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Supporting Information

A Scalable Biomimetic Synthesis of Resveratrol Dimers and Systematic Evaluation of their Antioxidant Activities**

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Supporting Information

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I. General Information:

Commercially available starting materials were used as received without further purification unless otherwise noted. Glassware was dried in a 170 °C oven or flame-dried under vacuum prior to use. Reactions were monitored by TLC and visualized by either dual short-wave/long-wave UV lamp or staining with an ethanolic solution of potassium permanganate or *p*-anisaldehyde. Flash chromatography was performed manually using 43-60 μm (230–400 mesh) silica gel or utilizing Redi*Sep*®*R*$_F$ Gold silica columns with a Teledyne Isco CombiFlash R_F automated purification system.

^{1}H and ^{13}C NMR spectra were recorded at ambient temperature at 117 kG and 176 kG (^{1}H 500 MHz, 700 MHz; ^{13}C 125 MHz and 175 MHz) using an internal deuterium lock on Varian Inova 500 or Varian vnmr 500 and 700 spectrometers. ^{1}H chemical shifts are expressed in parts per million (ppm) relative to the residual protio solvent resonance in $CDCl_3$ using δ 7.26 as standard for residual $CHCl_3$ or using the center line of the solvent signal as internal reference for acetone-d_6: δ 2.05. Multiplicity is reported as follows: (br = broad, s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet), and the corresponding coupling constants are indicated as *J* values in units of Hz. For ^{13}C spectra, the center line of the solvent signal was used as internal reference: $CDCl_3$ δ 77.23; $(CD_3)_2CO$ δ 29.92. Infrared spectra were recorded on a Perkin-Elmer Spectrum BX FT-IR spectrophotometer using an ATR mount with a ZnSe crystal. Absorption bands are expressed in wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were obtained on an Agilent quadrupolar time-of-flight (Q-TOF) mass spectrometer using electrospray ionization (ESI), positive ion mode. Chemical names were generated using ChemDraw Ultra 13.0 (PerkinElmer)–for racemic compounds, the name corresponds to the absolute configuration of the compound whose structure is shown.

Materials. Methyl linoleate, egg phosphatidylcholine, Triton™ X-100 and penicillin-streptomycin were purchased from Sigma-Aldrich. C11-BODIPY$^{581/591}$ (4,4-difluoro-5-(4-phenyl-1,3-butadienyl)-4-bora-3a,4a-diaza-s-indacene-3-undecano-ic acid), MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide), RPMI-1640 media with/without phenol red, fetal bovine serum (FBS), Hank's balanced salt solution (HBSS) were purchased from Invitrogen (life technologies). Phosphate buffered saline (PBS), 2, 2'-azobis(4-methoxy-2,4-dimethylvaleronitrile) (MeOAMVN), 2,2'-azobis-(2-amidinopropane) monohydrochloride (AAPH) and all other chemicals were used as received. The H_2B-PMHC fluorescent probe was prepared according to the previous literature.[1]

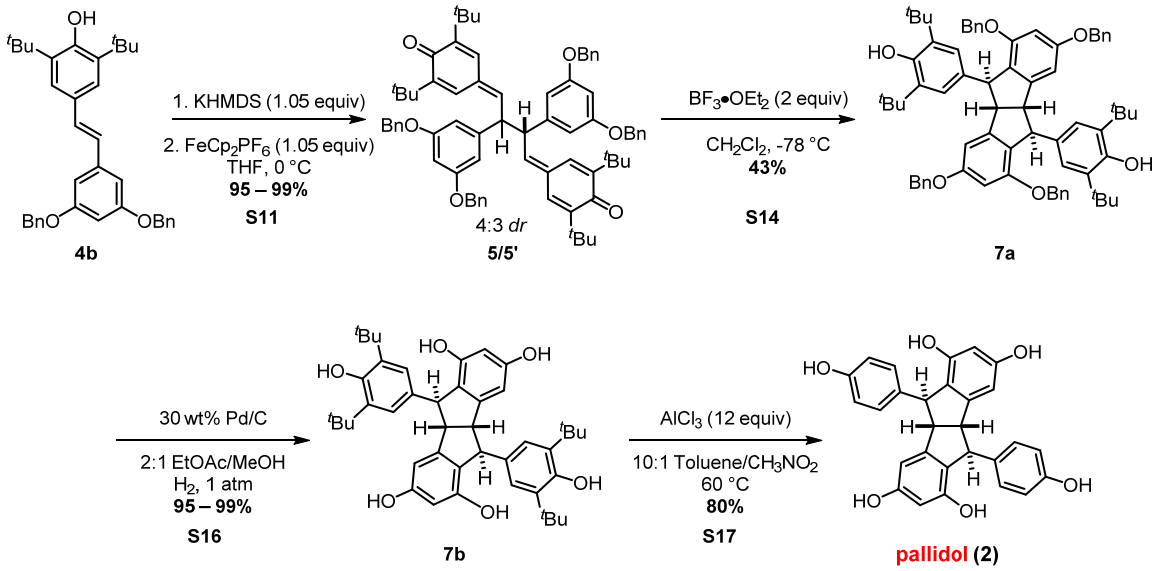
Radical Clock Experiments. Methyl linoleate (MeLn) was chromatographed on silica gel (5% EtOAc/ hexanes) prior to use. Stock solutions (0.02 M) of the tested compounds and methyl linoleate (1.0 M) were prepared in chlorobenzene separately. A stock solution of MeOAMVN (0.05 M) was prepared in benzene. Samples were prepared in 1.0 mL autosampler vials with a total reaction volume of 100 μL. The solutions were added in the following order to avoid premature oxidation: inhibitor (final concentration is 0.002 - 0.01 M), amount of chlorobenzene required to dilute samples to 100 μL, methyl linoleate (0.1 M), and MeOAMVN (0.01 M). The sealed samples were then incubated at 37 °C for 90 minutes. Stock solutions of BHT (1.0 M in hexanes) and PPh_3 (1.0 M in chlorobenzene) were prepared separately. Following the oxidation, the BHT solution (0.05 M) and then PPh_3 solution (0.05 M), were added to the samples and then diluted to 1 mL with HPLC grade hexanes, and analyzed by HPLC (0.5 % iPrOH/hexanes, 1.1 mL/min for 30 min, Sun-Fire Silica 5 mm 4.6 × 250 mm column, detection at 234 nm). The ratio of products (*E*,*Z*:*E*,*E*) was plotted versus the concentration of the tested compound to determine k_{inh} according to the reported procedure.[2]

Liposome Preparation and Oxidation. Liposome preparation and oxidations were performed following the procedure in one of our recent manuscripts.[3] To individual 21.4 μL aliquots of the 20 mM liposome solution were added increasing amounts (1.25, 2.5, 5, 7.5, 10 and 15 μL, respectively) of a solution of the test antioxidant in DMSO (857.5 μM) and 2.5 μL of a solution of H_2B-PMHC in acetonitrile (25.8 μM). Each resultant solution was then diluted to 400 μL with 10 mM phosphate buffered-saline (PBS) solution containing 150 mM NaCl (pH 7.4), from which 280 μL of each was loaded into a well of a 96-well microplate. The solution was equilibrated to 37 °C for 5 min, after which 20 μL of a solution of azo compound (40.5 mM in 2,2'-azobis-(2-amidinopropane)monohydrochloride, AAPH, in PBS or 10.1 mM in 2,2'-azobis-(4-methoxy-2,4-dimethylvaleronitrile, MeOAMVN, in acetonitrile was added to each well. The fluorescence was then monitored for 10 h at 60 s time intervals (λ_{ex} = 485 nm; λ_{em} = 520 nm). The final solutions in each well were 1 mM in lipids, 0.15 μM in H_2B-PMHC, 2.7 mM in AAPH or 0.68 mM in MeOAMVN and either 2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM in antioxidant. The rates of peroxyl radical trapping by the test compounds relative to the probe H_2B-PMHC were determined by re-plotting the data as $-\ln\{(I_\infty - I_t)/(I_\infty - I_0)\}$ versus $-\ln(1 - t/\tau)$ and determining the slope from the initial portion of the graph, which corresponds to $k_{inh}^{H_2B\text{-}PMHC}/k_{inh}^{unknown}$ as described in references [1] and [3].

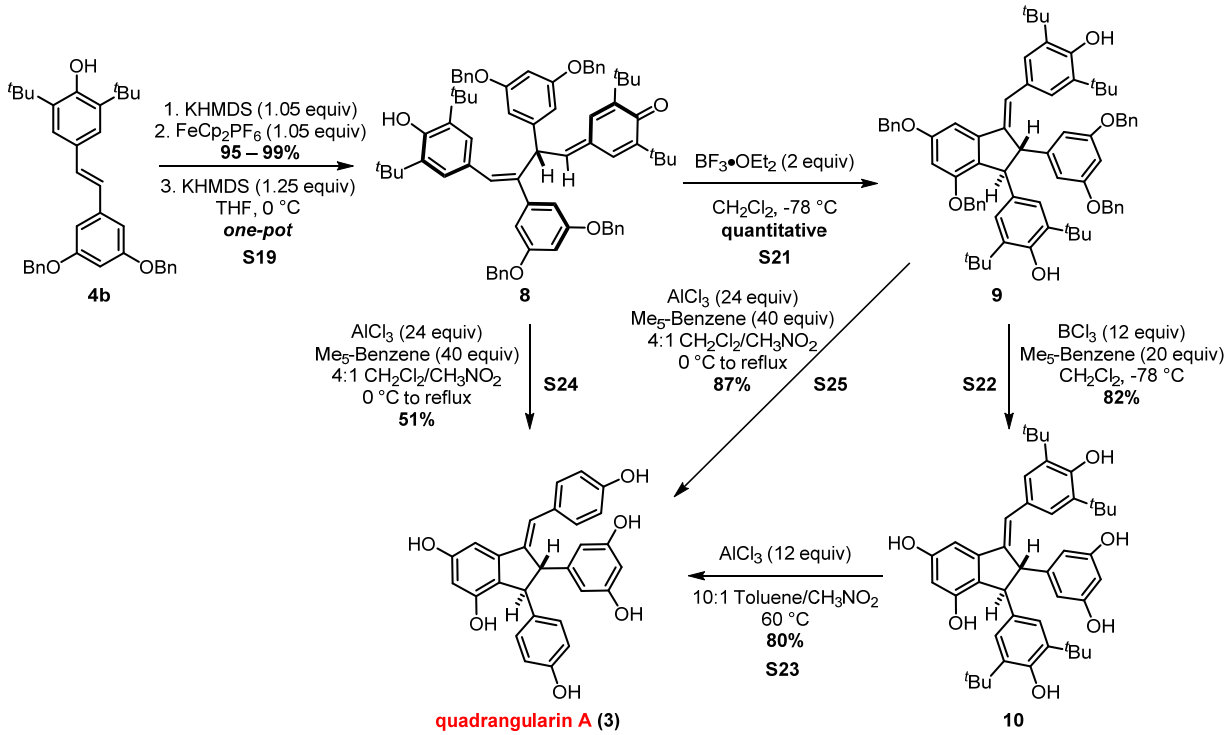
Cellular Lipid Peroxidation. TF1a cells were cultured in RPMI-1640 media (with phenol red) with 10 % FBS and 1 % penicillin-streptomycin. The cells (5×10^5 cells in 1 mL media) were treated with each antioxidant at final concentrations from 1.5 μM to 50 μM and incubated at 37 °C for 22 hours in phenol red-free RPMI-1640 media with 10 % FBS in humidified 5 % CO_2 atmosphere in 12-well plates. Cells were then treated with 1 μM C11-BODIPY$^{581/591}$ and incubated at 37 °C in the dark for 30 minutes after which oxidative stress was induced with diethylmaleate (9 mM) for 2 hours. Treated cells were then collected by centrifugation at 250×g for 4 minutes and washed with PBS. Cells were resuspended in PBS and analyzed by flow cytometry at a final concentration of 5×10^5 cells/ml (λ_{ex} = 488 nm; λ_{em} = 525±25 nm). Cells not treated with DEM were used as negative control. Cells not treated with antioxidants were used as positive control.

Cell Viability. TF1a cells (5×10^4 cells in 250 μL media) were treated with each antioxidant in DMSO at final concentrations ranging from 0.5 μM to 750 μM (final DMSO concentration was to not exceed 1% v/v) and incubated at 37°C for 22 hours in phenol red-free RPMI-1640 media with 10% FBS in a humidified 5 % CO_2 atmosphere on a 96-well plate. Each well was then treated with 50 μL of MTT (12.1 μM in HBSS) for 4h. The treated cells were collected by centrifugation at 250×g for 5 minutes and the solution was aspirated. The resultant purple crystals were dissolved with a 250 μL 1:4 water:DMSO (v/v) solution followed by 30 minutes incubation at room temperature. Absorbance (λ = 570 nm) was measured by microplate reader. Results were compared to a negative control (1 % DMSO) and a positive control (1 % Triton™ X-100).

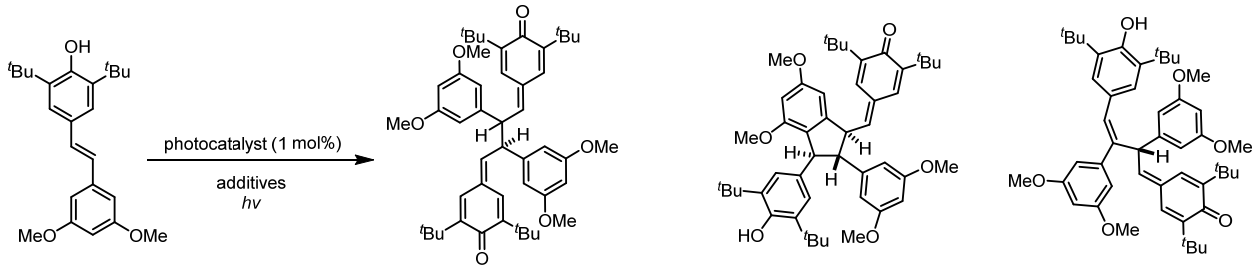
The Total Synthesis of Pallidol (2)



The Total Synthesis of Quadrangularin A (3)



Optimization of Photocatalytic/Aerobic Oxidative Resveratrol Dimerization:



4 OMe | **5/5' OMe** 3:2 *dr* | **6 OMe** | **8 OMe**

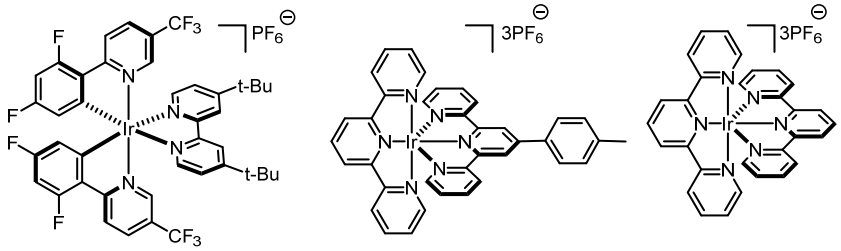
Entry	Photocatalyst	Solvent	Oxidant	Additive	Time	Yield	Product
1	$Ru(bpy)_3Cl_2$	MeCN	$BrCCl_3$	—	12h	Decomp.	—
2	$Ru(bpy)_3Cl_2$	MeCN	$(NH_4)_2S_2O_8$	—	2h	Decomp.	—
3	$Ir(tpy)_2(PF_6)_3$	MeCN	O_2	—	2d	7%[a]	**6**
4	$Ir(ttpy)(tpy)(PF_6)_3$	Acetone	O_2	—	2d	38%	**6**
5	$Ir(ttpy)(tpy)(PF_6)_3$	Acetone/MeOH	O_2	NaOMe	5h	47%	**8**
6	—	Acetone/MeOH	Degassed	NaOMe	2h	100%	E/Z **4**
7[b]	—	Acetone/MeOH	Degassed	NaOMe	2h	—	**4**
8[b]	$Ir(ttpy)(tpy)(PF_6)_3$	Acetone/MeOH	O_2	NaOMe	5h	45%	**8**
9[b]	—	Acetone/MeOH	O_2	NaOMe	2h	55%	**8**
10[b]	—	CCl_4[c]	O_2	KO^{t}Bu	1h	60-80%	**5**
11	—	THF	$FeCp_2PF_6$	KHMDS	30min	99%	**5**
12	$Ir[(dF\{CF_3\}ppy)_2(dtbbpy)]PF_6$	CCl_4	CCl_4	—	3d	0%	—

[a] Incomplete conversion

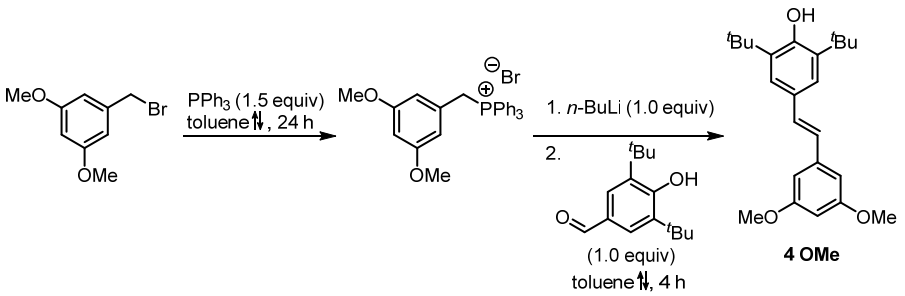
[b] Reaction was shielded from light

[c] Assuming that electron transfer to O_2 was the rate-limiting step in the dimerization, we performed the oxidation in solvents which are known to possess high oxygen solubility: N. J. Turro, V. Ramamurthy, J. C. Scaiano *Modern Molecular Photochemistry of Organic Molecules*, University Science Books, Sausalito, Calif, **2010**, pp. 1001-1042.

Photocatalyst Structure



$Ir[(dF\{CF_3\}ppy)_2(dtbbpy)]PF_6$ | **$Ir(ttpy)(tpy)(PF_6)_3$** | **$Ir(tpy)_2(PF_6)_3$**



(*E*)-2,6-di-tert-butyl-4-(3,5-dimethoxystyryl)phenol (4 OMe): A round bottom flask equipped with a reflux condenser and magnetic stir bar was charged with commercially available 3,5-dimethoxy benzyl bromide (6.00 g, 26.0 mmol, 1.00 equiv). The material was dissolved in anhydrous toluene (60 mL, 0.43 M) at room temperature under N_2. To the stirring mixture, PPh_3 (10.2 g, 38.9 mmol, 1.5 equiv) was added in a single portion and the solution was heated to reflux for 24 h. The reaction mixture was allowed to cool to room temperature and the product collected by vacuum filtration. The solid was washed with hexanes and dried under vacuum to give the desired phosphonium salt as a crystalline white solid (12.8 g, 26.0 mmol 99% yield). The phosphonium salt (5.00 g, 10.1 mmol, 1.00 equiv) was suspended in anhydrous toluene (200 mL, 0.05 M) in a flame-dried, 3-neck 500 mL round bottom flask equipped with a reflux condenser and magnetic stir bar. To the stirring suspension at room temperature under N_2, *n*-BuLi (4.00 mL, 2.5 M soln. in hexanes, 1.00 equiv) was added slowly, turning the mixture a brilliant red. The mixture was allowed to equilibrate at this temperature for 30 minutes, at which point the solution of the ylide was heated to reflux. Once reflux temperature was reached, 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (2.38 g, 10.1 mmol, 1.00 equiv, recrystallized from toluene and dried from benzene 3x prior to use) was added as a solid, portion wise under a stream of N_2. The reaction was allowed to stir at this temperature for 4 hours; reaction progress was monitored by TLC in 9:1 Hexanes/EtOAc. At 4 h, the reaction was quenched with methanol and the solvent removed by rotary evaporation. The crude residue was treated with cold diethyl ether to precipitate triphenylphosphine oxide, and filtered through a fritted funnel packed with Celite and a filter paper. The crude filtrate was then dried onto Celite and purified by flash chromatography using 97:2:1 Hexanes/EtOAc/CH_2Cl_2 as the mobile phase. The desired stilbene (**4 OMe**) was obtained as an amorphous white solid (2.90 g, 7.87 mmol, 78% yield).

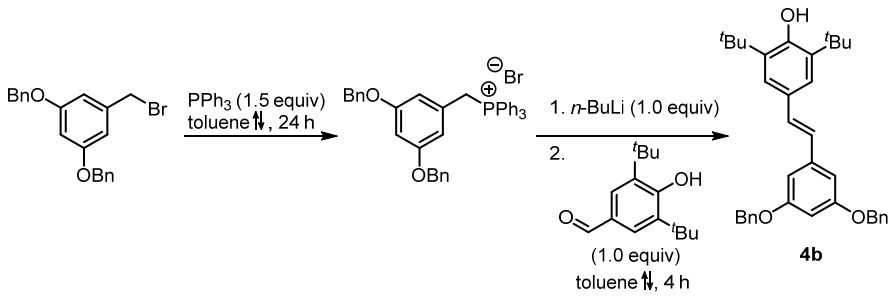
Rf (Hexanes/EtOAc, 9:1): 0.35

IR (Neat): 3624, 2956, 1590, 1456, 1436, 1358, 1236, 1204, 1150, 1066 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.34 (s, 2H), 7.05 (d, J = 16.1 Hz, 1H), 6.87 (d, J = 16.1 Hz, 1H), 6.66 (d, J = 2.2 Hz, 2H), 6.37 (t, J = 2.2 Hz, 1H), 5.29 (s, 1H), 3.84 (s, 6H), 1.48 (s, 18H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 161.2, 154.2, 140.2, 136.4, 130.3, 128.6, 126.0, 123.7, 104.4, 99.8, 55.6, 34.6, 30.5;

HRMS (ESI) *m/z* calculated for $C_{24}H_{33}O_3^+$ ($[M+H]^+$) 369.2244, found 369.2426.



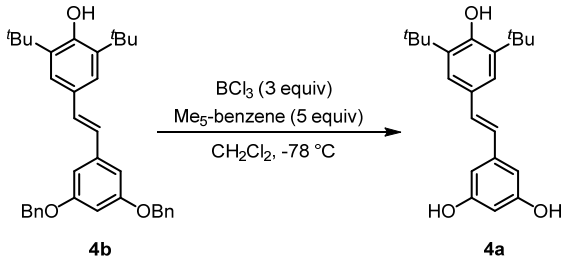
(*E*)-4-(3,5-bis(benzyloxy)styryl)-2,6-di-tert-butylphenol (4b): A round bottom flask equipped with a reflux condenser and magnetic stir bar was charged with commercially available 3,5-dibenzyloxy benzyl bromide (10.1 g, 26.4 mmol, 1.00 equiv). The material was dissolved in anhydrous toluene (60 mL, 0.44 M) at room temperature under N_2. To the stirring mixture, PPh_3 (10.4 g, 39.6 mmol, 1.50 equiv) was added in a single portion and the solution was heated to reflux for 24 h. The reaction mixture was allowed to cool to room temperature and the product collected by vacuum filtration. The solid was washed with hexanes and dried under vacuum to give the desired phosphonium salt as a crystalline white solid (16.9 g, 26.2 mmol 99% yield). The phosphonium salt (13.5 g, 22.4 mmol, 1.00 equiv) was suspended in anhydrous toluene (225 mL, 0.10 M) in a flame-dried, 3-neck 500 mL round bottom flask equipped with a reflux condenser and magnetic stir bar. To the stirring suspension at room temperature under N_2, *n*-BuLi (9.39 mL, 2.5 M soln. in hexanes, 1.05 equiv) was added slowly, turning the mixture a brilliant red. The mixture was allowed to equilibrate at this temperature for 30 minutes, at which point the solution of the ylide was heated to reflux. Once reflux temperature was reached, 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (5.77 g, 24.6 mmol, 1.10 equiv, recrystallized from toluene and dried from benzene 3x prior to use) was added as a solid, portionwise under a stream of N_2. The reaction was allowed to stir at this temperature for 4 hours; reaction progress was monitored by TLC in 9:1 Hexanes/EtOAc. At 4 h, the reaction was quenched with methanol and the solvent removed by rotary evaporation. The crude residue was treated with cold diethyl ether to precipitate triphenylphosphine oxide, and filtered through a fritted funnel packed with Celite and a filter paper. The crude filtrate was then dried onto Celite and purified by flash chromatography using 97:2:1 Hexanes/EtOAc/CH_2Cl_2 as the mobile phase. The desired stilbene (**4b**) was obtained as an amorphous white solid (9.57 g, 18.4 mmol, 82% yield), which was further purified to a crystalline white powder by sonication in ^{i}PrOH and collected by vacuum filtration.

Rf (Hexanes/EtOAc, 9:1): 0.35;

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.46 – 7.32 (m, 10H), 7.04 (d, J = 16.1 Hz, 1H), 6.87 (d, J = 16.1 Hz, 1H), 6.77 (d, J = 2.2 Hz, 2H), 6.52 (t, J = 2.2 Hz, 1H), 5.29 (s, 1H), 5.08 (s, 4H), 1.48 (s, 18H).

For additional characterization data, see:

W. Li, H. Li, Y. Li, Z. Hou, *Angew. Chem. Int. Ed.* **2006**, *45*, 7609–7611; *Angew. Chem.* **2006**, *118*, 7771–7773.



4b **4a**

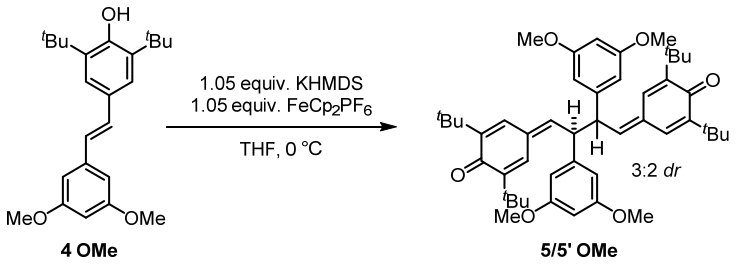
(*E*)-5-(3,5-di-tert-butyl-4-hydroxystyryl)benzene-1,3-diol (4a): A round bottom flask equipped with a septum and magnetic stir bar was charged with starting **4b** (1.75 g, 3.36 mmol, 1.00 equiv) and Me_5-benzene (2.49 g, 16.8 mmol, 5 equiv). The mixture was dissolved in anhydrous CH_2Cl_2 (57 mL, 0.05 M) at room temperature under N_2 and cooled to -78 °C. To the stirring mixture, BCl_3 (10.1 mL, 1.0 M soln. in CH_2Cl_2, 3 equiv) was added slowly, turning the reaction deep maroon. Upon completion of the addition, the reaction was quickly transferred to a 0 °C ice bath and stirred for an additional 40 minutes at this temperature, over which the reaction turned a bright transparent red color. The reaction was quenched at -78 °C by pipetwise addition of a 4:1 THF/sat. aq. $NaHCO_3$ mixture and the solution stirred vigorously under N_2 for several minutes as it decolorized. The contents were then transferred to a separatory funnel containing DI H_2O and the organic layer separated. The aqueous phase was extracted with CH_2Cl_2 (2x) and organic layers combined, dried over Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography using a gradient 5% to 15% EtOAc in $CHCl_3$ mobile phase to give **4a** as an amorphous white solid (1.05 g, 0.81 mmol, 91% yield) along with 45 mg (4%) of the corresponding (*Z*)-stilbene isomer. NOTE: **4a** is unstable to prolonged storage in air at room temperature, but could be stored indefinitely at -20 °C in a container sealed under N_2.

Rf (CH_2Cl_2/MeOH, 9:1): 0.48;

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31 (s, 2H), 7.02 (d, J = 16.4 Hz, 1H), 6.79 (d, J = 16.4 Hz, 1H), 6.56 (d, J = 2.2 Hz, 2H), 6.24 (t, J = 2.2 Hz, 1H), 5.30 (s, 1H), 4.66 (s, 2H), 1.47 (s, 18H).

For additional characterization data, see:

W. Li, H. Li, Y. Li, Z. Hou, *Angew. Chem. Int. Ed.* **2006**, *45*, 7609–7611; *Angew. Chem.* **2006**, *118*, 7771–7773.



4,4'-(2,3-bis(3,5-dimethoxyphenyl)butane-1,4-diylidene)bis(2,6-di-tert-butylcyclohexa-2,5-dien-1-one) (5 OMe): In a round bottom flask equipped with a septum and magnetic stir bar, a solution of **4 OMe** (2.00 g, 5.43 mmol, 1.00 equiv) in anhydrous THF (55 mL, 0.1 M) was cooled to 0 °C in an ice bath under inert atmosphere. To this, KHMDS (5.7 mL, 1.0 M soln. in THF, 1.05 equiv) was added slowly, turning the pale yellow solution a dark forest green. The solution was allowed to stir at temperature for 10 minutes, upon which the septum was removed and ferrocenium hexafluorophosphate (1.9 g, 97% purity, 5.70 mmol, 1.05 equiv.) was added in two 950 mg portions, separated by 15 minutes. The heterogeneous reaction slowly turns from blue-green to a dark yellow/orange color as the ferrocenium is reduced. After the reaction was deemed complete by TLC (ca. 30 min), the reaction mixture was dried on to Celite and the solvent removed completely under reduced pressure. The crude material was purified by flash chromatography over SiO_2 (100:0 Hexanes/EtOAc [to elute ferrocene], then gradient 95:2.5:2.5 to 90:5:5 Hexanes/EtOAc/CH_2Cl_2) to afford **5/5' OMe** as an amorphous yellow solid (1.94 g, 2.64 mmol, 97% yield), which further purified to a crystalline yellow powder by trituration from a minimum of CH_2Cl_2 with MeOH.

