# Phosphoric Acid-Catalyzed Asymmetric Synthesis of SPINOL Derivatives

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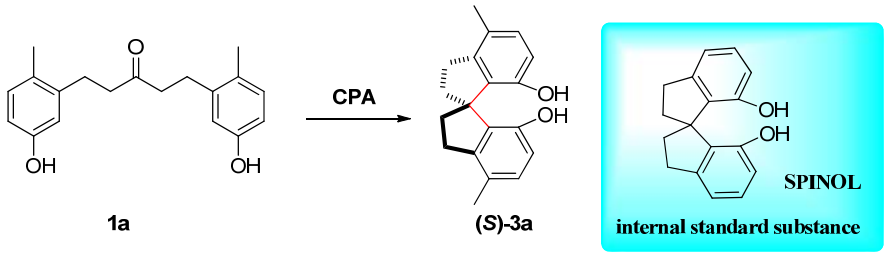
# General Information

Chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. Chiral phosphoric acid (**CPA**) was purchased from Daicel Chiral Technologies (China). Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 GF254 plates. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 0.040-0.063 mm). Visualization on TLC was achieved by use of UV light (254 nm) or iodine. $^{1}H$ and $^{13}C$ NMR spectra were recorded on Bruker DPX 400 spectrometer using $CDCl_3$, acetone-$d_6$ or DMSO-$d_6$ with tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in ppm and coupling constants are given in Hz. Data for 1H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet; d = doublet; t = triplet; q = quarter; p = pentet; m = multiplet; br = broad), coupling constant (Hz), integration. Data for 13C NMR are reported in terms of chemical shift (δ, ppm). Mass spectrometric data were obtained using Bruker Apex IV RTMS. The enantiomeric excess values were determined by chiral HPLC with an Agilent 1200 LC instrument and a Daicel CHIRALCEL AD-3 column or a Daicel CHIRALPAK OD-3 column. High resolution mass spectroscopy (HRMS) analyses were performed at a Bruker Daltonics. Inc mass instrument (ESI).

# Optimization of the Reaction Conditions

## Introduction of the yield based on RPLC

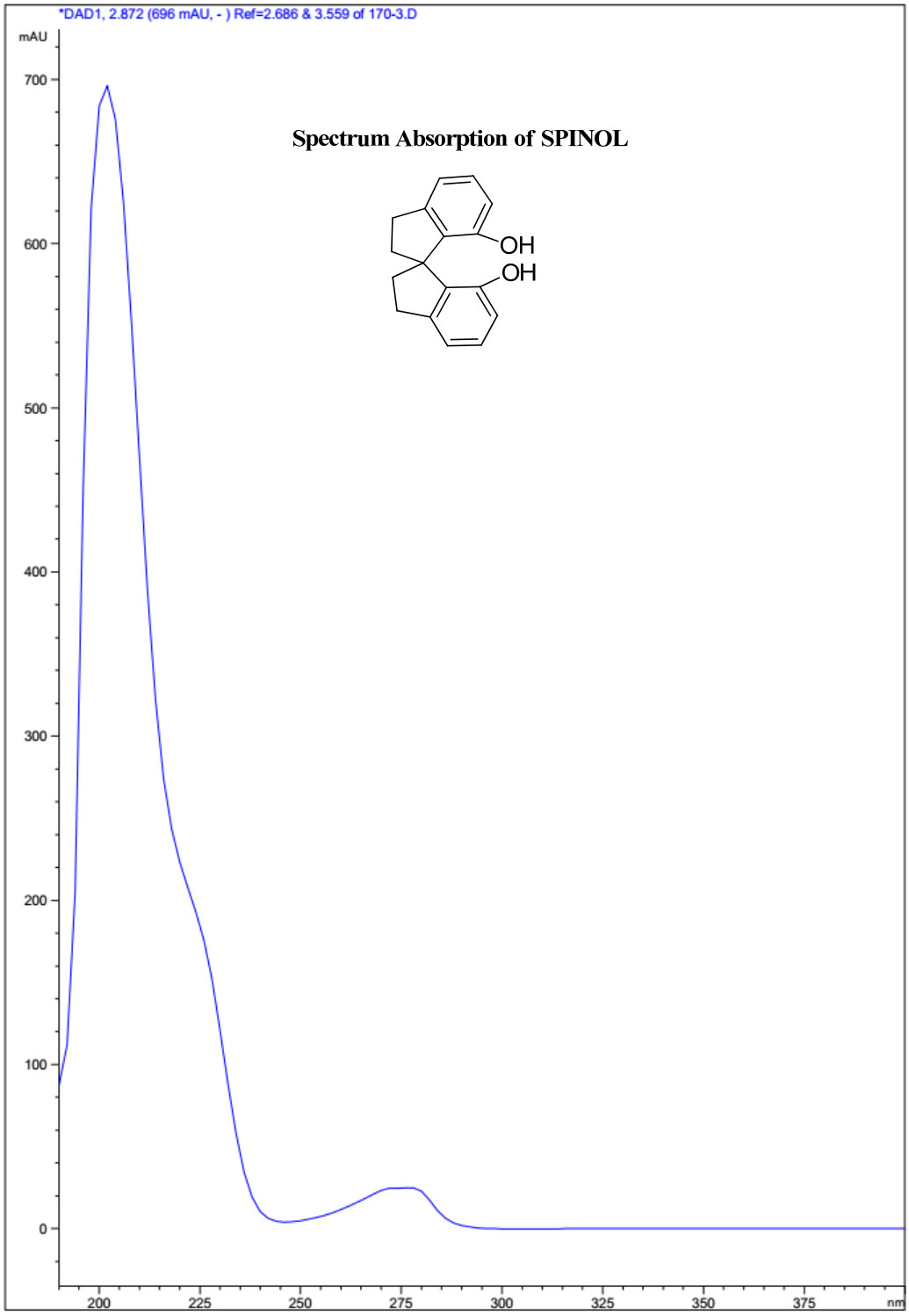



**1a** **(*S*)-3a**

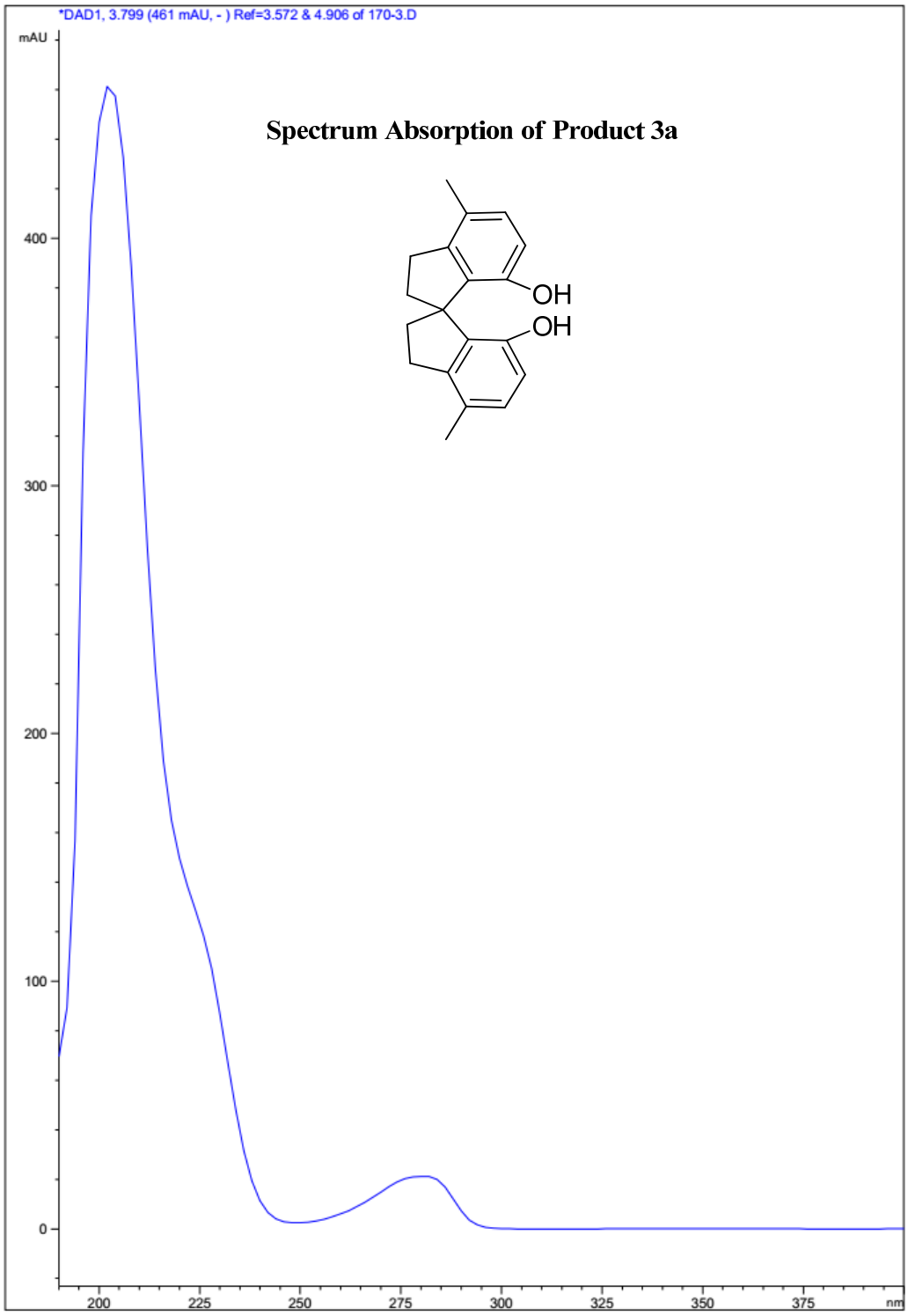
2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol(**SPINOL**) was used as the internal standard substance since its spectrum absorption is extremely similar to product **3a**. When the reaction was completed, a same equivalent internal standard substance (**SPINOL**) to the substrate was added. After evaporation of the solvent, the resulting residue was dissolved in methanol and analyzed by RPLC.

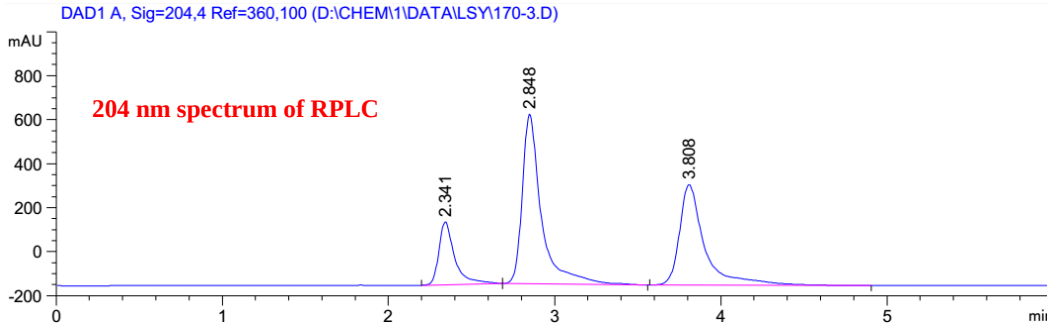
Unless otherwise noted, all yields of the reactions for screening conditions were calculated by RPLC. MeOH/$H_2O$ = 80/20, 1.0 mL/min, λ = 204 nm or 276 nm, $t_R$ (substrate **1a**) = 2.3 min, $t_R$ (**SPINOL**) = 2.8 min, $t_R$ (product **3a**) = 3.8 min. On the calibration curve, X axis represents peak area ratio between product **3a** and internal standard substance **SPINOL**, Y axis represents corresponding molar ratio. According to the below calculation formula: (**204nm**) *yield* = y = 0.9551x + 0.0005 or (**276nm**) *yield* = y = 0.7382x + 0.0016

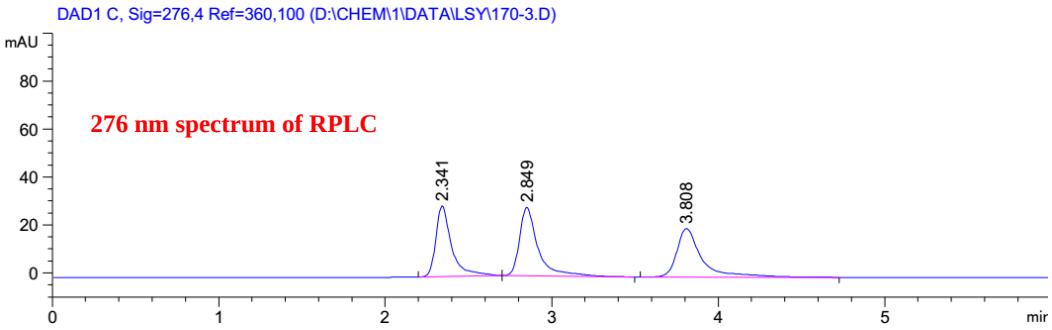
DAD1, 2.872 (696 mAU, - ) Ref=2.686 & 3.559 of 170-3.D

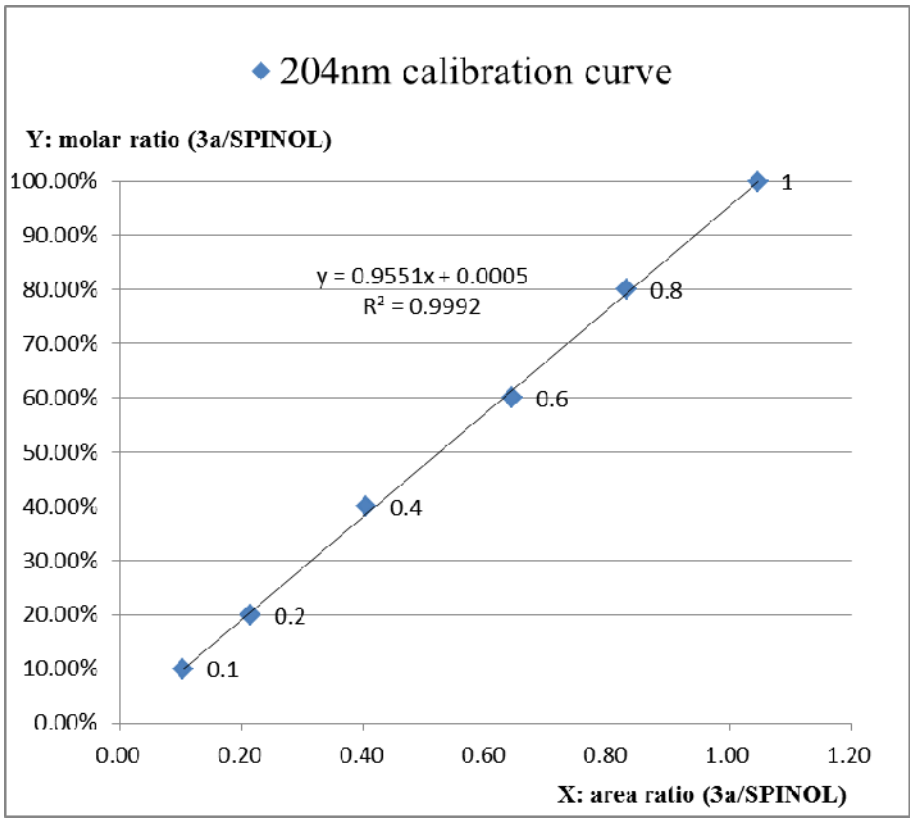


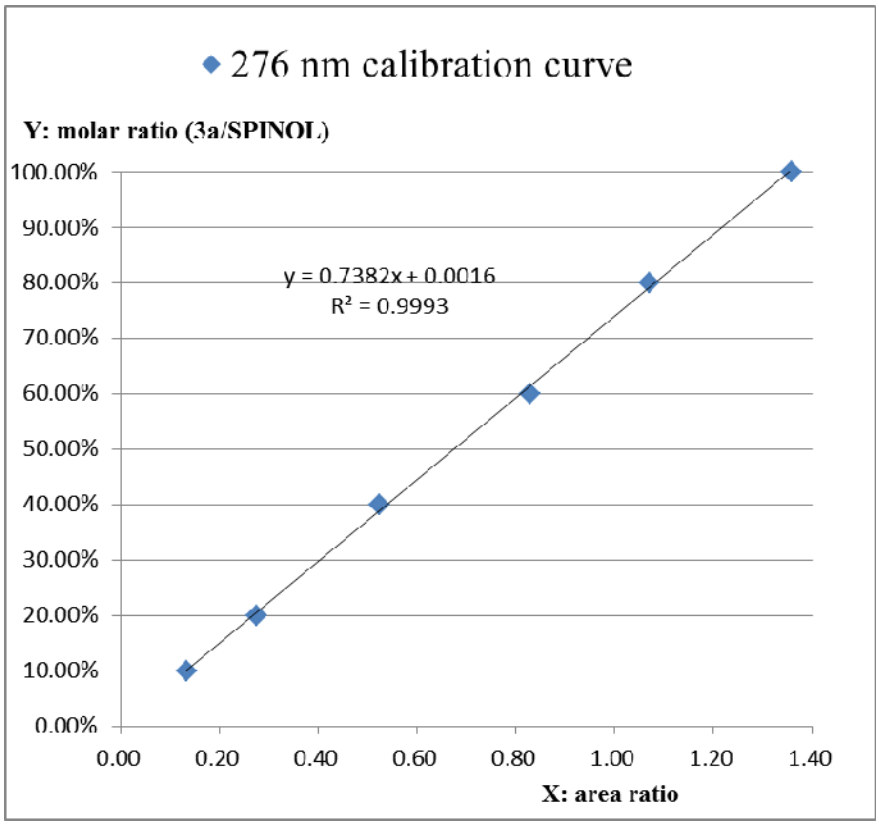
DAD1, 3.799 (461 mAU, - ) Ref=3.572 & 4.906 of 170-3.D



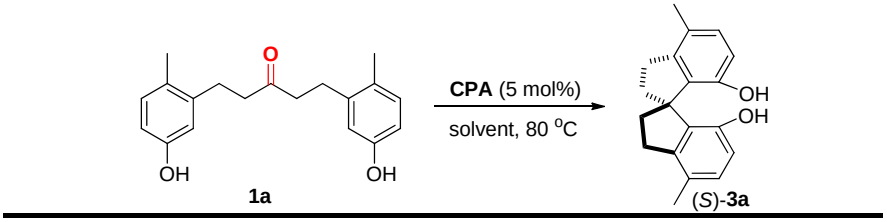

DAD1 A, Sig=204,4 Ref=360,100 (D:\CHEM\1\DATA\LSY\170-3.D)
mAU
204 nm spectrum of RPLC
2.341
2.848
3.808
min

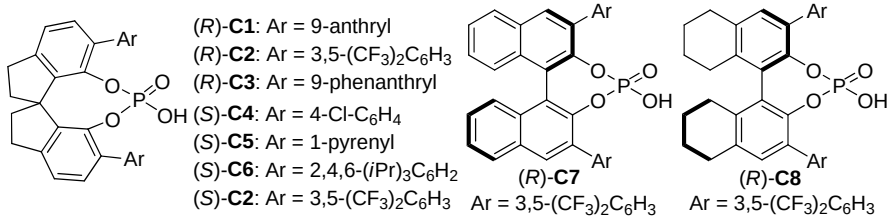

DAD1 C, Sig=276,4 Ref=360,100 (D:\CHEM\1\DATA\LSY\170-3.D)
mAU
276 nm spectrum of RPLC
2.341
2.849
3.808
min


204nm calibration curve
Y: molar ratio (3a/SPINOL)
y = 0.9551x + 0.0005
R² = 0.9992
0.1
0.2
0.4
0.6
0.8
1
X: area ratio (3a/SPINOL)




## Table S1: Screening of the reaction conditions for ketone transformation[a]



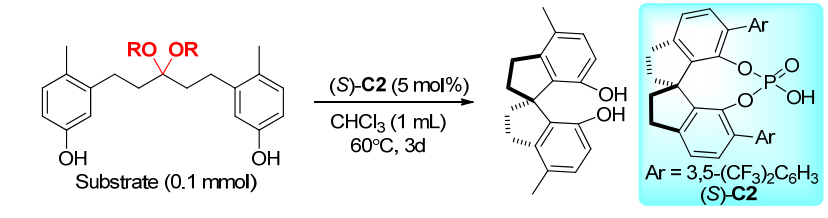



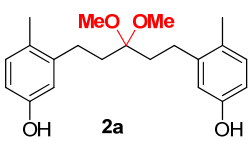

| entry | CPA | solvent | T (°C) | yield (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|
| 1 | (*R*)-**C1** | $CHCl_3$ | 80 | 17 | 41 |
| 2 | (*R*)-**C2** | $CHCl_3$ | 80 | 60 | 92 |
| 3 | (*R*)-**C3** | $CHCl_3$ | 80 | 23 | 40 |
| 4 | (*S*)-**C4** | $CHCl_3$ | 80 | 40 | -11 |
| 5 | (*S*)-**C5** | $CHCl_3$ | 80 | 43 | 0 |
| 6 | (*S*)-**C6** | $CHCl_3$ | 80 | NR | - |

| | | | | | |
|---|---|---|---|---|---|
| 7 | (*R*)-**C7** | $CHCl_3$ | 80 | trace | -36 |
| 8 | (*R*)-**C8** | $CHCl_3$ | 80 | 48 | -34 |
| 9 | (*R*)-**C2** | DCE | 80 | 54 | 83 |
| 10 | (*R*)-**C2** | toluene | 80 | 22 | 89 |
| 11 | (*R*)-**C2** | CCl4 | 80 | 30 | 66 |
| 12 | (*R*)-**C2** | *o*-xylene | 80 | 21 | 89 |
| 13 | (*R*)-**C2** | *m*-xylene | 80 | 18 | 86 |
| 14 | (*R*)-**C2** | trifluorotoluene | 80 | 34 | 83 |
| 15 | (*R*)-**C2** | $CH_3CN$ | 80 | trace | |
| 16 | (*R*)-**C2** | EA | 80 | ND | |
| 17 | (*R*)-**C2** | THF | 80 | ND | |
| 18 | (*R*)-**C2** | EtOH | 80 | ND | |
| 19[g] | (*R*)-**C2** | CPME | 120 | ND | |
| 20[d] | (*R*)-**C2** | $CHCl_3$ | 80 | 54 | 93 |
| 21[e] | (*R*)-**C2** | $CHCl_3$ | 80 | 38 | 93 |
| 22[d] | (*R*)-**C2** | $CHCl_3$ | 40 | NR | |
| 23[d] | (*R*)-**C2** | $CHCl_3$ | 60 | 13 | 94 |
| 24[d] | (*R*)-**C2** | $CHCl_3$ | 100 | 68 | 92 |
| 25[d] | (*R*)-**C2** | $CHCl_3$ | 120 | 90 | 90 |
| 26[d, f] | (*R*)-**C2** | $CHCl_3$ | 120 | 60 | 90 |
| 27[d, g] | (*R*)-**C2** | $CHCl_3$ | 120 | 98 | 90 |
| 28[d, g] | (*S*)-**C2** | $CHCl_3$ | 120 | 98 | -90 |

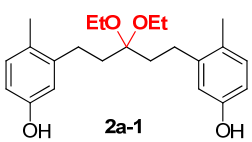
[a] Unless otherwise stated, all reactions were carried out with **1a** (0.1 mmol) and **CPA** (5 mol%) in 1 mL of solvent at 80℃ for three days under Ar. [b] Yield based on RPLC. [c] Determined by chiral HPLC analysis. [d] 3 mL of $CHCl_3$ was used. [e] 5 mL of $CHCl_3$ was used. [f] 1 mol% of **CPA** was used. [g] 10 mol% of **CPA** was used and reaction time was two days.

## Scheme S1: Evaluation of different ketals

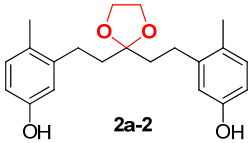



Isolated yield: 90%
ee: 93%

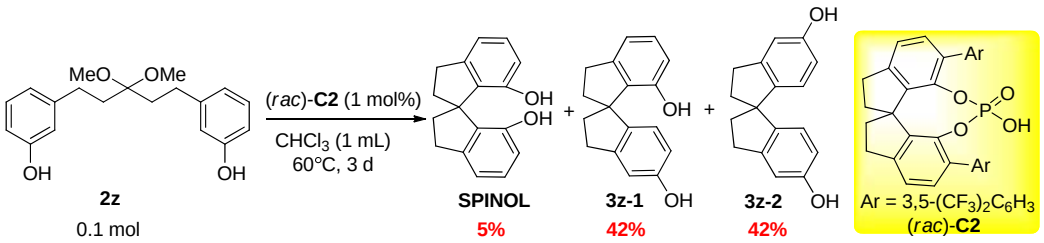



Isolated yield: 60%
ee: 93%

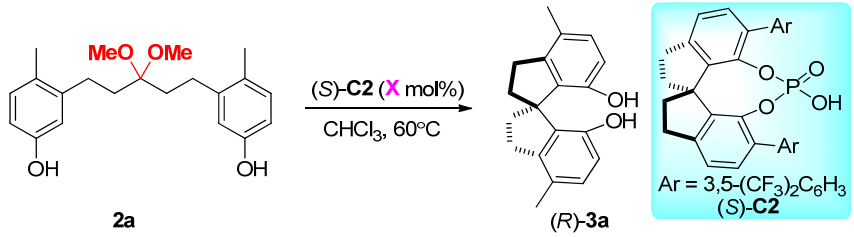



Isolated yield: trace

## Scheme S2: Investigation of the ketal without para substituent at the phenol




## Table S2: Screening of the reaction conditions for ketal transformation[a]

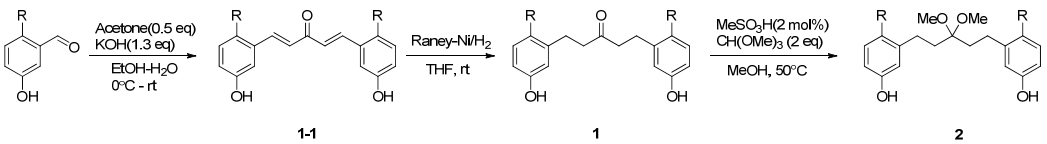



| entry | (*S*)-**C2** (X mol%) | $CHCl_3$ (mL) | time | yield (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|
| 1 | 5 | 0.5 | 15 h | 88 | 90.9 |
| 2 | 5 | 1 | 15 h | 92 | 92.9 |
| 3 | 5 | 2 | 15 h | 91 | 93.5 |
| 4 | 5 | 3 | 15 h | 92 | 94.4 |
| 5 | 5 | 6 | 15 h | 91 | 94.6 |
| 6 | 3 | 3 | 20 h | 88 | 94.5 |
| 7 | 2 | 3 | 30 h | 89 | 94.5 |
| 8 | 1 | 3 | 2 d | 90 | 94.3 |
| 9[d] | 1 | 3 | 3 d | NR | |
| 10[e] | 1 | 3 | 7 d | 73 | 96 |
| 11[f] | 1 | 3 | 2 d | 92 | 91.3 |

[a] Unless otherwise stated, all reactions were carried out with **1a** (0.1 mmol) and (*S*)-**C2** in $CHCl_3$ at 60℃ under Ar. [b] Isolated yield based on **2a**. [c] Determined by chiral HPLC analysis. [d] The reaction proceeded at room temperature. [e] The reaction was proceeded at 40℃. [f] The reaction was proceeded at 100℃.

# Procedure for the Synthesis of Substrates

## (a) Synthesis of the symmetrical substrates



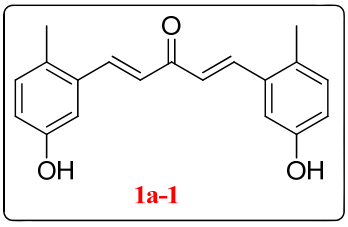
*Symmetrical 1,5-bis(3-hydroxyphenyl)pentan-3-ones **1** were prepared according to the patent:* (Wang, Y.-R.; Chin, C.-L.; Chen, W.-C.; Cheng, K.-L.; Liu, S.-H. Liquid crystal compounds, and liquid crystal displays and photochromic materials comprising the liquid crystal compounds, US 2013/0135574 A1)

5-Hydroxybenzaldehyde (10.0 mmol) was slowly added to a solution of KOH (13.0 mmol) in EtOH (4 mL) under an ice-bath to form a yellow sludge. After the mixture was cooled to 0-5℃, acetone (5.0 mmol) was added drop-wise through a funnel during 30 minutes. Then the reaction was warmed to room temperature and stirred for another 4 hours. After the reaction completion (monitored by TLC), 20 mL of ice water was added to the dark red solution. Subsequently, 0.8 mL of acetic acid was added slowly to neutralize the mixture. After vigorously stirring for 10 minutes, the resulting sludge was stood at ice bath for another 20 minutes. The bright yellow precipitate was filtrated and washed with plenty of water and small amount of EtOH/water (1/2) solution. The generated intermediate **1-1** was used directly in the next step after drying.

100 mg of Raney- Ni washed with THF for three times was added to a solution of intermediate **1-1** (6.0 mmol) in THF (15 mL). The resulting mixture was stirred at room temperature under $H_2$ atmosphere. When TLC indicated the reaction was completed, the solution was carefully poured into another bottle and the Raney-Ni attracted onto magnetic stirring bar was left. Then the obtained crude material was purified by silica gel column chromatography to afford the pure product **1**.

*3,3'-(3,3-Dimethoxypentane-1,5-diyl)diphenols **2** were prepared according to the reference*[1,2].

To a solution of ketone **1** (2.0 mmol) in anhydrous methanol (1 mL) were added methanesulfonic acid (0.04 mmol) and trimethyl orthoformate (4.0 mmol). The mixture was stirred at 50℃ for about 4 hours until the ketone was consumed completely. The mixture was diluted with 60 mL of EA and washed with 5 mL of ammonium hydroxide (25% solution) and 30 mL of saturated brine. The organic phase was dried over $Na_2SO_4$ and concentrated to obtain the pure ketal **2**, which was used directly without further purification.



**1a-1**

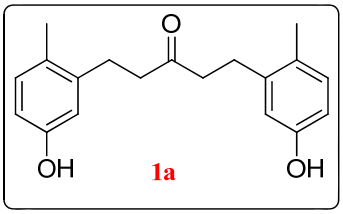
**(1*E*,4*E*)-1,5-bis(5-hydroxy-2-methylphenyl)penta-1,4-dien-3-one (1a-1)**

Yellow solid (12.5 g, 85% yield, 100.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.42 (s, 2H), 8.00 (d, *J* = 15.8 Hz, 2H), 7.25 (d, *J* = 2.6 Hz, 2H), 7.13 (d, *J* = 15.8 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 6.85 (dd, *J* = 2.6, 8.2 Hz, 2H), 2.30 (s, 6H);

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 188.26, 155.83, 140.21, 134.59, 131.75, 128.96, 126.58, 117.67, 112.65, 17.95.

**HRMS (ESI)** calcd for [M+H] $C_{19}H_{19}O_3$, m/z: 295.1329, found: 295.1322.



1a

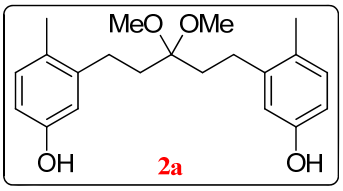
**1,5-bis(5-hydroxy-2-methylphenyl)pentan-3-one (1a)**

White solid (11.0 g, 92% yield, 40.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 7.93 (s, 2H), 6.94 (d, *J* = 7.8 Hz, 2H), 6.59-6.57 (m, 4H), 2.76-2.71 (m, 8H), 2.10 (s, 6H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.35, 155.53, 140.58, 130.88, 126.19, 115.53, 112.82, 42.49, 27.05, 17.52.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_3$, m/z: 297.1496, found: 297.1494.



2a

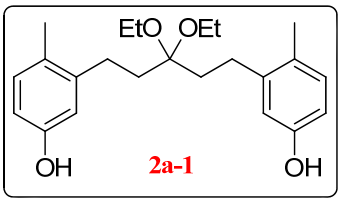
**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-methylphenol) (2a)**

White solid (3.4 g, 99% yield, 10.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 7.95 (s, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 2.6 Hz, 2H), 6.60 (dd, *J* = 8.0, 2.6 Hz, 2H), 3.24 (s, 6H), 2.61-2.56 (m, 4H), 2.27 (s, 6H), 1.92-1.87 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 155.68, 141.28, 130.95, 126.02, 115.63, 112.79, 102.53, 47.06, 33.23, 27.73, 17.76.

**HRMS (ESI)** calcd for [M-H] $C_{21}H_{27}O_4$, m/z: 343.1915, found: 343.1914.



2a-1

**3,3'-(3,3-diethoxypentane-1,5-diyl)bis(4-methylphenol) (2a-1)**

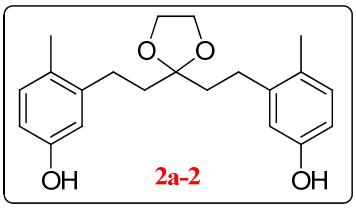
In the general procedure, methanol and trimethyl orthoformate were replaced with ethanol and triethyl orthoformate respectively for the synthesis of **2a-1**.

White solid (370 mg, 99% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 7.95 (s, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 2.4 Hz, 2H), 6.60 (dd, *J* = 8.0, 2.4 Hz, 2H), 3.54 (q, *J* = 6.8 Hz, 4H), 2.63-2.58 (m, 4H), 2.27 (s, 6H), 1.94-1.89 (m, 4H), 1.20 (t, *J* = 6.8 Hz, 6H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 155.67, 141.39, 130.93, 126.03, 115.61, 112.75, 102.35, 54.95, 34.18, 27.78, 17.76, 14.92.

**HRMS (ESI)** calcd for [M-H] $C_{23}H_{31}O_4$, m/z: 371.2228, found: 371.2223.




2a-2

**3,3'-((1,3-dioxolane-2,2-diyl)bis(ethane-2,1-diyl))bis(4-methylphenol) (2a-2)**

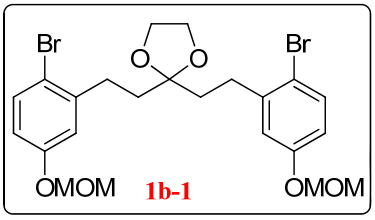
In the general procedure, the solvent methanol was replaced with ethylene glycol for the synthesis of **2a-2**.

White solid (340 mg, 99% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 7.91 (s, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 2.8 Hz, 2H), 6.58 (dd, *J* = 8.4, 2.8 Hz, 2H), 4.05 (s, 4H), 2.66-2.62 (m, 4H), 2.22 (s, 6H), 1.91-1.86 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 155.57, 141.54, 130.85, 126.09, 115.64, 112.63, 110.60, 64.91, 37.71, 27.67, 17.48.

**HRMS (ESI)** calcd for [M-H] $C_{21}H_{25}O_4$, m/z: 341.1758, found: 341.1757.




1b-1

**2,2-bis(2-bromo-5-(methoxymethoxy)phenethyl)-1,3-dioxolane (1b-1)**

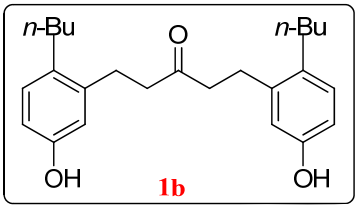
Under argon atmosphere, to a solution of ketone **1g** (10.0 mmol) in ethylene glycol (5 mL) was added methanesulfonic acid (0.2 mmol) and trimethyl orthoformate (20.0 mmol). The mixture was stirred at 50℃ for about 4 hours until the ketone was consumed completely. The mixture was diluted with 200 mL of EA and washed with 5 mL of ammonium hydroxide (25% solution) and 50 mL of saturated brine. The organic phase was dried over $Na_2SO_4$ and concentrated to obtain the ketal intermediate 4.7 g, which was used directly without further purification.

Under argon atmosphere, NaH (40.0 mmol) was added to the solution of above ketal intermediate (4.7 g) in 120 mL of anhydrous THF at 0℃ and the mixture was stirred for 30 minutes at same temperature. Then chloromethyl methyl ether (30.0 mmol) was added drop-wise to the reaction over 20 minutes. The reaction was warmed to room temperature and continued stirring another four hours. After completion of the reaction, the mixture was filtrated through celite and the solvent was evaporated. The resulting residue was purified by flash chromatography eluted with PE/EA = 10/1 to afford product **1b-1** as a colorless oil (5.5 g, 98% yield).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.38 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 2.8 Hz, 2H), 6.75 (dd, *J* = 8.8, 2.8 Hz, 2H), 5.12 (s, 4H), 4.03 (s, 4H), 3.44 (s, 6H), 2.83-2.79 (m, 4H), 2.00-1.96 (m, 4H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 156.72, 142.54, 133.38, 118.24, 116.21, 115.60, 110.63, 94.48, 65.18, 56.04, 37.12, 31.05.

**HRMS (ESI)** calcd for [M+H] $C_{23}H_{29}O_6Br_2$, m/z: 561.0305, found: 561.0300.




1b

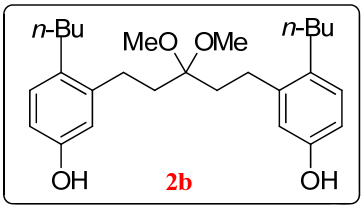
**1,5-bis(2-butyl-5-hydroxyphenyl)pentan-3-one (1b)**

Under argon atmosphere, **1b-1** (5.0 mmol), $Pd(Ph_3P)_4$ (0.02 mmol), butylboronic acid (15.0 mmol), $K_2CO_3$ (20.0 mmol), 1,4-dioxane (20 mL) and $H_2O$ (10 mL) were added in sequence to a 50 mL Schlenk tube with a magnetic stirring bar. Then the reaction proceeded at 100℃ for 12 hours. After completion of the reaction, evaporated the solvent and the residue was quickly purified by a short silica column eluted with PE/EA = 8/1 to afford the intermediate. Subsequently, 1 mL of 10 wt% aqueous HCl was added to the solution of above purified intermediate in methanol (10 mL). The reaction was stirred at 50℃ for 4 hours. After completion of the reaction, the mixture was diluted with 50 mL of EA and washed with saturated $NaHCO_3$. The separated organic phase was concentrated and purified by flash chromatography eluted with PE/EA = 3/1 to afford the pure **1b** as a white solid (1.5 g, 80% yield).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.07 (s, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.67-6.62 (m, 4H), 2.83-2.80 (m, 4H), 2.75-2.71 (m, 4H), 2.53 (t, *J* = 8.0 Hz, 4H), 1.54-1.48 (m, 4H), 1.40-1.35 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 6H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.57, 155.38, 140.10, 131.14, 130.18, 115.62, 113.06, 43.51, 33.76, 31.39, 26.37, 22.48, 13.57.

**HRMS (ESI)** calcd for [M-H] $C_{25}H_{33}O_3$, m/z: 381.2435, found: 381.2437.




2b

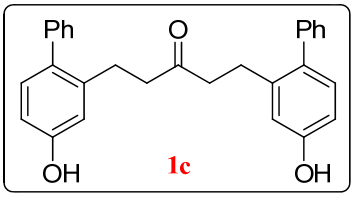
**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-butylphenol) (2b)**

Colorless thick oil (420 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 6.96 (d, *J* = 9.0 Hz, 2H), 6.64-6.62 (m, 4H), 6.51 (s, 2H), 3.22 (s, 6H), 2.53-2.49 (m, 8H), 1.94-1.89 (m, 4H), 1.52-1.48 (m, 4H), 1.36-1.31 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 153.61, 140.76, 132.70, 130.41, 116.01, 113.28, 103.59, 48.00, 33.74, 31.70, 27.15, 22.84, 14.08, an aliphatic carbon overlaps with others'.

**HRMS (ESI)** calcd for [M-H] $C_{27}H_{39}O_4$, m/z: 427.2854, found: 427.2851.




1c

**1,5-bis(4-hydroxy-[1,1'-biphenyl]-2-yl)pentan-3-one (1c)**

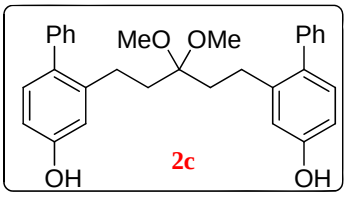
The synthetic procedure is same as the substrate **1b**.

White solid (1.8 g, 85% yield, 5.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.40 (s, 2H), 7.39-7.36 (m, 4H), 7.31-7.30 (m, 2H), 7.26-7.24 (m, 4H),7.01 (d, *J* = 8.0 Hz, 2H), 6.79-6.75 (m, 4H), 2.72 (t, *J* = 8.0 Hz, 4H), 2.46 (t, *J* = 8.0 Hz, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.50, 156.71, 141.75, 139.92, 133.40, 131.25, 129.41, 128.23, 126.59, 115.90, 113.28, 43.27, 27.19.

**HRMS (ESI)** calcd for [M-H] $C_{29}H_{25}O_3$, m/z: 421.1809, found: 421.1815.




**2c**

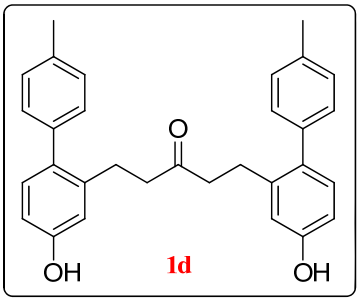
**2,2''-(3,3-dimethoxypentane-1,5-diyl)bis([1,1'-biphenyl]-4-ol) (2c)**

White powder (460 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, DMSO-$d_6$)** δ 9.39 (s, 2H), 7.39-7.35 (m, 4H), 7.28-7.21 (m, 6H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.66 (dd, *J* = 8.0, 2.0 Hz, 2H), 6.60 (d, *J* = 2.0 Hz, 2H), 2.60 (s, 6H), 2.21-2.17 (m, 4H), 1.39-1.35 (m, 4H).

**$^{13}$C NMR (100 MHz, DMSO-$d_6$)** δ 157.20, 141.91, 140.62, 132.76, 131.27, 129.70, 128.65, 126.92, 116.39, 113.42, 102.25, 46.99, 34.08, 27.57.

**HRMS (ESI)** calcd for [M-H] $C_{31}H_{31}O_4$, m/z: 467.2228, found: 467.2231.




**1d**

**1,5-bis(4-hydroxy-4'-methyl-[1,1'-biphenyl]-2-yl)pentan-3-one (1d)**

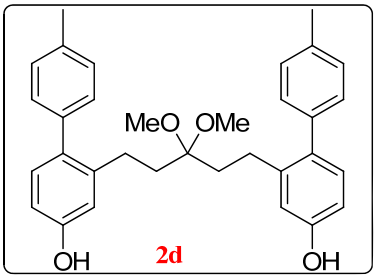
The synthetic procedure is same as the substrate **1b**.

White solid (1.8 g, 80% yield, 5.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.36 (s, 2H), 7.18 (d, *J* = 8.0 Hz, 4H), 7.13 (d, *J* = 8.0 Hz, 4H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.79-6.75 (m, 4H), 2.73 (t, *J* = 8.0 Hz, 4H), 2.47 (t, *J* = 8.0 Hz, 4H), 2.34 (s, 6H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.13, 156.59, 139.98, 138.82, 135.88, 133.27, 131.18, 129.24, 128.82, 115.75, 113.10, 43.30, 27.16, 20.40.

**HRMS (ESI)** calcd for [M-H] $C_{31}H_{29}O_3$, m/z: 449.2122, found: 449.2125.



2d

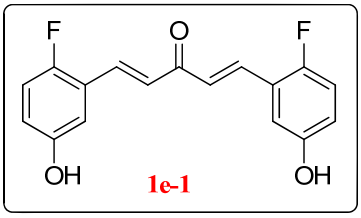
**2,2''-(3,3-dimethoxypentane-1,5-diyl)bis(4'-methyl-[1,1'-biphenyl]-4-ol) (2d)**

White powder (490 mg, 99% yield, 1.0 mmol material was used).

**$^{1}$H NMR (400 MHz, Acetone-$d_6$)** δ 8.28 (s, 2H), 7.20-7.13 (m, 8H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.71 (dd, *J* = 8.2, 2.6 Hz, 2H), 6.68 (d, *J* = 2.6 Hz, 2H), 2.73 (s, 6H), 2.28-2.23 (m, 10H), 1.51-1.47 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 156.64, 140.87, 139.00, 135.97, 133.24, 130.90, 129.35, 128.81, 116.01, 112.76, 102.12, 46.42, 34.04, 27.33, 20.18.

**HRMS (ESI)** calcd for [M-H] $C_{33}H_{35}O_4$, m/z: 495.2541, found: 495.2540.



1e-1

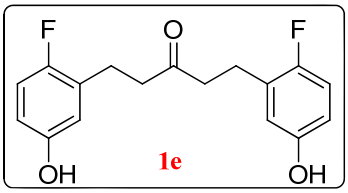
**(1*E*,4*E*)-1,5-bis(2-fluoro-5-hydroxyphenyl)penta-1,4-dien-3-one (1e-1)**

Yellow solid (1.43 g, 95% yield, 10.0 mmol material was used).

**$^{1}$H NMR (400 MHz, Acetone-$d_6$)** δ 8.57 (s, 2H), 7.83 (d, *J* = 16.0 Hz, 2H), 7.31-7.26 (m, 4H), 7.11-7.06 (m, 2H), 6.98-6.94 (m, 2H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 187.89, 155.41 (d, *J* = 242.0 Hz), 153.86, 134.93 (d, *J* = 3.0 Hz), 127.60 (d, *J* = 5.0 Hz), 123.12 (d, *J* = 13.0 Hz), 118. 91 (d, *J* = 8.0 Hz), 116.59 (d, *J* = 23.0 Hz), 114.17.

**HRMS (ESI)** calcd for [M+H] $C_{17}H_{13}O_3F_2$, m/z: 303.0827, found: 303.0821.



1e

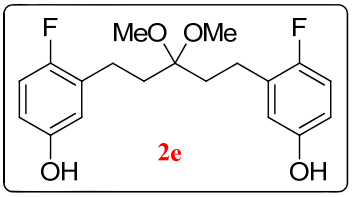
**1,5-bis(2-fluoro-5-hydroxyphenyl)pentan-3-one (1e)**

White solid (570 mg, 93% yield, 2.0 mmol material was used).

**$^{1}$H NMR (400 MHz, Acetone-$d_6$)** δ 8.16 (s, 2H), 6.88 (dd, *J* = 9.6, 8.8 Hz, 2H), 6.74 (dd, *J* = 6.4, 3.0 Hz, 2H), 6.68-6.64 (m, 2H), 2.84-2.75 (m, 8H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 207.43, 154.70 (d, *J* = 232.4 Hz), 153.41 (d, *J* = 1.6 Hz), 128.71 (d, *J* = 17.4 Hz), 116.73 (d, *J* = 4.5 Hz), 115.35 (d, *J* = 23.8 Hz), 113.80 (d, *J* = 8.0 Hz), 42.03, 22.88 (d, *J* = 2.4 Hz).

**HRMS (ESI)** calcd for [M-H] $C_{17}H_{15}O_3F_2$, m/z: 305.0995, found: 305.0995.



**2e**

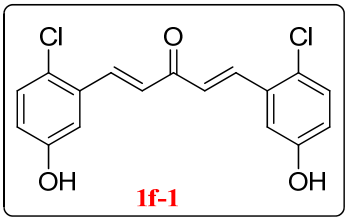
**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-fluorophenol) (2e)**

White powder (345 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.21 (s, 2H), 6.94-6.89 (m, 2H), 6.78 (dd, *J* = 6.2, 3.0 Hz, 2H), 6.70-6.66 (m, 2H), 3.21 (s, 6H), 2.63-2.58 (m, 4H), 1.95-1.91 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 154.75 (d, *J* = 232.2 Hz), 153.53 (d, *J* = 1.8 Hz), 129.35 (d, *J* = 7.6 Hz), 116.75 (d, *J* = 4.7 Hz), 115.43 (d, *J* = 24.0 Hz), 113.74 (d, *J* = 8.1 Hz), 102.23, 46.93, 32.93, 23.62 (d, *J* = 1.9 Hz).

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_4F_2$, m/z: 351.1413, found: 351.1412.



**1f-1**

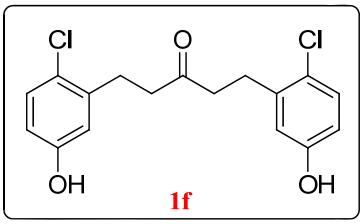
**(1*E*,4*E*)-1,5-bis(2-chloro-5-hydroxyphenyl)penta-1,4-dien-3-one (1f-1)**

Yellow solid (1.54 g, 92% yield, 10.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.90 (s, 2H), 8.07 (d, *J* = 15.6 Hz, 2H), 7.39 (d, *J* = 2.8 Hz, 2H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 15.6 Hz, 2H), 6.97 (dd, *J* = 8.7, 2.8 Hz, 2H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 187.72, 156.66, 138.33, 133.57, 130.84, 127.92, 125.11, 119.19, 114.06.

**HRMS (ESI)** calcd for [M+H] $C_{17}H_{13}O_3Cl_2$, m/z: 335.0236, found: 335.0228.



**1f**

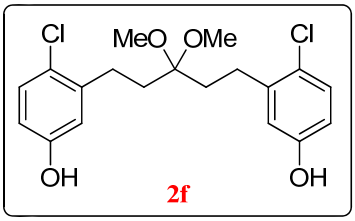
**1,5-bis(2-chloro-5-hydroxyphenyl)pentan-3-one (1f)**

White solid (405 mg, 60% yield, 2.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.45 (s, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 2.8 Hz, 2H), 6.71 (dd, *J* = 8.8, 2.8 Hz, 2H), 2.92-2.88 (m, 4H), 2.81-2.77 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 207.37, 156.39, 139.78, 129.93, 123.35, 117.31, 114.77, 41.72, 27.51.

**HRMS (ESI)** calcd for [M-H] $C_{17}H_{15}O_3Cl_2$, m/z: 337.0404, found: 337.0406.




2f

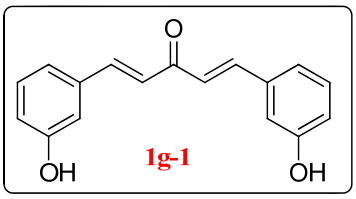
**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-chlorophenol) (2f)**

White powder (375 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.49 (s, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 2.8 Hz, 2H), 6.73 (dd, *J* = 8.8, 2.8 Hz, 2H), 3.25 (s, 6H), 2.75-2.71 (m, 4H), 1.96-1.92 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 156.56, 140.48, 130.03, 123.33, 117.26, 114.78, 102.27, 47.12, 32.72, 28.29.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_4Cl_2$, m/z: 383.0822, found: 383.0824.




1g-1

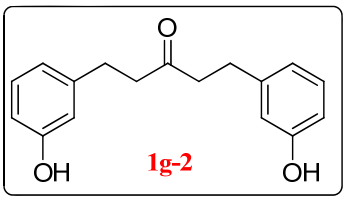
**(1*E*,4*E*)-1,5-bis(3-hydroxyphenyl)penta-1,4-dien-3-one (1g-1)**

Yellow solid (12.0 g, 90% yield, 100.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.56 (s, 2H), 7.73 (d, *J* = 16.0 Hz, 2H), 7.31-7.22 (m, 8H), 6.96-6.93 (m, 2H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 188.19, 157.83, 142.71, 136.57, 129.98, 125.65, 119.97, 117.56, 114.75.

**HRMS (ESI)** calcd for [M+H] $C_{17}H_{15}O_3$, m/z: 267.1016, found: 267.1009.




1g-2

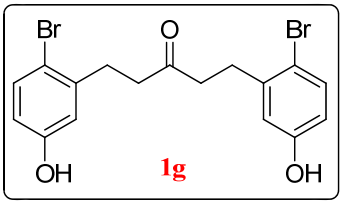
**1,5-bis(3-hydroxyphenyl)pentan-3-one (1g-2)**

Yellow solid (9.9 g, 92% yield, 40.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.15 (s, 2H), 7.09 (t, *J* = 7.8 Hz, 2H), 6.70-6.64 (m, 6H), 2.81-2.72 (m, 8H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 207.93, 157.17, 142.85, 129.08, 119.17, 115.01, 112.63, 43.50, 29.22.

**HRMS (ESI)** calcd for [M-H] $C_{17}H_{17}O_3$, m/z: 269.1183, found: 269.1183.



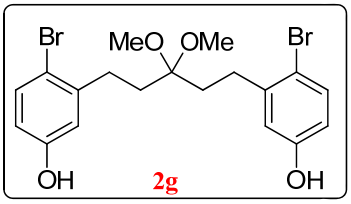

**1,5-bis(2-bromo-5-hydroxyphenyl)pentan-3-one (1g)**

8.1g (30.0 mmol) of **1g-2** was dissolved in 100 mL of $CH_3CN$. When the solution was cooled to -20℃, $Br_2$ (3.0 mmol) was added. After stirring for 10 minutes, NBS (60.0 mmol) was added to the reaction during 30 minutes. The resulting mixture was stirred at same temperature for another 30 minutes. When LCMS indicated the reaction was completed, 20 mL of saturated $Na_2SO_3$ was added at -20℃ to quench the reaction. Next, the mixture was evaporated to remove $CH_3CN$ and diluted with 200 mL of EA, subsequently washed with saturated brine for three times. The organic phase was concentrated and purified by flash chromatography eluted with PE/EA = 3/1 to afford 12.8 g of product **1g**, which was further recrystallized with DCE to obtain 11.5 g of pure **1g** as a white solid (90% yield).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.52 (s, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 2.8 Hz, 2H), 6.65 (dd, *J* = 8.8, 2.8 Hz, 2H), 2.92-2.89 (m, 4H), 2.81-2.77 (m, 4H).

**$^{13}$C NMR** (100 MHz, Acetone) δ 207.28, 157.06, 141.48, 133.23, 117.50, 115.29, 112.75, 41.91, 30.05.

**HRMS (ESI)** calcd for [M-H] $C_{17}H_{15}O_3Br_2$, m/z: 426.9373, found: 426.9370.



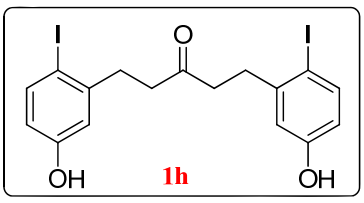

**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-bromophenol) (2g)**

White powder (465 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.52 (s, 2H), 7.37 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 3.2 Hz, 2H), 6.68 (dd, *J* = 8.8, 3.2 Hz, 2H), 3.27 (s, 6H), 2.77-2.73 (m, 4H), 1.97-1.92 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 157.21, 142.27, 133.30, 117.39, 115.29, 112.75, 102.20, 47.21, 32.92, 30.76.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_4Br_2$, m/z: 472.9792, found: 472.9790.




**1,5-bis(5-hydroxy-2-iodophenyl)pentan-3-one (1h)**

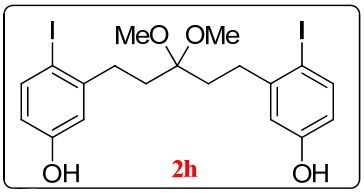
To a vial were added **1g-2** (5.0 mmol), PTSA (2.0 mmol) and DCM (50 mL), the mixture was

cooled to 0℃, then NIS (10.5 mmol) was added to the reaction over 20 minutes. The resulting mixture was stirred at same temperature for 2 hours. When LCMS indicated the reaction was completed, 10 mL of saturated $Na_2SO_3$ was added to quench the reaction. Then the solution was diluted with 200 mL of EA, subsequently washed with saturated brine. The organic phase was concentrated and purified by flash chromatography eluted with PE/EA = 4/1 to afford 1.95 g of pure **1g** as a white solid (75% yield).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.56 (s, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 2.8 Hz, 2H), 6.53 (dd, *J* = 8.8, 2.8 Hz, 2H), 2.91-2.87 (m, 4H), 2.80-2.76 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 207.06, 158.05, 144.82, 139.91, 117.00, 115.83, 86.52, 42.25, 34.58.

**HRMS (ESI)** calcd for [M-H] $C_{17}H_{15}O_3I_2$, m/z: 520.9116, found: 520.9121.




2h

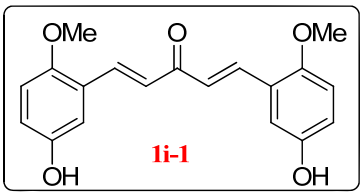
**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-iodophenol) (2h)**

White powder (556 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.56 (s, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 2.8 Hz, 2H), 6.55 (dd, *J* = 8.4, 2.8 Hz, 2H), 3.28 (s, 6H), 2.78-2.74 (m, 4H), 1.95-1.91 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 158.22, 145.83, 139.96, 116.85, 115.83, 102.08, 86.39, 47.40, 35.15, 33.24.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_4I_2$, m/z: 566.9535, found: 566.9538.




1i-1

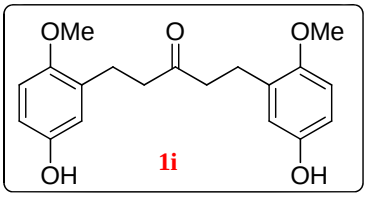
**(1*E*,4*E*)-1,5-bis(5-hydroxy-2-methoxyphenyl)penta-1,4-dien-3-one (1i-1)**

Yellow solid (1.1 g, 70% yield, 10.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.03 (d, *J* = 16.0 Hz, 2H), 7.23-7.19 (m, 4H), 6.96-6.94 (m, 4H), 3.87 (s, 6H), the two active protons of hydroxyl groups mix with the peak of solvent.

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 188.55, 152.41, 151.30, 137.36, 126.04, 124.28, 118.67, 114.08, 112.91, 55.68.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{17}O_5$, m/z: 325.1082, found: 325.1079.




1i

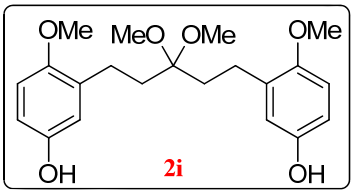
**1,5-bis(5-hydroxy-2-methoxyphenyl)pentan-3-one (1i)**

White powder (528 mg, 88% yield, 2.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 7.74 (s, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.68-6.62 (m, 4H), 3.75 (s, 6H), 2.79-2.75 (m, 4H), 2.70-2.66 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.70, 150.96, 150.89, 130.53, 116.92, 112.94, 111.58, 55.29, 42.28, 24.62.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_5$, m/z: 329.1395, found: 329.1395.




**3,3'-(3,3-dimethoxypentane-1,5-diyl)bis(4-methoxyphenol) (2i)**

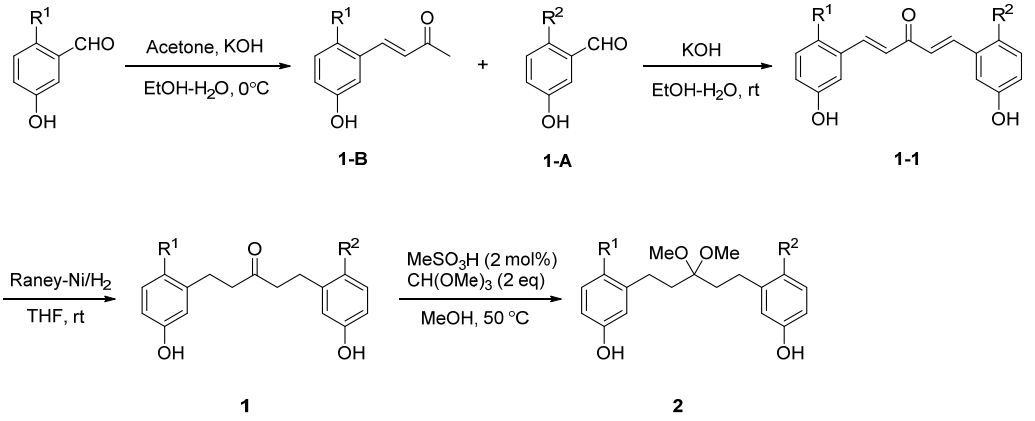
White powder (364 mg, 97% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 7.75 (s, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 2.8 Hz, 2H), 6.65 (dd, *J* = 8.8, 2.8 Hz, 2H), 3.80 (s, 6H), 3.22 (s, 6H), 2.60-2.56 (m, 4H), 1.90-1.85 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 151.10, 150.94, 131.49, 116.87, 112.76, 111.64, 102.67, 55.32, 46.79, 32.82, 24.99.

**HRMS (ESI)** calcd for [M-H] $C_{21}H_{27}O_6$, m/z: 375.1813, found: 375.1812.

**(b) Synthesis of the non-symmetrical substrates**



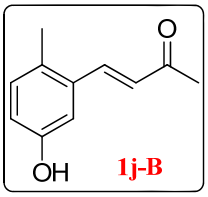

*Non-symmetrical (1E,4E)-1,5-bis(3-hydroxyphenyl)penta-1,4-dien-3-ones* ***1-1*** *were prepared according to the reference*[3]

To a solution of 5-hydroxybenzaldehyde (10.0 mmol) and acetone (3.7 mL, 50.0 mmol) in 20 mL EtOH at 0℃, 10% aqueous KOH (15 mL) was added over 15 minutes. The resulting mixture was stirred at the same temperature for 2 hours. After the reaction completion (monitored by TLC), the reaction mixture was diluted with water and acidified with 3 N HCl. Then the obtained crude material was purified by silica gel column chromatography to afford the pure intermediates **1-2**.

To a solution of the intermediate **1-2** (8.0 mmol) and another 5-hydroxybenzaldehyde (8.0 mmol) in EtOH, 10% aqueous KOH (12 mL) was added over 15 minutes at room temperature. The resulting mixture was stirred at the same temperature for 2 hours. After the reaction completion

(monitored by TLC), the reaction mixture was diluted with water and acidified with 3 N HCl. Then the obtained crude was collected by filtration. The yellow solid **1-3** was directly used in the next step.

The next two steps are same as the above-mentioned procedures for synthesis of symmetrical substrates.



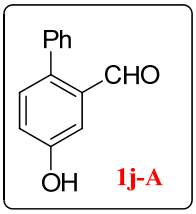

**(*E*)-4-(5-hydroxy-2-methylphenyl)but-3-en-2-one (1j-B)**

Yellow solid (1.5 g, 86% yield, 10.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.29 (s, 1H), 7.80 (d, *J* = 16.0 Hz, 1H), 7.14 (d, *J* = 2.4 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.84 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 2.35 (s, 6H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 197.20, 155.76, 140.22, 134.30, 131.76, 128.73, 127.92, 117.55, 112.47, 26.77, 17.85.

**HRMS (ESI)** calcd for [M-H] $C_{11}H_{11}O_2$, m/z: 175.0765, found: 175.0756.



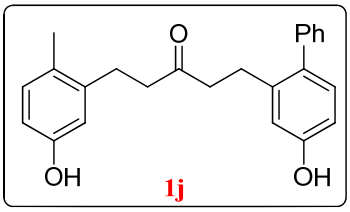

**4-hydroxy-[1,1'-biphenyl]-2-carbaldehyde (1j-A)**

Under argon atmosphere, 2-bromo-5-hydroxybenzaldehyde (10.0 mmol), $Pd(Ph_3P)_4$ (0.02 mmol), butylboronic acid (15.0 mmol), $K_2CO_3$ (20.0 mmol), 1,4-dioxane (20 mL) and $H_2O$ (10 mL) were added in sequence to a 50 mL Schlenk tube with a magnetic stirring bar. Then the reaction proceeded at 100℃ for 12 hours. After completion of the reaction, evaporated the solvent and the residue was purified by flash chromatography eluted with PE/EA = 4/1 to afford the pure **1j-A** as a white solid (1.2 g, 61% yield).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 9.91 (s, 1H), 8.89 (s, 1H), 7.52-7.37 (m, 7H), 7.22 (dd, *J* = 8.4, 2.8 Hz, 1H).

**$^{13}$C NMR (101 MHz, Acetone)** δ 205.34, 191.08, 157.09, 137.61, 134.80, 132.31, 130.14, 128.35, 127.54, 121.18, 112.52.

**HRMS (ESI)** calcd for [M-H] $C_{13}H_9O_2$, m/z: 197.0608, found: 197.0604.




1j

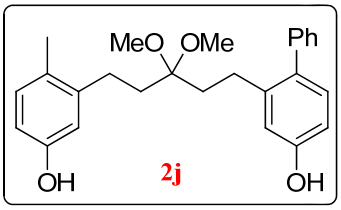
**1-(5-hydroxy-2-methylphenyl)-5-(4-hydroxy-[1,1'-biphenyl]-2-yl)pentan-3-one (1j)**

Colorless thick oil (576 mg, 80% yield for two steps, 2.0 mmol material **1j-B** was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.25 (s, 2H), 7.42 - 7.38 (m, 2H), 7.33-7.28 (m, 3H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.76 (dd, *J* = 8.0, 2.8 Hz, 1H), 6.17- 6.57 (m, 2H), 2.82-2.78 (m, 2H), 2.70-2.67 (m, 2H), 2.63-2.55 (m, 4H), 2.14 (s, 3H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.09, 156.78, 155.53, 141.82, 140.52, 139.97, 133.28, 131.09, 130.86, 129.36, 128.14, 126.49, 126.13, 115.77, 115.51, 113.08, 112.81, 43.34, 42.33, 27.16, 26.98, 17.55.

**HRMS (ESI)** calcd for [M-H] $C_{24}H_{23}O_3$, m/z: 359.1653, found: 359.1653.




2j

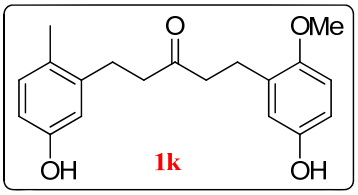
**2-(5-(5-hydroxy-2-methylphenyl)-3,3-dimethoxypentyl)-[1,1'-biphenyl]-4-ol (2j)**

Colorless thick oil (372 mg, 98% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.33-7.29 (m, 2H), 7.24-7.22 (m, 3H), 7.02 (d, *J* = 8.1 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.72-6.68 (m, 2H), 6.58 (dd, *J* = 8.1, 2.6 Hz, 1H), 6.47 (d, *J* = 2.6 Hz, 1H), 6.06 (s, 2H), 2.99 (s, 6H), 2.49-2.45 (m, 2H), 2.25-2.20 (m, 2H), 2.11 (s, 3H), 1.74-1.68 (m, 4H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 155.13, 153.74, 141.55, 141.45, 140.84, 134.73, 131.56, 131.34, 129.65, 128.34, 127.99, 126.88, 116.17, 115.95, 113.21, 113.07, 103.39, 47.77, 34.18, 32.45, 28.12, 27.43, 18.55.

**HRMS (ESI)** calcd for [M-H] $C_{26}H_{29}O_4$, m/z: 405.2071, found: 405.2073.




1k

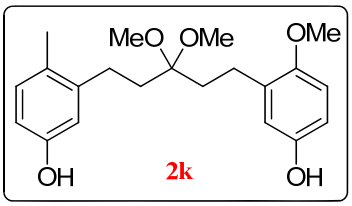
**1-(5-hydroxy-2-methoxyphenyl)-5-(5-hydroxy-2-methylphenyl)pentan-3-one (1k)**

Colorless thick oil (502 mg, 80% yield for two steps, 2.0 mmol material **1j-B** was used).

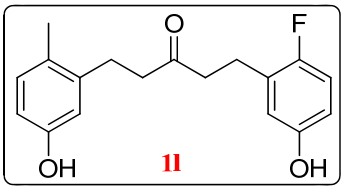
**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.10 (s, 2H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.75-6.67 (m, 4H), 6.63 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.72 (s, 3H), 2.83-2.66 (m, 8H), 2.18 (s, 3H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 209.43, 155.42, 150.92, 150.84, 140.60, 131.01, 130.40,

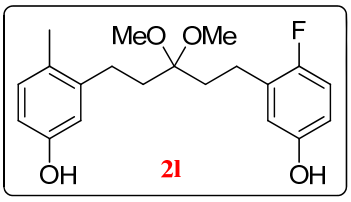
126.39, 117.01, 115.58, 113.14, 112.94, 111.64, 55.38, 42.44, 42.40, 27.08, 24.70, 17.70.
**HRMS (ESI)** calcd for [M-H] $C_{19}H_{21}O_4$, m/z: 313.1445, found: 313.1445.




**3-(5-(5-hydroxy-2-methoxyphenyl)-3,3-dimethoxypentyl)-4-methylphenol (2k)**
Colorless thick oil (352 mg, 98% yield, 1.0 mmol material was used).
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 6.92 (d, *J* = 8.0 Hz, 1H), 6.62-6.60 (m, 7H, containing 2OH), 3.68 (s, 3H), 3.21 (s, 6H), 2.49-2.47 (m, 4H), 2.20 (s, 3H), 1.89-1.87 (m, 4H).
**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 153.97, 151.59, 149.30, 141.47, 131.30, 131.27, 127.72, 117.45, 115.86, 113.42, 113.09, 111.64, 103.77, 55.82, 47.90, 32.75, 32.56, 27.57, 25.39, 18.47.
**HRMS (ESI)** calcd for [M-H] $C_{21}H_{27}O_5$, m/z: 359.1864, found: 359.1866.

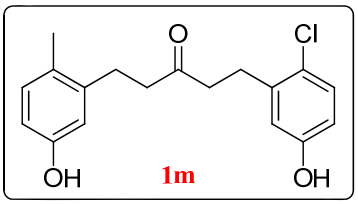



**1-(2-fluoro-5-hydroxyphenyl)-5-(5-hydroxy-2-methylphenyl)pentan-3-one (1l)**
White solid (512 mg, 85% yield for two steps, 2.0 mmol material **1j-B** was used).
**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.07 (s, 2H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.88 (t, *J* = 5.2 Hz, 1H), 6.74 (dd, *J* = 6.4, 3.2 Hz, 1H), 6.69-6.65 (m, 2H), 6.59 (dd, *J* = 8.0, 2.8 Hz, 1H), 2.85-2.75 (m, 6H), 2.74-2.70 (m, 2H), 2.18 (s, 3H).
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.07, 155.49, 154.73 (d, *J* = 232.0 Hz), 153.38 (d, *J* = 2.0 Hz), 140.55, 130.92, 128.75 (d, *J* = 17.0 Hz), 126.26, 116.78 (d, *J* = 4.0 Hz), 115.53, 115.28, 113.85 (d, *J* = 8.0 Hz), 112.86, 42.39, 42.15, 26.99, 22.98 (d, *J* = 2.0 Hz), 17.55.
**HRMS (ESI)** calcd for [M-H] $C_{18}H_{18}O_3F$, m/z: 301.1245, found: 301.1245.

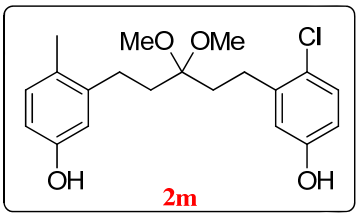



**4-fluoro-3-(5-(5-hydroxy-2-methylphenyl)-3,3-dimethoxypentyl)phenol (2l)**
White powder (337 mg, 97% yield, 1.0 mmol material was used).
**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.08 (s, 2H), 6.96-6.88 (m, 2H), 6.77 (dd, *J* = 6.3, 3.0 Hz, 1H), 6.71 (d, *J* = 2.6 Hz, 1H), 6.70-6.66 (m, 1H), 6.60 (dd, *J* = 8.1, 2.6 Hz, 1H), 3.21 (s, 6H), 2.63-2.54 (m, 4H), 2.25 (s, 3H), 1.96-1.85 (m, 4H).
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 155.64, 154.77 (d, *J* = 232.1 Hz), 153.52 (d, *J* = 1.9 Hz),

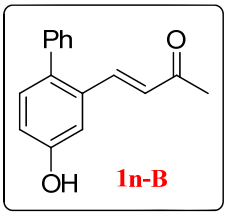
141.27, 130.96, 129.36 (d, *J* = 17.7 Hz), 126.09, 116.77 (d, *J* = 4.5 Hz), 115.66, 115.48 (d, *J* = 24.0 Hz), 113.78 (d, *J* = 8.0 Hz), 112.81, 102.40, 47.02, 33.12, 27.58, 23.83, 23.81, 17.72.
**HRMS (ESI)** calcd for [M-H] $C_{20}H_{24}O_4F$, m/z: 347.1664, found: 347.1665.




**1-(2-chloro-5-hydroxyphenyl)-5-(5-hydroxy-2-methylphenyl)pentan-3-one (1m)**
White solid (380 mg, 60% yield for two steps, 2.0 mmol material **1j-B** was used).
**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.22 (s, 2H), 7.18 (d, *J* = 8.8 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.71 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H), 6.58 (dd, *J* = 8.0, 2.4 Hz, 1H), 2.92-2.88 (m, 2H), 2.80-2.73(m, 6H), 2.19 (s, 3H).
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 207.84, 156.39, 155.55, 140.53, 139.85, 130.88, 129.94, 126.17, 123.35, 117.31, 115.53, 114.76, 112.83, 42.41, 41.78, 27.53, 27.02, 17.5.
**HRMS (ESI)** calcd for [M-H] $C_{18}H_{18}O_3Cl$, m/z: 317.0950, found: 317.0950.



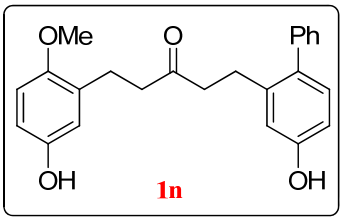

**4-chloro-3-(5-(5-hydroxy-2-methylphenyl)-3,3-dimethoxypentyl)phenol (2m)**
White powder (360 mg, 99% yield, 1.0 mmol material was used).
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.15 (d, *J* = 9.0 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.65-6.60 (m, 4H), 5.66 (s, 2H), 3.25 (s, 6H), 2.63-2.54 (m, 4H), 2.24 (s, 3H), 1.96-1.89 (m, 4H).
**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 154.65, 153.72, 141.42, 140.38, 131.46, 130.46, 128.10, 125.08, 117.38, 115.90, 114.92, 113.18, 103.53, 48.07, 32.78, 32.58, 28.62, 27.68, 18.60.
**HRMS (ESI)** calcd for [M-H] $C_{20}H_{24}O_4Cl$, m/z: 363.1369, found: 363.1372.




