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STEREOSELECTIVE RING-CLEAVAGE OF 3-*O*-BENZYL- AND 2,3-DI-*O*-BENZYL-4,6-*O*-BENZYLIDENEHEXOPYRANOSIDE DERIVATIVES WITH THE $LiAlH_4$–$AlCl_3$ REAGENT

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ABSTRACT

Hydrogenolysis of 3-*O*-benzyl- and 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-gluco- and -D-manno-pyranoside derivatives with $LiAlH_4$–$AlCl_3$ gives the corresponding 4-*O*-benzyl compounds. The direction of cleavage of the benzylidene ring is determined by the presence of a benzyl group at position 3, but it is not dependent on the anomeric configuration, substitution at O-2, or the character of the aglycon moiety. For 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-galactopyranoside derivatives, the ratio of the resulting 4- and 6-*O*-benzyl compounds is ~9:1 and is independent of the anomeric configuration. Substitution at O-3 with a group less-bulky than benzyl favours the formation of 6-*O*-benzyl compounds.

INTRODUCTION

Several reagents are known which decompose acetals by reductive cleavage, *e.g.*, di-isobutylaluminium hydride[1], decaborane[2], tetra-alkylsilanes[3], mixtures of $LiAlH_4$ and Lewis acids[4–8] (BF_3, $AlCl_3$), and borane[9].

The $LiAlH_4$–$AlCl_3$ reagent was used for the cleavage of acetals of carbohydrates by Gorin *et al.*[10–13]. The compounds studied contained various protecting groups, *e.g.*, orthoester, *O*-isopropylidene, *O*-cyclohexylidene, *O*-propylidene, *O*-ethylidene, *O*-methylene, and *O*-benzylidene groups. The reagent cleaves cyclic acetals into hydroxy-*O*-alkyl or hydroxy-*O*-aralkyl ethers. The cleavage of benzylidene derivatives is an important synthetic reaction, because of the formation of hydroxy-*O*-benzyl ethers. The polar effects which influence the direction of cleavage of 1,3-dioxane and 1,3-dioxolane rings have been extensively examined[8], but steric factors may also be involved.

RESULTS AND DISCUSSION

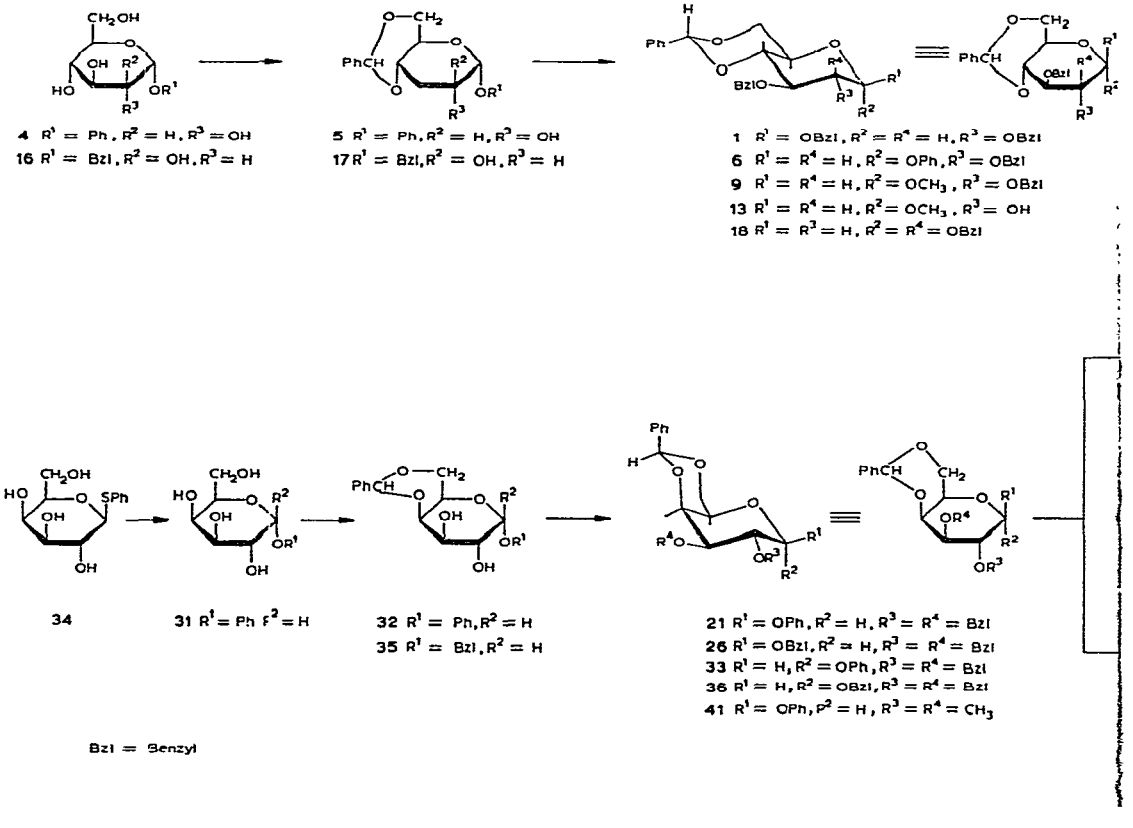
The direction of benzylidene-ring cleavage by $LiAlH_4$–$AlCl_3$ in phenyl 4,6-*O*-benzylidene-β-D-glucopyranoside derivatives is determined[14] by steric factors, namely, by the bulk of the O-3 substituent. The stereoselectivity of ring cleavage of

