*Electronic Supplementary Information*

# Synthesis of Diaryl Ether-components of Ellagitannins Using the Ortho-quinone with Consonant Mesomeric Effects

Hayato Konishi, Tsukasa Hirokane,[‡] Hajime Hashimoto, Kazutada Ikeuchi,[§] Shintaro Matsumoto, Shinnosuke Wakamori,* Hidetoshi Yamada*[,†]

*School of Science and Technology, Kwansei Gakuin University, Kwansei Gakuin University, 2-1 Gakuen, Sanda, Hyogo 669-1337, Japan. E-mail: shinnosuke1010@kwansei.ac.jp*

[†]Deceased on November 23, 2019. This paper is dedicated to the memory of Prof. Dr. Hidetoshi Yamada.

[‡]Present address: Faculty of Pharmaceutical Sciences, Tokushima Bunri University, 180 Nishihamaboji, Yamashiro-cho, Tokushima 770-1337, Japan.

[§]Present address:Department of Chemistry, Faculty of Science, Hokkaido University, West 8, North 10, Kita-ku, Sapporo, Hokkaido 060-0810, Japan.

*Table of Contents*

**Experiments for the reactions displayed in Scheme 4**

**ESI-1. Abbreviations used in the main text and the Supporting Information**

| | | | |
|---|---|---|---|
| Ac | acetyl | LRMS | low resolution mass spectra |
| ATR | attenuated total reflectance | m | multiplet |
| Bn | benzyl | M | molar (mol/L) |
| br | broad | Me | methyl |
| [Br] | bromination | min | minute(s) |
| calcd | calculated | MOM | methoxymethyl |
| d | doublet | mp | melting point |
| DBDMH | 1,3-dibromo-5,5-dimethylhydantoin | NAP | 2-naphthylmethyl |
| DDQ | 2,3-dichloro-5,6-dicyano-*p*-benzoquinone | NMR | nuclear magnetic resonance |
| | | *o*- | ortho- |
| DEPT | distortionless enhancement by polarization transfer | Obs | observed data |
| | | [Ox] | oxidation |
| DHDG | dehydrodigalloyl | Ph | phenyl |
| DMF | *N*,*N*-dimethylformamide | PIFA | phenyliodine bis(trifluoroacetate) |
| DMSO | dimethyl sulfoxide | q | quartet |
| ESI | electrospray ionization | [Rd] | reduction |
| | electronic supplementary material | rt | room temperature |
| Et | ethyl | s | singlet |
| h | hour(s) | TBAF | tetrabutylammonium fluoride |
| HHDP | hexahydroxydiphenoyl | t | triplet |
| HMQC | heteronuclear multiple quantum correlation | TES | triethylsilyl |
| | | THF | tetrahydrofuran |
| HMBC | heteronuclear multiple bond coherence | TLC | thin layer chromatography |
| HRMS | high resolution mass spectra | TMS | tetramethylsilane, trimethylsilyl |
| IPA | *iso*-propyl alcohol | UV | ultraviolet |
| IR | infrared spectroscopy | wt | weight |
| Lit | literature data | | |

**ESI-2. General experimental methods**

All commercially available reagents were used as received. All moisture and air sensitive reactions were carried out in glassware equipped with rubber septa (or a septum) under the positive pressure of nitrogen. When necessary, the glassware was dried under reduced pressure by heating with a heat-gun and solvents were distilled prior to use. The reactants were azeotropically dried if needed by evaporation of their acetonitrile or toluene solution several times to remove trace water that may be contained in the substrates. The reaction mixture was magnetically stirred. Concentration was carried out under reduced pressure.

The reactions were monitored by TLC and mass spectra. Anhydrous magnesium sulphate was used to dry organic layers after extraction, and it was removed by filtration through a cotton pad. The filtrate was concentrated and subjected to further purification protocols if necessary. This sequence was represented as "the general drying procedure" in the following experimental methods.

TLC was performed on Merck precoated silica gel 60 F-254 plates or Merck RP-19 F-254 plates. Spots were visualized by exposure to UV light or by immersion into a solution of 10% phosphomolybdic acid in ethanol followed by heating at ca. 200 °C.

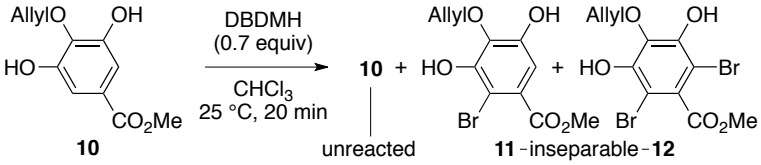
Column chromatography was performed on Merck silica gel 60 (63–200 or 40–63 μm) and Kanto Chemical silica gel 60 N (Spherical, neutral, 40–50 or 63–210 μm).

The melting points were determined using a Yanagimoto micro-melting point apparatus and uncorrected. IR spectra were recorded on Jasco FT/IR-4200 or Shimazu IRAffinity-1S with an ATR sampling unit, and the major absorbance bands are all reported in wavenumbers ($cm^{-1}$). HRMS were obtained on a JEOL JMS-T100LC spectrometer for ESI method. The data are reported in units of mass to charge.

NMR spectra were recorded on JEOL JNM-ECX-400 (400 MHz for $^{1}H$ and 101 MHz for $^{13}C$) or JNM-ECX-500 (500 MHz for $^{1}H$ and 126 MHz for $^{13}C$) with either tetramethylsilane or residual proton of deuterated solvent as internal reference in the indicated solvent in each parenthesis. The $^{1}H$ NMR spectroscopic data are indicated by a chemical shift (δ), with the multiplicity, the coupling constants, the integration and the assignments in parentheses in this order. The multiplicities are abbreviated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad. The $^{13}C$ NMR spectroscopic data are reported as the chemical shift (δ), with the hydrogen multiplicity obtained from the DEPT spectra and the assignments in parentheses. The multiplicities are abbreviated as s, C; d, CH; t, $CH_2$; and q, $CH_3$. When the number of the carbon was more than one, the number was added in the parentheses. In the case that there were very close but individual signals without overlap and when rounding chemical shifts of the signals at the second decimal place provides same values, their chemical shifts were written up to two decimal places.

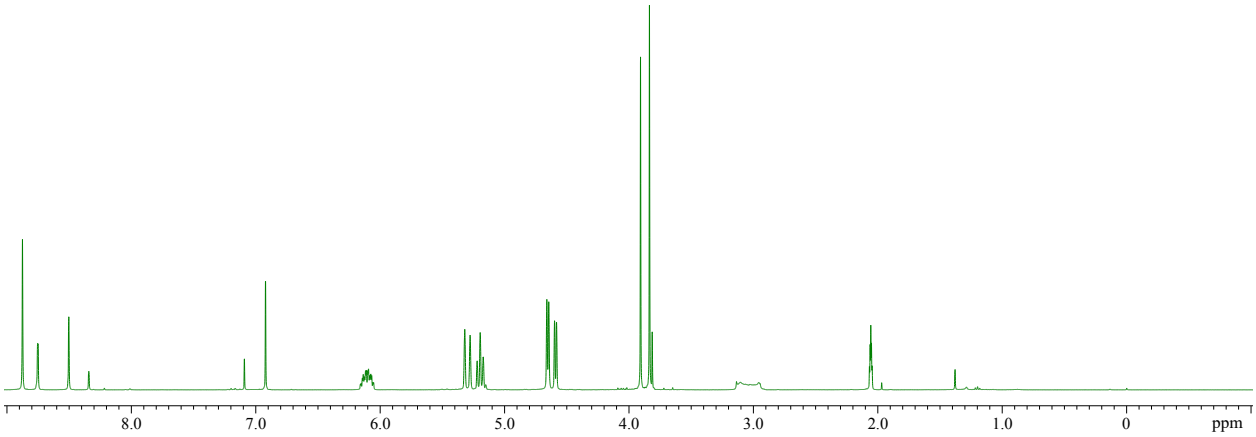
**Experiments displayed in Scheme 2**

**ESI-3. Bromination of 10 to a mixture of 11 and 12**

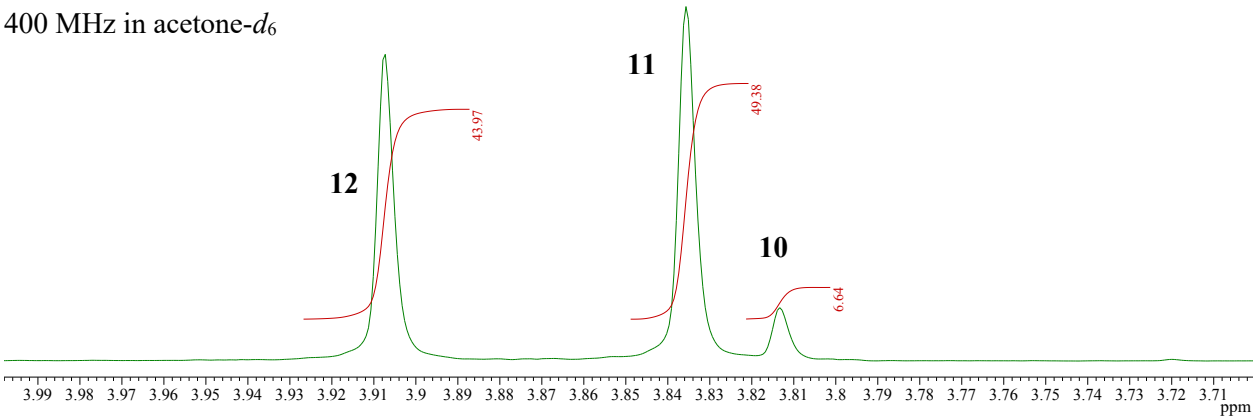



To a solution of **10** (1.50 g, 6.69 mmol) in chloroform (134 mL) was added 1,3-dibromo-5,5-dimethylhydantoin (1.34 g, 4.68 mmol) at 23 °C. The mixture was stirred for 20 min at 25 °C. Addition of 10% aqueous sodium thiosulfate (50 mL) quenched the reaction. The reaction mixture was extracted with chloroform. After the general drying procedure, the obtained crude product was a mixture of **10**, **11** and **12**. The ratio of **10**, **11** and **12** was 7:49:44 that was determined by integration values on a $^1$H NMR spectrum of the mixture. The mixture was purified by column chromatography (silica gel 50 g, hexane/ethyl acetate 6/1 to 4/1) to remove **10** (60.0 mg, 267 mmol, 4% yield) as a colourless solid and to obtain the mixture of **11** and **12** as a yellow oil.

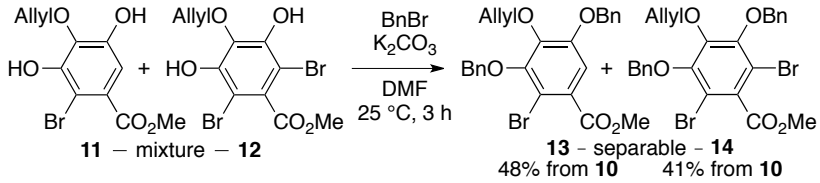
$^1$H NMR spectrum of the crude product (mixture of **10**, **11** and **12**), 400 MHz in acetone-$d_6$




Expanded $^1$H NMR spectrum of the crude product used for determination of the ratio **10**, **11** and **12**
400 MHz in acetone-$d_6$



**ESI-4. Synthesis of 13 and 14**




To a mixture of **11** and **12** in DMF (34 mL) were added potassium carbonate (2.78 g, 20.1 mmol) and benzyl bromide (3.43 g, 20.1 mmol) at 25 °C. The mixture was stirred for 3 h at 25 °C. To the reaction mixture were added diethyl ether (20 mL) and 1 M hydrochloric acid (20 mL). The reaction mixture was extracted with diethyl ether. The combined organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 20 g, hexane/toluene 2/1 to 1/2) to afford **13** (1.55 g, 3.21 mmol, 48% yield) as a colourless powder and **14** (1.54 g, 2.74 mmol, 41% yield) as a colourless oil.

Data for **13**

mp 64.8–66.3 °C.

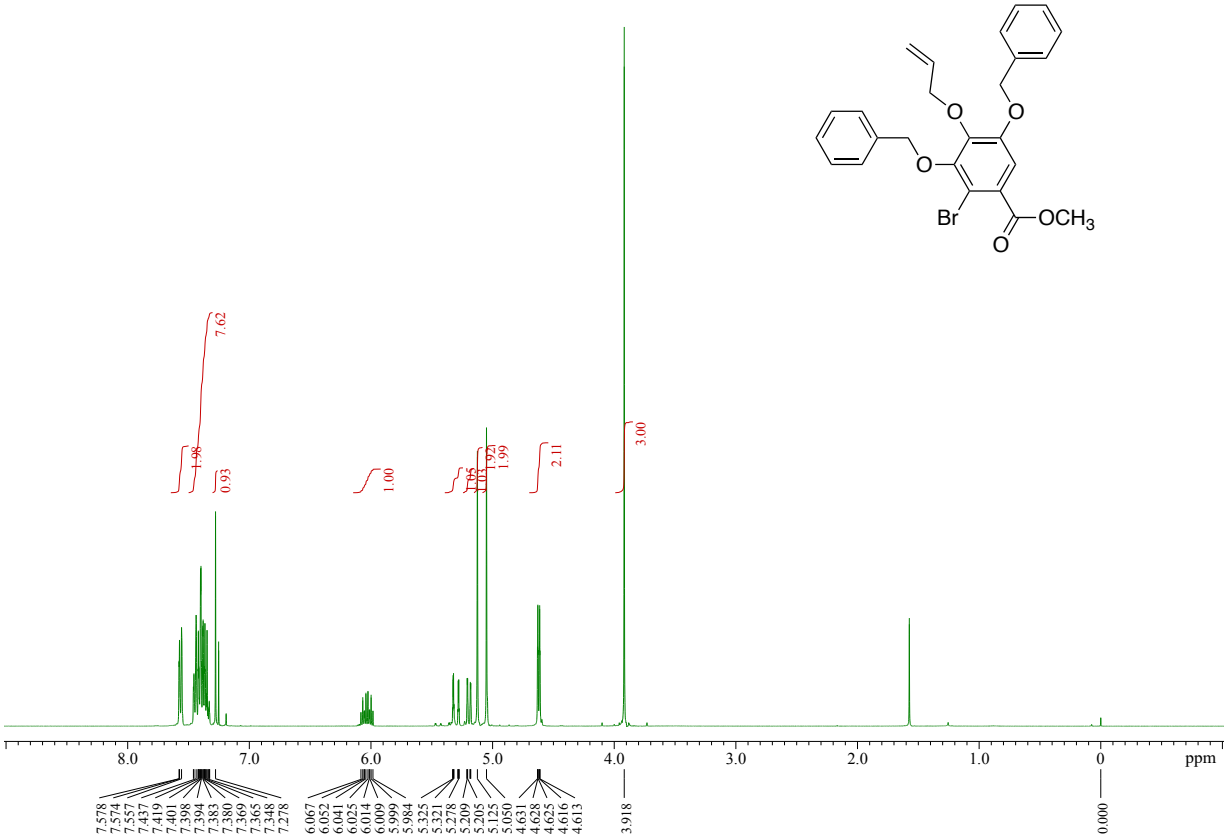
IR (ATR) 3090, 3032, 2951, 2876, 1734, 1560, 1476, 1433, 1406, 1364, 1337, 1204, 1099, 1024, 982, 739, 698 $cm^{-1}$.

$^{1}H$ NMR (400 MHz, chloroform-*d*, 21 °C) δ 7.58–7.55 (m, 2H, Bn), 7.46–7.32 (m, 8H, Bn), 7.28 (s, 1H, galloyl), 6.04 (ddt, *J* = 16.3, 10.3, 6.0 Hz, 1H, allyl), 5.31 (ddt, *J* = 16.3, 1.6, 1.4 Hz, 1H, allyl), 5.21 (br ddt, *J* = 10.3, 1.6, 1.1 Hz, 1H, allyl), 5.13 (s, 2H, Bn), 5.05 (s, 2H, Bn), 4.62 (ddd, *J* = 6.0, 1.4, 1.1 Hz, 2H, allyl), 3.92 (s, 3H, OMe).

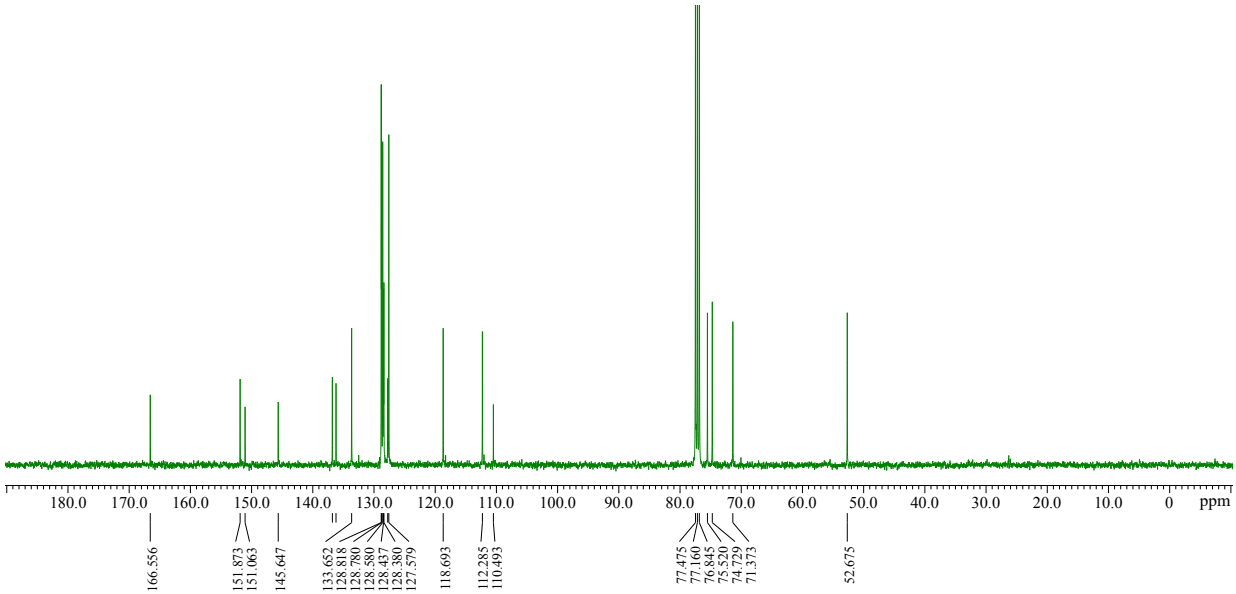
$^{13}C$ NMR (101 MHz, chloroform-*d*, 21 °C) δ 166.6 (s, ester), 151.9 (s, galloyl), 151.1 (s, galloyl), 145.6 (s, galloyl), 136.8 (s, Bn), 136.2 (s, Bn), 133.6 (d, allyl), 128.82 (d, 2C, Bn), 128.78 (d, 2C, Bn), 128.6 (d, 2C, Bn), 128.44 (d, Bn), 128.38 (d, Bn), 127.7 (s, galloyl), 127.6 (d, 2C, Bn), 118.7 (t, allyl), 112.3 (d, galloyl), 110.5 (s, galloyl), 75.5 (t, allyl or Bn), 74.7 (t, allyl or Bn), 71.3 (t, Bn), 52.7 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{23}O_5BrNa$ 505.0627, found 505.0632.

$^{1}$H NMR spectrum of **13**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **13**, 101 MHz in chloroform-*d*



Data for **14**

mp 47.9–49.3 °C.

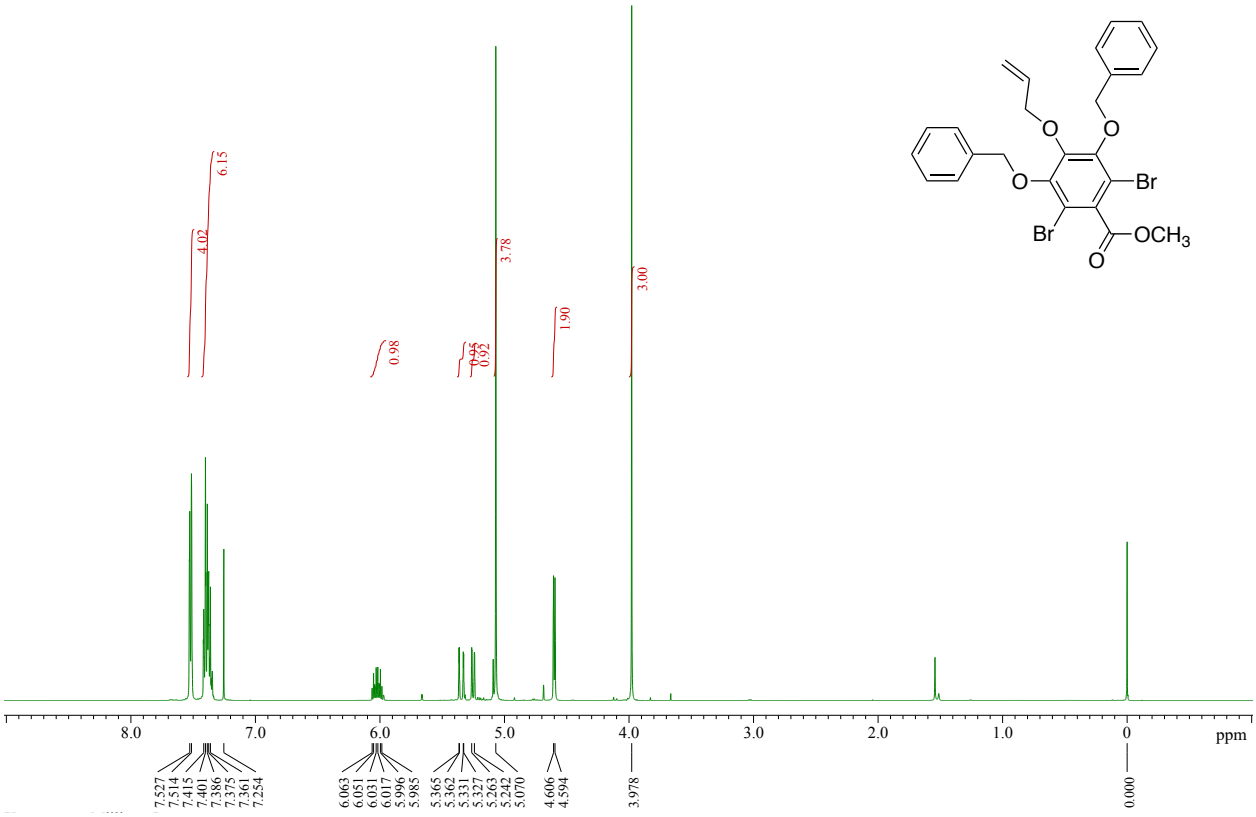
IR (ATR) 3032, 2949, 2876, 1740, 1429, 1404, 1356, 1333, 1221, 1086, 984, 733, 696 $cm^{-1}$.

$^1H$ NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.52 (br d, *J* = 6.9 Hz, 4H, Bn), 7.42–7.35 (m, 6H, Bn), 6.02 (ddt, *J* = 17.2, 10.9, 5.7 Hz, 1H, allyl), 5.35 (br ddt, *J* = 17.2, 1.7, 1.7 Hz, 1H, allyl), 5.25 (br ddt, *J* = 10.9, 1.7, 1.2 Hz, 1H, allyl), 5.07 (s, 4H, Bn), 4.60 (ddd, *J* = 5.7, 1.7, 1.2 Hz, 2H, allyl), 3.98 (s, 3H, OMe).

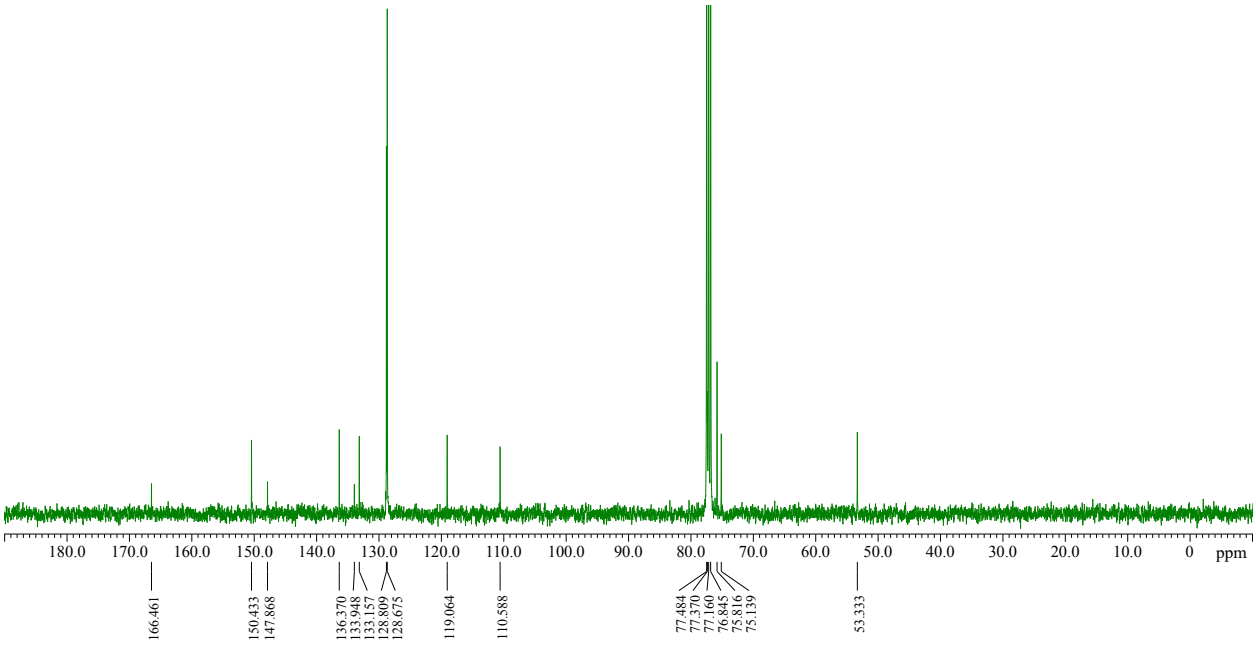
$^{13}C$ NMR (101 MHz, chloroform-*d*, 23 °C) δ 166.5 (s, ester), 150.4 (s, 2C, galloyl), 147.9 (s, galloyl), 136.4 (s, 2C, Bn), 134.0 (s, galloyl), 133.2 (d, allyl), 128.8 (d, 4C, Bn), 128.7 (d, 6C, Bn), 119.1 (t, allyl), 110.6 (s, 2C, galloyl), 75.8 (t, 2C, Bn), 75.1 (t, allyl), 53.3 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{22}O_5BrNa$ 582.9732, found 582.9724.

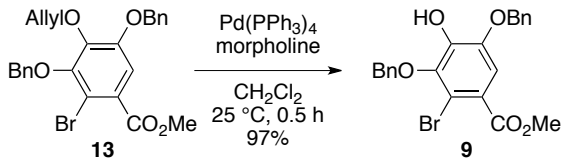
$^1H$ NMR spectrum of **14**, 500 MHz in chloroform-*d*



$^{13}$C NMR spectrum of **14**, 101 MHz in chloroform-*d*



**ESI-5. Synthesis of 9**




To a solution of **13** (80.0 mg, 166 μmol) in dichloromethane (2.0 mL) were added morpholine (20.0 mg, 232 μmol) and tetrakis(triphenylphosphine)palladium(0) (4.0 mg, 20.0 μmol) at 25 °C. The mixture was stirred for 0.5 h at 25 °C. To the reaction mixture were added dichloromethane (5 mL) and 1 M hydrochloric acid (5 mL). The reaction mixture was extracted with dichloromethane. After the general drying procedure, the mixture was purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 8/1) to afford **9** (71.4 mg, 161 μmol, 97% yield) as a colourless solid.

Data for **9**

mp 118.0–119.4 °C.

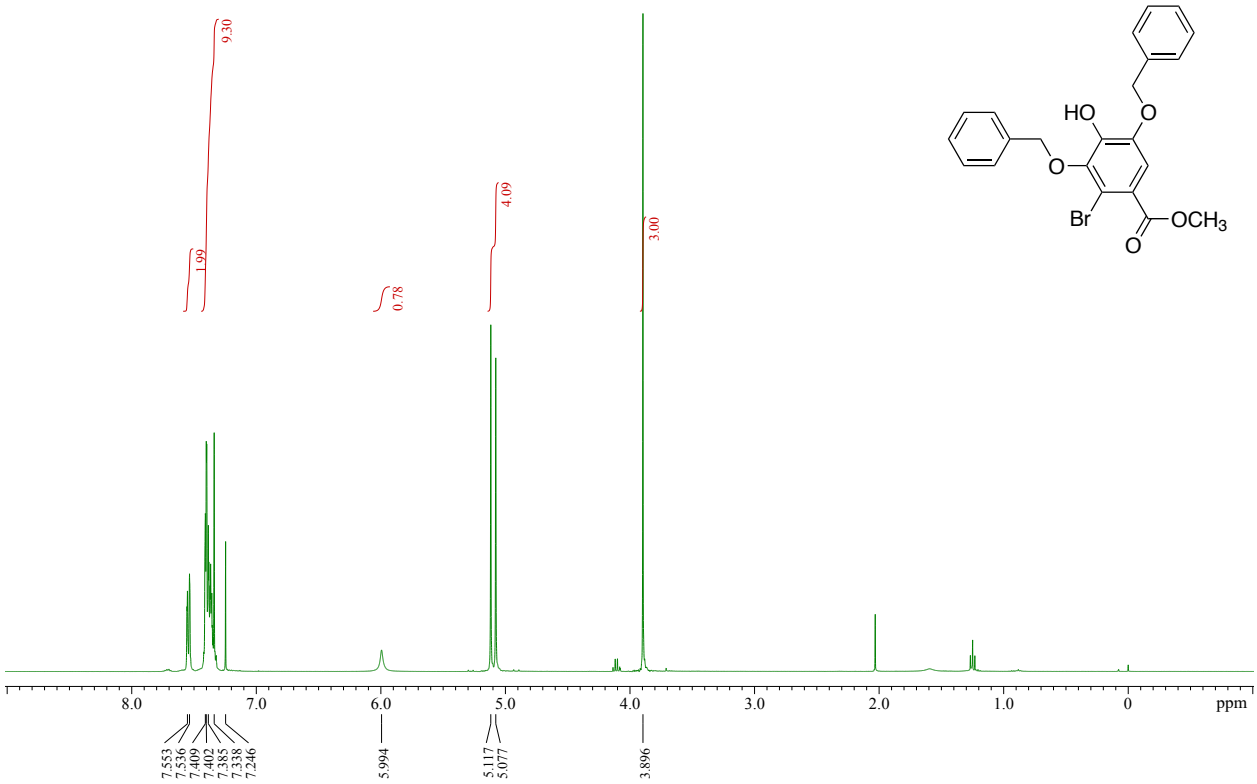
IR (ATR) 3447, 3063, 3032, 2949, 2880, 1719, 1593, 1497, 1435, 1354, 1307, 1211, 1026, 741, 698 $cm^{-1}$.

