SUPPORTING INFORMATION

An Efficient, Second-Generation Synthesis of the Signature Dioxabicyclo[3.2.1]octane Core of (+)-Sorangicin A and Elaboration of the (*Z*,*Z*,*E*)-Triene Acid System

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Experimental procedures and high field ^{1}H NMR and ^{13}C NMR spectra for all compounds.

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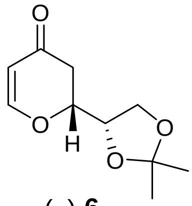
Experimental Section

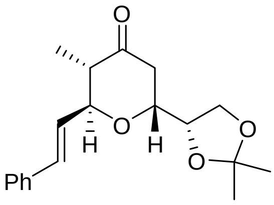
Materials and Methods: All solvents were reagent grade. Anhydrous dichloromethane (CH_2Cl_2), diethyl ether (Et_2O) and tetrahydrofuran (THF) were obtained from the Pure Solve^{TM} PS-400 under an argon atmosphere. All reagents were purchased from Aldrich or Acros and used as received. Reactions were magnetically stirred under an argon atmosphere and monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates. Flash chromatography was performed with silica gel 60 (particle size 0.040 – 0.062 mm) supplied by Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Infrared spectra were recorded on a Jasco Model FT/IR-480 Plus spectrometer. Proton and carbon-13 NMR spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported relative to either chloroform (δ 7.26) or benzene (δ 7.16) for ^{1}H NMR and either chloroform (δ 77.2) or benzene (δ 128.4) for ^{13}C NMR. Optical rotations were measured on a Perkin-Elmer model 241 polarimeter. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service Center.



(–)-**6**

Dihydropyrone (–)-**6.** A 50 ml oven-dried round bottomed flask was charged with the Jacobsen catalyst (1*R*,2*S*)-**9** (482 mg, 0.99 mmol) and BaO (4.0 g), and purged with argon for 20 min. EtOAc (2.8 mL) was added, and the resulting mixture was stirred at rt for 1 h in the dark, after which freshly distilled aldehyde (–)-**8** (2.83 g, 21.77 mmol) was added to the flask followed by 3×0.2 mL EtOAc rinse. The reaction mixture was cooled to 0 °C and stirred for 20 min. The Danishefsky diene 1-methoxy-3-[(trimethylsilyl)oxy]butadiene (3.85 mL, 19.79 mmol) was added, and the reaction mixture was stirred at 4 °C for 24 h in the dark. The reaction mixture was then cooled to 0 °C and CH_2Cl_2 (32 mL) was added followed by twenty drops of TFA. The reaction mixture was stirred at rt for 10 min, and then filtered through a plug of silica gel on Celite, and washed with copious Et_2O. The filtrate was concentrated in *vacuo* and the crude residue was purified by careful flash chromatography (10% to 40%

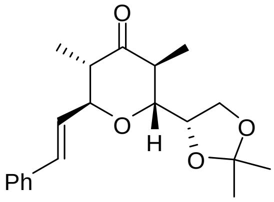
EtOAc:hexanes) to remove (*E*)-4-methoxybut-3-en-2-one and the minor diastereomer, and dihydropyrone (–)-**6** (3.3 g, 86%) was obtained as a brown oil. The crude NMR indicated a 33:1 dr. $[\alpha]^{24}_{\mathrm{D}}$ –122.4 (*c* 1.05, MeOH), literature data for dextrarotatory isomer: $[\alpha]^{20}_{\mathrm{D}}$ +120.6 (*c* 0.5, MeOH);[1] IR (neat, cm^{-1}) 1680, 1597, 1481, 1457, 1406, 1373, 1276, 1224, 1066; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33 (d, *J* = 5.8 Hz, 1H), 5.43 (d, *J* = 5.8 Hz, 1H), 4.35-4.26 (m, 2H), 4.14 (dd, *J* = 8.8, 5.9 Hz, 1H), 3.95 (dd, *J* = 8.8, 4.9 Hz, 1H), 2.67-2.59 (m, 2H), 1.43 (s, 3H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.8, 162.5, 110.4, 107.8, 79.4, 76.0, 66.2, 38.1, 26.6, 25.1.



(+)-**12**

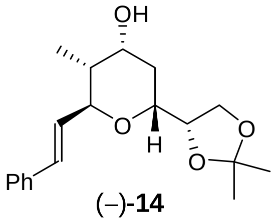
Tetrahydropyrone (+)-**12.** To a THF solution (55 mL) of *t*-BuLi (23 mL, 1.4 M in pentane, 32.24 mmol) at –78 °C was added a THF solution (8 mL) of β-bromostyrene (2.24 mL, 17.46 mmol) followed by 2×1 mL THF rinse. After 30 min at –78 °C Me_2Zn (9.7 mL, 1.8 M in toluene, 17.46 mmol) was introduced, and the reaction mixture was gradually warmed to 0 °C. After 15 min at 0 °C, the yellow mixture was recooled to –78 °C, and a THF solution (36 mL) of dihydropyrone (–)-**6** (2.66 g, 13.43 mmol) was slowly added over 1.5 h via syringe pump followed by 2×2 mL THF rinse. The resulting mixture was stirred for 30 min prior to the addition of HMPA (23.4 mL, 134.3 mmol). After another 10 min freshly prepared CuI•PBu_3 complex [by mixing Bu_3P (6.7 mL, 26.87 mmol) with CuI (2.04 g, 10.74 mmol) in THF (25 mL) at rt to generate a clear solution] was introduced. After 20 min, MeI (8.36 mL, 134.3 mmol) was added, and the resulting mixture was stirred at –20 °C for 2 days. The reaction mixture was quenched with saturated NH_4Cl solution (60 mL), and extracted with EtOAc (5×100 mL). The combined organic layers were dried over Na_2SO_4, filtered through a plug of silica gel on Celite to remove HMPA, and washed with copious EtOAc. The filtrate was concentrated in *vacuo* and the crude residue was purified by flash chromatography (5% to 20% EtOAc:hexanes) to afford tetrahydropyrone (+)-**12** (3.10 g, 73%) as a pale yellow oil. $[\alpha]^{25}_{\mathrm{D}}$ +24.7 (*c* 1.00, $CHCl_3$); IR (neat, cm^{-1}) 1718, 1453, 1375, 1066; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.4 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.20 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.41 (t, *J* = 6.8 Hz, 1H), 4.31 (dd, *J* = 11.8, 6.0 Hz, 1H), 4.18-4.12 (m, 2H), 3.76 (dd, *J* = 8.6, 6.0 Hz, 1H), 2.60 (d, *J* = 5.6

Hz, 2H), 2.53-2.48 (m, 1H), 1.40 (s, 3H), 1.34 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 136.1, 133.4, 128.6 (2C), 128.1, 127.7, 126.6 (2C), 110.4, 79.5, 77.6, 73.8, 66.8, 48.6, 40.4, 26.0, 25.0, 11.8; HRMS (ES) *m/z* $(M+H)^+$ calcd 317.1753, obsd 317.1758.



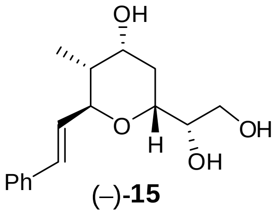
(+)-**13**

For bismethylation product (+)-**13**: $[\alpha]_D^{25}$ +37.7 (*c* 0.61, $CHCl_3$); IR (neat, cm^{-1}) 1715, 1377, 1211, 1067; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, *J* = 16.0, 7.0 Hz, 1H), 4.37-4.33 (m, 2H), 4.13 (dd, *J* = 8.4, 7.2 Hz, 1H), 3.83 (t, *J* = 4.4 Hz, 1H), 3.79 (dd, *J* = 8.2, 6.6 Hz, 1H), 2.66-2.54 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H), 1.32 (d, *J* = 7.2 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.3, 136.3, 133.3, 128.7 (2C), 128.2, 128.0, 126.8 (2C), 110.6, 80.0, 79.8, 77.8, 67.1, 45.8, 44.6, 26.0, 25.3, 16.1, 11.4; HRMS (CI) *m/z* M^+ calcd 330.1831, obsd 330.1829.



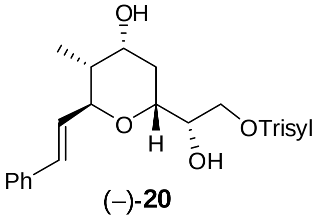
(–)-**14**

Alcohol (–)-14. L-Selectride (14.72 mL, 1.0 M in THF, 14.72 mmol) was added to a THF solution (210 mL) of tetrahydropyranone (+)-12 (3.10 mg, 9.81 mmol) at –78 °C. After 2 h, saturated NH_4Cl solution (200 mL) was added. After warming to rt, the aqueous layer was extracted with Et_2O (3×200 mL), and the combined extracts were washed with brine, dried over Na_2SO_4 and concentrated to give the crude residue, which was purified by flash chromatography (10% to 40% EtOAc:hexanes) to afford alcohol (–)-**14** (2.77 g, 89%) as a colorless oil. $[\alpha]_D^{25}$ -33.1 (*c* 0.57, $CHCl_3$); IR (neat, cm^{-1}) 3449, 1452, 1374, 1215, 1065; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2 H), 7.25 (d, *J* = 7.4 Hz, 1H), 6.59 (dd, *J* = 16.1, 1.0 Hz, 1H), 6.21 (dd, *J* = 16.1, 5.7 Hz, 1H), 4.35 (t, *J* = 5.2 Hz, 1H), 4.31 (dd, *J* = 12.8, 6.4 Hz, 1H), 4.12 (dd, *J* = 8.4, 6.4 Hz, 1H), 4.08-4.05 (m, 1H), 3.86 (dd, *J* = 8.4, 5.9 Hz, 1H), 3.76-3.72 (m, 1H), 2.04-1.93 (m, 2H), 1.83-1.77 (m, 1H), 1.43 (s, 3H), 1.38 (s, 3H), 1.08 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.6, 132.2, 128.7, 128.5 (2C), 127.7, 126.4 (2C), 109.5, 77.5, 77.0, 71.7, 67.6, 66.7, 38.5, 31.9, 26.6, 25.2, 12.4**;** HRMS (ES) *m/z* $(M+Na)^+$ calcd 341.1729, obsd 341.1712.



(–)-**15**

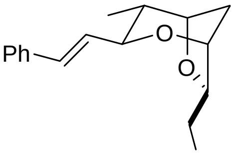
Triol (–)-**15.** Alcohol (–)-**14** (1.15 g, 3.62 mmol) was treated with acetic acid (45 mL) in water (15 mL), and the reaction mixture was stirred at rt overnight. The reaction mixture was quenched with saturated $NaHCO_3$ solution and solid $NaHCO_3$, and extracted with EtOAc (6×100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated to leave a crude residue, which was purified by flash chromatography (3% to 7% $MeOH:CH_2Cl_2$) to afford triol (–)-**15** (0.91 g, 91%) as a white foam. $[\alpha]_D^{25}$ -34.3 (*c* 0.45, $CHCl_3$); IR (neat, cm^{-1}) 3389, 1650, 1070; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.60 (dd, *J* = 16.1, 1.0 Hz, 1H), 6.20 (dd, *J* = 16.1, 5.8 Hz, 1H), 4.40 (t, *J* = 5.4 Hz, 1H), 4.10-4.07 (m, 1H), 3.98-3.94 (m, 1H), 3.89-3.86 (m, 1H), 3.78 (dd, *J* = 11.3, 3.6 Hz, 1H), 3.71 (dd, *J* = 11.3, 6.1 Hz, 1H), 2.00-1.96 (m, 1H), 1.93-1.81 (m, 2H), 1.06 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 132.5, 128.5 (2C), 128.3, 127.8, 126.4 (2C), 76.4, 72.8, 71.8, 66.9, 64.1, 38.5, 31.1, 12.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 301.1416, obsd 301.1426.



(–)-**20**

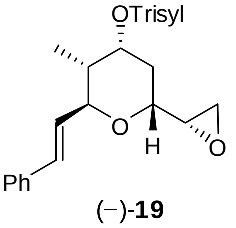
Sulfonate (–)-20. Triisopropylbenzenesulfonyl chloride (2.78 g, 9.17 mmol) was added to a solution of triol (–)-**15** (850 mg, 3.06 mmol) in pyridine (9 mL) and CH_2Cl_2 (14 mL) at 0 °C. The reaction mixture was stirred at rt for 18 h, and quenched with cold water (100 mL). The aqueous layer was extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (20% to 50% EtOAc:hexanes, silica gel was pretreated with 1% Et_3N) to afford sulfonate (–)-**20** (1.28 g, 77%) as a white foam. $[\alpha]_D^{25}$ -27.3 (*c* 0.67, $CHCl_3$); IR (neat, cm^{-1}) 3409, 1600, 1461, 1344, 1177; ^1H NMR

(500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.24 (d, *J* = 7.4 Hz, 1H), 7.18 (s, 2H), 6.56 (d, *J* = 16.1 Hz, 1H), 6.15 (dd, *J* = 16.1, 5.8 Hz, 1H), 4.34 (t, *J* = 5.8 Hz, 1H), 4.30 (dd, *J* = 10.5, 3.1 Hz, 1H), 4.23-4.21 (m, 1H), 4.16-4.06 (m, 5H), 3.81 (dd, *J* = 12.0, 6.8 Hz, 1H), 2.90 (sp, *J* = 7.0 Hz, 1H), 2.74 (br s, 1H), 1.96-1.86 (m, 3H), 1.25 (d, *J* = 6.7 Hz, 12H), 1.24 (d, *J* = 7.0 Hz, 6H), 1.03 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.8, 150.9 (2C), 136.5, 132.4, 129.0, 128.5 (2C), 128.3, 127.7, 126.4 (2C), 123.8 (2C), 76.7, 76.2, 70.9, 70.4, 66.9, 38.4, 34.2, 30.9, 29.6 (2C), 24.7 (4C), 23.4 (2C), 12.4; HRMS (ES) *m/z* $(M+H)^+$ calcd 545.2937, obsd 545.2919.



(–)-**18**

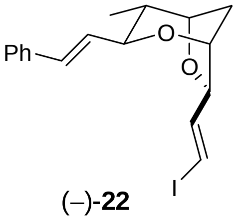
Alcohol (–)-18. To a THF solution (60 mL) of sulfonate (–)-**20** (1.07 g, 1.97 mmol) was added KHMDS (5.11 mL, 0.5 M in toluene, 2.56 mmol) at 0 °C. After 30 min, the ice bath was removed, and the reaction mixture was stirred at rt for 3 h. The reaction mixture was quenched with saturated NH_4Cl solution (120 mL), and extracted with EtOAc (3×120 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (30% to 70% EtOAc:hexanes) to afford alcohol (–)-**18** (465 mg, 91%) as a colorless oil. $[\alpha]_D^{25}$ -52 (*c* 0.26, CH_2Cl_2); IR (neat, cm^{-1}) 3420, 1450, 1144, 1052, 967; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 15.8 Hz, 1H), 6.12 (dd, *J* = 15.8, 7.5 Hz, 1H), 4.45 (br s, 1H), 4.32 (d, *J* = 6.6 Hz, 1H), 4.10-4.04 (m, 3H), 3.98-3.93 (m, 1H), 2.64 (d, *J* = 9.3 Hz, 1H), 2.10-2.06 (m, 1H), 1.94 (dd, *J* = 11.7, 1.0 Hz, 1H), 1.54 (dq, *J* = 6.8, 6.8 Hz, 1H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 132.5, 129.0, 128.5 (2C), 127.7, 126.5 (2C), 82.9, 79.7, 78.9, 74.4, 60.9, 41.6, 38.8, 15.2.



(–)-**19**

For oversulfonation product (–)-**19**: $[\alpha]_D^{29}$ –15 (*c* 1.00, $CHCl_3$); IR (neat, cm^{-1}) 1560, 1462, 1378, 1346, 1179, 1112, 860; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 7.18 (s, 2H), 6.52 (dd, *J* = 16.4, 2.0 Hz, 1H), 6.14 (dd, *J* = 16.4, 4.5 Hz, 1H), 5.04-5.00 (m, 1H), 4.47 (br t, *J* = 2.2 Hz, 1H), 4.18-

4.12 (m, 2H), 3.71-3.67 (m, 1H), 3.05-3.02 (m, 1H), 2.94-2.89 (m, 1H), 2.78 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.66 (dd, *J* = 5.0, 2.6 Hz, 1H), 2.45-2.35 (m, 1H), 1.97-1.91 (m, 1H), 1.85-1.82 (m, 1H), 1.26-1.20 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 138.2, 136.0, 133.2 (2C), 130.8, 128.7 (2C), 128.2, 127.3, 126.6 (2C), 123.9 (2C), 78.6, 76.4, 70.1, 53.4, 45.1, 36.5, 34.4, 29.8 (4C), 29.7, 24.8 (2C), 23.7 (2C), 12.2; HRMS (ES) *m/z* $(M+Na)^+$ calcd 549.2651, obsd 549.2659.

