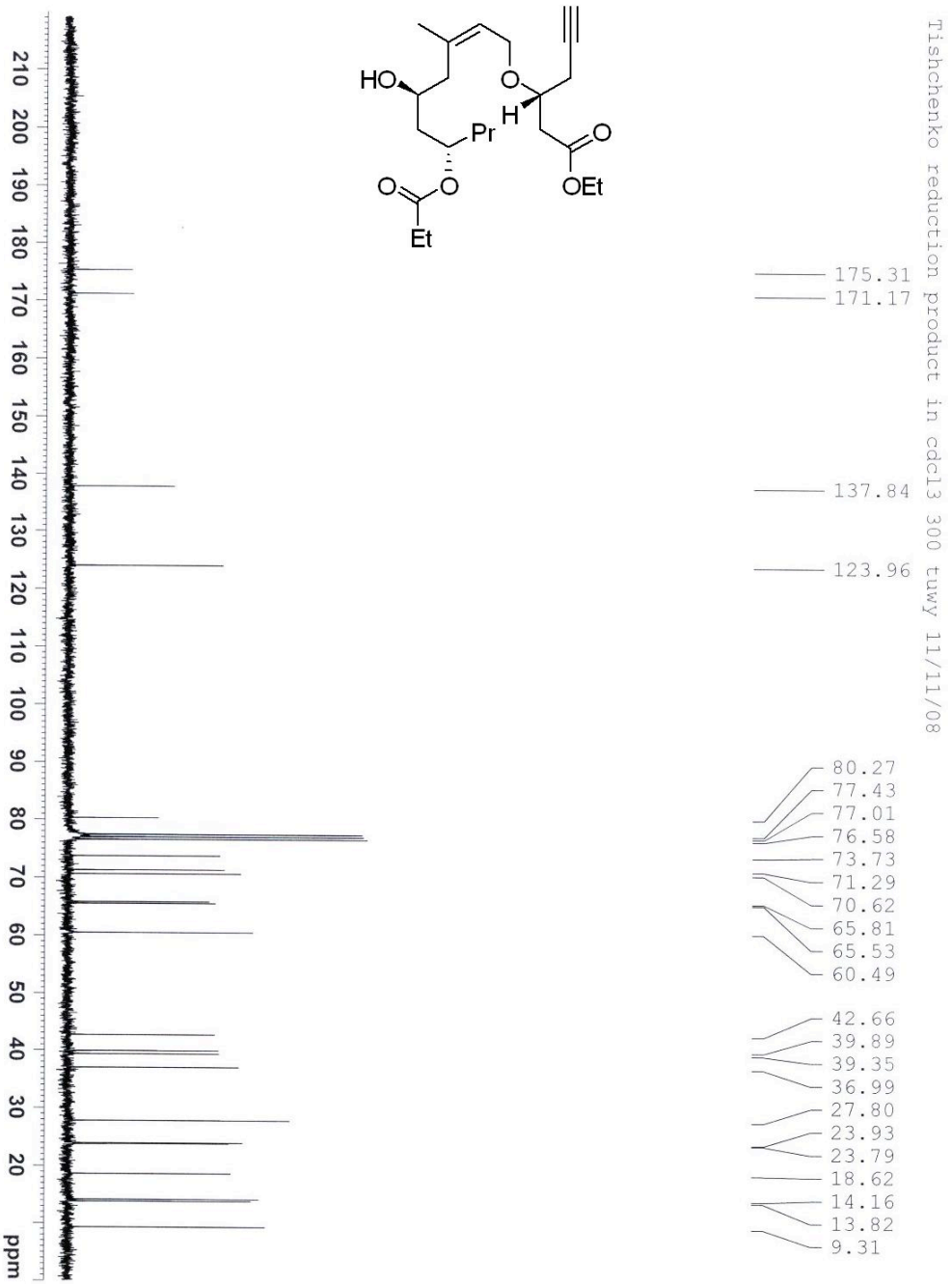

hydrosilylation in cdcl3 301 tuwy 01/15/09
209.10
171.21
133.76
125.07
80.16
77.43
77.00
76.58
73.83
70.66
67.39
66.07
60.55
48.58
47.38
39.35
38.63
24.32
23.79
18.62
14.15
13.91
ppm