$^{1}H$ NMR (400 MHz, chloroform-*d*, 24 °C) δ 7.56–7.53 (m, 2H), 7.41–7.35 (m, 8H, Bn), 7.34 (s, 1H, galloyl), 5.99 (br s, 1H, OH), 5.12 (s, 2H, Bn), 5.08 (s, 2H, Bn), 3.90 (s, 3H, OMe).

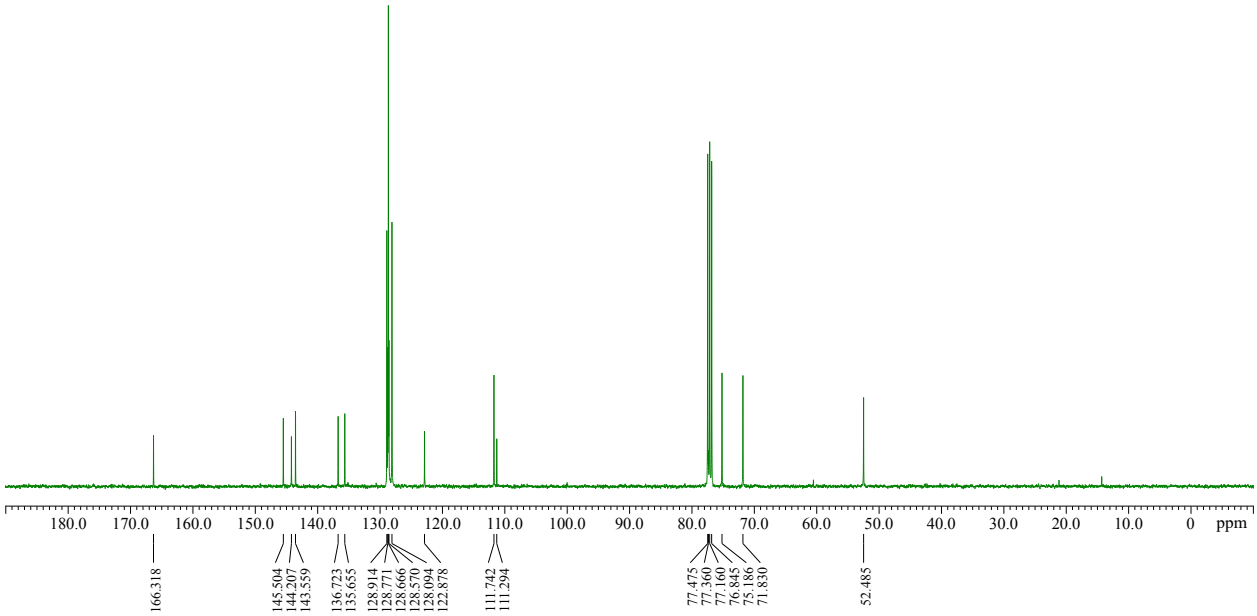
$^{13}C$ NMR (101 MHz, chloroform-*d*, 24 °C) δ 166.3 (s, ester), 145.5 (s, galloyl), 144.2 (s, galloyl), 143.6 (s, galloyl), 136.7 (s, Bn), 135.7 (s, Bn), 128.9 (d, 2C, Bn), 128.8 (d, Bn), 128.7 (d, 4C, Bn), 128.6 (d, Bn), 128.1 (d, 2C, Bn), 122.9 (s, galloyl), 111.7 (d, galloyl), 111.3 (s, galloyl), 75.2 (t, Bn), 71.8 (t, Bn), 52.5 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{19}O_5BrNa$ 465.0314, found 465.0304.

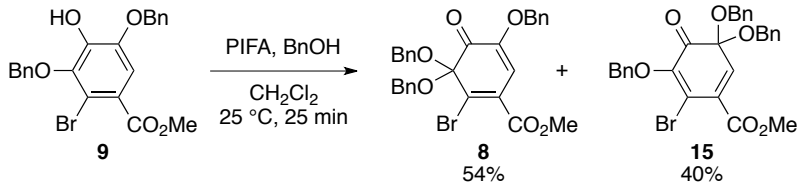
$^{1}$H NMR spectrum of **9**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **9**, 101 MHz in chloroform-*d*



**ESI-6. Synthesis of 8 and 15**



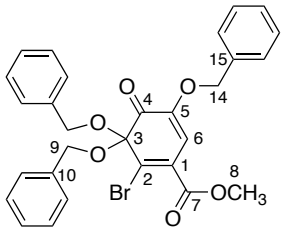

To a solution of **9** (100 mg, 226 μmol) in dichloromethane (4.5 mL) were added benzyl alcohol (733 mg, 6.78 mmol) and phenyliodine bis(trifluoroacetate) (145 mg, 338 μmol) at 25 °C. The mixture was stirred for 25 min at 25 °C. Addition 10% aqueous sodium thiosulfate (5 mL) quenched the reaction. The reaction mixture was extracted with dichloromethane. After the general drying procedure, the crude product was purified by column chromatography (silica gel 5 g, hexane/toluene 1/1 to 1/3) to afford **8** (67.0 mg, 122 μmol, 54% yield) as a yellow oil and its regioisomer **15** (49.7 mg, 90.4 μmol, 40% yield) as a yellow oil. The by-product **15** decomposed at room temperature.

Data for **8**

mp 115.2–117.0 °C.

IR (ATR) 3065, 3032, 2951, 1738, 1694, 1632, 1454, 1314, 1196, 1065, 1028, 737, 696 $cm^{-1}$.

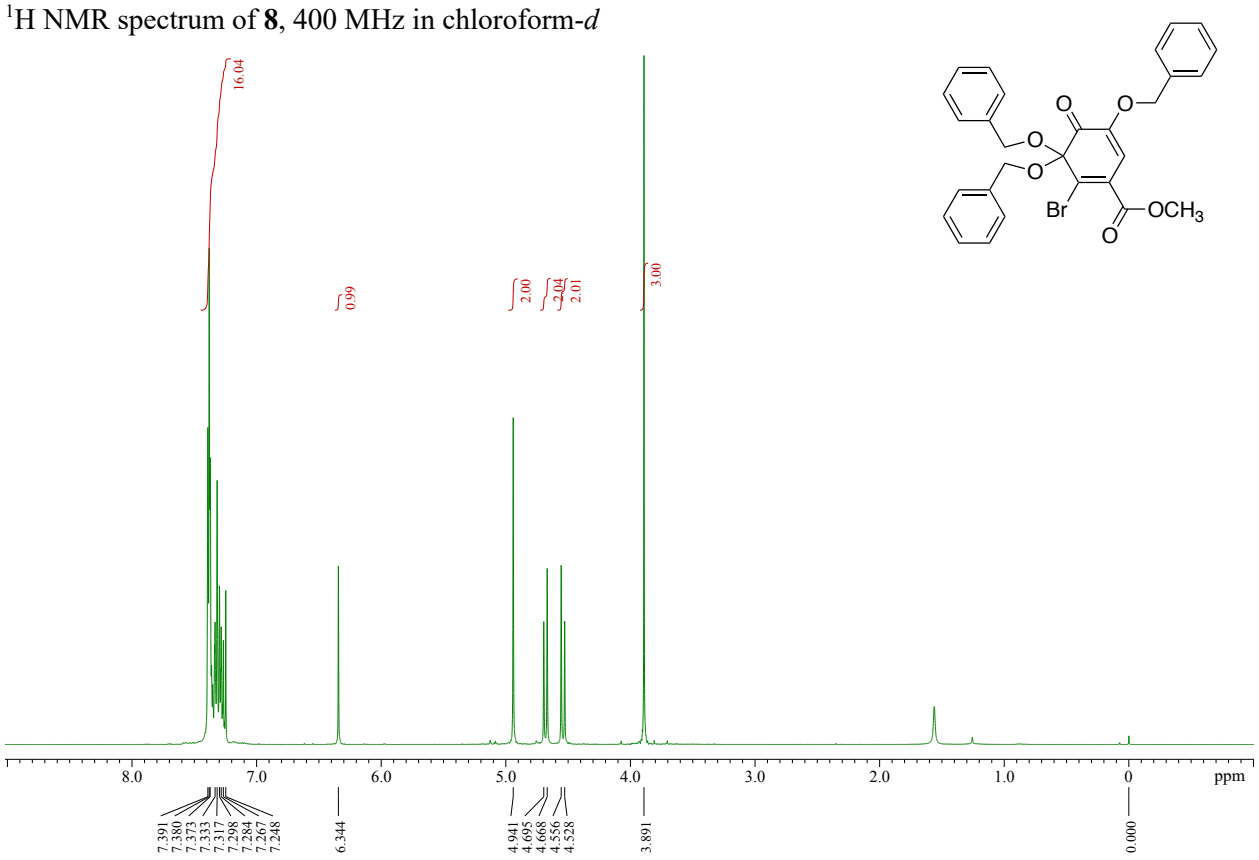
$^{1}H$ NMR (400 MHz, chloroform-*d*, 24 °C) δ 7.39–7.25 (m, 15H, Bn), 6.34 (s, 1H, H-6), 4.94 (s, 2H, Bn), 4.68 (d, *J* = 11.0 Hz, 2H, Bn), 4.54 (d, *J* = 11.0 Hz, 2H, Bn), 3.89 (s, 3H, H-8).



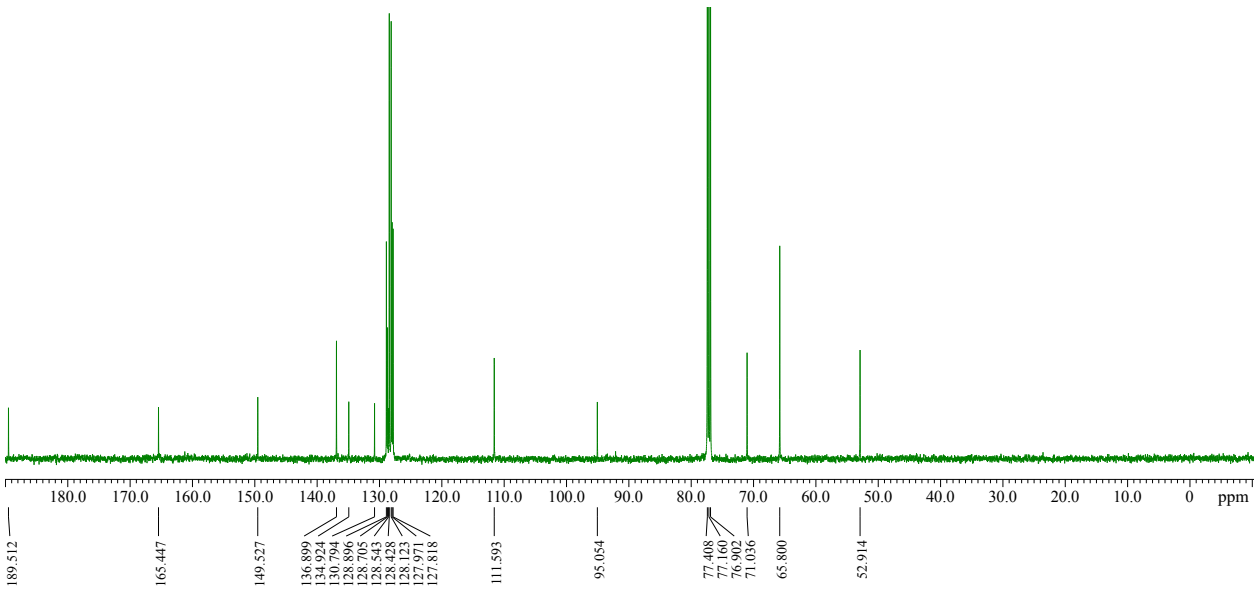

$^{13}C$ NMR (126 MHz, chloroform-*d*, 25 °C, HMQC and HMBC spectra were used for the assignments) δ 189.5 (s, C-4), 165.5 (s, C-7), 149.5 (s, C-5), 136.9 (s, 2C, C-10), 134.9 (s, C-15), 130.8 (s, C-1), 128.9 (d, 2C, Bn), 128.7 (d, Bn), 128.6 (s, C-2), 128.4 (d, 4C, Bn), 128.1 (d, 4C, Bn), 128.0 (d, 2C, Bn), 127.8 (d, 2C, Bn), 111.6 (d, C-6), 95.1 (s, C-3), 71.1 (t, C-14), 65.8 (t, 2C, C-9), 52.9 (q, C-8).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{25}O_6BrNa$ 571.0732, found 571.0729.

$^{1}$H NMR spectrum of **8**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **8**, 126 MHz in chloroform-*d*



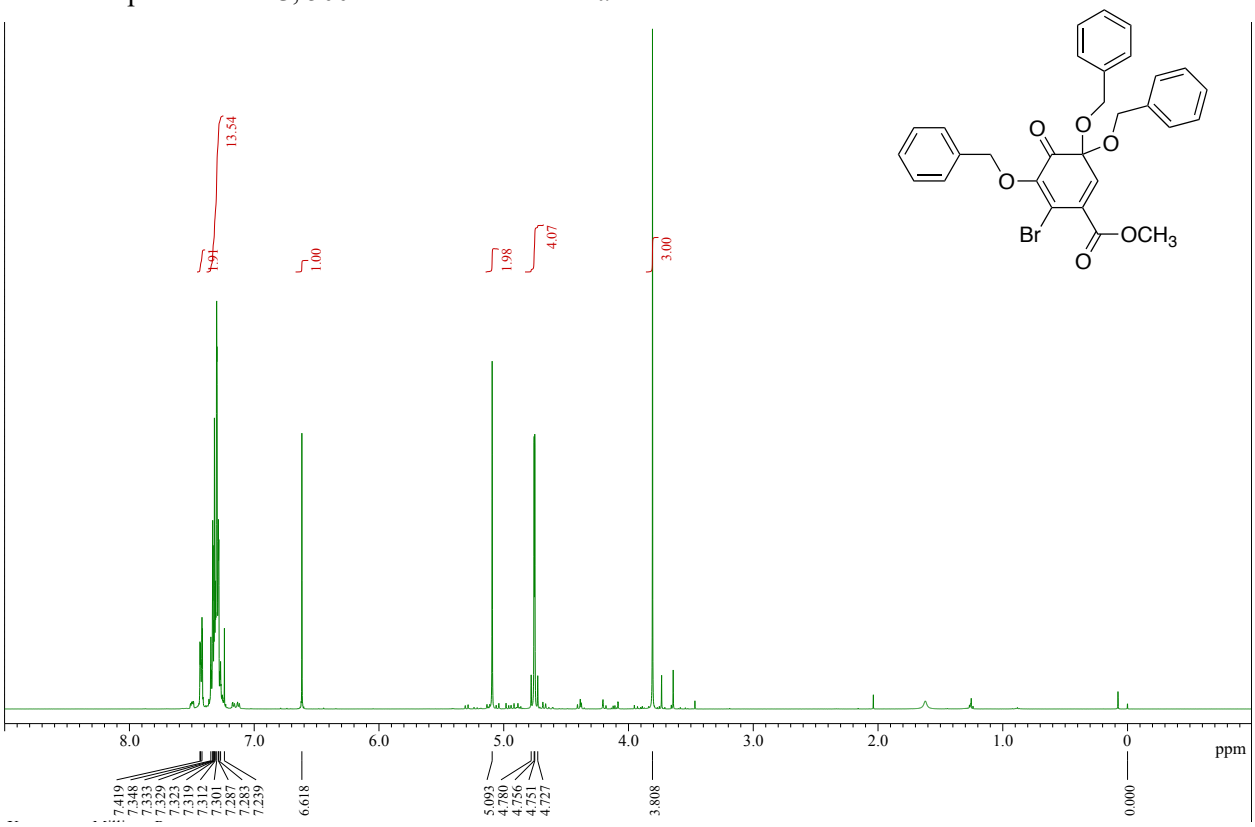
Data for **15**

$^{1}$H NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.44–7.41 (m, 2H, Bn), 7.35–7.25 (m, 13H, Bn), 6.62 (s, 1H, quinone), 5.09 (s, 2H, Bn), 4.77 (d, *J* = 12.0 Hz, 2H, Bn), 4.74 (d, *J* = 12.0 Hz, 2H, Bn), 3.81 (s, 3H, OMe).

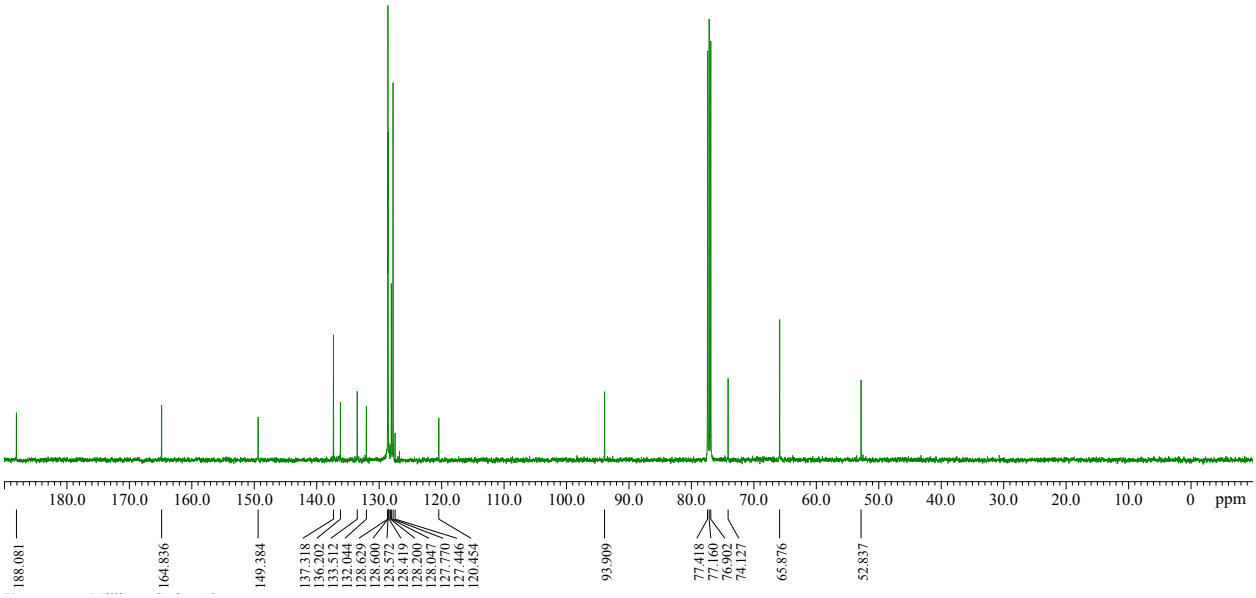
$^{13}$C NMR (126 MHz, chloroform-*d*, 23 °C) δ 188.1 (s, ketone), 164.8 (s, ester), 149.4 (s, quinone), 137.3 (s, 2C, Bn), 136.2 (s, Bn), 133.5 (d, quinone), 132.0 (s, quinone), 128.6–128.5 (d, overlapped 12 doublets: three peaks were observed, Bn), 128.0 (d, Bn), 127.8 (d, 2C, Bn), 120.5 (s, quinone), 93.9 (s, quinone), 74.1 (t, Bn), 65.9 (t, 2C, Bn), 52.8 (q, OMe).

HRMS (ESI) *m/z* [M + Na]$^{+}$ calcd for $C_{29}H_{25}O_6BrNa$ 571.0732, found 571.0724.

$^{1}$H NMR spectrum of **15**, 500 MHz in chloroform-*d*

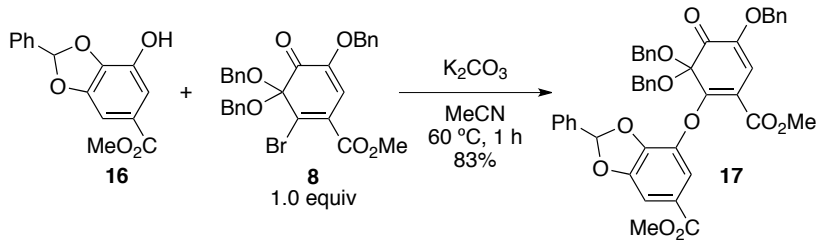


$^{13}$C NMR spectrum of **15**, 126 MHz in chloroform-*d*



**Experiments for the reactions displayed in Scheme 3**

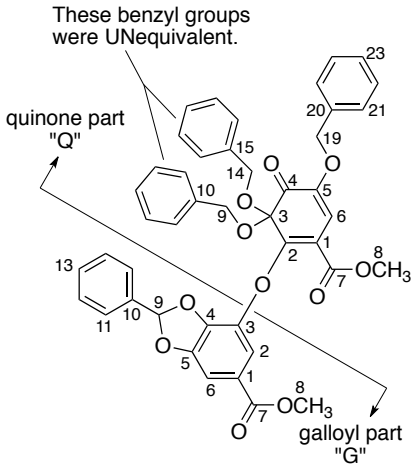
**ESI-7. Synthesis of 17** (The use of 1.0 equiv of **8**)




To a solution of **8** (66.0 mg, 120 μmol) in acetonitrile (1.2 mL) were added **16** (33.0 mg, 120 μmol) and potassium carbonate (33.0 mg, 239 μmol) at room temperature. The mixture was stirred for 1 h at 60 °C. After the mixture was cooled to 0 °C, ethyl acetate (3 mL) and 1 M hydrochloric acid (3 mL) were added to the mixture. The aqueous mixture was extracted with ethyl acetate. The organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (silica gel 2 g, hexane/ethyl acetate 20/3 to 2/1) to afford **17** (74.0 mg, 99.6 μmol, 83% yield) as a yellow amorphous solid.

Data for **17**

IR (ATR) 3067, 3032, 2951, 1715, 1626, 1497, 1437, 1364, 1331, 1302, 1215, 1180, 1061, 1016, 750, 696 $cm^{-1}$.

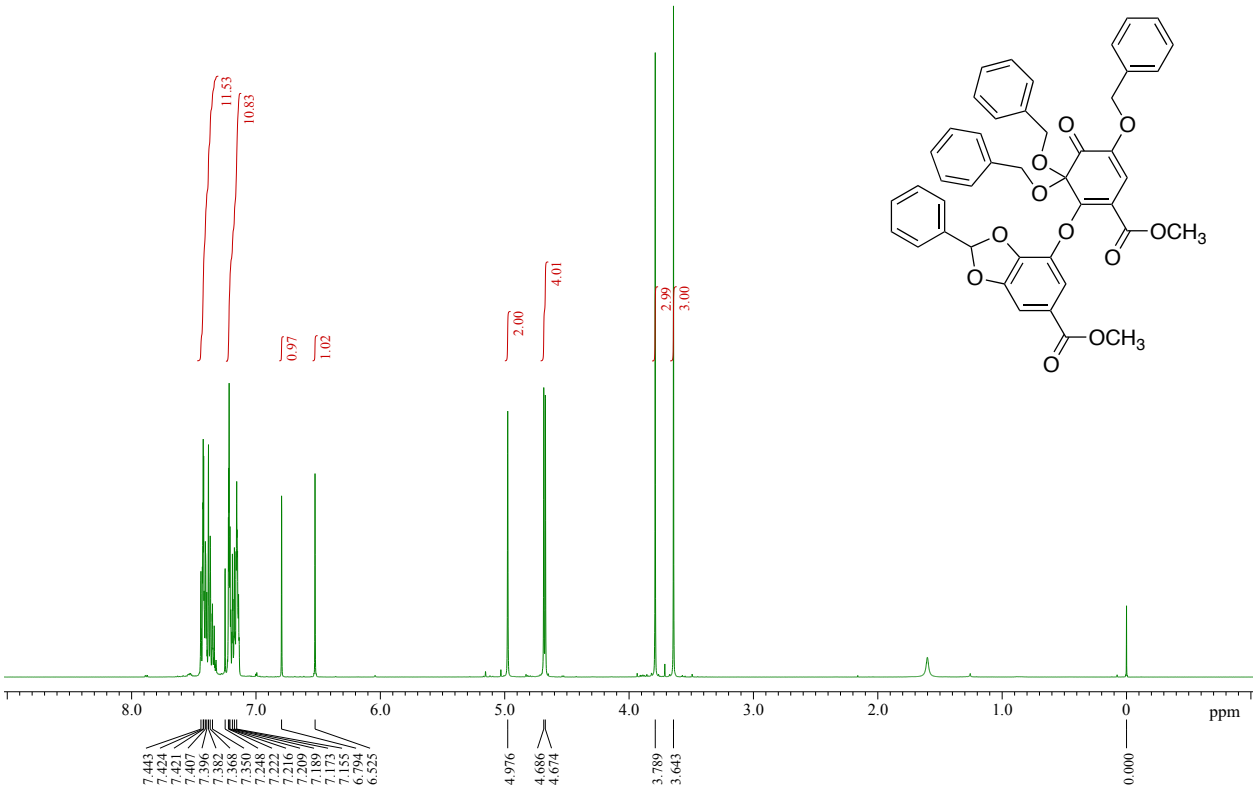



$^{1}H$ NMR (400 MHz, chloroform-*d*, 21 °C) δ 7.46–7.31 (m, 11H, aryl and H-2 or H-6 of G), 7.23–7.13 (m, 11H, aryl and H-2 or H-6 of G), 6.79 (s, 1H, H-9 of G), 6.53 (s, 1H, H-6 of Q), 4.98 (s, 2H, Bn), 4.68 (s, 2H, Bn), 4.67 (s, 2H, Bn), 3.79 (s, 3H, H-8 of G), 3.65 (s, 3H, H-8 of Q).

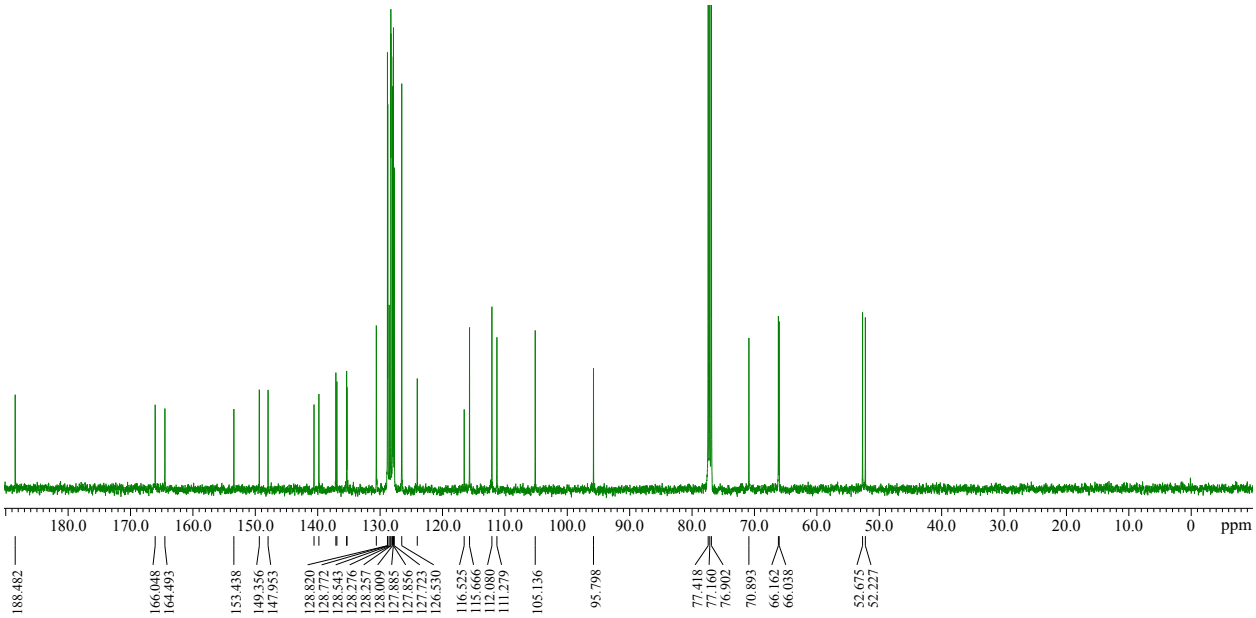
$^{13}C$ NMR (126 MHz, chloroform-*d*, 23 °C, HMQC and HMBC spectra were used for the assignments) δ 188.5 (s, Q4), 166.0 (s, G7), 164.5 (s, Q7), 153.4 (s, Q2), 149.4 (s, G5), 148.0 (s, Q5), 140.6 (s, G4), 139.8 (s, G3), 137.1 (s, Q10 or Q15), 136.9 (s, Q10 or Q15), 135.4 (s, Q20), 135.3 (s, G10), 130.6 (d, G13), 128.82 (d, 2C, Bn), 128.77 (d, 2C, Bn), 128.5 (d, Q23), 128.28 (d, 2C, Bn), 128.26 (d, 2C, Bn), 128.0 (d, 2C, Bn), 127.88 (d, 2C, Q21), 127.86 (d, 2C, Bn), 127.7 (d, 2C, Bn), 126.5 (d, 2C, G11), 124.0 (s, G1), 116.5 (s, Q1), 115.7 (d, G6), 112.1 (d, G9), 111.3 (d, Q6), 105.1 (d, G2), 95.8 (s, Q3), 70.9 (t, Q19), 66.2 (t, Q9 or Q14), 66.0 (t, Q9 or Q14), 52.7 (q, Q8), 52.2 (q, G8).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{44}H_{36}O_{11}Na$ 763.2155, found 763.2135.