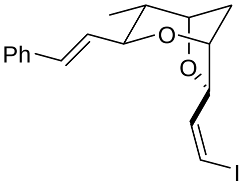


(–)-**22**

Vinyl iodide (–)-22. To a CH_2Cl_2 solution (6.2 mL) of alcohol (–)-**18** (310 mg, 1.19 mmol) was added *i*-Pr_2NEt (0.62 mL, 3.58 mmol) and DMSO (0.42 mL, 5.96 mmol). The mixture was cooled to 0 °C, and SO_3•Py was added in one portion. After 1 h, the reaction mixture was diluted with Et_2O (40 mL), washed sequentially with H_2O (40 mL), 1 M $KHSO_4$ (40 mL), H_2O (40 mL), and brine (40 mL). The organic layer was dried over Na_2SO_4, and evaporated to yield crude aldehyde **21** (300 mg) as a colorless oil. ^{1}H NMR (500 MHz, C_6D_6) δ 9.81 (s, 1H), 7.20 (d, *J* = 7.3 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 2H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.05 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.40 (br s, 1H), 3.94 (d, *J* = 6.4 Hz, 1H), 3.89 (br d, *J* = 2.8 Hz, 1H), 3.77 (dd, *J* = 9.0, 7.0 Hz, 1H), 1.44 (d, *J* = 11.6 Hz, 1H), 1.31-1.27 (m, 1H), 1.14-1.04 (m, 1H), 0.87 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 197.5, 137.1, 132.2, 128.8, 128.7, 128.6 (2C), 126.8 (2C), 87.5, 80.4, 80.0, 76.1, 41.7, 38.6, 15.0.

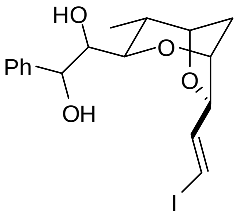
$CrCl_2$ (1.465 g, 11.9 mmol) was placed in 200 mL round bottom flask and was heated with heat gun under high vacuum before the flask was refilled with argon with cooling. The reaction flask was cooled to 0 °C, and degassed THF (10 mL) was added, then wrapped with aluminum foil. After 15 min, a dioxane solution (36 mL) of crude aldehyde **21** (300 mg) and CHI_3 (1.408 g, 3.58 mmol) was added slowly over 1 h via syringe pump, followed by 2×2 mL dioxane rinse. The resulting mixture was gradually warmed to rt and stirred overnight. The reaction mixture was quenched with brine (50 mL), and extracted with Et_2O (3×50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (5% to 15% EtOAc:hexanes, silica gel was pretreated with 1% Et_3N) to afford vinyl iodides (–)-**22** (230 mg, 52%) and (–)-**23** (70 mg, 16%) as white solids.

For (–)-**22**: $[\alpha]^{23}_{D}$ -25.1 (*c* 0.56, C_6H_6); IR (neat, cm^{-1}) 1604, 1450, 1140, 1068, 1040; ^{1}H NMR (500 MHz, C_6D_6) δ 7.21 (d, *J* = 7.2 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 2H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.88 (dd, *J* = 14.6, 4.8 Hz, 1H), 6.59 (d, *J* = 15.8 Hz, 1H), 6.50 (dd, *J* = 14.6, 1.8 Hz, 1H), 6.09 (dd, *J* = 15.8, 6.9 Hz, 1H), 4.20-4.17 (m, 1H), 3.93-3.91 (m, 2H), 3.87-3.85 (m, 1H), 1.48-1.40 (m, 2H), 1.15-1.09 (m, 1H), 0.81 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.9, 137.2, 131.6, 129.6, 128.6 (2C), 127.6, 126.7 (2C), 83.5, 79.3, 78.9, 78.5, 75.5, 41.7, 38.6, 15.0; HRMS (ES) *m/z* (M+H)$^+$ calcd 383.0508, obsd 383.0525.

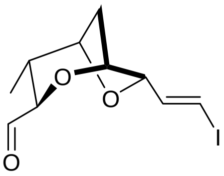


(–)-**23**

For (–)-**23**: $[\alpha]^{26}_{D}$ -136.6 (*c* 0.58, $CHCl_3$); IR (neat, cm^{-1}) 1608, 1449, 1270, 1142, 1070, 966; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.24 (d, *J* = 7.3 Hz, 1H), 6.78 (dd, *J* = 8.0, 6.5 Hz, 1H), 6.60-6.57 (m, 2H), 6.13 (dd, *J* = 16.0, 7.5 Hz, 1H), 4.66 (d, *J* = 1.5 Hz, 1H), 4.60 (dt, *J* = 6.5, 2.0 Hz, 1H), 4.34 (d, *J* = 6.5 Hz, 1H), 4.00 (dd, *J* = 9.0, 8.0 Hz, 1H), 2.14-2.10 (m, 1H), 2.00 (dd, *J* = 11.5, 1.5 Hz, 1H), 1.55 (dd, *J* = 7.0, 4.5 Hz, 1H), 0.97 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.8, 136.7, 132.7, 128.9, 128.7 (2C), 127.9, 126.7 (2C), 85.6, 84.3, 80.1, 79.7, 75.7, 41.8, 38.9, 15.3; HRMS (ES) *m/z* (M+H)$^+$ calcd 383.0508, obsd 383.0514.

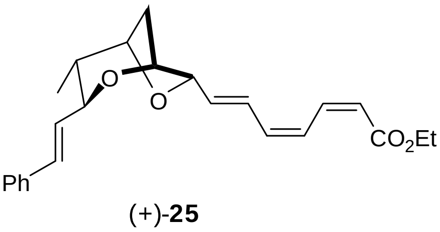


Diol. Vinyl iodide (–)-**22** (126 mg, 0.33 mmol) was dissolved in *t*-BuOH (7.5 mL) and H_2O (7.5 mL), and treated with $MeSO_2NH_2$ (32 mg, 0.33 mmol) and AD-mix-β (462 mg) at 0 °C. After 1 h the reaction mixture was warmed to rt and stirred for 20 h. TLC indicated presence of starting material, and the reaction mixture was treated with additional $MeSO_2NH_2$ (32 mg, 0.33 mmol) and AD-mix-β (462 mg). After 8 h, Na_2SO_3 (2 g) was added, and the mixture was vigorously stirred for 1 h, diluted with brine (50 mL), and extracted with EtOAc (3×50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (20% to 60% EtOAc:hexanes) to afford the diol shown above (104 mg, 76%) as a colorless oil. $[\alpha]_D^{25}$ -98.9 (*c* 1.86, C_6H_6); IR (neat, cm^{-1}) 3420, 1602, 1453, 1146, 1076, 1032; ^1H NMR (500 MHz, C_6D_6) δ 7.40 (d, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.14 (d, *J* = 7.3 Hz, 1H), 6.73 (dd, *J* = 14.6, 5.2 Hz, 1H), 6.37 (dd, *J* = 14.6, 1.6 Hz, 1H), 4.88 (d, *J* = 2.5 Hz, 1H), 3.85 (dd, *J* = 9.8, 3.8 Hz, 1H), 3.77-3.74 (m, 2H), 3.67 (br d, *J* = 1.6 Hz, 1H), 3.58 (dd, *J* = 3.6, 2.8 Hz, 1H), 1.36-1.26 (m, 1H), 1.22 (dd, *J* = 11.6, 1.2 Hz, 1H), 1.13-1.10 (m, 1H), 0.79 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.4, 141.4, 128.4 (2C), 127.6, 126.8 (2C), 83.1, 80.6, 79.9, 79.4, 76.5, 75.4, 72.5, 38.1, 38.0, 16.1; HRMS (ES) *m/z* $(M+Na)^+$ calcd 439.0382, obsd 439.0406.



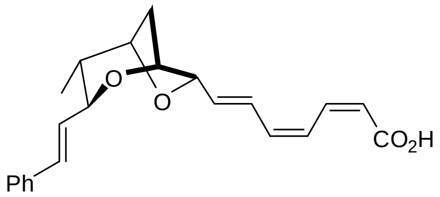
(–)-**2**

Bicycle (–)-2. A solution of the preceding diol (100 mg, 0.24 mmol) in THF (16.6 mL) and pH 7 buffer (3.3 mL) was treated with $NaIO_4$ (333 mg, 1.56 mmol) in one portion. The resulting mixture was stirred for 4 h, diluted with brine (50 mL), and extracted with Et_2O (3×50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (10% to 50% EtOAc:hexanes) to afford bicycle (–)-**2** (60 mg, 81%) as a colorless oil. $[\alpha]_D^{24}$ -85.6 (c 1.04, C_6H_6); IR (neat, cm^{-1}) 1736, 1603, 1454, 1220, 1075; ^1H NMR (500 MHz, C_6D_6) δ 9.35 (d, *J* = 1.6 Hz, 1H), 6.61 (dd, *J* = 14.5, 4.8 Hz, 1H), 6.39 (dd, *J* = 14.5, 1.8 Hz, 1H), 3.77 (dd, *J* = 10.1, 1.5 Hz, 1H), 3.74 (br d, *J* = 1.5 Hz, 1H), 3.70-3.67 (m, 2H), 1.22 (ddd, *J* = 11.8, 6.5, 2.7 Hz, 1H), 1.13 (dd, *J* = 11.8, 1.3 Hz, 1H), 1.08-1.05 (m, 1H), 0.83 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 199.6, 141.2, 83.2, 81.0, 79.1, 78.9, 75.2, 37.7, 36.6, 14.7.



(+)-**25**

Trienoate (+)-25. A 15 mL round bottom flask was charged with dienoate **24** (9.7 mg, 0.0233 mmol), vinyl iodide (–)-**22** (4.4 mg, 0.0116 mmol), and $Ph_2PO_2NBu_4$ (32 mg, 0.0699 mmol), and dissolved in degassed DMF (1.2 mL). $PdCl_2(PhCN)_2$ (0.22 mg, 0.00058 mmol) was added and the reaction mixture was purged with argon for 5 min, and stirred at rt in the dark overnight. The reaction mixture was diluted with hexanes (4 mL), filtered through Celite plug into brine (5 mL), and rinsed with Et_2O:hexanes (1:1, 20 mL). The mixture was extracted with Et_2O:hexanes (1:1, 3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (10% to 30% EtOAc:hexanes, silica gel was pretreated with 1% Et_3N) to afford trienoate (+)-**25** (4.2 mg, 96%) as a pale yellow oil. $[\alpha]^{28}_{\mathrm{D}}$ +104.3 (*c* 0.14, $CHCl_3$); IR (neat, cm^{-1}) 1712, 1612, 1448, 1219, 1183, 1038; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.21 (m, 6H), 7.13 (dt, *J* = 11.4, 0.8 Hz, 1H), 7.08-7.03 (m, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.46 (t, *J* = 11.0 Hz, 1H), 6.24 (dd, *J* = 15.1, 5.0 Hz, 1H), 6.10 (dd, *J* = 15.8, 7.5 Hz, 1H), 5.73 (d, *J* = 11.4 Hz, 1H), 4.57-4.55 (m, 1H), 4.47 (br d, *J* = 1.4 Hz, 1H), 4.35 (d, *J* = 6.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.12 (dd, *J* = 8.8, 8.0 Hz, 1H), 2.09 (ddd, *J* = 11.5, 6.4, 2.8 Hz, 1H), 1.99 (dd, *J* = 11.5, 1.4 Hz, 1H), 1.54-1.50 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 138.3, 136.7, 136.6, 133.4, 132.6, 129.0, 128.6 (2C), 127.8, 126.9, 126.7 (2C), 124.7, 118.3, 82.0, 79.7, 79.1, 76.6, 60.2, 41.7, 39.2, 15.2, 14.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 403.1885, obsd 403.1883.



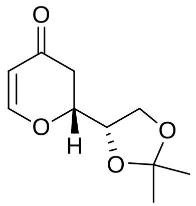
(+)-**26**

Acid (+)-26. A solution of trienoate (+)-**25** (4 mg, 0.0105 mmol) in THF (1.8 mL) and H_2O (0.6 mL) was treated with 1 M LiOH solution (0.8 mL). The reaction mixture was stirred for 2 days at rt in the dark. Brine (1 mL) was added and the pH value of reaction mixture was adjusted to ca. 3 with 1 M $NaHSO_4$. The mixture was extracted with EtOAc (4×2 mL), and the combined organic layers were washed dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (0.5% to 2.5% MeOH:CH_2Cl_2) to afford acid (+)-**26** (3 mg, 81%) as a pale yellow oil. $[\alpha]^{28}_{\mathrm{D}}$ +80.9 (*c* 0.15, $CHCl_3$); IR (neat, cm^{-1}) 2963 (br), 1688, 1607, 1451, 1239, 1145, 968; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.21 (m, 7H), 7.09-7.04 (m, 1H), 6.55-6.48 (m, 2H), 6.27 (dd, *J* = 15.1, 4.9 Hz, 1H), 6.10 (dd, *J* = 15.8, 7.4 Hz, 1H), 5.76 (d, *J* = 10.9 Hz, 1H), 4.58-4.57 (m, 1H), 4.48 (br d, *J* = 1.3 Hz, 1H), 4.36 (d, *J* = 6.4 Hz, 1H), 4.12 (dd, *J* = 9.2, 7.7 Hz, 1H), 2.10 (ddd, *J* = 11.5, 6.4, 2.7 Hz, 1H), 1.99 (dd, *J* = 11.5, 1.2 Hz, 1H), 1.56-1.52 (m, 1H), 0.97 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz,

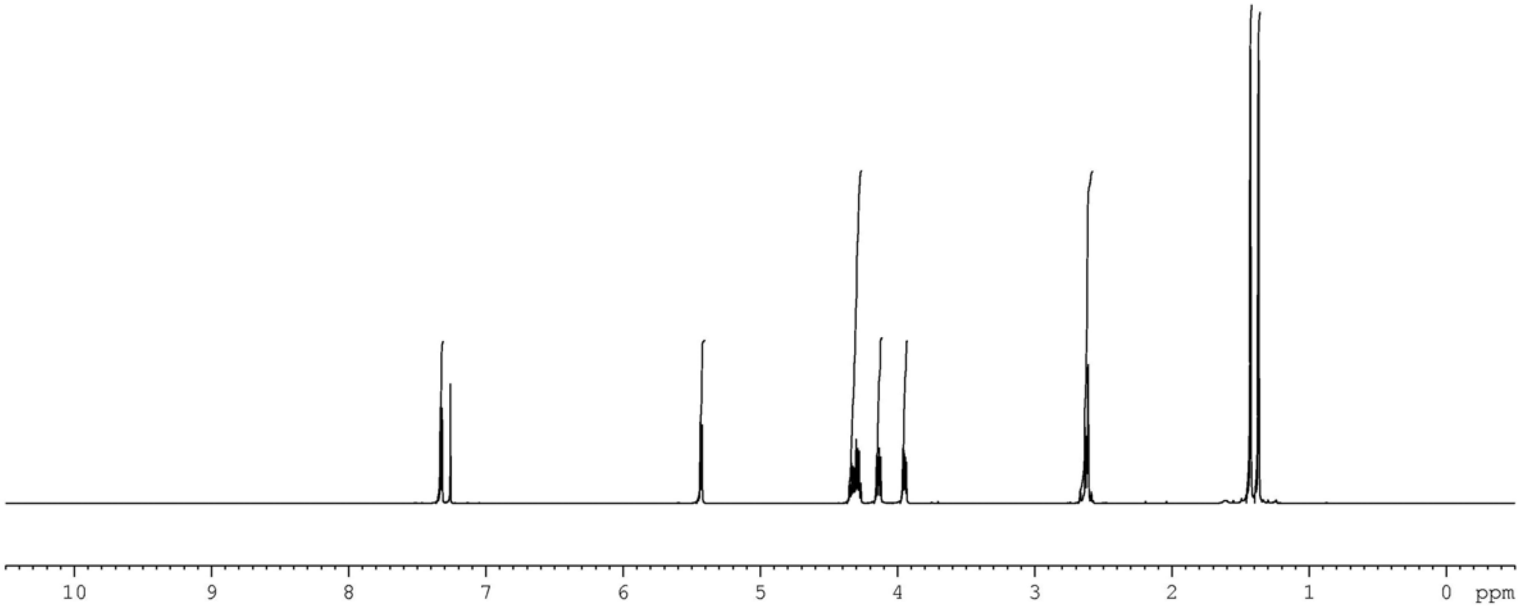
$CDCl_3$) δ 170.3, 140.5, 137.6, 136.7, 134.2, 132.6, 128.9, 128.6 (2C), 127.8, 126.7 (3C), 124.5, 117.1, 82.0, 79.8, 79.1, 76.6, 41.7, 39.2, 15.3; HRMS (ES) *m/z* $(M+Na)^+$ calcd 375.1572, obsd 375.1582.

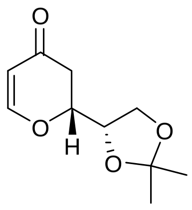
References

(1) Danishefsky, S. J.; Kobayashi, S.; Kerwin, J. F., Jr. *J. Org. Chem.* **1982**, *47*, 1981.