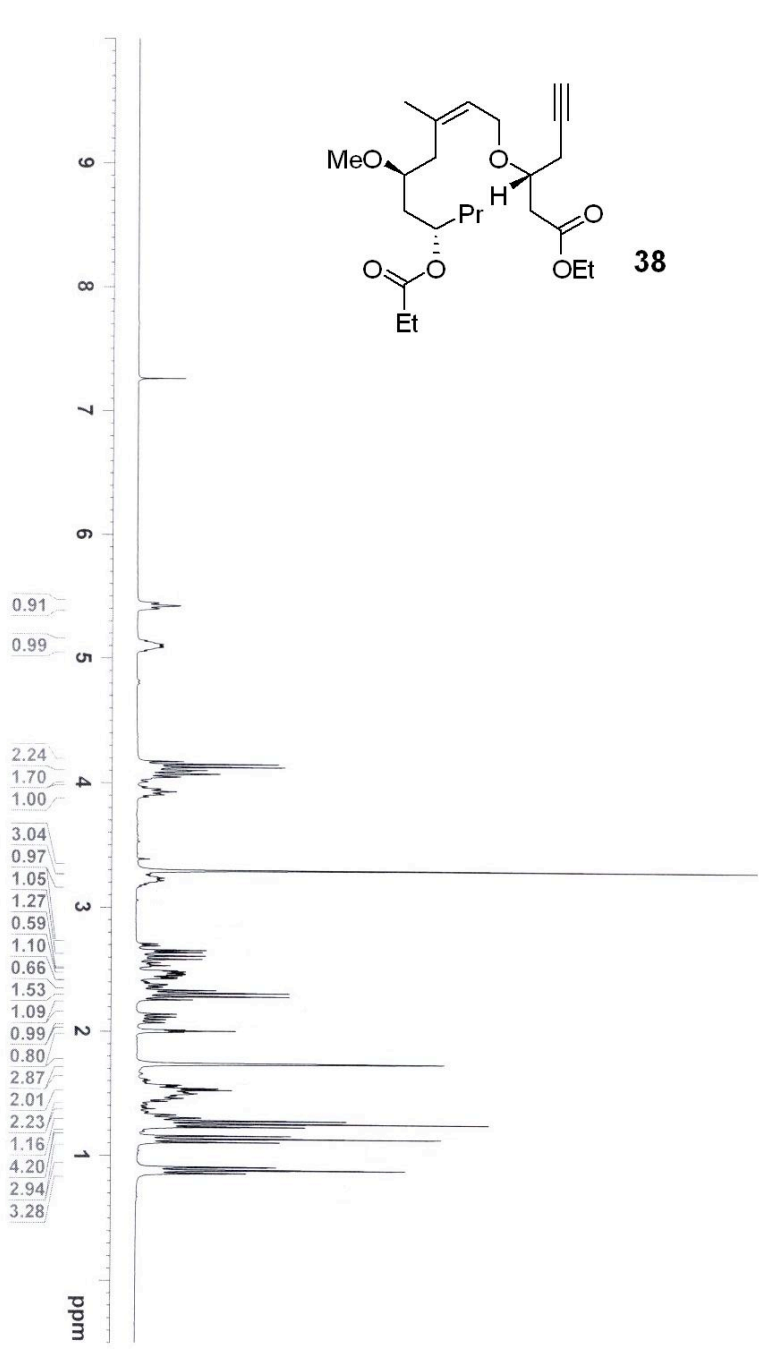
O
O
H
Pr
O
OH
OEt

37

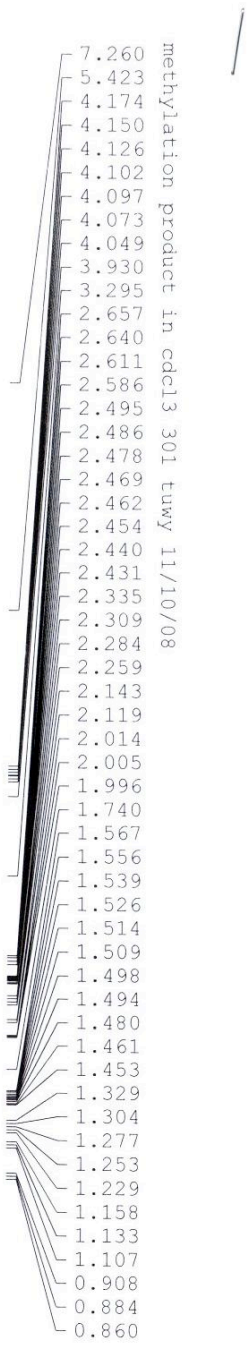

HO
O
H
Pr
O
O
OEt
O
Et
0.92
0.97
2.16
0.74
0.99
1.01
1.00
0.92
1.02
1.27
1.60
0.69
2.50
0.99
0.74
2.99
4.34
1.80
3.43
2.76
3.10
ppm

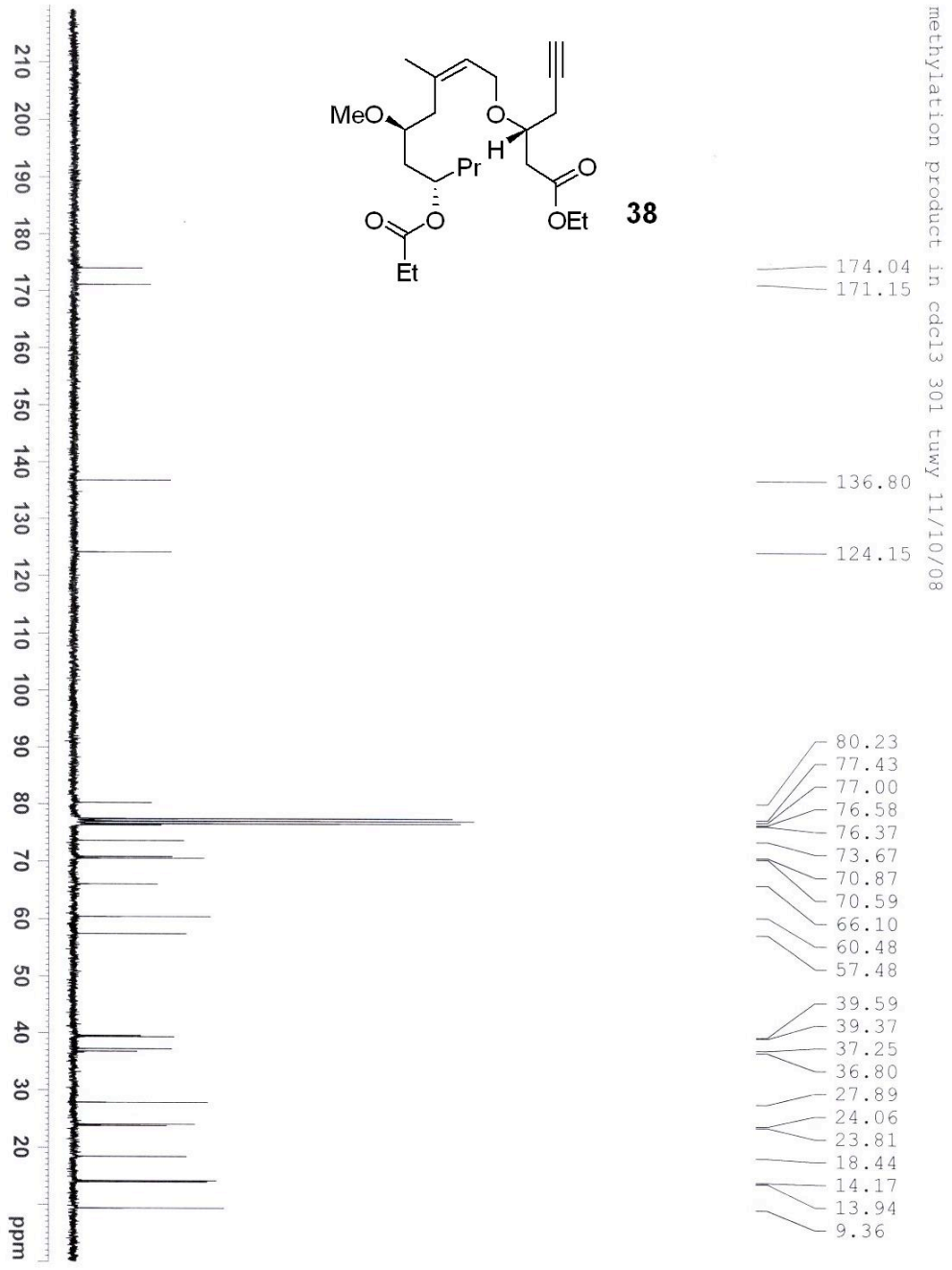

Tishchenko reduction product in cdcl3 300 tuwy 11/11/08
7.261
5.481
4.172
4.148
4.124
4.100
4.095
4.071
4.038
4.015
3.937
2.940
2.927
2.650
2.634
2.605
2.580
2.490
2.483
2.459
2.451
2.380
2.368
2.351
2.341
2.336
2.318
2.316
2.307
2.291
2.091
2.075
2.014
2.005
1.996
1.742
1.607
1.595
1.580
1.565
1.553
1.351
1.329
1.275
1.251
1.227
1.163
1.161
1.138
1.136
1.113
1.111
0.920
0.895
0.872

