Studies Relevant to Ellagitannin Chemistry: Strain-Energy Induced Opening of the D-Glucono-δ-lactone Ring of an Ellagitannin Derivative and the Synthesis of Ellagitannin Natural Products with a D-Gluconic Acid Moiety

Karamali Khanbabaee*[a] and Kerstin Lötzerich[a]

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The opening of the D-glucono-δ-lactone ring of the ellagitannin derivative **8**, which contains a hexabenzyloxydiphenoyl moiety, to the corresponding gluconic acid derivative **9** under mild acidic conditions was investigated. This transformation was found to occur quantitatively upon treatment of the D-glucono-δ-lactone derivative **8** with silica gel.

Introduction

Ellagitannins belong to the hydrolyzable tannin class of polyphenolic natural products which possess a broad range of biological activities.[1a] Lagerstannins A−C (**1**−**3**) have previously been isolated from *Lagerstroemia speciosa* (L.) Pers. (= *L. flos-reginae* RETZ.) (Lythraceae) and their chemical structures were assigned to the ellagitannins (**1**), (**2**) and (**3**).[2] It is known that the leaves and fruits of *Lagerstroemia speciosa* have hypoglycaemic properties in the treatment of diabetes mellitus.[2]

From a synthetic point of view, the ellagitannins **1**, **2** and **3** are of interest as challenging targets, due to the complexity of their regio- and stereochemistry combined with the stuctural feature of the gluconic acid. In this paper we describe the synthesis of the enantiomerically pure precursor **15** of the naturally occurring lagerstannin C. To the best of our knowledge, there is no report in the literature concerning the opening of the D-glucono-δ-lactone ring of ellagitannin derivatives, and this paper describes a practical route for the synthesis of ellagitannins with a D-gluconic acid moiety for the first time.

We assumed that oxidation of the glucopyranose **III** would increase the strain energy of the sugar ring and support the hydrolysis of the D-glucono-δ-lactone **IV** to the correponding gluconic acid derivative **V** (Figure 2). It should be noted that the D-glucono-δ-lactone derivatives **IV**, serving as possible key intermediates in the biosynthesis of ellagitannins with a D-gluconic acid moiety, have not been isolated until now. The formation and hydrolysis of the D-glucono-δ-lactone derivative **IV** to the corresponding gluconic acid derivative **V** under acidic conditions would be the first method for the synthesis of ellagitannins carrying a gluconic acid moiety (e.g. **1**, **2** and **3**). It would also show that such D-glucono-δ-lactone derivatives **IV** as important key intermediates in the biosynthesis of ellagitannins with

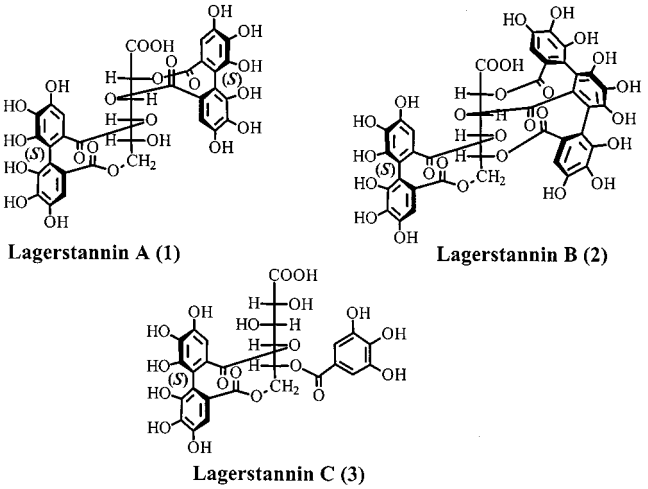

Figure 1. Chemical structures of the natural ellagitannins lagerstannins A−C (**1**−**3**)

a gluconic acid moiety are not stable under physiological (usually acidic) conditions in plants. Finally, the acylation of the free hydroxyl group of the gluconic acid derivative **V** at the C5 position with the protected gallic acid **VI** would then furnish the precusor of natural product lagerstannin C.

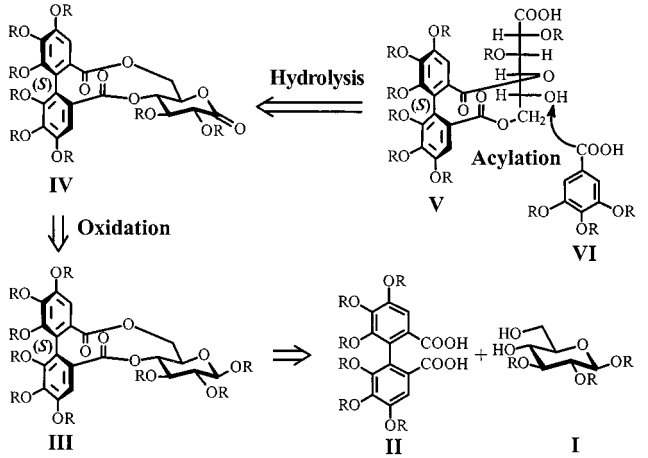

Figure 2. Retrosynthetic strategy for the synthesis of the carbon skeleton of the natural lagerstannin C (**3**)

[a] Universität-GH-Paderborn, Fachbereich 13, Chemie und Chemietechnik, Org. Chemie,
Warburger Str. 100, D-33098 Paderborn, Germany
Fax: (internat.) + 49-(0)5251/603245
E-mail: KKH@chemie.uni-paderborn.de

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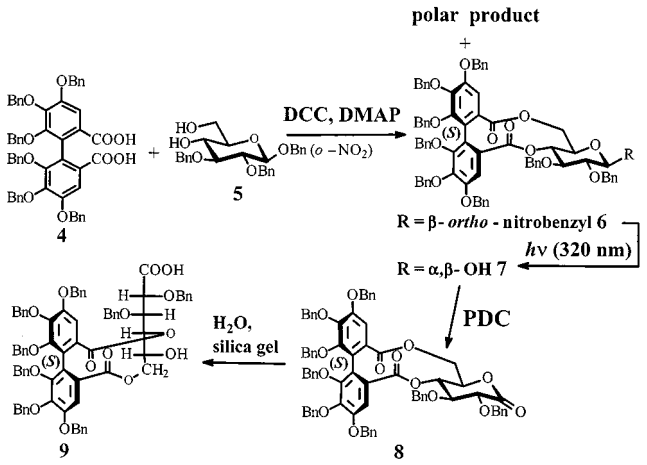
Results and Discussion

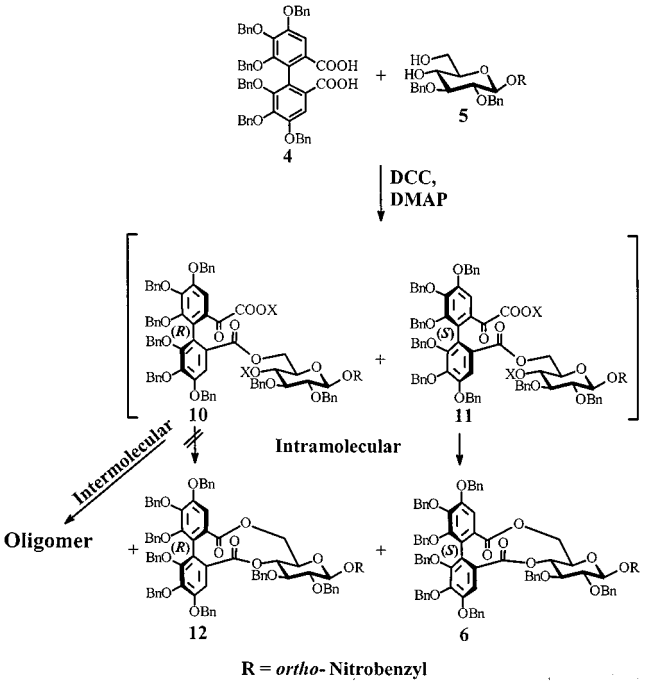
The absolute stereochemistry of the synthetic β−anomer **6** was established by an (*S*)-atropdiastereoselective esterification reaction of *rac*. hexabenzyloxydiphenic acid (**4**) with the appropriate sugar **5** under Steglich conditions [dicyclohexylcarbodiimide (DCC), 4-dimethylaminopyridine (DMAP)][3][4] to give the atropdiastereoisomer (*S*)-D **6** and a polar product (Scheme 1). The atropdiastereoselectivity of the esterification reaction of *rac*. hexabenzyloxydiphenic acid (**4**) with different 4,6-glucosediol derivatives under the same conditions was verified and the obtained (*S*)-atropdiastereoisomers were used as the enantiopure key intermediates in the total synthesis of the natural ellagitannins gemin D,[5] hippomanin A[5] and strictinin.[6]



