

# Synthesis of esters derived from 2,3,4-tri-*O*-benzyl- $\alpha$ -D-methylglucoside

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## Abstract

2,3,4-Tri-*O*-benzyl- $\alpha$ -D-methylglucoside was prepared and reacted with several acids: benzoic, phenylacetic, 2-(3-bromo-propoxy)-benzoic, acetylsalicylic and 4-(toluene-4-sulfonylamino)-benzoic. The products were isolated with low to fair yields and fully characterized by usual analytical techniques.

**Keywords:** Salicylic acid, benzoic acid, phenylacetic acid,  $\alpha$ -D-methylglucoside, esters.

## Introduction

Salicylic acid derivatives are widely known either as natural products or as synthetic derivatives displaying different types of activity. Salicylate esters display immunity against other organisms<sup>1,2</sup> in plants, regeneration effects<sup>3</sup> and possibly a protective effect against UV radiation in plants.<sup>4</sup> Synthetic salicylic acid derivatives are well known as biological active compounds such as analgesic and antifungal<sup>5</sup> and are also part of cosmetic formulations.<sup>6</sup>

Some recent works refer to application of salicylic esters and salicylic acid-based dendrimers as potential drug carriers.<sup>7,8</sup>

Carbohydrates and glycoconjugates are involved in many normal and pathologic biological processes including cellular recognition, tumour metastasis, bacterial and viral infections.<sup>9</sup> The biological activity of carbohydrates depends generally on their ability to bind to specific receptors namely those containing *O*-sulfate esters. These carbohydrate derivatives occur widely in nature and play an essential role in many biological processes.<sup>10</sup> The sulfate groups have been demonstrated to be essential for binding.<sup>11</sup> Due to their amphiphilic, emulsifying and bioactive properties carbohydrate fatty acid esters have become particularly important for pharmaceutical applications,<sup>12</sup> food and as biodegradable detergents.<sup>13</sup> The regiospecific synthesis of sugar esters is a difficult and challenging task. One approach

described in the literature involves sugar derivatives soluble in organic media, namely the esterification of methyl glucosides.<sup>14</sup>

It was decided to prepare a set of esters from the 6-hydroxyl group of the D-glucose which was obtained by published methods starting from methylglucoside.<sup>15a</sup>

As the acid components, derivatives of benzoic acid were used, including analogues of salicylic acid containing bromine as a reactive site for further modifications.

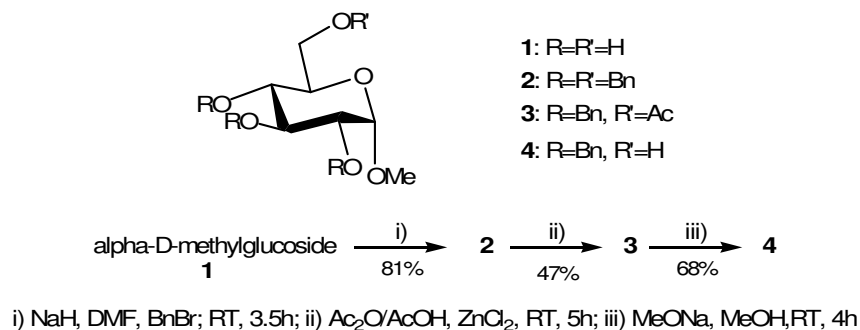
## Results and Discussion

Different methods of the preparation of the alcohol **4** starting from  $\alpha$ -methylglucoside are reported.<sup>15</sup> The availability of the reagents led us to use the route involving tetrabenylation, selective deprotection and simultaneous acetylation in position 6 followed by removal of the acetyl group.<sup>15a</sup>  $\alpha$ -D-Methylglucoside **1** was treated with sodium hydride and benzyl bromide in DMF and the tetrabenzylated product **2** was obtained in 81% yield.<sup>16</sup> Selective debenylation<sup>17</sup> using zinc chloride in  $\text{Ac}_2\text{O}$ -AcOH gave the product **3**, acetylated in position six, in 47% yield (Scheme 1). In the proton NMR it may be seen that one of the benzyl groups disappeared and had been replaced by a  $\text{COCH}_3$  group at 2.04 ppm.