**(*E*)-4-(4-hydroxy-[1,1'-biphenyl]-2-yl)but-3-en-2-one (1n-B)**
Yellow solid (975 mg, 82% yield, 5.0 mmol material was used).
**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.64 (s, 1H), 7.53 (d, *J* = 16.2 Hz, 1H), 7.48-7.30 (m, 6H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.03 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.68 (d, *J* = 16.2 Hz, 1H), 2.19 (s, 3H).
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 196.94, 157.01, 141.68, 140.05, 134.92, 133.60, 131.68,

129.89, 128.24, 127.84, 127.08, 117.69, 112.71, 26.68.

**HRMS (ESI)** calcd for [M-H] $C_{16}H_{13}O_2$, m/z: 237.0921, found: 237.0921.



**1n**

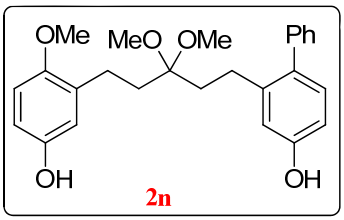
**1-(2-chloro-5-hydroxyphenyl)-5-(5-hydroxy-2-methoxyphenyl)pentan-3-one (1n)**

Colorless thick oil (564 mg, 75% yield for two steps, 2.0 mmol material **1n-B** was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.12 (s, 2H), 7.41-7.38 (m, 2H), 7.33-7.28 (m, 3H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.79-6.73 (m, 2H), 6.67-6.64 (m, 2H), 3.71 (s, 3H), 2.82-2.78 (m, 2H), 2.73-2.69 (m, 2H), 2.60-2.55 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.49, 156.75, 150.91, 150.84, 141.82, 140.02, 133.33, 131.13, 130.38, 129.38, 128.17, 126.51, 116.94, 115.80, 113.11, 113.00, 111.53, 55.29, 43.30, 42.22, 27.17, 24.58.

**HRMS (ESI)** calcd for [M-H] $C_{24}H_{23}O_4$, m/z: 375.1602, found: 375.1602.



**2n**

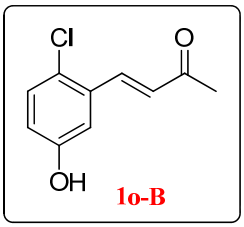
**2-(5-(5-hydroxy-2-methoxyphenyl)-3,3-dimethoxypentyl)-[1,1'-biphenyl]-4-ol (2n)**

Colorless thick oil (420 mg, 97% yield, 1.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.16 (s, 2H), 7.44-7.29 (m, 5H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.89 (d, *J* = 2.4 Hz, 1H), 6.78-6.76 (m, 2H), 6.66-6.61 (m, 2H), 3.76 (s, 3H), 2.99 (s, 6H), 2.61-2.57 (m, 2H), 2.31-2.27 (m, 2H), 1.72-1.67 (m, 4H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 156.88, 150.99, 150.83, 142.02, 141.07, 133.41, 131.20, 131.02, 129.50, 128.18, 126.50, 116.99, 116.00, 112.89, 112.74, 111.42, 102.38, 55.2, 46.62, 34.23, 32.60, 27.74, 24.78.

**HRMS (ESI)** calcd for [M-H] $C_{26}H_{29}O_5$, m/z: 421.2020, found: 421.2023.



**1o-B**

**(E)-4-(2-chloro-5-hydroxyphenyl)but-3-en-2-one (1o-B)**

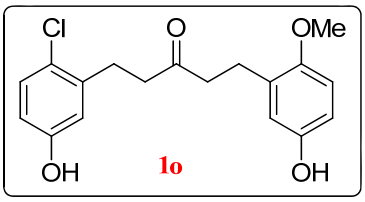
Yellow solid (880 mg, 90% yield, 5.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.76 (s, 1H), 7.84 (d, *J* = 16.4 Hz, 1H), 7.31 (d, *J* = 8.8 Hz,

1H), 7.27 (d, *J* = 2.8 Hz, 1H), 6.94 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.74 (d, *J* = 16.4 Hz, 1H), 2.37 (s, 3H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 196.97, 156.58, 137.85, 133.35, 130.79, 129.27, 124.86, 119.04, 113.89, 27.00.

**HRMS (ESI)** calcd for [M-H] $C_{10}H_8O_2Cl$, m/z: 195.0218, found: 195.0218.




**1o**

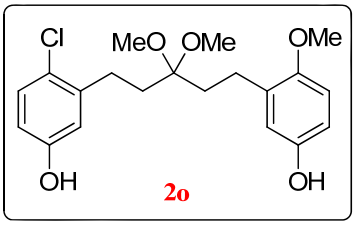
**1-(5-hydroxy-2-methoxyphenyl)-5-(4-hydroxy-[1,1'-biphenyl]-2-yl)pentan-3-one (1o)**

White solid (466 mg, 70% yield for two steps, 2.0 mmol material **1o-B** was used).

**$^{1}$H NMR (400 MHz, Acetone-$d_6$)** δ 8.07 (s, 2H), 7.17 (d, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 6.74-6.68 (m, 2H), 6.65 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.74 (s, 3H), 2.91-2.87.

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 208.28, 156.40, 150.94, 150.85, 139.86, 130.35, 129.95, 123.35, 117.33, 116.95, 114.78, 113.02, 111.54, 55.30, 42.30, 41.73, 27.55, 24.64.

**HRMS (ESI)** calcd for [M-H] $C_{18}H_{18}O_4Cl$, m/z: 333.0899, found: 333.0899.




**2o**

**4-chloro-3-(5-(5-hydroxy-2-methoxyphenyl)-3,3-dimethoxypentyl)phenol (2o)**

Colorless thick oil (398 mg, 98% yield, 1.0 mmol material was used).

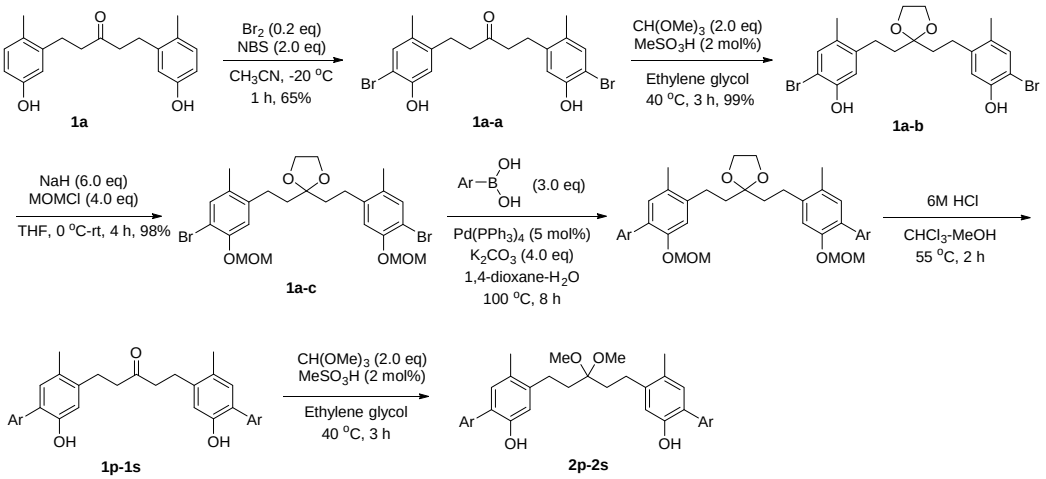
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.10 (d, *J* = 8.4 Hz, 1H), 6.63-6.58 (m, 7H, containing 2OH), 3.70 (s, 3H), 3.23 (s, 6H), 2.61-2.48 (m, 4H), 1.91-1.88 (m, 4H).

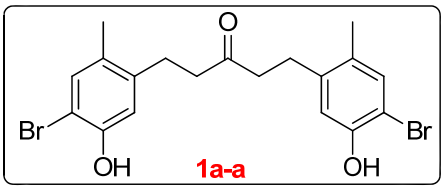
**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 154.74, 151.74, 149.13, 140.55, 131.36, 130.39, 125.00, 117.49, 117.30, 114.86, 113.51, 111.73, 103.73, 55.90, 47.98, 32.49, 32.45, 28.31, 25.30.

**HRMS (ESI)** calcd for [M-H] $C_{20}H_{24}O_5Cl$, m/z: 379.1318, found: 379.1320.

## (c) Synthesis of the symmetrical substrates 2p-2s

The bromination procedure from **1a** to **1a-a** is same as the synthetic procedure from **1g-2** to **1g**. And the sequential synthetic procedures from **1a-a** to **2p-2s** are similar to the routes from **1g** to **2b-2d**.



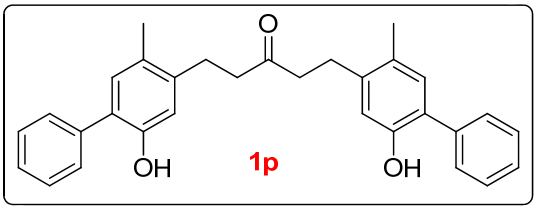

**1,5-bis(4-bromo-5-hydroxy-2-methylphenyl)pentan-3-one (1a-a)**

The bromination procedure is same as the substrate **1g**. White solid (2.96 g, 65% yield, 10.0 mmol material was used).

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.34 (s, 2H), 7.22 (s, 2H), 6.79 (s, 2H), 2.73-2.71 (m, 8H), 2.17 (s, 6H).

**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 207.81, 151.86, 140.46, 133.78, 128.69, 116.81, 106.40, 42.15, 26.48, 17.23.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{19}O_3Br_2$, m/z: 454.9686, found: 454.9690.



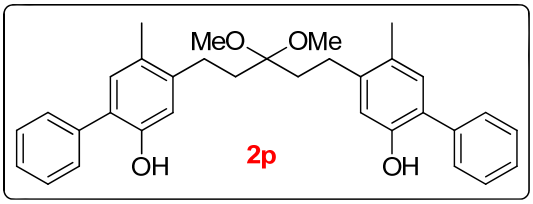

**1,5-bis(2-hydroxy-5-methyl-[1,1'-biphenyl]-4-yl)pentan-3-one (1p)**

Colorless thick oil (405 mg, 90% yield, 1.0 mmol **1a-c** was used).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.43-7.38 (m, 8H), 7.32-7.29 (m, 2H), 7.00 (s, 2H), 6.71 (s, 2H), 5.47 (s, 2H), 2.84 (t, $J$ = 7.6 Hz, 4H), 2.68 (t, $J$ = 7.6 Hz, 4H), 2.21 (s, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 210.08, 150.65, 149.99, 137.32, 132.02, 129.11, 129.05, 128.06, 127.52, 126.08, 116.07, 43.02, 26.99, 18.41.

**HRMS (ESI)** calcd for [M-H] $C_{31}H_{29}O_3$, m/z: 449.2122, found: 449.2126.



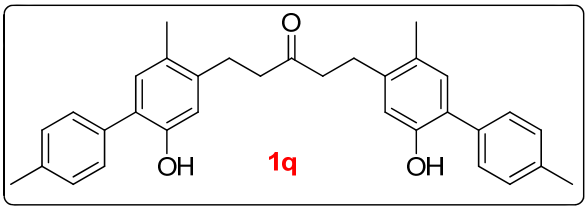

**4,4''-(3,3-dimethoxypentane-1,5-diyl)bis(5-methyl-[1,1'-biphenyl]-2-ol) (2p)**

Colorless thick oil (245 mg, 99% yield, 0.5 mmol **1p** was used).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.41 (m, 8H), 7.34-7.31 (m, 2H), 7.02 (s, 2H), 6.80 (s, 2H), 5.37 (s, 2H), 3.25 (s, 6H), 2.63-2.58 (m, 4H), 2.29 (s, 6H), 2.00-1.96 (m, 4H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.68, 141.08, 137.34, 131.94, 129.13, 129.13, 128.06, 127.57, 125.92, 116.17, 103.13, 48.01, 32.90, 27.60, 18.61.

**HRMS (ESI)** calcd for [M-H] $C_{33}H_{35}O_4$, m/z: 495.2541, found: 495.2542.



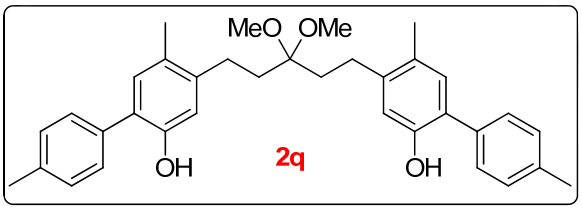

**1,5-bis(2-hydroxy-4',5-dimethyl-[1,1'-biphenyl]-4-yl)pentan-3-one (1q)**

Colorless thick oil (420 mg, 88% yield, 1.0 mmol **1a-c** was used).

**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.32 (d, *J* = 8.0 Hz, 4H), 7.21 (d, *J* = 8.0 Hz, 4H), 6.98 (s, 2H), 6.70 (s, 2H), 5.54 (s, 2H), 2.83 (t, *J* = 7.5 Hz, 4H), 2.67 (t, *J* = 7.5 Hz, 4H), 2.35 (s, 6H), 2.20 (s, 6H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 210.28, 150.76, 139.77, 137.30, 134.35, 132.02, 129.81, 129.00, 128.01, 126.08, 116.03, 43.09, 27.04, 21.29, 18.47.

**HRMS (ESI)** calcd for [M-H] $C_{33}H_{33}O_3$, m/z: 477.2435, found: 477.2436.



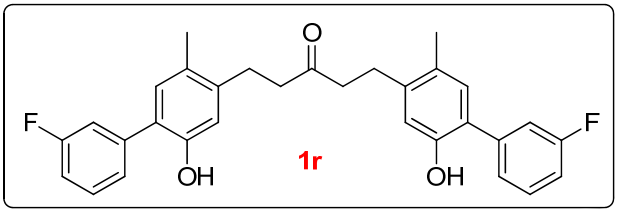

**4,4''-(3,3-dimethoxypentane-1,5-diyl)bis(4',5-dimethyl-[1,1'-biphenyl]-2-ol) (2q)**

Colorless thick oil (256 mg, 98% yield, 0.5 mmol **1q** was used).

**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.34 (d, *J* = 7.7 Hz, 4H), 7.24 (d, *J* = 7.7 Hz, 4H), 7.00 (s, 2H), 6.79 (s, 2H), 5.38 (s, 2H), 3.25 (s, 6H), 2.60 (t, *J* = 8.5 Hz, 4H), 2.37 (s, 6H), 2.29 (s, 6H), 1.97 (t, *J* = 8.5 Hz, 4H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 150.76, 140.86, 137.35, 134.29, 131.90, 129.89, 128.99, 127.98, 125.86, 116.07, 103.14, 48.01, 32.91, 27.61, 21.28, 18.65.

**HRMS (ESI)** calcd for [M+H] $C_{35}H_{41}O_4$, m/z: 525.2999, found: 525.3019.




**1,5-bis(3'-fluoro-2-hydroxy-5-methyl-[1,1'-biphenyl]-4-yl)pentan-3-one (1r)**

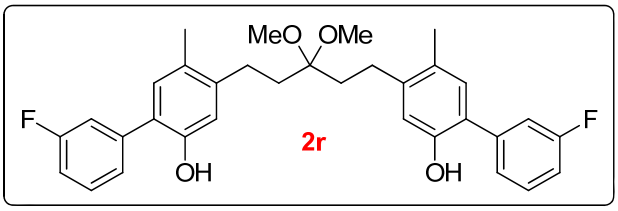
Colorless thick oil (435 mg, 90% yield, 1.0 mmol **1a-c** was used).

**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.41-7.37 (m, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 9.8 Hz, 2H), 7.05-7.02 (m, 4H), 6.72 (s, 2H), 6.02 (s, 2H), 2.87 (t, *J* = 7.5 Hz, 4H), 2.73 (t, *J* = 7.5 Hz, 4H), 2.25 (s, 6H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 211.06, 163.0 (d, *J* = 244.5 Hz), 150.69, 140.25, 139.84 (d, *J* = 7.5 Hz), 132.07, 130.24 (d, *J* = 7.5 Hz), 128.23, 125.02, 124.75 (d, *J* = 2.5 Hz), 116.46, 116.17 (d, *J* = 21.5 Hz), 114.16 (d, *J* = 20.8 Hz), 42.94, 26.98, 18.36.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -112.34.

**HRMS (ESI)** calcd for [M-H] $C_{31}H_{27}O_3F_2$, m/z: 485.1934, found: 485.1935.




**4,4''-(3,3-dimethoxypentane-1,5-diyl)bis(3'-fluoro-5-methyl-[1,1'-biphenyl]-2-ol) (2r)**

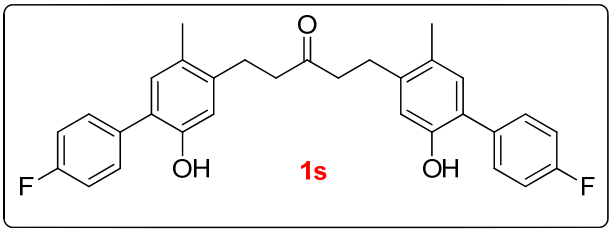
Colorless thick oil (263 mg, 99% yield, 0.5 mmol **1r** was used).

**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.37-7.34 (m, 2H), 7.25-7.18 (m, 4H), 7.02-6.99 (m, 4H), 6.75 (s, 2H), 5.67 (s, 2H), 3.25 (s, 6H), 2.57 (t, *J* = 8.0 Hz, 4H), 2.27 (s, 6H), 1.96 (t, *J* = 8.0 Hz, 4H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 163.06 (d, *J* = 245.0 Hz), 150.67, 141.37, 139.77 (d, *J* = 7.8 Hz), 131.96, 130.35 (d, *J* = 8.3 Hz), 128.23, 124.85, 124.71 (d, *J* = 16.0 Hz), 116.48, 116.18 (d, *J* = 21.5 Hz), 114.25 (d, *J* = 21.0 Hz), 103.25, 48.01, 32.80, 27.55, 18.56.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -112.30.

**HRMS (ESI)** calcd for [M-H] $C_{33}H_{33}O_4F_2$, m/z: 531.2352, found: 531.2352.




**1,5-bis(4'-fluoro-2-hydroxy-5-methyl-[1,1'-biphenyl]-4-yl)pentan-3-one(1s)**

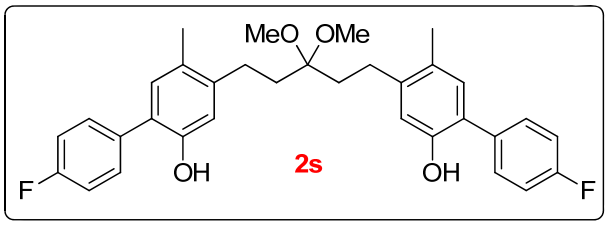
Colorless thick oil (456 mg, 94% yield, 1.0 mmol **1a-c** was used).

**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.42 (dd, *J* = 9.0, 5.5 Hz, 4H), 7.12 (t, *J* = 9.0 Hz, 4H), 6.99 (s, 2H), 6.71 (s, 2H), 5.25 (s, 2H), 2.86 (t, *J* = 7.5 Hz, 4H), 2.72 (t, *J* = 7.5 Hz, 4H), 2.24 (s, 6H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 209.74, 162.25 (d, *J* = 246 Hz), 150.49, 140.08, 133.15 (d, *J* = 2.9 Hz), 132.02, 130.78 (d, *J* = 8.0 Hz), 128.21, 125.09, 116.08, 115.90 (d, *J* = 21.2 Hz), 42.93, 26.87, 18.39.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -114.67.

**HRMS (ESI)** calcd for [M-H] $C_{31}H_{27}O_3F_2$, m/z: 485.1934, found: 485.1938.




**4,4''-(3,3-dimethoxypentane-1,5-diyl)bis(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-ol) (2s)**

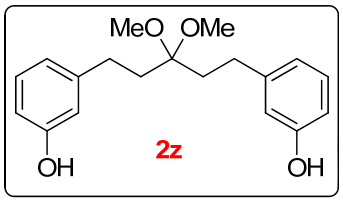
Colorless thick oil (260 mg, 98% yield, 0.5 mmol **1s** was used).

**$^{1}$H NMR (500 MHz, $CDCl_3$)** δ 7.43 (dd, *J* = 8.7, 5.6 Hz, 4H), 7.13 (t, *J* = 8.7 Hz, 4H), 7.00 (s, 2H), 6.78 (s, 2H), 5.24 (s, 2H), 3.27 (s, 6H), 2.61-2.58 (m, 4H), 2.29 (s, 6H), 2.03-1.96 (m, 4H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 162.26 (d, *J* = 245 Hz), 150.56, 141.12, 133.21 (d, *J* = 3.7 Hz), 131.97, 130.80 (d, *J* = 8.7 Hz), 128.18, 124.95, 116.21, 115.92 (d, *J* = 21.2 Hz), 103.03, 47.98, 32.81, 27.53, 18.55.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -114.69.

**HRMS (ESI)** calcd for [M-H] $C_{33}H_{33}O_4F_2$, m/z: 531.2352, found: 531.2156.



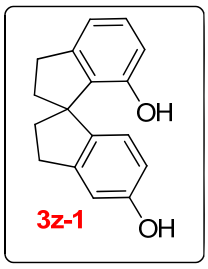

**3,3'-(3,3-dimethoxypentane-1,5-diyl)diphenol (2z)**

White solid (624 mg, 99% yield, 2.0 mmol material was used).

**$^{1}$H NMR (400 MHz, Acetone-$d_6$)** δ 8.15 (s, 2H), 7.10 (t, *J* = 8.0 Hz, 2H), 6.74-6.66 (m, 6H), 3.20 (s, 6H), 2.57-2.52 (m, 4H), 1.93-1.88 (m, 4H).

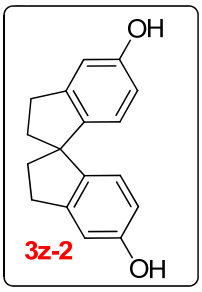
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 157.478, 143.77, 129.34, 119.38, 115.19, 112.75, 102.41, 46.92, 34.41, 29.99.

**HRMS (ESI)** calcd for [M-H] $C_{19}H_{23}O_4$, m/z: 315.1602, found: 315.1601.



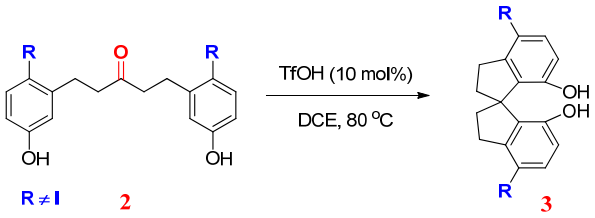

**2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-5,7'-diol (3z-1)**

**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.03 (s, 1H), 7.21 (s, 1H), 7.03-7.00 (m, 1H), 6.77 (dd, *J* = 7.4, 1.0 Hz, 1H), 6.74-6.71 (m, 2H), 6.60-6.57 (m, 2H), 2.98-2.88 (m, 4H), 2.58-2.51 (m, 1H), 2.31-2.25 (m, 1H), 2.19-2.14 (m, 1H), 2.07-1.98 (m, 1H).
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 156.47, 153.69, 145.99, 144.55, 140.78, 134.24, 128.06, 123.37, 115.87, 113.74, 113.58, 111.04, 59.16, 41.64, 37.66, 30.85, 30.81.

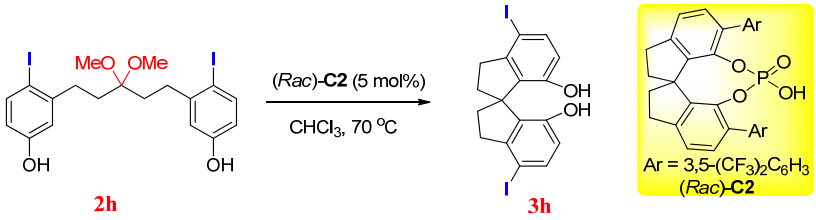



**2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-5,5'-diol (3z-2)**
**$^1$H NMR (400 MHz, Acetone-$d_6$)** δ 8.09 (s, 2H), 6.74 (d, *J* = 2.0, 2H), 6.69 (d, *J* = 8.0 Hz, 2H), 6.61 (dd, *J* = 8.0, 2.0 Hz, 2H), 2.92-2.87 (m, 4H), 2.28-.22 (m, 2H), 2.10-2.03 (m, 2H).
**$^{13}$C NMR (100 MHz, Acetone-$d_6$)** δ 156.49, 144.92, 141.63, 123.56, 113.68, 110.98, 59.13, 40.94, 30.42.

# Procedure for the Synthesis of Racemic SPINOL Derivatives



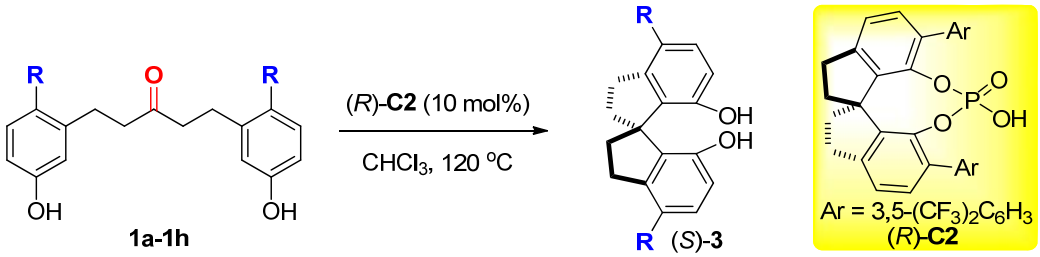

Generally, except for the racemic **3h** containing the iodo group, all the racemic products **3** were prepared according to the following synthetic route. To a vial were added substrate **2** (0.1 mmol), DCE (1 mL) and TfOH (0.01 mmol), then the reaction proceeded at 80℃ for about six hours. After the substrate was consumed completely, the reaction was diluted with 30 mL of EA and washed with aqueous $NaHCO_3$, the separated phase was concentrated and further purified by flash chromatography eluted with PE/EA to afford the corresponding desired product.




Under argon atmosphere, **2h** (0.1 mmol), (*Rac*)-**C2** (5 mol%) and 1 mL of anhydrous $CHCl_3$ were

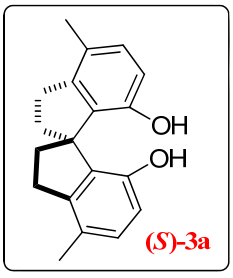
added to a 10 mL of oven-dried pressure Schlenk tube (purchased from Beijing Synthware Glass) with a magnetic stirring bar. Then the sealed reaction proceeded at 70℃ (the temperature of oil bath) for four days. After completion of the reaction, evaporated the solvent and the residue was purified by flash chromatography eluted with PE/EA = 8/1 to afford the racemic product **3h**.

# Procedure for the Asymmetric Synthesis of the SPINOL Derivatives (*S*)-3a-3h from Ketone Substrates




Under argon atmosphere, **2** (0.1 mmol), (*R*)-**C2** (10 mol% or 20 mol%) and 3 mL of anhydrous $CHCl_3$ were added to a 10 mL of oven-dried pressure Schlenk tube (purchased from Beijing Synthware Glass) with a magnetic stirring bar. Then the sealed reaction proceeded at 120℃ (the temperature of oil bath). After completion of the reaction, evaporated the solvent and the residue was purified by flash chromatography eluted with PE/EA = 8/1−4/1 to afford the product (*S*)-**3**.

**Reaction equipment**




**(*S*)-4,4'-dimethyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol** (**(*S*)-3a**)

According to the general procedure, **(*S*)-3a** was obtained in **97% yield** with **90% ee**.

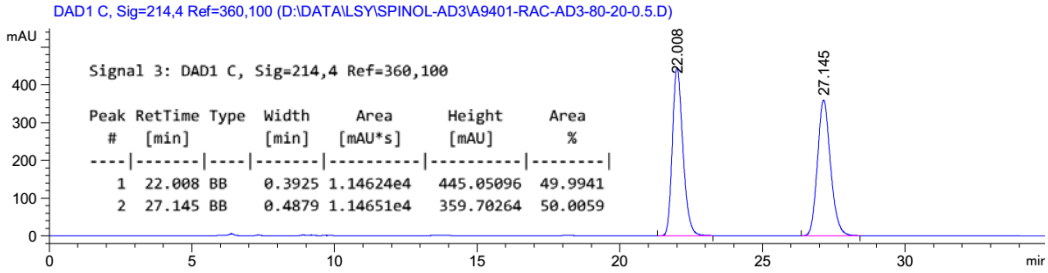
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 6.96 (d, *J* = 8.0 Hz, 2H), 6.59 (d, *J* = 8.0 Hz, 2H), 4.59 (s, 2H), 2.97-2.84 (m, 4H), 2.32– 2.27 (m, 2H), 2.22 (s, 6H), 2.20-2.14 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.89, 144.14, 130.51, 130.21, 126.53, 114.40, 58.17, 37.36, 30.00, 18.27.

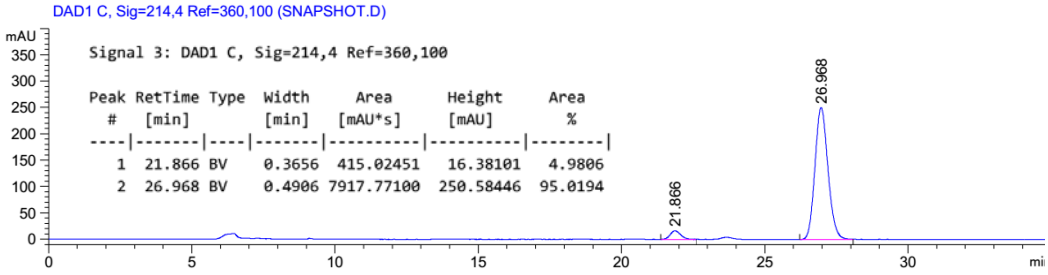
**HRMS (ESI)** calcd for [M+H] $C_{19}H_{21}O_2$, m/z: 281.1536, found: 281.1538.

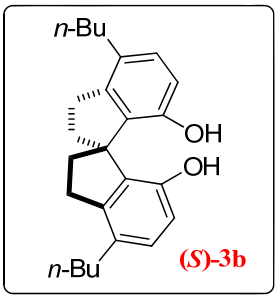
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 21.9 min, $t_R$ (major) = 27.0 min, ee = 90%.

*Chiral HPLC spectrum of racemic **3a***




*Chiral HPLC spectrum of **(S)-3a***




**(*S*)-4,4'-dibutyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol** (**(*S*)-3b**)

According to the general procedure, **(*S*)-3b** was obtained in **95% yield** with **91% ee**.

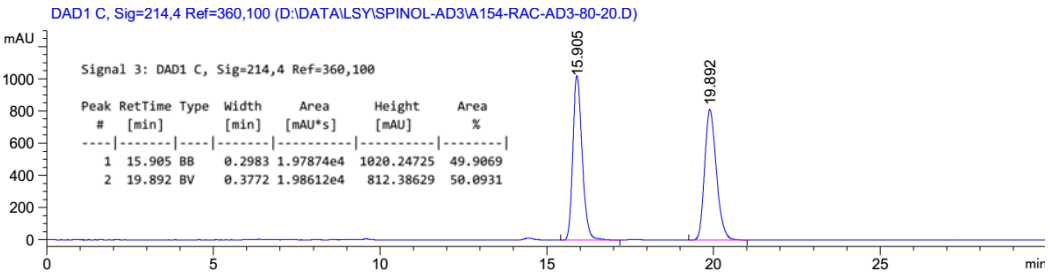
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 6.98 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 2H), 4.57 (s, 2H), 3.02-2.90 (m, 4H), 2.55-2.51 (m, 4H), 2.32-2.27 (m, 2H), 2.20-2.12 (m, 2H), 1.60-1.52 (m, 4H), 1.43-1.34 (m, 4H), 0.95 (t, *J* = 7.3 Hz, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.90, 143.67, 131.57, 130.14, 129.66, 114.48, 57.96, 37.35, 32.65, 32.41, 29.72, 22.69, 14.06.

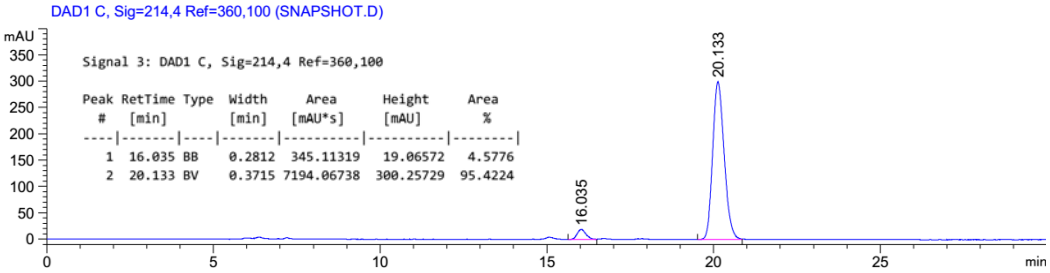
**HRMS (ESI)** calcd for [M+H] $C_{25}H_{33}O_2$, m/z: 365.2475, found: 365.2480.

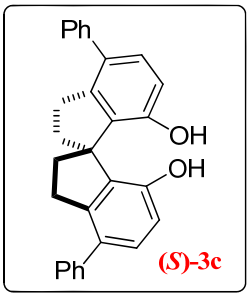
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 16.0 min, $t_R$ (major) = 20.1 min, ee = 91%.

*Chiral HPLC spectrum of racemic **3b***




*Chiral HPLC spectrum of **(S)-3b***




**(*S*)-4,4'-diphenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol** (**(*S*)-3c**)

According to the general procedure, **(*S*)-3c** was obtained in **90% yield** with **92% ee**.

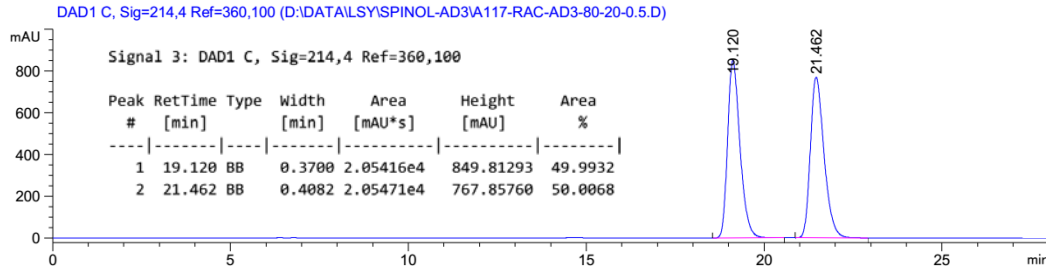
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.45-7.40 (m, 8H), 7.34-7.30 (m, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 8.2 Hz, 2H), 4.82 (s, 2H), 3.22-3.14 (m, 2H), 3.02(dd, *J* = 16.2, 8.4 Hz, 2H), 2.39 (dd, *J* = 12.8, 7.2 Hz, 2H), 2.24-2.16 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 152.37, 143.38, 140.80, 131.89, 130.64, 130.64, 128.66, 128.42, 126.78, 115.19, 58.07, 37.36, 31.41.

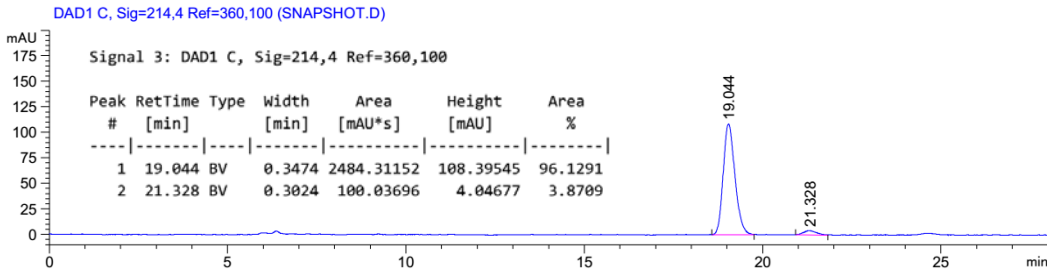
**HRMS (ESI)** calcd for [M+H] $C_{29}H_{25}O_2$, m/z: 405.1849, found: 405.1850.

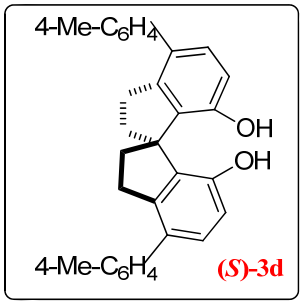
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 19.0 min, $t_R$ (minor) = 21.3 min, ee = 92%.

*Chiral HPLC spectrum of racemic **3c***




*Chiral HPLC spectrum of **(S)-3c***






**(*S*)-4,4'-di-p-tolyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol** (**(*S*)-3d**)

According to the general procedure, **(*S*)-3d** was obtained in **92% yield** with **93% ee**.

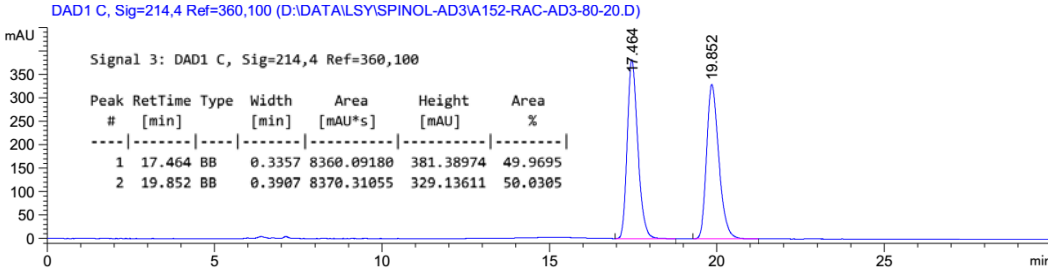
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.33 (d, *J* = 8.0 Hz, 4H), 7.24-7.20 (m, 6H), 6.77 (d, *J* = 8.0 Hz, 2H), 4.78 (s, 2H), 3.19-3.12 (m, 2H), 3.01 (dd, *J* = 16.2, 8.2 Hz, 2H), 2.39-2.35 (m, 8H), 2.23–2.17 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 152.11, 143.20, 137.79, 136.34, 131.74, 130.49, 130.45, 129.05, 128.42, 115.06, 57.95, 37.27, 31.34, 21.18.

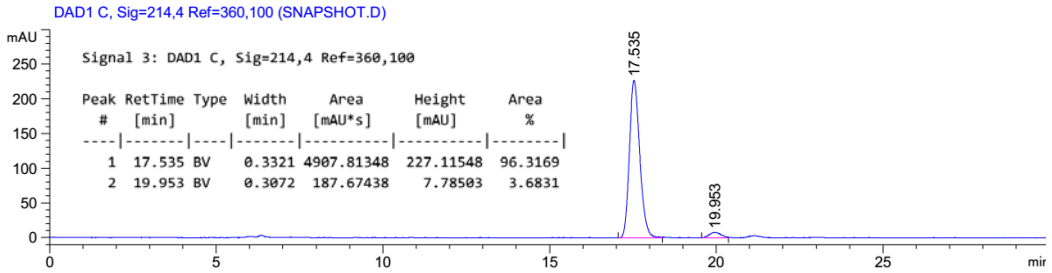
**HRMS (ESI)** calcd for [M+H] $C_{31}H_{29}O_2$, m/z: 433.2162, found: 433.2166.

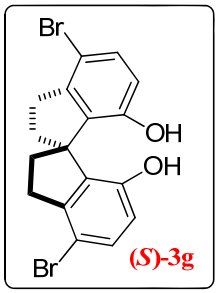
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 17.5 min, $t_R$ (minor) = 19.9 min, ee = 93%.

*Chiral HPLC spectrum of racemic **3d***




*Chiral HPLC spectrum of **(S)-3d***




**(*S*)-4,4'-dibromo-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol** (**(*S*)-3g**)

According to the general procedure, **(*S*)-3g** was obtained in **19% yield** with **93% ee**.

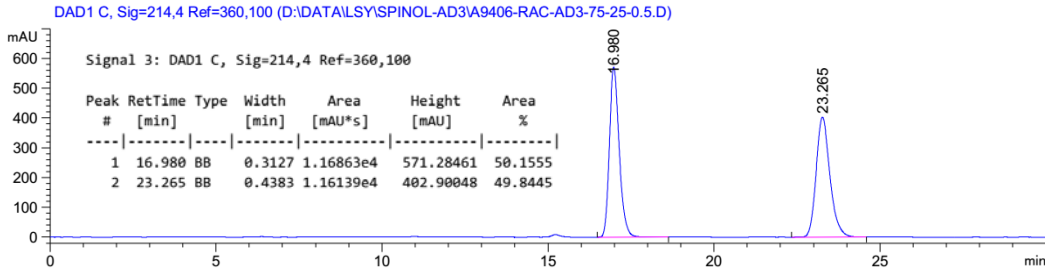
**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.28 (d, *J* = 8.5 Hz, 2H), 6.57 (d, *J* = 8.5 Hz, 2H), 4.71 (s, 2H), 3.00-2.94 (m, 4H), 2.32-2.15 (m, 4H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 151.96, 145.46, 132.53, 132.28, 116.57, 111.02, 60.35, 36.71, 32.74.

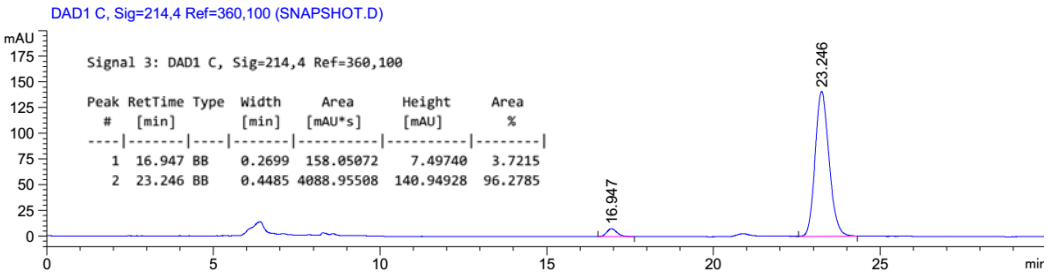
**HRMS (ESI)** calcd for [M-H] $C_{17}H_{13}O_2Br_2$, m/z: 408.9267, found: 408.9269.

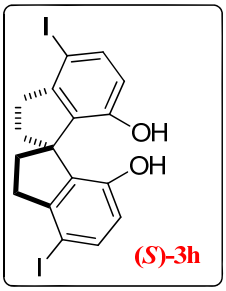
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 16.9 min, $t_R$ (major) = 23.2 min, ee = 93%.

*Chiral HPLC spectrum of racemic **3g***




*Chiral HPLC spectrum of **(S)-3g***




**(*S*)-4,4'-diiodo-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol** (**(*S*)-3h**)

According to the general procedure, **(*S*)-3h** was obtained in **20% yield** with **93% ee**.

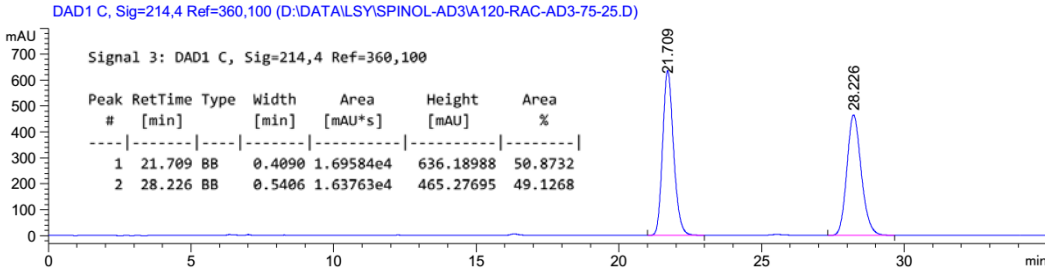
**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.50 (d, *J* = 8.5 Hz, 2H), 6.46 (d, *J* = 8.5 Hz, 2H), 4.74 (s, 2H), 2.98-2.95 (m, 4H), 2.29-2.25 (m, 2H), 2.20-2.13 (m, 2H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 153.05, 149.48, 138.59, 131.96, 117.00, 83.21, 61.16, 36.59, 36.29.

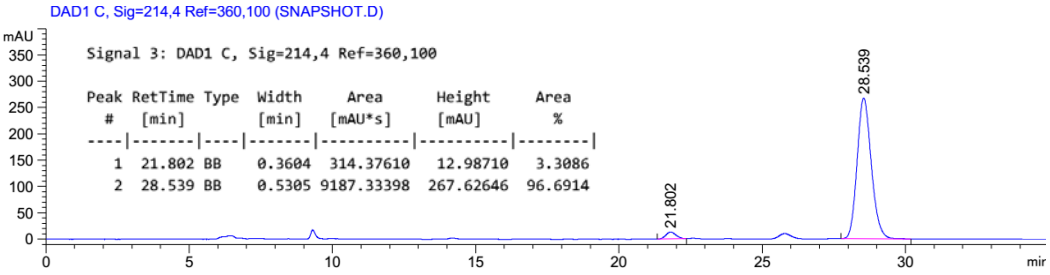
**HRMS (ESI)** calcd for [M-H] $C_{17}H_{13}O_2I_2$, m/z: 502.9010, found: 502.9016.

**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 21.8 min, $t_R$ (major) = 28.5 min, ee = 93%.

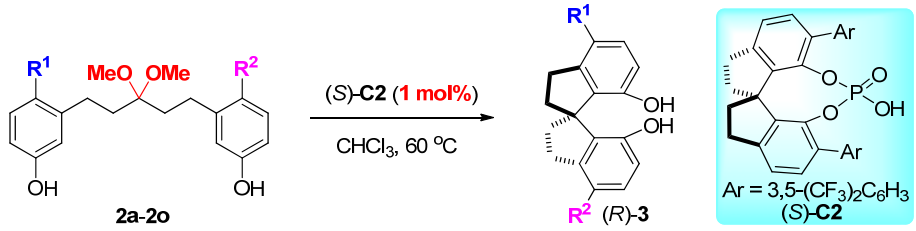
*Chiral HPLC spectrum of racemic **3h***



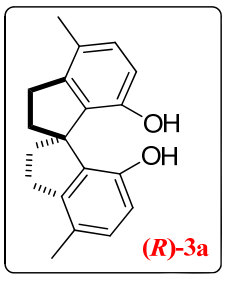

*Chiral HPLC spectrum of* ***(S)-3h***




# Procedure for the Asymmetric Synthesis of the SPINOL Derivatives (*R*)-3a-3o from Ketal Substrates




Under argon atmosphere, **2** (0.1 mmol), (*S*)-**C2** (1 mol% or 5 mol%) and 3 mL of anhydrous $CHCl_3$ were added to a 10 mL oven-dried pressure Schlenk tube (purchased from Beijing Synthware Glass) with a magnetic stirring bar. Then the sealed reaction proceeded at 60℃ or 70℃ (the temperature of oil bath) until the substrate was consumed completely. After evaporation of the solvent, the residue was purified by flash chromatography eluted with PE/EA = 8/1−4/1 to afford the product (*R*)-**3**.




**(*R*)-4,4'-dimethyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3a)**

According to the general procedure, **(*R*)-3a** was obtained in **90% yield** with **94% ee**.

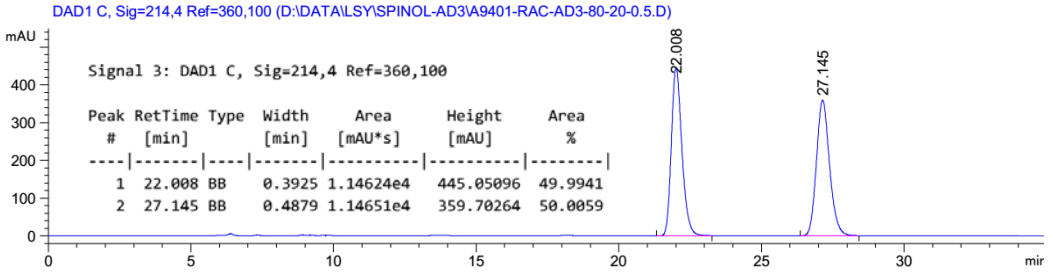
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.01 (d, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 8.0 Hz, 2H), 4.63 (s, 2H), 2.99-2.94 (m, 4H), 2.38– 2.32 (m, 2H), 2.27 (s, 6H), 2.24-2.10 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.90, 144.14, 130.51, 130.27, 126.52, 114.42, 58.20, 37.39, 30.01, 18.27.

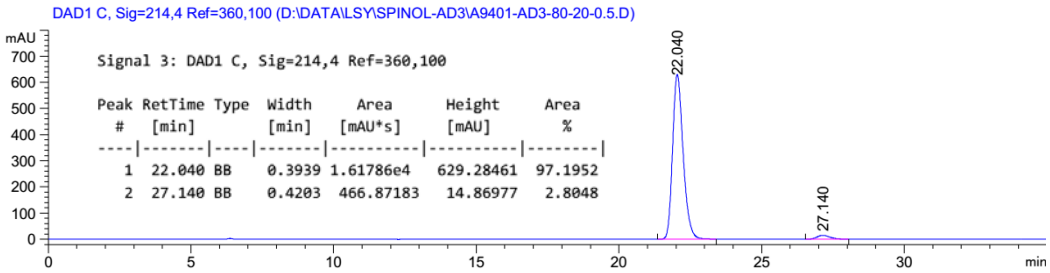
**HRMS (ESI)** calcd for [M-H] $C_{19}H_{19}O_2$, m/z: 279.1391, found: 279.1390.

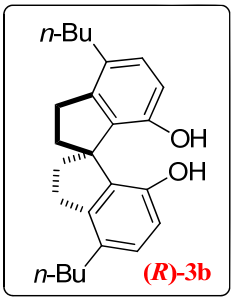
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 22.0 min, $t_R$ (minor) = 27.1 min, ee = 94%.

*Chiral HPLC spectrum of racemic **3a***




*Chiral HPLC spectrum of **(R)-3a***




**(*R*)-4,4'-dibutyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3b)**

According to the general procedure, **(*R*)-3b** was obtained in **95% yield** with **91% ee**.

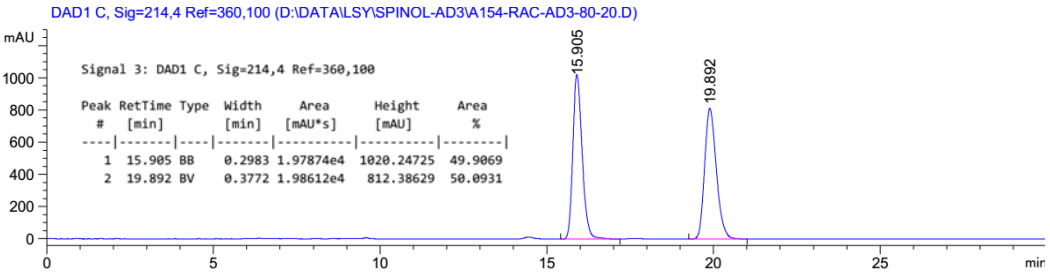
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 6.97 (d, *J* = 8.2 Hz, 2H), 6.61 (d, *J* = 8.2 Hz, 2H), 4.57 (s, 2H), 3.01-2.87 (m, 4H), 2.55-2.51 (m, 4H), 2.31-2.26 (m, 2H), 2.20-2.12 (m, 2H), 1.60-1.52 (m, 4H), 1.43-1.34 (m, 4H), 0.95 (t, *J* = 7.3 Hz, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.90, 143.67, 131.57, 130.19, 129.64, 114.48, 57.98, 37.36, 32.66, 32.42, 29.72, 22.69, 14.06.

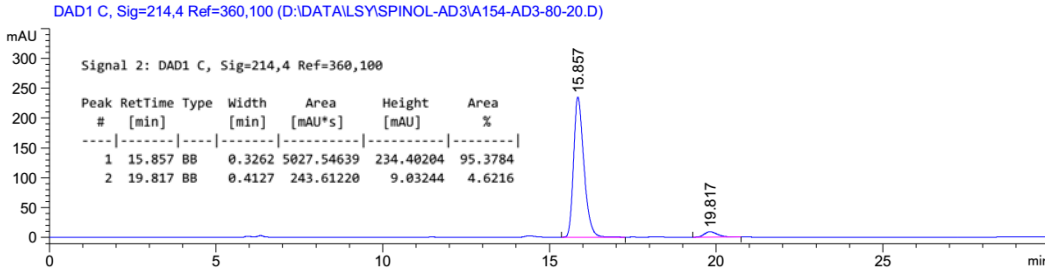
**HRMS (ESI)** calcd for [M-H] $C_{25}H_{31}O_2$, m/z: 363.2330, found: 363.2332.

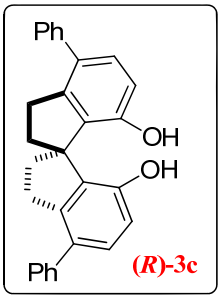
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 15.9 min, $t_R$ (minor) = 19.8 min, ee = 91%.

*Chiral HPLC spectrum of racemic **3b***




*Chiral HPLC spectrum of* ***(R)-3b***




**(*R*)-4,4'-diphenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3c)**

According to the general procedure, **(*R*)-3c** was obtained in **90% yield** with **94% ee**.

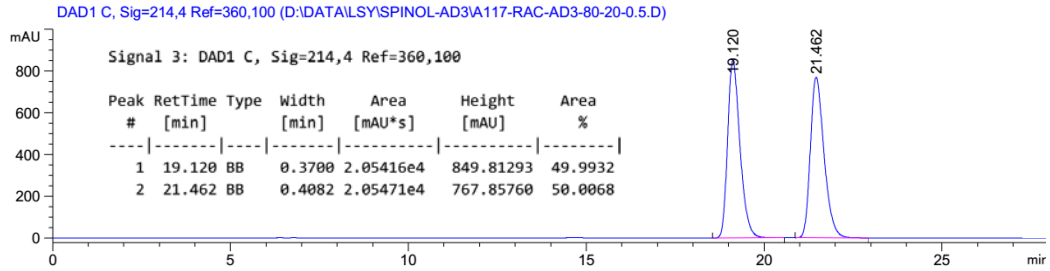
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.38 (m, 8H), 7.32-7.28 (m, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 4.86 (s, 2H), 3.18-3.12 (m, 2H), 3.00 (dd, *J* = 16.2, 8.4 Hz, 2H), 2.36 (dd, *J* = 12.8, 7.2 Hz, 2H), 2.23-2.18 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 152.33, 143.36, 140.80, 131.84, 130.76, 130.56, 128.64, 128.40, 126.75, 115.14, 58.08, 37.34, 31.39.

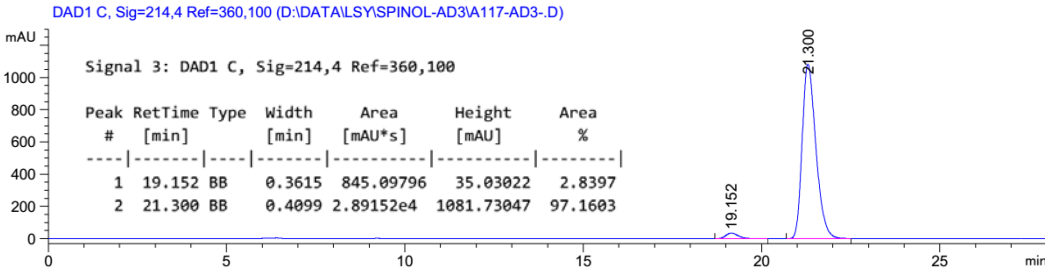
**HRMS (ESI)** calcd for [M-H] $C_{29}H_{23}O_2$, m/z: 403.1704, found: 403.1704.

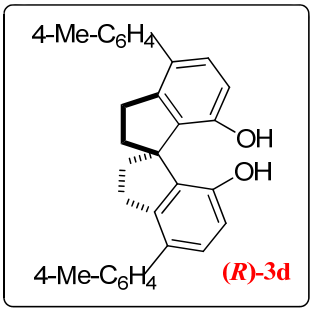
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 19.2 min, $t_R$ (major) = 21.3 min, ee = 94%.

*Chiral HPLC spectrum of racemic* ***3c***




*Chiral HPLC spectrum of* ***(R)-3c***




**(*R*)-4,4'-di-p-tolyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3d)**

According to the general procedure, **(*R*)-3d** was obtained in **92% yield** with **94% ee**.

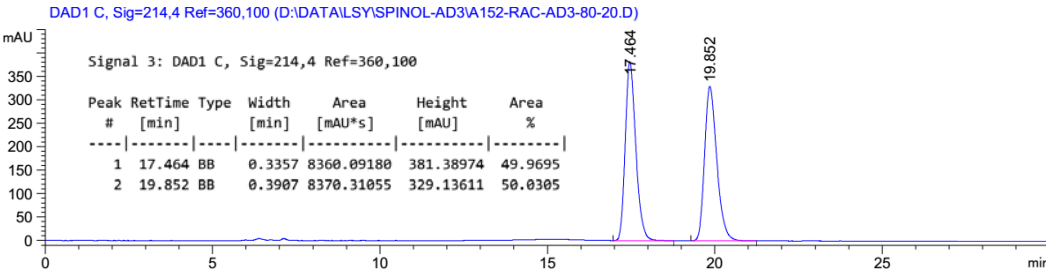
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.32 (d, *J* = 8.0 Hz, 4H), 7.22-7.19 (m, 6H), 6.75 (d, *J* = 8.0 Hz, 2H), 4.78 (s, 2H), 3.19-3.10 (m, 2H), 3.01 (dd, *J* = 16.2, 8.2 Hz, 2H), 2.38-2.33 (m, 8H), 2.22-2.14 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 152.13, 143.23, 137.85, 136.35, 131.76, 130.58, 130.48, 129.08, 128.46, 115.08, 58.01, 37.31, 31.37, 21.21.

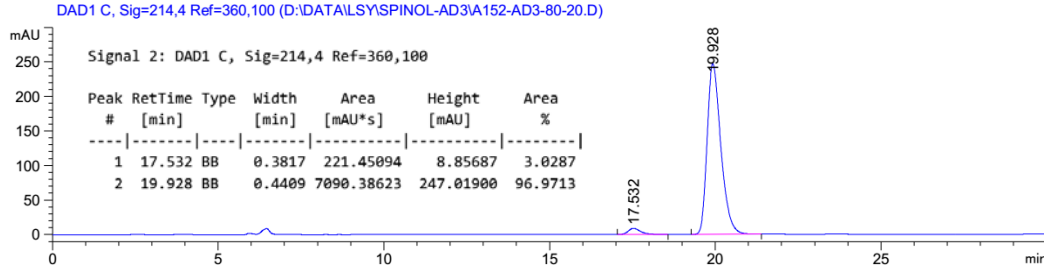
**HRMS (ESI)** calcd for [M-H] $C_{31}H_{27}O_2$, m/z: 431.2017, found: 431.2015.

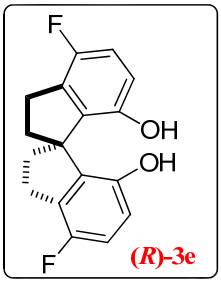
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 17.5 min, $t_R$ (major) = 19.9 min, ee = 94%.

*Chiral HPLC spectrum of racemic **3d***




*Chiral HPLC spectrum of* **(*R*)-*3d***






**(*R*)-4,4'-difluoro-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3e)**

According to the general procedure, **(*R*)-3e** was obtained in **72% yield** with **96% ee**.

**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 6.84 (dd, *J* = 8.5, 8.5 Hz, 2H), 6.59 (dd, *J* = 8.5, 3.8 Hz, 2H), 4.54 (s, 2H), 3.13-3.07 (m, 2H), 3.00-2.92 (m, 2H), 2.34-2.21 (m, 4H).

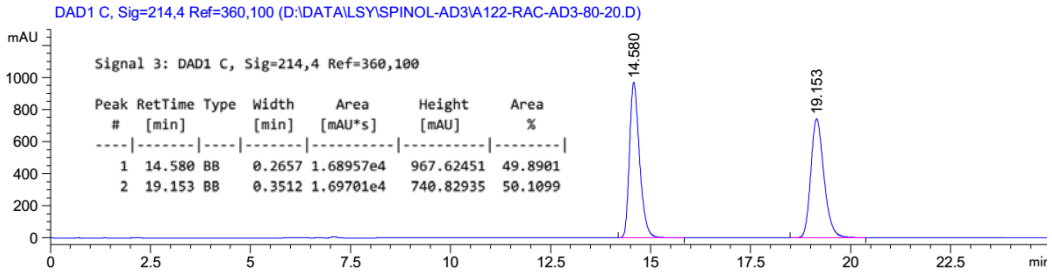
**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 153.90 (d, *J* = 237.9 Hz), 148.51 (d, *J* = 2.3 Hz), 132.87 (d, *J* = 4.8 Hz), 131.08 (d, *J* = 20.4 Hz), 115.93 (d, *J* = 22.6 Hz), 115.72 (d, *J* = 6.8 Hz), 59.06, 37.67, 27.31.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -127.66.

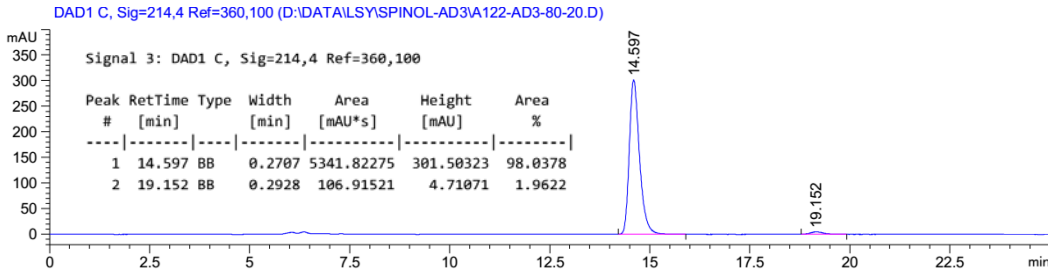
**HRMS (ESI)** calcd for [M-H] $C_{17}H_{13}O_2F_2$, m/z: 287.0889, found: 287.0890.

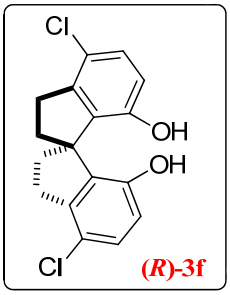
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 14.6 min, $t_R$ (minor) = 19.2 min, ee = 96%.

*Chiral HPLC spectrum of racemic **3e***




*Chiral HPLC spectrum of* ***(R)-3e***



**(*R*)-4,4'-dichloro-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3f)**

According to the general procedure, **(*R*)-3f** was obtained in **81% yield** with **96% ee**.

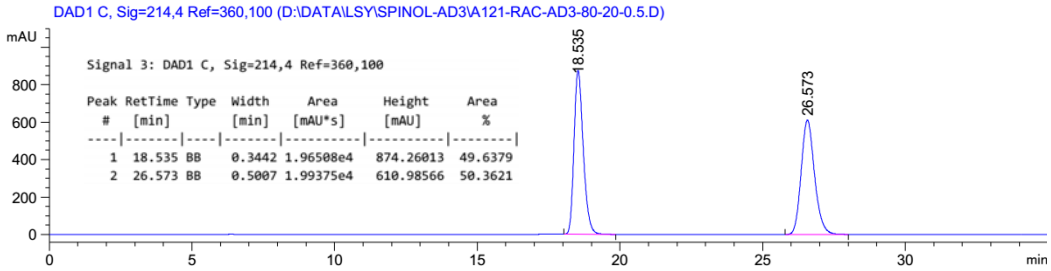
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.12 (d, *J* = 8.4 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 2H), 4.65 (s, 2H), 3.13-2.94 (m, 4H), 2.33-2.15 (m, 4H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 151.37, 143.47, 132.38, 129.57, 122.77, 116.20, 59.99, 37.03, 30.73.

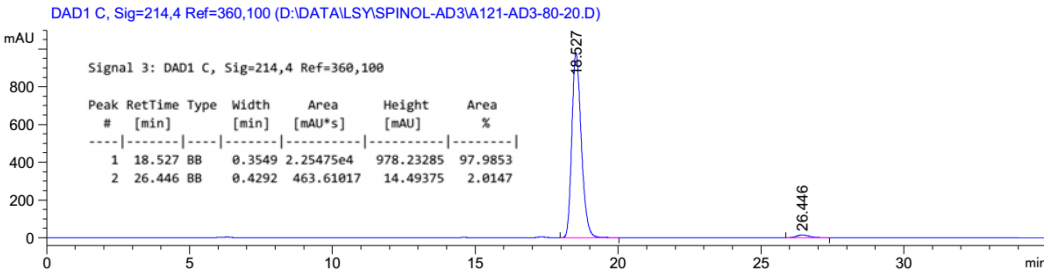
**HRMS (ESI)** calcd for [M-H] $C_{17}H_{13}O_2Cl_2$, m/z: 319.0298, found: 319.0299.

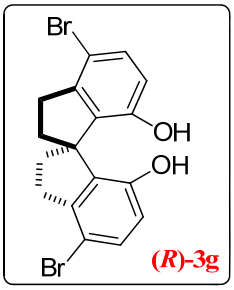
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 18.5 min, $t_R$ (minor) = 26.4 min, ee = 96%.

*Chiral HPLC spectrum of racemic **3f***




*Chiral HPLC spectrum of **(*R*)-3f***




**(*R*)-4,4'-dibromo-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3g)**

According to the general procedure, **(*R*)-3g** was obtained in **85% yield** with **96% ee**.

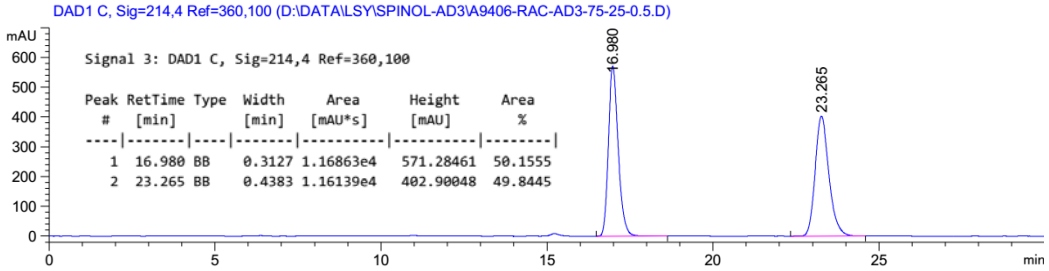
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.31 (d, *J* = 8.4 Hz, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 4.71 (s, 2H), 3.12-2.96 (m, 4H), 2.35-2.30 (m, 2H), 2.26-2.18 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 151.95, 145.45, 132.50, 132.39, 116.57, 111.03, 60.41, 36.75, 32.75.

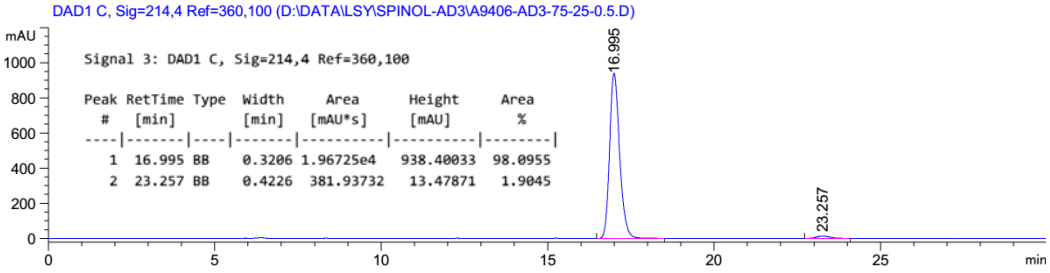
**HRMS (ESI)** calcd for [M-H] $C_{17}H_{13}O_2Br_2$, m/z: 408.9267, found: 408.9268.

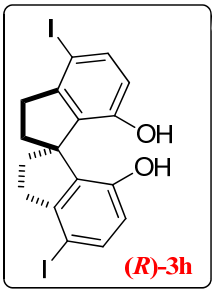
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 17.0 min, $t_R$ (minor) = 23.3 min, ee = 96%.

*Chiral HPLC spectrum of racemic **3g***




*Chiral HPLC spectrum of* ***(R)-3g***




**(*R*)-4,4'-diiodo-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3h)**

According to the general procedure, **(*R*)-3h** was obtained in **65% yield** with **95% ee**.

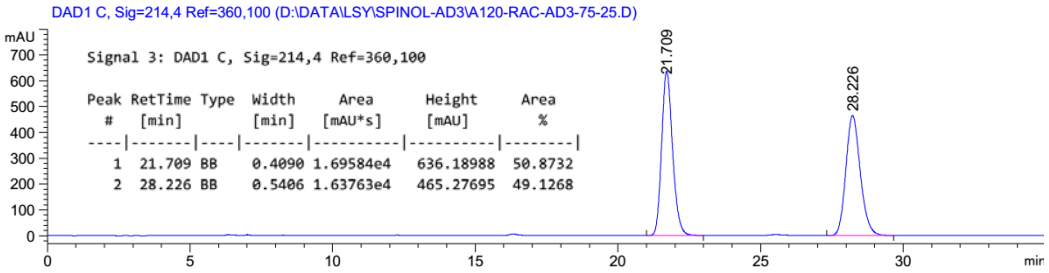
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.49 (d, *J* = 8.4 Hz, 2H), 6.45 (d, *J* = 8.4 Hz, 2H), 4.70 (s, 2H), 2.96 (dd, *J* = 9.6, 4.4 Hz, 4H), 2.30-2.24 (m, 2H), 2.20-2.12 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 153.14, 149.58, 138.71, 132.09, 117.11, 83.33, 61.29, 36.70.

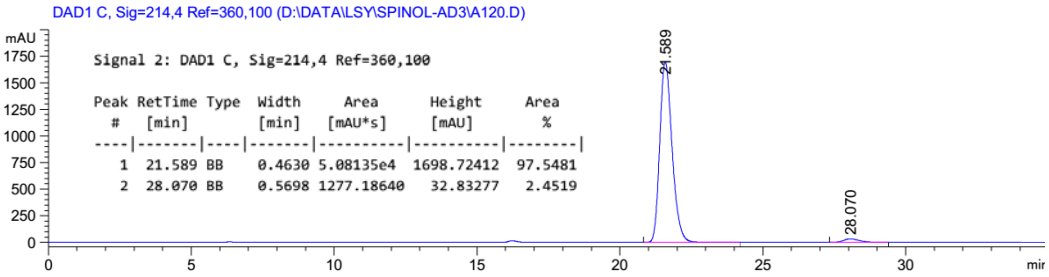
**HRMS (ESI)** calcd for [M-H] $C_{17}H_{13}O_2I_2$, m/z: 502.9010, found: 502.9014.

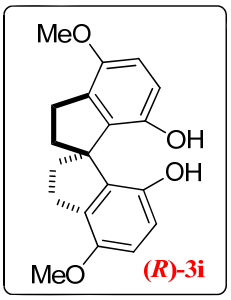
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 21.6 min, $t_R$ (minor) = 28.1 min, ee = 95%.

*Chiral HPLC spectrum of racemic* ***3h***




*Chiral HPLC spectrum of* ***(R)-3h***




**(*R*)-4,4'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3i)**

According to the general procedure, **(*R*)-3i** was obtained in **62% yield** with **90% ee**.

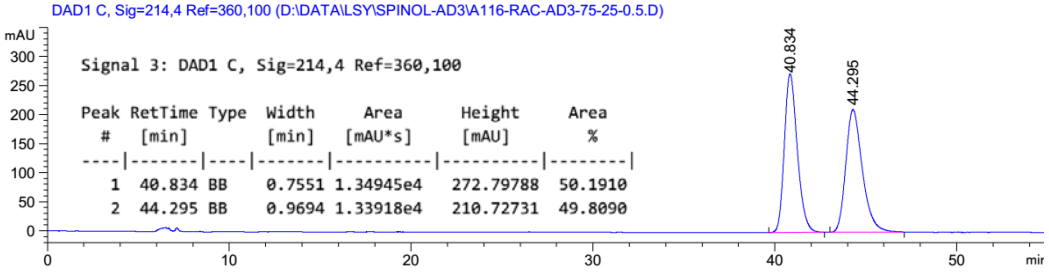
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 6.69-6.62 (m, 4H), 4.38 (s, 2H), 3.80 (s, 6H), 3.06-3.00 (m, 2H), 2.92-2.88 (m, 2H), 2.32-2.27 (m, 2H), 2.22-2.16 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.33, 146.68, 132.85, 132.54, 114.97, 111.40, 58.97, 55.78, 37.65, 28.05.

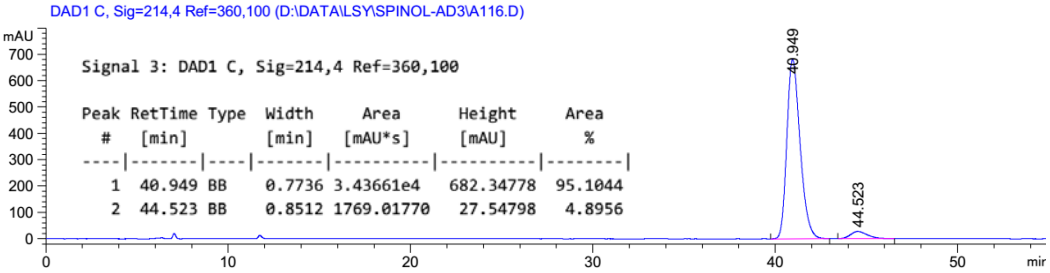
**HRMS (ESI)** calcd for [M-H] $C_{19}H_{19}O_4$, m/z: 311.1289, found: 311.1289.