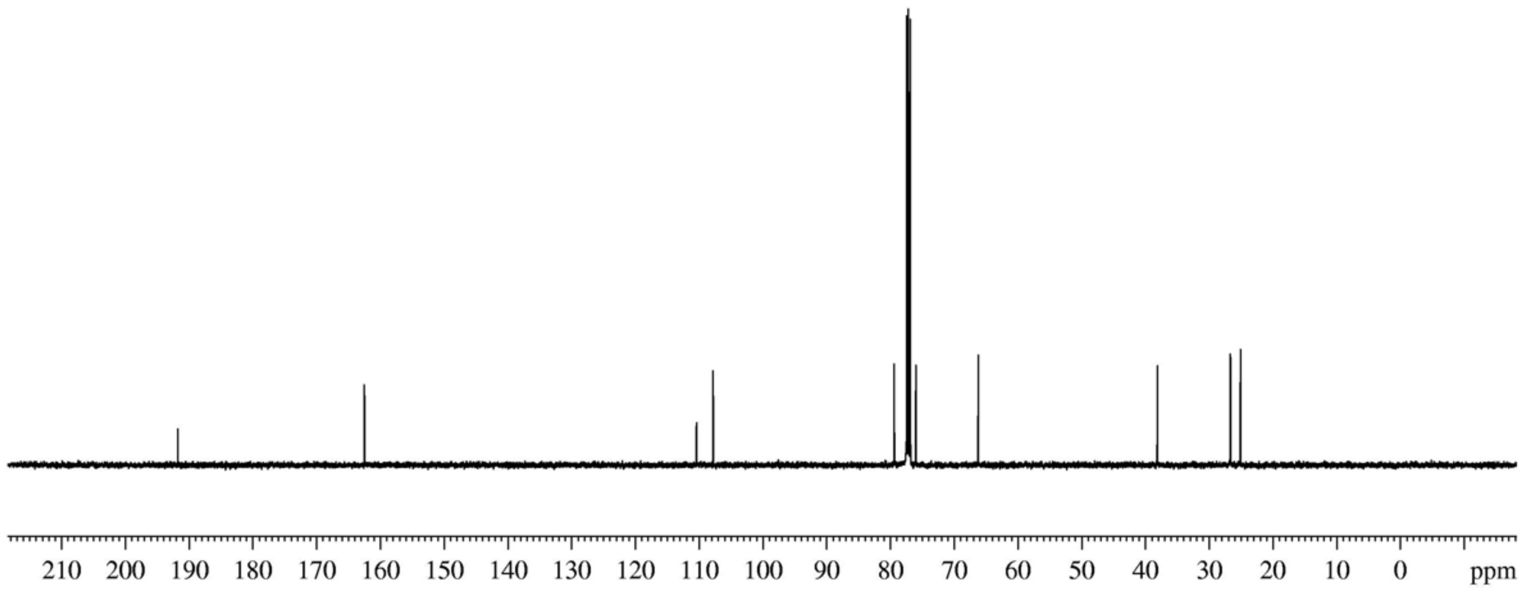


(−)-**6**, $CDCl_3$





(–)-**6**, $CDCl_3$



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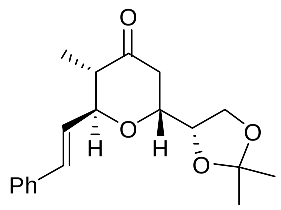

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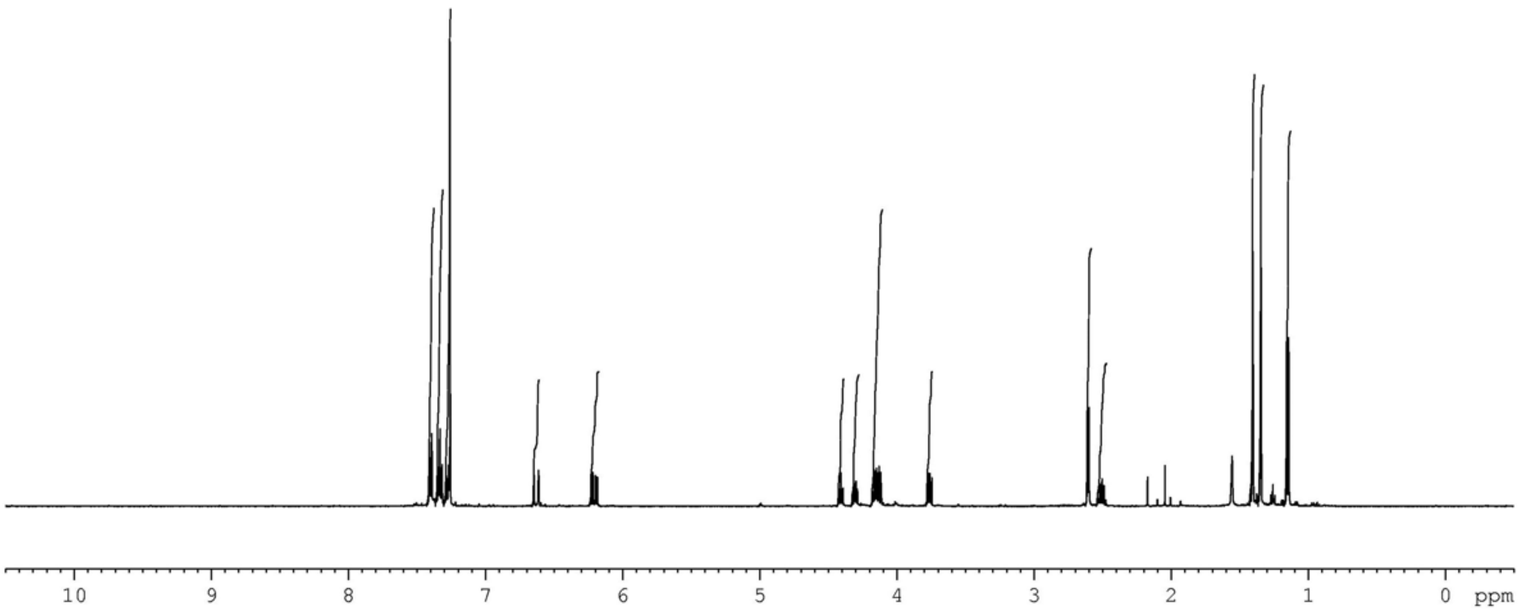

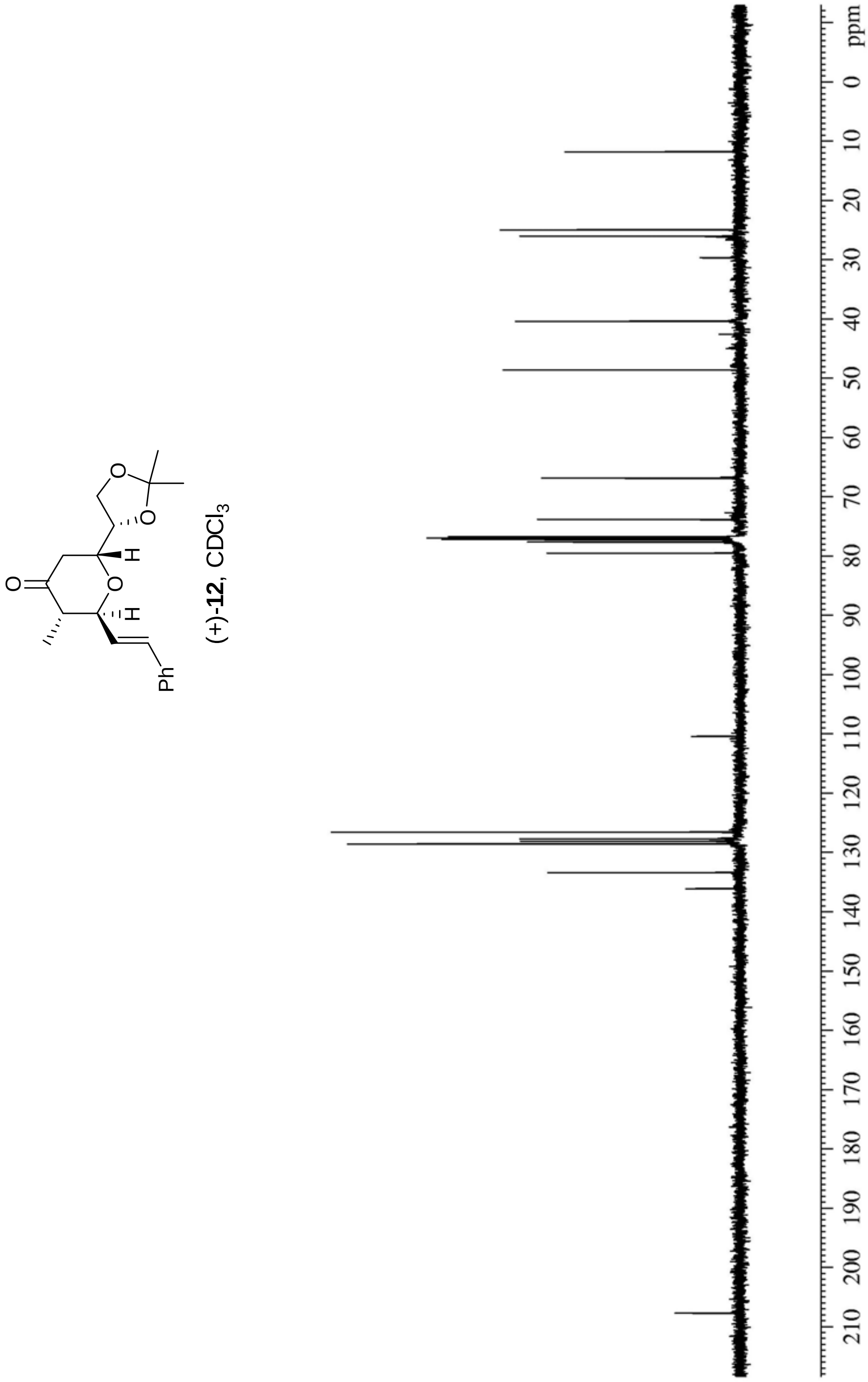

(+)-**12**, CDCl$_3$

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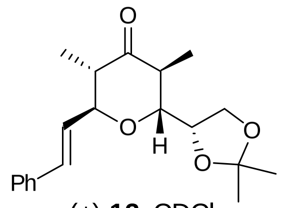

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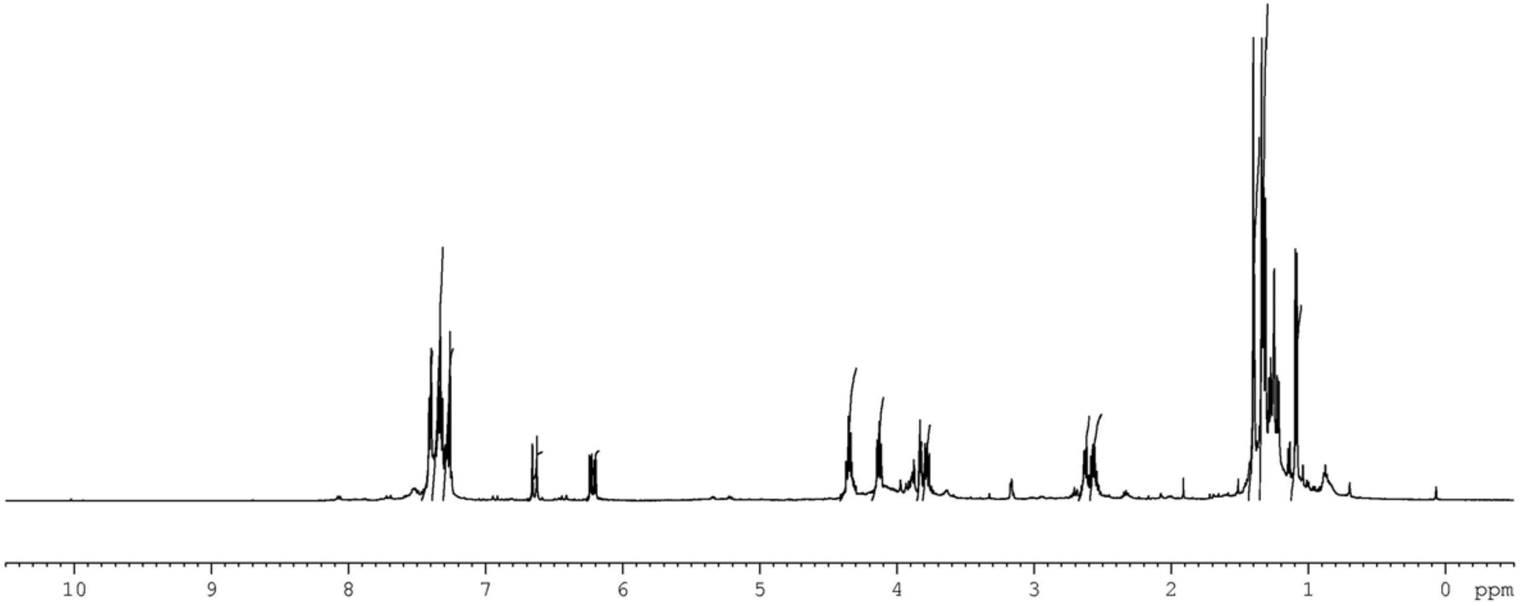

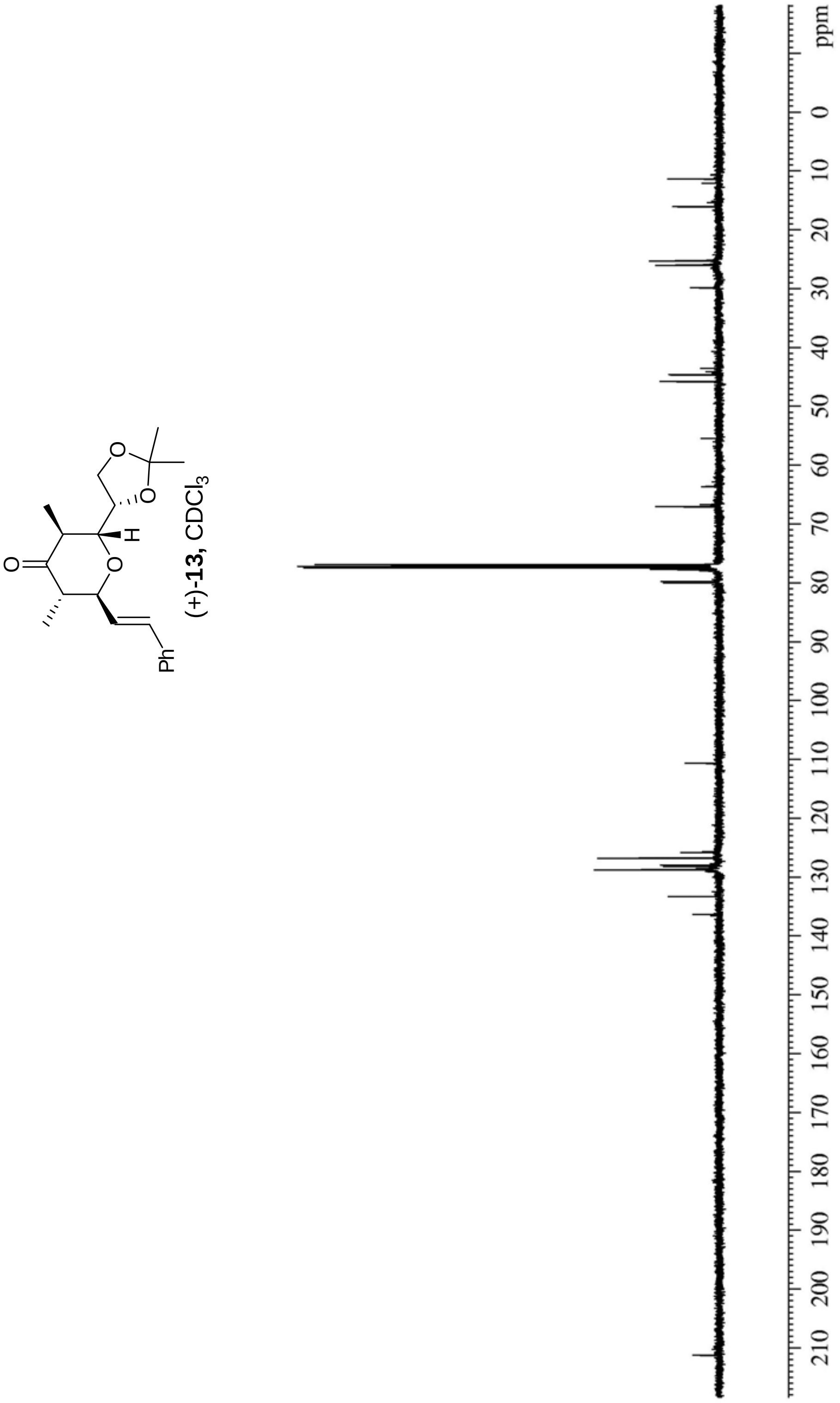
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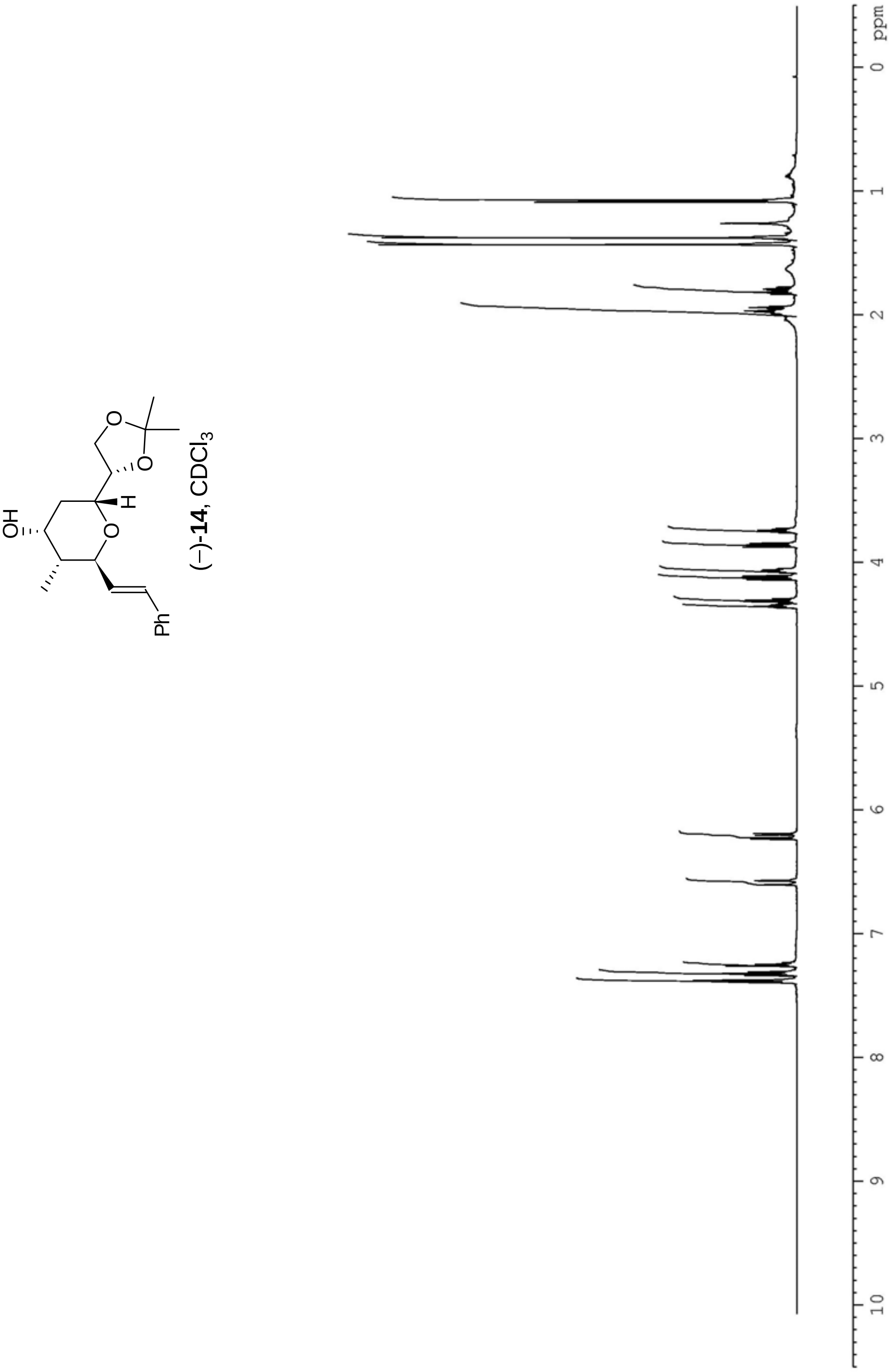
(+)-**13**, $CDCl_3$



