A bisphenolic honokiol analog outcompetes oral antimicrobial agent cetylpyridinium chloride via a membrane-associated mechanism

Cristian Ochoa[†], Amy E. Solinski[‡], Marcus Nowlan[†], Madeline M. Dekarske[‡], William M. Wuest*[‡], and Marisa C. Kozlowski*[†]

†Department of Chemistry, Roy and Diana Vagelos Laboratories, University of Pennsylvania, Philadelphia, Pennsylvania 19104, United States

‡Department of Chemistry, 1515 Dickey Drive, Emory University, Atlanta, Georgia 30322, United States

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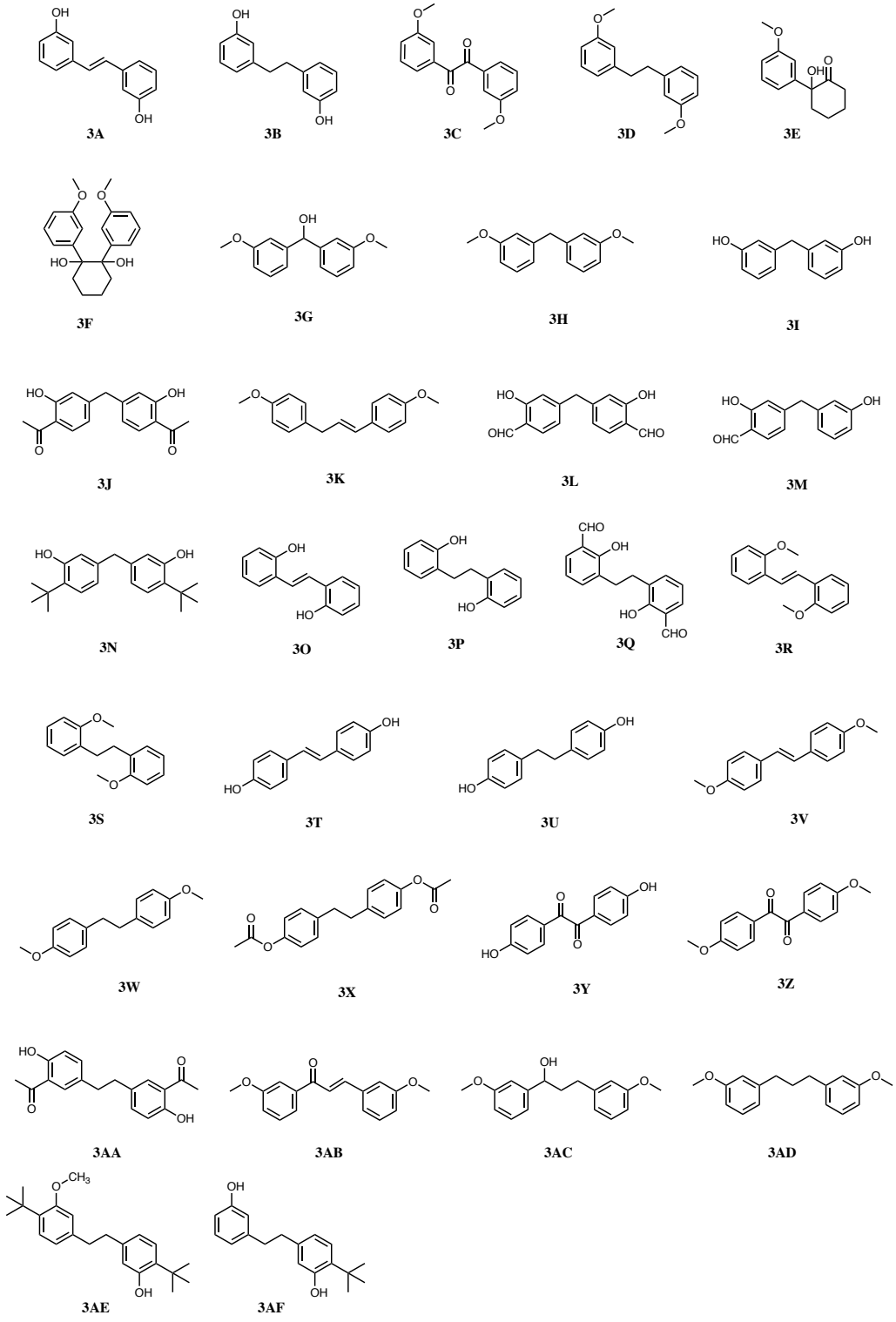
1. Supplemental Figures

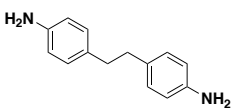
Figure S1. Comprehensive MIC Data

Compound	*S. mutans*	*S. gordonii*	*S. sanguinis*	*S. sobrinus*	*S. Mutans* MBC	$Lysis_{20}$	Therapeutic Index (TI)
3A-3M; 3O-3Z	>250 µM	-	-	-	-	-	-
3N	2 µM	2 µM	2 µM	4 µM	2 µM	63 µM	32
3AA-3AD	>250 µM	-	-	-	-	-	-
3AE	8 µM	-	-	-	-	-	-
3AF	16 µM	-	-	-	-	-	-
3AG-3AR	>250 µM	-	-	-	-	-	-
4A	>250 µM	-	-	-	-	-	-
4B	>250 µM	250 µM	250 µM	>250 µM	-	-	-
4C	32 µM	-	-	-	-	-	-
4D-4E	>250 µM	-	-	-	-	-	-
4F	16 µM	-	-	-	-	-	-
4G	4 µM	1 µM	1 µM	2 µM	4 µM	32 µM	8
4H	2 µM	4 µM	8 µM	8 µM	2 µM	63 µM	32
4I	>250 µM	>250 µM	63 µM	250 µM	-	-	-
4J	8 µM	-	-	-	-	-	-
4K	>250 µM	>250 µM	>250 µM	>250 µM	-	-	-
4L-4M	>250 µM	-	-	-	-	-	-
4N	>250 µM	-	-	-	-	-	-
4O	>250 µM	-	-	-	-	-	-
4P	32 µM	32 µM	32 µM	32 µM	-	-	-
4Q	16 µM	-	-	-	-	-	-
4R	8 µM	8 µM	8 µM	8 µM	8 µM	-	-
CPC	2 µM	1 µM	0.5 µM	0.5 µM	8 µM	16 µM	8
C2	2 µM	1 µM	1 µM	1 µM	4 µM	63 µM	32
Honokiol	250 µM	-	-	-	-	-	N/A

Figure S2. Bibenzyl Analog Structures



(Commercial Analogs)



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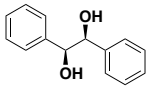

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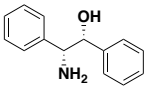

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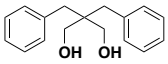

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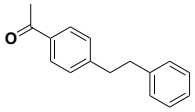

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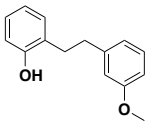

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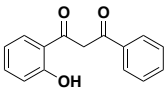

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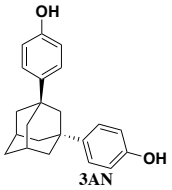

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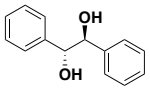

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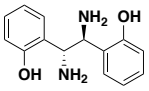

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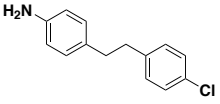

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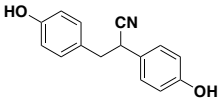

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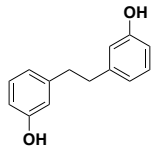

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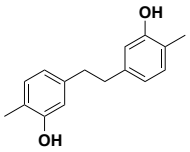

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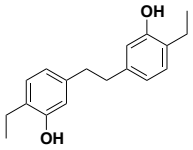

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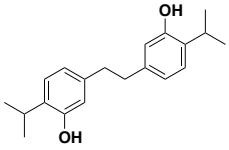

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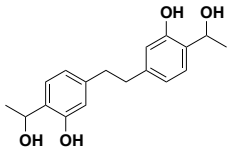

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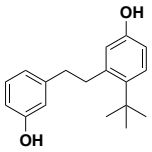

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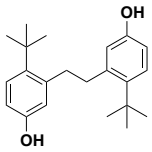

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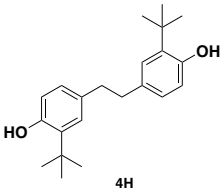

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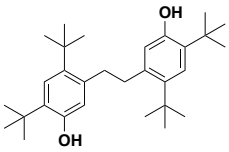

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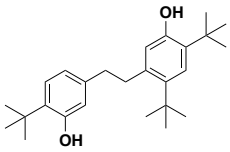

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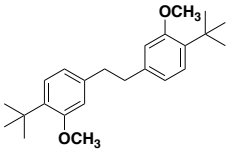

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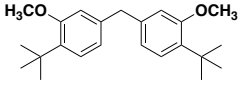

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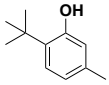

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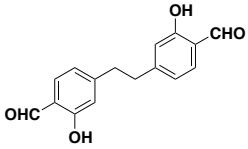

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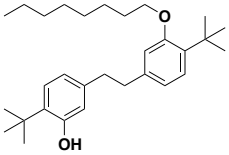

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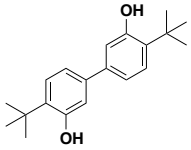

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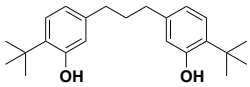

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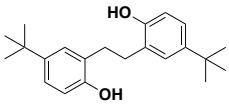

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Figure S3. Membrane Mechanism Data (3N)

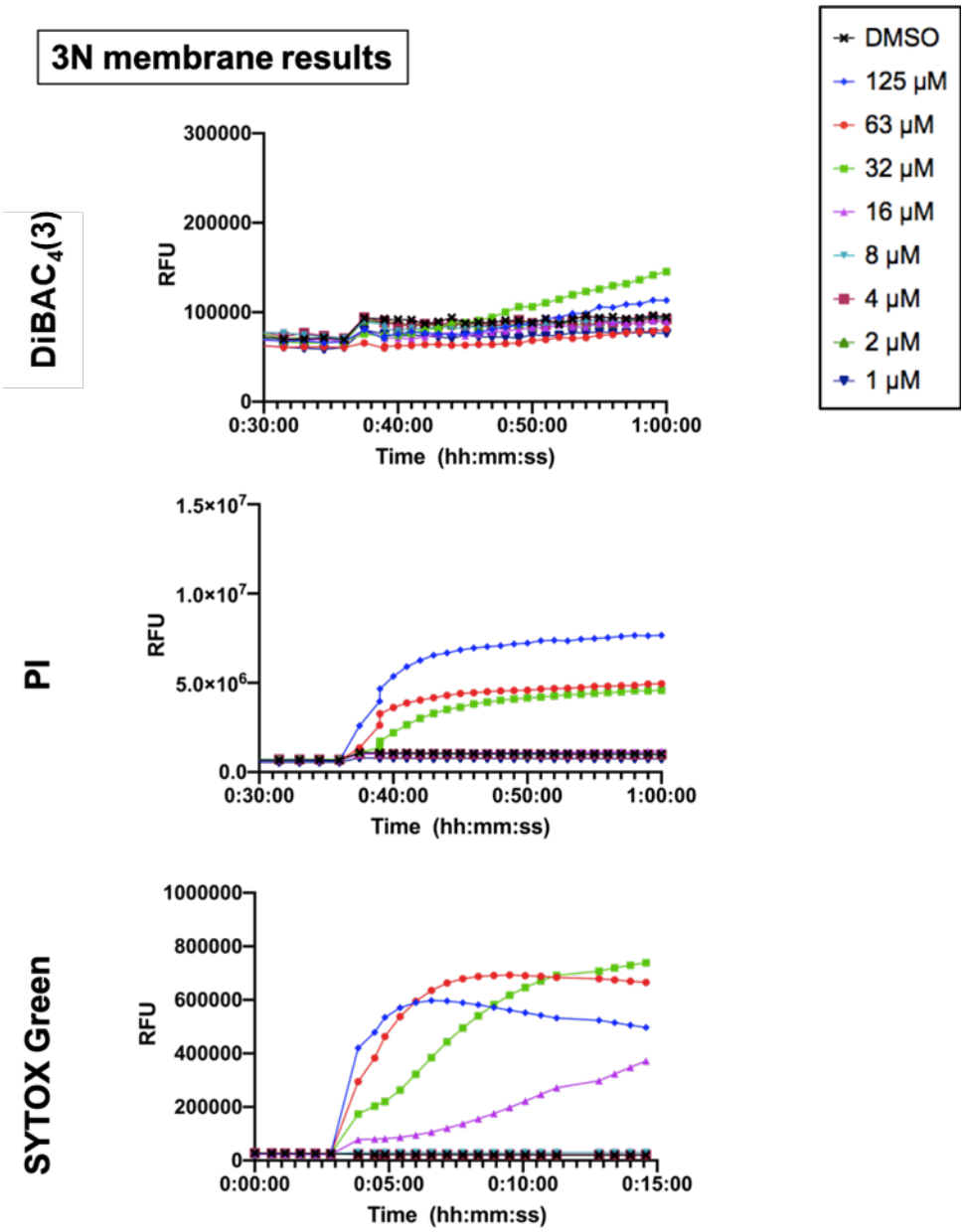


Figure S4. Membrane Mechanism Data (4B)

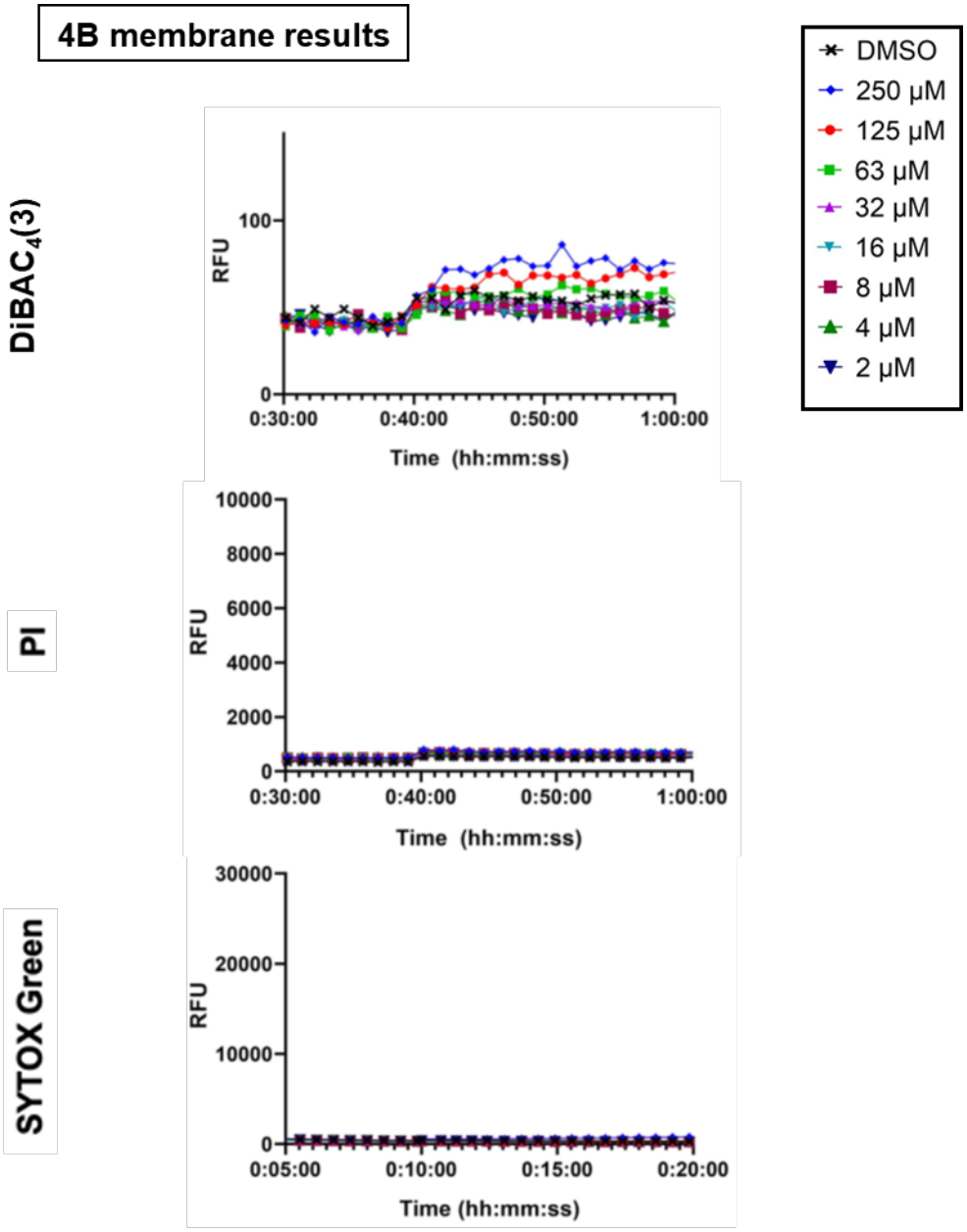
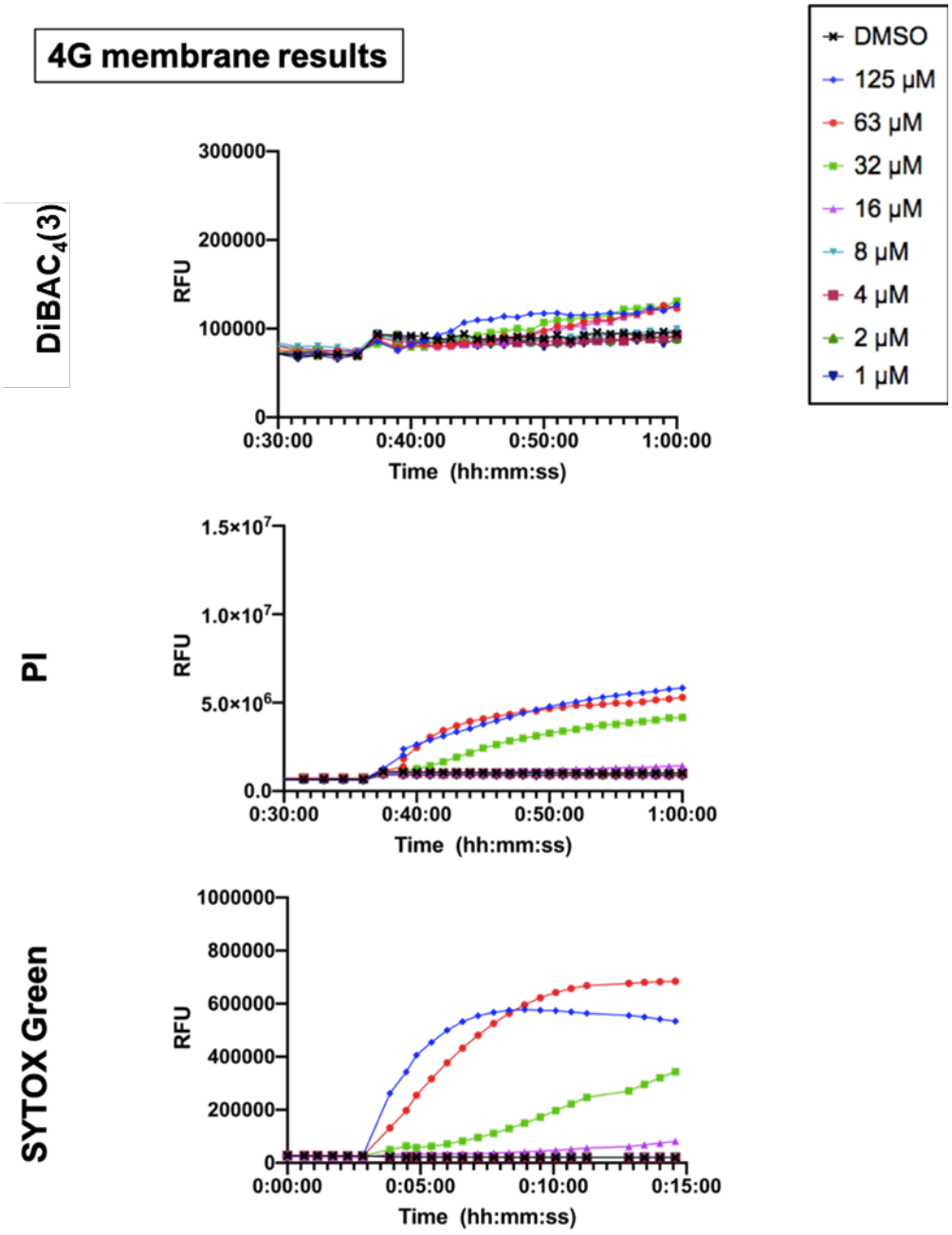


Figure S5. Membrane Mechanism Data (4G)



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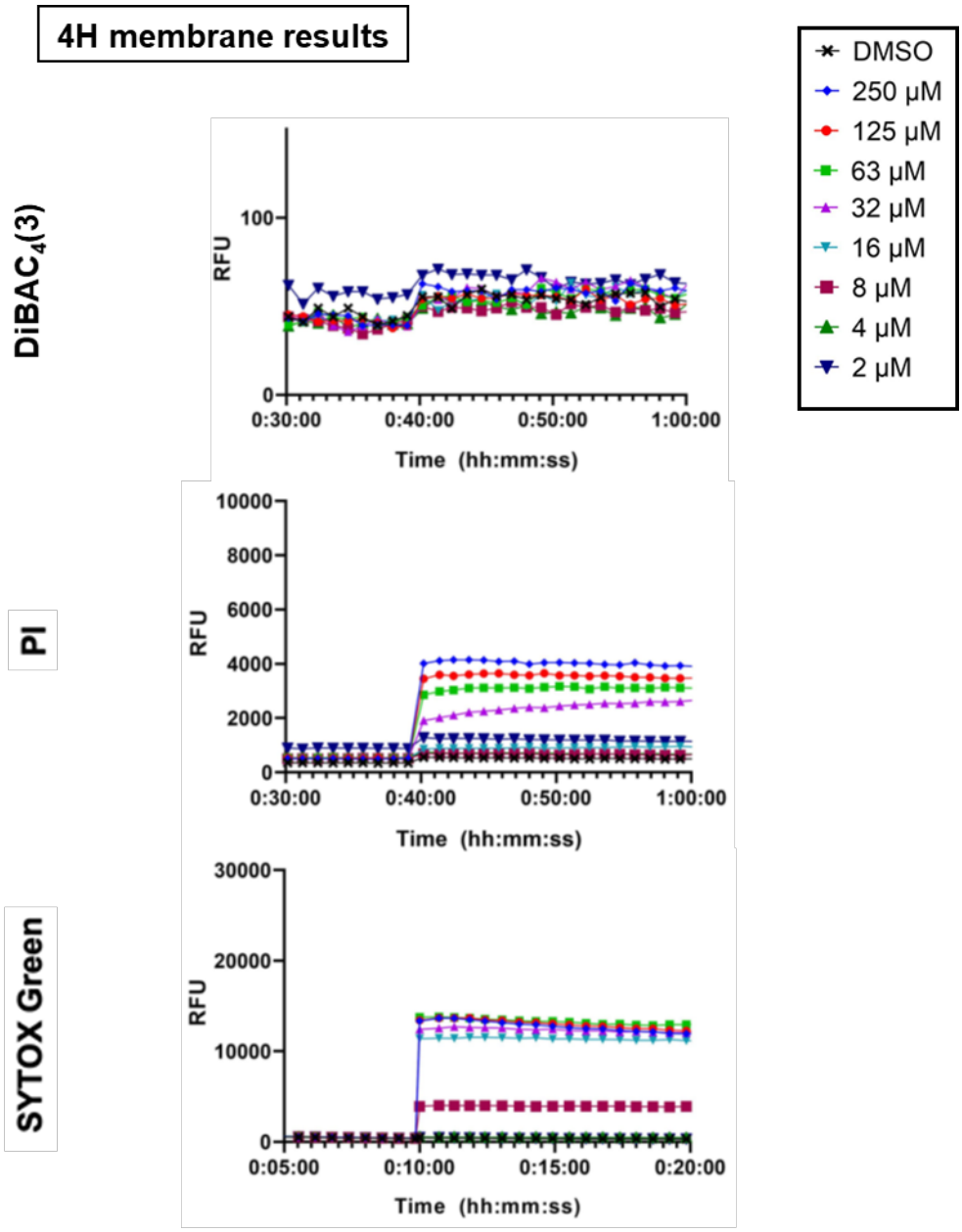


Figure S7. Membrane Mechanism Data (4l)

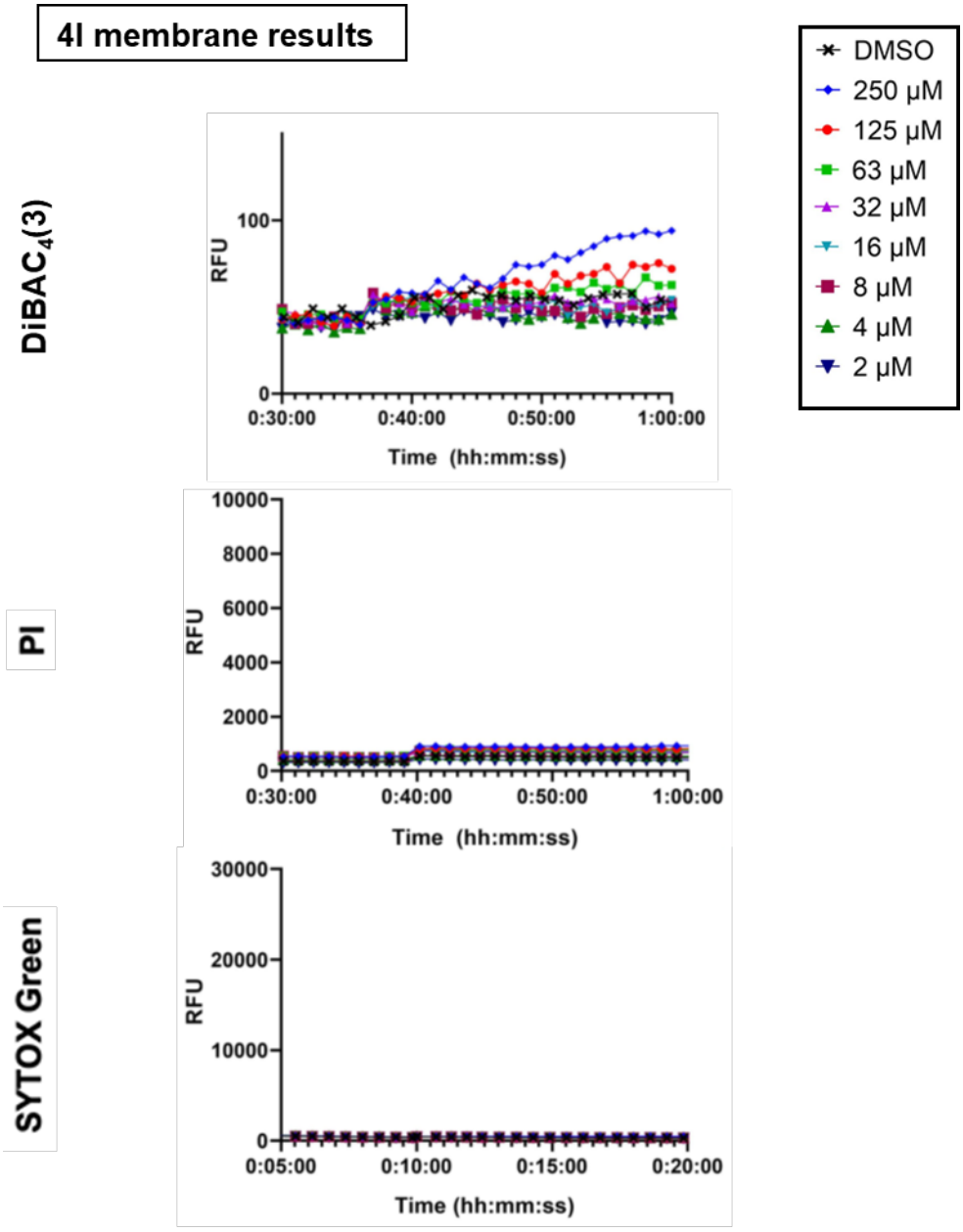
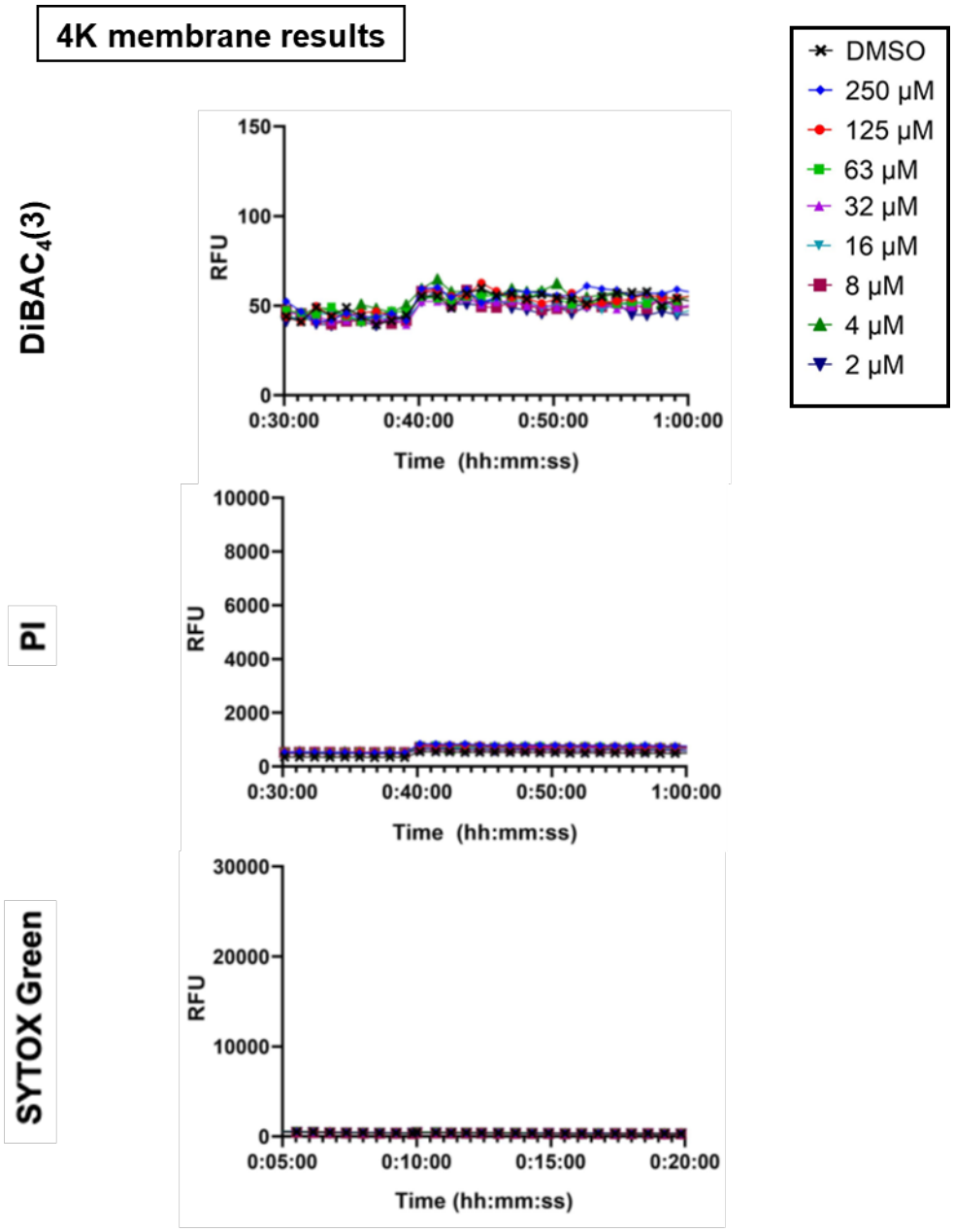


Figure S8. Membrane Mechanism Data (4K)



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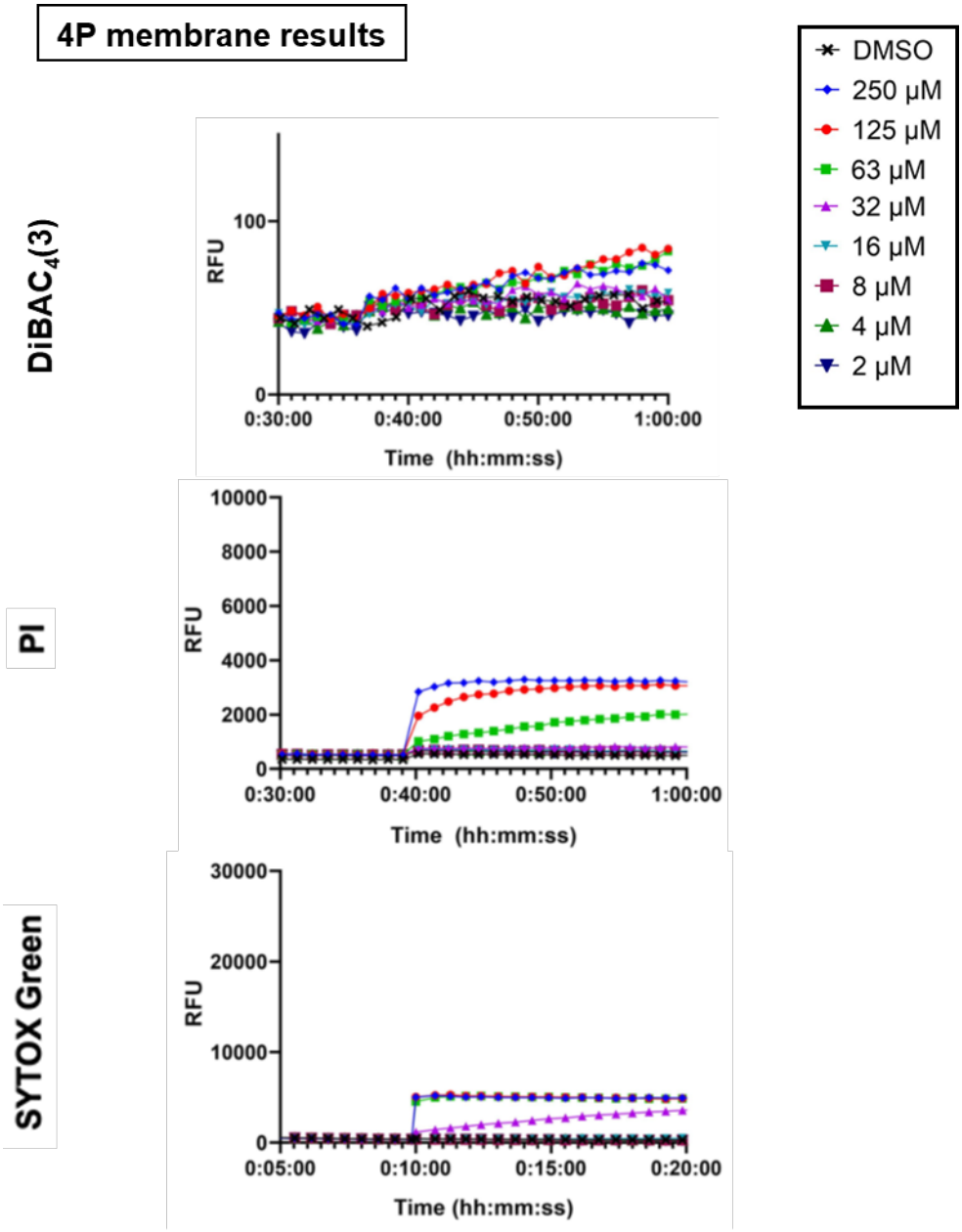

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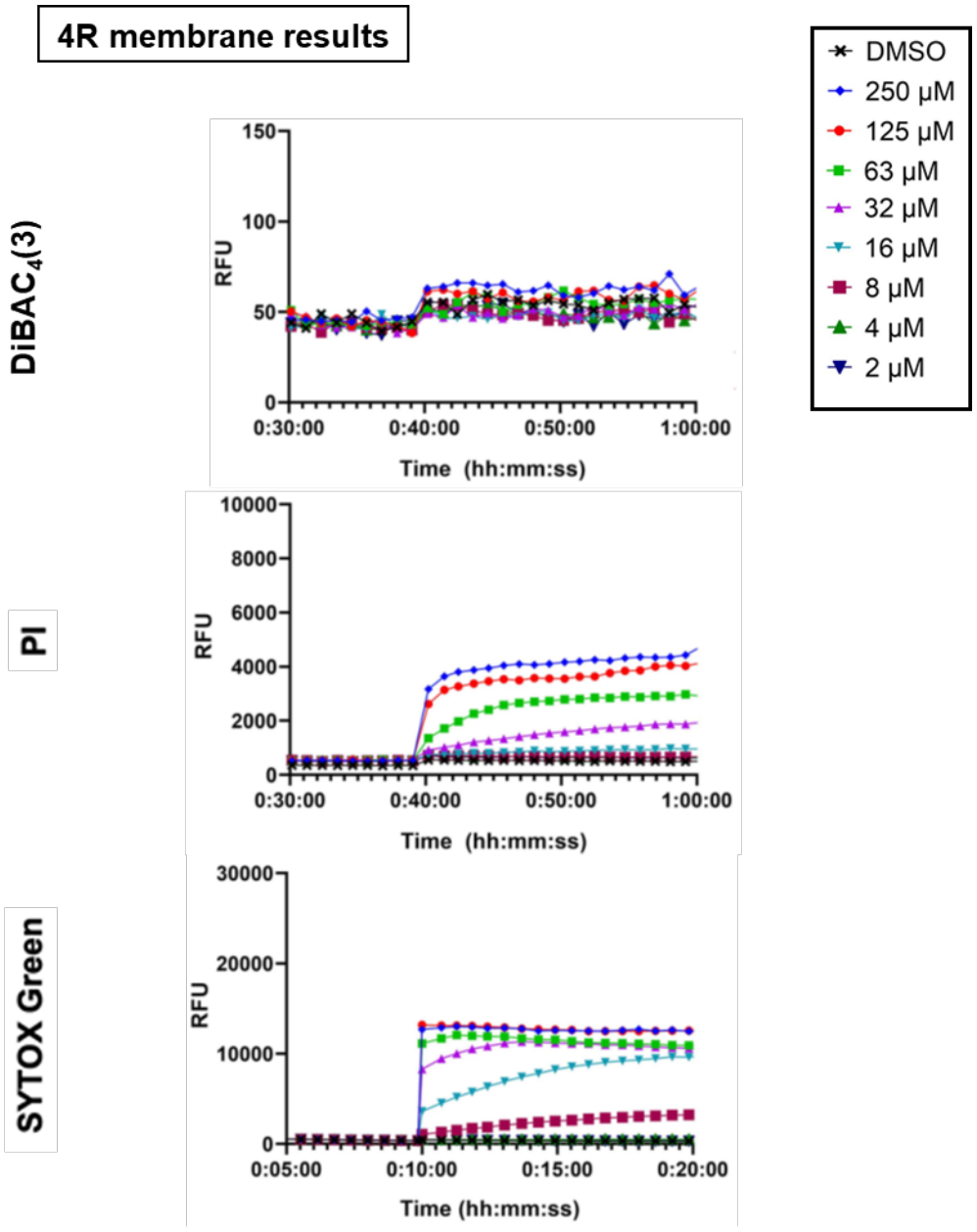


