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Note

From methyl D-glucopyranoside to methyl D-allopyranoside via the Mitsunobu reaction

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Abstract

Methyl β-D-glucopyranoside reacted with a 4-molar excess of the Mitsunobu reagents (triphenylphosphine–diethyl azodicarboxylate–benzoic acid) under Weinges et al. [*Carbohydr. Res.*, 164 (1987) 453–458] conditions to furnish four differently benzoylated methyl β-D-allopyranosides in a very good overall yield. The same reaction applied to methyl α-D-glucopyranoside yielded allosides in a low yield and nine other sugar products. These results give an insight into the course of the Mitsunobu esterification–inversion reaction. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Methyl α- and β-D-glucopyranosides; Benzoylated methyl α- and β-D-allopyranosides; Mitsunobu reaction

A preparative route to derivatives of D-allose consists of inversion of the hydroxyl group at C-3 in 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) via oxidation to 3-ulose and subsequent reduction of the keto group to 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**2**) [1]. Methyl D-allopyranosides can be obtained via inversion of configuration at C-3 in the properly substituted methyl D-glucopyranosides [2].

Looking for a shorter and more efficient route to methyl D-allopyranoside, we focused our attention on a procedure described by Weinges et al. [3]. Following these authors, treatment of methyl β-D-glucopyranoside (**3**) with an excess of the Mitsunobu reagents (triphenylphosphine, diethyl azodicarboxylate (DEAD) and benzoic acid, 1.2 mol equiv for each OH group, THF, reflux, 1 h) afforded a product which, after Zemplén deacylation, gave 70% of methyl β-D-allopyranoside (**5**). The transient product was not characterized and its homogeneity was left unknown.

We repeated Weinges' procedure and decided to analyze in detail the product obtained. In fact, it turned out that it was a mixture of compounds (93%) separable into five components identified as: methyl 3,6-di-*O*-benzoyl- (**6**, 16.2%), 4,6-di-*O*-benzoyl- (**7**, 21.3%), 3,4,6-tri-*O*-benzoyl- (**8**, 50.1%), 2,3,4,6-tetra-*O*-benzoyl- (**9**, 4.1%) -β-D-allopyranosides and methyl 3,6-anhydro-4-*O*-benzoyl-β-D-galactopyranoside (**10**, 1.6%). Products **6**–**8** could be readily interrelated by benzoylation to the same tetrabenzoate **9**. Their configuration and the localization of the ester grouping was deduced from ^{1}H NMR spectra. The structure of **10** was also assigned

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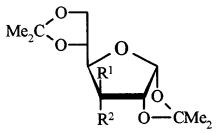
by its NMR data. Compounds **6**–**10** have not been described in the literature up to now.



1 R^1 =OH, R^2 =H
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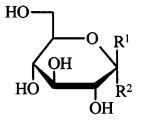

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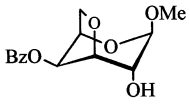

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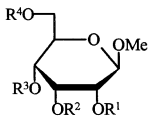
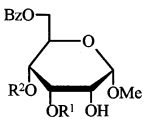
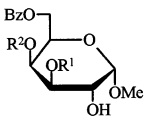


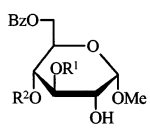
	R^1	R^2	R^3	R^4
5	H	H	H	H
6	H	Bz	H	Bz
7	H	H	Bz	Bz
8	H	Bz	Bz	Bz
9	Bz	Bz	Bz	Bz



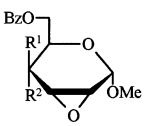
11 R^1 =Bz, R^2 =H
12 R^1 =Bz, R^2 =Bz



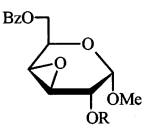
13 R^1 =H, R^2 =Bz
14 R^1 =Bz, R^2 =Bz



15 R^1 =Bz, R^2 =H
16 R^1 =Bz, R^2 =Bz



	R^1	R^2
17	H	OH
18	H	OBz
19	OBz	H



20 R=H
21 R=Bz

When, in this reaction, DEAD was replaced by diisopropyl azodicarboxylate (DIAD), four products were formed: dibenzoates **6** (3%) and **7** (30.5%), tribenzoate **8** (34.6%) and the anhydro compound **10** (6.2%).