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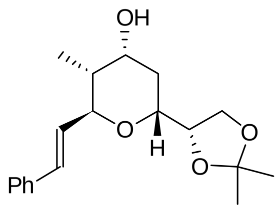

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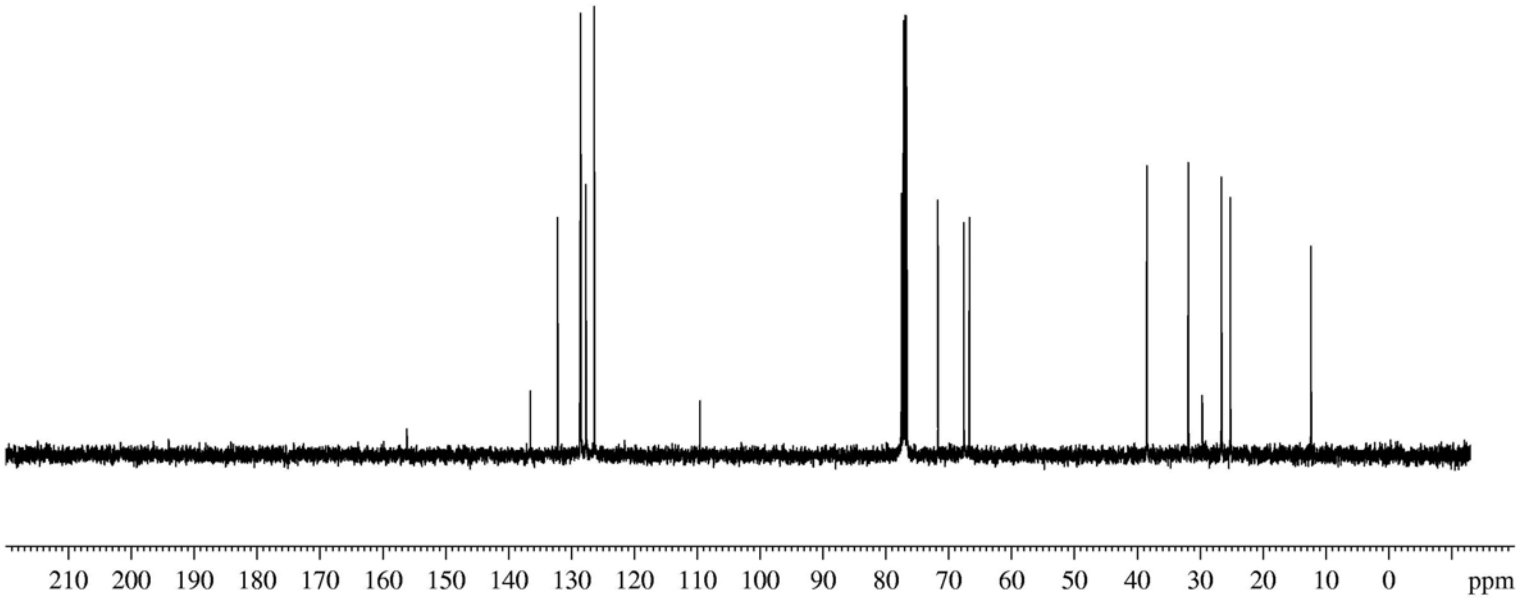
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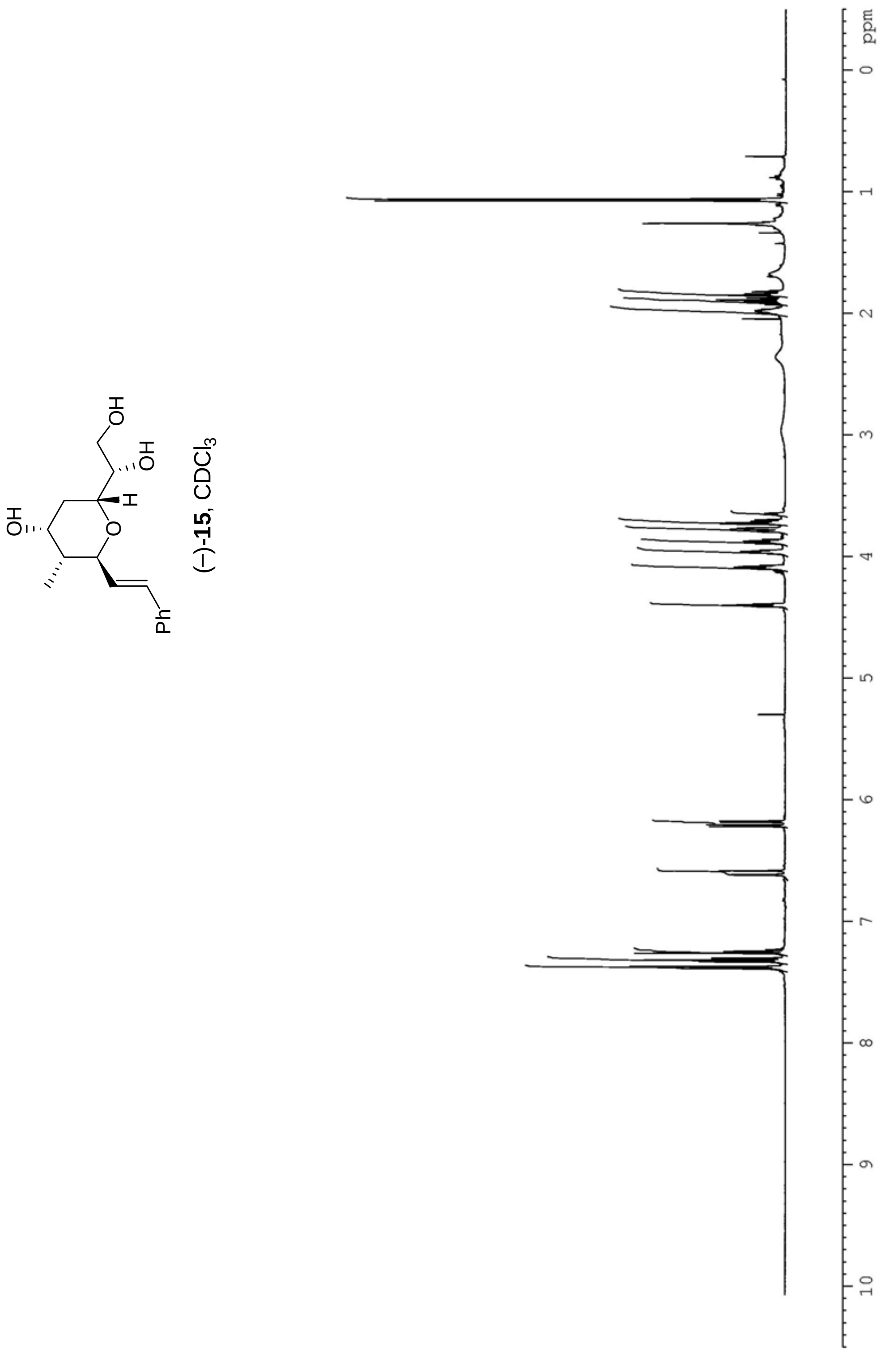

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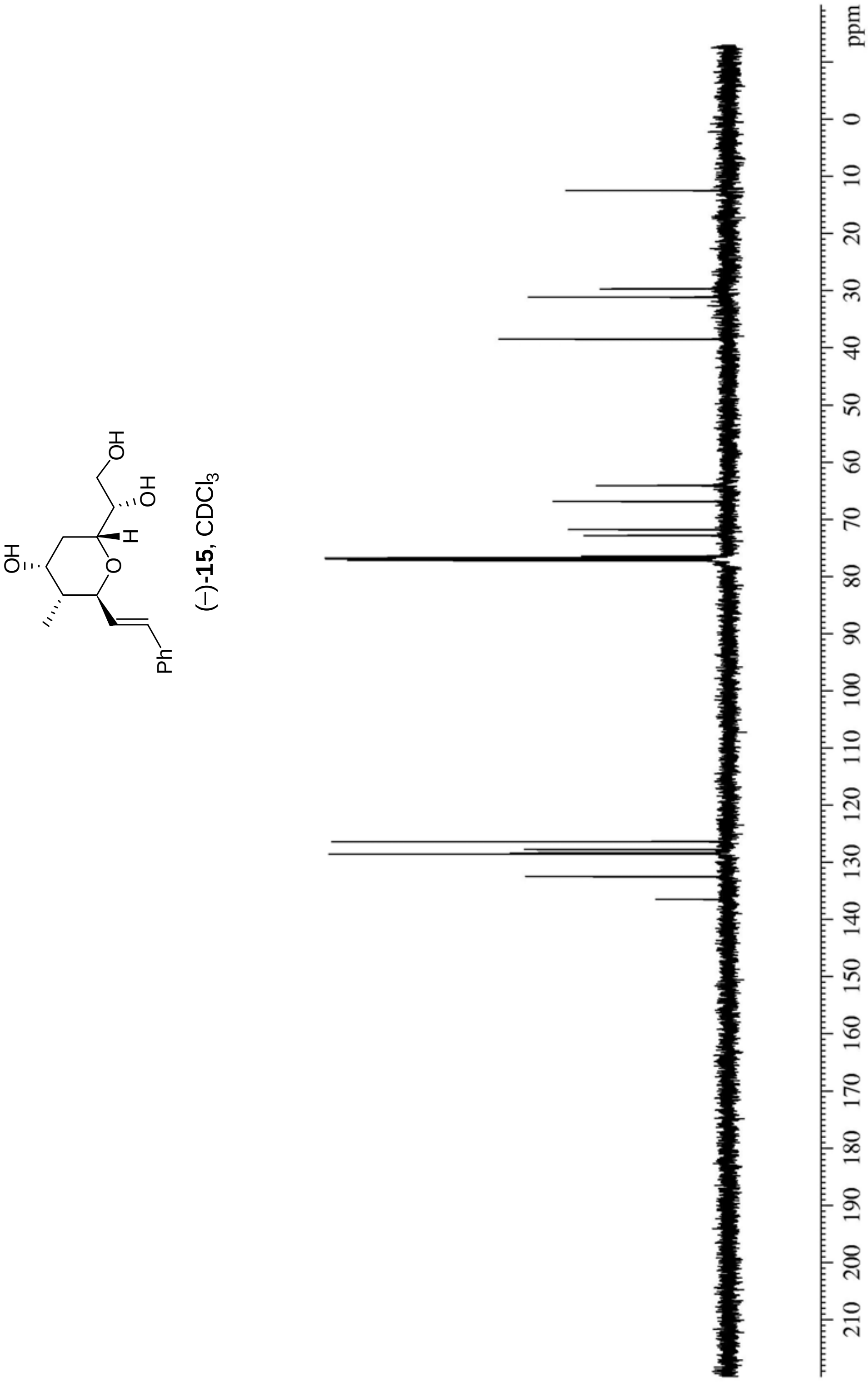

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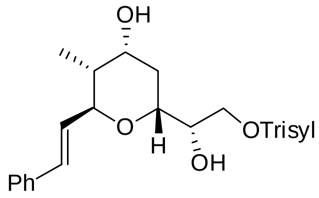

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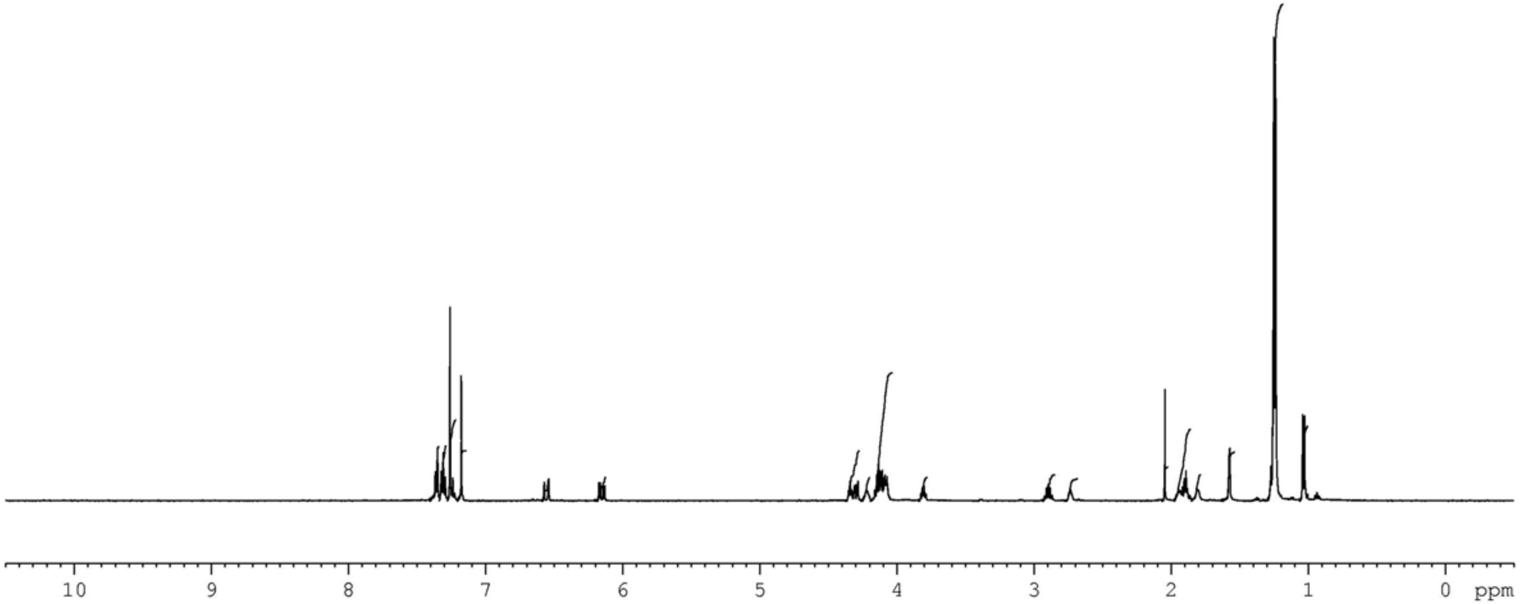

