The First Total Syntheses of Enantiomerically Pure Naturally Occuring Ellagitannins Gemin D and its Regioisomer Hippomanin A

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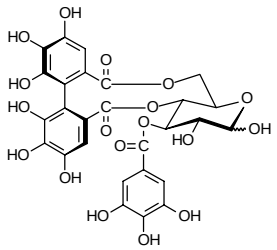
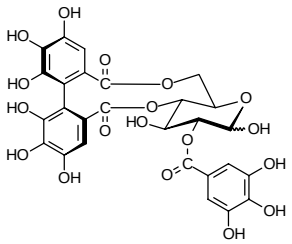
Abstract. The total syntheses of naturally occuring ellagitannins gemin D (**1**) and its regioisomer hippomanin A (**2**) are reported. In addition, the phase-transfer catalyzed benzylation reaction of the 2,3-glucopyranoside diols **3**–**7** is described. Our studies have illustrated the influence of the structure of 2,3-glucopyranoside diols on the regioselectivity of the phase-transfer catalyzed benzylation at their free 2,3-OH groups. We could show, that both phase-transfer catalyzed benzylations of 2,3-glucopyranoside diols using tetrabutylammonium hydrogensulfate (Bu_4NHSO_4) or using tetrabutylammonium iodide (Bu_4NI) disfavour the formation of the corresponding 3-*O*-monobenzylated products and preferentially give the 2-*O*-monobenzylated products. However, the ratio of the generated 2- *versus* 3-*O*-mono- and 2,3-dibenzylated products from these reactions also strongly depends upon the nature of the starting materials. The glucopyranosides **3** and **4** are the first examples, which allow the completely regioselective monobenzylation at the 2-OH positions by a phase-transfer catalyzed reaction.

The ellagitannin gemin D (**1**) [1, 2] and its regioisomer hippomanin A (**2**) [3] belong to a large family of polyphenolic natural products, obtained by extraction from a variety of higher plants and collectively named as tannins [4]. It has been shown that tannins exhibit a wide spectrum of biological effects [5]. Gemin D (**1**), for example, possesses antitumor [6] and anti-HIV [7] activities. The chemical structures of gemin D (**1**) and hippomanin A (**2**) were assigned as the 3-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-D-glucopyranose (**1**) [8, 9] and the 2-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-D-glucopyranose (**2**) [10, 11], respectively.



Gemin D (1)



Hippomanin A (2)

Our planned convergent syntheses of the natural products gemin D (**1**) and hippomannin A (**2**) involve the construction of monoacylated compounds **18** and **19** *via* an esterification reaction of the benzyl-protected gallic acid **17** with the suitably protected D-glucopyranoside derivatives **11** and **12**, in which only one OH group either at C-2 or at C-3 is unprotected.

A literature research for the 2-*O*-monoalkylation of the 2,3-glucopyranoside diols to synthesize such D-glucopyranoside derivatives with a free OH group at their C-3 revealed that several strategies have been employed so far. These include the control of the reaction time, or the application of an equimolar amount of alkylating agent or base [12]. A phase-transfer catalyzed regioselective 2-*O*-monobenzylation reaction of 2,3-glucopyranoside diols using tetrabutylammonium hydrogensulfate (Bu_4NHSO_4), has been developed by Garegg *et al*. [13]. However, this method led to the preferred formation of the 2-*O*-monobenzylated products with a considerable amount of the corresponding 3-*O*-mono and 2,3-dibenzylated compounds [13]. For example, the benzylation reaction of the glucopyranoside diol **6** led to the formation of a mixture of the corresponding 2,3-*O*-dibenzylated glucopyranoside (7%), 2-*O*-benzylated derivative **13** (50%) and 3-*O*-benzylated compound **14** (20%). The benzylation of the glucopyranoside diol **7** also gave a mixture of the corresponding 2,3-*O*-dibenzylated glucopyranoside (6%), 2-*O*-benzylated derivative **15** (54%) and 3-*O*-benzylated compound **16** (20%). As part of an ongoing program aimed at the synthesis of several enantiopure ellagitannins, a more practical route to the glucopyranosides with a free OH group at their C-3 was considered desirable. Here we report on the syntheses of the natural products gemin D (**1**), hippomannin A (**2**) based on benzylation of the 2,3-glucopyranoside diols **3**–**7** using tetrabutylammonium iodide (Bu_4NI) instead of Bu_4NHSO_4 as phase-transfer catalyst.

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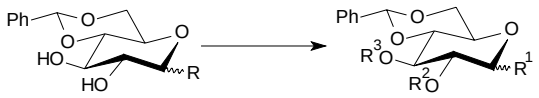
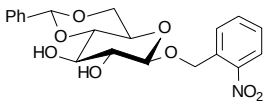
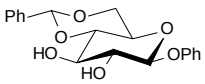
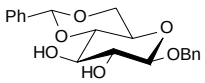
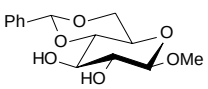
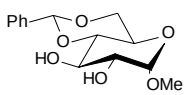
Results and Discussion

First, we investigated the benzylation reaction of the 2,3-glucopyranoside diol **3** using Bu_4NI as the phase-transfer catalyst. This reaction led to the formation of the 2-*O*-monobenzylated product **8** in a yield of 83% together with small amounts (5%) of dibenzylated product **9** (Tab. 1). None of the corresponding 3-*O*-monobenzylated product was detectable during this reaction. In addition, we investigated the benzylation reaction of other 2,3-glucopyranoside diols in order to find out the scope and limitation of this method (Tab. 1). The benzylation reaction of 2,3-glucopyranoside diol **4** exclusively gave the 2-*O*-monobenzylated product **10** in 72% yield. From 2,3-glucopyranoside diol **5** as the starting material, however, this reaction resulted in the formation of both regioisomers **11** and **12**, which could not be separated by chromatography on silica gel. The structures and the ratio of both regioisomers **11** and **12** were determined by comparison of the chemical shifts and the intensities of their ^{1}H NMR signals with those published for the glucopyranosides **11** [14, 15] and **12** [15]. The benzylation reaction of glucopyranoside diols **6** and **7** also produced a mixture of both corresponding monobenzylated regioisomers **13**, **14** and **15**, **16** with a negligible amount of the corresponding dibenzylated products.



	R	R^1	R^2	R^3
3	*β*-*O*-(*o*-Nitrobenzyl)	**8** *β*-*O*-(*o*-Nitrobenzyl)	Bn	H
4	*β*-*O*-(Phenyl)	**9** *β*-*O*-(*o*-Nitrobenzyl)	Bn	Bn
5	*β*-*O*-(Benzyl)	**10** *β*-*O*-(Phenyl)	Bn	H
6	*β*-*O*-(Methyl)	**11** *β*-*O*-(Benzyl)	Bn	H
7	*α*-*O*-(Methyl)	**12** *β*-*O*-(Benzyl)	H	Bn
		13 *β*-*O*-(Methyl)	Bn	H
		14 *β*-*O*-(Methyl)	H	Bn
		15 *α*-*O*-(Methyl)	Bn	H
		16 *α*-*O*-(Methyl)	H	Bn

Table 1 Partial Benzylation of Glucopyranoside Diols

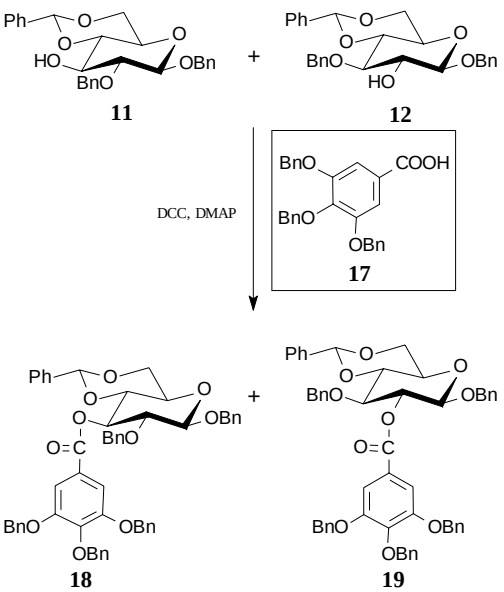
Starting material	Ether product	Yield (%)	$[\alpha]_D$ (degrees)	*m.p.* (°C)	Ref.
					
o-Nitrobenzyl 4,6-*O*-benzylidene-*β*-D-glucopyranoside (**3**) [16, 17]	2-benzyl **8**	83	– 27	152 – 153	s. exp.
	2,3-dibenzyl **9**	5	– 32	139 – 140	s. exp.
					