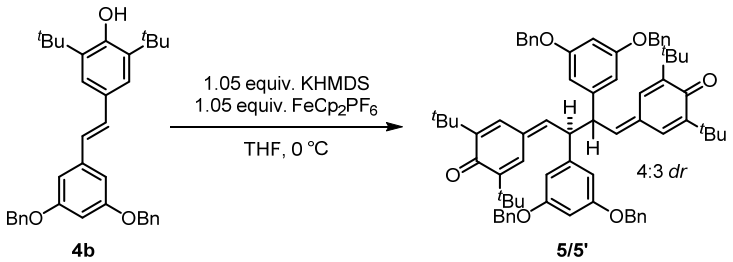
Rf (Hexanes/EtOAc, 9:1): 0.3;

IR (Neat): 2953, 1602, 1461, 1350, 1201, 1156, 1059, 925, 831, 696 cm^{-1};

^1H NMR ($CDCl_3$, 700 MHz): δ β-H's of quinone methides: 7.13 (major diastereomer, d, J = 1.9 Hz, 2H), 7.09 (minor diastereomer, d, J = 2.0 Hz, 2H), 6.82 (minor diastereomer, d, J = 2.2 Hz, 2H), 6.71 (major diastereomer, d, J = 2.2 Hz, 2H); δ-H's of quinone methides: 6.43 (minor diastereomer, m, 2H), 6.33 (major diastereomer, m, 2H); 6.35 (Ar-H major diastereomer, d, J = 2.1 Hz, 4H), 6.31 (Ar-H major diastereomer, t, J = 2.1 Hz, 2H), 6.29-6.27 (Ar-H's minor diastereomer, overlap, 6H), 4.34 – 4.30 (minor diastereomer sp^3 methines, m, 2H), 4.30 – 4.26 (major diastereomer sp^3 methines, m, 2H), 3.74 (major diastereomer –OMe's, s, 12H), 3.70 (minor diastereomer –OMe's, s, 12H), 1.25 (minor diastereomer ^{t}Bu's, s, 18H), 1.24 (major diastereomer ^{t}Bu's, s, 18H), 1.23 (minor diastereomer ^{t}Bu's, s, 18H), 1.22 (major diastereomer ^{t}Bu's, s, 18H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 186.67, 186.65, 161.3, 161.2, 149.2, 149.0, 147.7, 147.3, 145.3, 144.1, 143.3, 142.9, 134.8, 134.7, 133.1, 132.1, 126.1, 126.0, 106.9, 106.8, 99.0, 98.8, 55.54, 55.52, 51.6, 51.2, 35.6, 35.5, 35.1, 35.0, 29.7, 29.63, 29.62, 29.60;

HRMS (ESI) *m/z* calculated for $C_{48}H_{63}O_6^+$ ($[M+H]^+$) 735.4619, found 735.4613.



4,4'-(2,3-bis(3,5-bis(benzyloxy)phenyl)butane-1,4-diylidene)bis(2,6-di-tert-butylcyclohexa-2,5-dien-1-one) (5): In a round bottom flask equipped with a septum and magnetic stir bar, a solution of **4b** (1.88 g, 3.61 mmol, 1.00 equiv) in anhydrous THF (30 mL, 0.1 M) was cooled to 0 °C in an ice bath under inert atmosphere. To this, KHMDS (3.8 mL, 1.0 M soln. in THF, 1.05 equiv) was added slowly, turning the pale yellow solution a dark forest green. The solution was allowed to stir at temperature for 10 minutes, upon which the septum was removed and ferrocenium hexafluorophosphate (1.25 g, 97% purity, 3.79 mmol, 1.05 equiv) was added in two 625 mg portions, separated by 15 minutes. The heterogeneous reaction turns from blue-green to a dark yellow/orange color as the ferrocenium is reduced. After the reaction was complete by TLC (ca. 30 min), the reaction mixture was dried on to Celite and the solvent removed completely under reduced pressure. The crude material was purified by flash chromatography over SiO_2 (100% Hexanes [to elute ferrocene], then gradient 95:2.5:2.5 to 90:5:5 Hexanes/EtOAc/CH_2Cl_2) to afford **5/5'** (1.87 g, 1.81 mmol, 99% yield) as an amorphous yellow solid, which was further purified to a crystalline yellow powder by sonication in pH neutral CH_3NO_2. When ran on 10 gram scale, isolated 9.49 g of **5** (95% yield).

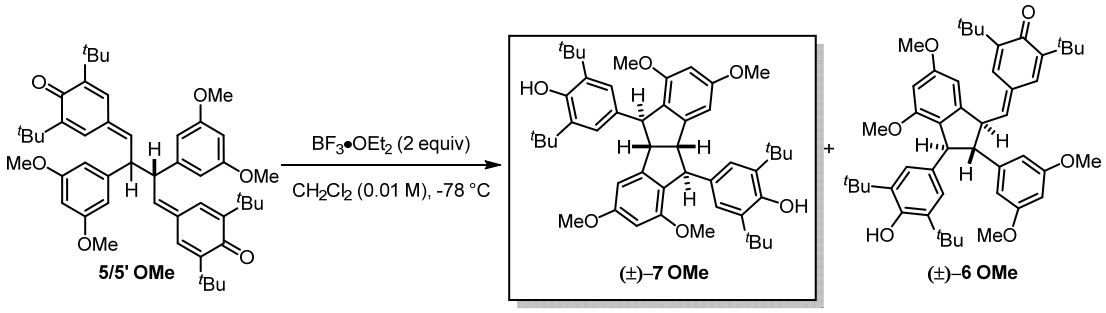
Rf (Hexanes/EtOAc, 9:1): 0.35;

IR (Neat): 2954, 1593, 1453, 1361, 1292, 1254, 1160, 1054, 930, 822, 734, 695 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.40 – 7.40 (m, 20H), β-H's of quinone methides: 7.12 (major diastereomer, d, J = 2.2 Hz, 2H), 7.02 (minor diastereomer, d, J = 2.0 Hz, 2H), 6.82 (minor diastereomer, d, J = 2.2 Hz, 2H), 6.72 (major diastereomer, d, J = 2.0 Hz, 2H); δ-H's of quinone methides: 6.41 – 6.37 (minor diastereomer, m, 2H), 6.33 – 6.29 (major diastereomer, m, 2H); 6.48 (major diastereomer, t, J = 2.1 Hz, 2H), 6.47 (minor diastereomer, t, J = 2.2 Hz, 2H), 6.45 (major diastereomer, d, J = 2.1 Hz, 4H), 6.38 (minor diastereomer, d, J = 2.2 Hz, 4H), 4.96 (major diastereomer, d, J = 11.5 Hz, 4H), 4.94 (major diastereomer, d, J = 11.5 Hz, 4H), 4.91 (minor diastereomer, d, J = 11.5 Hz, 4H), 4.89 (minor diastereomer, d, J = 11.5 Hz, 4H), 4.28 (m, overlap, sp^3 methines of both diastereomers, 4H), 1.26 (minor diastereomer ^{t}Bu's, s, 18H), 1.24 (major diastereomer ^{t}Bu's, s, 36H), 1.23 (minor diastereomer ^{t}Bu's, s, 18H).

^{13}C NMR ($CDCl_3$, 175 MHz): δ 186.70, 186.66, 160.5, 160.4, 149.2. 149.1, 147.7, 147.4, 145.2, 143.9, 143.3, 142.9, 136.7, 136.6, 134.9, 134.7, 133.2, 132.2, 128.85 (2C), 128.4, 127.81, 127.79, 126.2, 126.0, 108.2, 108.0, 100.6, 100.57, 100.54, 70.5, 51.8, 51.2, 35.57, 35.55, 35.11, 35.05, 29.7, 29.64, 29.62;

HRMS (ESI) *m/z* calculated for $C_{72}H_{79}O_6^+$ ($[M+H]^+$) 1039.5832, found 1039.5871.



4,4'-((4bS,5S,9bS,10S)-1,3,6,8-tetramethoxy-4b,5,9b,10-tetrahydroindeno[2,1-a]indene-5,10-diyl)bis(2,6-di-tert-butylphenol) (7 OMe): A solution of **5 OMe** (20 mg, 0.027 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (10 mL, 0.003 M) was cooled to -78 °C in a dry ice/acetone bath under inert atmosphere. To this, BF_3•OEt_2 (14 µL, 46.5% in diethyl ether, 2 equiv) was added dropwise, turning the reaction a brilliant magenta color. Temperature control is critical for the success of this reaction. The reaction was allowed to run for 40 minutes upon which the reaction was quenched with sat. aq. $NaHCO_3$ at temperature and allowed to warm to room temperature under vigorous stirring. The reaction was diluted with CH_2Cl_2 and transferred to a separatory funnel. The phases were separated and the aqueous layer was extracted with portions of CH_2Cl_2. The organic layers were combined, washed with sat. aq. $NaHCO_3$, brine, dried over sodium sulfate and concentrated *in vacuo*. The crude material was purified by column chromatography over SiO_2 (90:5:5 Hexanes/EtOAc/CH_2Cl_2) to afford **7 OMe** (8.5 mg, 0.012 mmol 43% yield) as a white amorphous solid. The remaining material was identified as compound **6 OMe** (see S13 for characterization data).

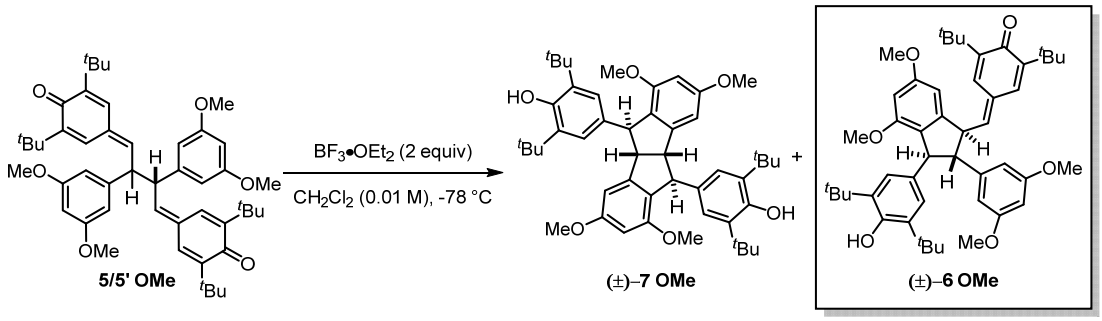
Rf (Hexanes/EtOAc 9:1): 0.1;

IR (Neat): 3646, 2988, 1600, 1436, cm^{-1};

^1H NMR ($CDCl_3$, 700 MHz): δ 7.12 (s, 4H), 6.66 (s, 2H), 6.23 (s, 2H), 5.03 (s, 2H, OH), 4.57 (s, 2H), 4.25 (s, 2H), 3.83 (s, 6H), 3.66 (s, 6H), 1.42 (s, 36H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 161.1, 157.1, 152.0, 148.5, 136.3, 135.4, 125.9, 124.3, 100.8, 97.6, 59.6, 55.7, 55.3, 54.2, 34.5, 30.6;

HRMS (ESI) *m/z* calculated for $C_{68}H_{63}O_6^+$ ($[M+H]^+$) 735.4650, found 735.4625.



2,6-di-tert-butyl-4-(((1S,2S,3S)-3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(3,5-dimethoxyphenyl)-4,6-dimethoxy-2,3-dihydro-1H-inden-1-yl)methylene)cyclohexa-2,5-dien-1-one (6 OMe)

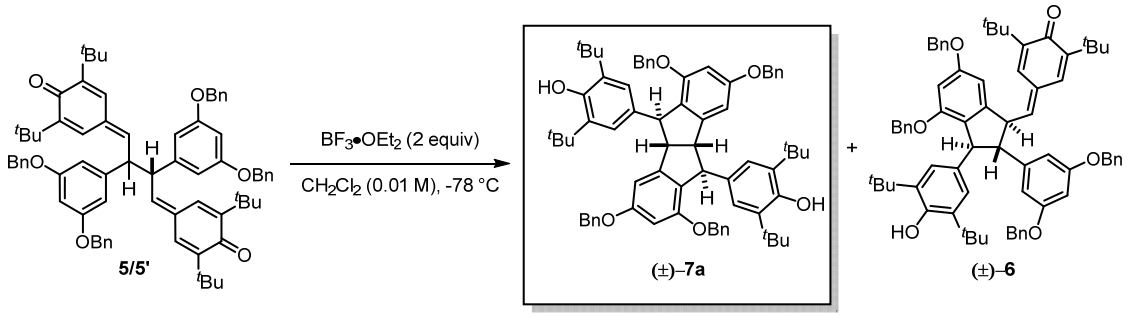
Rf (Hexanes/THF, 90:10): 0.33;

IR (Neat): 3640, 2953, 1594, 1460, 1434, 1360, 1202, 1152, 1070, 934, 882, 832 cm^{-1};

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.97 (d, *J* = 2.2 Hz, 1H), 6.85 (d, *J* = 2.2 Hz, 1H), 6.70 (s, 2H), 6.42 (d, *J* = 2.0 Hz, 1H), 6.39 (d, *J* = 10 Hz, 1H), 6.34 – 6.30 (m, 4H), 4.96 (s, 1H), 4.58 (dd, *J* = 9.2, 9.2 Hz, 1H), 4.48 (d, *J* = 7.8 Hz, 1H), 3.83 (s, 3H), 3.70 (s, 6H), 3.61 (s, 3H), 3.08 (dd, *J* = 8.1, 8.1 Hz, 1H), 1.32 (s, 18H), 1.26 (s, 9H), 1.16 (s, 9H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 186.8, 161.6, 161.0, 157.5, 152.1, 148.7, 147.8, 147.1, 146.7, 144.8, 135.1, 134.9, 133.9, 132.8, 127.0, 124.0, 123.8, 106.5, 100.9, 98.9, 98.7, 65.1, 56.6, 55.8, 55.5, 55.4, 52.9, 35.4, 35.0, 34.5, 30.6, 29.61, 29.56;

HRMS (ESI) *m/z* calculated for $C_{48}H_{63}O_6^+$ ($[M+H]^+$) 735.4619, found 735.4620.



4,4'-((4bS,5S,9bS,10S)-1,3,6,8-tetrakis(benzyloxy)-4b,5,9b,10-tetrahydroindeno[2,1-a]indene-5,10-diyl)bis(2,6-di-tert-butylphenol) (7a): A solution of **5** (800 mg, 0.77 mmol, 1.00 equiv) in CH_2Cl_2 (77 mL, 0.01M) was cooled to -78 °C in a dry ice/acetone bath under inert atmosphere. To this, BF_3•OEt_2 (390 μL, 46.5% in diethyl ether, 2 equiv) was added dropwise, turning the reaction a brilliant magenta color. Temperature control is critical for the success of this reaction. The reaction was allowed to run for 40 minutes upon which the reaction was quenched with sat. aq. $NaHCO_3$ at temperature and allowed to warm to room temperature under vigorous stirring. The reaction was diluted with CH_2Cl_2 and transferred to a separatory funnel. The phases were separated and the aqueous layer was extracted with portions of CH_2Cl_2. The organic layers were combined, washed with sat. aq. $NaHCO_3$, brine, dried over sodium sulfate and concentrated *in vacuo*. The crude material was purified by column chromatography over SiO_2 (95:5 Hexanes/THF gradient to 90:10 Hexanes/THF) to afford **7a** (340 mg, 0.33 mmol, 43% yield) as a white amorphous solid. The remaining material was identified as compound **6** (see S15 for characterization data).

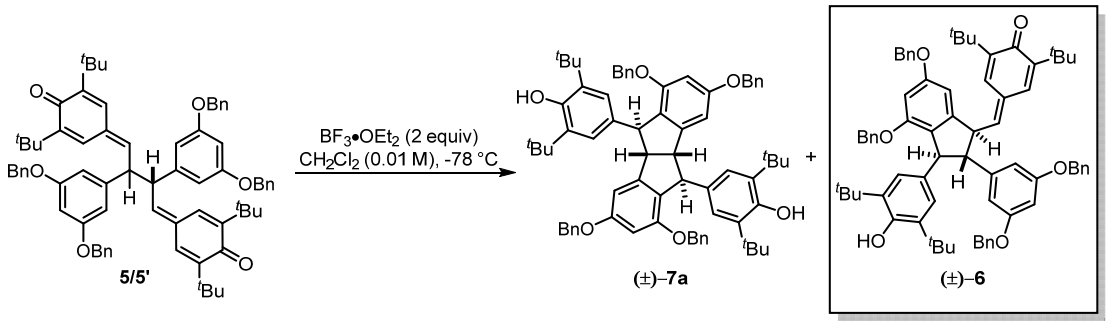
Rf (Hexanes/THF, 95:5): 0.19;

IR (Neat): 3636, 2954, 2908, 2870, 1598, 1433, 1316, 1135, 905, 727, 695 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.42 (d, *J* = 7.5 Hz, 4H), 7.35 (m, 5H), 7.29 (m, 2H), 7.22 (m, 5H), 7.03 (s, 4H), 7.01 (m, 4H), 6.73 (d, *J* = 2.0 Hz), 6.33 (d, *J* = 2.0 Hz), 5.04 (d, *J* = 11.2 Hz, 2H), 5.02 (d, *J* = 11.2 Hz, 2H), 5.01 (s, 2H, OH), 4.88 (d, *J* = 11.7 Hz, 2H), 4.82 (d, *J* = 11.7 Hz, 2H), 4.55 (s, 2 H), 4.24 (s, 2H), 1.36 (s, 36H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 160.2, 156.0, 152.1, 148.8, 137.3, 136.9, 135.6, 128.8, 128.6, 128.2, 127.9, 127.7, 127.1, 126.7, 124.3, 102.4, 99.5, 70.6, 69.6, 60.1, 55.4, 34.47 (2C), 30.6;

HRMS (ESI) *m/z* calculated for $C_{72}H_{79}O_6^+$ ($[M+H]^+$) 1039.5871, found 1039.5843.



4-(((1S,2S,3S)-4,6-bis(benzyloxy)-2-(3,5-bis(benzyloxy)phenyl)-3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,3-dihydro-1H-inden-1-yl)methylene)-2,6-di-tert-butylcyclohexa-2,5-dien-1-one (6):

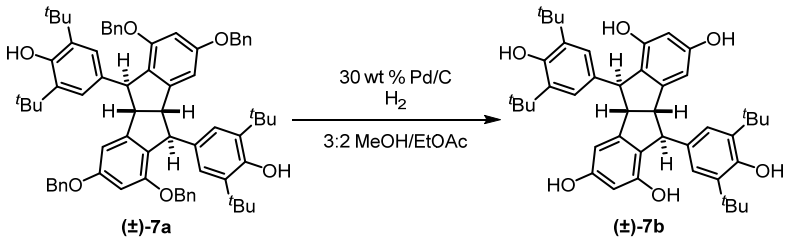
Rf (Hexanes/CH_2Cl_2/EtOAc, 85:10:5): 0.25;

IR (Neat): 3639, 2956, 1603, 1559, 1434, 1378, 1308, 1157, 1054, 1029 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.47 – 7.28 (m, 15H), 7.14 – 7.10 (m, 3H), 7.02 (d, *J* = 2 Hz, 1H), 6.89 (d, *J* = 2.4 Hz, 1H), 6.80 (S, 2H), 6.68 (d, *J* = 2.0 Hz, 1H), 6.66 (d, *J* = 2.0 Hz, 1H) 6.59 (d, *J* = 2.0 Hz, 1H), 6.47 (t, *J* = 2.2 Hz, 1H), 6.46 – 6.43 (m, overlap, 2H), 6.42 (d, *J* = 2.2 Hz, 2H), 5.08 (d, *J*= 11.2 Hz, 1H), 5.05 (d, *J*= 11.2 Hz, 1H), 5.03 (s, 1H), 4.91 (d, *J* = 11.2 Hz, 1H), 4.90 (d, *J* = 11.2 Hz, 2H), 4.87 (d, *J* = 11.2 Hz, 2H), 4.84 (d, *J* = 12.0 Hz, 1H), 4.65 (dd, *J* = 9.4, 9.4 Hz, 1H), 4.52 (d, *J* = 8.5 Hz, 1H), 3.14 (dd, *J* = 8.8, 8.8 Hz, 1H), 1.31 (s, 18H), 1.28 (s, 9H), 1.18 (s, 9H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 186.8, 160.7, 160.2, 156.2, 152.3, 148.8, 147.6, 147.2, 146.8, 144.0, 137.0, 136.9, 136.8, 135.5, 134.9, 134.2, 133.1, 128.82, 128.75, 128.4, 128.3, 128.2, 127.9, 127.8, 127.5, 127.1, 126.4, 124.8, 124.1, 107.6, 102.3, 100.5, 100.4, 70.7, 70.3, 69.6, 65.5, 57.0, 52.5, 35.4, 35.1, 34.5, 30.6, 29.66, 29.65;

HRMS (ESI) *m/z* calculated for $C_{72}H_{79}O_6^+$ ($[M+H]^+$) 1039.5871, found 1039.5849.



(4bS,5S,9bS,10S)-5,10-bis(3,5-di-tert-butyl-4-hydroxyphenyl)-4b,5,9b,10-tetrahydroindeno[2,1-a]indene-1,3,6,8-tetraol (7b): A heterogenous solution of **7a** (250 mg, 0.24 mmol, 1 equiv) and 30 wt % Pd/C (770 mg) in 5 mL of 3:2 EtOAc/MeOH was sparged with hydrogen gas for 30 min at room temperature. The walls of the vessel were rinsed down with a minimum of MeOH and the septum fitted with a full balloon of H_2. The reaction was allowed to stir at room temperature overnight under an atmosphere of hydrogen. The reaction solution was filtered over a pad of celite and concentrated to provide **7b** (155 mg, 0.23 mmol, 95% yield) as an amorphous white solid without need for further purification. NOTE: **7b** is unstable to prolonged storage in air at room temperature, but could be stored indefinitely at -20 °C in a container sealed under N_2.

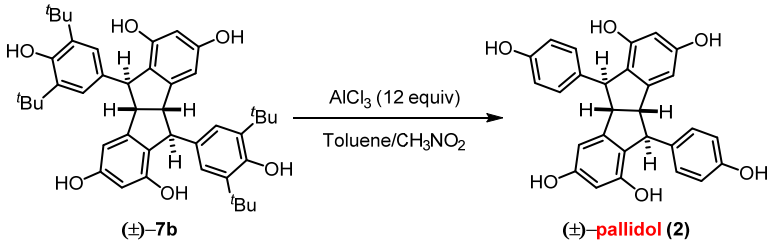
Rf (CH_2Cl_2/MeOH, 95:5): 0.09;

IR (Neat): 3367, 2956, 1600, 1458, 1435, 1254, 1233, 1126, 1042 cm^{-1};

^1H NMR (Acetone d_6, 700 MHz): δ 7.09 (s, 4H), 6.64 (s, 2H), 6.21 (s, 2H), 4.61 (s, 2H), 3.94 (s, 2H), 1.38 (s, 36H);

^{13}C NMR (Acetone d_6, 175 MHz): δ 159.2, 155.3, 152.7, 150.3, 137.8, 124.5, 123.4, 103.4, 102.3, 60.7, 54.6, 35.1, 30.8;

HRMS (ESI) *m/z* calculated for $C_{44}H_{55}O_6^+$ ($[M+H]^+$) 679.3993, found 679.3989.



(±)–**7b** (±)–**pallidol (2)**

Pallidol (2): The following procedure was adapted from Hou et. al.[4] To a solution of **7b** (150 mg, 0.22 mmol, 1 equiv) in anhydrous toluene (10.8 mL, 0.02 M) at room temperature under inert atmosphere, $AlCl_3$ (354 mg, 0.28 mmol, 12 equiv) was added as a solution in CH_3NO_2 (1.2 mL, 2.25 M). The reaction was immediately heated to 60 °C for 30 min upon which the reaction was removed from the heat source and transferred to a separatory funnel containing 1:1 ice/1 N HCl. The reaction flask was rinsed with EtOAc several times and the contents transferred to the separatory funnel. The phases were separated and the aqueous layer extracted with additional ethyl acetate (2x). The organic layers were combined, washed with sat. aq. $NaHCO_3$, brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography over SiO_2 (95:5 CH_2Cl_2/MeOH gradient to 90:10 CH_2Cl_2/MeOH) to afford pallidol (**2**) (80 mg, 0.17 mmol, 80%) as white amorphous solid.

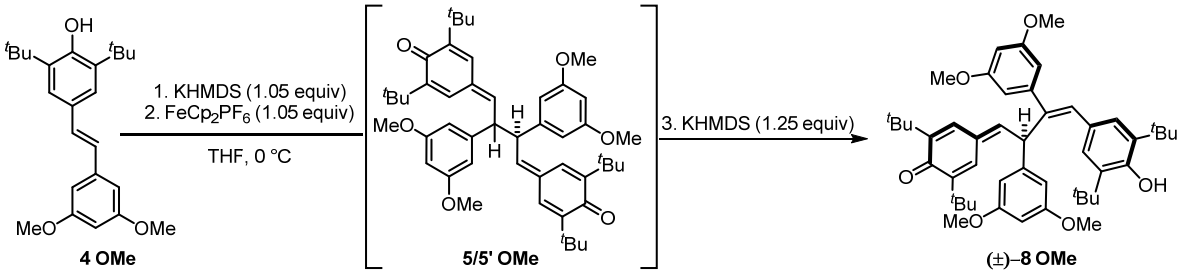
Rf (CH_2Cl_2/MeOH, 95:5): 0.09;

IR (Neat): 3296, 1598, 1508, 1464, 1334, 1238, 1128, 1147, 995, 831 cm^{-1};

^1H NMR (Acetone d_6, 500 MHz): δ8.02 (s, 2H, OH), 8.00 (s, 2H, OH), 7.77 (s, 2H, OH), 6.98 (d, J = 8.5 Hz, 4H), 6.70 (d, J = 8.5 Hz, 4H), 6.62 (d, J = 2.0 Hz, 2H), 6.19 (d, J = 2.2 Hz, 2H) 4.57 (s, 2H), 3.81 (s, 2H);

^{13}C NMR (Acetone d_6, 175 MHz): δ 159.4, 156.4, 155.4, 150.4, 137.8, 129.1, 123.3, 115.9, 103.4, 102.6, 60.6, 54.0;

HRMS (ESI) *m/z* calculated for $C_{28}H_{23}O_6^+$ ($[M+H]^+$) 455.1450, found 455.1457.



(*E*)-2,6-di-tert-butyl-4-(4-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,3-bis(3,5-dimethoxyphenyl)but-3-en-1-ylidene)cyclohexa-2,5-dien-1-one (8 OMe): In a round bottom flask equipped with a septum and magnetic stir bar, a solution of **4 OMe** (1.88 g, 2.60 mmol, 1.00 equiv) in anhydrous THF (75 mL, 0.02 M) was cooled to 0 °C in an ice bath under inert atmosphere. To this, KHMDS (2.73 mL, 1.0 M soln. in THF, 1.05 equiv) was added slowly. The solution was allowed to stir at temperature for 10 minutes, upon which the septum was removed and ferrocenium hexafluorophosphate (932 mg, 97% purity, 2.73 mmol, 1.05 equiv) was added in two 466 mg portions, separated by 15 minutes. After the reaction was deemed complete by TLC (ca. 30 min), KHMDS (3.25 mL, 1.0 M soln. in THF, 1.25 equiv), was added, turning the solution from yellow-orange to opaque. After 15 min, the reaction mixture was quenched by the addition of sat. aq. NH_4Cl, turning the organic phase bright red. The reaction was diluted with EtOAc and transferred to a separatory funnel containing DI H_2O. The phases were separated and the aqueous layer extracted with additional EtOAc (2x). The organic layers were combined and washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was taken up in CH_2Cl_2 and dried on to Celite and the solvent removed completely under reduced pressure. The crude material was purified by flash chromatography over a short plug of SiO_2 (100:0 Hexanes/EtOAc [to elute ferrocene] then 100% CH_2Cl_2) to afford **8** (1.88 g, 1.30 mmol, crude), which was taken directly on to the next step (see S18). For characterization, the material can instead be eluted with a gradient 95:2.5:2.5 to 90:5:5 Hexanes/EtOAc/CH_2Cl_2 mobile phase.

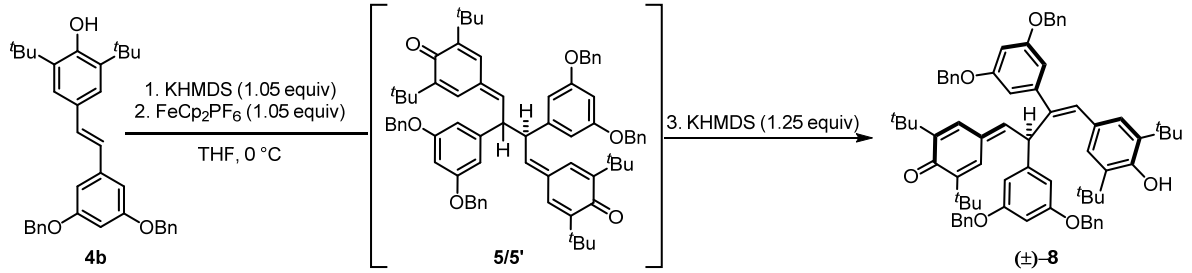
Rf (Hexanes/EtOAc, 95:5): 0.17;

IR (Neat): 3630, 2956, 2359, 1653, 1590, 1457, 1356, 1204, 1153, 1065, 833, 738 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 6.92 (s, 2H), 6.73 (d, J = 2.9 Hz, 1H), 6.52 (d, J = 2.2 Hz, 2H), 6.39 (d, J = 2.2 Hz, 2H), 6.31 (t, J = 2.2 Hz, 1H), 6.24 (d, J = 2.7 Hz, 1H), 6.23 (t, J = 2.2 Hz, 1H), 5.80 (d, J = 1.7 Hz, 1H), 5.00 (s, 1H), 4.97 (dd, J = 9.6, 1.8 Hz, 1H), 3.7 (s, 6H), 3.68 (s, 6H), 1.37 (s, 18H), 1.30 (s, 9H), 0.91 (s, 9H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 186.6, 160.9, 160.7, 152.8, 147.6, 146.6, 146.22, 146.15, 144.5, 141.6, 137.5, 135.4, 130.8, 127.8, 124.0, 106.9, 105.0, 100.2, 98.2, 65.3, 56.6, 55.5, 55.4, 54.6, 35.0, 34.8, 34.5, 30.5, 30.0, 29.3;

HRMS (ESI) *m/z* calculated for $C_{48}H_{63}O_6^+$ ($[M+H]^+$) 735.4619, found 735.4616.