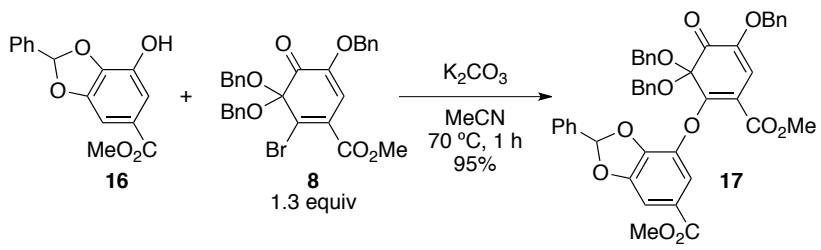
$^{1}$H NMR spectrum of **17**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **17**, 126 MHz in chloroform-*d*

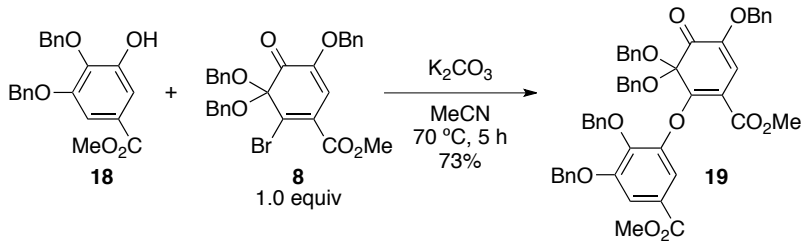


**ESI-8. Synthesis of 17** (The use of 1.3 equiv of **8**)




To a solution of **8** (240 mg, 436 μmol) in acetonitrile (5.0 mL) were added **16** (92.0 mg, 338 μmol) and potassium carbonate (122 mg, 883 μmol) at room temperature. The mixture was stirred for 1 h at 70 ºC. After the mixture was cooled to 0 °C, diethyl ether (10 mL) and 1 M hydrochloric acid (20 mL) were added to the mixture. The aqueous mixture was extracted with diethyl ether. The organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (Silica gel 20 g, hexane/ethyl acetate 20/3 to 4/1) to afford **17** (240 mg, 325 μmol, 95% yield) as a yellow amorphous solid.

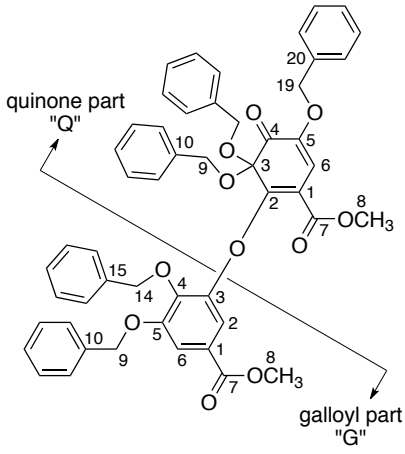
**ESI-9. Synthesis of 19** (The use of 1.0 equiv of **8**)




To a solution of **8** (37.4 mg, 68.1 μmol) in acetonitrile (1.0 mL) were added phenol **18** (24.8 mg, 68.1 μmol) and potassium carbonate (18.8 mg, 136 μmol) at room temperature. The mixture was stirred for 5 h at 70 °C. After the mixture was cooled to room temperature, diethyl ether (3 mL) and 1 M hydrochloric acid (3 mL) were added to the mixture. The aqueous mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 10 g, hexane/ethyl acetate 8/1 to 3/1) to afford **19** (41.3 mg, 49.6 μmol, 73% yield) as a yellow syrup.

Data for **19**

IR (ATR) 3065, 3032, 2949, 2880, 1717, 1643, 1595, 1499, 1454, 1423, 1331, 1213, 1065, 1003, 735, 696 $cm^{-1}$.

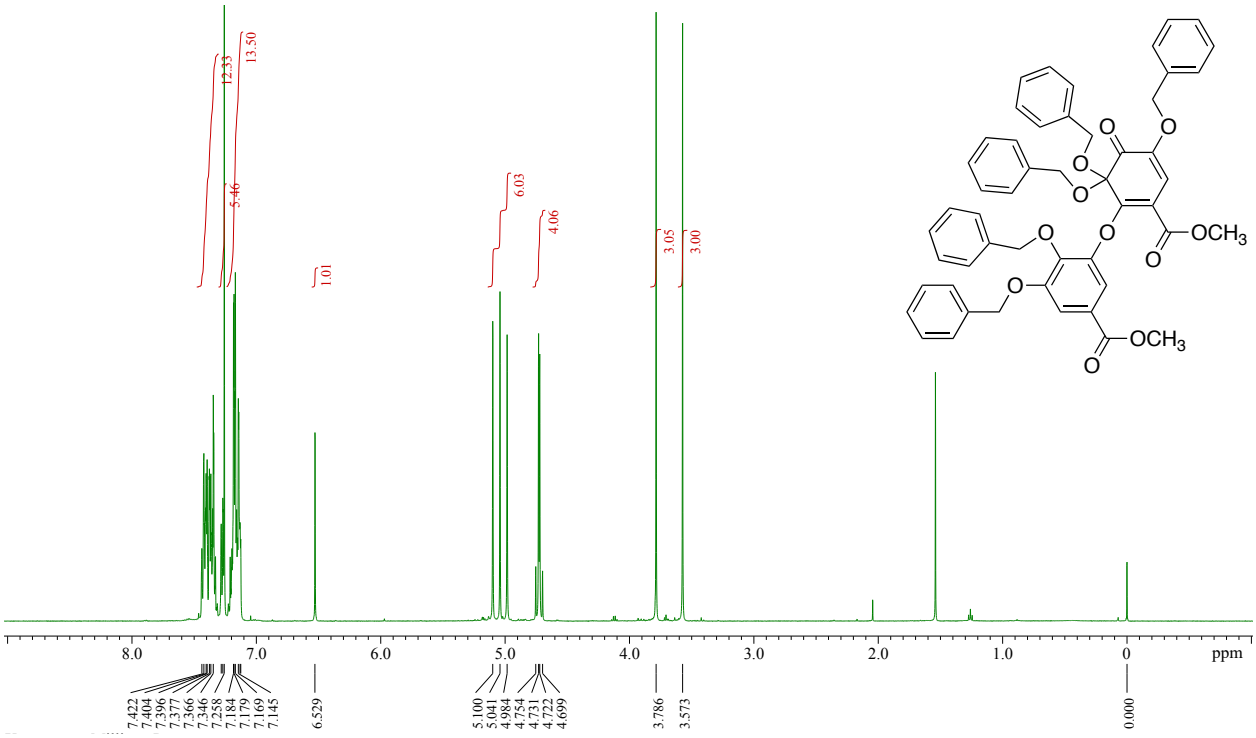



$^{1}H$ NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.44–7.33 (m, 12H, Bn, H-2 of G, H-6 of G), 7.28 (dd, *J* = 7.3, 1.7 Hz, 2H, Bn), 7.21–7.13 (m, 13H, Bn), 6.53 (s, 1H, H-6 of Q), 5.10 (s, 2H, Bn), 5.04 (s, 2H, Bn), 4.98 (s, 2H, Bn), 4.73 (d, *J* = 11.5 Hz, 2H, Bn), 4.69 (d, *J* = 11.5 Hz, 2H, Bn), 3.79 (s, 3H, H-8 of G), 3.57 (s, 3H, H-8 of Q).

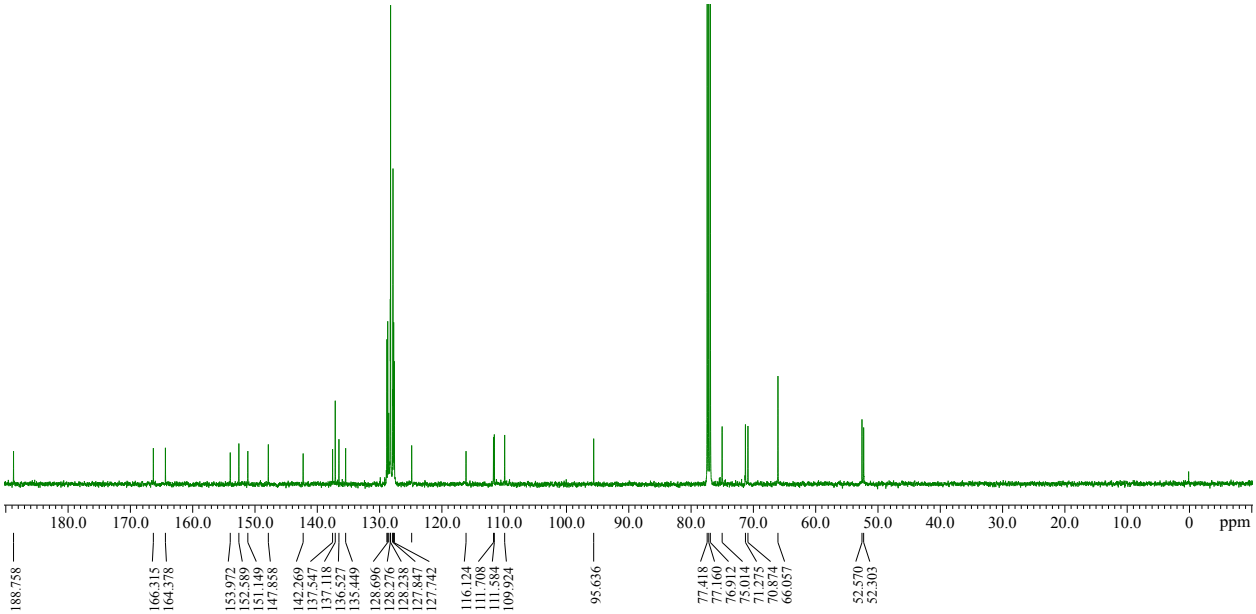
$^{13}C$ NMR (126 MHz, chloroform-*d*, 24 °C, HMQC and HMBC spectra were used for the assignments) δ 188.8 (s, Q4), 166.3 (s, G7), 164.4 (s, Q7), 154.0 (s, Q2), 152.6 (s, G5), 151.1 (s, G3), 147.9 (s, Q5), 142.3 (s, G4), 137.5 (s, G15), 137.1 (s, 2C, Q10), 136.5 (s, G10), 135.4 (s, Q20), 128.8–127.6 (d, overlapped 25 doublets: nine peaks were observed, 25C, Bn), 124.9 (s, G1), 116.1 (s, Q1), 111.7 (d, G2), 111.6 (d, Q6), 109.9 (d, G6), 95.6 (s, Q3), 75.0 (t, G14), 71.3 (t, G9), 70.9 (t, Q19), 66.1 (t, 2C, Q9), 52.6 (q, G8), 52.3 (q, Q8).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{51}H_{44}O_{11}Na$ 855.2781, found 855.2763.

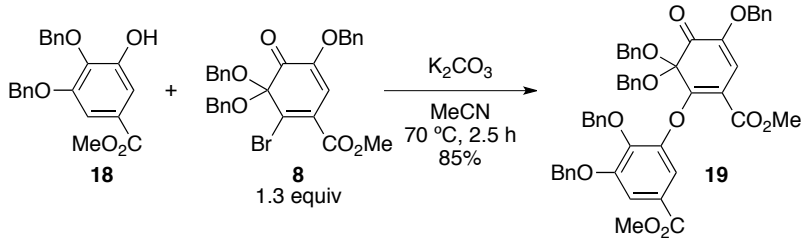
$^{1}$H NMR spectrum of **19**, 500 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **19**, 126 MHz in chloroform-*d*



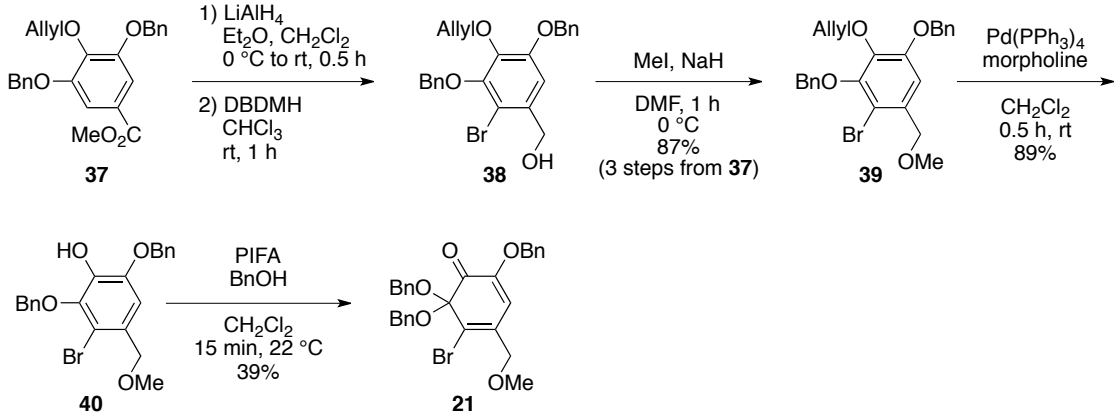
**ESI-10. Synthesis of 19** (The use of 1.3 equiv of **8**)



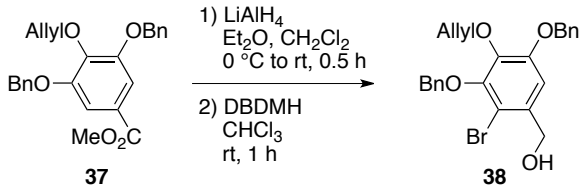

To a solution of **8** (97.0 mg, 177 μmol) in acetonitrile (1.0 mL) were added **18** (49.5 mg, 136 μmol) and potassium carbonate (37.6 mg, 272 μmol) at room temperature. The mixture was stirred for 2.5 h at 70 °C. After the mixture was cooled to room temperature, diethyl ether (3 mL) and 1 M hydrochloric acid (3 mL) were added to the mixture. The aqueous mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 15 g, hexane/ethyl acetate 8/1 to 4/1) to afford **19** (96.3 mg, 115 μmol, 85% yield) as a yellow syrup.

**ESI-11. Overview of synthesis of 21**

The "keto-ether" **21** was synthesized from **37**[21] in five steps. Reduction of **37** and subsequent bromination by DBDMH provided **38**, which was methylated using sodium hydride and methyl iodide to give **39** in 87% yield from **37**. Tetrakis(triphenylphosphine)palladium(0) catalyzed deallylation of **39** gave phenol **40**, oxidation of which using PIFA in the presence of BnOH produced desired **21**.



**ESI-12. Synthesis of 38**



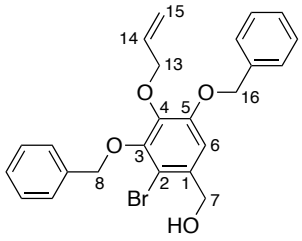

To a solution of **37** (1.00 g, 2.47 mmol) in diethyl ether (25 mL) and dichloromethane (5 mL) was added of lithium aluminum hydride (47.0 mg, 1.24 mmol) at 0 °C. The mixture was stirred for 0.5 h at 0 °C. To the mixture was added further lithium aluminum hydride (47.0 mg, 1.24 mmol) at 0 °C. The mixture was stirred for additional 0.5 h at 24 °C. To the mixture was added sodium sulphate decahydrate (3.0 g). The mixture was stirred for additional 30 min at 24 °C. The mixture was filtered through a cotton-Celite pad to remove aluminum salts and wet sodium sulphate. The filtrate was concentrated to give the corresponding primary alcohol, which was used without further purification.

To a solution of crude product of the above reaction in chloroform (50 mL) was added 1,3-dibromo-5,5-dimethylhydantoin (355 mg, 1.24 mmol) at 23 °C. The mixture was stirred for 1 h at 23 °C. Addition of 10% aqueous sodium thiosulfate (20 mL) quenched the reaction. The reaction mixture was extracted with chloroform. After the general drying procedure, the obtained crude product, the main content of which was **38**, was used without further purification.

Data for **38**

IR (ATR) 3600–3120, 3063, 3032, 2870, 1570, 1497, 1476, 1455, 1418, 1385, 1327, 1173, 1098, 984, 931, 841, 748, 698 $cm^{-1}$.

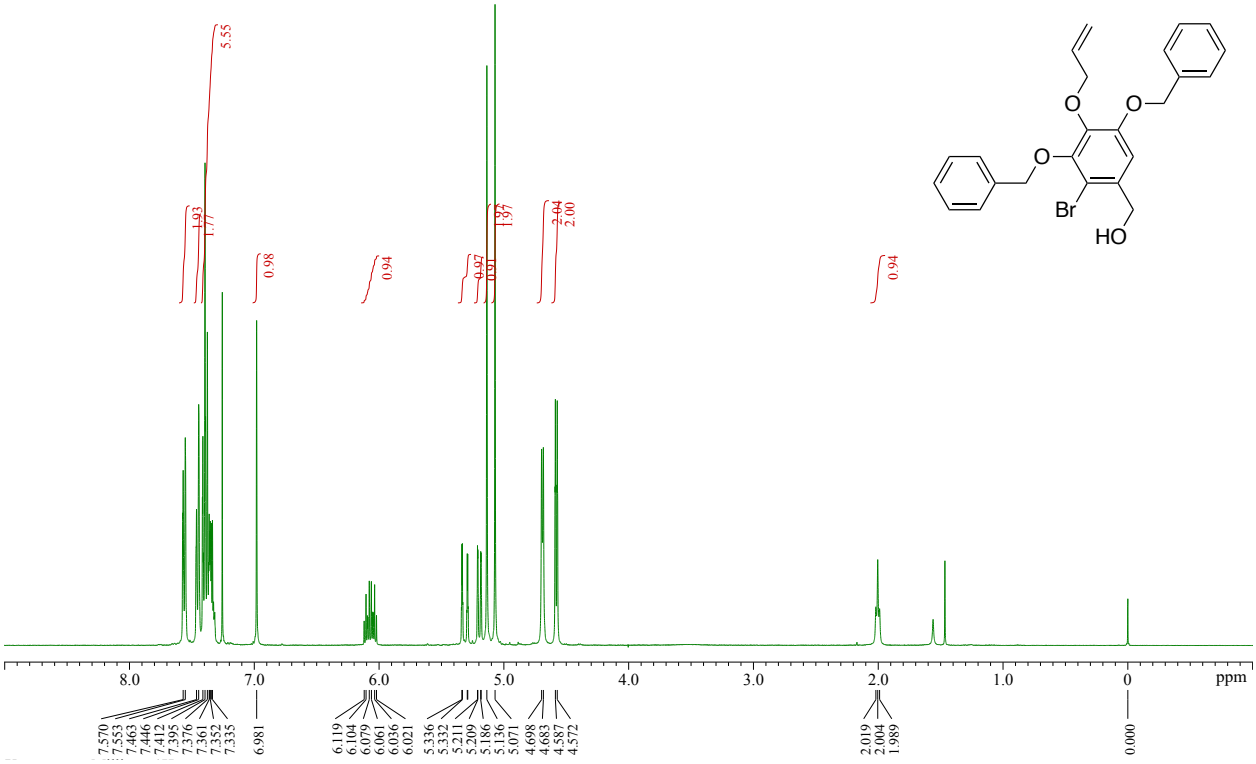
$^1H$ NMR (400 MHz, chloroform-*d*, 21 °C) δ 7.58–7.54 (m, 2H, Bn), 7.47–7.44 (m, 2H, Bn), 7.42–7.31 (m, 6H, Bn), 6.98 (s, 1H, H-6), 6.06 (ddt, *J* = 17.2, 10.3, 6.0 Hz, 1H, H-14), 5.31 (ddt, *J* = 17.2, 1.5, 1.0 Hz, 1H, H-15), 5.20 (ddt, *J* = 10.3, 1.5, 1.1 Hz, 1H, H-15), 5.14 (s, 2H, H-8 or H-16), 5.07 (s, 2H, H-8 or H-16), 4.69 (d, *J* = 6.0 Hz, 2H, H-7), 4.58 (ddd, *J* = 6.0, 1.1, 1.0 Hz, 2H, H-13), 2.00 (t, *J* = 6.0 Hz, 1H, OH).



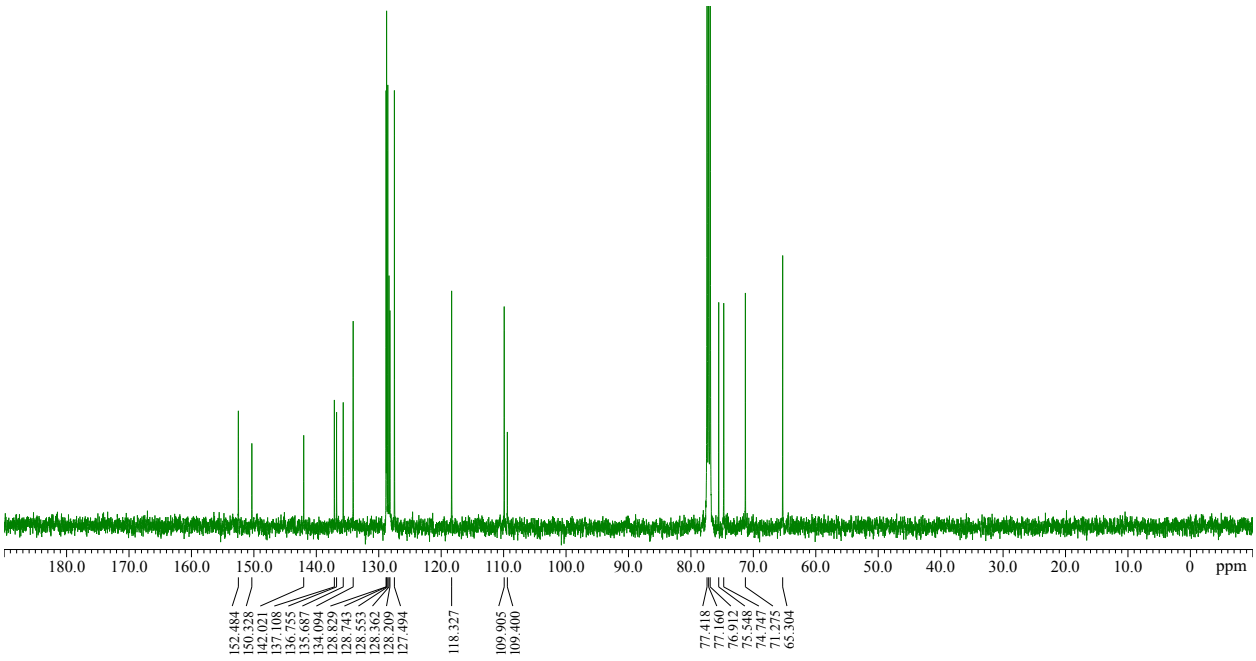

$^{13}C$ NMR (126 MHz, chloroform-*d*, 24 °C) δ 152.5 (s, C-3 or C-5), 150.3 (s, C-3 or C-5), 142.0 (s, C-4), 137.1 (s, Bn), 136.8 (s, Bn), 135.7 (s, C-1), 134.1 (d, C-14), 128.8 (d, 2C, Bn), 128.7 (d, 2C, Bn), 128.6 (d, 2C, Bn), 128.4 (d, Bn), 128.2 (d, Bn), 127.5 (d, 2C, Bn), 118.3 (t, C-15), 109.9 (d, C-6), 109.4 (s, C-2), 75.5 (t, C-8 or C-16), 74.7 (t, C-13), 71.3 (t, C-8 or C-16), 65.3 (t, C-7).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{24}H_{23}O_4BrNa$ 477.06774, found 477.0672.

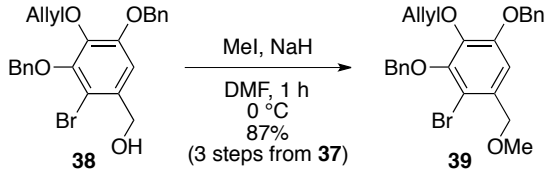
$^{1}$H NMR spectrum of **38**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **38**, 126 MHz in chloroform-*d*



**ESI-13. Synthesis of 39**




To a solution of crude **38** in DMF (25 mL) were added methyl iodide (526 mg, 3.71 mmol) and sodium hydride (60% in mineral oil, 150 mg, 89.0 mg as NaH, 3.71 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C. To the reaction mixture were added diethyl ether (30 mL) and 1 M hydrochloric acid (40 mL). The aqueous mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 20 g, hexane/ethyl acetate 9/1) to afford **39** (1.00 g, 2.13 mmol, 87% yield in 3 steps) as a colourless syrup.

Data for **39**

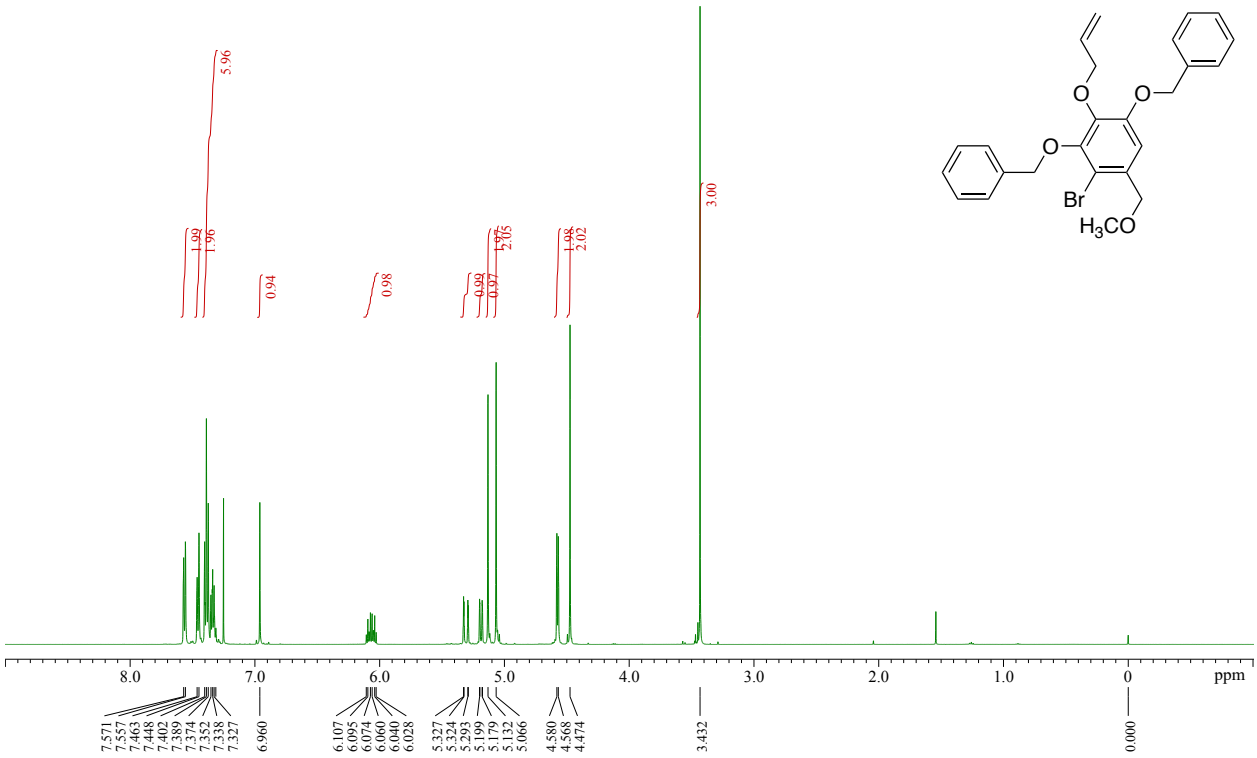
IR (ATR) 3065, 3032, 2984, 2928, 2868, 2822, 1570, 1454, 1418, 1369, 1327, 1177, 1098, 984, 737, 696 $cm^{-1}$.

$^{1}H$ NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.56 (br d, *J* = 6.9 Hz, 2H, Bn), 7.46 (br d, *J* = 7.5 Hz, 2H, Bn), 7.40–7.37 (m, 4H, Bn), 7.35–7.31 (m, 2H, Bn), 6.96 (s, 1H, aryl), 6.07 (ddt, *J* = 17.2, 10.3, 5.7 Hz, 1H, allyl), 5.31 (ddt, *J* = 17.2, 1.7, 1.7 Hz, 1H, allyl), 5.19 (ddt, *J* = 10.3, 1.7, 1.2 Hz, 1H, allyl), 5.13 (s, 2H, Bn), 5.07 (s, 2H, Bn), 4.57 (ddd, *J* = 5.7, 1.7, 1.2 Hz, 2H, allyl), 4.47 (s, 2H, -$CH_2O$-), 3.43 (s, 3H, OMe).

