

Supporting Information

Total Synthesis of Muamvatin

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Experimental Procedures

General Methods. Anhydrous solvents were distilled under argon atmosphere as follows: Tetrahydrofuran (THF) from benzophenone sodium ketyl; CH_2Cl_2 from CaH_2 ; MeOH from $\text{Mg}(\text{OMe})_2$; DMSO from CaH_2 at reduced pressure (stored over 4Å molecular sieves). All experiments involving air- and/or moisture-sensitive compounds were conducted in an oven dried round-bottom flask capped with a rubber septum, and attached via a needle and connecting tubing to an argon manifold equipped with mercury bubbler (ca. 5 mm positive pressure of argon). Low temperature baths were: ice/water (0 °C), $\text{CO}_{2(\text{s})}/\text{CH}_3\text{CN}$ (−50 °C), and $\text{CO}_{2(\text{s})}/\text{acetone}$ (−78 °C). Unless otherwise noted, reaction temperatures refer to that of the bath. Concentration refers to removal of volatiles at water aspirator pressure on a rotary evaporator. Preparative TLC (PTLC) was carried out on glass plates (20×20 cm) pre-coated (0.25 mm) with silica gel 60 F₂₅₄. Materials were detected by visualization under an ultraviolet lamp (254 nm) and/or by treating a 1 cm vertical strip removed from the plate with a solution of phosphomolybdic acid (5%) containing a trace of ceric sulfate in aqueous sulfuric acid (5% v/v) followed by charring on a hot plate. Flash column chromatography (FCC) was performed according to Still et al.¹ with silica gel 60 (40–63 µm). All mixed solvent eluents are reported as v/v solutions. Unless otherwise noted, all reported compounds were homogeneous by thin layer chromatography (TLC) and by ¹H NMR.

Spectral Data. High resolution mass spectra (HRMS) and low resolution mass spectra (LRMS) were obtained on a double focusing high resolution spectrometer; only partial data are reported. EI ionization was accomplished at 70 eV and CI ionization at 50 eV with ammonia as the reagent gas; only partial data are reported. Alternatively, HRMS were obtained on an LC-MS/MS time-of-flight high resolution spectrometer with electrospray ionization (ESI) from acetonitrile solution. IR spectra were recorded on a Fourier transform interferometer using a diffuse reflectance cell (DRIFT); only diagnostic and/or intense peaks are reported. Unless otherwise noted, NMR spectra were measured in CDCl_3 solution at 500 MHz for ¹H and 125 MHz for ¹³C. Signals due to the solvent (¹³C NMR) or residual protonated solvent (¹H NMR) served as the internal standard: CDCl_3 (7.26 δ_{H} , 77.23 δ_{C}); C_6D_6 (7.16 δ_{H} , 128.39 δ_{C}). The ¹H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), ap (apparent); the list of couplings constants (*J*) corresponds to the order of the multiplicity assignment. Coupling constants (*J*) are reported to the nearest 0.5 Hz (i.e., ±0.25 Hz as consistent with the digital resolution ca. 0.2 Hz/pt). The ¹H NMR assignments were made based on chemical shift and multiplicity and were confirmed by homonuclear decoupling and/or two-dimensional correlation experiments (gCOSY, gHSQC, gHMBC).² The ¹³C NMR assignments were made on the basis of chemical shift and multiplicity³ (as determined by ¹³C-DEPT or gHSQC) and were confirmed by two-dimensional ¹H/¹³C correlation experiments (gHSQC and/or gHMBC).² Specific rotations ($[\alpha]_{\text{D}}$) are the average of 5 determinations at ambient temperature using a 1 mL, 10 dm cell; the units are 10^{−1} deg cm² g^{−1}, the concentrations (*c*) are reported in g/100 mL, and the values are rounded to reflect the accuracy of the measured concentrations (the major source of error).

Materials. The following compounds and reagents were prepared as described previously: (−)-**S1** (>98% ee);⁴ **7**;⁵ **19**;⁶ W-2 Raney nickel.⁷ 2,6-Lutidine was distilled from CaH_2 and stored over 4Å molecular sieves. All other reagents were commercially available and unless otherwise noted, were used as received.

¹ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

² Reynolds, W. F.; Enríquez, R. G. *J. Nat. Prod.* **2002**, *65*, 221–244.

³ The multiplicity of ¹³C NMR signals refers to the number of attached H's (i.e., s = C, d = CH, t = CH₂, q = CH₃)

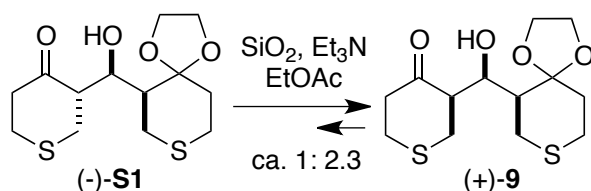
⁴ Ward, D. E.; Jheengut, V.; Beye, G. E.; Gillis, H. M.; Karagiannis, A.; Becerril-Jimenez, F. *Synlett* **2011**, 508–512.

⁵ Dahmann, G.; Hoffmann, R. W. *Liebigs Ann. Chem.* **1994**, 837–845.

⁶ Tanaka, S.; Saburi, H.; Kitamura, M. *Adv. Synth. Catal.* **2006**, *348*, 375–378.

⁷ Mozingo, R. *Org. Synth.* **1941**, *21*, 15–17 (*Coll. Vol. III* **1955**, 181–183).

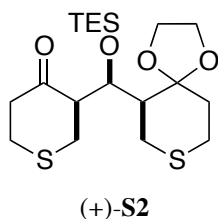
(3R)-3-[(R)-(6S)-1,4-Dioxo-8-thiaspiro[4.5]dec-6-yl(hydroxy)methyl]tetrahydro-4H-thiopyran-4-one (9). The



isomerization of (-)-S1 to (+)-9 (1 g scale) in the presence of silica gel and Et₃N was reported previously.⁸ Using the same procedure, a slurry of silica gel 60 (230-400 mesh, 12.1 g) and Et₃N (7.2 mL, 5.2 g, 51 mmol) were added to a solution of (-)-S1 (>98% ee; 4.03 g, 13.2 mmol) in ethyl acetate (52 mL) at room temperature. The resulting

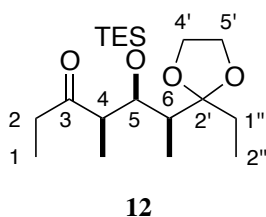
slurry was stirred for 8 h to obtain a (2.3:1 equilibrium mixture of (+)-9 and (-)-S1, respectively. The mixture was filtered and silica gel was washed with ethyl acetate. The combined filtrate and ethyl acetate washings were concentrated and fractionated by FCC (15 % diethyl ether in dichloromethane) to give (+)-9 as a colorless oil (2.56 g, 63%) and a mixture of (-)-S1 and (+)-9 (1.42 g) which subjected to the same reaction conditions (4.3 g silica gel, 2.6 mL Et₃N, 18 mL ethyl acetate) to give (-)-S1 (435 mg, 11%) and additional (+)-9 (960 mg 23%; 86% over 2 cycles): [α]_D +65 (c 1.0 CHCl₃) (lit.⁸ [α]_D +64; c 1.0, CHCl₃). Spectroscopic data for (+)-9 closely matched that previously reported for (±)-9.⁹

(3R)-3-[(R)-(6S)-1,4-Dioxo-8-thiaspiro[4.5]dec-6-yl(triethylsilyloxy)methyl]tetrahydro-4H-thiopyran-4-one



(S1). Using the same procedure previously described for the preparation of (±)-S2,¹⁰ 2,6-lutidine (4.0 mL, 3.7 g, 34 mmol), TES-OTf (6.0 mL, 6.9 g, 26 mmol) were added sequentially in to a solution of (+)-9 (5.34 g, 17.5 mmol) in CH₂Cl₂ (78 mL) at 0 °C. After 1 h, MeOH (1 mL) was added, and the reaction mixture were diluted with CH₂Cl₂ (100 mL) and washed sequentially with NaHCO₃ and brine. The organic layer was dried over Na₂SO₄, concentrated, and fractionated by FCC (15% ethyl acetate in hexane) to give the title compound (6.68 g, 91%) ([α]_D +12; c 1.3 CHCl₃). Spectroscopic data for (+)-S2 was consistent with that previously reported for (±)-S2.¹⁰

(4R,5R,6S)-6-(2-Ethyl-1,3-dioxolan-2-yl)-4-methyl-5-((triethylsilyl)oxy)heptan-3-one (12). A suspension of



Raney nickel (W2; 70 mL settled volume) in EtOH (150 mL) was added to (+)-S2 (4.90 g, 11.7 mmol) and the mixture was heated under reflux with vigorous stirring. After 2 h (reaction was complete by TLC analysis), the mixture was decanted and the solid was suspended in EtOH (200 mL) and heated under reflux with vigorous stirring for several min. This washing procedure was repeated twice with acetone, and twice with methanol. The combined organic layers were filtered

through Celite®, concentrated, and fractionated by FCC (10% ethyl acetate in hexane) to give the title compound (3.28 g, 78%): colorless oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); [α]_D -60 (c 1.0, CHCl₃); IR (DRIFT) ν_{max} 1710 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.15 (1H, br dd, *J* = 3, 4 Hz, HC-5), 3.95-3.87 (4H, m, H₂C-4', H₂C-5'), 2.75 (1H, dq, *J* = 4, 6.5 Hz, HC-4), 2.64 (1H, dq, *J* = 18, 7 Hz, HC-2), 2.41 (1H, dq, *J* = 18, 7 Hz, HC-2), 1.85 (1H, dq, *J* = 3, 7 Hz, HC-6), 1.68 (1H, dq, *J* = 14.5, 7.5 Hz, HC-1''), 1.59 (1H, dq, *J* = 14.5, 7.5 Hz, HC-1''), 1.03 (3H, d, *J* = 6.5 Hz, H₃CC-4), 1.02 (3H, t, *J* = 7.5 Hz, H₃C-1), 0.96 (9H, t, *J* = 8 Hz, H₃CCCSi × 3), 0.84 (3H, t, *J* = 7 Hz, H₃C-2''), 0.83 (3H, d, *J* = 7 Hz, H₃CC-6), 0.62 (6H, ap q, *J* = 8 Hz, H₂CSi × 3); ¹³C NMR (125 MHz, CDCl₃) δ 214.1 (s, C-3), 113.8 (s, C-2'), 72.9 (d, C-5), 65.2 (t, C-4'), 65.1 (t, C-5'), 52.7 (d, C-4), 41.9 (d, C-6), 36.4 (t, C-2), 26.9 (t, C-1''), 12.5 (q, CH₃C-4), 10.6 (q, CH₃C-6), 7.8 (q, C-2''), 7.4 (q, C-1), 7.3 (q × 3, CH₃CSi), 5.6 (t × 3, CH₂Si); LRMS

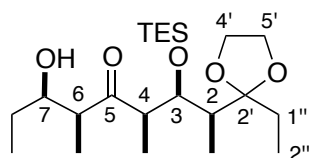
⁸ Ward, D. E.; Jheengut, V.; Beye, G. E. *J. Org. Chem.* **2006**, *71*, 8989-8992.

⁹ Ward, D. E.; Sales, M.; Man, C. C.; Shen, J.; Sasmal, P. K.; Guo, C. *J. Org. Chem.* **2002**, *67*, 1618-1629.

¹⁰ Ward, D. E.; Becerril-Jimenez, F.; Zahedi, M. M. *J. Org. Chem.* **2009**, *74*, 4447-4454.

(Cl, NH₃), m/z (relative intensity): 359 ([M+1]⁺, 0.5), 329 (2), 273 (2), 227 (8), 101 (100), 57 (2); **HRMS** m/z calcd for C₁₉H₃₈O₄Si+H: 359.2618; found: 359.2611 (Cl, NH₃).

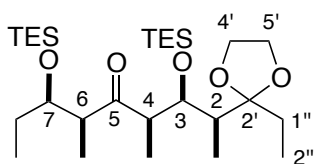
(2S,3R,4R,6S,7R)-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-4,6-dimethyl-3-(triethylsilyloxy)nonan-5-one (13). A



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solution of (-)-**12** (3.61 g, 10.1 mmol) in Et₂O (15 mL) was added dropwise via syringe to a stirred solution of Et₃N (3.1 mL, 2.2 g, 22 mmol) and 9-BBN-OTf (0.5 M in hexane; 40 mL, 20 mmol) in Et₂O (220 mL) at -78 °C under argon. After 2 h, a solution of propanal (3.6 mL, 2.9 g, 50 mmol) in Et₂O (30 mL) was slowly added via syringe. After 4 h, the reaction was quenched by sequential addition of MeOH (90 mL), phosphate buffer (pH 7; 300 mL), and 30% aqueous H₂O₂ (90 mL). The reaction vessel was transferred to an ice bath and after vigorous stirring for 20 min, the mixture was extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, concentrated to give the crude product whose ¹H NMR spectrum indicated the presence of 2.4:1 mixture of a single adduct (>20:1 dr) and (-)-**12**, respectively. Fractionation of the crude by FCC (20% ethyl acetate in hexane) gave recovered (-)-**12** (0.80 g, 22%) and the title compound (2.6 g, 62%): colorless oil, TLC R_f = 0.3 (16% ethyl acetate in hexane); [α]_D +92 (c 1.7, CHCl₃); **IR** (DRIFT) ν_{max} 3510, 1696, 2878 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.09 (1H, dd, *J* = 3, 4.5 Hz, HC-3), 3.94-3.85 (5H, m, H₂C-4', H₂C-5', HC-7), 3.29 (1H, br d, *J* = 1.5 Hz, HOC-3), 2.99 (1H, dq, *J* = 4.5, 7 Hz, HC-4), 2.82 (1H, dq, *J* = 2, 7.5 Hz, HC-6), 1.91 (1H, dq, *J* = 3, 7 Hz, HC-2), 1.66 (1H, dq, *J* = 14.5, 7.5 Hz, HC-1''), 1.61-1.51 (2H, m, HC-1'', HC-8), 1.10 (3H, d, *J* = 7.5 Hz, H₃CC-6), 1.01 (3H, d, *J* = 7 Hz, H₃CC-4), 0.96 (9H, t, *J* = 8 Hz, H₃CCSi ×3), 0.93 (3H, d, *J* = 7.5 Hz, H₃C-9), 0.84 (3H, t, *J* = 7.5 Hz, H₃C-2''), 0.82 (3H, d, *J* = 7 Hz, H₃C-1), 0.62 (6H, ap q, *J* = 8 Hz, H₂CSi ×3); **¹³C NMR** (125 MHz, CDCl₃) δ 220.3 (s, C-5), 113.7 (s, C-2'), 73.0 (d, C-3), 72.2 (d, C-7), 65.1 (t, C-4'), 65.0 (t, C5'), 51.3 (d, C-4), 49.3 (d, C-6), 41.2 (d, C-2), 26.9 (t, C-1''), 26.7 (t, C-8), 13.0 (q, CH₃C-4), 10.6 (q, C-1 or C-9), 10.5 (q, C-1 or C-9), 9.3 (q, CH₃C-6), 7.5 (q, C-2''), 7.2 (q ×3, CH₃CSi), 5.5 (t ×3, CH₂Si); **LRMS** (Cl, NH₃), m/z (relative intensity): 417 ([M+1]⁺, 6), 387 (20), 355 (30), 329 (30), 297 (23), 229 (13), 199 (10), 165 (6), 101 (100); **HRMS** (Cl, NH₃), m/z calcd for C₂₂H₄₄O₅Si+H: 417.3036; found: 417.3040.

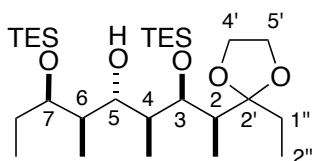
2S,3R,4R,6S,7R)-2-(2-Ethyl-1,3-dioxolan-2-yl)-4,6-dimethyl-3,7-bis[(triethylsilyl)oxy]nonan-5-one (S3). TES-Cl



S3

(1.40 mL, 1.27 g, 8.43 mmol) and imidazole (0.62 g, 9.0 mmol) were added sequentially to a stirred solution of (+)-**13** (2.50 g, 6.01 mmol) in DMF (20 mL) at ambient temperature under argon. After 18 h, the mixture was diluted by ethyl acetate, washed with 1 M aq HCl, dried over Na₂SO₄, concentrated, and fractionated by FCC (10% ethyl acetate in hexane) to give the title compound (2.84 g, 89%): colorless oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); [α]_D +16 (c 0.5, CHCl₃); **IR** (DRIFT) ν_{max} 1704 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.26 (1H, dd, *J* = 4.5, 4.5 Hz, HC-3), 3.95-3.86 (4H, m, H₂C-4', H₂C-5'), 3.82 (1H, ddd, *J* = 5, 5.5, 6 Hz, HC-7), 2.95 (1H, dq, *J* = 4.5, 7 Hz, HC-4), 2.85 (1H, dq, *J* = 6, 7 Hz, HC-6), 1.83 (1H, dq, *J* = 4.5, 7 Hz, HC-2), 1.69 (1H, dq, *J* = 14.5, 7.5 Hz, HC-1''), 1.58 (1H, dq, *J* = 14.5, 7.5 Hz, HC-1''), 1.49 (1H, ddq, *J* = 4.5, 14.5, 7.5 Hz, HC-8), 1.32 (1H, ddq, *J* = 4.5, 14.5, 7.5 Hz, HC-8), 1.12 (3H, d, *J* = 7 Hz, H₃CC-4), 1.07 (3H, d, *J* = 7 Hz, H₃CC-6), 0.96 (9H, t, *J* = 8 Hz, H₃CCSi ×3), 0.95 (9H, t, *J* = 8 Hz, H₃CCSi ×3), 0.90 (3H, d, *J* = 7 Hz, H₃C-1), 0.88 (3H, t, *J* = 7.5 Hz, H₃C-9), 0.84 (3H, t, *J* = 7.5 Hz, H₃C-2''), 0.65-0.59 (12H, m, H₂CSi ×6); **¹³C NMR** (125 MHz, CDCl₃) δ 216.0 (s, C-5), 113.8 (s, C-2'), 74.8 (d, C-7), 71.1 (d, C-3), 65.2 (t ×2, C-4', C-5'), 52.4 (d, C-4), 49.7 (d, C-6), 43.1 (d, C-2), 28.0 (t, C-8), 27.2 (t, C-1''), 13.5 (q, CH₃C-6), 12.4 (q, CH₃C-4), 11.2 (q, C-1), 9.7 (q, C-9), 7.5 (q, C-2''), 7.4 (q ×3, CH₃CSi), 7.2 (q ×3, CH₃CSi), 5.6 (t ×3, CH₂Si), 5.4 (t ×3, CH₂Si); **LRMS** (Cl, NH₃), m/z (relative intensity): 531 ([M+1]⁺, 0.4), 501 (1), 399 (12), 337 (7), 273 (5), 173 (32), 132 (31), 101 (100); **HRMS** (Cl, NH₃), m/z calcd for C₂₈H₅₈O₅Si₂+H: 531.3901; found: 531.3897.

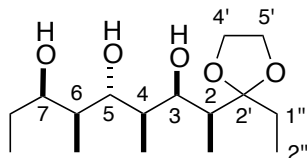
(2*S*,3*R*,4*S*,5*S*,6*R*,7*R*)-2-(2-Ethyl-1,3-dioxolan-2-yl)-4,6-dimethyl-3,7-bis((triethylsilyl)oxy)nonan-5-ol (S4).



S4

LiHBEt₃ (1 M in THF; 1.5 mL, 1.5 mmol) was added dropwise via syringe to a pre-cooled, stirred solution of **S3** (270 mg, 0.51 mmol) in THF (24 mL) at 0 °C under argon. The reaction mixture was removed from the ice bath and allowed to slowly warm to ambient temperature. After 18 h, the reaction mixture was cooled to 0 °C and quenched by sequential addition of MeOH (4 mL), phosphate buffer (pH 7; 5 mL), and 30% aqueous H₂O₂ (3 mL) with vigorous stirring. After 20 min, the mixture was diluted with water and extracted with CH₂Cl₂. The combined organic layers were washed with H₂O, dried over Na₂SO₄, and concentrated to give crude product whose ¹H NMR spectrum indicated the presence of a 7:1 mixture of diastereomers (283 mg). Fractionation of the crude by FCC (10% ethyl acetate in hexane) gave the title compound (219 mg, 81%): colorless oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); [α]_D -11 (c 1.1, CHCl₃); **IR** (DRIFT) ν_{max} 3512 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.30 (1H, dd, *J* = 1, 6.5 Hz, HC-3), 4.04 (1H, ddd, *J* = 1.5, 5.5, 9.5 Hz, HC-7), 3.95-3.86 (4H, m, H₂C-4', H₂C-5'), 3.48 (1H, ap d, *J* = 8.5 Hz, HO), 3.29 (1H, ddd, *J* = 3.5, 8.5, 9.5 Hz, HC-5), 1.93 (1H, dq, *J* = 6.5, 7 Hz, HC-2), 1.88 (1H, ddq, *J* = 1, 9.5, 7 Hz, HC-4), 1.79-1.67 (2H, m, HC-1'', HC-6), 1.66-1.54 (3H, m, HC-1'', H₂C-8), 1.04 (3H, d, *J* = 7 Hz, H₃CC-6), 0.98 (3H, d, *J* = 7 Hz, H₃C-1), 0.96 (9H, t, *J* = 8 Hz, H₃CCSi ×3), 0.95 (9H, t, *J* = 8 Hz, H₃CCSi ×3), 0.84 (3H, t, *J* = 7.5 Hz, H₃C-2''), 0.81 (3H, t, *J* = 7.5 Hz, H₃C-9), 0.71 (3H, d, *J* = 7 Hz, H₃CC-4), 0.65 (6H, ap q, *J* = 8 Hz, H₂CSi ×3), 0.62 (6H, ap q, *J* = 8 Hz, H₂CSi ×3); **¹³C NMR** (125 MHz, CDCl₃) δ 114.2 (s, C-2'), 77.5 (s, C-5), 75.1 (d, C-7), 71.5 (d, C-3), 65.3 (t, C-4'), 65.1 (t, C-5'), 43.8 (d, C-4), 43.5 (d, C-2), 34.2 (d, C-6), 28.0 (t, C-8), 27.1 (t, C-1''), 13.1 (q, C-1), 11.1 (q, CH₃C-6), 10.2 (q, C-9), 9.9 (q, CH₃C-4), 7.6 (q, C-2''), 7.4 (q ×3, CH₃CSi), 7.1 (q ×3, CH₃CSI), 5.8 (t ×3, CH₂Si), 5.7 (t ×3, CH₂Si); **LRMS** (CI, NH₃), *m/z* (relative intensity): 533 ([M+1]⁺, 1), 401 (6), 373 (7), 339 (39), 201 (11), 173 (12), 132 (31), 132 (11), 101 (100). **HRMS** *m/z* calcd for C₂₈H₆₀O₅Si₂+H: 533.4058; found: 533.4032 (CI, NH₃).

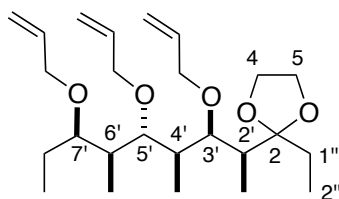
(2*S*,3*R*,4*S*,5*S*,6*S*,7*R*)-2-(2-Ethyl-1,3-dioxolan-2-yl)-4,6-dimethylnonane-3,5,7-triol (14).



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LiHBEt₃ (1 M in THF; 17.0 mL, 17 mmol) was added dropwise via syringe to a stirred solution of **S3** (2.96 g, 5.57 mmol) in THF (200 mL) at 0 °C under argon. The reaction vessel was removed from the ice bath and allowed to slowly warm to ambient temperature. After 18 h, the reaction mixture was cooled to 0 °C and quenched by sequential addition of MeOH (20 mL), phosphate buffer (pH 7; 40 mL), and 30% aqueous H₂O₂ (20 mL) with vigorous stirring. After 20 min, the mixture was diluted with water and extracted with CH₂Cl₂. The combined organic layers were washed with H₂O, dried over Na₂SO₄, and concentrated to give the crude product **S4** (3.15 g) that was taken up in THF (20 mL). TBAF (1.2 g, 4.6 mmol) was added to the stirred solution of **S4** at ambient temperature. After 4 h, the mixture was diluted with CH₂Cl₂, washed with saturated aq NH₄Cl, dried over Na₂SO₄, concentrated, and fractionated by FCC (40% ether in dichloromethane) to give the title compound (1.22 g, 72%): colorless oil, TLC R_f = 0.3 (40% ether in CH₂Cl₂): colorless oil, TLC R_f = 0.3 (40% ether in CH₂Cl₂); [α]_D -13 (c 0.1, CHCl₃); **IR** (DRIFT) ν_{max} 3431 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 4.48 (1H, br s, HOC-5), 4.23 (1H, br s, HC-3), 4.01-3.94 (4H, m, H₂C-4', H₂C-5'), 3.83 (1H, br dd, *J* = 5.5, 7 Hz, HC-7), 3.68 (1H, br dd, *J* = 7, 8 Hz, HC-5), 3.48 (1H, br s, HOC-7), 2.98 (1H, br s, HOC-3), 2.06 (1H, ddq, *J* = 3.5, 7, 7 Hz, HC-4), 2.02 (1H, dq, *J* = 1.5, 7 Hz, HC-2), 1.82 (1H, ddq, *J* = 1.5, 6, 7 Hz, HC-6), 1.73-1.60 (2H, m, H₂C-1''), 1.56 (1H, ddq, *J* = 7, 13.5, 7.5 Hz, HC-8), 1.42 (1H, ddq, *J* = 5.5, 13.5, 7.5 Hz, HC-8), 1.08 (3H, d, *J* = 7 Hz, H₃C-1), 0.97 (3H, d, *J* = 7 Hz, H₃CC-6), 0.96 (3H, t, *J* = 7.5 Hz, H₃C-9), 0.93 (3H, d, *J* = 7 Hz, H₃CC-4), 0.89 (3H, t, *J* = 7.5 Hz, H₃C-2''); **¹³C NMR** (125 MHz, CDCl₃) δ 115.1 (s, C-2'), 80.6 (d, C-5), 74.2 (d, C-7), 72.1 (d, C-3), 65.4 (t, C-4'), 65.1 (t, C-5'), 40.0 (d, C-2), 39.6 (d, C-4), 38.3 (d, C-6), 27.1 (t, C-1'' or C-8), 27.0 (t, C-1'' or C-8), 13.2 (q, CH₃C-4), 11.8 (q, CH₃C-6), 11.0 (q, C-9), 10.1 (q, C-1), 8.1 (q, C-2''); **LRMS** (CI, NH₃), *m/z* (relative intensity): 305 ([M+1]⁺, 6), 243 (38), 225 (44), 101 (100); **HRMS** (CI, NH₃), *m/z* calcd for C₁₆H₃₂O₅+H: 305.2328; found: 533.2325.

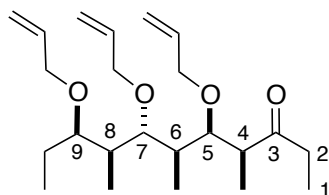
2-[(2*S*,3*R*,4*S*,5*S*,6*S*,7*R*)-3,5,7-Tris(allyloxy)-4,6-dimethylnonan-2-yl]-2-ethyl-1,3-dioxolane (15). A solution of



15

of **14** (993 mg, 3.26 mmol) in THF (20 mL) was added dropwise via syringe to stirred suspension of KH (oil free; 0.52 g, 13 mmol) and DMPU (1.6 mL, 1.7 g, 13 mmol) in THF (100 mL) at 0 °C. After 10 min, allyl bromide (1.7 mL, 2.4 g, 19 mmol) was added dropwise via syringe. The reaction mixture was allowed to warm to ambient temperature and after 18 h, was cooled down to 0 °C and quenched by slow addition of MeOH (6 mL). The mixture was diluted with CH₂Cl₂, washed sequentially with saturated aq NH₄Cl and brine, dried over Na₂SO₄, and fractionated by FCC (10% ethyl acetate in hexane) to give the title compound (1.18 g, 85%): colorless oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); [α]_D –25 (c 1.0, CHCl₃); **IR** (DRIFT) ν_{max} 3088, 1646 cm^{–1}; **¹H NMR** (500 MHz, CDCl₃) δ 5.95–5.86 (3H, m, HC= ×3), 5.25 (3H, br d, *J* = 17 Hz, HC= ×3), 5.11–5.06 (3H, m, HC= ×3), 4.09–4.01 (5H, m, H₂CO-allyl ×2.5), 3.96–3.88 (5H, m, H₂C-4, H₂C-5, H₂CO-allyl ×0.5), 3.76 (1H, dd, *J* = 3, 4.5 Hz, HC-3'), 3.50 (1H, ddd, *J* = 3, 6, 7 Hz, HC-7'), 3.21 (1H, dd, *J* = 5, 7 Hz, HC-5'), 1.91 (1H, ddq, *J* = 4.5, 5, 7 Hz, HC-4'), 1.87 (1H, dq, *J* = 3, 7 Hz, HC-2'), 1.81 (1H, ddq, *J* = 3, 7, 7 Hz, HC-6'), 1.76, 1.63 (3H, m, H₂C-1'', HC-8'), 1.46 (1H, ddq, *J* = 7, 14, 7.5 Hz, HC-8'), 1.01 (3, d, *J* = 7 Hz, H₃C-1'), 0.99 (3, d, *J* = 7 Hz, H₃CC-4'), 0.94 (3, d, *J* = 7 Hz, H₃CC-6'), 0.89 (3, t, *J* = 7.5 Hz, H₃C-9'), 0.86 (3, t, *J* = 7.5 Hz, H₃C-2''); **¹³C NMR** (125 MHz, CDCl₃) δ 136.1 (d, CH=), 136.0 (d, CH=), 135.9 (d, CH=), 115.9 (t, CH₂=), 115.5 (t, CH₂=), 115.3 (t, CH₂=), 114.2 (s, C-2), 84.2 (d, C-5'), 80.5 (d, C-7'), 77.3 (d, C-3'), 72.8 (t, CH₂O), 72.4 (t, CH₂O), 71.0 (t, CH₂O), 65.6 (t, C-4), 65.1 (t, C-5), 44.6 (d, C-2'), 41.8 (d, C-4'), 38.6 (d, C-6'), 27.2 (t, C-1''), 25.0 (t, C-8'), 12.8 (q, CH₃C-4'), 11.3 (q, CH₃C-6'), 10.4 (q, C-9'), 10.1 (q, C-1'), 7.5 (q, C-2''); **LRMS** (CI, NH₃), *m/z* (relative intensity): 425 ([M+1]⁺, 5), 367 (4), 237 (26), 141 (3), 101 (100), 99 (12), 57 (4); **HRMS** (CI, NH₃), *m/z* calcd for C₂₅H₄₄O₅+H: 425.3267; found: 425.3259.

