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STUDIES ON THE REACTION WITH *N*-BROMOSUCCINIMIDE OF FIXED 2-PHENYL-1,3-DIOXOLANE SYSTEMS IN METHYL DI-*O*-BENZYLIDENE-α-D-HEXOPYRANOSIDES

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ABSTRACT

The reaction of methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside (**5**) with *N*-bromosuccinimide gave mainly three, isomeric dibromo dibenzoates, identified as the 3,6-dibromo-*altro* (**1**), 3,6-dibromo-*manno* (**2**), and 4,6-dibromo-*ido* (**3**) derivatives by subsequent chemical transformation and by extended n.m.r.-spectral studies. The reaction of methyl 2,3:4,6-di-*O*-benzylidene-α-D-allopyranoside (**22**) with *N*-bromosuccinimide gave two isomeric dibromo dibenzoates, the 2,6-dibromo-*altro* (**23**) and 3,6-dibromo-*gluco* (**24**) products, and their structures were similarly assigned. A similar reaction-sequence with methyl 2,3:4,6-di-*O*-benzylidene-α-D-glucopyranoside (**32**), however, yielded two isomeric monobenzoates **33** and **34**, which could be identified straightforwardly. The results are consistent with the intermediate formation of benzoxonium ions that undergo favored axial attack. Thus the observed products and their ratios in reactions of **5** and of **22** with *N*-bromosuccinimide are explicable. Compound **32**, however, does not appear to react by way of an intermediate, five-membered 2,3-*trans* benzoxonium ion.

INTRODUCTION

In connection with synthetic approaches towards deoxygenated disaccharides, we were interested in applying the Hanessian–Hullar reaction[1] to several di-*O*-benzylidene disaccharide derivatives carrying the benzylidene acetal groups exclusively on secondary positions. Preliminary experiments gave confusing results, and it seemed necessary and of interest to perform initial studies on various sterically fixed, alkyl di-*O*-benzylidenehexopyranosides.

There is ample information on the opening of 1,3-dioxane systems in hexopyranose derivatives[2], but very little on the opening of 1,3-dioxolane systems, and this only in furanose derivatives[3]. However, there has been one report on the reaction with *N*-bromosuccinimide in a sterically fixed, six-membered ring-system, namely, in methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside[4] (**5**).

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Because of the unclear results obtained with the more-complicated disaccharide derivatives, we decided to reexamine the reported reaction, and have observed quite different products. Consequently, extension of these studies to analogous di-*O*-benzylidenehexopyranosides was the next step. Similar reports on a reexamination of the reaction of **5** with *N*-bromosuccinimide came to our knowledge recently[5].

RESULTS AND DISCUSSION

Treatment of methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside[6] (**5**) with *N*-bromosuccinimide in carbon tetrachloride in the presence of barium carbonate gave a mixture of four compounds. One (a minor byproduct) could be separated by column chromatography, whereas the other three gave one spot on t.l.c. in various solvent-systems. Analysis of the mixture indicated that all of the compounds contained two bromine atoms, as expected for the opening of a dibenzylidene acetal. N.m.r. spectroscopy (270 MHz) of the mixture showed three signals, at δ 3.65, 3.66, and 3.71, for the methoxyl groups, in the ratios 5:7:10. After treatment of the mixture with sodium methoxide at room temperature, a two-fold column-chromatographic separation allowed isolation of the three, deacylated compounds, one of which proved to be methyl 2,3-anhydro-6-bromo-6-deoxy-α-D-mannopyranoside (**6**). N.m.r. spectroscopy of its acetate (**7**) and the corresponding benzoate (**8**), prepared by reaction with *N*-bromosuccinimide of the readily available methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside[8] (**14**), showed characteristic couplings[7] of epoxy-group protons H-2 and H-3 ($J_{2,3}$ 3.25 Hz), a broad singlet for H-1 ($J_{1,2} < 0.3$ Hz), and a broad doublet for H-4 with $J_{3,4} < 0.3$ and $J_{4,5}$ 10.0 Hz.

The second product, obtained in minor amount, was methyl 3,6-dibromo-3,6-dideoxy-α-D-mannopyranoside (**9**); it was identified by n.m.r. spectroscopy of its 2,4-diacetate **10**. The chemical shift of H-3 bearing a secondary bromine atom, could be assigned by INDOR experiments, and the coupling values ($J_{1,2}$ 1.7, $J_{2,3}$ 3.2, and $J_{3,4} = J_{4,5} = 10.0$ Hz) are fully in agreement with the *manno* configuration.