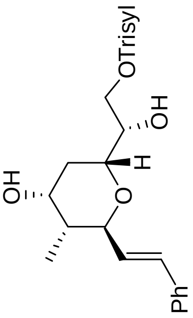
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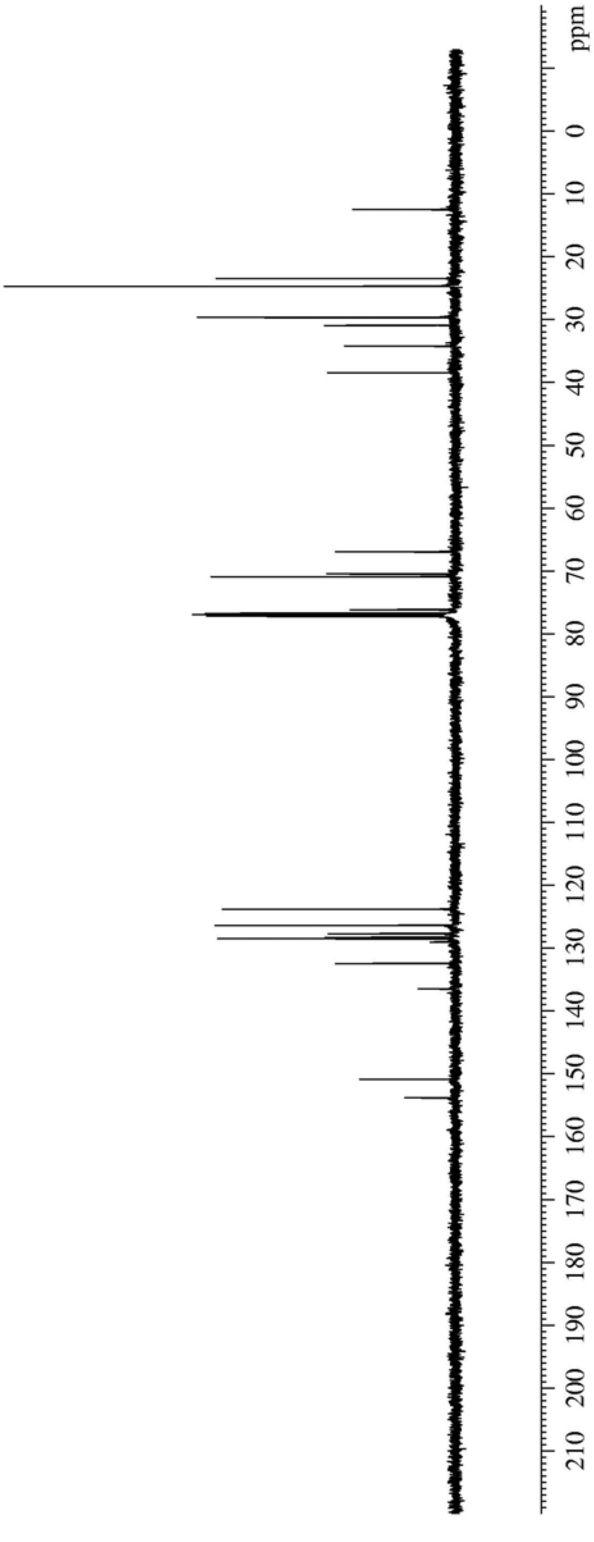
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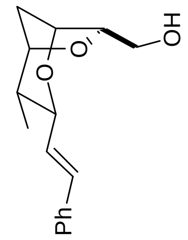

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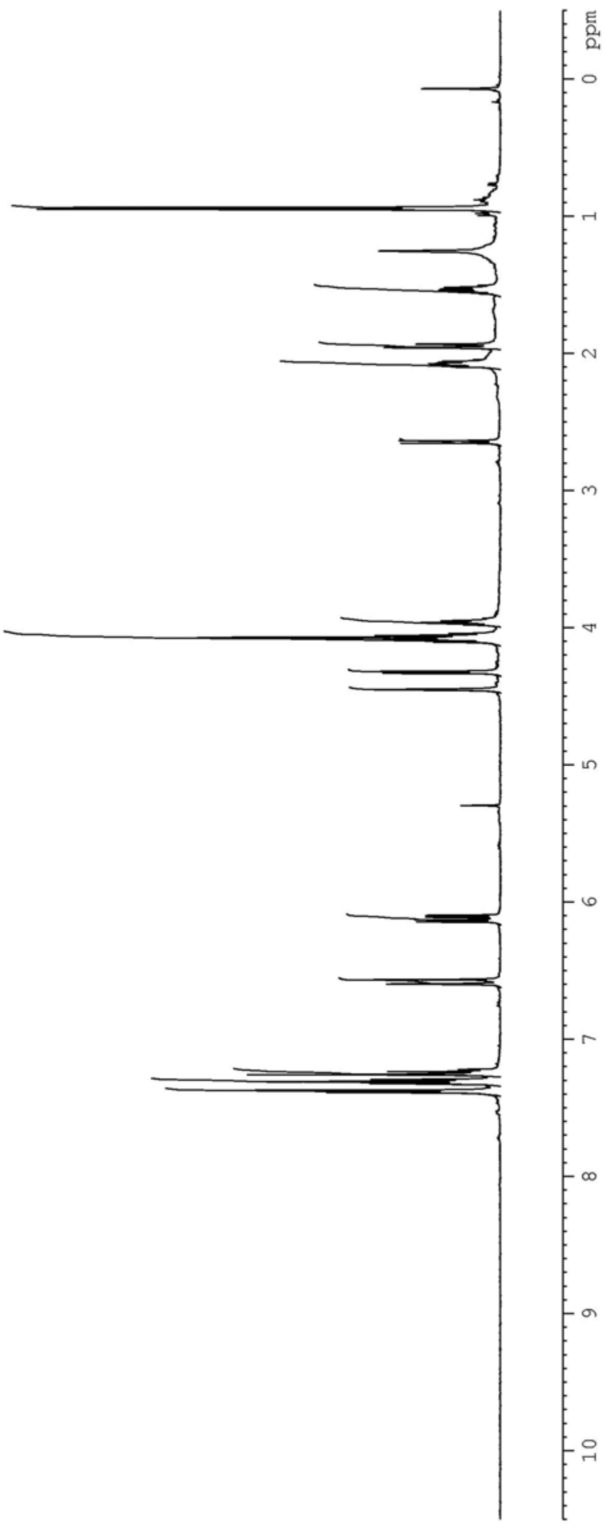

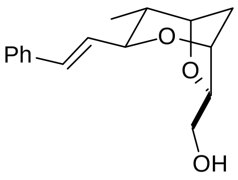
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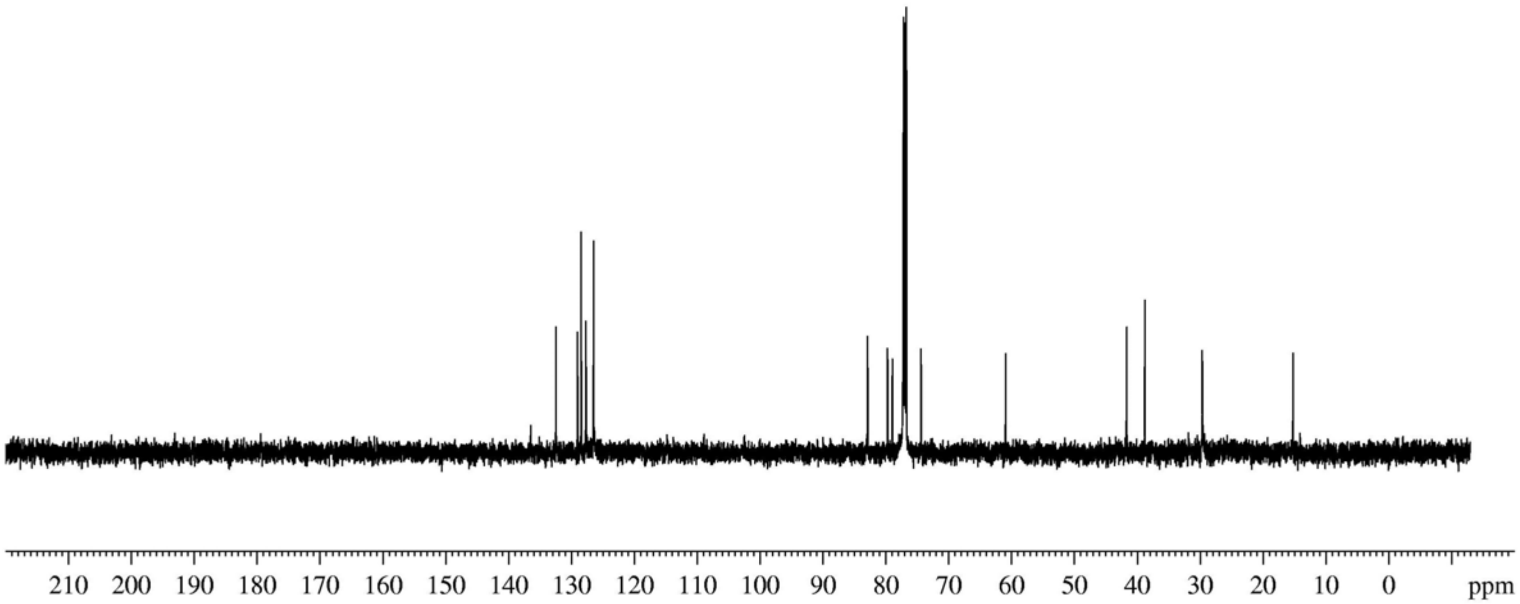
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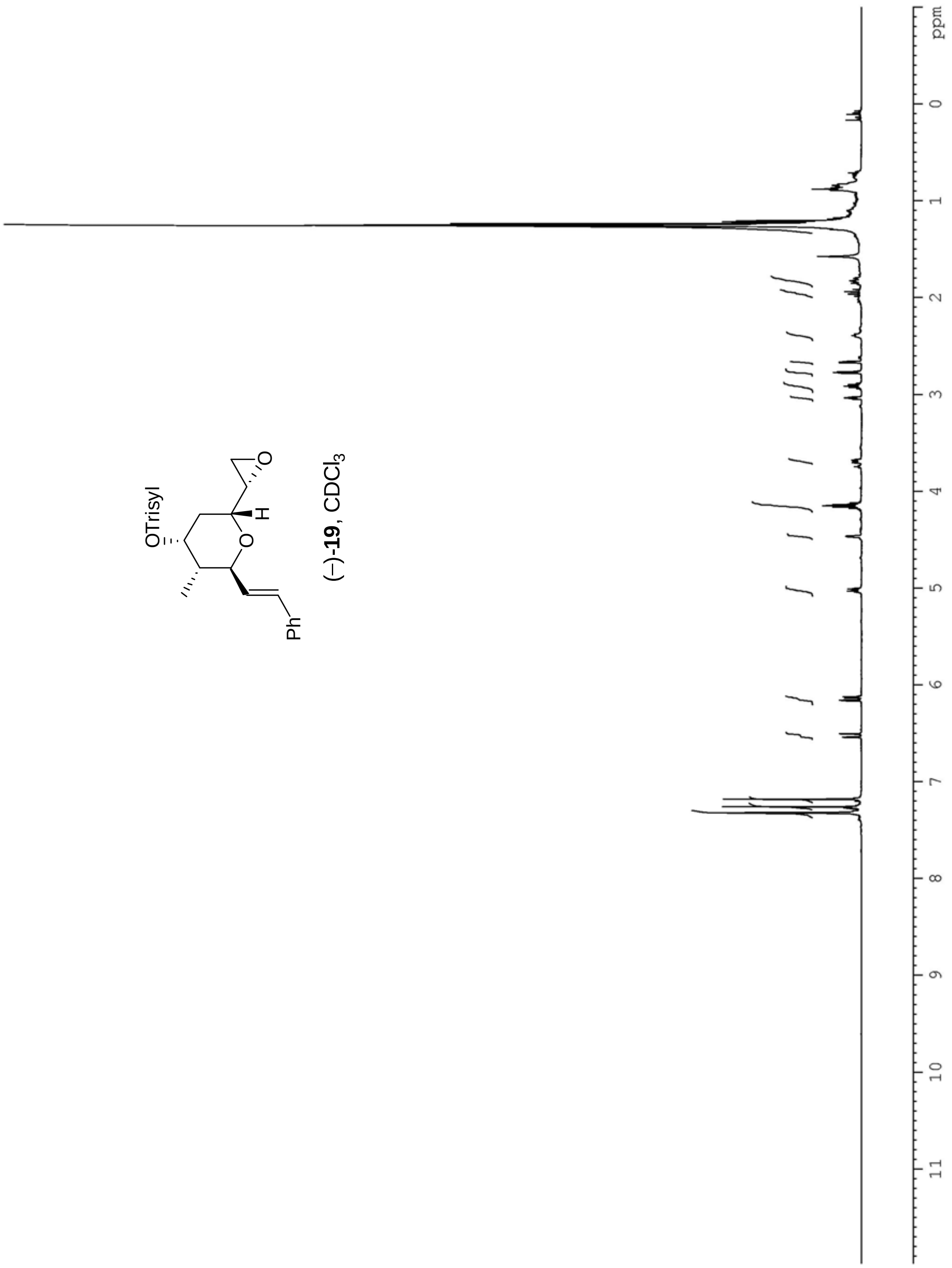

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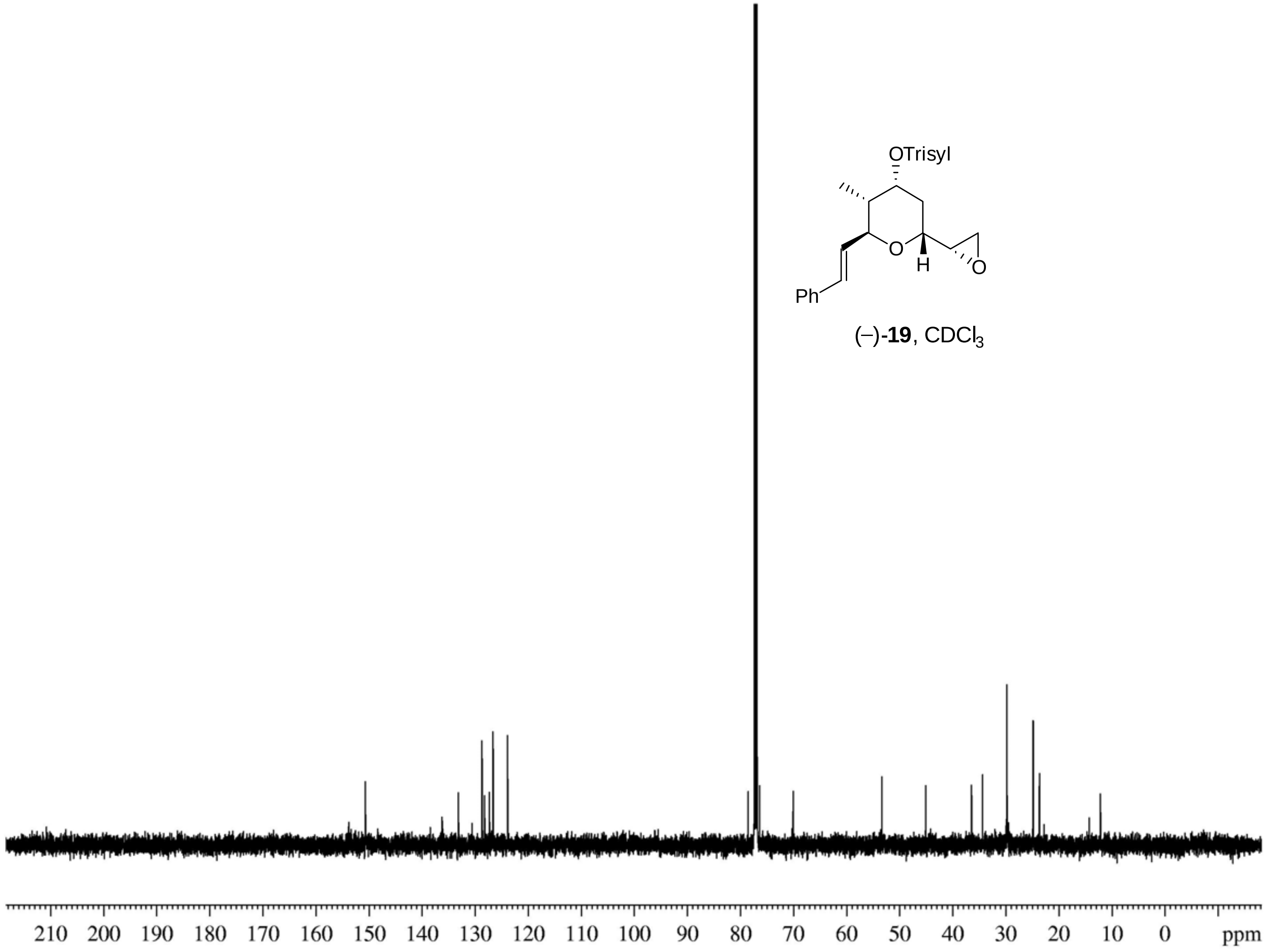