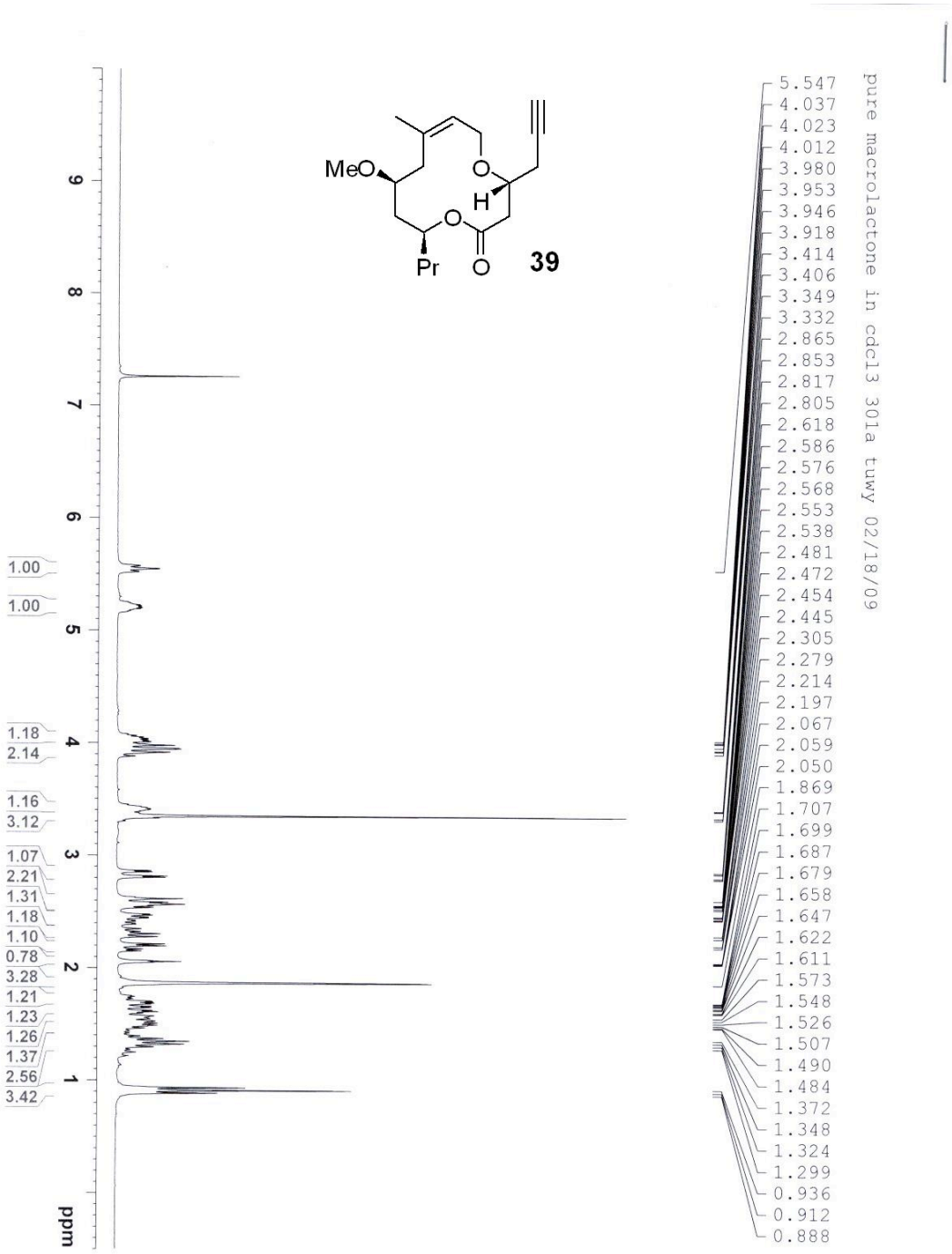

HO
O
H
Pr
O
OEt
O
O
Et
Tishchenko reduction product in cdcl3 300 tuwy 11/11/08
175.31
171.17
137.84
123.96
80.27
77.43
77.01
76.58
73.73
71.29
70.62
65.81
65.53
60.49
42.66
39.89
39.35
36.99
27.80
23.93
23.79
18.62
14.16
13.82
9.31
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

