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THE REGIOSELECTIVITY OF TRIBUTYLTIN ETHER-MEDIATED BENZYLATION OF 1,6-ANHYDRO-β-D-HEXOPYRANOSES*

M. CARMEN CRUZADO AND MANUEL MARTIN-LOMAS
Instituto de Química Orgánica, C.S.I.C., Juan de la Cierva 3, 28006 Madrid (Spain)
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ABSTRACT

The benzylation of 1,6-anhydro-β-D-galactopyranose and the *manno, allo, altro, gulo, talo, gluco*, and *ido* isomers, using bis(tributyltin) oxide and *N*-methylimidazole, tetrabutylammonium bromide, tetrabutylammonium iodide, or tetrabutylammonium fluoride as catalyst, has been studied. The results confirm the importance of the catalyst in the benzylation reactions and indicate that the presence of a *cis*-axial hydroxyl group seems to be necessary for regioselective benzylation.

INTRODUCTION

The utility of organotin derivatives of alcohols in regioselective acylation, alkylation, and oxidation reactions has been demonstrated[1]. Dibutyltin oxide and bis(tributyltin) oxide have been used to selectively enhance the nucleophilicity of hydroxyl groups in carbohydrate derivatives and an understanding of this activation is important in designing synthesis strategies. The reaction of carbohydrate derivatives with bis(tributyltin) oxide and subsequent treatment with acyl halides results in regioselective acylation, which can be explained on the basis of the formation of a co-ordinated tributyltin ether in which the oxygen atom is more nucleophilic than the original hydroxyl group[2,3]. These acylations are fast reactions at room temperature, but alkylations usually require extended periods of heating[4]. Alkylation is catalysed by quaternary ammonium bromides[4] and the enhanced reactivity of the alkoxide under these conditions has been attributed to the formation of an ion pair $RO^- {}^+NBu_4$ with a large cation–anion separation. *N*-Methylimidazole, which alters the regioselectivity of benzoylation *via* stannylene derivatives[5], is as efficient a catalyst as tetrabutylammonium bromide in the selective benzylation of lactose derivatives[6]. We now report on a systematic study of the selective benzylation of the conformationally rigid 1,6-anhydro-β-D-hexopyranoses (**1–8**), using bis(tributyltin) oxide and various catalysts.

*Dedicated to Professor Rezső Bognár in the year of his 75th birthday.

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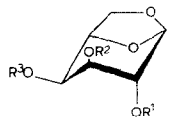
RESULTS AND DISCUSSION

1,6-Anhydro-β-D-galactopyranose (**1**) and the *manno* (**2**), *allo* (**3**), *altro* (**4**), *gulo* (**5**), *talo* (**6**), *gluco* (**7**), and *ido* (**8**) analogues were each reacted with 1.5 mol. equiv. of bis(tributyltin) oxide in toluene, and then treated with an excess of benzyl bromide in the presence variously of *N*-methylimidazole and tetrabutylammonium halides (fluoride, bromide, and iodide) as catalysts. The products were isolated by column chromatography or analysed by g.l.c. of the trimethylsilyl derivatives. The results are summarised in Table I.



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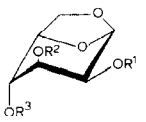
10 $R^1 = R^3 = H, R^2 = Bzl$
11 $R^1 = R^3 = Ac, R^2 = Bzl$



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12 $R^1 = Bzl, R^2 = R^3 = H$
13 $R^1 = R^3 = H, R^2 = Bzl$
14 $R^1 = Bzl, R^2 = R^3 = Ac$
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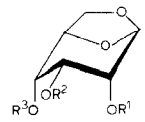
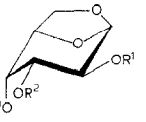
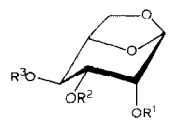


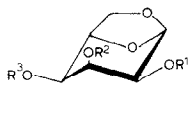
3 $R^1 = R^2 = R^3 = H$
16 $R^1 = R^2 = H, R^3 = Bzl$
17 $R^1 = R^3 = H, R^2 = Bzl$
18 $R^1 = Bzl, R^2 = R^3 = H$
19 $R^1 = R^2 = Ac, R^3 = Bzl$
20 $R^1 = R^3 = Ac, R^2 = Bzl$
21 $R^1 = Bzl, R^2 = R^3 = Ac$