benzyl β-D-glucopyranoside derivatives was also examined. Thus, benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside[15] (**1**) gave only the 4-*O*-benzyl derivative **2**, which was isolated in 90% yield. The structure of **2** was confirmed by methylation to afford the 6-*O*-methyl derivative **3**. The synthesis of **2** *via* the corresponding trityl derivative was reported by Zissis and Fletcher[16].

To determine the effect of anomeric configuration, the bulk of the aglycon moiety, and substitution at O-2 on the direction of ring-cleavage, the following experiments were performed in the D-glucose series.

With $LiAlH_4$–$AlCl_3$, phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**6**), obtained from phenyl α-D-glucopyranoside[17] (**4**) *via* the 4,6-*O*-benzylidene derivative **5**, gave only the 4-*O*-benzyl compound **7**. The structure of **7** was confirmed by conversion into the 6-*O*-methyl derivative **8**.

Likewise, methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[18] (**9**) gave the (syrupy) 4-*O*-benzyl derivative **10**, which was characterized as the 6-*p*-nitrobenzoate **11**. The structure of **10** was confirmed by the preparation of the 6-*O*-methyl derivative **12**. The cleavage of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[19] (**13**) gave only one product, namely, methyl 3,4-di-*O*-benzyl-α-D-glucopyranoside (**14**), which was also converted into the 2,6-di-*O*-methyl derivative **15**.

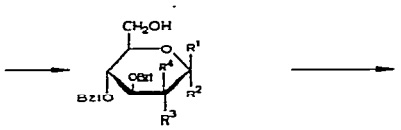


The results obtained with **9** and **13** showed that the size of the substituent at position 3 is the only structural factor determining the direction of ring-cleavage.

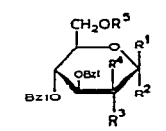
As expected, the cleavage of benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**18**) with $LiAlH_4$–$AlCl_3$ gave only the 4-*O*-benzyl compound **19**, which was converted into the corresponding 6-*O*-methyl derivative **20**. Compound **18** was prepared from benzyl α-D-mannopyranoside (**16**) by formic acid-catalyzed benzylidenation to give **17**[20] followed by benzylation.

Each of the above-mentioned gluco- and manno-pyranoside derivatives contains a *trans*-fused ring system and *trans*-diequatorial orientation of O-3 and O-4. Accordingly, $AlCl_3$ or $AlHCl_2$ can form a complex only with the free electron-pair of O-6, because of the shielding of O-4 by the bulky 3-*O*-benzyl group. Consequently, the benzylidene ring cleaves at position 6.

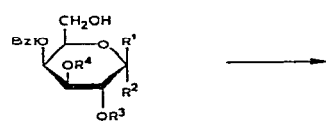
In the galactopyranoside series, the ring fusion is *cis*, and O-3 and O-4 are in *cis*-equatorial,axial relationship. After treatment of methyl 4,6-*O*-benzylidene-α-D-galactopyranoside with $LiAlH_4$–$AlCl_3$, Gorin and Bhattacharjee[10] isolated only the 6-*O*-benzyl derivative, whereas cleavage of 4,6-*O*-benzylidene derivatives of 2-amino-2-deoxy-D-galactose resulted in low yields of products and the formation of both 4- and 6-*O*-benzyl compounds. The effect of substitution at position 3 on the



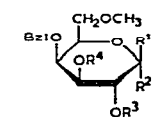
2 $R^1 = R^3 = OBzl, R^2 = R^4 = H$
7 $R^2 = OPh, R^3 = OBzl, R^1 = R^4 = H$
10 $R^1 = R^4 = H, R^2 = OCH_3, R^3 = OBzl$
14 $R^1 = R^4 = H, R^2 = OCH_3, R^3 = OH$
19 $R^1 = R^3 = H, R^2 = R^4 = OBzl$



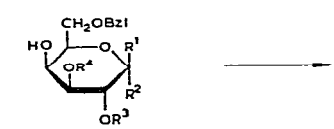
3 $R^1 = R^3 = OBzl, R^2 = R^4 = H, R^5 = CH_3$
8 $R^2 = OPh, R^3 = OBzl, R^1 = R^4 = H, R^5 = CH_3$
11 $R^1 = R^4 = H, R^2 = OCH_3, R^3 = OBzl, R^5 = p\text{-}NO_2\text{—}Bz$
12 $R^1 = R^4 = H, R^2 = OCH_3, R^3 = OBzl, R^5 = CH_3$
15 $R^1 = R^4 = H, R^2 = R^3 = OCH_3, R^5 = CH_3$
20 $R^1 = R^3 = H, R^2 = R^4 = OBzl, R^5 = CH_3$



