A Catalytic Enantioselective Tandem Allylation Strategy for Rapid Terpene Construction: Application to the Synthesis of Pumilaside Aglycon

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Supporting Information
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General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), a Varian Inova-500 (500 MHz), or a Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent), and coupling constants. ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), a Varian Inova-500 (125 MHz), or a Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$ 77.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, νmax cm-1. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High resolution mass spectrometry (ESI) was performed at the Mass Spectrometry Facility, Boston College.

Liquid Chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230x450 mesh) purchased from Silicycle. Thin Layer Chromatography was performed on 25 μmolm silica gel plates purchased from Silicycle. Visualization was performed using ultraviolet light (254 nm), potassium permanganate (KMnO4) in water, or phosphomolybdic acid (PMA) in ethanol. Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector. Optical rotations were measured on a Atago AP-300 Polarimeter. Melting point determination was performed with Digimelt MPA160.

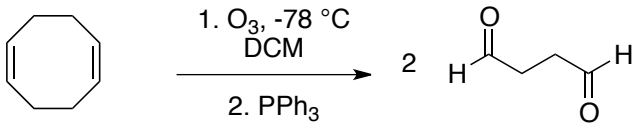
All reactions were conducted in oven- or flamed-dried glassware under an inert atmosphere of nitrogen or argon, unless otherwise noted. Tetrahydrofuran (THF), toluene (PhMe), and dichloromethane (DCM) were purified using a Pure Solv MD-4 solvent purification system from Innovative Technology Inc. by passing through two activated alumina columns after being purged with argon. Triethylamine was distilled from calcium hydride. Bis(pinacolato)diboron was generously donated by Allychem Co., Ltd. and was recrystallized from pentane prior to use. Cyclooctadiene was purchased from Aldrich and distilled over sodium metal prior to use. All other reagents were purchased from either Aldrich, Alfa-Aesar or Acros and used without further purification.

Experimental Procedures

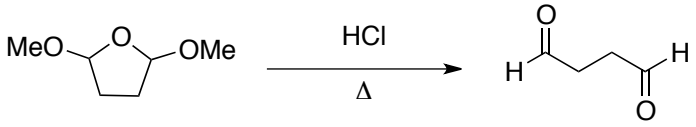
I. Preparation of 1,4-dicarbonyl compounds.

Preparation of succinaldehyde.

The following two procedures can be used interchangeably for the diboration/double allylation reaction. The ozonolysis procedure is the preferred method, however, both were used over the course of the reaction development.

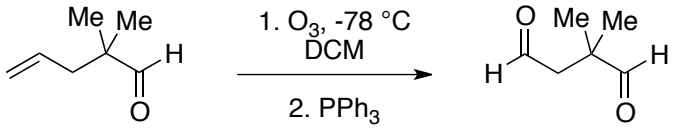


a) The title compound was prepared according to the literature procedure[1] with slight modification. To a 2-dram vial equipped with a stir bar was added cyclooctadiene (40.6 μL, 0.33 mmol) and DCM (6.6 mL, 0.5 M). The solution was cooled to -78 °C, and ozone was bubbled through until the reaction solution was blue in color. The mixture was then purged with N_2 until the blue color dissipated. Next, triphenylphosphine (173 mg, 0.66 mmol) was added in a single portion. The vial was sealed and allowed to warm to room temperature and stir overnight. The solution was carefully concentrated until triphenylphosphine oxide began to precipitate.



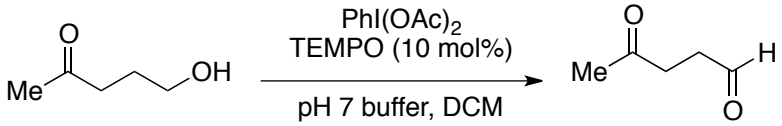
b) The title compound was prepared according to the literature procedure[2] with slight modification. To a 6-dram vial equipped with a stir bar was added 2,5-dimethoxytetrahydrofuran (0.5 mL, 3.83 mmol) and 1.0 M hydrochloric acid (2.0 mL, 2.0 mmol). The solution was stirred and heated with in an oil bath at 60 °C for 30 minutes. Upon cooling, solid powdered $NaHCO_3$ was added until a pH = 6 was reached. The aqueous solution was extracted 3 x 5 mL EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated carefully on the rotary evaporator. Due to the mild evaporation conditions, the dialdehyde was isolated as a mixture with ethyl acetate, starting material and polymeric byproduct; the typical weight percent of product was between 30-40%.

Preparation of 2,2-dimethylsuccinaldehyde



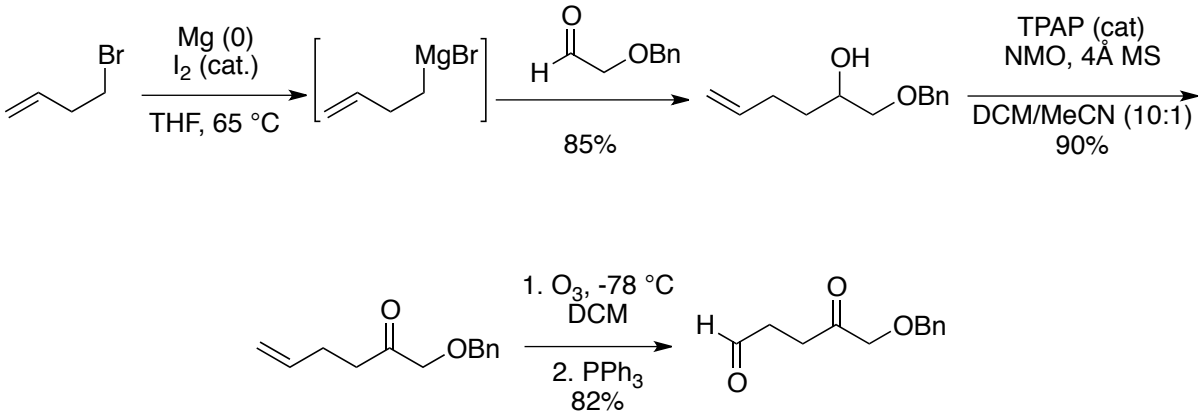
To a 2-dram vial equipped with a stir bar was added 2,2-dimethyl-4-pentenal (34 uL, 0.25 mmol) and DCM (1.5 mL). The solution was cooled to -78 °C and ozone was bubbled through until the reaction solution was blue in color. The mixture was then purged with N_2 until the blue color dissipated. Next, triphenylphosphine (0.275 mmol, 72.1 mg) was added as a single portion. The vial was sealed and allowed to warm to room temperature and stir overnight, then carefully concentrated until triphenylphosphine oxide began to precipitate.

Preparation of 4-oxopentanal



The title compound was prepared from 5-hydroxy-2-pentanone according to the literature procedure[3] with slight modification. To an aluminum foil-covered round bottom flask equipped with a stir bar was added $PhI(OAc)_2$ (17.467 g, 54.23 mmol) and TEMPO (770.3 mg, 4.93 mmol). The flask was sealed with a septum and purged with N_2. The solids were dissolved in DCM (50 mL, 1.0 M), and 5-hydroxy-2-pentanone (5.0 mL, 49.30 mmol) and pH 7 buffer (12 mL) were added in succession *via* syringe. The solution was allowed to stir at room temperature for 1 hour. Upon completion, the reaction was quenched with the addition of 15 mL saturated aqueous sodium thiosulfate. The mixture was transferred to a separatory funnel and washed with DCM (3 x 30 mL) and the combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (100% pentane, then 1:1 - 3:1 Et_2O:pentane, R_f = 0.18 in 1:1 Et_2O:pentane, stain in $KMnO_4$) to afford the ketoaldehyde as a yellow-brown oil. The title compound was then distilled with the Kugelrohr under vacuum at 65 °C to afford a colorless oil (2.907 g, 59% yield).

Preparation of 5-(benzyloxy)-4-oxopentanal



To a flame-dried 2-neck round bottom flask equipped with a reflux condenser and a stir bar was added ground magnesium turnings (148 mg, 6.1 mmol). The apparatus was flamed dried three times and put under positive N_2 pressure. A crystal of I_2 was added, and the magnesium was suspended in THF (6 mL, 1.0 M). Next, 1-bromobutene (0.61 mL, 6.0 mmol) was added slowly, and the reaction was warmed to 65 °C and refluxed for 2 hours. Of this stock solution, 4.9 mL was transferred to a flame-dried round bottom flask equipped with a stir bar. The solution was cooled to 0 °C, and benzyloxyacid aldehyde (0.5 mL, 3.56 mmol) was added dropwise as a solution in THF (7.12 mL, 0.5 M). The solution was stirred at 0 °C for 2 hours, then quenched with saturated aqueous ammonium chloride solution (5 mL). The mixture was transferred to a separatory funnel and washed with 3 x 20 mL EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The bis-homoallylic alcohol was purified by column chromatography on SiO_2 (5:1 hexanes/ethyl acetate, R_f = 0.19 in 5:1 hexanes/ethyl acetate, stain in $KMnO_4$) to afford 1-(benzyloxy)hex-5-en-2-ol as a clear, colorless oil (625 mg, 85%).

To a round bottom flask equipped with a stir bar was added 4Å MS. The apparatus was flamed dried and placed under positive pressure of N_2. Dichloromethane (5 mL) was charged to the flask, followed by the addition of 1-(benzyloxy)hex-5-en-2-ol (550 mg, 2.67 mmol). The remaining DCM (5 mL) and acetonitrile (1 mL) were then added to the solution. *N*-Methylmorpholine *N*-oxide (468.7 mg, 4.0 mmol) was added in a single portion. The flask was sealed with a septum, purged with N_2, and allowed to stir at room temperature for 20 minutes. Upon the addition of NMO, the solution changed color from cloudy white to black. Next, TPAP (46.8 mg, 0.133 mmol) was added as a single portion, followed by a N_2 purge of the flask atmosphere. The reaction was allowed to stir at room temperature until complete by TLC. The solution was then concentrated until acetonitrile was removed, redissolved in DCM, filtered over SiO_2,

and concentrated *in vacuo*. The resulting oil was used in the next step without further purification (492.2 mg, 90%).

To a round bottom flask equipped with a stir bar was added 1-(benzyloxy)hex-5-en-2-one (417 mg, 2.0 mmol) and DCM (8.0 mL, 0.25 M). The flask was loosely closed with a plastic yellow cap with a N_2 source and a vent needle. Next, solution was cooled to – 78 °C, the N_2 needle removed, and ozone was bubbled through until a blue color persisted. The solution was purged with N_2 until the blue color dissipated, then triphenylphosphine (642 mg, 2.45 mmol) was added in a single portion. The reaction was sealed and allowed to warm to room temperature and stir for 14 hours. The solution was then the concentrated *in vacuo*. The resulting mixture was purified by column chromatography on SiO_2 (3:1 Et_2O/pentane, R_f = 0.21 in 3:1 Et_2O/pentane, stain in PMA) to afford a clear, colorless oil (372.6 mg, 82% yield). The ^1H and ^{13}C spectra were in accordance with the literature.[4]

II. Representative procedure for Diboration/Oxidation I - Ozonolysis-Derived Dicarbonyls

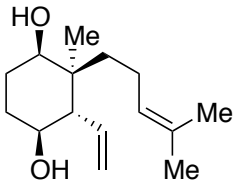
To an oven-dried 2-dram vial equipped with a magnetic stir bar in the glove box was added $Pt(dba)_3$ (3 mol%), (*R,R*)-3,5-di-*iso*-propylphenyl-TADDOL-PPh (3.6 mol%), $B_2(pin)_2$ (1.05 equiv), and toluene ([substrate] = 1.0 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for 20 minutes. The vial was cooled to room temperature, returned to the glove box and charged with diene (1.0 equiv.) The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 hours. After cooling to room temperature, the dicarbonyl compound (2.0 equiv) was transferred quantitatively to the flask using minimal toluene. The vial was purged with N_2 , sealed and heated to 60 °C for 24 hours. The reaction mixture was then cooled to room temperature, transferred to a 6-dram scintillation vial with THF (2 mL), and stirred with 2mL of 3M NaOH for 3 hours. The reaction mixture was diluted with ethyl acetate (5 mL), transferred to a separatory funnel and washed with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by column chromatography on SiO_2.

Representative Procedure for Diboration/Double Allylation II - neat dicarbonyl addition

To an oven-dried 2-dram vial equipped with a magnetic stir bar in the glove box was added $Pt(dba)_3$ (3 mol%), ((*R,R*)-3,5-di-*iso*-propylphenyl-TADDOL-PPh (3.6 mol%), $B_2(pin)_2$ (1.05 equiv), and toluene ([substrate] = 1.0 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for

20 minutes. The vial was cooled to room temperature, returned to the glove box and charged with diene (1.0 equiv.) The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 hours. After cooling to room temperature, the dicarbonyl compound (1.0 equiv.) was added by mass. The vial was purged with N_2 , sealed and heated to 60 °C for 24 hours. The reaction mixture was then cooled to room temperature, transferred to a 6-dram scintillation vial with THF (2 mL), and stirred with 2 mL of 3M NaOH for 3 hours. The reaction mixture was diluted with ethyl acetate (5 mL), transferred to a separatory funnel and washed with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by column chromatography on SiO_2.

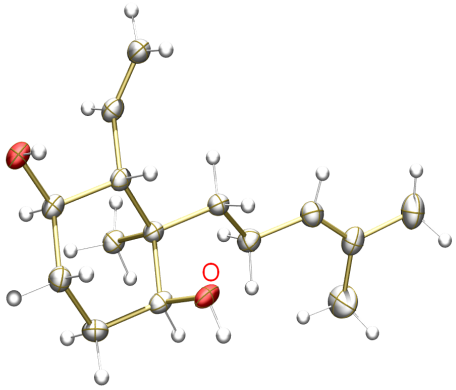
III. Characterization and Proof of Stereochemistry



(1*R*,2*S*,3*S*,4*S*)-2-methyl-2-(4-methylpent-3-en-1-yl)-3-vinylcyclohexane-1,4-diol (6). The diboration was performed according to Representative Diboration/Double Allylation Procedure I with (*E*)-4,8-dimethylnona-1,3,7-triene (50.0 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.9 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 11.9 μmol), $B_2(pin)_2$ (87.9 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M) and succinaldehyde (56.8 mg, 0.66 mmol). The crude reaction mixture was purified by column chromatography on SiO_2 (75:25 - 60:40 hexanes/ethyl acetate, R_f = 0.21 in 50:50 hexanes/ethyl acetate, stain in PMA) to afford a white solid (64.0 mg, 81%, d.r. >15:1 *syn*:*anti* diol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (1H, dt, *J* = 17.1 Hz, 10.1 Hz), 5.27 (1H, dd, *J* = 10.0 Hz, 2.2 Hz), 5.19 (1H, ddd, *J* = 17.1 Hz, 2.2 Hz, 0.5 Hz), 5.11-5.07 (1H, m), 3.63 (1H, br s), 3.56 (1H, dt, *J* = 4.6 Hz, 10.5 Hz), 2.04 (1H, t, *J* = 10.0 Hz), 2.00-1.84 (3H, m), 1.79-1.70 (3H, m), 1.69-1.60 (1H, m), 1.65 (3H, d, *J* = 1.0 Hz), 1.58 (3H, s), 1.45-1.39 (2H, m), 1.23-1.17 (1H, m), 0.86 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 131.7, 124.8, 120.7, 70.6, 67.9, 55.2, 40.5, 38.6, 27.2, 27.0, 25.7, 21.3, 18.3, 17.6; IR (neat): 3382.9 (br), 2966.7 (m), 2931.3 (s), 1444.7 (m), 1378.2 (m), 1263.1 (w), 1036.5 (m), 995.6 (m), 914.9 (m) cm^{-1}; HRMS-(ESI+) for $C_{15}H_{27}O_2$ [M+H]: calculated: 239.2011, found: 239.2005. $[\alpha]_D^{23}$: +10.98 (*c* = 0.91, $CHCl_3$, *l* = 10 mm**).**

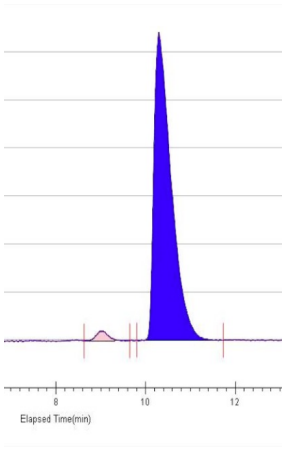
Analysis of Stereochemistry:

The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by crystallography using anomalous dispersion. Flack parameter = 0.03.

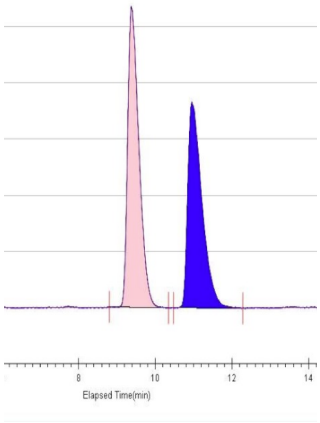


(*S,S*)-*i*Pr$_2$TADDOL-PPh used when this crystal structure was obtained

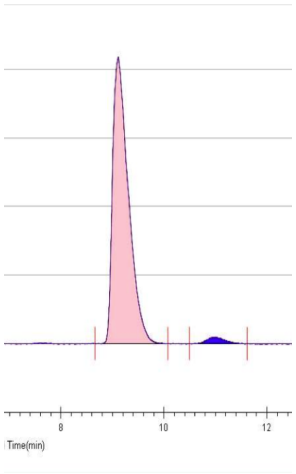
Chiral SFC (AD-H, Chiraldex, 5 mL/min, 3% i-PrOH, 100 bar, 35 °C)-analysis of the bis (benzoate) of the reaction product.



Product from
(*R,R*)-*i*Pr$_2$TADDOL-PPh



Mixture of products from
(*R,R*)- and (*S,S*)-ligands



Product from
(*S,S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	2.2257	194.0318	9.02	10.0518	0.0087
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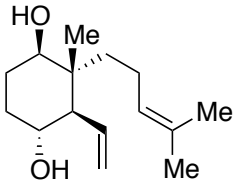
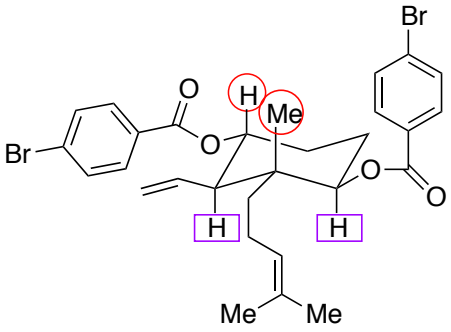
Total:	100	8717.8875			



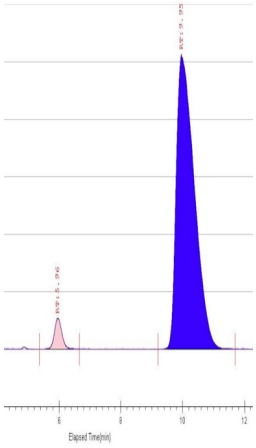
(1*R*,2*R*,3*R*,4*R*)-2-methyl-2-(4-methylpent-3-en-1-yl)-3-vinylcyclohexane-1,4-diol (4a). The diboration was performed according to Representative Diboration/Double Allylation Procedure I with (*Z*)-4,8-dimethylnona-1,3,7-triene (50.0 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.9 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 11.9 μmol), $B_2(pin)_2$ (87.9 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M) and succinaldehyde (56.8 mg, 0.66 mmol). The crude reaction mixture was purified by column chromatography on SiO_2 (67:33−50:50 hexanes/ethyl acetate, R_f = 0.22 in 50:50 hexanes/ethyl acetate, stain in PMA) to afford a colorless oil (82.3 mg, 5:1:1 d.r., mixture of three diastereomers and pinacol, combined yield 73%). The major diastereomer was isolated after the second column chromatography purification (80:1 dichloromethane/methanol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.71 (1H, dt, *J* = 17.1 Hz, 10.0 Hz), 5.31 (1H, dd, *J* = 10.3 Hz, 2.0 Hz), 5.22 (1H, ddd, *J* = 17.1 Hz, 2.0 Hz, 0.5 Hz), 5.07-5.03 (1H, m), 3.59 (1H, dd, *J* = 11.5 Hz, 4.4 Hz), 3.54 (1H, dt, *J* = 4.6 Hz, 10.8 Hz), 2.10-2.05 (1H, m), 1.96-1.91 (2H, m), 1.89 (1H, t, *J* = 9.8 Hz), 1.81-1.75 (1H, m), 1.65 (3H, d, *J* = 1.0 Hz), 1.63-1.55 (1H, m), 1.57 (3H, s), 1.46-1.39 (1H, m), 1.35-1.27 (1H, m), 1.25-1.18 (1H, m), 0.84 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.6, 131.6, 124.5, 120.5, 72.2, 67.6, 55.2, 41.0, 37.3, 31.6, 28.4, 25.7, 20.8, 17.6, 15.0; IR (neat): 3385.9 (br), 2969.5 (m), 2930.5 (s), 1448.9 (m), 1376.7 (w), 1115.7 (w), 1044.2 (s), 1011.3 (m), 954.1 (m), 915.3 (w) cm^{-1}; HRMS-(ESI+) for $C_{15}H_{27}O_2$ [M+H]: calculated: 239.2011, found: 239.2017. $[\alpha]_D^{23}$ = −24.10 (*c* = 0.93, $CHCl_3$, *l* = 10 mm**).**

Analysis of Stereochemistry:

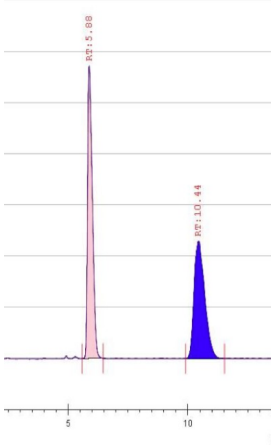
The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-*i*Pr$_2$TADDOL-PPh. The relative stereochemistry was determined by NOESY analysis of the bis-4-bromobenzoate of the reaction product (prepared using 4-bromobenzoyl chloride, triethylamine, and DMAP). The following NOEs were observed:



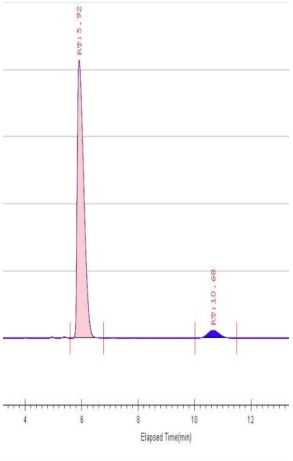
Chiral SFC (AD-H, Chiraldex, 3 mL/min, 5% MeOH, 100 bar, 35 °C)-analysis of the bis (benzoate) of reaction product ***4a****.*



Product from (*R,R*)-*i*Pr$_2$TADDOL-PPh



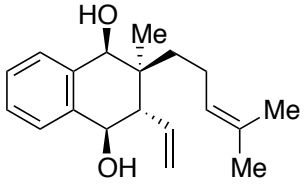
Mixture of products from (*R,R*)- and (*S,S*)-ligands



Product from (*S,S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

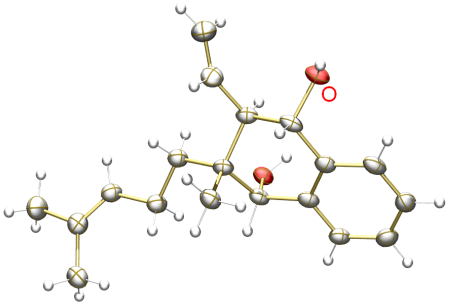
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.126	1796.7898	5.96	107.404	0.0057
2	95.874	41751.6838	9.95	1026.2145	0.0095
Total:	100	43548.4736			



(1*S*,2*S*,3*S*,4*R*)-2-methyl-2-(4-methylpent-3-en-1-yl)-3-vinyl-1,2,3,4-tetrahydronaphthalene-1,4-diol (4b). The diboration was performed according to Representative Diboration/Double Allylation Procedure II with (*E*)-4,8-dimethylnona-1,3,7-triene (50.0 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.9 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 11.9 μmol), $B_2(pin)_2$ (87.9 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M) and phthalaldehyde (44.3 mg, 0.33 mmol). The crude reaction mixture was purified by column chromatography on SiO_2 (80:20 hexanes/ethyl acetate, R_f = 0.22 in 75:25 hexanes/ethyl acetate, stain in PMA) to afford a white solid (78.9 mg, 83% combined yield, d.r. = 2.8:1 *syn*:*anti* diol). The two diastereomers was separated after a purification by column chromotography (85:15–75:25 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (1H, d, *J* = 7.6 Hz), 7.36-7.33 (1H, m), 7.30-7.26 (2H, m), 5.81 (1H, dt, *J* = 16.9 Hz, 9.8 Hz), 5.33 (1H, dd, *J* = 10.3 Hz, 2.0 Hz), 5.30 (1H, ddd, *J* = 16.9, 2.0, 0.5 Hz), 5.16-5.12 (1H, m), 4.48 (1H, d, *J* = 9.5 Hz), 4.35 (1H, s), 2.54 (1H, t, *J* = 9.8 Hz), 2.20-2.13 (1H, m), 2.06-1.98 (1H, m), 1.68 (3H, s), 1.63 (3H, s), 1.61-1.55 (1H, m), 1.28-1.22 (1H, m), 0.81 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.0, 136.9, 136.2, 131.5, 129.9, 128.7, 128.1, 127.9, 124.8, 120.2, 73.8, 69.2, 52.4, 39.5, 37.8, 25.7, 21.2, 17.7, 16.4; IR (neat): 3374.0 (br), 2966.1 (m), 2921.7 (m), 1453.5 (w), 1380.0 (m), 996.9 (s), 918.1 (w), 765.0 (m), 745.8 (s) cm^{-1}; HRMS-(ESI+) for $C_{19}H_{25}O_1$ [M+H-H_2O]: calculated: 269.1905, found: 269.1909. $[\alpha]_D^{23}$: -14.37 (*c* = 1.39, $CHCl_3$, *l* = 10 mm).

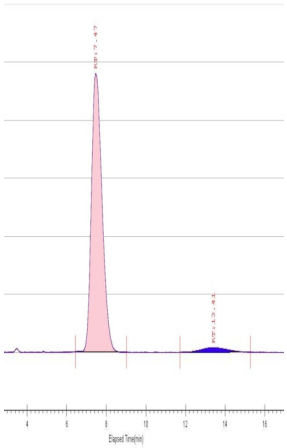
Analysis of Stereochemistry:

The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-*i*Pr$_2$TADDOL-PPh, and reconfirmed by anomalous dispersion effects in diffraction measurements on the crystal.