Phenyl 4,6-O-benzylidene-*β*-D-glucopyranoside (**4**) (Aldrich)	2-benzyl **10**	72	– 24	138 – 139	s. exp.
	2,3-dibenzyl	trace	–	–	[18]
					
Benzyl 4,6-O-benzylidene-*β*-D-gluco pyranoside (**5**) [19, 20]	2-benzyl **11**	55	–	–	[14, 15]
	3-benzyl **12**	19	–	–	[15]
	2,3-dibenzyl	trace	–	–	[19, 20]
					
Methyl 4,6-O-benzylidene-*β*-D-glucopyranoside (**6**) [21, 22]	2-benzyl **13**	56	– 28	125 – 126	[13, 23, 24]
	3-benzyl **14**	20	– 47	188 – 189	[13, 23, 24]
	2,3-dibenzy	trace	–	–	[13, 23]
					
Methyl 4,6-O-benzylidene-*α*-D-glucopyranoside (**7**) (Lancaster)	2-benzyl **15**	50	+ 34	131 – 132	[25, 13]
	3-benzyl **16**	28	+ 79	187 – 188	[25, 13]
	2,3-dibenzyl	trace	–	–	[25, 13]

In fact, the 2,3-glucopyranoside diols **3** and **4** are the first examples, which allow a completely regioselective phase-transfer catalyzed benzylation of their 2-OH, without accompanying formation of the corresponding 3-*O*-monobenzylated regioisomers.

The results of the benzylation reactions on 2,3-glucopyranoside diols **3**–**7** are summarized in Table 1.

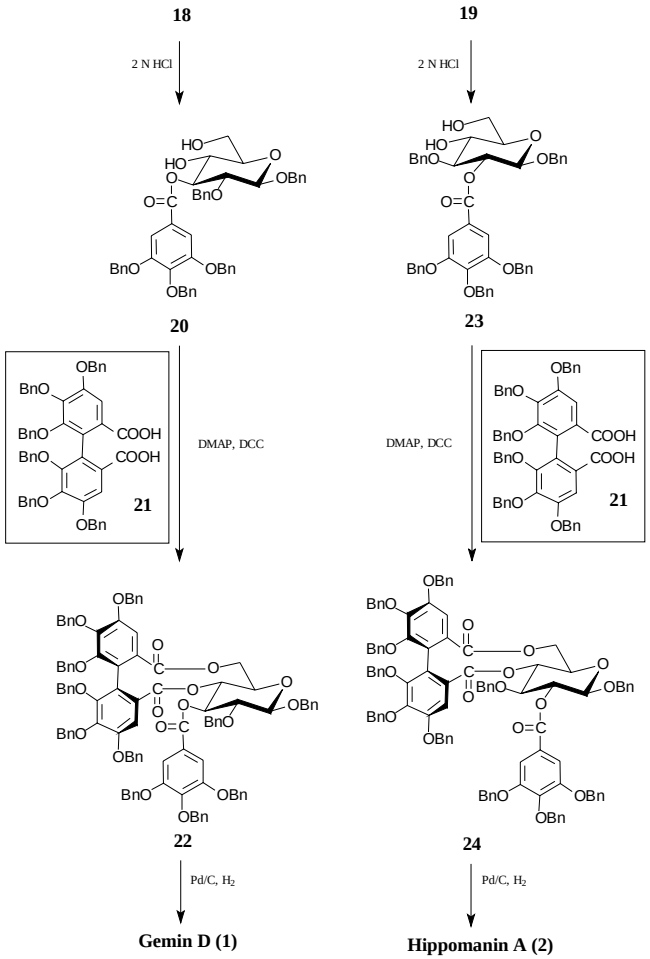
For comparison of the results of the benzylation reaction of 2,3-glucopyranoside diols using Bu_4NI with those based on the use of Bu_4NHSO_4, we also benzylated the 2,3-glucopyranoside diol **3** using Bu_4NHSO_4 as the phase-transfer catalyst. This benzylation reaction led to the formation of monobenzylated product **8** in a yield of 79% together with a small amount of the corresponding dibenzylated product **9** in 7% yield. The results for the benzylation reactions of **3**, **6** and **7** using Bu_4NHSO_4 are similar to those obtained for the benzylation reaction of the glucopyranoside **3**, **6** and **7** using Bu_4NI as the phase-transfer catalyst. Obviously, both phase-transfer catalyzed benzylation reactions of the 2,3-glucopyranosides preferentially form the corresponding 2-*O*-monobenzylated products, while the formation of the corresponding 3-*O*-monobenzylated regioisomers is prevented. Nevertheless, these similarities indicate, that the ratio of generated 2-*O*- *versus* 3-*O*-monobenzylated regioisomer depends not only on the nature of the used catalyst, but also strongly on the nature of the starting glucopyranosides.

Accordingly, we decided to acylate the mixture of both regioisomers **11** and **12** with the benzyl-protected gallic acid **17** [26] to assemble the frameworks of **1** and **2**. The acylation reaction of both regioisomers **11** and **12** with the benzyl-protected gallic acid **17** [26] in the presence of 4-(dimethylamino)pyridine (DMAP) and 1,3-dicyclohexylcarbodiimide (DCC) afforded a mixture of the monoacylated compounds **18** and **19**, respectively (Scheme 1).



Scheme 1

The resulting regioisomers **18** and **19** were then separated by chromatography and converted into the corresponding diols **20** and **23** by cleavage of the benzylidene acetal using 2N HCl in THF (Scheme 2). The esterification reaction of the racemic hexabenzyloxydiphenic acid (**21**) [26] with diols **20** and **23** proceeded diastereoselectively to produce both diastereoisomers **22** and **24**, respectively. The absolut configuration of the obtained diastereoisomers **22** and **24** were determined to be (*S*) after completion of the syntheses of both naturally occuring ellagitannins gemin D (**1**) and hippomanin A (**2**) by hydrogenolysis of the benzyl groups of the diastereoisomers **22** and **24**. All spectroscopic data of the synthetic ellagitannins **1** and **2** are in agreement with those published for the natural products gemin D (**1**) and hippomanin A (**2**), respectively.



Scheme 2

We thank the Deutsche Forschungsgemeinschaft for financial support (Totalsynthese 21/2-1), the Universität-GH Paderborn for the donation of a doctoral fellowship to K. Lötzerich and Professor K. Krohn for his helpful support.

Experimental

Analytical instruments and general methods were described previously [26].

Monobenzylation of Glucopyranoside Diols 3–7 (General Method A)

A mixture of the respective glucopyranoside diol (1.50 mmol), tetra-*n*-butylammonium iodide (*n*-Bu_4NI) (0.50 mmol, 0.33 eq), freshly distilled benzyl bromide (BnBr) (1.85 mmol, 1.23 eq) and diluted aqueous NaOH (2.42 mmol, 1.61 eq, 0.68M) in CH_2Cl_2 (30 ml) was stirred for 24 h at rt. The organic phase was separated and washed once with water (30 ml) and dried (Na_2SO_4). The solvent was removed under reduced pressure to give the crude product, which was purified by chromatography on silica gel to yield monobenzylated glucopyranoside as major product.

o-Nitrobenzyl 2-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (**8**) and *o-Nitrobenzyl 2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside* (**9**)

A solution of glucopyranoside diol **3** (500 mg, 1.24 mmol) in CH_2Cl_2 was treated with BnBr, according to the general method A, to afford after chromatography (CH_2Cl_2) 2-*O*-monobenzyl glucopyranoside **8** (508 mg, 83%, *m.p.* 152–153 °C) and its regioisomer 3-*O*-monobenzyl glucopyranoside **9** (36 mg, 5%, *m.p.* 139–140 °C) both as white powders.