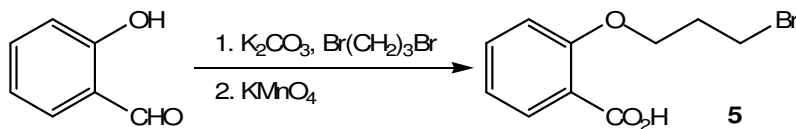
Selective de-*O*-acetylation was accomplished by a known method.<sup>18</sup> The overall yield for the preparation of the alcohol **4** was 26%. In its proton NMR spectrum the loss of the singlet at 2.04 ppm and the change of the signals of protons in position 6 to higher field, confirmed the structure.

As acid components, for the preparation of the esters, were used benzoic acid, phenylacetic acid, acetylsalicylic acid (these three compounds were commercially available), 2-(3-bromo-propoxy)-benzoic acid **5** and 4-(toluene-4-sulfonylamino)-benzoic acid **6**.

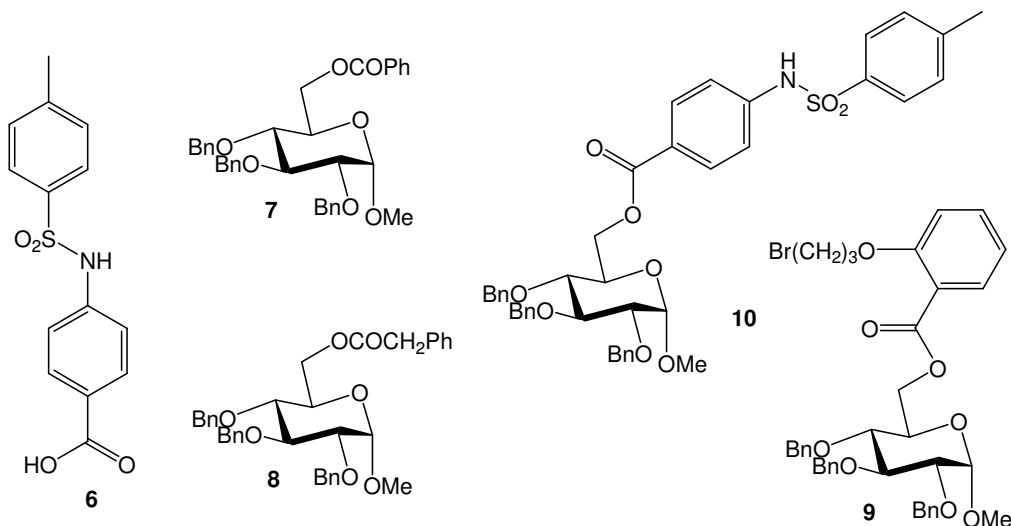
Acid component **5**<sup>19</sup> was prepared in 14% yield by alkylation of salicylaldehyde and further oxidation of the product (Scheme 2). The sulphonamide **6** (Figure 1) was prepared according to a literature method.<sup>20</sup>



**Scheme 1.** Preparation of the alcohol **4**



**Scheme 2.** Preparation of 2-(3-bromo-propoxy)-benzoic acid **5**



**Figure 1.** Structures of compounds **6-10**

The reactions between each carboxylic acid and the alcohol **4** were performed using DCC and DMAP.<sup>21</sup> The preparation of the esters **8** and **9** were achieved in high yields (75 and 77%), however compounds **7** and **10** were obtained in 27 and 9 % yields, respectively. The low yields for the latter esters were possibly due to difficulties in purification. For compound **10** selective precipitation of the urea by-product followed by preparative chromatography caused a greater loss of the target compound.

When the same preparative conditions were applied to acetylsalicylic acid with the alcohol **4**, the only product isolated was the 2,3,4-tri-*O*-benzyl-6-*O*-acetyl- $\alpha$ -D-methylglucoside **3**, in 53% yield. Under these conditions, the acetyl group was transferred to the OH group of the glucose derivative and this transesterification was the only reaction observed.

From the NMR data it may be observed that position of protons **6** give information on the acylation since for the alcohol **4** the chemical shifts are lower, below 3.8 ppm, than for the ester derivatives. The highest values are observed for compound **7**, 4.50 ppm for H-6'<sub>a</sub> (J=12 and 4.8 Hz) and 4.58 ppm for H-6'<sub>b</sub> (J=12 and 2.0 Hz).

