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Dioxolanylium Ions Derived from Carbohydrates. V. Rearrangement of Derivatives of 1,6-Anhydro-β-D-Glycopyranoses and their Reaction with Nucleophiles

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The relative stability of a series of equilibrating 2-phenyl-1,3-dioxolanylium ions *6*⇌*7* and *18*⇌*19*, derived from 1,6-anhydro-β-D-glycopyranoses has been measured in acetonitrile. On reaction with nucleophiles, the reaction with water is faster than the equilibration between the ions, and gives the *cis* hydroxybenzoates in the same ratio as the equilibrium concentrations of dioxolanylium ions, while *trans* opening with bromide ion is slower than the ion equilibration, allowing preferential attack on the more reactive, rather than on the more abundant dioxolanylium ion. An efficient synthesis of 1,6-anhydro-β-D-gulopyranose from 1,6-anhydro-β-D-galactopyranose is described.

In two preceding papers in this series it was shown that certain benzylidene derivatives of carbohydrates can be converted into benzoxonium ions by hydride abstraction with triphenylmethyl fluoroborate.[1,2] These ions reacted with bromide ion to give *trans* bromodeoxybenzoates, in most cases *trans* diequatorial isomers as opposed to the *trans* diaxial compounds, obtained when benzoxonium ions derived from *trans* decalin or steroids are treated with bromide ion.[3] In order to learn whether this difference is due to increased conformational mobility of carbohydrate derivatives, as compared to the rigid decalin or steroid systems, the reaction of benzoxonium ions derived from 1,6-anhydro-β-D-hexopyranoses with bromide ion has now been studied.

1,6-Anhydro-β-D-hexopyranoses with *manno-*, *altro-*, *galacto-*, or *gulo*-configurations all have a pair of *cis*-oriented hydroxy groups suitable for the formation of benzaldehyde acetals and, subsequently, benzoxonium ions. They also have one hydroxy group *trans* to this pair, and when acylated this group may excert a neighbouring group attack to give a rearranged acyloxonium ion. The rearrangement of acyloxonium ions and subsequent reaction with water to give *cis* hydroxy – acyloxy compounds is well known,[4,5] but little is known about acyloxonium ion rearrangements followed by *trans* opening with nucleophiles such as bromide ion.[6–8] This is probably due to the fact that most acyloxonium ion rearrangements have been carried out in strong acids [4,5] (hydrogen fluoride, trifluoromethane sulfonic acid, or antimony pentachloride) which do not allow the presence of nucleophiles. Formation of benzoxonium ions by hydride abstraction, as used in the present work, poses no limitations on the nucleophiles and has therefore allowed a study of the potentially useful sequence: benzoxonium ion formation, rearrangement, and *trans* opening with a nucleophile.

Treatment of the benzylidene derivatives of D-mannosan (*8f*), D-altrosan (*5a*), D-galactosan (*17a*) and D-gulosan (*20f*), and of the corresponding *p*-toluenesulfonates *8g*, *5b*, *17b*, and *20g* with triphenylmethyl fluoroborate in acetonitrile solution gave the corresponding benzoxonium ions as seen from the ^1H and ^{13}C NMR spectra of the solutions (Tables 1 and 2).

Reaction of the altrosan ions *6a* and *6b* with bromide ion gave solely the 3-bromo-3-deoxy-D-mannosan derivatives *9a* and *9b*. Similarly, the gulosan ions *19f* and *19g* gave only the 3-bromo-3-deoxy-D-galactosan derivatives *24f* and

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Table 1. ^{1}H NMR spectra of benzoxonium ions in acetonitrile-d_3 solution.

Compound	Chemical shifts (δ-values)								Coupling constants (Hz)							
	H1	H2	H3	H4	H5	$H6_{en}$	$H6_{ex}$	CH_3	J_{12}	J_{23}	J_{34}	J_{45}	J_{5en}	J_{5ex}	J_{enex}	
6a	5.56	4.13	5.97	5.94	5.36	4.13	3.96		3.1	3.0	8.7	≃0	1.0	5.9	9.0	
6b	5.57	4.88	6.08	5.90	5.40	4.18	3.97	2.48	3.1	3.7	9.0	0.7	1.3	5.6	9.0	
6c	5.89	5.47	6.33	6.11	5.47	4.26	4.08		3.7	3.4	9.2	≃0	1.6	5.8	9.0	
6e	5.90	5.51	6.36	6.11	5.49	4.27	4.09		3.7	3.2	9.3	≃0	1.6	5.9	9.0	
6h	5.85	5.38	6.17	5.95	5.37	4.22	4.04	3.98	3.8	3.4	8.8	≃0	1.7	6.0	9.0	
7c	5.87	6.20	5.9	6.0	5.10	4.16	3.91		2.8	≃8			1.2	5.6	8.9	
7d	5.89	6.03	5.79	5.81	5.06	4.11	3.86	3.99	2.9	7.7			≃1	5.8	8.9	
7f	5.81	6.08	5.70	4.60	4.84	3.91	3.76		2.7	7.5	≃1	1.5	1.5	5.2	8.8	
7g	5.85	6.12	5.77	5.38	4.84	3.98	3.77		2.8	7.6	≃1	1.5	1.4	5.6	9.3	
7i	5.95	6.23	6.00	5.89	5.11	4.17	3.90		2.7	7.7	≃1	≃1.5	1.3	5.6	9.3	
18a	5.58	4.39	5.73	6.39	5.17	3.7 – 3.8			<1	<1	9.2	6.5				
18b	5.58	4.96	5.78	6.38	5.26	3.88	3.70	2.45	<1	<1	9.7	6.7	<1	4.2	10.2	$J_{13}\simeq 1$ Hz
18e	5.82	5.52	6.05	6.49	5.34	3.95	3.79		<1	<1	9.6	6.6	<1	4.2	10.0	
18h	5.74	5.41	5.78	6.24	5.22	3.84	3.76	4.01	<1	<1	9	7	<1	4	10	270 MHz
19c	6.14	5.78	6.35	5.78	5.06	4.35	3.88		<1	9.4	3.7	6.3	1.3	5.5	8.7	
19d	6.09	5.63	6.18	5.70	5.03	4.31	3.86	4.00	<1	9.2	3.8	6.3	1.3	5.5	8.7	
19f	6.14	5.63	6.07	4.49	4.75	4.15	3.74		<1	9.2	4.0	6.3	1.3	5.5	8.5	
19g	6.13	5.69	6.20	5.25	4.87	4.20	3.87	2.51	<1	9.2	3.9	6.4	1.3	5.5	9.0	
19h	6.11	5.71	6.28	5.74	5.03	4.31	3.9	3.85	<1	9	4		1		9	270 MHz
19i	6.16	5.78	6.40	5.82	5.09	4.39	3.92		<1	9.3	3.6	6.3	1.1	5.5	8.8	

Table 2. ^{13}C NMR spectra of benzoxonium ions in acetonitrile-d_3 solution.

Compound	Chemical shifts (δ-values)						
	C1	C2	C3	C4	C5	C6	C+
6a	99.2	69.7	90.3 [a]	87.3 [a]	70.9	64.9	181.2
6b	97.3	75.2	86.1	87.1	70.9	65.3	181.3
6c	97.0	70.4 [a]	86.5	87.1	71.1 [a]	64.8	181.3
6e	96.8	71.1 [a]	86.2	87.1	70.9 [a]	64.8	181.3
6h	96.9	71.2 [a]	85.1	85.8	70.7 [a]	64.8	178.9
7c	94.5	81.4	84.5	67.5	73.7	65.6	
7d	94.8	80.1	83.1	67.6	73.6	65.5	179.7
7f	94.5	81.5	87.0	65.8	75.9	65.4	182.0
7g	94.3	81.0	84.0	71.6	74.0	65.2	182.0
7i	94.5	81.3	84.2	68.1	73.6	65.6	182.2
18a	100.8	67.4	88.0	78.9	68.7	62.9	181.7
18b	98.7	72.6	84.6	78.4	68.4	63.1	
18e	98.7	69.3	85.0	78.8	68.8	63.3	182.1
18h	98.7	68.9 [a]	83.8	77.5	68.7 [a]	63.1	179.4
19c	95.6	83.9	87.0	68.2	70.2	63.6	181.3
19d	95.8	82.9	85.5	68.5	70.2	63.5	179.0
19e	95.6	85.0	88.5	68.0	70.4	63.8	
19f	95.1	84.0	90.5	67.0	72.5	62.5	
19g	95.4	84.0	86.1	73.0	70.6	63.1	181.4
19h	95.6	83.8	87.1	67.9	70.4	63.6	181.3
19i	95.6	84.0	86.7	68.9	70.1	63.7	181.1

[a] Assignment may be reversed.

