Supporting Information to Accompany " Pyran Annulation: Asymmetric Synthesis of 2,6-Disubstituted-4-Methylene Tetrahydropyrans"

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Includes Experimental Details, Spectral and Characterization Data, Copies of NMR Spectra

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General Procedures. All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware. Solvents were purified according to the guidelines in Purification of Common Laboratory Chemicals (Perrin, Armarego, and Perrin, Pergamon: Oxford, 1966). Reagent grade benzyloxyacetaldehyde, propionaldehyde, trimethylorthoformate, and trimethylsilyl trifluoromethanesulfonate were purchased from Aldrich and used without further purification. Technical grade hydrocinnamaldehyde was purchased from Aldrich and used directly, accounting for its 90% purity. Furaldehyde was purchased from Aldrich and distilled prior to use. Yields were calculated for material judged homogeneous by TLC and NMR. TLC was performed on EM Science silica gel 60 F254 plates, visualizing with a 254 nm UV lamp and staining with an ethanol solution of 12-molybdo-phosphoric acid. Flash column chromatography was performed with Silicycle UltraPure 230-400 mesh silica gel, slurry packed in glass columns. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Unity-500 (500 MHz) spectrometer. The chemical shifts are reported on the δ scale (ppm) downfield from tetramethylsilane. The abbreviations s, d, t, q, m, ABq, etc. stand for the resonance multiplicities singlet, doublet, triplet, quartet, multiplet, AB quartet, etc. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 125 MHz on a Unity-500 spectrometer. The chemical shifts are reported in ppm relative to the center line of the triplet at 77.0 ppm for $CDCl_3$. Infrared (IR) spectra were measured with a Mattson FTIR 3000 infrared spectrophotometer. Optical rotations were determined with a PerkinElmer 343 polarimeter. Mass spectra were obtained with a Finnigan MAT 95 high-resolution gas chromatograph/mass spectrometer with a Finnigan MAT ICIS II operating system. Elemental analysis were performed by Atlantic Microlabs, Inc., Norcross, GA. HPLC analyses were carried out on a 25 cm CHIRACEL OD-H column, using isopropanol in hexanes as the mobile phase and a refractive index detector.

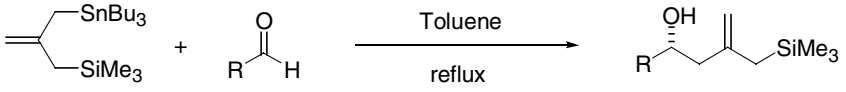
Representative Experimental Procedure for the Asymmetric Synthesis of β-Hydroxy Allylsilanes

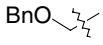
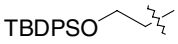
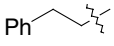
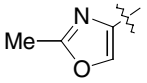
Preparation of (1*R*)-3-(2,2-dimethyl-2-silapropyl)-1-(2-methyl(1,3-oxazol-4-yl))but-3-en-1-ol (**2d**): A mixture of (*R*)-(+)-BINOL (81 mg, 0.28 mmol), 1M $Ti(O^iPr)_4$ in CH_2Cl_2 (0.14 mL, 0.14 mmol), oven-dried powdered 4-Å molecular sieves (0.56 g), and 0.1 M trifluoroacetic acid in CH_2Cl_2 (43 μL, 0.0043 mmol), in CH_2Cl_2 (9.0 mL) was heated at reflux for 1h. The red-brown mixture was cooled to ambient temperature and 2-methyl-1,3-oxazole-4-carbaldehyde (0.158 g, 1.42 mmol) was added. After stirring for 10 min the mixture was cooled to –78 °C, and stannane **1** (1.20 g, 2.84 mmol) was added. The mixture was stirred for 10 min and then placed in a –20 °C freezer for 72 h. Saturated aqueous $NaHCO_3$ solution (3.0 mL) was added, and the mixture was stirred for 1 h before being transferred to a separatory funnel. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined and washed with brine (20 mL), dried over $MgSO_4$, and then filtered through a plug of Celite. After concentration under reduced pressure, the crude material was purified by flash chromatography, eluting with 35% ethyl acetate in hexanes to afford (1*R*)-3-(2,2-dimethyl-2-silapropyl)-1-(2-methyl(1,3-oxazol-4-yl))but-3-en-1-ol (**2d**) (0.313 g, 92%) as an oily solid. The enantiomeric purity was determined to be 96% *via* chiral HPLC. Note: in the one instance (entry 2e) where baseline resolution of the enantiomers could not be achieved with HPLC, the Mosher ester derivatives were synthesized and their ^{19}F NMR spectra were analyzed to obtain the enantiomeric excess.

Representative Experimental Procedure for the Racemic Synthesis of β-Hydroxy Allylsilanes

Preparation of 4-(2,2-dimethyl-2-silapropyl)-1-(phenylmethoxy)pent-4-en-2-ol (**±2a**): Stannane **1** (0.335 g, 0.803 mmol) and benzyloxyacetaldehyde (0.107 g, 0.712 mmol) were combined with toluene (0.7 mL) and heated at reflux for 3 h. The toluene was evaporated and the crude material was purified by flash chromatography, eluting with 20% ethyl acetate in hexanes to afford 4-(2,2-dimethyl-2-silapropyl)-1-(phenylmethoxy)pent-4-en-2-ol (**±2a**) as a clear colorless oil (0.187 g, 95%). Analysis by HPLC using a 25 cm Chiracel OD-H column gave retention times of 20.4 min and 19.0 min for the (*R*) and (*S*) enantiomers respectively, using 3% 2-propanol in hexanes. Retention times for the other cases are summarized in the table below.

Table of Results for the Racemic Synthesis of β-Hydroxy Allylsilanes and Retention Times for *R* and *S* Enantiomers



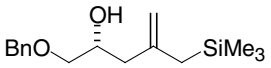
R	Yield (%)	R_t (*R*) (min)	R_t (*S*) (min)	Eluent (% ^{i}PrOH/Hexane)
	95	20.4	19.0	3
	76	12.0	10.5	1
	82	22.6	12.0	3
	99	17.4	21.0	3
	90	80.59 ppm[a]	80.38 ppm[a]	—

a) ^{19}F Chemical shift of trifluoromethyl fluorines of Mosher ester derivatives relative to TFA @ 76.55 ppm.

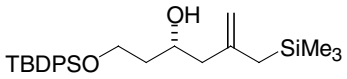
Representative Experimental Procedure for the Preparation of 2,6-*cis*-Disubstituted 4-Methylenetetrahydropyrans *via* TMSOTf Promoted Cyclization of β-Hydroxy Allylsilanes

Preparation of 1-(2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl](3,5,6-trihdro-2H-pyran-2-yl)}ethoxy)-2,2-dimethyl-1,1-diphenyl-1silapropane (**3c**): To a solution of β-hydroxy allylsilane **2a** (19.5 mg, 0.0700 mmol) in diethyl ether (2.00 mL), 3-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)propanal (44.0 mg, 0.140 mmol) was added, and the mixture was cooled to –78 °C. TMSOTf (23.3 mg, 0.105 mmol) was added and the mixture was stirred for 20 min. Aqueous

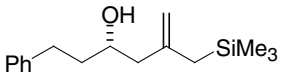
NaOH solution (1 mL of 1 M) was added and the mixture was brought to rt, then transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The organic layers were combined and washed with brine (5 mL), then dried over $MgSO_4$. The solvents were evaporated under reduced pressure and the crude material was purified by flash chromatography, eluting with 10% ethyl acetate in hexanes to afford 1-(2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl](3,5,6-trihdro-2H-pyran-2-yl)}ethoxy)-2,2-dimethyl-1,1-diphenyl-1silapropane (**3c**) (34.0 mg, 97%) as a clear colorless oil.



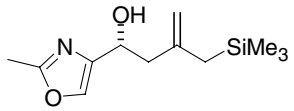
Analytical data for (2*R*)-4(2,2-dimethyl-2-silapropyl)-1-(phenylmethoxy)pent-4-en-2-ol (**2a**): R*f* 0.21 (20% EtOAc in Hexanes); $[\alpha]_D^{20}$ –8.33° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.27-7.40 (m, 5 H), 4.70 (m, 1 H), 4.66 (m, 1 H), 4.58 (s, 2H), 4.00 (dddd, *J* = 10.8, 7.0, 3.7, 3.7 Hz, 1H), 3.54 (dd, J = 9.5, 3.7 Hz, 1H), 3.42 (dd, J = 9.4, 7.0 Hz, 1 H), 2.46 (br s, 1H), 2.17 (d, J = 6.6 Hz, 2 H), 1.58 (ABq, J = 13.4 Hz, ΔAB = 16.8 Hz, 2 H), 0.05 (s, 9H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 144.0, 138.2, 128.6, 127.9, 127.9, 110.4, 74.3, 73.5, 68.5, 42.5, 26.8, -1.2; IR (neat) cm^{-1} 3459 (br), 3069, 3031, 2953, 2897, 2862, 1632; Anal. calcd for $C_{16}H_{26}O_2Si$: C, 69.01; H, 9.41. Found: C, 68.75; H, 9.44.



