Linear Free Energy Relationship Analysis of a Catalytic Desymmetrization Reaction of a Diarymethane-(Bis)phenol

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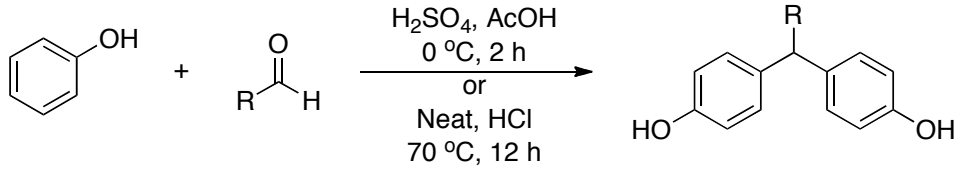
Supplementary Information

I. General Procedures.

Proton NMR spectra were recorded on a 400 or 500 MHz spectrometer. Proton chemical shifts were reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00 ppm), or with the solvent reference relative to TMS employed as the internal standard ($CDCl_3$, δ 7.26 ppm; CD_3OD, δ 3.30 ppm). Spectral data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), and multiplet (m)], coupling constants [Hz], integration). Carbon NMR spectra were recorded on a 500 (125) MHz spectrometer with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to the residual solvent signal ($CDCl_3$, δ 77.0 ppm; CD_3OD, δ 49.0 ppm;). NMR data were collected at ambient temperature unless otherwise indicated. Infrared spectra (thin film and attenuated total reflectance (ATR-IR)) were obtained on a Nicolet 6700 FT-IR spectrometer; υ_{max} (cm^{-1}) are partially reported. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 Å F254 pre-coated plates (0.25 mm thickness). TLC R_f values are reported and visualization was accomplished by irradiation with a UV lamp and/or staining with cerium ammonium molybdate (CAM), ninhydrin, or $KMnO_4$ solutions. Flash column chromatography was performed using Silica Gel 60 Å (32-63 micron) or using a Biotage SP4 flash purification system. Gradient elution volumes are reported as column volumes (CV). Optical rotations were recorded on a Perkin-Elmer Polarimeter 341 at the sodium D line (1.0 dm path length). High resolution mass spectra were acquired from the Mass Spectrometry Facility at the Keck Center of Yale University. The method of ionization is given in parentheses. In place of HRMS for some samples, ultra high performance liquid chromatography-mass spectrometry (UPLC/MS) was performed on a Waters UPLC/MS instrument equipped with a reverse-phase C_{18} column (1.7 μm particle size, 2.1 x 50 mm), dual atmospheric pressure chemical ionization (API)/electrospray (ESI) mass spectrometry detector, and photodiode array detector. Chiral analytical normal phase HPLC was performed at a column temperature of 20 °C on a Hewlett-Packard or Agilent 1100 Series chromatograph equipped with a diode array detector (210 nm, 230 nm or 254 nm). Solvents were purified using a Seca Solvent Purification System by GlassContour. All other chemicals were purchased commercially and used as received unless indicated otherwise.

II. Preparation of 4,4'-(1,1-diyl)diphenols (2-13).



Method 1

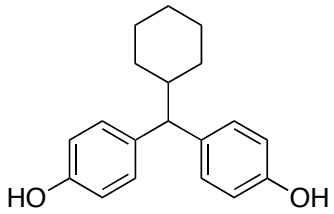
To a schlenk flask under nitrogen containing 50 mL acetic acid and 50 mL concentrated sulfuric acid at 0 °C was charged aldehyde (40 mmol) via syringe. Phenol (80 mmol) was then added in four parts over five minutes. The solution was then left to stir for 2 hours at 0 °C. The crude mixture was then neutralized with saturated $NaHCO_3$, and extracted into ethyl acetate (3 x 150 mL), washed with brine (2 x 150 mL), dried with sodium sulfate, and concentrated. Flash chromatography was then used ($CHCl_3$:MeOH, 10:1) to yield a white solid.

Method 2

Phenol (80 mmol), and aldehyde (20 mmol) were charged to a round bottom flask and heated to 70 ^{o}C in an oil bath. 1 mL of concentrated HCl was then added to the melt, which was left to stir for 12 hours. Upon cooling, the mixture was extracted in to DCM (2 x 100 mL), washed with water, dried with sodium sulfate, and concentrated down. The resulting oil was then dissolved in $CHCl_3$ and left to sit in -25 ^{o}C freezer until solid crashed out. Filtration, and subsequent recrystallizations of solid resulted in pure bis(phenol).

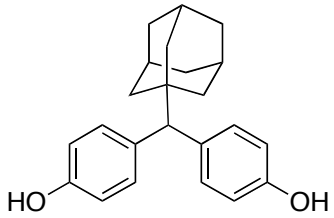
Compounds **2-6** have been previously characterized.[2, 3]

(7)



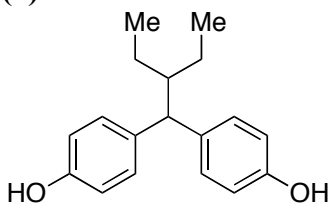
Method 2, (1.95 g, 60% yield); **^{1}H NMR** (500 MHz, CD_3OD) δ 7.01 (d, *J* = 8.5, 4H), 6.65 (d, *J* = 8.5, 4H), 4.85 (s, 2H), 3.26 (d, *J* = 11.1, 1H), 2.01 – 1.91 (m, 1H), 1.65 – 1.52 (m, 5H), 1.27 – 1.04 (m, 3H), 0.82 – 0.73 (m, 2H); **^{13}C NMR** (CD_3OD, 125 MHz) δ 156.1, 137.5, 129.9, 116.0, 59.0, 42.8, 33.3, 27.7, 27.4; **IR** (film, cm^{-1}) 3399, 3288, 2815, 1514, 1228; **TLC** R_f 0.28 (9:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{19}H_{22}O_2Na$ $[M+Na]^+$ 305.1512 found 305.1510.

(8)



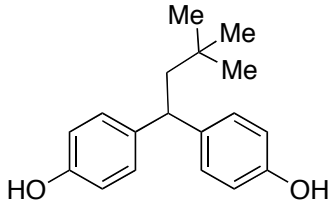
Method 2, (1.05 g, 34% yield); **^{1}H NMR** (500 MHz, CD_3OD) δ 6.95 (d, *J* = 8.5, 4H), 6.56 (d, *J* = 8.5, 4H), 3.18 (d, *J* = 10.9, 1H), 1.94 – 1.80 (m, 1H), 1.67 – 1.38 (m, 5H), 1.25 – 0.94 (m, 3H), 0.80 – 0.61 (m, 2H); **^{13}C NMR** (126 MHz, CD_3OD) δ 156.2, 137.6, 129.9, 116.0, 59.1, 42.9, 33.3, 27.7, 27.4; **IR** (film, cm^{-1}) 3317, 2891, 2838, 1502; **TLC** R_f 0.29 (10:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{23}H_{26}O_2Na$ $[M+Na]^+$ 357.1825, found 357.1852.

(9)



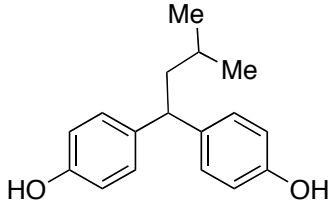
Method 2, (2.04 g, 61% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.09 (d, J = 8.6, 4H), 6.70 (d, J = 8.6, 4H), 3.55 (d, J = 11.0, 1H), 2.13 – 2.03 (m, 1H), 1.43 – 1.29 (m, 2H), 1.23 – 1.13 (m, 2H), 0.77 (t, J = 7.4, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.4, 137.4, 129.3, 115.5, 54.2, 43.6, 22.4, 10.3; **IR** (film, cm^{-1}) 3399, 2955, 2926, 1868, 1508; **TLC** R_f 0.25 (9:1 $CHCl_3$:MeOH); **HRMS** (ESI) *m/z* calc'd for $C_{18}H_{22}O_2Na$ $[M+Na]^+$ 293.1512 found 293.1514.

(10)



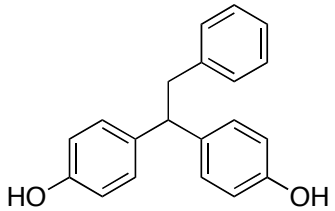
Method 2, (312 mg, 12% yield); **^{1}H NMR** (CD_3OD, 500 MHz) 7.05 (d, J = 8.6, 4H), 6.63 (d, J = 8.6, 4H), 3.86 (t, J = 6.8, 1H), 1.96 (d, J = 6.8, 2H), 0.78 (s, 9H); **^{13}C NMR** (CD_3OD, 125 MHz) δ 156.1, 139.8, 129.5, 115.9, 51.0, 47.9, 32.1, 30.7; **IR** (film, cm^{-1}) 3422, 3189, 2932, 1505; **TLC** R_f 0.63 (1:1 hexane:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{18}H_{22}O_2Na$ $[M+Na]^+$ 293.1512, found 299.1505.

(11)



Method 2, (505 mg, 25% yield); **^{1}H NMR** (500 MHz, CD_3OD) δ 7.05 (d, J = 8.6, 4H), 6.70 (d, J = 8.5, 4H), 3.85 (t, J = 8.1, 1H), 1.90 – 1.73 (m, 2H), 1.42 (m, 1H), 0.92 (d, J = 6.6, 6H); **^{13}C NMR** (CD_3OD, 125 MHz) δ 156.7, 138.1, 130.1, 116.4, 48.9, 47.2, 27.1, 23.4; **IR** (film, cm^{-1}) 3282, 2938, 2903, 1514; **TLC** R_f 0.60 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{17}H_{20}O_2Na$ $[M+Na]^+$ 279.1356, found 279.1354.

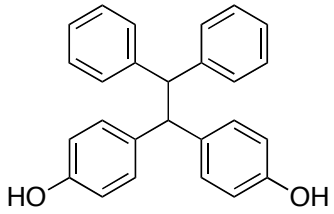
(12)



Method 2, (400 mg, 40% yield); **^{1}H NMR** 1H NMR (400 MHz, CD_3OD) δ 7.18 – 7.03 (m, 4H), 7.03 – 6.98 (obscured d, 5H), 6.64 (d, J = 8.5, 4H), 4.05 (t, J = 7.9, 1H), 3.22 (d, J = 7.9, 2H); **^{13}C NMR** (126 MHz, CD_3OD) δ 156.8, 142.5, 138.0, 130.6, 130.3, 129.3, 127.0, 116.3, 53.4, 44.1; **IR** (film, cm^{-1}) 3375, 3084, 2926, 1502; **TLC** R_f 0.24 (9:1

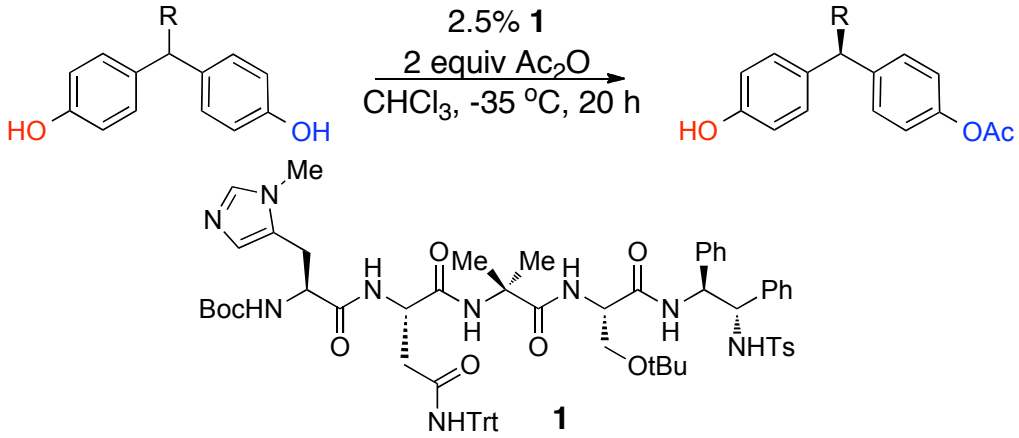
$CHCl_3$:MeOH); **HRMS** (ESI) *m/z* calc'd for $C_{18}H_{22}O_2Na$ $[M+Na]^+$ 313.1199 found 313.1196.

(13)



Method 2, (500 mg, 92% yield**);** **^{1}H NMR** (500 MHz CD_3OD) δ 7.24 (d, *J* = 7.1, 4H), 7.08 (t, *J* = 7.7, 4H), 7.04 (d, *J* = 8.6, 4H), 6.97 (t, *J* = 7.4, 2H), 6.52 (d, *J* = 8.6, 4H), 4.75 (d, *J* = 12.5, 1H), 4.71 (d, *J* = 12.4, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.2, 143.5, 136.2, 129.4, 128.5, 128.1, 125.7, 114.9, 56.7, 54.5; **IR** (film, cm^{-1}) 3399, 3288, 1590, 1491; **TLC** R_f 0.28 (4:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{26}H_{22}O_2Na$ $[M+Na]^+$ 389.1512 found 389.1515.

III. General Procedure for the Acylation of (Bis)phenol 2-13.

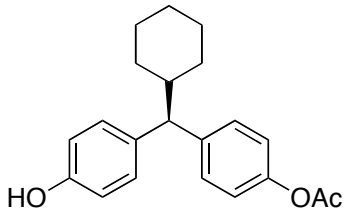


To a flame dried flask was charged the bis(phenol) (**2-13**, 0.160 mmol) and peptide **1** (4.7 mg, 3.93 μmol). The flask was then charged with 4.76 mL of $CHCl_3$ along with 20 μL of THF. This solution was then cooled to -35 °C over 30 minutes. Freshly distilled acetic anhydride (28.5 μL, 0.301 mmol) was then added via syringe. The solution was stirred for 18 h at -40 °C and then quenched with 0.2 mL of methanol while still cold. Silica gel chromatography (Hex/EtOAc 3/1 v/v) was used to purify the products.