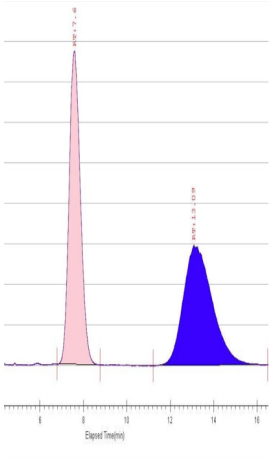


(*S,S*)-*i*Pr$_2$TADDOL-PPh used when this crystal structure was obtained

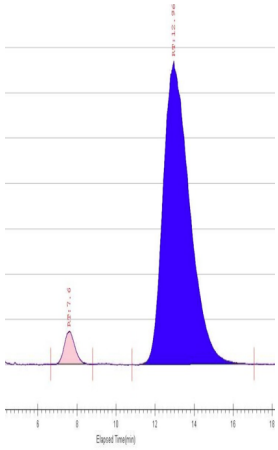
Chiral SFC (AD-H, Chiraldex, 3 mL/min, 5% MeOH, 100 bar, 35 °C)-analysis of the bis (benzoate) of reaction product ***4b****.*



Product from (*R,R*)-*i*Pr$_2$TADDOL-PPh



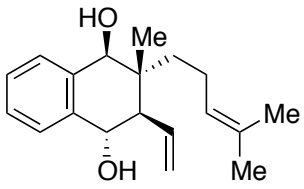
Mixture of products from (*R,R*)- and (*S,S*)-ligands



Product from (*S,S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

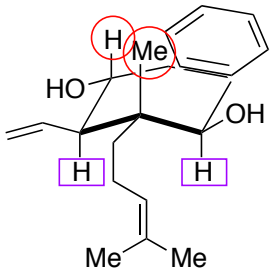
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	95.9863	35913.7946	7.47	960.8472	0.006
2	4.0137	1501.7331	13.41	16.884	0.0108
Total:	100	37415.5277			



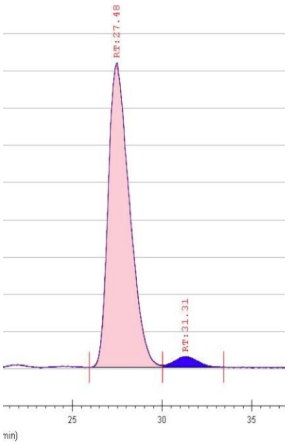
(1*S*,2*R*,3*R*,4*S*)-2-methyl-2-(4-methylpent-3-en-1-yl)-3-vinyl-1,2,3,4-tetrahydronaphthalene-1,4-diol (4c). The diboration was performed according to Representative Diboration/Double Allylation Procedure II with (*Z*)-4,8-dimethylnona-1,3,7-triene (50.0 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.9 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 11.9 μmol), $B_2(pin)_2$ (87.9 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M) and phthalaldehyde (44.3 mg, 0.33 mmol). The crude reaction mixture was purified by column chromatography on SiO_2 (75:25−60:40 hexanes/ethyl acetate, stain in PMA) to afford a heterogeneous mixture (77.5 mg, 82% combined yield, d.r. = 1.2:1 *anti:syn* diol [with 8% of minor diastereomer from first allylation]). A second purification was used to separate the two major diastereomers (85:15−75:25 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60-7.55 (2H, m), 7.32-7.27 (2H, m), 5.88 (1H, dt, *J* = 16.9 Hz, 10.0 Hz), 5.38 (1H, dd, *J* = 10.5 Hz, 2.0 Hz), 5.34 (1H, ddd, *J* = 17.1 Hz, 2.0 Hz, 0.5 Hz), 5.10-5.07 (1H, m), 4.79 (1H, d, *J* = 4.6 Hz), 4.58 (1H, d, *J* = 9.8 Hz), 2.34 (1H, t, *J* = 9.8 Hz), 2.03 (2H, q, *J* = 7.9 Hz), 1.67 (3H, d, *J* =0.7 Hz), 1.64-1.58 (1H, m), 1.59 (3H, s), 1.38-1.32 (1H, m), 0.81 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.2, 136.1, 135.3, 131.7, 128.0, 127.4, 127.3, 126.1, 124.3, 120.1, 72.3, 69.3, 53.9, 41.3, 37.1, 25.7, 21.0, 17.7, 14.9; IR (neat): 3383.9 (br), 2967.6 (m), 2921.7 (s), 1452.2 (m), 1380.2 (m), 1129.0 (w), 1027.2 (m), 1010.3 (s), 918.0 (w), 762.1 (s), 680.7 (w), 668.1 (w) cm^{-1}; HRMS-(ESI+) for $C_{19}H_{25}O_1$ [M+H-H_2O]: calculated: 269.1905, found: 269.1902. $[\alpha]_D^{23}$= +16.63 (*c* = 0.60, $CHCl_3$, *l* = 10 mm). R_f = 0.32 in 75:25 hexanes/ethyl acetate.

Analysis of Stereochemistry:

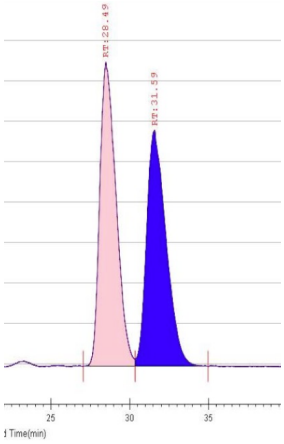
The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-*i*Pr_2TADDOL-PPh. The relative stereochemistry was determined by NOESY analysis. The following NOEs were observed:



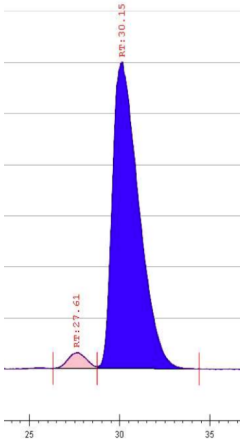
Chiral SFC (AD-H, Chiraldex, 1.5 mL/min, 4% MeOH, 100 bar, 35 °C)-analysis of the bis (benzoate) of reaction product ***4c****.*



Product from (*R,R*)-*i*Pr$_2$TADDOL-PPh



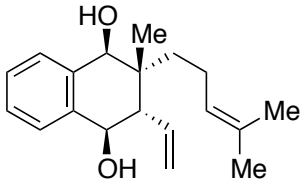
Mixture of products from (*R,R*)- and (*S,S*)-ligands



Product from (*S,S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

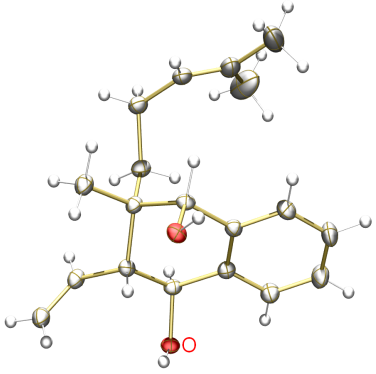
Peak No	**% Area**	**Area**	**RT (min)**	**Height (mV)**	**K'**
1	96.3551	33728.0439	27.48	409.9959	0.0374
2	3.6449	1275.8455	31.31	14.4836	0.0427
Total:	100	35003.8894			



(1*S*,2*R*,3*S*,4*R*)-2-methyl-2-(4-methylpent-3-en-1-yl)-3-vinyl-1,2,3,4-tetrahydronaphthalene-1,4-diol (*syn* diastereomer from reaction producing **4c**). R_f = 0.27 in 67:33 hexanes/ethyl acetate. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (1H, d, *J* = 7.3 Hz), 7.37-7.33 (1H, m), 7.30-7.28 (2H, m), 5.88 (1H, dt, *J* = 16.9 Hz, 9.9 Hz), 5.34-5.29 (2H, m), 4.92-4.88 (1H, m), 4.57 (1H, dd, *J* = 9.5 Hz, 4.7 Hz), 4.47 (1H, s), 2.66 (1H, t, *J* = 9.7 Hz), 2.02-1.93 (1H, m), 1.89-1.81 (1H, m), 1.58 (3H, d, *J* = 0.7 Hz), 1.46 (3H, s), 1.41-1.35 (1H, m), 1.13-1.01 (1H, m), 1.09 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2, 136.8, 136.2, 131.6, 129.8, 128.7, 128.2, 128.1, 124.4, 120.2, 74.2, 69.2, 52.6, 40.2, 32.7, 25.6, 22.3, 21.8, 17.4; IR (neat): 3301.5 (br s), 2966.1 (s), 2923.5 (m), 2864.7 (w), 1453.9 (w), 1040.8 (m), 1005.5 (s), 987.2 (s), 926.8 (m), 765.8 (w), 743.7 (w) cm^{-1}; HRMS-(ESI+) for $C_{19}H_{25}O_1$ [M+H-H_2O]: calculated: 269.1905, found: 269.1902. $[\alpha]_D^{23}$= −108.00 (*c* = 0.37, $CHCl_3$, *l* = 10 mm**).**

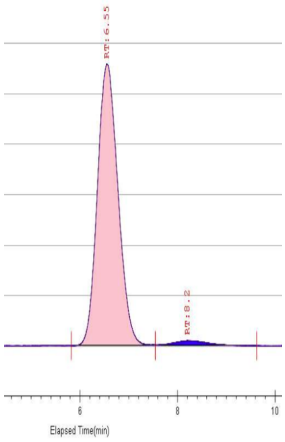
Analysis of Stereochemistry:

The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by crystallography using anomalous dispersion. Flack parameter = 0.34.

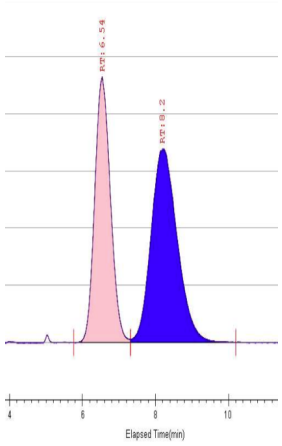


(*S,S*)-*i*Pr_2TADDOL-PPh used when this crystal structure was obtained

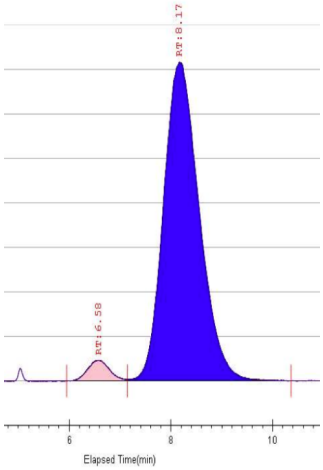
Chiral SFC (AD-H, Chiraldex, 3 mL/min, 5% MeOH, 100 bar, 35 °C)-analysis of the bis (benzoate) of reaction product ***4c*** *minor diastereomer.*



Product from
(*R,R*)-*i*Pr$_2$TADDOL-PPh



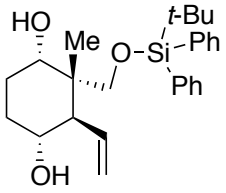
Mixture of products from
(*R,R*)- and (*S,S*)-ligands



Product from
(*S,S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

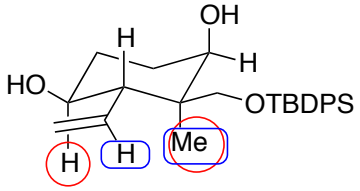
Peak No	**% Area**	**Area**	**RT (min)**	**Height (mV)**	**K'**
1	97.1229	16401.5583	6.55	559.9962	0.0064
2	2.8771	485.8737	8.2	10.1418	0.008
Total:	100	16887.432			



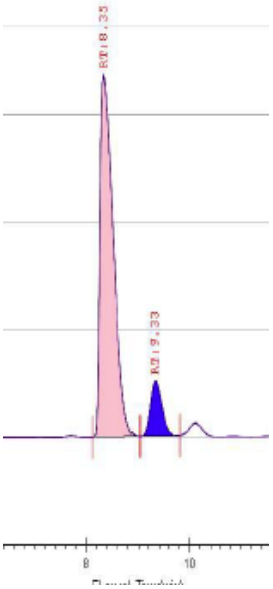
(1*R*,2*R*,3*S*,4*S*)-2-(((*tert*-butyldiphenylsilyl)oxy)methyl)-2-methyl-3-vinylcyclohexane-1,4-diol (4d). The diboration was performed according the Representative Procedure I with slight modification using (*E*)-*tert*-butyl((2-methylpenta-2,4-dien-1-yl)oxy)diphenylsilane (111.0 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.0 μmol), (*S,S*)-3,5-di-*iso*-propylphenyl-PPh (10.8 mg, 12.0 μmol), $B_2(pin)_2$ (88.0 mg, 0.35 mmol), toluene (0.33 mL, 1.0M), and succinaldehyde (56.8 mg, 0.66 mmol). Upon completion of the double allylation, the mixture was transferred to a 6-dram scintillation vial with 2 mL of THF and cooled to 0 °C. To the solution was then added 2 mL pH 7 buffer, followed by the dropwise addition of 30% H_2O_2. The mixture was allowed to stir and warmed to room temperature over 6 hours, then quenched with a saturated solution of sodium thiosulfate (2 mL). The reaction mixture was then diluted with ethyl acetate (5 mL) and isolated as previously described. The crude reaction mixture was purified by column chromatography on SiO_2 (70:30 - 40:60 hexanes/ethyl acetate, R_f = 0.28 in 50:50 hexanes/ethyl acetate, stain in PMA) to afford a clear, colorless oil (99.5 mg, 71%, d.r. = 10:1 *syn:anti* diol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 - 7.62 (4H, m), 7.45 - 7.35 (6H, m), 5.56 (1H, dt, *J* = 17.1 Hz, 10.0 Hz), 5.23 - 5.16 (2H, m), 4.07 (1H, br s), 3.82 (1H, t, *J* = 2.7 Hz), 3.60 (1H, dt, *J* = 9.8 Hz, 6.9 Hz), 3.51 (1H, d, *J* = 10.3 Hz), 3.44 (1H, d, *J* = 10.3 Hz), 2.58 (1H, dd, *J* = 10.0 Hz, 9.8 Hz), 1.87 - 1.82 (2H, m), 1.80 - 1.66 (3H, m), 1.06 (9H, s), 0.69 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.8, 135.7, 135.61, 135.48, 135.55, 135.4, 132.3, 132.1, 130.0, 129.90, 127.82, 127.76, 127.74, 120.9, 77.2, 74.0, 71.5, 68.3, 49.0, 42.0, 27.2, 26.91, 26.86, 26.82, 19.1, 16.4; IR (neat): 3424.6 (br w), 3071.2 (w), 29292 (m), 2856.7 (w), 1784.4 (w), 1470.5 (2), 1442.5 (w), 1427.4 (m), 1390.2 (w), 1361.5 (w), 1264.8 (w), 1109.7 (w), 1078.1 (s), 1031.9 (m), 999.4 (m), 966.3 (w), 938.7 (w), 822.0 (m), 740.8 (m), 701.4 (s), 614.0 (m), 504.2 (s) cm^{-1}; HRMS-(ESI+) for $C_{26}H_{37}O_3Si$ [M+H]: calculated: 425.2512, found: 245.2515; $[\alpha]_D^{22}$: -10.37 (*c* = 2.890, $CHCl_3$, *l* = 10 mm).

Analysis of Stereochemistry:

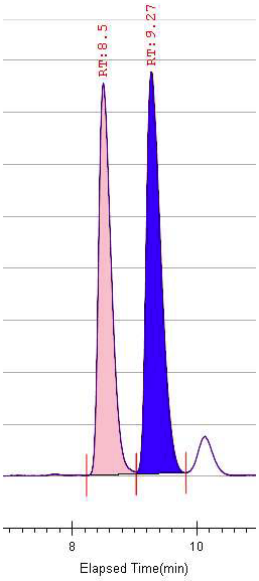
The enantioselectivity was determined by SFC analysis of the reaction product. A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*S,S*)-*i*Pr$_2$TADDOL-PPh. The relative stereochemistry was assigned by NOESY analysis. The following NOEs were observed:



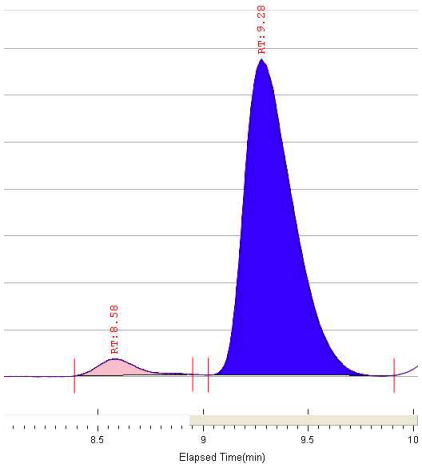
Chiral SFC (AD-H, Chiraldex, 3 mL/min, 8% i-PrOH, 100 bar 35 °C) - analysis of reaction product ***4d.***



Product from
(*R*,*R*)-*i*Pr$_2$TADDOL-PPh



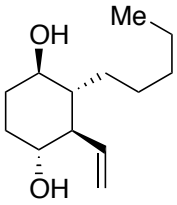
Mixture of products from
(*R*,*R*)- and (*S*,*S*)-ligands



Product from
(*S*,*S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

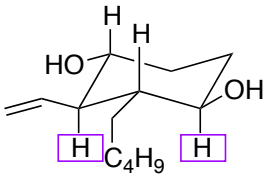
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	3.9127	438.6183	8.58	34.5948	0.0091
2	96.0873	10771.5411	9.28	672.8939	0.0098
Total:	100	11210.1594			



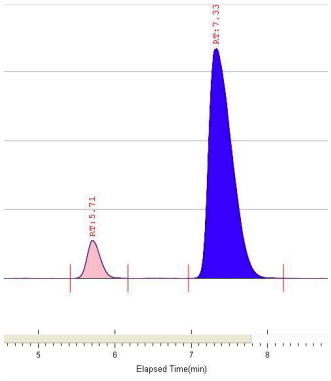
(1*R*,2*R*,3*S*,4*S*)-2-pentyl-3-vinylcyclohexane-1,4-diol (4e). The diboration was performed according to Representative Diboration/Double Allylation Procedure I with slight modification using (*Z*)-nona-1,3-diene (41.0 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.9 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 19.8 μmol), $B_2(pin)_2$ (87.9 mg, 0.35 mmol), and THF (0.66 mL, 0.5 M). After cooling to room temperature, the diboration reaction solvent was removed *in vacuo*. The reaction mixture was transferred to a vial containing succinaldehyde (85.2 mg, 0.99 mmol) with 0.5 mL DCM (0.5 M), purged with N_2, sealed and stirred at room temperature for 24 hours. Upon completion, the reaction mixture was warmed to room temperature, transferred to a 6-dram scintillation vial with THF (2 mL), and stirred with 2 mL of 3M NaOH for 3 hours. the reaction mixture was diluted with ethyl acetate (5 mL), transferred to a separatory funnel and washed with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified twice by column chromatography on silica gel (70:30 - 40:60 hexanes/ethyl acetate, then 30:1 - 20:1 DCM/methanol. R_f = 0.19 in 25:1 DCM/ methanol, stain in PMA) to afford a single diastereomer of the title compound as a white solid (27.0 mg, 39%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.50 (1H, dt, *J* = 17.1 Hz, 10.0 Hz), 5.24 (1H, dd, *J* = 10.0 Hz, 1.7 Hz), 5.17 (1H, dd, *J* = 17.1 Hz, 2.0 Hz), 3.44 (1H, dt, *J* = 10.3 Hz, 4.7 Hz), 3.26 - 3.21 (1H, m), 2.05 - 1.98 (2H, m), 1.96-1.95 (1H, m), 1.81 (1H, ddd, *J* = 9.5 Hz, 9.5 Hz, 9.5 Hz), 1.61 - 1.54 (1H, m), 1.41 - 1.31 (3H, m), 1.30 - 1.16 (9H, m), 0.85 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 119.2, 71.4, 71.3, 53.6, 45.8, 33.0, 32.4, 31.0, 28.2, 23.8, 22.6, 14.0; IR (neat): 3344.0 (m br), 3075.9 (2), 2921.1 (s), 2873.4 (s), 2859.6 (s), 1643.0 (2), 1456.7 (m), 1354.3 (m), 1151.0 (w), 1113.7 (w), 1069.7 (m), 1032.4 (s), 990.0 (m), 915.2 (m), 724.9 (2), 682.8 (m), 567.2 (w); HRMS-(ESI+) for $C_{13}H_{23}O_1$ [M+1-H_2O]: calculated: 195.1749, found: 195.1746. $[\alpha]_D^{23}$: -11.04 (*c* = 0.905, $CHCl_3$, *l* = 10 mm).

Analysis of Stereochemistry:

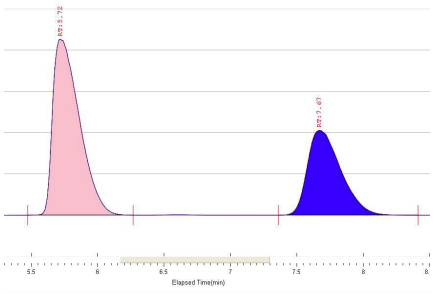
The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-*i*Pr$_2$TADDOL-PPh. The relative stereochemistry was assigned by 2D-NMR analysis. A COSY was used to elucidate the identity of the carbinol signals, and the following NOE was observed during NOESY analysis:



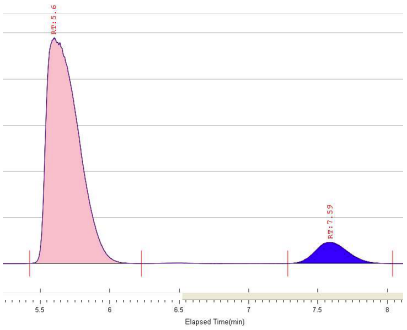
Chiral SFC (AD-H, Chiraldex, 3 mL/min, 5% MeOH, 100 bar, 35 °C) - analysis of reaction product ***4e****-bisbenzoate.*



Product from
(*R*,*R*)-*i*Pr$_2$TADDOL-PPh



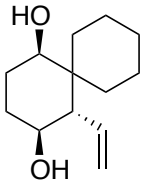
Mixture of products from
(*R*,*R*)- and (*S*,*S*)-ligands



Product from
(*S*,*S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

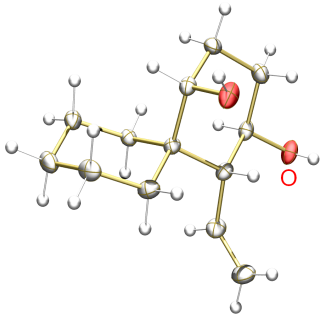
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	8.7479	3307.7824	5.71	274.7333	0.0053
2	91.2521	34504.479	7.33	1666.1093	0.0069
Total:	100	37812.2614			



(1R,4S,5S)-5-vinylspiro[5.5]undecane-1,4-diol (4f). The diboration was performed according to Representative Diboration/Double Allylation Procedure I with allylidenecyclohexane[3] (40.3 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.9 μmol), (*R,R*)-di-iso-propylTADDOL-PPh (10.8 mg, 11.9 μmol), $B_2(pin)_2$ (87.9 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M) and and succinaldehyde (56.8 mg, 0.66 mmol). The crude reaction mixture was purified by column chromatography on SiO_2 (67:33–50:50 hexanes/ethyl acetate) to afford a colorless oil (4.8 mg, 7%, *anti* diol) and a white solid (44.0 mg, 63%, *syn* diol, R_f = 0.14 in 50:50 hexanes/ethyl acetate, stain in PMA). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.72 (1H, dt, *J* = 16.9 Hz, 10.3 Hz), 5.31 (1H, dd, *J* = 10.0 Hz, 2.2 Hz), 5.18 (1H, ddd, *J* = 16.9 Hz, 2.2 Hz, 0.5 Hz), 4.20 (1H, t, *J* = 2.9 Hz), 3.59 (1H, dt, *J* = 4.5 Hz, 10.8 Hz), 2.05 (1H, t, *J* = 10.0 Hz), 1.90-1.83 (1H, m), 1.81-1.77 (1H, m), 1.76-1.08 (12H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.1, 121.1, 67.5, 65.8, 55.0, 40.9, 32.1, 28.6, 27.4, 26.33, 26.29, 21.2, 21.1; IR (neat): 3320.4 (br), 2923.0 (s), 2858.2 (m), 1451.1 (m), 1089.6 (w), 1064.7 (m), 1023.9 (m), 993.9 (s), 970.5 (m), 912.6 (m), 634.2 (m) cm^{-1}; HRMS-(ESI+) for $C_{13}H_{21}O_1$ [M+H-H_2O]: calculated: 193.1592, found: 193.1596. $[\alpha]_D^{23}$ = −46.83: (c = 0.64, $CHCl_3$, *l* = 10 mm).

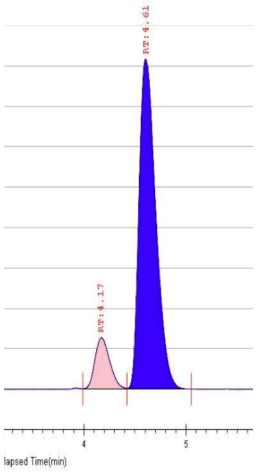
Analysis of Stereochemistry:

The enantioselectivity was determined by SFC analysis of the bis(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by crystallography using anomalous dispersion. Flack parameter = 0.18.

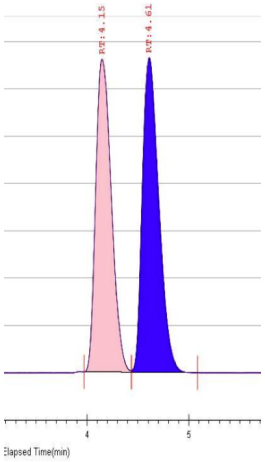


(*S,S*)-*i*Pr$_2$TADDOL-PPh used when this crystal structure was obtained

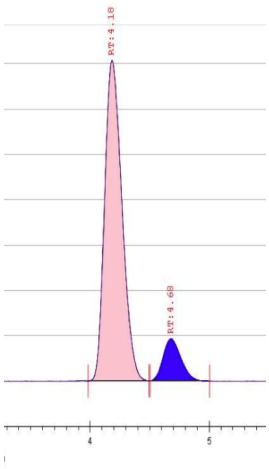
Chiral SFC (AD-H, Chiraldex, 3 mL/min, 10% MeOH, 100 bar, 35 °C)-analysis of the bis (benzoate) of reaction product ***4f****.*



Product from (*R*,*R*)-*i*Pr$_2$TADDOL-PPh



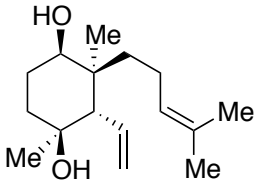
Mixture of products from (*R*,*R*)- and (*S*,*S*)-ligands



Product from (*S*,*S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

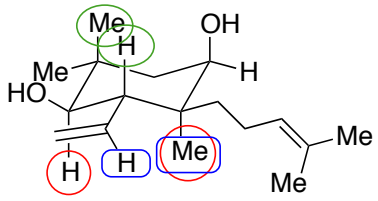
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	11.9326	2514.401	4.17	253.2321	0.0034
2	88.0674	18557.3147	4.61	1631.3881	0.0037
Total:	100	21071.7157			



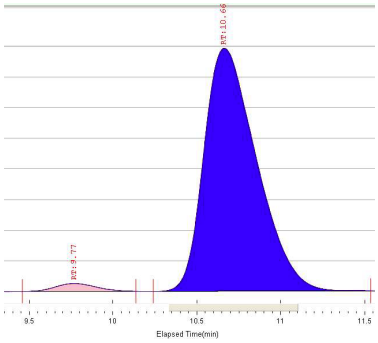
(1*S*,2*S*,3*S*,4*R*)-1,3-dimethyl-3-(4-methylpent-3-en-1-yl)-2-vinylcyclohexane-1,4-diol (4g): The diboration/double allylation was performed according to Representative Diboration/Double Allylation Procedure II using (*E*)-4,8-dimethylnona-1,3,7-triene (50 mg, 0.33 mmol), $Pt(dba)_3$ (8.9 mg, 9.0 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 12.0 μmol), $B_2(pin)_2$ (88.0 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M), and 4-oxopentenal (33.0 mg, 0.33 mmol). The crude reaction mixture was purified twice on SiO_2 (first purification: 70:30 - 40:60 hexanes/ethyl acetate, R_f = 0.26 in 25:1 DCM/methanol, stain in PMA) to afford a clear, colorless oil (64.9 mg, 78%, 11:1 *syn:anti* diol). A second purification on SiO_2 (25:1 DCM/methanol) was used to separate the diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.73 (1H, dt, *J* = 16.9 Hz, 10.3 Hz), 5.23 (1H, dd, *J* = 10.3 Hz, 2.4 Hz), 5.14 (1H, dd, *J* = 16.9 Hz, 2.2 Hz), 5.11 - 5.07 (1H, m), 3.61 (1H, t, *J* = 3.4 Hz), 2.18 (1H, d, *J* = 10.5 Hz), 1.99 - 1.92 (2H, m), 1.89 - 1.81 (2H, m), 1.76 - 1.72 (2H, m), 1.65 (3H, s), 1.59 - 1.55 (1H, m), 1.59 (3H, s), 1.43 (1H, br s), 1.39 (1H, br s), 1.34 - 1.29 (2H, m), 1.18 (3H, s), 0.91 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.0, 131.6, 124.9, 120.4, 71.4, 71.3, 57.7, 39.9, 38.5, 33.5, 26.6, 25.7, 25.6, 21.6, 19.1, 17.6; IR (neat): 3416.7 (m br), 3072.0 (w), 2965.8 (m), 2924.9 (s), 1634.8 (w), 1451.3 (m), 1419.2 (w), 1381.8 (s), 1328.1 (w), 1279.5 (w), 1197.2 (m), 1107.7 (m), 1062.9 (s), 1039.9 (m), 1017.4 (s), 974.0 (m), 910.0 (s), 883.8 (w), 833.5 (w), 809.4 (w), 651.9 w), 548.3 (w), 448.1 (w); HRMS-(ESI+): for $C_{16}H_{27}O_1$ [M+1-H_2O]: calculated: 235.20619, found: 235.20727. $[\alpha]_D^{22}$: -52.58 (*c* = 0.95, $CHCl_3$, *l* = 10 mm).