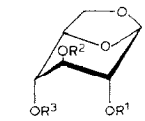
4 $R^1 = R^2 = R^3 = H$
22 $R^1 = R^3 = H, R^2 = Bzl$
23 $R^1 = R^2 = H, R^3 = Bzl$
24 $R^1 = R^3 = Ac, R^2 = Bzl$
25 $R^1 = R^2 = Ac, R^3 = Bzl$



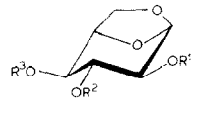
5 $R^1 = R^2 = R^3 = H$
26 $R^1 = R^3 = H, R^2 = Bzl$
27 $R^1 = Bzl, R^2 = R^3 = H$
28 $R^1 = R^3 = Ac, R^2 = Bzl$
29 $R^1 = Bzl, R^2 = R^3 = Ac$



6 $R^1 = R^2 = R^3 = H$
30 $R^1 = R^3 = Bzl, R^2 = H$
31 $R^1 = R^3 = Bzl, R^2 = Ac$



7 $R^1 = R^2 = R^3 = H$
32 $R^1 = Bzl, R^2 = R^3 = H$
33 $R^1 = R^2 = H, R^3 = Bzl$
34 $R^1 = Bzl, R^2 = R^3 = Ac$
35 $R^1 = R^2 = Ac, R^3 = Bzl$



8 $R^1 = R^2 = R^3 = H$
36 $R^1 = R^3 = H, R^2 = Bzl$
37 $R^1 = R^2 = H, R^3 = Bzl$
38 $R^1 = Bzl, R^2 = R^3 = H$
39 $R^1 = R^3 = Ac, R^2 = Bzl$
40 $R^1 = R^2 = Ac, R^3 = Bzl$
41 $R^1 = Bzl, R^2 = R^3 = Ac$

The regioselectivity of the benzylation was invariably high and the best results were obtained when *N*-methylimidazole or tetrabutylammonium fluoride was used as catalyst. The influence of the catalyst on both the regioselectivity and the rate of reaction is evident. As expected, the equatorial HO-4 of **1** was benzylated preferentially to give 1,6-anhydro-4-*O*-benzyl-β-D-galactopyranose (**9**), but some of the 3-*O*-benzyl derivative **10** was also formed. Lower regioselectivity was observed for **2** in which the equatorial HO-2 reacted preferentially to afford 1,6-anhydro-2-*O*-benzyl-β-D-mannopyranose (**12**) as the major product and the 3-*O*-benzyl derivative **13** as the minor product. The equatorial HO-3 of **3** was selectively benzylated to give 1,6-anhydro-3-*O*-benzyl-β-D-allopyranose (**17**), and the 2- (**18**, 11%) and 4-*O*-benzyl derivative (**16**, 10%) were also formed. Neither **17** and **18** nor the corresponding diacetates (**20** and **21**) could be isolated and their relative proportions were determined by n.m.r. spectroscopy. The equatorial HO-3 groups of **4** and **5** were also benzylated selectively to give 1,6-anhydro-3-*O*-benzyl-β-D-altropyranose (**22**) and 1,6-anhydro-3-*O*-benzyl-β-D-gulopyranose (**26**), respectively. Benzylation