compound 8 $[\alpha]_D^{20}$ = –27° (c = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3491, 3064, 3038, 2882, 1868, 1773, 1530, 1497. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 271 (3.36). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.42–3.62 (m, 3H, H-2, H-4, H-5), 3.78 (t, $J_{gem.}$ = 10.2 Hz, 1H, H-6), 3.91 (t, $J_{3,2}$ = 8.9 Hz, $J_{3,4}$ = 9.0 Hz, 1H, H-3), 4.39 (dd, $J_{6,5}$ = 4.9 Hz, $J_{gem.}$ = 10.5 Hz, 1H, H-6), 4.71 (d, $J_{1,2}$ = 7.7 Hz, 1H, H-1), 4.84 (d, $J_{gem.}$ = 11.4 Hz, 1H, OC$\underline{H}_2$Ph), 4.97 (d, $J_{gem.}$ = 11.4 Hz, 1H, OC$\underline{H}_2$Ph), 5.13 (d, $J_{gem.}$ = 15.3 Hz, 1H, H-7), 5.33 (d, $J_{gem.}$ = 15.3 Hz, 1H, H-7), 5.45 (s, 1H, H-14), 7.27–7.52 (m, 11H, H-12, H-Ar), 7.59 (dt, $J_{11,10}$ = 7.9 Hz, $J_{11,12}$ = 7.6 Hz, $J_{11,13}$ = 1.2 Hz, 1H, H-11), 7.86 (d, $J_{13,12}$ = 7.6 Hz, 1H, H-13), 8.13 (dd, $J_{10,11}$ = 7.9 Hz, $J_{10,12}$ = 1.2 Hz, 1H, H-10). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 65.98 (d, C-5), 67.79 (t, C-7), 68.44 (t, C-6), 73.31 (d, C-3), 74.93 (t, O$\underline{C}H_2$Ph), 80.24 (d, C-4), 81.81 (d, C-2), 101.64 (d, C-14), 102.85 (d, C-1), 124.64 (d, C-10), 126.09, 127.80, 127.87, 128.01, 128.13, 128.35, 128.52 and 129.06 (d, C–Ar), 133.63 (s, C–Ar), 133.92 (d, C–Ar), 136.77 (s, C–Ar), 137.90 (s, C–Ar), 146.84 (s, C-9). – MS (FAB/NBA): *m/z* (%) = 494 (8) [M^+ + H], 493 (2) [M^+], 341 (7) [(M^+ + H) – $C_7H_7NO_3$], 329 (12), 307 (12), 289 (8), 176 (34), 153 (36) [$C_7H_7NO_3^+$], 136 (100) [$C_7H_6NO_2^+$], 107 (38) [$C_7H_7O^+$], 91 (80) [$C_7H_7^+$], 77 (32), 63 (12).

$C_{27}H_{27}NO_8$	calcd.:	C 65.71	H 5.51	N 2.84
(493.51)	found:	C 65.68	H 5.38	N 2.66.

compound 9 $[\alpha]_D^{20}$ = –32° (c = 1, $CHCl_3$) – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3087, 3062, 3032, 2906, 2872, 1612, 1528, 1498. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 271 (3.06). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.47–3.55 (m, 1H, H-5), 3.69 (t, $J_{2,1}$ = 7.8 Hz, $J_{2,3}$ = 8.2 Hz, 1H, H-2), 3.78–3.92 (m, 3H, H-3, H-4, H-6), 4.45 (dd, $J_{6,5}$ = 5.0 Hz, $J_{gem.}$ = 10.4 Hz, 1H, H-6), 4.74 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1), 4.89 (d, $J_{gem.}$ = 11.4 Hz, 1H, OC$\underline{H}_2$Ph), 4.96 (s, 1H, OC$\underline{H}_2$Ph), 4.97 (s, 1H, OC$\underline{H}_2$Ph), 5.03 (d, $J_{gem.}$ = 11.4 Hz, 1H, OC$\underline{H}_2$Ph), 5.19 (d, $J_{gem.}$ = 15.6 Hz, 1H, H-7), 5.38 (d, $J_{gem.}$ = 15.6 Hz, 1H, H-7), 5.65 (s, 1H, H-14), 7.33–7.60 (m, 17H, H-11, H-12, H-Ar), 7.92 (d, $J_{13,12}$ = 7.7 Hz, 1H, H-13), 8.15 (dd, $J_{10,11}$ = 8.1 Hz, $J_{10,12}$ = 1.3 Hz, 1H, H-10). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 65.98 (d, C-5), 67.73 (t, C-7), 68.56 (t, C-6), 75.00 (t, O$\underline{C}H_2$Ph), 75.45 (t, O$\underline{C}H_2$Ph), 80.97 (d, C-3), 81.42 (d, C-4), 81.98 (d, C-2), 101.02 (d, C-14), 103.08 (d, C-1), 124.65 (d, C-10), 125.89 (d, C-11), 127.55, 127.64, 127.92, 127.94, 128.12, 128.16, 128.18, 128.21 and 128.24 (d, C–Ar), 128.49 (d, C-13), 128.83 (d, C–Ar), 134.17 (d, C-12), 137.16, 138.06 and 138.31 (s, C-8 and C–Ar), 146.78 (s, C-9). – MS (CI/NH_3, 160 °C): *m/z* (%) = 584 (38) [M^+ + H], 583 (100) [M^+], 493 (6) [(M^+ + H) – C_7H_7], 491 (6), 339 (12) [(M^+ – $C_7H_7NO_3$) – C_7H_7], 328 (10), 249 (6) [(M^+ + H) – $C_7H_7NO_3$) – $2C_7H_7$], 209 (12), 147 (14), 136 (12) [$C_7H_7O^+$], 79 (28).

$C_{34}H_{33}NO_8$	calcd.:	C 69.97	H 5.70	N 2.40
(583.63)	found:	C 69.82	H 5.59	N 2.31.

Phenyl 2-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (**10**)

A solution of the glucopyranoside diol (**4**) (500 mg, 1.45 mmol) in CH_2Cl_2 was treated with BnBr, according to the general method A, to afford after chromatography (CH_2Cl_2/EtOAc, 98:2) 2-*O*-monobenzyl glucopyranoside **10** (455 mg, 72%, *m.p.* 138–139 °C) as a white powder, along with a negligible amount of a less polar product. The less polar product is probably phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside [18] and was not further characterized. – $[\alpha]_D^{20}$ = –24° (c = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3467, 3061, 3036, 2900, 2878, 1728, 1598, 1595, 1491, 1454. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 268 (3.22). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 3.53–4.02 (m, 5H, H-2, H-3, H-4, H-5, H-6), 4.43 (dd, $J_{6,5}$ = 4.5 Hz, $J_{gem.}$ = 10.4 Hz, 1H, H-6), 4.90 (d, $J_{gem.}$ = 11.3 Hz, 1H, OC$\underline{H}_2$Ph), 5.09 (d, $J_{gem.}$ = 11.3 Hz, 1H, OC$\underline{H}_2$Ph), 5.19 (d, $J_{1,2}$ = 7.6 Hz, 1H, H-1), 5.59 (s, 1H, H-7), 7.30–7.58 (m, 15H, H-Ar). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 66.70 (d, C-5), 69.10 (t, C-6), 73.69 (d, C-3), 75.48 (t, O$\underline{C}H_2$Ph), 80.63 and 82.00 (d, C-2 and C-4), 102.15 (d, C-7), 102.30 (d, C-1), 117.28, 123.57, 126.49, 126.76, 128.51, 128.70, 128.75, 128.79, 128.93, 129.02, 129.73 and 130.05 (d, C–Ar), 137.37, 138.40 and 157.38 (s, C–Ar). – MS (DCI/NBA): *m/z* (%) = 435 (100) [M^+ + H], 391 (10), 358 (12), 341 (6), 250 (28), 235 (20) [M^+ – C_7H_7 – C_7H_8O], 183 (16), 168 (14) 125 (14), 106 (66).

$C_{26}H_{26}O_6$	calcd.:	C 71.88	H 6.03	
(434.49)	found:	C 71.70	H 6.10.	