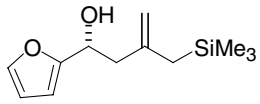
Analytical data for (2*R*)-1-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)-5-(2,2-dimethyl-2-silapropyl)hex-5-en-3-ol (**2b**): R*f* 0.22 (10% EtOAc in Hexanes); $[\alpha]_D^{20}$ –4.02° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.70-7.73 (m, 4H), 7.40-7.48 (m, 6H), 4.70 (m, 1H), 4.68 (m, 1H), 4.07 (dddd, J = 6.4, 5.9, 5.9, 5.4 Hz, 1H), 3.90 (ddd, J = 10.3, 5.4, 5.4 Hz, 1H), 3.85-3.89 (m, 1H), 2.98 (m, 1H), 2.21 (ddd, J = 13.7, 7.8, 1.0 Hz, 1H), 2.15 (ddd, J = 13.7, 5.4, 1.0 Hz, 1H), 1.76 (d, J = 5.9 Hz, 1H), 1.74 (dd, J = 4.9, 2.0 Hz, 1H), 1.59 (ABq, J = 13.2 Hz, ΔAB = 20.0 Hz, 2H), 1.09 (s, 9H), 0.07 (s, 9H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 144.7, 135.8, 135.8, 133.5, 133.5, 130.0, 128.0, 110.3, 68.7, 63.0, 46.7, 38.7, 27.1, 26.9, 19.3, -1.1; IR (neat) cm^{-1} 3506 (br), 3071, 3051, 2954, 2932, 1632; HR CI-MS for $C_{26}H_{38}OSi_2$ (M+1-18) requires m/z 423.25395. Found 423.25378; Anal. calcd for $C_{26}H_{39}O_2Si_2$: C, 70.85; H, 9.15. Found: C, 70.79; H, 9.06.



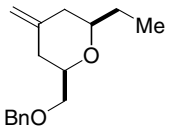
Analytical data for (3*S*)-5-(2,2-dimethyl-2-silapropyl)-1-phenylhex-5-ene-3-ol (**2c**): R*f* 0.46 (20% EtOAc in Hexanes); $[\alpha]_D^{20}$ –37.17° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.19-7.32 (m, 5 H), 4.71 (m, 2 H), 3.75 (br s, 1 H), 2.81-2.89 (m, 1 H), 2.68-2.75 (m, 1 H), 2.19 (dd, J = 13.7, 2.4 Hz, 1 H), 2.07 (dd, J = 13.7, 9.5 Hz, 1 H), 1.92 (s, 1 H), 1.75-1.86 (m, 2H), 1.54 (ABq, J = 13.7 Hz, ΔAB = 39.1 Hz, 2H), 0.04 (s, 9 H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 144.8, 142.4, 128.7, 128.6, 126.0, 110.7, 68.1, 46.9, 38.9, 32.4, 26.9, -1.1; IR (neat) cm^{-1} 3403 (br), 3075, 3023, 2943, 1632; Anal. calcd for $C_{16}H_{26}OSi$: C, 73.22; H, 9.98. Found: C, 73.07; H, 9.98.



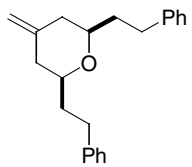
Analytical data for (1*R*)-3-(2,2-dimethyl-2-silapropyl)-1-(2-methyl(1,3-oxazol-4-yl))but-3-en-1-ol (**2d**): R*f* 0.13 (35% EtOAc in Hexanes); $[\alpha]_D^{20}$ +9.22° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.45 (s, 1H), 4.73-4.77 (m, 3H), 2.56 (m, 1H), 2.50 (dd, J = 13.7, 3.9 Hz, 1H), 2.44 (s, 3H), 2.40 (dd, J = 13.7, 9.3 Hz, 1H), 1.58 (ABq, J = 13.4 Hz, ΔAB = 25.6 Hz, 2H), 0.04 (s, 9H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 161.9, 144.1, 143.2, 134.3, 111.3, 64.9, 45.9, 26.7, 14.2, -1.2; IR (neat) cm^{-1} 3358 (br), 3074, 2954, 1634; Anal. calcd for $C_{12}H_{21}NO_2Si$: C, 60.21; H, 8.84. Found: C, 60.07; H, 8.92.



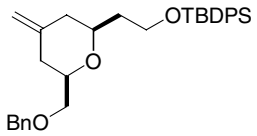
Analytical data for (1*R*)-3-(2,2-dimethyl-2-silapropyl)-1-(2-furyl)but-3-en-1-ol (**2e**): R*f* 0.26 (20% EtOAc in Hexanes); $[\alpha]_D^{20}$ +11.60° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.38 (dd, J = 2.0, 1.0 Hz, 1H), 6.34 (dd, J = 3.4, 2.0 Hz, 1H), 6.27 (d, J = 3.4 Hz, 1H), 4.83 (ddd, J = 6.8, 6.8, 2.4 Hz, 1H), 4.77 (m, 1H), 4.73 (m, 1H), 2.51 (dd, J = 6.8, 1.0 Hz, 2H), 2.27 (br s, 1H), 1.55 (ABq, J = 13.7 Hz, ΔAB = 23.9 Hz, 2H) 0.05 (s, 9H).125-MHz ^{13}C NMR ($CDCl_3$) δ 156.3, 143.7, 142.1, 111.3, 110.4, 106.2, 65.5, 44.8, 26.7, -1.2; IR (neat) cm^{-1} 3404 (br), 3075, 2954, 2897, 1634; HR CI-MS for $C_{12}H_{19}OSi$ (M+1-18) requires m/z 207.12052. Found 207.12089.



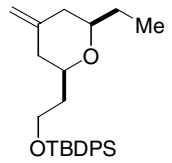
Analytical data for ((2*R*,6*R*)-6-ethyl-4-methylene(3,5,6-trihydro-2H-pyran-2-yl))(phenylmethoxy)methane (**3a**): R*f* 0.58 (20% EtOAc in Hexanes); $[\alpha]_D^{20}$ +3.24° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.38-7.27 (m, 5H), 4.75 (m, 2H), 4.61 (ABq, J = 12.2 Hz, ΔAB = 22.5 Hz, 2H), 3.47-3.59 (m, 3H), 3.22 (dddd, J = 13.2, 6.4, 6.4, 2.0 Hz, 1H), 2.23-2.27 (m, 2H), 2.00-2.05 (m, 1H), 1.90-1.95 (m, 1H) 1.66 (dq, J = 21.0, 7.3, Hz, 1H), 1.52 (dq, J = 21.0, 7.3 Hz, 1H), 0.97 (t, J = 7.3 Hz, 3H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 144.7, 138.6, 128.5, 127.9, 127.7, 108.8, 80.1, 77.7, 73.6, 73.5, 40.4, 37.7, 29.3, 10.2; IR (neat) cm^{-1} 3069, 3030, 2962, 2937, 2881, 2856, 1652; Anal. calcd for $C_{16}H_{22}O$: C, 78.01; H, 9.00. Found: C, 78.26; H, 9.05.



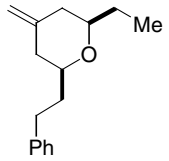
Analytical data for (6*R*,2*S*)-2,6-bis(2-phenylethyl)-4-methylene-3,5,6-trihydro-2H-pyran (**3b**): R*f* 0.47 (10% EtOAc in Hexanes); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.30-7.33 (m, 4H), 7.20-7.27 (m, 6H), 4.70 (s, 2H), 3.23-3.29 (m, 2H), 2.91 (ddd, J = 14.2, 9.8, 5.4, Hz, 2H), 2.77 (ddd, J = 14.2, 9.3, 7.3 Hz, 2H), 2.22 (dd, J = 13.7, 1.5 Hz, 2H), 1.92-2.03 (m, 4H), 1.80 (dddd, J = 13.2, 10.7, 6.8, 3.9 Hz, 2H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 145.1, 142.5, 128.7, 128.5, 125.9, 108.6, 77.5, 41.2, 38.2, 32.1; IR (neat) cm^{-1} 3064, 3026, 2940, 2855, 1651; HR CI-MS for $C_{22}H_{27}O$ (M+1) requires m/z 307.20619. Found 307.2044; Anal. calcd for $C_{22}H_{26}O$: C, 86.23; H, 8.55. Found: C, 85.99; H, 8.65.



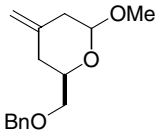
Analytical data for 1-(2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl](3,5,6-trihdro-2H-pyran-2-yl)}ethoxy)-2,2-dimethyl-1,1-diphenyl-1silapropane (**3c**): R*f* 0.26 (10% EtOAc in Hexanes); $[\alpha]_D^{20}$ +3.18° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.67-7.69 (m, 4H), 7.27-7.45 (m, 11H), 4.75-4.77 (m 2H), 4.59 (s, 2H), 3.86 (ddd, J = 10.3, 7.8, 5.4 Hz, 1H), 3.78 (ddd, J = 10.3, 5.8, 5.8 Hz, 1H), 3.45-3.59 (m, 4H), 2.23-2.29 (m, 1H), 1.94-2.01 (m, 1H), 1.88 (dddd, J = 13.7, 7.8, 5.4, 5.4 Hz, 1H), 1.77 (dddd, J = 13.7, 7.8, 5.9, 5.9 Hz, 1H), 1.06 (s, 9H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 144.6, 138.6, 135.8, 134.2, 134.1, 129.8, 129.8, 128.6, 127.9, 127.8, 127.8, 127.8, 127.8, 109.0, 77.7, 75.7, 73.6, 73.4, 60.5, 41.1, 39.3, 37.7, 27.1, 19.5; IR (neat) cm^{-1} 3070, 2955, 2890, 2856, 1651; Anal. calcd for $C_{32}H_{40}O_2Si$,: C, 76.75; H, 8.05. Found: C, 76.69; H, 8.09.