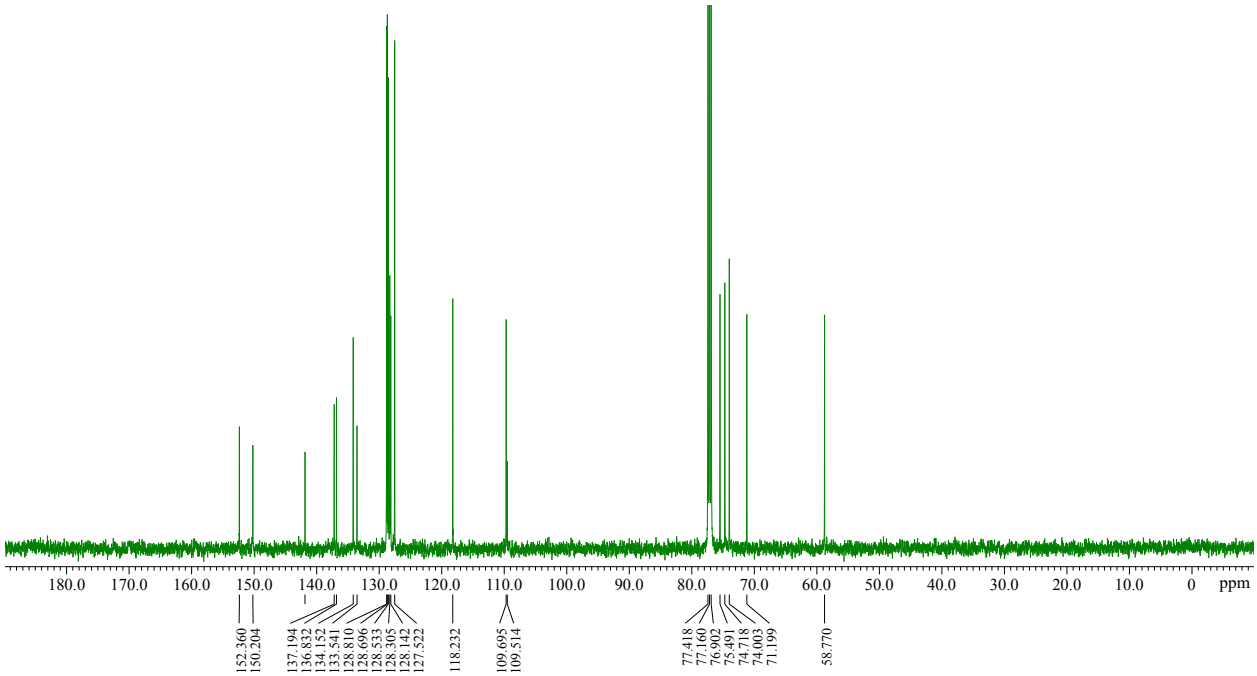
$^{13}C$ NMR (126 MHz, chloroform-*d*, 23 °C) δ 152.4 (s, aryl), 150.2 (s, aryl), 141.9 (s, aryl), 137.2 (s, Bn), 136.8 (s, Bn), 134.2 (d, allyl), 133.5 (s, aryl), 128.8 (d, 2C, Bn), 128.7 (d, 2C, Bn), 128.5 (d, 2C, Bn), 128.3 (d, Bn), 128.1 (d, Bn), 127.5 (d, 2C, Bn), 118.2 (t, allyl), 109.7 (d, aryl), 109.5 (s, aryl), 75.5 (t, Bn), 74.7 (t, allyl), 74.0 (t, -$CH_2O$-), 71.2 (t, Bn), 58.8 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{25}O_4BrNa$ 491.0834, found 491.0822.

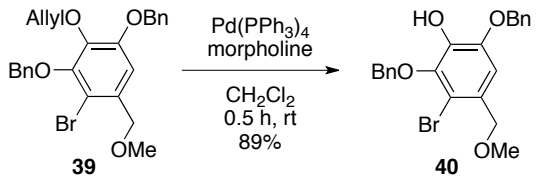
$^{1}$H NMR spectrum of **39**, 500 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **39**, 126 MHz in chloroform-*d*



**ESI-14. Synthesis of 40**




To a solution of **39** (821 mg, 1.75 mmol) in dichloromethane (15 mL) were added morpholine (305 mg, 3.50 mmol) and tetrakis(triphenylphosphine)palladium (40.0 mg, 34.6 μmol) at 22 °C. The mixture was stirred for 0.5 h at 22 °C. To the reaction mixture were added dichloromethane (10 mL) and 1 M hydrochloric acid (20 mL). The reaction mixture was extracted with $CHCl_3$. After the general drying procedure, the mixture was purified by column chromatography (silica gel 20 g, hexane/ethyl acetate 10/1 to 8/1) to afford **40** (669 mg, 1.56 mmol, 89% yield) as a colourless solid.

Data for **40**

mp 73.3–74.0 °C.

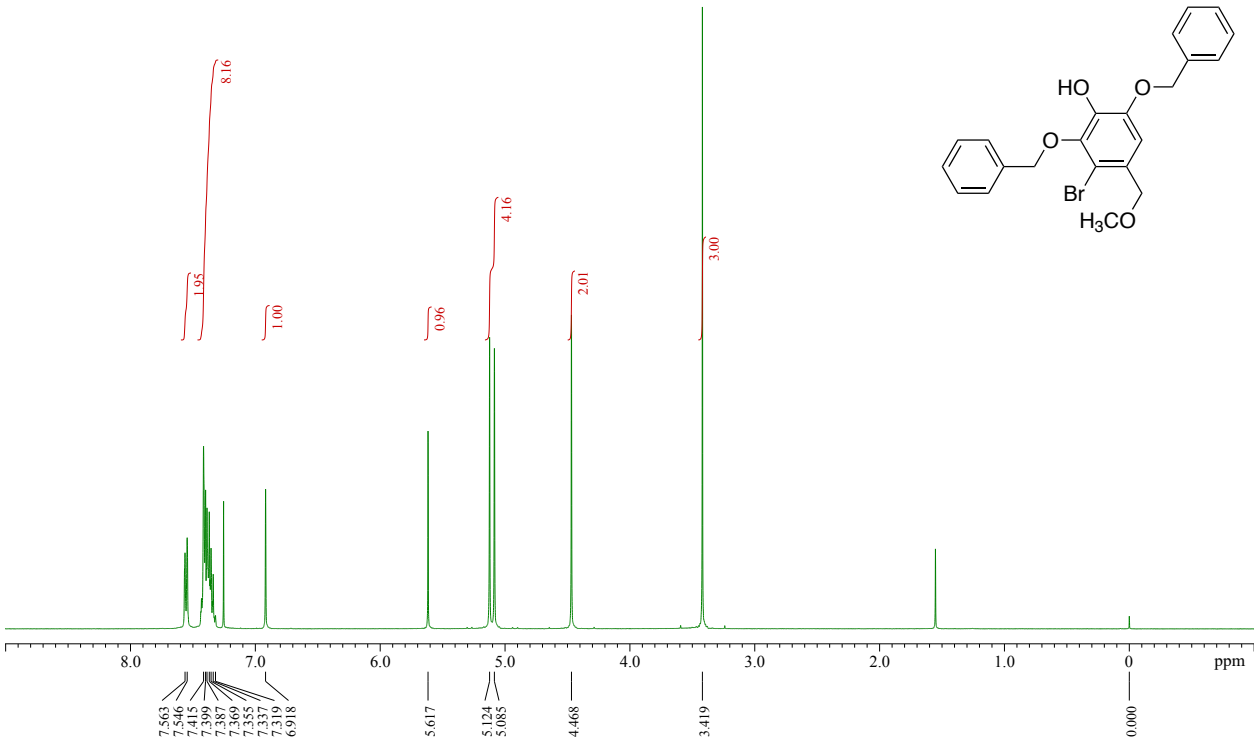
IR (ATR) 3550–3130, 3032, 2930, 2876, 2822, 1595, 1493, 1454, 1423, 1373, 1306, 1173, 1086, 1074, 1028, 907, 841, 735, 696 $cm^{-1}$.

$^1H$ NMR (400 MHz, chloroform-*d*, 21 °C) δ 7.56 (d, *J* = 7.1 Hz, 2H, Bn), 7.41–7.34 (m, 8H, Bn), 6.92 (s, 1H, aryl), 5.61 (s, 1H, OH), 5.12 (s, 2H, Bn), 5.09 (s, 2H, Bn), 4.47 (s, 2H, -$CH_2$O-), 3.42 (s, 3H, OMe).

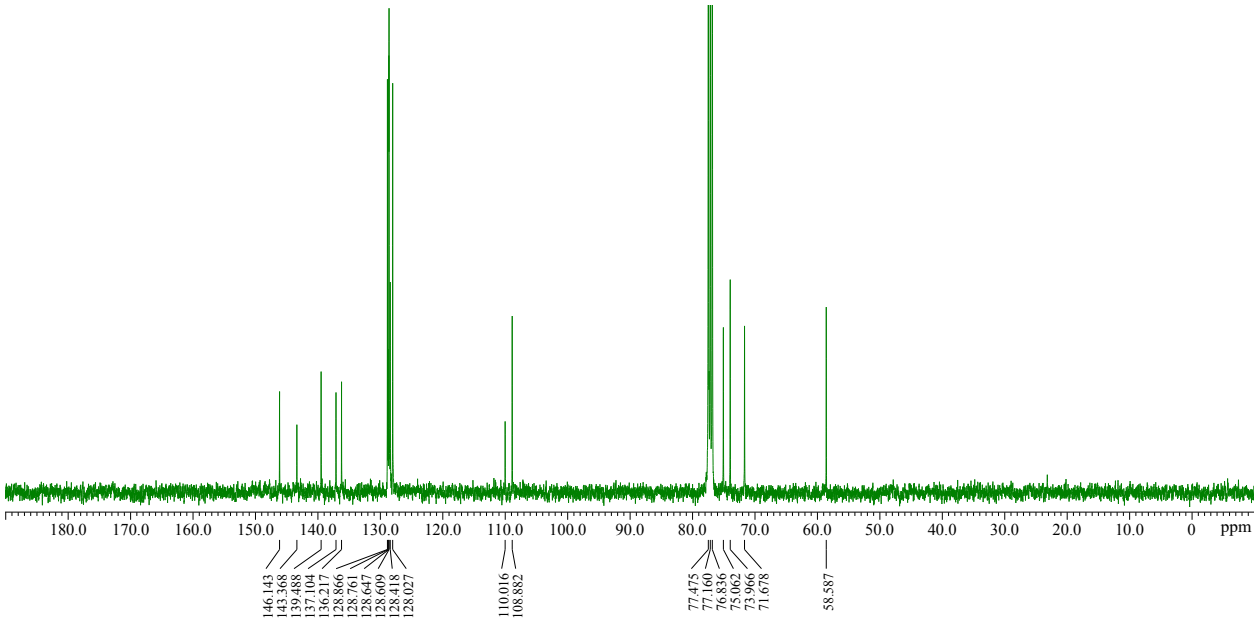
$^{13}C$ NMR (101 MHz, chloroform-*d*, 22 °C) δ 146.1 (s, aryl), 143.4 (s, aryl), 139.5 (s, aryl), 137.1 (s, Bn), 136.2 (s, Bn), 128.9 (d, 2C, Bn), 128.8 (s, aryl), 128.6 (d, 2C, Bn), 128.6 (d, 2C, Bn), 128.6 (d, Bn), 128.4 (d, Bn), 128.0 (d, 2C, Bn), 110.0 (s, aryl), 108.9 (d, aryl), 75.1 (t, Bn), 74.0 (t, -$CH_2$O-), 71.7 (t, Bn), 58.6 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{22}H_{21}O_4BrNa$ 451.0521, found 451.0515.

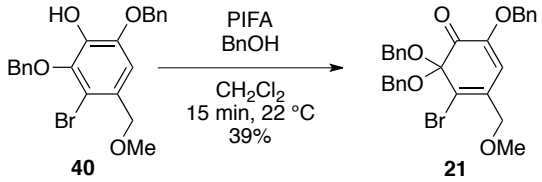
$^{1}$H NMR spectrum of **40**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **40**, 101 MHz in chloroform-*d*



**ESI-15. Synthesis of 21**



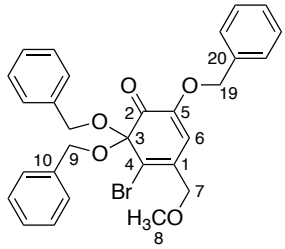

To a solution of **40** (90.0 mg, 210 μmol) in dichloromethane (2.0 mL) were added benzyl alcohol (250 μL) and phenyliodine bis(trifluoroacetate) (108 mg, 251 μmol) at 22 °C. The mixture was stirred for 15 min at 22 °C. Addition of dichloromethane (5 mL) and 10% aqueous sodium thiosulfate (5 mL) quenched the reaction. The reaction mixture was extracted with dichloromethane. After the general drying procedure, the crude product was purified by successive column chromatography (silica gel 10 g, toluene; followed by silica gel 10 g, hexane/toluene 8/1 to 4/1; and finally silica gel 10 g, toluene) to afford **21** (40.9 mg, 76.4 μmol, 39% yield) as a yellow syrup.

Data for **21**

IR (ATR) 3062, 3032, 2930, 2874, 1694, 1643, 1580, 1497, 1454, 1364, 1296, 1184, 1130, 1067, 1028, 910, 854, 737, 698 $cm^{-1}$.

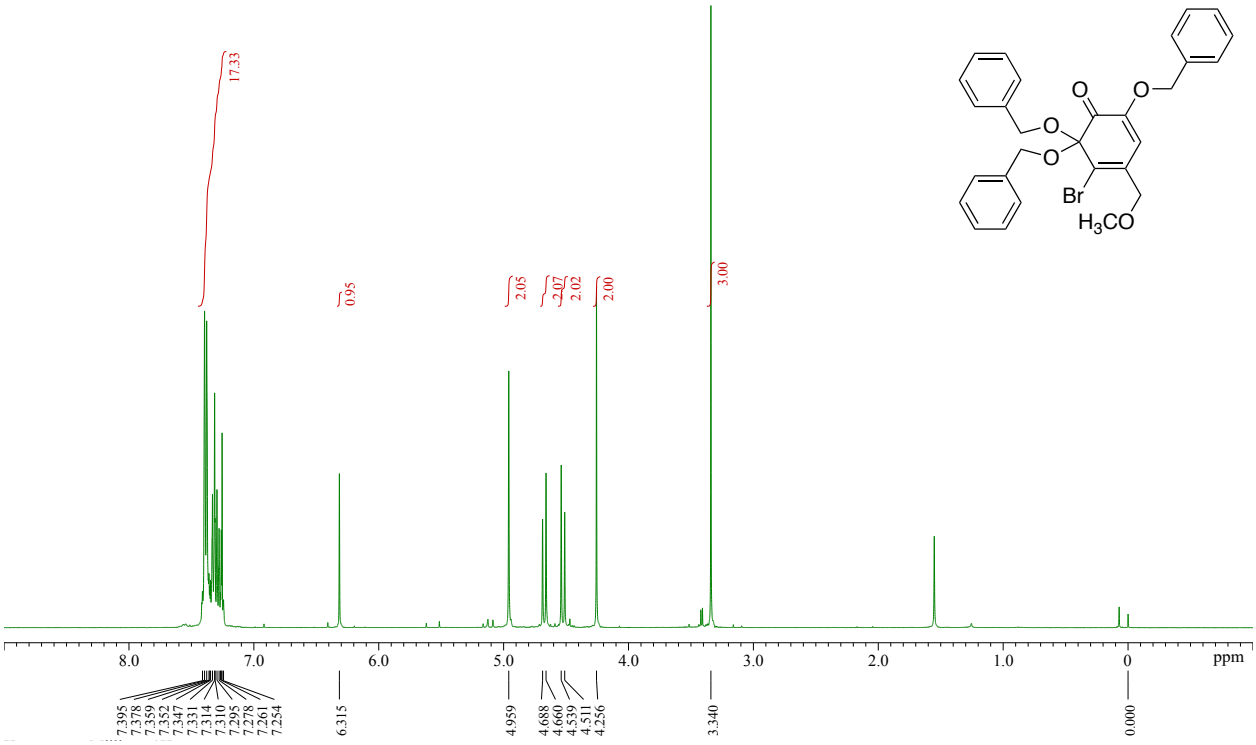
$^{1}H$ NMR (400 MHz, chloroform-*d*, 24 °C) δ 7.42–7.35 (m, 6H, Bn), 7.33–7.25 (m, 9H, Bn), 6.32 (s, 1H, H-6), 4.96 (s, 2H, Bn), 4.67 (d, *J* = 11.2 Hz, 2H, Bn), 4.53 (d, *J* = 11.2 Hz, 2H, Bn), 4.26 (s, 2H, H-7), 3.34 (s, 3H, H-8).

$^{13}C$ NMR (126 MHz, chloroform-*d*, 24 °C, HMQC and HMBC spectra were used for the assignments) δ 190.7 (s, C-2), 149.6 (s, C-5), 137.3 (s, 2C, C-10), 135.3 (s, C-20), 135.0 (s, C-1), 128.8 (d, 2C, Bn), 128.6 (d, Bn), 128.4 (d, 4C, Bn), 128.1 (d, 4C, Bn), 127.8 (d, 2C, Bn), 127.8 (d, 2C, Bn), 121.7 (s, C-4), 112.4 (d, C-6), 94.8 (s, C-3), 73.1 (t, C-7), 70.8 (t, C-19), 65.6 (t, 2C, C-9), 58.5 (q, C-8).

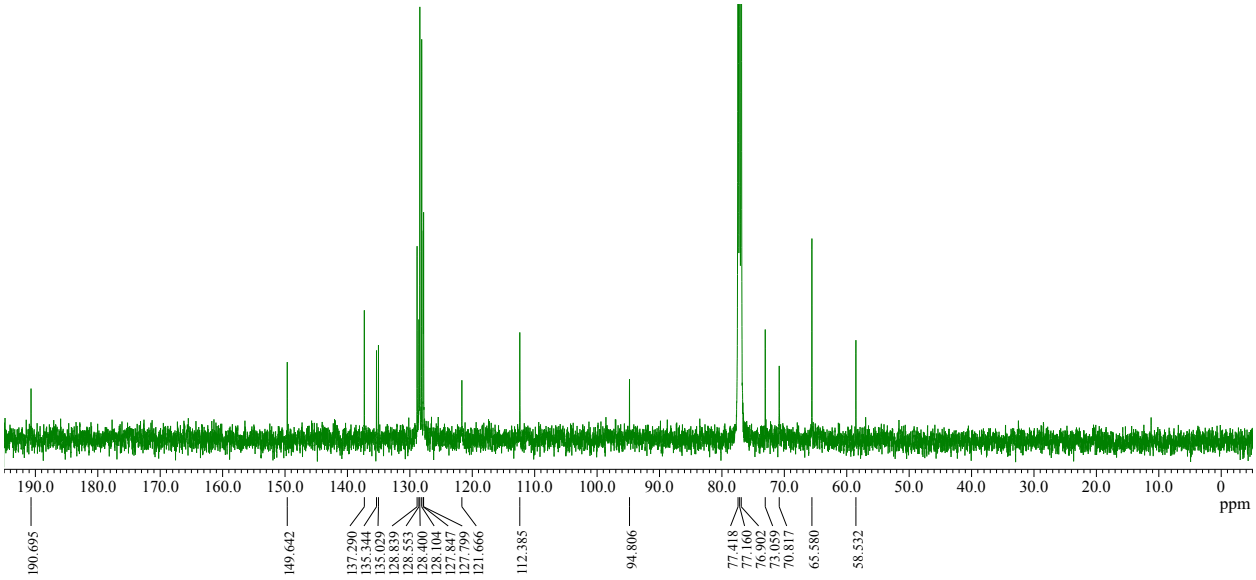



HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{29}H_{27}BrO_5Na$ 557.09340, found 557.0924.

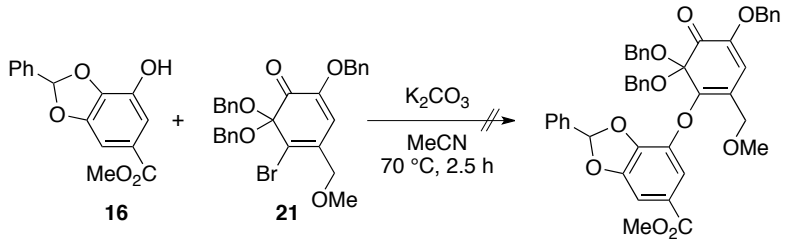
$^{1}$H NMR spectrum of **21**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **21**, 126 MHz in chloroform-*d*



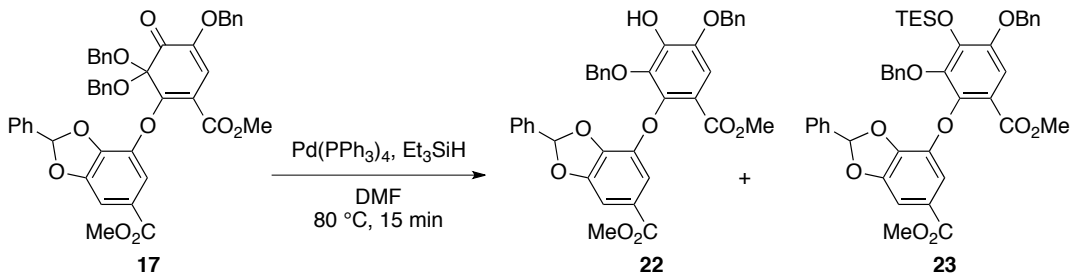
**ESI-16. An attempt of *oxa*-addition to 21**




To a solution of **21** (40.0 mg, 74.7 μmol) in MeCN (1.0 mL) were added phenol **16** (16.0 mg, 58.8 μmol) and potassium carbonate (12.0 mg, 86.8 μmol) at room temperature. The mixture was stirred for 2.5 h at 70 ºC. The reaction was monitored by TLC (hexane/EtOAc = 3/1) and LRMS-ESI, but the desired coupled compound was not obtained.

**Experiments for Table 1**

**ESI-17. Synthesis of 22 and 23** (Table 1, Entry 1)




A trial that marked the best yield of **22** when $Pd(PPh_3)_4$ and $Et_3SiH$ were used.

To a solution of **17** (53.3 mg, 72.0 μmol) in DMF (1.0 mL) were added tetrakis(triphenylphosphine)palladium (10.2 mg, 8.83 μmol) and triethylsilane (21.8 mg, 181 μmol) at room temperature. The mixture was stirred for 15 min at 80 °C. After the mixture was cooled to 0 °C, addition of diethyl ether (10 mL) and 1 M hydrochloric acid (10 mL) quenched the reaction. The aqueous mixture was extracted with diethyl ether. The organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 7/1 to 3/1) to afford **22** (rf 0.35 with hexane/ethyl acetate 2/1, 37.9 mg, 56.7 μmol, 83% yield) as a colourless amorphous solid and almost pure **23**. The almost pure **23** was further purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 7/1) to afford **23** (rf 0.59 with hexane/ethyl acetate 2/1, 9.20 mg, 12.3 μmol, 17% yield) as a colourless syrup.

A trial that marked the worst yield of **22** when $Pd(PPh_3)_4$ and $Et_3SiH$ were used.

To a solution of **17** (52.0 mg, 70.2 μmol) in DMF (1.0 mL) were added tetrakis(triphenylphosphine)palladium (2.00 mg, 1.73 μmol) and triethylsilane (16.0 mg, 138 μmol) at room temperature. The mixture was stirred for 10 min at 80 °C. After the mixture was cooled to room temperature, addition of diethyl ether (5 mL) and 1 M hydrochloric acid (3 mL) quenched the reaction. The aqueous mixture was extracted with diethyl ether. The organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (silica gel 10 g, hexane/ethyl acetate 7/1 to 4/1) to afford **23** (rf 0.61 hexane/ethyl acetate 2/1, 31.4 mg, 41.9 μmol, 60% yield) as a colourless syrup and **22** (rf 0.29 hexane/ethyl acetate 2/1, 16.4 mg, 25.9 μmol, 37% yield) as a colourless amorphous solid.

Data for **22**

mp 177.1–179.5 °C.

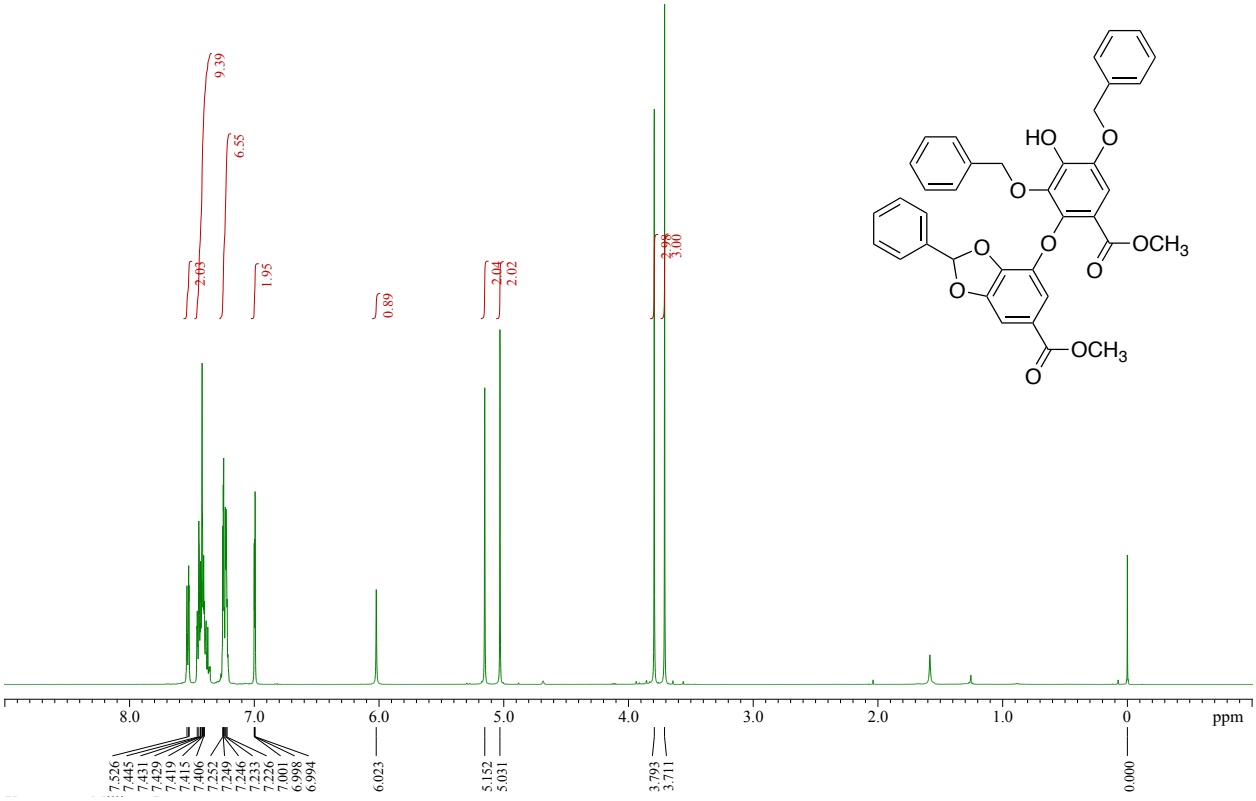
IR (ATR) 3550–3150, 3067, 3032, 2951, 1717, 1634, 1501, 1437, 1362, 1308, 1217, 1080, 758, 696 $cm^{-1}$.

$^{1}$H NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.55–7.52 (m, 2H, aryl), 7.47–7.35 (m, 9H, aryl and DHDG), 7.26–7.20 (m, 6H, aryl and DHDG), 7.00 (d, *J* = 1.2 Hz, 1H, DHDG), 6.99 (s, 1H, benzylidene), 6.02 (s, 1H, OH), 5.15 (s, 2H, Bn), 5.03 (s, 2H, Bn), 3.79 (s, 3H, OMe), 3.71 (s, 3H, OMe).

