Regiodivergent Reactions through Catalytic Enantioselective Silylation of Chiral Diols. Synthesis of Sapinofuranone A

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Supporting Information

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General information

Infrared (**IR**) spectra ν_{max} are reported in cm^{-1}; bands are characterized as broad (br), strong (s), medium (m), and weak (w). **^{1}H NMR** spectra chemical shifts are reported in ppm with the solvent reference as the internal standard ($CHCl_3$: δ 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), and coupling constants (Hz). **^{13}C NMR** spectra chemical shifts are reported in ppm with the solvent reference as the internal standard ($CHCl_3$: δ 77.23). Melting points (**mp**) were uncorrected. **Enantiomeric ratios** were determined by gas liquid chromategraphy (GLC).[1]

Reagents and catalyst

Racemic diols (Substrates in Table 1) were prepared according to literature procedure.[2] Catalyst **1** was prepared according to the literature procedure[3] and is also commercially available. Chlorotriethylsilane (TESCl) was distilled from 3 Å molecular sieves prior to use. Citric Acid, *tert*-butyldimethylsilyl chloride (TBSCl), diisopropylethylamine (DIPEA), and imidazole were used as received. Tetrahydrofuran (THF) was dried on alumina columns by a solvent dispensing system prior to use.

General procedure for the regiodivergent reaction on a racemic mixture of 1,2-*syn* diols through catalytic enantioselective silylation with TBSCl

Catalyst **1** (19 mg, 0.06 mmol) and the diol substrate (0.2 mmol) were weighed into a 10 x 75 mm test tube. THF (48 μL) and DIPEA (52 μL, 0.3 mmol) were added with a mechanical pipettor. The tube was capped with a septum, and the mixture was allowed to cool to –78 °C. TBSCl (45 mg, 0.3 mmol) was dissolved in THF (55 μL, total volume ~100 μL) and added to the test tube with a Gilson Pipetman. The test tube was capped with a septum, wrapped with Teflon tape and the mixture was allowed to stir at the appropriate temperature (see below for details) in a cryocool apparatus for the reported period of time. The reaction was quenched by addition of DIPEA (25 μL) and MeOH (25 μL). The mixture was allowed to warm to room temperature, diluted with EtOAc (20 mL) and washed with 10% citric acid (10 mL). The aqueous layer was washed with EtOAc (2 x 15 mL) and the combined organic layer was dried over $MgSO_4$, filtered and concentrated to afford a yellow oil. The reaction mixture was purified by silica gel chromatography (10% Et_2O in hexanes to 1:1 Et_2O:hexanes) and analyzed by GLC (Supelco Beta, or Gamma Dex 120).

The aqueous layer was basified with $NaOH_{(aq)}$ (3 N) until pH 12 and washed with CH_2Cl_2 (3 x 15 mL). The combined organic layer was dried over $MgSO_4$, filtered and concentrated under high vacuum to provide the recovered catalyst **1** as a white solid (mass recovery > 90%). The recovered catalyst was used directly for subsequent silylation reactions with the same efficiency and selectivity.

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[1] Due to resolution issues during photocopying/scanning, some of the GLC spectra were digitally darkened to improve readability.

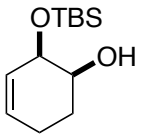
[2] B. Jung, S. Kang, *Proc. Nat. Acad. Sci.* **2007**, *104*, 1473–1475.

[3] Y. Zhao, J. Rodrigo, A. H. Hoveyda, M. L. Snapper, *Nature* **2006**, *443*, 67–70.

General procedure for the regiodivergent reaction on a racemic mixture of 1,2-*syn* diols through catalytic enantioselective silylation with TESCl

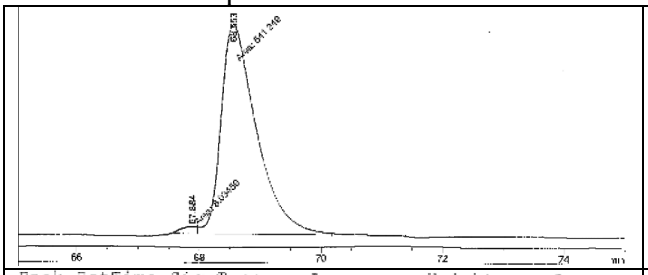
Catalyst **1** (12 mg, 0.04 mmol) and the diol substrate (0.2 mmol) were weighed into a 10 x 75 mm test tube. THF (148 μL) and DIPEA (52 μL, 0.3 mmol) were added with a mechanical pipettor. The tube was capped with a septum, and the mixture was allowed to cool to -78 °C. TESCl (42 μL, 0.25 mmol) was dissolved in THF (158 μL, total volume ~200 μL) and added to the test tube with a mechanical pipettor. The test tube was capped with a septum, wrapped with Teflon tape and the mixture was allowed to stir at –78 °C in a cryocool apparatus for 48 h. The reaction was quenched by addition of DIPEA (25 μL) and MeOH (25 μL). The mixture was allowed to warm to room temperature, diluted with EtOAc (20 mL) and washed with 10% citric acid (10 mL). The aqueous layer was washed with EtOAc (2 x 15 mL) and the combined organic layer was dried over $MgSO_4$, filtered and concentrated to afford a yellow oil. The crude product was purified by silica gel chromatography (10% diethyl ether in hexanes to 1:1 Et_2O:hexanes) and analyzed by GLC (Supelco Beta, or Gamma Dex 120).

Characterization Data



(1S, 2R)-2-(tert-butyldimethylsilyloxy)cyclohex-3-enol (Table 1, entry 1, regioisomer A, (+)-4): IR (neat, thin film): 3570 (br), 3031 (br), 2955 (s), 2928 (s), 2858 (s), 1729 (s), 1462 (w), 1078 (s), 837 (s), 778 (m) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.81 (1H, dtd, *J* = 10.0, 3.8, 1.2 Hz), 5.53 (1H, ddt, *J* = 10.0, 3.4, 2.0 Hz), 4.18 (1H, m) 3.77 (1H, m), 2.56 (1H, d, *J* = 5.6 Hz), 2.26 -2.17 (1H, m) 2.01-1.83 (2H, m), 1.67 (1H, dtd, *J* = 12.8, 6.4, 2.8 Hz), 0.910 (9H, s), 0.114 (3H, s), 0.109 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 130.5, 127.5, 77.6, 76.9, 68.5, 68.2, 26.5, 26.1, 25.9, 22.8, -3.9, -4.4. **HRMS** $[M+H]^+$: Calculated for $C_{12}H_{25}O_2Si$: 229.1624; Found: 229.1628. **Optical Rotation**: $[\alpha]^{25}_D$ +21 (*c* = 1.0, $CHCl_3$).

Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 140 °C hold 110 min, 15 psi.); chromatograms are illustrated below for a 97% ee sample:



Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
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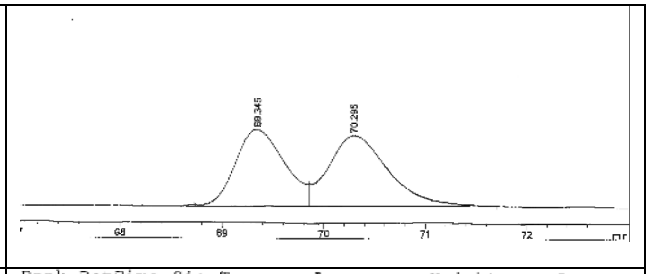
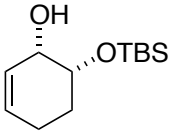


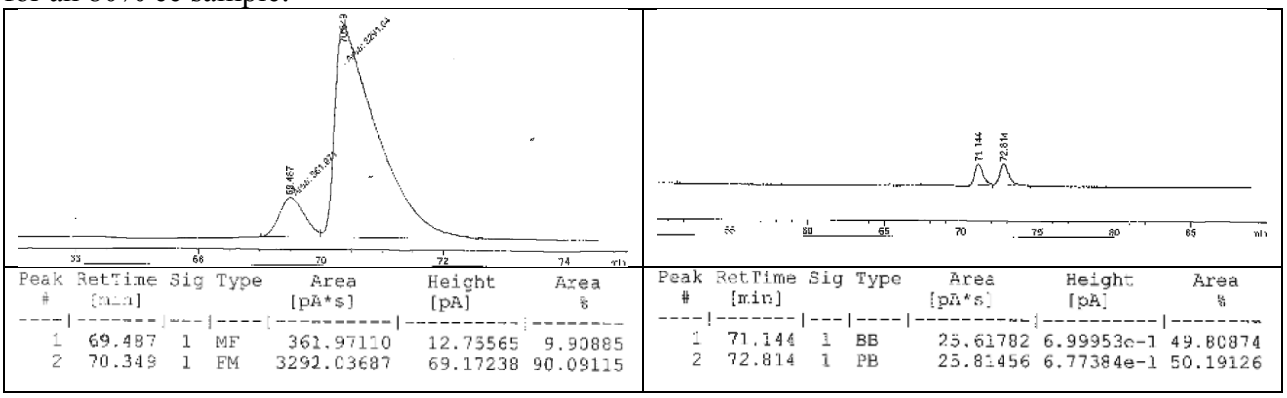
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	69.345	1	BV	191.49962	5.73710	46.95528
2	70.295	1	VB	216.33443	5.28549	53.04472



(1S, 6R)-6-(tert-butyldimethylsilyloxy)cyclohex-2-enol (Table 1, entry 1, regioisomer B, (-)-5): IR (neat, thin film): 3561 (br), 3029 (br), 2952 (s), 2929 (s), 2857 (s), 1471 (w), 1096 (s), 837 (s), 776 (m) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.85 (1H, m), 5.73 (1H, ddt, *J* = 9.6, 4.0, 2.0 Hz), 4.01 (1H, m), 3.86 (1H, dt, *J* = 10.4, 3.2 Hz), 2.63 (1H, d, *J* = 4.0 Hz), 2.25-2.14 (1H, m) 2.06-1.95 (1H, m), 1.88-1.78 (1H, m), 1.62 -1.55 (1H, m), 0.911 (9H, s), 0.106 (3H, s), 0.096 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz):

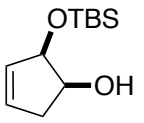
δ 131.0, 127.2, 77.5, 76.9, 70.5, 66.8, 26.4, 26.1, 24.1, 18.4, -4.2, -4.6. **HRMS** $[M\text{-}OH]^+$: Calculated for $C_{12}H_{23}OSi$: 211.1518; Found: 211.1516. **Optical Rotation**: $[\alpha]^{20}_D$ -92 (*c* = 3.8, $CHCl_3$).

Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 140 °C hold 110 min, 15 psi.); chromatograms are illustrated below for an 80% ee sample:



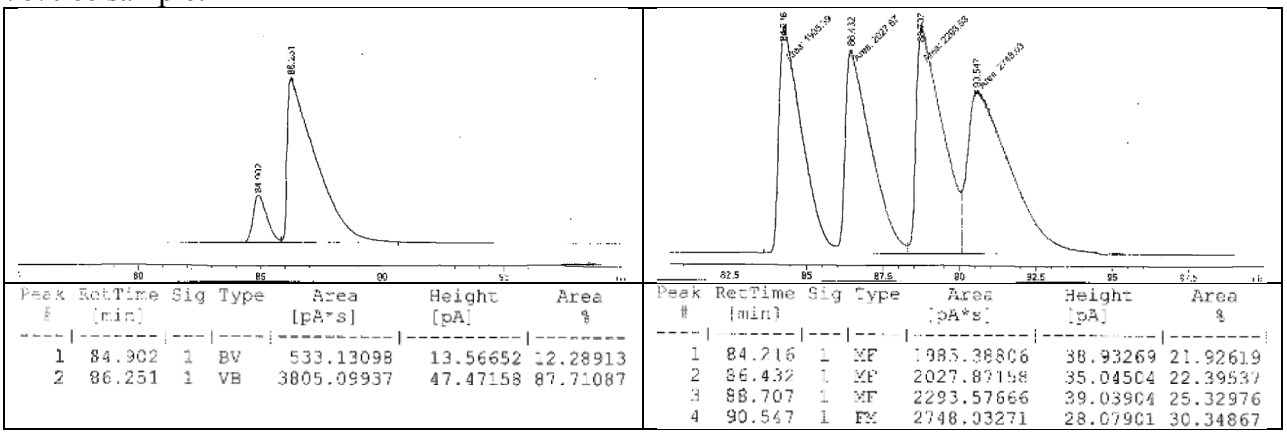
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	69.487	1	MF	361.97110	12.75565	9.90885
2	70.349	1	FM	3292.03687	69.17238	90.09115

Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	71.144	1	BB	25.61782	6.99953e-1	49.80874
2	72.814	1	BB	25.81456	6.77384e-1	50.19126



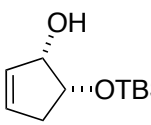
(1S, 2R)-2-(tert-butyldimethylsilyloxy)cyclopent-3-enol (Table 1, entry 2, regioisomer A): IR (neat, thin film): 3538 (br), 3062 (m), 2953 (m), 2929 (m), 2888 (m), 2857 (m), 1082 (m), 923 (m), 836 (s), 778 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.86 (1H, m), 5.82 (1H, dq, *J* = 6.0, 2.0 Hz), 4.32 (1H, t, *J* = 5.2 Hz), 4.34 (1H, td, *J* = 6.4, 3.6 Hz), 2.95 (1H, d, *J* = 5.6 Hz), 2.51 (1H, ddt, *J* = 16.8, 5.6, 2.0 Hz), 2.30 (1H, ddq, *J* = 16.4, 3.6, 2.0 Hz), 0.91 (9H, s), 0.12 (3H, s), 0.11 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 132.6, 132.1, 77.5, 76.9, 75.4, 72.1, 40.1, 26.1, 18.4, –4.4, –4.7. **HRMS** $[M\text{-}OH]^+$: Calculated for $C_{11}H_{21}OSi$: 197.1361; Found: 197.1370. **Optical Rotation**: $[\alpha]^{20}_D$ +14 (*c* = 2.5, $CHCl_3$).

Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 °C isothermal, 15 psi.); chromatograms are illustrated below for a 76% ee sample:



Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	84.902	1	BV	533.13098	13.56652	12.28913
2	86.251	1	VB	3805.09937	47.47158	87.71087

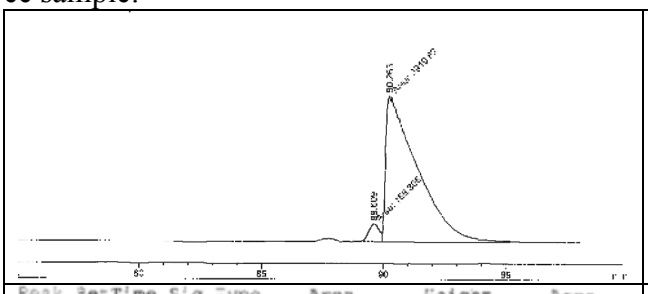
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	84.216	1	MF	1985.38806	38.93269	21.92619
2	86.432	1	MF	2027.87198	35.04504	22.39537
3	88.707	1	MF	2293.57666	39.03904	25.32976
4	90.547	1	FM	2748.03271	28.07901	30.34867



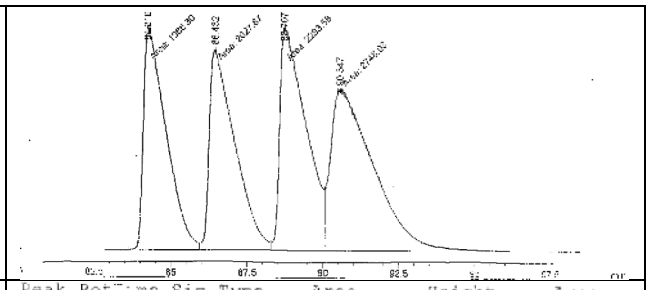
(1S,5R)-5-(tert-butyldimethylsilyloxy)cyclopent-2-enol (Table 1, entry 2, regioisomer B): **IR** (neat, thin film): 3529 (br), 3061 (br), 2953 (m), 2929 (m), 2899 (m), 2857 (m), 1078 (s), 938 (m), 835 (s), 776 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.87 (1H, dqd, *J* = 4.4, 2.0, 1.2 Hz), 5.65 (1H, dq, *J* = 6.0, 2.0 Hz), 4.63 (1H, m), 4.20 (1H, qd, *J* = 5.6, 2.8 Hz), 3.03 (1H, d, *J* = 4.8 Hz), 2.49 (1H, ddtd, *J* = 17.2, 6.0, 2.4,

0.8 Hz), 2.34 (1H, m), 0.91 (9H, s), 0.12 (3H, s), 0.11 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 132.7, 131.4, 77.5, 77.0, 76.9, 70.7, 39.9, 26.1, 18.4, -4.2, -4.6. **HRMS** $[M+H]^+$: Calculated for $C_{11}H_{23}O_2Si$: 215.1467; Found: 215.1459. **Optical Rotation**: $[\alpha]^{20}_D$ -230 (*c* = 3.8, $CHCl_3$).

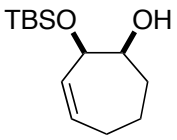
Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 80 °C isothermal, 15 psi); chromatograms are illustrated below for a 92% ee sample:



Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	89.609	1	MF	158.30453	5.46931	3.88179
2	90.263	1	FM	3919.82275	44.29568	96.11821

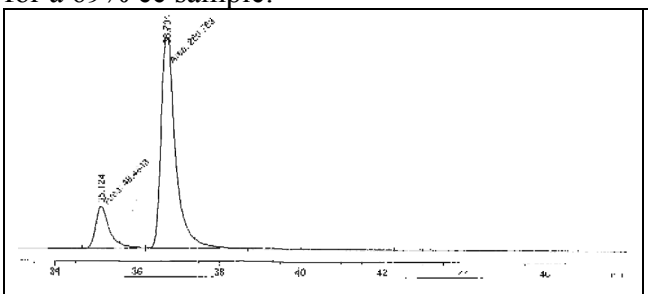


Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	84.216	1	MF	1985.38806	38.93269	21.92619
2	86.432	1	MF	2027.87158	35.04504	22.39537
3	88.707	1	MF	2293.57666	39.03904	25.32976
4	90.547	1	FM	2748.03271	28.07901	30.34867

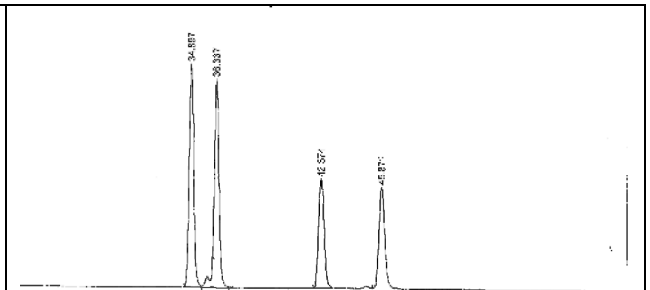


(1S,2R)-2-(tert-butyldimethylsilyloxy)cyclohept-3-enol (Table 1, entry 3, regioisomer A): **IR** (neat, thin film): 3467 (br), 3021 (m), 2928 (m), 2885 (m), 2856 (m), 1251 (m), 835 (s), 775 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.85 (1H, dddd, *J* = 11.6, 7.2, 5.6, 2.0 Hz), 5.50 (1H, ddt, *J* = 11.6, 4.0, 1.6 Hz), 4.42 (1H, dq, *J* = 3.2, 1.6 Hz), 3.80 (1H, m), 2.22 (1H, dtd, *J* = 15.6, 7.6, 2.4 Hz), 2.13 (1H, d, *J* = 5.2 Hz), 2.11-1.94 (2H, m), 1.79-1.60 (2H, m), 1.47 (1H, m), 0.904 (9H, s), 0.076 (3H, s), 0.073 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 132.9, 132.3, 77.5, 76.9, 74.9, 73.0, 34.0, 28.9, 26.1, 21.5, 18.4, -4.3, -4.6. **HRMS** $[M\text{-}OH]^+$: Calculated for $C_{13}H_{25}OSi$: 225.1675; Found: 225.1680. **Optical Rotation**: $[\alpha]^{20}_D$ -110 (*c* = 1.0, $CHCl_3$).

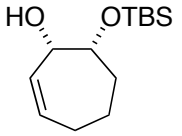
Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 130 °C hold 60 min, 15 psi.); chromatograms are illustrated below for a 69% ee sample:



Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	35.124	1	MF	48.48462	2.09692	15.67826
2	36.704	1	FM	260.76291	11.04851	84.32174

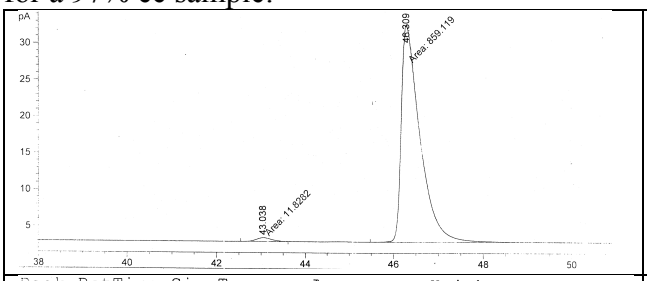


Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	34.897	BV	0.2721	3.85863e4	2163.15918	31.96473
2	36.337	VB	0.2857	3.68778e4	2013.53394	30.54944
3	42.374	BB	0.3221	2.25785e4	1053.09424	18.70390
4	45.871	VB	0.3546	2.26727e4	977.67871	18.78194



(1S,7R)-7-(tert-butyldimethylsilyloxy)cyclohept-2-enol (Table 1, entry 3, regioisomer B): **IR** (neat, thin film): 3446 (br), 3026 (br), 2951 (m), 2929 (m), 2885 (m), 2856 (m), 1251 (m), 836 (s), 775 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 5.86 (1H, dtd, *J* = 12.4, 6.4, 1.6 Hz), 5.55 (1H, dd, *J* = 11.6, 5.2 Hz), 4.25 (1H, m), 3.89 (1H, dt, *J* = 8.4, 2.4 Hz), 2.3-1.96 (4H, m), 1.75-1.65 (2H, m), 1.5-1.3 (1H, m), 0.895 (9H, s), 0.076 (3H, s), 0.070 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 133.2, 131.0, 77.6, 76.9, 74.2, 73.9, 34.4, 28.8, 26.1, 22.5, 18.4, -4.2, -4.6. **HRMS** $[M\text{-}OH]^+$: Calculated for $C_{13}H_{25}OSi$: 225.1675; Found: 225.1665. **Optical Rotation**: $[\alpha]^{20}_D$ +18 (*c* = 1.0, $CHCl_3$).

Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 130 °C hold 60 min, 15 psi.); chromatograms are illustrated below for a 97% ee sample:



Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
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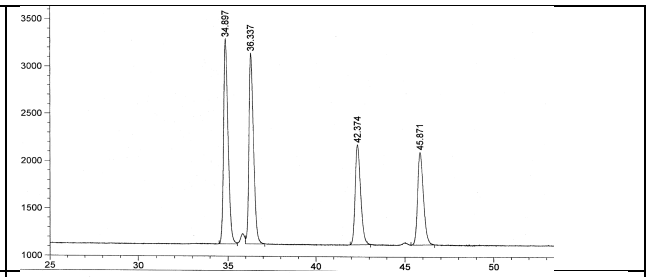
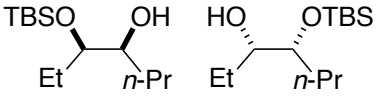
2	46.309	1	MM	859.11871	29.70036	98.64191

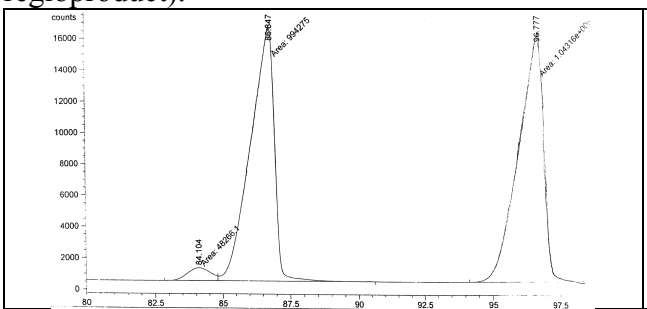


Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	34.897	BV	0.2721	3.85863e4	2163.15918	31.96473
2	36.337	VB	0.2857	3.68778e4	2013.53394	30.54944
3	42.374	BB	0.3221	2.25785e4	1053.09424	18.70390
4	45.871	VB	0.3546	2.26727e4	977.67871	18.78194

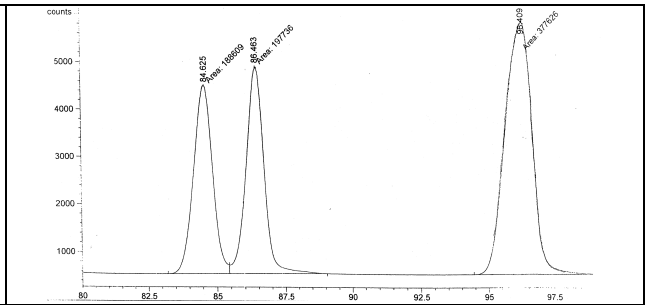


(3R,4S)-3-(triethylsilyloxy)heptan-4-ol (Table 1, entry 4, regioisomer A) and (3S,4R)-4-(triethylsilyloxy)heptan-3-ol (Table 1, entry 4, regioisomer B) *the enantiomeric purity was established on the direct products resulting from the enantioselective catalytic silylation. The chromatograms are illustrated below for 95% ee samples:*

Enantiomeric purity was established by GLC analysis (Supelco Beta Dex 120 (30 m x 0.15 mm x 0.25 μm film thickness), 130 °C hold 60 min, 15 psi.); chromatograms are illustrated below for a 91% ee sample (Note: Because only one of the regioisomeric products can be resolved by GLC, Horeau's equation is applied to the system in order to derive the enantiopurity for the unresolved regioproduct).

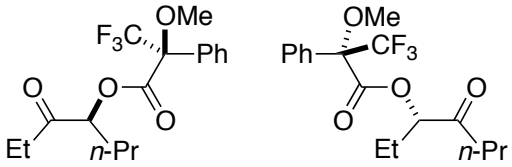


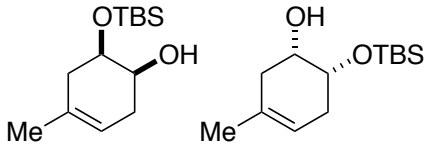
Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	84.104	MF	0.9770	4.82661e4	823.36060	2.31415
2	86.847	FM	1.0221	9.94275e5	1.62127e4	47.67112
3	96.777	MM	1.0889	1.04316e6	1.59671e4	50.01473



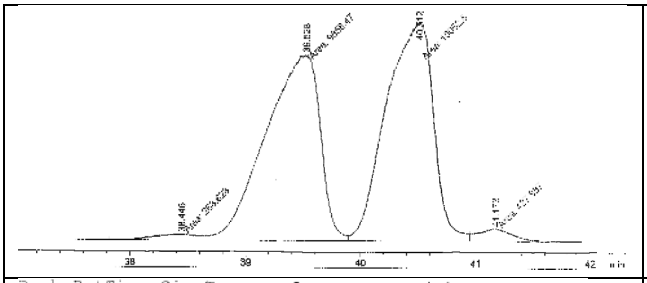
Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	84.625	MF	0.7897	1.88609e5	3980.45947	24.68800
2	86.463	FM	0.7524	1.97736e5	4380.38086	25.88268
3	96.409	MM	1.1826	3.77626e5	5321.94287	49.42933

This mixture of regioisomeric products was derivatized to the corresponding Mosher ester products according to known literature precedent.[4] The product mixture was directly desilylated under the conditions of SiO_2/MeOH. This mixture of alcohols was oxidized under standard conditions[5] to afford a mixture of pseudodiastereomeric products. These products were purified by silica gel chromatography (5% EtOAc/hexanes) to afford the following products:

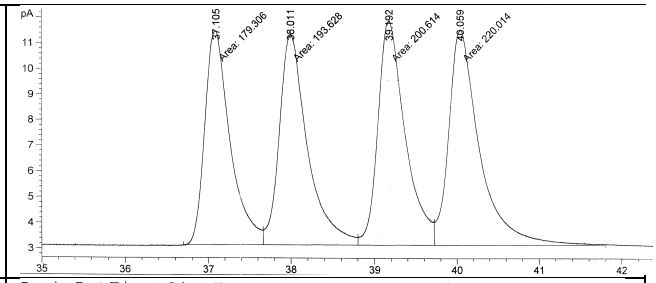




(1S,2R)-2-(*tert*-butyldimethylsilyloxy)-4-methylcyclohex-4-ene-1-ol (Table 1, entry 5, regioisomer A) and (1R,2S)-1-(*tert*-butyldimethylsilyloxy)-4-methylcyclohex-4-ene-2-ol (Table 1, entry 5, regioisomer B) were derivatized to characterize the products of this transformation, although the enantiomeric purity was established on the direct products resulting from the enantioselective catalytic silylation. Chromatograms are illustrated below for 93% ee samples:

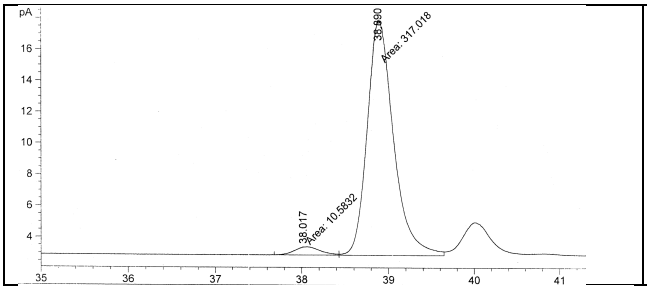


Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	38.446	1	MF	268.62799	8.86141	1.30354
2	39.528	1	FM	9858.46582	299.39127	47.83913
3	40.512	1	MF	1.00525e4	353.52789	48.78048
4	41.173	1	FM	427.98700	19.44015	2.07685

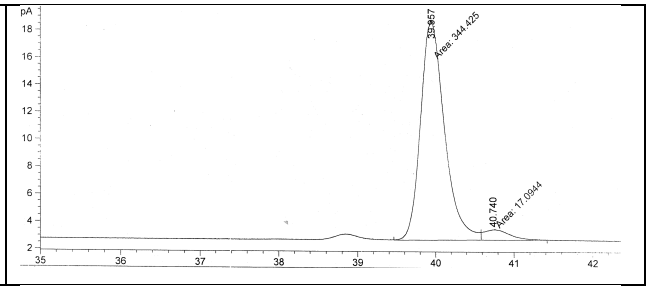


Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	37.105	1	MF	179.30583	8.34321	22.59507
2	38.011	1	FM	193.62781	8.21185	24.39984
3	39.192	1	MF	200.61395	8.74224	25.28020
4	40.059	1	FM	220.01408	8.38990	27.72489

Below are examples of optically and regioisomerically enriched samples obtained after silica gel chromatography:



Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	38.017	1	MF	10.58323	5.38564e-1	3.23053
2	38.890	1	MF	317.01773	15.01729	96.76947

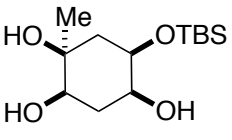


Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	39.957	1	MF	344.42480	16.05192	95.27151
2	40.740	1	FM	17.09441	7.55596e-1	4.72849

[4] T. R. Hoye, C. S. Jeffrey, F. Shao, *Nature Protocols* **2007**, *2*, 2451-2458.

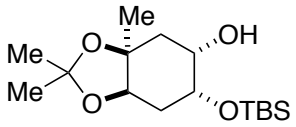
[5] E. J. Corey, W. Suggs, *Tetrahedron Lett.* **1975**, *16*, 2647–2650.

This mixture of regioisomeric products was subjected to Sharpless asymmetric dihydroxylation (AD-mix-β) according to known literature precedent.[6] The products were purified by silica gel chromatography (60% EtOAc/hexanes) to afford the following product:

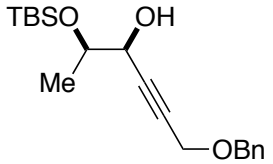


IR (neat, thin film): 3422 (br), 2953 (m), 2929 (m), 2885 (m), 2857 (m), 1462 (w), 1289 (m), 1061 (s), 1021 (s), 832 (s), 775 (s), 730 (m), 670 (m), 435 (w) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 4.00 (1H, ddd, *J* = 9.2, 7.2, 3.2 Hz), 3.76 (1H, q, *J* = 3.2 Hz), 3.79 (1H, m), 2.41 (1H, s), 2.03 (1H, dt, *J* = 13.6, 4.4 Hz), 1.96- 1.74 (4H, m), 1.25 (3H, s), 0.89 (9H, s), 0.084 (3H, s), 0.076 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 72.3, 70.4, 70.3, 69.1, 39.8, 34.1, 27.6, 26.0, 18.3, -4.3, -4.6. **HRMS** $[M+H]^+$: Calculated for $C_{13}H_{29}O_4Si$: 277.1835; Found: 277.1828. **Optical Rotation**: $[\alpha]^{20}_D$ -2.0 (*c* = 1.0, $CHCl_3$).

In order to obtain a pure sample of the other regioproduct (contaminated with methane sulfonamide after column chromatography), the acetonide derivative was prepared according to a known procedure.[7] The product was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the following product:



IR (neat, thin film): 3574 (br), 2984 (m), 2955 (m), 2931 (m), 2859 (m), 1371 (m), 1234 (m), 1185 (s), 1097 (s), 1074 (s), 927 (m), 812 (s), 778 (s), 671 (m), 519 (w) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 4.00 (1H, ddd, *J* = 10.8, 5.2, 3.2 Hz), 3.91 (1H, m), 3.81 (1H, m), 2.31 (1H, dd, *J* = 2.0, 1.6 Hz), 2.10-1.80 (4H, m), 1.46 (3H, s), 1.43 (3H, s), 1.33 (3H, s), 0.893 (9H, s), 0.099 (3H, s), 0.091 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 107.3, 79.9, 77.9, 69.8, 67.9, 39.3, 29.5, 28.5, 27.2, 26.4, 26.0, 18.2, -4.2, -4.5. **HRMS** $[M+H]^+$: Calculated for $C_{16}H_{33}O_4Si$: 317.2148; Found: 317.2157. **Optical Rotation**: $[\alpha]^{20}_D$ -1.0 (*c* = 1.0, $CHCl_3$).



(2R,3S)-6-(benzyloxy)-2-(tert-butyldimethylsilyloxy)hex-4-yn-3-ol (Table 1, entry 6, regioisomer A): **IR** (neat, thin film): 2953 (m), 2929 (m), 2885 (m), 2856 (m), 1472 (w), 1454 (w), 1254 (m), 1097 (s) 835 (s), 777 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.38-7.28 (5H, m), 4.61 (2H, s), 4.34 (1H, br), 4.23 (2H, dd, *J* = 2.4, 1.6 Hz), 3.95 (1H, qd, *J* = 6.0, 4.0 Hz), 2.42 (1H, d, *J* = 5.2 Hz), 1.25 (3H, d, *J* = 6.4 Hz), 0.907 (9H, s), 0.103 (6H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 137.6, 128.6, 128.2, 128.0, 84.8, 82.2, 71.7, 71.2, 67.3, 57.6, 26.0, 18.5, 18.3, -4.1, -4.5. **HRMS** $[M+H]^+$: Calculated for $C_{19}H_{31}O_3Si$: 335.2043; Found: 335.2057. **Optical Rotation**: $[\alpha]^{20}_D$ 0 (*c* = 1.0, $CHCl_3$).

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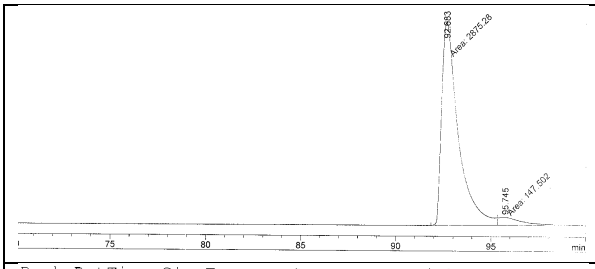
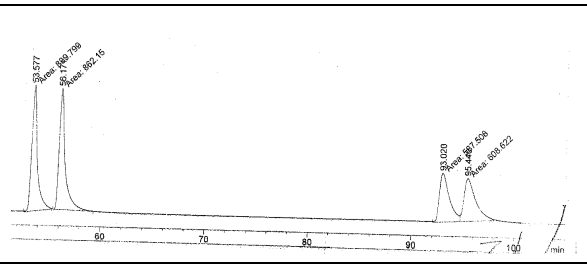
[6] D. P. G. Hamon, K. L. Tuck, H. S. Christie, *Tetrahedron* **2001**, *57*, 9499-9508.

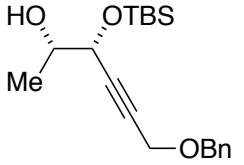
[7] Z. Liu, B. –H. Hu, P. B. Messersmith, *Tetrahedron Lett.* **2008**, *49*, 5519–5521.



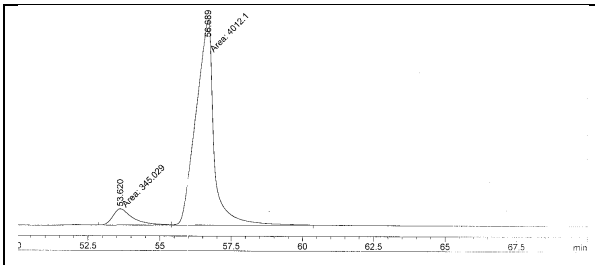
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	92.683	1	MF	2875.27661	47.75792	95.12031
2	95.745	1	FM	147.50224	1.84325	4.87969



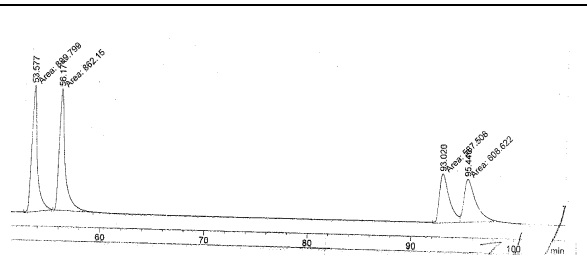
Peak #	Ret Time [min]	Area %
1	93.020	587.508
2	95.440	608.622



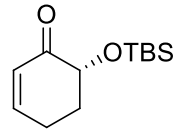
(2S,3R)-6-(benzyloxy)-3-(*tert*-butyldimethylsilyloxy)hex-4-yn-2-ol (Table 1, entry 6, regioisomer B): IR (neat, thin film): 2955 (m), 2929 (m), 2889 (m), 2856 (m), 1472 (w), 1463 (w), 1252 (m), 1098 (s) 838 (s), 778 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.37-7.27 (5H, m), 4.60 (2H, s), 4.34 (1H, dt, *J* = 4.4, 1.6 Hz), 4.23 (2H, d, *J* = 1.6 Hz), 3.81 (1H, qd, *J* = 6.0, 4.4 Hz), 2.32 (1H, br), 1.25 (3H, d, *J* = 6.0 Hz), 0.928 (9H, s), 0.184 (3H, s) 0.150 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 137.6, 128.6, 128.2, 128.0, 85.1, 82.4, 71.7, 70.9, 68.1, 57.6, 26.0, 18.5, 18.0, -4.2, -4.8. **HRMS** $[M+H]^+$: Calculated for $C_{19}H_{31}O_3Si$: 335.2043; Found: 335.2039. **Optical Rotation**: $[\alpha]^{20}_D$ -22 (*c* = 1.0, $CHCl_3$).



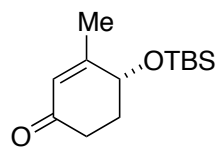
Peak #	RetTime [min]	Sig	Type	Area [pA*s]	Height [pA]	Area %
1	53.620	1	MF	345.02911	7.20918	7.91873
2	56.689	1	FM	4012.09741	90.67001	92.08127



Peak #	Ret Time [min]	Area %
1	53.577	889.799
2	56.171	862.150



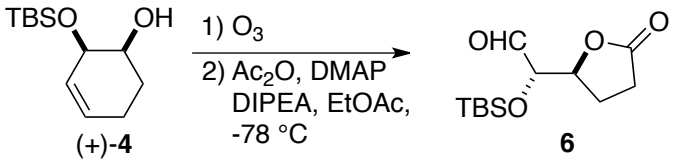
(*R*)-6-(*tert*-butyldimethylsilyloxy)cyclohex-2-enone (7, Scheme 3): IR (neat, thin film): 2954 (m), 2929 (m), 2888 (w), 2856 (m), 1699 (s), 1255 (m), 1141 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 6.89 (1H, dddd, *J* = 16.5, 8.0, 5.0, 1.5 Hz), 5.98 (1H, ddd, *J* = 11.0, 2.5, 1.5 Hz), 4.17 (1H, dd, *J* = 11.5, 5.0 Hz), 2.47-2.54 (1H, m), 2.38-2.46 (1H, m), 2.14-2.19 (1H, m), 2.01-2.09 (1H, m), 0.91 (1H, s), 0.16 (3H, s), 0.08 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 198.9, 149.6, 128.7, 74.4, 32.7, 26.0, 25.5, 18.7, -4.3, -5.2. **HRMS** $[M+H]^+$: Calculated for $C_{12}H_{22}O_2Si$: 226.1389; Found: *submitted*. **Optical Rotation**: $[\alpha]^{20}_D$ +47 (*c* = 0.6, $CDCl_3$).



(R)-4-(*tert*-butyldimethylsilyloxy)-3-methylcyclohex-2-enone (8, Scheme 3): IR (neat, thin film): 2954 (m), 1674 (s), 1628 (w), 1253 (s), 1102 (s) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): 5.83 (1H, br. s), 4.35 (1H, dd, *J* = 8.0, 5.0 Hz),

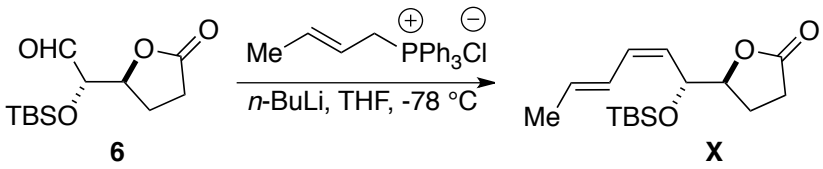
2.56 (1H, dt, *J* = 16.5, 5.0 Hz), 2.31 (1H, ddd, *J* = 16.5, 12.0, 5.0 Hz), 2.16 (1H, m), 1.99 (1H, m), 1.98 (3H, s), 0.92 (9H, s), 0.14 (3H, s), 0.13 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 198.8, 164.4, 126.8, 69.9, 35.4, 32.8, 26.0, 21.3, 18.3, -4.0, -4.6. **HRMS** $[M+H]^+$: Calculated for $C_{13}H_{25}O_2Si$: 241.1624; Found: 241.1619. **Optical Rotation**: $[\alpha]^{20}_D$ +15 (*c* = 0.5, $CDCl_3$).

