

Symmetric Macrocycles by a Prins Dimerization and Macrocyclization Strategy

Michael R. Gesinski, Kwanruthai Tadpetch, and Scott D. Rychnovsky*

Department of Chemistry, 1102 Natural Sciences II, University of California, Irvine, California, 92697-2025

srychnov@uci.edu

SUPPORTING INFORMATION

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General Experimental Details. All reactions were run in flame- or oven-dried glassware under an inert atmosphere of argon using standard syringe and septa techniques, unless otherwise stated. All commercially available reagents were used as received unless otherwise stated. Tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were degassed with Ar and then passed through two 4×36 inch columns of anhydrous neutral alumina A-2 (8×14 mesh, LaRoche Chemicals; activated under a flow of Ar 350°C for 12 h) to remove H_2O according to the procedure described by Grubbs.¹ Dimethylformamide (DMF) was distilled over BaO. Trimethylsilylacetate (TMSOAc) was distilled under an inert atmosphere of argon. Acetic acid (AcOH) was distilled over CrO_3 . Triphenylsilyl perrhenate ($\text{O}_3\text{ReOSiPh}_3$) was prepared according to the procedure described by in our previous work.² (1*S*,2*S*,5*R*)-1-(1-methylallyl)menthol and (1*R*,2*R*,5*S*)-1-(1-methylallyl)menthol were prepared according to McDonald's procedure.³ Compounds **2**,⁴ **18**,⁵ **19**,⁵ **18a**,⁵ **19a**,⁵ and **22**⁶ were prepared according to published procedures. Column chromatography was performed using forced flow (flash chromatography) of the indicated eluant on Sorbent Technologies 230–400 mesh silica gel. Thin layer chromatography (TLC) was performed on Whatman 250 μm layer silica gel plates and developed plates were visualized by vanillin or *p*-anisaldehyde. All melting points (mp) were obtained using a Mel-Temp melting point apparatus and are not corrected.

¹H NMR spectra were recorded at either 500 or 600 MHz and ¹³C NMR spectra were recorded at either 125 MHz or 150 MHz and were referenced to residual solvent peaks. Chemical shifts (δ) were referenced to the residual solvent peaks. Data are presented as follows:

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J.; *Organometallics* **1996**, *15*, 1518–1520.

² Tadpetch, K.; Rychnovsky, S. D. *Org. Lett.* **2008**, *10*, 4839–4832.

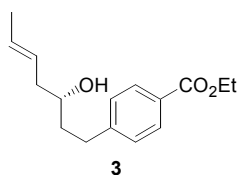
³ Wiseman, J. M.; McDonald, F. E.; Liotta, D. C. *Org. Lett.* **2005**, *7*, 3155–3157.

⁴ Watson, S. E.; Taylor, E. C.; Patel, H. *Synth. Commun.* **1998**, *28*, 1897–1905.

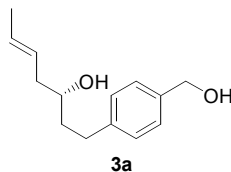
⁵ Nelson, S. G.; Spencer, K. L. *J. Org. Chem. Soc.* **2000**, *65*, 1227–1230.

⁶ Eggen, M.; Mossman, C. J.; Buck, S. B.; Nair, S. K.; Bhat, L.; Ali, S. M.; Reiff, E. A.; Boge, T. C.; Georg, G. I. *J. Org. Chem.* **2000**, *65*, 7792–7799.

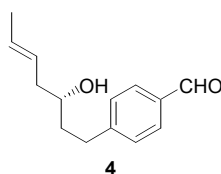
chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quarter, m = multiplet, br = broad), coupling constants (in Hertz), and integration. Infrared spectra were recorded on an FT-IR spectrometer. Optical rotations were measured on a digital polarimeter and are reported as follows: $[\alpha]_D^{25}$, concentration (g/100 mL), and solvent. High resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center.



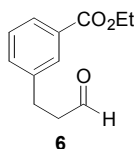
(*R,E*)-Ethyl 4-(3-hydroxyhept-5-enyl)benzoate (3). *p*-Toluenesulfonic acid (392 mg, 2.06 mmol) was added to a solution of aldehyde **2** (2.02 g, 9.78 mmol) and (1*S*,2*S*,5*R*)-1-(1-methylallyl)menthol (4.05 g, 19.3 mmol) in 60 mL of CH₂Cl₂. After 21 h, 50 mL of saturated aqueous NaHCO₃ was added and the mixture was extracted with CH₂Cl₂ (4 × 25 mL). The combined organic layers were then dried with MgSO₄ and concentrated *in vacuo*. Purification by column chromatography (5%–10% EtOAc/CH₂Cl₂) yielded the title compound as a yellow oil (2.22 g, 87%): *R*_f = 0.41 (3:7 EtOAc/hexanes); $[\alpha]_D^{24} = +15.3$ (*c* 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.96 (d, *J* = 8.3, 2H), 7.27 (d, *J* = 7.9, 2H), 5.57 (app dq, *J* = 15.2, 6.4, 1H), 5.41 (dtq, *J* = 15.2, 7.9, 1.5, 1H), 4.36 (q, *J* = 7.1, 2H), 3.62–3.56 (m, 1H), 2.89–2.83 (m, 1H), 2.74 (ddd, *J* = 13.8, 8.4, 7.8, 1H), 2.27–2.22 (m, 1H), 2.10 (ddd, *J* = 14.9, 8.0, 7.7, 1H), 1.79–1.73 (m, 2H), 1.69 (app dd, *J* = 6.3, 3H), 1.64 (d, *J* = 3.7, 1H), 1.39 (t, *J* = 7.1, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 166.7, 147.7, 129.8, 129.6, 128.5, 128.2, 126.8, 70.0, 60.8, 40.9, 30.9, 32.2, 18.1, 14.4; IR (thin film) 3458, 2981, 2933, 1716, 1279, 1107 cm⁻¹; HRMS (ES/MeOH) *m/z* calcd for C₁₆H₂₂NaO₃ [*M* + Na]⁺ 285.1467, found 285.1458.



(*R,E*)-1-(4-(Hydroxymethyl)phenyl)hept-5-en-3-ol (3a). To a suspension of LiAlH_4 (492 mg, 13.0 mmol) in 40 mL of THF was added dropwise a solution of homoallylic alcohol **3** (2.22 g, 8.46 mmol) in 10 mL of THF over 5 min. The reaction mixture was diluted with 15 mL of THF and was heated at reflux (77 °C) for 4 h. The excess LiAlH_4 was quenched at 0 °C by sequential addition of 10 mL of H_2O , 10 mL of 15% aqueous NaOH, and 30 mL of H_2O . The cloudy mixture was then filtered through a pad of Celite. The organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic phases were dried with MgSO_4 and concentrated *in vacuo*. Purification by column chromatography (30%–40% EtOAc/hexanes) of the crude residue produced diol **3a** as a light yellow oil (1.80 g, 95%): $R_f = 0.15$ (3:7 EtOAc/hexanes); $[\alpha]_D^{24} = +12.5$ (c 1.00, CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.28 (d, $J = 7.9$, 2H), 7.20 (d, $J = 8.0$, 2H), 5.56 (app dq, $J = 15.2$, 6.4, 1H), 5.42 (dtq, $J = 15.2$, 7.9, 1.5, 1H), 4.66 (s, 2H), 3.63–3.58 (m, 1H), 2.83–2.77 (m, 1H), 2.68 (ddd, $J = 13.8$, 8.3, 7.7, 1H), 2.27–2.22 (m, 1H), 2.09 (ddd, $J = 15.4$, 8.0, 7.9, 1H), 1.78–1.73 (m, 2H), 1.69 (d, $J = 6.3$, 3H), 1.62 (br s, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 141.8, 138.4, 129.4, 128.7, 127.3, 126.9, 70.2, 65.3, 40.9, 38.5, 31.8, 18.2; IR (thin film) 3350, 3022, 2929, 1450, 1016, 968 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$ 243.1361, found 243.1361.

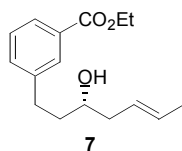


(*R,E*)-4-(3-Hydroxyhept-5-enyl)benzaldehyde (4). Activated manganese(IV) oxide (85%) (4.30 g, 43.7 mmol) was added to a solution of diol **3a** (1.80 g, 8.17 mmol) in 36 mL of CH₂Cl₂. After 18 h, the reaction mixture was filtered through a pad of Celite and concentrated *in vacuo*. Purification by column chromatography (30%–40% EtOAc/hexanes) of the crude residue produced aldehyde **4** as a colorless oil (1.53 g, 86%): $R_f = 0.41$ (2:3 EtOAc/hexanes); $[\alpha]_D^{24} = +20.4$ (c 1.02, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 9.97 (s, 1H), 7.80 (d, $J = 8.1$, 2H), 7.37 (d, $J = 8.0$, 2H), 5.58 (dq, $J = 15.2$, 6.3, 1H), 5.42 (app dtq, $J = 15.2$, 6.4, 1.4, 1H), 3.60 (tt, $J = 7.9$, 4.7, 1H), 2.90 (ddd, $J = 14.1$, 8.8, 6.7, 1H), 2.77 (ddd, $J = 14.0$, 8.4, 7.7, 1H), 2.28–2.23 (m, 1H), 2.10 (ddd, $J = 15.2$, 8.6, 8.0, 1H), 1.80–1.76 (m, 2H), 1.70 (d, $J = 6.3$, 3H), 1.63 (br s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 192.1, 149.9, 134.6, 130.0, 129.7, 129.2, 126.7, 69.9, 41.0, 38.0, 32.4, 18.2; IR (thin film) 3417, 3026, 2931, 1695, 1606, 1169 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₁₄H₁₈NaO₂ [M + Na]⁺ 241.1205, found 241.1198.



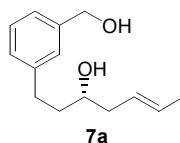
Ethyl 3-(3-oxopropyl)benzoate (6). Palladium(II) acetate (120 mg, 0.535 mmol) was added to a suspension of ethyl-3-iodobenzoate (1.50 mL, 8.91 mmol), allyl alcohol (0.91 mL, 13.4 mmol), NaHCO₃ (1.87 g, 22.3 mmol), tetrabutylammonium bromide (2.87 g, 8.91 mmol), and powdered 3 Å mol sieves (1.78 g) in 30 mL of DMF. The mixture was heated to 70 °C and allowed to stir for 3 h. The brown suspension was then cooled to room temperature and filtered through a plug of Celite, diluting with EtOAc (200 mL). The brown slurry was then poured over H₂O (200 mL) and extracted with EtOAc (2 × 200 mL). The combined organic fractions were then dried with

MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (4:1 hexanes/EtOAc) afforded aldehyde **6** (1.52 g, 83%) as a brown oil that was ~95% pure by NMR analysis: $R_f = 0.37$ (4:1 hexanes/EtOAc); ¹H NMR (600 MHz, CDCl₃) δ 9.83 (s, 1H), 7.91–7.89 (m, 2H), 7.41–7.34 (m, 2H), 4.39 (q, $J = 7.1$, 2H), 3.01 (t, $J = 7.6$, 2H), 2.82 (t, $J = 7.6$, 2H), 1.41 (t, $J = 7.1$, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 201.3, 166.8, 140.8, 130.1, 131.0, 129.6, 128.8, 127.8, 61.2, 45.3, 28.0, 14.5; IR (neat) 2983, 2727, 1716, 1446, 1284 cm⁻¹; HRMS (ES/CH₂Cl₂) m/z calcd for C₁₂H₁₄O₃ [M + Na]⁺ 229.0841, found 229.0835.

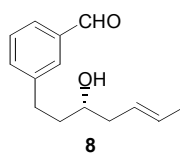


(S,E)-Ethyl 3-(3-hydroxyhept-5-enyl)benzoate (7). *p*-Toluenesulfonic acid (230 mg, 1.21 mmol) was added to a solution of aldehyde **6** (500 mg, 2.42 mmol) and (1*R*,2*R*,5*S*)-1-(1-methylallyl)menthol (765 mg, 3.64 mmol) in 24 mL of CH₂Cl₂. After 72 h, 50 mL of saturated aqueous NaHCO₃ was added and the mixture was extracted with CH₂Cl₂ (2 × 50 mL). The combined organic layers were then dried with MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (4:1 hexanes/EtOAc) yielded the title compound (580 mg, 91%) as a clear oil: $R_f = 0.23$ (4:1 hexanes/EtOAc); $[\alpha]_D^{24} = -13.7$ (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.89 (s, 1H), 7.87 (d, $J = 7.6$, 1H), 7.40 (d, $J = 7.6$, 1H), 7.35 (t, $J = 7.6$, 1H), 5.57 (dq, $J = 15.2, 6.4$, 1H), 5.43 (dt, $J = 15.2, 7.8$, 1H), 4.37 (q, $J = 7.1$, 2H), 3.64–3.56 (m, 1H), 2.85 (ddd, $J = 15.2, 9.0, 6.5$, 1H), 2.73 (ddd, $J = 16.5, 9.1, 7.3$, 1H), 2.29–2.21 (m, 1H), 2.10 (dt, $J = 13.4, 8.0$, 1H), 1.82–1.75 (m, 2H), 1.69 (d, $J = 6.3$, 3H), 1.64 (s, 1H), 1.40 (t, $J = 7.2$, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.1, 142.7, 133.3, 130.8, 129.73, 129.68, 128.6,

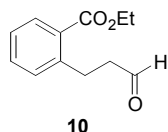
127.3, 127.0, 70.3, 61.2, 41.1, 38.5, 32.1, 18.3, 14.6; IR (neat) 3446, 2979, 1699, 1444, 1198 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3$ $[\text{M} + \text{Na}]^+$ 285.1467, found 285.1471.



(S,E)-1-(3-(Hydroxymethyl)phenyl)hept-5-en-3-ol (7a). LiAlH_4 (159 mg, 4.19 mmol) was added to a solution of homoallylic alcohol **7** (550 mg, 2.10 mmol) in 7 mL of THF. After 1 h, the excess LiAlH_4 was quenched by sequential addition of 0.3 mL of H_2O , 0.3 mL of 3 M aqueous NaOH, and 0.3 mL of H_2O . The grey sludge was then filtered and rinsed with 200 mL of Et_2O . The solution was finally dried with MgSO_4 and concentrated *in vacuo*. Purification by column chromatography (1:1 hexanes/ EtOAc) of the crude residue produced the title diol (363 mg, 78%) as a clear oil: $R_f = 0.30$ (1:1 hexanes/ EtOAc); $[\alpha]_D^{24} = -11.7$ (c 1.07, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.28 (t, $J = 7.5$, 1H), 7.22 (s, 1H), 7.19 (d, $J = 7.5$, 1H), 7.14 (d, $J = 7.5$, 1H), 5.56 (dq, $J = 15.2$, 6.5, 1H), 5.43 (dt, $J = 15.2$, 7.4, 1H), 4.68 (s, 2H), 3.65–3.57 (m, 2H), 2.80 (ddd, $J = 15.2$, 7.4, 5.1, 1H), 2.70 (ddd, $J = 16.4$, 8.5, 7.4, 1H), 2.29–2.21 (m, 1H), 2.10 (dt, $J = 13.9$, 7.9, 1H), 1.80–1.74 (m, 2H), 1.69 (d, $J = 6.3$, 1H), 1.63 (br s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 142.8, 141.2, 129.5, 128.8, 128.0, 127.3, 127.0, 124.7, 70.4, 65.6, 41.1, 38.6, 32.2, 18.3; IR (neat) 3316, 2931, 1448, 1045 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$ $[\text{M} + \text{Na}]^+$ 243.1361, found 243.1366.

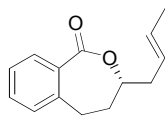


(*S,E*)-3-(3-Hydroxyhept-5-enyl)benzaldehyde (8). Activated manganese(IV) oxide (1.38 g, 15.9 mmol) was added to a solution of diol **7a** (350 mg, 1.59 mmol) in 20 mL of CH₂Cl₂. After 18 h, the reaction mixture was filtered through a pad of Celite and diluted with 500 mL of CH₂Cl₂. The solution was then concentrated to give aldehyde **8** (335 mg, 97%) as a viscous yellow oil that was deemed pure without additional purification: *R_f* = 0.60 (1:1 hexanes/EtOAc); $[\alpha]_D^{24} = -15.1$ (*c* 1.05, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 10.0 (s, 1H), 7.73 (s, 1H), 7.70 (d, *J* = 7.4, 1H), 7.45 (d, *J* = 7.6, 1H), 7.45 (t, *J* = 7.5, 1H), 5.57 (dq, *J* = 15.1, 6.4, 1H), 5.42 (dt, *J* = 15.2, 7.9, 1H), 3.60 (qd, *J* = 8.2, 4.2, 1H), 2.90 (ddd, *J* = 14.2, 9.0, 6.4, 1H), 2.77 (ddd, *J* = 16.4, 9.0, 7.4, 1H), 2.29–2.21 (m, 1H), 2.10 (dt, *J* = 13.9, 7.9, 1H), 1.83–1.75 (m, 2H), 1.69 (d, *J* = 6.3, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 192.8, 143.6, 136.8, 135.0, 126.7, 129.6, 129.2, 127.9, 126.9, 70.1, 41.1, 38.3, 32.0, 18.3; IR (neat) 3426, 2918, 1699, 1587, 1450 cm⁻¹; HRMS (ES/MeOH) *m/z* calcd for C₁₄H₁₈O₂ [M + Na]⁺ 241.1205, found 241.1207.



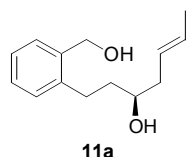
Ethyl 2-(3-oxopropyl)benzoate (10). Palladium(II) acetate (163 mg, 0.726 mmol) was added to a suspension of ethyl-2-iodobenzoate (2.00 mL, 12.1 mmol), allyl alcohol (1.20 mL, 18.2 mmol), NaHCO₃ (2.50 g, 30.3 mmol), tetrabutylammonium bromide (3.90 g, 12.1 mmol), and powdered 3 Å mol sieves (2.40 g) in 40 mL of DMF. The mixture was heated to 70 °C and allowed to stir for 18 h. The brown suspension was then cooled to room temperature and filtered through a plug of Celite, diluting with EtOAc (200 mL). The brown slurry was then poured over H₂O (200 mL) and extracted with EtOAc (2 × 200 mL). The combined organic fractions were then dried with

MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (7:1 hexanes/EtOAc) afforded aldehyde **10** (1.84 g, 74%) as a yellow oil that was ~80% pure by NMR analysis: $R_f = 0.22$ (7:1 hexanes/EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 9.82 (s, 1H), 8.44 (d, $J = 8.4$, 1H), 7.43 (td, $J = 7.5$, 1.3, 1H), 7.28 (t, $J = 7.5$, 2H), 4.35 (q, $J = 7.2$, 2H), 3.27 (t, $J = 7.7$, 2H), 2.82 (t, $J = 7.8$, 2H), 1.39 (t, $J = 7.1$, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 201.8, 167.3, 142.4, 132.3, 131.1, 131.0, 130.3, 126.5, 61.0, 45.7, 27.4, 14.4; IR (neat) 2981, 2721, 1716, 1684, 1257, 1084 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₁₂H₁₄O₃ [M + Na]⁺ 229.0841, found 229.0845.

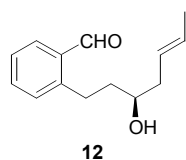
**11**

Lactone 11. *p*-Toluenesulfonic acid (230 mg, 1.21 mmol) was added to a solution of aldehyde **6** (500 mg, 2.42 mmol) and (1*R*,2*R*,5*S*)-1-(1-methylallyl)menthol (763 mg, 3.63 mmol) in 20 mL of CH₂Cl₂. After 5 d, 50 mL of saturated aqueous NaHCO₃ was added and the mixture was extracted with CH₂Cl₂ (2 × 50 mL). The combined organic layers were then dried with MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (9:1 hexanes/EtOAc) yielded the title compound (375 mg, 72%) as a yellow oil: $R_f = 0.24$ (9:1 hexanes/EtOAc); $[\alpha]_D^{24} = -130.5$ (c 1.05, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.71 (dd, $J = 7.6$, 1.2, 1H), 7.46 (td, $J = 7.5$, 1.4, 1H), 7.35 (t, $J = 7.6$, 1H), 7.19 (d, $J = 7.5$, 1H), 5.52 (dq, $J = 15.2$, 6.3, 1H), 5.41 (dtd, $J = 15.2$, 6.9, 1.5, 1H), 4.08–4.03 (m, 1H), 2.99 (td, $J = 13.4$, 8.0, 1H), 2.75 (dd, $J = 13.8$, 7.0, 1H), 2.46 (dt, $J = 13.1$, 6.7, 1H), 2.33 (dt, $J = 14.3$, 6.1, 1H), 2.10 (tdd, $J = 13.4$, 8.0, 1.0, 1H), 1.99–1.90 (m, 1H), 1.64 (dd, $J = 6.3$, 1.2, 3H); ¹³C NMR (125 MHz,

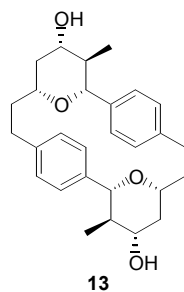
CDCl₃) δ 171.9, 138.2, 132.7, 132.2, 130.2, 129.1, 128.7, 127.5, 125.8, 78.4, 38.0, 33.6, 29.9, 18.2; IR (neat) 2945, 1722, 1454, 1261, 1088 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₁₄H₁₆O₂ [M + Na]⁺ 239.1048, found 239.1043.



(S,E)-1-(2-(Hydroxymethyl)phenyl)hept-5-en-3-ol (11a). LiAlH₄ (129 mg, 3.40 mmol) was added to a solution of lactone **7** (368 mg, 1.70 mmol) in 6 mL of THF. After 45 min, the excess LiAlH₄ was quenched by sequential addition of 0.3 mL of H₂O, 0.3 mL of 3 M aqueous NaOH, and 0.3 mL of H₂O. The grey sludge was then filtered and rinsed with 200 mL of Et₂O. The solution was finally dried with MgSO₄ and concentrated *in vacuo*. Purification by column chromatography (3:2 hexanes/EtOAc) of the crude residue produced the title diol (342 mg, 91%) as a clear oil: R_f = 0.31 (1:1 hexanes/EtOAc); $[\alpha]_D^{24}$ = -36.6 (*c* 0.99, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.33 (d, J = 7.5, 1H), 7.29–7.18 (m, 3H), 5.55 (dq, J = 15.2, 6.4, 1H), 5.39 (dt, J = 16.7, 7.2, 1H), 4.79 (d, J = 12.3, 1H), 4.63 (d, J = 12.3, 1H), 3.52 (tt, J = 8.5, 3.8, 1H), 2.91–2.81 (m, 2H), 2.25–2.17 (m, 1H), 2.14–2.04 (m, 1H), 1.89–1.81 (m, 1H), 1.80–1.72 (m, 1H), 1.68 (d, J = 6.3, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 140.7, 138.8, 129.63, 129.56, 129.5, 128.4, 127.0, 126.4, 69.6, 63.8, 41.1, 38.2, 27.8, 18.3; IR (neat) 3336, 2918, 1452, 1011, 968 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₁₄H₂₀O₂ [M + Na]⁺ 243.1361, found 243.1353.

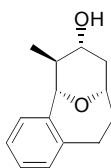


(*S,E*)-2-(3-Hydroxyhept-5-enyl)benzaldehyde (12). Activated manganese(IV) oxide (1.30 g, 15.0 mmol) was added to a solution of diol **7a** (331 mg, 1.50 mmol) in 15 mL of CH₂Cl₂. After 18 h, the reaction mixture was filtered through a pad of Celite and diluted with 500 mL of CH₂Cl₂. The solution was then concentrated to give aldehyde **12** (306 mg, 93%) as a pale yellow wax that was deemed pure without additional purification: $R_f = 0.43$ (2:1 hexanes/EtOAc); $[\alpha]_D^{24} = -22.7$ (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 10.3 (s, 1 H), 7.82 (dd, $J = 7.6, 1.2$, 1H), 7.51 (td, $J = 7.5, 1.4$, 1H), 7.38 (td, $J = 7.5, 0.9$, 1H), 7.32 (d, $J = 7.6$, 1H), 5.55 (dq, $J = 15.2, 6.3$, 1H), 5.43 (dt, $J = 15.3, 7.8$, 1H), 3.63 (qd, $J = 8.0, 4.0$, 1H), 3.22 (ddd, $J = 13.3, 9.5, 5.4$, 1H), 3.13 (ddd, $J = 13.4, 9.4, 7.0$, 1H), 2.27–2.20 (m, 1H), 2.13 (dt, 14.0, 7.7, 1H), 1.88 (d, $J = 4.0$, 1H), 1.83–1.70 (m, 2H), 1.68 (dd, $J = 6.3, 1.0$, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 193.2, 145.3, 134.1, 134.0, 132.8, 131.5, 129.4, 127.1, 126.8, 70.2, 41.0, 39.1, 28.9, 18.3; IR (neat) 3574, 2917, 1695, 1601, 1452, 1210 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₁₄H₁₈O₂ [M + Na]⁺ 241.1205, found 241.1202.



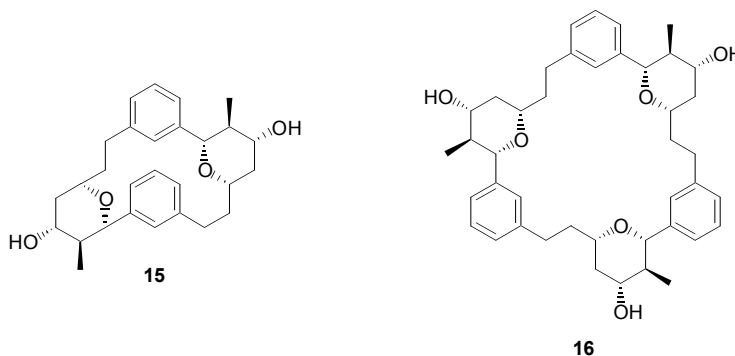
[5,5]-*para*-Cyclophane 13. O₃ReOSiPh₃ (29.2 mg, 0.0573 mmol) was added to a solution of aldehyde **4** (50.0 mg, 0.229 mmol) in 4.6 mL of CH₂Cl₂. After 24 h, a pink, immiscible wax had formed that turned white upon addition of Et₃N (0.5 mL). The mixture was then concentrated under reduced pressure and purified by column chromatography (60% EtOAc/hexanes) to afford the title cyclophane (25.5 mg, 51%) as a white powder: $R_f = 0.28$ (4:1 EtOAc/hexanes); mp 198–

200 °C; $[\alpha]_D^{24} = -74.3$ (*c* 0.28, MeOH); ^1H NMR (500 MHz, CDCl_3) δ 6.99 (d, *J* = 8.0, 2H), 6.83 (d, *J* = 7.7, 4H), 6.59 (d, *J* = 7.4, 2H), 3.43–3.38 (m, 4H), 3.31 (d, *J* = 10.0, 2H), 2.93 (dt, *J* = 13.7, 3.7, 2H), 2.46 (td, *J* = 13.2, 3.7, 2H), 1.92 (ddd, *J* = 12.4, 4.6, 1.2, 2H), 1.87 (dtd, *J* = 13.2, 9.7, 3.6, 2H), 1.74 (dt, *J* = 14.4, 3.7, 2H), 1.44–1.36 (m, 6H), 0.67 (d, *J* = 6.5, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.6 (2), 137.0 (2), 128.7 (2), 128.0 (2), 127.3 (2), 125.1 (2), 84.0 (2), 77.6 (2), 74.6 (2), 44.0 (2), 42.0 (2), 36.5 (2), 35.4 (2), 13.2 (2); IR (KBr) 3378, 2916, 2831, 1093, 1047, 804 cm^{-1} ; HRMS (ES/MeOH) *m/z* calcd for $\text{C}_{28}\text{H}_{36}\text{NaO}_4$ $[\text{M} + \text{Na}]^+$ 459.2511, found 459.2509.