Proof of Stereochemistry:

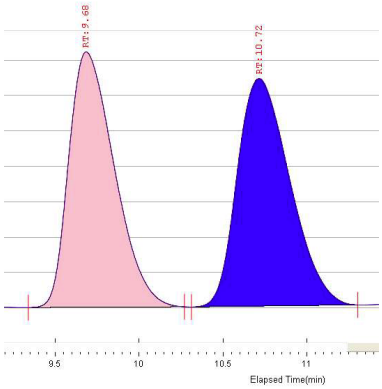
The enantioselectivity was determined by SFC analysis of the mono(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-*i*Pr$_2$TADDOL-PPh. The relative stereochemistry was assigned by NOESY analysis. The following NOEs were observed:



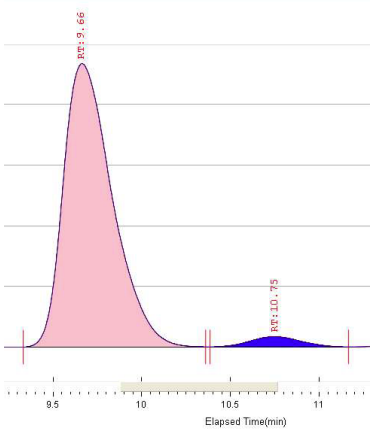
Chiral SFC (AD-H, Chiraldex, 1.5 mL/min, 5% MeOH, 100 bar, 35 °C)- analysis of reaction the mono(benzoate) of reaction product ***4g****.*



Product from
(*R,R*)-*i*Pr$_2$TADDOL-PPh



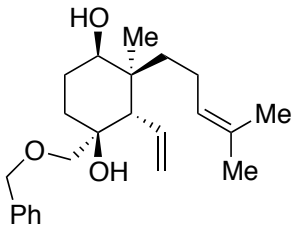
Mixture of products from
(*R,R*)- and (*S,S*)-ligands



Product from
(*S,S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

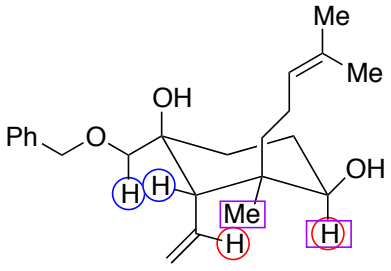
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	2.4744	437.3655	9.77	25.9145	0.012
2	97.5256	17238.2324	10.66	792.2277	0.0131
Total:	100	17675.5979			



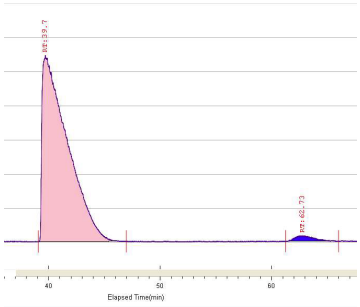
(1*R*,2*R*,3*S*,4*R*)-1-((benzyloxy)methyl)-3-methyl-3-(4-methylpent-3-en-1-yl)-2-vinylcyclohexane-1,4-diol (4h): The diboration/double allylation was performed according to Representative Diboration/Double Allylation Procedure II using 5-(benzyloxy)-4-oxopentanal (50 mg, 0.33 mmol) $Pt(dba)_3$ (8.9 mg, 9.0 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (10.8 mg, 12.0 μmol)), $B_2(pin)_2$ (88.0 mg, 0.35 mmol), toluene (0.33 mL, 1.0 M), and 4-oxopentenal (68.0 mg, 0.33 mmol). The crude reaction mixture was purified on SiO_2 (5:1 - 3:1 hexanes/ethyl acetate, R_f = 0.26 in 1:1 hexanes/ethyl acetate, stain in PMA) to afford a colorless oil (71.0 mg, 60%, d.r. = > 20:1 *syn:anti* diol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 - 7.31 (2H, m), 7.29 - 7.25 (3H, m), 5.60 (1H, dt, *J* = 16.6 Hz, 10.0 Hz), 5.13 (1H, tt, *J* = 7.1 Hz, 1.5 Hz), 5.07 - 5.01 (2H, m), 4.50 (1H, d, *J* = 12.0 Hz), 4.45 (1H, d, *J* = 12.0 Hz), 3.59 (1H, dd, *J* = 10.0 Hz, 3.7 Hz), 3.32 (1H, d, *J* = 9.1 Hz), 3.18 (1H, d, *J* = 8.8 Hz), 2.66 (1H, s), 2.41 (1H, d, *J* = 10.0 Hz), 2.07 - 1.98 (2H, m), 1.95 - 1.85 (2H, m), 1.75 - 1.70 (1H, m), 1.66 (3H, s), 1.65 - 1.53 (2H, m), 1.60 (3H, s), 1.38 (1H, br s), 1.32 - 1.26 (1H, m), 0.87 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.1, 135.7, 131.0, 128.3, 127.6, 127.5, 125.4, 118.2, 76.9, 74.9, 73.4, 72.8, 54.0, 39.9, 33.7, 30.2, 26.2, 25.7, 23.9, 22.4, 17.6; IR (neat): 3444.4 (br w), 3069.4 (w), 3029.0 (w), 2961.9 (m), 2928.8 (m), 2859.1 (m), 1496.4 (w), 1452.8 (m), 1375.4 (m), 1252.1 (w), 1202.2 (w), 1092.4 (s), 1058.7 (s), 1028.5 (m), 998.5 (m), 915.4 (m), 839.7 (w), 735.9 (s), 697.5 (s), 579.1 (w), 357.4 (w), 412.5 (m); HRMS-(ESI+): for $C_{23}H_{33}O_2$ [M+H-H_2O]: calculated: 342.2481, found: 341.2475. $[\alpha]_D^{22}$: -52.58 (*c* = 0.95, $CHCl_3$, *l* = 10 mm).

Proof of Stereochemistry:

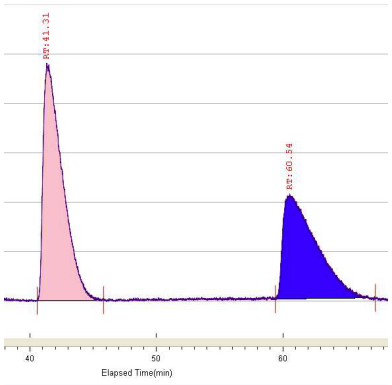
The enantioselectivity was determined by SFC analysis of the reaction product. A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-di-*iso*-propylTADDOL-PPh. The relative stereochemistry was determined by NOESY analysis. The following NOEs were observed:



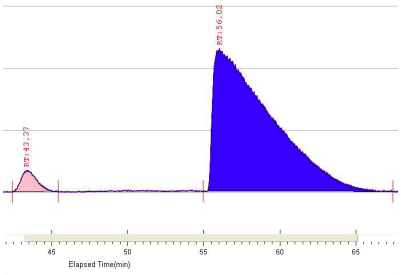
Chiral SFC (AD-H, Chiraldex, 3.0 mL/min, 5% i-PrOH, 100 bar, 35 °C) - analysis of reaction product ***4h.***



Product from
(*R*,*R*)-*i*Pr$_2$TADDOL-PPh



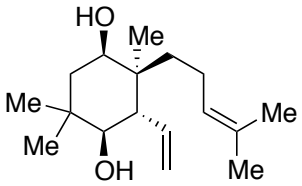
Mixture of products from
(*R*,*R*)- and (*S*,*S*)-ligands



Product from
(*S*,*S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

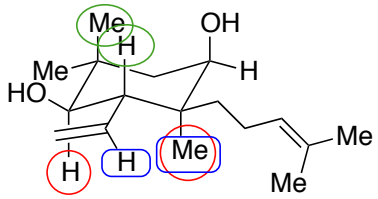
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	97.9452	43039.9397	39.7	272.5994	0.0412
2	2.0548	902.9478	62.73	8.087	0.0651
Total:	100	43942.8875			



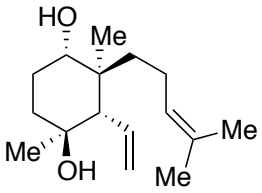
(1*R*,2*S*,3*S*,4*R*)-2,5,5-trimethyl-2-(4-methylpent-3-en-1-yl)-3-vinylcyclohexane-1,4-diol (4i): The diboration was performed according to Representative Diboration/Double Allylation Procedure I with slight modification using (*E*)-4,8-dimethylnona-1,3,7-triene (75.1 mg, 0.50 mmol), $Pt(dba)_3$ (13.5 mg, 15.0 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (16.4 mg, 18.0 μmoll), $B_2(pin)_2$ (133.3 mg, 0.525 mmol), and toluene (0.5 mL, 1.0 M). After cooling to room temperature, the reaction mixture was transferred to a vial containing 2,2-dimethylsuccinaldehyde (28.5 mg, 0.25 mmol) using minimal toluene. The crude reaction mixture was purified on SiO_2 (10:1 - 30:70 hexanes/ethyl acetate, R_f = 0.24 in 6:1 hexanes/ethyl acetate, stain in PMA) to afford a single diastereomer of the title compound as a yellow oil (36.4 mg, 54% yield, >20:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (1H, dt, *J* = 16.9 Hz, 10.0 Hz), 5.28 (1H, dd, *J* = 9.2 Hz, 2.0 Hz), 5.19 (1H, dd, *J* = 16.9 Hz, 2.0 Hz), 5.10 (1H, dt, *J* = 7.1 Hz, 1.2 Hz), 3.63 (1H, t, *J* = 2.9 Hz), 3.34 (1H, d, *J* = 10.8 Hz), 2.23 (1H, t, *J* = 10.3 Hz), 1.99 - 1.86 (2H, m), 1.65 (3H, s), 1.63 - 1.54 (2H, m), 1.58 (3H, s), 1.46 - 1.39 (2H, m), 1.23 - 1.17 (2H, m), 1.09 (3H, s), 1.02 (3H, s), 0.88 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.6, 131.7, 124.8, 120.7, 74.8, 72.6, 50.9, 41.5, 41.1, 38.5, 34.8, 30.9, 25.7, 22.0, 21.3, 18.2, 17.6; IR (neat): 3477.0 (br m), 3072.6 (w), 2965.6 (s), 2922.1 (s), 1636.5 (w), 1452.4 (m), 1377.6 (m), 1363.9 (m), 1260.0 (m), 1092.3 (m), 1037.8 (s), 1019.4 (s), 1000.5 (s), 965.6 (m), 919.8 (m), 882.7 (w), 811.0 (w), 743.3 (w), 663.7 (w), 539.5 (w), 522.6 (w), 455.7 (w), 445.4 (w), 416.5 (w); HRMS-(ESI+) for $C_{17}H_{29}O_1$ [M+H-H_2O]: calculated: 249.2218, found: 249.2228; $[\alpha]_D^{22}$: -88.65 (*c* = 1.465, $CHCl_3$, *l* = 10 mm).

Analysis of Stereochemistry:

Due to difficulties in dervitizing the title compound with a chromophore, the enantioselectivity was assigned by analogy to diboration/double allylation products derived from the geranial-diene and (*R,R*)-*i*Pr_2TADDOL-PPh. The absolute stereochemistry was assigned by analogy to other products derived from (*R,R*)-di-*iso*-propylTADDOL-PPh. The relative stereochemistry was assigned by NOESY analysis. The following NOEs were observed:



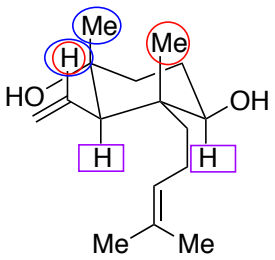
IV. Synthesis and Characterization of Pumilaside B aglycon



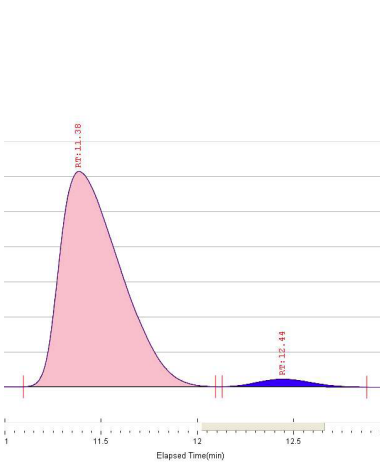
(1*S*,2*S*,3*R*,4*R*)-1,3-dimethyl-3-(4-methylpent-3-en-1-yl)-2-vinylcyclohexane-1,4-diol (8): The diboration/double allyation was performed according to Representative Diboration/Double Allylation Procedure II with slight modification using (*Z*)-4,8-dimethylnona-1,3,7-triene (1.476 g, 9.822 mmol) $Pt(dba)_3$ (88.2 mg, 98.2 μmol), (*R,R*)-di-*iso*-propylTADDOL-PPh (107.2 mg, 117.8 μmol), $B_2(pin)_2$ (2.619 g, 10.31 mmol), toluene (9.8 mL, 1.0 M), and 4-oxopentenal (1.18 g, 11.79 mmol) in a large pressure vessel. The crude reaction mixture was purified twice on SiO_2 (first purification: 70:30 - 40:60 hexanes/ethyl acetate, second purification: 30:1 - 20:1 DCM/methanol, R_f = 0.25 in 25:1 DCM/methanol, stain in PMA) to afford a clear, colorless oil (1.66 g, 67%, d.r. = 5:1 *anti:syn* diol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.82 (1H, dt, *J* = 17.1 Hz, 10.3 Hz), 5.29 (1H, dd, *J* = 10.3 Hz, 2.2 Hz), 5.19 (1H, dd, *J* = 17.1 Hz, 2.4 Hz), 5.02 (1H, dt, *J* = 7.1 Hz, 1.0 Hz), 3.56 (1H, dd, *J* = 10.8 Hz, 3.4 Hz), 2.05 (1H, d, *J* = 10.5 Hz), 2.00 (1H, br s), 1.91 (2H, dd, *J* = 7.8 Hz, 7.6 Hz), 1.80 - 1.75 (2H, m), 1.64 (3H, s), 1.62 - 1.47 (2H, m), 1.56 (3H, s), 1.42 - 1.36 (2H, m), 1.23 - 1.17 (1H, m), 1.18 (3H, s), 0.89 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.7, 131.5, 124.5, 120.5, 72.9, 71.1, 57.3, 40.5, 38.7, 38.0, 28.2, 25.7, 25.1, 21.2, 17.6, 16.0; IR (neat): 3420.2 (br m), 3072.3 (w), 2968.6 (m), 2924.9 (s), 2872.4 (m), 1634.7 (w), 1555.5 (m), 1450.1 (m), 1381.7 (m), 1312.5 (w), 1130.2 (m), 1075.3 (s), 1037.0 (s), 1001.3 (m), 951.8 (s), 916.0 (s), 879.2 (w), 832.1 (w), 812.0 (w), 670.6 (m), 558.0 (w), 437.3 (w); HRMS-(ESI+): for $C_{16}H_{27}O_1$ [M+H-H_2O]: calculated 235.2062, found: 235.2070. $[\alpha]_D^{23}$: +6.70 (c = 1.490, $CHCl_3$, *l* = 10 mm).

Proof of Stereochemistry:

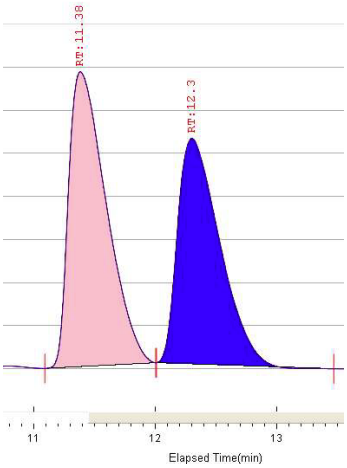
The enantioselectivity was determined by SFC analysis of the mono(benzoate) of the reaction product (prepared using benzoic anhydride, triethylamine, and catalytic DMAP). A mixture of the products made using (*R,R*)-di-*iso*-propylTADDOL-PPh and (*S,S*)-di-*iso*-propylTADDOL-PPh as the ligands in the diboration reaction were used to determine separation conditions.The relative stereochemistry was assigned by NOESY analysis. The following NOEs were observed:



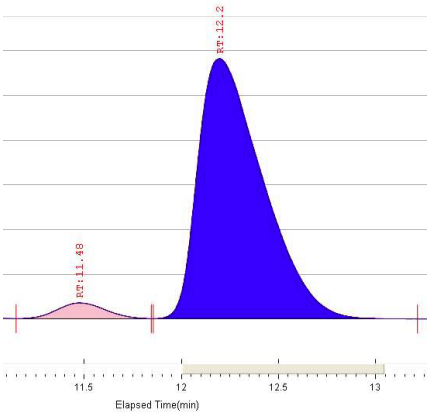
Chiral SFC (AD-H, Chiraldex, 1.5 mL/min, 5% MeOH, 100 bar , 35 °C)- analysis of mono (benzoate) of reaction product* ***8****.*



Product from
(*R*,*R*)-*i*Pr$_2$TADDOL-PPh



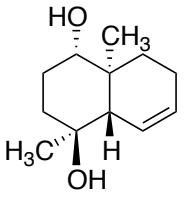
Mixture of products from
(*R*,*R*)- and (*S*,*S*)-ligands



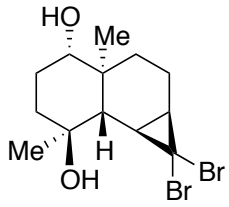
Product from
(*S*,*S*)-*i*Pr$_2$TADDOL-PPh

Peak Info

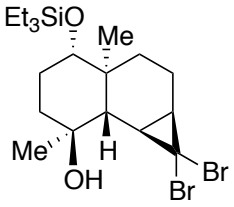
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.2653	1199.9207	11.48	70.2127	0.0152
2	95.7347	26932.0117	12.2	1163.3115	0.0162
Total:	100	28131.9324			



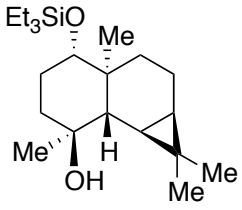
(1*S*,4*S*,4a*S*,8a*S*)-1,4a-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalene-1,4-diol (9): To a flame-dried 3-neck round bottom flask equipped with a stir bar and a reflux condensor was added the diol from the previous step (48 mg, 0.19 mmol). The flask was purged with N_2, and benzene (1.9 mL, 0.1 M) was added. Hoveyda-Grubbs Catalyst 2nd Generation (14.3 mg, 22.8 μmol) was added in a single portion, and the flask was resealed with a septum and purged with N_2. The reaction was then heated to 60 °C for 12 hours, slowly purging the entire solvent volume over the reaction time. Upon completion, the mixture was transferred to a 6-dram scintillation vial with diethyl ether and concentrated. The crude reaction mixture was purified on SiO_2 (25:1 DCM/methanol, R_f = 0.18 in 25:1 DCM/MeOH, stain in PMA) to afford an off-white foamy solid (37.0 mg, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.73 - 5.68 (2H, m), 3.38 (1H, dd, *J* = 11.3 Hz, 4.2 Hz), 2.08 - 2.06 (3H, m), 1.83 - 1.75 (3H, m), 1.70 - 1.61 (1H, m), 1.53 - 1.47 (1H,m), 1.34 - 1.28 (2H, m), 1.23 (1H, s), 01.12 (3H, s), 0.86 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 127.1, 124.8, 77.9, 71.5 52.4, 40.7, 37.9, 35.7, 28.9, 22.6, 22.5, 12.2; IR (neat): 3352.5 (br m), 3024.5 (w), 2970.8 (w), 2925.1 (m), 2857.0 (m), 1455.5 (m), 1381.3 (m), 1337.2 (m), 1235.6 (w), 1183.1 (m), 1159.7 (m), 1117.3 (m), 1069.7 (s), 1046.3 (s), 1031.1 (m), 1010.4 (m), 996.3 (m), 973.6 (m), 952.5 (m), 912.2 (s), 854.5 (w), 826.9 (m), 784.0 (m), 658.6 (s), 636.6 (s), 581.6 (m), 454.2 (w); HRMS-(ESI+) for $C_{12}H_{19}O_1$ [M+H-H_2O]: calculated: 179.1436, found: 179.1442; $[\alpha]_D^{24}$: +28.04 (*c* = 1.425, $CHCl_3$, *l* = 10 mm).



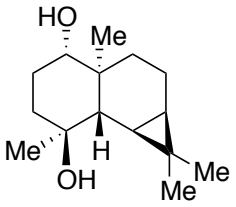
(1a*R*,3a*S*,4*S*,7*S*,7a*S*,7b*S*)-1,1-dibromo-3a,7-dimethyldecahydro-1*H*-cyclopropa[*a*]naphthalene-4,7-diol (10): The title compound was prepared according to the literature procedure.[5] To a 6-dram scintillation vial equipped with a stir bar was added the diol from the previous step (232.0 mg, 1.182 mmol), DCM (2.3 mL, 0.5 M), and bromoform (4.1 mL, 47.28 mmol). Finely powdered NaOH (804.0 mg, 20.09 mmol) was then added in a single portion. The vial was sealed with a teflon-lined cap and heated to 50 °C for 64 hours. Upon cooling, the solution was diluted with water (10 mL) and washed with DCM (3x10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified on SiO_2 (25:1 - 20:1 DCM/methanol, R_f = 0.28 in 25:1 DCM/methanol, stain in PMA) to afford a foamy white solid (325.3 mg, 70% yield, single diastereomer). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.27 (1H, dd, *J* = 10.5 Hz, 3.9 Hz), 1.91 - 1.81 (3H, m), 1.79 - 1.74 (3H, m), 1.65 - 1.51 (4H, m), 1.28 (3H, s), 1.23 (1H, s), 1.20 (1H, d, *J* = 5.4 Hz), 0.95 (1H, dt, *J* = 12.7 Hz, 7.6 Hz), 0.81 (3H, s) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 77.6, 72.0, 51.1, 40.6, 40.4, 37.3, 34.1, 28.8, 27.9, 26.6, 23.3, 16.6, 14.0; IR (neat): 3675.3 (br m), 2970.4 (m), 2934.5 (m), 2870.3 (m), 1559.4 (w), 1458.0 (w), 1438.4 (w), 1384.0 (m), 1338.9 (w), 1279.3 (w), 1279.3 (w), 1247.5 (w), 1162.3 (w), 1112.3 (m), 1085.2 (m), 1075.0 (m), 1058.1 (m), 1033.3 (s), 1002.6 (w), 951.8 (w), 911.8 (w), 859.0 (w), 835.8 (w), 722.0 (m), 709.7 (s), 668.8 (m), 643.4 (m), 571.8 (w), 495.8 (w), 452.5 (w); HRMS-(ESI+) for $C_{13}H_{24}N_1Br_2O_2$ [M+NH_4]: calculated: 384.0174, found: 384.0169. $[\alpha]_D^{23}$: +8.72 (*c* = 1.145, $CHCl_3$, *l* = 10 mm).



(1a*R*,3a*S*,4*S*,7*S*,7a*S*,7b*S*)-1,1-dibromo-3a,7-dimethyl-4-((triethylsilyl) oxy)decahydro-1*H*-cyclopropa[*a*]naphthalen-7-ol: To a round bottom flask equipped with a stir bar was added the diol from the previous step (92 mg, 0.25 mmol) and imidazole (20.4 mg, 0.299 mmol). The flask was sealed with a septum and purged with N_2. Next, imidazole was added as a single portion, and the solution changed from clear and colorless to cloudy white. The reaction was allowed to stir at room temperature for 2.5 hours. Upon completion, the solution was diluted with water (15 mL), transferred to a separatory funnel and washed with DCM (3x15 mL). The combined organic layers were dried over MgSO4, filtered, and concentrated *in vacuo*. The crude mixture was purified on SiO_2 (5:1 - 2:1 pentane/ether, R_f = 0.33 in 5:1 pentane/ether, stain in PMA) to afford a foamy white solid (89.0 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.26 - 3.19 (1H, m), 1.89 - 1.78 (3H, m), 1.76 - 1.70 (2H, m), 1.66 - 1.59 (2H, m), 1.55 - 1.47 (2H, m), 1.31 (1H, br s), 1.27 (3H, s), 1.16 (1H, d, *J* = 5.5 Hz), 0.91 (9H, t, *J* = 8.0 Hz), 0.82 (1H, dt, *J* = 12.5 Hz, 7.5 Hz), 0.76 (3H, s), 0.57 - 0.49 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 78.2, 72.0, 51.2, 41.0, 40.5, 37.9, 34.4, 29.3, 28.2, 26.9, 23.3, 16.8, 14.4, 6.9, 5.2; IR (neat): 3360.0 (br w), 2947.5 (m), 2912.1 (m), 2874.2 (m), 1458.4 (m), 1412.7 (w), 1385.0 (m), 1356.2 (w), 1332.6 (w), 1237.9 (w), 1163.0 (2), 1096.8 (s), 1067.4 (s), 1052.2 (m), 1004.0 (m), 972.2 (w), 956.1 (w), 935.4 (w), 913.8 (w), 878.0 (w), 859.7 (w), 840.8 (m), 825.1 (m), 771.3 (m), 740.0 (s), 724.9 (s), 711.1 (s), 670.9 (m), 550.7 (2), 520.3 (w), 488.4 (w), 415.8 (w); HRMS-(ESI+): for $C_{19}H_{33}Br_2O_1Si$ [M+H-H_2O]: calculated: 463.0667, found: 463.0661; $[\alpha]_D^{24}$: +18.54 (*c* = 2.155, $CHCl_3$, *l* = 10 mm)



(1a*R*,3a*S*,4*S*,7*S*,7a*S*,7b*R*)-1,1,3a,7-tetramethyl-4-((triethylsilyl)oxy) decahydro-1*H*-cyclopropa[*a*]naphthalen-7-ol: The title compound was prepared according to the literature procedure[6] with slight modificaiton. To an aluminum foil-wrapped flame-dried round bottom flask equipped with a stir bar was added CuI (748 mg, 3.93 mmol), and the flask was purged with N_2. The CuI was suspended in anhydrous Et_2O (2.0 mL) and cooled to – 78 °C. Upon cooling, a 1.71 M solution of MeLi (4.61 mL, 7.88 mmol) was added slowly over 30 minutes, then slowly warmed to – 20 °C and stirred for an additional 10 minutes. The solution was then re-cooled to – 78 °C, and the dibromide from the previous step (190 mg, 0.393 mmol) was added as a solution in anhydrous Et_2O (0.6 mL, 0.66 M). The flask was sealed with parafilm and kept at 4 °C in the cold room for 28 hrs. The solution was then re-cooled to – 20 °C and iodomethane (0.98 mL, 15.72 mmol) was added slowly. The reaction was allowed to warm to room temperature and stir for 6 hours. The reaction was then diluted with $CHCl_3$ (5 mL) and Cu-salts precipitated as a white solid. The heterogeneous mixture was filtered over SiO_2 and concentrated *in vacuo*. The crude reaction mixture was purified on SiO_2 (8:1 - 4:1 pentane/Et_2O, R_f = 0.36 in 4:1 pentane/Et_2O, stain in PMA) to afford a white solid (75.2 mg, 54%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.22 - 3.14 (1H, m), 1.79 - 1.70 (2H, m), 1.63 - 1.58 (3H, m), 1.52 (1H, dd, *J* = 14.9 Hz, 7.6 Hz), 1.48 - 1.37 (2H, m), 1.24 (3H, s), 1.03 (3H, s), 0.94 - 0.90 (13H, m), 0.80 (3H, s), 0.61 - 0.49 (8H, m), 0.45 (1H, dd, *J* = 9.3 Hz, 6.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 78.9, 72.3, 48.0, 40.0, 38.2, 37.3, 29.3, 29.2, 23.1, 19.5, 18.8, 17.6, 15.5, 15.3, 13.5, 7.0, 5.2; IR (neat): 3447.1 (br w), 2936.9 (m), 2874.7 (m), 1468.6 (w), 1413.9 (w), 1381.8 (w), 1355.5 (w), 1332.1 (w), 1310.9 (w), 1237.3 (w), 1191.7 (w), 1162.6 (w), 1091.1 (s), 1057.0 (w), 1041.5 (w), 1002.9 (m), 983.8 (w), 956.6 (w), 933.8 (2), 915.3 (2), 868.3 (w), 828.3 (w), 797.3 (w), 741.7 (m), 725.8 (m), 688.2 (w); HRMS-(ESI+): for $C_{21}H_{41}O_2Si$ [M+H]: calculated: 335.2770, found: 355.2763; $[\alpha]_D^{23}$: +12.89 (*c* = 0.775, $CHCl_3$, *l* = 10 mm)



Pumilaside B aglycon: The title compound was prepared according to the literature procedure[7] with slight modification. To a 6-dram scintillation vial equipped with a stir bar was added the silyl ether from the previous step (61.7 mg, 0.175 mmol), followed by a 3:1:1 mixture of glacial acetic acid, water, and THF (1.0 mL, 0.35 mL, 0.35 mL, total concentration 0.1M). The reaction was stirred at room temperature for 3 hours until complete by TLC. The solution was diluted with water (15 mL) and transferred to a separatory funnel and washed with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified on SiO_2 (25:1 DCM/methanol, R_f = 0.25 in 25:1 DCM/methanol, stain in PMA) to afford a white solid (41 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.20 (1H, dd, *J* = 11.0 Hz, 4.2 Hz), 1.80 (1H, dt, *J* = 12.2 Hz, 2.9 Hz), 1.77 - 1.70 (2H, m), 1.65 - 1.61 (1H, m), 1.59 - 1.53 (2H, m), 1.50 - 1.44 (2H, m), 1.25 (3H, s), 1.03 (3H, s), 0.96 (1H, d, *J* = 6.1 Hz), 0.91 (3H, s), 0.83 (3H, s), 0.67 (1H, dt, *J* = 13.0 Hz, 7.6 Hz), 0.62 (1H, t, *J* = 9.1 Hz), 0.47 (1H, dd, *J* = 9.3 Hz, 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 78.4, 72.2, 47.9, 39.9, 37.6, 36.9, 29.2, 28.7, 23.1, 19.3, 18.6, 17.6, 15.4, 15.1, 13.2; IR (neat): 3397.5 (br m), 2928.3 (s), 2861.5 (m), 1708.0 (w), 1673.1 (w), 1458.7 (m), 1381.6 (m), 1343.3 (w), 1285.9 (w), 1257.4 (w), 1185.7 (2), 1161.3 (m), 1122.3 (w), 1103.8 (w), 1077.9 (m), 1037.4 (m), 1014.2 (w), 1000.0 (m), 982.8 (m), 953.4 (w), 928.1 (w), 882.0 (w), 832.0 (w), 798.0 (w), 751.6 (w), 643.0 (m); HRMS-(ESI+) for $C_{15}H_{25}O_1$ [M+1-H_2O]: calculated: 221.1905, found: 221.1912. $[\alpha]_D^{23}$: +49.95 (*c* = 0.200, MeOH, *l* = 10 mm); melting point: 108.6 - 110.4 °C.