Scheme 1. The formation and the opening of the D-glucono-δ-lactone

The photolabile *ortho*-nitrobenzyl group of **6** was then removed by irradiation at 320 nm in a photochemical apparatus (PYREX). The purification of the crude product was carried out easily by column chromatography on silica gel to give the anomerically deprotected derivative **7** (Scheme 1). The ^{13}C NMR spectrum of compound **7** shows duplicated signals for C-1 of the sugar moiety. On the basis of their chemical shifts, and their intensities, these signals could be assigned to the corresponding α- and β-anomers (α/β, 85:15). The oxidation of the α/β-anomeric mixture **7** by treatment with pyridinium dichromate (PDC) led exclusively to the formation of the corresponding D-glucono-δ-lactone derivative **8**. Surprisingly, the lactone ring of **8** was spontaneously hydrolyzed by treatment with silica gel yielding the desired gluconic acid derivative **9**. In light of these results it is not surprising that such kinds of D-glucono-δ-lactones are not abundant in nature.

We assume that, first, one of the two chemically equivalent carboxylic acid groups of the hexabenzyloxydiphenic acid (**4**) reacts with the more reactive hydroxyl group at C6 of the glucopyranose **5** to produce diastereoisomers **10** and **11** (Scheme 2). This transformation step was found to be very fast by the rapid disappearance of the starting materials from the reaction mixture (TLC). The intermediates **10** and **11** from the first transformation step can now react in two possible ways: (a) in an intermolecular way to yield more polar products, or (b) in an intramolecular ester cyclization reaction to yield the desired cyclic atropdiastereoisomers. Unusually, the (*R*)-intermediate **10** was found to react intermolecularly to produce polar products, whereas the (*S*)-intermediate **11** underwent an intramolecular cyclization to form the desired material **6** (Scheme 2). These results are in agreement with the molecular mechanics calculations and chemical results obtained by Feldman.[1a,1b]



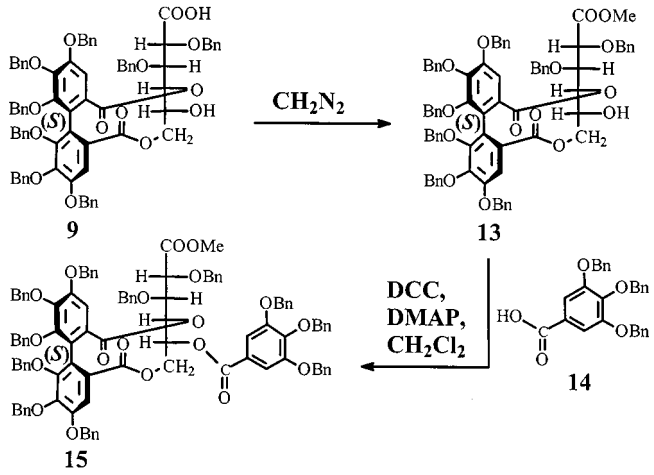
Scheme 2. Atropdiastereoselective esterification reaction

Alkaline hydrolysis of both polar and cyclic products from this reaction using anhydrous potassium hydroxide (potassium *tert*-butoxide, H_2O, THF)[7] led to the (*R*)-, and the (*S*)-hexabenzyloxydiphenic acid, respectively.[8] Thus, the atropisomerism of the biphenyl bond of the polar and the cyclic products was unequivocally established to be in the (*R*)-, and in the (*S*)-series by comparison of their specific optical rotations with those reported for the (*R*)-, and the (*S*)-hexabenzyloxydiphenic acids.[9]

All attempts to acylate the hydroxyl group at C5 of the gluconic acid derivative **9** with tribenzylgallic acid **14** under Steglich conditions, or by a trimethylsilyl trifluoromethanesulfonate (TMSOTf)-catalyzed esterification reaction[10] with tribenzylgalloyl anhydride, failed. Therefore, the carboxyl group of **9** was first protected as a methyl ester by treatment with diazomethane and then the free hydroxyl group of **13** was acylated with tribenzylgallic acid **14** to form the precusor **15** of the naturally occurring lagerstannin C.

Experimental Section

General Remarks: General methods and instrumentation were as described elsewhere.[8] HBDP and HHDP represent the hexa-



Scheme 3. The formation of the precursor of natural product lagerstannin C **15**

benzyloxy-, and hexahydroxydiphenoyl moiety, respectively. Gall represents the galloyl moiety, (*R*)-D and (*S*)-D the (*R*)-, and (*S*)-diastereoisomers, respectively.