Benzyl 2-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (**11**) and *Benzyl 3-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside* (**12**)

A solution of glucopyranoside diol **5** (2.00 g, 5.58 mmol) in CH_2Cl_2 was treated with BnBr, according to the general method A, to afford after chromatography (CH_2Cl_2) 2-*O*-monobenzyl glucopyranoside **11** [14] and its regioisomer 3-*O*-monobenzyl glucopyranoside **12** [15] (1.84 g together, 74%) as a white powder, which could not be separated by chromatography on silica gel. However, on the basis of their intensities, these signals could be assigned to the monobenzylated regioisomers **11** and **12** present in a 3:1 ratio. A negligible amount

of a less polar product could also be detected by t.l.c.. The less polar product is probably benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside [19, 20] and was not further characterized.

compounds 11 and 12 ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 2.69 (br. s., 2H, OH from **11** and **12**), 3.42–3.94 (m, 10H, H-2, H-3, H-4, H-5 and H-6 from **11**, H-2, H-3, H-4, H-5 and H-6 from **12**), 4.45 (dd, $J_{6,5}$ = 4.8 Hz, $J_{gem.}$ = 10.4 Hz, 2H, H-6 from **11** and **12**), 4.57 (d, $J_{1,2}$ = 6.0 Hz, 1H, H-1 from **12**), 4.68–5.11 (m, 9H, H-1 and OC$\underline{H}_2$Ph from **11**, OC$\underline{H}_2$Ph from **12**), 5.59 (s, 1H, H-7 from **11**), 5.64 (s, 1H, H-7 from **12**), 7.30–7.59 (m, 30H, H-Ar from **11** and **12**) – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 66.60 (d, C-5 from **11**), 66.91 (d, C-5 from **12**), 69.20 (t, C-6 from **11** and **12**), 71.80 (t, O$\underline{C}H_2$Ph anomeric center from **12**), 71.99 (t, O$\underline{C}H_2$Ph anomeric center from **11**), 73.66 (d, C-3 from **11**), 74.82 (d, C-2 from **12**), 75.06 (t, O$\underline{C}H_2$Ph from **12**), 75.34 (t, O$\underline{C}H_2$Ph from **11**), 80.73 (d, C-4 from **12**), 80.94 (d, C-4 from **11**), 81.80 (d, C-3 from **12**), 82.36 (d, C-2 from **11**), 101.73 (d, C-7 from **12**), 102.24 (d, C-7 from **11**), 102.74 (d, C-1 from **12**), 103.22 (d, C-1 from **11**), 126.54, 126.82, 128.23, 128.38, 128.49, 128.56, 128.60, 128.80, 128.89, 128.98, 129.48 and 129.69 (d, C–Ar from **11** and **12**), 137.36 (s, C–Ar from **12**), 137.51 and 137.55 (s, C–Ar from **11**), 137.77 (s, C–Ar from **12**), 138.69 (s, C–Ar from **11**), 138.89 (s, C–Ar from **12**).

Methyl 2-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (**13**) and *Methyl 3-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside* (**14**)

A solution of the glucopyranoside diol **6** (500 mg, 1.77 mmol) in CH_2Cl_2 was treated with BnBr, according to the general method A, to afford after chromatography (CH_2Cl_2) glucopyranosides **13** (369 mg, 56%, *m.p.* 125–126 °C; Lit. [13] 124–125 °C, Lit. [24] 124–125 °C, Lit. [23] 125–126 °C) and **14** (132 mg, 20%, *m.p.* 188–189 °C; Lit. [13] 184–185 °C, Lit. [24] 189–190 °C, Lit. [23] 190 °C) both as white powders, along with a negligible amount of a less polar product. The less polar product is probably methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside [13, 23] and was not further characterized.

compound 13 $[\alpha]_D^{20}$ = –28° (c = 1, $CHCl_3$); Lit. [13] $[\alpha]_D^{20}$ = –27° (c = 1, $CHCl_3$), Lit. [24] $[\alpha]_D^{20}$ = –27.6° (c = 1, $CHCl_3$), Lit. [23] $[\alpha]_D$ = –26° (c = 0.68, $CHCl_3$). – ^{1}H NMR (200 MHz, DMSO-d_6): δ/ppm = 3.18 (t, $J_{2,1}$ = 7.9 Hz, $J_{2,3}$ = 8.3 Hz, 1H, H-2), 3.40–3.56 (m, 2H, H-4, H-5), 3.47 (s, 3H, OCH_3), 3.62–3.79 (m, 2H, H-3, H-6), 4.25 (dd, $J_{6,5}$ = 3.5 Hz, $J_{gem.}$ = 9.8 Hz, 1H, H-6), 4.49 (d, $J_{1,2}$ = 7.9 Hz, 1H, H-1), 4.78 (s, 2H, OC$\underline{H}_2$Ph), 5.60 (d, *J* = 5.7 Hz, 1H, OH-3), 5.62 (s, 1H, H-7), 7.28–7.49 (m, 10H, H-Ar). – ^{13}C NMR (50 MHz, DMSO-d_6): δ/ppm = 57.48 (q, OCH_3), 66.43 (d, C-5), 68.78 (t, C-6), 73.14 (d, C-3), 74.77 (t, O$\underline{C}H_2$Ph), 81.53 (d, C-4), 83.57 (d, C-2), 101.57 (d, C-7), 104.99 (d, C-1), 127.24, 128.12, 128.35, 128.91 and 129.74 (d, C–Ar), 138.59 and 139.84 (s, C–Ar).

compound 14 $[\alpha]_D^{20}$ = –47° (c = 1, $CHCl_3$); Lit. [13] $[\alpha]_D^{20}$ = –48° (c = 1, $CHCl_3$), Lit. [24] $[\alpha]_D$ = –47.2° (c = 1, $CHCl_3$), Lit. [23] $[\alpha]_D$ = –45.5° (c = 0.88, $CHCl_3$). – ^{1}H NMR (200 MHz, DMSO-d_6): δ/ppm = 3.29–3.95 (m, 5H, H-2, H-3, H-4, H-5, H-6), 3.43 (s, 3H, OCH_3), 4.25 (dd, $J_{6,5}$ = 4.6 Hz, $J_{gem.}$ = 9.9 Hz, 1H, H-6), 4.33 (d, $J_{1,2}$ = 7.6 Hz, 1H, H-1), 4.80 (s, 2H, OC$\underline{H}_2$Ph), 5.63 (d, *J* = 5.4 Hz, 1H, OH-2), 5.67 (s, 1H, H-7), 7.27–7.41 (m, 10H, H-Ar). – ^{13}C NMR (50 MHz, DMSO-d_6): δ/ppm = 57.37 (q, OCH_3), 66.29 (d, C-5), 66.78 (t, C-6), 74.28 (t, O$\underline{C}H_2$Ph), 74.58 (d, C-2), 81.25 (d, C-4), 81.72 (d, C-3), 100.94 (d, C-7), 105.28 (d, C-1), 126.82, 128.07, 128.32, 128.86, 128.95 and 129.60 (d, C-Ar), 138.56 and 139.92 (s, C-Ar).

Methyl 2-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (**15**) and *Methyl 3-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside* (**16**)

A solution of the glucopyranoside diol **7** (500 mg, 1.77 mmol) in CH_2Cl_2 was treated with BnBr, according to the general method A, to afford after chromatography (CH_2Cl_2/EtOAc, 96:4) glucopyranosides **15** (330 mg, 50%, *m.p.* 131–132 °C; Lit. [13] 131–132 °C, Lit. [25] 130–131 °C) and **16** (185 mg, 28%, *m.p.* 187–188 °C; Lit. [13] 187–188 °C, Lit. [25] 186–187 °C) both as white powders, along with a negligible amount of a less polar product. This product is probably methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside [13, 25] and was not further characterized.

compound 15 $[\alpha]_D^{20}$ = +34° (c = 1, $CHCl_3$); Lit. [13] $[\alpha]_D^{20}$ = +35° (c = 1, $CHCl_3$), Lit. [25] $[\alpha]_D^{20}$ = +33° (c = 0.25). – ^{1}H NMR (200 MHz, DMSO-d_6): δ/ppm = 3.31–3.56 (m, 2H, H-2, H-4), 3.36 (s, 3H, OCH_3), 3.63–3.76 (m, 2H, H-5, H-6), 3.81–3.95 (m, 1H, H-3), 4.23–4.26 (m, 1H, H-6), 4.71 (d, $J_{gem.}$ = 12.0 Hz, 1H, OC$\underline{H}_2$Ph), 4.77 (d, $J_{gem.}$ = 12.0 Hz, 1H, OC$\underline{H}_2$Ph), 4.86 (d, $J_{1,2}$ = 3.4 Hz, 1H, H-1), 5.54 (d, *J* = 5.2 Hz, 1H, OH-3), 5.64 (s, 1H, H-7), 7.33–7.54 (m, 10H, H-Ar). – ^{13}C NMR (50 MHz, DMSO-d_6): δ/ppm = 55.64 (q, OCH_3), 63.17 (d, C-5), 69.08 (t, C-6), 70.16 (d, C-3), 72.84 (t, O$\underline{C}H_2$Ph), 80.69 (d, C-2), 82.22 (d, C-4), 99.24 (d, C-1), 101.89 (d, C-7), 127.33, 128.30, 128.55, 128.91, 129.04 and 129.76 (d, C–Ar), 138.68 and 139.66 (s, C–Ar).