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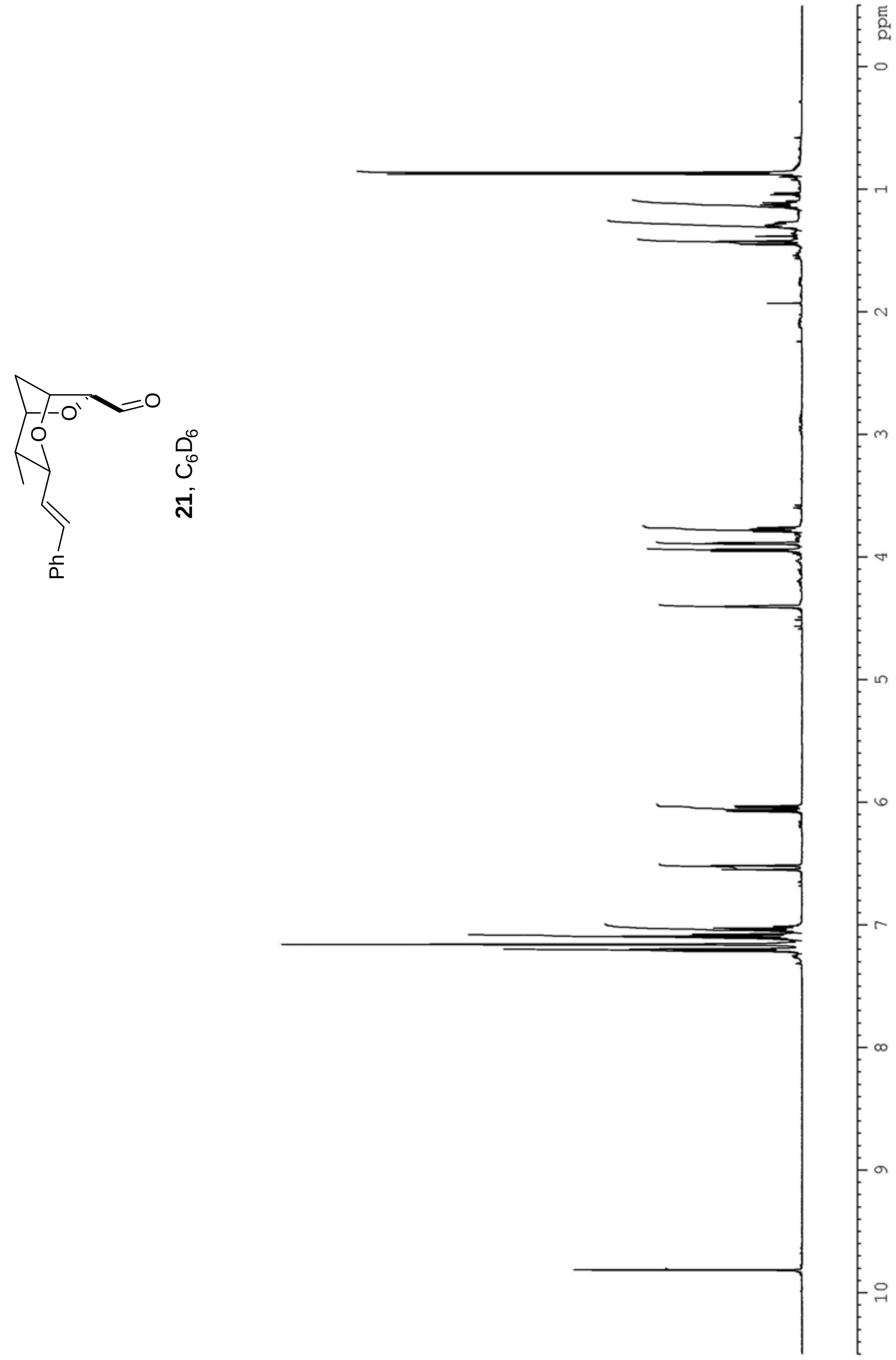

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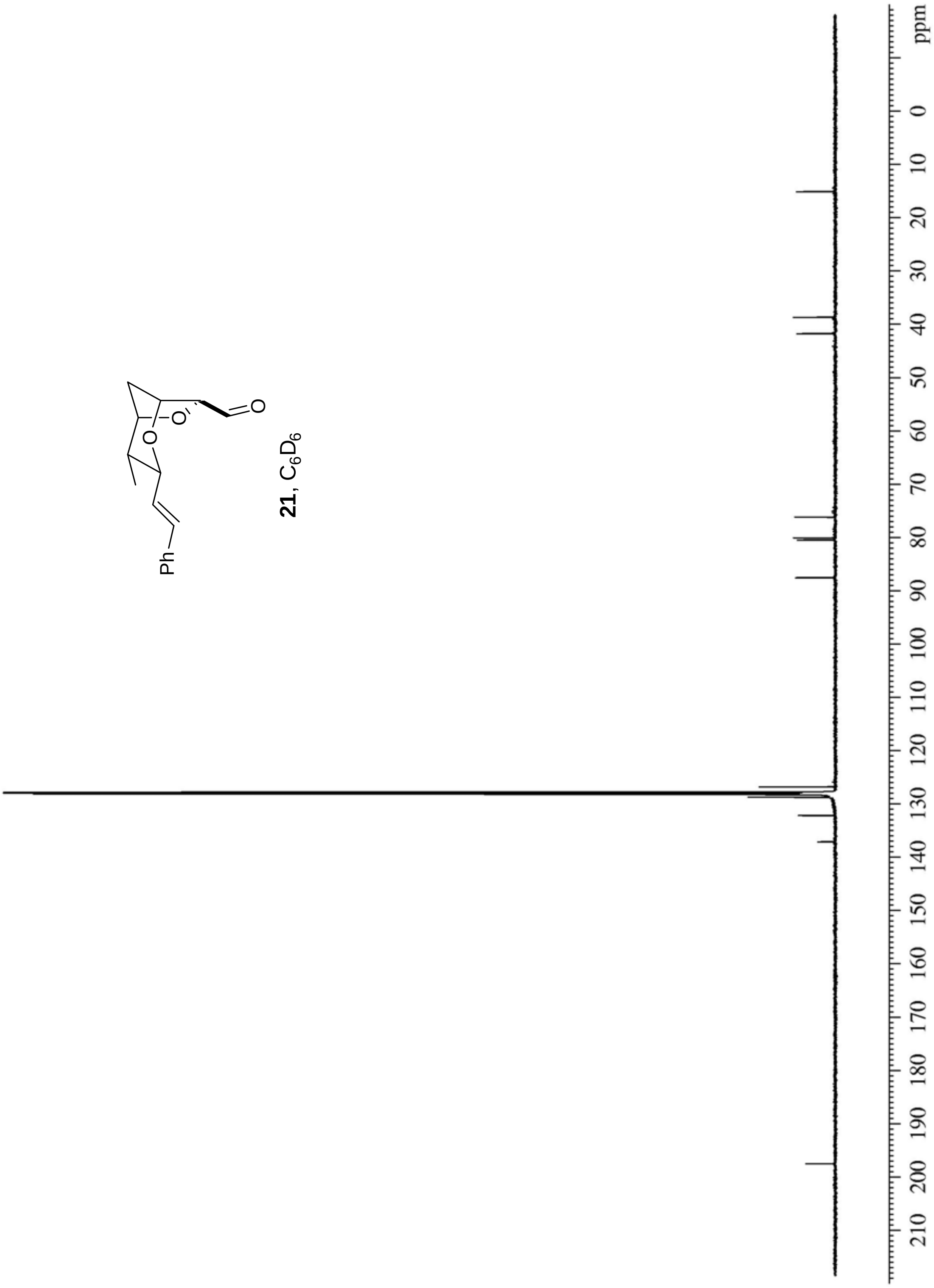

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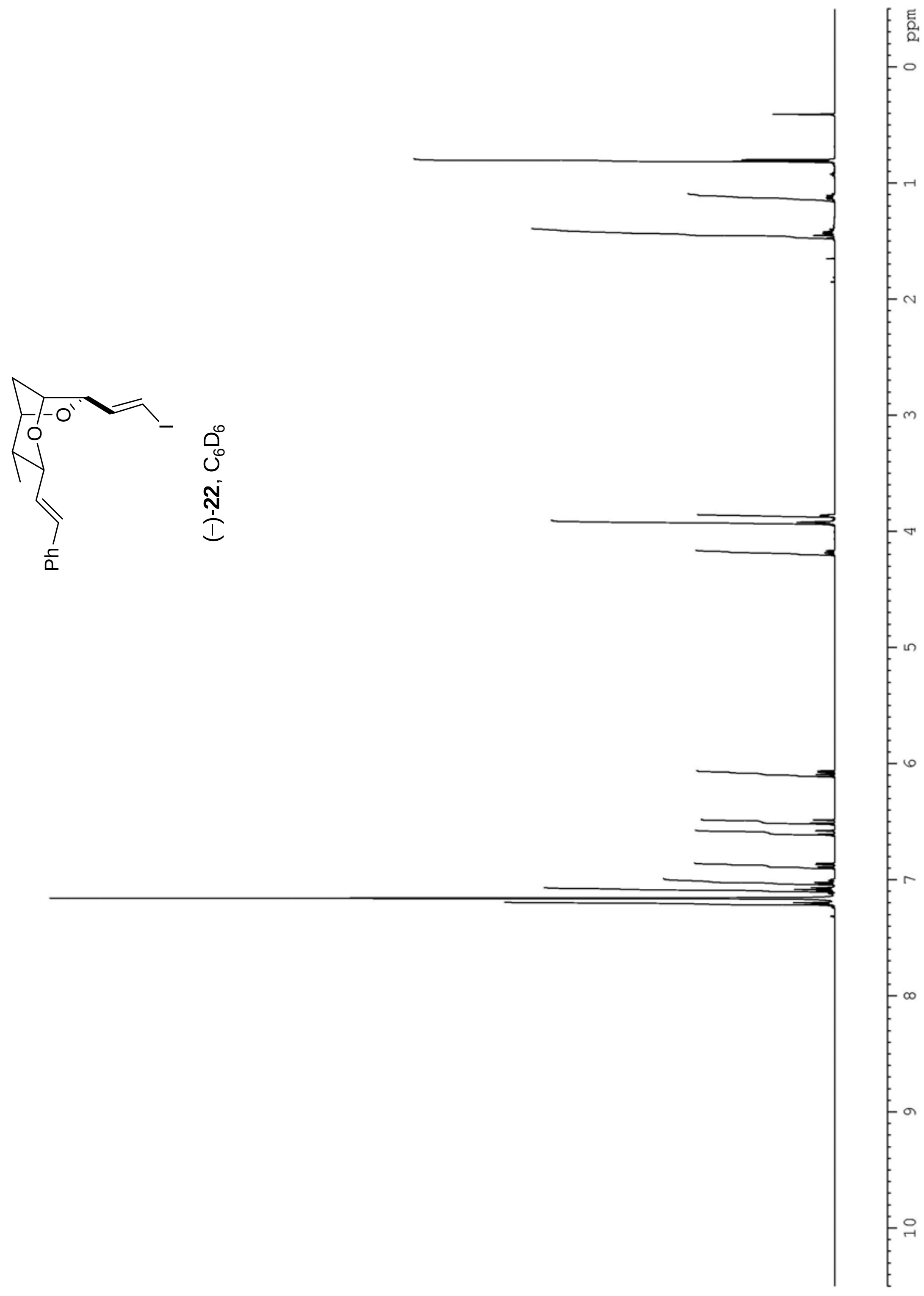

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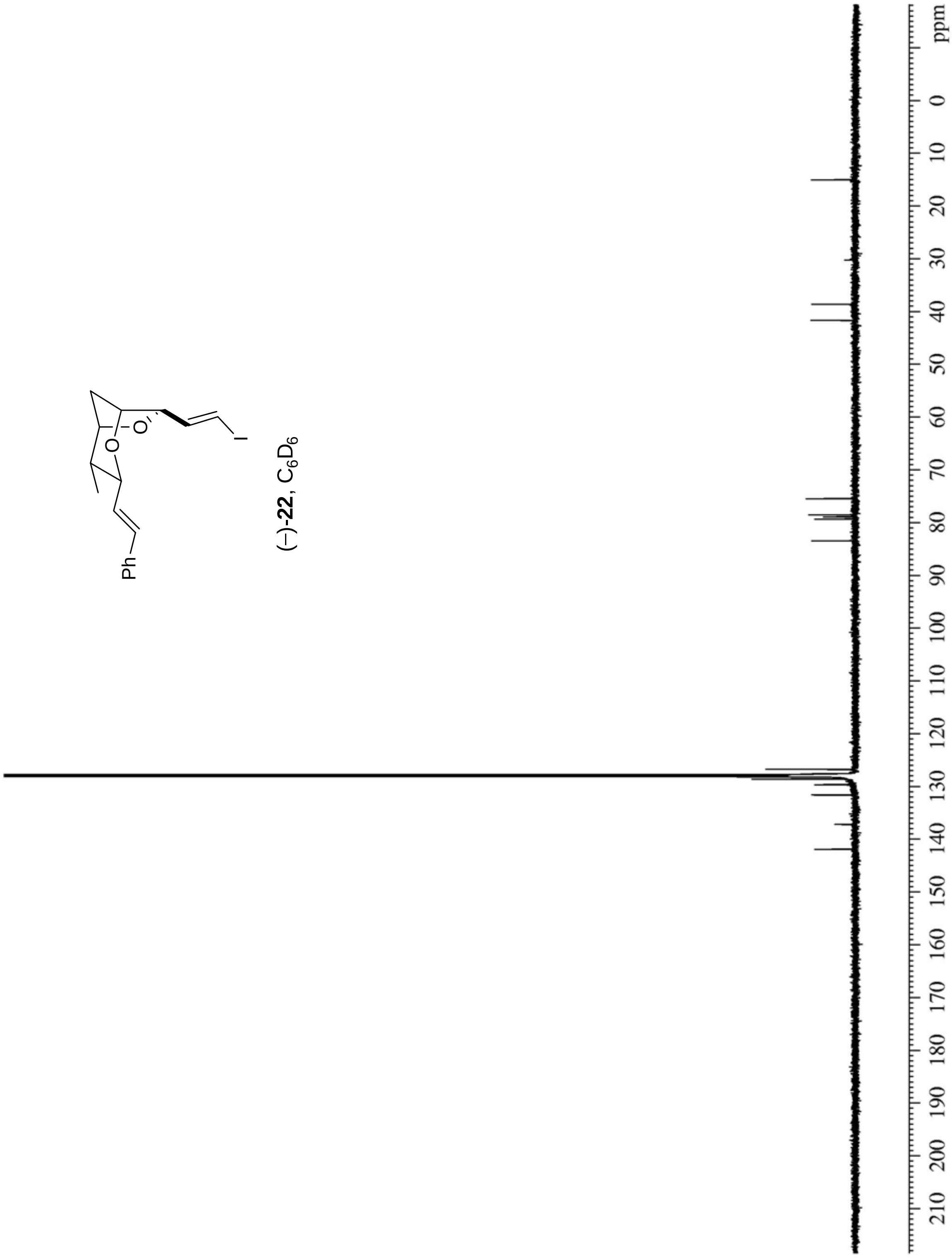

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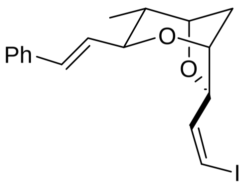

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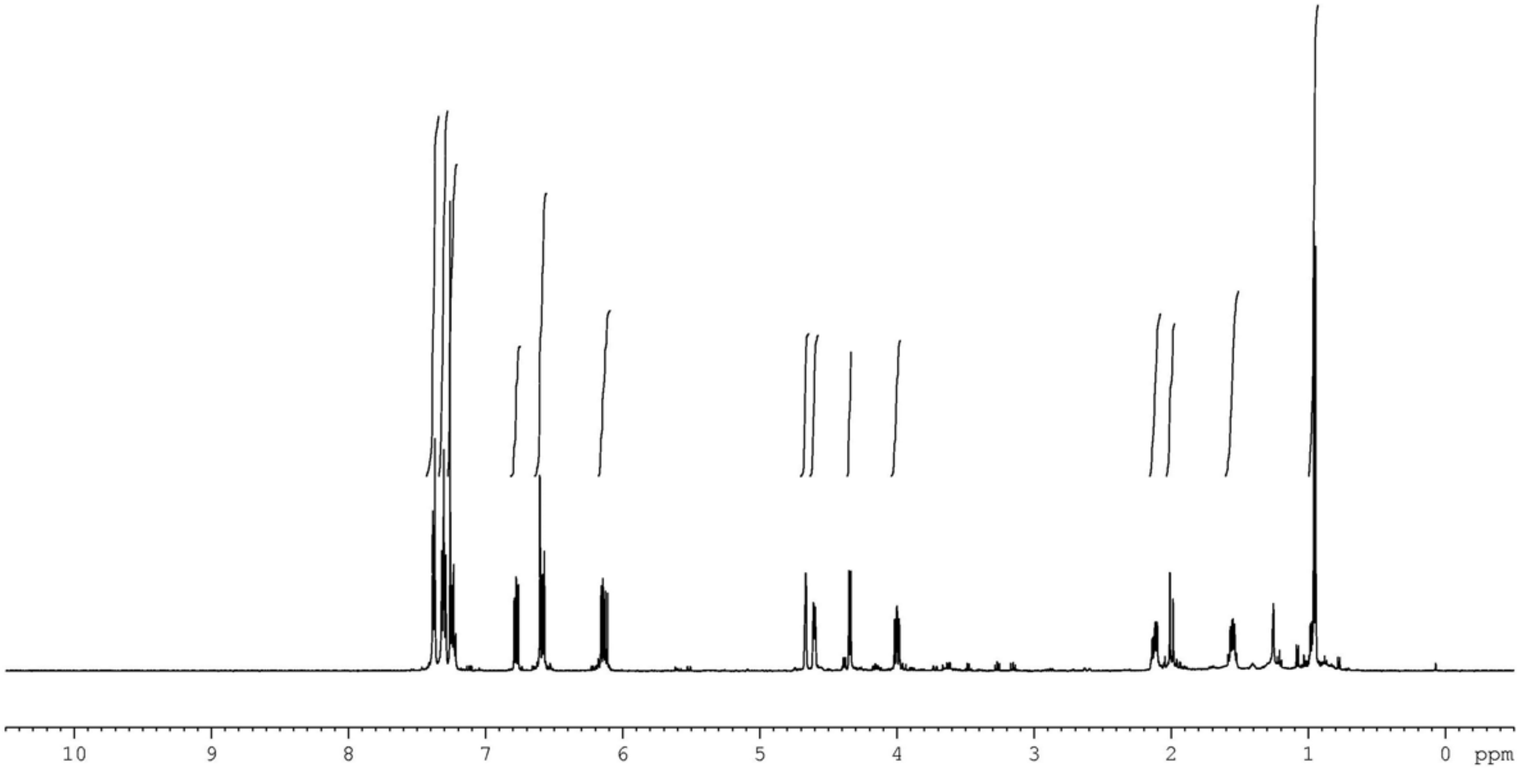