TABLE I

RESULTS OF THE BENZYLATION REACTIONS OF 1,6-ANHYDRO-β-D-HEXOPYRANOSES

Starting material	*Catalyst (equiv.)*[a]	*Rection time (h)*	*Products (%)*
1	A (1)	1.5	**9** (93)
	B (0.35)	1.25	**9** (81), **10** (19)[b]
	C (0.35)	2.5	**9** (85), **10** (15)[b]
	A (0.35)	4	**9** (89), **10** (11)[b]
	D (0.35)	7	**9** (80), **10** (20)[b]
	E	5 days	**9** (60) + other products
2	A (1)	2	**12** (65), **13** (25)
	C (0.35)	3	**12** (62), **13** (28)
	A (0.35)	4.5	**12** (58), **13** (32)
	D (0.35)	8	**12** (52), **13** (38)
3	A (1)	0.8	**16** (11), **17** and **18** (89)[b]
4	A (1)	1.5	**22** (78), **23** (22)[b]
5	A (1)	1.5	**26** (90), **27** (8)[b]
6	A (1)	2	**30** (95)
	A (0.35)	4	**30** (96)
	C (0.35)	3	**30** (93)
7	A (1)	7.5	**32** (39), **33** (52)[b]
8	A (1)	4.5	**36** (50), **37** and **38** (40)

[a]A, *N*-Methylimidazole; tetrabutylammonium iodide (B), fluoride (C), and bromide (D); E, no catalyst. [b]Determined by g.l.c.

of the *cis*-axial HO-2 in **4** and HO-4 in **5** occurred also to give **23** and **27**, respectively. Benzylation of the equatorial HO-4 in **4** or HO-2 in **5** was not observed. Benzylation of the *talo* isomer **6** gave the 2,4-di-*O*-benzyl derivative **30** and no mono-*O*-benzyl derivatives could be isolated. Poor regioselectivity was observed in the benzylation of the *gluco* (**7**) and *ido* (**8**) isomers.

The above results confirm the importance of the catalyst in the benzylation reaction. The hypothesis of the reversible formation of an anionic pentaco-ordinate tin species on addition of the catalyst to a preferentially formed, equatorially oriented trialkyltinalkoxide accounts for the results, although the presence of a *cis*-axial hydroxyl group seems to be necessary for regioselective benzylation. This situation has been demonstrated with methyl 3,6-anhydro-α-D-galactopyranoside (**42**), which gave the 2- (**43**) and 4-*O*-benzyl (**44**) derivatives in approximately equal amounts when treated with bis(tributyltin) oxide and then with benzyl bromide. Therefore, it may be postulated that a reversible formation of an equatorial trialkylstannyl ether with participation of an adjacent *cis*-hydroxyl group is the first step. This intermediate may reversibly give an anionic pentaco-ordinate tin species on addition of the catalyst, which reacts irreversibly with benzyl bromide with possible participation of a *cis*-hydroxyl group to give the selectively benzylated derivative.

EXPERIMENTAL

General. — Melting points were measured in capillary tubes and are uncorrected. T.l.c. was performed on Silica Gel GF_{254} (Merck) with detection by charring with sulfuric acid. Column chromatography was performed on Merck type I (70–230 Mesh) silica gel. ^{1}H-N.m.r. spectra were recorded with Varian XL-300 and Bruker AM-200 spectrometers, and ^{13}C-n.m.r. spectra (20 MHz) with a Bruker WP-80 spectrometer. Optical rotations were determined with a Perkin–Elmer 141 polarimeter. G.l.c. was performed at 180°, using a Perkin–Elmer 900 chromatograph equipped with a capillary column with OV-1 as the stationary phase. For the preparation of samples for g.l.c., an aliquot of the reaction mixture was percolated through Silica Gel GF_{254} (Merck), and the resulting mixture (~1 mg) of partially benzylated 1,6-anhydrohexopyranoses was treated with 1-(trimethylsilyl)imidazole (0.1 mL) in pyridine (0.1 mL) for 30 min at 65° and then injected into the gas chromatograph.

Benzylation reactions. — A stirred mixture of the 1,6-anhydro-β-D-hexopyranose (0.1 g, 0.56 mmol), powdered molecular sieve, type 3A (0.5 g), and bis(tributyltin) oxide (0.44 mL, 0.84 mmol) in toluene (8 mL) was heated under argon at 120°. After 15 h, benzyl bromide (0.2 mL, 3.36 mmol) and the catalyst (see Table I) were added. When the reaction was complete, the molecular sieve was collected and washed with chloroform and methanol, the combined filtrate and washings were concentrated, and the residue was fractionated by column chromatography (3:2 ethyl acetate–hexane).

(*a*) From **1**, 1,6-anhydro-4- (**9**) and -3-*O*-benzyl-β-D-galactopyranose (**10**) were obtained.