The third product turned out to be methyl 3,4-anhydro-6-bromo-6-deoxy-α-D-altropyranoside (**11**), identified by n.m.r. spectroscopy of its 2-acetate **12**. The H-1 and H-2 resonances appeared as singlets, because of their small coupling ($J_{1,2} \approx J_{2,3} < 0.3$ Hz), and again there was a small coupling[7] ($J_{3,4}$ 3.3 Hz) between the epoxy-group protons. These n.m.r. data agree with the $^1H_0$ (D) conformation of **12**, which is expected to be favored, because of the bulky equatorial bromomethyl group.

These products **6**, **9**, and **11** provide evidence for their corresponding precursors, the isomeric dibromides obtained from **5**. Obviously, the reaction with molar amounts of sodium methoxide at room temperature causes, in addition to the expected trans-esterification of the benzoate groups, the loss of a bromine atom from two of the compounds, but not from the third one. It is well known[10], that *trans*-diaxial dispositions of leaving group and alkoxy anion lead to epoxide formation at room temperature, whereas a *trans*-diequatorial arrangement normally requires elevated temperatures for reaction. Consequently, the *altro* derivative **1** should be the pre-

cursor of the *manno*-2,3-epoxide **6**, and the *ido* derivative **3** that of the *altro*-3,4-epoxide **11**, whereas the *manno* isomer **2**, having the *trans*-diequatorial arrangement of Br-3 and the benzoate groups at C-2 and C-4, should merely yield the transesterification product **9**.

It may be supposed that compounds **6** and **11** are interconvertible by an epoxide rearrangement under these alkaline conditions. Rearrangements of this type have been shown[18] to occur between the *manno*-2,3-epoxide–*altro*-3,4-epoxide pairs **15** ⇄ **18**, **16** ⇄ **19** (ref. 12), and **17** ⇄ **20** (ref. 12). Similarly, the equilibrium between **6** and **11** could be shown to lie far (90%) on the side of the *manno*-epoxide **6**, in accord with results for analogous compounds[11, 12]. The rearrangement of **11** with sodium methoxide, monitored by n.m.r. spectroscopy, indicated that, after ~45 min, 50% of **11** is detectable in the mixture, corresponding to an actual ratio between **6** and **11** of ~1:1. The ratio of the products **1** and **3** was about 7:10; with the presumption of a fast reaction of **1** to **6**, and of **3** to **11**, and the observed equilibrium ratio between **6** and **11** after 45 min, the final ratio should be ≃12:5, which is in overall accord with the experimental ratio of 2:1 obtained.

Treatment of **5** with trityl tetrafluoroborate and subsequent addition of tetraethylammonium bromide yields methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-bromo-3-deoxy-α-D-altropyranoside[13] (**13**).

By treatment of **13*** with *N*-bromosuccinimide, the 3,6-dibromo *altro* derivative **1** could be prepared; its n.m.r. spectrum is readily interpreted and is in accordance with data for similar compounds[5]. The signals for **1** could also be assigned in the spectrum of the mixture of **1** + **2** + **3**. In addition to the three main products, a small proportion (2% of the total amount of **1** + **2** + **3**) of methyl 2,4-di-*O*-benzoyl-6-bromo-6-deoxy-α-D-mannopyranoside (**4**) was detected as a by-product. The configuration of **4** could be assigned unequivocally by n.m.r. spectroscopy. The six-line signal at δ 4.36 may be attributed to H-3, because exchange of the HO-3 group with CD_3OD eliminated the coupling $J_{3,OH}$ 9.0 Hz.

In view of these results, former reports[4] claiming the epimeric methyl 3,4-di-*O*-benzoyl-2,6-dibromo-2,6-dideoxy-α-D-gluco- and -mannopyranosides as products before reduction to the dideoxy analogs should be corrected.