Figure S11. Membrane Mechanism Data (PBS)

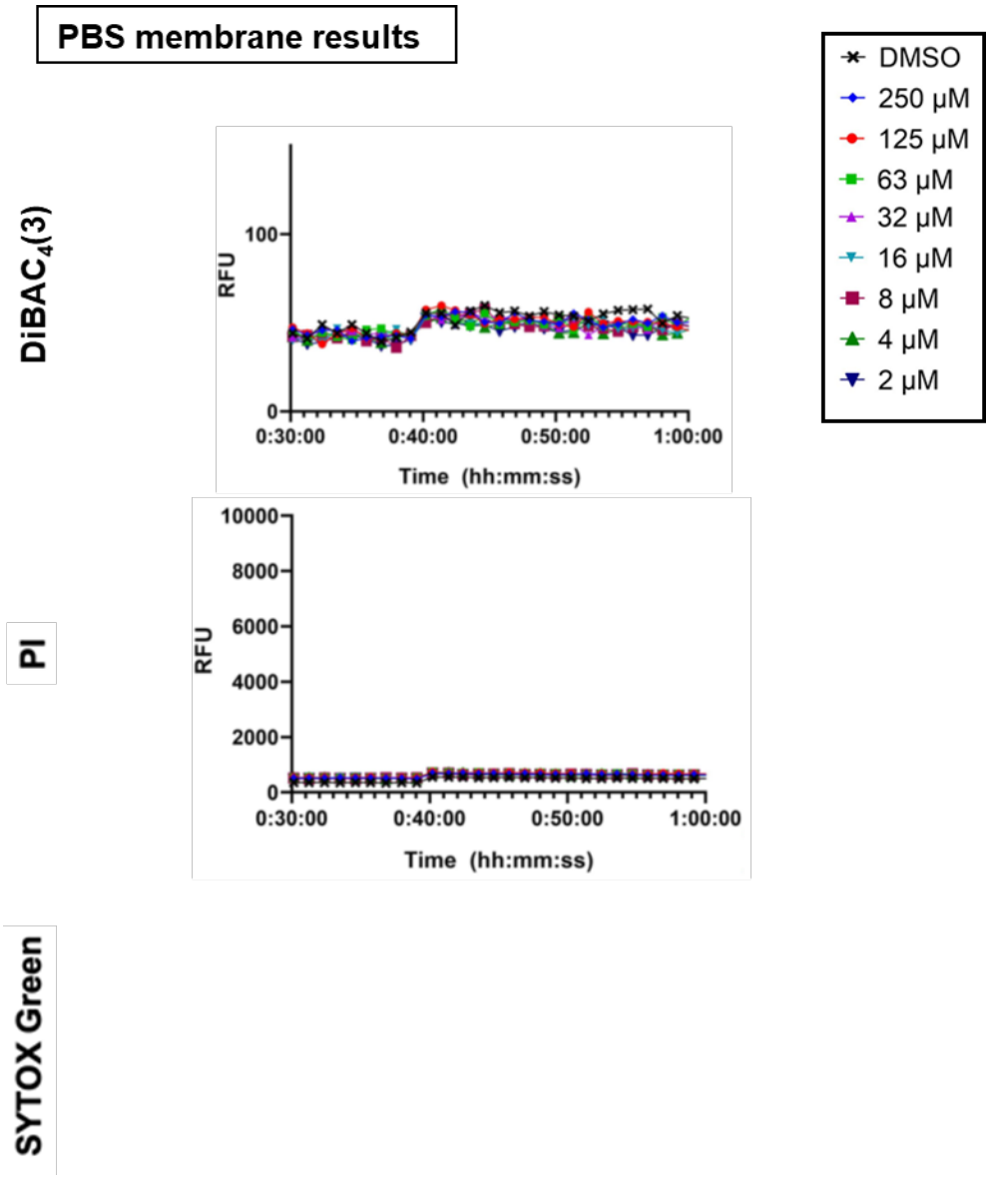
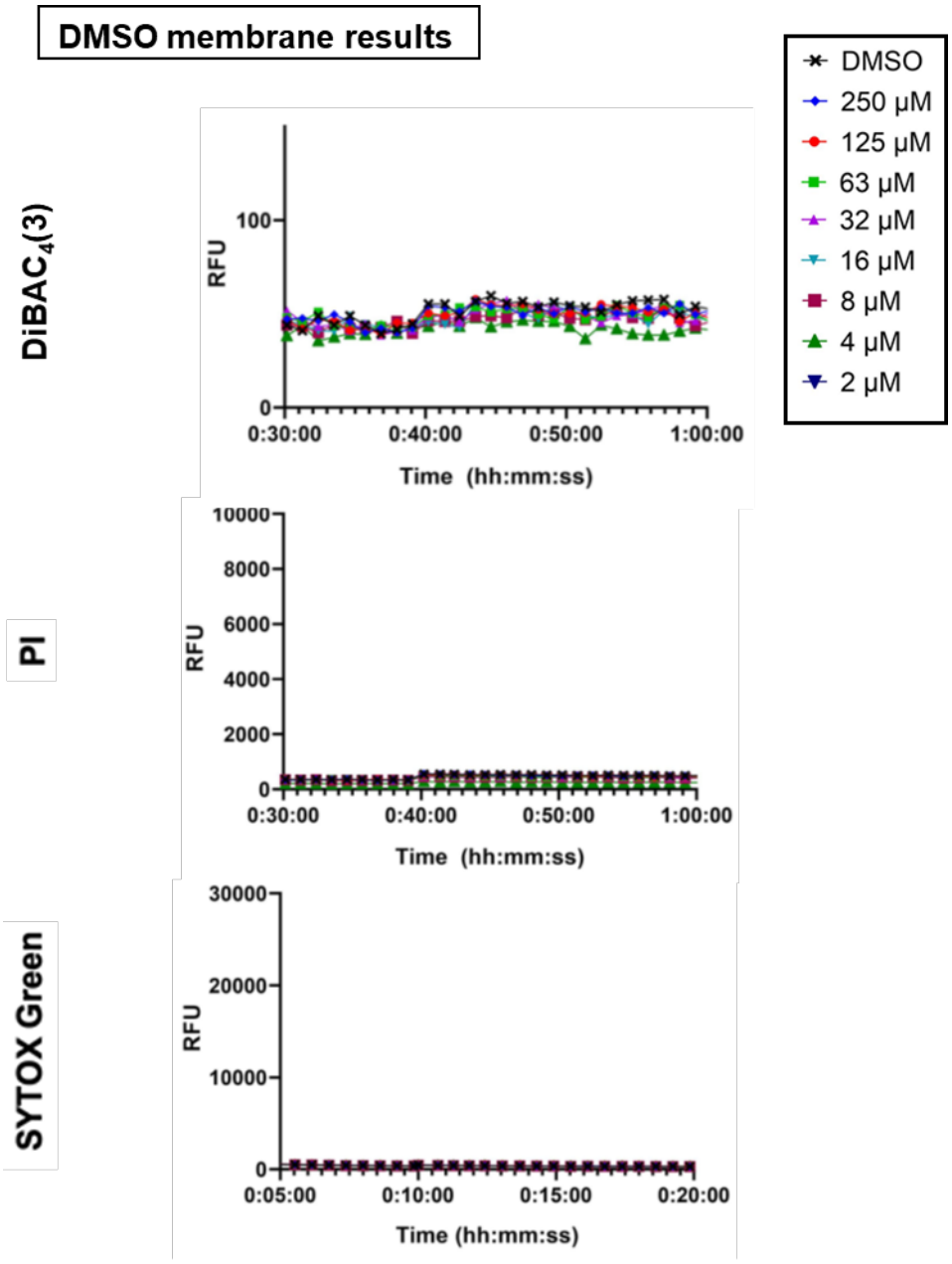


Figure S12. Membrane Mechanism Data (DMSO)



2. Biological Methods

Materials: The bacterial strain *Streptococcus Sobrinus* SL1 [CCM 6070, CNCTC 9/89], was purchased from the American Type Culture Collection. *Streptococcus mutans* wild-type strain UA159 was provided by Dr. Bettina Buttaro from Temple University Medical School, Philadelphia, PA. *Streptococcus gordonii* strain DL1 and *Streptococcus sanguinis* strain 10904 were provided by Dr. Robert G. Quivey from University of Rochester Medical School. Bacteria were routinely maintained on in BactoTM Todd- Hewitt (TH) agar plates and liquid cultures were grown in in BactoTM Todd-Hewitt broth (THB). For growth of biofilms, THB was supplemented with 0.1% sucrose. Incubation was stagnant at 37 °C with 5% CO_2. Optical density (OD) measurements were performed on a Molecular Devices SpectraMax iD3 plate reader for *S. mutans*, *S. gordonii* and *S. sanguinis*. Optical density (OD) measurements were performed on a BioTek plate reader spectrophotometer for *S. sobrinus.*

Minimum Inhibitory Concentration (MIC) Assay (*S. sobrinus*): Stock solutions of bibenzyl analogs, 10 mM, were serial diluted in brain heart infusion in flat-bottom 96-well microtiter plates (volume 100 μL). Bacterial cultures were grown overnight and then inoculated into the 96-well plate (total volume 200 μL). Plates are inoculated at 37 °C for 20-24 hours after which the OD_{630} values were evaluated with a BioTek Plate Reader spectrophotometer. The MIC is determined as the lowest concentration of compound resulting in no bacterial growth visible to the naked eye and the difference of measured and background OD_{630} is less than 0.1. DMSO controls corresponding to each test concentration were performed. Biological triplicates were performed to confirm results.

Minimum Inhibitory Concentration (MIC) Assay (*S. mutans*, *S. gordonii*, *S. sanguinis*): Stock solution of bibenzyl analogs, 10 mM, were serial diluted in THB media in flat-bottom 96-well microtiter plates (total volume 100 μL). Bacterial cultures were grown to mid-exponential phase, back diluted to an OD of 0.1 and then inoculated into the 96-well plate to reach a final volume of 200 μL. Plates were incubated at 37 °C in 5% CO_2 for 20-24 hours upon which time wells are evaluated visually for bacterial growth. The MIC is determined as the lowest concentration of compound resulting in no bacterial growth visible to the naked eye. DMSO controls corresponding to each test concentration were performed. Biological triplicates were performed to confirm results.

***S. mutans* biofilm model.** Stock solution of bibenzyl analogs, 10 mM, were serial diluted in THB media supplemented with 0.1% sucrose (w/v) in flat-bottom 96-well microtiter plates (total volume 100 μL). Bacterial cultures are grown to mid-exponential phase, back diluted to an OD of 0.1 and then inoculated into the 96-well plate to reach a final volume of 200 μL. Plates are incubated at 37 °C in 5% CO_2 for 24 hours (early stage biofilm) upon which time wells are evaluated visually for bacterial growth. DMSO controls

corresponding to each test concentration were performed. Biological triplicates were performed to confirm results.

***S. mutans* $MBIC_{50}$ assay**. Biofilms were prepared with above procedure, evaluated visually, OD_{600} of bacterial growth was recorded, and then emptied by inverting carefully, as to not disturb the biofilm. Wells were washed with 200 µL of phosphate buffer solution (PBS) and dried overnight at 37°C. Once dry, plates were incubated for 10 min at room temperature with 200 µL of 1% w/v crystal violet in DI H_2O. Excess crystal violet was removed by aspirating off the liquid and performing DI H_2O rinses until the run off was colorless. Plates were then inverted and dried overnight at 37°C. Crystal violet stained biofilm was redissolved with 200 µL of 10% acetic acid in DI H_2O. The crystal violet plate with acetic acid solution was allowed to incubate at room temperature for 10-30 minutes to allow for full dissolution. Then 100 µL was transferred to a fresh flat-bottom 96-well plate for absorbance measurements at 595 nm. DMSO controls corresponding to each test concentration were performed. Three biological replicates were performed. Crystal violet reading was set relative to bacterial growth (OD_{595}/OD_{600}) to allow for appropriate comparison of biofilm mass formation. $MBIC_{50}$ refers to the concentration at which biofilm growth is inhibited by 50% compared to the control.

Hemolysis Assay ($Lysis_{20}$) Hemolysis assays were performed on mechanically defibrinated sheep blood (Hemostat Labs: DSB030). 1.5 mL of blood was placed into a microcentrifuge tube and centrifuged at 10,000 rpm for ten minutes. The supernatant was removed and then the cells were resuspended with 1 mL of phosphate-buffered saline (PBS). The suspension was centrifuged as previously, the supernatant was removed, and cells were resuspended two more times. The final cell suspension was diluted twentyfold with PBS. The twentyfold suspension dilution was then aliquoted into microcentrifuge tubes containing compound serially diluted in PBS. TritonX (1% by volume) served as a positive control (100% lysis marker) and sterile PBS served as a negative control (0% lysis marker). Samples were then placed in an incubator at 37 ◦C and shaken at 200 rpm. After 1 hour, the samples were centrifuged at 10,000 rpm for ten minutes. The absorbance of the supernatant was measured with a UV spectrometer at a 540 nm wavelength.

Adapted from: Peng, L.; DeSousa, J.; Su, Z.; Novak, B.M.; Nevzorov, A.A.; Garland, E.R.; Melander, C. *Chem. Comm.* **2011**, *47*, 4896-4898.

SYTOX Assay. Bacterial overnight cultures were regrown to mid-log phase in THB media and the culture was centrifuged, and washed with PBS three times. Cells were then suspended in the same volume of PBS corresponding to the original regrow volume, and SYTOX green solution (5 mM in DMSO) was added to reach a final concentration of 5 µM. Cells were incubated at room temperature and in the dark for 30 minutes. 150 µL of cells were then added to a black, clear bottom 96-well plate. Fluorescence was recorded

for 10 minutes in plate reader to allow equilibration (excitation wavelength 485 nm and emission wavelength 525 nm). In a new 96-well plate, test compounds (10 mM DMSO stock solutions) were serially diluted in PBS. 50 µL of serially diluted compound was added to the SYTOX prepared cells in the plate reader and fluorescence was recorded overtime (excitation wavelength 485 nm, emission wavelength 525 nm). Biological triplicates were completed. Controls: DMSO vehicle control, PBS control, and CPC positive control.

Adapted from Steele, A. D.; Ernouf, G.; Lee, Y. E. and Wuest W.M. Diverted Total Synthesis of the Baulamycins and Analogues Reveals an Alternate Mechanism of Action. *Organic Letters* **2018** *20* (4), 1126-1129. doi: 10.1021/acs.orglett.8b00054.

Detecting Membrane Depolarization and Rupture. Bacterial overnight cultures were regrown to mid-log phase in THB media and the culture was centrifuged, and washed with PBS three times. Cells were then suspended in the same volume of PBS corresponding to the original regrow volume. To 20 mLs of cell suspension, 500 µl of 1 M sterile filter glucose solution was added (Final glucose concentration = 24.4 mM). Cells were incubated for 15 minutes at 37˚C. Then 100 µl of 50 µM solution of $DIBAC_4(3)$ was added (Final concentration = 243 nM). Next, 400 µl of 2 mg/ml solution of PI was added (Final concentration 19 µg/ml). The sample was mixed thoroughly and 150 µL of sample was added into the wells of a black, clear bottom 96-well plate. The plate was then placed in a pre-warmed (37˚C) fluorescence detection plate reader. The measurements were recorded until readings stabilized (~40 mins). In a new 96-well plate, test compounds (10 mM DMSO stock solutions) were serially diluted in PBS. The fluorescence plate was ejected, 50 µl of test compound was added and then quickly returned to the plate reader. Fluorescence was recorded overtime (measurements below). Biological triplicates were completed. Controls: DMSO vehicle control, PBS control, and CPC positive control.

Measurements

1. $DiBAC_4(3)$ measures changes in polarity. (490 nm excitation and 516 nm emission) detection
2. PI measures cell rupture. (535 nm excitation and 617 nm emission) detection

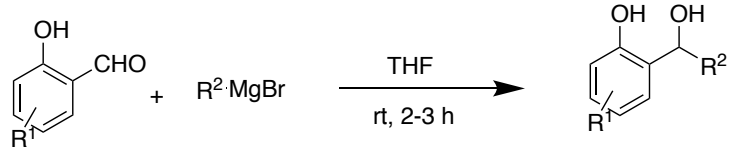
Adapted from Clementi, E. A., Marks, L. R., Roche-Håkansson, H., Håkansson, A. P. Monitoring Changes in Membrane Polarity, Membrane Integrity, and Intracellular Ion Concentrations in *Streptococcus pneumoniae* Using Fluorescent Dyes. *J. Vis. Exp.* (84), e51008, doi:10.3791/51008 (2014).

TEM Imaging. Cells were grown to mid-log phase in THB media, centrifuged, and washed with PBS three times. Cells were then suspended to the original volume with PBS. The cells were then incubated with test compound for 30 minutes at 37˚C. Following treatment, cells were collected, washed, and prepared for transmission electron microscopy by fixing the cells in 2.5% glutaraldehyde in 0.1 M cacodylate buffer. Images were recorded on a JEOL JEM-1400 Transmission electron microscope at the Integrated Cellular Imaging Core at Emory University.

3. Synthetic Procedures

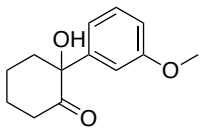
All non-aqueous reactions were carried out under an atmosphere of dry argon unless otherwise noted. Commercial reagents were used as received without additional purification unless otherwise noted. Anhydrous THF, toluene, dichloromethane, and 1,2-dichloroethane were obtained from a Pure Process Technology solvent purification system. Bibenzyls 3A, 3D, 3G, 3H, 3I, 3O, 3P, 3R, 3S, 3T, 3U, 3V, and 3W were prepared according to the literature.[1-4] Compounds 3C, 3Z and 4M were purchased from Sigma Aldrich. Reactions were monitored by thin layer chromatography (TLC) using Silicycle glass-backed TLC plates with 250 μM silica and F254 indicator. Visualization was accomplished by UV light or iodine staining. All compounds with inhibitory ability greater than 250 μM were analyzed for purity by UPLC and characterized by 1H NMR and decoupled ^{13}C NMR. All final compounds were found to have >95% purity by UPLC unless otherwise noted. Nominal mass accuracy LCMS data were obtained by use of a Waters Acquity UPLC system equipped with a Waters TUV detector (254 nm) and a Waters SQD single quadrupole mass analyzer with electrospray ionization. LC gradient A 500 μL/min: 30 second hold 95:5 (water:acetonitrile 0.1% v/v formic acid), 2 minute gradient to 5:95, and 30 second hold. LC gradient B 500 μL/min: 30 second hold 50:50 (water:acetonitrile 0.1% v/v formic acid), 2 minute gradient to 5:95, and 30 second hold. Acquity UPLC BEH C18, 1.7 μm, 2.1 x 50 mm column. ^{1}H NMR spectra were recorded on a 500 MHz spectrometer. Chemical shifts are reported in ppm from the solvent resonance ($CDCl_3$ 7.26 ppm, acetone-d_6 2.05 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants, and number of protons. Decoupled ^{13}C NMR spectra were recorded at 125 MHz. IR spectra were taken on an FT-IR spectrometer. Accurate mass measurement analyses were conducted via time-of-flight mass analyzer GCMS with electron ionization (EI) or via time-of-flight mass analyzer LCMS with electrospray ionization (ESI). The signals were measured against an internal reference of perfluorotributylamine for EI-GCMS and leucine enkephalin for ESI-LCMS. The instrument was calibrated, and measurements were made using neutral atomic masses; the mass of the electron removed or added to create the charged species is not taken into account.

General Procedure A: Grignard Addition to Aryl Aldehydes

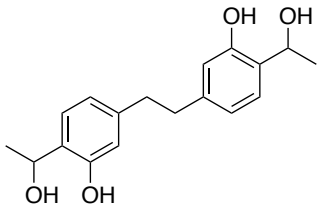


Salicylaldehyde Grignard

To a solution of salicylaldehyde (1.0 mmol) in anhydrous THF (0.2 M) was slowly added a solution of Grignard reagent (4.5 mmol, 1.0 M in diethyl ether) at 0 °C. The reaction mixture was stirred for 2-3 h at room temperature. The reaction mixture was cooled to 0 °C and quenched *via* drop-wise addition of saturated ammonium chloride solution (5 mL). After stirring at room temperature for 10 min, the product was extracted with diethyl ether (5 x 20 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed using 30% ethyl acetate/hexane to afford the product.

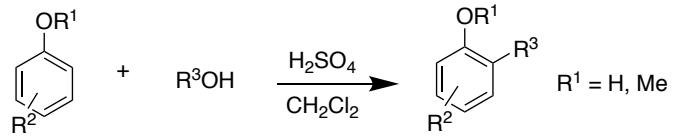


2-Hydroxy-2-(3-methoxyphenyl)cyclohexan-1-one (3E). Following general procedure A, the product was obtained as a clear yellow liquid (0.266 g, 1.20 mmol) in 45% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, J = 7.8 Hz, 1H), 6.89-6.85 (m, 3H), 4.47 (s, 1H), 3.80 (s, 3H), 2.98-2.95 (m, 1H), 2.56-2.51 (m, 1H), 2.45 (m, 1H), 2.07-2.04 (m, 1H), 1.88-1.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.7, 160.3, 141.6, 130.3, 118.8, 113.6, 112.7, 80.2, 55.5, 39.11, 39.05, 28.4, 23.2; IR (neat) 3341, 2937, 1676, 1599, 1585, 1487, 1454, 1433, 1317, 1256, 1153, 1040, 872, 784, 735, 699, 564, 465 cm^{-1}; HRMS (ESI-TOF) *m/z* = 220.1099 calc for $C_{13}H_{16}O_3$ [M]$^+$, found 220.1095.

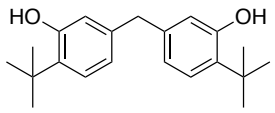


5,5'-(Ethane-1,2-diyl)bis(2-(1-hydroxyethyl)phenol) (4E). Following general procedure A, the product was obtained as an amorphous white solid (39 mg, 0.13 mmol) in 70% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 8.57 (s, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.69-6.68 (m, 4H), 5.10-5.06 (m, 2H), 4.84 (s, 2H), 2.79 (s, 4H), 1.44 (d, J = 6.5 Hz, 6H; ^{13}C NMR (125 MHz, Acetone-D_6) δ 155.0, 141.9, 128.5, 126.1, 119.4, 115.9, 68.1, 37.1, 23.7; IR (neat) 3318, 2927, 1619, 1580, 1428, 1371, 1250, 1122, 1067, 1008, 958, 872, 815 cm^{-1}; HRMS (EI-TOF) *m/z* = 266.1307 calc for $C_{18}H_{18}O_2$ [M-2H_2O]$^-$, found 266.1315.

General Procedure B: Friedel-Crafts Electrophilic Aromatic Substitution

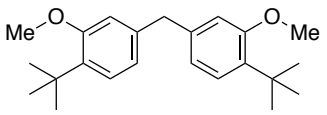


To a solution of the arene (1.0 equiv) dissolved in dichloromethane (0.2 M) at 0 °C was added R^2OH (2.2 equiv) and H_2SO_4 (2.0 equiv). The resultant mixture was stirred for 18 h and monitored *via* TLC. When the complete, the mixture was quenched with a saturated solution of $NaHCO_3$ (10 mL), extracted with dichloromethane (5 x 15 mL) and ethyl acetate (5 x 15 mL), and washed with brine (5 x 10 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed using 10% ethyl acetate/hexane to afford the product.

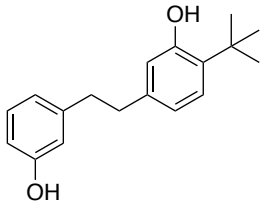


5,5'-Methylenebis(2-(*tert*-butyl)phenol) (3N). Following general procedure B, the product was obtained as an amorphous light brown solid (8.9 mg, 0.03 mmol) in 12% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 8.0 Hz, 2H), 6.70 (dd, J = 8.0, 1.5 Hz, 2H), 6.43 (d, J =1.5 Hz, 2H), 4.63 (s, 2H), 3.77 (s, 2H), 1.37 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 140.2, 134.1, 127.3, 121.3, 117.3, 40.5, 34.5, 29.9; IR (neat) 3521, 2956, 2912, 2870, 1614, 1573, 1514, 1483, 1414, 1391, 1362, 1333, 1296, 1262, 1185, 1136, 1080, 977, 811, 762, 734,

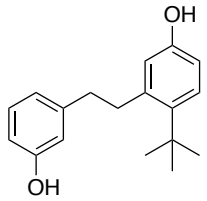
502 cm^{-1}; HRMS (EI-TOF) *m/z* = 312.2089 calc for $C_{21}H_{28}O_2$ $[M]^+$, found 312.2092. >95% purity. UPLC t_R = 2.37 min gradient A.



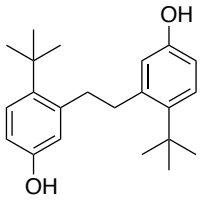
Bis(4-(*tert*-butyl)-3-methoxyphenyl)methane (4L). Following general procedure B, the product was obtained as a light yellow liquid (13 mg, 0.04 mmol) in 18% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, J = 8.2 Hz, 2H), 6.73 (m, 4H), 3.91 (s, 2H), 3.80 (s, 6H), 1.36 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 139.9, 135.9, 126.5, 120.6, 112.3, 55.0, 41.4, 34.5, 29.8; IR (neat) 2955, 1608, 1570, 1501, 1464, 1411, 1359, 1254, 1172, 1087, 1041, 811 cm^{-1}; HRMS (EI-TOF) *m/z* = 340.2402 calc for $C_{23}H_{32}O_2$ $[M]^+$, found 340.2397.



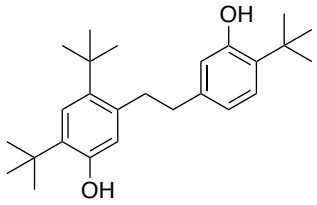
2-(*tert*-Butyl)-5-(3-hydroxyphenethyl)phenol (4AF). Following general procedure B, the product was obtained as a dark yellow solid (46 mg, 0.17 mmol) in 18% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04-7.00 (m, 3H), 6.87 (dd, J = 8.0, 2.0 Hz, 1H), 6.75 (dd, J = 6.5, 2.0 Hz, 2H), 6.58 (d, J = 8.0 Hz, 1H), 2.81 (s, 4H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, Acetone-D_6) δ 157.3, 155.5, 143.5, 140.5, 133.1, 129.1, 126.3, 119.4, 119.1, 116.2, 115.2, 112.7, 37.3, 36.7, 33.9, 29.0; IR (neat) 3400, 2954, 2864, 1653, 1611, 1513, 1442, 1419, 1364, 1211, 1085, 821, 758, 553, 515 cm^{-1}; HRMS (EI-TOF) *m/z* = 270.1620 calc for $C_{18}H_{22}O_2$ $[M]^+$, found 270.1618. mp = 125 – 127 °C. >95% purity. UPLC t_R = 2.37 min gradient A.



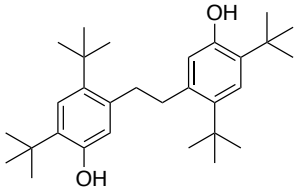
4-(*tert*-Butyl)-3-(3-hydroxyphenethyl)phenol (4F). Following general procedure B, the product was obtained as a red gel (0.396 g, 1.47 mmol) in 34% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, J = 8.0 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 6.87-6.82 (m, 3H), 6.57 (s, 1H), 6.22 (s, 1H), 5.48 (s, 1H), 2.92-2.90 (m, 4H), 1.56 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 154.1, 143.9, 140.8, 133.8, 129.6, 127.1, 121.0, 120.5, 116.6, 115.3, 112.9, 37.4, 36.8, 34.3, 29.7; IR (neat) 3389, 2955, 2867, 1699, 1613, 1589, 1483, 1455, 1417, 1391, 1363, 1297, 1263, 1202, 1153, 1079, 1023, 1000, 941, 860, 818, 788, 735, 694, 677, 632, 572, 537, 501 cm^{-1}; HRMS (EI-TOF) *m/z* = 270.1620 calc for $C_{18}H_{22}O_2$ $[M]^+$, found 270.1613. >95% purity. UPLC t_R = 2.47 min gradient A.



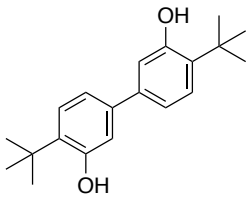
3,3'-(Ethane-1,2-diyl)bis(4-(*tert*-butyl)phenol) (4G). Following general procedure B, the product was obtained as a brown solid (0.660 , 2.02 mmol) in 47% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 8.06 (s, 2H), 7.09 (d, J = 8.0 Hz, 2H), 6.70 (d, J = 2.0 Hz, 2H), 6.64 (dd, J = 8.0, 2.0 Hz, 2H), 2.73 (s, 4H), 1.37 (s, 18H); ^{13}C NMR (125 MHz, Acetone-D_6) δ 154.7, 141.1, 134.1, 127.1, 120.3, 116.9, 36.9, 34.5, 29.9; IR (neat) 3520, 2955, 2868, 1703, 1615, 1574, 1517, 1483, 1454, 1416, 1391, 1363, 1297, 1263, 1187, 1137, 1079, 1023, 960, 859, 818, 736, 696, 635, 572, 502 cm^{-1}; HRMS (EI-TOF) *m/z* = 326.2246 calc for $C_{22}H_{30}O_2$ [M]$^+$, found 326.2262. mp = 137 – 139 °C. >95% purity. UPLC t_R = 2.86 min gradient A.



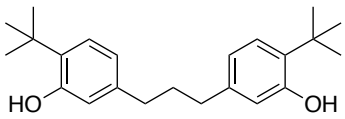
2,4-Di-*tert*-butyl-5-(4-(*tert*-butyl)-3-hydroxyphenethyl)phenol (4J). Following general procedure B, the product was obtained as a brown gel (39 mg, 0.10 mmol) in 11% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (d, J = 2.0 Hz, 1H), 6.98 (m, 2H), 6.89 (dd, J = 8.0, 2.0 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 5.03 (s, 1H), 4.64 (s, 1H), 2.81 (s, 4H), 1.43 (s, 18H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 151.8, 135.7 (2C), 135.6, 134.0 (2C), 132.5, 127.1, 126.6, 124.8, 116.3, 38.0, 37.6, 34.4, 34.2 (2C), 30.3 (2C), 29.6; IR (neat) 3643, 3519, 2955, 2868, 1704, 1646, 1608, 1506, 1483, 1434, 1419, 1391, 1363, 1317, 1248, 1232, 1200, 1121, 1084, 1022, 932, 885, 814, 768, 741, 704, 620, 494 cm^{-1}; HRMS (EI-TOF) *m/z* = 382.2872 calc for $C_{26}H_{38}O_2$ [M]$^+$, found 382.2888. 90% purity. UPLC t_R = 2.88 min gradient B.



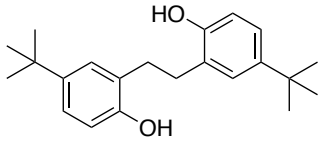
5,5'-(Ethane-1,2-diyl)bis(2,4-di-*tert*-butylphenol) (4I). Following general procedure B, the product was obtained as an amorphous yellow solid (7.3 mg, 0.02 mmol) in 2% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (m, 4H), 5.02 (s, 2H), 2.82 (s, 4H), 1.43 (s, 36H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.7, 135.6 (2C), 132.7, 124.8 (2C), 37.9, 34.2 (2C), 30.3 (2C); IR (neat) 3646, 2955, 1435, 1391, 1361, 1315, 1232, 1157, 1120, 877, 768 cm^{-1}; HRMS (EI-TOF) *m/z* = 438.3998 calc for $C_{30}H_{46}O_2$ [M]$^+$, found 438.3995. 93% purity. UPLC t_R = 3.02 min gradient A.



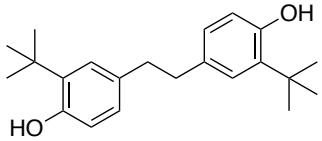
4,4'-Di-*tert*-butyl-[1,1'-biphenyl]-3,3'-diol (4P). Following general procedure B, the product was obtained as a white solid (42 mg, 0.14 mmol) in 53% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 8.33 (s, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 1.8 Hz, 2H), 6.96 (dd, J = 8.0, 1.8 Hz, 2H), 1.40 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.3, 139.4, 135.3, 127.5, 119.1, 115.0, 34.4, 29.7; IR (neat) 3516, 2957, 2870, 1694, 1611, 1555, 1504, 1484, 1420, 1399, 1387, 1361, 1293, 1264, 1241, 1187, 1138, 1104, 1078, 1049, 1022, 961, 858, 815, 741, 567, 500 cm^{-1}; HRMS (EI-TOF) *m/z* = 298.1933 calc for $C_{26}H_{26}O_2$ $[M]^+$, found 298.1940. mp = 177 – 179 °C. >95% purity. UPLC t_R = 2.79 min gradient A.



5,5'-(Propane-1,3-diyl)bis(2-(*tert*-butyl)phenol) (4Q). Following general procedure B, the product was obtained as a yellow liquid (5.6 mg, 0.02 mmol) in 13% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 7.9 Hz, 2H), 6.70 (d, J = 7.9 Hz, 2H), 6.49 (s, 2H), 4.67 (s, 2H), 2.56 (t, J = 7.6 Hz, 4H), 1.91 (pentet, J = 7.6 Hz, 2H), 1.39 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 141.5, 133.6, 127.0, 120.6, 116.8, 34.7, 34.4, 31.1, 29.8; IR (neat) 3518, 2926, 2857, 1616, 1574, 1417, 1391, 1363, 1297, 1262, 1181, 1138, 1080, 863, 816, 573 cm^{-1}; HRMS (EI-TOF) *m/z* = 340.2402 calc for $C_{23}H_{32}O_2$ $[M]^+$, found 340.2411. >95% purity. UPLC t_R = 2.94 min gradient B.



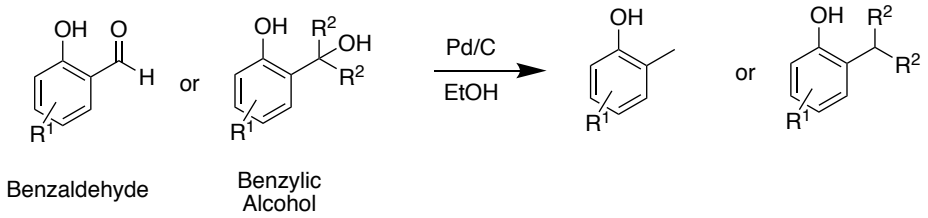
2,2'-(Ethane-1,2-diyl)bis(4-(*tert*-butyl)phenol) (4R). Following general procedure B, the product was obtained as an amorphous white solid (3.0 mg, 0.01 mmol) in 7% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (m, 4H), 6.80 (d, J = 8.7 Hz, 2H), 5.98 (s, 2H), 2.85 (s, 4H), 1.30 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.5, 143.9, 127.2, 127.2, 124.6, 115.1, 34.2, 32.4, 31.7; IR (neat) 3339, 2953, 2868, 1612, 1590, 1500, 1462, 1423, 1392, 1363, 1265, 1219, 1180, 1153, 1121, 1105, 1087, 984, 888, 819, 752, 739, 635, 478 cm^{-1}; HRMS (EI-TOF) *m/z* = 326.2246 calc for $C_{22}H_{30}O_2$ $[M]^+$, found 326.2237. >95% purity. UPLC t_R = 2.47 min gradient A.



4,4'-(Ethane-1,2-diyl)bis(2-(*tert*-butyl)phenol) (4H). Following general procedure B, the product was obtained as an amorphous light yellow solid (9.3 mg, 0.03 mmol) in 6% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (d, J = 2.2 Hz, 2H), 6.87 (dd, J = 6.0, 2.2 Hz, 2H), 6.58 (d, J = 6.0 Hz, 2H), 4.69 (s, 2H), 2.80 (s, 4H), 1.39

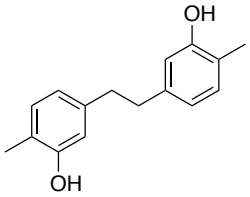
(s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 135.9, 134.0, 127.4, 126.8, 116.5, 37.8, 34.6, 29.8; IR (neat) 3528, 2955, 2866, 1608, 1504, 1484, 1456, 1418, 1391, 1363, 1329, 1248, 1182, 1084, 890, 815, 769, 496 cm^{-1}; HRMS (EI-TOF) *m/z* = 326.2246 calc for $C_{22}H_{30}O_2$ $[M]^+$, found 326.2233. >95% purity. UPLC t_R = 2.78 min gradient B.

General Procedure C: Reduction of Benzaldehydes and Benzylic Alcohols

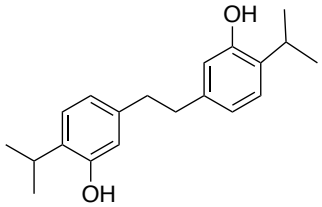


Benzaldehyde Benzylic Alcohol

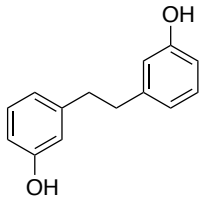
Benzaldehyde or benzylic alcohol (1.0 equiv) and 10% Pd/C (0.9 equiv) were added to anhydrous ethanol (0.1 M). The flask was evacuated and backfilled with H_2 gas three times and the mixture was allowed to stir under H_2 balloon for 18 h. After completion of the reaction, the flask was purged with argon and filtered through a bed of Celite. The solvent was evaporated and product was chromatographed using 10% ethyl acetate/hexane to afford the product.



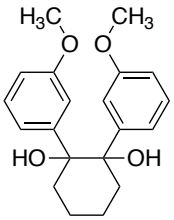
5,5'-(Ethane-1,2-diyl)bis(2-methylphenol) (4B). Following general procedure C, the product was obtained as a white solid (15 mg, 0.06 mmol) in 68% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 6.95 (d, J = 7.5 Hz, 2H), 6.67 (d, J = 1.5 Hz, 2H), 6.59 (dd, J = 7.5, 1.5 Hz, 2H), 2.74 (s, 4H), 2.14 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 140.7, 130.5, 121.4, 119.4, 114.7, 37.3, 14.9; IR (neat) 3392, 2925, 1622, 1578, 1513, 1458, 1419, 1379, 1247, 1177, 1152, 1116, 996, 861, 815, 752 cm^{-1}; HRMS (EI-TOF) *m/z* = 242.1307 calc for $C_{16}H_{18}O_2$ $[M]^+$, found 242.1316. mp = 165 – 166 °C. >95% purity. UPLC t_R = 2.24 min gradient A.