## Experimental Section

**General.** Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected.  $^1\text{H}$  NMR (300 MHz) and  $^{13}\text{C}$  NMR (75.4 MHz) spectra were recorded on a Varian Unity Plus Spectrometer at 298 K or on a Bruker Avance II 400 spectrometer (400 MHz for  $^1\text{H}$  and 100.6 MHz for  $^{13}\text{C}$ ) or on a AC Bruker 250 MHz spectrometer. Chemical shifts are reported in ppm relative to solvent peak or TMS; coupling constants ( $J$ ) are given in Hz; C-q stands for quaternary carbon. Double resonance, HMQC (heteronuclear multiple quantum coherence) and HMBC (heteronuclear multiple bond correlation) experiments were carried out for complete assignment of  $^1\text{H}$  and  $^{13}\text{C}$  signals in the NMR spectra. High-resolution mass spectra (ESI-TOF) were obtained on a Bruker FTMS APEXIII spectrometer. Elemental analyses were obtained on a Leco CHNS-932 instrument. TLC was carried out on plates coated with silica gel 60 F254. Column chromatography was performed on silica gel (70-230 or 230-400 mesh). Light petroleum refers to the fraction boiling in the range 40-60°C.

**2,3,4,6-Tetra-*O*-benzyl- $\alpha$ -D-methylglucoside (2).** A suspension of sodium hydride (80%, 9.36 g, 0.312 mol) in DMF (40 mL) was cooled to 0°C with stirring and a solution of  $\alpha$ -D-methylglucoside **1** (5.0 g, 0.026 mol) in DMF (5 mL) and benzyl bromide (25 mL, 0.208 mol) were added slowly. The mixture was stirred at room temperature for 3.5 hours. After cooling to 0-5°C, diethyl ether (250 mL) and water (150 mL) were added. The organic layer was washed with water (5 x 150 mL), dried ( $\text{MgSO}_4$ ) and concentrated to give an oily residue. This residue was submitted to column chromatography (elution with mixtures of light petroleum and ethyl acetate) affording the glucoside **2** as a pure oil (81%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.39 (3H, s,  $\text{OCH}_3$ ), 3.57 (1H, dd  $J = 9.6$  and  $3.6$  Hz, H-2), 3.60-3.78 (4H, m, H-4, H-5 and 2x H-6), 3.99 (1H, t,  $J = 9.0$  Hz, H-3), 4.45-5.02 (8H, m, 4x  $\text{CH}_2$ ), 4.64 (1H, d  $J = 3.6$  Hz, H-1), 7.10-7.40 (20H, m, 4x5 Ar-H).  $^{13}\text{C}$  NMR (100.6 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.15 ( $\text{OCH}_3$ ), 68.48 (C-6), 70.04 (C-5), 73.37 ( $\text{CH}_2$ ), 73.47 ( $\text{CH}_2$ ), 75.01 ( $\text{CH}_2$ ), 75.73 ( $\text{CH}_2$ ), 77.66 (C-4), 79.83 (C-2), 82.11 (C-3), 98.19 (C-1), 127.56, 127.64, 127.66, 127.83, 127.88, 127.95, 128.12, 128.34, 128.37, 128.43, 128.98, 129.73 (CH-Ar), 137.91 (C-q), 138.16 (C-q), 138.25 (C-q), 138.79 (C-q).

**2,3,4-Tri-*O*-benzyl-6-*O*-acetyl- $\alpha$ -D-methylglucoside (3).** To a solution of the glucoside **2** (5.2 g, 9.36 mmol) in  $\text{Ac}_2\text{O}/\text{AcOH}$  (2:1, 52 mL)  $\text{ZnCl}_2$  (1M solution in diethyl ether, 70 mL, 70 mmol) was added. The mixture was stirred at room temperature for 8 hours and kept in the refrigerator overnight. Water was added (150 mL) and the mixture was extracted with diethyl ether (4 x 50 mL). The combined organic extracts were washed with aqueous saturated  $\text{Na}_2\text{CO}_3$  (2 x 100 mL), and water (3 x 100 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to give a yellowish syrup. This residue was submitted to dry flash chromatography (elution with mixtures of light petroleum and ethyl acetate of increasing polarity). The acetylated compound **3** was obtained as an oil (2.24 g, 47 %). The starting glucoside **2** (1.93 g, 37%) was also recovered.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.04 (3H, s,  $\text{COCH}_3$ ), 3.39 (3H, s,  $\text{OCH}_3$ ), 3.49 (1H, app t,  $J = 9.0$  Hz, H-4), 3.55 (1H, dd,  $J = 10.0$  and  $3.6$  Hz, H-2), 3.79-3.86 (1H, m, H-5), 4.02 (1H, t,  $J = 9.2$  Hz, H-3), 4.25-4.29 (2H, m, 2x H-6), 4.61 (1H, d,  $J = 3.6$  Hz, H-1), 4.55-5.05 (6H, m, 3x  $\text{CH}_2$ ), 7.25-7.40 (15H, m, 3x5 Ar-H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,