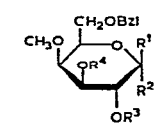
22 $R^1 = OPh, R^2 = H, R^3 = R^4 = Bzl$
27 $R^1 = OBzl, R^2 = H, R^3 = R^4 = Bzl$
37 $R^1 = H, R^2 = OPh, R^3 = R^4 = Bzl$
38 $R^1 = H, R^2 = OBzl, R^3 = R^4 = Bzl$
42 $R^1 = OPh, R^2 = H, R^3 = R^4 = CH_3$



24 $R^1 = OPh, R^2 = H, R^3 = R^4 = Bzl$
29 $R^1 = OBzl, R^2 = H, R^3 = R^4 = Bzl$
39 $R^1 = H, R^2 = OPh, R^3 = R^4 = Bzl$
40 $R^1 = H, R^2 = OBzl, R^3 = R^4 = Bzl$
44 $R^1 = OPh, R^2 = H, R^3 = R^4 = CH_3$



23 $R^1 = OPh, R^2 = H, R^3 = R^4 = Bzl$
28 $R^1 = OBzl, R^2 = H, R^3 = R^4 = Bzl$
43 $R^1 = OPh, R^2 = H, R^3 = R^4 = CH_3$



25 $R^1 = OPh, R^2 = H, R^3 = R^4 = Bzl$
30 $R^1 = OBzl, R^2 = H, R^3 = R^4 = Bzl$
45 $R^1 = OPh, R^2 = H, R^3 = R^4 = CH_3$

direction of the opening of the benzylidene ring in galactoside derivatives was therefore examined.

Cleavage of phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside[21] (**21**) with $LiAlH_4$–$AlCl_3$, followed by fractional crystallization of the products, gave the 4- (**22**) and 6-*O*-benzyl (**23**) derivatives in yields of 68 and 12%, respectively. Compounds **22** and **23** were identical with phenyl 2,3,4- and 2,3,6-tri-*O*-benzyl-β-D-galactopyranoside, respectively, synthesised by Dyong and Werner[22] in six steps starting from **21**. The structures of **22** and **23** were also confirmed by the n.m.r. data for the respective *O*-methyl derivatives **24** and **25**.

Cleavage of benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside[23] (**26**) gave a similar result; the yields of 4- (**27**) and 6-*O*-benzyl (**28**) derivatives were 91.8 and 4.4%, respectively. Chromatography[24] was necessary to isolate **28**. The postulated structures were completely supported by the n.m.r. data for the respective, crystalline 6- (**29**) and 4-*O*-methyl (**30**) derivatives.

That the yield of **28** (4%) from **26** is less than that (12%) of **23** from **21** is not due to steric effects associated with the anomeric substituent was shown when cleavage of phenyl (**33**) and benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranoside (**36**) did not yield a higher proportion of the 6-*O*-benzyl products. The yield of 6-*O*-benzyl product was $<10\%$ (t.l.c.) in each reaction, and only the 4-*O*-benzyl compounds (**37** and **38**) were isolated. Methylation of **37** and **38** gave the corresponding 6-*O*-methyl derivatives **39** and **40**. The synthesis of **38**, using the 6-*O*-allyl intermediate, has recently been reported[25].

Compound **33** was prepared from phenyl α-D-galactopyranoside[26] (**31**) by benzylidenation (→**32**) followed by benzylation.

Solvolysis of phenyl 1-thio-β-D-galactopyranoside[27] (**34**) with benzyl alcohol in tetrahydrofuran, in the presence of HgO and $HgSO_4$, gave benzyl α-D-galactopyranoside, which was converted without isolation into benzyl 4,6-*O*-benzylidene-α-D-galactopyranoside (**35**, 65%) by treatment with benzaldehyde and $ZnCl_2$. The α-configuration of **35** was indicated by the $J_{1,2}$ value of 1.5 Hz.

The effect of the benzyl group at position 3 on the direction of ring-cleavage of benzylidene D-galactopyranosides by $LiAlH_4$–$AlCl_3$ is indirectly shown by the behaviour of phenyl 4,6-*O*-benzylidene-2,3-di-*O*-methyl-β-D-galactopyranoside[21] (**41**). The 4- (**42**) and 6-*O*-benzyl (**43**) products were formed in the ratio 4:6, which was determined by n.m.r. spectroscopy after methylation of the product mixture. The increase in proportion of the 6-*O*-benzyl compound reflects the increased reactivity of O-4. Methylation of **42** and **43** gave the benzyltrimethyl derivatives **44** and **45**, respectively.