compound 16 $[\alpha]_D^{20}$ = +79° (c = 1, $CHCl_3$); Lit. [13] $[\alpha]_D^{20}$ = +78° (c = 1, $CHCl_3$), Lit. [25] $[\alpha]_D^{20}$ = +78° (c = 0.25). – ^{1}H NMR (200 MHz, DMSO-d_6): δ/ppm = 3.25–3.76 (m, 5H, H-2, H-3, H-4, H-5, H-6), 3.35 (s 3H, OCH_3), 4.20–4.24 (m, 1H, H-6), 4.69 (d, $J_{1,2}$ = 3.0 Hz, 1H, H-1), 4.78 (s, 2H, OC$\underline{H}_2$Ph), 5.28 (d, *J* = 6.9 Hz, 1H, OH-2), 5.67 (s, 1H, H-7), 7.27–7.42 (m, 10H, H-Ar). – ^{13}C NMR (50 MHz, DMSO-d_6): δ/ppm = 55.65 (q, OCH_3), 63.22 (d, C-5), 69.03 (t, C-6), 72.86 (d, C-2), 74.24 (t, O$\underline{C}H_2$Ph), 79.23 and 81.77 (d, C-3 and C-4), 101.18 (d, C-7), 101.47 (d, C-1), 126.88, 128.03, 128.31, 128.83, 128.95 and 129.61 (d, C–Ar), 138.62 and 140.04 (s, C–Ar).

Esterification Reaction of Carboxylic Acids with Glucopyranoside Derivatives (General Method B)

A mixture of the suitably protected glucopyranoside, carboxylic acid, DCC and DMAP in dry CH_2Cl_2 was stirred at rt under Argon. After 24 h, the white precipitate (dicyclohexylurea) was filtered off. The solution was washed twice with water, dried (Na_2SO_4), filtered off, and the solvent was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel to afford the corresponding glucopyranoside ester.

Benzyl 2-O-benzyl-3-O-(3,4,5-tri-O-benzylgalloyl)-4,6-O-benzylidene-β-D-glucopyranoside (**18**) and *benzyl 3-O-benzyl-2-O-(3,4,5-tri-O-benzylgalloyl)-4,6-O-benzylidene-β-D-gluco-pyranoside* (**19**)

A mixture of both regioisomers **11** and **12** (1.60 g, 3.57 mmol), 3,4,5-tri-*O*-benzylgallic acid (**17**) (1.90 g, 4.28 mmol), DCC (0.89 g, 4.28 mmol), DMAP (0.53 g, 4.28 mmol) in dry CH_2Cl_2 (50 ml), was stirred, according to the general method B, to afford after column chromatography (CH_2Cl_2/*n*-hexane, 96:4 vol.%) benzylidene acetals **18** (1.85 g, 60%, *m.p.* 141–142 °C) and **19** (0.78 g, 25%, *m.p.* 161–162 °C) both as faintly yellow powders.

compound 18 $[\alpha]_D^{20}$ = –24° (c = 1.25, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3062, 3030, 2925, 2867, 1722, 1588, 1499, 1453, 1428, 1334, 1208, 1090, 1008, 737, 694. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 272 (3.50). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 3.70–4.02 (m, 4H, H-2, H-4, H-5, H-6), 4.55 (dd, $J_{6,5}$ = 4.4 Hz, $J_{gem.}$ = 10.1 Hz, 1H, H-6), 4.72 (d, $J_{gem.}$ = 11.6 Hz, 1H, OC<u>H</u>$_2$Ph at C-2), 4.86 (d, $J_{gem.}$ = 12.0 Hz, 1H, OC<u>H</u>$_2$Ph at C-1), 4.90–4.97 (m, 2H, H-1, OC<u>H</u>$_2$Ph at C-2), 5.14 (d, $J_{gem.}$ = 12.0 Hz, 1H, OC<u>H</u>$_2$Ph at C-1), 5.23 (s, 4H, Gall-OC<u>H</u>$_2$Ph at Gall-C-3 and Gall-C-5), 5.29 (s, 2H, Gall-OC<u>H</u>$_2$Ph at Gall-C-4), 5.63 (s, 1H, H-7), 5.72 (t, $J_{3,2}$ = 9.3 Hz, $J_{3,4}$ = 9.3 Hz, 1H, H-3), 7.22–7.55 (m, 32H, H-Ar). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 66.73 (d, C-5), 69.31 (t, C-6), 71.76 (t, Gall-O<u>C</u>H$_2$Ph at Gall-C-3 and Gall-C-5), 72.23 (t, O<u>C</u>H$_2$Ph at C-1), 73.95 (d, C-3), 74.92 (t, O<u>C</u>H$_2$Ph at C-2), 75.67 (t, Gall-O<u>C</u>H$_2$Ph at Gall-C-4), 79.35 (d, C-4), 80.04 (d, C-2), 101.90 (d, C-7), 103.70 (d, C-1), 110.06 (d, Gall-C-2 and Gall-C-6), 125.49 (s, Gall-C-1), 126.74, 127.43, 128.05, 128.52, 128.55, 128.73, 128.85, 129.10 and 129.55 (d, C–Ar), 137.26, 137.48, 137.54, 137.99 and 138.16 (s, C–Ar), 143.03 (s, Gall-C-4), 152.95 (s, Gall-C-3 and Gall-C-5), 165.54 (s, COOR). – MS (FAB/NBA): *m/z* (%) = 871 (21) [M$^+$ + H], 870 (26) [M$^+$], 763 (57) [(M$^+$ + H) – C_7H_8O], 673 (21) [M$^+$ – C_7H_6O – C_7H_7], 461 (21), 423 (90) [3,4,5-tri-*O*-benzylgalloyl ($C_{28}H_{23}O_4^+$)], 327 (70), 91 (100) [$C_7H_7^+$].
$C_{55}H_{50}NO_{10}$ calcd.: C 75.85 H 5.79
(870.99) found: C 75.88 H 5.81.

compound 19 $[\alpha]_D^{20}$ = –3° (c = 0.57, CH_2Cl_2) .– IR (KBr): $\tilde{\nu}$/cm^{-1} = 3062, 3030, 2928, 2868, 1730, 1591, 1499, 1454, 1428, 1337, 1207, 1126, 1090, 1020, 746, 696. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 279 (4.04). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 3.55–3.66 (m, 1H, H-5), 3.88–4.04 (m, 3H, H-3, H-4, H-6), 4.54 (dd, $J_{6,5}$ = 4.8 Hz, $J_{gem.}$ = 10.4 Hz, 1H, H-6), 4.71 (d, $J_{gem.}$ = 12.5 Hz, 1H, OC<u>H</u>$_2$Ph at C-1), 4.73 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1), 4.77 (d, $J_{gem.}$ = 11.8 Hz, 1H, OC<u>H</u>$_2$Ph at C-3), 4.94 (d, $J_{gem.}$ = 11.8 Hz, 1H, OC<u>H</u>$_2$Ph at C-3), 4.98 (d, $J_{gem.}$ = 12.5 Hz, 1H, OC<u>H</u>$_2$Ph at C-1), 5.20 (s, 4H, Gall-OC<u>H</u>$_2$Ph at Gall-C-3 and Gall-C-5), 5.34 (s, 2H, Gall-OC<u>H</u>$_2$Ph at Gall-C-4), 5.49 (t, $J_{2,1}$ = 8.0 Hz, $J_{2,3}$ = 8.2 Hz, 1H, H-2), 5.73 (s, 1H, H-7), 7.11–7.68 (m, 32H, H-Ar). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 66.83 (d, C-5), 69.25 (t, C-6), 70.99 (t, O<u>C</u>H$_2$Ph at C-1), 71.74 (t, Gall-O<u>C</u>H$_2$Ph at Gall-C-3 and Gall-C-5), 73.99 (d, C-2), 74.39 (t, O<u>C</u>H$_2$Ph at C-3), 75.62 (t, Gall-O<u>C</u>H$_2$Ph at Gall-C-4), 78.19 (d, C-4), 82.24 (d, C-3), 100.44 (d, C-1), 101.82 (d, C-7), 109.97 (d, Gall-C-2 and Gall-C-6), 125.31 (s, Gall-C-1), 126.59, 128.07, 128.35, 128.60, 128.69, 128.77, 128.85, 129.12, 129.17 and 129.61 (d, C-Ar), 137.20, 137.36, 137.81, 137.94 and 138.43 (s, C-Ar), 142.92 (s, Gall-C-4), 152.98 (s, Gall-C-3 and Gall-C-5), 165.10 (s, COOR). – MS (FAB/Glycerol + CF_3COOH): *m/z* (%) = 870 (1) [M$^+$], 782 (13), 675 (94), 585 (24), 493 (12), 423 (75) [3,4,5-tri-*O*-benzylgalloyl ($C_{28}H_{23}O_4^+$)], 331 (57), 304 (21), 271 (26), 241 (43), 91 (100) [$C_7H_7^+$].
$C_{55}H_{50}NO_{10}$ calcd.: C 75.85 H 5.79
(870.99) found: C 75.80 H 5.79.