1-*O*-(*o*-Nitrobenzyl)-2,3-di-*O*-benzyl-4,6-*O*-[(*S*)-2,2′,3,3′,4,4′-hexabenzyloxydiphenoyl]-β-D-glucopyranose (6): A mixture of glucopyranose derivative **5** (6.50 g, 13.12 mmol), *rac*-diphenic acid derivative **4** (13.83 g, 15.74 mmol, 1.2 equiv.), DCC (8.20 g, 39.36 mmol, 3 equiv.) and DMAP (4.86 g, 39.36 mmol, 3 equiv.) in dry CH_2Cl_2 (300 mL) was stirred at room temp. under argon for 24 h. The white precipitate (dicyclohexylurea) was then removed by filtration, the organic phase washed twice with water (150 mL) and dried (Na_2SO_4). The solvent was removed in vacuo to give an oil, which was purified by TLC (CH_2Cl_2/*n*-hexane, 95:5) on silica gel. Pure **6** (5.62 g, 32%) was obtained as a pale yellow powder. − m.p. 73−75°C. − $[\alpha]_D^{20} = -45°$ (*c* = 0.28, CH_2Cl_2). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.79−3.98 (m, 4 H, H-2, H-3, H-4, H-5), 4.11 (d, $J_{gem.}$ = 13.0 Hz, 1 H, H-6), 4.74 (d, $J_{1,2}$ = 7.2 Hz, 1 H, H-1), 4.81−5.34 (m, 18 H, H-6, H-7, OCH_2Ph), 5.47 (d, $J_{gem.}$ = 15.4 Hz, 1 H, H-7), 6.79 and 7.06 (s, 2 H, HBDP-H-5 and HBDP-H-5′), 6.93−7.61 (m, 41 H, H-11, H-Ar), 7.66 (dt, $J_{12,11}$ = 7.7 Hz, $J_{12,13}$ = 7.5 Hz, 1 H, H-12), 7.96 (br. d, $J_{13,12}$ = 7.5 Hz, 1 H, H-13), 8.21 (dd, $J_{10,11}$ = 8.1 Hz, $J_{10,12}$ = 1.3 Hz, 1 H, H-10). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 64.06 (t, C-6), 68.50 (t, C-7), 71.71 and 71.81 (t, O*C*H_2Ph), 72.23 and 72.39 (d, C-4 and C-5), 75.35, 75.58, 75.96 and 76.09 (t, O*C*H_2Ph), 81.94 and 83.08 (d, C-2 and C-3), 103.84 (d, C-1), 108.45 (d, HBDP-C-5 and HBDP-C-5′), 124.08 and 124.88 (s, HBDP-C-1 and HBDP-C-1′), 125.34 (d, C-10), 127.93, 128.05, 128.13, 128.39, 128.50, 128.56, 128.62, 128.75, 128.87, 128.94, 129.02 and 129.09 (d, C-11 and C-Ar), 129.41 (d, C-13), 134.44 (d, C-12), 134.62 (s, C-8), 136.98, 137.02, 137.97, 138.07, 138.22, 138.43, 138.51 and 138.61 (s, C-Ar), 144.94 and 145.39 (s, HBDP-C-3 and HBDP-C-3′), 147.40 (s, C-9), 152.83, 152.88, 152.97 and 153.07 (s, HBDP-C-2, HBDP-C-2′, HBDP-C-4 and HBDP-C-4′), 167.30 and 168.31 (s, COOR). − IR (KBr): $\tilde{\nu}$ = 3061 cm^{-1}, 3029, 2935, 2872, 1746, 1592, 1525, 1497, 1454, 1366, 1334, 1188. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 271 nm (4.25). − MS (DCI/NH_3); *m*/*z* (%) = 1338 (5) [M^+ + H], 1337 (6) [M^+], 1305 (9), 1216 (5) [(M^+ + H) − $C_6H_4NO_2$], 1215 (3) [M^+ − $C_6H_4NO_2$], 1111 (36) [(M^+ + H) − $C_7H_6NO_2$ − C_7H_7], 1021 (16), 1020 (9) [(M^+ + H) − $C_7H_6NO_2$ − 2 × C_7H_7], 878 (9) [HBDPS$^+$], 877 (13), 787 (9), 697 (4), 571 (5). − $C_{83}H_{71}NO_{16}$ (1338.46): calcd. C 74.48, H 5.35, N 1.05; found C 74.34, H 5.26, N 1.13.