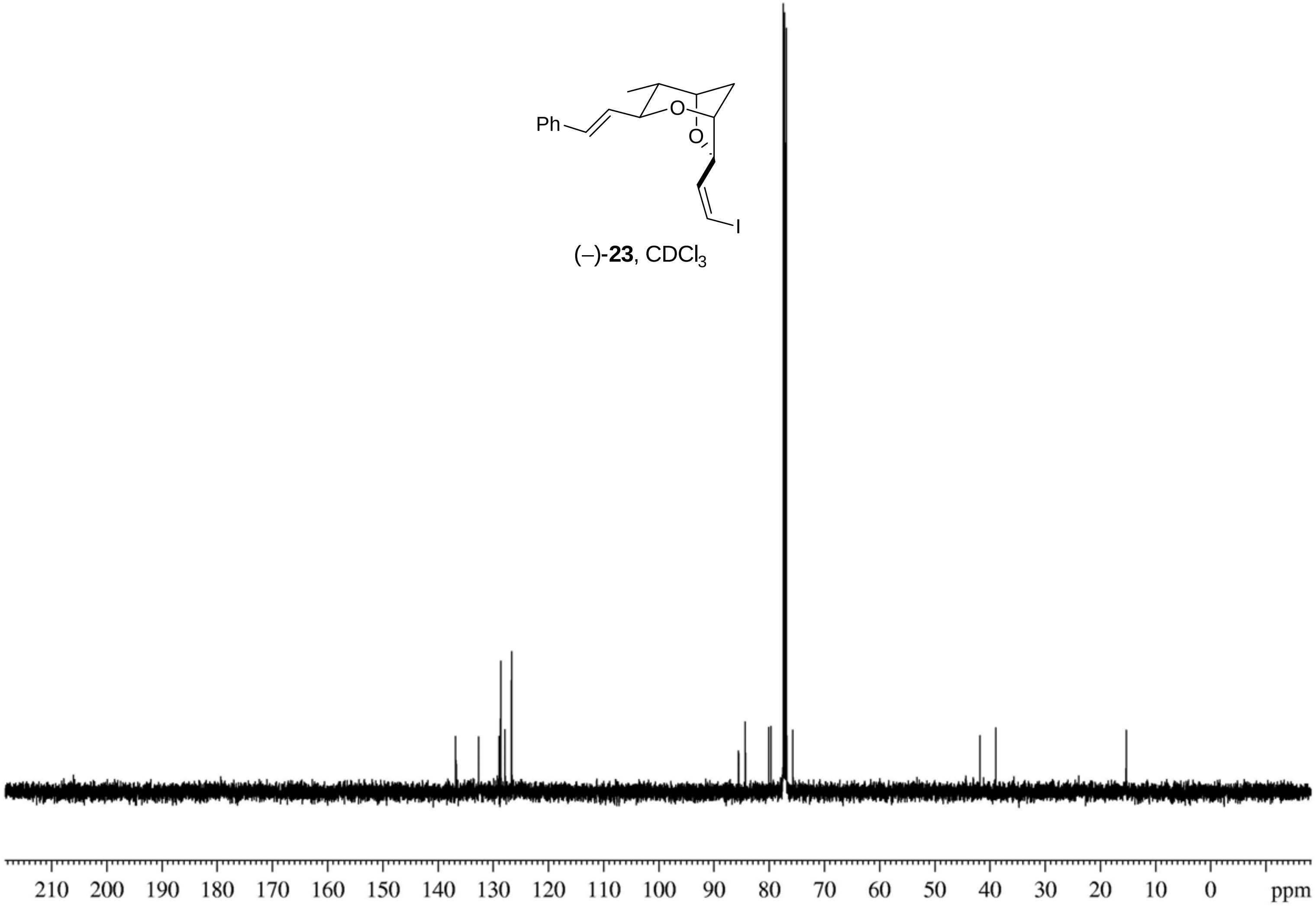
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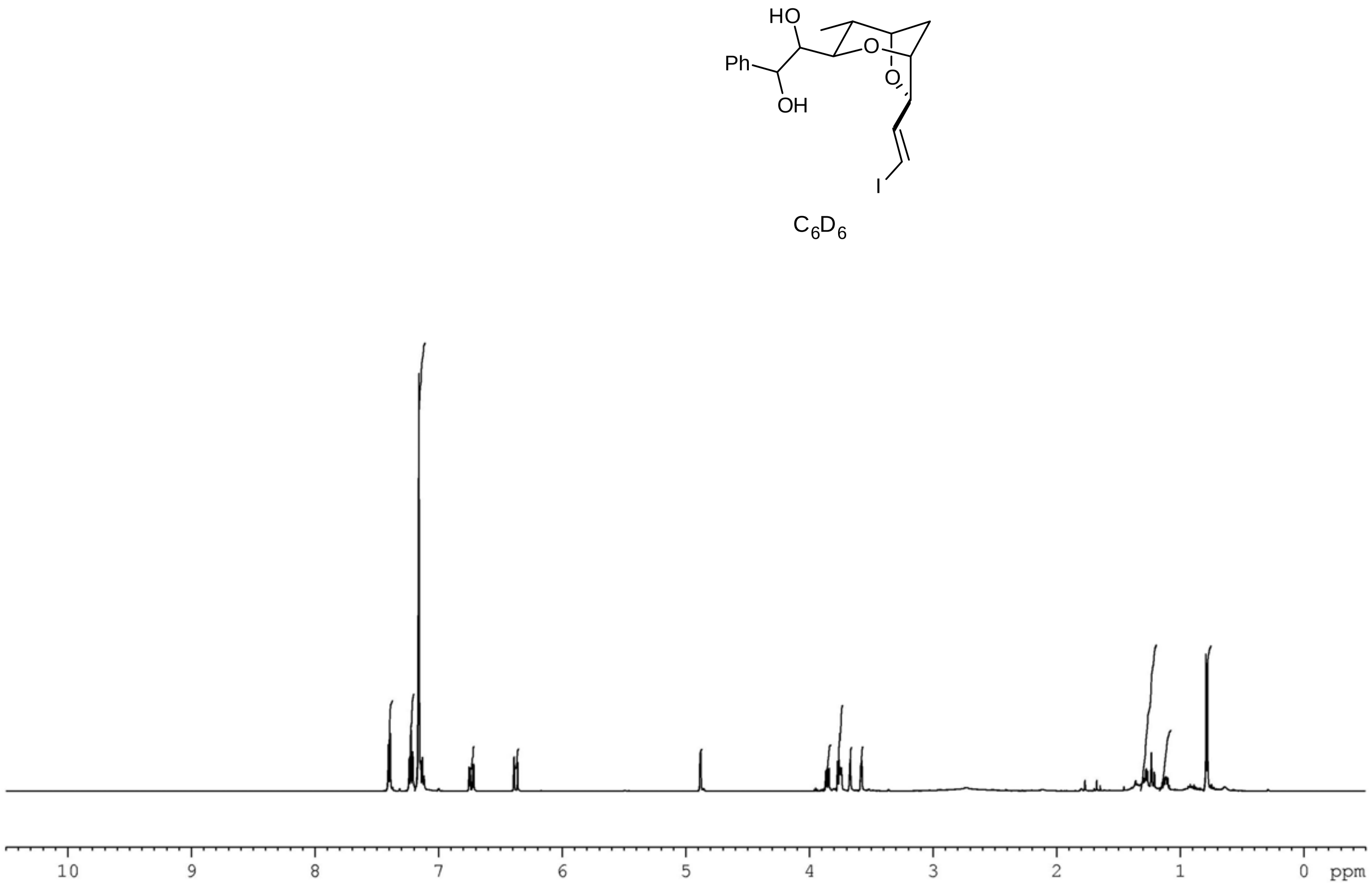
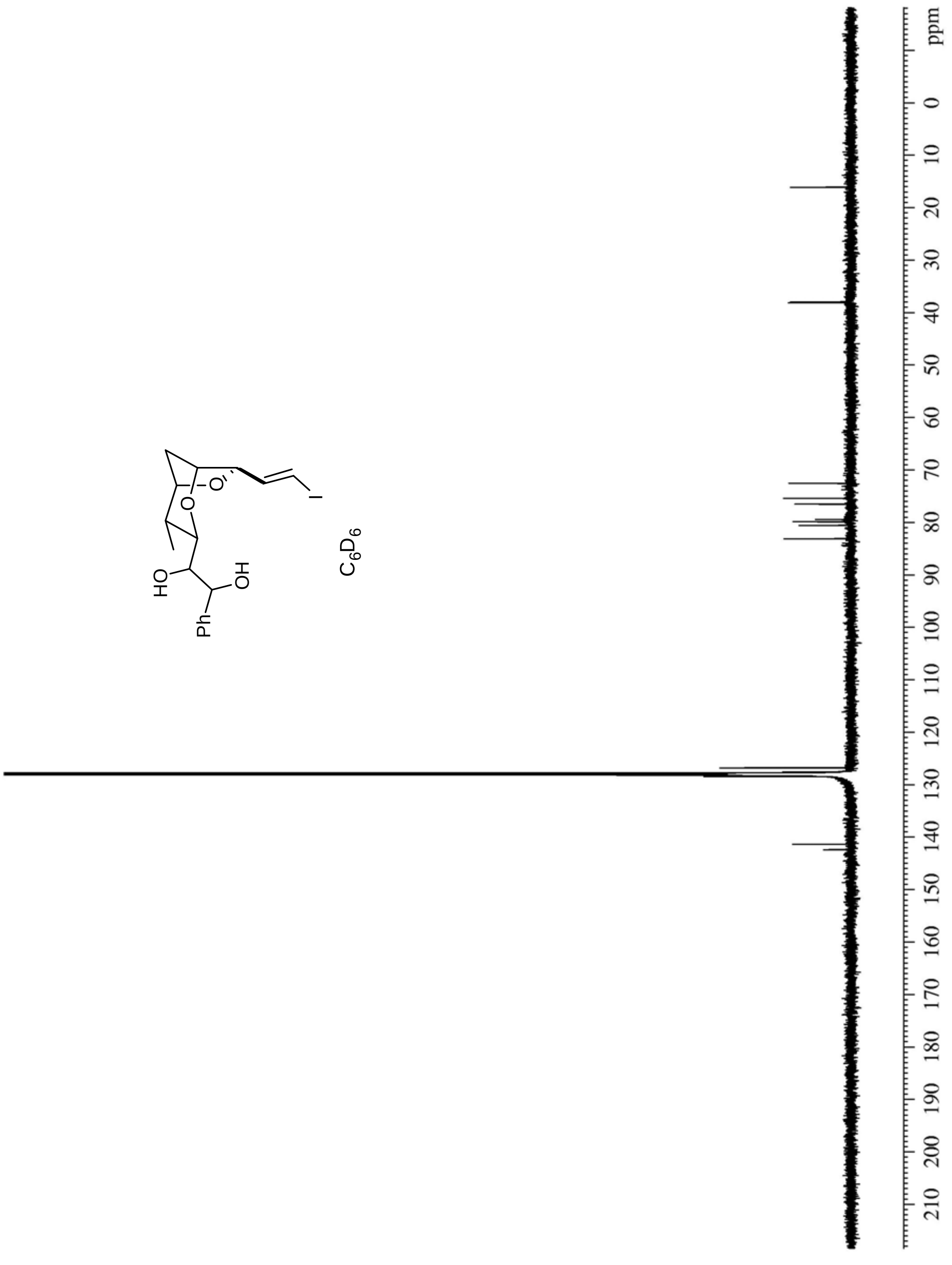
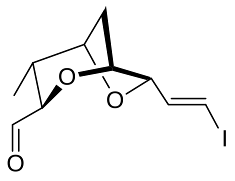
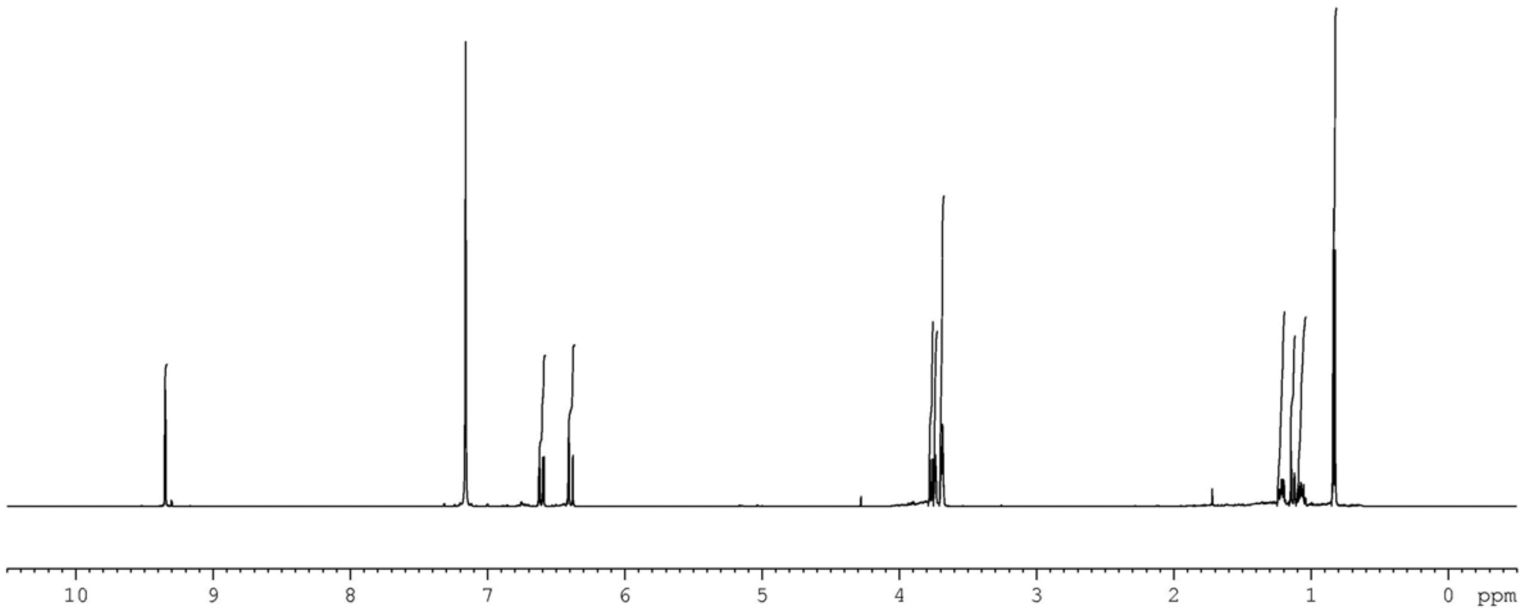