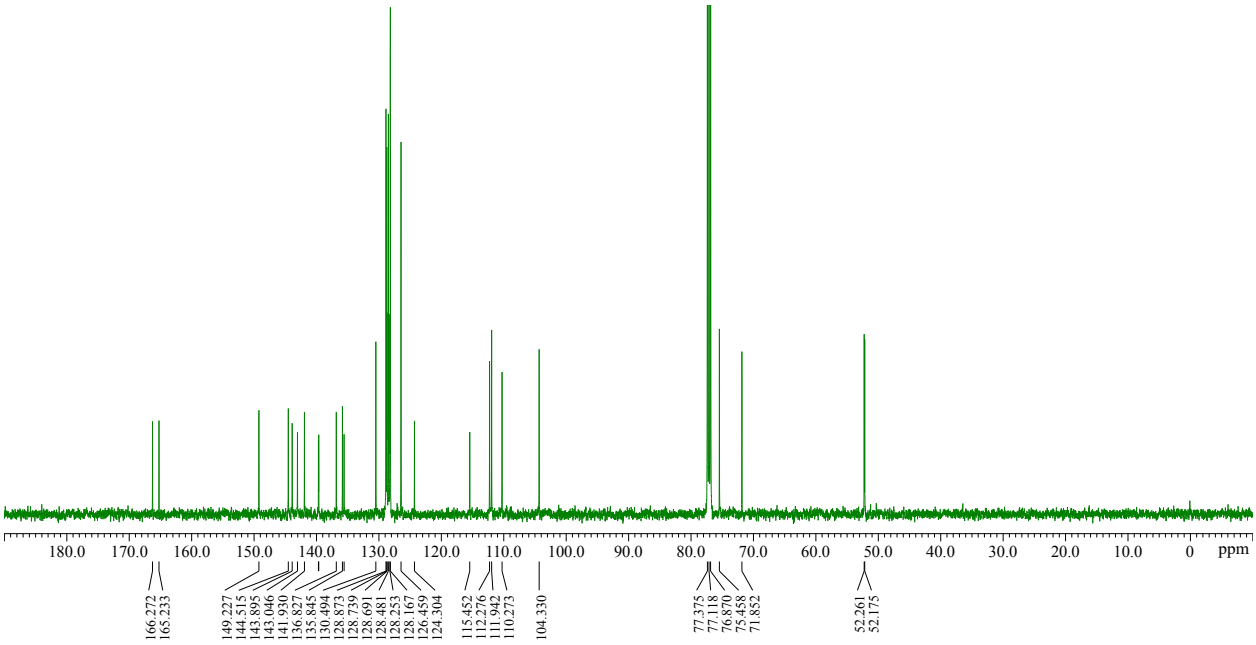
$^{13}$C NMR (126 MHz, chloroform-*d*, 23 °C) δ 166.3 (s, ester), 165.3 (s, ester), 149.3 (s, DHDG), 144.6 (s, DHDG), 143.9 (s, DHDG), 143.1 (s, DHDG), 142.0 (s, DHDG), 139.73 (s, DHDG), 139.68 (s, DHDG), 136.9 (s, aryl), 135.9 (s, aryl), 135.6 (s, aryl), 130.5 (d, aryl), 128.9 (d, 2C, aryl), 128.8 (d, 2C, aryl), 128.7 (d, aryl), 128.5 (d, 2C, aryl), 128.3 (d, aryl), 128.2 (d, 4C, aryl), 126.5 (d, 2C, aryl), 124.3 (s, DHDG), 115.5 (s, DHDG), 112.3 (d, DHDG), 112.0 (d, DHDG), 110.3 (d, benzylidene), 104.4 (d, DHDG), 75.5 (t, Bn), 71.9 (t, Bn), 52.3 (q, OMe), 52.2 (q, OMe).

HRMS (ESI) *m/z* [M + Na]$^{+}$ calcd for $C_{37}H_{30}O_{10}Na$ 657.1737, found 657.1725.

$^{1}$H NMR spectrum of **22**, 500 MHz in chloroform-*d*



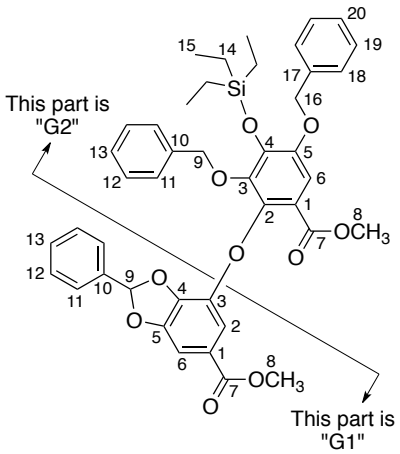
$^{13}$C NMR spectrum of **22**, 126 MHz in chloroform-*d*




Data for **23**

IR (ATR) 2953, 2876, 1719, 1634, 1499, 1435, 1356, 1308, 1219, 1086, 1016, 746, 696 cm$^{-1}$.

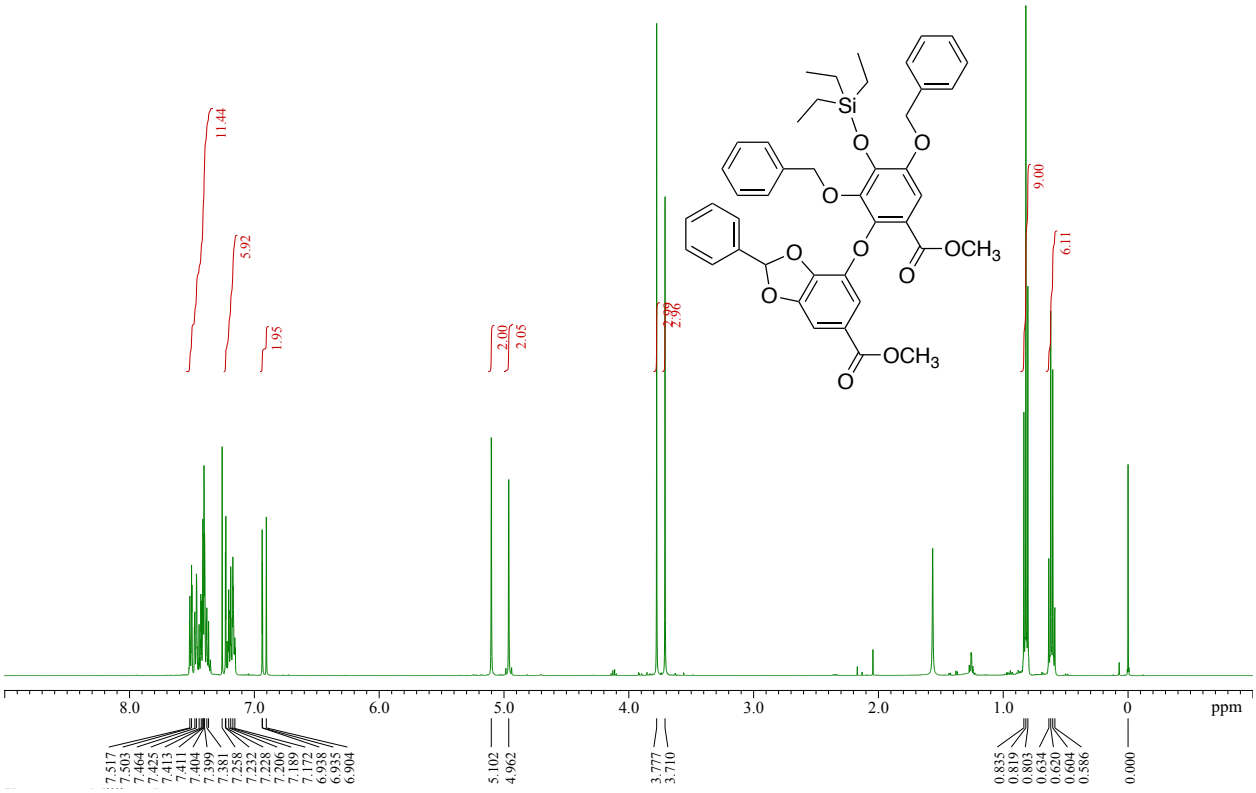
$^{1}$H NMR (500 MHz, chloroform-*d*, 23 °C, HMQC and HMBC spectra were used for the assignments) δ 7.52–7.49 (m, 2H, aryl), 7.47–7.37 (m, 9H, aryl and H-6 of G2), 7.23 (d, *J* = 1.2 Hz, 1H, H-6 of G1), 7.22–7.15 (m, 5H, aryl), 6.94 (d, *J* = 1.2 Hz, 1H, H-2 of G1), 6.90 (s, 1H, H-9 of G1), 5.10 (s, 2H, H-16 of G2), 4.96 (s, 2H, H-9 of G2), 3.78 (s, 3H, H-8 of G2), 3.71 (s, 3H, H-8 of G1), 0.82 (t, *J* = 8.0 Hz, 9H, H-15 of G2), 0.61 (q, *J* = 8.0 Hz, 6H, H-14 of G2).



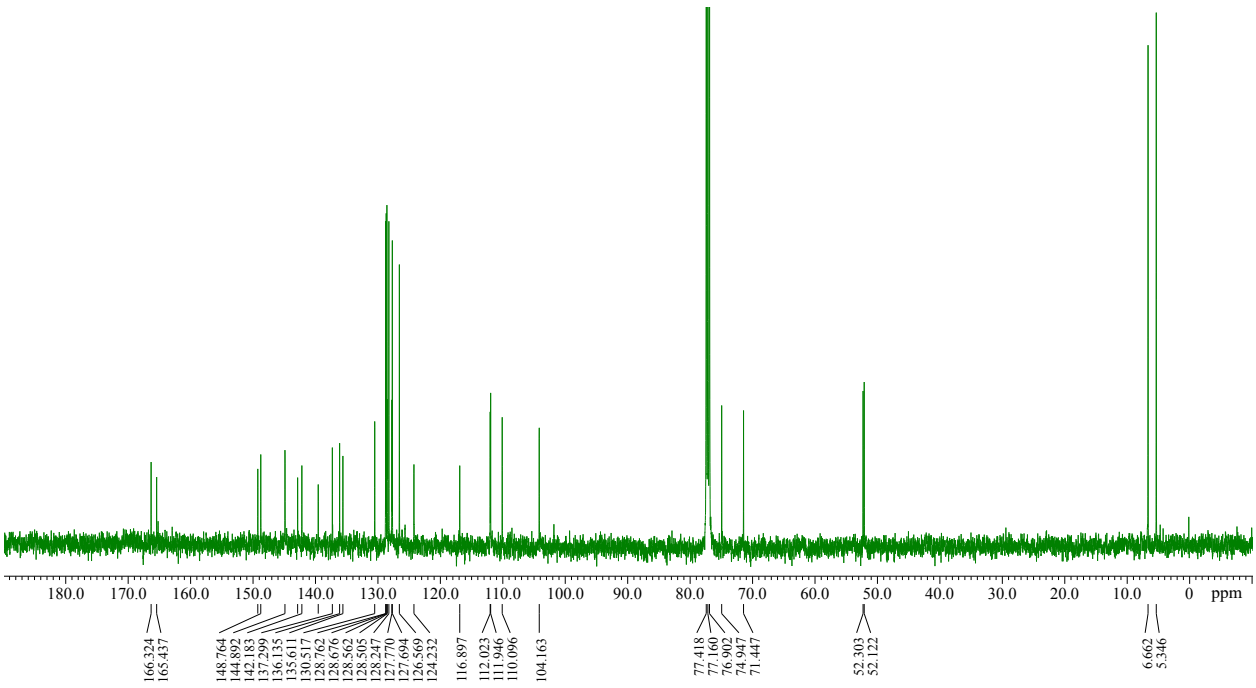

$^{13}$C NMR (126 MHz, chloroform-*d*, 23 °C, HMQC and HMBC spectra were used for the assignments) δ 166.3 (s, G1-7), 165.4 (s, G2-7), 149.2 (s, G2-3), 148.8 (s, G2-5), 144.9 (s, 2C, G2-2 and G1-5), 142.9 (s, G2-4), 142.2 (s, G1-3), 139.6 (s, G1-4), 137.3 (s, G2-10), 136.1(s, G2-17), 135.6 (s, G1-10), 130.5 (d, G1-13), 128.8 (d, 2C, aryl), 128.7 (d, 2C, G2-18), 128.6 (d, 2C, aryl), 128.5 (d, aryl), 128.2 (d, 2C, aryl), 127.8 (d, aryl), 127.7 (d, 2C, G2-11), 126.6 (d, 2C, G1-11), 124.2 (s, G1-1), 116.9 (s, G2-1), 112.0 (d, G1-2), 111.9 (d, G1-9), 110.1 (d, G2-6), 104.2 (d, G1-6), 74.9 (t, G2-9), 71.4 (t, G2-16), 52.3 (q, G1-8), 52.1 (q, G2-8), 6.7 (q, 3C, G2-15), 5.3 (t, 3C, G2-14).

HRMS (ESI) *m/z* [M + Na]$^{+}$ calcd for $C_{43}H_{44}O_{10}SiNa$ 771.2601, found 771.2589.

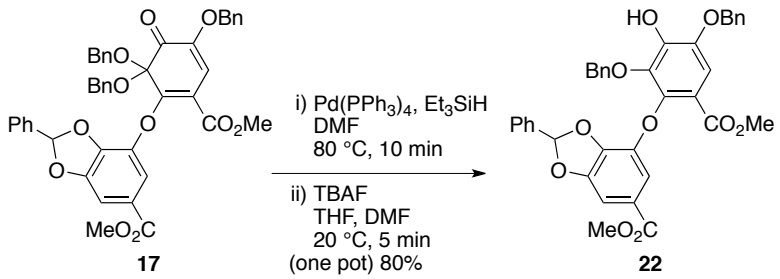
$^{1}$H NMR spectrum of **23**, 500 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **23**, 126 MHz in chloroform-*d*

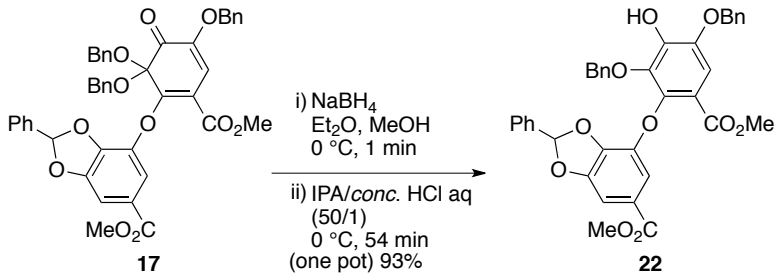


**ESI-18. Synthesis of 22** (Table 1, Entry 2)



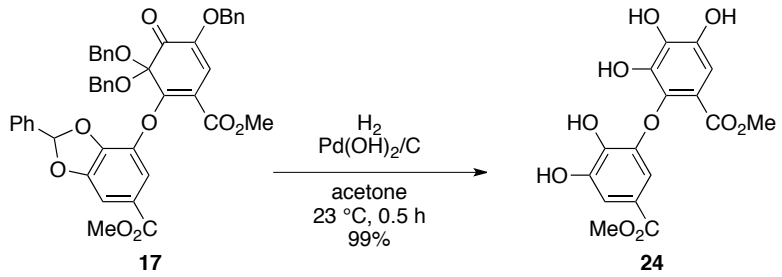

To a solution of **17** (29.0 mg, 39.1 μmol) in DMF (0.5 mL) were added tetrakis(triphenylphosphine)palladium (1.00 mg, 865 nmol) and triethylsilane (9.10 mg, 78.3 μmol) at room temperature. The mixture was stirred for 10 min at 80 °C. The production of **22** and silylated **23** was observed by monitoring TLC (hexane/ethyl acetate 2/1). After the mixture was cooled to 20 °C, the reaction mixture was added TBAF (1.0 mol/L in THF, 39.0 μL, 39.0 μmol) and stirred for 5 min at 20 °C. Addition of diethyl ether (3 mL) and 1 M hydrochloric acid (3 mL) quenched the reaction. The aqueous mixture was extracted with diethyl ether. The organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 4/1) to afford **22** (19.7 mg, 31.1 μmol, 80% yield) as a colourless solid.

**ESI-19. Synthesis of 22** (Table 1, Entry 3)




To a solution of **17** (36.5 mg, 49.3 μmol) in diethyl ether (0.3 mL) and methanol (0.3 mL) was added sodium borohydride (9.0 mg, 24 μmol) at 0 °C. The mixture was stirred for 1 min at 0 °C. The reaction mixture was added IPA/conc. hydrochloric acid (v/v 50/1, 2 mL) and stirred for 54 min at 23 °C. After addition of diethyl ether (10 mL) and 1 M hydrochloric acid (10 mL), the mixture was extracted with diethyl ether. The organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 3/1) to afford **22** (29.1 mg, 45.9 μmol, 93% yield) as a colourless solid.

**ESI-20. Synthesis of 24** (Table 1, Entry 4)




A mixture of **17** (42.1 mg, 56.8 μmol) and palladium hydroxide on carbon (20 wt %, 40.0 mg, 56.8 μmol) in acetone (1.0 mL) was stirred for 0.5 h at 23 °C under a hydrogen atmosphere. The mixture was filtered through a cotton–Celite pad to remove the catalyst and carbon. The filtrate was concentrated to afford a crude product, the main content of which was **24** (20.5 mg, 66.0 μmol, 99% yield) as a pale purple syrup.

Data for **24**

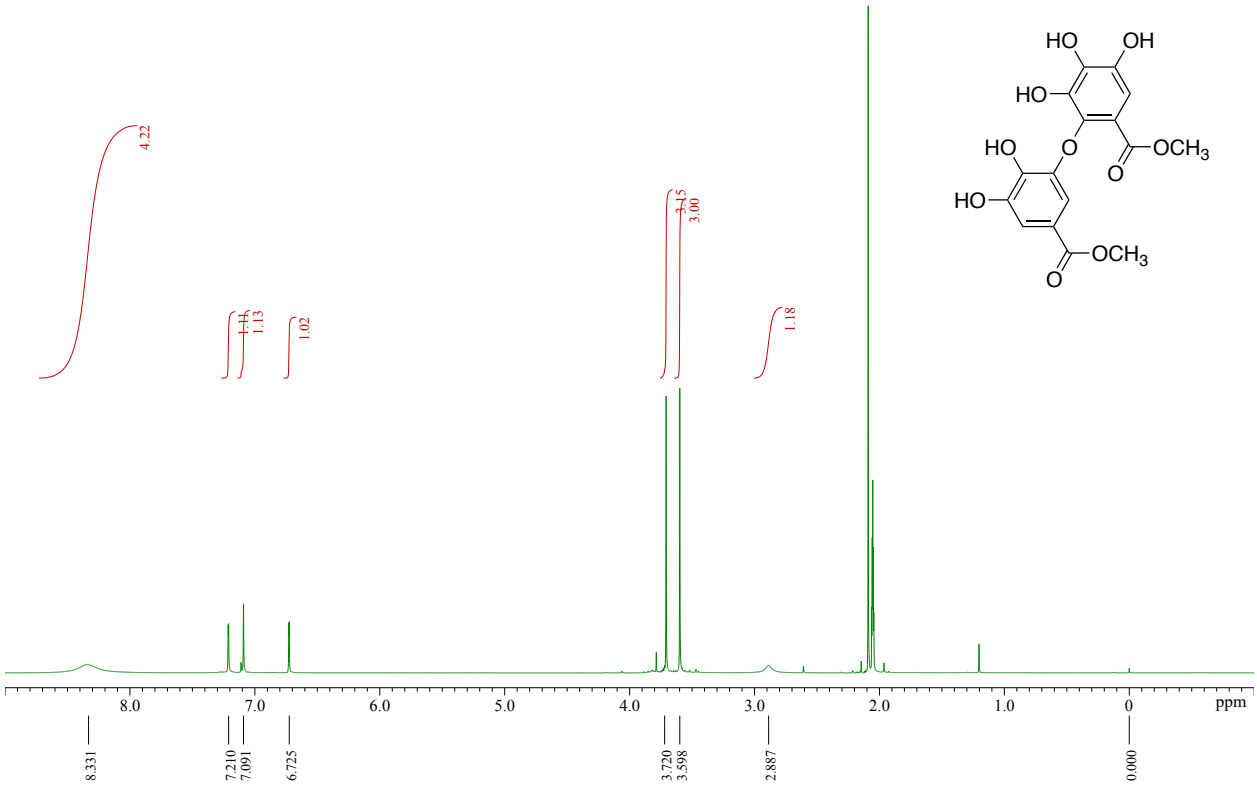
IR (ATR) 3700–2850, 2955, 1697, 1607, 1518, 1435, 1356, 1310, 1221, 1182, 1038, 1001, 959, 770 $cm^{-1}$.

$^{1}H$ NMR (500 MHz, acetone-$d_6$, 23 °C) δ 8.33 (br s Hz, 4H, OH), 7.21 (d, $J$ = 1.7 Hz, 1H, DHDG), 7.09 (s, 1H, DHDG), 6.73 (d, $J$ = 1.7 Hz, 1H, DHDG), 3.71 (s, 3H, OMe), 3.60 (s, 3H, OMe).

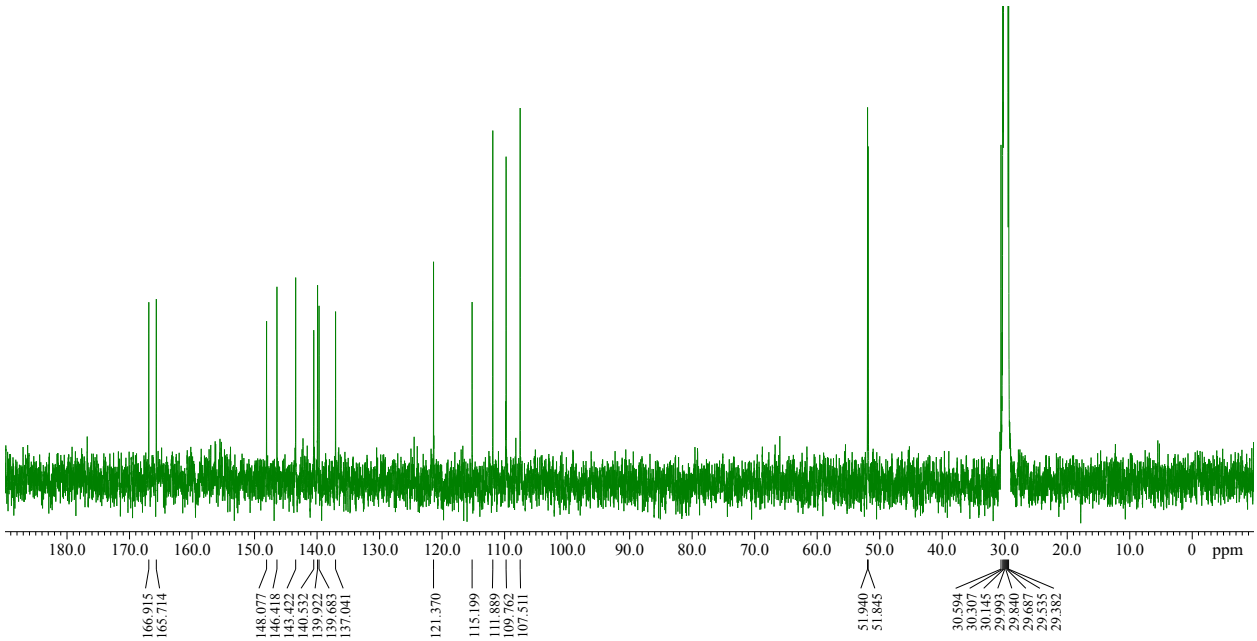
$^{13}C$ NMR (126 MHz, acetone-$d_6$, 23 °C) δ 166.9 (s, DHDG), 165.7 (s, DHDG), 148.1 (s, DHDG), 146.4 (s, DHDG), 143.4 (s, DHDG), 140.5 (s, DHDG), 139.9 (s, DHDG), 139.7 (s, DHDG), 137.0 (s, DHDG), 121.4 (s, DHDG), 115.2 (s, DHDG), 111.9 (d, DHDG), 109.8 (d, DHDG), 107.5 (d, DHDG), 51.9 (q, OMe), 51.8 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{16}H_{14}O_{10}Na$ 365.0509, found 365.0502.

$^{1}$H NMR spectrum of **24**, 500 MHz in acetone-$d_6$

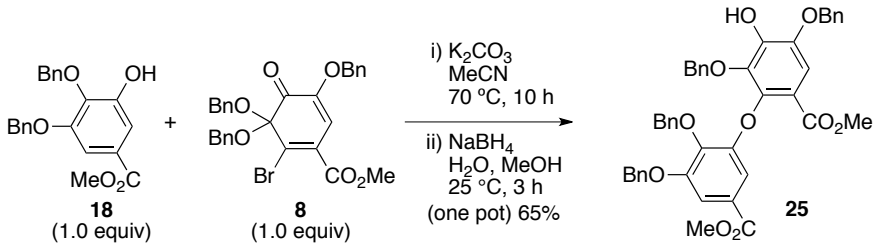



$^{13}$C NMR spectrum of **24**, 126 MHz in acetone-$d_6$



**Experiments for the reactions displayed in Scheme 4**

**ESI-21. One-pot synthesis of 25**




To a solution of **8** (32.3 mg, 58.7 μmol) in acetonitrile (0.7 mL) were added **18** (21.4 mg, 58.7 μmol) and potassium carbonate (16.3 mg, 118 μmol) at room temperature. The mixture was stirred for 10 h at 70 °C. After the mixture was cooled to room temperature, to the mixture were added water (0.3 mL), sodium borohydride (9.0 mg, 238 μmol) and methanol (1.0 mL) at 25 °C. The mixture was stirred for 3 h at 25 °C. Addition of diethyl ether (3 mL) and 1 M hydrochloric acid (3 mL) quenched the reaction. The aqueous mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 7/1 to 4/1) to afford **25** (27.9 mg, 38.3 μmol, 65% yield) as a colourless amorphous solid.

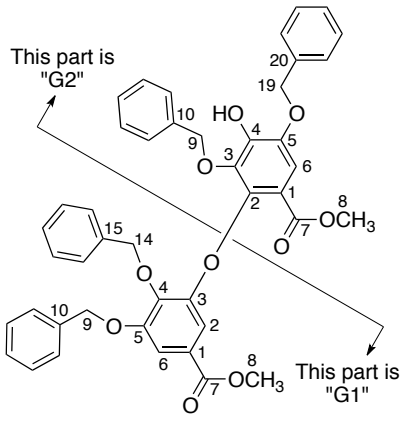
Data for **25**

mp 146.5–149.2 °C.

IR (ATR) 3550–3130, 3065, 3032, 2949, 1715, 1589, 1501, 1449, 1425, 1335, 1308, 1213, 1086, 1074, 1009, 750, 696, 696 $cm^{-1}$.

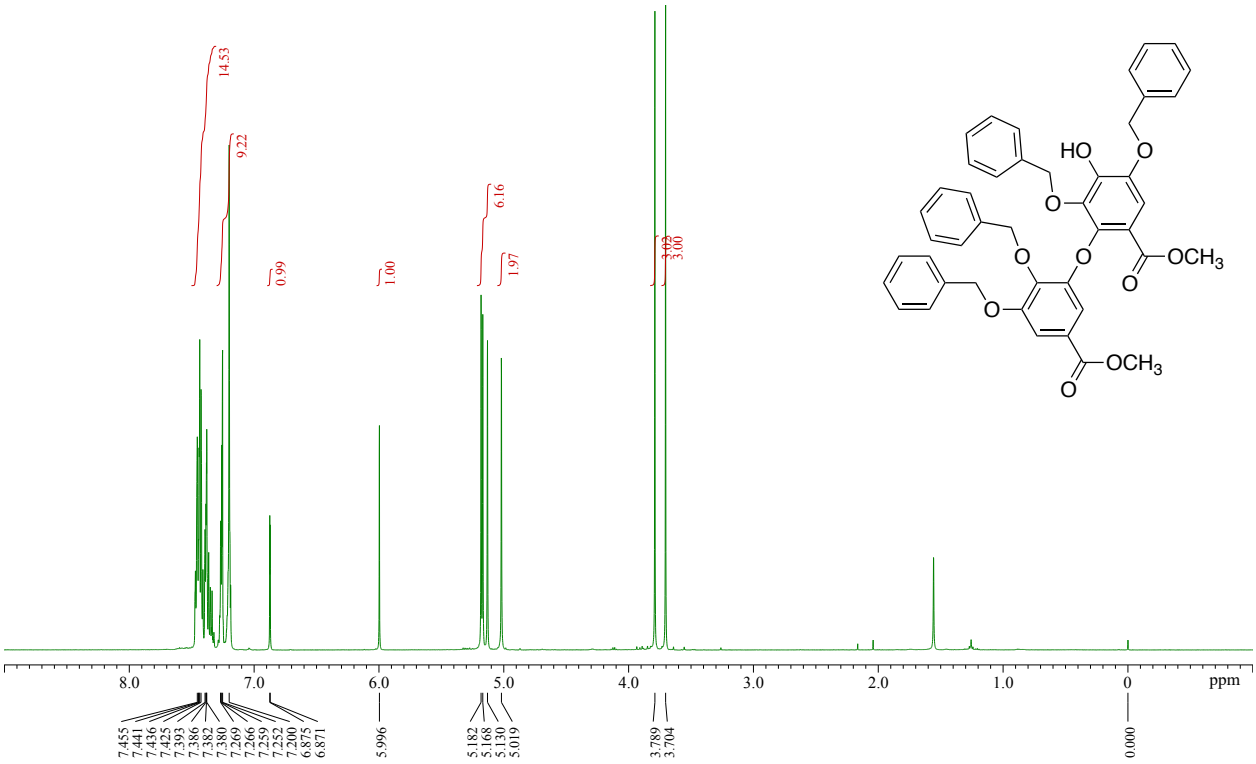
$^1H$ NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.47–7.34 (m, 14H, aryl), 7.28–7.25 (m, 3H, Bn), 7.22–7.19 (m, 5H, Bn), 6.87 (d, *J* = 1.7 Hz, 1H, DHDG), 6.00 (s, 1H, OH), 5.18 (s, 2H, Bn), 5.17 (s, 2H, Bn), 5.13 (s, 2H, Bn), 5.02 (s, 2H, Bn), 3.79 (s, 3H, OMe), 3.70 (s, 3H, OMe).

$^{13}C$ NMR (126 MHz, chloroform-*d*, 23°C, HMQC and HMBC spectra were used for the assignments) δ 166.6 (s, G1-7), 165.3 (s, G2-7), 152.8 (s, G1-3), 152.6 (s, G1-5), 144.7 (s, G2-2), 143.7 (s, G2-3), 142.9 (s, G2-4), 141.8 (s, G1-4), 139.5 (s, G2-5), 137.9 (s, G2-10), 136.8 (s, G1-10), 136.7 (s, G2-20), 136.0 (s, G1-15), 128.9 (d, 2C, Bn), 128.70 (d, Bn), 128.66 (d, 2C, Bn), 128.6 (d, 2C, Bn), 128.5 (d, 2C, Bn), 128.42 (d, 2C, Bn), 128.35 (d, Bn), 128.3 (d, 2C, Bn), 128.2 (d, 2C, Bn), 128.1 (d, Bn), 127.9 (d, Bn), 127.7 (d, 2C, Bn), 125.2 (s, G1-1), 115.6 (s, G2-1), 110.5 (d, G2-6), 109.2 (d, G1-6), 109.1 (d, G1-2), 75.5 (t, G2-19), 75.3 (t, G2-9), 71.9 (t, G1-14), 71.4 (t, G1-9), 52.3 (q, G2-8), 52.2 (q, G1-8).

