

Iridium-Catalyzed Allylation of Chiral β -Stereogenic Alcohols: Bypassing Discrete Formation of Epimerizable Aldehydes

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General Information: All reactions were run under an atmosphere of argon. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under a nitrogen atmosphere. Anhydrous solvents were transferred by oven-dried syringe. Sealed tubes (13x100 mm²) were purchased from Fisher Scientific (catalog number 14-959-35C) and were dried in an oven overnight and cooled under a stream of argon prior to use.¹ All ligands were used as received from Strem Chemicals Inc. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Adsorbents F254). Visualization was accomplished with UV light followed by dipping in a p-anisaldehyde solution or ceric ammonium molybdate and heating. Purification of reaction products was carried out by flash column chromatography using Silicycle silica gel (40-63 μ m).

Spectroscopy and Spectrometry: Infrared spectra were recorded on a Thermo Nicolet 380 spectrometer. Low-resolution mass spectra (LRMS) were obtained on an Agilent 6530 QTOF and are reported as *m/z* (relative intensity). Accurate masses are reported for the molecular ion (*M*+*H*, *M* or *M*-*H*) or a suitable fragment ion. ¹H NMR spectra were recorded on a Varian Gemini (400 MHz) spectrometer at ambient temperature unless otherwise noted. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane or ppm relative to the center of the singlet at 7.26 ppm for deuteriochloroform. Data are reported as: multiplicity (*s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet), integration and coupling constant(s) in Hz. ¹³C NMR spectra were recorded on a Varian Gemini (100 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are

(1) Welker, M., *J. Org. Chem.*, **2009**, 74, 8290.

reported in ppm from tetramethylsilane, with the residual solvent resonance employed as the internal standard (CDCl₃ at 77.0 ppm).

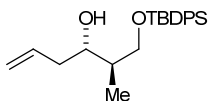
Preparation of (R)-Ir-b-NO₂: A pressure tube equipped with a magnetic stirbar was charged with [Ir(cod)Cl]₂ (103 mg, 0.15 mmol, 100 mol%), (R)-Cl,OMe-BIPHEP (200 mg, 0.31 mmol, 200 mol%), Cs₂CO₃ (195 mg, 0.60 mmol, 400 mol%) and 4-NO₂-3-NO₂BzOH (127 mg, 0.60 mmol, 400 mol%). The tube was purged with argon for 5 minutes, followed by the addition of allyl acetate (81 μL, 0.75 mmol, 500 mol%) and THF (4.0 mL, 0.05 M). The mixture was stirred for 30 min at room temperature under argon. The reaction mixture was then stirred for 90 min at 80 °C. Upon cooling to ambient temperature, the reaction mixture was diluted with CH₂Cl₂ (10 mL), filtered through a celite plug, washed with CH₂Cl₂ (50 mL) and concentrated *in vacuo* at ambient temperature. The compound was purified by flash chromatography (SiO₂, 20% Et₂O/CH₂Cl₂) and concentrated *in vacuo* at ambient temperature. A magnetic stirbar was added and the yellow gum was dissolved in 3 mL THF, stirred and precipitated upon rapid addition of 50 mL HPLC grade hexanes. Gravity filtration, followed by removal of trace solvents *in vacuo* gives a bright yellow powder (196 mg, 0.18 mmol, 60% yield).

A small amount of the powder was recrystallized by slow diffusion of Et₂O into CH₂Cl₂ at ambient temperature to give small orange crystals. Single crystal X-ray diffraction data has been deposited in the CSD.

Preparation of (S)-Ir-b-NO₂: (S)- Ir-b-NO₂ was prepared as above, but using (S)-Cl,OMe-BIPHEP.

Experimental Procedures and Spectroscopic Data for Table 1

(2R,3S)-1-(tert-butyldiphenylsilyloxy)-2-methylhex-5-en-3-ol (2a)



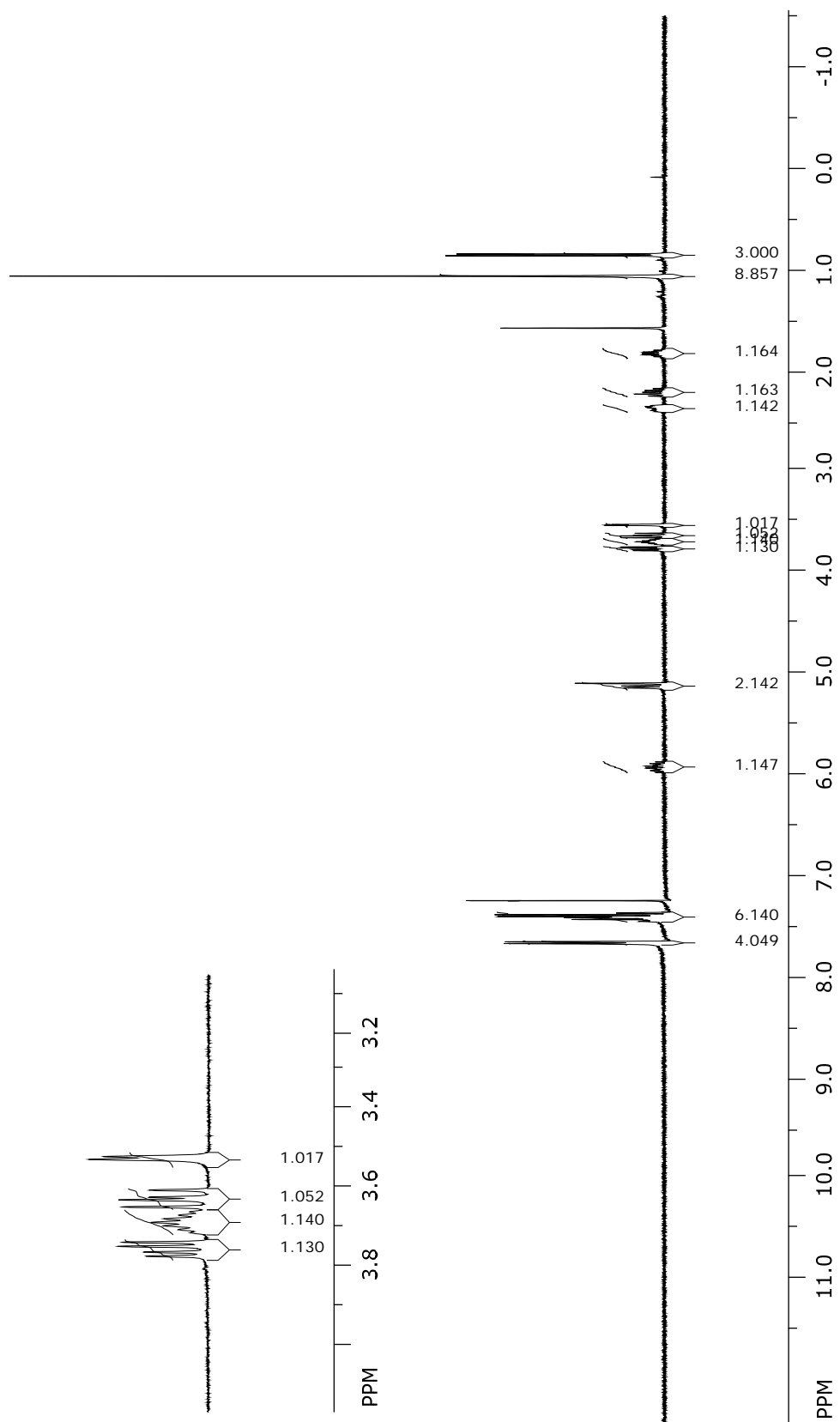
To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*S*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.2 mmol, 100 mol%) and alcohol **1**² (66 mg, 0.2 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 2.0 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 100 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 3% EtOAc/hexanes) to furnish the title compound (58 mg, 0.157 mmol, d.r. = 97:3) as a colorless oil in 79% yield. Spectroscopic data was consistent with previously reported values.³

¹H NMR (400 MHz, CDCl₃) Major diastereomer: δ 7.70 (d, *J* = 8 Hz, 4H), 7.47-7.38 (m, 6H), 5.98-5.88 (m, 1H), 5.15-5.10 (m, 2H), 3.78 (dd, *J* = 4, 8 Hz, 1H), 3.72 -3.67 (m, 1H), 3.65 (dd, *J* = 8, 8.4 Hz, 1H), 3.53 (d, *J* = 4 Hz, 1H), 2.40-2.34 (m, 1H), 2.24-2.17 (m, 1H), 1.16 (m, 1H), 1.05 (s, 9H), 0.85 (d, *J* = 6 Hz, 3H).

[α]_D²⁸ = -17 (c = 2.4, CH₂Cl₂).

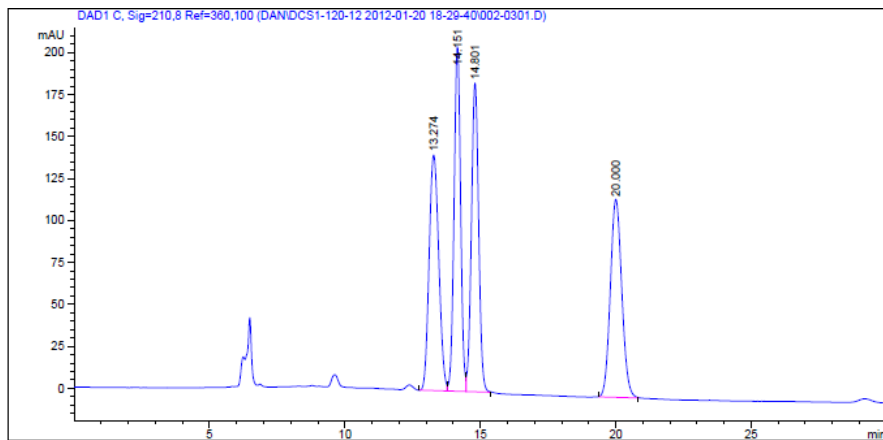
(2) Takayama, H.; Konno, K.; Fujishima, T.; Maki, S.; Liu, Z.; Miura, D.; Chokki, M.; Ishizuka, S.; Smith, C.; DeLuca, H. F.; Nakagawa, K.; Kurobe, M.; Okano, T. *Steroids*, **2001**, 66, 277.

(3) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, 55, 4117.



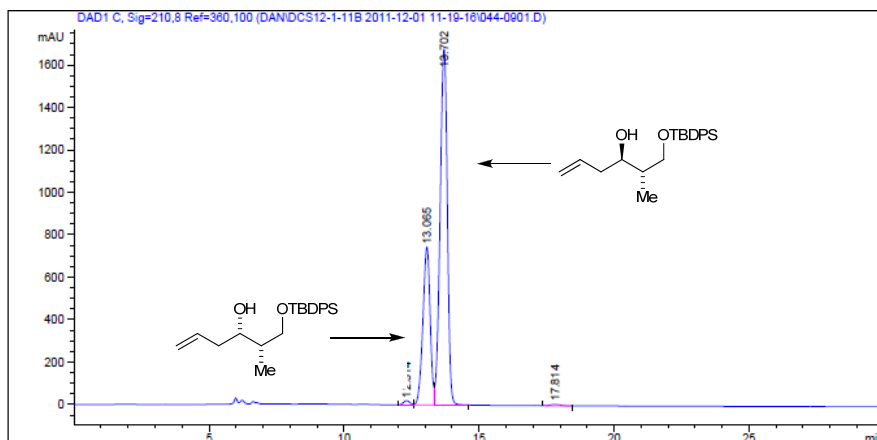
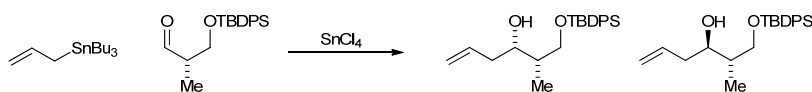
Determination of Diastereomeric Ratio and Stereochemistry Confirmation

Racemic Sample (stereoisomeric mixture (1:1 dr))



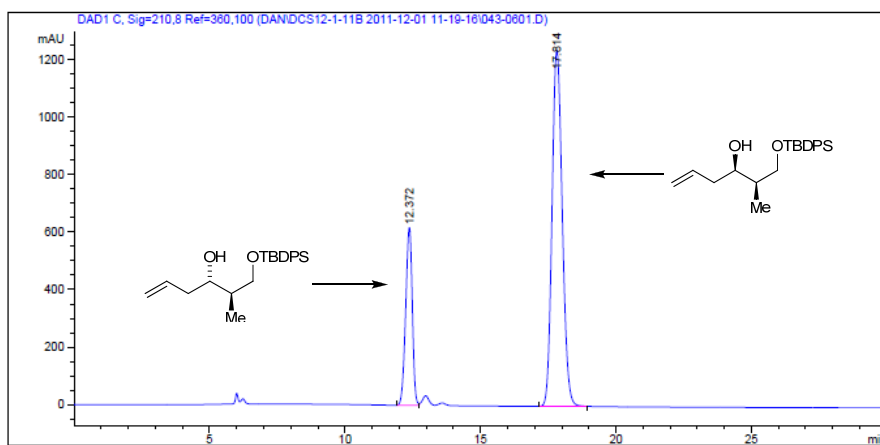
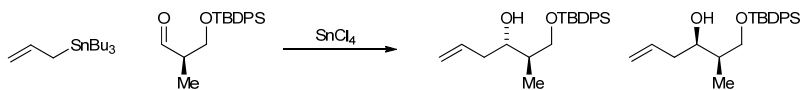
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.274	VV	0.3911	3478.26929	140.38019	25.2086
2	14.151	VV	0.2597	3446.84326	205.51695	24.9808
3	14.801	VB	0.2881	3407.47876	183.94016	24.6955
4	20.000	BB	0.4565	3465.35571	118.03324	25.1150

Authentic Sample Derived from an Allylation of the Enantioenriched (*S*)-Aldehyde with Allyltributyltin (*anti:syn* = 2.3:1)



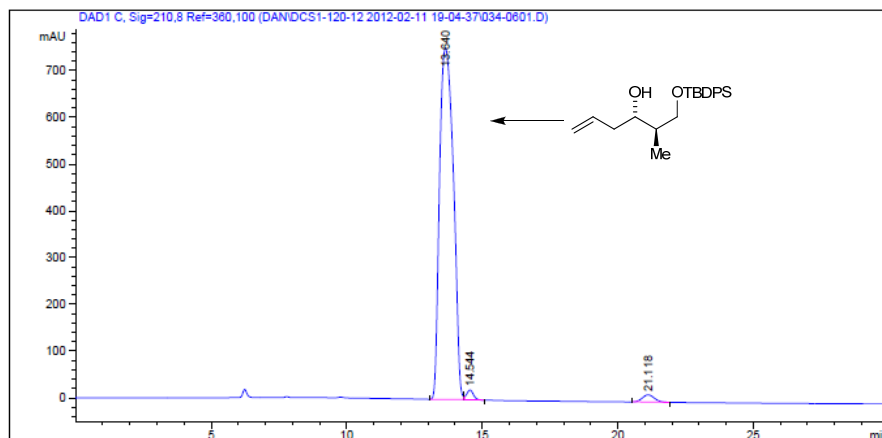
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.314	BV	0.2607	334.71622	19.84868	0.7328
2	13.065	VV	0.2879	1.38965e4	744.01239	30.4227
3	13.702	VB	0.2913	3.12869e4	1679.93335	68.4943
4	17.814	BB	0.3865	159.97112	6.37958	0.3502

Authentic Sample Derived from an Allylation of the Enantioenriched (*R*)-Aldehyde with Allyltributyltin (*syn:anti* = 3.2:1)



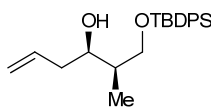
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.372	BV	0.2662	1.05198e4	619.10040	24.4667
2	17.814	BB	0.4101	3.24766e4	1237.85889	75.5333

Sample 2a



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.640	BV	0.6169	2.66200e4	752.12677	96.8941
2	14.544	VB	0.2662	366.33865	21.13297	1.3334
3	21.118	BB	0.4720	486.95258	15.60812	1.7725

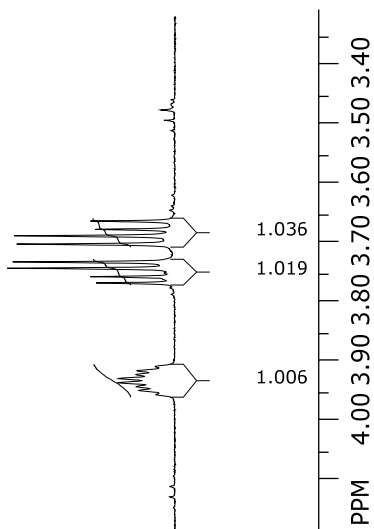
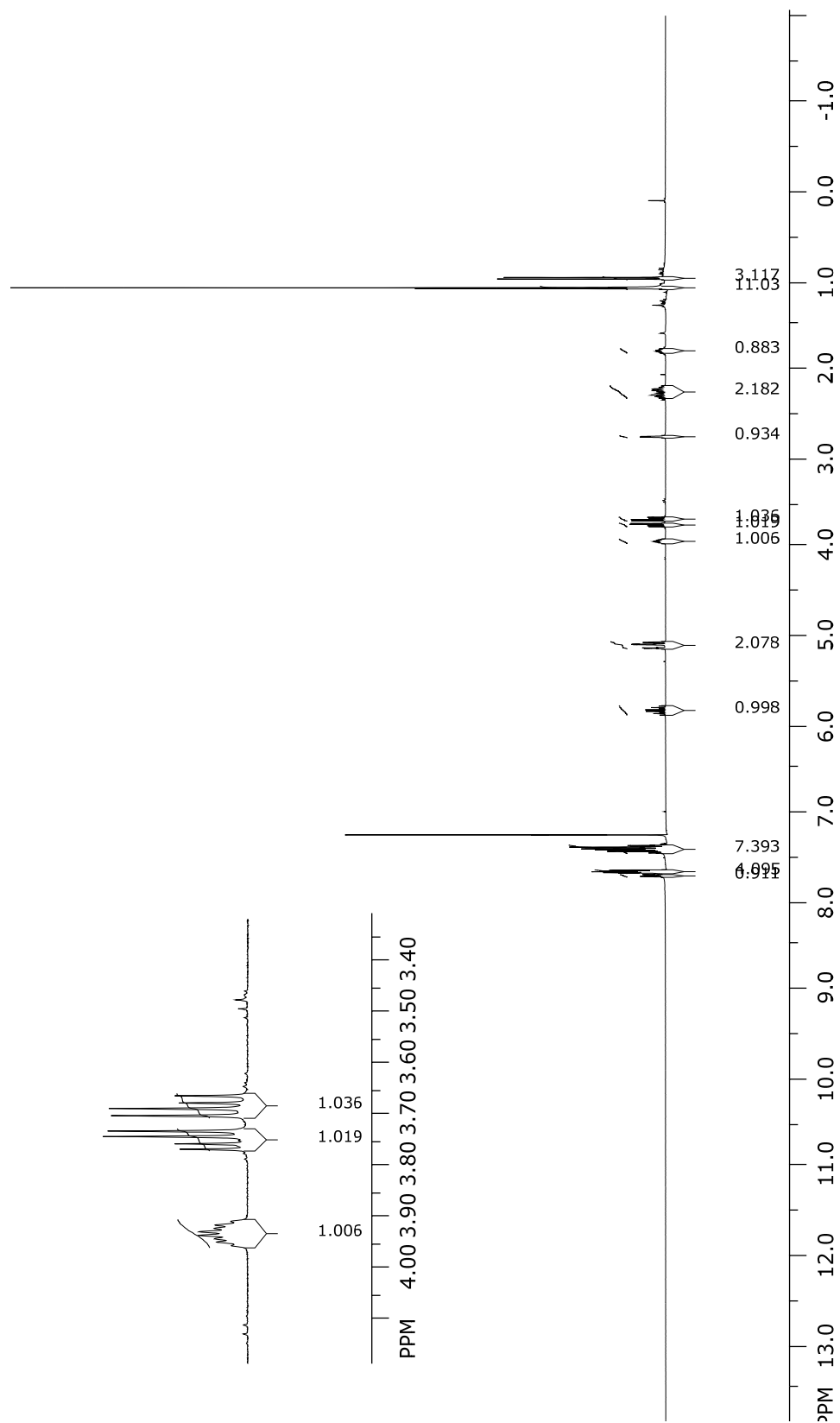
(2*R*,3*R*)-1-(tert-butyldiphenylsilyloxy)-2-methylhex-5-en-3-ol (2b)

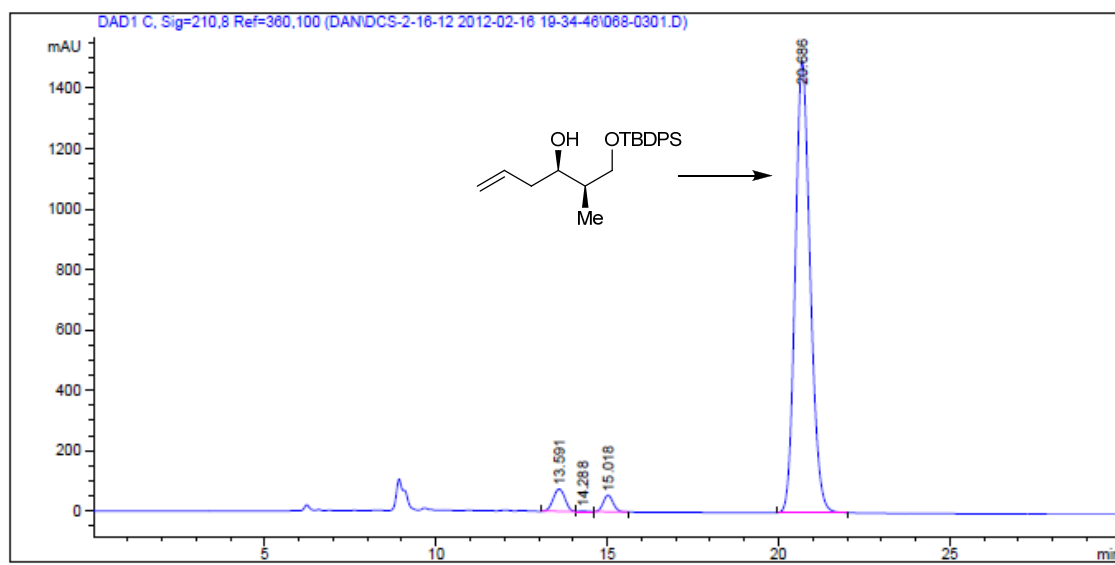


To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*R*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.2 mmol, 100 mol%) and alcohol **1**² (66 mg, 0.2 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 0.2 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 100 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 3% EtOAc/hexanes) to furnish the title compound (59.0 mg, 0.16 mmol, d.r. = 94:6) as a colorless oil in 80% yield. The spectroscopic data was in good agreement with previously reported values.³

¹H NMR (400 MHz, CDCl₃) Major diastereomer: δ 7.69-7.66 (m, 4H), 7.45-7.38 (m, 6H), 5.90-5.88 (m, 1H), 5.15-5.08 (m, 2H), 3.96-3.90 (m, 1H), 3.77 (dd, *J* = 4.4, 8 Hz, 1H), 3.70 (dd, *J* = 4, 8 Hz, 1H), 2.75 (d, *J* = 1.6 Hz, 1H), 2.34-2.17 (m, 2H), 1.8-1.75 (m, 1H), 1.06 (s, 3H), 0.96 (d, *J* = 6.4 Hz, 3H)

[α]_D²⁵ = -6.3 (c = 3.4, CH₂Cl₂).

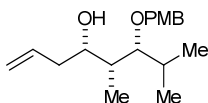




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.591	BV	0.3838	1773.61340	73.94410	3.6637
2	14.288	VV	0.2685	31.06278	1.82581	0.0642
3	15.018	VB	0.3135	1112.09717	55.08386	2.2972
4	20.686	BB	0.4670	4.54934e4	1495.22375	93.9749

Experimental Procedures and Spectroscopic Data for Table 2

(4S,5R,6R)-6-(4-methoxybenzyloxy)-5,7-dimethyloct-1-en-4-ol (4a)



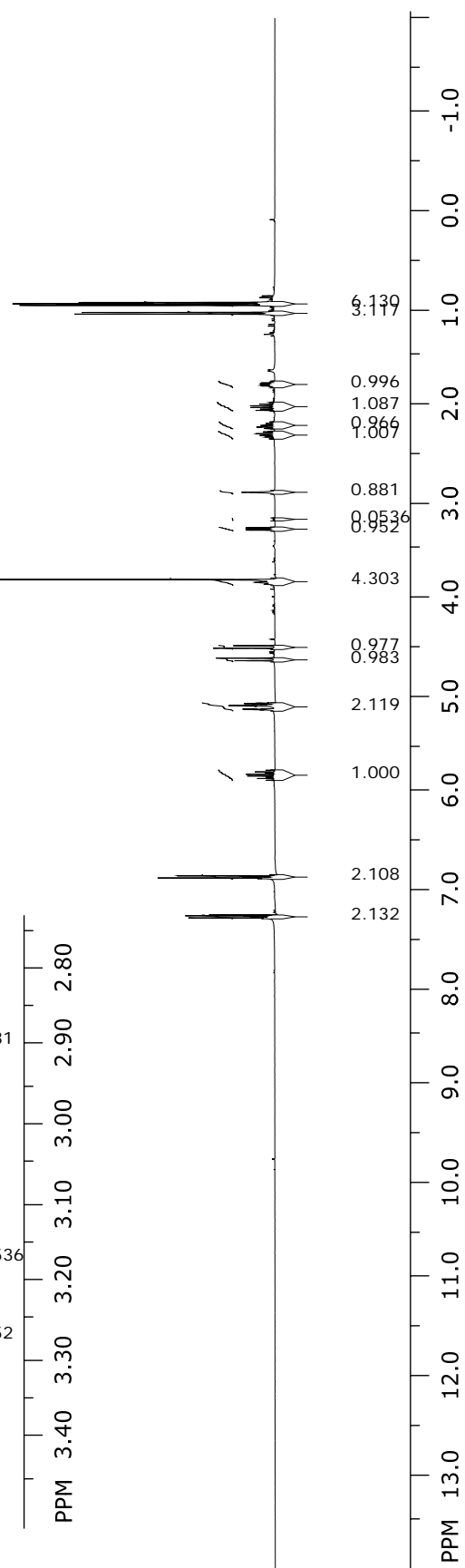
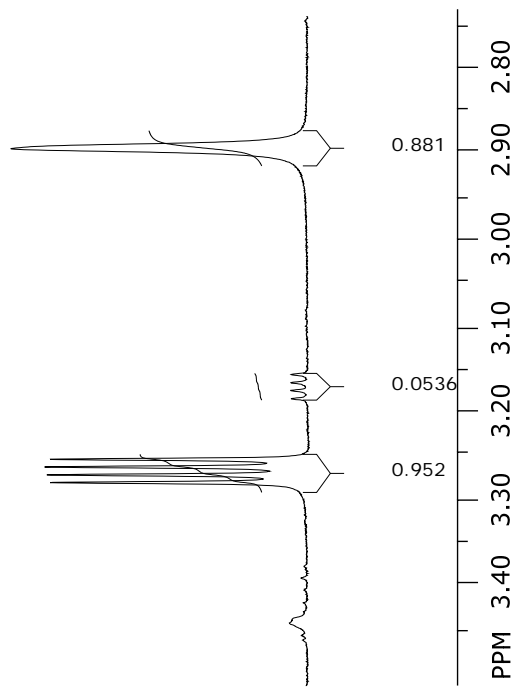
To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*S*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.2 mmol, 100 mol%) and alcohol *syn*-**3**⁴ (50.5 mg, 0.2 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 0.2 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 7% EtOAc/hexanes) to furnish the title compound (40.2 mg, 0.14 mmol, d.r. = 17:1) as a colorless oil in 69% yield. The spectroscopic data was consistent with reported values.⁴

¹H NMR (400 MHz, CDCl₃) Major diastereomer: δ 7.29 (d, *J* = 8.6, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.82 (m, 1H), 5.11 (m, 2H), 4.62 (d, *J* = 10.4 Hz, 1H), 4.49 (d, *J* = 10.4, 1H), 3.83 (m, 1H), 3.80 (s, 3H), 3.27 (dd, *J* = 3.5, 7.4 Hz, 1H), 2.93 (s, 1H), 2.29 (m, 1H), 2.22 (m, 1H), 2.01 (m, 1H), 1.77 (m, 1H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H).