Enantioselective synthesis of sapinofuranone A



(S)-2-(tert-butyldimethylsilyloxy)-2-((S)-5-oxotetrahydrofuran-2-yl)acetaldehyde (6, Scheme 3): A solution of TBS ether **(+)-4** (0.19 g, 0.83 mmol) in EtOAc (100 mL) at -78 °C was purged with O_3 until the solution turned blue. The system was then purged with N_2 until the blue color had disappeared (approximately 15 min). To this solution were added Ac_2O (0.25 g, 2.5 mmol) and DIPEA (0.52 g, 4.0 mmol) using a microsyringe. The mixture was allowed to stir for 5 min. prior to the addition of DMAP (0.01 g, 0.08 mmol). The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ solution (50 mL). The mixture was partitioned and the organic layer was collected. The aqueous layer was washed with EtOAc (2 x 50 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The mixture was filtered and solvent was removed in vacuo to yield a light yellow oil (~300 mg). This was purified by Florisil® chromatography (200 mesh, 30% EtOAc/hexanes) to yield desired product **6** as a colorless oil (0.18 g, 83% yield over 2 steps).

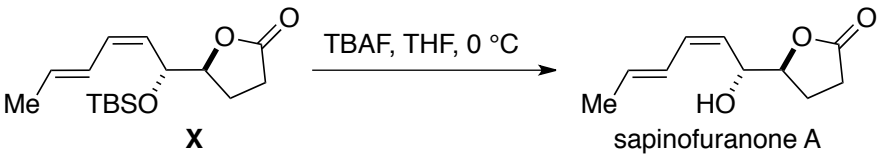
IR (neat, thin film): 2956 (s), 2930 (s), 2857 (s), 1781 (s), 1734 (s), 1463 (w), 1361 (w) 1256 (m), 1135 (s), 838 (s), 780 (m), 541 (w) cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 9.68 (1H, s), 4.87 (1H, td, *J* = 7.2, 2.8 Hz), 3.51 (1H, d, *J* = 10.0 Hz), 3.45 (1H, d, *J* = 10.8 Hz), 2.77 (1H, s), 2.36 (1H, s), 1.11 (3H, s), 0.935 (9H, s), 0.143 (3H, s), 0.120 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 201.7, 176.8, 79.3, 78.8, 28.5, 25.9, 21.7, 18.4, -4.67, -4.73. **HRMS** $[M+H]^+$: Calculated for $C_{12}H_{23}O_4Si$: 259.1366; Found: 259.1359. **Optical Rotation**: $[\alpha]^{20}_D$ -15 (*c* = 1.0, $CHCl_3$).



(S)-5-((R,2Z,4E)-1-(tert-butyldimethylsilyloxy)hexa-2,4-dienyl)dihydrofuran-2(3H)-one (TBS-sapinofuranone A, Scheme 3): A suspension of the Wittig salt (0.25 g, 0.71 mmol) in THF (5 mL) is deprotonated by the slow addition (approximately 5 min.) of freshly titrated *n*-BuLi (323 μL, 0.71 mmol) by microsyringe. This deep red mixture is allowed to stir at room temperature for 1 h. The contents of this mixture are then transferred to a syringe and fitted to a syringe pump. This mixture is then added slowly (over 5 h) to a solution of aldehyde **6** (0.18 g, 0.68 mmol) in THF (5 mL) at -78 °C. The reaction is allowed to stir at this temperature for an additional 12 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ solution (50 mL) and diluted with EtOAc (50 mL). The mixture was partitioned and the organic layer was collected. The

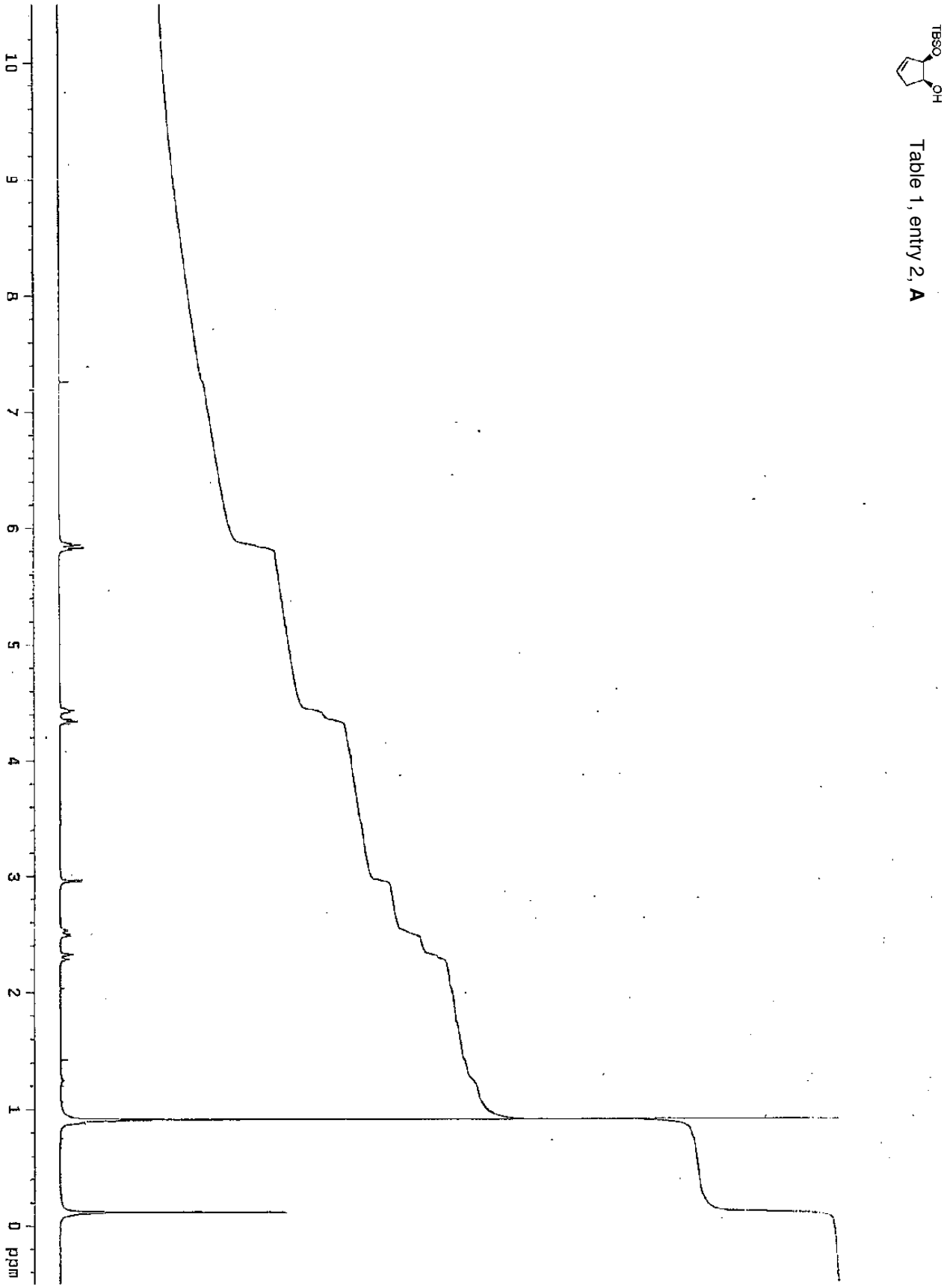
aqueous layer was washed with EtOAc (2 x 50 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The mixture was filtered and solvent was removed in vacuo to yield an orange oil. This reaction mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to yield desired product **X** as a colorless oil (0.11 g, 55% yield).

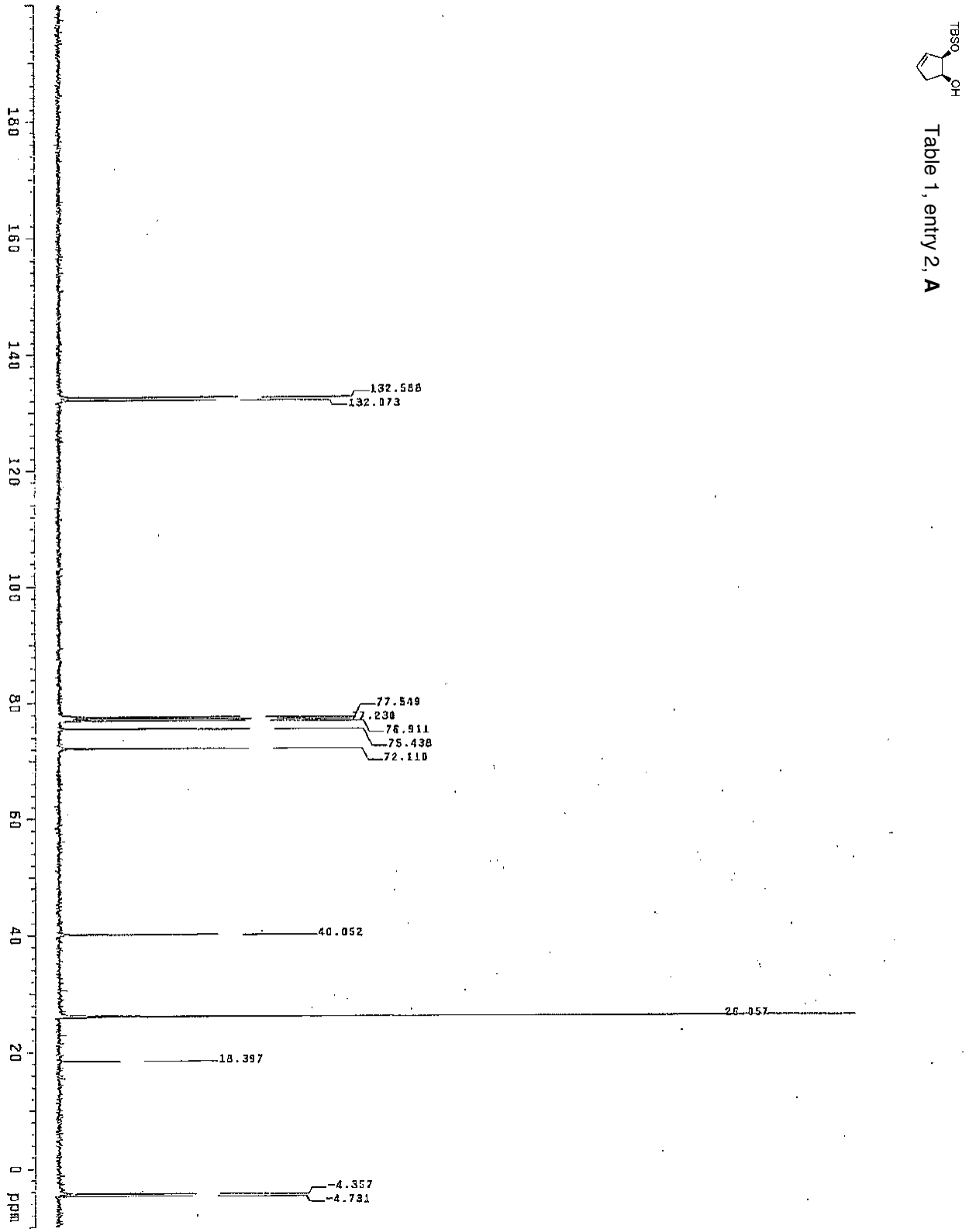
IR (neat, thin film): 2956 (m), 2930 (m), 2886 (m), 2857 (m), 1781 (s), 1471 (m), 1255 (m), 1105 (m), 894 (m), 835 (s), 779 (m). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 6.24 (1H, dd, *J* = 13.6, 12.4 Hz), 6.03 (1H, t, *J* = 10.8 Hz), 5.79 (1H, dq, *J* = 14.0, 6.8 Hz), 5.14 (1H, dd, *J* = 11.2, 8.0 Hz), 4.85 (1H, d, *J* = 8.4 Hz), 4.42 (1H, ddd, *J* = 8.0, 4.4, 2.4 Hz), 2.60 (1H, m), 2.42 (1H, ddd, *J* = 17.6, 10.8, 5.6 Hz) 2.33-2.25(1H, m), 2.16-2.07 (1H, m), 1.81 (3H, d, *J* = 6.8 Hz), 0.87 (9H, s), 0.066 (3H, s), 0.044 (3H, s). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 177.7, 133.4, 131.1, 126.7, 126.2, 82.6, 70.5, 28.9, 26.0, 21.2, 18.7, 18.3, -4.4, -4.7. **HRMS** $[M+H]^+$: Calculated for $C_{16}H_{29}O_3Si$: 297.1886; Found: 297.1901. **Optical Rotation**: $[\alpha]^{20}_D$ +47 (*c* = 1.0, $CHCl_3$).

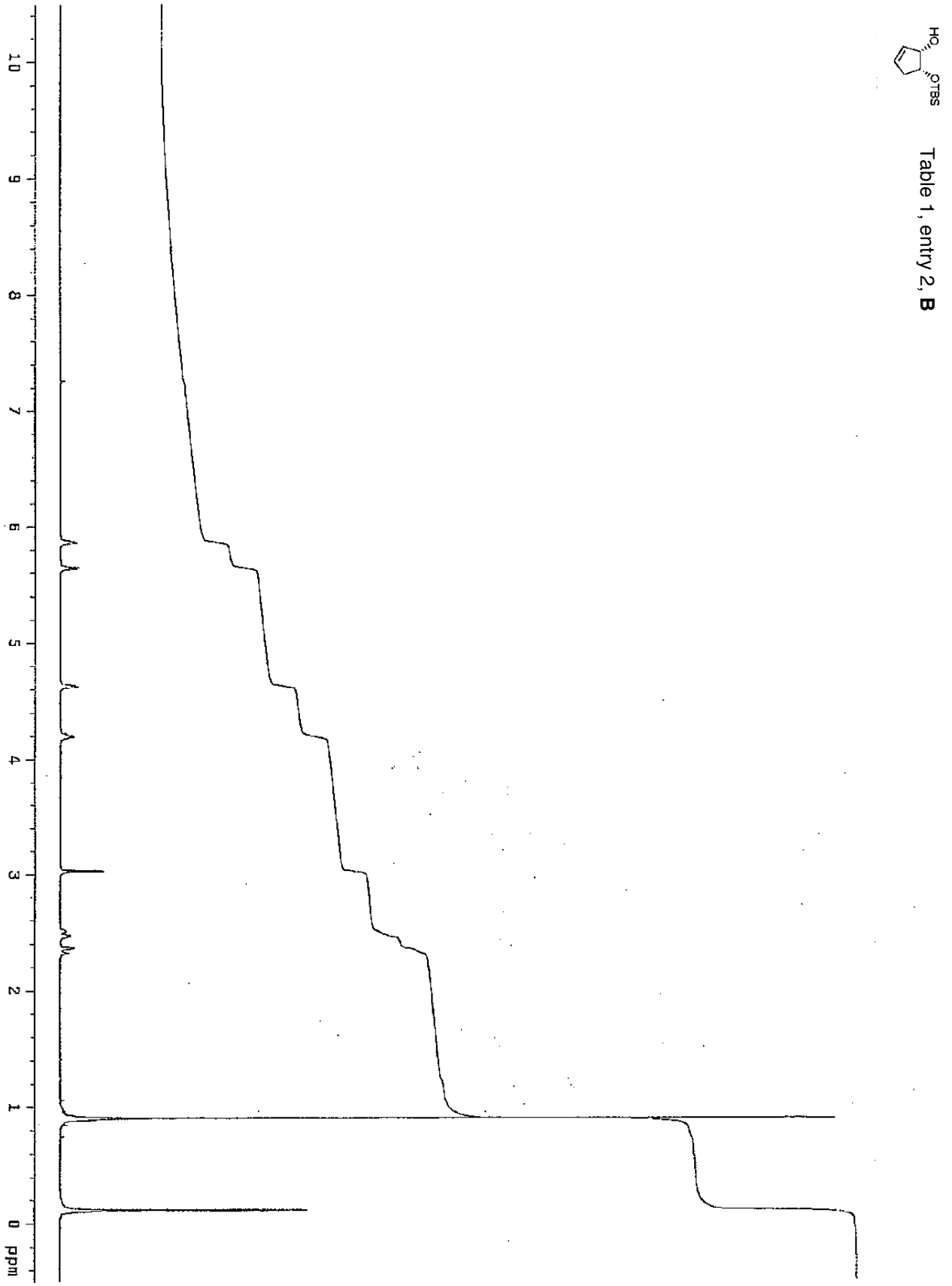


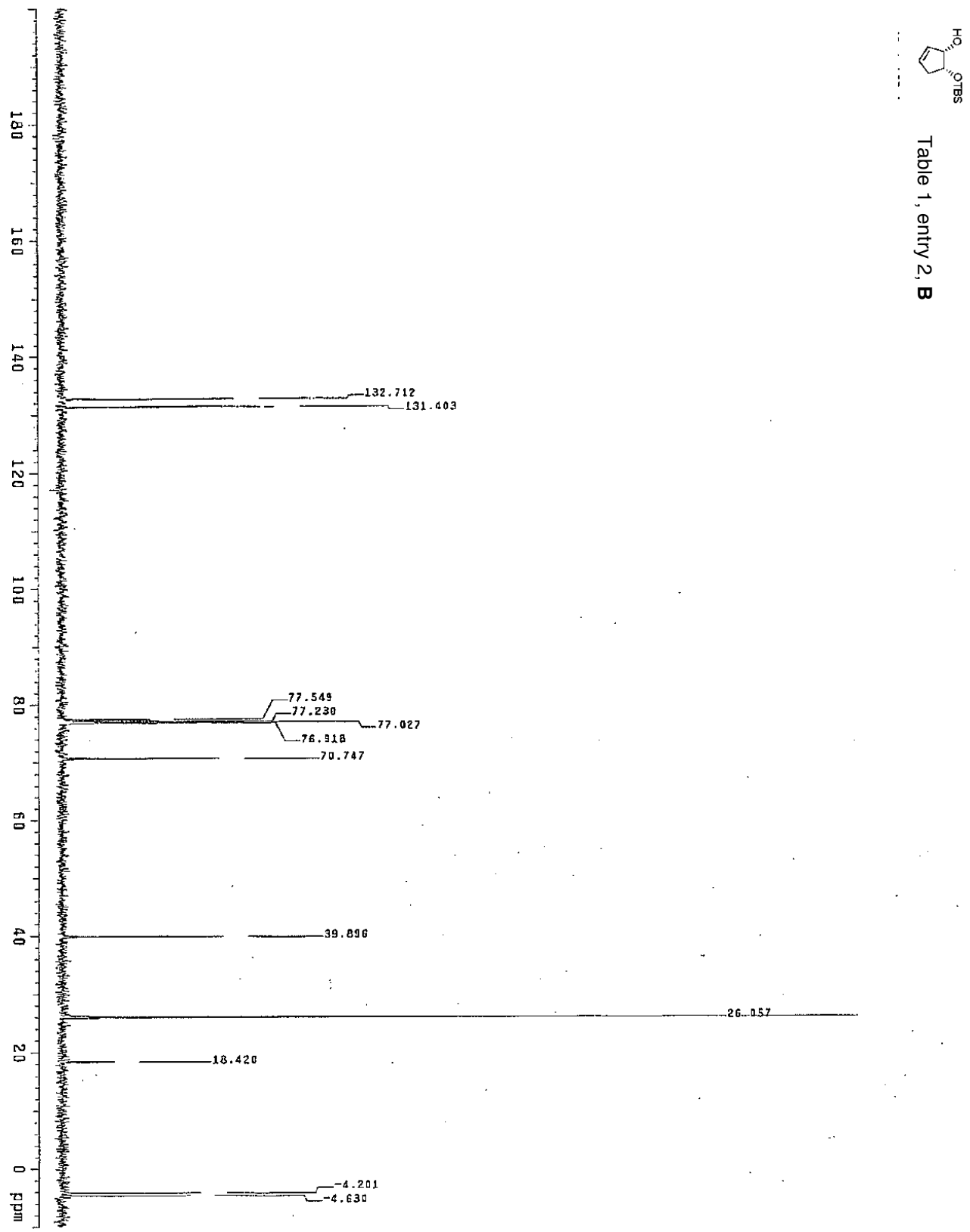
Sapinofuranone A (Scheme 3): To lactone **X** (25.0 mg, 0.084 mmol) in THF (2 mL) at 0 ºC was added a solution of TBAF in THF (1 M, 101 μL, 0.10 mmol). The reaction was allowed to stir at this temperature for 45 min. The reaction mixture was diluted with Et_2O (50 mL) and quenched by the addition of a $HCl_{(aq.)}$ solution (1 M, 25 mL). The mixture was partitioned and the organic layer was collected. The aqueous layer was washed with diethyl ether (2 x 50 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The mixture was filtered and solvent was removed in vacuo to yield a yellow oil. This reaction mixture was purified by silica gel chromatography (35% EtOAc/hexanes) to yield desired product **Sapinofuranone A** as a colorless oil (14.4 mg, 94% yield).