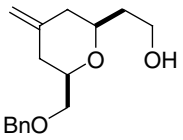
Analytical data for 1-(2-((2*R*,6*R*)-6-ethyl-4-methylene(3,5,6-trihydro-2H-pyran-2-yl))ethoxy)-2,2-dimethyl-1,1-diphenyl-1-silapropane (**3d**): R*f* 0.54 (10% EtOAc in Hexanes); $[\alpha]_D^{20}$ –3.81° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.67-7.70 (m, 4H), 7.37-7.44 (m, 6H), 4.72 (s, 2H), 3.85-3.90 (m, 1H), 3.77 (ddd, J = 10.6, 5.4, 5.4, Hz, 1H), 3.50-3.52 (m, 1H), 3.12-3.18 (m, 1H), 2.20-2.26 (m, 2H), 1.85-1.96 (m, 2H), 1.73-1.85 (m, 2H), 1.57 (dq, J = 21.0, 7.3 Hz, 1H), 1.47 (dq, J = 21.0,7.3 Hz, 1H), 1.06 (s, 9H), 0.94 (t, J= 7.3 Hz, 3H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 145.5, 135.8, 135.8, 134.3, 134.2, 129.7, 129.7, 127.8, 127.8, 108.3, 80.0, 75.2, 60.5, 41.3, 40.8, 39.5, 29.5, 27.1, 19.5, 10.2; IR (neat) cm^{-1} 3071, 2960, 2936, 2857, 1652; HR CI-MS for $C_{26}H_{36}O_2Si$ (M+1) requires m/z 409.25628. Found 409.25604.



Analytical data for (6*R*,2*S*)-6-ethyl-4-methylene-2-(2-phenylethyl)-3,5,6-trihydro-2H-pyran (**3e**): R*f* 0.53 (10% EtOAc in Hexanes); $[\alpha]_D^{20}$ –24.56° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.17-7.33 (m, 5H), 4.68-4.72 (m, 2H), 3.11-3.27 (m, 2H), 2.68-2.90 (m, 2H), 2.16-2.28 (m, 2H), 1.86-2.02 (m, 3H), 1.46-1.81 (m, 3H), 1.03 (t, J = 7.5 Hz, 3H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 145.4, 142.5, 128.8, 128.5, 125.9, 108.4, 80.0, 77.3, 41.3, 40.9, 38.2, 32.0, 29.6, 10.5; IR (neat) cm^{-1} 3069, 3026, 2936, 2887, 2846, 1651; HR CI-MS for $C_{16}H_{23}O$ (M+1) requires m/z 231.17489. Found 231.17398.



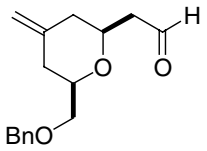
Analytical data for ((2*R*)-6-methoxy-4-methylene(3,5,6-trihydro-2H-pyran-2-yl))(phenylmethoxy)methane (**4**): R*f* 0.31, 0.38; spectral data for higher R*f* isomer: (20% EtOAc in Hexanes); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.27–7.37 (m, 5H), 4.83 (m, 2H), 4.61 (ABq, J = 11.7 Hz, ΔAB = 20.0 Hz , 2H), 4.31 (dd, J = 9.3, 2.4 Hz, 1H), 3.55-3.65 (m, 3H), 3.53 (s, 3H), 2.46 (d, J = 13.2, 1H), 2.26 (d, J = 13.7 Hz, 1H), 2.16 (dd, J = 12.2, 10.5 Hz, 1H), 2.03 (dd, J = 13.7, 11.7, 1H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 141.9, 138.5, 128.6, 127.9, 127.8, 111.4, 103.2, 74.8, 73.7, 73.1, 56.5, 40.9, 37.0; IR (neat) cm^{-1} 3072, 3030, 2955, 2901, 2859, 2834, 1652; Anal. calcd for $C_{15}H_{20}O_3$,: C, 72.55; H, 8.12. Found: C, 72.56; H, 8.20.



Preparation of 2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl]-3,5,6-trihydro-2H-pyran-2-yl}ethan-1-ol: To a solution of 1-(2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl](3,5,6-trihdro-2H-pyran-2-yl)}ethoxy)-2,2-dimethyl-1,1-diphenyl-1silapropane (**3c**, 0.180 g, 0.360 mmol) in THF (25 mL) was added a solution of tetrabutylammonium fluoride in THF (1 M, 0.44 mL, 0.44 mmol) dropwise at rt, and the pale-yellow solution was stirred 2 h. Saturated aqueous $NaHCO_3$ solution (5 mL) was added, the mixture was diluted with H_2O (5 mL), and the THF was removed *in vacuo*. The aqueous residue was diluted with methylene chloride, the layers were separated, and the aqueous phase was extracted with methylene chloride (3 × 30 mL). The combined organic layers were washed with brine (30 mL), then dried over Na_2SO_4 and $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash chromatography (27 × 3.5 cm silica gel) with gradient elution (20% ethyl acetate in hexanes to

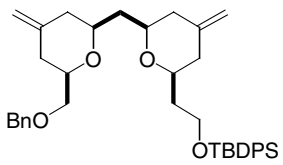
35% ethyl acetate in hexanes) to afford 2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl]-3,5,6-trihydro-2H-pyran-2-yl}ethan-1-ol as a clear, colorless oil (79.4 mg, 84%).

R*f* 0.16 (35% EtOAc in Hexanes); $[\alpha]_D^{20}$ –2.06° (c 0.1, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.26-7.36 (m, 5H), 4.75 (s, 2H), 4.55 (ABq, J = 12.2 Hz, ΔAB = 15.1 Hz , 2H), 3.78-3.81 (m, 2H), 3.53-3.61 (m, 2H), 3.50 (dd, J = 10.3, 6.3 Hz, 1H), 3.45 (dd, J = 10.3, 4.2 Hz, 1H), 3.03 (br s, 1H), 2.18-2.23 (m, 2H), 1.98-2.08 (m, 2H), 1.79-1.87 (m, 1H), 1.69-1.74 (m, 1H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 143.5, 138.2, 128.6, 127.9, 127.8, 109.6, 79.2, 77.6, 73.6, 73.3, 61.6, 40.8, 38.0, 37.1; IR (neat) cm^{-1} 3421 (br), 3069, 3030, 2940, 2888, 2862, 1651; HR CI-MS for $C_{16}H_{23}O_3$ (M+1) requires m/z 263.16472. Found 263.16372.



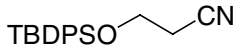
Preparation of 2-{(6*R*, 2*S*)-4-methylene-6-[(phenylmethoxy)methyl]-3,5,6-trihydro-2H-pyran-2-yl}ethanal (**5**): To a solution of 2-{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl]-3,5,6-trihydro-2H-pyran-2-yl}ethan-1-ol (44 mg, 0.17 mmol) in methylene chloride (1.0 mL) were added 4 Å molecular sieves (84 mg), 4-methylmorpholine-N-oxide (30 mg, 0.25 mmol), and then tetrapropylammonium perruthenate (3.5 mg, 0.010 mmol). The initial green color quickly turned black. Thin-layer chromatography analysis at 15 min. indicated complete reaction. The reaction was quenched by passing it through a column of silica gel (2 × 12 cm) equilibrated with methylene chloride. The column was washed with methylene chloride (100 mL), then with ethyl acetate (150 mL). The desired product (33 mg) was contained within the ethyl acetate fraction. The crude aldehyde is typically quite pure and used without further purification; however, in this case it was purified by flash chromatography (2 × 15 cm silica gel, 35% ethyl acetate in hexanes) to give 2-{(6*R*, 2*S*)-4-methylene-6-[(phenylmethoxy)methyl]-3,5,6-trihydro-2H-pyran-2-yl}ethanal (**5**) (29 mg, 66%).

R*f* 0.40 (35% EtOAc in Hexanes); $[\alpha]_D^{20}$ –16.75° (c 0.04, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 9.81 (app t, J = 2.2 Hz, 1H), 7.26-7.36 (m, 5H), 4.77-4.80 (m, 2H), 4.57 (s, 2H), 3.86 (dddd, J = 12.2, 7.3, 4.9, 2.5 Hz, 1H), 3.58 (dddd, J = 12.2, 5.9, 4.4, 2.4 Hz, 1H), 3.52 (dd, J = 10.3, 5.4 Hz, 1H), 3.48 (dd, J = 10.3, 3.9 Hz, 1H), 2.70 (ddd, J = 16.6, 7.8, 2.4 Hz, 1H), 2.54 (ddd, J = 16.6, 4.9, 2.0 Hz, 1H), 2.22-2.30 (m, 2H), 1.99-2.09 (m, 2H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 201.2, 143.1, 138.4, 128.6, 127.9, 127.8, 110.1, 78.0, 73.8, 73.6, 73.1, 49.8, 40.5, 37.1; IR (neat) cm^{-1} 3069, 3030, 2940, 2893, 2859, 1730, 1651.



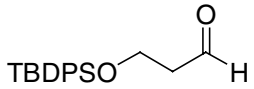
Preparation of 1-{2-[(6*R*,2*S*)-6-[{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl](3,5,6-trihydro-2H-pyran-2yl)}methyl]-4-methylene(3,5,6-trihydro-2H-pyran-2-yl)]ethoxy}-2,2-dimethyl-1,1-diphenyl-1-silapropane.(**6**): A solution of (2*S*)-1-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)-5-(2,2-dimethyl-2-silapropyl)hex-5-en-3-ol (20 mg, 0.078 mmol), and 2-{(6*R*, 2*S*)-4-methylene-6-[(phenylmethoxy)methyl]-3,5,6-trihydro-2H-pyran-2-yl}ethanal (**5**) (17 mg, 0.039 mmol), in diethyl ether (1.0 mL) was cooled to –78 °C, then TMSOTf (11 mg, 0.050 mmol) was added. The mixture was stirred for 20 min before adding aqueous NaOH solution (1.0 mL of 1 M). The mixture was brought to rt, then transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The organic layers were combined and washed with brine (5 mL), then dried over $MgSO_4$. The solvents were evaporated and the crude material was purified by flash chromatography, eluting with 10% ethyl acetate in hexanes to afford 1-{2-[(6*R*,2*S*)-6-[{(6*R*,2*S*)-4-methylene-6-[(phenylmethoxy)methyl](3,5,6-trihydro-2H-pyran-2yl)}methyl]-4-methylene(3,5,6-trihydro-2H-pyran-2-yl)]ethoxy}-2,2-dimethyl-1,1-diphenyl-1-silapropane.(**6**) as a clear, colorless oil (20 mg, 83%).