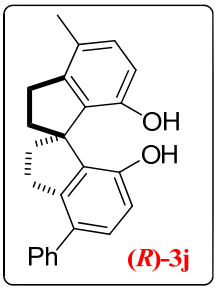
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 40.9 min, $t_R$ (minor) = 44.5 min, ee = 90%.

*Chiral HPLC spectrum of racemic **3i***




*Chiral HPLC spectrum of **(*R*)-3i***






**(*R*)-4-methyl-4'-phenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3j)**

According to the general procedure, **(*R*)-3j** was obtained in **99% yield** with **94% ee**.

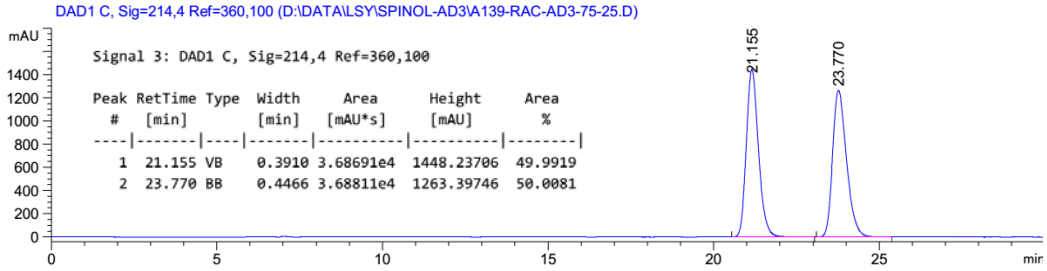
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.37 (m, 4H), 7.32-7.28 (m, 1H), 7.21-7.19 (m, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.60 (d, *J* = 8.1 Hz, 1H), 4.81 (s, 1H), 4.59 (s, 1H), 3.19-3.10 (m, 1H), 3.00-2.85 (m, 3H), 2.41-2.36 (m, 1H), 2.29-2.12 (m, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 152.26, 150.95, 144.27, 143.19, 140.81, 131.69, 131.07, 130.67, 130.38, 129.87, 128.58, 128.32, 126.66, 126.65, 115.04, 114.51, 58.12, 37.75, 36.94, 31.30, 30.07, 18.30.

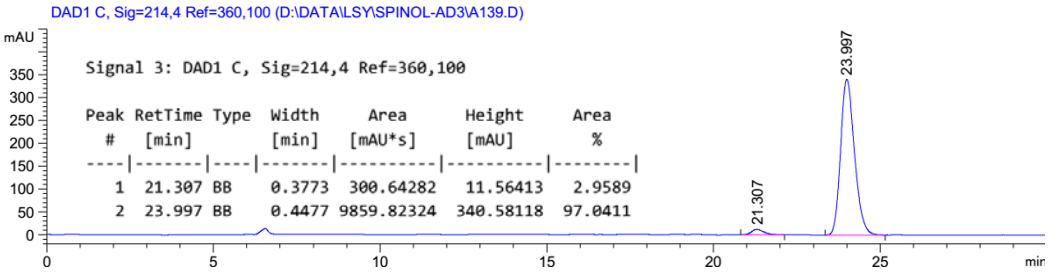
**HRMS (ESI)** calcd for [M+H] $C_{24}H_{23}O_2$, m/z: 343.1693, found: 343.1687.

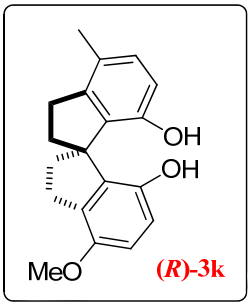
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 21.3 min, $t_R$ (major) = 24.0 min, ee = 94%.

*Chiral HPLC spectrum of racemic **3j***




*Chiral HPLC spectrum of* **(*R*)-*3j***



**(*R*)-4-methoxy-4'-methyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3k)**

According to the general procedure, **(*R*)-3k** was obtained in **50% yield** with **95% ee**.

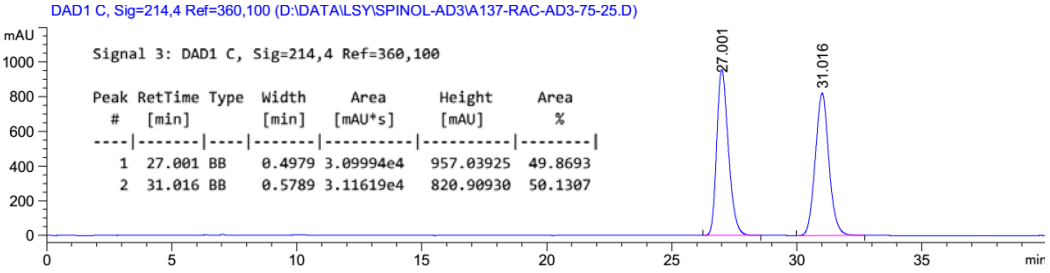
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 6.96 (d, *J* = 8.0 Hz, 1H), 6.69-6.65 (m, 2H), 6.59 (d, *J* = 8.0 Hz, 1H), 4.56 (s, 1H), 4.39 (s, 1H), 3.80 (s, 3H), 3.04-2.86 (m, 4H), 2.33-2.26 (m, 2H), 2.21 (s, 3H), 2.18-2.13 (m, 2H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 150.81, 150.22, 146.64, 144.24, 132.64, 132.59, 130.54, 130.01, 126.55, 114.83, 114.42, 111.27, 58.51, 55.68, 37.61, 37.28, 30.01, 27.93, 18.27.

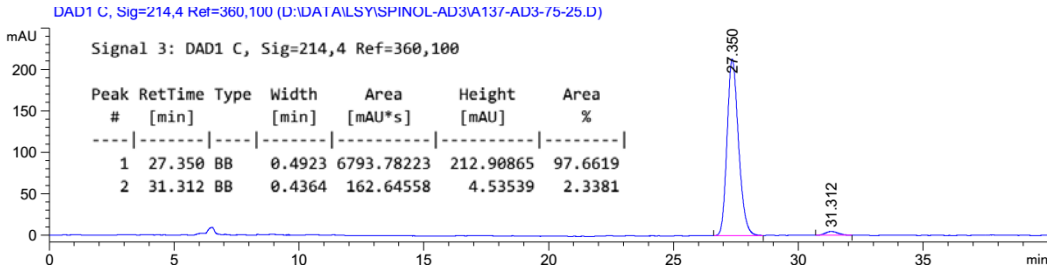
**HRMS (ESI)** calcd for [M+H] $C_{19}H_{21}O_3$, m/z: 297.1485, found: 297.1482.

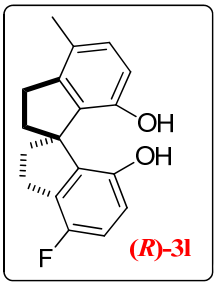
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 27.3 min, $t_R$ (minor) = 31.3 min, ee = 95%.

*Chiral HPLC spectrum of racemic **3k***




*Chiral HPLC spectrum of **(*R*)-3k***




**(*R*)-4-fluoro-4'-methyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3l)**

According to the general procedure, **(*R*)-3l** was obtained in **93% yield** with **93% ee**.

**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 6.95 (d, *J* = 8.0 Hz, 1H), 6.81 (dd, *J* = 8.5, 8.5 Hz, 1H), 6.59-6.54 (m, 2H), 4.62 (s, 2H), 3.10-3.04 (m, 1H), 2.99-2.87 (m, 3H), 2.33-2.21 (m, 7H).

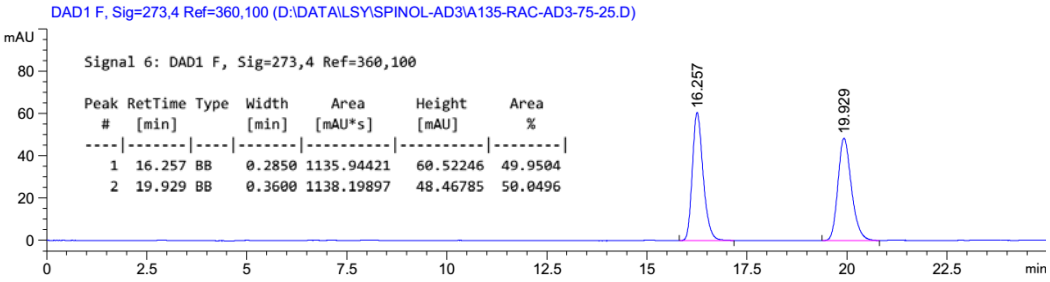
**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 153.75 (d, *J* = 237.5 Hz), 150.71, 148.55 (d, *J* = 1.9 Hz), 144.48, 133.74, 130.68, 130.00 (d, *J* = 9.7 Hz), 126.74, 115.52 (d, *J* = 22.5 Hz), 115.51, 115.44, 114.50, 58.64, 37.69, 37.27, 30.01, 27.20, 18.25.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -128.04.

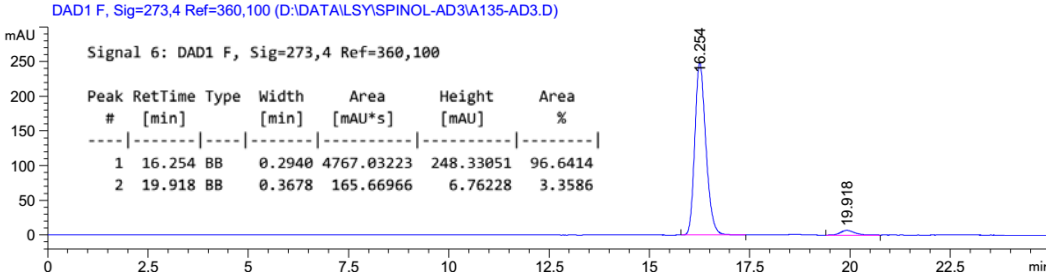
**HRMS (ESI)** calcd for [M-H] $C_{18}H_{16}O_2F$, m/z: 283.1140, found: 283.1142.

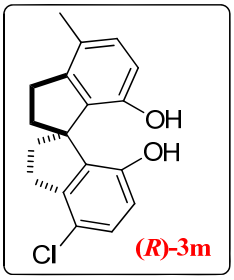
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 273 nm, $t_R$ (major) = 16.3 min, $t_R$ (minor) = 19.9 min, ee = 93%.

*Chiral HPLC spectrum of racemic **3l***




*Chiral HPLC spectrum of **(*R*)-3l***




**(*R*)-4-chloro-4'-methyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3m)**

According to the general procedure, **(*R*)-3m** was obtained in **96% yield** with **94% ee**.

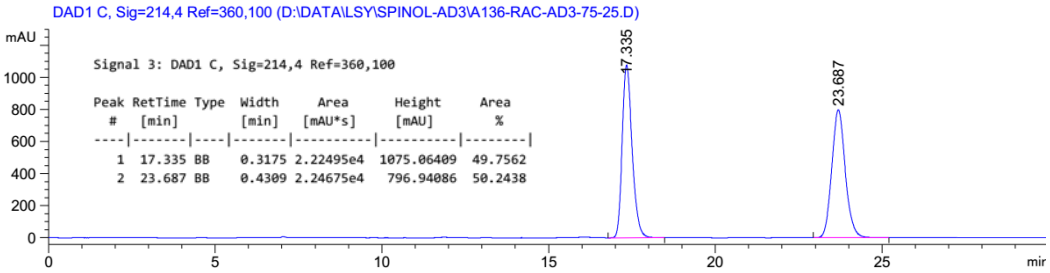
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.10 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 4.65 (s, 2H), 3.11-2.88 (m, 4H), 2.34-2.16 (m, 7H, containing a $CH_3$).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 151.43, 150.74, 144.44 143.05, 133.14, 130.75, 129.46, 129.19, 126.78, 122.47, 116.05, 114.50, 59.08, 37.37, 36.96, 30.66, 29.97, 18.26.

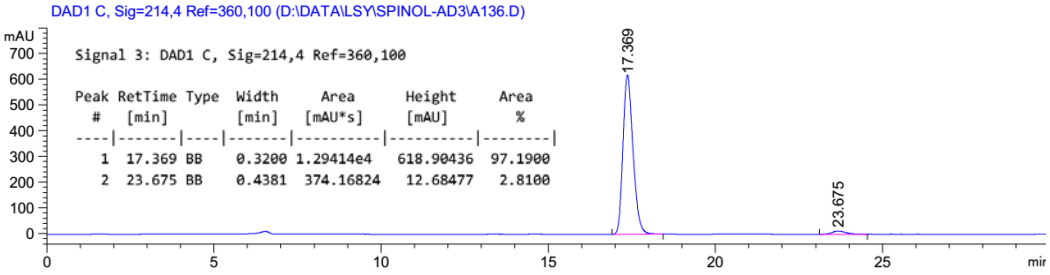
**HRMS (ESI)** calcd for [M-H] $C_{18}H_{16}O_2Cl$, m/z: 299.0844, found: 299.0846.

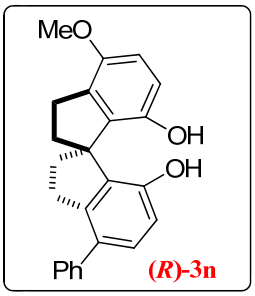
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 17.4 min, $t_R$ (minor) = 23.7 min, ee = 94%.

*Chiral HPLC spectrum of racemic **3m***




*Chiral HPLC spectrum of* ***(R)-3m***




**(*R*)-4-methoxy-4'-phenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3n)**

According to the general procedure, **(*R*)-3n** was obtained in **92% yield** with **93% ee**.

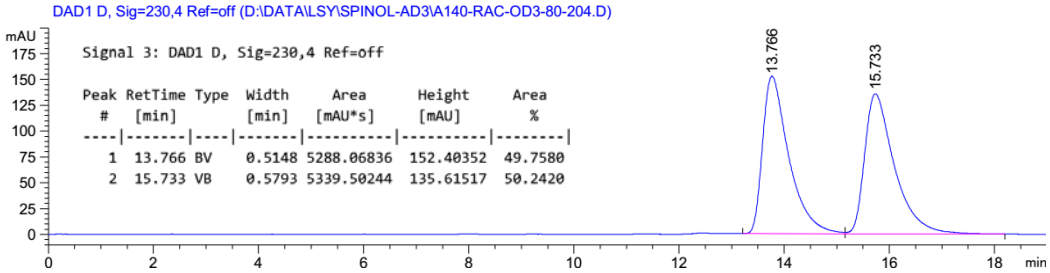
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.38 (m, 4H), 7.32-7.30 (m, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.68 (d, *J* = 8.6 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 4.86 (s, 1H), 4.49 (s, 1H), 3.80 (s, 3H), 3.16-2.85 (m, 4H), 2.40-2.10 (m, 4H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 152.18, 150.30, 146.67, 143.29, 140.78, 132.80, 132.35, 131.67, 130.95, 130.38, 128.58, 128.33, 126.66, 115.03, 114.93, 111.39, 58.47, 55.72, 37.67, 37.17, 31.32, 28.01.

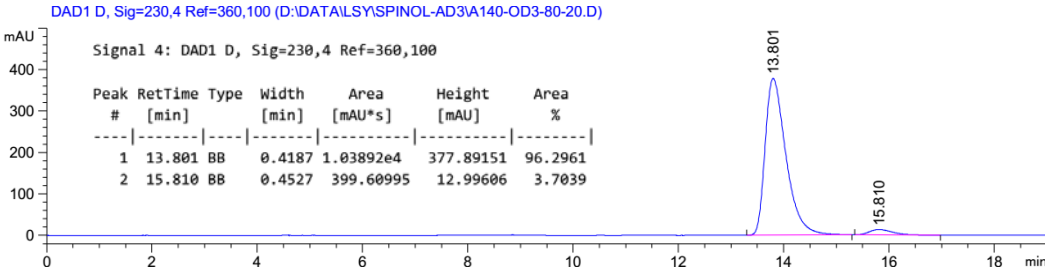
**HRMS (ESI)** calcd for [M+H] $C_{24}H_{23}O_3$, m/z: 359.1642, found: 359.1637.

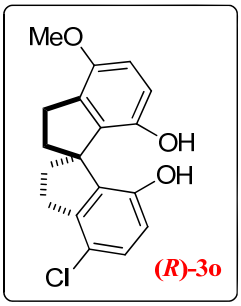
**HPLC analysis**: HPLC DAICEL CHIRALCEL OD-3, hexane/isopropanol = 80/20, 0.4 mL/min, λ = 230 nm, $t_R$ (major) = 13.8 min, $t_R$ (minor) = 15.8 min, ee = 93%.

*Chiral HPLC spectrum of racemic* ***3n***




*Chiral HPLC spectrum of* ***(R)-3n***




**(*R*)-4-chloro-4'-methoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3o)**

According to the general procedure, **(*R*)-3o** was obtained in **61% yield** with **92% ee**.

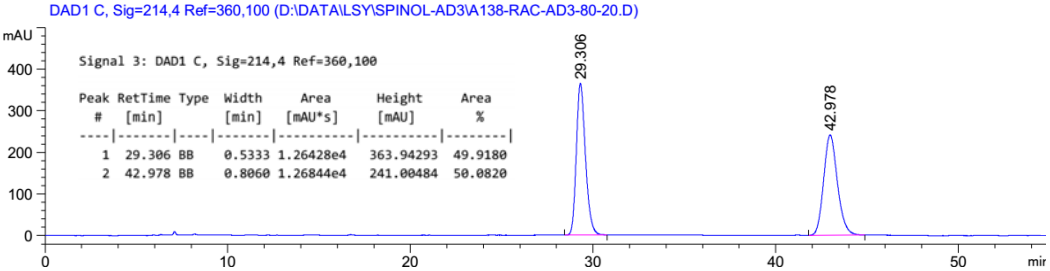
**$^{1}$H NMR (400 MHz, $CDCl_3$)** δ 7.10 (d, *J* = 8.4 Hz, 1H), 6.68 (d, *J* = 8.6 Hz, 1H), 6.62 (d, *J* = 8.6 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 4.76 (s, 1H), 4.43 (s, 1H), 3.80 (s, 3H), 3.11-2.83 (m, 4H), 2.34-2.18 (m, 4H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 151.37, 150.33, 146.46, 143.15, 132.98, 132.93, 131.87, 129.22, 122.47, 116.06, 114.96, 111.45, 59.40, 55.70, 37.61, 36.88, 30.67, 27.91.

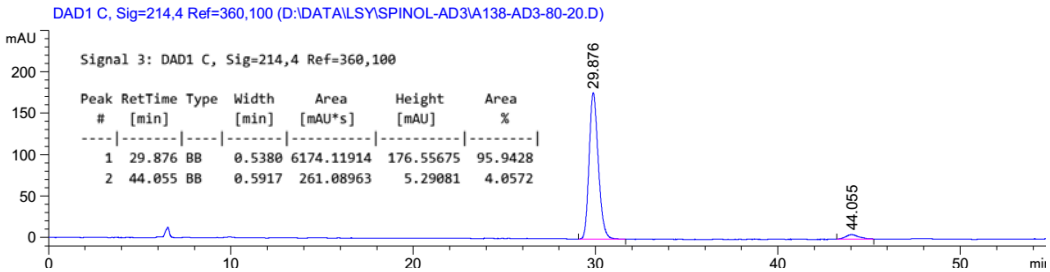
**HRMS (ESI)** calcd for [M-H] $C_{18}H_{16}O_3Cl$, m/z: 315.0793, found: 315.0797.

**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 29.9 min, $t_R$ (minor) = 44.0 min, ee = 92%.

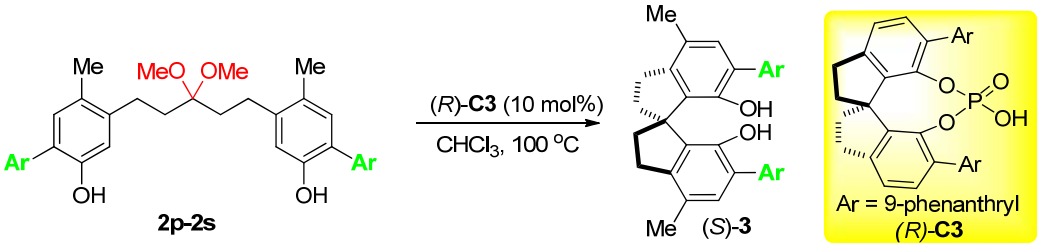
*Chiral HPLC spectrum of racemic **3o***



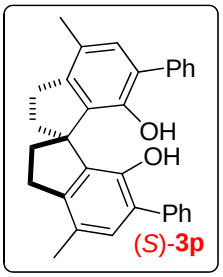

*Chiral HPLC spectrum of **(*R*)-3o***



# Procedure for the Asymmetric Synthesis of the 6,6'-diaryl-SPINOL Derivatives (*S*)-3p-3s from Ketal Substrates




Under argon atmosphere, **2** (0.1 mmol), (*R*)-**C3** (10 mol%) and 5 mL of anhydrous $CHCl_3$ were added to a 10 mL oven-dried pressure Schlenk tube (purchased from Beijing Synthware Glass) with a magnetic stirring bar. Then the sealed reaction proceeded at 100℃ (the temperature of oil bath) for five days. After evaporation of the solvent, the residue was purified by flash chromatography eluted with PE/EA = 50/1−20/1 to afford the corresponding product (*S*)-**3**.




**(*S*)-4,4'-dimethyl-6,6'-diphenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*S*)-3p)**

According to the general procedure, **(*S*)-3p** was obtained in **61% yield** with **90% ee**.

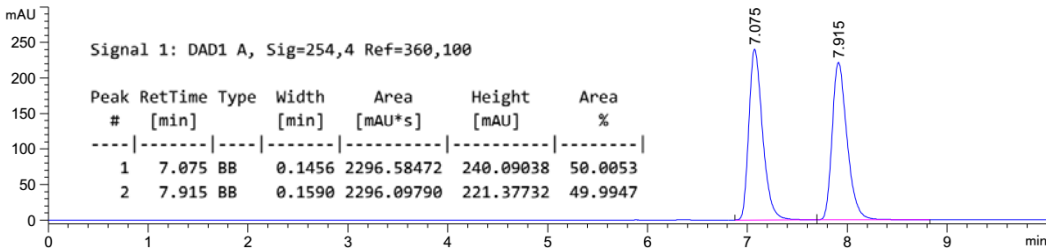
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.47-7.44 (m, 4H), 7.38-7.34 (m, 4H), 7.28-7.24 (m, 2H), 7.00 (s, 2H), 4.95 (s, 2H), 3.03-2.89 (m, 4H), 2.04-2.35 (m, 4H), 2.25 (s, 6H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 147.51, 143.74, 137.73, 131.88, 131.31, 129.35, 128.59, 127.16, 127.10, 126.27, 59.15, 37.79, 29.98, 18.37.

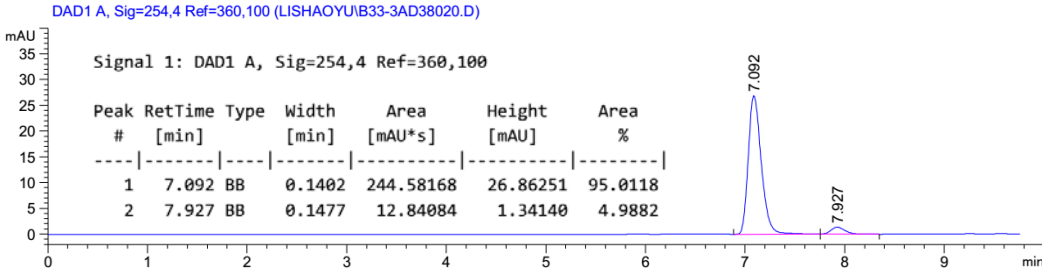
**HRMS (ESI)** calcd for [M+H] $C_{31}H_{29}O_2$, m/z: 433.2162, found: 433.2155.

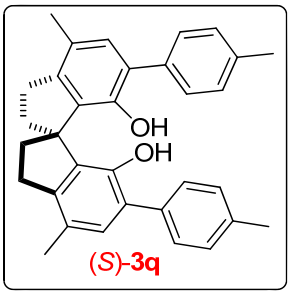
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 254 nm, $t_R$ (major) = 7.09 min, $t_R$ (minor) = 7.92 min, ee = 90%.

*Chiral HPLC spectrum of racemic **3p***



*Chiral HPLC spectrum of* ***(S)-3p***




**(*S*)-4,4'-dimethyl-6,6'-di-p-tolyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*S*)-3q)**

According to the general procedure, **(*S*)-3q** was obtained in **58% yield** with **83% ee**.

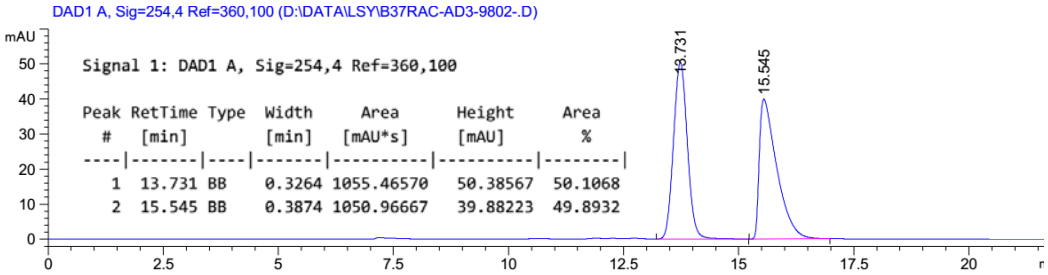
**$^{1}$H NMR (500 MHz, $CDCl_3$)** δ 7.48 (d, *J* = 8.0 Hz, 4H), 7.18 (d, *J* = 8.0 Hz, 4H), 6.99 (s, 2H), 4.95 (s, 2H), 3.00-2.92 (m, 4H), 2.39-2.34 (m, 10H), 2.24 (s, 6H).

**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 147.46, 143.44, 136.82, 134.67, 131.83, 131.13, 129.28, 129.14, 126.97, 126.11, 59.11, 37.70, 29.90, 21.20, 18.33.

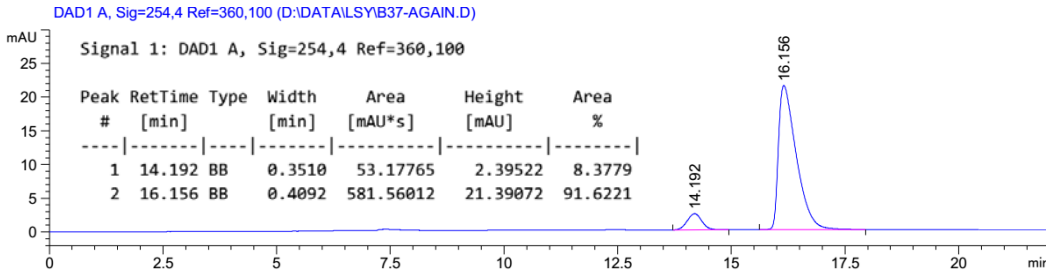
**HRMS (ESI)** calcd for [M+H] $C_{33}H_{33}O_2$, m/z: 461.2475, found: 461.2473.

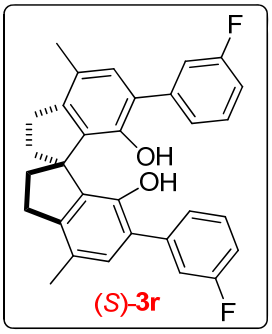
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 98/2, 0.5 mL/min, λ = 254 nm, $t_R$ (minor) = 14.1 min, $t_R$ (major) = 16.1 min, ee = 83%.

*Chiral HPLC spectrum of racemic* ***3q***




*Chiral HPLC spectrum of* ***(S)-3q***






**(*S*)-6,6'-bis(3-fluorophenyl)-4,4'-dimethyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*S*)-3r)**

According to the general procedure, **(*S*)-3r** was obtained in **62% yield** with **95% ee**.

**$^1$H NMR (500 MHz, $CDCl_3$)** δ 7.34-7.30 (m, 2H), 7.24 (d, *J* = 6.0 Hz, 2H), 7.20 (dd, *J* = 10.0, 1.5 Hz, 2H), 7.02 (s, 2H), 6.99-6.95 (m, 2H), 4.91 (s, 2H), 3.03-2.93 (m, 4H), 2.39-2.34 (m, 4H), 2.26 (s, 6H).

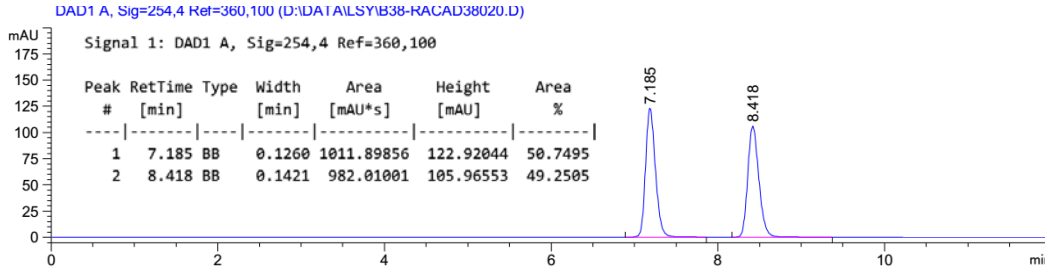
**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 162.82 (d, *J* = 244 Hz), 147.46, 144.24, 139.88 (d, *J* = 7.7 Hz), 131.51, 131.36, 129.84 (d, *J* = 8.4 Hz), 126.59, 125.91 (d, *J* = 1.5 Hz), 124.88 (d, *J* = 2.6 Hz), 116.32 (d, *J* = 21.6 Hz), 113.91 (d, *J* = 20.8 Hz), 58.95, 37.64, 29.91, 18.29.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -113.13.

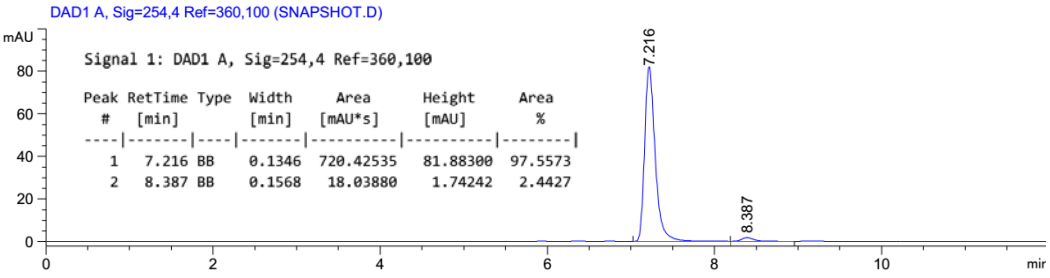
**HRMS (ESI)** calcd for [M-H] $C_{31}H_{25}O_2F_2$, m/z: 467.1828, found: 467.1827.

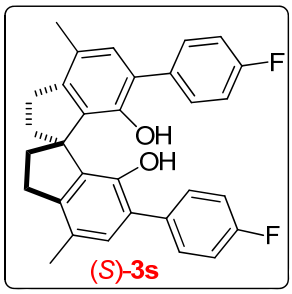
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 80/20, 0.5 mL/min, λ = 254 nm, $t_R$ (major) = 7.2 min, $t_R$ (minor) = 8.3 min, ee = 95%.

*Chiral HPLC spectrum of racemic **3r***




*Chiral HPLC spectrum of **(*S*)-3r***






**(*S*)-6,6'-bis(4-fluorophenyl)-4,4'-dimethyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*S*)-3s)**

According to the general procedure, **(*S*)-3r** was obtained in **60% yield** with **95% ee**.

**$^{1}$H NMR (500 MHz, $CDCl_3$)** δ 7.43 (dd, *J* = 8.7, 5.5 Hz, 4H), 7.06 (t, *J* = 8.7 Hz, 4H), 6.99 (s, 2H), 4.86 (s, 2H), 3.03-2.91 (m, 4H), 2.38-2.34 (m, 4H), 2.25 (s, 6H).

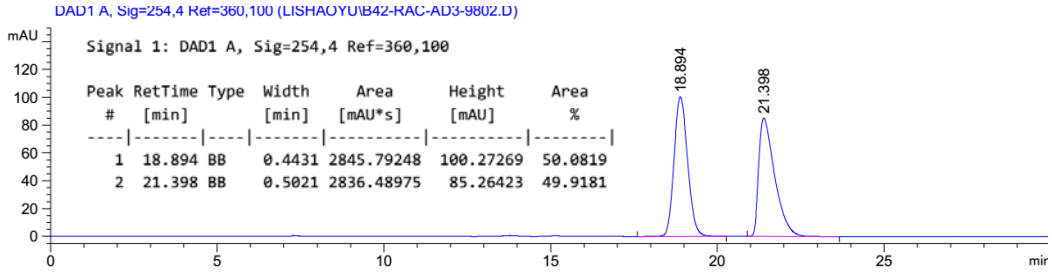
**$^{13}$C NMR (125 MHz, $CDCl_3$)** δ 162.02 (d, *J* = 245 Hz), 147.43, 143.77, 133.56 (d, *J* = 3.7 Hz), 131.45, 131.42, 130.94 (d, *J* = 7.5 Hz), 126.49, 126.17, 115.31 (d, *J* = 22.5 Hz), 58.93, 37.66, 29.88, 18.28.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -115.47.

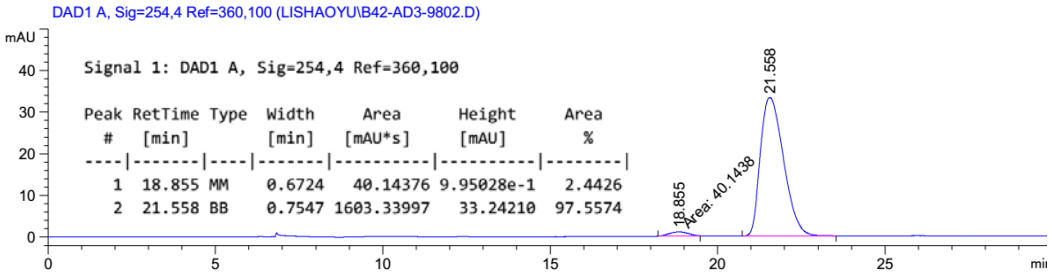
**HRMS (ESI)** calcd for [M-H] $C_{31}H_{25}O_2F_2$, m/z: 467.1828, found: 467.1830.

**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 98/2, 0.5 mL/min, λ = 254 nm, $t_R$ (minor) = 18.8 min, $t_R$ (major) = 21.5 min, ee = 95%.

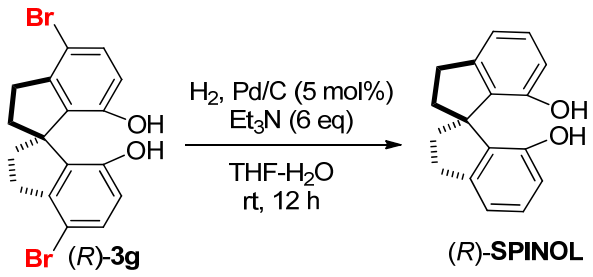
*Chiral HPLC spectrum of racemic **3s***




*Chiral HPLC spectrum of **(S)-3s***

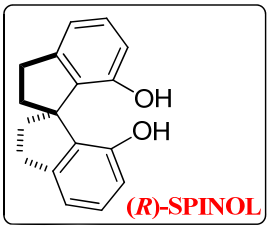


# Confirmation of the Absolute Configuration




According to the reference[5], to a vial with a magnetic stirring bar were added (*R*)-**3g** with 95% ee (0.2 mmol), Pd/C (5 mol%), $Et_3N$ (1.2 mmol), THF (6 mL) and $H_2O$ (3 mL). Then the mixture was stirred under hydrogen atmosphere at room temperature for 12 hours. After completion of the reaction monitored by TLC, the catalyst was filtrated off and the solution was diluted with 60 mL of EA, washed with saturated brine for two times and dried over $Na_2SO_4$. The organic phase was concentrated and further purified by flash chromatography eluted with PE/EA = 6/1 to afford the product (*R*)-**SPINOL** in 98% yield with 95% ee.

The absolute configuration of this product proved to be "***R***" by comparison of chiral HPLC spectra with the known (*R*)-SPINOL and (*S*)-SPINOL purchased from Daicel Chiral Technologies Company (China).




**(*R*)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-SPINOL)**

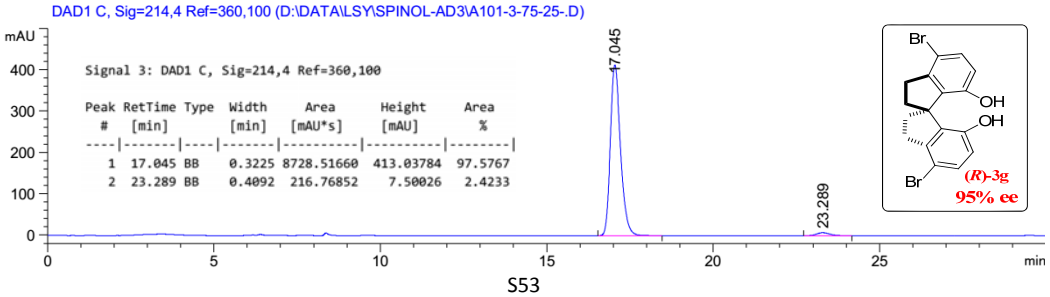
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.16 (dd, *J* = 8.0, 7.2 Hz, 2H), 6.88 (d, *J* = 7.2 Hz, 2H), 6.66 (d, *J* = 8.0 Hz, 2H), 4.66 (s, 2H), 3.07-2.96 (m, 4H), 2.32-2.14 (m, 4H).

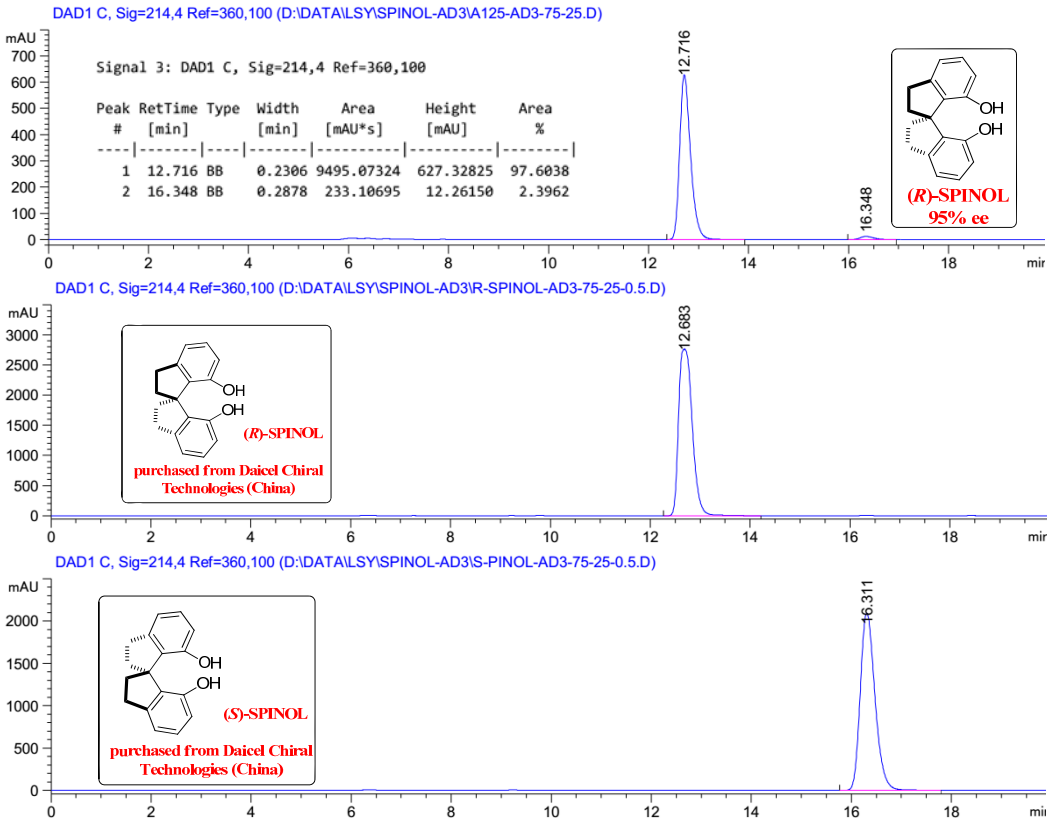
**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 153.07, 145.98, 130.66, 130.00, 117.81, 114.42, 57.60, 37.55, 31.36.

**HRMS (ESI)** calcd for [M-H] $C_{17}H_{15}O_2$, m/z: 251.1078, found: 251.1076.

**(*R*)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol**

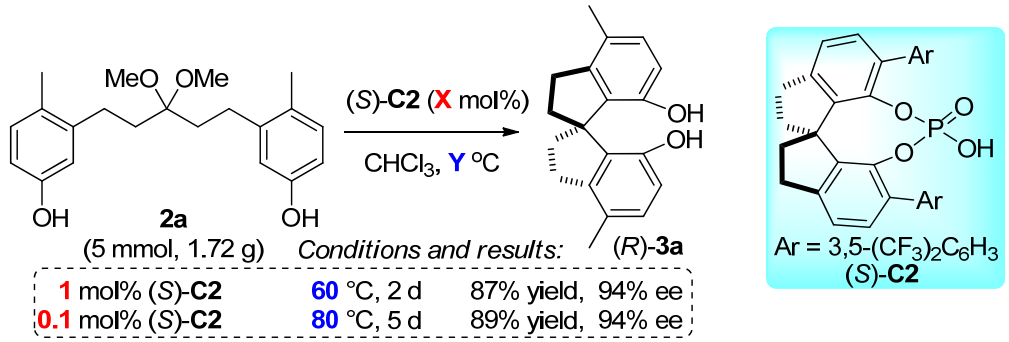
**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 12.7 min, $t_R$ (minor) = 16.3 min, ee = 95%.






# Gram Scale Reactions and recrystallization experiment

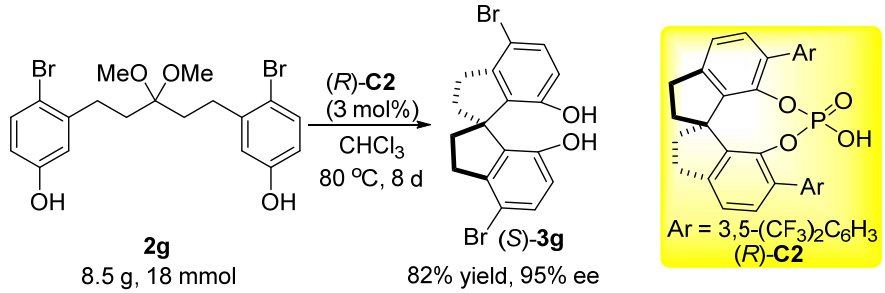
## (a) Synthesis of (*R*)-3a




Under argon atmosphere, to a 250 mL of oven-dried ***pressure Schlenk bottle (purchased from Beijing Synthware Glass)*** with a magnetic stirring bar were added **2a** (1.72 g, 5.0 mmol), (*S*)-**C2** (37 mg, 0.05 mmol) and 150 mL of anhydrous $CHCl_3$. Then the sealed reaction was stirred at 60℃ for two days. After completion of the reaction monitored by TLC, the solvent was evaporated and the residue was purified by flash chromatography eluted with PE/EA = 6/1 to afford the product (*R*)-**3a** in 87% yield with 94% ee value.

When the reaction proceeded at 80℃ for five days in the presence of 0.1 mol% of (*S*)-**C2**, product (*R*)-**3a** could be obtained in 89% yield with 94% ee value.

## (b) Synthesis of (*S*)-3g and a resolution to enrich to 99% ee




**2g**
8.5 g, 18 mmol

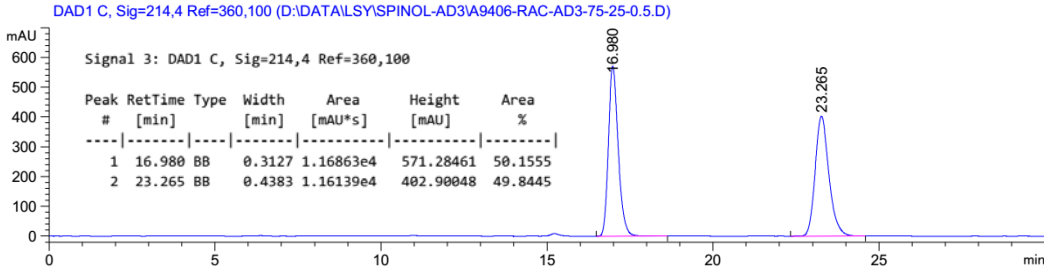
Br (*S*)-**3g**
82% yield, 95% ee

Under argon atmosphere, to a 500 mL of oven-dried ***pressure Schlenk bottle (purchased from Beijing Synthware Glass)*** with a magnetic stirring bar were added **2g** (8.5 g, 18.0 mmol), (*R*)-**C2** (400 mg, 0.54 mmol) and 400 mL of anhydrous $CHCl_3$. Then the sealed reaction was stirred at 80℃ for eight days. After completion of the reaction monitored by TLC, the solvent was evaporated and the residue was purified by flash chromatography eluted with PE/EA = 6/1 to afford the product (*S*)-**3g** in 82% yield with 95% ee value.

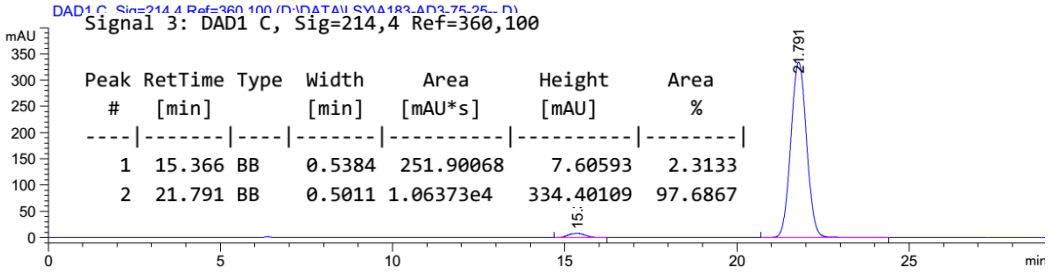
The product **3g** with 95% ee was recrystallized once with hexane/ethyl acetate (50/1), enantiopure product **3g** with >99% ee could be obtained in 89% yield.

**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 16.9 min, $t_R$ (major) = 23.2 min, ee = 95%. After once recrystallization, ee > 99%

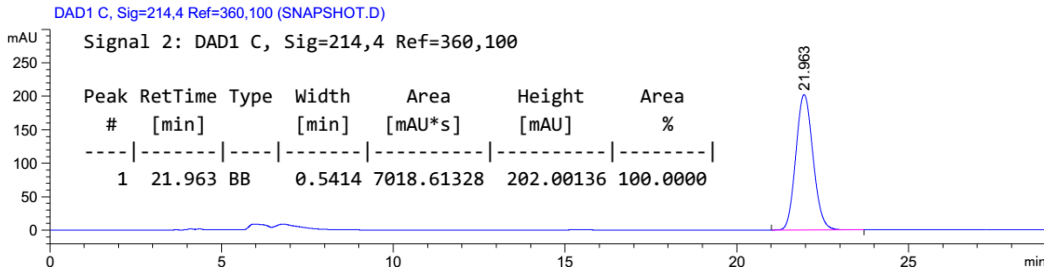
*Chiral HPLC spectrum of racemic **3g***



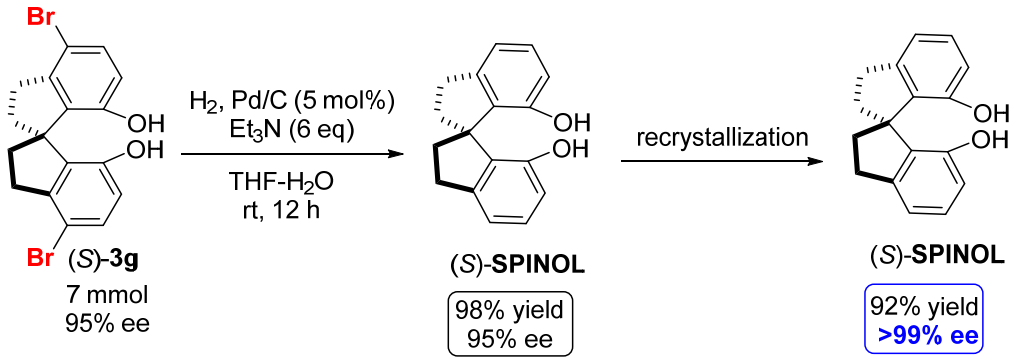

*Chiral HPLC spectrum of (S)-**3g***




*Chiral HPLC spectrum of (S) -**3g*** after recrystallization



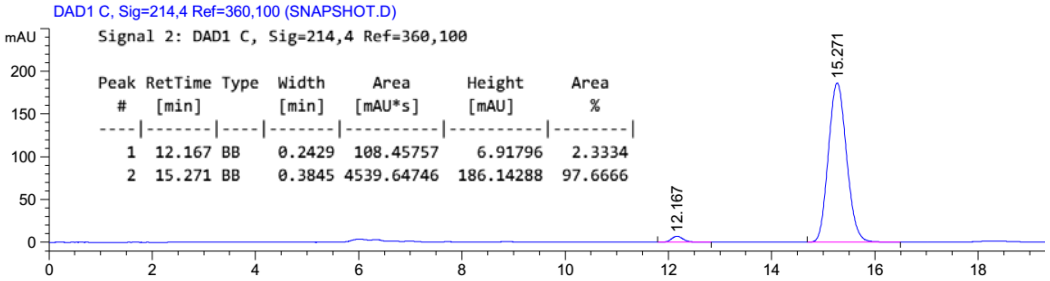
## (c) Synthesis of (*S*)-SPINOL via debromination



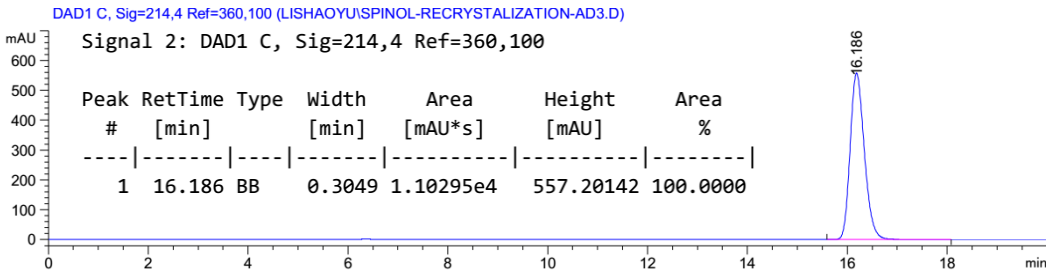

According to the reference[5], to a vial with a magnetic stirring bar were added (*S*)-**3g** with 95% ee (7.0 mmol), Pd/C (5 mol%), $Et_3N$ (42.0 mmol), THF (60 mL) and $H_2O$ (30 mL). Then the mixture was stirred under hydrogen atmosphere at room temperature for 12 hours. After completion of the reaction monitored by TLC, the catalyst was filtrated off and the solution was evaporated to remove THF, then diluted with 100 mL of EA, washed with saturated brine for two times and dried over $Na_2SO_4$. The organic phase was concentrated and further purified by flash chromatography eluted with PE/EA = 6/1 to afford the product (*S*)-**SPINOL** in 98% yield with 95% ee, which was recrystallized with hexane/EA (50:1) to afford the optically pure (*S*)-**SPINOL** (yield = 92%, ee > 99%).

**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 75/25, 0.5 mL/min, λ = 214 nm, $t_R$ (minor) = 12.1 min, $t_R$ (major) = 15.2 min, ee = 95%. After recrystallization, ee > 99%

*Chiral HPLC spectrum of (S)-**SPINOL***

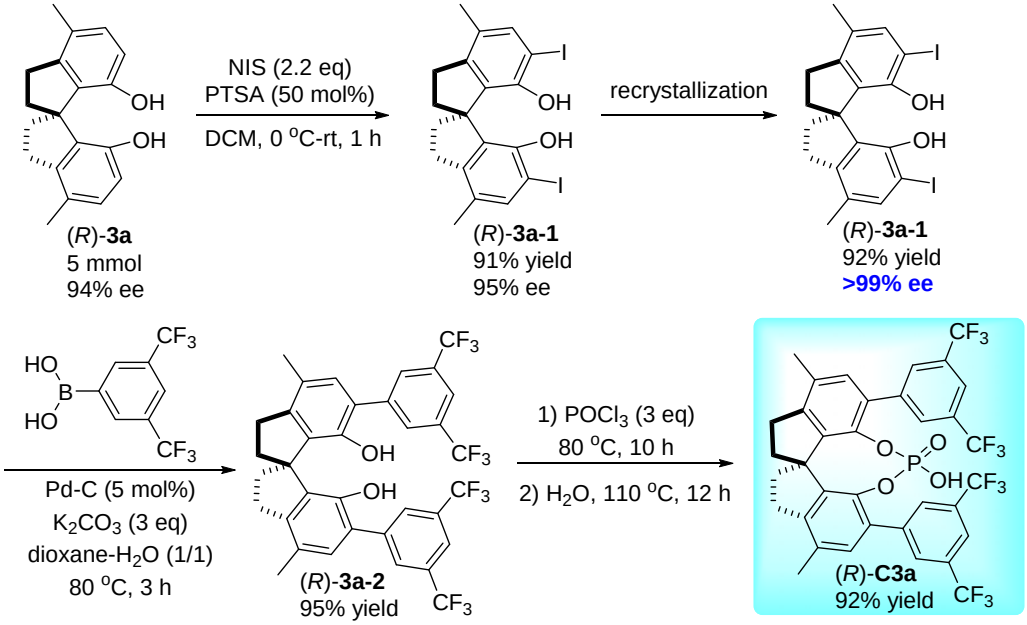



*Chiral HPLC spectrum of (S)-**SPINOL*** after recrystallization



# Synthesis and application of SPINOL-phosphoric acid derivative (*R*)-C3a.

## (a) Synthesis of (*R*)-C3a




**Synthesis of (R)-6,6'-diiodo-4,4'-dimethyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3a-1)**

Under argon atmosphere, to a solution of (*R*)-**3a** (5.0 mmol, 94% ee) in DCM (50 mL) was added PTSA (2.5 mmol). When the mixture was cooled to 0℃, NIS (11.0 mmol) was added to the reaction during 15 minutes. Then the mixture was stirred at room temperature for about 2 hours. After completion of the reaction monitored by TLC, 20 mL of saturated $Na_2S_2O_3$ was added to quench the reaction. The separated organic phase was dried over $Na_2SO_4$ and concentrated to obtain the crude product (*R*)-**3a-1**, which was purified by flash chromatography eluted with PE/EA = 10/1 to afford 2.42 g of (*R*)-**3a-1** as a white solid in 91% yield with 95% ee. After recrystallization with hexane/EA(v/v=50:1), 2.23 g of optically pure (*R*)-**3a-1** was obtained (yield=92%, ee>99%).

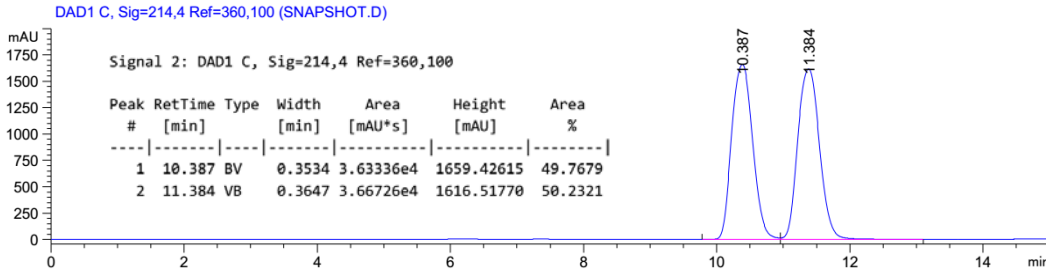
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.35 (s, 2H), 4.97 (s, 2H), 2.97-2.79 (m, 4H), 2.31-2.18 (m, 10H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 149.30, 145.26, 137.98, 132.36, 128.45, 83.12, 60.39, 37.60, 29.99, 17.97.

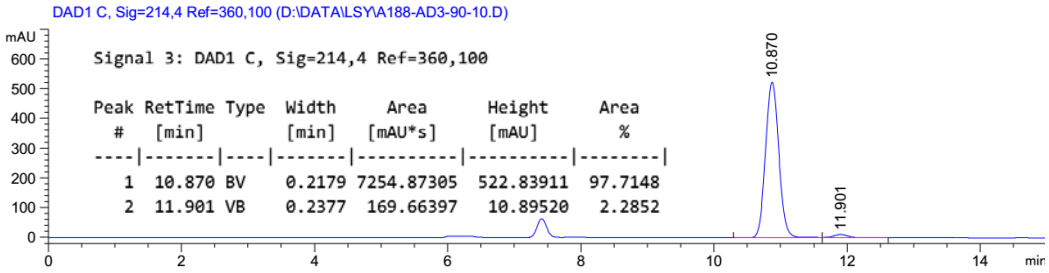
**HRMS (ESI)** calcd for [M-H] $C_{19}H_{17}O_2I_2$, m/z: 530.9323, found: 530.9323.

**HPLC analysis**: HPLC DAICEL CHIRALCEL AD-3, hexane/isopropanol = 90/10, 0.5 mL/min, λ = 214 nm, $t_R$ (major) = 10.45 min, $t_R$ (minor) = 11.46 min, ee = 95%. After recrystallization: ee > 99%.

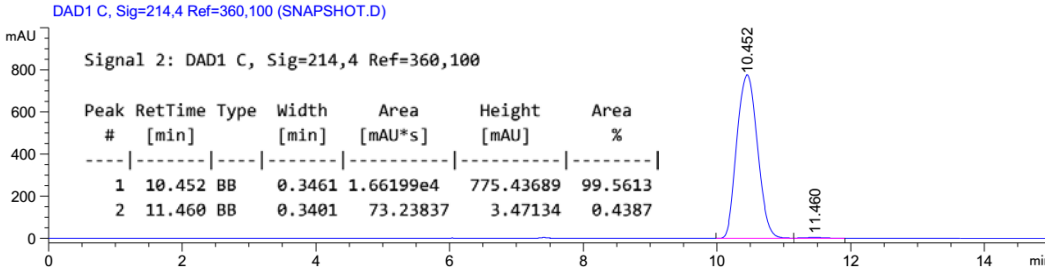
*Chiral HPLC spectrum of racemic* ***(R)-3a-1***




*Chiral HPLC spectrum of* ***(R)-3a-1***




*Chiral HPLC spectrum of* ***(R)-3a-1*** after recrystallization




**Synthesis of (*R*)-6,6'-bis(3,5-bis(trifluoromethyl)phenyl)-4,4'-dimethyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol ((*R*)-3a-2)**

According the reference[4], under argon atmosphere, (*R*)-**3a-1** (3.0 mmol), 10% Pd/C (0.06 mmol), 3,5-Bis(trifluoromethyl)benzeneboronic acid (10.5 mmol), $K_2CO_3$ (10.5 mmol), 1,4-dioxane (30 mL) and $H_2O$ (30 mL) were added in sequence to a 100 mL Schlenk tube with a magnetic stirring bar. Then the reaction proceeded at 80℃ for 3 hours. After completion of the reaction, the mixture was filtrated through kieselguhr and evaporated to remove 1,4-dioxane. Subsequently, the mixture was diluted with 100 mL of EA and 20 mL of 10 wt% aqueous HCl. The organic phase was washed with brine, dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by flash chromatography eluted with PE/EA = 10/1 to afford the coupling product (*R*)-**3a-2** as a white solid (2.0 g, 95% yield).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.98 (s, 4H), 7.78 (s, 2H), 7.10 (s, 2H), 4.84 (s, 2H), 3.10-2.95 (m, 4H), 2.49-2.44 (m, 2H), 2.38-2.44 (m, 8H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 147.78, 145.46, 139.82, 132.12, 131.40 (q, $J$ = 33 Hz), 130.46, 129.48, 127.64, 124.64, 123.46 (q, $J$ = 271 Hz), 120.53(q, $J$ = 3.8 Hz), 58.58, 37.57, 29.93, 18.20.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -62.83.

**HRMS (ESI)** calcd for [M-H] $C_{35}H_{23}O_2F_{12}$, m/z: 703.1512, found: 703.1509.

**Synthesis of (*R*)-1,10-bis(3,5-bis(trifluoromethyl)phenyl)-12-hydroxy-3,8-dimethyl-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide ((*R*)-C3a)**

Under argon atmosphere, $POCl_3$ (6.0 mmol) was added to the solution of (*R*)-**3a-2** (2.0 mmol) in pyridine (10 mL) at 0°C, then the mixture was heated to 80°C for 10 h. After the mixture was cooled to 0°C, water (10 mL) was added very slowly. Then the mixture was heated with stirring at 100 °C for another 12 h. Next it was cooled to 0°C and diluted with DCM (100 mL), washed with 30 mL of 3N HCl. The organic layer was separated, and the aqueous layer was extracted with DCM (2×30 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated. The residue was purified by silica gel column chromatography (DCM/MeOH = 20:1). The obtained CPA was redissolved in DCM (100 mL) and treated with 50 mL of 3 M HCl. The mixture was stirred vigorously for 1 h. The organic layer was separated, dried over $Na_2SO_4$, and evaporated to give the desired catalyst (*R*)-**C3a** as a white solid (1.41 g, 92% yield).

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.82 (s, 4H), 7.56 (s, 2H), 7.01 (s, 2H), 2.99-2.85 (m, 4H), 2.32-2.18 (m, 10H).

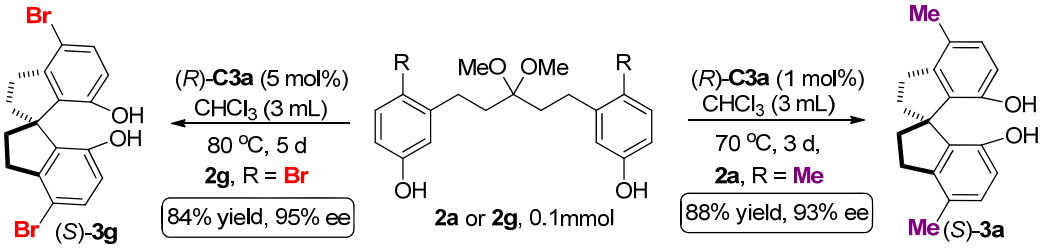
**$^{13}$C NMR (101 MHz, $CDCl_3$)** δ 145.46, 140.63, 140.58, 131.92, 131.80, 131.76, 131.02 (q, $J$ = 33 Hz), 130.92, 129.59, 123.40 (q, $J$ = 271 Hz), 120.11, 60.31, 38.35, 29.12, 18.30.

**$^{19}$F NMR (376 MHz, $CDCl_3$)** δ -62.76.

**$^{31}$P NMR (162 MHz, $CDCl_3$)** δ -8.08.

**HRMS (ESI)** calcd for [M-H] $C_{35}H_{22}O_4F_{12}P$, m/z: 765.1070, found: 765.1065.

## (b) Application of (*R*)-C3a

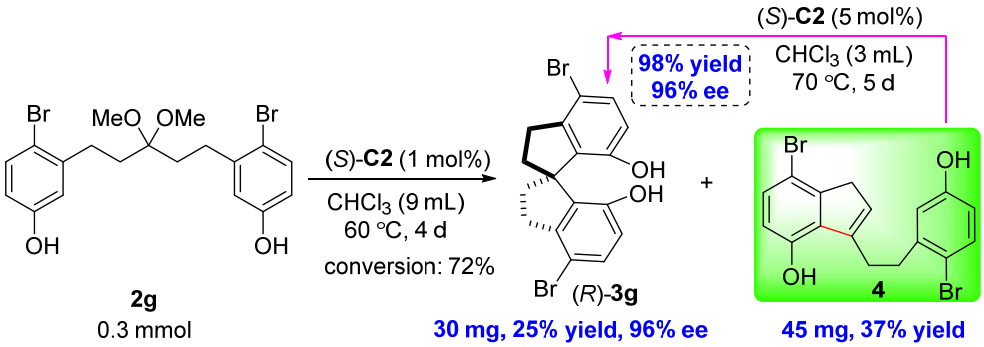



Under argon atmosphere, to a 10 mL of oven-dried pressure Schlenk tube (purchased from Beijing Synthware Glass) with a magnetic stirring bar were added **2a** (0.1 mmol), (*R*)-**C3a** (1 mol%) and 3 mL of anhydrous $CHCl_3$. Then the sealed reaction was stirred at 70℃ (the temperature of oil bath) for three days. After completion of the reaction monitored by TLC, the solvent was evaporated and the residue was purified by flash chromatography eluted with PE/EA = 6/1 to afford the product (*S*)-**3a** in 88% yield with 93% ee value.

In addition, the (*S*)-**3g** could be isolated in 84% yield with 95% ee value in presence of 5 mol% of (*R*)-**C3a** at 80℃ for five days.

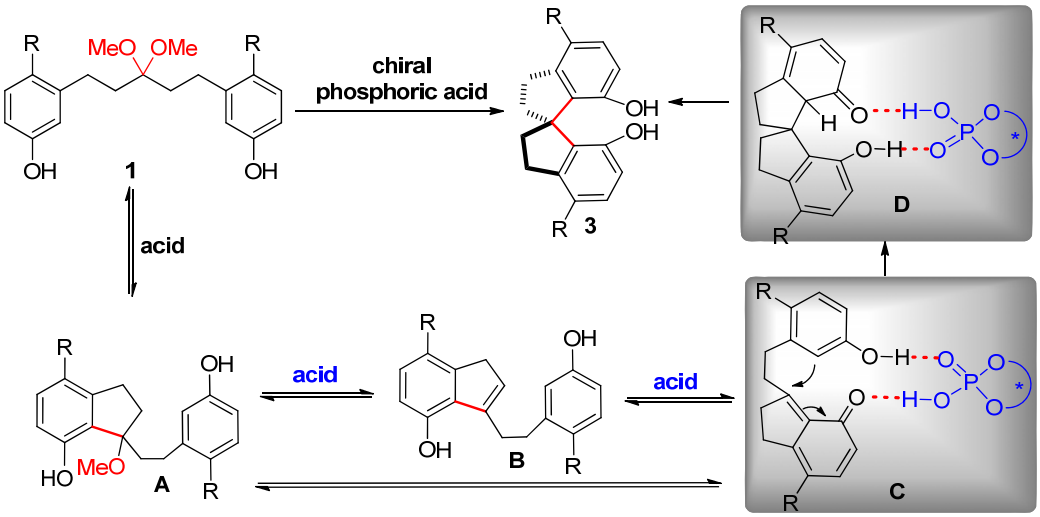
# Investigation of the Reaction Mechanism

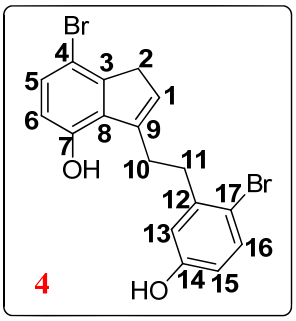
## Scheme S3: Isolation of the key intermediate and control experiment




To gain further insight into the reaction mechanism, control experiments were tested to rationalize the current reaction process and its stereochemistry. When ketal **2g** was conducted under the similar reaction conditions by using 1 mol% of catalyst (*S*)-**C2** for just four days, the key intermediate **4** was formed in 37% yield and accompanied with formation of the desired product in 25% yield with 96% ee (Scheme S3). The structure of intermediate **4** has been confirmed through the spectra of $^{1}$H-NMR, $^{13}$C-NMR, H-H COSY and NOESY. Furthermore, treating the intermediate **4** with 5 mol% of (*S*)-**C2** at 70 $^{o}$C for five days, the final product (*R*)-**3g** was formed in almost quantitative yield with the same enantioselectivity (Scheme S2). On the basis of the above observations and previous reports,[6,7] the reaction may initially form an intermediate **B** in situ generated from **A** and further go through an active o-QM intermediate **C** to deliver the SPINOL derivatives. The excellent stereocontrol was attributed to the simultaneous interaction between the bifunctional phosphoric acid and intermediate C via hydrogen bonding (Scheme S4).

## Scheme S4: Proposed Concept for Enantioselective Axially Chiral SPINOLs



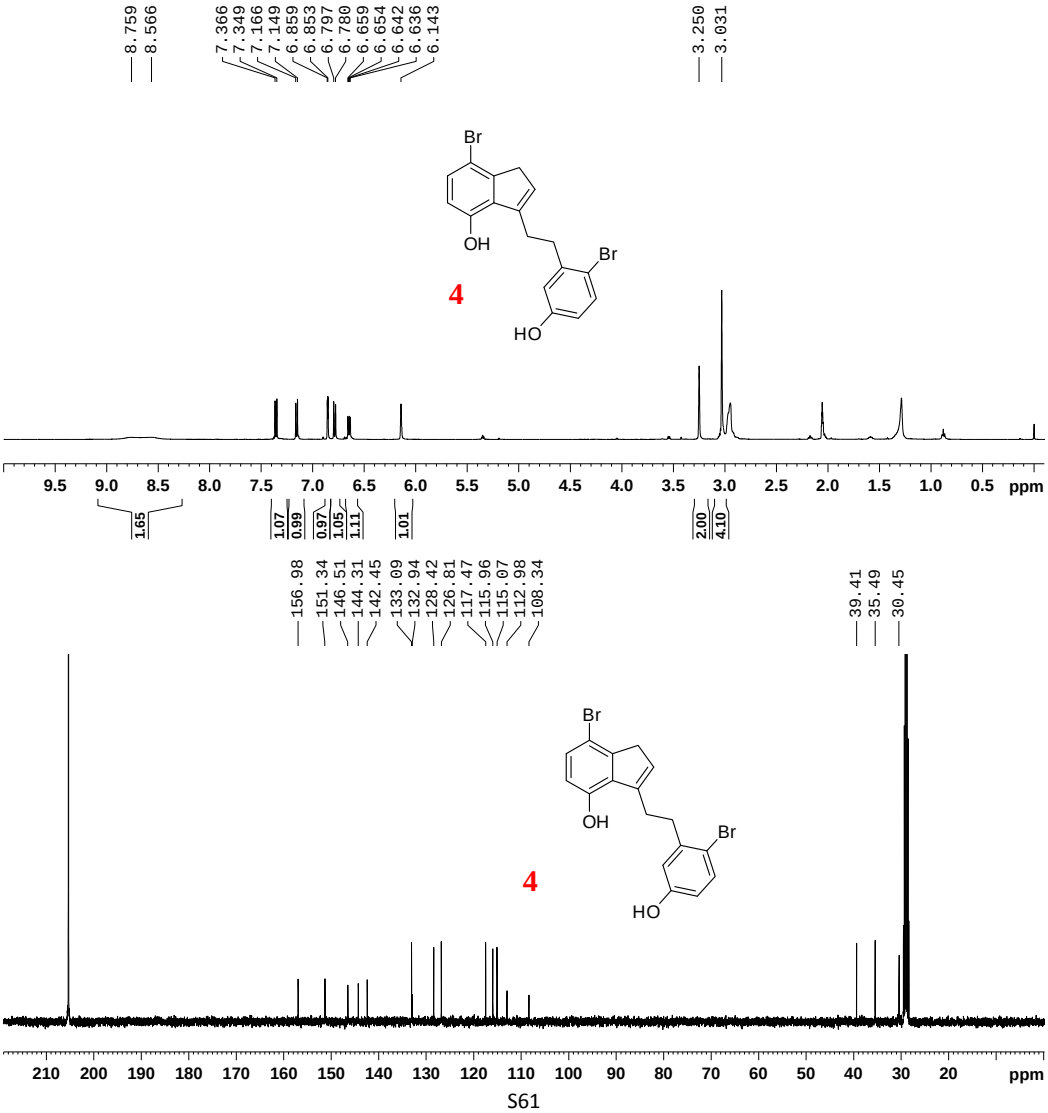



**7-bromo-3-(2-bromo-5-hydroxyphenethyl)-1H-inden-4-ol (4)**

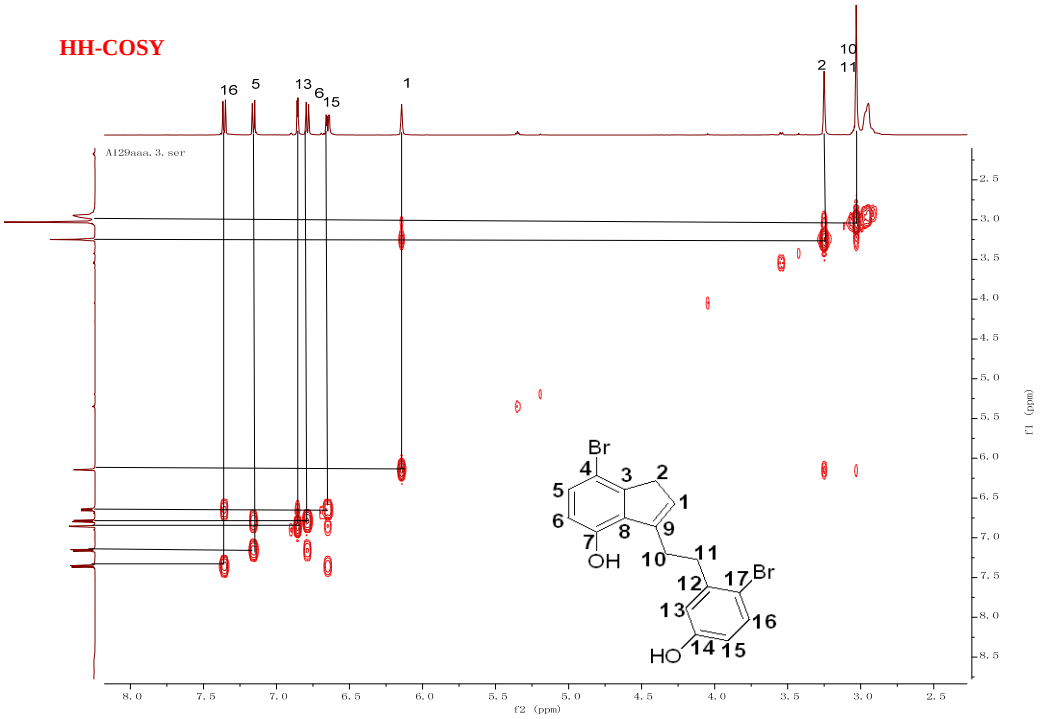
**$^{1}$H NMR (500 MHz, Acetone-d6)** δ 8.76 (s, 1H), 8.57 (s, 1H), 7.36 (d, J = 8.5 Hz, 1H), 7.15 (d, J = 8.5 Hz, 1H), 6.85 (d, J = 3.0 Hz, 1H), 6.79 (d, J = 8.5 Hz, 1H), 6.65 (dd, J = 8.5, 3.0 Hz, 1H), 6.14 (s, 1H), 3.25 (s, 2H), 3.03 (s, 4H).