As with compound **5** methyl 2,3:4,6-di-*O*-benzylidene-α-D-allopyranoside (**22**) possesses a *cis*-1,3-dioxolane benzylidene acetal group. Methyl 4,6-*O*-benzylidene-α-D-allopyranoside[14] (**21**) could be prepared readily from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside by a selective benzoylation[15] at O-2, oxidation[16] at C-3 with dimethyl sulfoxide–P_4O_{10}, and reduction with sodium borohydride, followed by treatment with sodium methoxide[14]. In contrast to the ready formation of **5**, reaction of **21** with benzaldehyde–zinc chloride did not yield **22**, whereas treatment with α,α-dichlorotoluene in pyridine[17] gave **22** in 55% yield. T.l.c. showed that methyl α-D-allopyranoside (**25**) does not give **22** with benzaldehyde–zinc chloride, and with α,α-dichlorotoluene in pyridine the desired compound **22** was obtained in approxi-

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mately 10% yield, presumably because of the simultaneous formation of methyl 3,4-*O*-benzylidene-α-D-allopyranoside. The structure of **22** was assigned straightforwardly from its n.m.r. spectrum (see Tables I and II).

On treatment of **22** with *N*-bromosuccinimide, a mixture of two compounds was obtained (60%), showing signals of the methoxyl groups at δ 3.55 and 3.49 p.p.m. in the ratio of 10:17. The n.m.r. spectrum (270 MHz) of the mixture indicated a mixture of methyl 3,4-di-*O*-benzoyl-2,6-dibromo-2,6-dideoxy-α-D-altropyranoside (**23**) and methyl 2,4-di-*O*-benzoyl-3,6-dibromo-3,6-dideoxy-α-D-glucopyranoside (**24**).

Compound **23** shows mainly small couplings, except in the H-4 quadruplet at δ 5.75 resulting from a *trans*-diaxial coupling of 9.6 Hz and a smaller one of 3.4 Hz. Furthermore, the downfield location (δ 5.79) of the H-3 triplet demonstrates the presence of the benzoate group at C-3. The H-2 signal appears at higher field (δ 4.32) as a quadruplet showing small couplings $J_{1,2}$ 1.2 and $J_{2,3}$ 3.4 Hz.

In contrast, the other isomer (**24**) should have the *gluco* configuration, which is in accordance with large couplings (10–11 Hz) of the *trans*-diaxial protons at C-2,3,4, and 5, and the smaller $J_{1,2}$ value of 3.5 Hz. Because of the attached benzoate groups, H-2 and H-4 resonate further downfield whereas H-3 resonates upfield (δ 4.66) because of the bromine substituent.

Analysis of the mixture supports the formation of two, isomeric dibromo dibenzoates. Separation by crystallization or chromatography was not feasible and thus further chemical proofs were necessary.

Treatment of the mixture with ammonia in methanol (4 days, 20°) gave two compounds, **27** and **29**, which could be separated by column chromatography. Compound **29** proved to be the dibromide resulting from simple debenzoylation of the *gluco* compound **24**. After acetylation to the 2,4-diacetate **30** an n.m.r. spectrum similar to that of **24** was obtained. The other product gave an analysis in accord with formulation as the monobromo anhydride **27**. Methyl 2,3-anhydro-6-bromo-6-deoxy-α-D-allopyranoside (**27**) could be identified by reference to authentic **27** prepared [9,18] from the disulfonate **26**. N.m.r. and other physical data were fully in agreement with this assignment.

The formation of **27** from **23** corresponds to the ready formation of an epoxide[10], whereas **24** merely undergoes transterification under these mild conditions. In agreement with expectation, treatment of **24** with sodium methoxide under reflux gave the same anhydride **27**.

In view of the foregoing results, it was of interest to study the reaction with methyl 2,3:4,6-di-*O*-benzylidene-α-D-glucopyranoside (**32**), in which the 1,3-dioxolane ring is fused *trans*-diequatorially. Compound **32** has been prepared before[19] in 15% yield, after separation from methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**35**). We improved the yield of **32** to 32% by application of the α,α-dichlorotoluene–pyridine method[17] to **36**, and purification by column filtration over alkali-treated silica gel.