24g. Thus all four benzoxonium ions underwent exclusive *trans* diaxial opening with bromide ion. The ion *7f* reacted with bromide ion to give a 3-bromo-3-deoxy-D-altrosan derivative *10f* with *trans* diequatorial opening. The corresponding tosylate *7g*, on the other hand, gave a mixture of the 3-bromo-3-deoxy-D-altrosan derivative *10g* and the 2-bromo-2-deoxy-D-glucosan derivative *11g* in a ratio of 3:1. The ion *18a* with bromide ion yielded a mixture of the 3-bromo-D-gulosan derivative *23a* and the 4-bromo-D-glucosan derivative *22a* corresponding to a 2:1 preference for *trans* diequatorial opening relative to *trans* diaxial opening of the benzoxonium ion. The tosylate ion *18a*, on the other hand, gave exclusively the *trans* diaxial product *22b*.

These results agree with those of King and Allbutt [3] who found that the diaxial opening is favoured by *ca.* 20:1 unless an axial substituent interacts with the incoming nucleophile. In the manno-ions *7* a 1,3-diaxial interaction will occur between the substituent at C-4 and the bromide ions attacking at C-2. A similar interaction is found in the galacto-ions *18*; therefore it is reasonable that substitution of these ions with bromide ion to some extent yields the *trans* equatorial products, *10* and *23*, respectively. It may be noted that an axial hydroxy group favours equatorial substitution more than an axial tosyloxy group. The altro-ions *6* and the gulo-ions *19* yield exclusively the *trans* diaxial products *9* and *24*, respectively, although the 1,6-anhydro bridge might hinder axial attack upon C-3. Dreiding models show, however, that the pyranose ring of 1,6-anhydro-β-D-pyranoses is flattened considerably in the area around C-2, C-3, and C-4, thus leaving C-3 open for nucleophilic attack. A similar effect has been found in the opening of steroid 2α,3α-epoxides with hydrogen bromide; again, the lack of 1,3-diaxial hindrance from the C-19 methyl group was explained by flattening of the steroid A-ring.[3]

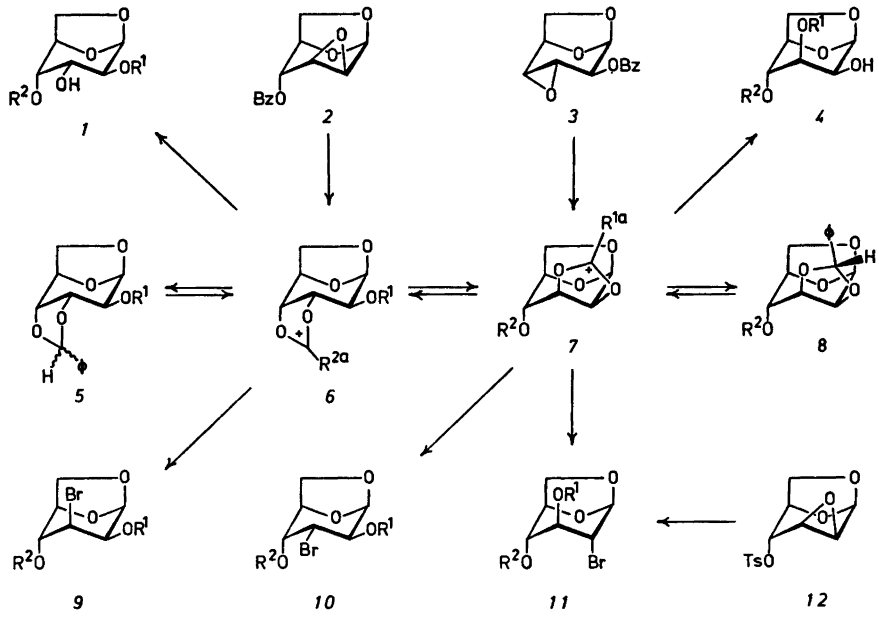
Reaction of 3,4-*O*-benzylidene-2-*O*-benzoyl-1,6-anhydro-β-D-galactose (*17c*) with trityl fluoroborate in acetonitrile would be expected to give the galacto-ion *18c*, but ^1H and ^{13}C NMR spectra showed that the solution contained more than 95 % of the gulo-ion *19c*, resulting from benzoxonium ion rearrangement of *18c*. After hydrolysis, debenzoylation, and acetylation tri-*O*-acetyl-1,6-anhydro-β-D-gulose could be crystallized in 85 % yield. Examination of

the mother liquor showed that it contained 3–4 % of galactosan triacetate corresponding to 3–4 % of the galacto-ion *18c* in equilibrium with *19c*. Similarly, the methoxy-benzoate *17d* gave the gulo-ion *19d* as the only detectable ion as seen from NMR spectra, and work-up as described above yielded 95 % of D-gulosan triacetate. The mother liquor contained *ca.* 0.2 % of D-galactosan triacetate corresponding to a twenty-fold shift of the equilibrium between *18* and *19* towards *19*, when compared with the unsubstituted benzoxonium ions described above. Any unintentional hydrolysis of the benzylidene galactosan *17*, prior to its conversion to the benzoxonium ion, would increase the amount of galactosan triacetate in the product. In view of the small amount of galactosan obtained even a low degree of hydrolysis would therefore underrate the stabilizing effect of the *p*-methoxy-group. Another system, *18h*⇌*19h* suggests that the *p*-methoxy group increases the equilibrium constant by a factor of 50 rather than 20 (see below). The *p*-nitrobenzoate *17e* also gave some (10–15 %) of the gulo-ion *19e* as seen from ^{13}C NMR spectra, but due to destabilization of benzoxonium ions by a nitro group [9] the equilibrium was now shifted towards *18e* (85–90 %). This corresponds to a 200-fold decrease in the equilibrium constant compared to that of the benzoxonium ions *18c* and *19c*.

Oxidation of 2,3-*O*-benzylidene-4-*O*-benzoyl-1,6-anhydro-β-D-gulopyranose (*20c*) with trityl fluoroborate gave the same gulo-ion *19c* as that obtained from *17c*. Likewise the *p*-nitrobenzoate *20i* exclusively yielded the gulo-ion *19i*, whereas the *p*-methoxybenzoate *20h* gave a mixture containing 65 % galacto-ion *18h* and 35 % gulo-ion *19h*, corresponding to a 50-fold decrease in the equilibrium constant (Table 3).

Reaction of benzylidene-altrosan benzoate (*5c*), or benzylidene-mannosan benzoate (*8c*), with trityl carbonium ion gave an equilibrium mixture consisting of 60 % of the altro-ion *6c* and 40 % manno-ion *7c*. Its composition was observed directly by means of ^{1}H and ^{13}C NMR spectroscopy and indirectly after hydrolysis, benzoylation, and separation of the resulting altrosan and mannosan tribenzoates. Again, the equilibrium could be shifted by electron donating or withdrawing substituents on the benzoxonium ions as shown in Table 4.

The hydrolysis of benzoxonium ions with water is rapid; the hydrolysis products obtained



R^1, R^{1a}, R^2 and R^{2a} see Table 4

Table 3. Galacto- and gulobenzoxonium ions, their equilibria and their reactions with bromide ion.

	R¹	R¹ᵃ	R²	R²ᵃ	Obs. equil. *18* %	Obs. equil. *19* %	Product from reaction between bromide ion and *18*	Product from reaction between bromide ion and *19*
18a	H		Bz	C_6H_5			36 % *22a*	
							64 % *23a*	
18b	Ts		Bz	C_6H_5			100 % *22b*	
18c⇌*19c*	Bz	C_6H_5	Bz	C_6H_5	4	96		100 % *24c*
18d⇌*19d*		*p*-CH_3O-C_6H_5	Bz	C_6H_5	0.2	99.8		
18e⇌*19e*		*p*-NO_2-C_6H_5	Bz	C_6H_5	90	10		
19f		C_6H_5	H					100 % *24f*
19g	Bz	C_6H_5	Ts					100 % *24g*
18h⇌*19h*	Bz	C_6H_5	*p*-CH_3O-Bz	*p*-CH_3O-C_6H_5	65	35	7 % *22h*	93 % *24h*
18i⇌*19i*	Bz	C_6H_5	*p*-NO_2-Bz	*p*-NO_2-C_6H_5	⩽5	⩾95		100 % *24i*

from a pair of equilibrating ions, such as *6* or *7*, therefore correspond to the equilibrium mixture.[7] The *trans* opening of benzoxonium ions with bromide ion is much slower and the products obtained are determined by the relative reactivity of the two ions towards bromide ion more than by their relative amount.[7]

When the equilibrating mixture of gulo- *19* and galacto-benzoxonium ions *18* was treated with bromide ion the major and, in most cases, the only product was a 3-bromo-3-deoxy-D-galactosan derivative *24*, resulting from bromide attack on the gulo-ion. This was the result, not only when the gulo-benzoxonium ion *19* was the dominating species present, but also when a stabilizing *p*-methoxy group in the galacto-benzoxonium ion or a destabilizing *p*-nitro group in the gulo-benzoxonium ion had shifted the equilibrium towards the galacto-ion *18* (Table 3). Thus, the gulo-ion *19* is more reactive towards bromide ion than the galacto-ion.