2,3-Di-*O*-benzyl-4,6-*O*-[(*S*)-2,2′,3,3′,4,4′-hexabenzyloxydiphenoyl]-α/β-D-glucose (7): A solution of β-D-glucopyranose **6** (4.50 g, 3.36 mmol) in a solvent mixture of THF (200 mL), EtOH (200 mL) and H_2O (20 mL) was irradiated at 320 nm in a PYREX-Apparatus under argon for 6 h. The solvent was removed in vacuo to give an oil, which was purified by TLC (CH_2Cl_2/Et_2O, 99:1) on silica gel. Pure **7** (3.36 g, 90%) was obtained as a yellow powder (m.p. 75−77°C), which was identified as a mixture of α- and β-anomers by NMR spectroscopy (α/β, 85:15). − $[\alpha]_D^{20} = -48°$ (*c* = 0.90, $CHCl_3$). − **α−anomer:** ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.51 (s, 1 H, 1-OH), 3.80 (dd, $J_{2,1}$ = 3.5 Hz, $J_{2,3}$ = 9.1 Hz, 1 H, H-2), 3.97 (d, $J_{gem.}$ = 13.3 Hz, 1 H, H-6), 4.13 (t, $J_{3,2}$ = 9.1 Hz, $J_{3,4}$ = 9.8 Hz, 1 H, H-3), 4.54 (dd, $J_{5,4}$ = 9.9 Hz, $J_{5,6}$ = 5.8 Hz, 1 H, H-5), 4.73−5.32 (m, 19 H, H-1, H-4, H-6, OCH_2Ph), 6.83 and 7.05 (s, 2 H, HBDP-H-5 and HBDP-H-5′), 7.17−7.55 (m, 40 H, H-Ar). − **α−anomer:** ^{13}C NMR (50 MHz, $CDCl_3$): δ = 64.43 (t, C-6), 67.82 (d, C-5), 71.69 and 71.77 (t, O*C*H_2Ph), 72.65 (d, C-4), 74.18, 75.19, 75.41, 75.63 and 76.09 (t, O*C*H_2Ph), 79.70 (d, C-3), 80.56 (d, C-2), 92.29 (d, C-1), 108.41 (d, HBDP-C-5 and HBDP-C-5′), 124.08 and 124.83 (s, HBDP-C-1 and HBDP-C-1′), 127.99, 128.10, 128.15, 128.57, 128.79, 128.89, 128.97, 129.13 and 129.57 (d, C-Ar), 136.96, 137.01, 137.96, 138.00, 138.07, 138.25, 138.51 and 138.84 (s, C-Ar), 144.87 and 145.30 (s, HBDP-C-3 and HBDP-C-3′), 152.86, 152.99 and 153.05 (s, HBDP-C-2, HBDP-C-2′, HBDP-C-4 and HBDP-C-4′), 167.52 and 168.52 (s, COOR). − IR (KBr): $\tilde{\nu}$ = 3087 cm^{-1}, 3029, 2935, 2875, 1745, 1592, 1454, 1367, 1328, 1198, 1095. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 270 nm (4.43) . − MS (DCI/NH_3): *m*/*z* (%) = 1201 (13) [M^+], 1112 (75) [(M^+ + H) − C_7H_7], 1111 (100) [M^+ − C_7H_7], 1021 (49) [(M^+ + H) − 2 × C_7H_7], 931 (26), 878 (12) [HBDPS$^+$], 877 (18), 841 (9), 787 (26), 697 (11). − $C_{76}H_{66}O_{14}$ (1203.34): calcd. C 75.86, H 5.53; found C 76.01, H 5.42.

2,3-Di-*O*-benzyl-4,6-*O*-[(*S*)-2,2′,3,3′,4,4′-hexabenzyloxydiphenoyl]-D-glucono-δ-lactone (8) and 2,3-Di-*O*-benzyl-4,6-*O*-[(*S*)-2,2′,3,3′,4,4′-hexabenzyloxydiphenoyl]-D-gluconic acid (9): A solution of the α/β−anomeric mixture 7 (1.90 g, 1.58 mmol) in dry CH_2Cl_2 (8 mL) was treated with PDC (0.90 g, 2.37 mmol, 1.5 equiv.), freshly activated molecular sieve powder (1.20 g, 3 Å, 5 h at 300°C in vacuo) and dry acetic acid (150 μL) and the reaction mixture was stirred for 45 min at room temp. Celite (0.75 g) was added and the reaction mixture was stirred for an additional 20 min. The precipitate was filtered off and washed with CH_2Cl_2 (30 mL). Toluene (3 mL) was added and the solvent was evaporated in vacuo in order to remove the acetic acid. The residue was redissolved in CH_2Cl_2 (10 mL) and dried (Na_2SO_4). The solvent was removed in vacuo to give an oil. The product was purified by thin layer chromatography on silica gel to give D-glucono-δ-lactone 8 (m.p. 183−184°C) as yellow powder. Column chromatography of the product on silica gel (CH_2Cl_2/MeOH, 92:8) gave the corresponding D-gluconic acid derivative 9 (1.52 g, 79%, m.p. 135−137°C) also as a yellow powder.