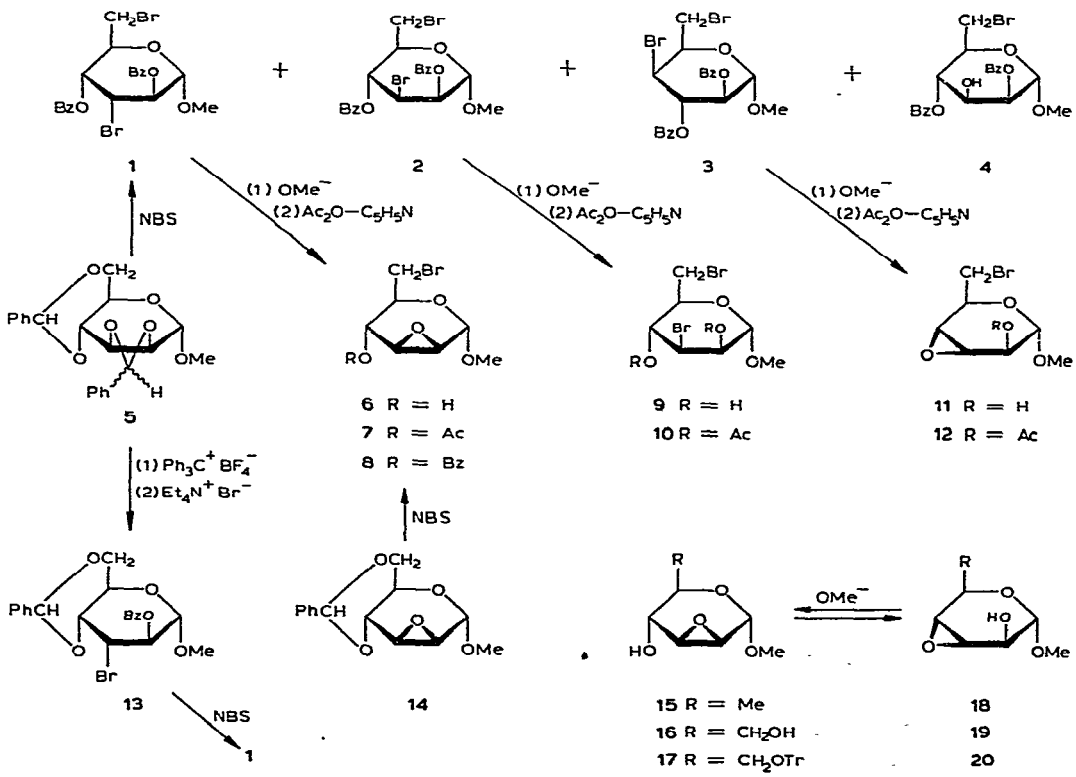
Compound **32** was obtained in much lower yield from methyl α-D-glucopyranoside. As might be expected, compound **32** is obtained as an ~2:1 mixture of the *endo*

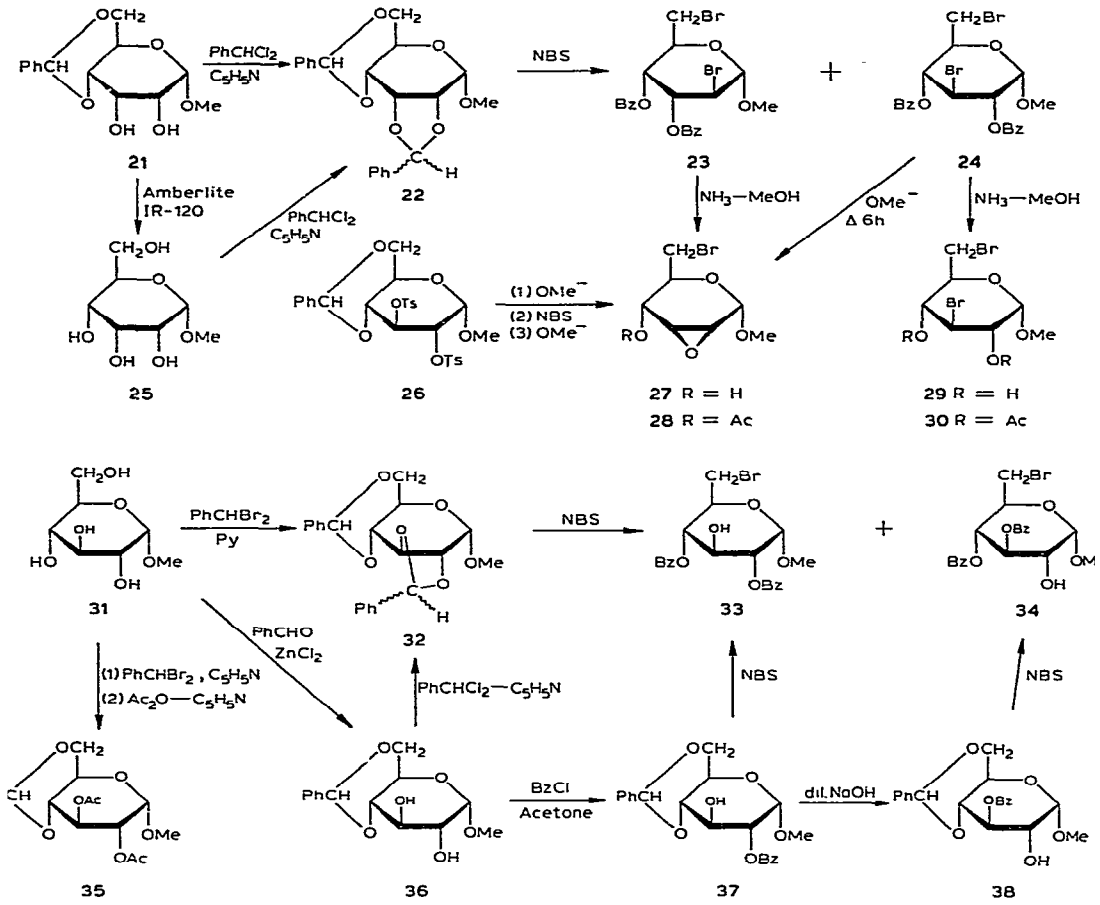
(or *exo*) and *exo* (or *endo*) isomers. The n.m.r. spectrum (270 MHz) shows four signals for the methine protons in the 1,3-dioxane ring (δ 6.11 and 6.13) and the 1,3-dioxolane ring (δ 6.14 and 6.16), as well as two doublets for H-1 (δ 5.12 and 5.23, $J_{1,2}$ 3.5 Hz).