Pumilaside B aglycon ^{1}H NMR (d_5-pyridine):

Reported (ppm)	Found (ppm)	Δδ (ppm)	ΔHz
0.64 (3H, t) *J* = 6.5Hz	0.65 (3H, t) *J* = 8.6 Hz	+0.01	+2.1
0.91 (1H, dd) *J* = 9.0 Hz, 6.0 Hz	0.90-0.98 (2H, m)		
1.05 (3H, s)	1.06 (3H, s)	+0.01	
1.10 (3H, s)	1.10 (3H, s)	0	
1.22 (3H, s)	1.22 (3H, s)	0	
1.42 (1H, d) *J* = 6.0 Hz)	1.42 (1H, d) *J* = 5.9 Hz	0	-0.01
1.53 (3H, s)	1.54 (3H, s)	+0.01	
nd	1.67 (1H, dd) *J* = 14.7, 7.1 Hz		
nd	1.98-1.87 (2H, m)		
nd	2.07-2.00 (3H, m)		
nd	2.18 (1H, dd) *J* = 13.0, 8.3 Hz		
3.59 (1H, t) *J* = 7.0 Hz	3.59 (1H, t) *J* = 6.6 Hz	0	-0.4

Pumilaside B aglycon ^{13}C NMR (d_5-pyridine):

Reported (ppm)	Found (ppm)	Δδ (ppm)
78.12	78.15	+0.03
71.63	71.64	+0.01
48.63	48.67	+0.04
41.89	41.93	+0.04
38.51	38.54	+0.03
37.83	37.86	+0.03
30.09	30.13	+0.04
29.61	29.64	+0.03
23.74	23.78	+0.04
21.08	21.12	+0.04
18.99	19.04	+0.05
17.53	17.55	+0.02
16.02	16.05	+0.03
15.74	15.76	+0.02
14.45	14.45	0

References*:*

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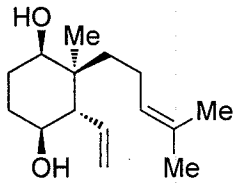
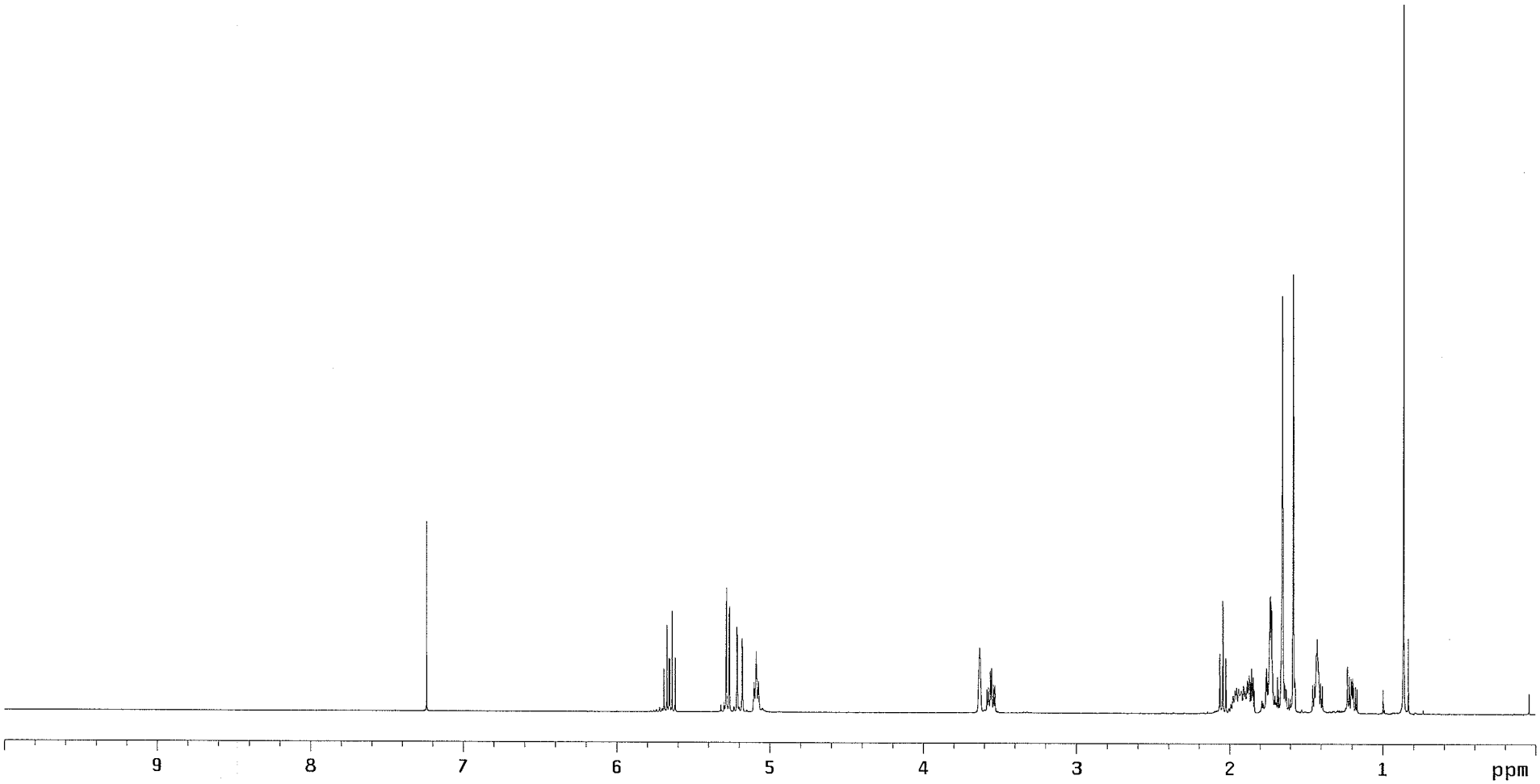
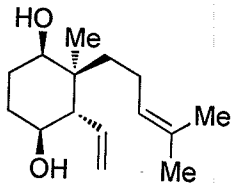
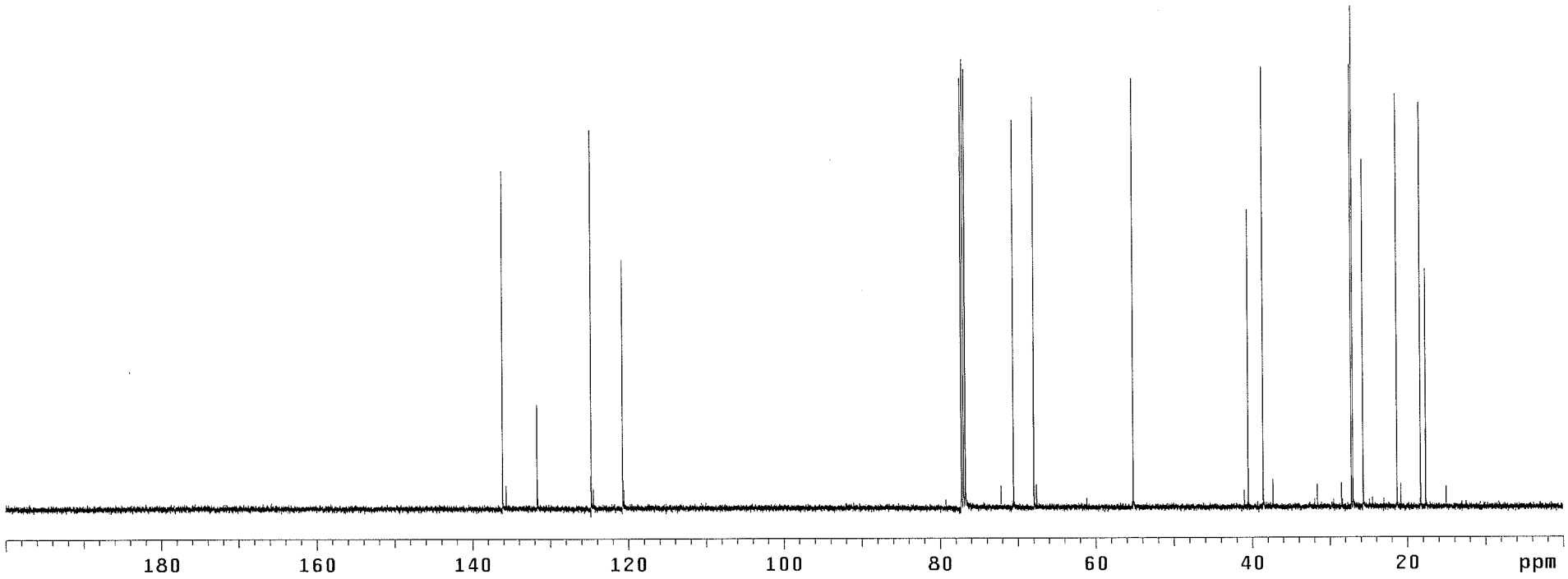


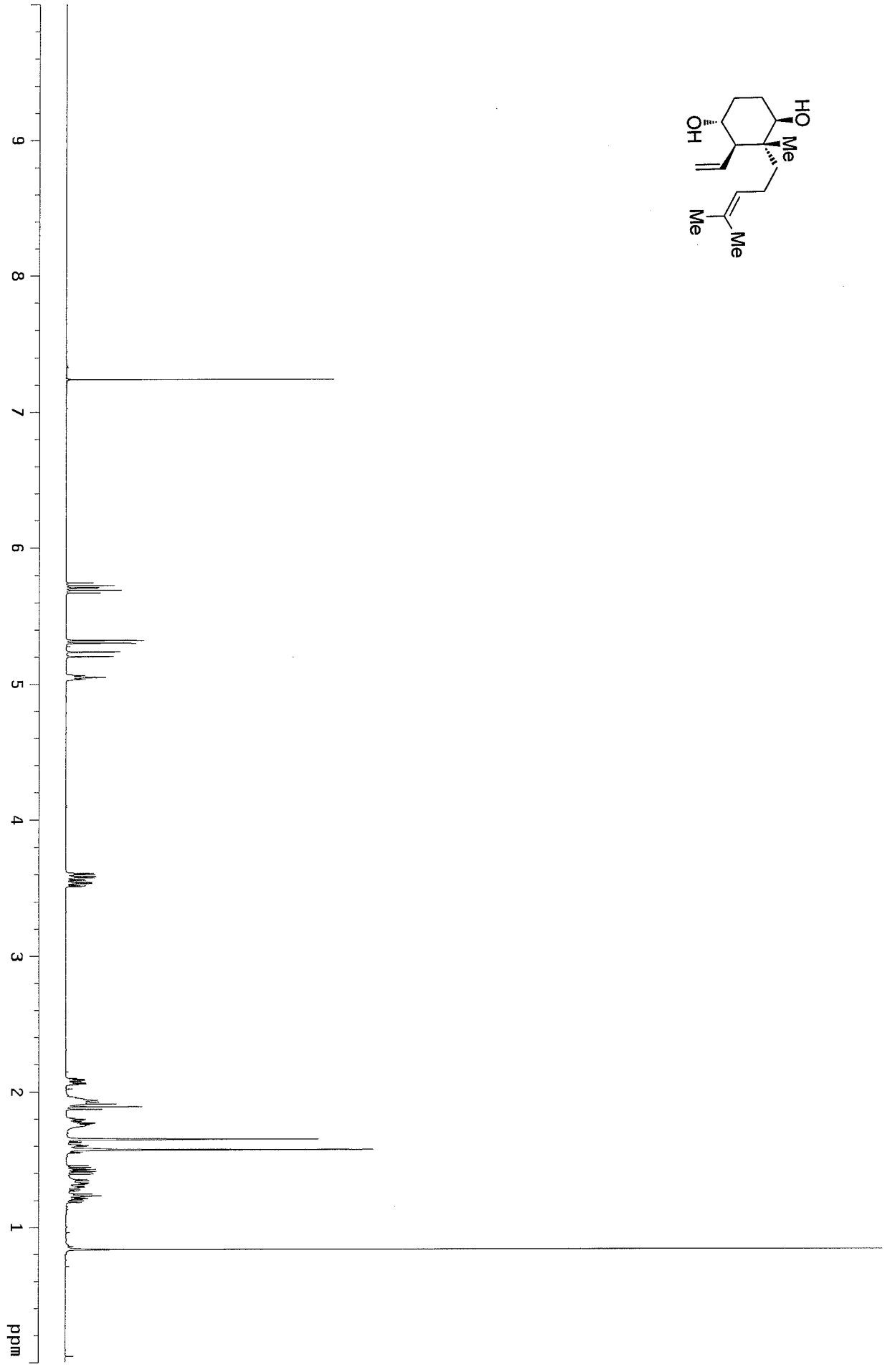
with minor diastereomer





with minor diastereomer

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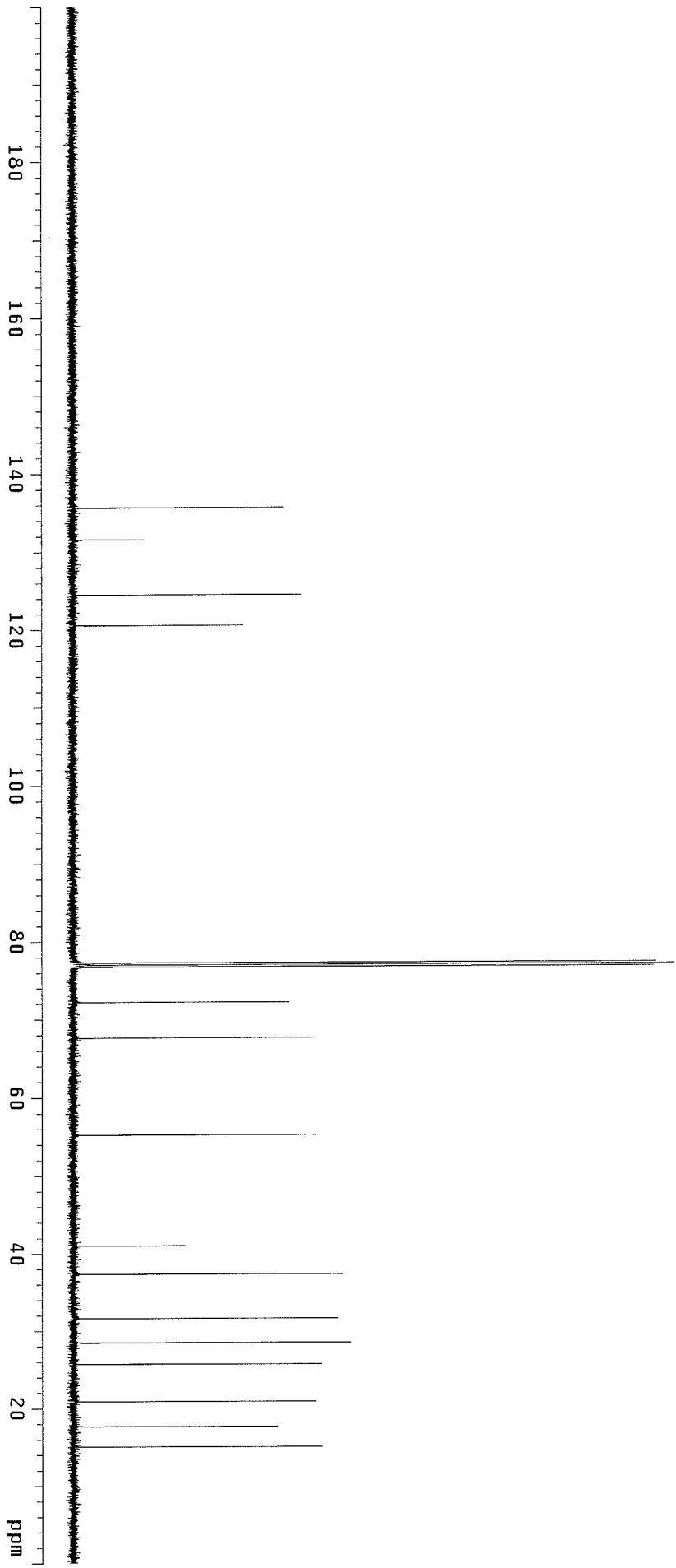
Me
Me
9
8
7
6
5
4
3
2
1
ppm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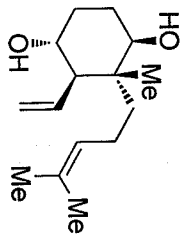
140
120
100
80
60
40
20
ppm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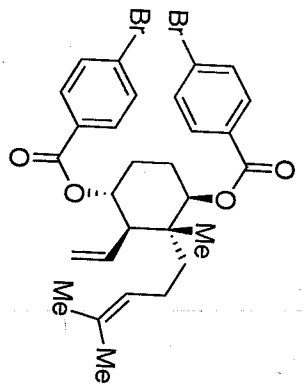
OH
Me
Me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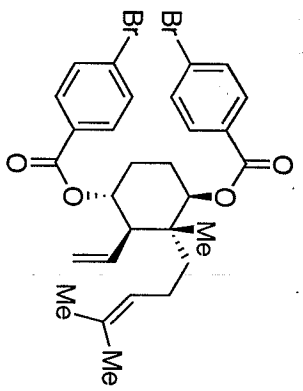
Br
O
O
O
O
Me
Me
Me

8
7
6
5
4
3
2
1
ppm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Br
O
O
O
O
Me
Me
Me

F1 (ppm)
F2 (ppm)
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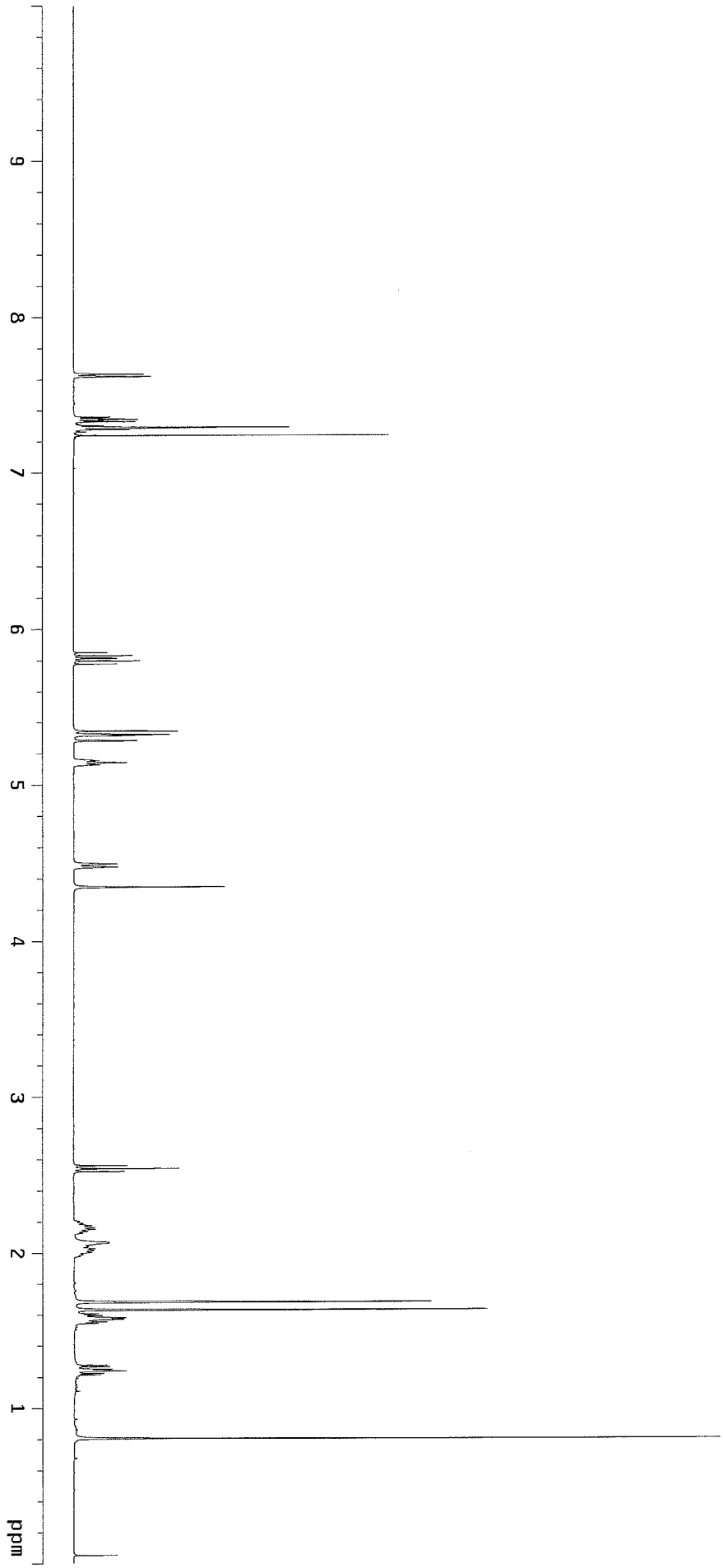
7
6
5
4
3
2
1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4
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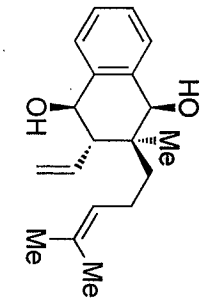
ppm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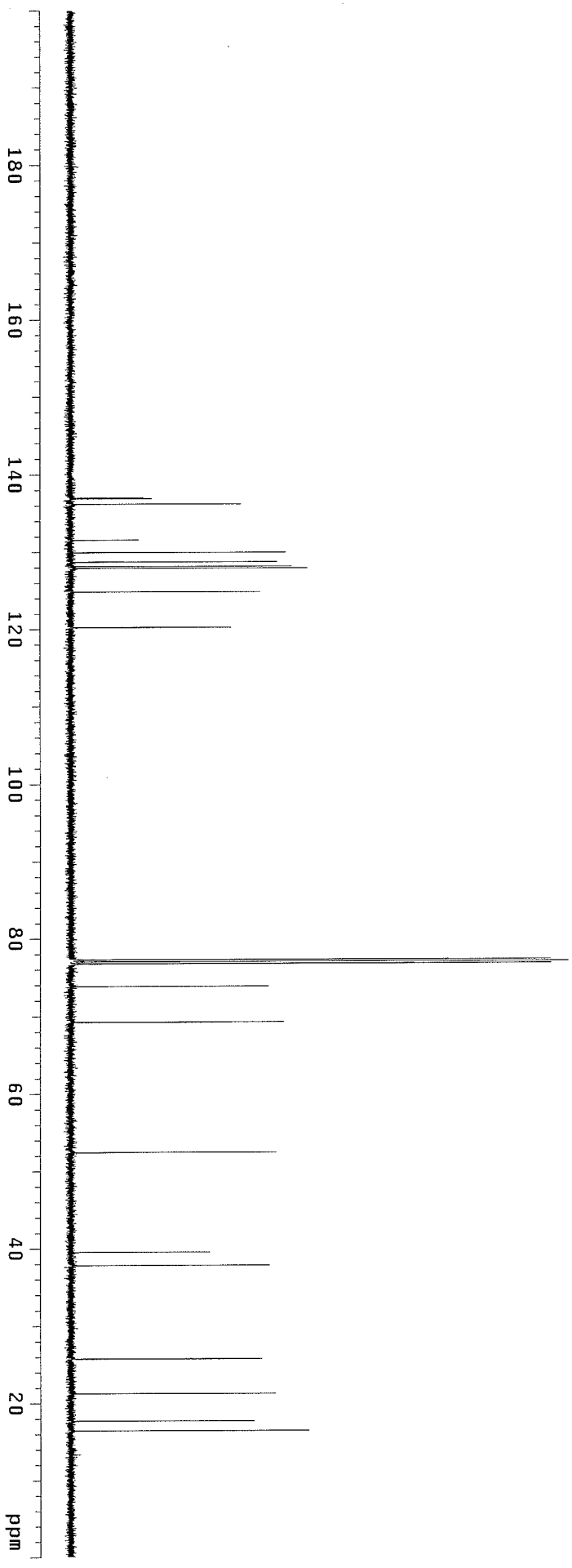
OH
Me
Me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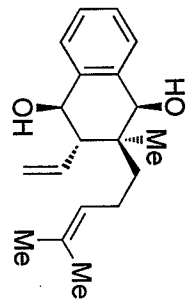
80
60
40
20
ppm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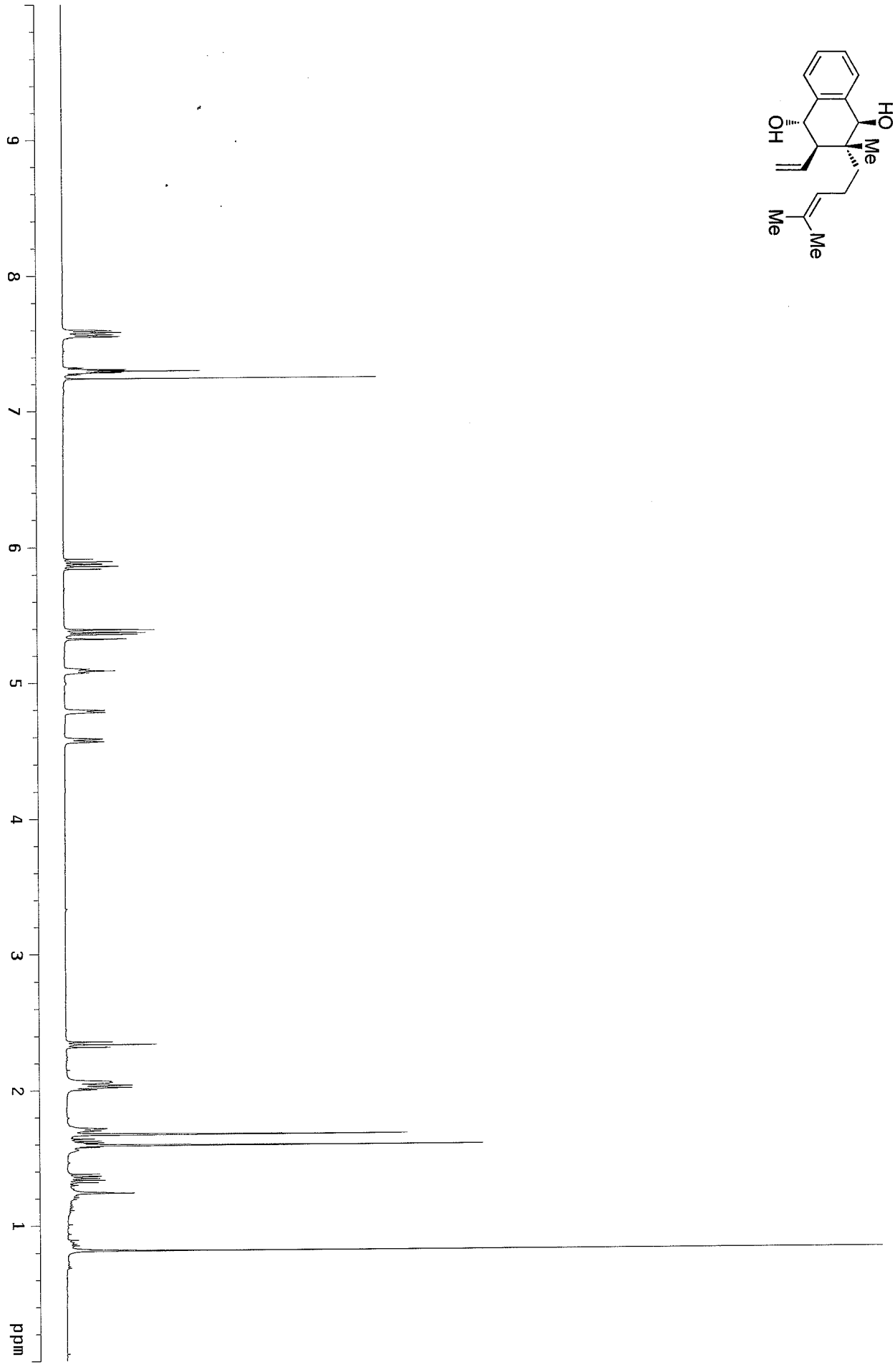
OH
Me
Me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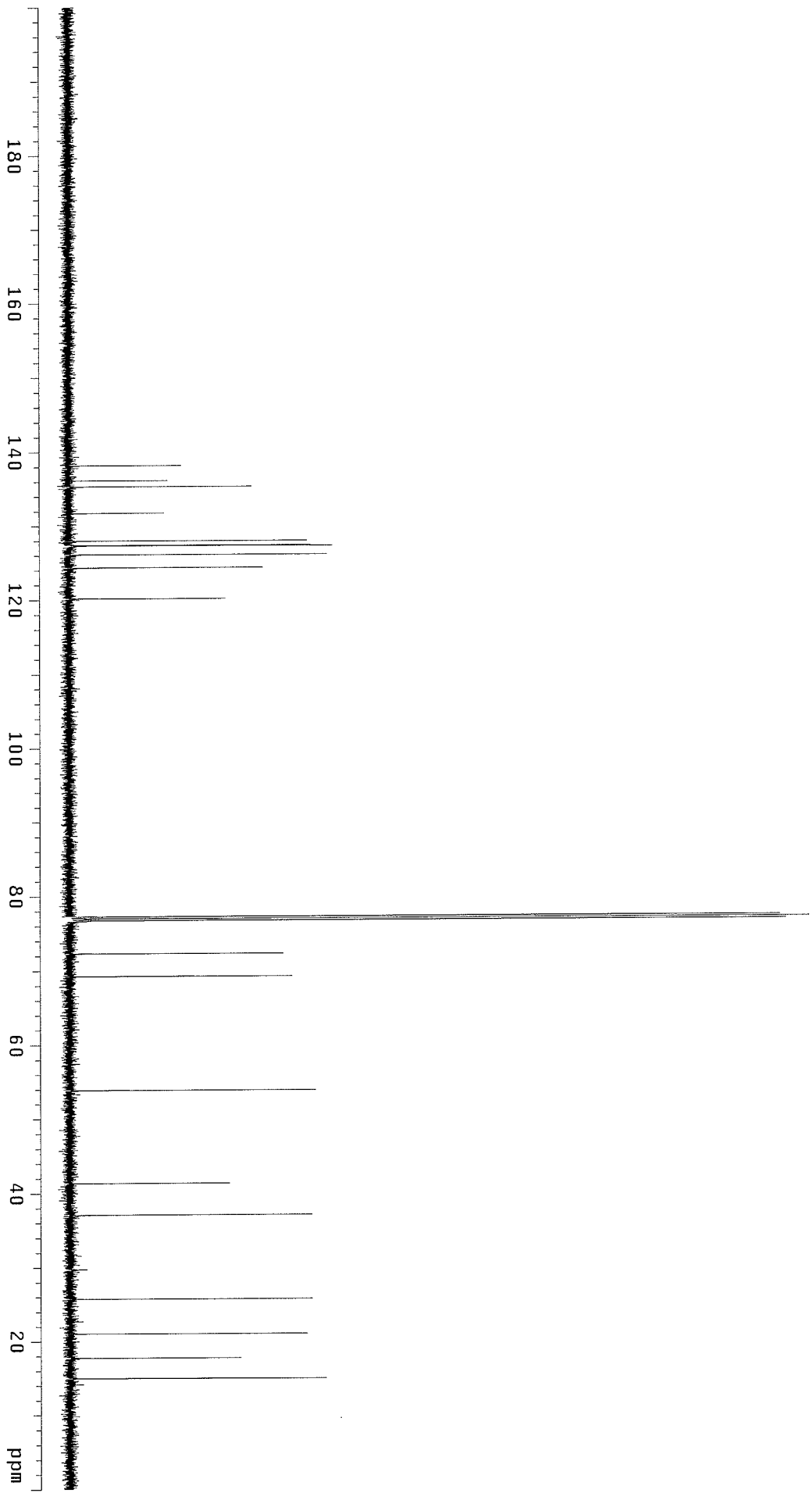
7
6
5
4
3
2
1
ppm