D-Glucono-δ-lactone 8: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.03 (dd, $J_{3,2}$ = 2.2 Hz, $J_{3,4}$ = 7.9 Hz, 1 H, H-3), 4.22 (d, $J_{gem.}$ = 13.2 Hz, 1 H, H-6), 4.30 (d, $J_{2,3}$ = 2.2 Hz, 1 H, H-2), 4.48 (d, $J_{gem.}$ = 12.0 Hz, 1 H, OCH_2Ph), 4.69 (d, $J_{gem.}$ = 12.0 Hz, 1 H, OCH_2Ph), 4.73 (d, $J_{gem.}$ = 12.0 Hz, 1 H, OCH_2Ph), 5.00 (dd, $J_{5,4}$ = 7.5 Hz, $J_{5,6}$ = 2.6 Hz, 1 H, H-5), 4.86−5.44 (m, 15 H, H-4, H-6, OCH_2Ph), 6.81 and 7.05 (s, 2 H, HBDP-H-5 and HBDP-H-5′), 7.14−7.56 (m, 40 H, H-Ar). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 62.94 (t, C-6), 71.62 and 71.70 (t, O*C*H_2Ph), 71.82 (d, C-4), 72.15 and 73.29 (t, O*C*H_2Ph), 74.04 (d, C-5), 75.49, 75.60, 76.02 and 76.07 (t, O*C*H_2Ph), 78.90 (d, C-2), 79.62 (d, C-3), 108.13 and 108.31 (d, HBDP-C-5 and HBDP-C-5′), 123.60 and 124.93 (s, HBDP-C-1

and HBDP-C-1′), 127.94, 128.11, 128.16, 128.35, 128.48, 128.53, 128.58, 128.72, 128.76, 128.89, 128.99, 129.11 and 129.23 (d, C-Ar), 136.52, 136.82, 136.89, 137.46, 137.88, 137.93, 138.10 and 138.46 (s, C-Ar), 144.86 and 145.48 (s, HBDP-C-3 and HBDP-C-3′), 152.75, 152.91, 153.07 and 153.20 (s, HBDP-C-2, HBDP-C-2′, HBDP-C-4 and HBDP-C-4′), 166.84 (s, HBDP-COOR), 167.75 (s, lactone-COOR), 168.13 (s, HBDP-COOR). − IR (KBr): $\tilde{\nu}$ = 3087 cm^{-1}, 3029, 2925, 2873, 1751, 1592, 1454, 1367, 1330, 1184, 1078. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 270 nm (4.44). − MS (DCI/NH_3): *m/z* (%) = 1200 (4) [M^+], 1109 (80) [$M^+ - C_7H_7$], 1019 (100), 929 (50), 878 (36) [HBDPS$^+$], 823 (30), 787 (38), 733 (20), 697 (18), 607 (10). − $C_{76}H_{64}O_{14}$ (1201.33): calcd.C 75.99, H 5.37; found C 75.87, H 5.46.

D-Gluconic acid derivative 9: $[\alpha]_D^{20}$ = +15° (*c* = 0.15, CH_2Cl_2). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.96 (d, $J_{gem.}$ = 11.4 Hz, 1 H, H-6), 4.13−5.27 (m, 21 H, H-2, H-3, H-4, H-5, H-6, OC*H*$_2$Ph), 6.67 (s, 1 H, HBDP-H-5 or HBDP-H-5′), 6.93−7.59 (m, 41 H, HBDP-H-5 or HBDP-H-5′, H-Ar). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 67.39 (d, C-4), 68.40 (t, C-6), 69.86, 70.45, 71.45, 72.35, 74.39, 74.55, 74.76 and 74.91 (t, O*C*H$_2$Ph), 76.69 (d, C-3), 78.89 (d, C-2), 80.27 (d, C-5), 106.94 and 107.62 (d, HBDP-C-5 and HBDP-C-5′), 121.85 and 122.47 (s, HBDP-C-1 and HBDP-C-1′), 126.95, 127.11, 127.30, 127.45, 127.62, 127.86, 127.93, 127.98, 128.11, 128.17, 128.38, 128.42, 129.20 and 130.14 (d, C-Ar), 136.04, 136.66, 137.07, 137.16, 137.22, 137.38, 139.18 and 139.43 (s, C-Ar), 142.86 and 143.24 (s, HBDP-C-3 and HBDP-C-3′), 151.22, 151.37, 151.76 and 152.02 (s, HBDP-C-2, HBDP-C-2′, HBDP-C-4 and HBDP-C-4′), 166.57 and 168.25 (s, COOR), 175.53 (s, COOH). − IR (KBr): $\tilde{\nu}$ = 3439 cm^{-1}, 3087, 3062, 3031, 2938, 2874, 1740, 1593, 1497, 1454, 1388, 1333, 1191, 1096. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 270 nm (4.10). − MS (FAB/NBA): *m/z* (%) = 1219 (21) [M^+ + H], 1218 (14) [M^+], 830 (17), 753 (25), 645 (46), 553 (100). − $C_{76}H_{66}O_{15}$ (1219.34): calcd. C 74.86, H 5.46; found C 74.37, H 5.50.