**$^{13}$C NMR (100 MHz, Acetone-d6)** δ 156.98, 151.34, 146.51, 144.31, 142.45, 133.09, 132.94, 128.42, 126.81, 117.47, 115.96, 115.07, 112.98, 108.34, 39.41, 35.49, 30.45.

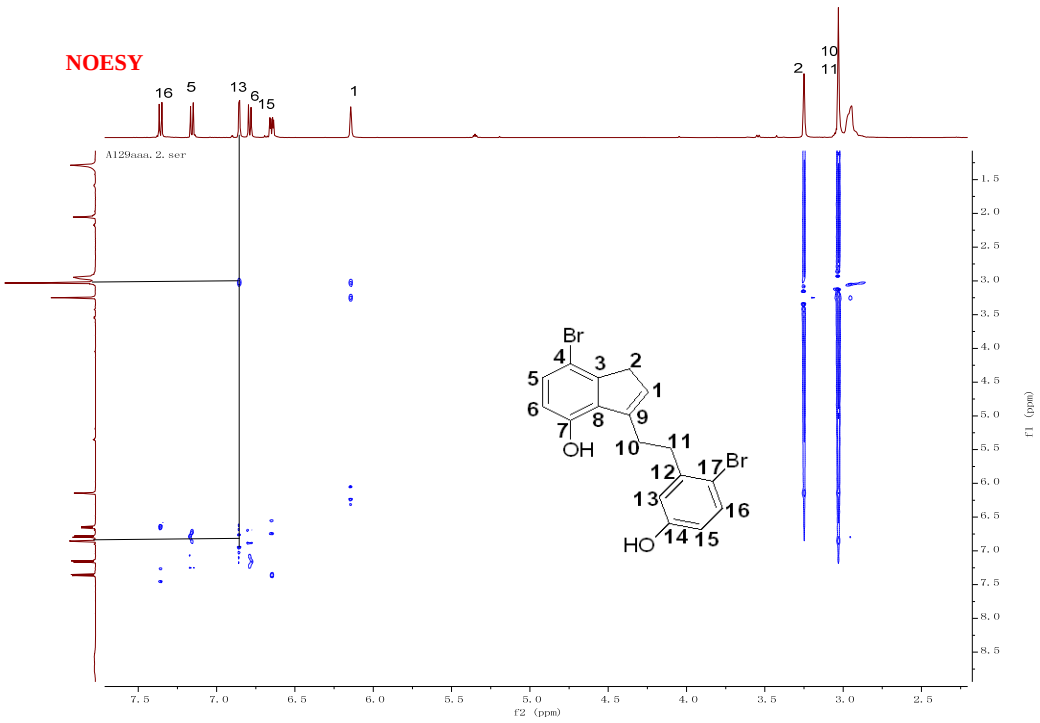
**HRMS (ESI)** calcd for [M-H] $C_{18}H_{15}O_4Br_2$, m/z: 408.9256, found: 408.9264.



**HH-COSY**




**NOESY**



# References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(4) Xu, F.; Huang, D.; Han, C.; Shen, W.; Lin, X.; Wang, Y. *J. Org. Chem.* **2010**, *75*, 8677.

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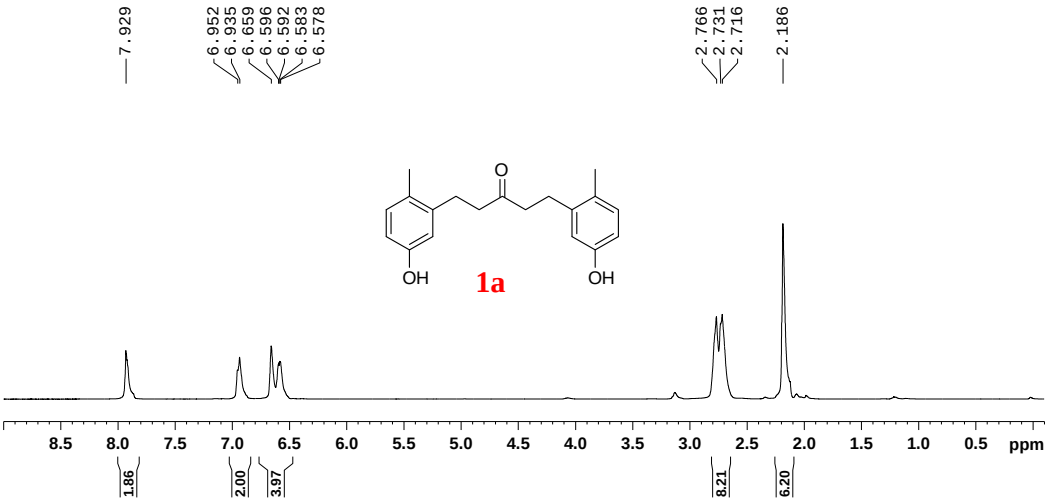
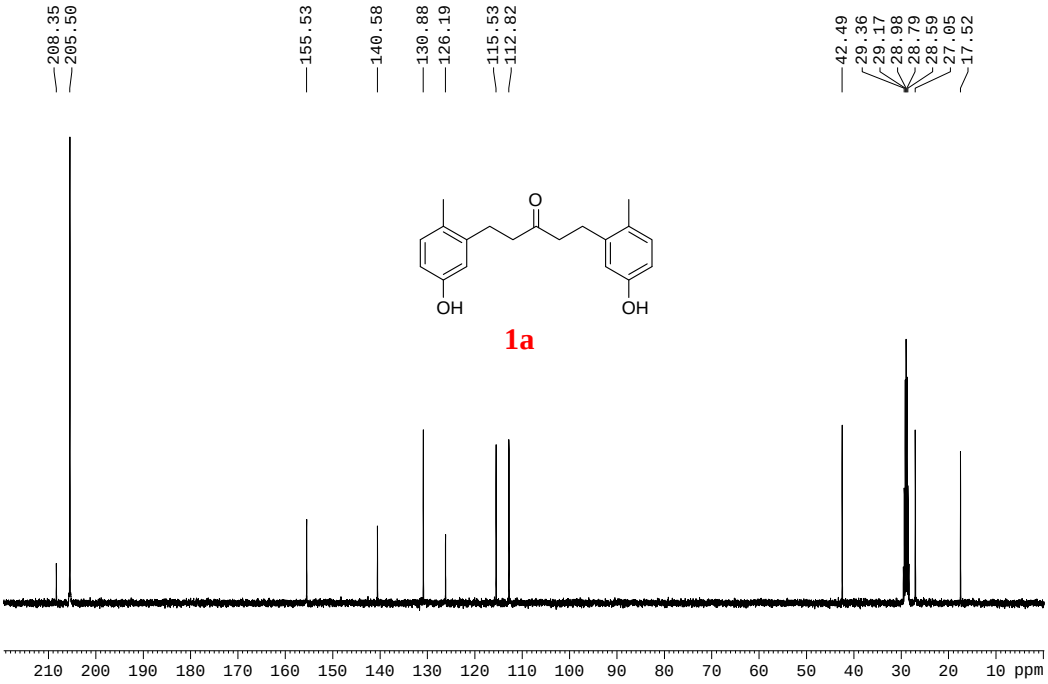
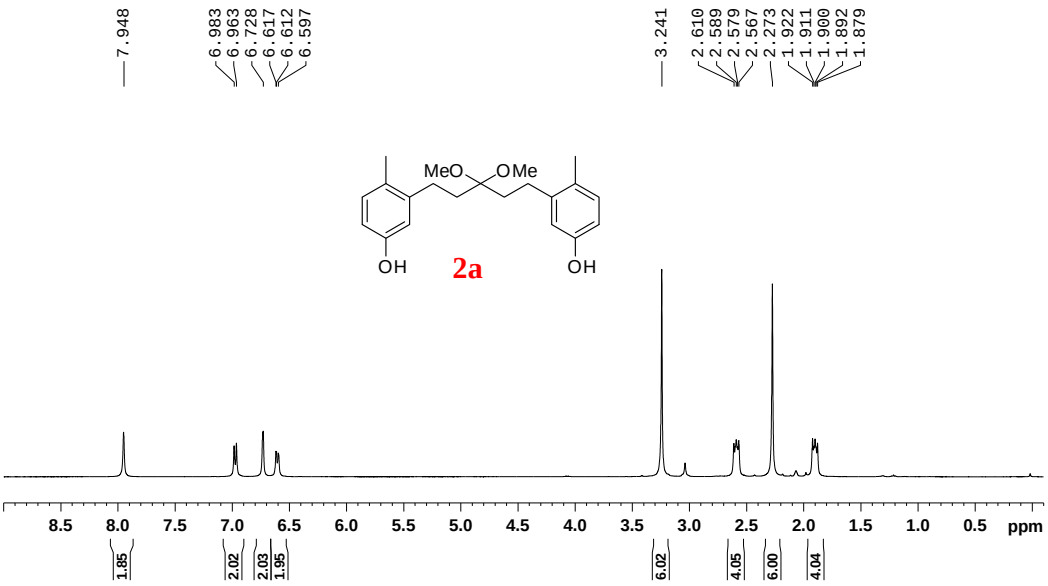
(6) Zhao, W.; Wang, Z.; Chu, B.; Sun, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 1910.

(7) Wang, Z.; Ai, F.; Wang, Z.; Zhao, W.; Zhu, G.; Lin, Z.; Sun, J. *J. Am. Chem. Soc.* **2015**, *137*, 383.

# Copies of $^{1}H$ and $^{13}C$ NMR Spectra of Substrates 1 and 2

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6.597
3.241
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2.589
2.579
2.567
2.273
1.922
1.911
1.900
1.892
1.879
MeO
OMe
OH
OH
2a
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
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ppm
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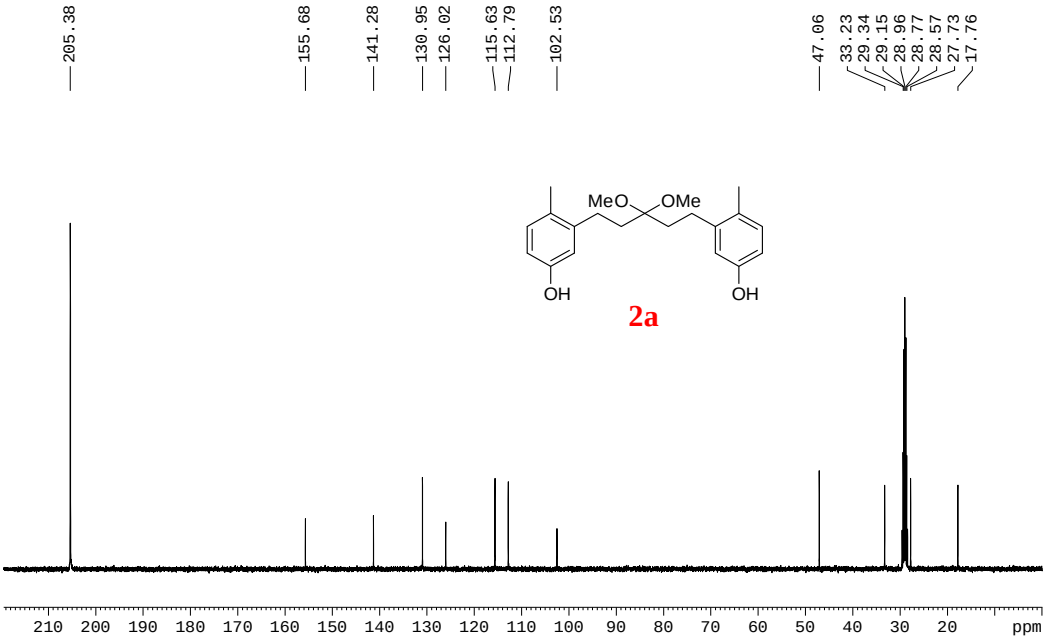
2.02
2.03
1.95
6.02
4.05
6.00
4.04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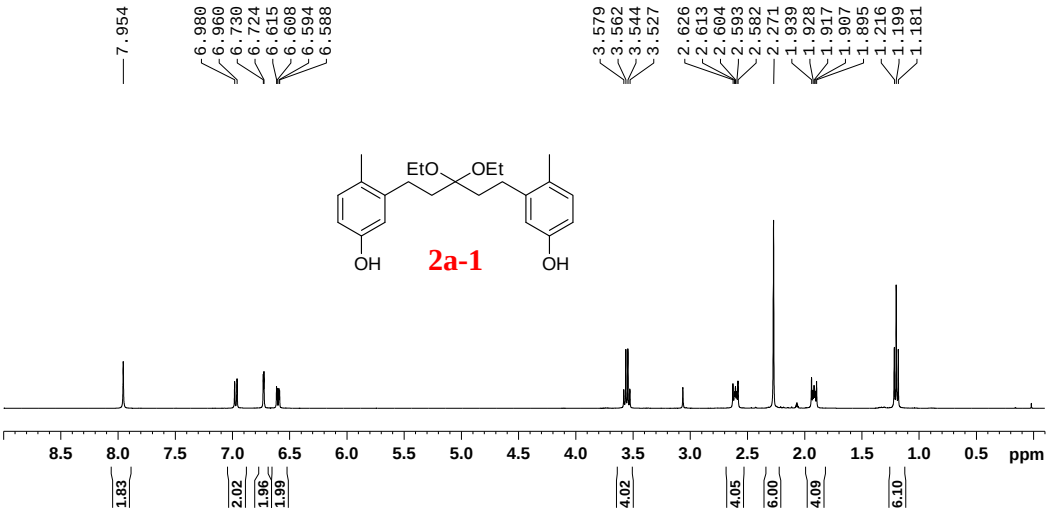
130.95
126.02
115.63
112.79
102.53
47.06
33.23
29.34
29.15
28.96
28.77
28.57
27.73
17.76
MeO
OMe
OH
OH
2a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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6.960
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6.594
6.588
3.579
3.562
3.544
3.527
2.626
2.613
2.604
2.593
2.582
2.271
1.939
1.928
1.917
1.907
1.895
1.216
1.199
1.181
EtO
OEt
OH
OH
2a-1
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
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0.5
ppm
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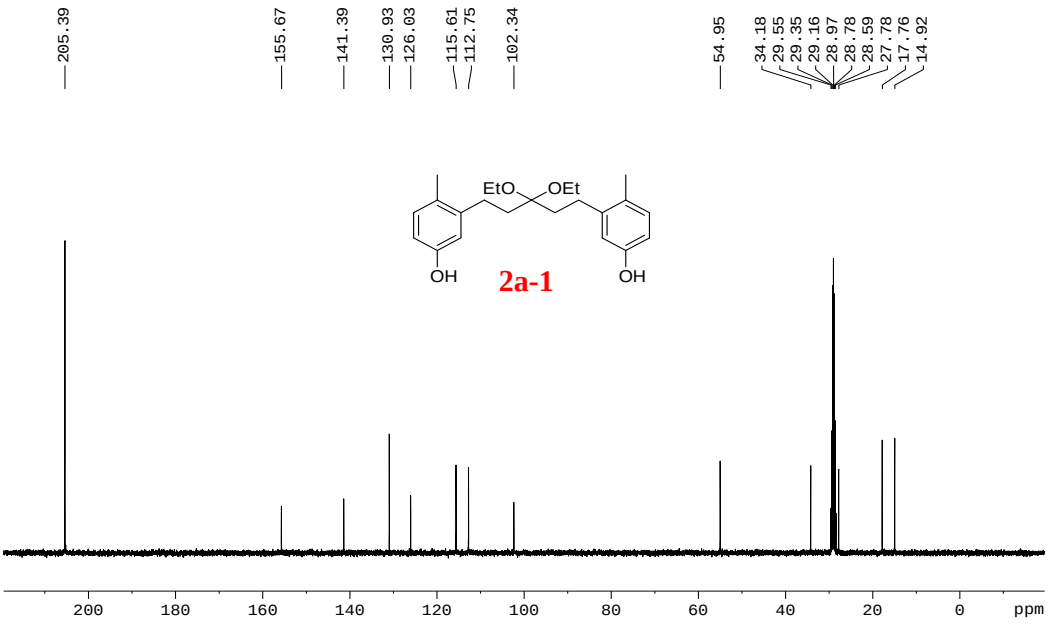
1.96
1.99
4.02
4.05
6.00
4.09
6.10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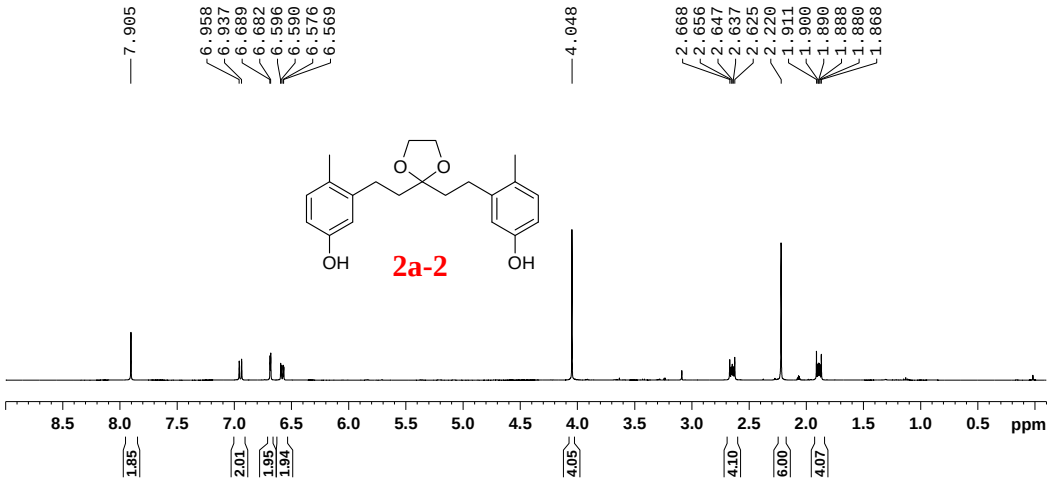
112.75
102.34
54.95
34.18
29.55
29.35
29.16
28.97
28.78
28.59
27.78
17.76
14.92
EtO
OEt
OH
OH
2a-1
200
180
160
140
120
100
80
60
40
20
0
ppm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6.937
6.689
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6.590
6.576
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4.048
2.668
2.656
2.647
2.637
2.625
2.220
1.911
1.900
1.890
1.888
1.880
1.868
OH
OH
2a-2
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
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1.0
0.5
ppm
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2.01
1.95
1.94
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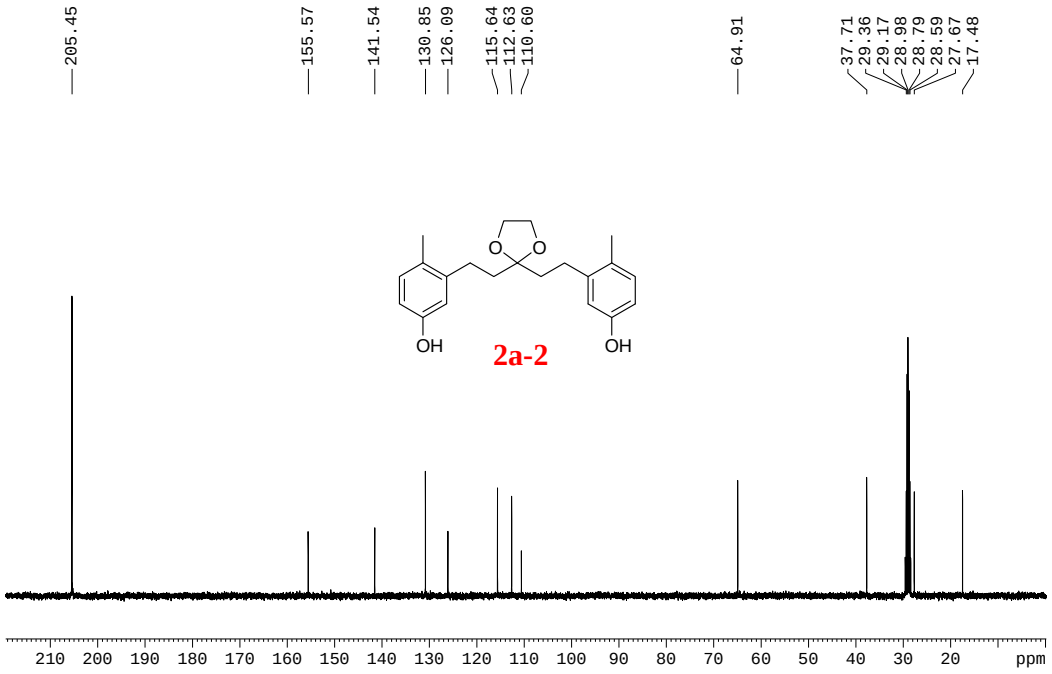
4.10
6.00
4.07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126.09
115.64
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110.60
64.91
37.71
29.36
29.17
28.98
28.79
28.59
27.67
17.48
OH
OH
2a-2
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200
190
180
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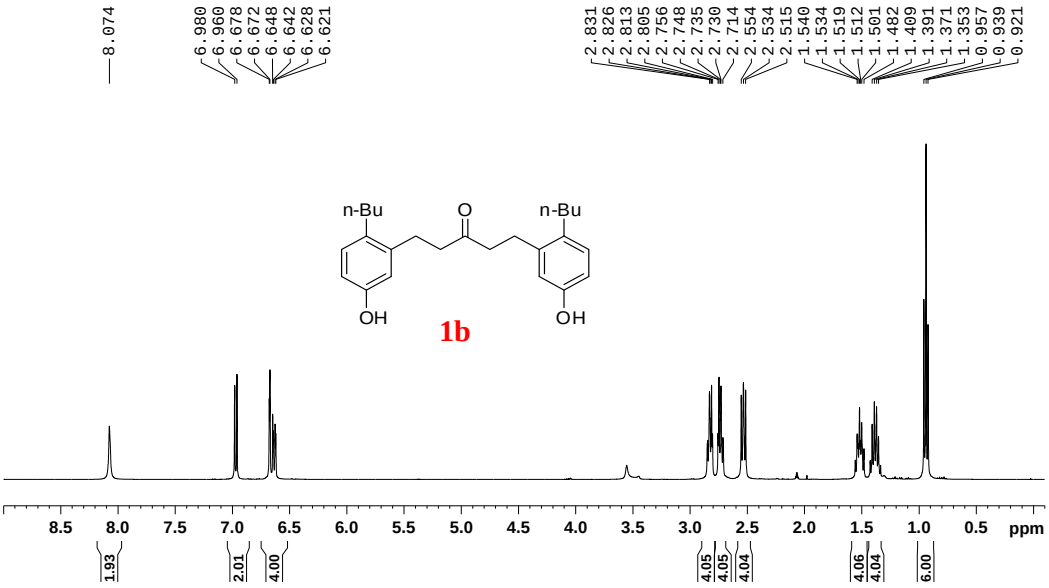
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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6.678
6.672
6.648
6.642
6.628
6.621
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2.826
2.813
2.805
2.756
2.748
2.735
2.730
2.714
2.554
2.534
2.515
1.540
1.534
1.519
1.512
1.501
1.482
1.409
1.391
1.371
1.353
0.957
0.939
0.921
n-Bu
O
n-Bu
OH
OH
1b
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
0.5
ppm
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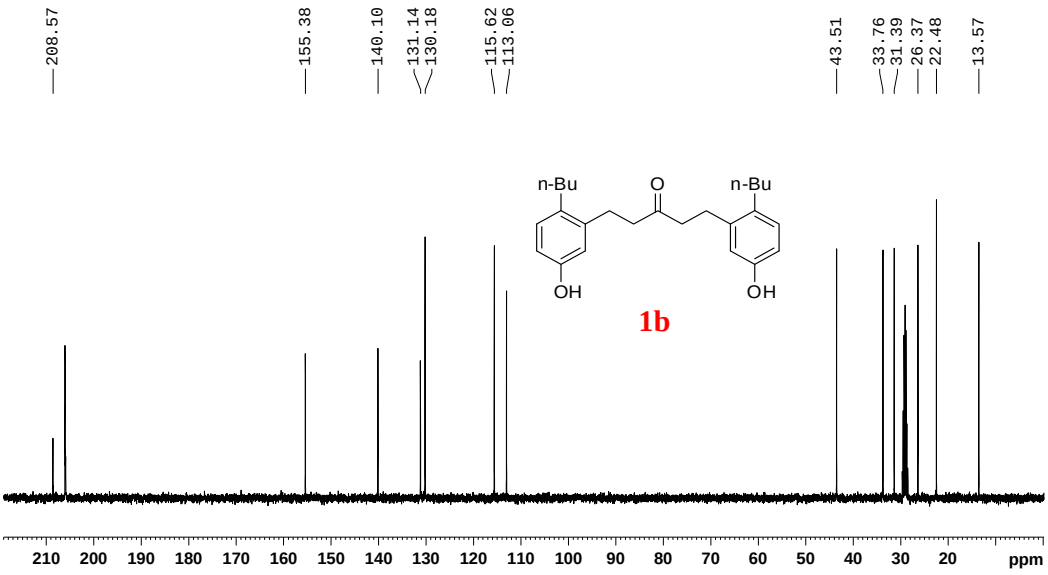
4.00
4.05
4.05
4.04
4.06
4.04
6.00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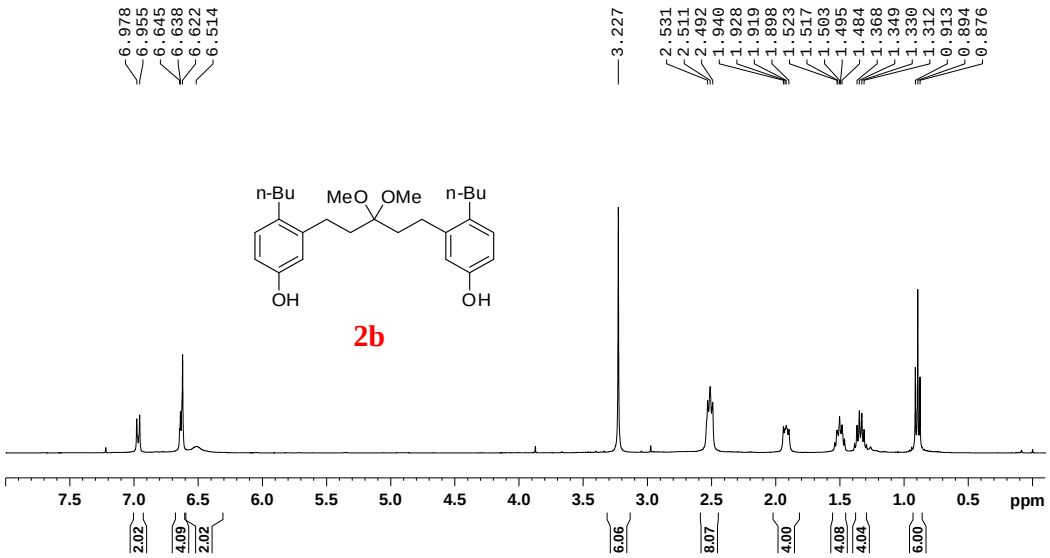
155.38
140.10
131.14
130.18
115.62
113.06
43.51
33.76
31.39
26.37
22.48
13.57
n-Bu
O
n-Bu
OH
OH
1b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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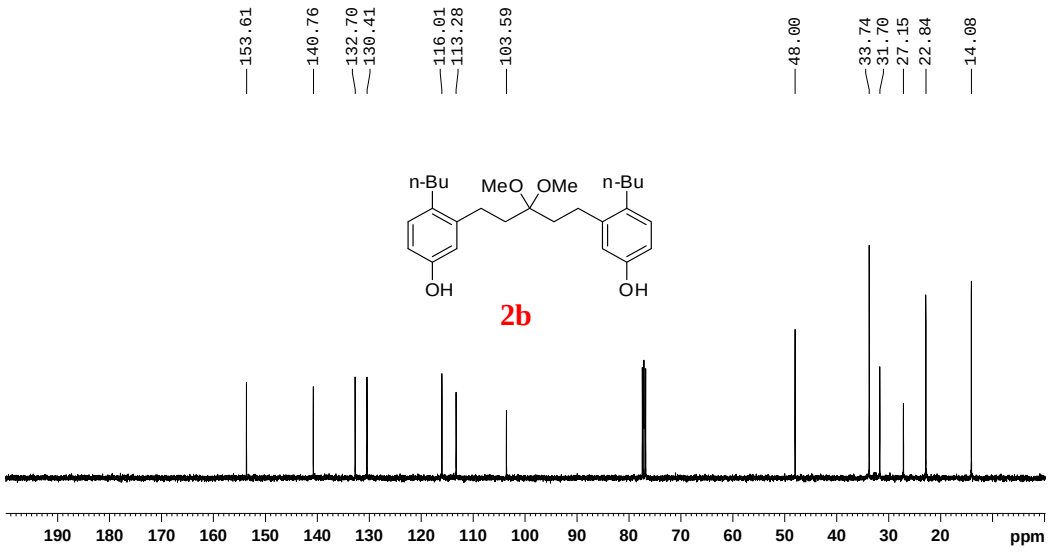
6.645
6.638
6.622
6.514
3.227
2.531
2.511
2.492
1.940
1.928
1.919
1.898
1.523
1.517
1.503
1.495
1.484
1.368
1.349
1.330
1.312
0.913
0.894
0.876
n-Bu
MeO
OMe
n-Bu
OH
OH
2b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.02
4.09
2.02
6.06
8.07
4.00
4.08
4.04
6.00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140.76
132.70
130.41
116.01
113.28
103.59
48.00
33.74
31.70
27.15
22.84
14.08
n-Bu
MeO
OMe
n-Bu
OH
OH
2b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

8.397
7.397
7.380
7.361
7.319
7.316
7.300
7.261
7.258
7.241
7.021
7.001
6.790
6.784
6.779
6.773
6.759
6.753
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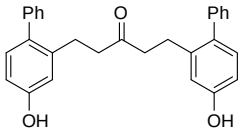
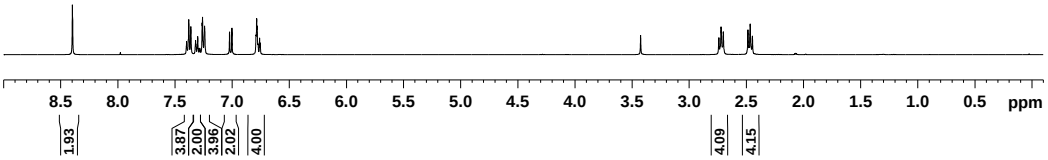
2.721
2.700
2.485
2.465
2.446


Ph
O
Ph
OH
OH

**1c**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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
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ppm
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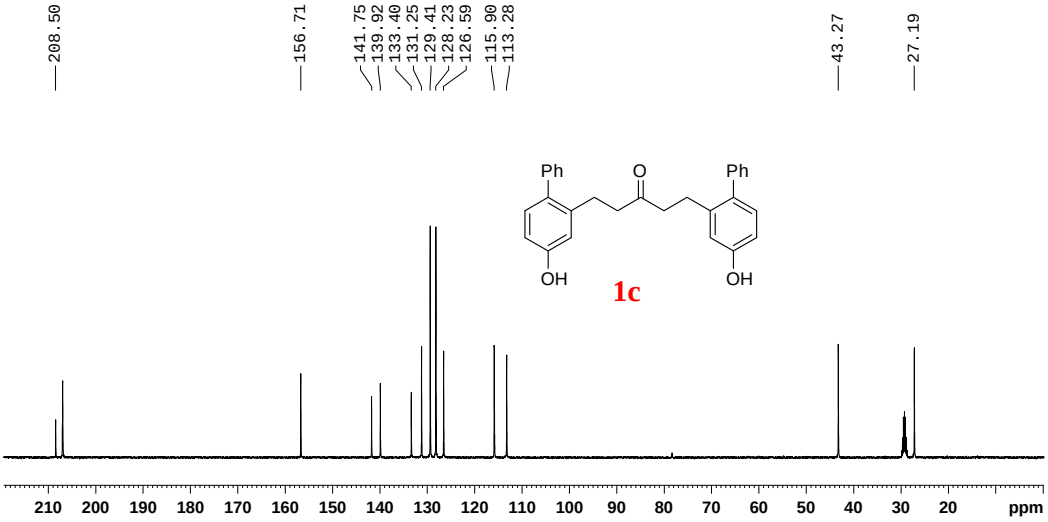
2.00
3.96
2.02
4.00
4.09
4.15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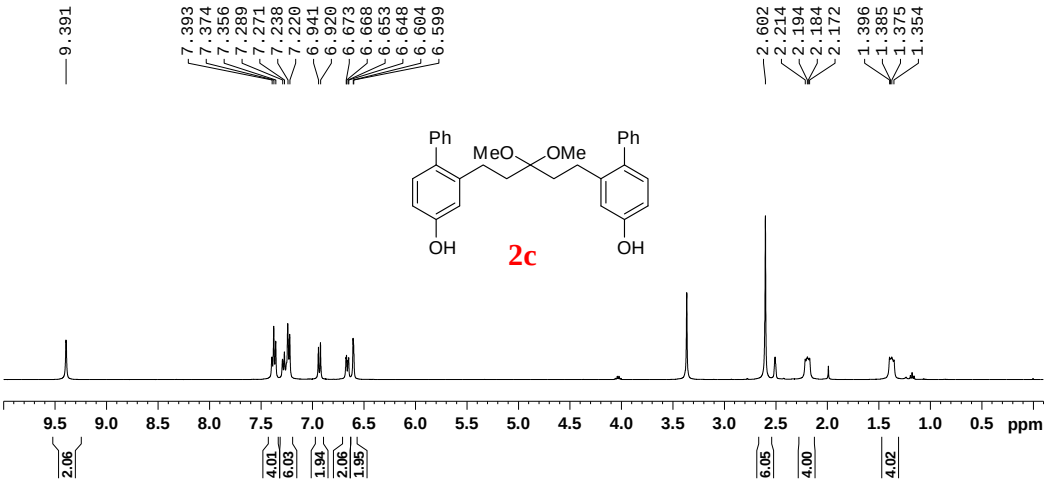
156.71
141.75
139.92
133.40
131.25
129.41
128.23
126.59
115.90
113.28
43.27
27.19
Ph
O
Ph
OH
OH
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

**1c**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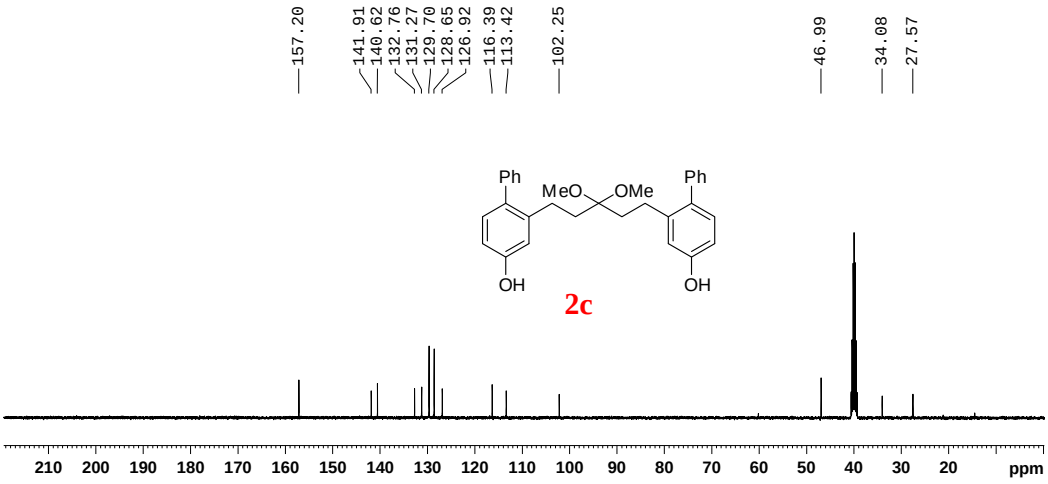
7.356
7.289
7.271
7.238
7.220
6.941
6.920
6.673
6.668
6.653
6.648
6.604
6.599
2.602
2.214
2.194
2.184
2.172
1.396
1.385
1.375
1.354
Ph
MeO
OMe
Ph
OH
OH
2c
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.06
4.01
6.03
1.94
2.06
1.95
6.05
4.00
4.02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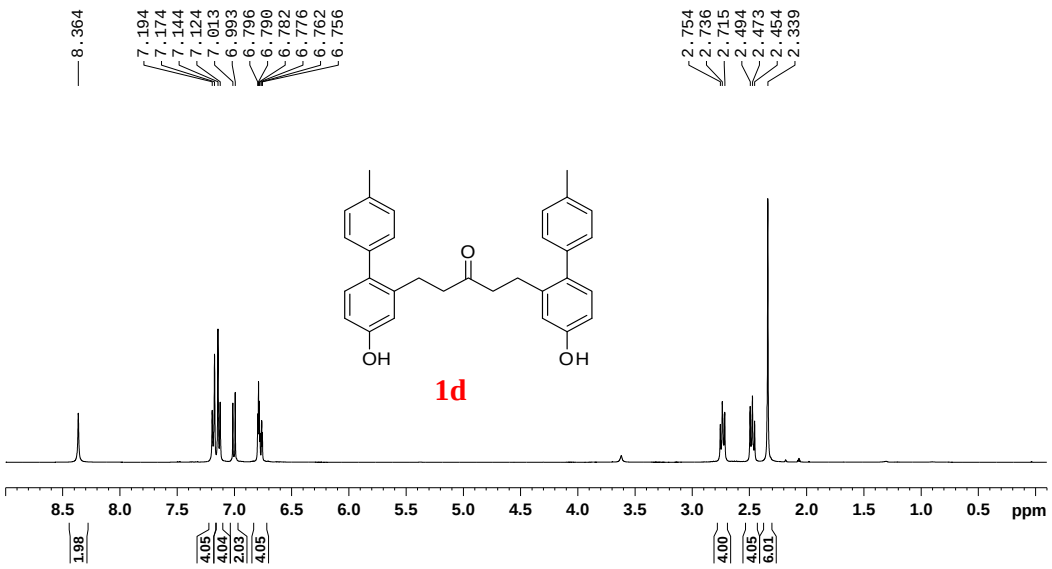
132.76
131.27
129.70
128.65
126.92
116.39
113.42
102.25
46.99
34.08
27.57
Ph
MeO
OMe
Ph
OH
OH
2c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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6.776
6.762
6.756
2.754
2.736
2.715
2.494
2.473
2.454
2.339
O
OH
OH
1d
8.5
8.0
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
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0.5
ppm
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4.05
4.04
2.03
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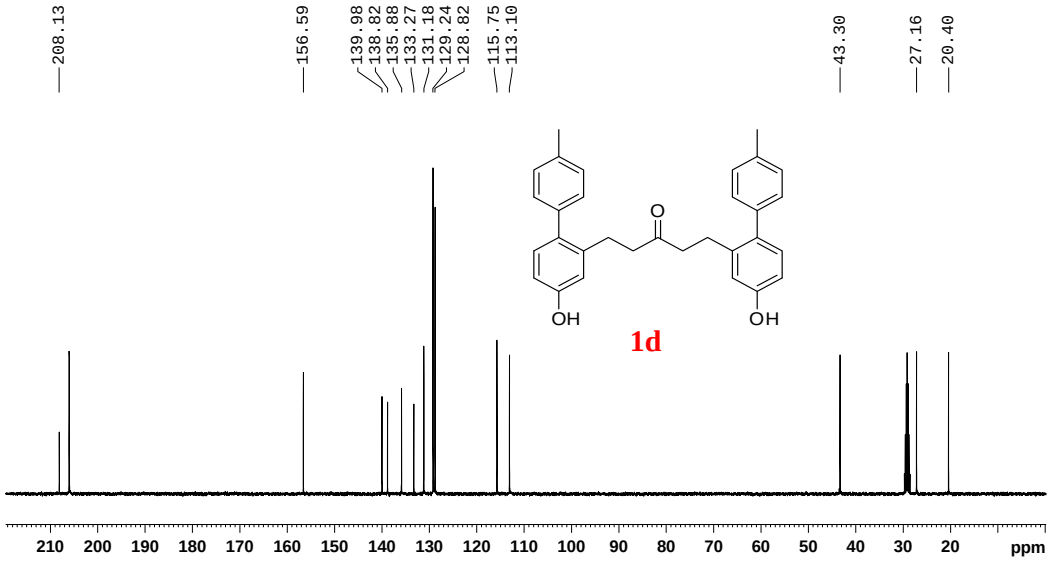
4.00
4.05
6.01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138.82
135.88
133.27
131.18
129.24
128.82
115.75
113.10
43.30
27.16
20.40
O
OH
OH
1d
210
200
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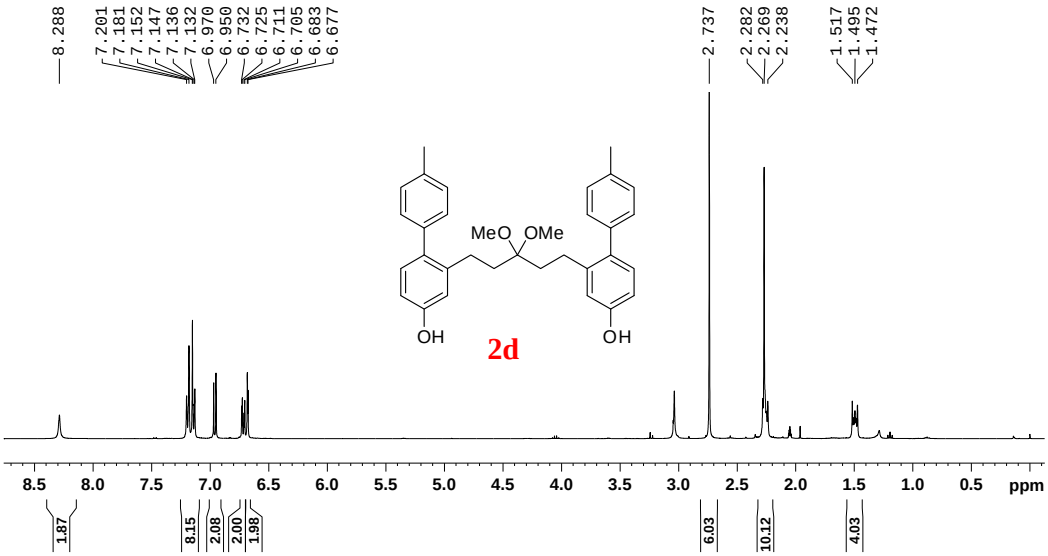
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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7.152
7.147
7.136
7.132
6.970
6.950
6.732
6.725
6.711
6.705
6.683
6.677
2.737
2.282
2.269
2.238
1.517
1.495
1.472
MeO OMe
OH
OH
2d
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
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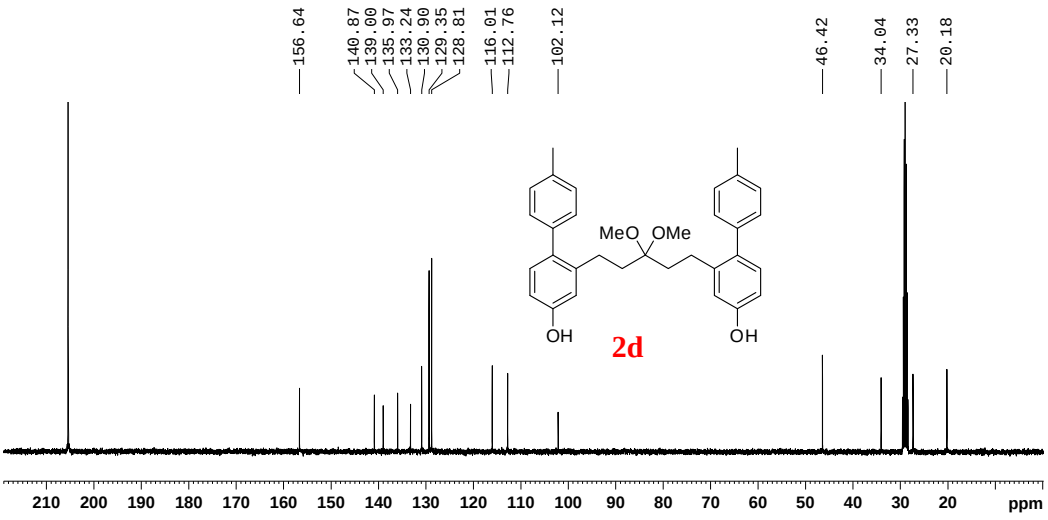
8.15
2.08
2.00
1.98
6.03
10.12
4.03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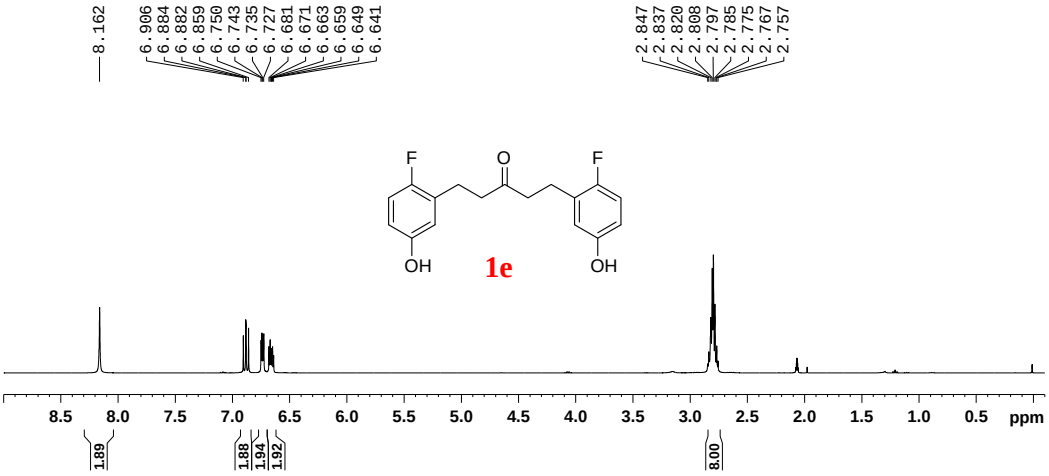
139.00
135.97
133.24
130.90
129.35
128.81
116.01
112.76
102.12
46.42
34.04
27.33
20.18
MeO OMe
OH
OH
2d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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6.884
6.882
6.859
6.750
6.743
6.735
6.727
6.681
6.671
6.663
6.659
6.649
6.641
2.847
2.837
2.820
2.808
2.797
2.785
2.775
2.767
2.757
F
O
F
OH
OH
1e
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
0.5
ppm
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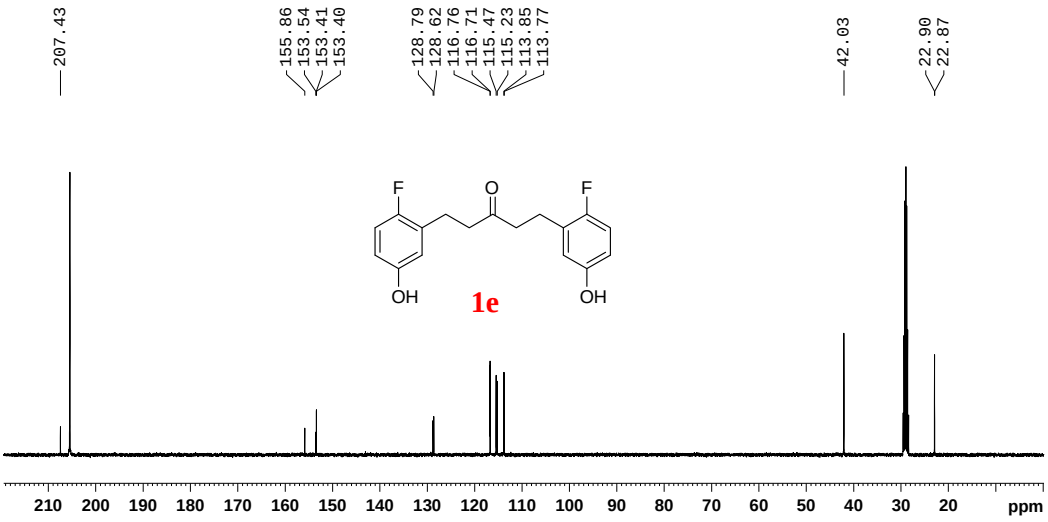
1.94
1.92
8.00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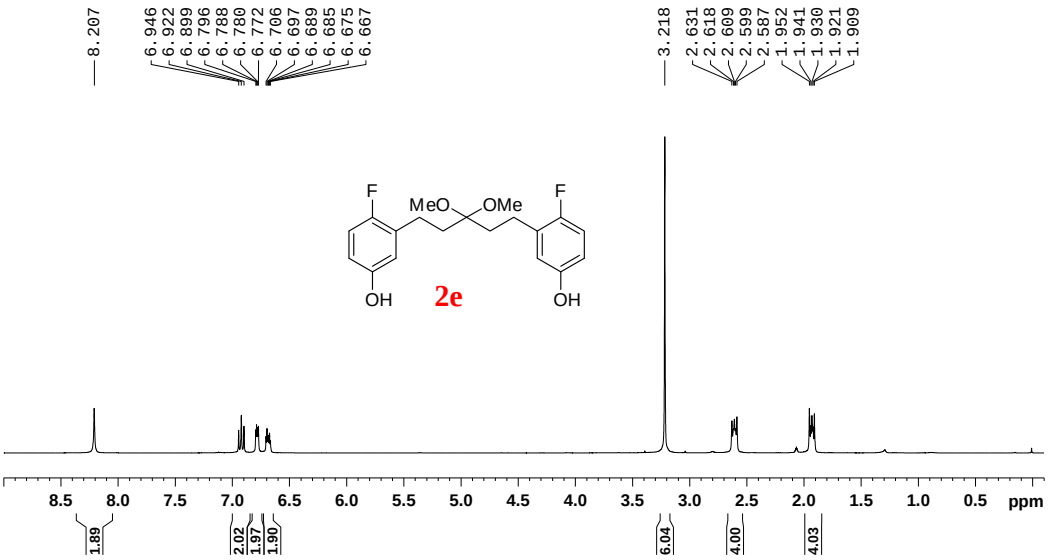
153.41
153.40
128.79
128.62
116.76
116.71
115.47
115.23
113.85
113.77
42.03
22.90
22.87
F
O
F
OH
OH
1e
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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6.697
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6.685
6.675
6.667
3.218
2.631
2.618
2.609
2.599
2.587
1.952
1.941
1.930
1.921
1.909
F
MeO
OMe
F
OH
2e
OH
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 0.5 ppm
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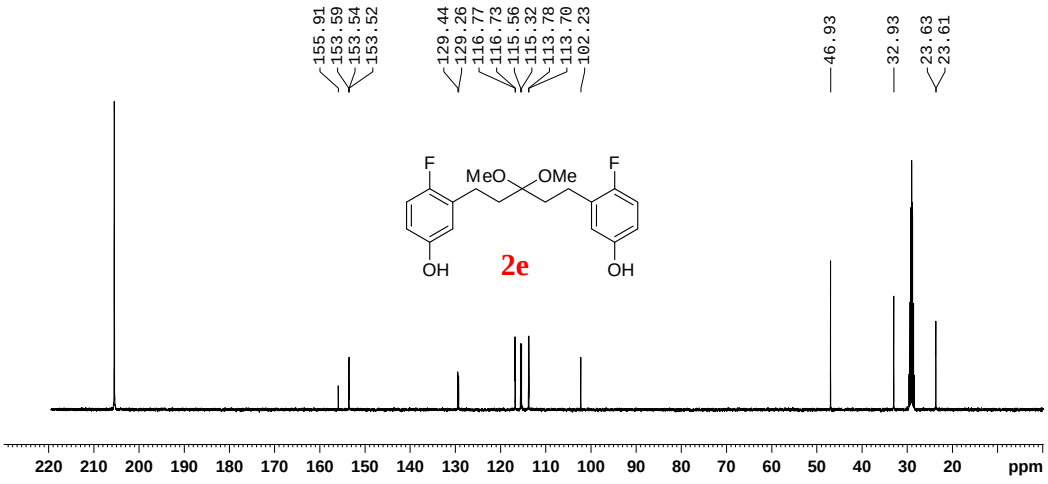
2.02
1.97
1.90
6.04
4.00
4.03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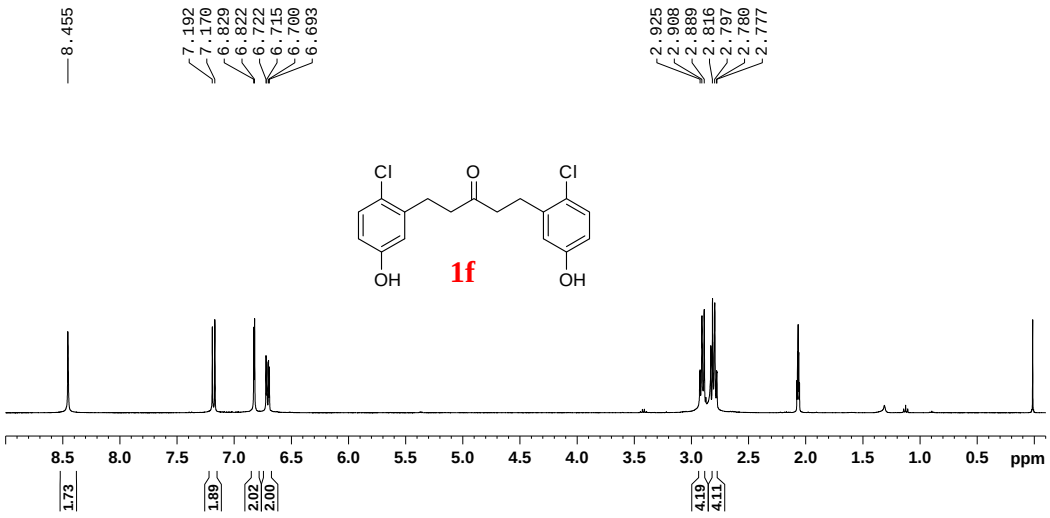
153.54
153.52
129.44
129.26
116.77
116.73
115.56
115.32
113.78
113.70
102.23
46.93
32.93
23.63
23.61
F
MeO
OMe
F
OH
2e
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.170
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6.822
6.722
6.715
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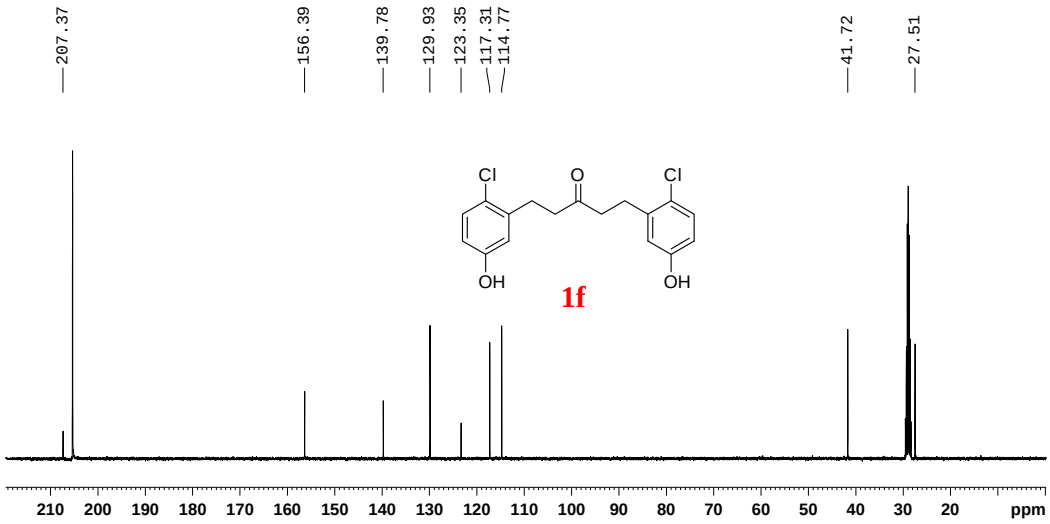
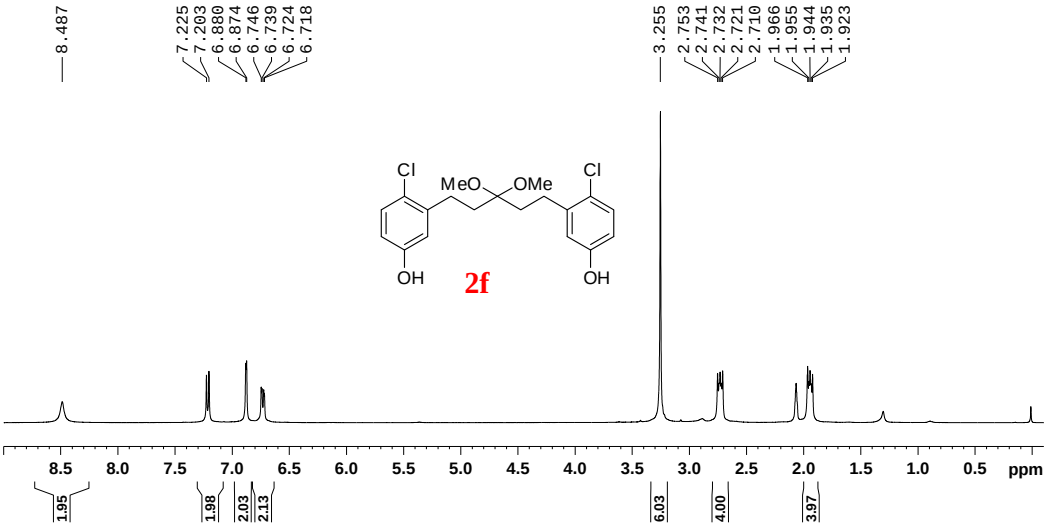
2.925
2.908
2.889
2.816
2.797
2.780
2.777
Cl
O
Cl
OH
OH
1f
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.73
1.89
2.02
2.00
4.19
4.11


207.37
156.39
139.78
129.93
123.35
117.31
114.77
41.72
27.51
Cl
O
Cl
OH
OH
1f
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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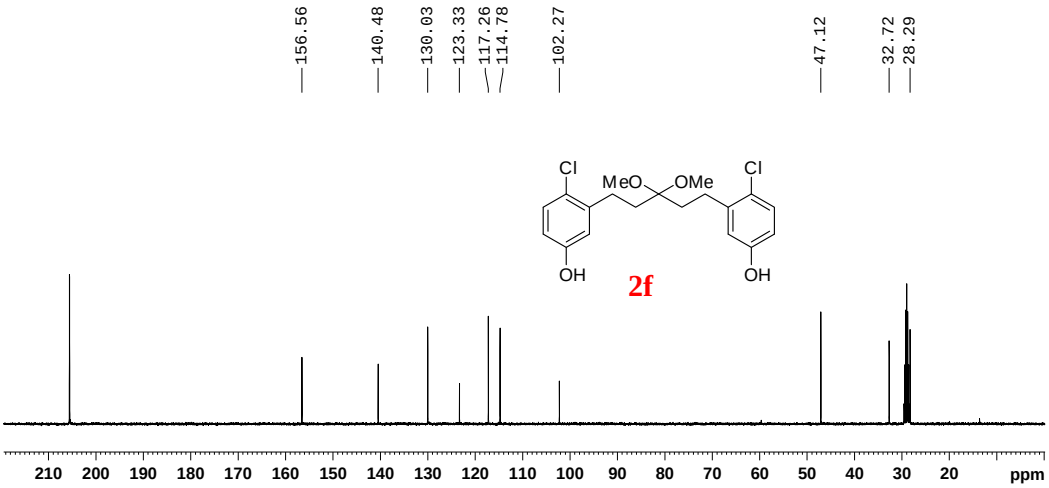
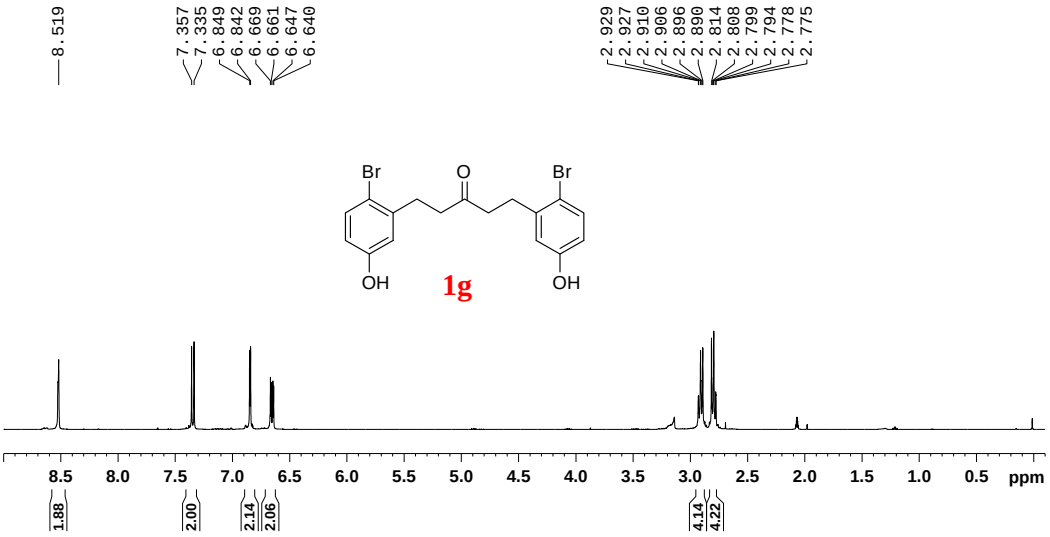
7.225
7.203
6.880
6.874
6.746
6.739
6.724
6.718
3.255
2.753
2.741
2.732
2.721
2.710
1.966
1.955
1.944
1.935
1.923
Cl
MeO
OMe
Cl
OH
OH
2f
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.95
1.98
2.03
2.13
6.03
4.00
3.97


156.56
140.48
130.03
123.33
117.26
114.78
102.27
47.12
32.72
28.29
Cl
MeO
OMe
Cl
OH
OH
2f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.357
7.335
6.849
6.842
6.669
6.661
6.647
6.640
2.929
2.927
2.910
2.906
2.896
2.890
2.814
2.808
2.799
2.794
2.778
2.775
Br
O
Br
OH
OH
1g
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
0.5
ppm
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2.00
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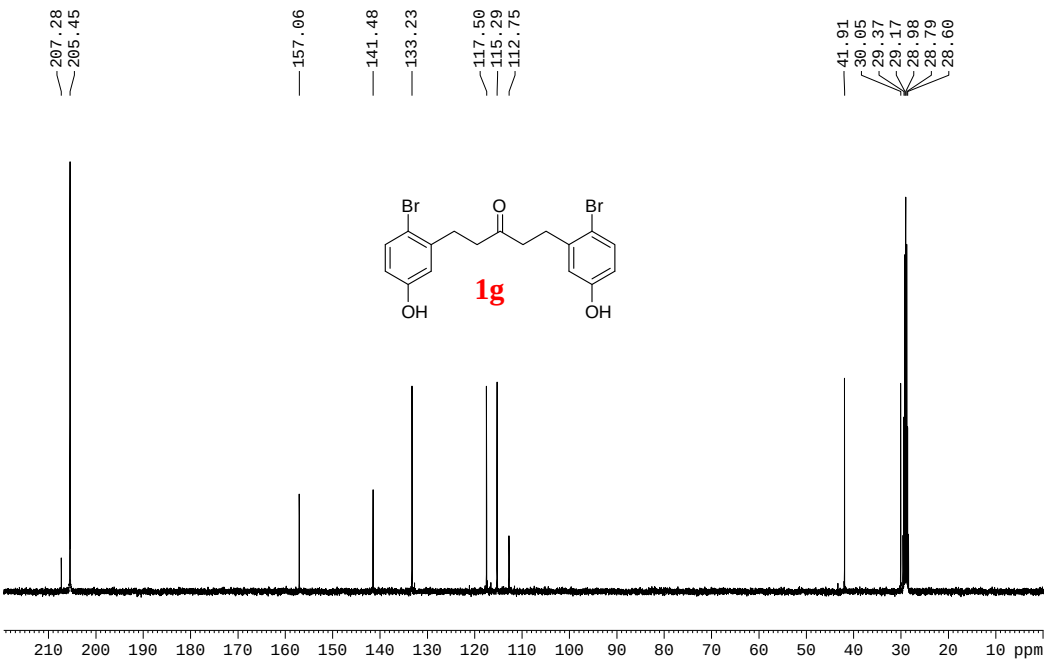
2.06
4.14
4.22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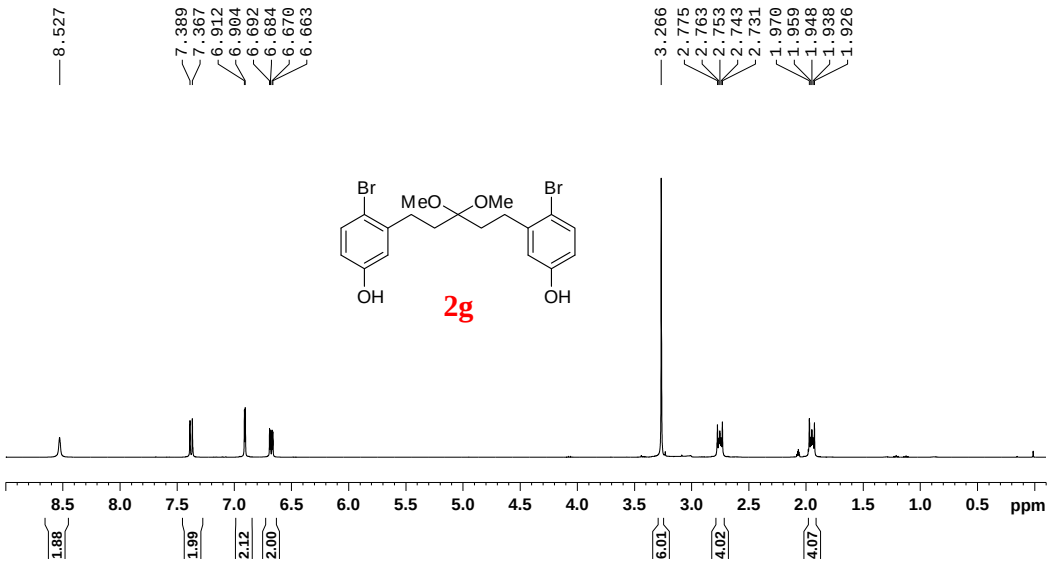
205.45
157.06
141.48
133.23
117.50
115.29
112.75
41.91
30.05
29.37
29.17
28.98
28.79
28.60
Br
O
Br
OH
OH
1g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm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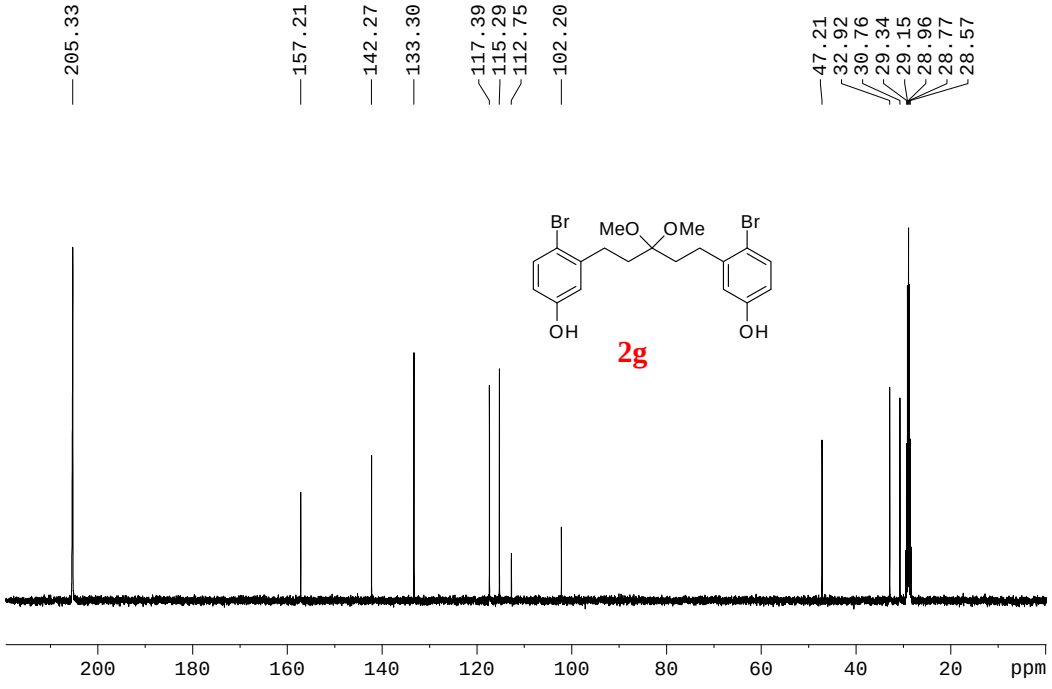
7.389
7.367
6.912
6.904
6.692
6.684
6.670
6.663
3.266
2.775
2.763
2.753
2.743
2.731
1.970
1.959
1.948
1.938
1.926
Br
MeO
OMe
Br
OH
OH
2g
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.88
1.99
2.12
2.00
6.01
4.02
4.07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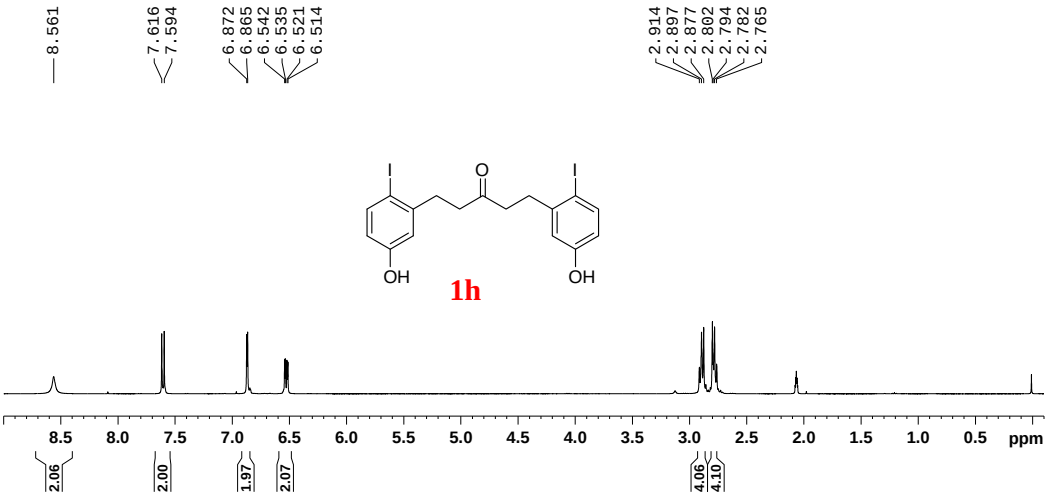
157.21
142.27
133.30
117.39
115.29
112.75
102.20
47.21
32.92
30.76
29.34
29.15
28.96
28.77
28.57
Br
MeO
OMe
Br
OH
OH
2g
200
180
160
140
120
100
80
60
40
20
ppm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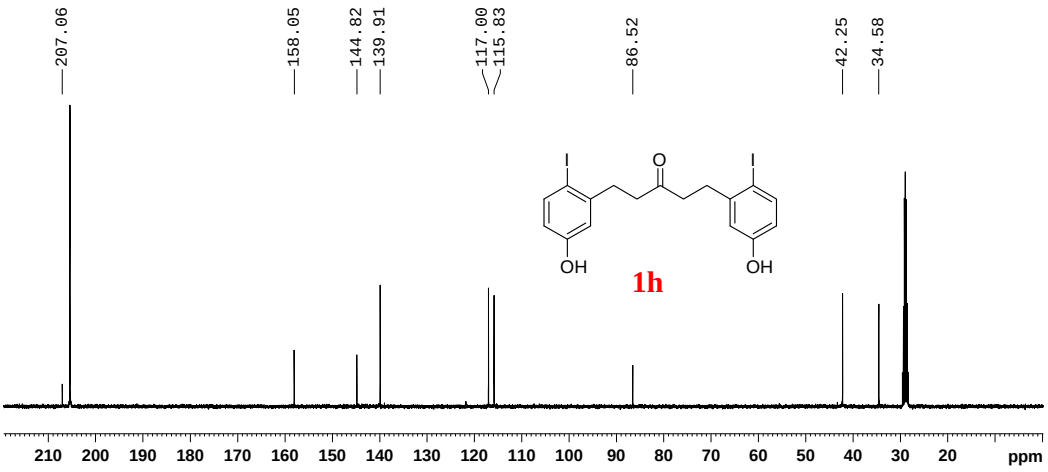
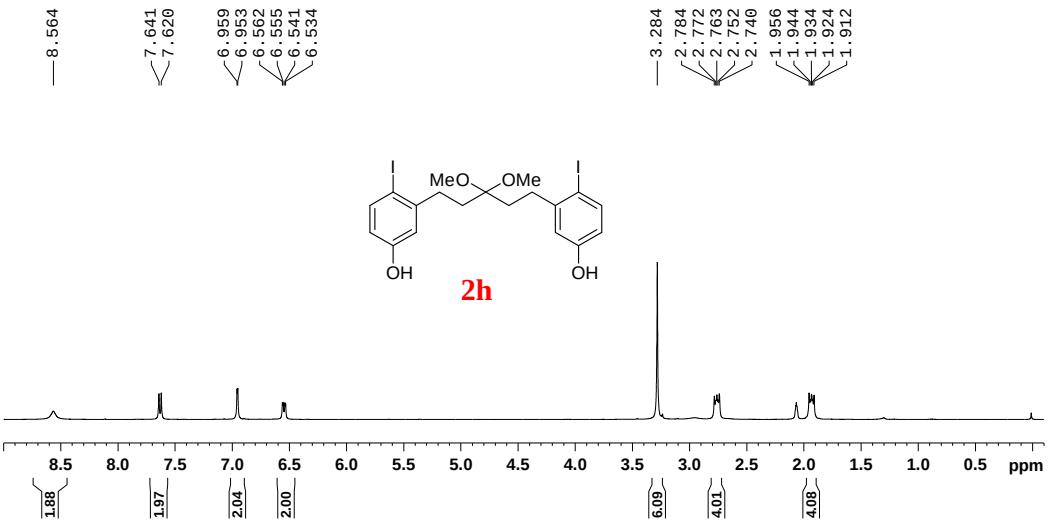
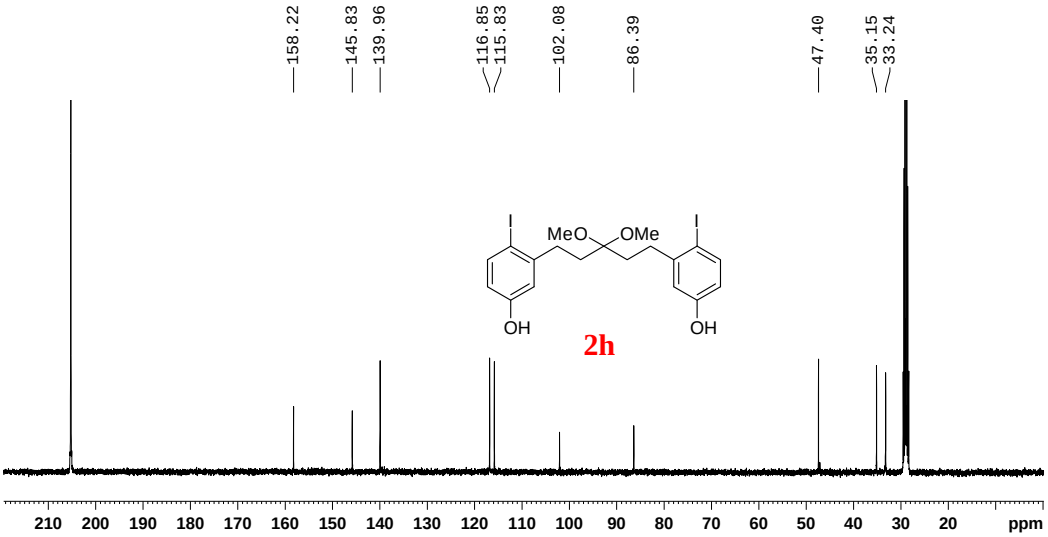
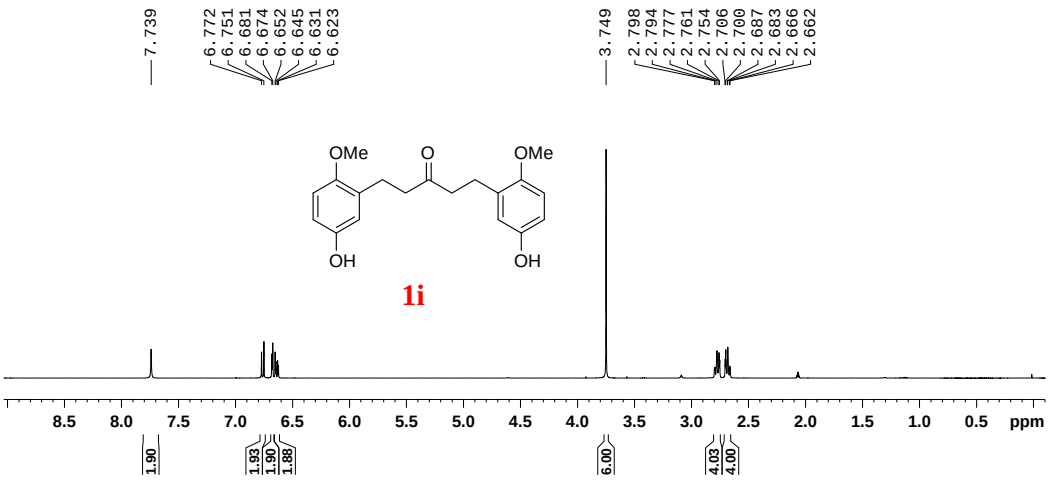
7.616
7.594
6.872
6.865
6.542
6.535
6.521
6.514
2.914
2.897
2.877
2.802
2.794
2.782
2.765
I
O
I
OH
OH
1h
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.06
2.00
1.97
2.07
4.06
4.10