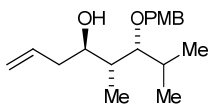
[α]_D²⁵ = -101 (c = 1.0, CHCl₃).

(4) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G.; Livingston, A. B. *J. Am. Chem. Soc.* **1995**, *117*, 6619.

X 8.000



(4S,5R,6R)-6-(4-methoxybenzyloxy)-5,7-dimethyloct-1-en-4-ol (4b)



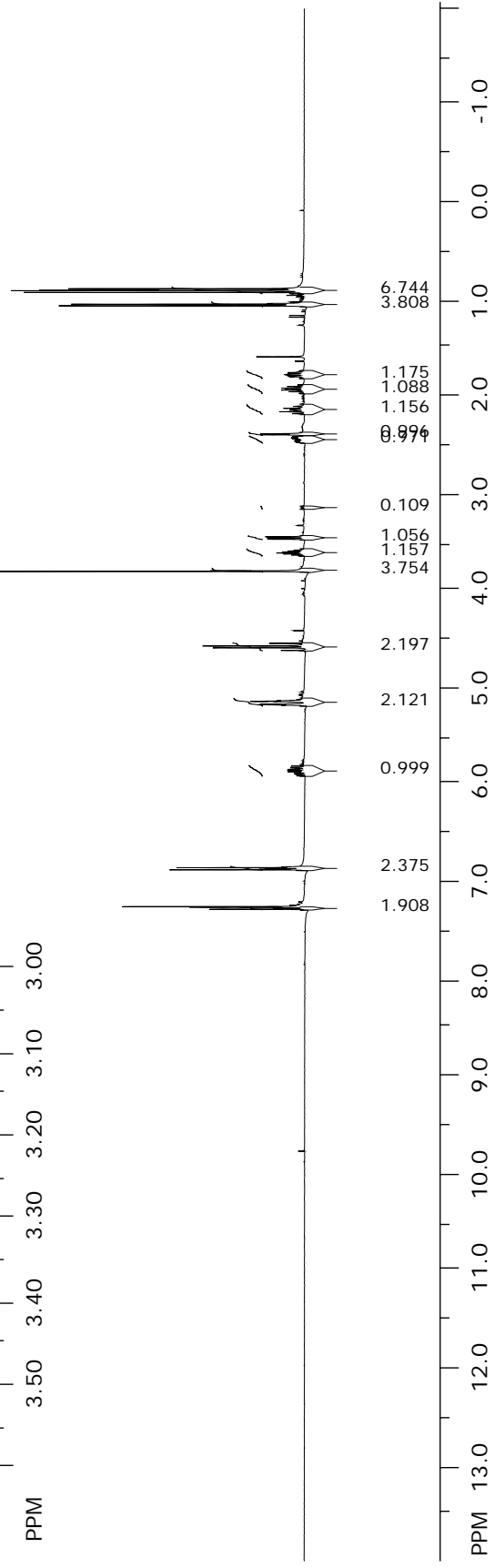
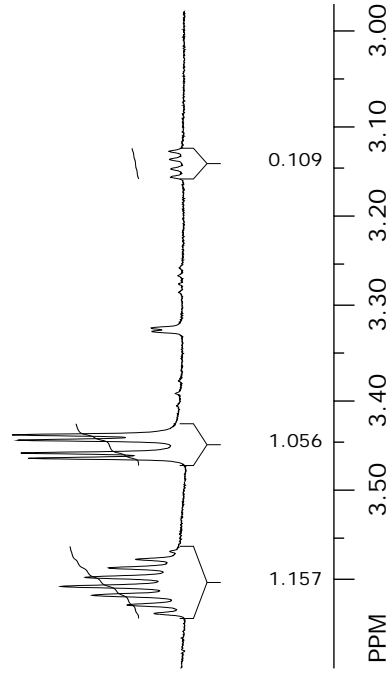
To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*R*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.2 mmol, 100 mol%) and alcohol *syn*-**3**⁴ (50.5 mg, 0.2 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 0.2 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 7% EtOAc/hexanes) to furnish the title compound (40.2 mg, 0.14 mmol, d.r. = 9:1) as a colorless oil in 69% yield. The spectroscopic data is consistent with values reported in the literature.⁴

¹H NMR (400 MHz, CDCl₃) Major diastereomer: δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.85 (m, 1H), 5.16 (d, *J* = 5.1 Hz, 2H), 4.69 (d, *J* = 10.9 Hz, 1H), 4.60 (d, *J* = 10.9 Hz, 1H), 4.56 (d, *J* = 10.9 Hz, 1H), 3.20 (s, 3H), 3.61 (m, 1H), 3.45 (dd, *J* = 2.3, 8.1 Hz, 1H), 2.42 (m, 2H), 2.13 (m, 1H), 1.92 (m, 1H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H).

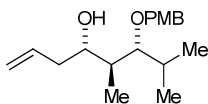
[α]_D²⁵ = -68 (c = 1.68, CHCl₃).

SpinWorks 3:

X 4.000



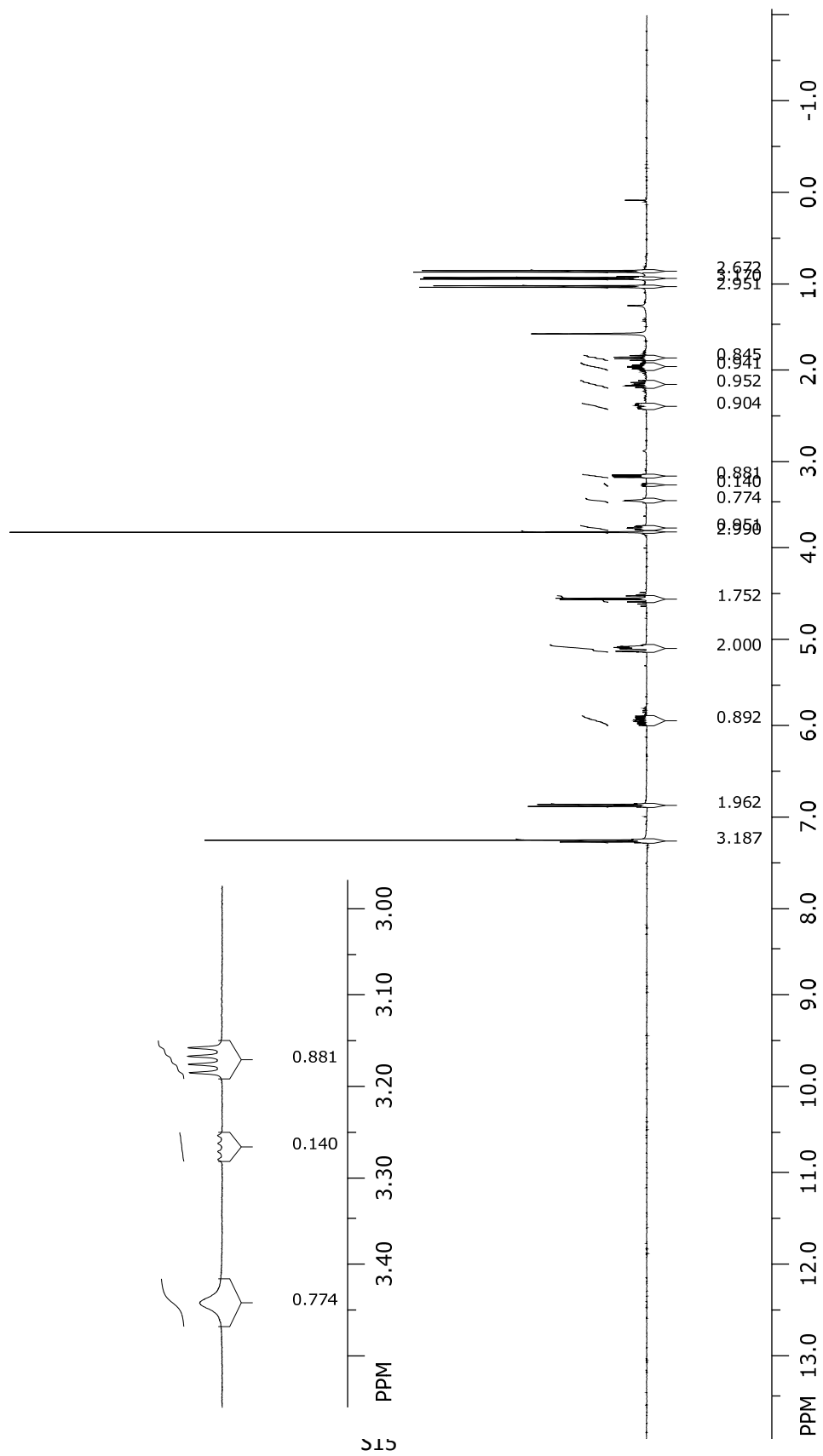
(4S,5S,6R)-6-(4-methoxybenzyloxy)-5,7-dimethyloct-1-en-4-ol (4c)



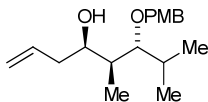
To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*S*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.2 mmol, 100 mol%) and alcohol *anti*-**3** (prepared by oxazolidinone *anti*-aldol, as reported by Evans⁴) (50.5 mg, 0.2 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 0.2 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 7% EtOAc/hexanes) to furnish the title compound (32 mg, 0.11 mmol, d.r. = 6:1) as a colorless oil in 55% yield. The spectroscopic data was in good agreement with values previously reported.⁴

¹H NMR (400 MHz, CDCl₃) Major diastereomer: δ 7.27 (m, 2H), 6.87 (m, 2H), 5.92 (m, 2H), 5.11 (m, 2H), 4.57 (d, *J* = 10.6 Hz, 1H), 4.53 (d, *J* = 10.6 Hz, 1H), 3.80 (s, 3H), 3.76 (m, 1H), 3.46 (d, *J* = 1.8 Hz, 1H), 3.17 (dd, *J* = 7.5, 3.8 Hz, 1H), 2.40 (m, 1H), 2.13 (m, 1H), 1.94 (m, 1H), 1.84 (m, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 7, 3H).

[α]_D²⁸ = -103 (c = 0.22, CHCl₃).



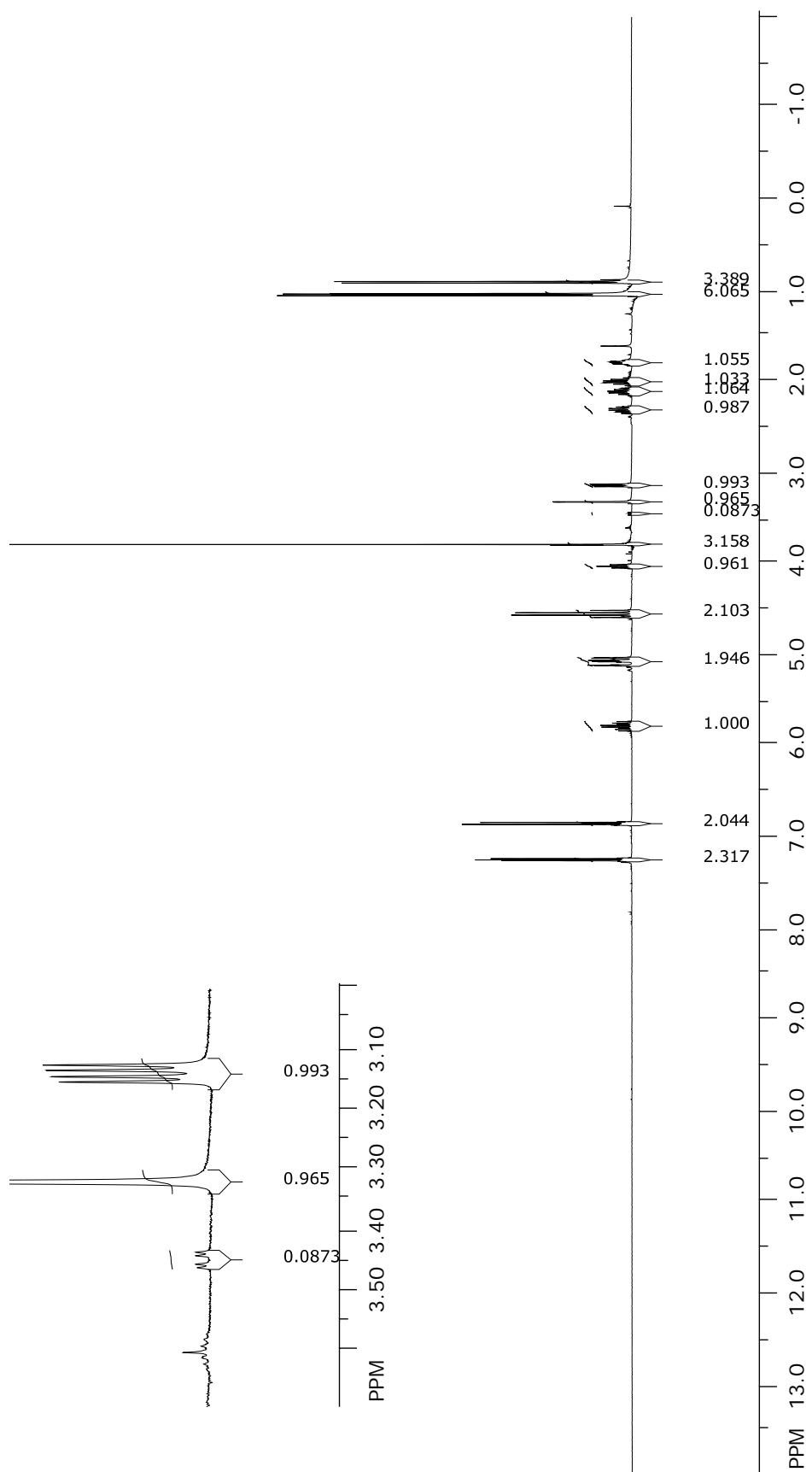
(4R,5S,6R)-6-(4-methoxybenzyloxy)-5,7-dimethyloct-1-en-4-ol (4d)



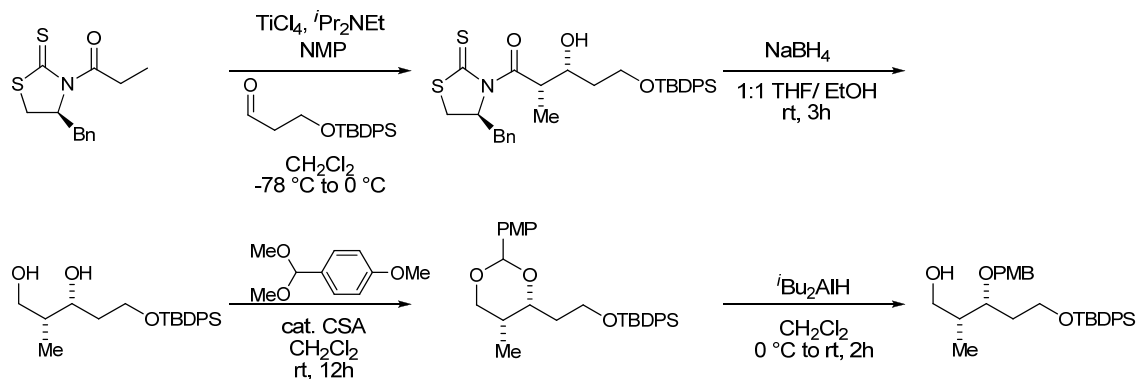
To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*R*)-Ir-b-NO₂ (13.7 mg, 0.013 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (5.3 mg, 0.025 mmol, 10 mol%), cesium carbonate (81 mg, 0.25 mmol, 100 mol%) and alcohol *anti*-**3**⁴ (63 mg, 0.25 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.63 mL, 0.4 M concentration with respect to alcohol), water (45 μ L, 2.5 mmol, 10 equiv) and allyl acetate (54 μ L, 0.5 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 7% EtOAc/hexanes) to furnish the title compound (57 mg, 0.19 mmol, d.r. = 12:1) as a colorless oil in 78% yield. The spectroscopic data was in good agreement with reported values.⁴

¹H NMR (400 MHz, CDCl₃) Major diastereomer: δ 7.26 (m, 2H), 6.86 (m, 2H), 5.79 (m, 1H), 5.10 (dd, *J* = 15.4, 1.4 Hz, 1H), 5.05 (dd, *J* = 10.2, 0.8 Hz, 1H), 4.55 (q, *J* = 10.3 Hz, 2H), 4.03 (t, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.35 (s, 1H), 3.14 (dd, *J* = 3.5, 7.8 Hz, 1H), 2.31 (m, 1H), 2.10 (m, 1H), 1.99 (m, 1H), 1.79 (m, 1H), 1.05 (d, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H).

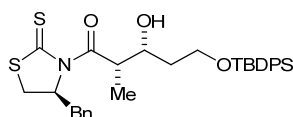
[α]_D²⁸ = -215 (c = 0.61, CHCl₃).



Experimental Procedures and Spectroscopic Data for the Preparation of Alcohol 5



(2S,3R)-1-((S)-4-benzyl-2-thioxothiazolidin-3-yl)-5-(tert-butyldiphenylsilyloxy)-3-hydroxy-2-methylpentan-1-one (**S1**)



To a flamed dried 25 mL round bottom flask was added (S)-1-(4-benzyl-2-thioxothiazolidin-3-yl)propan-1-one⁵ (212 mg, 0.8 mmol, 1.0 equiv) and DCM (8 mL, 0.1 M with respect to thione). The reaction vessel was cooled to 0 °C and TiCl₄ (90 µL, 0.84 mmol, 1.05 equiv) was added dropwise to form an orange slurry. After stirring 5 min, *i*Pr₂NEt (120 µL, 0.88 mmol, 1.1 equiv) was added dropwise. The resultant dark red solution was allowed to stir for 40 min at 0 °C and then NMP (150 µL, 1.60 mmol, 2 equiv) was added followed by 15 min of additional stirring. The reaction was cooled to -78 °C and 3-((tert-butyldiphenylsilyl)oxy)propanal⁶ (300 mg, 0.96 mmol, 1.2 equiv) was added in 1 mL DCM. The reaction was stirred for 2 hours at -78 °C and one hour at 0 °C and was then poured into a separatory funnel containing saturated aqueous ammonium chloride (100 mL). The organic phase was separated and the remaining aqueous phase was washed with two additional portions of dichloromethane (10 mL each). The combined organic portions were dried over sodium sulfate, filtered and concentrated under reduced pressure. Flash chromatography (15% EtOAc/hexanes) delivered aldol adduct **S1** as a yellow oil (350 mg, 76%, >20:1 d.r.).

¹H NMR (400 MHz, CDCl₃): δ 7.7-7.66 (m, 4H), 7.44-7.37 (m, 6H), 7.35-7.27 (m, 5H), 5.42-5.37 (m, 1H), 4.74-4.68 (m, 1H), 4.37-4.32 (m, 1H), 3.90-3.83 (m, 2H), 3.39 (dd, *J* = 8, 12 Hz, 1H), 3.27 (d, *J* = 4 Hz, 1H), 3.26 (dd, *J* = 8, 14 Hz, 1H), 2.90 (dd, *J* = 8 Hz, 1H), 1.87-1.79 (m, 1H), 1.70-1.64 (m, 1H), 1.24 (d, *J* = 4 Hz, 3H), 1.05 (s, 9H).

¹³C NMR (100 MHz, CDCl₃): δ 201.4, 177.42, 136.45, 135.57, 134.79, 133.30, 133.25, 129.74, 129.65, 129.44, 128.89, 127.74, 127.24, 70.28, 68.91, 62.45, 43.37, 37.03, 35.95, 31.81, 26.85, 26.55, 19.2, 11.4.

(5) Crimmins, M. T.; Christie, H. S.; Hughes, C. O. *Org. Synth.* **2011**, 88, 364.

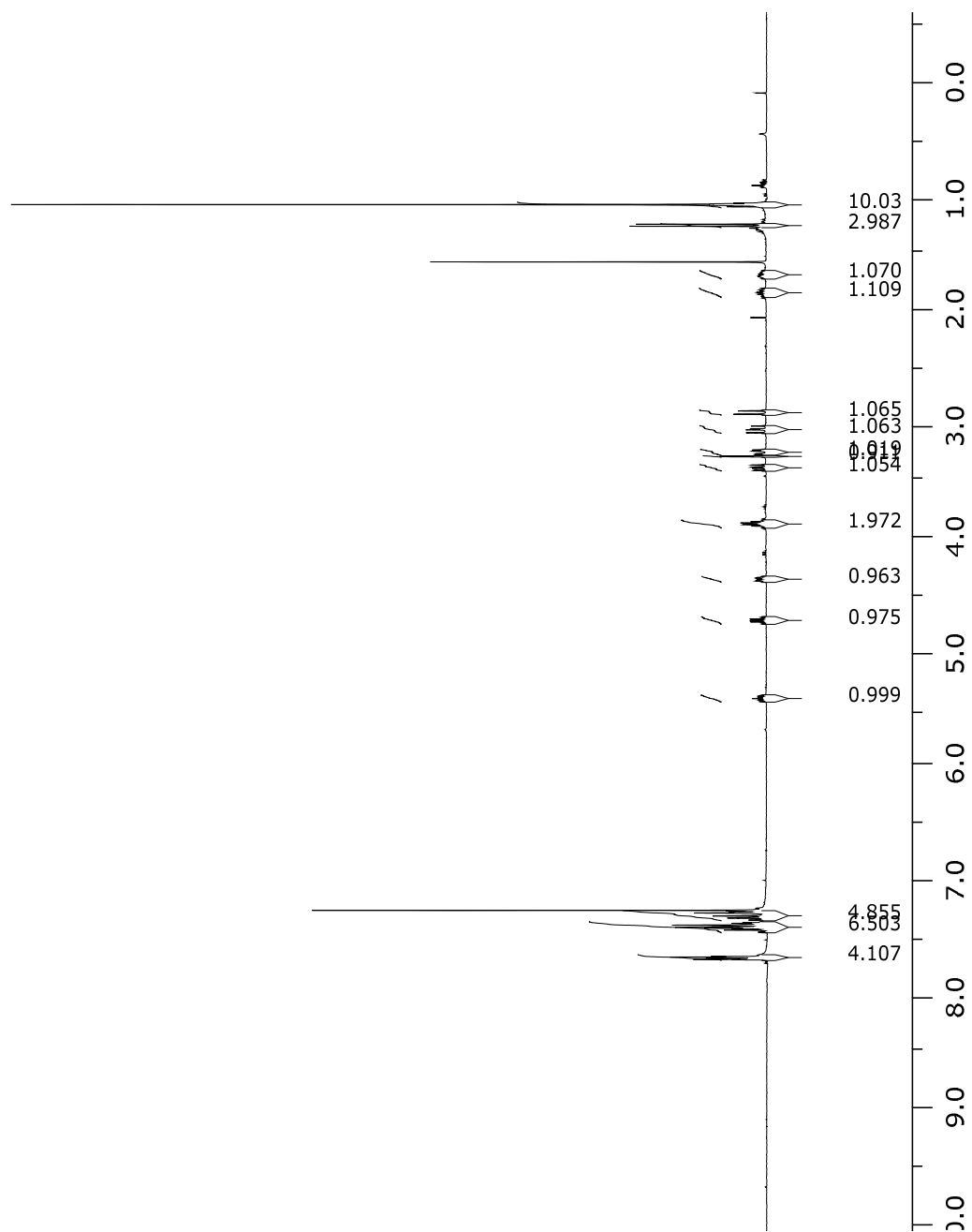
(6) Ferrie, L.; Boulard, L.; Bouzbouz, S.; Reymond, S.; Capdevielle, P.; Cossy, J. *J. Org. Chem.* **2008**, 73, 1864.