Compound **9**, isolated as a syrup, had $[\alpha]_D$ −22° (*c* 0.5, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (200 MHz): δ 7.34 (m, 5 H, Ph), 5.35 (s, 1 H, H-1), 4.63 (d, 2 H, PhC*H*$_2$), 4.39 (t, 1 H, $J_{4,5} \approx J_{5,6exo} \approx 4.6$ Hz, H-5), 4.28 (d, 1 H, $J_{6endo,6exo}$ ~7.4 Hz, H-6*endo*), 4.00 (dd, 1 H, $J_{2,3}$ ~1.4, $J_{3,4}$ ~4.8 Hz, H-3), 3.82 (m, 2 H, H-2,4), 3.60 (dd, 1 H, H-6*exo*); ^{13}C, δ 128.75 (2 C), 128.38 (2 C), 127.88 (2 C), 101.61 (C-1), 72.70, 71.79 (2 C), 71.50, 69.92, 64.21 (C-6).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.85; H, 6.76.

The 2,4-diacetate (**11**) of **10** was a syrup, $[\alpha]_D$ −71° (*c* 0.5, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (200 MHz): δ 7.32 (m, 5 H, Ph), 5.37 (s, 1 H, H-1), 4.91 (t, 1 H, $J_{3,4} \approx J_{4,5} \approx 4.8$ Hz, H-4), 4.85 (s, 1 H, H-2), 4.40 (m, 4 H, H-5,6*endo*, PhC*H*$_2$), 3.86 (dd, 1 H, $J_{2,3}$ ~1.4 Hz, H-3), 3.64 (t, 1 H, $J_{exo,endo}$~6.1 Hz, H-6*exo*), 2.06 (s, 3 H, Ac), 1.95 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.75; H, 6.13.

(*b*) From **2**, 1,6-anhydro-2- (**12**) and -3-*O*-benzyl-β-D-mannopyranose (**13**) were obtained.

Compound **12** was isolated as a syrup, $[\alpha]_D$ −60° (*c* 0.6, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.74; H, 6.50.

The 3,4-diacetate (**14**) of **12** was a syrup, $[\alpha]_D$ −42° (*c* 0.8, chloroform).

N.m.r. data ($CDCl_3$): ^1H (300 MHz): δ 7.30 (m, 5 H, Ph), 5.33 (s, 1 H, H-1), 5.29 (dd, 1 H, $J_{2,3}$ ~5.2, $J_{3,4}$ ~1.4 Hz, H-3), 4.72 (s, 1 H, H-4), 4.57 (d, 1 H, PhCH_2), 4.50 (m, 1 H, H-5), 4.42 (d, 1 H, PhCH_2), 4.14 (d, 1 H, $J_{6endo,exo}$ ~7.7 Hz, H-6*endo*), 3.76 (dd, 1 H, $J_{5,6exo}$ ~5.9 Hz, H-6*exo*), 3.52 (dd, 1 H, $J_{1,2}$ ~1.8 Hz, H-2), 2.11 (s, 3 H, Ac), 2.06 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00; Found: C, 60.31; H, 6.14.

Compound **13** was isolated as a syrup, $[\alpha]_D$ −21° (*c* 0.4, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.96; H, 6.33.

The 2,4-diacetate (**15**) of **13** was a syrup, $[\alpha]_D$ −31° (*c* 0.4, chloroform). N.m.r. data ($CDCl_3$): ^1H (200 MHz): δ 7.31 (m, 5 H, Ph), 5.38 (s, 1 H, H-1), 4.87 (s, 1 H, H-4), 4.66 (dd, 1 H, $J_{1,2}$ ~1.8, $J_{2,3}$ ~5.6 Hz, H-2), 4.64 (d, 1 H, PhCH_2), 4.51 (d, 1 H, PhCH_2), 4.50 (m, 1 H, H-5), 4.28 (d, 1 H, $J_{6exo,6endo}$ ~7.5 Hz, H-6*endo*), 3.85 (dd, 1 H, $J_{3,4}$ ~1.4 Hz, H-3), 3.76 (dd, 1 H, $J_{5,6exo}$ ~5.9 Hz, H-6*exo*), 2.16 (s, 3 H, Ac), 2.03 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.80; H, 6.21.