R*f* 0.42 (20% EtOAc in Hexanes); $[\alpha]_D^{20}$ +4.00° (c 0.06, $CHCl_3$); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.64-7.67 (m, 4H), 7.25-7.43 (m, 11H), 4.70-4.72 (m, 3H), 4.66-4.68 (m, 1H), 4.52 (ABq, J = 12.2 Hz, ΔAB = 17.1 Hz , 2H), 3.72-3.83 (m, 2H), 3.44-3.55 (m, 6H), 2.19-2.26 (m, 4H), 1.89-2.03 (m, 5H), 1.79 (dddd, J= 14.2, 8.3, 5.9, 5.9, 1H), 1.67-1.74 (m, 1H), 1.53-1.60 (m, 1H), 1.04 (s, 9H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 145.1, 144.3, 138.6, 135.8, 134.2, 134.2, 129.7, 129.7, 128.6, 128.0, 127.7, 109.2, 108.7, 77.8, 75.4, 75.4, 75.0, 73.6, 73.5, 60.7, 42.7, 41.2, 40.9, 40.7, 39.4, 37.7, 27.1, 19.4; IR (neat) cm^{-1}; 3071, 2926, 2855, 1651; HR CI-MS for $C_{39}H_{51}SiO_4$ (M+1) requires m/z 611.35566. Found 611.35217.



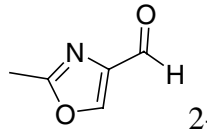
Preparation of 3-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)propanal: A solution of 3-hydroxypropionitrile (2.5 g, 35 mmol) in dichloromethane (50 mL) was cooled to 0 °C. Imidazole (6.0 g, 88 mmol) was added and the mixture was stirred 10 min before adding *tert*-butylchlorodiphenylsilane (18 mL, 70 mmol). The cold bath was removed after 2 h and stirring was continued for another 12 h. Saturated aqueous ammonium chloride solution (100 mL) was added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were washed with brine (200 mL) and dried over $MgSO_4$. After evaporating the solvents, *a portion* of the crude material was purified by flash chromatography (10% acetone in hexanes, 5 × 22 cm) to give 5.0 g of 3-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)propionitrile.

R*f* 0.33 (20% EtOAc in Hexanes); 500-MHz ^{1}H NMR ($CDCl_3$) δ 7.67-7.69 (m, 4H), 7.38-7.48 (m, 6H), 3.85 (t, J = 6.3 Hz, 2H), 2.54 (t, J = 6.3 Hz, 2H), 1.08 (s, 9H) ; 125-MHz ^{13}C NMR ($CDCl_3$) δ 135.7, 132.9, 130.2, 128.1, 118.1, 59.2, 26.9, 21.7, 19.4; IR (neat) cm^{-1} 3072, 3051, 2959, 2932, 2888, 2858, 2253; HR CI-MS for $C_{19}H_{24}NOSi$ (M+1) requires m/z 310.1627. Found 310.1628; Anal. calcd for $C_{19}H_{23}NOSi$: C, 73.74; H, 7.49. Found: C, 74.01; H, 7.53.

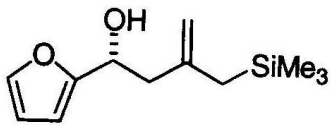


Preparation of 3-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)propanal: A stirring solution of 3-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)propionitrile (1.07 g, 3.45 mmol) in dichloromethane (30.0 mL) was cooled to 0 °C, and diisobutylaluminum hydride (1 M in hexanes, 3.80 mL, 3.80 mmol) was added dropwise. After 1h, aqueous potassium phthalate buffer solution (pH 4.00, 15 mL) was added, and the cold bath was removed. The mixture was stirred until two distinct layers formed (2 h). The layers were separated, and the aqueous phase was diluted with saturated aqueous potassium sodium tartrate solution (50 mL), then extracted with dichloromethane (3 × 20 mL). The combined organic layers were washed with brine (50 mL), and dried over $MgSO_4$. After removal of solvents under reduced pressure, the crude material was purified by flash chromatography (20% ethyl acetate in hexanes, 3.5 × 23 cm) to give 3-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)propanal as a white solid (0.99g, 92%).

R*f* 0.41 (20% EtOAc in Hexanes); m.p. = 40.5-42.0 °C 500-MHz ^{1}H NMR ($CDCl_3$) δ 9.84 (app t, J = 2.2 Hz, 1H), 7.66-7.69 (m, 4H), 7.39-7.47 (m, 6H), 4.04 (t, J = 6.1 Hz, 2H), 2.62 (dt, J = 2.0, 5.9 Hz, 1H), 1.05 (s, 9H); 125-MHz ^{13}C NMR ($CDCl_3$) δ 202.1, 135.8, 133.5, 130.0, 128.0, 58.5, 46.6, 27.0, 19.4; IR (neat) cm^{-1} 3071, 3050, 2958, 2931, 2889, 2858, 1730; Anal. calcd for $C_{19}H_{24}O_2Si$,: C, 73.03; H, 7.74. Found: C, 72.94; H, 7.77.