Reaction of the mixture of altro- *6* and manno-benzoxonium ions *7* with bromide ion afforded two products: a 3-bromo-3-deoxy-mannosan *9* and a 3-bromo-3-deoxy-altrosan derivative *10*. When no substituents were present in the benzoxonium ions the equilibrium mixture, which contained 40 % of the manno-ion *7c*, reacted with bromide ion to give 90 % of *9c*, resulting from substitution on *6c*, and only 10 % of *10c*. This corresponds to a six-fold lower reactivity of *7c* relative to *6c*, assuming that the equilibration is much faster than the reaction with bromide ion. A methoxy group in the manno-benzoxonium ion shifts the equilibrium so far towards this ion *7d* that the altro-ion *6d* could not be observed in the NMR spectrum (< 5 %). Assuming a 50 times increase in the equilibrium constant, as found for the galacto-gulo pair discussed above, the amount of *6d* was calculated to be *ca.* 3 %. This shift in concentration of ions relative to the benzoxonium ions *6c* and *7c* was not reflected in the outcome of the reaction with bromide ion since the amount of product *9d* resulting from attack on the altro-ion only decreased from 90 to 70 %. This indicates that the reactivity of the manno-ion *7d* is seventy times lower than that of the altro-ion *6d*. The only difference between the ions *6c* and *6d* is the presence of a benzoyl or a *p*-

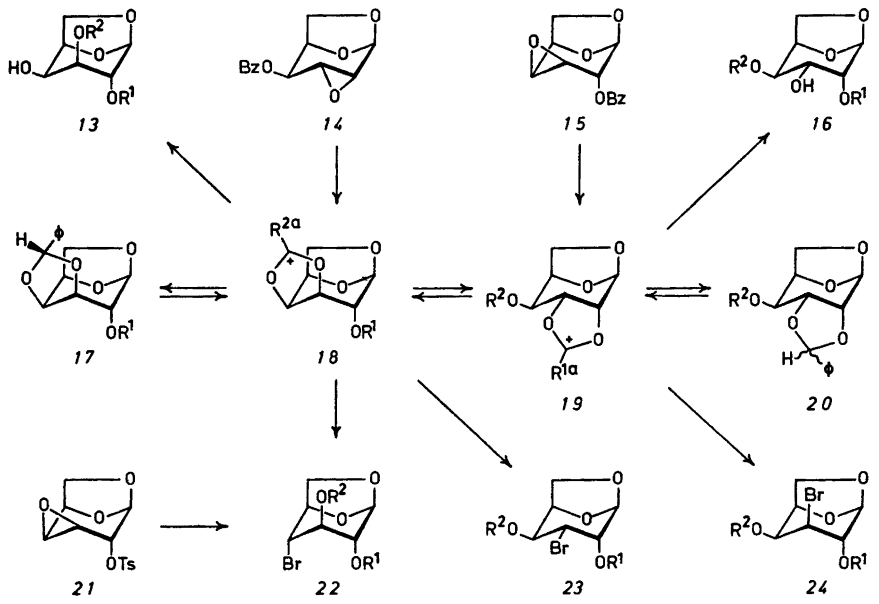
Table 4. Altro- and mannobenzoxonium ions, their equilibria and their reactions with bromide ion.

	R^1	R^{1a}	R^2	R^{3a}	Obs. equil. 6 %	Obs. equil. 7 %	Calc. equil. 6 %	Calc. equil. 7 %	Product from reaction between bromide ion and 6	Product from reaction between bromide ion and 7
6a	H		Bz	C_6H_5					100 % *9a*	
6b	Ts		Bz	C_6H_5					100 % *9b*	
6c⇌*7c*	Bz	C_6H_5	Bz	C_6H_5	60	40			90 % *9c*	10 % *10c*
6d⇌*7d*	*p*-CH_3O-Bz	*p*-CH_3O-C_6H_5	Bz	C_6H_5	<5	>95	3	97	70 % *9d*	30 % *10d*
6e⇌*7e*	*p*-NO_2-Bz	*p*-NO_2-C_6H_5	Bz	C_6H_5	>95	<5	99.7	0.3	100 % *9e*	
7f	Bz	C_6H_5	H							100 % *10f*
7g	Bz	C_6H_5	Ts							27 % *11g*
										73 % *10g*
6h⇌*7h*	Bz	C_6H_5	*p*-CH_3O-Bz	*p*-CH_3O-C_6H_5	>95	<5	98.7	1.3	96 % *9h*	4 % *10h*
6i⇌*7i*	Bz	C_6H_5	*p*-NO_2-Bz	*p*-NO_2-C_6H_5	<5	>95	0.7	99.3	35 % *9i*	65 % *10i*

methoxy-benzoyl grouping which would probably not cause any major difference in the reactivity of the benzoxonium ion. If *6c* and *6d* are assumed to have the same reactivity the *p*-methoxy substituted mannobenzoxonium ion *7d* must react 12 times slower with bromide than the corresponding unsubstituted ion *7c*. In a similar experiment, a *p*-methoxy-group was introduced into the altro-benzoxonium ion *6h* causing a shift of the equilibrium in favour of this ion. In this case it was found that the methoxybenzoxonium ion *7h* reacted 18 times slower than the corresponding benzoxonium ion *7c* (Table 4). This lower reactivity means that although the amount of *p*-methoxybenzoxonium ion is increased by a factor of 50 the amount of product *9h* arising from it is only 3 – 4 times larger. The effect of a *p*-nitro-group can be deduced from the *p*-nitro-substituted altro-benzoxonium ion *6i*. The destabilization, causing the equilibrium constant to shift by a factor of 200 in favour of the manno-ion *7i*, increases the reactivity of *6i* sufficiently to shift the product ratio only by a factor of 15 – 20 in favour of *10i* (Table 4).

Hydrolysis of the benzoxonium ions described above gives products with an axial benzoyloxy group and an equatorial hydroxy group.[10] In the case of equilibrating benzoxonium ions, the hydrolysis reaction is sufficiently fast to give the products in the same ratio as that observed spectroscopically between the benzoxonium ions. The synthetic utility of this reaction for the preparation of selectively acylated 1,6-anhydrides is limited by the tendency of the hydroxy-benzoates to undergo acyl migration on chromatography or storage.

The structures of the products were determined from NMR spectra. The products with *altro*-, *manno*-, *galacto*-, and *gulo*-configurations show characteristic coupling constants,[11] the starting materials serving as model compounds. In products with the *gluco*-configuration, H1 – H4 appeared as broad singlets with a half-width of 3 – 4 Hz due to a large number of small vicinal and long-range coupling constants. Therefore, 3-*O*-benzoyl-2-bromo-2-deoxy-4-*O*-tosyl- and 3-*O*-benzoyl-4-bromo-4-deoxy-2-*O*-tosyl-1,6-anhydro-β-D-glucopyranose (*11b* and *22b*), respectively, were synthesized independently by *trans* diaxial opening with hydrogen



R^1, R^{1a}, R^2 and R^{2a} see Table 3

bromide of the tosylates of 2,3:1,6-dianhydro-β-D-mannopyranose (*12*) and 3,4:1,6-dianhydro-β-D-galactopyranose (*21*), respectively, followed by benzoylation.

The benzylidene compounds were either prepared from the free 1,6-anhydro sugars by acid catalyzed acetalization [1,2] with benzaldehyde or benzaldehyde dimethyl acetal [12,13] or from 1,6-anhydrides containing an epoxide group and a vicinal *trans* benzoyloxy-group by rearrangement to a benzoxonium ion with boron trifluoride followed by reduction to the benzylidene compound with sodium borohydride.[14]

EXPERIMENTAL

Thin-layer chromatography (TLC) was performed on silica gel PF_{254} (Merck); for preparative work 1 mm layers were used on 20 × 40 cm plates. Compounds were visualized by UV light. Melting points are uncorrected. Optical rotations were measured in chloroform solution on a Perkin-Elmer 141 instrument. ^1H NMR spectra were measured on Bruker HXE 90 and HX 270 instruments and ^{13}C NMR spectra on a Bruker WH90 as previously recorded. All spectra were measured in deuteriochloroform unless otherwise specified.

Benzylidene derivatives

Method 1. To a solution of 50 mmol of the appropriate epoxy-benzoate in acetonitrile (100 ml) at 0 °C was added 50 mmol of boron trifluoride etherate and the solution was stirred for 15 min. To this solution was added 75 mmol of finely powdered sodium borohydride under vigorous stirring. After 15 min at 0 °C and 15 min at room temperature water was added and the resulting solution was neutralized with acetic acid. The crude benzylidene derivative either crystallized directly or was extracted with chloroform. The following compounds were prepared in this manner:

2,3-O-(S)-Benzylidene-1,6-anhydro-β-D-mannopyranose (8f). 2-*O*-Benzoyl-1,6:3,4-dianhydro-β-D-altropyranose (*3*) [15] gave *8f* which crystallized directly, m.p. 189–192 °C. Recrystallization from ethyl acetate gave 54 % of *8f*, m.p. 191–194 °C, $[\alpha]_D^{25}$ −85° (*c* 1.2) [lit.[16] m.p. 188–189 °C, $[\alpha]_D$ −79° (*c* 1.0)].