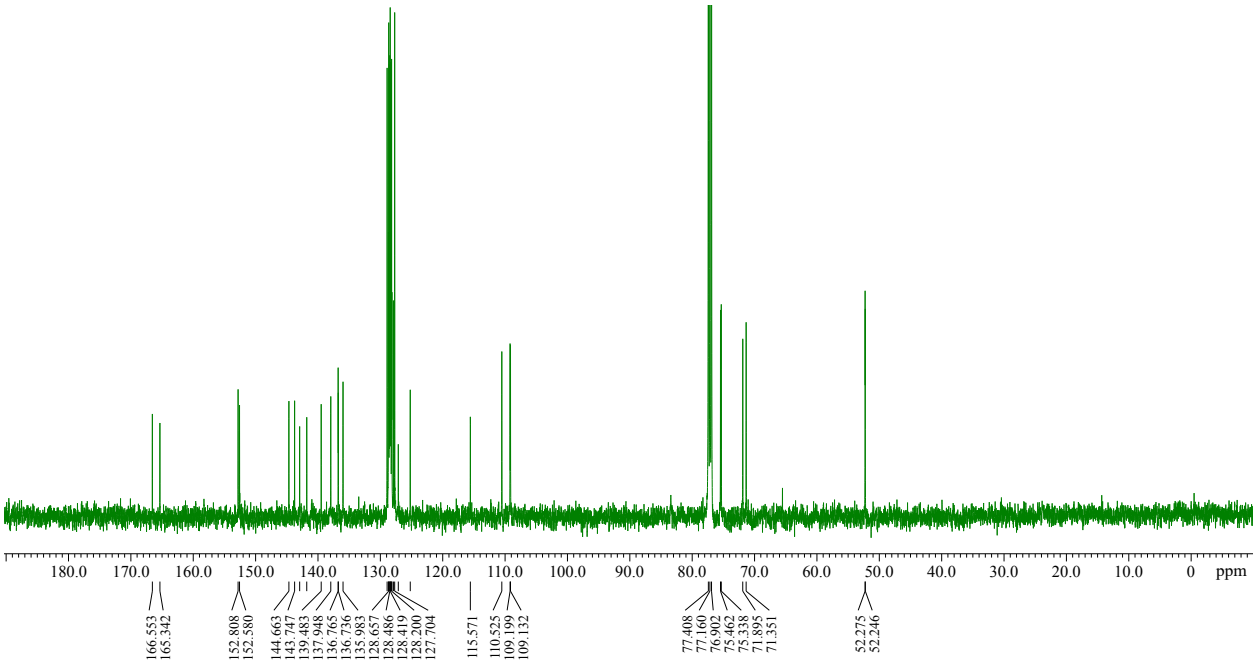



HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{44}H_{38}O_{10}Na$ 749.2363, found 749.2341.

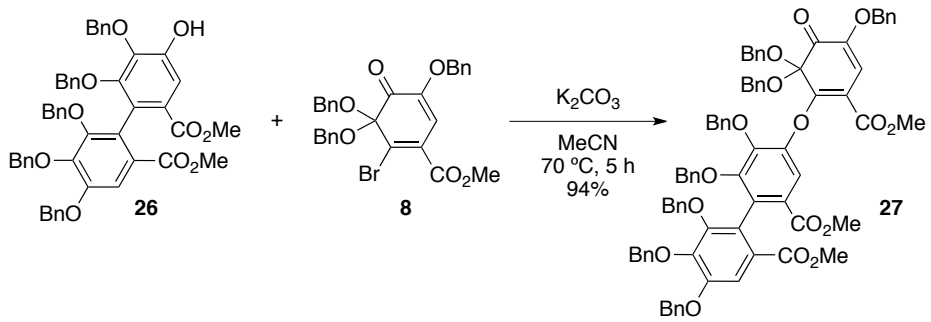
$^{1}$H NMR spectrum, 500 MHz in chloroform-*d* of **25**




$^{13}$C NMR spectrum of **25**, 126 MHz in chloroform-*d*



**ESI-22. Synthesis of 27**




To a solution of **26** (63.0 mg, 77.1 μmol) in acetonitrile (1.0 mL) were added **8** (127 mg, 231 μmol) and potassium carbonate (21.0 mg, 154 μmol) at room temperature. The mixture was stirred for 5 h at 70 ºC. After the mixture was cooled to 0 °C, diethyl ether (3 mL) and 1 M hydrochloric acid (3 mL) were added to the mixture. The aqueous mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 10 g, hexane/ethyl acetate 7/1 to 2/1) to afford **27** (93.0 mg, 72.4 μmol, 94% yield) as a yellow syrup. Although the isolated **27** was not perfectly pure, which included very small amount of unknown by-product, the product was used as the starting material for the next step.

Data for **27**

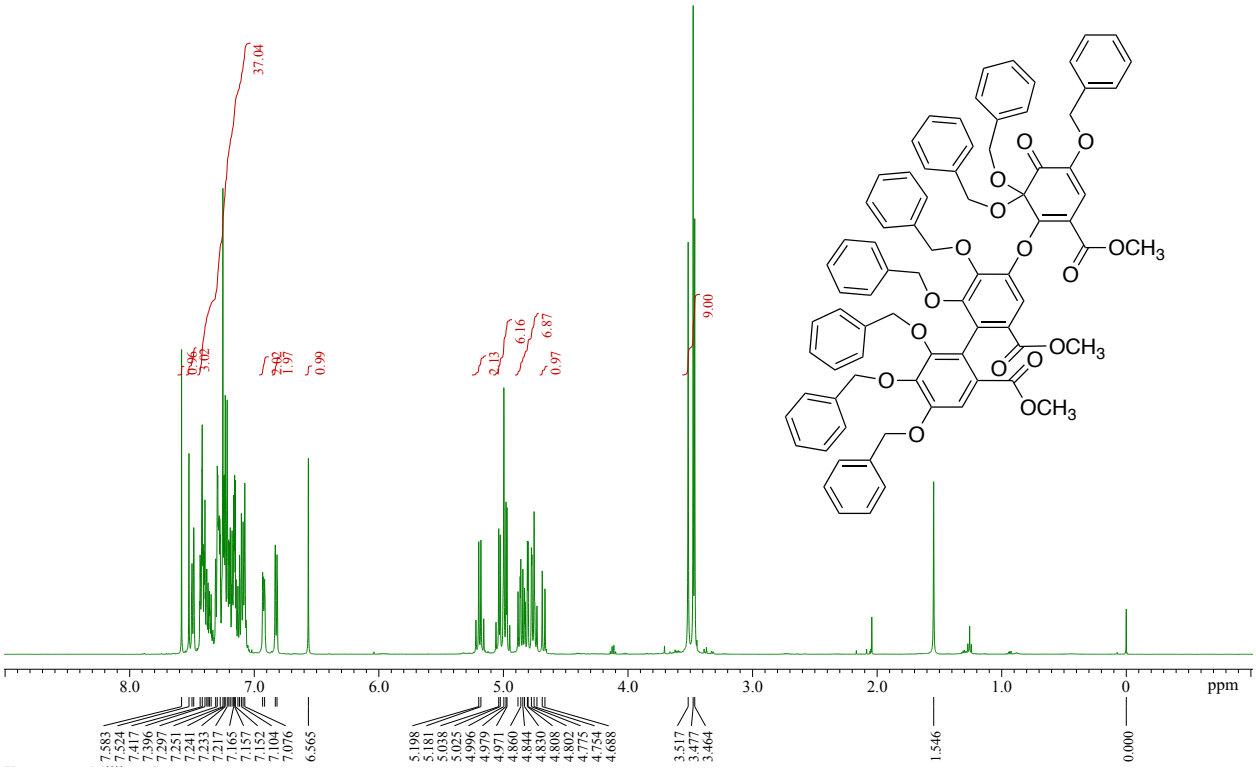
IR (ATR) 3065, 3032, 2949, 2876, 1726, 1593, 1433, 1366, 1323, 1180, 1065, 1028, 910, 735, 696 $cm^{-1}$.

$^1H$ NMR (500 MHz, chloroform-*d*, 24 °C) δ 7.58 (s, 1H, HHDP), 7.52 (s, 1H, HHDP), 7.49 (dd, *J* = 7.7, 1.7 Hz, 2H, Bn), 7.44–7.33 (m, 8H, Bn), 7.31–7.27 (m, 6H, Bn), 7.26–7.06 (m, 17H, Bn), 6.92 (dd, *J* = 7.7, 1.7 Hz, 2H, Bn), 6.82 (dd, *J* = 7.7, 1.7 Hz, 2H, Bn), 6.57 (s, 1H, quinone), 5.21 (d, *J* = 11.5 Hz, 1H, Bn), 5.17 (d, *J* = 11.5 Hz, 1H, Bn), 5.05 (d, *J* = 10.9 Hz, 1H, Bn), 5.01 (d, *J* = 10.9 Hz, 1H, Bn), 5.00 (s, 2H, Bn), 4.99 (d, *J* = 10.9 Hz, 1H, Bn), 4.96 (d, *J* = 10.9 Hz, 1H, Bn), 4.87 (d, *J* = 11.5 Hz, 1H, Bn), 4.86 (d, *J* = 10.9 Hz, 1H, Bn), 4.82 (d, *J* = 11.5 Hz, 1H, Bn), 4.81 (d, *J* = 11.5 Hz, 1H, Bn), 4.77 (d, *J* = 11.5 Hz, 1H, Bn), 4.76 (d, *J* = 11.5 Hz, 1H, Bn), 4.74 (d, *J* = 11.5 Hz, 1H, Bn), 4.68 (d, *J* = 10.9 Hz, 1H, Bn), 3.52 (s, 3H, OMe), 3.48 (s, 6H, OMe), 3.46 (s, 3H, OMe).

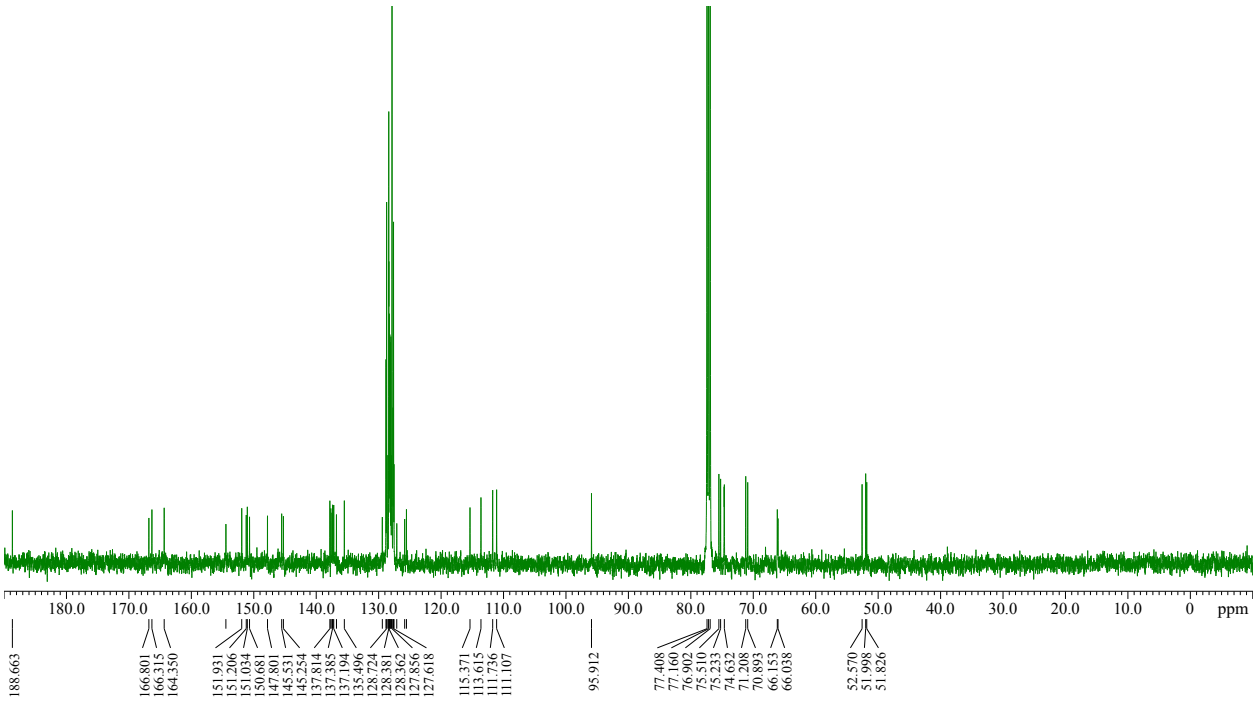
$^{13}C$ NMR (126 MHz, chloroform-*d*, 23 °C) δ 188.7 (s, ketone), 166.8 (s, ester), 166.3 (s, ester), 164.3 (s, ester), 154.4 (s, HHDP or quinone), 151.9 (s, HHDP or quinone), 151.2 (s, HHDP or quinone), 151.0 (s, HHDP or quinone), 150.7 (s, HHDP or quinone), 147.8 (s, HHDP or quinone), 145.5 (s, HHDP or quinone), 145.3 (s, HHDP or quinone), 137.8 (s, Bn), 137.7 (s, Bn), 137.5 (s, Bn), 137.4 (s, Bn), 137.3 (s, Bn), 137.2 (s, Bn), 136.8 (s, Bn), 135.5 (s, Bn), 129.4 (s, HHDP), 128.8–127.5 (d, overlapped 32 doublets: 16 peaks were observed, 40C, Bn), 127.1 (s, HHDP), 125.8 (s, HHDP), 125.5 (s, HHDP), 115.4 (s, quinone), 113.6 (d, HHDP or quinone), 111.7 (d, HHDP or quinone), 111.1 (d, HHDP or quinone), 95.9 (s, quinone), 75.5 (t, Bn), 75.2 (t, Bn), 74.7 (t, Bn), 74.6 (t, Bn), 71.2 (t, Bn), 70.9 (t, Bn), 66.2 (t, Bn), 66.0 (t, Bn), 52.6 (q, OMe), 52.0 (q, OMe), 51.8 (q, OMe).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{80}H_{68}O_{16}Na$ 1307.4405, found 1307.4383.

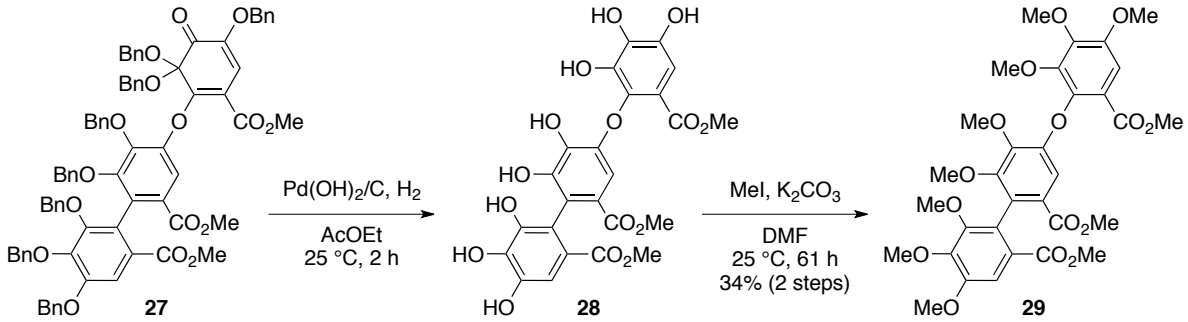
$^{1}$H NMR spectrum, 500 MHz in chloroform-*d* of **27**




$^{13}$C NMR spectrum of **27**, 126 MHz in chloroform-*d*

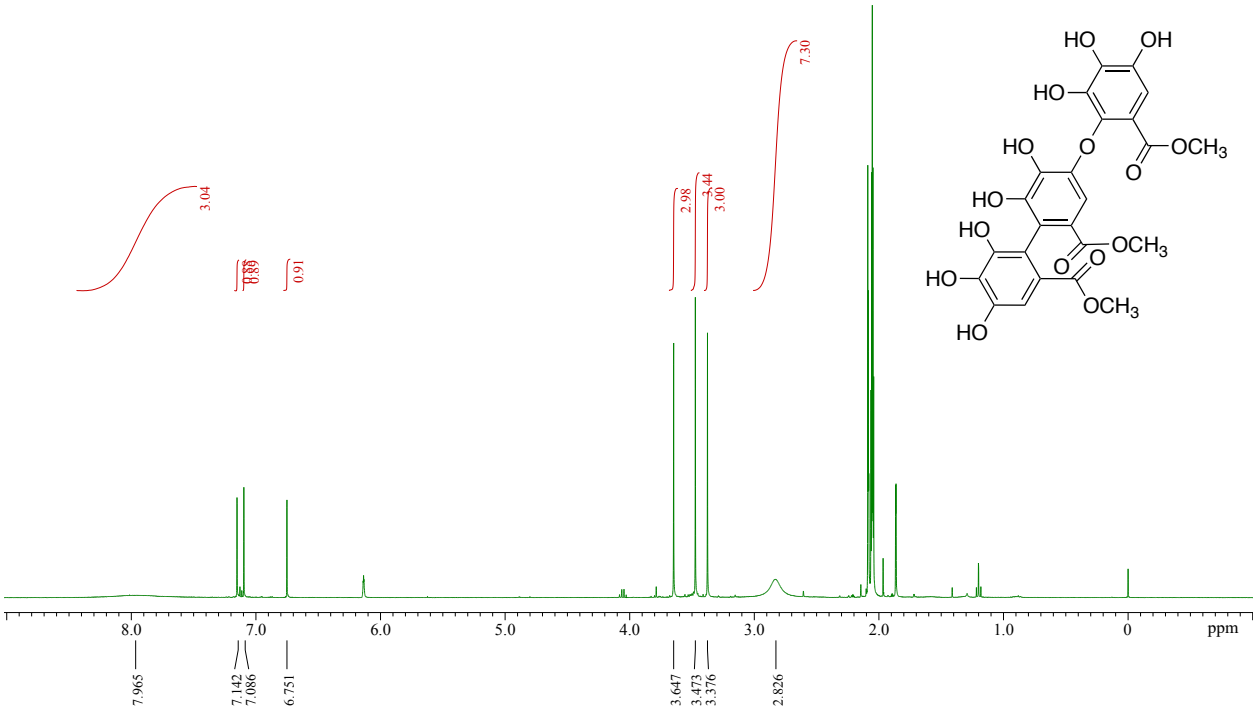


**ESI-23. Synthesis of 29**




A mixture of **27** (almost pure, 80.0 mg, 62.2 μmol) and palladium hydroxide on carbon (20 wt %, 87.0 mg, 124 μmol) in ethyl acetate (1.0 mL) was stirred for 2 h at 25 °C under a hydrogen atmosphere. The mixture was filtered through a cotton–Celite pad to remove the catalyst and carbon. The filtrate was concentrated to afford a crude product, the main content of which was **28**, which was used in the next reaction without further purification.

$^1$H NMR spectrum of the crude **28**, 400 MHz in acetone-$d_6$




To a solution of crude **28** in DMF (1.0 mL) were added methyl iodide (176 mg, 1.24 mmol) and potassium carbonate (170 mg, 1.24 mmol) at 25 °C. The mixture was stirred for 13 h at 25 °C. To the mixture was added further methyl iodide (684 mg, 4.82 mmol). The mixture was stirred for additional 48 h. Diethyl ether (5 mL) and 1 M hydrochloric acid (5 mL) were added to the mixture. The aqueous mixture was extracted with diethyl ether. The combined organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 5 g,

hexane/ethyl acetate 4/1 to 3/2) to afford **29** (13.8 mg, 20.9 μmol, 34% yield) as a colourless syrup. $^{1}$H NMR data for **29** were identical to the literature data.[19]

Data for **29**

IR (ATR) 2994 , 2945 , 2843 , 1728 , 1595 , 1429 , 1327 , 1215 , 1086 , 1036 , 1002 , 760 $cm^{-1}$.

$^{1}$H NMR (400 MHz, chloroform-*d*, 24 °C) δ 7.35 (s, 1H, valoneoyl), 7.30 (s, 1H, valoneoyl), 6.93 (s, 1H, valoneoyl), 4.08 (s, 3H, OMe), 3.98 (s, 3H, OMe), 3.943 (s, 6H, OMe), 3.935 (s, 3H, OMe), 3.78 (s, 6H, OMe), 3.68 (s, 3H, OMe), 3.60 (s, 3H, OMe), 3.57 (s, 3H, OMe), 3.48 (s, 3H, OMe).

$^{13}$C NMR (101 MHz, chloroform-*d*, 24 °C) δ 167.2 (s, ester), 166.8 (s, ester), 165.6 (s, ester), 152.2 (s, valoneoyl), 151.7 (s, valoneoyl), 151.6 (s, valoneoyl), 151.3 (s, valoneoyl), 150.3 (s, valoneoyl), 147.3 (s, valoneoyl), 147.2 (s, valoneoyl), 145.51 (s, valoneoyl), 145.49 (s, valoneoyl), 142.7 (s, valoneoyl), 127.5 (s, valoneoyl), 126.5 (s, valoneoyl), 125.3 (s, valoneoyl), 125.0 (s, valoneoyl), 119.4 (s, valoneoyl), 111.8 (d, valoneoyl), 109.0 (d, valoneoyl), 108.9 (d, valoneoyl), 61.4 (q, OMe), 61.3 (q, O-Me), 61.1 (q, O-Me), 61.0 (q, O-Me), 60.8 (q, O-Me), 60.6 (q, O-Me), 56.4 (q, O-Me), 56.1 (q, O-Me), 52.4 (q, O-Me), 51.9 (q, O-Me), 51.8 (q, O-Me).

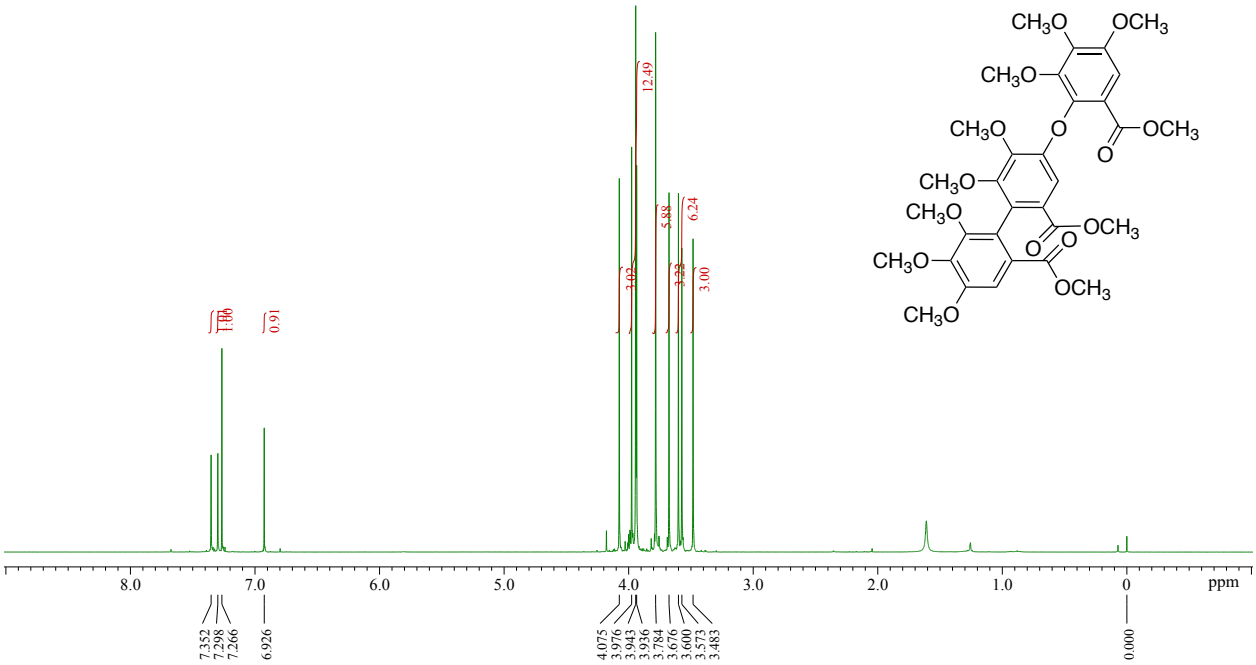
HRMS (ESI) *m/z* $[M + Na]^{+}$ calcd for $C_{32}H_{36}O_{15}Na$ 683.1952, found 683.1946.

Comparison of $^{1}$H NMR data of **29** to the literature data.

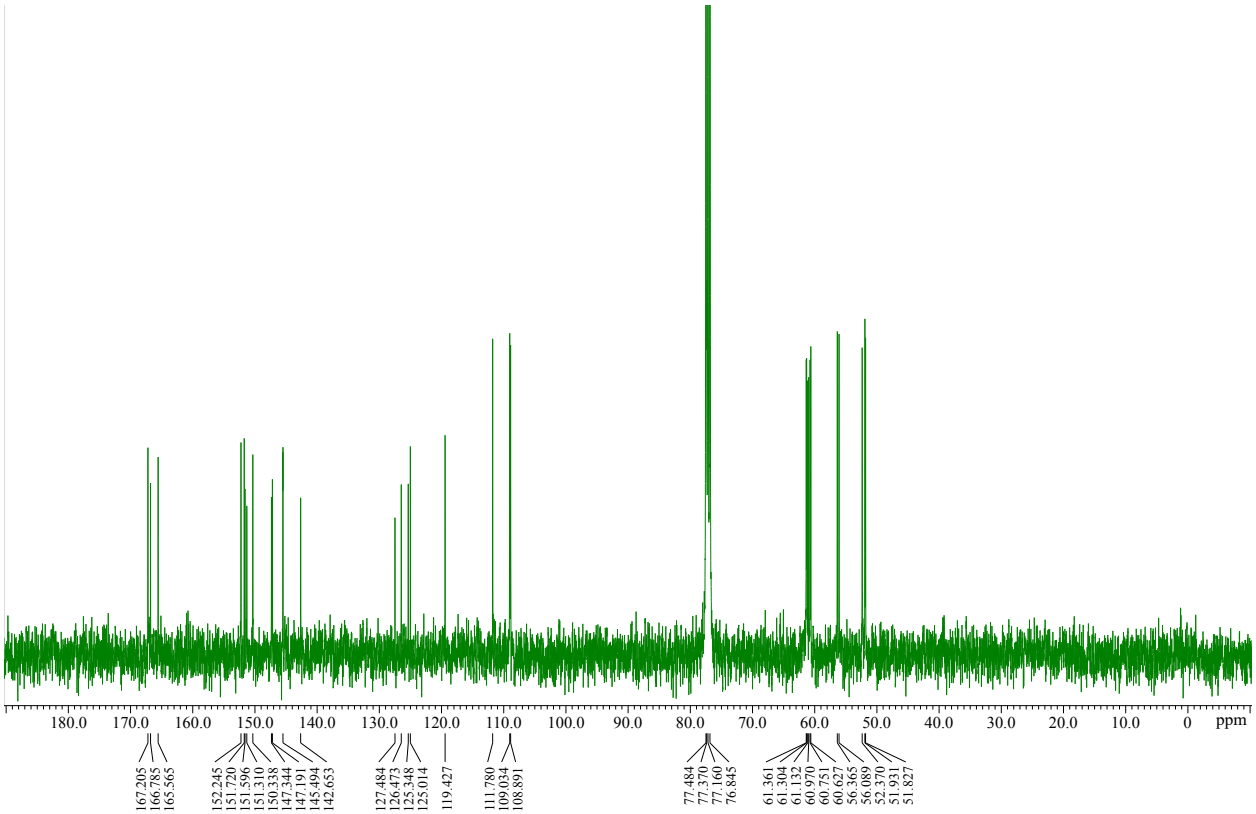
| Position | Lit. data (ppm) | Synthesized **29** (ppm) | Δ(Lit – Obs) (ppm) |
|---|---|---|---|
| Aryl | 7.35 | 7.35 | 0.00 |
| | 7.30 | 7.30 | 0.00 |
| | 6.93 | 6.93 | 0.00 |
| OMe | 4.08 | 4.08 | 0.00 |
| | 3.98 | 3.98 | 0.00 |
| | 3.94 | 3.943 | –0.003 |
| | | 3.935 | 0.005 |
| | 3.78 | 3.78 | 0.00 |
| | 3.68 | 3.68 | 0.00 |
| | 3.60 | 3.60 | 0.00 |
| | 3.58 | 3.57 | 0.01 |
| | 3.49 | 3.48 | 0.01 |

The literature data are in reference 19.

$^{1}$H NMR spectrum of **29**, 400 MHz in chloroform-*d*

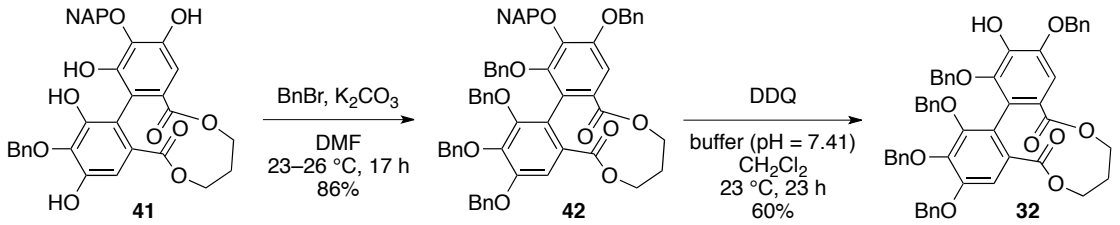



$^{13}$C NMR spectrum of **29**, 101 MHz in chloroform-*d*



**ESI-24. Synthesis of 32**

Compound **32**, a phenolic nucleophile for the synthesis of the tergalloyl group (Scheme 4, d), was prepared from known **41**[9] via benzylation of the phenolic hydroxy groups and removal of the 2-naphthylmethyl (NAP) group.