207.06
158.05
144.82
139.91
117.00
115.83
86.52
42.25
34.58
I
O
I
OH
OH
1h
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


8.564
7.641
7.620
6.959
6.953
6.562
6.555
6.541
6.534
3.284
2.784
2.772
2.763
2.752
2.740
1.956
1.944
1.934
1.924
1.912
MeO
OMe
I
I
OH
OH
2h
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
0.5
ppm
1.88
1.97
2.04
2.00
6.09
4.01
4.08


158.22
145.83
139.96
116.85
115.83
102.08
86.39
47.40
35.15
33.24
MeO
OMe
I
I
OH
OH
2h
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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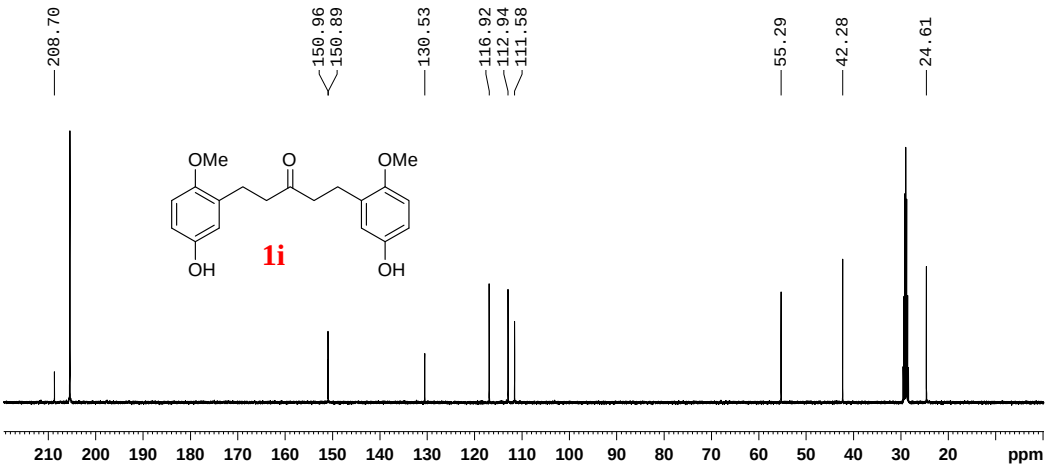
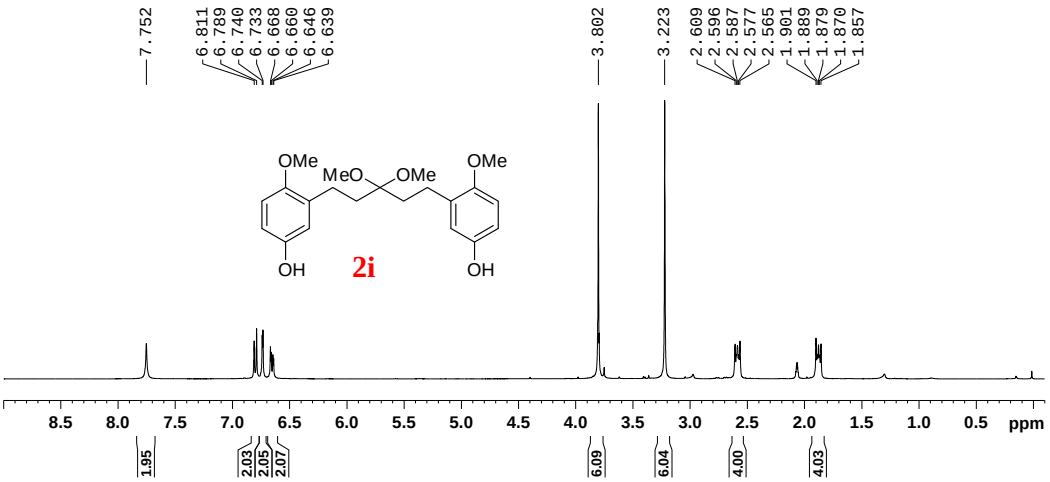
6.772
6.751
6.681
6.674
6.652
6.645
6.631
6.623
3.749
2.798
2.794
2.777
2.761
2.754
2.706
2.700
2.687
2.683
2.666
2.662
OMe
O
OMe
OH
OH
1i
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.90
1.93
1.90
1.88
6.00
4.03
4.00


208.70
150.96
150.89
130.53
116.92
112.94
111.58
55.29
42.28
24.61
OMe
O
OMe
OH
OH
1i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.752
6.811
6.789
6.740
6.733
6.668
6.660
6.646
6.639
3.802
3.223
2.609
2.596
2.587
2.577
2.565
1.901
1.889
1.879
1.870
1.857
OMe
MeO
OMe
OMe
OH
OH
2i
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 0.5 ppm
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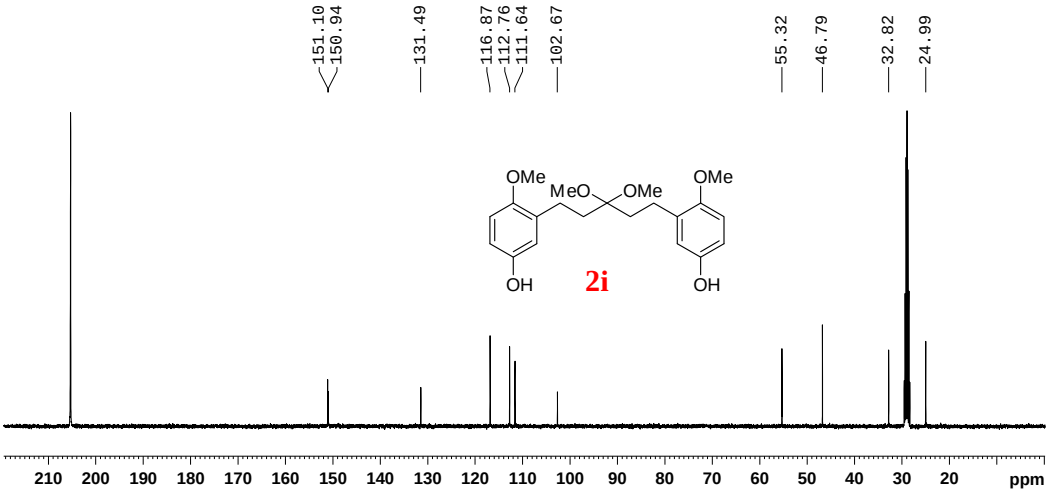
2.03
2.05
2.07
6.09
6.04
4.00
4.03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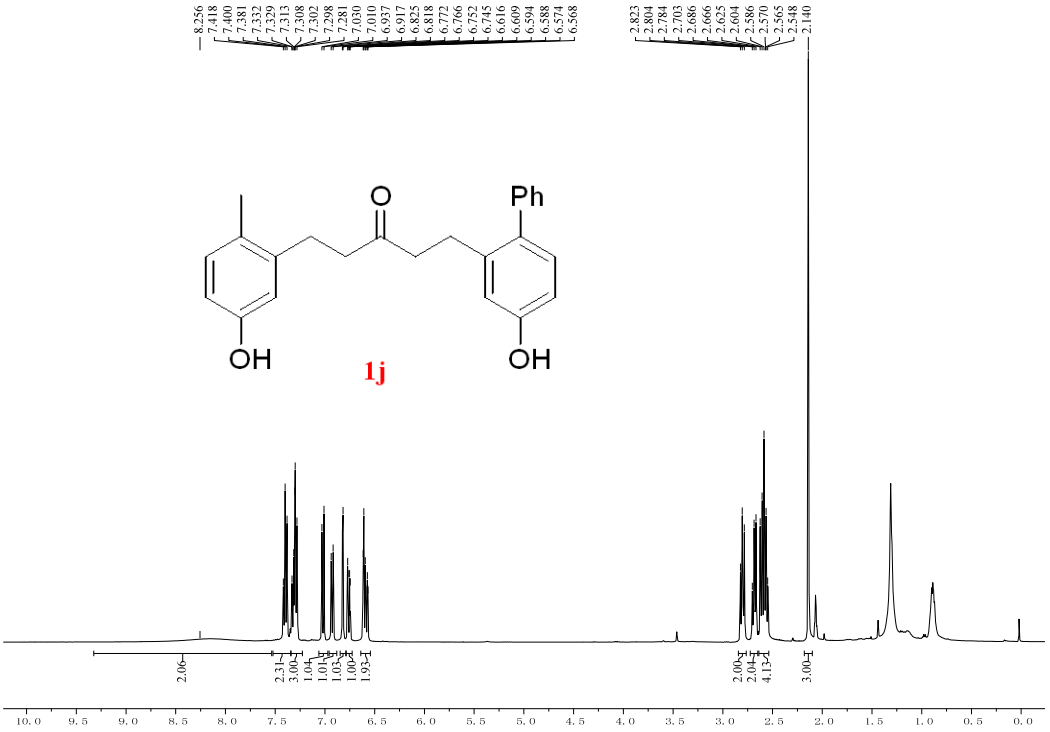
150.94
131.49
116.87
112.76
111.64
102.67
55.32
46.79
32.82
24.99
OMe
MeO
OMe
OMe
OH
OH
2i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.400
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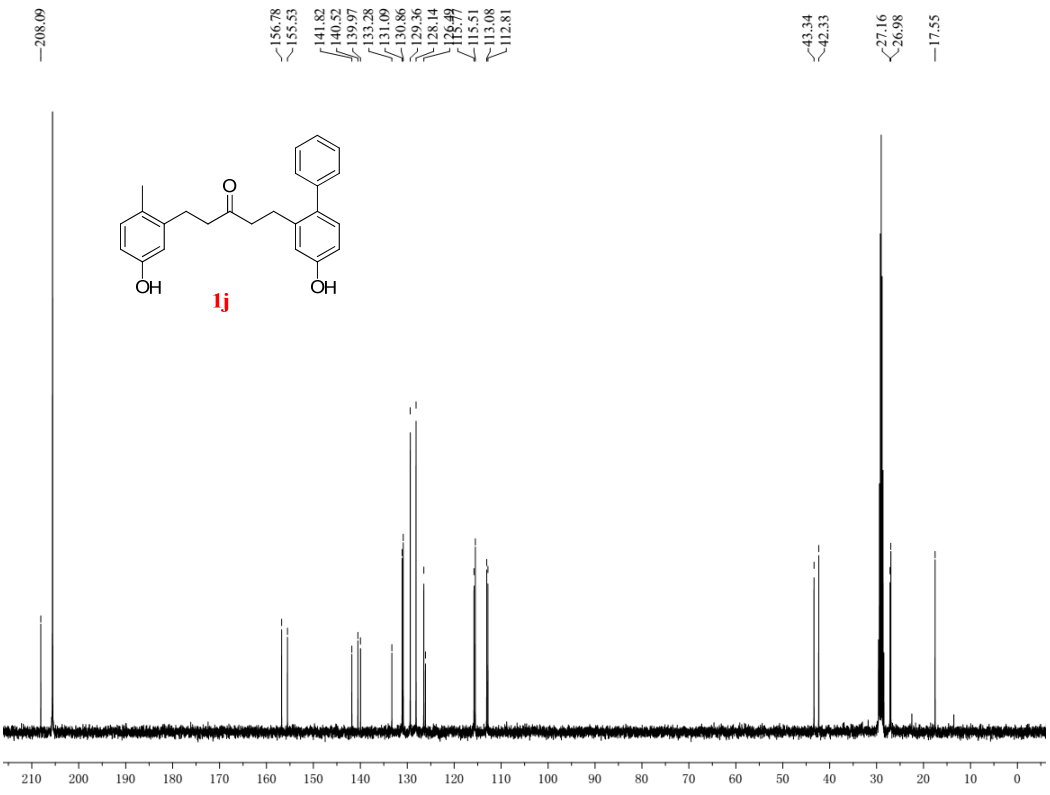
7.332
7.329
7.313
7.308
7.302
7.298
7.281
7.030
7.010
6.937
6.917
6.825
6.818
6.772
6.766
6.752
6.745
6.616
6.609
6.594
6.588
6.574
6.568
2.823
2.804
2.784
2.703
2.686
2.666
2.625
2.604
2.586
2.570
2.565
2.548
2.140
O
Ph
OH
OH
1j
2.06
2.31
3.00
1.04
1.01
1.03
1.06
1.93
2.00
2.04
4.13
3.00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141.82
140.52
139.97
133.28
131.09
130.86
129.36
128.14
126.49
118.47
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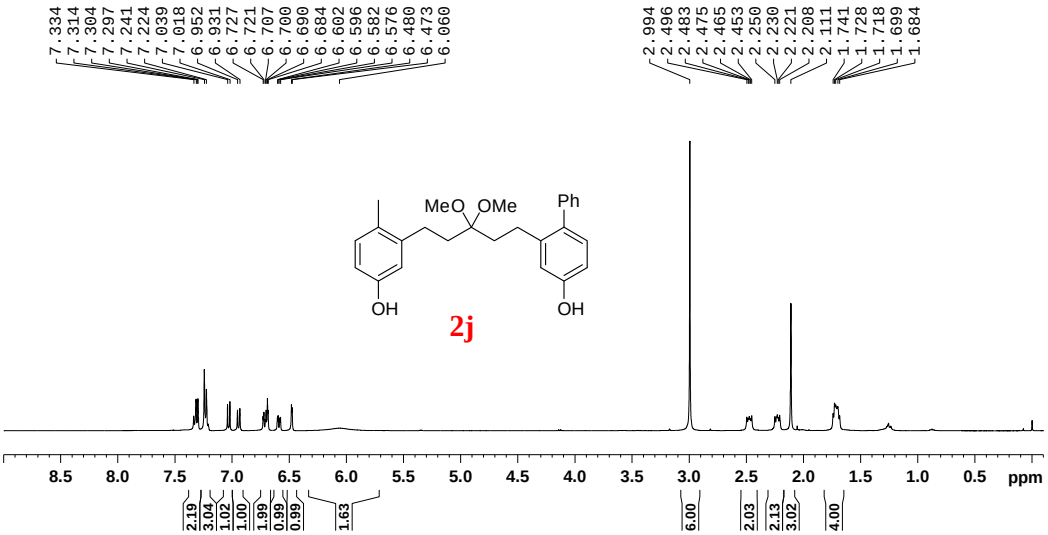
113.08
112.81
43.34
42.33
27.16
26.98
17.55
O
OH
OH
1j


7.334
7.314
7.304
7.297
7.241
7.224
7.039
7.018
6.952
6.931
6.727
6.721
6.707
6.700
6.690
6.684
6.602
6.596
6.582
6.576
6.480
6.473
6.060
2.994
2.496
2.483
2.475
2.465
2.453
2.250
2.230
2.221
2.208
2.111
1.741
1.728
1.718
1.699
1.684
MeO
OMe
Ph
OH
OH
2j
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
0.5
ppm
2.19
3.04
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1.99
0.99
0.99
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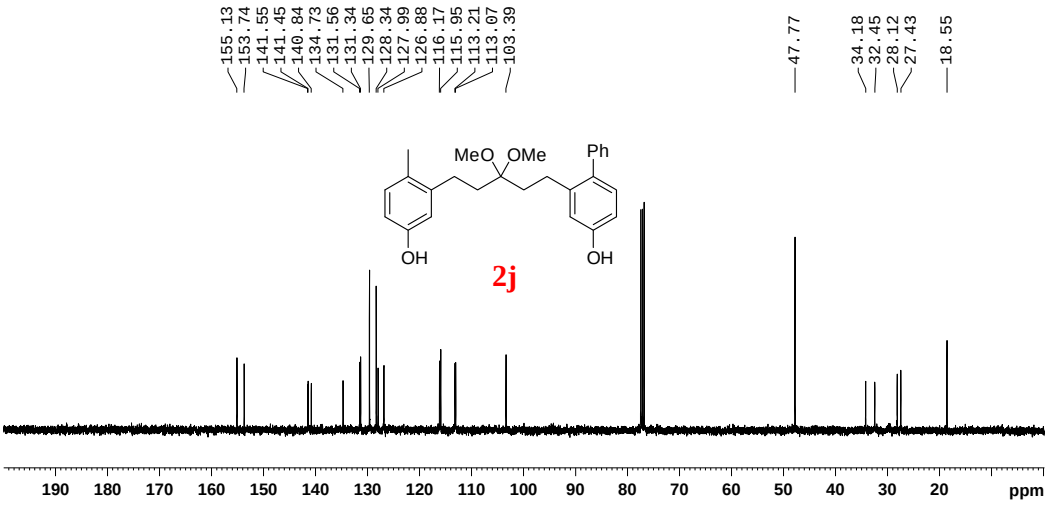
2.13
3.02
4.00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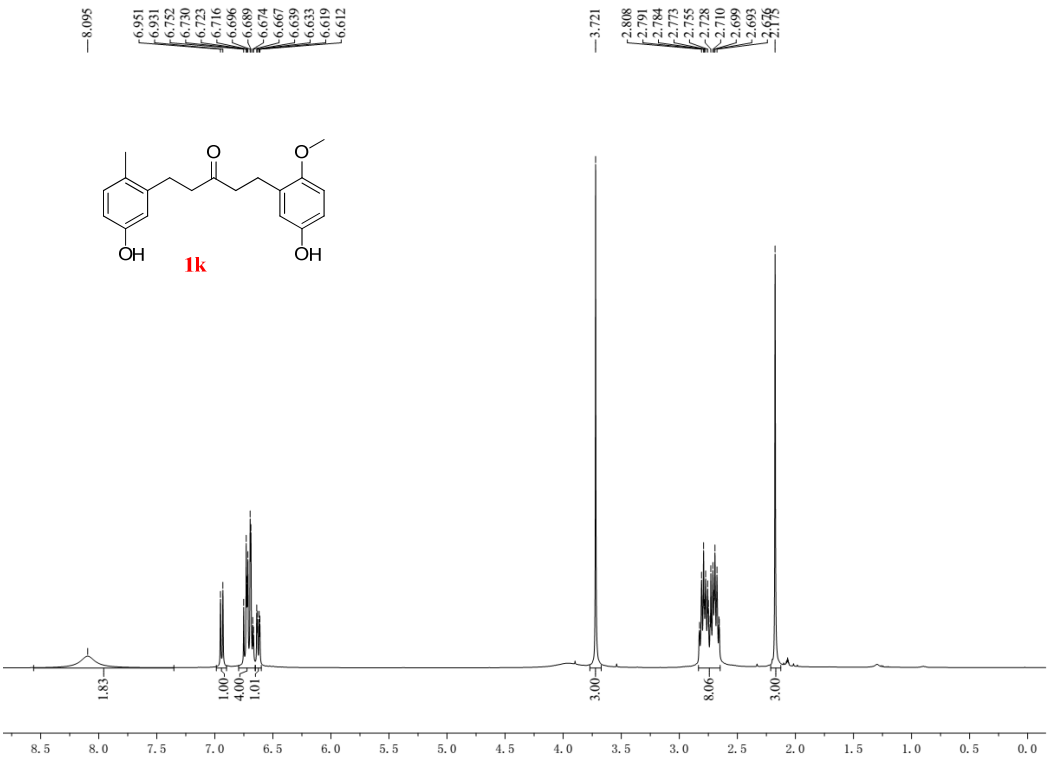
141.55
141.45
140.84
134.73
131.56
131.34
129.65
128.34
127.99
126.88
116.17
115.95
113.21
113.07
103.39
47.77
34.18
32.45
28.12
27.43
18.55
MeO
OMe
Ph
OH
OH
2j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


8.095
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6.931
6.752
6.730
6.723
6.716
6.696
6.689
6.674
6.667
6.639
6.633
6.619
6.612
3.721
2.808
2.791
2.784
2.773
2.755
2.728
2.710
2.699
2.693
2.676
2.175
O
O
OH
OH
1k
1.83
1.00
4.00
1.01
3.00
8.06
3.00
8.5
8.0
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
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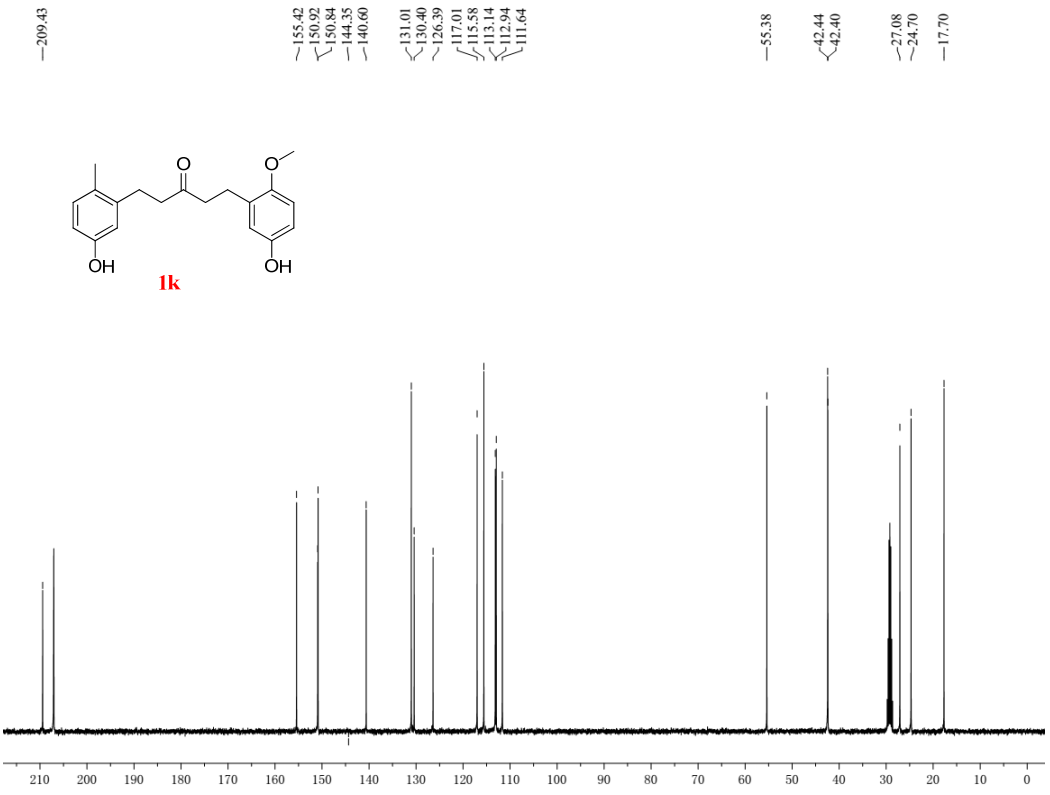
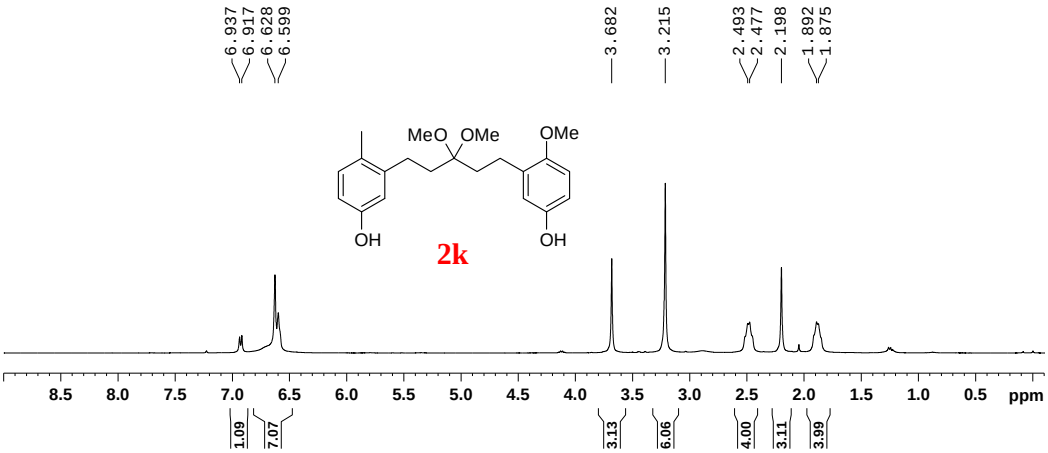

209.43
155.42
150.92
150.84
144.35
140.60
131.01
130.40
126.39
117.01
115.58
113.14
112.94
111.64
55.38
42.44
42.40
27.08
24.70
17.70
O
O
OH
OH
1k
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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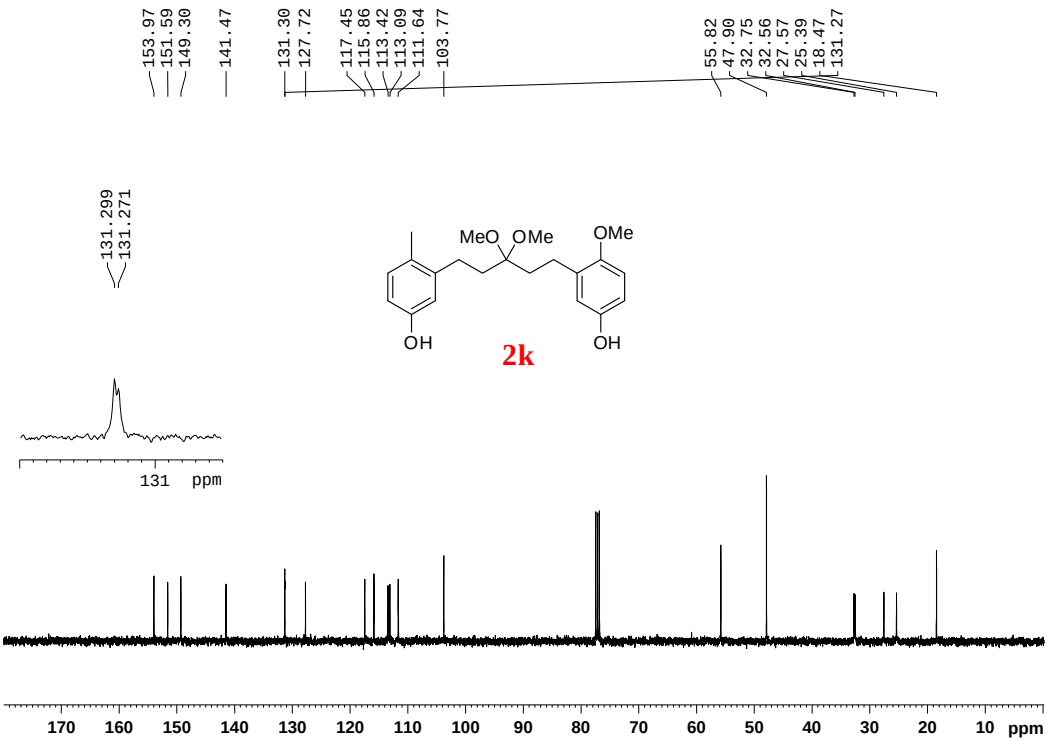
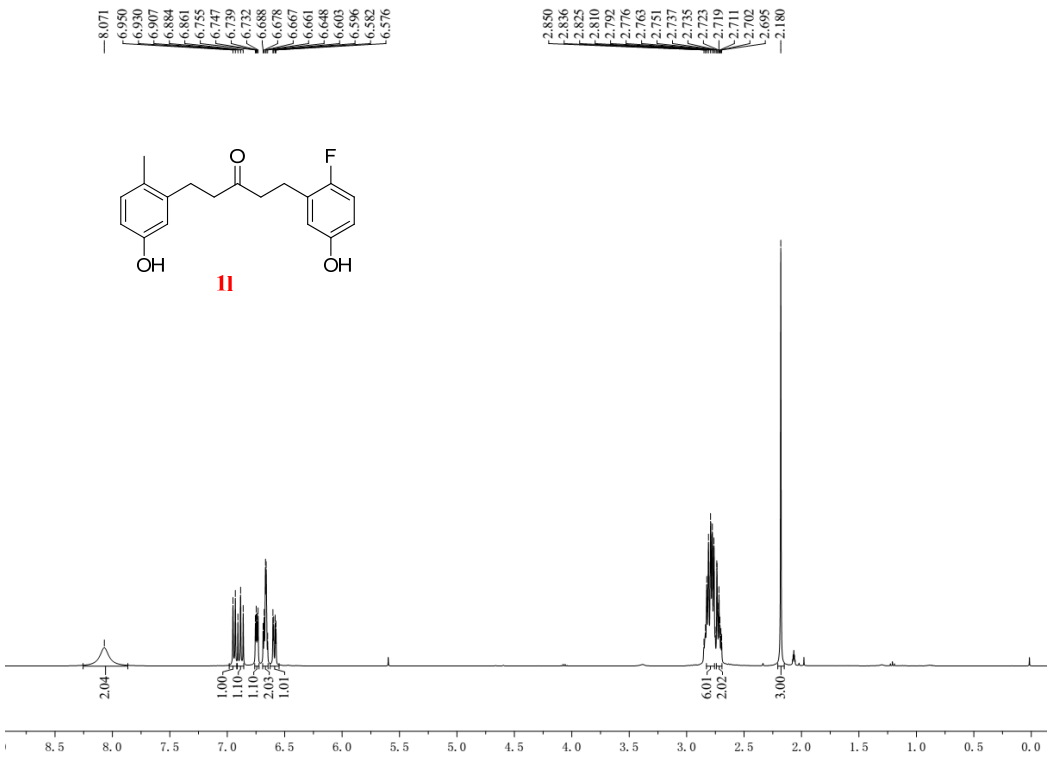
6.917
6.628
6.599
3.682
3.215
2.493
2.477
2.198
1.892
1.875
MeO
OMe
OMe
OH
OH
2k
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.09
7.07
3.13
6.06
4.00
3.11
3.99


153.97
151.59
149.30
141.47
131.30
127.72
117.45
115.86
113.42
113.09
111.64
103.77
55.82
47.90
32.75
32.56
27.57
25.39
18.47
131.27
131.299
131.271
MeO
OMe
OMe
OH
OH
2k
131 ppm
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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6.950
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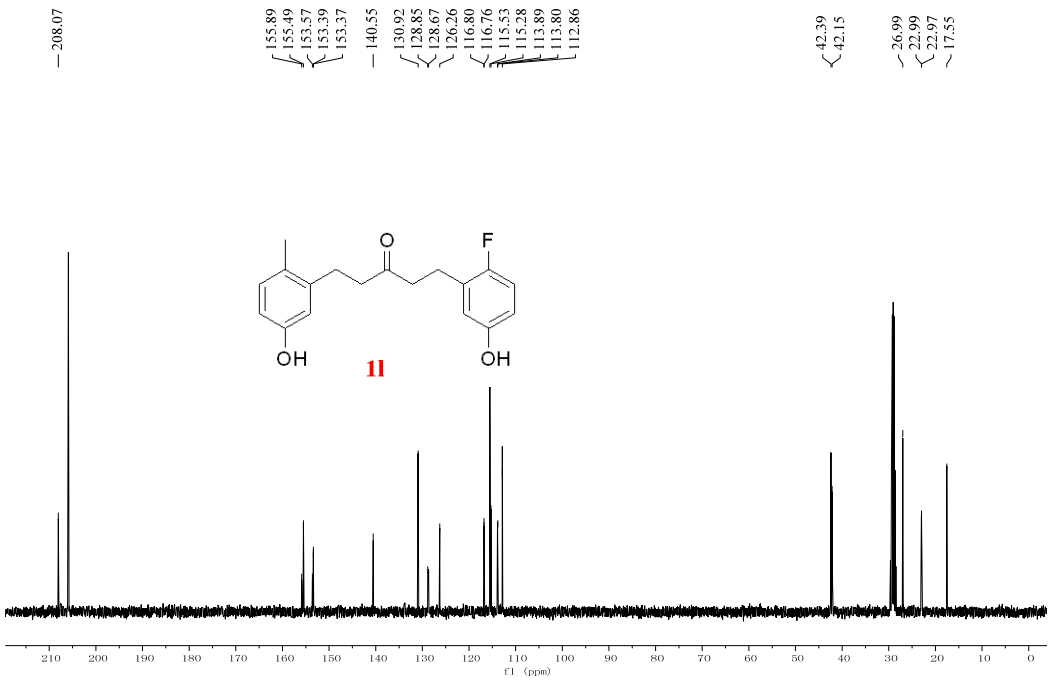
6.907
6.884
6.861
6.755
6.747
6.739
6.732
6.688
6.678
6.667
6.661
6.648
6.603
6.596
6.582
6.576
2.850
2.836
2.825
2.810
2.792
2.776
2.763
2.751
2.737
2.735
2.723
2.719
2.711
2.702
2.695
2.180
O
F
OH
OH
2.04
1.00
1.10
1.10
2.03
1.01
6.01
2.02
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

**1l**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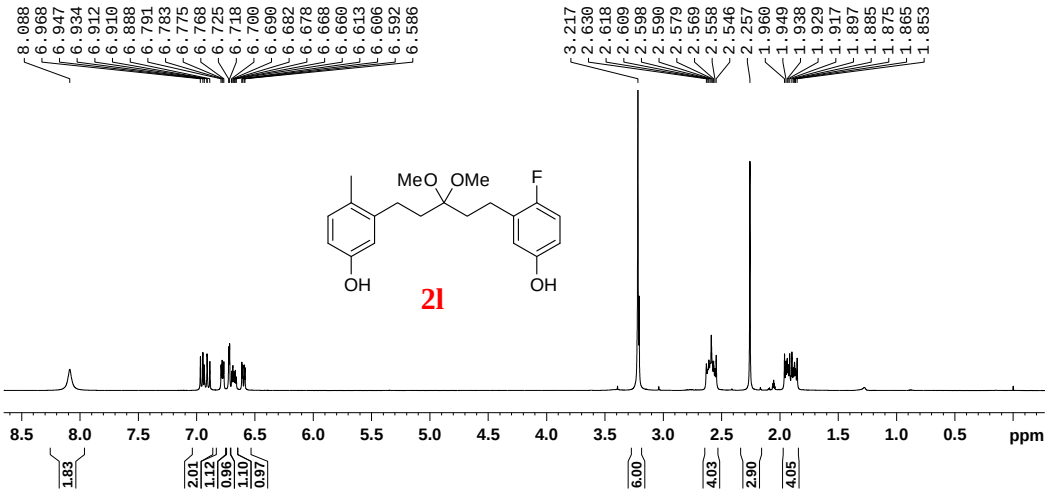
155.89
155.49
153.57
153.39
153.37
140.55
130.92
128.85
128.67
126.26
116.80
116.76
115.53
115.28
113.89
113.80
112.86
42.39
42.15
26.99
22.99
22.97
17.55
O
F
OH
OH
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

**1l**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6.968
6.947
6.934
6.912
6.910
6.888
6.791
6.783
6.775
6.768
6.725
6.718
6.700
6.690
6.682
6.678
6.668
6.660
6.613
6.606
6.592
6.586
3.217
2.630
2.618
2.609
2.598
2.590
2.579
2.569
2.558
2.546
2.257
1.960
1.949
1.938
1.929
1.917
1.897
1.885
1.875
1.865
1.853
MeO
OMe
F
OH
OH
2l
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
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ppm
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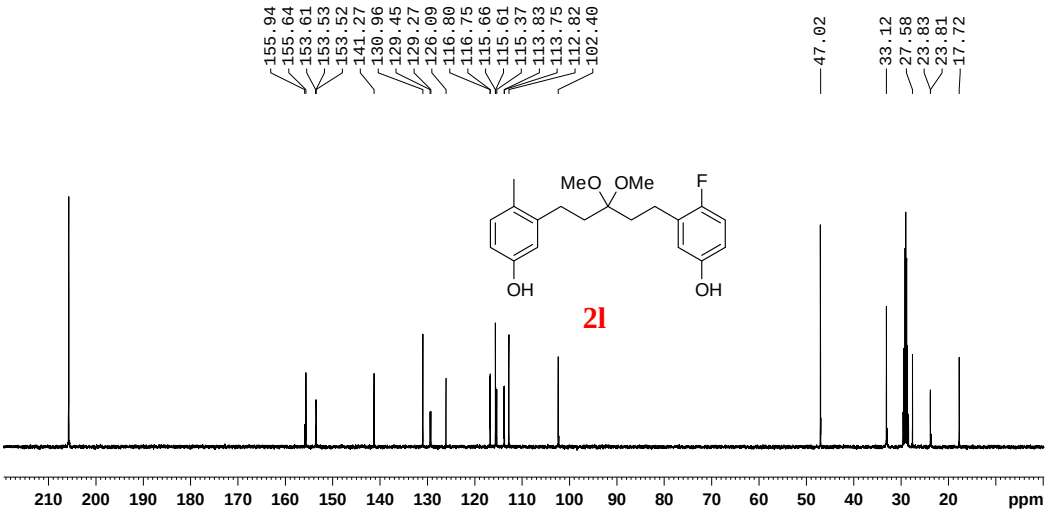
2.01
1.12
0.96
1.10
0.97
6.00
4.03
2.90
4.05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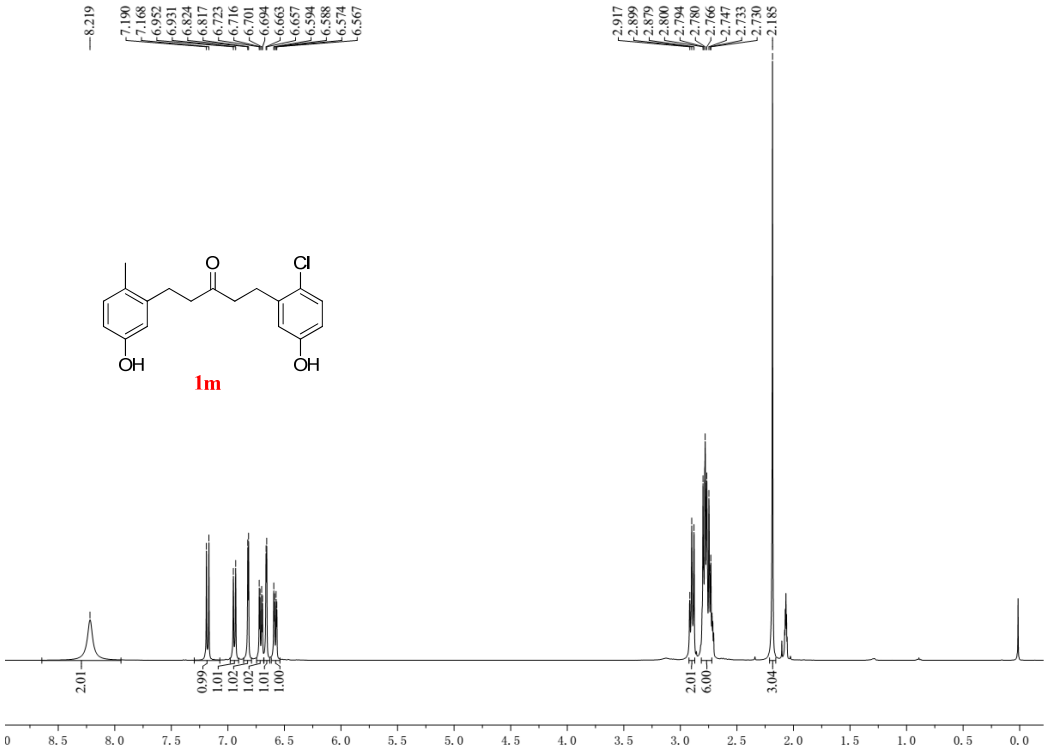
155.64
153.61
153.53
153.52
141.27
130.96
129.45
129.27
126.09
116.80
116.75
115.66
115.61
115.37
113.83
113.75
112.82
102.40
47.02
33.12
27.58
23.83
23.81
17.72
MeO
OMe
F
OH
OH
2l
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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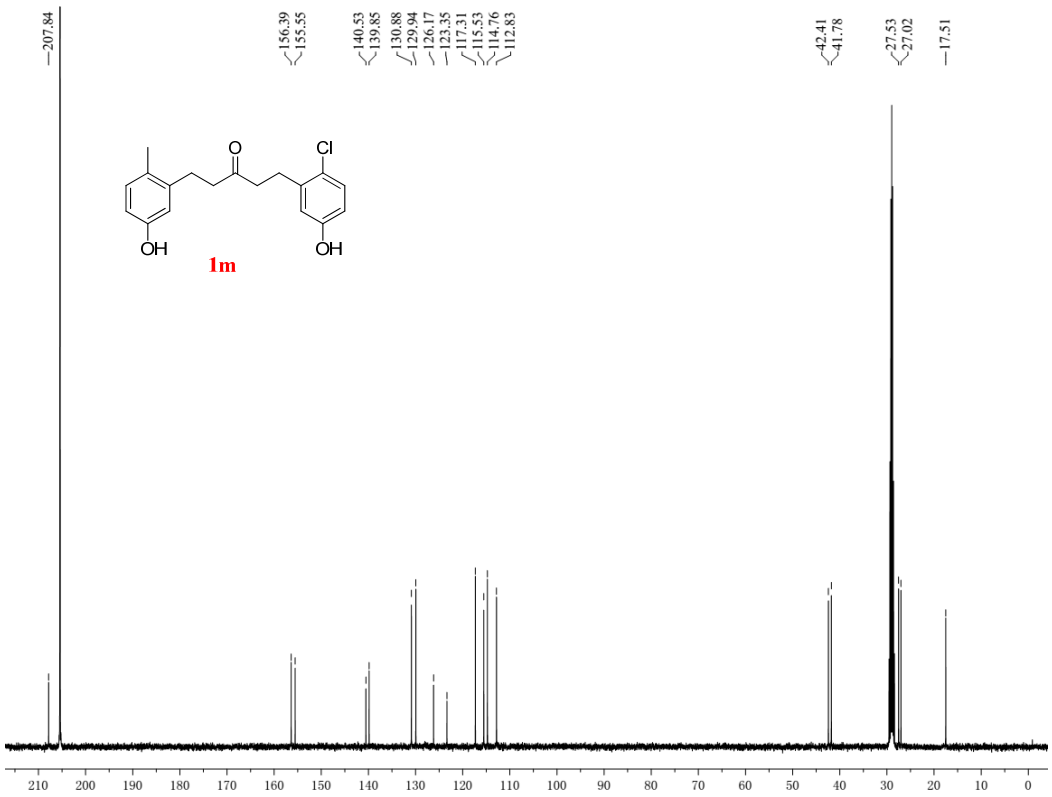
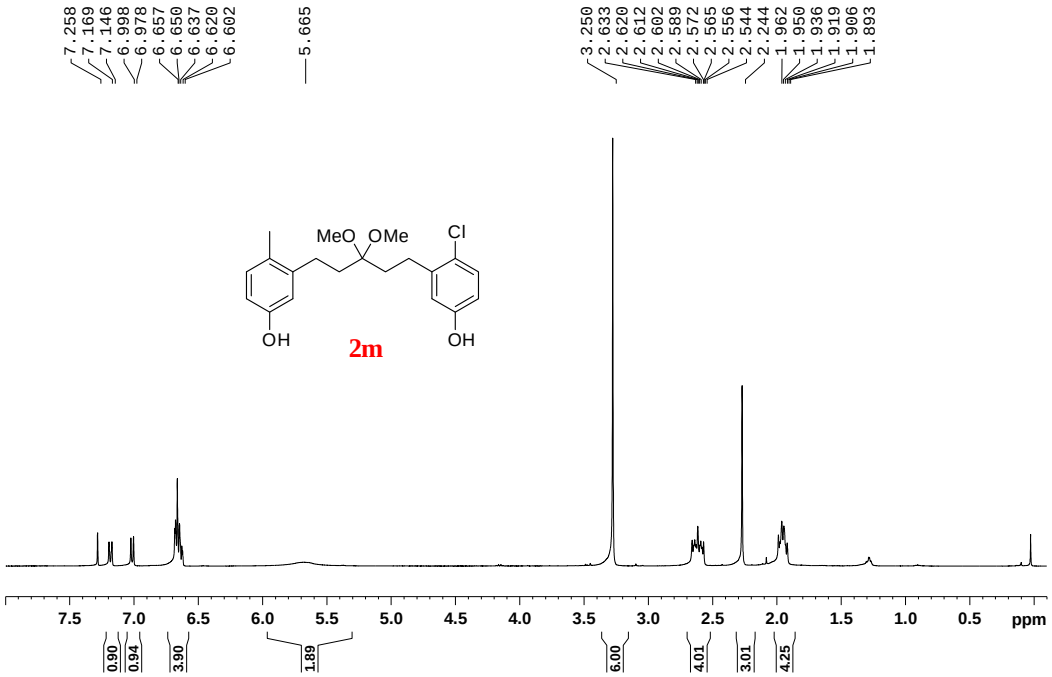
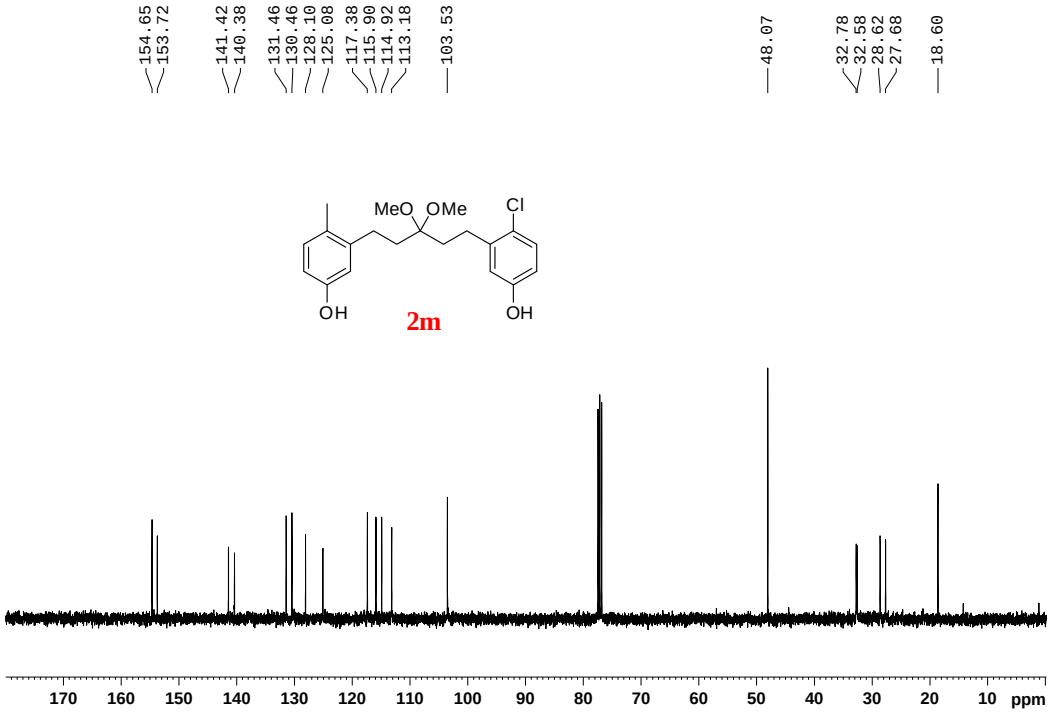
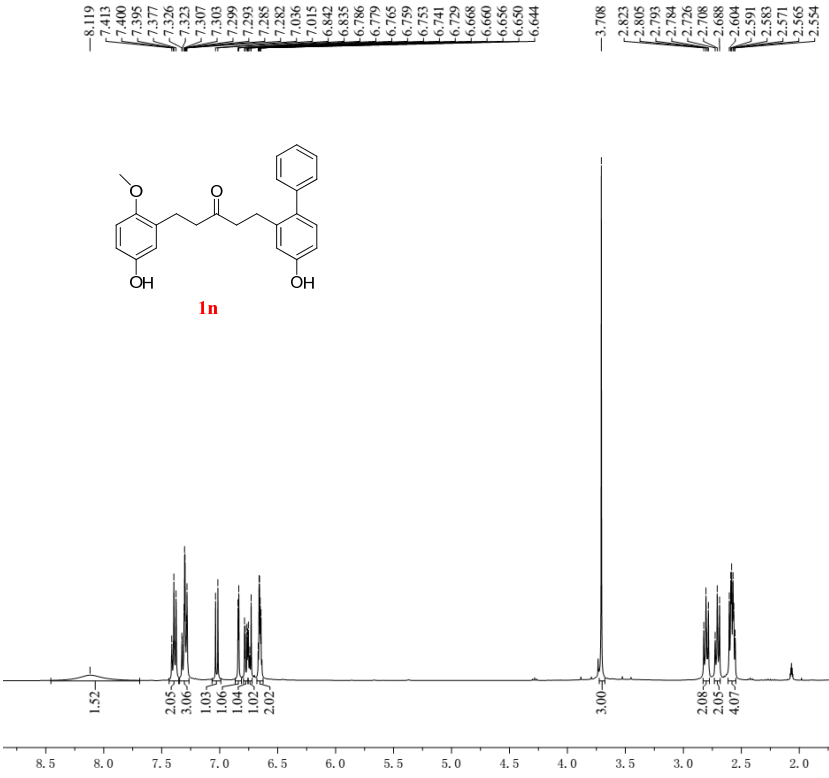
7.190
7.168
6.952
6.931
6.824
6.817
6.723
6.716
6.701
6.694
6.663
6.657
6.594
6.588
6.574
6.567
2.917
2.899
2.879
2.800
2.794
2.780
2.766
2.747
2.733
2.730
2.185
O
Cl
OH
OH
1m
2.01
0.99
1.01
1.02
1.02
1.01
1.00
2.01
6.00
3.04


207.84
156.39
155.55
140.53
139.85
130.88
129.94
126.17
123.35
117.31
115.53
114.76
112.83
42.41
41.78
27.53
27.02
17.51
O
Cl
OH
OH
1m


7.258
7.169
7.146
6.998
6.978
6.657
6.650
6.637
6.620
6.602
5.665
3.250
2.633
2.620
2.612
2.602
2.589
2.572
2.565
2.556
2.544
2.244
1.962
1.950
1.936
1.919
1.906
1.893
MeO
OMe
Cl
OH
OH
2m
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
ppm
0.90
0.94
3.90
1.89
6.00
4.01
3.01
4.25


154.65
153.72
141.42
140.38
131.46
130.46
128.10
125.08
117.38
115.90
114.92
113.18
103.53
48.07
32.78
32.58
28.62
27.68
18.60
MeO
OMe
Cl
OH
OH
2m
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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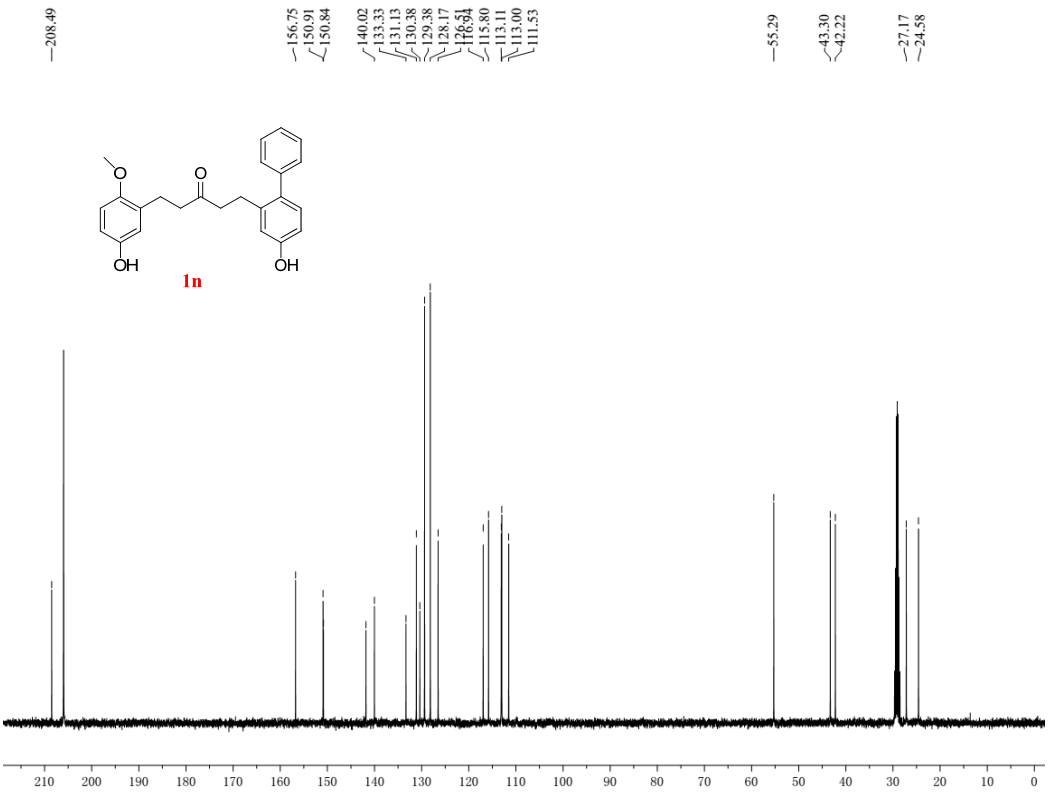
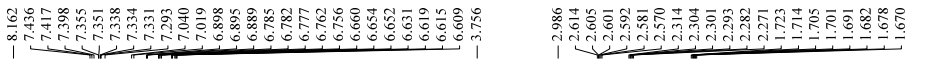
7.413
7.400
7.395
7.377
7.326
7.323
7.307
7.303
7.299
7.293
7.285
7.282
7.036
7.015
6.842
6.835
6.786
6.779
6.765
6.759
6.753
6.741
6.729
6.668
6.660
6.656
6.650
6.644
3.708
2.823
2.805
2.793
2.784
2.726
2.708
2.688
2.604
2.591
2.583
2.571
2.565
2.554
O
O
OH
OH
1n
1.52
2.05
3.06
1.03
1.06
1.04
1.02
2.02
3.00
2.08
2.05
4.07
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
0.5
0.0


208.49
156.75
150.91
150.84
140.02
133.33
131.13
130.38
129.38
128.17
126.51
116.94
115.80
113.11
113.00
111.53
55.29
43.30
42.22
27.17
24.58
O
O
OH
OH
1n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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7.436
7.417
7.398
7.355
7.351
7.338
7.334
7.331
7.293
7.040
7.019
6.898
6.895
6.889
6.785
6.782
6.777
6.762
6.756
6.660
6.654
6.652
6.631
6.619
6.615
6.609
3.756
2.986
2.614
2.605
2.601
2.592
2.581
2.570
2.314
2.304
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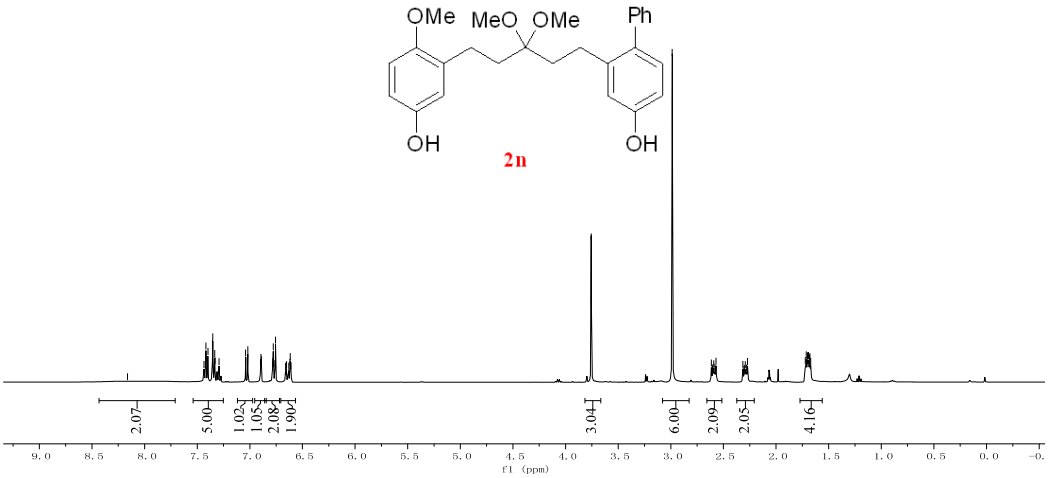
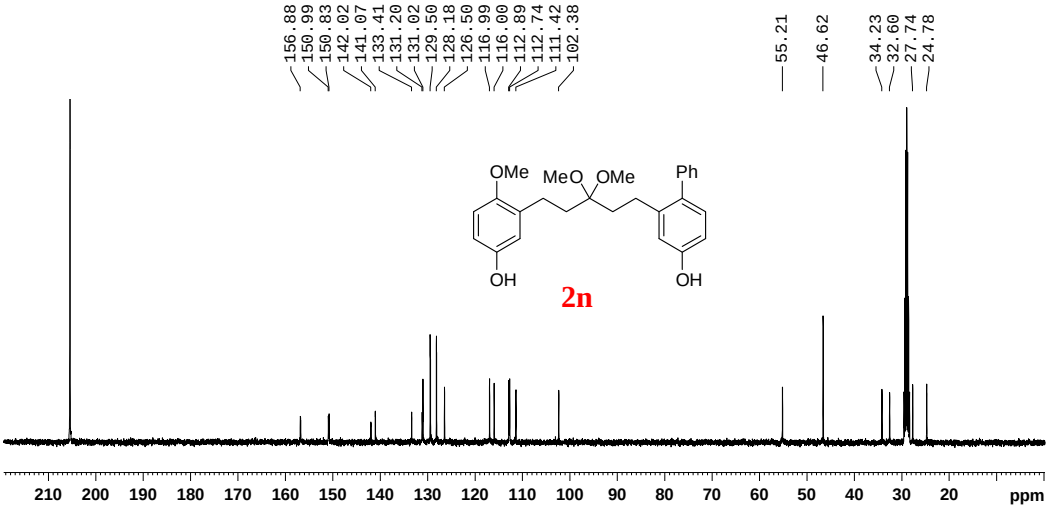
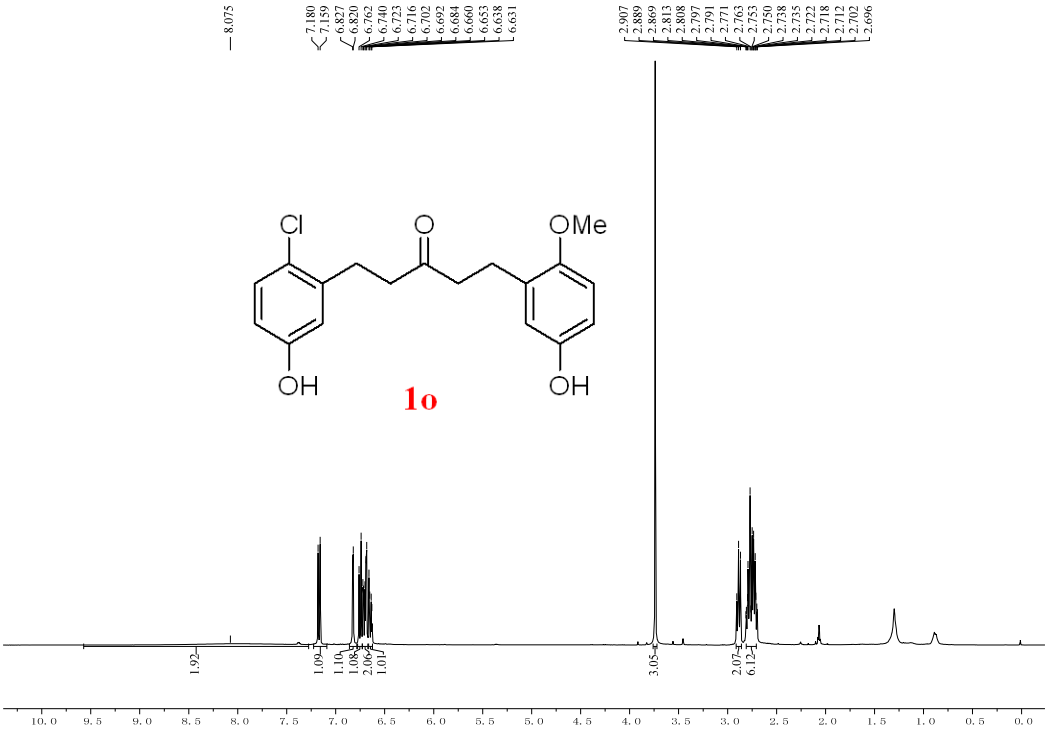
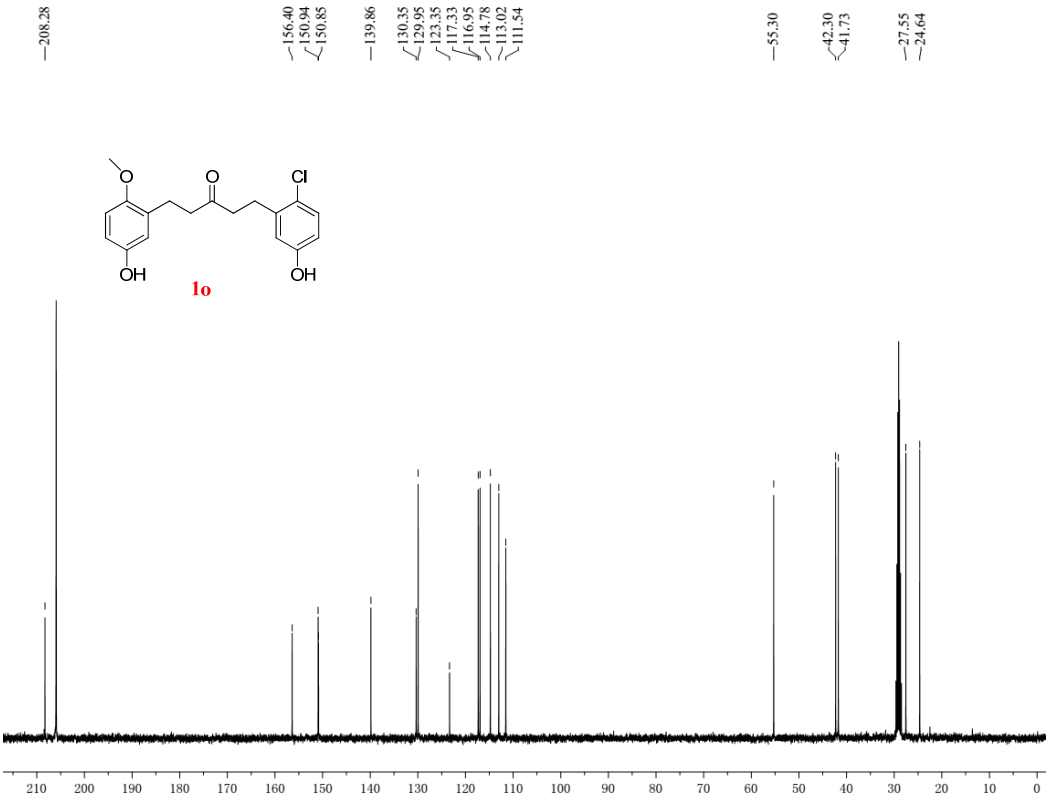
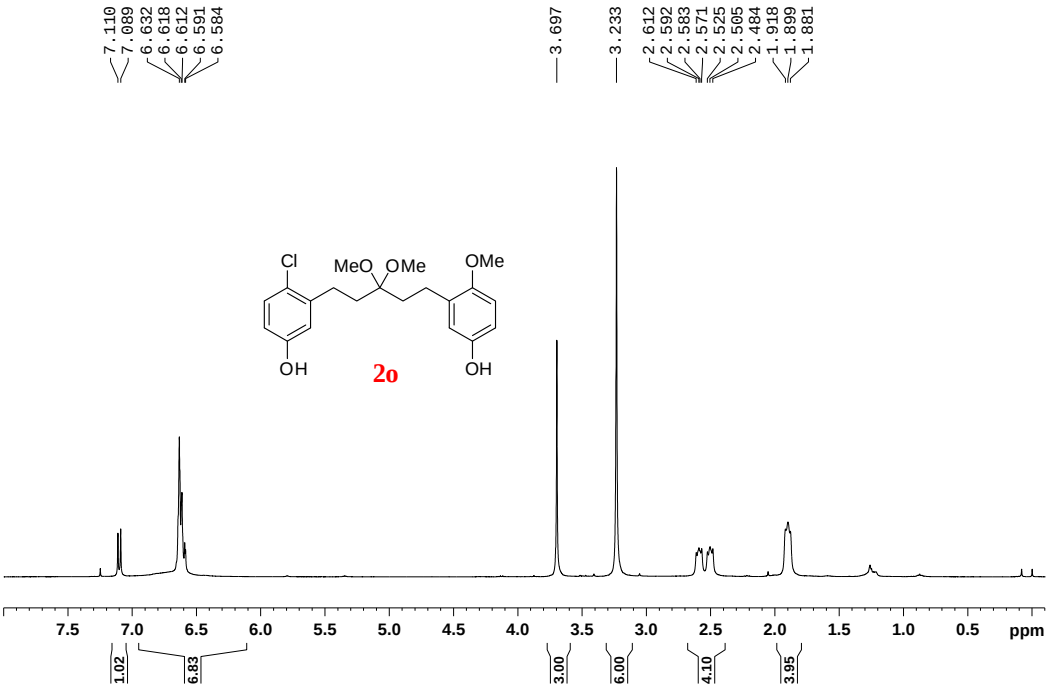
1.682
1.678
1.670

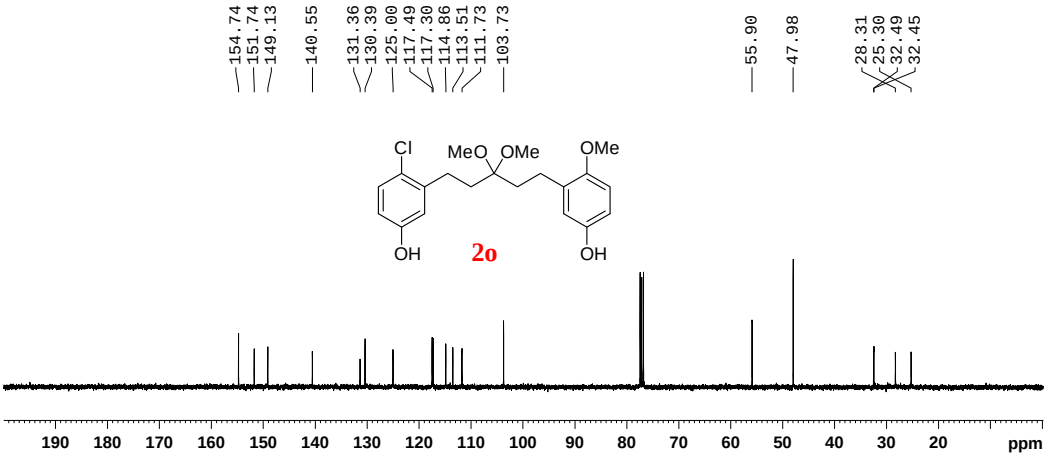

OMe
MeO
OMe
Ph
OH
OH
2n
2.07
5.00
1.02
1.05
2.08
1.90
3.04
6.00
2.09
2.05
4.16
f1 (ppm)

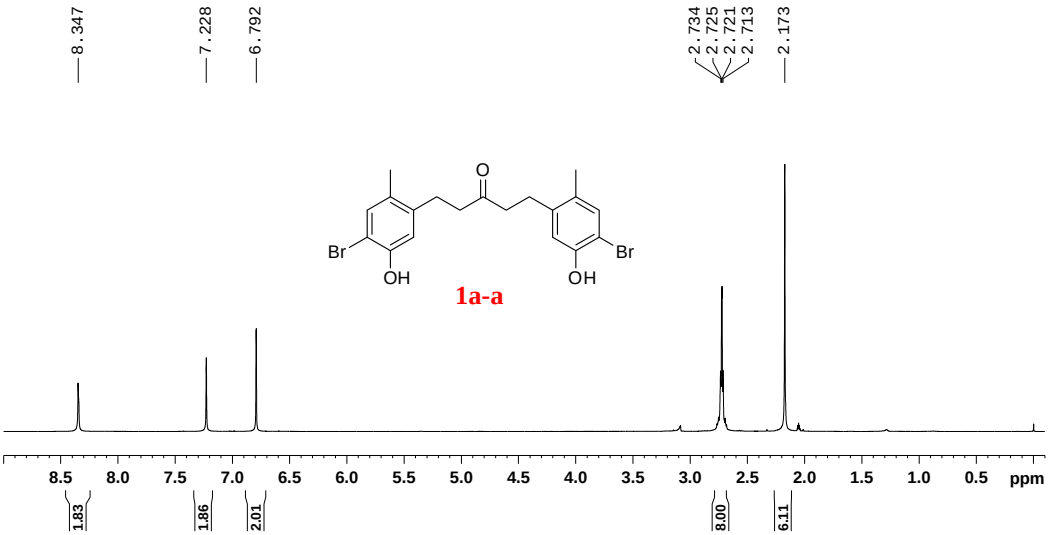

156.88
150.99
150.83
142.02
141.07
133.41
131.20
131.02
129.50
128.18
126.50
116.99
116.00
112.89
112.74
111.42
102.38
55.21
46.62
34.23
32.60
27.74
24.78
OMe
MeO
OMe
Ph
OH
OH
2n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