The structures of the compounds obtained after cleavage of the benzylidene derivatives with $LiAlH_4$–$AlCl_3$ were determined by methylation. The positions of methyl groups were assigned on the basis of their chemical shifts[28–30] in n.m.r. spectroscopy. For the thirteen partially methylated hexopyranosides shown in Table I. the variation of the chemical shifts for each locus of a methyl group is ± 0.15 p.p.m. Consequently, n.m.r. spectroscopy can be used for structure assignment.

TABLE I

THE CHEMICAL SHIFTS (δ) FOR OMe PROTONS IN SOME METHYLATED HEXOPYRANOSIDE DERIVATIVES

	Chemical shift (δ) *Compounds*												
	3	**8**	**12**	**15**	**20**	**24**	**25**	**29**	**30**	**39**	**40**	**44**	**45**
MeO-1	—	—	3.35	3.43	—	—	—	—	—	—	—	—	—
MeO-2	—	—	—	3.53	—	—	—	—	—	—	—	3.51	3.55
MeO-3	—	—	—	—	—	—	—	—	—	—	—	3.68	3.68
MeO-4	—	—	—	—	—	—	3.58	—	3.59	—	—	—	3.58
MeO-6	3.39	3.26	3.30	3.36	3.38	3.26	—	3.33	—	3.19	3.25	3.27	—

The isolable main product of the cleavage of each of the 2,3-di-*O*-benzyl- and 3-O-benzyl-4,6-*O*-benzylidene-gluco-, -manno-, and -galacto-pyranosides with $LiAlH_4$–$AlCl_3$ was the corresponding 4-*O*-benzyl compound. The yields were >65% and 80% for the glucosides. Thus, the method represents a new selective procedure which is equivalent to tritylation, with the advantage that the isolation of the products is more convenient.

Experiments to utilise the products of the foregoing cleavage reactions, *e.g.*, for the synthesis of oligosaccharides, uronic acids, and 6-deoxy sugars, are in progress.

EXPERIMENTAL

Melting points were obtained with a Kofler apparatus and are uncorrected. Optical rotations were measured on solutions in $CHCl_3$ with a Polamat A (Zeiss) automatic photoelectric polarimeter. N.m.r. spectra were recorded on Varian A-60A and Jeol MH-100 instruments for solutions in $CDCl_3$ with Me_4Si as the internal standard. Reactions were monitored and the purity of products assessed by t.l.c. on Kieselgel G (Merck). Kieselgel G was also used for short-column chromatography[24], using benzene–methanol mixtures, the proportions of which are given in brackets where R_F values are stated.

*Benzyl 2,3,4-tri-*O*-benzyl-β-*D*-glucopyranoside* (**2**). — To a solution of **1**[15] (3 g) in 1:1 ether–dichloromethane (60 ml), 1 g of $LiAlH_4$ was added in three portions with stirring, and the mixture was slowly heated to the boiling point. To the hot solution, $AlCl_3$ (3 g) in ether (30 ml) was added during 30 min, and boiling was continued for 1.5–2 h. When t.l.c. indicated the absence of starting material, the mixture was cooled, the excess of $LiAlH_4$ was decomposed with ethyl acetate (8–10 ml), and $Al(OH)_3$ was precipitated by the addition of water (15 ml). After dilution with ether (50 ml), the organic layer was separated and the residue was washed with a little ether. The organic phase was washed with water (3 × 20 ml), dried, and concentrated to yield **2** (2.68 g, 89.5%), m.p. 104–105°, $[\alpha]_D$ −11.5° (*c* 0.5), R_F 0.42 (97:3); lit.[16] m.p. 105–106°, $[\alpha]_D$ −9.2°. N.m.r. data: δ 7.45–7.15 (m, 20 H, aromatic

protons), 5.10–4.45 (m, 9 H, benzyl and anomeric protons), 3.90–3.15 (m, 6 H, skeleton protons), 1.85 (t, 1 H, *J* 6.5 Hz, HO).

*Benzyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-β-*D*-glucopyranoside* (**3**). — To a mixture of **2** (1 g) and methyl iodide (1.25 ml, 10 mol.) in *N*,*N*-dimethylformamide (15 ml), Ag_2O (1.25 g) was added in three portions. After shaking for 24 h, the mixture was diluted with chloroform and filtered. The filtrate was successively washed with 1% aqueous KCN (3 × 20 ml) and water (3 × 20 ml), dried ($CaCl_2$), and concentrated to give **3** (0.92 g, 89.7%), m.p. 122–123°, $[\alpha]_D$ −22° (*c* 0.5), R_F 0.69 (95:5). N.m.r. data: δ 7.50–7.20 (m, 20 H, aromatic protons), 5.18–4.40 (m, 9 H, benzyl and anomeric protons), 3.85–3.40 (m, 6 H, skeleton protons), 3.39 (s, 3 H, OMe).