3,4-O-Benzylidene-1,6-anhydro-β-D-altropyranose (5a). 4-*O*-Benzoyl-1,6:2,3-dianhydro-β-D-mannopyranose (*2*) [15] gave *5a* as a diastereomeric mixture (1:1), which was crystallized from ethanol to give 48 % of *5a* m.p. 70–120 °C. Further recrystallizations from ethanol gave the pure (*S*)-*5a*, m.p. 129–130 °C, $[\alpha]_D^{25}$ −121° (*c* 1.5). Anal. $C_{13}H_{14}O_5$: C, H. ^1H NMR: δ 5.46 (H1), 3.80 (H2), 4.46 (H3), 4.14 (H4), 4.84 (H5), 4.02 (H6ex), 3.82 (H6en), 6.11

(ArCH); J_{12} = 2.4 Hz, J_{23} = 5.2, J_{34} = 6.4, J_{45} = 1.3, $J_{5\text{ex}}$ = 4.6, $J_{5\text{en}}$ = 2.2, $J_{\text{en,ex}}$ = 7.6.

2,3-O-Benzylidene-1,6-anhydro-β-D-gulopyranose (20f). 2-*O*-Benzoyl-1,6:3,4-dianhydro-β-D-galactopyranose (*15*)[17] gave crude *20f* as a sirup which was crystallized from a small amount of ether at −20 °C to give 55 % of *20f* as a diastereomeric mixture (1:1). Recrystallization from ethyl acetate-pentane gave m.p. 103–107 °C. Anal. $C_{13}H_{14}O_5$: C, H.

3,4-O-Benzylidene-1,6-anhydro-β-D-galactopyranose (17a). 4-*O*-Benzoyl-1,6:2,3-dianhydro-β-D-galactopyranose (*14*) gave *17a* which crystallized from ethyl acetate in 63 % yield as a diastereomeric mixture with the (*S*) isomer predominating (9:1), m.p. 171–176 °C.

Method II: The 1,6-anhydro sugar was acetalized with benzaldehyde under forced conditions as previously described.[1] The following compounds were prepared:

8f was isolated as a diastereomeric mixture from which the *S*-isomer was crystallized in 54 % yield from ether. Equilibration of the mother liquors with *p*-toluenesulfonic acid in refluxing chloroform gave a further 6 % of (*S*)−*8f*. Recrystallization from ethyl acetate gave m.p. 195–198 °C. $[\alpha]_D^{25}$ −78° (*c* 0.5).

5a (68 %) from ether as a diastereomeric mixture (≃1:1), m.p. 90–100 °C.

17a (50 %) from ethyl acetate–pentane as a diastereomeric mixture, m.p. 160–170 °C, with the (*S*)-isomer predominating (9:1). Equilibration of the mother liquors with *p*-toluenesulfonic acid in refluxing chloroform gave a further 10 % of *17a*. Recrystallization from ethyl acetate–pentane gave pure (*S*)-*17a*, m.p. 175–177 °C, $[\alpha]_D^{25}$ +7.6° (*c* 0.9). Anal. $C_{13}H_{14}O_5$: C, H. ^{1}H NMR (270 MHz, DMSO): δ 5.27 (H1), 3.75 (H2), 4.10 (H3), 4.50 (H4), 4.59 (H5), 3.92 (H6en), 3.39 (H6ex), 5.80 (ArCH); J_{12}, J_{23} and $J_{5\text{en}}$ ≃0 Hz J_{34} = 7.6, J_{45} = 5.9, $J_{5\text{ex}}$ = 5.6, $J_{\text{en,ex}}$ = 7.5.

Method III: Transacetalization of the 1,6-anhydro sugar with benzaldehyde dimethylacetal by analogy to the procedure described for methyl α-D-glucopyranoside.[13]

17a (80 %) from ethyl acetate–pentane, m.p. 173–176 °C as essentially pure (NMR) (*S*) isomer.

Esters of the benzylidene-1,6-anhydro-sugars were prepared by acylation with the appropriate acid chloride in pyridine.

2,3-O-(S)-Benzylidene-4-O-p-toluenesulfonyl-1,6-anhydro-β-D-mannopyranose (8g), m.p. 155–156 °C from acetone–ethanol $[\alpha]_D^{25}$ −76° (*c* 1.2) Anal. $C_{20}H_{20}O_7S$: C, H, S. ^{1}H NMR: δ 5.52 (H1), 4.20 (H2, H3), 4.81 (H4), 4.65 (H5), 4.00 (H6en), 3.80 (H6ex), 5.72 (ArCH), 2.47 (CH_3Ar); J_{12} ≃1 Hz, J_{34}, J_{45} ≃0, $J_{5\text{en}}$ = 1.5, $J_{5\text{ex}}$ = 6.2, $J_{\text{en,ex}}$ = 7.9.

4-O-Benzoyl-2,3-O-(S)-benzylidene-1,6-anhydro-β-D-mannopyranose (8c), m.p. 153–155 °C from ethyl acetate–pentane. $[\alpha]_D^{25}$ −150° (*c* 1.2). Anal. $C_{20}H_{18}O_6$: C, H. ^{1}H NMR (270 MHz): δ 5.60 (H1), 4.29 (H2), 4.33 (H3), 5.39 (H4), 4.77 (H5), 4.17 (H6en), 3.90 (H6ex), 5.80 (ArCH); J_{12} = 2.9 Hz, J_{23} = 6.9, J_{34} = 1.3, J_{45} = 1.3, $J_{5\text{en}}$ = 1.4, $J_{5\text{ex}}$ = 6.4, $J_{\text{en,ex}}$ = 7.6, J_{13} ≃1.3.

2,3-O-(S)-Benzylidene-4-O-p-Methoxybenzoyl-1,6-anhydro-β-D-mannopyranose (8h), m.p. 154–155 °C from acetone–ethanol, $[\alpha]_D^{25}$ −163° (*c* 1.2). Anal. $C_{21}H_{20}O_7$: C, H. ^{1}H NMR: δ 5.61 (H1), 4.32 (H2, H3), 5.37 (H4), 4.77 (H5), 4.17 (H6en), 3.88 (H6ex), 5.81 (ArCH), 3.88 (CH_3O); J_{12} ≃1 Hz, J_{34}, J_{45} ≃0, $J_{5\text{en}}$ = 1.5, $J_{5\text{ex}}$ = 6.2, $J_{\text{en,ex}}$ = 7.8.

2,3-O-(S)-Benzylidene-4-O-p-nitrobenzoyl-1,6-anhydro-β-D-mannopyranose (8i), m.p. 210–212 °C from acetone, $[\alpha]_D^{25}$ −150° (*c* 1.1). Anal. $C_{21}H_{17}NO_8$: C, H, N. ^{1}H NMR: δ 5.64 (H1), 4.37 (H2, H3), 5.44 (H4), 4.81 (H5), 4.22 (H6en), 3.96 (H6ex), 5.85 (ArCH); J_{12} ≃1 Hz, J_{34}, J_{45} ≃0, $J_{5\text{en}}$ = 1.6, $J_{5\text{ex}}$ = 6.2, $J_{\text{en,ex}}$ = 7.5.

3,4-O-Benzylidene-2-O-p-toluenesulfonyl-1,6-anhydro-β-D-altropyranose (5b), diastereomeric mixture, m.p. 153–158 °C from ethyl acetate–pentane. Anal. $C_{20}H_{20}O_7S$: C, H, S.

2-O-Benzoyl-3,4-O-benzylidene-1,6-anhydro-β-D-altropyranose (5c), m.p. 85–95 °C from ethyl acetate–pentane. Preparative TLC (ether–pentane 3:1) gave (*R*)-*5c*, m.p. 107–108 °C, $[\alpha]_D^{21}$ −254° (*c* 1.4). Anal. $C_{20}H_{18}O_6$: C, H. ^{1}H NMR: δ 5.74 (H1), 5.14 (H2), 4.63 (H3), 4.36 (H4), 5.03 (H5), ≃4.0 (H6ex,en), 5.98 (ArCH); J_{12} = 2.5 Hz, J_{23} = 5.0, J_{34} = 6.8, J_{45} ≃1, followed by (*S*)-*5c*, m.p. 106–108 °C, $[\alpha]_D^{21}$ −178° (*c* 1.2), anal. C, H. ^{1}H NMR: δ 5.73 (H1), 5.23 (H2), 4.83 (H3), 4.32 (H4), 4.96 (H5), 3.9 (H6en,ex), 6.24 (ArCH); J_{12} = 2.1 Hz, J_{23} = 5.9, J_{34} = 6.4, J_{45} ≃1.