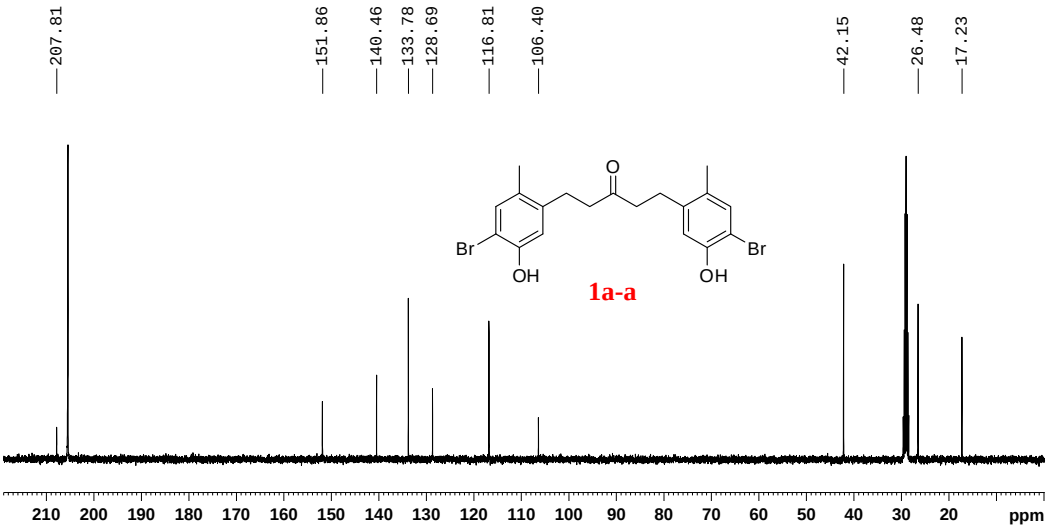

8.075
7.180
7.159
6.827
6.820
6.762
6.740
6.723
6.716
6.702
6.692
6.684
6.660
6.653
6.638
6.631
2.907
2.889
2.869
2.813
2.808
2.797
2.791
2.771
2.763
2.753
2.750
2.738
2.735
2.722
2.718
2.712
2.702
2.696
Cl
O
OMe
OH
OH
1o
1.92
1.09
1.10
1.08
2.06
1.01
3.05
2.07
6.12

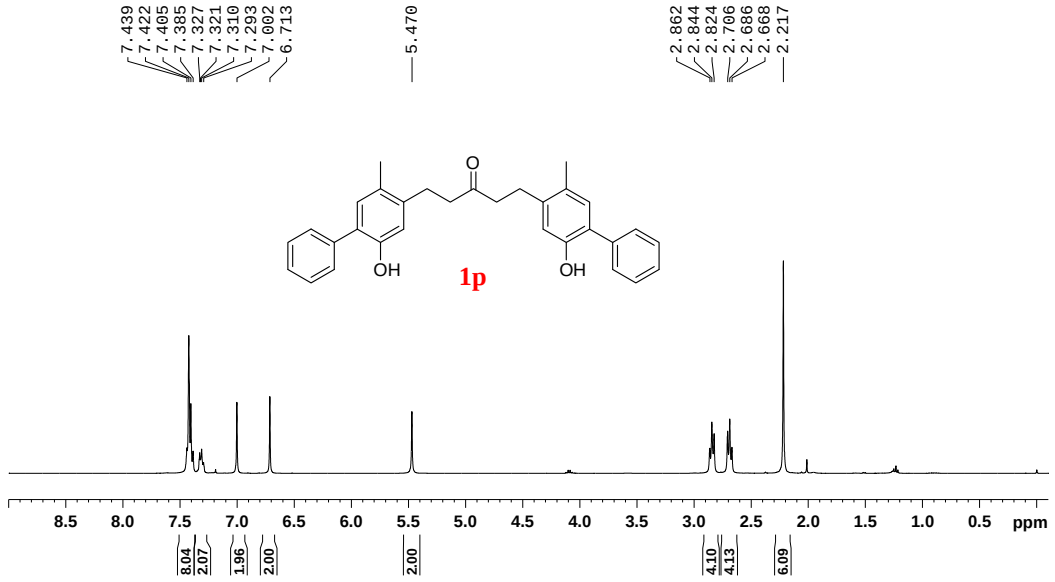

208.28
156.40
150.94
150.85
139.86
130.35
129.95
123.35
117.33
116.95
114.78
113.02
111.54
55.30
42.30
41.73
27.55
24.64
O
O
Cl
OH
OH
1o


7.110
7.089
6.632
6.618
6.612
6.591
6.584
3.697
3.233
2.612
2.592
2.583
2.571
2.525
2.505
2.484
1.918
1.899
1.881
Cl
MeO
OMe
OMe
OH
OH
2o
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
ppm
1.02
6.83
3.00
6.00
4.10
3.95


154.74
151.74
149.13
140.55
131.36
130.39
125.00
117.49
117.30
114.86
113.51
111.73
103.73
55.90
47.98
28.31
25.30
32.49
32.45
Cl
MeO
OMe
OMe
OH
OH
2o
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


8.347
7.228
6.792
2.734
2.725
2.721
2.713
2.173
O
Br
OH
Br
OH
1a-a
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 0.5 ppm
1.83
1.86
2.01
8.00
6.11


207.81
151.86
140.46
133.78
128.69
116.81
106.40
42.15
26.48
17.23
O
Br
OH
Br
OH
1a-a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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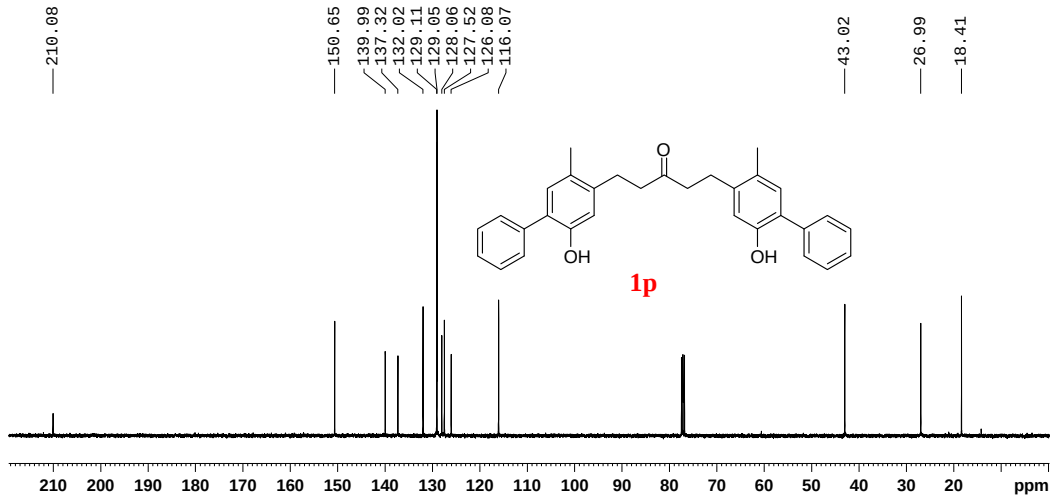
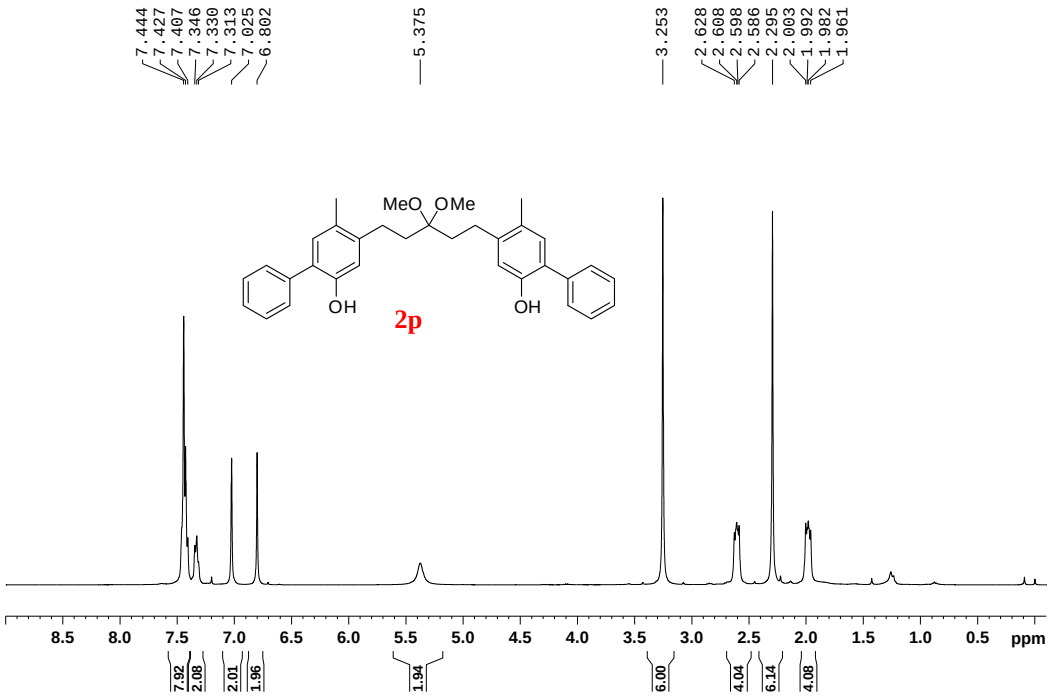
7.422
7.405
7.385
7.327
7.321
7.310
7.293
7.002
6.713
5.470
2.862
2.844
2.824
2.706
2.686
2.668
2.217
O
OH
OH
1p
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
8.04
2.07
1.96
2.00
2.00
4.10
4.13
6.09


210.08
150.65
139.99
137.32
132.02
129.11
129.05
128.06
127.52
126.08
116.07
43.02
26.99
18.41
O
OH
OH
1p
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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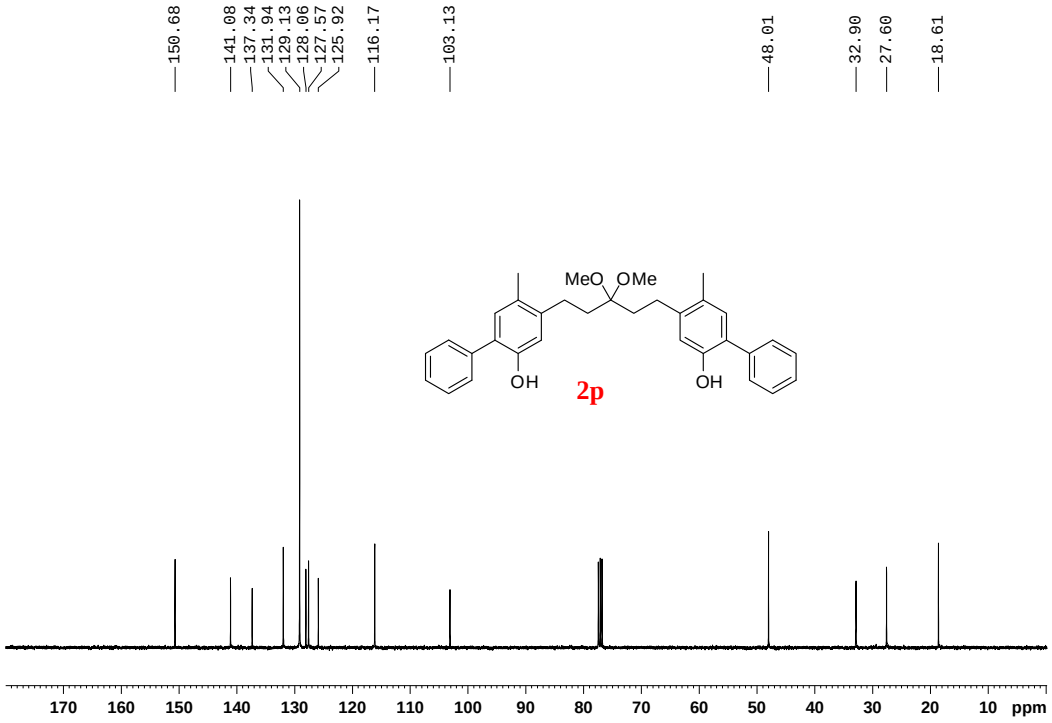
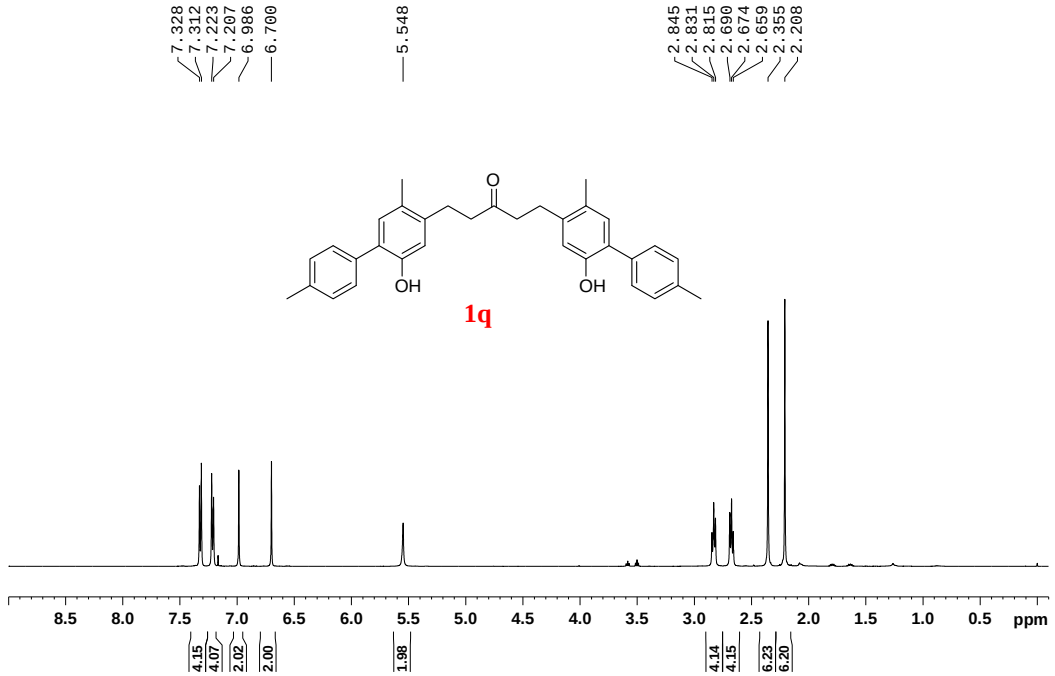
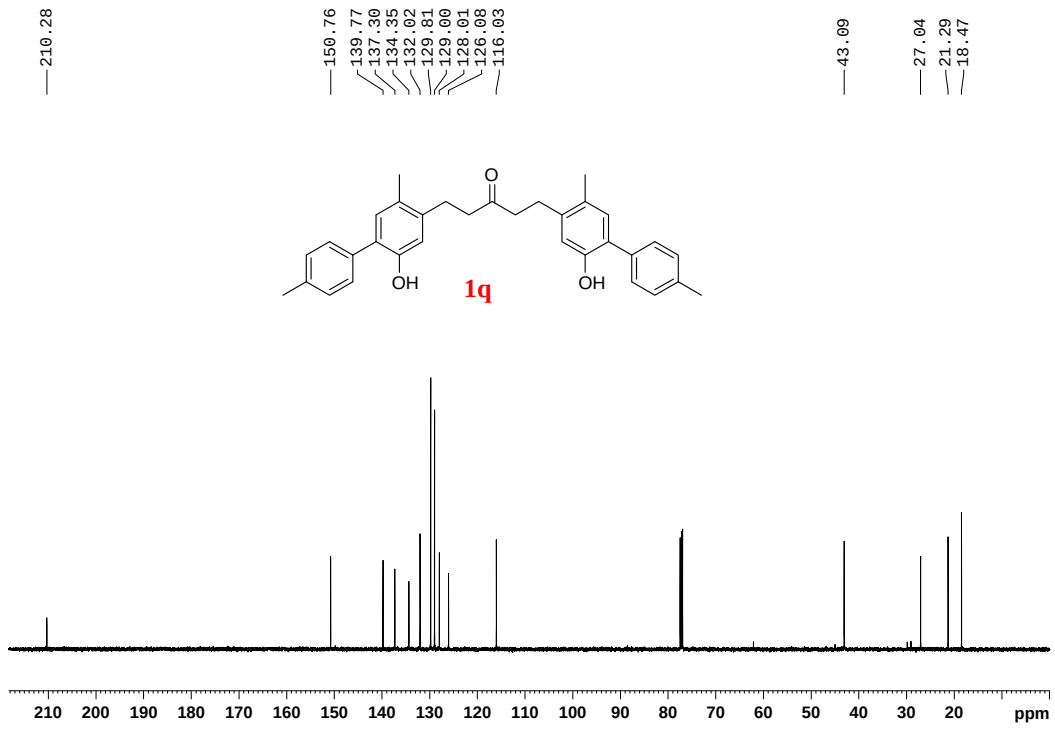
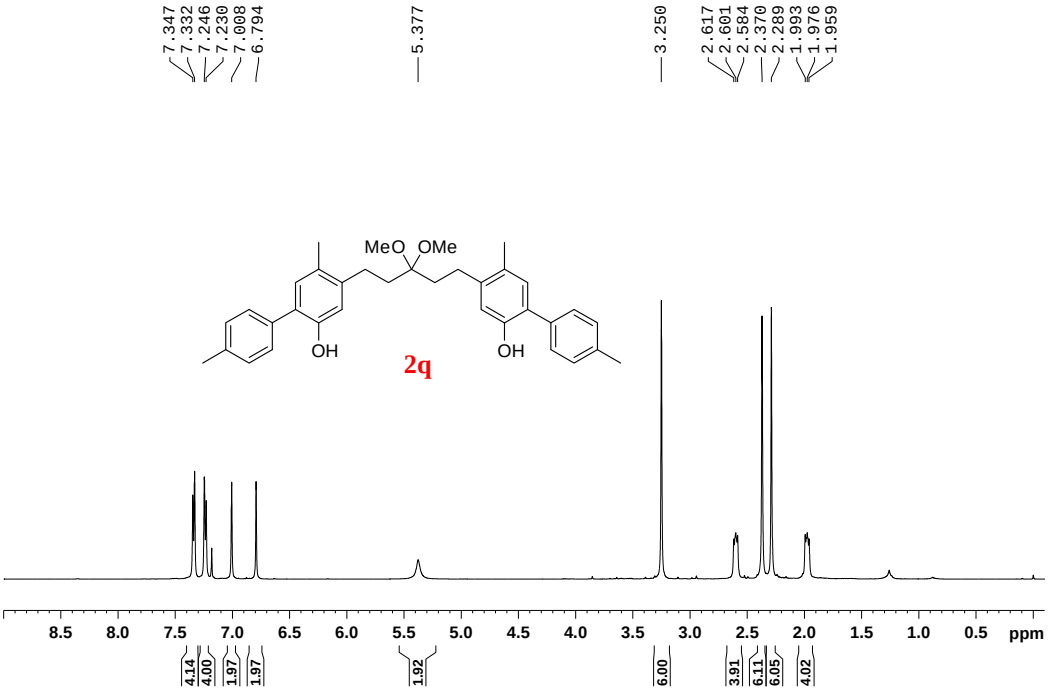
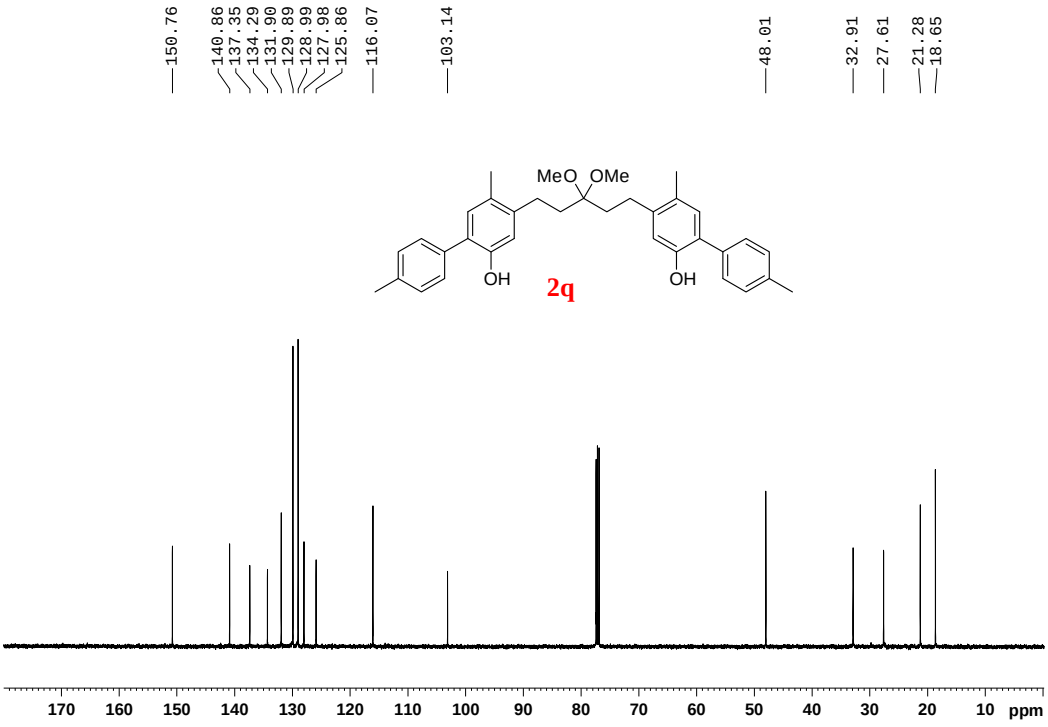
7.427
7.407
7.346
7.330
7.313
7.025
6.802
5.375
3.253
2.628
2.608
2.598
2.586
2.295
2.003
1.992
1.982
1.961
MeO
OMe
OH
OH
2p
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
7.92
2.08
2.01
1.96
1.94
6.00
4.04
6.14
4.08

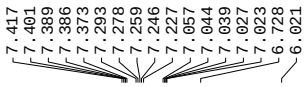

150.68
141.08
137.34
131.94
129.13
128.06
127.57
125.92
116.17
103.13
48.01
32.90
27.60
18.61
MeO
OMe
OH
OH
2p
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

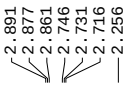

7.328
7.312
7.223
7.207
6.986
6.700
5.548
2.845
2.831
2.815
2.690
2.674
2.659
2.355
2.208
O
OH
OH
1q
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.15
4.07
2.02
2.00
1.98
4.14
4.15
6.23
6.20

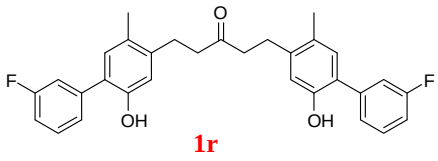

210.28
150.76
139.77
137.30
134.35
132.02
129.81
129.00
128.01
126.08
116.03
43.09
27.04
21.29
18.47
O
OH
OH
1q
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.347
7.332
7.246
7.230
7.008
6.794
5.377
3.250
2.617
2.601
2.584
2.370
2.289
1.993
1.976
1.959
MeO OMe
OH
OH
2q
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 0.5 ppm
4.14
4.00
1.97
1.97
1.92
6.00
3.91
6.11
6.05
4.02

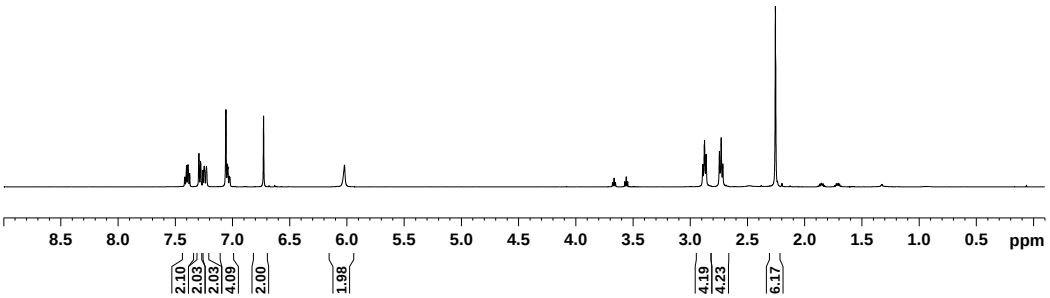

150.76
140.86
137.35
134.29
131.90
129.89
128.99
127.98
125.86
116.07
103.14
48.01
32.91
27.61
21.28
18.65
MeO OMe
OH
OH
2q
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

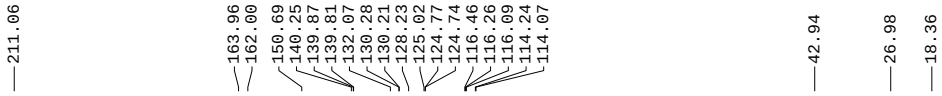

7.417
7.401
7.389
7.386
7.373
7.293
7.278
7.259
7.246
7.227
7.057
7.044
7.039
7.027
7.023
6.728
6.021

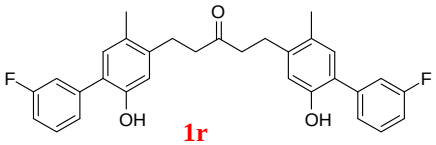

2.891
2.877
2.861
2.746
2.731
2.716
2.256


O
F
OH
OH
F

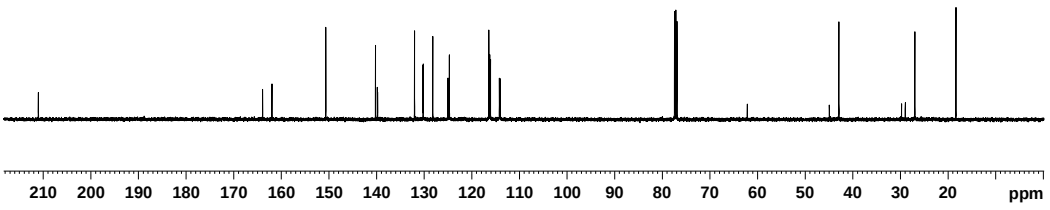
**1r**

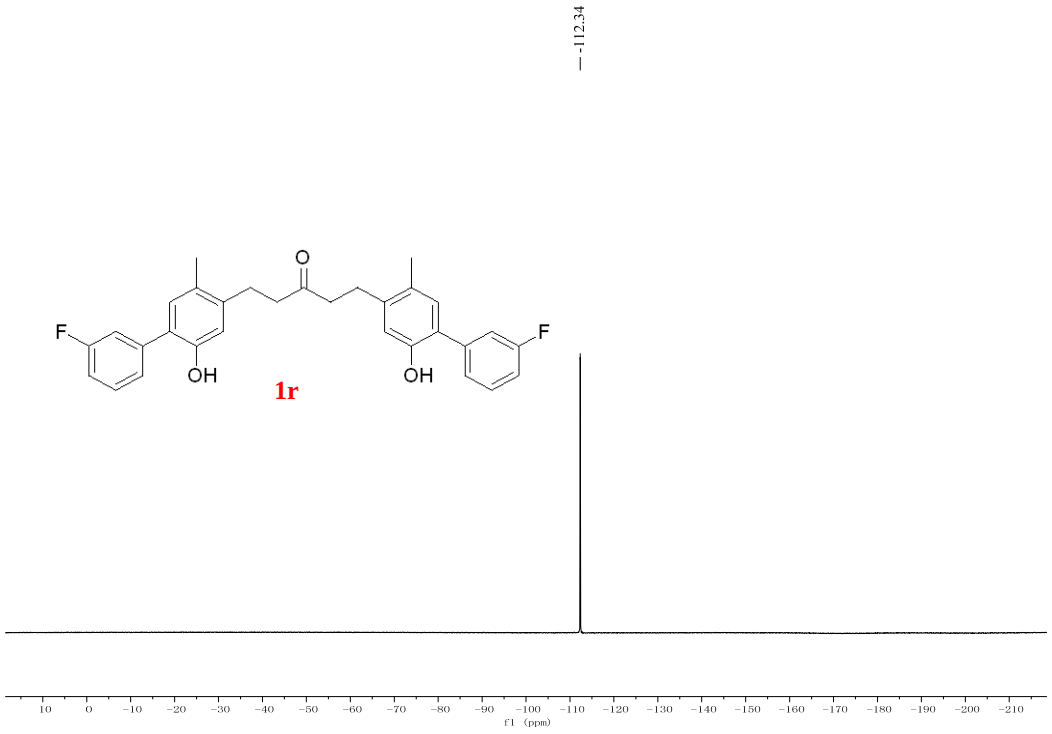

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.10
2.03
2.03
4.09
2.00
1.98
4.19
4.23
6.17

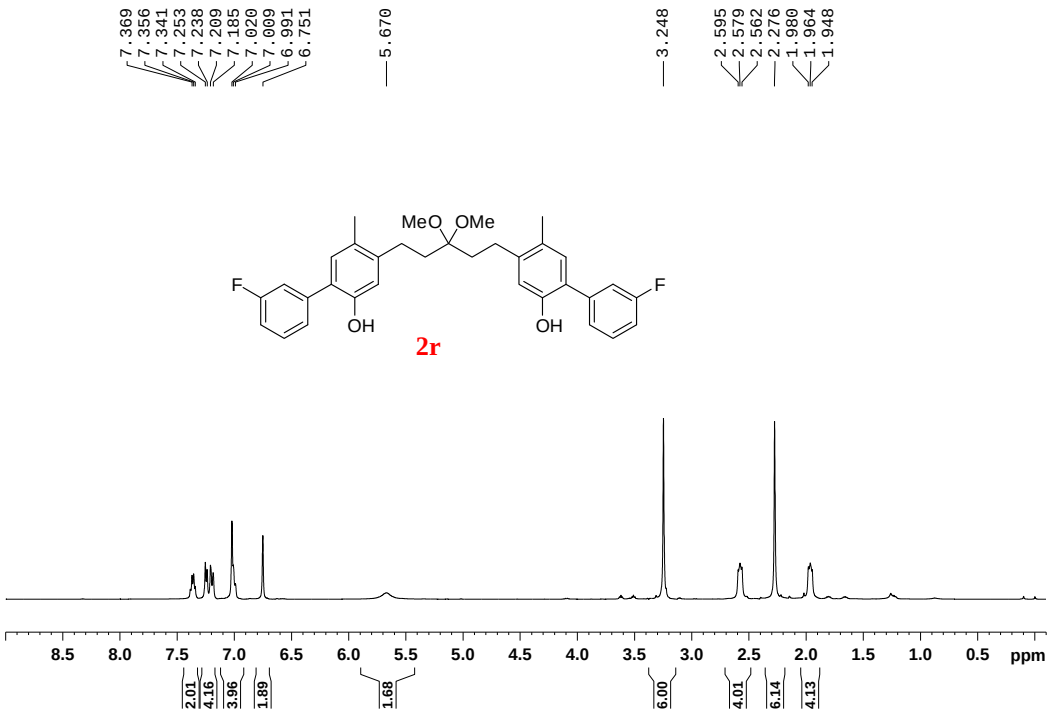

211.06
163.96
162.00
150.69
140.25
139.87
139.81
132.07
130.28
130.21
128.23
125.02
124.77
124.74
116.46
116.26
116.09
114.24
114.07
42.94
26.98
18.36

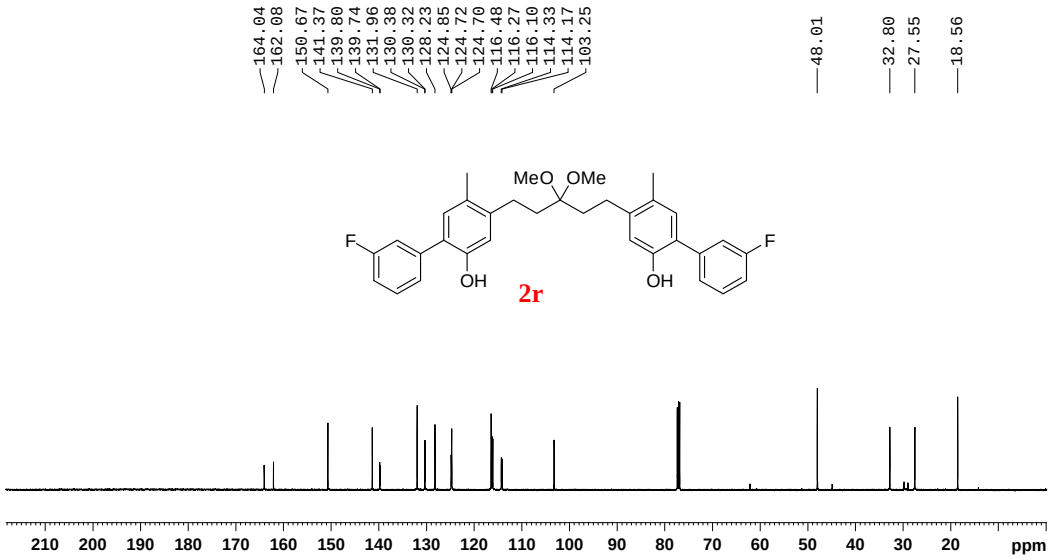

O
F
OH
OH
F

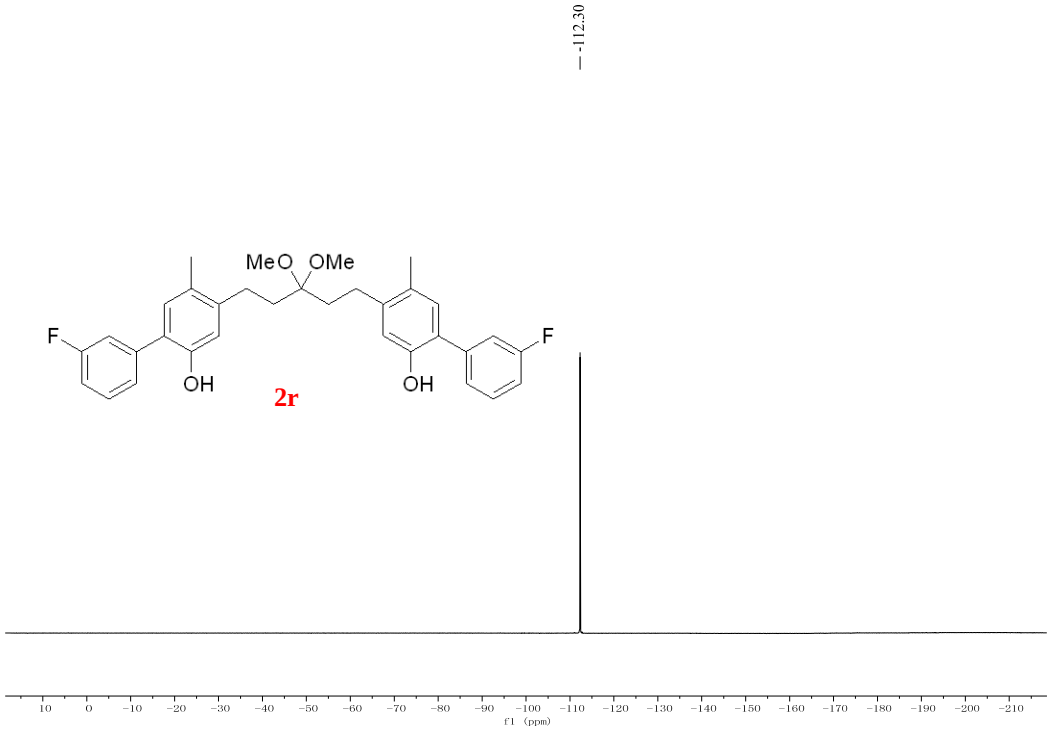
**1r**

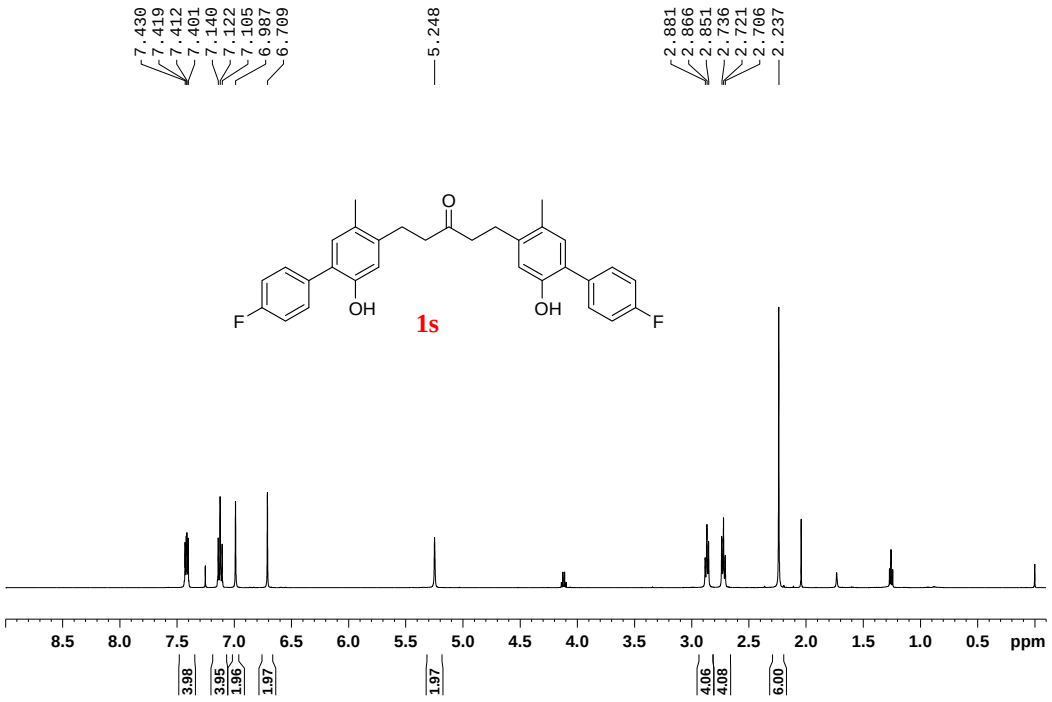

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

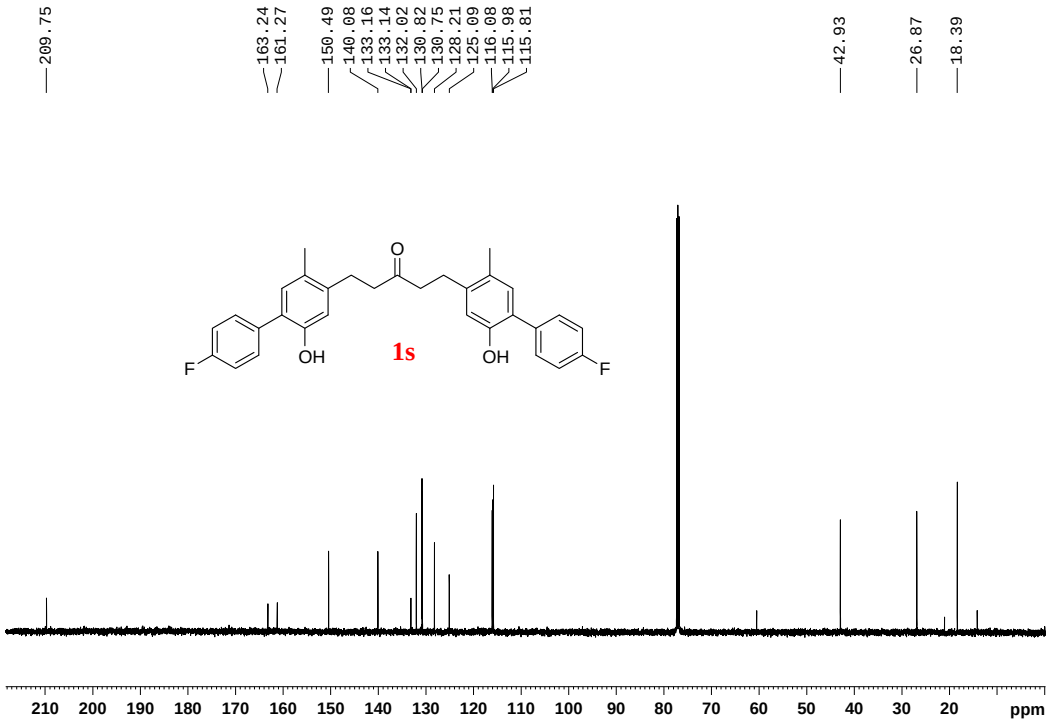

-112.34
O
F
OH
OH
F
1r
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

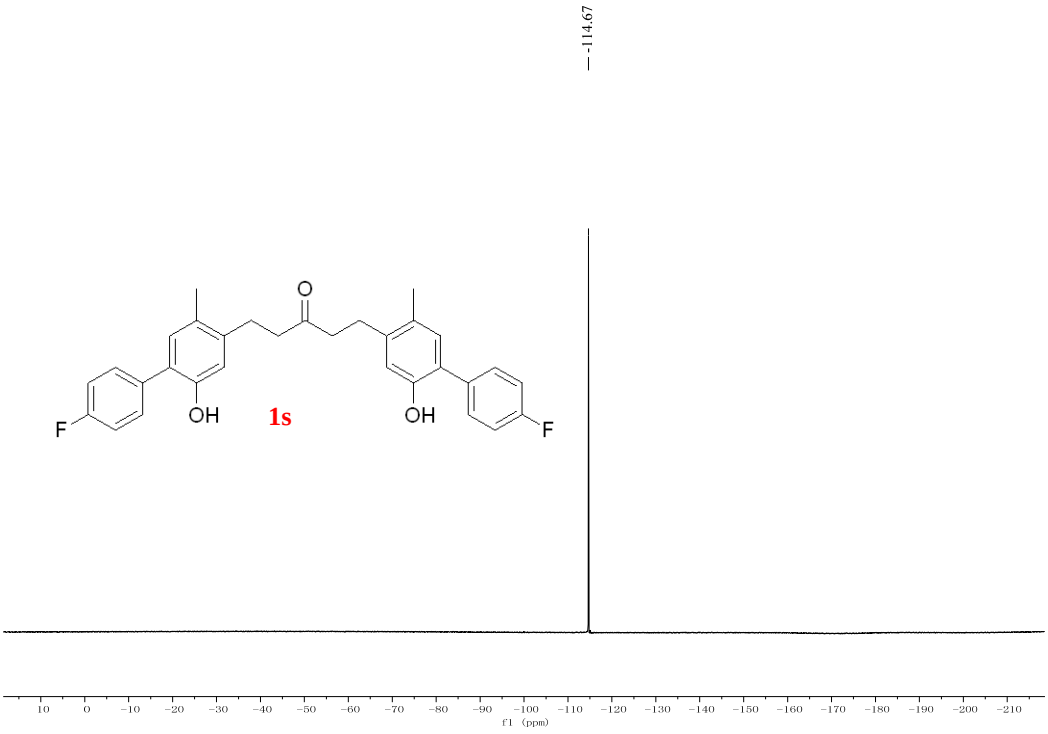

7.369
7.356
7.341
7.253
7.238
7.209
7.185
7.020
7.009
6.991
6.751
5.670
3.248
2.595
2.579
2.562
2.276
1.980
1.964
1.948
MeO
OMe
F
OH
OH
F
2r
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.01
4.16
3.96
1.89
1.68
6.00
4.01
6.14
4.13

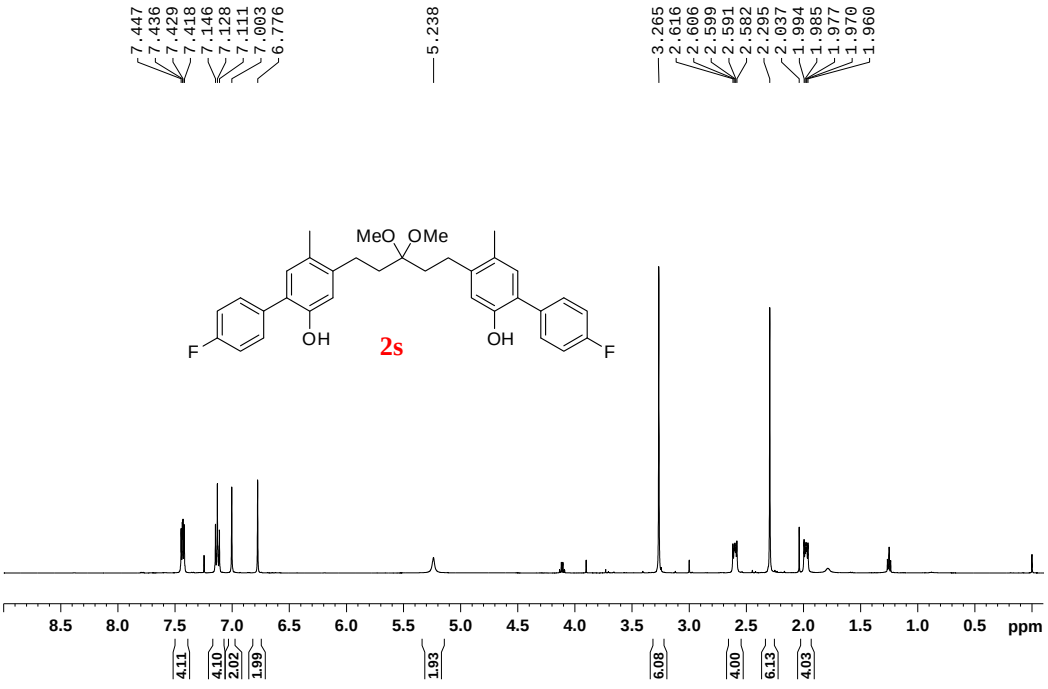

164.04
162.08
150.67
141.37
139.80
139.74
131.96
130.38
130.32
128.23
124.85
124.72
124.70
116.48
116.27
116.10
114.33
114.17
103.25
48.01
32.80
27.55
18.56
MeO
OMe
F
OH
OH
F
2r
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

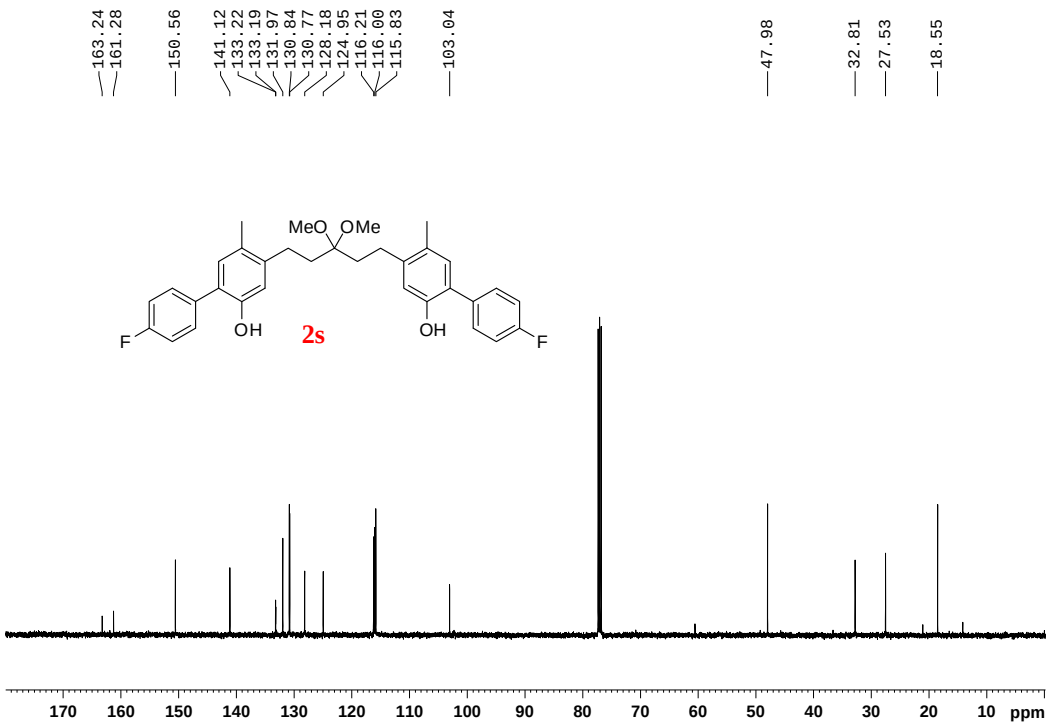

-112.30
MeO
OMe
F
OH
OH
F
2r
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

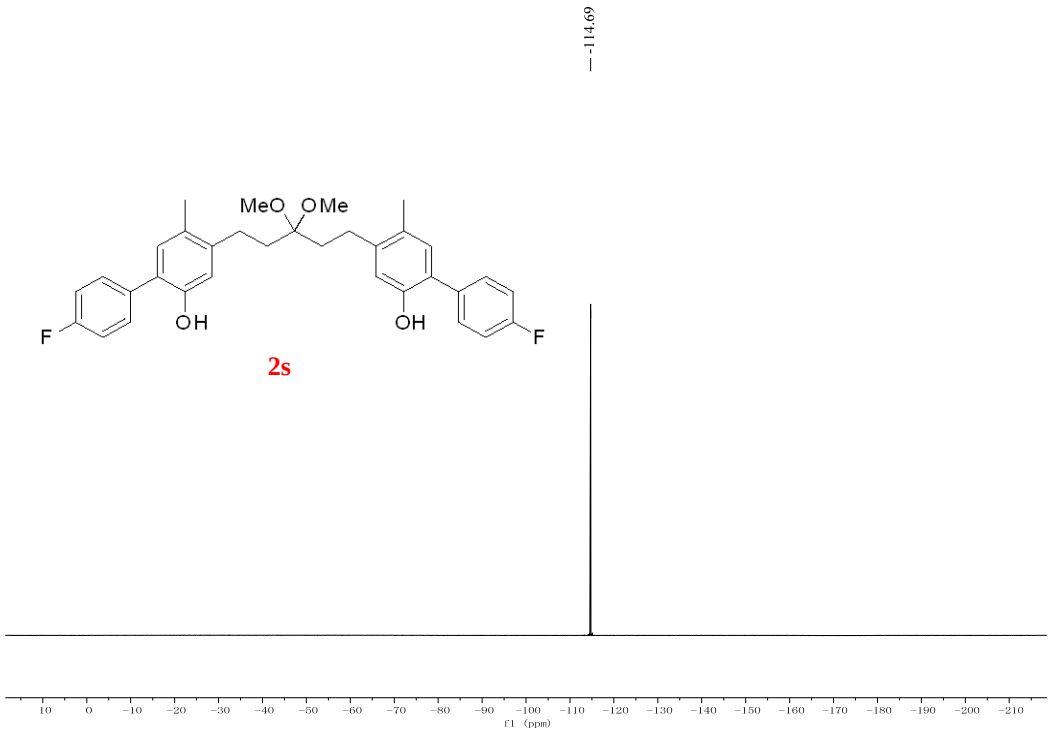

7.430
7.419
7.412
7.401
7.140
7.122
7.105
6.987
6.709
5.248
2.881
2.866
2.851
2.736
2.721
2.706
2.237
O
OH
OH
F
F
1s
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
3.98
3.95
1.96
1.97
1.97
4.06
4.08
6.00

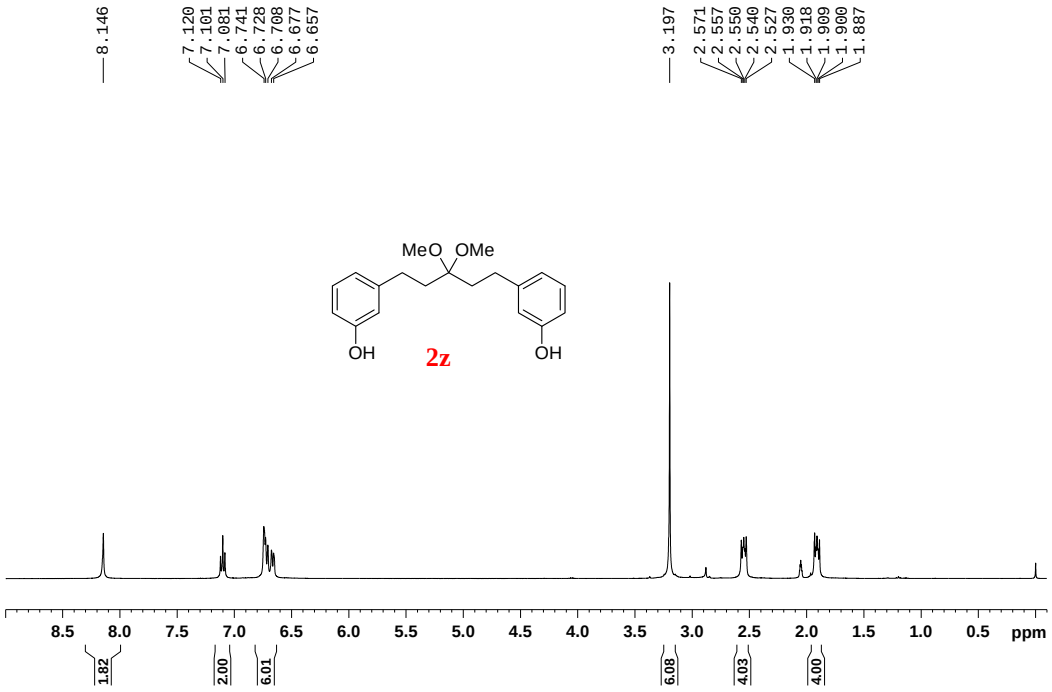

209.75
163.24
161.27
150.49
140.08
133.16
133.14
132.02
130.82
130.75
128.21
125.09
116.08
115.98
115.81
42.93
26.87
18.39
O
OH
OH
F
F
1s
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

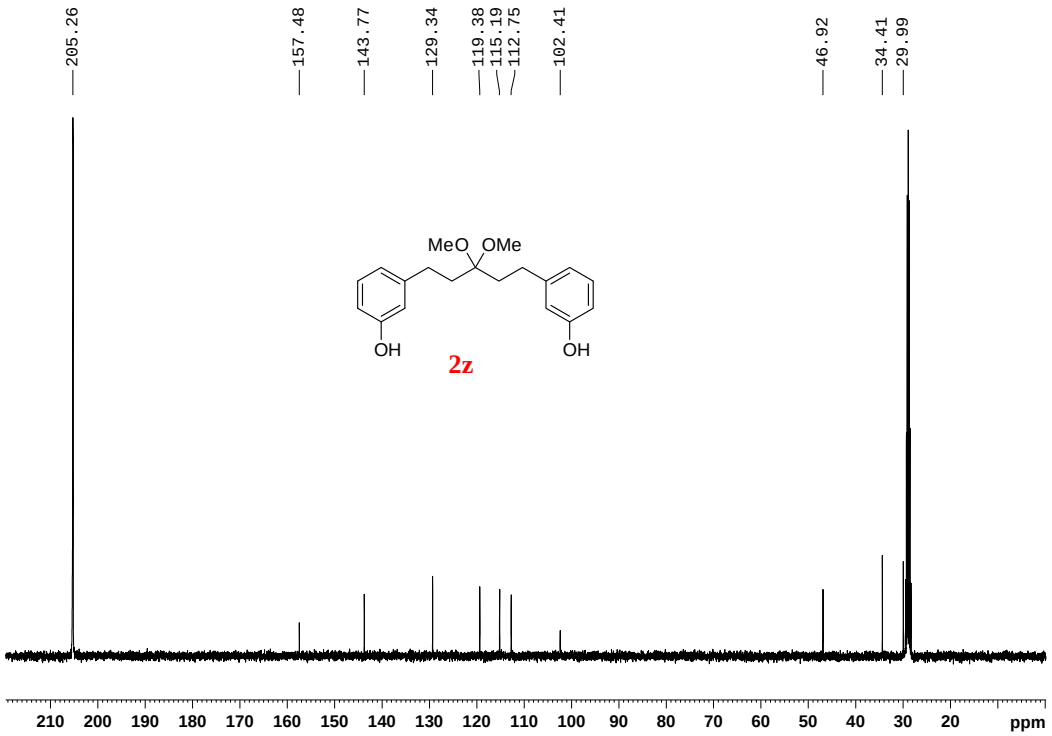

-114.67
O
F
OH
1s
OH
F
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)


7.447
7.436
7.429
7.418
7.146
7.128
7.111
7.003
6.776
5.238
3.265
2.616
2.606
2.599
2.591
2.582
2.295
2.037
1.994
1.985
1.977
1.970
1.960
MeO
OMe
OH
2s
OH
F
F
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 0.5 ppm
4.11
4.10
2.02
1.99
1.93
6.08
4.00
6.13
4.03

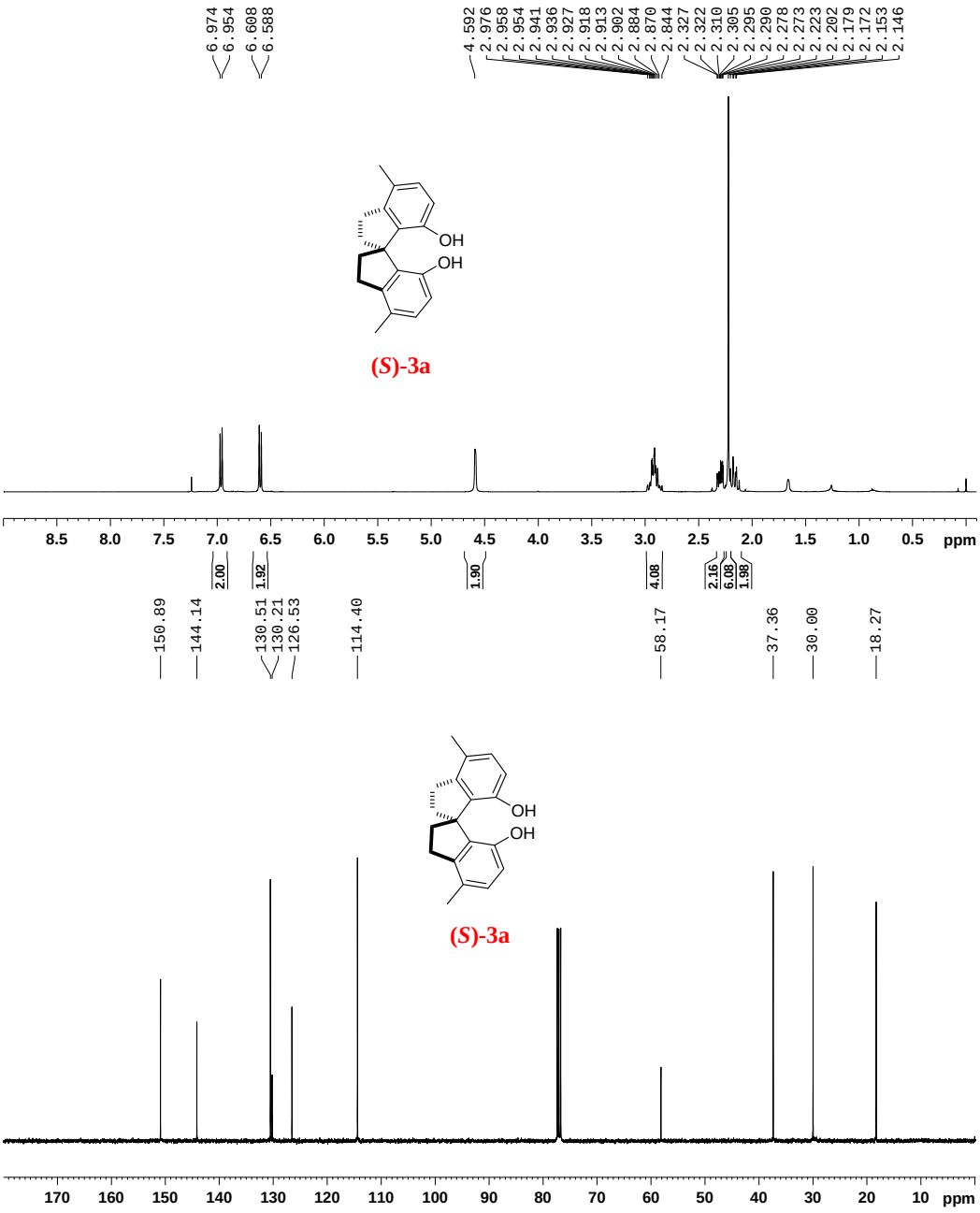

163.24
161.28
150.56
141.12
133.22
133.19
131.97
130.84
130.77
128.18
124.95
116.21
116.00
115.83
103.04
47.98
32.81
27.53
18.55
MeO
OMe
OH
OH
F
F
2s
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

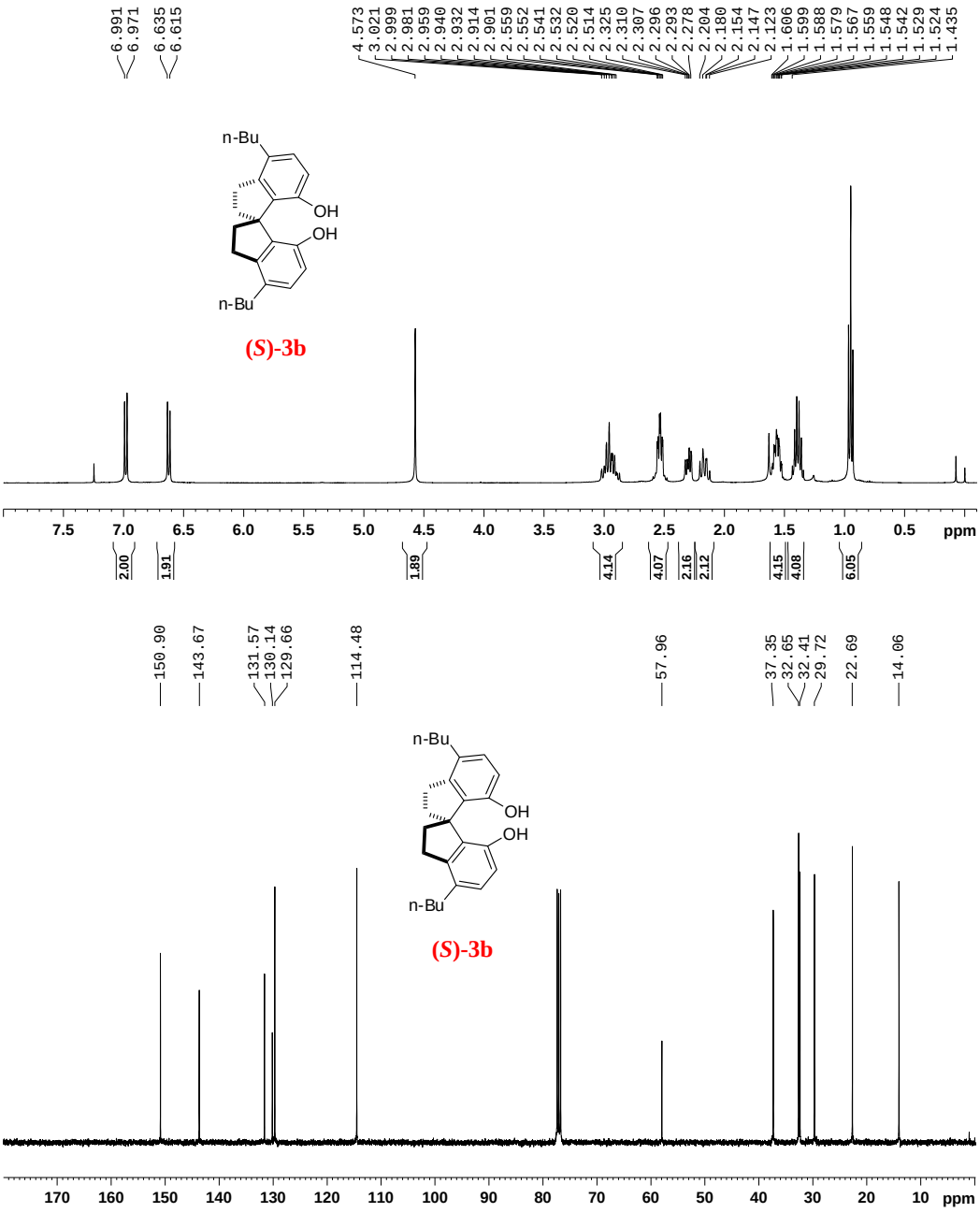

-114.69
MeO
OMe
OH
OH
F
F
2s
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

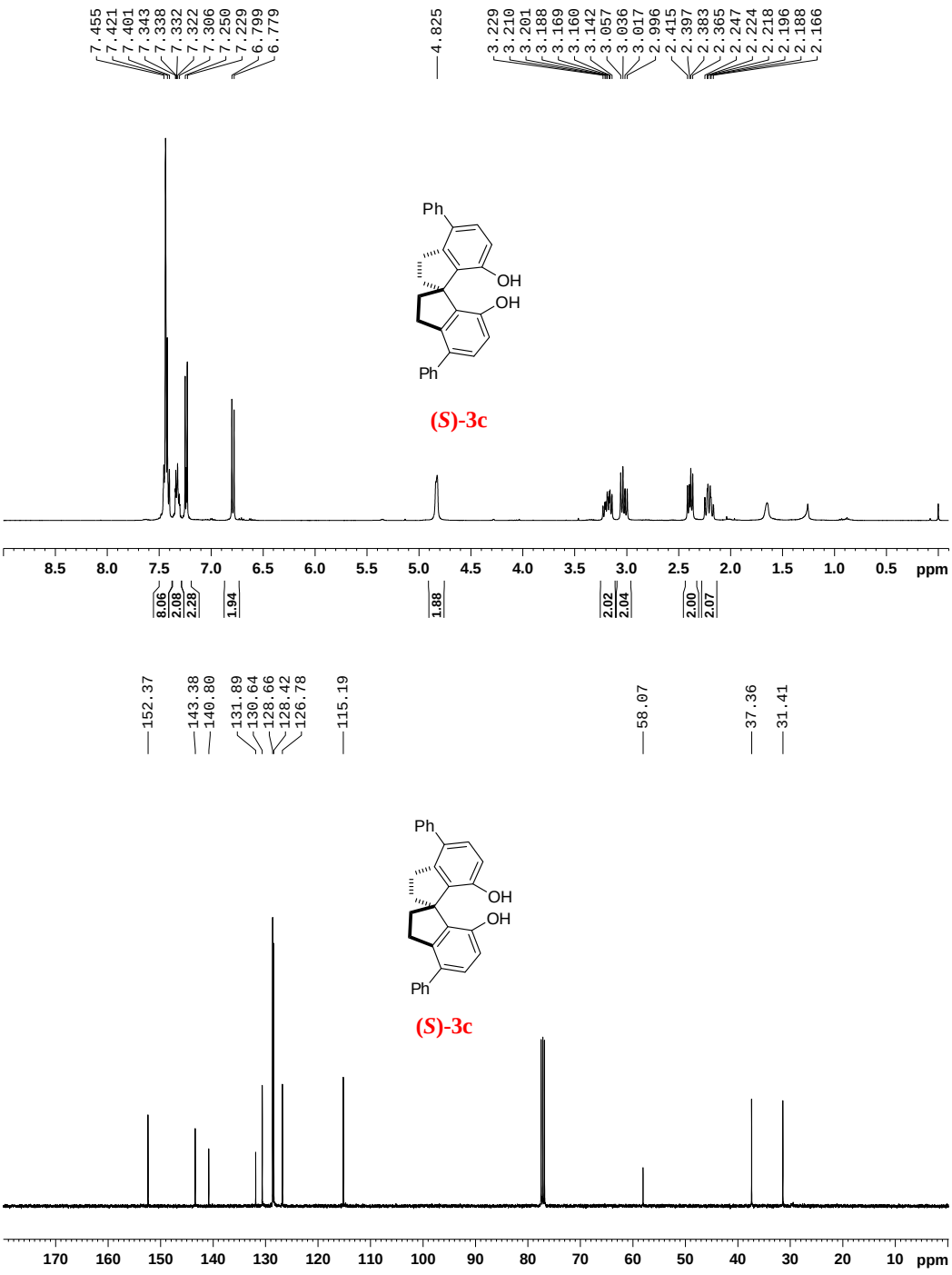

8.146
7.120
7.101
7.081
6.741
6.728
6.708
6.677
6.657
3.197
2.571
2.557
2.550
2.540
2.527
1.930
1.918
1.909
1.900
1.887
MeO
OMe
OH
OH
2z
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.82
2.00
6.01
6.08
4.03
4.00

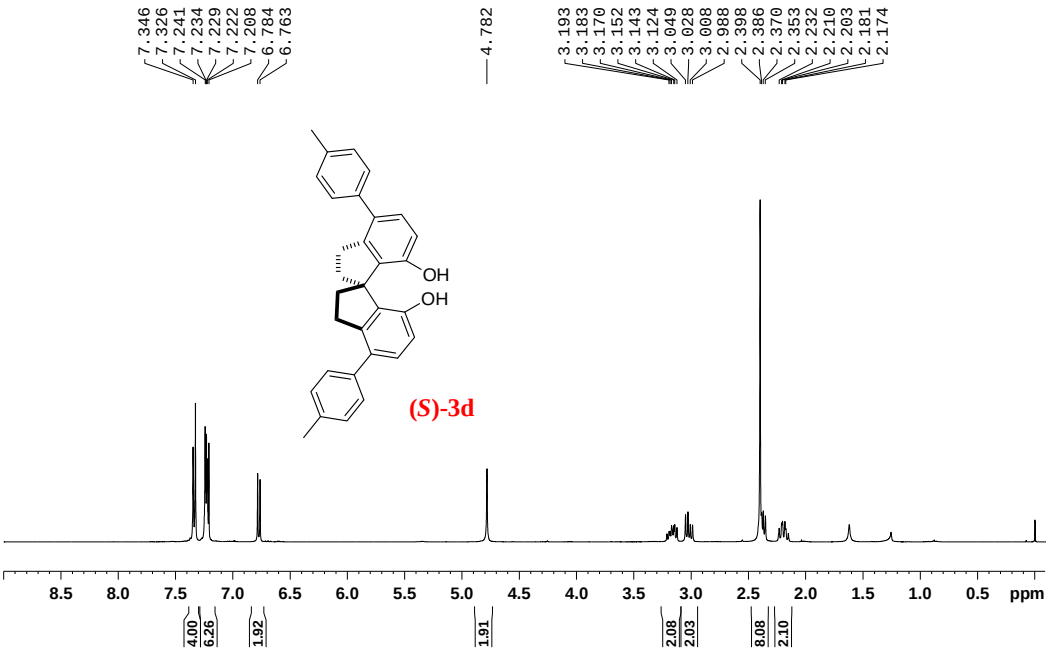

205.26
157.48
143.77
129.34
119.38
115.19
112.75
102.41
46.92
34.41
29.99
MeO
OMe
OH
OH
2z
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

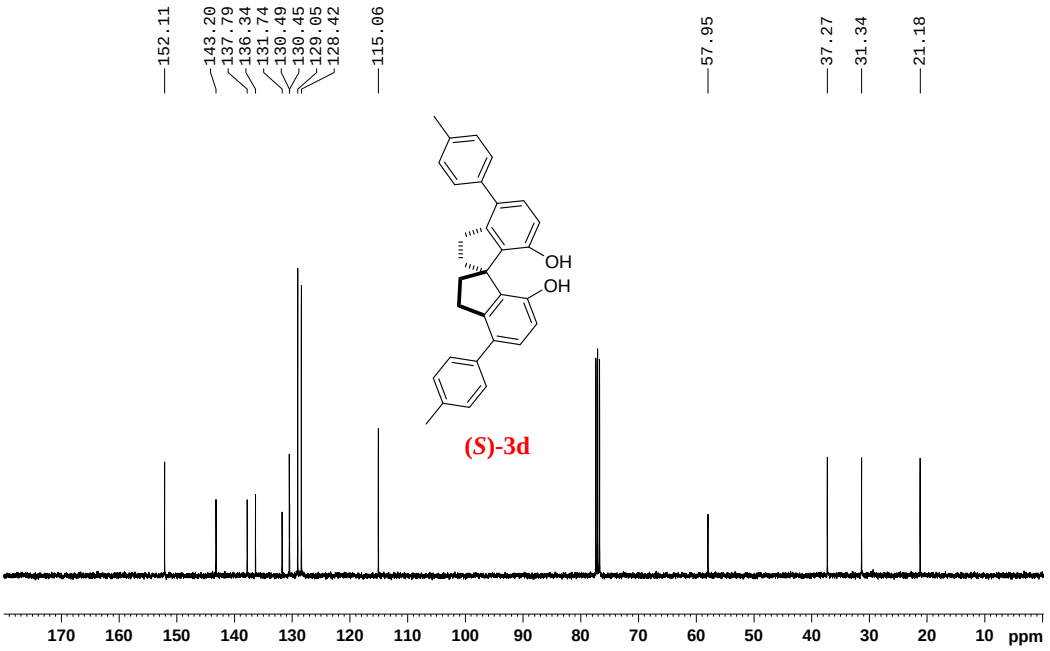
# Copies of $^{1}H$ and $^{13}C$ NMR Spectra of products 3