Anal. Calc. for $C_{35}H_{38}O_6$: C, 75.78; H, 6.91. Found: C, 74.89; H, 6.69.

*Phenyl 4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**5**). — Compound **4**[17] (1.35 g) was treated with benzaldehyde (5 ml) and freshly fused $ZnCl_2$ (2 g). Crystallization of the product from ethanol afforded **5** (1.62 g, 89.5%), m.p. 209–211°, $[\alpha]_D$ +174° (*c* 1.05), R_F 0.53 (8:2).

Anal. Calc. for $C_{19}H_{20}O_6$: C, 66.26; H, 5.85. Found: C, 66.43; H, 5.71.

*Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**6**). — Compound **5** (2 g) was benzylated with benzyl chloride (24 ml) and powdered KOH (4 g). Crystallization of the product from ethanol gave **6** (2.15 g, 70.7%), m.p. 139–139.5°, $[\alpha]_D$ +84° (*c* 0.76), R_F 0.72 (98:2).

Anal. Calc. for $C_{33}H_{32}O_6$: C, 75.56; H, 6.14. Found: C, 75.32; H, 6.04.

*Phenyl 2,3,4-tri-*O*-benzyl-α-*D*-glucopyranoside* (**7**). — Compound **6** (1 g) was hydrogenolysed, according to the procedure described above for **2**, to give **7** (0.7 g, 67.9%), m.p. 74–75°, $[\alpha]_D$ +114.5° (*c* 1.13), R_F 0.42 (97:3).

Anal. Calc. for $C_{33}H_{34}O_6$: C, 75.26; H, 6.50. Found: C, 74.99; H, 6.38.

*Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-*D*-glucopyranoside* (**8**). — Compound **7** (0.3 g) was methylated, as described above for **3**, to give **8** as a syrup (0.17 g, 55.1%), $[\alpha]_D$ +100° (*c* 0.96), R_F 0.79 (97:3). N.m.r. data: δ 7.40–6.84 (m, 20 H, aromatic protons), 5.45 (d, *J* 3.5 Hz, H-1), 5.12–4.48 (m, 6 H, benzyl protons), 4.32–3.32 (m, 6 H, skeleton protons), 3.26 (s, 3 H, OMe).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 75.71; H, 6.81.

*Methyl 2,3,4-tri-*O*-benzyl-α-*D*-glucopyranoside* (**10**). — Compound **9** (2 g) was hydrogenolysed, as described above for **2**, to give syrupy **10** (1.89 g, 94.1%), $[\alpha]_D$ +20° (*c* 0.55), R_F 0.27 (97:3).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.08; H, 6.83.

*Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(p-nitrobenzoyl)-α-*D*-glucopyranoside* (**11**). — Compound **10** (1 g) was treated with *p*-nitrobenzoyl chloride (0.48 g, 1.2 mol.) in anhydrous pyridine at room temperature for 24 h. The mixture was then poured into ice–water and extracted with chloroform. The organic layer was washed till neutral and then concentrated, and the residue was crystallized from ethanol to give **11** (0.4 g, 30.3%), m.p. 81–83°, $[\alpha]_D$ +69° (*c* 0.84), R_F 0.65 (97:3).

Anal. Calc. for $C_{35}H_{35}NO_9$: C, 68.50; H, 5.74. Found: C, 68.24; H, 5.52.

*Methyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-*D*-glucopyranoside* (**12**). — Methylatior

of **10** (1.1 g) was carried out as described above for **3**, to give syrupy **12** (0.85 g, 75.2%), $[\alpha]_D$ +8° (*c* 0.71), R_F 0.67 (97:3). N.m.r. data: δ 7.40–7.26 (m, 15 H, aromatic protons), 5.05–4.48 (m, 7 H, benzyl and anomeric protons), 4.10–3.40 (m, 6 H, skeleton protons), 3.35 and 3.30 (2 s, 6 H, 2 MeO).

Anal. Calc. for $C_{29}H_{34}O_6$: C, 72.77; H, 7.16. Found: C, 72.85; H, 7.03.

*Methyl 3,4-di-*O*-benzyl-α-*D*-glucopyranoside* (**14**). — Compound **13**[19] (2 g) was hydrogenolysed as described above for **2**. Crystallization of the product from cyclohexane gave **14** (1.67 g, 83.0%), m.p. 95.5–96°, $[\alpha]_D$ +69° (*c* 0.8), R_F 0.32 (9:1).

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 6.99. Found: C, 67.99; H, 6.51.

*Methyl 3,4-di-*O*-benzyl-2,6-di-*O*-methyl-α-*D*-glucopyranoside* (**15**). — Compound **14** (0.5 g) was methylated in the usual manner to give syrupy **15** (0.31 g, 58.5%), $[\alpha]_D$ +73° (*c* 1.2), R_F 0.44 (97:3). N.m.r. data: δ 7.44–7.08 (m, 10 H, aromatic protons), 5.04–4.50 (m, 5 H, benzyl and anomeric protons), 4.05–3.55 (m, 6 H, skeleton protons), 3.53, 3.43, 3.36 (3 s, 9 H, 3 MeO).