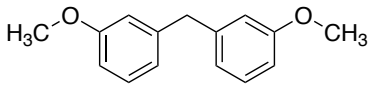
5,5'-(Ethane-1,2-diyl)bis(2-isopropylphenol) (4D). Following general procedure C, the product was obtained as an amorphous white solid (2.3 mg, 0.01 mmol) in 26% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, J = 7.8 Hz, 2H), 7.76 (d, J = 7.8 Hz, 2H), 6.59 (s, 2H), 4.60 (s, 2H), 3.15 (hep, J = 7.4 Hz, 2H), 2.80 (s, 4H), 1.24 (d, J = 7.0 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 140.9, 132.1, 126.5, 121.0, 115.4, 37.4, 27.0, 22.9; IR (neat) 3405, 2960, 2926, 2869, 1712, 1617, 1581, 1518, 1457, 1422, 1382, 1363, 1342, 1290, 1225, 1185, 1152, 1112, 1085, 1060, 956, 861, 818, 738, 635, 581, 492 cm^{-1}; HRMS (EI-TOF) *m/z* = 298.1933 calc for $C_{16}H_{18}O_2$ $[M]^+$, found 298.1933.



3,3'-(Ethane-1,2-diyl)diphenol (4A). To a solution of 1,2-bis(3-methoxyphenyl)ethane (0.600 g, 2.78 mmol) in anhydrous dichloromethane (11 mL, 0.2 M) at –78 °C was added BBr_3 (1 M solution in dichloromethane, 6.4 mL, 6.40 mmol) dropwise under an argon flow. The mixture stirred for 30 min, then slowly raised to room temperature and stirred for 12 h. The reaction was quenched *via* drop wise addition of H_2O, and extracted using ethyl acetate (5 x 30 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1). The demethylated product was obtained as a white solid (535.6 mg, 2.50 mmol) in 90% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 8.11 (s, 2H), 7.08 (t, J = 7.8 Hz, 2H), 6.72-6.69 (m, 4H), 6.66-6.64 (m, 2H), 2.81 (s, 4H); ^{13}C NMR (125 MHz, Acetone-D_6) δ 157.5, 143.6, 129.3, 119.7, 115.5, 112.9, 37.6; IR (neat) 3328, 2927, 1589, 1491, 1455, 1254, 1155, 939, 865, 783, 693 cm^{-1}; HRMS (ESI-TOF) *m/z* = 214.0994 calc for $C_{14}H_{14}O_2$ [M]$^+$, found 214.0991. mp = 130 – 134 °C.

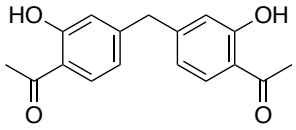


1,2-Bis(3-methoxyphenyl)cyclohexane-1,2-diol (3F). To a solution of 2-hydroxy-2-(3-methoxyphenyl)cyclohexan-1-one (60 mg, 0.27 mmol) and vacuum dried $CeCl_3$ (0.608 g, 1.63 mmol) in anhydrous THF (1.0 mL, 0.3 M) was slowly added a solution of (3-methoxyphenyl)magnesium bromide (1.0 M in diethyl ether, 1.10 mL, 1.10 mmol) at 0 °C. The mixture was stirred for 2-3 hours at room temperature. After cooling to 0 °C, the reaction was quenched *via* drop-wise addition of saturated ammonium chloride solution (2 mL). After stirring at room temperature for 10 min, the product was extracted with diethyl ether (5 x 10 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1).[5] The product was obtained as a brown liquid (60 mg, 0.18 mmol) in 67% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (t, J = 8.0 Hz, 2H), 6.79 (d, J = 7.8 Hz, 2H), 6.72 (dd, J = 7.6, 2.5 Hz, 2H), 6.63 (d, J = 1.8 Hz, 2H), 3.57 (s, 6H), (td, J = 8.1, 3.3 Hz, 2H), 1.92 (q, J = 9.2 Hz, 2H), 1.72-1.65 (m, 4H); ^{13}C NMR (125 MHz, Acetone-D_6) δ 158.4, 147.7, 127.0, 119.8, 113.3, 111.6, 76.3, 54.2, 34.7, 20.8; IR (neat) 3480, 2934, 2863, 2835, 1600, 1582, 1486, 1464, 1429, 1313, 1289, 1252, 1197, 1168, 1149, 1078, 1043, 1011, 997, 946, 895, 879, 851, 804, 786, 735, 700, 590, 571, 522, 492 cm^{-1}; HRMS (EI-TOF) *m/z* = 328.1675 calc for $C_{20}H_{24}O_4$ [M]$^+$, found 328.1671.

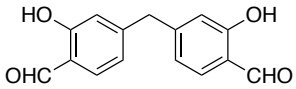


Bis(3-methoxyphenyl)methane (3H). To a round bottom flask with bis(3-methoxyphenyl)methanol (200 mg, 0.82 mmol) and 10% Pd/C (80 mg, 0.75 mmol) was added anhydrous ethanol (6.0 mL, 0.1 M). The flask was evacuated and backfilled with hydrogen gas three times and then allowed to stir for 18 h. After completion of the reaction, the flask was purged with argon and the mixture was filtered through a bed of Celite. The solvent was evaporated and the product was chromatographed (hexane/EtOAc, 10:1). The product was obtained as a

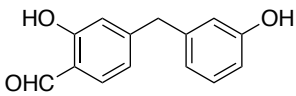
clear liquid (118 mg, 0.52 mmol) in 63% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (m, 2H), 6.83 (d, J = 7.6 Hz, 2H), 6.79-6.78 (m, 4H), 3.96 (s, 2H), 3.80 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 142.6, 129.5, 121.5, 114.9, 111.5, 55.3, 42.1; IR (neat) 3001, 2939, 2835, 1596, 1583, 1487, 1464, 1453, 1434, 1310, 1280, 1256, 1190, 1149, 1089, 1044, 996, 946, 873, 774, 774, 737, 691, 572, 554 cm^{-1}; HRMS (ESI-TOF) *m/z* = 228.1150 calc for $C_{15}H_{16}O_2$ $[M]^+$, found 228.1157.



1,1'-(Methylenebis(2-hydroxy-4,1-phenylene))bis(ethan-1-one) (3J). To a solution of bis(3-methoxyphenyl)methane (100 mg, 0.44 mmol) in anhydrous toluene (1.1 mL, 0.4 M), $TiCl_4$ (0.11 mL, 0.96 mmol) was added slowly. The mixture was stirred until gas evolution ceased. Acetyl chloride (0.09 mL, 1.31 mmol) was slowly added and the solution stirred for 0.25 h. The solution was brought to 100 °C and stirred for an additional1 h. The mixture was quenched *via* drop wise addition of H_2O (5 mL) and then extracted with dichloromethane (5 x 10 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1).[6] The product was obtained as a brown liquid (31.2 mg, 0.10 mmol) in 25% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 12.29 (s, 2H), 7.82 (d, J = 8.0 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 6.81 (s, 2H), 3.97 (s, 2H), 2.60 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.7, 163.5, 150.6, 132.6, 120.8, 119.2, 118.9, 42.5, 23.4; IR (neat) 3254, 3012, 2921, 2872, 1647, 1620, 1569, 1504, 1420, 1363, 1322, 1301, 1281, 1245, 1221, 1165, 1148, 1023, 983, 959, 822, 794, 759, 750, 704, 602 cm^{-1}; HRMS (ESI-TOF) *m/z* = 284.1049 calc for $C_{17}H_{16}O_4$ $[M]^+$, found 284.1048.

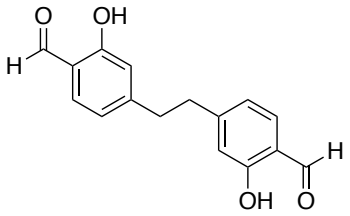


4,4'-Methylenebis(2-hydroxybenzaldehyde) (3L). To a solution of 3,3'-methylenediphenol (40.0 mg, 0.20 mmol) and anhydrous $MgCl_2$ (38.0 mg, 0.40 mmol) in THF (1.0 mL, 0.2 M) was added triethylamine (0.06 mL, 0.40 mmol). The mixture was stirred for 0.25 h whereupon paraformaldehyde (48.0 mg, 1.60 mmol) was added and After heating to reflux for 18 h, the mixture was quenched with 3 M aqueous HCl (20 mL), extracted with diethyl ether (5 x 15 mL), and washed with H_2O (3 x 20 mL) and saturated aqueous NaCl (3 x 20 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1)[7]. The product was obtained as a white solid (10.6 mg, 0.04 mmol) in 21% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 11.03 (s, 2H), 9.97 (s, 2H), 7.71 (d, J = 7.9 Hz, 2H), 7.00 (d, J = 7.9 Hz, 2H), 6.90 (s, 2H), 4.07 (s, 2H); ^{13}C NMR (125 MHz, Acetone-D_6) δ 196.7, 161.6, 150.2, 134.1, 120.9, 119.6, 117.3, 41.8; IR (neat) 3262, 3076, 2856, 1644, 1622, 1569, 1498, 1450, 1410, 1381, 1344, 1321, 1269, 1229, 1205, 1155, 1131, 983, 926, 888, 805, 733, 709, 637, 610, 598, 559, 475 cm^{-1}; HRMS (ESI-TOF) *m/z* = 256.0736 calc for $C_{15}H_{12}O_4$ $[M]^+$, found 256.0722. mp = 139 – 140 °C.

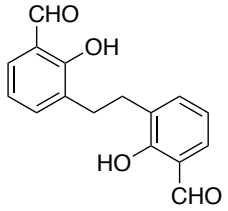


2-Hydroxy-4-(3-hydroxybenzyl)benzaldehyde (3M). To a solution of 3,3'-methylenediphenol (40.0 mg, 0.20 mmol) and anhydrous $MgCl_2$ (38.0 mg, 0.40 mmol) in THF (1.0 mL, 0.2 M) was added triethylamine (0.06 mL, 0.40 mmol). The mixture was stirred for 0.25 h whereupon paraformaldehyde (48.0 mg, 1.60 mmol) was added. After heating at reflux for 18 h, the reaction was quenched with 3 M aqueous HCl (20 mL), extracted with diethyl

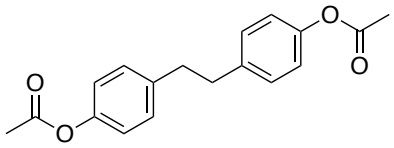
ether (5 x 15 mL), and washed with H_2O (3 x 20 mL) and saturated solution of NaCl (3 x 20 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1)[7]. The product was obtained as a light red solid (12.3 mg, 0.05 mmol) in 27% yield: ^{1}H NMR (500 MHz, Acetone-D_6) δ 9.95 (s, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.12 (t, J = 7.8 Hz, 1H), 6.95 (d, J = 7.3 Hz, 1H), 6.84 (s, 1H), 6.74-6.68 (m, 3H), 3.93 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 161.8, 155.7, 151.2, 141.0, 133.7, 129.8, 121.5, 120.7, 119.1, 117.7, 115.9, 113.5, 42.0; IR (neat) 3365, 2925, 2852, 1651, 1627, 1589, 1569, 1502, 1490, 1454, 1371, 1322, 1279, 1227, 1206, 1158, 1128, 1081, 1000, 975, 878, 809, 786, 749, 697, 674, 622, 557, 469 cm^{-1}; HRMS (EI-TOF) *m/z* = 228.0786 calc for $C_{14}H_{12}O_3$ $[M]^+$, found 228.0779. mp = 136 – 138 °C.



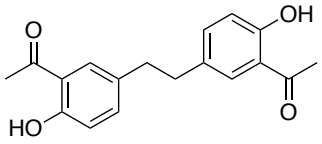
4,4'-(Ethane-1,2-diyl)bis(2-hydroxybenzaldehyde) (4N). To a solution of 3,3'-(ethane-1,2-diyl)diphenol (0.700 mg, 3.27 mmol) and anhydrous $MgCl_2$ (1.24 g, 13.1 mmol) in THF (17.0 mL, 0.2 M) was added triethylamine (1.8 mL, 13.1 mmol). The mixture was stirred for 0.25 h whereupon paraformaldehyde (0.784 g, 26.14 mmol) was added. After heating at reflux for 18 h, the reaction was quenched with 3 M aqueous HCl (50 mL), extracted with diethyl ether (5 x 35 mL), and washed with H_2O (3 x 30 mL) and saturated solution of NaCl (3 x 30 mL)[7]. The combined organic fractions were dried over Na_2SO_4, concentrated, and recrystallized using acetone. The product was obtained as a white solid (0.400 mg, 1.48 mmol) in 45% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 2H), 7.45 (d, J = 7.9 Hz, 2H), 6.80 (m, 4H), 2.94 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 162.0, 151.4, 133.9, 120.5, 119.3, 117.3, 37.3; IR (neat) 3242, 2923, 2852, 2759, 1667, 1565, 1503, 1439, 1381, 1299, 1198, 969, 814, 736, 714, 551 cm^{-1}; HRMS (EI-TOF) *m/z* = 270.0892 calc for $C_{16}H_{14}O_4$ $[M]^+$, found 270.0903. mp = 107 – 108 °C.



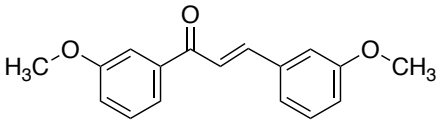
3,3'-(Ethane-1,2-diyl)bis(2-hydroxybenzaldehyde) (3Q). To a solution of 3,3'-methylenediphenol (50.0 mg, 0.23 mmol) and anhydrous $MgCl_2$ (44.4 mg, 0.47 mmol) in THF (1.2 mL, 0.2 M) was added triethylamine (0.07 mL, 0.47 mmol). The mixture was stirred for 0.25 h whereupon paraformaldehyde (56 mg, 1.87 mmol) was added. After heating at reflux for 18 h, the reaction was quenched with 3 M aqueous HCl (20 mL), extracted with diethyl ether (5 x 15 mL), and washed with H_2O (3 x 20 mL) and saturated solution of NaCl (3 x 20 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1)[7]. The product was obtained as an amorphous white solid (4.2 mg, 0.02 mmol) in 7% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.32 (d, J = 0.5 Hz, 2H), 9.89 (s, 2H), 7.42 (dd, J = 7.5, 1.7 Hz, 2H), 7.33 (dd, J = 7.5, 1.5 Hz, 2H), 6.91 (t, J = 7.5 Hz, 2H), 3.00 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 159.8, 137.4, 131.8, 130.2, 120.2, 119.4, 28.9; IR (neat) 3178, 3084, 2928, 2845, 1645, 1615, 1484, 1443, 1385, 1352, 1325, 1265, 1239, 1218, 1153, 1076, 978, 853, 792, 756, 733, 696, 645, 464 cm^{-1}; HRMS (ESI-TOF) *m/z* = 270.0892 calc for $C_{16}H_{14}O_4$ $[M]^+$, found 270.0908.



Ethane-1,2-diylbis(4,1-phenylene) diacetate (3X). To a solution of 1,2-bis(4-methoxyphenyl)ethane (50.0 mg, 0.21 mmol) in anhydrous toluene (0.5 mL, 0.4 M), $TiCl_4$ (50.0 μL, 0.45 mmol) was added slowly. The mixture was stirred until gas evolution ceased. Acetyl chloride (30.0 μL, 0.45 mmol) was added slowly and the solution stirred for 0.25 h. The mixture was brought to 100 °C and stirred for an additional 1 h. The mixture was quenched *via* drop-wise addition of H_2O (5 mL) and then extracted with dichloromethane (5 x 10 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1)[6]. The product was obtained as a brown liquid (29.4 mg, 0.10 mmol) in 48% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 4H), 7.29 (d, J = 8.0 Hz, 4H), 2.51 (s, 6H), 2.37 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 143.4, 134.9, 129.0, 128.2, 25.6, 20.5; IR (neat) 2922, 1679, 1605, 1573, 1511, 1429, 1405, 1356, 1265, 1211, 1181, 1112, 1074, 1037, 1018, 953, 814, 713, 673, 637, 591, 567, 460 cm^{-1}; HRMS (ESI-TOF) *m/z* = 299.1283 calc for $C_{18}H_{19}O_4$ $[M+H]^+$, found 299.1277.

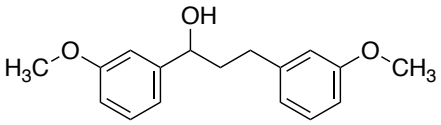


1,1'-(Ethane-1,2-diylbis(6-hydroxy-3,1-phenylene))bis(ethan-1-one) (3AA). To a solution of 1,2-bis(4-methoxyphenyl)ethane (50.0 mg, 0.21 mmol) in anhydrous toluene (0.5 mL, 0.4 M), was added $TiCl_4$ (50.0 μL, 0.45 mmol) slowly. The mixture was stirred until gas evolution ceased. Acetyl chloride (30.0 μL, 0.45 mmol) was added slowly and the solution stirred for 0.25 h. The mixture was brought to 100 °C and stirred for 1 h. The mixture was quenched *via* drop-wise addition of H_2O (5 mL) and then extracted with dichloromethane (5 x 10 mL)[6]. The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1). The product was obtained as a light brown solid (14 mg, 0.05 mmol) in 24% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.12 (s, 2H), 7.38 (d, J = 2.2 Hz, 2H), 7.26 (dd, J = 8.5, 2.2 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 2.86 (s, 4H), 2.56 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.5, 160.9, 137.1, 131.5, 130.4, 119.5, 118.5, 37.2, 26.8; IR (neat) 3340, 3033, 2861, 1643, 1586, 1480, 1421, 1366, 1345, 1321, 1303, 1263, 1201, 1147, 1125, 1069, 1024, 960, 886, 845, 788, 635, 541, 472 cm^{-1}; HRMS (ESI-TOF) *m/z* 299.1283 calc for $C_{18}H_{19}O_4$ $[M+H]^+$, found 299.1293. mp = 107 – 108 °C.

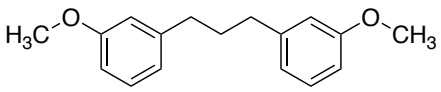


(*E*)-1,3-Bis(3-methoxyphenyl)prop-2-en-1-one (3AB). To a flame dried round bottom flask was added 3-methoxybenzaldehyde (2.44 mL, 20.0 mmol), 1-(3-methoxyphenyl)ethan-1-one (2.74 mL, 20.0 mmol), and BF_3•OEt_2 (1.24 mL, 10.0 mmol). The mixture was stirred for 4 h, then quenched with H_2O (30 mL) and extracted with ethyl acetate (5 x 40 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed (hexane/EtOAc, 10:1)[8]. The product was obtained as a brown liquid (0.943 g, 3.52 mmol) in 18% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 15.7 Hz, 1H), 7.59 (dt, J = 7.6, 1.1 Hz, 1H), 7.54 (dd, J = 2.1, 1.0 Hz, 1H), 7.48 (d, J = 15.7 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 7.7 Hz, 1H), 7.14 (t, J = 2.1 Hz, 1H), 7.11 (ddd, J = 9, 2.7, 0.8 Hz, 1H) 6.94 (ddd, J = 8.8, 2.5, 0.5 Hz,

1H), 3.85 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 160.0, 159.9, 144.7, 139.6, 136.3, 130.0, 129.6, 122.4, 121.12, 121.07, 119.3, 116.3, 113.5, 113.0, 55.5, 55.3; IR (neat) 3002, 2938, 2835, 1662, 1578, 1485, 1452, 1430, 1314, 1286, 1257, 1195, 1165, 1088, 1028, 993, 979, 878, 847, 776, 728, 683, 568, 549, 502 cm^{-1}; HRMS (EI-TOF) *m/z* = 268.1099 calc for $C_{17}H_{16}O_3$ [M]$^+$, found 268.1101.

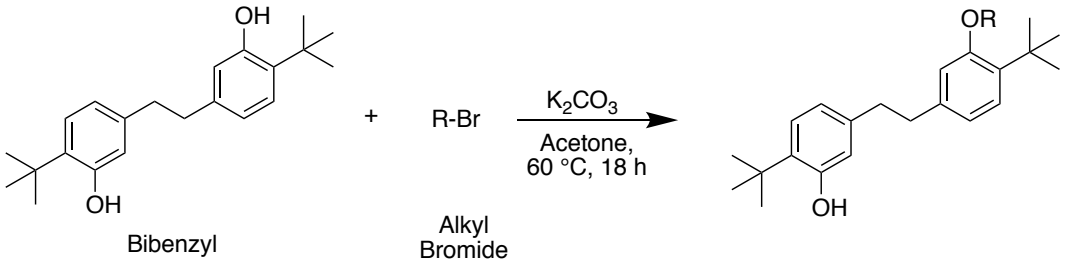


1,3-Bis(3-methoxyphenyl)propan-1-ol (3AC). To a flame dried round bottom flask, was added $Pd(OAc)_2$ (20 mg, 0.09 mmol) and $NaBH_4$ (33.1 mg, 0.88 mmol). (*E*)-1,3-Bis(3-methoxyphenyl)prop-2-en-1-one (235 mg, 0.88 mmol) was dissolved in $CHCl_3$ (1.0 mL, 0.9 M) and the solution added. With a balloon as an outlet for H_2 gas produced, MeOH (4.0 mL, 0.2 M) was slowly added. After completion, the mixture was filtered through Celite. The solvent was evaporated and the product was chromatographed (hexane/EtOAc, 10:1). The product was obtained as a clear liquid (31.6 mg, 0.12 mmol) in 13% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, J = 8.0 Hz, 1H), 7.21 (t, J = 7.7 Hz, 1H), 6.94-6.92 (m, 2H), 6.84-6.81 (m, 1H), 6.80 (d, J = 7.5 Hz, 1H), 6.76-6.73 (m, 2H), 4.66 (dd, J = 6.4, 2.2 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 2.77-2.63 (m, 2H), 2.15-1.99 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 159.7, 147.8, 143.9, 129.1, 128.9, 120.5, 118.0, 113.9, 112.1, 111.3, 111.0, 72.5, 54.4, 54.4, 41.2, 31.9; IR (neat) 3417, 2939, 2835, 1600, 1584, 1487, 1454, 1434, 1316, 1256, 1191, 1151, 1039, 995, 938, 867, 780, 725, 696, 561, 502, 471 cm^{-1}; HRMS (ESI-TOF) *m/z* = 272.1412 calc for $C_{17}H_{20}O_3$ [M]$^+$, found 272.1404.

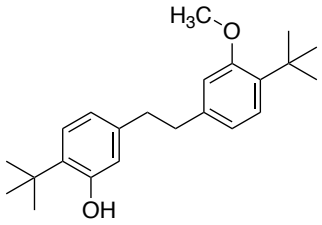


1,3-Bis(3-methoxyphenyl)propane (3AD). To a flame dried round bottom flask, was added $Pd(OAc)_2$ (20 mg, 0.09 mmol) and $NaBH_4$ (33.1 mg, 0.88 mmol). (*E*)-1,3-Bis(3-methoxyphenyl)prop-2-en-1-one (0.235 g, 0.88 mmol) was dissolved in $CHCl_3$ (1.0 mL, 0.9 M) and the solution added. With a balloon as an outlet for H_2 gas produced, MeOH (4.0 mL, 0.2 M) was slowly added. After reaction completion, the mixture was filtered through Celite. The solvent was evaporated and the product was chromatographed (hexane/EtOAc, 10:1). The product was obtained as a dark orange liquid (17 mg, 0.07 mmol) in 8% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (dd, J = 8.2, 1.2 Hz, 2H), 6.79 (d, J = 7.5, 2H) 6.75-6.73 (m, 4H), 3.80 (s, 6H), 2.64 (t, J = 7.5, 4H), 1.96 (m, 2H); ^{13}C NMR (125 MHz, Acetone-D_6) δ 159.8, 143.8, 129.1, 120.5, 113.9, 111.0, 54.4, 35.2, 32.8. IR (neat) 2936, 2834, 1601, 1583, 1487, 1453, 1436, 1313, 1286, 1258, 1190, 1164, 1151, 1084, 1044, 996, 866, 775, 752, 737, 694, 571 cm^{-1}; HRMS (EI-TOF) *m/z* = 256.1463 calc for $C_{17}H_{20}O_2$ [M]$^+$, found 256.1439.

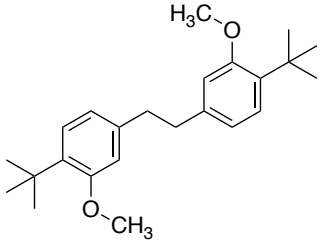
General Procedure D: Monoalkylation of Bibenzyl Analogs



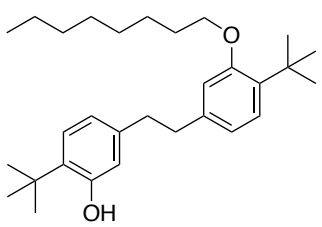
To a 10 mL microwave vial was added the bibenzyl analog (1.0 equiv), K_2CO_3 (1.5 equiv), and HPLC grade acetone (0.2 M). The vial was sealed with a septum and, under an inert atmosphere, the alkyl bromide (0.9 equiv) added. The septum was replaced with a crimping cap and the vessel sealed and stirred for the indicated time at 60 °C. When the reaction was finished, it was quenched with H_2O (15 mL). The mixture was extracted with dichloromethane (5 x 15 mL) and ethyl acetate (5 x 15 mL). The combined organic layers were washed with brine (5 x 10 mL), dried over Na_2SO_4, concentrated, and chromatographed (10% ethyl acetate/hexane) to afford the product.



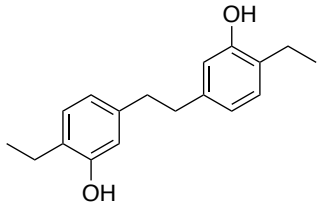
2-(*tert*-Butyl)-5-(4-(*tert*-butyl)-3-methoxyphenethyl)phenol (3AE). Following general procedure D, the product was obtained as a white solid (7 mg, 0.02 mmol) in 40% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 8.0 Hz, 2H), 6.64 (s, 1H), 6.50 (s, 1H), 4.62 (s, 1H), 3.78 (s, 3H), 2.84 (m, 4H), 1.39 (s, 9H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4 154.0, 141.1, 140.8, 135.9, 133.7, 127.0, 126.5, 120.5, 119.9, 116.7, 112.0, 54.97, 37.4, 37.0, 34.6, 34.3, 29.8, 29.7; IR (neat) 3527, 2997, 2954, 2867, 1612, 1571, 1504, 1484, 1463, 1412, 1390, 1360, 1296, 1258, 1188, 1173, 1137, 1087, 1040, 943, 889, 853, 817, 729, 638, 572, 541, 502 cm^{-1}; HRMS (EI-TOF) *m/z* = 340.2402 calc for $C_{23}H_{32}O_2$ $[M]^+$, found 340.2395. 94% purity. UPLC t_R = 3.13 min gradient A.



1,2-Bis(4-(*tert*-butyl)-3-methoxyphenyl)ethane (4K). Following general procedure D, the product was obtained as a white solid (6 mg, 0.02 mmol) in 17% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, J = 7.9 Hz, 2H), 6.77 (d, J = 7.9 Hz, 2H), 6.65 (s, 2H), 3.79 (s, 6H), 2.89 (s, 4H), 1.37 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 140.9, 135.8, 126.4, 120.0, 112.1, 55.0, 37.6, 34.5, 29.8; IR (neat) 2996, 2953, 2864, 1611, 1571, 1504, 1484, 1464, 1411, 1390, 1359, 1295, 1257, 1173, 1151, 1087, 1041, 933, 851, 817, 724, 639, 543 cm^{-1}; HRMS (EI-TOF) *m/z* = 354.2559 calc for $C_{24}H_{34}O_2$ $[M]^+$, found 354.2574. mp = 129 – 130 °C. >95% purity. UPLC t_R = 2.88 min gradient B.



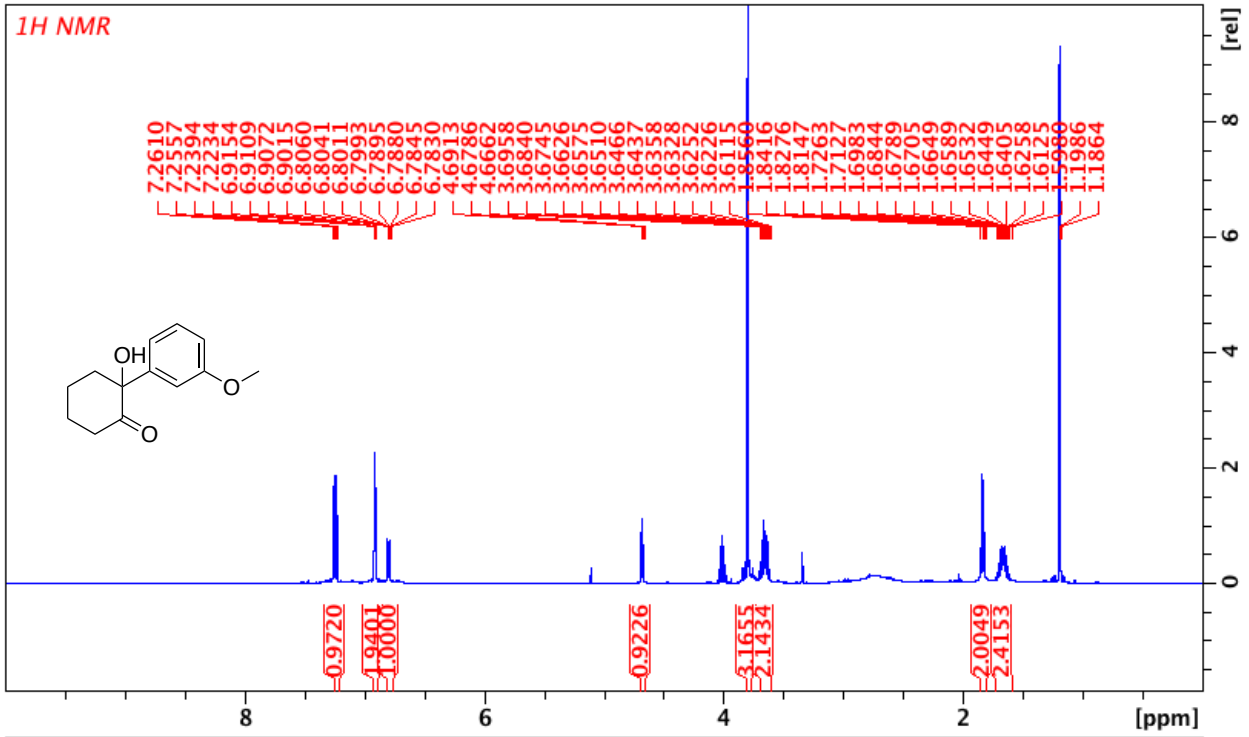
2-(*tert*-Butyl)-5-(4-(*tert*-butyl)-3-(octyloxy)phenethyl)phenol (4O). Following general procedure D, the product was obtained as a light yellow liquid (15 mg, 0.03 mmol) in 49% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, J = 7.9, 1.8 Hz, 2H) 6.77-6.74 (m, 2H), 6.66 (s, 1H), 6.53 (s, 1H), 4.69 (s, 1H), 3.93 (t, J = 6.5 Hz, 2H), 2.85-2.83 (m, 4H), 1.83 (pentet, J = 7.0 Hz, 2H), 1.51 (m, 3H), 1.41 (s, 9H), 1.39 (s, 9H), 1.34-1.26 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 154.0, 141.2, 140.7, 135.6, 133.7, 127.0, 126.5, 120.5, 119.6, 116.7, 112.1, 67.7, 37.4, 37.0, 34.6, 34.3, 31.8, 29.9, 29.7, 29.5, 29.3, 29.2, 26.4, 22.7, 14.1; IR (neat) 3527, 2925, 2857, 1611, 1572, 1503, 1467, 1416, 1390, 1360, 1297, 1258, 1179, 1138, 1084, 1033, 852, 817, 724, 637, 572, 502 cm^{-1}; HRMS (EI-TOF) *m/z* = 438.3498 calc for $C_{30}H_{46}O_2$ $[M]^+$, found 438.3493.

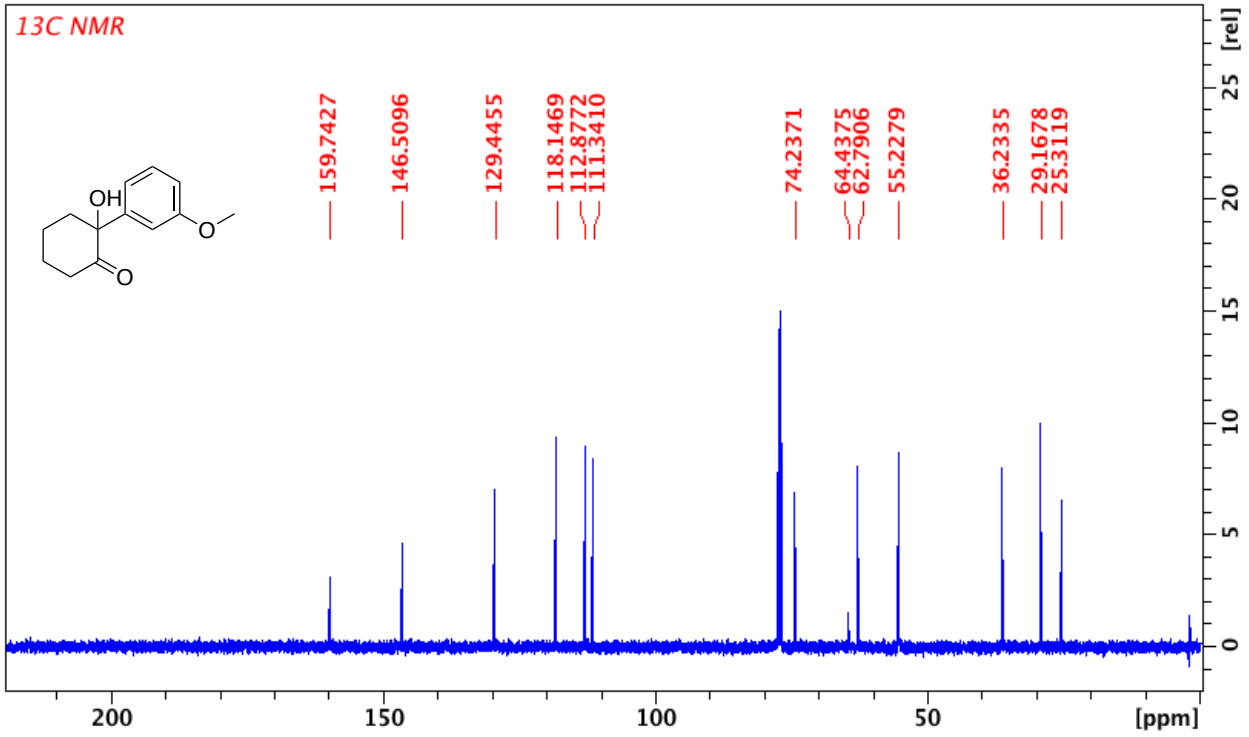


5,5'-(Ethane-1,2-diyl)bis(2-ethylphenol) (4C). In a microwave vial, 5,5'-(ethane-1,2-diyl)bis(2-(1-hydroxyethyl)phenol) (15 mg, 0.05 mmol) was dissolved in chlorobenzene (0.1 M). The solution was cooled to 0 °C, then BH_3•SMe_2 was added slowly dropwise. The solution stirred at rt for 0.25 h, raised to 80 °C for 3 h, then raised to 130 °C for 18 h. The mixture was quenched with Na_2CO_3 (10 mL), extracted with dichloromethane (5 x 10 mL) and washed with brine (5 x 10 mL). The combined organic fractions were dried over Na_2SO_4, concentrated, and chromatographed(hexane/EtOAc, 10:1). The product was obtained as an amorphous white solid (10 mg, 0.04 mmol) in 74% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, J = 7.6 Hz, 2H), 6.72 (d, J = 7.6 Hz, 2H), 6.59 (s, 2H), 4.63 (s, 2H), 2.80 (s, 4H), 2.59 (q, J = 7.5 Hz, 4H), 1.22 (t, J = 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 141.0, 129.2, 127.3, 120.9, 115.2, 37.3, 30.9, 22.6; IR (neat) 3270, 2965, 2921, 2872, 2860, 1621, 1586, 1427, 1243, 1120, 862, 821 cm^{-1}; HRMS (EI-TOF) *m/z* = 270.1620 calc for $C_{18}H_{22}O_2$ $[M]^+$, found 270.1617. >95% purity. UPLC t_R = 2.46 min gradient A.