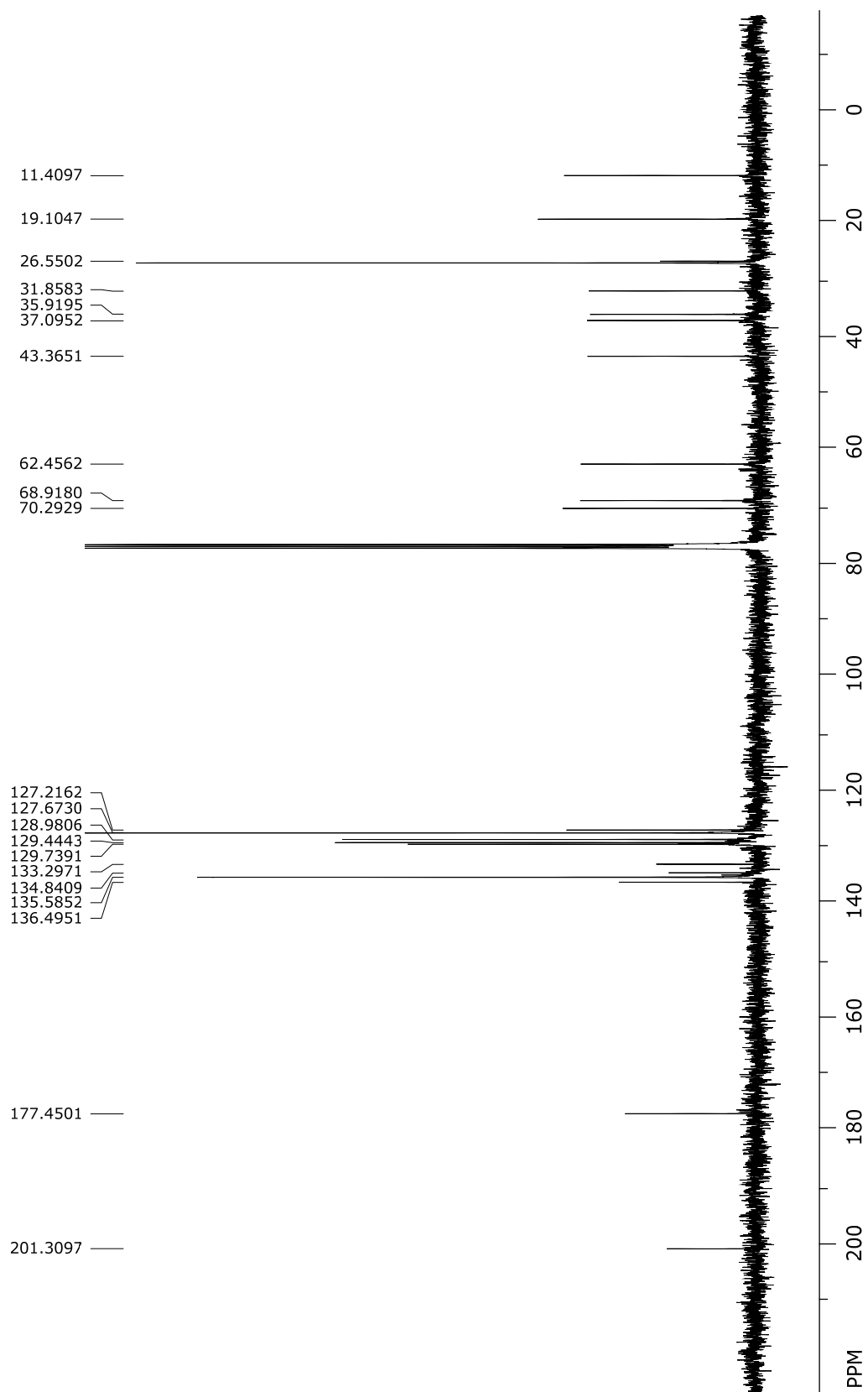
LRMS (ESI) Calcd.For C₃₂H₃₉NO₃S₂Si(M+H): 600.2, Found: 600.2.

FTIR (neat): 3480, 2930, 2856, 2358, 1692, 1470, 1454, 1427, 1340, 1291, 1030 cm⁻¹.

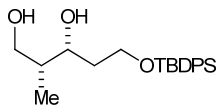
R_f = 0.30 (4:1 Hexane/EtOAc).

[α]_D²⁷ = +33 (c =0.52, CH₂Cl₂).





(2R,3R)-5-((tert-butyldiphenylsilyl)oxy)-2-methylpentane-1,3-diol (S2)



To a 250 mL round bottom flask was added **S1** (5.05 g, 8.75 mmol, 1.0 equiv) in 1:1 THF/EtOH (100 mL total). To this was added NaBH₄ (330 mg, 8.75 mmol, 1.0 equiv). The reaction was stirred at room temperature for 3 h, and quenched by the addition of saturated ammonium chloride (50 mL). Ethyl acetate (75 mL) was added and the layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 75 mL), dried (MgSO₄), and was concentrated *in vacuo*. Flash chromatography (25% EtOAc/Hexanes to 50% EtOAc/Hexanes) gave diol **S2** as a clear oil (2.23 g, 68%).

¹H NMR (400 MHz, CDCl₃): δ 7.69-7.66 (m, 4H), 7.47-7.39 (m, 6H), 4.15-4.11 (m, 1H), 3.94-3.84 (m, 1H), 3.70 (brs, 3H), 2.79 (brs, 1H), 1.93-1.83 (m, 2H), 1.56-1.50 (m, 1H), 1.05 (s, 9H), 0.92 (d, *J* = 7.1, 3H).

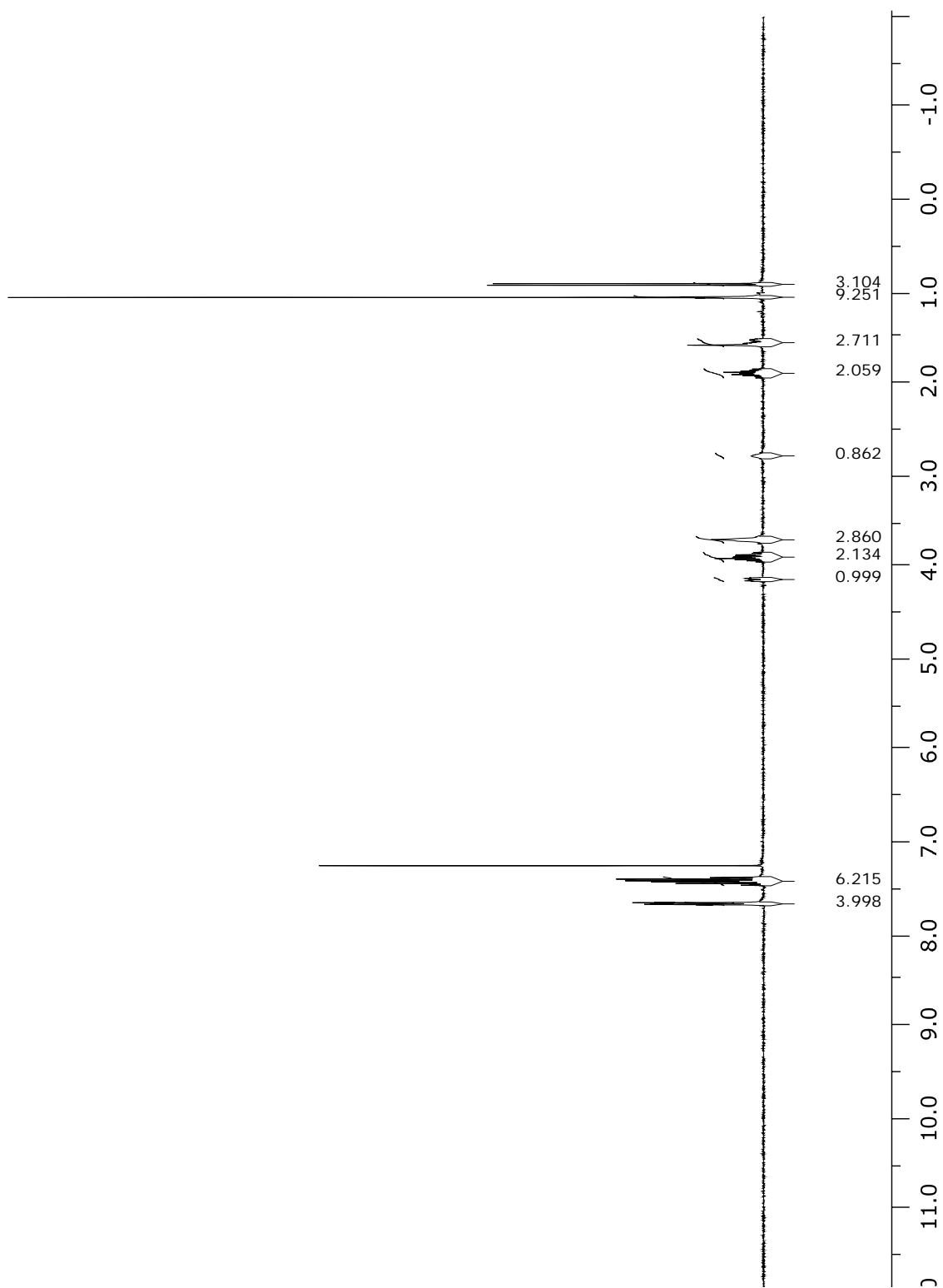
¹³C NMR (100 MHz, CDCl₃): δ 135.6, 132.8, 132.6, 129.9, 127.8, 75.7, 66.8, 64.2, 39.5, 34.4, 26.8, 19.1, 11.1.

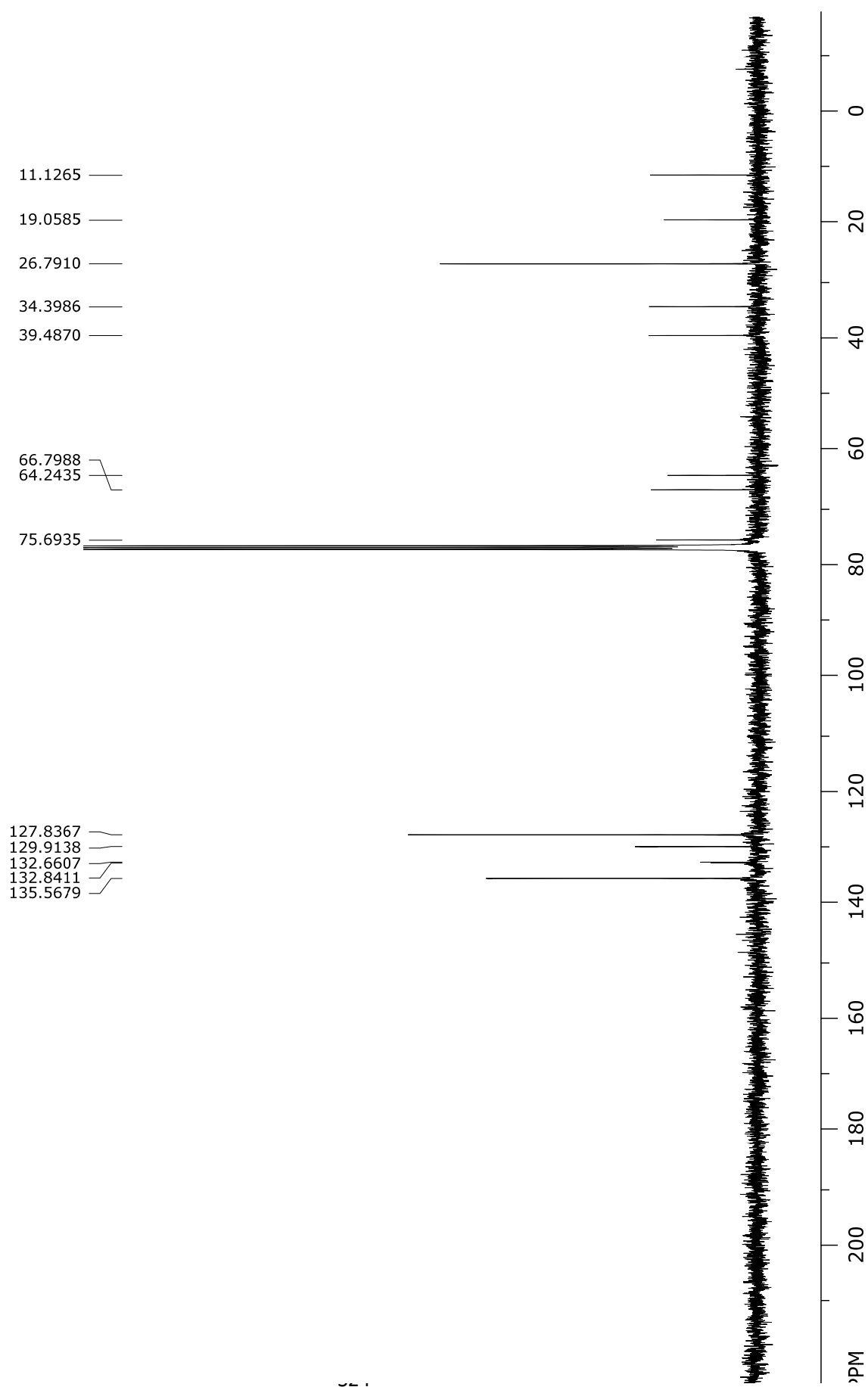
LRMS (ESI) Calcd. For C₂₂H₃₂O₃Si(M+Na): 395.2, Found: 395.2.

FTIR (neat): 3343, 2931, 2854, 2117, 1744, 1710, 1642, 1433, 1349, 1206, 1111 cm⁻¹.

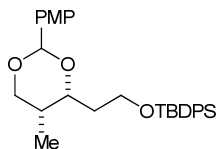
R_f = 0.43 (3:2 Hexanes/EtOAc).

[α]_D²⁸ = -277 (c = 0.44, CH₂Cl₂).





tert-butyl(2-((4R,5R)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl)ethoxy)diphenylsilanediol (S3)



To a dry 150 mL round bottom flask was added **S2** (2.23 g, 6.00 mmol, 1.0 equiv) in 60 mL DCM (0.1 M). To this was added CSA (130 mg, 0.6 mmol, 10 mol%), and *p*-anisaldehyde dimethyl acetal (1.1 mL, 6.59 mmol, 1.1 equiv). The reaction was stirred at room temperature for 12 h, and quenched by the addition of saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous phase was further extracted with DCM (3 x 20 mL). The organic layer was evaporated and EtOAc (10 mL) and sodium bisulfite (1 g) and water (10 mL) were added. The reaction was stirred for 10 minutes and then concentrated. The aqueous phase was extracted with EtOAc (20 mL x 3), dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography (10% EtOAc/Hexanes) provided the product as a clear oil (2.11 g, 71%).

¹H NMR(400 MHz, CDCl₃): δ 7.68-7.63 (m, 4H), 7.42-7.30 (m, 8H), 6.89-6.86 (m, 2H), 4.22-4.18 (m, 2H), 4.09 (dd, J = 1.6, 12 Hz, 1H), 4.01 (dd, J = 1.2, 11.6 Hz, 1H), 3.88-3.79 (m, 1H), 3.80 (s, 3H), 3.77-3.73 (m, 1H), 1.90-1.81 (m, 1H), 1.73-1.65 (m, 1H), 1.54-1.48 (m, 1H), 1.16 (d, J = 8 Hz, 3H), 1.06 (s, 9H).

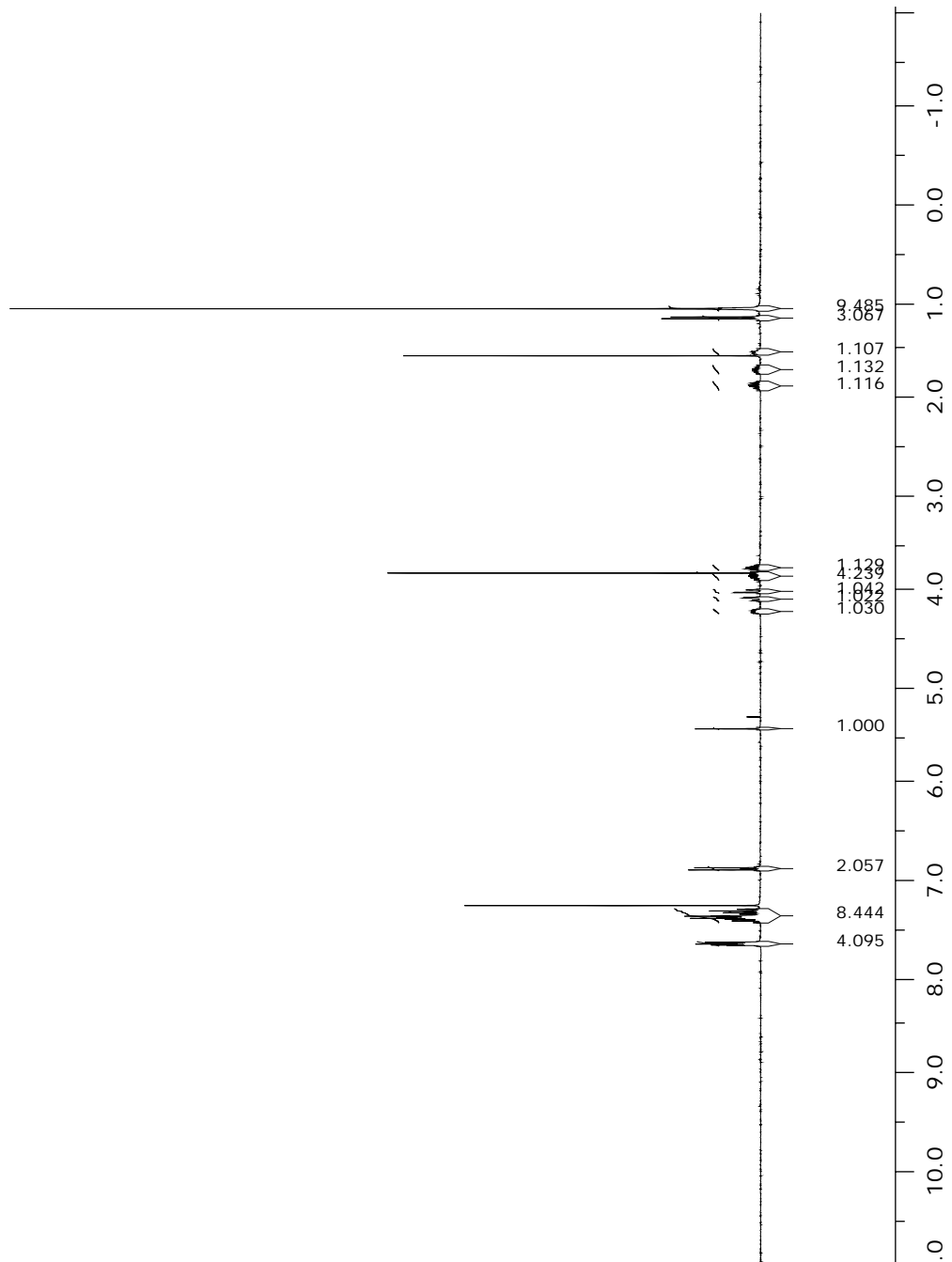
¹³C NMR (100 MHz, CDCl₃): δ 159.8, 135.4, 133.9, 133.8, 131.5, 129.5, 127.7, 127.6, 127.4, 76.1, 73.9, 59.9, 53.3, 35.8, 32.0, 26.9, 19.3, 11.3.

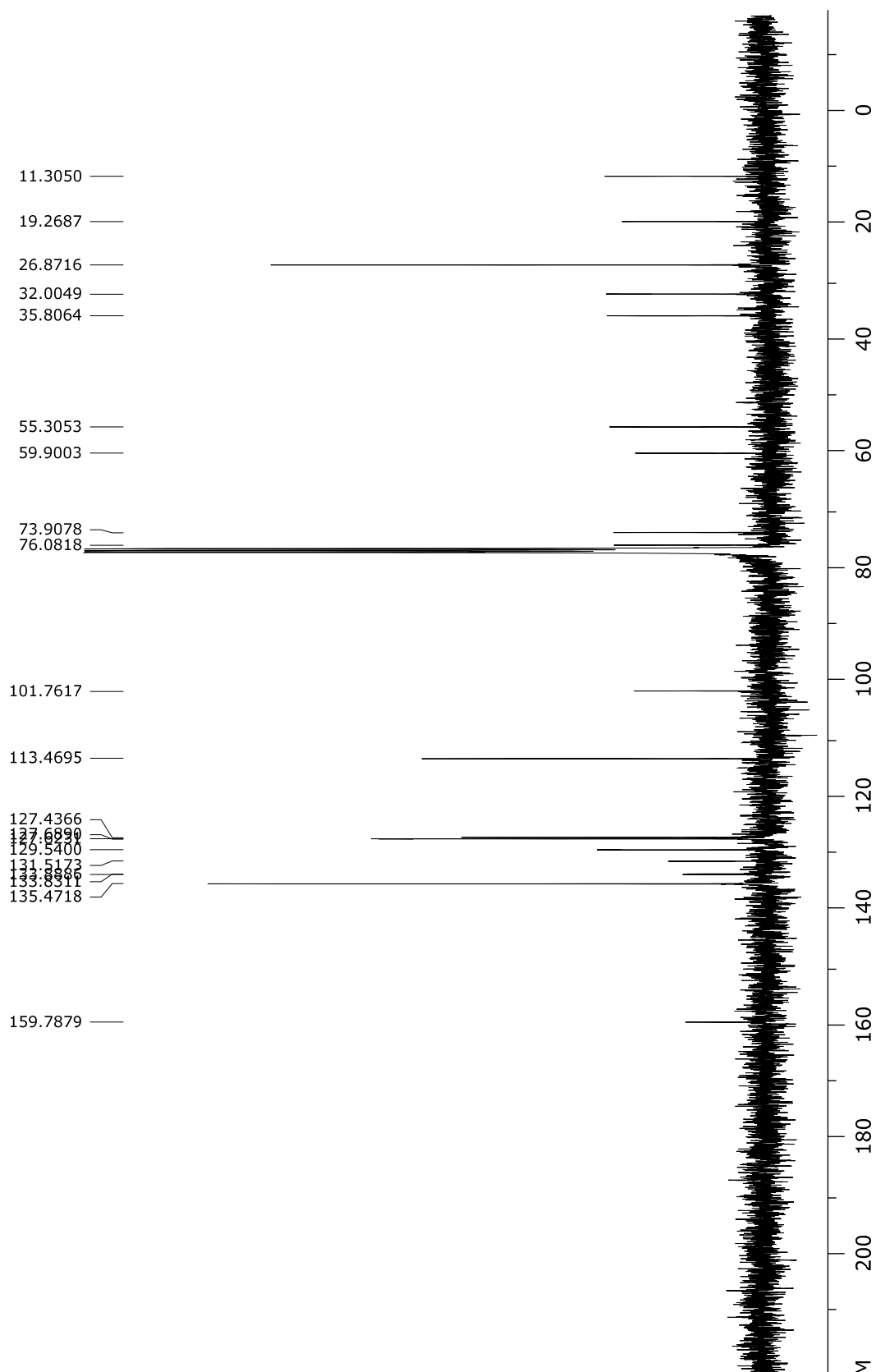
LRMS (ESI) Calcd.For C₃₀H₃₈O₄Si(M+Na): 513.2, Found: 513.2.

FTIR (neat): 2956, 2930, 2855, 1615, 1462, 1427, 1389, 1357, 1339, 1302, 1160, 1063 cm⁻¹.

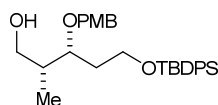
R_f = 0.57 (4:1 Hexane/EtOAc).

[α]_D²⁶ = -86 (c = 0.7, CH₂Cl₂).





(2R,3R)-5-(tert-butylidiphenylsilyloxy)-3-(4-methoxybenzyloxy)-2-methylpentan-1-ol (5)



To a dry 100 mL round bottom flask was added **S3** (2.11 g, 4.3 mmol, 1.0 equiv) in 43 mL DCM (0.1 M). The flask was cooled to 0 °C, and to this was added dropwise ^tBu₂AlH (1M solution in hexanes, 8.6 mmol, 8.6 mL 2.0 equiv). The reaction was gradually warmed to room temperature over 2 h and was quenched by the addition of a saturated aqueous solution of Rochelle's salt. After stirring an additional 2 h, the layers were partitioned, and the aqueous layer further extracted with DCM (3 x 15 mL). The organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography (10% EtOAc/hexanes) provided the product as a clear oil (2.09 g, 99%)

¹H NMR (400 MHz, CDCl₃): δ 7.68-7.64 (m, 4H), 7.45-7.36 (m, 6H), 7.18-7.16 (m, 2H), 6.84-6.82 (m, 2H), 4.52 (d, J = 12 Hz, 1H), 4.40 (d, J = 8 Hz, 1H), 3.80-3.73 (m, 3H), 3.79 (s, 3H), 3.68-3.62 (m, 1H), 3.55-3.49 (m, 1H), 2.61 (dd, J = 4, 8 Hz, 1H), 2.15-2.08 (m, 1H), 1.80-1.73 (m 2H), 1.06 (s, 9H), 0.85 (d, J = 6.8 Hz, 3H).

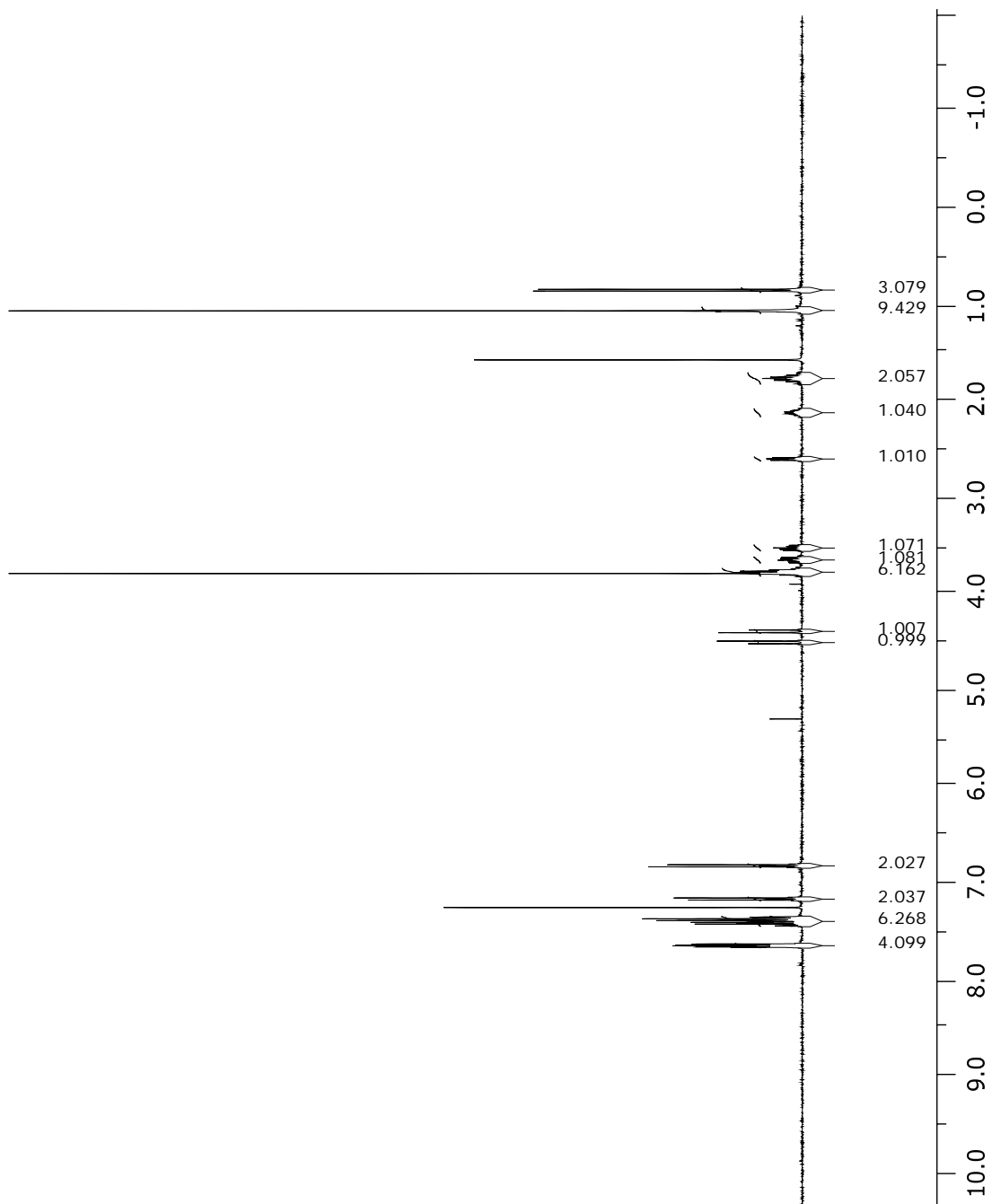
¹³C NMR (100 MHz, CDCl₃): δ 159.3, 135.5, 133.8, 130.4, 129.6, 129.5, 127.6, 79.0, 71.6, 66.0, 60.7, 55.3, 36.6, 32.7, 26.9, 19.2, 12.2.