HO
Me
OH
Me
Me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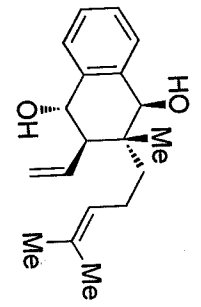
20
ppm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Me
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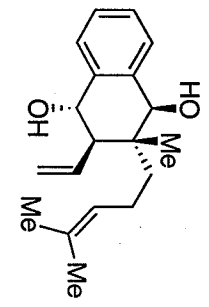
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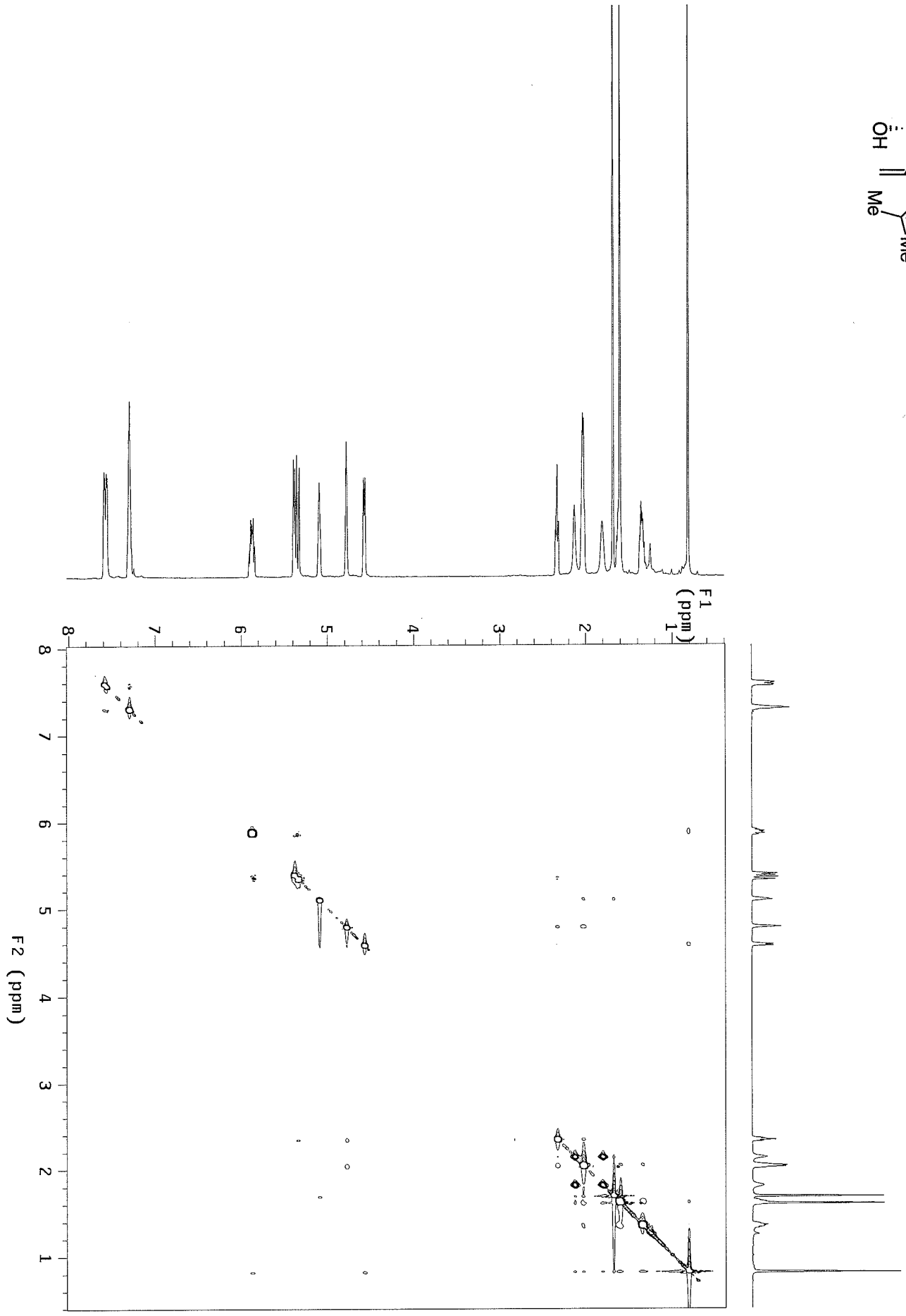
OH
Me
Me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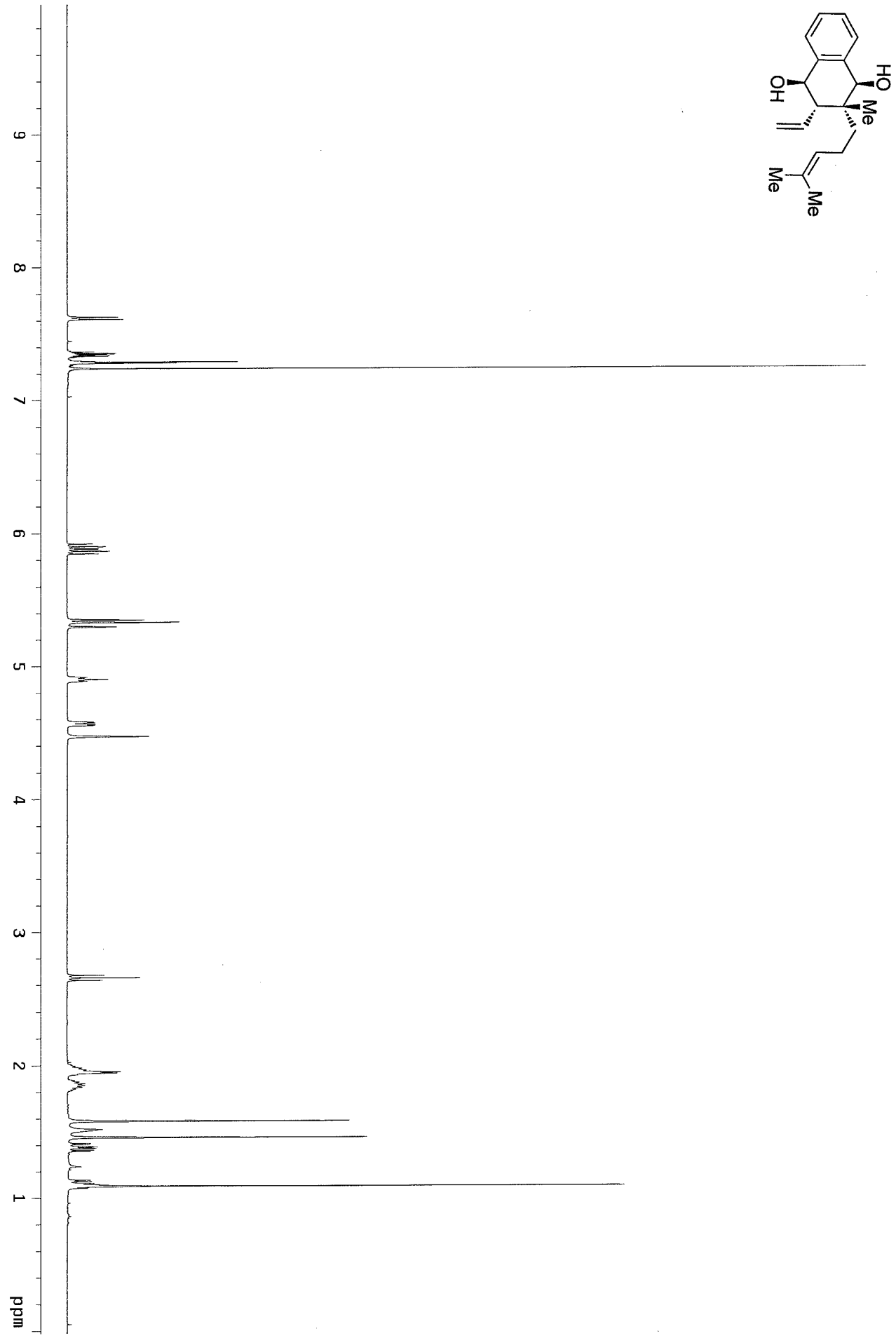
F2 (ppm)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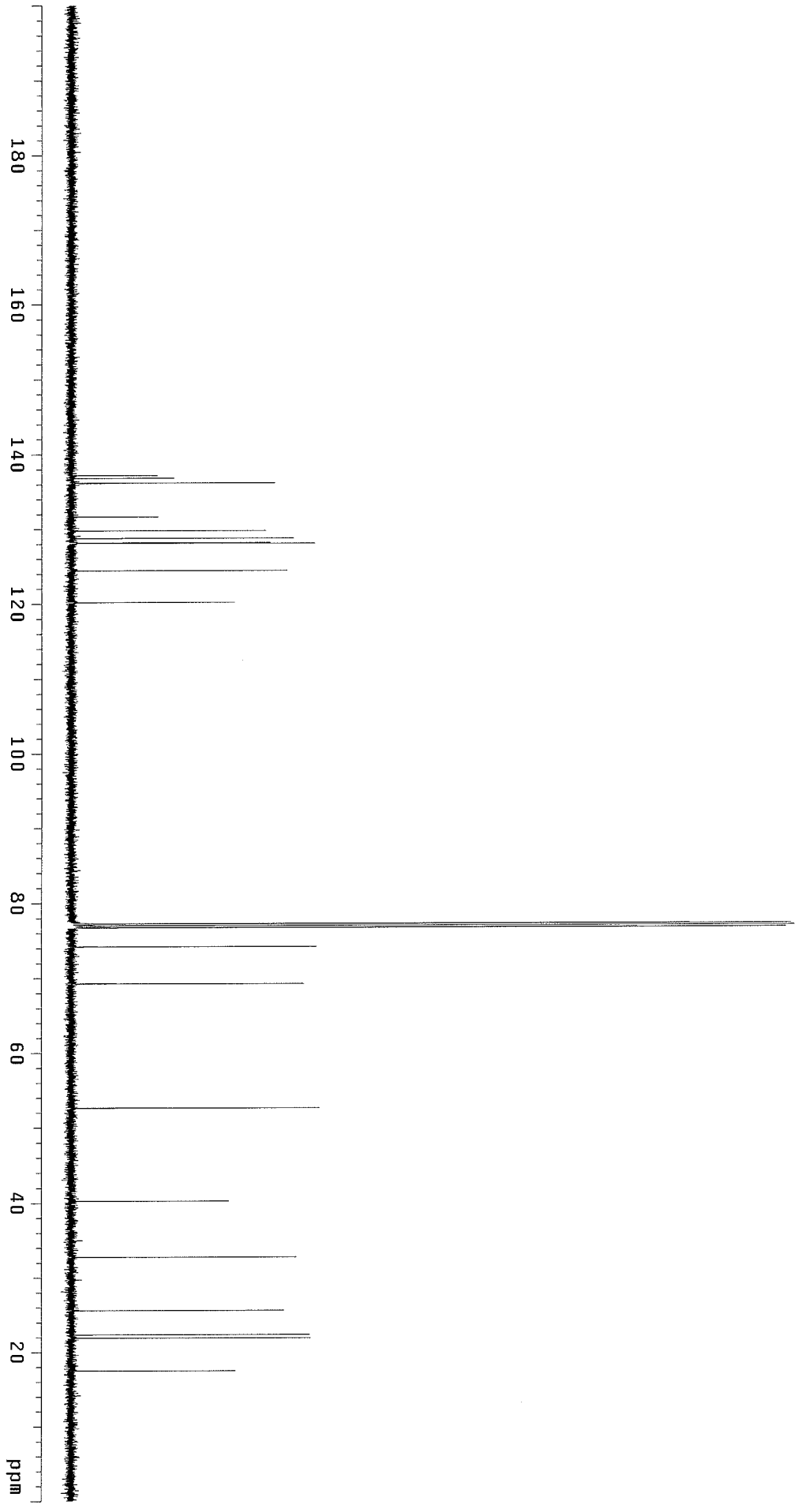
OH
Me
Me
9
8
7
6
5
4
3
2
1
ppm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40
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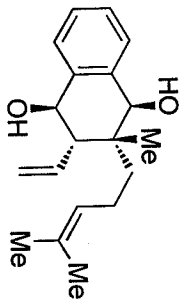
ppm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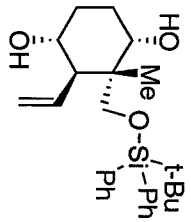
OH
Me
Me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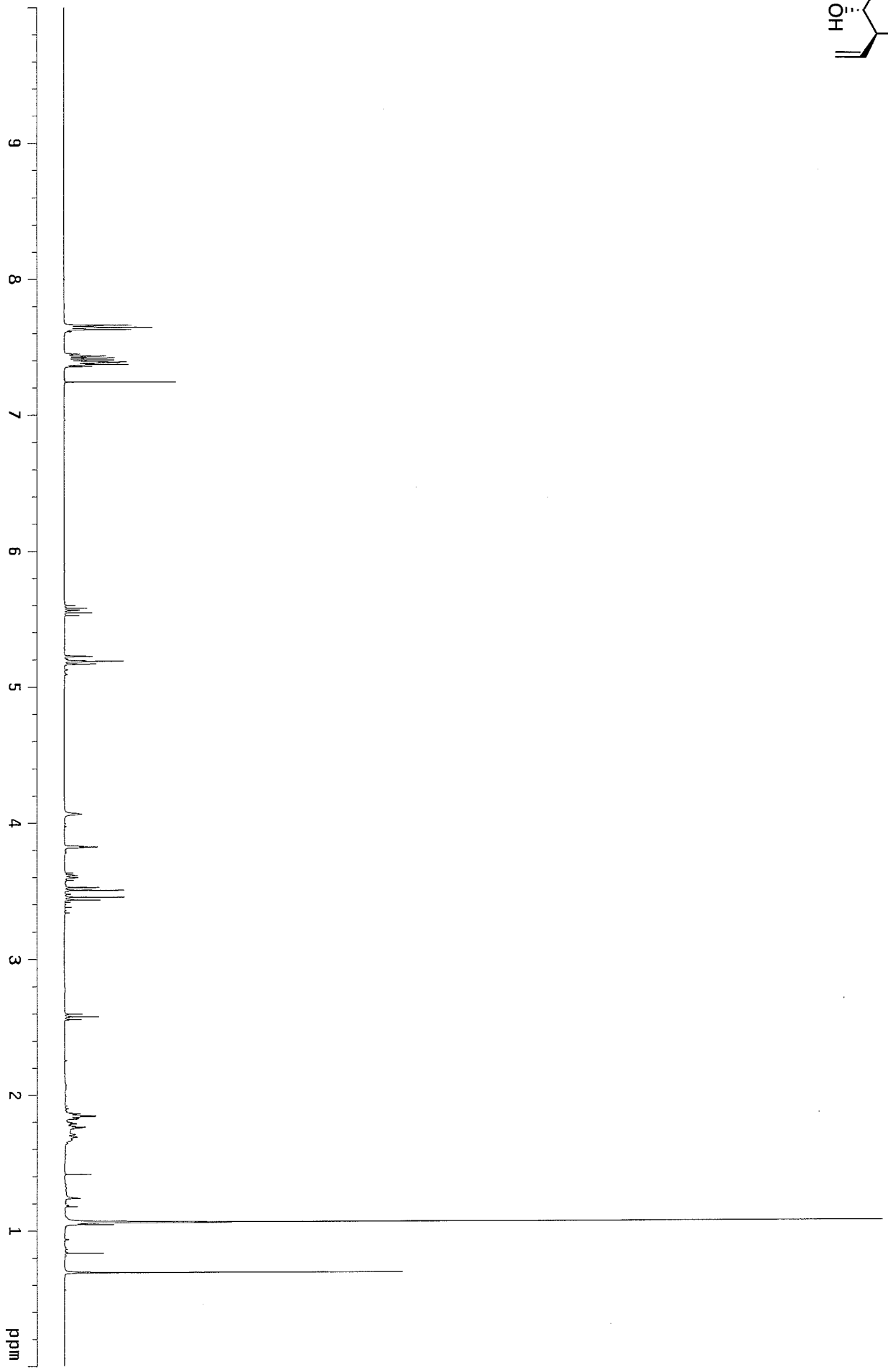
OH
Me
O-Si-Ph
t-Bu
Ph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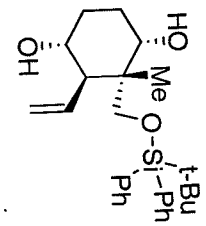
4
3
2
1
ppm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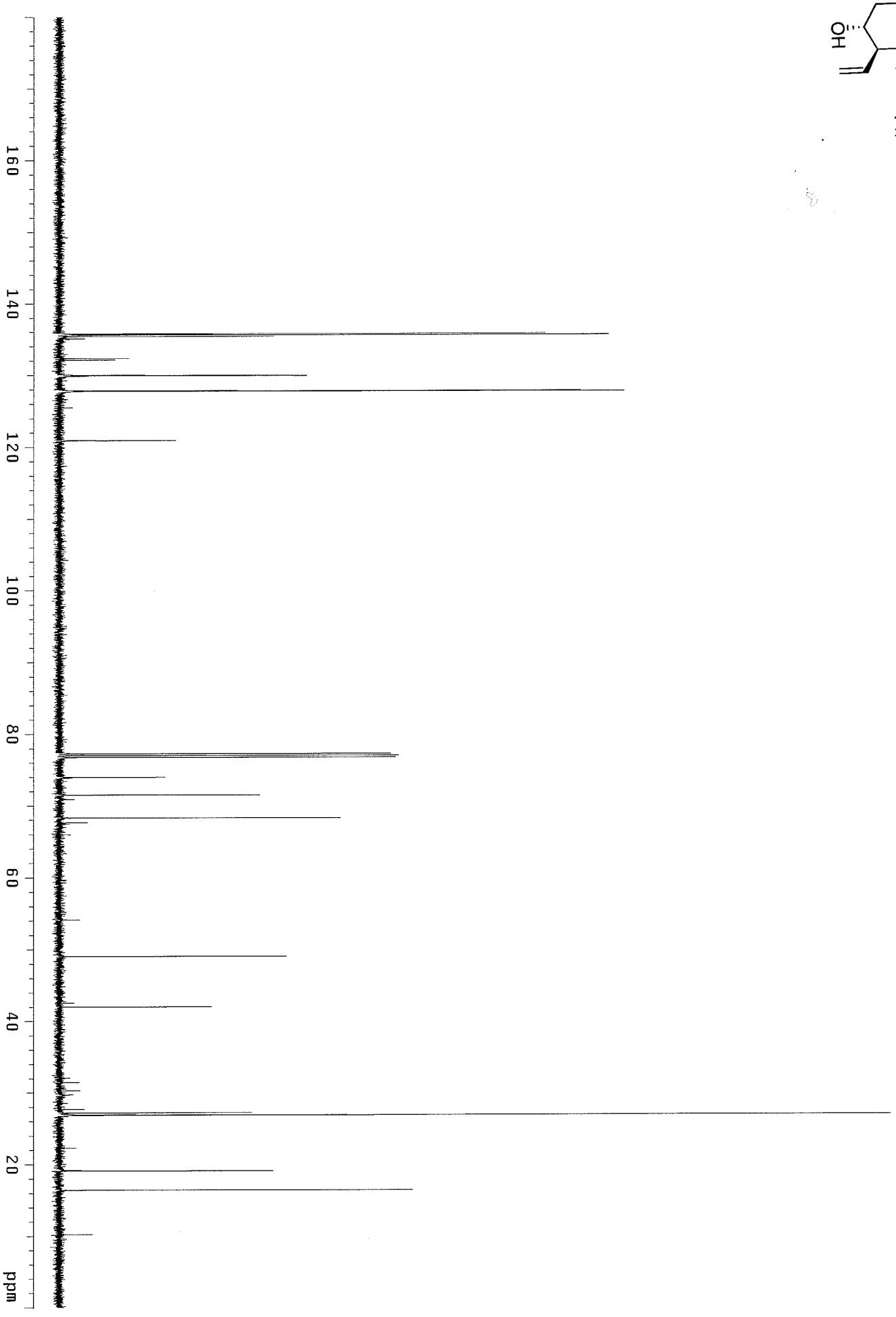
t-Bu
Ph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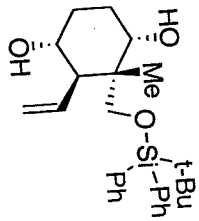
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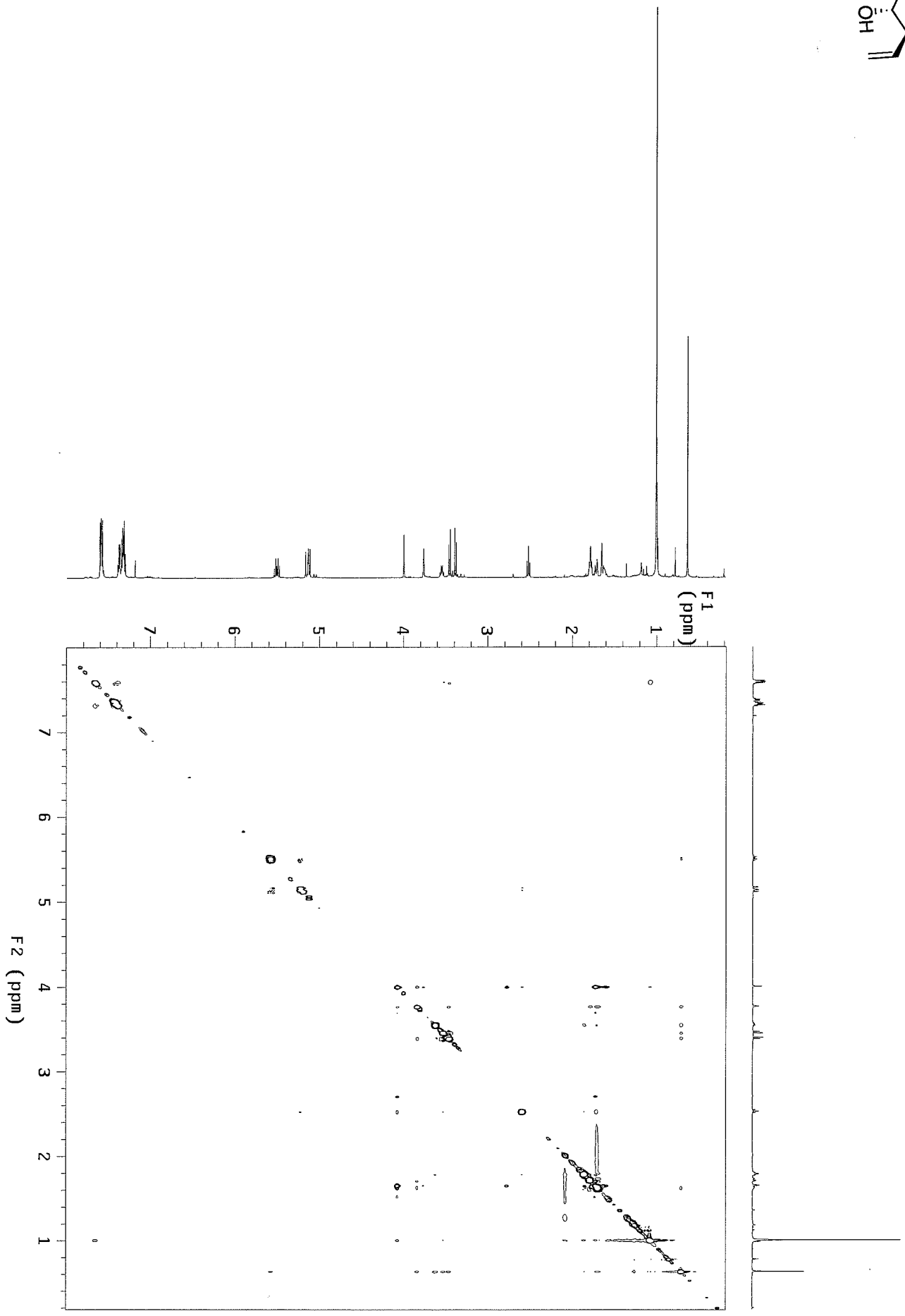
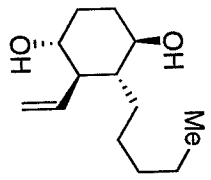
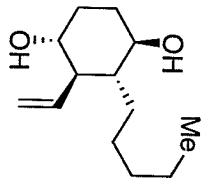
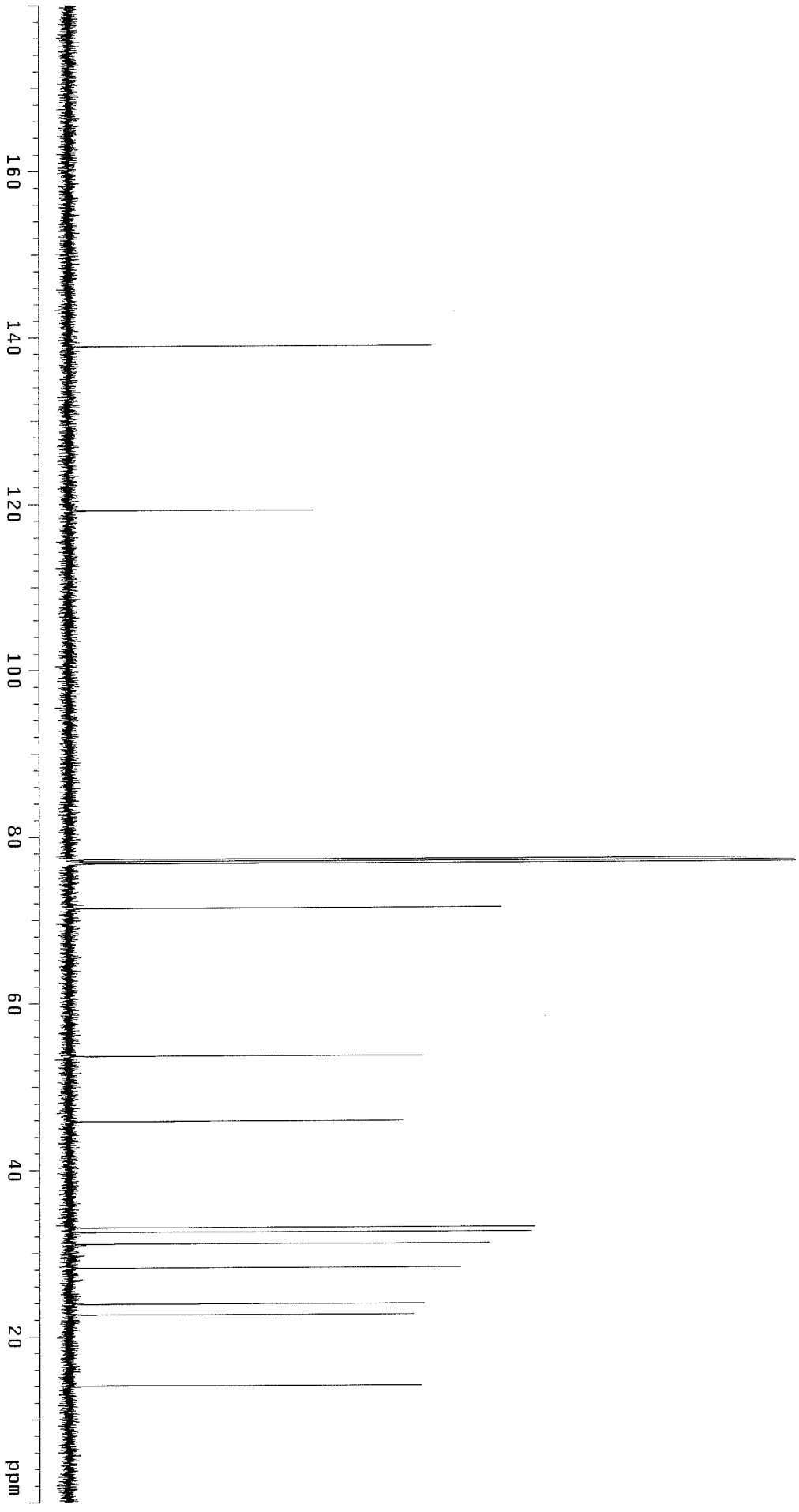
t-Bu
Ph