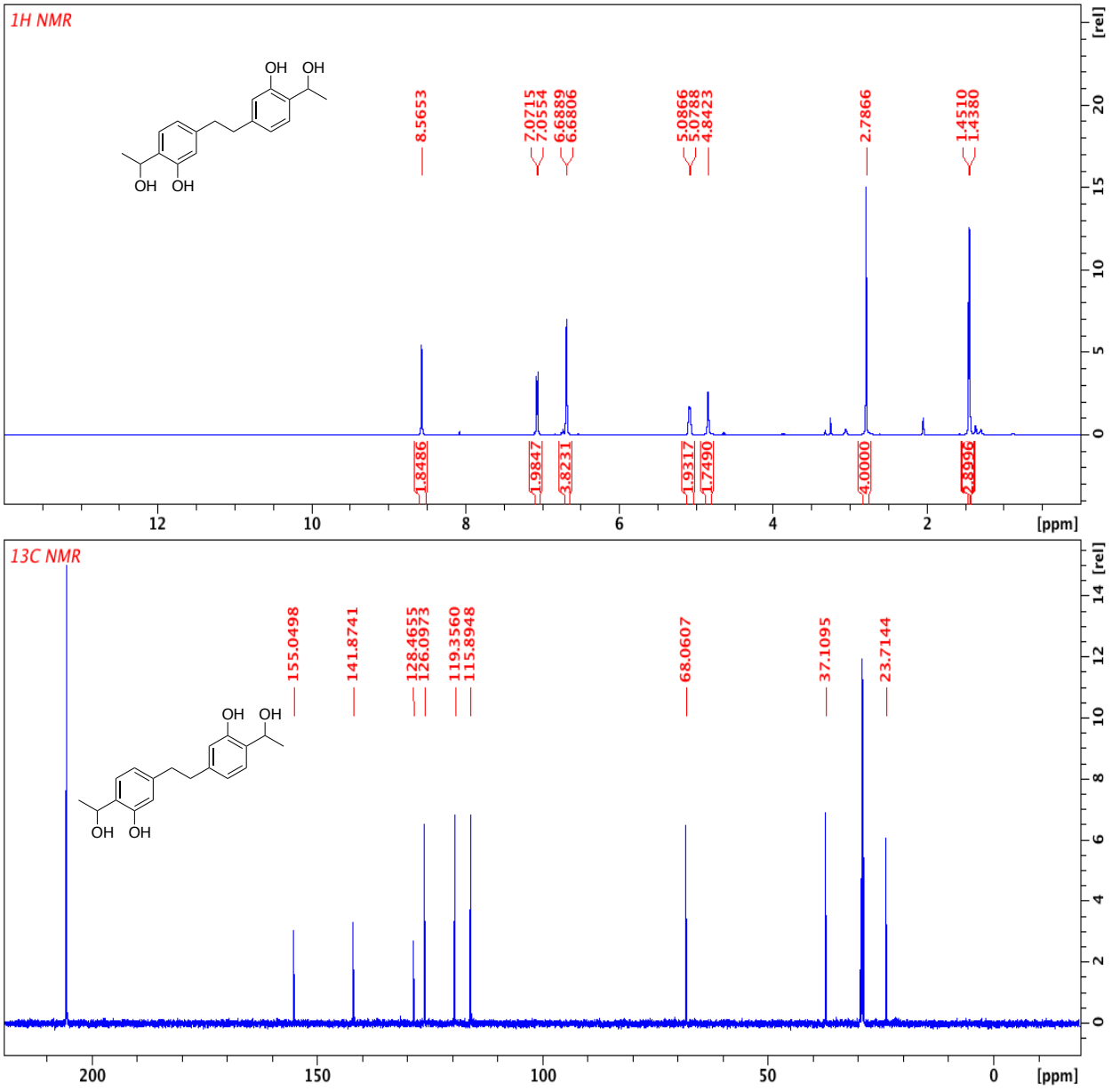
4. Experimental Spectra

2-Hydroxy-2-(3-methoxyphenyl)cyclohexan-1-one (3E)

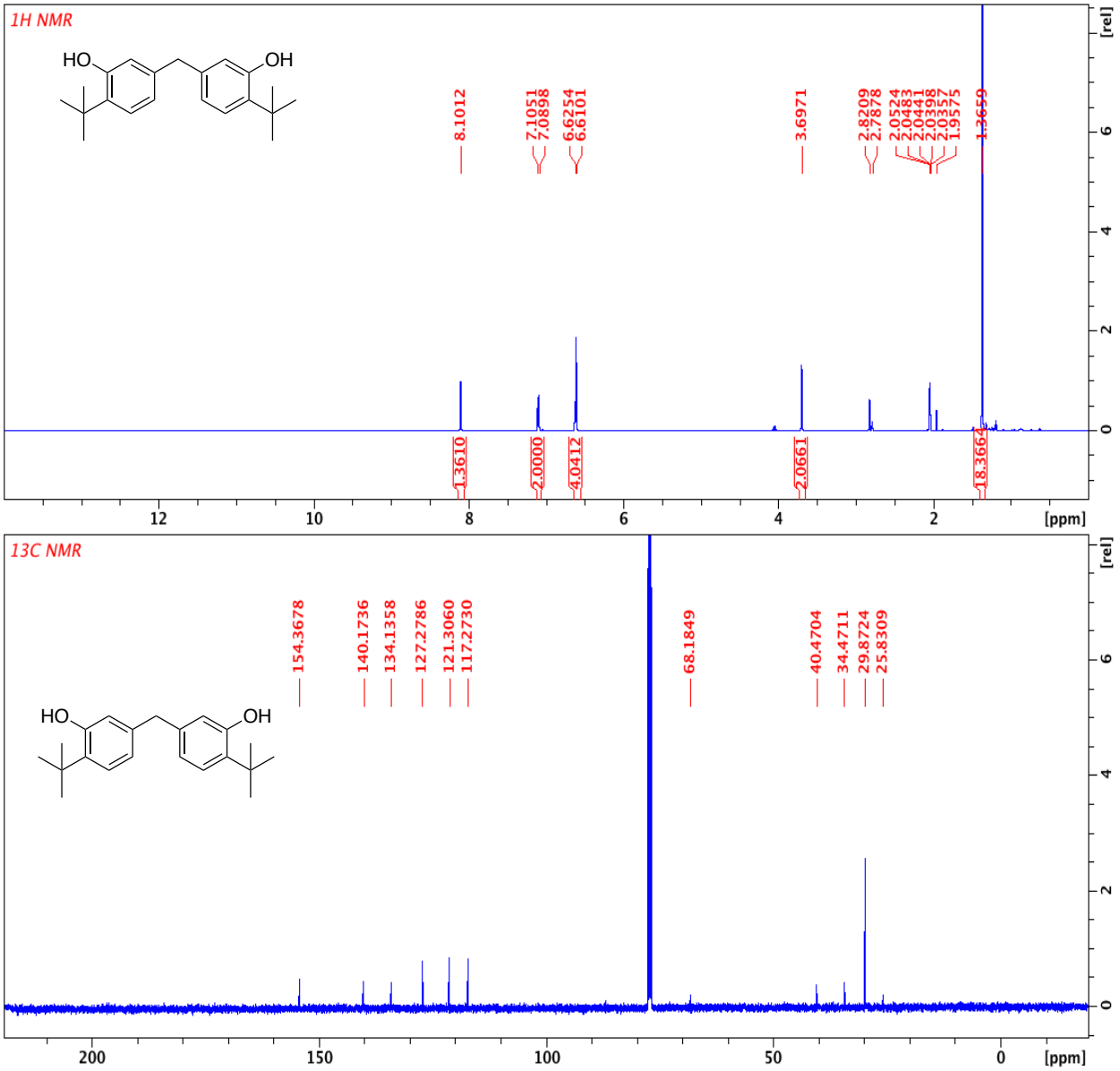




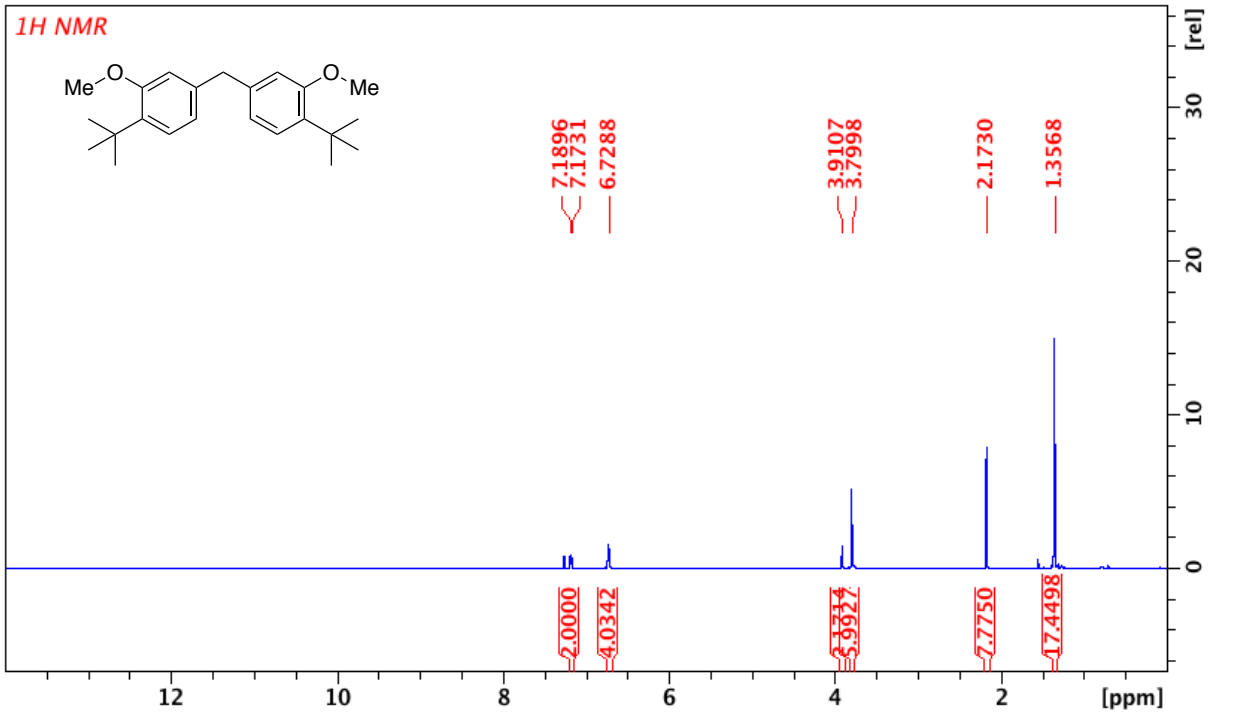
5,5'-(Ethane-1,2-diyl)bis(2-(1-hydroxyethyl)phenol) (4E)

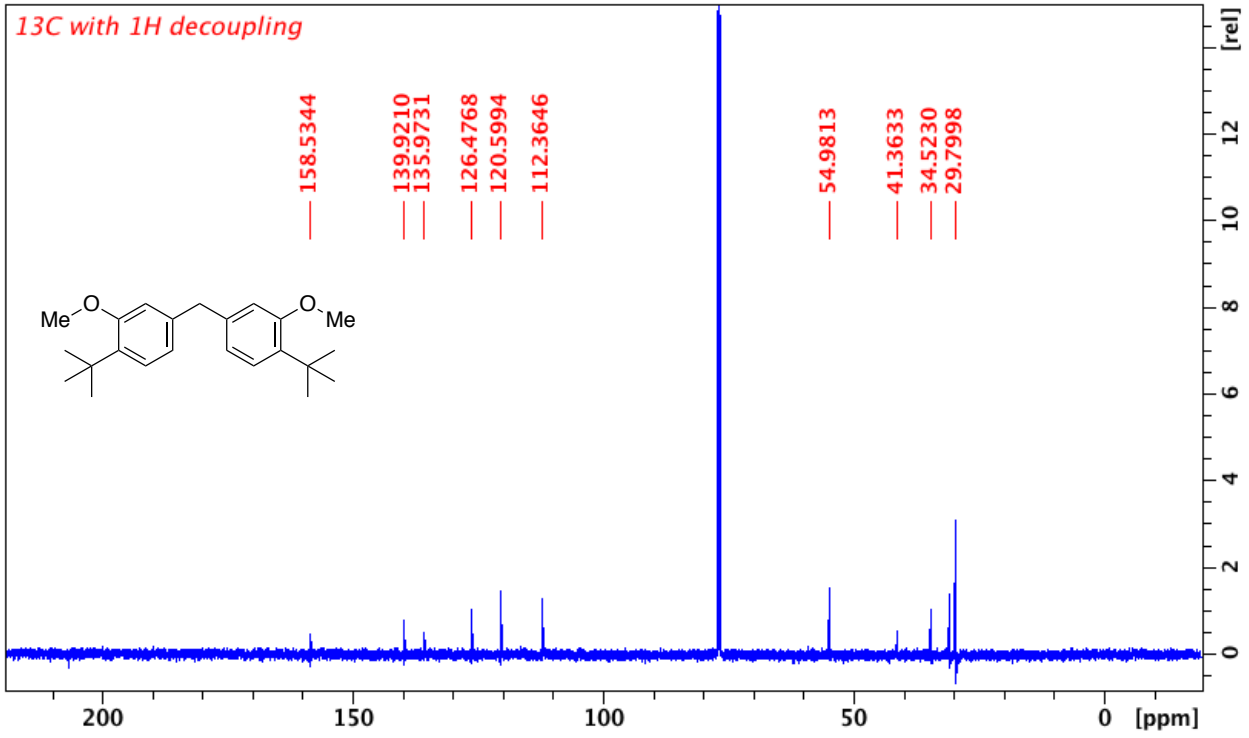


5,5'-Methylenebis(2-(*tert*-butyl)phenol) (3N)

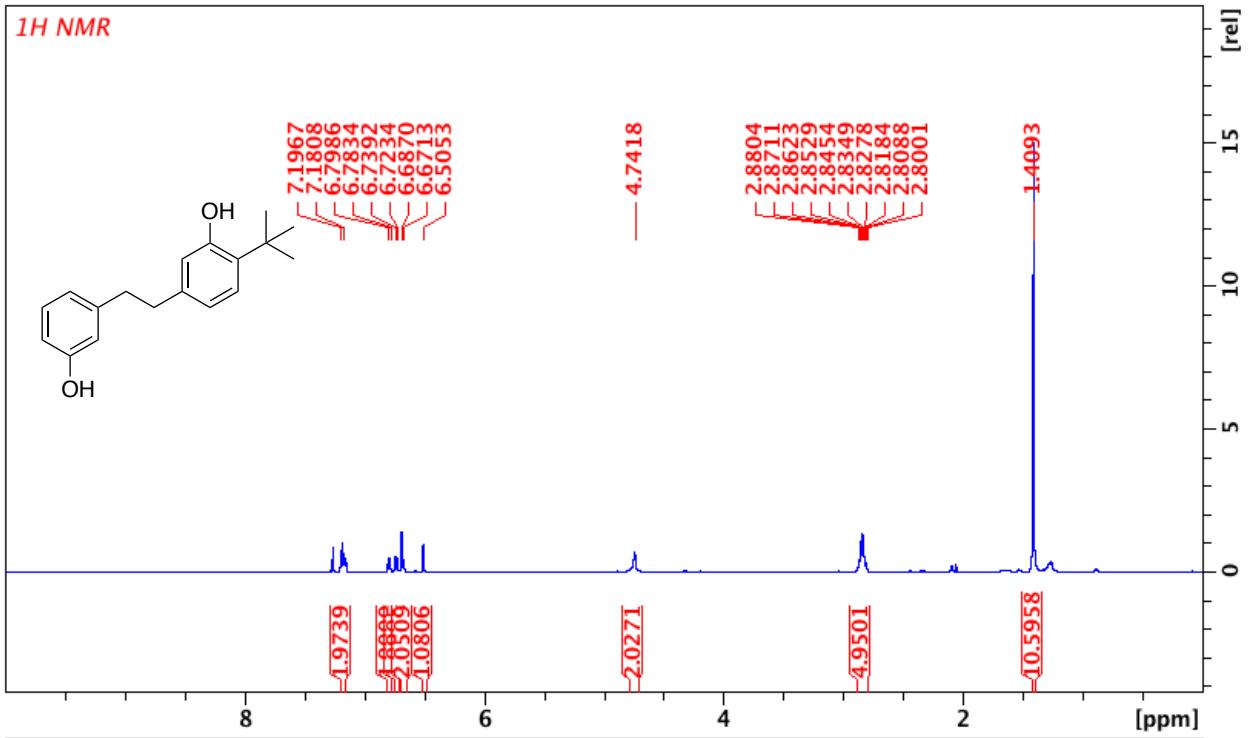


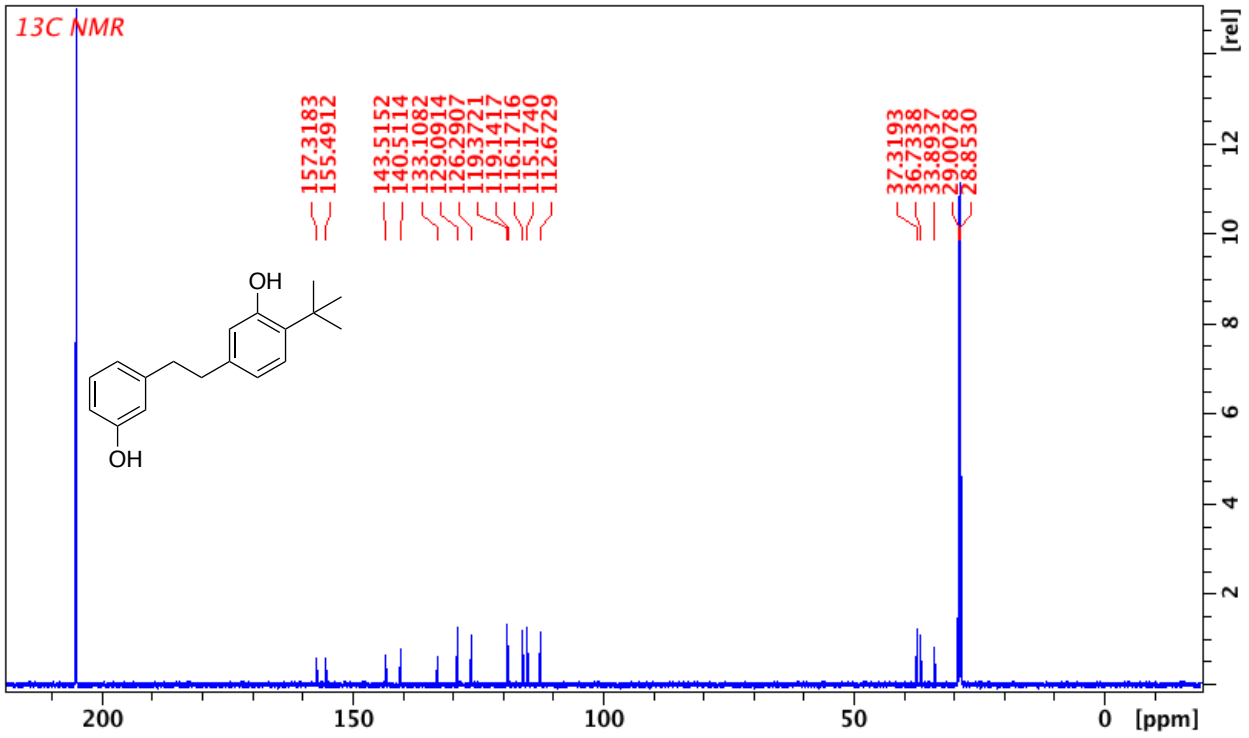
Bis(4-(*tert*-butyl)-3-methoxyphenyl)methane (4L)



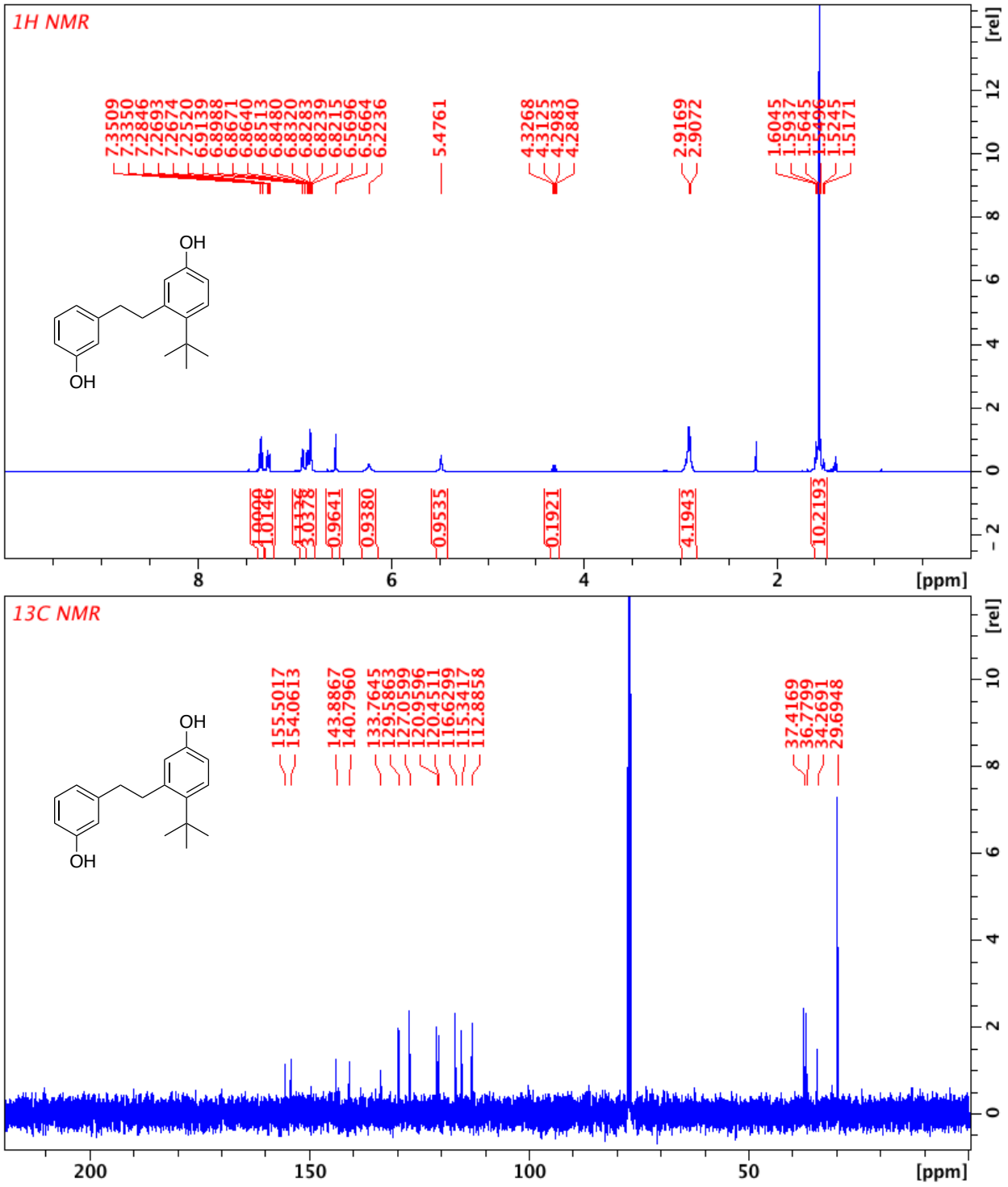


2-(*tert*-Butyl)-5-(3-hydroxyphenethyl)phenol (4AF)

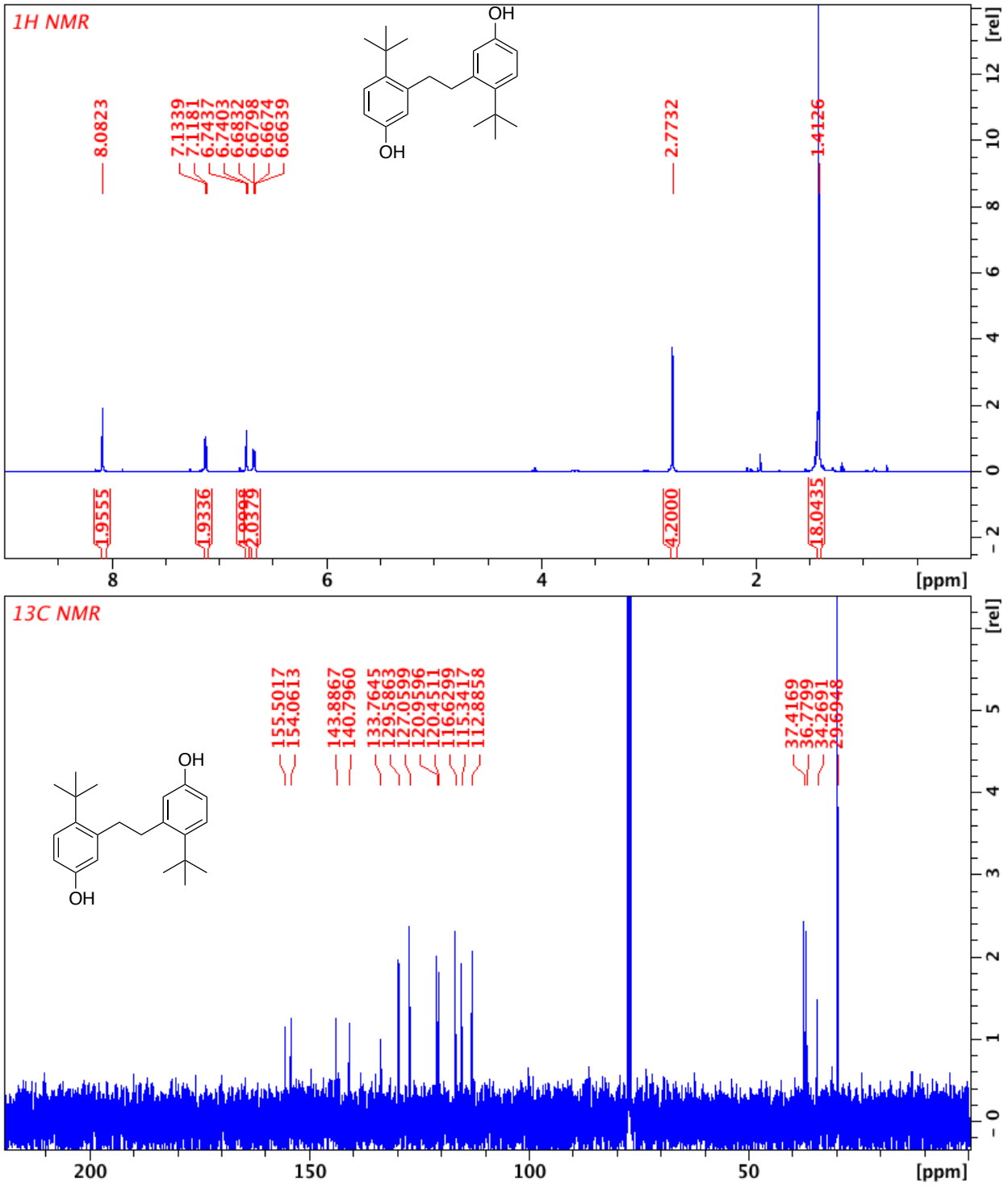




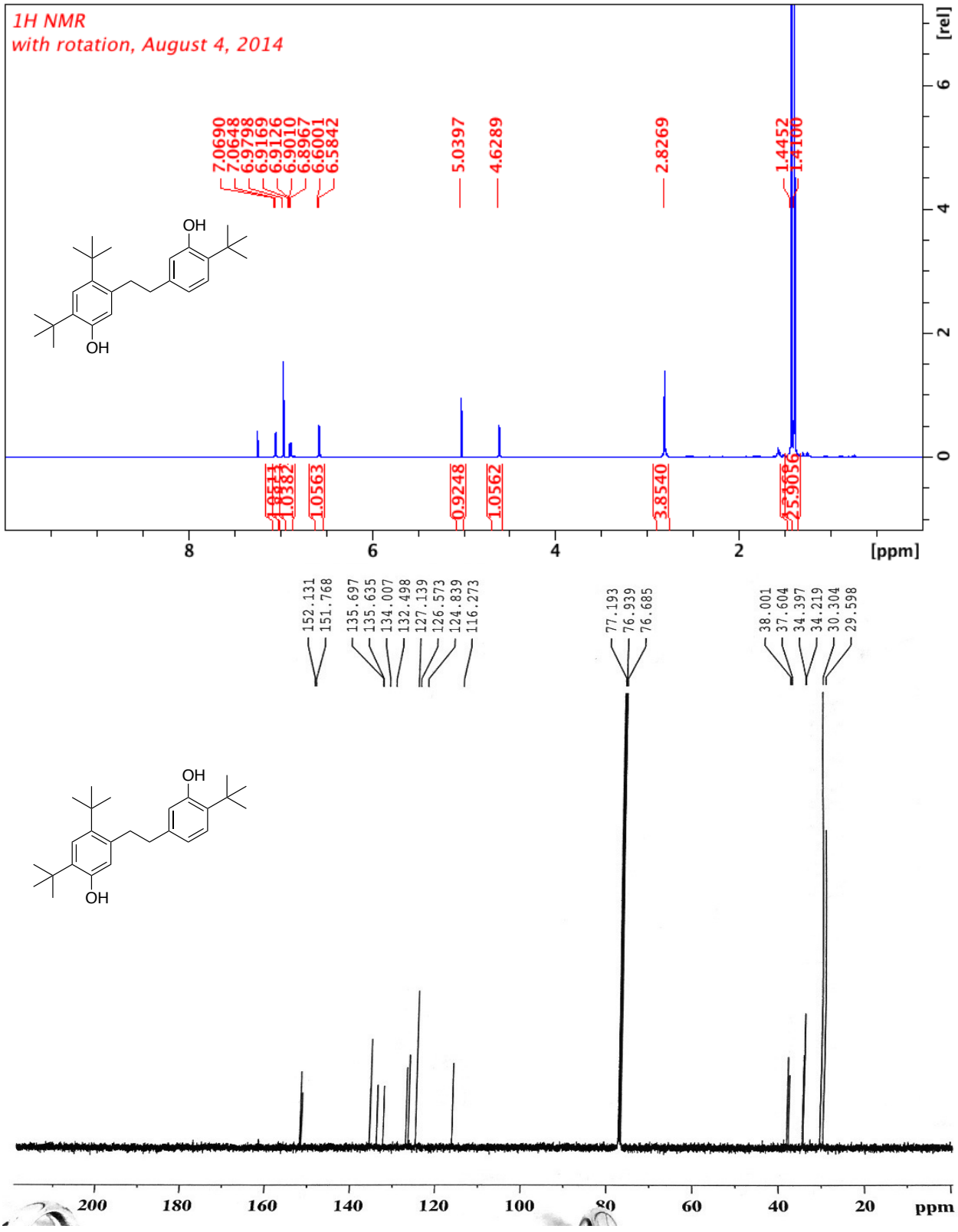
4-(*tert*-Butyl)-3-(3-hydroxyphenethyl)phenol (4F)



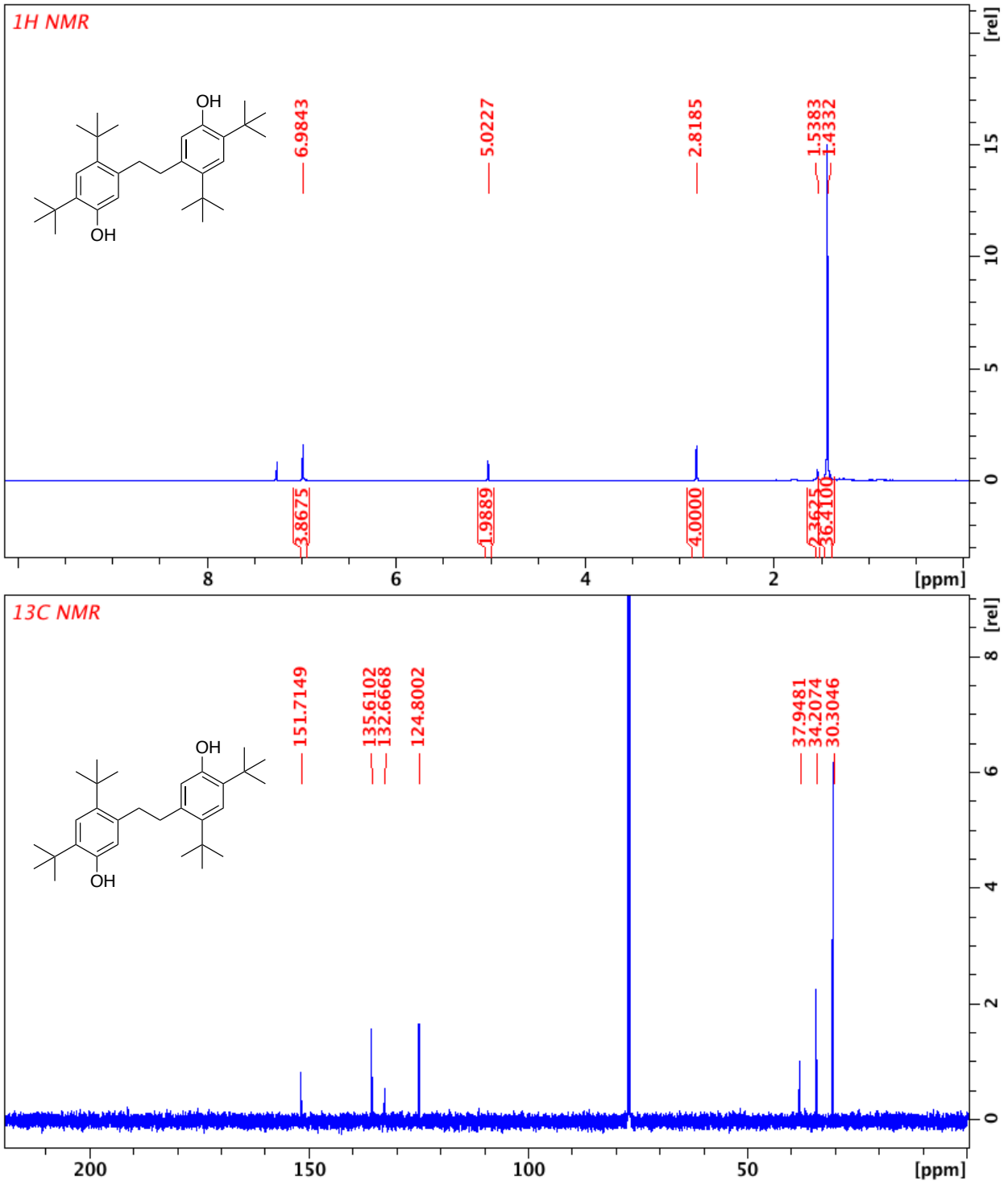
3,3'-(Ethane-1,2-diyl)bis(4-(*tert*-butyl)phenol) (4G)



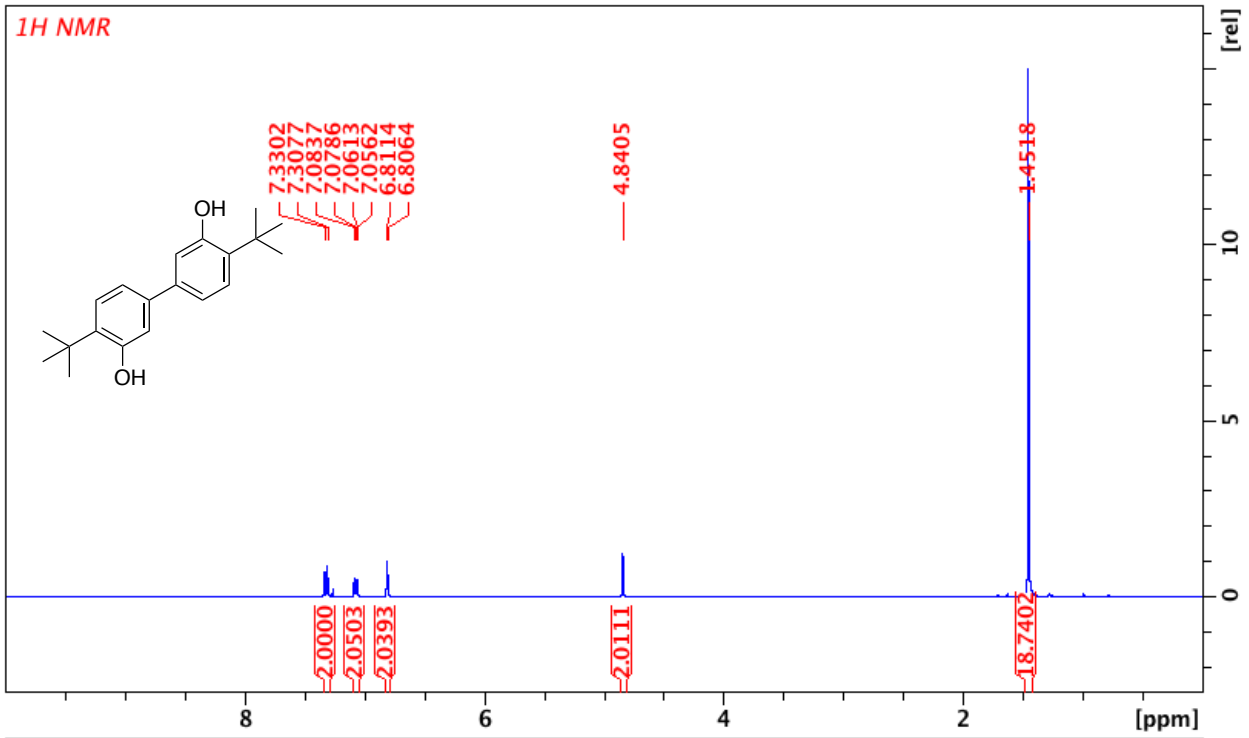
2,4-Di-*tert*-butyl-5-(4-(*tert*-butyl)-3-hydroxyphenethyl)phenol (4J)

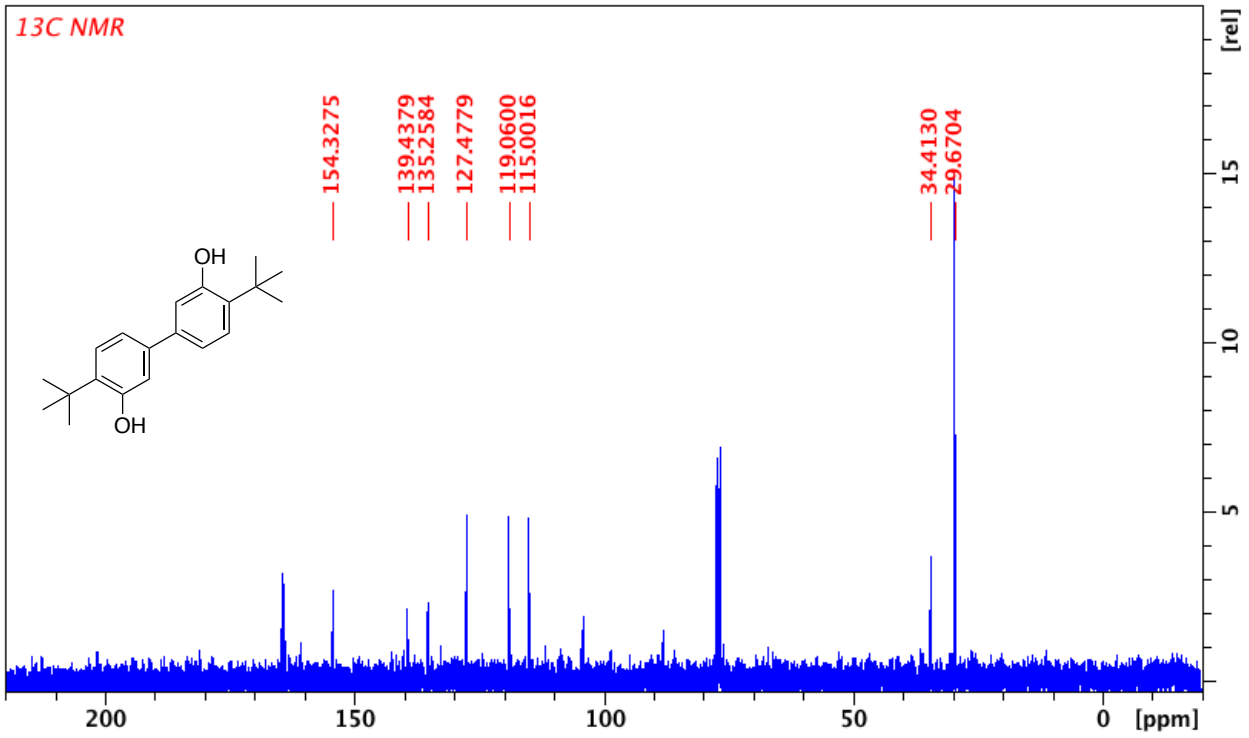


5,5'-(Ethane-1,2-diyl)bis(2,4-di-*tert*-butylphenol) (4I).