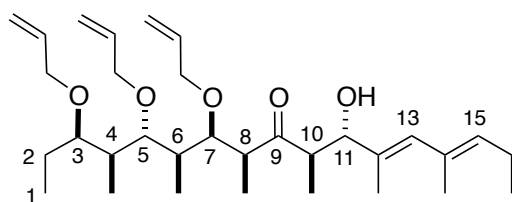
(4*S*,5*R*,6*S*,7*S*,8*S*,9*R*)-5,7,9-Tris(allyloxy)-4,6,8-trimethylundecan-3-one (16). FeCl₃·6H₂O (150 mg, 0.55 mmol)



16

was added to a stirred solution of **15** (603 mg, 1.42 mmol) in THF (8.5 mL) and CH₂Cl₂ (8.5 mL). After 19 h, the reaction mixture was diluted with CH₂Cl₂, washed sequentially with H₂O and brine, dried over Na₂SO₄, and concentrated to give the title compound (538 mg, quantitative) that was homogeneous by TLC and ¹H NMR: colorless oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); [α]_D –4 (c 2.2, CHCl₃); **IR** (DRIFT) ν_{max} 3087, 1711, 1646 cm^{–1}; **¹H NMR** (500 MHz, CDCl₃) δ 5.93–5.83 (3H, m, HC= ×3), 5.26–5.21 (3H, m, HC= ×3), 5.10–5.07 (3H, m, HC= ×3), 4.12–3.96 (5H, m, H₂CO ×2.5), 3.86 (1H, dddd, *J* = 1.5, 1.5, 5, 12.5 Hz, H₂CO ×0.5), 3.76 (1H, dd, *J* = 3, 6.5 Hz, HC-5), 3.50 (1H, ddd, *J* = 3, 5.5, 8 Hz, HC-9), 3.16 (1H, dd, *J* = 4, 7.5 Hz, HC-7), 2.84 (1H, dq, *J* = 7, 7 Hz, HC-4), 2.53 (1H, dq, *J* = 18, 7.5 Hz, HC-2), 2.46 (1H, dq, *J* = 18, 7.5 Hz, HC-2), 1.76 (1H, ddq, *J* = 3, 7, 7 Hz, HC-8), 1.73–1.63 (2H, m, HC-6, HC-10), 1.44 (1H, ddq, *J* = 8, 14, 7.5 Hz, HC-10), 1.13 (3H, d, *J* = 7 Hz, H₃CC-4), 1.02 (3H, t, *J* = 7 Hz, H₃C-1), 1.00 (3H, d, *J* = 7 Hz, H₃CC-6), 0.87 (3H, t, *J* = 7.5 Hz, H₃C-11), 0.86 (3H, d, *J* = 7 Hz, H₃CC-8); **¹³C NMR** (125 MHz, CDCl₃) δ 214.3 (s, C-3), 136.0 (d, CH=), 135.8 (d, CH=), 135.5 (d, CH=), 116.1 (t, CH₂=), 115.7 (t, CH₂=), 115.5 (t, CH₂=), 85.0 (d, C-7), 80.3 (d, C-9), 80.0 (d, C-5), 73.3 (t, CH₂O), 72.8 (t, CH₂O), 70.8 (t, CH₂O), 50.2 (d, C-4), 38.9 (d, C-6 or C-8), 38.8 (d, C-6 or C-8), 35.8 (t, C-2), 24.7 (t, C-10), 13.6 (q, CH₃C-6), 13.1 (q, CH₃C-4), 11.0 (q, CH₃C-8), 10.5 (q, C-11), 7.9 (q, C-1); **LRMS** (CI, NH₃), *m/z* (relative intensity): 381 ([M+1]⁺, 100), 323 (39), 265 (33), 237 (34), 195 (47), 155 (17), 101 (18), 99 (32), 57 (10); **HRMS** (CI, NH₃), *m/z* calcd for C₂₃H₄₀O₄+H: 381.3005; found: 381.2997.

(3*R*,4*S*,5*S*,6*S*,7*R*,8*S*,10*R*,11*S*,12*E*,14*E*)-3,5,7-Tris(allyloxy)-11-hydroxy-4,6,8,10,12,14-hexamethylheptadeca-

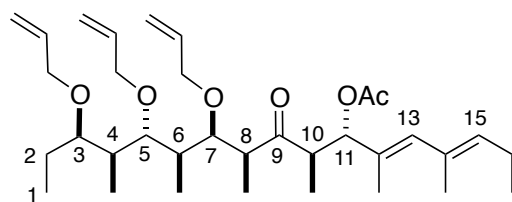


17

12,14-dien-9-one (17). (*c*-Hex)₂BCl (1 M in hexane, 1.6 mL, 1.6 mmol), and Et₃N (0.24 mL, 0.17 g, 1.7 mmol) were added sequentially via syringe to a stirred solution of **16** (200 mg, 0.53 mmol) in Et₂O (9 mL) at 0 °C under argon. After 1 h, the reaction mixture was cooled to -78 °C and a solution of the aldehyde **7** (145 mg, 1.05 mmol) in Et₂O (1 mL) was added dropwise via syringe. After 18 h, the reaction was quenched by sequential addition of MeOH (5 mL), phosphate buffer (pH 7; 10 mL), and 30%

aqueous H₂O₂ (5 mL) with vigorous stirring. The reaction vessel was transferred to an ice bath and after 15 min, was extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, concentrated, and fractionated by FCC (10% ethyl acetate in hexane) to give the title compound (220 mg, 80%): colorless oil, TLC R_f = 0.5 (15% ethyl acetate in hexane); [α]_D +14 (*c* 0.8, CHCl₃); **IR** (DRIFT) ν_{max} 3444, 3087, 1707, 1646 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 5.94-5.86 (3H, m, HC= ×3), 5.84 (1H, br s, HC-13), 5.32 (1H, dd, *J* = 7, 7 Hz, HC-15), 5.28-5.22 (3H, m, HC= ×3), 5.10-5.07 (3H, m, HC= ×3), 4.13-3.99 (6H, m, H₂CO ×2.5, HC-11), 3.91-3.85 (2H, m, H₂CO ×0.5, HC-7), 3.53 (1H, ddd, *J* = 2.5, 5.5, 8 Hz, HC-3), 3.19 (1H, dd, *J* = 4, 7.5 Hz, HC-5), 3.04 (1H, dq, *J* = 7, 7 Hz, HC-8), 2.92 (1H, dq, *J* = 9, 7 Hz, HC-10), 2.14 (1H, d, *J* = 3.5 Hz, HO), 2.09 (2H, ap qn, *J* = 7.5 Hz, H₂C-16), 1.88-1.79 (2H, m, HC-4, HC-6), 1.75 (3H, br s, H₃CC-12), 1.72 (3H, br s, H₃CC-14), 1.72-1.64 (1H, m, HC-2), 1.46 (1H, ddq, *J* = 8, 14, 7.5 Hz, HC-2), 1.18 (3H, d, *J* = 7 Hz, H₃CC-8), 1.06 (3H, d, *J* = 7 Hz, H₃CC-6), 0.99 (3H, t, *J* = 7.5 Hz, H₃C-17), 0.93 (3H, d, *J* = 7 Hz, H₃CC-10), 0.89 (3H, d, *J* = 7 Hz, H₃CC-4), 0.89 (3H, t, *J* = 7.5 Hz, H₃C-1); **¹³C NMR** (125 MHz, CDCl₃) δ 217.8 (s, C-9), 136.1 (d, CH=), 135.9 (d, CH=), 135.7 (d, CH=), 133.8 (s, C-12 or C-14), 133.2 (d ×2, C-13, C-15), 131.5 (s, C-12 or C-14), 116.0 (t, CH₂=), 115.8 (t, CH₂=), 115.5 (t, CH₂=), 85.1 (d, C-5), 81.2 (d, C-11), 80.4 (d, C-3), 79.2 (d, C-7), 73.4 (t, CH₂O), 73.0 (t, CH₂O), 70.8 (t, CH₂O), 50.8 (d, C-8), 49.0 (d, C-10), 39.4 (d, C-6), 38.9 (d, C-4), 24.7 (t, C-2), 21.6 (t, C-16), 16.9 (q, CH₃C-14), 14.8 (q, CH₃C-10), 14.3 (q, C-17), 13.8 (q, CH₃C-6), 12.8 (q, CH₃C-8), 12.6 (q, CH₃C-12), 11.0 (q, CH₃C-4), 10.5 (q, C-1); **LRMS** (CI, NH₃), *m/z* (relative intensity): 536 ([M+18]⁺, 1), 519 ([M+1]⁺, 3), 501 (12), 381 (100), 351 (16), 323 (25), 265 (43), 237 (56), 195 (15), 109 (82); **HRMS** (CI, NH₃), *m/z* calcd for C₃₂H₅₄O₅+NH₄: 536.4315; found: 536.4335.

(3*R*,4*S*,5*S*,6*S*,7*R*,8*S*,10*R*,11*S*,12*E*,14*E*)-3,5,7-Tris(allyloxy)-4,6,8,10,12,14-hexamethyl-9-oxoheptadeca-12,14-



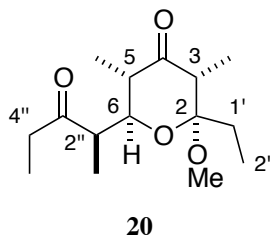
18

dien-11-yl Acetate (18). Ac₂O (100 μL, 108 mg, 1.05 mmol), ⁱPr₂EtN (0.27 mL, 0.20 g, 1.6 mmol), and DMAP (10 mg, 0.08 mmol) were added sequentially to a stirred solution of **17** (136 mg, 0.262 mmol) in CH₂Cl₂ (8 mL). After 18 h, the mixture was diluted with CH₂Cl₂, washed with saturated aq NaHCO₃, dried over Na₂SO₄, concentrated, and fractionated by PTLC (10% ethyl acetate in hexane) to give the title compound (146 mg, quantitative): colorless oil, TLC R_f = 0.7 (15% ethyl

acetate in hexane); [α]_D +4 (*c* 1.3, CHCl₃); **IR** (DRIFT) ν_{max} 3086, 1745, 1711 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 5.99 (1H, br s, HC-5), 5.94-5.84 (3H, m, HC= ×3), 5.33 (1H, br dd, *J* = 7, 7 Hz, HC-3), 5.28-5.21 (4H, m, HC= ×3, HC-11), 5.11-5.08 (3H, m, HC= ×3), 4.14-3.96 (5H, m, H₂CO ×2.5), 3.87 (1H, dddd, *J* = 1.5, 1.5, 5, 12.5 Hz, H₂CO ×0.5), 3.84 (1H, dd, *J* = 3.5, 6 Hz, HC-7), 3.53 (1H, ddd, *J* = 3, 5.5, 8 Hz, HC-3), 3.19 (1H, dd, *J* = 4, 8 Hz, HC-5), 3.10 (1H, dq, *J* = 10.5, 7 Hz, HC-10), 2.97 (1H, dq, *J* = 6, 7 Hz, HC-8), 2.11-2.03 (2H, m, H₂C-16), 1.91 (3H, s, H₃CCO), 1.84 (1H, ddq, *J* = 3, 8, 7 Hz, HC-4), 1.71 (1H, ddq, *J* = 3.5, 4, 7 Hz, HC-6), 1.74-1.64 (1H, m, HC-2), 1.72 (6H, s, H₃CC-12, H₃CC-14), 1.46 (1H, ddq, *J* = 8, 14, 7.5 Hz, HC-2), 1.19 (3H, d, *J* = 7 Hz, H₃CC-8), 1.07 (3H, d, *J* = 7 Hz, H₃CC-6), 0.97 (3H, t, *J* = 7.5 Hz, H₃C-17), 0.96 (3H, d, *J* = 7 Hz, H₃CC-10), 0.88 (3H, t, *J* = 7.5 Hz, H₃C-1), 0.87 (3H, d, *J* = 7 Hz, H₃CC-4); **¹³C NMR** (125 MHz, CDCl₃) δ 214.3 (s, C-9), 169.5 (s, O=CO), 136.0 (d, CH=), 135.8 (d, CH=), 135.7 (d, C-13), 135.5 (d, CH=), 133.8 (d, C-3), 131.4 (s, C-12 or C-14), 129.6 (s, C-12 or C-14), 116.0 (t, CH₂=), 115.7 (t, CH₂=), 115.6 (t, CH₂=), 85.0 (d, C-5), 82.0 (d, C-11), 80.4 (d, C-3), 79.0 (d, C-7),

73.4 (t, CH₂O), 72.9 (t, CH₂O), 70.7 (t, CH₂O), 50.3 (d, C-8), 46.8 (d, C-10), 39.5 (d, C-6), 38.8 (d, C-4), 24.5 (t, C-2), 21.6 (t, C-16), 21.4 (q, CH₃CO), 16.8 (q, CH₃C-14), 14.7 (q, CH₃C-10), 14.2 (q, C-17), 13.9 (q, CH₃C-6), 13.3 (q, CH₃C-12), 12.6 (q, CH₃C-8), 10.9 (q, CH₃C-4), 10.5 (q, C-1); **LRMS** (CI, NH₃), *m/z* (relative intensity): 578 ([M+18]⁺, 17), 561 ([M+1]⁺, 3), 535 (18), 501 (27), 443 (22), 351 (55), 295 (15), 237 (100), 99 (58); **HRMS** (CI, NH₃), *m/z* calcd for C₃₄H₅₆O₆+NH₄: 578.4415; found: 578.4408.

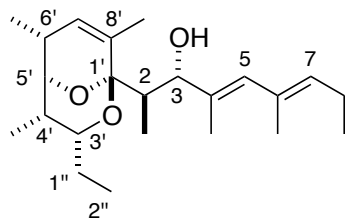
(2R,3S,5S,6S)-2-Ethyl-2-methoxy-3,5-dimethyl-6-((R)-3-oxopentan-2-yl)dihydro-2H-pyran-4(3H)-one (20). A



solution of **16** (10 mg, 0.026 mmol) in methanol (1.3 mL) was added via syringe to a dry Schlenk flask containing a magnetic stir bar and Ru(IV) catalyst **19** (0.3 mg, 0.6 μmol) under argon. Stirring was initiated and after 10 min, the mixture was diluted with ethyl acetate and washed with distilled water (×3). The organic layer was dried over Na₂SO₄, concentrated to give the crude product (8 mg) whose ¹H NMR spectrum indicated a single compound without any allyl groups. The crude product was taken up in DMSO (1 mL) and IBX (15 mg, 0.05 mmol) was added to the stirred solution at ambient temperature. After 2 h, the mixture was diluted with

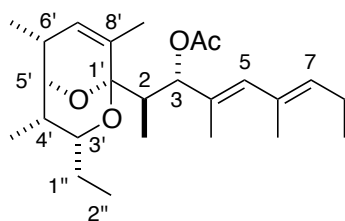
ethyl acetate, and washed sequentially with NaHCO₃ and brine, dried over Na₂SO₄, concentrated, and fractionated by PTLC (15% ethyl acetate in hexane) to give the title compound (5.1 mg, 72 %); white solid, TLC R_f = 0.3 (15% ethyl acetate in hexane); [α]_D -118 (c 0.1, CHCl₃); **IR** (neat) ν_{max} 1722, 1703 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 3.55 (1H, dd, *J* = 3, 10.5 Hz, HC-6), 3.15 (3H, s, H₃CO), 2.77 (1H, dq, *J* = 3, 7 Hz, HC-1'), 2.66 (1H, dq, *J* = 18.5, 7 Hz, HC-4''), 2.63 (1H, dq, *J* = 1, 6.5 Hz, HC-3), 2.55 (1H, dq, *J* = 18.5, 7 Hz, HC-4''), 2.45 (1H, ddq, *J* = 1, 10.5, 6.5 Hz, HC-5), 1.95 (1H, dq, *J* = 13.5, 7.5 Hz, HC-1'), 1.56 (1H, dq, *J* = 13.5, 7.5 Hz, HC-1'), 1.34 (3H, d, *J* = 7 Hz, H₃C-1''), 1.05 (3H, t, *J* = 7 Hz, H₃C-5''), 1.03 (3H, d, *J* = 6.5 Hz, H₃CC-5), 0.99 (3H, d, *J* = 6.5 Hz, H₃CC-3), 0.98 (3H, t, *J* = 7.5 Hz, H₃C-2''); **¹³C NMR** (125 MHz, CDCl₃) δ 213.3 (s, C-4 or C-3''), 208.8 (s, C-4 or C-3''), 106.2 (s, C-2), 78.5 (d, C-6), 49.4 (d, C-3), 49.0 (d, C-2''), 47.8 (q, CH₃O), 47.2 (d, C-5), 35.0 (t, C-4'), 26.4 (t, C-1'), 14.4 (q, C-1''), 9.9 (q, C-5''), 8.9 (q, CH₃C-3 or CH₃C-5), 8.4 (q, CH₃C-3 or CH₃C-5), 7.7 (q, C-2''); **LRMS** (EI), *m/z* (relative intensity): 270 ([M]⁺, 1), 185 (13), 182 (20), 153 (53), 126 (42), 108 (15), 100 (100), 69 (25), 57 (75); **HRMS** (EI), *m/z* calcd for C₁₅H₂₆O₄: 270.1831; found: 270.1839.

(2R,3S,4E,6E)-2-((1R,3R,4S,5R,6R)-3-Ethyl-4,6,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-1-yl)-4,6-dimethylnona-4,6-dien-3-ol (21a). A solution of **17** (11 mg, 0.017 mmol) in methanol (8 mL) was added via syringe to a dry Schlenk flask containing Ru(IV) catalyst **190** (0.4 mg, 0.8 μmol) under argon. The stirred reaction mixture was kept at 30 °C. After 20 min, the reaction mixture was diluted with ethyl acetate, washed sequentially with distilled water and brine, dried over Na₂SO₄, concentrated, and fractionated by PTLC (40 % ethyl acetate in hexane) to give the title compound (5 mg, 79%); colorless oil, TLC R_f = 0.7 (40% ethyl acetate in hexane); **IR** (DRIFT) ν_{max} 3479 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ



5.90 (1H, br s, HC-5), 5.76 (1H, br d, *J* = 5 Hz, HC-7'), 5.31 (1H, br t, *J* = 7 Hz, HC-7), 5.06 (1H, br s, HO), 4.44 (1H, d, *J* = 9 Hz, HC-3), 3.95 (1H, ddd, *J* = 3, 5.5, 8 Hz, HC-3'), 3.67 (1H, br s, HC-5'), 2.11-2.02 (3H, m, HC-2, H₂C-8), 1.98 (, br dq, *J* = 5, 7 Hz, HC-6'), 1.77 (3H, s, H₃CC-4), 1.72 (3H, s, H₃CC-6), 1.61 (3H, s, H₃CC-8'), 1.53 (1H, ddq, *J* = 8, 13, 7.5 Hz, HC-1''), 1.41-1.31 (2H, m, HC-1', HC-4'), 1.15 (3H, d, *J* = 7 Hz, H₃CC-4'), 1.09 (3H, d, *J* = 7 Hz, H₃CC-6'), 0.98 (3H, t, *J* = 7.5 Hz, H₃C-9), 0.86 (3H, t, *J* = 7.5 Hz, H₃C-2''), 0.65 (3H, d, *J* = 7 Hz, H₃C-1); **¹³C NMR** (125 MHz, CDCl₃) δ 135.0 (s, C-4), 132.6 (d, C-5), 132.02 (d, C-7), 131.93 (s, C-6), 131.1 (d, C-7'), 129.9 (s, C-8'), 101.3 (s, C-9'), 79.94 (d, C-3 or C-5'), 79.86 (d, C-3 or C-5'), 72.1 (d, C-3'), 40.5 (d, C-2), 36.6 (d, C-4'), 34.7 (d, C-6'), 25.7 (t, C-1''), 21.6 (t, C-8), 20.6 (q, CH₃C-6'), 18.2 (q, CH₃C-8'), 17.0 (q, CH₃C-6), 14.4 (q, C-9), 13.1 (q, CH₃C-4'), 12.5 (q, CH₃C-4), 12.2 (q, C-1), 10.0 (q, C-2''); **LRMS** (EI), *m/z* (relative intensity): 362 ([M]⁺, 4), 224 (37), 139 (35), 137 (100), 122 (10), 109 (24), 69 (14), 57 (16); **HRMS** (EI), *m/z* calcd for C₂₃H₃₈O₃: 362.2821; found: 362.2825.

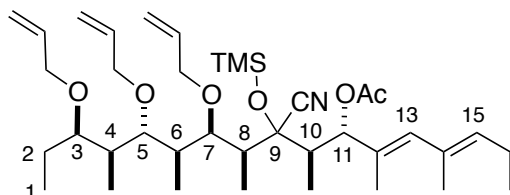
(2R,3S,4E,6E)-2-((1R,3R,4S,5R,6R)-3-Ethyl-4,6,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-1-yl)-4,6-



21b

ν_{\max} 1737 cm^{-1} ; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.98 (1H, s, HC-5), 5.74 (1H, d, $J = 8.5$ Hz, HC-3), 5.72 (1H, dq, $J = 5, 1.5$ Hz, HC-7'), 5.33 (1H, br dd, $J = 7, 7$ Hz, HC-7), 3.78 (1H, ddd, $J = 3, 5.5, 8$ Hz, HC-3'), 3.61 (1H, br s, HC-5'), 2.25 (1H, dq, $J = 8.5, 7$ Hz, HC-2), 2.07 (2H, ap dq, $J = 7, 7.5$ Hz, H_2C -8), 1.97 (3H, s, H_3CCO), 1.95-1.90 (1H, m, HC-6'), 1.75 (3H, d, $J = 1$ Hz, H_3CC -4), 1.72 (3H, br s, H_3CC -6), 1.59 (3H, dd, $J = 1.5, 1.5$ Hz, H_3CC -8'), 1.45-1.36 (1H, ddq, $J = 8, 13, 7.5$ Hz, HC-1''), 1.30-1.21 (2H, m, HC-1'', HC-4'), 1.08 (3H, d, $J = 7$ Hz, H_3CC -4'), 1.05 (3H, d, $J = 7$ Hz, H_3CC -6'), 0.97 (3H, t, $J = 7.5$ Hz, H_3C -9), 0.82 (3H, t, $J = 7.5$ Hz, H_3C -2''), 0.7 (3H, d, $J = 7$ Hz, H_3C -1); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 169.9 (s, CO), 133.8 (d, C-5), 133.0 (d, C-7), 131.9 (s, C-4 or C-6), 131.7 (s, C-4 or C-6), 130.9 (d, C-7'), 130.4 (s, C-8'), 99.5 (s, C-9'), 80.0 (d, C-5'), 79.5 (d, C-3), 71.2 (d, C-3'), 39.5 (d, C-2), 36.7 (d, C-4'), 35.0 (d, C-6'), 25.6 (t, C-1''), 21.9 (q, CH_3CO), 21.6 (t, C-8), 20.6 (q, CH_3C -6'), 18.5 (q, CH_3C -8'), 16.9 (q, CCH_3C -6), 14.3 (q, C-9), 13.8 (q, CCH_3C -4), 13.3 (q, CH_3C -4'), 12.1 (q, C-1), 10.1 (q, C-2''); **LRMS** (EI), m/z (relative intensity): 404 ($[\text{M}]^+$, 9), 344 (23), 228 (13), 207 (14), 149 (28), 137 (100), 121 (60), 109 (33), 93 (16), 69 (29); **HRMS** (EI), m/z calcd for $\text{C}_{25}\text{H}_{40}\text{O}_4$: 404.2927; found: 404.2918..

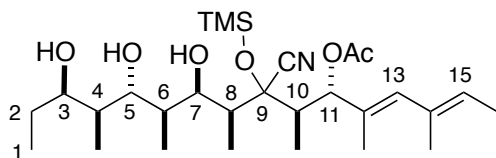
(3R,4S,5S,6S,7R,8S,10R,11S,12E,14E)-3,5,7-Tris(allyloxy)-9-cyano-4,6,8,10,12,14-hexamethyl-9-((trimethylsilyloxy)heptadeca-12,14-dien-11-yl) Acetate (22).



22

colorless oil, TLC $R_f = 0.9$ (10% ethyl acetate in hexane); **IR** (DRIFT) ν_{\max} 3079, 1743, 1646 cm^{-1} ; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.03-5.86 (4H, m, $\text{HC} = \times 3$, HC-13), 5.33-5.22 (4H, m, $\text{HC} = 3$, HC-15), 5.14-5.06 (4H, m, $\text{HC} = \times 3$, HC-11), 4.26-3.85 (6.6H, m, $\text{H}_2\text{C} \times 3$, HC-7 $\times 0.6$), 3.77 (0.4H, br dd, $J = 3, 3$ Hz, HC-7), 3.46 (0.6H, ddd, $J = 4, 5.5, 7$ Hz, HC-3), 3.36 (0.4H, ddd, $J = 4, 6, 7$ Hz, HC-3), 3.22 (1H, ap t, $J = 6$ Hz, HC-5), 2.50 (0.6H, dq, $J = 9.5, 7$ Hz, HC-10), 2.43 (0.4H, dq, $J = 9.5, 7$ Hz, HC-10), 2.12-2.00 (3H, m, HC-8, H_2C -16), 2.08 (1H, s, H_3CCO), 2.02 (2H, s, H_3CCO), 1.90-1.75 (2H, m, HC-4, HC-6), 1.72 (s) and 1.71 (s) (6H, s, H_3C -12, H_3C -14), 1.71-1.41 (2H, m, H_2C -2), 1.19 (1H, d, $J = 7$ Hz, H_3CC -8), 1.15 (2H, d, $J = 7$ Hz, H_3CC -8), 1.02 (2H, d, $J = 7$ Hz, H_3C -10), 1.01-0.86 (9H, m, $\text{CH}_3 \times 3$), 0.72 (1H, d, H_3C -10), 0.31 (5.4H, s, $J = 7$ Hz, $\text{H}_3\text{CSi} \times 3$), 0.28 (3.6H, s, $\text{H}_3\text{CSi} \times 3$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ (* major isomer) 170.5* (s, C=O), 169.6 (s, C=O), 135.9 (d, CH=), 135.83 (d, CH=), 135.77 (d, CH=), 135.7 (d $\times 2$, CH=), 135.5 (d, CH=), 135.2* (d) and 133.8* (d), 135.1 (d) and 133.6 (d), 131.3 (s) and 130.7 (s), 131.2* (s) and 130.6* (s), 120.9* (s, CN), 120.8 (s, CN), 116.1 (t $\times 2$, $\text{CH}_2 =$), 115.9 (t $\times 2$, $\text{CH}_2 =$), 115.6 (t, $\text{CH}_2 =$), 115.4 (t, $\text{CH}_2 =$), 84.42* (d, C-5), 84.37 (d, C-5), 80.7 (d, C-3 or C-11), 80.64* (d, C-11), 80.56 (d, C-3 or C-11), 80.5* (d, C-3), 77.35* (s, C-9; confirmed by DEPT), 76.2 (d, C-7), 75.8* (d, C-7), 73.4 (t, CH_2O), 73.2* (t, CH_2O), 73.1 (t, CH_2O), 72.4* (t, CH_2O), 71.0 (t, CH_2O), 70.6* (t, CH_2O), 47.3 (d, C-8), 46.4* (d, C-8), 42.6 (d, C-4), 42.2* (d $\times 2$, C-4, C-10), 40.5 (d, C-10), 38.63 (d, C-6), 38.56* (d, C-6), 25.1 (t, C-2), 24.7* (t, C-2), 21.7 (q, CH_3CO), 21.62* (t $\times 2$, C-16), 21.57* (q, CH_3CO), 16.7* (q $\times 2$, CH_3C -14), 14.2* (q $\times 2$, C-17), 13.6 (q, CH_3C -12), 13.4* (q, CH_3C -10), 13.3* (q, CH_3C -12), 12.4 (q), 12.0 (q), 11.7* (q), 10.94 (q), 10.89 (q), 10.85 (q), 10.3* (q, C-1), 10.1 (q, C-1), 2.1* (q $\times 6$, CH_3Si); **HRMS** (ESI), m/z calcd for $\text{C}_{38}\text{H}_{65}\text{NO}_6\text{Si} + \text{Na}$: 682.4479; found: 682.4486.

(3R,4S,5S,6S,7R,8S,10R,11S,12E,14E)-9-Cyano-3,5,7-trihydroxy-4,6,8,10,12,14-hexamethyl-9-((trimethylsilyl)-oxy)heptadeca-12,14-dien-11-yl Acetate (23).

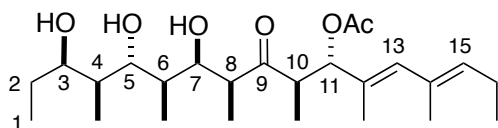


23

A solution of **22** (81 mg, 0.12 mmol) in MeOH (4 mL) was added via syringe to a dry Schlenk flask containing a magnetic stir bar and the Ru(IV) catalyst **19** (1.2 mg, 1.1 μ mol) under argon. The reaction mixture was stirred at 30 °C for 20 min, and then additional Ru(IV) catalyst **19** (1.2 mg, 1.1 μ mol) was added. After 20 min, the mixture was diluted with ethyl acetate and washed sequentially with water ($\times 3$)

and brine, dried over Na₂SO₄, concentrated, and fractionated by FCC (40% ethyl acetate in hexane) to give the title compound as a 1.1:1 mixture of diastereomers (44 mg, 67%): colorless oil, TLC R_f = 0.3 (40% ethyl acetate in hexane); **IR** (DRIFT) ν_{max} 3439, 1742 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 5.93 (0.6H, br s, HC-13), 5.90 (0.4H, br s, HC-13), 5.35-5.31 (1H, m, HC-15), 5.20 (0.4H, d, *J* = 9 Hz, HC-11), 5.11 (0.6H, d, *J* = 9 Hz, HC-11), 4.40 (0.4H, br s, HC-7), 4.33 (0.6H, br s, HC-7), 4.30-4.22 (1H, m, HOC-5), 3.88-3.84 (1H, m, *J* = 7 Hz, HC-3), 3.61-3.57 (1H, m, HC-5), 3.20 (0.4H, br s, HOC-3), 3.07 (0.4H, br s, HOC-7), 2.99 (1.2H, br s, HOC-3, HOC-7), 2.52 (0.4H, dq, *J* = 9, 7 Hz, HC-10), 2.36 (0.6H, dq, *J* = 9, 7 Hz, HC-10), 2.14-2.01 (3H, m, HC-8, H₂C-16), 2.07 (1.8H, s, H₃CCO), 2.03 (1.2H, s, H₃CCO), 1.94-1.76 (2H, m, HC-4, HC-6), 1.73-1.71 (6H, m, H₃CC-12, H₃CC-14), 1.60-1.50 (1H, m, HC-2), 1.49-1.38 (1H, m, HC-2), 1.22 (1.2H, d, *J* = 7 Hz, H₃CC-8), 1.16 (1.8H, d, *J* = 7 Hz, H₃CC-8), 1.08 (1.2H, d, H₃CC-8), 1.00-0.92 (10.8H, m, H₃C $\times 3.6$), 0.89 (1.8H, d, *J* = 7 Hz, H₃CC-10), 0.88 (1.2H, d, *J* = 7 Hz, H₃C $\times 0.4$), 0.31 (9, s, H₃C-Si $\times 3$), 0.28 (9, s, H₃C-Si $\times 3$); **¹³C NMR** (125 MHz, CDCl₃) δ (* major isomer) 170.1* (s, CO), 169.7 (s, CO), 135.45* (d, C-13), 135.40 (d, C13), 134.03 (d, C15), 133.95* (d, C-15), 131.19* (s, C-12 or C-14), 131.18 (s, C-12 or C-14), 130.35 (s, C-12 or C-14), 130.33* (s, C-12 or C-14), 121.1 (s, CN), 121.0* (s, CN), 80.8* (d, C-11), 80.5 (d, C-11), 80.2 (d, C-5), 79.9* (d, C-5), 79.6 (s, C-9), 78.9* (s, C-9), 74.5* (d, C-3), 73.8 (d, C-3), 71.2* (d, C-7), 71.0 (d, C-7), 44.8* (d, C-8), 44.1 (d, C-8), 41.4* (d, C-10), 41.3* (d, C-4), 41.2 (d $\times 2$, C-4, C-10), 38.0* (d, C-6), 37.4 (d, C-6), 27.3 (t, C-2), 26.9* (t, C-2), 21.62* (t $\times 2$, C-16), 21.61* (q $\times 2$, CH₃CO), 16.76 (q, CH₃C-14), 16.73* (q, CH₃C-14), 14.2* (q $\times 3$, C-17, CH₃C-10), 13.7* (q, CH₃C-12), 13.6 (q, CH₃C-12), 13.0* (q, CH₃C-10), 12.3 (q), 12.2* (q), 11.7* (q), 11.6 (q), 11.2 (q, CH₃C-8), 10.9* (q), 10.8 (q), 10.1* (q, CH₃C-8), 1.98* (q $\times 3$, CH₃Si), 1.93 (q $\times 3$, CH₃Si); **LRMS** (EI), *m/z* (relative intensity): 539 ([M]⁺, 2), 479 (3), 334 (10), 334 (10), 276 (8), 167 (22), 149 (100), 139 (56), 121 (37), 69 (40); **HRMS** (EI), *m/z* calcd for C₂₉H₅₃NO₆Si: 539.3642; found: 539.3637.

(3R,4S,5S,6S,7R,8S,10R,11S,12E,14E)-3,5,7-Trihydroxy-4,6,8,10,12,14-hexamethyl-9-oxoheptadeca-12,14-



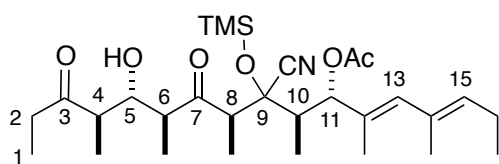
24

dien-11-yl Acetate (24). Pyridine (48 μ L, 47 mg, 0.6 mmol), HF-pyridine (32 μ L), and water (2 μ L) were added sequentially to a stirred solution of **23** (10.6 mg, 19.6 μ mol) in THF (0.6 mL). After 24 h, the reaction mixture was diluted with ethyl acetate and washed sequentially with saturated aq NaHCO₃, saturated aq

NH₄Cl and brine, dried over Na₂SO₄, and concentrated. The resulting crude product (cyanohydrin) was taken up in a 1:1 (v/v) mixture of water and MeOH and heated to 60 °C. After 3 h, the mixture was diluted with CH₂Cl₂ and washed with water. The aqueous phase was extracted with CH₂Cl₂ and the combined organic layers were dried over Na₂SO₄, concentrated, and fractionated by PTLC to give the title compound as a 3:1 mixture of keto and hemiacetal forms, respectively (6.3 mg, 73%): colorless oil, TLC R_f = 0.2 (40% ethyl acetate in hexane); **IR** (DRIFT) ν_{max} 3398, 1743, 1711 cm⁻¹; **¹H NMR** (500 MHz, CDCl₃) δ 5.91 (0.75H, s, HC-13), 5.90 (0.25H, s, HC-13), 5.33 (0.75H, dd, *J* = 7, 7 Hz, HC-15), 5.32 (0.25H, dd, *J* = 7, 7 Hz, HC-15), 5.19 (0.75H, d, *J* = 10.5 Hz, HC-11), 5.18 (0.25H, d, *J* = 9.5 Hz, HC-11), 4.54 (0.75H, br s, HO), 4.20 (0.75H, br d, *J* = 8.5 Hz, HC-7), 3.91-3.85 (1H, m, OH, HC-3), 3.78 (0.75H, ddd, *J* = 2.5, 6, 7 Hz, HC-3), 3.67-3.62 (1H, m, HC-5), 3.28 (0.25H, dd, *J* = 9.5 Hz, HC-7), 3.06 (0.75H, dq, *J* = 10.5, 7 Hz, HC-10), 2.90 (0.75H, dq, *J* = 8.5, 7 Hz, HC-8), 2.86 (0.75H, br s, HO), 2.40 (0.25H, br d, *J* = 1 Hz, HO), 2.32 (0.25, dq, *J* = 9.5, 7 Hz, HC-10), 2.10-2.03 (2.75H, m, HC-4, H₂C-16), 2.03 (0.75H, s, H₃CCO), 1.93 (2.25H, s, H₃CCO), 1.85-1.80 (0.25H, m, HC-4), 1.74-1.66 (6.75H, m, H₃CC-12, H₃CC-14, HC-8), 1.65-1.57

(0.75H, s, HC-2, HC-4, HC-6), 1.54-1.47 (1.5H, s, H₂C-2), 1.39-1.32 (0.25H, m, HC-2), 1.27 (2.25H, d, $J = 7$ Hz, H₃C-8), 1.14 (0.75H, d, $J = 7$ Hz, H₃C-4), 1.04 (2.25H, d, $J = 7$ Hz, H₃C-6), 1.02- 0.89 (9.75H, m, H₃C \times 3.25), 0.87 (0.75H, d, $J = 7$ Hz, H₃CC-10), 0.83 (2.25H, d, $J = 7$ Hz, H₃CC-4); ¹³C NMR (125 MHz, CDCl₃) δ (* major isomer) 216.0* (s, C-9), 169.8 (s, COO), 169.5* (s, COO), 135.9* (d, C-13), 135.1 (d, C-13), 134.0* (d, C-15), 133.7 (d, C-15), 131.3* (s, C-12 or C-14), 130.6 (s, C-12 or C-14), 129.1* (s \times 2, C-12 or C-14), 100.9 (s, C-9), 82.8* (d, C-11), 81.7 (d, C-11), 80.1* (d, C-5), 78.9 (d, C-5), 76.9* (d, C-3), 75.8 (d, C-7), 71.34* (d, C-7), 71.26 (d, C-3), 50.8* (d, C-8), 47.5* (d, C-10), 44.1 (d), 42.4 (d, C-10), 40.6 (d), 39.4* (d, C-4), 36.3* (d, C-6), 35.4 (d), 27.7 (t, C-2), 25.2* (t, C-2), 21.64* (t \times 2, C-16), 21.61 (q, CH₃CO), 21.3* (q, CH₃CO), 16.77* (q, CH₃C-14), 16.75 (q, CH₃C-14), 14.9* (q, CH₃C-10), 14.4 (q), 14.3* (q, CH₃C-8 or C-17), 14.2* (q, CH₃C-8 or C-17), 13.5 (q \times 2), 13.2* (q, CH₃C-12), 13.0 (q), 12.4 (q), 12.3* (q, CH₃C-4 or CH₃C-6), 12.0* (q, CH₃C-4 or CH₃C-6), 11.3 (q), 11.2* (q, C-1), 11.1 (q), 10.8 (q); LRMS (EI), m/z (relative intensity): 422 ([M-18]⁺, 0.5), 362 (4), 235 (10), 195 (17), 149 (62), 138 (68), 121 (121), 109 (46), 69 (42); HRMS (ESI), m/z calcd for C₂₅H₄₄O₆+Na: 463.3030; found: 463.3043.

(4R,5S,6S,8R,10R,11S,12E,14E)-9-Cyano-5-hydroxy-4,6,8,10,12,14-hexamethyl-3,5-dioxo-9-((trimethylsilyl)-

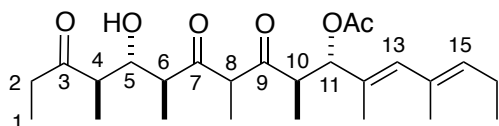


S5

oxy)heptadeca-12,14-dien-11-yl Acetate (S5). Oxalyl chloride (140 μ L, 201 mg, 1.6 mmol) was added to a stirred solution of DMSO (0.23 mL, 25 mg, 3.2 mmol) and CH₂Cl₂ (1 mL) at -78 °C under argon. After 30 min, a solution of **23** (44 mg, 0.08 mmol) in CH₂Cl₂ (0.4 mL) was added dropwise via syringe to the above Swern reagent. After 2 h, Et₃N (0.66 mL, 480 mg, 4.7 mmol) was added to the reaction mixture. After 30 min, the

reaction mixture was transferred to a -50 °C bath. After 30 min, the mixture was diluted with ethyl acetate, washed with saturated aq NaHCO₃ solution (\times 2), dried over Na₂SO₄, concentrated, and fractionated by PTLC (40% ethyl acetate in hexane) to give the title compound as a 1.2:1 mixture of diastereomers (27.5 mg, 63%): colorless oil, TLC R_f = 0.5 (40% ethyl acetate in hexane); IR (DRIFT) ν_{max} 3472, 1741, 1717, 1702 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.90 (1H, s, HC-13), 5.35-5.29 (1H, m, HC-15), 5.14 (0.5H, d, $J = 9$ Hz, HC-11), 5.07 (0.5H, d, $J = 10$ Hz, HC-11), 3.71 (0.5H, ddd, $J = 5, 7, 7$ Hz, HC-5), 3.66 (10.5H, ddd, $J = 3, 8.5, 9.5$ Hz, HC-5), 3.60 (0.5H, d, $J = 9.5$ Hz, OH), 3.43 (0.5H, q, $J = 7$ Hz, HC-8), 3.25 (0.5H, d, $J = 7$ Hz, OH), 3.17 (0.5H, q, $J = 7$ Hz, HC-8), 2.89-2.80 (1H, m, HC-4 or HC-6), 2.78-2.67 (1H, m, HC-4 or HC-6), 2.66-2.55 (1H, m, HC-2), 2.53 (0.5H, dq, $J = 10, 7$ Hz, HC-10), 2.51-2.40 (1H, m, HC-2), 2.37 (0.5H, dq, $J = 9, 7$ Hz, HC-10), 2.16 (s) and 2.06 (s) (3H, , H₃CCO), 2.10-2.03 (2H, m, H₂C-16), 1.73-1.68 (6H, m, H₃CC-12, H₃CC-14), 1.38 (1.5H, d, $J = 7$ Hz, H₃CC-8), 1.27 (1.5H, d, $J = 7$ Hz, H₃CC-8), 1.26 (1.5H, d, $J = 7$ Hz, H₃CC-4 or H₃CC-6), 1.21 (1.5H, d, $J = 7$ Hz, H₃CC-4 or H₃CC-6), 1.16 (1.5H, d, $J = 7$ Hz, H₃CC-4 or H₃CC-6), 1.08 (1.5H, d, $J = 7$ Hz, H₃CC-10), 1.06 (1.5H, t, $J = 7$ Hz, H₃C-1), 1.04 (1.5H, d, $J = 7$ Hz, H₃CC-4 or H₃CC-6), 1.03 (1.5H, t, $J = 7$ Hz, H₃C-1), 0.98 (1.5H, t, $J = 7.5$ Hz, H₃C-17), 0.97 (1.5H, t, $J = 7.5$ Hz, H₃C-17), 0.80 (1.5H, d, $J = 7$ Hz, H₃CC-10), 0.28 (s) and 0.24 (s) (, , H₃CSi \times 3); ¹³C NMR (125 MHz, CDCl₃) δ 217.8 (s), 216.5 (s), 213.9 (s), 213.7 (s), 170.6 (s), 169.6 (s), 135.5 (d), 135.0 (d), 134.0 (d), 133.6 (d), 131.3 (s), 131.2 (s), 130.8 (s), 130.3 (s), 119.7 (s), 119.4 (s), 80.6 (d), 80.4 (d), 78.1 (d), 77.9 (s), 77.0 (d), 74.7 (s), 55.1 (d), 50.8 (d), 50.3 (d), 49.3 (d), 47.9 (d), 46.1 (d), 41.7 (d), 41.4 (d), 36.4 (t), 35.9 (t), 21.8 (q), 21.63 (t), 21.61 (t), 21.57 (q), 16.8 (q \times 2), 15.5 (q), 15.0 (q), 14.9 (q), 14.22 (q), 14.20 (q \times 2), 14.16 (q), 13.7 (q), 13.5 (q), 13.4 (q), 12.7 (q), 11.2 (q), 7.7 (q), 7.6 (q), 2.1 (q \times 3), 1.8 (q \times 3); HRMS (ESI), m/z calcd for C₂₉H₅₃NO₆Si+Na: 558.3221; found: 558.3226.

4R,5S,6S,8R,10R,11S,12E,14E)-9-cyano-5-hydroxy-4,6,8,10,12,14-hexamethyl-3,5-dioxo-9-((trimethylsilyl)-

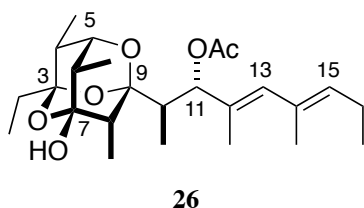


25

oxy)heptadeca-12,14-dien-11-yl Acetate (25). Pyridine (96 μ L, 94 mg, 1.2 mmol), HF \cdot pyridine (70 μ L), and water (4 μ L) were added sequentially to a solution of **S5** (27.5 mg, 51.3 μ mol) in THF (1.2 mL). After 24 h, the reaction mixture was diluted with ethyl acetate and washed sequentially with saturated aq NaHCO₃, saturated aq NH₄Cl and brine. The

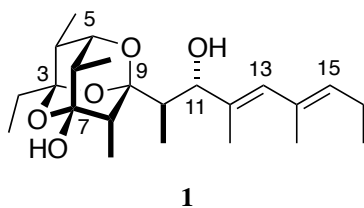
organic layer was dried over Na_2SO_4 , and concentrated to give the crude product (29.2 mg) as a 1.2:1 mixture cyanohydrin diastereomers. The above crude was taken up in ethyl acetate (1 mL) and silica gel 60 (100 mg) was added. The resulting suspension was stirred for 2 h and then filtered. The combined filtrate and ethyl acetate washings were concentrated to give the title compound as a mixture of ring-chain and keto-enol tautomers (20.3 mg, 91%): colorless oil, TLC R_f = 0.4 (40% ethyl acetate in hexane); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ (partial data) 16.97 (0.16H, s, HO-enol), 6.04-5.89 (1H, several s, HC-13), 5.34 (1H, bt, HC-15), 5.28-5.15 (1H, several d, J = 5-6 Hz, HC-11), 4.99 (0.05, s, HO-hemiacetal), 4.02 (q) and 4.01 (q) (0.7H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ (partial data) 199.1 (s, CO) & 193.6 (s, CO) & 105.0 (s, C-8) (enol form), 169.6 (s, CO) & 169.5 (s, CO) & 169.35 (s, CO) (acetate carbonyls), 82.3 (d, C-11) & 82.1 (d, C-11) & 81.9 (d, C-11), 61.8 (d, C-8) & 59.8 (d, C-8) (2 keto diastereomers); **LRMS** (CI, NH_3), m/z (relative intensity): 454 ($[\text{M}+18]^+$, 17), 378 (26), 377 (100), 359 (54), 263 (58), 195 (37), 149 (30), 115 (13), 109 (11); **HRMS** (CI, NH_3), m/z calcd for $\text{C}_{25}\text{H}_{40}\text{O}_6+\text{NH}_4$: 454.3169; found: 454.3161.

11-O-Acetylmumvatin (26). Pyridine (48 μL , 47 mg, 0.6 mmol), HF-pyridine (32 μL), and water (2 μL) was added sequentially to a solution of **25** (10 mg, 23 μmol) in THF (0.6 mL). After 10 days, the reaction mixture was diluted with ethyl acetate and washed sequentially with saturated solution of NaHCO_3 ($\times 3$), saturated aq NH_4Cl ($\times 3$), and brine (5 mL). The organic layer was dried over Na_2SO_4 , concentrated, and fractionated by PTLC (40% ethyl acetate in hexane) to give recovered **25** (5.1 mg, 51 %) and the title compound (4.8 mg, 48%). The recovered **25** was



resubjected to the above reaction conditions to give **25** (2.4 mg, 24%) and additional title compound (2.1 mg, 21%): colorless oil, TLC R_f = 0.6 (40% ethyl acetate in hexane); $[\alpha]_D^{+40}$ (c 0.2, CHCl_3); **IR** (DRIFT) ν_{max} 3435, 1737 cm^{-1} ; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.94 (1H, s, HC-13), 5.53 (1H, d, J = 8.5 Hz, HC-11), 5.33 (1H, br dd, J = 7, 7.5 Hz, HC-15), 3.80 (1H, br s, HC-5), 2.56 (1H, br s, HO), 2.21 (1H, dq, J = 8.5, 7.5 Hz, HC-10), 2.10-2.04 (3H, m, HC-8, $\text{H}_2\text{C}-16$), 1.97 (3H, s, H_3CCO), 1.89 (1H, dq, J = 1, 7 Hz, HC-6), 1.72 (6H, br s, $\text{H}_3\text{C}-12$, $\text{H}_3\text{C}-14$), 1.63-1.54 (2H, m, HC-2, HC-4), 1.47 (1H, dq, J = 14, 7.5 Hz, HC-2), 1.12 (3H, d, J = 7 Hz, $\text{H}_3\text{CC}-6$), 1.09 (3H, d, J = 7 Hz, $\text{H}_3\text{CC}-4$), 1.01 (3H, d, J = 6.5 Hz, $\text{H}_3\text{CC}-8$), 0.97 (3H, t, J = 7.5 Hz, $\text{H}_3\text{C}-17$), 0.93 (3H, t, J = 7.5 Hz, $\text{H}_3\text{C}-1$), 0.78 (3H, d, J = 7.5 Hz, $\text{H}_3\text{CC}-10$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 169.9 (s, CO), 134.0 (d, C-13), 133.2 (d, C-15), 131.7 (s, C-12 or C-14), 131.6 (s, C-12 or C-14), 103.4 (s, C-9), 102.5 (s, C-3), 97.7 (s, C-7), 79.6 (d, C-11), 78.9 (d, C-5), 43.4 (d, C-6), 39.9 (d, C-10), 38.0 (d, C-4), 35.0 (d, C-8), 30.0 (t, C-2), 21.8 (q, CH_3CO), 21.6 (t, C-16), 16.9 (q, $\text{CH}_3\text{C}-14$), 14.3 (q, C-17), 14.0 (q, $\text{CH}_3\text{C}-12$), 13.6 (q, $\text{CH}_3\text{C}-4$ or $\text{CH}_3\text{C}-6$), 13.4 (q, $\text{CH}_3\text{C}-4$ or $\text{CH}_3\text{C}-6$), 10.5 (q, $\text{CH}_3\text{C}-10$), 7.2 (q, $\text{CH}_3\text{C}-8$), 6.1 (q, C-1); **LRMS** (EI), m/z (relative intensity): 436 ($[\text{M}]^+$, 4), 419 (3), 376 (10), 195 (29), 176 (20), 153 (18), 149 (100), 139 (50), 121 (87), 57 (55); **HRMS** (EI), m/z calcd for $\text{C}_{25}\text{H}_{40}\text{O}_6$: 436.2825; found: 436.2816.

Mumvatin (1). DIBAL-H (1 M in toluene; 50 μL , 50 μmol) was added to a stirred solution of ?? (6.8 mg, 15



μmol) in Et_2O (2 mL) at -78°C under argon. After 2 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with aq Rochelle's salt (1.4 M). The aqueous layer was back extracted with CH_2Cl_2 . The combined organic layers were dried over Na_2SO_4 , concentrated, and fractionated by PTLC (40% ethyl acetate in hexane) to give the titled compound (5.6 mg, 91%): colorless oil, TLC R_f = 0.5 (40% ethyl acetate in hexane); $[\alpha]_D^{+60}$ (c 0.13, CH_2Cl_2); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.87 (1H, br s, HC-13), 5.31 (1H, br dd, J = 7, 7 Hz, HC-15), 4.40 (1H, d, J = 9 Hz, HC-11), 4.38 (1H, br s, HOC-11), 3.88 (1H, br s, HC-5), 2.59 (1H, br s, HOC-7), 2.13-2.05 (3H, m, HC-8, $\text{H}_2\text{C}-16$), 2.00-1.92 (2H, m, HC-6, HC-10), 1.76 (3H, br s, $\text{H}_3\text{CC}-12$), 1.72 (3H, br s, $\text{H}_3\text{C}-14$), 1.70-1.65 (2H, m, HC-4, HC-2), 1.59-1.51 (1H, m, HC-2), 1.18 (3H, d, J = 7 Hz, $\text{H}_3\text{CC}-4$), 1.14 (3H, d, J = 7 Hz, $\text{H}_3\text{CC}-6$), 1.03 (3H, d, J = 7 Hz, $\text{H}_3\text{CC}-8$), 0.98 (3H, t, J = 7.5 Hz, $\text{H}_3\text{C}-17$), 0.95 (3H, t, J = 7.5 Hz, $\text{H}_3\text{C}-1$), 0.72 (3H, t, J = 7 Hz, $\text{H}_3\text{CC}-10$); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 134.7 (s, C-12), 132.9 (d, C-13), 132.3 (d, C-15), 131.7 (s, C-14), 105.4 (s, C-9), 103.2

(s, C-3), 97.7 (s, C-7), 79.6 (d, C-11), 78.8 (d, C-5), 43.1 (d, C-6), 40.9 (d, C-10), 37.8 (d, C-4), 35.2 (d, C-8), 30.1 (t, C-2), 21.6 (t, C-16), 16.9 (q, CH₃C-14), 14.4 (q, C-17), 13.45 (q, CH₃C-4 or CH₃C-6), 13.41 (q, CH₃C-4 or CH₃C-6), 12.5 (q, CH₃C-12), 10.6 (q, CH₃C-10), 6.9 (q, CH₃C-8), 6.1 (q, C-1); **LRMS** (EI), *m/z* (relative intensity): 394 ([M]⁺, 4), 376 (10), 294 (11), 256 (31), 238 (29), 183 (39), 153 (41), 109 (48), 86 (28), 57 (100); **HRMS** (EI), *m/z* calcd for C₂₃H₃₈O₅: 394.2719; found: 394.2715.

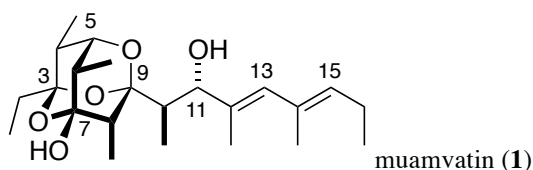


Table S1. Comparison of ¹H NMR spectra (CDCl₃) of natural **1** and synthetic **1**.

Natural ^a				Synthetic		
δ _H	multiplicity	<i>J</i> (Hz)	Assignment	δ _H	multiplicity	<i>J</i> (Hz)
0.96	t	7.46	H ₃ C-1	0.95	t	7.5
1.56	dq	14.34, 7.46	HC-2	1.59-1.51	m	
1.69	dq	14.34, 7.46	HC-2	1.70-1.65	2H m	
1.69	q	6.93	HC-4			
1.18	d	7.93	H ₃ CC-4	1.18	d	7
3.88	br s		HC-5	3.88	br s	
1.15	d	7.03	H ₃ CC-6	1.14	d	7
1.97	q	7.03	HC-6	2.00-1.92	2H m	
1.97	dq	9.02, 7.18	HC-10			
			HOC-7	2.59	br s	
2.10	dq	7.19, 7.52	H ₂ C-16	2.13-2.05	2H m	
2.10	q	6.74	HC-8			
1.03	d	6.74	H ₃ CC-8	1.03	d	7
0.73	d	7.18	H ₃ CC-10	0.72	t	7
4.40	d	9.02	HC-11	4.40	d	9
			HOC-11	4.38	br s	
1.76	s		H ₃ CC-12	1.76	br s	
5.87	br s		HC-13	5.87	s	
1.72	s		H ₃ CC-14	1.72	br s	
5.32	br t	7.19	HC-15	5.31	br t	7
0.98	t	7.52	H ₃ C-17	0.98	t	7.5

^a Data and assignments according to Ireland et al. (ref. 11); numbering according to Paterson et al. (ref 12).

¹¹ Roll, D. M.; Biskupiak, J. E.; Mayne, C. L.; Ireland, C. M. *J. Am. Chem. Soc.* **1986**, *108*, 6680-6682.

¹² Paterson, I.; Perkins, M. V. *J. Am. Chem. Soc.* **1993**, *115*, 1608-1610.

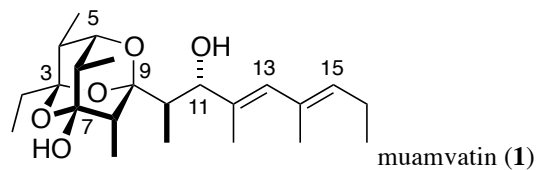


Table S2. Comparison of ^{13}C NMR spectra (CDCl_3) of natural **1** and synthetic **1**.

Natural ^a		Synthetic	
δ_{C}	Assignment	δ_{C}	$\Delta\delta_{\text{C}}$ ^b
5.8	C-1	6.1	0.3
29.9	C-2	30.1	0.2
102.1	C-3	103.2	0.1
37.7	C-4	37.8	0.1
78.7	C-5	78.8	0.1
43.0	C-6	43.1	0.1
97.5	C-7	97.7	0.1
35.0	C-8	35.2	0.2
105.2	C-9	105.4	0.2
40.7	C-10	40.9	0.2
79.4	C-11	79.6	0.2
134.6	C-12	134.7	0.3
132.7	C-13	132.9	0.2
131.6	C-14	131.7	0.1
132.1	C-15	132.3	0.2
21.4	C-16	21.6	0.2
14.1	C-17	14.4	0.3
16.7	$\text{CH}_3\text{C-14}$	16.9	0.2
12.3	$\text{CH}_3\text{C-12}$	12.5	0.2
10.4	$\text{CH}_3\text{C10}$	10.6	0.2
6.6	$\text{CH}_3\text{C-8}$	6.9	0.3

^a Data and assignments according to Ireland et al. (ref. 11); numbering according to Paterson et al. (ref 12).

^b δ_{C} (synthetic) - δ_{C} (natural). The consistent $\Delta\delta_{\text{C}}$ of ca. 0.2 is presumably due to a different reference standard; we used $\delta_{\text{C}}(\text{CDCl}_3) = 77.23$ while Ireland et. al likely used $\delta_{\text{C}}(\text{CDCl}_3) = 77.0$.

Structure Determination for Triol 14

Triol **14** was converted into an inseparable 7:3 mixture of **S6a** and **S6b**, respectively. The ^{13}C NMR spectrum for the mixture clearly indicated that each acetonide was derived from a 1,3-*anti* diol (acetonide Me's at δ 25.4 & 23.7 for **S6a** and δ 25.3 & 23.6 for **S6b**),¹³ thereby establishing a 3,5-*anti*-, 5,7-*anti* relative configuration for **14**. In the major isomer **S6a**, the ^1H NMR spectra indicated $^3J_{\text{H-H}}$ coupling constants of 4.5 and 8 Hz for HC-6''-HC-5'' and HC-5''-HC-4'', respectively, indicating 4'',5''-*anti*-, 6'',5''-*syn* relative configuration in **S6a** and therefore a 5,6-*anti*-, 6,7-*syn* relative configuration in **14**. The 2,3-*syn*-, 3,4-*syn* relative configuration in **14** is determined by the structure of **9**. Thus the relative and absolute configurations of **12**, **13**, **S2**, **S3**, and **14** are established as indicated.

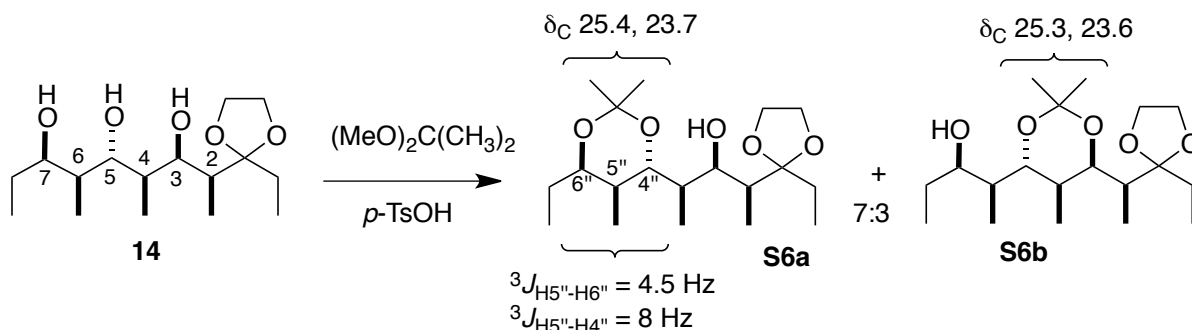
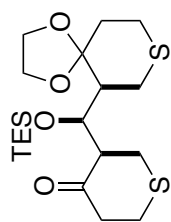
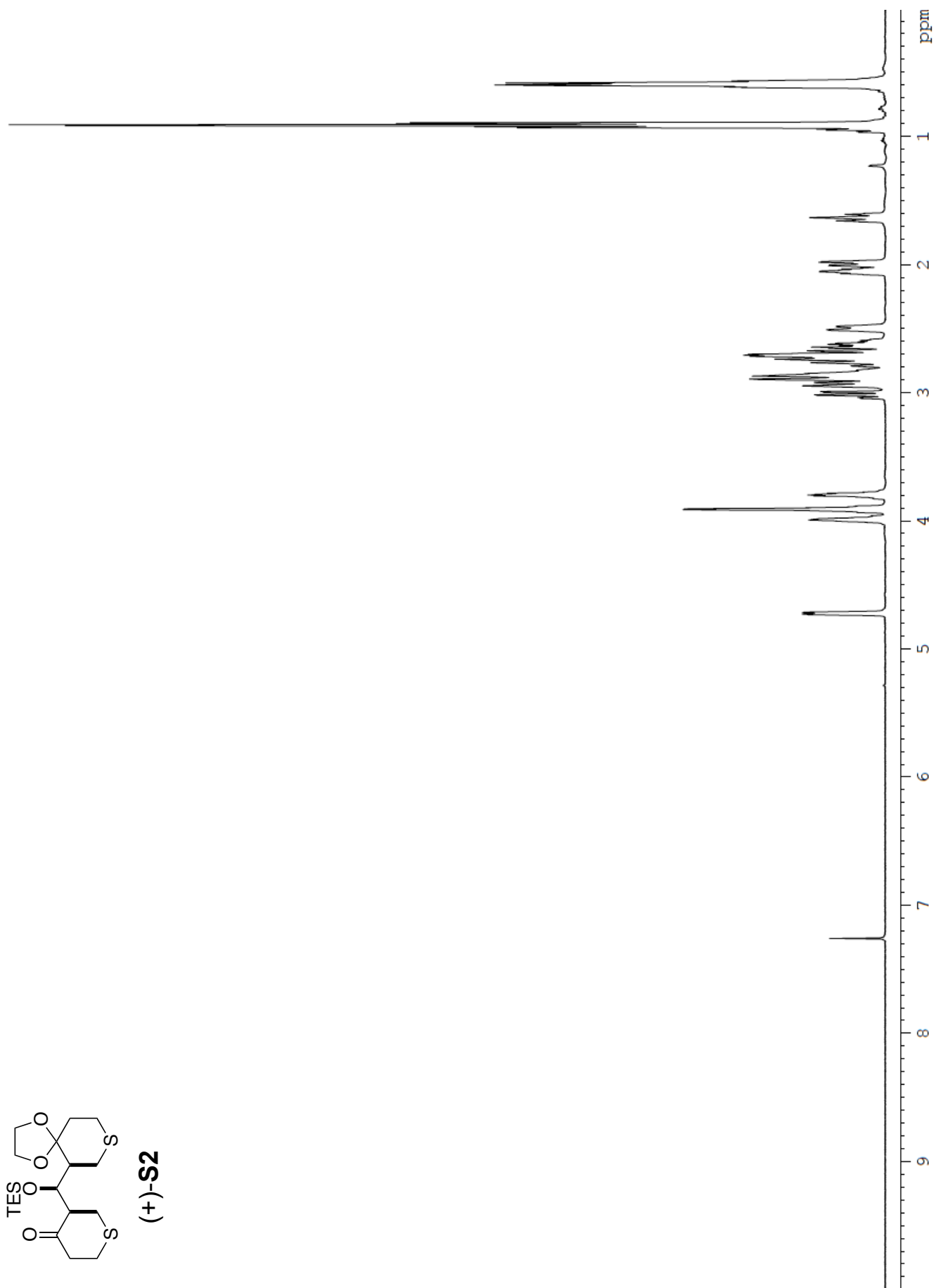


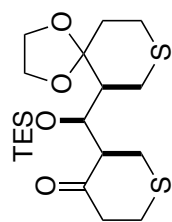
Figure S1. Determination of the relative configuration of **14** by conversion to acetonides **S6a** and **S6b**.

(2*S*,3*R*,4*R*)-2-(2-Ethyl-1,3-dioxolan-2-yl)-4-[(4*R*,5*S*,6*R*)-6-ethyl-2,2,5-trimethyl-1,3-dioxan-4-yl]pentan-3-ol (**S6a**) and (2*S*,3*R*)-2-[(4*S*,5*S*,6*R*)-6-((*S*)-1-(2-Ethyl-1,3-dioxolan-2-yl)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl]pentan-3-ol (**S6b**).

S6a and **S6b** were prepared from triol **14** (10 mg, 0.033 mmol) in CH_2Cl_2 (1 mL) and 2,2-dimethoxypropane (0.5 mL) in the presence of $p\text{-TsOH} \cdot \text{H}_2\text{O}$ (2.5 mg, 0.01 mmol) for 5 min. The mixture was diluted with CH_2Cl_2 , washed with saturated aq NaHCO_3 , dried over Na_2SO_4 , concentrated, and fractionated by PTLC (20% ethyl acetate in hexane) to give an inseparable 7:3 mixture of **S6a** and **S6b**, respectively (8 mg, 70%): colorless oil, TLC R_f = 0.6 (20% ethyl acetate in hexane); ^1H NMR (500 MHz, C_6D_6) δ (* major isomer) 4.31 (0.7H, ddd, J = 1, 3.5, 5 Hz, *HC-3), 4.08 (0.3H, dd, J = 4.5, 7.5 Hz, HC-6'), 4.05-4.01 (0.3H, m, HC-3), 3.73 (0.7H, ddd, J = 4.5, 4.5, 9 Hz, *HC-6'' [$^3J_{\text{HC-5''}} = 4.5$ Hz]), 3.48 (4H, br s, *H₂C-C-4', H₂C-4''', *H₂C-5', H₂C-5'''), 3.36 (1H, ap dd, J = 4, 8 Hz, *HC-4'', HC-4'), 3.24 (0.7H, d, J = 1 Hz, *HOC-3), 3.11 (0.3H, d, J = 2 Hz, HOC-3), 2.17 (0.7H, dq, J = 5, 7 Hz, *HC-2), 2.14-2.04 (1.3H, m, *HC-4, HC-1'', HC-5'), 1.91 (0.7H, ddq, J = 4.5, 8, 7 Hz, *HC-5'' [$^3J_{\text{HC-6''}} = 4.5$ Hz, $^3J_{\text{HC-4''}} = 8$ Hz]), 1.85 (0.7H, dq, J = 14, 7.5 Hz, *HC-1'''), 1.81-1.60 (2H, m, *HC-1'', H₂C-1''', HC-4), 1.56 (0.3H, ddq, J = 2.5, 4, 7 Hz, HC-2), 1.44 (0.7H, ddq, J = 9, 13.5, 7.5 Hz, *HC-1'''), 1.39 (2.1H, d, J = 7 Hz, *H₃C-1), 1.37-1.30 (0.3H, m, HC-4), 1.29 (2.1H, s, *H₃C-2''), 1.27 (2.1H, d, J = 7 Hz, *H₃C-5), 1.26 (0.9H, s, H₃C-2'), 1.23 (2.1H, s, *H₃C-2''), 1.23 (0.9H, d, J = 7 Hz, H₃C-2''), 1.22 (0.9H, s, H₃C-2'), 1.15 (0.7H, ddq, J = 4.5, 13.5, 7.5 Hz, *HC-1'''), 1.06 (0.9H, t, J = 7 Hz, H₃C-5), 1.06 (0.9H, d, J = 7 Hz, HC-2), 0.98 (2.1H, t, J = 7.5 Hz, *H₃C-2'''), 0.97 (0.9H, d, J = 7 Hz, H₃CC-5'), 0.93 (0.9H, t, J = 7.5 Hz, H₃C-2'''), 0.88 (2.1H, t, J = 7.5 Hz, *H₃C-2'''), 0.81 (2.1H, d, J = 7 Hz, *H₃CC-5''); ^{13}C NMR (125 MHz, CDCl_3) δ (* major isomer) 114.4* (s), 113.8 (s), 101.2 (s), 100.9* (s), 81.0 (d), 80.2* (d), 73.7 (d), 71.5* (d), 70.8* (d), 69.3 (d), 65.3 (t), 65.23* (t), 65.21* (t), 65.0 (t), 42.4* (d), 40.0* (d), 39.8 (d), 39.2 (d), 39.0 (d), 37.0* (d), 27.4 (t), 26.78* (t), 26.73 (t), 25.4* (q, CH₃C-2''), 25.3 (q, CH₃C-2'), 23.8* (t), 23.7* (q, CH₃C-2''), 23.6 (q, CH₃C-2'), 13.6 (q), 12.4 (q), 12.34* (q), 12.29* (q), 12.0 (q), 11.2 (q), 10.8* (q \times 2), 7.6* (q), 7.4 (q); HRMS m/z calcd for $\text{C}_{19}\text{H}_{36}\text{O}_5 + \text{Na}$: 367.2454; found: 367.2443 (ESI).

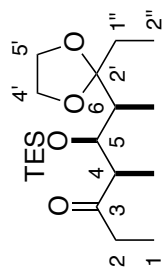
¹³ Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, 58, 3511-3515.

**(+)-S2**

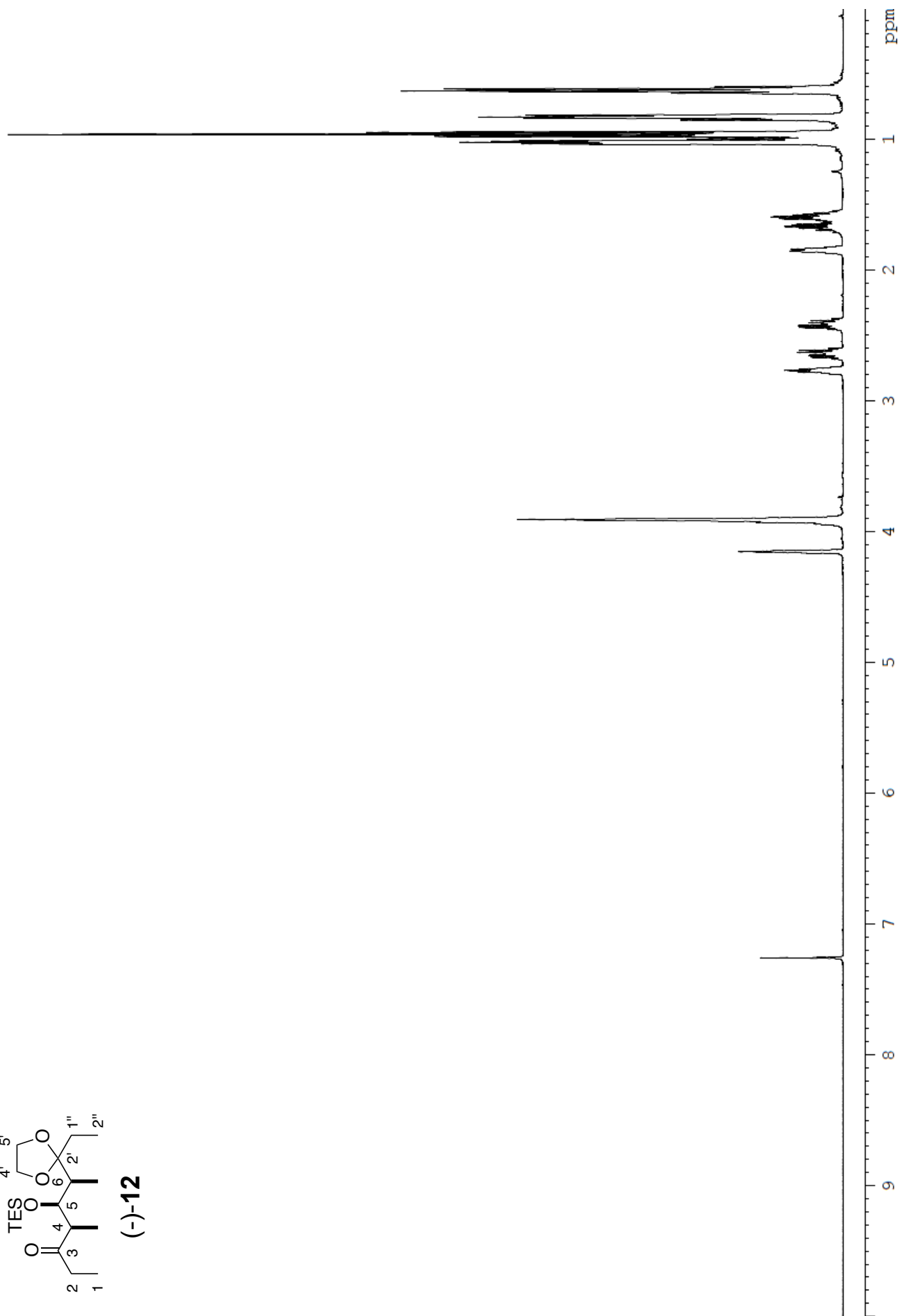


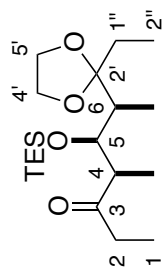
(+)-**S2**



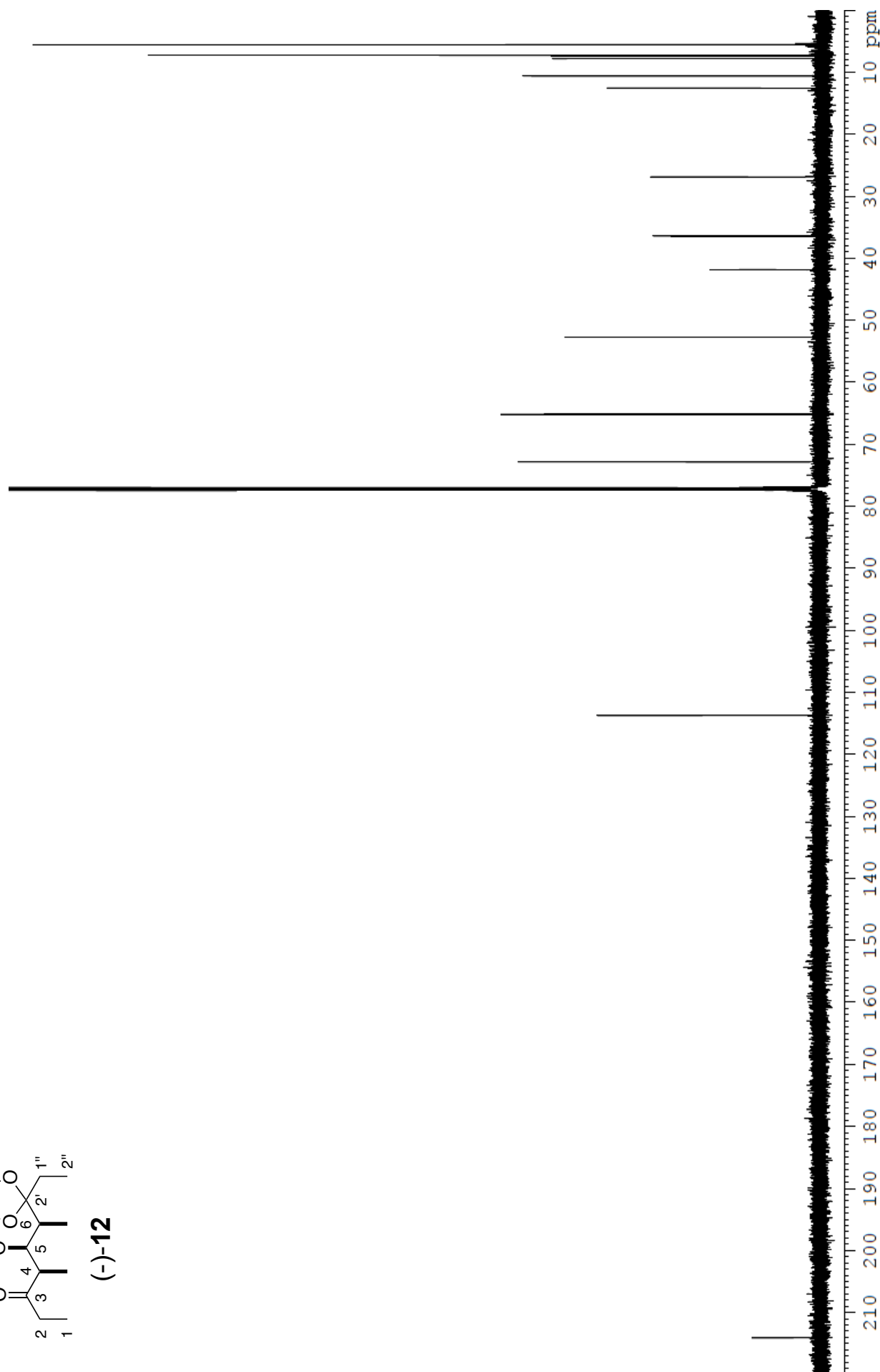


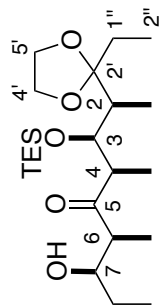
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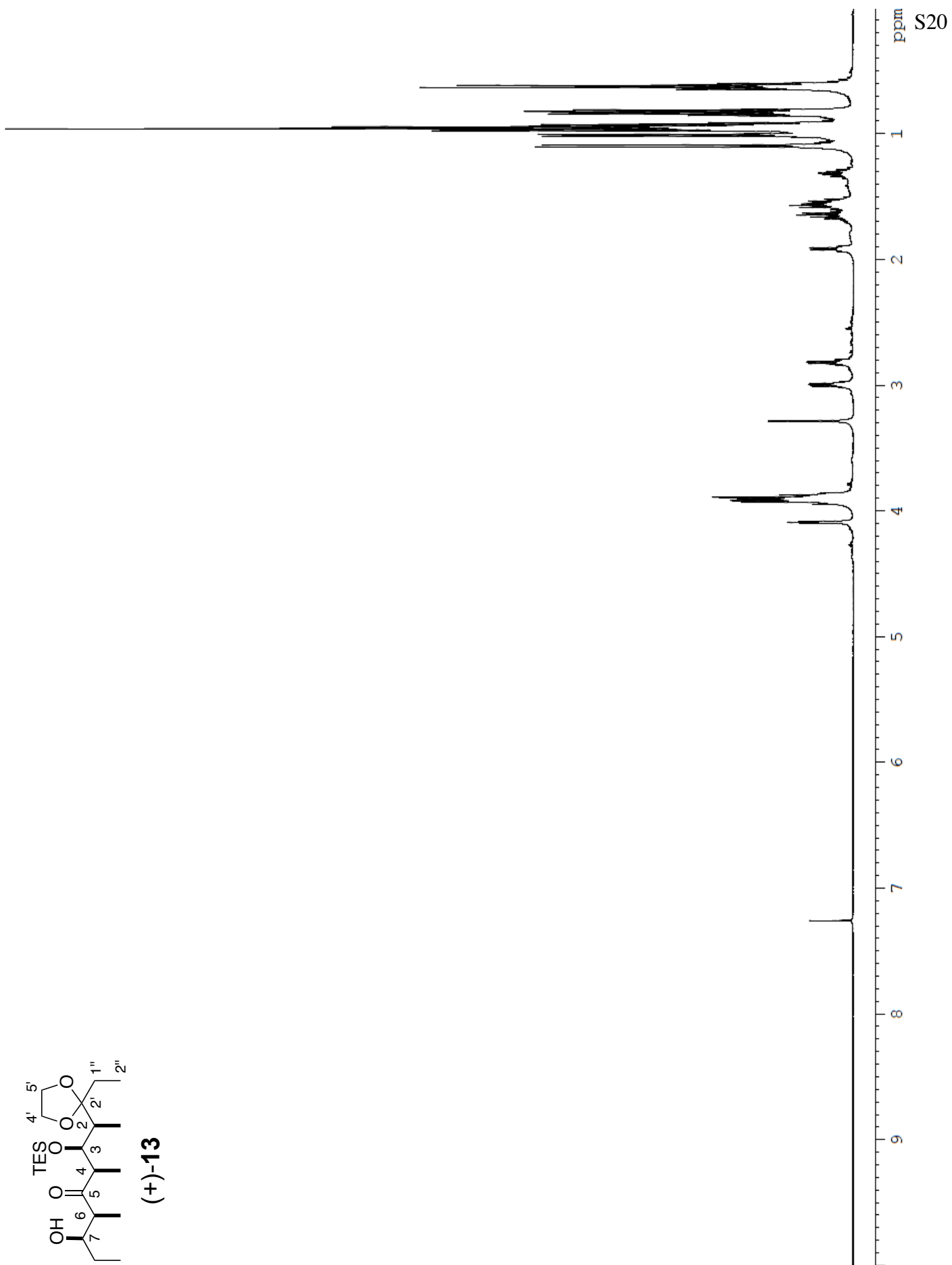


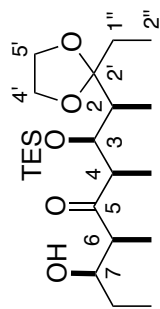
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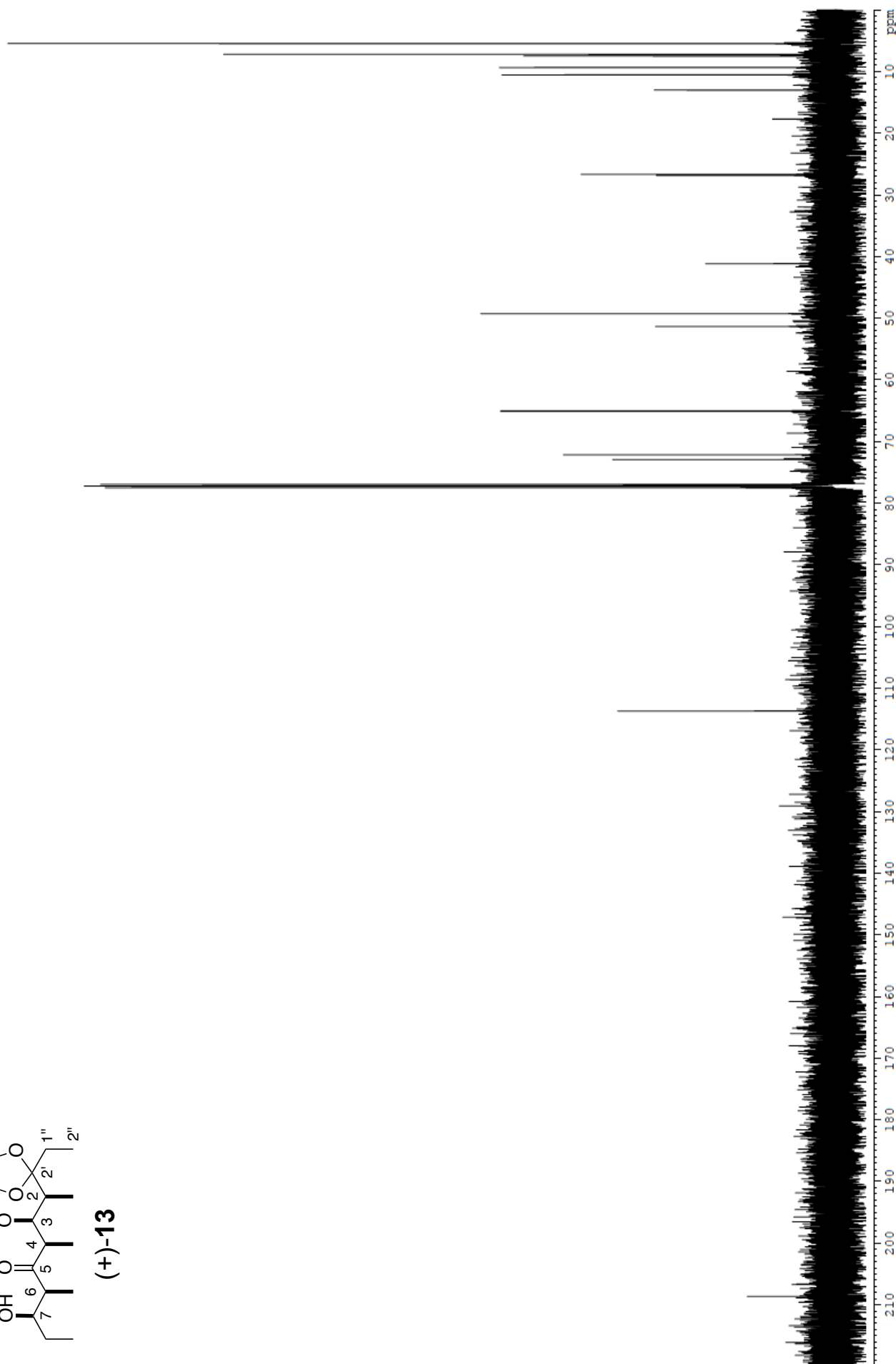


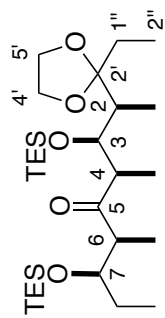
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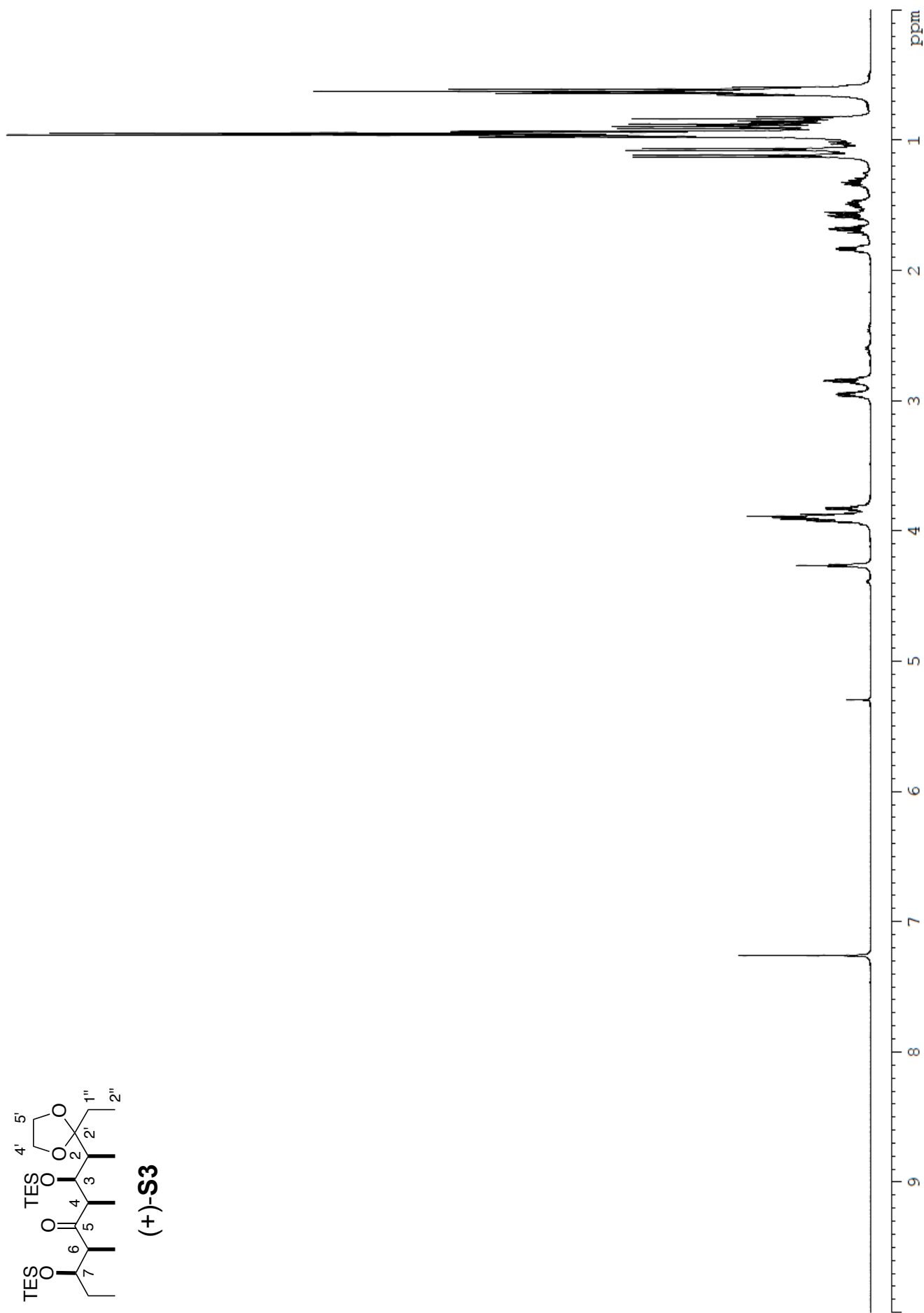


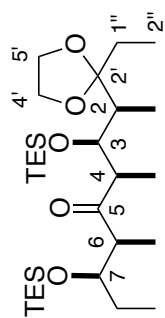
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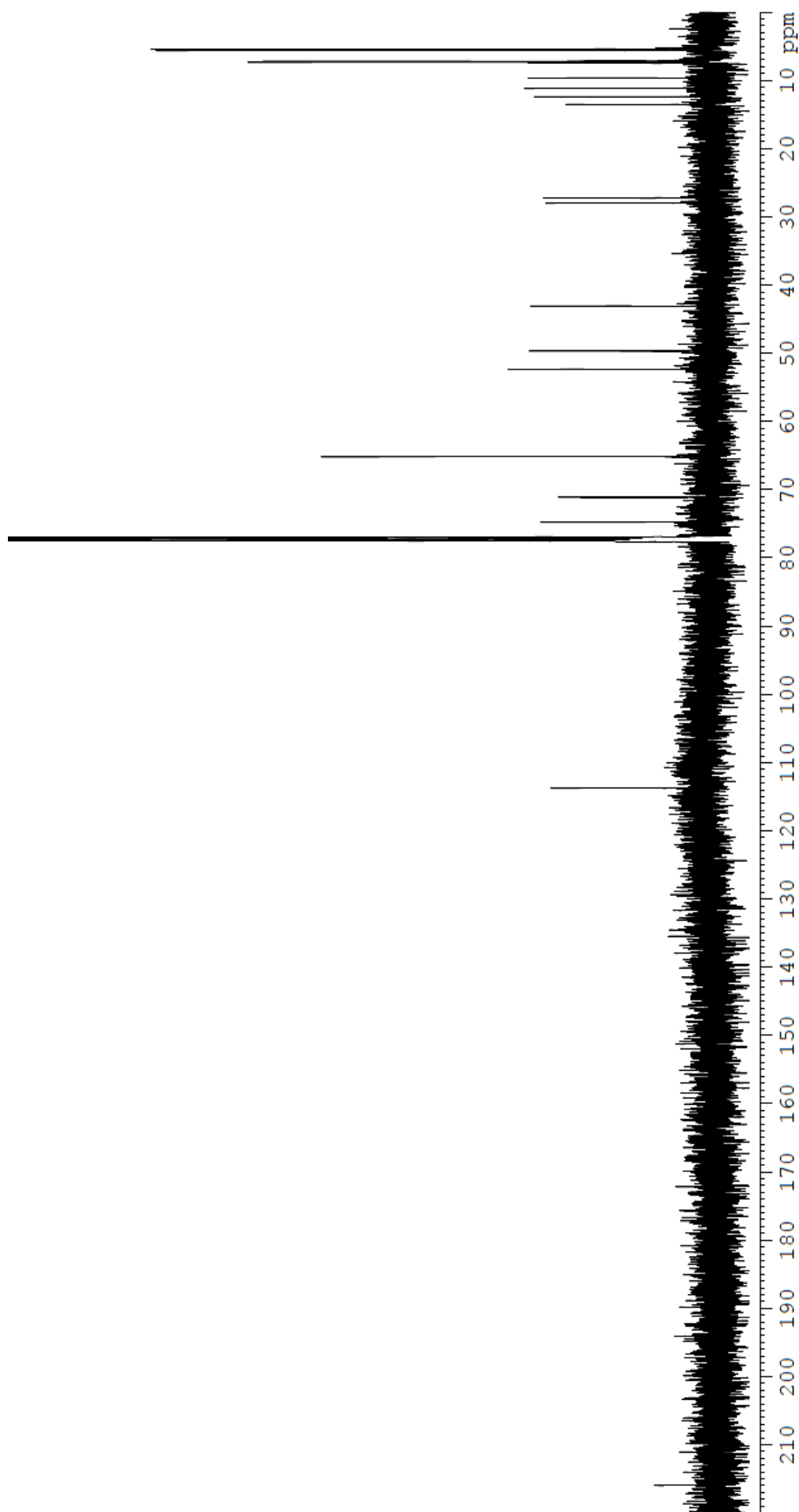


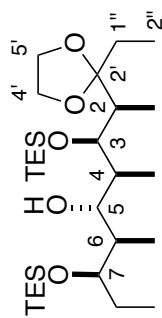
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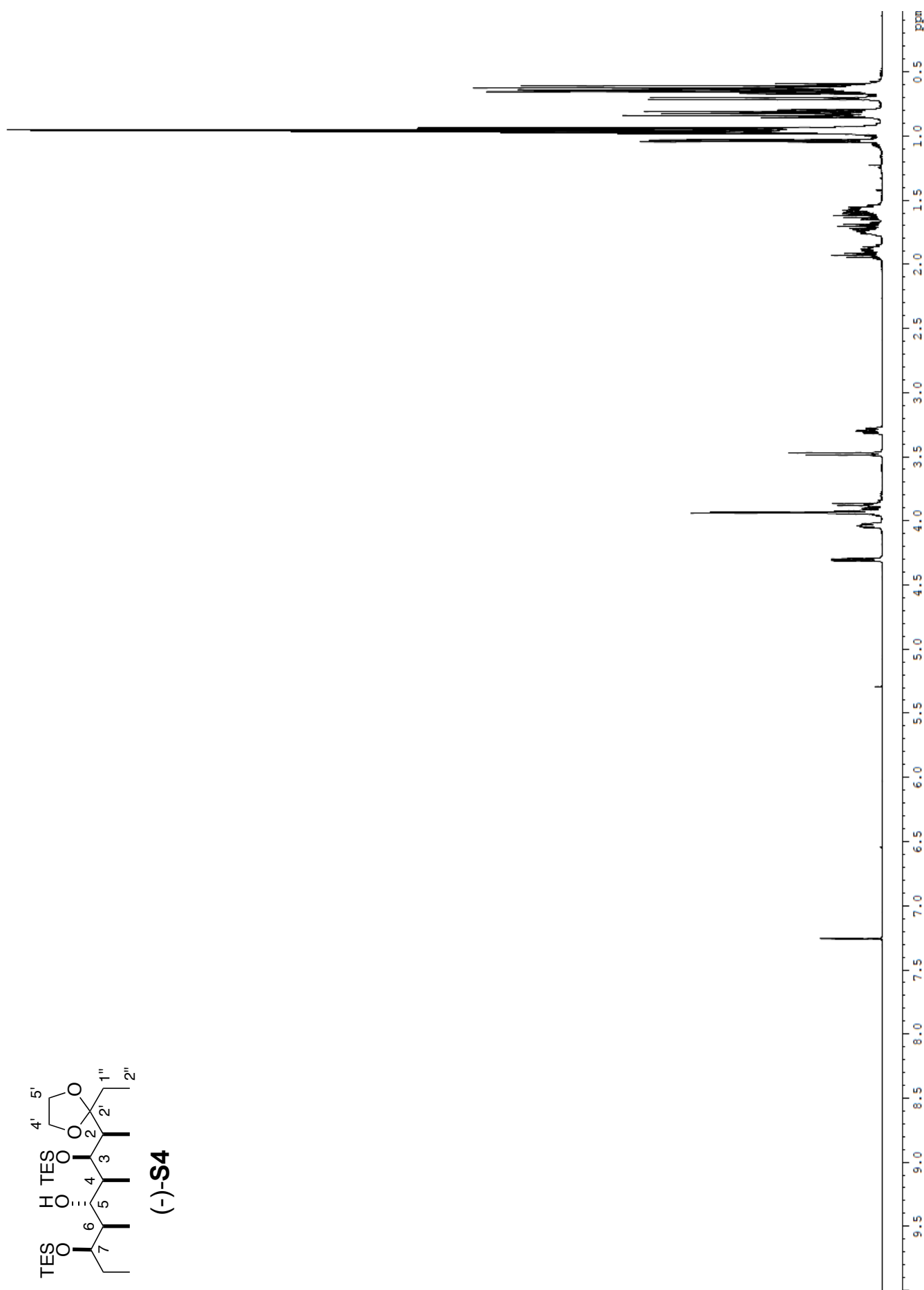


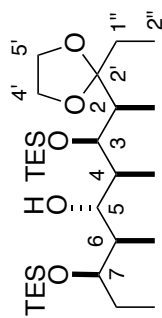
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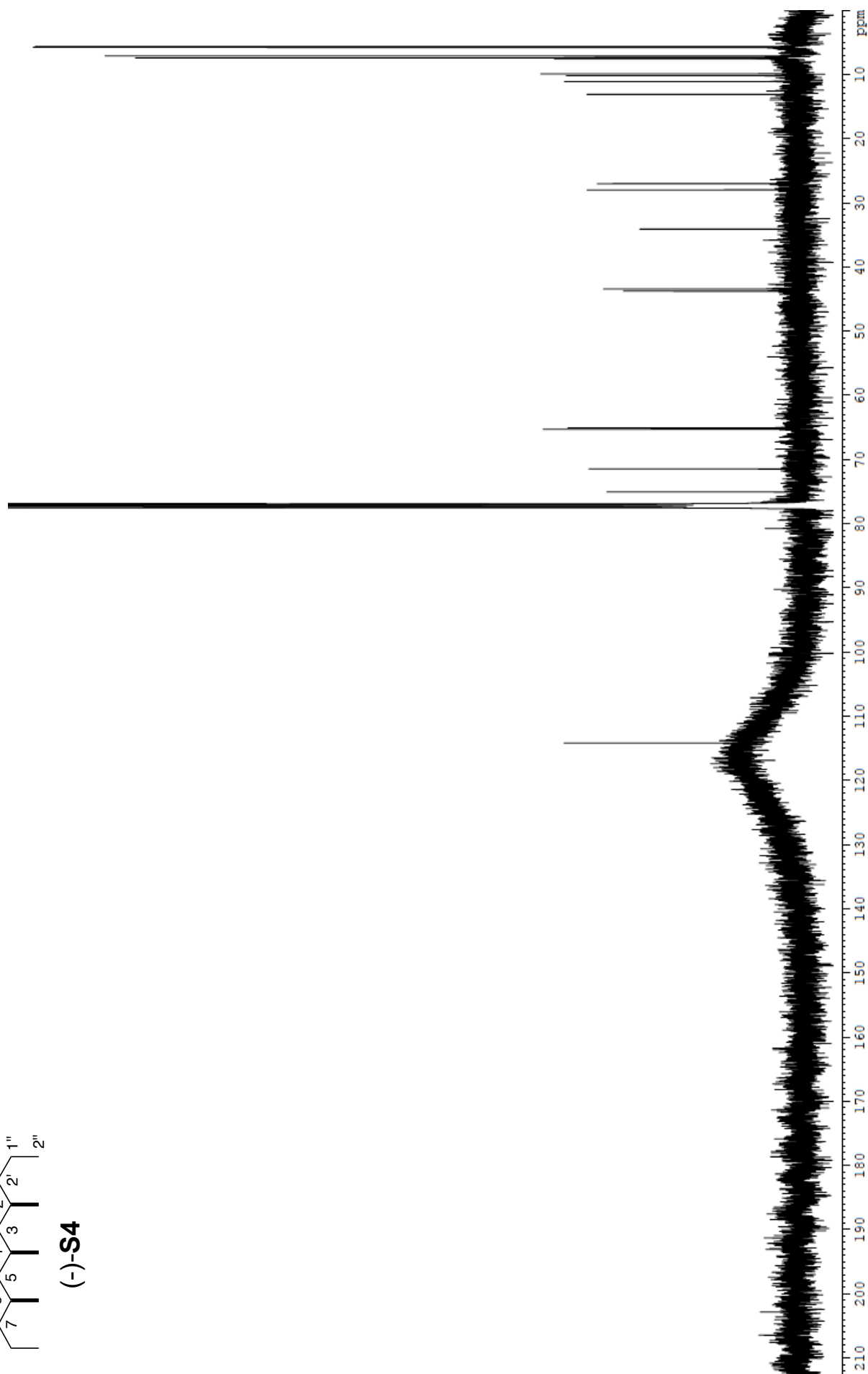


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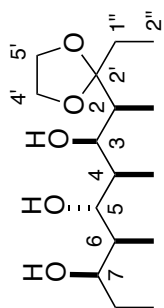




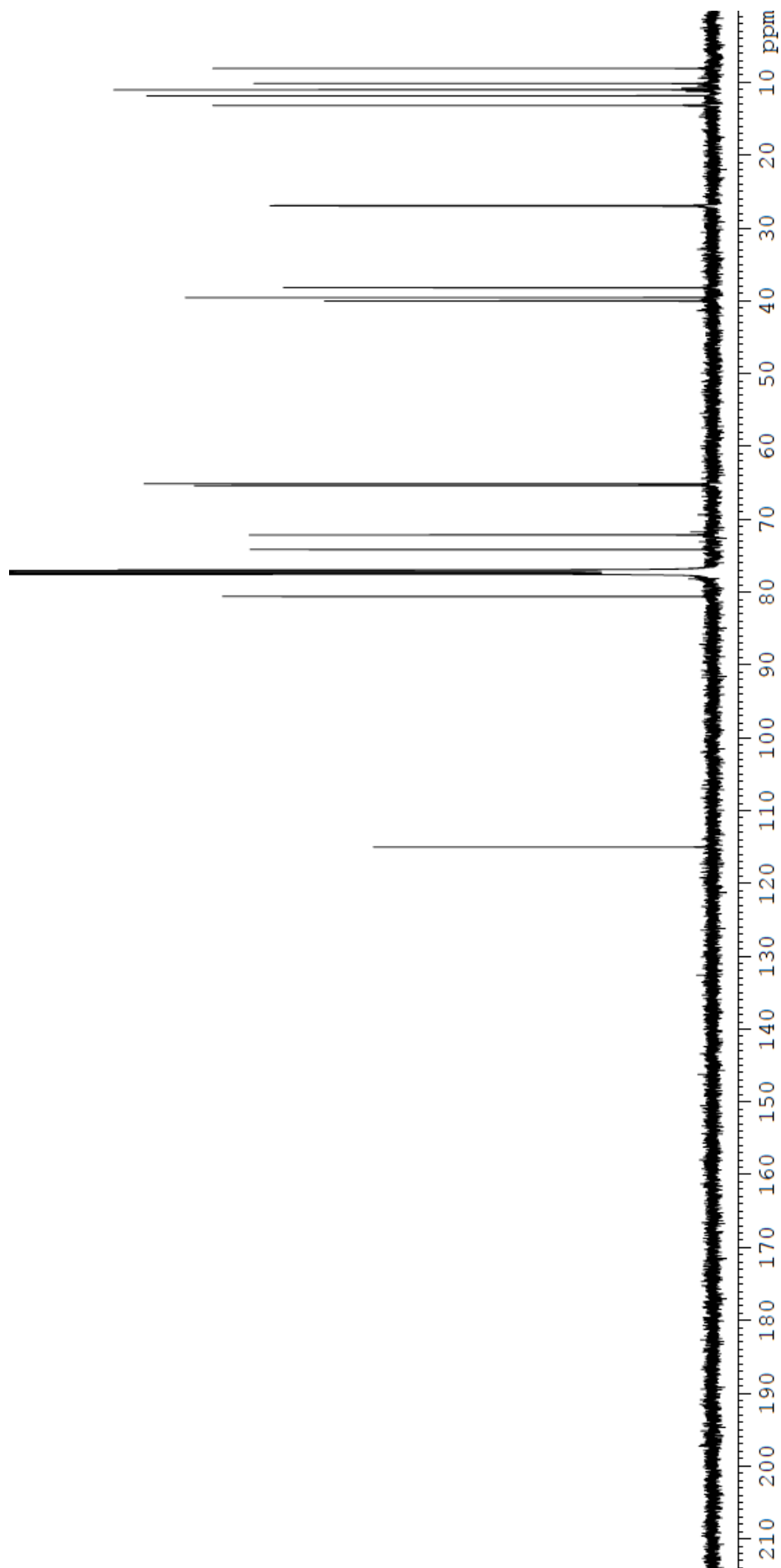
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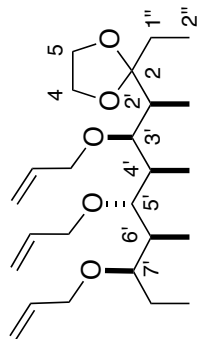




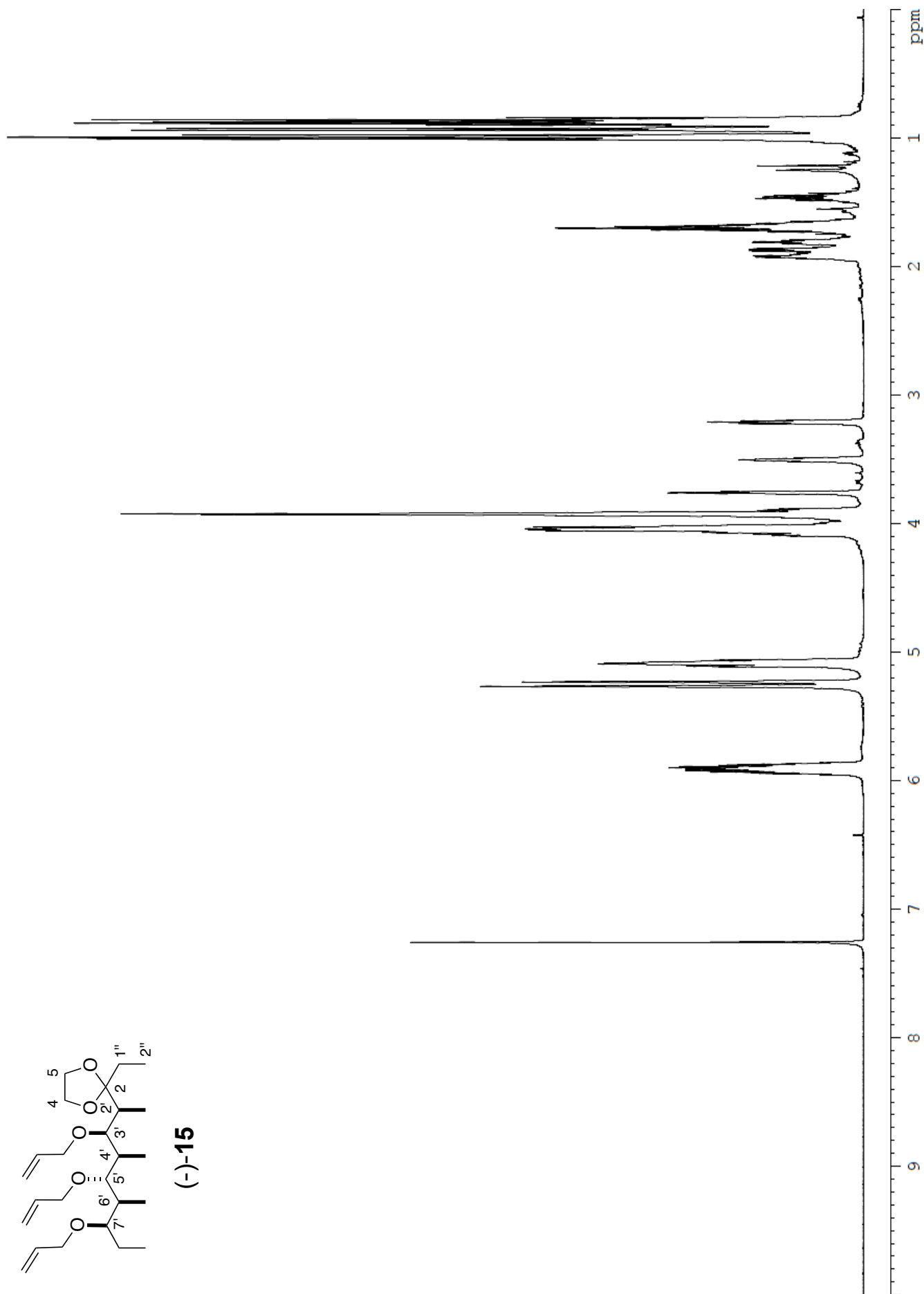


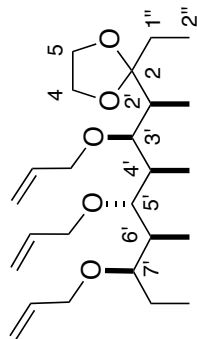
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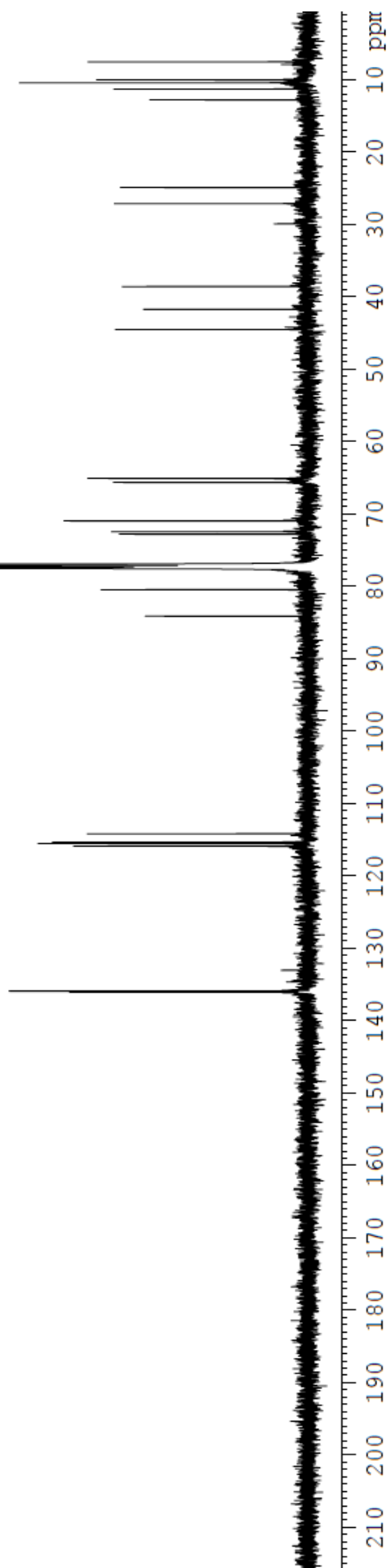


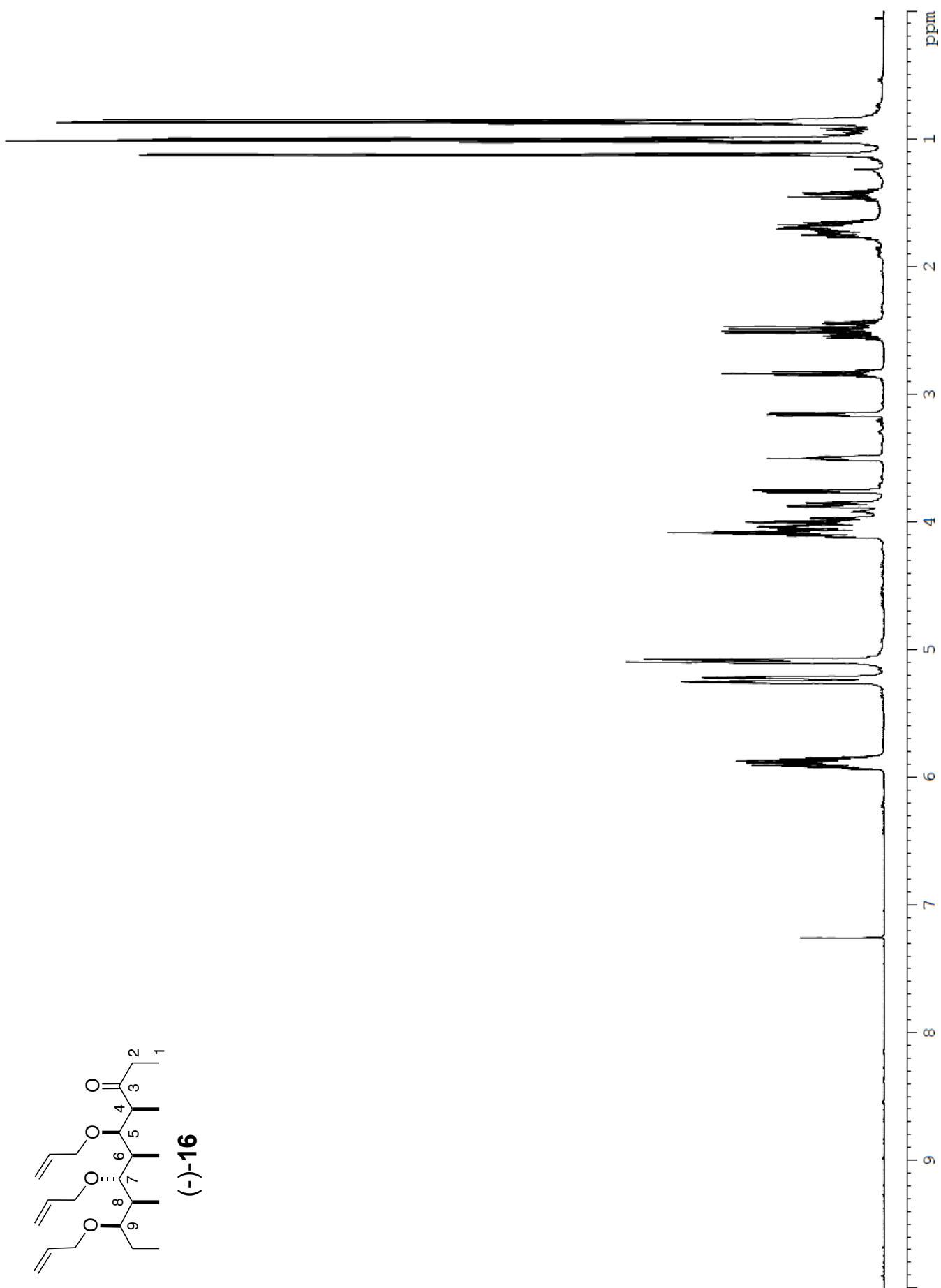
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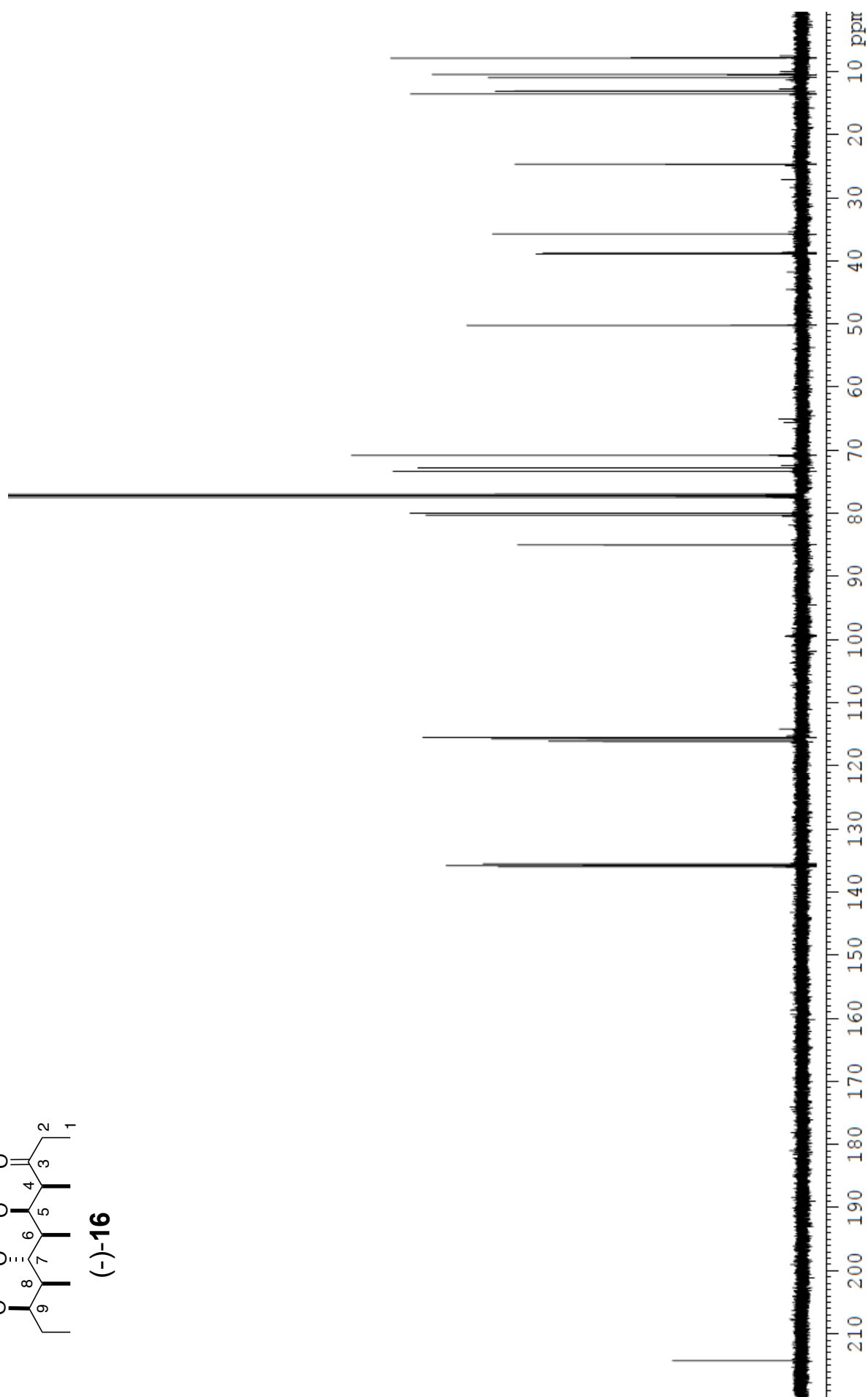
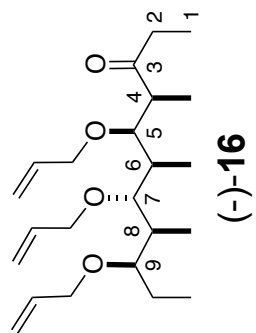


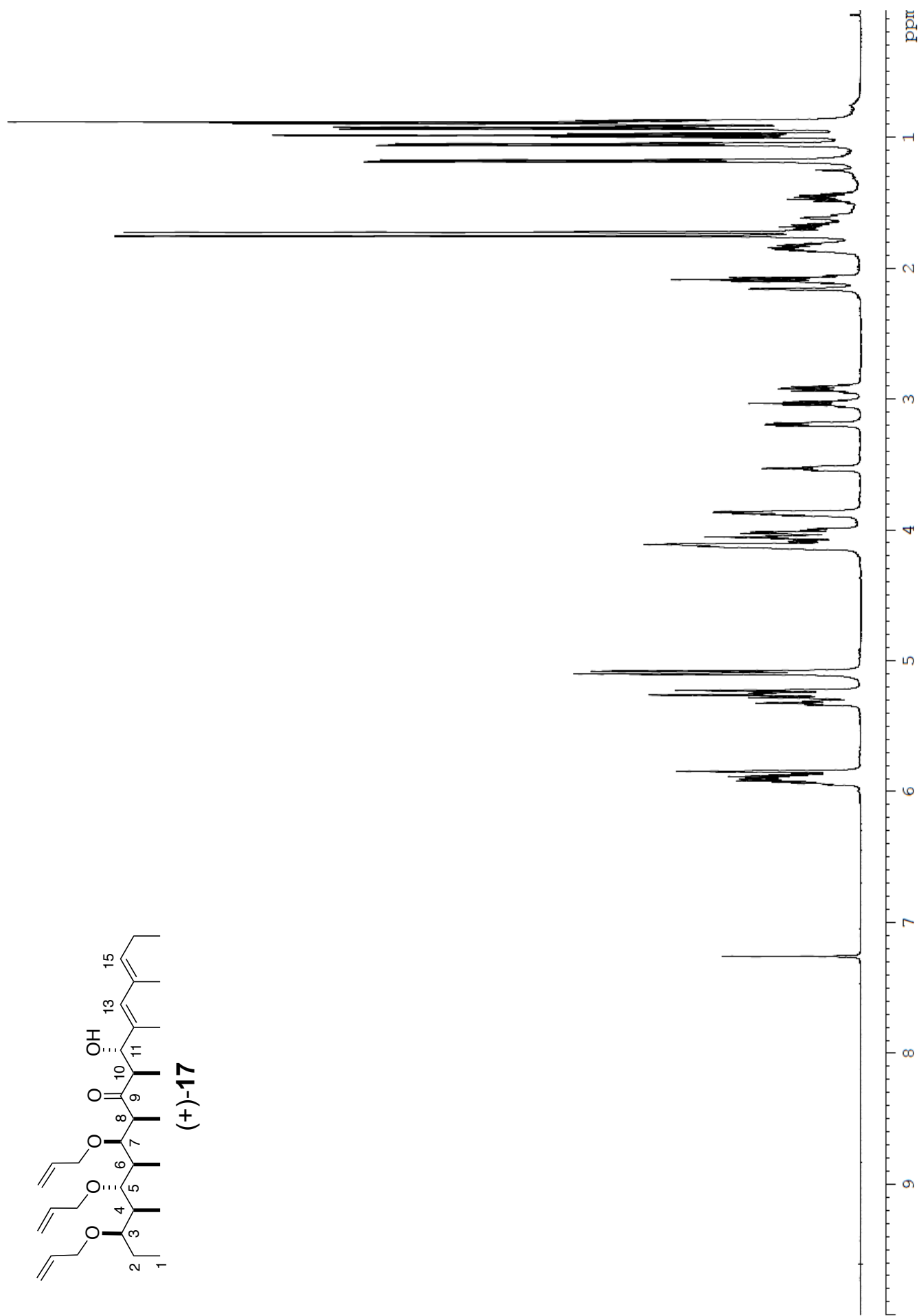
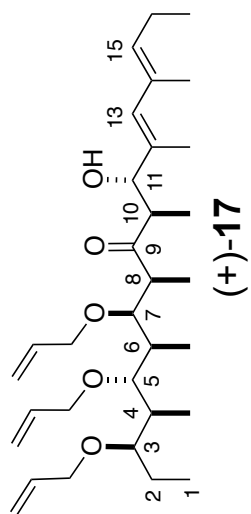


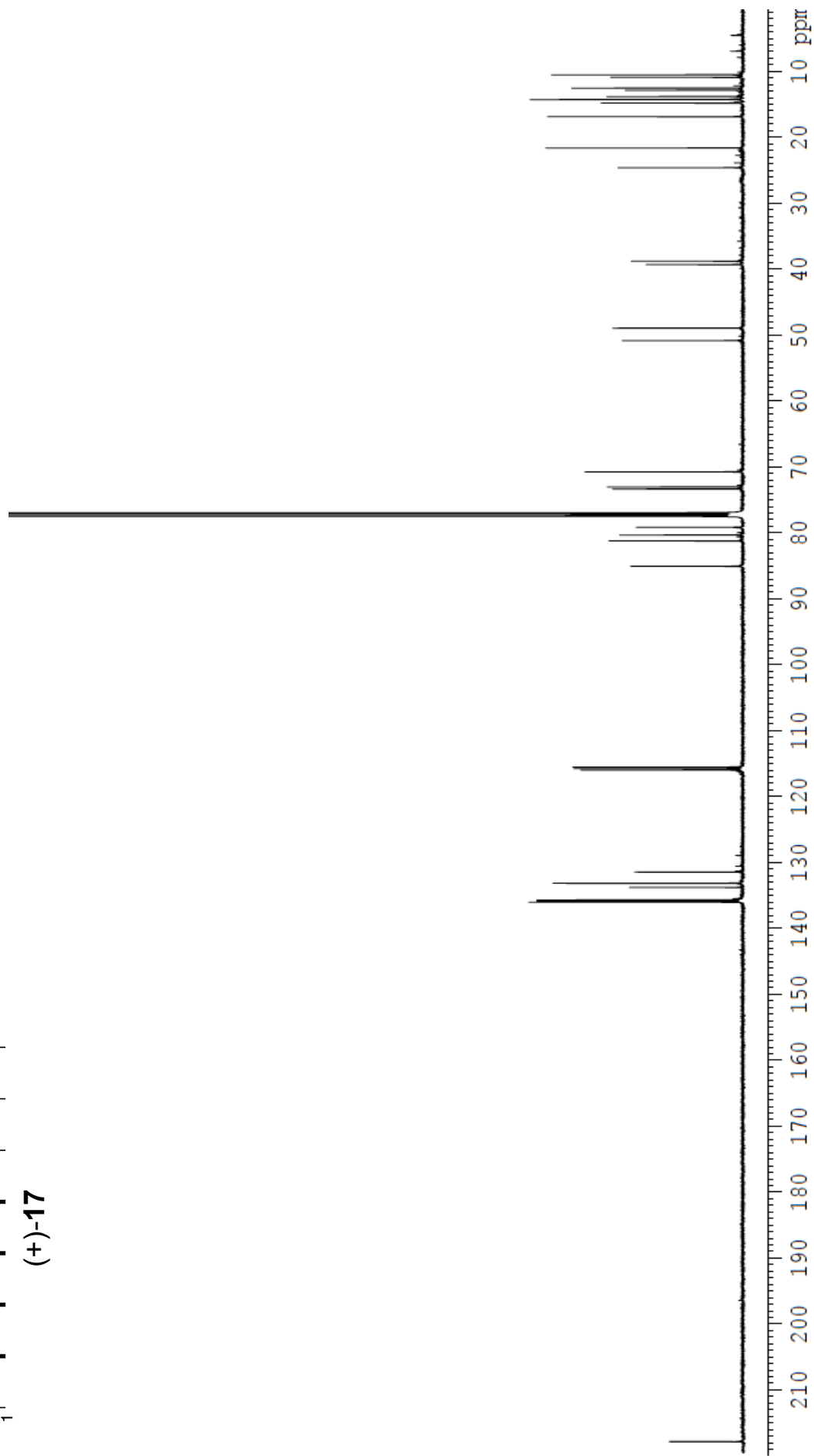
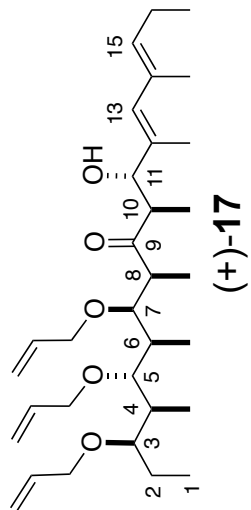
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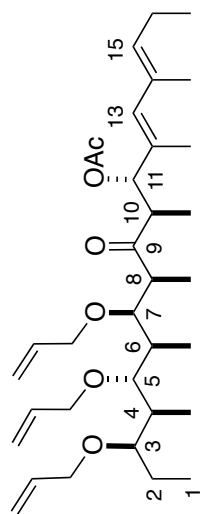




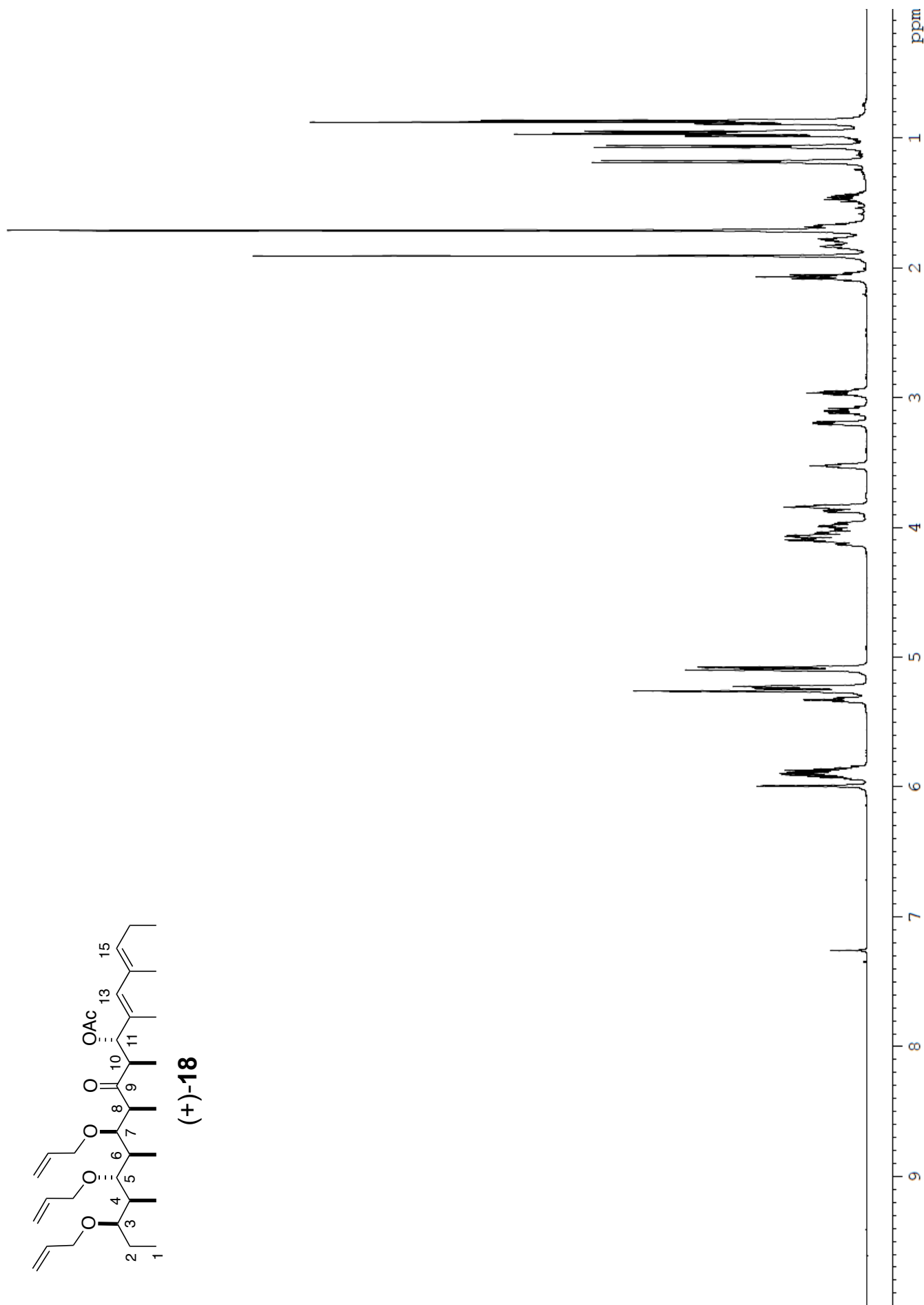


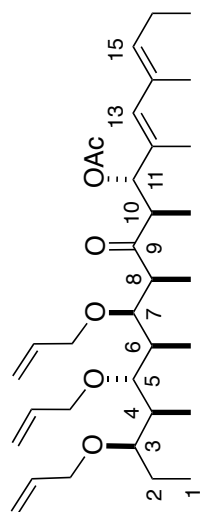




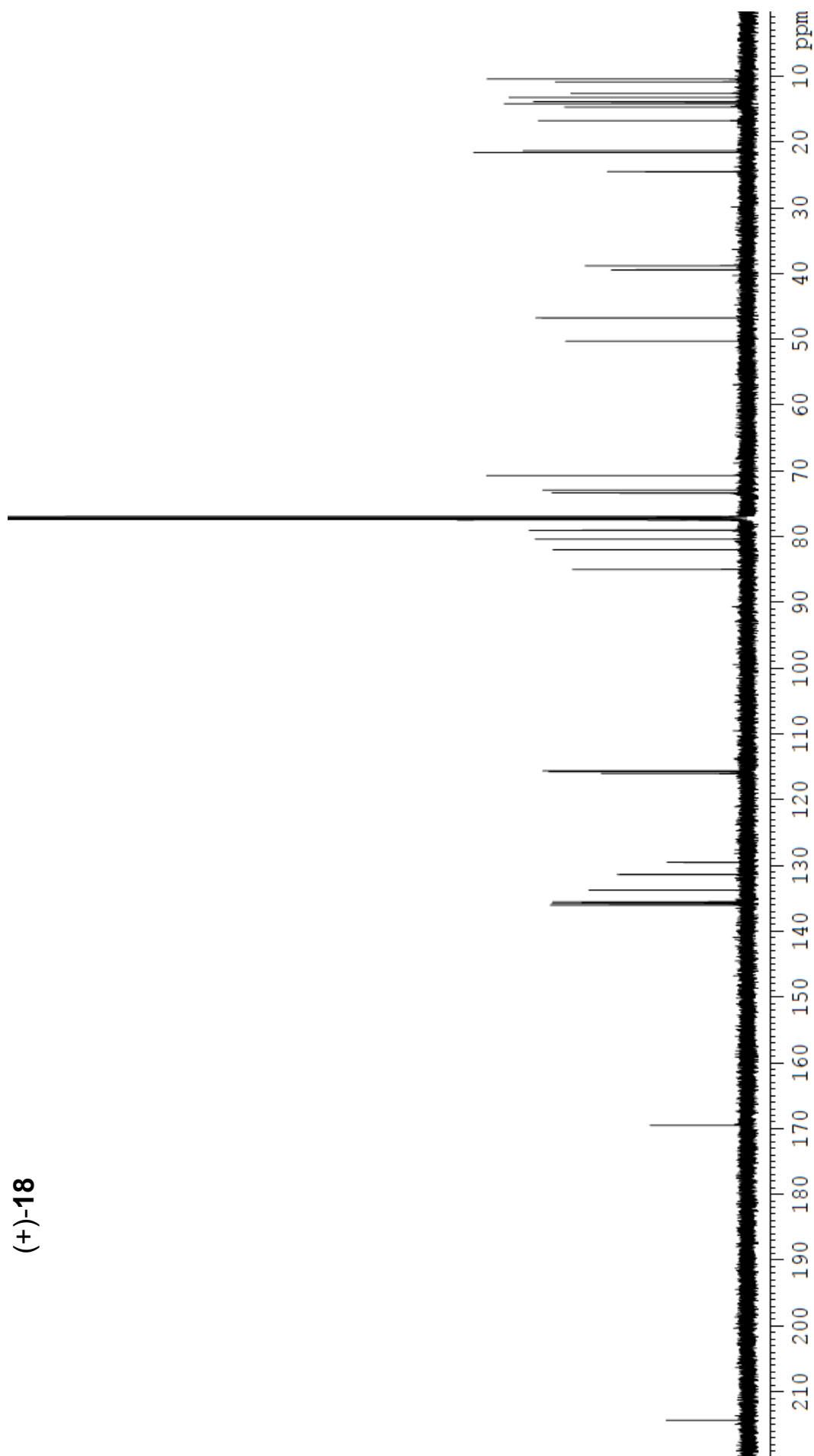


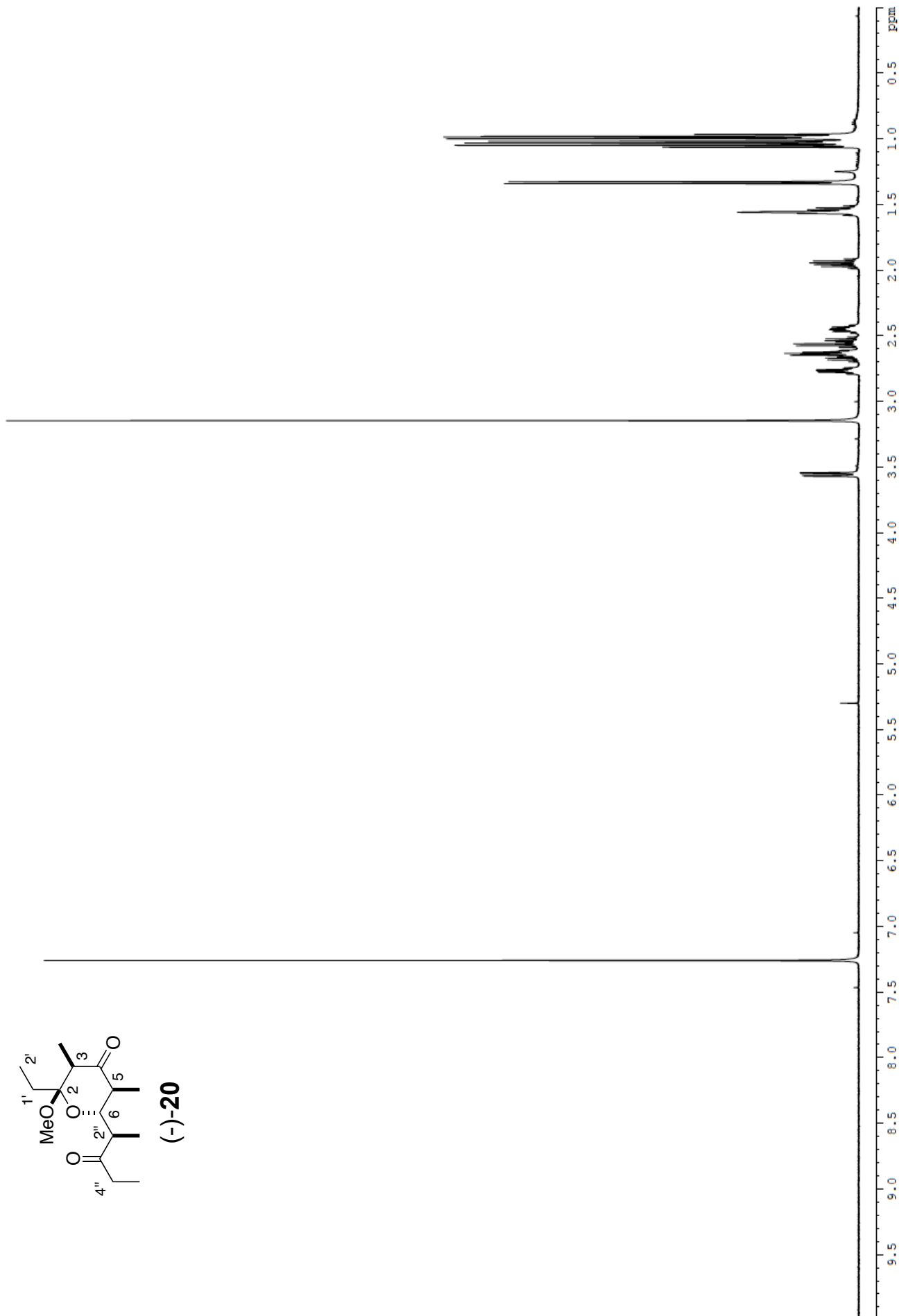
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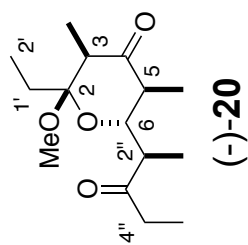




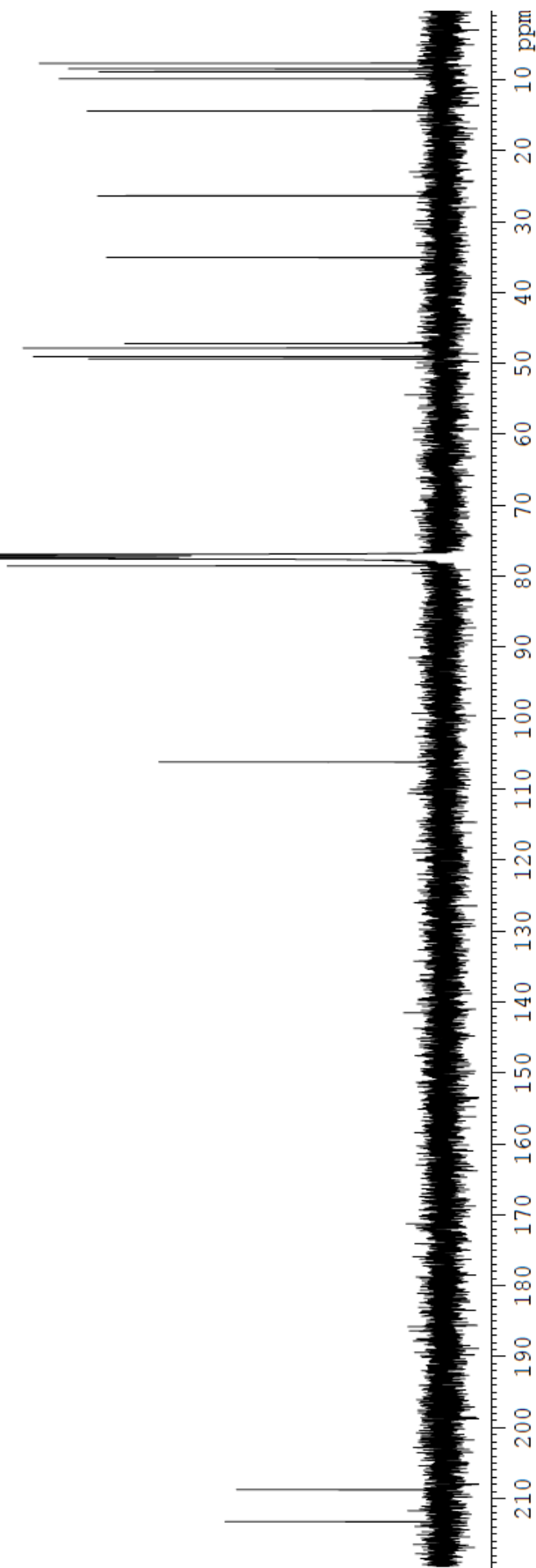
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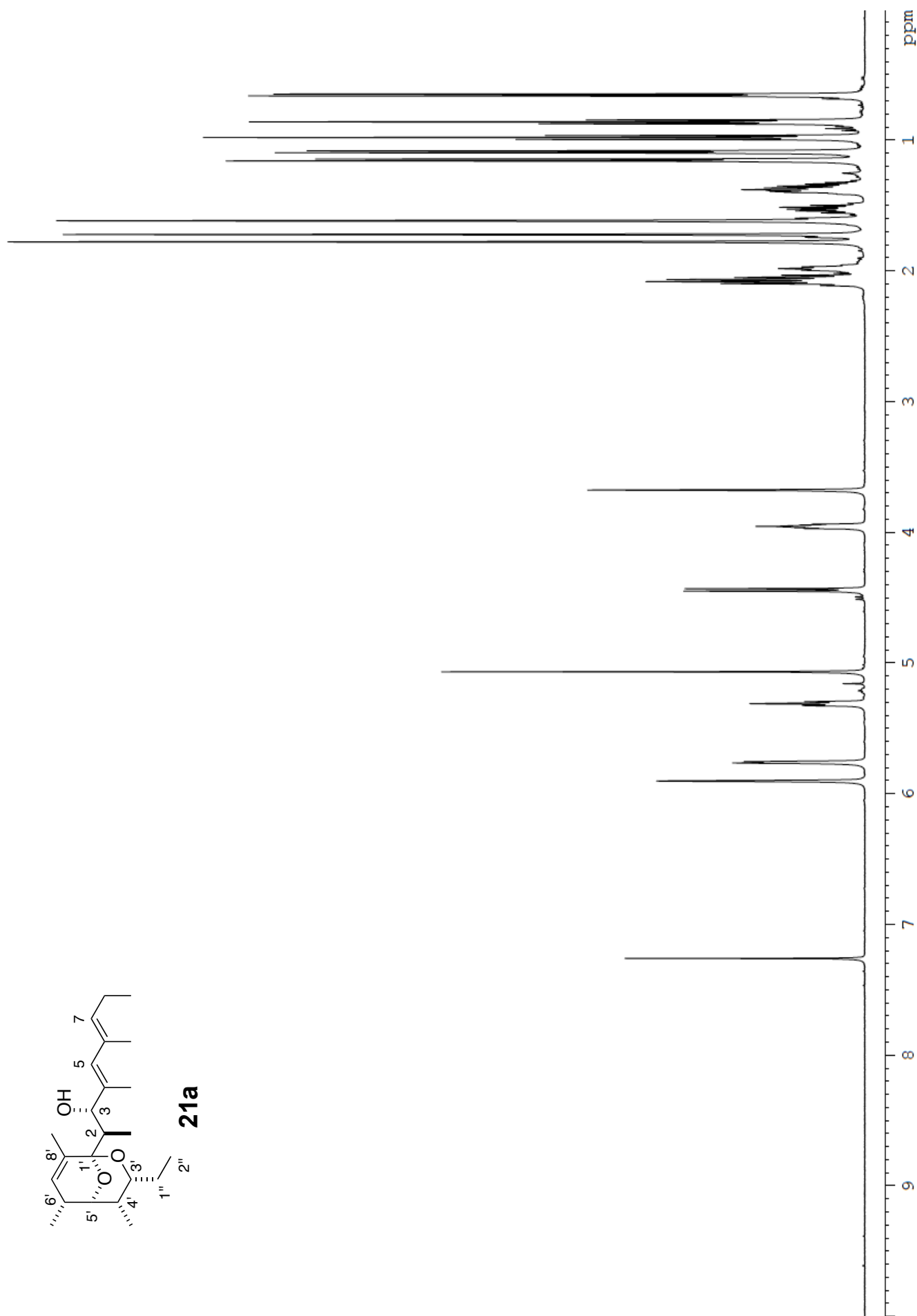
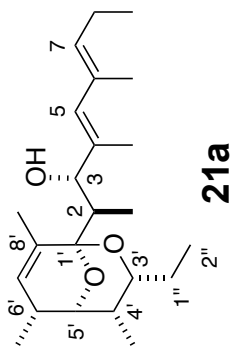


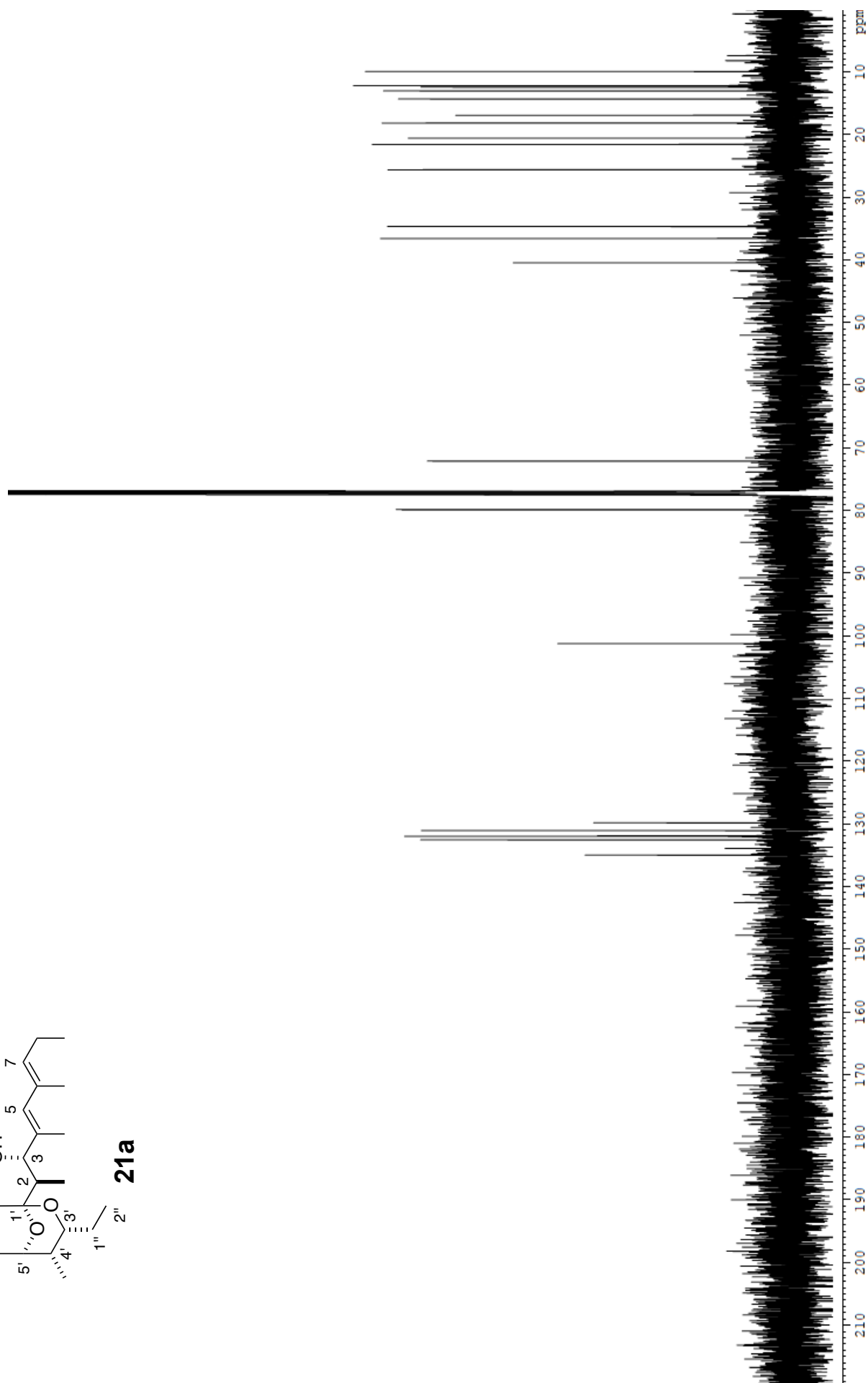
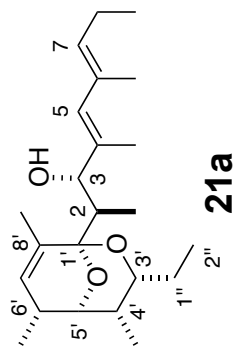


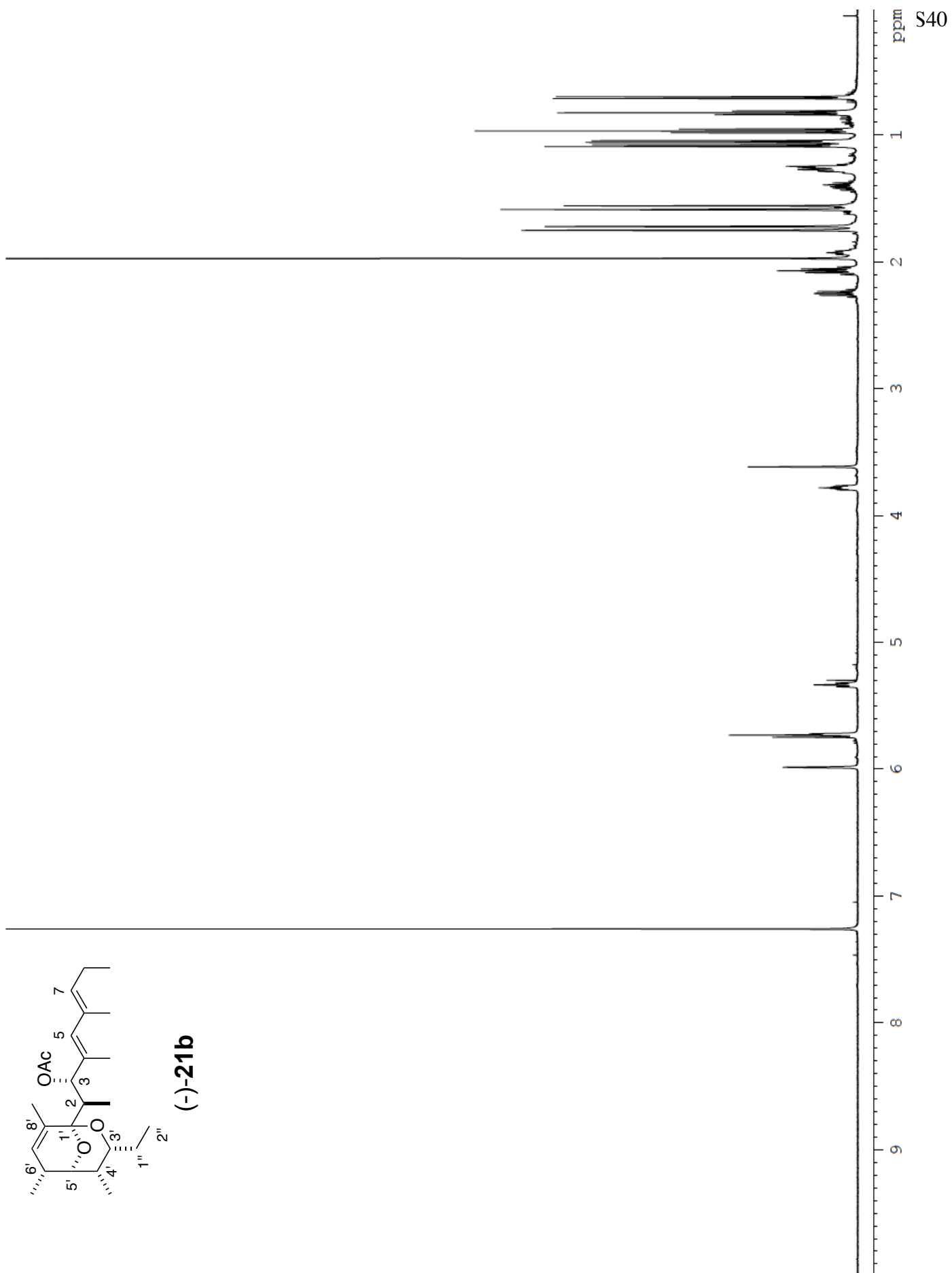
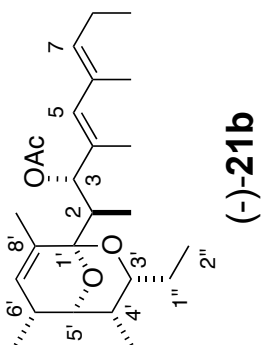


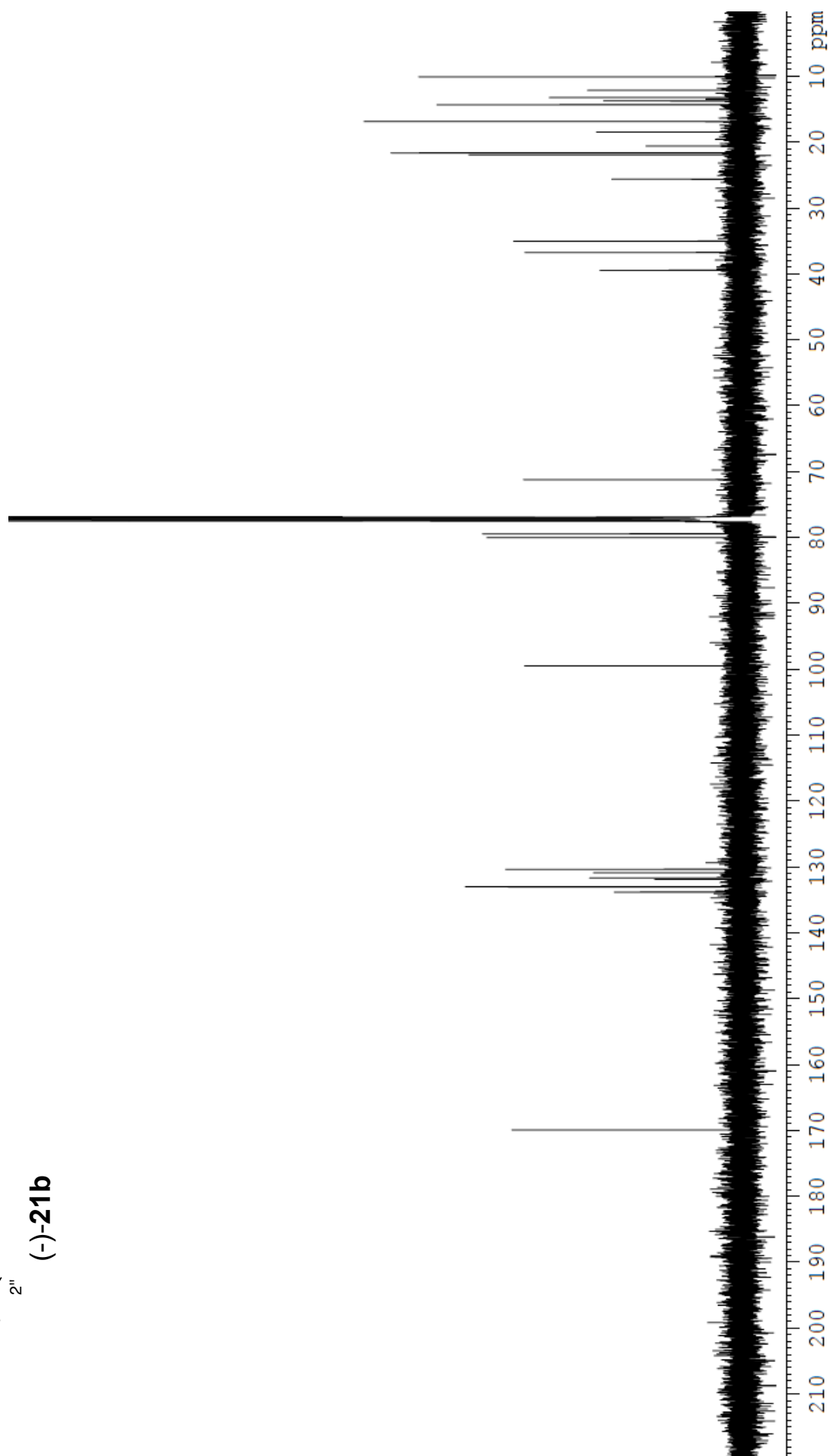
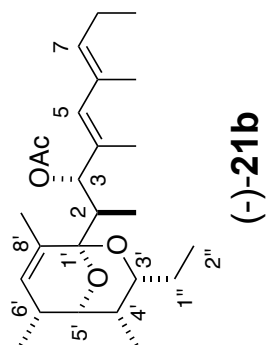
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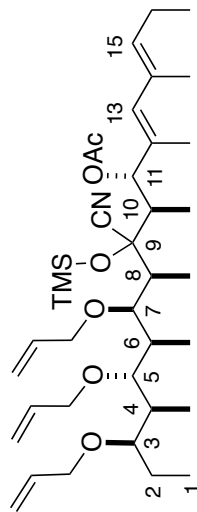




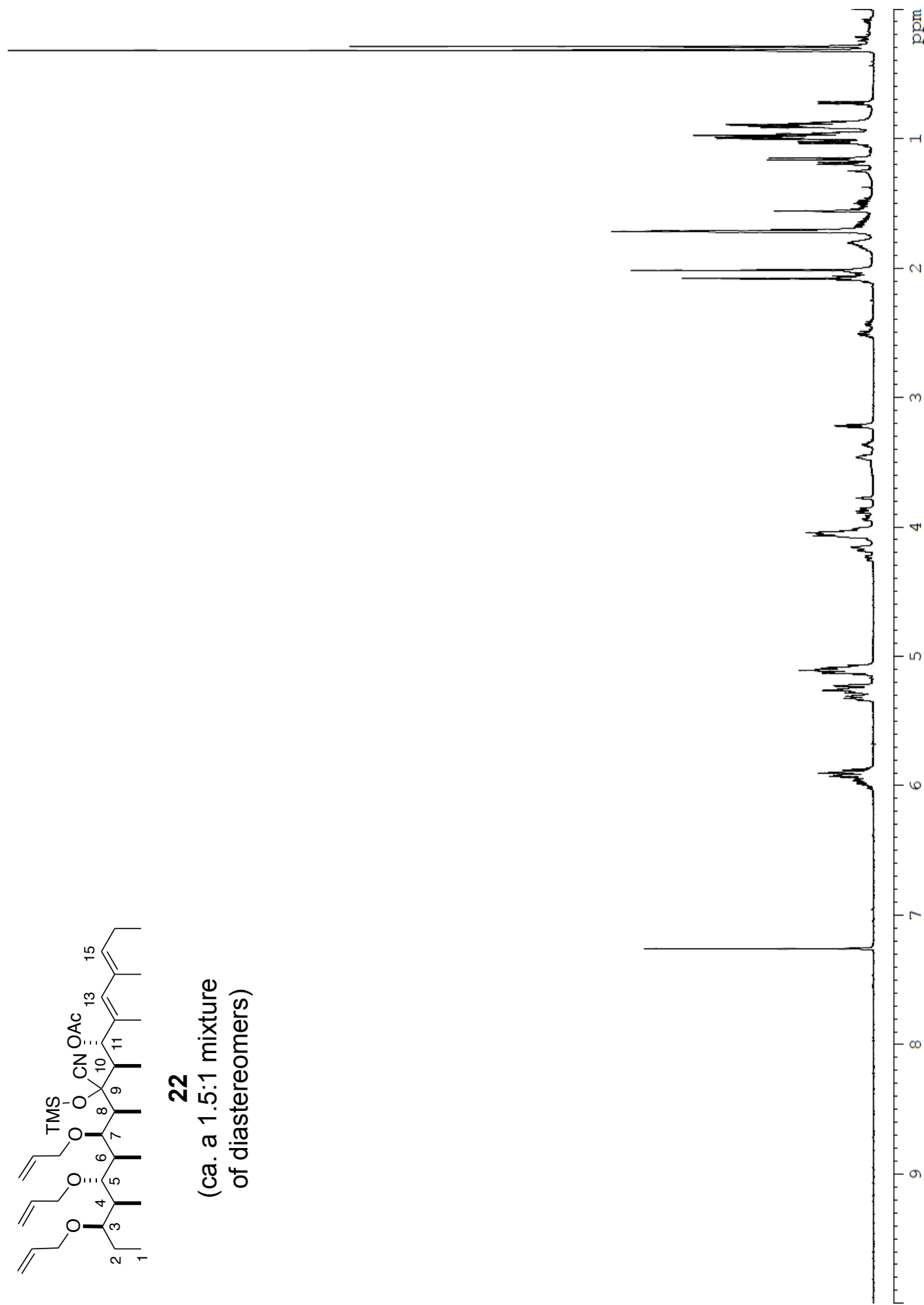


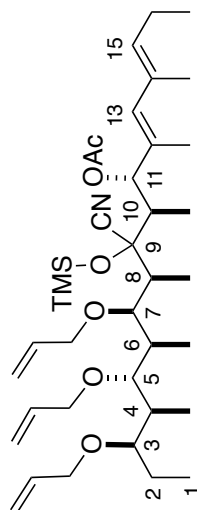






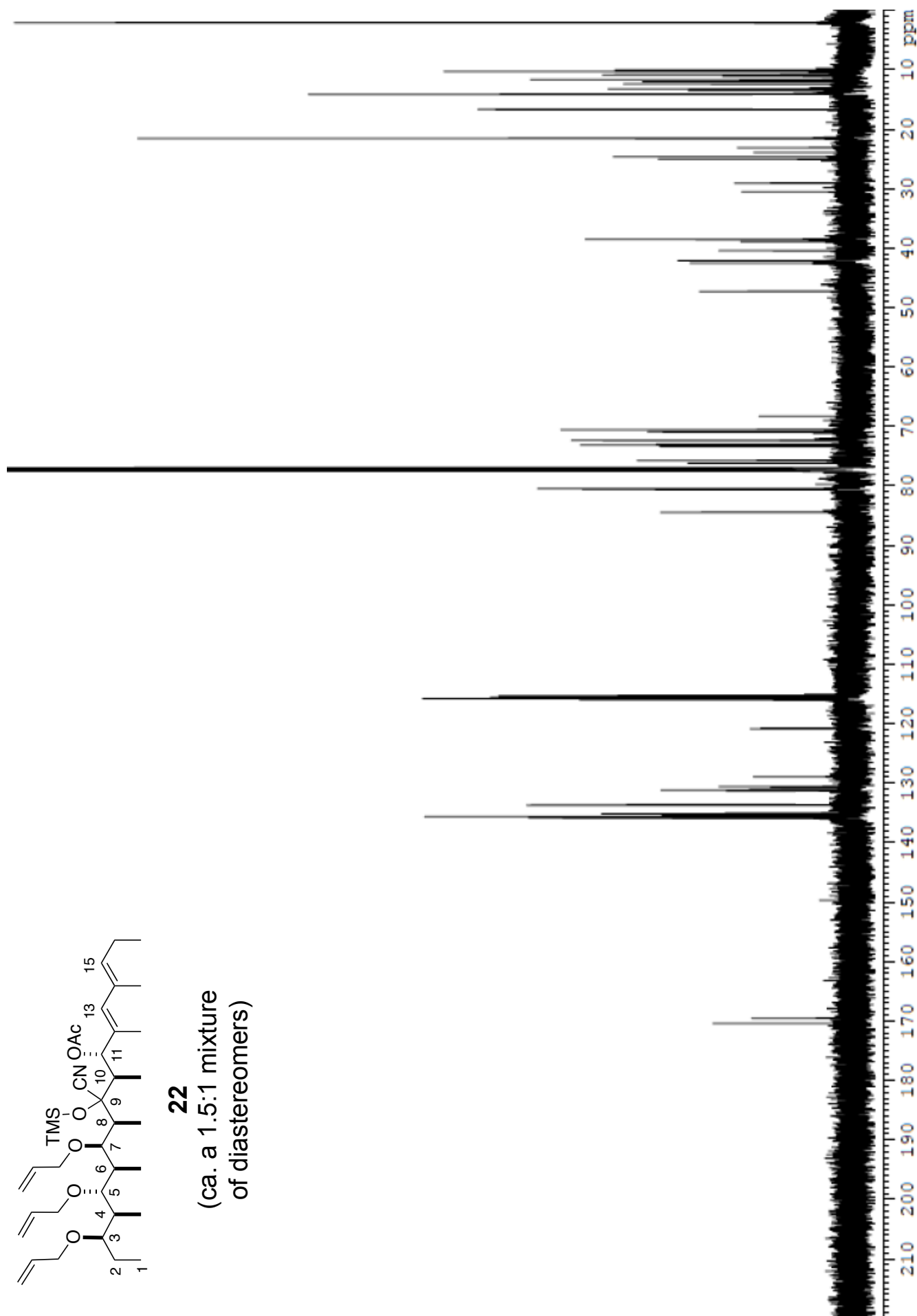
22
(ca. a 1.5:1 mixture
of diastereomers)

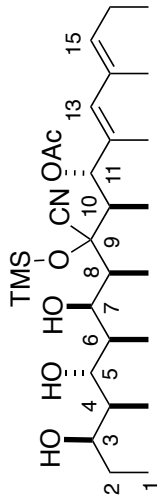




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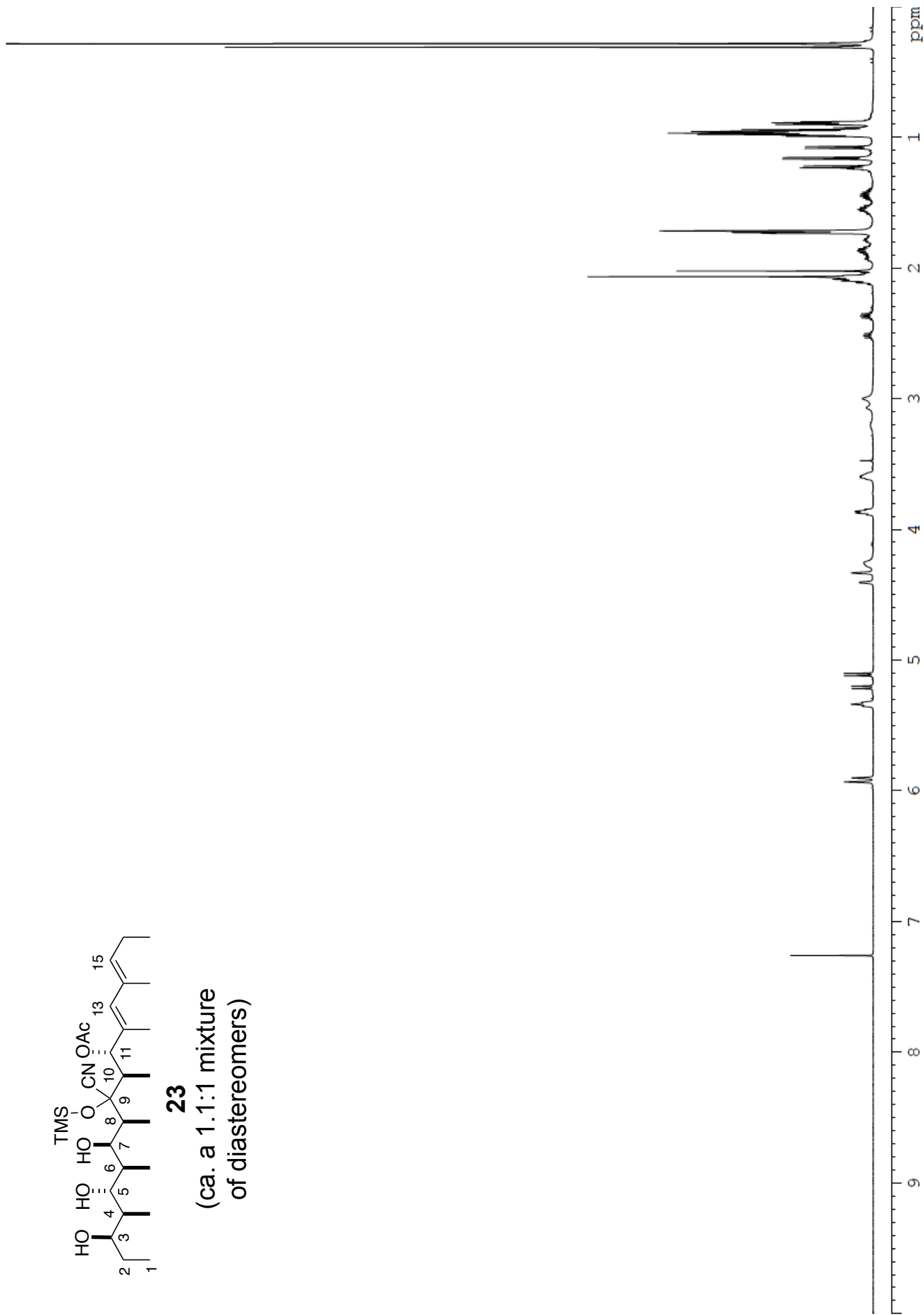
(ca. a 1.5:1 mixture
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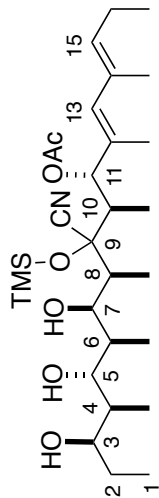


23

(ca. a 1:1:1 mixture of diastereomers)

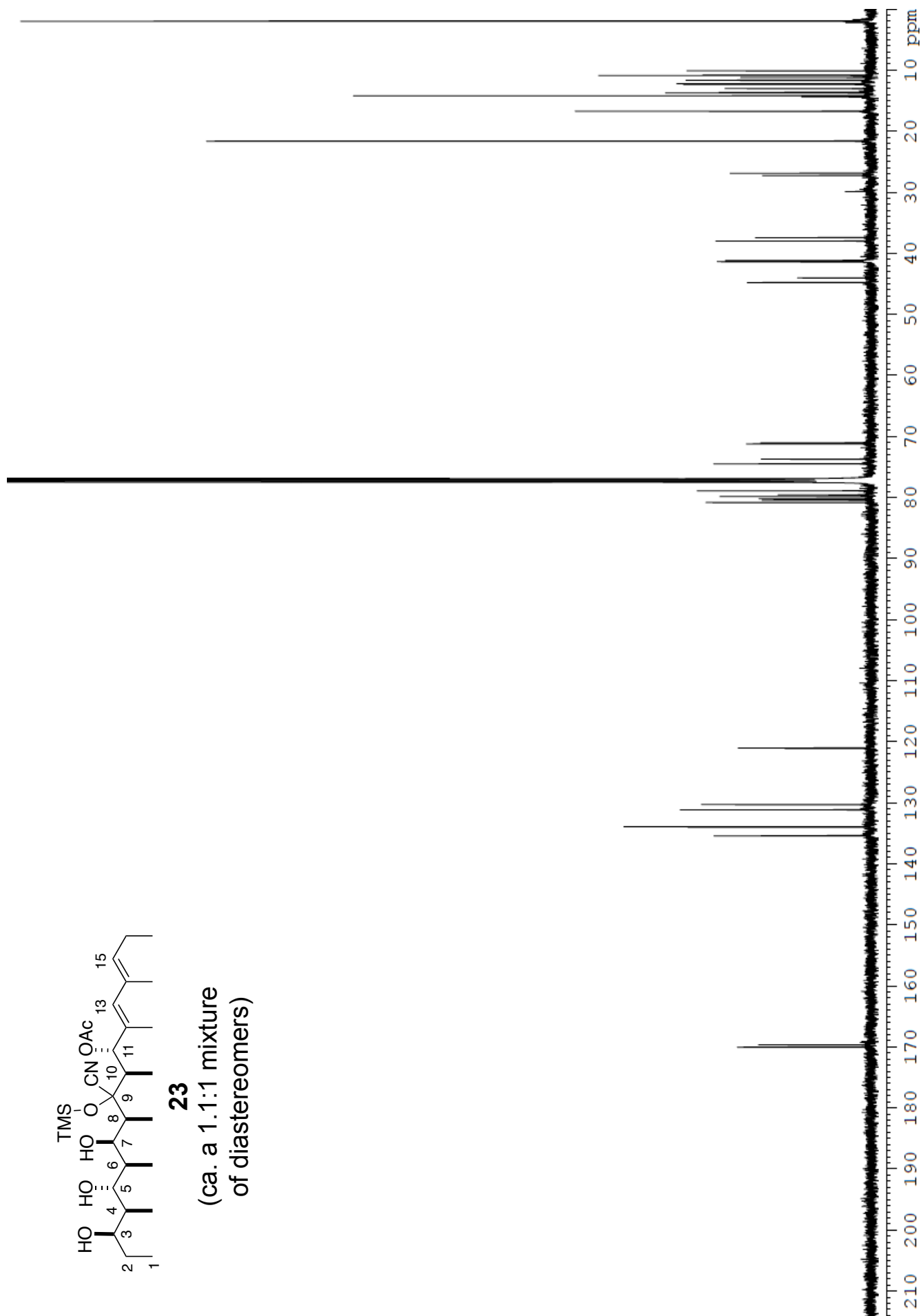


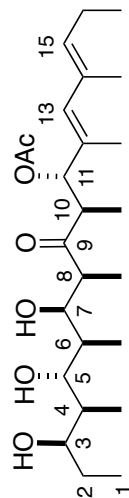
S44



23

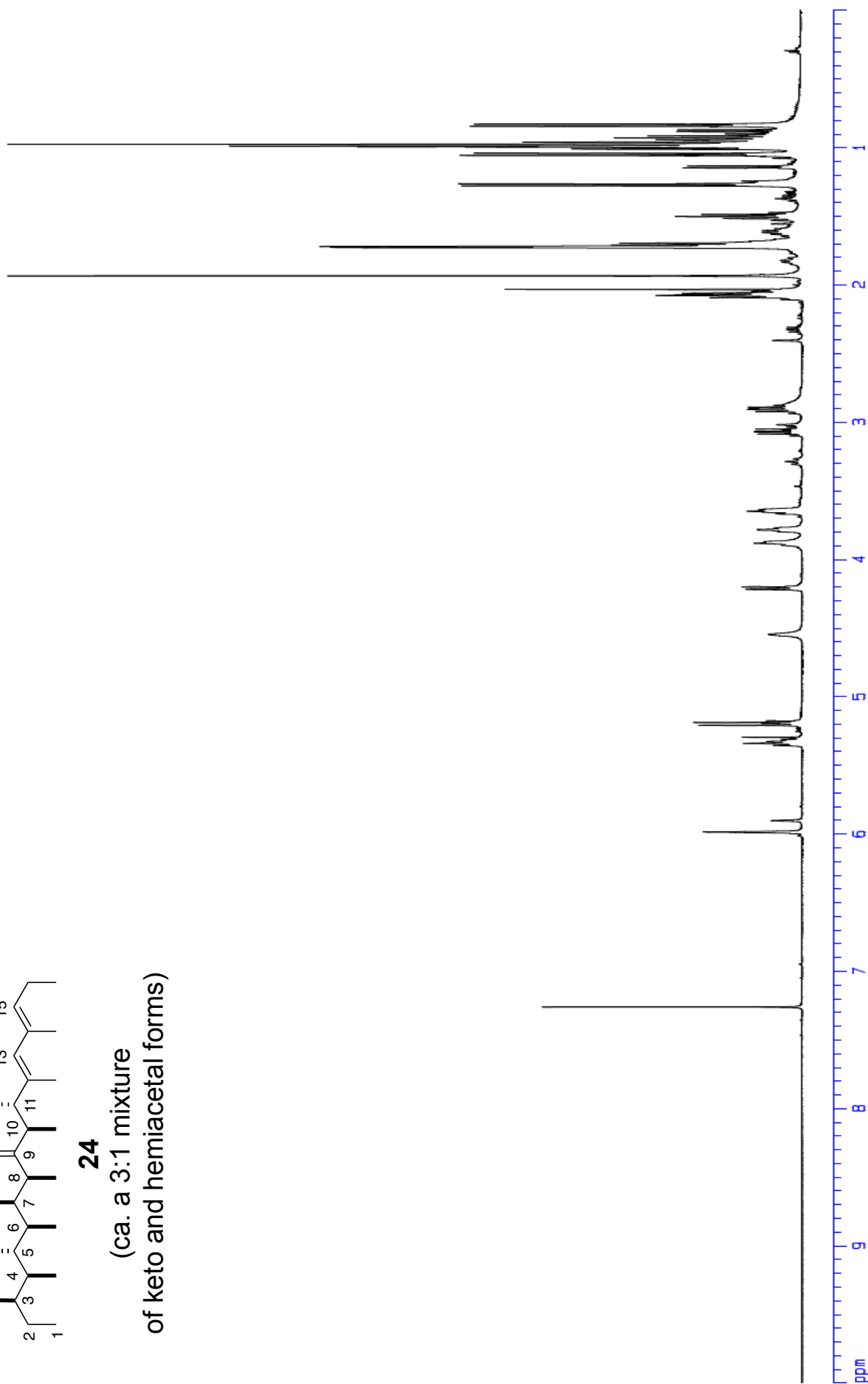
(ca. a 1:1:1 mixture
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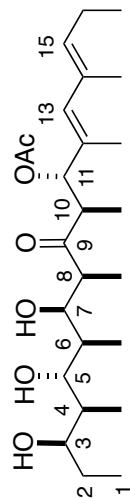




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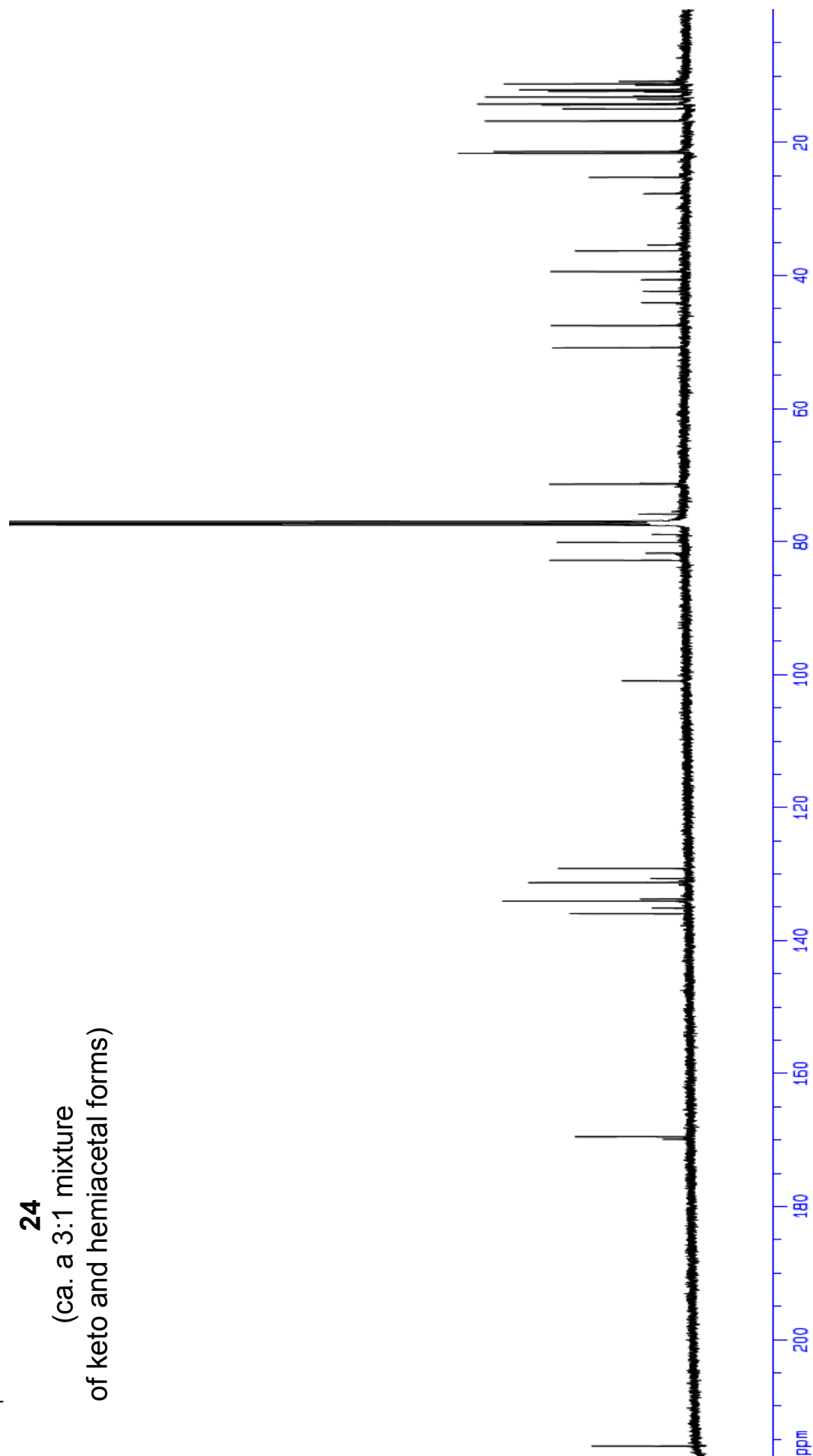
(ca. a 3:1 mixture
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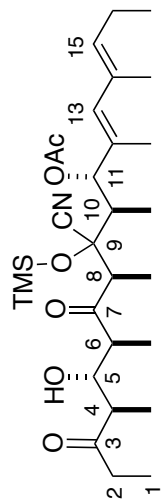




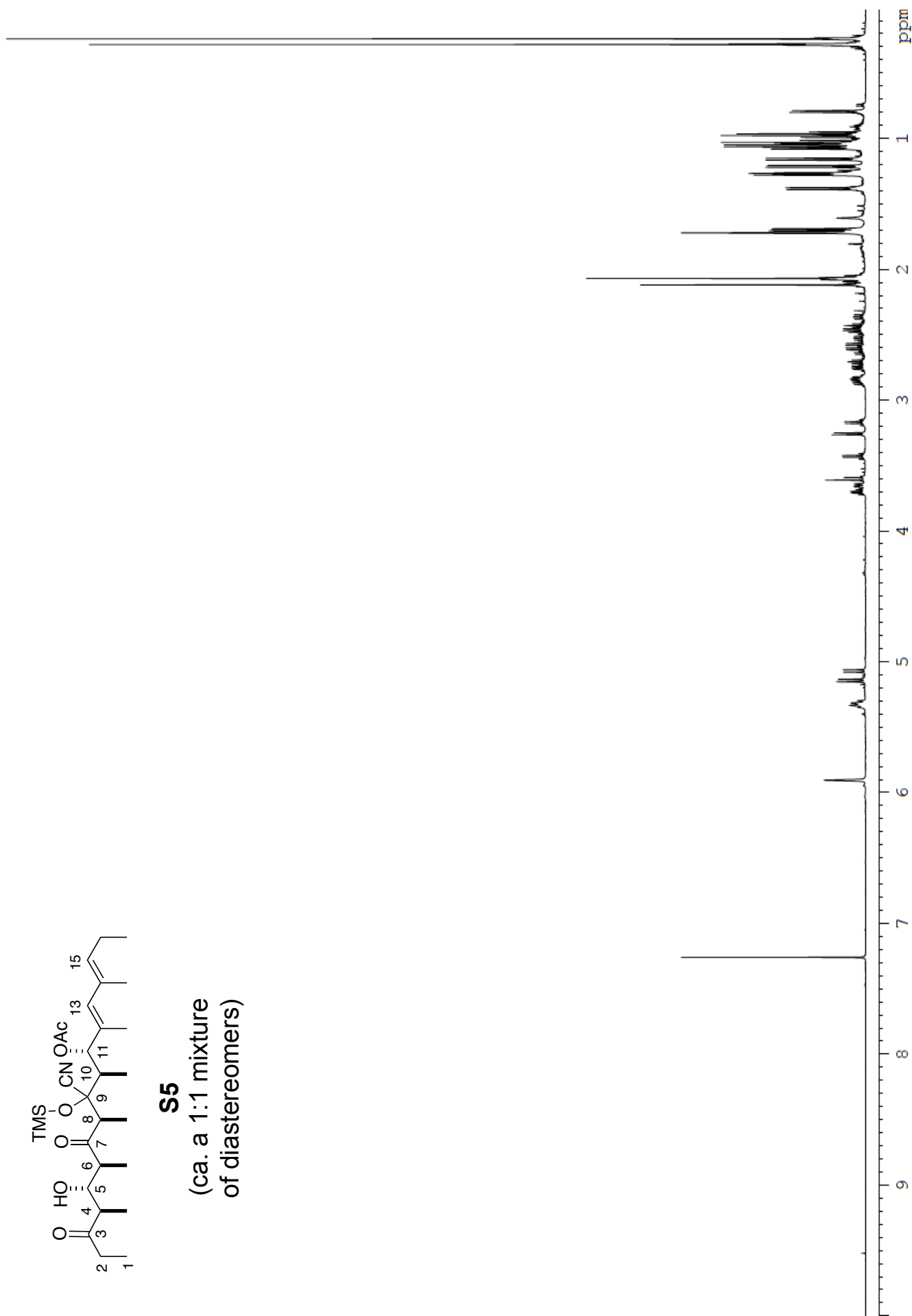
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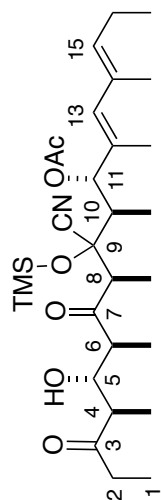
(ca. a 3:1 mixture
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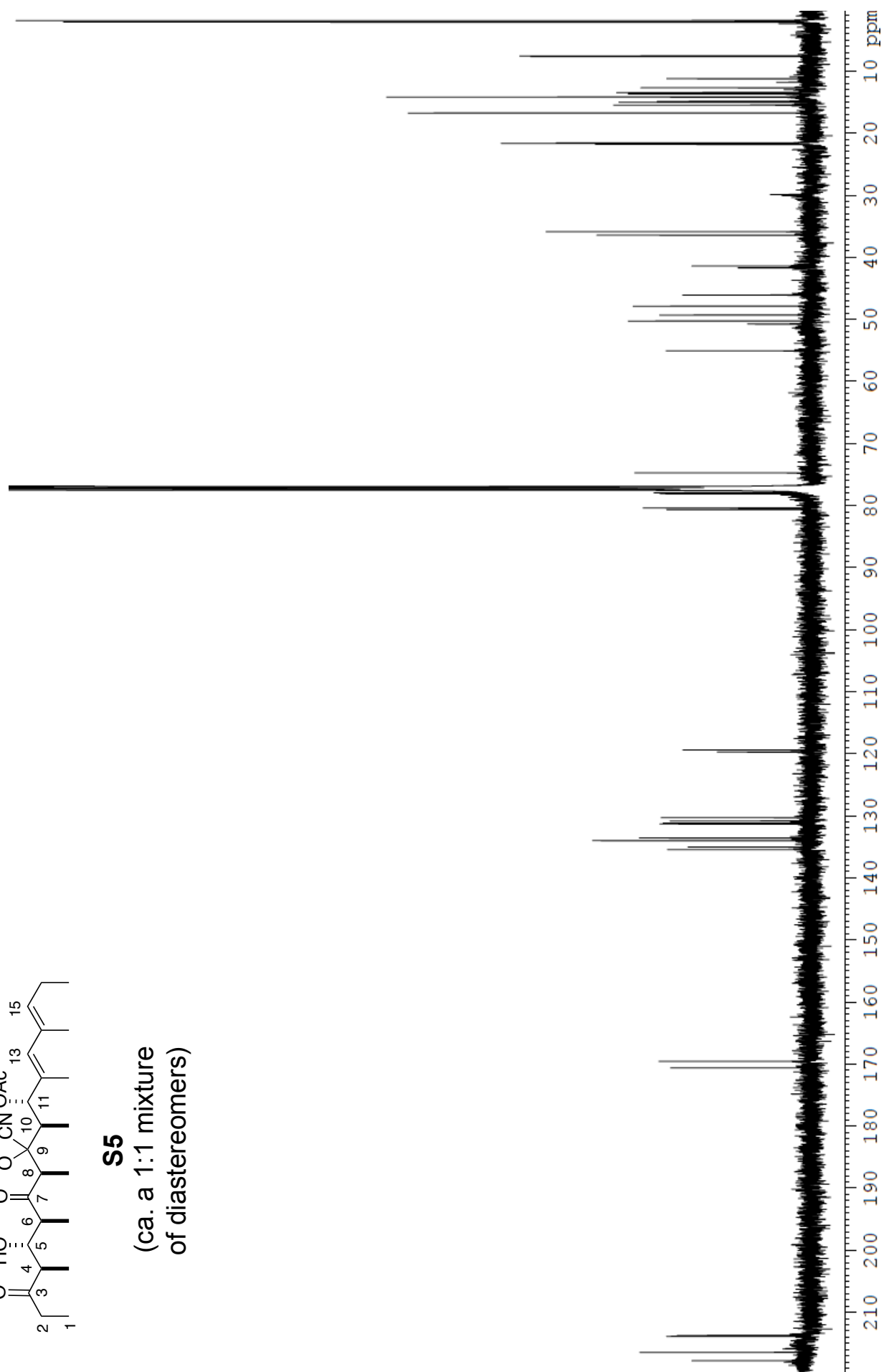


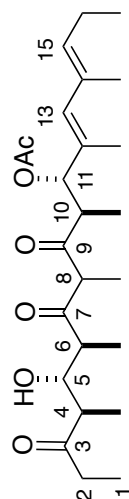
S5
(ca. a 1:1 mixture
of diastereomers)





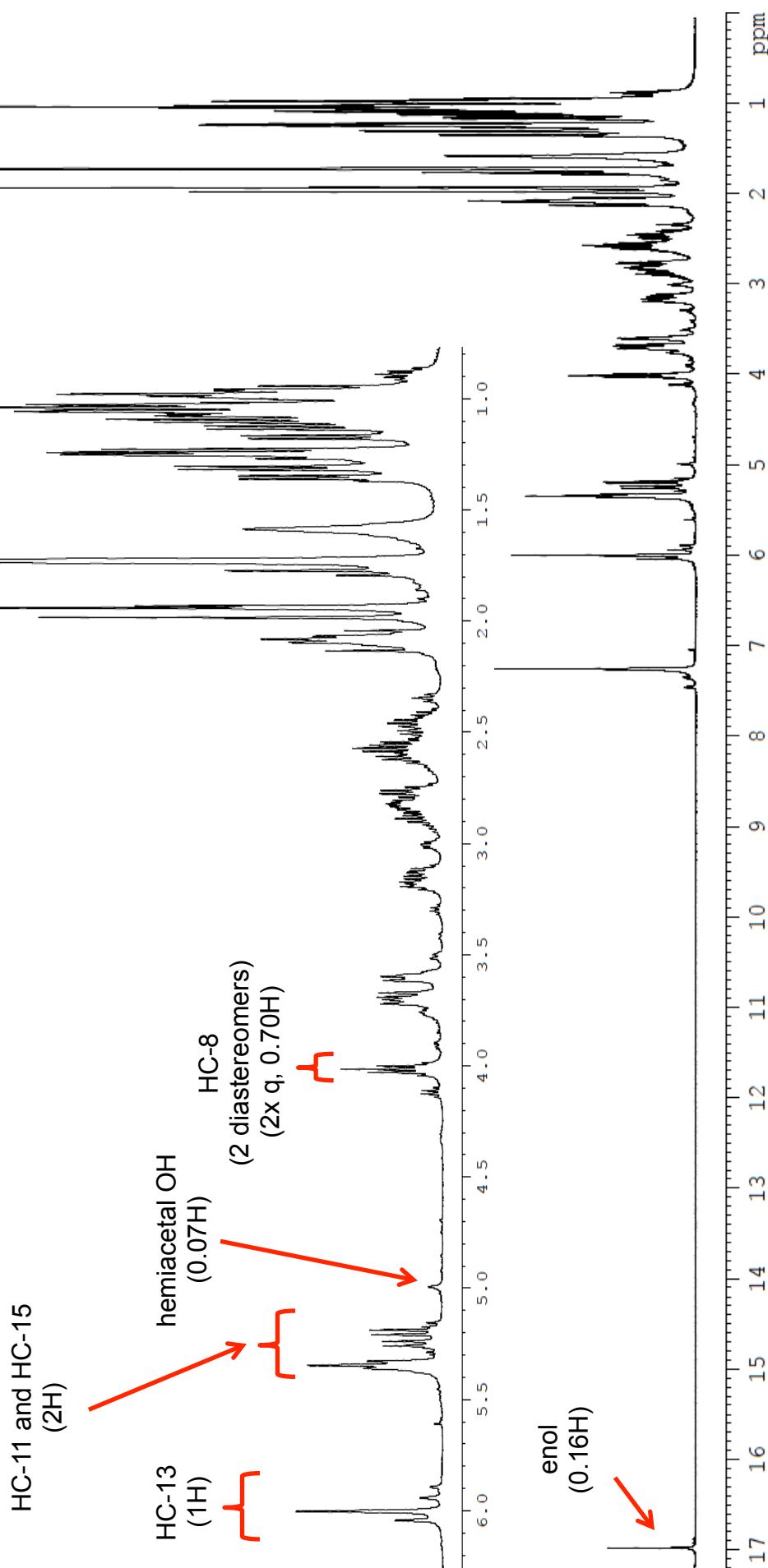
S5
(ca. a 1:1 mixture
of diastereomers)

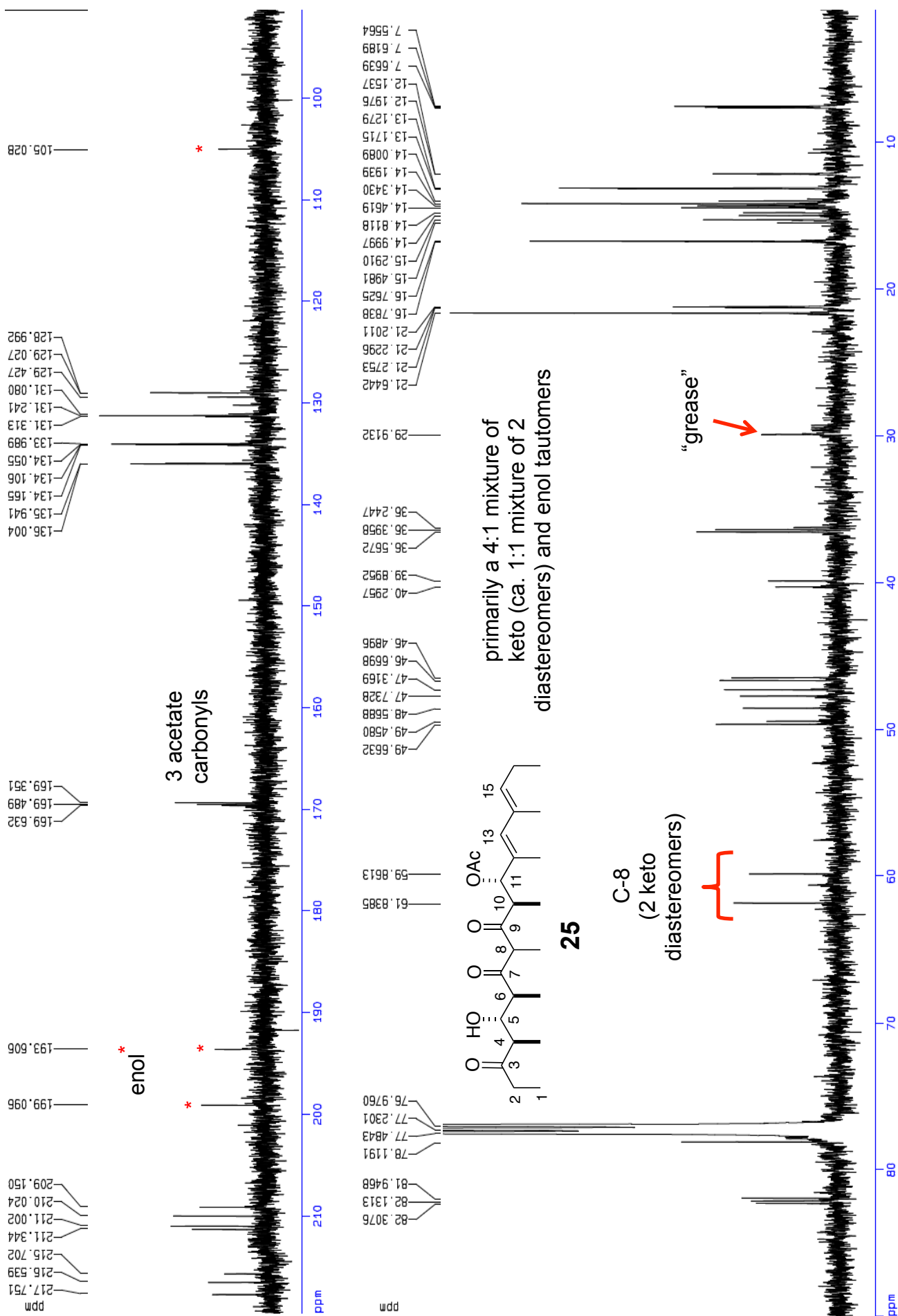


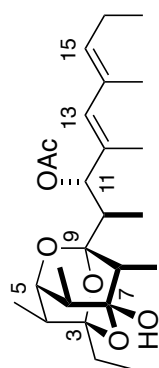


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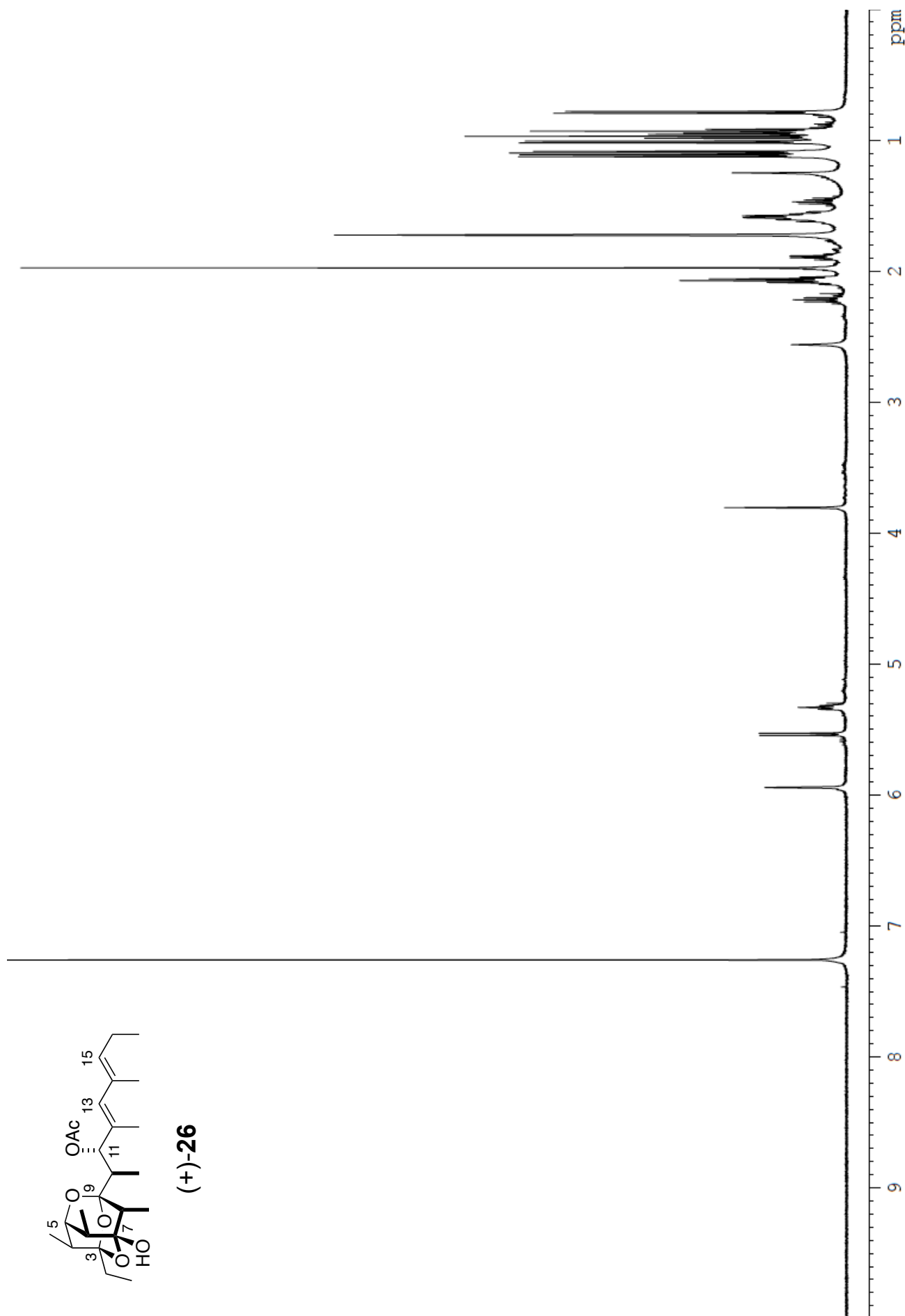
primarily a 4:1 mixture of keto (ca. 1:1 mixture of 2 diastereomers) and enol tautomers

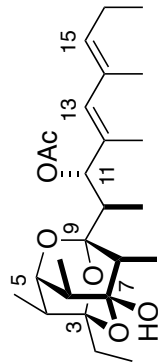




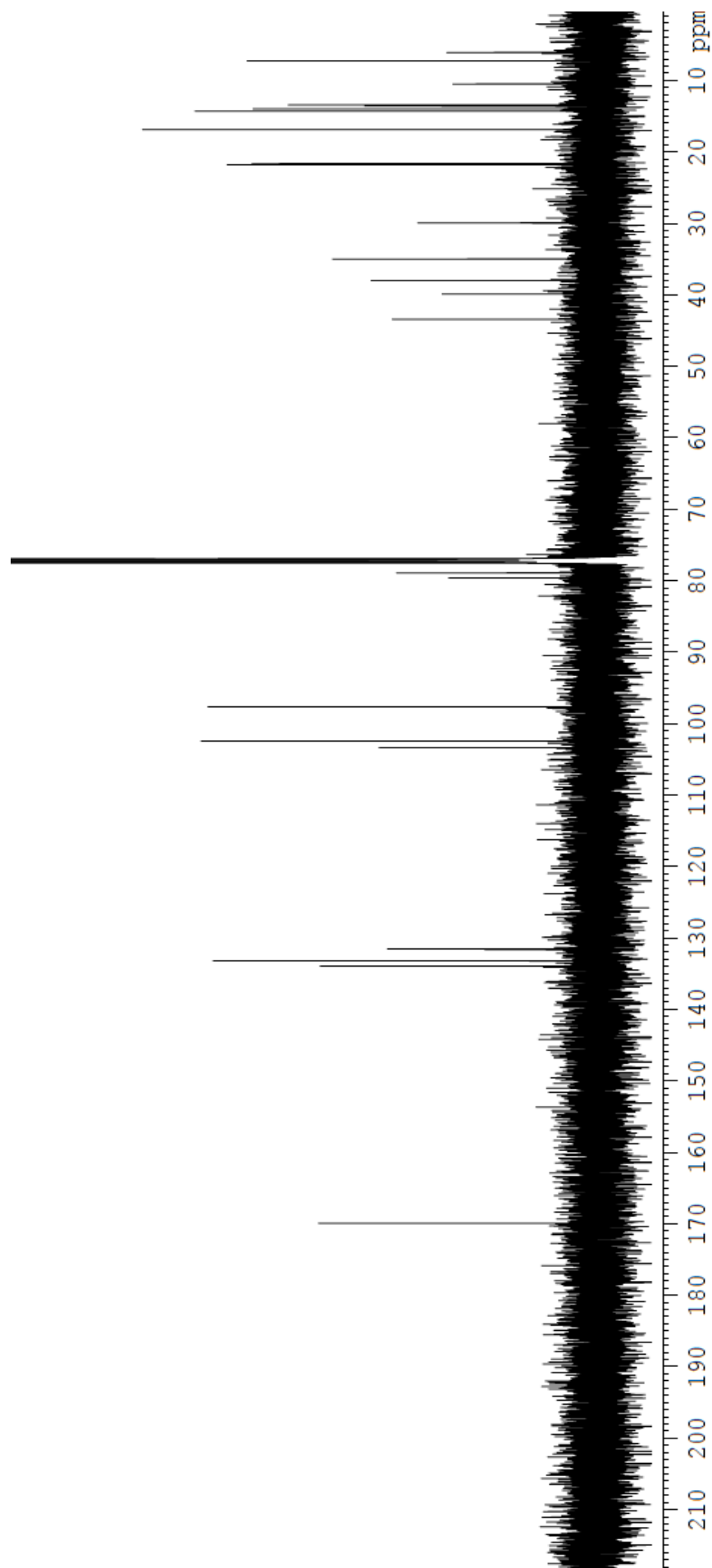


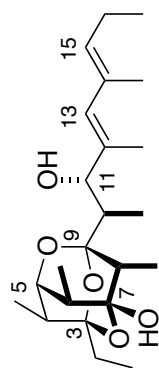
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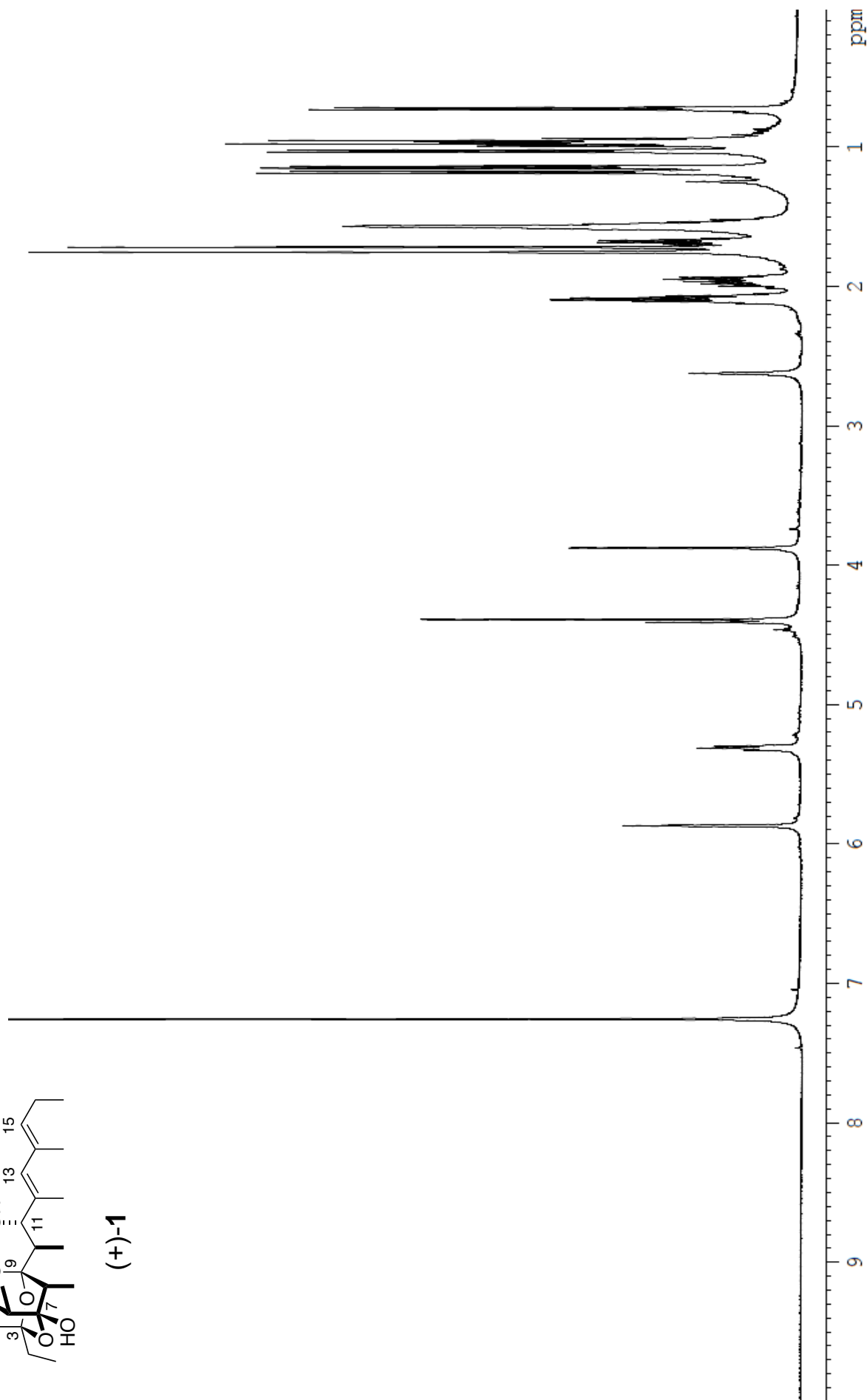


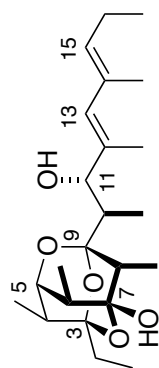
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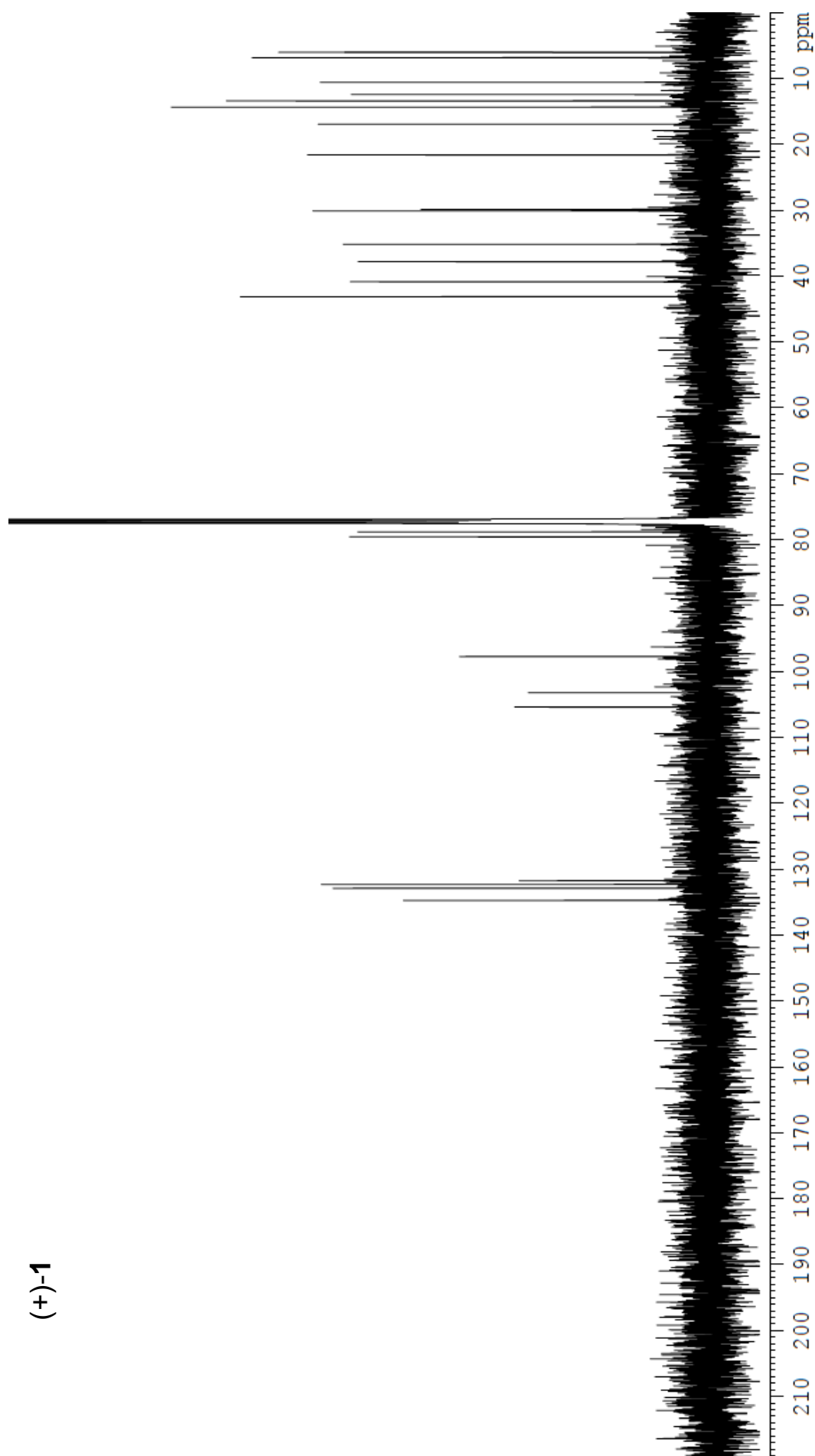


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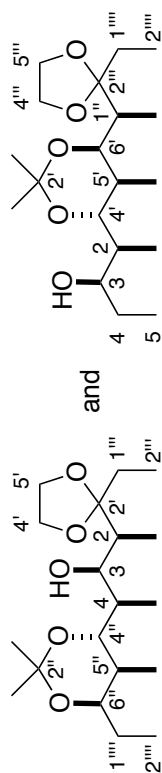
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7:3





and

7:3

S6a (major)

S6b (minor)