To a solution of **41** (50.5 mg, 83.0 μmol) in DMF (1.0 mL) were added potassium carbonate (68.8 mg, 498 μmol) and benzyl bromide (85.2 mg, 498 μmol) at 26 °C. The mixture was stirred for 15 h at 23–26 °C. To the mixture were added further potassium carbonate (28.2 mg, 204 μmol) and benzyl bromide (28.8 mg, 168 μmol). The mixture was stirred for additional 2 h at 23 °C. To the reaction mixture were added diethyl ether (3 mL) and 1 M hydrochloric acid (5 mL). The reaction mixture was extracted with diethyl ether. The combined organic layer was successively washed with 1 M hydrochloric acid and brine. After the general drying procedure, the mixture was purified by column chromatography (silica gel 3 g, hexane/ethyl acetate 6/1 to 4/1) to afford **42** (69.2 mg, 71.4 μmol, 86% yield) as a colourless amorphous solid.

Data for **42**

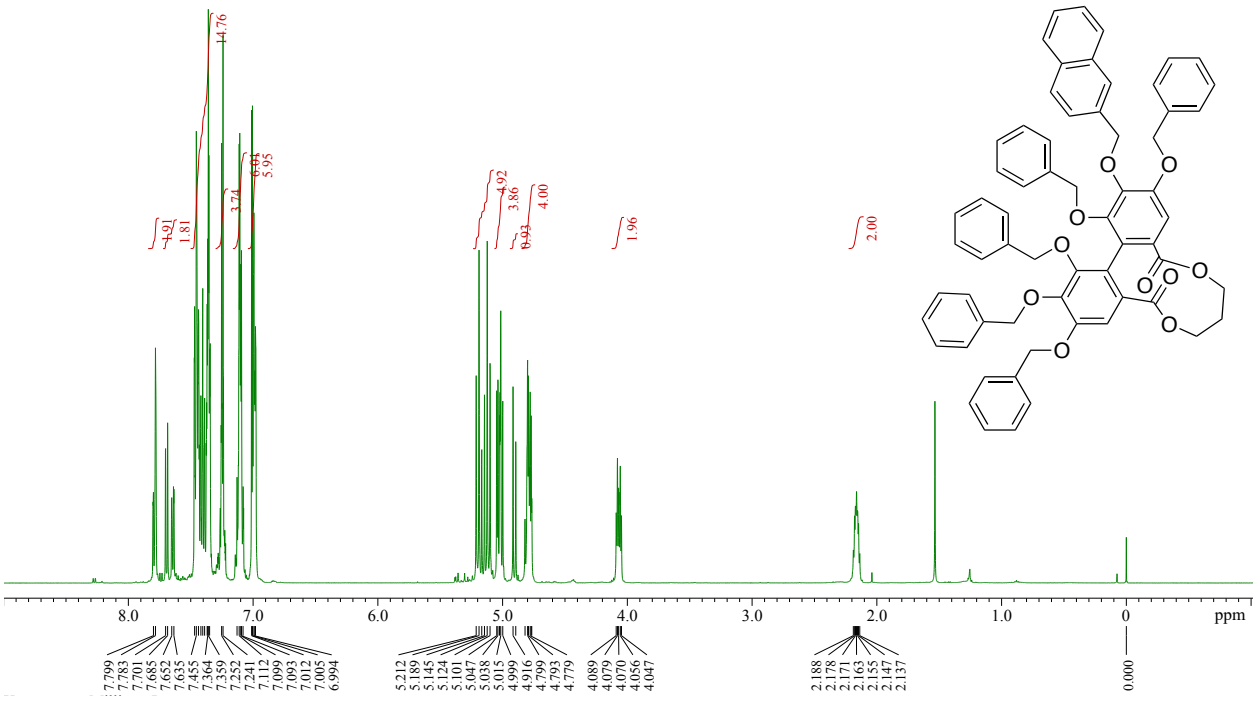
IR (ATR) 3063, 3030, 2874, 1736, 1591, 1368, 1327, 1192, 1094, 908, 735, 696 $cm^{-1}$.

$^1H$ NMR (500 MHz, chloroform-*d*, 23 °C) δ 7.79 (dd, *J* = 8.9, 1.7 Hz, 1H, NAP), 7.78 (br s, 1H, NAP), 7.69 (d, *J* = 8.0 Hz, 1H, NAP), 7.64 (dd, *J* = 6.9, 1.7 Hz, 1H, NAP), 7.47–7.34 (m, 15H, aryl), 7.26–7.23 (m, 3H, aryl), 7.13–7.08 (m, 6H, aryl), 7.01 (s, 1H, HHDP), 7.01 (s, 1H, HHDP), 6.99–6.98 (m, 4H, aryl), 5.20 (d, *J* = 11.5 Hz, 2H, Bn), 5.16 (d, *J* = 10.9 Hz, 1H, NAP), 5.11 (d, *J* = 11.5 Hz, 2H, Bn), 5.05–4.99 (m, 4H, Bn, NAP), 4.91 (d, *J* = 10.9 Hz, 1H, Bn), 4.82–4.77 (m, 4H, Bn and propylene), 4.07 (dt, *J* = 11.5, 5.2 Hz, 2H, propylene), 2.16 (br m, 2H, propylene).

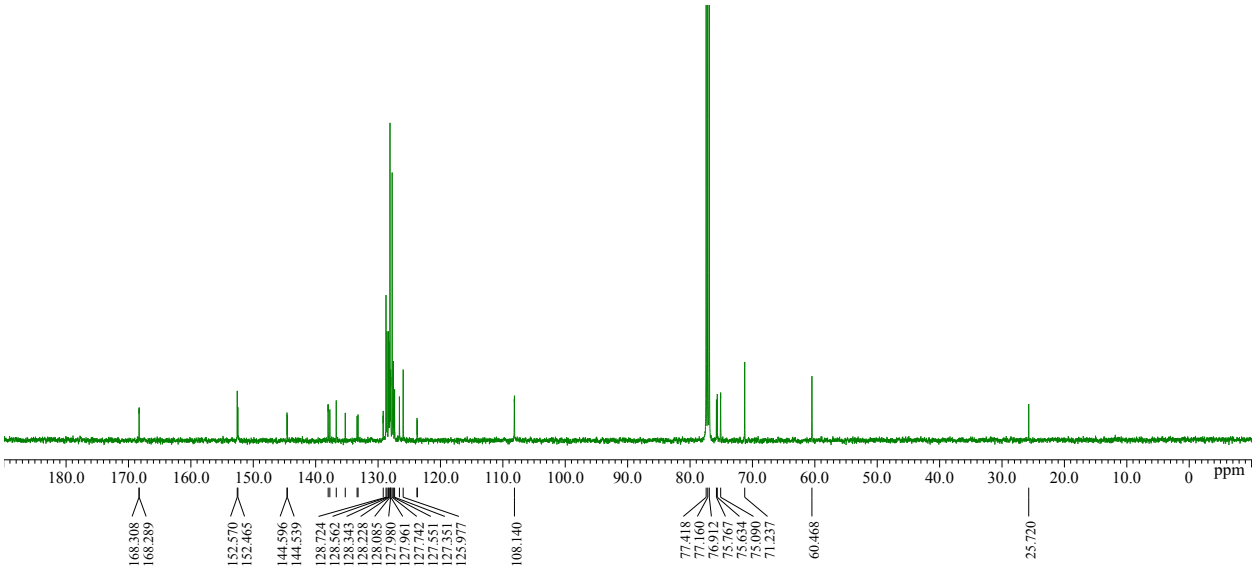
$^{13}C$ NMR (126 MHz, chloroform-*d*, 24 °C) δ 168.31 (s, ester), 168.29 (s, ester), 152.6 (s, 2C, HHDP), 152.5 (s, 2C, HHDP), 144.6 (s, HHDP), 144.5 (s, HHDP), 138.02 (s, Bn), 138.00 (s, Bn), 137.7 (s, Bn), 136.7 (s, 2C, Bn), 135.3 (s, NAP), 133.4 (s, NAP), 133.2 (s, NAP), 129.20 (s, HHDP), 129.17 (s, HHDP), 128.7–127.4 (d, overlapped 29 doublets: ten peaks were observed, Bn and NAP), 126.6 (d, NAP), 126.0 (d, 2C, NAP), 123.8 (s, HHDP), 123.7 (s, HHDP), 108.2 (d, HHDP), 108.1 (d, HHDP), 75.8 (t, NAP), 75.6 (t, Bn), 75.12 (t, Bn), 75.09 (t, Bn), 71.2 (t, 2C, Bn), 60.5 (t, 2C, propylene), 25.7 (t, propylene).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{63}H_{52}O_{10}Na$ 991.3458, found 991.3447.

$^{1}$H NMR spectrum of **42**, 500 MHz in chloroform-*d*



$^{13}$C NMR spectrum of **42**, 126 MHz in chloroform-*d*



To a solution of **42** (800 mg, 826 µmol) in dichloromethane (10 mL) were added DDQ (562 mg, 2.48 mmol) and phosphate buffer (pH = 7.41, 2.0 mL) at 23 °C. The mixture was stirred for 23 h at 23 °C. Addition of 10% aqueous sodium thiosulfate (20 mL) quenched the reaction. The aqueous mixture was extracted with dichloromethane. After the general drying procedure, the mixture was purified by column chromatography (silica gel 20 g, hexane/ethyl acetate 8/1 to 3/1) to afford **32** (414 mg, 499 µmol, 60% yield) as a colourless amorphous solid.

Data for **32**

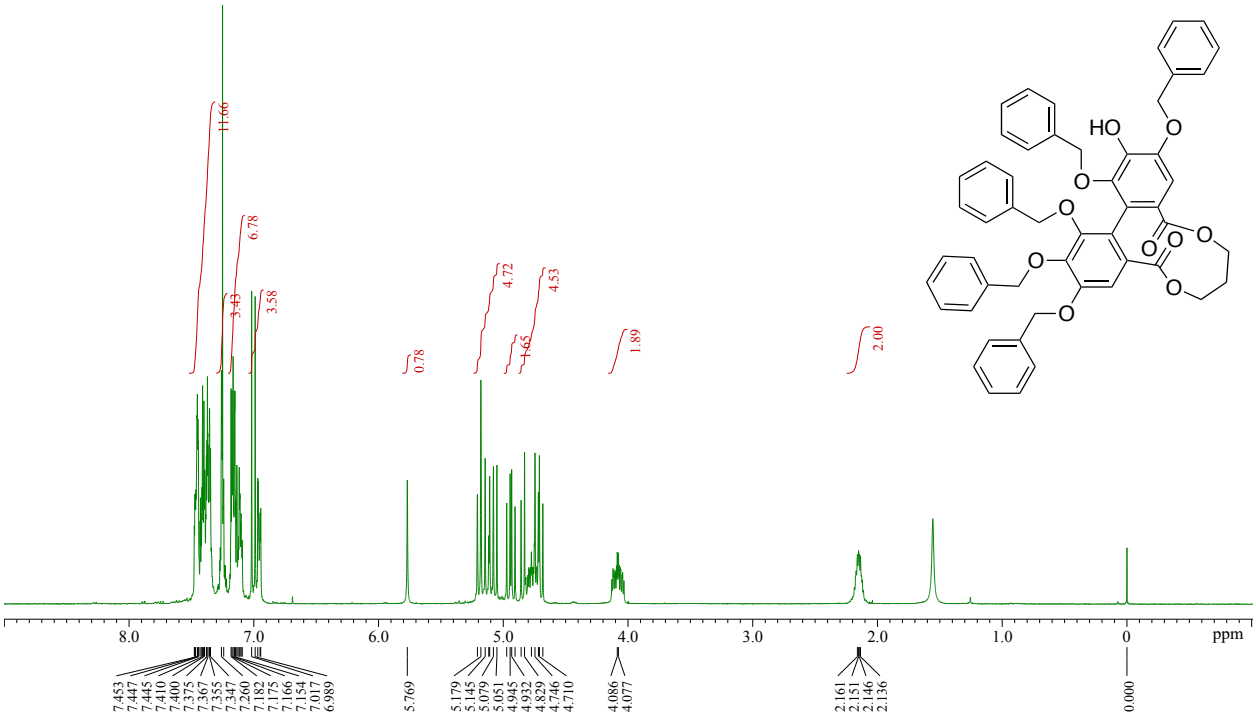
IR (ATR) 3550–3200, 3063, 3030, 2953, 2876, 1734, 1593, 1497, 1454, 1368, 1331, 1192, 1088, 1057, 746, 696 $cm^{-1}$.

$^1H$ NMR (400 MHz, chloroform-*d*, 25 °C) δ 7.48–7.34 (m, 12H, Bn), 7.27–7.24 (m, 4H, Bn), 7.18–7.09 (m, 7H, Bn), 7.02 (s, 1H, HHDP), 6.99 (s, 1H, HHDP), 6.96 (dd, *J* = 7.3, 1.8 Hz, 2H, Bn), 5.77 (br s, 1H, OH), 5.19 (d, *J* = 11.2 Hz, 2H, Bn), 5.13 (d, *J* = 11.2 Hz, 1H, Bn), 5.09 (d, *J* = 11.2 Hz, 1H, Bn), 5.07 (d, *J* = 11.0 Hz, 1H, Bn), 4.96 (d, *J* = 11.0 Hz, 1H, Bn), 4.92 (d, *J* = 11.0 Hz, 1H, Bn), 4.84 (d, *J* = 11.2 Hz, 1H, Bn), 4.82–4.72 (m, 2H, propylene), 4.73 (d, *J* = 11.0 Hz, 1H, Bn), 4.70 (d, *J* = 11.2 Hz, 1H, Bn), 4.13–4.03 (m, 2H, propylene), 2.16 (br m, 2H, propylene).

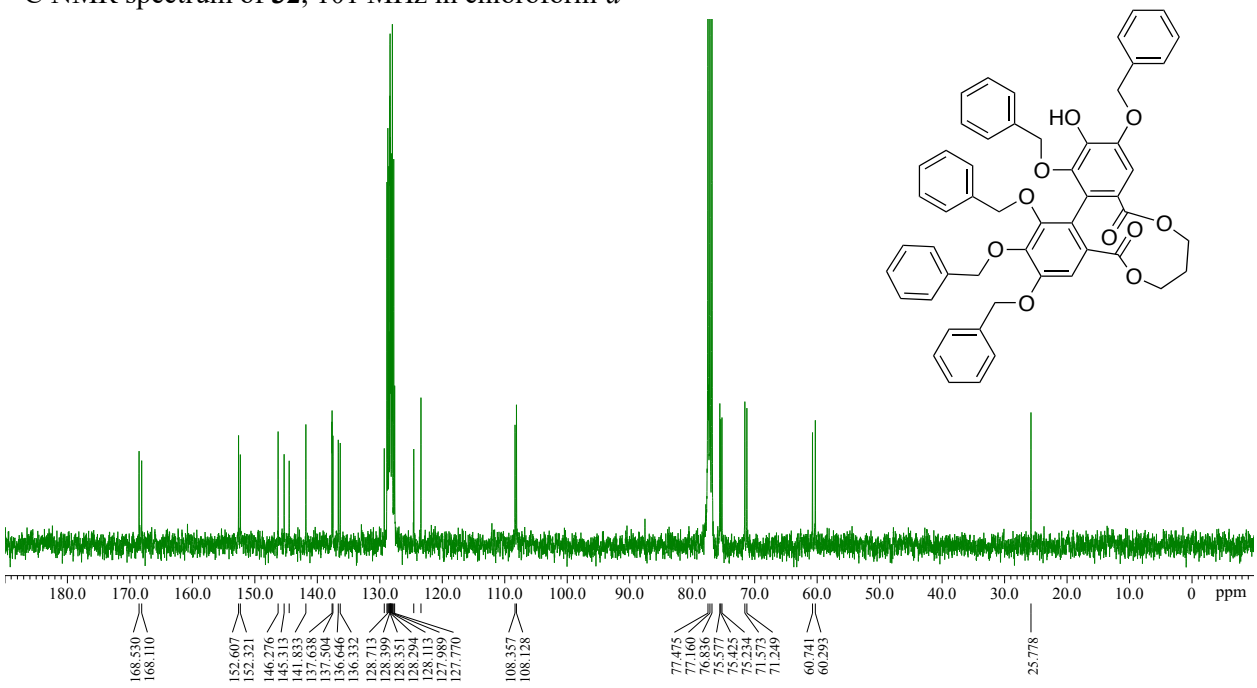
$^{13}C$ NMR (101 MHz, chloroform-*d*, 25 °C) δ 168.5 (s, ester), 168.1 (s, ester), 152.6 (s, HHDP), 152.3 (s, HHDP), 146.3 (s, HHDP), 145.3 (s, HHDP), 144.5 (s, HHDP), 141.8 (s, HHDP), 137.7 (s, Bn), 137.6 (s, Bn), 137.5 (s, Bn), 136.6 (s, Bn), 136.3 (s, Bn), 129.3 (s, Bn), 128.9–127.6 (d, 26C, overlapped 25 doublets and 1 singlet: 13 peaks were observed, Bn and HHDP), 124.6 (s, HHDP), 123.4 (s, HHDP), 108.4 (d, HHDP), 108.1 (d, HHDP), 75.6 (t, Bn), 75.4 (t, Bn), 75.2 (t, Bn), 71.6 (t, Bn), 71.2 (t, Bn), 60.7 (t, propylene), 60.3 (t, propylene), 25.8 (t, propylene).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{52}H_{44}O_{10}Na$ 851.2817, found 851.2832.

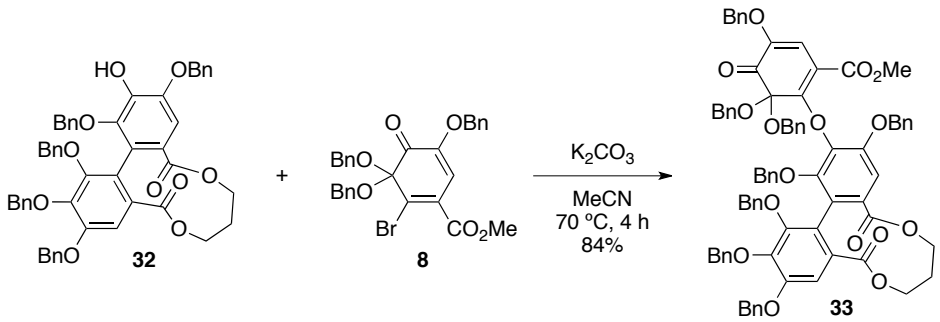
$^1H$ NMR spectrum of **32**, 400 MHz in chloroform-*d*



$^{13}$C NMR spectrum of **32**, 101 MHz in chloroform-*d*



**ESI-25. Synthesis of 33**




To a solution of **32** (17.4 mg, 21.0 μmol) in acetonitrile (0.5 mL) were added **8** (46.0 mg, 83.7 μmol) and potassium carbonate (6.0 mg, 43 μmol) at room temperature. The mixture was stirred for 4 h at 70 °C. To the mixture was added further potassium carbonate (6.0 mg, 43 μmol). The mixture was stirred for additional 3.5 h at 70 °C. After the mixture was cooled to 0 °C, diethyl ether (5 mL) and 1 M hydrochloric acid (5 mL) were added to the mixture. The aqueous mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 10 g, hexane/ethyl acetate 8/1 to 3/1) to afford **33** (22.8 mg, 17.6 μmol, 84% yield) as a yellow amorphous solid.

Data for **33**

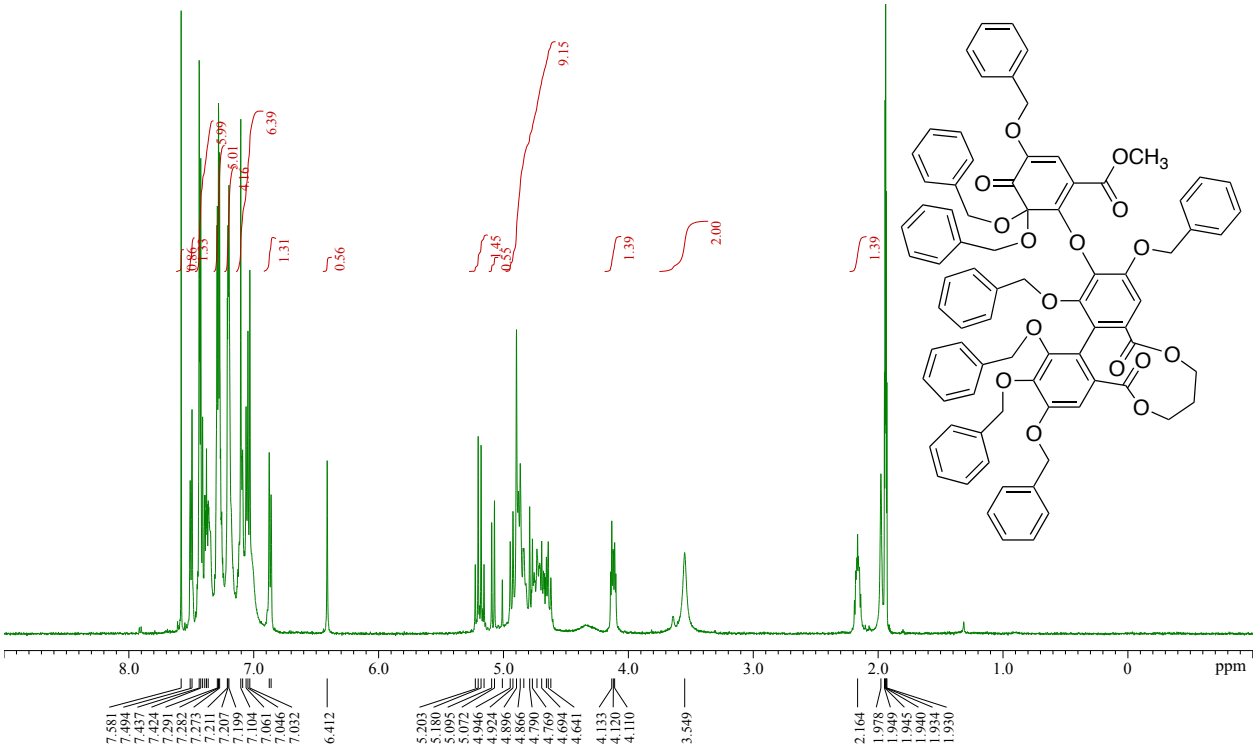
IR (ATR) 3065, 3032, 2940, 2880, 1738, 1645, 1591, 1497, 1454, 1369, 1333, 1192, 1096, 1061, 910, 735, 696 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CD_3CN$, 75 °C) δ 7.50 (d, $J$ = 7.5 Hz, 2H, Bn), 7.46–6.98 (m, 38H, Bn), 6.87 (d, $J$ = 7.5 Hz, 2H, Bn), 6.41 (s, 1H, quinone), 5.21 (d, $J$ = 11.5 Hz, 1H, Bn), 5.17 (d, $J$ = 11.5 Hz, 1H, Bn), 5.10 (d, $J$ = 11.5 Hz, 1H, Bn), 4.94 (d, $J$ = 10.9 Hz, 1H, Bn), 4.90–4.82 (m, 7H, Bn), 4.78 (d, $J$ = 10.9 Hz, 1H, Bn), 4.75–4.60 (m, 6H, Bn + propylene), 4.12 (dt, $J$ = 11.5, 5.2 Hz, 2H, propylene), 3.55 (br s, 3H, OMe), 2.19–2.14 (m, 2H, propylene).

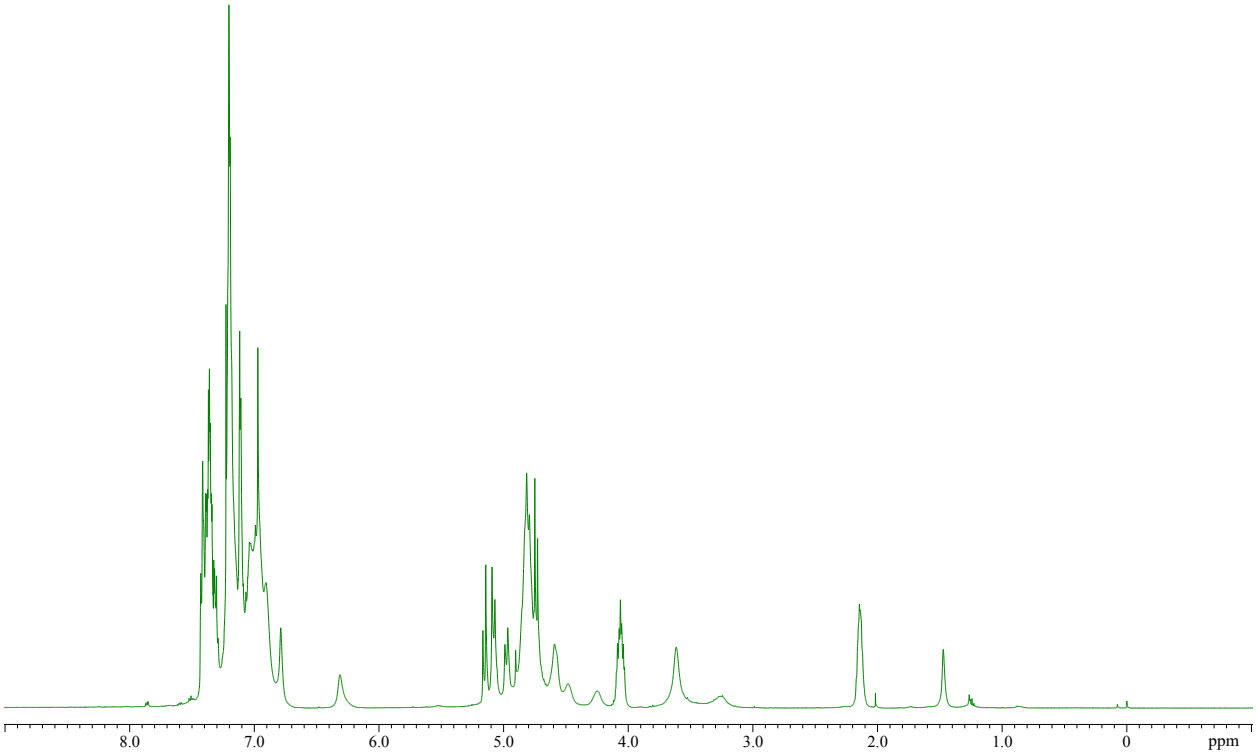
$^{13}C$ NMR (126 MHz, $CD_3CN$, 75 °C) Because of broad signals due to existence of rotational isomers even at 75 °C, specific chemical shifts could not be displayed.

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{81}H_{68}O_{16}Na$ 1319.4405, found 1319.43818.