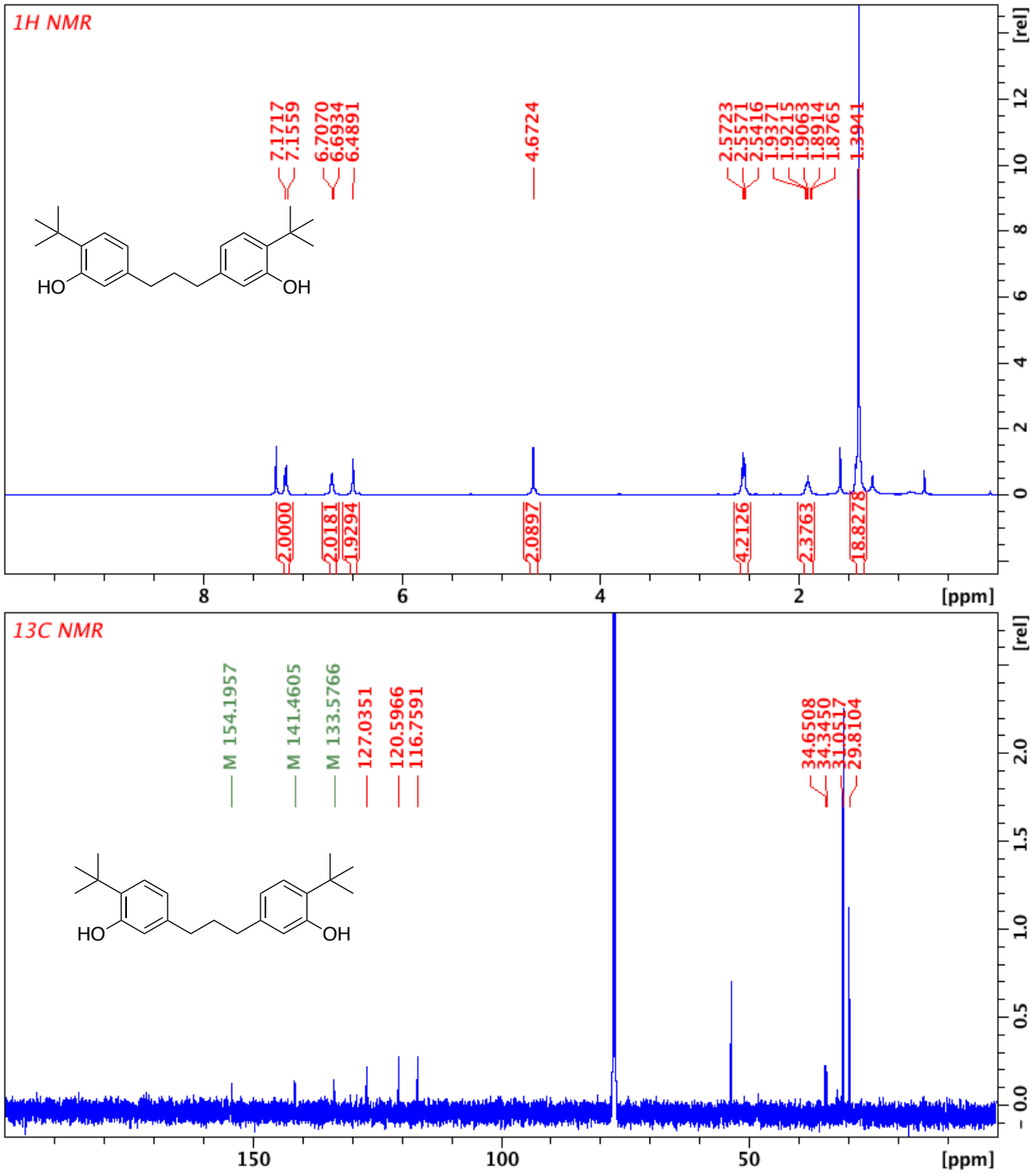


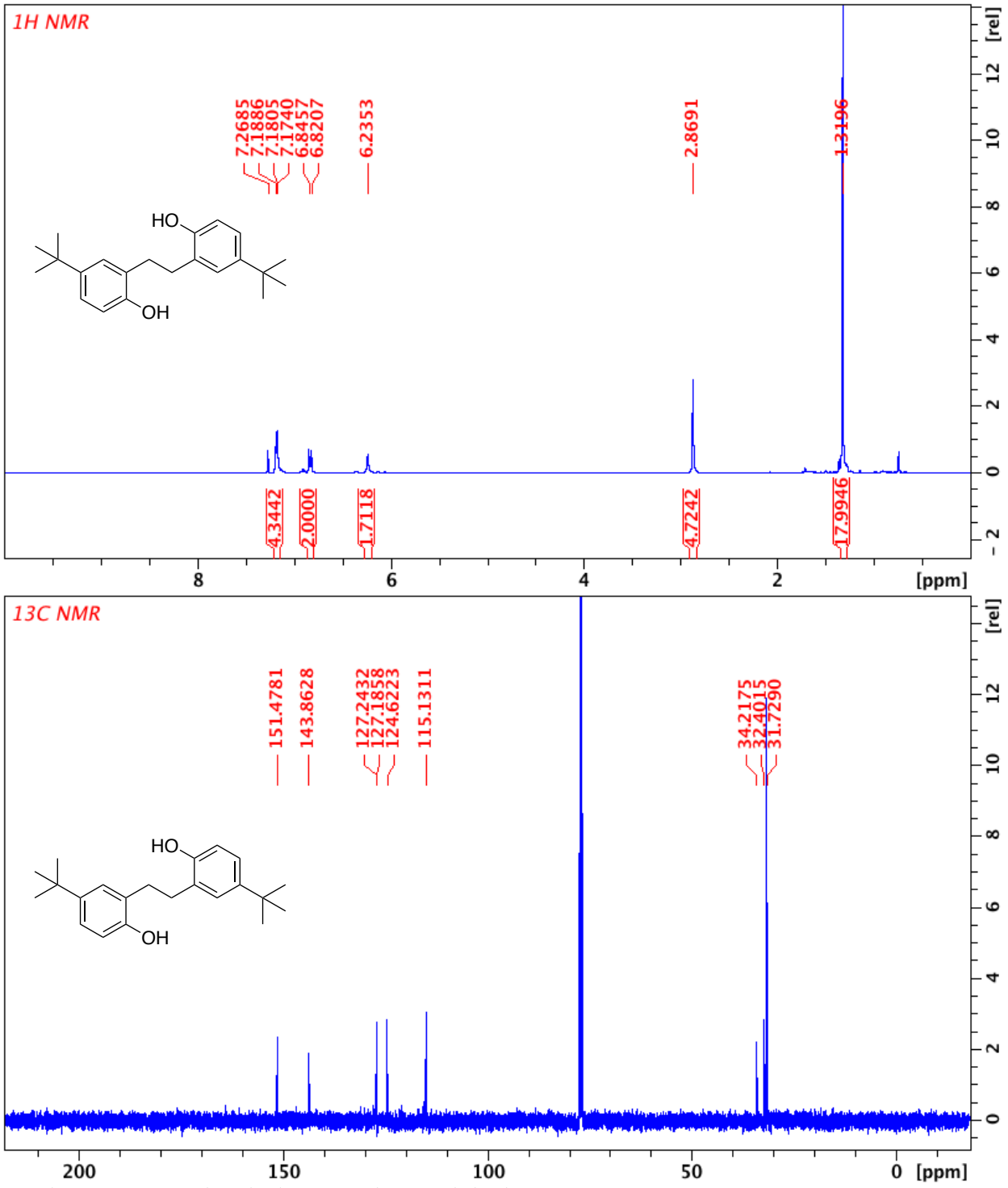
4,4'-Di-*tert*-butyl-[1,1'-biphenyl]-3,3'-diol (4P)





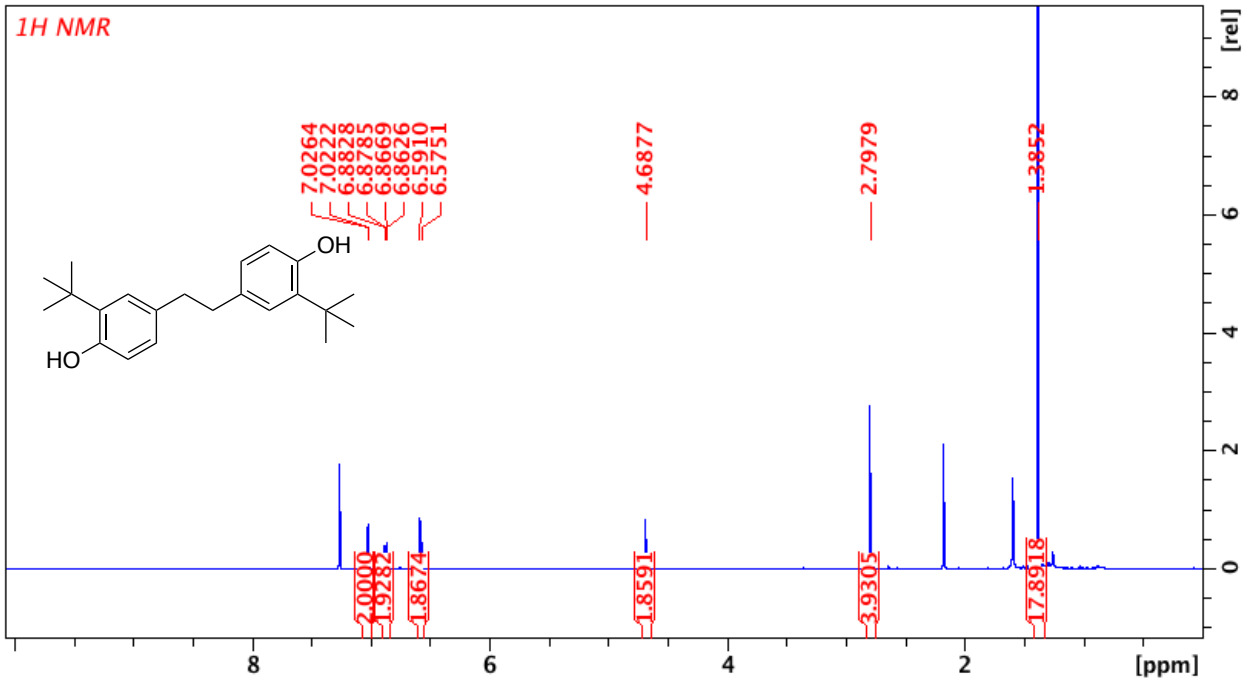
5,5'-(Propane-1,3-diyl)bis(2-(*tert*-butyl)phenol) (4Q)

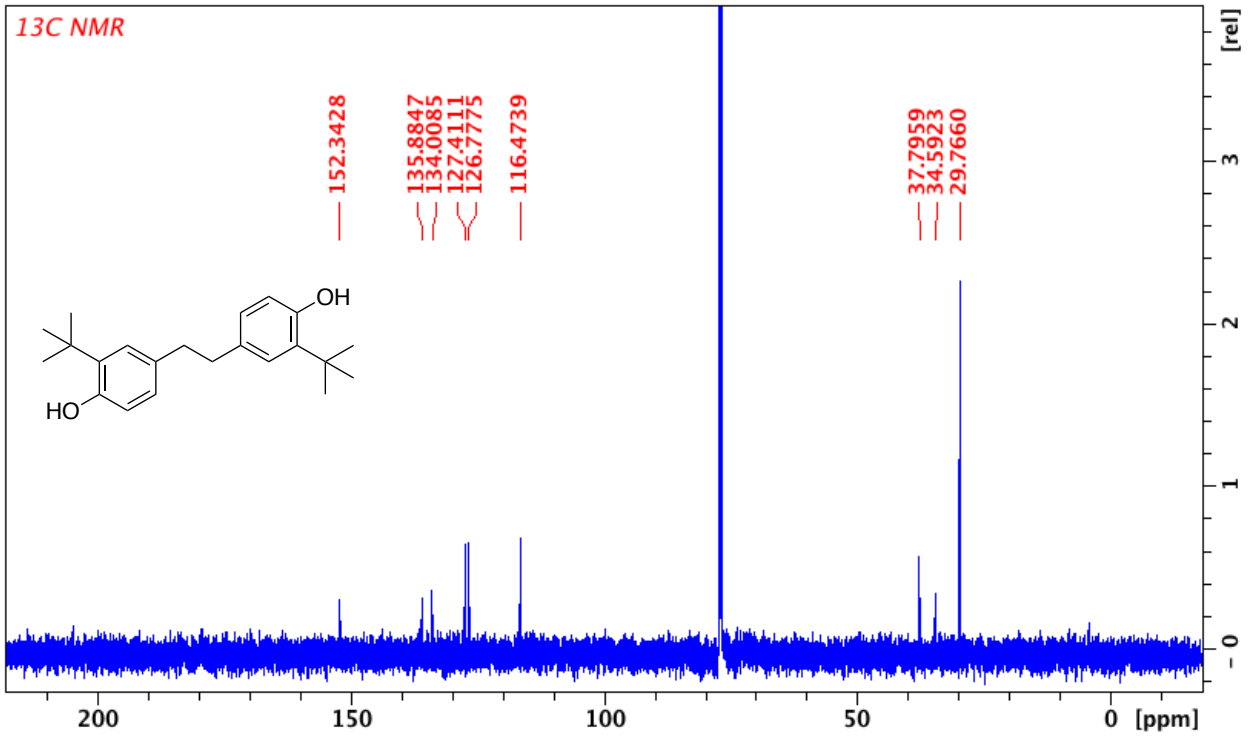




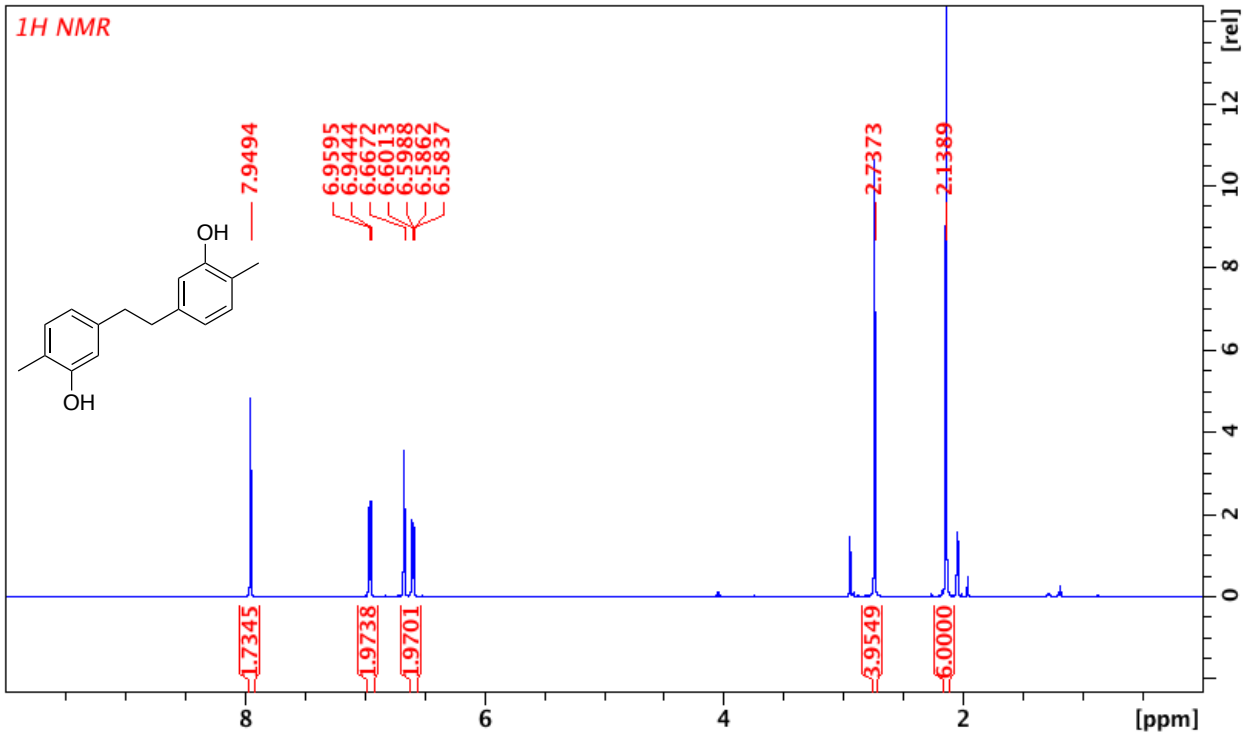
2,2'-(Ethane-1,2-diyl)bis(4-(*tert*-butyl)phenol) (4R)

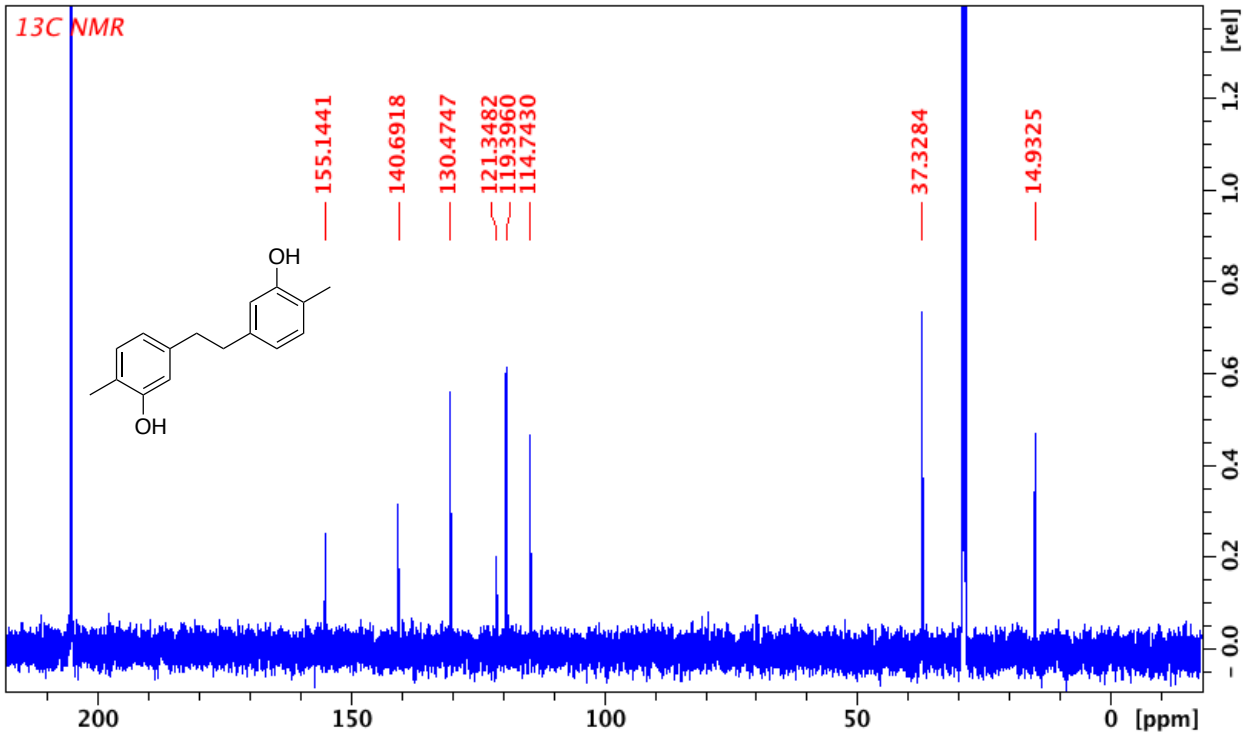
4,4'-(Ethane-1,2-diyl)bis(2-(*tert*-butyl)phenol) (4H)



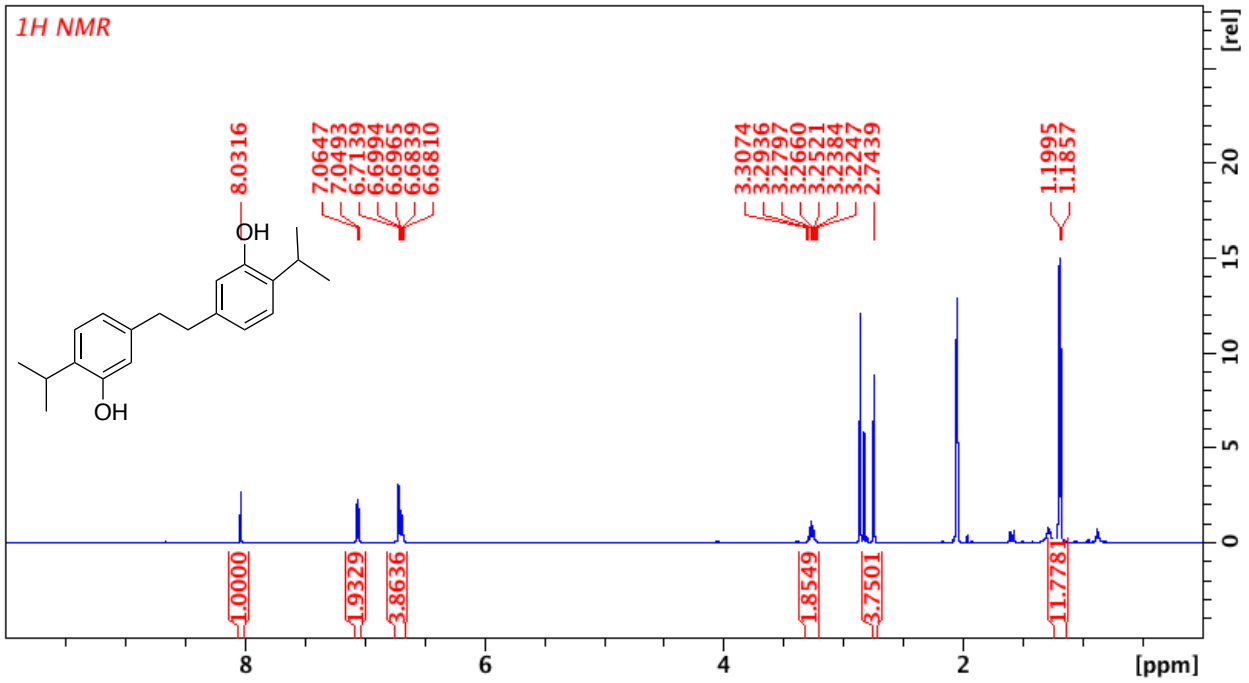


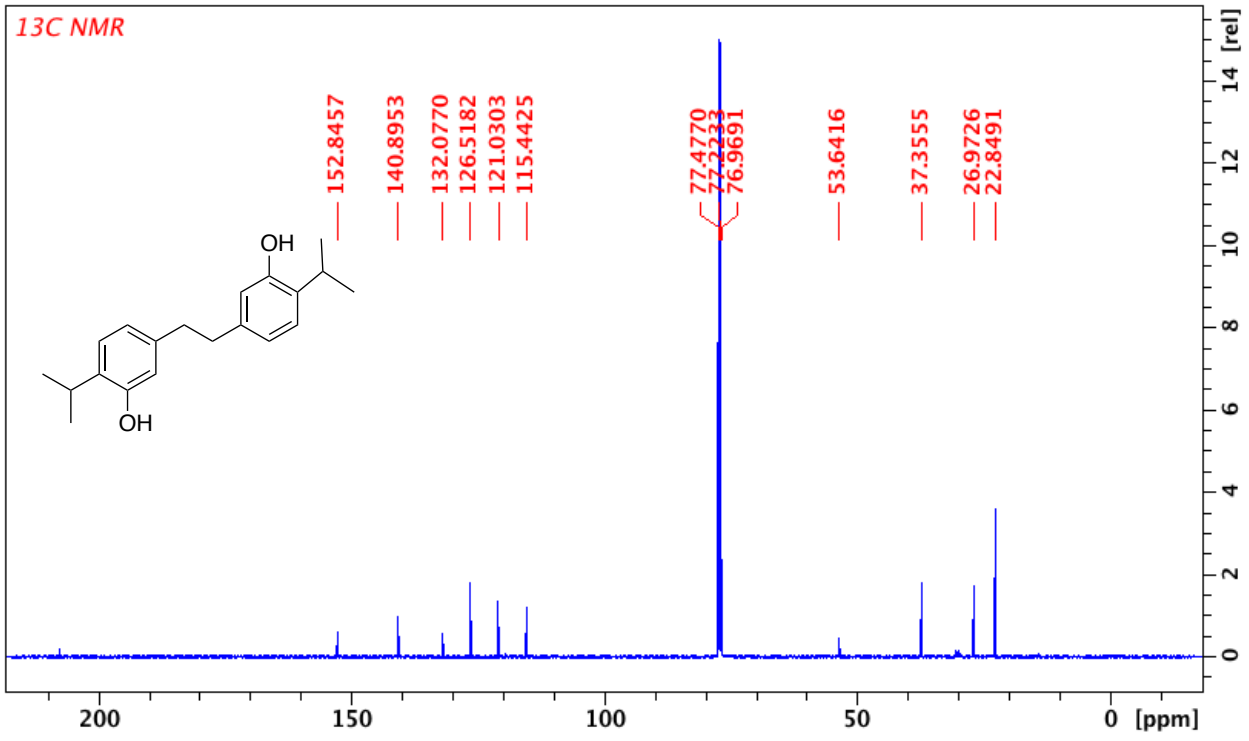
5,5'-(Ethane-1,2-diyl)bis(2-methylphenol) (4B).



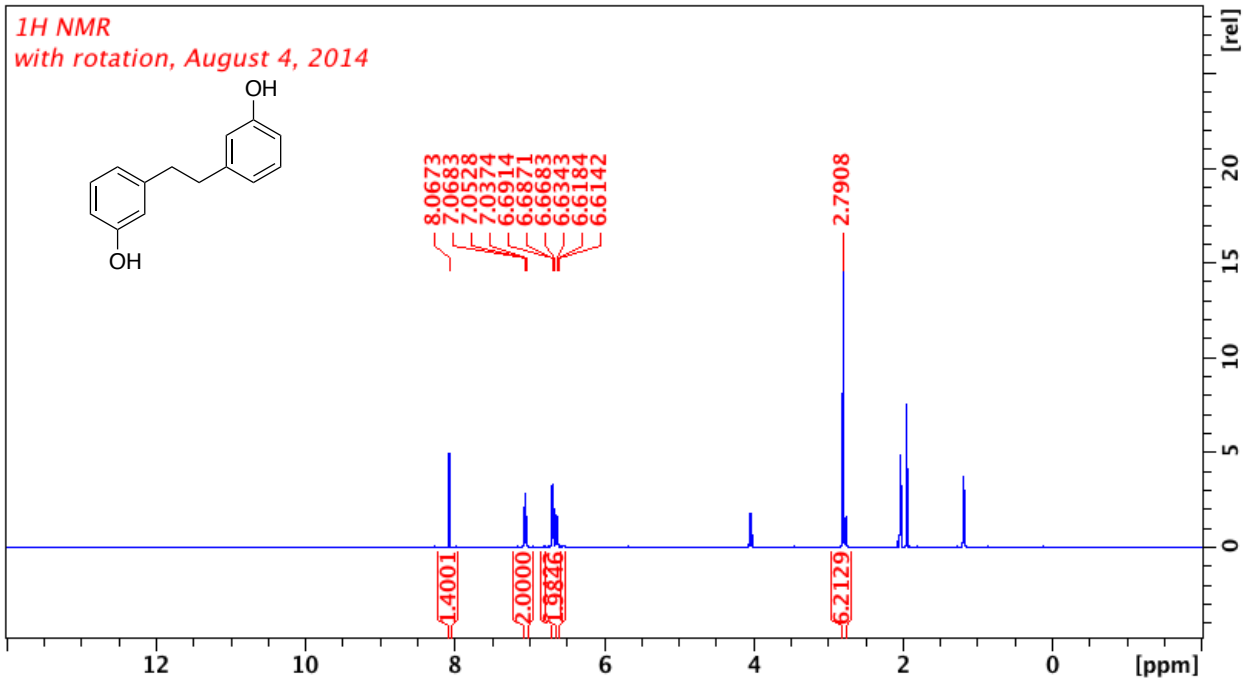


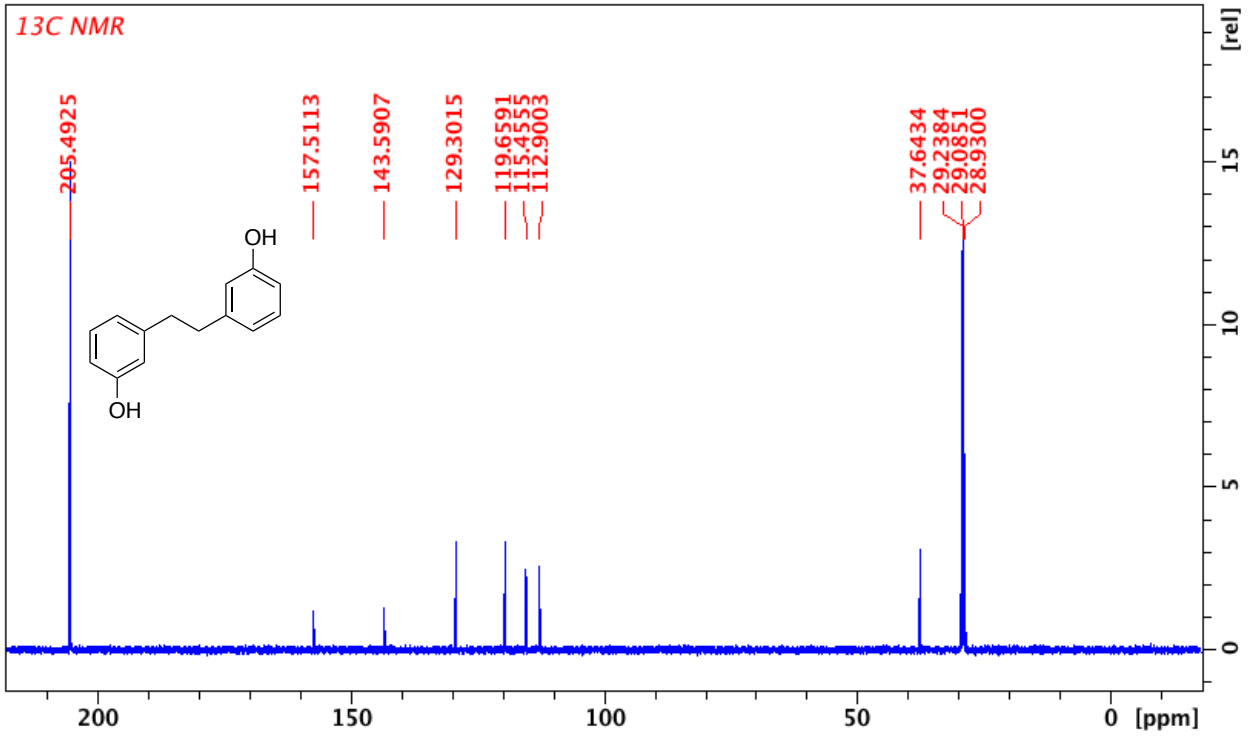
5,5'-(Ethane-1,2-diyl)bis(2-isopropylphenol) (4D).



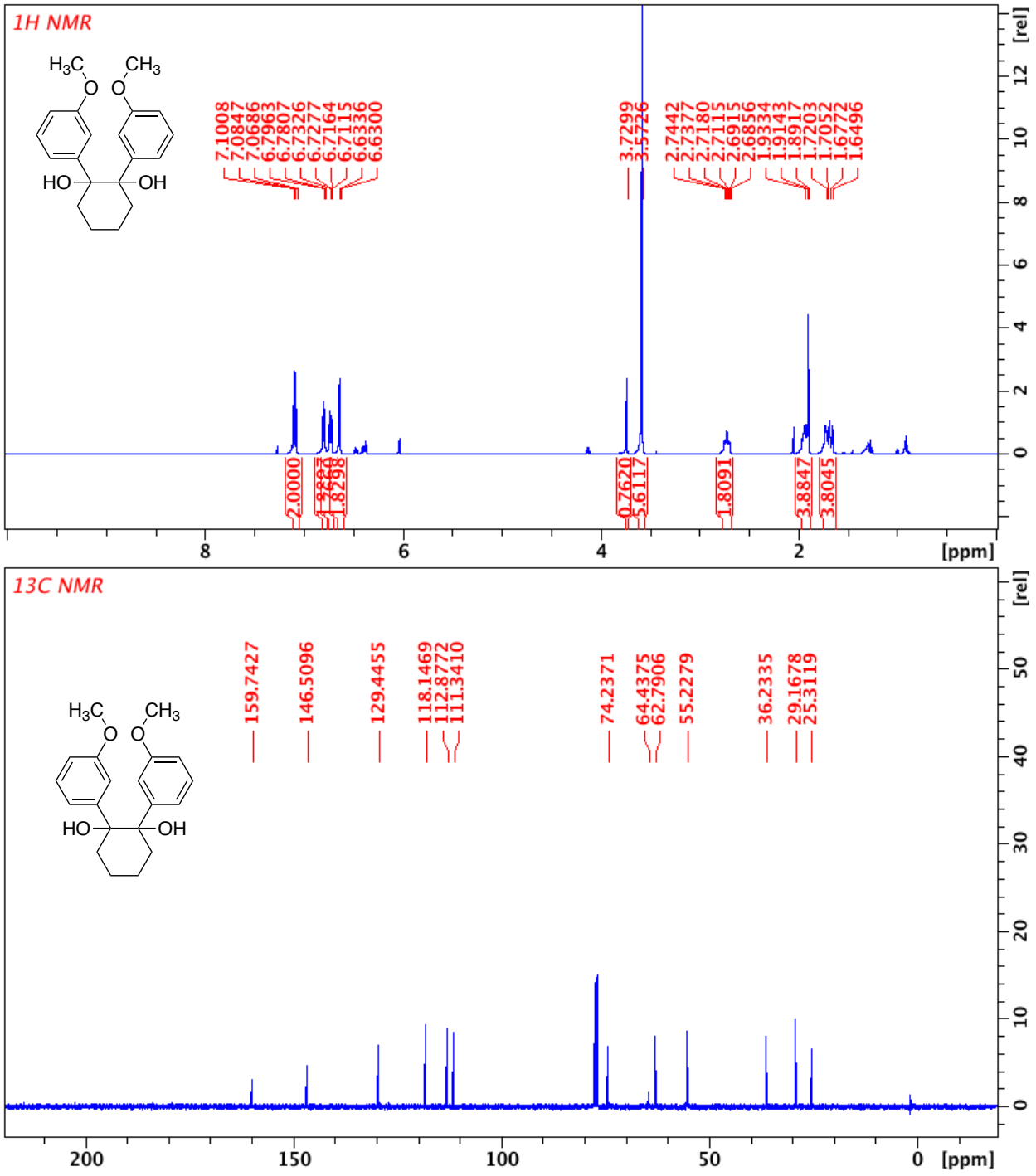

13C NMR
152.8457
140.8953
132.0770
126.5182
121.0303
115.4425
77.4770
77.2233
76.9691
53.6416
37.3555
26.9726
22.8491
OH
OH
200
150
100
50
0
[ppm]
0
2
4
6
8
10
12
14
[rel]

3,3'-(Ethane-1,2-diyl)diphenol (4A)

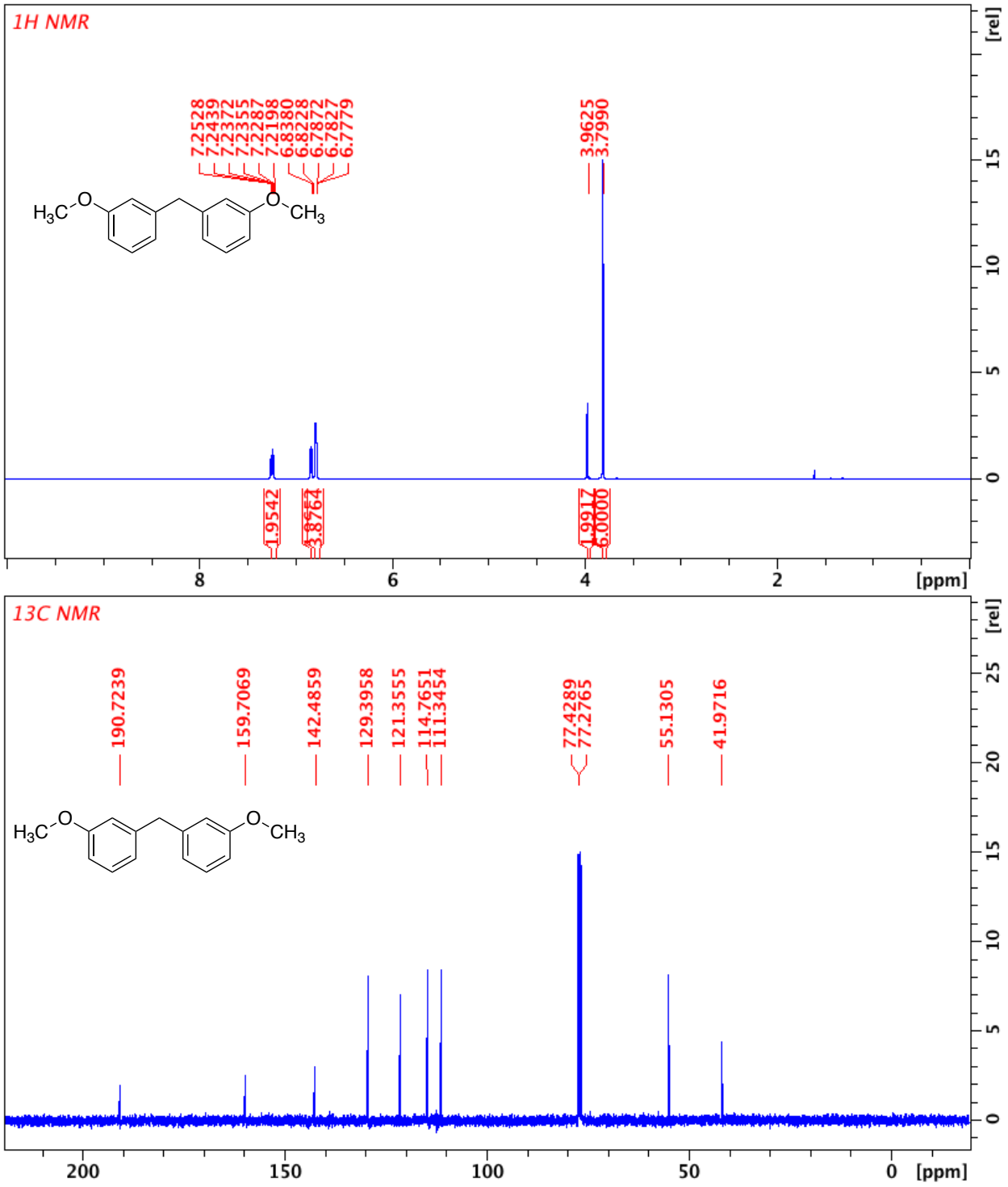




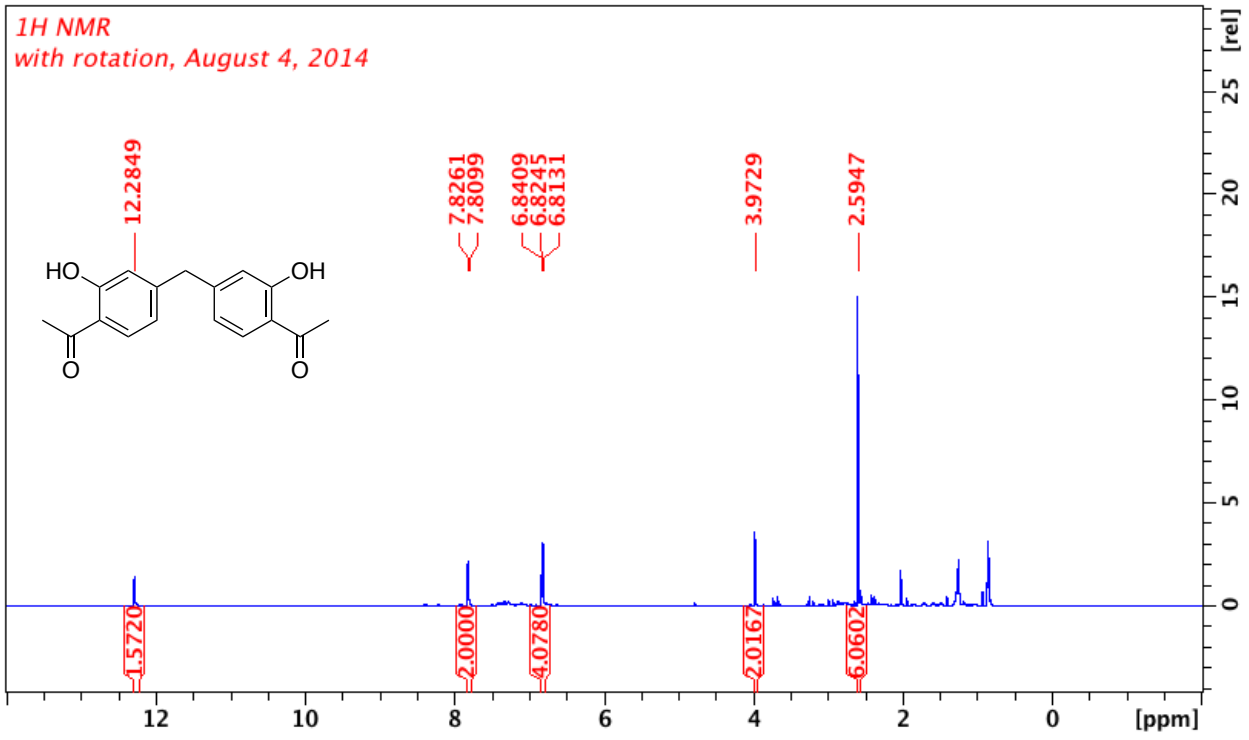
1,2-Bis(3-methoxyphenyl)cyclohexane-1,2-diol (3F)