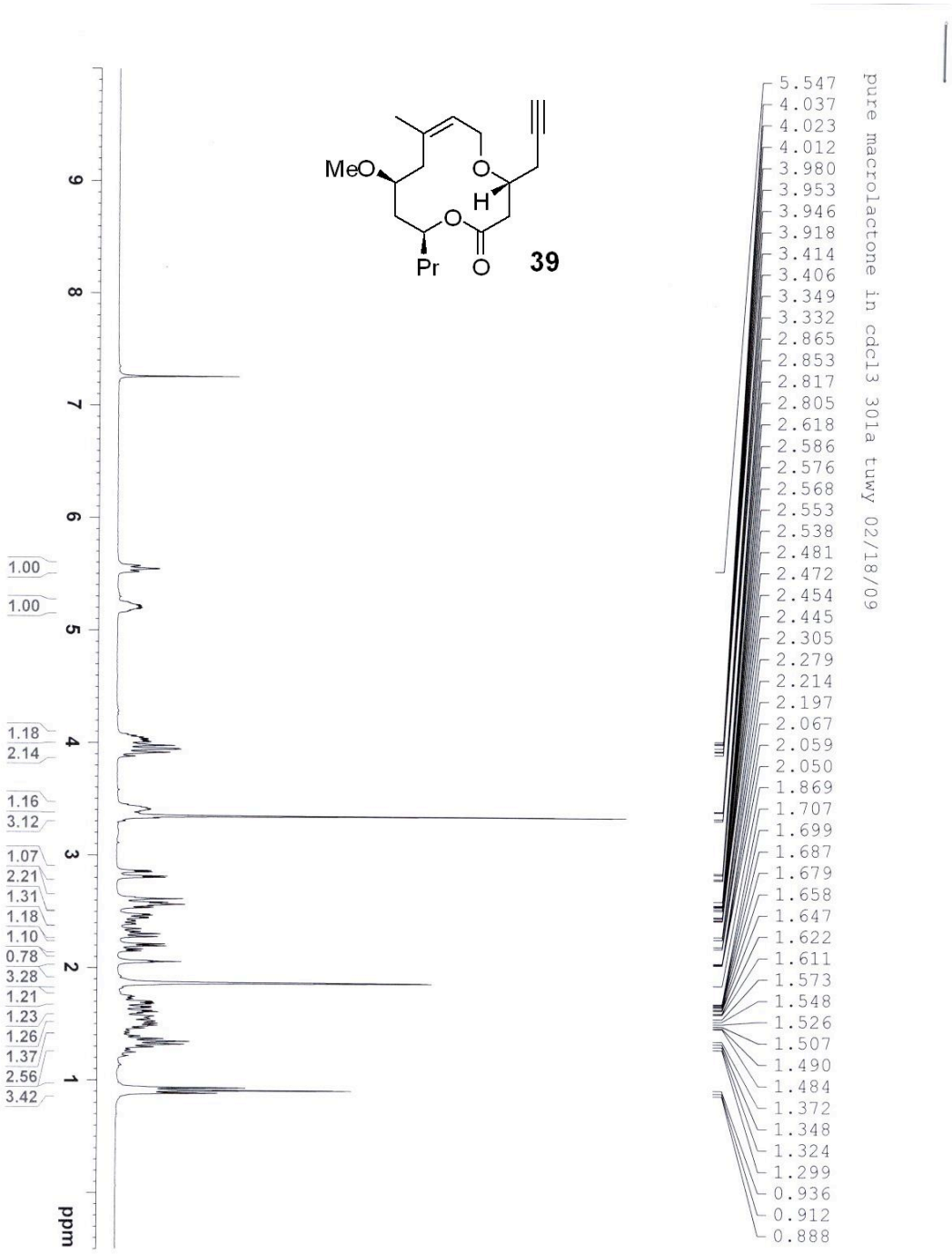

MeO
O
H
Pr
O
OEt
O
O
Et
38

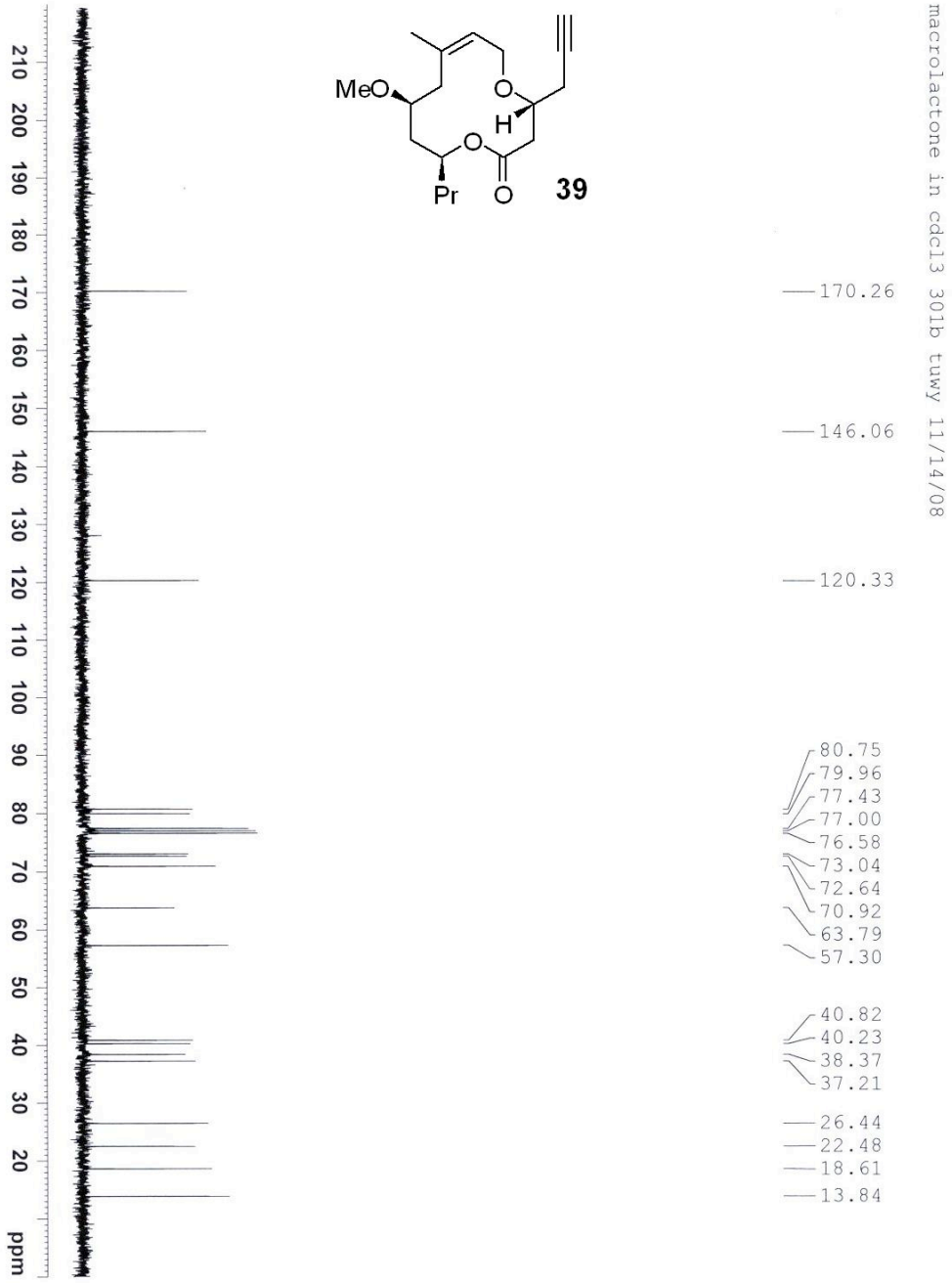
0.91
0.99
2.24
1.70
1.00
3.04
0.97
1.05
1.27
0.59
1.10
0.66
1.53
1.09
0.99
0.80
2.87
2.01
2.23
1.16
4.20
2.94
3.28
ppm