HO
Ph
OH
O
O
I
C$_6$D$_6$
10
9
8
7
6
5
4
3
2
1
0
ppm

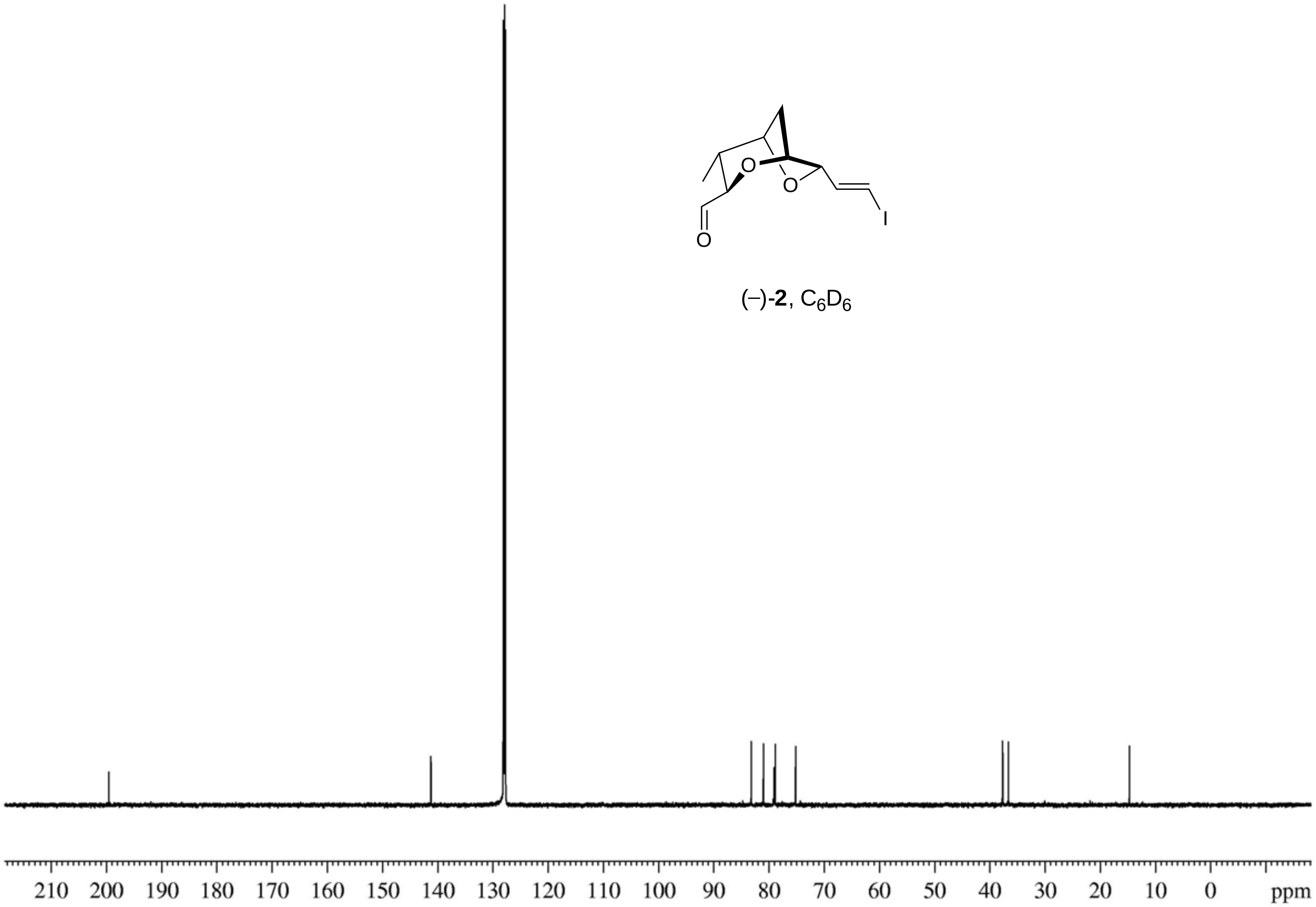


HO
OH
Ph
O
O
I
C$_6$D$_6$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



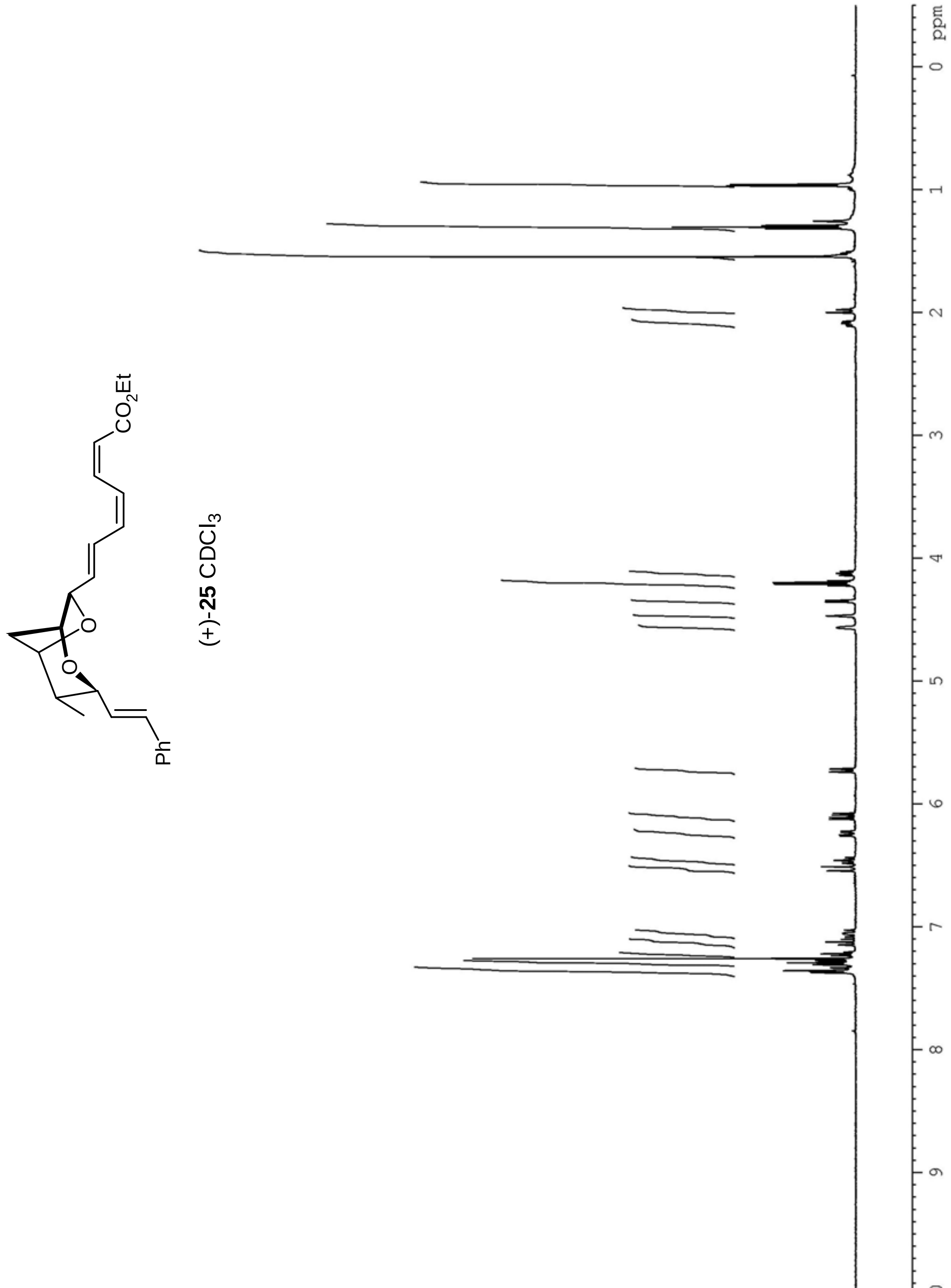
(–)-**2**, C_6D_6



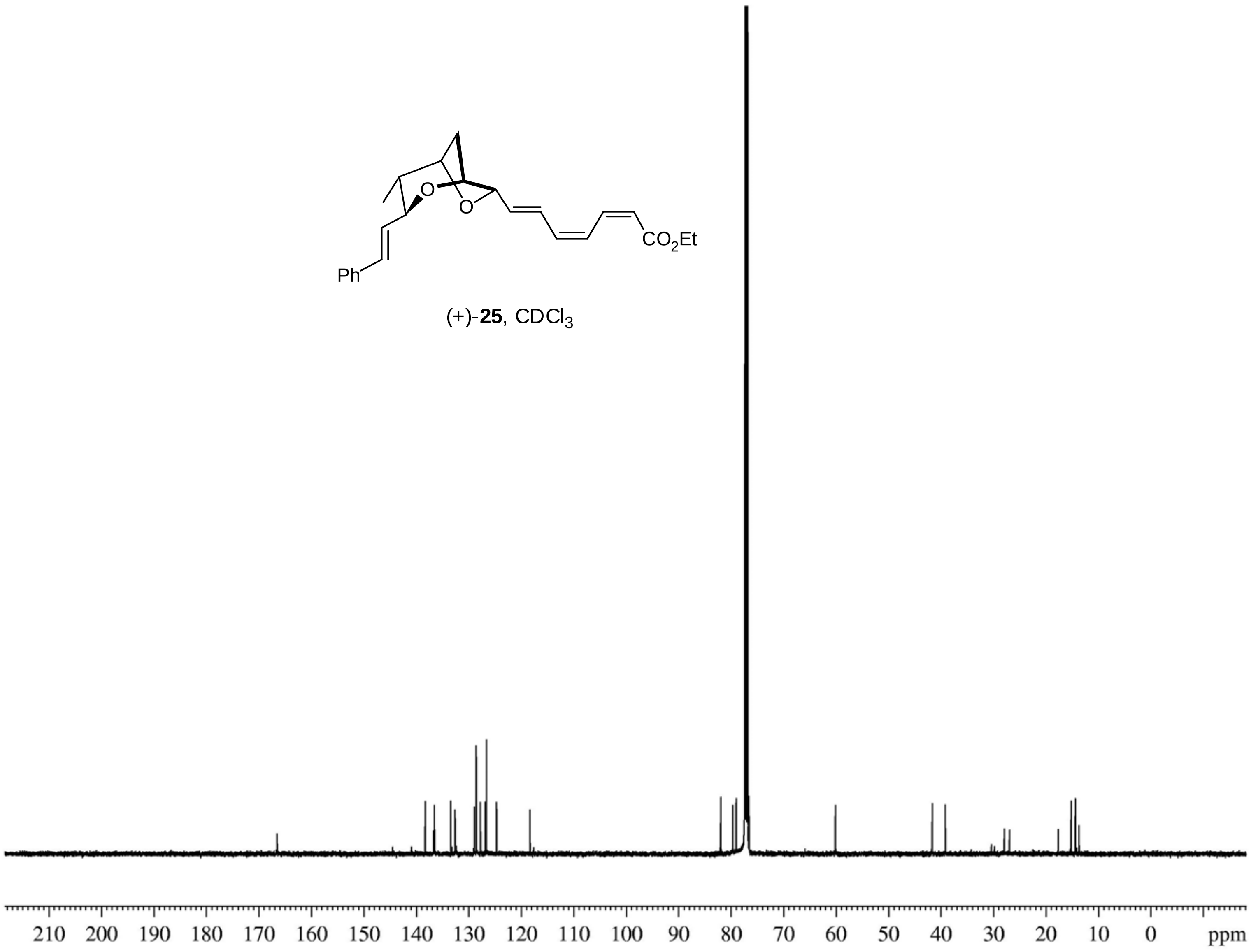


(−)-**2**, C_6D_6

O
O
O
I
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

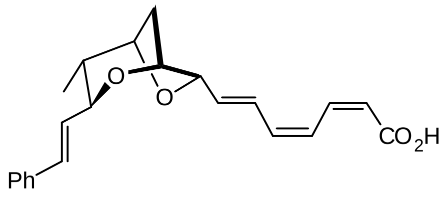


(+)-**25** $CDCl_3$

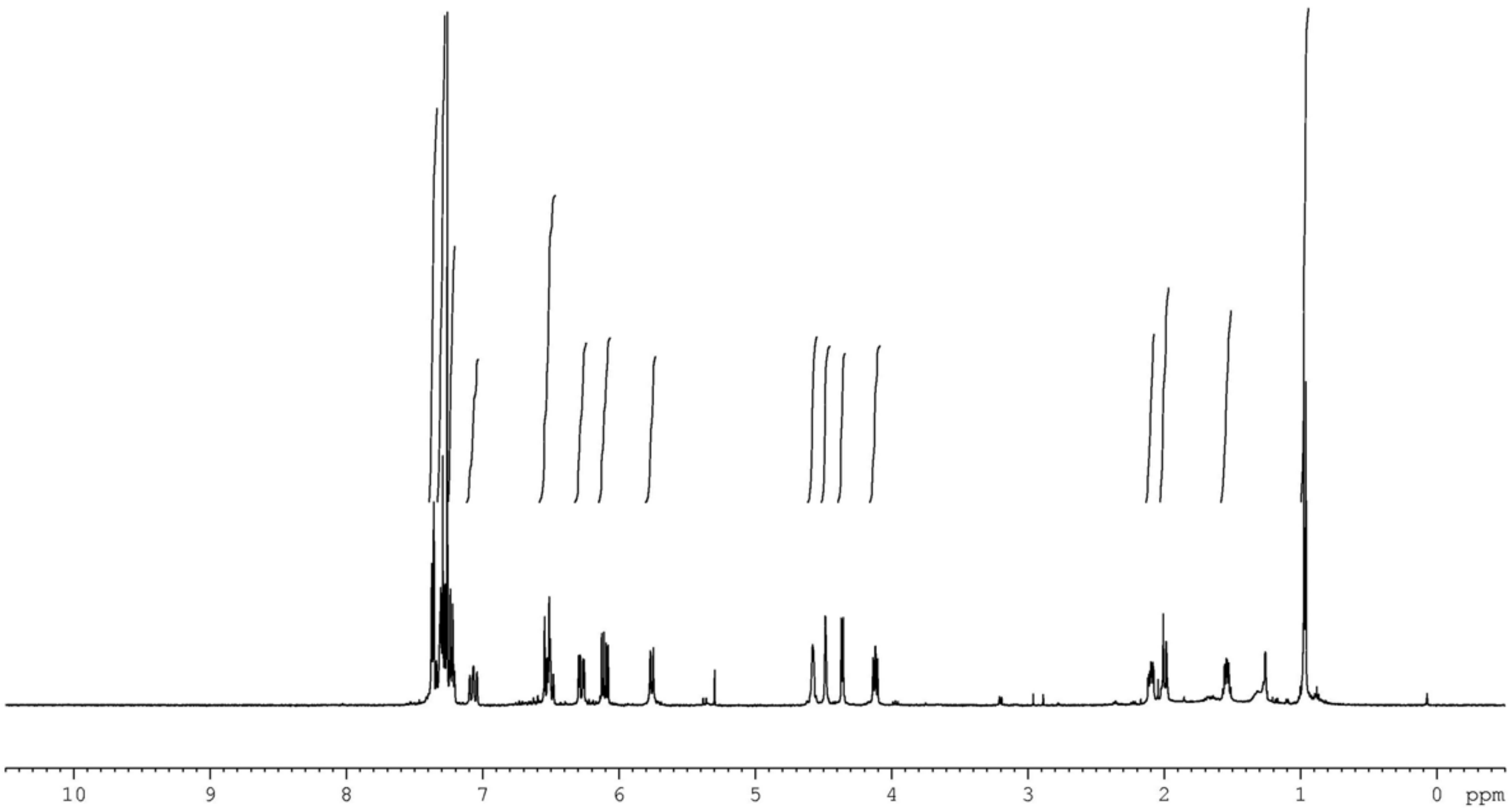


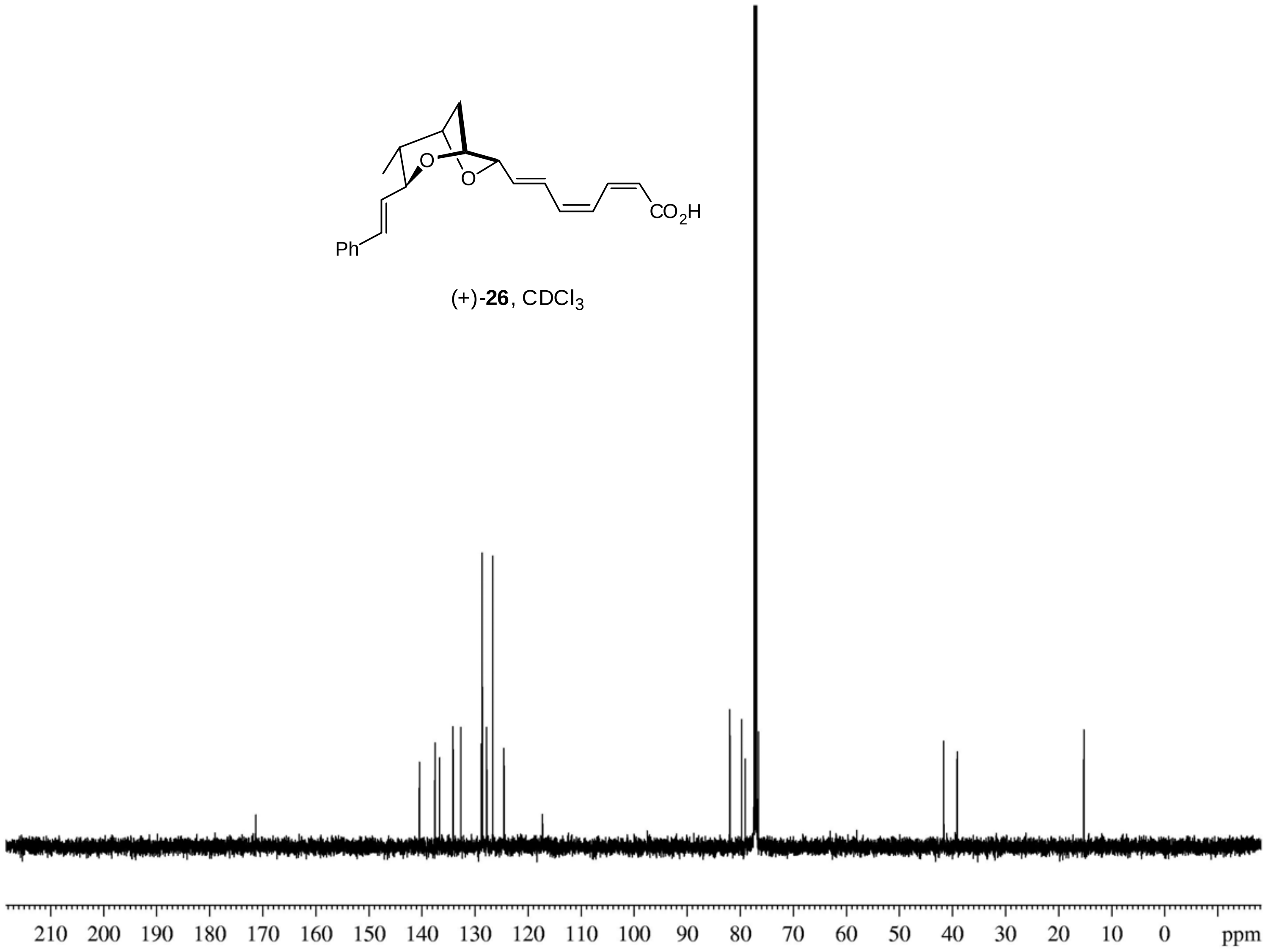
(+)-**25**, $CDCl_3$

Ph
O
O
CO_2Et
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



(+)-**26**, $CDCl_3$





(+)-**26**, $CDCl_3$

Ph
O
O
CO_2H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm