



## Supporting Information

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## Supporting Information

### **Solid-Phase Synthesis of Epigallocatechin Gallate Derivatives .**

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## General Techniques

NMR spectra were recorded on a JEOL Model ECP-400 (400 MHz for <sup>1</sup>H, 100 MHz for <sup>13</sup>C) instrument in the indicated solvent. Chemical shifts are reported in units parts per million (ppm) relative to the signal (0 ppm) for internal tetramethylsilane for solutions in CDCl<sub>3</sub>. <sup>1</sup>H NMR spectrum data are reported as follows: CDCl<sub>3</sub> (7.26 ppm) or CD<sub>3</sub>OD (3.30 ppm), acetone-*d*<sub>6</sub> (2.00 ppm), DMSO-*d*<sub>6</sub> (2.50 ppm). <sup>13</sup>C NMR spectrum data are reported as follows: CDCl<sub>3</sub> (77.1 ppm) or acetone-*d*<sub>6</sub> (30.3 ppm) as internal standard for D<sub>2</sub>O. Multiplicities are reported by using the following abbreviations: s; singlet, d; doublet, t; triplet, q; quartet, m; multiplet, br; broad, *J*; coupling constants in Hertz.

IR spectra was recorded on a Perkin-Elmer Spectrum One FT-IR spectrophotometer. Only the strongest and/or structurally important peaks are reported as the IR data given in cm<sup>-1</sup>.

All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light, visualized by 10% ethanolic phosphomolybdic acid, *p*-anisaldehyde solution.

Merck silica gel was used for column chromatography.

Gel permeation chromatography (GPC) for qualitative analysis were performed on Japan Analytical Industry Model LC908 (recycling preparative HPLC), on a Japan Analytical Industry Model RI-5 refractive index detector and on a Japan Analytical Industry Model 310 ultra violet detector with a polystyrene gel column (JAIGEL-1H, 20mm x 600 mm), using chloroform as solvent (3.5 mL / min).

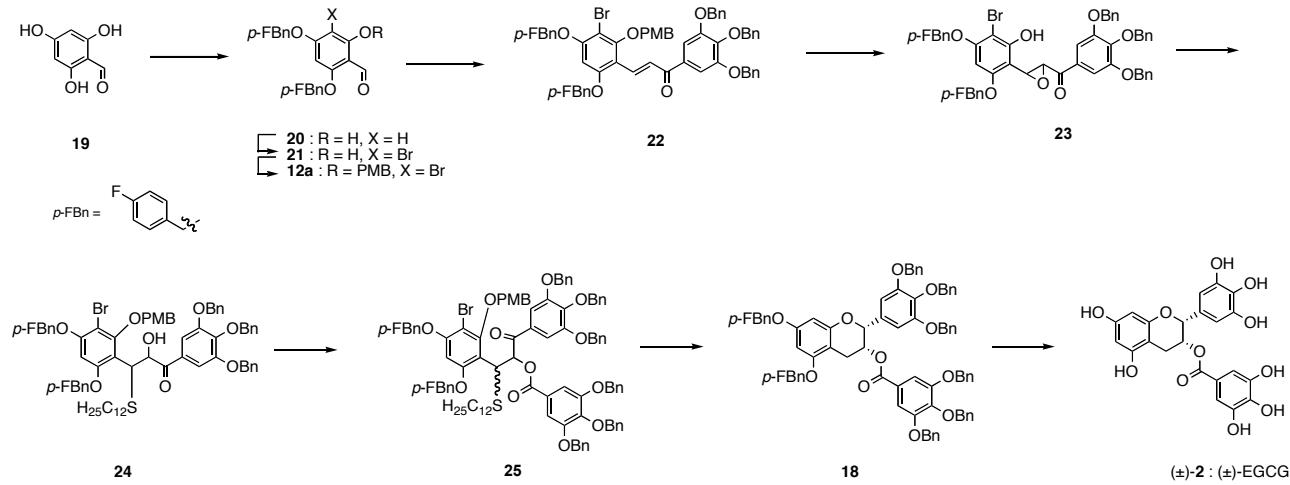
ESI-TOF Mass spectra were measured with Waters LCT Premier<sup>TM</sup> XE.

Dry dichloromethane was distilled from P<sub>2</sub>O<sub>5</sub>. Dry triethylamine and dry acetonitrile were distilled from CaH<sub>2</sub>.

LC/MS were obtained on Hewlett-Pachard Series 1100 (GL Science Inc. Inertsil ODS-3, 3 $\mu$ m, 4.6 x 75 mm with a linear gradient of 10 % acetonitrile containing 0.1% formic acid/water containing 0.1% formic acid to 80% acetonitrile containing 0.1% formic acid/water containing 0.1% formic acid over 3 min, to 100% acetonitrile containing 0.1% formic acid further 10 min at 10 mL mon-1 flow rat).

## Experimental Section

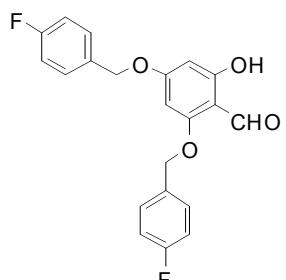
### Solution-Phase Synthesis of Epigallocatechin-3-gallate (2)



### 2,4-Bis(4-fluorobenzyloxy)-6-hydroxybenzaldehyde (20)

To a suspension of 2,4,6-trihydroxybenzaldehyde (**19**) (5.00 g, 26.3 mmol, 1.00 eq.) in DMF (55.0 mL) was added  $\text{K}_2\text{CO}_3$  (8.36 g, 60.5 mmol, 2.30 eq.) at 0 °C under argon. After the reaction mixture was stirred at the same temperature for 5 min, a solution of 4-fluorobenzyl bromide (6.55 mL, 52.6 mmol, 2.00 eq.) in DMF (15.0 mL) was added dropwise to the reaction mixture. After being stirred at the room temperature for 16 h, the reaction mixture was poured into the mixture of 1 M aqueous HCl and ethyl acetate at 0 °C. The aqueous layer was extracted with two portions of ethyl acetate. The combined organic layers were washed with three portions of  $\text{H}_2\text{O}$  and brine, dried over  $\text{MgSO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (elution with chloroform), and recrystallized from  $\text{CH}_2\text{Cl}_2$ -hexane to afford benzaldehyde **20** (2.86 g, 7.65 mmol, 29% yield) as a white solid.

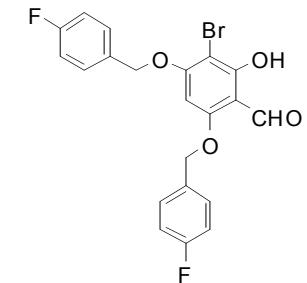
TLC  $R_f$  0.49 (hexane/ethyl acetate = 2/1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  12.50 (s, 1H), 10.14 (s, 1H), 7.38 (dd,  $J$  = 8.2 Hz,  $J_{\text{H},\text{F}}$  = 5.3 Hz, 2H), 7.37 (dd,  $J$  = 8.2 Hz,  $J_{\text{H},\text{F}}$  = 5.3 Hz, 2H), 7.09 (dd,  $J$  = 8.2 Hz,  $J_{\text{H},\text{F}}$  = 8.7 Hz, 4H), 6.10 (d,  $J$  = 1.9 Hz, 1H), 6.04 (d,  $J$  = 1.9 Hz, 1H), 5.04 (s, 2H), 5.03 (s, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.9, 166.9, 166.4, 162.8x2 ( $J_{\text{C},\text{F}}$  = 247 Hz), 162.5, 131.5 ( $J_{\text{C},\text{F}}$  = 3.0 Hz), 131.4 ( $J_{\text{C},\text{F}}$  = 3.0 Hz), 129.6 ( $J_{\text{C},\text{F}}$  = 8.4 Hz), 129.4 ( $J_{\text{C},\text{F}}$  = 8.4 Hz), 115.8 ( $J_{\text{C},\text{F}}$  = 21.3 Hz), 106.4, 94.2, 92.4, 70.0, 69.8; FT-IR (solid) 3037, 2873, 1624, 1575, 1510, 1291, 1153, 828, 795, 585, 504  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{21}\text{H}_{16}\text{F}_2\text{O}_4$ : C, 68.11; H, 4.35. Found: C, 67.80; H, 4.47.



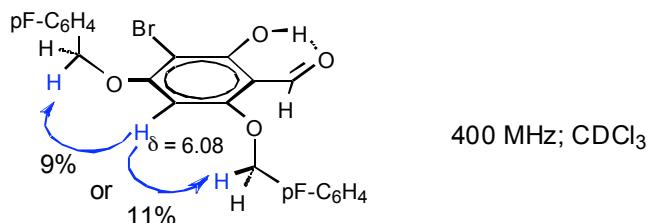
### 4,6-Bis(4-fluorobenzyl)oxy-3-bromo-2-hydroxybenzaldehyde (12a)

To a solution of the benzaldehyde **20** (1.51 g, 4.09 mmol, 1.00 eq.) in  $\text{CH}_2\text{Cl}_2$  (10.0 mL) was added dropwise a solution of bromine (209  $\mu\text{L}$ , 4.09 mmol, 1.00 eq.) in  $\text{CH}_2\text{Cl}_2$  at 0 °C under argon. After being stirred at the same temperature for 20 min, the reaction mixture was poured into the mixture of 10 wt% aqueous  $\text{Na}_2\text{S}_2\text{O}_3$ , saturated aqueous  $\text{NaHCO}_3$  and ethyl acetate at 0 °C. The aqueous layer was extracted with two portions of ethyl acetate. The combined organic layers were washed with brine, dried over  $\text{MgSO}_4$ , and concentrated *in vacuo*. The residue was recrystallized from  $\text{CH}_2\text{Cl}_2$ -hexane to afford bromide **12a** (1.51 g, 3.37 mmol, 82% yield) as a pale yellow solid. Structure determination of the bromide **12a** was achieved by analysis of  $^1\text{H}$  nOe spectra.

TLC  $R_f$  0.41 (hexane/ethyl acetate = 2/1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  12.94 (s, 1H), 10.12 (s, 1H), 7.40 (dd,  $J$  = 8.2 Hz,  $J_{\text{H},\text{F}}$  = 5.3 Hz, 2H), 7.35 (dd,  $J$  = 8.2 Hz,  $J_{\text{H},\text{F}}$  = 5.3 Hz, 2H), 7.09 (dd,  $J$  = 8.2 Hz,  $J_{\text{H},\text{F}}$  = 8.7 Hz, 4H), 6.08 (s, 1H), 5.16 (s, 2H), 5.07 (s, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.6, 164.0, 162.9 ( $J_{\text{C},\text{F}}$  = 247 Hz), 162.7 ( $J_{\text{C},\text{F}}$  = 247 Hz), 162.6, 162.1, 161.6, 131.1 ( $J_{\text{C},\text{F}}$  = 3.0 Hz), 131.0 ( $J_{\text{C},\text{F}}$  = 3.0 Hz), 129.4 ( $J_{\text{C},\text{F}}$  = 7.6 Hz), 128.8 ( $J_{\text{C},\text{F}}$  = 8.4 Hz), 116.0 ( $J_{\text{C},\text{F}}$  = 21.3 Hz), 115.9 ( $J_{\text{C},\text{F}}$  = 22.1 Hz), 106.8, 91.8, 89.7, 70.5, 70.3; FT-IR (solid) 3048, 2924, 1646, 1604, 1515, 1301, 1240, 1199, 1118, 972, 787, 716  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{21}\text{H}_{15}\text{BrF}_2\text{O}_4$ : C, 56.14; H, 3.37. Found: C, 56.26; H, 3.37.



#### nOe observation



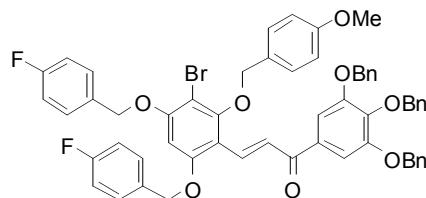
### 3-[4,6-Bis(4-fluorobenzyl)oxy-3-bromo-2-(4-methoxybenzyl)oxyphenyl]-1-[3,4,5-tris(benzyl)phenyl]prop-2-en-1-one (22)

To a suspension of benzaldehyde **12a** (894 mg, 1.99 mmol, 1.00 eq.) and  $\text{Cs}_2\text{CO}_3$  (1.30 g, 3.98 mmol, 2.00 eq.) in DMF (10.0 mL) was added 4-methoxybenzyl chloride (565  $\mu\text{L}$ , 4.15 mmol, 2.08 eq.) and sodium iodide (120 mg, 796  $\mu\text{mol}$ , 0.40 eq.) at room temperature under argon. After being stirred at the same temperature for 11 h, the reaction mixture was poured into the mixture of  $\text{H}_2\text{O}$  and ethyl acetate. The aqueous layer was extracted with two portions of ethyl acetate. The combined organic layers were washed with two portions of  $\text{H}_2\text{O}$  and brine, dried over  $\text{MgSO}_4$ , and concentrated *in vacuo*. The crude mixture was used for the next reaction without further purification.

To a solution of the above residue in THF (5.00 mL) was added 3',4',5'-tris(benzyl)acetophenone (**11a**) (829 mg, 1.89 mmol, 0.95 eq.) and sodium methoxide (322 mg, 5.97 mmol, 3.00 eq.) at room temperature. After being stirred at the same temperature for 3 h, the reaction mixture was poured into the mixture of  $\text{H}_2\text{O}$  and ethyl

acetate at 0 °C. The aqueous layer was extracted with two portions of ethyl acetate. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated *in vacuo*. The residue was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>-hexane to afford chalcone **22** (1.62 g, 1.64 mmol, 82% yield in 2 steps) as a pale yellow solid.

TLC R<sub>f</sub> 0.57 (toluene/acetone = 20/1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.16 (d, *J* = 15.9 Hz, 1H), 7.95 (d, *J* = 15.9 Hz, 1H), 7.31-7.45 (m, 21H), 7.22 (s, 2H), 7.10 (dd, *J* = 8.2 Hz, 8.7 Hz, 2H), 7.04 (dd, *J* = 8.2 Hz, 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.42 (s, 1H), 5.11 (s, 4H), 5.09 (s, 2H), 4.95 (s, 4H), 4.84 (s, 2H), 3.64 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 189.7, 162.7 (*J*<sub>C,F</sub> = 248 Hz), 160.0, 158.9, 157.6, 157.5, 152.7, 142.5, 137.6, 136.7, 135.3, 133.8, 131.6x2 (*J*<sub>C,F</sub> = 3.0 Hz), 130.8, 129.1 (*J*<sub>C,F</sub> = 7.6 Hz), 128.9 (*J*<sub>C,F</sub> = 8.4 Hz), 128.5, 128.2x2, 128.0x2, 127.8, 123.9, 115.9 (*J*<sub>C,F</sub> = 21.3 Hz), 115.8 (*J*<sub>C,F</sub> = 21.3 Hz), 114.0, 113.8, 108.3, 101.1, 96.0, 75.3, 75.2, 71.2, 70.6x2, 55.2; FT-IR (solid) 3031, 2936, 1643, 1586, 1251, 1184, 1159, 1093, 1031, 885, 799, 733, 698 cm<sup>-1</sup>; Anal. Calcd for C<sub>58</sub>H<sub>47</sub>BrF<sub>2</sub>O<sub>8</sub>: C, 70.37; H, 4.79. Found: C, 70.22; H, 4.81.

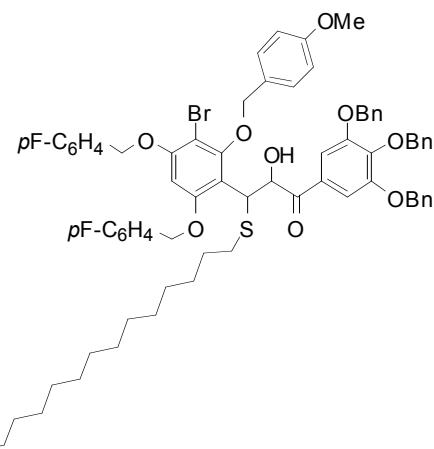


### 3-[4,6-Bis(4-fluorobenzyl)oxy]-3-bromo-2-(4-methoxybenzyl)phenyl]-3-dodecylsulfanyl-2-hydroxy-1-[3,4,5-tris(benzyl)phenyl]propan-1-one (24)

To a solution of chalcone **22** (200 mg, 202 μmol, 1.00 eq.) in CH<sub>2</sub>Cl<sub>2</sub> (3.00 mL) was added 30 wt% aqueous H<sub>2</sub>O<sub>2</sub> (2.29 mL, 20.2 mmol, 100 eq.), 3 M aqueous KOH (1.00 mL) and Bu<sub>4</sub>N · HSO<sub>4</sub> (137 mg, 404 μL, 2.00 eq.) at room temperature. After being stirred at the same temperature for 26 h, the reaction mixture was poured into saturated aqueous Na<sub>2</sub>SO<sub>3</sub> and ethyl acetate at 0 °C. The aqueous layer was extracted with two portions of ethyl acetate. The combined organic layers were washed with saturated aqueous Na<sub>2</sub>SO<sub>3</sub>, brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The crude mixture was used for the next reaction without further purification.

To a solution of the crude in acetonitrile (2.02 mL) and CH<sub>2</sub>Cl<sub>2</sub> (750 μL) was added 1-dodecanethiol (73.0 μL, 303 μmol, 1.50 eq.) and Zn(OTf)<sub>2</sub> (14.7 mg, 40.4 μmol, 0.20 eq.) at room temperature under argon. After being stirred at the same temperature for 15 min, the mixture was quenched by addition of triethylamine and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (elution with 20% ethyl acetate in hexane) to afford a diastereo mixture of α-hydroxyketones **24** (210 mg, 174 μmol, 86% in 2 steps) as a white solid.

TLC R<sub>f</sub> 0.45 (hexane/ethyl acetate = 3/1); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 7.02-8.31 (m, 45H), 6.96 (d, *J* = 8.2 Hz, 1.3H), 6.85 (d, *J* = 8.2 Hz, 0.7H), 6.75 (s, 0.32H), 6.66 (s, 0.09H), 6.62 (s, 0.59H), 6.25 (d, *J* = 7.7 Hz, 0.64H), 6.16 (d, *J* = 6.8 Hz, 0.05H), 6.09 (d, *J* = 7.3 Hz, 0.31H), 5.71 (br t, *J* = 9.7, 8.2 Hz, 0.38H), 5.61 (br t, *J* = 8.7 Hz, 0.62H), 4.77-5.29 (m, 12.4H), 4.57 (d, *J* = 9.7 Hz, 0.60H), 3.75 (s,

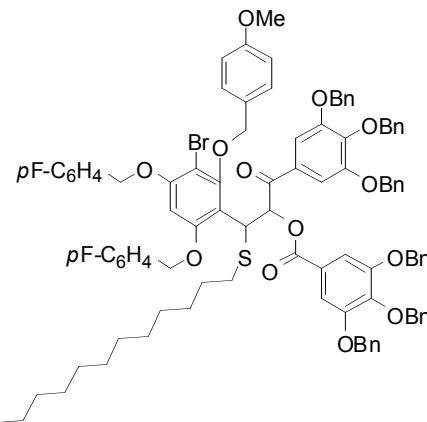


2.1H), 3.60 (s, 0.9H), 2.60-2.71 (m, 2H), 0.83-1.49 (m, 23H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  198.9, 198.7, 161.7 ( $J_{\text{C},\text{F}} = 244$  Hz), 161.6 ( $J_{\text{C},\text{F}} = 244$  Hz), 159.1, 156.7, 155.6, 155.2, 155.1, 154.8, 153.4, 151.8x2, 141.2, 141.0, 137.3, 136.5, 132.6 ( $J_{\text{C},\text{F}} = 2.3$  Hz), 132.5 ( $J_{\text{C},\text{F}} = 2.3$  Hz), 131.7, 131.5, 130.0, 129.6 ( $J_{\text{C},\text{F}} = 8.4$  Hz), 129.4 ( $J_{\text{C},\text{F}} = 7.6$  Hz), 128.8, 128.3, 128.1, 128.0x2, 127.9, 127.7, 127.6, 117.1, 115.2 ( $J_{\text{C},\text{F}} = 21.3$  Hz), 113.7, 107.1, 106.7, 99.1, 74.4, 74.3, 74.0, 73.5, 72.6, 70.3, 70.1, 69.9, 69.8x2, 69.4, 55.0, 54.8, 44.6, 40.4, 33.6, 33.4, 31.3, 29.7, 29.6, 29.0, 28.7, 28.6, 28.5, 28.4, 22.1; FT-IR (solid) 3471, 2924, 2855, 1674, 1608, 1589, 1514, 1103, 914, 824, 733, 697  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{70}\text{H}_{74}\text{F}_2\text{BrO}_9\text{S} [\text{M}+\text{H}]^+$  1207.4205, found 1207.4204.

**3-[4,6-Bis(4-fluorobenzyl)oxy]-3-bromo-2-(4-methoxybenzyl)oxyphenyl]-3-dodecylsulfanyl-1-[3,4,5-tris(benzyl)oxy]propan-1-one-2-yl 3,4,5-tris(benzyl)oxybenzoate (25)**

To a solution of hydroxyketone **24** (195 mg, 162  $\mu\text{mol}$ , 1.00 eq.) in pyridine (800  $\mu\text{L}$ ) was added 3,4,5-tris(benzyl)benzoic acid (**7a**) (92.5 mg, 210  $\mu\text{mol}$ , 1.30 eq.), EDCI  $\cdot$  HCl (55.3 mg, 288  $\mu\text{mol}$ , 1.78 eq.) and DMAP (3.90 mg, 32.4  $\mu\text{mol}$ , 0.20 eq.) at room temperature under argon. After being stirred at the same temperature for 20 h, the reaction mixture was poured into 1 M aqueous HCl and ethyl acetate at 0  $^{\circ}\text{C}$ . The aqueous layer was extracted with two portions of ethyl acetate. The combined organic layers were washed with 1 M aqueous HCl, saturated aqueous  $\text{NaHCO}_3$ , brine, dried over  $\text{MgSO}_4$ , and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (elution with toluene) to afford a diastereo mixture of acyloxyketones **25** (219 mg, 134  $\mu\text{mol}$ , 83% yield) as a white solid.

TLC  $R_f$  0.51 (hexane/ethyl acetate = 2/1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.70-7.65 (m, 46H), 6.40 (s, 0.05H), 6.13 (s, 0.36H), 5.94 (s, 0.59H), 5.39 (d,  $J = 9.2$  Hz, 0.31H), 4.65-5.17 (m, 19.69H), 3.79 (s, 0.15H), 3.70 (s, 1.86H), 3.65 (s, 0.99H), 2.61-2.88 (m, 2H), 0.85-1.66 (m, 23H); FT-IR (solid) 3020, 2928, 1713, 1691, 1588, 1514, 1216, 1107, 927, 757, 669  $\text{cm}^{-1}$ .

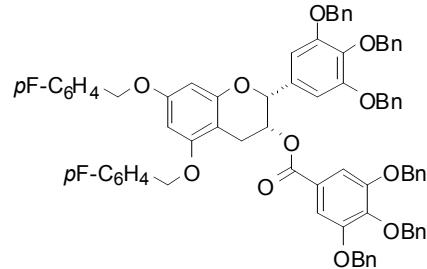


**cis-5,7-Bis(4-fluorobenzyl)oxy-2-[3,4,5-tris(benzyl)oxyphenyl]chroman-3-yl 3,4,5-tris(benzyl)oxybenzoate (18)**

To a solution of acyloxyketone **25** (100 mg, 61.5  $\mu\text{mol}$ , 1.00 eq.) in  $\text{CH}_2\text{Cl}_2$  (1.50 mL) was added trifluoroacetic acid (300  $\mu\text{L}$ ) at -10  $^{\circ}\text{C}$  under argon. After being stirred at -10  $^{\circ}\text{C}$  for 2 h, the reaction mixture was treated with triethylsilane (200  $\mu\text{L}$ ). After being stirred at the same temperature for further 1 h, the reaction mixture was quenched by addition of triethylamine, diluted with toluene, and concentrated *in vacuo*. The residue was purified by gel permeation chromatography (GPC) to afford chroman **18** (64.7 mg, 53.2  $\mu\text{mol}$ , 87% yield) as a white solid.

TLC  $R_f$  0.43 (hexane/ethyl acetate = 2/1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.19-7.39 (m, 36H), 7.00-7.07 (m, 4H),

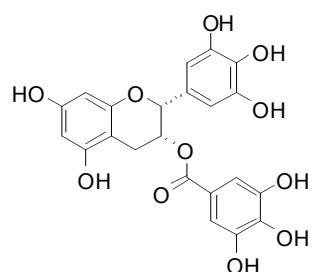
6.73 (s, 2H), 6.38 (d,  $J$  = 1.9 Hz, 1H), 6.30 (d,  $J$  = 1.9 Hz, 1H), 5.65 (br s, 1H), 5.04 (s, 1H), 4.66-5.01 (m, 16H), 3.10 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 4.4 Hz, 1H), 3.03 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 2.4 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  164.9, 162.6x2 ( $J_{\text{C,F}} = 247$  Hz), 158.8, 158.0, 155.8, 153.0, 152.5, 142.9, 138.6, 137.8, 137.5, 137.0, 136.5, 133.2, 132.6 ( $J_{\text{C,F}} = 3.0$  Hz), 129.4 ( $J_{\text{C,F}} = 8.4$  Hz), 129.1 ( $J_{\text{C,F}} = 8.4$  Hz), 128.6x2, 128.5, 128.4, 128.3, 128.2x2, 128.0, 127.9, 127.8, 127.6x2, 125.0, 115.6 ( $J_{\text{C,F}} = 22.1$  Hz), 109.3, 106.9, 101.2, 94.8, 94.1, 78.1, 75.2, 75.1, 71.3, 71.2, 69.6, 69.5, 68.3, 26.3; FT-IR (solid) 3033, 2870, 1717, 1620, 1594, 1512, 1455, 1369, 1220, 1118, 909, 819, 734, 696, 502  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{78}\text{H}_{64}\text{F}_2\text{O}_{11}$   $[\text{M}+\text{H}]^+$  1215.4495, found 1215.4495.; Anal. Calcd for  $\text{C}_{78}\text{H}_{64}\text{F}_2\text{O}_{11}$ : C, 77.08; H, 5.31. Found: C, 76.76; H, 5.41.



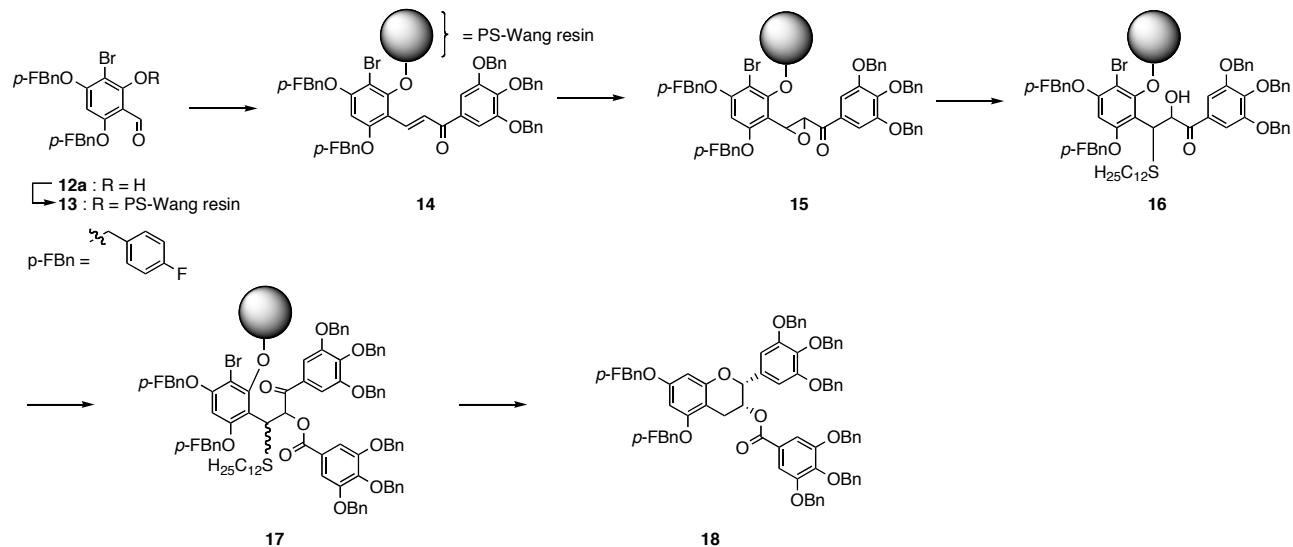
### ( $\pm$ )-Epigallocatechin-3-gallate (2)

To a stirred solution of chroman **52** (9.10 mg, 7.45  $\mu\text{mol}$ , 1.00 eq.) in THF/methanol (1:1, 2.00 mL) was added 20 wt%  $\text{Pd}(\text{OH})_2$  (19.1 mg) and formic acid (5.00  $\mu\text{L}$ ) at room temperature. The reaction mixture was hydrogenolyzed for 29 h under hydrogen gas atmosphere. The reaction mixture was filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (elution with 10% methanol in  $\text{CH}_2\text{Cl}_2$ ) to afford epigallocatechin-3-gallate (**1**) (2.80 mg, 6.11  $\mu\text{mol}$ , 82% yield) as a white solid.

$^1\text{H}$  NMR (400 MHz, acetone- $d_6$ / $\text{D}_2\text{O}$  = 1/1);  $\delta$  6.86 (s, 2H), 6.51 (s, 2H), 5.89 (s, 2H), 5.27 (br s, 1H), 4.89 (s, 1H), 2.87 (dd,  $J_{\text{gem}} = 17.4$  Hz,  $J$  = 4.4 Hz, 1H), 2.76 (br d,  $J_{\text{gem}} = 17.4$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz, acetone- $d_6$ / $\text{D}_2\text{O}$  = 1/1)  $\delta$  167.3, 157.0, 156.9, 156.8, 146.0, 145.7, 139.3, 133.0, 130.6, 121.0, 110.2, 106.8, 99.0, 96.5, 95.8, 77.9, 70.3, 26.4; FT-IR (solid) 3508, 1687, 1608, 1451, 1227, 1029, 730, 549  $\text{cm}^{-1}$ .



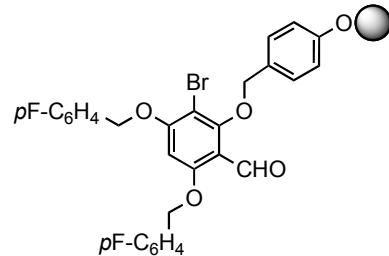
## Solid-Phase Synthesis



## Polymer-supported 4,6-bis(4-fluorobenzyloxy)-3-bromo-2-hydroxybenzaldehyde (13)

PS-Wang-Br resin<sup>®</sup> (Novabiochem, 1.6 mmol/g loading, 140 mg) was placed in a syringe-shaped vessel. To this reaction vessel was added a suspension of hydroxybenzaldehyde **12a** (180 mg, 400  $\mu\text{mol}$ ) in DMF (2.00 mL),  $\text{Cs}_2\text{CO}_3$  (130 mg, 400  $\mu\text{mol}$ ) and sodium iodide (15.0 mg, 120  $\mu\text{mol}$ ) at room temperature. After being shaken at the same temperature for 24 h, the solvent was removed and the resin was rinsed with DMF (10 min). The remained resin was washed consecutively with DMF/H<sub>2</sub>O (2:1, 10 min x 3), DMF (10 min x 3), methanol (10 min x 3),  $\text{CH}_2\text{Cl}_2$  (10 min x 3), and dried under reduced pressure to afford polymer-supported benzaldehyde **13** (202.5 mg).

FT-IR (solid) 3025, 2909, 1685, 1615, 1104, 923, 851, 701, 576  $\text{cm}^{-1}$ .



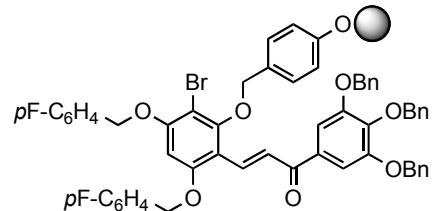
## Procedure for Cleavage from PS resins

A part of the polymer-supported benzaldehyde **13** (84.8 mg) was placed in a syringe-shaped vessel. To this reaction vessel was added a solution of trifluoroacetic acid (50.0  $\mu\text{L}$ ) in  $\text{CH}_2\text{Cl}_2$  (1.95 mL) at room temperature. After being shaken at the same temperature for 1 h, the reaction vessel was filtered and washed with  $\text{CH}_2\text{Cl}_2$  (5 min x 3). The filtrate was concentrated *in vacuo*. The residue was purified by short-pad column chromatography (elution with chloroform) to afford benzaldehyde **12a** (20.3 mg, 45.2  $\mu\text{mol}$ , 48% yield based on the resin).

**Polymer-supported 3-[4,6-bis(4-fluorobenzyl)oxy]-3-bromo-2-(4-methoxybenzyl)phenyl]-1-[3,4,5-tris(benzyl)oxy]prop-2-en-1-one (14)**

Polymer-supported benzaldehyde **13** (118 mg, 62.5  $\mu$ mol) was placed in a syringe-shaped vessel. To this reaction vessel was added 3',4',5'-tris(benzyl)acetophenone (**11a**) (329 mg, 750  $\mu$ mol) in THF (1.20 mL) at room temperature. After being shaken for 15 min, the reaction mixture was added 0.5 M sodium methoxide in methanol (300  $\mu$ L). After being shaken for 24 h, the solvent was removed and rinsed with THF (10 min). The remained resin was washed consecutively with THF (10 min x 3), methanol (10 min x 3),  $\text{CH}_2\text{Cl}_2$  (10 min x 3), and dried under reduced pressure to afford polymer-supported chalcone **14**.

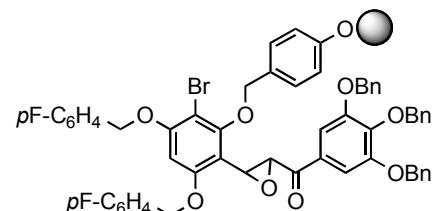
FT-IR (solid) 3028, 2925, 1655, 1583, 1174, 1104, 828, 740  $\text{cm}^{-1}$ .



**Polymer-supported 3-[4,6-bis(4-fluorobenzyl)oxy]-3-bromo-2-(4-methoxybenzyl)phenyl]-2,3-epoxy-1-[3,4,5-tris(benzyl)oxy]propan-1-one (15)**

The polymer-supported chalcone **14** was placed in a syringe-shaped vessel. To this reaction vessel was added 5.5 M *t*-butyl hydrogen peroxide in decane (380  $\mu$ L, 2.09 mmol),  $\text{CH}_2\text{Cl}_2$  (1.00 mL) and 2.5 M KOH in methanol (120  $\mu$ L) at room temperature. After being shaken for 72 h, the solvent was removed and the resin was rinsed with  $\text{CH}_2\text{Cl}_2$  (10 min). The remained resin was washed consecutively with methanol (10 min x 4),  $\text{CH}_2\text{Cl}_2$  (10 min x 4), and dried under reduced pressure to afford the polymer-supported epoxide **15**.

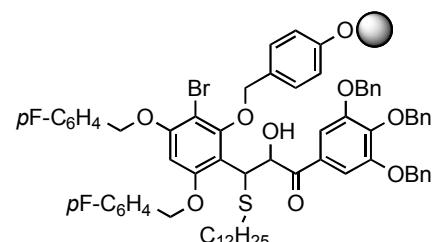
FT-IR (solid) 3464, 3027, 2921, 1676, 1610, 1158, 1078, 1028, 829, 739  $\text{cm}^{-1}$ .



**Polymer-supported 3-[4,6-bis(4-fluorobenzyl)oxy]-3-bromo-2-(4-methoxybenzyl)phenyl]-3-dodecylsulfanyl-2-hydroxy-1-[3,4,5-tris(benzyl)oxy]propan-1-one (16)**

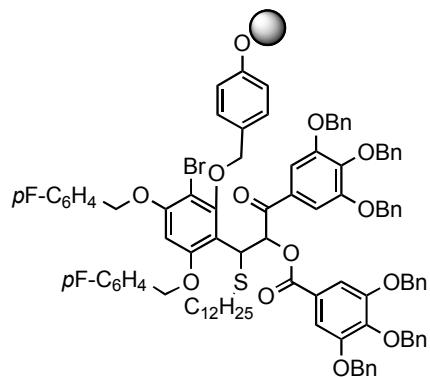
Polymer-supported epoxide **15** was placed in a syringe-shaped vessel. To this reaction vessel was added dodecanethiol (180  $\mu$ L, 2.09 mmol),  $\text{CH}_2\text{Cl}_2$  (750  $\mu$ L) and 0.02 M  $\text{Zn}(\text{OTf})_2$  in acetonitrile (750  $\mu$ L, 15.0  $\mu$ mol) at room temperature. After being shaken for 3 h, the solution was quenched by addition of triethylamine, and the solvent was removed and the resin was rinsed with  $\text{CH}_2\text{Cl}_2$  (10 min). The remained resin was washed consecutively with acetonitrile (10 min x 2), methanol (10 min x 4),  $\text{CH}_2\text{Cl}_2$  (10 min x 4), and dried under reduced pressure to afford polymer-supported hydroxyketone **16**.

FT-IR (solid) 3490, 3028, 2927, 1667, 1173, 1079, 1030, 829, 737  $\text{cm}^{-1}$ .



**Polymer-supported 3-[4,6-bis(4-fluorobenzyl)oxy]-3-bromo-2-(4-methoxybenzyl)phenyl]-3-dodecylsulfanyl-1-[3,4,5-tris(benzyl)oxy]phenyl]propan-1-one-2-yl 3,4,5-tris(benzyl)benzoate (17)**

Polymer-supported  $\alpha$ -hydroxyketone **16** was packed in MacroKan<sup>TM</sup>. In flask, to a suspension of MacroKan<sup>TM</sup> and 3,4,5-tris(benzyl)benzoic acid (441 mg, 1.00 mmol), in pyridine/DMF (1:1, 5.00 mL) was added EDCI  $\cdot$  HCl (192 mg, 1.00 mmol) and DMAP (36.6 mg, 300  $\mu$ mol) at 50 °C. After being stirred at the same temperature for 48 h, the reaction mixture was filtered and the MacroKan<sup>TM</sup> was rinsed with DMF (10 min). The MacroKan<sup>TM</sup> was washed consecutively with DMF (10 min x 3), DMF/H<sub>2</sub>O (2:1, 10 min x 3), CH<sub>2</sub>Cl<sub>2</sub> (10 min x 3), methanol (10 min x 3), and dried under reduced pressure to afford polymer-supported acyloxyketone **17**. FT-IR (solid) 3029, 2932, 1718, 1676, 1028, 1017, 828, 737, 702 cm<sup>-1</sup>.



**Procedure for the Release and cyclization of **17** to provide (**18**)**

To a suspension of polymer-supported acyloxyketone **17** was added trifluoroacetic acid (0.600 mL) in CH<sub>2</sub>Cl<sub>2</sub> (2.00 mL). After being stirred at -10 °C for 5 h, to the reaction mixture was added triethylsilane (0.400 mL). After being stirred at the same temperature for further 19 h, the reaction mixture was filtered. The remained resin was rinsed with ethyl acetate and the filtrate was concentrated *in vacuo*. The residue was purified by gel permeation chromatography (GPC) to afford chroman **18**.

**Parallel synthesis of 60-membered EGCG analogues**

**General Procedure for Loading of 4,6-*O*-protective-2-hydroxybenzaldehyde**

Each MiniKans<sup>TM</sup> contained PS-Wang-Br resin<sup>®</sup> (Novabiochem, 1.6 mmol/g loading, ca. 70 mg) and color tag. To suspension of hydroxybenzaldehydes **12a-b** (0.2 M) and MiniKans<sup>TM</sup> in DMF was added Cs<sub>2</sub>CO<sub>3</sub> (0.2 M) and sodium iodide (0.06 M) at room temperature. After being shaken at the same temperature for 24 h, the reaction mixture was filtered. The resin was washed with DMF/H<sub>2</sub>O (2:1, 10 min x 3), DMF (10 min x 3), methanol (10 min x 3), CH<sub>2</sub>Cl<sub>2</sub> (10 min x 3), and dried under reduced pressure to afford the polymer-supported benzaldehydes, respectively.

**General Procedure for Cleavage from PS resins**

To a MiniKans<sup>TM</sup> in 10 mL vial was added a solution of trifluoroacetic acid (50.0  $\mu$ L) in CH<sub>2</sub>Cl<sub>2</sub> (1.95 mL) at room temperature. After being shaken at the same temperature for 1 h, MiniKans<sup>TM</sup> was filtered and washed with CH<sub>2</sub>Cl<sub>2</sub> (5 min x 3). The filtrate was concentrated *in vacuo*. The residue was purified by short-pad column chromatography (elution with chloroform).