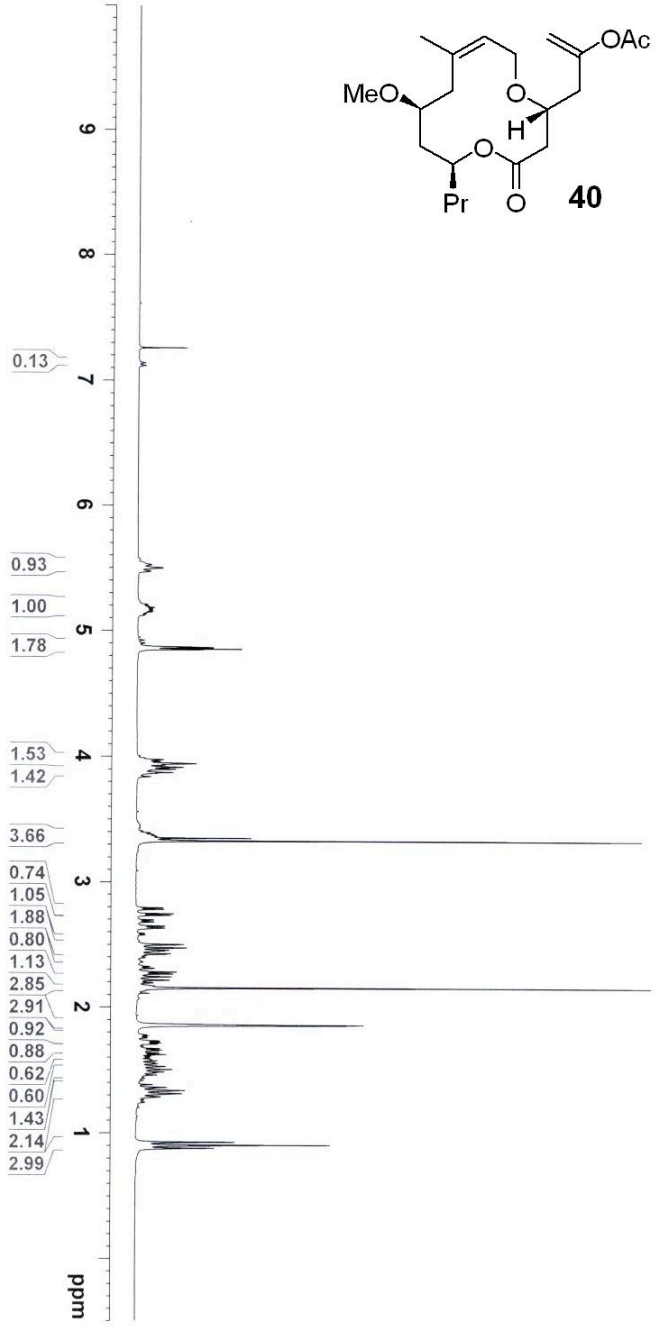

methylation product in cdcl3 301 tuwy 11/10/08
7.260
5.423
4.174
4.150
4.126
4.102
4.097
4.073
4.049
3.930
3.295
2.657
2.640
2.611
2.586
2.495
2.486
2.478
2.469
2.462
2.454
2.440
2.431
2.335
2.309
2.284
2.259
2.143
2.119
2.014
2.005
1.996
1.740
1.567
1.556
1.539
1.526
1.514
1.509
1.498
1.494
1.480
1.461
1.453
1.329
1.304
1.277
1.253
1.229
1.158
1.133
1.107
0.908
0.884
0.860

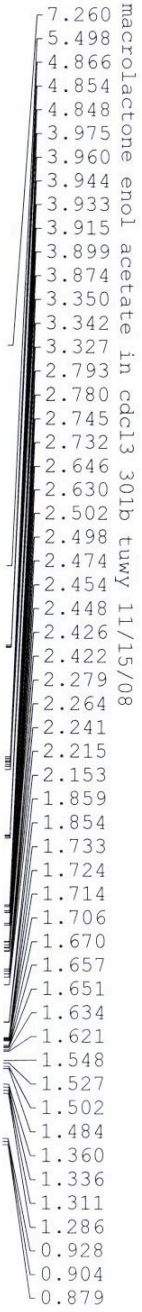

MeO
O
H
Pr
O
OEt
O
O
Et
38
methylation product in cdcl3 301 tuwy 11/10/08
174.04
171.15
136.80
124.15
80.23
77.43
77.00
76.58
76.37
73.67
70.87
70.59
66.10
60.48
57.48
39.59
39.37
37.25
36.80
27.89
24.06
23.81
18.44
14.17
13.94
9.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

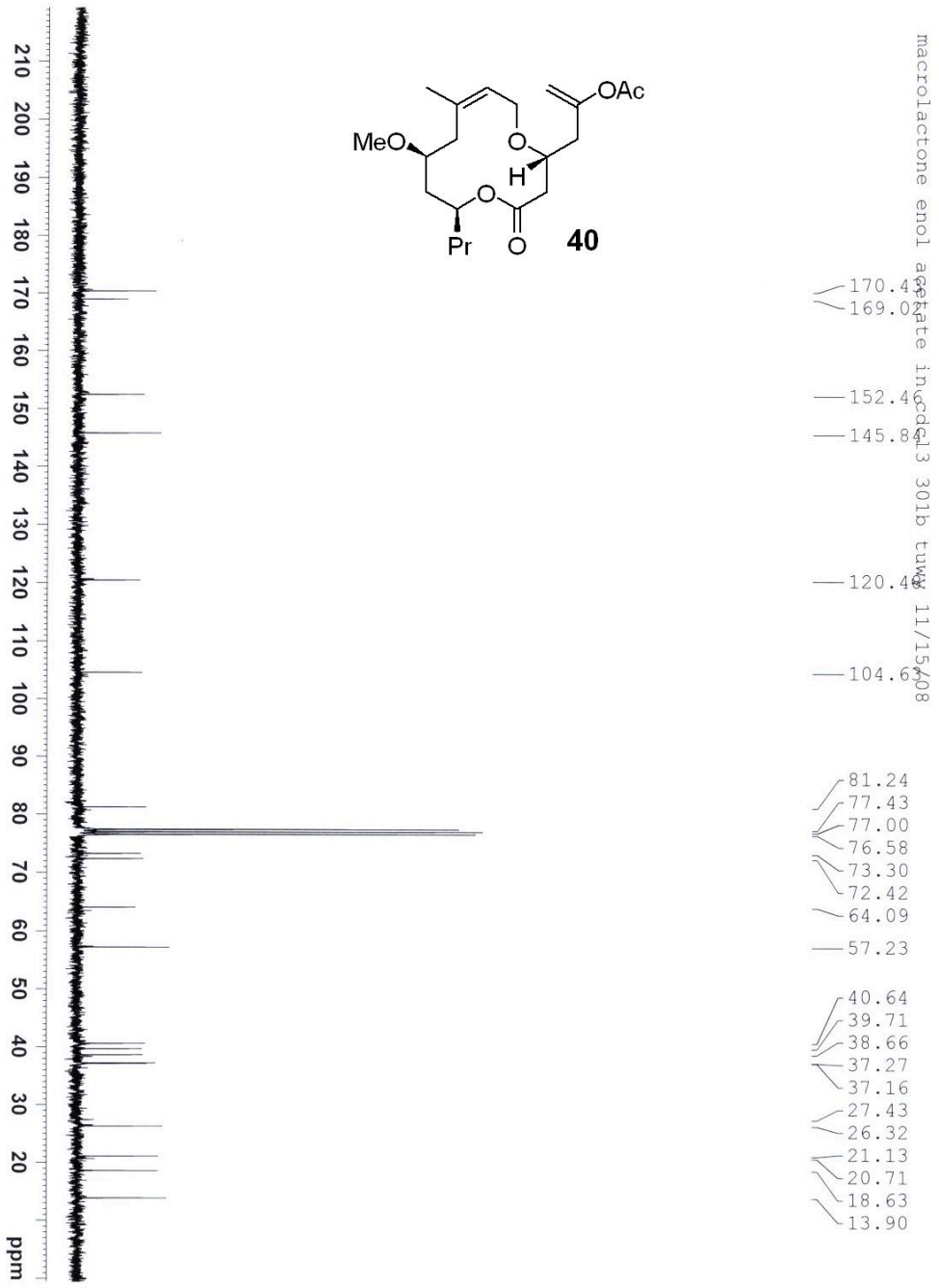

MeO
O
H
O
Pr
O
39
pure macrolactone in cdcl3 301a tuwy 02/18/09
5.547
4.037
4.023
4.012
3.980
3.953
3.946
3.918
3.414
3.406
3.349
3.332
2.865
2.853
2.817
2.805
2.618
2.586
2.576
2.568
2.553
2.538
2.481
2.472
2.454
2.445
2.305
2.279
2.214
2.197
2.067
2.059
2.050
1.869
1.707
1.699
1.687
1.679
1.658
1.647
1.622
1.611
1.573
1.548
1.526
1.507
1.490
1.484
1.372
1.348
1.324
1.299
0.936
0.912
0.888
1.00
1.00
1.18
2.14
1.16
3.12
1.07
2.21
1.31
1.18
1.10
0.78
3.28
1.21
1.23
1.26
1.37
2.56
3.42
ppm