Reaction of **32** with *N*-bromosuccinimide gave mainly two products, in 1:1 ratio. Separation by chromatography gave the pure compounds, both of which, surprisingly, gave analyses consistent with monobromo dibenzoates having one free hydroxyl group. Identification was readily achieved by n.m.r. spectroscopy and by preparation of the compounds by different routes.

Thus, the reaction of **37** (ref. 16) with *N*-bromosuccinimide gave **33**, a compound identical in all respects with one of the reaction products from **32**. Rearrangement of **37** gave[20] the isomeric 3-benzoate **38**, which yielded **34** on treatment with *N*-bromosuccinimide and this compound was identical with the other product of the reaction of **32** with *N*-bromosuccinimide. The n.m.r. spectra of **33** and **34** were in agreement with formulation as the *gluco* derivatives methyl 2,4-di-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**33**) and methyl 3,4-di-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**34**).

Concerning the *manno* (Scheme 1) and the *allo* derivatives (Scheme 2), the results of the foregoing reaction may be rationalized and interpreted readily following





Hanessian and Plessos's[2,3] original suggestion of a "radical hydrogen-abstraction step followed by ionic termination".

However, for the *gluco* derivative (Scheme 3) the formation of products cannot be interpreted according to the reactions observed for its isomers, and conclusive evidence of a possible intermediate, 2,3-*trans* benzoxonium-ion cannot yet be offered.

EXPERIMENTAL

General methods. — Reactions were monitored by t.l.c. on silica gel 60 F_{254} (Merck) in A, 9:1 chloroform–ether; B, 3:1 petroleum ether (b.p. 60–70)–ethyl acetate; C, 4:1 toluene–ethanol; D, ether. Column chromatography was performed on silica gel 60 (Merck) with the foregoing eluents. Detection was by sulfuric acid, u.v. illumination, and 0.2% 1,2-naphthalenediol in 1:1 ethanol–M sulfuric acid. Melting points were taken on a Kofler hot-stage microscope and are uncorrected. Optical rotations were measured in 1-dm cells with Perkin–Elmer 141 and 241