**General Procedure for aldol condensation with ketones **11a-f****

The 60 MiniKans™ were sorted and distributed into six sets of 10 MiniKans™. To a suspension of each set of MiniKans™ and ketones **11a-f** (7.50 mmol) in THF (12.0 mL) was added a solution of sodium methoxide (81.0 mg, 1.50 mmol) in methanol (3.00 mL) at room temperature. After being shaken for 36 h, the reaction mixture was filtered and the MiniKans™ were rinsed with THF (10 min). All MiniKans™ were pooled together, and washed consecutively with THF (10 min x 3), THF/H<sub>2</sub>O (2:1, 10 min x 3), CH<sub>2</sub>Cl<sub>2</sub> (10 min x 3), methanol (10 min x 3), and dried under reduced pressure.

#### Procedure for epoxidation

The 60 MiniKans™ in CH<sub>2</sub>Cl<sub>2</sub> (50.0 mL) at room temperature were treated with a solution of 5.5 M *t*-butyl hydrogen peroxide in decane (19.0 mL) and a solution of 2.5 M KOH in methanol (19.0 mL). After being shaken for 72 h, the solvent was removed. The MiniKans™ were rinsed with CH<sub>2</sub>Cl<sub>2</sub> (10 min). The MiniKans™ were washed consecutively with CH<sub>2</sub>Cl<sub>2</sub> (10 min x 4), methanol (10 min x 4), and dried under reduced pressure.

#### Procedure for epoxide opening

The 60 MiniKans™ in dry CH<sub>2</sub>Cl<sub>2</sub>/acetonitrile (1:1, 80.0 mL) at room temperature were treated with dodecanol (9.59 mL, 40.0 mmol) and Zn(OTf)<sub>2</sub> (291 mg, 800  $\mu$ mol). After being vigorously shaken for 3 h, the solution was quenched by addition of triethylamine, and the solvent was removed and the MiniKans™ were rinsed with acetonitrile (10 min). The MiniKans™ were washed consecutively with acetonitrile (10 min x 3), CH<sub>2</sub>Cl<sub>2</sub> (10 min x 3), methanol (10 min x 3), and dried under reduced pressure.

#### General Procedure for acylation with acid **7a-e**

The 60 MiniKans™ were sorted and distributed into five sets of 12 MiniKans™. To a suspension of each set of MiniKans™ and acids **7a-e** (3.00 mmol) in pyridine/DMF (1:1, 15.0 mL) was added EDCI • HCl (575 mg, 3.00 mmol) and DMAP (36.6 mg, 300  $\mu$ mol) at room temperature. And the solution of acids **7a-e** was added to the reaction mixture at 50 °C. After being shaken at the same temperature for 48 h, the reaction mixture was filtered, and rinsed with DMF (10 min). All MiniKans™ were pooled together, and washed consecutively with DMF (10 min x 3), DMF/H<sub>2</sub>O (2:1, 10 min x 3), CH<sub>2</sub>Cl<sub>2</sub> (10 min x 3), methanol (10 min x 3), and dried under reduced pressure.

#### General Procedure for cleavage of the **60** polymer supported acyloxyketones

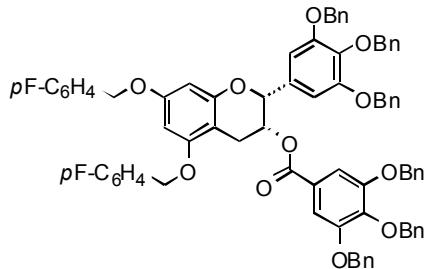
Each MiniKans™ was treated with a solution of trifluoroacetic acid (600  $\mu$ L) in CH<sub>2</sub>Cl<sub>2</sub> (2.00 mL) in the presence of PS-benzaldehyde resin (Argonaut, 1.13 mmol/g loading, 200 mg) at -10 °C. After the reaction mixture was shaken at the same temperature for 5 h, triethylsilane (400  $\mu$ L) was added to the mixture. After being shaken at the same temperature for further 19 h, the reaction mixture was filtered to remove the MiniKans™. The MiniKans™ was rinsed with ethyl acetate. The filtrate was concentrated *in vacuo*. The residue was purified by gel permeation chromatography (GPC) to afford EGCG analogues.

Entry	aldehyd e	ketone	acid	Product	Crude yield(%)	Purity (%)	Isolated Yield (mg)	Isolated Yield (%)
1	<b>12a</b>	<b>11a</b>	<b>7a</b>	<b>2</b>	89	20	8.5	13
2	<b>12a</b>	<b>11a</b>	<b>7b</b>	<b>5aab</b>	129	27	10.8	17
3	<b>12a</b>	<b>11a</b>	<b>7c</b>	<b>5aac</b>	105	32	7.3	12
4	<b>12a</b>	<b>11a</b>	<b>7d</b>	<b>5aad</b>	114	16	3.1	5
5	<b>12a</b>	<b>11a</b>	<b>7e</b>	<b>5aae</b>	135	35	16.4	28
6	<b>12a</b>	<b>11b</b>	<b>7a</b>	<b>5aba</b>	87	15	8.0	13
7	<b>12a</b>	<b>11b</b>	<b>7b</b>	<b>5abb</b>	111	48	26.4	45
8	<b>12a</b>	<b>11b</b>	<b>7c</b>	<b>5abc</b>	143	51	14.3	26
9	<b>12a</b>	<b>11b</b>	<b>7d</b>	<b>5abd</b>	-	-	-	-
10	<b>12a</b>	<b>11b</b>	<b>7e</b>	<b>5abe</b>	118	49	21.6	39
11	<b>12a</b>	<b>11c</b>	<b>7a</b>	<b>5aca</b>	96	12	2.4	4
12	<b>12a</b>	<b>11c</b>	<b>7b</b>	<b>5acb</b>	108	22	6.5	12
13	<b>12a</b>	<b>11c</b>	<b>7c</b>	<b>5acc</b>	107	18	3.6	7
14	<b>12a</b>	<b>11c</b>	<b>7d</b>	<b>5acd</b>	115	31	3.2	6
15	<b>12a</b>	<b>11c</b>	<b>7e</b>	<b>5ace</b>	98	23	8.0	16
16	<b>12a</b>	<b>11d</b>	<b>7a</b>	<b>5ada</b>	64	23	5.7	10
17	<b>12a</b>	<b>11d</b>	<b>7b</b>	<b>5adb</b>	104	43	10.6	21
18	<b>12a</b>	<b>11d</b>	<b>7c</b>	<b>5adc</b>	152	57	20.3	44
19	<b>12a</b>	<b>11d</b>	<b>7d</b>	<b>5add</b>	111	45	8.7	18
20	<b>12a</b>	<b>11d</b>	<b>7e</b>	<b>5ade</b>	140	40	24.2	52
21	<b>12a</b>	<b>11e</b>	<b>7a</b>	<b>5aea</b>	142	7	1.5	3
22	<b>12a</b>	<b>11e</b>	<b>7b</b>	<b>5aeb</b>	110	48	8.3	16
23	<b>12a</b>	<b>11e</b>	<b>7c</b>	<b>5aec</b>	118	18	6.4	13
24	<b>12a</b>	<b>11e</b>	<b>7d</b>	<b>5aed</b>	85	9	-	-
25	<b>12a</b>	<b>11e</b>	<b>7e</b>	<b>5aee</b>	104	25	9.0	18
26	<b>12a</b>	<b>11f</b>	<b>7a</b>	<b>5afa</b>	93	11	3.6	6
27	<b>12a</b>	<b>11f</b>	<b>7b</b>	<b>5afb</b>	106	25	10.4	18
28	<b>12a</b>	<b>11f</b>	<b>7c</b>	<b>5afc</b>	141	15	8.0	15
29	<b>12a</b>	<b>11f</b>	<b>7d</b>	<b>5afd</b>	102	20	3.3	5
30	<b>12a</b>	<b>11f</b>	<b>7e</b>	<b>5afe</b>	152	18	9.4	18
31	<b>12b</b>	<b>11a</b>	<b>7a</b>	<b>5baa</b>	87	25	11.6	18
32	<b>12b</b>	<b>11a</b>	<b>7b</b>	<b>5bab</b>	80	27	9.0	15
33	<b>12b</b>	<b>11a</b>	<b>7c</b>	<b>5bac</b>	100	11	6.1	11
34	<b>12b</b>	<b>11a</b>	<b>7d</b>	<b>5bad</b>	75	18	4.0	7
35	<b>12b</b>	<b>11a</b>	<b>7e</b>	<b>5bae</b>	134	41	13.4	24
36	<b>12b</b>	<b>11b</b>	<b>7a</b>	<b>5bba</b>	100	8	-	-
37	<b>12b</b>	<b>11b</b>	<b>7b</b>	<b>5bbb</b>	173	22	10.2	18
38	<b>12b</b>	<b>11b</b>	<b>7c</b>	<b>5bbc</b>	117	40	10.1	20
39	<b>12b</b>	<b>11b</b>	<b>7d</b>	<b>5bbd</b>	66	23	4.6	9
40	<b>12b</b>	<b>11b</b>	<b>7e</b>	<b>5bbe</b>	99	47	16.1	32
41	<b>12b</b>	<b>11c</b>	<b>7a</b>	<b>5bca</b>	82	8	-	-
42	<b>12b</b>	<b>11c</b>	<b>7b</b>	<b>5bcb</b>	91	41	7.5	15
43	<b>12b</b>	<b>11c</b>	<b>7c</b>	<b>5bcc</b>	83	6	-	-
44	<b>12b</b>	<b>11c</b>	<b>7d</b>	<b>5bcd</b>	78	5	-	-
45	<b>12b</b>	<b>11c</b>	<b>7e</b>	<b>5bce</b>	87	6	-	-
46	<b>12b</b>	<b>11d</b>	<b>7a</b>	<b>5bda</b>	208	16	-	-
47	<b>12b</b>	<b>11d</b>	<b>7b</b>	<b>5bdb</b>	93	16	-	-
48	<b>12b</b>	<b>11d</b>	<b>7c</b>	<b>5bdc</b>	134	45	11.3	28
49	<b>12b</b>	<b>11d</b>	<b>7d</b>	<b>5bdd</b>	80	33	9.7	22

50	<b>12b</b>	<b>11d</b>	<b>7e</b>	<b>5bde</b>	73	59	10.3	25
51	<b>12b</b>	<b>11e</b>	<b>7a</b>	<b>5bea</b>	63	23	6.0	10
52	<b>12b</b>	<b>11e</b>	<b>7b</b>	<b>5beb</b>	85	32	10.8	19
53	<b>12b</b>	<b>11e</b>	<b>7c</b>	<b>5bec</b>	-	26	2.1	4
54	<b>12b</b>	<b>11e</b>	<b>7d</b>	<b>5bed</b>	96	26	3.5	6
55	<b>12b</b>	<b>11e</b>	<b>7e</b>	<b>5bee</b>	79	37	10.4	20
56	<b>12b</b>	<b>11f</b>	<b>7a</b>	<b>5bfa</b>	66	25	20.3	30
57	<b>12b</b>	<b>11f</b>	<b>7b</b>	<b>5fbf</b>	67	25	12.2	20
58	<b>12b</b>	<b>11f</b>	<b>7c</b>	<b>5bfc</b>	86	29	12.2	22
59	<b>12b</b>	<b>11f</b>	<b>7d</b>	<b>5bfd</b>	59	24	5.5	9
60	<b>12b</b>	<b>11f</b>	<b>7e</b>	<b>5bfe</b>	90	25	15.6	28

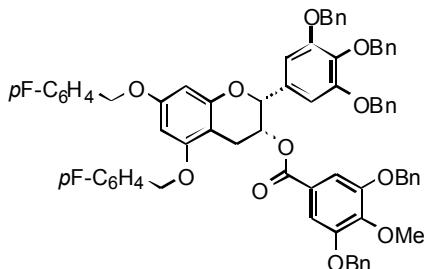
## Epicatechin Analogues

### *Cis*-5,7-bis(4-fluorobenzyloxy)-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (18)

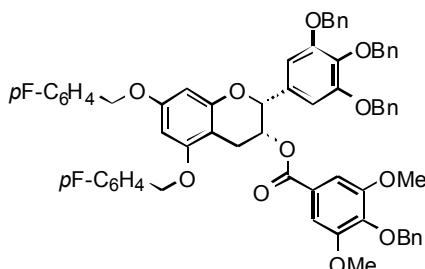


Yield 8.5 mg; Purity 32%; Retention Time 13.23 minutes;

### *Cis*-5,7-bis(4-fluorobenzyloxy)-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5aab)

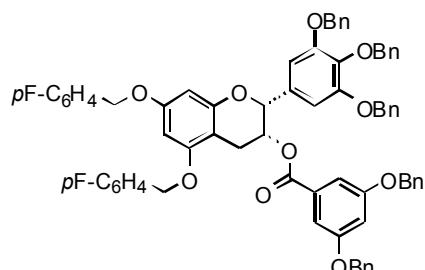


Yield 10.8 mg; Purity 27%; Retention Time 12.23 minutes; HRMS (ESI-TOF) calcd for  $C_{72}H_{61}F_2O_{11}$   $[M+H]^+$  1139.4182, found 1139.4186.



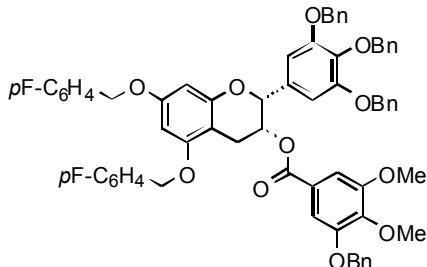
### *Cis*-5,7-bis(4-fluorobenzyloxy)-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5aac)

Yield 7.3 mg; Purity 20%; Retention Time 11.67 minutes; MS (ESI-TOF) calcd for  $C_{66}H_{57}F_2O_{11}$   $[M+H]^+$  1063.4, found 1063.4.



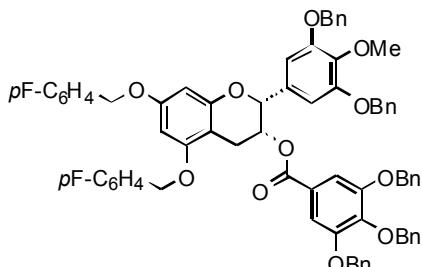
**Cis-5,7-bis(4-fluorobenzyloxy)-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3,5-bis(benzyloxy)benzoate (5aad)**

Yield 3.1 mg; Purity 16%; Retention Time 12.75 minutes; HRMS (ESI-TOF) calcd for  $C_{71}H_{59}F_2O_{10}$   $[M+H]^+$  1109.4076, found 1109.4076.



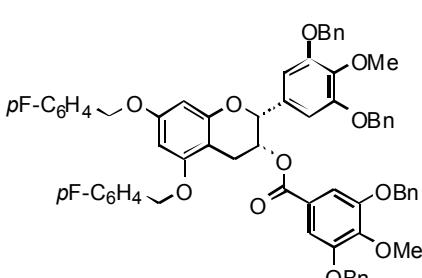
**Cis-5,7-bis(4-fluorobenzyloxy)-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5aae)**

Yield 16.4 mg; Purity 35%; Retention Time 11.27 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.20-7.39 (m, 25H), 7.18x2 (t,  $J$  = 8.2, 8.7 Hz, 2H), 6.75 (s, 2H), 6.36 (d,  $J$  = 2.4 Hz, 1H), 6.29 (d,  $J$  = 2.4 Hz, 1H), 5.65 (br s, 1H), 5.05 (br s, 1H), 4.97-5.07 (m, 9H), 4.84 (d,  $J$  = 11.6 Hz, 2H), 4.72 (d,  $J$  = 11.6 Hz, 2H), 3.78 (s, 3H), 3.78 (s, 3H), 3.11 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 4.3$  Hz, 1H), 3.04 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 2.4$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.0, 162.6x2 ( $J_{C,F} = 246$  Hz), 158.8, 158.0, 155.8, 153.3, 153.0, 151.8, 143.3, 138.6, 137.8, 137.0, 136.5, 133.3, 132.6 ( $J_{C,F} = 2.3$  Hz), 129.4 ( $J_{C,F} = 7.6$  Hz), 129.1 ( $J_{C,F} = 7.6$  Hz), 128.7, 128.6, 128.5, 128.2, 128.0, 127.9, 127.8x2, 127.5, 124.9, 115.6x2 ( $J_{C,F} = 22.1$  Hz), 109.1, 107.4, 106.9, 101.1, 94.8, 94.0, 78.0, 75.2, 71.4, 71.1, 69.6, 69.5, 68.4, 60.9, 56.4, 26.2; FT-IR (solid) 3421, 3032, 2932, 1713, 1590, 1511, 1220, 1107, 1001, 823, 754, 696  $\text{cm}^{-1}$ ; MS (ESI-TOF) calcd for  $C_{66}H_{57}F_2O_{11}$   $[M+H]^+$  1063.4, found 1063.2.



**Cis-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5aba)**

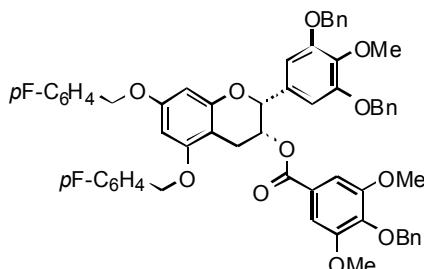
Yield 8.0 mg; Purity 15%; Retention Time 12.15 minutes; MS (ESI-TOF) calcd for  $C_{72}H_{61}F_2O_{11}$   $[M+H]^+$  1139.4, found 1139.3.



***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**3,5-bis(benzyloxy)-4-methoxybenzoate (5abb)**

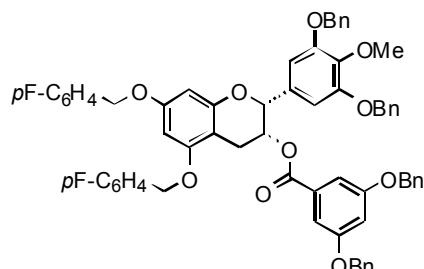
Yield 26.4 mg; Purity 48%; Retention Time 11.10 minutes; MS (ESI-TOF) calcd for  $C_{66}H_{57}F_2O_{11}$   $[M+H]^+$  1063.4, found 1063.4.



***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**4-benzyloxy-3,5-dimethoxybenzoate (5abc)**

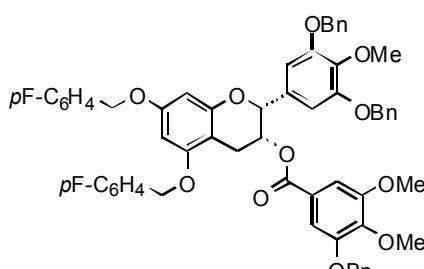
Yield 14.3 mg; Purity 51%; Retention Time 10.33 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.27-7.43 (m, 19H), 7.18 (s, 2H), 7.03-7.11 (m, 4H), 6.78 (s, 2H), 6.30 (d,  $J$  = 2.4 Hz, 1H), 6.25 (d,  $J$  = 2.4 Hz, 1H), 5.62 (ddd,  $J$  = 1.5, 3.4, 4.4 Hz, 1H), 5.05 (br s, 1H), 4.88-5.02 (m, 10H), 3.84 (s, 3H), 3.76 (s, 6H), 3.10 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 4.4$  Hz, 1H), 3.04 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 3.4$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.3, 162.6x2 ( $J_{C,F} = 247$  Hz), 158.7, 157.9, 155.7, 153.4, 152.7, 141.7, 139.9, 137.5, 137.0, 133.1, 132.7 ( $J_{C,F} = 3.0$  Hz), 132.6 ( $J_{C,F} = 3.0$  Hz), 129.4 ( $J_{C,F} = 8.4$  Hz), 129.1 ( $J_{C,F} = 8.4$  Hz), 128.6, 128.3x2, 128.0x2, 127.4, 125.2, 115.6x2 ( $J_{C,F} = 22.1$  Hz), 107.4, 107.2, 101.1, 94.8, 94.0, 77.7, 75.0, 71.5, 69.6, 69.5, 68.6, 61.0, 56.4, 26.0; FT-IR (solid) 2999, 2935, 1712, 1590, 1509, 1223, 1129, 1102, 959, 833, 731, 696, 492  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $C_{60}H_{53}F_2O_{11}$   $[M+H]^+$  987.3556, found 987.3556.



***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**3,5-bis(benzyloxy)benzoate (5abd)**

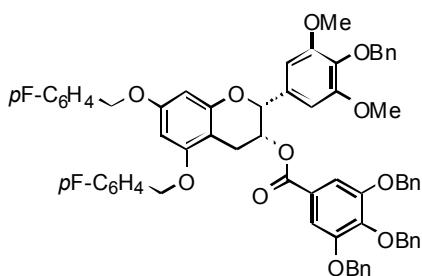
Yield - mg; Purity -%; Retention Time - minutes;



***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**3-benzyloxy-4,5-dimethoxybenzoate (5abe)**

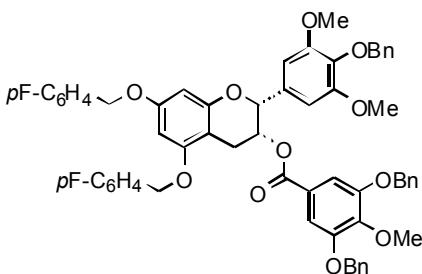
Yield 21.6 mg; Purity 49%; Retention Time 10.03 minutes;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28-7.37 (m, 20H), 7.18 (d,  $J$  = 1.0 Hz, 1H), 7.03-7.07 (m, 4H), 6.73 (s, 2H), 6.35 (d,  $J$  = 1.9 Hz, 1H), 6.29 (d,  $J$  = 1.9 Hz, 1H), 5.64 (br s, 1H), 4.99-5.07 (m, 7H), 4.87 (d,  $J_{\text{gem}}$  = 12.1 Hz, 2H), 4.76 (d,  $J_{\text{gem}}$  = 12.1 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 6H), 3.10 (dd,  $J_{\text{gem}}$  = 17.9 Hz,  $J$  = 4.3 Hz, 1H), 3.03 (dd,  $J_{\text{gem}}$  = 17.9 Hz,  $J$  = 2.4 Hz, 1H); FT-IR (solid) 3034, 2935, 1714, 1591, 1512, 1423, 1224, 1112, 1002, 827, 737, 697  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{60}\text{H}_{53}\text{F}_2\text{O}_{11}$   $[\text{M}+\text{H}]^+$  987.3556, found 987.3570.



***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**3,4,5-tris(benzyloxy)benzoate (5aca)**

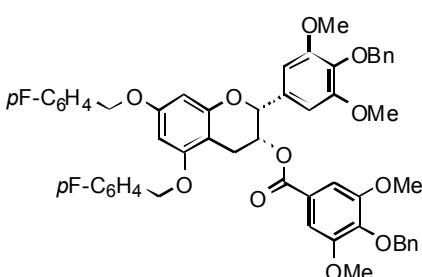
Yield 2.4 mg; Purity 12%; Retention Time 11.45 minutes; MS (ESI-TOF) calcd for  $\text{C}_{66}\text{H}_{57}\text{F}_2\text{O}_{11}$   $[\text{M}+\text{H}]^+$  1063.4, found 1063.5.



***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**3,5-bis(benzyloxy)-4-methoxybenzoate (5acb)**

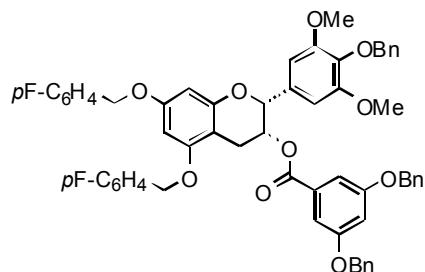
Yield 6.5 mg; Purity 22%; Retention Time 10.23 minutes; HRMS (ESI-TOF) calcd for  $\text{C}_{60}\text{H}_{53}\text{F}_2\text{O}_{11}$   $[\text{M}+\text{H}]^+$  987.3556, found 987.3552.



***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

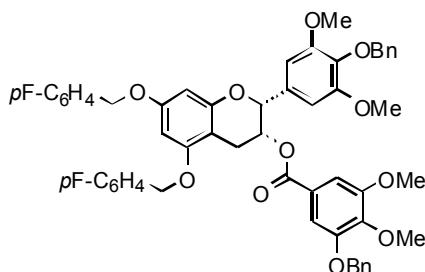
**4-benzyloxy-3,5-dimethoxybenzoate (5acc)**

Yield 3.6 mg; Purity 18%; Retention Time 9.38 minutes; HRMS (ESI-TOF) calcd for  $C_{54}H_{49}F_2O_{11}$   $[M+H]^+$  911.3243, found 911.3243.



***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3,5-bis(benzyloxy)benzoate (5acd)**

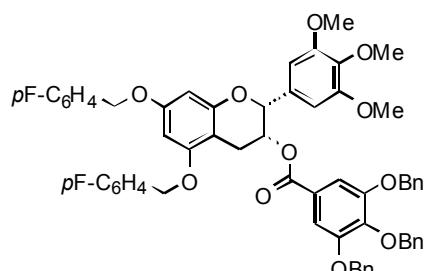
Yield 3.2 mg; Purity 31%; Retention Time 10.93 minutes; HRMS (ESI-TOF) calcd for  $C_{59}H_{51}F_2O_{10}$   $[M+H]^+$  957.3450, found 957.3447.



***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

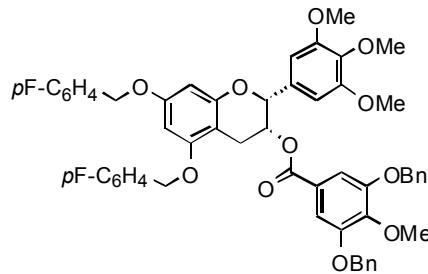
**3-benzyloxy-4,5-dimethoxybenzoate (5ace)**

Yield 8.0 mg; Purity 23%; Retention Time 9.12 minutes; HRMS (ESI-TOF) calcd for  $C_{54}H_{49}F_2O_{11}$   $[M+H]^+$  911.3243, found 911.3224.



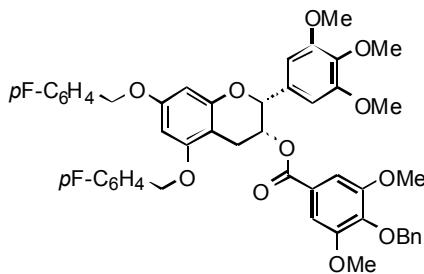
**Cis-5,7-bis(4-fluorobenzyloxy)-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5ada)**

Yield 5.7 mg; Purity 23%; Retention Time 10.28 minutes; HRMS (ESI-TOF) calcd for  $C_{60}H_{53}F_2O_{11}$   $[M+H]^+$  987.3556, found 987.3552.



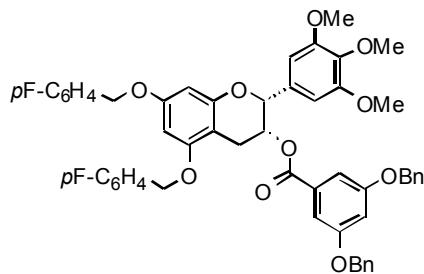
**Cis-5,7-bis(4-fluorobenzyloxy)-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5adb)**

Yield 10.6 mg; Purity 43%; Retention Time 8.95 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.28-7.40 (m, 16H), 7.04 (t,  $J$  = 8.7 Hz, 2H), 7.02 (t,  $J$  = 8.7 Hz, 2H), 6.60 (s, 2H), 6.40 (d,  $J$  = 2.4 Hz, 1H), 6.30 (d,  $J$  = 2.4 Hz, 1H), 5.67 (br s, 1H), 4.99-5.09 (m, 9H), 3.89 (s, 3H), 3.78 (s, 3H), 3.53 (s, 6H), 3.11 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 4.3$  Hz, 1H), 3.04 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 1.9$  Hz, 1H); HRMS (ESI-TOF) calcd for  $C_{54}H_{49}F_2O_{11}$   $[M+H]^+$  911.3243, found 911.3281.



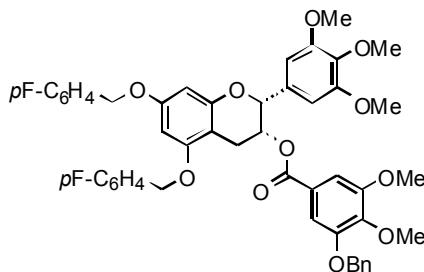
**Cis-5,7-bis(4-fluorobenzyloxy)-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5adc)**

Yield 20.3 mg; Purity 57%; Retention Time 8.08 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.29-7.45 (m, 9H), 7.17 (s, 2H), 7.03-7.11 (m, 4H), 6.69 (s, 2H), 6.33 (d,  $J$  = 2.4 Hz, 1H), 6.26 (d,  $J$  = 2.4 Hz, 1H), 5.66 (br s, 1H), 5.09 (s, 1H), 5.06 (s, 2H), 5.00 (s, 2H), 4.98 (s, 2H), 3.80 (s, 3H), 3.78 (s, 6H), 3.69 (s, 6H), 3.15 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 3.9$  Hz, 1H), 3.07 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J = 2.9$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.2, 162.6 ( $J_{C,F} = 247$  Hz), 162.5 ( $J_{C,F} = 246$  Hz), 158.7, 157.9, 155.7, 153.3, 153.2, 141.4, 138.1, 137.5, 137.3, 133.3, 132.6x2 ( $J_{C,F} = 3.0$  Hz), 129.4 ( $J_{C,F} = 7.6$  Hz), 129.1 ( $J_{C,F} = 7.6$  Hz), 128.5, 128.3, 128.1, 125.2, 115.6 ( $J_{C,F} = 21.3$  Hz), 115.5 ( $J_{C,F} = 21.3$  Hz), 107.3, 104.1, 101.1, 94.8, 94.0, 78.0, 75.0, 69.5, 69.4, 68.6, 60.9, 56.3, 56.1, 26.2; FT-IR (solid) 2937, 1715, 1587, 1510, 1220, 1123, 1009, 825, 754  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $C_{48}H_{45}F_2O_{11}$   $[M+H]^+$  835.2930, found 835.2915.



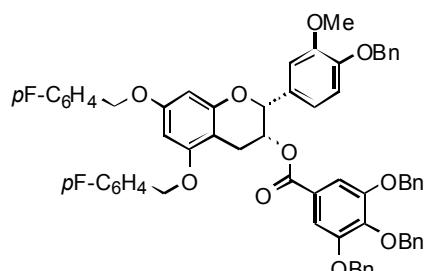
**Cis-5,7-bis(4-fluorobenzyloxy)-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3,5-bis(benzyloxy)benzoate (5add)**

Yield 8.7 mg; Purity 45%; Retention Time 9.63 minutes;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31-7.39 (m, 14H), 7.20 (d,  $J$  = 2.4 Hz, 2H), 7.03-7.07 (m, 4H), 6.75 (t,  $J$  = 2.4 Hz, 1H), 6.68 (s, 2Hc), 6.36 (d,  $J$  = 2.4 Hz, 1H), 6.26 (d,  $J$  = 2.4 Hz, 1H), 5.64 (t,  $J$  = 2.9 Hz, 1H), 5.07 (s, 1H), 4.99-5.00 (m, 8H), 3.80 (s, 3H), 3.67 (s, 6H), 3.05-3.17 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  165.3, 162.6x2 ( $J_{\text{C},\text{F}}$  = 247 Hz), 159.8, 158.8, 158.0, 155.7, 153.3, 138.1, 136.4, 133.2, 132.7 ( $J_{\text{C},\text{F}}$  = 3.0 Hz), 132.6 ( $J_{\text{C},\text{F}}$  = 3.0 Hz), 129.5 ( $J_{\text{C},\text{F}}$  = 8.4 Hz), 129.1 ( $J_{\text{C},\text{F}}$  = 8.4 Hz), 128.8, 128.3, 127.8, 115.6 ( $J_{\text{C},\text{F}}$  = 21.3 Hz), 108.8, 106.9, 104.1, 101.1, 95.1, 94.2, 78.2, 70.4, 69.6, 69.5, 68.8, 60.9, 56.1, 26.3; FT-IR (solid) 3431, 2928, 1719, 1591, 1510, 1221, 1125, 1050, 823, 736, 696, 667, 502  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{53}\text{H}_{47}\text{F}_2\text{O}_{10}$   $[\text{M}+\text{H}]^+$  881.3137, found 881.3133.



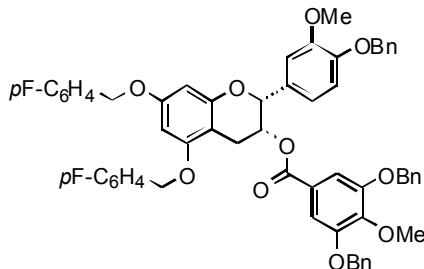
**Cis-5,7-bis(4-fluorobenzyloxy)-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5ade)**

Yield 24.2 mg; Purity 40%; Retention Time 7.82 minutes; HRMS (ESI-TOF) calcd for  $\text{C}_{48}\text{H}_{45}\text{F}_2\text{O}_{11}$   $[\text{M}+\text{H}]^+$  835.2930, found 835.2950.



**Cis-2-(4-benzyloxy-3-methoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5aea)**

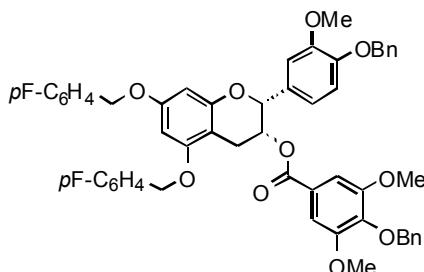
Yield 1.5 mg; Purity 7%; Retention Time 11.52 minutes; MS (ESI-TOF) calcd for  $C_{65}H_{55}F_2O_{10}$   $[M+H]^+$  1033.4, found 1033.3.



**Cis-2-(4-benzyloxy-3-methoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

**3,5-bis(benzyloxy)-4-methoxybenzoate (5aeb)**

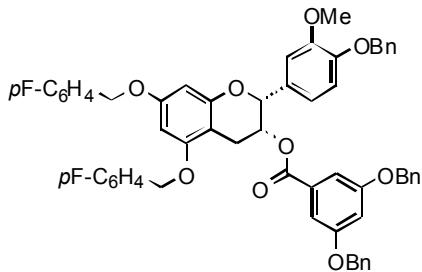
Yield 8.3 mg; Purity 48%; Retention Time 10.17 minutes; HRMS (ESI-TOF) calcd for  $C_{59}H_{51}F_2O_{10}$   $[M+H]^+$  957.3450, found 957.3452.



**Cis-2-(4-benzyloxy-3-methoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

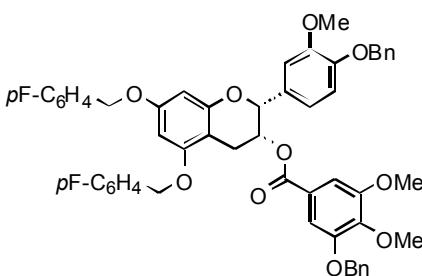
**4-benzyloxy-3,5-dimethoxybenzoate (5aec)**

Yield 6.4 mg; Purity 18%; Retention Time 9.32 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.29-7.45 (m, 14H), 7.15 (s, 2H), 7.02-7.10 (m, 5H), 6.94 (dd,  $J$  = 8.2, 1.9 Hz, 1H), 6.88 (d,  $J$  = 8.2 Hz, 1H), 6.31 (d,  $J$  = 1.9 Hz, 1H), 6.24 (d,  $J$  = 1.9 Hz, 1H), 5.61 (br s 1H), 5.12 (br s, 3H), 5.05 (s, 2H), 4.99 (s, 2H), 4.97 (s, 2H), 3.77 (s, 6H), 3.68 (s, 3H), 3.11 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 4.3 Hz, 1H), 3.06 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 2.9 Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.4, 162.6 ( $J_{C,F} = 247$  Hz), 162.5 ( $J_{C,F} = 246$  Hz), 158.7, 157.9, 155.8, 153.3, 149.7, 148.2, 141.4, 137.4, 137.1, 132.7 ( $J_{C,F} = 3.0$  Hz), 132.6 ( $J_{C,F} = 3.0$  Hz), 130.9, 129.4 ( $J_{C,F} = 7.6$  Hz), 129.1 ( $J_{C,F} = 8.4$  Hz), 128.6, 128.5, 128.3, 128.1, 127.9, 127.3, 125.2, 119.1, 115.6 ( $J_{C,F} = 22.1$  Hz), 115.6 ( $J_{C,F} = 21.3$  Hz), 113.4, 110.7, 107.3, 101.2, 94.8, 94.0, 77.7, 75.1, 71.1, 69.6, 69.5, 68.9, 56.3, 56.0, 26.1; FT-IR (solid) 2936, 1714, 1592, 1511, 1224, 1128, 1036, 825, 733, 697  $cm^{-1}$ ; HRMS (ESI-TOF) calcd for  $C_{53}H_{47}F_2O_{10}$   $[M+H]^+$  881.3137, found 881.3141.



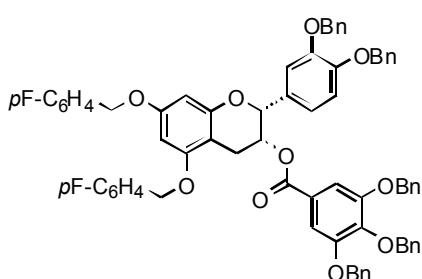
**Cis-2-(4-benzyloxy-3-methoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3,5-bis(benzyloxy)benzoate (5aed)**

Yield mg; Purity 9%; Retention Time 10.83 minutes; HRMS (ESI-TOF) calcd for  $C_{58}H_{49}F_2O_9$   $[M+H]^+$  927.3, found 927.1.



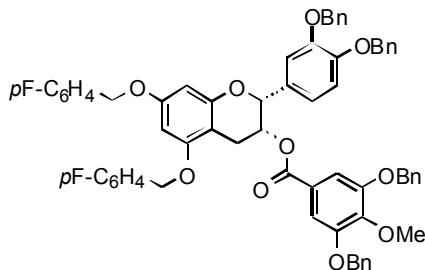
**Cis-2-(4-benzyloxy-3-methoxyphenyl)-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5aee)**

Yield 9.0 mg; Purity 25%; Retention Time 9.07 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.25-7.40 (m, 15H, aromatic-H), 7.15 (d,  $J$  = 1.4 Hz, 1H), 7.02-7.07 (m, 4H), 6.96 (d,  $J$  = 1.9 Hz, 1H), 6.89 (dd,  $J$  = 8.7, 1.4 Hz, 1H), 6.79 (d,  $J$  = 8.7 Hz, 1H), 6.35 (d,  $J$  = 2.4 Hz, 1H), 6.26 (d,  $J$  = 2.4 Hz, 1H), 5.62 (dd,  $J$  = 4.3, 2.9 Hz, 1H), 4.98-5.10 (m, 9H), 3.88 (s, 3H), 3.81 (s, 3H), 3.56 (s, 3H), 3.10 (dd,  $J_{\text{gem}}$  = 17.9 Hz,  $J$  = 4.3 Hz, 1H), 3.04 (dd,  $J_{\text{gem}}$  = 17.9 Hz,  $J$  = 2.9 Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.1, 162.6 ( $J_{C,F}$  = 247 Hz), 162.5 ( $J_{C,F}$  = 246 Hz), 158.7, 158.0, 155.9, 153.2, 151.8, 149.6, 148.2, 143.2, 137.1, 136.6, 132.6x2 ( $J_{C,F}$  = 3.0 Hz), 130.8, 129.4 ( $J_{C,F}$  = 8.4 Hz), 129.1 ( $J_{C,F}$  = 7.6 Hz), 128.7, 128.6, 128.2, 127.9, 127.8, 127.3, 124.9, 119.2, 115.6x2 ( $J_{C,F}$  = 21.3 Hz), 113.8, 110.6, 109.1, 107.4, 101.2, 94.8, 94.0, 77.8, 71.1, 71.0, 69.6, 69.4, 68.7, 61.0, 56.3, 55.8, 26.2; FT-IR (solid) 3030, 2936, 1713, 1592, 1512, 1223, 1143, 1116, 1002, 821, 738, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $C_{53}H_{47}F_2O_{10}$   $[M+H]^+$  881.3137, found 881.3142.



***Cis*-2-[3,4-bis(benzyloxy)phenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5afa)**

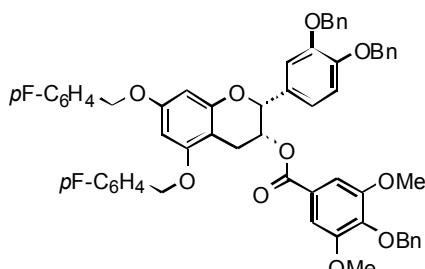
Yield 3.6 mg; Purity 11%; Retention Time 11.35 minutes; HRMS (ESI-TOF) calcd for  $C_{71}H_{59}F_2O_{10}$   $[M+H]^+$  1109.4076, found 1109.4076.



***Cis*-2-[3,4-bis(benzyloxy)phenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl**

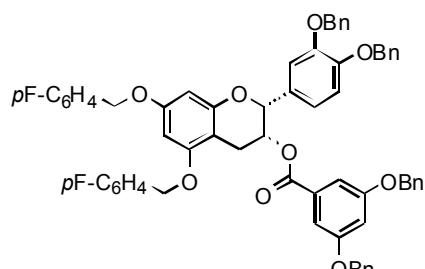
**3,5-bis(benzyloxy)-4-methoxybenzoate (5afb)**

Yield 10.4 mg; Purity 25%; Retention Time 11.28 minutes; HRMS (ESI-TOF) calcd for  $C_{65}H_{50}F_2O_{10}$   $[M+H]^+$  1033.3763, found 1033.3767.