100.6 MHz):  $\delta$  20.80 (CH<sub>3</sub>), 55.20 (O CH<sub>3</sub>), 63.02 (C-6), 68.52 (C-5), 73.38 (CH<sub>2</sub>), 75.00 (CH<sub>2</sub>), 75.79 (CH<sub>2</sub>), 77.29 (C-4), 79.85 (C-2), 82.02 (C-3), 98.03 (C-1), 127.67, 127.87, 127.89, 127.96, 127.98, 128.02, 128.05, 128.09, 128.17, 128.42, 128.45, 128.47, 128.50, 128.52 (CH-Ar), 137.82 (C-q), 138.01 (C-q), 138.57 (C-q), 170.71 (C=O).

**2,3,4-Tri-*O*-benzyl- $\alpha$ -D-methylglucoside (4).** To a solution of 2,3,4-tri-*O*-benzyl-6-*O*-acetyl- $\alpha$ -D-methylglucoside **3** (0.62 g, 1.22 mmol) in MeOH (20 mL) sodium methoxide (0.21 g, 3.69 mmol) was added. The mixture was stirred at room temperature for 1.5 hours. Water (150 mL) was added, the methanol was partly distilled and the mixture was extracted (6 x 50 mL) with dichloromethane. The evaporation of dried (Na<sub>2</sub>SO<sub>4</sub>) organic phase afforded an oily residue which was purified by dry flash chromatography (mixtures of increasing polarity of light petroleum and ethyl acetate). The alcohol **4** was obtained as a colourless oil (0.39 g, 69%) that later solidified, m.p. 45.5 – 48.0°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  3.38 (3H, s, OCH<sub>3</sub>), 3.49-3.58 (2H, m, H-2 and H-4), 3.64-3.74 (2H, m, H-5 and H-6a), 3.78 (1H, dd, *J* = 11.6 and 2.4 Hz, H-6b), 4.02 (1H, t, *J* = 9.2 Hz, H-3), 4.58 (1H, d, *J* = 3.6 Hz, H-1), 4.63-5.04 (6H, m, 3x CH<sub>2</sub>), 7.25-7.38 (15H, m, Ar-H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100.6 MHz)  $\delta$ : 55.17 (OCH<sub>3</sub>), 61.86 (C-6), 70.63 (C-5), 73.41 (CH<sub>2</sub>), 75.01 (CH<sub>2</sub>), 75.73 (CH<sub>2</sub>), 77.38 (C-4), 79.96 (C-2), 81.94 (C-3), 98.17 (C-1), 127.60, 127.86, 127.95, 127.95, 128.02, 128.11, 128.39, 128.46 (CH-Ar), 138.10 (q), 138.12 (q), 138.71 (q). Anal. Calcd. for C<sub>28</sub>H<sub>32</sub>O<sub>2</sub>·H<sub>2</sub>O: C, 69.69; H, 7.10. Found: C, 69.61; H, 6.72%.