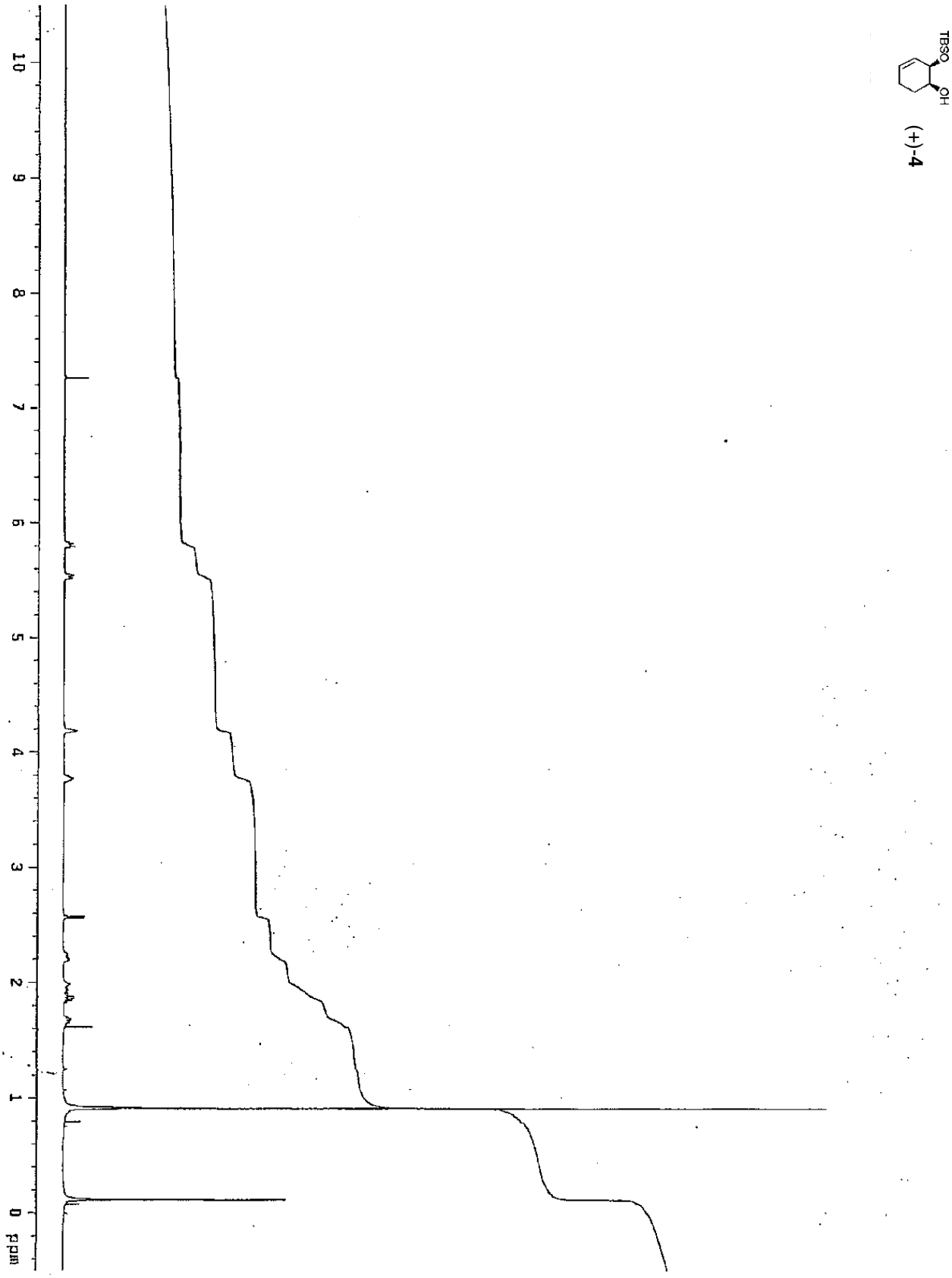
IR (neat, thin film): 3432 (br), 3023 (w), 2916 (w), 2853 (w), 1771 (s), 1655 (w), 1186 (m), 951 (m), 823 (m), 755 (w), 672 (w), 533 (w). **^{1}H NMR**: ($CDCl_3$, 400 MHz): δ 6.30 (1H, ddq, *J* = 13.7, 11.2, 1.8 Hz), 6.15 (1H, dd, *J* = 11.2, 11.0 Hz), 5.82 (1H, dq, *J* = 13.7, 6.8 Hz), 5.20 (1H, dd, *J* = 11.0, 8.4 Hz), 4.88 (1H, dd, *J* = 8.4, 3.1 Hz), 4.51 (1H, dt, *J* = 7.2, 3.1 Hz), 2.51 (2H, m), 2.20 (2H, m), 1.80 (3H, dd, *J* = 6.8, 1.8 Hz). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 177.5, 134.0, 133.3, 126.2, 123.9, 82.5, 68.8, 28.8, 21.6, 18.6. $[M\text{-}OH]^+$: Calculated for $C_{10}H_{13}O_2$: 165.0916; Found: 165.0910. **Optical Rotation**: $[\alpha]^{20}_D$ +16 (*c* = 1.3, $CDCl_3$).

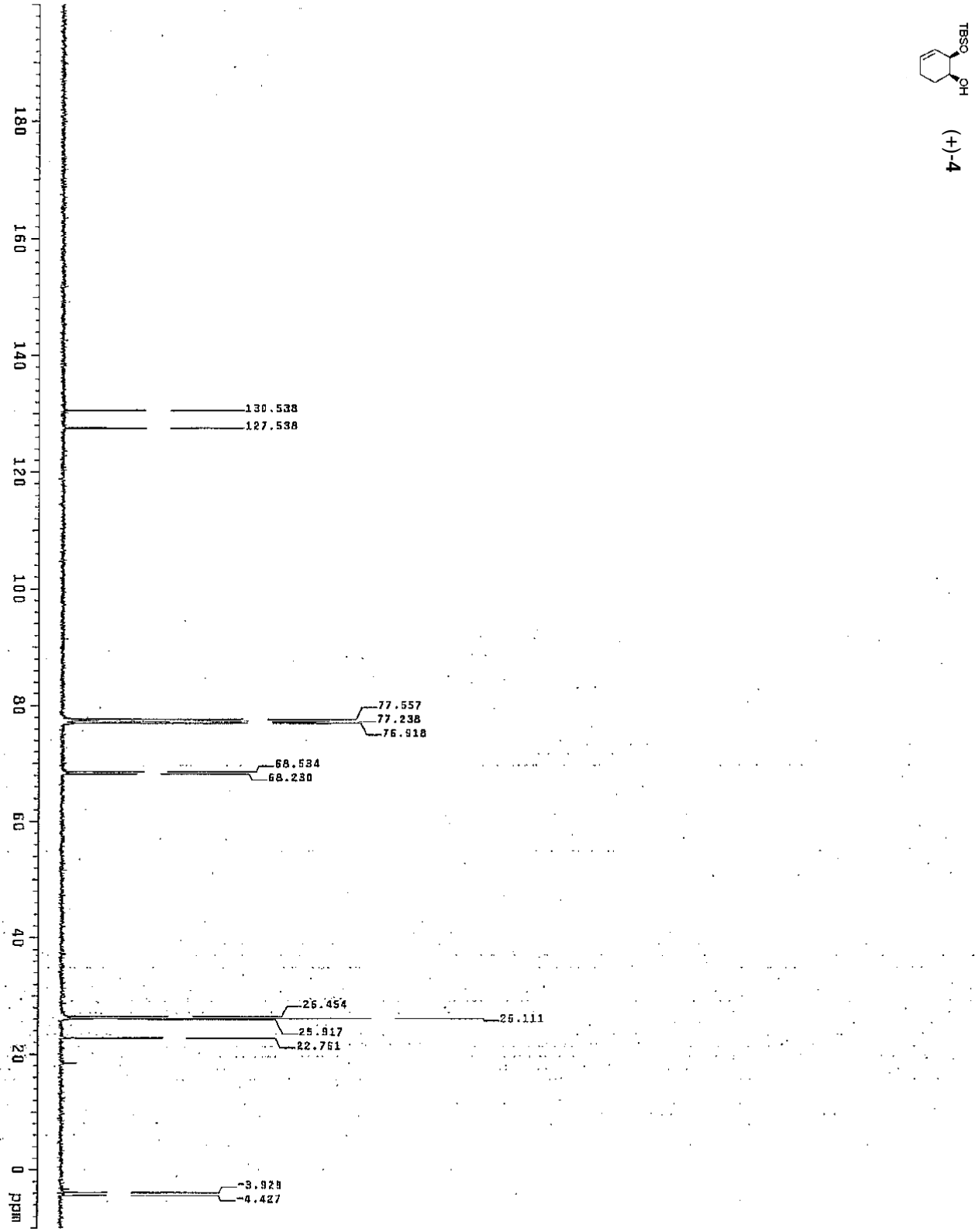

TBSO
OH
Table 1, entry 2, **A**
10
9
8
7
6
5
4
3
2
1
0
ppm

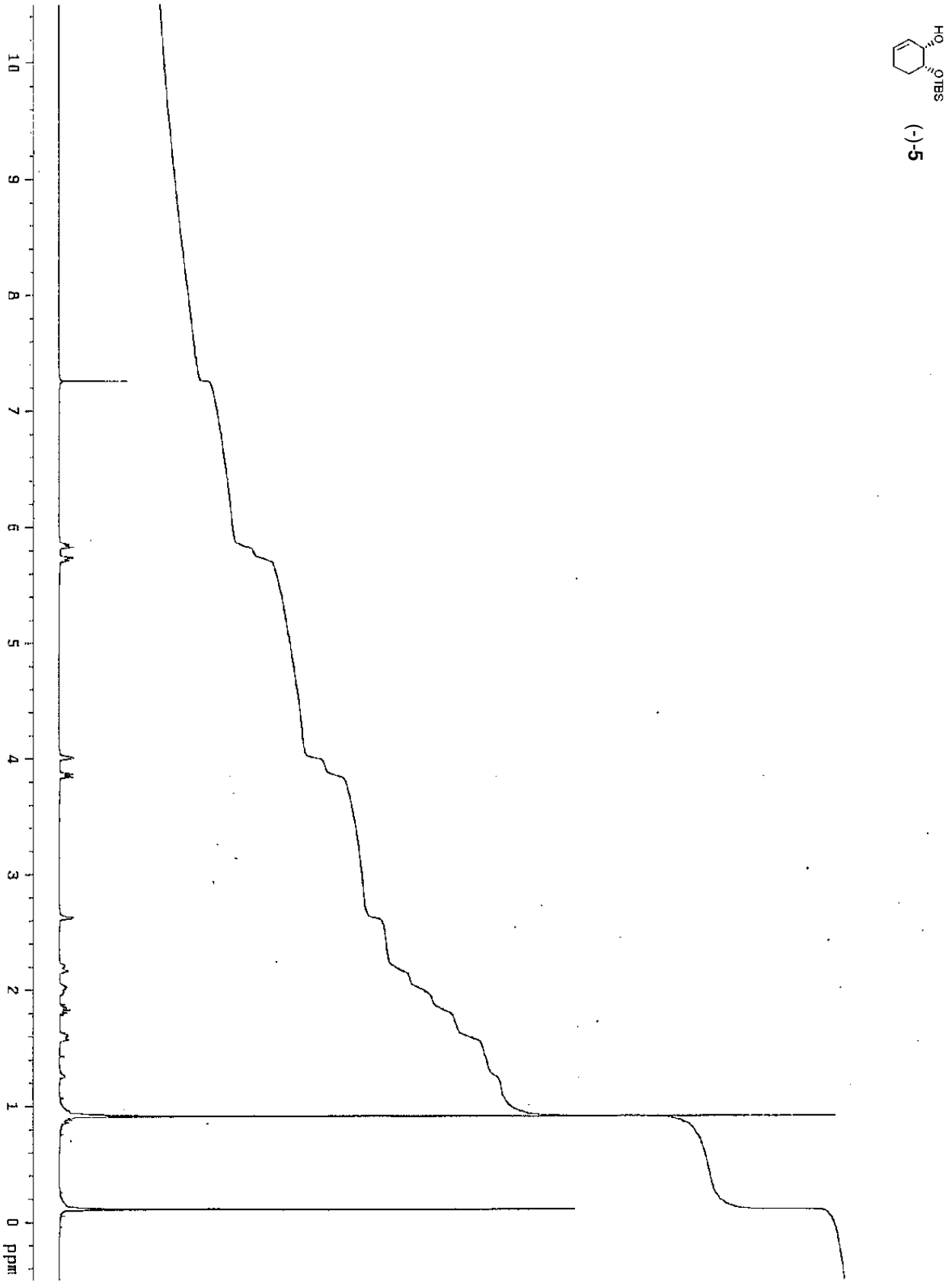

TBSO
OH
Table 1, entry 2, **A**
132.588
132.073
77.549
77.230
76.911
75.438
72.110
40.052
26.057
18.397
-4.357
-4.731
ppm

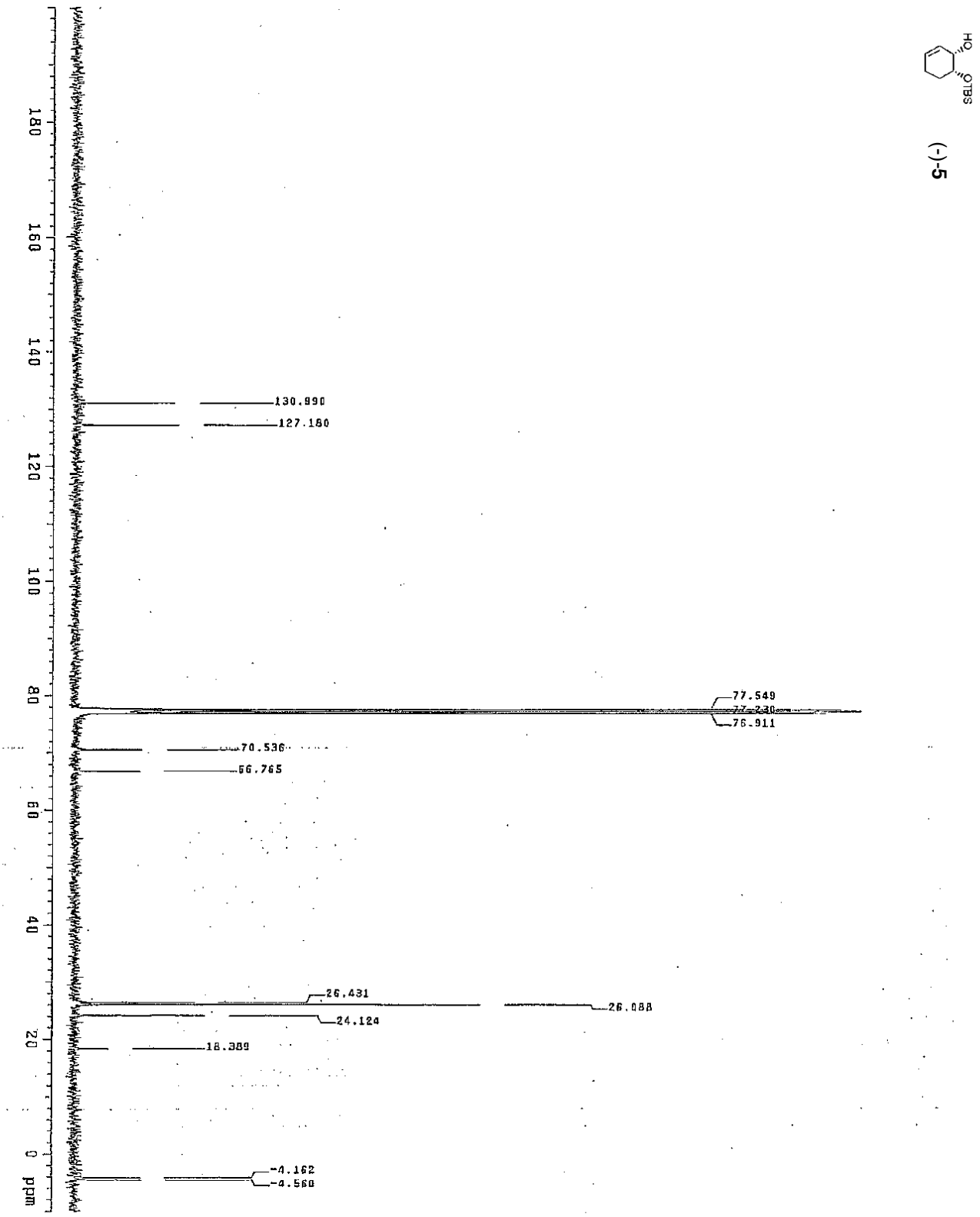

HO
OTBS
Table 1, entry 2, **B**
10
9
8
7
6
5
4
3
2
1
0 ppm

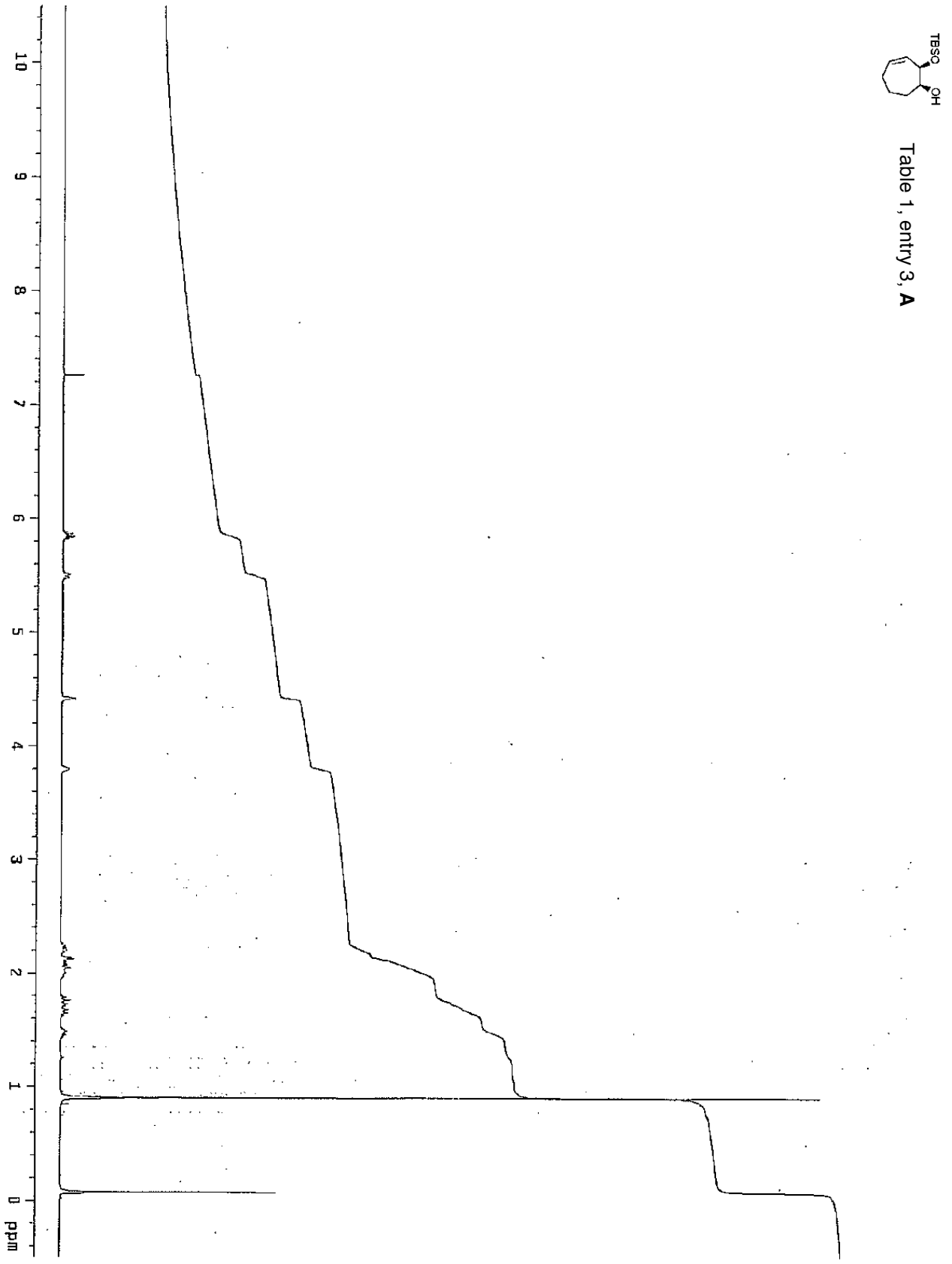

HO
OTBS
Table 1, entry 2, **B**
180
160
140
120
100
80
60
40
20
0
ppm
132.712
131.403
77.549
77.230
77.027
76.918
70.747
39.896
26.057
18.420
-4.201
-4.630