***Cis*-2-[3,4-bis(benzyloxy)phenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5afc)**

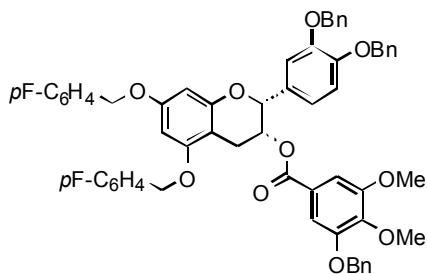
Yield 8.0 mg; Purity 15%; Retention Time 10.55 minutes; HRMS (ESI-TOF) calcd for  $C_{59}H_{51}F_2O_{10}$   $[M+H]^+$  957.3450, found 957.3464.



***Cis*-2-[3,4-bis(benzyloxy)phenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3,5-bis(benzyloxy)benzoate (5afd)**

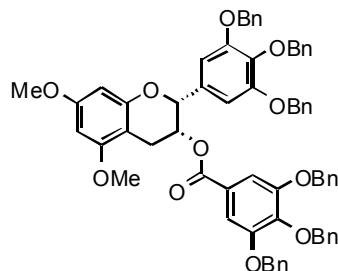
Yield 3.3 mg; Purity 20%; Retention Time 11.85 minutes;

MS (ESI-TOF) calcd for  $C_{64}H_{53}F_2O_9$   $[M+H]^+$  1103.4, found 1103.2.



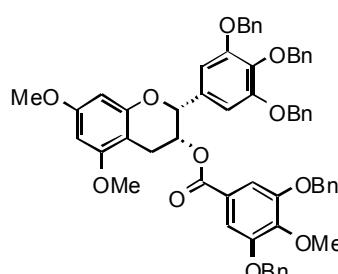
**Cis-2-[3,4-bis(benzyloxy)phenyl]-5,7-bis(4-fluorobenzyloxy)chroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5afe)**

Yield 9.4 mg; Purity 18%; Retention Time 10.20 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.27-7.42 (m, 19H), 7.16 (d,  $J$  = 1.9 Hz, 1H), 7.02-7.07 (m, 6H), 6.94 (dd,  $J$  = 1.9, 8.2 Hz, 1H), 6.85 (d,  $J$  = 8.2 Hz, 1H), 6.34 (d,  $J$  = 2.4 Hz, 1H), 6.26 (d,  $J$  = 2.4 Hz, 1H), 5.60 (s, 1H), 5.11 (s, 1H), 4.98-5.09 (m, 8H), 4.81 (d,  $J_{\text{gem}} = 11.6$  Hz, 1H), 4.70 (d,  $J_{\text{gem}} = 11.6$  Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.10 (dd,  $J_{\text{gem}} = 17.9, 4.4$  Hz, 1H), 3.03 (dd,  $J_{\text{gem}} = 17.9, 2.9$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.1, 162.6 ( $J_{C,F} = 247$  Hz), 162.5 ( $J_{C,F} = 246$  Hz), 158.7, 158.0, 155.8, 153.2, 151.8, 149.1, 143.1, 137.2, 137.1, 136.6, 132.6x2 ( $J_{C,F} = 3.0$  Hz), 131.1, 129.4 ( $J_{C,F} = 8.4$  Hz), 129.1 ( $J_{C,F} = 8.4$  Hz), 128.7, 128.5, 128.4, 128.2, 127.8x2, 127.5, 127.3, 124.9, 121.3, 120.1, 115.6x2 ( $J_{C,F} = 21.3$  Hz), 114.8, 113.9, 109.1, 107.4, 101.1, 94.8, 94.0, 77.7, 71.4, 71.3, 71.1, 69.6, 69.4, 68.6, 61.0, 56.3, 26.1; FT-IR (solid) 3032, 2936, 1716, 1592, 1511, 1422, 1224, 1112, 1015, 824, 755, 697, 628  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $C_{59}H_{51}F_2O_{10}$   $[M+H]^+$  957.3450, found 957.3430.



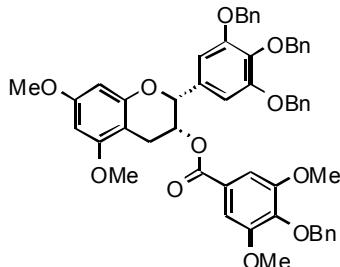
**Cis-5,7-dimethoxy -2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5baa)**

Yield 11.6 mg; Purity 25%; Retention Time 11.88 minutes; HRMS (ESI-TOF) calcd for  $C_{66}H_{59}O_{11}$   $[M+H]^+$  1027.4057, found 1027.4050.



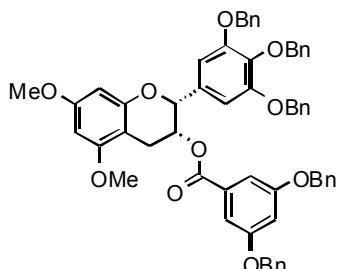
**Cis-5,7-dimethoxy -2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5bab)**

Yield 9.0 mg; Purity 27%; Retention Time 10.62 minutes; MS (ESI-TOF) calcd for  $C_{60}H_{55}O_{11}$   $[M+H]^+$  951.4, found 951.4.



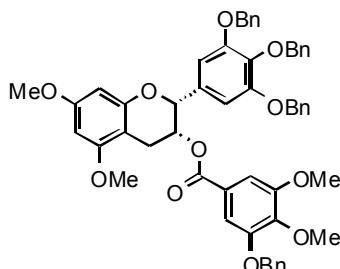
**Cis-5,7-dimethoxy -2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5bac)**

Yield 6.1 mg; Purity 11%; Retention Time 9.80 minutes; HRMS (ESI-TOF) calcd for  $C_{54}H_{51}O_{11}$   $[M+H]^+$  875.3431, found 875.3434.



**Cis-5,7-dimethoxy-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3,5-bis(benzyloxy)benzoate (5bad)**

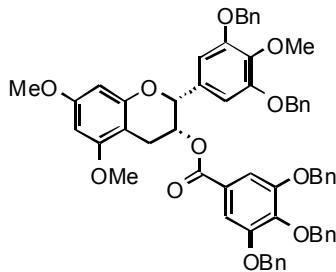
Yield 4.0 mg; Purity 18%; Retention Time 11.32 minutes; HRMS (ESI-TOF) calcd for  $C_{59}H_{53}O_{10}$   $[M+H]^+$  921.3639, found 921.3639.



**Cis-5,7-dimethoxy-2-[3,4,5-tris(benzyloxy)phenyl]chroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5bae)**

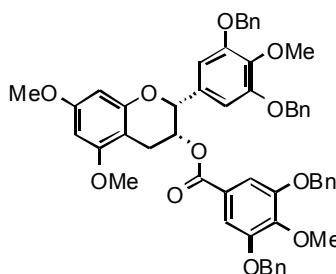
Yield 13.4 mg; Purity 41%; Retention Time 9.50 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.18-7.39 (m, 22H), 6.76 (s, 2H), 6.28 (d,  $J$  = 2.4 Hz, 1H), 6.16 (d,  $J$  = 2.4 Hz, 1H), 5.66 (br s, 1H), 4.97-5.05 (m, 5H), 4.86 (d,  $J_{\text{gem}} = 11.6$  Hz, 2H), 4.72 (d,  $J_{\text{gem}} = 11.6$  Hz, 2H), 3.80x2 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.06 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 4.3 Hz, 1H), 3.00 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 3.9 Hz 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.0, 159.9, 159.0, 155.6, 153.2, 153.0, 151.8, 143.3, 138.6, 137.9, 137.0, 136.5, 133.4, 128.7, 128.6x2, 128.5, 128.2, 127.9, 127.8x2, 127.6, 127.5, 125.0, 109.2, 107.5, 106.9, 100.3, 93.4, 92.1, 77.9, 75.2, 71.6, 71.4, 71.1, 68.5, 60.9, 56.4, 55.5x2, 26.0; FT-IR (solid) 3434, 2939, 1712, 1590, 1498, 1334, 1205, 1118, 1001, 812, 733, 696, 505  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $C_{54}H_{51}O_{11}$   $[M+H]^+$

875.3431, found 875.3423.



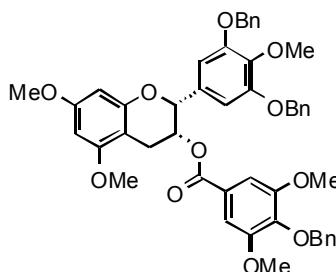
***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-dimethoxychroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5bba)**

Yield mg; Purity 8%; Retention Time 10.65 minutes; HRMS (ESI-TOF) calcd for  $C_{60}H_{55}O_{11}$   $[M+H]^+$  951.3744, found 951.3745.



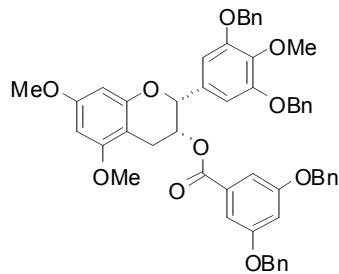
***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5bbb)**

Yield 10.2 mg; Purity 22%; Retention Time 9.25 minutes; HRMS (ESI-TOF) calcd for  $C_{54}H_{51}O_{11}$   $[M+H]^+$  875.3431, found 875.3439.



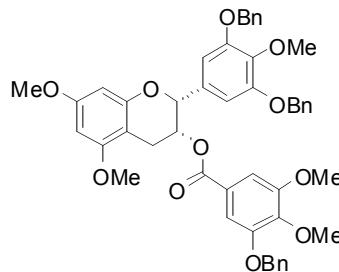
***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-dimethoxychroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5bbc)**

Yield 10.1 mg; Purity 40%; Retention Time 8.42 minutes; MS (ESI-TOF) calcd for  $C_{48}H_{47}O_{11}$   $[M+H]^+$  799.3, found 799.3.



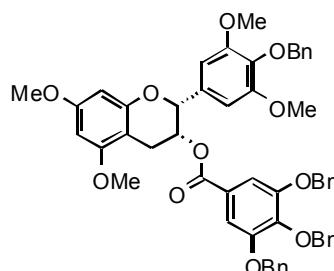
***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)benzoate (5bbd)**

Yield 4.6 mg; Purity 23%; Retention Time 10.00 minutes; HRMS (ESI-TOF) calcd for  $C_{53}H_{49}O_{10}$   $[M+H]^+$  845.3326, found 845.3321.



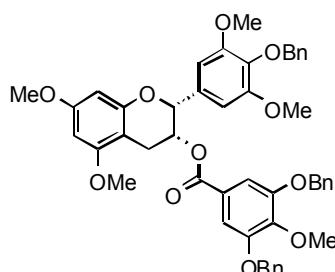
***Cis*-2-[3,5-bis(benzyloxy)-4-methoxyphenyl]-5,7-dimethoxychroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5bbe)**

Yield 16.1 mg; Purity 47%; Retention Time 8.12 minutes; HRMS (ESI-TOF) calcd for  $C_{48}H_{47}O_{11}$   $[M+H]^+$  799.3118, found 799.3121.



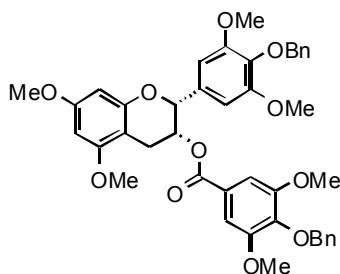
***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5bca)**

Yield mg; Purity 8%; Retention Time 9.67 minutes; HRMS (ESI-TOF) calcd for  $C_{54}H_{51}O_{11}$   $[M+H]^+$  875.3431, found 875.3430.



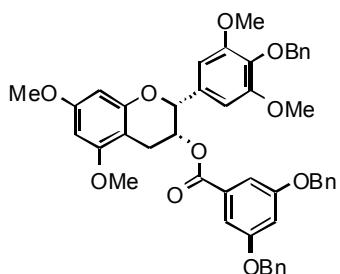
***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5bcb)**

Yield 7.5 mg; Purity 41%; Retention Time 8.28 minutes;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27-7.42 (m, 15H), 7.26 (s, 2H, a), 6.61 (s, 2H), 6.33 (d,  $J$  = 2.4 Hz, 1H), 6.17 (d,  $J$  = 2.4 Hz, 1H), 5.66 (br t,  $J$  = 2.9 Hz, 1H), 5.05-5.07 (m, 5H), 4.93 (s, 3H), 3.88 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.51 (s, 6H), 3.06 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 3.9 Hz, 1H), 3.00 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 2.4 Hz 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  164.9, 159.9, 159.1, 155.7, 153.5, 152.1, 143.9, 137.9, 137.0, 136.6, 133.5, 128.7, 128.5, 128.2, 127.8x2, 127.6, 124.9, 109.4, 104.1, 100.3, 93.4, 92.1, 78.1, 75.0, 71.1, 68.5, 61.1, 56.0, 55.5x2, 26.2; FT-IR (solid) 3429, 3006, 2939, 1714, 1591, 1427, 1217, 1098, 1001, 847, 742, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{48}\text{H}_{47}\text{O}_{11}$   $[\text{M}+\text{H}]^+$  799.3118, found 799.3119.



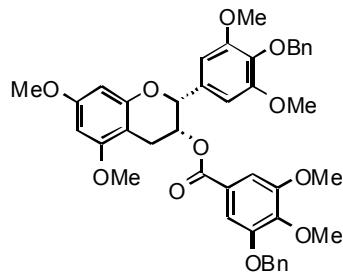
***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-dimethoxychroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5bcc)**

Yield mg; Purity 6%; Retention Time 7.33 minutes; MS (ESI-TOF) calcd for  $\text{C}_{42}\text{H}_{43}\text{O}_{11}$   $[\text{M}+\text{H}]^+$  723.2805, found 723.2798.