Anal. Calc. for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 67.95; H, 7.43.

*Benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-mannopyranoside* (**18**). — Compound **17**[20] (2.3 g) was benzylated with benzyl chloride (9.2 ml) and powdered KOH (4.6 g) to give syrupy **18** (2.24 g, 65%), $[\alpha]_D$ +69° (*c* 0.77, pyridine), R_F 0.72 (97:3).

Anal. Calc. for $C_{34}H_{34}O_6$: C, 75.81; H, 6.36. Found: C, 74.99; H, 6.51.

*Benzyl 2,3,4-tri-*O*-benzyl-α-*D*-mannopyranoside* (**19**). — Hydrogenolysis of **18** (2 g), as described above for **2**, gave syrupy **19** (1.72 g, 86%), $[\alpha]_D$ +54° (*c* 0.3), R_F 0.73 (9:1).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 76.12; H, 6.53.

*Benzyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-*D*-mannopyranoside* (**20**). — Compound **19** (0.23 g) was methylated with methyl iodide and Ag_2O in the usual manner to give syrupy **20** (0.19 g, 82.5%), $[\alpha]_D$ +57° (*c* 0.7), R_F 0.67 (97:3). N.m.r. data: δ 7.40–7.05 (m, 20 H, aromatic protons), 5.00–4.28 (m, 9 H, benzyl and anomeric protons), 4.0–3.44 (m, 6 H, skeleton protons), 3.38 (s, 3 H, OMe).

Anal. Calc. for $C_{35}H_{38}O_6$: C, 75.78; H, 6.91. Found: C, 75.02; H, 6.73.

*Phenyl 2,3,4-tri-*O*-benzyl-β-*D*-galactopyranoside* (**22**) *and phenyl 2,3,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**23**). — Compound **21**[21] (3 g) was hydrogenolysed as described above for **2**. The product contained components having R_F 0.62 and 0.50 (97:3). The latter component crystallized from cyclohexane to give **22** (4.07 g, 65.4%), m.p. 114°, $[\alpha]_D$ −47° (*c* 0.68); lit.[22] m.p. 111°, $[\alpha]_D$ −36°. N.m.r. data: δ 7.40–6.80 (m, 20 H, aromatic protons), 5.15–4.42 (m, 7 H, benzyl and anomeric protons), 4.30–3.27 (m, 6 H, skeleton protons), 1.56 (t, 1 H, *J* 3.5 Hz, OH).

After removal of **22**, the filtrate was concentrated and the residue was crystallized from ethanol to give **23** (0.73 g, 11.7%), m.p. 119°, $[\alpha]_D$ −23° (*c* 1.56); lit.[22] m.p. 119°, $[\alpha]_D$ −16.5°. N.m.r. data: δ 7.45–6.93 (m, 20 H, aromatic protons), 5.15–4.50 (m, 7 H, benzyl and anomeric protons), 4.15–3.43 (m, 6 H, skeleton protons), 2.57 (d, 1 H, *J* 2.5 Hz, OH).

*Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-β-*D*-galactopyranoside* (**24**). — Methylation of **22** (1.05 g) as described for **3**, with crystallization of the product from

cyclohexane, gave **24** (0.93 g, 86.9%), m.p. 98–100°, $[\alpha]_D$ −20° (*c* 0.79), R_F 0.70 (97:3). N.m.r. data: δ 7.40–6.92 (m, 20 H, aromatic protons), 5.10–4.58 (m, 7 H, benzyl and anomeric protons), 4.24–3.44 (m, 6 H, skeleton protons), 3.26 (s, 3 H, OMe).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 74.26; H, 6.55.

*Phenyl 2,3,6-tri-*O*-benzyl-4-*O*-methyl-β-*D*-galactopyranoside* (**25**). — Compound **23** (0.3 g) was methylated, as described above for **3**, to give **25** (0.26 g, 84.3%), m.p. 120–122°, $[\alpha]_D$ −32° (*c* 0.69), R_F 0.73. N.m.r. data: δ 7.36–6.90 (m, 20 H, aromatic protons), 5.05–4.47 (m, 7 H, benzyl and anomeric protons), 4.12–3.46 (m, 6 H, skeleton protons), 3.58 (s, 3 H, OMe).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 74.78; H, 6.54.

*Benzyl 2,3,4-tri-*O*-benzyl-β-*D*-galactopyranoside* (**27**) *and benzyl 2,3,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**28**). — Compound **26**[23] (3 g) was hydrogenolysed as described above for **2**. The product contained components having R_F 0.56 and 0.31 (97:3). The latter component was crystallized from cyclohexane to give **27**[31] (2.75 g, 91.8%), m.p. 96°, $[\alpha]_D$ −49° (*c* 1.3); lit.[31] m.p. 96–96.5°, $[\alpha]_D$ −46.1°. N.m.r. data: δ 7.45–7.10 (m, 20 H, aromatic protons), 5.10–4.47 (m, 9 H, benzyl and anomeric protons), 4.08–3.10 (m, 6 H, skeleton protons), 1.53 (s, 1 H, OH).