(*c*) From **3**, 1,6-anhydro-4-*O*-benzyl-β-D-allopyranose (**16**) and a mixture of the 3- (**17**) and 2-*O*-benzyl derivative (**18**) was obtained.

Compound **16** had m.p. 109–111°, $[\alpha]_D$ −76° (*c* 0.6, chloroform); lit.[7] m.p. 113°, $[\alpha]_D$ −79° (chloroform). The 2,3-diacetate (**19**) of **16** was a syrup, $[\alpha]_D$ −67° (*c* 1.3, chloroform). N.m.r. data ($CDCl_3$): ^1H (300 MHz): δ 7.35 (m, 5 H, Ph), 5.51 (d, 1 H, $J_{1,2}$ ~1.4 Hz, H-1), 5.14 (m, 2 H, H-2,3), 4.73 (d, 2 H, PhCH_2), 4.68 (m, 1 H, H-5), 3.78 (m, 3 H, H-6*endo*,6*exo*,4), 2.20 (s, 3 H, Ac), 2.06 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.29; H, 6.13.

Acetylation of the mixture of **17** and **18** gave a 6:1 mixture of **20** and **21**. The proportions were determined by n.m.r. spectroscopy. ^1H-N.m.r. data ($CDCl_3$, 300 MHz): for **20**, δ 5.42 (d, $J_{1,2}$ ~2.6 Hz, H-1), 5.11 (m, H-2,4), 4.57 (m, H-5), 2.10 (s, Ac), 2.08 (s, Ac); **21**, δ 5.39 (d, $J_{1,2}$ ~2.5 Hz, H-1), 5.05 (t, $J_{2,3} \approx J_{3,4} \approx 5.6$ Hz, H-3), 2.12 (s, Ac), 1.95 (s, Ac).

(*d*) From **4**, 1,6-anhydro-3- (**22**) and -4-*O*-benzyl-β-D-altropyranose (**23**) were identified, and **22** was isolated as a syrup, $[\alpha]_D$ −123° (*c* 0.8, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.49; H, 6.51.

The 2,4-diacetate (**24**) of **22** was a syrup, $[\alpha]_D$ −152° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): ^1H (200 MHz): δ 7.30 (m, 5 H, Ph), 5.46 (d, 1 H, $J_{1,2}$ ~1.6 Hz, H-1), 5.29 (dd, 1 H, $J_{3,4}$ ~4.6, $J_{4,5}$ ~2.5 Hz, H-4), 4.97 (dd, 1 H, $J_{2,3}$ ~9.2 Hz, H-2), 4.62 (m, 2 H, PhCH_2, H-5), 4.44 (d, 1 H, PhCH_2), 3.77 (m, 3 H, H-3,6*endo*,6*exo*), 2.16 (s, 3 H, Ac), 2.07 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.31; H, 5.87.

Compound **23** had m.p. 123–126°, $[\alpha]_D$ −137° (*c* 0.5, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.68; H, 6.22.

The 2,3-diacetate (**25**) of **23** was a syrup, $[\alpha]_D$ −129° (*c* 0.9, chloroform). N.m.r. data ($CDCl_3$): ^1H (200 MHz): δ 7.35 (m, 5 H, Ph), 5.43 (d, 1 H, $J_{1,2}$ ~1.5 Hz, H-1), 5.06 (dd, 1 H, $J_{2,3}$ ~9.5 Hz, H-2), 4.95 (dd, 1 H, $J_{3,4}$ ~4.5 Hz, H-3), 4.57

(m, 3 H, PhCH_2, H-5), 3.90 (dd, 1 H, $J_{4,5}$ ~2.5 Hz, H-4), 3.74 (m, 2 H, H-6*endo*,6*exo*), 2.06 (s, 3 H, Ac), 1.96 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.21; H, 6.15.

(*e*) From **5**, 1,6-anhydro-3- (**26**) and -2-*O*-benzyl-β-D-gulopyranose (**27**) were obtained.