2-methyl-1,3-oxazole-4-carbaldehyde: This material was prepared as described by Boger and Curran: Boger, D. L.; Curran, T. T. *J. Org. Chem.* **1992**, *57*, 2235-2244.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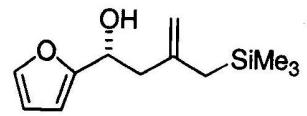
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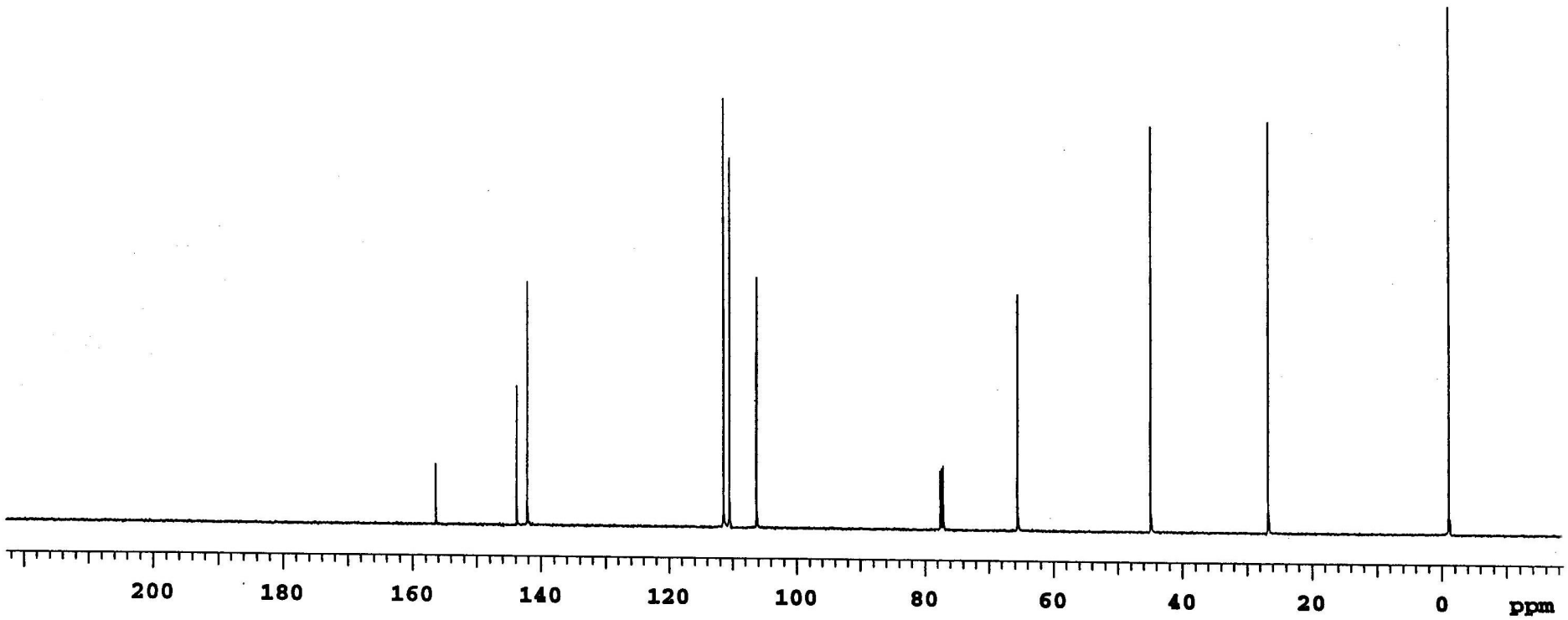
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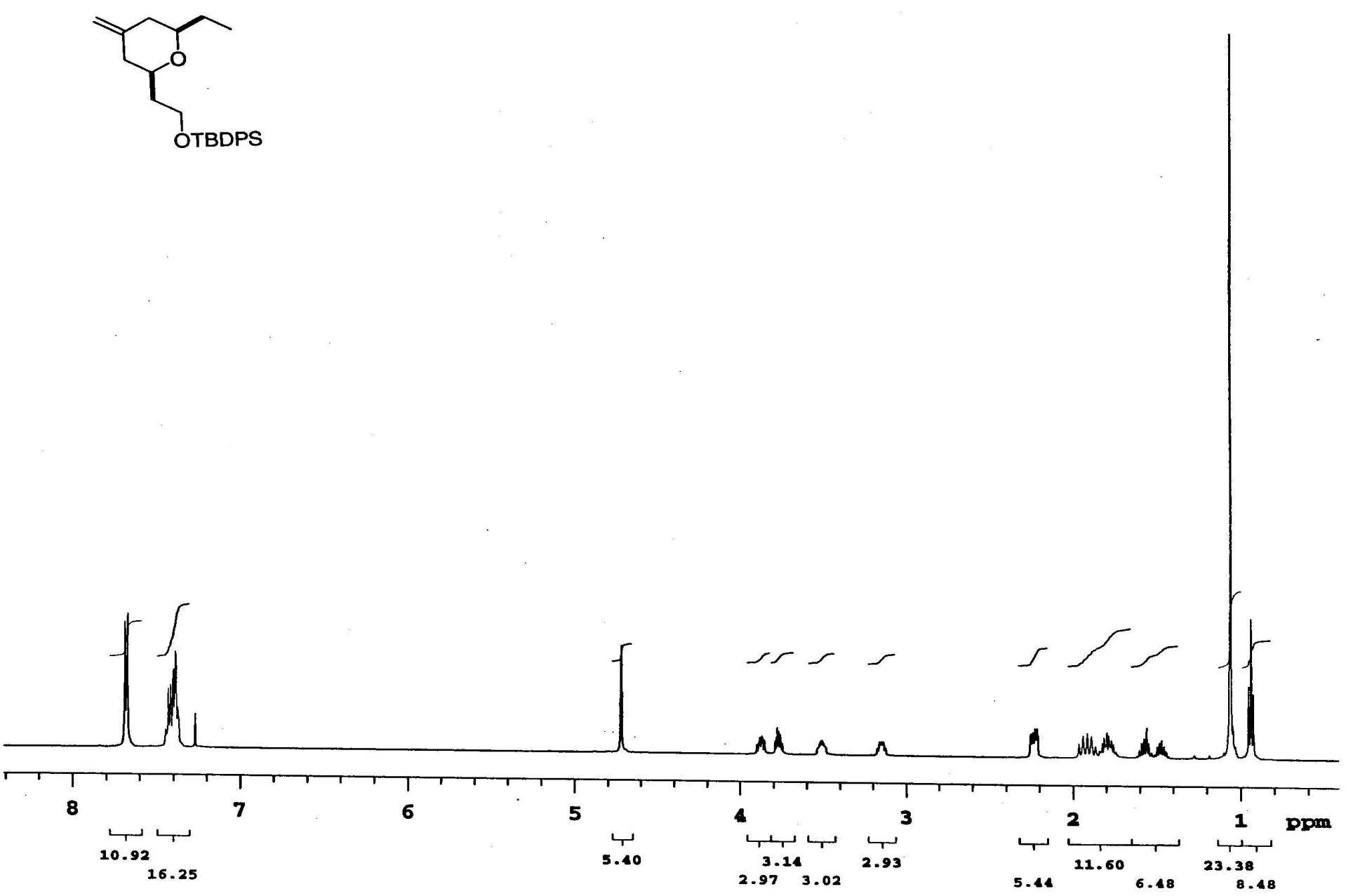