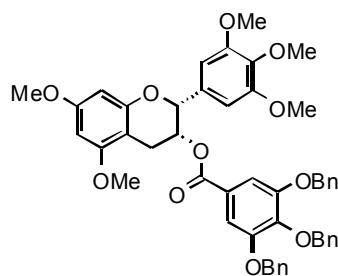
***Cis*-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)benzoate (5bcd)**

Yield mg; Purity 5%; Retention Time 8.93 minutes; HRMS (ESI-TOF) calcd for  $\text{C}_{47}\text{H}_{45}\text{O}_{10}$   $[\text{M}+\text{H}]^+$  769.3013, found 769.3013.



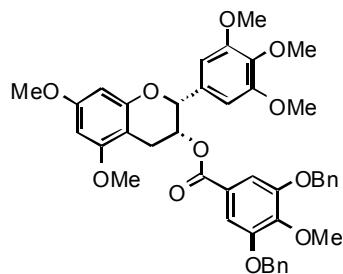
**Cis-2-(4-benzyloxy-3,5-dimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5bce)**

Yield mg; Purity 6%; Retention Time 7.13 minutes; HRMS (ESI-TOF) calcd for  $C_{42}H_{43}O_{11}$   $[M+H]^+$  723.2805, found 723.2791.



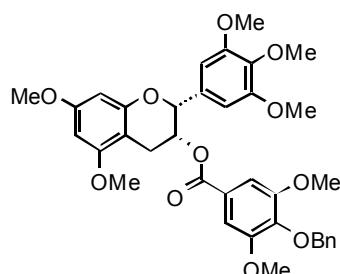
**Cis-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5bda)**

Yield mg; Purity 16%; Retention Time 8.27 minutes; HRMS (ESI-TOF) calcd for  $C_{48}H_{47}O_{11}$   $[M+H]^+$  799.3118, found 799.3123.



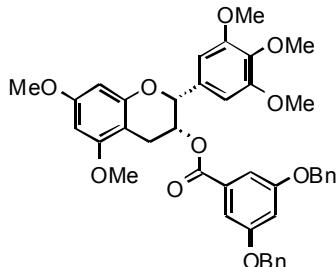
**Cis-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5bdb)**

Yield mg; Purity 16%; Retention Time 6.95 minutes; HRMS (ESI-TOF) calcd for  $C_{42}H_{42}O_{11}$   $[M+H]^+$  723.3, found 723.3.



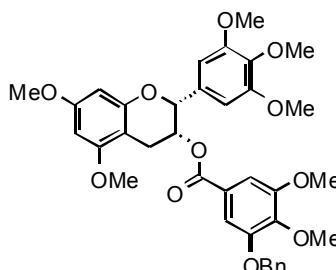
**Cis-5,7-dimethoxy -2-(3,4,5-trimethoxyphenyl)chroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5bdc)**

Yield 11.3 mg; Purity 45%; Retention Time 6.23 minutes;  $\delta$  7.28-7.44 (m, 5H), 7.16 (s, 2H), 6.69 (s, 2H), 6.25 (d,  $J$  = 2.4 Hz, 1H), 6.13 (d,  $J$  = 2.4 Hz, 1H), 5.66 (br s, 1H), 5.08 (s, 1H), 5.50 (s, 2H), 3.70-3.80 (m, 21H), 3.04-3.10 (m, 2H); HRMS (ESI-TOF) calcd for  $C_{36}H_{39}O_{11}$   $[M+H]^+$  647.2492, found 647.2480.



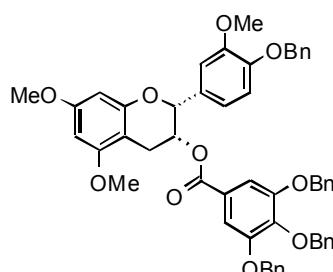
**Cis-5,7-dimethoxy -2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3,5-bis(benzyloxy)benzoate (5bdd)**

Yield 9.7 mg; Purity 33%; Retention Time 7.60 minutes; HRMS (ESI-TOF) calcd for  $C_{41}H_{41}O_{10}$   $[M+H]^+$  693.2690, found 693.2700.



**Cis-5,7-dimethoxy -2-(3,4,5-trimethoxyphenyl)chroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5bde)**

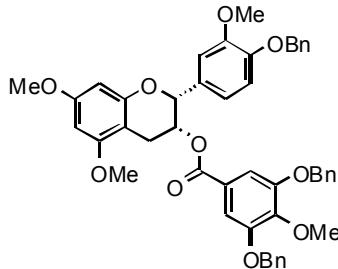
Yield 10.3 mg; Purity 59%; Retention Time 6.08 minutes; HRMS (ESI-TOF) calcd for  $C_{36}H_{39}O_{11}$   $[M+H]^+$  647.2492, found 647.2490.



**Cis-2-(4-benzyloxy-3-trimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5bea)**

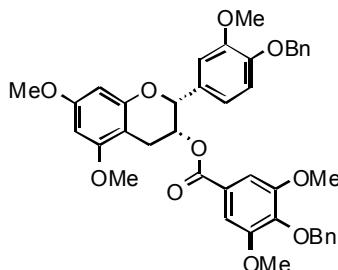
Yield 6.0 mg; Purity 23%; Retention Time 9.71 minutes;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.25-7.36 (m, 22H, aromatic-H), 6.93 (d,  $J$  = 1.5 Hz, 1H), 6.86 (dd,  $J$  = 1.5 Hz, 8.2 Hz, 1H), 6.77 (s,  $J$  = 8.2 Hz, 1H), 6.29 (d,  $J$  = 1.9 Hz, 1H), 6.15 (d,  $J$  = 1.9 Hz, 1H), 5.61 (br s, 1H), 5.09 (s, 1H), 5.00-5.07 (m, 8H), 3.80 (s, 3H), 3.79 (s, 3H, h), 3.47 (s, 3H), 3.05 (dd,  $J_{\text{gem}} = 17.9$  Hz,  $J$  = 3.9 Hz, 1H), 3.04 (br d,  $J_{\text{gem}} = 17.9$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  165.1, 159.8, 159.1, 155.8, 152.4, 149.6, 148.2, 142.5, 137.5, 137.1, 136.6, 131.0, 128.7, 128.6, 128.3, 128.1x2, 127.9, 127.8,

127.3, 125.1, 119.2, 113.8, 110.6, 109.2, 100.3, 93.3, 92.0, 77.8, 75.2, 71.1, 71.0, 68.7, 55.8, 55.5x2, 26.1; FT-IR (solid) 3031, 2937, 1715, 1593, 1429, 1217, 1145, 1116, 815, 753, 697, 474  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{53}\text{H}_{49}\text{O}_{10}$   $[\text{M}+\text{H}]^+$  845.3326, found 845.3328.



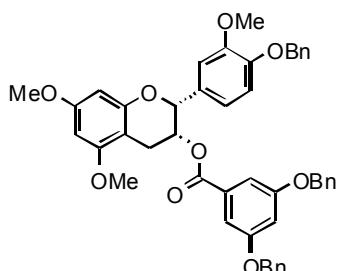
**Cis-2-(4-benzyloxy-3-trimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5beb)**

Yield 10.8 mg; Purity 32%; Retention Time 8.23 minutes; HRMS (ESI-TOF) calcd for  $\text{C}_{47}\text{H}_{45}\text{O}_{10}$   $[\text{M}+\text{H}]^+$  769.3013, found 769.3012.



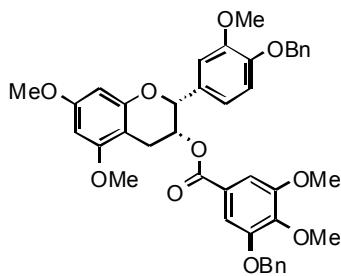
**Cis-2-(4-benzyloxy-3-trimethoxyphenyl)-5,7-dimethoxychroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5bec)**

Yield 2.1 mg; Purity 25%; Retention Time 7.37 minutes; HRMS (ESI-TOF) calcd for  $\text{C}_{41}\text{H}_{41}\text{O}_{10}$   $[\text{M}+\text{H}]^+$  693.3, found 693.2.



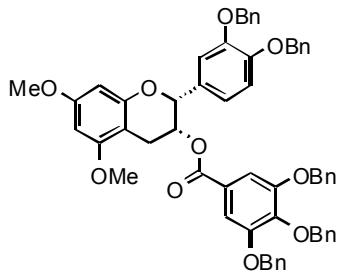
**Cis-2-(4-benzyloxy-3-trimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)benzoate (5bed)**

Yield 3.5 mg; Purity 26%; Retention Time 8.92 minutes; HRMS (ESI-TOF) calcd for  $\text{C}_{46}\text{H}_{43}\text{O}_9$   $[\text{M}+\text{H}]^+$  739.2907, found 739.2903.



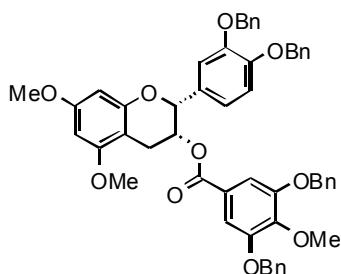
**Cis-2-(4-benzyloxy-3-trimethoxyphenyl)-5,7-dimethoxychroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5bee)**

Yield 10.4 mg; Purity 37%; Retention Time 7.13 minutes; HRMS (ESI-TOF) calcd for  $C_{41}H_{41}O_{10}$   $[M+H]^+$  693.2700, found 693.2676.



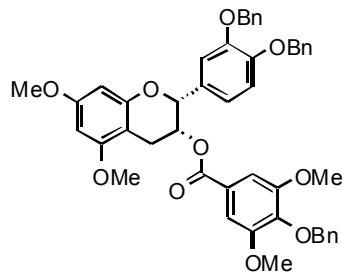
**Cis-2-[3,4-bis(benzyloxy)phenyl]-5,7-dimethoxychroman-3-yl 3,4,5-tris(benzyloxy)benzoate (5bfa)**

Yield 20.3 mg; Purity 25%; Retention Time 10.82 minutes; HRMS (ESI-TOF) calcd for  $C_{59}H_{53}O_{10}$   $[M+H]^+$  921.3639, found 921.3638.



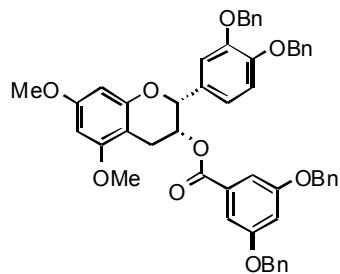
**Cis-2-[3,4-bis(benzyloxy)phenyl]-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)-4-methoxybenzoate (5bfb)**

Yield 12.2 mg; Purity 25%; Retention Time 9.43 minutes; HRMS (ESI-TOF) calcd for  $C_{53}H_{49}O_{10}$   $[M+H]^+$  845.3326, found 845.3323.



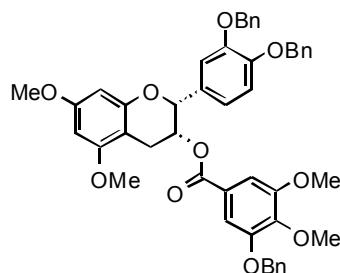
**Cis-2-[3,4-bis(benzyloxy)phenyl]-5,7-dimethoxychroman-3-yl 4-benzyloxy-3,5-dimethoxybenzoate (5bfc)**

Yield 12.2 mg; Purity 29%; Retention Time 8.58 minutes; HRMS (ESI-TOF) calcd for C<sub>47</sub>H<sub>45</sub>O<sub>10</sub> [M+H]<sup>+</sup> 769.3013, found 769.3021.



**Cis-2-[3,4-bis(benzyloxy)phenyl]-5,7-dimethoxychroman-3-yl 3,5-bis(benzyloxy)benzoate (5bfd)**

Yield 5.5 mg; Purity 24%; Retention Time 10.13 minutes; HRMS (ESI-TOF) calcd for C<sub>52</sub>H<sub>47</sub>O<sub>9</sub> [M+H]<sup>+</sup> 815.3220, found 815.3205.



**Cis-2-[3,4-bis(benzyloxy)phenyl]-5,7-dimethoxychroman-3-yl 3-benzyloxy-4,5-dimethoxybenzoate (5bfe)**

Yield 15.6 mg; Purity 25%; Retention Time 8.25 minutes; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.25-7.38 (m, 16H, aromatic-H), 7.16 (d, *J* = 1.4 Hz, 1H), 7.07 (d, *J* = 1.9 Hz, 1H), 6.95 (dd, *J* = 1.9, 8.2 Hz, 1H), 6.85 (s, *J* = 8.2 Hz, 1H), 6.25 (d, *J* = 2.4 Hz, 1H), 6.13 (d, *J* = 2.4 Hz, 1H), 5.59 (br t, *J* = 2.9 Hz 1H), 5.04-5.09 (m, 5H), 4.82 (d, *J*<sub>gem</sub> = 11.6 Hz, 1H), 4.70 (d, *J*<sub>gem</sub> = 11.6 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 9H), 3.04 (dd, *J*<sub>gem</sub> = 17.4 Hz, *J* = 4.3 Hz, 1H), 2.99 (dd, *J*<sub>gem</sub> = 17.4 Hz, *J* = 2.9 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  165.2, 159.8, 159.0, 155.7, 153.1, 151.8, 149.1, 149.0, 143.1, 137.1, 136.6, 131.3, 128.7, 128.5, 128.4, 128.2, 127.8x2, 127.6, 127.4, 127.3, 125.0, 120.1, 114.9, 113.8, 109.1, 107.3, 100.3, 93.3, 92.0, 77.6, 71.4, 71.3, 71.0, 68.6, 60.9, 56.3, 55.5x2, 25.9; FT-IR (solid) 3447, 3008, 2939, 1715, 1596, 1455, 1220, 1118, 1025, 1006, 815, 752, 698 cm<sup>-1</sup>; HRMS (ESI-TOF) calcd for C<sub>47</sub>H<sub>45</sub>O<sub>10</sub> [M+H]<sup>+</sup> 769.3013, found 769.3026.