IV. Characterization of acylated (Bis)Phenols 2-13.

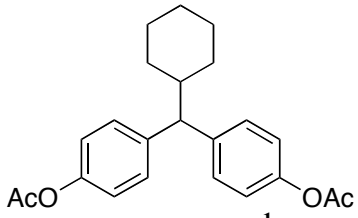
Compounds **2-Ac**–**6-Ac**, and **2-Ac$_2$**–**6-Ac$_2$ have** been previously characterized.[2, 3]

(7-Ac)



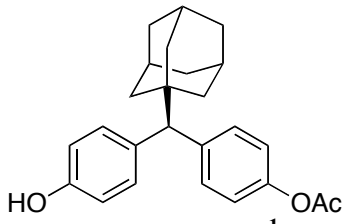
(22.0 mg, 44% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.6, 2H), 7.02 (d, *J* = 8.5, 2H), 6.89 (d, *J* = 8.5, 2H), 6.64 (d, *J* = 8.5, 2H), 4.72 (s, 1H), 3.34 (d, *J* = 10.8, 1H), 2.19 (s, 3H), 1.97 – 1.87 (m, *J* = 11.0, 1H), 1.64 – 1.45 (m, 5H), 1.22 – 1.08 (m, 3H), 0.84 – 0.67 (m, 2H); **^{13}C NMR** (126 MHz, CDCl3) δ 170.1, 154.1, 149.1, 142.8, 136.9, 129.6, 129.3, 121.7, 115.7, 58.4, 41.9, 32.5, 32.4, 26.9, 26.7, 26.7, 21.6; **IR** (film, cm^{-1}) 3422, 2926, 2850, 1730, 1508, 1199; **TLC** R_f 0.38 (1:1 hexanes:EtOAc); $[\alpha]_D^{20.0} = +0.4$ (*c* = 1.0, $CHCl_3$); **HRMS** (ESI) *m/z* calc'd for $C_{21}H_{25}O_3$ $[M+H]^+$ 325.1798, found 325.1797;
Chiral HPLC Analysis: 65% ee, chiral HPLC utilized a Chiralcel OD (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 1.0 mL/min with 90% hexanes/isopropanol. Retention times: $R_{T(Major)}$ = 13.8 min. $R_{T(Minor)}$ = 16.3 min.

(7-Ac$_2$)



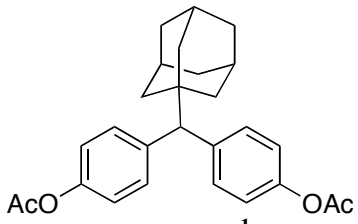
(4.0 mg, 8% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.6, 4H), 6.90 (d, *J* = 8.6, 4H), 3.41 (d, *J* = 10.8, 1H), 2.18 (s, 6H), 2.05 – 1.83 (m, 1H), 1.74 – 1.39 (m, 5H), 1.19 – 0.91 (m, 3H), 0.93 – 0.58 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.4, 148.8, 141.6, 128.9, 121.3, 58.2, 41.4, 32.0, 26.4, 26.3, 21.1; **IR** (film, cm^{-1}) 2920, 2856, 1747, 1508, 1199; **TLC** R_f 0.50 (3:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{23}H_{27}O_4$ $[M+H]^+$ 367.1904, found 367.1902.

(8-Ac)



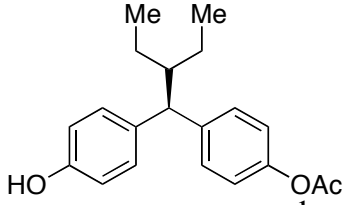
(44 mg, 55% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6, 2H), 7.17 (d, *J* = 8.6, 2H), 6.90 (d, *J* = 8.7, 2H), 6.64 (d, *J* = 8.7, 2H), 4.81 (s, 1H), 3.35 (s, 1H), 2.19 (s, 3H), 1.85 (s, 3H), 1.66 – 1.38 (m, 12H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.6, 153.9, 148.8, 140.0, 134.1, 131.0, 130.7, 120.7, 114.7, 64.8, 60.5, 41.0, 36.8, 36.8, 28.7, 21.1, 14.1; **IR** (film, cm^{-1}) 3393, 2903, 2850, 1718, 1502, 1199; **TLC** R_f 0.60 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{25}H_{28}O_3Na$ $[M+Na]^+$ 399.19, found 399.1935; $[\alpha]_D^{20.0} = +0.8$ (*c* = 1.0, $CHCl_3$);
Chiral HPLC Analysis: 95% ee, chiral HPLC utilized a Chiralpak AD (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 0.75 mL/min with 90% hexanes/isopropanol. Retention times: $R_{TMinor)}$ = 18.4 min. $R_{T(Major)}$ = 20.6 min.

(8-Ac$_2$)



(3 mg, 5% yield) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.6, 4H), 6.91 (d, *J* = 8.6, 4H), 3.43 (s, 1H), 2.19 (s, 6H), 1.86 (s, 3H), 1.66 – 1.40 (m, 12H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.3, 149.0, 139.4, 130.8, 120.8, 65.1, 41.0, 36.8, 36.8, 28.7, 21.1; **IR** (film, cm^{-1}) 2903, 2839, 1759, 1508, 1187; R_f 0.85 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{27}H_{30}O_4K$ $[M+K]^+$ 457.18, found 457.1756.

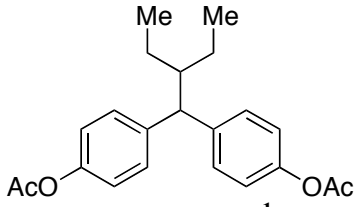
(9-Ac)



(50.0 mg, 85% yield); **^{1}H NMR** (500 MHz, CDCl3) δ 7.18 (d, *J* = 8.5, 2H), 7.04 (d, *J* = 8.6, 2H), 6.89 (d, *J* = 8.6, 2H), 6.63 (d, *J* = 8.6, 2H), 4.84 (s, 1H), 3.56 (d, *J* = 11.1, 1H), 2.19 (s, 3H), 2.04 (m, 1H), 1.30 (m, 2H), 1.23 – 1.02 (m, 2H), 0.70 (t, *J* = 7.4, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.2, 154.3, 149.0, 143.1, 137.0, 129.5, 129.3, 121.7, 115.7, 68.4, 54.5, 43.6, 22.4, 22.3, 21.6, 10.4; **IR** (film, cm^{-1}) 3428, 2955, 2874, 1747, 1520, 1217; **TLC** R_f 0.38 (9:1 $CHCl_3$:MeOH); **HRMS** (ESI) *m/z* calc'd for $C_{20}H_{24}O_3Na$ $[M+Na]^+$ 335.1618, found 335.1615; $[\alpha]_D^{20.0}$ = +0.1 (*c* = 1.0, $CHCl_3$);

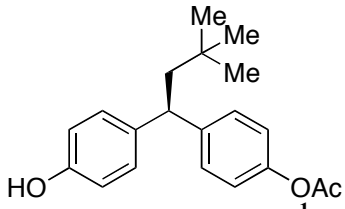
Chiral HPLC Analysis: 84% ee, chiral HPLC utilized a Chiralcel OD (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 0.75 mL/min with 90% hexanes/isopropanol. Retention times: $R_{T(Major)}$ = 14.7 min. $R_{T(Minor)}$ = 17.7 min.

(9-Ac$_2$)



(4.5 mg, 5% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.6, 4H), 6.90 (d, *J* = 8.6, 4H), 3.64 (d, *J* = 11.1, 1H), 2.19 (s, 6H), 2.15 – 1.99 (m, 1H), 1.39 – 1.23 (m, 2H), 1.21 – 1.07 (m, 2H), 0.71 (t, *J* = 7.4, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.8, 149.3, 142.3, 129.3, 121.8, 54.8, 43.5, 22.3, 21.5, 10.3; **IR** (film, cm^{-1}) 2967, 2868, 1765, 1491, 1205; **TLC** R_f 0.62 (9:1 $CHCl_3$:MeOH); **HRMS** (ESI) *m/z* calc'd for $C_{22}H_{26}O_4Na$ $[M+Na]^+$ 377.1723, found 377.1722.

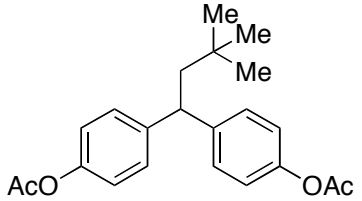
(10-Ac)



(19.0 mg, 41% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.6, 2H), 7.05 (d, *J* = 8.6, 2H), 6.89 (d, *J* = 8.6, 2H), 6.64 (d, *J* = 8.6, 2H), 4.67 (s, 1H), 3.92 (t, *J* = 6.7, 1H), 2.19 (s, 3H), 2.03 – 1.86 (m, 2H), 0.74 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.6, 153.6, 148.5, 144.7, 138.6, 128.9, 128.5, 121.3, 115.2, 49.7, 46.9, 31.3, 30.2, 21.1; **IR** (film, cm^{-1}) 3405, 2944, 2862, 1736, 1496, 1199; **TLC** R_f 0.68 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{20}H_{25}O_3$ $[M+H]^+$ 313.1798, found 313.1798; $[\alpha]_D^{20.0}$ = +1.4 (*c* = 1.0, $CHCl_3$);

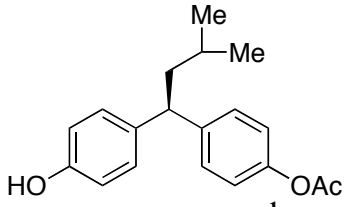
Chiral HPLC Analysis: 55% ee, chiral HPLC utilized a Chiralcel OD (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 0.75 mL/min with 97% hexanes/isopropanol. Retention times: $R_{T(Major)}$ = 43.7 min. $R_{T(Minor)}$ = 48.6 min.

(10-Ac$_2$)



(8.0 mg, 9% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 7.1, 4H), 6.90 (d, *J* = 8.4, 4H), 3.98 (t, *J* = 6.6, 1H), 2.19 (s, 6H), 1.98 (d, *J* = 6.7, 2H), 0.75 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.9, 149.2, 144.3, 129.1, 121.8, 50.1, 47.6, 31.9, 30.6, 21.6; **IR** (film, cm^{-1}) 2944, 2856, 1760, 1496, 1199; **TLC** R_f 0.76 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{21}H_{24}O_4$ $[M+H]^+$ 341.1747, found 341.1746.

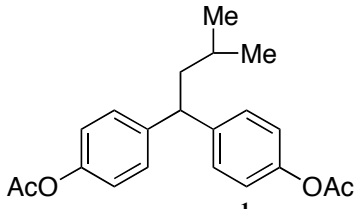
(11-Ac)



(24 mg, 53% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.5, 2H), 7.00 (d, *J* = 8.5, 2H), 6.90 (d, *J* = 8.6, 2H), 6.65 (d, *J* = 8.6, 2H), 4.87 (s, 1H), 3.87 (t, *J* = 8.0, 1H), 2.20 (s, 3H), 1.90 – 1.70 (m, 2H), 1.35 (m, 1H), 0.82 (d, *J* = 6.6, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.7, 153.8, 148.6, 143.2, 137.1, 128.9, 128.6, 121.2, 115.2, 47.3, 45.2, 25.3, 22.6, 22.4, 21.1; **IR** (film, cm^{-1}) 3393, 2955, 1742, 1601, 1508, 1211; **TLC** R_f 0.66 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{19}H_{23}O_3$ $[M+H]^+$ 299.1641, found 299.1639; $[\alpha]_D^{20.0}$ = +0.70 (*c* = 1.0, $CHCl_3$);

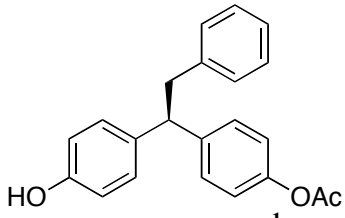
Chiral HPLC Analysis: 40% ee, chiral HPLC utilized a Chiralcel OJ-H (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 0.75 mL/min with 97% hexanes/ethanol. Retention times: $R_{T(major)}$=143.9 min, $R_{T(minor)}$ = 158.4 min.

(11-Ac$_2$)



(3 mg, 5% yield) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6, 4H), 7.03 (d, *J* = 8.6, 4H), 4.05 (t, *J* = 7.9, 1H), 2.30 (s, 6H), 1.91 (t, *J* = 7.5, 2H), 1.54 – 1.42 (m, 1H), 0.94 (d, *J* = 6.6, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.9, 149.3, 142.8, 129.1, 121.8, 48.0, 45.5, 25.7, 23.0, 21.6; **IR** (film, cm^{-1}) 3037, 2961, 1753, 1508, 1195; R_f 0.78 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{21}H_{25}O_4$ $[M+H]^+$ 341.1747, found 341.1746.

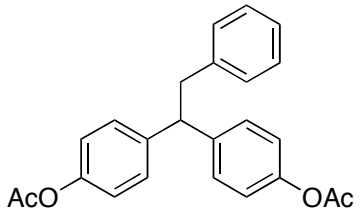
(12-Ac)



(13 mg, 46% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.12 – 7.07 (m, 4H), 7.06 – 7.01 (m, 1H), 6.95 (d, *J* = 8.5, 2H), 6.89 (t, *J* = 8.5, 4H), 6.62 (d, *J* = 8.6, 2H), 4.08 (t, *J* = 7.8, 1H), 3.21 (d, *J* = 7.8, 2H), 2.19 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.6, 152.9, 147.9, 141.4, 139.1, 135.3, 128.2, 128.0, 127.8, 127.1, 124.9, 120.2, 114.1, 50.6, 41.3, 20.1; **IR** (film, cm^{-1}) 3399, 3078, 2955, 1730, 1508, 1211; **TLC** R_f 0.50 (9:1 $CHCl_3$:MeOH); **HRMS** (ESI) *m/z* calc'd for $C_{22}H_{20}O_4Na$ $[M+Na]^+$ 355.1305, found 355.1293; $[\alpha]_D^{20.0}$ = +0.35 (*c* = 1.0, $CHCl_3$);

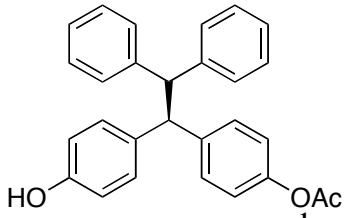
Chiral HPLC: 43% ee, chiral HPLC utilized a Chiralpak AD (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 0.75 mL/min with 95% hexanes/isopropanol. Retention times: $R_{T(major)}$=33.5 min, $R_{T(minor)}$ = 38.7 min.

(12-Ac)



(13 mg, 46% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.13 – 7.08 (m, 6H), 7.08 – 7.03 (m, 1H), 6.93 – 6.87 (m, 6H), 4.15 (t, *J* = 7.8, 1H), 3.24 (d, *J* = 7.8, 2H), 2.19 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.9, 149.4, 142.0, 140.2, 129.5, 129.4, 128.6, 126.5, 121.8, 52.3, 42.7, 21.6; **IR** (film, cm^{-1}) 3025, 2926, 1747, 1496, 1193; **TLC** R_f 0.67 (1:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{24}H_{22}O_4Na$ $[M+Na]^+$ 397.1410, found 397.1400.