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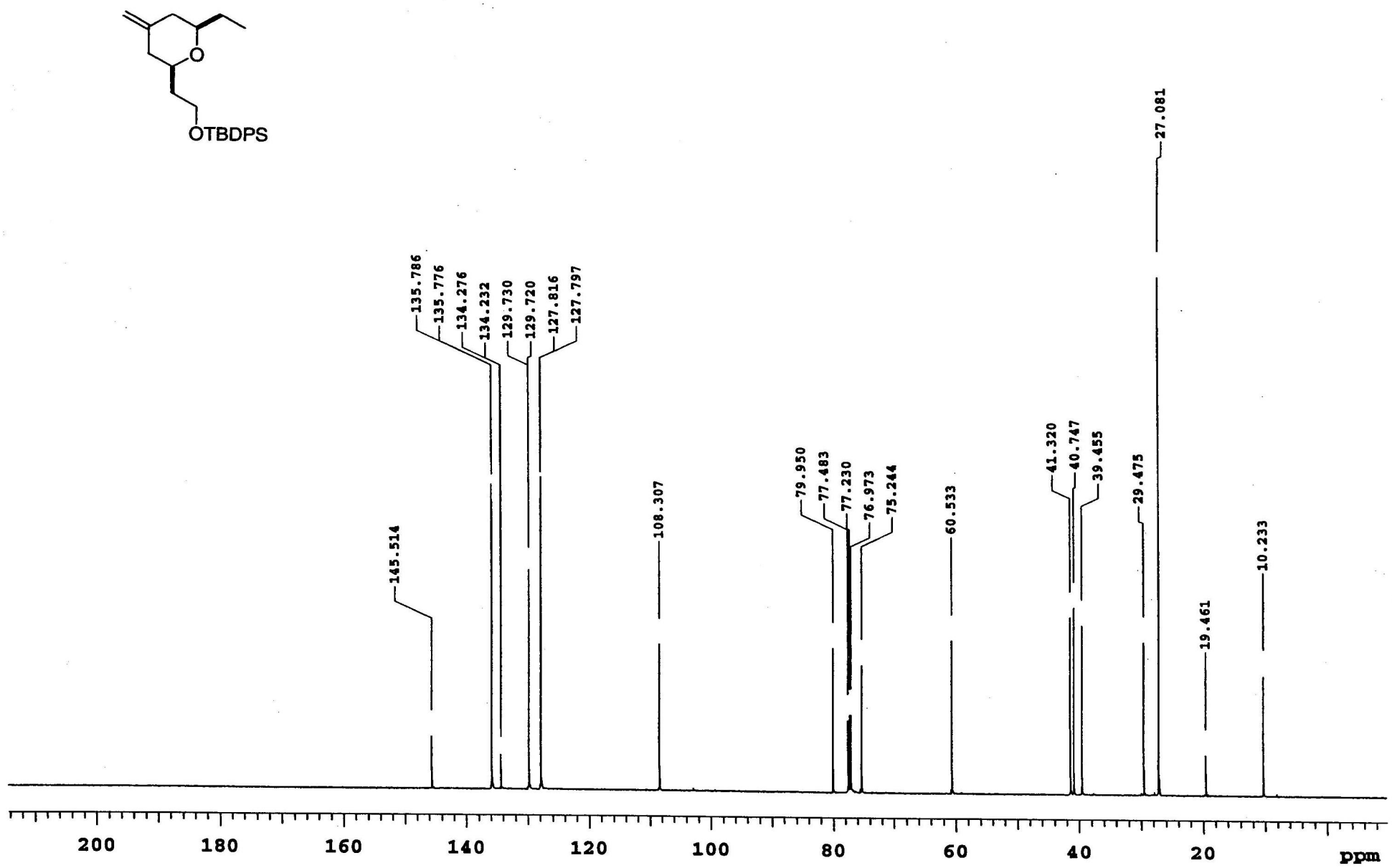
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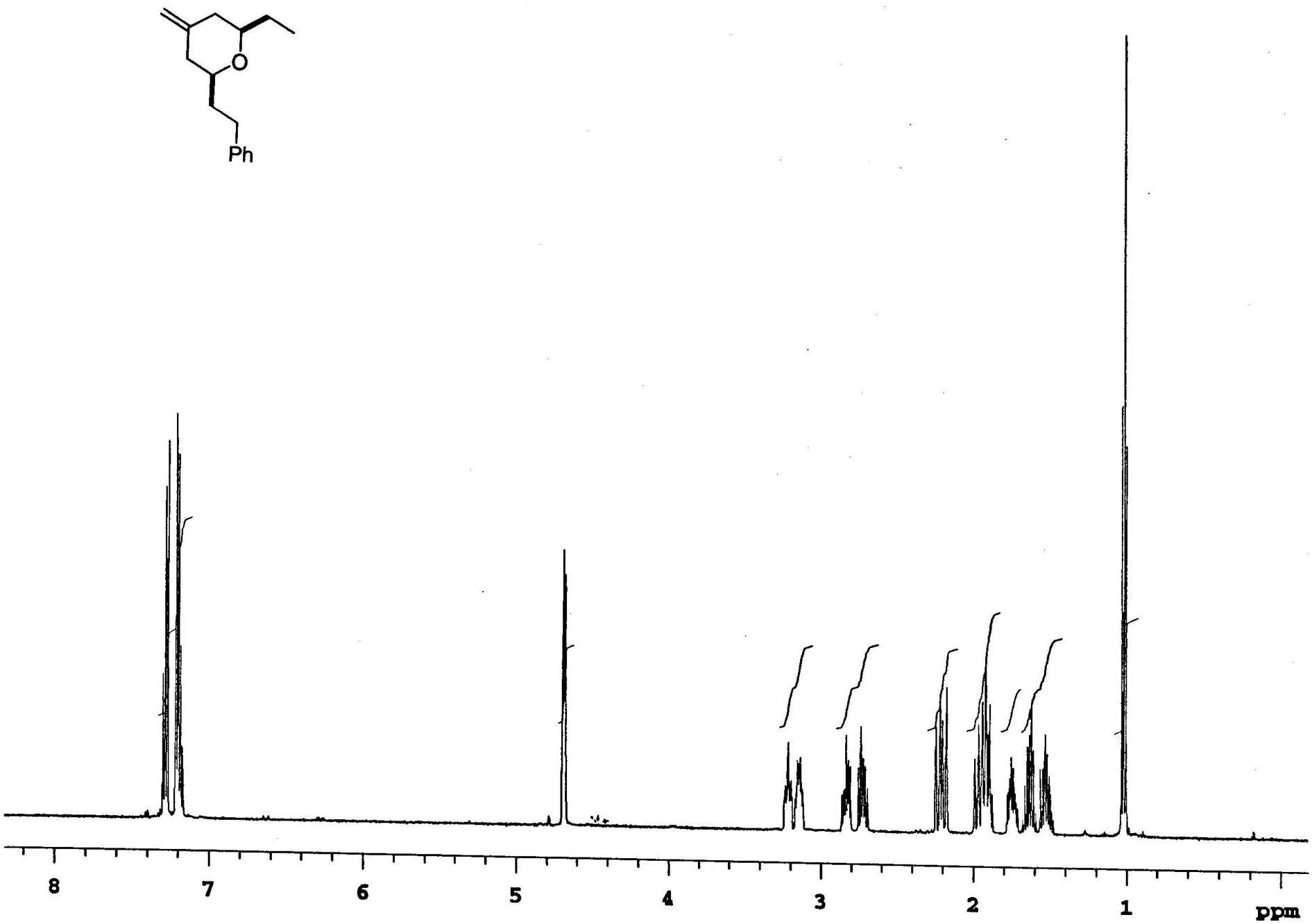
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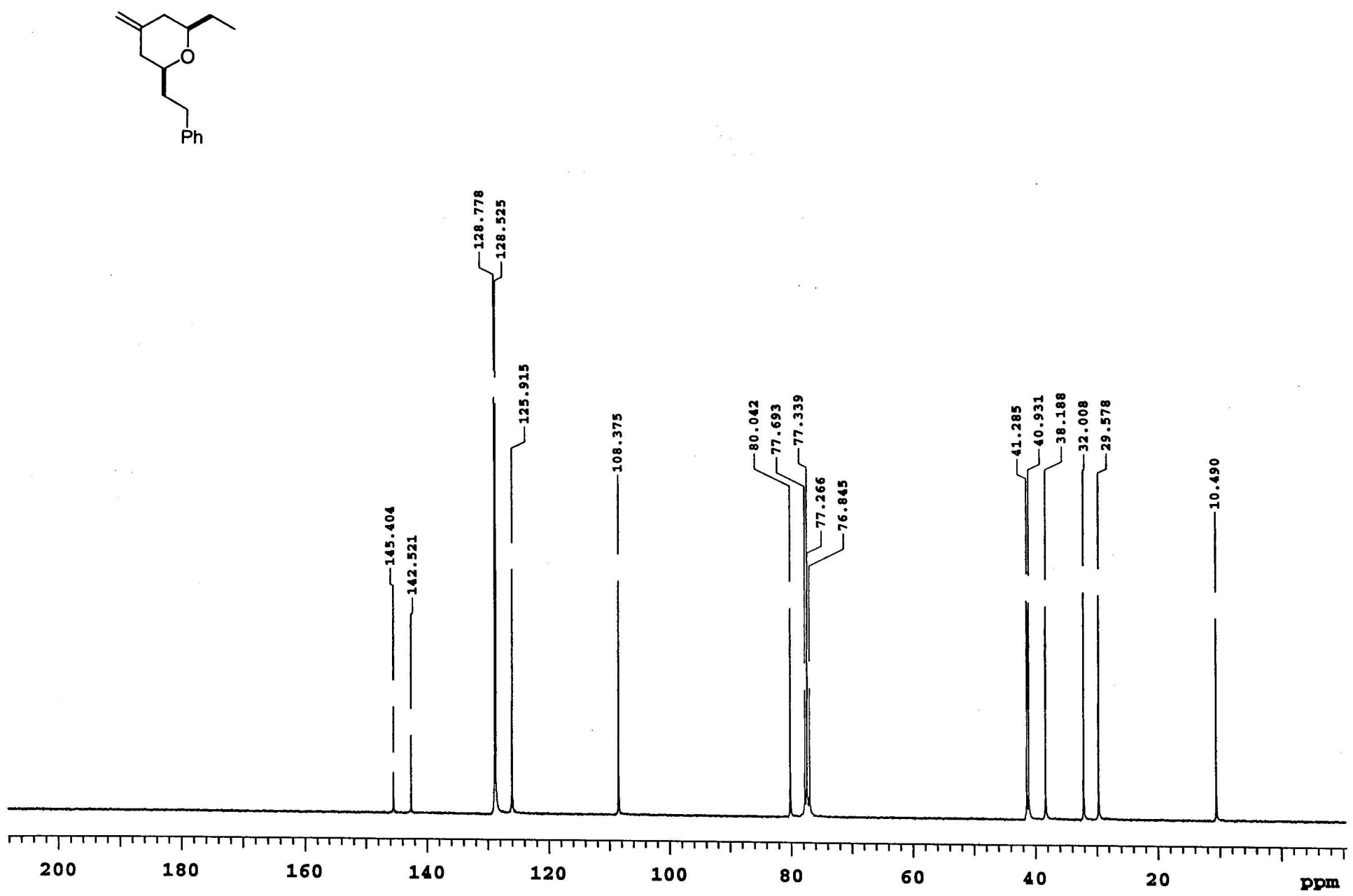
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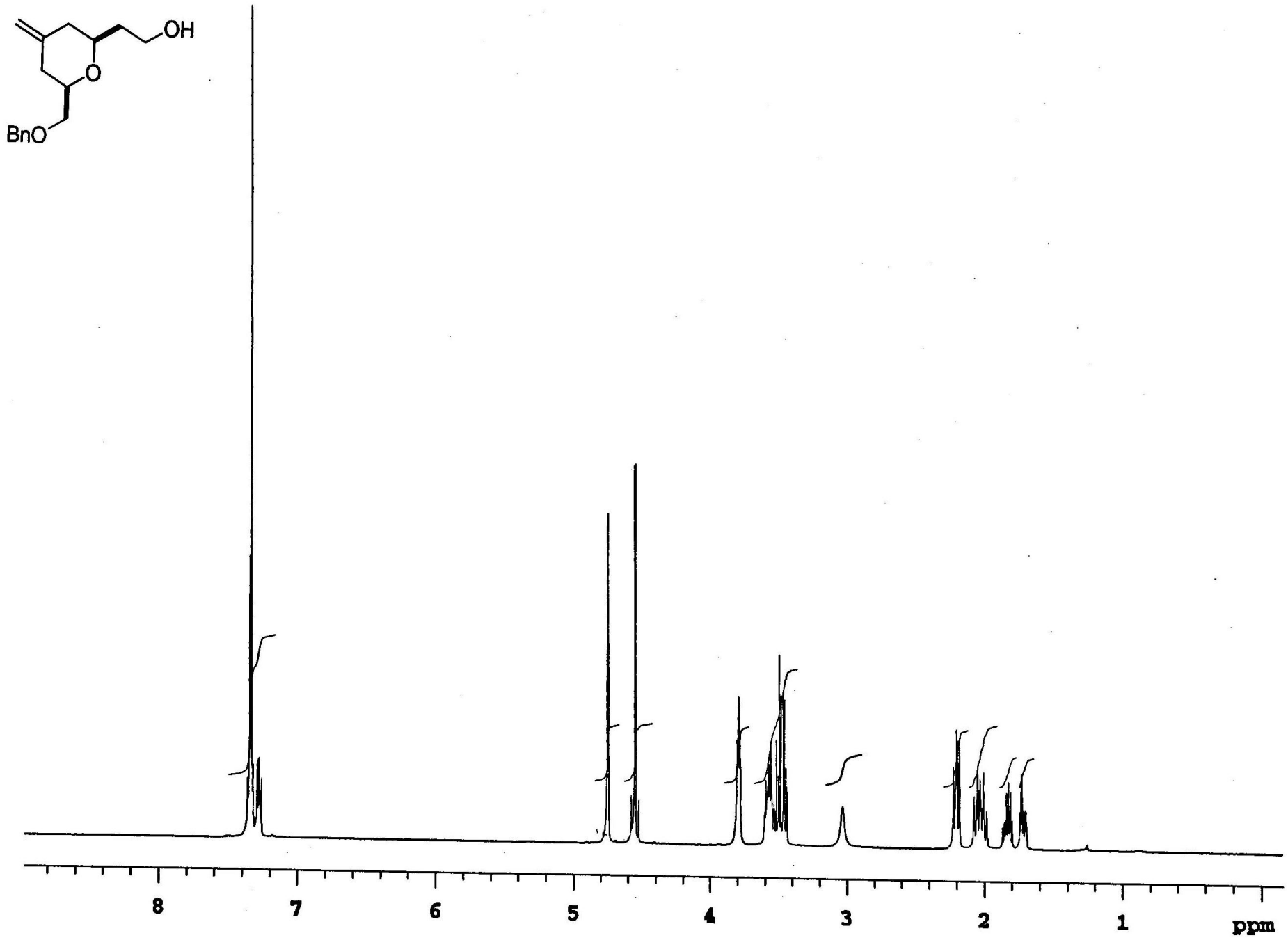
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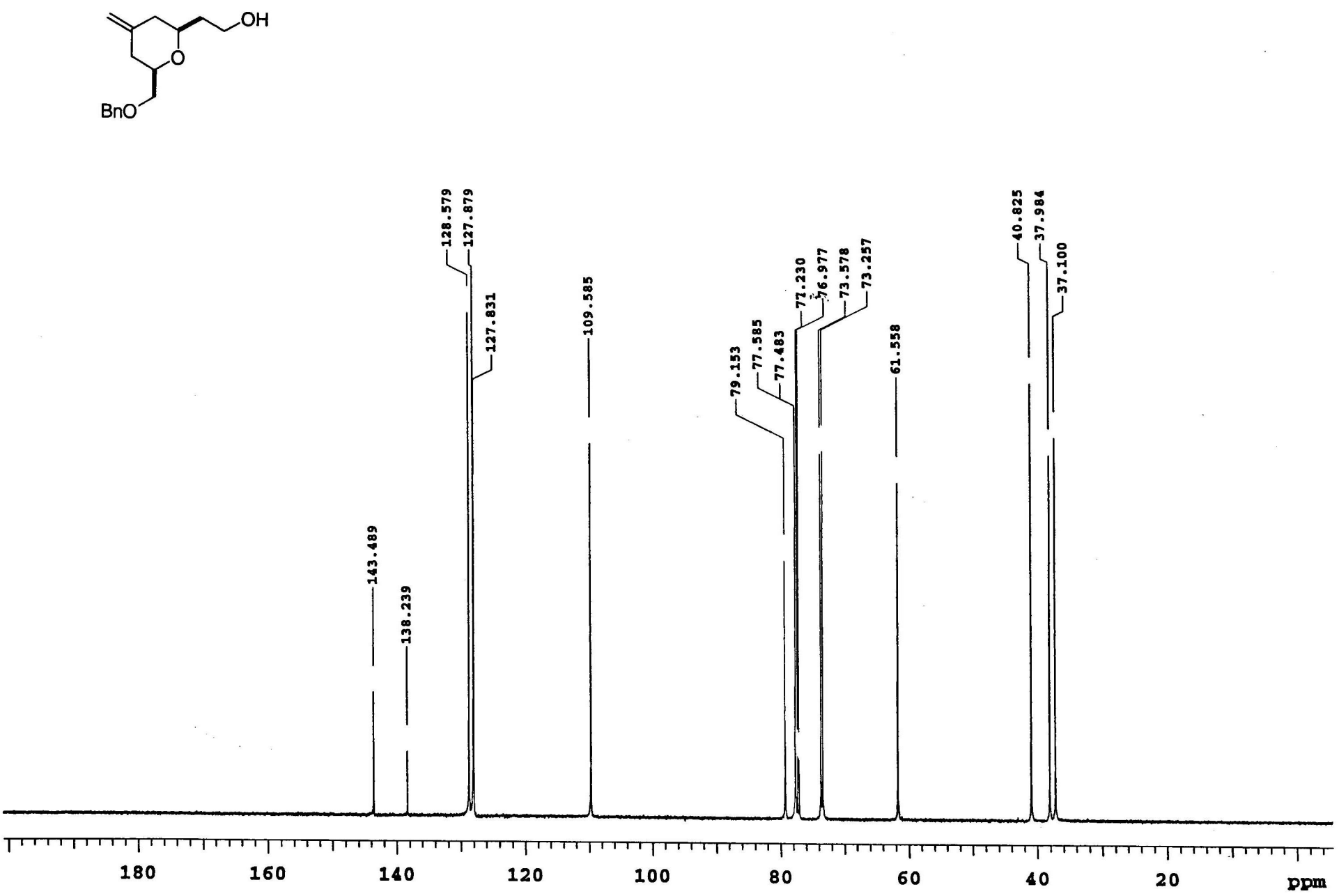
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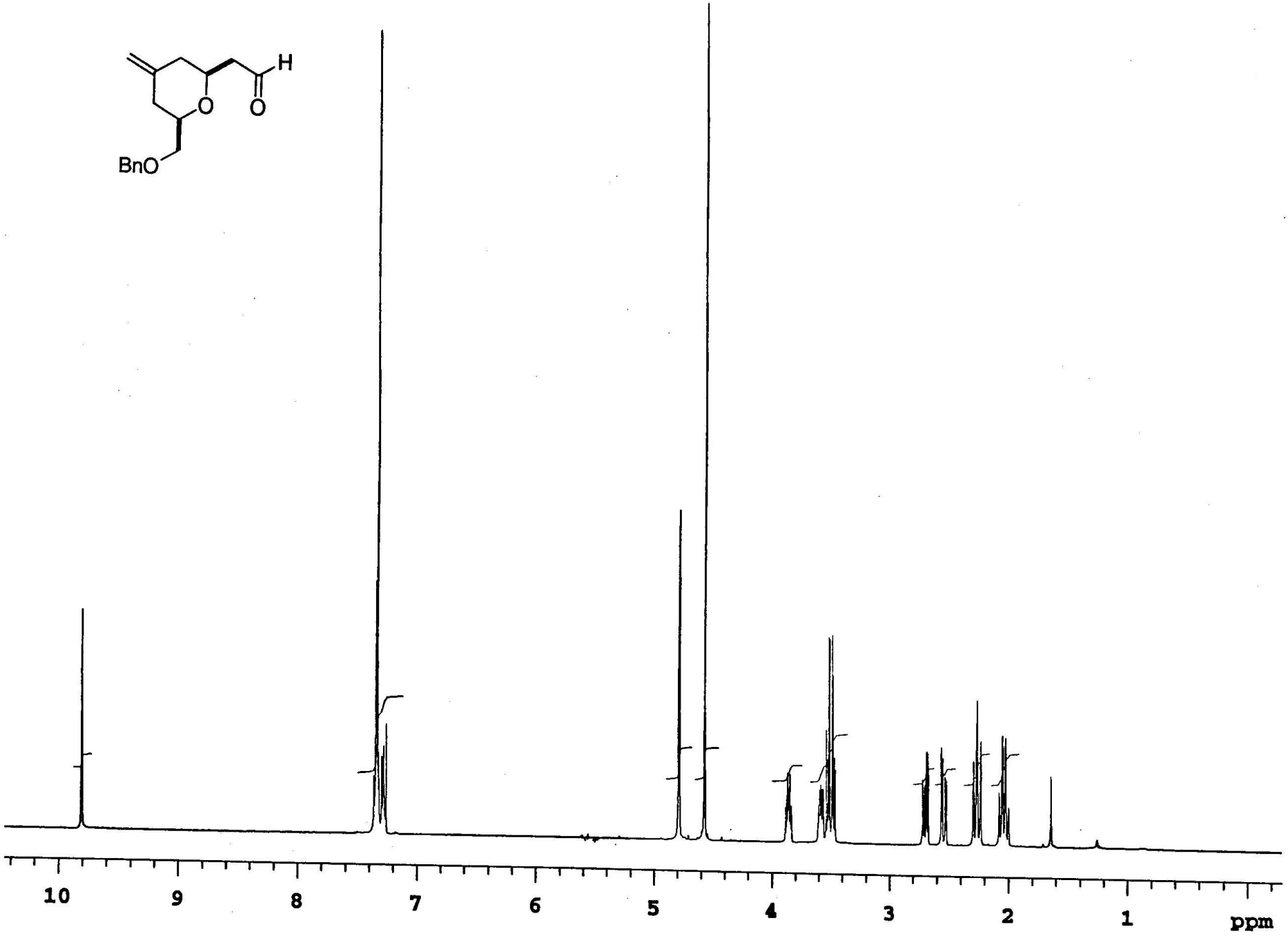