**Preparation of 2-(3-bromo-propoxy)-benzoic acid<sup>19</sup> (5).** To a solution of salicylaldehyde (1.00 g, 8.2 mmol) in acetonitrile (100 mL), 1,3-dibromopropane (8.26 g, 41 mmol) and potassium carbonate (2.26 g, 16 mmol) were added and the mixture was refluxed for 4 hours. To the reaction mixture dichloromethane and water were added and the organic layer was washed with water, dried (MgSO<sub>4</sub>) and the solvent was evaporated giving a yellow oil. Purification by column chromatography (ethyl acetate:*n*-hexane; 1:9) gave the 2-(3-bromo-propoxy)-benzaldehyde as a yellow oil (1.08 g, 54%). <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$  2.45-2.50 (2H, m, CH<sub>2</sub>), 3.63 (2H, t, *J* = 6.0 Hz, Br-CH<sub>2</sub>), 4.25 (2H, t, *J* = 6.0 Hz, O-CH<sub>2</sub>), 6.90-7.10 (2H, m, 3 and H-5), 7.56 (1H, dt, *J* = 7.4 and 1.8 Hz, H-4), 7.84 (1H, dd, *J* = 7.4 and 1.8 Hz, H-6), 10.49 (1H, s, CHO). The above derivative was dissolved in acetone (10 mL) and cooled to 0°C. A 1M aqueous solution of KMnO<sub>4</sub> (12 mL, 12 mmol) was added dropwise and the reaction was left stirring for 24 hours. The solid was filtered and washed with acetone. After removal of the acetone from the filtrate the solution was acidified to pH 2 (with 2M HCl) and extracted with ethyl acetate. The organic extract was dried (MgSO<sub>4</sub>) and the solvent was evaporated giving a thick oil which solidified in light petroleum, under vigorous stirring, overnight. The final product was obtained as a light brown solid (0.28 g, 25%), m.p. 62.3-64.5°C. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$  2.35-2.55 (2H, m, CH<sub>2</sub>), 3.62 (2H, t, *J* = 6.0 Hz, Br-CH<sub>2</sub>), 4.41 (2H, t, *J* = 6.0 Hz, OCH<sub>2</sub>), 7.06-7.19 (2H, m, H-3 and H-5), 7.56 (1H, dt, *J* = 1.8 and 7.6 Hz, H-4), 8.16 (1H, dd, *J* = 8.0 and 1.8 Hz, H-6). The signal due to COOH is not observed. Anal. Calcd. for C<sub>10</sub>H<sub>11</sub>BrO<sub>3</sub>: C, 46.33; H, 4.25%. Found: C, 46.03; H, 4.25%.

**2',3',4'-Tri-*O*-benzyl-6'-*O*-benzoyl- $\alpha$ -D-methylglucoside (7).** A solution of alcohol **4** (0.15 g, 0.325 mmol), DCC (74 mg, 0.358 mmol), benzoic acid (40 mg, 0.325 mmol) and DMAP (40 mg, 0.325 mmol) in dichloromethane (8 mL) was stirred at room temperature for 5 hours.

The *N,N'*-dicyclohexylurea was filtered off and the filtrate was washed with water (3x20 mL), 5% acetic acid solution (2 x 20 mL), again with water (3 x 20 mL) and then dried ( $\text{Na}_2\text{SO}_4$ ). After evaporation an oil was obtained which was submitted to column chromatography (eluted with mixtures of light petroleum and ethyl acetate of increasing polarity). The ester **7** was obtained as an oil (60 mg) still containing some urea. After PLC (chloroform:methanol; 9.7:0.3) product **7** was obtained as an oil (50 mg, 27%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.42 (3H, s,  $\text{OCH}_3$ ), 3.58-3.68 (2H, m, H-2' and H-4'), 3.95-4.02 (1H, m, H-5'), 4.09 (1H, t,  $J = 9.2$  Hz, H-3'), 4.50 (1H, dd,  $J = 12.0$  and 4.8 Hz, H-6'b), 4.58 (1H, dd,  $J = 12.0$  and 2.0 Hz, H-6'a), 4.65 (1H, d,  $J = 3.3$  Hz, H-1'), 4.62-5.08 (6H, m, 3x  $\text{CH}_2$ ), 7.23 -7.43 (15H, m, Ar-H), 7.45 (2H, t,  $J = 7.2$  Hz, H-3 and H-5), 7.58 (1H, t,  $J = 7.2$  Hz, H-4) and 8.03 (2H, d,  $J = 7.2$  Hz, H-2 and H-6).  $^{13}\text{C}$  NMR (100.6 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.18 ( $\text{OCH}_3$ ), 63.42 (C-6'), 68.70 (C-5'), 73.38 ( $\text{CH}_2$ ), 75.13 ( $\text{CH}_2$ ), 75.92 ( $\text{CH}_2$ ), 77.61 (C-4'), 80.04 (C-2'), 82.06 (C-3'), 97.95 (C-1'), 127.72 (CH-Ar), 127.87, 127.93, 128.00, 128.03, 128.08, 128.27, 128.32, 128.32, 128.43, 128.45 (CH-Ar), 129.59 (C-2 and C-6), 129.85 (C-1), 133.01 (C-3 and C-5), 137.74 (C-q), 138.01 (C-q), 138.48 (C-q), 166.17 (C=O). HR-ESI-TOF: Calcd. for  $\text{C}_{35}\text{H}_{36}\text{NaO}_7$ : 591.23532. Found: 591.23472 [ $\text{M}$ ] $^+$ .