Benzyl 2-O-benzyl-3-O-(3,4,5-tri-O-benzylgalloyl)-β-D-glucopyranoside (**20**)

To a stirred solution of the benzylidene acetal **18** (1.68 g, 1.94 mmol) in THF (20 ml) 20 ml of 2N HCl was added slowly at 60 °C. The mixture was stirred at 78 °C for 7 h. After cooling to rt the reaction mixture was quenched with saturated $NaHCO_3$, extracted 3 times with CH_2Cl_2 (60 ml). Drying of the combined organic extracts (Na_2SO_4) and evaporation under reduced pressure gave an oily residue. The crystallization of the oily residue (CH_2Cl_2/*n*-hexane) afforded the monoester **20** (1.30 g, 86%, *m.p.* 149–150 °C) as a white powder. – $[\alpha]_D^{20}$ = +39° (c = 0.79, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3412, 3284, 3061, 3028, 2948, 2934, 2865, 2862, 1720, 1588, 1498, 1429, 1373, 1333, 1100, 1091, 736, 697. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 274 (4.00). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.46–3.51 (m, 1H, H-5), 3.59 (dd, $J_{2,1}$ = 7.9 Hz, $J_{2,3}$ = 9.2 Hz, 1H, H-2), 3.81–4.00 (m, 3H, H-4, H-6), 4.61 (d, $J_{gem.}$ = 11.7 Hz, 1H, OC<u>H</u>$_2$Ph at C-2), 4.74 (d, $J_{1,2}$ = 7.9 Hz, 1 H, H-1), 4.76 (d, $J_{gem.}$ = 11.9 Hz, 1H, OC<u>H</u>$_2$Ph at C-1), 4.86 (d, $J_{gem.}$ = 11.7 Hz, 1H, OC<u>H</u>$_2$Ph at C-2), 5.01 (d, $J_{gem.}$ = 11.9 Hz, 1H, OC<u>H</u>$_2$Ph at C-1), 5.11 (s, 4H, Gall-OC<u>H</u>$_2$Ph at Gall-C-3 and Gall-C-5), 5.22 (s, 2H, Gall-OC<u>H</u>$_2$Ph at Gall-C-4), 5.33 (t, $J_{3,2}$ = 9.2 Hz, $J_{3,4}$ = 9.3 Hz, 1H, H-3), 7.08–7.49 (m, 27H, H-Ar). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 62.13 (t, C-6), 69.62 (d, C-4), 70.99 (t, Gall-O<u>C</u>H$_2$Ph at Gall-C-3 and Gall-C-5), 71.54 (t, O<u>C</u>H$_2$Ph at C-1), 74.19 (t, O<u>C</u>H$_2$Ph at C-2), 74.99 (t, Gall-O<u>C</u>H$_2$Ph at Gall-C-4), 75.30 (d, C-5), 77.93 (d, C-3), 78.64 (d, C-2), 102.56 (d, C-1), 109.19 (d, Gall-C-2 and Gall-C-6), 124.39 (s, Gall-C-1), 127.41, 127.45, 127.57, 127.65, 127.68, 127.70, 127.72, 127.78, 127.88, 127.92, 127.99, 128.07, 128.11, 128.23, 128.29, 128.33, 128.35, 128.37, 128.41, 128.44, 128.48, 128.58, 128.59, 128.61 and 128.65 (d, C-Ar), 136.47, 137.09, 137.21 and 137.60 (s, C–Ar), 142.42 (s, Gall-C-4), 152.34 (s, Gall-C-3 and Gall-C-5), 166.54 (s, COOR). – MS (FAB/NBA): *m/z* (%) = 783 (25) [M$^+$ + H], 782 (6) [M$^+$], 693 (21), 692 (7) [(M$^+$ + H) – C_7H_7], 675 (20) [(M$^+$ + H) – C_7H_8O], 585 (20), 461 (21), 423 (40) [3,4,5-tri-*O*-benzylgalloyl ($C_{28}H_{23}O_4^+$)], 369 (53), 333 (55), 304 (28), 185 (83), 93 (100), 91 (32) [$C_7H_7^+$].
$C_{48}H_{46}NO_{10}$ calcd.: C 73.64 H 5.92
(782.88) found: C 73.60 H 5.97.

Benzyl 2-O-benzyl-3-O-(3,4,5-tri-O-benzylgalloyl)-4,6-O-[(S)-2,2',3,3',4,4'-hexabenzyloxydiphenoyl]-β-D-glucopyranoside (**22**)

A mixture of the glucopyranoside diol **20** (1.20 g, 1.53 mmol), 2,2',3,3',4,4'-hexabenzyloxy-6,6'-diphenic acid (**21**) (2.02 g, 2.30 mmol), DCC (0.96 g, 4.60 mmol), and DMAP (0.57 g, 4.60 mmol) in dry CH_2Cl_2 (35 ml) was stirred, according to general method B, to afford after column chromatography (CH_2Cl_2/*n*-hexane, 90:10) the triester **22** (846 mg, 34%, *m.p.* 91–93 °C) as a white powder. – $[\alpha]_D^{20}$ = –28° (c = 0.31,

CH_2Cl_2). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3061, 3029, 2937, 2871, 1744, 1724, 1588, 1498, 1429, 1368, 1332, 1184, 1097, 737, 695. – UV (CH_2Cl_2): $\lambda_{max/nm}$ (lg ε) = 271 (4.36). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.83 (dd, $J_{2,1}$ = 7.9 Hz, $J_{2,3}$ = 9.2 Hz, 1H, H-2), 4.17 (ddd, $J_{5,4}$ = 10.0 Hz, $J_{5,6}$ = 1.7 Hz, 6.1 Hz, 1H, H-5), 4.23 (d, $J_{gem.}$ = 13.0 Hz, 1H, H-6), 4.76 (d, J_{gem} = 11.7 Hz, 1 H, OC$\underline{H}_2$Ph), 4.89 (d, $J_{1,2}$ = 7.9 Hz, 1H, H-1), 4.92–5.32 (m, 20H, OC$\underline{H}_2$Ph), 5.36 (d, $J_{gem.}$ = 11.7 Hz, 1H, OC$\underline{H}_2$Ph), 5.42 (t, $J_{4,3}$ = 9.7 Hz, $J_{4,5}$ = 10.0 Hz, 1H, H-4), 5.50 (dd, $J_{6,5}$ = 6.1 Hz, $J_{gem.}$ = 13.0 Hz, 1H, H-6), 5.71 (t, $J_{3,2}$ = 9.2 Hz, $J_{3,4}$ = 9.7 Hz, 1H, H-3), 7.08 (s, 1H, HBDP-H-5 or HBDP-H-5'), 7.15 (s, 1H, HBDP-H-5 or HBDP-H-5'), 7.02–7.65 (m, 57H, H-Ar). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 63.39 (t, C-6), 70.42 (d, C-4), 70.96 and 71.06 (t, O$\underline{C}H_2$Ph), 71.38 (d, C-5), 71.59 (t, O$\underline{C}H_2$Ph), 74.07 (d, C-3), 74.28, 74.85, 75.01, 75.12, 75.39 and 75.43 (t, O$\underline{C}H_2$Ph), 78.88 (d, C-2), 103.06 (d, C-1), 107.55 and 107.77 (HBDP-C-5 and HBDP-C-5'), 109.34 (d, Gall-C-2 and Gall-C-6), 123.36 (s, Gall-C-1), 123.50 and 124.60 (s, HBDP-C-1 and HBDP-C-1'), 127.36, 127.40, 127.46, 127.55, 127.63, 127.87, 127.90, 127.97, 127.99, 128.08, 128.12, 128.14, 128.19, 128.32, 128.34, 128.38, 128.43, 128.45, 128.48, 128.53, 128.55, 128.59 and 128.77 (d, C–Ar), 136.32, 136.36, 136.48, 136.88, 137.33, 137.35, 137.40, 137.48, 137.58 and 137.66 (s, C–Ar), 142.52, (s, Gall-C-4), 144.22 and 144.56 (s, HBDP-C-3 and HBDP-C-3'), 152.12, 152.31, 152.38, 152.56 and 152.58 (s, HBDP-C-2, HBDP-C-2', HBDP-C-4, HBDP-C-4', Gall-C-3 and Gall-C-5), 165.69 (s, Gall-COOR), 166.96 and 167.59 (s, HBDP-COOR).