After removal of **27**, the filtrate was concentrated and the residue was subjected to short-column chromatography to give syrupy **28** (0.82 g, 4.54%), $[\alpha]_D$ −24° (*c* 1.1), R_F 0.56 (97:3).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 74.92; H, 6.92.

*Benzyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-β-*D*-galactopyranoside* (**29**). — Compound **27**[31] (0.5 g) was methylated as described above for **3**. Crystallization of the product from cyclohexane gave **29** (0.42 g, 82.3%), m.p. 80–81°, $[\alpha]_D$ −30° (*c* 0.80), R_F 0.73 (97:3). N.m.r. data: δ 7.55–7.12 (m, 20 H, aromatic protons), 5.17–4.35 (m, 9 H, benzyl and anomeric protons), 4.10–3.95 (m, 6 H, skeleton protons), 3.33 (s, 3 H, OMe).

Anal. Calc. for $C_{35}H_{38}O_6$: C, 75.78; H, 6.91. Found: C, 75.47; H, 6.63.

*Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-methyl-β-*D*-galactopyranoside* (**30**). — Compound **28** (0.71 g) was methylated in the usual manner. Crystallization of the product from cyclohexane and hexane gave **30** (0.53 g, 66.2%), m.p. 79–81°, $[\alpha]_D$ −43° (*c* 0.50), R_F 0.64 (97:3). N.m.r. data: δ 7.40–7.15 (m, 20 H, aromatic protons), 5.04–4.36 (m, 9 H, benzyl and anomeric protons), 3.90–3.35 [m, 9 H, skeleton protons and OMe (δ 3.59)].

Anal. Calc. for $C_{35}H_{38}O_6$: C, 75.78; H, 6.91. Found: C, 76.13; H, 6.81.

*Phenyl 4,6-*O*-benzylidene-α-*D*-galactopyranoside* (**32**). — Compound **31**[26] (3.1 g) was treated with benzaldehyde (20 ml) and freshly fused $ZnCl_2$ (5 g). Crystallization of the product from ethanol gave **32** (4.08 g, 95.3%), m.p. 192–194°, $[\alpha]_D$ +95° (*c* 0.54, pyridine), R_F 0.39 (9:1).

Anal. Calc. for $C_{19}H_{20}O_6$: C, 66.26; H, 5.85. Found: C, 65.73; H, 5.69.

*Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-galactopyranoside* (**33**). — Compound **32** (3 g) was benzylated with benzyl chloride (10 ml) and powdered KOH (3 g).

Crystallization of the product from acetone–ethanol gave **33** (3.72 g, 81.3%), m.p. 132°, $[\alpha]_D$ +108° (*c* 1.48), R_F 0.72 (97:3).

Anal. Calc. for $C_{33}H_{32}O_6$: C, 75.56; H, 6.14. Found: C, 74.28; H, 5.98.

*Phenyl 2,3,4-tri-*O*-benzyl-α-*D*-galactopyranoside* (**37**). — Compound **33** was hydrogenolysed as described above for **2**. Crystallisation of the product from cyclohexane gave **37** (1.8 g, 87.8%), m.p. 57–58°, $[\alpha]_D$ +81° (*c* 0.57), R_F 0.59 (97:3).

Anal. Calc. for $C_{33}H_{34}O_6$: C, 75.26; H, 6.50. Found: C, 74.39; H, 6.38.

*Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-*D*-galactopyranoside* (**39**). — Methylation of **37** (0.2 g), as described above for **3**, gave syrupy **39** (0.14 g, 68.3%), $[\alpha]_D$ +110.5° (*c* 0.3), R_F 0.73 (97:3). N.m.r. data: δ 7.50–6.94 (m, 20 H, aromatic protons), 5.50 (d, 1 H, *J* 2.5 Hz, H-1), 5.10–4.55 (m, 6 H, benzyl protons), 4.25–3.30 (m, 6 H, skeleton protons), 3.19 (s, 3 H, OMe).

Anal. Calc. for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 74.83; H, 6.51.