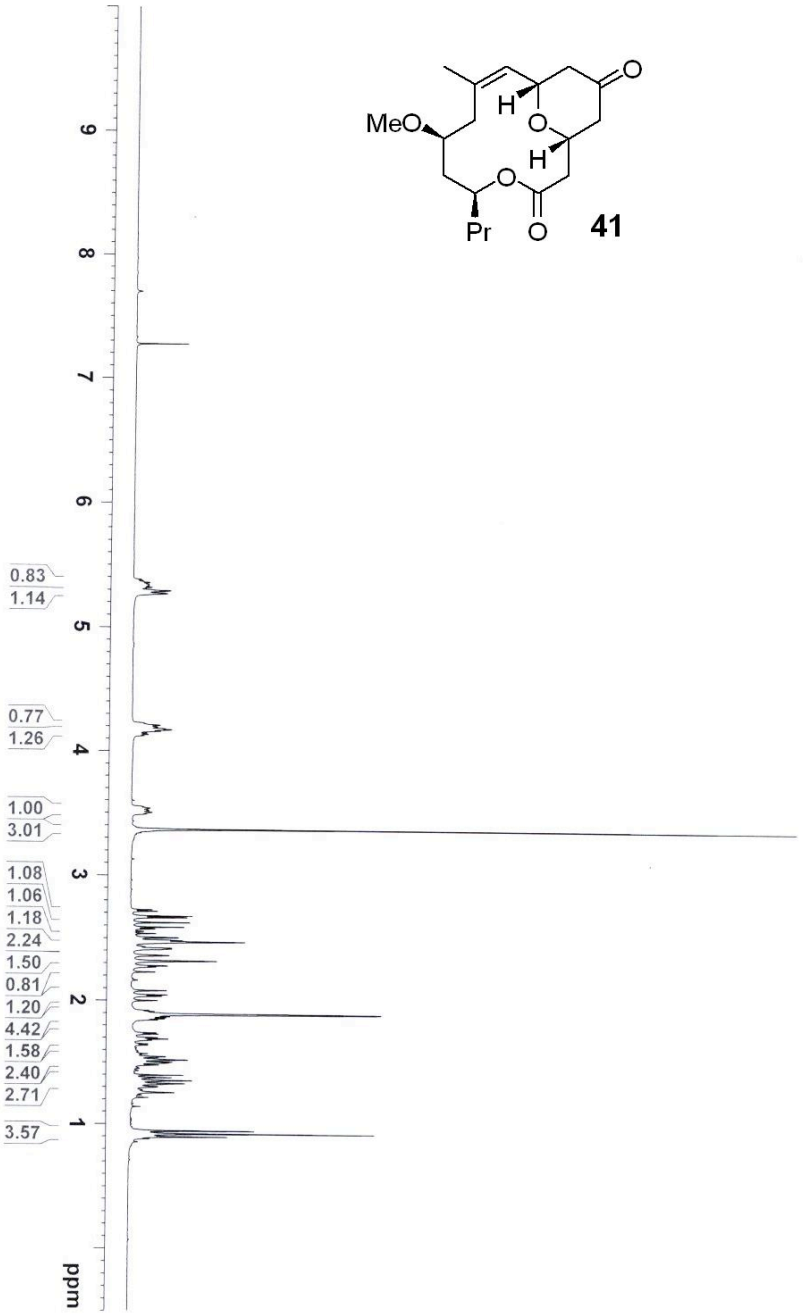

MeO
O
H
O
Pr
O
39
pure macrolactone in cdcl3 301a tuwy 02/18/09
5.547
4.037
4.023
4.012
3.980
3.953
3.946
3.918
3.414
3.406
3.349
3.332
2.865
2.853
2.817
2.805
2.618
2.586
2.576
2.568
2.553
2.538
2.481
2.472
2.454
2.445
2.305
2.279
2.214
2.197
2.067
2.059
2.050
1.869
1.707
1.699
1.687
1.679
1.658
1.647
1.622
1.611
1.573
1.548
1.526
1.507
1.490
1.484
1.372
1.348
1.324
1.299
0.936
0.912
0.888
1.00
1.00
1.18
2.14
1.16
3.12
1.07
2.21
1.31
1.18
1.10
0.78
3.28
1.21
1.23
1.26
1.37
2.56
3.42
ppm

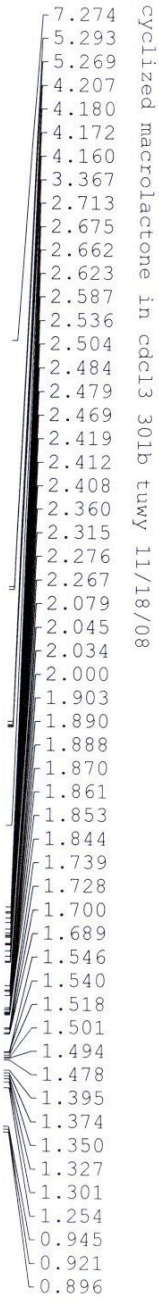

MeO
O
H
O
Pr
O
39
macrolactone in cdcl3 301b tuwy 11/14/08
170.26
146.06
120.33
80.75
79.96
77.43
77.00
76.58
73.04
72.64
70.92
63.79
57.30
40.82
40.23
38.37
37.21
26.44
22.48
18.61
13.84
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