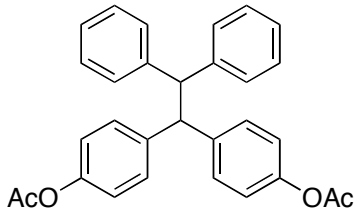
(13-ac)



(26.0 mg, 49% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.10 – 7.00 (m, 10H), 6.98 – 6.93 (m, 2H), 6.91 (d, *J* = 8.6, 2H), 6.76 (d, *J* = 8.6, 2H), 6.49 (d, *J* = 8.6, 2H), 4.64 (d, *J* = 12.2, 1H), 4.58 (d, *J* = 12.2, 1H), 2.14 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.4, 153.5, 148.5, 143.3, 143.3, 141.3, 135.5, 129.6, 129.3, 128.5, 128.4, 128.2, 128.2, 125.9, 125.8, 120.9, 115.1, 56.6, 54.8, 21.1; **IR** (film, cm^{-1}) 3439, 2908, 2827, 1724, 1508, 1216; **TLC** R_f 0.71 (9:1 $CHCl_3$:MeOH); **HRMS** (ESI) *m/z* calc'd for $C_{28}H_{24}O_3Na$ $[M+Na]^+$ 431.1618, found 431.1606; $[\alpha]_D^{20.0} = +19.3$ (*c* = 1.0, $CHCl_3$);

Chiral HPLC Analysis: 70% ee, chiral HPLC utilized a Chiralpak AD (Daicel, 0.46 cm x 20 cm, 10 μM, 20°C), eluting at 1.00 mL/min with 85% hexanes/isopropanol. Retention times: $R_{T(Major)}$ = 7.4 min. $R_{T(Minor)}$ = 8.2 min.

(13-Ac_2)



(8.0 mg, 9% yield); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.07 – 7.00 (m, 12H), 6.97 – 6.92 (m, 2H), 6.77 (d, *J* = 8.6, 4H), 4.70 (d, *J* = 12.2, 1H), 4.59 (d, *J* = 12.2, 1H), 2.13 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.2, 148.7, 143.0, 140.6, 129.4, 128.4, 128.2, 126.0, 121.1, 56.6, 55.0, 21.1; **IR** (film, cm^{-1}) 3066, 2920, 2844, 1753, 1502, 1199; **TLC** R_f 0.62 (10:1 hexanes:EtOAc); **HRMS** (ESI) *m/z* calc'd for $C_{30}H_{26}O_4Na$ $[M+Na]^+$ 473.1723, found 473.1728.

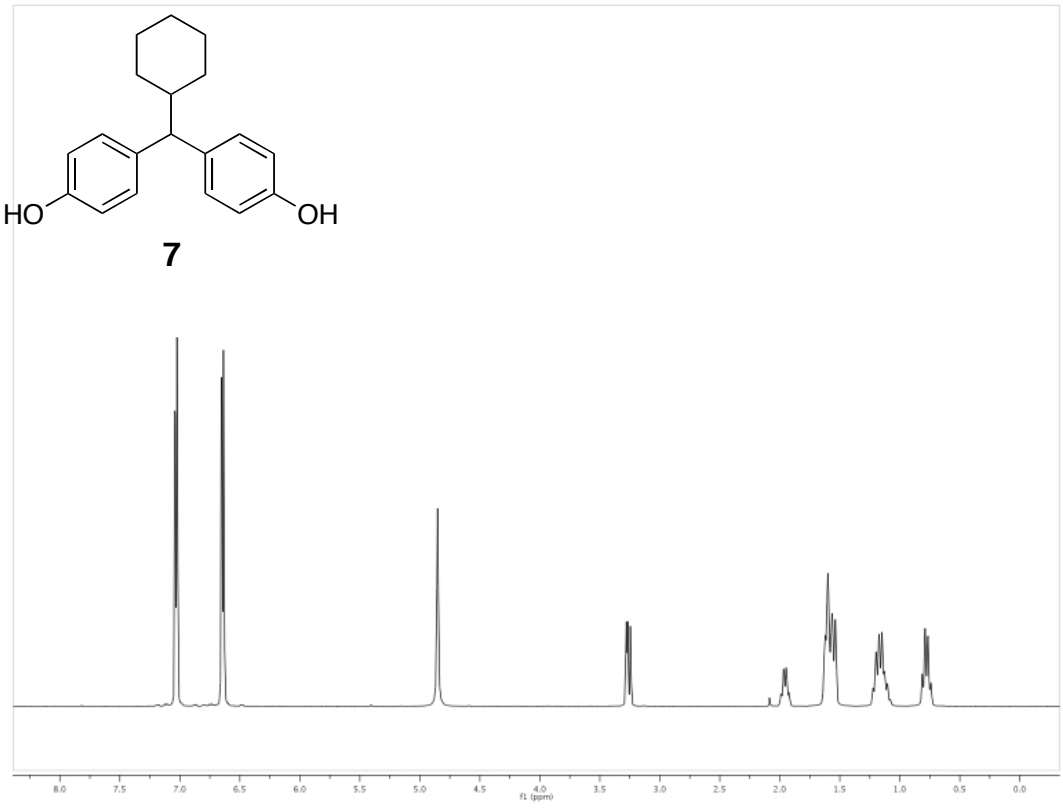
V. References.

[1]Rogers, E.; Brown. H.; Rasmussen, I.; Heal, R. *J. Am. Chem. Soc.,* **1953**, *75*, 2991.

[2]Lewis, C. A.; Chiu, A.; Kubryk, M.; Balsells, J.; Pollard, D.; Esser, C. K.; Murry, J.; Reamer, R. A.; Hansen, K. B.; Miller, S. J. *J. Am. Chem. Soc.* **2006**, *128,* 16454-16455.

[3]Lewis, C. A.; Gustafson, J. L.; Chiu, A.; Balsells, J.; Pollard, D.; Murry, J.; Reamer, R. A.; Hansen, K. B.; Miller, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 16358-16365.

IV. NMR Spectra.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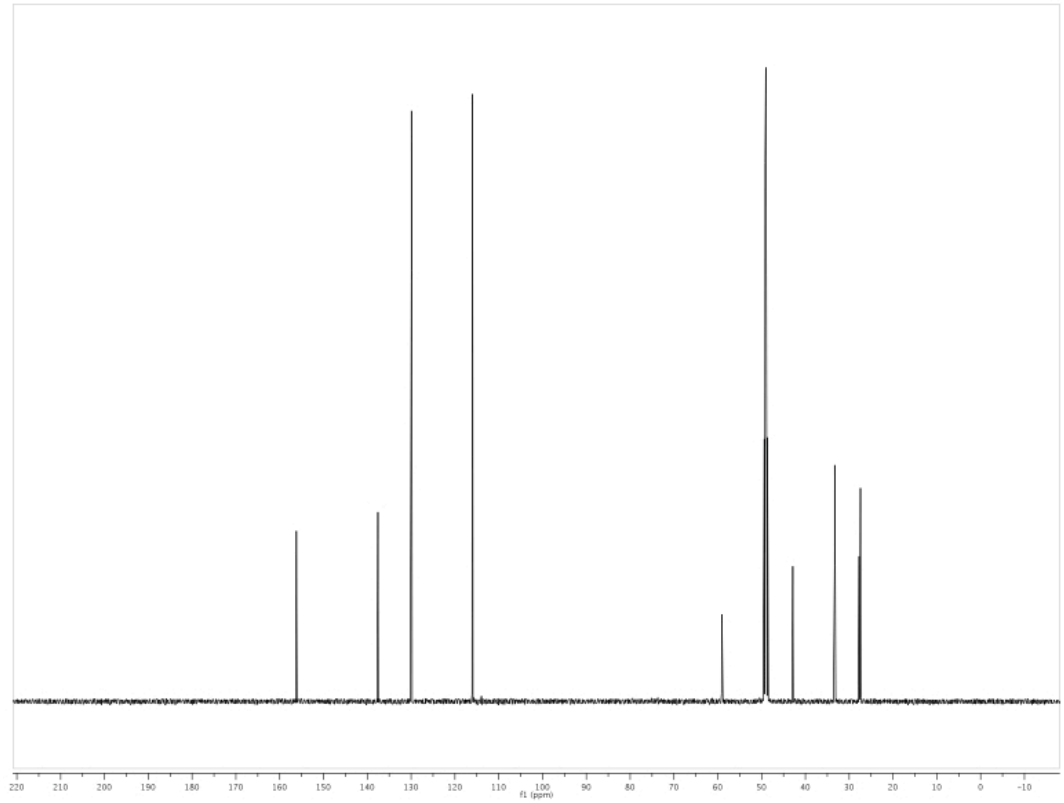
f1 (ppm)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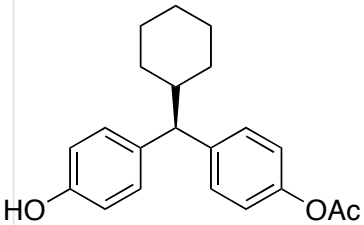
0
-10
f1 (ppm)


HO
OAc

7-Ac

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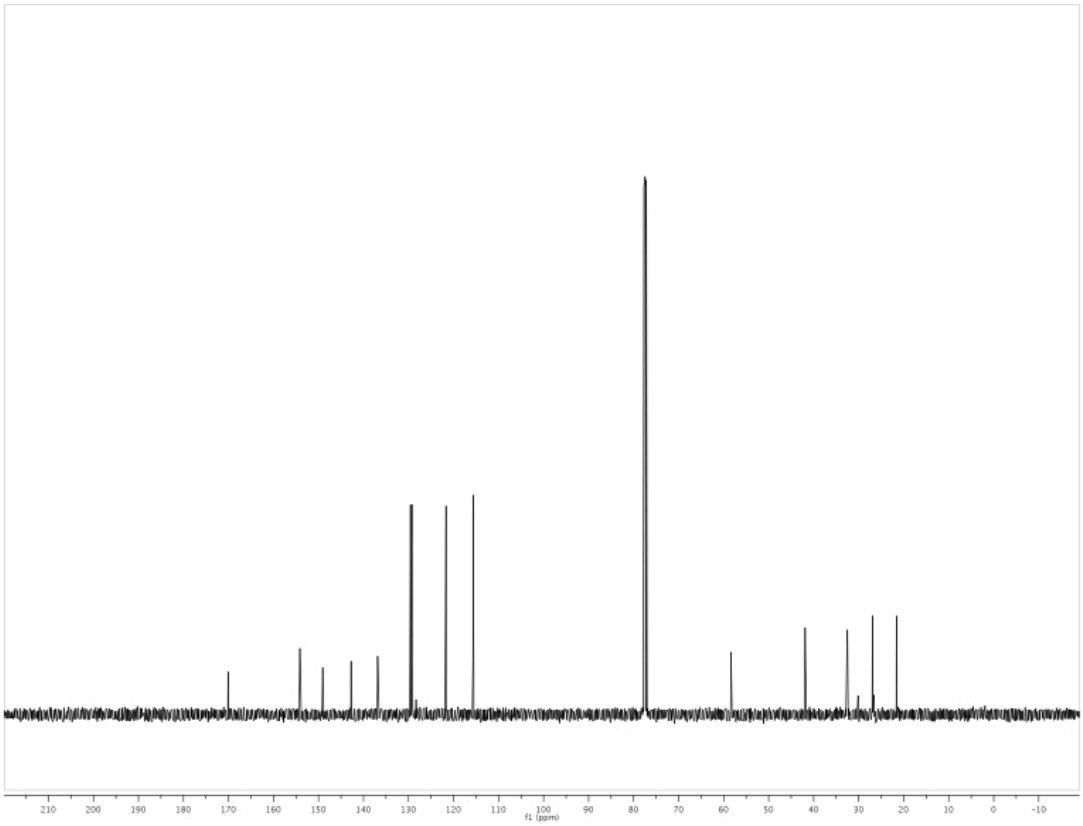
1.0
0.5
f1 (ppm)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30
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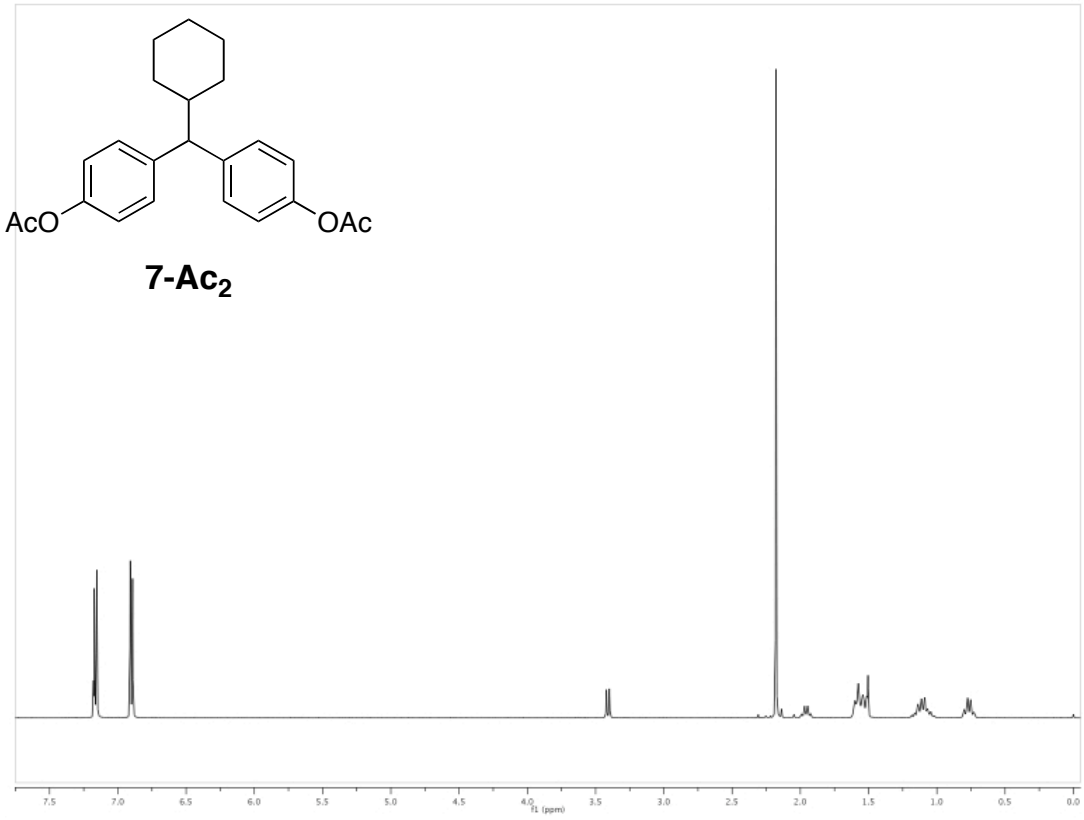
10
0
-10
f1 (ppm)