F1 (ppm)
F2 (ppm)
1
2
3
4
5
6
7


OH
OH
Me

9
8
7
6
5
4
3
2
1
0
ppm


OH
OH
Me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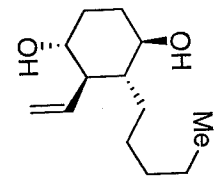
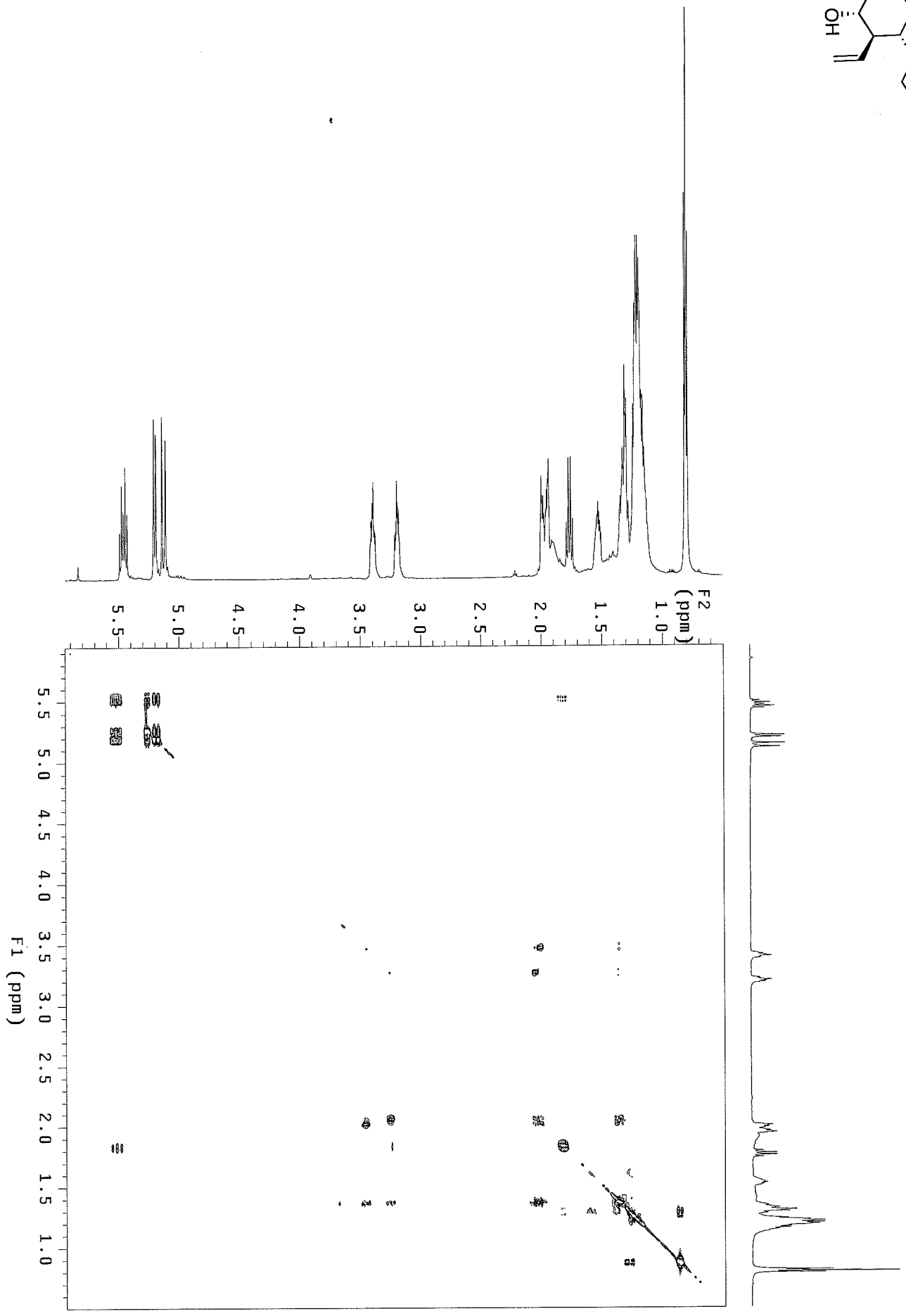

OH
OH
Me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3.0
2.5
2.0
1.5
1.0
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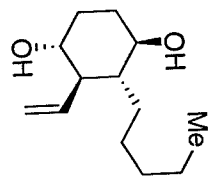
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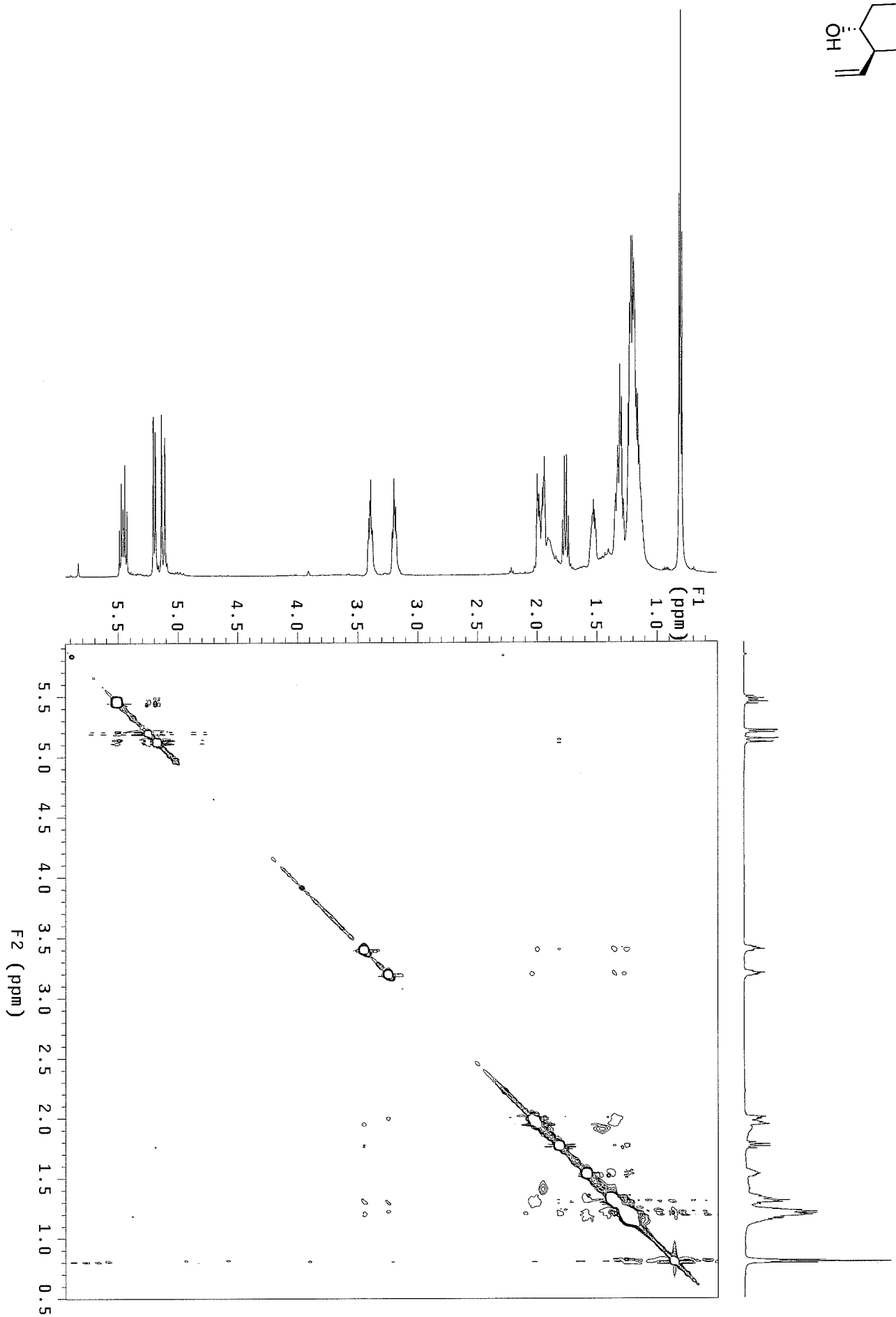
Me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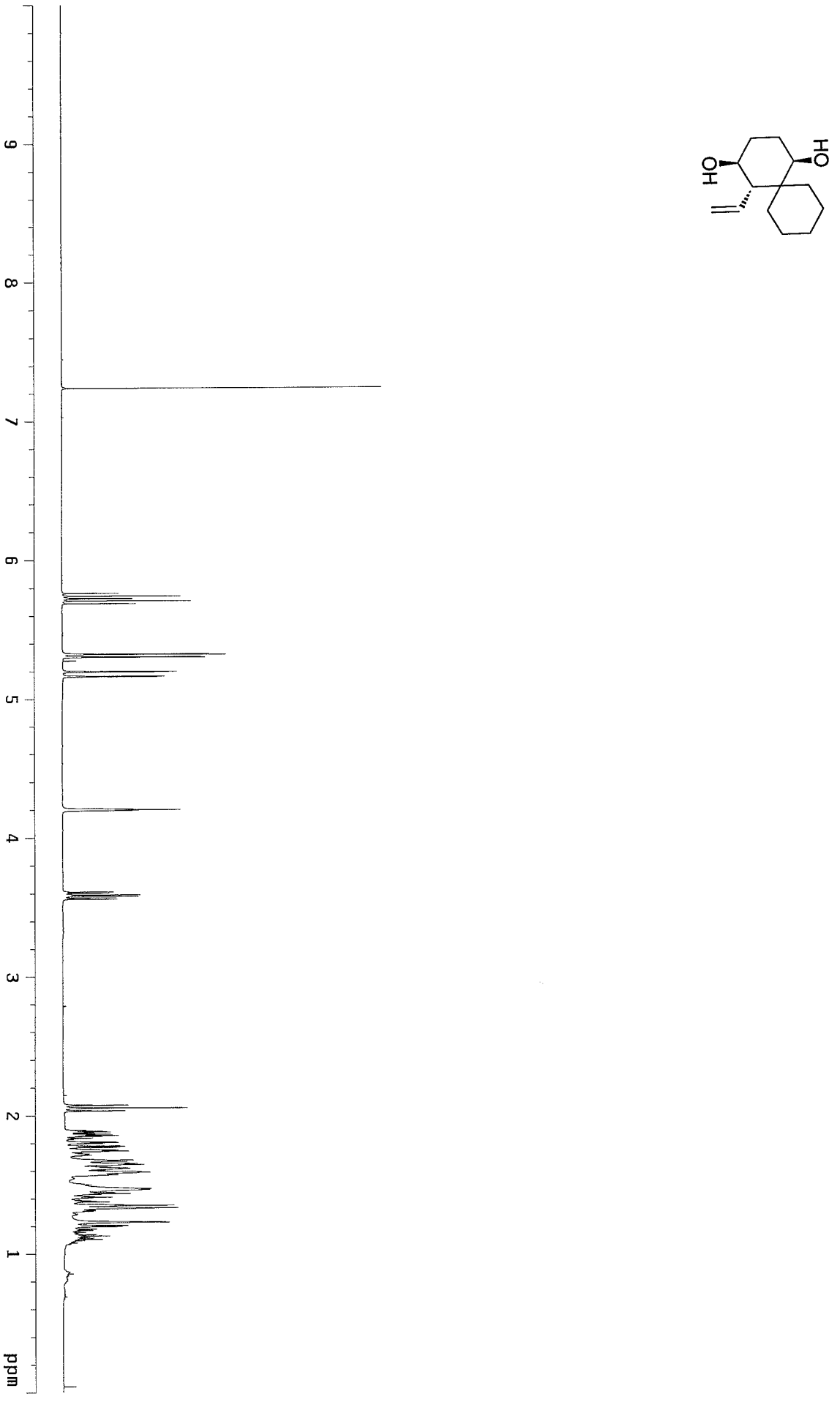
F2 (ppm)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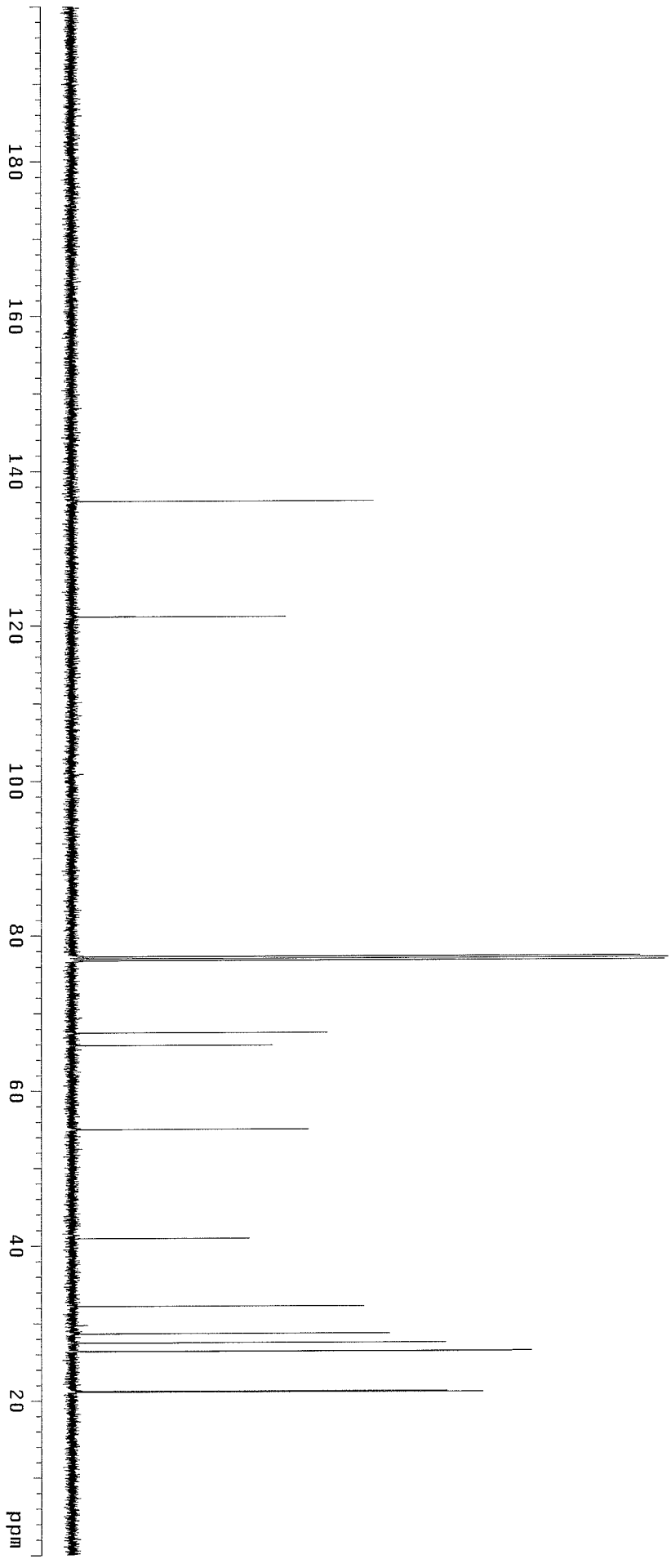
5
4
3
2
1
ppm

HO
OH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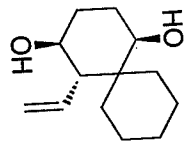
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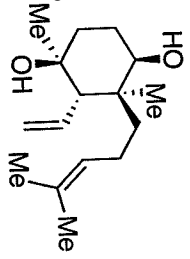
HO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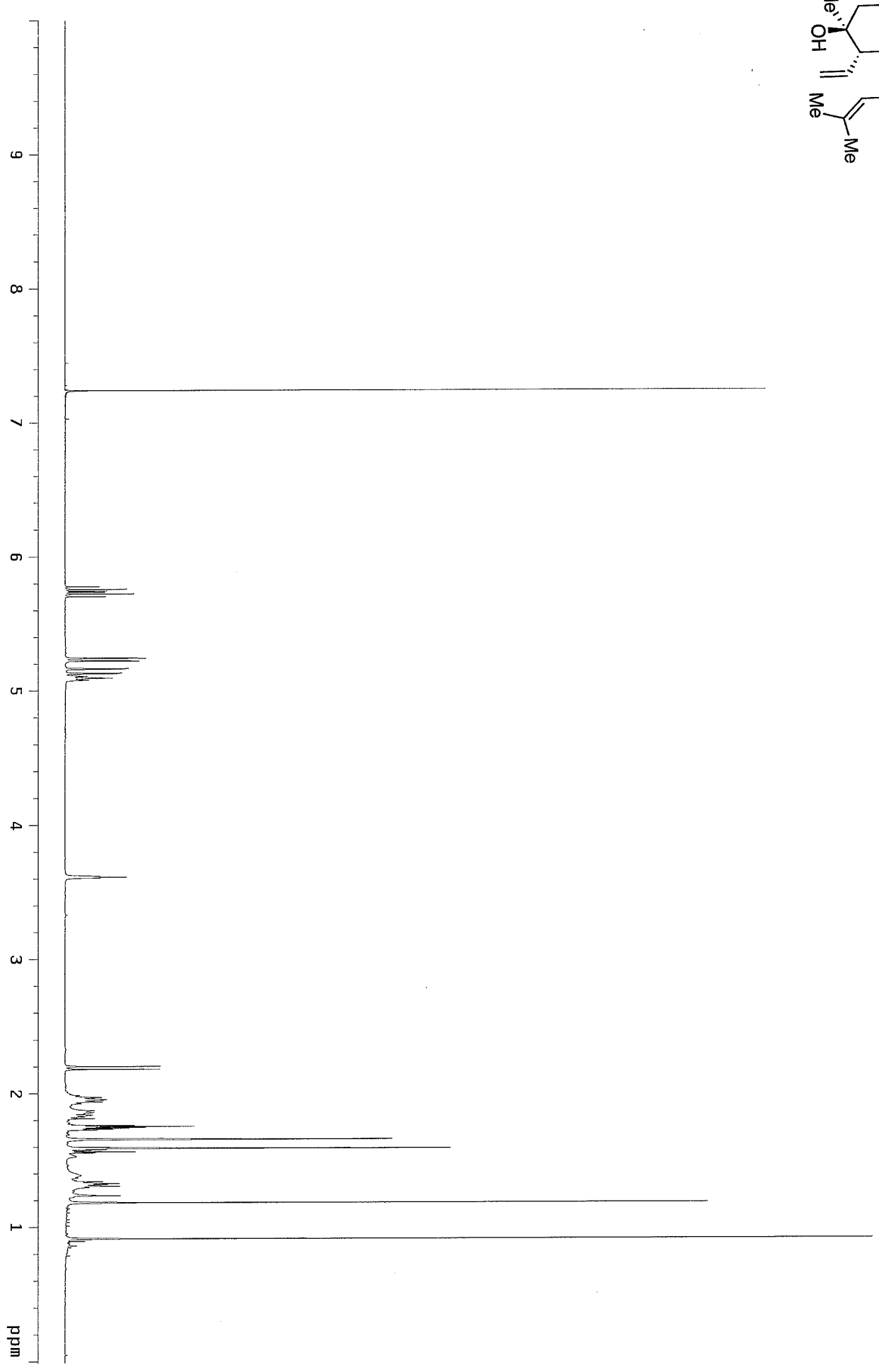
Me
Me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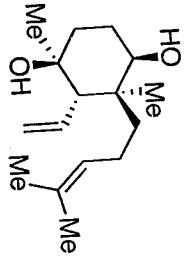
3
2
1
ppm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Me
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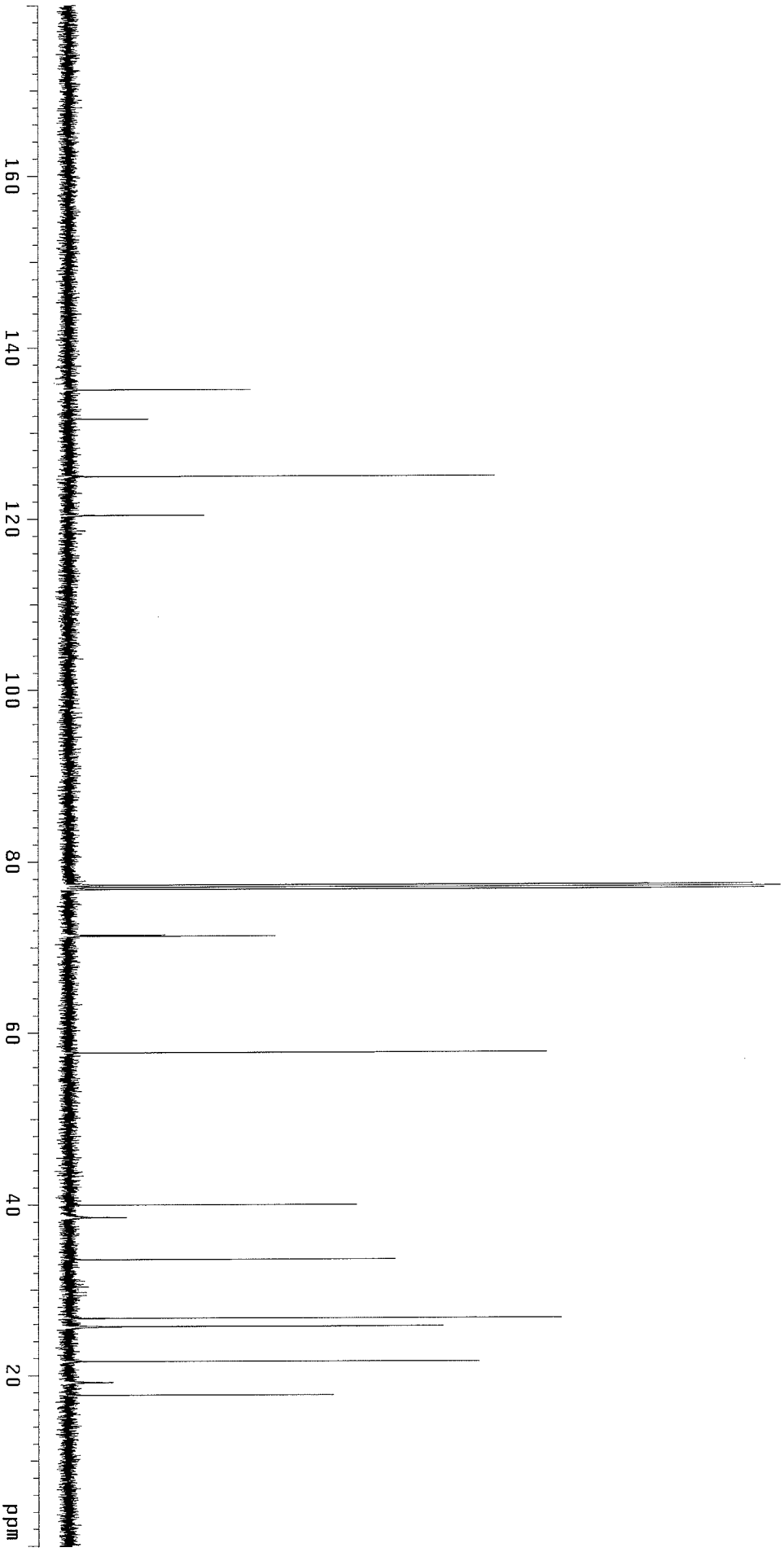
Me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80
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40
20
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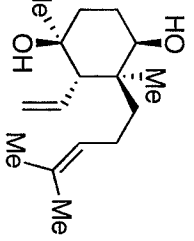
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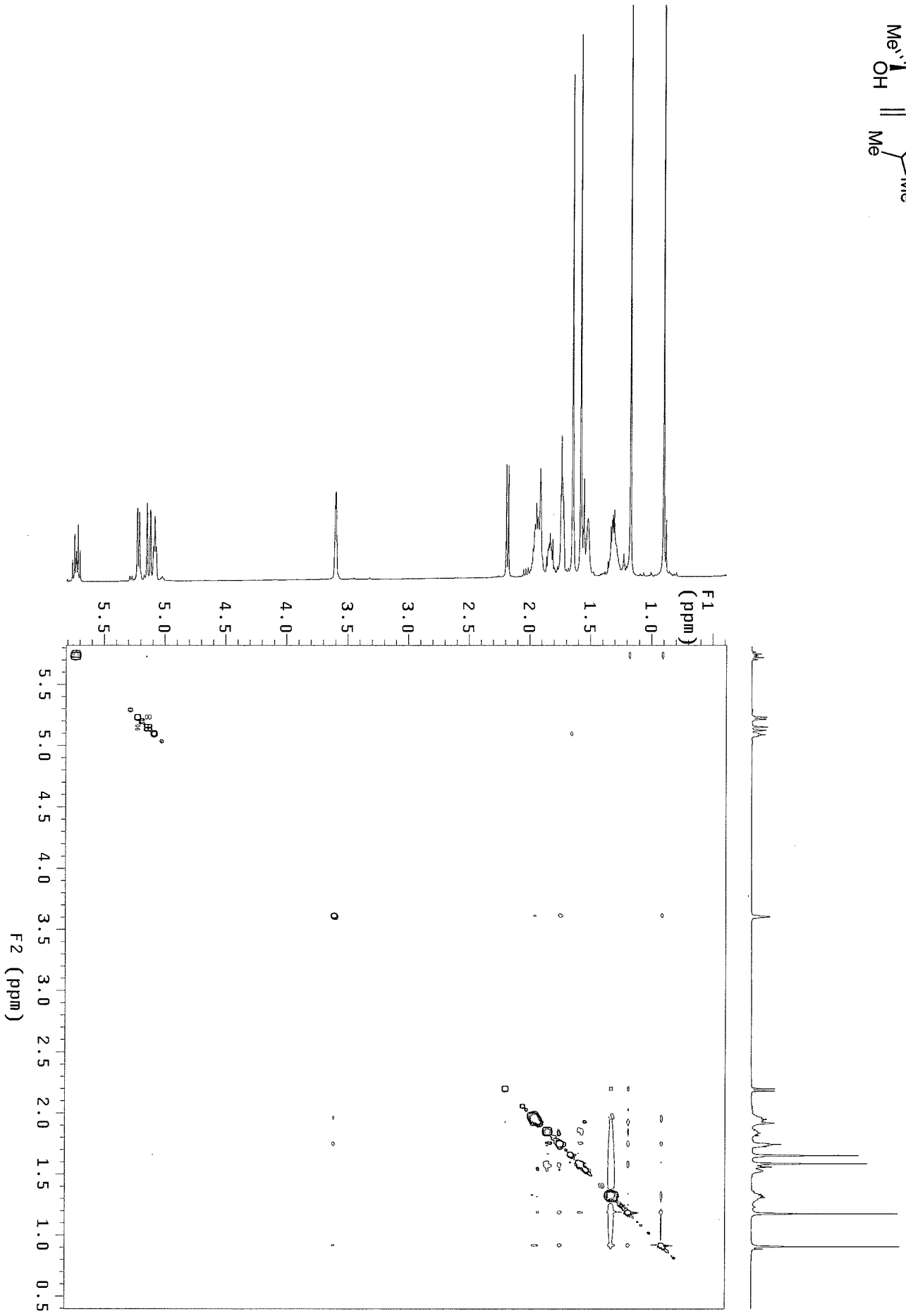
Me
OH
Me
Me
Me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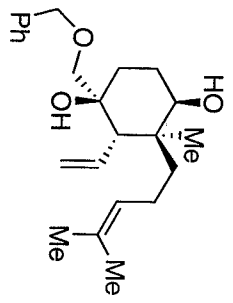
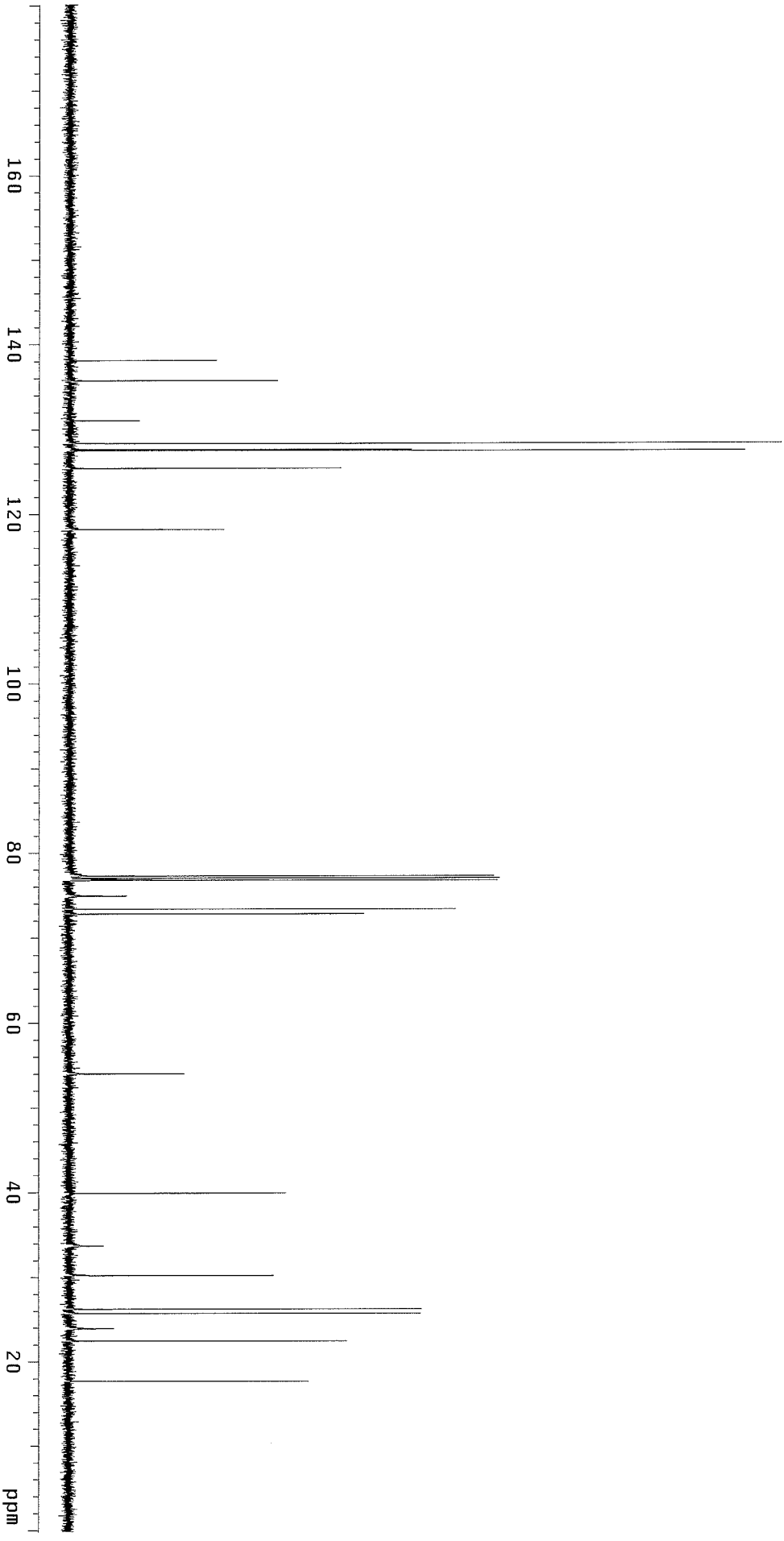
F2 (ppm)