2,3-Di-*O*-benzyl-4,6-*O*-[(*S*)-2,2′,3,3′,4,4′-hexabenzyloxydiphenoyl]-D-gluconic acid methyl ester (13): A portion of the gluconic acid **9** (250 mg, 0.21 mmol) was treated with freshly prepared ethereal diazomethane solution (0.41 mL, 0.21 mmol) and the suspension was stirred at room temp. for 1 h. After 1 h one drop of acetic acid was added to the reaction mixture to destroy the diazomethane excess and the solvent was removed in vacuo. The product was chromatographed on silica gel (CH_2Cl_2/Et_2O, 105:5) to give methyl ester **13** (178 mg, 70%, m.p. 197−199°C) as yellow powder. − $[\alpha]_D^{20}$ = −8° (*c* = 0.10, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.78 (br. s, 1 H, 5-OH), 3.58 (s, 3 H, OCH_3), 3.87 (d, $J_{gem.}$ = 12.2 Hz, 1 H, H-6), 4.13 (t, $J_{3,2}$ = 4.6 Hz, $J_{3,4}$ = 4.6 Hz, 1 H, H-3), 4.23 (d, $J_{2,3}$ = 4.6 Hz, 1 H, H-2), 4.34 (d, $J_{gem.}$ = 11.2 Hz, 1 H, OC*H*$_2$Ph), 4.45 (d, $J_{5,4}$ = 7.3 Hz, 1 H, H-5), 4.64−5.03 (m, 15 H, H-6, OC*H*$_2$Ph), 5.11 (d, $J_{gem.}$ = 11.2 Hz, OC*H*$_2$Ph), 5.25 (dd, $J_{4,3}$ = 4.6 Hz, $J_{4,5}$ = 7.3 Hz, 1 H, H-4), 6.79 and 6.87 (s, 2 H, HBDP-H-5 and HBDP-H-5′), 6.91−7.38 (m, 40 H, H-Ar). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.90 (q, OCH_3), 66.78 (t, C-6), 69.47 (d, C-5), 71.43 (t, O*C*H$_2$Ph), 72.97 (d, C-4), 73.67, 74.64, 75.45 and 75.94 (t, O*C*H$_2$Ph), 79.26 (d, C-3), 79.43 (d, C-2), 107.88 and 108.41 (d, HBDP-C-5 and HBDP-C-5′), 123.08 and 124.14 (s, HBDP- C-1 and HBDP-C-1′), 127.89, 128.05, 128.41, 128.52, 128.64, 128.84 and 128.98 (d, C-Ar), 129.72 (s, C-Ar), 136.91, 136.97, 137.34, 137.88, 137.99, 138.17 and 138.28 (s, C-Ar), 144.53 and 144.97 (s, HBDP-C-3 and HBDP-C-3′), 152.69, 152.78, 152.91 and 153.05 (s, HBDP-C-2, HBDP-C-2′, HBDP-C-4 and HBDP-C-4′), 167.32 and 168.55 (s, HBDP-COOR), 171.09 (s, COOR). − IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1}, 3062, 3031, 2944, 2876, 1741, 1594, 1498, 1455, 1369, 1337, 1249, 1193. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 270 nm (4.02). − MS (DCI/NH_3): *m/z* (%) = 1232 (3) [M^+], 1200 (1) [$M^+ - CH_4O$], 1141 (100) [$M^+ - C_7H_7$], 1109 (45), 1051 (13) [(M^+ + H) − 2 × C_7H_7], 929 (14). − $C_{77}H_{68}O_{15}$ (1233.37): calcd. C 74.99, H 5.56; found C 74.88, H 5.48.