$C_{104}H_{88}NO_{18}$	calcd.:	C 76.83	H 5.46
(1625.82)	found:	C 76.85	H 5.49.

3-O-Galloyl-4,6-O-[(S)-2,2',3,3',4,4'-hexahydroxydiphenoyl]-D-glucopyranose (Gemin D) (**1**)

A suspension of triester **22** (250 mg, 0.15 mmol), Pd/C (0.10 g, 10%) and dry THF (15 ml) was first degased with Argon (3 times) to remove O_2, and H_2 was conducted slowly through the reaction mixture for 24 h at room temperature.The reaction mixture was filtered through celite, and the celite was washed with a mixture of acetone/MeOH (80:20, 50 mL). The solvent was removed under reduced pressure to give an oily residue. The purification of the crude product was carried out by crystallization [MeOH/(acetone:CH_2Cl_2:*n*-hexane, 1:2:4)] to afford Gemin D (91 mg, 89%, *m.p.* >250 °C) as an anomeric mixture (α:β, 1.2:1) as a powder. – $[\alpha]_D^{20}$ = +40 ° (c = 0.5, MeOH). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3432, 2938, 2827, 1727, 1620, 1449, 1356, 1235, 1028, 760, 593. – UV (CH_2Cl_2): $\lambda_{max/nm}$ (lg ε) = 278 (4.37). – ^{1}H NMR (300 MHz, acetone-d_6/D_2O): δ/ppm = 3.58–3.85 (m, 5H, H-2α, H-2β, H-5β, H-6α, H-6β), 4.55 (dd, $J_{5\alpha,4\alpha}$ = 9.8 Hz, $J_{5\alpha,6\alpha}$ = 6.5 Hz, 1H, H-5α), 4.76 (d, $J_{1\beta,2\beta}$ = 7.0 Hz, 1H, H-1β), 4.92 (t, $J_{4\alpha,3\alpha}$ = 9.9 Hz, $J_{4\alpha,5\alpha}$ = 9.9 Hz, 1H, H-4α), 4.95 (t, $J_{4\beta,3\beta}$ = 9.9 Hz, $J_{4\beta,5\beta}$ = 9.8 Hz, 1H, H-4β), 5.19 (dd, $J_{6\alpha,5\alpha}$ = 6.5 Hz, $J_{gem.}$ = 13.0 Hz, 1H, H-6α), 5.21 (dd, $J_{6\beta,5\beta}$ = 6.5 Hz, $J_{gem.}$ = 13.0 Hz, 1H, H-6β), 5.24–5.33 (m, 2H, H-1α, H-3β), 5.47 (t, $J_{3\alpha,2\alpha}$ = 9.8 Hz, $J_{3\alpha,4\alpha}$ = 9.8 Hz, 1H, H-3α), 6.46, 6.47, 6.62 and 6.63 (s, 4H, HHDP-H-5α, HHDP-H-5'α, HHDP-H-5β and HHDP-H-5'β), 7.03 (s, 4H, Gall-H-2α, Gall-H-2β, Gall-H-6α and Gall-H-6β). – ^{13}C NMR (75 MHz, acetone-d_6/D_2O): δ/ppm = 64.15 (t, C-6α/6β), 67.40 (d, C-5α), 71.55 (d, C-4α), 71.66 (d, C-4β), 71.84 (d, C-5β), 72.00 (d, C-2α), 74.39 (d, C-3α), 74.79 (d, C-2β), 76.36 (d, C-3β), 93.91 (d, C-1α), 98.68 (d, C-1β), 108.08 and 108.29 (d, HHDP-C-5α/5β and HHDP-C-5'α/5'β), 110.47 (d, Gall-C-2α/2β and Gall-C-6α/6β), 116.11 (s, Gall-C-1α/1β), 121.13 and 121.21 (s, HHDP-C-1α/1β and HHDP-C-1'α/1'β), 126.13, 126.15, 126.52 and 126.57 (s, HHDP-C-6α/6β and HHDP-C-6'α/6'β), 136.58 and 136.74 (s, HHDP-C-3α/3β and HHDP-C-3'α/3'β), 139.34 and 139.37 (s, Gall-C-4α/4β), 144.66, 144.69, 145.49, 145.85 and 146.04 (s, HHDP-C-2α/2β, HHDP-C-2'α/2'β, HHDP-C-4α/4β, HHDP-C-4'α/4'β, Gall-C-3α/3β and Gall-C-5α/5β), 167.84, 168.03, 168.40, 168.46, 169.09 and 169.16 (s, HHDP-COORα/COORβ and Gall-COORα/COORβ).

$C_{27}H_{22}O_{18}\cdot 7\ H_2O$	calcd.:	C 42.64	H 4.77
(760.57)	found:	C 42.65	H 4.12.

Benzyl 3-O-benzyl-2-O-(3,4,5-tri-O-benzylgalloyl)-β-D-glucopyranoside (**23**)

A solution of benzylidene acetal **19** (0.68 g, 0.78 mmol) in THF (9 ml) was treated with 2N HCl (9 ml), according to the procedure for the glucopyranoside diol **20**, to give after crystallization (CH_2Cl_2/*n*-hexane) the 4,6-*O*-deprotected glucopyranoside **23** (0.50 g, 81%, *m.p.* 129–130 °C) as a white powder. – $[\alpha]_D^{20}$ = –4° (0.55, CH_2Cl_2) .– IR (KBr): $\tilde{\nu}$/cm^{-1} = 3423, 3409, 3062, 3031, 2926, 2875, 1723, 1588, 1499, 1454, 1427, 1335, 1204, 1100, 1038, 736, 696. – UV (MeOH): $\lambda_{max/nm}$ (lg ε) = 276 (3.94). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.44–3.47 (m 1H, H-5), 3.67 (t, $J_{3,2}$ = 9.1 Hz, $J_{3,4}$ = 9.2 Hz, 1H, H-3), 3.85–4.02 (m, 3H, H-4, H-6), 4.61–4.69 (m, 4H, H-1, OC$\underline{H}_2$Ph), 4.88 (d, $J_{gem.}$ = 12.7 Hz, 1H, OC$\underline{H}_2$Ph), 5.14 (s, 4H, Gall-OC$\underline{H}_2$Ph at Gall-C-3 and Gall-C-5), 5.24 (s, 2H, Gall-OC$\underline{H}_2$Ph at Gall-C-4), 5.50 (t, $J_{2,1}$ = 8.0 Hz, $J_{2,3}$ = 9.1 Hz, 1H, H-2), 7.14–7.51 (m, 27H, H-Ar). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 62.07 (t, C-6), 70.40 (d, C-4), 70.43 (t, O$\underline{C}H_2$Ph), 71.16 (t, Gall-O$\underline{C}H_2$Ph at Gall-C-3 and Gall-C-5), 73.50 (d, C-2), 74.36 (t, O$\underline{C}H_2$Ph), 75.00 (t, Gall-O$\underline{C}H_2$Ph at Gall-C-4), 75.33 (d, C-5), 81.97 (d, C-3), 99.51 (d, C-1), 109.39 (d, Gall-C-2 and Gall-C-6), 124.68 (s, Gall-C-1), 127.31, 127.33, 127.39, 127.61, 127.68, 127.79, 127.92, 128.03, 128.09, 128.19, 128.23, 128.37, 128.43 and 128.46 (d, C–Ar), 136.52, 136.91, 137.25 and 137.78 (s, C–Ar), 142.46 (s, Gall-C-4), 152.36 (s, Gall-C-3 and Gall-C-5), 164.65 (s, COOR). – MS (FAB/NBA): *m/z* (%) = 782 (10) [M^+], 675 (50) [$M^+ - C_7H_7O$], 585 (8), 461 (19), 423 (65) [3,4,5-tri-*O*-benzylgalloyl ($C_{28}H_{23}O_4^+$)], 307 (66), 91 (100) [$C_7H_7^+$].