AcO
OAc

7-Ac$_2$

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3.5
3.0
2.5
2.0
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1.0
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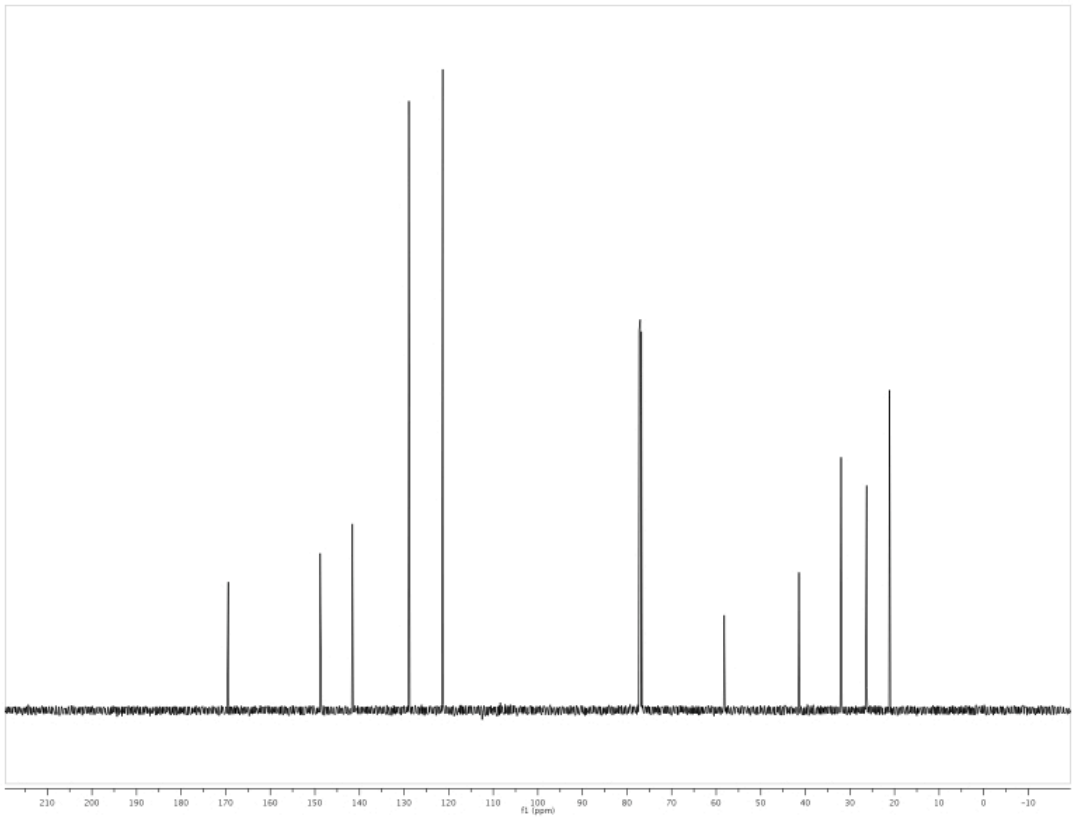
0.0
f1 (ppm)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30
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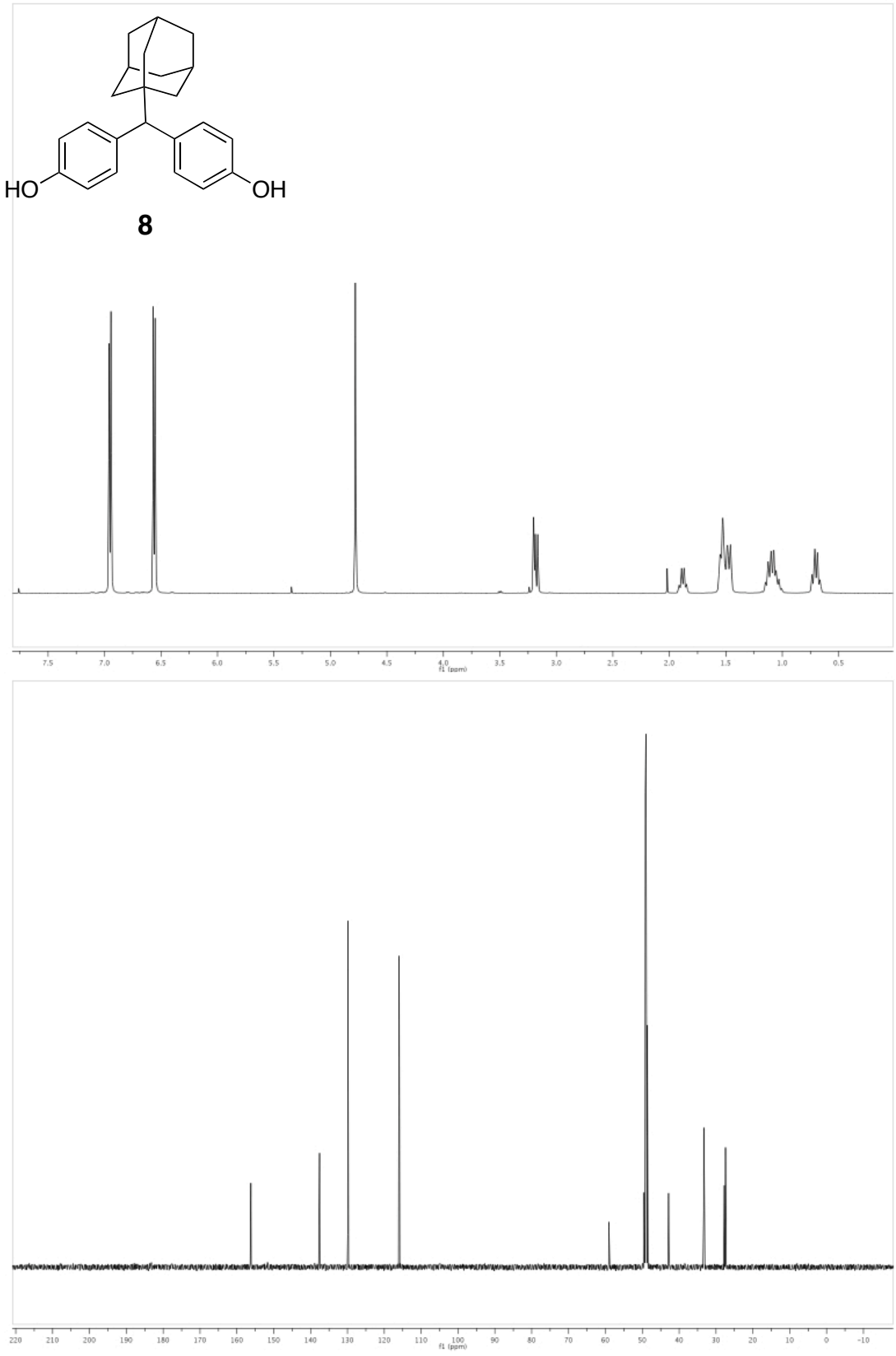
10
0
-10
f1 (ppm)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3.5
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2.5
2.0
1.5
1.0
0.5
f1 (ppm)
220
210
200
190
180
170
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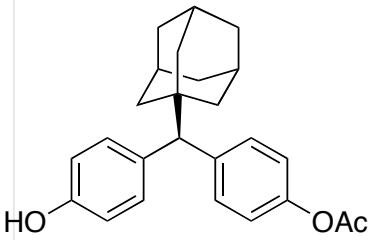
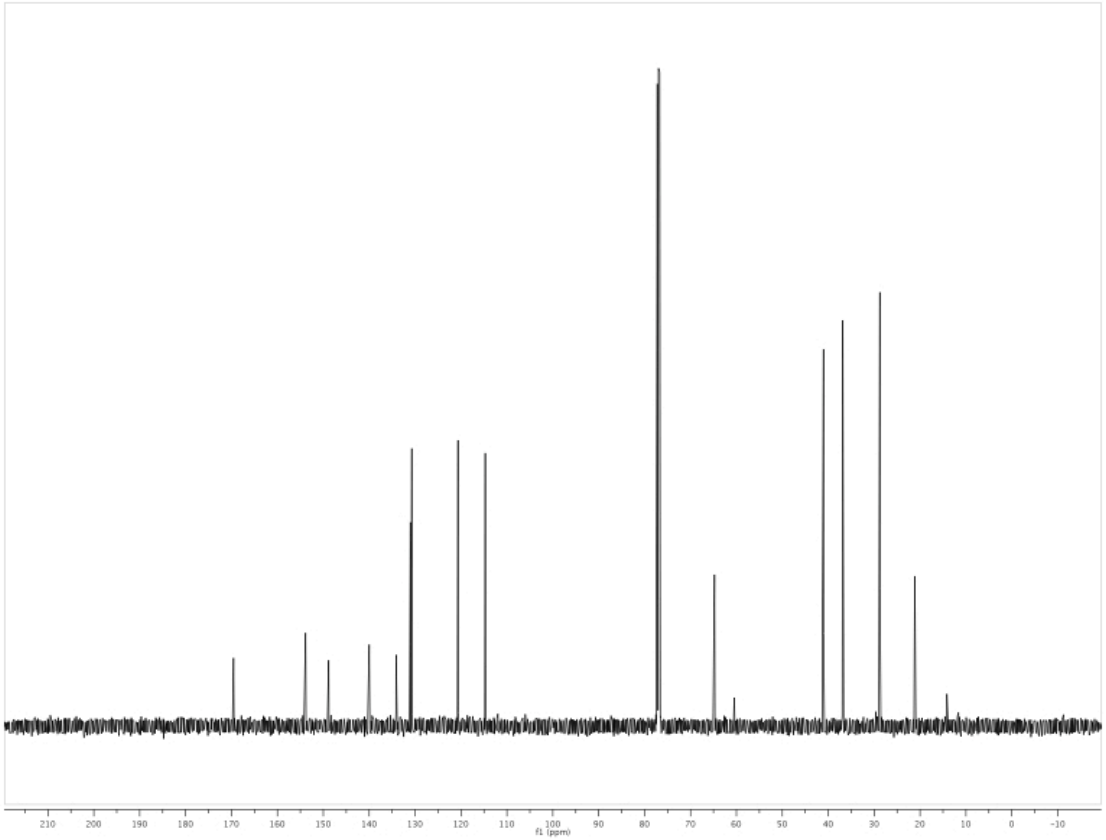
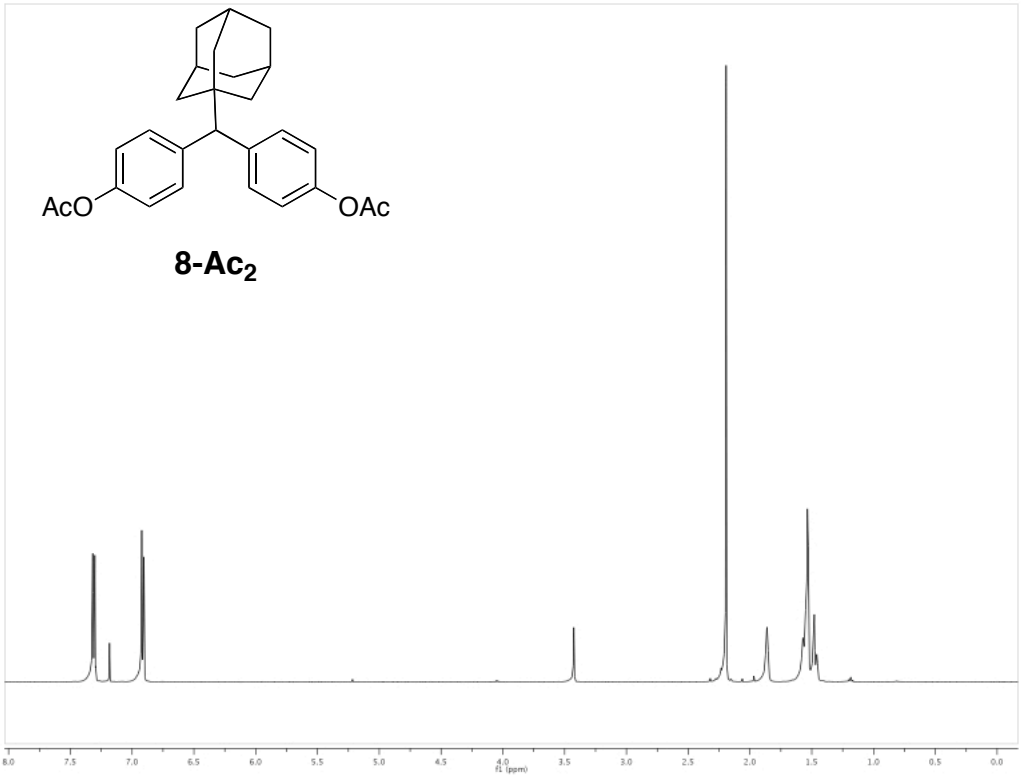
f1 (ppm)

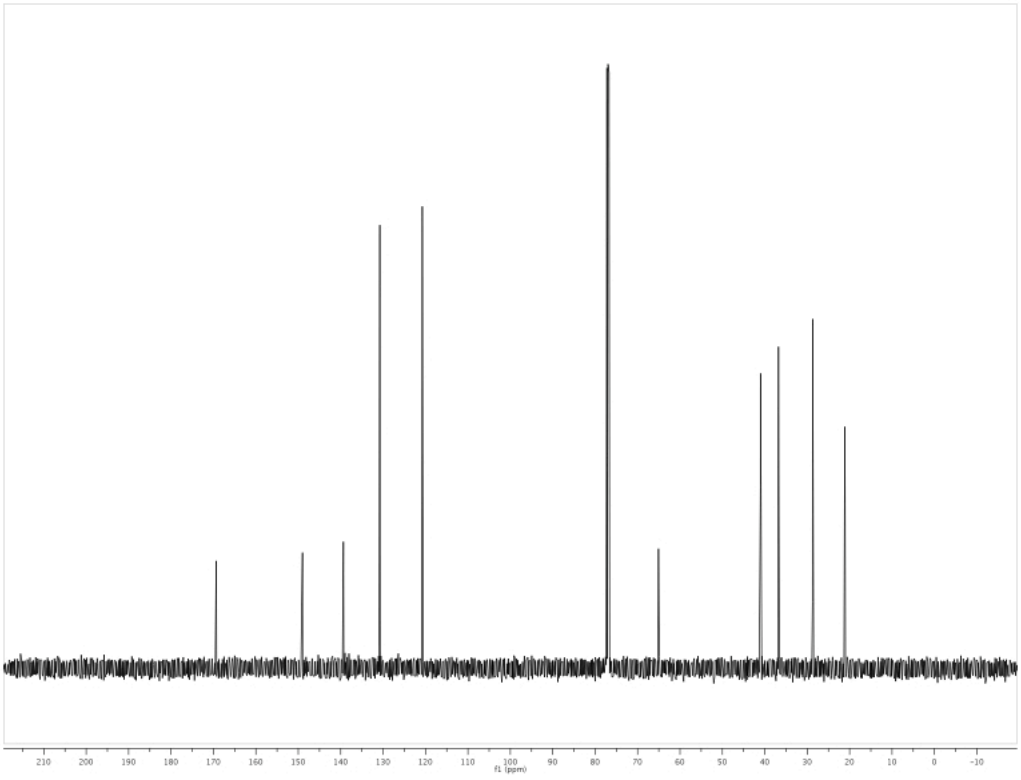


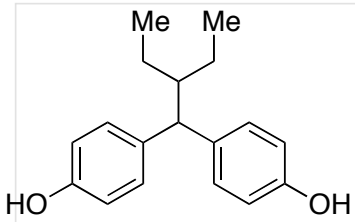
8-Ac





8-Ac$_2$





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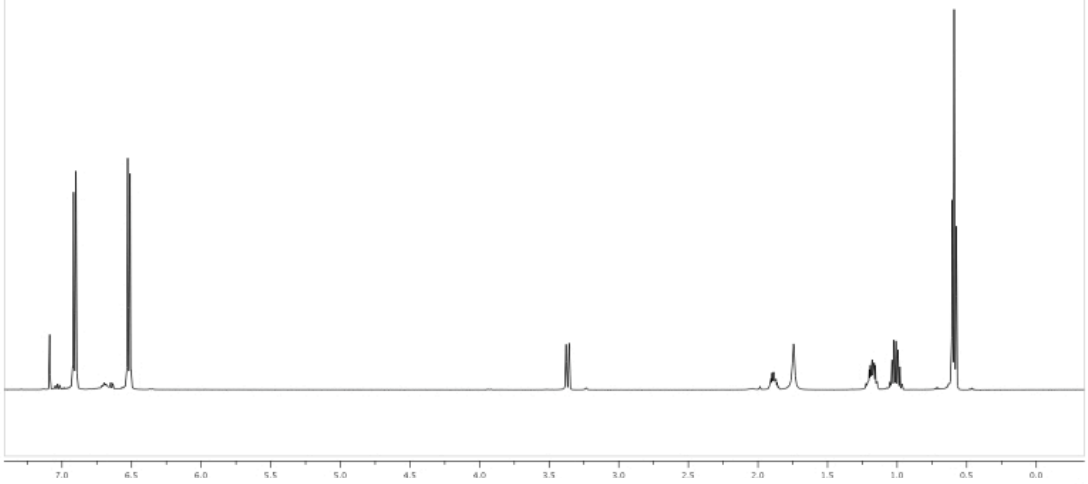