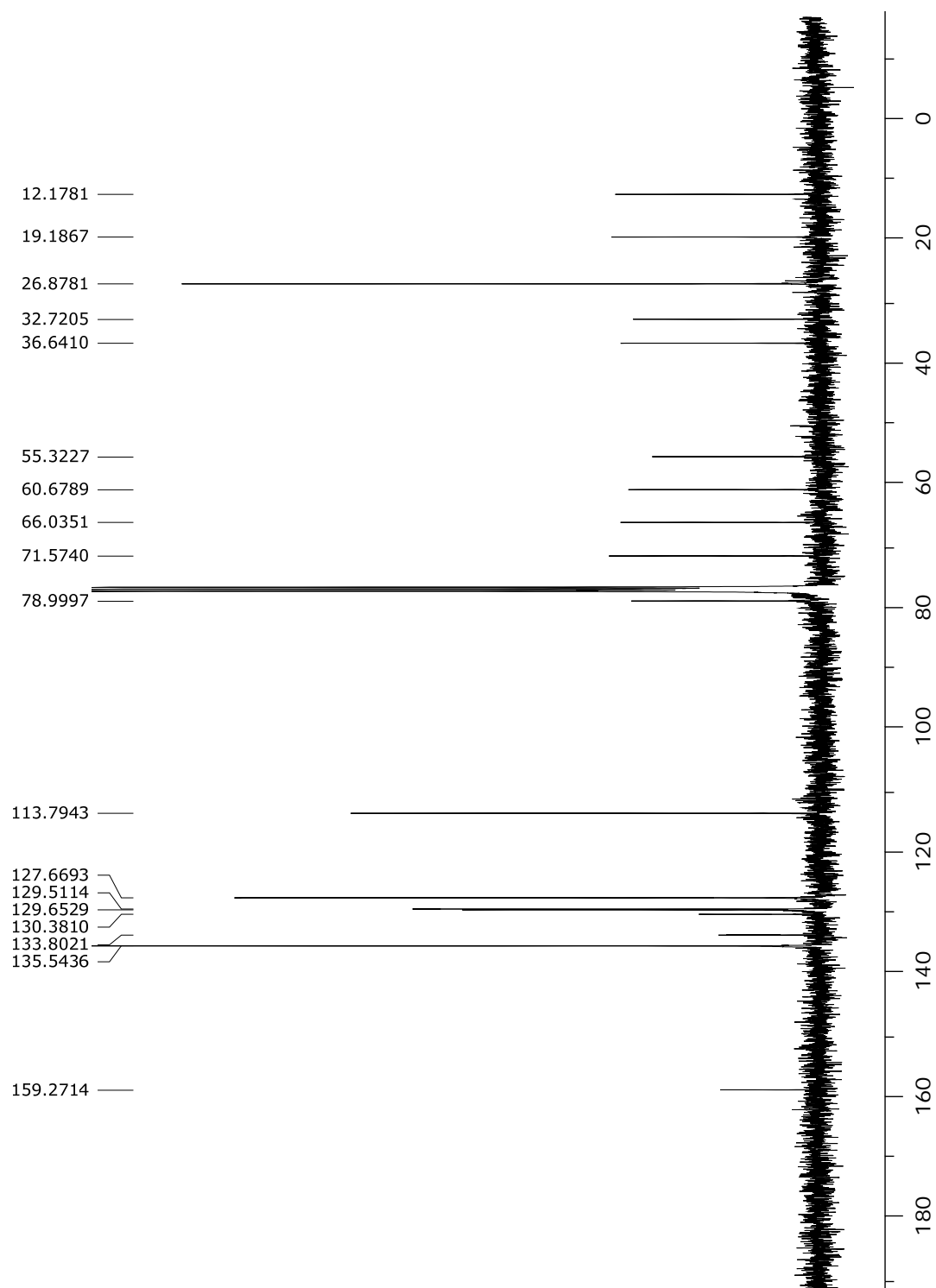
LRMS (ESI) Calcd.For C₃₀H₄₀O₄Si(M+Na): 515.3, Found: 515.3

FTIR (neat): 3470 2930, 2856, 1587, 1513, 1462, 1427, 1390, 1356, 1301, 1246, 1173, 1108, 1082 cm⁻¹.

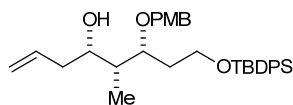
R_f = 0.18 (4:1 Hexane/EtOAc).

[α]_D²⁸ = -33 (c = 0.27, CH₂Cl₂).





(4*S*,5*R*,6*R*)-8-(tert-butyldiphenylsilyloxy)-6-(4-methoxybenzyloxy)-5-methyloct-1-en-4-ol
(6a)



To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*S*)-Ir-b-NO₂ (9.3 mg, 0.0085 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (3.6 mg, 0.017 mmol, 10 mol%), cesium carbonate (55 mg, 0.17 mmol, 100 mol%) and alcohol **5** (84 mg, 0.17 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.43 mL, 0.4 M concentration with respect to alcohol), water (31 μ L, 1.7 mmol, 10 equiv) and allyl acetate (37 μ L, 0.34 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 100 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 10% EtOAc/hexanes) to furnish the title compound (62 mg, 0.116 mmol, d.r. = 9:1) as a colorless oil in 68% yield.

¹H NMR (400 MHz, CDCl₃): δ 7.69-7.65 (m, 4H), 7.46-7.38 (m, 6H), 7.21-7.19 (m, 2H), 6.89-6.84 (m, 2H), 5.84-5.74 (m, 1H), 5.13-5.05 (m, 1H), 4.54 (d, *J* = 12 Hz, 1H), 4.37 (d, *J* = 12, 1H), 3.85-3.79 (m, 2H), 3.80 (s, 3H), 3.77-3.66 (m, 2H), 3.16 (brs, 1H), 2.32-2.25 (m, 1H), 2.18-2.10 (m, 1H), 2.03-1.95 (m, 1H), 1.82-1.74 (m, 1H), 1.71-1.66 (m, 1H), 1.07 (s, 9H), 0.93 (d, *J* = 12 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 159.2, 135.5, 133.6, 130.2, 129.7, 129.4, 127.7, 117.0, 113.9, 81.1, 77.3, 74.6, 70.9, 60.8, 55.2, 39.8, 38.8, 33.5, 26.9, 19.2, 6.2.

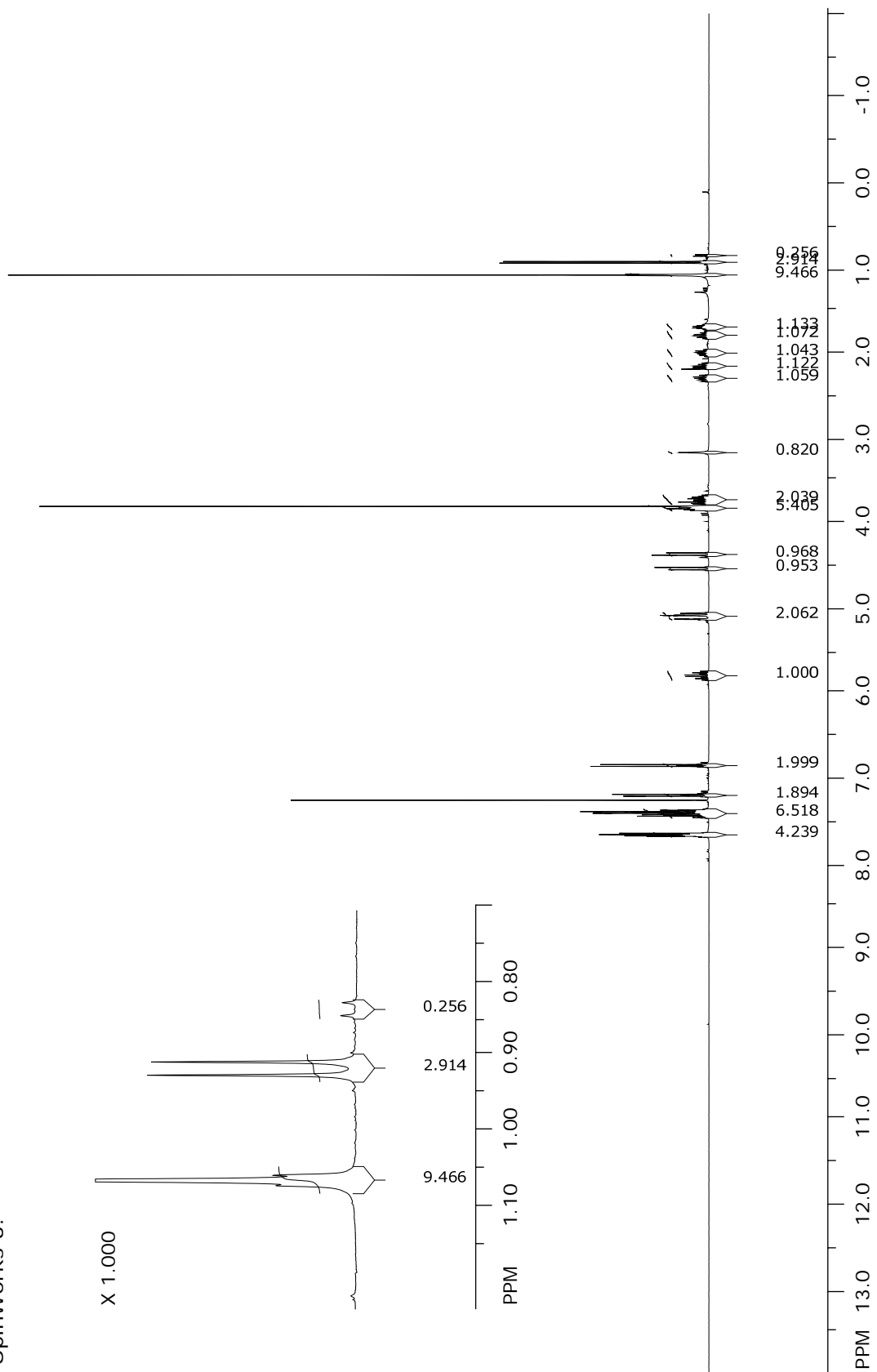
LRMS (ESI) Calcd.For C₃₃H₄₄O₄Si(M+Na): 555.3, Found: 555.3

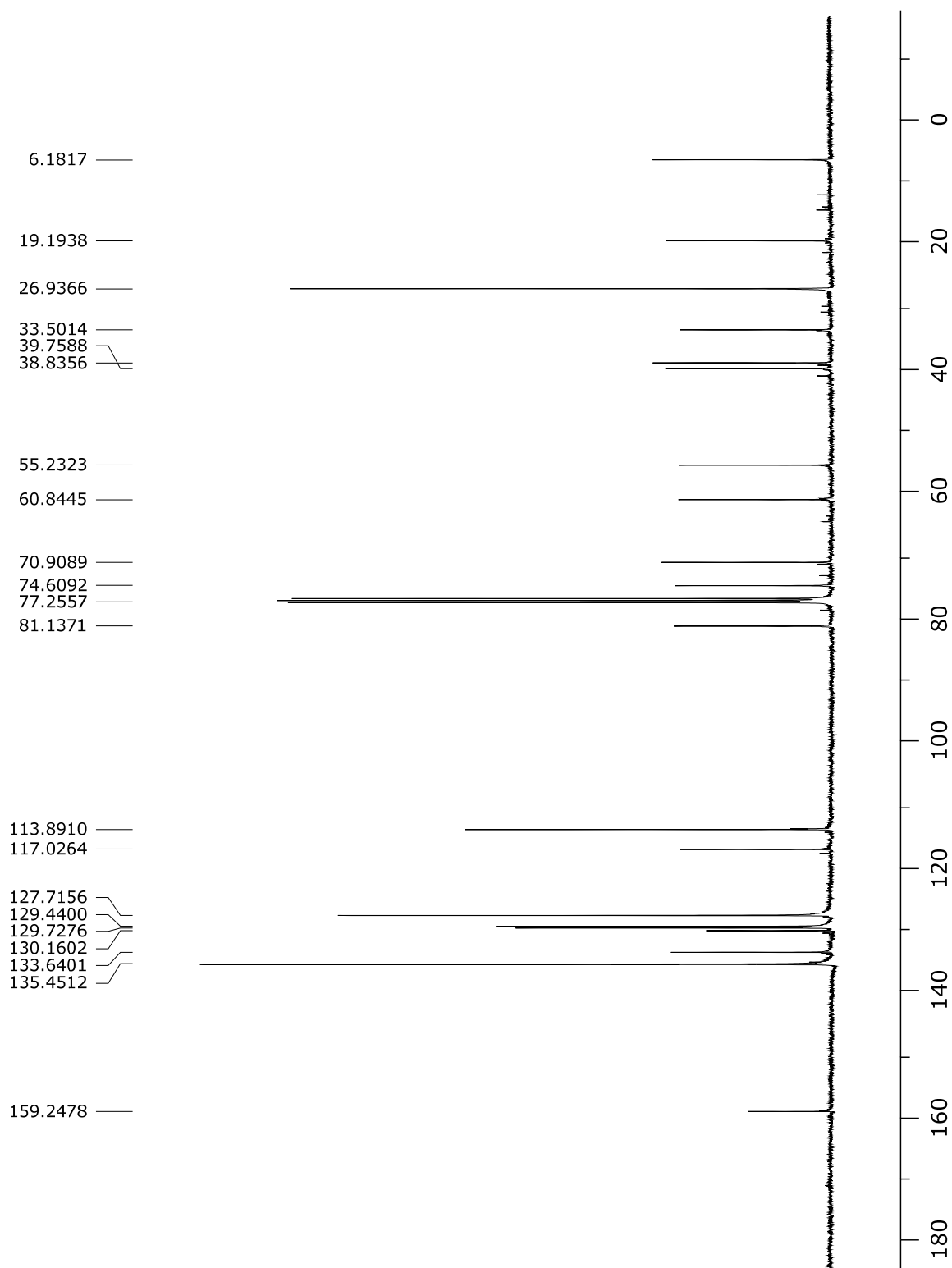
FTIR (neat): 2931, 2857, 1612, 1587, 1513, 1463, 1427, 1390, 1360, 1302, 1248, 1173 cm⁻¹.

R_f = 0.40 (4:1 Hexane/EtOAc).

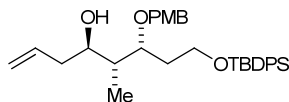
[α]_D²⁷ = -43 (c = 2.76, CH₂Cl₂).

SpinWorks 3:





(4*R*,5*R*,6*R*)-8-(tert-butyldiphenylsilyloxy)-6-(4-methoxybenzyloxy)-5-methyloct-1-en-4-ol
(6b)



To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*R*)-Ir-b-NO₂ (8.2 mg, 0.0075 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (3.2 mg, 0.015 mmol, 10 mol%), cesium carbonate (49 mg, 0.15 mmol, 100 mol%) and alcohol **5** (74 mg, 0.15 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.38 mL, 0.4 M concentration with respect to alcohol), water (27 μ L, 1.5 mmol, 10 equiv) and allyl acetate (32 μ L, 0.3 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 100 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 5% EtOAc/hexanes to 7% EtOAc/hexanes) to furnish the title compound (56 mg, 0.105 mmol, d.r. = 4:1) as a colorless oil in 70% yield.

¹H NMR (400 MHz, CDCl₃): δ 7.67-7.64 (m, 4H), 7.46-7.35 (m, 6H), 7.19-7.16 (m, 2H), 6.83-6.81 (m, 2H), 5.98-5.88 (m, 1H), 5.13-5.08 (m, 2H), 4.58 (d, *J* = 12 Hz, 1H), 4.37 (d, *J* = 12, 1H), 3.89-3.85 (m, 2H), 3.71-3.74 (m, 5H), 3.70-3.65 (m, 1H), 2.40-2.32 (m, 1H), 2.18-2.10 (m, 1H), 2.00-1.91 (m, 1H), 1.86-1.71 (m, 2H), 1.05 (s, 9H), 0.85 (d, *J* = 8 Hz, 3H).

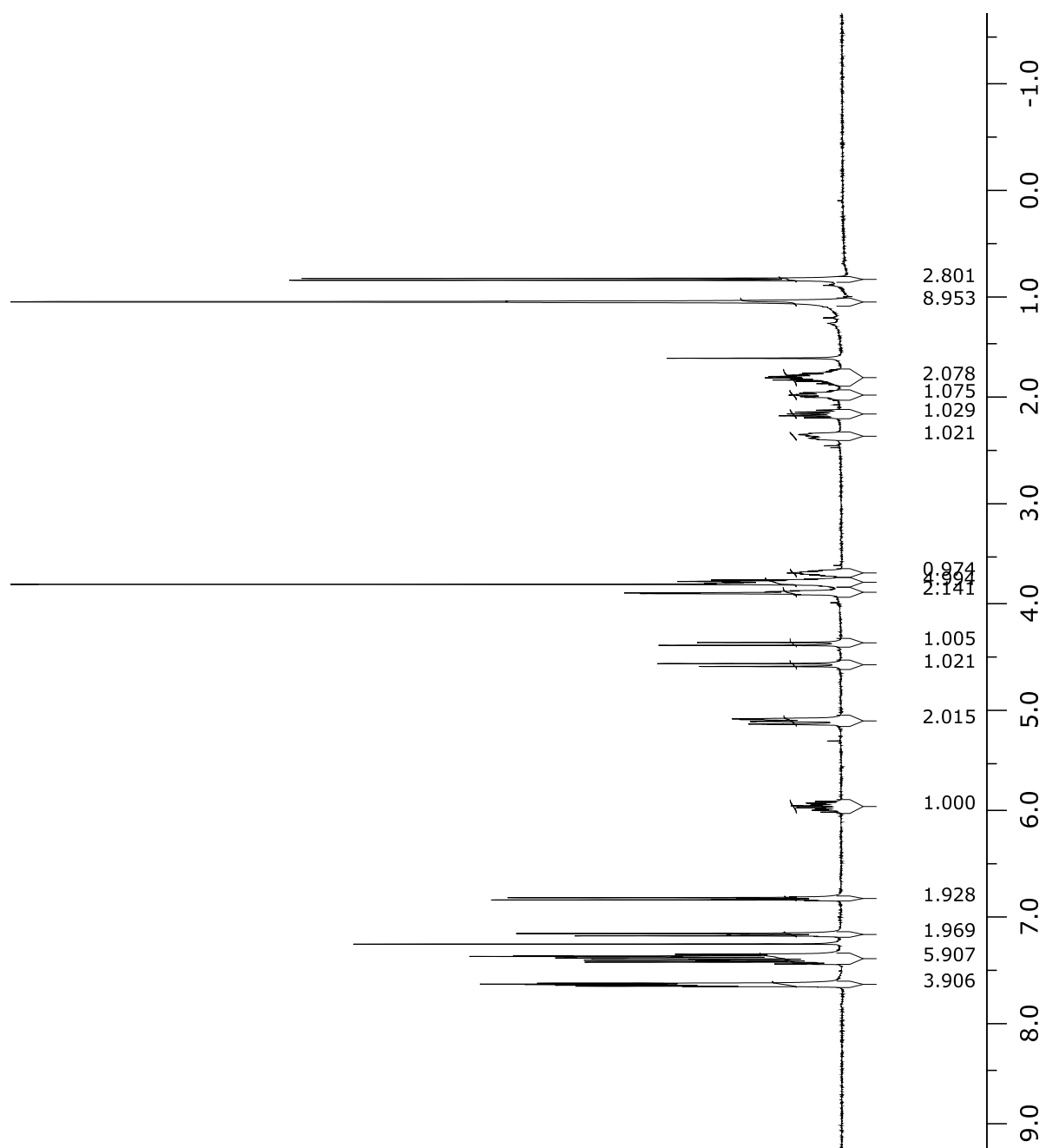
¹³C NMR (100 MHz, CDCl₃): δ 159.2, 135.5, 135.2, 133.7, 133.8, 130.0, 129.6, 129.5, 127.7, 116.9, 113.8, 79.3, 73.1, 71.3, 60.6, 55.2, 39.7, 38.2, 32.7, 26.8, 19.2, 12.8.

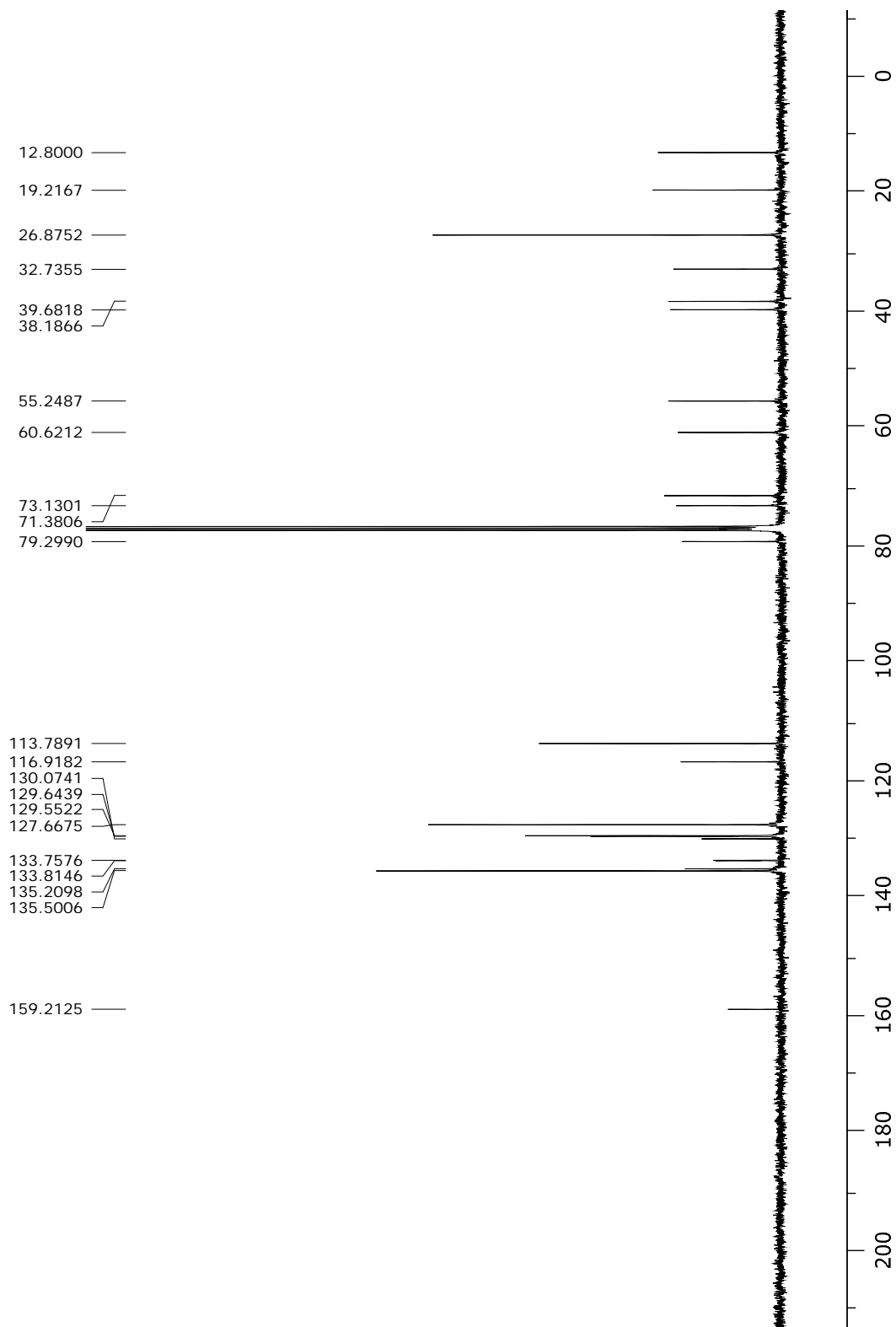
LRMS (ESI) Calcd.For C₃₃H₄₄O₄Si(M+Na): 555.3, Found: 555.3

FTIR (neat): 3462, 3070, 2930, 2856, 2359, 1640, 1612, 1587, 1513, 1463, 1427, 1389, 1359, 1302, 1247, 1173 cm⁻¹.

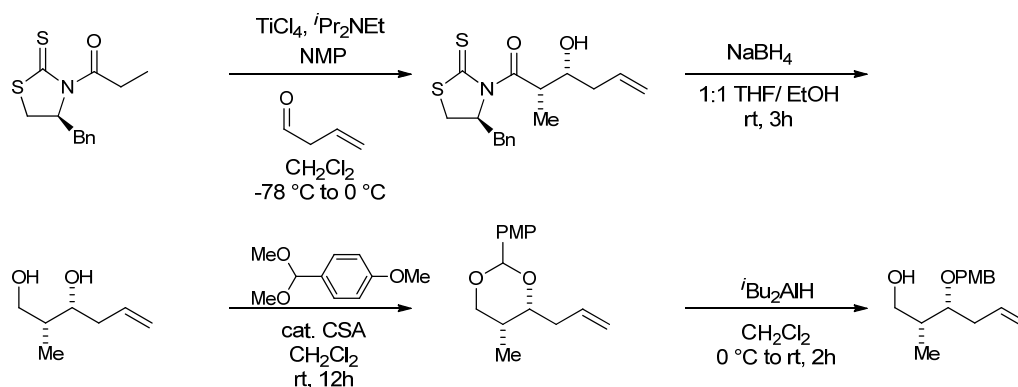
R_f = 0.51 (4:1 Hexane/EtOAc).

[α]_D²⁷ = -91.1 (c = 0.41, CH₂Cl₂).

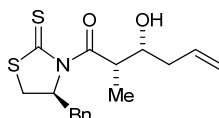




Experimental Procedures and Spectroscopic Data for the Preparation of Alcohol 7



(2S,3R)-1-((S)-4-benzyl-2-thioxothiazolidin-3-yl)-3-hydroxy-2-methylhex-5-en-1-one (S4)



To a flamed dried 1 L round bottom flask was added (S)-1-(4-benzyl-2-thioxothiazolidin-3-yl)propan-1-one⁵ (12.15 g, 45.7 mmol, 1.0 equiv) and DCM (385 mL, 0.1 M with respect to thione). The reaction vessel was cooled to 0°C and TiCl_4 (5.3 mL, 48.2 mmol, 1.05 equiv) was added dropwise to form an orange slurry. After stirring 5 min, $i\text{Pr}_2\text{NEt}$ (7.1 mL, 50.3 mmol, 1.1 equiv) was added dropwise. The resultant dark red solution was allowed to stir for 40 min at 0°C and then NMP (8.8 mL, 91.4 mmol, 2 equiv) was added followed by 15 min of additional stirring. The reaction was cooled to -78°C and 3-butenal⁷ (6.4 g, 91.4 mmol, 2.0 equiv) was added in 75 mL DCM. The reaction was stirred for 2 hours at -78°C and one hour at 0°C and was then poured into a separatory funnel containing saturated aqueous ammonium chloride (200 mL). The organic phase was separated and the remaining aqueous phase was washed with two additional portions of dichloromethane (100 mL each). The combined organic portions were dried over sodium sulfate, filtered and concentrated under reduced pressure. Flash chromatography (10% to 20% EtOAc/hexanes) delivered aldol adduct **S4** as a yellow oil (9.6 g, 63%, >20:1 d.r.).