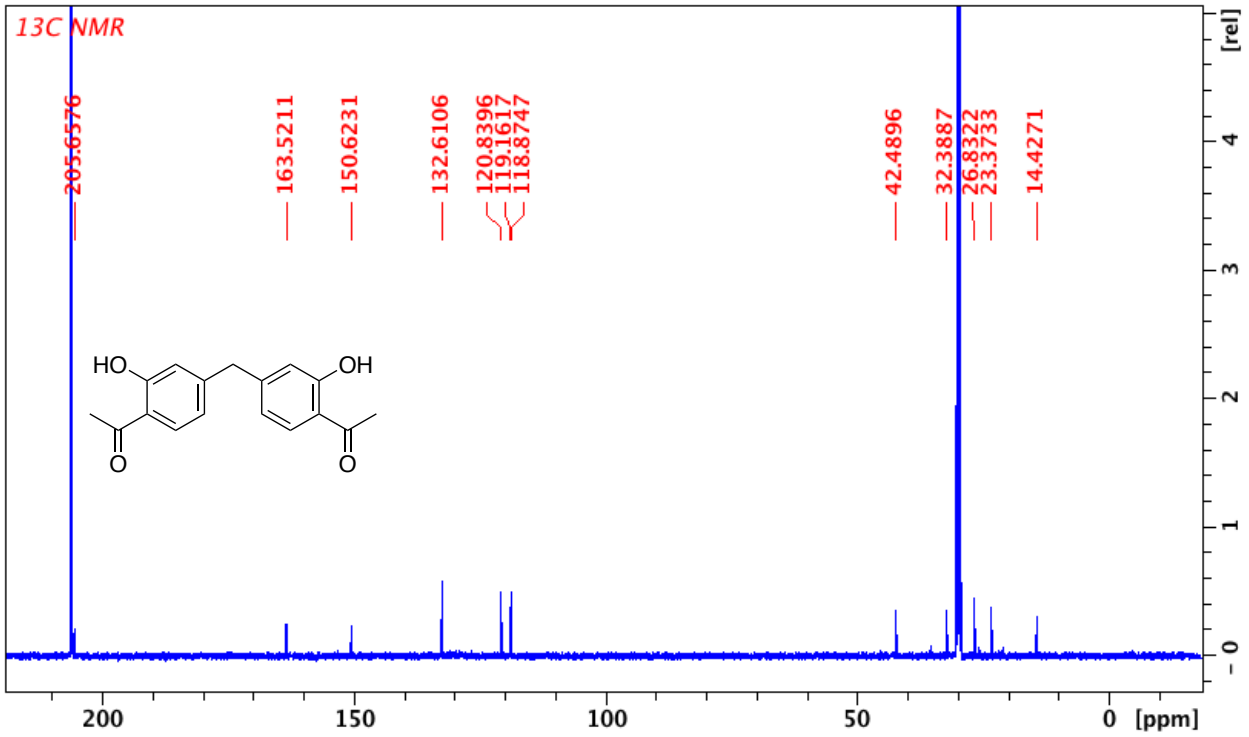


Bis(3-methoxyphenyl)methane (3H)

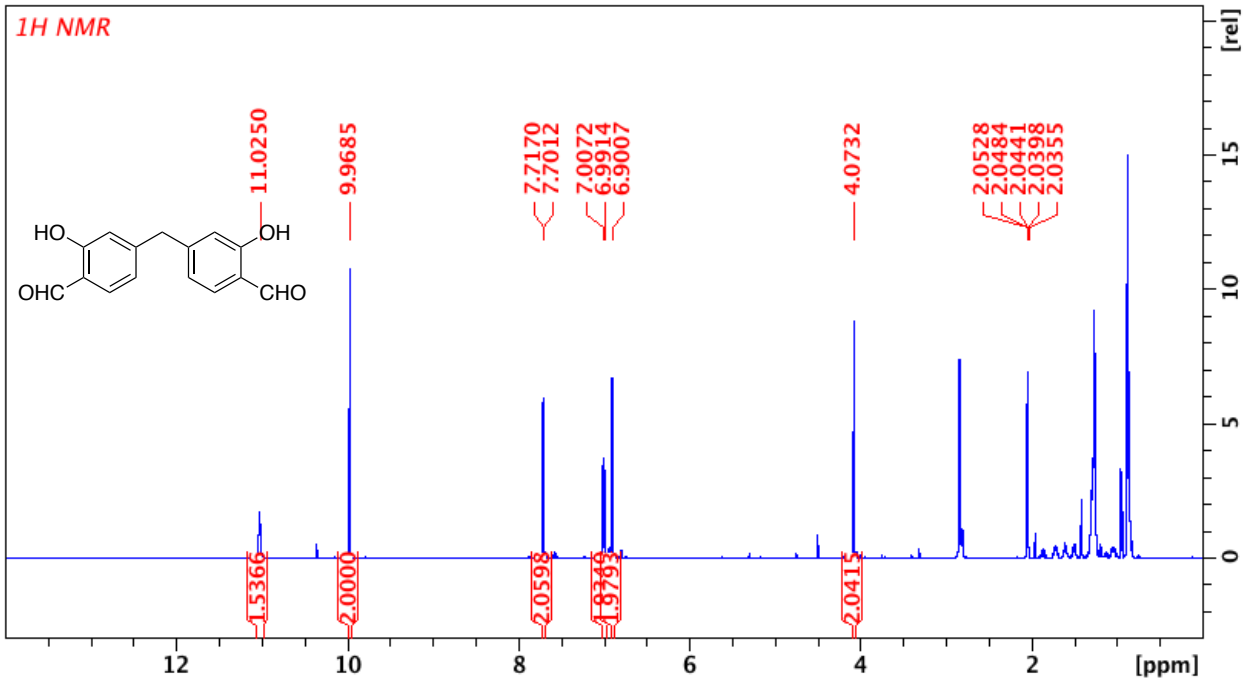


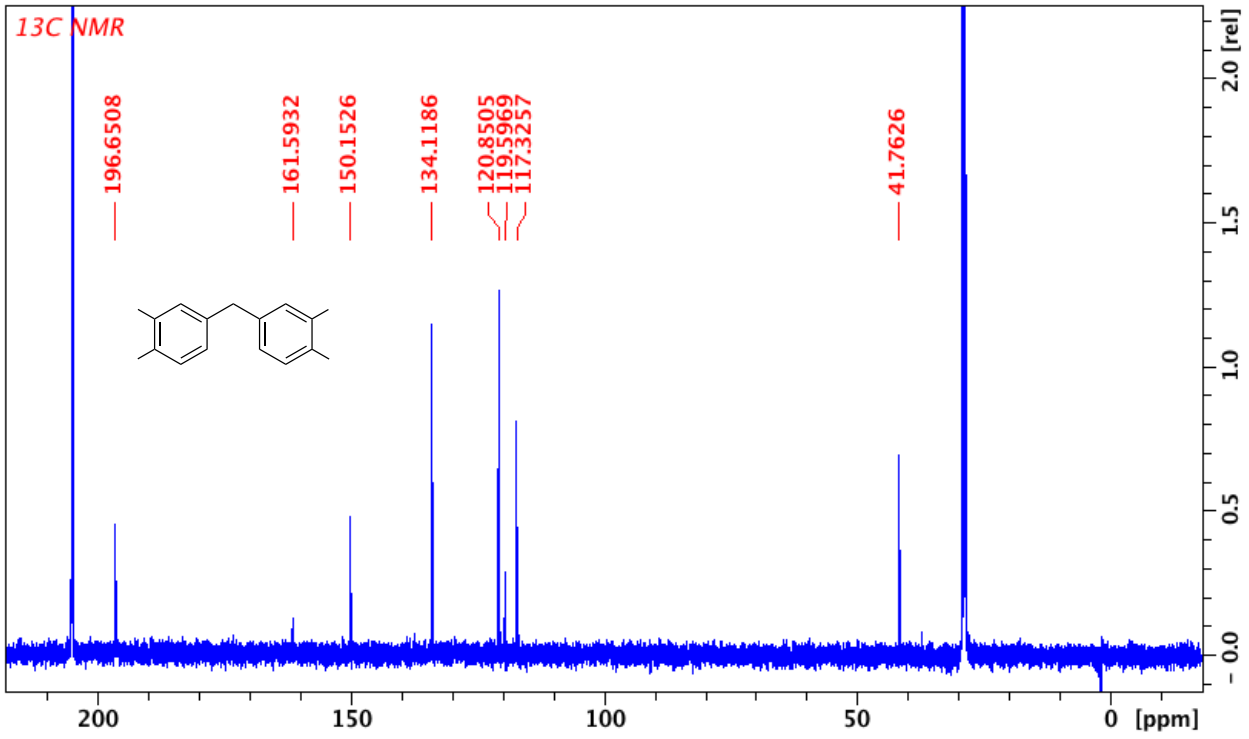
1,1'-(Methylenebis(2-hydroxy-4,1-phenylene))bis(ethan-1-one) (3J)



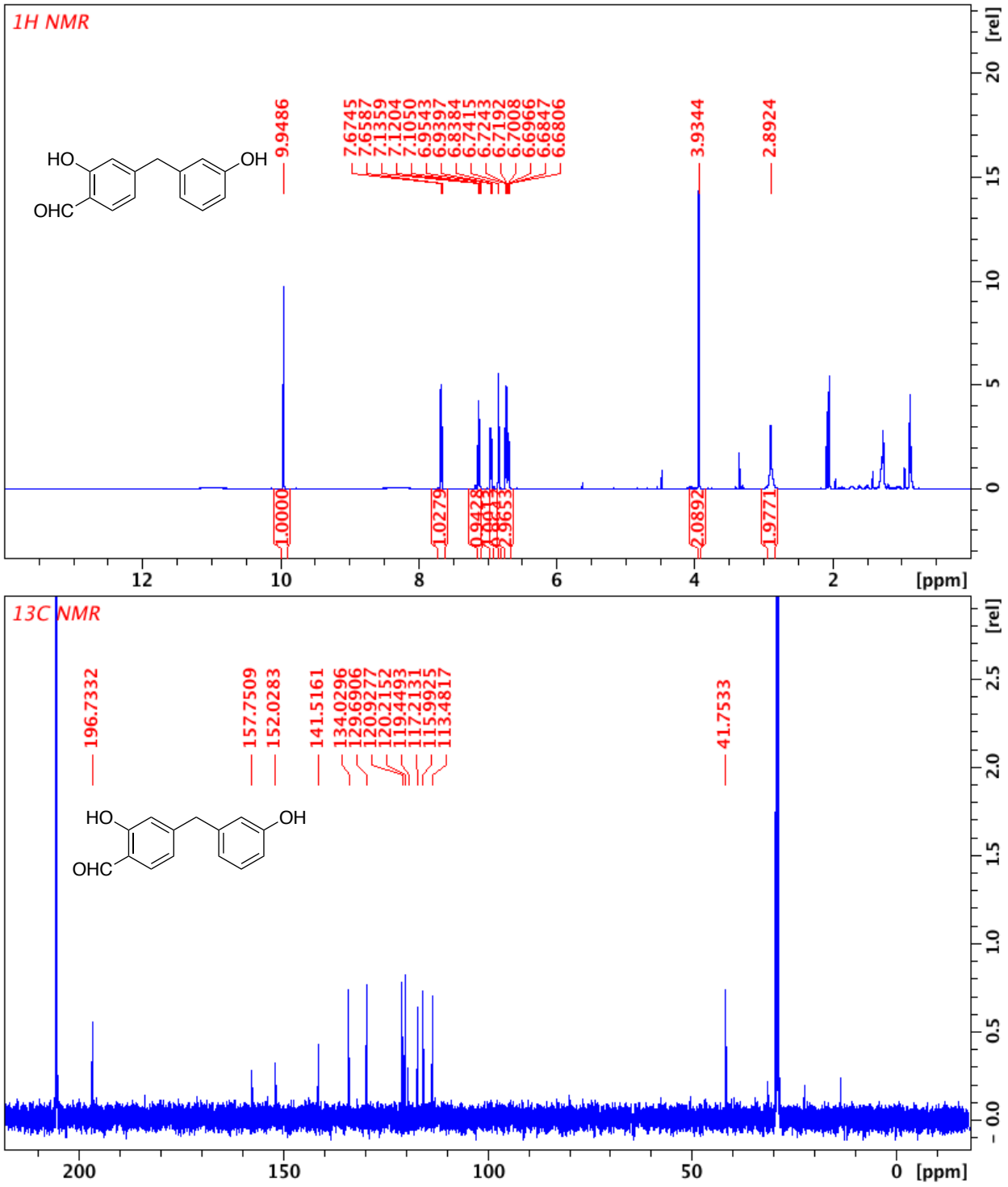


4,4'-Methylenebis(2-hydroxybenzaldehyde) (3L)

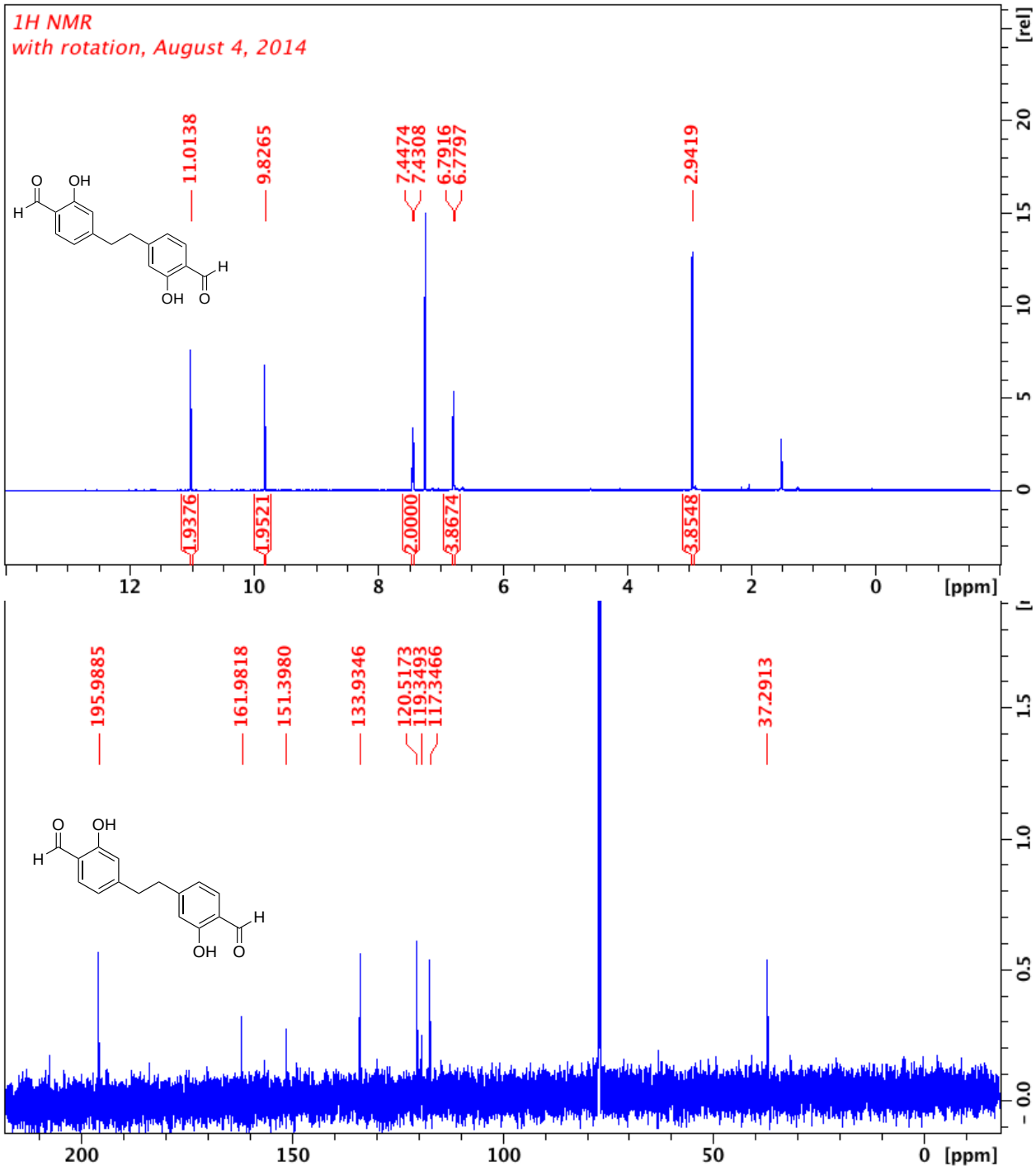



13C NMR
196.6508
161.5932
150.1526
134.1186
120.8505
119.5969
117.3257
41.7626
200
150
100
50
0 [ppm]
2.0 [rel]
1.5
1.0
0.5
- 0.0

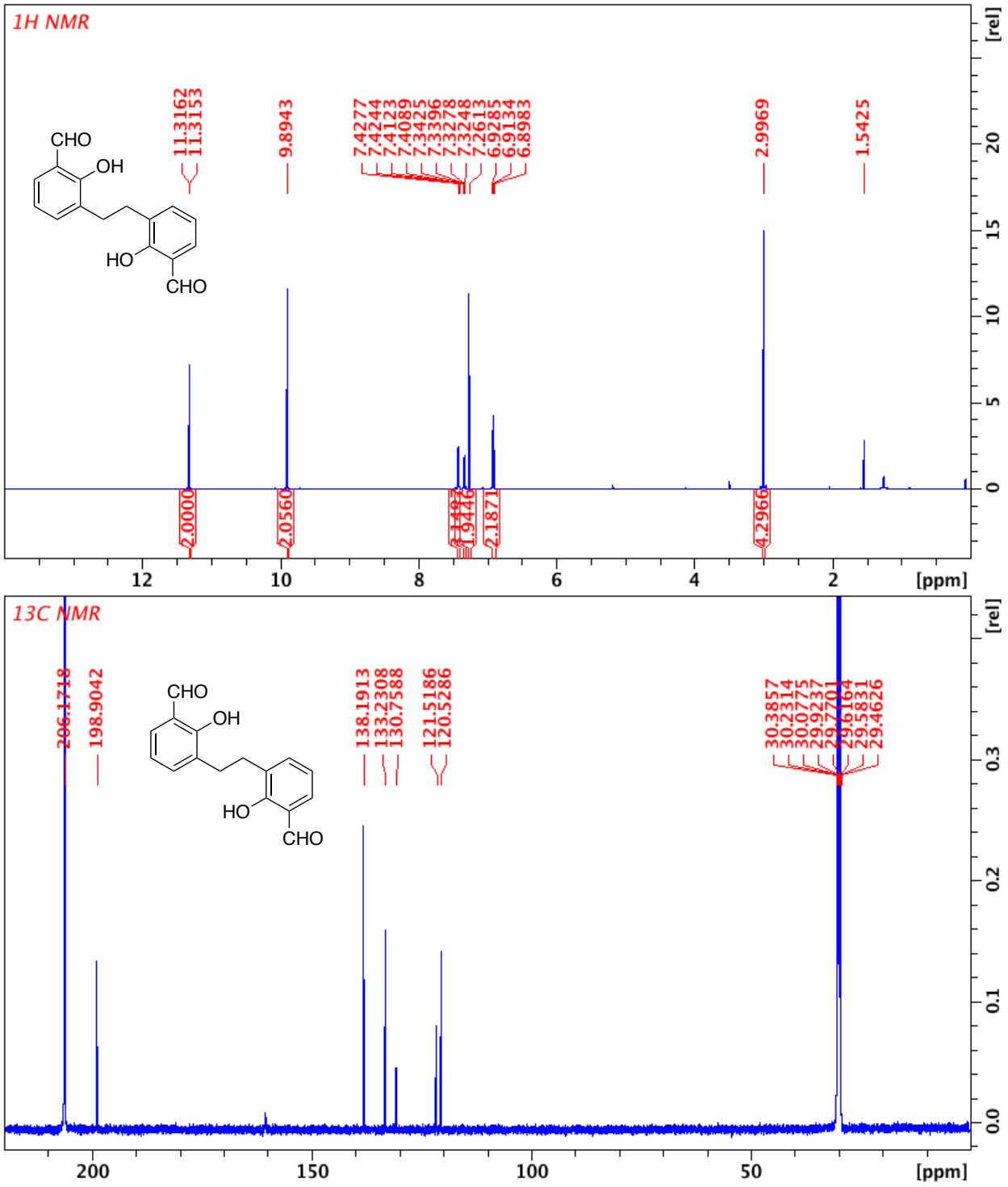
2-Hydroxy-4-(3-hydroxybenzyl)benzaldehyde (3M)



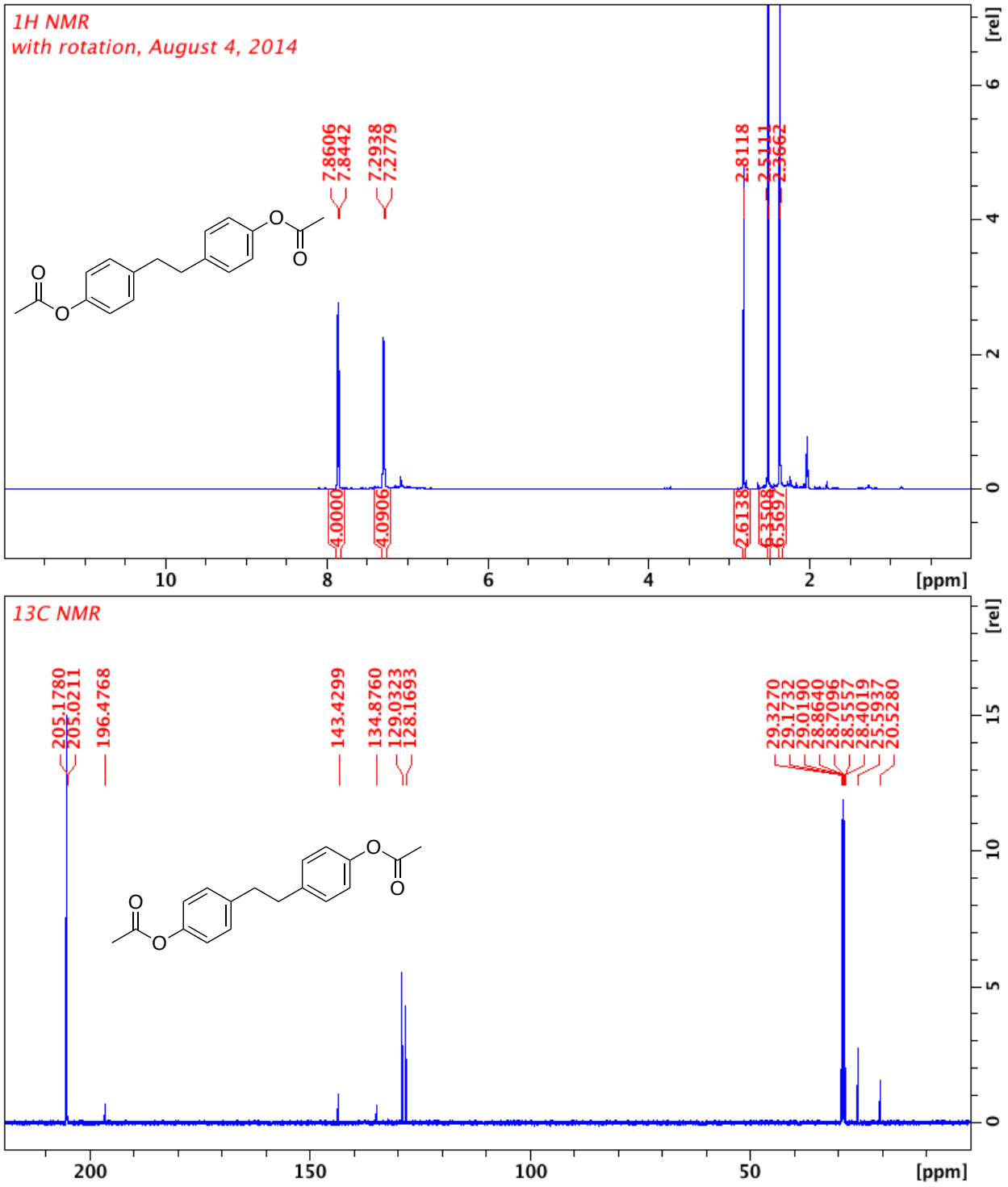
4,4'-(Ethane-1,2-diyl)bis(2-hydroxybenzaldehyde) (4N)



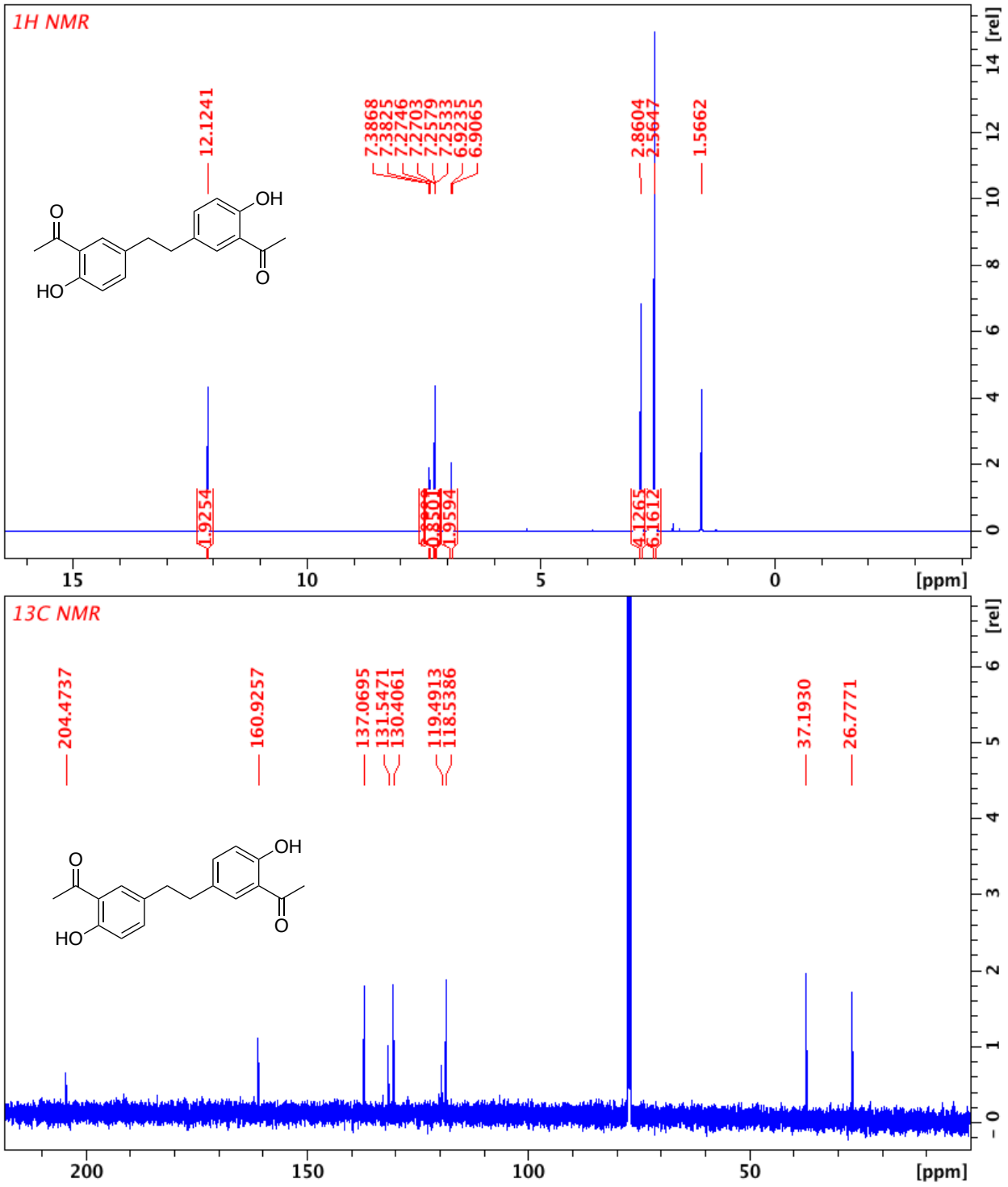
3,3'-(Ethane-1,2-diyl)bis(2-hydroxybenzaldehyde) (3Q)



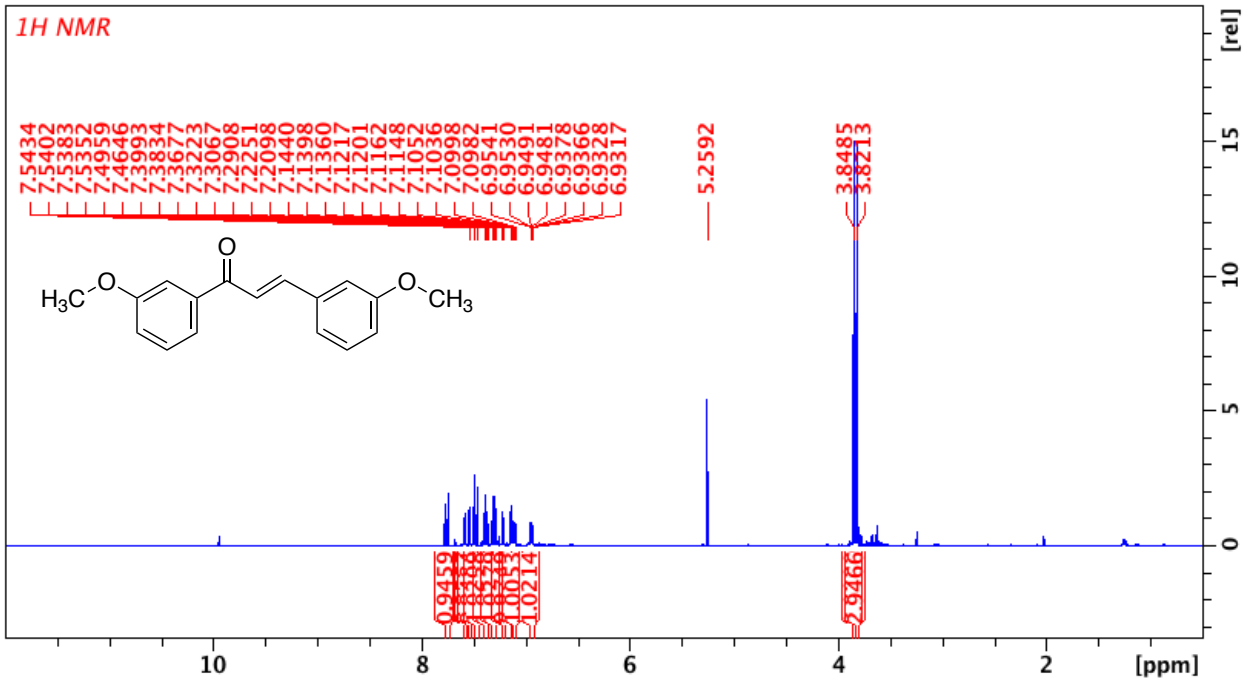
Ethane-1,2-diylbis(4,1-phenylene) diacetate (3X)

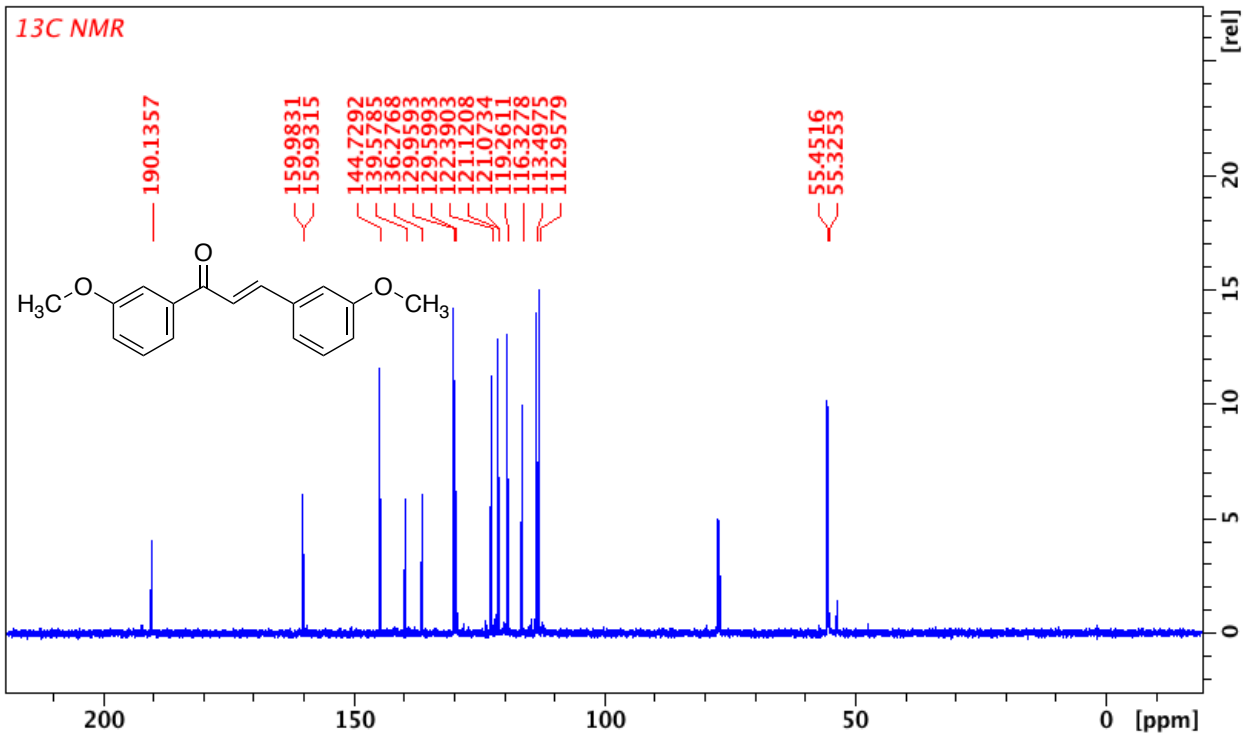


1,1'-(Ethane-1,2-diylbis(6-hydroxy-3,1-phenylene))bis(ethan-1-one) (3AA)

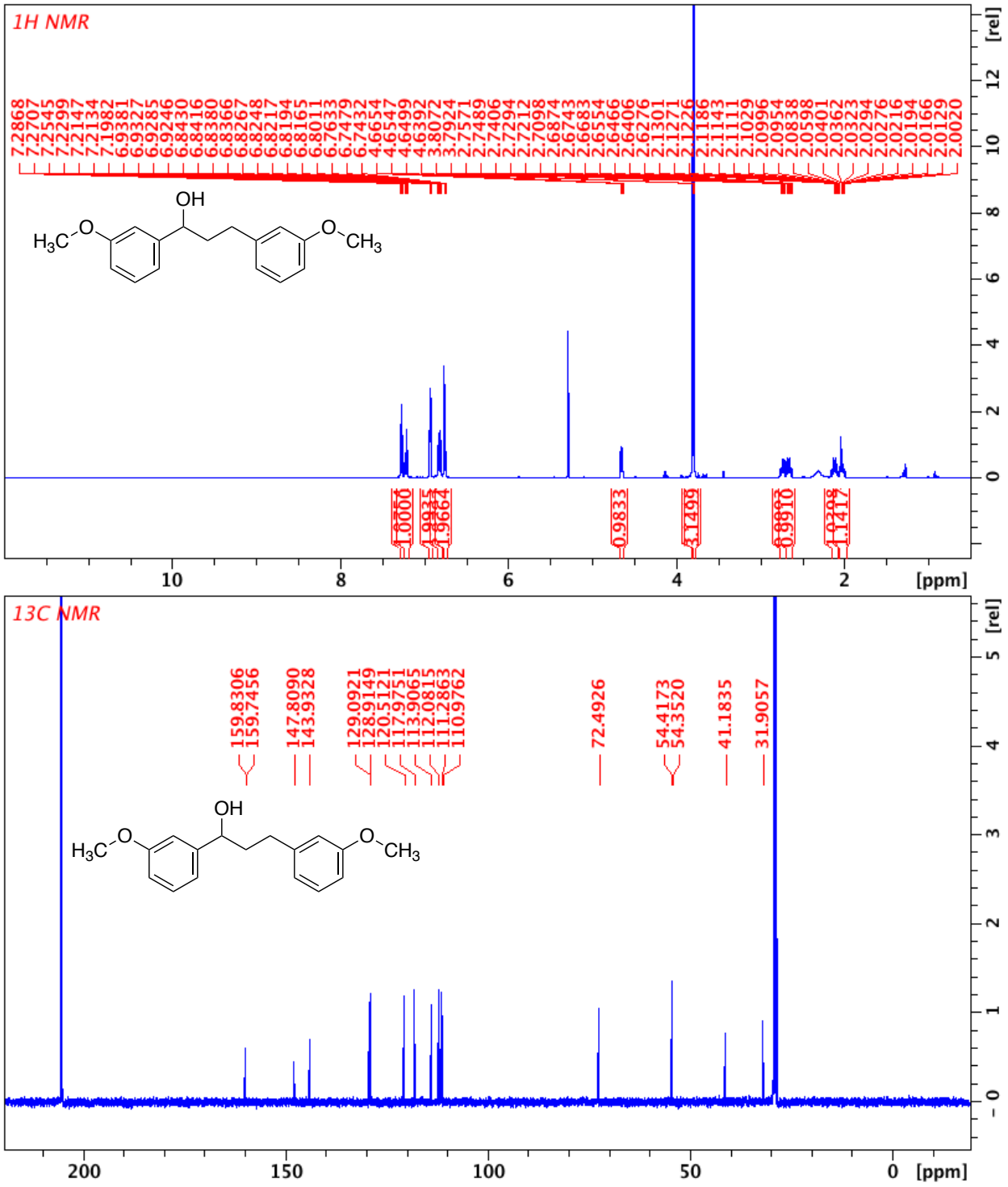


(*E*)-1,3-Bis(3-methoxyphenyl)prop-2-en-1-one (3AB)