$C_{48}H_{46}NO_{10}$	calcd.:	C 73.64	H 5.92
(782.88)	found:	C 73.57	H 5.98.

Benzyl 3-O-benzyl-2-O-(3,4,5-tri-O-benzylgalloyl)-4,6-O-[(S)-2,2',3,3',4,4'-hexabenzyloxydiphenoyl]-β-D-glucopyranoside (**24**)

A mixture of glucopyranoside diol **23** (0.40 g, 0.51 mmol), diphenic acid derivative **21** (0.67 g, 0.77 mmol), DCC (0.32 g, 1.53 mmol), and DMAP (0.19 g, 1.53 mmol) in dry CH_2Cl_2 (12 ml) was stirred, according to the general method B, to afford after column chromatography (CH_2Cl_2/*n*-hexane, 90:10) the triester **24** (247 mg, 33%, *m.p.* 128–129 °C) as a white powder. – $[\alpha]_D^{20}$ = –15° (c = 0.18, CH_2Cl_2) .– IR (KBr): $\tilde{\nu}$/cm^{-1} = 3061, 3029, 2931, 2874, 1745, 1588, 1498, 1428, 1368, 1331, 1184, 1097, 738, 695. – UV (CH_2Cl_2): $\lambda_{max/nm}$

(lg ε) = 272 (4.34). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 3.96–4.04 (m, 2H, H-3, H-5), 4.61 (d, $J_{gem.}$ = 13.0 Hz, 1H, H-6), 4.64–4.74 (m, 2H, H-1, OC$\underline{H}_2$Ph), 4.88–5.36 (m, 22H, H-6, OC$\underline{H}_2$Ph), 5.42 (t, $J_{4,3}$ = 9.8 Hz, $J_{4,5}$ = 9.8 Hz, 1H, H-4), 5.54 (t, $J_{2,1}$ = 8.0 Hz, $J_{2,3}$ = 9.0 Hz, 1H, H-2), 6.86 (s, 1H, HBDP-H-5 or HBDP-H-5'), 7.07 (s, 1H, HBDP-H-5 or HBDP-H-5'), 7.09–7.59 (m, 57H, H-Ar). – ^{13}C NMR (75 MHz, $CDCl_3$): δ/ppm = 63.47 (t, C-6), 70.28, 71.11 and 71.15 (t, O$\underline{C}H_2$Ph), 71.58 (d, C-4), 71.68 (d, C-5), 72.77 (t, O$\underline{C}H_2$Ph), 73.39 (d, C-2), 74.93, 75.02 and 75.45 (t, O$\underline{C}H_2$Ph), 78.96 (d, C-3), 99.71 (d, C-1), 107.74 and 107.82 (d, HBDP-C-5 and HBDP-C-5'), 109.31 (d, Gall-C-2 and Gall-C-6), 123.22 (s, Gall-C-1), 124.36 and 124.54 (s, HBDP-C-1 and HBDP-C-1'), 127.30, 127.39, 127.44, 127.56, 127.62, 127.75, 127.79, 127.84, 127.90, 127.93, 128.00, 128.10, 128.15, 128.28, 128.30, 128.36, 128.40, 128.50 and 128.68 (d, C–Ar), 136.30, 136.37, 136.49, 136.61, 137.23, 137.33, 137.40, 137.46, 137.54 and 137.86 (s, C–Ar), 142.43 (s, Gall-C-4), 144.33 and 144.80 (s, HBDP-C-3 and HBDP-C-3'), 152.17, 152.32, 152.36, 152.39 and 152.55 (s, HBDP-C-2, HBDP-C-2', HBDP-C-4, HBDP-C-4', Gall-C-3 and Gall-C-5), 164.22 (s, Gall-COOR), 166.36 and 166.80 (s, HBDP-COOR).

$C_{104}H_{88}NO_{18}$	calcd.:	C 76.83	H 5.46
(1625.82)	found:	C 76.84	H 5.50.

2-O-Galloyl-4,6-O-[(S)-2,2',3,3',4,4'-hexahydroxydiphenoyl]-D-glucopyranose (hippomanin A) (**2**)

A suspension of the triester **24** (160 mg, 0.10 mmol), Pd/C (0.09 g, 10%) in dry THF (10 ml) was treated with H_2, according to the procedure for Gemin D (**1**), to afford after crystallization [MeOH/(acetone:CH_2Cl_2:*n*-hexane, 1:2:4)] hippomanin A (**2**) (59 mg, 88%, *m.p.* >250 °C) as an anomeric mixture (α:β, 1.3:1) as a powder. – $[\alpha]_D^{20}$ = +60° (c = 0.5, MeOH) .– IR (KBr): $\tilde{\nu}$/cm^{-1} = 3417, 2964, 1727, 1621, 1449, 1349, 1261, 1230, 1096, 1024, 800, 696. – UV (CH_2Cl_2): $\lambda_{max/nm}$ (lg ε) = 278 (4.15). – ^{1}H NMR (200 MHz, acetone-d_6/D_2O): δ/ppm = 3.71–4.52 and 4.85–5.04 (2m, 10H, H-2α, H-2β, H-3α, H-3β, H4α, H-4β, H-5α, H-5β, H-6α, H-6β), 4.88 (d, $J_{1\beta,2\beta}$ = 7.8 Hz, 1H, H-1β), 5.20 (dd, $J_{6\alpha/6\beta,5\alpha/5\beta}$ = 6.5 Hz, $J_{gem.}$ = 12.7 Hz, 2H, H-6α, H-6β), 5.43 (d, $J_{1\alpha,2\alpha}$ = 3.5 Hz, 1H, H-1α), 6.55, 6.56, 6.64 and 6.67 (s, HHDP-H-5α, HHDP-H-5'α, HHDP-H-5β and HHDP-H-5'β), 7.13 and 7.15 (s, 4H, Gall-H-2α, Gall-H-2β, Gall-H-6α and Gall-H-6β). – ^{13}C NMR (75 MHz, acetone-d_6/D_2O): δ/ppm = 63.49 (t, C-6α/6β), 66.61, 69.74, 71.47, 72.41, 72.74, 74.65 and 76.06 (d, C-2α, C-2β, C-3α, C-3β, C-4α, C-4β, C-5α and C-5β), 90.49 (d, C-1α), 95.88 (d, C-1β), 107.41 and 107.66 (d, HHDP-C-5α/5β and HHDP-C-5'α/5'β), 109.88 (d, Gall-C-2α/2β and Gall-C-6α/6β), 116.07, 116.27, 120.35 and 120.77 (s, HHDP-C-1α/1β, HHDP-C-1'α/1'β, Gall-C-1α/1β), 125.59 and 125.92 (s, HHDP-C-6α/6β and HHDP-C-6'α/6'β), 136.27 and 136.51 (s, HHDP-C-3α/3β and HHDP-C-3'α/3'β), 138.95 and 139.12 (s, Gall-C-4α/4β), 144.47, 144.99 and 145.59 (s, HHDP-C-2α/2β, HHDP-C-2'α/2'β, HHDP-C-4α/4β, HHDP-C-4'α/4'β, Gall-C-3α/3β and Gall-C-5α/5β), 166.65, 166.97, 168.62, 168.89 and 169.08 (s, HHDP-COORα/COORβ and Gall-COORα/COORβ).

$C_{27}H_{22}O_{18} \cdot 7\ H_2O$	calcd.:	C 42.64	H 4.77
(760.57)	found:	C 42.65	H 4.07.

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