**Reaction of acetylsalicylic acid with alcohol 4.** This reaction was performed under the same conditions as described above and the only product isolated was the acetylated glucoside **3** (53%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.04 (3H, s,  $\text{COCH}_3$ ), 3.39 (3H, s,  $\text{OCH}_3$ ), 3.50 (1H, t,  $J = 9.8$  Hz, H-4'), 3.56 (1H, dd,  $J = 9.8$  and 3.0 Hz, H-2'), 3.79-3.84 (1H, m, H-5'), 4.03 (1H, t,  $J = 9.0$  Hz, H-3') 4.22-4.34 (2H, m, 2xH-6'), 4.60 (1H, d,  $J = 3.3$  Hz, H-1'), 4.54-5.06 (6H, m, 3x $\text{CH}_2$ ), 7.23-7.44 (15H, m, Ar-H).

**2',3',4'-Tri-*O*-benzyl-6'-*O*-phenylacetyl- $\alpha$ -D-methylglucoside (**8**).** A solution of the alcohol **4** (0.124 g, 0.27 mmol), DCC (67 mg, 0.323 mmol), phenylacetic acid (40 mg, 0.30 mmol) and DMAP (36 mg, 0.30 mmol) in dichloromethane (8 mL) was stirred at room temperature for 3 hours. The *N,N'*-dicyclohexylurea was filtered off and the filtrate was evaporated to give an oil (0.36 g) which was submitted to dry flash chromatography. The ester **8** was obtained as an oil (0.12 g, 75%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.31 (3H, s,  $\text{OCH}_3$ ), 3.38 (1H, app t,  $J = 10.0$  Hz, H-4'), 3.49 (1H, dd,  $J = 9.6$  and 3.6 Hz, H-2'), 3.64 (2H, s,  $\text{CH}_2$ ), 3.76-3.82 (1H, m, H-5'), 3.99 (1H, t,  $J = 9.2$  Hz, H-3'), 4.25 (1H, dd,  $J = 12.0$  and 4.8 Hz, H-6'a), 4.35 (1H, dd,  $J = 12.0$  and 2.0 Hz, H-6'b), 4.58 (1H, d,  $J = 3.6$  Hz, H-1'), 4.35-5.30 (6H, m, 3x  $\text{CH}_2$ ), 7.20-7.40 (20H, m, Ar-H).  $^{13}\text{C}$  NMR (100.6 MHz,  $\text{CDCl}_3$ ):  $\delta$  41.29 ( $\text{COCH}_3$ ), 55.08 ( $\text{OCH}_3$ ), 63.33 (C-6'), 68.56 (C-5'), 73.32 ( $\text{CH}_2$ ), 74.97 ( $\text{CH}_2$ ), 75.68 ( $\text{CH}_2$ ), 77.50 (C-4'), 79.75 (C-2'), 81.89 (C-3'), 97.93 (C-1'), 127.11, 127.62, 127.81, 127.89, 127.92, 127.93, 128.06, 128.38, 128.40, 128.46, 128.54, 129.26 (CH-Ar), 133.80 (C-q), 137.81 (C-q), 138.02 (C-q), 138.61 (C-q), 171.15 (C=O). HR-ESI-TOF: Calcd. for  $\text{C}_{36}\text{H}_{38}\text{NaO}_7$ : 605.25097. Found: 605.25278 [ $\text{M}$ ] $^+$ .

**2',3',4'-Tri-*O*-benzyl-6'-*O*-[2-(3-bromopropoxy)]benzoyl- $\alpha$ -D-methylglucoside (**9**).** A solution of the alcohol **4** (0.235 g, 0.33 mmol), DCC (84 mg, 0.40 mmol), (3-bromopropoxy)benzoic acid **5** (96 mg, 0.37 mmol) and DMAP (5 mg, 0.040 mmol) in dichloromethane (10 mL) was heated at reflux for 2 h and then stirred at room temperature for 5 days. The *N,N'*-dicyclohexylurea was filtered off and the filtrate, after evaporation, was submitted to column chromatography (elution with mixtures of light petroleum and ethyl