3,4-O-Benzylidene-2-O-p-methoxybenzoyl-1,6-anhydro-β-D-altropyranose (5d), m.p. 105–120 °C from ethyl acetate–pentane. Preparative TLC (ether–pentane 3:1) gave (*R*)-*5d*, m.p. 138–140 °C, $[\alpha]_D^{21}$ −245° (*c* 1.1), anal. $C_{21}H_{20}O_7$: C, H. ^{1}H NMR: δ 5.71 (H1), 5.10 (H2), 4.61 (H3), 4.33 (H4), 5.01 (H5), 3.9 (H6en,ex), 5.97 (ArCH); J_{12} = 2.3 Hz, J_{23} = 5.1, J_{34} = 6.9, J_{45} ≃1, followed by (*S*)-*5c*, m.p. 139–140 °C, $[\alpha]_D^{21}$ −190° (*c* 1.1), anal. C, H. ^{1}H NMR: δ 5.72 (H1), 5.21 (H2), 4.82 (H3), 4.32 (H4), 4.95 (H5), 3.9 (H6en,ex), 6.24 (ArCH); J_{12} = 2.3 Hz, J_{23} = 5.9, J_{34} = 6.3, J_{45} ≃1.

3,4-O-Benzylidene-2-O-p-nitrobenzoyl-1,6-anhydro-β-D-altropyranose (5e), diastereomeric mixture, foam. Anal. $C_{20}H_{17}NO_8$: C, H, N.

3,4-O-(S)-Benzylidene-2-O-p-toluenesulfonyl-1,6-anhydro-β-D-galactopyranose (17b), m.p. 148–150 °C from ethanol, $[\alpha]_D^{25}$ +7.2° (*c* 1.1). Anal. $C_{20}H_{20}O_7S$: C, H, S. ^{1}H NMR: δ 5.34 (H1), 4.69 (H2), 4.30 (H3), 4.58 (H4, H5), 4.09 (H6en), 3.49 (H6ex), 5.80 (ArCH); J_{12}, J_{23}, $J_{5\text{en}}$ ≃0 Hz, $J_{5\text{ex}}$ ≃6, $J_{\text{en,ex}}$ = 7.8.

2-O-Benzoyl-3,4-O-(S)-benzylidene-1,6-anhydro-β-D-galactopyranose (17c), m.p. 153–154 °C from ethanol, $[\alpha]_D^{25}$ +87° (*c* 1.1). Anal $C_{20}H_{18}O_6$: C, H. ^{1}H NMR (DMSO-d_6): δ 5.63 (H1), 5.12 (H2), 4.37 (H3), 4.65 (H4), 4.81 (H5), 4.08 (H6en), 3.51 (H6ex), 5.88 (ArCH);

J_{12}, J_{23} = 0-1 Hz, J_{34} = 7.2, J_{45} = 6.3, $J_{56en} \simeq 0$, J_{56ex} = 5.4, J_{6en6ex} = 7.6.

3,4-O-(S)-Benzylidene-2-O-p-methoxybenzoyl-1,6-anhydro-β-D-galactopyranose (17d), m.p. 161–163 °C from acetone–ethyl acetate, $[\alpha]_D^{25}$ +102° (*c* 1.0). Anal. $C_{21}H_{20}O_7$: C, H. ^{1}H NMR: δ 5.57 (H1), 5.33 (H2), 4.31 (H3), 4.64 (H4, H5), 4.18 (H6en), 3.58 (H6ex), 5.87 (ArCH); J_{12}, J_{23}, J_{56en} = 0-1 Hz, J_{6en6ex} = 7.6.

3,4-O-(S)-Benzylidene-2-O-p-nitrobenzoyl-1,6-anhydro-β-D-galactopyranose (17e), m.p. 173–174 °C from acetone–ethanol, $[\alpha]_D^{25}$ +99° (*c* 1.0). Anal. $C_{20}H_{17}NO_8$: C, H, N. ^{1}H NMR: δ 5.59 (H1), 5.36 (H2), 4.34 (H3), 4.68 (H4, H5), 4.21 (H6en), 3.59 (H6ex), 5.88 (ArCH); J_{12}, J_{23}, J_{56en} = 0–1 Hz, J_{6en6ex} = 7.7.

2,3-O-Benzylidene-4-O-p-toluenesulfonyl-1,6-anhydro-β-D-gulopyranose (20g), diastereomeric mixture, m.p. 103–106 °C from ethyl acetate–pentane. Anal. $C_{20}H_{20}O_7S$: C, H, S.

4-O-Benzoyl-2,3-O-benzylidene-1,6-anhydro-β-D-gulopyranose (20c), diastereomeric mixture, m.p. 102–107 °C from ethyl acetate–pentane. Anal. $C_{20}H_{18}O_6$: C, H.

2,3-O-Benzylidene-4-O-p-methoxybenzoyl-1,6-anhydro-β-D-gulopyranose (20h), diastereomeric mixture, m.p. 93–97 °C from ether. Anal. $C_{21}H_{20}O_7$: C, H.

2,3-O-Benzylidene-4-O-p-nitrobenzoyl-1,6-anhydro-β-D-gulopyranose (20i), diastereomeric mixture, foam. Anal. $C_{20}H_{17}NO_8$: C, H, N.

Conversion of benzylidene derivatives to hydroxybenzoates

3-O-Benzoyl-4-O-p-toluenesulfonyl-1,6-anhydro-β-D-mannopyranose (4g). *8g* (456 mg) was treated with trityl fluoroborate (506 mg) in acetonitrile (10 ml) for 16 h at room temperature. Addition of aqueous $NaHCO_3$ and extraction with chloroform gave a crude reaction mixture, which was crystallized from a small amount of ether at −20 °C to give 380 mg (80 %) of *4g*, m.p. 112–118 °C. Two recrystallizations from ethyl acetate–pentane gave 215 mg, m.p. 117–118 °C, $[\alpha]_D^{20}$ −145° (*c* 1.2). Anal. $C_{20}H_{20}O_6S$: C, H, S. ^{1}H NMR (DMSO-d_6): δ 5.37 (H1), 3.74 (H2), 5.29 (H3), 4.88 (H4), 4.53 (H5), 4.25 (H6en), 3.74 (H6ex); J_{12} = 1 Hz, J_{23} = 5.5, J_{34} = J_{45} = 1.5, $J_{56en} \simeq 0$, J_{56ex} = 5.5, J_{6en6ex} = 8.4.

1,6-Anhydro-β-D-altro- and mannopyranose tribenzoates. 5c (300 mg) was reacted with trityl fluoroborate (350 mg) in acetonitrile for 16 h at room temperature. Hydrolysis with aqueous $NaHCO_3$ and extraction with chloroform gave a crude product which was benzoylated with benzoyl chloride in pyridine. Preparative TLC (ether–pentane 1:1) of a part of the product yielded 77 mg of 1,6-anhydro-β-D-mannopyranose tribenzoate and 177 mg of 1,6-anhydro-β-D-altropyranose tribenzoate.

3-O-Benzoyl-1,6-anhydro-β-D-galactopyranose (13a). *17a* (999 mg) was reacted with trityl fluoroborate (1.7 g) in acetonitrile at room temperature for 16 h. Addition of aqueous $NaHCO_3$ and extraction with chloroform gave a crude reaction mixture, which was extracted with pentane (2 × 50 ml) and crystallized from ethyl acetate–pentane. One recrystallization from ethyl acetate–pentane gave 326 mg (31 %) of *13a*, m.p. 140–142 °C, homogeneous on NMR. Chromatographic (ether–pentane 5:1) work-up instead of direct crystallization gave 63 % of *13a*, m.p. 145–147 °C, $[\alpha]_D^{20}$ −25° (*c* 0.8). Anal. $C_{13}H_{14}O_6$: C, H. ^{1}H NMR (DMSO-d_6): δ 5.32 (H1), 3.59 (H2), 5.26 (H3), 4.16 (H4), 4.39 (H5), 4.41 (H6en), 3.74 (H6ex); J_{12}, $J_{23} \simeq 1.5$ Hz, J_{34} = 5.2, J_{45} = 3.8, $J_{56en} \simeq 0$, J_{56ex} = 5.5, J_{6en6ex} = 7.5.

2,4-Di-O-benzoyl-1,6-anhydro-β-D-gulopyranose (16c). *17c* (1.90 g) was reacted with trityl fluoroborate (2.16 g) in acetonitrile at room temperature for 20 h. Addition of aqueous $NaHCO_3$ and extraction with chloroform gave a crude product, which, after extraction with pentane (2 × 50 ml), was crystallized from ethyl acetate–pentane. Decantation of the mother liquors and one recrystallization from the same medium gave 1.25 g (63 %) of *16c*, m.p. 138–141 °C. One further recrystallization followed by drying over P_2O_5 gave m.p. 140–142 °C. $[\alpha]_D^{20}$ +133 (*c* 1.0). Anal. $C_{20}H_{18}O_7$: C, H. ^{1}H NMR: δ 5.68 (H1), 5.40 (H2), 4.36 (H3), 5.44 (H4), 4.78 (H5), 4.18 (H6en), 3.78 (H6ex); J_{12} = 2.4, J_{23} = 5.0, J_{34} = 9.5, $J_{45} \simeq 4.5$, $J_{56} \simeq 0$, J_{56ex} = 4.9, J_{6en6ex} = 8.0.