Ph
O
OH
HO
Me
Me
Me

9
8
7
6
5
4
3
2
1
ppm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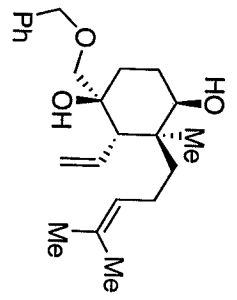
60
40
20
ppm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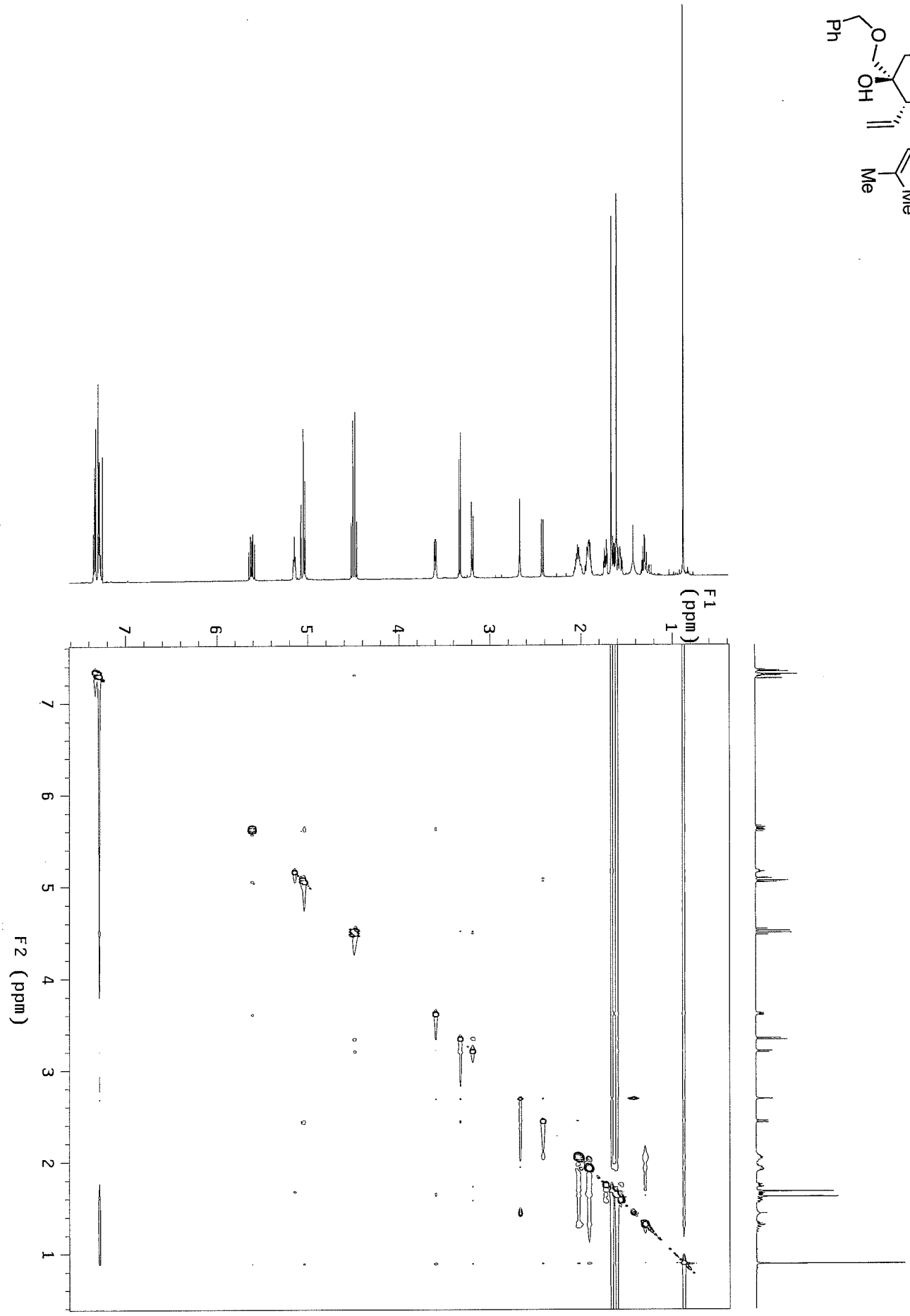
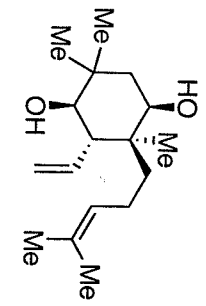
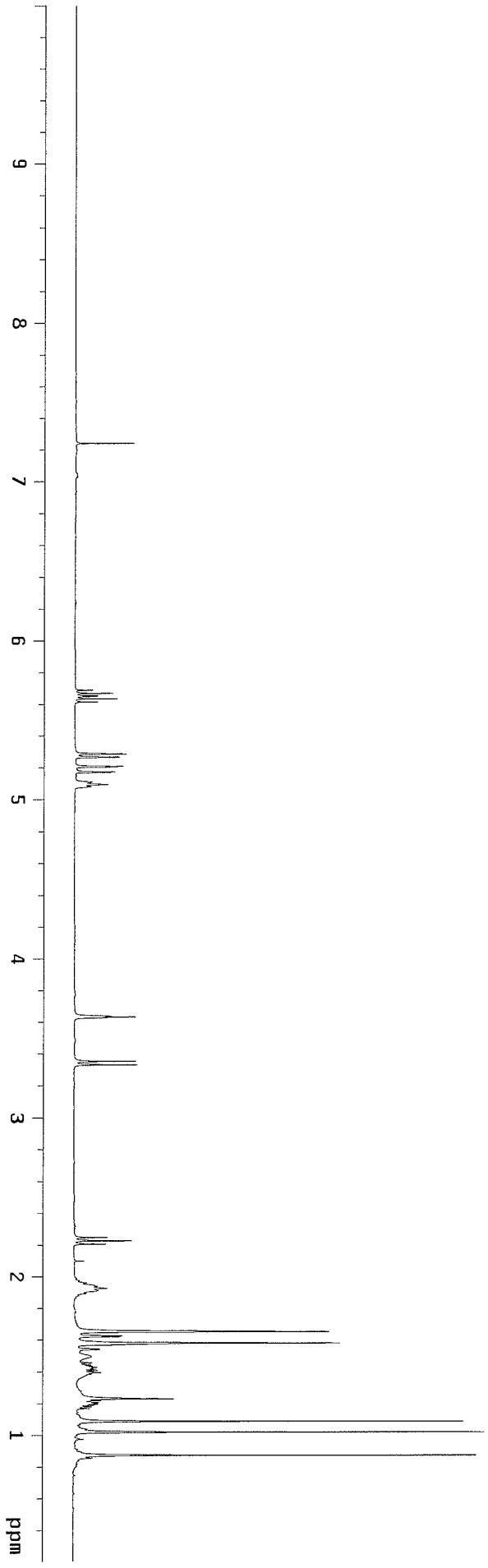
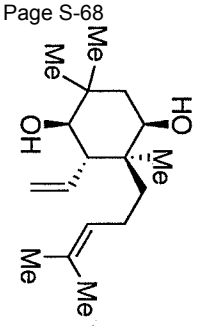
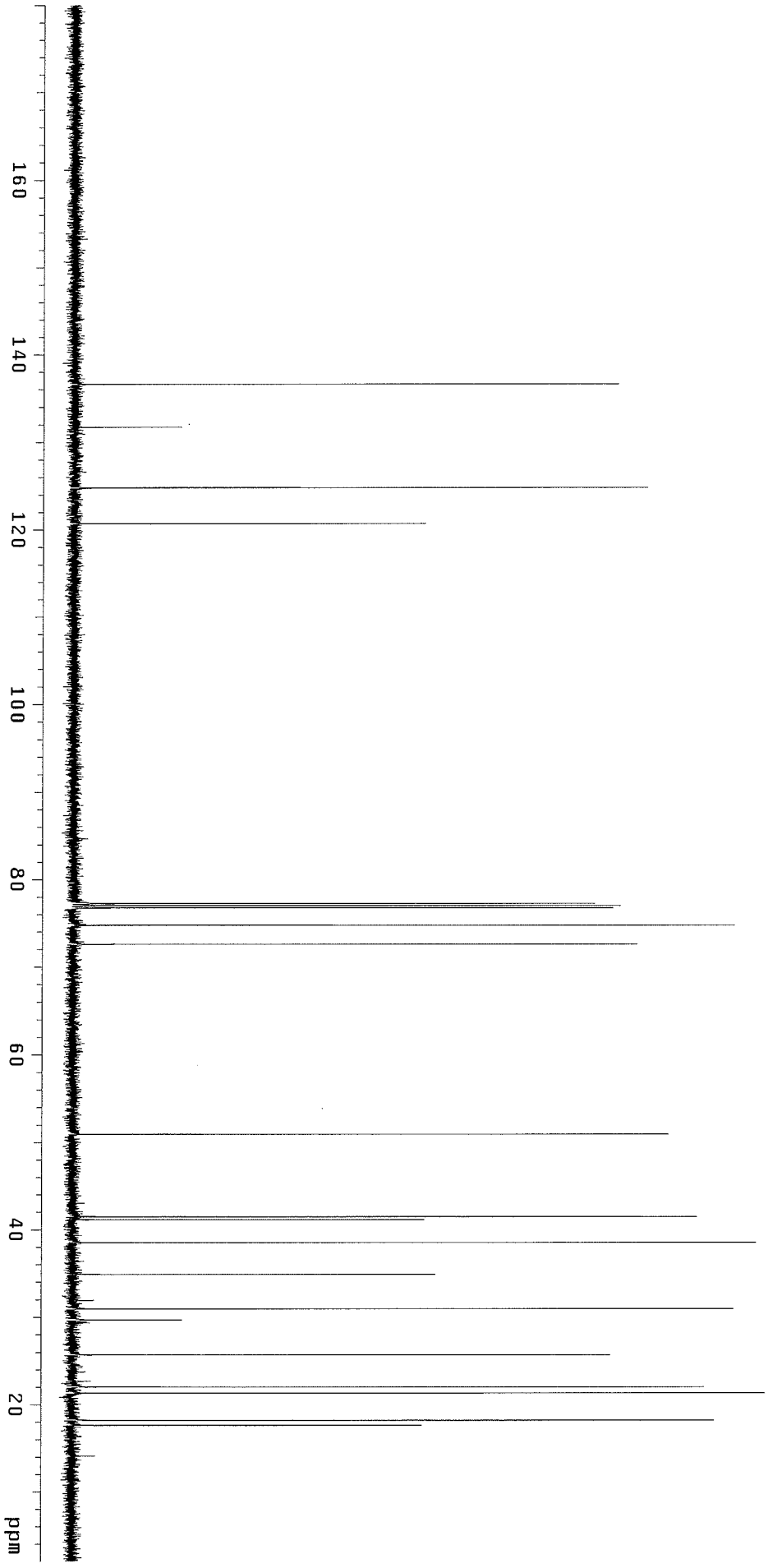
O
OH
HO
Me
Me
Me

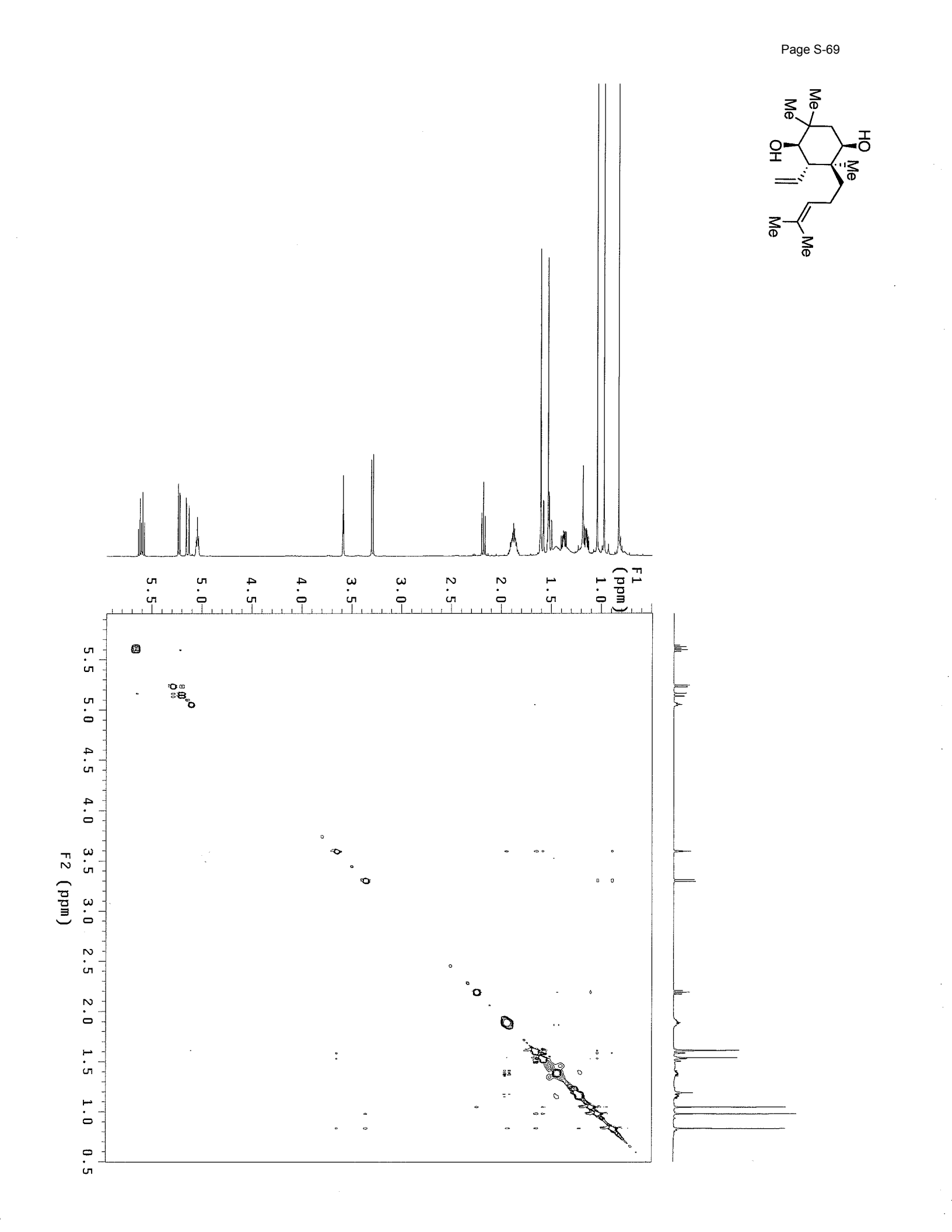

HO
Me
OH
Me
Me
O
Ph
F1 (ppm)
F2 (ppm)

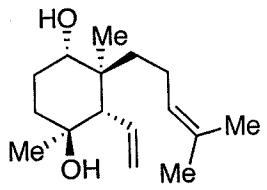

Me
Me
HO
OH
Me
Me
Me

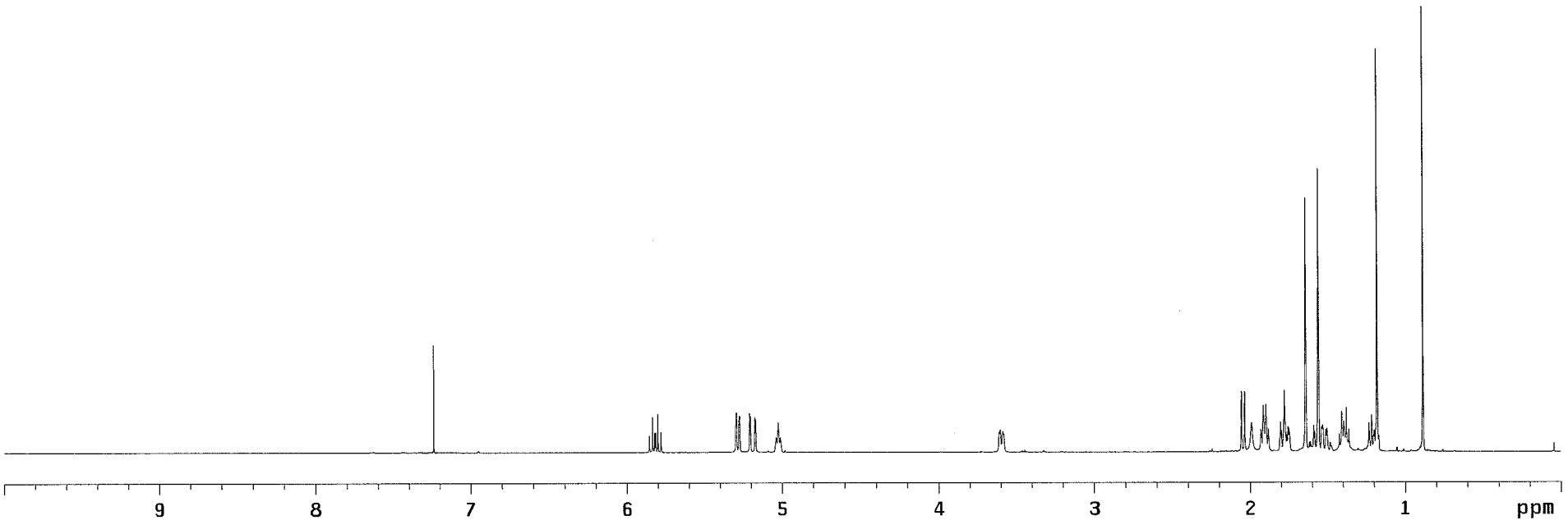

9
8
7
6
5
4
3
2
1
ppm

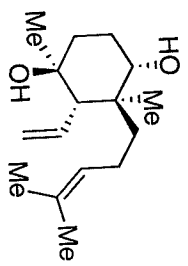

Me
Me
HO
OH
Me
Me
Me

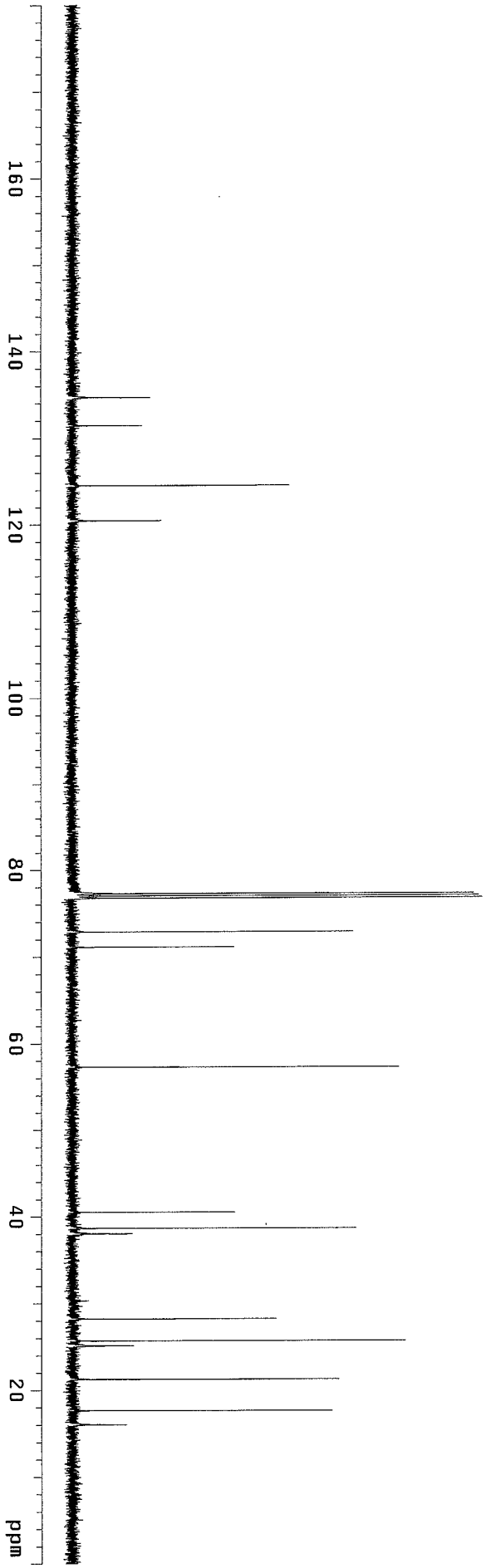

160
140
120
100
80
60
40
20
ppm


Me
Me
OH
HO
Me
Me
Me
F1 (ppm)
F2 (ppm)