¹H NMR (400 MHz, CDCl_3): δ 7.39-7.19 (m, 5H), 5.78-5.67 (m, 1H), 5.30-5.24 (m, 1H), 5.10-5.04 (m, 2H), 4.47-4.40 (m, 1H), 3.98-3.90 (m, 1H), 3.34 (dd, $J = 4, 12$ Hz, 1H), 3.17 (dd, $J = 8, 16$ Hz, 1H), 3.00 (dd, $J = 8, 12$ Hz, 1H), 2.57 (d, $J = 4$ Hz, 1H), 2.27 (d, $J = 4$ Hz, 1H), 2.27-2.11 (m, 1H), 1.21 (d, $J = 8$ Hz, 3H).

¹³C NMR (100 MHz, CDCl_3): δ 201.3, 177.9, 136.4, 134.2, 129.4, 128.9, 127.3, 118.2, 71.6, 68.7, 42.7, 38.9, 36.8, 32.1, 10.7.

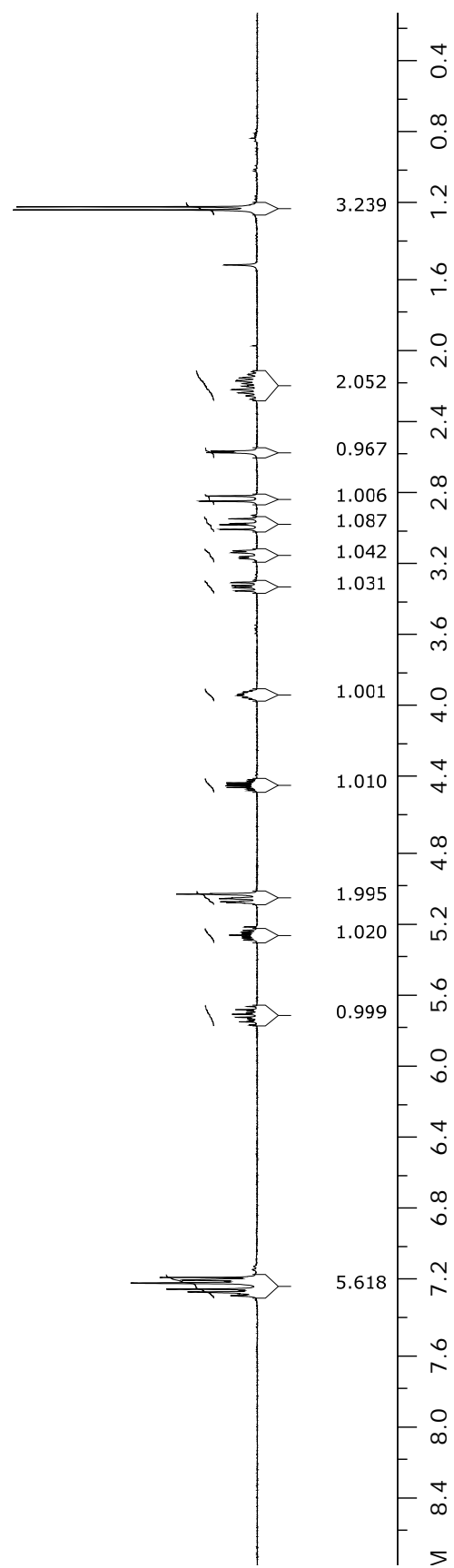
LRMS (ESI) Calcd. For $\text{C}_{19}\text{H}_{27}\text{NO}_2\text{S}_2$ $\text{M}+\text{Na}$): 358.1, Found: 358.1.

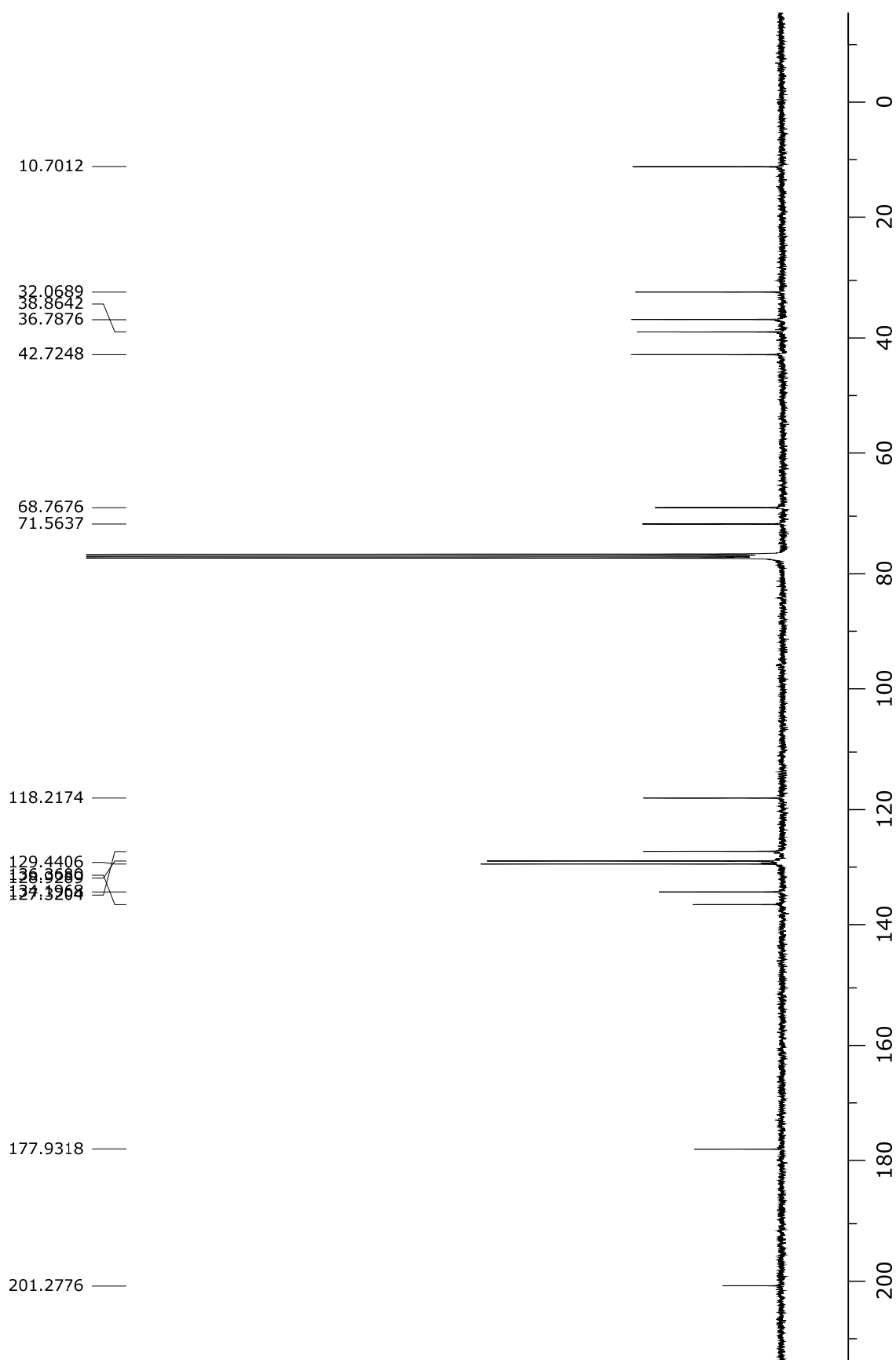
FTIR (neat): 3435, 2932, 1683, 1494, 1454, 1291, 1258, 1163, 1135 cm^{-1} .

(7) Crimmins, M. T.; Choy, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 5653.

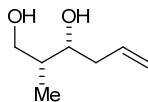
$\underline{R}_f = 0.18$ (4:1 Hexane/EtOAc).

$[\alpha]_D^{25} = +140$ (c = 1.35, CH₂Cl₂).





(2R,3R)-2-methylhex-5-ene-1,3-diol (S5)



To a 250 mL round bottom flask was added **S4** (1.1 g, 3.3 mmol, 1.0 equiv) in 1:1 THF/EtOH (40 mL total). To this was added NaBH₄ (124 mg, 3.3 mmol, 1.0 equiv). The reaction was stirred at room temperature for 3 h, and quenched by the addition of saturated ammonium chloride (50 mL). Ethyl acetate was added and the layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 25 mL), dried (MgSO₄), and concentrated under reduced pressure. Flash chromatography (25% EtOAc/Hexanes to 50% EtOAc/Hexanes) gave diol **S5** as a clear oil (300 mg, 2.31 mmol, 70%).

¹H NMR (400 MHz, CDCl₃): δ 5.87-5.77 (m, 1H), 5.18-5.12 (m, 2H), 3.89 (ddd, *J* = 2, 4, 8 Hz, 1H), 3.70 (d, *J* = 5.6 Hz, 2H), 2.45 (brs, 2H), 2.26 (m, 2H), 1.88-1.70 (m, 1H), 0.95 (d, *J* = 8 Hz, 3H).

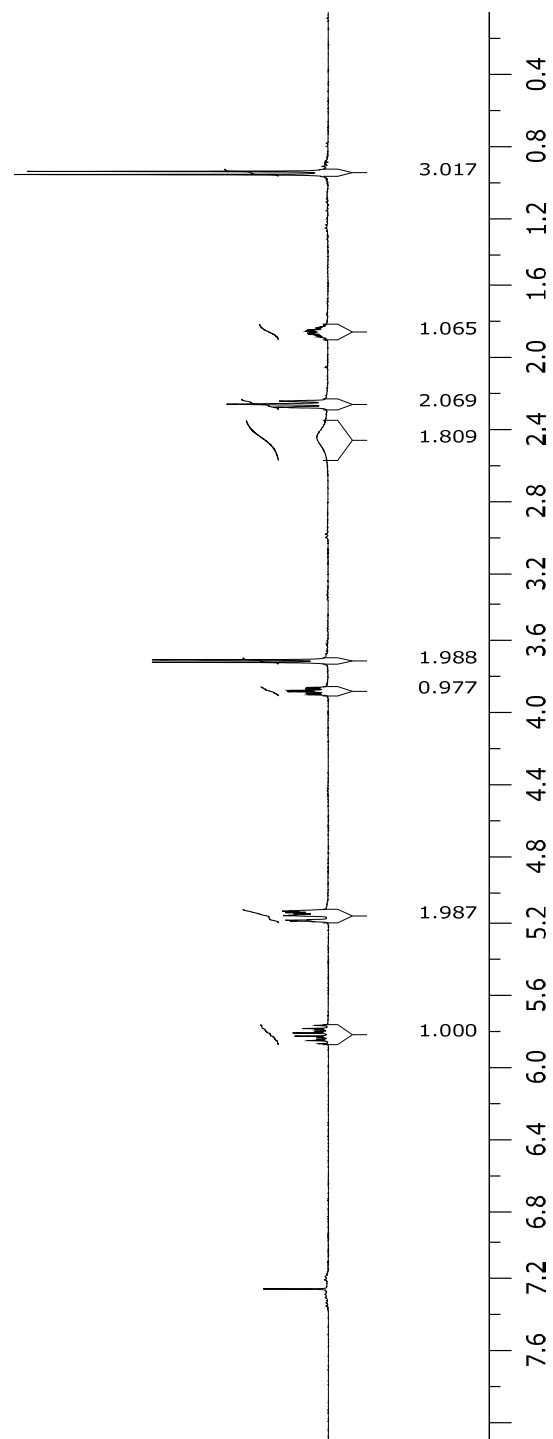
¹³C NMR (100 MHz, CDCl₃): δ 135.1, 118.0, 73.3, 67.0, 38.7, 38.7, 10.3.

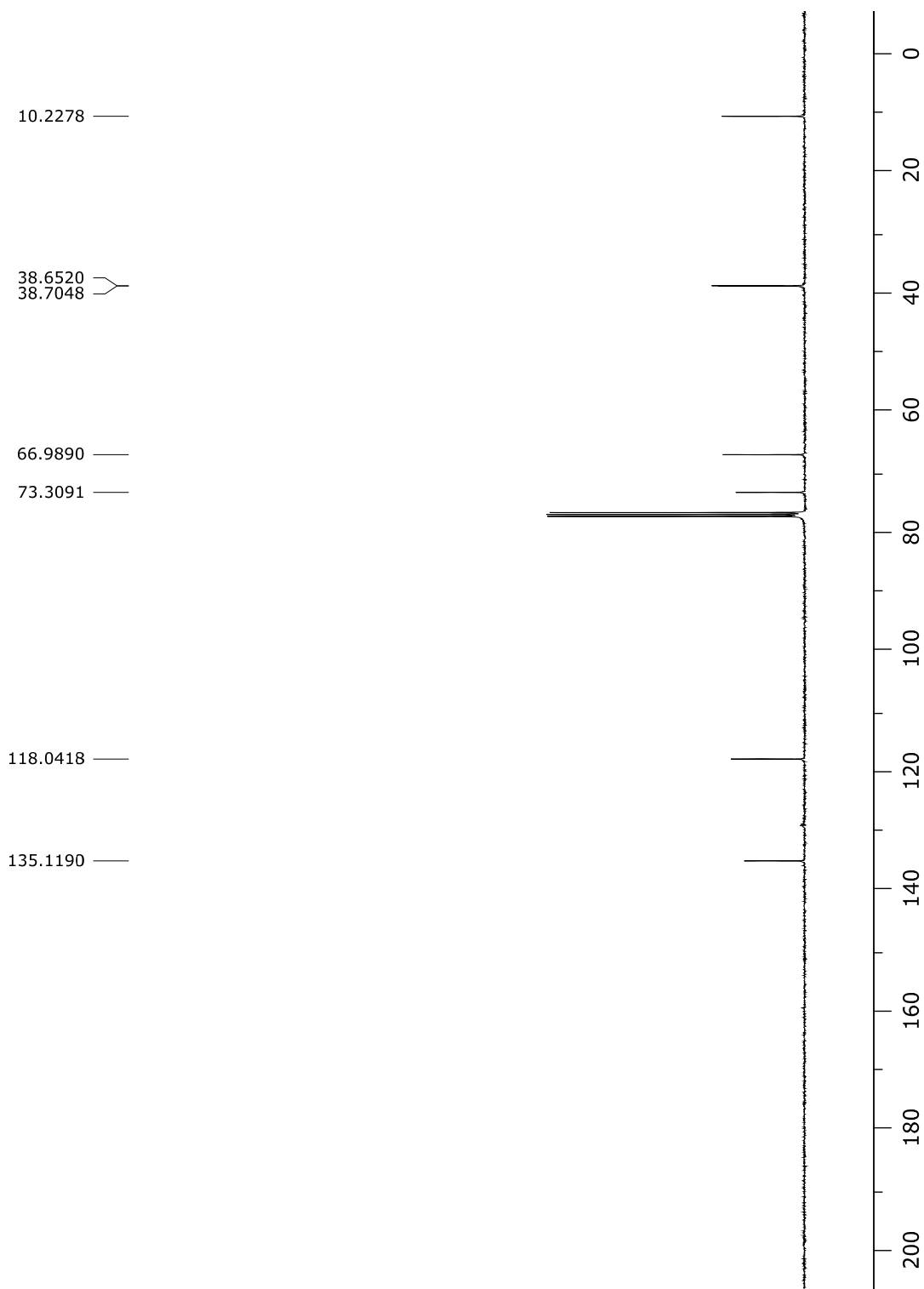
LRMS (ESI) Calcd. For C₇H₁₄O₂(M+Na): 153.1, Found: 153.1.

FTIR (neat): 3348, 2931, 1432, 1021, 979 cm⁻¹.

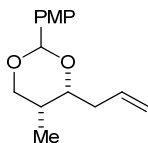
R_f = 0.19 (3:2 Hexane/EtOAc).

[α]_D²⁵ = -64 (c = 1.35, CHCl₃).





(4*R*,5*R*)-4-allyl-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (S6)



To a dry 150 mL round bottom flask was added **S5** (1.37 g, 10.5 mmol, 1.0 equiv) in 10.5 mL DCM (1 M). To this was added CSA (240 mg, 1.05 mmol, 10 mol%), and *p*-anisaldehyde dimethyl acetal (1.97 mL, 11.6 mmol, 1.1 equiv). The reaction was stirred at room temperature for 12 h, and quenched by the addition of saturated sodium bicarbonate solution. The layers were separated, and the aqueous phase was further extracted with DCM (3 x 15 mL). The organic layer was evaporated and EtOAc (10 mL) and sodium bisulfite (1 g) and water (10 mL) were added. The reaction was stirred for 10 minutes and then concentrated. The aqueous phase was extracted with EtOAc (20 mL x 3), dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography (5% EtOAc/Hexanes) provided the product as a clear oil (2.33 g, 9.4 mmol, 89%).

¹H NMR (400 MHz, CDCl₃): δ 7.44 (d, *J* = 8 Hz, 2H), 6.90 (d, *J* = 8 Hz, 2H), 5.88-5.77 (m, 1H), 5.47 (s, 1H), 5.18-5.07 (m, 2H), 4.09-3.95 (m, 3H), 3.80 (s, 3H), 2.48-2.40 (m, 1H), 2.26-2.19 (m, 1H), 1.62 (m, 1H), 1.21 (d, *J* = 8 Hz, 3H).

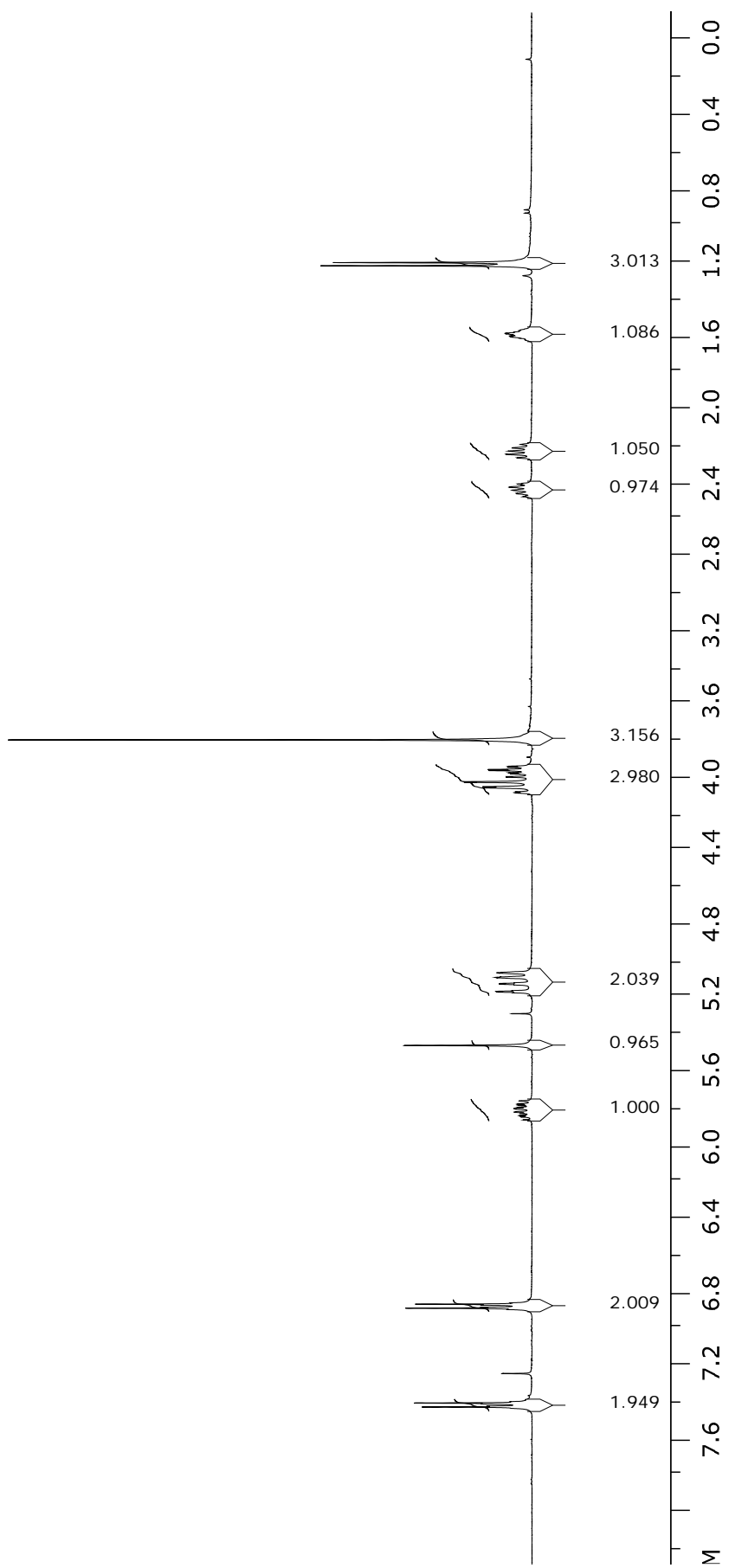
¹³C NMR (100 MHz, CDCl₃): δ 159.9, 134.0, 131.4, 127.4, 117.2, 113.6, 110.8, 79.3, 73.8, 55.3, 37.2, 31.2, 11.0.

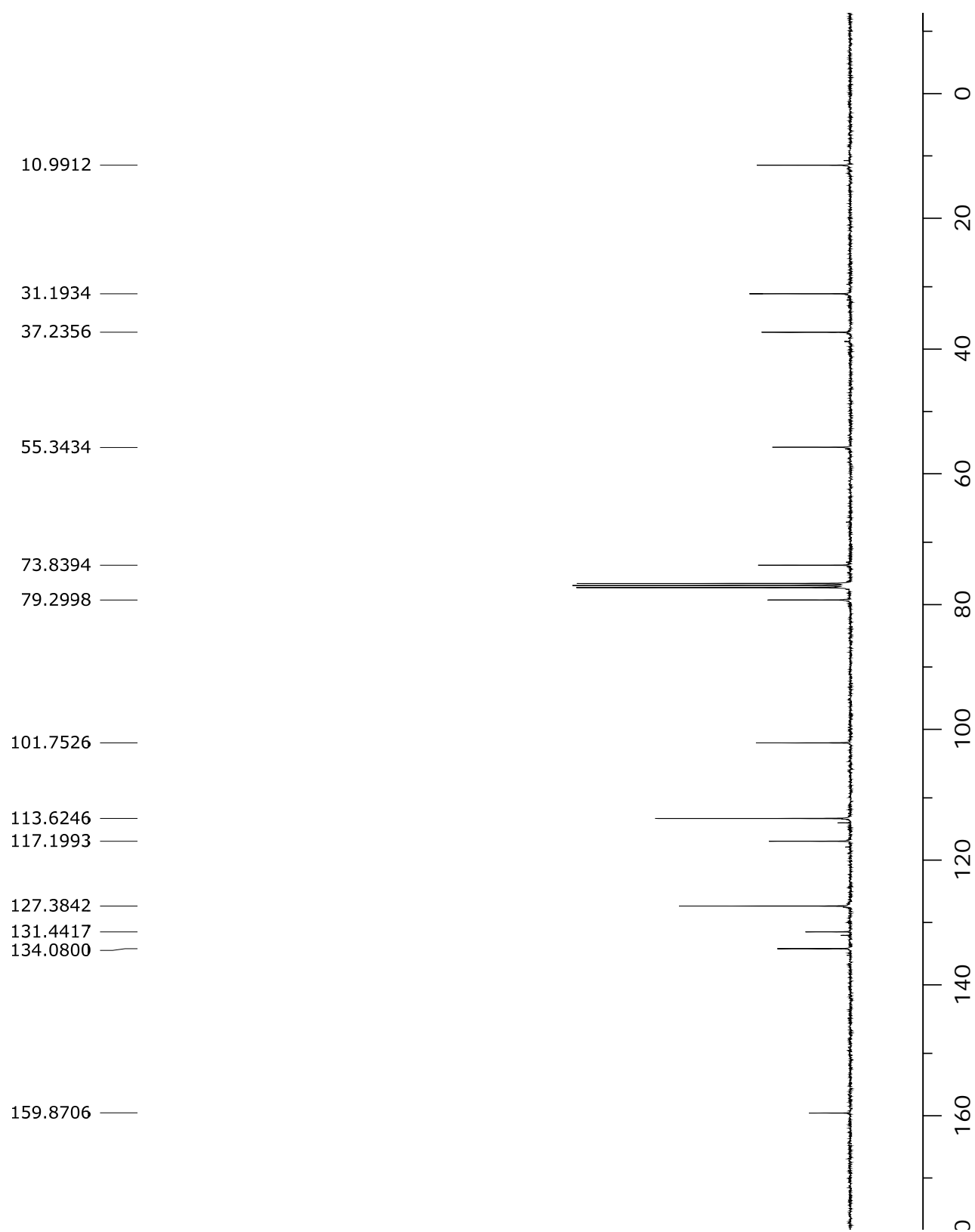
LRMS (ESI) Calcd. for C₁₇H₂₆O₃(M+Na): 271.1, Found: 271.1.

FTIR (neat): 2963, 2838, 1615, 1517, 1462, 1441, 1395, 1356, 1338, 1301, 1214, 1162 cm⁻¹.

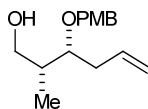
R_f = 0.63 (4:1 Hexane/EtOAc).

[α]_D²⁵ = +10.4 (c = 1.5, CHCl₃).





(2*R*,3*R*)-3-(4-methoxybenzyloxy)-2-methylhex-5-en-1-ol (7)



To a dry 100 mL round bottom flask was added **S6** (1.22 g, 4.9 mmol, 1.0 equiv) in 20 mL DCM (0.2 M). The flask was cooled to 0 °C, and to this was added dropwise *i*Bu₂AlH (1M solution in hexanes, 12.3 mmol, 12.3 mL, 2.0 equiv). The reaction was warmed to room temperature and quenched by the addition of a saturated aqueous solution of Rochelle's salt. After stirring 2 h, the layers were partitioned, and the aqueous layer further extracted with DCM (3 x 15 mL). The organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography (20% EtOAc/hexanes) provided the product as a clear oil (1.02 g, 4.07 mmol, 83%).