*Benzyl 4,6-*O*-benzylidene-α-*D*-galactopyranoside* (**35**). — Phenyl 1-thio-β-D-galactopyranoside[26] (**34**, 5 g) was dissolved in tetrahydrofuran (150 ml), and the solution was boiled and stirred with $HgSO_4$ (5 g), HgO (4 g), and benzyl alcohol (50 ml) for 24 h. The filtered solution was steam-distilled and then concentrated, and the residue was dried over P_2O_5. The resulting product was treated with benzaldehyde (10 ml) and freshly fused $ZnCl_2$ (5 g) in the usual manner. Crystallization of the product from ethanol gave **35** (3.96 g, 60.2%), m.p. 108–109°, $[\alpha]_D$ +117° (*c* 0.2), R_F 0.55 (8:2). N.m.r. data: δ 7.53–7.16 (m, 10 H, aromatic protons), 5.46 (s, 1 H, benzylidene proton), 5.08 (d, 1 H, *J* 1.5 Hz, H-1), 4.64 (AB quartet, benzyl protons, *J* 11 Hz), 4.14–3.50 (m, 6 H, skeleton protons), 2.58 (s, 2 H, OH).

Anal. Calc. for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 65.62; H, 6.35.

*Benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-galactopyranoside* (**36**). — Compound **35** (0.47 g) was benzylated according to the procedure described above. Crystallization of the product from ethanol gave **36** (0.49 g, 69.3%), m.p. 140°, $[\alpha]_D$ +111° (*c* 0.5), R_F 0.69 (97:3).

Anal. Calc. for $C_{34}H_{34}O_6$: C, 75.80; H, 6.36. Found: C, 79.05; H, 6.98.

*Benzyl 2,3,4-tri-*O*-benzyl-α-*D*-galactopyranoside* (**38**). — Hydrogenolysis of **36** (0.29 g), as described above for **2**, gave **38**[25] (0.24 g, 82.4%), m.p. 91–91.5°, $[\alpha]_D$ +58° (*c* 0.55); R_F 0.6 (95:5); lit.[25] m.p. 96–98°, $[\alpha]_D$ +51.5°.

*Benzyl 2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-*D*-galactopyranoside* (**40**). — Compound **38**[25] (0.2 g) was methylated in the usual manner to give syrupy **40** (0.15 g, 73.8%), $[\alpha]_D$ +70° (*c* 0.71), R_F 0.7 (97:3). N.m.r. data: δ 7.52–7.05 (m, 20 H, aromatic protons), 5.04–4.40 (m, 9 H, benzyl and anomeric protons), 4.08–3.12 [m, 9 H, skeleton protons and OMe (δ 3.25)].

Anal. Calc. for $C_{35}H_{38}O_6$: C, 75.78; H, 6.90. Found: C, 75.51; H, 6.81.

*Phenyl 4-*O*-benzyl-2,3-di-*O*-methyl-β-*D*-galactopyranoside* (**42**) *and phenyl 6-*O*-benzyl-2,3-di-*O*-methyl-β-*D*-galactopyranoside* (**43**). — Compound **41**[21] (3 g) was hydrogenolysed as described above for **2**. The product (2.1 g, 69.5%) contained components having R_F 0.52 and 0.55 (97:3). Crystallization from cyclohexane–hexane gave **42** (0.8 g, 26.5%), m.p. 107°, $[\alpha]_D$ −80° (*c* 0.94). N.m.r. data: δ 7.44–6.90

(m, 10 H, aromatic protons), 5.04–4.58 (m, 3 H benzyl and anomeric protons), 3.85–3.20 [m, 12 H, skeleton protons and OMe (δ 3.70, 3.58)], 1.71 (s, 1 H, HO).

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 6.99. Found: C, 66.85; H, 6.71.

After removal of **42**, the filtrate was concentrated and the residue was subjected to column chromatography with a high loss. Compound **43** (0.2 g, 6.6%), when crystallized from cyclohexane, had m.p. 63–65°, $[\alpha]_D$ −34° (*c* 0.52).

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 6.99. Found: C, 68.03; H, 6.81.

Phenyl 4-O-benzyl-2,3,6-tri-O-methyl-β-D-galactopyranoside (**44**). — Compound **42** (0.6 g) was methylated, as described above for **3**, to give **44** (0.45 g, 72.5%), m.p. 77–78°, $[\alpha]_D$ −65° (*c* 0.55), R_F 0.57 (97:3). N.m.r. data: δ 7.48–6.85 (m, 20 H, aromatic protons), 5.02–4.56 (m, 3 H, benzyl and anomeric protons), 3.96–3.15 [m, 15 H, skeleton protons and OMe (δ 3.68, 3.51, 3.27)].

Anal. Calc. for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 66.98; H, 7.09.

Phenyl 6-O-benzyl-2,3,4-tri-O-methyl-β-D-galactopyranoside (**45**). — Methylation of **43** (0.1 g) in the usual manner gave **45** (0.08 g, 76.9%), m.p. 88.5–89°, $[\alpha]_D$ −47° (*c* 0.46), R_F 0.51 (97:3). N.m.r. data: δ 7.32–6.84 (m, 10 H, aromatic protons), 4.83 (d, 1 H, *J* 8 Hz, H-1), 4.54 (s, 2 H, benzyl CH_2), 3.80–3.15 [m, 15 H, skeleton protons and OMe (δ 3.68, 3.58, 3.55)].

Anal. Calc. for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 68.85; H, 7.11.

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