acetate of increasing polarity). The ester was obtained as a chromatographically pure oil (0.180 g, 77%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 2.25-2.40 (2H, m, CH<sub>2</sub>CH<sub>2</sub>Br), 3.40 (3H, s, OCH<sub>3</sub>), 3.55-3.66 (2H, m, H-2' and H-4'), 3.62 (2H, t, J=6.4 Hz, CH<sub>2</sub>), 3.92-3.98 (1H, m, H-5'), 4.06 (1H, t, J = 9.2 Hz, H-3'), 4.17 (2H, t, J = 5.6 Hz, CH<sub>2</sub>O), 4.43 (1H, dd, J = 12.0 and 2.0 Hz, H-6'b), 4.56 (1H, dd, J= 12.0 and 4.4 Hz, H-6'a), 4.66 (1H, d, J=3.3 Hz, H-1'), 4.58-5.05 (6H, m, 3xCH<sub>2</sub>Ar), 6.94-7.03 (2H, m, H-3 and H-5), 7.22-7.41 (15H, m, 3xAr-H), 7.45 (1H, dt, J = 8.0 and 1.6 Hz, H-4), 7.78 (1H, dd, J = 8.0 and 1.6 Hz, H-6). <sup>13</sup>C NMR (100.6 MHz, CDCl<sub>3</sub>): δ 30.29 (CH<sub>2</sub>), 32.23 (CH<sub>2</sub>), 55.22 (OCH<sub>3</sub>), 63.23 (C-6'), 66.11 (CH<sub>2</sub>), 68.70 (C-5'), 73.30 (CH<sub>2</sub>), 75.12 (CH<sub>2</sub>), 75.84 (CH<sub>2</sub>), 77.66 (C-2' or C-4'), 79.71 (C-4' or C-2'), 82.02 (C-3'), 97.98 (C-1'), 113.18 (C-3 ou C-5), 119.97 (C-1), 120.37 (C-3 ou C-5), 127.67, 127.84, 127.93, 128.01, 128.06, 128.42, 128.45 (CH-Ar), 131.73 (C-6), 133.61 (C-4), 137.83 (C-q), 138.03 (C-q), 138.58 (C-q), 158.44 (C-2), 165.51 (CO).

HR-ESI-TOF: Calcd. for C<sub>38</sub>H<sub>41</sub>BrNaO<sub>8</sub>: 727.18770. Found: 729.18740 [M]<sup>+</sup>.

### **2',3',4'-Tri-O-benzyl-6'-O[4-(toluene-4-sulfonylamino)]benzoyl-α-D-methylglucoside**

**(10)**. A solution of the alcohol **4** (0.14 g, 0.30 mmol), DCC (68 mg, 0.33 mmol), 4-(toluene-4-sulfonylamino)benzoic acid **6** (87 mg, 0.30 mmol) and DMAP (37 mg, 0.30 mmol) in dichloromethane (10 mL) was stirred at room temperature for 3 days. The reaction mixture was heated at 40°C for 10 hours. The *N,N'*-dicyclohexylurea was filtered off, the filtrate was washed with water (50 mL), 20% acetic acid solution (50 mL) and water (2x50 mL) and dried (Na<sub>2</sub>SO<sub>4</sub>). The brown oil obtained after evaporation was dissolved in acetone and cooled. Some more urea precipitated out which was filtered, the filtrate was evaporated and the residue (136 mg) was purified by PLC (light petroleum:ethyl acetate, 2:1). The pure compound **10** was obtained as an oil (20 mg, 9%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.38 (3H, s, ArCH<sub>3</sub>), 3.38 (3H, s, OCH<sub>3</sub>), 3.50-3.60 (2H, m, H-2' and H-4'), 3.88-3.96 (1H, m, H-5'), 4.05 (1H, t, J = 9.3 Hz, H-3'), 4.20 (1H, dd, J = 12 and 4.8 Hz, H-6'a), 4.48 (1H, dd, J = 11.7 and 2.1 Hz, H-6'b), 4.83 (1H, d, J = 3.3 Hz, H-1'), 4.56-5.50 (6H, m, 3xCH<sub>2</sub>), 7.10-7.42 (23H, m, Ar-H), 7.77 (2H, d, J = 9.3 Hz, 2x Ar-H) and 7.83 (2H, d, J = 9.3 Hz, 2x Ar-H). HR-ESI-TOF: Calcd. for C<sub>42</sub>H<sub>43</sub>NNaO<sub>9</sub> S: 760.25507. Found: 760.25569 [M]<sup>+</sup>.

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