(*E*)-4-(2,3-bis(3,5-bis(benzyloxy)phenyl)-4-(3,5-di-tert-butyl-4-hydroxyphenyl)but-3-en-1-ylidene)-2,6-di-tert-butylcyclohexa-2,5-dien-1-one (8): In a round bottom flask equipped with a septum and magnetic stir bar, a solution of **4b** (1.00 g, 1.92 mmol, 1.00 equiv) in anhydrous THF (75 mL, 0.02 M) was cooled to 0 °C in an ice bath under inert atmosphere. To this, KHMDS (1 M solution in THF, 1.61 mL, 1.05 equiv) was added slowly. The solution was allowed to stir at temperature for 10 minutes, upon which the septum was removed and ferrocenium hexafluorophosphate (655 mg, 97% purity, 2.04 mmol, 1.05 equiv) was added in two 328 mg portions, separated by 15 minutes. After the reaction was complete by TLC (ca. 30 min), KHMDS (1.92 mL, 1.0 M soln. in THF, 1.25 equiv), was added, turning the solution from yellow-orange to opaque. After 15 min, the reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The reaction was diluted with EtOAc and transferred to a separatory funnel containing DI H_2O. The phases were separated and the aqueous layer extracted with EtOAc (2x). The organic layers were combined and washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was taken up in CH_2Cl_2 and dried on to Celite and the solvent removed under reduced pressure. Purification by flash chromatography over a short plug of SiO_2 (100% Hexanes [to elute ferrocene], then 100% CH_2Cl_2) afforded **8** (1.00 g, 0.96 mmol, crude), which was taken directly on to the next step (see S19). For characterization, the material can instead be eluted with a gradient 95:2.5:2.5 to 90:5:5 Hexanes/EtOAc/CH_2Cl_2 mobile phase.

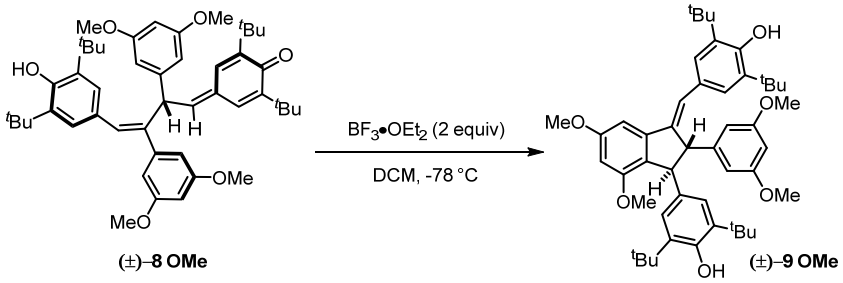
Rf (Hexanes/EtOAc/CH_2Cl_2, 85:10:5): 0.25;

IR (Neat): 3641, 2952, 1654, 1590, 1435, 1373, 1264, 1151, 1054, 1028, 834, 733, 696 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.39 – 7.29 (m, 20H), 6.91 (s, 2H), 6.71 (d, J = 2.7 Hz, 1H), 6.64 (d, J = 2.2 Hz, 2H), 6.52 (d, J = 2.2 Hz, 2H), 6.50 (t, J = 2.2 Hz, 1H), 6.42 (t, J = 2.2 Hz, 1H), 6.23 (d, J = 2.7 Hz, 1H), 5.79 (d, J = 2.0 Hz, 1H), 5.02 (s, 1H), 4.95 (d, J = 11.5 Hz, 2H), 4.94 (d, J = 11.5 Hz, 2H), 4.89 (d, J = 11.5 Hz, 2H), 4.88 (d, J = 11.5 Hz, 2H), 3.66 (d, J = 9.8 Hz, 1H), 1.38 (s, 18 H), 1.31 (s, 9H), 0.92 (s, 9H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 186.6, 160.2, 159.9, 152.9, 147.6, 146.5, 146.2, 144.4, 141.6, 137.5, 137.0, 136.9, 135.4, 130.9, 128.80, 128.78, 128.76, 128.2, 127.9, 127.82, 127.76, 127.7, 124.0, 108.2, 106.3, 102.0, 100.3, 70.32, 70.27, 65.2, 56.6, 54.7, 35.0, 34.8, 34.5, 30.5, 30.0, 29.3;

HRMS (ESI) *m/z* calculated for $C_{72}H_{79}O_6^+$ ($[M+H]^+$) 1039.5832, found 1039.5838.



2,6-di-tert-butyl-4-((1S,2S)-3-((E)-3,5-di-tert-butyl-4-hydroxybenzylidene)-2-(3,5-dimethoxyphenyl)-5,7-dimethoxy-2,3-dihydro-1H-inden-1-yl)phenol (9 OMe): A solution of crude **8 OMe** (S12) (260 mg, 0.35 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (35 mL, 0.01 M) was cooled to -78 °C in a dry ice/acetone bath. To this, BF_3•OEt_2 (175 µL, 46.5% in diethyl ether, 2 equiv) was added dropwise, turning the solution into a deep ruby red color. After 5 min, the reaction was quenched with sat. aq. $NaHCO_3$ at -78 °C and allowed to warm to room temperature with vigorous stirring. The reaction mixture was diluted with CH_2Cl_2 and transferred to a separatory funnel containing additional sat. aq. $NaHCO_3$. The phases were separated and the aqueous layer was extracted with additional CH_2Cl_2 (2x). The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The crude residue was purified by flash chromatography using a 90:5:5 Hexanes/EtOAc/CH_2Cl_2 mobile phase to afford **9 OMe** (235 mg, 0.32 mmol, 90% yield over 3 steps) as a pale yellow amorphous solid.

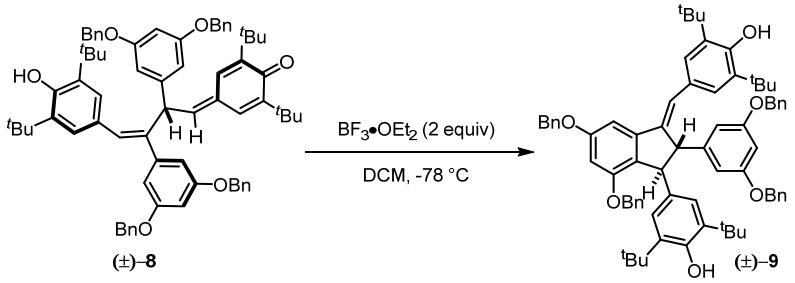
Rf (Hexanes/EtOAc, 90:10): 0.33;

IR (Neat): 3633, 2965, 1593, 1435, 13783, 1304, 1234, 1153, 1050, 1028, 736 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.13 (s, 1H), 7.08 (s, 2H), 7.06 (s, 2H), 6.83 (d, J = 1.7 Hz, 1H), 6.50 (d, J = 2.2 Hz, 2H), 6.29 (d, J = 2.0 Hz, 2H), 5.18 (s, 1H), 4.99 (s, 1H), 4.49 (s, 1H), 4.32 (s, 1H), 3.92 (s, 3H), 3.73 (s, 6H), 3.65 (s, 3H), 1.35 (s, 18H), 1.31 (s, 18H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 161.3, 161.0, 160.8, 157.5, 153.1, 152.0, 147.9, 145.1, 142.5, 136.3, 135.8, 135.3, 128.9, 127.2, 126.3, 125.9, 124.1, 123.9, 106.0, 104.9, 98.9, 98.3, 95.5, 58.8, 57.0, 55.8, 55.4, 55.3, 34.50, 34.45, 30.5, 30.4;

HRMS (ESI) *m/z* calculated for $C_{48}H_{63}O_6^+$ ($[M+H]^+$) 735.4625, found 735.4648.



4-((1S,2S)-5,7-bis(benzyloxy)-2-(3,5-bis(benzyloxy)phenyl)-3-((E)-3,5-di-tert-butyl-4-hydroxybenzylidene)-2,3-dihydro-1H-inden-1-yl)-2,6-di-tert-butylphenol (9): A solution of crude **8** (S13) (1.00 g, 0.96 mmol, 1.00 equiv) in anhydrous CH_2Cl_2 (96 mL, 0.01 M) was cooled to -78 °C in a dry ice/acetone bath under inert atmosphere. To this, BF_3•OEt_2 (511 µL, 46.5% in diethyl ether 2 equiv) was added dropwise, turning the solution into a deep ruby red color. After 5 min, the reaction was quenched with sat. aq. $NaHCO_3$ at -78 °C and allowed to warm to room temperature with vigorous stirring. The reaction mixture was diluted with CH_2Cl_2 and transferred to a separatory funnel containing additional sat. aq. $NaHCO_3$. The phases were separated and the aqueous layer was extracted with additional CH_2Cl_2 (2x). The organic layers were combined, washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The crude residue was purified by flash chromatography using a 90:5:5 Hexanes/EtOAc/CH_2Cl_2 mobile phase to afford **9** (898 mg, 0.86 mmol, 90% yield over 3 steps) as a pale yellow amorphous solid.

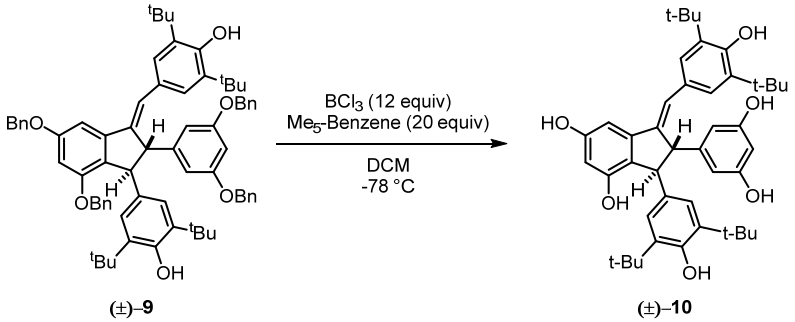
Rf (Hexanes/CH_2Cl_2/EtOAc, 85:10:5): 0.27;

IR (Neat): 3632, 2953, 1592, 1451, 1434, 1372, 1304, 1154, 1048, 774, 696 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.50 (m, 2H), 7.41 – 7.28 (m, 13H, benzyl group overlap), 7.21 (m, 3H), 7.14 (d, J = 0.7 Hz, 1H), 7.04 (s, 2H), 7.03-7.01 (m, 2H, benzyl group H's), 7.00 (s, 2H), 6.95 (d, J = 1.7 Hz, 1H), 6.59 (d, J = 2.2 Hz, 2H), 6.42 (t, J = 2.2 Hz, 1H), 6.41 (d, J = 1.7 Hz, 1H), 5.30 (s, 2H), 5.16 (s, 1H, OH), 5.15 (s, 2H), 4.99 (s, 1H, OH), 4.95 (d, J = 12.2 Hz, 2H), 4.93 (d, J = 12.2 Hz, 2H), 4.90 (d, J = 12.0 Hz, 1H), 4.84 (d, J = 12.0Hz, 1H), 4.40 (s, 1H), 4.32 (s, 1H), 1.31 (s, 18H), 1.29 (s, 18H);

^{13}C NMR ($CDCl_3$, 175 MHz): δ 160.5, 160.2, 156.4, 153.2, 152.1, 148.1, 145.3, 142.5, 137.3, 137.20, 137.16, 136.6, 135.7, 135.5, 128.9, 128.80, 128.77, 128.7, 128.6, 128.5, 128.21, 128.18, 128.1, 128.0, 127.9, 127.8, 127.7, 127.2, 127.1, 126.0, 124.2, 124.1, 107.1, 100.8, 100.1, 97.0, 70.6, 70.2, 69.6, 58.9, 57.6, 34.5, 34.4, 30.6, 30.5, 30.4;

HRMS (ESI) *m/z* calculated for $C_{72}H_{79}O_6^+$ ($[M+H]^+$) 1039.5871, found 1039.5829.



(±)–**9** (±)–**10**

(2S,3S)-1-((E)-3,5-di-tert-butyl-4-hydroxybenzylidene)-3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2-(3,5-dihydroxyphenyl)-2,3-dihydro-1H-indene-4,6-diol: A solution of **9** (460 mg, 0.44 mmol, 1.00 equiv) and pentamethylbenzene (1.30 g, 8.8 mmol, 20 equiv) in anhydrous CH_2Cl_2 (22 mL, 0.02 M) was cooled to -78 °C in a dry ice/acetone bath under inert atmosphere. To this, BCl_3 (5.3 mL, 1.0 M soln. in CH_2Cl_2, 12 equiv) was added dropwise turning the yellow solution a brilliant magenta color. Reaction was maintained at -78 °C until deemed complete by TLC (ca. 2h). At this point, the reaction was quenched with a 4:1 THF/sat. aq. $NaHCO_3$ mixture at -78 °C and allowed to warm to room temperature while stirring vigorously. Upon thawing, the solution returned to a yellow color. The reaction was diluted with ethyl acetate (50 mL) and transferred to a separatory funnel containing additional sat. aq. $NaHCO_3$. The phases were separated and the aqueous layer extracted with additional EtOAc (2x). The organic layers were combined and washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by flash chromatography over SiO_2 (98:2 CH_2Cl_2/MeOH gradient to 90:10 CH_2Cl_2/MeOH) to afford **10** (245 mg, 0.36 mmol, 82% yield) as a white amorphous solid. NOTE: **10** is unstable to prolonged storage in air at room temperature, but could be stored indefinitely at -20 °C in a container sealed under N_2.

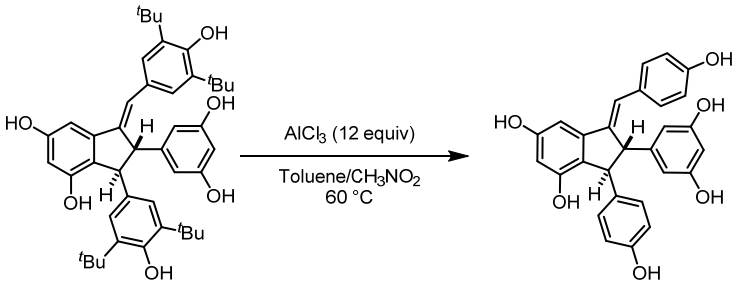
Rf (CH_2Cl_2/MeOH, 95:5): 0.09;

IR (Neat): 3376, 2957, 1599, 1547, 1467, 1434, 1341, 1237, 1157, 1006, 838 cm^{-1};

^1H NMR (Acetone d_6, 700 MHz): δ 8.13 (br. s., 4H, OH), 7.86 (br. s., 2H, OH), 7.15 (s, 2H), 7.12 (s, 1H), 7.05 (s, 2H), 6.80 (s, 1H), 6.38 (s, 2H), 6.29 (s, 1H), 6.20 (s, 1H), 5.99 (s, 1H), 5.73 (s, 1H), 4.33 (s, 1H), 4.26 (s, 1H), 1.34 (s, 18H), 1.31 (s, 18H);

^{13}C NMR (Acetone d_6, 175 MHz): δ 159.6, 159.5, 155.9, 154.0, 152.9, 148.8, 147.2, 143.0, 137.9, 137.8, 137.6, 130.0, 126.6, 124.4, 107.0, 103.6, 101.5, 98.8, 60.5, 58.0, 35.2, 30.8, 30.7;

HRMS (ESI) *m/z* calculated for $C_{44}H_{55}O_6^+$ ($[M+H]^+$) 679.3993, found 679.3989.



(±)–**10** (±)–**quadrangularin A (3)**

Quadrangularin A (3): The following procedure was adapted from Hou et. al.[4] To a solution of **10** (80.0 mg, 0.12 mmol, 1.00 equiv) in anhydrous toluene (5.4 mL, 0.022 M) at room temperature under inert atmosphere, $AlCl_3$ (190 mg, 1.44 mmol, 12.0 equiv) was added as a solution in CH_3NO_2 (600 µL, 2.33 M). The reaction was immediately heated to 60 °C for 30 min upon which the reaction was removed from the heat source and transferred to a separatory funnel containing 1:1 ice/1 N HCl. The reaction flask was rinsed with EtOAc several times and the contents transferred to the separatory funnel. The phases were separated and the aqueous layer extracted with additional ethyl acetate (2x). The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash chromatography over SiO_2 (95:5 CH_2Cl_2/MeOH gradient to 90:10 CH_2Cl_2/MeOH) to afford quadrangularin A (**3**) (43 mg, 0.095 mmol 80%) as a tan amorphous solid.

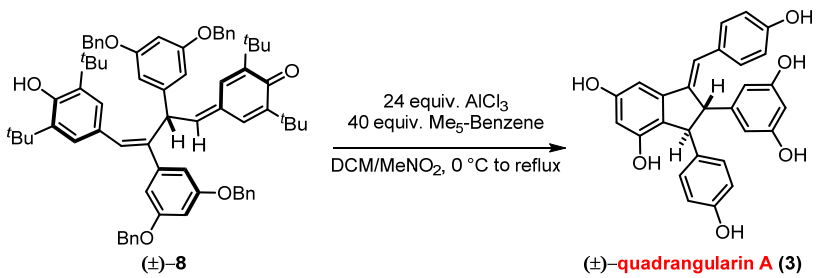
Rf (CH_2Cl_2/MeOH, 95:5): 0.09;

IR (Neat): 3245, 1596, 1509, 1446, 1334, 1233, 1172, 1147, 1005, 831 cm^{-1};

^1H NMR (Acetone d_6, 500 MHz): δ 8.16 (s, 6H), 7.21 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 1.0 Hz, 1H), 6.92 (d, J = 8.5 Hz), 6.79 (d, J = 2.0 Hz, 1H), 6.68 (d, J = 5.4 Hz, 2H), 6.67 (d, J = 5.4 Hz, 2H), 6.31 (d, J = 2.2 Hz, 2H), 6.30 (d, J = 2.0 Hz, 1H), 6.19 (t, J = 2.2 X 2 Hz, 1H), 4.27 (s, 1H), 4.14 (s, 1H);

^{13}C NMR (Acetone d_6, 175 MHz): δ 159.7, 159.7, 157.4, 156.6, 155.9, 149.1, 147.1, 142.7, 137.8, 131.1, 129.8, 128.8, 124.6, 123.0, 116.0, 115.9, 106.3, 103.7, 101.6, 98.4, 60.7, 57.7;

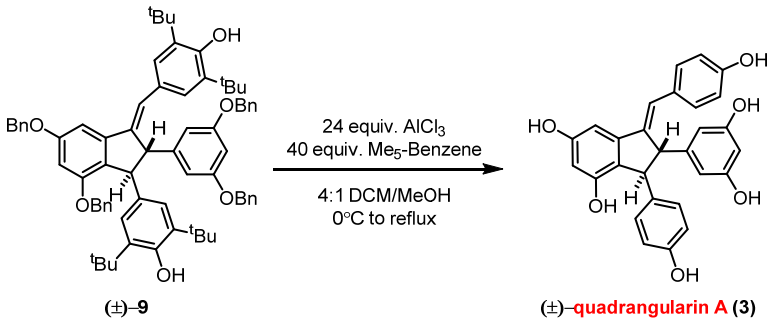
HRMS (ESI) *m/z* calculated for $C_{28}H_{23}O_6^+$ ($[M+H]^+$) 455.1489, found 455.1485.



(±)–**8** (±)–quadrangularin A (**3**)

Friedel-Crafts Cyclization – Global Deprotection of 8 with $AlCl_3$

A solution of **8** (370 mg, 0.34 mmol, 1 equiv) and pentamethylbenzene (2.1 g, 14.1 mmol, 40 equiv) in anhydrous CH_2Cl_2 (57 mL, 0.005 M) was cooled to 0 °C in an ice bath under inert atmosphere. To this, $AlCl_3$ (1.14 g, 8.6 mmol, 25 equiv) was added slowly as a solution in CH_3NO_2 (14 mL, 0.6 M) via syringe turning the clear yellow solution a deep red color. Upon addition, the reaction flask was fitted with a reflux condenser and heated to 60 °C, allowing the reaction to stir at this temperature for 15 minutes. The reaction was removed from the heat and the contents transferred to a separatory funnel containing 1:1 ice/1N HCl. The reaction flask was rinsed with EtOAc several times and the contents transferred to the separatory funnel. The phases were separated and the aqueous layer extracted with additional ethyl acetate (2x). The organic layers were combined, washed with sat. aq. $NaHCO_3$, brine, dried over Na_2SO_4, and concentrated *in vacuo*. The dry crude material was dissolved in a minimal amount of diethyl ether using sonication. Then hexane was added dropwise to the sonicating material to precipitate out crude quadrangularin A as a brown amorphous solid, which was collected by vacuum filtration. This crude material (nearly pure by NMR), was purified via flash chromatography (95:2.5:2.5 gradient to 90:5:5 Chloroform/Acetone/MeOH) to yield quadrangularin A (**3**) (82 mg, 0.18 mmol, 51%) as a tan amorphous solid (see S23 for characterization data).



(±)–**9** (±)–**quadrangularin A (3)**

Global Deprotection of 9 with $AlCl_3$

A solution of **9** (30 mg, 0.03 mmol, 1 equiv) and pentamethylbenzene (170 mg, 1.14 mmol, 40 equiv.) in CH_2Cl_2 (4.5 mL, 0.005 M) was cooled to 0 °C in an ice bath under inert atmosphere. To this, $AlCl_3$ (92 mg, 0.70 mmol, 24 equiv) was added as a solution in CH_3NO_2 (1.5 mL, 0.48 M) via syringe, turning the clear yellow solution a deep red color. Upon addition, the reaction flask was fitted with a reflux condenser and heated to 60 °C, allowing the reaction to stir at this temperature for 1 hour. The reaction was cooled down to 0 °C, quenched with sat. aq. $NaHCO_3$, and stirred until the solution turned from red to clear yellow. The reaction was transferred to a separatory funnel and washed with ice cold 1N HCl (CO_2 evolution). The organic layer was removed and the aqueous layer was extracted with EtOAc (2x). The organic layers were combined, washed with sat. aq. $NaHCO_3$, brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by flash chromatography over SiO_2 (17:2:1 Chloroform/MeOH/Acetone) to yield quadrangularin A (**3**) (11.5 mg, 88%, 5:1 ratio of quadrangularin A and its internal alkene isomer) as a tan amorphous solid (see S23 for characterization data).

Radical Clock Experiments with 4b, 7a, 9, and BHT

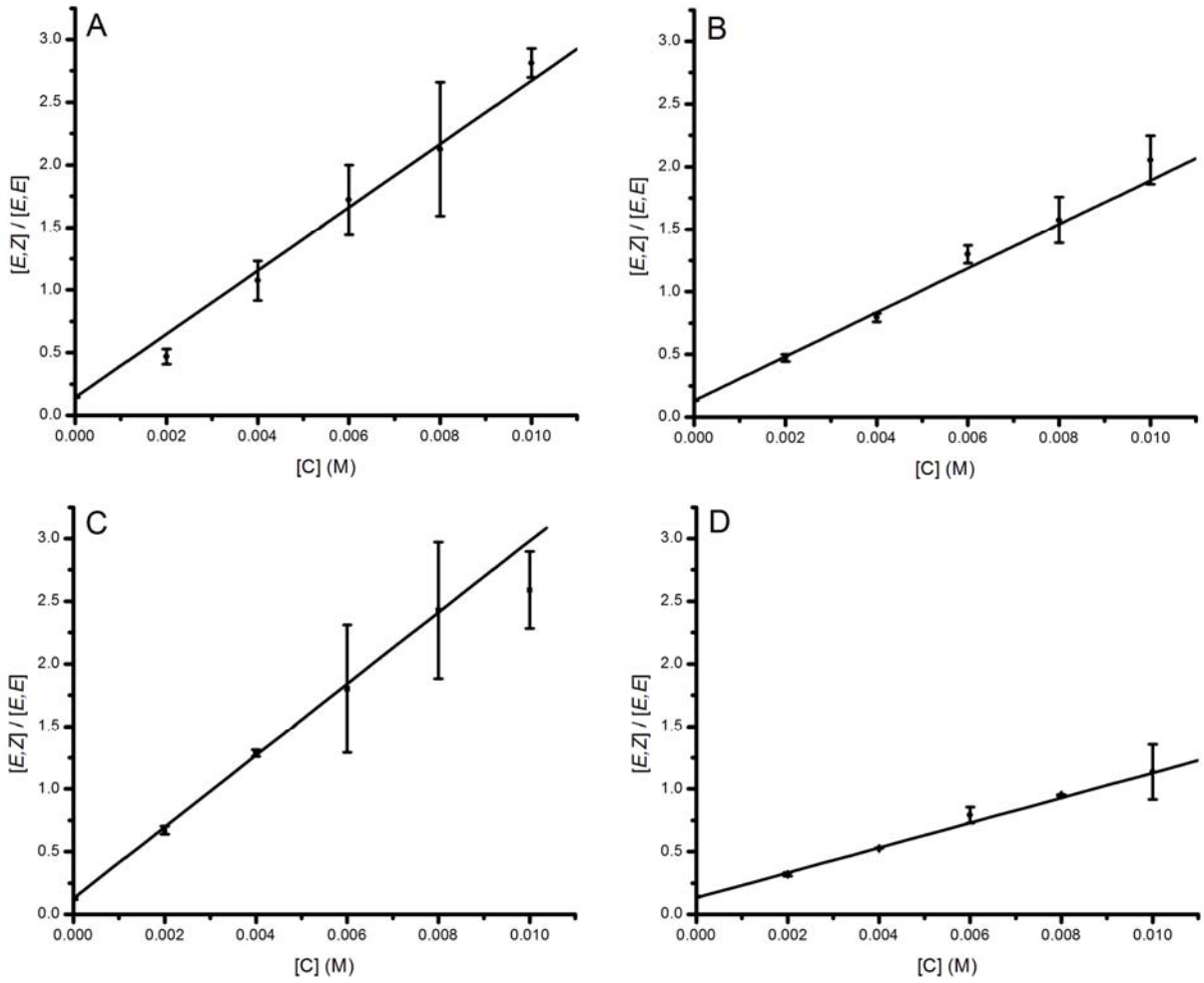


Figure S1. Ratio of [*E,Z*]:[*E,E*] products versus concentration of *t*-Bu_2-resveratrol (**4b**) (A), *t*-Bu_2-pallidol (**7a**) (B), *t*-Bu_2-quadrangularin A B (**9**) (C), and BHT (D) in the MeOAMVN-initiated (0.01 M) autoxidation of methyl linoleate (0.1 M) in chlorobenzene at 37°C.

Inhibited Oxidations of Phosphatidylcholine Liposomes

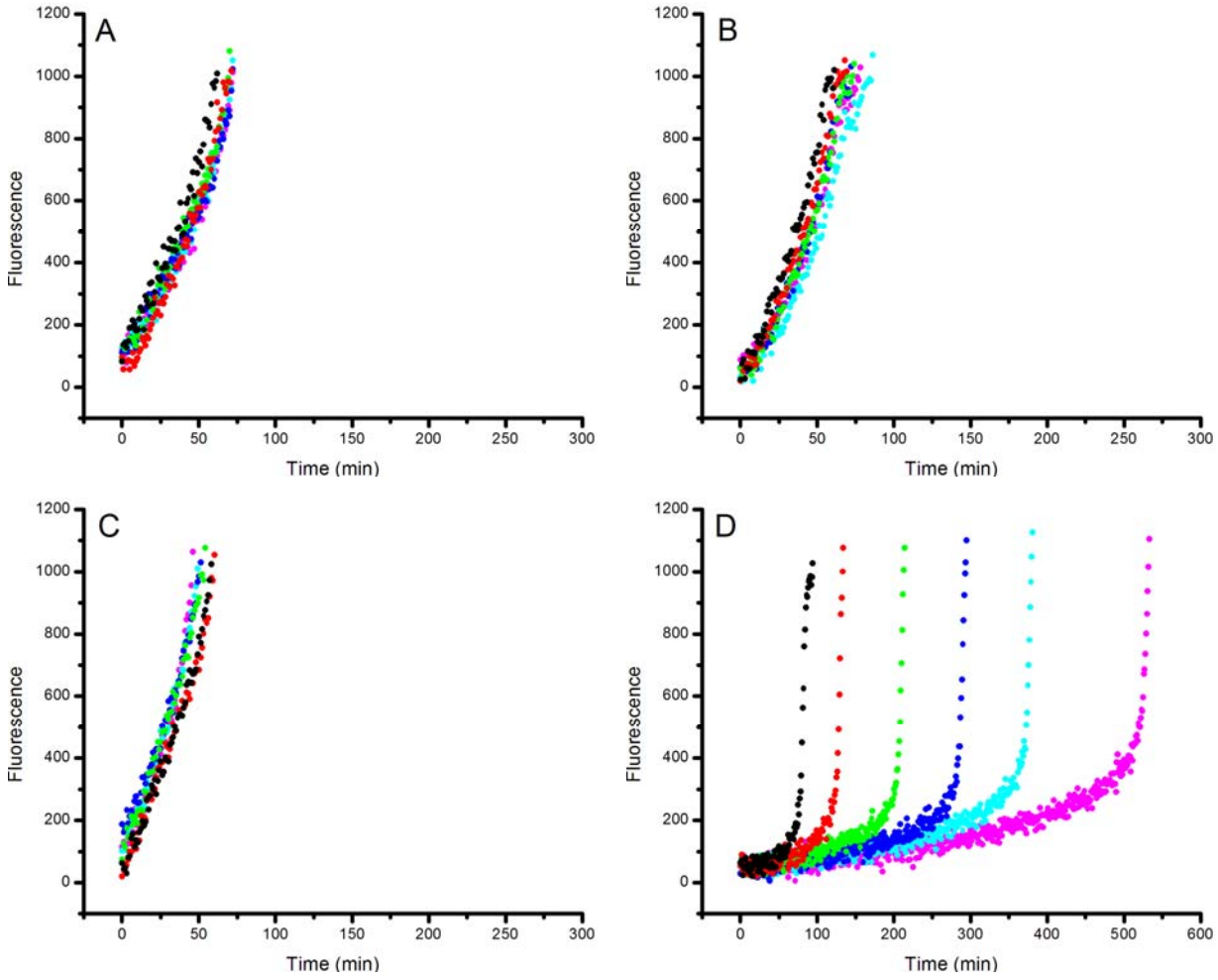


Figure S2. Representative fluorescence intensity-time profiles from MeOAMVN-mediated (0.68 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in pH 7.4 PBS buffer) containing 0.15 μM H_2B-PMHC probe and increasing concentrations (2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM) of resveratrol (**1**) (A), pallidol (**2**) (B), quadrangularin A (**3**) (C) and PMHC (D). Fluorescence (λ_{ex} = 485 nm, λ_{em} = 520 nM) was recorded every 60s.