¹H NMR (400 MHz, CDCl₃): δ 7.27 (m, 2H), 6.89 (m, 2H), 5.87-5.76 (m, 1H), 5.15-5.04 (m, 2H), 4.57 (d, *J* = 12 Hz, 1H), 4.47 (d, *J* = 12 Hz, 1H), 3.80 (s, 3H), 3.67-3.53 (m, 3H), 2.49-2.41 (m, 1H), 2.04-1.96 (m, 1H), 0.92 (d, *J* = 8 Hz, 3H).

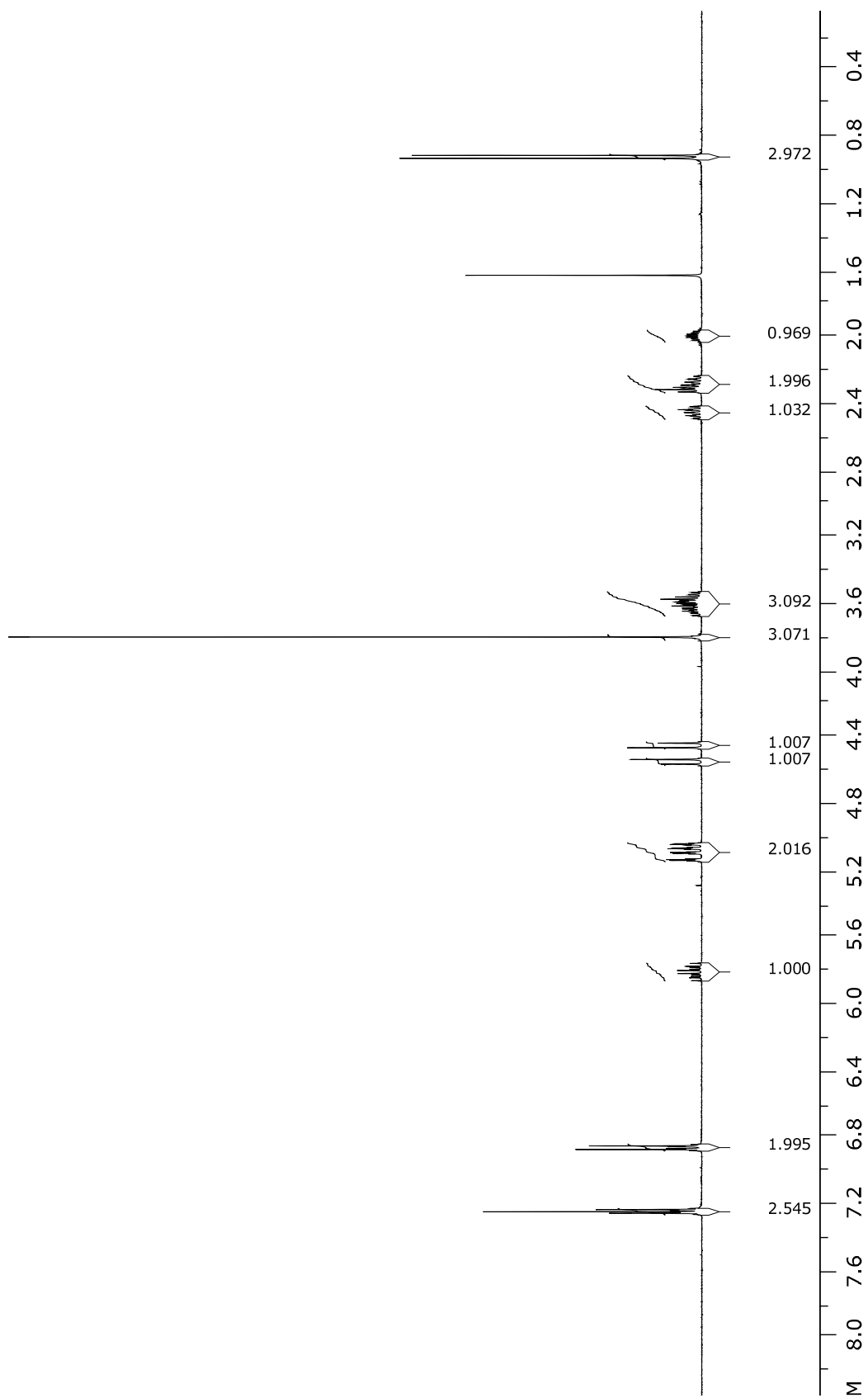
¹³C NMR (100 MHz, CDCl₃): δ 159.3, 135.3, 130.4, 129.5, 117.0, 113.8, 80.9, 71.4, 66.1, 55.2, 37.3, 34.9, 11.2.

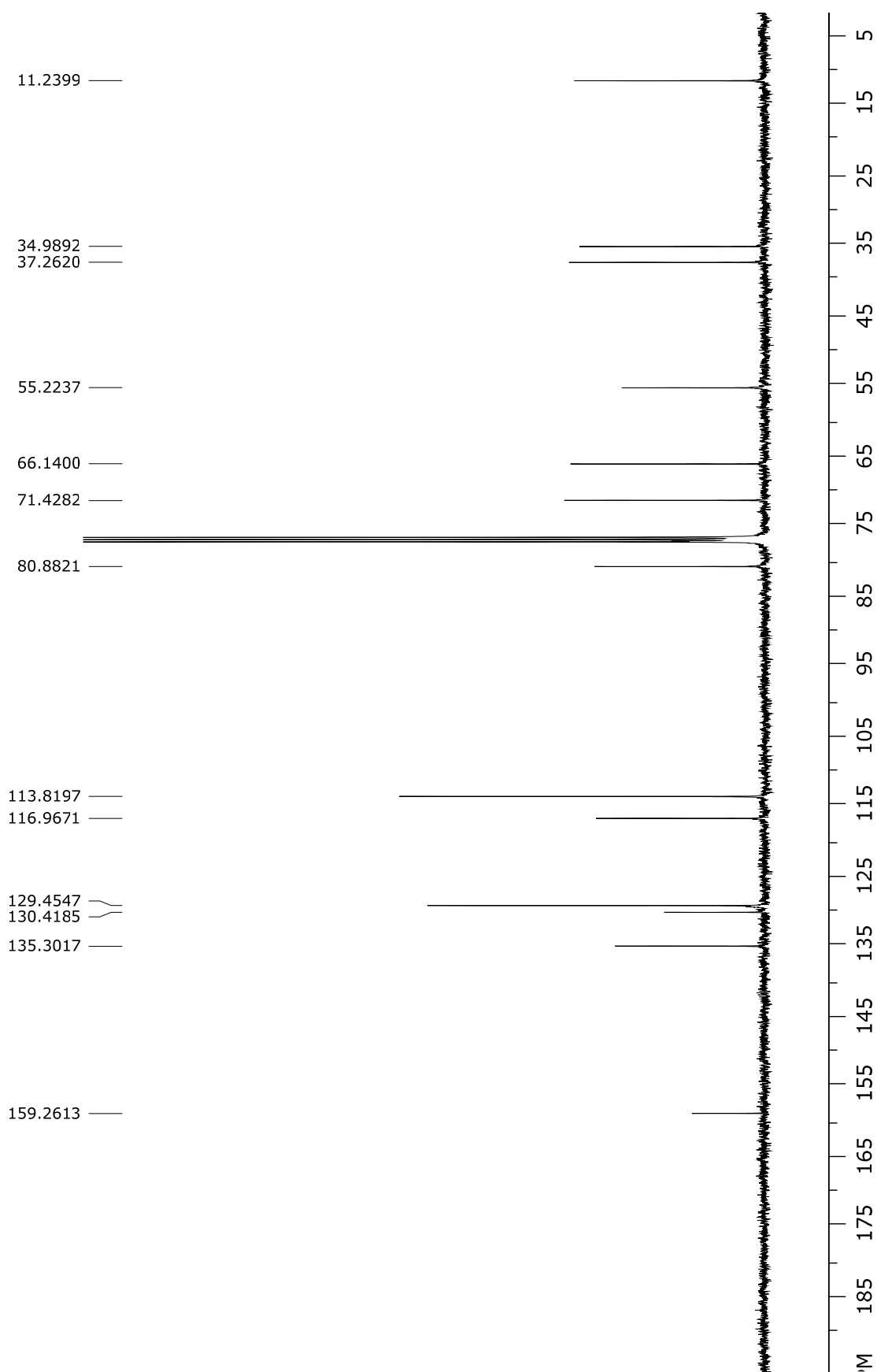
LRMS (ESI) Calcd. For C₁₅H₂₂O₃(M+Na): 273.1, Found: 273.1.

FTIR (neat): 3404, 2934, 1737, 1639, 1612, 1586, 1513, 1463, 1441, 1350, 1301, 1172 cm⁻¹.

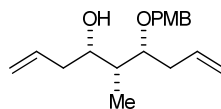
R_f = 0.26 (4:1 Hexane/EtOAc).

[*α*]_D²⁵ = -31.3 (c = 0.75, CHCl₃).





(4*S*,5*R*,6*R*)-6-(4-methoxybenzyloxy)-5-methylnona-1,8-dien-4-ol (8a)



To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*S*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.20 mmol, 100 mol%) and alcohol **7** (50 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 0.4 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 5% EtOAc/hexanes to 10% EtOAc/hexanes) to furnish the title compound (48 mg, 0.165 mmol, d.r. = 12:1) as a colorless oil in 83% yield.

¹H NMR(400 MHz, CDCl₃): δ 7.26 (d, *J* = 12 Hz, 2H), 6.88 (d, *J* = 8 Hz, 2H), 5.85-5.70 (m, 2H), 5.16 (m, 4H), 4.65 (d, *J* = 12 Hz, 1H), 4.40 (d, *J* = 10.8 Hz, 1H), 3.84-3.79 (m, 4H), 3.67-3.63 (m, 1H), 3.23 (s, 1H), 2.60-2.54 (m, 1H), 2.33-2.25 (m, 2H), 2.18-2.11 (m, 1H), 1.72-1.65 (m, 1H), 0.97 (d, *J* = 12 Hz, 3H).

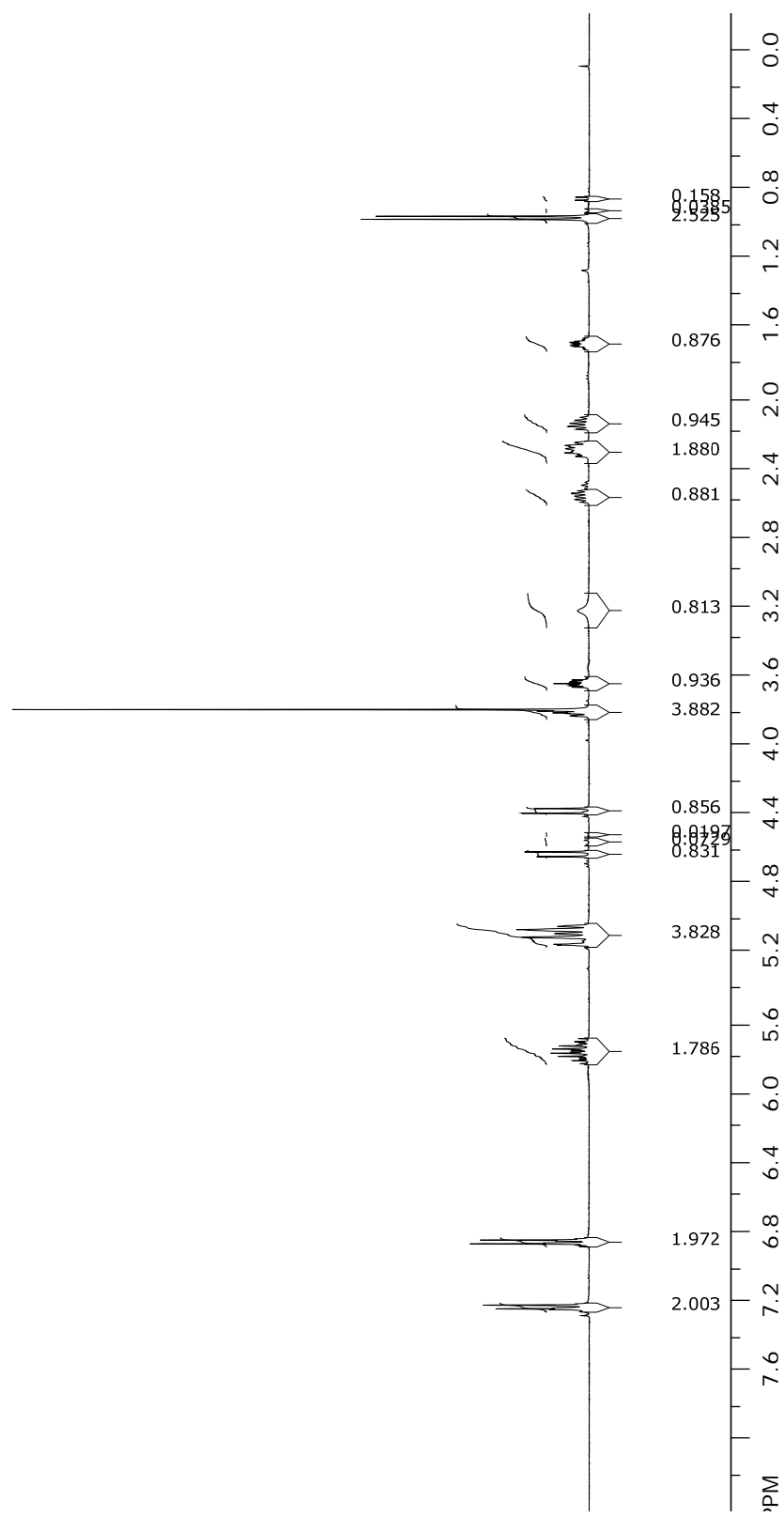
¹³C NMR (100 MHz, CDCl₃): δ 159.3, 135.5, 134.5, 130.0, 129.4, 117.4, 117.0, 113.9, 88.3, 74.8, 70.9, 55.3, 39.6, 38.6, 35.4, 5.65.

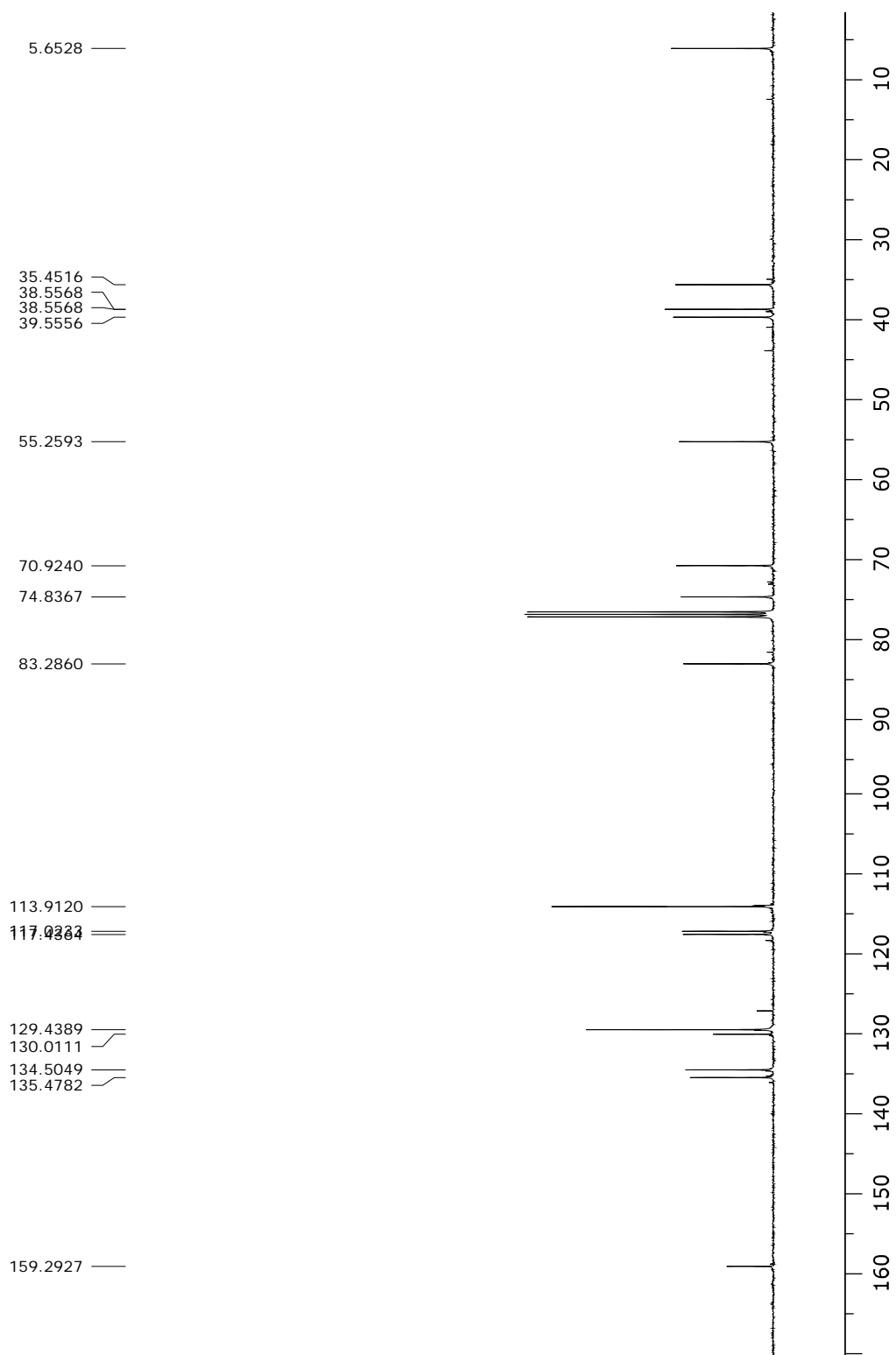
LRMS (ESI) Calcd. for C₁₈H₂₆O₃(M+Na): 313.2, Found: 313.2.

FTIR (neat): 3467, 2974, 2939, 2878, 1710, 1669, 1629, 1458, 1412, 1374, 1109 cm⁻¹.

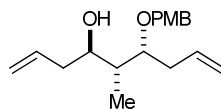
R_f = 0.46 (4:1 Hexane/EtOAc).

[α]_D²⁵ = -64 (c = 1.35, CH₂Cl₂).





(4*R*,5*R*,6*R*)-6-(4-methoxybenzyloxy)-5-methylnona-1,8-dien-4-ol (8b)



To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*R*)-Ir-b-NO₂ (10.9 mg, 0.01 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (4.2 mg, 0.02 mmol, 10 mol%), cesium carbonate (65 mg, 0.20 mmol, 100 mol%) and alcohol **7** (50 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.50 mL, 0.4 M concentration with respect to alcohol), water (36 μ L, 2.0 mmol, 10 equiv) and allyl acetate (43 μ L, 0.4 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 5% EtOAc/hexanes to 10% EtOAc/hexanes) to furnish the title compound (42 mg, 0.14 mmol, d.r. = 6:1) as a colorless oil in 72% yield.

¹H NMR (400 MHz, CDCl₃): δ 7.26 (d, *J* = 8 Hz, 2H), 6.88 (d, *J* = 8 Hz, 2H), 5.93 (m, 2H), 5.14 (m, 4H), 4.55 (dd, *J* = 12 Hz, 16 Hz, 2H), 3.80 (s, 3H), 3.75-3.71 (m, 1H), 3.68-3.62 (m, 1H), 3.34 (d, *J* = 4 Hz, 1H), 2.53-2.45 (m, 1H), 2.37-2.11 (m, 3H), 1.84 (m, 1H), 1.66 (brs, 1H), 0.92 (d, *J* = 8 Hz, 3H).

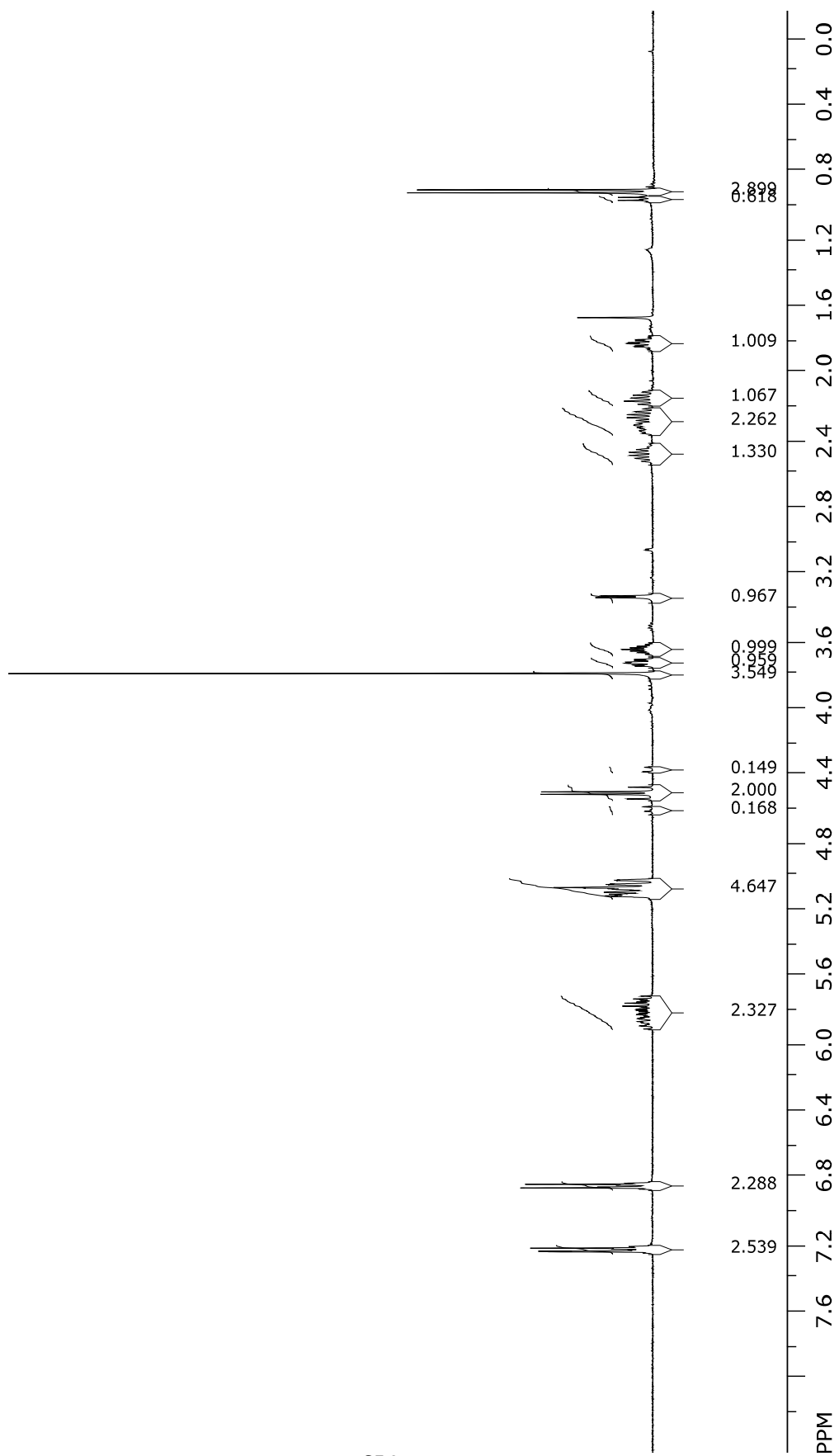
¹³C NMR (100 MHz, CDCl₃): δ 159.3, 135.3, 135.2, 130.2, 129.5, 117.2, 116.9, 113.8, 80.4, 73.2, 71.2, 55.3, 39.8, 38.9, 34.9, 11.7.

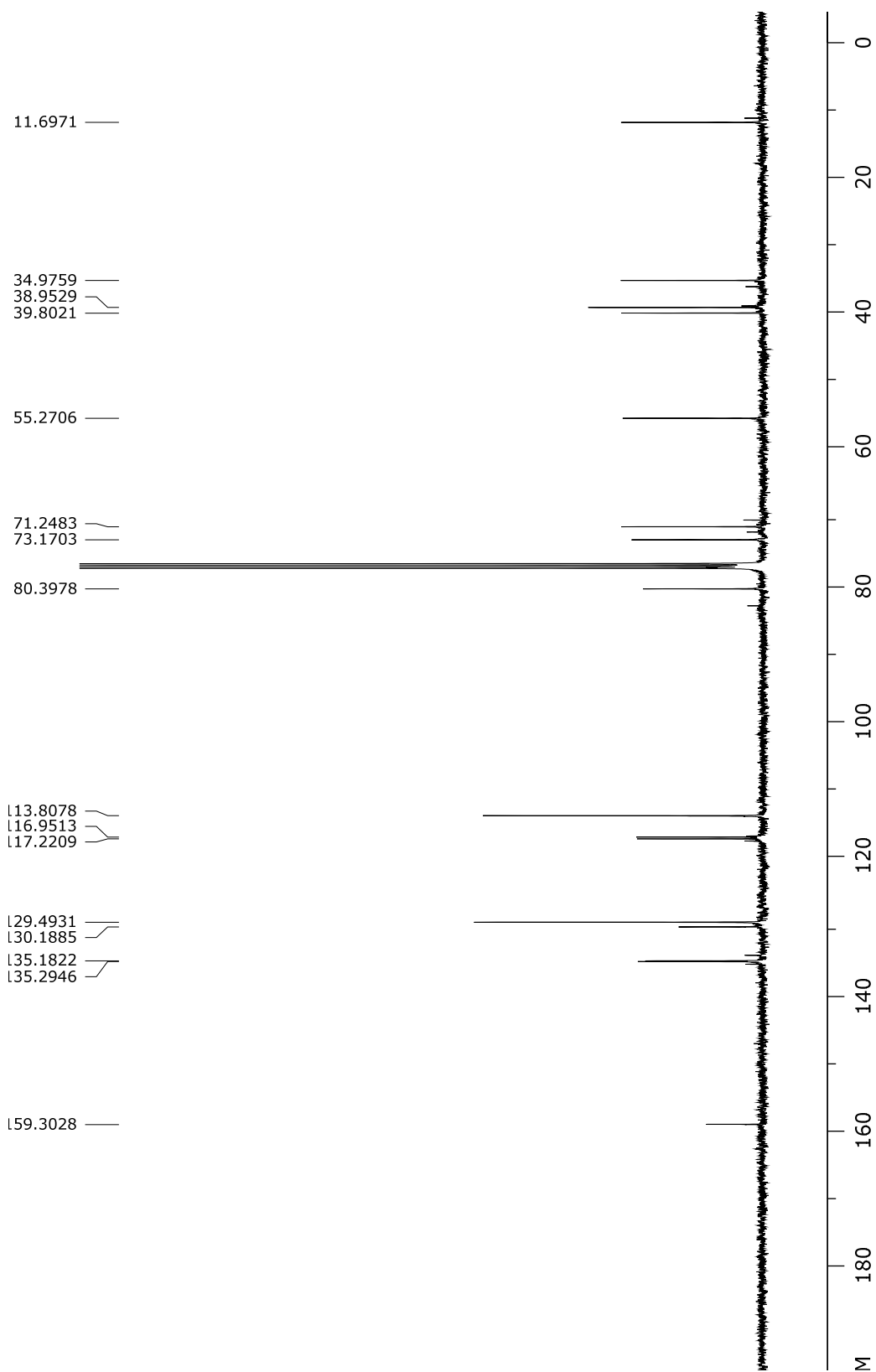
LRMS (ESI) Calcd. For C₁₈H₂₆O₃(M+Na): 313.2, Found: 313.2.