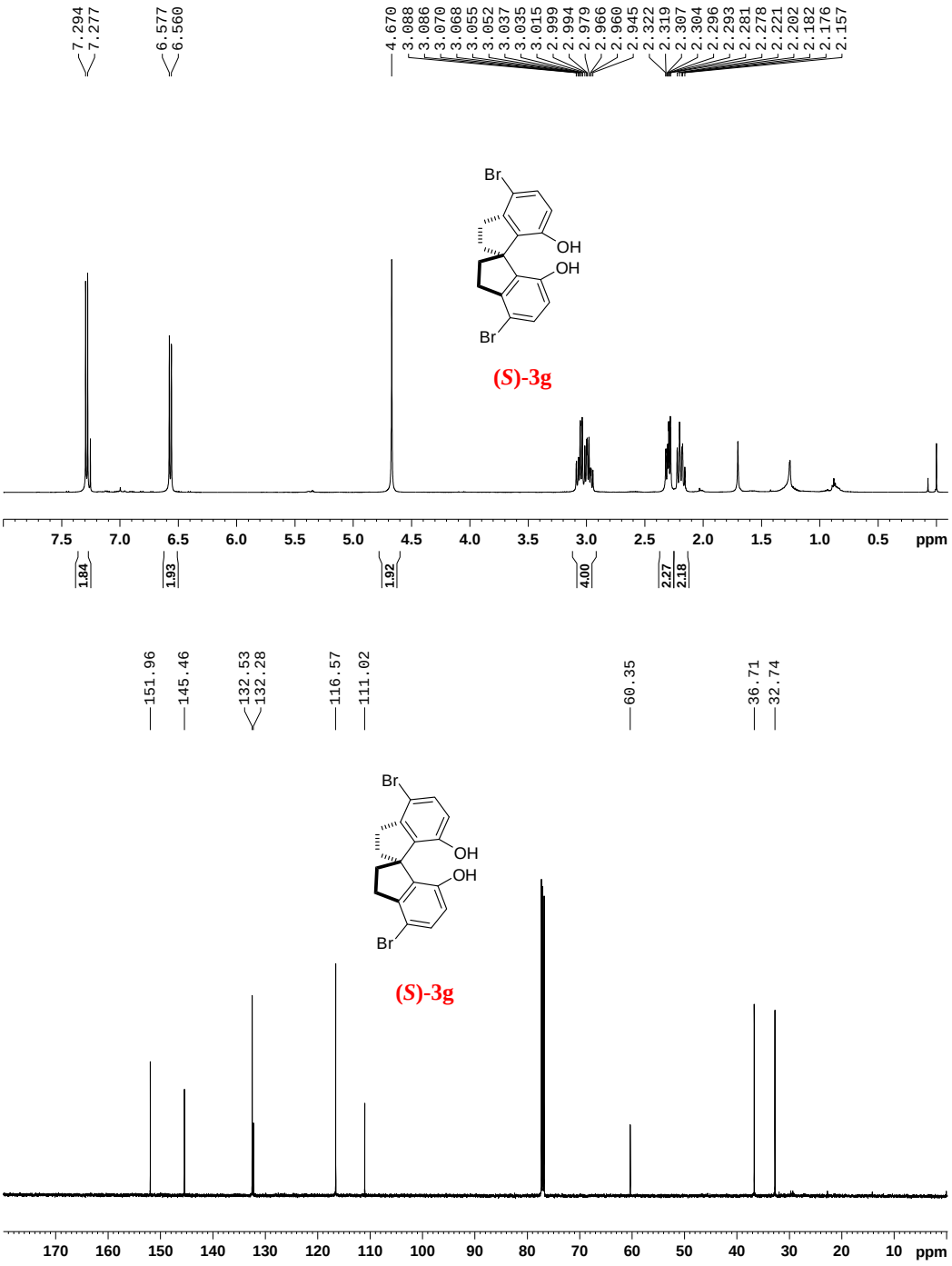


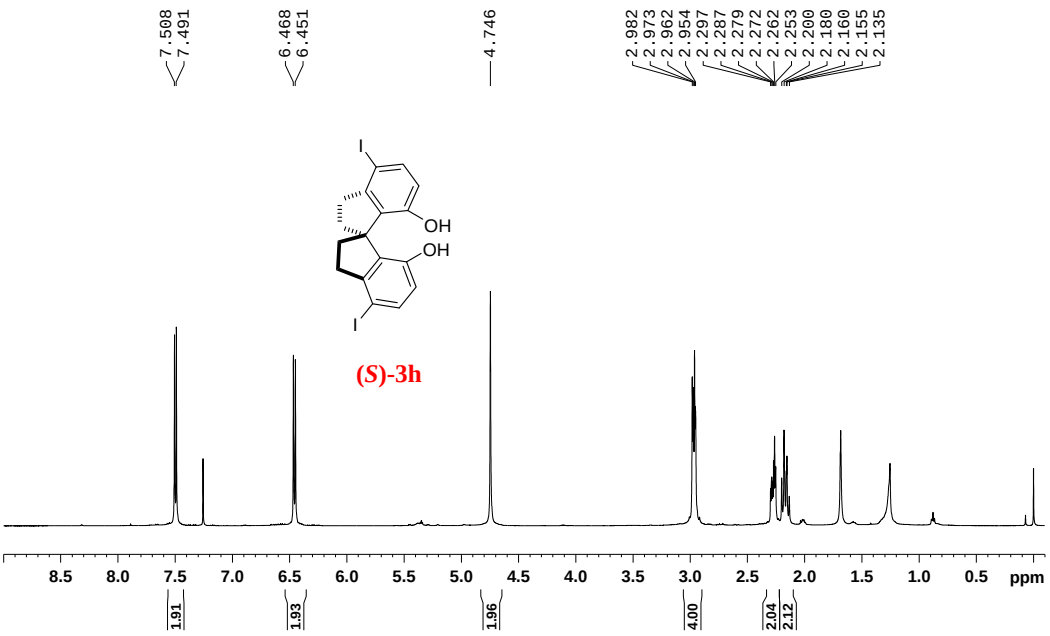

6.991
6.971
6.635
6.615
4.573
3.021
2.999
2.981
2.959
2.940
2.932
2.914
2.901
2.559
2.552
2.541
2.532
2.520
2.514
2.325
2.310
2.307
2.296
2.293
2.278
2.204
2.180
2.154
2.147
2.123
1.606
1.599
1.588
1.579
1.567
1.559
1.548
1.542
1.529
1.524
1.435
n-Bu
OH
OH
n-Bu
(S)-3b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.91
1.89
4.14
4.07
2.16
2.12
4.15
4.08
6.05
150.90
143.67
131.57
130.14
129.66
114.48
57.96
37.35
32.65
32.41
29.72
22.69
14.06
n-Bu
OH
OH
n-Bu
(S)-3b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

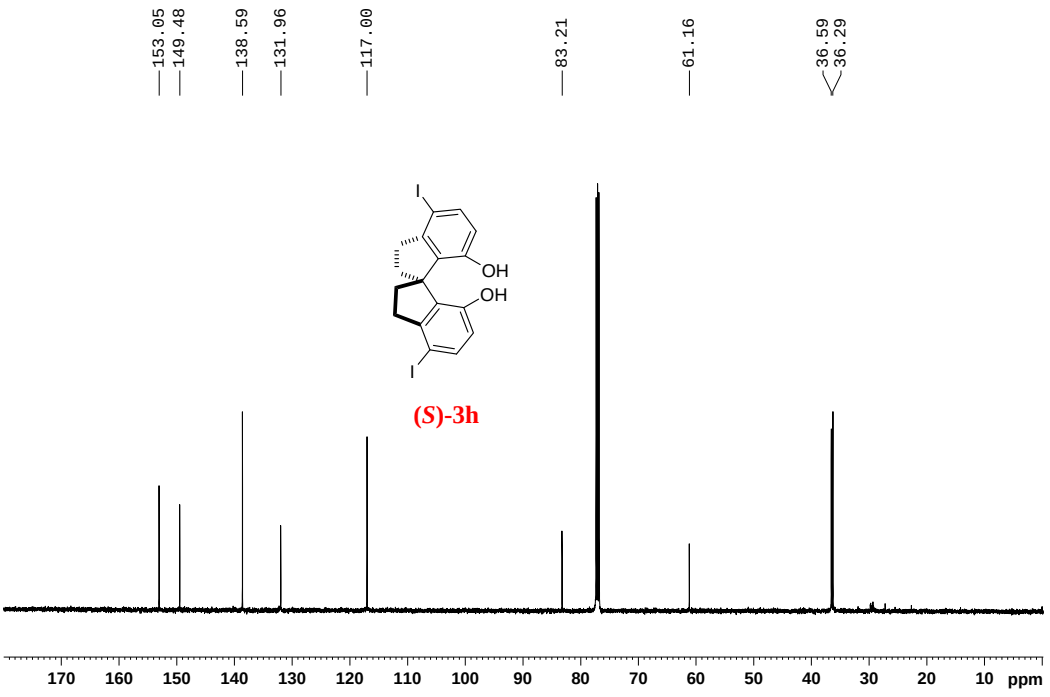

7.455
7.421
7.401
7.343
7.338
7.332
7.322
7.306
7.250
7.229
6.799
6.779
4.825
3.229
3.210
3.201
3.188
3.169
3.160
3.142
3.057
3.036
3.017
2.996
2.415
2.397
2.383
2.365
2.247
2.224
2.218
2.196
2.188
2.166
Ph
OH
OH
Ph
(S)-3c
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
8.06
2.08
2.28
1.94
1.88
2.02
2.04
2.00
2.07
152.37
143.38
140.80
131.89
130.64
128.66
128.42
126.78
115.19
58.07
37.36
31.41
Ph
OH
OH
Ph
(S)-3c
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

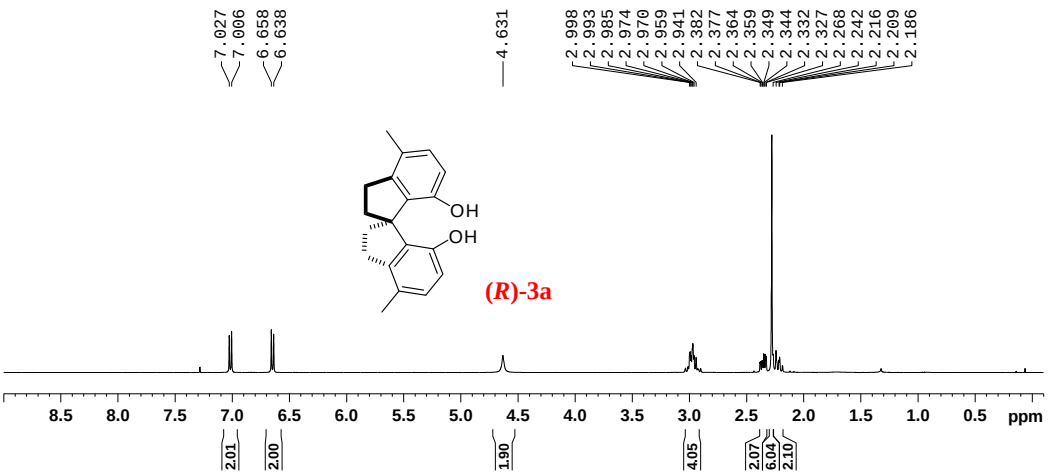

7.346
7.326
7.241
7.234
7.229
7.222
7.208
6.784
6.763
4.782
3.193
3.183
3.170
3.152
3.143
3.124
3.049
3.028
3.008
2.988
2.398
2.386
2.370
2.353
2.232
2.210
2.203
2.181
2.174
OH
OH
(S)-3d
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
4.00
6.26
1.92
1.91
2.08
2.03
8.08
2.10

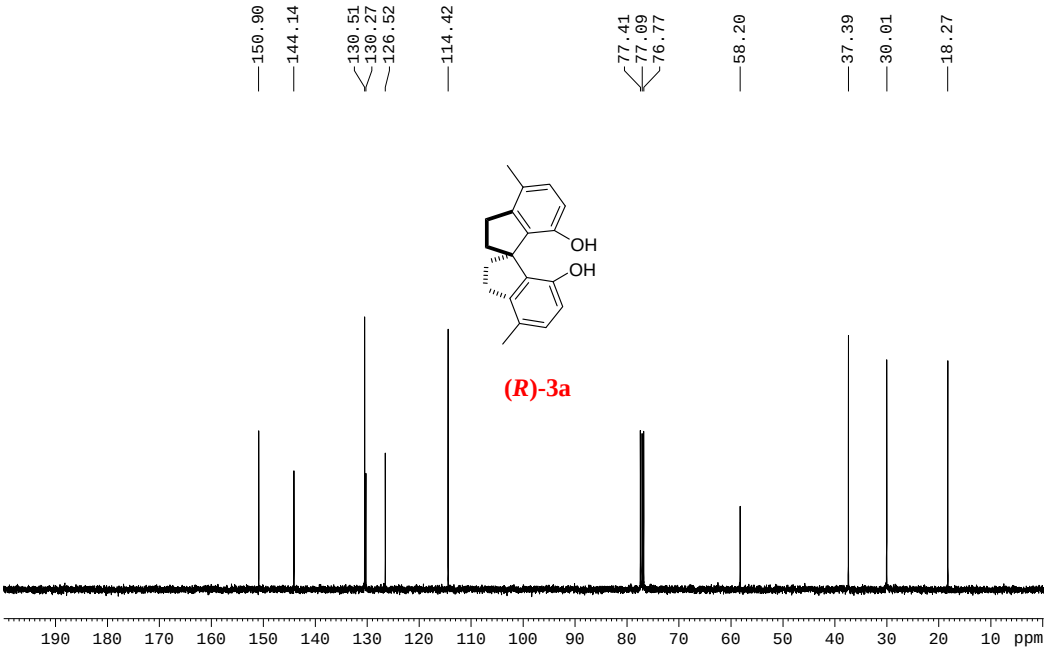

152.11
143.20
137.79
136.34
131.74
130.49
130.45
129.05
128.42
115.06
57.95
37.27
31.34
21.18
OH
OH
(S)-3d
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

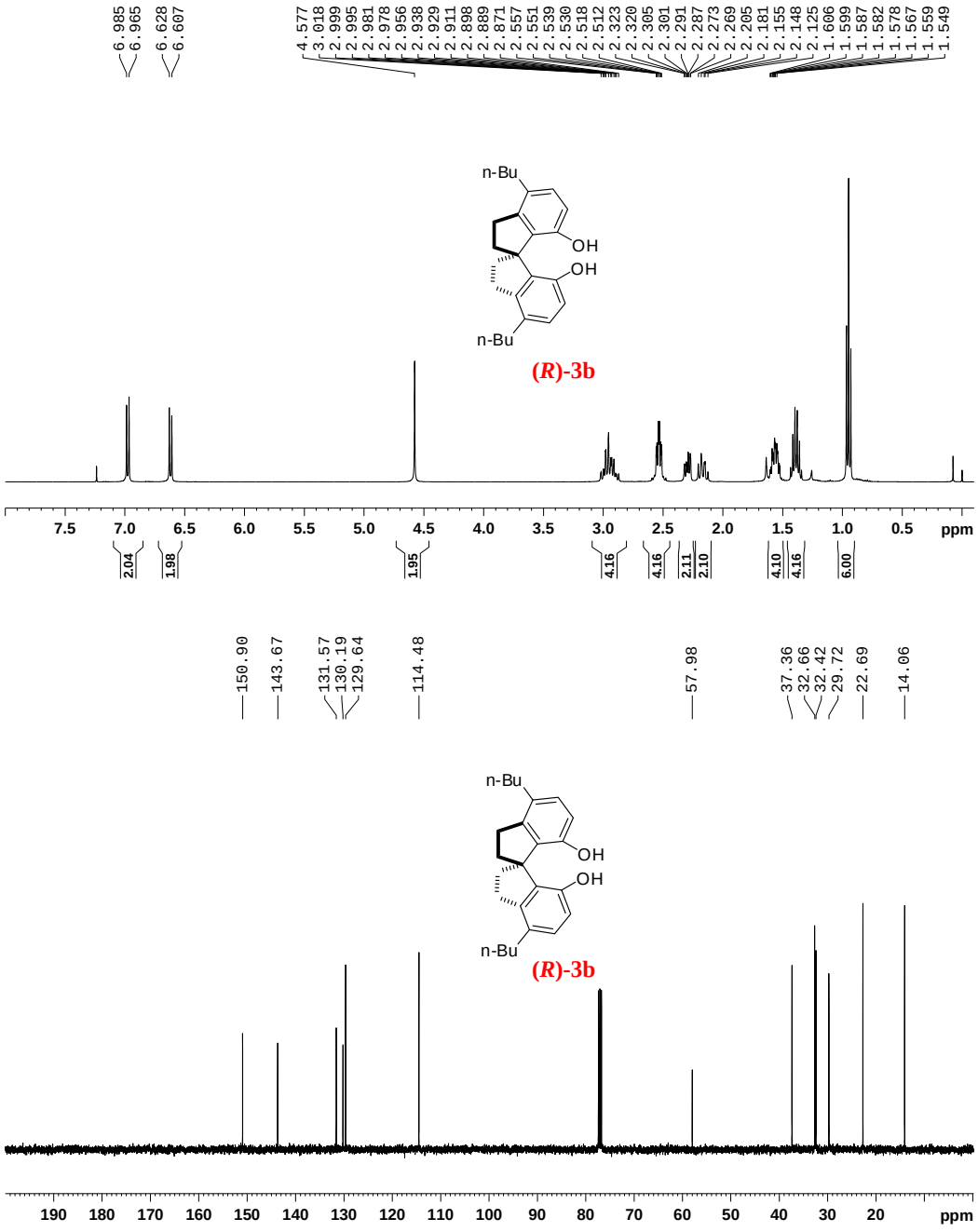

7.294
7.277
6.577
6.560
4.670
3.088
3.086
3.070
3.068
3.055
3.052
3.037
3.035
3.015
2.999
2.994
2.979
2.966
2.960
2.945
2.322
2.319
2.307
2.304
2.296
2.293
2.281
2.278
2.221
2.202
2.182
2.176
2.157
Br
OH
OH
Br
(S)-3g
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.84
1.93
1.92
4.00
2.27
2.18
151.96
145.46
132.53
132.28
116.57
111.02
60.35
36.71
32.74
Br
OH
OH
Br
(S)-3g
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

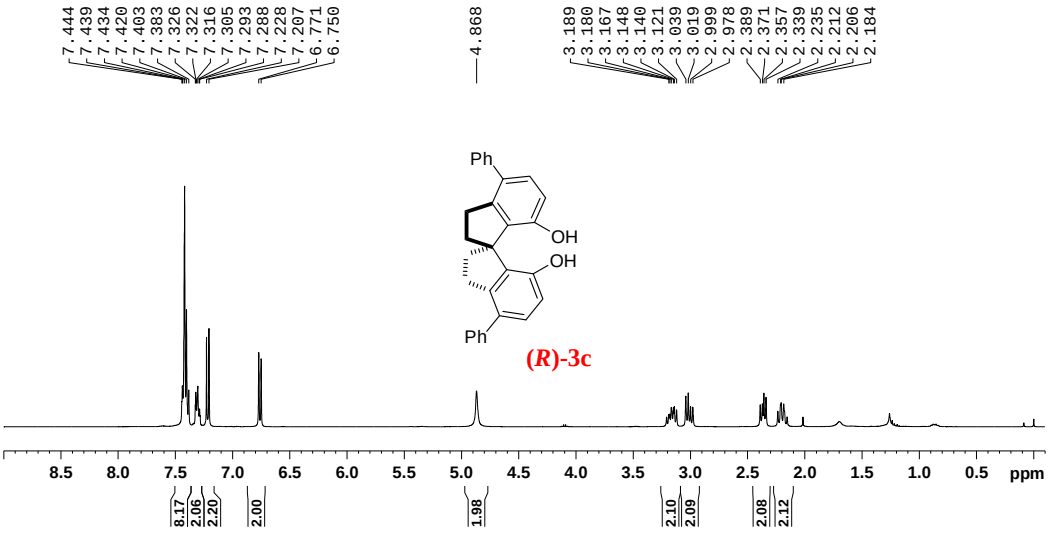

7.508
7.491
6.468
6.451
4.746
2.982
2.973
2.962
2.954
2.297
2.287
2.279
2.272
2.262
2.253
2.200
2.180
2.160
2.155
2.135
I
OH
OH
I
(S)-3h
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.91
1.93
1.96
4.00
2.04
2.12

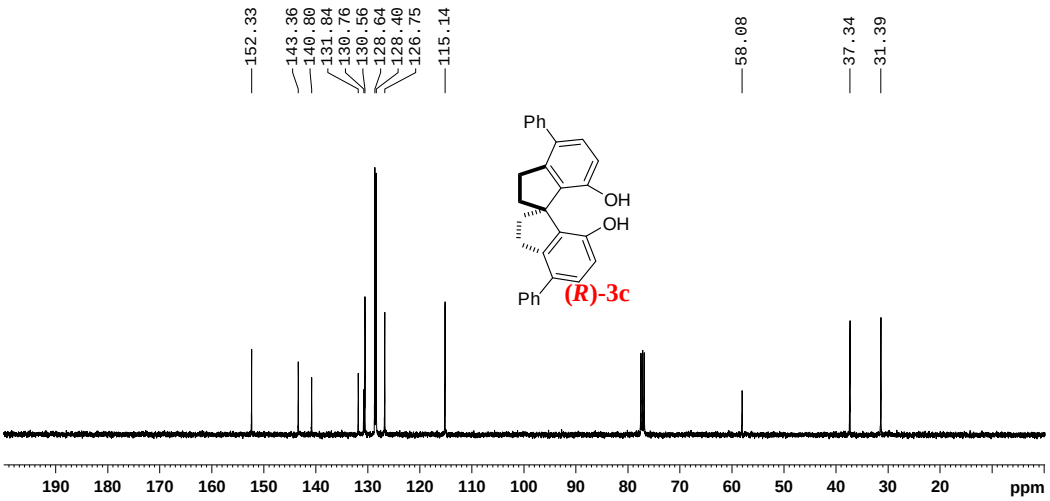

153.05
149.48
138.59
131.96
117.00
83.21
61.16
36.59
36.29
I
OH
OH
I
(S)-3h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

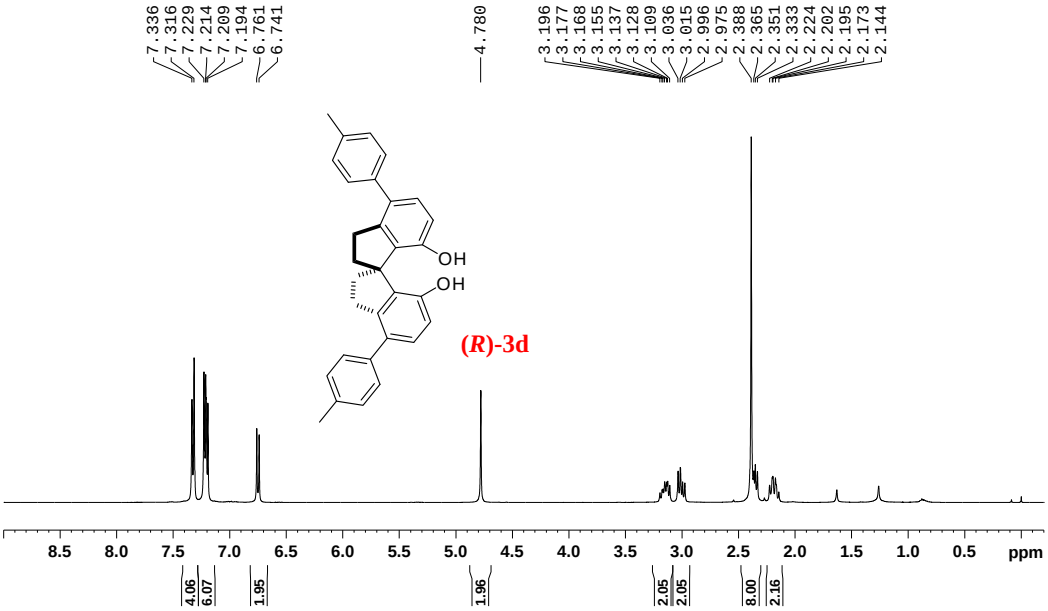

7.027
7.006
6.658
6.638
4.631
2.998
2.993
2.985
2.974
2.970
2.959
2.941
2.382
2.377
2.364
2.359
2.349
2.344
2.332
2.327
2.268
2.242
2.216
2.209
2.186
OH
OH
(R)-3a
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.01
2.00
1.90
4.05
2.07
6.04
2.10

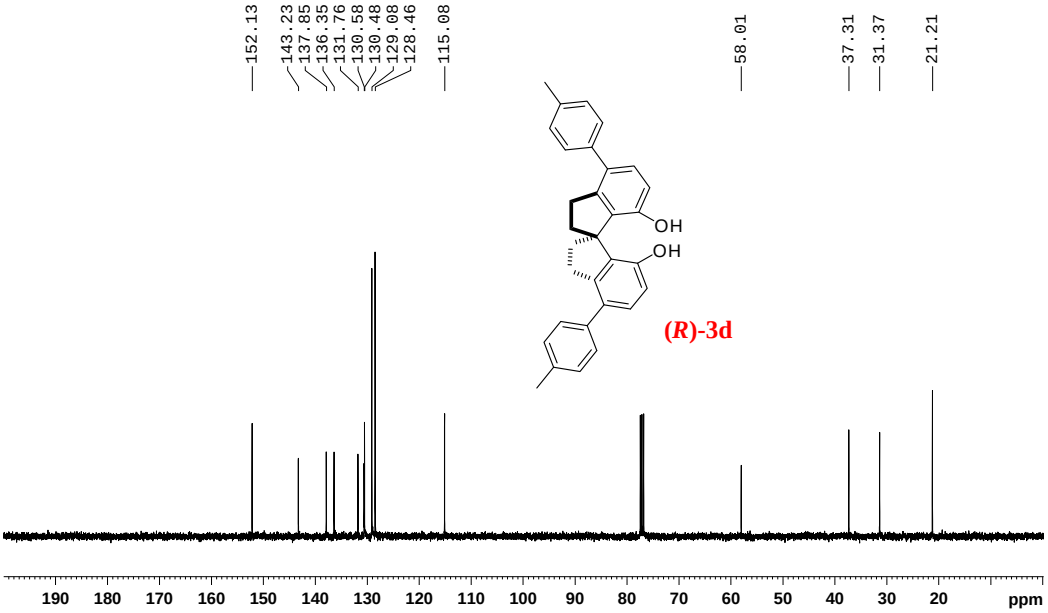

150.90
144.14
130.51
130.27
126.52
114.42
77.41
77.09
76.77
58.20
37.39
30.01
18.27
OH
OH
(R)-3a
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

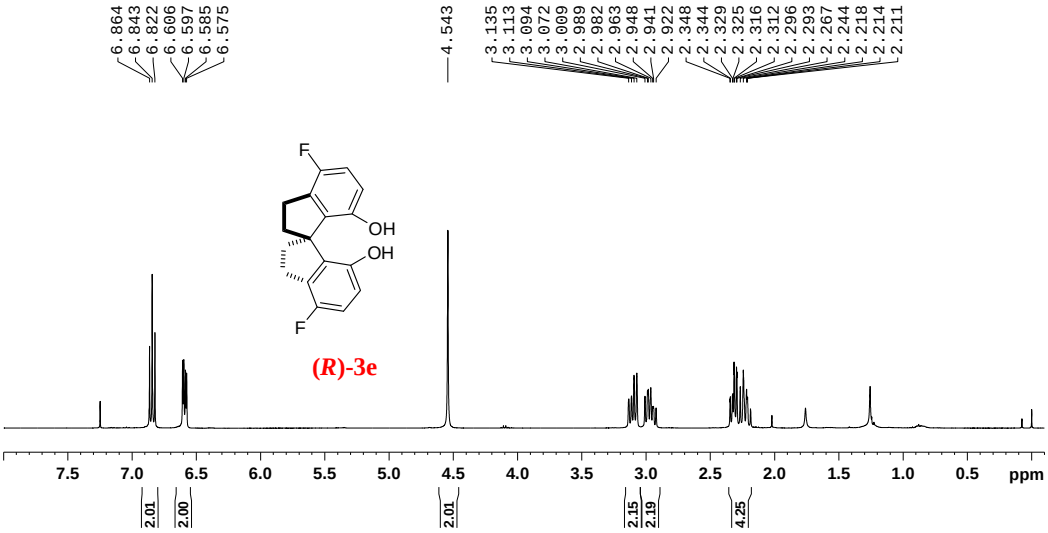

6.985
6.965
6.628
6.607
4.577
3.018
2.999
2.995
2.981
2.978
2.956
2.938
2.929
2.911
2.898
2.889
2.871
2.557
2.551
2.539
2.530
2.518
2.512
2.323
2.320
2.305
2.301
2.291
2.287
2.273
2.269
2.205
2.181
2.155
2.148
2.125
1.606
1.599
1.587
1.582
1.578
1.567
1.559
1.549
n-Bu
OH
OH
n-Bu
(R)-3b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.04
1.98
1.95
4.16
4.16
2.11
2.10
4.10
4.16
6.00
150.90
143.67
131.57
130.19
129.64
114.48
57.98
37.36
32.66
32.42
29.72
22.69
14.06
n-Bu
OH
OH
n-Bu
(R)-3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

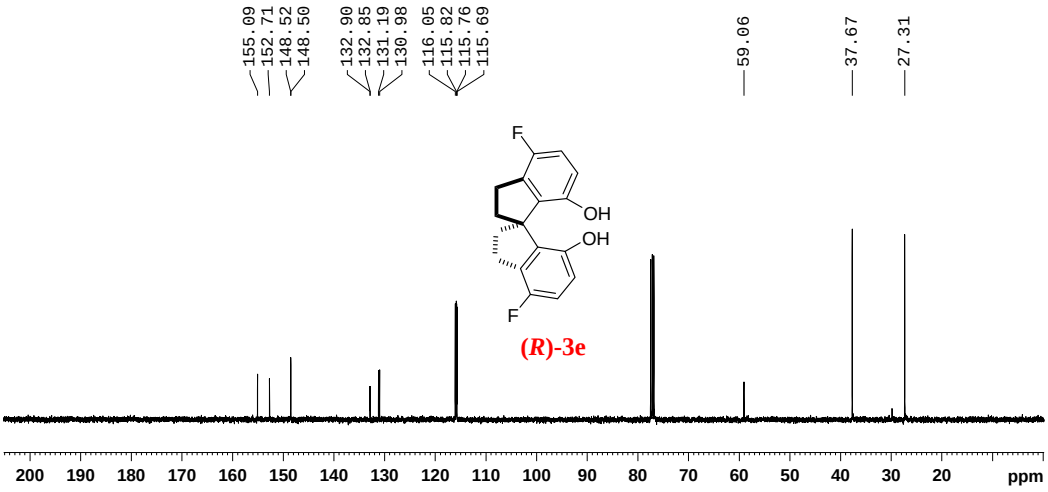

7.444
7.439
7.434
7.420
7.403
7.383
7.326
7.322
7.316
7.305
7.293
7.288
7.228
7.207
6.771
6.750
4.868
3.189
3.180
3.167
3.148
3.140
3.121
3.039
3.019
2.999
2.978
2.389
2.371
2.357
2.339
2.235
2.212
2.206
2.184
Ph
OH
OH
Ph
(R)-3c
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
8.17
2.06
2.20
2.00
1.98
2.10
2.09
2.08
2.12

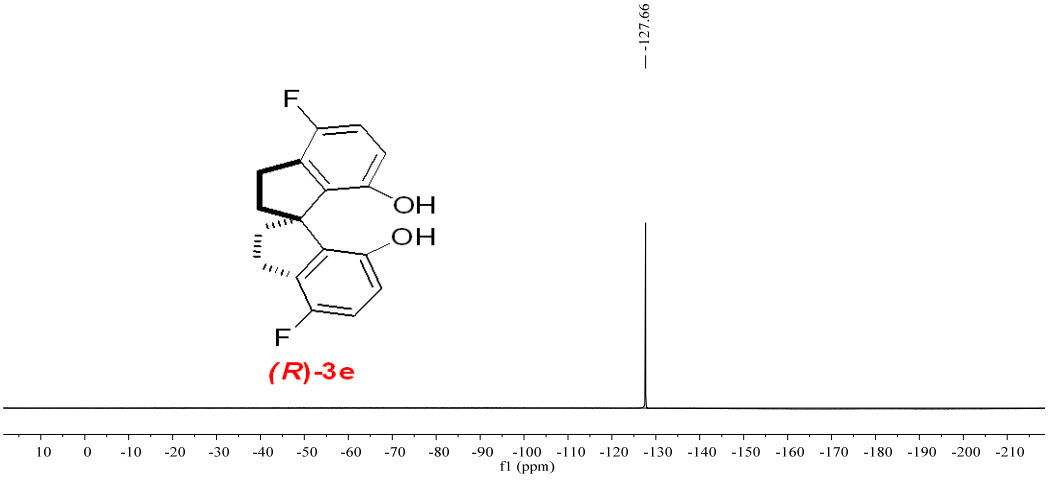

152.33
143.36
140.80
131.84
130.76
130.56
128.64
128.40
126.75
115.14
58.08
37.34
31.39
Ph
OH
OH
Ph
(R)-3c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

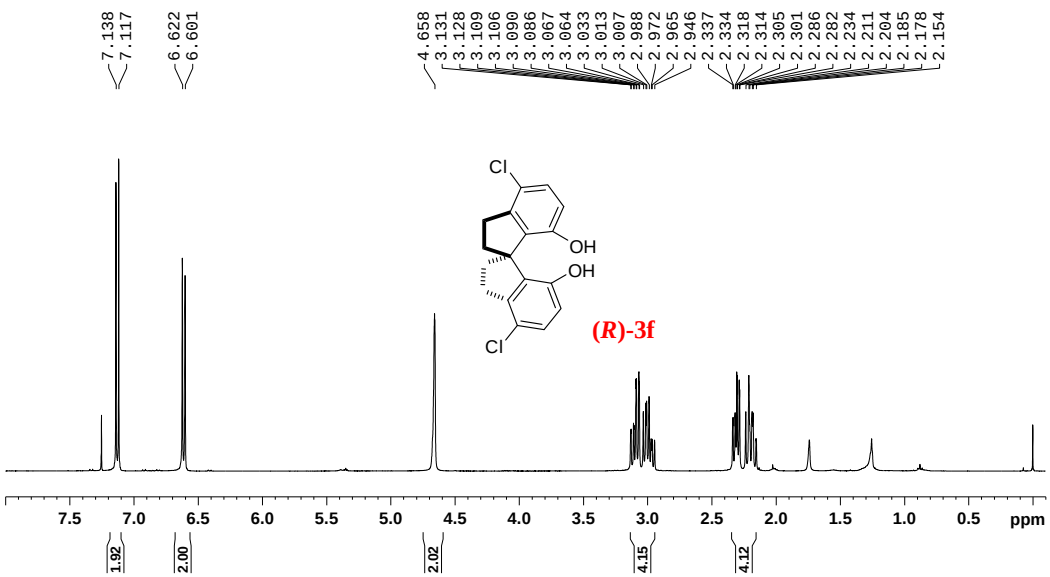

7.336
7.316
7.229
7.214
7.209
7.194
6.761
6.741
4.780
3.196
3.177
3.168
3.155
3.137
3.128
3.109
3.036
3.015
2.996
2.975
2.388
2.365
2.351
2.333
2.224
2.202
2.195
2.173
2.144
OH
OH
(R)-3d
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.06
6.07
1.95
1.96
2.05
2.05
8.00
2.16

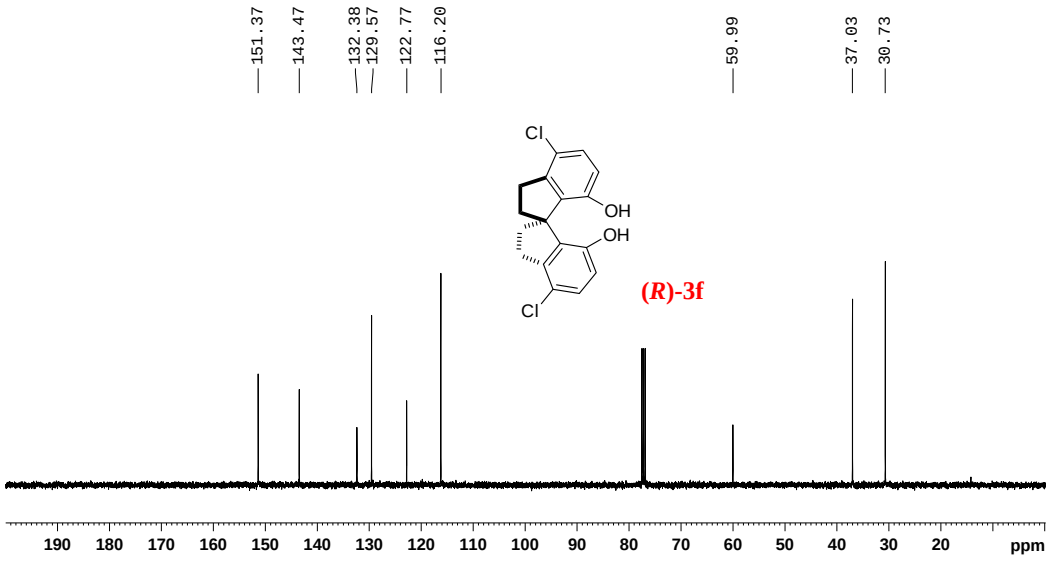

152.13
143.23
137.85
136.35
131.76
130.58
130.48
129.08
128.46
115.08
58.01
37.31
31.37
21.21
OH
OH
(R)-3d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

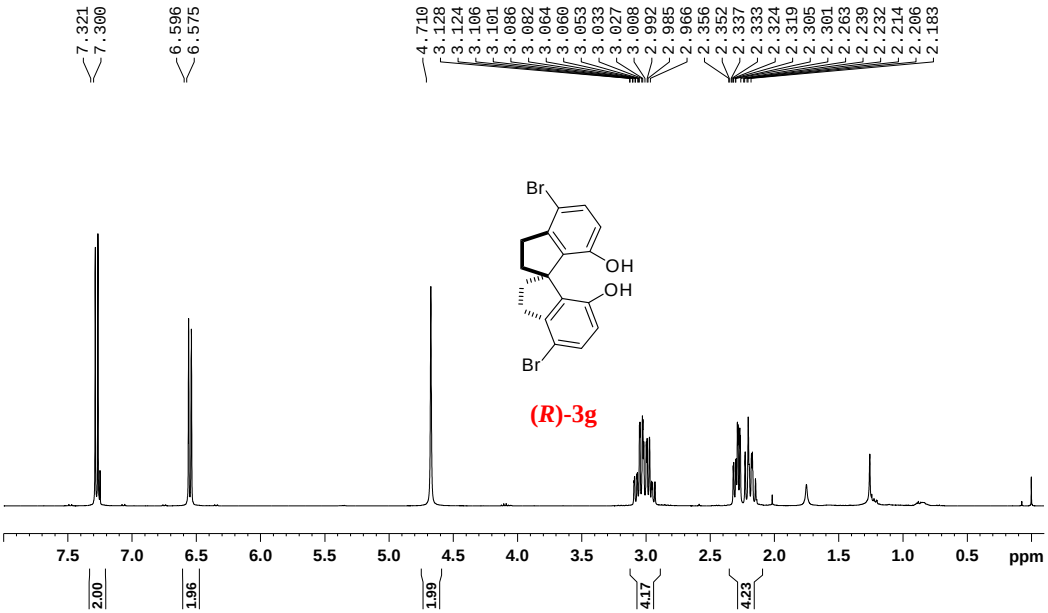

6.864
6.843
6.822
6.606
6.597
6.585
6.575
4.543
3.135
3.113
3.094
3.072
3.009
2.989
2.982
2.963
2.948
2.941
2.922
2.348
2.344
2.329
2.325
2.316
2.312
2.296
2.293
2.267
2.244
2.218
2.214
2.211
F
OH
OH
F
(R)-3e
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.01
2.00
2.01
2.15
2.19
4.25

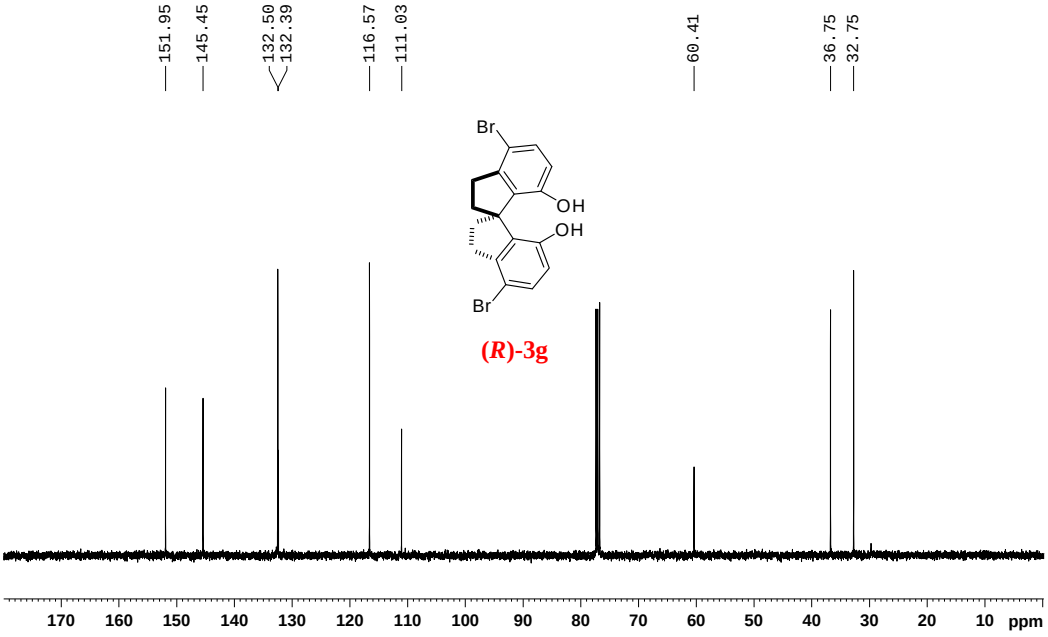

155.09
152.71
148.52
148.50
132.90
132.85
131.19
130.98
116.05
115.82
115.76
115.69
59.06
37.67
27.31
F
OH
OH
F
(R)-3e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

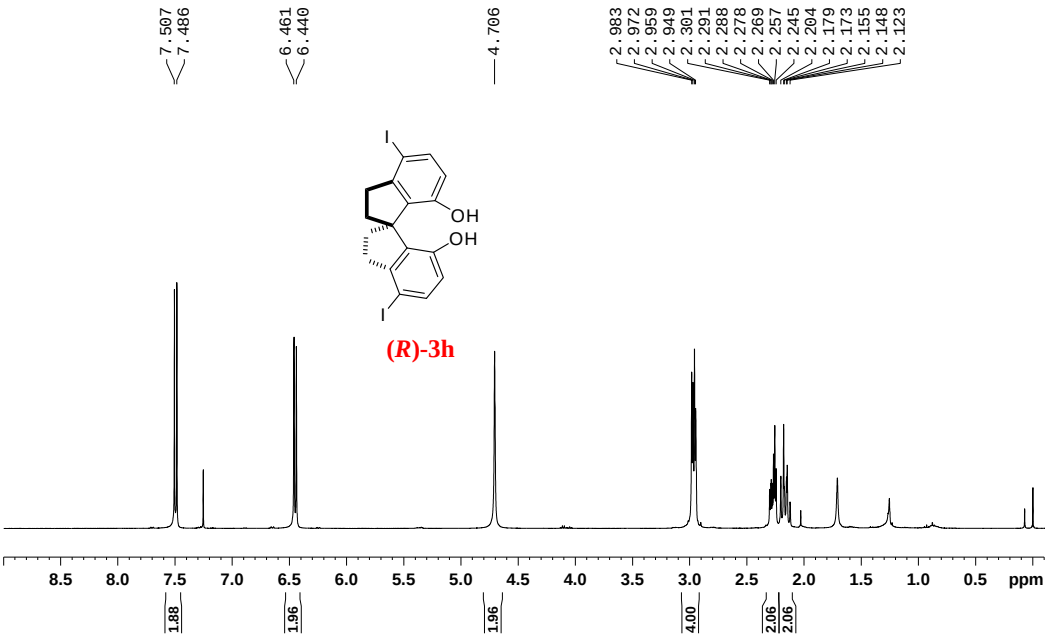

-127.66
F
OH
OH
F
(R)-3e
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


7.138
7.117
6.622
6.601
4.658
3.131
3.128
3.109
3.106
3.090
3.086
3.067
3.064
3.033
3.013
3.007
2.988
2.972
2.965
2.946
2.337
2.334
2.318
2.314
2.305
2.301
2.286
2.282
2.234
2.211
2.204
2.185
2.178
2.154
Cl
OH
OH
Cl
(R)-3f
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
ppm
1.92
2.00
2.02
4.15
4.12

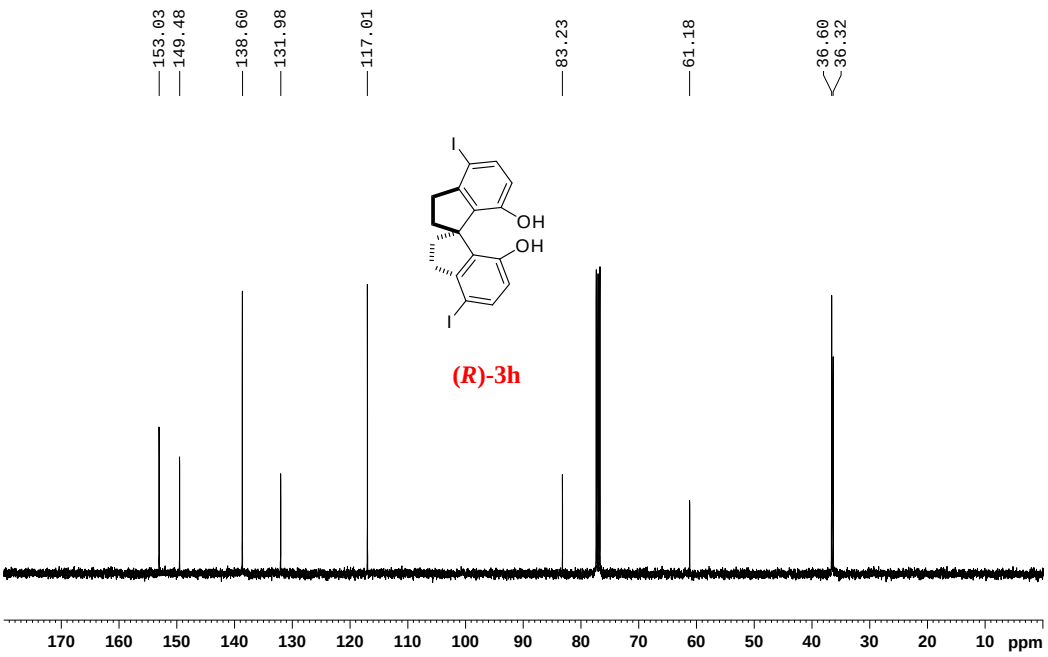

151.37
143.47
132.38
129.57
122.77
116.20
59.99
37.03
30.73
Cl
OH
OH
Cl
(R)-3f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.321
7.300
6.596
6.575
4.710
3.128
3.124
3.106
3.101
3.086
3.082
3.064
3.060
3.053
3.033
3.027
3.008
2.992
2.985
2.966
2.356
2.352
2.337
2.333
2.324
2.319
2.305
2.301
2.263
2.239
2.232
2.214
2.206
2.183
Br
OH
OH
Br
(R)-3g
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
ppm
2.00
1.96
1.99
4.17
4.23

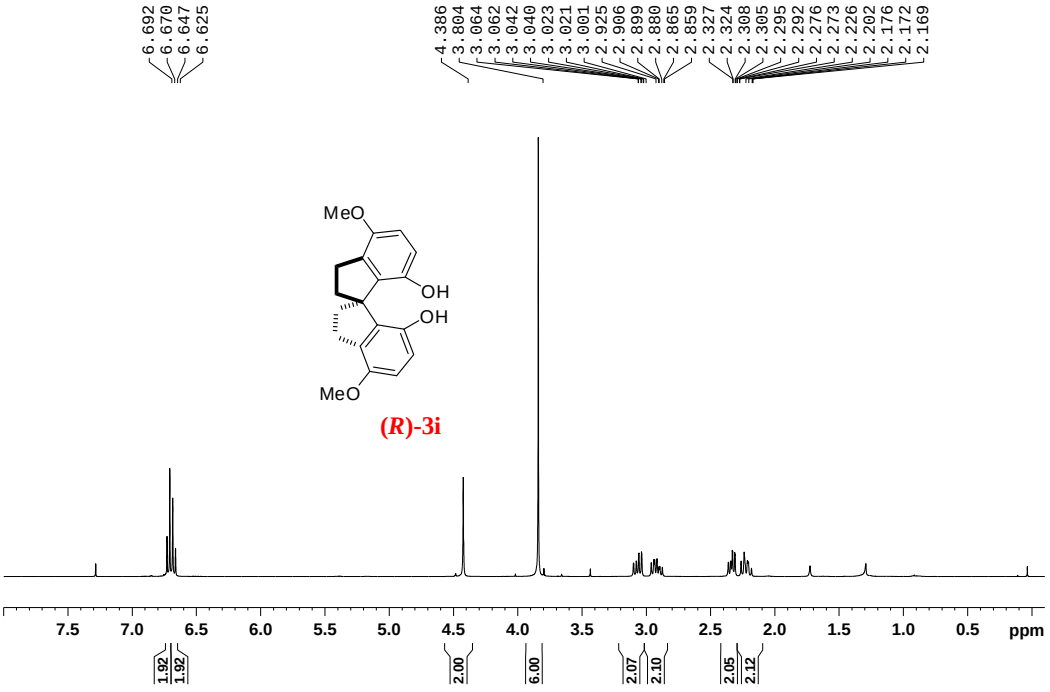

151.95
145.45
132.50
132.39
116.57
111.03
60.41
36.75
32.75
Br
OH
OH
Br
(R)-3g
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.507
7.486
6.461
6.440
4.706
2.983
2.972
2.959
2.949
2.301
2.291
2.288
2.278
2.269
2.257
2.245
2.204
2.179
2.173
2.155
2.148
2.123
I
OH
OH
I
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 0.5 ppm
1.88
1.96
1.96
4.00
2.06
2.06

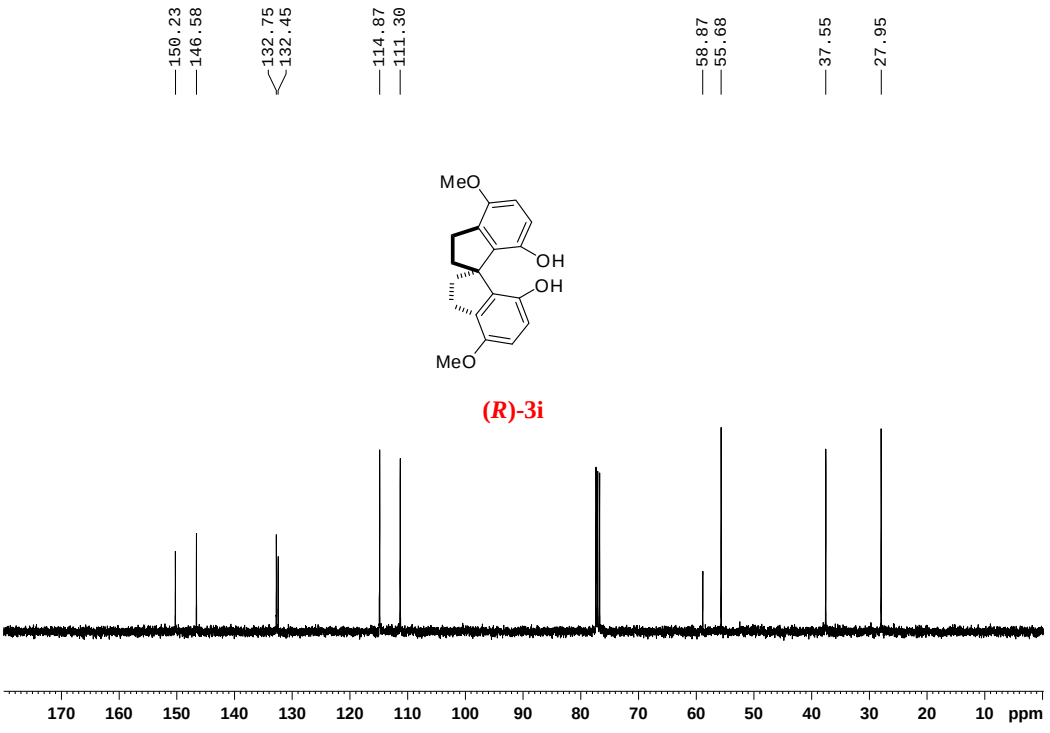
**(*R*)-3h**


153.03
149.48
138.60
131.98
117.01
83.23
61.18
36.60
36.32
I
OH
OH
I
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

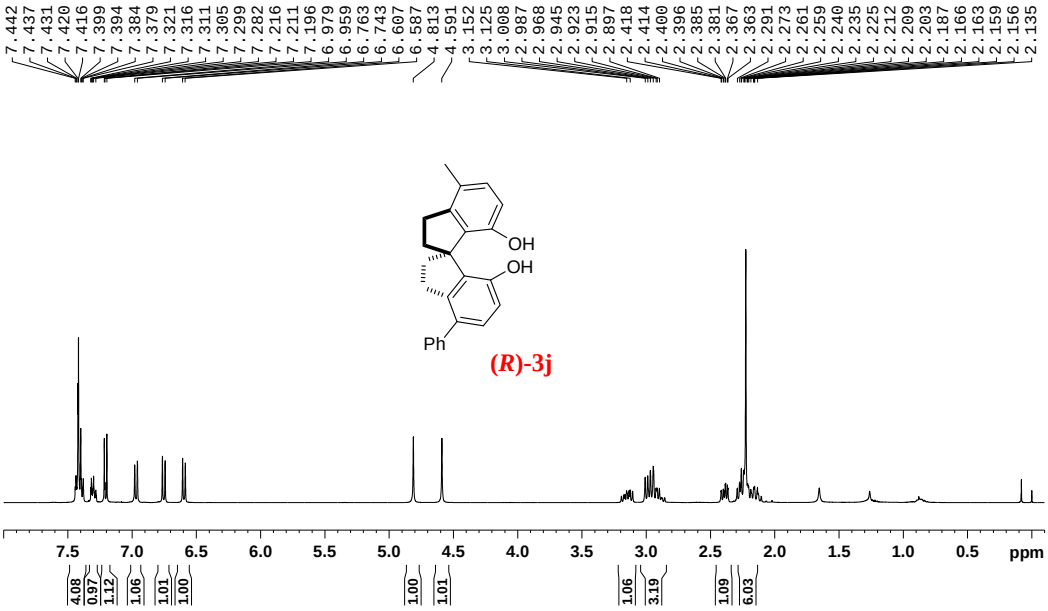
**(*R*)-3h**

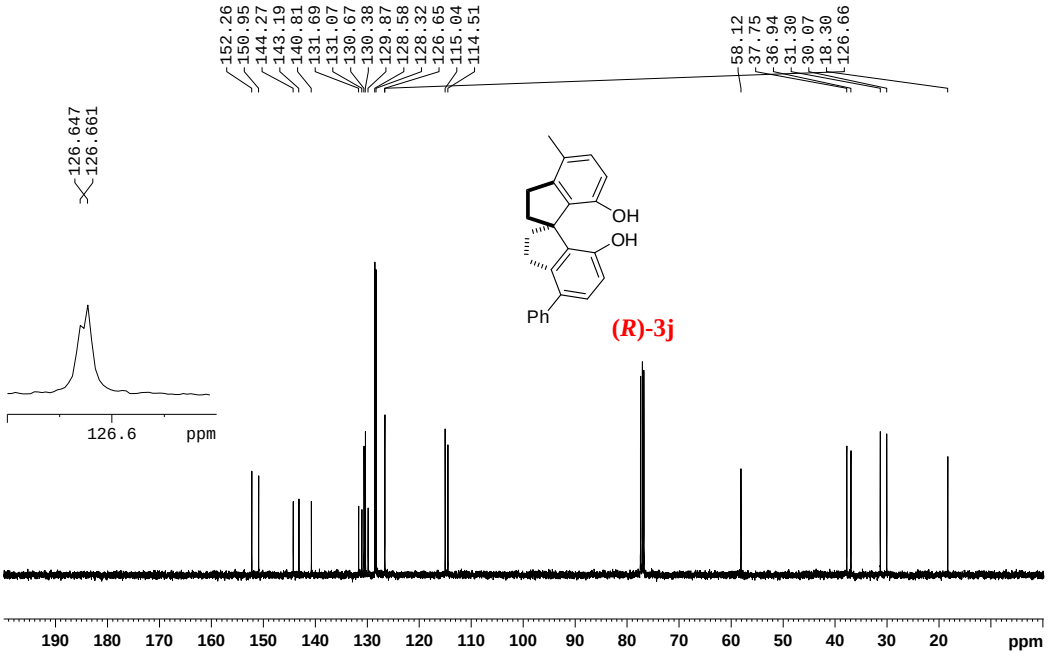

6.692
6.670
6.647
6.625
4.386
3.804
3.064
3.062
3.042
3.040
3.023
3.021
3.001
2.925
2.906
2.899
2.880
2.865
2.859
2.327
2.324
2.308
2.305
2.295
2.292
2.276
2.273
2.226
2.202
2.176
2.172
2.169
MeO
OH
OH
MeO
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.92
1.92
2.00
6.00
2.07
2.10
2.05
2.12

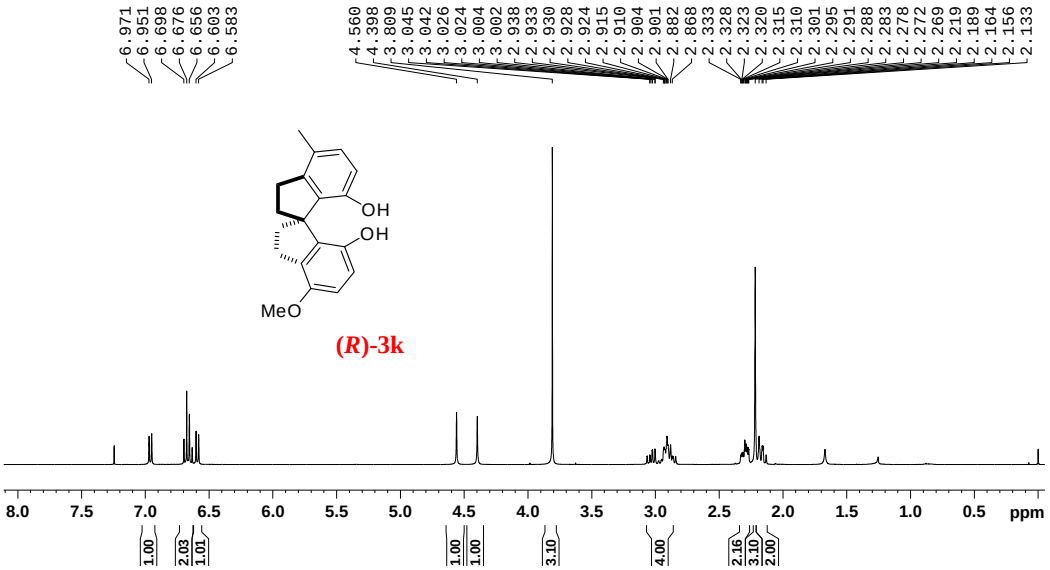
**(*R*)-3i**


150.23
146.58
132.75
132.45
114.87
111.30
58.87
55.68
37.55
27.95
MeO
OH
OH
MeO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

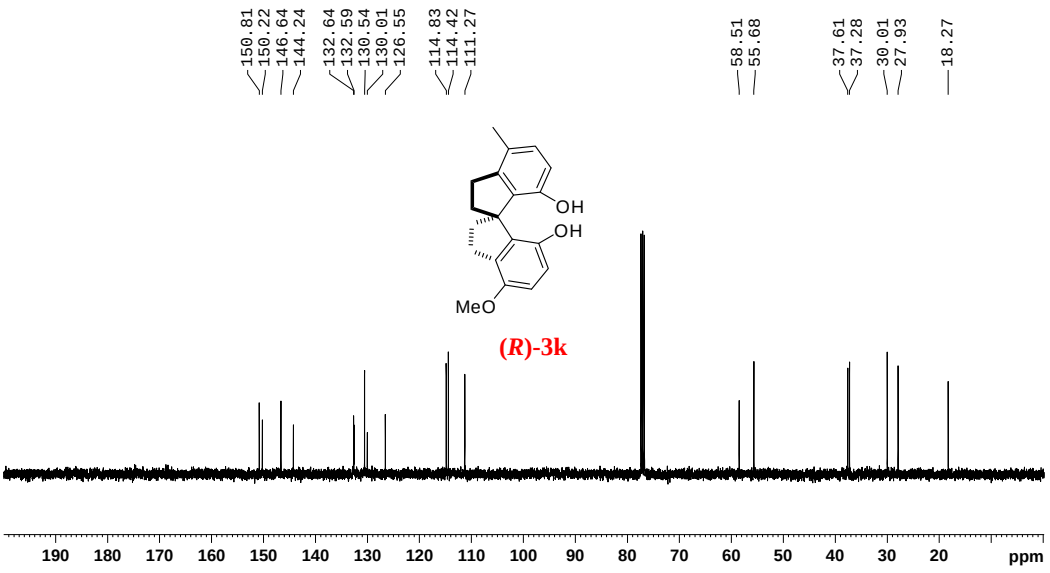
**(*R*)-3i**


7.442
7.437
7.431
7.420
7.416
7.399
7.394
7.384
7.379
7.321
7.316
7.311
7.305
7.299
7.282
7.216
7.211
7.196
6.979
6.959
6.763
6.743
6.607
6.587
4.813
4.591
3.152
3.125
3.008
2.987
2.968
2.945
2.923
2.915
2.897
2.418
2.414
2.400
2.396
2.385
2.381
2.367
2.363
2.291
2.273
2.261
2.259
2.240
2.235
2.225
2.212
2.209
2.203
2.187
2.166
2.163
2.159
2.156
2.135
OH
OH
Ph
(R)-3j
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
ppm
4.08
0.97
1.12
1.06
1.01
1.00
1.00
1.01
1.06
3.19
1.09
6.03

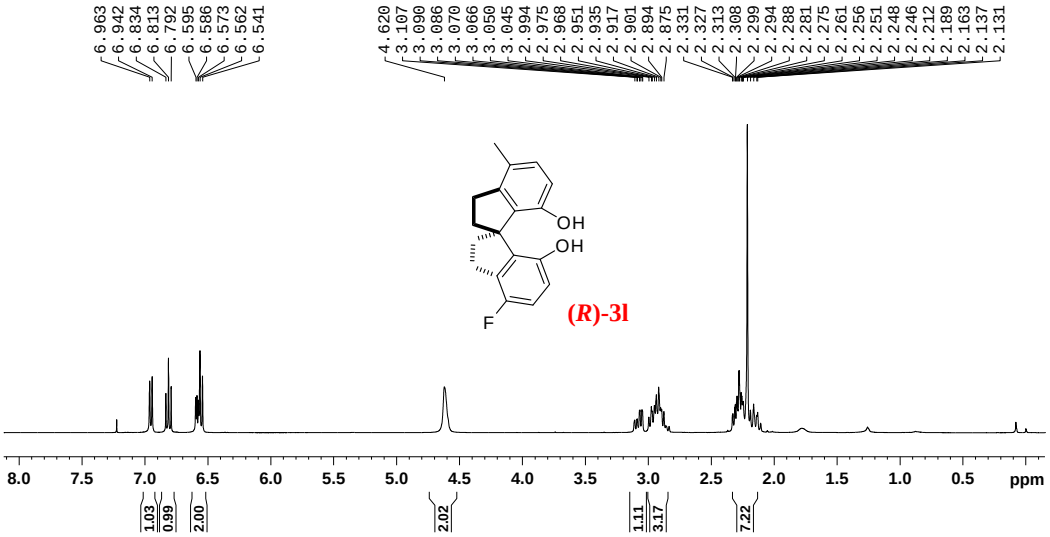

152.26
150.95
144.27
143.19
140.81
131.69
131.07
130.67
130.38
129.87
128.58
128.32
126.65
115.04
114.51
58.12
37.75
36.94
31.30
30.07
18.30
126.66
126.647
126.661
126.6
ppm
OH
OH
Ph
(R)-3j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

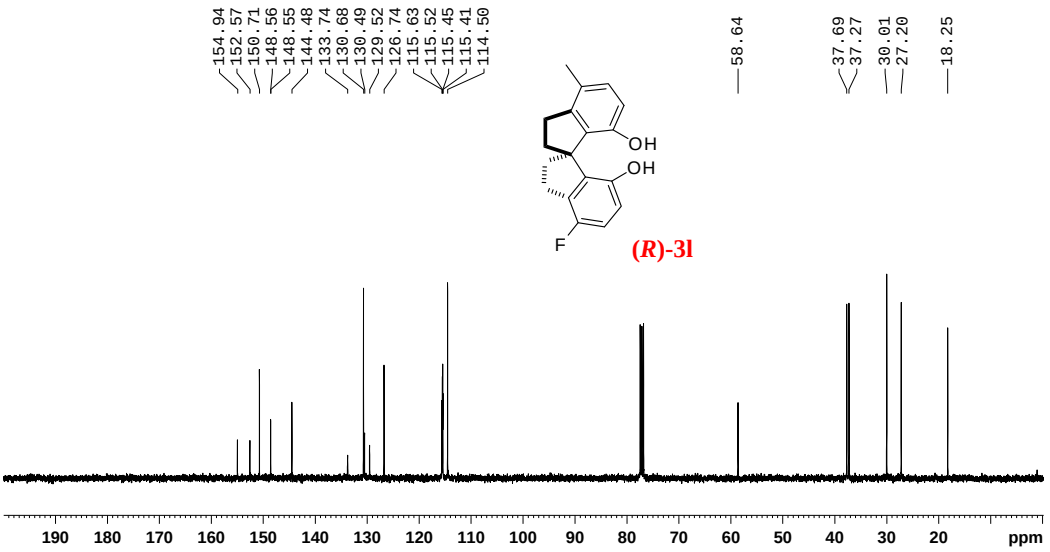

6.971
6.951
6.698
6.676
6.656
6.603
6.583
4.560
4.398
3.809
3.045
3.042
3.026
3.024
3.004
3.002
2.938
2.933
2.930
2.928
2.924
2.915
2.910
2.904
2.901
2.882
2.868
2.333
2.328
2.323
2.320
2.315
2.310
2.301
2.295
2.291
2.288
2.283
2.278
2.272
2.269
2.219
2.189
2.164
2.156
2.133
OH
OH
MeO
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
2.03
1.01
1.00
1.00
3.10
4.00
2.16
3.10
2.00

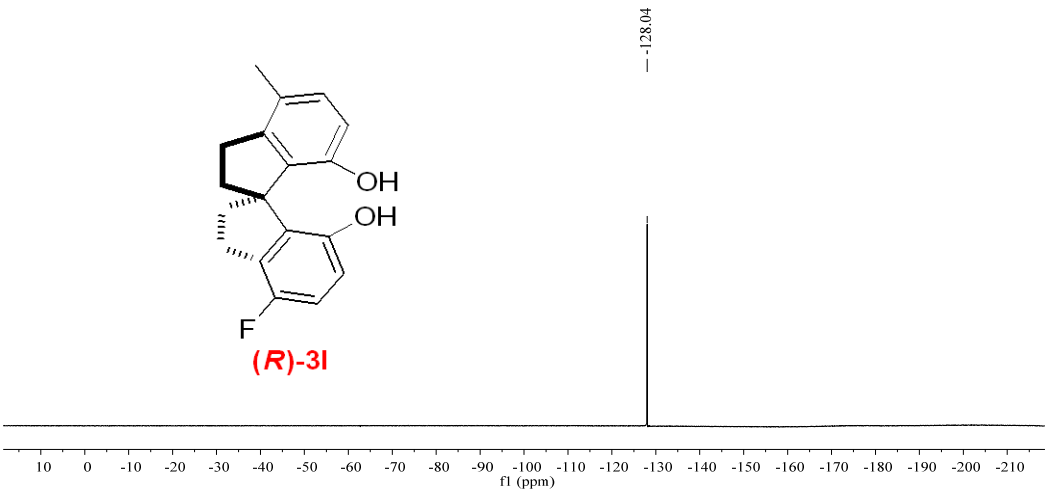
**(*R*)-3k**

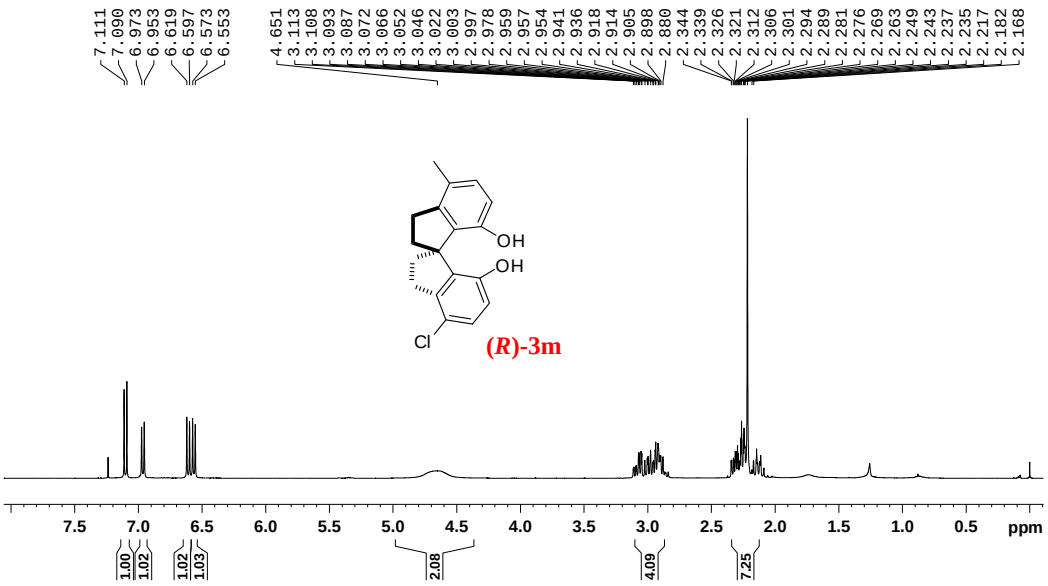

150.81
150.22
146.64
144.24
132.64
132.59
130.54
130.01
126.55
114.83
114.42
111.27
58.51
55.68
37.61
37.28
30.01
27.93
18.27
OH
OH
MeO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

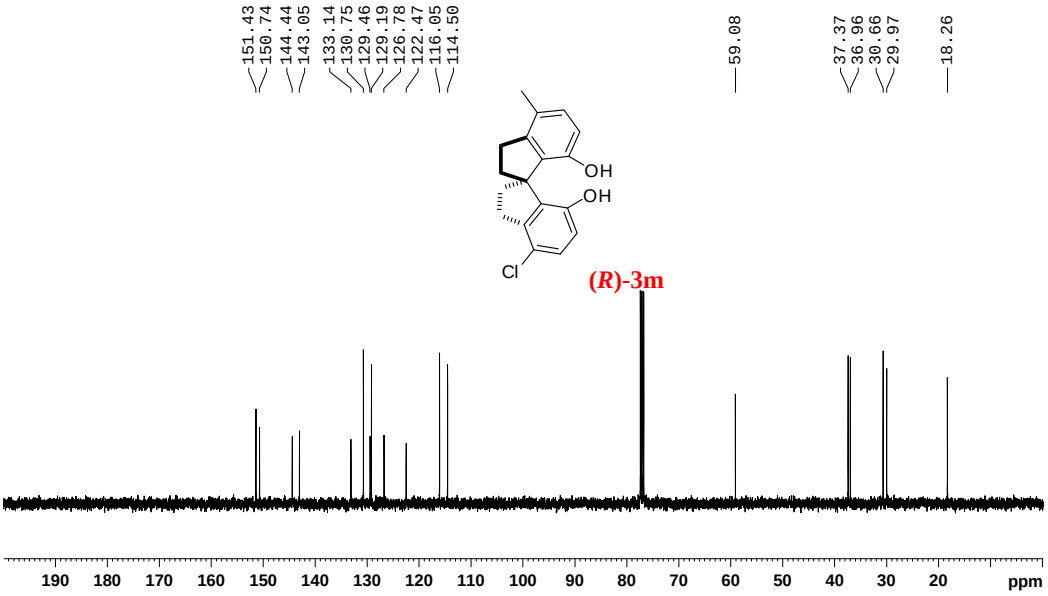
**(*R*)-3k**

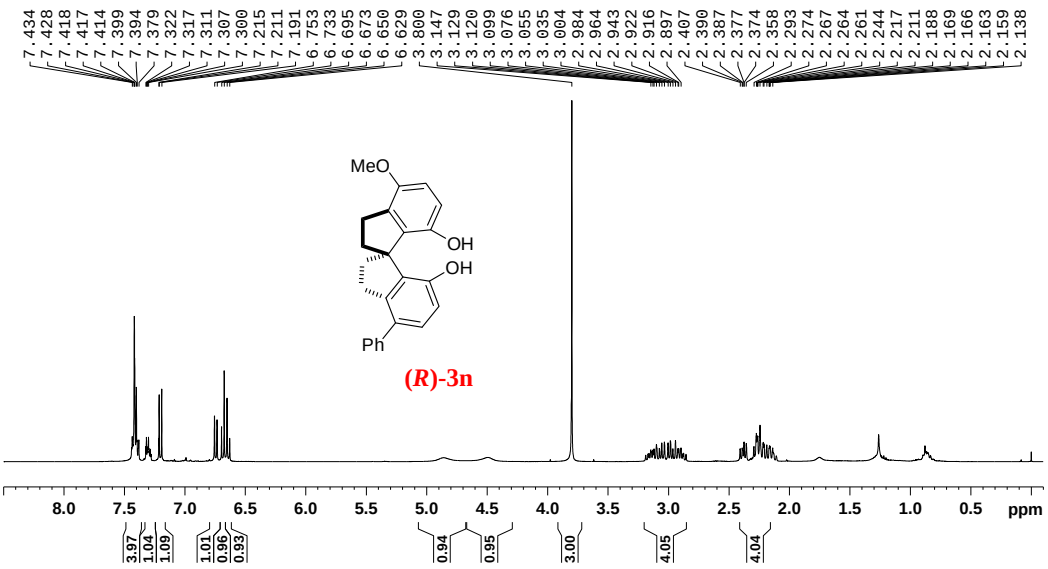

6.963
6.942
6.834
6.813
6.792
6.595
6.586
6.573
6.562
6.541
4.620
3.107
3.090
3.086
3.070
3.066
3.050
3.045
2.994
2.975
2.968
2.951
2.935
2.917
2.901
2.894
2.875
2.331
2.327
2.313
2.308
2.299
2.294
2.288
2.281
2.275
2.261
2.256
2.251
2.248
2.246
2.212
2.189
2.163
2.137
2.131
OH
OH
F
(R)-3l
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.03
0.99
2.00
2.02
1.11
3.17
7.22