Successful conversion of methyl β-D-glucoside to methyl β-D-alloside was required in order to perform the same reactions with the cheap methyl α-D-glucopyranoside (**4**). The reaction of **4** with Mitsunobu reagents under Weinges' conditions led to a complex mixture of products. This mixture was separated by a combination of column chromatography and high-performance liquid chromatography (HPLC), resulting in 11 products, which were identified on the basis of analytical and spectral data. Two of them, formed in 4.6 and 3.1% yields were, in fact, methyl α-D-allopyranosides, having benzoate groupings located at C-3 and -6 (**11**) and C-3, -4 and -6 (**12**). Furthermore, two methyl α-D-galactopyranosides have been isolated, esterified at C-4 and -6 (**13**, 1.2%) and C-3, -4 and -6 (**14**, 3.0%), and two methyl α-D-glucopyranosides benzoylated in positions C-3 and -6 (**15**, 10.6%) and C-3, -4 and -6 (**16**, 3.5%). The remaining compounds, constituting the major portion of products, were sugar epoxides i.e., two methyl 2,3-anhydro-α-D-allopyranosides esterified at C-6 (**17**, 10.1%) and at C-4 and -6 (**18**, 14.8%), methyl 2,3-anhydro-4,6-di-*O*-benzoyl-α-D-gulopyranoside (**19**, 17.0%), and two methyl 3,4-anhydro-α-D-galactopyranosides benzoylated at C-6 (**20**, 9.0%) and at C-2 and -6 (**21**, 4.8%).

1. Discussion

The results of the Mitsunobu reaction with methyl β-D-glucopyranoside can be rationalized by assuming initial formation of oxyphosphonium cations at the primary (C-6) and secondary (C-3) alcohol positions in **3** followed by the attack of benzoic acid molecules, leading to **6**. Formation of **7** can be explained if we assume a migration of the benzoate grouping from O-3 to O-4. The most abundant tribenzoate **8** was probably formed from **6** by an esterification of O-4 without inversion of configuration. Esterification with retention of configuration was observed earlier [4]. The tetrabenzoate **9** was obtained probably by a similar process. Of particular interest is the formation of the anhydro compound **10**. Here an intramolecular attack of 3-OH on the C-6 phosphonium cation leads to a 3,6-anhydro bridge, and then a C-4 phosphonium salt is formed undergoing inversion of configuration by attack of a benzoic acid molecule leading to **10**.

The Mitsunobu benzoylation reaction of methyl α-D-glucopyranoside (**4**) was studied in 1979 by Grynkiewicz [5]. He found that, with 1.5 mmol of the reagents (PPh_3, benzoic acid, DEAD) in refluxing 9:1 dioxane–pyridine, only a single product was formed methyl 6-*O*-benzoyl-α-D-glucopyranoside (cf. also [6]). However, we found that with an excess of the reagents, under relatively harsh Weinges conditions, a variety of products was formed. Their identification allowed us to deduce the course of all consecutive reactions. Thus, all products **11**–**21** have the benzoate residue at C-6, which indicates again a facile formation of the oxyphosphonium cation at the primary position [5] followed by the reaction with benzoic acid. From the remaining three secondary

alcohol positions, the Mitsunobu betaine prefers position 3 (as in the case of **3**) to form the next oxyphosphonium cation. In methyl β-D-glucopyranoside (**3**), there is no steric hindrance from the axial methoxy group, therefore the attack of benzoic acid does not meet any serious opposition and the inversion of configuration at C-3 is facile. In the α anomer **4**, direct reaction with benzoic acid can occur only with difficulty (Richardson's "β-trans-axial effect" [7]) and therefore formation of alloside is very limited. A preferred reaction pathway for the C-3 oxyphosphonium salt is the intramolecular attack of the the C-2 hydroxyl group leading to the 2,3-anhydro compounds, **17** and its 4-O-benzoylated derivative **18**. The most abundant (17%) gulo epoxide **19** was probably formed from **17** by inversion of the configuration at C-4. All 2,3-anhydro compounds **17**–**19** were formed in almost 42% overall yield.