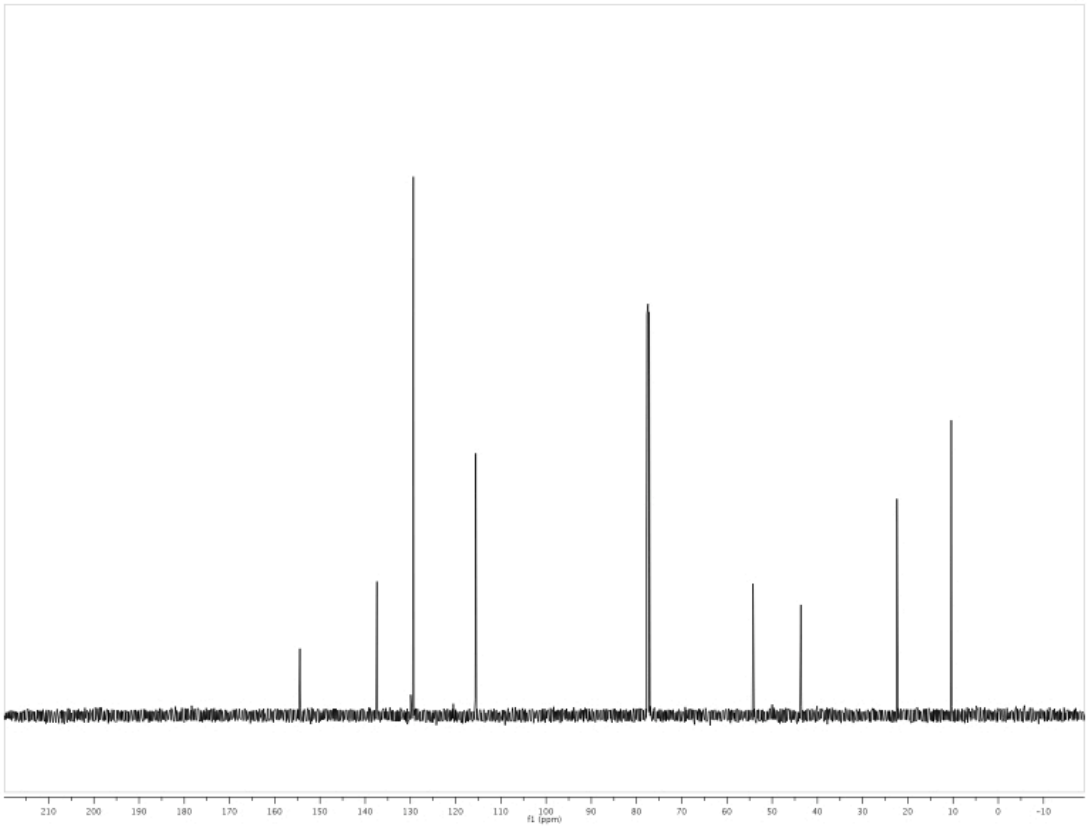

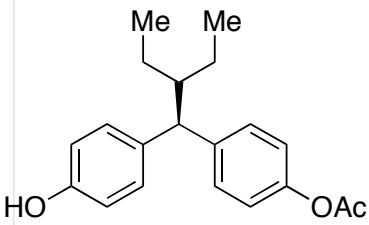
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Me
HO
OAc

9-Ac

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f1 (ppm)
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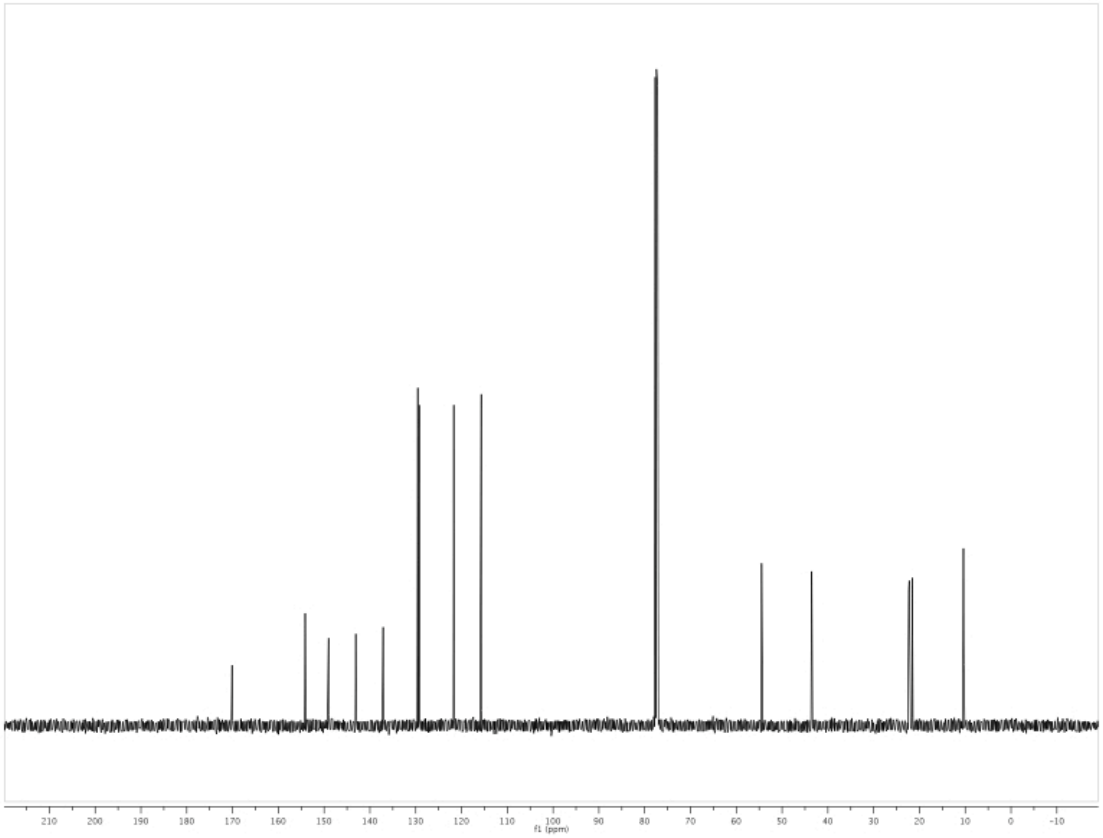
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f1 (ppm)
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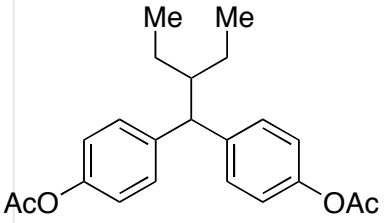
Me
Me
AcO
OAc

9-Ac$_2$

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6.5
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4.5
4.0
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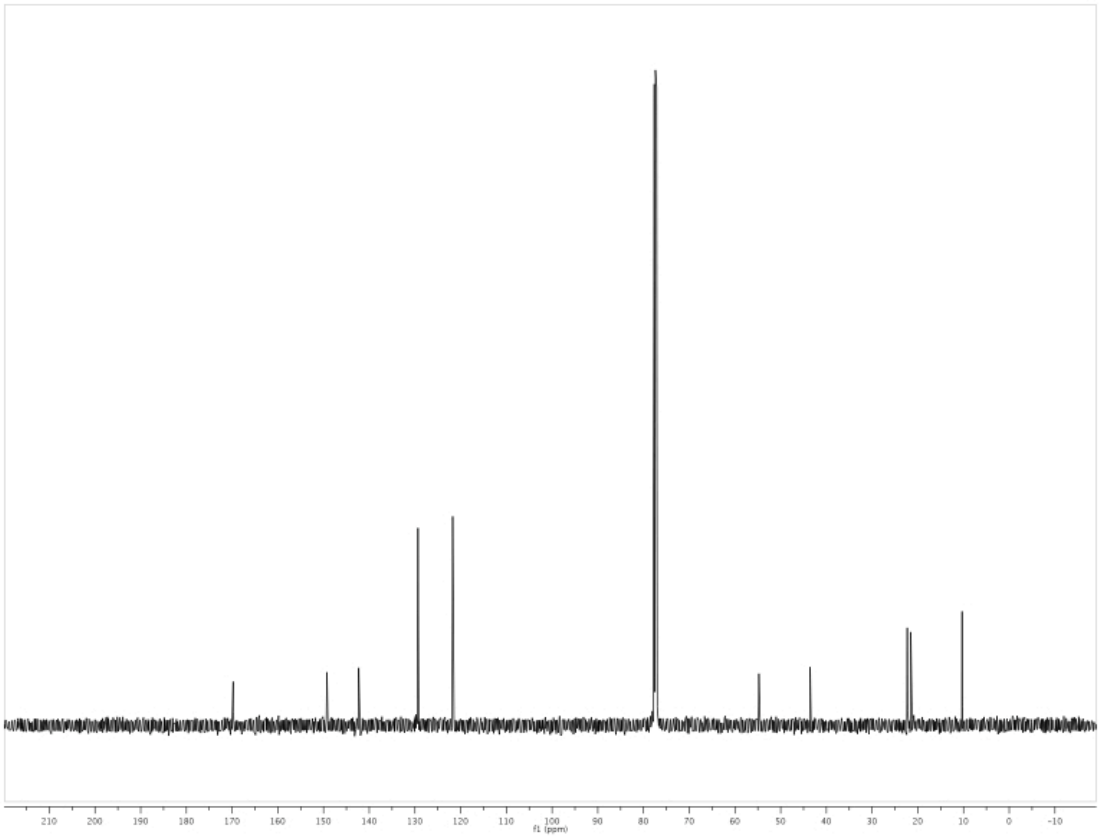
f1 (ppm)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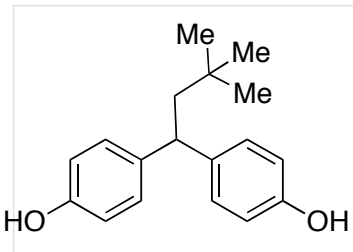
f1 (ppm)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Me
Me
HO
OH