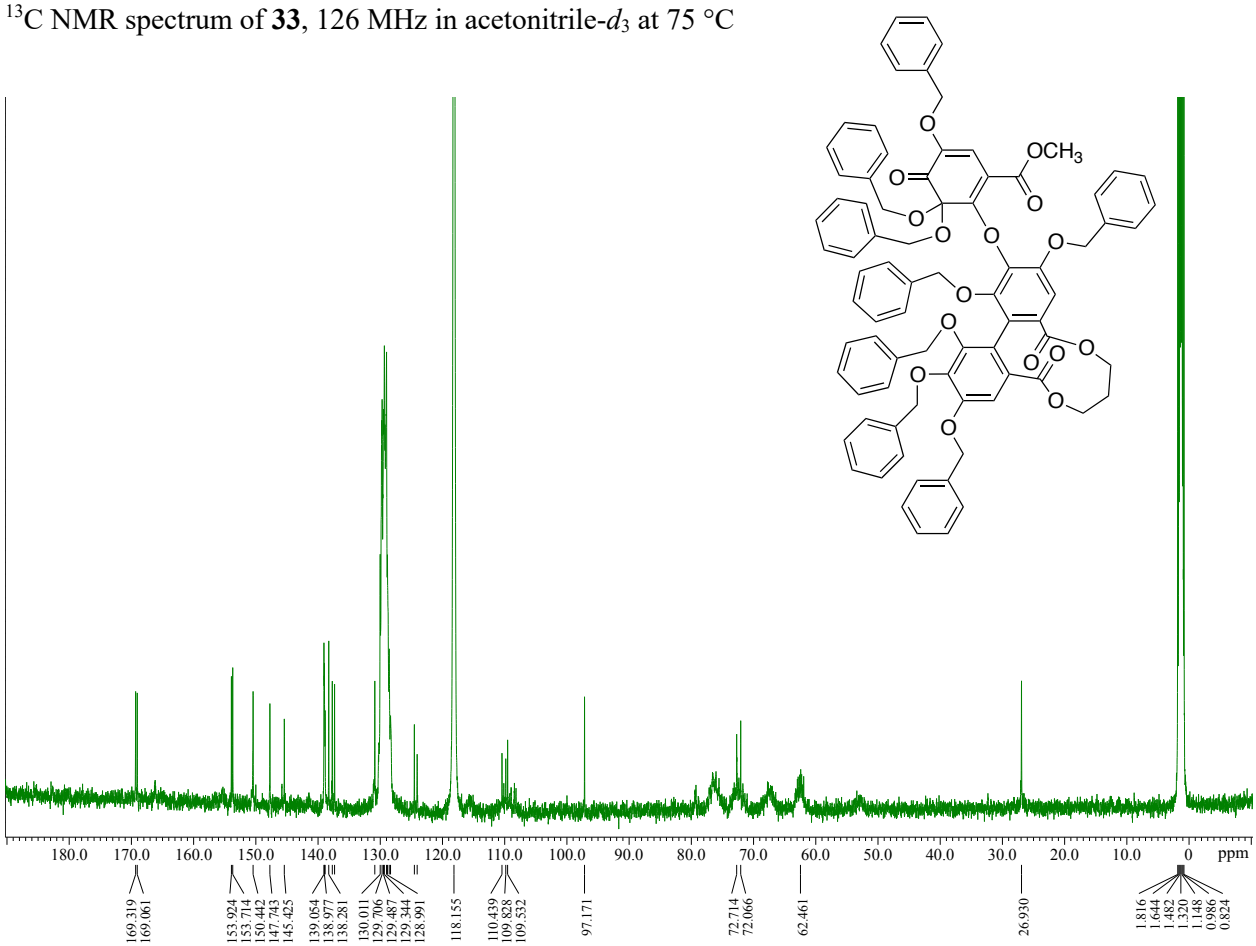
$^{1}$H NMR spectrum of **33**, 500 MHz in acetonitrile-$d_3$ at 75 °C



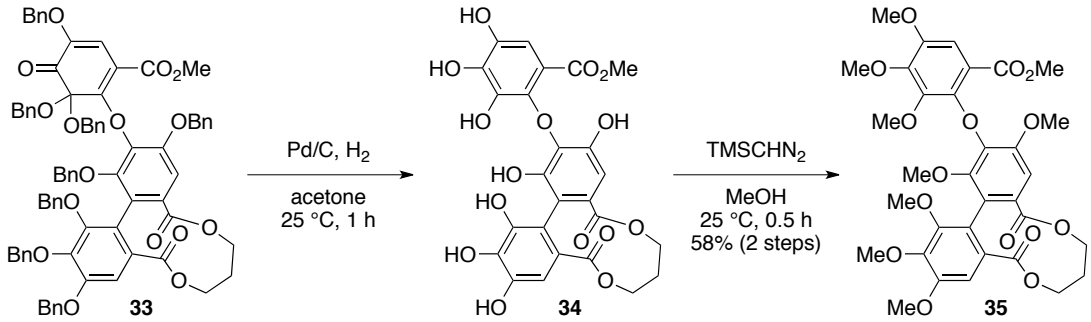

$^{1}$H NMR spectrum of **33**, 500 MHz in acetonitrile-$d_3$ at 50 °C



$^{13}$C NMR spectrum of **33**, 126 MHz in acetonitrile-$d_3$ at 75 °C

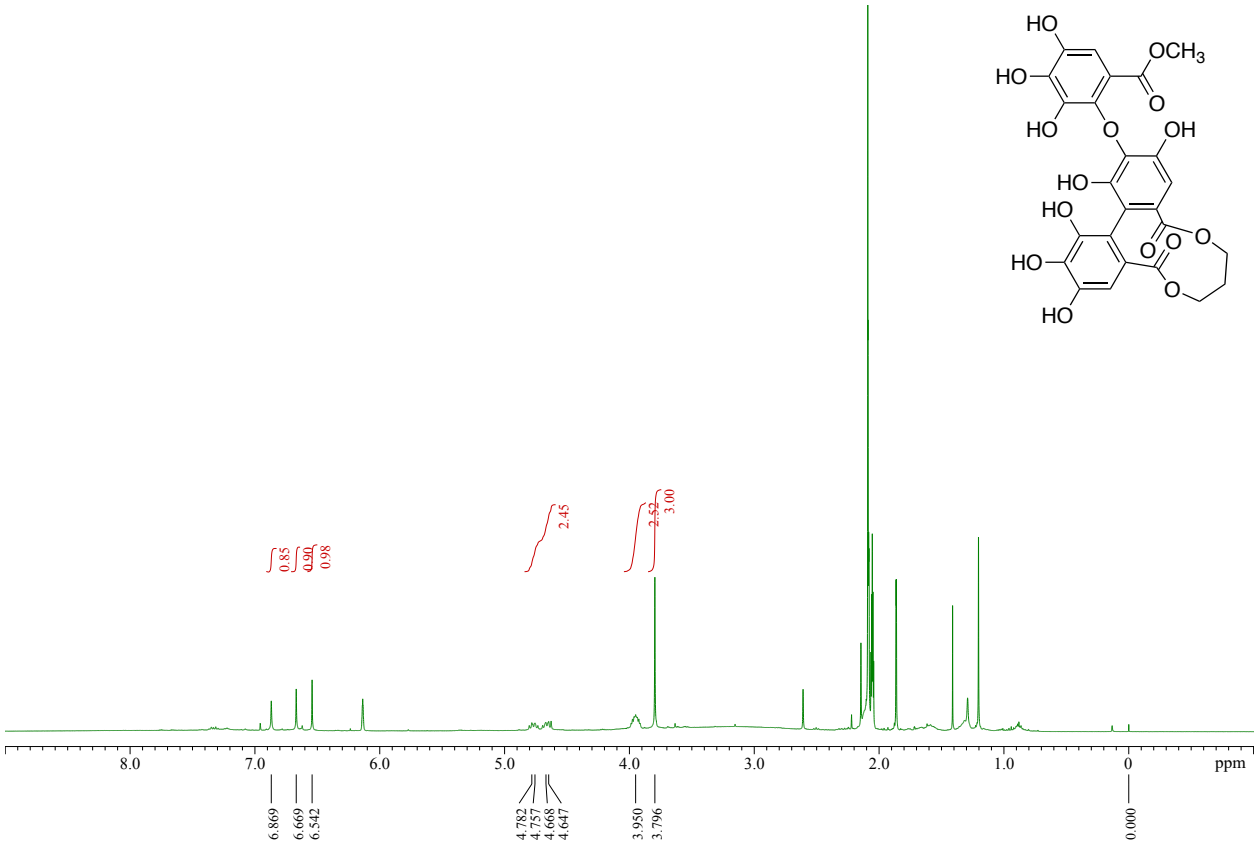


**ESI-26. Synthesis of 35**




A mixture of **33** (88.0 mg, 67.8 μmol) and palladium on carbon (20 wt %, 72.0 mg, 136 μmol) in acetone (1.0 mL) was stirred for 1 h at 25 °C under a hydrogen atmosphere. The mixture was filtered through a cotton–Celite pad to remove the catalyst and carbon. The filtrate was concentrated to afford a crude product, the main content of which was **34**. The crude product was used in the next reaction without further purification.

$^1$H NMR spectrum of the crude **34**, 400 MHz in acetone-$d_6$



To a solution of crude **34** in MeOH (1.0 mL) was added trimethylsilyldiazomethane (2.0 M in diethyl ether, 0.70 mL, 1.40 mmol) at 25 °C. The mixture was stirred for 0.5 h at 25 °C. Acetic acid (1 mL) was added to the mixture. After removal of solvents, the mixture was purified by column chromatography (silica gel 5 g, hexane/ethyl acetate 4/1 to 1/1) to afford **35** (26.4 mg, 39.2 μmol, 58% yield) as a yellow amorphous solid.

Data for **35**

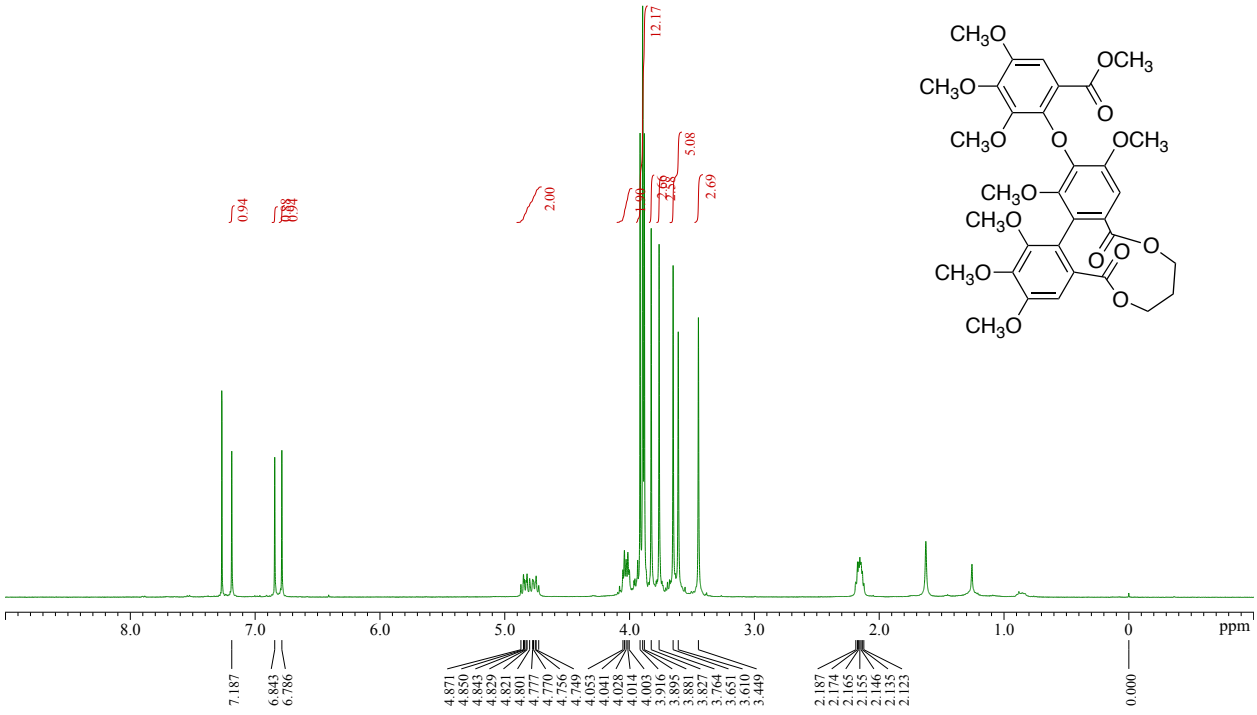
IR (ATR) 2995, 2941, 2843, 1736, 1595, 1483, 1460, 1431, 1414, 1395, 1341, 1211, 1172, 1103, 1057, 1030, 988, 916, 731, 648 $cm^{-1}$.

$^1H$ NMR (400 MHz, chloroform-*d*, 22 °C) δ 7.19 (s, 1H, tergalloyl), 6.84 (s, 1H, tergalloyl), 6.79 (s, 1H, tergalloyl), 4.87–4.73 (m, 2H, propylene), 4.05–4.00 (m, 2H, propylene), 3.92 (s, 3H, OMe), 3.89 (s, 6H, OMe), 3.88 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.76 (s, 3H, OMe), 3.65 (s, 3H, OMe), 3.61 (s, 3H, OMe), 3.45 (s, 3H, OMe), 2.19–2.12 (m, 2H, propylene).

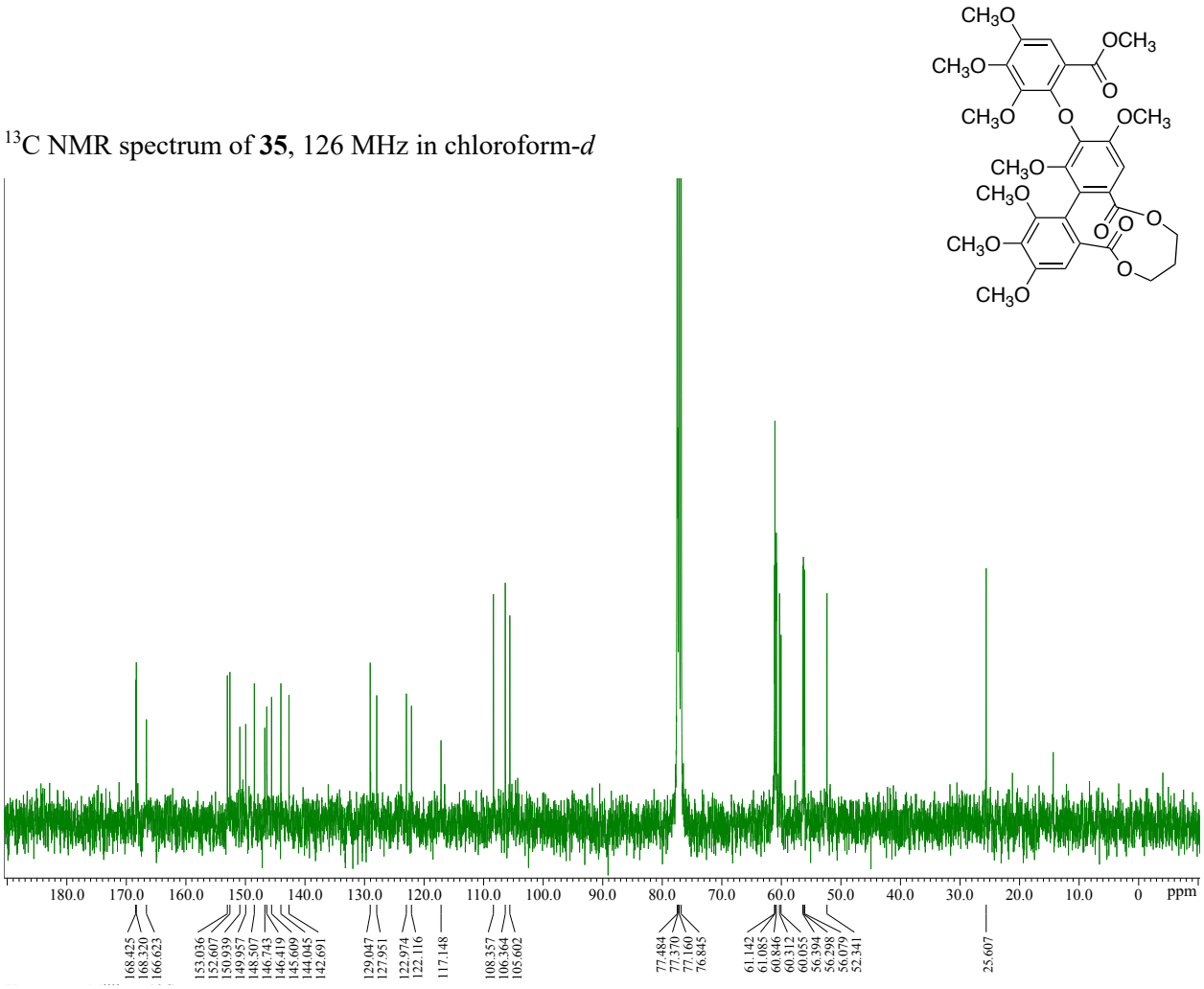
$^{13}C$ NMR (126 MHz, chloroform-*d*, 23 °C) δ 168.4 (s, ester), 168.3 (s, ester), 166.6 (s, ester), 153.0 (s, tergalloyl), 152.6 (s, tergalloyl), 150.9 (s, tergalloyl), 149.9 (s, tergalloyl), 148.5 (s, tergalloyl), 146.7 (s, tergalloyl), 146.4 (s, tergalloyl), 145.6 (s, tergalloyl), 144.0 (s, tergalloyl), 142.7 (s, tergalloyl), 129.0 (s, tergalloyl), 127.9 (s, tergalloyl), 123.0 (s, tergalloyl), 122.1 (s, tergalloyl), 117.1 (s, tergalloyl), 108.3 (d, tergalloyl), 106.3 (d, tergalloyl), 105.6 (d, tergalloyl), 61.1 (q, OMe), 61.1 (q, 2C, OMe), 60.8 (q, OMe), 60.8 (q, OMe), 60.3 (t, propylene), 60.0 (t, propylene), 56.4 (q, OMe), 56.3 (q, OMe), 56.1 (q, OMe), 52.3 (q, OMe), 25.6 (t, propylene).

HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{33}H_{36}O_{15}Na$ 695.1952, found 695.1943.

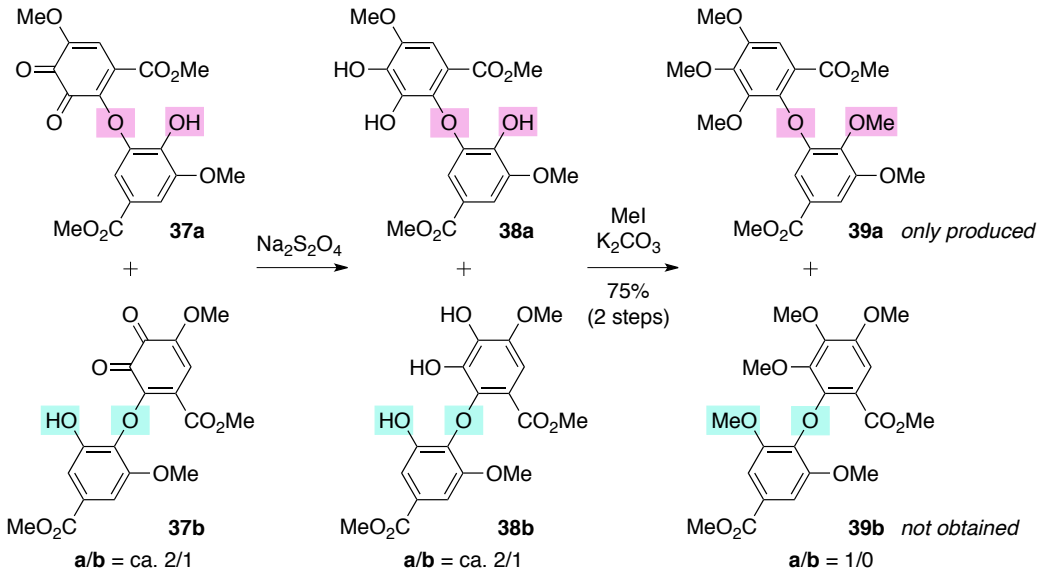
$^1H$ NMR spectrum of **35**, 400 MHz in chloroform-*d*



$^{13}$C NMR spectrum of **35**, 126 MHz in chloroform-*d*

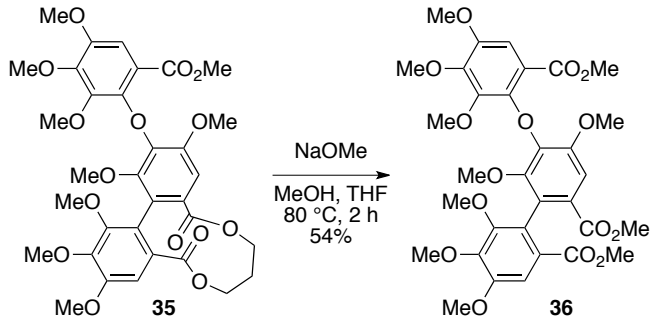



Smiles rearrangement reported by Feldman *et al*.



Feldman and co-workers reported Smiles rearrangement-mediated equilibration of catechol products during methylation reaction.[7] Reduction of a ~2/1 mixture of **37a** and **37b** with sodium hydrosulfite followed by methylation of produced crude mixture of **38a** and **38b** (**a**/**b** = ~2/1) using methyl iodide and potassium carbonate provided only **39a** in 75% yield (2 steps). To prevent this equilibration to less hindered regioisomers, trimethylsilyldiazomethane was used for the methylation of **34**.

**ESI-27. Synthesis of 36**




To a solution of **35** (26.4 mg, 39.2 μmol) in methanol and THF (v/v 1/1, 1.0 mL) was added sodium methoxide (28% MeOH solution 48.0 μL, 196 μmol) at room temperature. The mixture was stirred for 2 h at 80 °C. After the mixture was cooled to 0 °C, diethyl ether (3 mL) and 1 M hydrochloric acid (3 mL) were added to the mixture. The reaction mixture was extracted with diethyl ether. The organic layer was washed with 1 M hydrochloric acid. After the general drying procedure, the mixture was purified by column chromatography (silica gel 2 g, hexane/ethyl acetate 3/1 to 2/1) to afford **36** (13.8 mg, 20.9 μmol, 54% yield) as a colourless syrup. $^{1}$H NMR data for **36** were identical to the literature data.[20]

Data for **36**

IR (ATR) 2995, 2945, 2843, 1726, 1595, 1458, 1429, 1331, 1215, 1171, 1103, 1036, 995, 758 cm$^{-1}$.

$^{1}$H NMR (400 MHz, chloroform-*d*, 24 °C) δ 7.40 (s, 1H, tergalloyl), 7.34 (s, 1H, tergalloyl), 7.18 (s, 1H, tergalloyl), 3.93 (s, 3H, OMe), 3.92 (s, 3H, OMe), 3.880 (s, 3H, OMe), 3.877 (s, 3H, OMe), 3.76 (s, 3H, OMe), 3.63 (s, 3H, OMe), 3.62 (s, 6H, OMe), 3.61 (s, 3H, OMe), 3.38 (s, 3H, OMe), (s, 3H, OMe).

$^{13}$C NMR (101 MHz, chloroform-*d*, 25 °C) δ 167.01 (s, Me ester), 166.98 (s, Me ester), 166.3 (s, Me ester), 152.2 (s, tergalloyl), 151.5 (s, tergalloyl), 149.9 (s, tergalloyl), 148.6 (s, 2C, tergalloyl), 146.7 (s, tergalloyl), 146.2 (s, tergalloyl), 145.7 (s, tergalloyl), 145.5 (s, tergalloyl), 144.0 (s, tergalloyl), 127.3 (s, tergalloyl), 126.5 (s, tergalloyl), 125.3 (s, tergalloyl), 124.1 (s, tergalloyl), 117.1 (s, tergalloyl), 109.7 (d, tergalloyl), 108.9 (d, tergalloyl), 108.3 (d, tergalloyl), 61.2 (q, OMe), 61.1 (q, OMe), 60.9 (q, OMe), 60.7 (q, OMe), 60.6 (q, OMe), 56.4 (q, OMe), 56.3 (q, OMe), 56.1 (q, OMe), 52.3 (q, OMe), 51.9 (q, 2C, OMe).

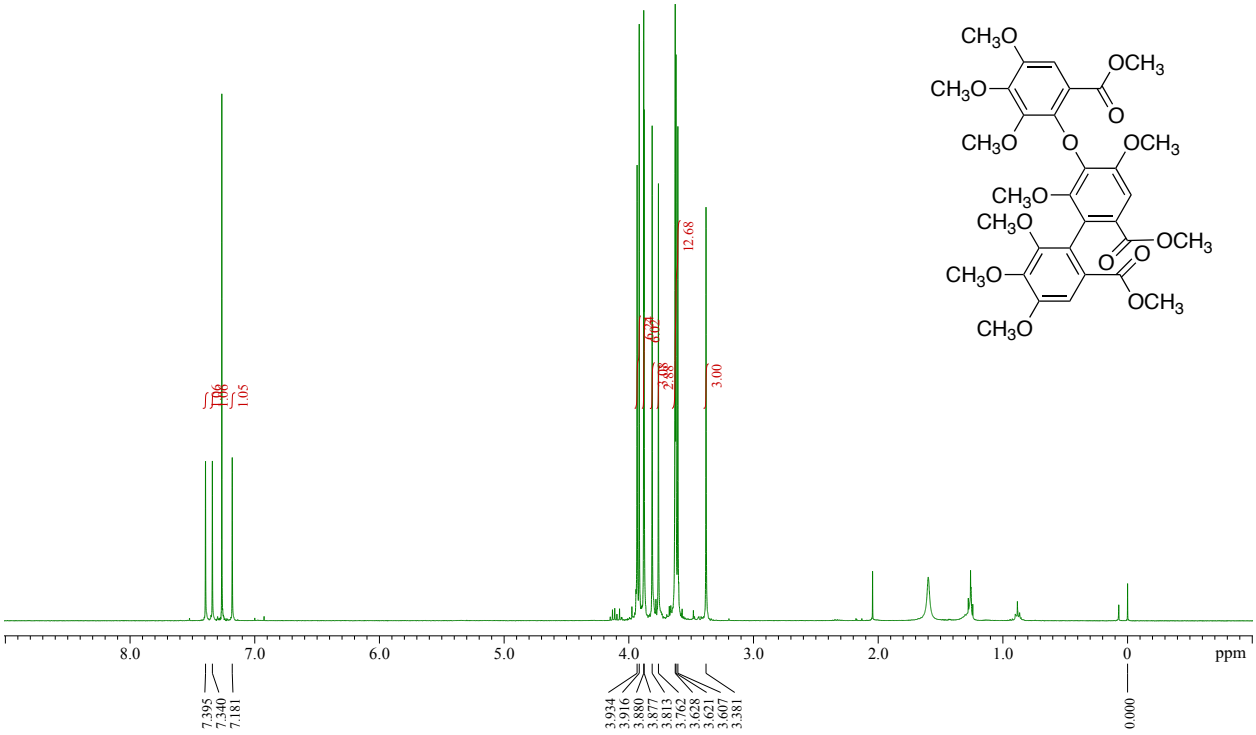
HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{32}H_{36}O_{15}Na$ 683.1952, found 683.1945.

Comparison of $^{1}$H NMR data of **36** to the literature data.

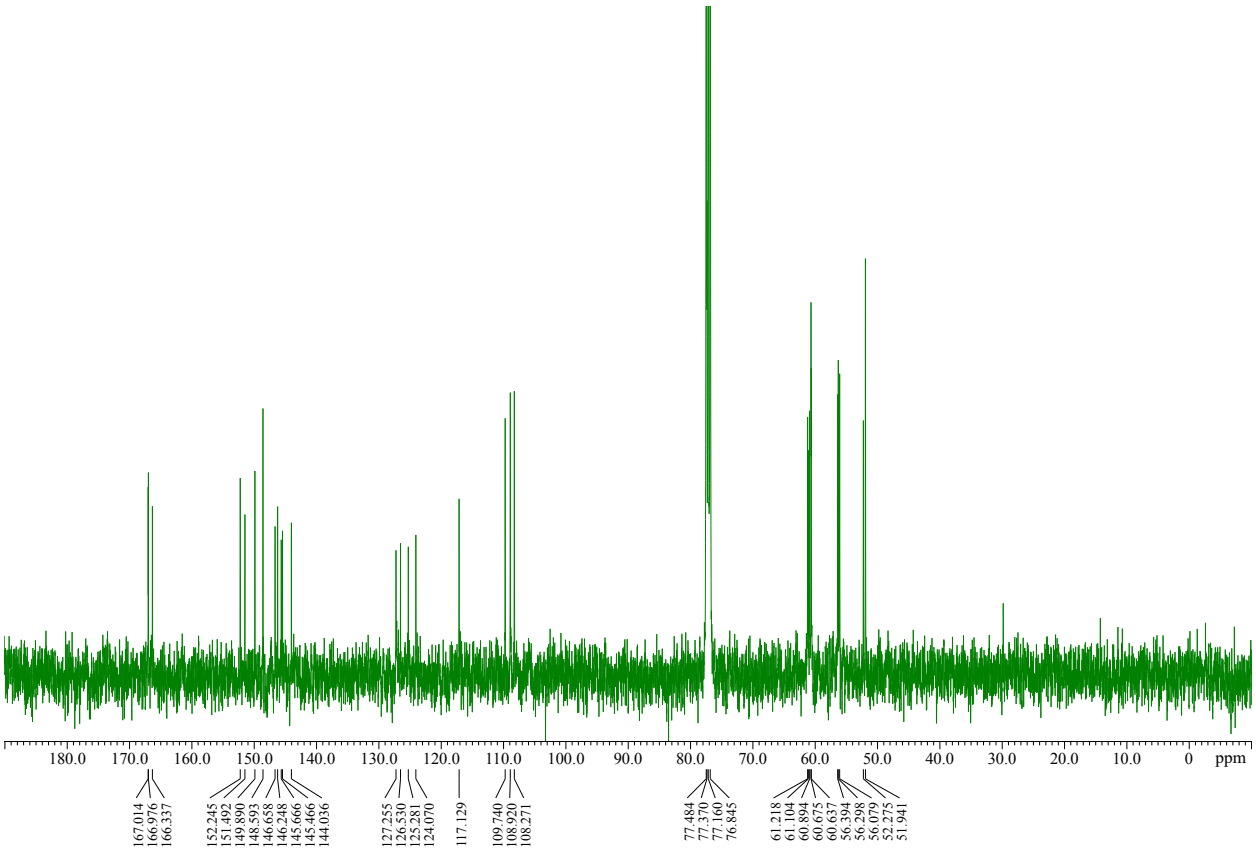
| Position | Lit. data (ppm) | Synthesized **36** (ppm) | Δ(Lit – Obs) (ppm) |
|---|---|---|---|
| Aryl | 7.39 | 7.40 | –0.01 |
| | 7.34 | 7.34 | 0.00 |
| | 7.18 | 7.18 | 0.00 |
| OMe | 3.93 | 3.93 | 0.00 |
| | 3.91 | 3.92 | –0.01 |
| | 3.88 | 3.880 | 0.00 |
| | | 3.877 | 0.003 |
| | 3.81 | 3.81 | 0.00 |
| | 3.76 | 3.76 | 0.00 |
| | 3.63 | 3.63 | 0.00 |
| | 3.62 | 3.62 | 0.00 |
| | 3.61 | 3.61 | 0.00 |
| | 3.38 | 3.38 | 0.00 |

The literature data are in reference 20.

$^{1}$H NMR spectrum of **36**, 400 MHz in chloroform-*d*




$^{13}$C NMR spectrum of **36**, 101 MHz in chloroform-*d*



**ESI-28. Additional Reference**

(21) G. Cainelli, C. Angeloni, R. Cervellati, P. Galletti, D. Giacomini, S. Hrelia and R. Sinisi, *Chem. Biodivers*., 2008, **5**, 811.