FTIR (neat): 3467, 2974, 2939, 2878, 1710, 1669, 1629, 1458, 1415, 1347, 1374, 1199, 1109 1029 cm⁻¹.

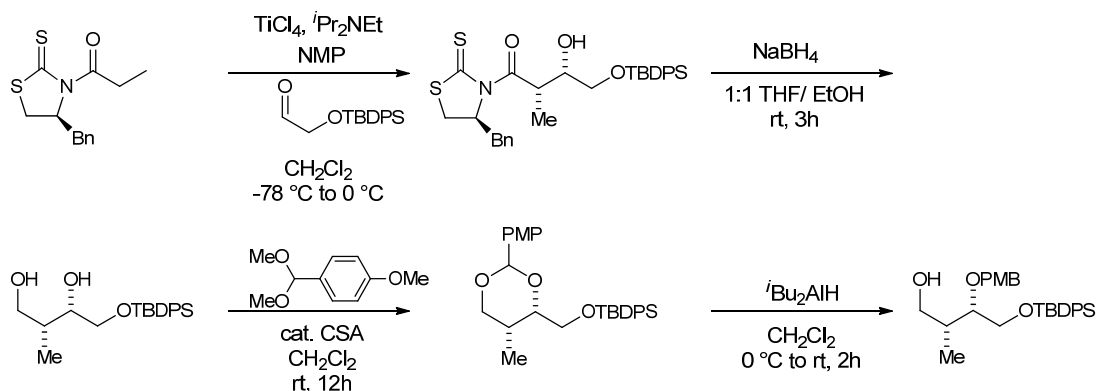
R_f = 0.46 (4:1 Hexane/EtOAc).

[α]_D²⁵ = -144 (c = 0.3, CHCl₃).

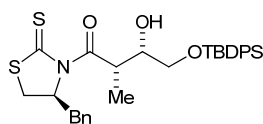




Experimental Procedures and Spectroscopic Data for the Preparation of Alcohol 9



(2S,3S)-1-((S)-4-benzyl-2-thioxothiazolidin-3-yl)-4-(tert-butyldiphenylsilyloxy)-3-hydroxy-2-methylbutan-1-one (S7)



To a flamed dried 500 mL round bottom flask was added (*S*)-1-(4-benzyl-2-thioxothiazolidin-3-yl)propan-1-one⁵ (3.22 g, 12.1 mmol, 1.0 equiv) and DCM (115 mL, 0.1 M with respect to thione). The reaction vessel was cooled to 0 °C and TiCl₄ (1.39 mL, 12.7 mmol, 1.05 equiv) was added dropwise to form an orange slurry. After stirring 5 min, *i*Pr₂NEt (1.81 mL, 13.3 mmol, 1.1 equiv) was added dropwise. The resultant dark red solution was allowed to stir for 40 min at 0 °C and then NMP (2.3 mL, 24.2 mmol, 2 equiv) was added followed by 15 min of additional stirring. The reaction was cooled to -78 °C and 2-((tert-butyldiphenylsilyl)oxy)acetaldehyde (3.60 g, 12.1 mmol, 1.0 equiv) was added in 10 mL DCM. The reaction was stirred for 2 hours at -78 °C and one hour at 0 °C and was then poured into a separatory funnel containing saturated aqueous ammonium chloride (200 mL). The organic phase was separated and the remaining aqueous phase was washed with two additional portions of dichloromethane (100 mL each). The combined organic portions were dried over sodium sulfate, filtered and concentrated under reduced pressure. Flash chromatography (10% to 20% EtOAc/hexanes) delivered aldol adduct **S7** as a yellow oil (3.8 g, 56%, >20:1 d.r.).

¹H NMR (400 MHz, CDCl₃): δ 7.58-7.55 (m, 4H), 7.35-7.19 (m, 11H), 5.17 (m, 1H), 4.65-4.58 (m, 1H), 4.02-3.96 (m, 1H), 3.59 (d, *J* = 4 Hz, 1H), 3.17-3.09 (m, 2H), 2.98 (dd, *J* = 12 Hz, 1H), 2.77 (d, *J* = 12 Hz, 1H), 2.68 (d, *J* = 4 Hz, 1H), 1.19 (d, *J* = 8 Hz, 3H), 0.98 (s, 9H).

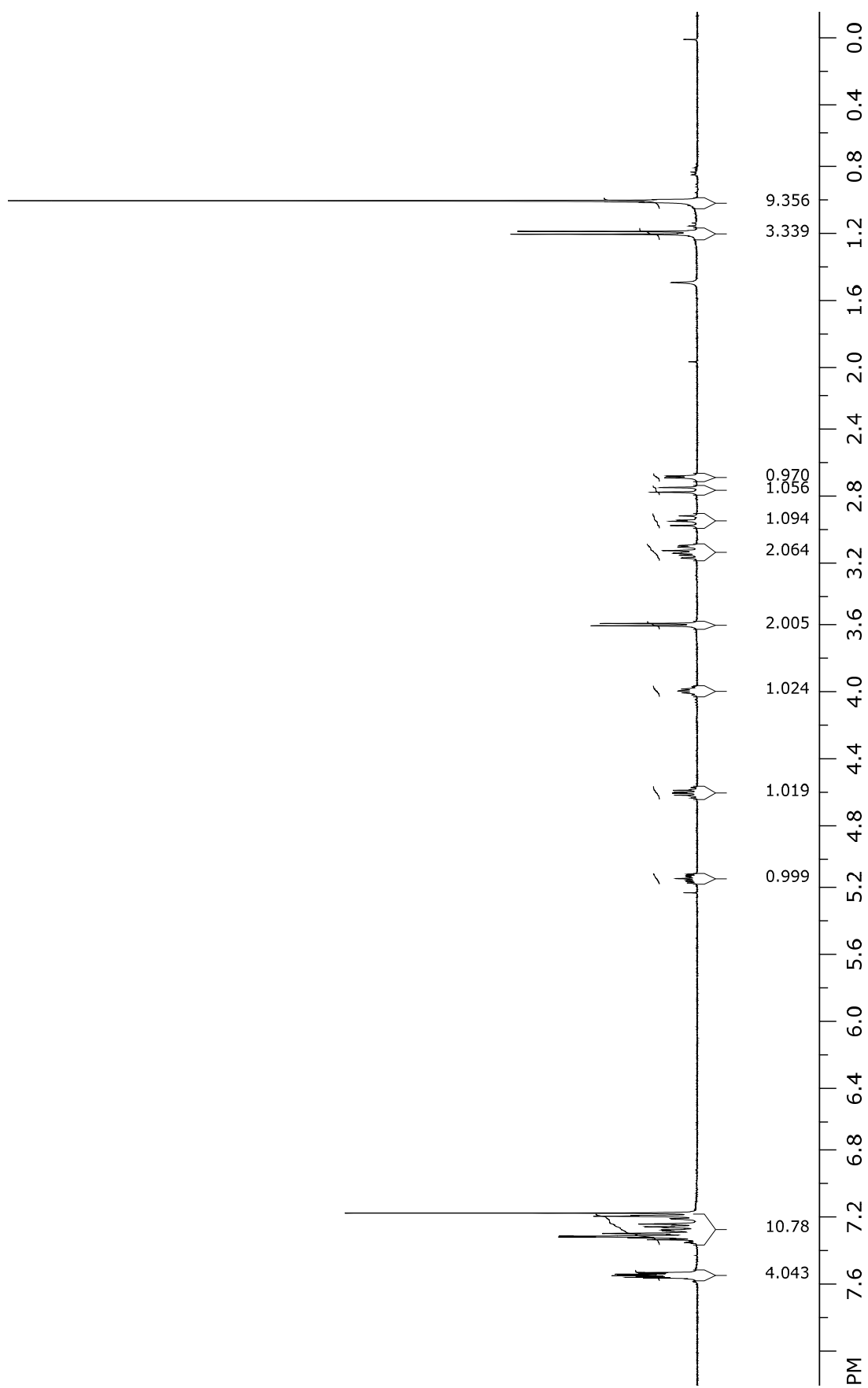
¹³C NMR (100 MHz, CDCl₃): δ 200.9, 177.3, 136.5, 135.5, 133.0, 132.9, 129.9, 129.8, 129.4, 128.9, 127.8, 127.2, 72.8, 68.8, 65.0, 40.9, 36.7, 31.9, 26.9, 19.2, 11.6.

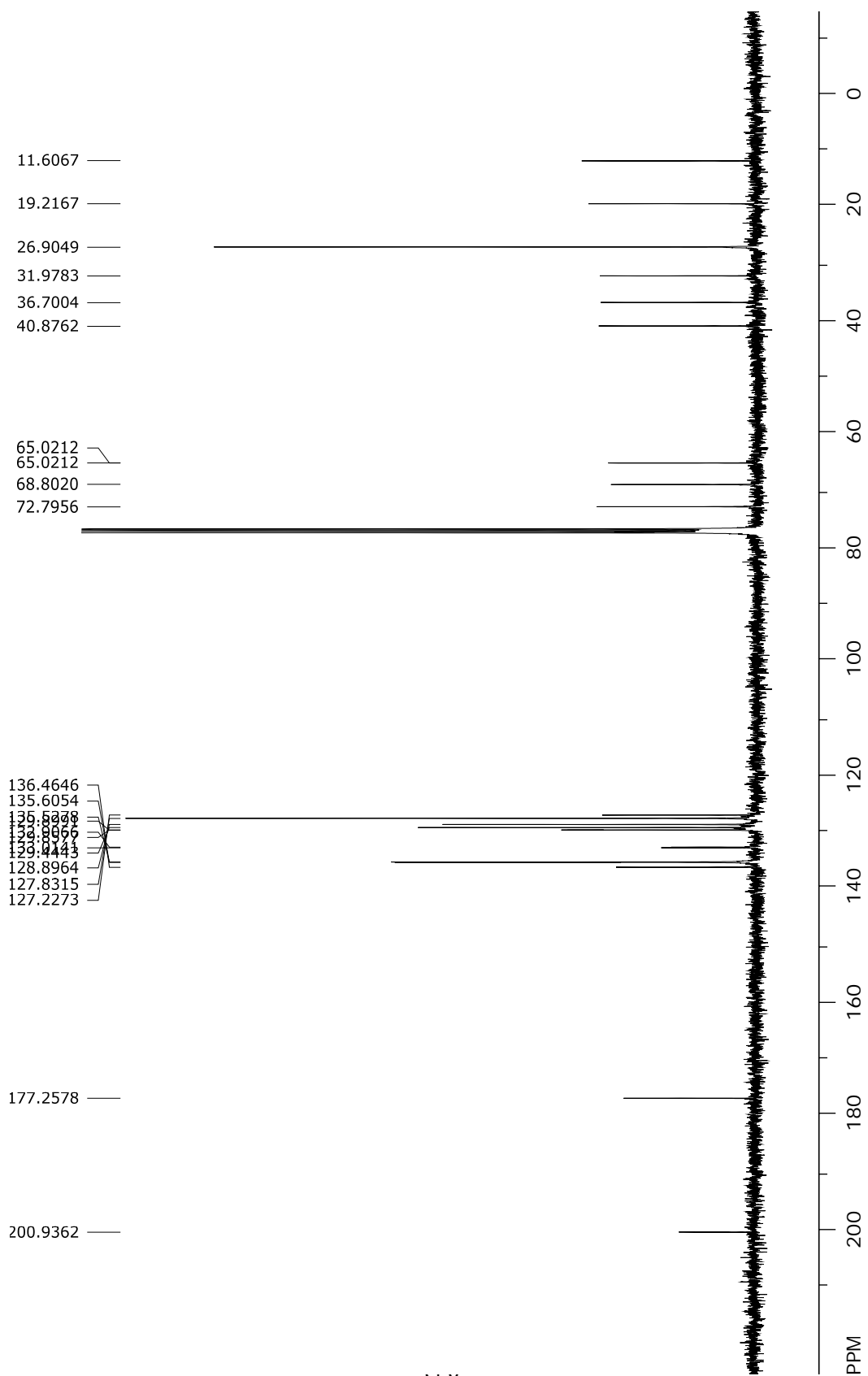
LRMS (ESI) Calcd. For C₃₁H₃₇NO₃S₂Si (M+H): 564.2, Found: 564.2.

FTIR (neat): 3435, 1687, 1454, 1427, 1361, 1340, 1291, 1191, 1163, 1029 cm⁻¹.

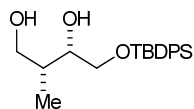
R_f = 0.65 (4:1 Hexane/EtOAc).

[α]_D²⁷ = +90 (c = 1.85, CHCl₃).





(2R,3S)-4-(tert-butyldiphenylsilyloxy)-2-methylbutane-1,3-diol (S8)



To a 250 mL round bottom flask was added **S7** (3.8 g, 6.7 mmol, 1.0 equiv) in 1:1 THF/EtOH (100 mL total). To this was added NaBH₄ (255 mg, 6.7 mmol, 1.0 equiv). The reaction is stirred at room temperature for 3h, and quenched by the addition of saturated aqueous ammonium chloride (50 mL). Ethyl acetate was added and the layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 25 mL), dried (MgSO₄) and concentrated under reduced pressure. Flash chromatography (25% EtOAc/Hexanes) gave diol **S8** as a clear oil (1.9 g, 5.3 mmol, 79%).

¹H NMR (400 MHz, CDCl₃): δ 7.677.64 (m, 4H), 7.47-7.37 (m, 6H), 3.93 (m, 1H), 3.68-3.62 (m, 4H), 1.06 (s, 9H), 0.89 (d, *J* = 8 Hz, 3H).

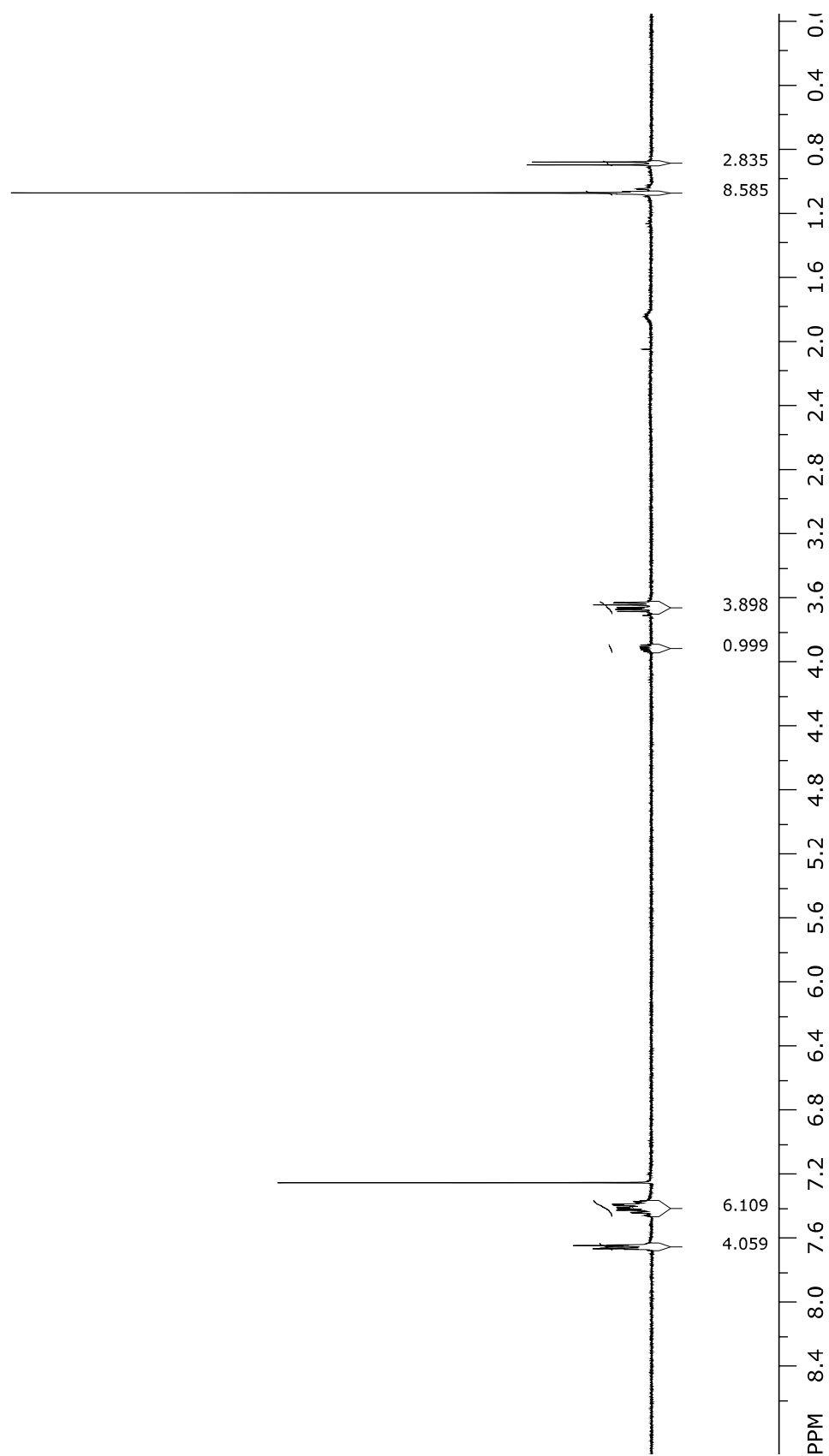
¹³C NMR (100 MHz, CDCl₃): δ 135.6, 132.9, 131.5, 129.9, 127.8, 74.3, 66.6, 65.8, 36.9, 26.7, 19.2, 10.9.

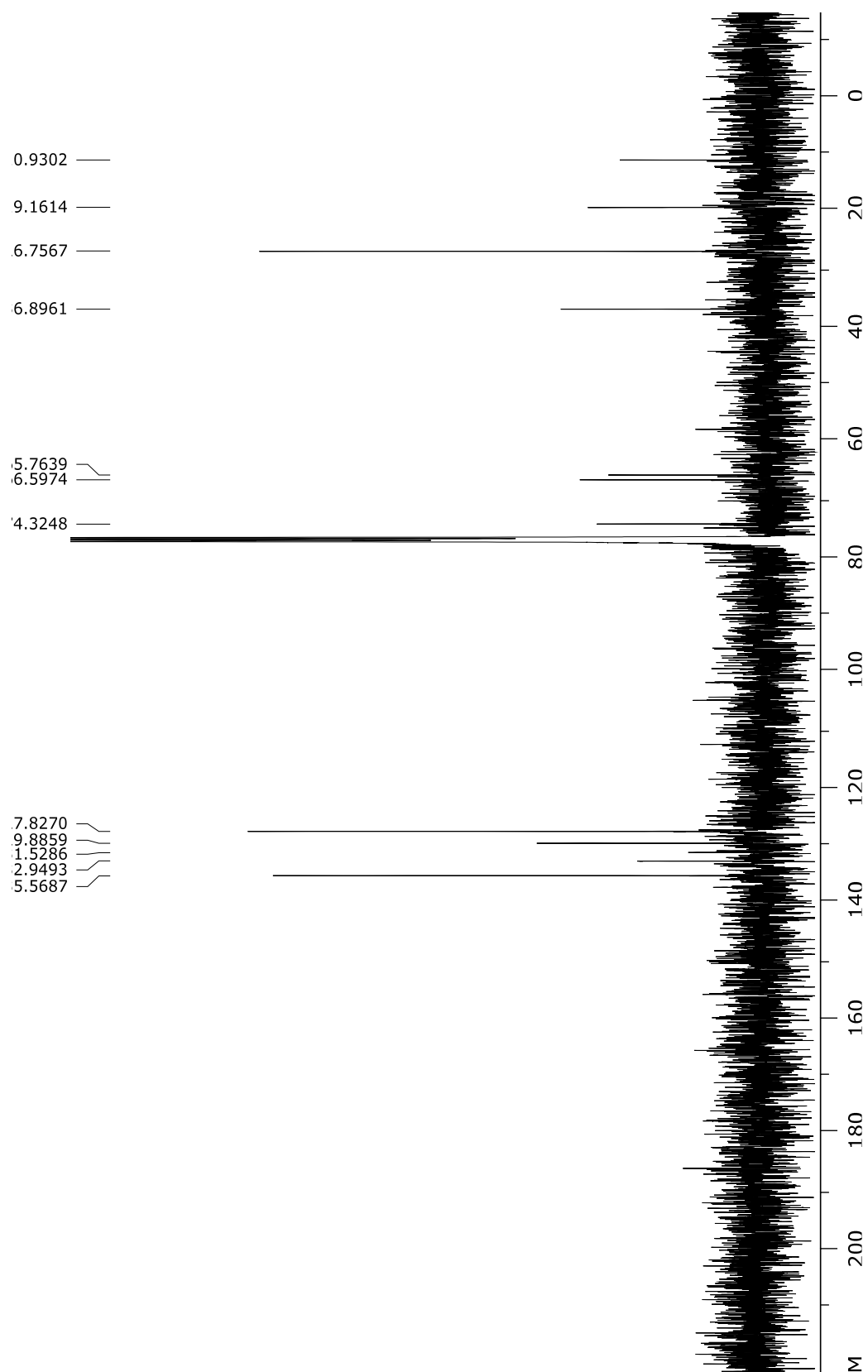
LRMS (ESI) Calcd.For C₂₁H₃₀O₃Si(M+Na): 381.2, Found: 381.2.

FTIR (neat): 3376, 2929, 2857, 1427, 1110, 1029 cm⁻¹.

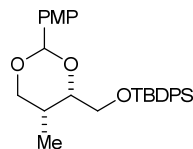
R_f = 0.31 (7:3 Hexane/EtOAc)

[α]_D²⁸ = -6.5 (c = 1.44, CHCl₃).





tert-butyl(((4S,5R)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl)methoxy)diphenylsilane (S9)



To a dry 150 mL round bottom flask was added **S8** (1.90 g, 5.3 mmol, 1.0 equiv) in 5.3 mL DCM (1M). To this was added CSA (123 mg, 0.53 mmol, 10 mol%), and *p*-anisaldehyde dimethyl acetal (0.99 mL, 5.8 mmol, 1.1 equiv). The reaction was stirred at room temperature for 12 h, and quenched by the addition of saturated sodium bicarbonate solution. The layers were separated, and the aqueous phase was further extracted with DCM (3 x 15 mL), dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography (5% EtOAc/Hexanes) provided the product as a clear oil (1.23 g, 1.64 mmol, 49%).

¹H NMR (400 MHz, CDCl₃): δ 7.69-7.66 (m, 4H), 7.43-7.34 (m, 8H), 6.88 (d, *J* = 8 Hz, 2H), 5.47 (s, 1H), 4.14-4.09 (m, 2H), 4.04 (dd, *J* = 4, 12 Hz, 1H), 3.82 (m, 4H), 3.68 (dd, *J* = 9.2, 12 Hz, 1H), 1.82 (m, 1H), 1.16 (d, *J* = 8 Hz, 3H), 1.06 (s, 9H).

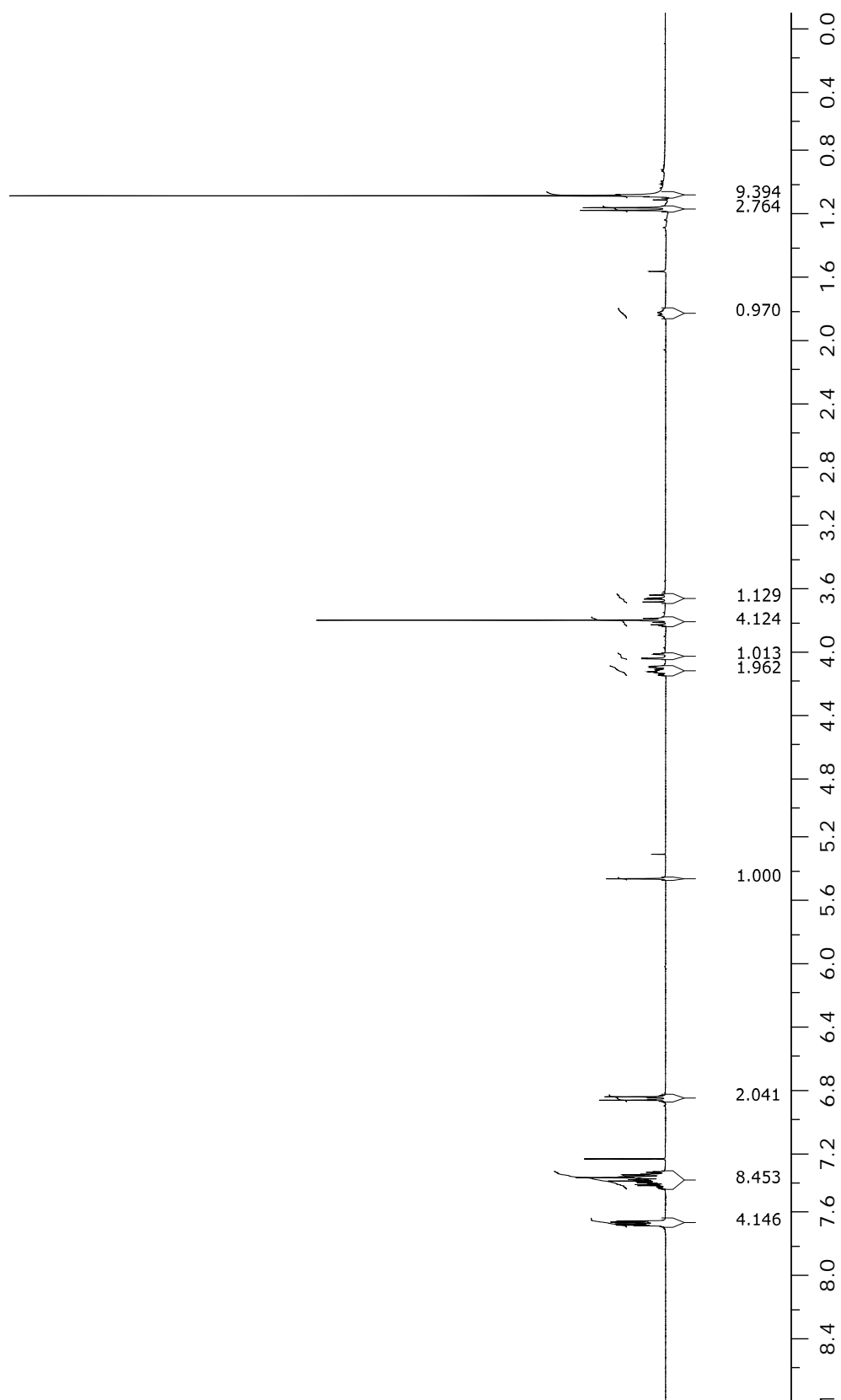
¹³C NMR (100 MHz, CDCl₃): δ 159.9, 135.6, 133.6, 133.5, 131.3, 129.7, 129.6, 127.7, 127.1, 127.0, 113.6, 101.6, 79.5, 73.8, 63.9, 55.3, 29.5, 26.8, 19.3, 11.0.