10

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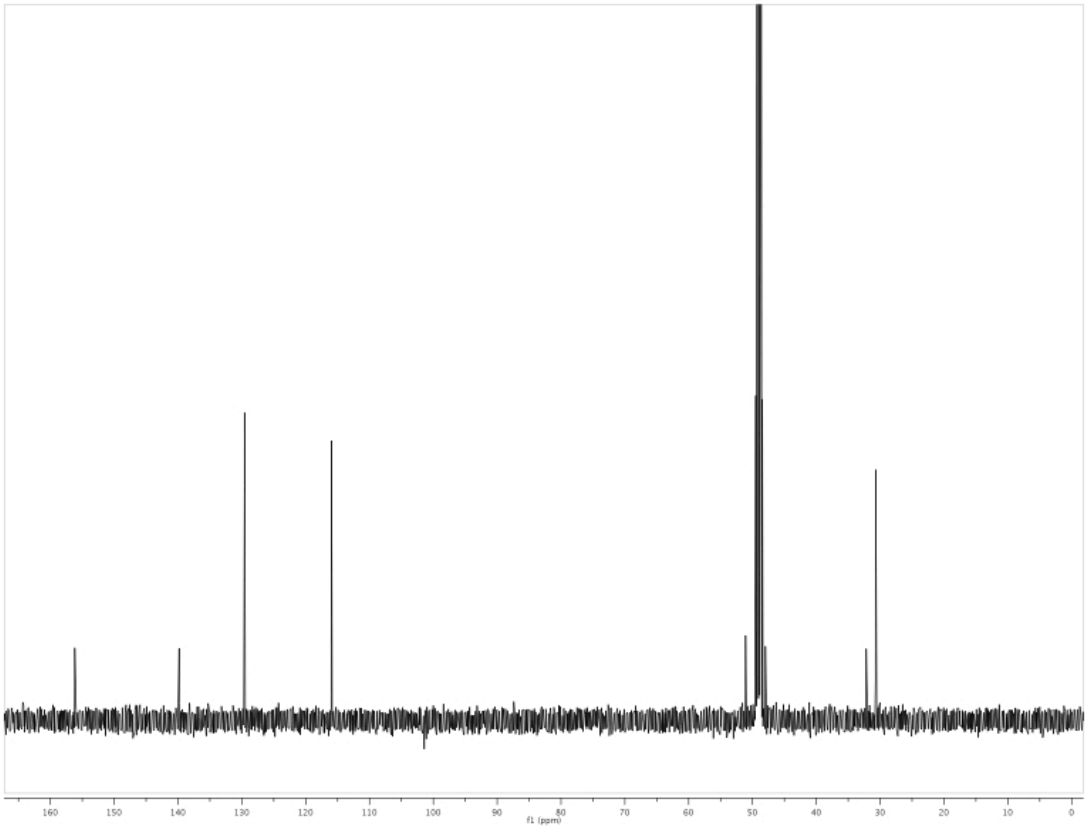
0.5
f1 (ppm)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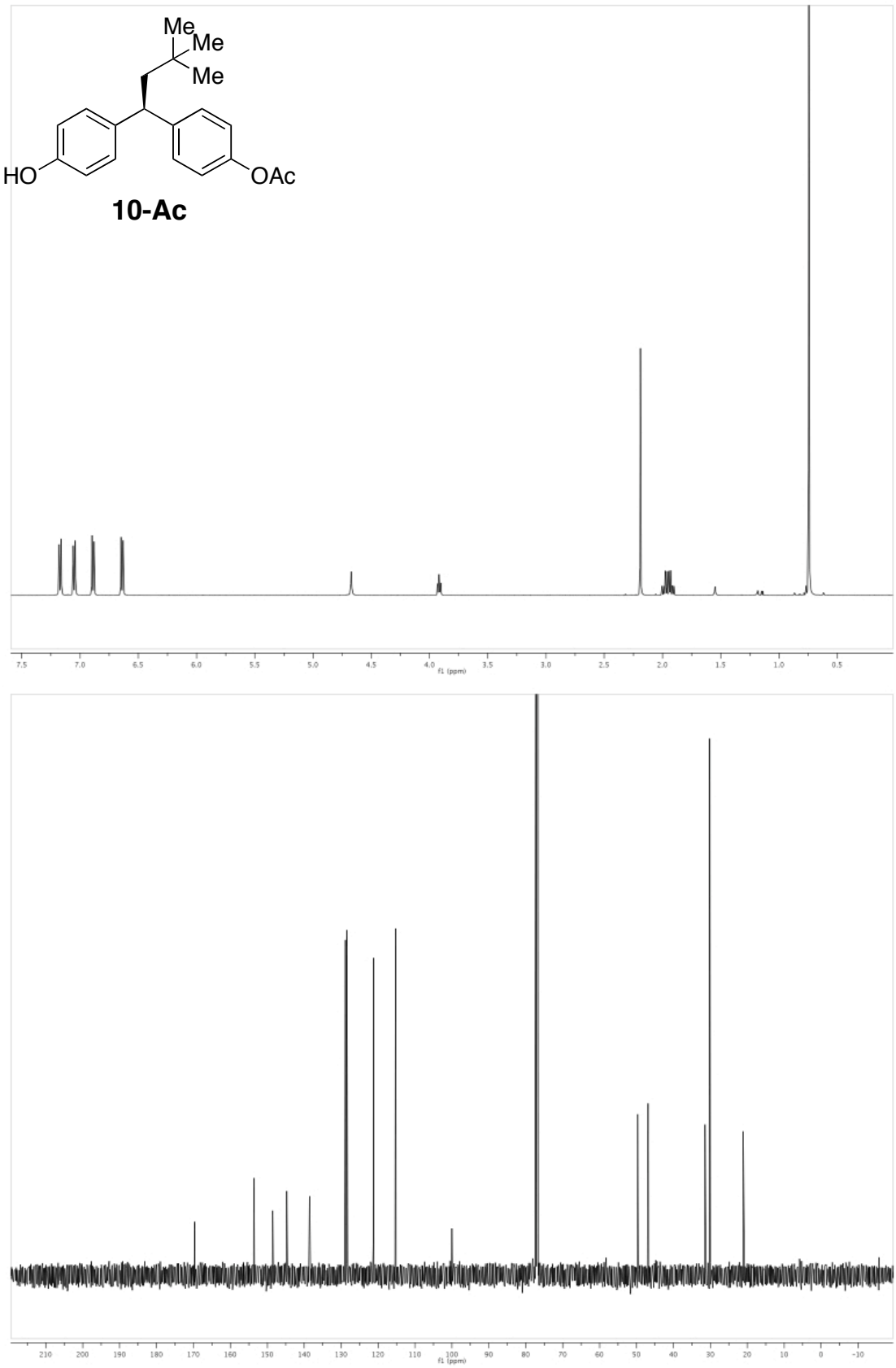
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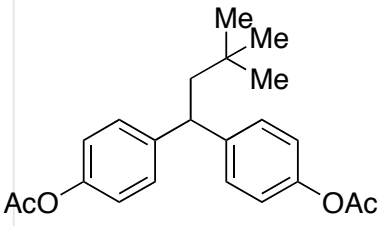
Me
Me
HO
OAc
10-Ac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Me
Me
AcO
OAc

10-Ac$_2$

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6.0
5.5
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4.5
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3.5
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2.5
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1.5
1.0
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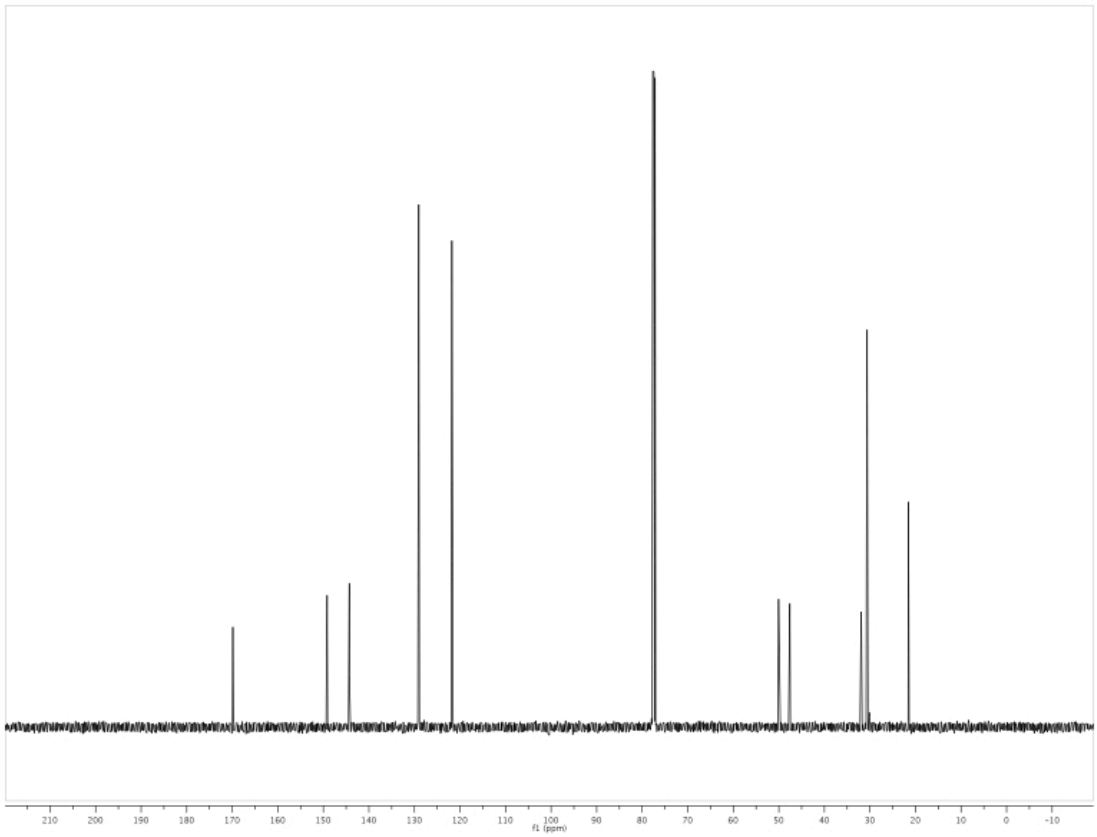
0.0
f1 (ppm)


210
200
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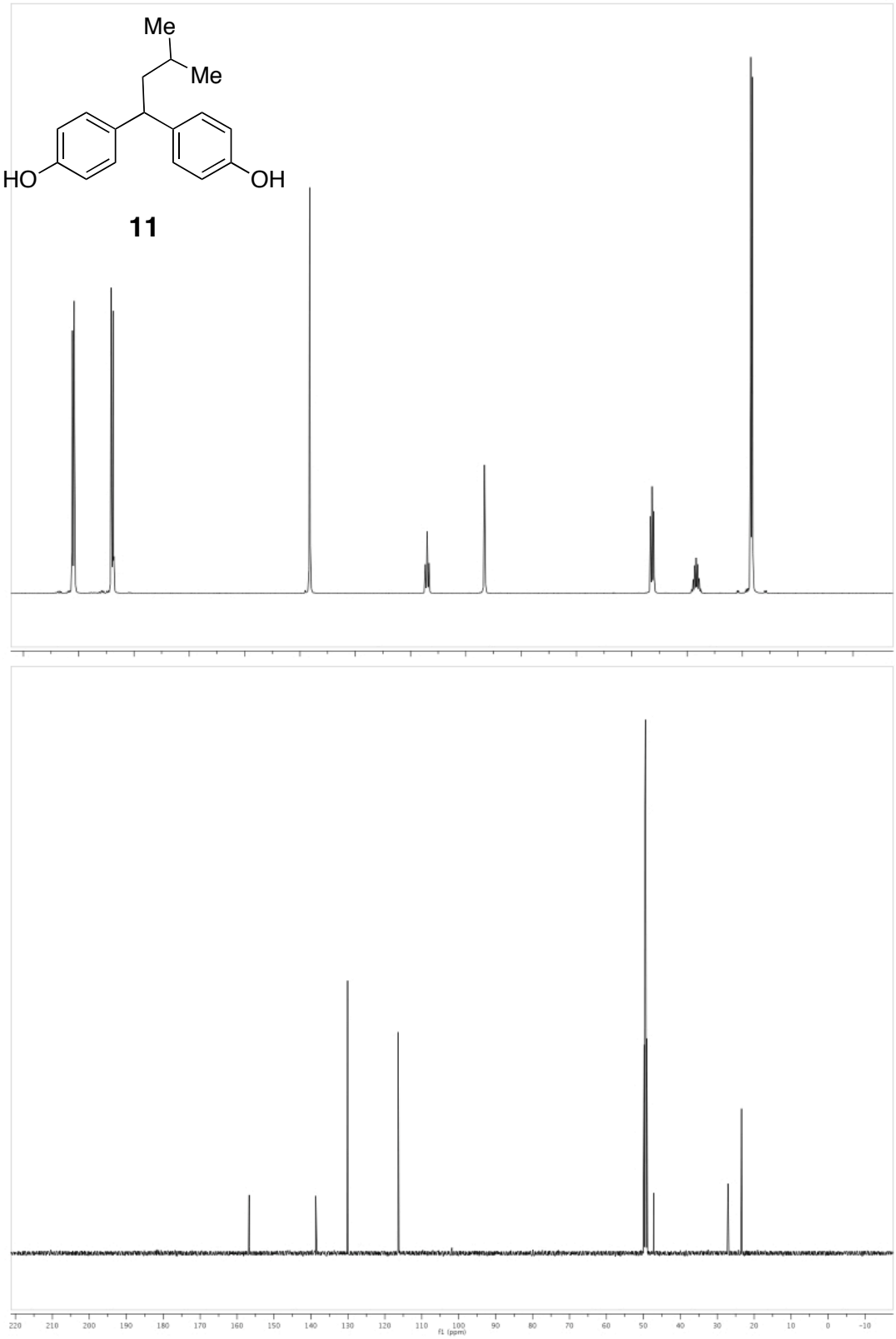
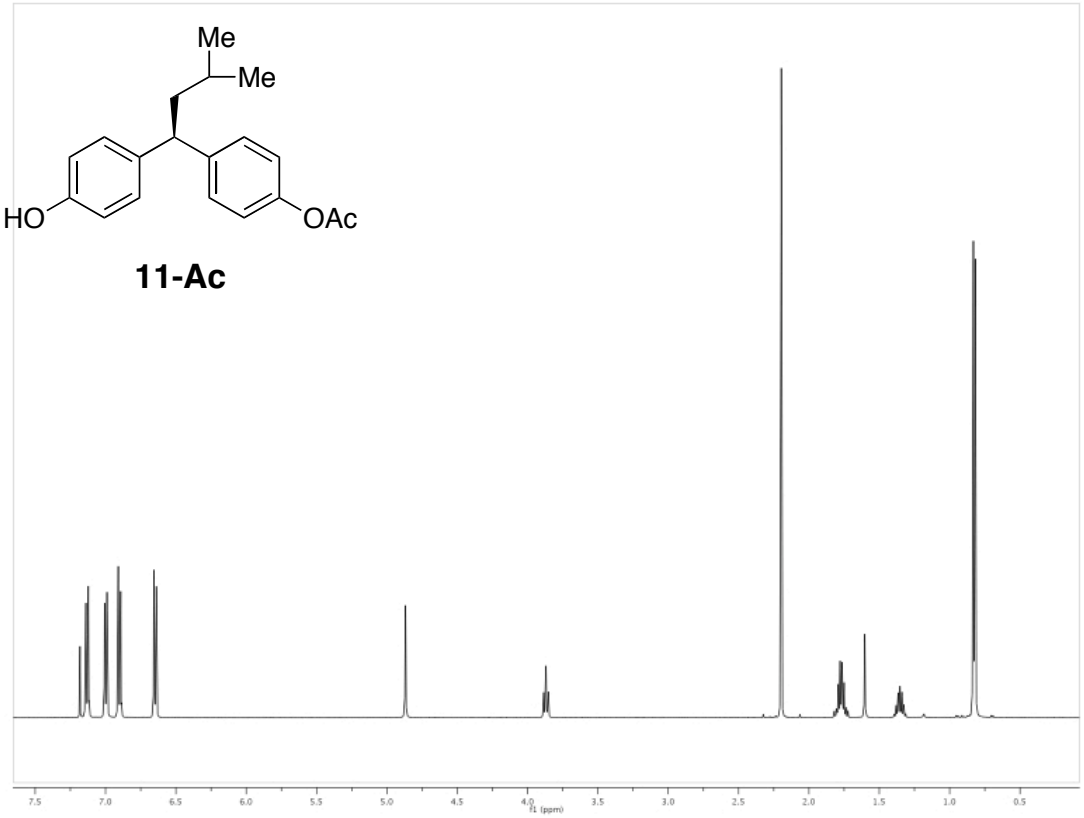
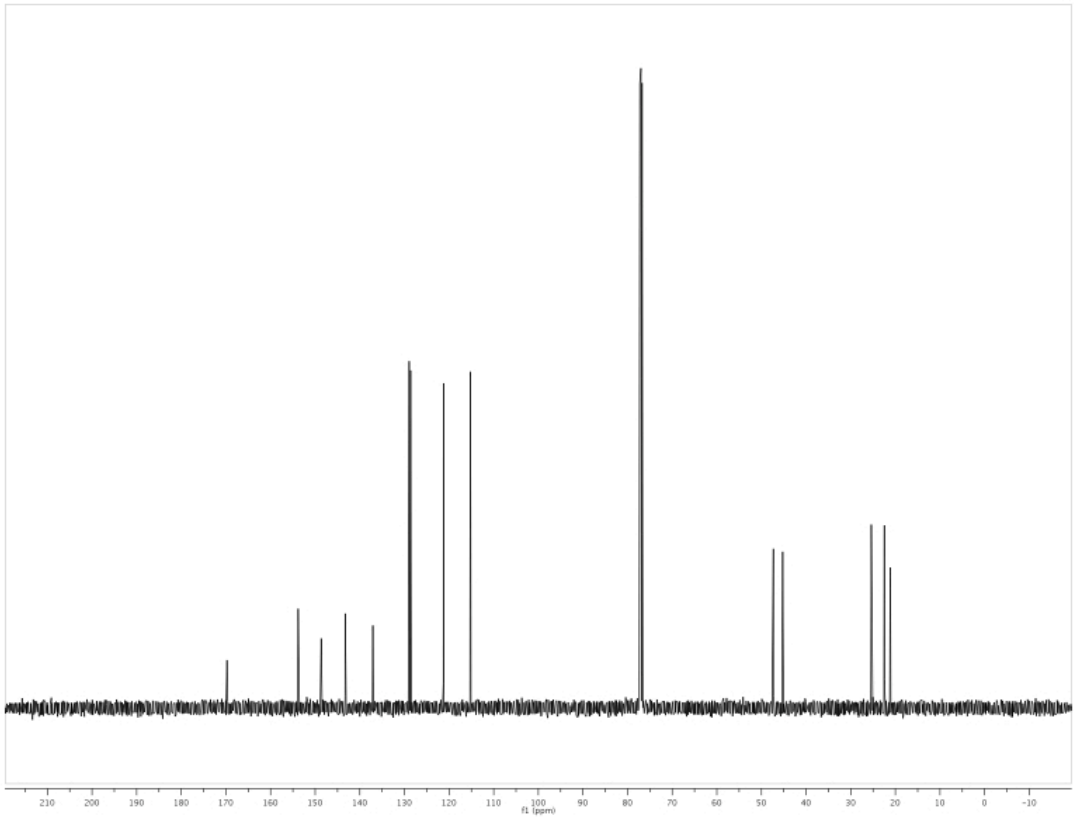
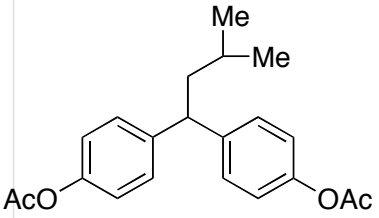
0
-10
f1 (ppm)