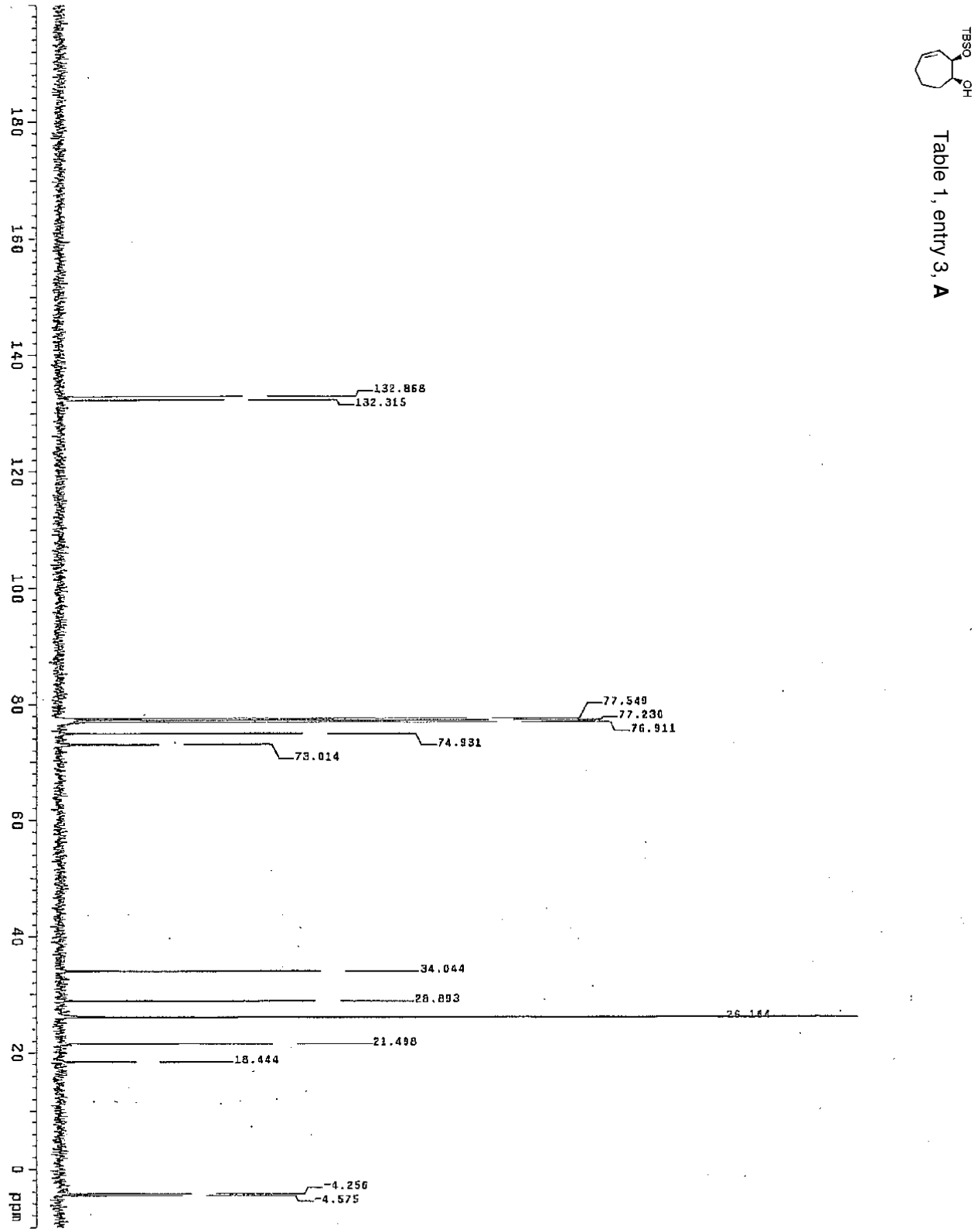

TBSO
OH
(+)-4
10
9
8
7
6
5
4
3
2
1
0
ppm

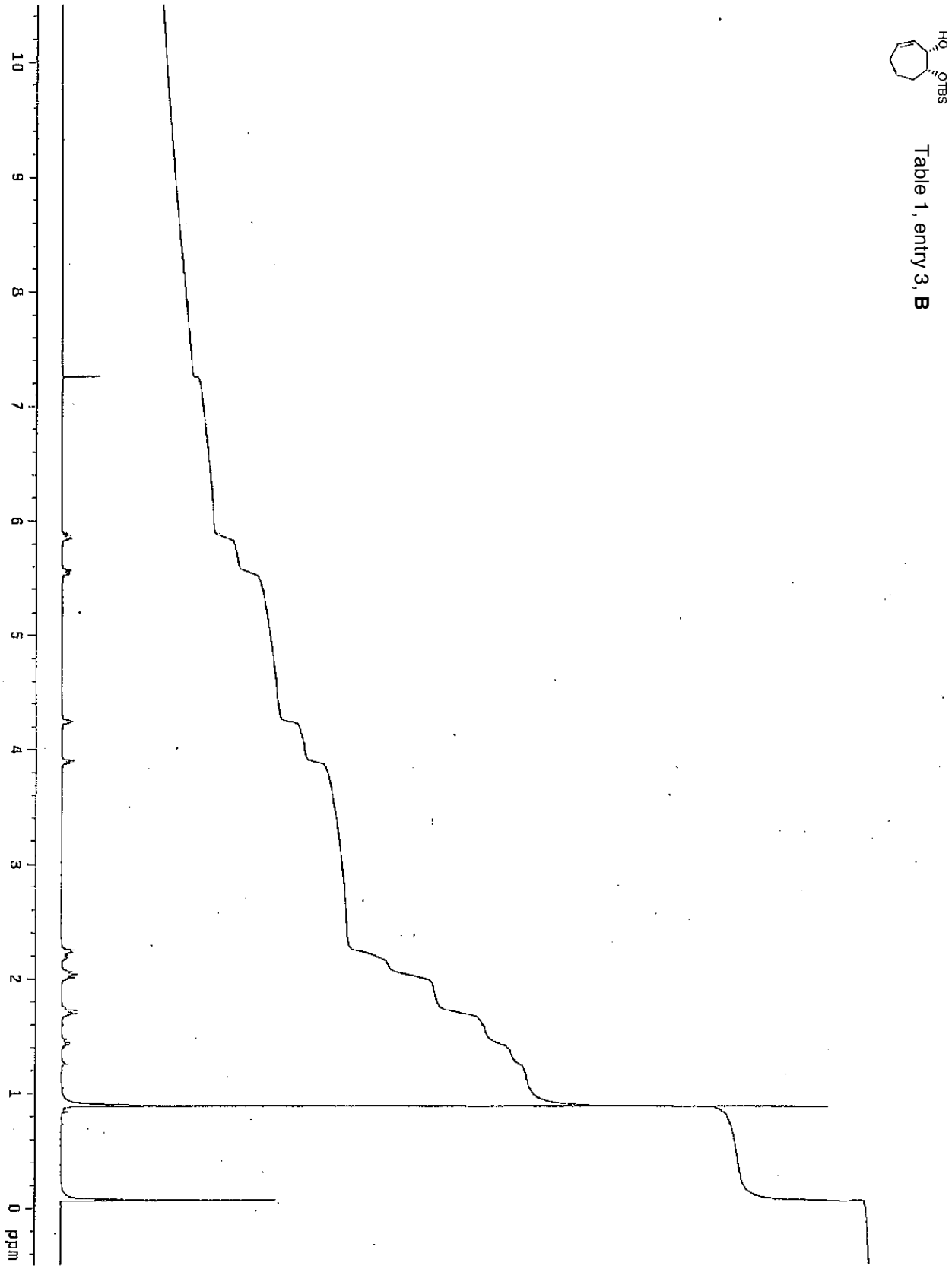

TBSO
OH
(+)-4
180
160
140
120
100
80
60
40
20
0
ppm
130.538
127.538
77.557
77.238
76.918
68.534
68.230
26.454
25.111
25.917
22.761
-3.929
-4.427

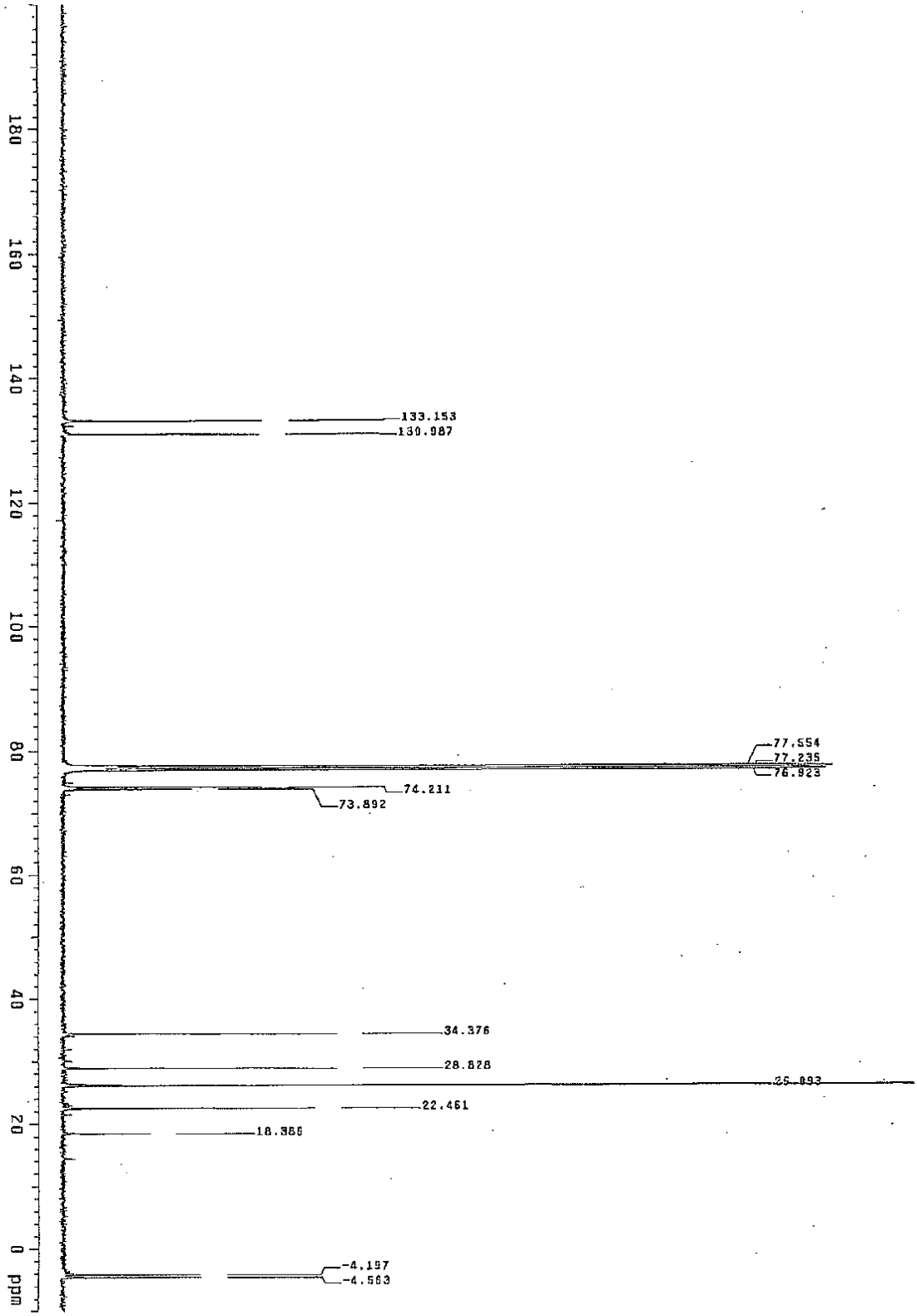

HO
OTBS
(-)-5
10
9
8
7
6
5
4
3
2
1
0 ppm

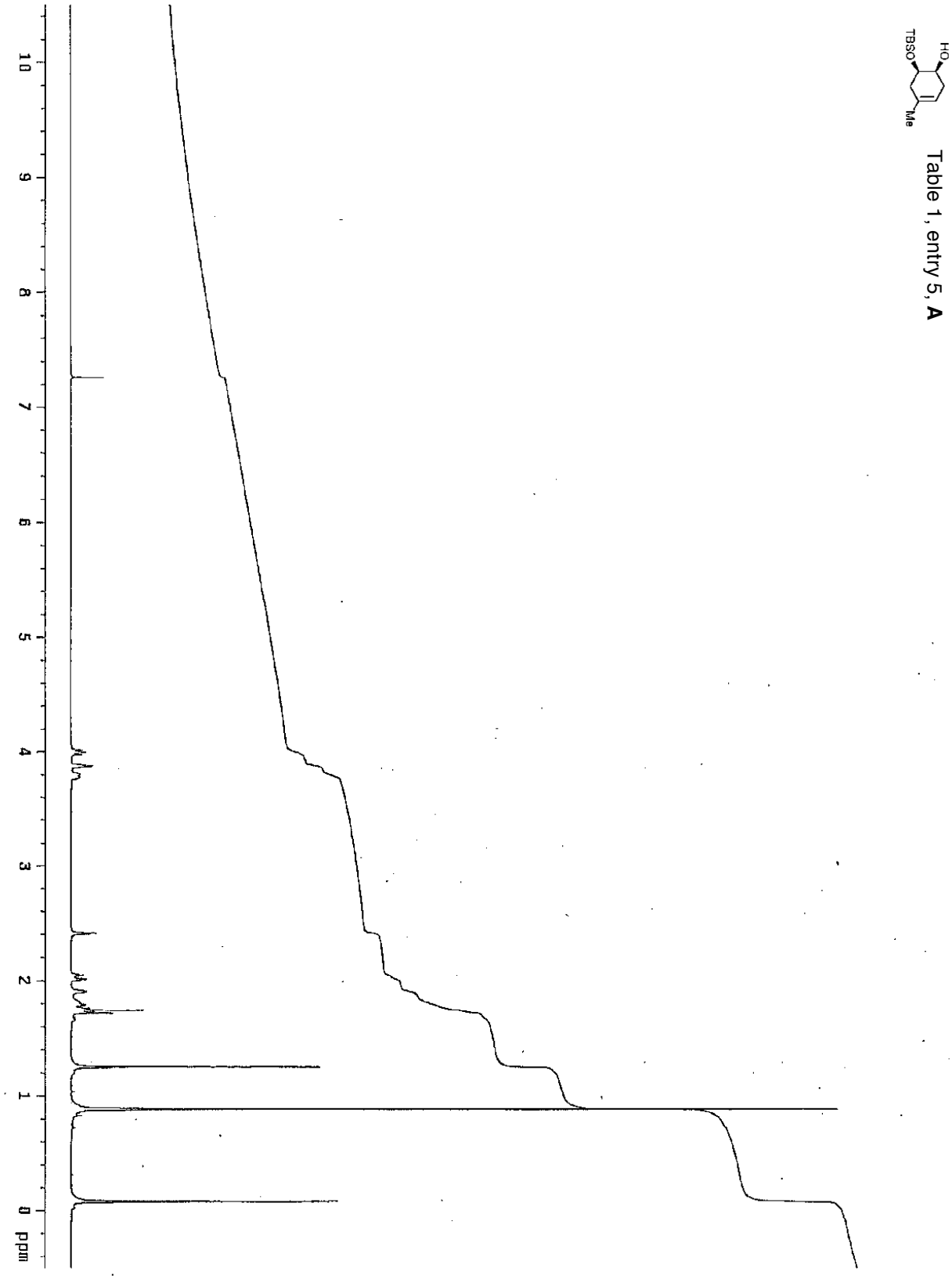

(-)-5
OTBS
OH
180
160
140
120
100
80
60
40
20
0
ppm
130.990
127.180
77.549
77.230
76.911
70.536
66.765
26.431
26.088
24.124
18.389
-4.162
-4.560

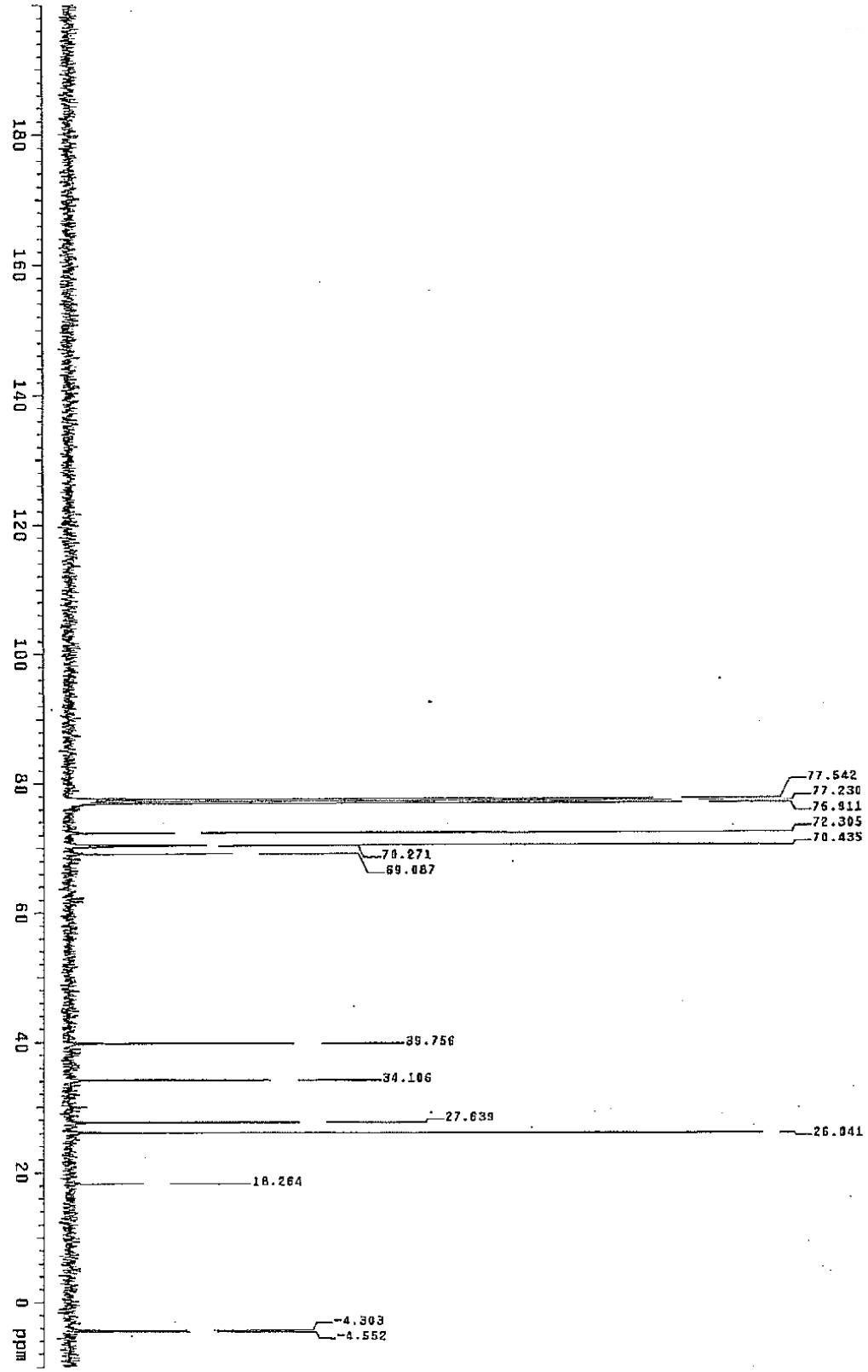

TBSO
OH
Table 1, entry 3, **A**
10
9
8
7
6
5
4
3
2
1
0
ppm

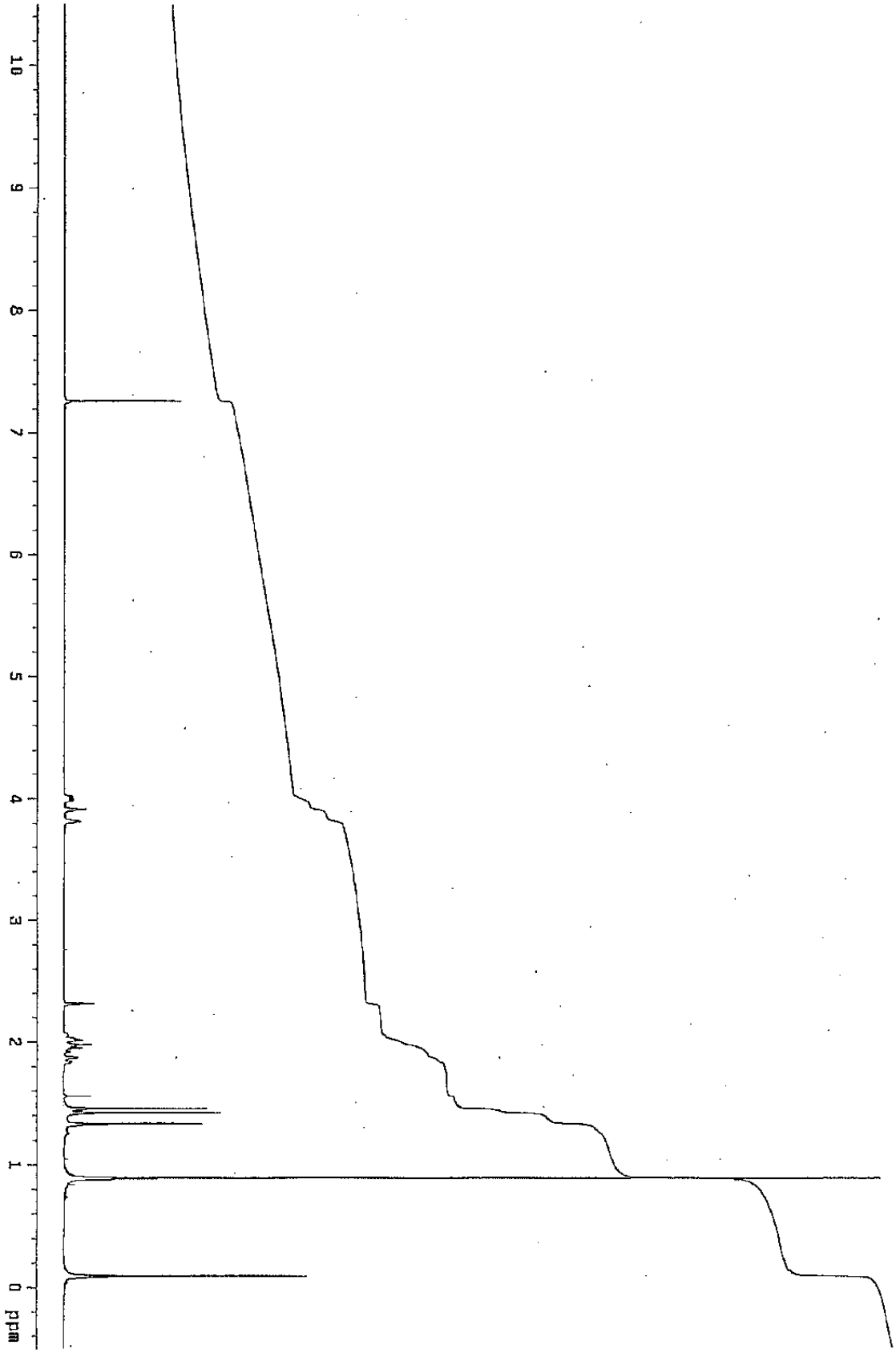

TBSO
OH
Table 1, entry 3, **A**
180
160
140
120
100
80
60
40
20
0
ppm
132.858
132.315
77.549
77.230
76.911
74.931
73.014
34.044
28.893
26.164
21.498
18.444
-4.256
-4.575