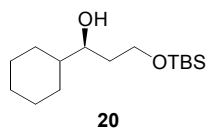
14

Tetrahydropyran 14. $\text{O}_3\text{ReOSiPh}_3$ (29.2 mg, 0.0573 mmol) was added to a solution of aldehyde **12** (50.0 mg, 0.229 mmol) in 4.6 mL of CH_2Cl_2 . After 24 h, Et_3N was added to the brown solution and the mixture was concentrated under reduced pressure. Purification by column chromatography (40% EtOAc/hexanes) provided the title compound (44.8 mg, 90%) as a viscous, colorless oil: $R_f = 0.26$ (3:2 hexanes/EtOAc); $[\alpha]_D^{24} = +10.0$ (*c* 0.45, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.19 (d, *J* = 6.8, 1H), 7.15–7.10 (m, 3H), 4.72–4.68 (m, 2H), 3.90 (dt, *J* = 12.5, 6.3, 1H), 3.12 (td, *J* = 14.6, 3.1, 1H), 2.79 (dt, *J* = 16.0, 3.9, 1H), 2.49–2.42 (m, 1H), 2.22–2.15 (m, 1H), 2.08 (dd, *J* = 12.6, 9.2, 1H), 1.98 (tt, *J* = 13.9, 3.1, 1H), 1.73 (dq, *J* = 14.2, 3.3, 1H), 1.24 (d, *J* = 6.2, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.8, 140.5, 131.0, 128.1, 127.5, 126.2, 86.5, 80.7, 71.1, 54.0, 33.9, 33.0, 32.0, 22.2; IR (neat) 3421, 2964, 2927, 1454, 1049 cm^{-1} ; HRMS (ES/MeOH) *m/z* calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ $[\text{M} + \text{Na}]^+$ 241.1205, found 241.1211.

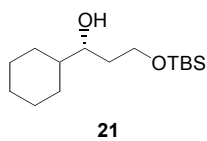


[5,5]-meta-Cyclophanes 15 and 16. $\text{O}_3\text{ReOSiPh}_3$ (29.2 mg, 0.0573 mmol) was added to a solution of aldehyde **8** (50.0 mg, 0.229 mmol) in 4.6 mL of CH_2Cl_2 . After 24 h, a 0.5 mL of Et_3N was added. The mixture was then concentrated under reduced pressure and purified by column chromatography (50%–70% EtOAc/hexanes) to afford dimeric cyclophane **15** (14.0 mg, 28%) as a white solid and the trimeric cyclophane **16** (6.5 mg, 13%) as white film. **15**: $R_f = 0.45$ (3:7 hexanes/EtOAc); mp 202–203 °C; $[\alpha]_D^{24} = -137.8$ (c 1.13, CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.25 (s, 2H), 7.21 (t, $J = 7.5$, 2H), 7.10 (d, $J = 7.5$, 2H), 7.02 (d, $J = 7.5$, 2H), 3.67 (d, $J = 10.1$, 2H), 3.46–3.39 (m, 4H), 2.90 (ddd, $J = 14.4$, 10.9, 3.5, 2H), 2.70 (dt, $J = 14.6$, 4.5, 2H), 2.12–2.03 (m, 2H), 2.01–1.96 (m, 4H), 1.62 (br s, 2H), 1.56–1.48 (m, 4H), 0.73 (d, $J = 6.6$, 6H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 142.5 (2), 139.7 (2), 130.4 (2), 127.6 (2), 127.3 (2), 124.2 (2), 84.9 (2), 74.9 (2), 74.4 (2), 44.2 (2), 40.6 (2), 34.6 (2), 34.6 (2), 30.5 (2), 13.4 (2); IR (neat) 3376, 2922, 2852, 1450, 1045 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{28}\text{H}_{36}\text{O}_4$ $[\text{M} + \text{Na}]^+$ 459.2511; found 459.2509. **16**: $R_f = 0.16$ (3:7 hexanes/EtOAc); $[\alpha]_D^{24} = -77.6$ (c 0.39, CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.26 (t, $J = 7.6$, 3H), 7.19 (s, 3H), 7.14 (d, $J = 7.6$, 3H), 7.10 (d, $J = 7.6$, 3H), 3.87 (d, $J = 10.0$, 3H), 3.51–3.40 (m, 6H), 2.76–2.70 (m, 6H), 2.04–1.95 (m, 3H), 1.81–1.72 (m, 3H), 1.65–1.50 (m, 6H), 0.78 (d, $J = 6.5$, 9H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 142.4 (3), 140.7 (3), 128.54 (3), 128.46 (3), 128.2 (3), 84.7 (3), 74.6 (3), 74.3 (3), 45.0 (3), 41.2

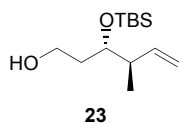
(3), 37.4 (3), 31.6 (3), 13.7 (3); IR (neat) 3391, 2927, 2854, 1454, 1047 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{42}\text{H}_{54}\text{O}_6$ $[\text{M} + \text{Na}]^+$ 677.3818, found 677.3819.



(S)-3-(*tert*-Butyldimethylsilyloxy)-1-cyclohexylpropan-1-ol (20). *tert*-Butyldimethylchlorosilane (317 mg, 2.10 mmol) was added to a solution of (*S*)-Diol **18a** (302 mg, 1.91 mmol) and imidazole (143 mg, 2.10 mmol) in 10 mL of CH_2Cl_2 . After 90 min, saturated aqueous NaHCO_3 (20 mL) was added to the suspension which was diluted with 20 mL of EtOAc. The biphasic mixture was separated and the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic fractions were then dried with MgSO_4 and concentrated under reduced pressure. Purification by column chromatography (9:1 hexanes/EtOAc) of the crude residue afford the title compound (454 mg, 87%) as a clear oil: $R_f = 0.35$ (9:1 hexanes/EtOAc); $[\alpha]_D^{24} = +7.4$ (c 1.22, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 3.91 (dt, $J = 10.1, 4.6$, 1H), 3.80 (dt, $J = 10.1, 6.6$, 1H), 3.57 (td, $J = 5.8, 5.7$, 1H), 3.30 (s, 1H), 1.89–1.83 (m, 1H), 1.80–1.71 (m, 2H), 1.70–1.62 (m, 4H), 1.38–1.29 (m, 1H), 1.28–1.09 (m, 3H), 1.08–0.97 (m, 2H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 76.9, 63.6, 44.1, 35.4, 29.1, 28.5, 26.8, 26.6, 26.5, 26.1 (3), 18.3, $-5.31, -5.33$; IR (neat) 3438, 2927, 2856, 1471, 1255, 1086 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{15}\text{H}_{32}\text{O}_2\text{Si}$ $[\text{M} + \text{Na}]^+$ 295.2069, found 295.2075.

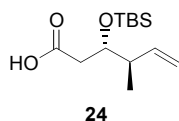


(*R*)-3-(*tert*-Butyldimethylsilyloxy)-1-cyclohexylpropan-1-ol (21). *tert*-Butyldimethylchlorosilane (376 mg, 2.50 mmol) was added to a solution of (*R*)-Diol **19a** (359 mg, 2.27 mmol) and imidazole (170 mg, 2.50 mmol) in 12 mL of CH₂Cl₂. After 2.5 h, saturated aqueous NaHCO₃ (20 mL) was added to the suspension which was diluted with 20 mL of EtOAc. The biphasic mixture was separated and the aqueous layer was washed with EtOAc (3 × 20 mL). The combined organic fractions were then dried with MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (9:1 hexanes/EtOAc) of the crude residue afford the title compound (571 mg, 92%) as a clear oil: *R*_f = 0.35 (9:1 hexanes/EtOAc); [α]_D²⁴ = −7.5 (*c* 1.09, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 3.91 (dt, *J* = 10.1, 4.6, 1H), 3.81 (dt, *J* = 10.1, 7.1, 1H), 3.60–3.54 (m, 1H), 3.35 (d, *J* = 2.1, 1H), 1.89–1.83 (m, 1H), 1.80–1.71 (m, 2H), 1.70–1.62 (m, 4H), 1.38–1.29 (m, 1H), 1.28–1.09 (m, 3H), 1.08–0.97 (m, 2H), 0.90 (s, 9H), 0.08 (s, 6 H); ¹³C NMR (125 MHz, CDCl₃) δ 76.8, 63.6, 44.1, 35.4, 29.1, 28.5, 26.8, 26.6, 26.5, 26.1 (3), 18.3, −5.31, −5.33; IR (neat) 3438, 2927, 2856, 1471, 1255, 1086 cm^{−1}; HRMS (ES/MeOH) *m/z* calcd for C₁₅H₃₂O₂Si [M + Na]⁺ 295.2069, found 295.2069.



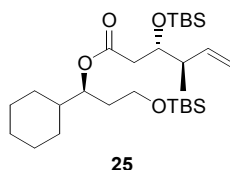
(3*S*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-4-methylhex-5-en-1-ol (23). 2,3-Dichloro-5,6-dicyanobenzoquinone (2.40 g, 10.6 mmol) was added to a biphasic mixture of silyl ether **22** (2.57 g, 7.05 mmol) in CH₂Cl₂ (176 mL) and 18 mL of phosphate buffer (pH = 7). After 1 h, 100 mL of saturated aqueous NaHCO₃ solution was added and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (150 mL) and the combined organic layers were dried with MgSO₄ and concentrated under reduced pressure. This crude residue was then dissolved in

MeOH (55 mL) and NaBH₄ (533 mg, 14.1 mmol) was added. After 30 min, a 10% aqueous H₂SO₄ solution was added drop-wise to quench any excess NaBH₄. The mixture was then diluted with 75 mL of water and extracted with EtOAc (2 × 150 mL). The combined organic layers were then dried with MgSO₄ and concentrated *in vacuo*. Purification by column chromatography (5:1 hexanes/EtOAc) afforded the title compound (1.51 g, 88%) as a clear oil: $R_f = 0.14$ (8:1 hexanes/EtOAc); $[\alpha]_D^{24} = -6.5$ (c 1.79, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.75 (ddd, $J = 17.1, 13.5, 7.3$, 1H), 5.06–5.00 (m, 2H), 3.82 (dt, $J = 7.0, 4.3$, 1H), 3.78–3.68 (m, 2H), 2.43–2.35 (m, 1H), 1.95 (s, 1H), 1.69–1.64 (m, 2H), 1.01 (d, $J = 6.9$, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 140.9, 114.9, 74.5, 60.7, 43.4, 34.7, 26.0 (3), 18.2, 14.1, -4.2, -4.5; IR (neat) 3345, 2958, 2860, 1639, 1473, 1255 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₁₃H₂₈O₂Si [M + Na]⁺ 267.1756, found 267.1756.



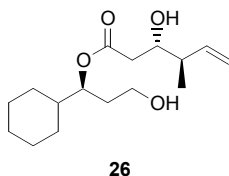
(3S,4R)-3-(tert-Butyldimethylsilyloxy)-4-methylhex-5-enoic acid (24). A solution of pyridinium dichromate (44.0 g, 117 mmol) in 50 mL of DMF was added to a solution of alcohol **23** in 100 mL of DMF. After 3 d, water (200 mL) was added and the mixture was extracted with EtOAc (2 × 200 mL). The combined organic fractions were then washed with brine (2 × 200 mL), dried with MgSO₄, and concentrated. The crude residue was then purified by column chromatography (4:1 hexanes/EtOAc) to yield carboxylic acid **24** (1.80 g, 66%) as a yellow oil: $R_f = 0.23$ (4:1 hexanes/EtOAc); $[\alpha]_D^{24} = -8.2$ (c 1.74, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 11.2–10.2 (br s, 1H), 5.75 (ddd, $J = 17.0, 10.7, 7.4$, 1H), 5.09–5.03 (m, 2H), 4.11 (dt, $J = 6.6, 5.1$, 1H), 2.49–2.42 (m, 2H), 2.41–2.33 (m, 1H), 1.04 (d, $J = 6.9$, 3H), 0.89 (s, 9H), 0.09 (s, 3H),

0.06 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 178.5, 139.6, 115.7, 72.4, 43.6, 39.1, 25.9, 25.8, 25.7, 18.1, 14.5, -4.6, -4.7; IR (neat) 3078, 2931, 2860, 1714, 1464, 1255 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{13}\text{H}_{26}\text{O}_3\text{Si}$ $[\text{M} + \text{Na}]^+$ 281.1549, found 281.1550.



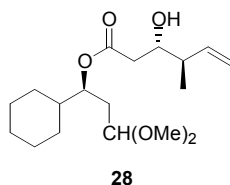
Bis-silyl ether 25. Carboxylic acid **24** (260 mg, 0.950 mmol) and (*S*)-alcohol **20** (246 mg, 0.950 mmol) were dissolved in 3 mL of CH_2Cl_2 . DMAP (23.0 mg, 0.19 mmol) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (201 mg, 1.05 mmol) were then added sequentially. After 18 h, water (10 mL) was added and the biphasic mixture was extracted with hexanes (2×20 mL). The combined organic phases were then dried with MgSO_4 and concentrated under reduced pressure. Purification by column chromatography (19:1 hexanes/ Et_2O) yielded the title compound (303 mg, 62%) as a clear oil: $R_f = 0.48$ (19:1 hexanes/ EtOAc); $[\alpha]_D^{24} = -21.8$ (c 1.20, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.78 (ddd, $J = 17.3, 10.4, 7.7$, 1H), 5.07–4.98 (m, 2H), 4.82 (dt, $J = 7.9, 4.8$, 1H), 4.11 (td, $J = 6.3, 3.2$, 1H), 3.65–3.54 (m, 2H), 2.44 (dd, $J = 16.0, 6.4$, 1H), 2.35 (dd, $J = 16.0, 6.2$, 2H), 1.81–1.71 (m, 4H), 1.70–1.61 (m, 3H), 1.57–1.49 (m, 1H), 1.26–1.09 (m, 3H), 1.03 (d, $J = 6.9$, 3H), 1.01–0.94 (m, 2H), 0.88 (s, 18H), 0.08 (s, 3H), 0.05 (s, 3H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.8, 140.0, 115.6, 72.2, 60.2, 43.5, 41.6, 39.8, 34.4, 28.9, 28.3, 26.6, 26.34 (2), 26.32 (3), 26.13 (3), 26.07, 18.5, 18.3, 15.9, -4.3, -4.6, -5.1(2); IR (neat) 2956, 2858, 1734, 1471, 1254 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{28}\text{H}_{56}\text{O}_4\text{Si}_2$ $[\text{M} + \text{Na}]^+$ 535.3615, found 535.3601.

Bis-silyl ether 25. Carboxylic acid **24** (517 mg, 1.90 mmol) and (*R*)-Alcohol **21** (490 mg, 1.90 mmol) were azeotroped in benzene (3×15 mL) and concentrated together. The mixture was then dissolved in THF (30 mL) and triphenylphosphine (1.49 g, 5.69 mmol) was added. The solution was then cooled to -40 °C and diisopropyl azodicarboxylate (1.2 mL, 6.07 mmol) was added. After 20 h, the suspension was warmed to room temperature and ~ 200 mg of silica gel was added. The solution was then concentrated to give a yellow powder that was loaded onto a column for purification (19:1 hexanes/Et₂O) affording the title compound (789 mg, 81%) as a clear oil. The ¹H NMR and ¹³C NMR spectra matched data reported above.

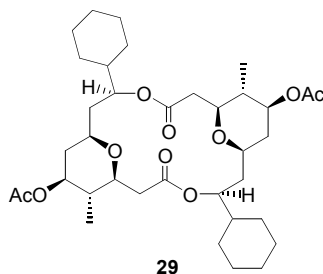


Diol 26. Pyridine hydrofluoride (0.90 mL, 70% v/v HF) was added to a solution of bis-TBS ether **25** (290 mg, 0.565 mmol) in THF (5 mL). After 3 h, saturated aqueous NaHCO₃ was added dropwise until gas evolution halted. The mixture was then extracted with EtOAc (2×30 mL) and the combined organic layers were dried with MgSO₄ and concentrated. Purification by column chromatography (1:1 hexanes/EtOAc) afforded diol **26** (142 mg, 88%) as a colorless oil: $R_f = 0.23$ (1:1 hexanes/EtOAc); $[\alpha]_D^{24} = -39.5$ (c 0.40, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.79 (ddd, $J = 17.1, 10.4, 8.1$, 1H), 5.13–5.08 (m, 2H), 4.93 (ddd, $J = 10.4, 6.0, 2.7$, 1H), 3.93 (ddd, $J = 9.6, 5.4, 3.2$, 1H), 3.68–3.61 (m, 1H), 3.59–3.52 (m, 1H), 2.73 (br s, 1H), 2.50 (dd, $J = 15.6, 3.2$, 1H), 2.44 (dd, $J = 15.6, 9.6$, 1H), 2.28 (app sextet, $J = 6.8$, 1H), 1.89–1.80 (m, 1H), 1.78–1.72 (m, 3H), 1.71–1.64 (m, 1H), 1.29–1.09 (m, 3H), 1.07 (d, $J = 6.9$, 3 H), 1.05–0.95 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 174.1, 139.7, 116.7, 76.0, 71.7, 59.0, 43.9, 41.9, 39.5, 34.5,

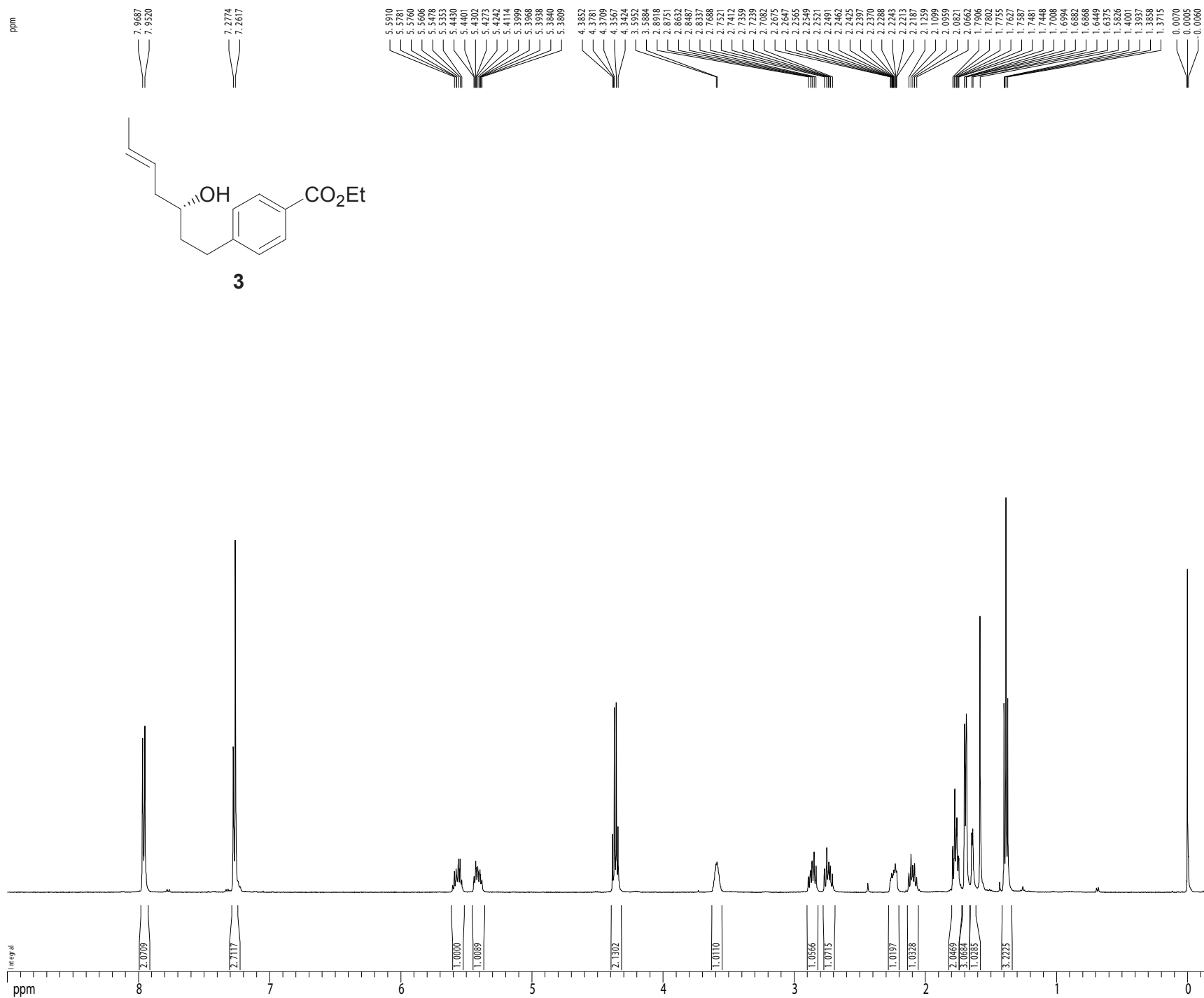
29.2, 28.5, 26.5, 26.23, 26.17, 16.1; IR (neat) 3408, 2929, 2856, 1716, 1450, 1176 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{16}\text{H}_{28}\text{O}_4$ $[\text{M} + \text{Na}]^+$ 307.1885, found 307.1880.

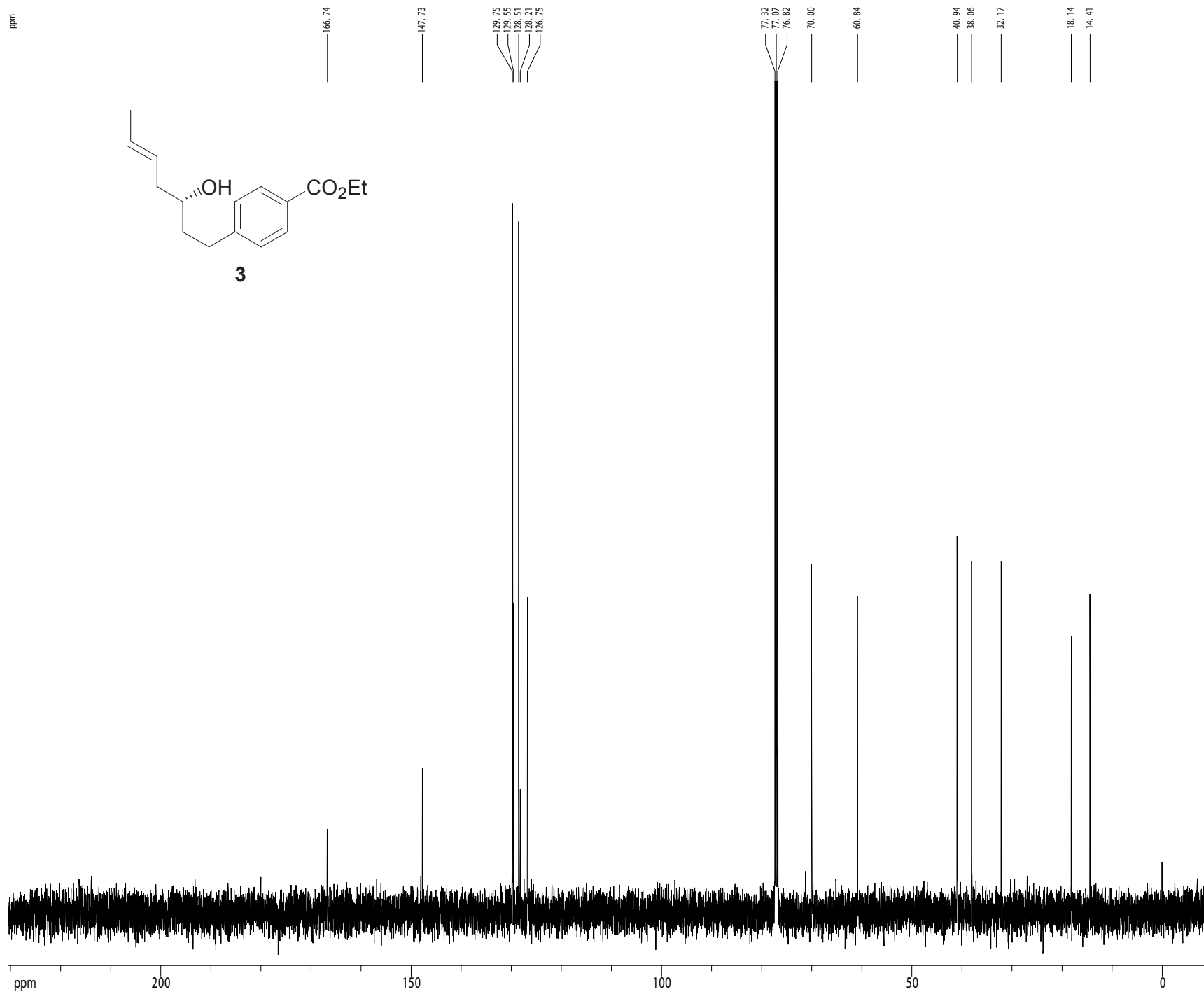


Acetal 28. 2,2,6,6,-Tetramethylpiperidine-1-oxyl (7.7 mg, 0.049 mmol) was added to a solution of diol **26** (70.0 mg, 0.250 mmol) and [bis(acetoxy)iodo]benzene (87.0 mg, .0270 mmol) in CH_2Cl_2 (2 mL). After 8 h, 5 mL of saturated aqueous NaHCO_3 was added and the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic fractions were then dried with MgSO_4 and concentrated under reduced pressure. The crude brown residue was then dissolved in 2 mL of MeOH and DL-camphorsulfonic acid (5.7 mg, 0.025 mmol) was added. After 20 h, saturated aqueous NaHCO_3 (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic phases were then dried with MgSO_4 and concentrated *in vacuo*. Purification by column chromatography (5:1 hexanes/EtOAc with 1% Et_3N) afforded the title compound (62.3 mg, 77%) as a colorless oil: $R_f = 0.20$ (4:1 hexanes/EtOAc); $[\alpha]_D^{24} = -37.1$ (c 1.00, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.82 (ddd, $J = 17.1, 10.5, 8.0$, 1H), 5.12–5.06 (m, 2H), 4.95 (q, $J = 6.0$, 1H), 4.41 (t, $J = 5.6$, 1H), 3.96–3.90 (m, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 2.96 (s, 1H), 2.48–2.38 (m, 2H), 2.29 (app sextet, $J = 6.9$, 1H), 1.83 (t, $J = 1.83$, 2H), 1.78–1.63 (m, 5H), 1.55–1.44 (m, 1H), 1.29–1.10 (m, 3H), 1.07 (d, $J = 6.9$, 3H), 1.05–0.91 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.0, 139.9, 116.2, 102.6, 75.0, 71.6, 53.3, 53.2, 43.6, 42.0, 39.5, 34.7, 29.0, 28.2, 26.5, 26.23, 26.22, 16.1; IR (neat) 3487, 2931, 2856, 1731, 1639, 1452 cm^{-1} ; HRMS (ES/MeOH) m/z calcd for $\text{C}_{18}\text{H}_{32}\text{O}_5$ $[\text{M} + \text{Na}]^+$ 351.2148, found 351.2145.