Me
Me
HO
OH
11
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



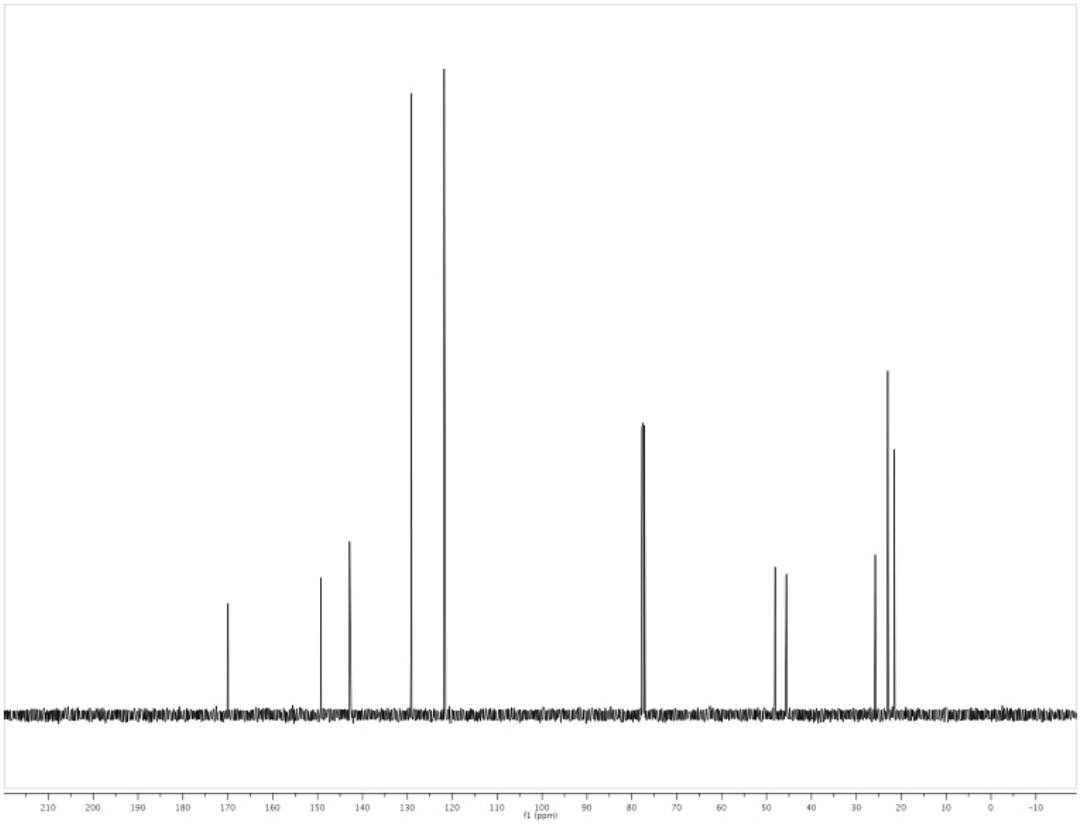
11-Ac




Me
Me
AcO
OAc

11-Ac$_2$

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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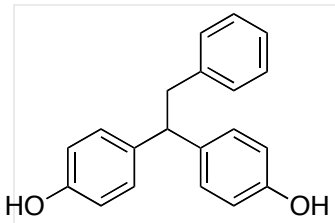
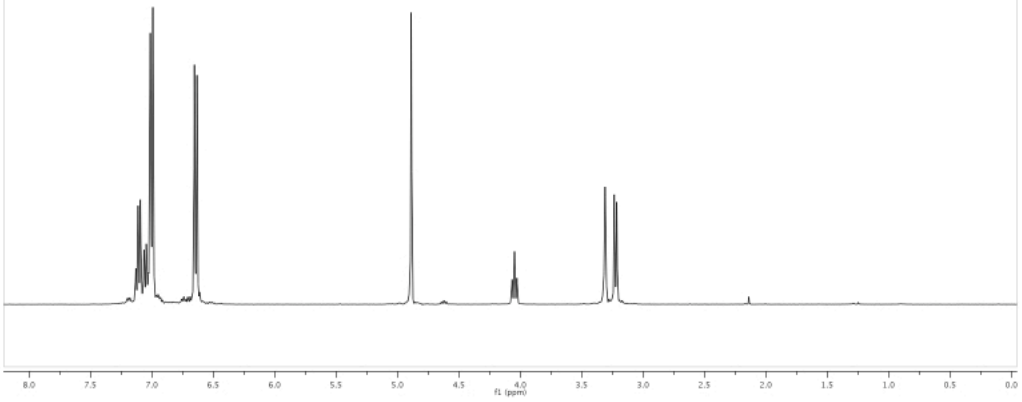
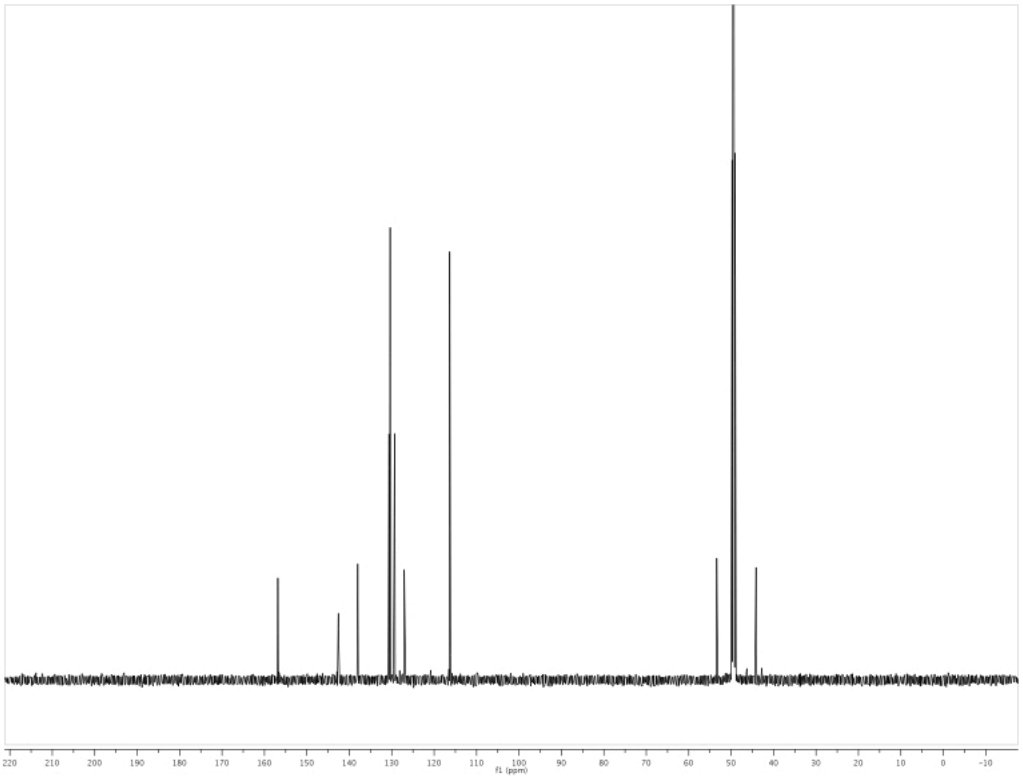
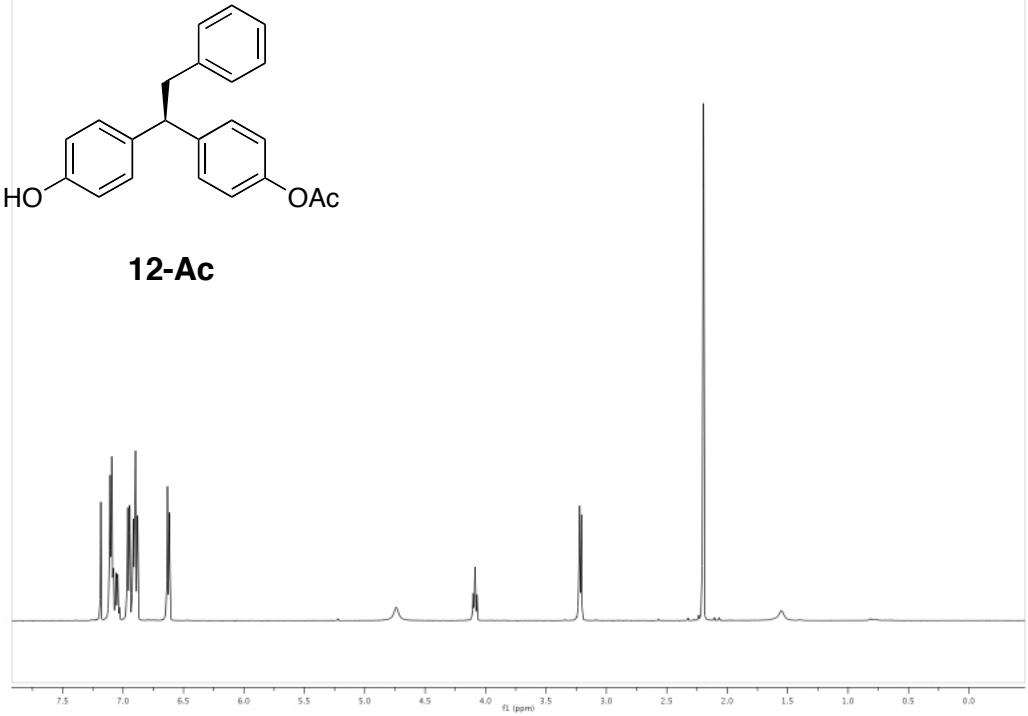
0
-10
f1 (ppm)