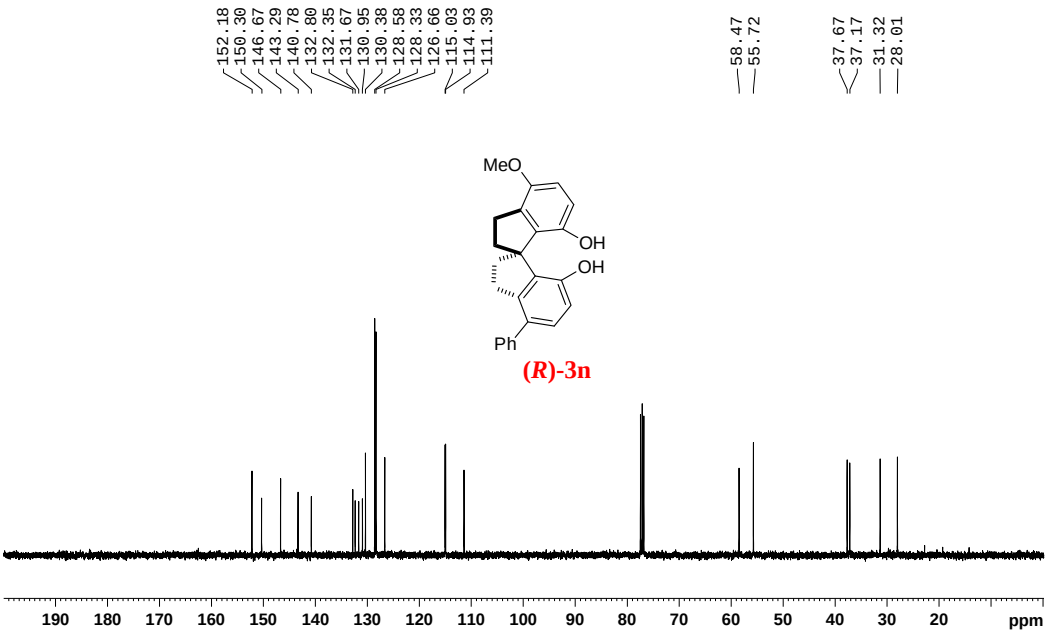

154.94
152.57
150.71
148.56
148.55
144.48
133.74
130.68
130.49
129.52
126.74
115.63
115.52
115.45
115.41
114.50
58.64
37.69
37.27
30.01
27.20
18.25
OH
OH
F
(R)-3l
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

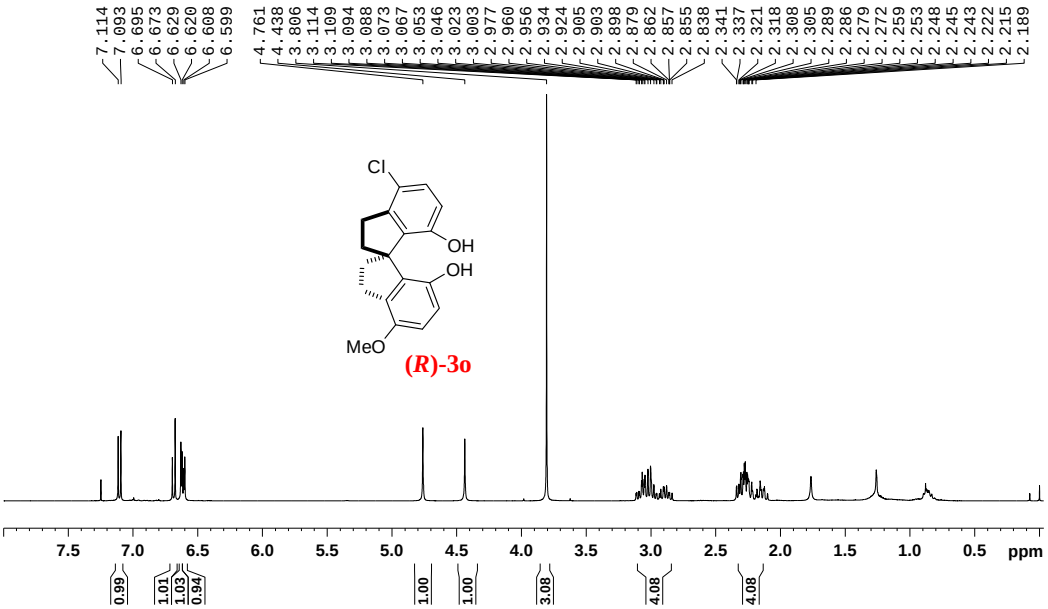

-128.04
OH
OH
F
(R)-3l
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

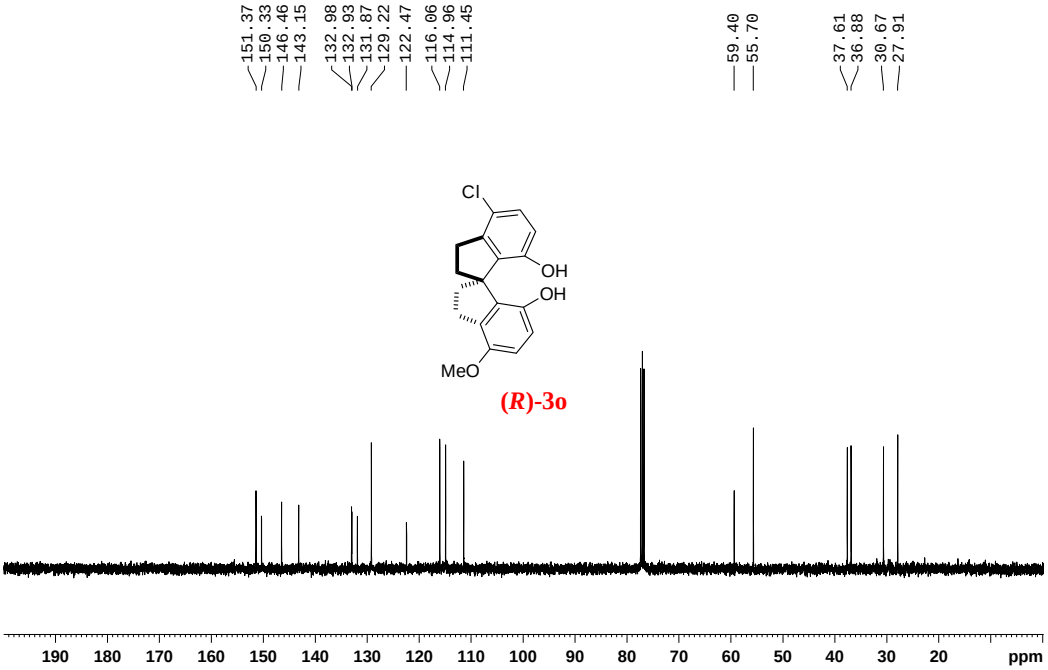

7.111
7.090
6.973
6.953
6.619
6.597
6.573
6.553
4.651
3.113
3.108
3.093
3.087
3.072
3.066
3.052
3.046
3.022
3.003
2.997
2.978
2.959
2.957
2.954
2.941
2.936
2.918
2.914
2.905
2.898
2.880
2.344
2.339
2.326
2.321
2.312
2.306
2.301
2.294
2.289
2.281
2.276
2.269
2.263
2.249
2.243
2.237
2.235
2.217
2.182
2.168
OH
OH
Cl
(R)-3m
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
ppm
1.00
1.02
1.02
1.03
2.08
4.09
7.25

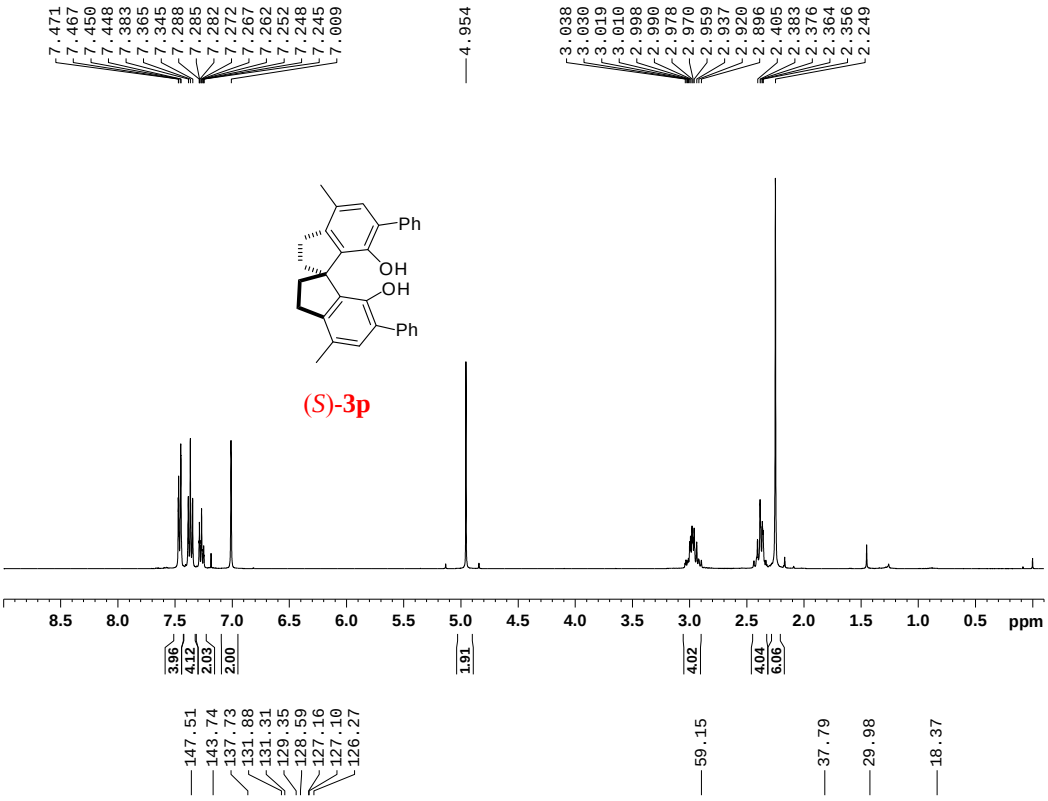

151.43
150.74
144.44
143.05
133.14
130.75
129.46
129.19
126.78
122.47
116.05
114.50
59.08
37.37
36.96
30.66
29.97
18.26
OH
OH
Cl
(R)-3m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

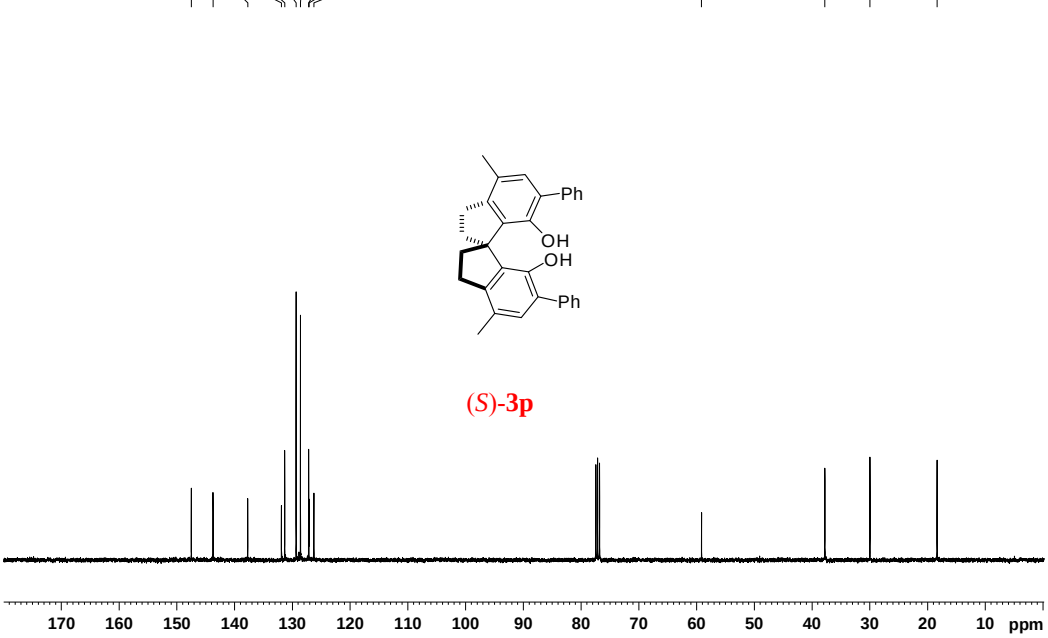

7.434
7.428
7.418
7.417
7.414
7.399
7.394
7.379
7.322
7.317
7.311
7.307
7.300
7.215
7.211
7.191
6.753
6.733
6.695
6.673
6.650
6.629
3.800
3.147
3.129
3.120
3.099
3.076
3.055
3.035
3.004
2.984
2.964
2.943
2.922
2.916
2.897
2.407
2.390
2.387
2.377
2.374
2.358
2.293
2.274
2.267
2.264
2.261
2.244
2.217
2.211
2.188
2.169
2.166
2.163
2.159
2.138
MeO
OH
OH
Ph
(R)-3n
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
0.5
ppm
3.97
1.04
1.09
1.01
0.96
0.93
0.94
0.95
3.00
4.05
4.04

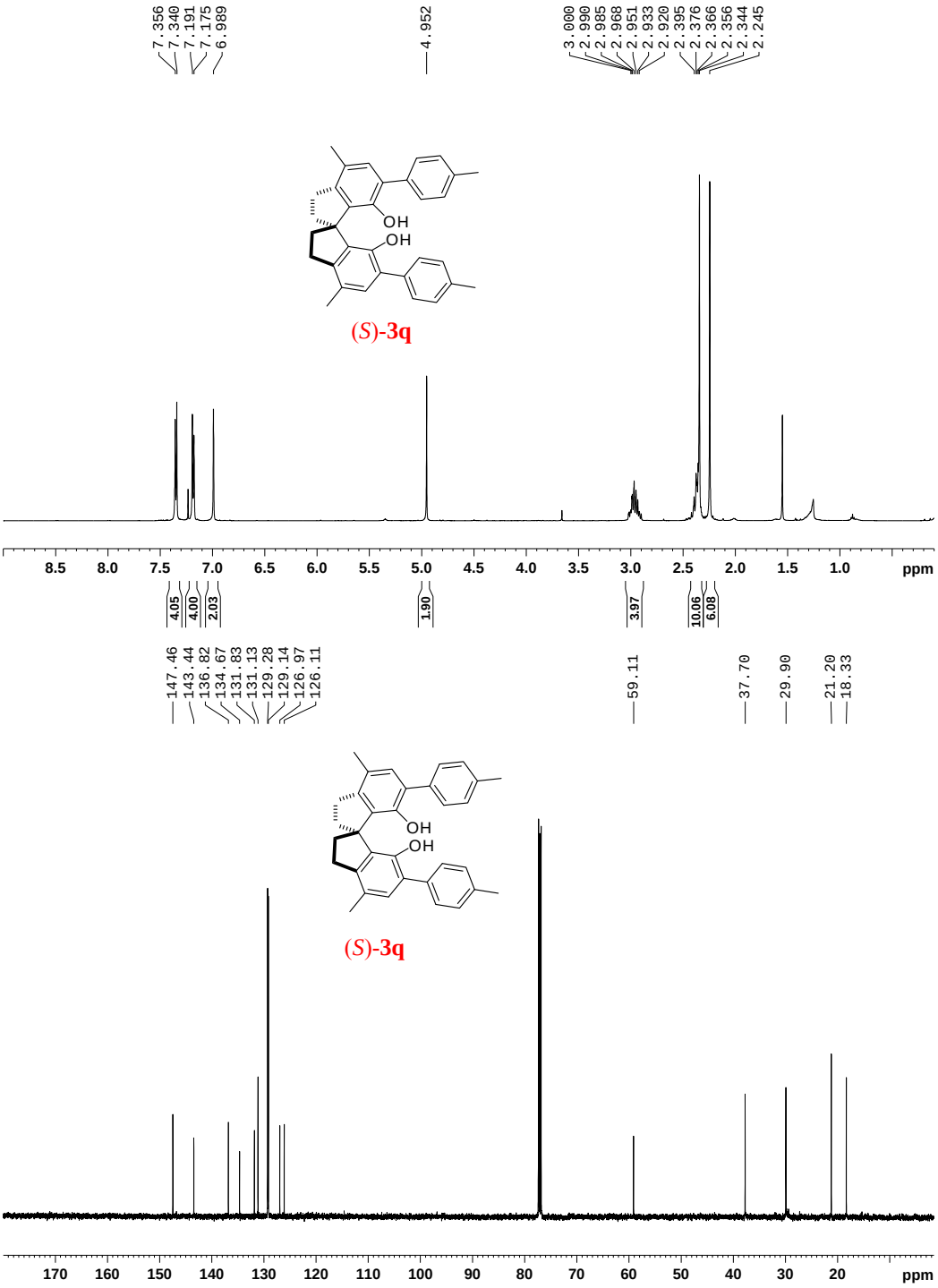

152.18
150.30
146.67
143.29
140.78
132.80
132.35
131.67
130.95
130.38
128.58
128.33
126.66
115.03
114.93
111.39
58.47
55.72
37.67
37.17
31.32
28.01
MeO
OH
OH
Ph
(R)-3n
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

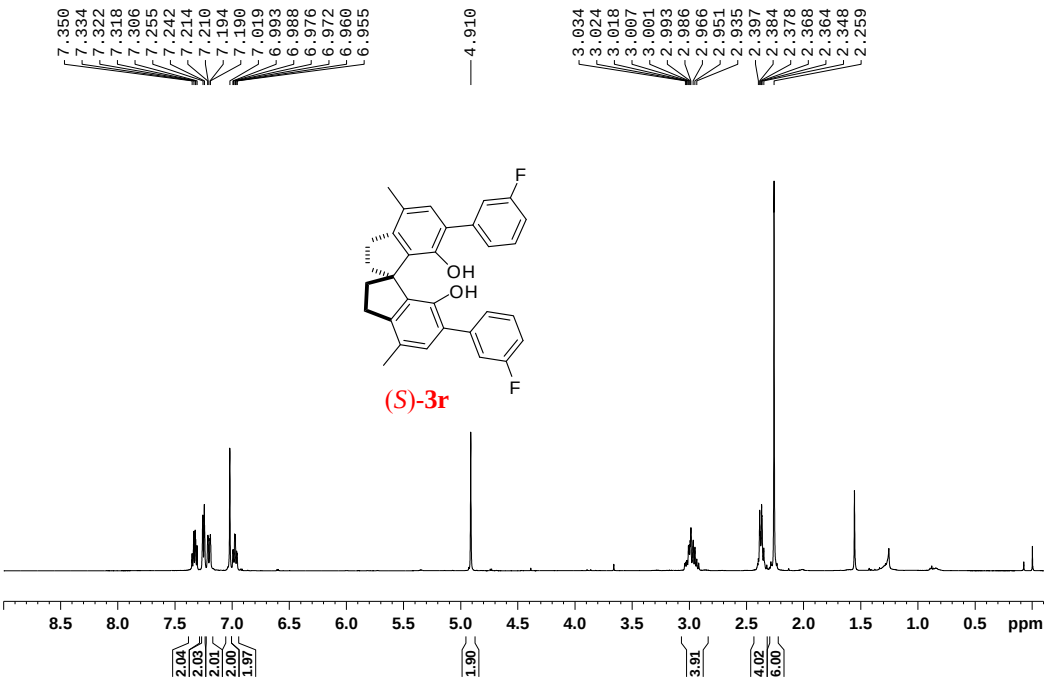

7.114
7.093
6.695
6.673
6.629
6.620
6.608
6.599
4.761
4.438
3.806
3.114
3.109
3.094
3.088
3.073
3.067
3.053
3.046
3.023
3.003
2.977
2.960
2.956
2.934
2.924
2.905
2.903
2.898
2.879
2.862
2.857
2.855
2.838
2.341
2.337
2.321
2.318
2.308
2.305
2.289
2.286
2.279
2.272
2.259
2.253
2.248
2.245
2.243
2.222
2.215
2.189
Cl
OH
OH
MeO
(R)-3o
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
ppm
0.99
1.01
1.03
0.94
1.00
1.00
3.08
4.08
4.08

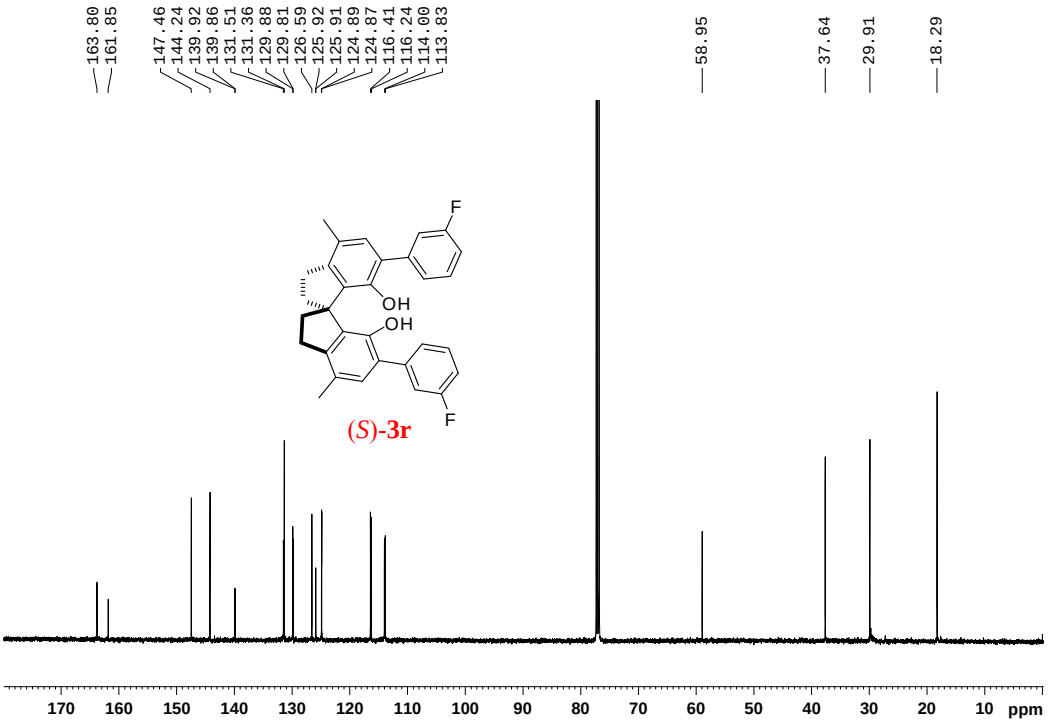

151.37
150.33
146.46
143.15
132.98
132.93
131.87
129.22
122.47
116.06
114.96
111.45
59.40
55.70
37.61
36.88
30.67
27.91
Cl
OH
OH
MeO
(R)-3o
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

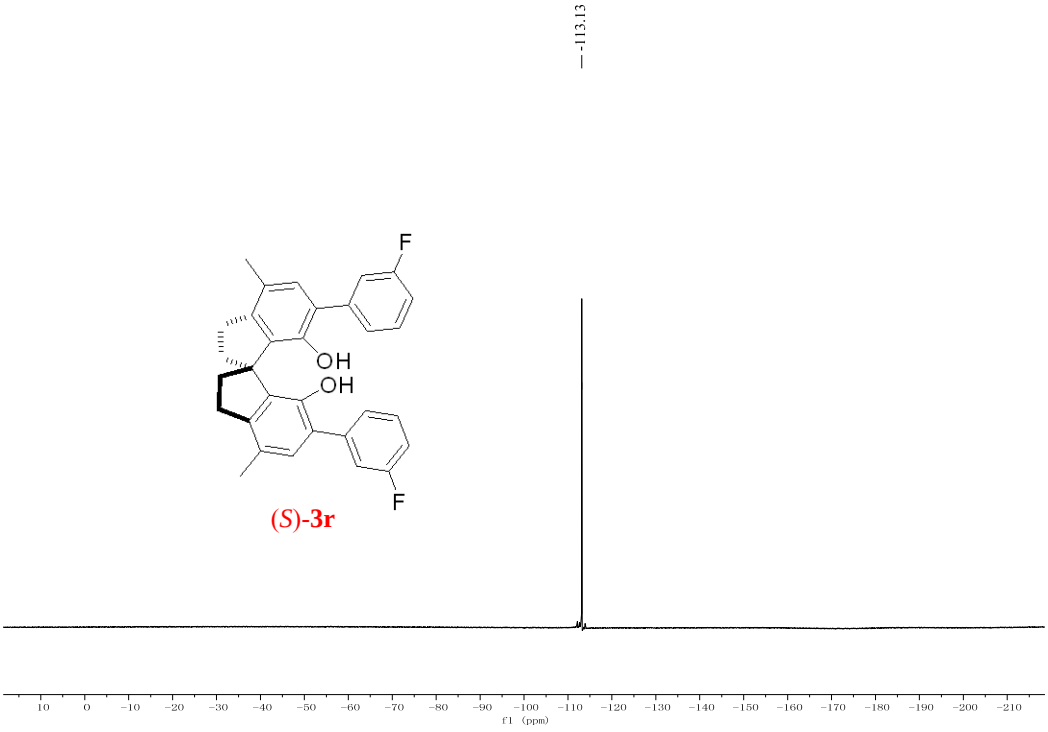

7.471
7.467
7.450
7.448
7.383
7.365
7.345
7.288
7.285
7.282
7.272
7.267
7.262
7.252
7.248
7.245
7.009
4.954
3.038
3.030
3.019
3.010
2.998
2.990
2.978
2.970
2.959
2.937
2.920
2.896
2.405
2.383
2.376
2.364
2.356
2.249
Ph
OH
OH
Ph
(S)-3p
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.96
4.12
2.03
2.00
1.91
4.02
4.04
6.06


147.51
143.74
137.73
131.88
131.31
129.35
128.59
127.16
127.10
126.27
59.15
37.79
29.98
18.37
Ph
OH
OH
Ph
(S)-3p
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

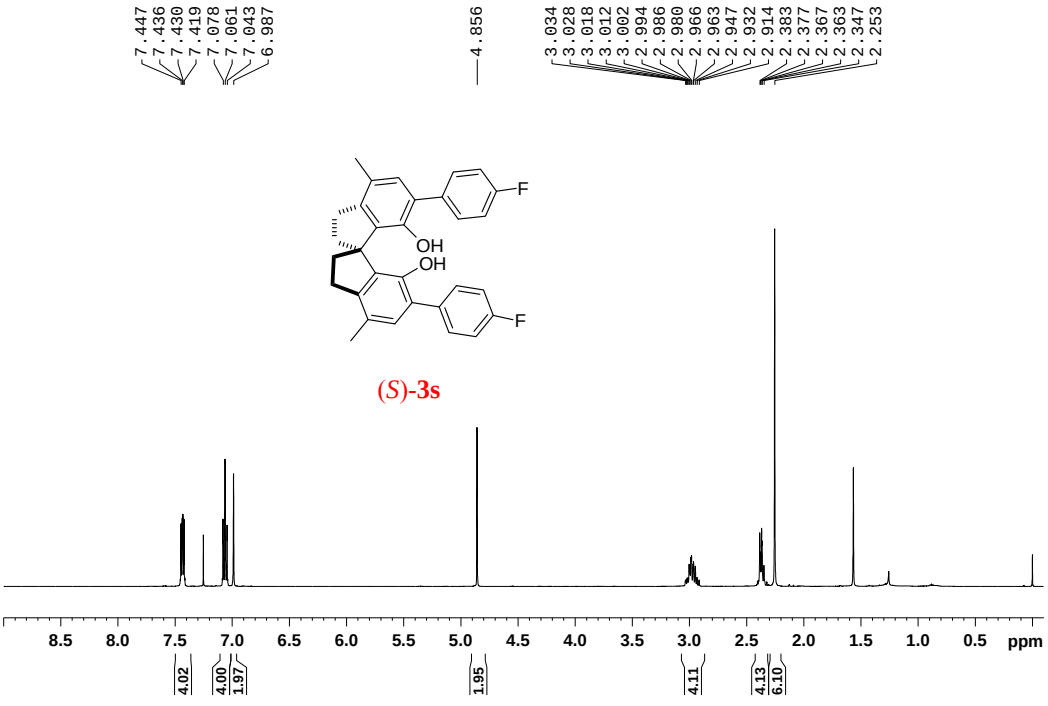

7.356
7.340
7.191
7.175
6.989
4.952
3.000
2.990
2.985
2.968
2.951
2.933
2.920
2.395
2.376
2.366
2.356
2.344
2.245
OH
OH
(S)-3q
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
4.05
4.00
2.03
1.90
3.97
10.06
6.08
147.46
143.44
136.82
134.67
131.83
131.13
129.28
129.14
126.97
126.11
59.11
37.70
29.90
21.20
18.33
OH
OH
(S)-3q
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.350
7.334
7.322
7.318
7.306
7.255
7.242
7.214
7.210
7.194
7.190
7.019
6.993
6.988
6.976
6.972
6.960
6.955
4.910
3.034
3.024
3.018
3.007
3.001
2.993
2.986
2.966
2.951
2.935
2.397
2.384
2.378
2.368
2.364
2.348
2.259
F
OH
OH
F
(S)-3r
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
0.5
ppm
2.04
2.03
2.01
2.00
1.97
1.90
3.91
4.02
6.00

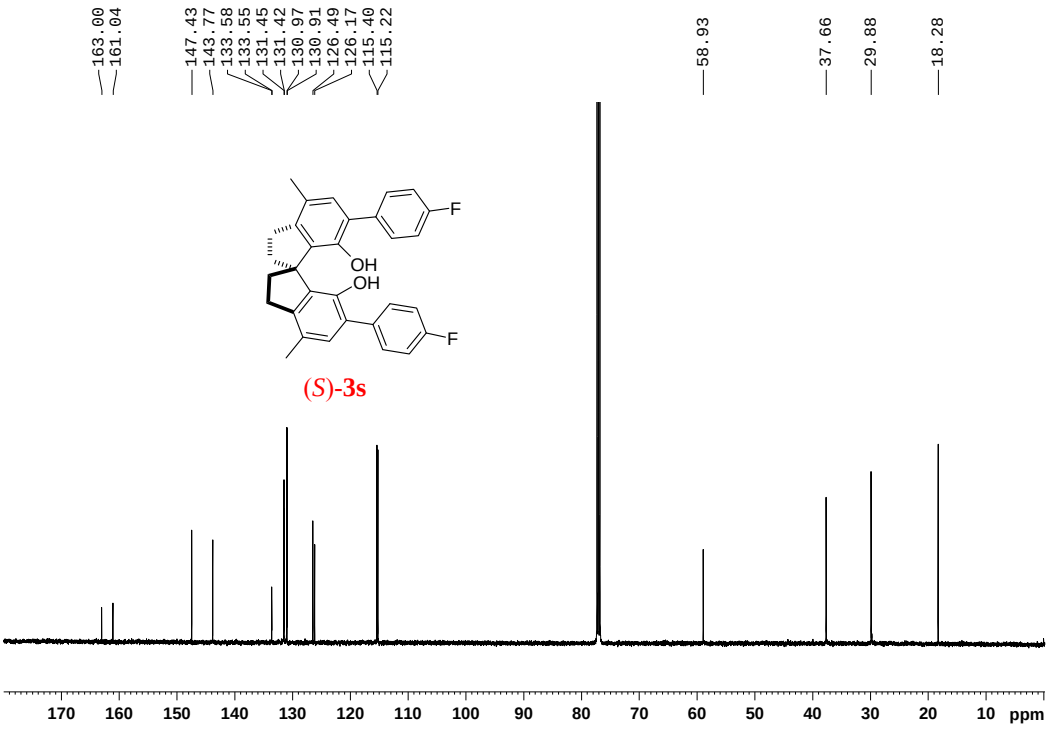

163.80
161.85
147.46
144.24
139.92
139.86
131.51
131.36
129.88
129.81
126.59
125.92
125.91
124.89
124.87
116.41
116.24
114.00
113.83
58.95
37.64
29.91
18.29
F
OH
OH
F
(S)-3r
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


-113.13
F
OH
OH
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

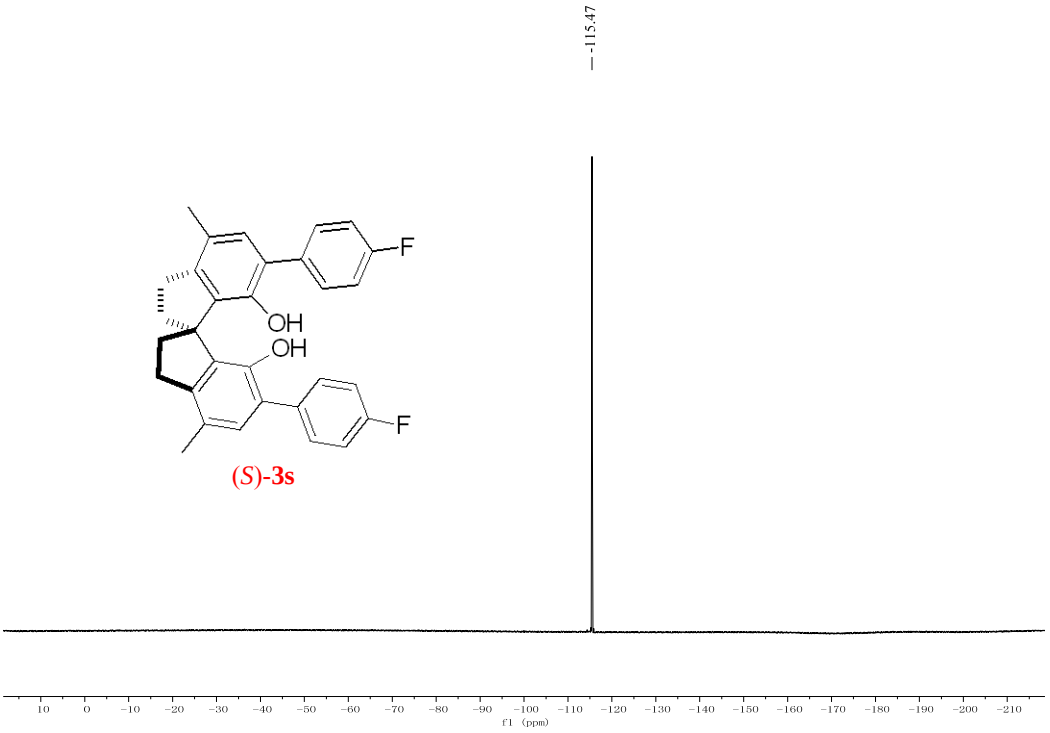
(*S*)-**3r**


7.447
7.436
7.430
7.419
7.078
7.061
7.043
6.987
4.856
3.034
3.028
3.018
3.012
3.002
2.994
2.986
2.980
2.966
2.963
2.947
2.932
2.914
2.383
2.377
2.367
2.363
2.347
2.253
F
OH
OH
F
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 0.5 ppm
4.02
4.00
1.97
1.95
4.11
4.13
6.10

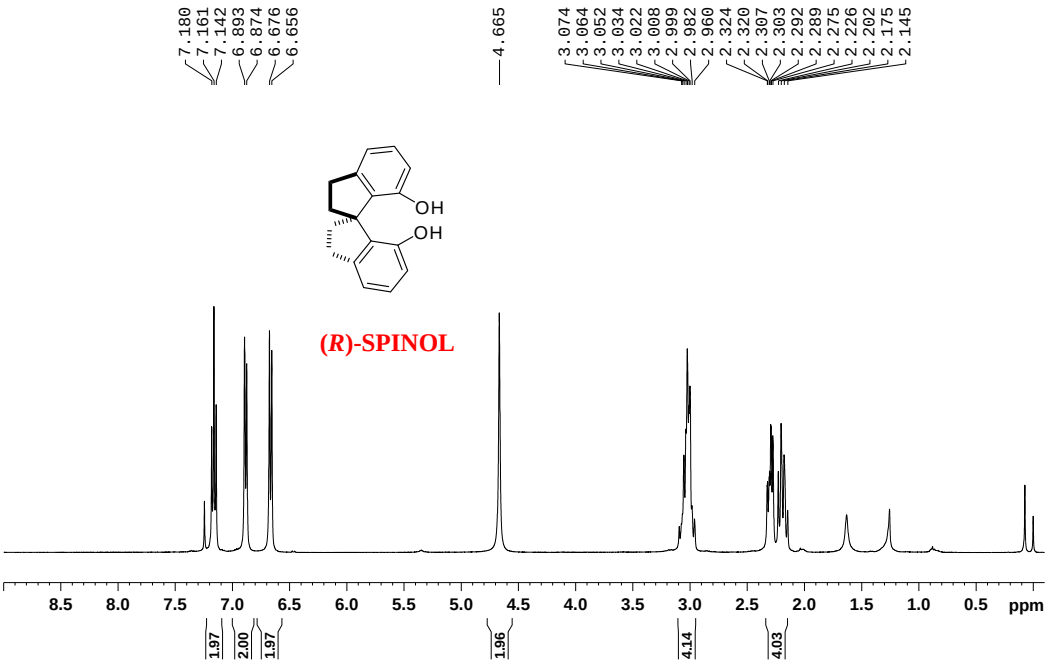
(*S*)-**3s**

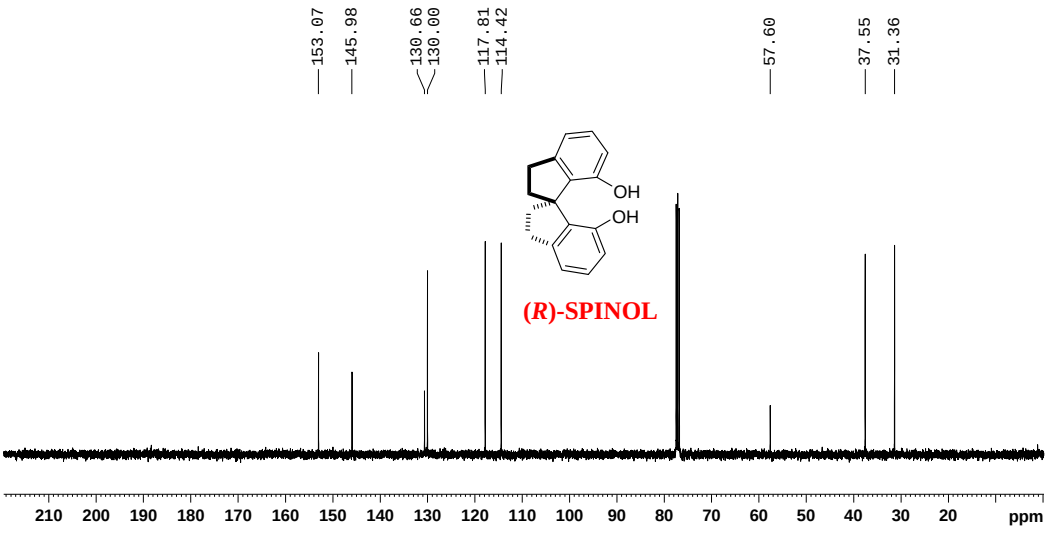

163.00
161.04
147.43
143.77
133.58
133.55
131.45
131.42
130.97
130.91
126.49
126.17
115.40
115.22
58.93
37.66
29.88
18.28
F
OH
OH
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

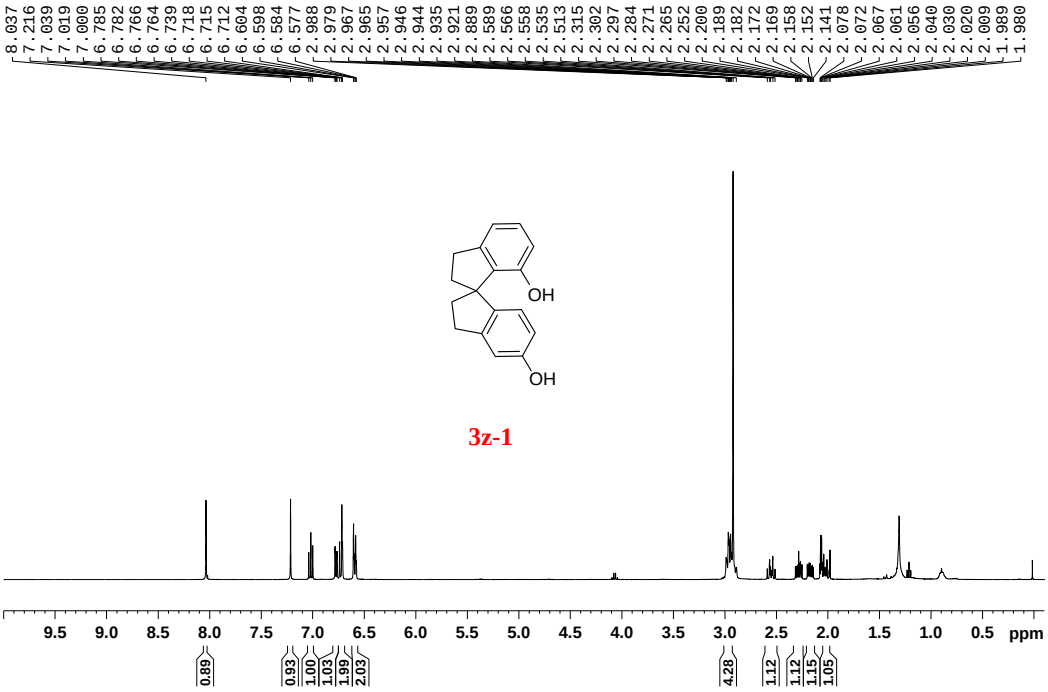
(*S*)-**3s**


-115.47
F
OH
OH
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

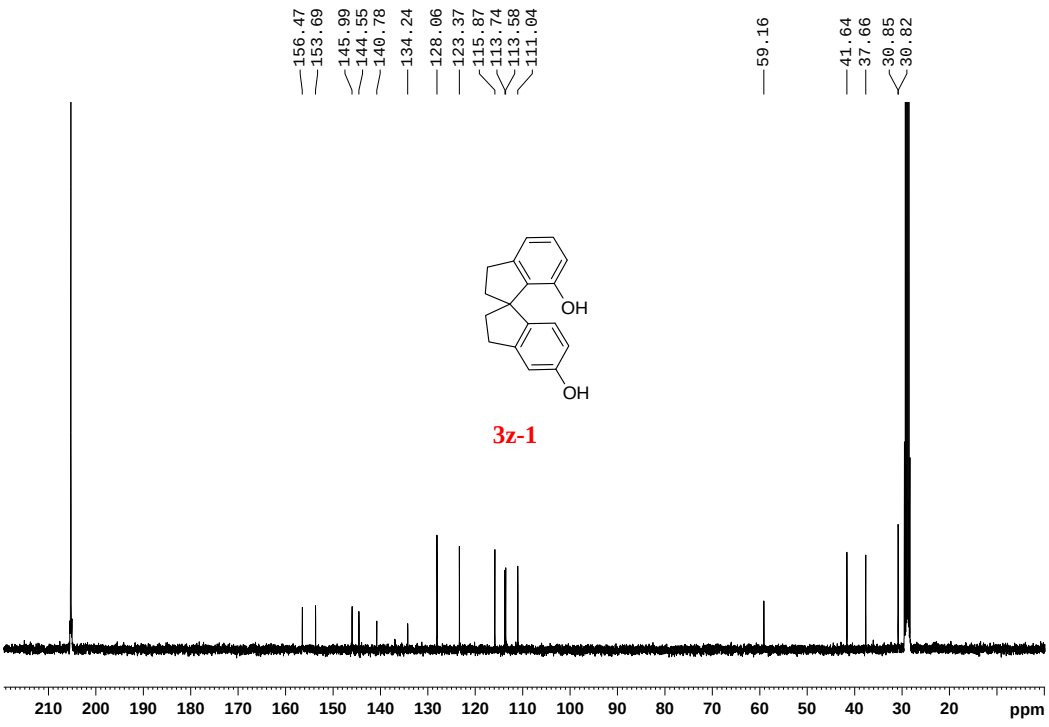
(*S*)-**3s**


7.180
7.161
7.142
6.893
6.874
6.676
6.656
4.665
3.074
3.064
3.052
3.034
3.022
3.008
2.999
2.982
2.960
2.324
2.320
2.307
2.303
2.292
2.289
2.275
2.226
2.202
2.175
2.145
OH
OH
(R)-SPINOL
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
0.5
ppm
1.97
2.00
1.97
1.96
4.14
4.03

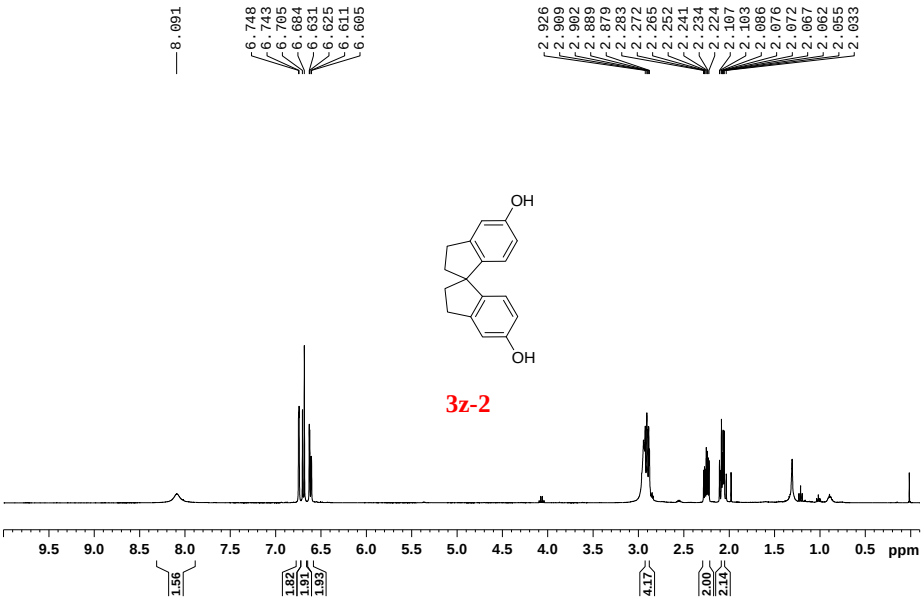

153.07
145.98
130.66
130.00
117.81
114.42
57.60
37.55
31.36
OH
OH
(R)-SPINOL
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

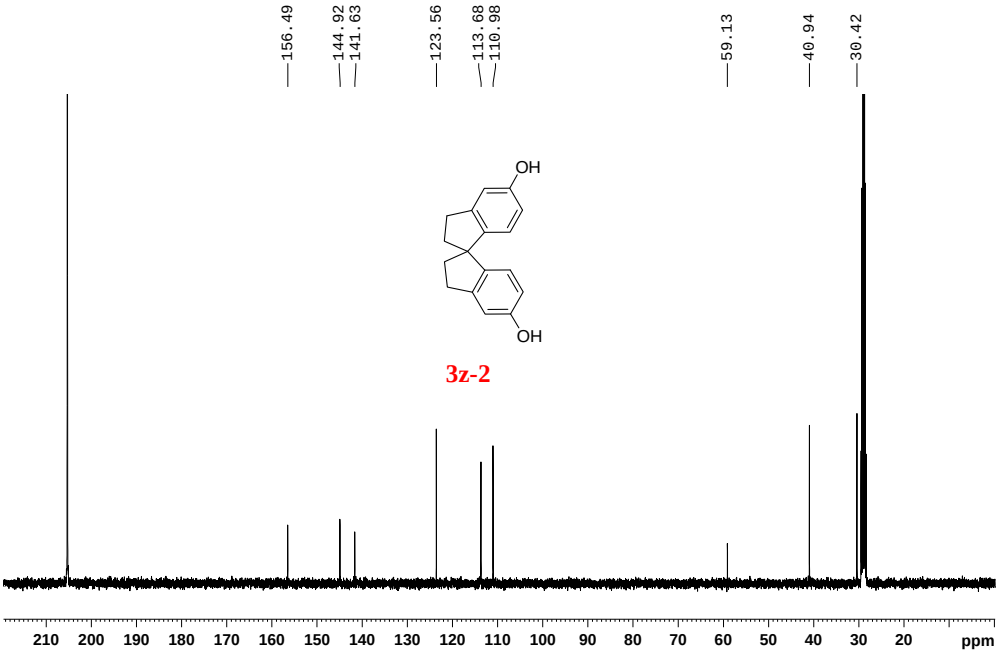

8.037
7.216
7.039
7.019
7.000
6.785
6.782
6.766
6.764
6.739
6.718
6.715
6.712
6.604
6.598
6.584
6.577
2.988
2.979
2.967
2.965
2.957
2.946
2.944
2.935
2.921
2.889
2.589
2.566
2.558
2.535
2.513
2.315
2.302
2.297
2.284
2.271
2.265
2.252
2.200
2.189
2.182
2.172
2.169
2.158
2.152
2.141
2.078
2.072
2.067
2.061
2.056
2.040
2.030
2.020
2.009
1.989
1.980
OH
OH
9.5 9.0 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 0.5 ppm
0.89
0.93
1.00
1.03
1.99
2.03
4.28
1.12
1.12
1.15
1.05

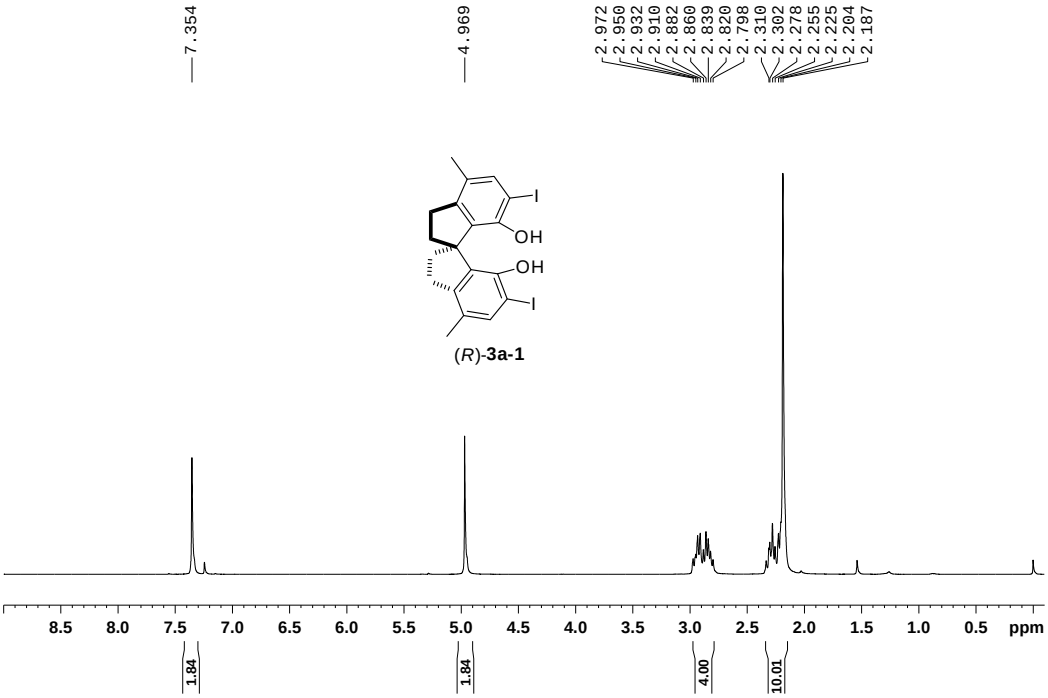
**3z-1**

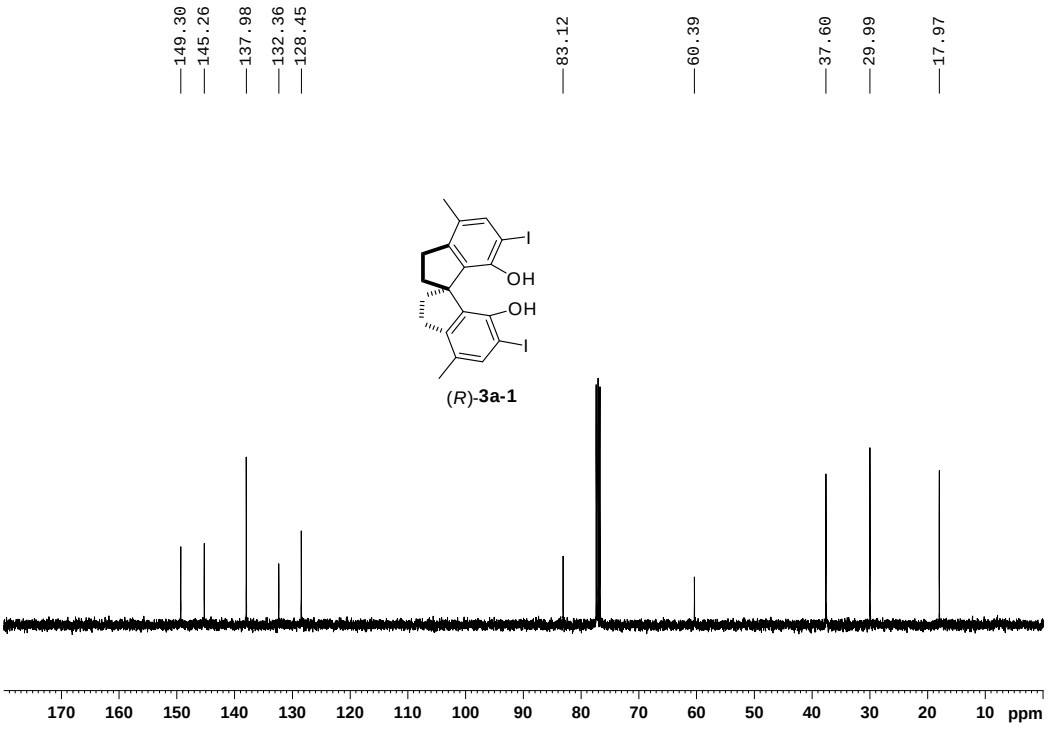

156.47
153.69
145.99
144.55
140.78
134.24
128.06
123.37
115.87
113.74
113.58
111.04
59.16
41.64
37.66
30.85
30.82
OH
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

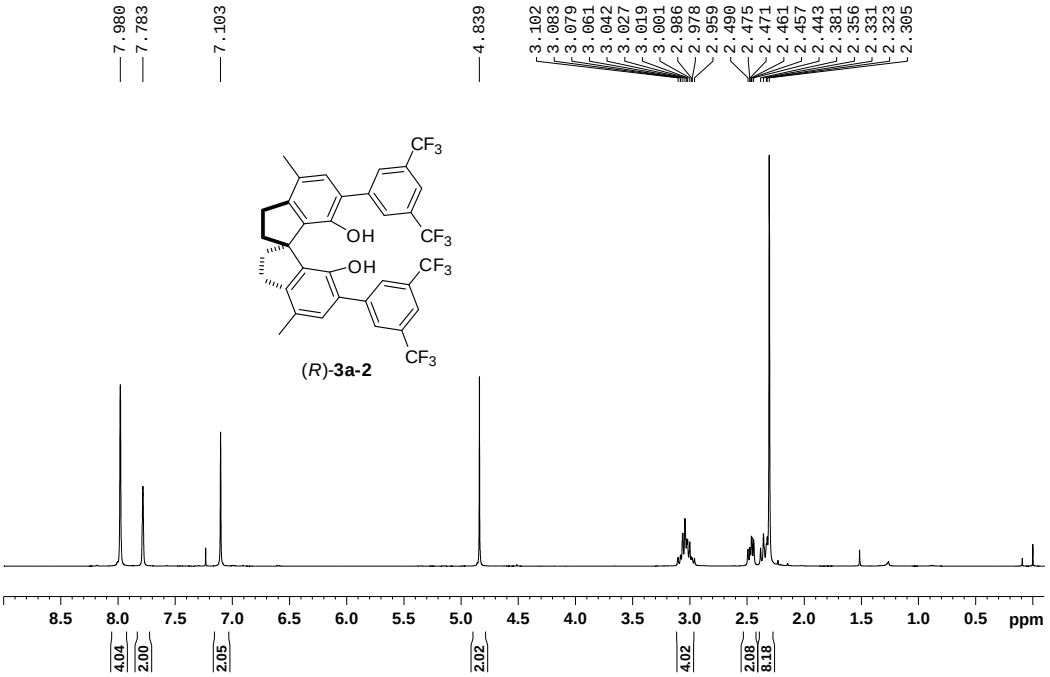
**3z-1**

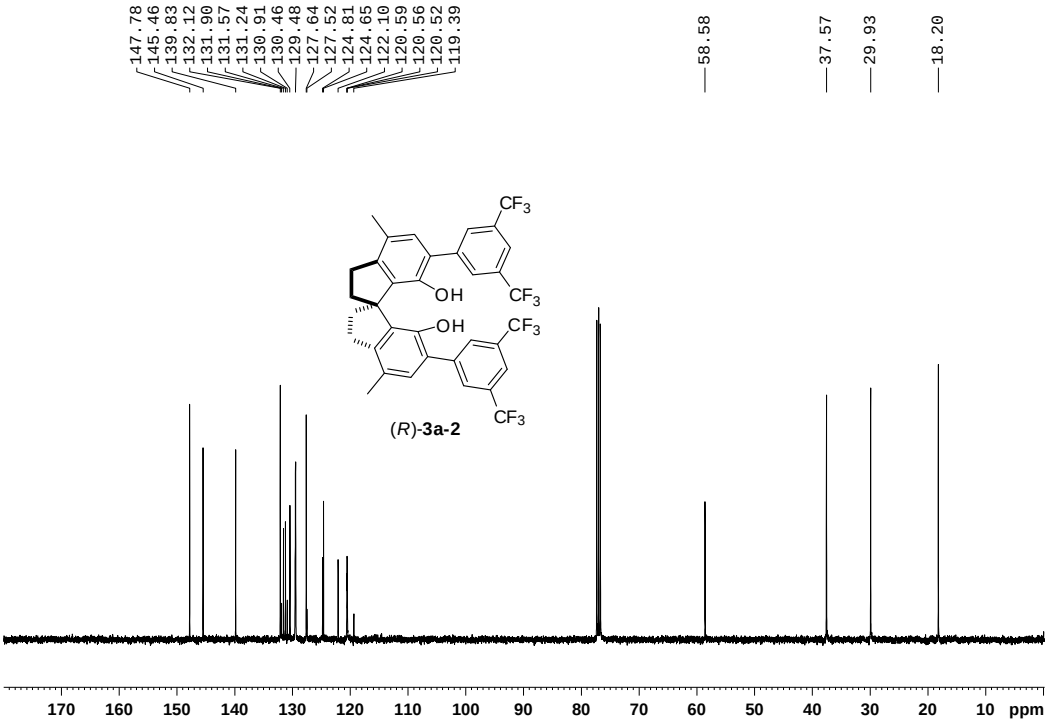

8.091
6.748
6.743
6.705
6.684
6.631
6.625
6.611
6.605
2.926
2.909
2.902
2.889
2.879
2.283
2.272
2.265
2.252
2.241
2.234
2.224
2.107
2.103
2.086
2.076
2.072
2.067
2.062
2.055
2.033
OH
OH
3z-2
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.56
1.82
1.91
1.93
4.17
2.00
2.14

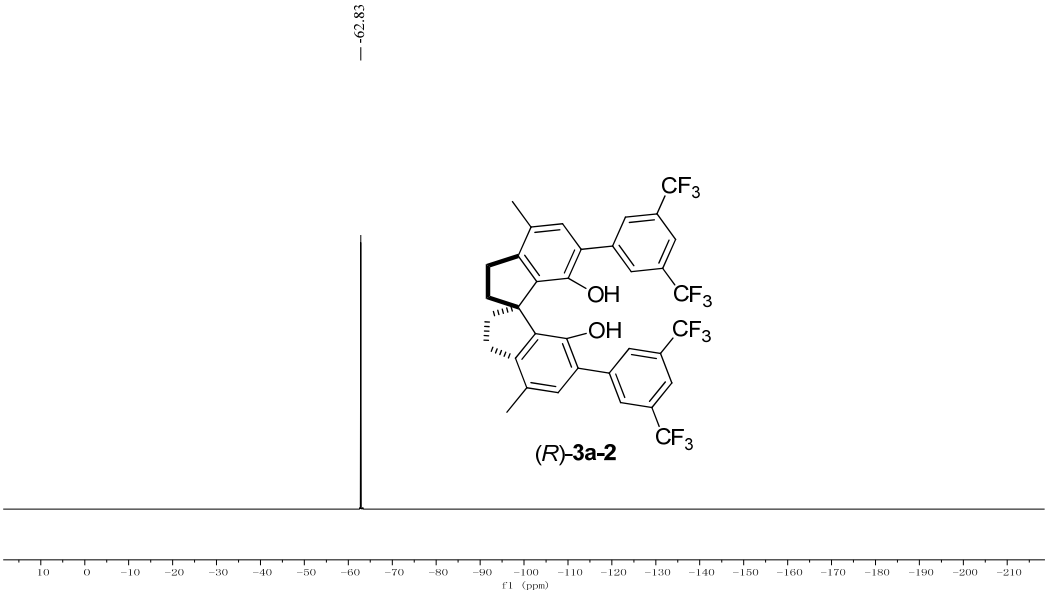

156.49
144.92
141.63
123.56
113.68
110.98
59.13
40.94
30.42
OH
OH
3z-2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

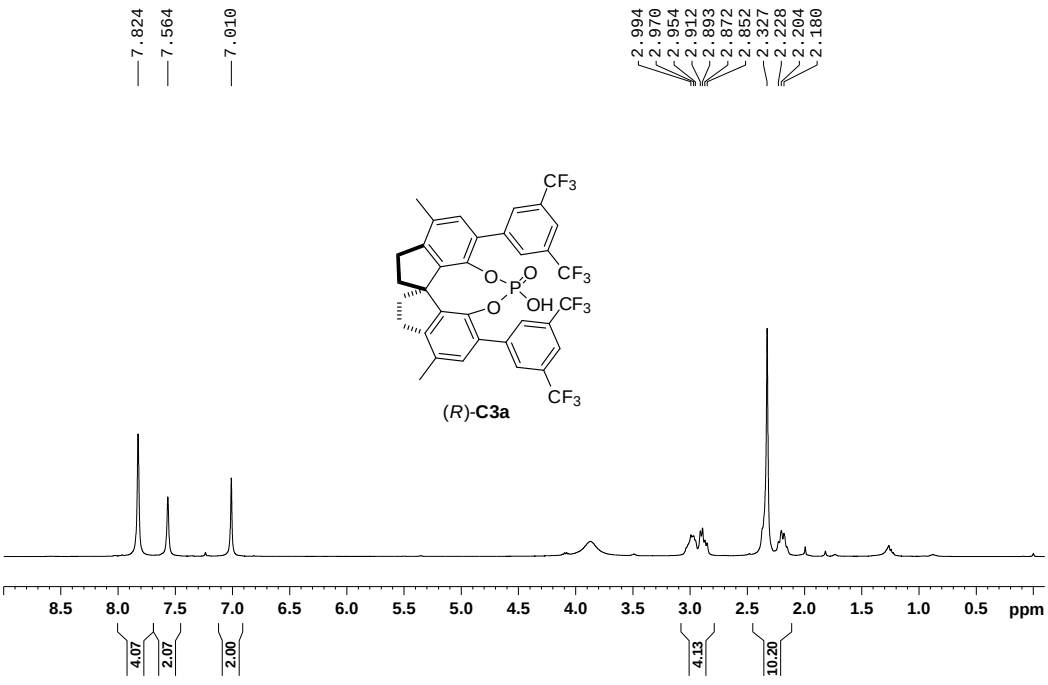

7.354
4.969
2.972
2.950
2.932
2.910
2.882
2.860
2.839
2.820
2.798
2.310
2.302
2.278
2.255
2.225
2.204
2.187
I
OH
OH
I
(R)-3a-1
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.84
1.84
4.00
10.01

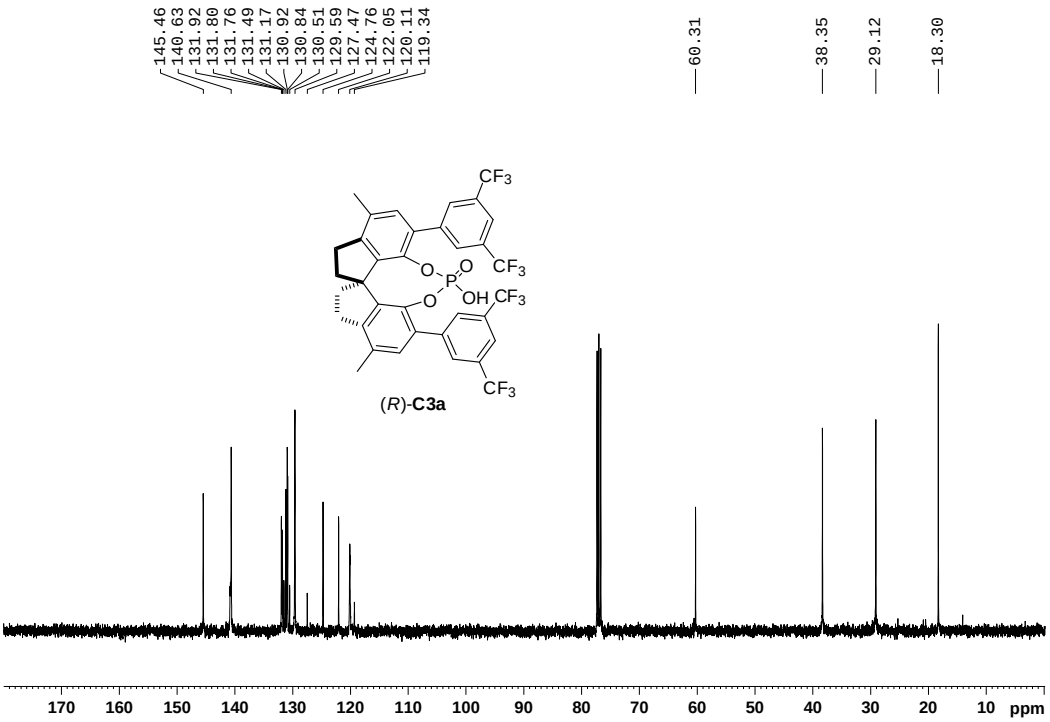

149.30
145.26
137.98
132.36
128.45
83.12
60.39
37.60
29.99
17.97
I
OH
OH
I
(R)-3a-1
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

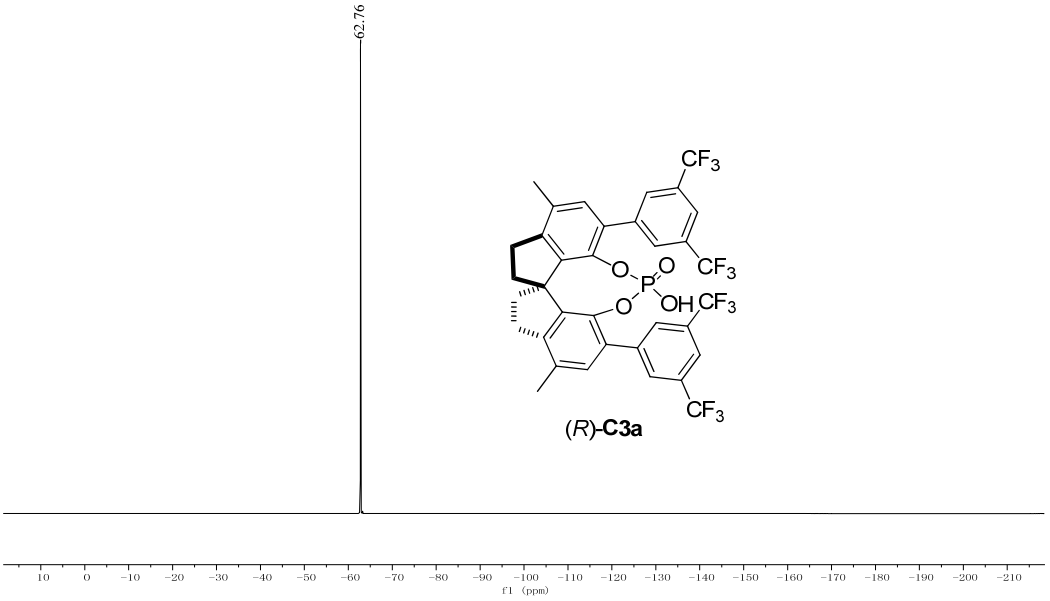

7.980
7.783
7.103
4.839
3.102
3.083
3.079
3.061
3.042
3.027
3.019
3.001
2.986
2.978
2.959
2.490
2.475
2.471
2.461
2.457
2.443
2.381
2.356
2.331
2.323
2.305
CF3
OH
OH
CF3
CF3
CF3
CF3
(R)-3a-2
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.04
2.00
2.05
2.02
4.02
2.08
8.18

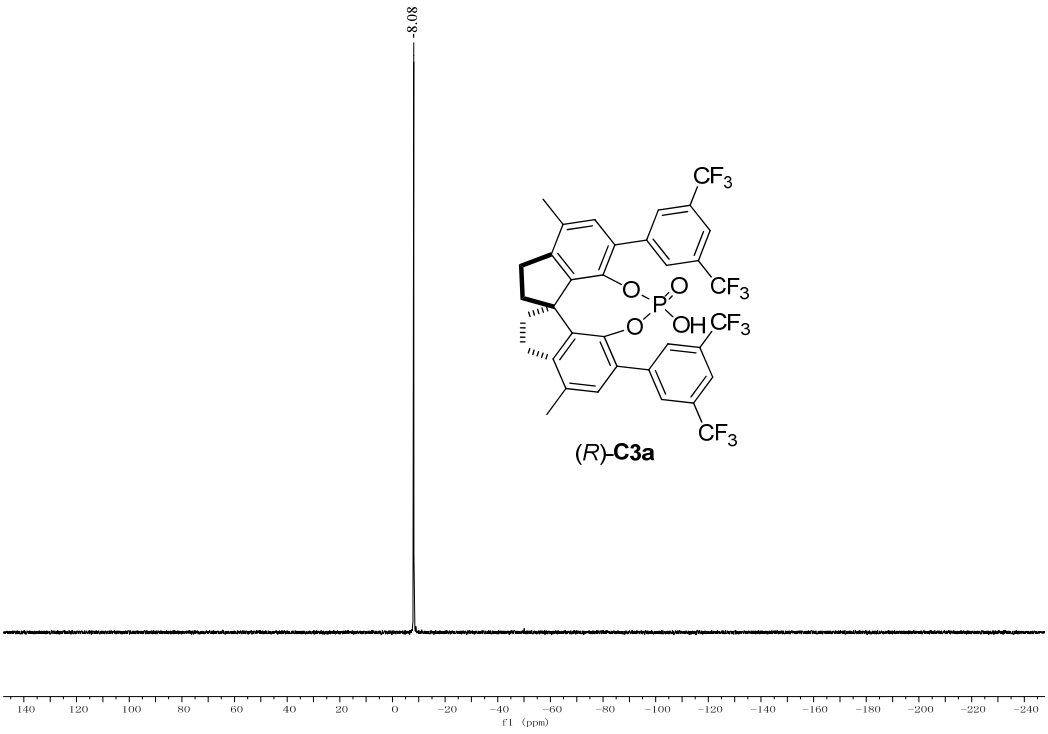

147.78
145.46
139.83
132.12
131.90
131.57
131.24
130.91
130.46
129.48
127.64
127.52
124.81
124.65
122.10
120.59
120.56
120.52
119.39
58.58
37.57
29.93
18.20
CF3
OH
OH
CF3
CF3
CF3
CF3
(R)-3a-2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


-62.83
CF3
OH
CF3
OH
CF3
CF3
(R)-3a-2
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


7.824
7.564
7.010
2.994
2.970
2.954
2.912
2.893
2.872
2.852
2.327
2.228
2.204
2.180
CF3
O
O
P
O
OH
CF3
CF3
CF3
(R)-C3a
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 0.5 ppm
4.07
2.07
2.00
4.13
10.20


145.46
140.63
131.92
131.80
131.76
131.49
131.17
130.92
130.84
130.51
129.59
127.47
124.76
122.05
120.11
119.34
60.31
38.35
29.12
18.30
CF3
CF3
CF3
CF3
O
P
O
O
OH
(R)-C3a
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


62.76
CF3
CF3
CF3
CF3
O
P
O
O
OH
(R)-C3a
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)


-8.08
CF3
CF3
CF3
CF3
O
O
P
O
OH
140
120
100
80
60
40
20
0
−20
−40
−60
−80
−100
−120
−140
−160
−180
−200
−220
−240
f1 (ppm)

(*R*)-**C3a**