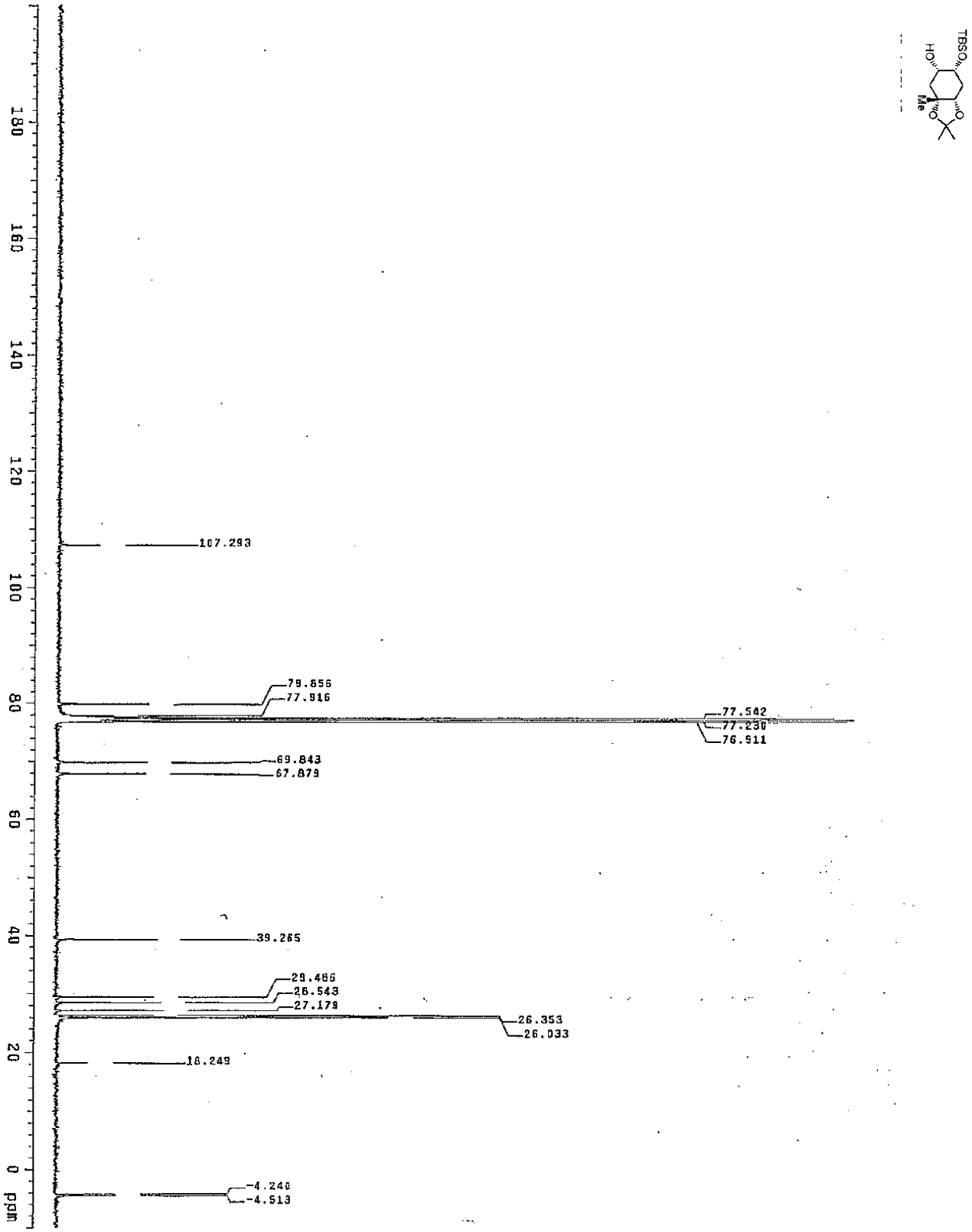

HO
OTBS
Table 1, entry 3, **B**
10
9
8
7
6
5
4
3
2
1
0
ppm


HO
OTBS
Table 1, entry 3, **B**
133.153
130.987
77.554
77.235
76.923
74.231
73.892
34.376
28.828
25.893
22.461
18.356
-4.197
-4.563
ppm


HO
TBSO
Me
Table 1, entry 5, **A**
10
9
8
7
6
5
4
3
2
1
0
ppm


TBSO
HO
Me
Table 1, entry 5, **A**
77.542
77.230
76.911
72.305
70.435
70.271
69.087
39.759
34.106
27.639
26.041
18.264
-4.303
-4.552
ppm


TBSO
HO
Me
O
O
10
9
8
7
6
5
4
3
2
1
0 ppm


TBSO
HO
Me
O
O
180
160
140
120
100
80
60
40
20
0
ppm
107.293
79.856
77.916
77.542
77.230
76.911
69.843
67.879
39.265
29.486
28.543
27.179
26.353
26.033
18.249
-4.240
-4.513

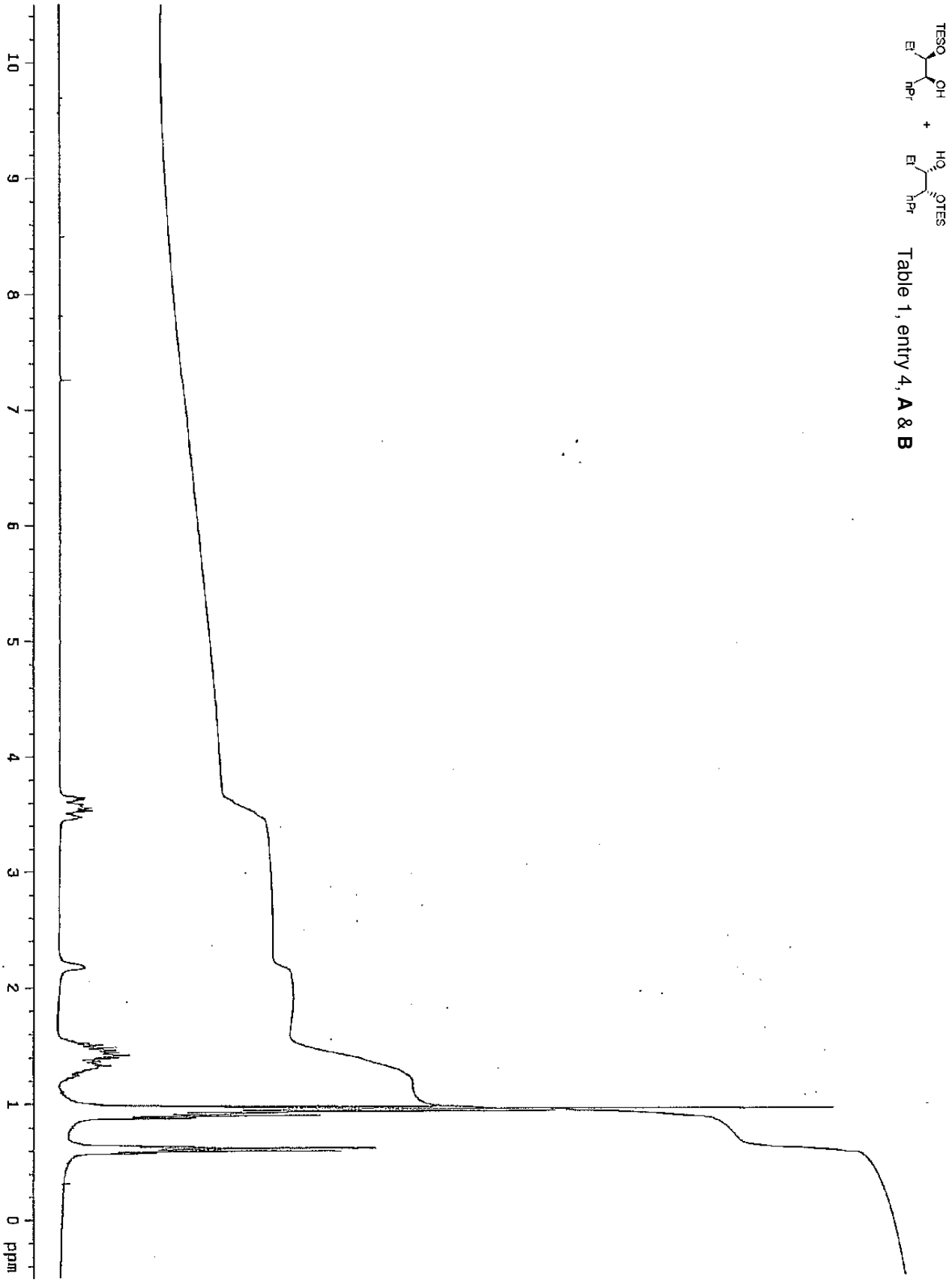
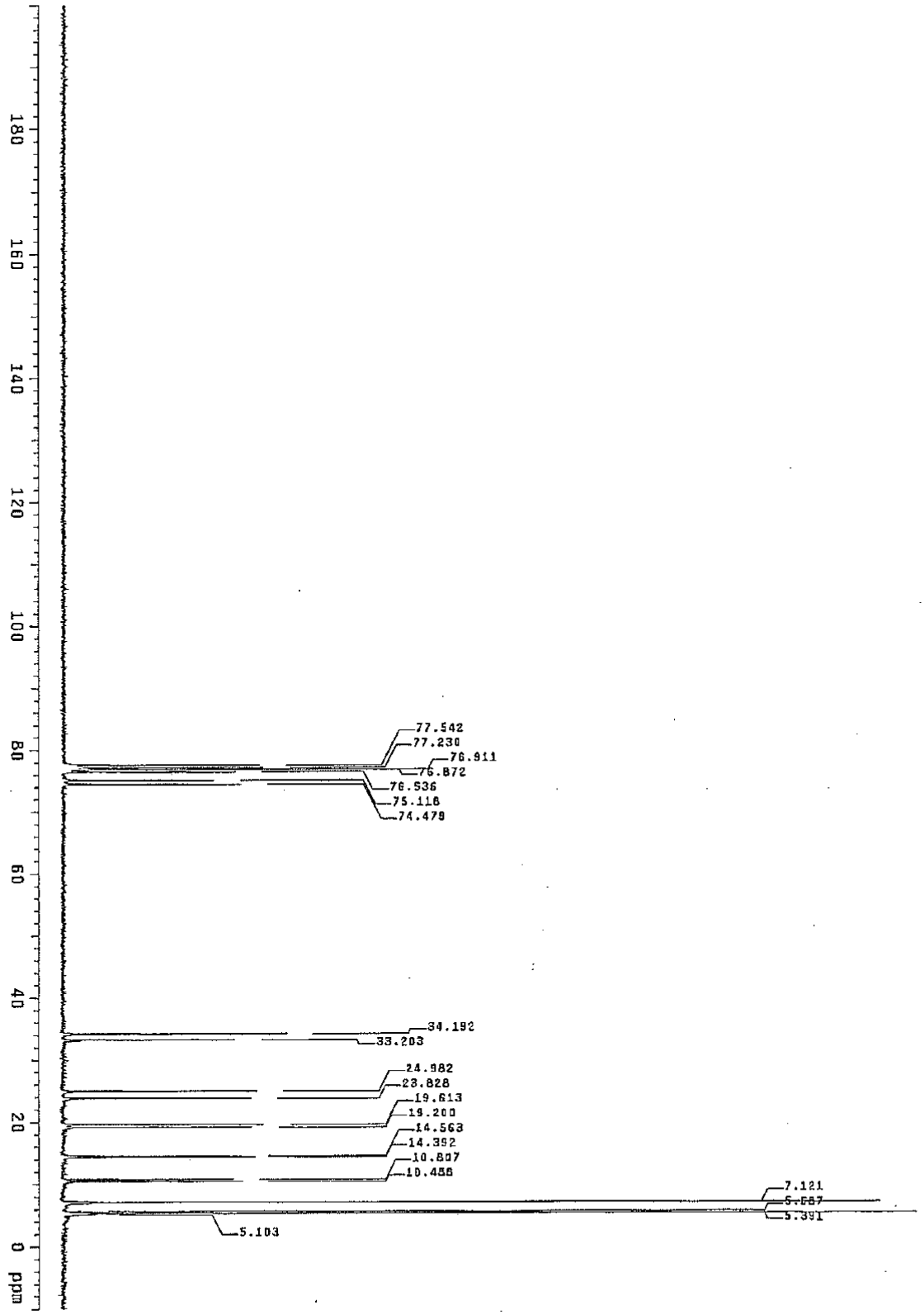
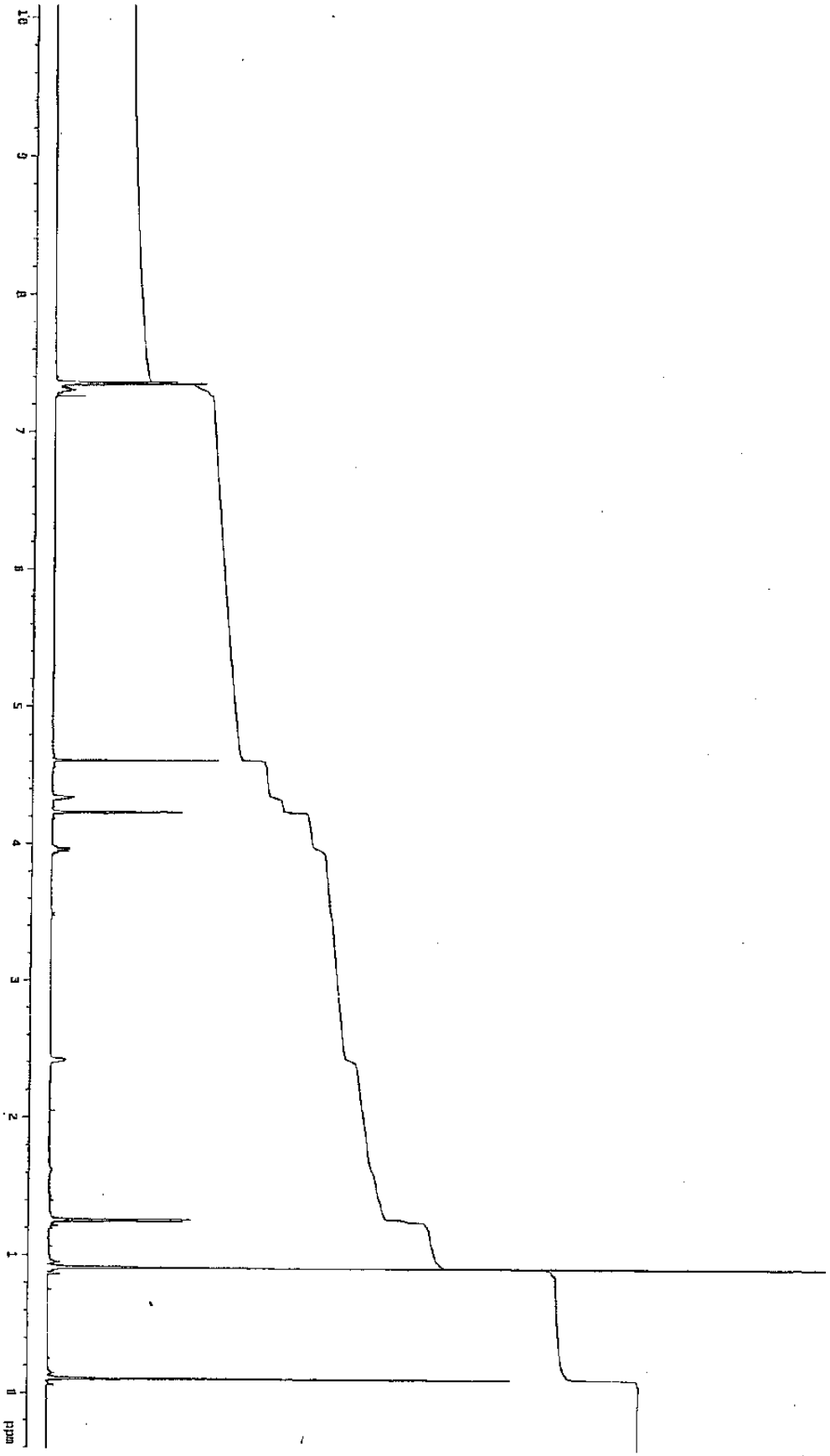
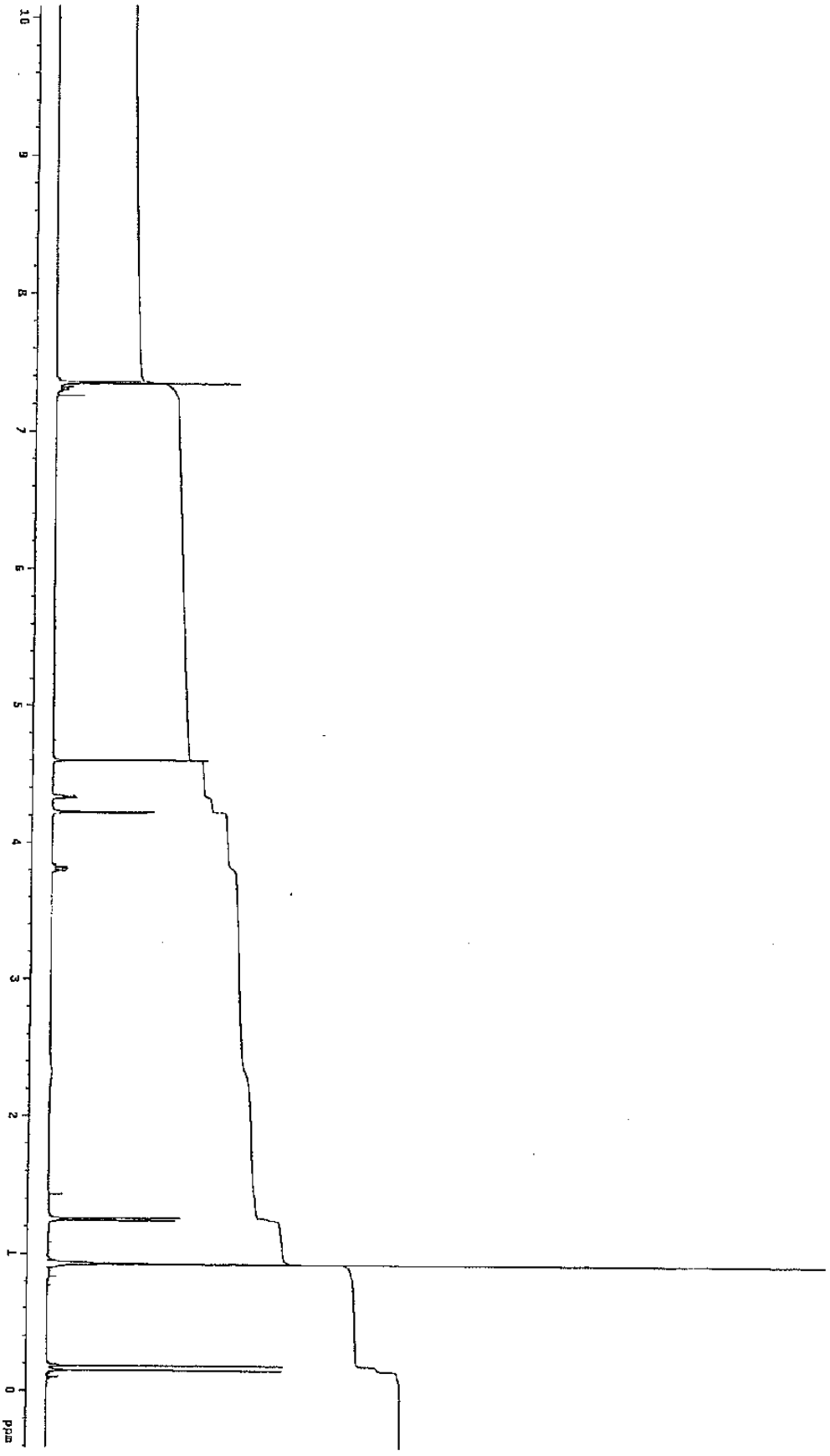