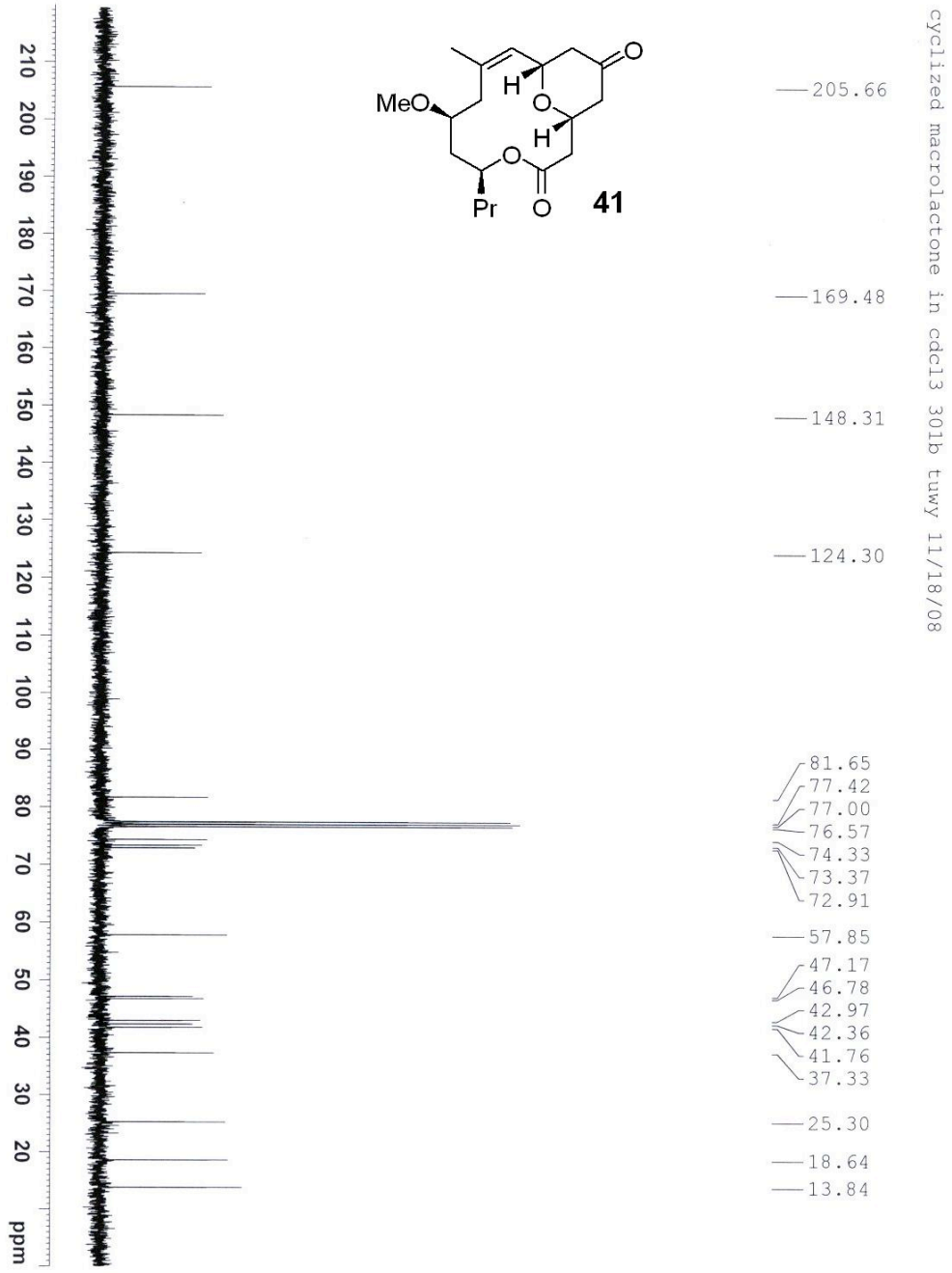

MeO
OAc
O
H
O
Pr
O
40
0.13
0.93
1.00
1.78
1.53
1.42
3.66
0.74
1.05
1.88
0.80
1.13
2.85
2.91
0.92
0.88
0.62
0.60
1.43
2.14
2.99
ppm
9
8
7
6
5
4
3
2
1

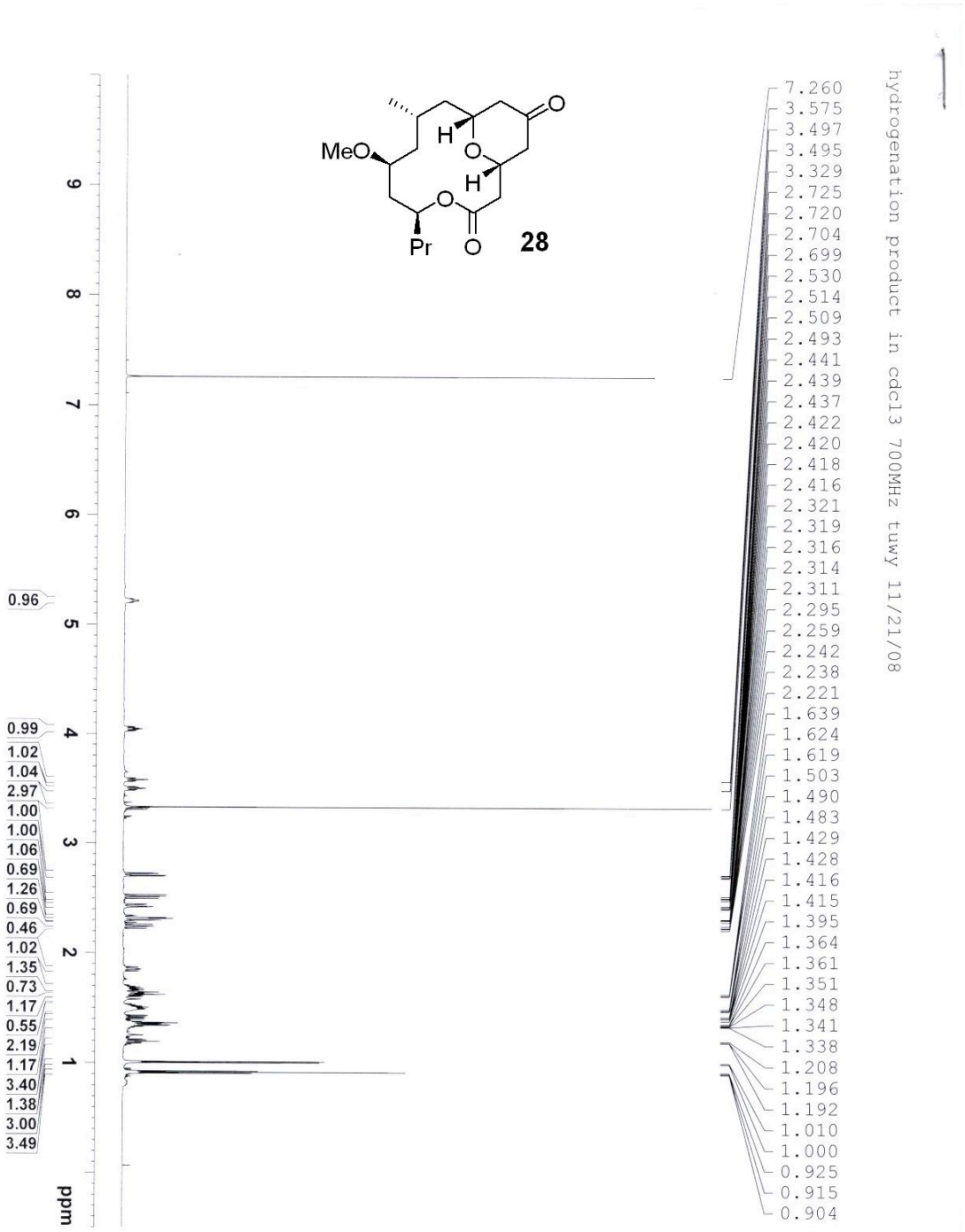

macrolactone enol acetate in cdcl3 301b tuwy 11/15/08
7.260
5.498
4.866
4.854
4.848
3.975
3.960
3.944
3.933
3.915
3.899
3.874
3.350
3.342
3.327
2.793
2.780
2.745
2.732
2.646
2.630
2.502
2.498
2.474
2.454
2.448
2.426
2.422
2.279
2.264
2.241
2.215
2.153
1.859
1.854
1.733
1.724
1.714
1.706
1.670
1.657
1.651
1.634
1.621
1.548
1.527
1.502
1.484
1.360
1.336
1.311
1.286
0.928
0.904
0.879