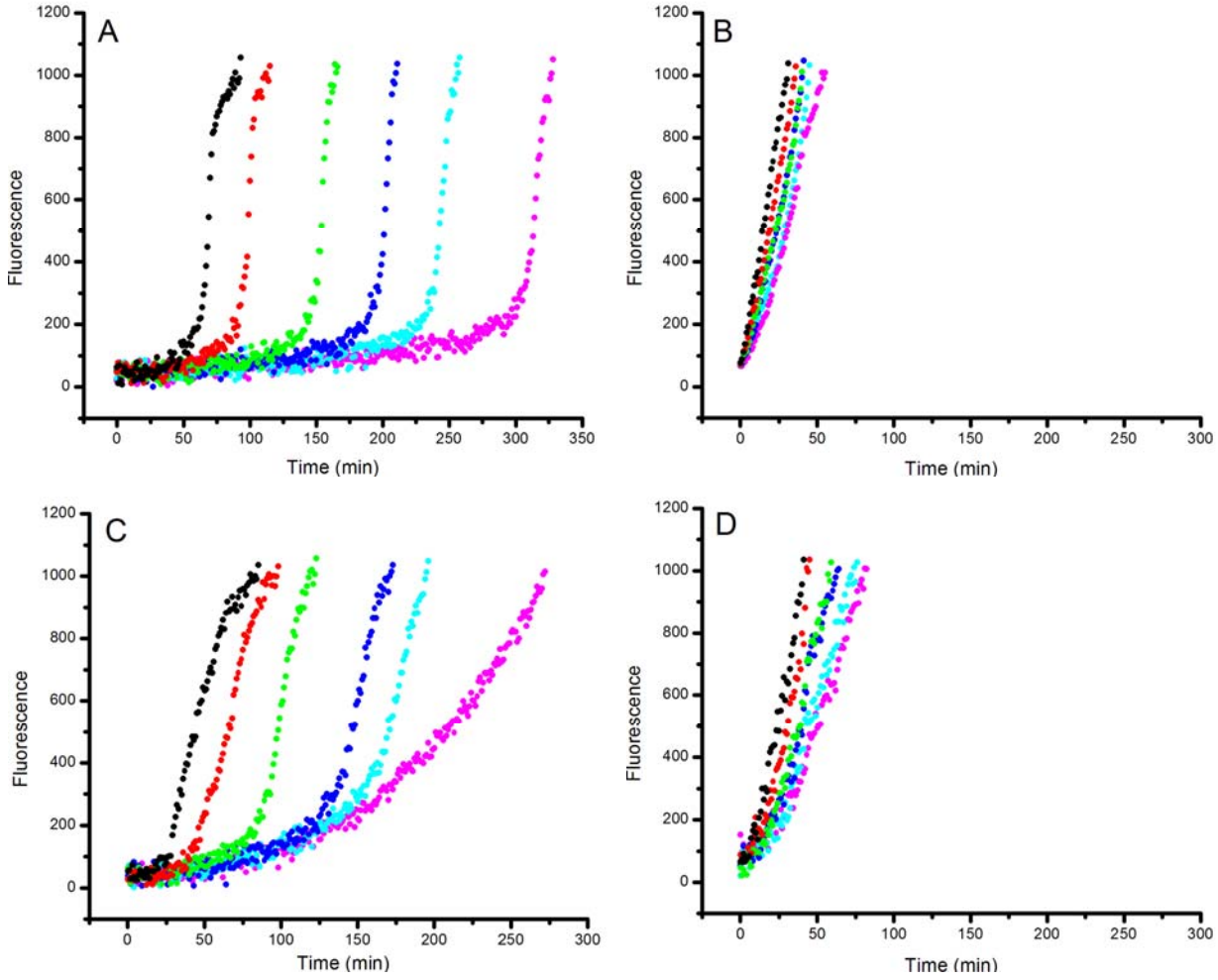


Figure S3. Representative fluorescence intensity-time profiles from MeOAMVN-mediated (0.68 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in pH7.4 PBS buffer) containing 0.15 μM H_2B-PMHC and increasing concentrations (2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM) of *t*-Bu_2-resveratrol (**4a**) (A), *t*-Bu_2-pallidol (**7b**) (B), *t*-Bu_2-quadrangularin A (**10**) (C) and BHT (D). Fluorescence (λ_{ex} = 485 nm; λ_{em} = 520 nM) was recorded every 60s.

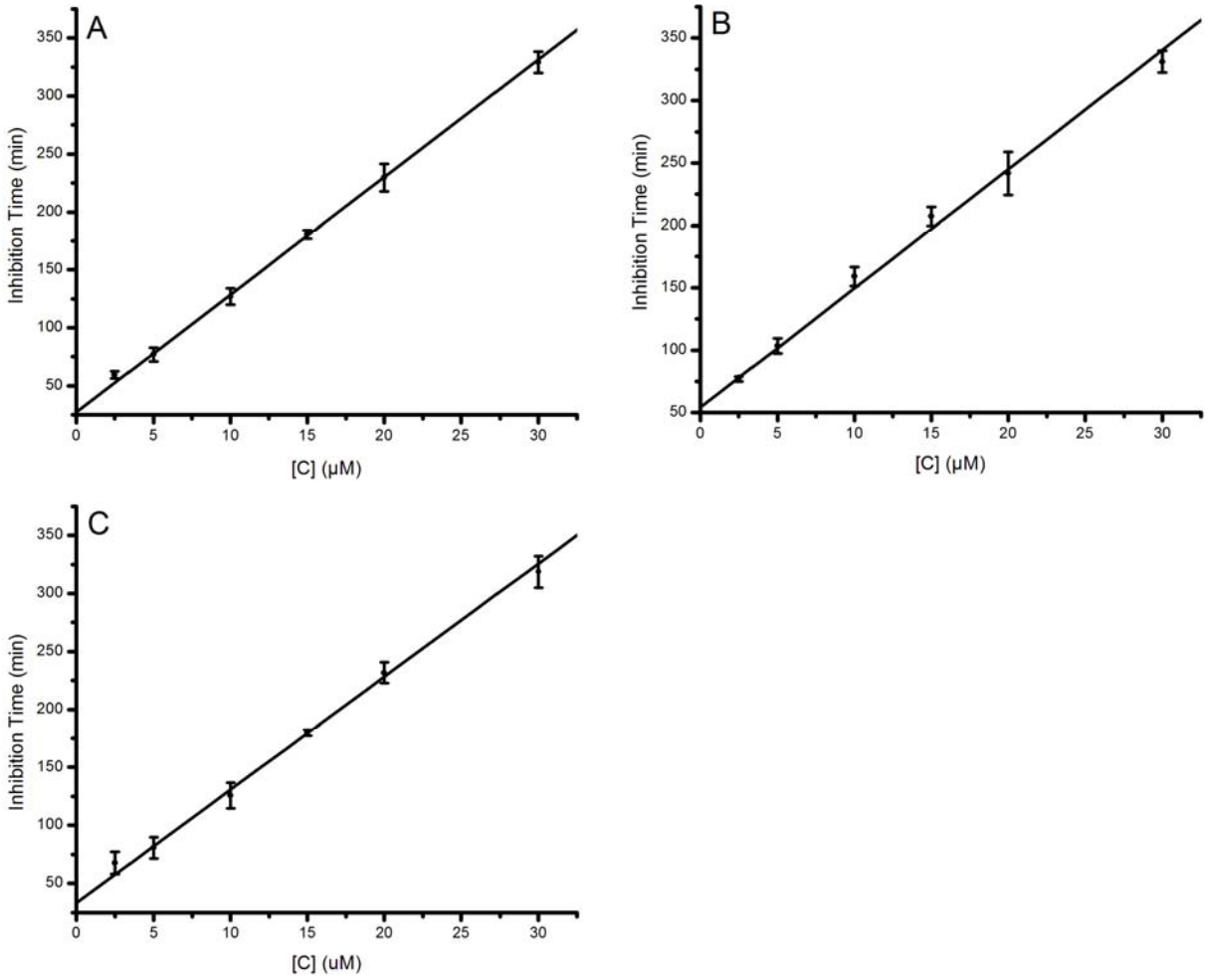


Figure S4. Inhibition time-concentration profiles from MeOAMVN-mediated (0.68 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in pH 7.4 PBS buffer) containing 0.15 μM H_2B-PMHC and increasing concentrations (2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM) of the inhibitors which display a clear inhibited period: PMHC (A), *t*-Bu_2-resveratrol (**4**) (B), and *t*-Bu_2-quadrangularin A (**10**) (C). The stoichiometric numbers (*n*) were calculated based on the slopes of the line of best fit relative to PMHC, for which *n*=2.

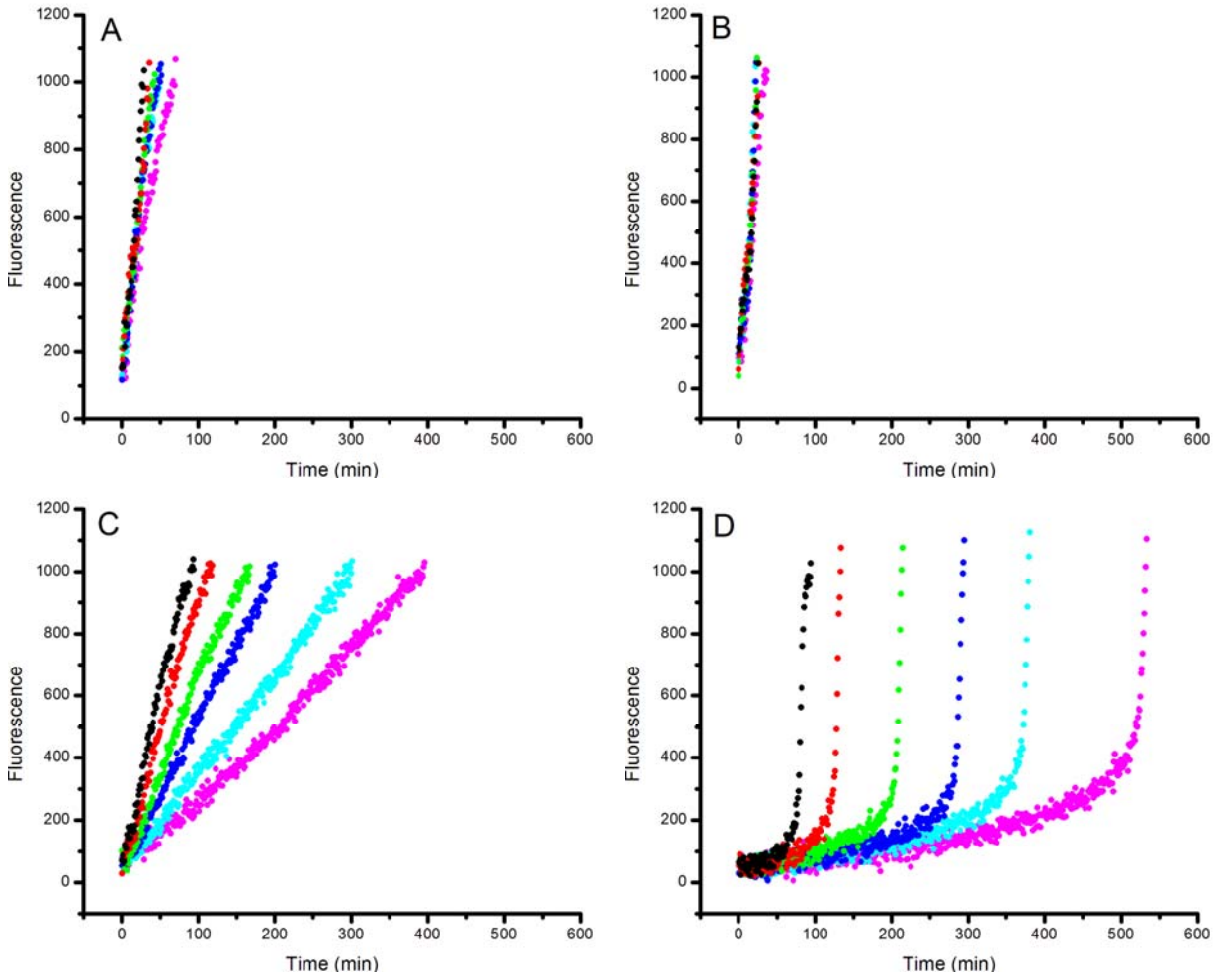


Figure S5. Representative fluorescence intensity-time profiles from AAPH-mediated (2.7 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in pH 7.4 PBS buffer) containing 0.15 μM H_2B-PMHC and increasing concentrations (2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM) of resveratrol (**1**) (A), pallidol (**2**) (B), quadrangularin A (**3**) (C) and PMHC (D). Fluorescence (λ_{ex} = 485 nm; λ_{em} = 520 nM) was recorded every 60s.

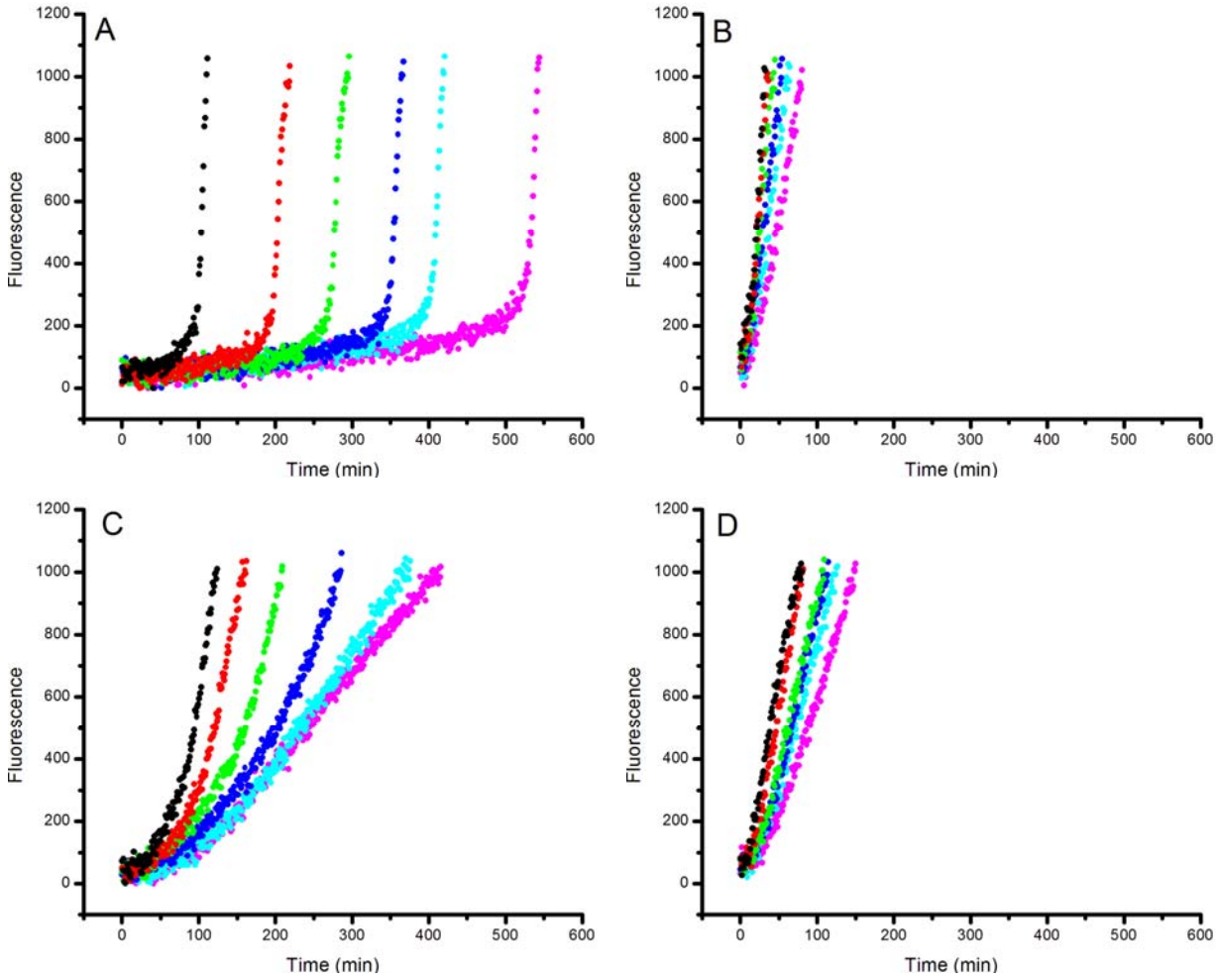


Figure S6. Representative fluorescence intensity-time profiles from AAPH-mediated (2.7 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in pH 7.4 PBS buffer) containing 0.15 μM H_2B-PMHC and increasing concentrations (2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM) of *t*-Bu_2-resveratrol (**4a**) (A), *t*-Bu_2-pallidol (**7b**) (B), *t*-Bu_2-quadrangularin A (**10**) (C) and BHT (D). Fluorescence (λ_{ex} = 485 nm; λ_{em} = 520 nM) was recorded every 60s.

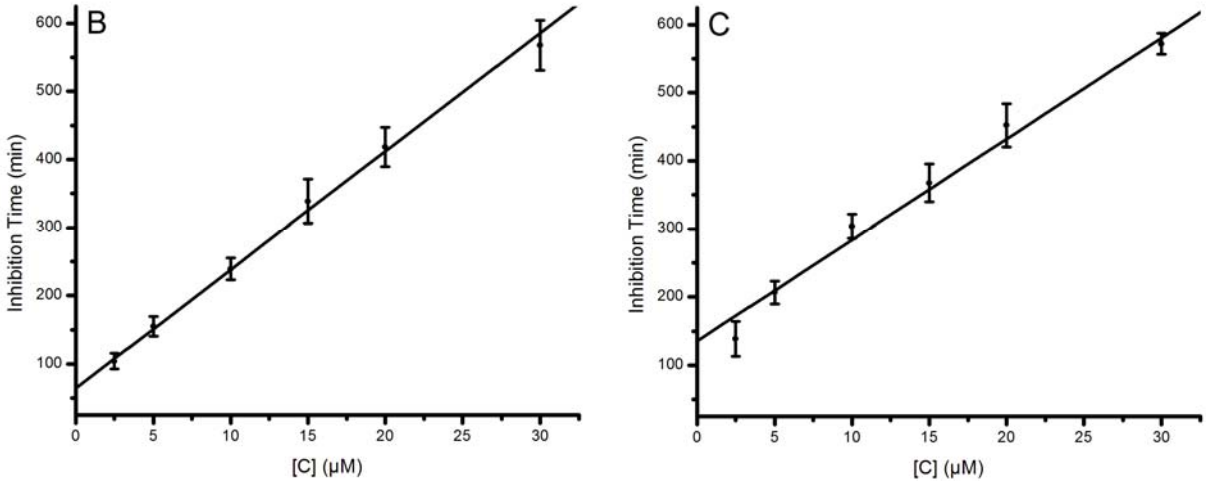


Figure S7. Inhibition time-concentration profiles from AAPH-mediated (2.7 mM) oxidations of egg phosphatidylcholine liposomes (1 mM in pH 7.4 PBS buffer) containing 0.15 μM H_2B-PMHC and increasing concentrations (2.5 μM, 5.0 μM, 10 μM, 15 μM, 20 μM, 30 μM) of the inhibitors which display a clear inhibited period: PMC (B) and *t*-Bu_2-resveratrol (**4a**) (C). The stoichiometric numbers (*n*) were calculated based on the slopes of the line of best fit relative to PMHC, for which *n*=2.

Cellular Lipid Peroxidation Assay

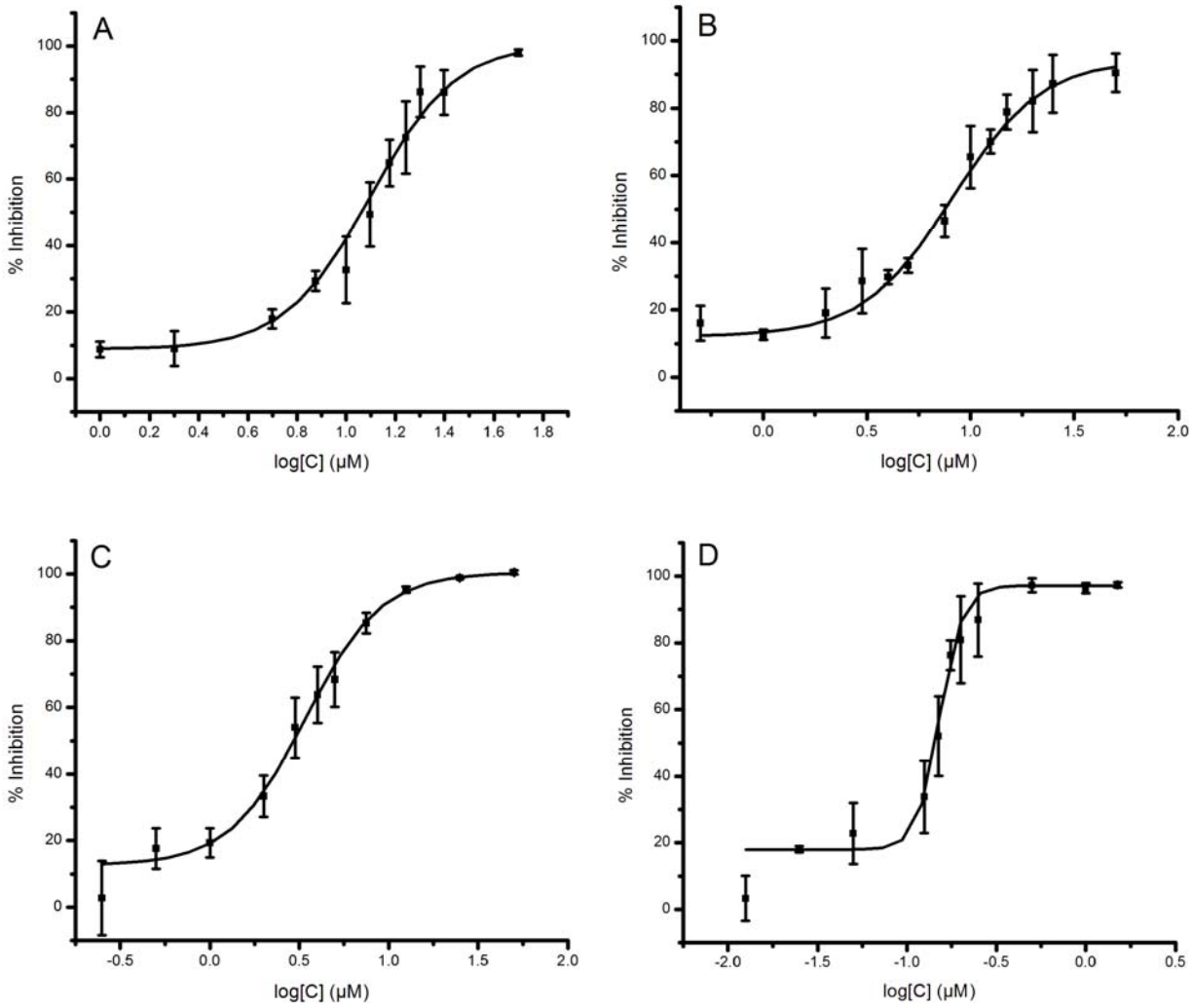


Figure S8. Dose-response curves obtained from flow cytometry (5×10^5 cells/ mL; λ_{ex} = 488 nm, λ_{em} = 525±25 nm; 10,000 events) following induction of oxidative stress with diethylmaleate (DEM, 9 mM) in TF1a cells grown in media containing resveratrol (**1**) (A), pallidol (**2**) (B), quadrangularin A (**3**) (C) and α-tocopherol (D) (0.015-50 μM) for 22 hours at 37 °C. Cells were incubated with the lipid peroxidation reporter C11-BODIPY$^{581/591}$ (1 μM) for 30 minutes prior to DEM treatment.

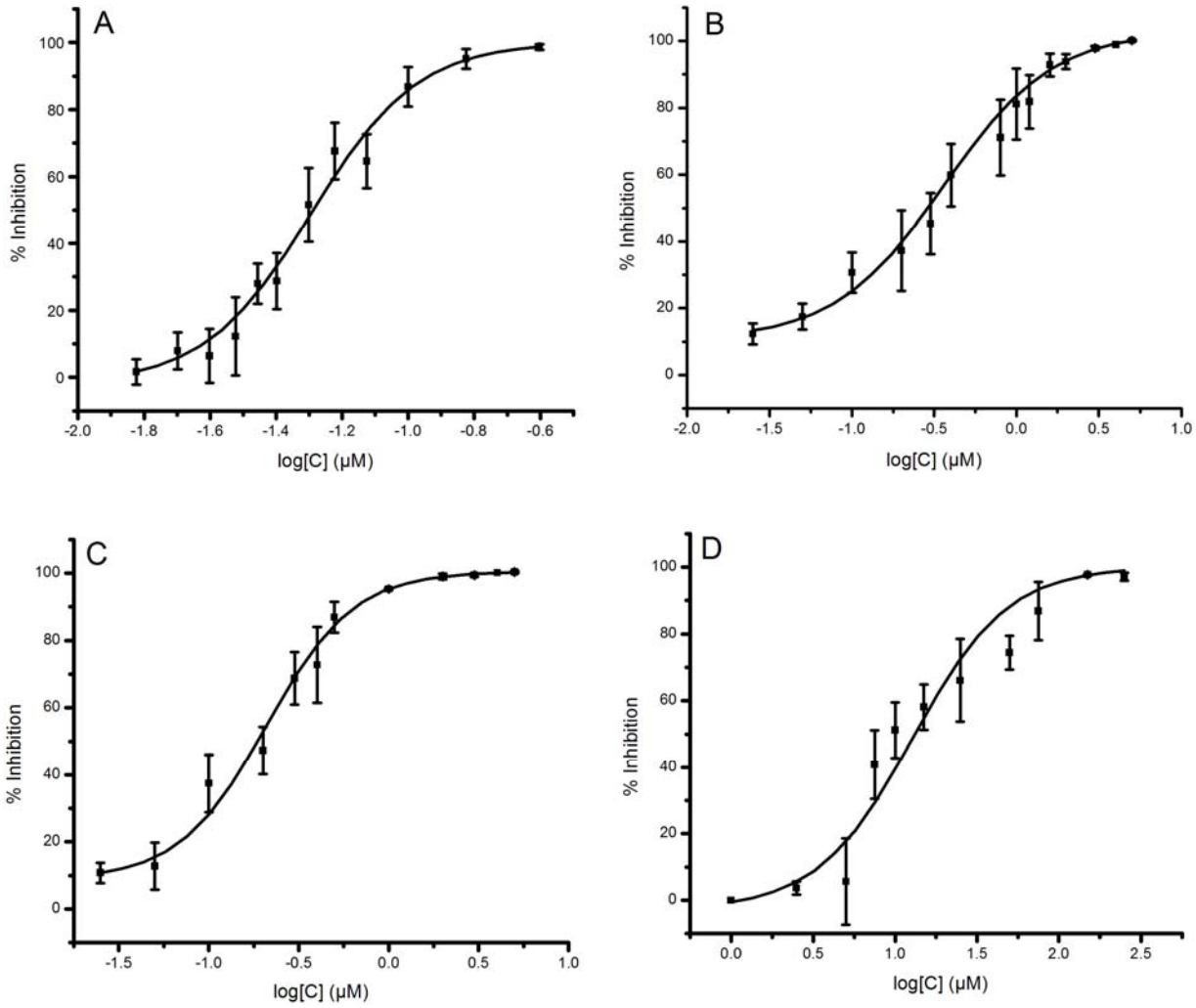


Figure S9. Dose-response curves obtained from flow cytometry (5×10^5 cells/ mL; λ_{ex} = 488 nm, λ_{em} = 525±25 nm; 10,000 events) following induction of oxidative stress with diethylmaleate (DEM, 9 mM) in TF1a cells grown in media containing *t*-Bu_2-resveratrol (**4a**) (A), *t*-Bu_2-pallidol (**7b**) (B), *t*-Bu_2-quadrangularin A (**10**) (C) and BHT (D) (0.015-50 μM) for 22 hours at 37 °C. Cells were incubated with the lipid peroxidation reporter C11-BODIPY$^{581/591}$ (1 μM) for 30 minutes prior to DEM treatment.