Compound **26** had m.p. 137–139°, $[\alpha]_D$ +56° (*c* 0.6, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.62; H, 6.09.

The 2,4-diacetate (**28**) of **26** had m.p. 73–75°, $[\alpha]_D$ +67° (*c* 0.6, chloroform). N.m.r. data ($CDCl_3$): ^1H (300 MHz): δ 7.31 (m, 5 H, Ph), 5.47 (d, 1 H, $J_{1,2}$ ~2.5 Hz, H-1), 5.33 (dd, 1 H, $J_{2,3}$ ~4.7 Hz, H-2), 5.16 (dd, 1 H, $J_{3,4}$ ~9.5, $J_{4,5}$ ~4.2 Hz, H-4), 4.64 (d, 1 H, PhCH_2), 4.60 (t, 1 H, $J_{5,6exo}$ ~4.2 Hz, H-5), 4.44 (d, 1 H, PhCH_2), 3.95 (d, 1 H, $J_{6exo,6endo}$ ~7.9 Hz, H-6*endo*), 3.79 (dd, 1 H, H-3), 3.67 (dd, 1 H, H-6*exo*), 2.16 (s, 3 H, Ac), 2.05 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.53; H, 6.20.

Compound **27** was isolated as a syrup, $[\alpha]_D$ +31° (*c* 0.4, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.72; H, 6.45.

The 3,4-diacetate (**29**) of **27** was a syrup, $[\alpha]_D$ +20° (*c* 0.4, chloroform). N.m.r. data ($CDCl_3$): ^1H (300 MHz): δ 7.27 (m, 5 H, Ph), 5.28 (d, 1 H, $J_{1,2}$ ~2.4 Hz, H-1), 5.24 (ddd, 1 H, $J_{3,4}$ ~9.7, $J_{4,5}$ ~4.2, $J_{4,6exo}$ ~0.9 Hz, H-4), 5.16 (dd, 1 H, $J_{2,3}$ ~4.9 Hz, H-3), 4.58 (d, 1 H, PhCH_2), 4.52 (t, 1 H, $J_{5,6exo}$ ~4.3 Hz, H-5), 4.47 (d, 1 H, PhCH_2), 3.96 (d, 1 H, $J_{6endo,6exo}$ ~8 Hz, H-6*endo*), 3.86 (dd, 1 H, H-2), 3.60 (ddd, 1 H, H-6*exo*), 1.99 (s, 3 H, Ac), 1.97 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.25; H, 6.20.

(*f*) From **6**, 1,6-anhydro-2,4-di-*O*-benzyl-β-D-talopyranose (**30**) was obtained as a syrup, $[\alpha]_D$ −19° (*c* 0.6, chloroform).

Anal. Calc. for $C_{26}H_{22}O_5$: C, 70.14; H, 6.48. Found: C, 70.32; H, 6.29.

The 3-acetate (**31**) of **30** was a syrup, $[\alpha]_D$ −26° (*c* 0.5, chloroform). N.m.r. data ($CDCl_3$): ^1H (200 MHz): δ 7.28 (m, 10 H, 2 Ph), 5.89 (t, 1 H, $J_{2,3} \approx J_{3,4} \approx 4.7$ Hz, H-3), 5.33 (s, 1 H, H-1), 4.68–4.41 (m, 4 H, 2 PhCH_2), 4.49 (d, 1 H, $J_{6exo,6endo}$ ~8.3 Hz, H-6*endo*), 4.36 (t, 1 H, $J_{4,5} \approx J_{5,6exo} \approx 4.6$ Hz, H-5), 3.72 (m, 2 H, H-4,6*exo*), 3.46 (dd, 1 H, $J_{1,2}$ ~1.7 Hz, H-2), 2.17 (s, 3 H, Ac).

Anal. Calc. for $C_{22}H_{24}O_6$: C, 68.72; H, 6.30. Found: C, 68.79; H, 6.47.