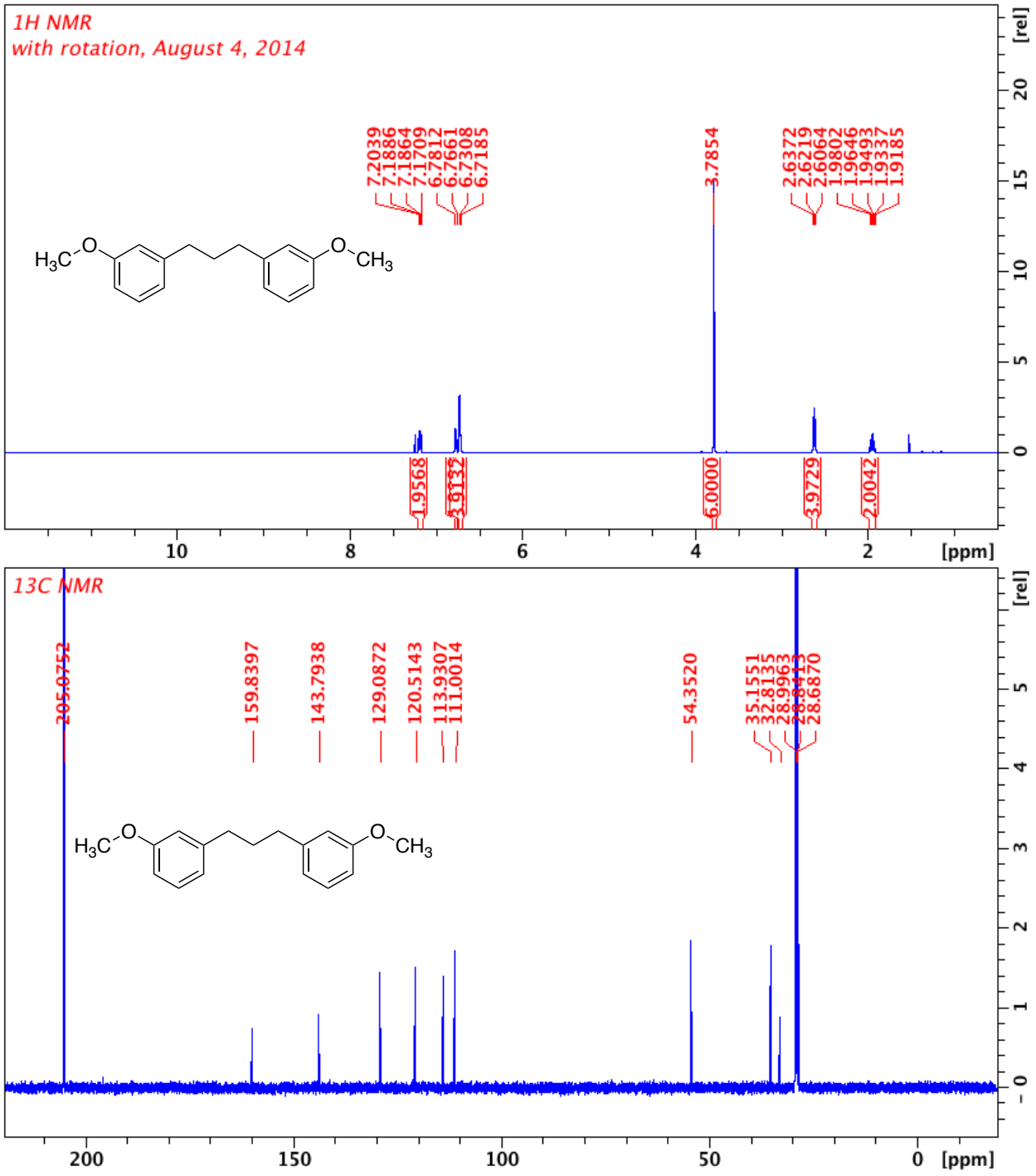




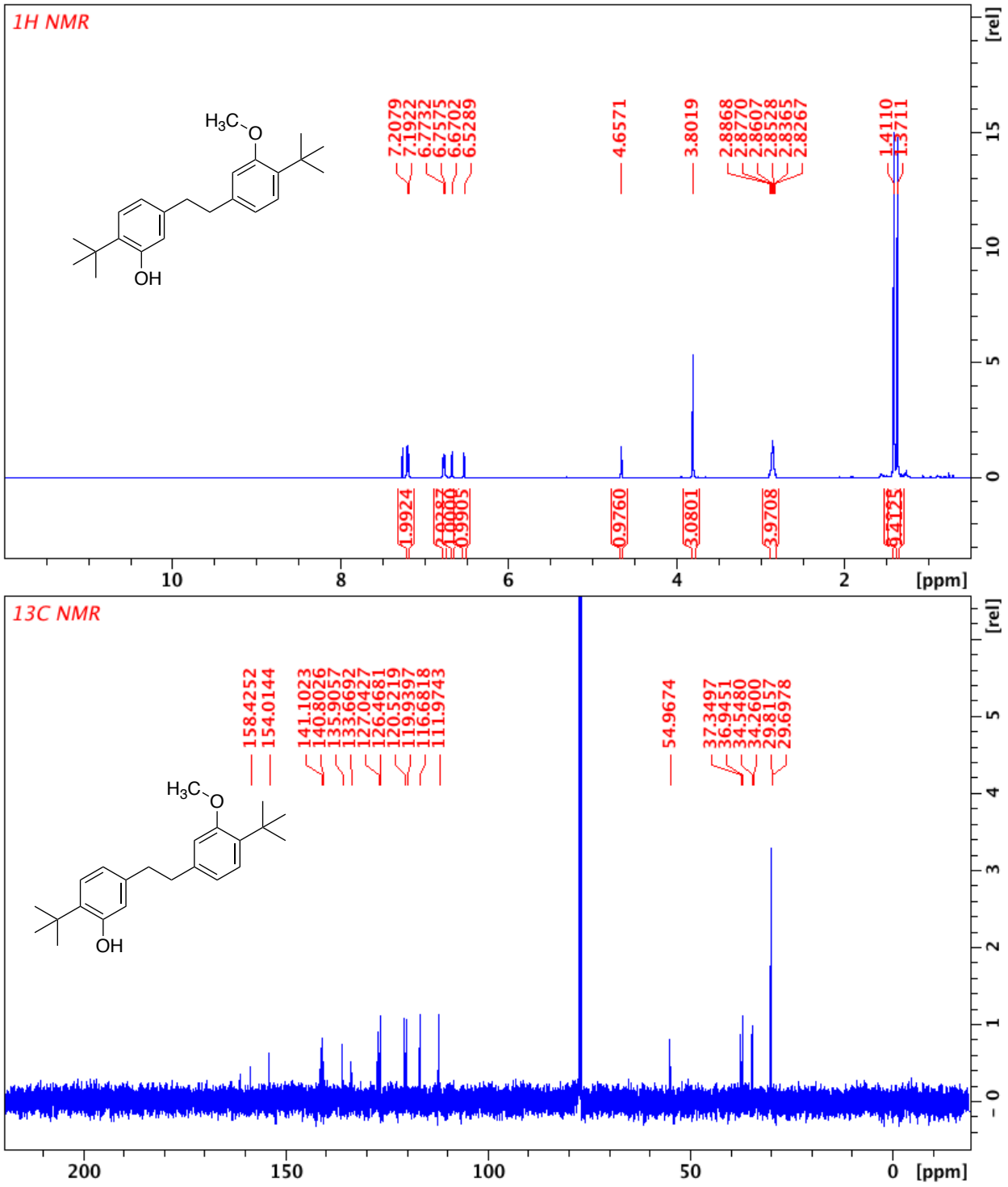
1,3-Bis(3-methoxyphenyl)propan-1-ol (3AC)



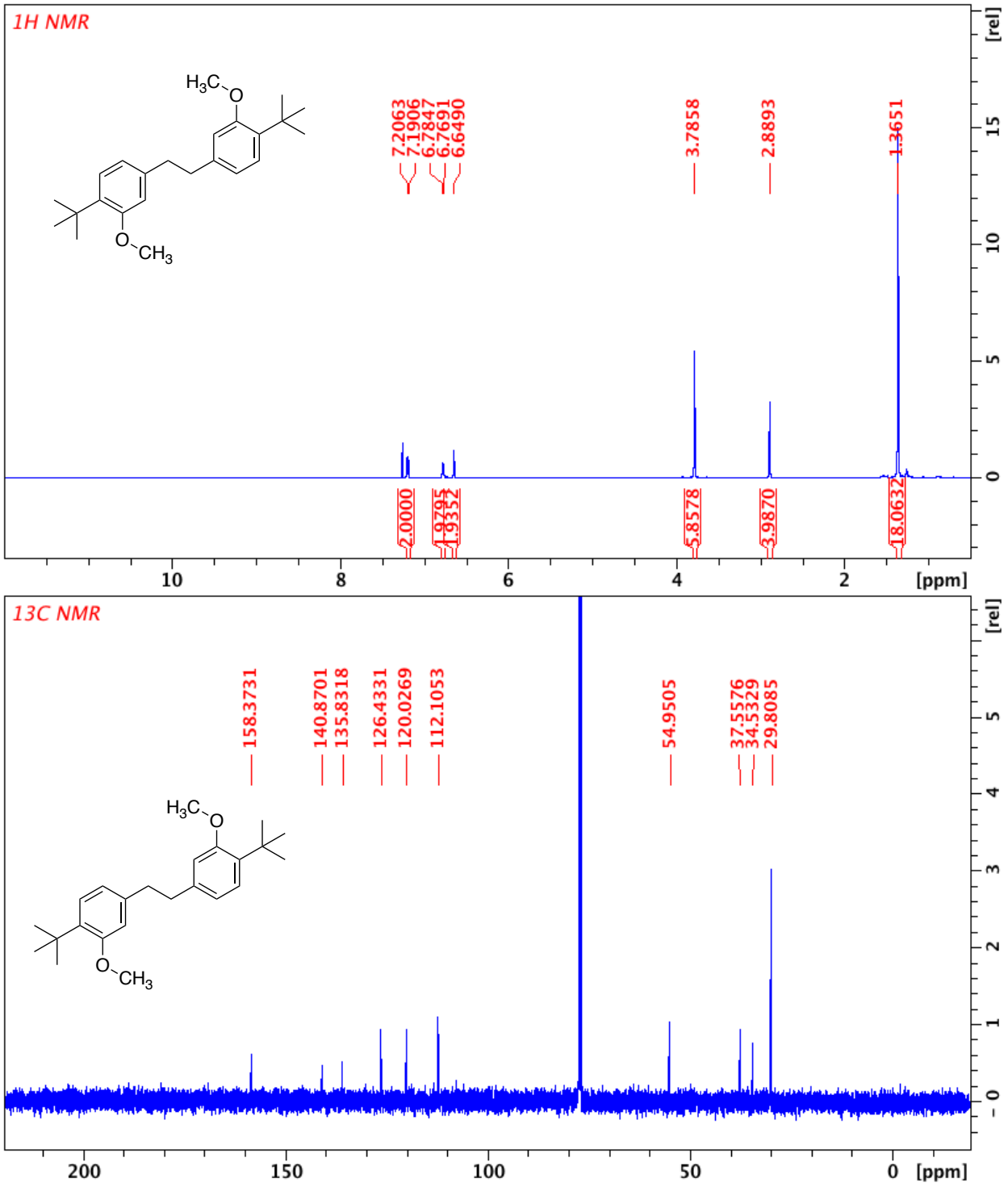
1,3-Bis(3-methoxyphenyl)propane (3AD)



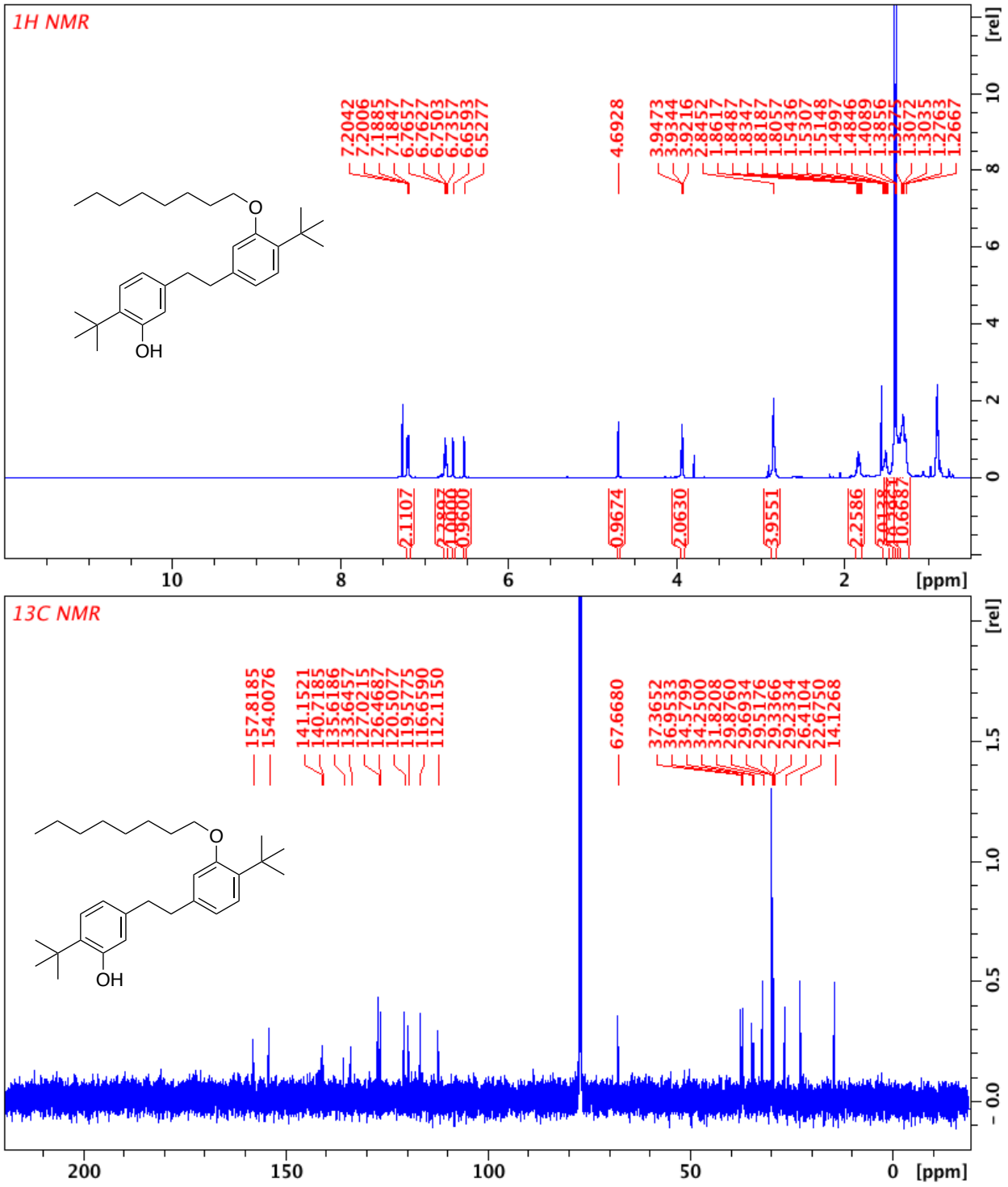
2-(*tert*-Butyl)-5-(4-(*tert*-butyl)-3-methoxyphenethyl)phenol (3AE)



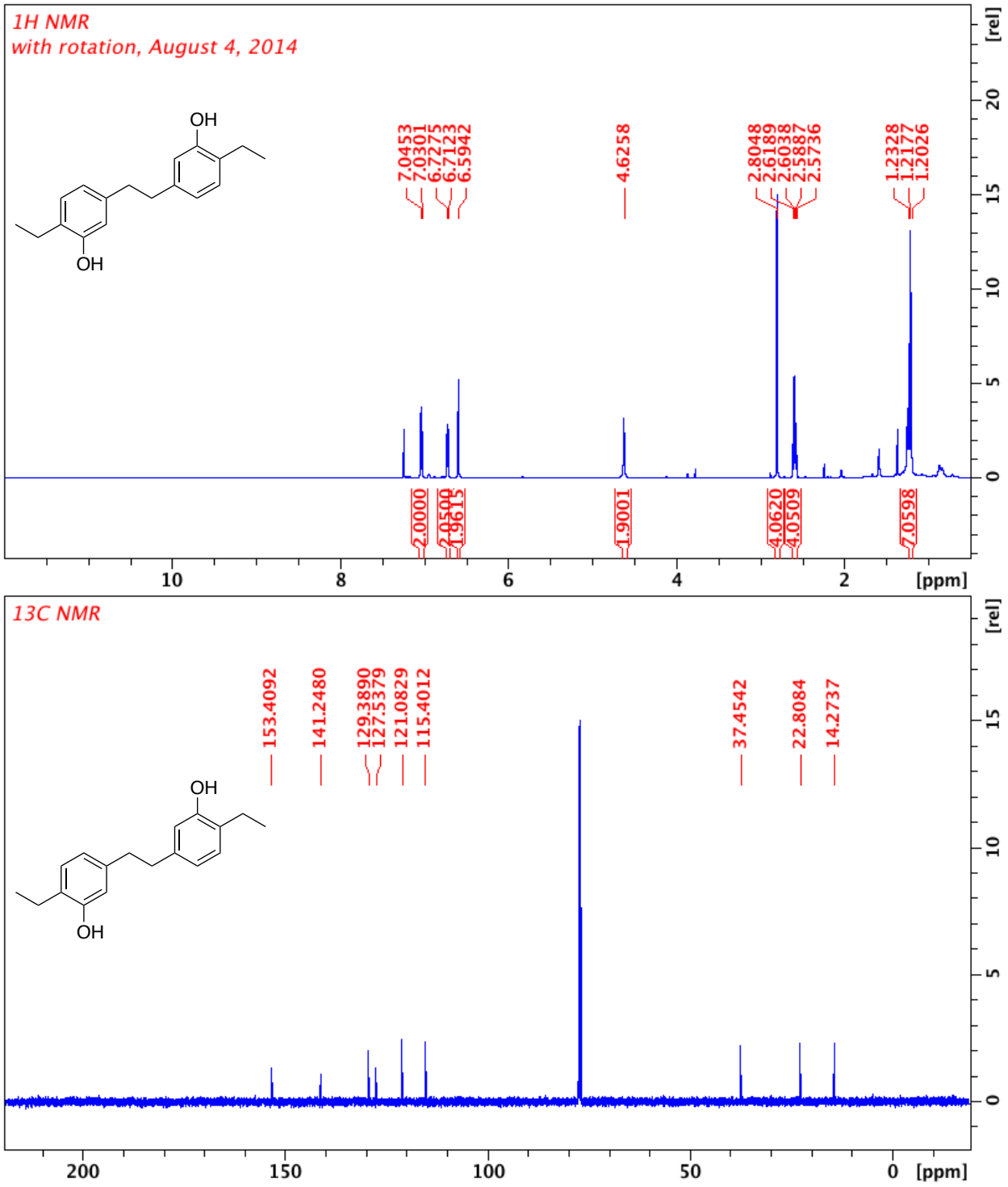
1,2-Bis(4-(*tert*-butyl)-3-methoxyphenyl)ethane (4K)



2-(*tert*-Butyl)-5-(4-(*tert*-butyl)-3-(octyloxy)phenethyl)phenol (4O)

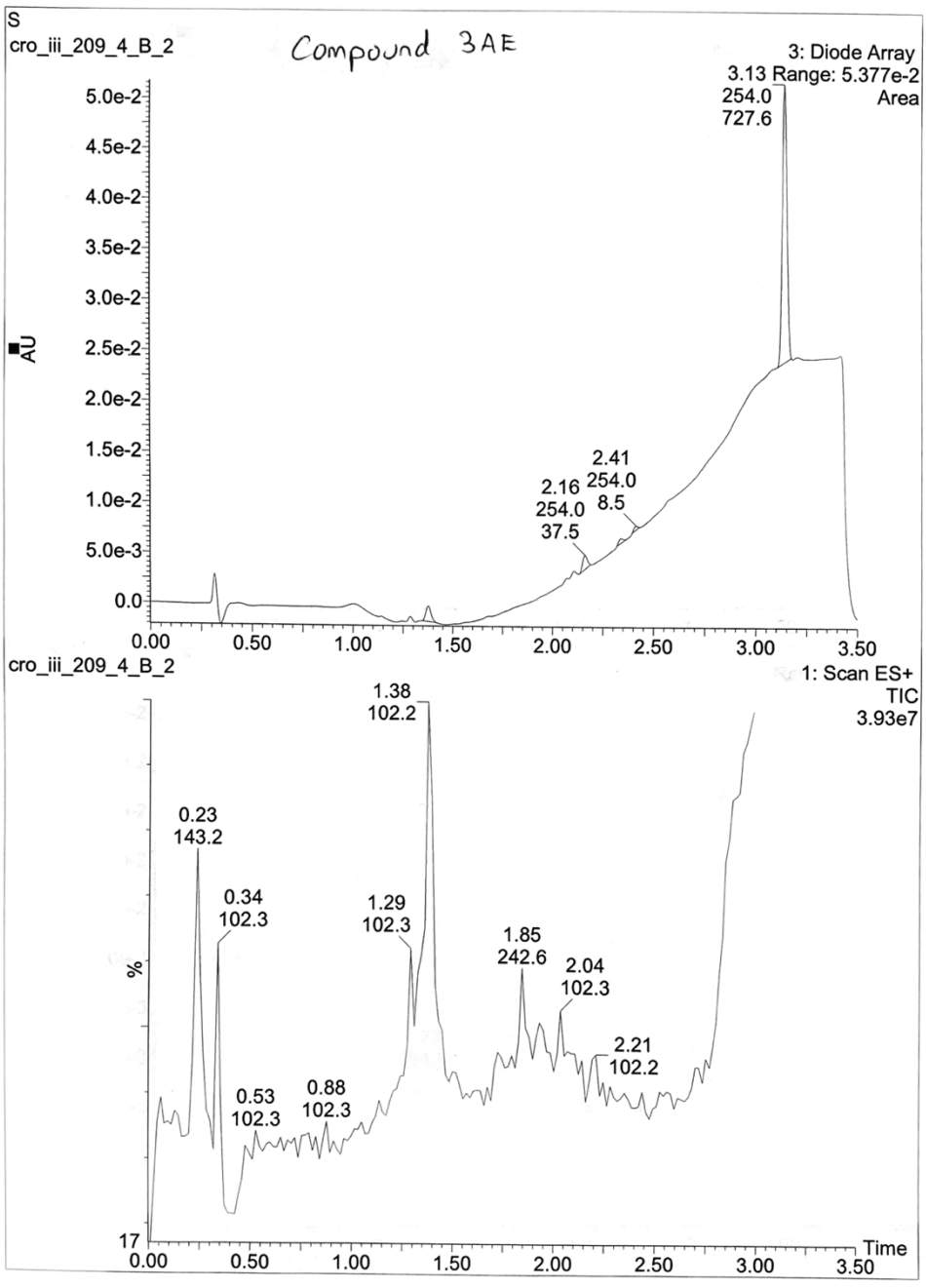


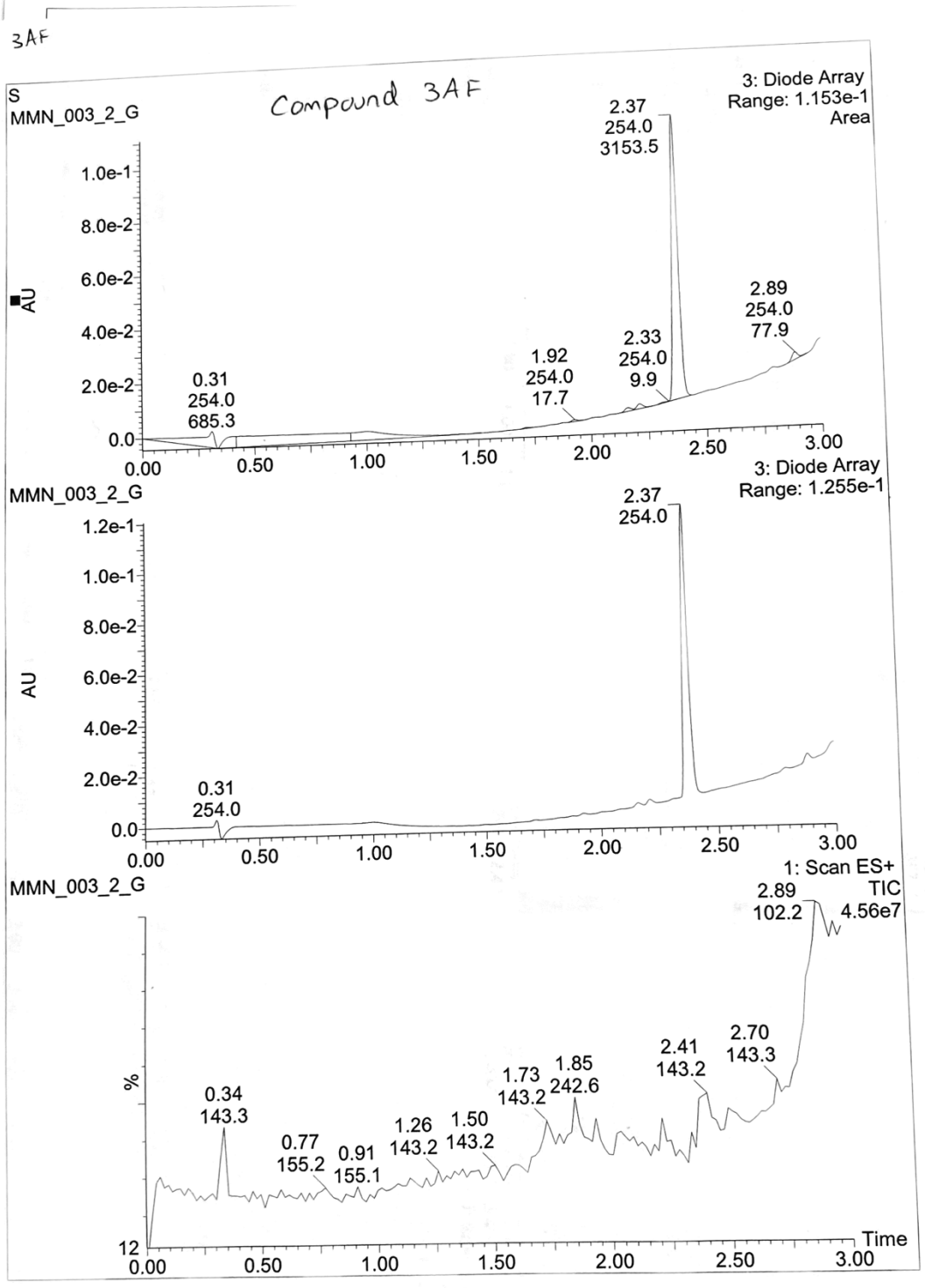
5,5'-(Ethane-1,2-diyl)bis(2-ethylphenol) (4C)

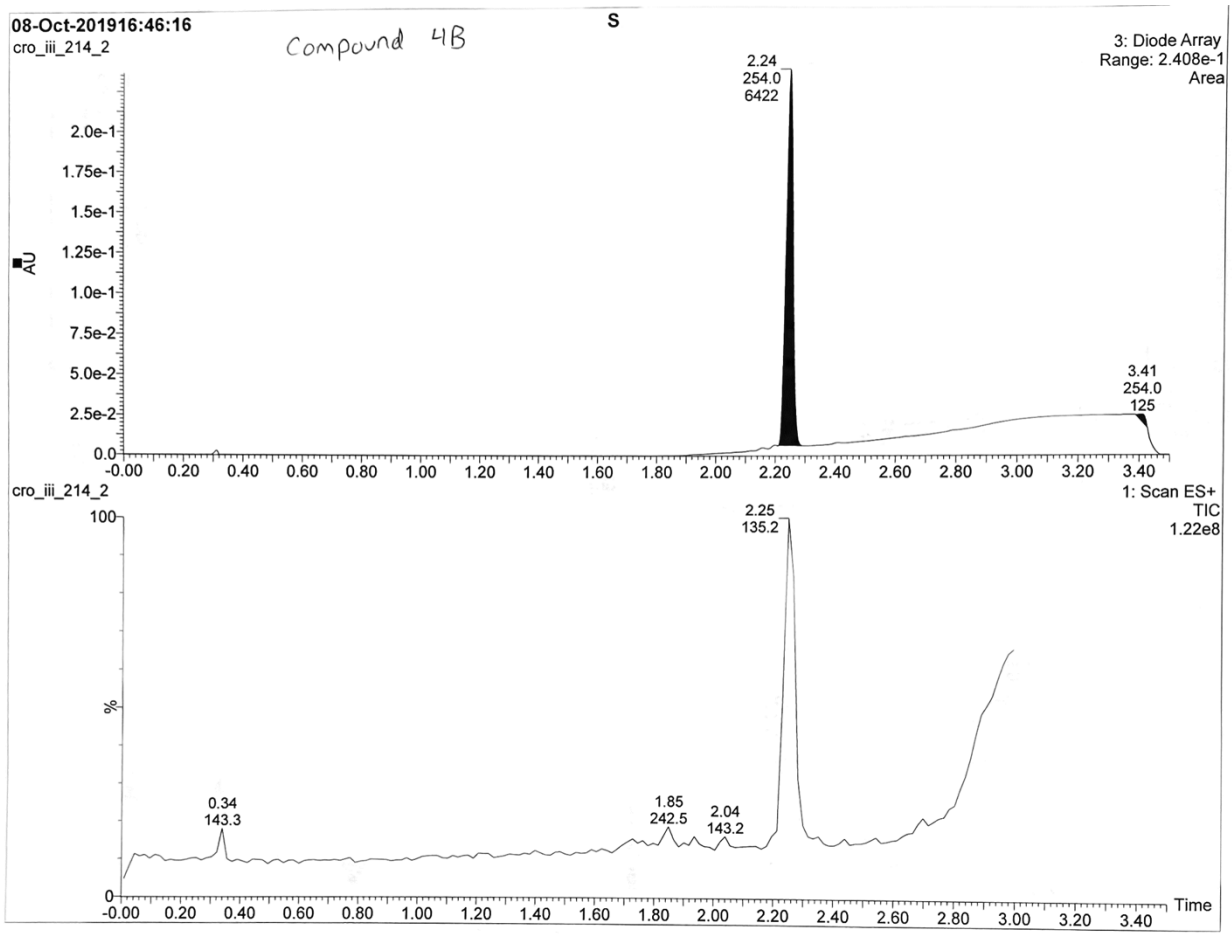


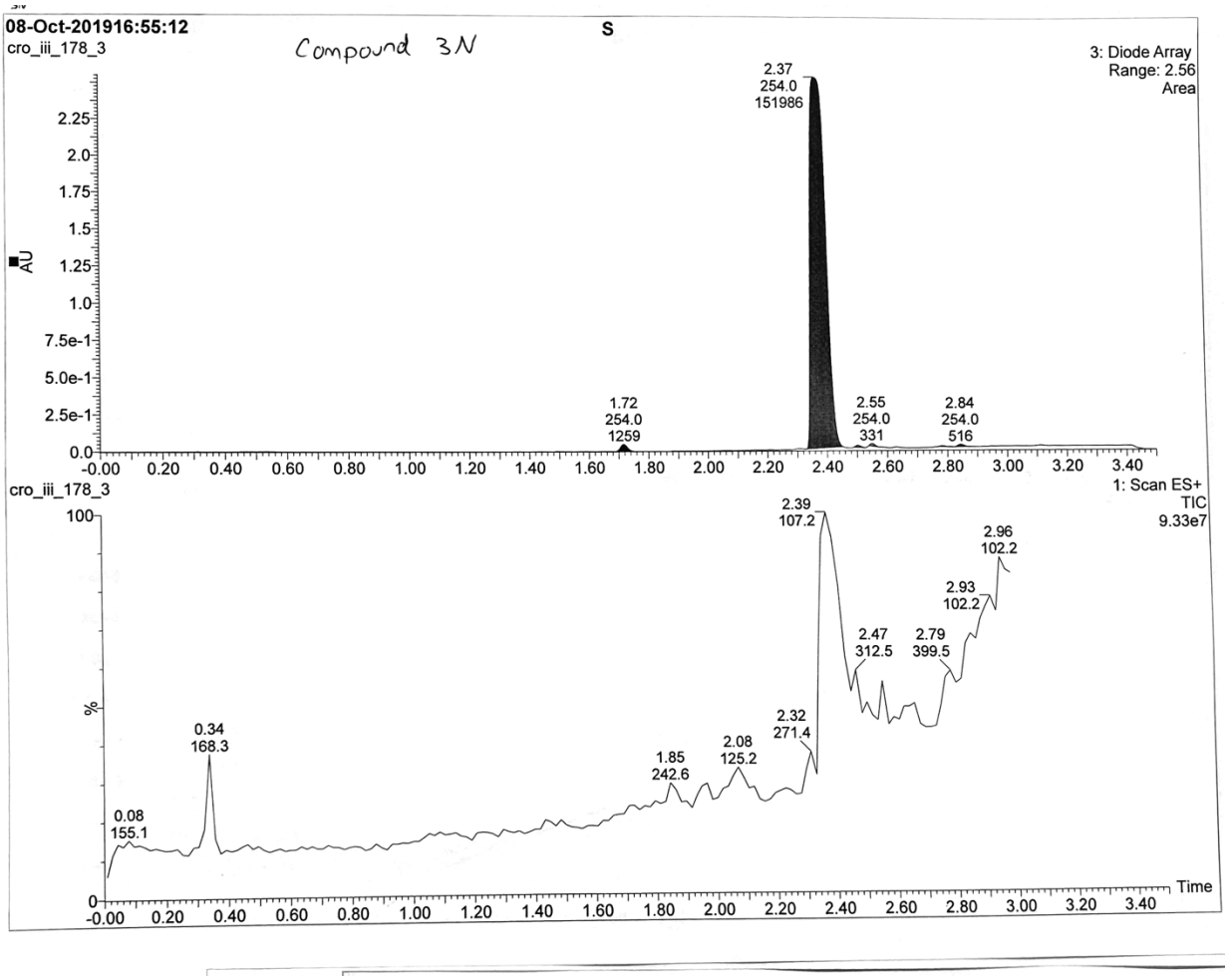
5. UPLC Traces

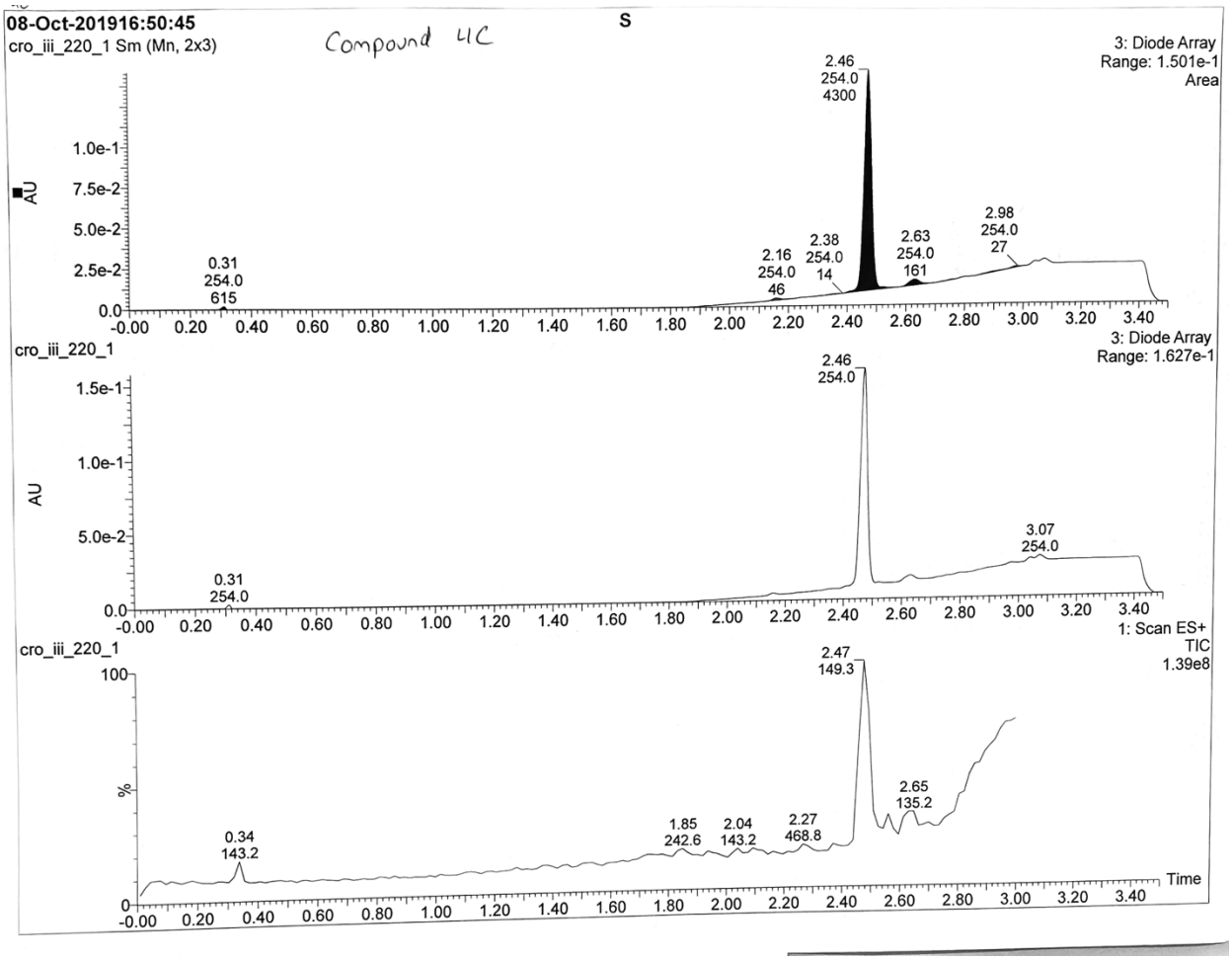
3AE

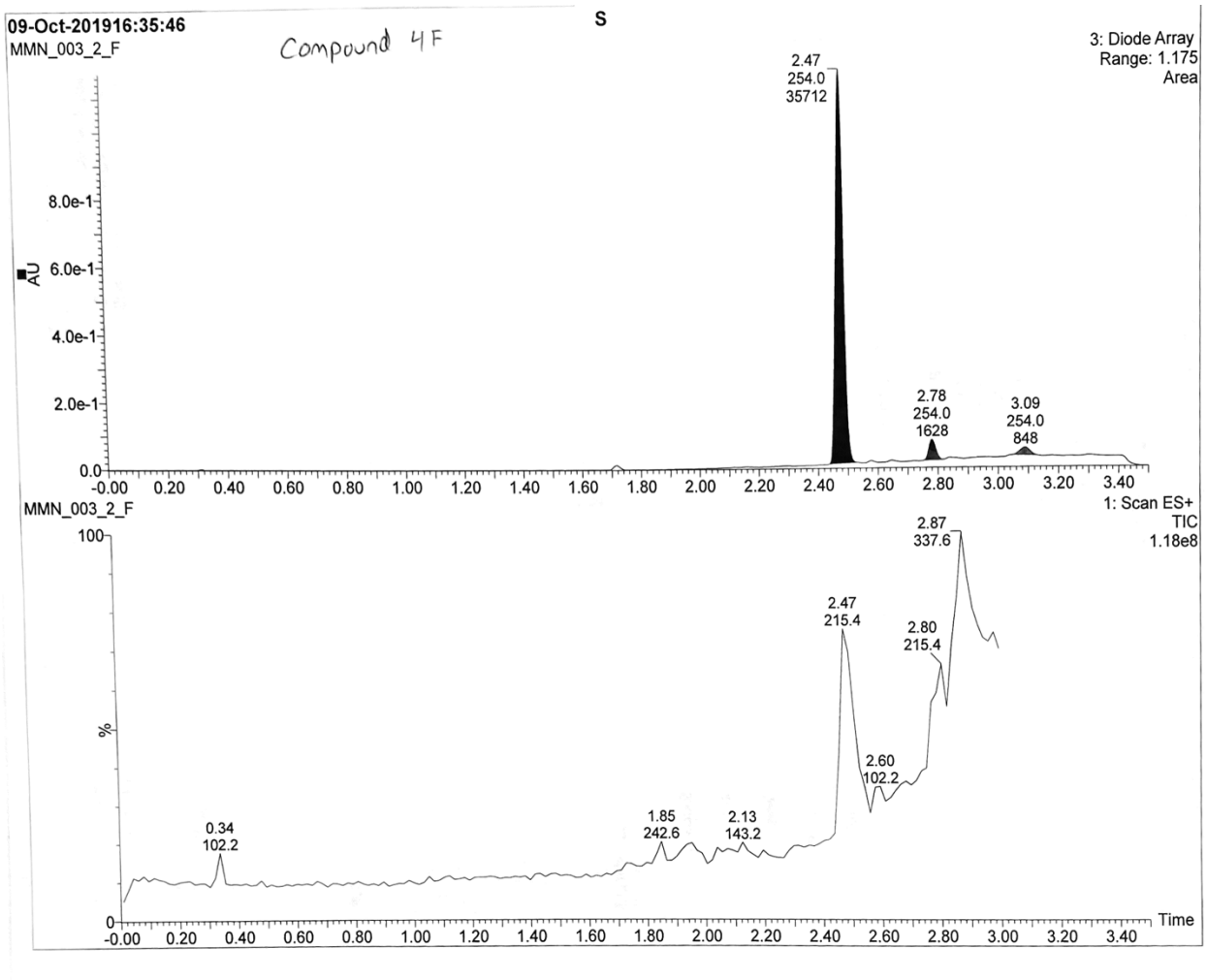



3AF
Compound 3AF
S
MMN_003_2_G
3: Diode Array
Range: 1.153e-1
Area
AU
2.37
254.0
3153.5
2.89
254.0
77.9
2.33
254.0
9.9
1.92
254.0
17.7
0.31
254.0
685.3
MMN_003_2_G
3: Diode Array
Range: 1.255e-1
AU
2.37
254.0
0.31
254.0
MMN_003_2_G
1: Scan ES+
TIC
4.56e7
2.89
102.2
%
0.34
143.3
0.77
155.2
0.91
155.1
1.26
143.2
1.50
143.2
1.73
143.2
1.85
242.6
2.41
143.2
2.70
143.3
Time
09-Oct-201916:35:46
MMN_003_2_F
S