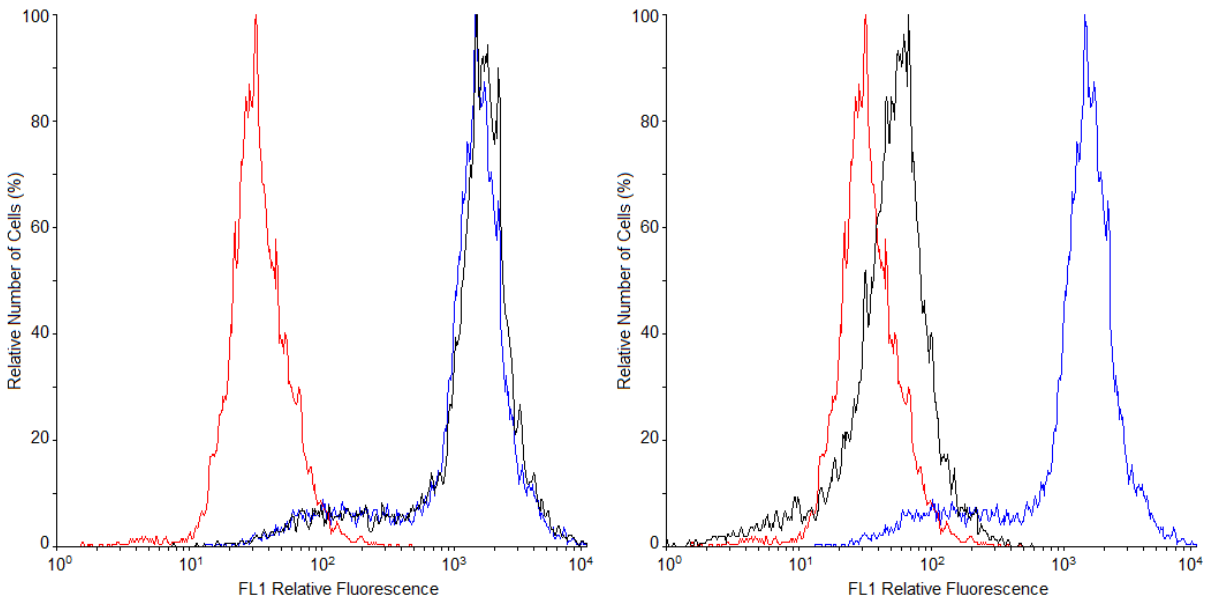


Figure S10. Representative histograms obtained from flow cytometry (5×10^5 cells/ mL; λ_{ex} = 488 nm, λ_{em} = 525±25 nm; 10,000 events) following induction of oxidative stress with diethylmaleate (DEM, 9 mM) in TF1a cells grown in media containing resveratrol (left black: 5 μM, right black: 50 μM) for 22 hours at 37 °C. Cells were incubated with the lipid peroxidation reporter C11-BODIPY$^{581/591}$ (1 μM) for 30 minutes prior to DEM treatment. Cells not treated with DEM were used as negative control (red). Cells not treated with antioxidants were used as positive control (blue).

Cell Viability Studies

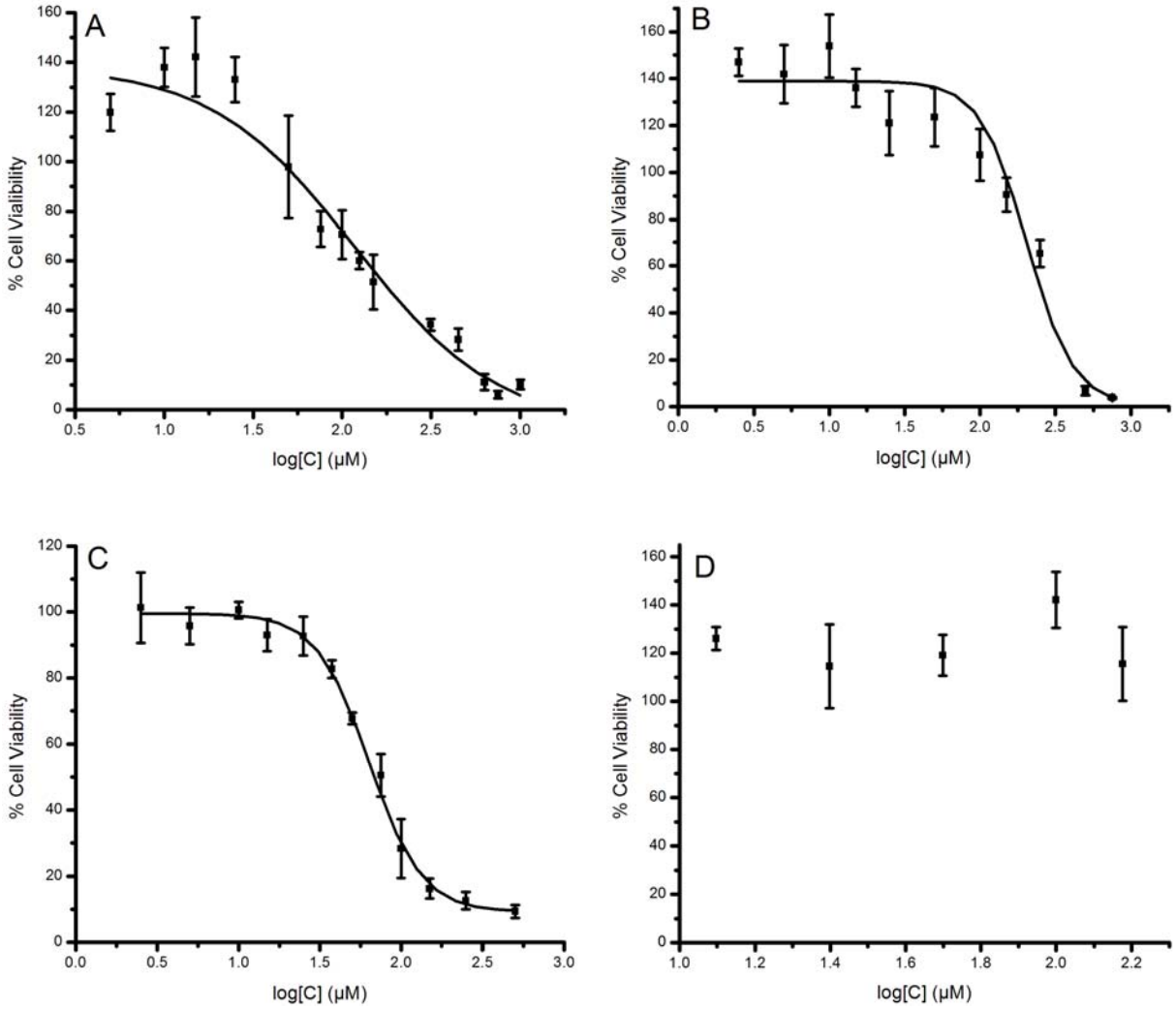


Figure S11. Dose-response curves obtained from MTT cell viability studies with TF1a erythroblasts (0.2 × 10^6 cells/ mL) containing varying concentrations of resveratrol (**1**) (A), pallidol (**2**) (B), quadrangularin A (**3**) (C), α-tocopherol (D) incubated at 37 °C for 22h.

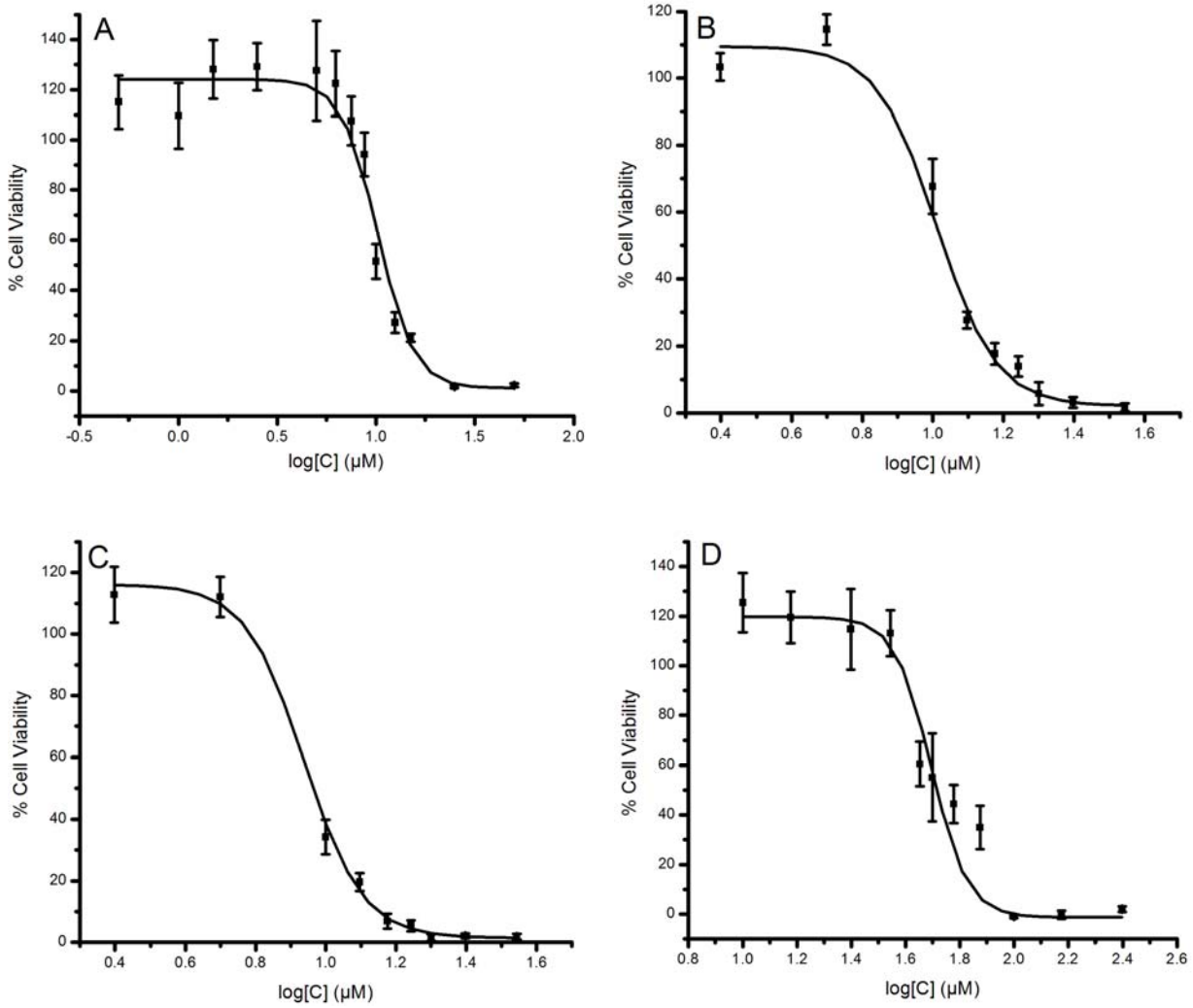
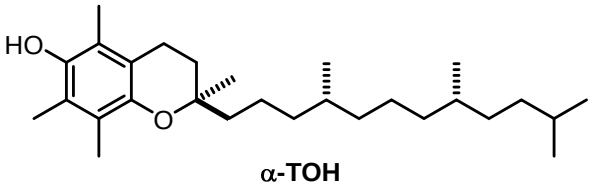
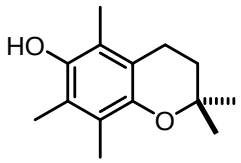


Figure S12. Dose-response curves obtained from MTT cell viability studies with TF1a erythroblasts (0.2 × 10^6 cells/ mL) containing varying concentrations of *t*-Bu2-resveratrol (**4a**) (A), *t*-Bu2-pallidol (**7b**) (B), *t*-Bu2-quadrangularin A (**10** (C), BHT (D) incubated at 37 °C for 22h.

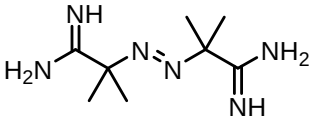
Compound Structures for Antioxidant Studies



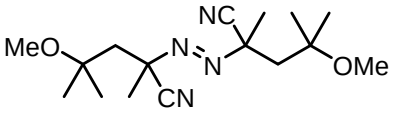
α-TOH
α-Tocopherol



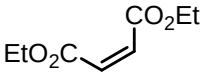
PMHC
2,2,5,7,8-pentamethyl-6-hydroxy-chromane



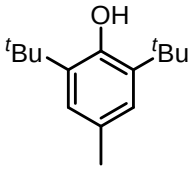
AAPH
2,2'-azobis-(2-amidinopropane)-dihydrochloride



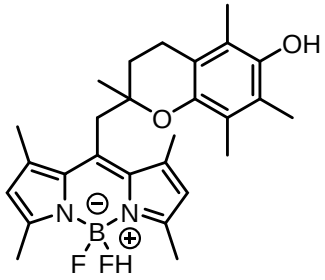
MeOAMVN
2,2'-azobis-(4-methoxy-2,4-imethylvaleronitrile)



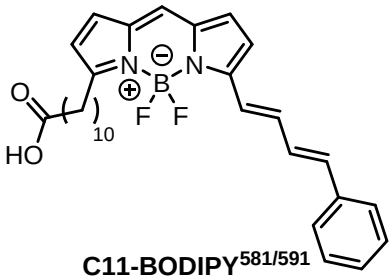
DEM
Diethylmaleate



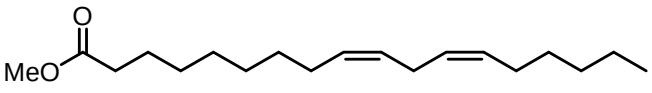
BHT
2,6-di-*tert*-butyl-4-hydroxytoluene



H_2B-PMHC
BODIPY-2,2,5,7,8-pentamethyl-6-hydroxy-chromane



C11-BODIPY$^{581/591}$



Methyl Lineolate

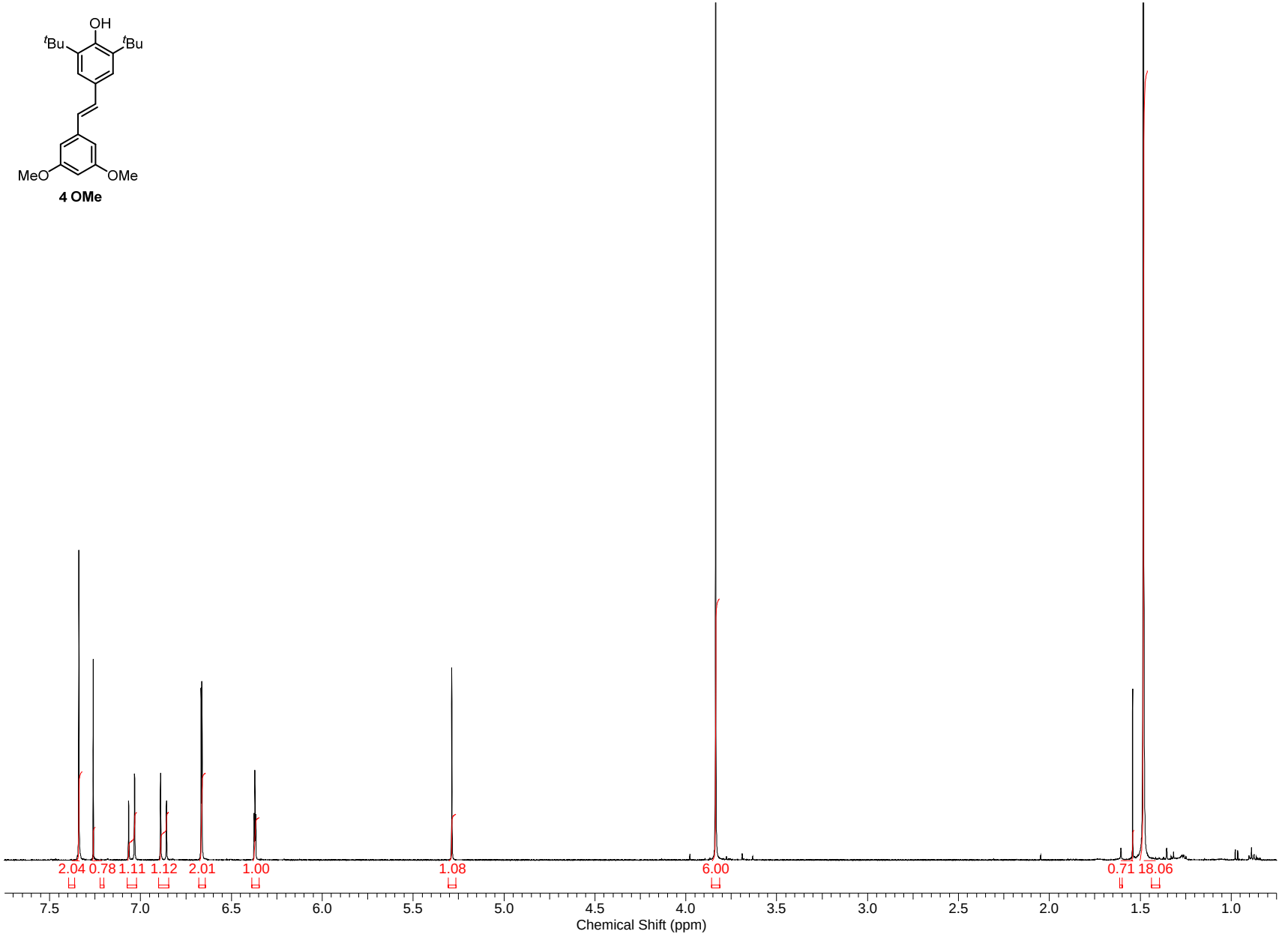
References

[1] K. Krumova, S. Friedland, G. Cosa, *J. Am. Chem. Soc.* **2012**, *134*, 10102–10113.

[2] B. Roschek, K. A. Tallman, C. L. Rector, J. G. Gillmore, D. A. Pratt, C. Punta, N. A. Porter, *J. Org. Chem.* **2006**, *71*, 3527–3532.

[3] B. Li, J. R. Harjani, N. S. Cormier, H. Madarati, J. Atkinson, G. Cosa, D. A. Pratt, *J. Am. Chem. Soc.* **2013**, *135*, 1394–1405.