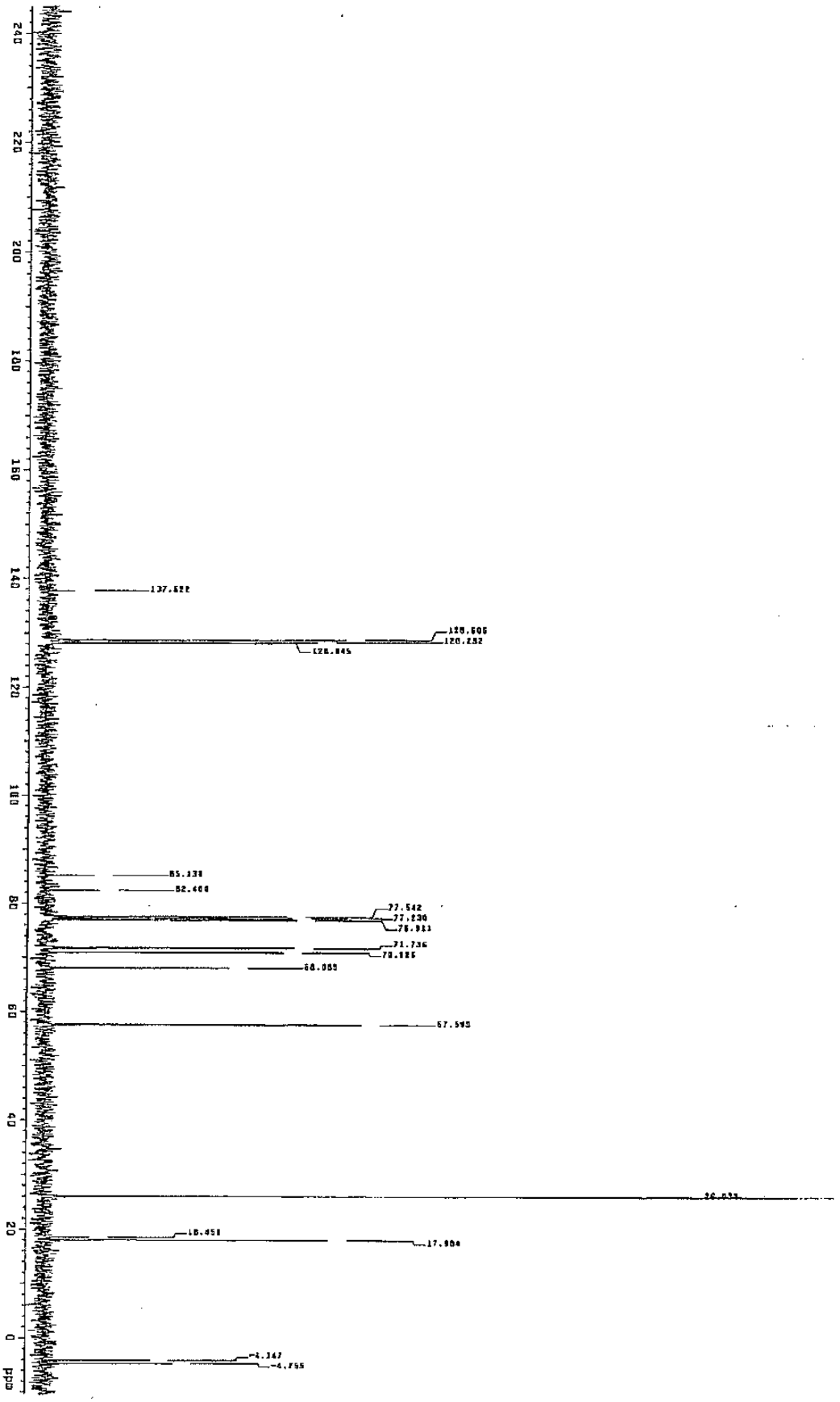
Table 1, entry 4, **A** & **B**

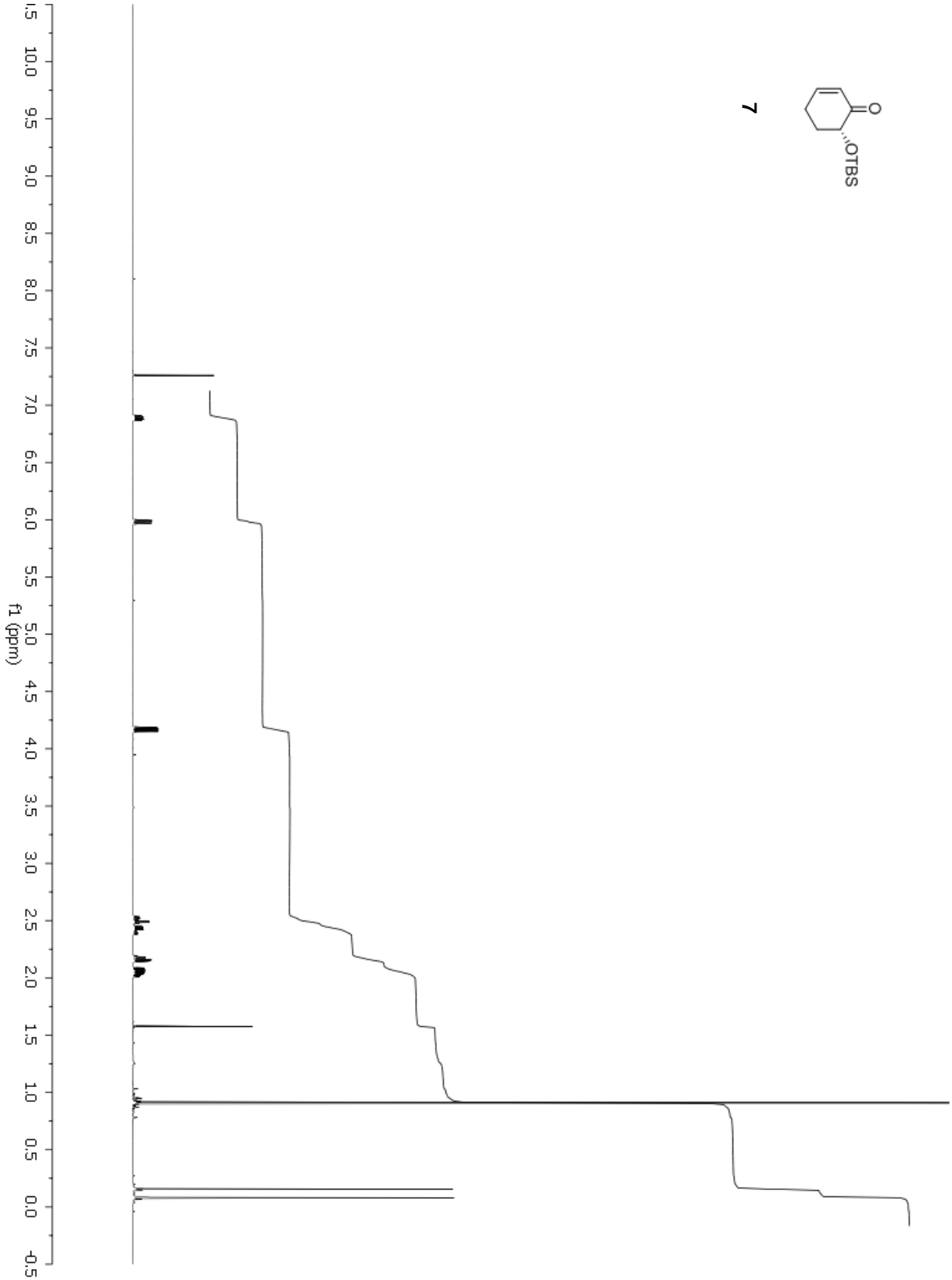

TESO
Et
OH
nPr
+
HO
Et
OTES
nPr
Table 1, entry 4, **A** & **B**
180
160
140
120
100
80
60
40
20
0 ppm
77.542
77.230
76.911
76.872
76.536
75.116
74.479
34.192
33.203
24.982
23.828
19.613
19.200
14.563
14.352
10.807
10.456
7.121
5.587
5.391
5.103

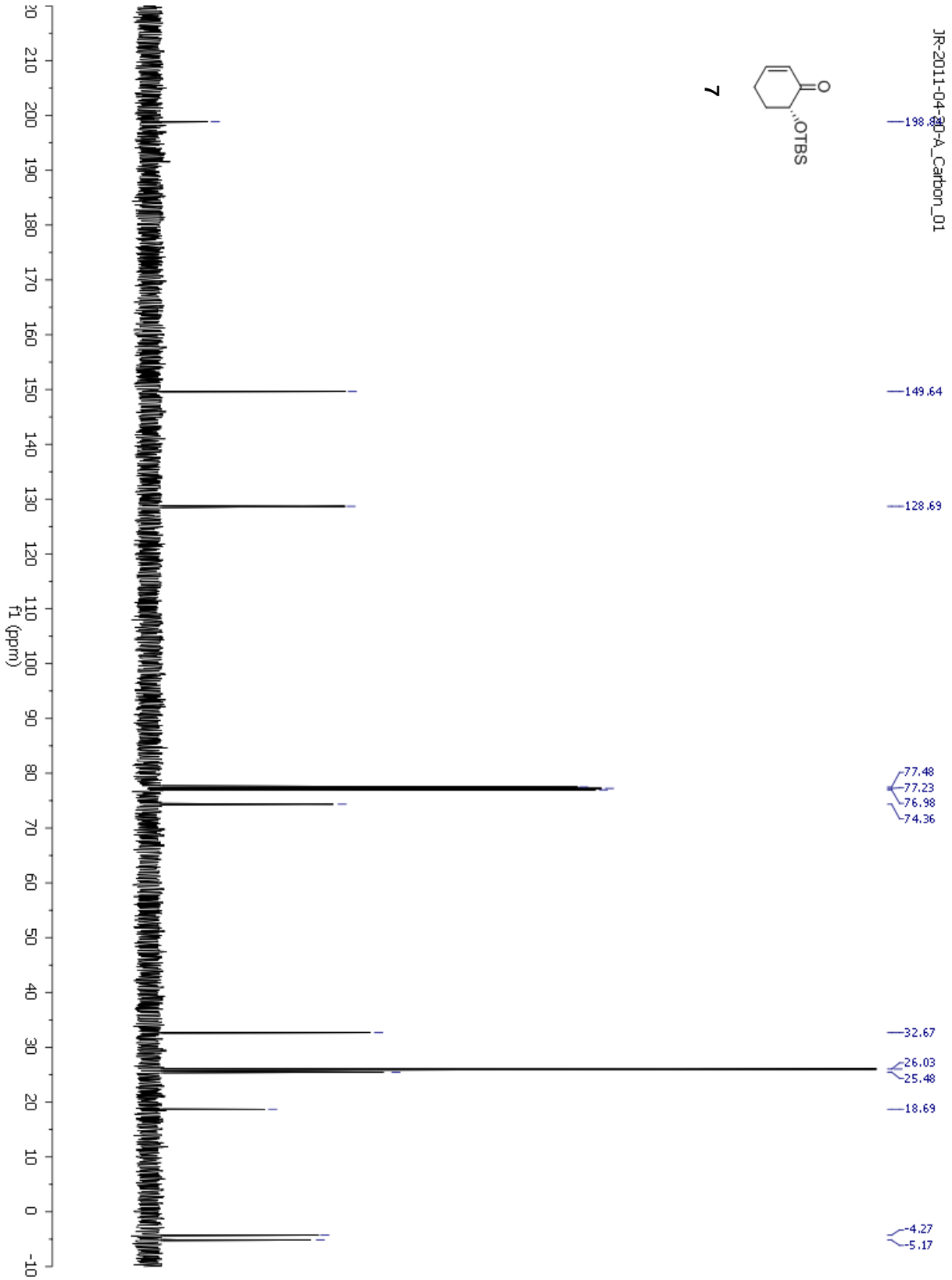

TBSO
Me
OH
OBn
Table 1, entry 6, **A**
10
9
8
7
6
5
4
3
2
1
0
ppm

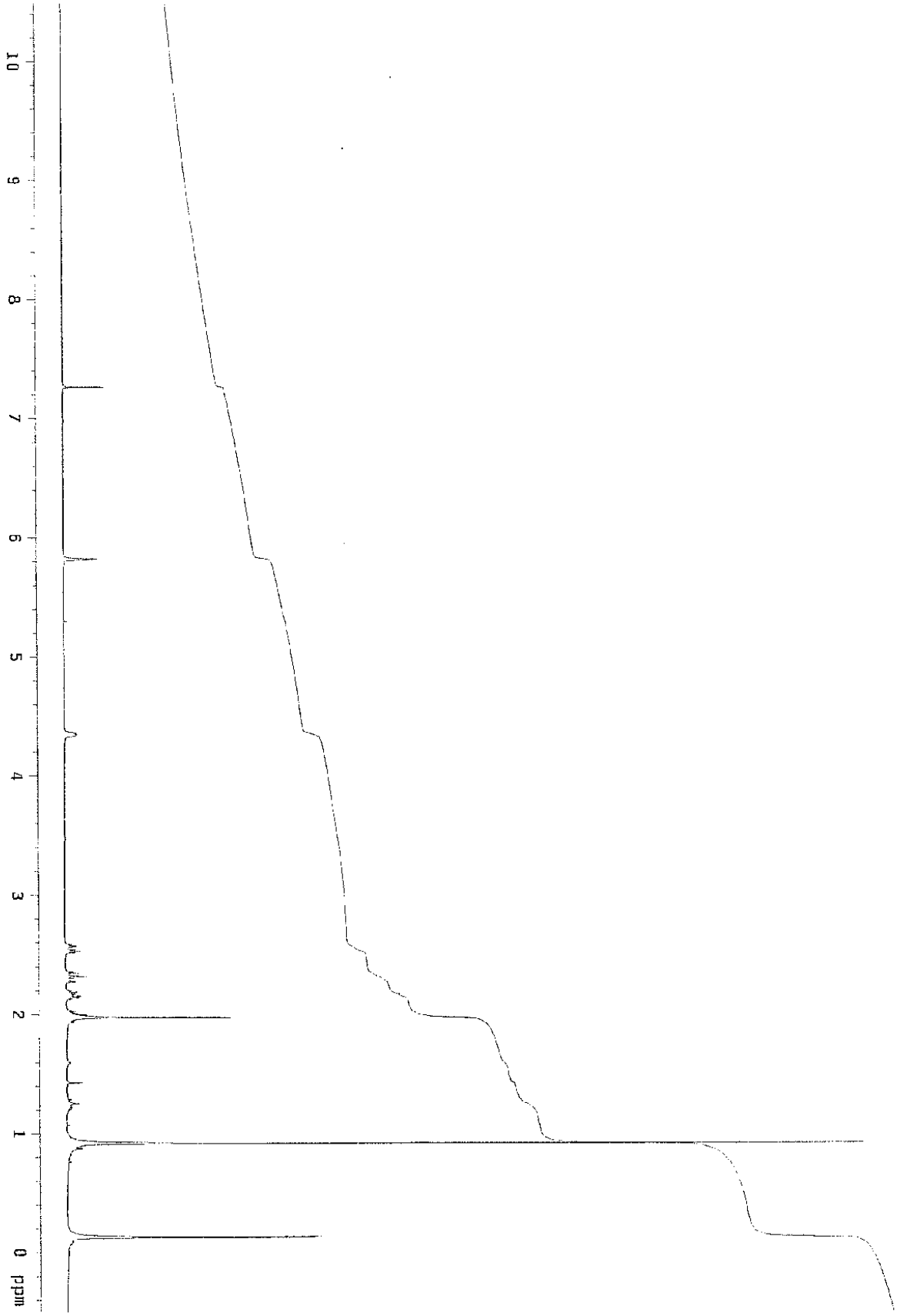

TBSO
Me
OH
OBn
Table 1, entry 6, **A**
ppm
137.606
128.553
127.675
84.755
82.176
77.628
77.207
76.807
71.888
67.295
57.588
26.015
18.489
-4.162
-4.552

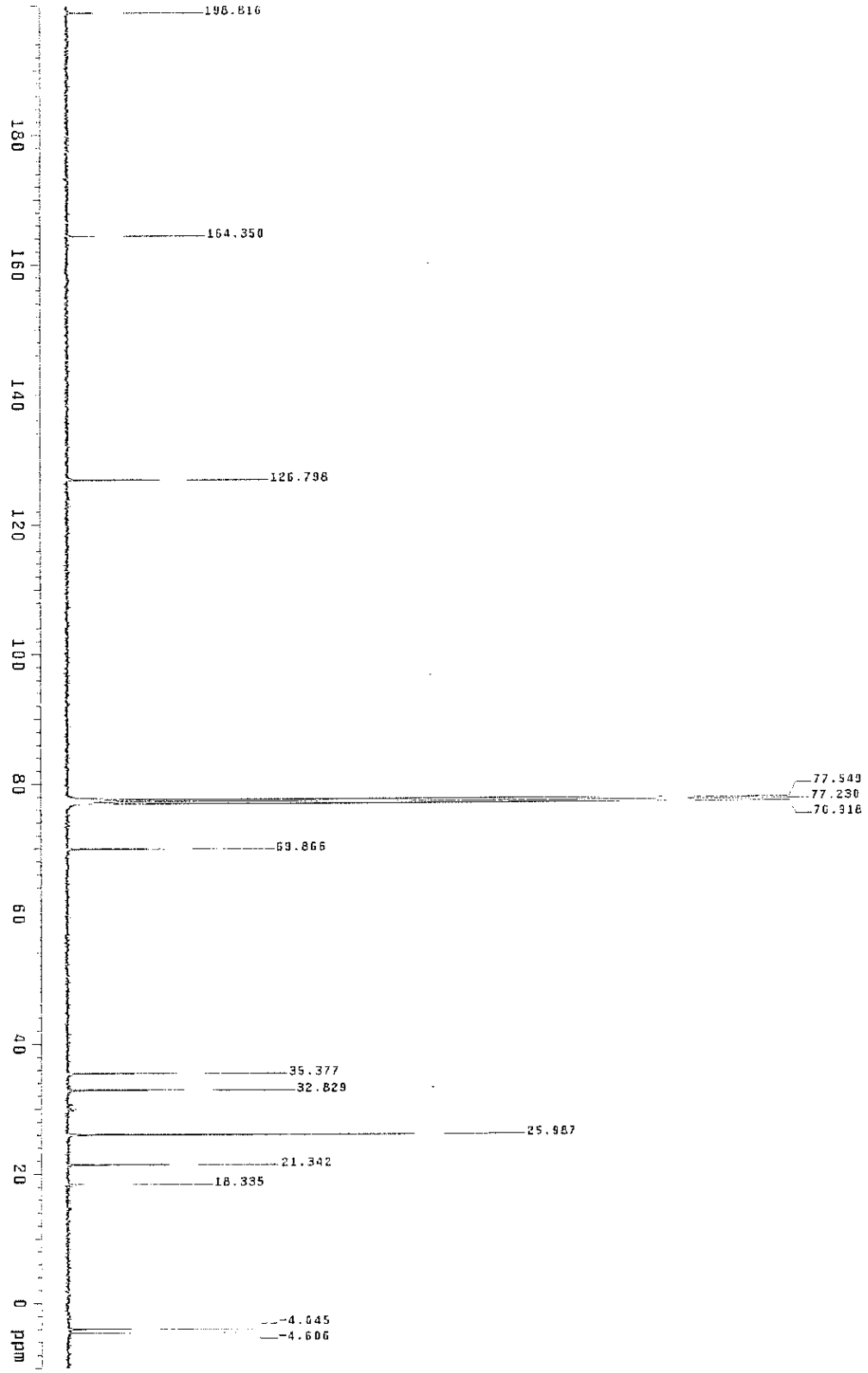

HO
Me
OTBS
OBn
Table 1, entry 6, **B**
10
9
8
7
6
5
4
3
2
1
0
ppm

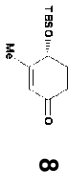

HO
Me
OTBS
OBn
Table 1, entry 6, **B**
137.622
128.606
128.252
126.845
85.138
82.468
77.542
77.230
76.911
71.736
70.185
68.085
57.595
26.033
18.451
17.884
-4.347
-4.755
ppm


7
OTBS
O
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

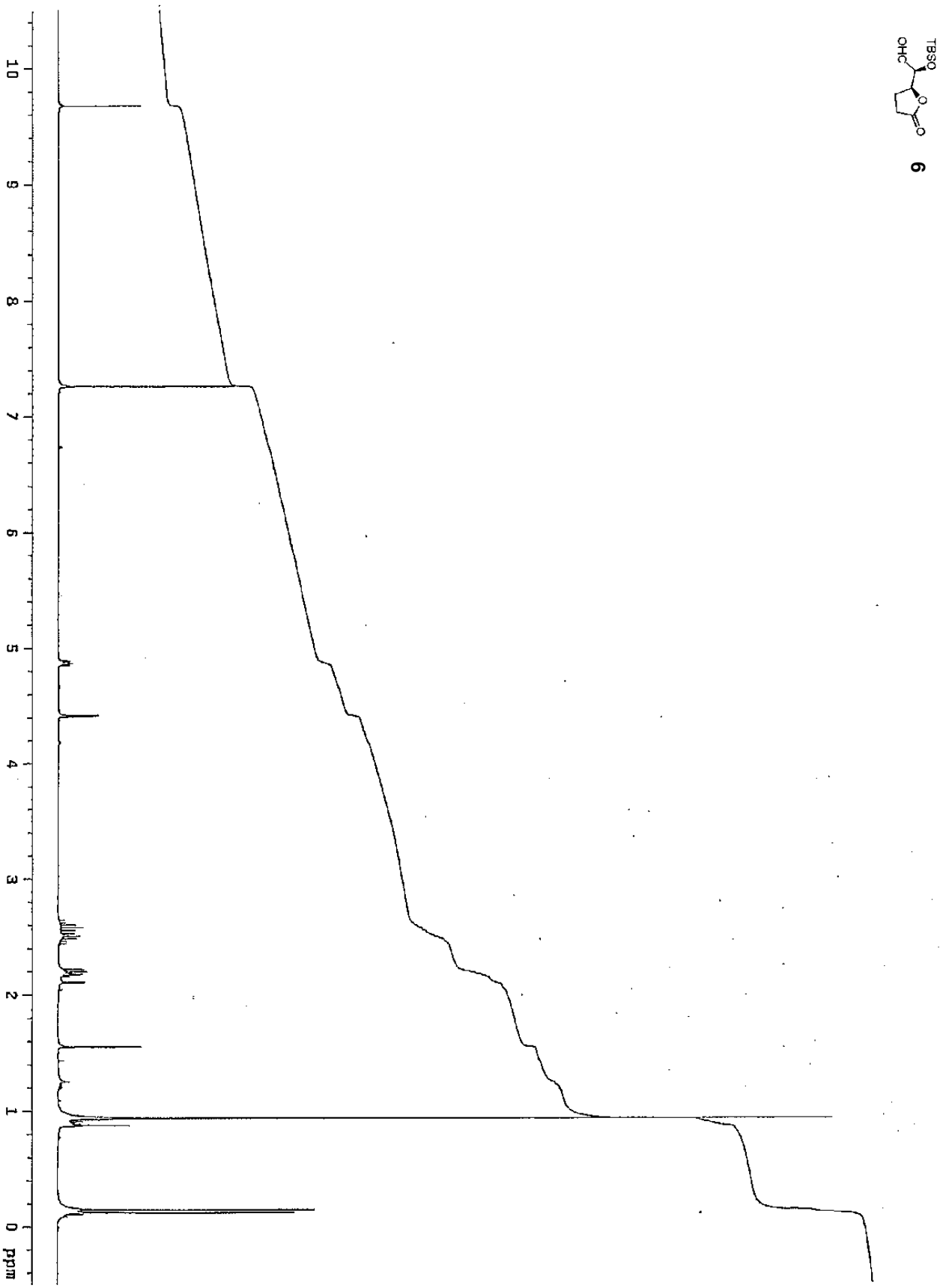

JR-2011-04-30-A_Carbon_01
7
OTBS
198.88
149.64
128.69
77.48
77.23
76.98
74.36
32.67
26.03
25.48
18.69
-4.27
-5.17
f1 (ppm)