Formation of the *galacto* compounds can be interpreted by reactions involving an intermediate C-4 oxyphosphonium cation. Direct inversion at C-4 of **4** with benzoic acid leads to galactosides **13** and **14**. The C-4 oxyphosphonium cation must also be responsible for the formation of both *galacto* epoxides **20** and **21** via an intramolecular attack of the C-3 hydroxyl group followed by esterification of the C-2 hydroxyl group in the case of **21**. It is remarkable that none of the products can be derived from a C-2 oxyphosphonium cation. Benzoates of the unchanged substrate, **15** and **16**, were most probably formed by a direct esterification process [4].

From the results described following Weinges methodology applied to methyl β-D-glucopyranoside (**3**), a practical preparative route to methyl β-D-allopyranoside (**5**) emerges including detailed knowledge of the products formed in the reaction. The wealth of products obtained with methyl α-D-glucopyranoside (**4**) is certainly of interest with regard to the mechanism of the Mitsunobu reaction in a polyol system.

2. Experimental

General methods.—Optical rotations were measured for solutions in $CHCl_3$ at 20 ± 2 °C with a Jasco DIP 360 automatic polarimeter. Melting points were determined on a Kofler apparatus and are uncorrected. NMR spectra were recorded with a Varian Gemini AC-200 (200 MHz). Mass spectra (LSI MS, positive-ion mode) were recorded with an AMD-604 mass spectrometer. Thin-layer chromatography (TLC) was performed on Kieselgel 60 F_{254} ready plates and column chromatography on Silica Gel 230-400 or 70-230 mesh (E. Merck). High-performance liquid chromatography (HPLC) was carried out on a Shimadzu apparatus C-R4A, pump unit LC-8A, UV spectrometric detector SPD250-6A on a column SP250/21 Nucleosil 100-7 (Macherey–Nagel). All reagents used were of commercial origin.

To a suspension of methyl D-glucopyranoside (β: **3**, α: **4**) in dry THF (10 mL/mmol) were added 4.8 mol equiv (1.2 mol equiv for every hydroxyl group) each of triphenylphosphine and benzoic acid. The mixture was refluxed, and a solution of 4.8 mol equiv of dialkyl azodicarboxylate in dry THF was added dropwise. Time of additional heating to complete the reaction [until no trace of the substrate was detected by TLC (35:15:3 $CHCl_3$–MeOH–2 M AcOH)] is given below for each case. The solution was concentrated to dryness under reduced pressure and, unless otherwise stated, the residue was taken up in benzene (3 mL/mmol). Dialkyl hydrazinodicarboxylate crystallized on cooling. The precipitate was filtered off and the filtrate was concentrated. The residue was treated with ether (5 mL/mmol) and the precipitate was filtered off. The filtrate was washed twice with satd aq $NaHCO_3$ and twice with water, the organic layer was dried ($MgSO_4$) and concentrated to dryness under reduced pressure. The residue was separated by column chromatography, preparative TLC, and by HPLC.

Reaction with methyl β-D-glucopyranoside (**3**) *and diethyl azodicarboxylate.*—A suspension of **3** (semihydrate, 1 g, 4.9 mmol) in THF (50 mL) containing triphenylphosphine (PPh_3, 6.20 g) and benzoic acid (2.88 g) was treated with a solution of DEAD (4.11 g) in THF (10 mL) as described above. Time of additional heating was 1 h. The mixture of products was separated by column chromatography with hexane–EtOAc (10:1 → 1:2) to give (in order

of elution): **9** (0.123 g, 4.1%), **10** (0.022 g, 1.6%), **8** (1.248 g, 50.1%), **6** (0.315 g, 15.9%), and **7** (0.421 g, 21.3%).