[4] W. Li, H. Li, Y. Li, Z. Hou, *Angew. Chem. Int. Ed.* **2006**, *45*, 7609–7611; *Angew. Chem.* **2006**, *118*, 7771–7773.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tBu
tBu
MeO
OMe
4 OMe
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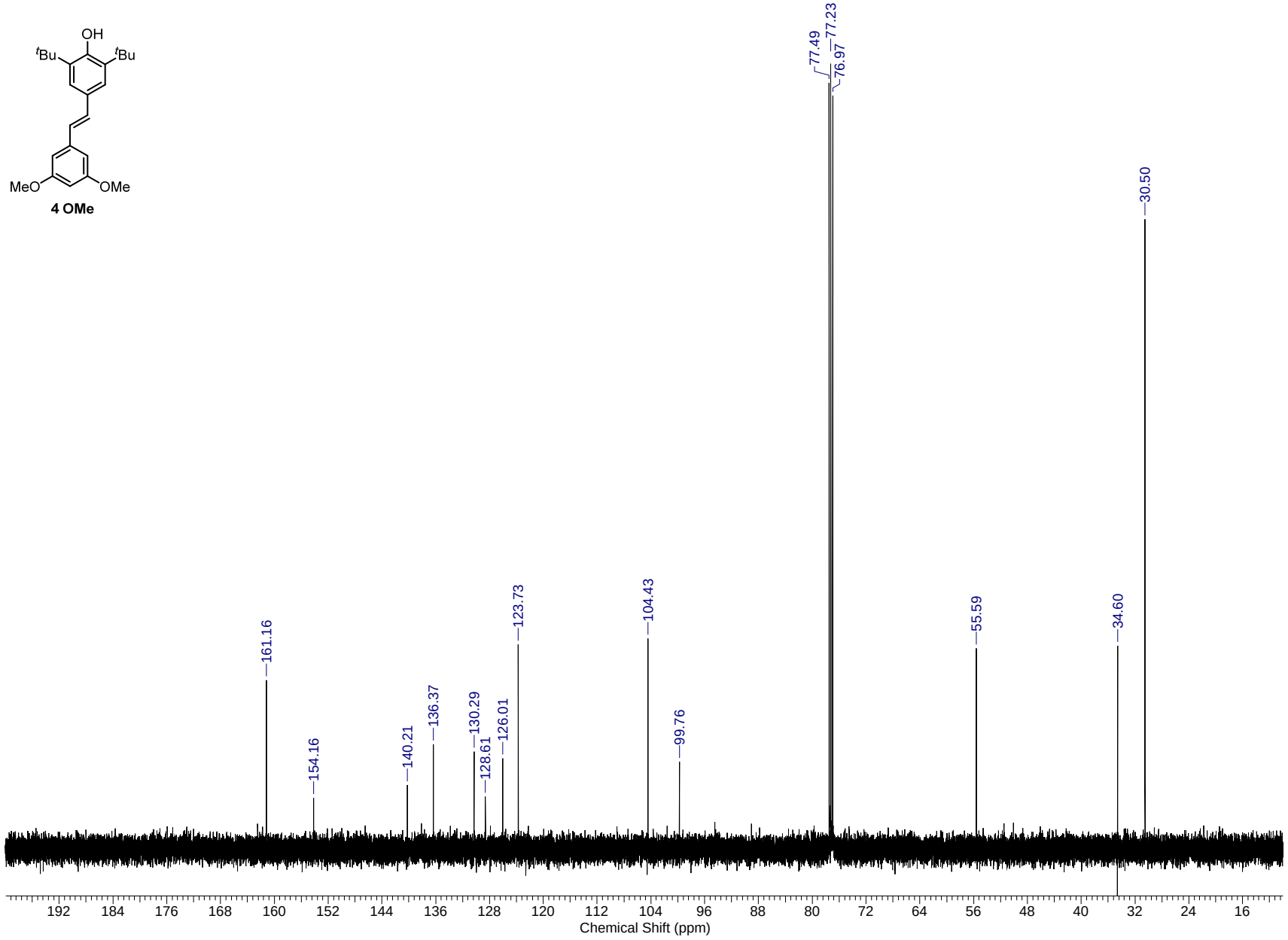
0.78
1.11
1.12
2.01
1.00
1.08
6.00
0.71
18.06
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)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tBu
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OMe
4 OMe
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76.97
30.50
161.16
154.16
140.21
136.37
130.29
128.61
126.01
123.73
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99.76
55.59
34.60
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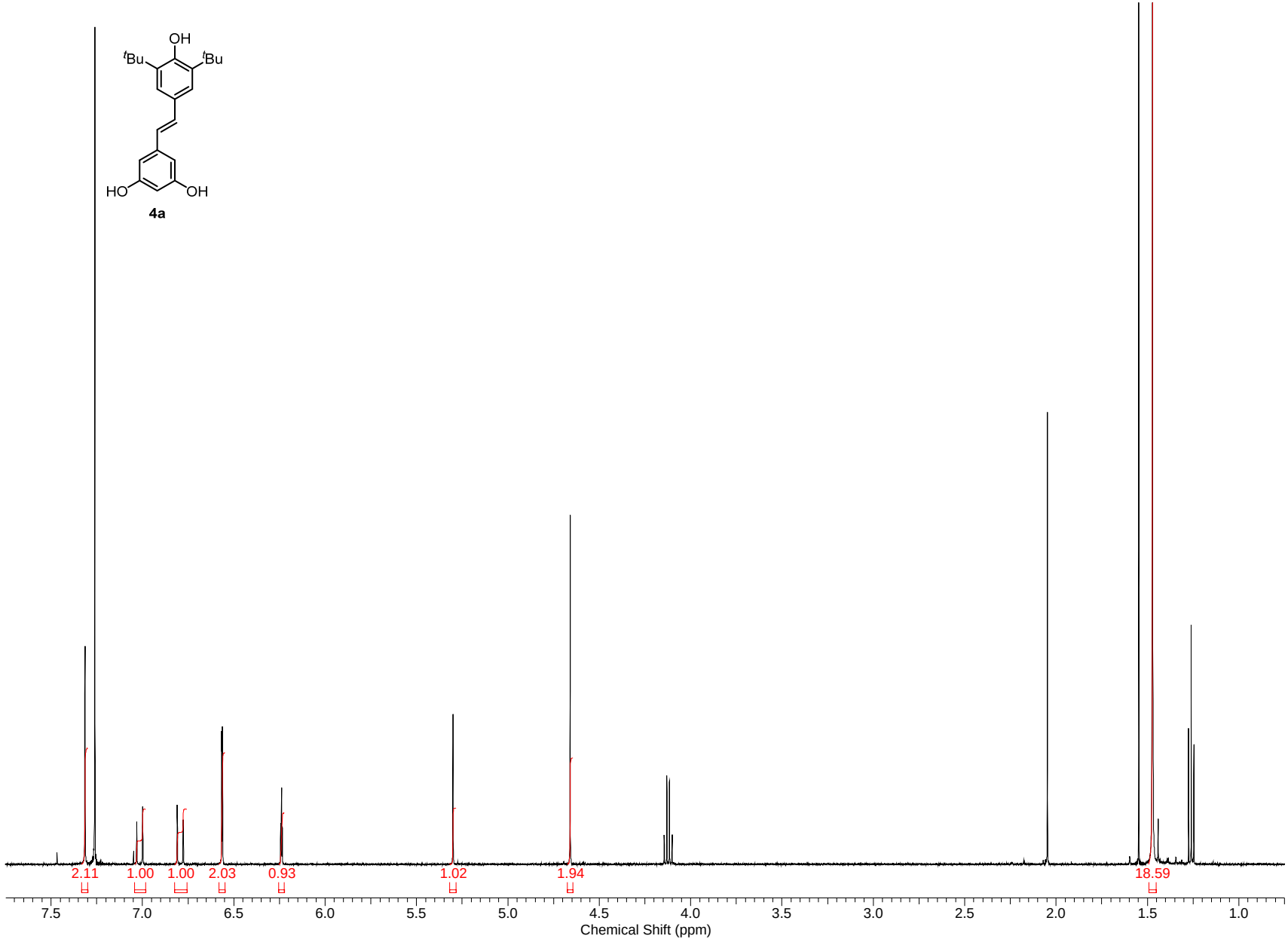
Chemical Shift (ppm)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1.02
1.94
18.59
7.5
7.0
6.5
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4.5
4.0
3.5
3.0
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2.0
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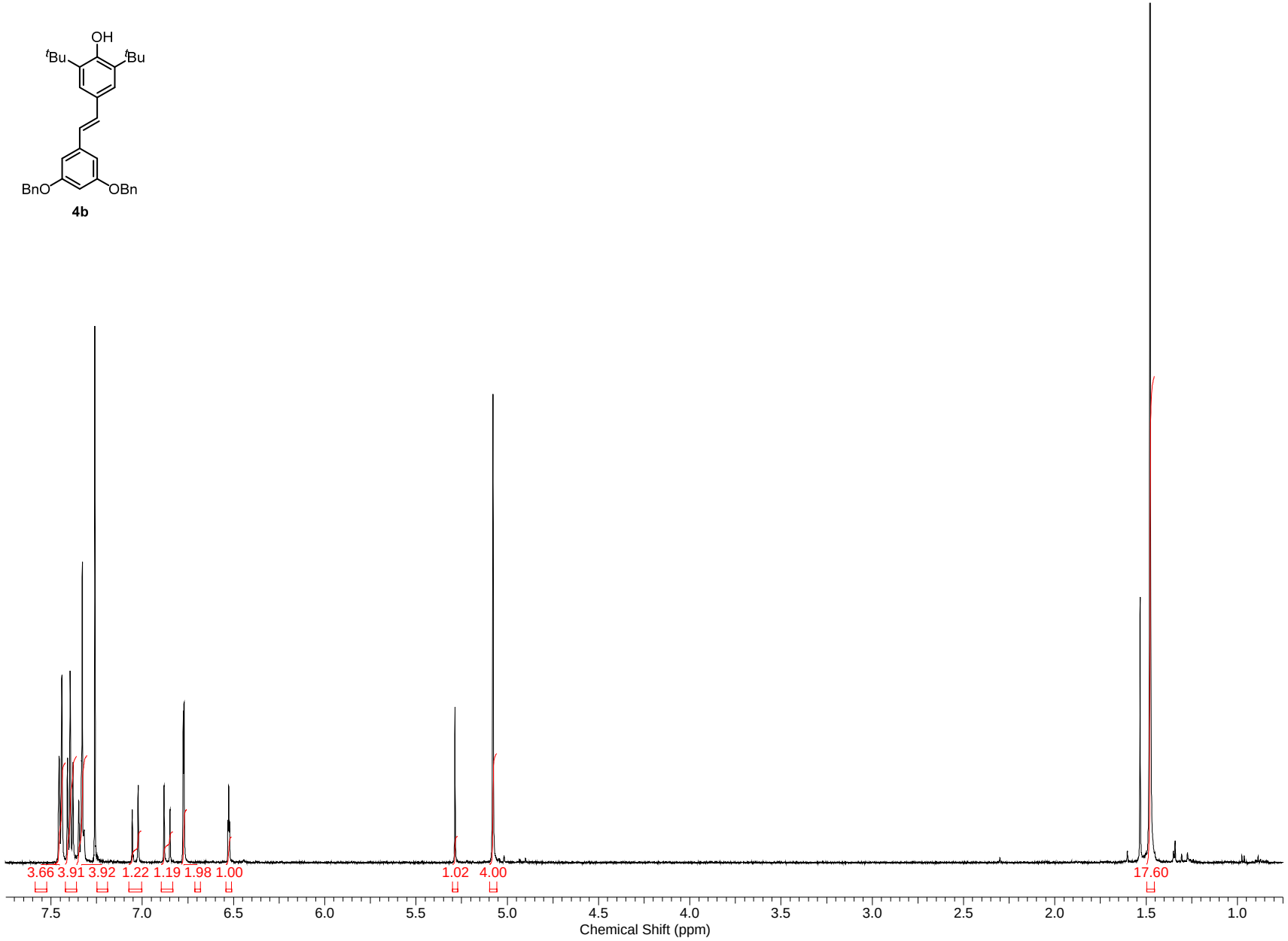
1.0
Chemical Shift (ppm)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tBu
BnO
OBn
4b
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1.02 4.00
17.60
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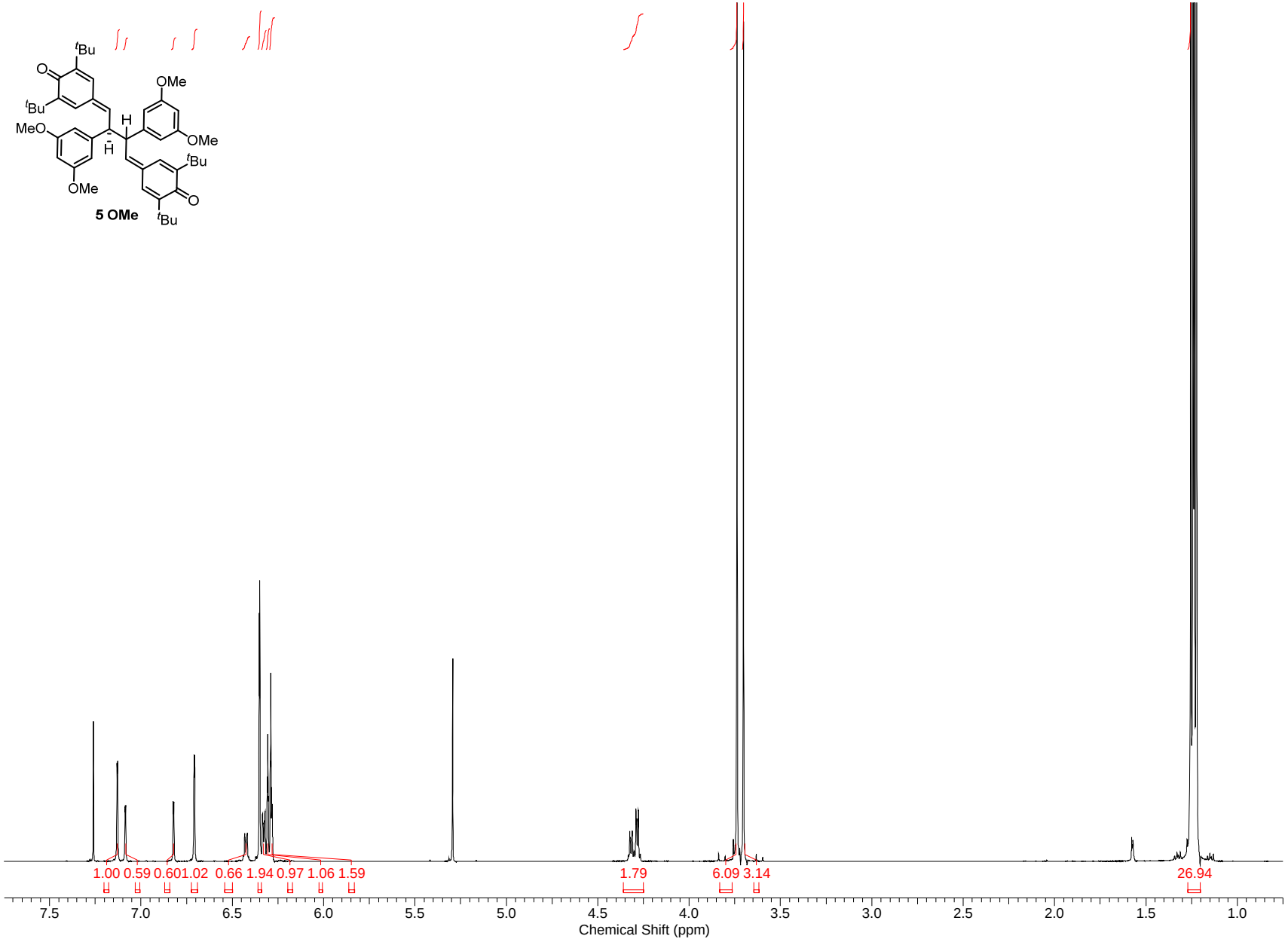
Chemical Shift (ppm)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1.79
6.09 3.14
26.94
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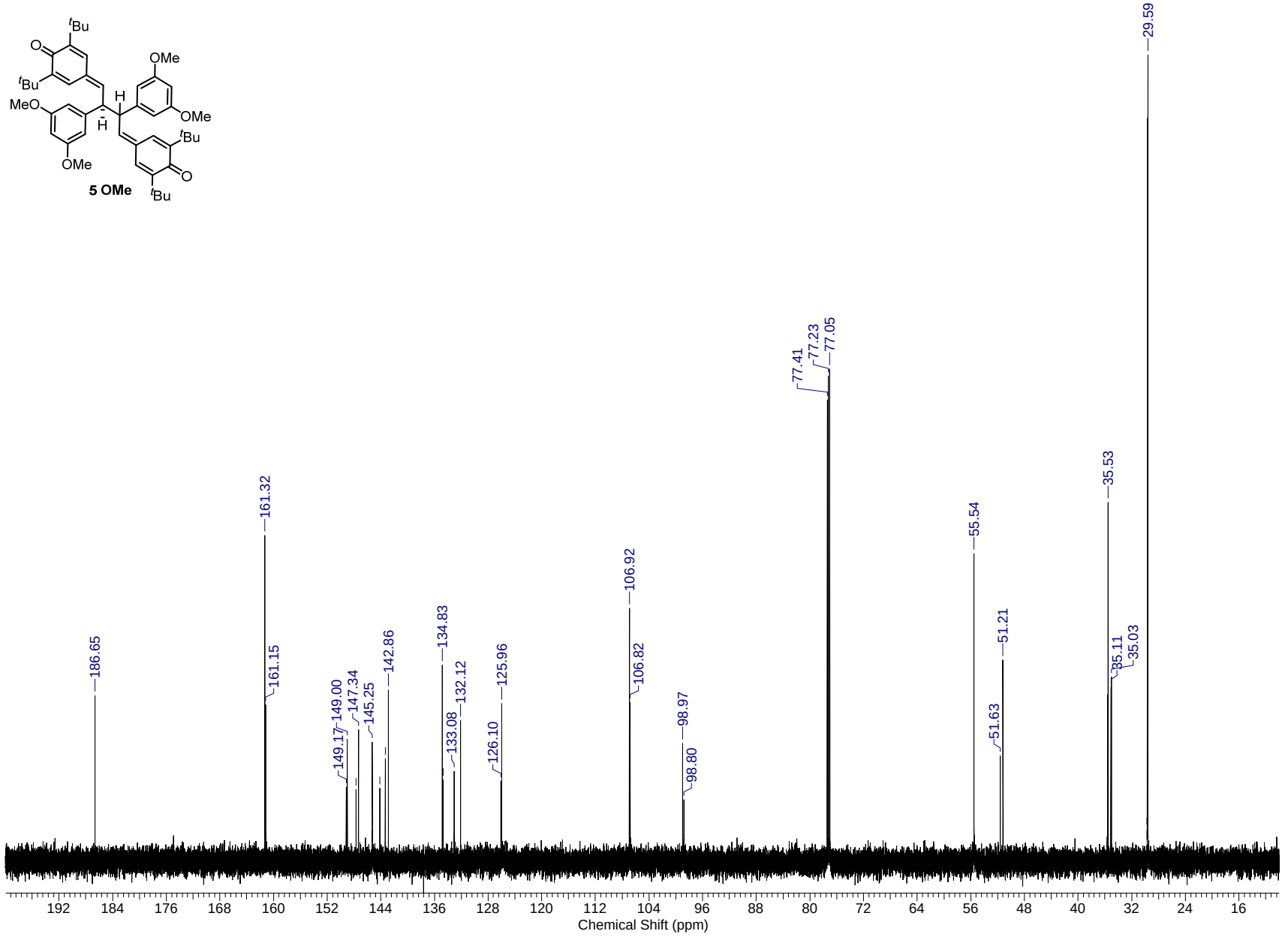
Chemical Shift (ppm)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133.08
132.12
126.10
125.96
106.92
106.82
98.97
98.80
77.41
77.23
77.05
55.54
51.63
51.21
35.53
35.11
35.03
29.59
192
184
176
168
160
152
144
136
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120
112
104
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88
80
72
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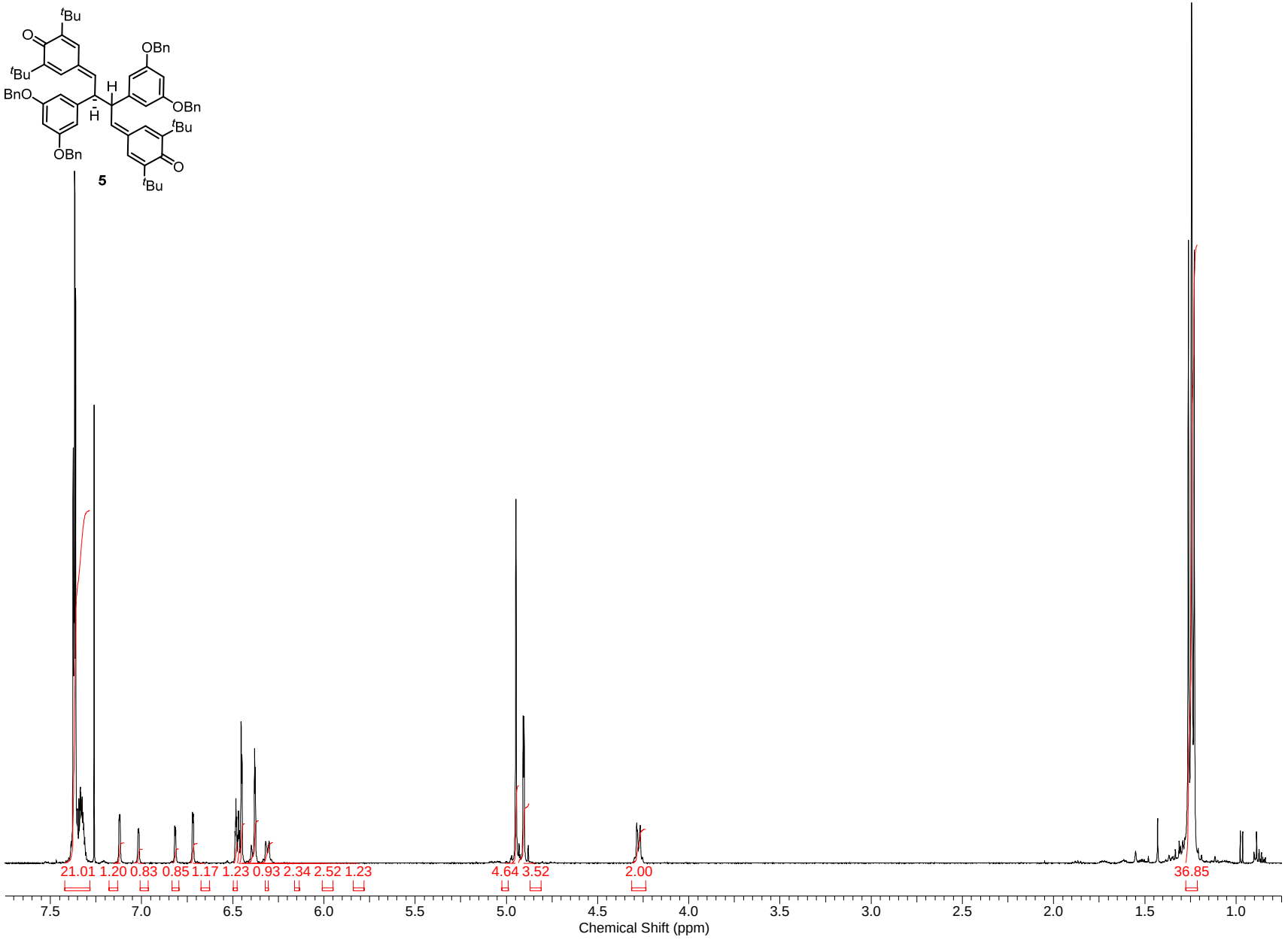
56
48
40
32
24
16
Chemical Shift (ppm)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BnO
H
H
OBn
OBn
tBu
OBn
O
tBu
5
21.01 1.20 0.83 0.85 1.17 1.23 0.93 2.34 2.52 1.23
4.64 3.52
2.00
36.85
7.5
7.0
6.5
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5.5
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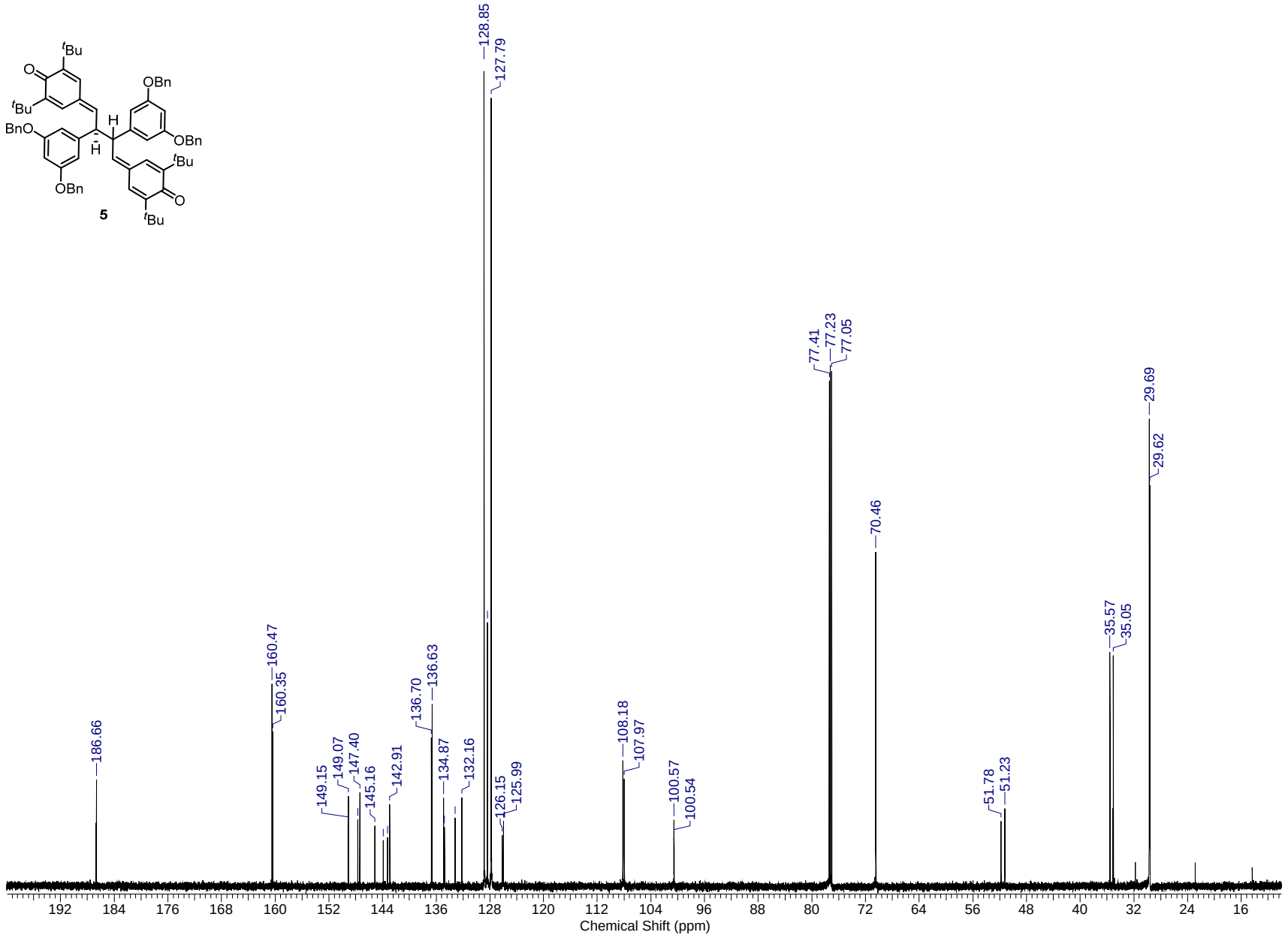
1.0
Chemical Shift (ppm)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tBu
OBn
H
BnO
H
OBn
tBu
OBn
O
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5
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127.79
77.41
77.23
77.05
29.69
29.62
70.46
35.57
35.05
160.47
160.35
136.63
136.70
186.66
149.15
149.07
147.40
145.16
142.91
134.87
132.16
126.15
125.99
108.18
107.97
100.57
100.54
51.78
51.23
192
184
176
168
160
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88
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72
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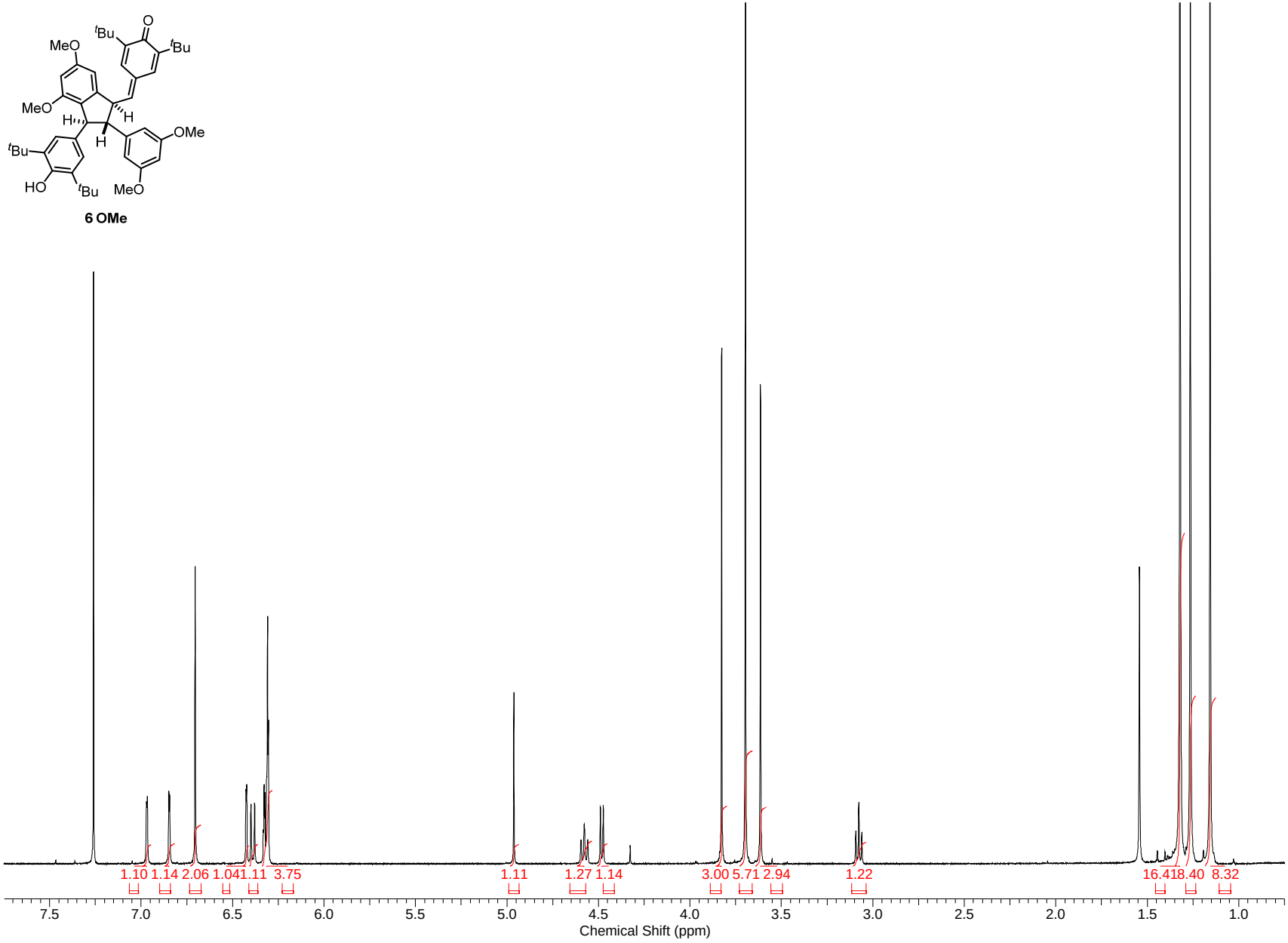
56
48
40
32
24
16
Chemical Shift (ppm)


MeO
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O
tBu
MeO
H
H
H
OMe
tBu
HO
tBu
MeO
6 OMe
1.10 1.14 2.06 1.04 1.11 3.75
1.11
1.27 1.14
3.00 5.71 2.94
1.22
16.41 8.40 8.32
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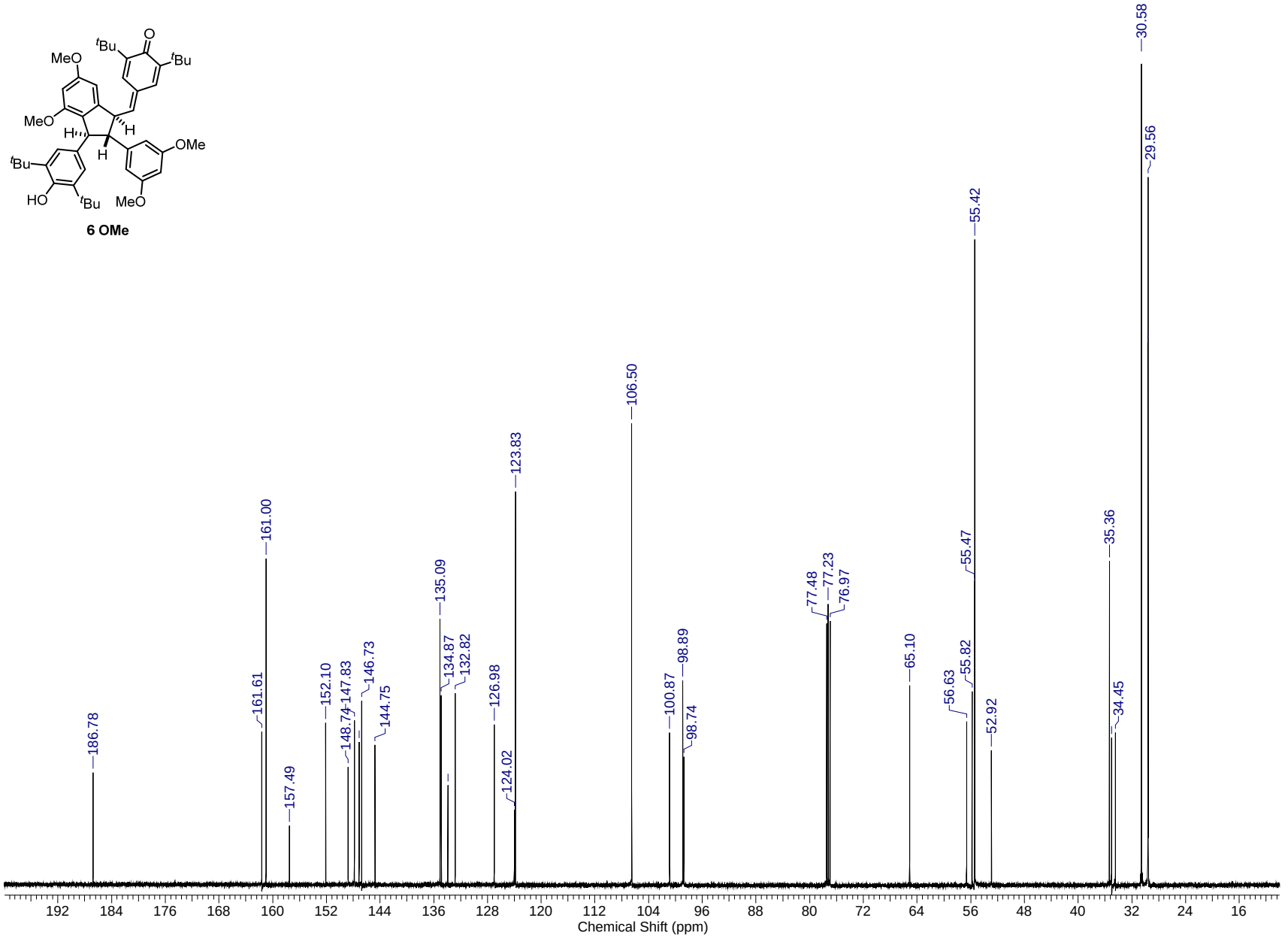
Chemical Shift (ppm)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147.83
146.73
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132.82
126.98
124.02
123.83
106.50
100.87
98.89
98.74
77.48
77.23
76.97
65.10
56.63
55.82
55.47
55.42
52.92
35.36
34.45
30.58
29.56
192
184
176
168
160
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88
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56
48
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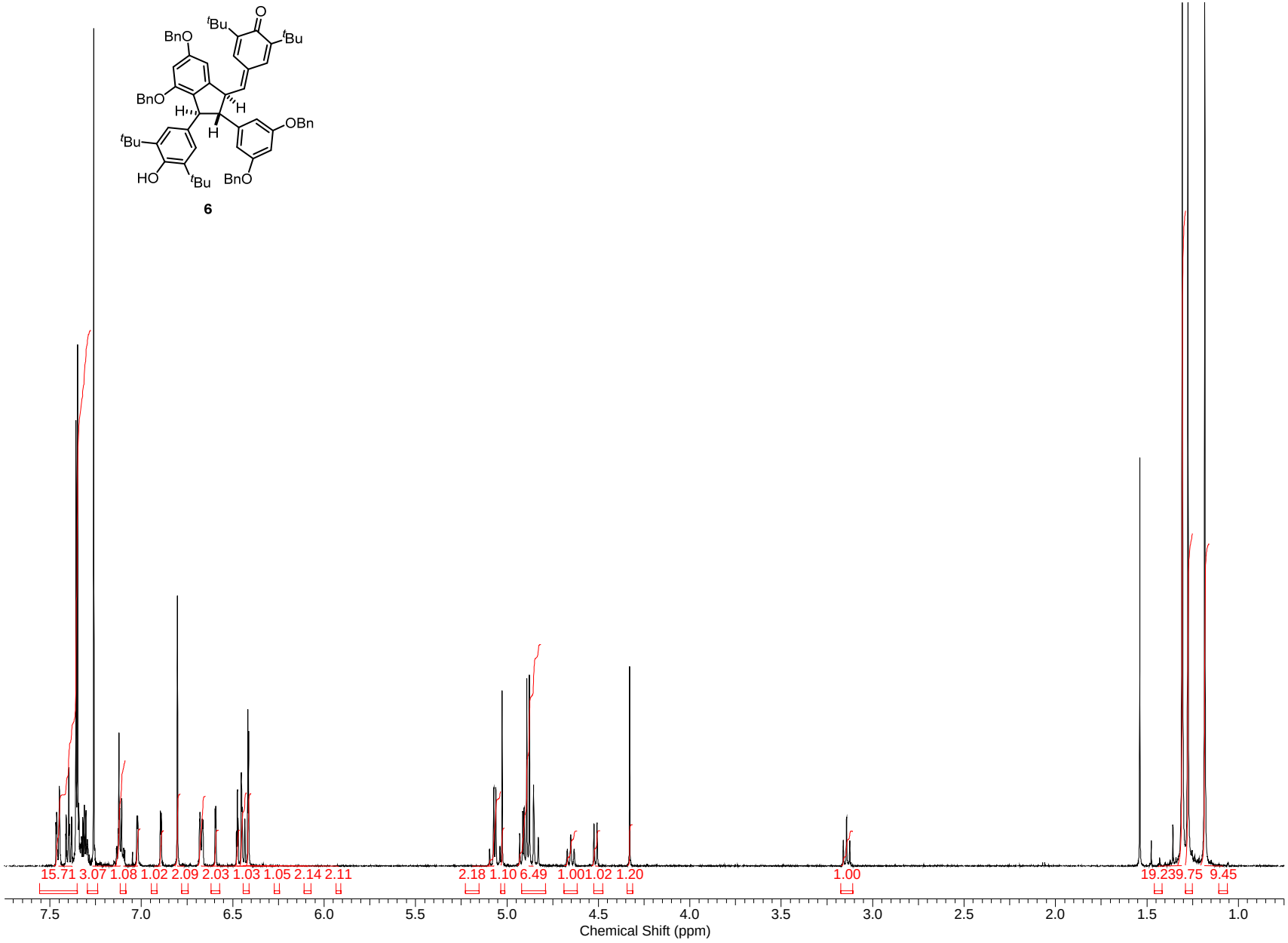
24
16
Chemical Shift (ppm)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BnO
H
H
H
OBn
tBu
HO
tBu
BnO
6
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2.18 1.10 6.49 1.00 1.02 1.20
1.00
19.23 9.75 9.45
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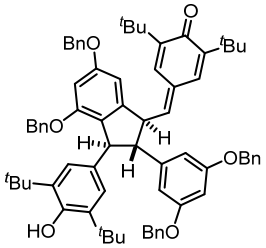
Chemical Shift (ppm)


BnO
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O
tBu
BnO
H
H
H
OBn
tBu
HO
tBu
BnO