HO
Me
Me
OH
Me
Me


9
8
7
6
5
4
3
2
1
ppm


HO
Me
Me
OH
Me
Me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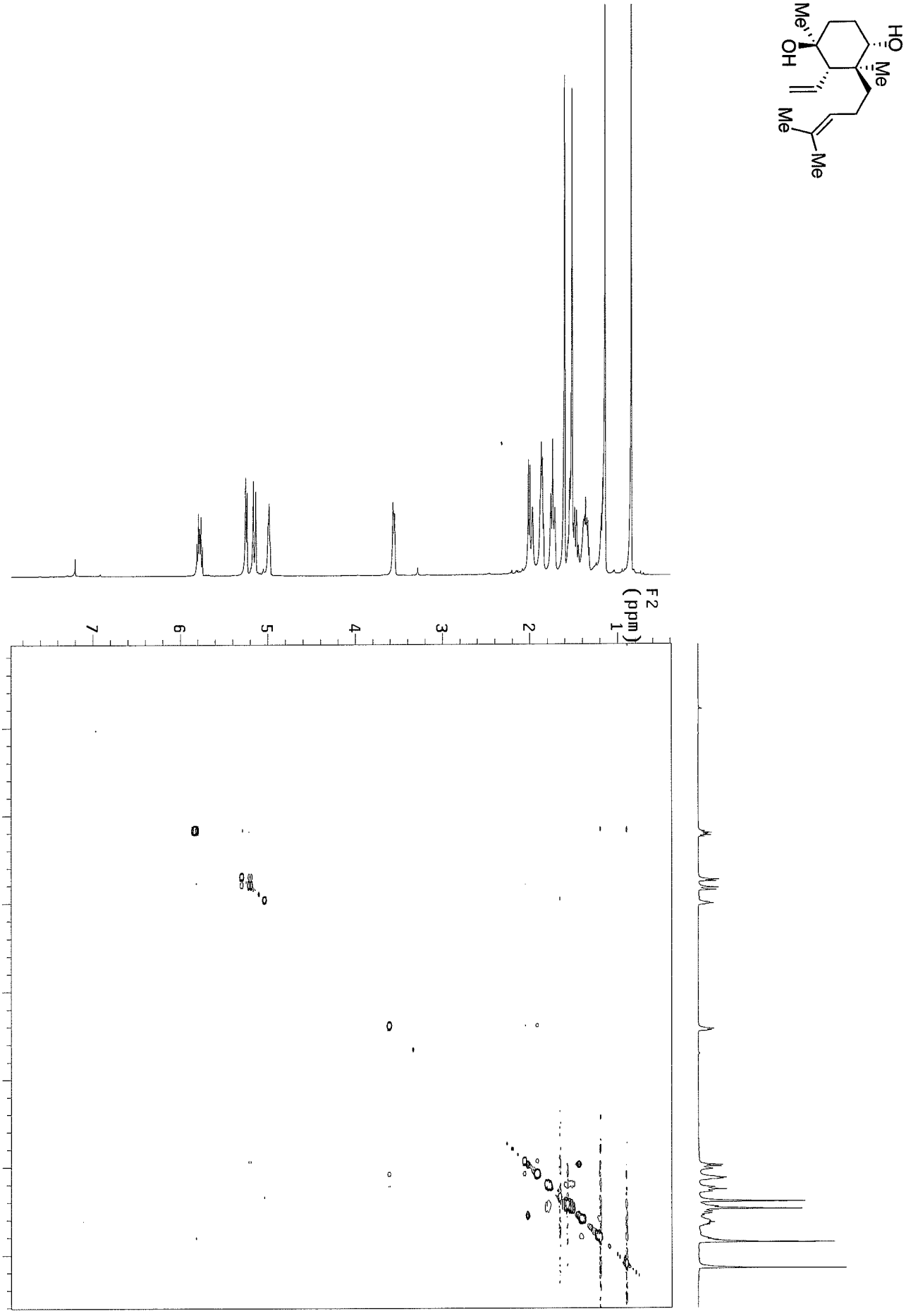
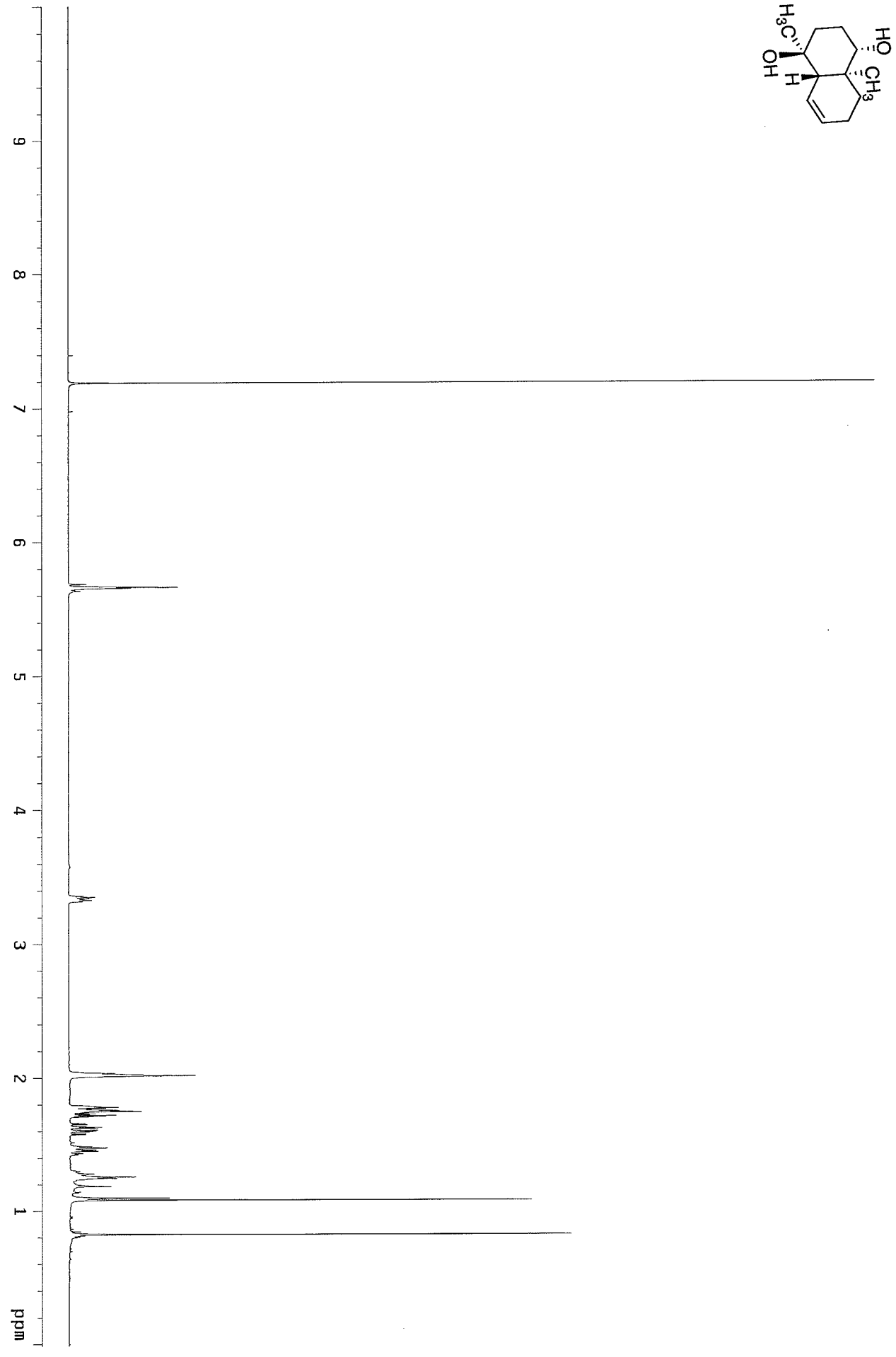
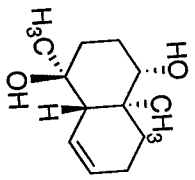
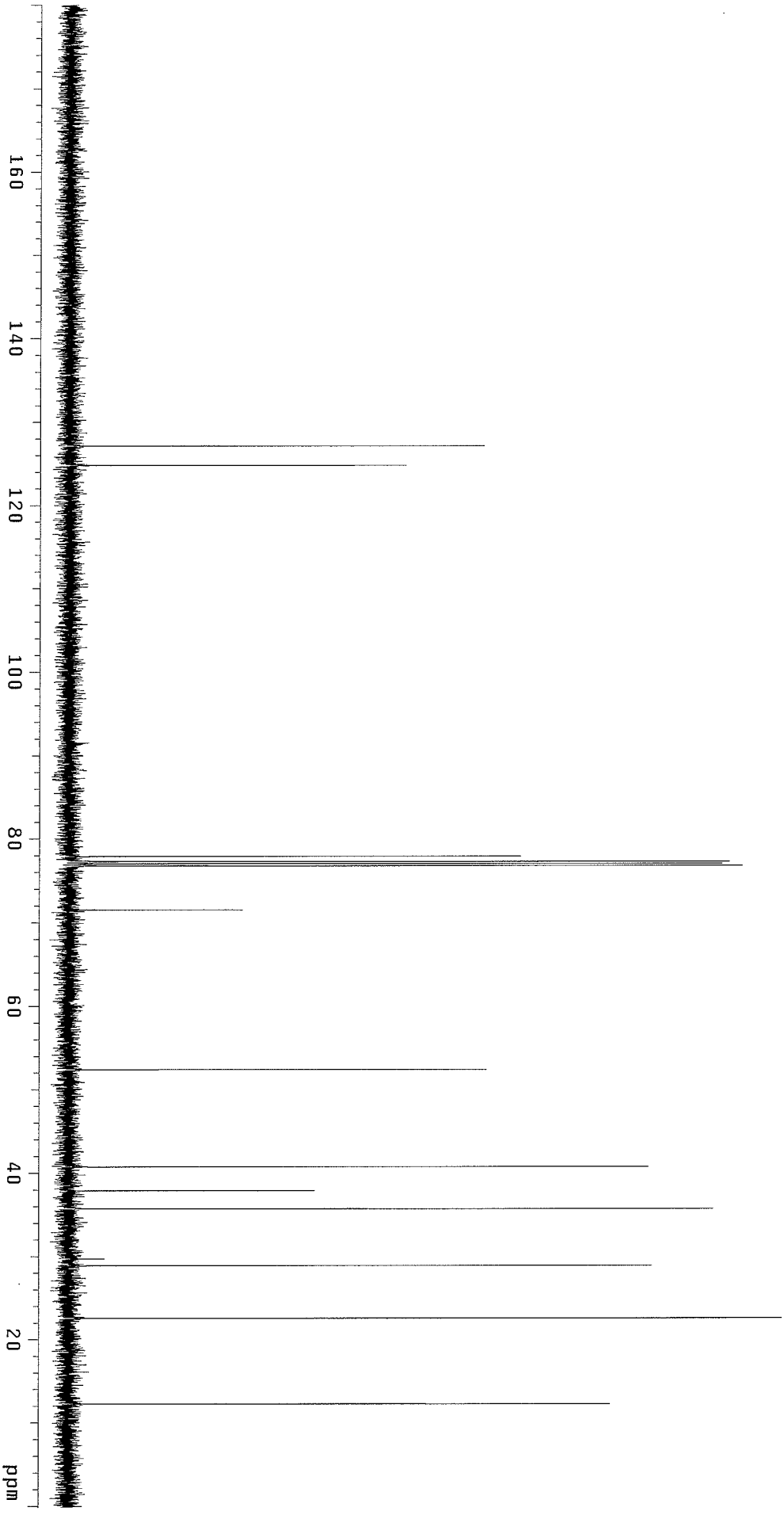
140
120
100
80
60
40
20
ppm


HO
Me
OH
Me
Me
Me
F2 (ppm)
F1 (ppm)


9
8
7
6
5
4
3
2
1
ppm

HO
H3C
OH
H
CH3


HO
CH3
H3C
OH
H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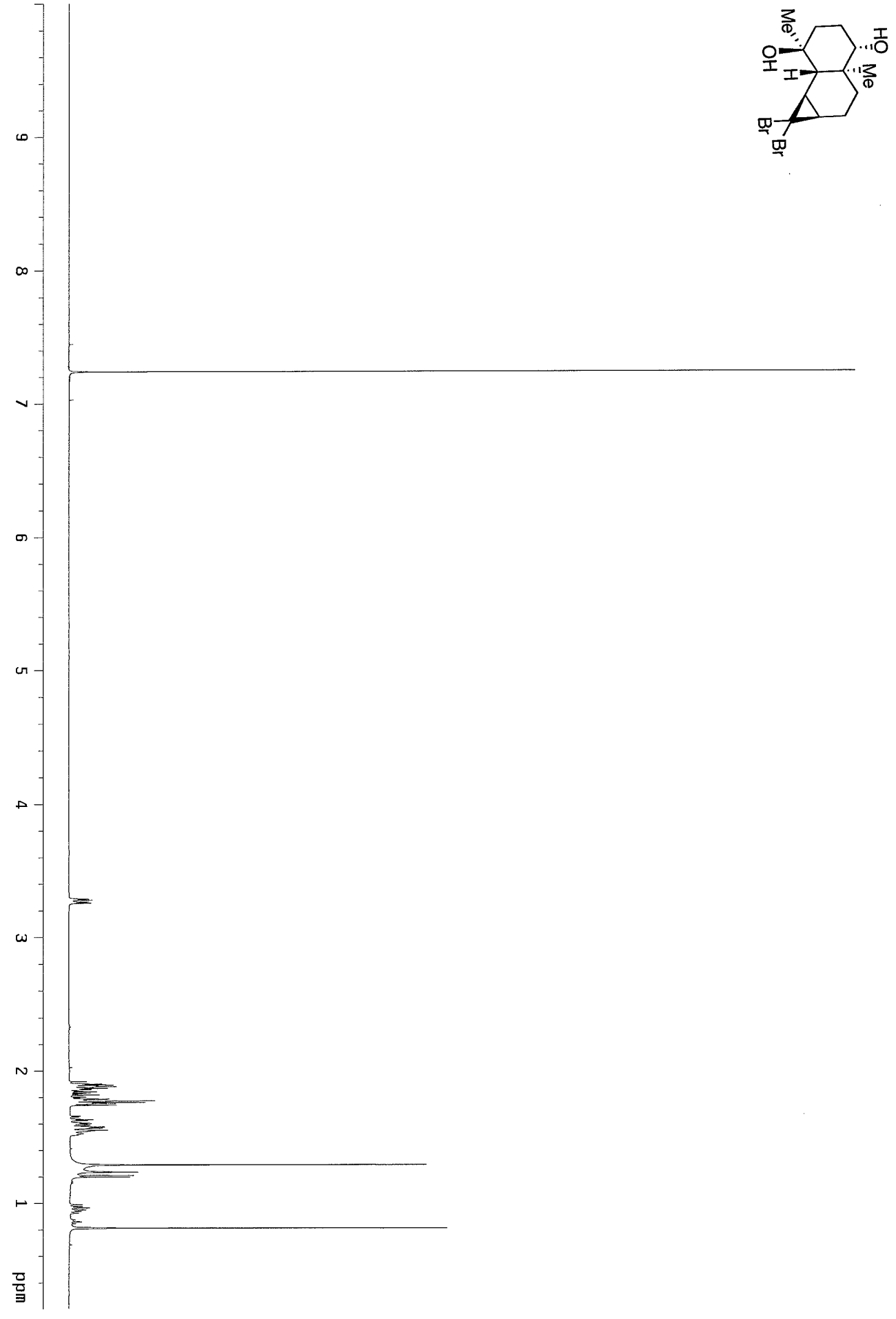
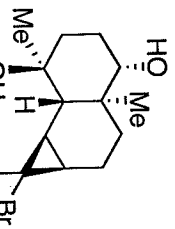
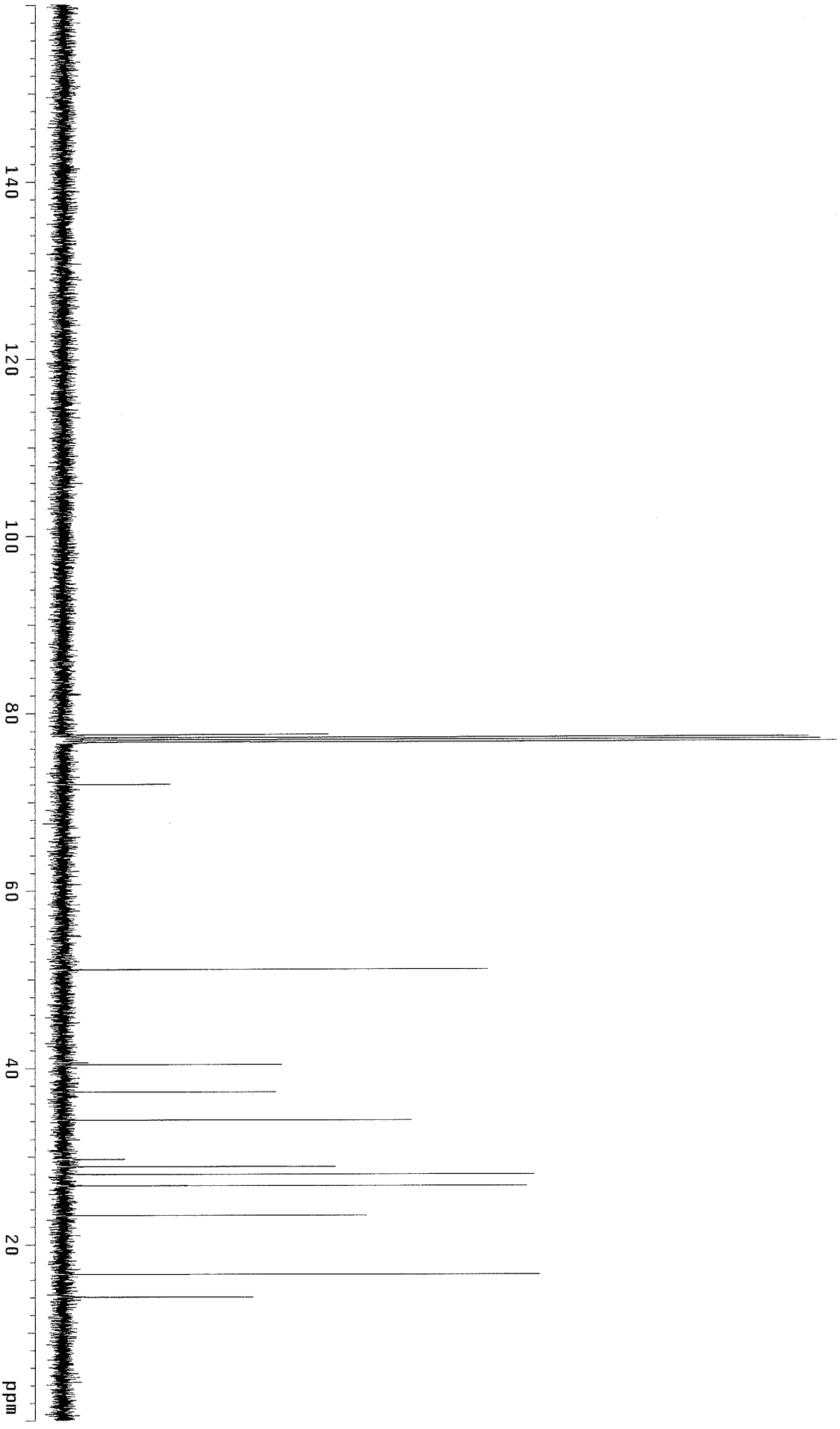
140
120
100
80
60
40
20
ppm


HO
Me
H
OH
Me
Br
Br
9
8
7
6
5
4
3
2
1
ppm


HO
Me
H
OH
Me
Br
Br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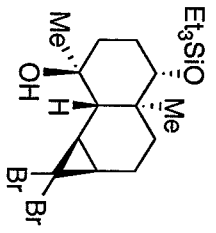
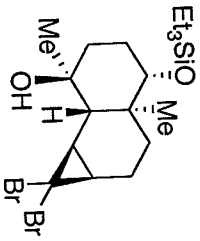
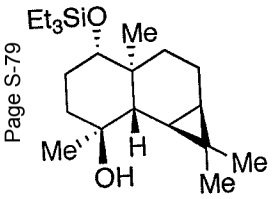
120
100
80
60
40
20
ppm


Et3SiO
Me
H
OH
Me
Br
Br

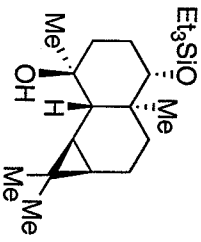
9
8
7
6
5
4
3
2
1
ppm

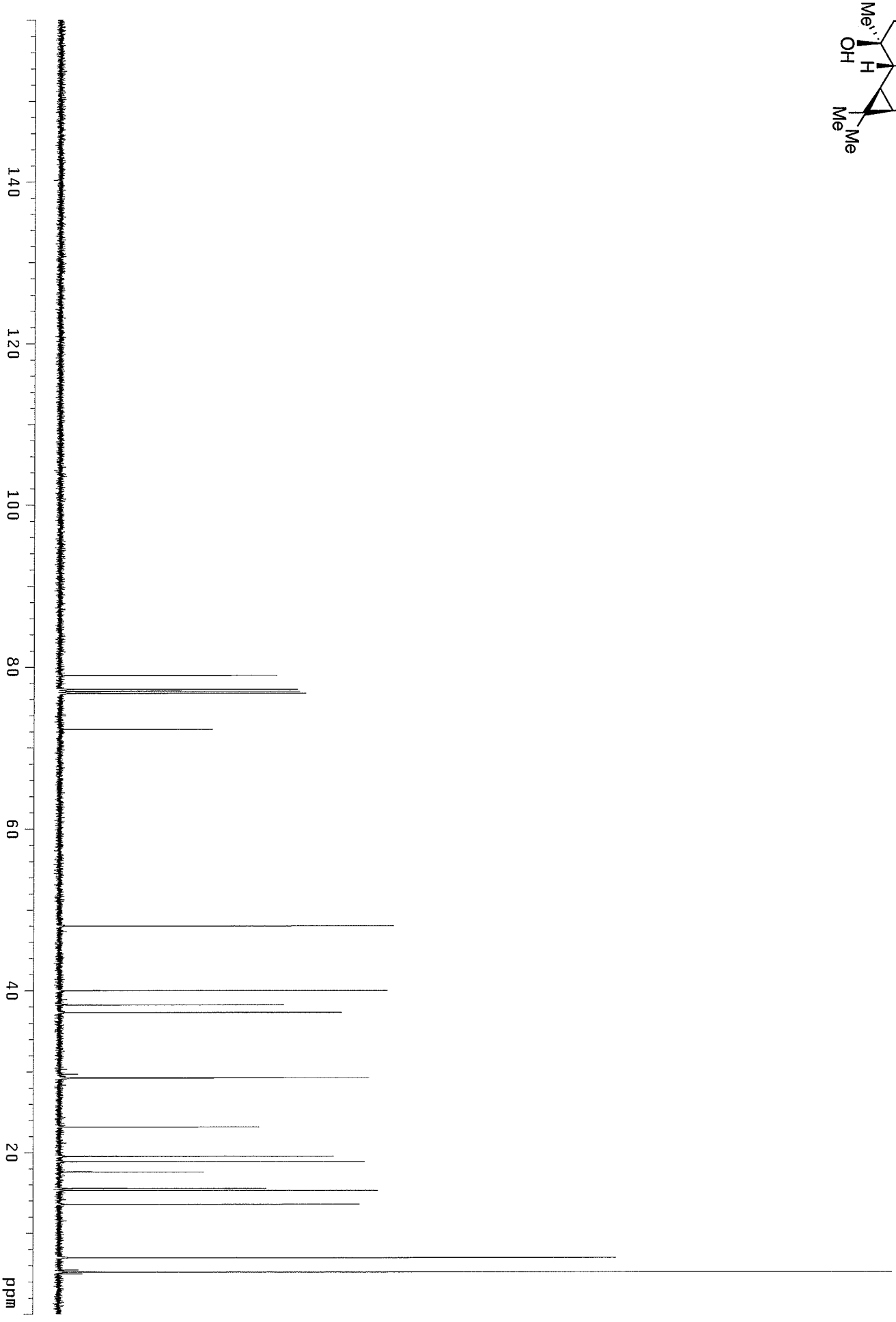

Et3SiO
Me
Me
H
OH
Br
Br

140
120
100
80
60
40
20
0
ppm


Et3SiO
Me
Me
H
OH
Me
Me

9
8
7
6
5
4
3
2
1
ppm


Et3SiO
Me
Me
H
OH
Me
Me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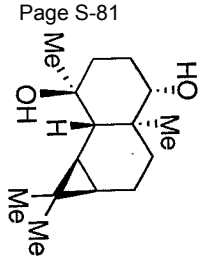
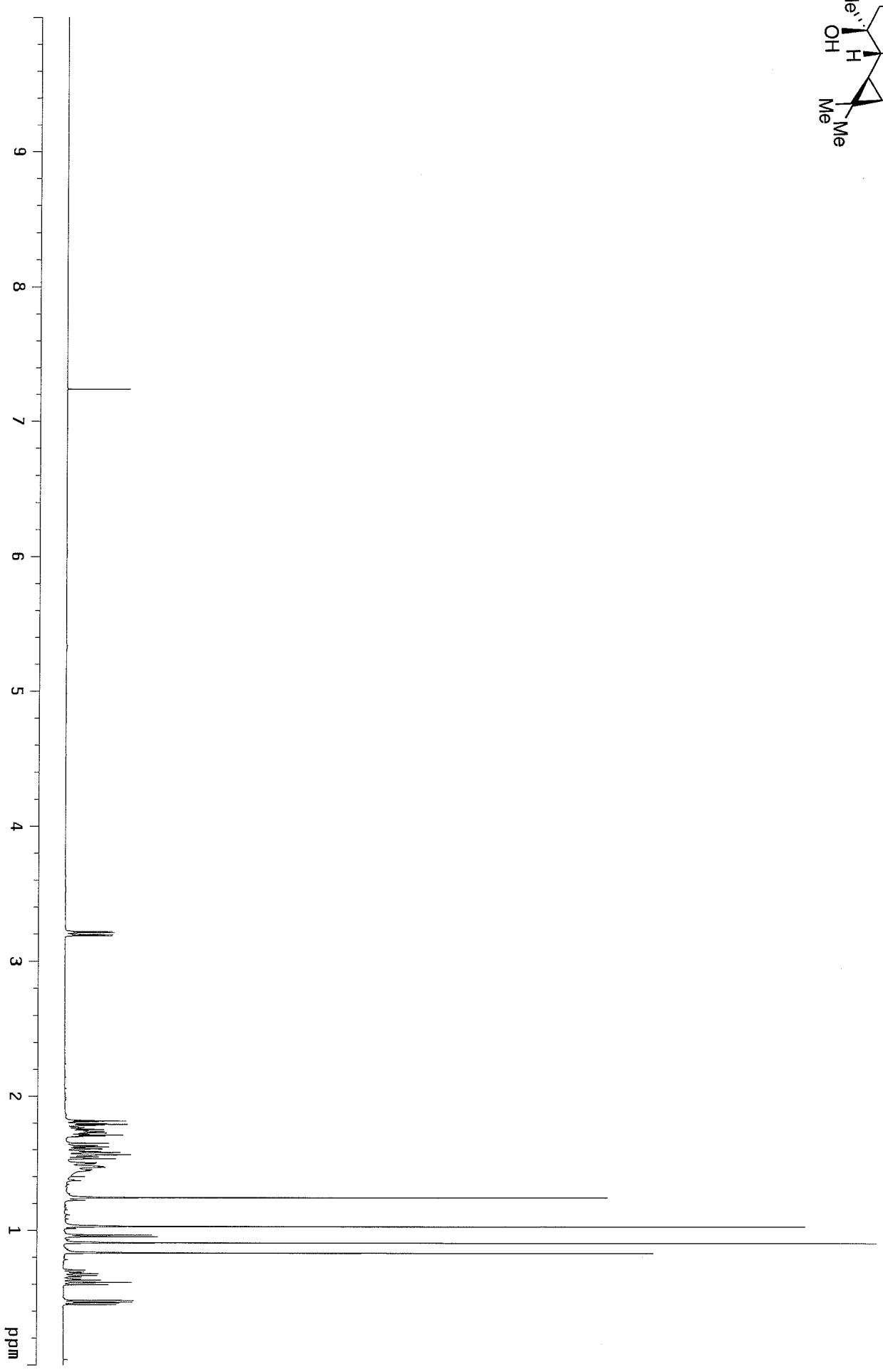

HO
Me
OH
H
Me
Me
Me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8
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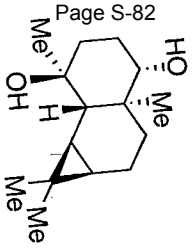
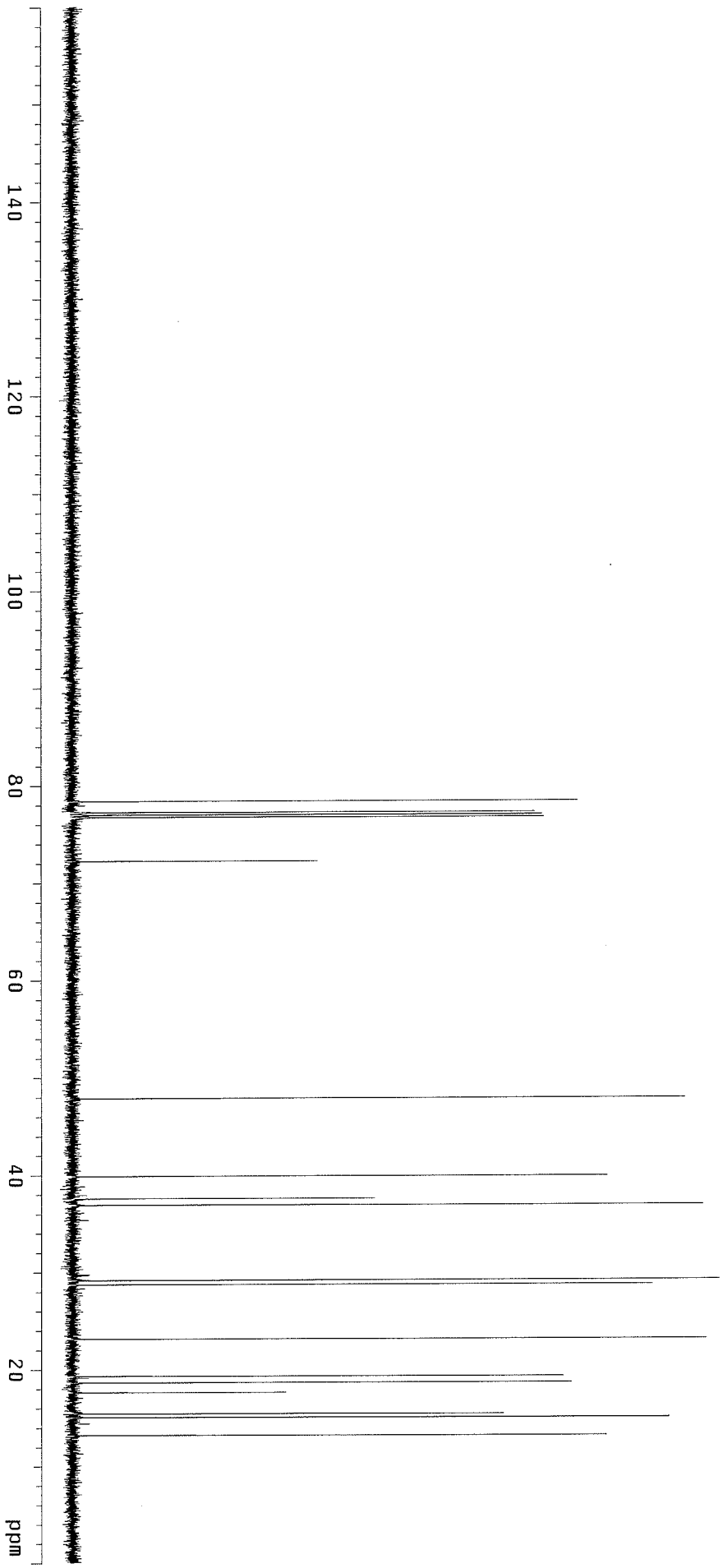
6
5
4
3
2
1
ppm


HO
Me
Me
OH
H
Me


140
120
100
80
60
40
20
ppm