Reaction with diisopropyl azodicarboxylate.—A suspension of **3** (5 g, 24.6 mmol) in THF (250 mL) was treated as described in General methods [PPh_3 (30.95 g), DIAD [23.86 g in THF (50 mL), benzoic acid (14.41 g)]. After 2 h of reflux the solution was concentrated to dryness under reduced pressure and the residue was taken up in toluene. The mixture of triphenylphosphine oxide and diisopropyl hydrazinodicarboxylate crystallized on cooling. The work-up of the reaction mixture followed the general method. Then chromatographic column was washed first with 1:2 hexane–ether and then with 2:1 toluene–ether to furnish **6** (0.294 g, 3.0%), **7** (3.020 g, 30.5%), **8** (4.308 g, 34.6%) and **10** (0.430 g, 6.2%).

Reaction between methyl α-D-glucopyranoside (**4**) *and diethyl azodicarboxylate.*—A suspension of **4** (1 g, 5.15 mmol) in THF (50 mL) was treated as described in General methods [PPh_3 (6.45 g), DEAD (4.31 g in 10 mL THF), benzoic acid (3.02 g)]. After 2 h of reflux and work-up as above, the mixture was separated by chromatography with 10:1 → 1:6 hexane–ether into five fractions, which were further separated by preparative TLC or HPLC to give **11** (0.095 g, 4.6%), **12** (0.082 g, 3.1%), **13** (0.030 g, 1.2%), **14** (0.077 g, 3.0%), **15** (0.219 g, 10.6%), **16** (0.090 g, 3.5%), **17** (0.146 g, 10.1%), **18** (0.293 g, 14.8%), **19** (0.337 g, 17.0%), **20** (0.130 g, 9.0%), and **21** (0.095 g, 4.8%).

Benzoylation of **8**, **7** and **6** under standard conditions gave **9**. Similarly, benzoylation of **17** gave **18**, and of **20** gave **21**. New compounds were fully characterized; physical and spectral data of known compounds agreed with the literature values.

Methyl 3,6-di-O-benzoyl-β-D-allopyranoside (**6**).—Syrup, $[\alpha]_D - 55°$ (*c* 2.41); ^1H NMR ($CDCl_3$): δ 8.12–8.03, 7.65–7.38 (m, 10 H, 2 Ph), 5.85 (t, 1 H, $J_{3,4}$ 3.0, $J_{3,2}$ 3.1 Hz, H-3), 4.72 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.68–4.60 (m, 2 H, H-6a, 6b), 4.11 (dt, 1 H, $J_{5,4}$ 9.5, $J_{5,6a}$ 3.5, $J_{5,6b}$ 4.0 Hz, H-5), 3.93 (dd, 1 H, H-4), 3.73 (dd, 1 H, H-2), 3.59 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$): δ 167.08, 166.90 (2 × C=O), 133.56, 133.47, 133.21, 130.09, 129.88, 129.77, 129.68, 129.44, 128.58, 128.49, 128.37 (Ar), 101.86 (C-1), 73.09, 73.09, 70.17, 67.24 (C-2, 3, 4, 5), 64.07 (C-6), 57.09 (OMe). HRMS (LSI MS): Calcd for $C_{21}H_{22}O_8 + Na^+$ $[M + Na]^+$, 425.12125. Found: 425.12132.

Methyl 4,6-di-O-benzoyl-β-D-allopyranoside (**7**).—Syrup, $[\alpha]_D + 33°$ (*c* 1.35); ^1H NMR ($CDCl_3$): δ 8.08–7.96, 7.61–7.33 (m, 10 H, 2 Ph), 5.17 (dd, 1 H, $J_{4,3}$ 2.8, $J_{4,5}$ 9.8 Hz, H-4), 4.67 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.69–4.58 (m, 1 H, H-5), 4.53 (t, 1 H, $J_{3,2}$ 2.9 Hz, H-3), 4.50–4.36 (m, 2 H, H-6a, 6b), 3.61 (dd, 1 H, H-2), 3.56 (s, 3 H OMe); ^{13}C NMR ($CDCl_3$): δ 166.21, 165.21 (2 × C=O), 133.48, 133.00, 129.79, 129.63, 129.16, 128.47, 128.35, 128.27 (Ar), 101.43 (C-1), 70.78, 69.92, 69.50, 68.69 (C-2, 3, 4, 5), 63.77 (C-6), 57.17 (OMe). HRMS (LSI MS): Calcd for $C_{21}H_{22}O_8 + Na^+$ $[M + Na]^+$, 425.12125. Found: 425.12356.