6

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127.82
128.75
126.38
77.41
77.23
77.05
29.66
160.16
160.71
156.24
152.33
148.81
147.20
146.83
143.99
137.01
136.93
135.47
134.93
134.23
124.14
107.61
102.32
100.46
100.37
186.84
70.28
70.70
69.57
65.54
57.04
52.45
35.43
34.48
192
184
176
168
160
152
144
136
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120
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104
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88
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72
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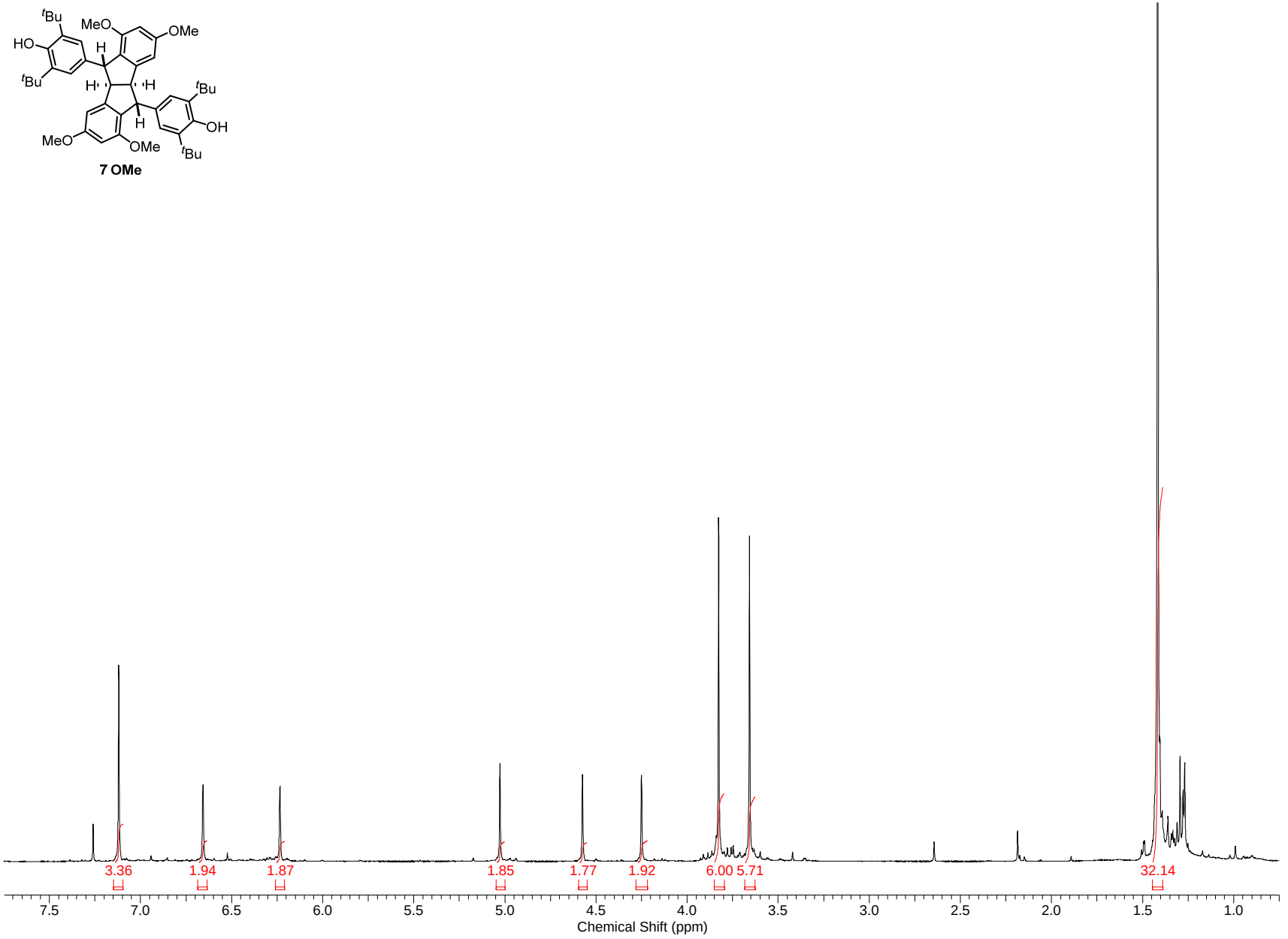
56
48
40
32
24
16
Chemical Shift (ppm)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OMe
HO
H
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H
H
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H
OH
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OMe
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3.36
1.94
1.87
1.85
1.77
1.92
6.00
5.71
32.14
7.5
7.0
6.5
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2.0
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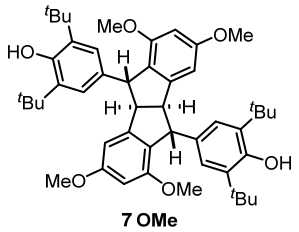
1.0
Chemical Shift (ppm)


tBu
MeO
OMe
HO
H
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H
H
tBu
H
OH
MeO
OMe
tBu

7 OMe

30.59
34.50
77.41
77.23
77.05
124.28
135.43
161.05
157.05
152.00
148.49
136.27
125.85
100.77
97.57
59.58
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55.28
54.23
192
184
176
168
160
152
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136
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112
104
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88
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72
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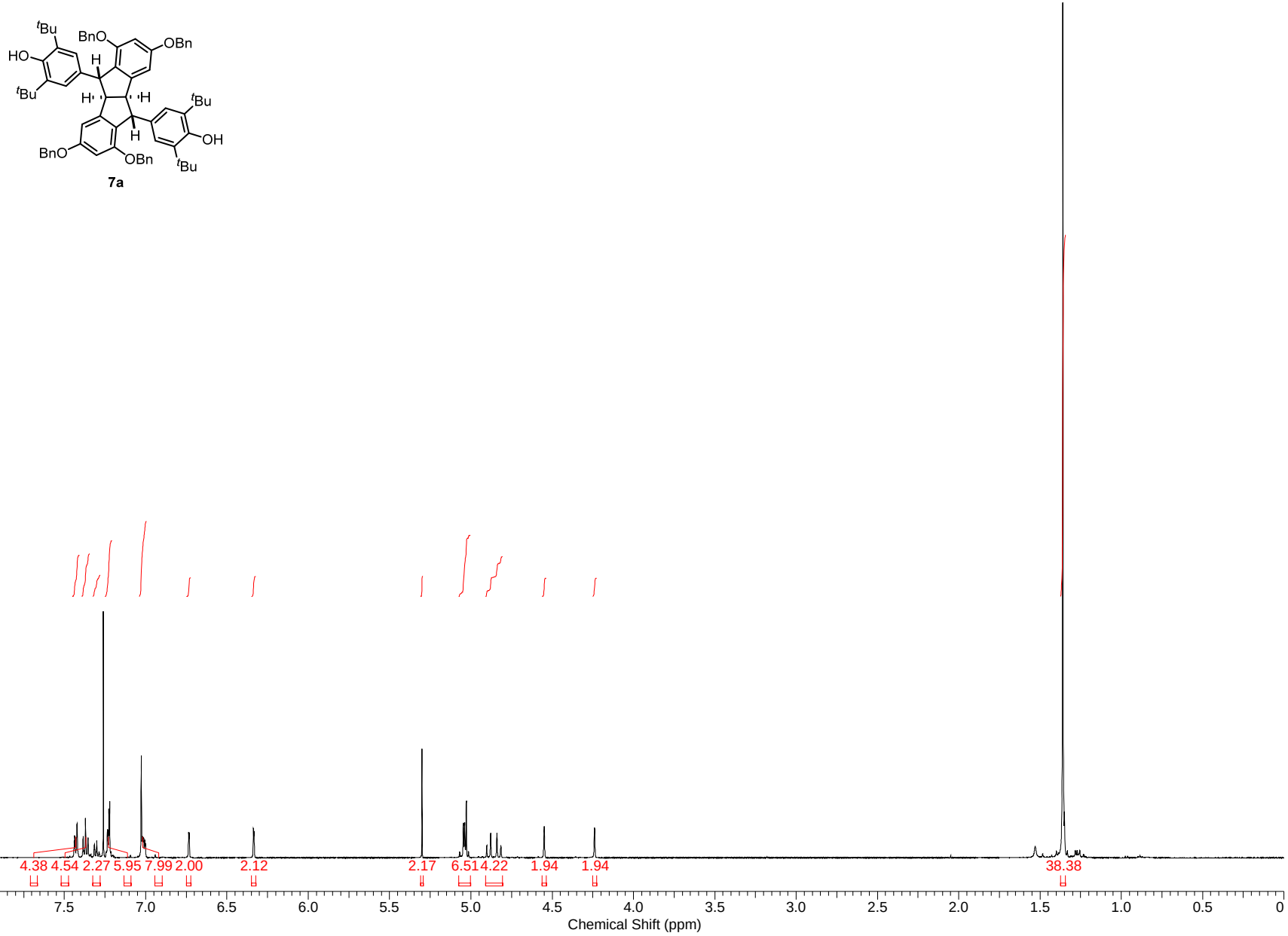
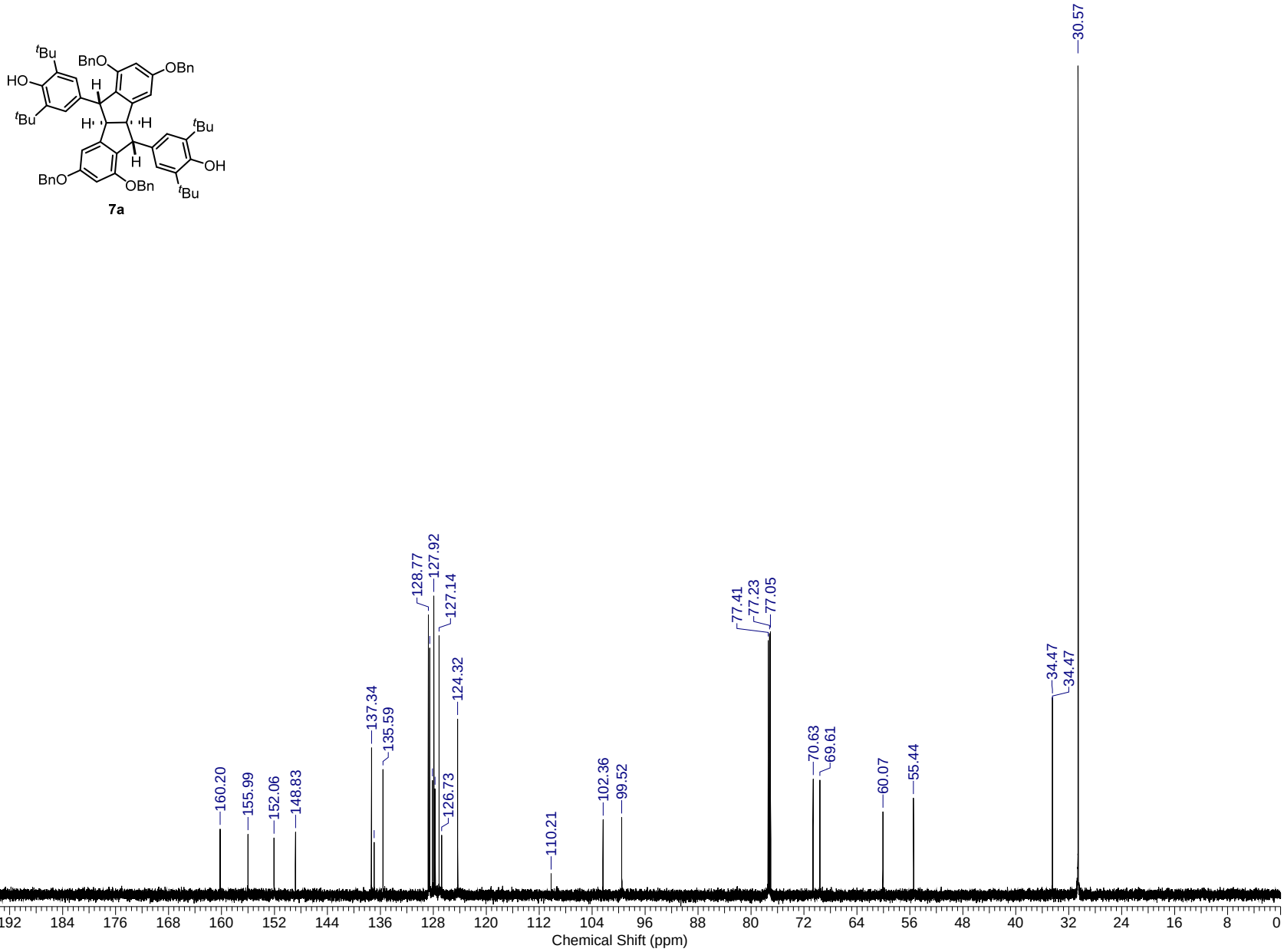
56
48
40
32
24
16
Chemical Shift (ppm)


tBu
BnO
OBn
HO
H
tBu
H
H
H
tBu
BnO
OBn
H
OH
tBu
7a
4.38 4.54 2.27 5.95 7.99 2.00 2.12 2.17 6.51 4.22 1.94 1.94 38.38
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
Chemical Shift (ppm)


tBu
BnO
OBn
HO
H
tBu
H
H
tBu
H
OH
BnO
OBn
tBu
7a
30.57
160.20
155.99
152.06
148.83
137.34
135.59
128.77
127.92
127.14
124.32
126.73
110.21
102.36
99.52
77.41
77.23
77.05
70.63
69.61
60.07
55.44
34.47
34.47
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
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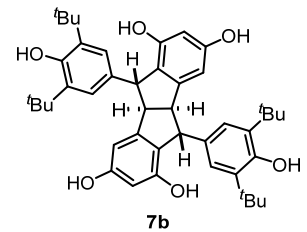
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


tBu
HO
OH
HO
H
tBu
H
H
tBu
H
OH
HO
OH
tBu

7b

4.03
2.08
2.10
2.04
1.96
36.00
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
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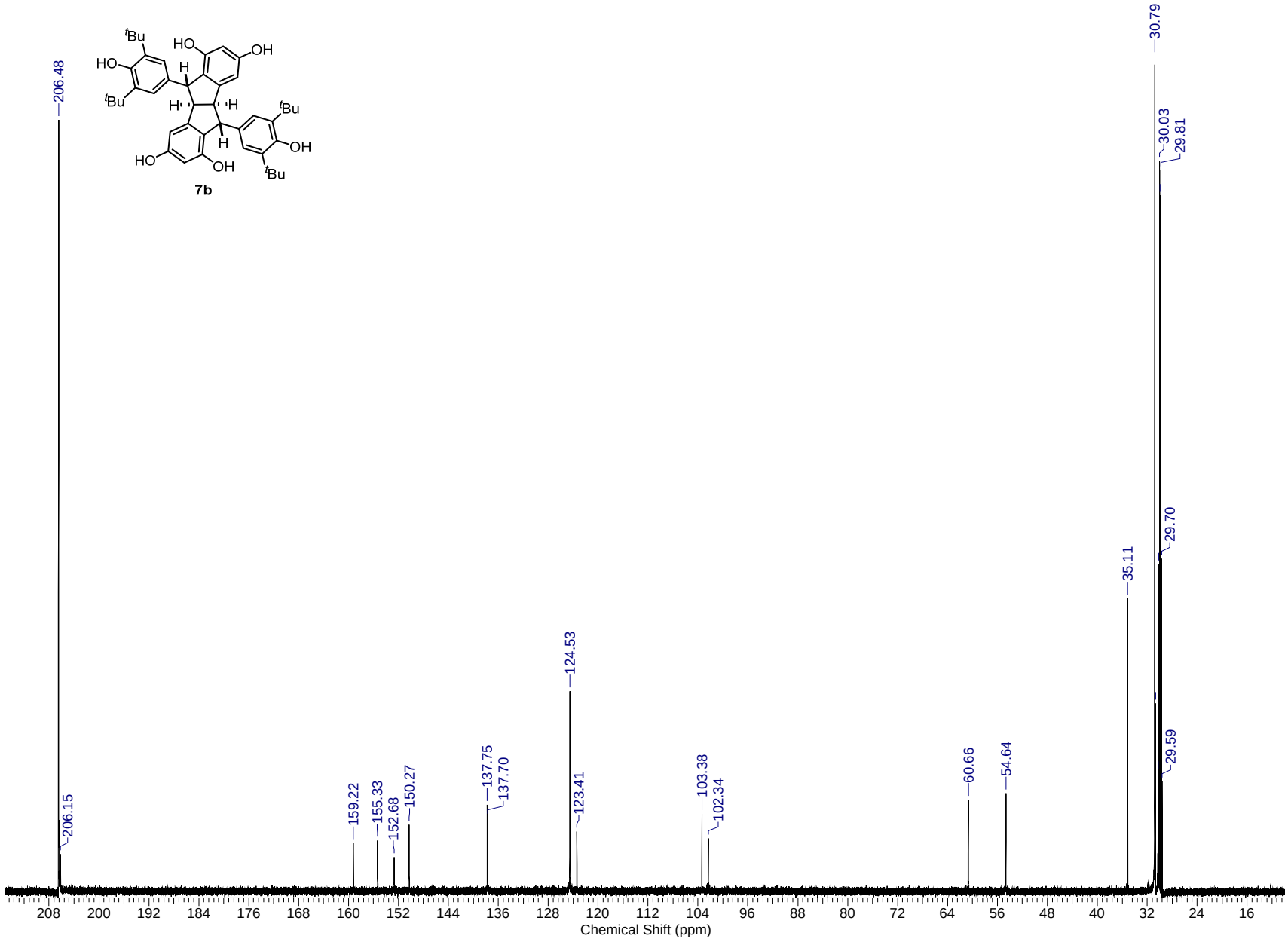
2.0
1.5
1.0
Chemical Shift (ppm)


7b
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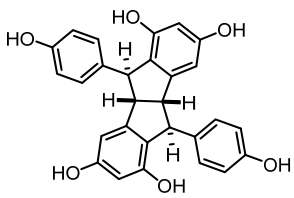
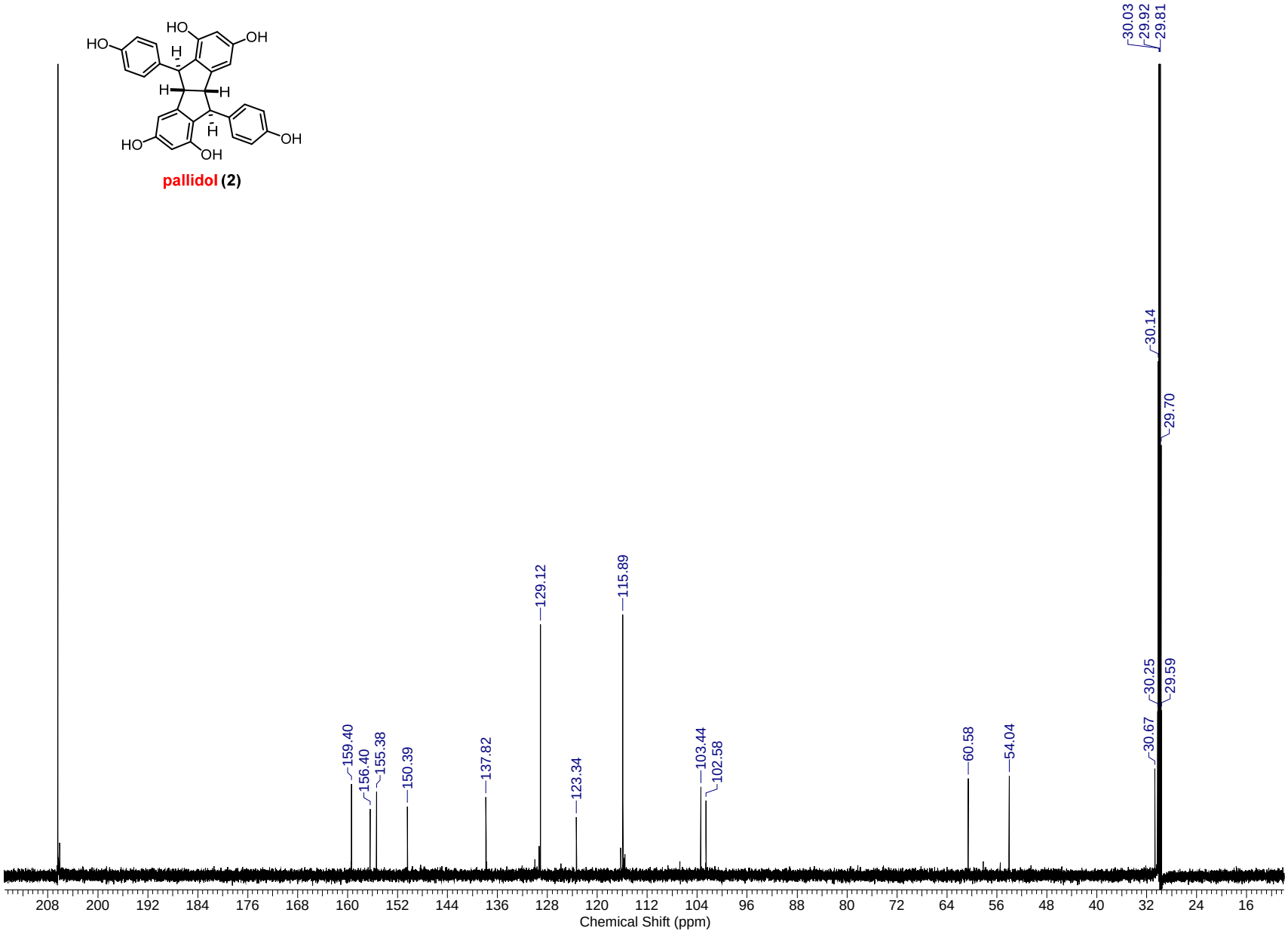
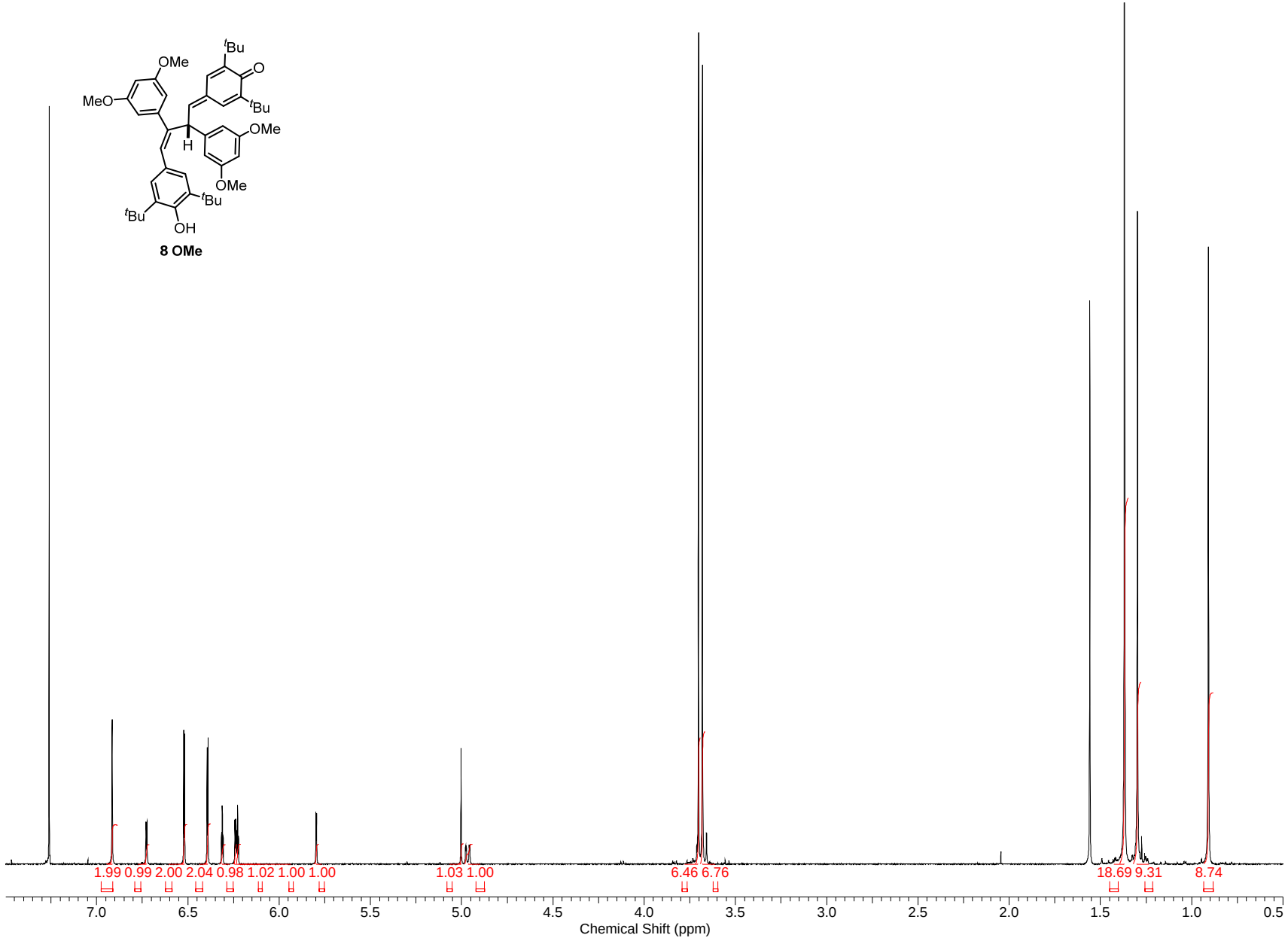
152.68
150.27
137.75
137.70
124.53
123.41
103.38
102.34
60.66
54.64
35.11
30.79
30.03
29.81
29.70
29.59
Chemical Shift (ppm)

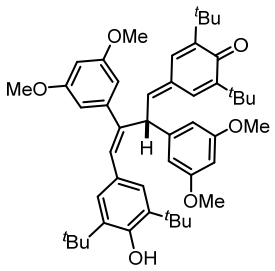

HO
OH
H
H
H
H
HO
OH
OH

pallidol (2)

3.62
1.61
3.94
3.91
1.98
1.98
2.00
2.02
8.0
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
Chemical Shift (ppm)

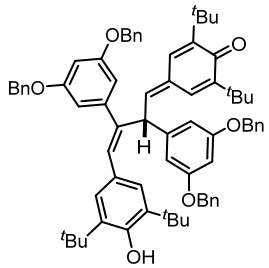

HO
OH
H
H
H
H
HO
OH
HO
OH
pallidol (2)
30.03
29.92
29.81
30.14
29.70
159.40
156.40
155.38
150.39
137.82
129.12
123.34
115.89
103.44
102.58
60.58
54.04
30.25
29.59
30.67
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


OMe
MeO
tBu
O
tBu
H
OMe
OMe
tBu
tBu
OH
8 OMe
1.99 0.99 2.00 2.04 0.98 1.02 1.00 1.00
1.03 1.00
6.46 6.76
18.69 9.31
8.74
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
Chemical Shift (ppm)


tBu
OMe
O
MeO
tBu
H
OMe
OMe
tBu
tBu
OH

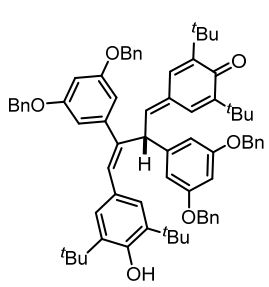
8 OMe

30.51
77.41
77.23
77.05
29.26
34.45
160.90
160.67
152.84
147.55
146.64
146.15
144.49
141.60
137.47
135.39
130.77
127.84
124.02
106.86
104.99
100.19
98.23
65.34
55.49
55.39
56.56
54.63
35.04
34.82
186.61
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


tBu
OBn
O
BnO
tBu
H
OBn
OBn
tBu
tBu
OH

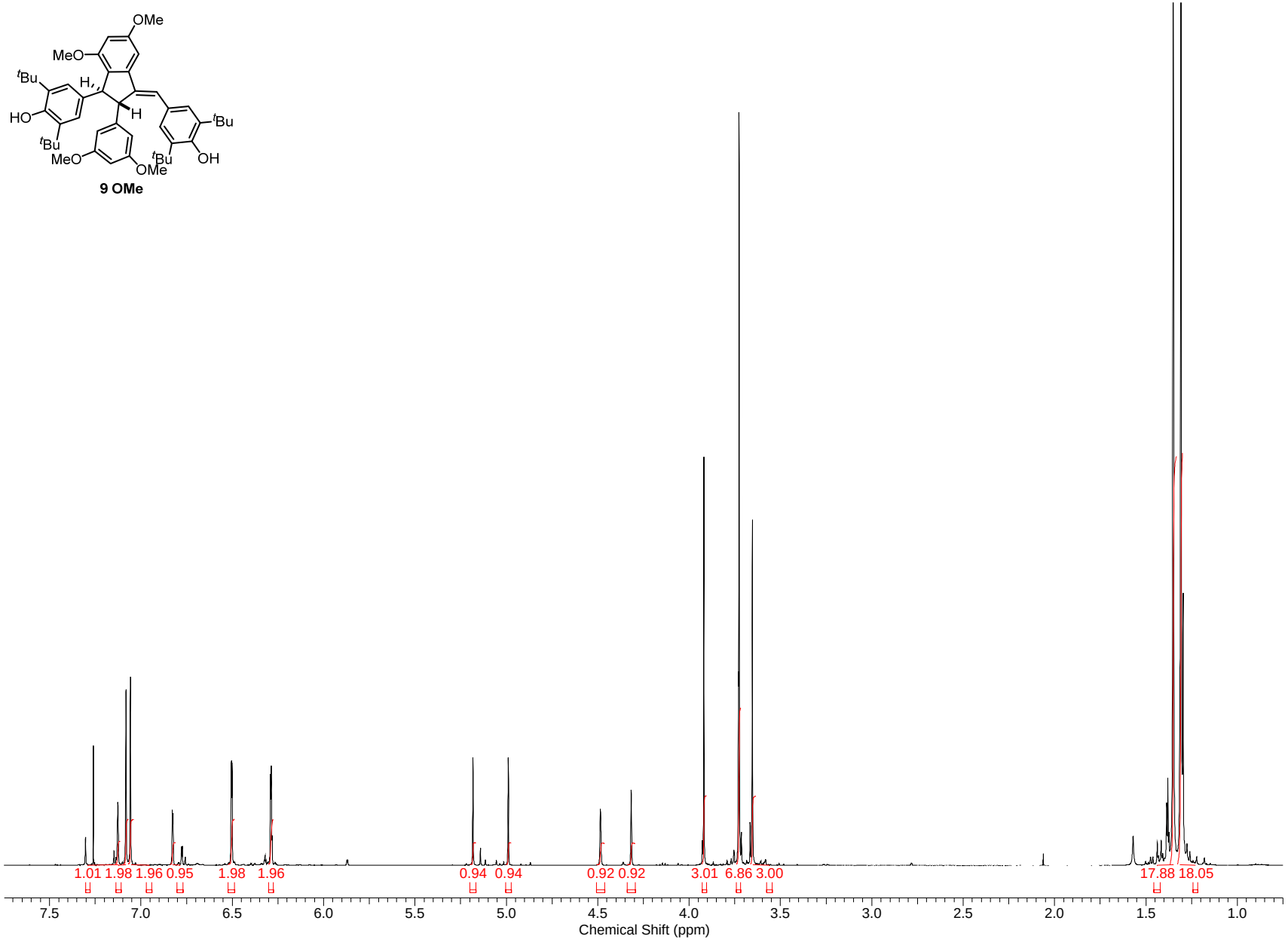
8

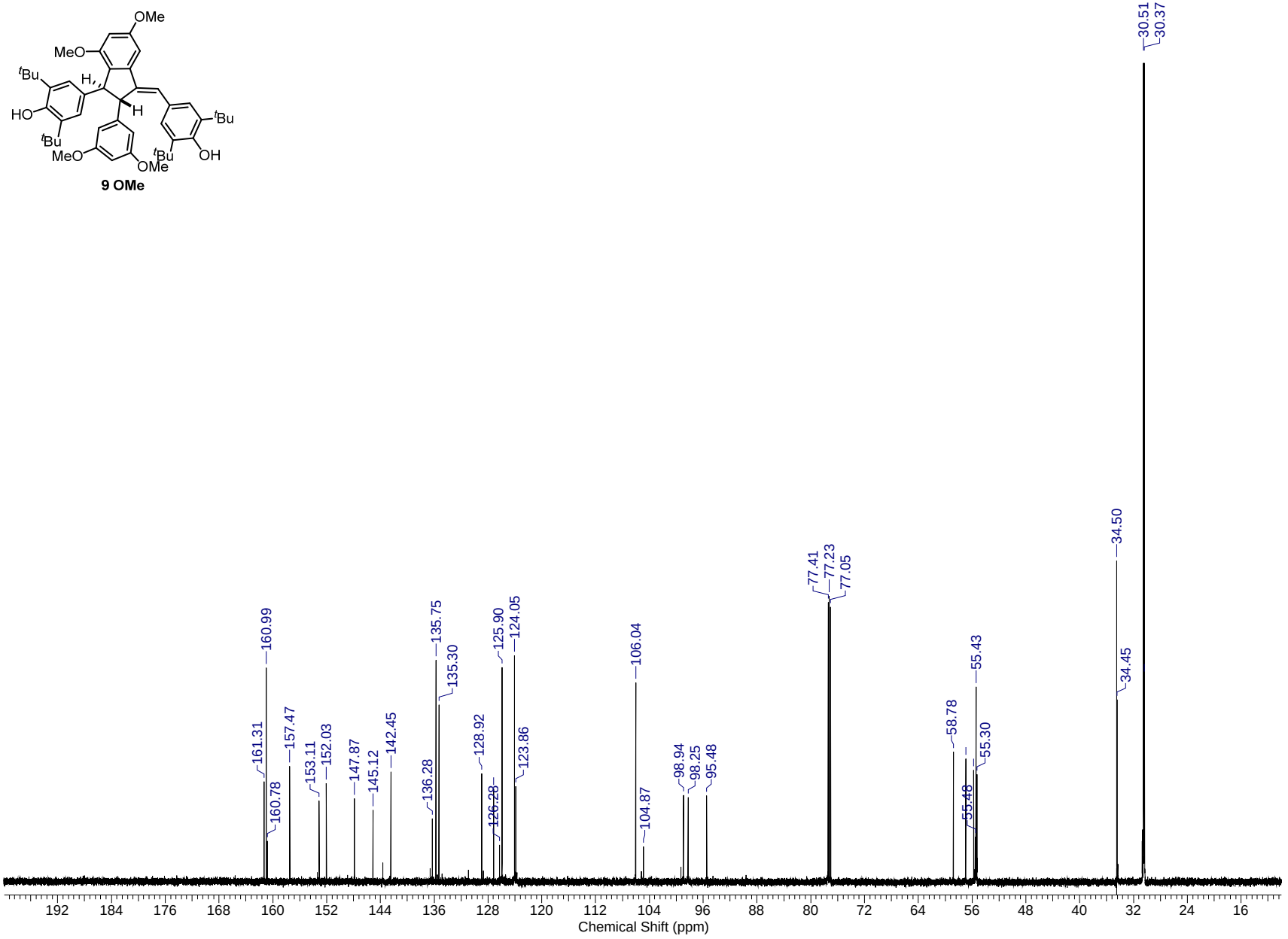
24.26
2.17
1.07
2.21
2.23
1.12
1.07
1.05
1.04
1.29
10.62
1.00
20.06
10.43
9.83
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