(*g*) From **7**, 1,6-anhydro-2- (**32**) and -4-*O*-benzyl-β-D-glucopyranose (**33**) were isolated; **32** had m.p. 70–73°, $[\alpha]_D$ −67° (*c* 0.4, ethanol) {lit.[8] m.p. 73–74°, $[\alpha]_D$ −64° (ethanol)}, and **33** had m.p. 50–52°, $[\alpha]_D$ −41° (*c* 0.7, ethanol) {lit.[9] m.p. 53–54°, $[\alpha]_D$ −43° (ethanol)}.

(*h*) From **8**, 1,6-anhydro-3- (**36**), -4- (**37**), and -2-*O*-benzyl-β-D-idopyranose (**38**) were formed.

Compound **36** had m.p. 157–158°, $[\alpha]_D$ −36° (*c* 0.5, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.70; H, 6.42.

The 2,4-diacetate (**39**) of **36** was a syrup, $[\alpha]_D$ −35° (*c* 1.2, chloroform). N.m.r. data ($CDCl_3$): ^1H (300 MHz): δ 7.24 (m, 5 H, Ph), 5.37 (d, 1 H, $J_{1,2}$ ~1.7 Hz, H-1), 4.98 (ddd, 1 H, $J_{3,4}$ ~8.6, $J_{4,5}$ ~4.3, $J_{4,6exo}$ ~1 Hz, H-4), 4.76 (dd, 1 H,

$J_{2,3}$ ~8.4 Hz, H-2), 4.57 (s, 2 H, PhCH_2), 4.53 (t, 1 H, $J_{4,5} \approx J_{5,6exo} \approx 4.6$ Hz, H-5), 3.94 (d, 1 H, $J_{6exo,6endo}$ ~8.0 Hz, H-6*endo*), 3.78 (t, 1 H, H-3), 3.65 (dd, 1 H, H-6*exo*), 1.99 (s, 3 H, Ac), 1.95 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.29; H, 6.31.

Compounds **37** and **38** were isolated as a mixture that was acetylated to give a 1:1 mixture of **40** and **41**, which was fractionated by column chromatography (7:3 hexane–ethyl acetate). Compound **40** was isolated as a syrup, $[\alpha]_D$ −67° (*c* 0.4, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (300 MHz): δ 7.25 (m, 5 H, Ph), 5.30 (d, 1 H, $J_{1,2}$ ~2.0 Hz, H-1), 5.22 (t, 1 H, $J_{2,3} \approx J_{3,4} \approx 8.5$ Hz, H-3), 4.69 (dd, 1 H, H-2), 4.51 (m, 2 H, PhCH_2), 4.42 (t, 1 H, $J_{4,5} \approx J_{5,6exo} \approx 4.3$ Hz, H-5), 4.15 (d, 1 H, $J_{6endo,6exo}$ ~7.7 Hz, H-6*endo*), 3.67 (m, 2 H, H-4,6*exo*), 1.99 (s, 3 H, Ac), 1.91 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.51; H, 6.13.

Compound **41** was isolated as a syrup, $[\alpha]_D$ −20° (*c* 0.5, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (300 MHz): δ 7.25 (m, 5 H, Ph), 5.33 (d, 1 H, $J_{1,2}$ ~1.7 Hz, H-1), 5.24 (t, 1 H, $J_{2,3} \approx J_{3,4} \approx 8.5$ Hz, H-3), 4.92 (ddd, $J_{4,5}$ ~4.3, $J_{4,6exo}$ ~1.1 Hz, H-4), 4.54 (m, 2 H, PhCH_2), 4.44 (t, 1 H, $J_{5,6exo}$ ~4.4 Hz, H-5), 4.10 (d, 1 H, $J_{6exo,6endo}$ ~7.9 Hz, H-6*endo*), 3.70 (ddd, 1 H, H-6*exo*), 3.44 (dd, 1 H, H-2), 1.97 (s, 3 H, Ac), 1.90 (s, 3 H, Ac).

Anal. Calc. for $C_{17}H_{20}O_7$: C, 60.69; H, 6.00. Found: C, 60.47; H, 6.29.

(*i*) Methyl 3,6-anhydro-α-D-galactopyranoside (**42**), after 1 day, gave (t.l.c.) two monobenzyl derivatives in approximately equal amounts and 50% of **42**.

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