Methyl 3,4,6-tri-O-benzoyl-β-D-allopyranoside (**8**).—Mp 177–178 °C (from toluene); $[\alpha]_D + 79°$ (*c* 1.71); ^1H NMR ($CDCl_3$): δ 8.10–7.23 (m, 15 H, 3 Ph), 6.12 (t, 1 H, $J_{3,2}$ 3.0, $J_{3,4}$ 3.0 Hz, H-3), 5.41 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.83 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.73–4.62 (m, 1 H, H-5), 4.55–4.38 (m, 2 H, H-6a, 6b), 3.90 (dd, 1 H, H-2), 3.64 (s, 3 H, OMe), 2.50 (bs, 1 H, OH); ^{13}C NMR ($CDCl_3$): δ 166.14, 165.80, 164.93 (3 × C=O), 133.39, 133.34, 133.08, 129.75, 129.66, 129.55, 128.92, 128.53, 128.33 (Ar), 101.94 (C-1), 70.68, 70.45, 69.96, 68.08 (C-2, 3, 4, 5), 63.53 (C-6), 57.18 (OMe). HRMS (LSI MS): Calcd for $C_{28}H_{26}O_9 + Na^+$ $[M + Na]^+$, 529.14746. Found: 529.14798. Anal. Calcd for $C_{28}H_{26}O_9$: C, 66.40; H, 5.17. Found: C, 66.18; H, 5.24.

Methyl 2,3,4,6-tetra-O-benzoyl-β-D-allopyranoside (**9**).—Mp 163–164 °C (from EtOH); $[\alpha]_D + 17°$ (*c* 1.61); ^1H NMR ($CDCl_3$) δ 8.10–7.27 (m, 20 H, 4 Ph), 6.22 (t, 1 H, $J_{3,2}$ 3.1, $J_{3,4}$ 2.9 Hz, H-3), 5.58 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 5.41 (dd, 1 H, $J_{2,1}$ 8.1 Hz, H-2), 5.11 (d, 1 H, H-1), 4.72 (dd, 1 H, $J_{6a,5}$ 2.4, $J_{6a,6b}$ 11.4 Hz, H-6a), 4.56 (ddd, 1 H, $J_{5,6b}$ 5.0 Hz, H-5), 4.49 (dd, 1 H, H-6b), 3.59 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$): δ 166.19, 165.18, 164.81, 164.71 (4 × C=O), 133.49, 133.37, 133.17, 129.81, 129.72, 129.68, 129.61, 129.53, 129.32, 128.89, 128.66, 128.38, 128.26 (Ar), 100.07 (C-1), 70.78, 69.68, 69.38, 67.59 (C-2, 3, 4, 5),

63.39 (C-6), 56.94 (OMe). HRMS (LSI MS): Calcd for $C_{35}H_{30}O_{10} + Na^+$ $[M + Na]^+$, 633.17365. Found: 633.17234. Anal. Calcd for $C_{35}H_{30}O_{10}$: C, 68.85; H, 4.95. Found: C, 68.77; H, 4.86.

*Methyl 3,6-anhydro-4-*O*-benzoyl-β-*D*-galactopyranoside* (**10**).—Syrup, $[\alpha]_D - 142°$ (*c* 2.14); ^{1}H NMR ($CDCl_3$): δ 8.15–7.98, 7.67–7.42 (m, 5 H, Ph), 5.21 (dd, 1 H, $J_{4,3}$ 5.5, $J_{4,5}$ 3.1 Hz, H-4), 4.80 (bs, 1 H, H-1), 4.63 (t, 1 H, $J_{5,6a} < 1$, $J_{5,6b}$ 3.2 Hz, H-5), 4.48 (dd, 1 H, $J_{3,2}$ 3.6 Hz, H-3), 4.37 (dd, 1 H, $J_{6a,6b}$ 10.1 Hz, H-6a), 4.02 (dd, 1 H, H-6b), 3.95 (bd, 1 H, H-2), 3.47 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$): δ 165.55 (C=O), 133.66, 133.59, 130.11, 129.61, 129.05, 128.72, 128.41 (Ar), 104.04 (C-1), 72.74, 71.83, 71.63, 71.57 (C-2, 3, 4, 5), 70.79 (C-6), 55.84 (OMe). HRMS (LSI MS): Calcd for $C_{14}H_{16}O_6 + Na^+$ $[M + Na]^+$, 303.08447. Found: 303.08487.