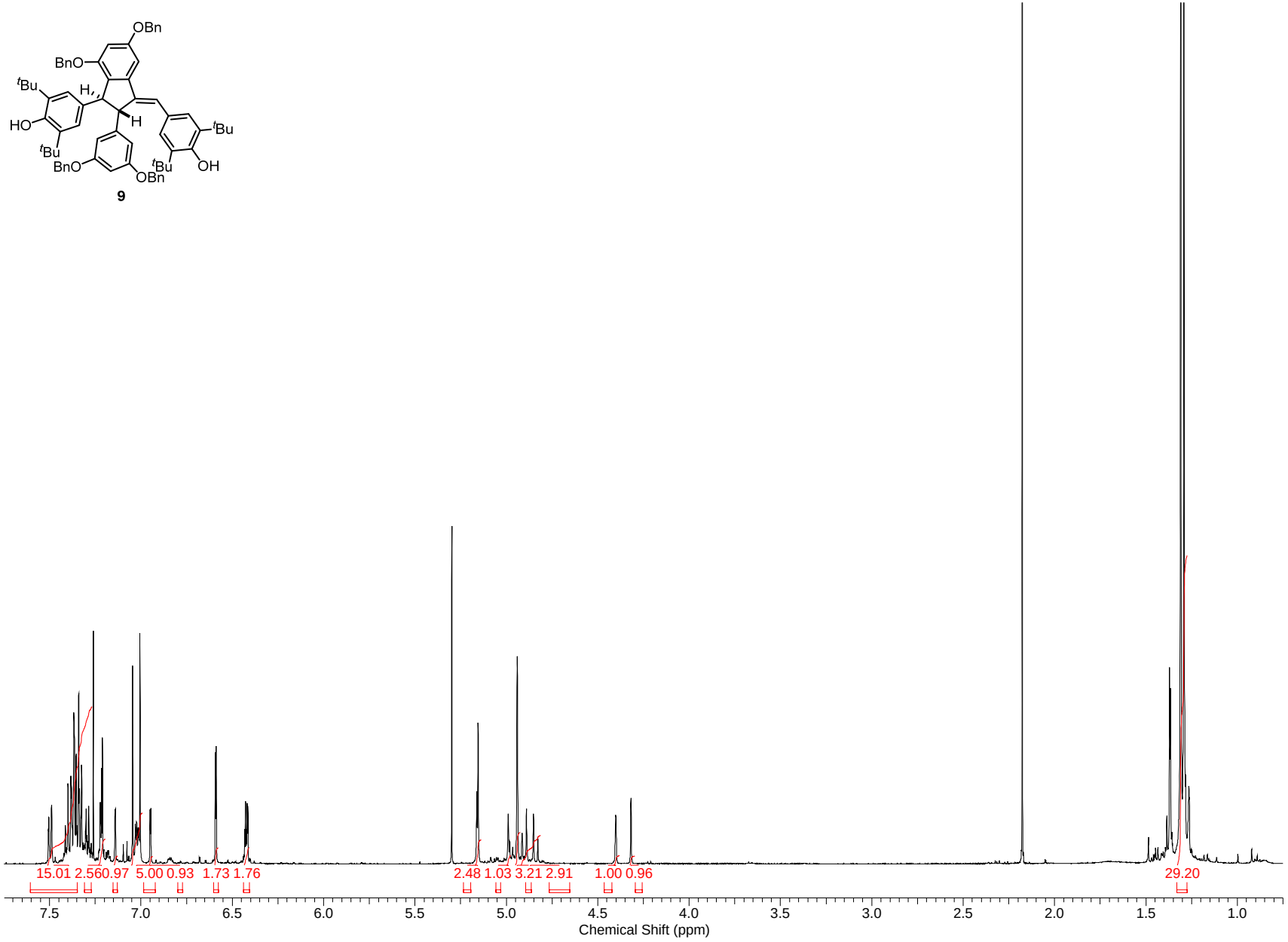

tBu
OBn
O
BnO
tBu
H
OBn
OBn
tBu
tBu
OH

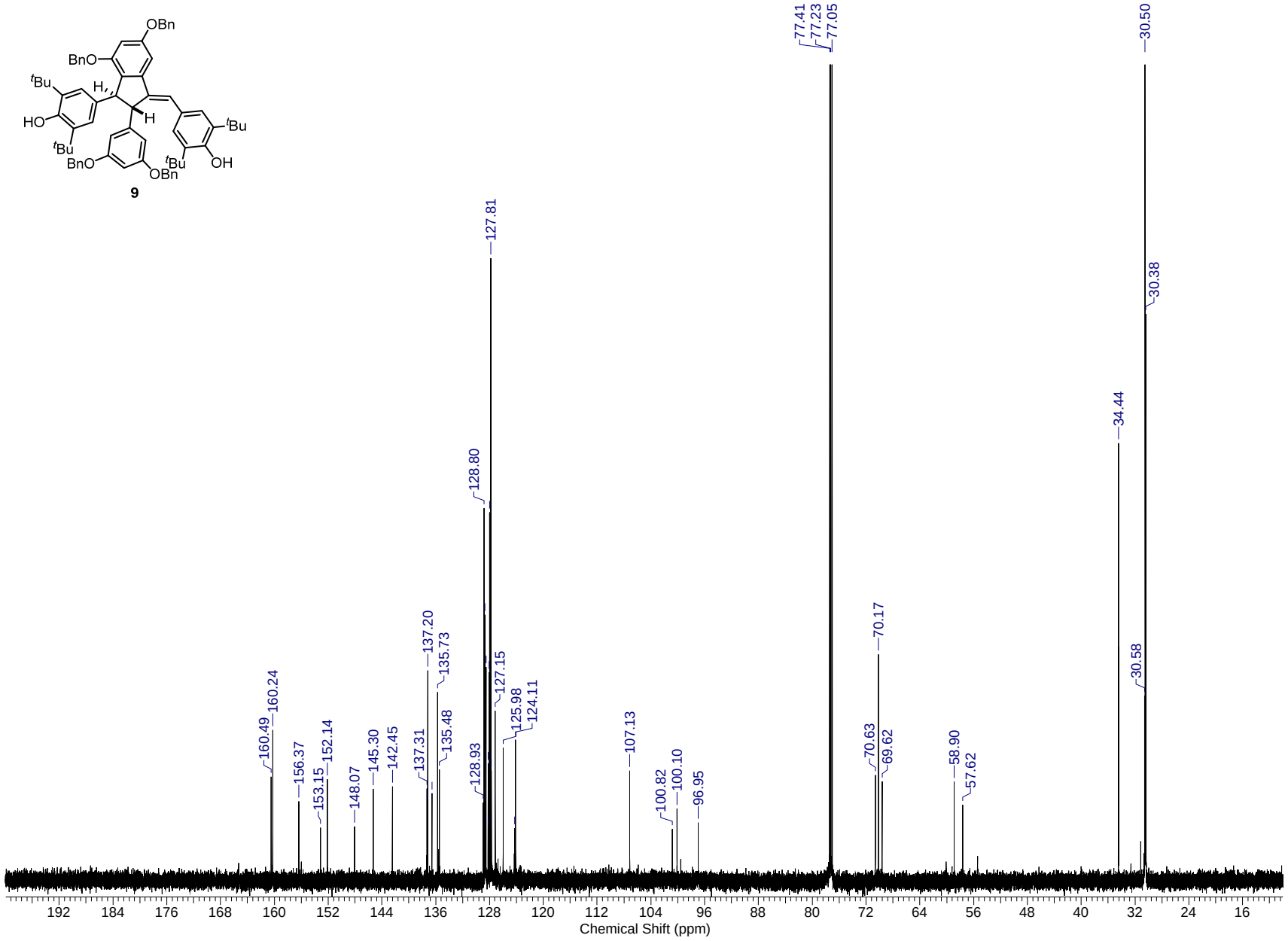
8

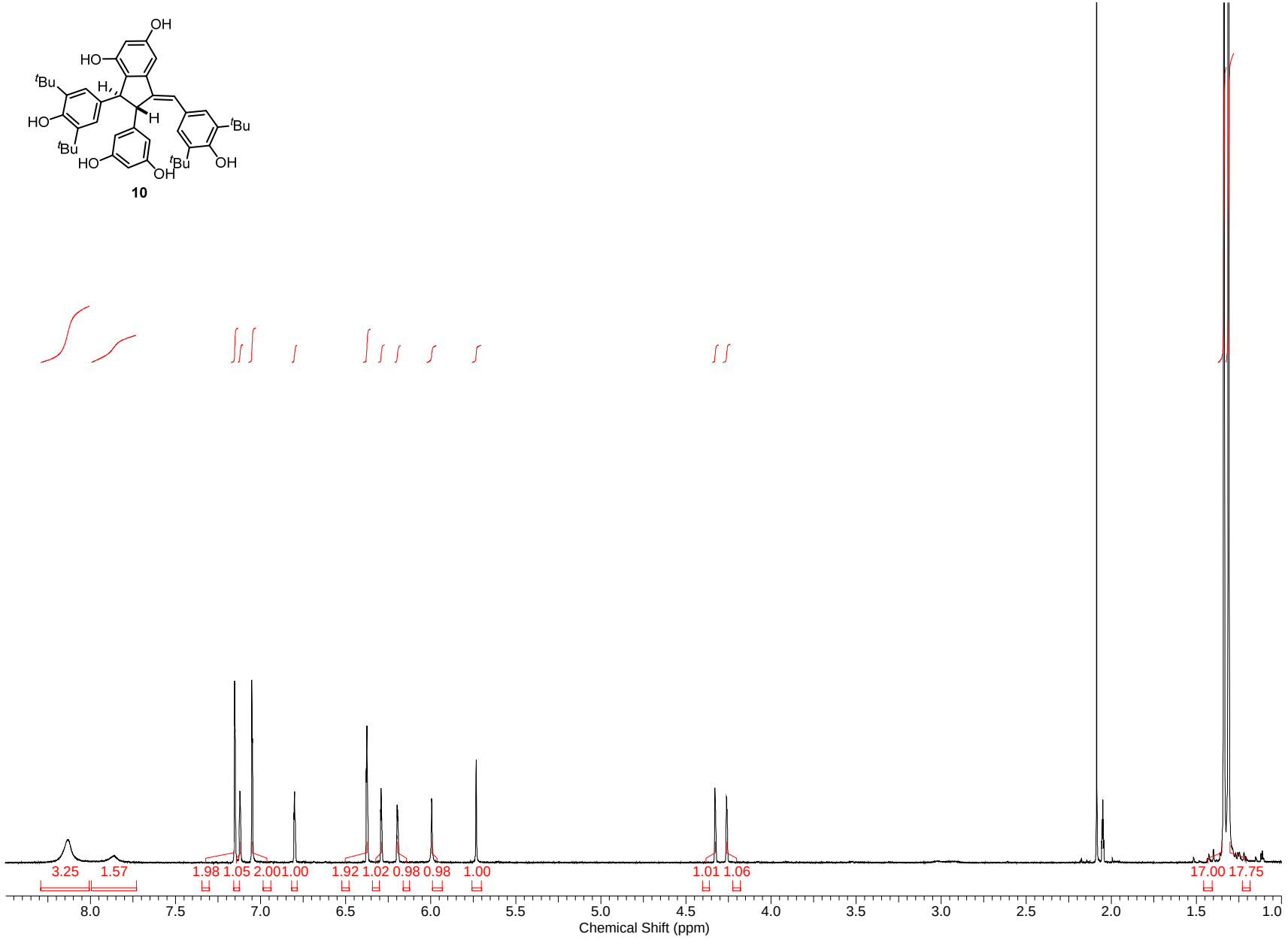
77.41
77.23
77.05
30.54
128.78
127.82
34.47
30.02
29.27
70.32
70.27
136.98
136.88
160.15
159.89
35.04
34.83
56.56
152.86
147.56
146.51
146.23
144.44
137.46
135.42
130.85
127.67
124.02
108.15
106.26
101.96
100.27
65.18
54.70
186.58
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

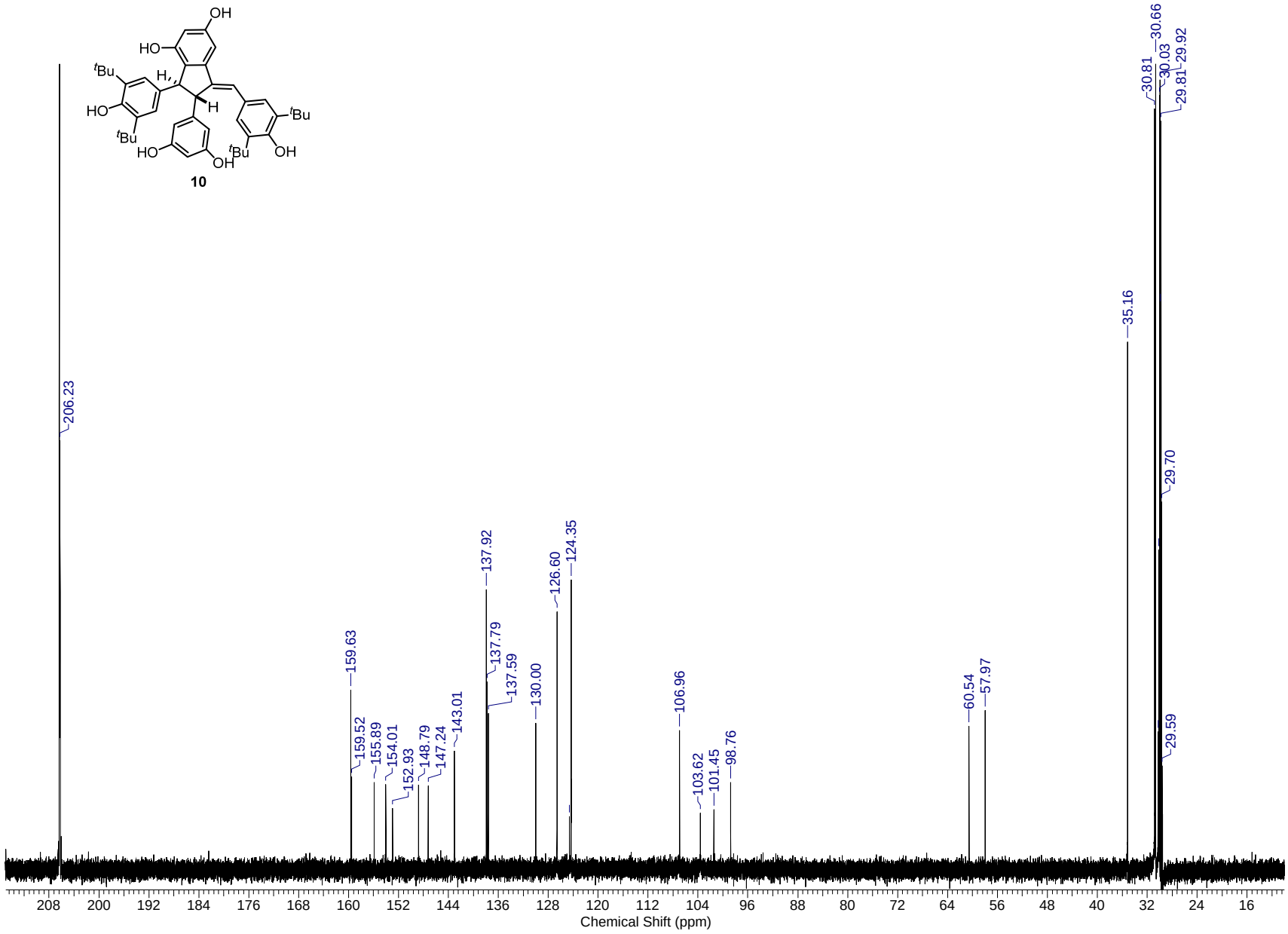

OMe
MeO
tBu
H
HO
H
tBu
tBu
MeO
tBu
OMe
OH
9 OMe
1.01 1.98 1.96 0.95 1.98 1.96
0.94 0.94
0.92 0.92
3.01 6.86 3.00
17.88 18.05
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
Chemical Shift (ppm)

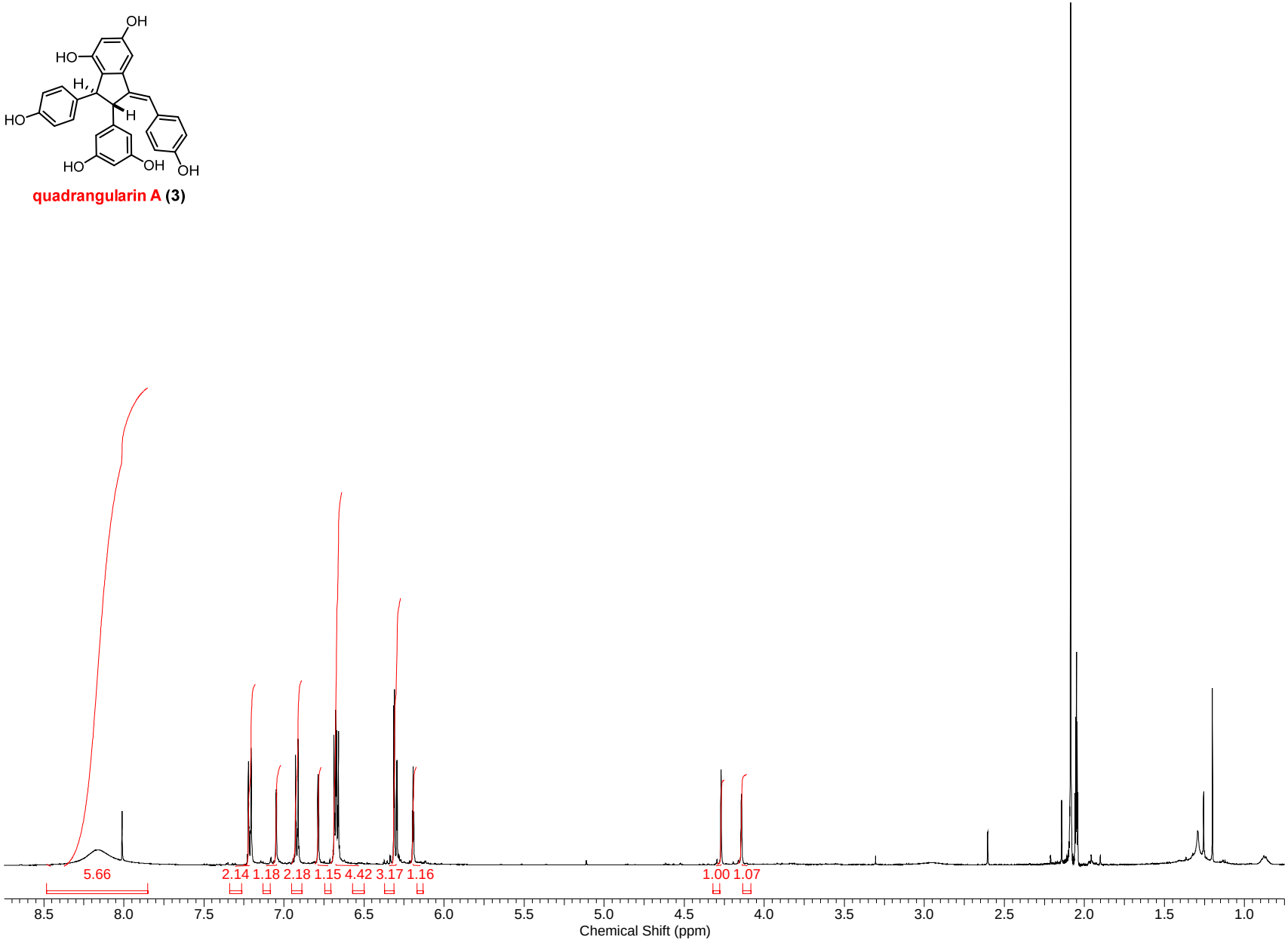

OMe
MeO
tBu
H
HO
H
tBu
tBu
MeO
OMe
tBu
OH
9 OMe
30.51
30.37
34.50
34.45
77.41
77.23
77.05
160.99
161.31
160.78
157.47
153.11
152.03
147.87
145.12
142.45
136.28
135.75
135.30
128.92
126.28
125.90
124.05
123.86
106.04
104.87
98.94
98.25
95.48
58.78
55.48
55.43
55.30
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

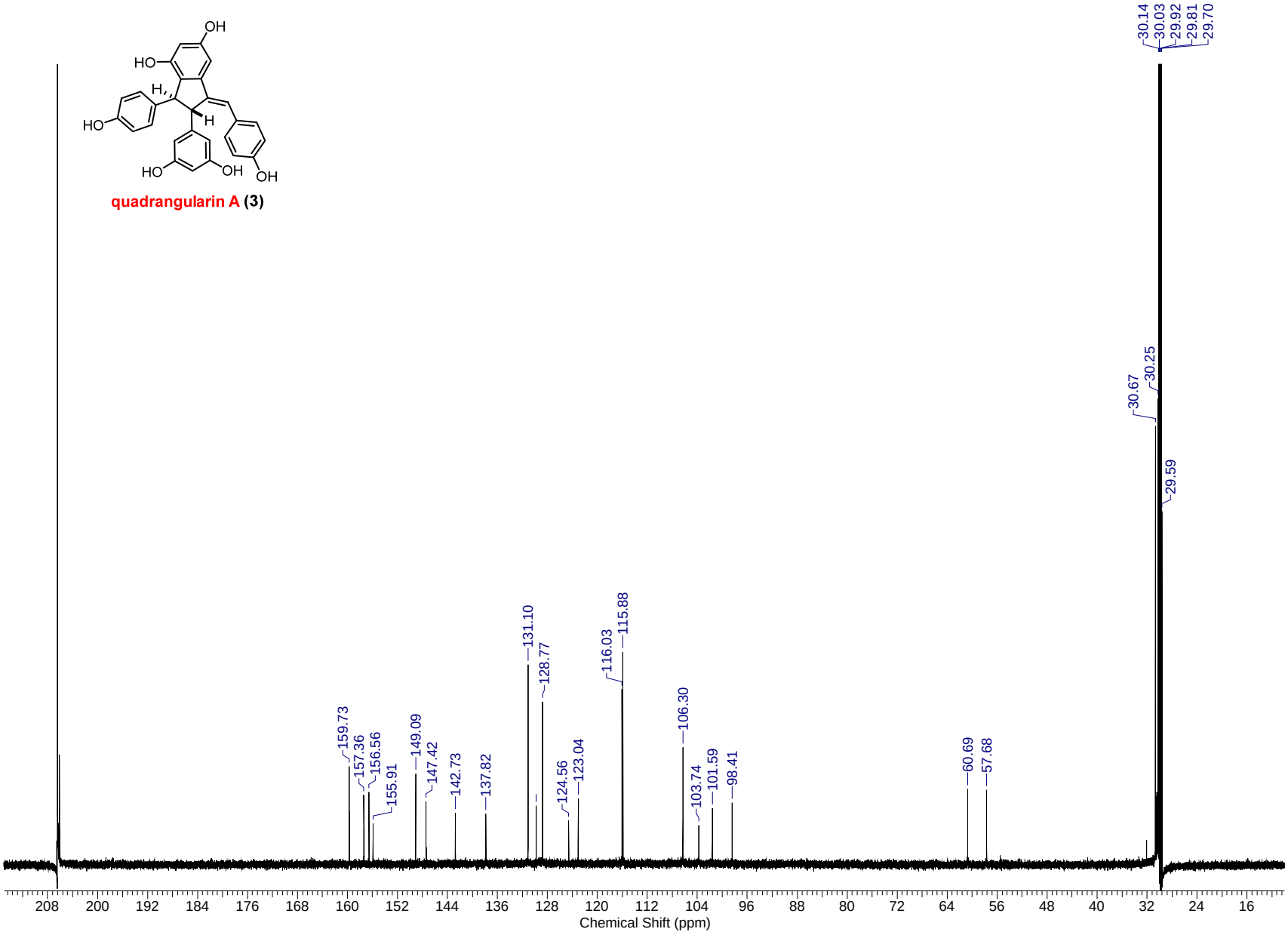

OBn
BnO
tBu
H
HO
H
tBu
tBu
BnO
tBu
OH
OBn
9
15.01 2.56 0.97 5.00 0.93 1.73 1.76
2.48 1.03 3.21 2.91
1.00 0.96
29.20
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
Chemical Shift (ppm)


OBn
BnO
tBu
H
HO
H
tBu
tBu
BnO
tBu
OH
OBn
9
77.41
77.23
77.05
30.50
127.81
30.38
34.44
128.80
160.49
160.24
156.37
153.15
152.14
148.07
145.30
142.45
137.31
137.20
135.73
135.48
128.93
127.15
125.98
124.11
107.13
100.82
100.10
96.95
70.17
70.63
69.62
58.90
57.62
30.58
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


OH
HO
tBu
H
H
HO
tBu
tBu
HO
OH
tBu
OH
10
3.25
1.57
1.98
1.05
2.00
1.00
1.92
1.02
0.98
0.98
1.00
1.01
1.06
17.00
17.75
8.0
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
Chemical Shift (ppm)


OH
HO
tBu
H
HO
H
tBu
tBu
HO
OH
tBu
OH
10
206.23
159.63
159.52
155.89
154.01
152.93
148.79
147.24
143.01
137.92
137.79
137.59
130.00
126.60
124.35
106.96
103.62
101.45
98.76
60.54
57.97
35.16
30.81
30.66
30.03
29.92
29.81
29.70
29.59
208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16
Chemical Shift (ppm)


OH
HO
H
H
HO
HO
OH
OH
quadrangularin A (3)
5.66
2.14
1.18
2.18
1.15
4.42
3.17
1.16
1.00
1.07
8.5
8.0
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
Chemical Shift (ppm)


OH
HO
H
HO
H
HO
OH
OH
quadrangularin A (3)
30.14
30.03
29.92
29.81
29.70
30.67
30.25
29.59
159.73
157.36
156.56
155.91
149.09
147.42
142.73
137.82
131.10
128.77
124.56
123.04
116.03
115.88
106.30
103.74
101.59
98.41
60.69
57.68
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)