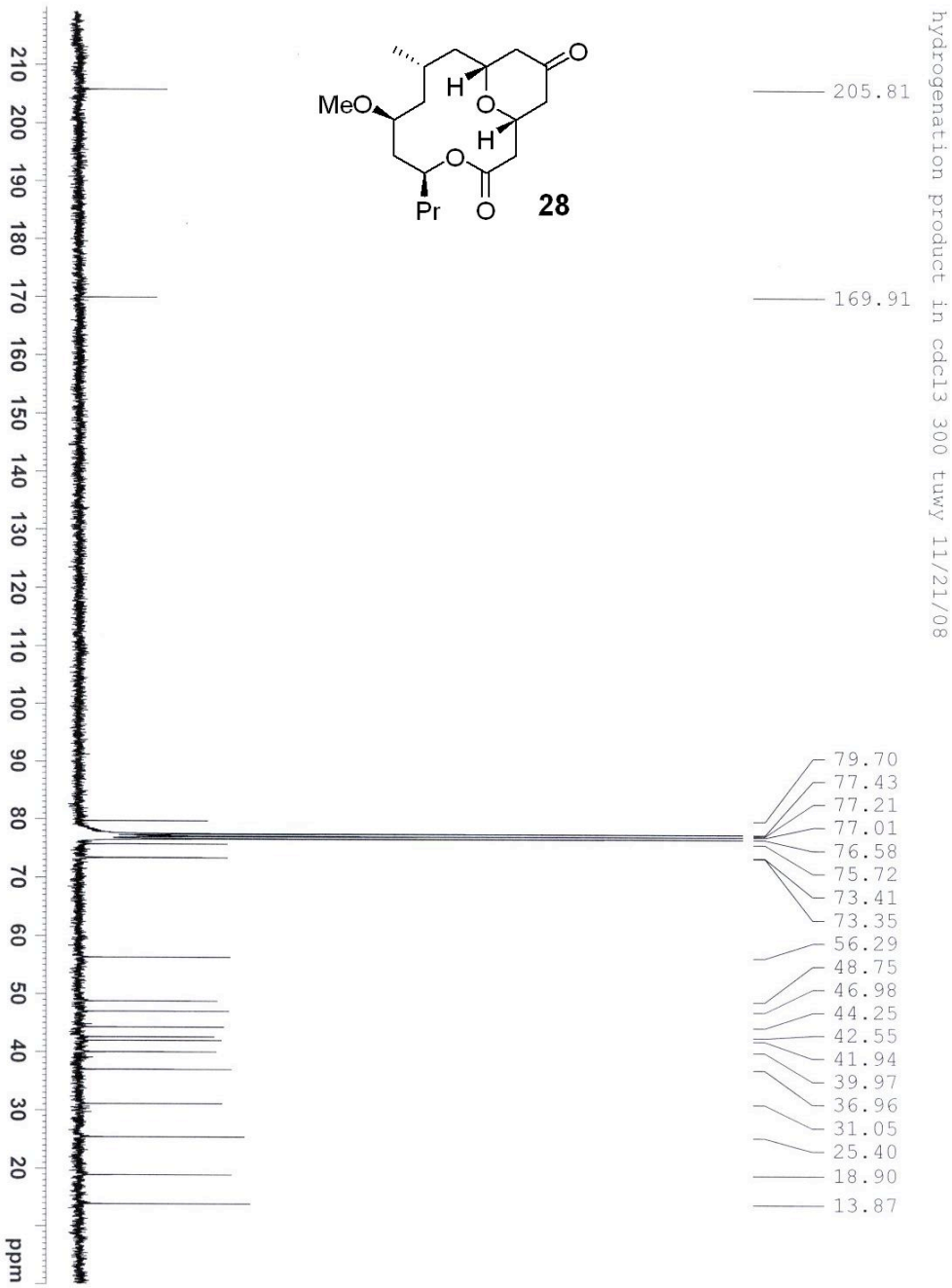

macrolactone enol acetate in cdcl3 301b tuww 11/15/08
170.42
169.02
152.42
145.84
120.44
104.67
81.24
77.43
77.00
76.58
73.30
72.42
64.09
57.23
40.64
39.71
38.66
37.27
37.16
27.43
26.32
21.13
20.71
18.63
13.90
MeO
OAc
O
H
O
Pr
O
40
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm


MeO
H
O
O
H
Pr
O
O
41
0.83
1.14
0.77
1.26
1.00
3.01
1.08
1.06
1.18
2.24
1.50
0.81
1.20
4.42
1.58
2.40
2.71
3.57
ppm
9
8
7
6
5
4
3
2
1


cyclized macrolactone in cdcl3 301b tuwy 11/18/08
7.274
5.293
5.269
4.207
4.180
4.172
4.160
3.367
2.713
2.675
2.662
2.623
2.587
2.536
2.504
2.484
2.479
2.469
2.419
2.412
2.408
2.360
2.315
2.276
2.267
2.079
2.045
2.034
2.000
1.903
1.890
1.888
1.870
1.861
1.853
1.844
1.739
1.728
1.700
1.689
1.546
1.540
1.518
1.501
1.494
1.478
1.395
1.374
1.350
1.327
1.301
1.254
0.945
0.921
0.896


cyclized macrolactone in cdcl3 301b tuwy 11/18/08
MeO
H
O
H
O
Pr
O
O
41
205.66
169.48
148.31
124.30
81.65
77.42
77.00
76.57
74.33
73.37
72.91
57.85
47.17
46.78
42.97
42.36
41.76
37.33
25.30
18.64
13.84
ppm


MeO
H
O
H
O
O
Pr
O
28
hydrogenation product in cdcl3 700MHz tuwy 11/21/08
7.260
3.575
3.497
3.495
3.329
2.725
2.720
2.704
2.699
2.530
2.514
2.509
2.493
2.441
2.439
2.437
2.422
2.420
2.418
2.416
2.321
2.319
2.316
2.314
2.311
2.295
2.259
2.242
2.238
2.221
1.639
1.624
1.619
1.503
1.490
1.483
1.429
1.428
1.416
1.415
1.395
1.364
1.361
1.351
1.348
1.341
1.338
1.208
1.196
1.192
1.010
1.000
0.925
0.915
0.904
0.96
0.99
1.02
1.04
2.97
1.00
1.00
1.06
0.69
1.26
0.69
0.46
1.02
1.35
0.73
1.17
0.55
2.19
1.17
3.40
1.38
3.00
3.49
ppm


hydrogenation product in cdcl3 300 tuwy 11/21/08
205.81
169.91
79.70
77.43
77.21
77.01
76.58
75.72
73.41
73.35
56.29
48.75
46.98
44.25
42.55
41.94
39.97
36.96
31.05
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