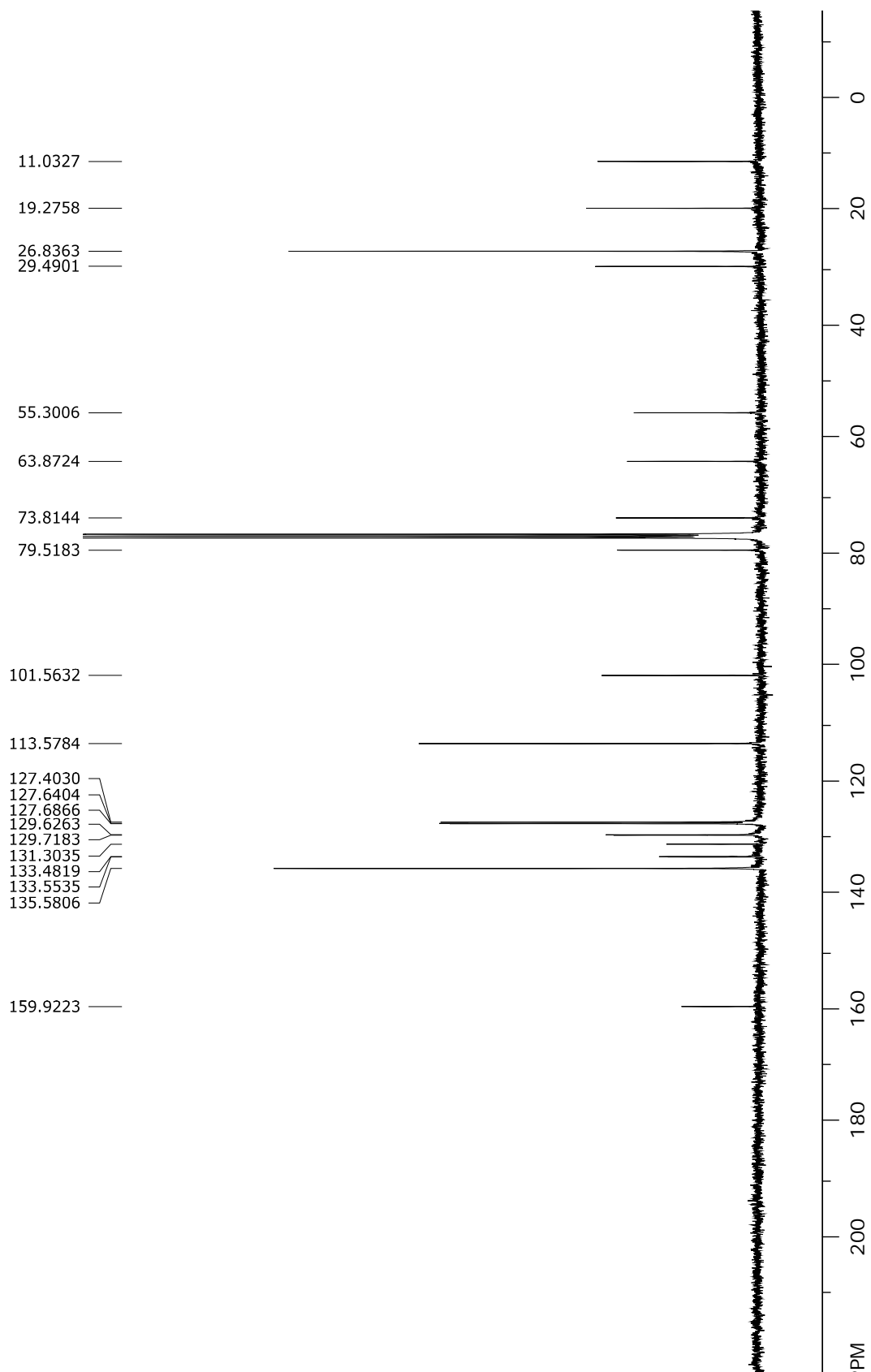
LRMS (ESI) Calcd. For C₂₉H₃₆O₄Si (M+H): 477.2, Found: 477.2.

FTIR (neat): 2930, 2856, 1615, 1588, 1517, 1462, 1382, 1359, 1338, 1302 cm⁻¹.

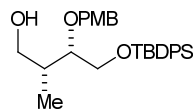
R_f = 0.15 (95:5 Hexane/EtOAc).

[α]_D²⁸ = -19.4 (c = 1.9, CHCl₃).





(2R,3S)-4-(tert-butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy)-2-methylbutan-1-ol (9)



To a dry 100 mL round bottom flask was added **S9** (630 mg, 1.32 mmol, 1.0 equiv) in 13 mL DCM (0.1M). The flask was cooled to 0 °C, and to this was added dropwise *i*Bu₂AlH (1M solution in hexanes, 2.64 mmol, 2.64 mL, 2.0 equiv). The reaction was warmed to room temperature and quenched by the addition of a saturated aqueous solution of Rochelle's salt. After stirring 2 h, the layers were partitioned, and the aqueous layer further extracted with DCM (3 x 15 mL). The organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography (20% EtOAc/hexanes) provided the product as clear oil (496 mg, 1.03 mmol, 79%).

¹H NMR (400 MHz, CDCl₃): δ 7.7-7.69 (m, 4H), 7.46-7.37 (m, 6H), 7.20 (d, *J* = 8 Hz, 2H), 6.86 (d, *J* = 12 Hz, 2H), 4.57 (d, *J* = 12 Hz, 1H), 4.40 (d, *J* = 12 Hz, 1H), 3.87 (m, 4H), 3.75 (dd, *J* = 4, 8 Hz, 1H), 3.61 (m, 3H), 2.34 (brs, 1H), 2.01 (m, 1H), 1.07 (s, 9H), 0.88 (d, *J* = 12 Hz, 3H).

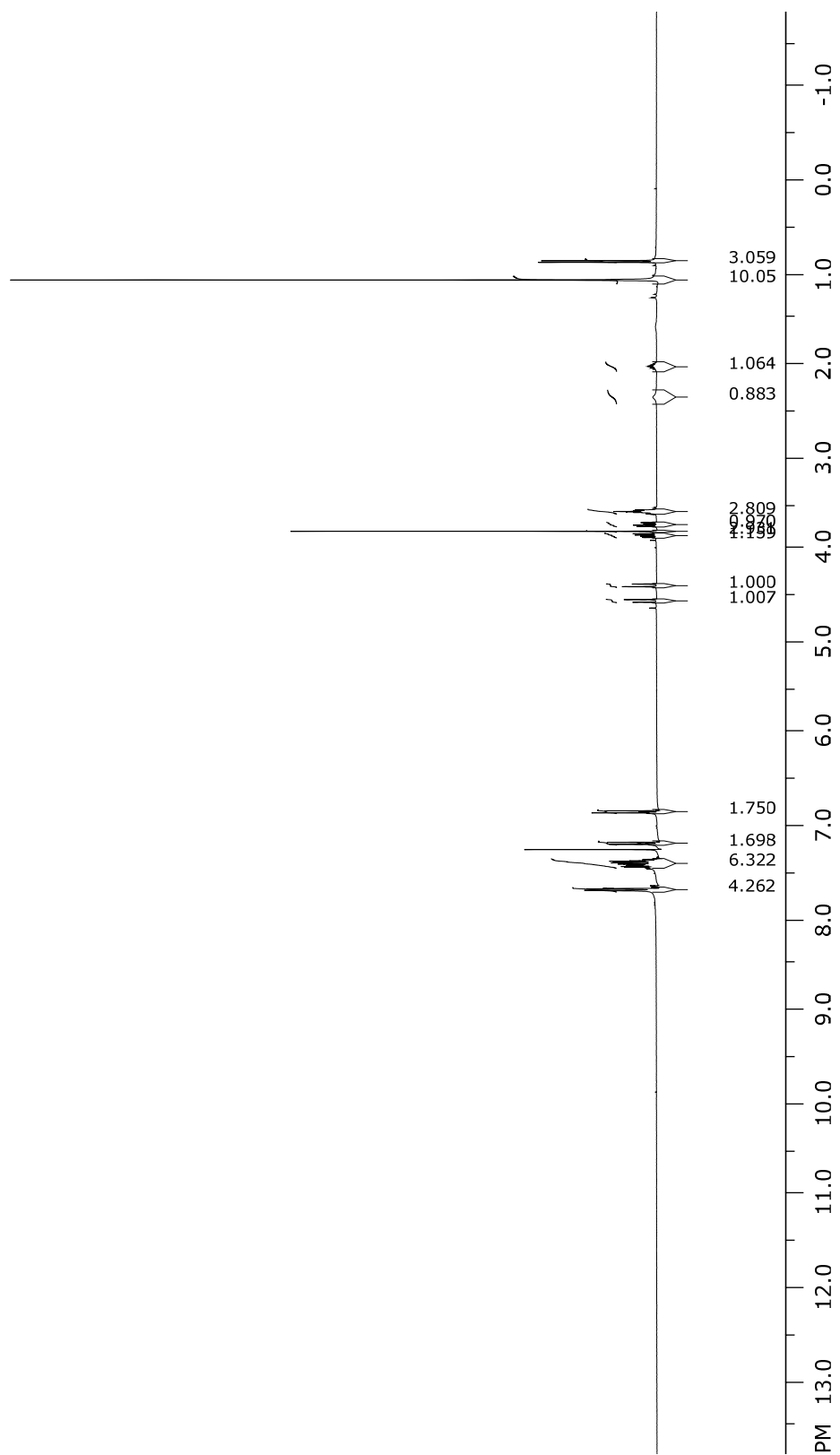
¹³C NMR (100 MHz, CDCl₃): δ 159.2, 135.7, 135.68, 135.62, 133.3, 133.1, 130.6, 129.8, 129.4, 127.8, 113.8, 81.2, 72.1, 66.0, 64.1, 55.2, 37.3, 26.8, 19.2, 11.7.

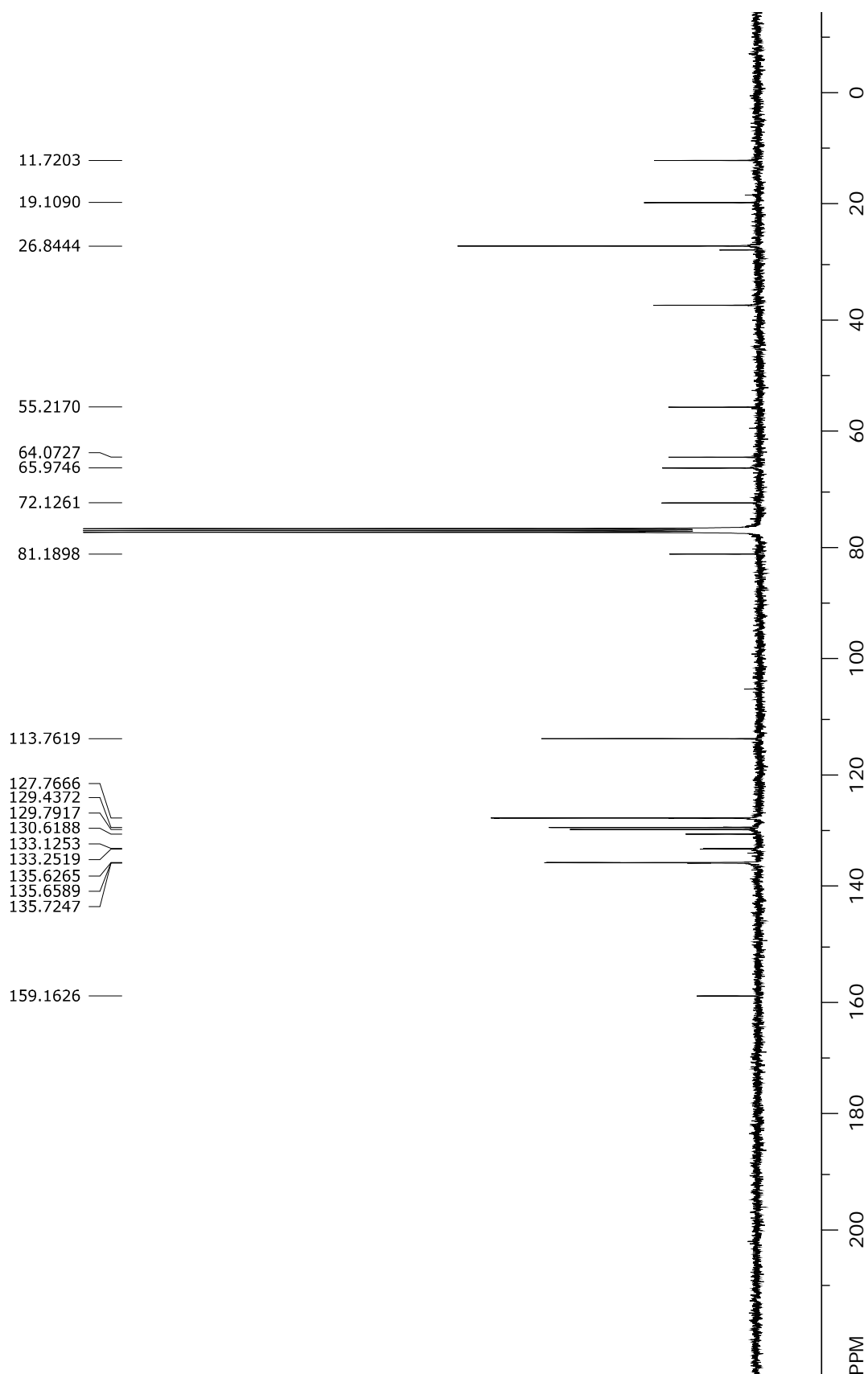
LRMS (ESI) Calcd. for C₂₉H₃₈O₄Si(M+Na): 501.5, Found: 501.5.

FTIR (neat): 3438, 2929, 2856, 1612, 1587, 1513, 1462, 1427, 1389, 1359, 1301, 1172 cm⁻¹.

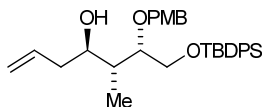
R_f = 0.20 (4:1 Hexane/EtOAc).

[α]_D²⁸ = -61.5 (c = 0.76, CHCl₃).





**(4R,5R,6S)-7-(tert-butyldiphenylsilyloxy)-6-(4-methoxybenzyloxy)-5-methylhept-1-en-4-ol
(10b)**



To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*R*)-Ir-b-NO₂ (8.0 mg, 0.007 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (3.2 mg, 0.015 mmol, 10 mol%), cesium carbonate (49 mg, 0.15 mmol, 100 mol%) and alcohol **9** (70 mg, 0.15 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.38 mL, 0.4 M concentration with respect to alcohol), water (27 μL, 1.5 mmol, 10 equiv) and allyl acetate (32 μL, 0.3 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 7% EtOAc/hexanes) to furnish the title compound (55 mg, 0.11 mmol, d.r. = 5:1) as a colorless oil in 73% yield.

¹H NMR (400 MHz, CDCl₃): δ 7.60 (m, 4H), 7.33 (m, 6H), 7.15(d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8 Hz, 2H), 5.77 (m, 1H), 5.03 (m, 2H), 4.58 (d, *J* = 12 Hz, 1H), 4.44 (d, *J* = 12 Hz, 1H), 3.84 (m, 2H), 3.72 (s, 3H), 3.63 (m, 1H), 3.51 (m, 1H), 2.98 (d, *J* = 4), 2.19 (m, 1H), 2.08 (m, 1H), 1.80 (m, 1H), 0.90 (s, 9H), 0.77 (d, *J* = 10 Hz, 3H).

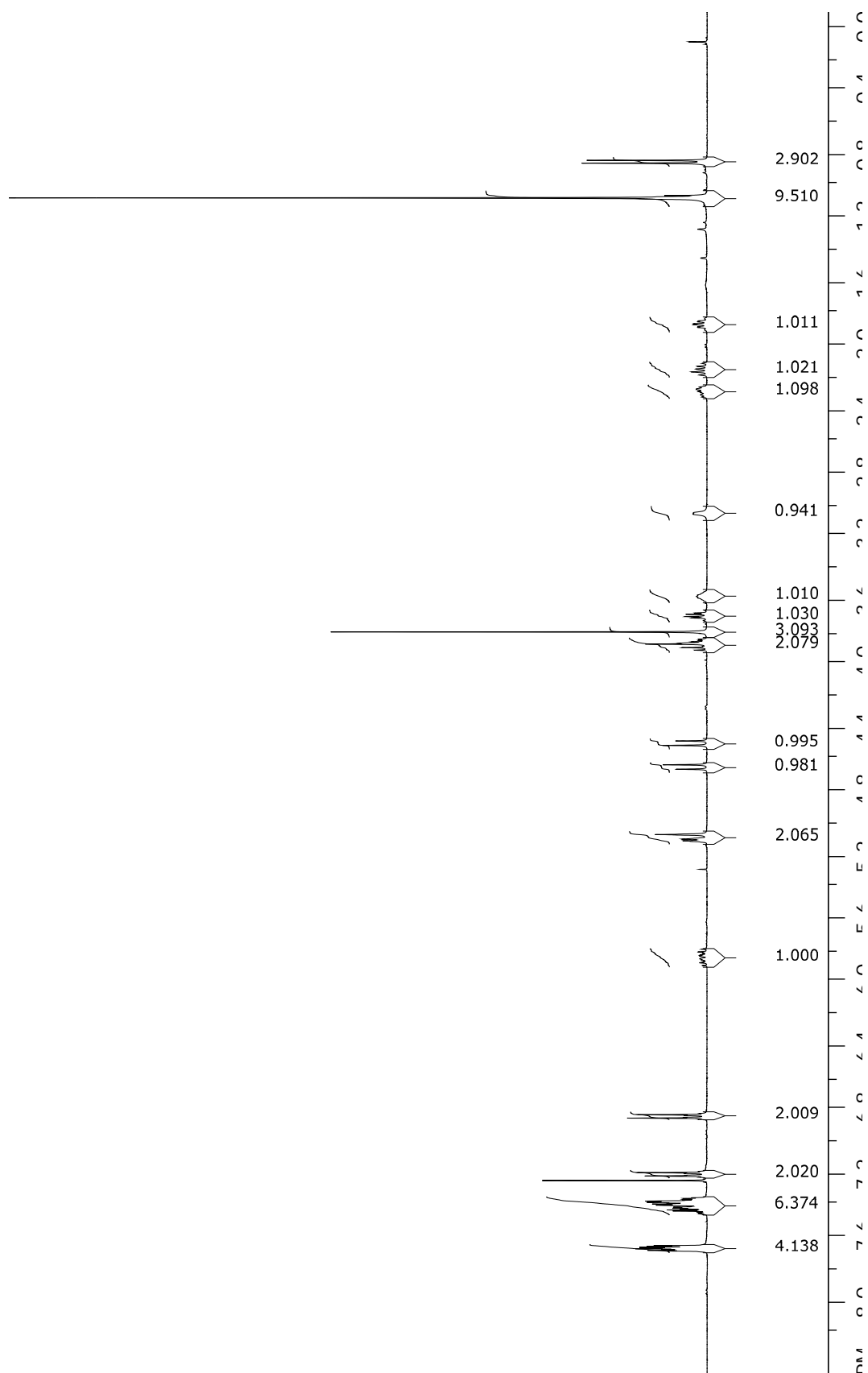
¹³C NMR (100 MHz, CDCl₃): δ 159.5, 135.9, 135.4, 133.5, 130.1, 129.6, 128.2, 117.5, 114.1, 80.8, 73.7, 72.4, 64.4, 55.5, 40.0, 38.7, 27.0, 19.4, 11.9.

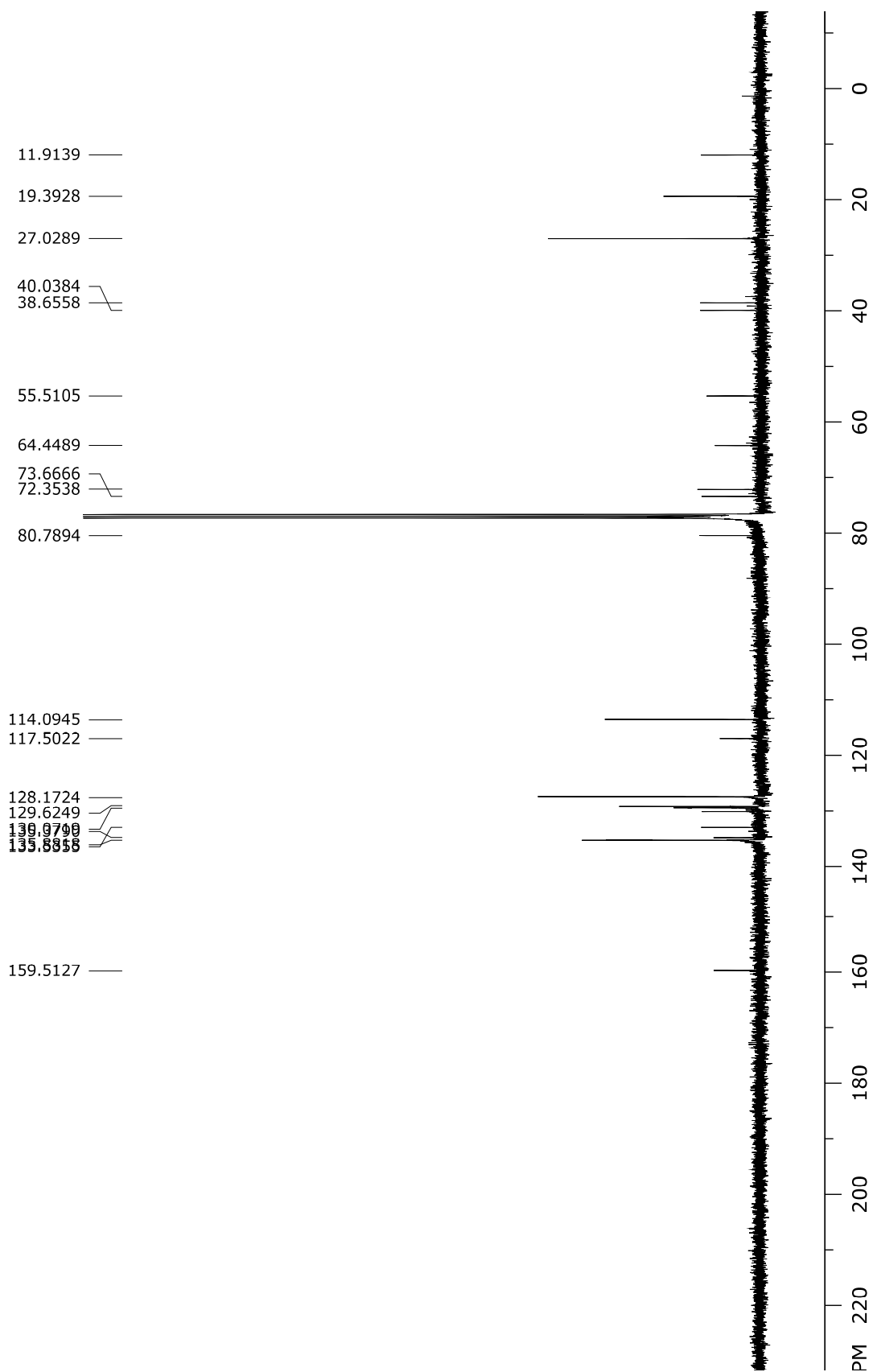
LRMS (ESI) Calcd.For C₃₂H₄₂O₄Si(M+Na): 541.50, Found: 541.50.

FTIR (neat): 3432, 2931, 2857, 1612, 1587, 1513, 1462, 1427, 1390, 1361, 1302, 1248, 1173, 1035 cm⁻¹.

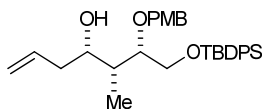
R_f = 0.37 (4:1 Hexane/EtOAc)

[α]_D²⁶ = -100 (c = 0.5, CH₂Cl₂).





(4S,5R,6S)-7-(tert-butyldiphenylsilyloxy)-6-(4-methoxybenzyloxy)-5-methylhept-1-en-4-ol (10a)



To a resealable pressure tube (13 x 100 mm) equipped with a magnetic stirbar was added (*S*)-Ir-b-NO₂ (8.0 mg, 0.007 mmol, 5 mol%), 4-NO₂-3NO₂BzOH (3.2 mg, 0.015 mmol, 10 mol%), cesium carbonate (49 mg, 0.15 mmol, 100 mol%) and alcohol **9** (70 mg, 0.15 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with argon. THF (0.38 mL, 0.4 M concentration with respect to alcohol), water (27 μ L, 1.5 mmol, 10 equiv) and allyl acetate (32 μ L, 0.3 mmol, 2 equiv) were added and the rubber septum was quickly replaced with a screw cap. The mixture was heated at 100 °C (oil bath temperature) for 24 h, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (SiO₂; 15% EtOAc/hexanes) to furnish the title compound (60 mg, 0.12 mmol, d.r. = 10:1) as a colorless oil in 77% yield.

¹H NMR (400 MHz, CDCl₃): δ 7.70 (m, 4H), 7.48-7.37 (m, 6H), 7.18 (d, *J* = 8 Hz, 2H), 6.85-6.83 (d, *J* = 8 Hz, 2H), 5.85 (m, 1H), 5.13 (m, 2H), 4.61 (d, *J* = 12 Hz, 1H), 4.39 (d, *J* = 12 Hz, 1H), 3.89 (m, 2H), 3.80 (m, 4H), 3.67 (m, 2H), 2.33 (m, 1H), 2.19 (m, 1H), 1.91 (m, 1H), 1.07 (s, 9H), 0.89 (d, *J* = 4 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 159.3, 135.7, 135.6, 135.5, 133.3, 133.1, 130.3, 129.8, 129.5, 127.8, 117.0, 113.9, 83.7, 73.9, 72.0, 63.8, 55.3, 29.3, 37.7, 26.9, 19.1, 6.4.

LRMS (ESI) Calcd. For C₃₂H₄₂O₄Si(M+Na): 541.50, Found: 541.50.

FTIR (neat): 3471, 2930, 2857, 1612, 1587, 1463, 1427, 1390, 1360, 1301, 1172 cm⁻¹.

R_f = 0.54 (4:1 Hexane/EtOAc)

[α]_D²⁸ = -22.7 (c = 2.60, CHCl₃).