2,3-Di-*O*-benzyl-4,6-*O*-[(*S*)-2,2′,3,3′,4,4′-hexabenzyloxydiphenoyl]-5-*O*-(3,4,5-tri-*O*-benzyl-galloyl)-D-gluconic acid methyl ester (15): A solution of 13 (67 mg, 0.05 mmol), 3,4,5-tri-*O*-benzylgallic acid (14) (36 mg, 0.08 mmol, 1.5 equiv.), DCC (18 mg, 0.08 mmol, 1.5 equiv.) and DMAP (11 mg, 0.08 mmol, 1.5 equiv.) in dry CH_2Cl_2 (5 mL) was stirred at room temp. under argon for 4 h. The white precipitate (dicyclohexylurea) was then filtered off, the organic phase was washed twice with water (20 mL) and dried (Na_2SO_4). The solvent was removed in vacuo to give an oil. The product was chromatographed on silica gel (CH_2Cl_2/*n*-hexane, 95:5) to give the acylated product 15 (68 mg, 75%, m.p. 68−70°C) as yellow powder. − $[\alpha]_D^{20}$ = −10° (*c* = 0.14, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.59 (s, 3 H, OCH_3), 4.06 (dd, $J_{3,2}$ = 5.3 Hz, $J_{3,4}$ = 2.9 Hz, 1 H, H-3), 4.15 (d, $J_{gem.}$ = 12.9 Hz, 1 H, H-6), 4.27 (d, $J_{2,3}$ = 5.3 Hz, 1 H, H-2), 4.36 (d, $J_{gem.}$ = 11.0 Hz, 1 H, OC*H*$_2$Ph), 4.47 (d, $J_{gem.}$ = 11.0 Hz, 1 H, OC*H*$_2$Ph), 4.63 (br. d, $J_{gem.}$ = 11.0 Hz, 2 H, OC*H*$_2$Ph), 4.73−5.08 (m, 19 H, H-6, OC*H*$_2$Ph), 5.56 (dd, $J_{4,3}$ = 2.9 Hz, $J_{4,5}$ = 7.7 Hz, 1 H, H-4), 5.78 (br. d, $J_{5,4}$ = 7.7 Hz, 1 H, H-5), 6.85 and 6.88 (s, 2 H, HBDP-H-5 and HBDP-H-5′), 6.89−7.39 (m, 57 H, H-Ar). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.29 (q, OCH_3), 63.83 (t, C-6), 69.90, 69.99, 70.22, 72.46, 72.94, 73.99, 74.11, 74.45 and 74.49 (t, O*C*H$_2$Ph), 69.63, 76.87 and 78.43 (d, C-2, C-3, C-4 and C-5), 106.47 and 107.26 (d, HBDP-C-5 and HBDP-C-5′), 108.30 (d, Gall-C-2 and Gall-C-6), 121.90 and 122.56 (s, HBDP-C-1 and HBDP-C-1′), 123.39 (s, Gall-C-1), 126.51, 126.58, 126.65, 126.72, 126.75, 126.85, 126.90, 126.95, 127.01, 127.07, 127.21, 127.33, 127.37, 127.44, 127.51 and 127.59 (d, C-Ar), 128.04, 135.28, 135.50, 135.56, 135.95, 136.25, 136.37, 136.40, 136.53, 136.67 and 136.81 (s, C-Ar), 141.71, 143.22 and 143.57 (s, HBDP-C-3, HBDP-C-3′ and Gall-C-4), 151.21, 151.37, 151.47 and 151.57 (s, HBDP-C-2, HBDP- C-2′, HBDP-C-4, HBDP-C-4′, Gall-C-3 and Gall-C-5), 164.00 (s, Gall-COOR), 166.03 and 166.83 (s, HBDP-COOR), 169.87 (s, COOR). − IR (KBr): $\tilde{\nu}$ = 3063 cm^{-1}, 3031, 2960, 2925, 2860, 1744, 1631, 1593, 1493, 1454, 1370, 1261, 1184, 1097. − UV/Vis ($CHCl_3$): λ_{max} (lg ε) = 271 nm (4.33). − MS (DCI/NH_3): *m/z* (%) = 1654 (1) [M^+], 1564 (15) [(M^+ + H) − C_7H_7], 1473 (25) [(M^+ + H) − 2 × C_7H_7], 1383 (24), 1335 (2), 1294 (5), 1245 (2). − $C_{105}H_{90}O_{19}$ (1655.85): calcd. C 76.16, H 5.48; found C 76.10 H 5.57.

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