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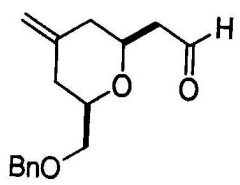
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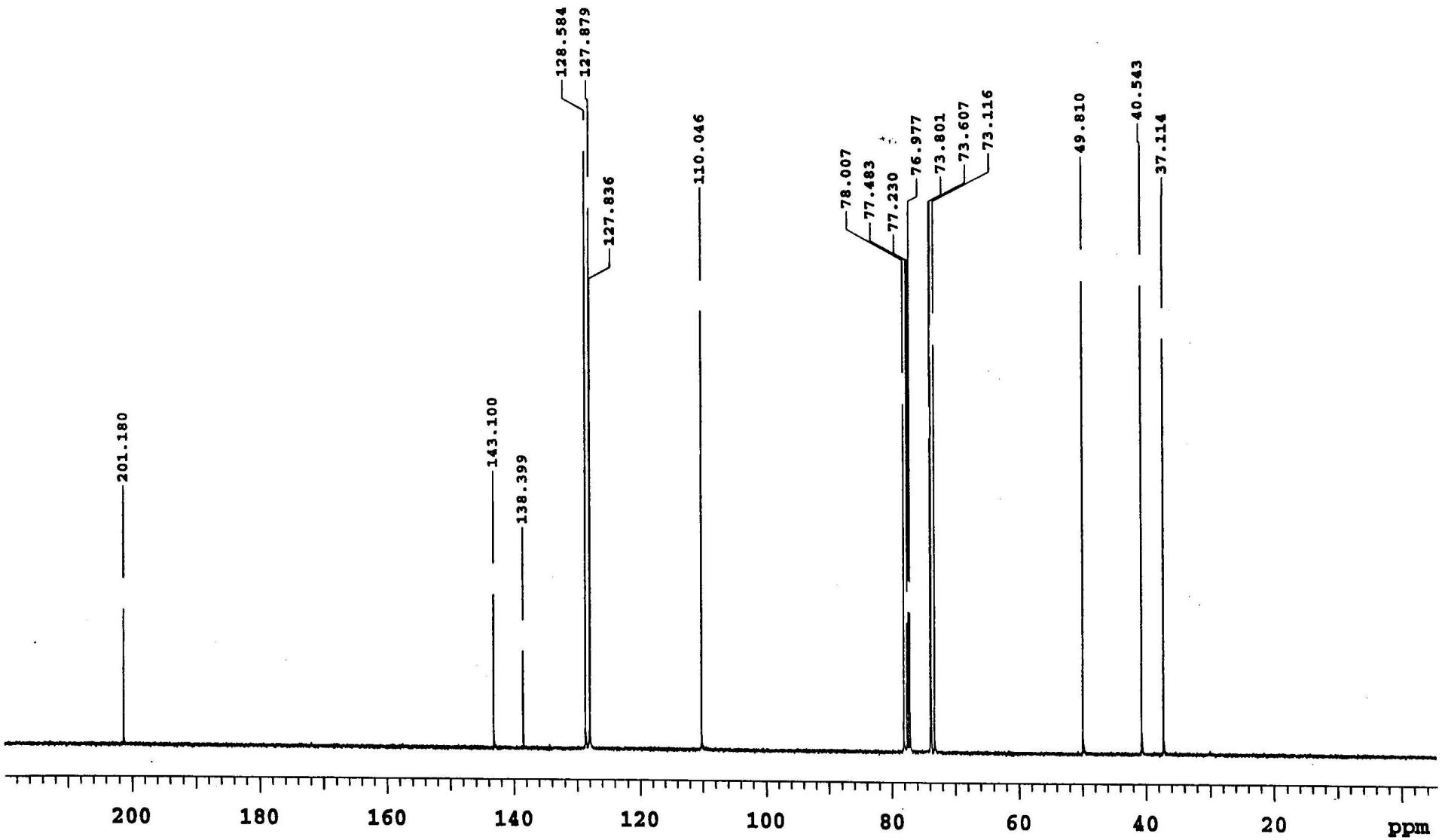
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127.836
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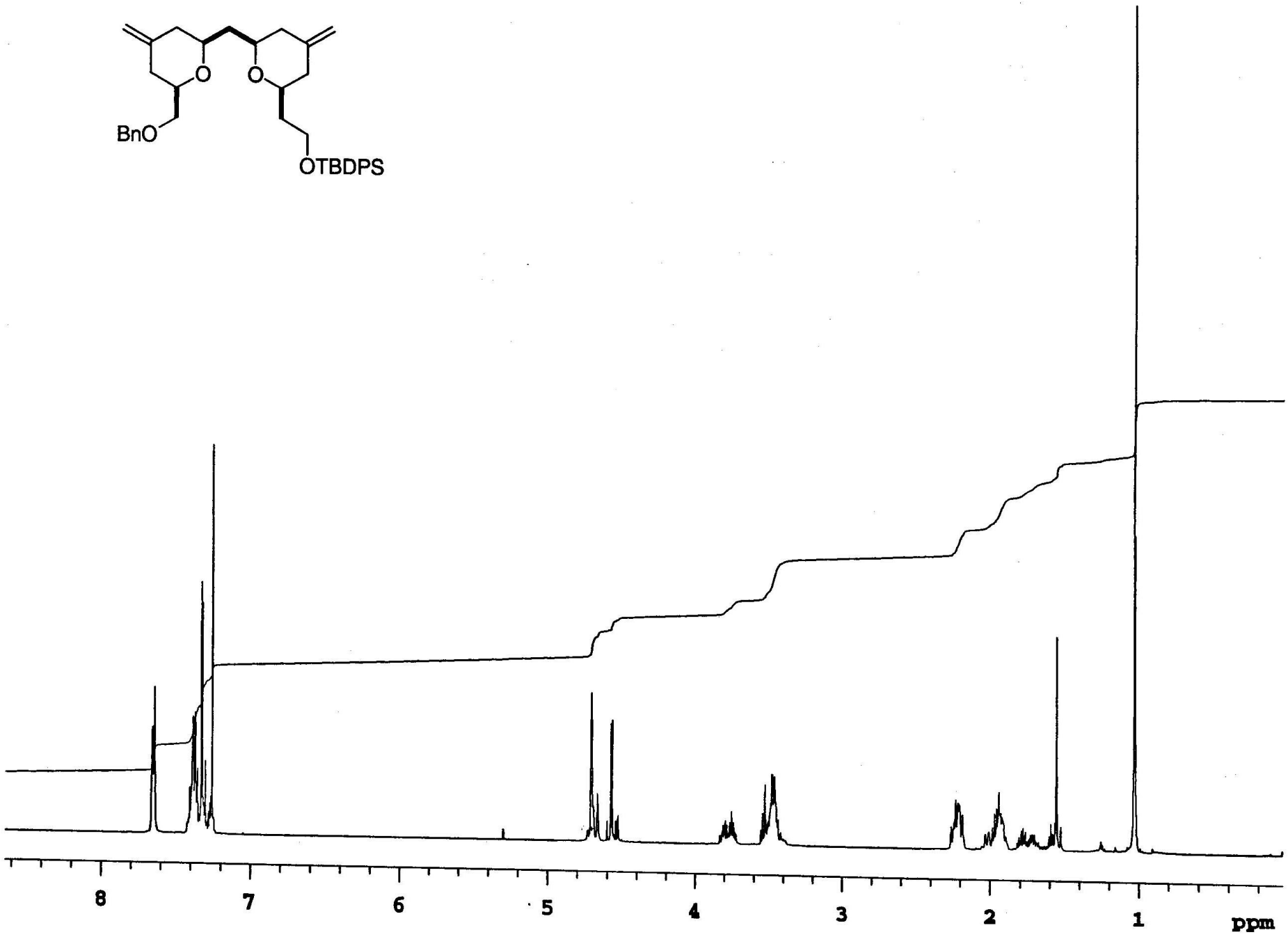
77.230
76.977
73.801
73.607
73.116
49.810
40.543
37.114
200
180
160
140
120
100
80
60
40
20
ppm