*Methyl 3,6-di-*O*-benzoyl-α-*D*-allopyranoside* (**11**).—Syrup, $[\alpha]_D + 43°$ (*c* 0.94); ^{1}H NMR ($CDCl_3$): δ 8.17–8.02, 7.65–7.39 (m, 10 H, 2 Ph), 5.76 (t, 1 H, $J_{3,2}$ 3.4, $J_{3,4}$ 3.3 Hz, H-3), 4.83 (d, 1 H, $J_{1,2}$ 4.4 Hz, H-1), 4.67 (dd, 1 H, $J_{6a,5}$ 4.6, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.59 (dd, 1 H, $J_{6b,5}$ 2.7 Hz, H-6b), 4.21 (ddd, 1 H, $J_{5,4}$ 9.9 Hz, H-5), 3.98–3.85 (m, 1 H, H-2), 3.88 (dd, 1 H, H-4), 3.57 (s, 3 H, OMe), 2.64 (bd, 1 H, $J_{OH,2}$ 9.6 Hz, OH); ^{13}C NMR ($CDCl_3$): δ 167.30, 166.82 (2 × C=O), 133.40, 133.16, 129.98, 129.69, 129.48, 128.46, 128.36 (Ar), 98.67 (C-1), 72.87, 67.14, 66.66, 66.01 (C-2, 3, 4, 5), 63.77 (C-6), 56.13 (OMe). HRMS (LSI MS): Calcd for $C_{21}H_{22}O_8 + Na^+$ $[M + Na]^+$, 425.12124. Found: 425.12052.

*Methyl 3,4,6-tri-*O*-benzoyl-α-*D*-allopyranoside* (**12**).—Syrup, $[\alpha]_D + 141°$ (*c* 1.71); lit [8]: $[\alpha]_D + 117°$ (*c* 1, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.15, 165.79, 164.90 (3 × C=O), 133.33, 133.33, 133.25, 133.10, 129.89, 129.70, 129.63, 129.05, 128.51, 128.37, 128.27 (Ar), 98.88 (C-1), 70.05, 67.34, 66.81, 63.57 (C-2, 3, 4, 5), 63.18 (C-6), 56.32 (OMe).

*Methyl 2,4,6-tri-*O*-benzoyl-α-*D*-galactopyranoside* (**13**).—Syrup, $[\alpha]_D + 102°$ (*c* 2.66); lit [9]: $[\alpha]_D + 104°$ (*c* 1.0, $CHCl_3$).

*Methyl 3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranoside* (**14**).—Syrup, $[\alpha]_D + 102°$ (*c* 1.10); lit [10]: $[\alpha]_D + 102°$ (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.14, 165.96, 165.46 (3 × C=O), 133.47, 133.16, 133.10, 129.81, 129.74, 129.62, 129.44, 129.35, 129.28, 128.55, 128.39, 128.19 (Ar), 99.81 (C-1), 71.40, 69.28, 67.95, 67.17 (C-2, 3, 4, 5), 62.59 (C-6), 55.78 (OMe).

*Methyl 3,6-di-*O*-benzoyl-α-*D*-glucopyranoside* (**15**).—Mp 135–136 °C (from EtOAc–hexane); $[\alpha]_D + 135°$ (*c* 1.07); lit [8]: mp 136–137 °C (from EtOAc), $[\alpha]_D + 136°$ (*c* 1 $CHCl_3$); ^{1}H NMR ($CDCl_3 + D_2O$): δ 8.12–8.00, 7.63–7.37 (m, 10 H, 2 Ph), 5.37 (t, 1 H, $J_{3,2}$ 9.5, $J_{3,4}$ 9.5 Hz, H-3), 4.87 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.74 (dd, 1 H, $J_{6a,5}$ 4.6, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.59 (dd, 1 H, $J_{6b,5}$ 2.4 Hz, H-6b), 4.00 (ddd, 1 H, $J_{5,4}$ 9.9 Hz, H-5), 3.78 (dd, 1 H, H-2), 3.71 (t, 1 H, H-4).