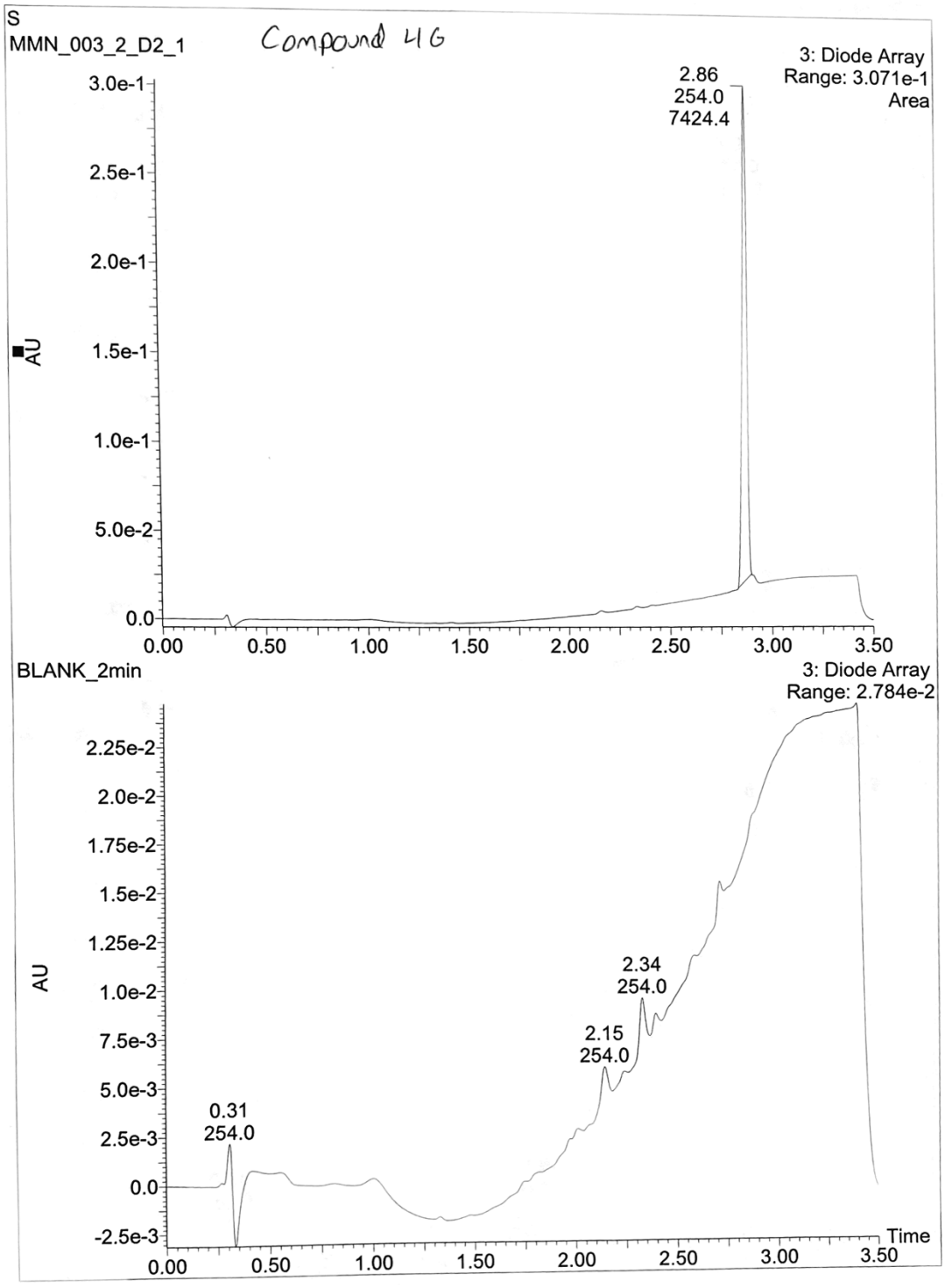

08-Oct-201916:46:16
S
cro_iii_214_2
Compound 4B
3: Diode Array
Range: 2.408e-1
Area
2.24
254.0
6422
3.41
254.0
125
AU
2.0e-1
1.75e-1
1.5e-1
1.25e-1
1.0e-1
7.5e-2
5.0e-2
2.5e-2
0.0
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40 1.60 1.80 2.00 2.20 2.40 2.60 2.80 3.00 3.20 3.40
cro_iii_214_2
1: Scan ES+
TIC
1.22e8
2.25
135.2
0.34
143.3
1.85
242.5
2.04
143.2
100
%
0
Time

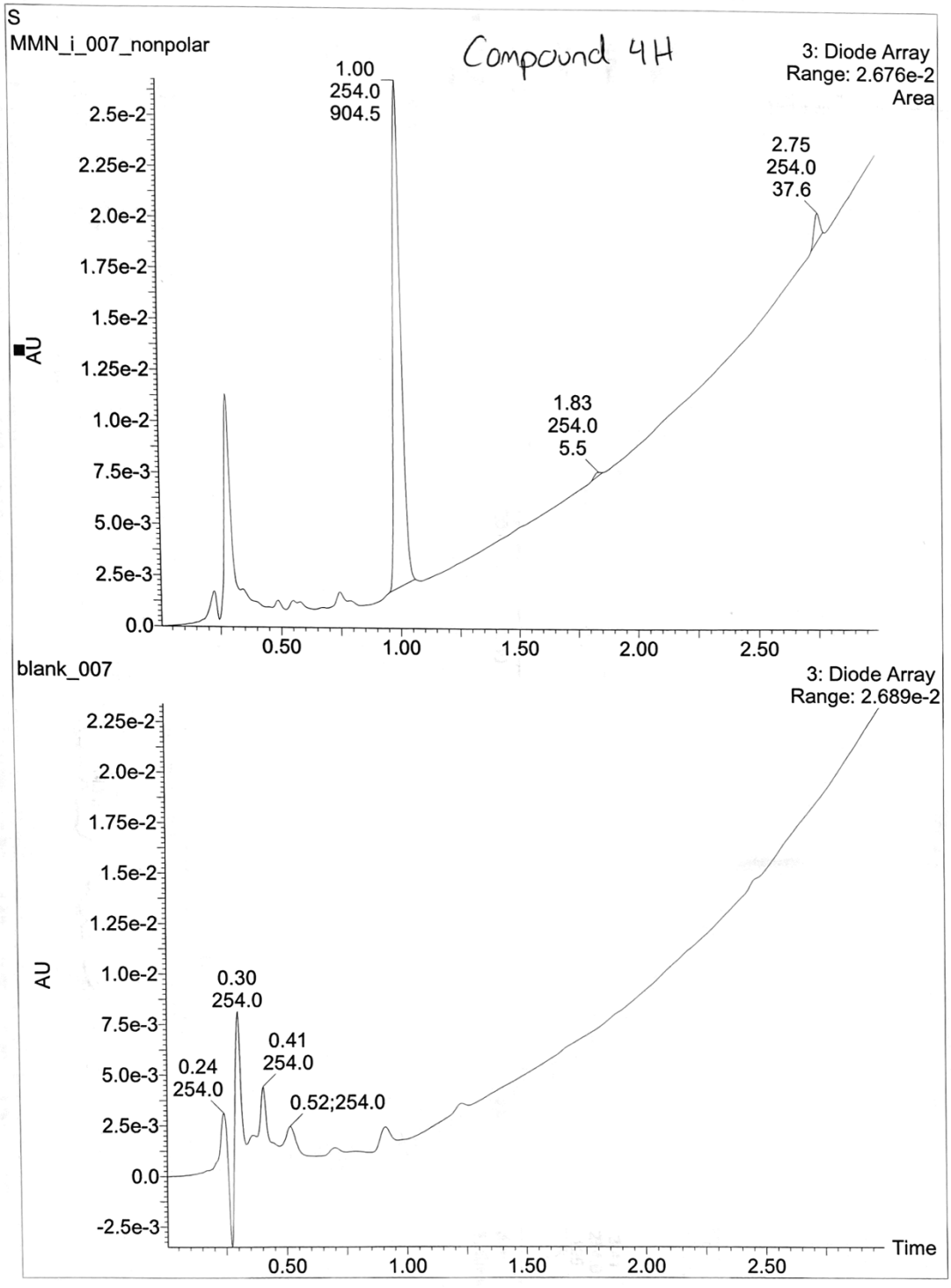

08-Oct-201916:55:12
S
cro_iii_178_3
Compound 3N
3: Diode Array
Range: 2.56
Area
2.37
254.0
151986
AU
1.72
254.0
1259
2.55
254.0
331
2.84
254.0
516
cro_iii_178_3
1: Scan ES+
TIC
9.33e7
2.39
107.2
2.96
102.2
2.93
102.2
2.47
312.5
2.79
399.5
2.32
271.4
2.08
125.2
1.85
242.6
0.34
168.3
0.08
155.1
%
Time


08-Oct-201916:50:45
S
cro_iii_220_1 Sm (Mn, 2x3)
Compound 41C
3: Diode Array
Range: 1.501e-1
Area
AU
2.46
254.0
4300
0.31
254.0
615
2.16
254.0
46
2.38
254.0
14
2.63
254.0
161
2.98
254.0
27
cro_iii_220_1
3: Diode Array
Range: 1.627e-1
2.46
254.0
3.07
254.0
0.31
254.0
1: Scan ES+
TIC
1.39e8
2.47
149.3
2.65
135.2
1.85
242.6
2.04
143.2
2.27
468.8
0.34
143.2
%
Time

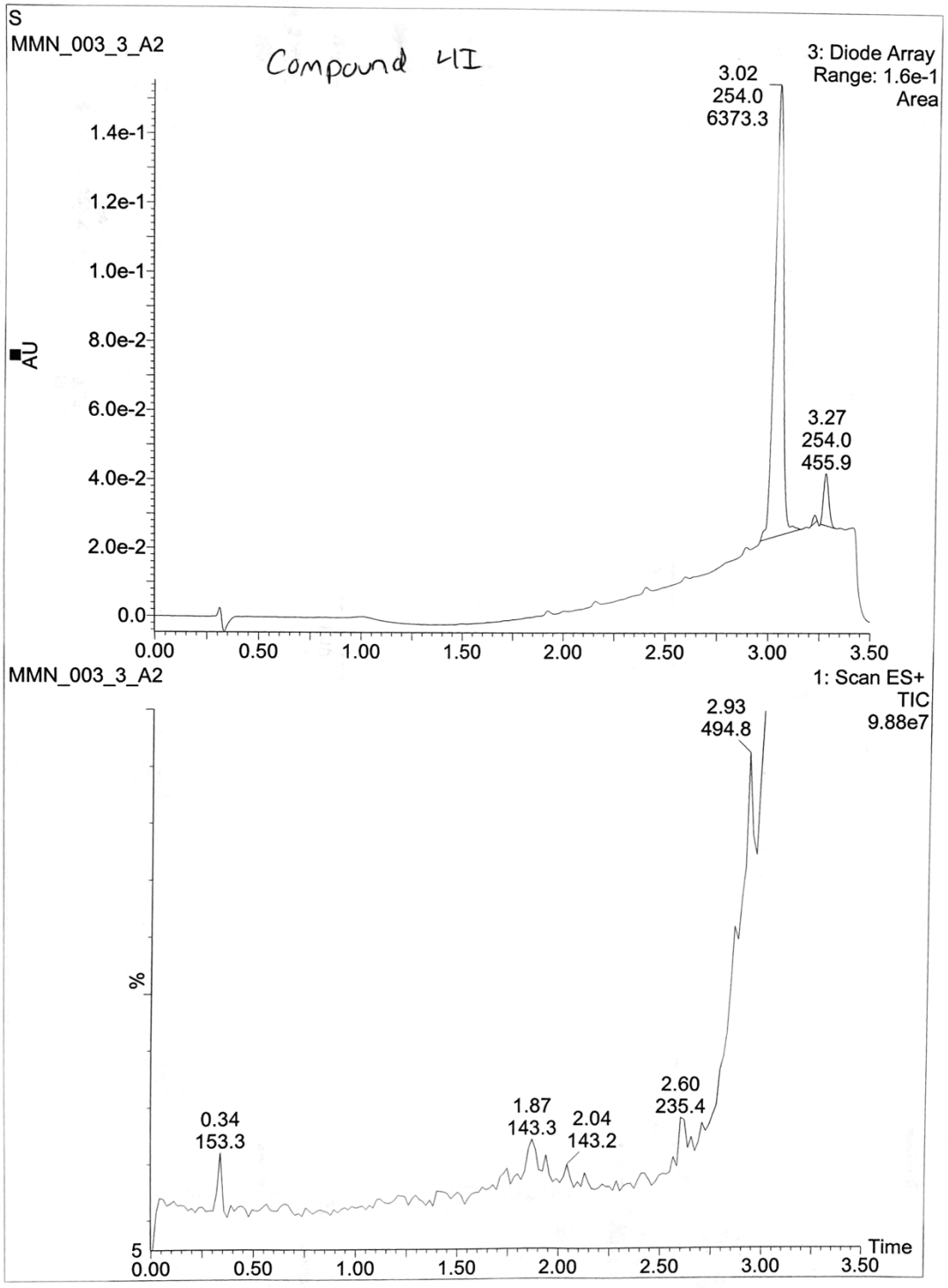

09-Oct-201916:35:46
MMN_003_2_F
Compound 4F
S
3: Diode Array
Range: 1.175
Area
2.47
254.0
35712
2.78
254.0
1628
3.09
254.0
848
AU
8.0e-1
6.0e-1
4.0e-1
2.0e-1
0.0
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40 1.60 1.80 2.00 2.20 2.40 2.60 2.80 3.00 3.20 3.40
MMN_003_2_F
1: Scan ES+
TIC
1.18e8
2.87
337.6
2.47
215.4
2.80
215.4
2.60
102.2
1.85
242.6
2.13
143.2
0.34
102.2
%
100
0
Time
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40 1.60 1.80 2.00 2.20 2.40 2.60 2.80 3.00 3.20 3.40

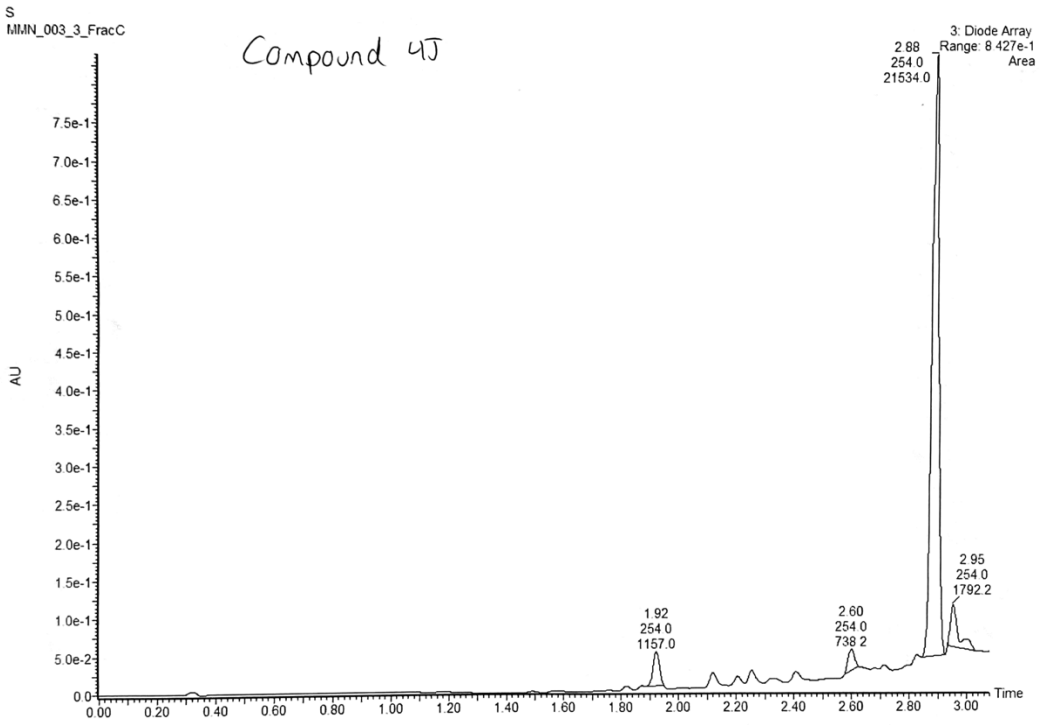
4G

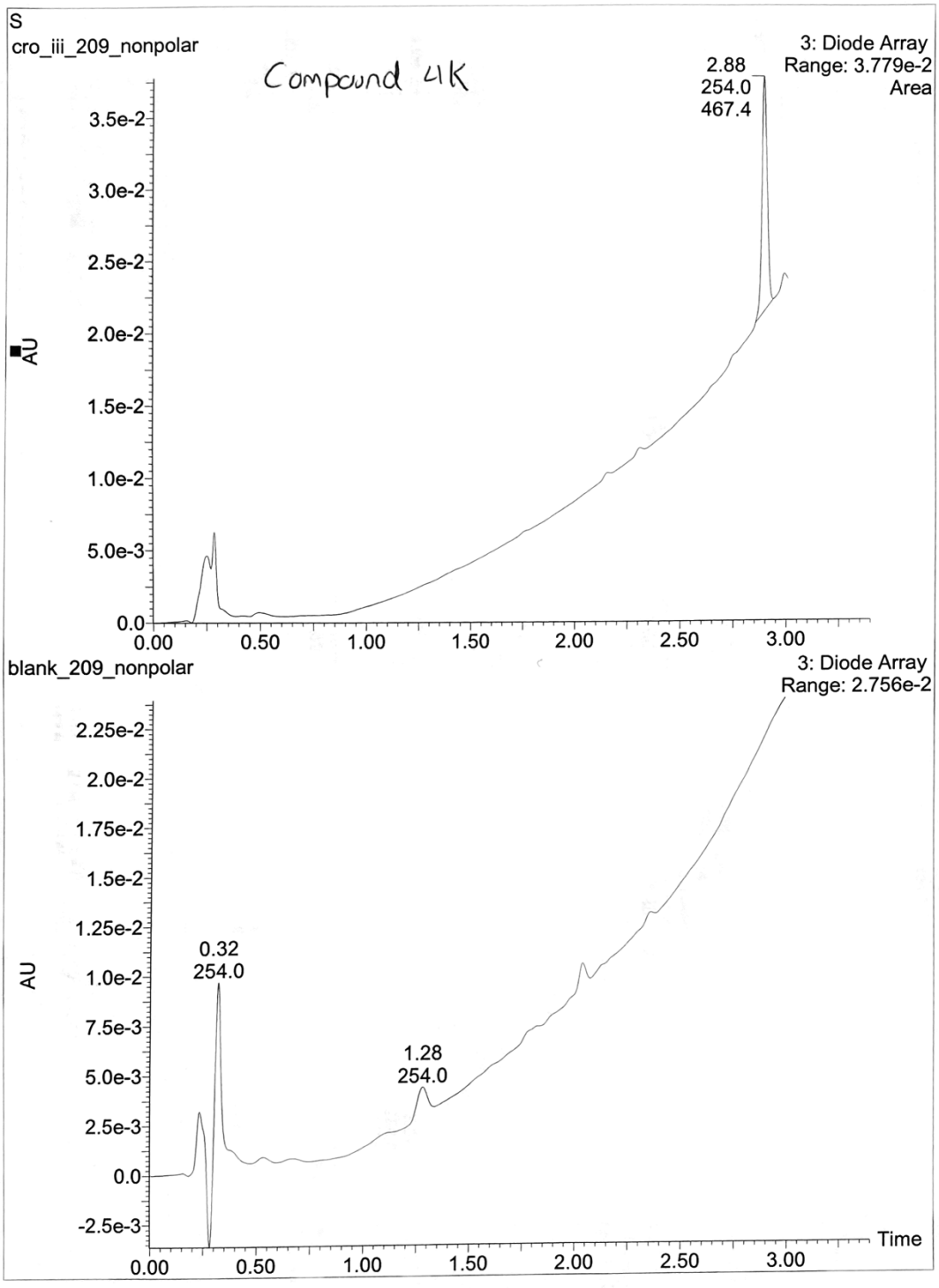

S
MMN_003_2_D2_1
Compound 4G
3: Diode Array
Range: 3.071e-1
Area
2.86
254.0
7424.4
AU
3.0e-1
2.5e-1
2.0e-1
1.5e-1
1.0e-1
5.0e-2
0.0
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
BLANK_2min
3: Diode Array
Range: 2.784e-2
2.25e-2
2.0e-2
1.75e-2
1.5e-2
1.25e-2
1.0e-2
7.5e-3
5.0e-3
2.5e-3
0.0
-2.5e-3
0.31
254.0
2.15
254.0
2.34
254.0
Time

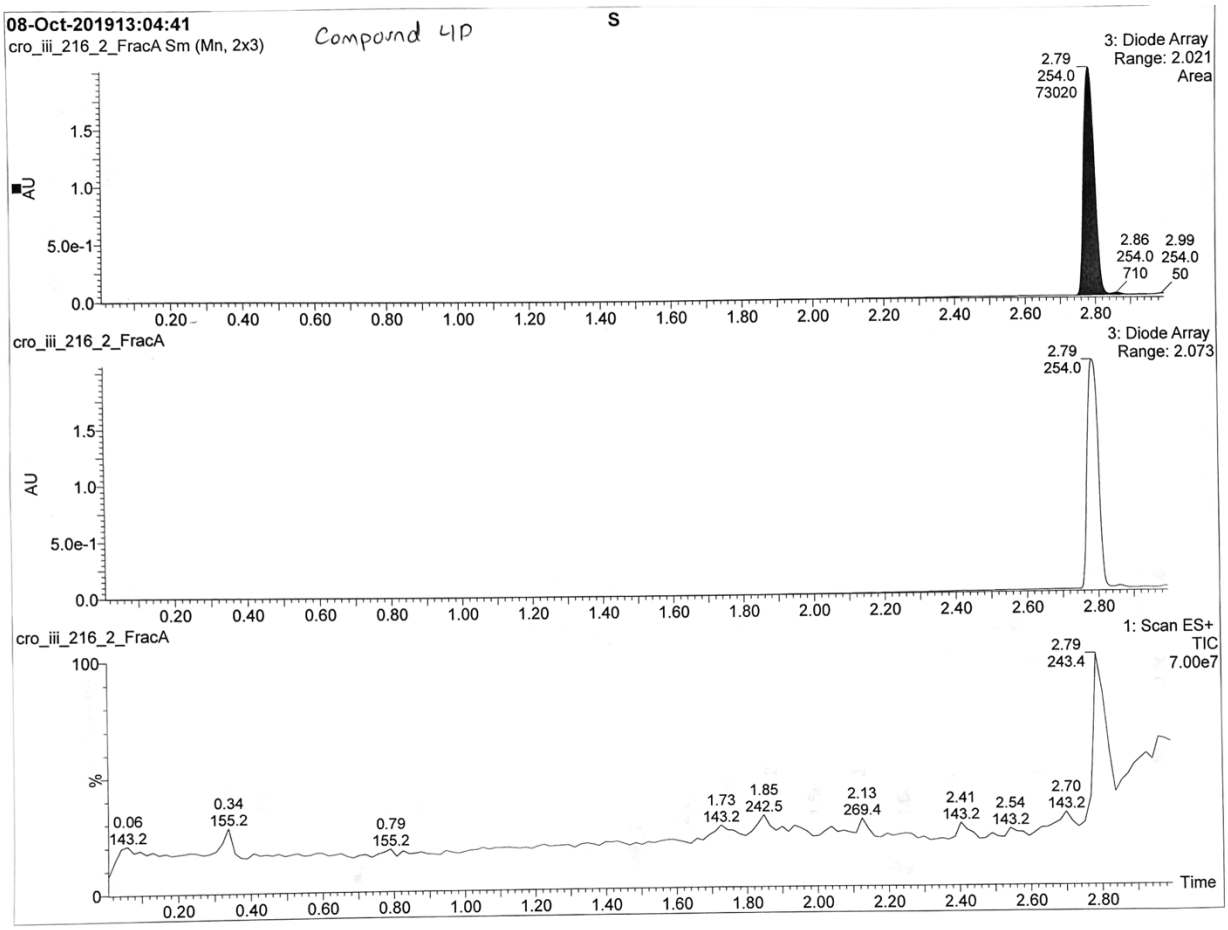

S
MMN_i_007_nonpolar
Compound 4H
3: Diode Array
Range: 2.676e-2
Area
1.00
254.0
904.5
2.75
254.0
37.6
1.83
254.0
5.5
AU
2.5e-2
2.25e-2
2.0e-2
1.75e-2
1.5e-2
1.25e-2
1.0e-2
7.5e-3
5.0e-3
2.5e-3
0.0
0.50
1.00
1.50
2.00
2.50
blank_007
3: Diode Array
Range: 2.689e-2
0.30
254.0
0.41
254.0
0.24
254.0
0.52;254.0
-2.5e-3
Time

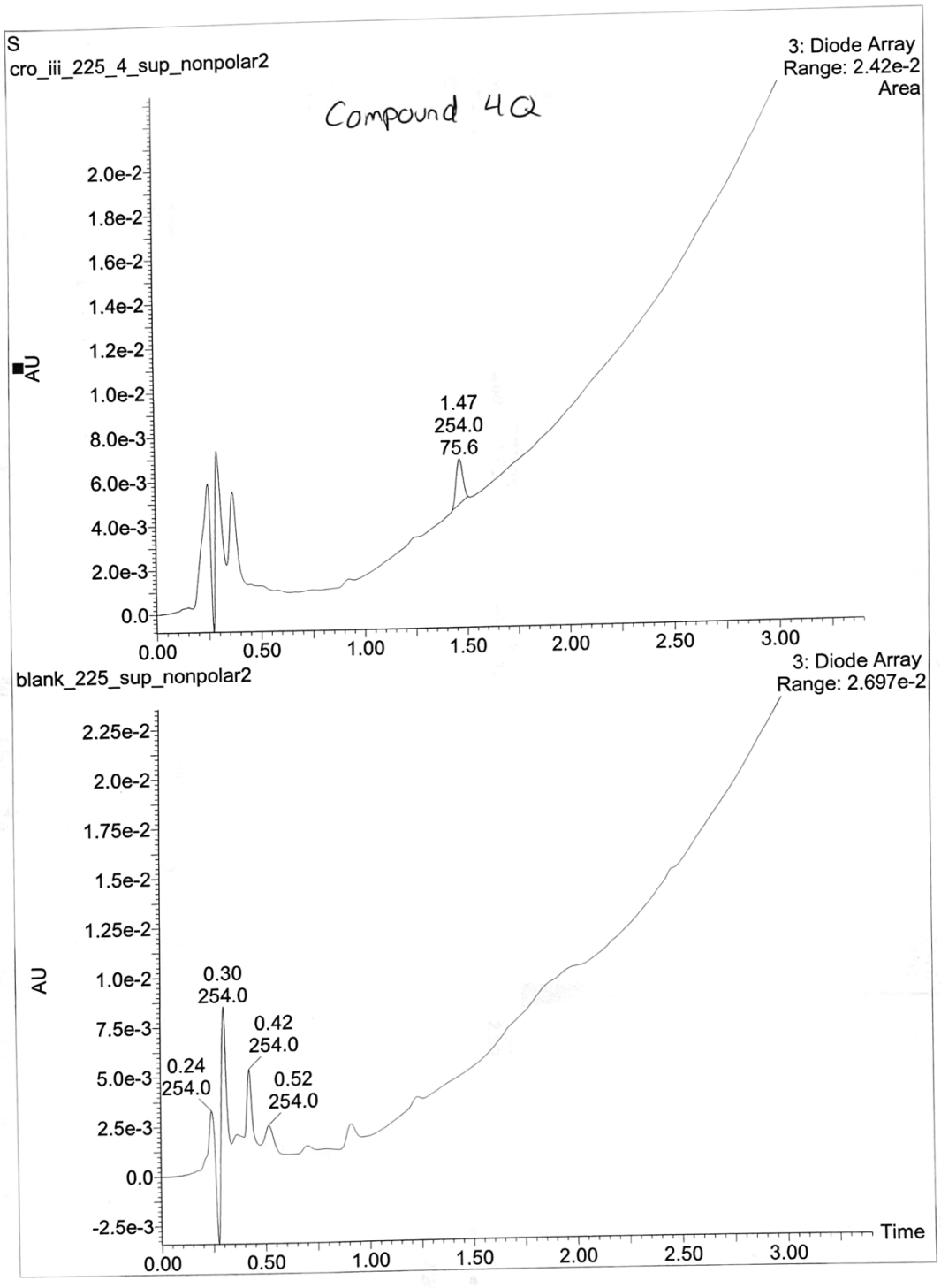
4I

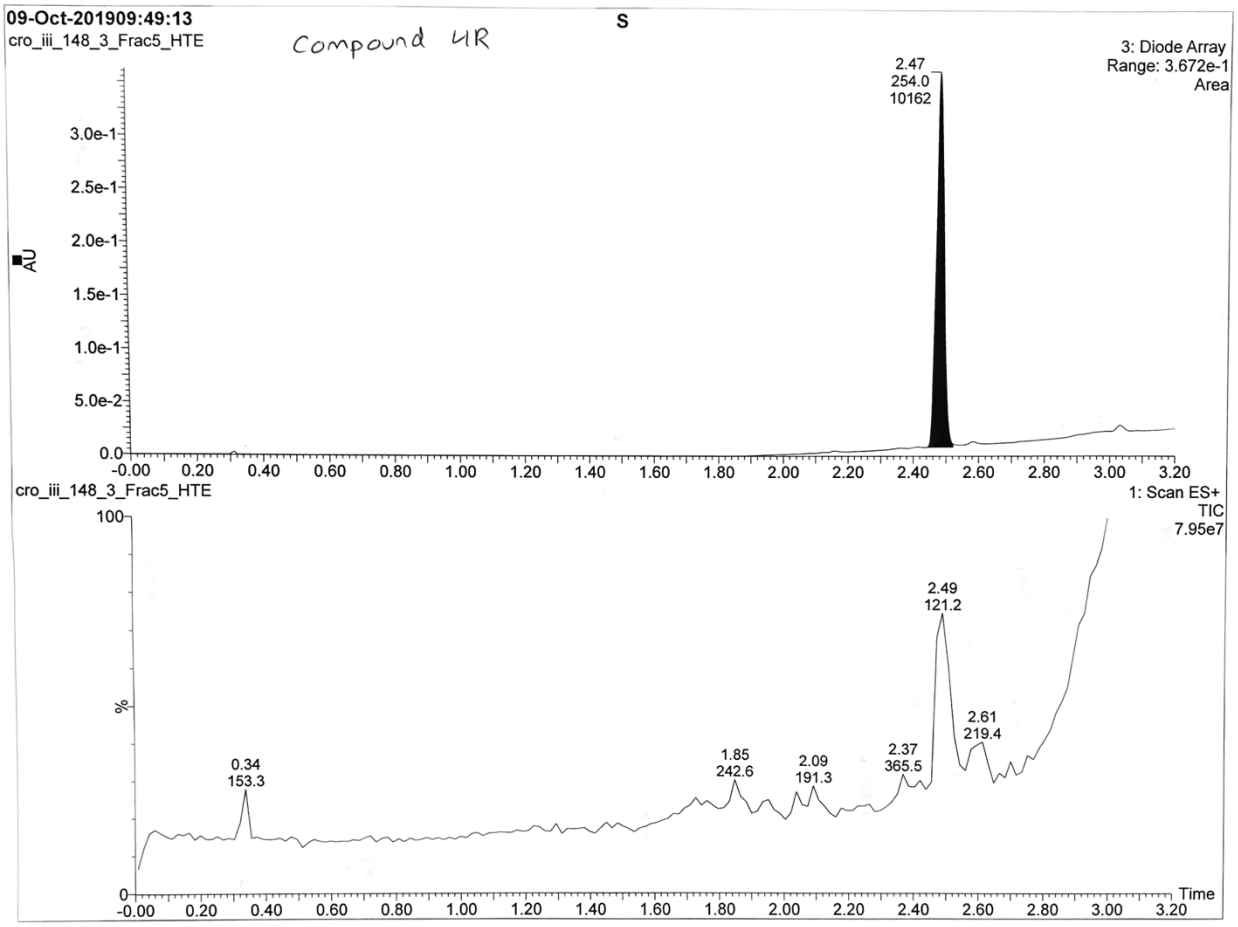

S
MMN_003_3_A2
Compound 4I
3: Diode Array
Range: 1.6e-1
Area
3.02
254.0
6373.3
3.27
254.0
455.9
AU
1.4e-1
1.2e-1
1.0e-1
8.0e-2
6.0e-2
4.0e-2
2.0e-2
0.0
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
MMN_003_3_A2
1: Scan ES+
TIC
9.88e7
2.93
494.8
%
0.34
153.3
1.87
143.3
2.04
143.2
2.60
235.4
5
Time


S
MMN_003_3_FracC
Compound 4J
3: Diode Array
Range: 8.427e-1
Area
2.88
254.0
21534.0
2.95
254.0
1792.2
1.92
254.0
1157.0
2.60
254.0
738.2
AU
Time
7.5e-1
7.0e-1
6.5e-1
6.0e-1
5.5e-1
5.0e-1
4.5e-1
4.0e-1
3.5e-1
3.0e-1
2.5e-1
2.0e-1
1.5e-1
1.0e-1
5.0e-2
0.0
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
2.20
2.40
2.60
2.80
3.00


S
cro_iii_209_nonpolar
Compound 41K
3: Diode Array
Range: 3.779e-2
Area
2.88
254.0
467.4
AU
3.5e-2
3.0e-2
2.5e-2
2.0e-2
1.5e-2
1.0e-2
5.0e-3
0.0
0.00
0.50
1.00
1.50
2.00
2.50
3.00
blank_209_nonpolar
3: Diode Array
Range: 2.756e-2
AU
2.25e-2
2.0e-2
1.75e-2
1.5e-2
1.25e-2
1.0e-2
7.5e-3
5.0e-3
2.5e-3
0.0
-2.5e-3
0.32
254.0
1.28
254.0
Time
0.00
0.50
1.00
1.50
2.00
2.50
3.00


08-Oct-201913:04:41
cro_iii_216_2_FracA Sm (Mn, 2x3)
Compound 4P
S
3: Diode Array
Range: 2.021
Area
2.79
254.0
73020
2.86
254.0
710
2.99
254.0
50
AU
cro_iii_216_2_FracA
3: Diode Array
Range: 2.073
2.79
254.0
1: Scan ES+
TIC
7.00e7
2.79
243.4
0.06
143.2
0.34
155.2
0.79
155.2
1.73
143.2
1.85
242.5
2.13
269.4
2.41
143.2
2.54
143.2
2.70
143.2
%
Time


S
cro_iii_225_4_sup_nonpolar2
3: Diode Array
Range: 2.42e-2
Area
Compound 4Q
AU
1.47
254.0
75.6
blank_225_sup_nonpolar2
3: Diode Array
Range: 2.697e-2
AU
0.30
254.0
0.42
254.0
0.24
254.0
0.52
254.0
Time


09-Oct-201909:49:13
S
cro_iii_148_3_Frac5_HTE
Compound 4R
3: Diode Array
Range: 3.672e-1
Area
2.47
254.0
10162
AU
3.0e-1
2.5e-1
2.0e-1
1.5e-1
1.0e-1
5.0e-2
0.0
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40 1.60 1.80 2.00 2.20 2.40 2.60 2.80 3.00 3.20
cro_iii_148_3_Frac5_HTE
1: Scan ES+
TIC
7.95e7
100
%
0
2.49
121.2
2.61
219.4
0.34
153.3
1.85
242.6
2.09
191.3
2.37
365.5
Time
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40 1.60 1.80 2.00 2.20 2.40 2.60 2.80 3.00 3.20

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