BnO
O
O
OTBDPS
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7
6
5
4
3
2
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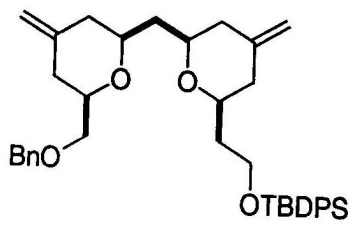
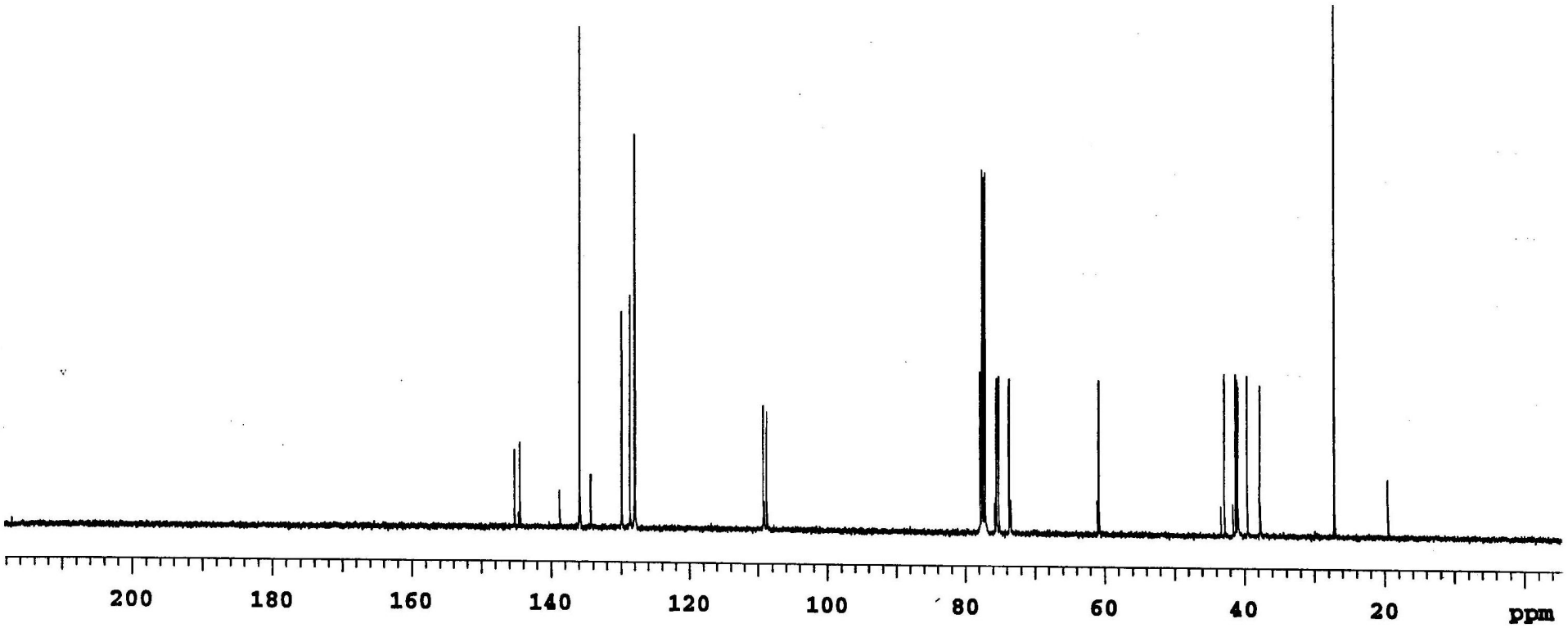

BnO
O
O
OTBDPS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120
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80
60
40
20
ppm