*Methyl 3,4,6-tri-*O*-benzoyl-α-*D*-glucopyranoside* (**16**).—Amorphous solid, $[\alpha]_D + 76°$ (*c* 2.26); lit [11]: $[\alpha]_D + 75°$ (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3 + D_2O$): δ 8.07–7.88, 7.60–7.27 (m, 15 H, 3 Ph), 5.73 (t, 1 H, $J_{3,2}$ 9.5, $J_{3,4}$ 9.7 Hz, H-3), 5.56 (t, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.94 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.59 (dd, 1 H, $J_{6a,5}$ 2.9, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.45 (dd, 1 H, $J_{6b,5}$ 5.2 Hz, H-6b), 4.32 (ddd, 1 H, H-5), 3.92 (dd, 1 H, H-2), 3.54 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$): δ 166.73, 166.08, 165.25 (3 × C=O), 133.34, 133.15, 133.05, 129.74, 129.62, 129.25, 128.86, 128.34, 128.25 (Ar), 99.36 (C-1), 73.90, 71.43, 69.02, 67.91 (C-2, 3, 4, 5), 63.10 (C-6), 55.71 (OMe).

*Methyl 2,3-anhydro-6-*O*-benzoyl-α-*D*-allopyranoside* (**17**).—Mp 141–143 °C (from EtOH); $[\alpha]_D + 87°$ (*c* 1.67); lit [12]: mp 140–142 °C, $[\alpha]_D + 74°$ (*c* 0.3, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.86 (C=O), 133.19, 130.10, 129.67, 128.38 (Ar), 94.50 (C-1), 67.72, 65.84 (C-4,5), 64.10 (C-6), 55.69, 55.39, 53.81 (C-2, 3, OMe).

*Methyl 2,3-anhydro-4,6-di-*O*-benzoyl-α-*D*-allopyranoside* (**18**).—Mp 122–124 °C (from EtOH–hexane); $[\alpha]_D + 202°$ (*c* 1.08); lit [13]: mp 125–126 °C (from ether–hexane); $[\alpha]_D + 199°$ (*c* 3.48, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 166.09, 165.76 (2 × C=O), 133.53, 133.05, 129.85, 129.69, 129.58, 129.07, 128.47, 128.34 (Ar), 94.54 (C-1), 68.07, 64.85 (C-4, 5), 63.52 (C-6), 55.84, 54.75, 51.39 (C-2, 3, OMe).

*Methyl 2,3-anhydro-4,6-di-*O*-benzoyl-α-*D*-gulopyranoside* (**19**).—Mp 100–101 °C (from EtOAc–hexane); $[\alpha]_D - 35°$ (*c* 1.26), ^{1}H NMR (C_6D_6): δ 8.18–8.06, 7.18–6.92 (m, 10 H, 2 Ph), 5.44–5.39 (m, 1 H, H-4), 4.62 (d, 1 H, $J_{1,2}$

2.9 Hz, H-1), 4.61 (dd, 1 H, $J_{6a,5}$ 7.9, $J_{6a,6b}$ 11.0 Hz, H-6a), 4.44 (ddd, 1 H, $J_{5,6b}$ 4.4, $J_{5,4}$ 1.6 Hz, H-5), 4.18 (dd, 1 H, H-6b), 3.20 (dd, 1 H, $J_{4,3}$ 2.4, $J_{3,2}$ 3.6 Hz, H-3), 3.17 (s, 3 H, OMe), 2.84 (d, 1 H, H-2); ^{13}C NMR ($CDCl_3$): δ 165.97, 165.70 (2 × C=O), 133.62, 133.10, 129.88, 129.55, 129.02, 128.54, 128.44, 128.37 (Ar), 94.72 (C-1), 66.16, 65.02 (C-4, 5), 63.37 (C-6), 55.58, 51.29, 49.94 (C-2, 3, OMe). Anal. Calcd for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.72; H, 5.26. HRMS (LSI MS) Calcd for $C_{21}H_{20}O_7 + H^+$ $[M + H]^+$, 385.12873. Found: 385.12665.