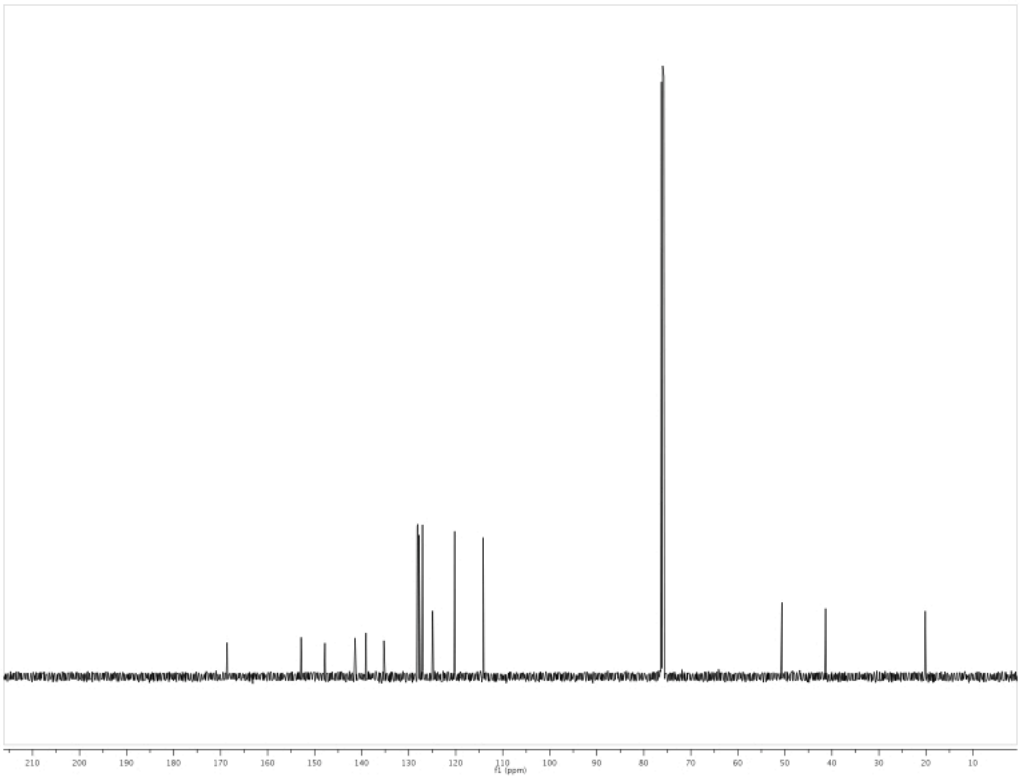
12

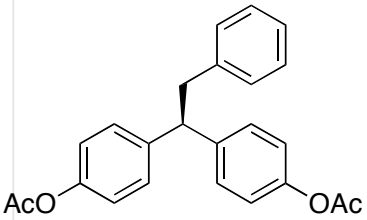




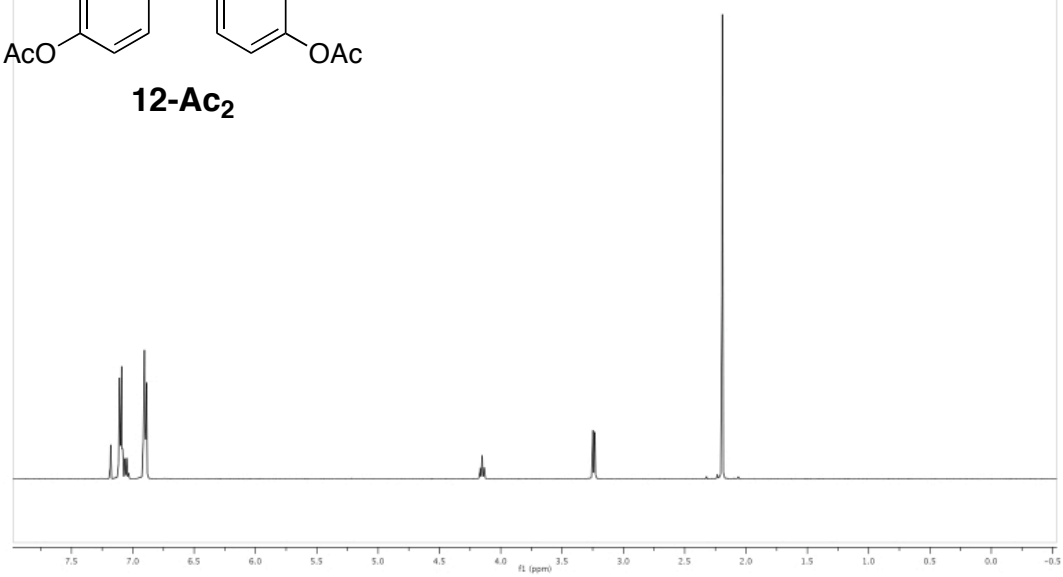


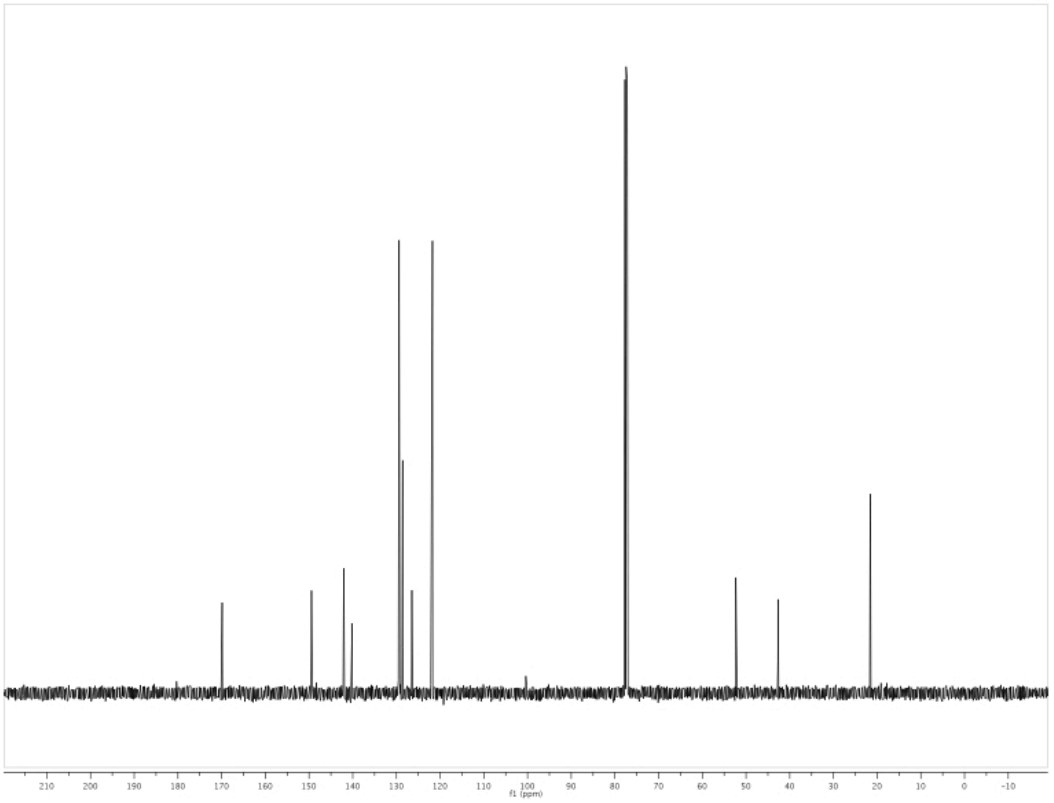
12-Ac




AcO
OAc

12-Ac$_2$


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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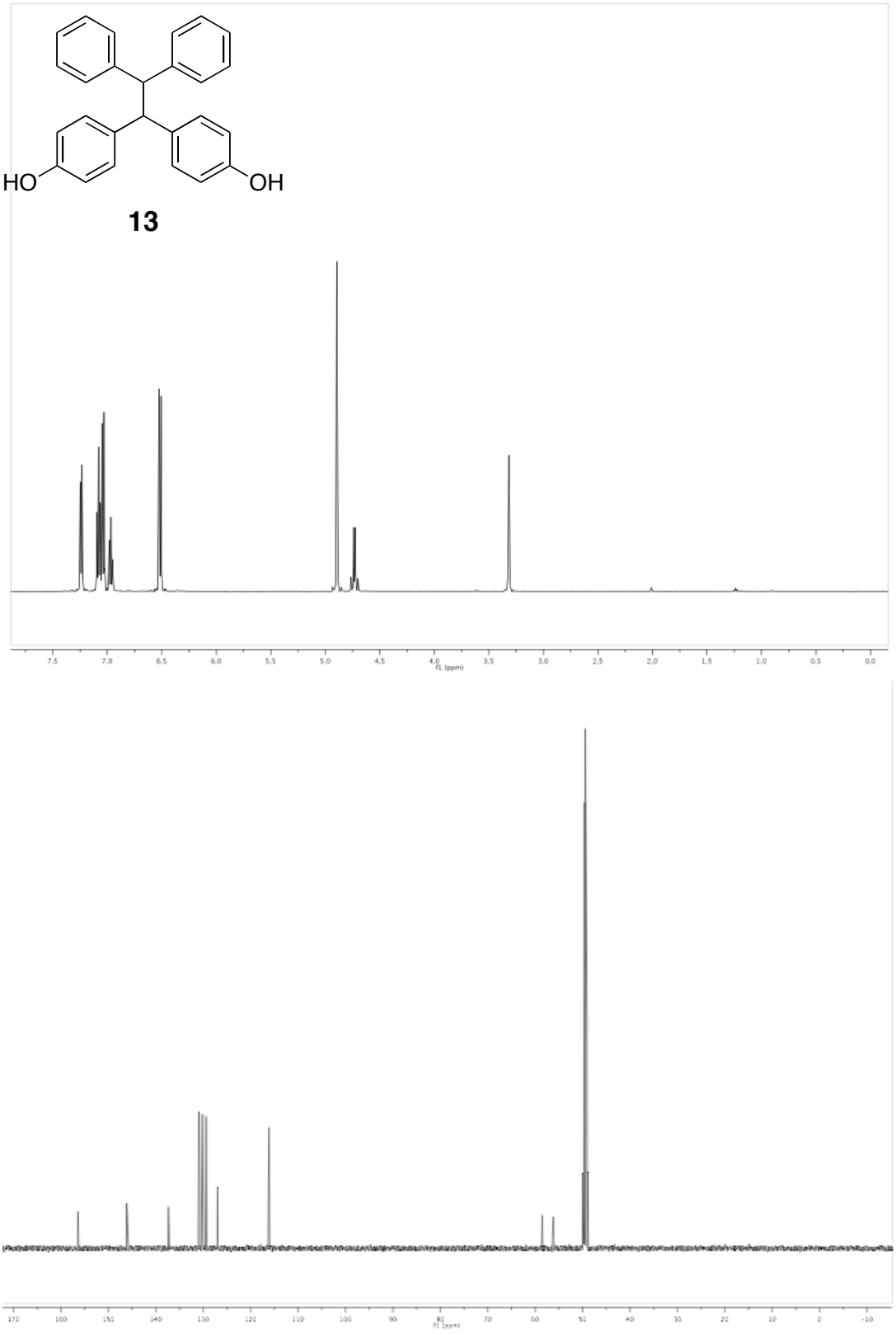
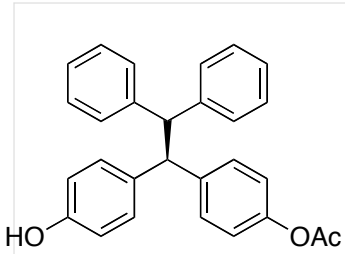
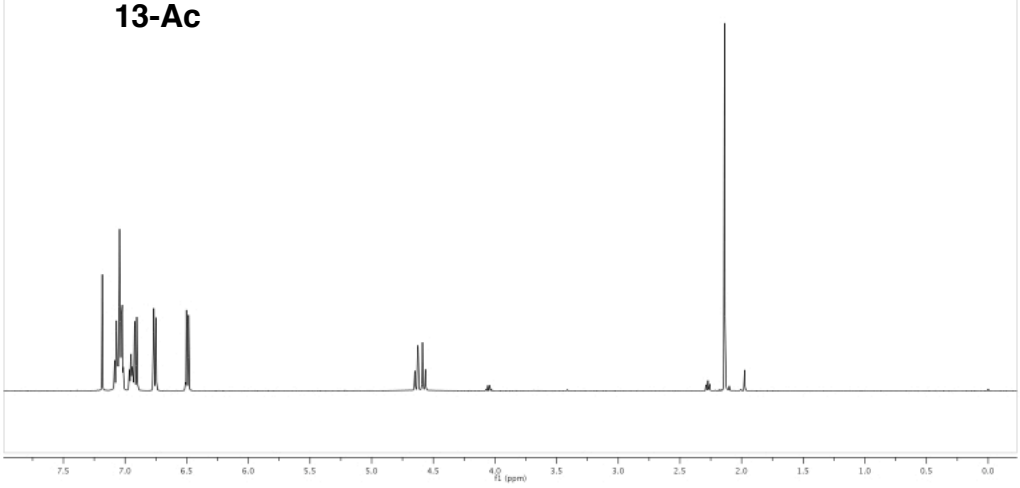
f1 (ppm)



13


HO
OAc

13-Ac


7.5
7.0
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4.5
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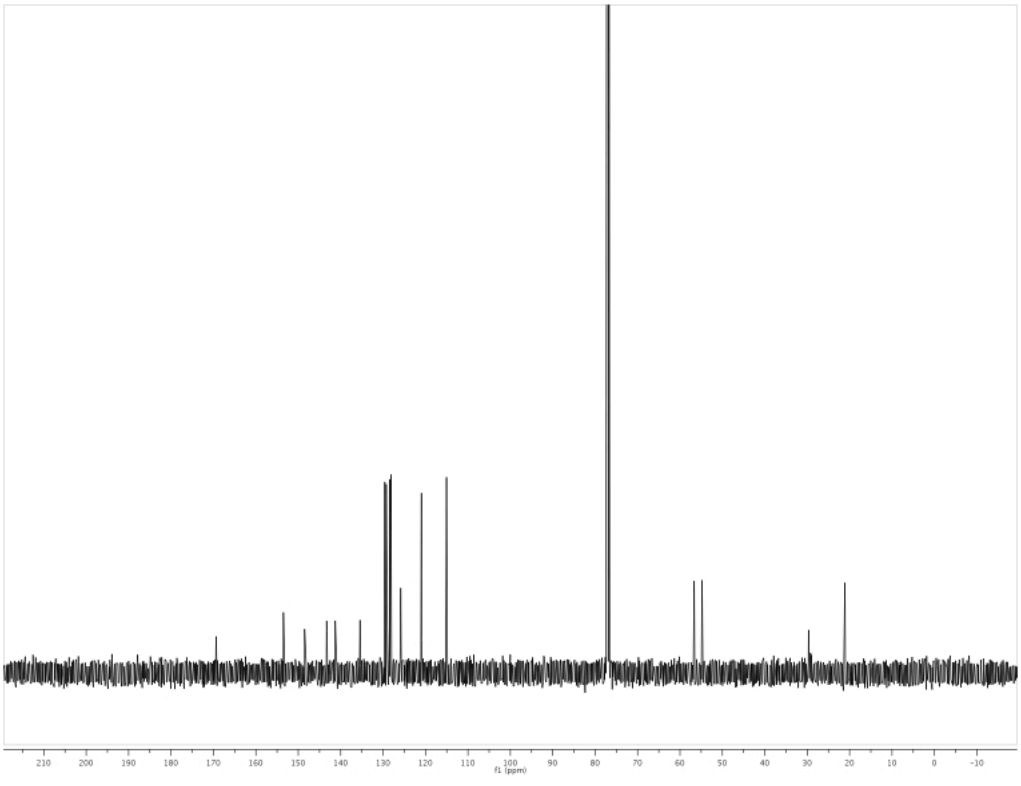
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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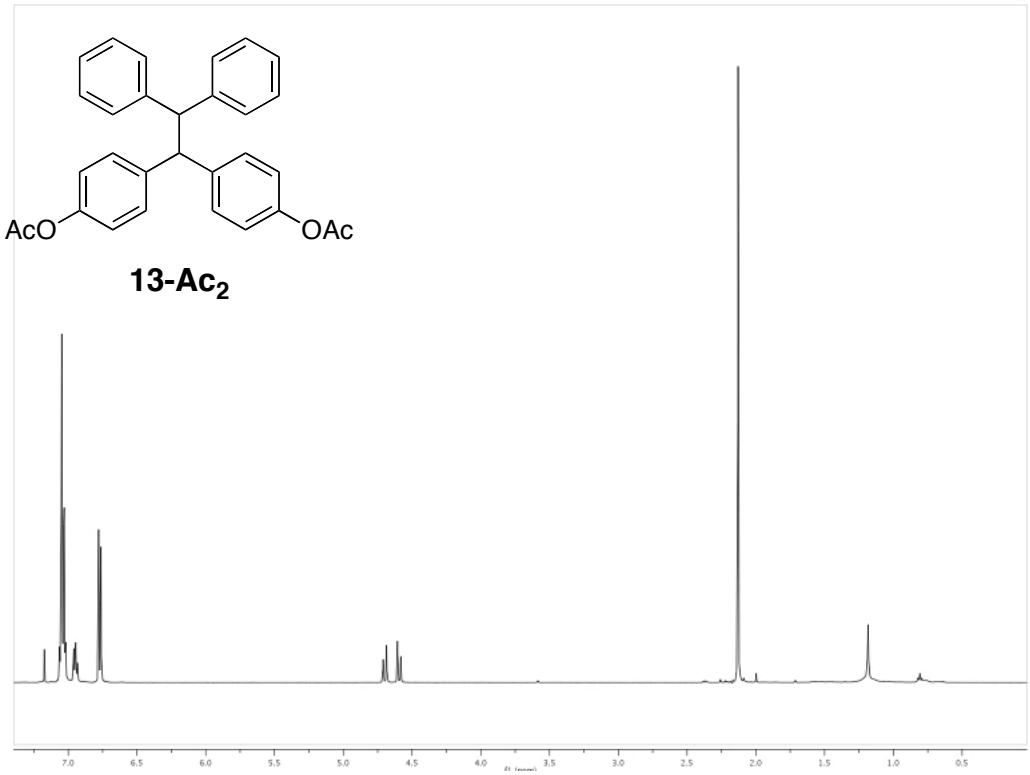
f1 (ppm)



13-Ac$_2$