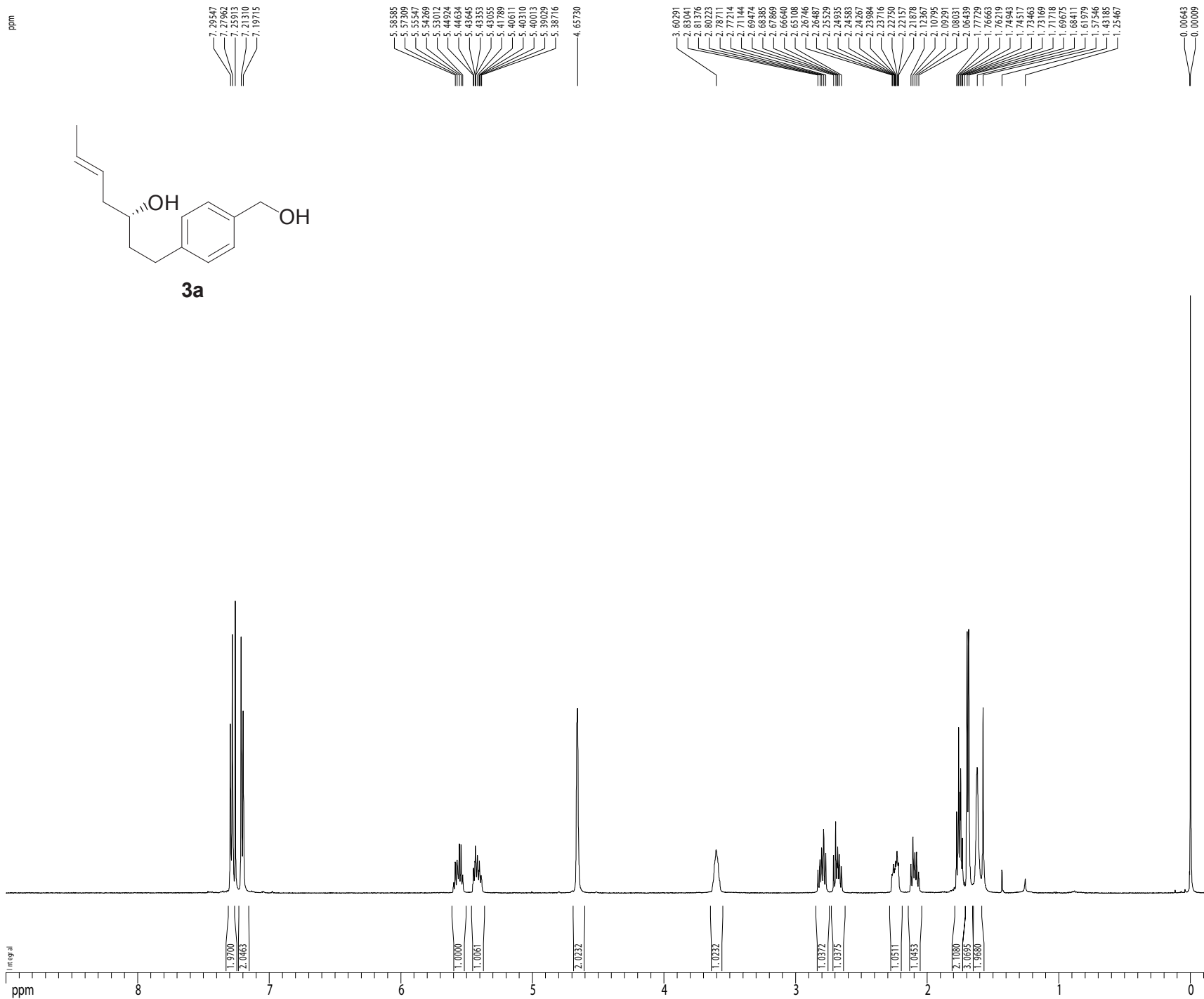


Dimeric macrolide 29. Triethylsilyl trifluoromethanesulfonate (0.55 mL, 2.42 mmol) was added to a solution of acetal **28** (39.8 mg, 0.121 mmol) and trimethylsilyl acetate (0.56 mL, 3.64 mmol) in 4 mL of acetic acid. After 2 h, the brown/orange solution was diluted with 10 mL of Et₂O and saturated aqueous NaHCO₃ was carefully added until gas evolution ceased. The aqueous layer was then extracted with Et₂O (2 × 10 mL) and the combined organic fractions were dried with MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (6:1 hexanes/EtOAc) afforded the dimeric macrolide (16.7 mg, 43%) as a white film: $R_f = 0.30$ (4:1 hexanes/EtOAc); $[\alpha]_D^{24} = +49.7$ (c 0.31, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.90 (td, $J = 7.9, 2.0, 2H$), 4.58 (td, $J = 10.7, 4.3, 2H$), 3.62–3.55 (m, 4H), 2.53 (dd, $J = 18.1, 4.0, 2H$), 2.44 (dd, $J = 18.1, 5.9, 2H$), 2.05 (s, 6H), 2.03–1.98 (m, 2H), 1.75–1.63 (m, 10H), 1.59–1.56 (m, 4H), 1.49–1.41 (m, 2H), 1.30–1.10 (m, 10H), 0.98–0.86 (m, 4H), 0.82 (d, $J = 6.5, 6H$); ¹³C NMR (125 MHz, CDCl₃) δ 170.9 (2), 170.8 (2), 77.1 (2), 76.7 (2), 75.5 (4), 42.5 (2), 41.0 (2), 39.2 (2), 38.2 (2), 37.9 (2), 28.5 (2), 28.4 (2), 26.6 (2), 26.2 (4), 21.4 (2), 13.0 (2); IR (neat) 2929, 2854, 1738, 1240, 1029 cm⁻¹; HRMS (ES/MeOH) m/z calcd for C₃₆H₅₆O₁₀ [M + Na]⁺ 671.3771, found 671.3788.

^1H NMR; 500 MHz, CDCl_3 

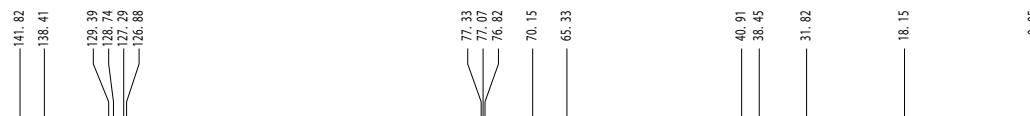
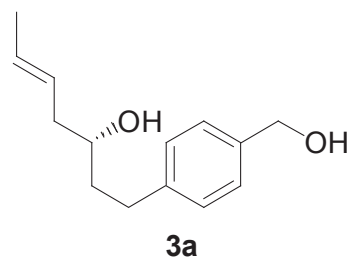
13C NMR; 125 MHz, CDCl₃

¹H NMR; 500 MHz, CDCl₃



^{13}C NMR; 125 MHz, CDCl_3

ppm



ppm

200

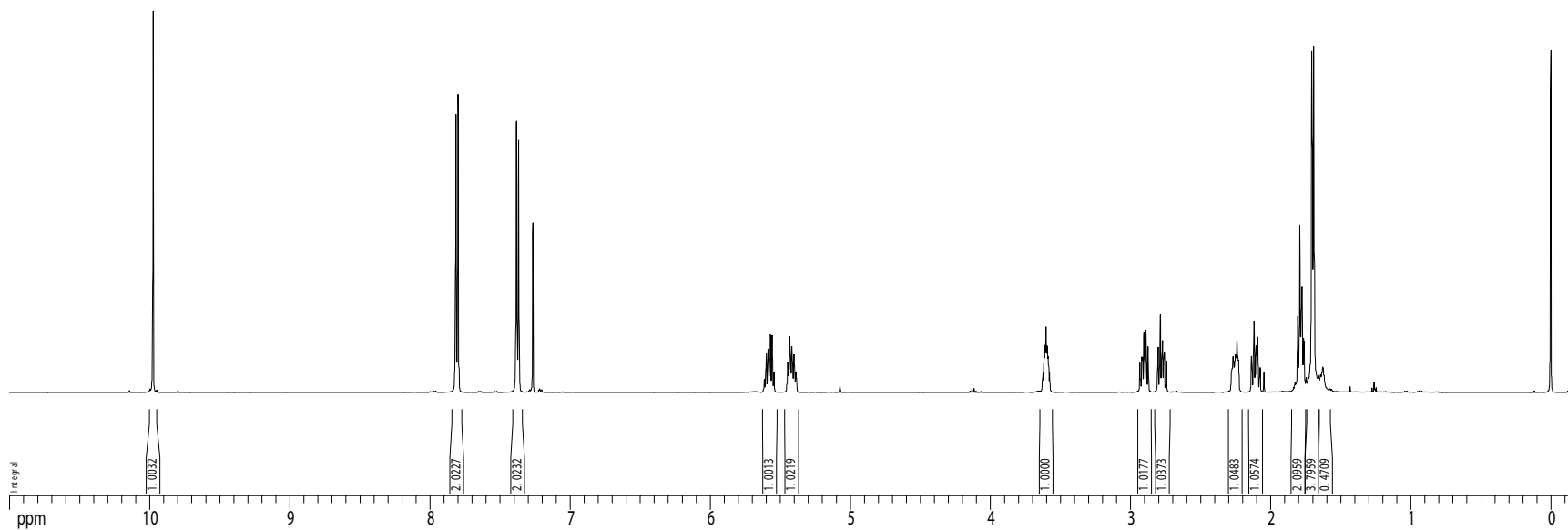
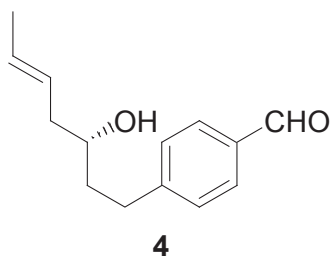
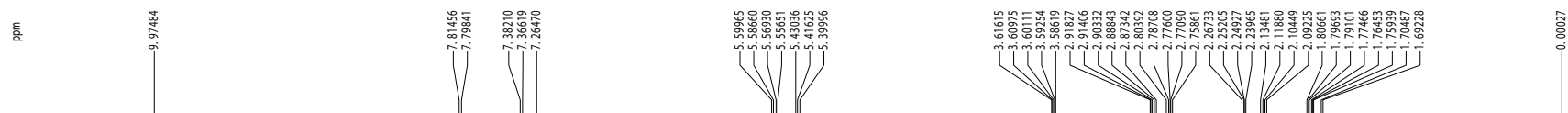
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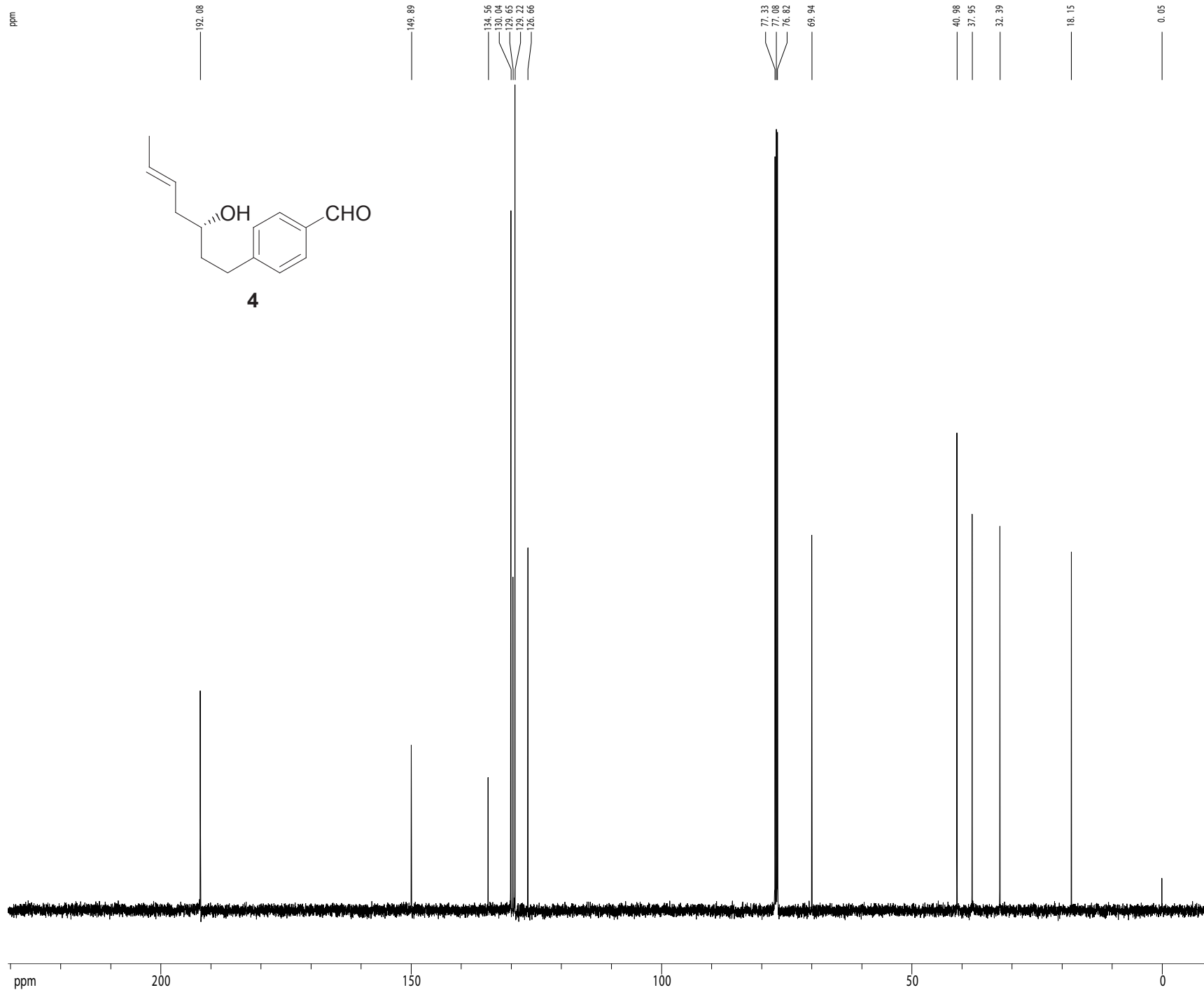
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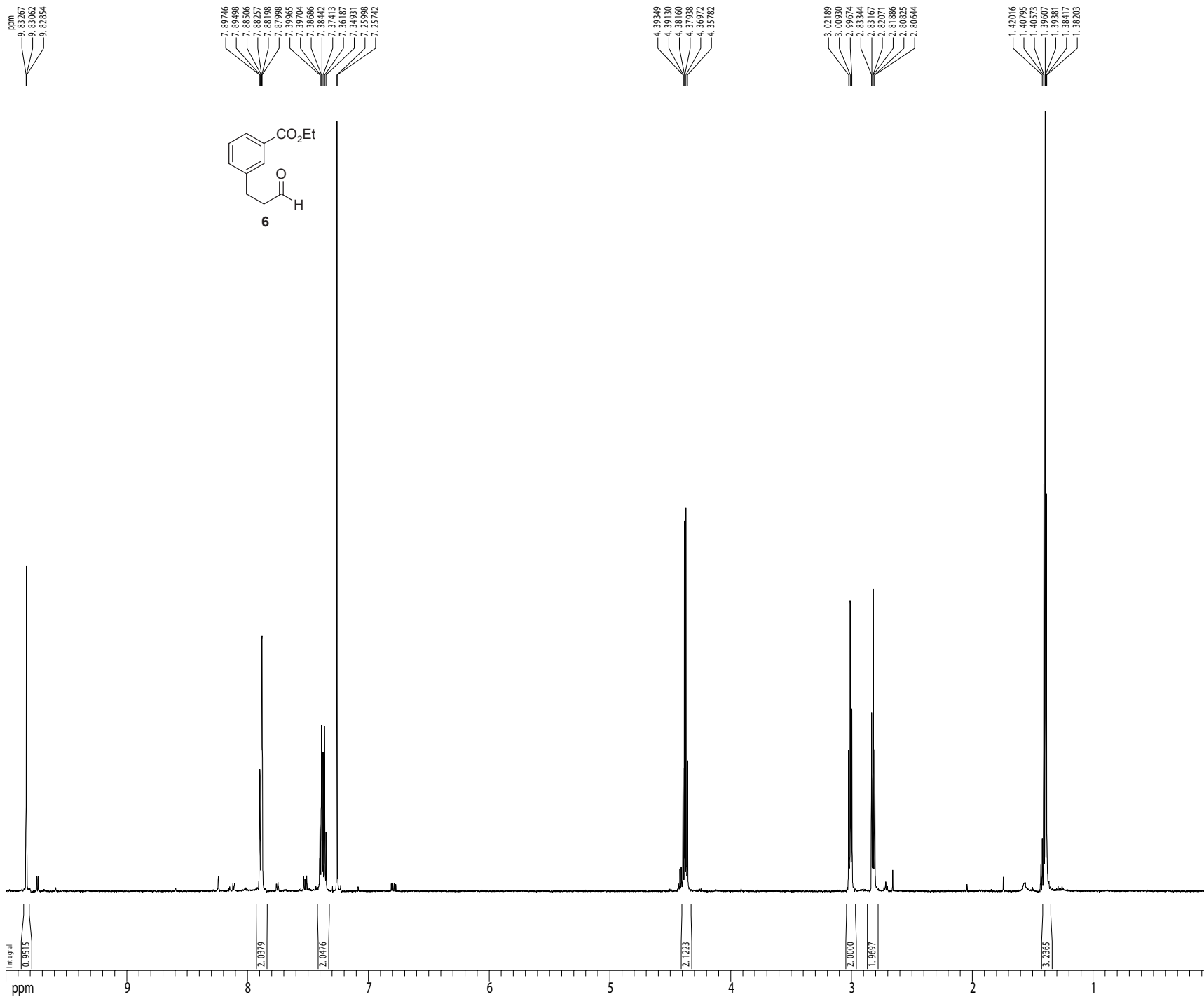
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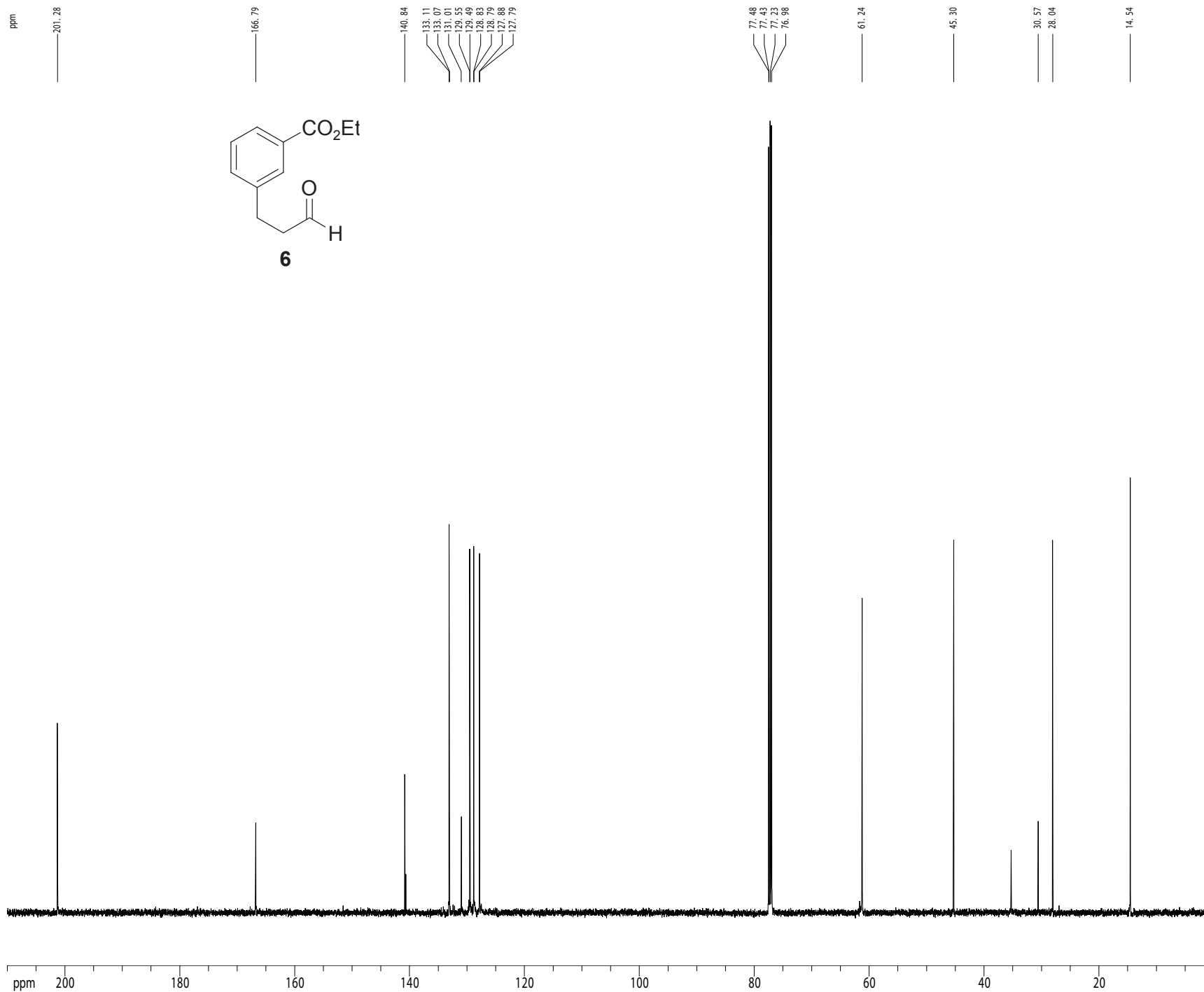
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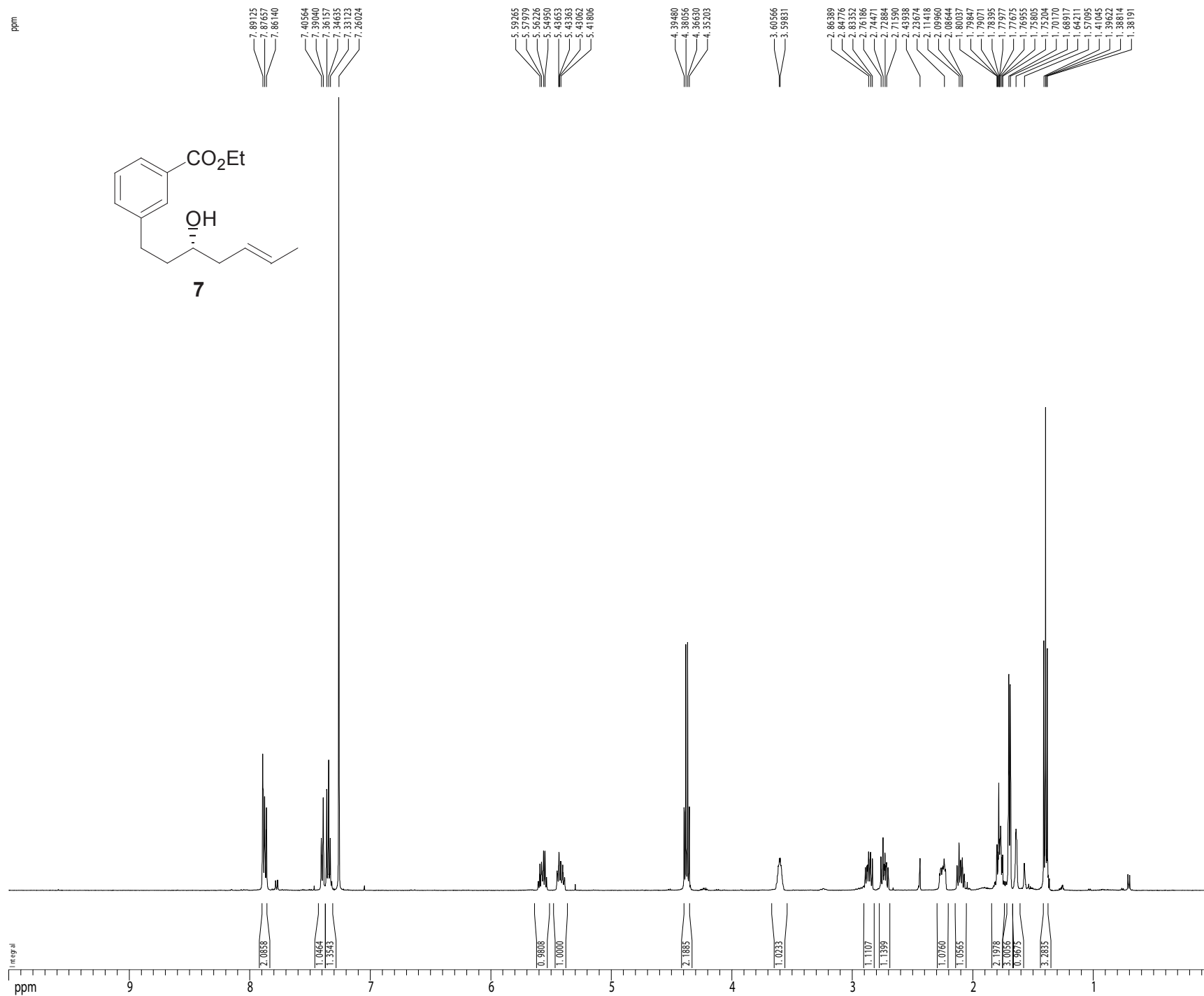
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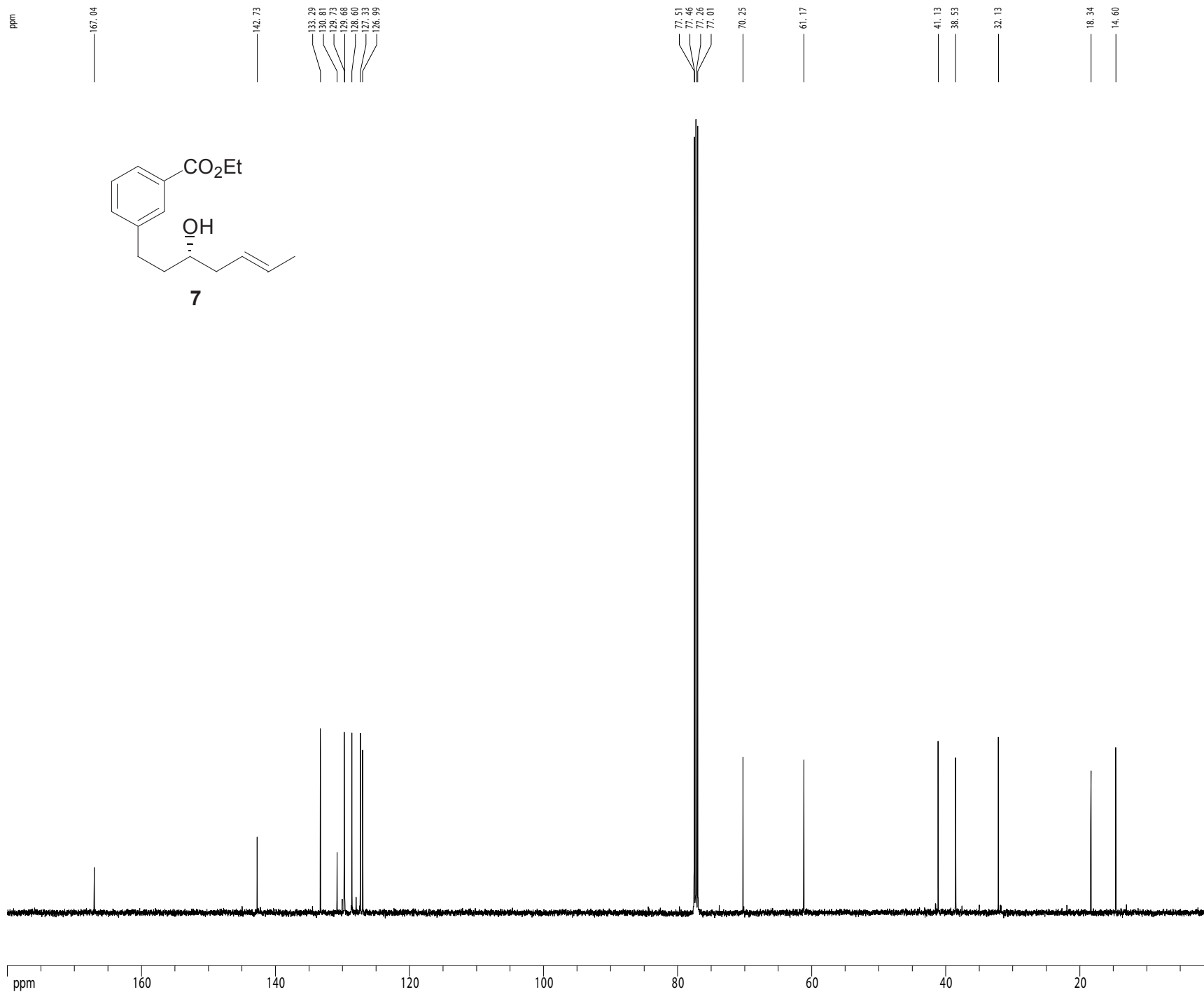
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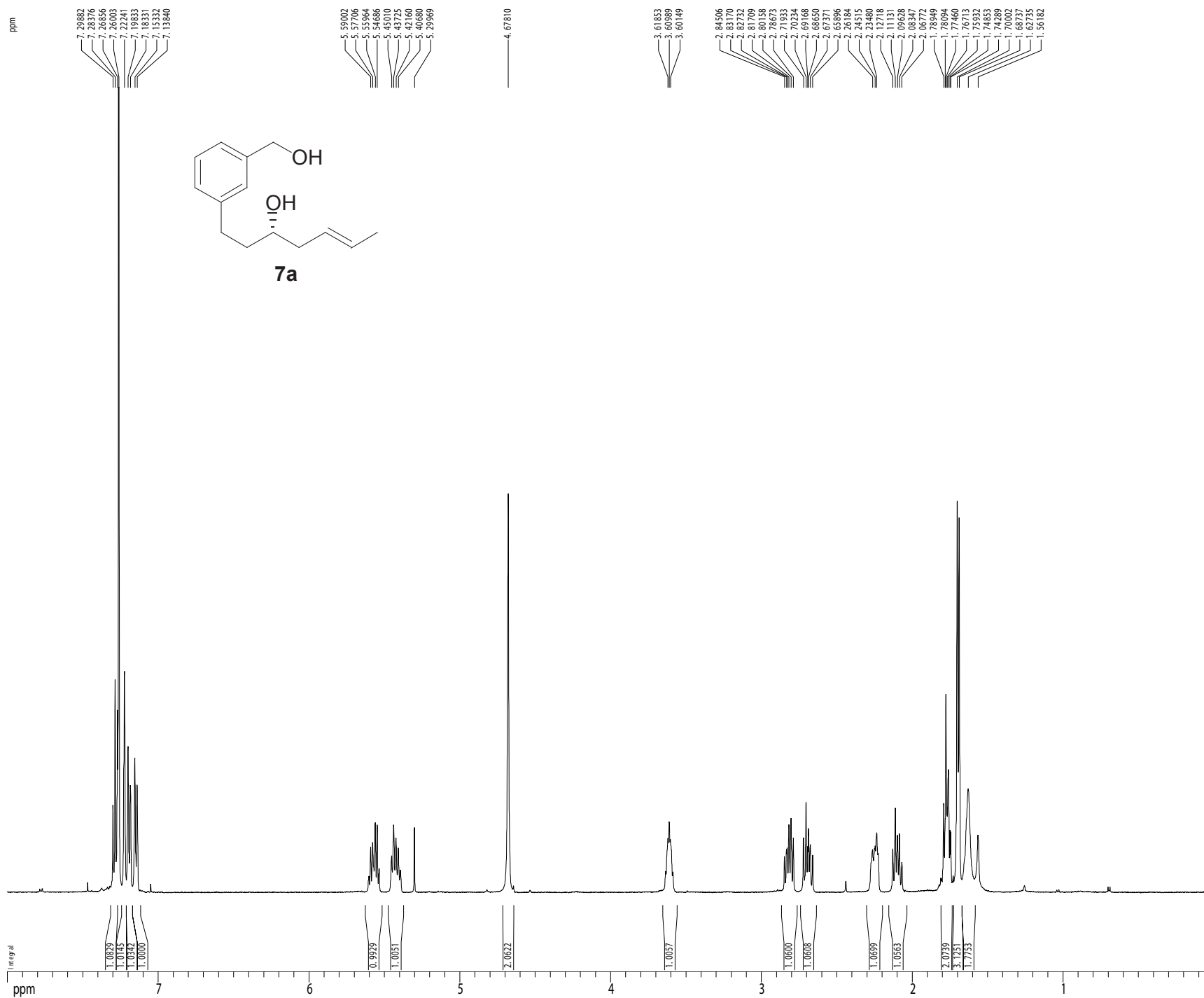
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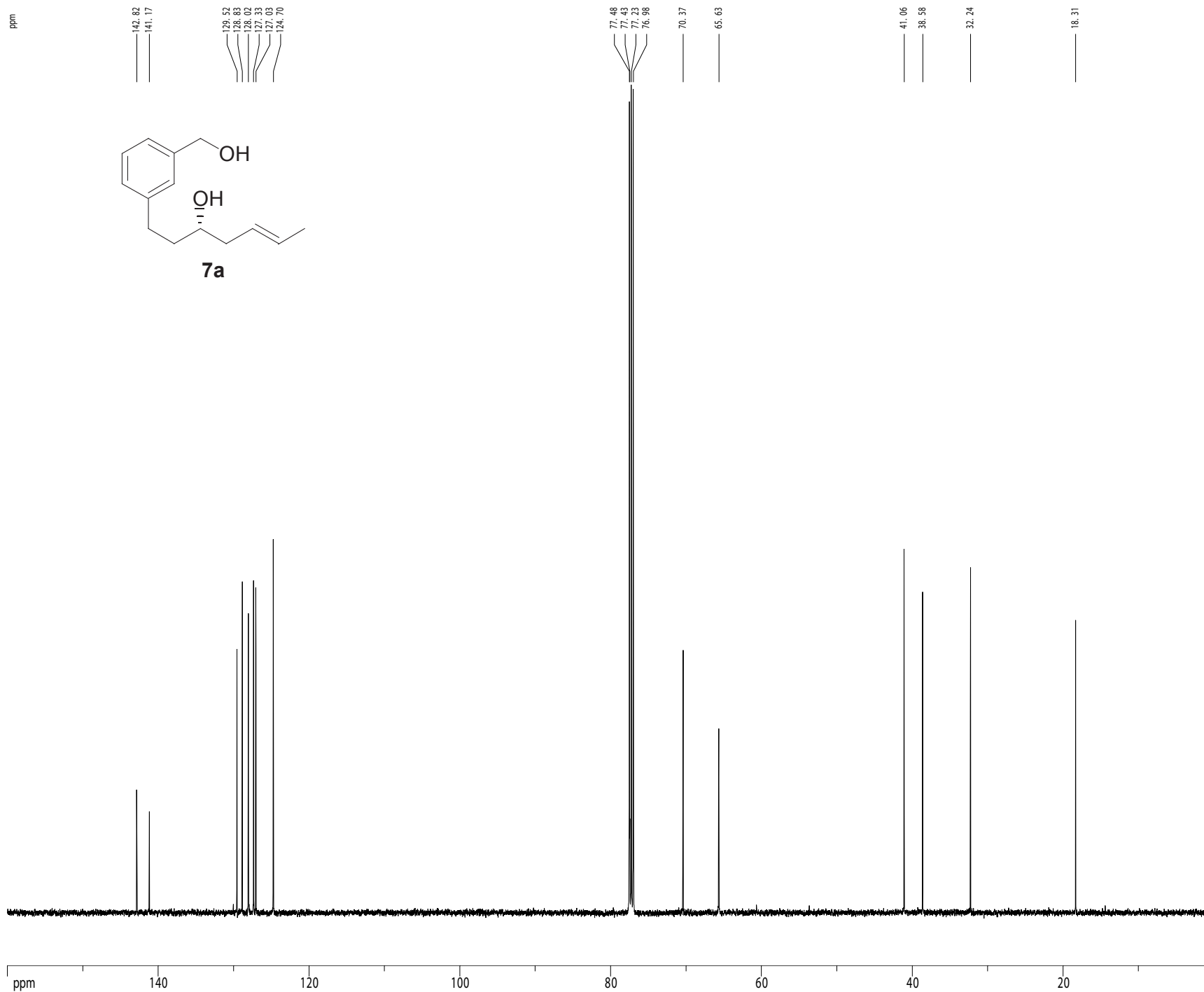
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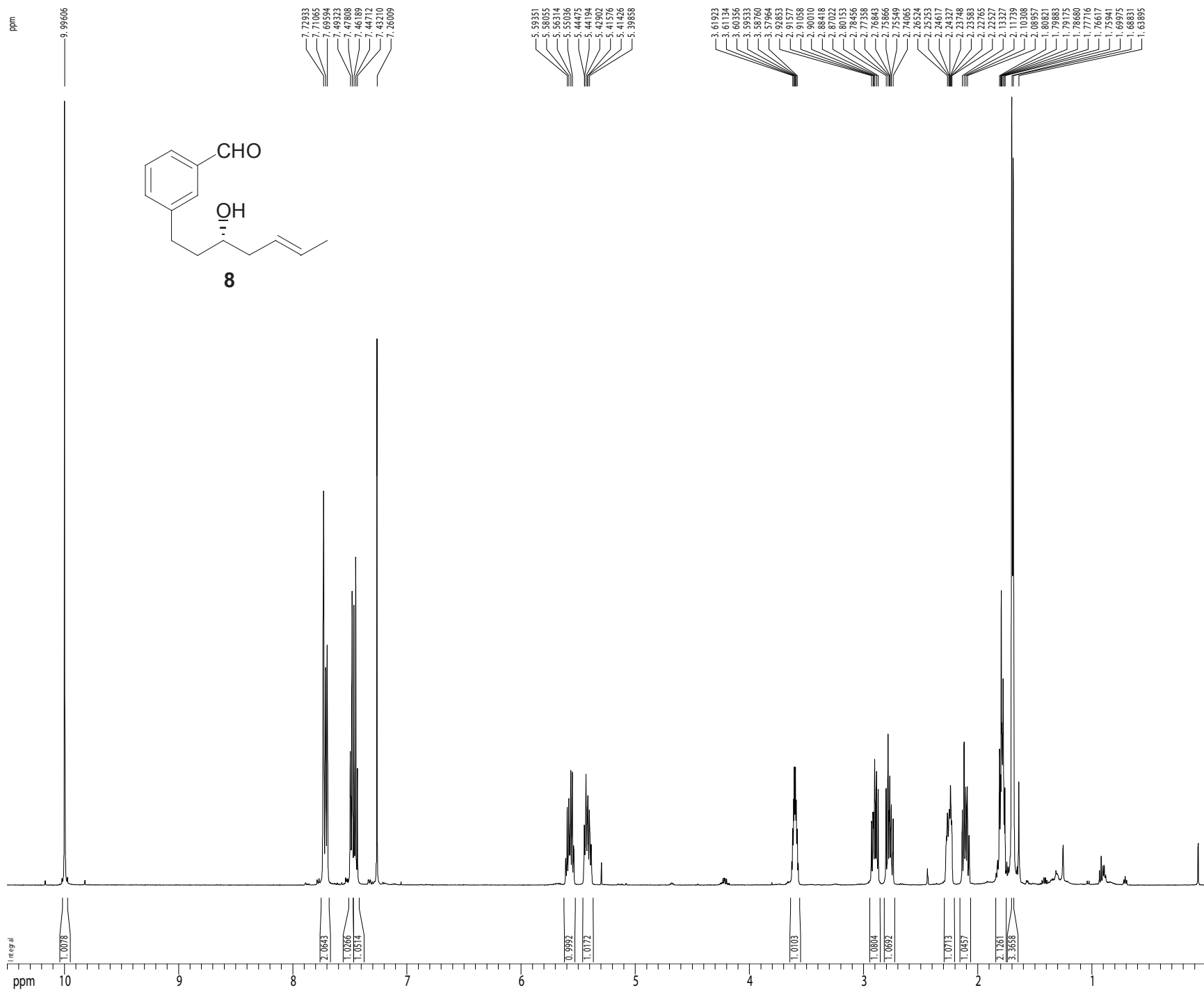


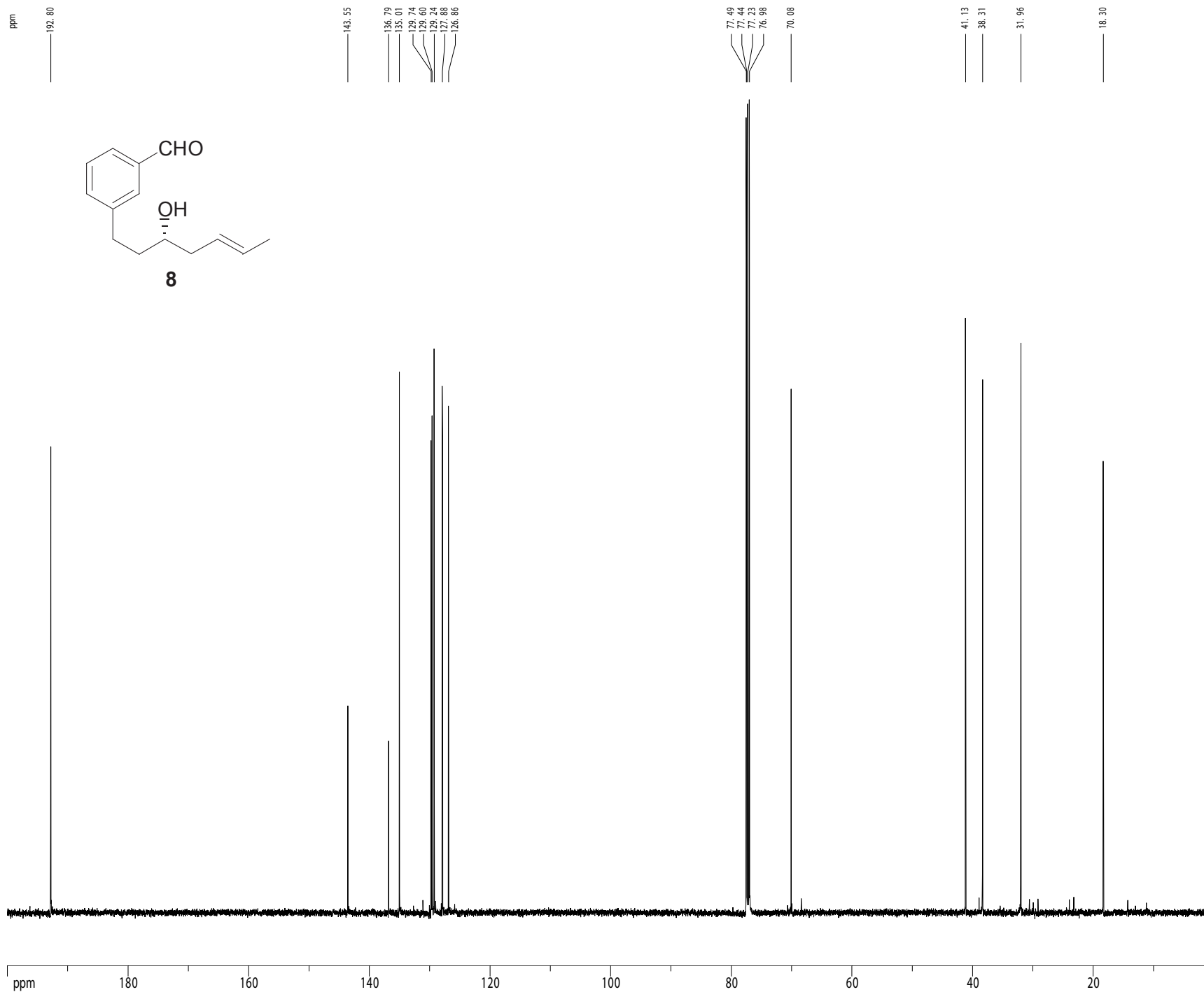
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1H NMR; 500 MHz, CDCl3

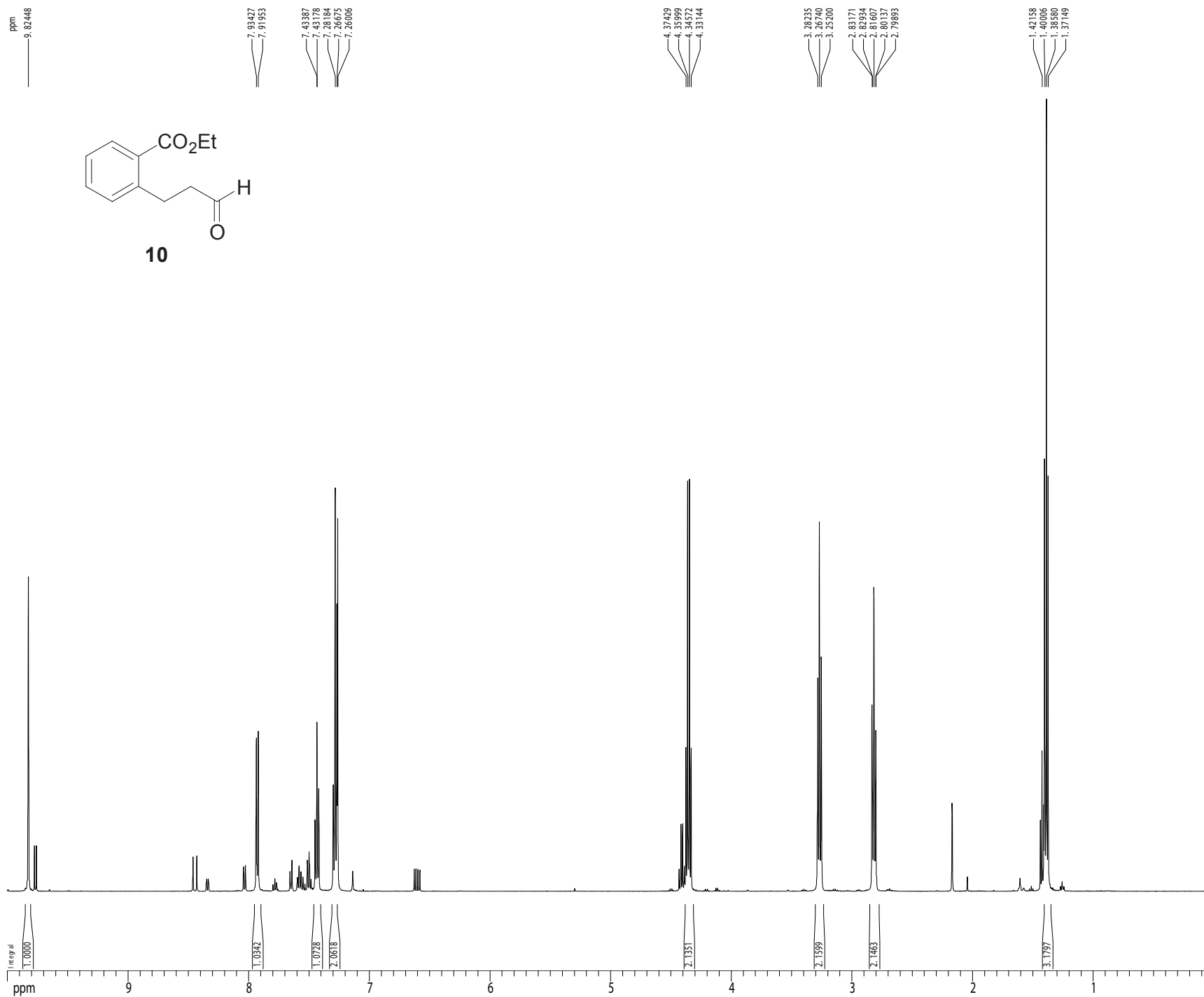


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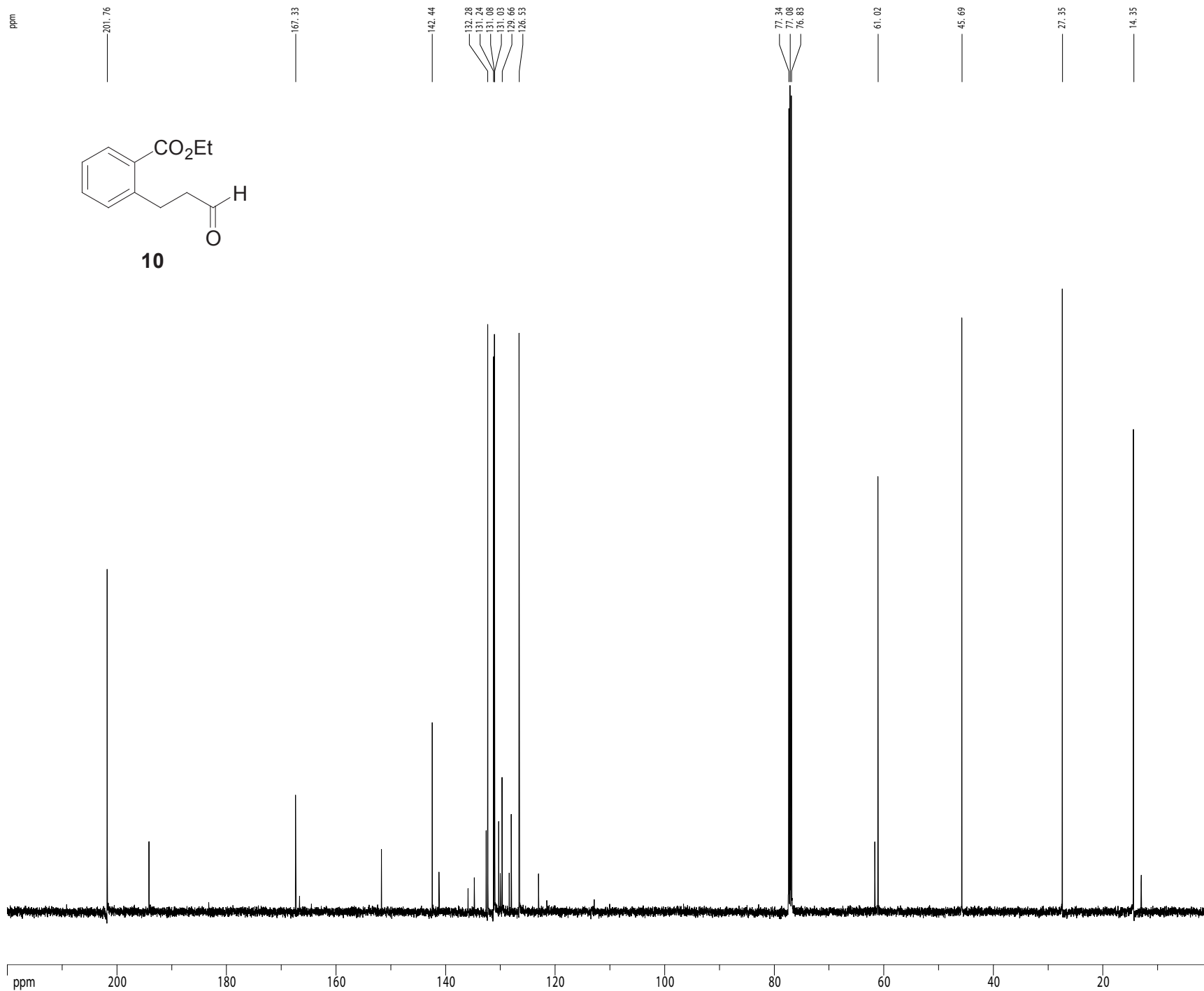
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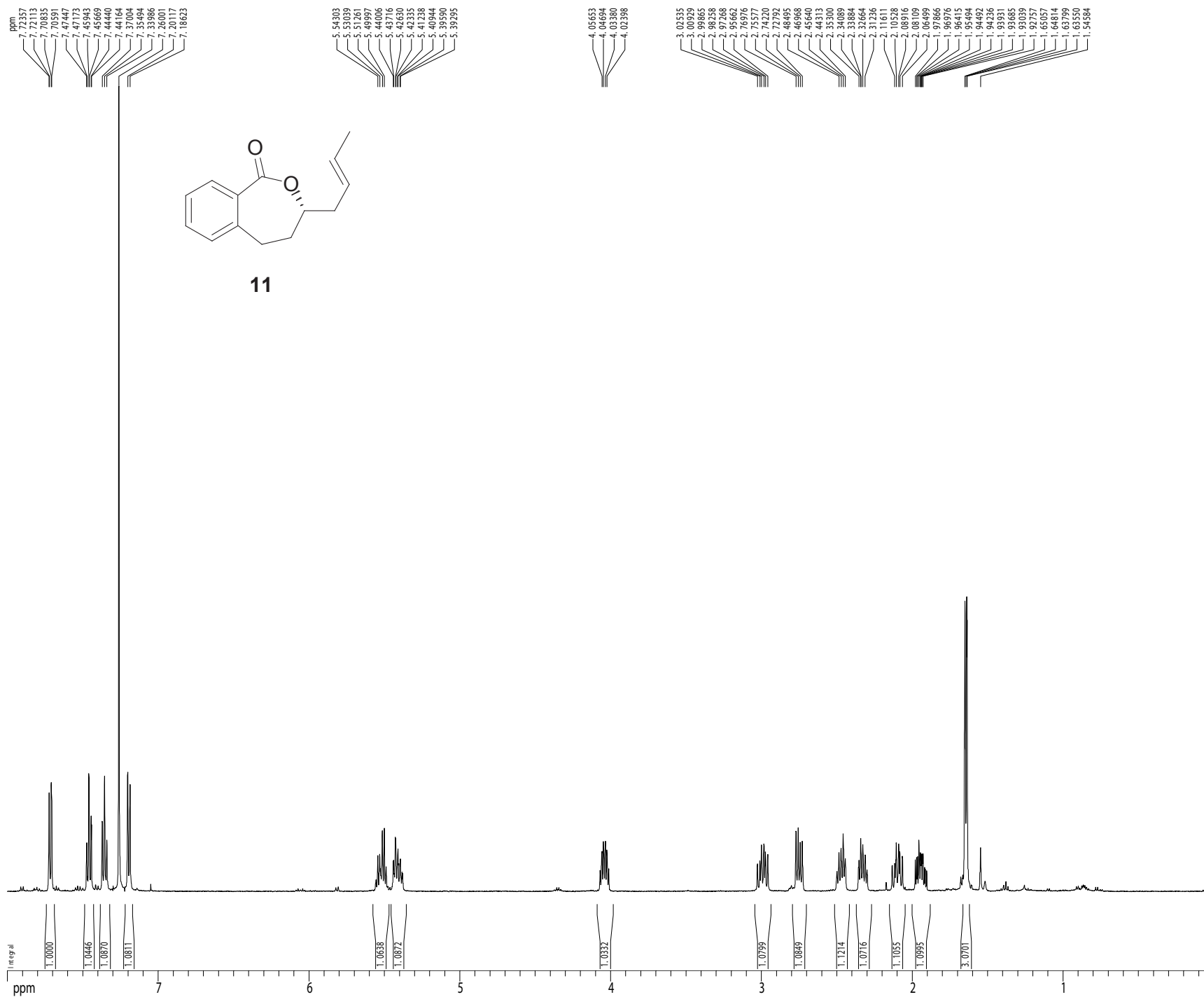
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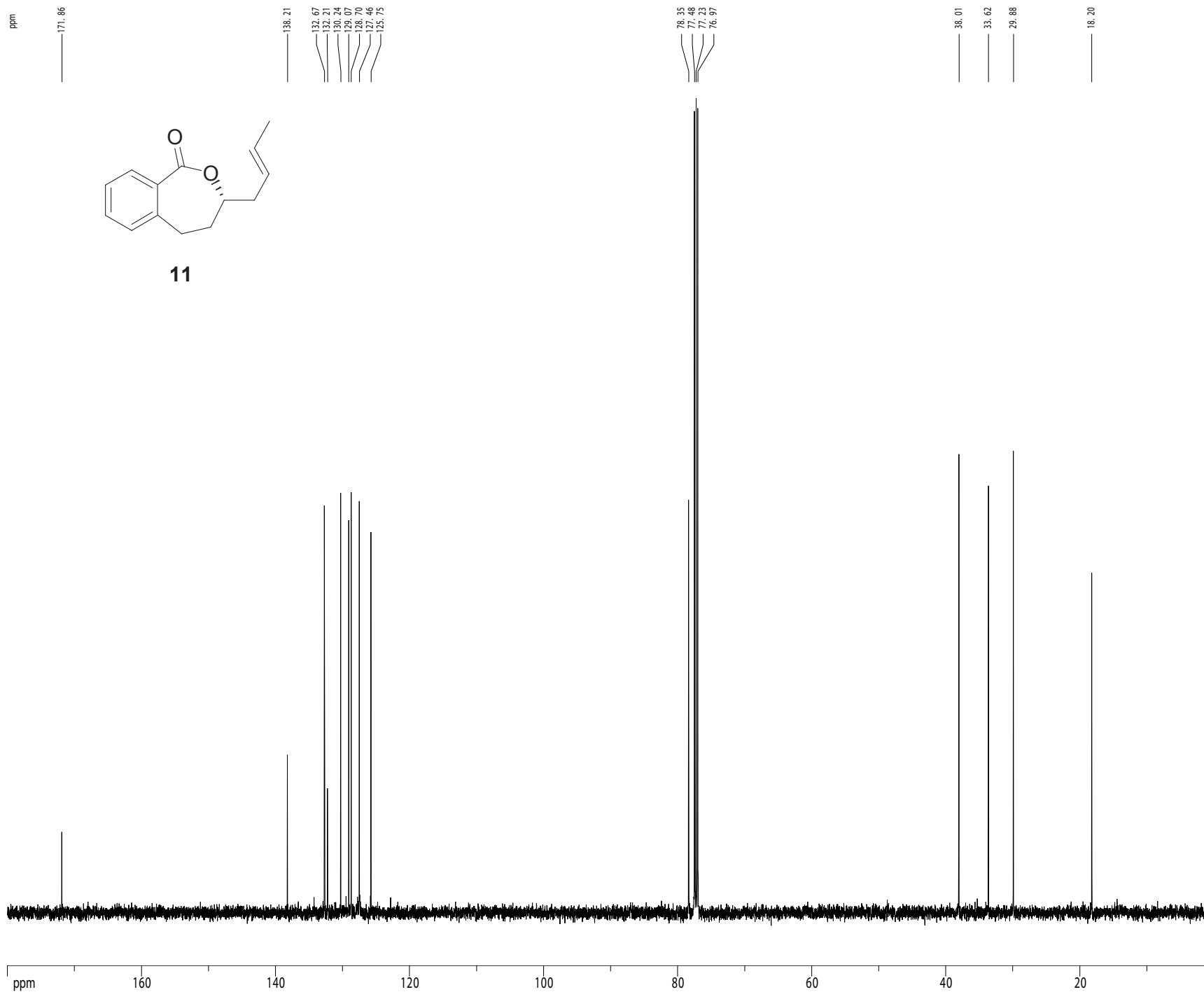
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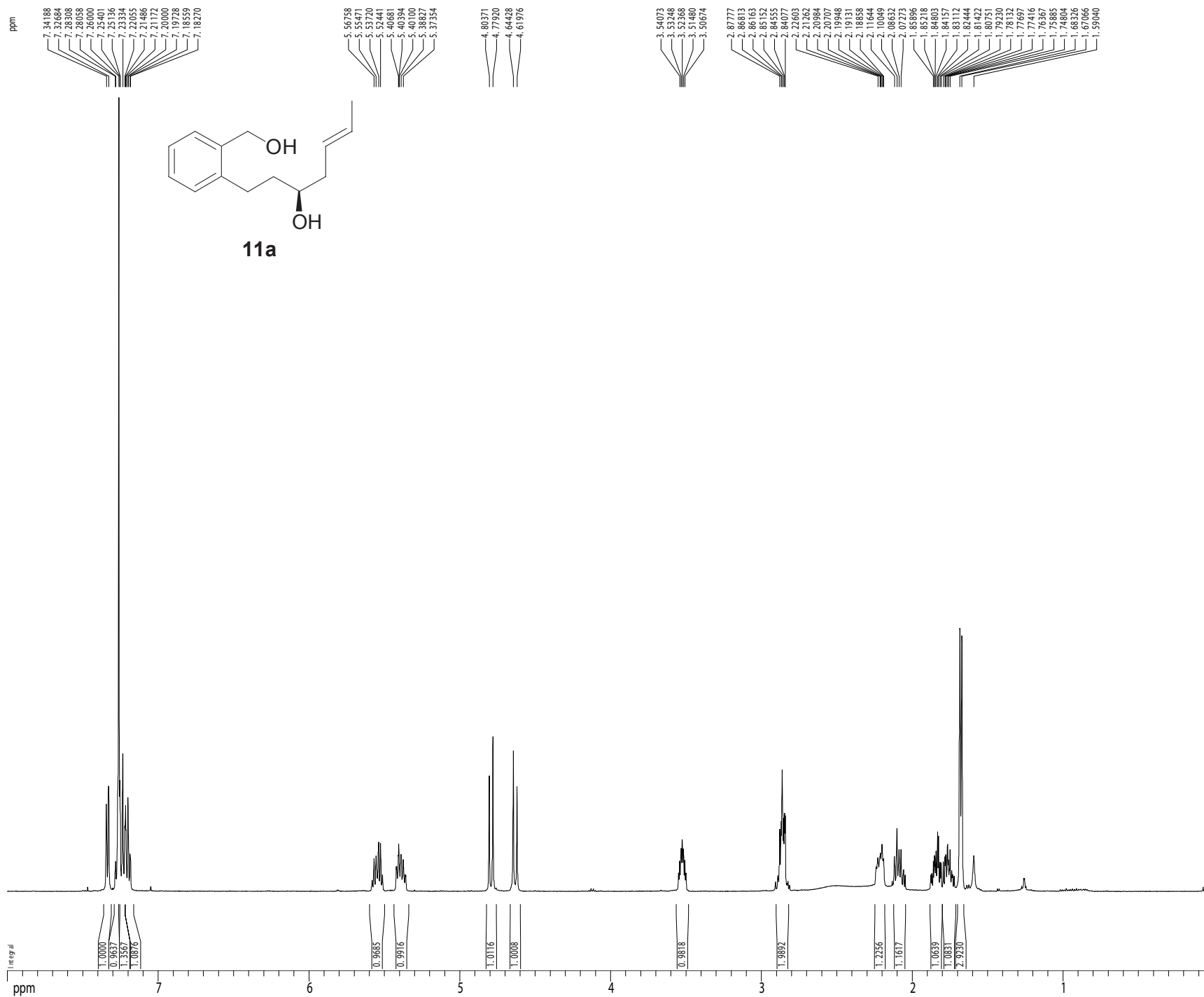


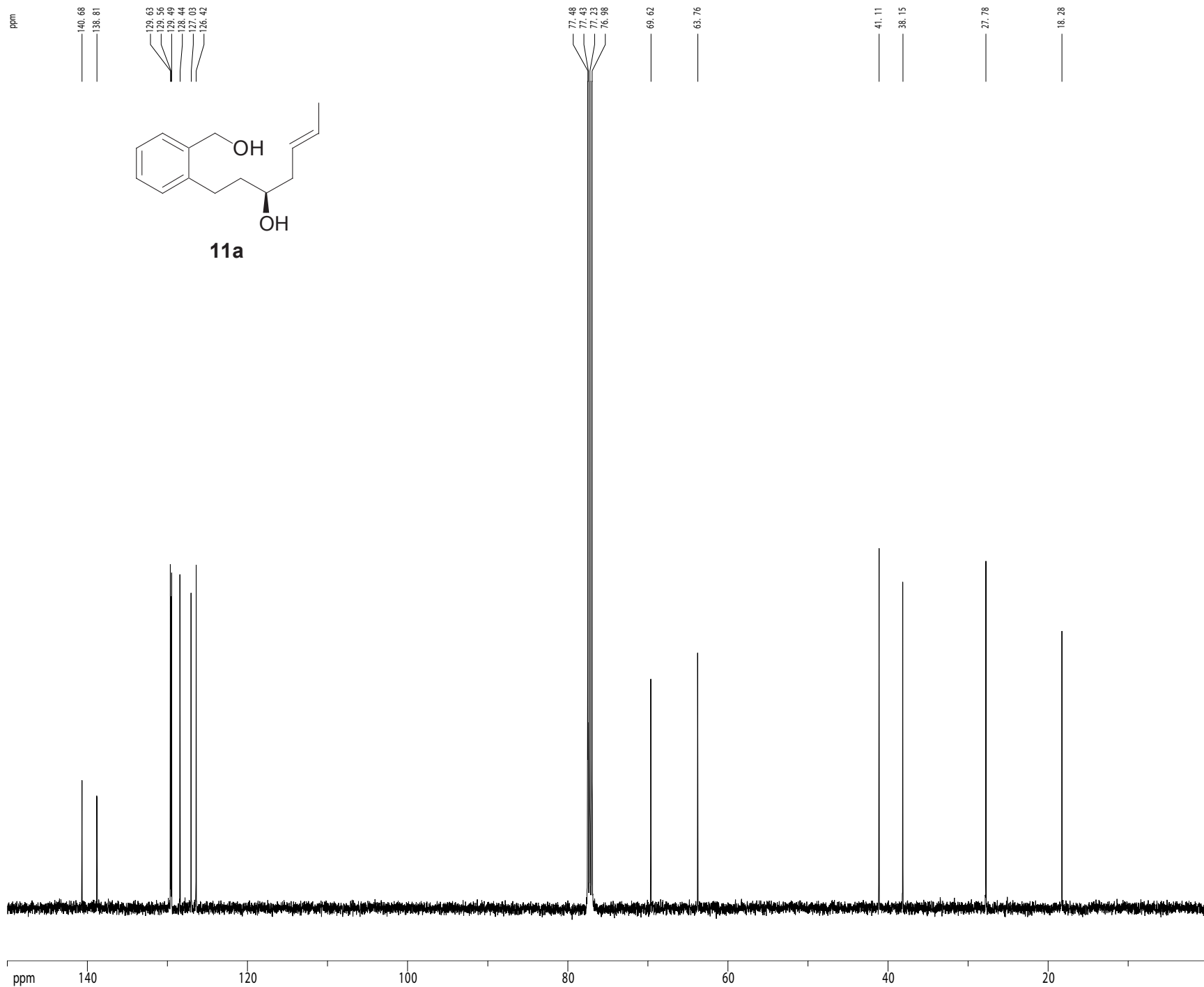
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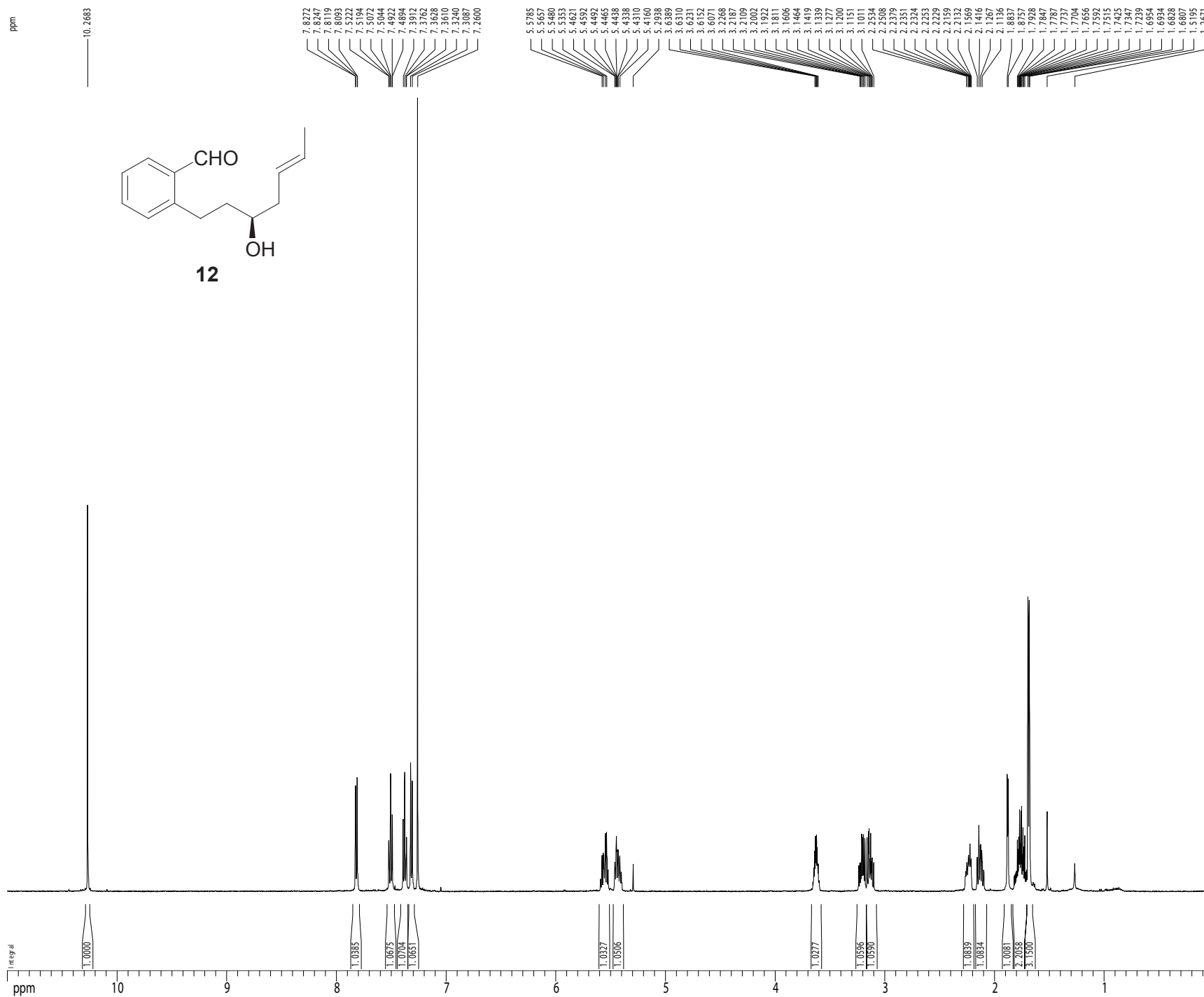


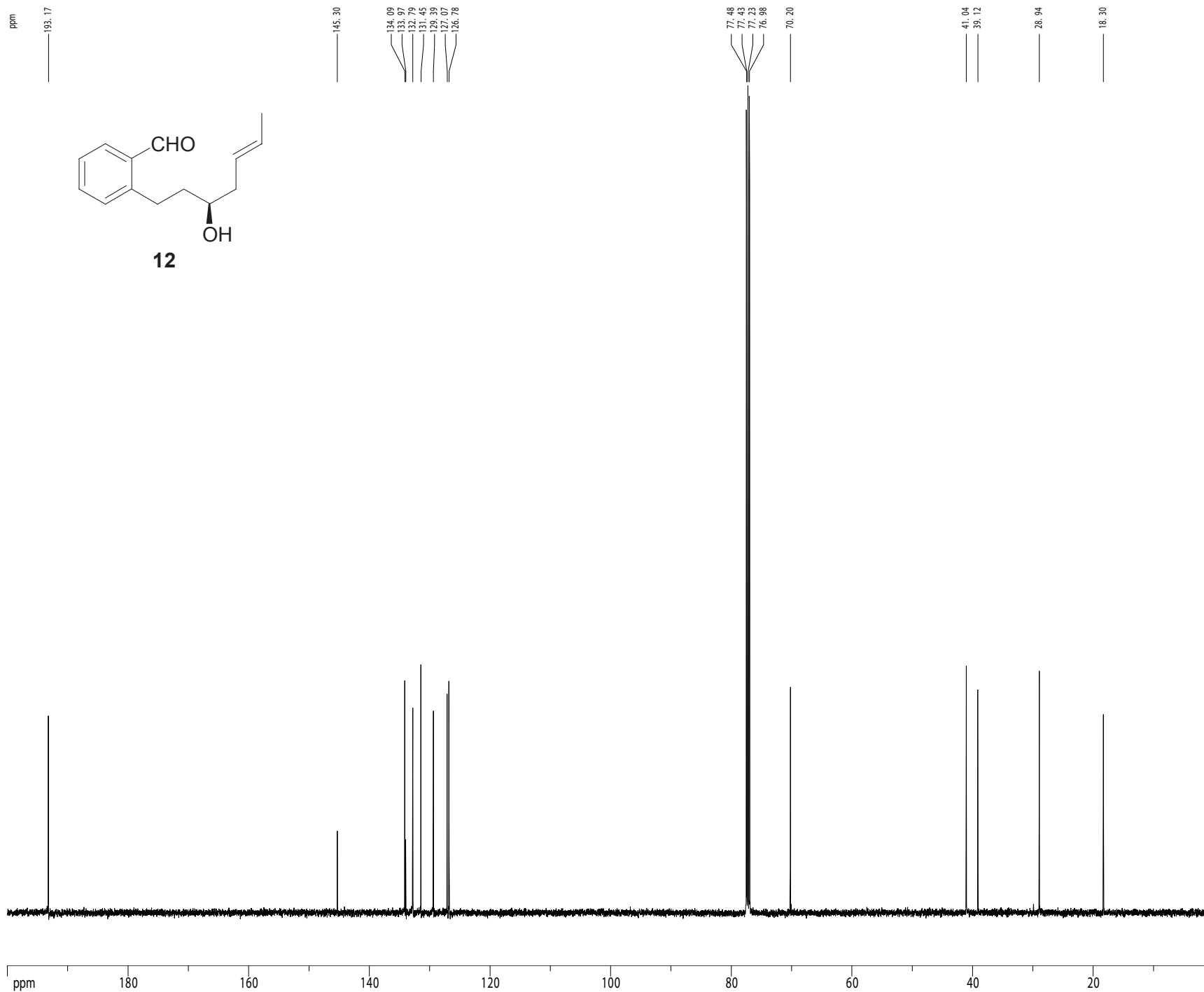
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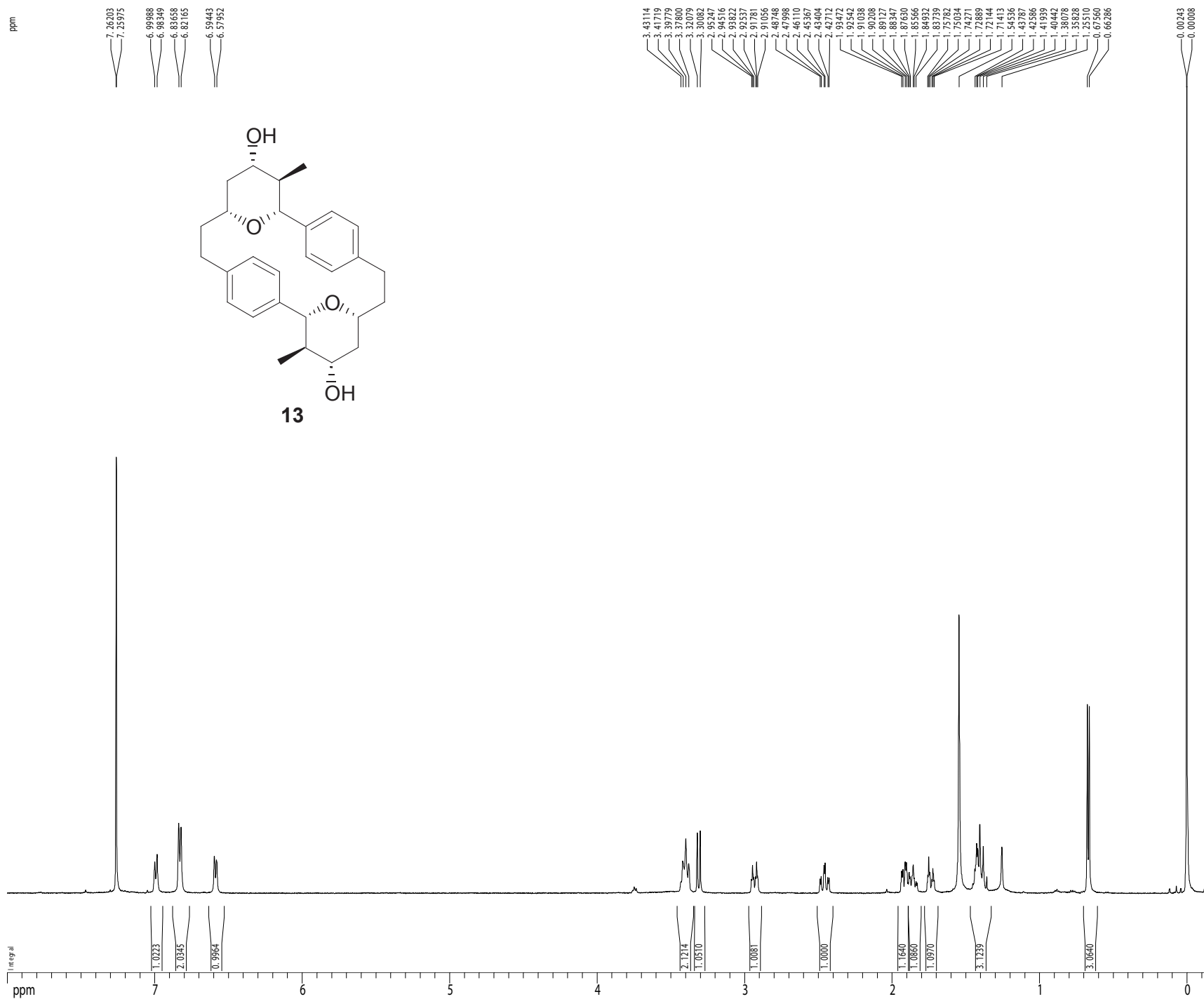
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1H NMR; 500 MHz, CDCl₃

^{13}C NMR; 125 MHz, CDCl_3 

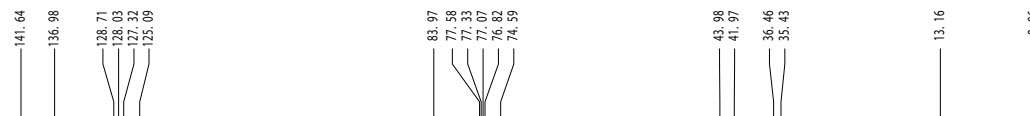
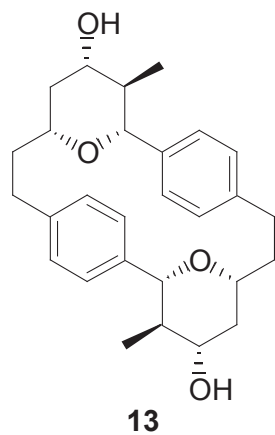
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^{13}C NMR; 125 MHz, CDCl_3 

^1H NMR; 500 MHz, CDCl_3 

13C NMR; 125 MHz, CDCl₃

ppm



ppm

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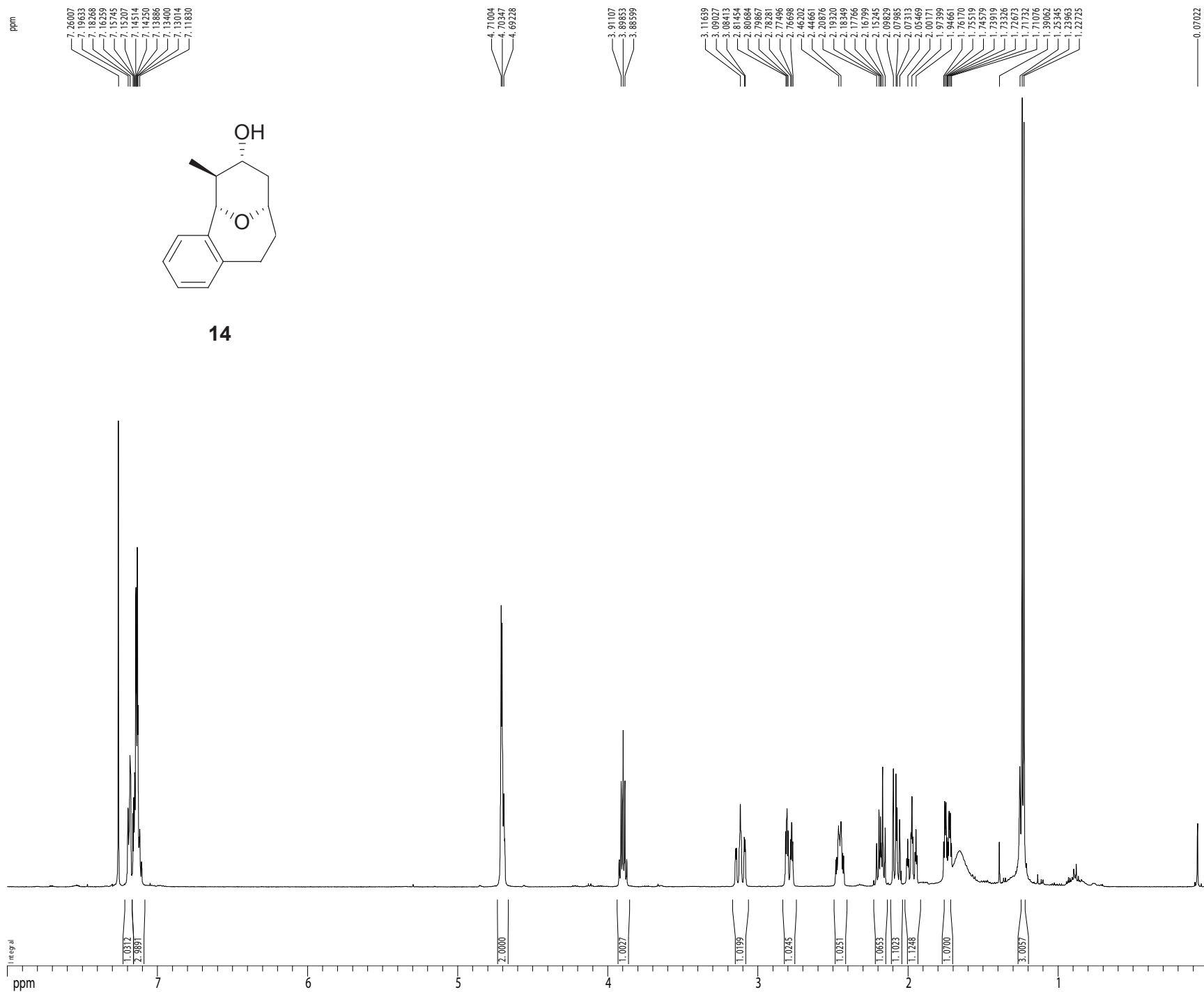
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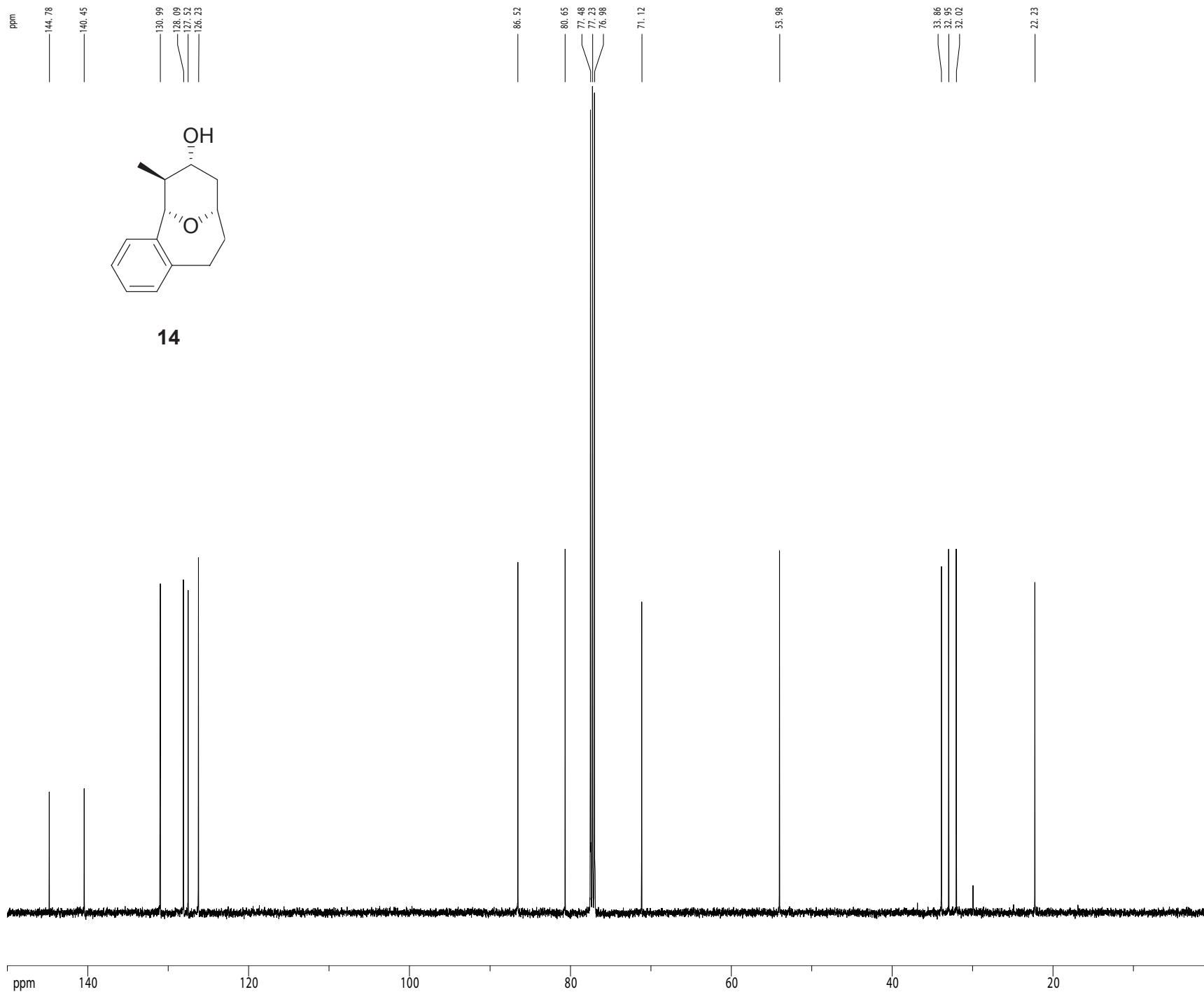
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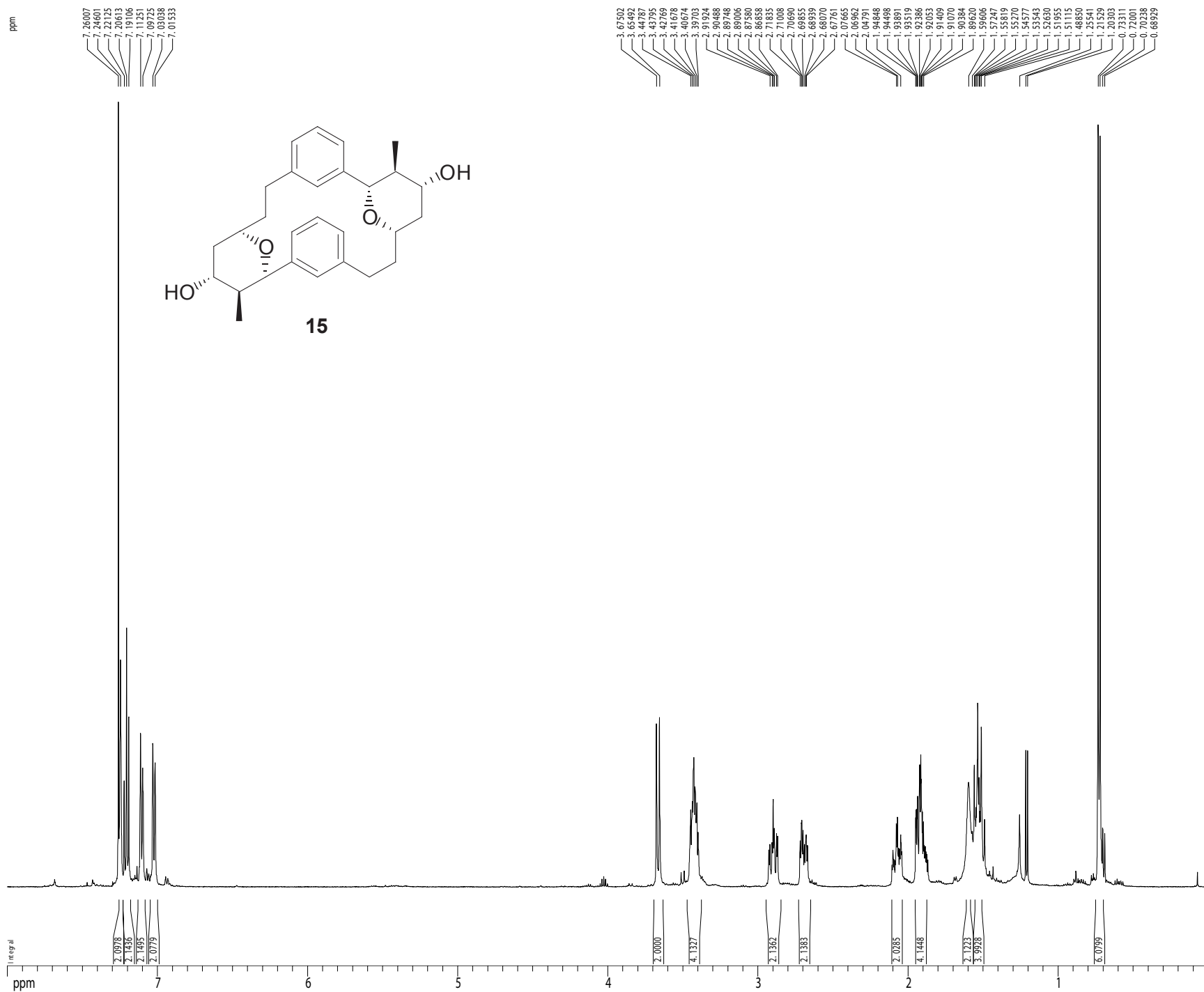
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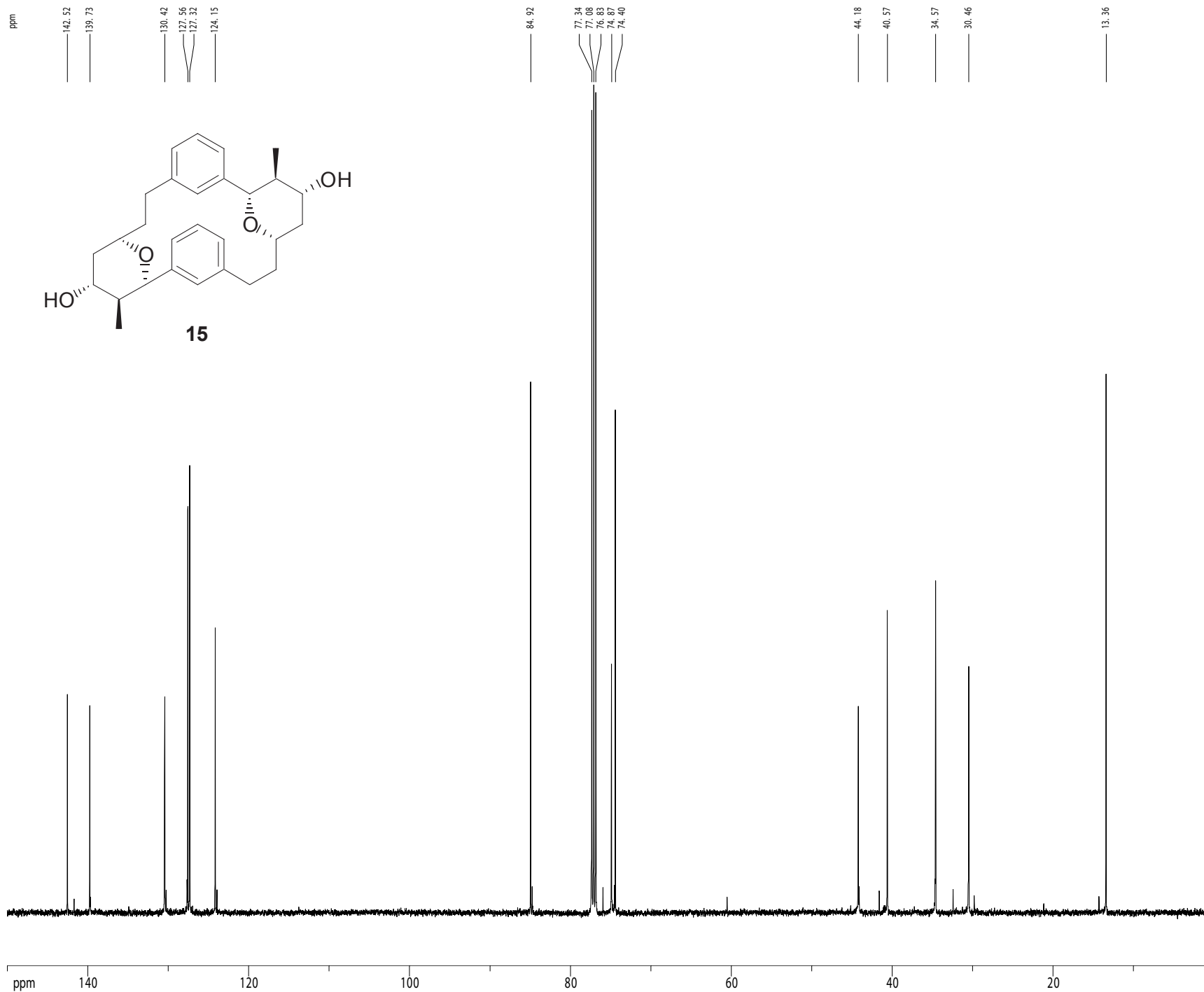
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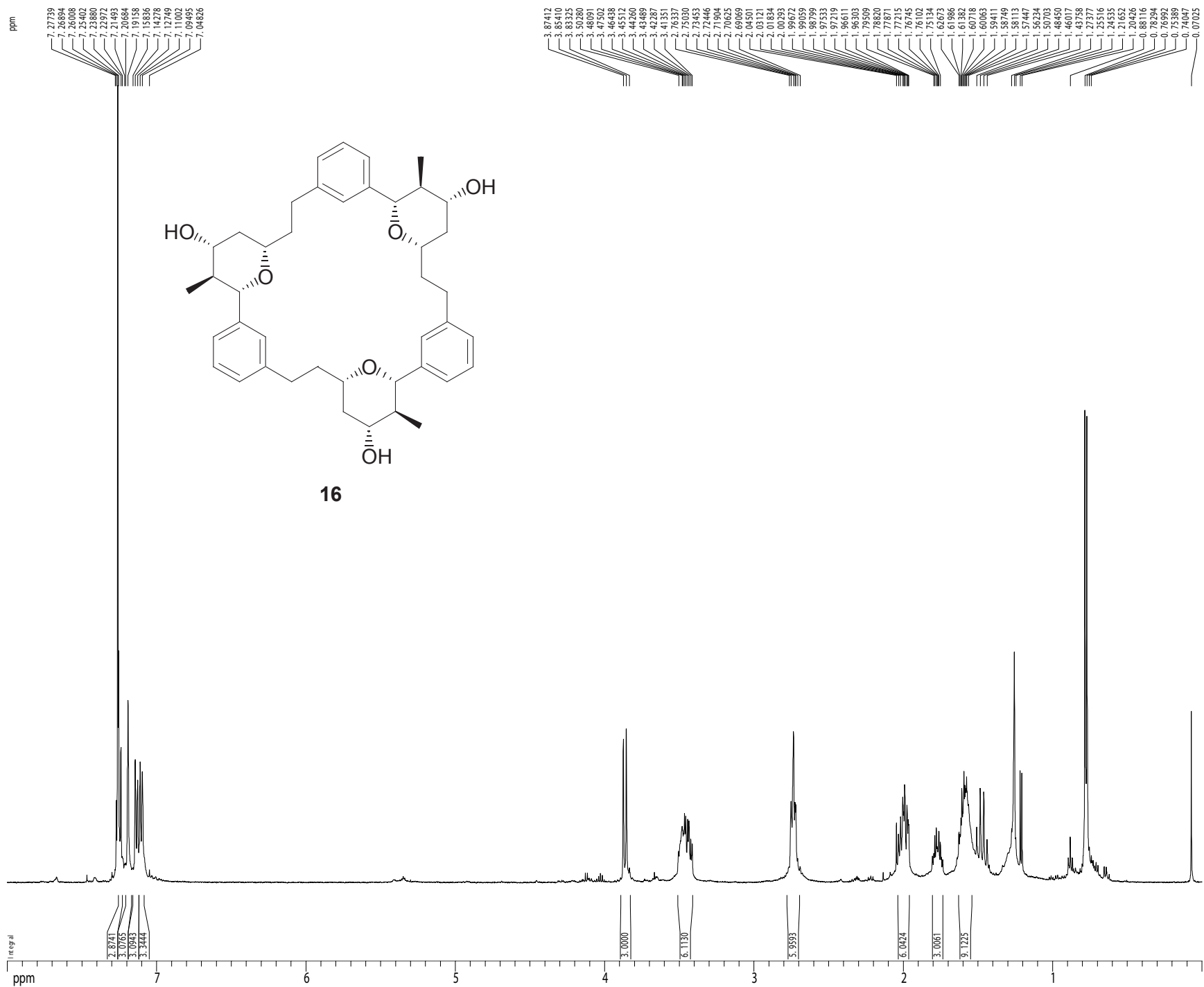


$^1\text{H NMR}$; 500 MHz, CDCl_3 

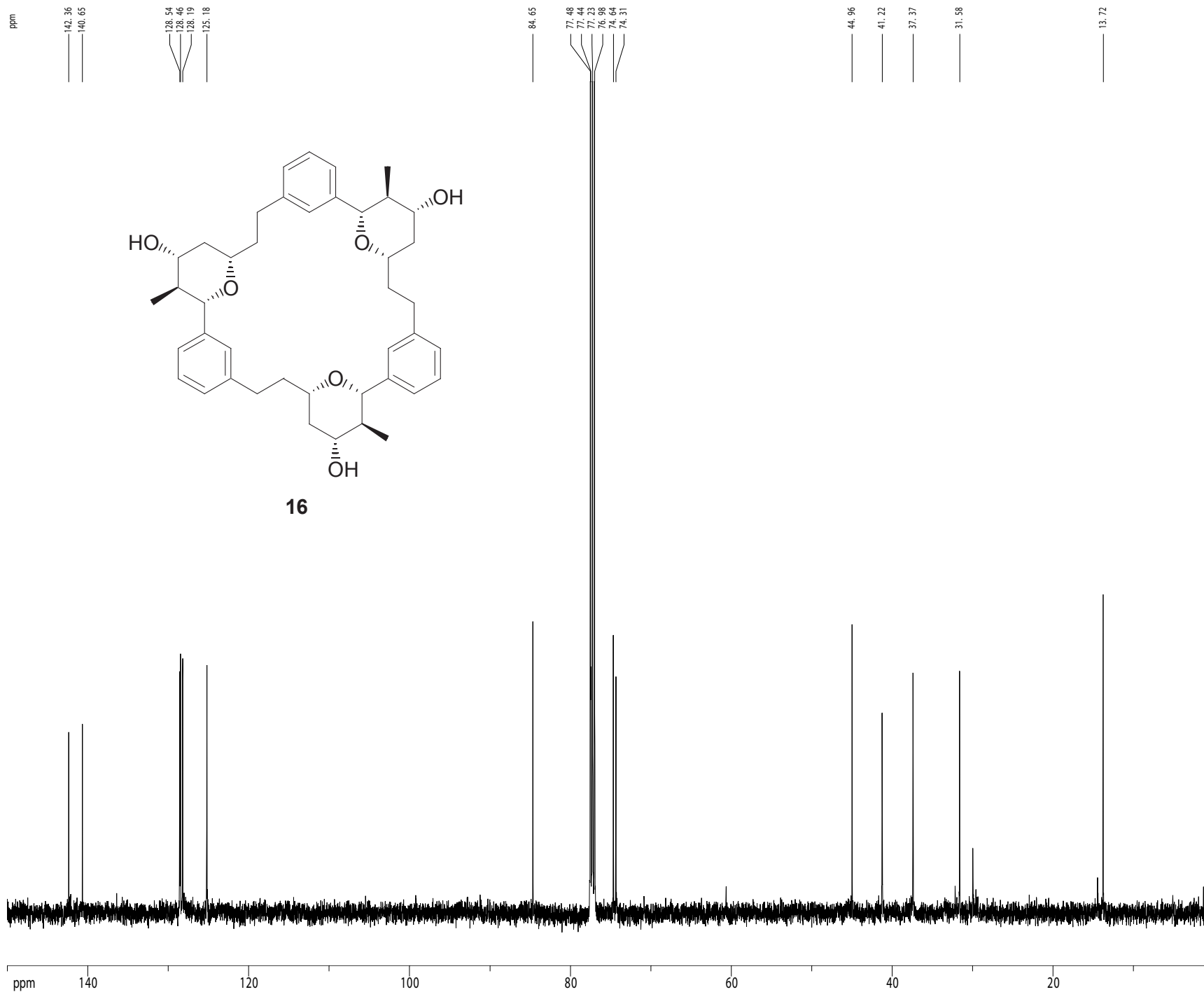
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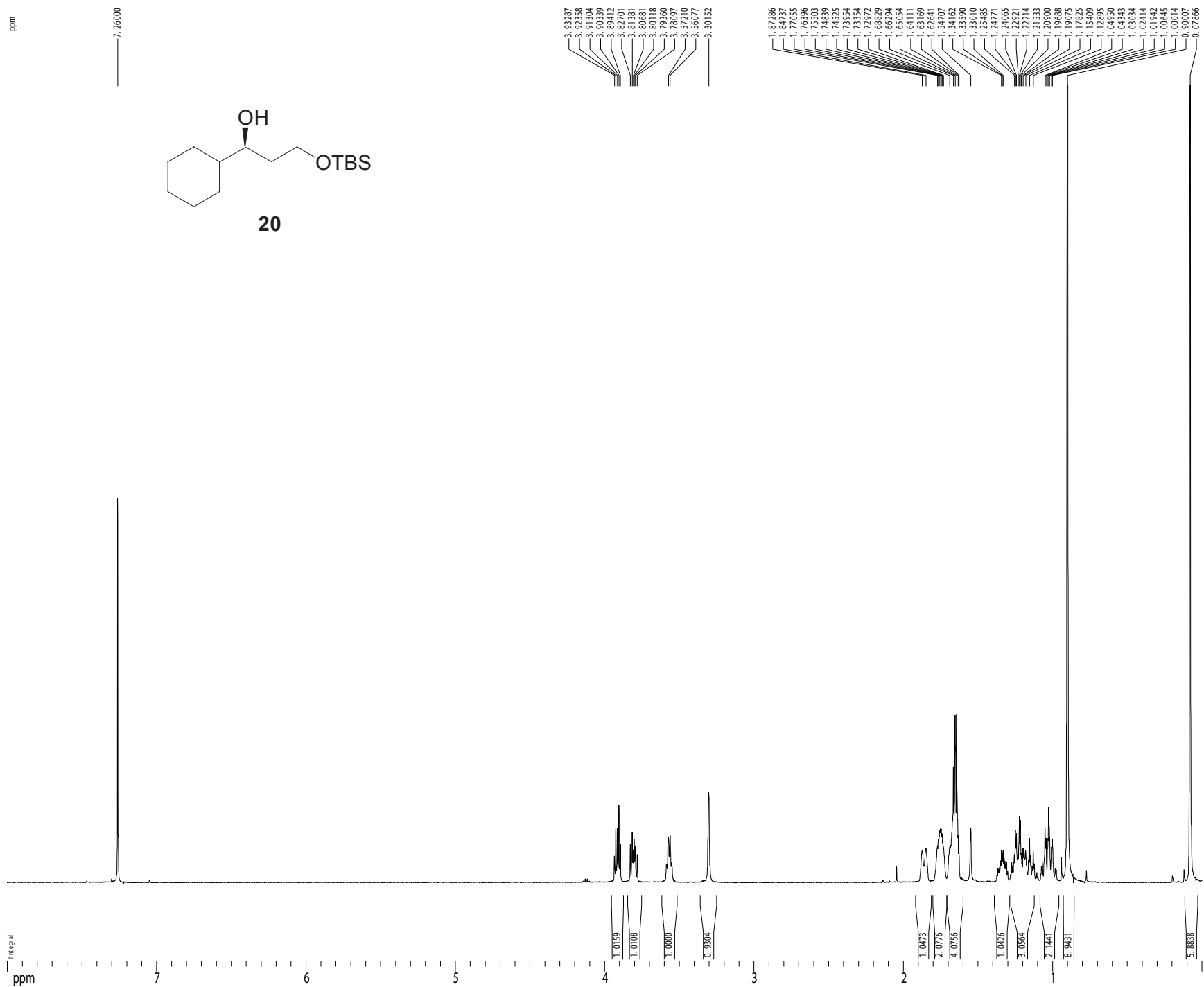
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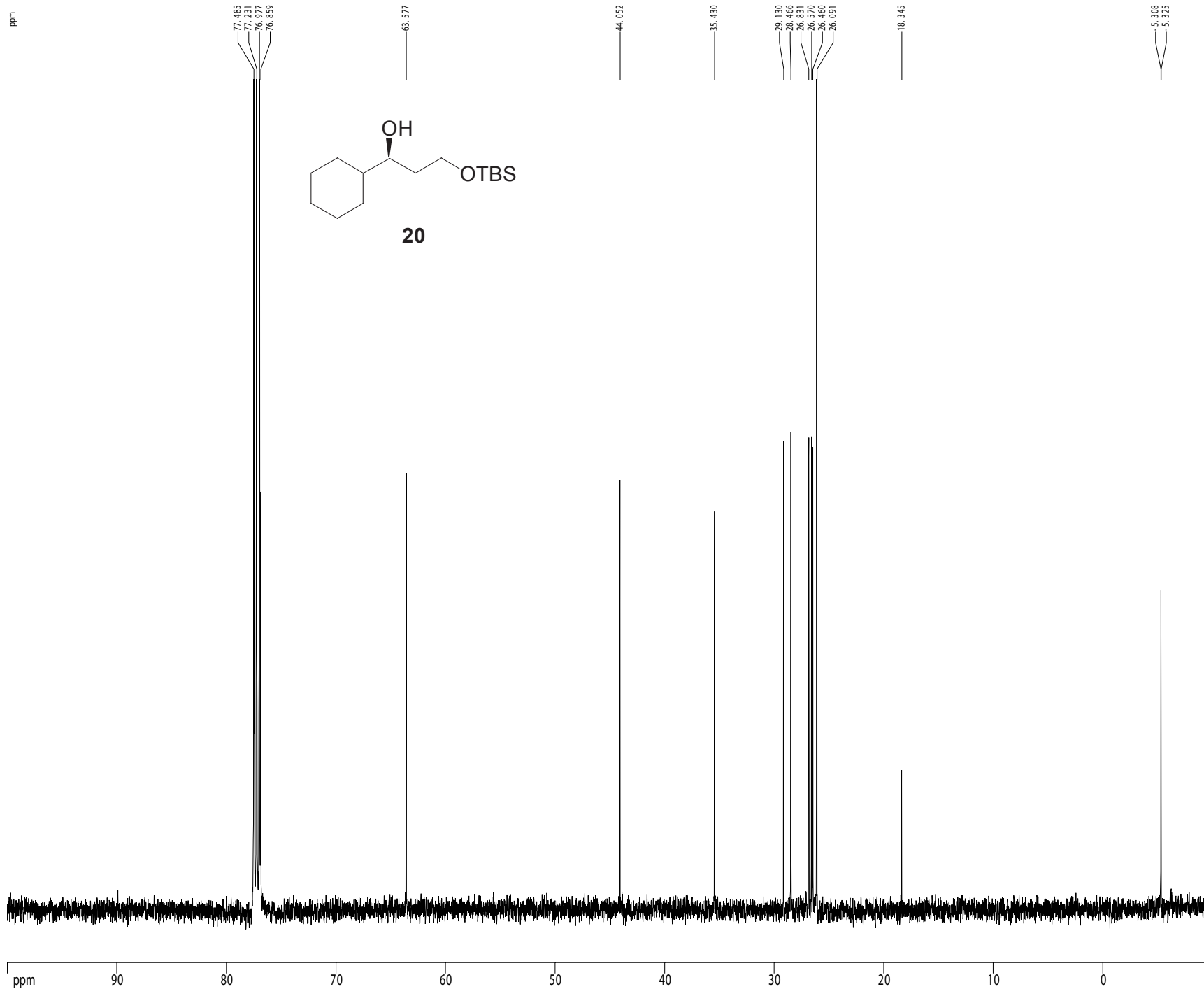
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$^1\text{H NMR}$; 500 MHz, CDCl_3 

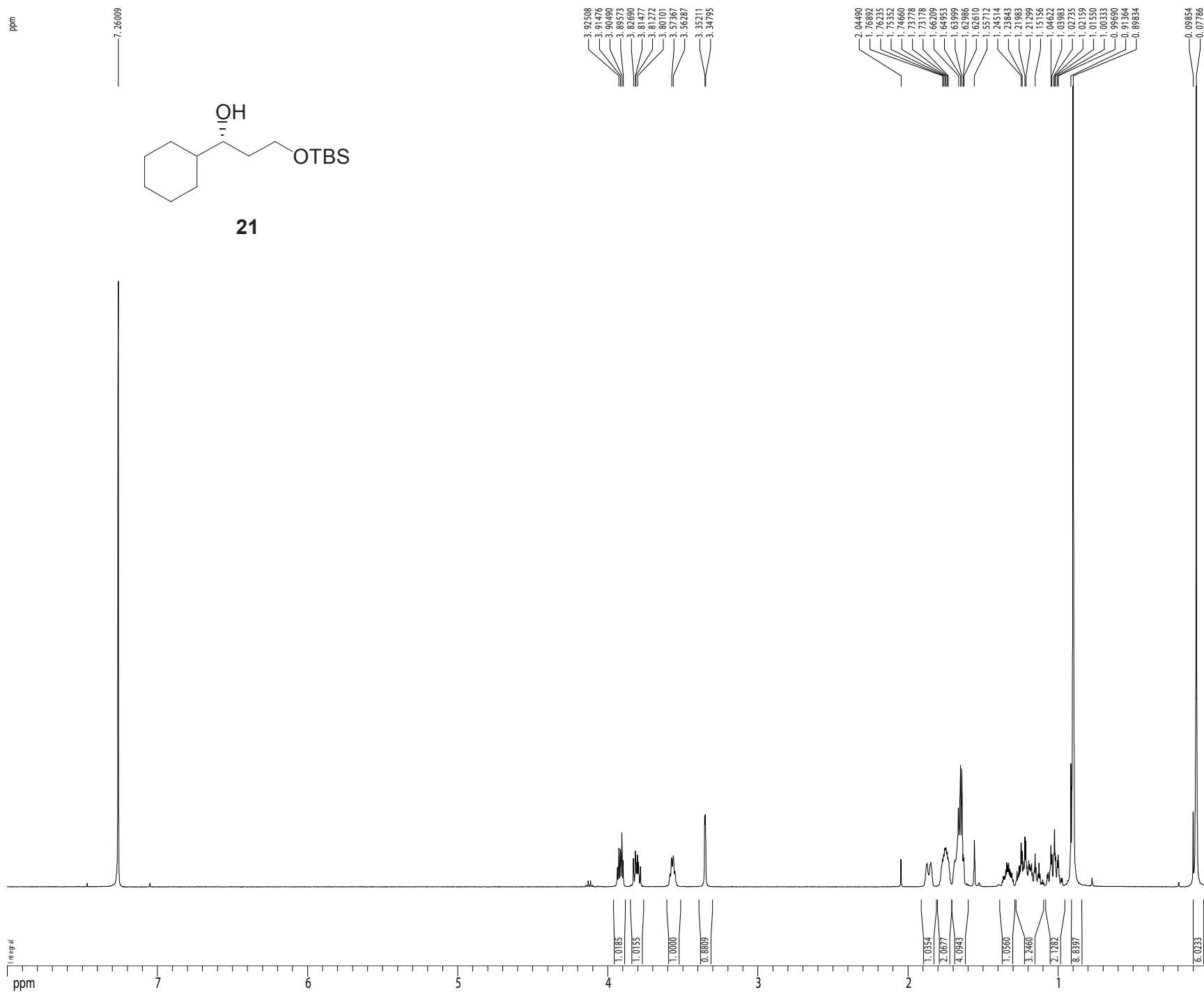
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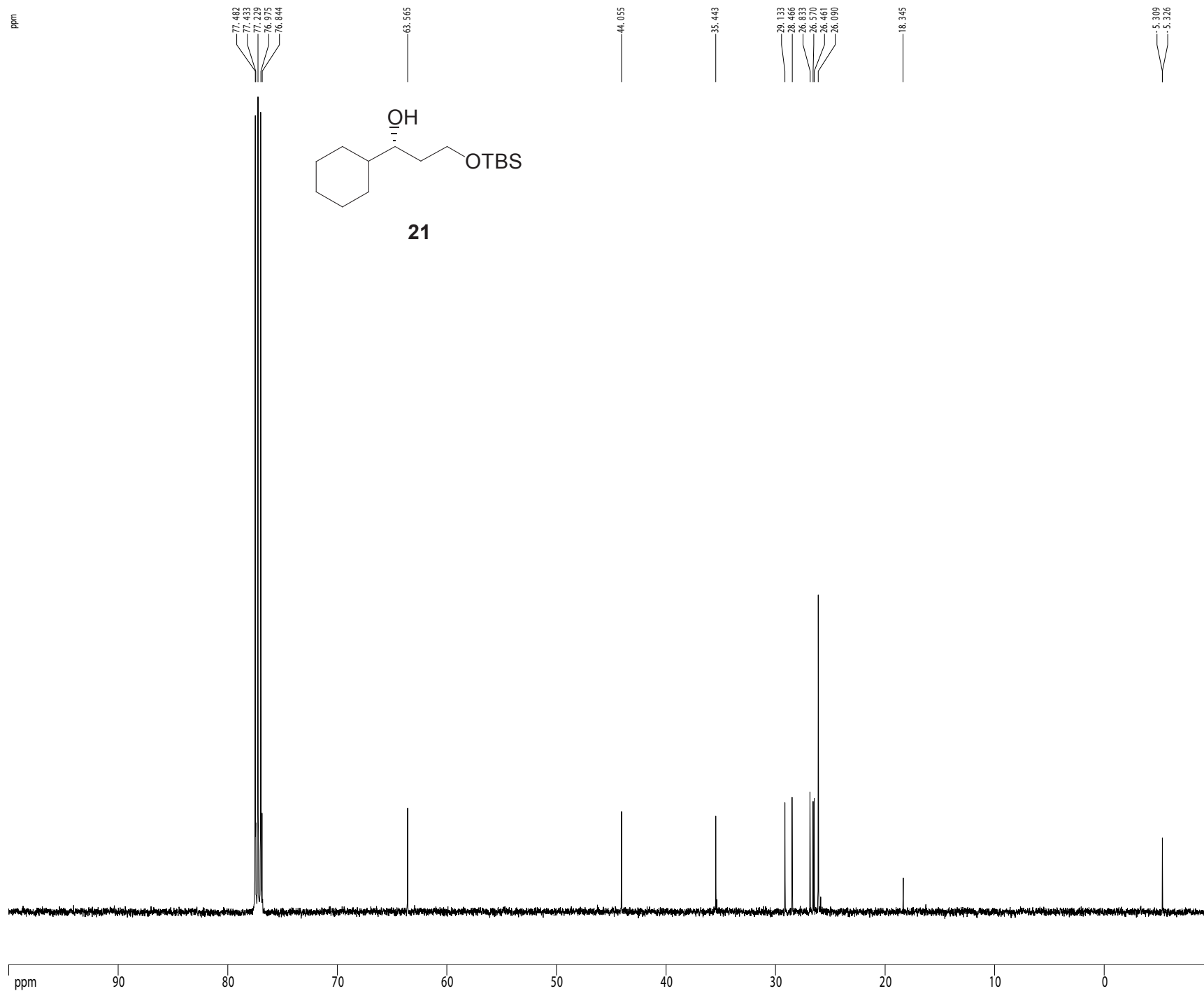


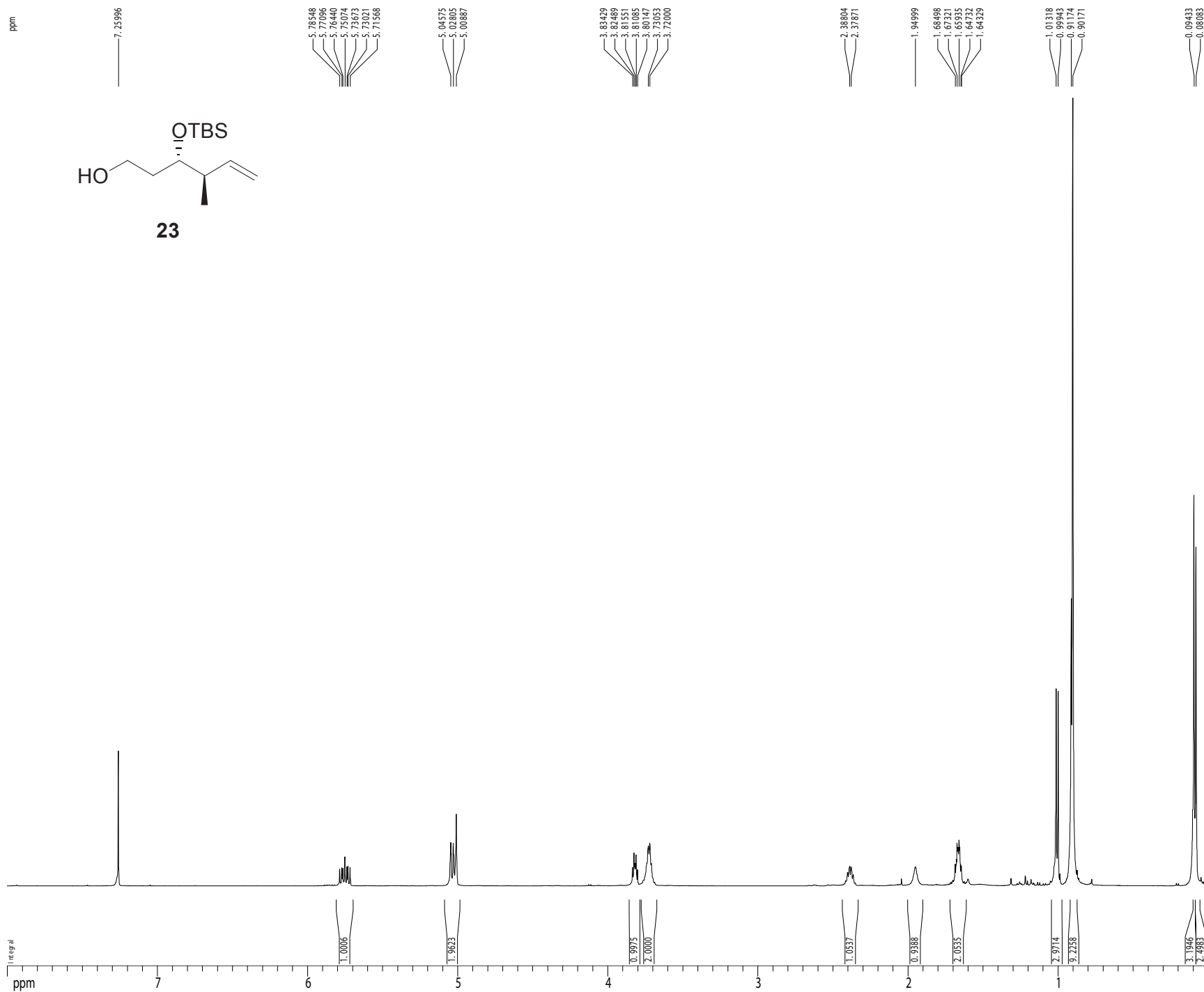
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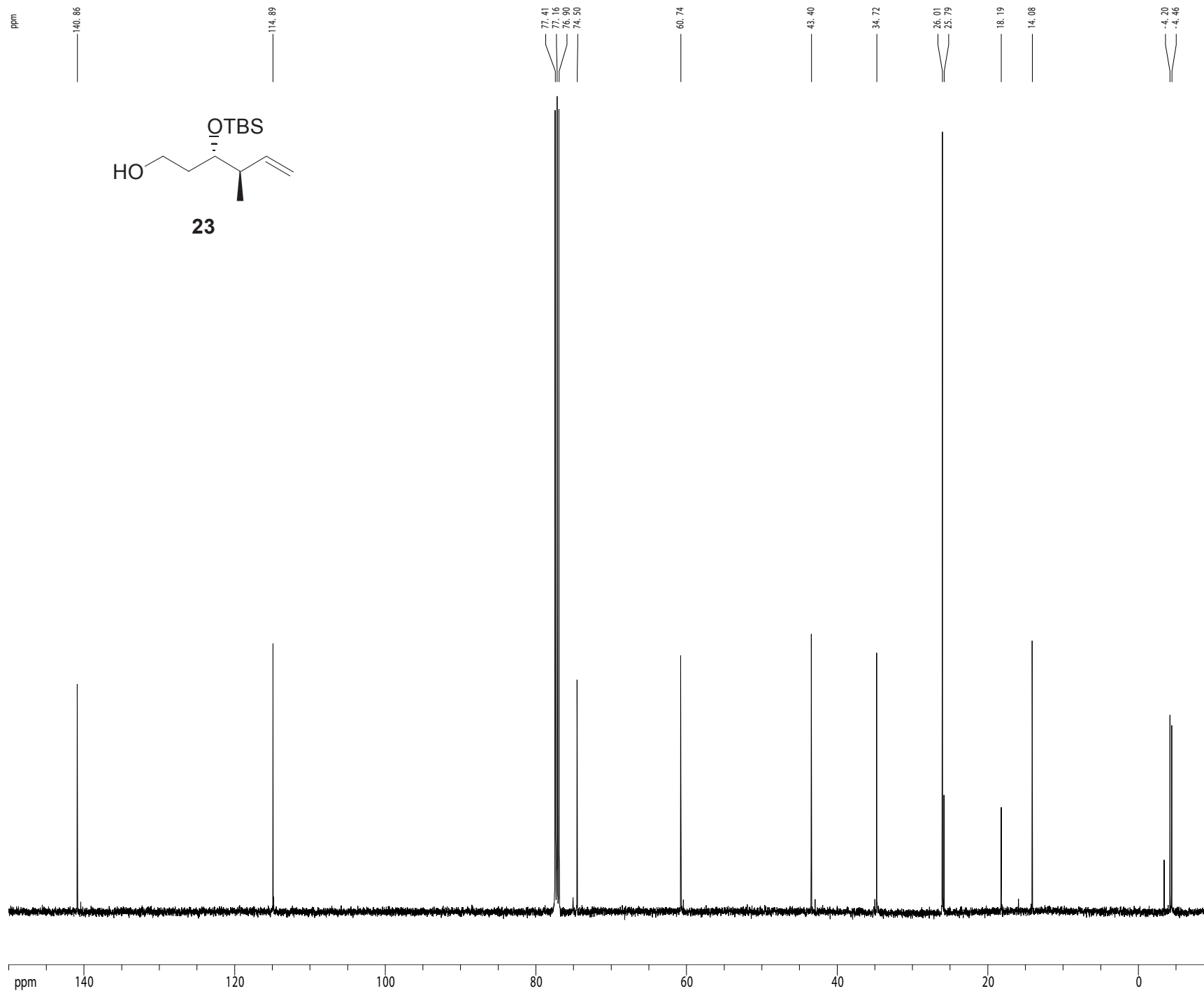
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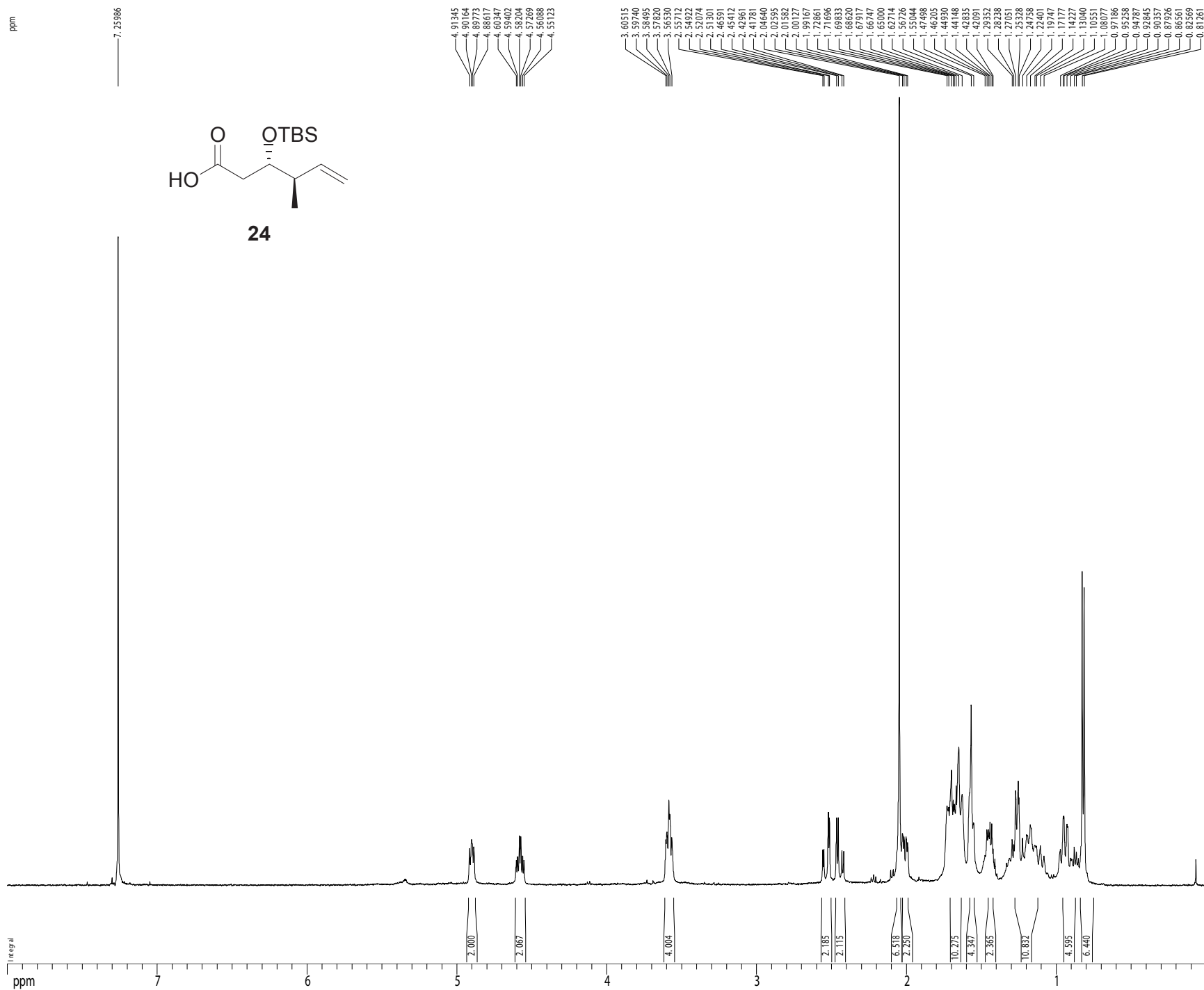


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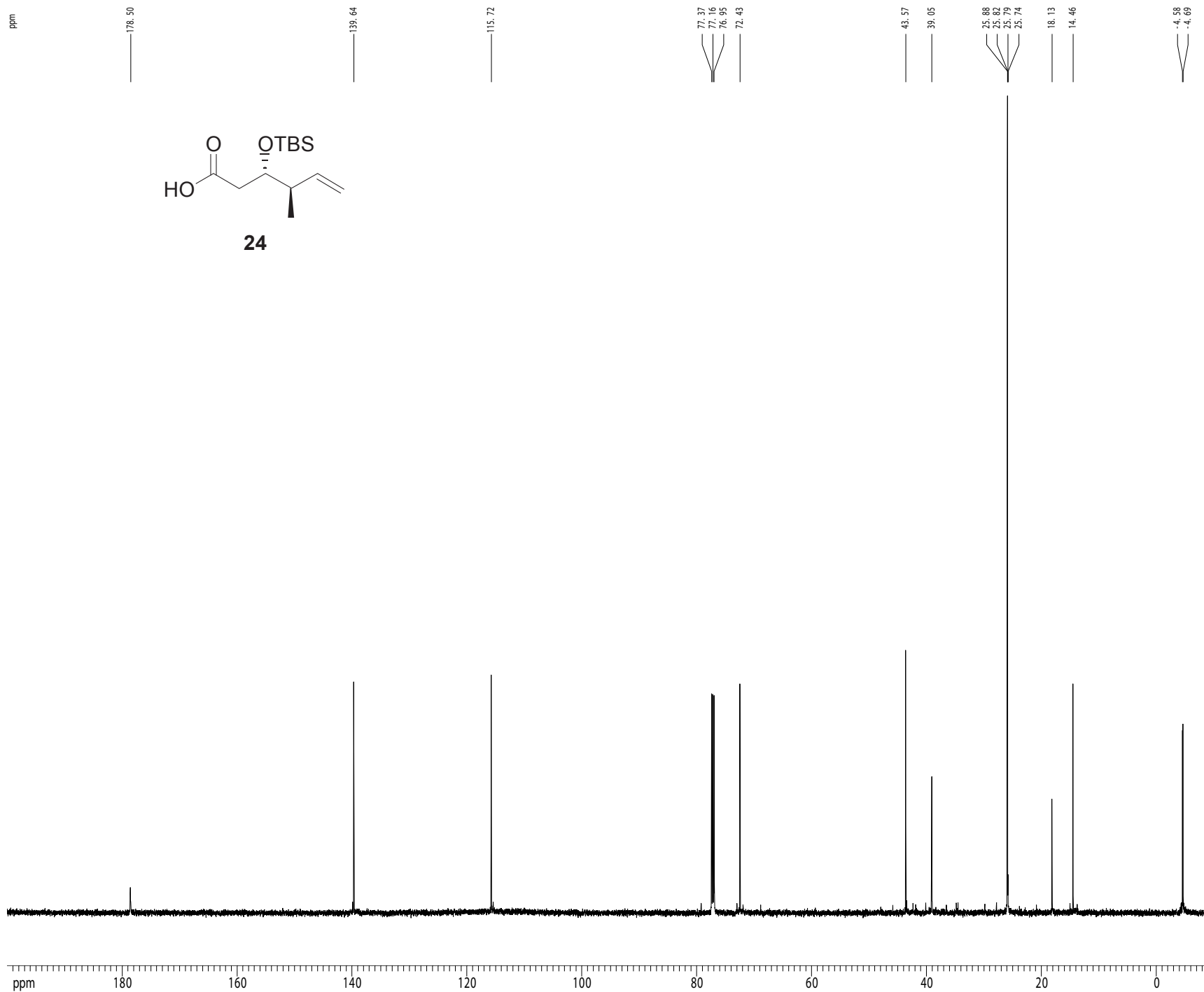
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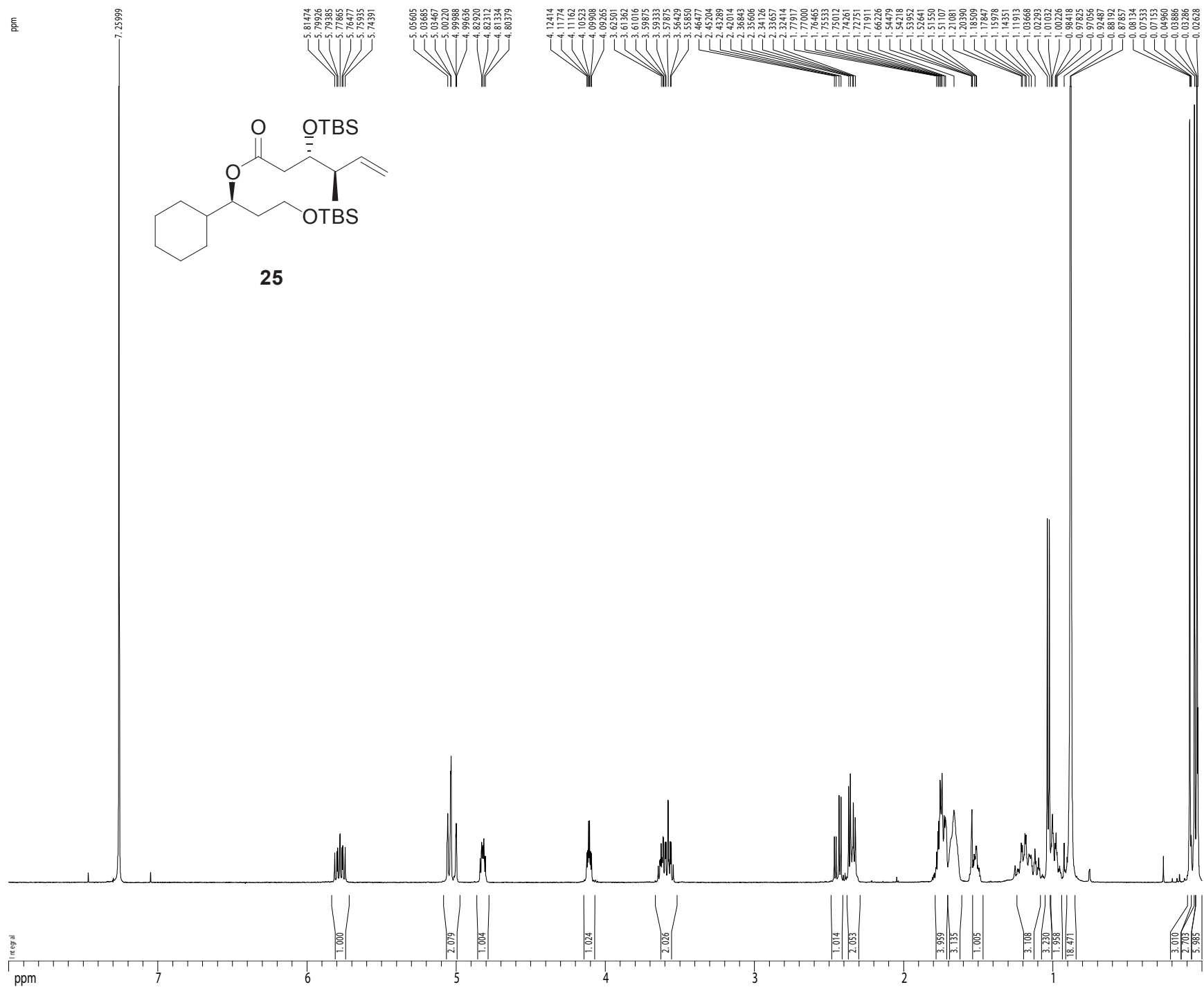
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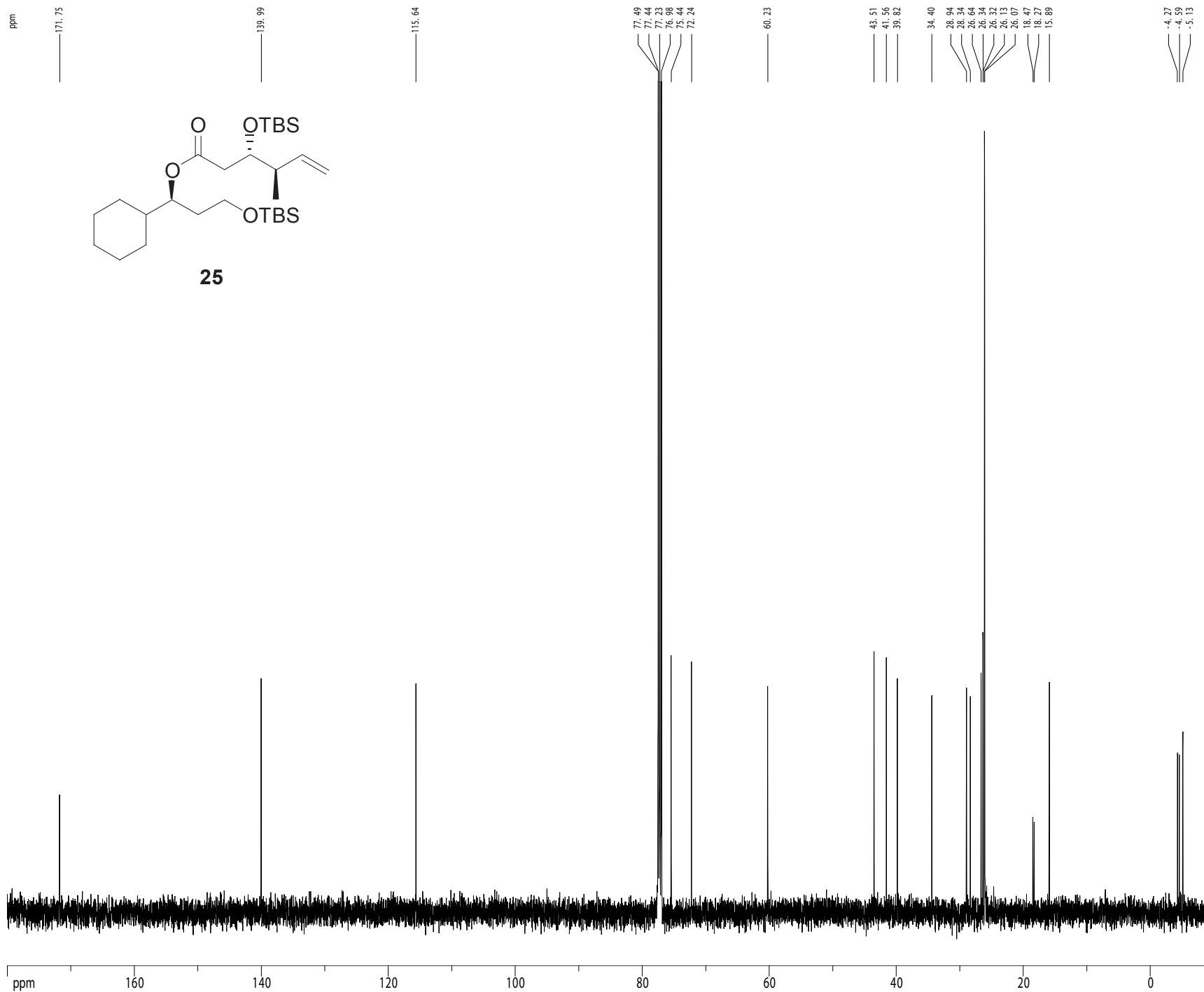
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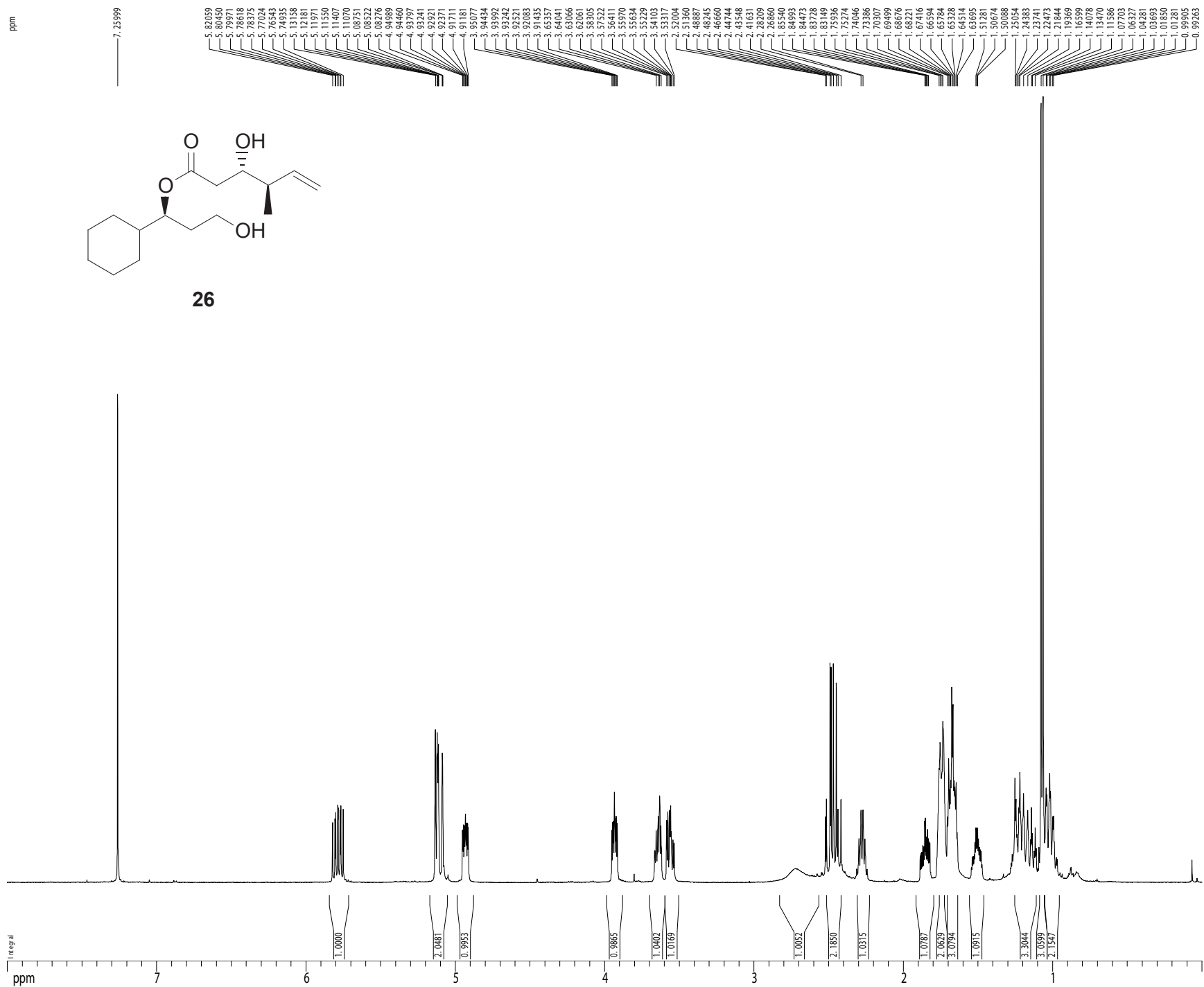


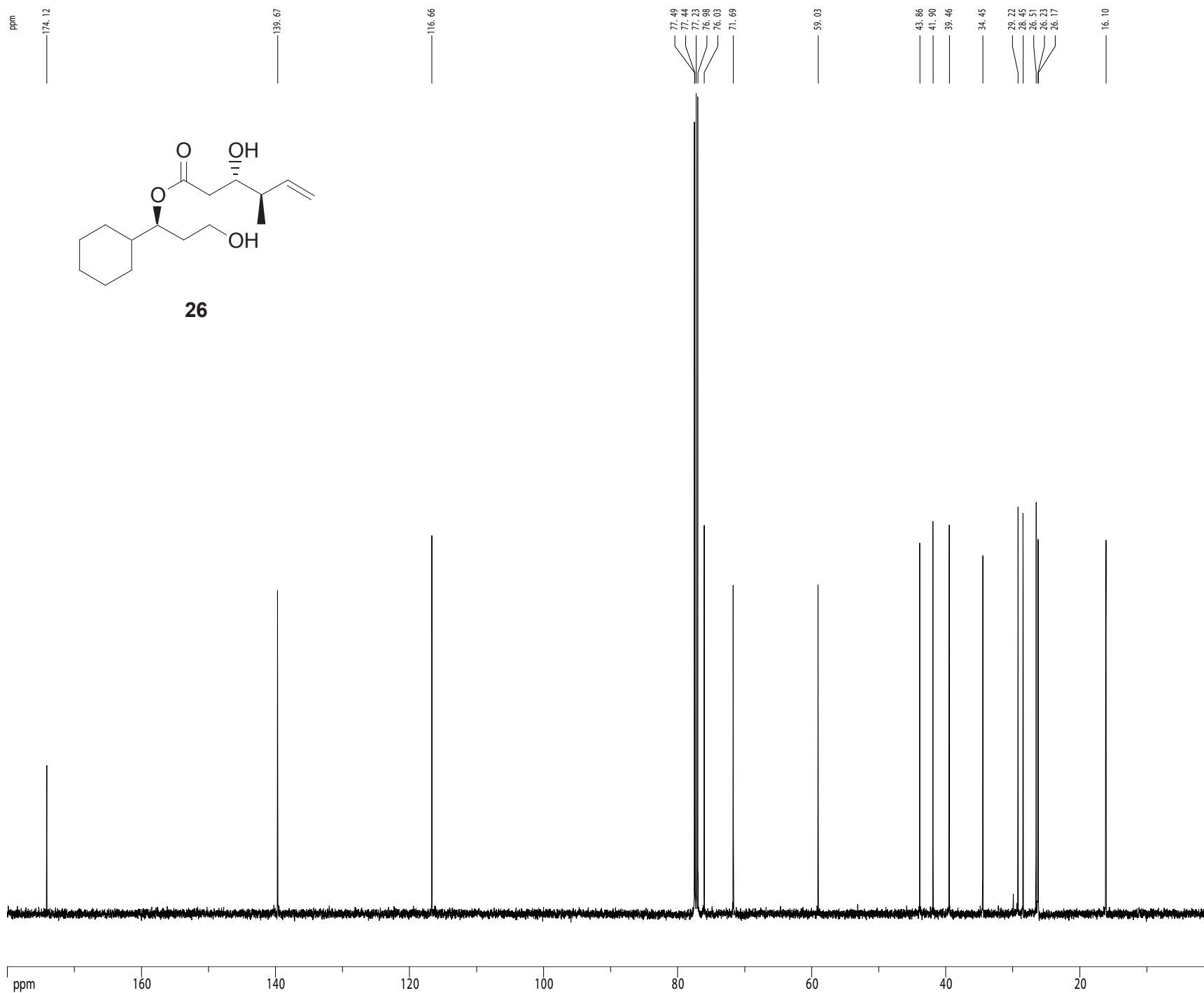
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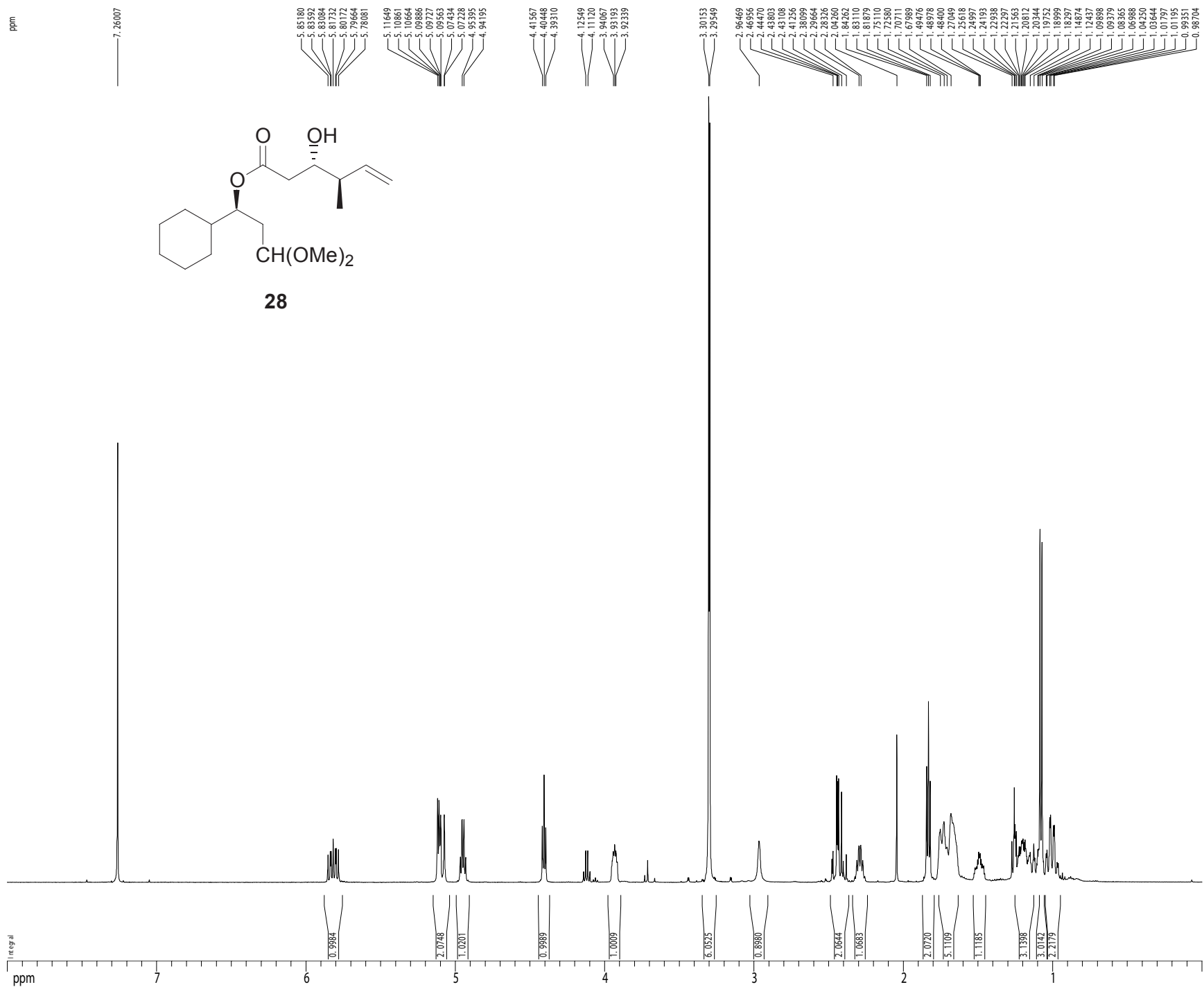
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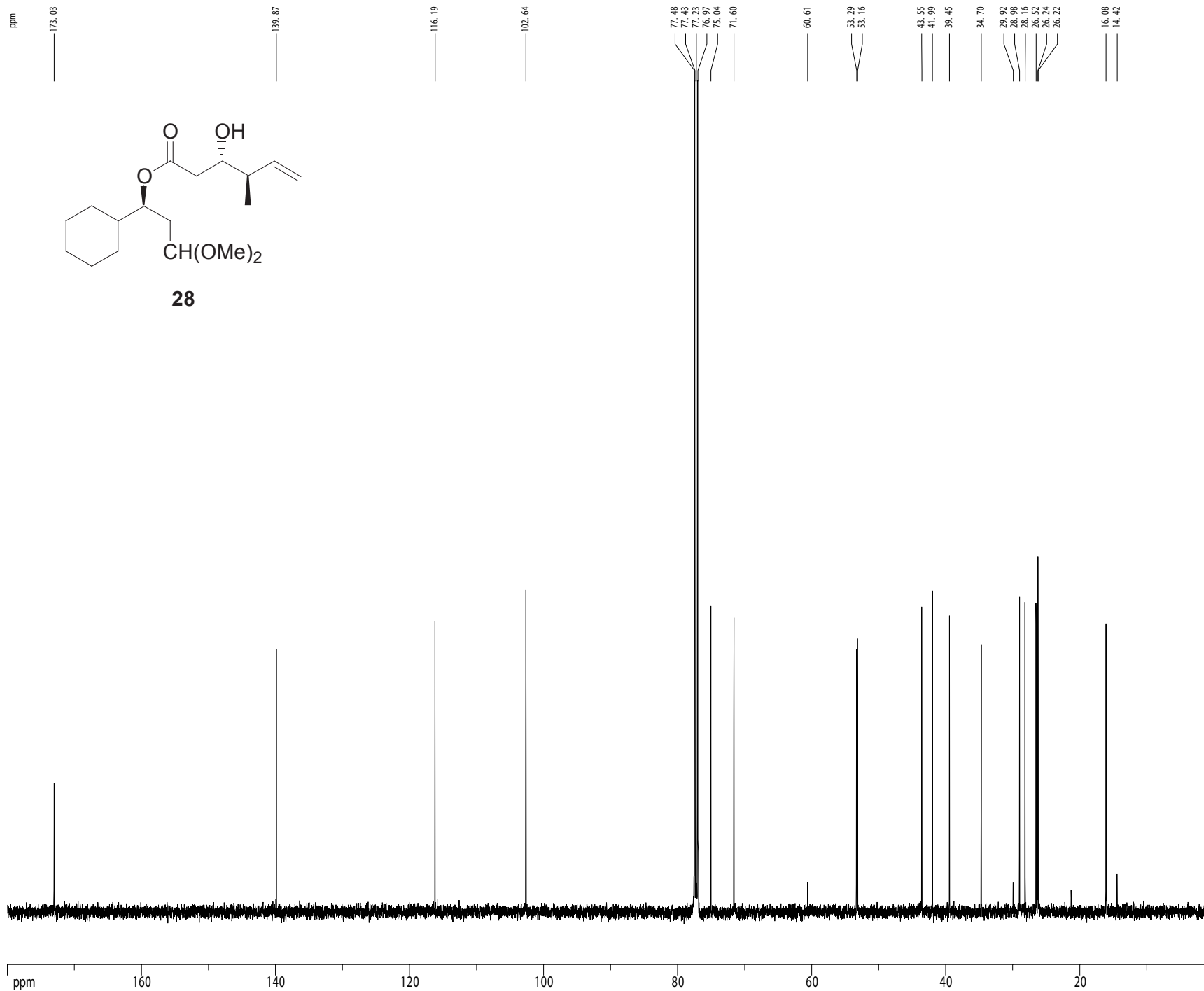
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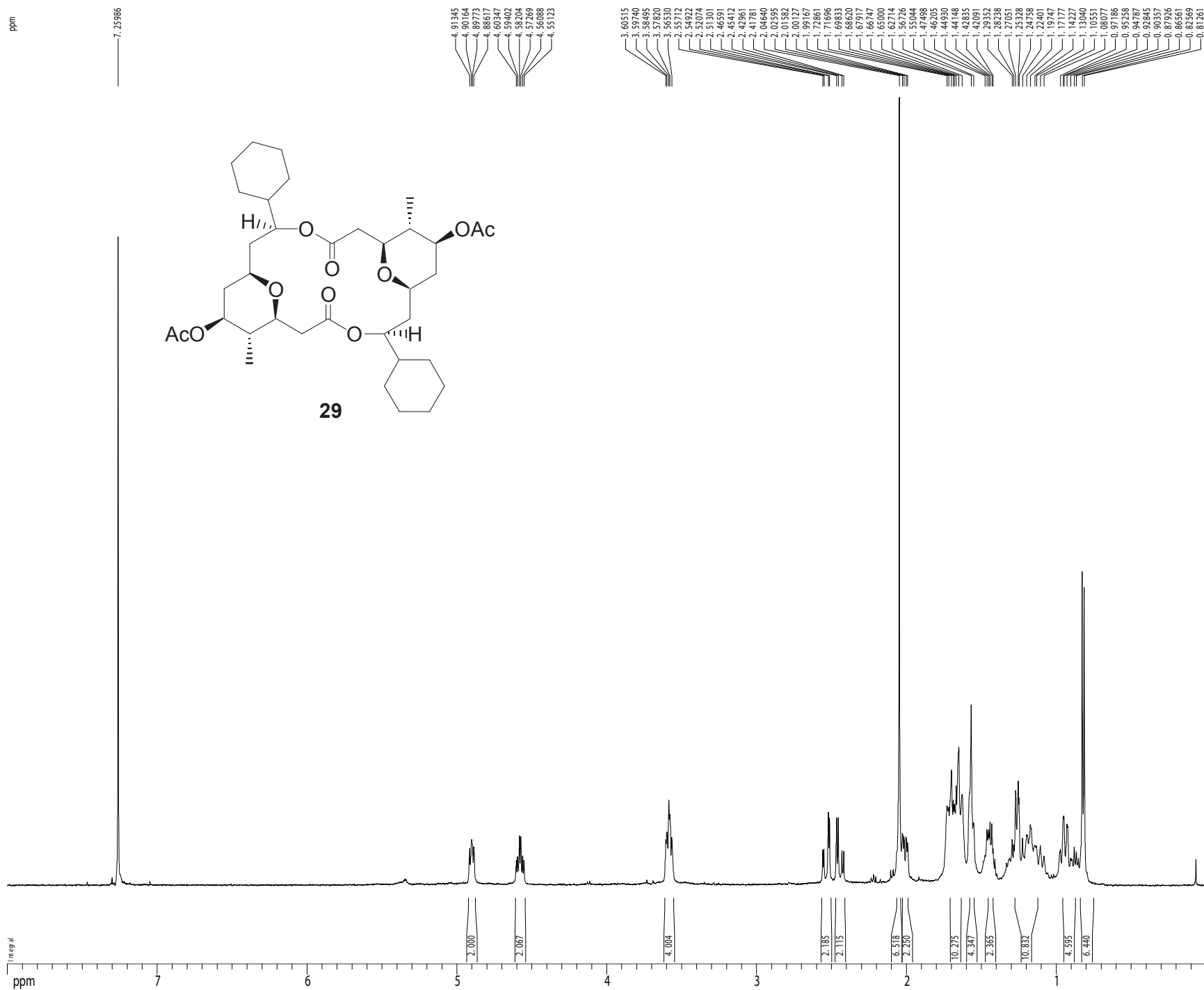
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1H NMR; 500 MHz, CDCl3



^{13}C NMR; 125 MHz, CDCl_3 

1H NMR; 500 MHz, CDCl3



^{13}C NMR; 125 MHz, CDCl_3 