*Methyl 3,4-anhydro-6-*O*-benzoyl-α-*D*-galactopyranoside* (**20**).—Mp 122–123 °C (from EtOH–hexane); $[\alpha]_D + 39°$ (*c* 0.59); ^{1}H NMR ($CDCl_3$): δ 8.12–8.00, 7.62–7.38 (m, 5 H, Ph), 4.72 (d, 1 H, $J_{1,2}$ 4.7 Hz, H-1), 4.59–4.51 (m, 2 H, H-6a, 6b), 4.31 (bt, 1 H, $J_{5,6a}$ 6.0, $J_{5,6b}$ 6.2, $J_{5,4} < 1$ Hz, H-5), 3.87 (dd, 1 H, $J_{2,OH}$ 10.4 Hz, H-2), 3.49 (s, 3 H, OMe), 3.34–3.26 (m, 2 H, H-3, 4), 2.51 (d, 1 H, OH); ^{1}H NMR (C_6D_6): δ 8.19–8.11, 7.18–6.95 (m, 5 H, Ph), 4.50 (dd, 1 H, $J_{6a,5}$ 6.7, $J_{6a,6b}$ 11.2 Hz, H-6a), 4.43 (dd, 1 H, $J_{6b,5}$ 5.5 Hz, H-6b), 4.30 (d, 1 H, $J_{1,2}$ 4.6 Hz, H-1), 3.96 (ddd, 1 H, $J_{5,4}$ 0.7 Hz, H-5), 3.78 (bd, 1 H, $J_{2,3} < 1$ Hz, H-2), 3.04 (dd, 1 H, $J_{3,4}$ 4.0 Hz, H-3), 2.86 (s, 3 H, OMe), 2.72 (dd, 1 H, H-4); ^{13}C NMR ($CDCl_3$): δ 166.20 (C=O), 133.16, 129.66, 128.39 (Ar), 95.92 (C-1), 64.19, 63.65 (C-2, 5), 64.03 (C-6), 55.92 (OMe), 53.12, 50.11 (C-3, 4). HRMS (LSI MS): Calcd for $C_{14}H_{16}O_6 + H^+$ $[M + H]^+$, 281.10251. Found: 281.10346. Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.76. Found: C, 59.85; H, 5.98.

*Methyl 3,4-anhydro-2,6-di-*O*-benzoyl-α-*D*-galactopyranoside* (**21**).—Syrup, $[\alpha]_D + 34°$ (*c* 1.22); ^{1}H NMR (C_6D_6): δ 8.22–8.10, 7.20–6.95 (m, 10 H, 2 Ph), 5.13 (d, 1 H, $J_{1,2}$ 4.4 Hz, H-1), 4.89 (dd, 1 H, H-2), 4.62 (dd, 1 H, $J_{6a,5}$ 6.6, $J_{6a,6b}$ 11.2 Hz, H-6a), 4.49 (dd, 1 H, $J_{6b,5}$ 5.5 Hz, H-6b), 4.11 (ddd, 1 H, $J_{5,4}$ 0.9 Hz, H-5), 3.12 (dd, 1 H, $J_{3.2}$ 1.1, $J_{3,4}$ 4.0 Hz, H-3), 2.95 (s, 3 H, OMe), 2.82 (dd, 1 H, H-4); ^{13}C NMR ($CDCl_3$): δ 166.18, 165.44 (2 × C=O), 133.41, 133.14, 129.81, 129.67, 128.42, 128.38 (Ar), 94.40 (C-1), 66.26, 64.05 (C-2, 5), 64.02 (C-6), 55.97 (OMe), 51.24, 49.84 (C-3, 4). HRMS (LSI MS): Calcd for $C_{21}H_{20}O_7 + H^+$ $[M + H]^+$, 385.12873. Found: 385.12919.

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