1,6-Anhydro-β-D-gulopyranose triacetate (25). *17d* (11.65 g) was treated with trityl fluoroborate (12.50 g) in acetonitrile at room temperature for 16 h. Addition of aqueous $NaHCO_3$ and extraction with chloroform gave, after evaporation, a crude product which was debenzoylated with a catalytic amount of sodium methoxide in methanol overnight. After neutralization with CO_2 and concentration, the semisolid product was partitioned between water and chloroform, the aqueous phase extracted twice with chloroform and evaporated to dryness. The crude 1,6-anhydro-β-D-gulopyranose was acetylated with acetic anhydride (20 ml), in pyridine (30 ml). Work-up in the usual manner gave 8.4 g of crude *25*, m.p. 110–112 °C. Recrystallization from ethyl acetate (150 ml)–pentane (150 ml) yielded 7.15 g (85 %) of gulosan triacetate (*25*), m.p. 111–112 °C. $[\alpha]_D^{25}$ +22.2° (*c* 1.4) (lit.[18] m.p. 114–115 °C, $[\alpha]_D^{25}$ +22.1°). Fractional crystallization of the mother liquors gave further 1.03 g (12 %) of *25*, m.p. 111–112 °C and 176 mg of mother liquor containing 18 mg (0.2 %) of 1,6-anhydro-β-D-galactose triacetate (*26*), 150 mg *25* and *ca.* 10 mg of an unidentified compound as seen from a ^{13}C NMR spectrum.

When the same reaction sequence was carried out starting from the benzoate (*17c*) (10.0 g) 5.9 g (76 %) of *25* could be crystallized directly,

m.p. 111–112 °C. Concentration of the mother liquors gave further 0.8 g (10 %) of *25*, m.p. 110–112 °C and 850 mg of a semisolid mass which on ^{13}C NMR was shown to contain only gulosan triacetate (*25*), 560 mg (7.2 %), and galactosan triacetate (*26*), 280 mg (3.6 %).

Reaction of benzoxonium ions with bromide ion

General procedure. The benzylidene compound (500 mg) was treated with a 25 % molar excess of trityl fluoroborate in acetonitrile (10 ml) overnight. A 2–3-fold molar excess of tetraethylammonium bromide (dried over P_2O_5) was added and the solution stirred at room temperature for 1–2 h. Addition of aqueous $NaHCO_3$ and extraction with chloroform gave the crude reaction product, which was either crystallized directly or separated by preparative TLC (ether–pentane 3:1) to give triphenylmethane and triphenylcarbinol moving with the solvent front, followed by the bromodeoxy compounds. As the slowest moving compound(s) was usually isolated a small amount (5–15 %) of the hydroxy-benzoates, resulting from direct hydrolysis of the benzoxonium ions. The properties and yields of the individual bromo-deoxy-1,6-anhydro-hexopyranoses are given below in the order of elution on preparative TLC under the heading of the benzylidene compound from which they were prepared.

3,4-O-Benzylidene-1,6-anhydro-β-D-altropyranose (5a). The crude reaction mixture was crystallized from ether to give 63 % of 4-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-mannopyranose (*9a*), m.p. 128–131 °C. Preparative TLC of the mother liquors gave a further 19 % of *9a*, which on recrystallization from ethyl acetate–pentane gave m.p. 132–133 °C. $[\alpha]_D^{25}$ −200° (*c* 1.5). Anal. $C_{13}H_{13}BrO_5$: C, H, Br. ^1H NMR (acetone-d_6): δ 5.47 (H1), 3.91 (H2), 4.65 (H3), 5.57 (H4), 4.82 (H5), 4.56 (H6en), 3.85 (H6ex); $J_{12} \simeq 2$ Hz, $J_{23} = 6.1$, $J_{34} \simeq 2$, $J_{45} \simeq 2$, $J_{5\text{6en}} = 0.7$, $J_{5\text{6ex}} = 5.6$, $J_{\text{6en6ex}} = 8.1$.

3,4-O-Benzylidene-2-O-p-toluenesulfonyl-1,6-anhydro-β-D-altropyranose (5b). Preparative TLC gave 58 % of 4-*O*-benzoyl-3-bromo-3-deoxy-2-*O*-*p*-toluenesulfonyl-1,6-anhydro-β-D-mannopyranose (*9b*). Recrystallization from ethyl acetate–pentane gave m.p. 119–120 °C. $[\alpha]_D^{25}$ −130° (*c* 0.9). Anal. $C_{20}H_{19}BrO_7S$: C, H, Br, S. ^1H NMR (acetone-d_6): δ 5.53 (H1), 4.76 (H2), 4.46 (H3), 5.53 (H4), 4.87 (H5), 4.59 (H6en), 3.90 (H6ex); $J_{12} = 2.1$ Hz, $J_{23} = 6.2$, $J_{34} = 2.1$, $J_{45} = 1.5$, $J_{5\text{6en}} = 0.8$, $J_{5\text{6ex}} = 5.7$, $J_{\text{6en6ex}} = 8.3$, $J_{13} = 1.1$, $J_{24} = 0.6$, $J_{35} = 1.5$.

2-O-Benzoyl-3,4-O-benzylidene-1,6-anhydro-β-D-altropyranose (5c). Preparative TLC gave 70 % of 2,4-di-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-mannopyranose (*9c*). Crystallization from a small amount of ether gave m.p. 106–108 °C, $[\alpha]_D^{25}$ −233° (*c* 0.7). Anal. $C_{20}H_{17}BrO_6$: C, H, Br. ^1H NMR (270 MHz): δ 5.74 (H1), 5.15 (H2), 4.69 (H3), 5.54 (H4), 4.79 (H5), 4.60 (H6en), 3.96 (H6ex); $J_{12} = 2.3$ Hz, $J_{23} = 6.1$, $J_{34} = 2.3$, $J_{45} = 1.7$, $J_{5\text{6en}} = 0.8$, $J_{5\text{6ex}} = 5.8$, $J_{\text{6en6ex}} = 8.0$, $J_{13} = 1.3$, $J_{24} = 0.6$, $J_{35} = 1.5$. A slower moving minor product (8 %) was 2,4-di-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-altropyranose (*10c*). Crystallization from ether and from ethyl acetate–pentane gave m.p. 137–138 °C, $[\alpha]_D^{25}$ −301° (*c* 0.9). Anal. C, H. ^1H NMR: δ 5.74 (H1), 5.50 (H2), 4.64 (H3), 5.48 (H4), 4.92 (H5), 4.08 (H6en), 3.97 (H6ex); $J_{12} = 1.2$ Hz, $J_{23} = 10.4$, $J_{34} = 4.5$, $J_{45} = 2.4$, $J_{5\text{6en}} = 1.4$, $J_{5\text{6ex}} = 5.0$, $J_{\text{6en6ex}} = 8.7$.

3,4-O-Benzylidene-2-O-p-methoxybenzoyl-1,6-anhydro-β-D-altropyranose (5d). Preparative TLC gave two products. 44 % was 4-*O*-benzoyl-3-bromo-3-deoxy-2-*O*-*p*-methoxybenzoyl-1,6-anhydro-β-D-mannopyranose (*9d*), sirup, $[\alpha]_D^{25}$ −234° (*c* 3.6). Anal. $C_{21}H_{19}BrO_7$: C, H, Br. ^1H NMR: δ 5.76 (H1), 5.16 (H2), 4.72 (H3), 5.57 (H4), 4.81 (H5), 4.62 (H6en), 3.97 (H6ex); $J_{12} = 2.3$ Hz, $J_{23} = 6.1$, $J_{34} \simeq 2$, $J_{45} \simeq 2$, $J_{5\text{6en}} \simeq 1$, $J_{5\text{6ex}} = 5.8$, $J_{\text{6en6ex}} = 8.2$. 21 % was 4-*O*-benzoyl-3-bromo-3-deoxy-2-*O*-*p*-methoxybenxoyl-1,6-anhydro-β-D-altropyranose (*10d*), m.p. 139–140 °C, $[\alpha]_D^{25}$ −288° (*c* 3.0). Anal. C, H, Br. ^1H NMR: δ 5.73 (H1), 5.47 (H2), 4.63 (H3), 5.47 (H4), 4.91 (H5), 4.07 (H6en), 3.95 (H6ex); $J_{12} = 1.3$ Hz, $J_{23} = 10.4$, $J_{34} = 4.4$, $J_{45} = 2.4$, $J_{5\text{6en}} = 1.5$, $J_{5\text{6ex}} = 5.0$, $J_{\text{6en6ex}} = 8.6$.