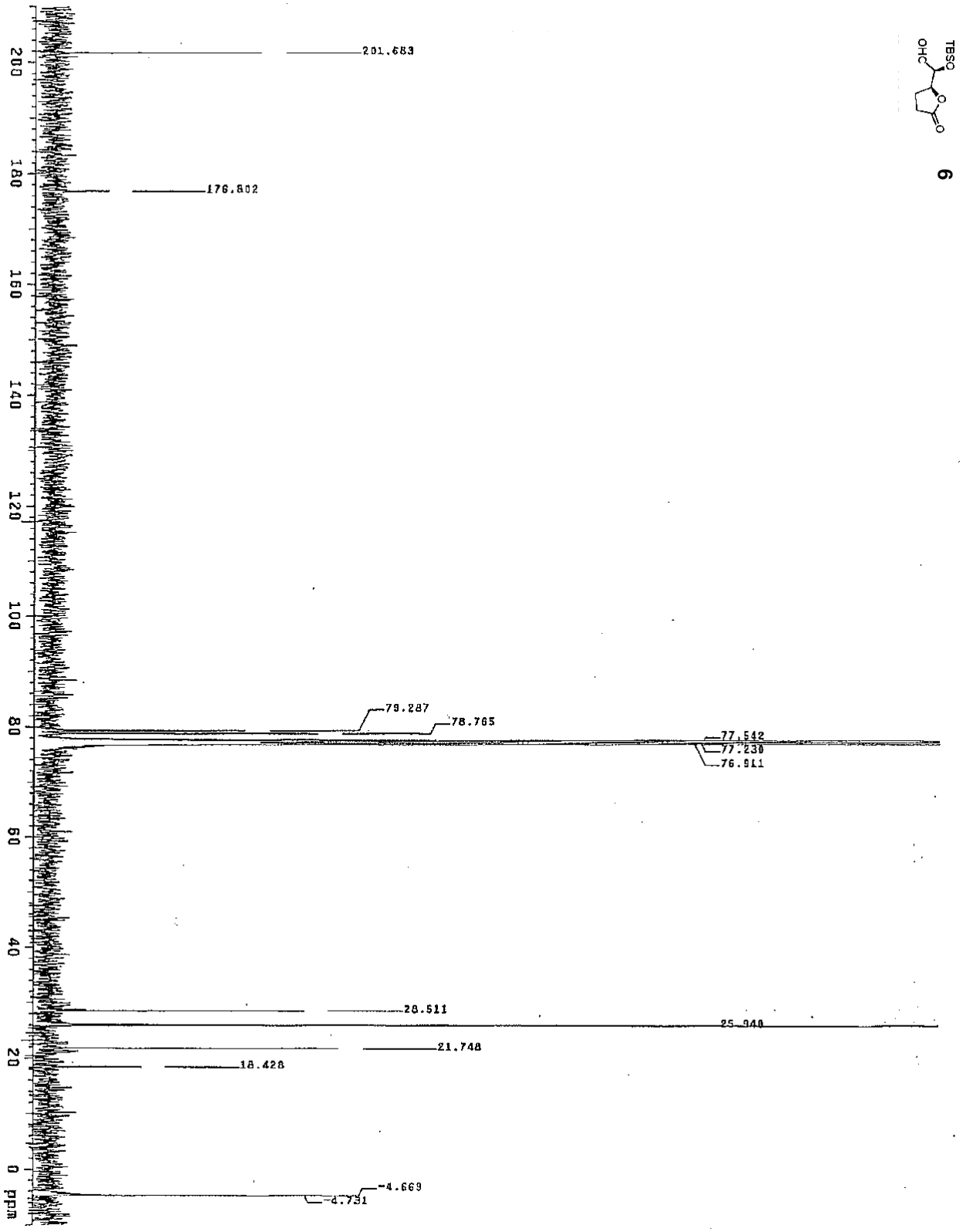

TBSO
Me
O
8
10
9
8
7
6
5
4
3
2
1
0
ppm

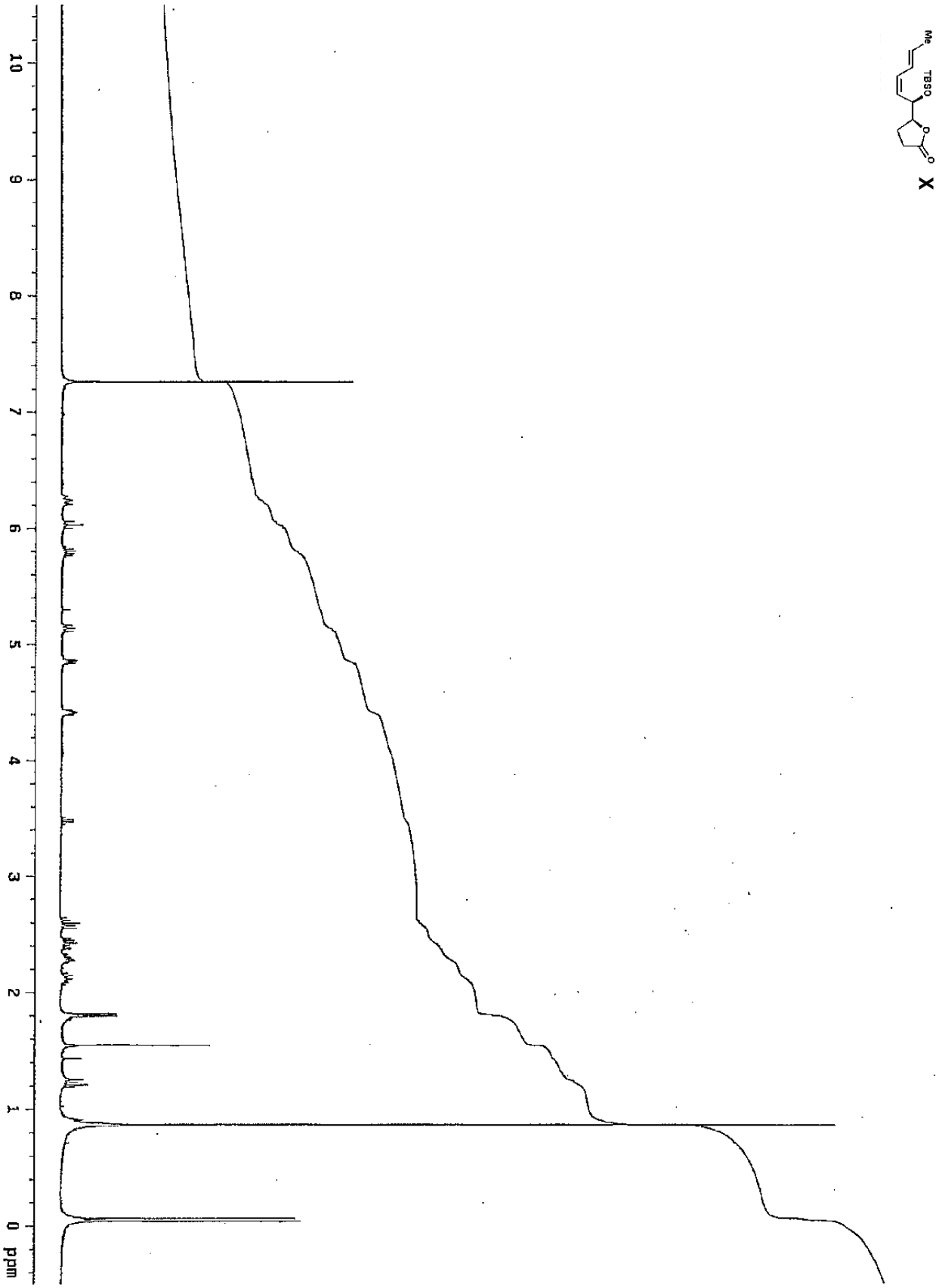

198.816
164.350
126.798
77.549
77.230
76.916
69.866
35.377
32.829
25.987
21.342
18.335
-4.645
-4.606
180
160
140
120
100
80
60
40
20
0
ppm

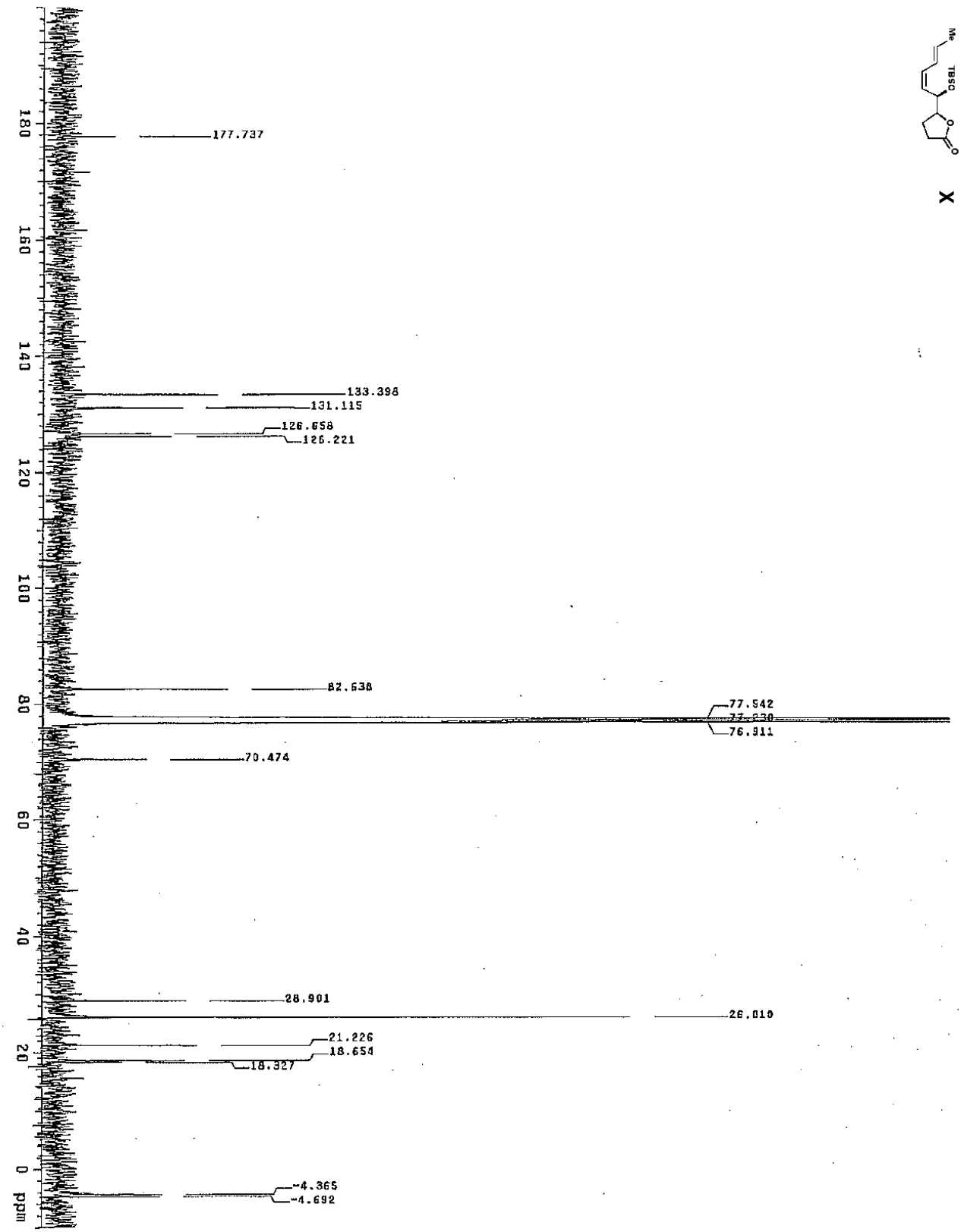

TBSO
Me
O

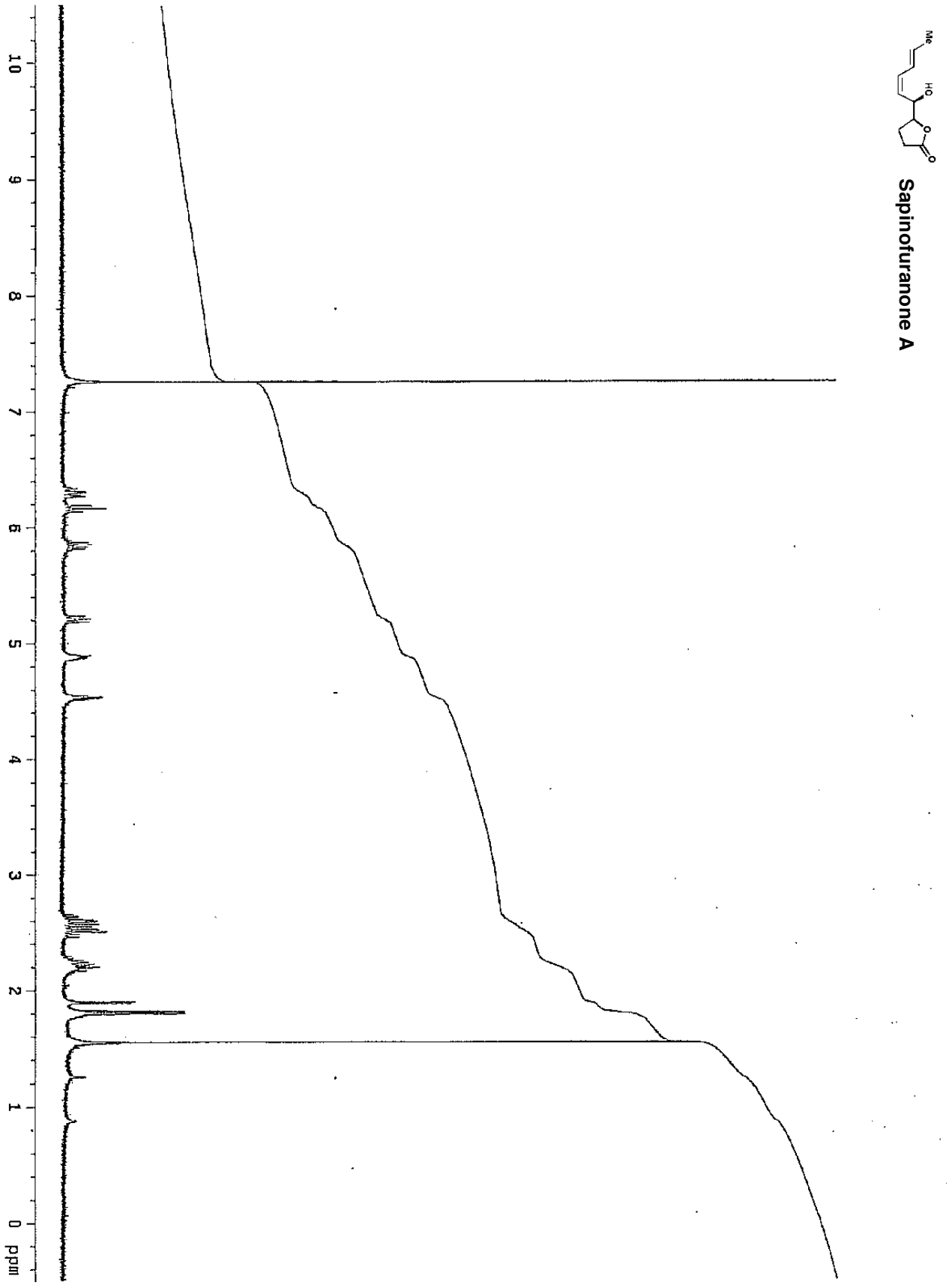
8

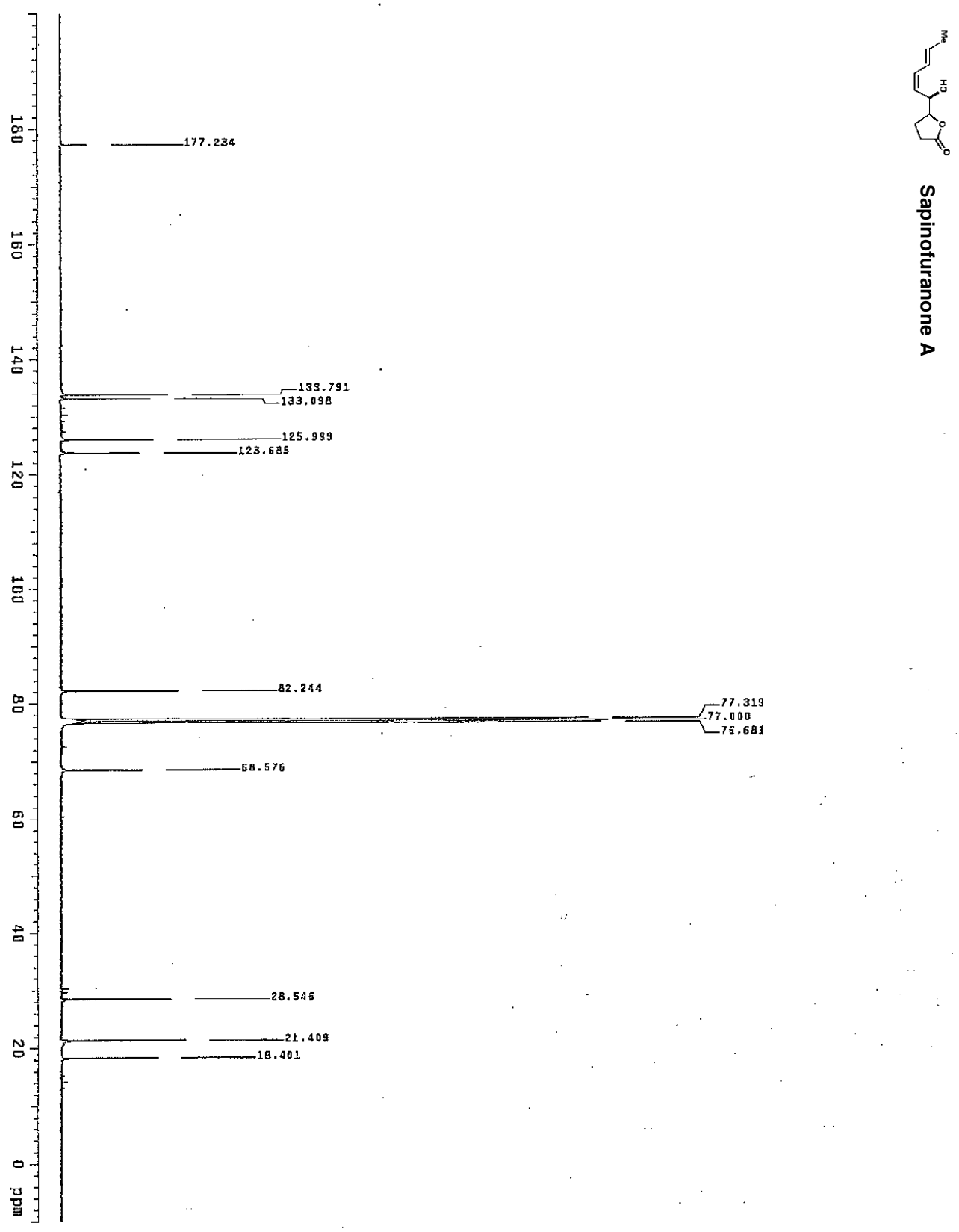

TBSO
OHC
O
O
O
6
10
9
8
7
6
5
4
3
2
1
0
ppm


201.683
176.802
79.287
78.765
77.542
77.230
76.911
28.511
25.948
21.748
18.428
-4.669
-4.731
ppm
TBSO
OHC
O
O
6


Me
TBSO
O
O
X
10
9
8
7
6
5
4
3
2
1
0
ppm


Me
TBSO
O
O
177.737
133.398
131.115
126.658
126.221
82.638
77.542
76.911
70.474
28.901
26.010
21.226
18.654
18.327
-4.365
-4.692
ppm


Me
HO
O
O
Sapinofuranone A
10
9
8
7
6
5
4
3
2
1
0 ppm


Me
HO
O
O
Sapinofuranone A
177.234
133.791
133.098
125.999
123.685
82.244
77.319
77.000
76.681
68.576
28.546
21.409
18.401
180
160
140
120
100
80
60
40
20
0
ppm