3,4-O-Benzylidene-2-O-p-nitrobenzoyl-1,6-anhydro-β-D-altropyranose (5e). The crude product was crystallized from a small amount of ether to give 51 % of 4-*O*-benzoyl-3-bromo-3-deoxy-2-*O*-*p*-nitrobenzoyl-1,6-anhydro-β-D-mannopyranose (*9e*), m.p. 165–170 °C. Preparative TLC of the mother liquors gave a further 19 % of *9e*, which on recrystallization from ethyl acetate–pentane gave m.p. 175–176 °C, $[\alpha]_D^{25}$ −288° (*c* 1.2). Anal. $C_{20}H_{12}BrNO_8$: C, H, Br, N. ^1H NMR: δ 5.70 (H1), 5.19 (H2), 4.70 (H3), 5.56 (H4), 4.81 (H5), 4.59 (H6en), 3.97 (H6ex); $J_{12} = 2.2$ Hz, $J_{23} = 6.0$, J_{34}, $J_{45} \simeq 2$, $J_{5\text{6en}} \simeq 1$, $J_{5\text{6ex}} = 5.6$, $J_{\text{6en6ex}} = 8.1$.

2,3-O-Benzylidene-1,6-anhydro-β-D-mannopyranose (8f). The crude product was crystallized from a small amount of ether to give 55 % of 2-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-altropyranose (*10f*), m.p. 163–166 °C. Preparative TLC gave a further 26 % of *10f*, which on recrystallization from ethyl acetate–pentane gave m.p. 167–169 °C, $[\alpha]_D^{25}$ −251° (*c* 1.2). Anal. $C_{13}H_{13}BrO_5$: C, H, Br. ^1H NMR (acetone-d_6): δ 5.59 (H1), 5.35 (H2), 4.65 (H3), 4.15 (H4), 4.78 (H5), 4.15 (H6en), 3.82 (H6ex); $J_{12} = 1.6$ Hz, $J_{23} = 10.4$, $J_{34} = 4.1$, $J_{45} = 2.8$, $J_{5\text{6en}} = 1.0$, $J_{5\text{6ex}} = 5.5$, $J_{\text{6en6ex}} = 8.2$.

2,3-O-Benzylidene-4-O-p-toluenesulfonyl-1,6-anhydro-β-D-mannopyranose (8g). Preparative TLC gave 13 % of 3-*O*-benzoyl-2-bromo-2-deoxy-4-*O*-*p*-toluenesulfonyl-1,6-anhydro-β-D-glucopyranose (*11g*) m.p. 149–150 °C from ethyl acetate–pentane, $[\alpha]_D^{25}$ −23.6° (*c* 1.1).

Anal. $C_{20}H_{19}O_7BrS$: C, H, Br, S. ^1H NMR: δ 5.66 (H1), 3.83 (H2), 5.36 (H3), 4.63 (H4), 4.83 (H5), 4.26 (H6en), 3.88 (H6ex); $J_{12}<1$ Hz, $J_{23}=1.5$, $J_{34}=1.5$, $J_{45}=2.0$, $J_{5\text{6en}}=1.0$, $J_{5\text{6ex}}=5.7$, $J_{\text{6en6ex}}=8.0$, J_{13}, J_{24}, $J_{35}\simeq 1.5$. The next fraction gave 35 % of 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-toluenesulfonyl-1,6-anhydro-β-D-altropyranose (*10g*), sirup, $[\alpha]_D^{25}$ −213° (*c* 1.0). Anal. C, H, Br, S. ^1H NMR: δ 5.63 (H1), 5.26 (H2), 4.43 (H3), 4.93 (H4, H5), 3.92 (H6en, H6ex); $J_{12}=1.5$ Hz, $J_{23}=10.3$, $J_{34}=4.0$. The major product (39 %) was, however, the hydroxy-benzoates resulting from hydrolysis of the benzoxonium ion.

*2,3-O-Benzylidene-4-*O-p-*methoxybenzoyl-1,6-anhydro-β-*D-*mannopyranose* (8h). Preparative TLC gave two products. The faster−moving (71 %) was 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-methoxybenzoyl-1,6-anhydro-β-D-mannopyranose (*9h*), m.p. 111−113 °C from ethyl acetate−pentane, $[\alpha]_D^{25}$ −215° (*c* 1.1). Anal. $C_{21}H_{19}BrO_7$: C, H, Br. ^1H NMR: δ 5.76 (H1), 5.18 (H2), 4.71 (H3), 5.53 (H4), 4.79 (H5), 4.60 (H6en), 3.96 (H6ex); $J_{12}=2.3$ Hz, $J_{23}=6.0$, J_{34}, $J_{45}\simeq 2$, $J_{5\text{6en}}\simeq 1$, $J_{5\text{6ex}}=5.7$, $J_{\text{6en6ex}}=8.1$. The slower-moving product (3 %) was 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-methoxybenzoyl-1,6-anhydro-β-D-altropyranose (*10h*) identified only through its ^1H NMR spectrum: δ 5.76 (H1), 5.51 (H2), 4.64 (H3), 5.46 (H4), 4.93 (H5), 4.07 (H6en), 3.97 (H6ex); $J_{12}=1.5$ Hz, $J_{23}=10.5$, $J_{34}=4.5$, $J_{45}=2.6$, $J_{5\text{6en}}=1.4$, $J_{5\text{6ex}}=5.4$, $J_{\text{6en6ex}}=8.5$.

*2,3-O-Benzylidene-4-*O-p-*nitrobenzoyl-1,6-anhydro-β-*D-*mannopyranose* (8i). Preparative TLC gave 24 % of 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-nitrobenzoyl-1,6-anhydro-β-D-mannopyranose (*9i*), m.p. 145−146 °C from ethyl acetate−pentane, $[\alpha]_D^{25}$ −235° (*c* 0.6). Anal. $C_{20}H_{16}BrNO_8$: C, H, Br, N. ^1H NMR: δ 5.77 (H1), 5.17 (H2), 4.74 (H3), 5.61 (H4), 4.82 (H5), 4.63 (H6en). 3.99 (H6ex); $J_{12}=2.3$ Hz, $J_{23}=6.2$, J_{34}, $J_{45}\simeq 2$, $J_{5\text{6en}}\simeq 1$, $J_{5\text{6ex}}=5.8$, $J_{\text{6en6ex}}=8.2$. The major product (44 %) was 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-nitrobenzoyl-1,6-anhydro-β-D-altropyranose (*10i*), m.p. 133−134 °C from ethyl acetate−pentane. $[\alpha]_D^{25}$ −291° (*c* 1.0). Anal. C, H, Br, N. ^1H NMR: δ 5.73 (H1), 5.46 (H2), 4.64 (H3), 5.48 (H4), 4.91 (H5), 4.08 (H6en), 3.98 (H6ex); $J_{12}=1.4$ Hz, $J_{23}=10.4$, $J_{34}=4.4$, $J_{45}=2.3$, $J_{5\text{6en}}=1.4$, $J_{5\text{6ex}}=5.2$, $J_{\text{6en6ex}}=8.6$.

3,4-O-Benzylidene-1,6-anhydro-β-D-galactopyranose (17a). The crude product was crystallized from chloroform (−20 °C) to give 42 % of 4-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-gulopyranose (*23a*), m.p. 180−187 °C. Preparative TLC of the mother liquors gave one fraction containing 24 % of 3-*O*-benzoyl-4-bromo-4-deoxy-1,6-anhydro-β-D-glucopyranose (*22a*) as well as a further 12 % of *23a*. Crystallization from a small amount of ether removed most of the *23a* present, to give a mother liquor of almost pure *22a*, identified only through its NMR spectrum: δ 5.64 (H1), 3.74 (H2), 5.48 (H3), 4.13 (H4), 4.79 (H5), 4.27 (H6en), 3.91 (H6ex); J_{12}, J_{23}, J_{34}, $J_{45}<2$ Hz, $J_{5\text{6en}}=1.1$, $J_{5\text{6ex}}=5.6$, $J_{\text{6en6ex}}=8.0$. Tosylation of this mother liquor with tosyl chloride in pyridine gave 3-*O*-benzoyl-4-bromo-4-deoxy-2-*O*-*p*-toluenesulfonyl-1,6-anhydro-β-D-glucopyranose (*22b*). Crystallization from ethyl acetate−pentane gave 18 % of *23b*, m.p. 129−131 °C, identical (NMR, mixed m.p.) with the authentic product described below.

The combined fractions of *23a* were recrystallized from ethyl acetate−pentane to give m.p. 189−190 °C (dec), $[\alpha]_D^{25}$ +118° (*c* 0.9). Anal. $C_{13}H_{13}BrO_5$: C, H, Br. ^1H NMR: δ 5.57 (H1), 4.02 (H2), 4.46 (H3), 5.54 (H4), 4.80 (H5), 4.16 (H6en), 3.87 (H6ex); $J_{12}=2.2$ Hz, $J_{23}=4.1$, $J_{34}=10.6$, $J_{45}=4.0$, $J_{5\text{6en}}\simeq 0$, $J_{5\text{6ex}}=4.9$, $J_{\text{6en6ex}}=8.4$, $J_{46\text{ex}}=1.4$.

*3,4-O-Benzylidene-2-*O-p-*toluenesulfonyl-1,6-anhydro-β-*D-*galactopyranose* (17b). Two crystallizations of the crude product from ether−pentane gave 38 % of 3-*O*-benzoyl-4-bromo-4-deoxy-2-*O*-*p*-toluenesulfonyl-1,6-anhydro-β-D-glucopyranose (*22b*), m.p. 126−129 °C. Preparative TLC of the combined mother liquors gave 17 % of recovered *17b*, and a further 13 % of *22b*, which on recrystallization from ethyl acetate−pentane gave m.p. 129−131 °C, $[\alpha]_D^{25}$ −84° (*c* 1.1). Anal. $C_{20}H_{19}BrO_7S$: C, H, Br, S. ^1H NMR: δ 5.61 (H1), 4.48 (H2), 5.34 (H3), 4.00 (H4), 4.78 (H5), 4.15 (H6en), 3.85 (H6ex); $J_{12}<1$ Hz, J_{23}, J_{34}, $J_{45}\simeq 1.5$, $J_{5\text{6en}}=1.1$, $J_{5\text{6ex}}=5.2$, $J_{\text{6en6ex}}=7.9$, J_{13}, J_{24}, $J_{35}\simeq 1.5$.

2-O-Benzoyl-3,4-O-benzylidene-1,6-anhydro-β-D-galactopyranose (17c). Preparative TLC gave 81 % of 2,4-di-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-galactopyranose (*24c*), as a sirup which was difficult to pyrify completely. Analysis, found: C 56.14, H 3.89. Calc. for $C_{20}H_{17}BrO_6$: C 55.44; H 3.96. $[\alpha]_D^{25}$ +116° (*c* 3.0). An authentic sample was prepared by benzoylation of 2-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-galactopyranose (*24f*) (see below) with benzoyl chloride in pyridine to give a pure sample of *24c*, $[\alpha]_D^{25}$ +118° (*c* 1.1). Anal. C, H, Br identical (NMR) with the product described above. ^1H NMR (benzene-d_6): δ 5.61 (H1), 5.48 (H2), 4.49 (H3), 5.31 (H4), 4.29 (H5), 4.60 (H6en), 3.36 (H6ex); $J_{12}=1.8$ Hz, $J_{23}\simeq 1$, $J_{34}=6.5$, $J_{45}=3.8$, $J_{5\text{6en}}=0$, $J_{5\text{6ex}}=5.0$, $J_{\text{6en6ex}}=7.8$, $J_{13}=1.6$.

2,3-O-Benzylidene-1,6-anhydro-β-D-gulopyranose (20f). Preparative TLC gave 68 % of 2-*O*-benzoyl-3-bromo-3-deoxy-1,6-anhydro-β-D-galactopyranose (*24f*), which slowly crystallized. Recrystallization from ethyl acetate−pentane gave m.p. 99−100 °C, $[\alpha]_D^{20}$ +78° (*c* 1.1). Anal. $C_{13}H_{13}BrO_5$: C, H, Br. ^1H NMR: δ 5.58 (H1), 5.50 (H2), 4.54 (H3), 4.18 (H4), 4.57 (H5), 4.62 (H6en), 3.70 (H6ex); $J_{34}=6.0$ Hz, $J_{45}=4.4$, $J_{5\text{6en}}\simeq 0$, $J_{5\text{6ex}}=5.1$, $J_{\text{6en6ex}}=8.0$ and in benzene-d_6 $J_{12}=1.8$, $J_{23}\simeq 1$.

*2,3-O-Benzylidene-4-*O-p-*toluenesulfonyl-1,6-anhydro-β-*D-*gulopyranose* (20g). Preparative TLC gave 58 % of 2-*O*-benzoyl-3-bromo-3-

deoxy-4-*O*-*p*-toluenesulfonyl-1,6-anhydro-β-D-galactopyranose (*24g*) in a mixture with 17 % recovered *20g*. Reflux for 1 h with 80 % acetic acid and rechromatography gave pure *24g* as a sirup, $[\alpha]_D^{20}$ +47° (*c* 1.2). Anal. $C_{20}H_{19}O_7BrS$: C, H, Br, S. ^{1}H NMR: δ 5.57 (H1), 5.43 (H2), 4.21 (H3), 4.94 (H4), 4.59 (H5), 4.70 (H6en), 3.70 (H6ex); J_{12}, $J_{23} \simeq 1.5$ Hz, $J_{34} = 6.0$, $J_{45} = 4.3$, $J_{5\text{en}} \simeq 0$, $J_{5\text{ex}} = 5.0$, $J_{\text{en,ex}} = 8.0$.

2,3-O-Benzylidene-4-O-p-methoxybenzoyl-1,6-anhydro-β-D-gulopyranose (20h). Preparative TLC gave 69 % of 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-methoxybenzoyl-1,6-anhydro-β-D-galactopyranose (*24h*), m.p. 108–110 °C from ethyl acetate–pentane, $[\alpha]_D^{20}$ +138° (*c* 1.1). Anal. $C_{21}H_{19}BrO_7$: C, H, Br. ^{1}H NMR: δ 5.67 (H1), 5.56 (H2), 4.68 (H3), 5.41 (H4), 4.74 (H5), 4.81 (H6en), 3.82 (H6ex); J_{12}, $J_{23} \simeq 1.5$ Hz, $J_{34} = 6.0$, $J_{45} = 4.5$, $J_{5\text{en}} \simeq 0$, $J_{5\text{ex}} = 4.8$, $J_{\text{en,ex}} = 8.0$. A slower-moving minor product (5 %) was 2-*O*-benzoyl-4-bromo-4-deoxy-3-*O*-*p*-methoxybenzoyl-1,6-anhydro-β-D-glucopyranose (*22h*) identified only through its ^{1}H NMR spectrum: δ 5.76 (H1), 5.07 (H2), 5.52 (H3), 4.17 (H4), 4.85 (H5), 4.27 (H6en), 3.94 (H6ex); J_{12}, J_{23}, J_{34}, $J_{45} < 2$ Hz, $J_{5\text{en}} \simeq 1$, $J_{5\text{ex}} = 5.5$, $J_{\text{en,ex}} = 7.9$.

2,3-O-Benzylidene-4-O-p-nitrobenzoyl-1,6-anhydro-β-D-gulopyranose (20i). The crude product was crystallized from ethyl acetate–pentane to give 47 % of 2-*O*-benzoyl-3-bromo-3-deoxy-4-*O*-*p*-nitrobenzoyl-1,6-anhydro-β-D-galactopyranose (*24i*), m.p. 188–191 °C. Preparative TLC of the mother liquors gave a further 17 % of *24i*. Recrystallization from ethyl acetate–pentane gave m.p. 191–193 °C, $[\alpha]_D^{25}$ +125° (*c* 0.9). Anal. $C_{20}H_{16}BrNO_8$: C, H, Br, N. ^{1}H NMR: δ 5.68 (H1), 5.55 (H2), 4.73 (H3), 5.46 (H4), 4.78 (H5), 4.82 (H6en), 3.86 (H6ex); J_{12}, $J_{23} \simeq 1.5$ Hz, $J_{34} = 6.0$, $J_{45} = 4.5$, $J_{5\text{en}} \simeq 0$, $J_{5\text{ex}} = 5.0$, $J_{\text{en,ex}} = 7.9$.

Reaction of epoxides with hydrogen bromide

3-O-Benzoyl-4-bromo-4-deoxy-2-O-p-toluenesulfonyl-1,6-anhydro-β-D-glucopyranose (22b). 2-*O*-*p*-toluenesulfonyl-1,6:3,4-dianhydro-β-D-galactopyranose[19] (*21*) (600 mg) in methylene chloride (5 ml) was treated with 25 ml 0.6 M solution of hydrogen bromide in benzene for 15 min. Addition of water and extraction with chloroform yielded a crude bromo-hydrin, which on benzoylation with benzoyl chloride in pyridine yielded 724 mg (75 %) of *22b*, m.p. 132–133 °C from ethyl acetate–pentane, identical (NMR, mixed m.p.) with the products described above.

3-O-Benzoyl-2-bromo-2-deoxy-4-O-p-toluenesulfonyl-1,6-anhydro-β-D-glucopyranose (11g). Following the same procedure 4-*O*-*p*-toluenesulfonyl-1,6:2,3-dianhydro-β-D-mannopyranose[20] (*12*) (600 mg) gave 463 mg (47 %) of *11g* after two recrystallizations from ethyl acetate–pentane, m.p. 149–150 °C, identical (NMR, mixed m.p.) with the product described above.

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