TABLE I

CHEMICAL SHIFTS (δ, p.p.m.) IN $CDCl_3$ AT 270 MHZ

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*OMe*	*OAc*	*OBz*	*OH*
1	4.91s	5.45d	4.75dd	5.34dd	4.56m	3.6 –3.9m		3.66s		7.40–8.15m	
4	4.97d	5.40dd	4.36dt	5.48t	4.16m	3.42–3.69m		3.47s		7.19–7.71m	2.34d
7	4.93s	3.21d	3.10d	4.78d	3.89m	3.46dd	3.32dd	3.55s	2.13s		
8	5.00s	3.35d	3.16d	5.05d	4.07m	3.53dd	3.38dd	3.60s		7.40–8.30m	
10[a]	4.72d	5.20dd	4.42dd	5.22t	3.94m	3.30–3.60m		3.46s	2.14s 2.18s		
12	4.59s	4.98s	3.32d	3.28d	4.29t	3.56–3.69m		3.41s	2.15s		
22[b]	4.89d	4.48–4.58m		3.82dd	4.27dt	3.74t	4.40dd	3.49s			
23	5.05d	4.32dd	5.79t	5.75dd	4.10m	3.41–3.70m		3.55s		7.26–8.29m	
24	5.13d	5.29dd	4.66dd	5.41t	4.10m	3.41–3.70m		3.49s		7.26–8.29m	
27[c]	4.35d	2.85dd	2.77dd	3.30t	3.68m	3.36dd	2.56dd	3.21s			
28	4.96d	3.56dd	3.59dd	5.02dd	4.08m	3.53dd	3.39dd	3.53s	2.08s		
30	4.89d	5.03dd	4.27dd	5.08t	3.92m	3.44dd	3.36dd	3.40s	2.13s		
33	5.13d	5.09dd	4.41dt	5.19dd	4.16m	3.40–3.63m		3.49s		7.33–8.15m	2.63d
34[d]	4.93d	3.90dd	5.73t	5.36t	4.19m	3.20–3.65m		3.54s		7.15–8.15m	

[a]At 90 MHz. [b]PhC*H* (2.3) 6.32s; PhC*H* (4.6) 5.58s; C_6H_5 7.0–7.7m. [c]In C_6D_6 + D_2O. [d]At 90 MHz in $CDCl_3$ + D_2O.

TABLE II

COUPLING CONSTANTS (Hz)

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
1	<0.3	3.6	4.0	8.8			
4[a]	1.6	3.4	9.4	9.4			
7	<0.3	3.25	<0.3	10.0	2.5	8.0	11.0
8	<0.3	3.25	<0.3	10.0	2.25	8.5	11.3
10	1.7	3.2	10.0	10.0			
12	<0.3	<0.3	3.3	<0.3	5.50		
22	5.0		3.1	9.8	5.1	10.0	10.0
23	1.2	3.4	3.4	9.6			
24	3.5	11.0	10.0	10.0			
27	3.0	4.0	1.4	9.0	1.0	7.0	11.0
28	2.8	4.2	1.6	9.6	2.5	6.8	11.0
30	3.4	11.0	10.4	10.4	3.5	7.8	11.2
33[b]	3.6	9.5	9.4	9.8			
34	4.0	9.3	9.3	9.3			

[a]$J_{3,OH}$ 9.0 Hz. [b]$J_{3,OH}$ 5.7 Hz.

polarimeters; n.m.r. spectra were recorded with Varian T-60 (60 MHz), Perkin–Elmer R 32 (90 MHz), and Bruker WH 270 (270 MHz) instruments in various solvents, with Me_4Si as the internal standard.

*Methyl 2,4-di-*O*-benzoyl-3,6-dibromo-3,6-dideoxy-α-*D*-altropyranoside* (**1**). —

A. Compound **13** (ref. 13) (352 mg, 1.0 mmol) was boiled under reflux for 1 h with *N*-bromosuccinimide (250 mg, 1.4 mmol) and barium carbonate (1 g) in carbon tetrachloride (20 ml), with stirring. After cooling, the mixture was filtered and the filter washed with carbon tetrachloride. The filtrate was washed twice with aqueous sodium hydrogensulfite, twice with aqueous sodium hydrogencarbonate, and then dried (sodium sulfate) and evaporated *in vacuo* (standard isolation conditions). Chromatography on silica gel with solvent *B* gave **1** (120 mg, 23%).

B. Compound **13** (ref. 13) (352 mg, 1.0 mmol) was boiled under reflux with *N*-bromosuccinimide (250 mg, 1.4 mmol) and benzoyl peroxide (3 mg) in benzene (20 ml) for 45 min. Standard isolation followed by chromatography on silica gel with solvent *B* gave **1** (160 mg, 32%), $[\alpha]_D^{20}$ −25.0° (*c* 0.8, chloroform).

Anal. Calc. for $C_{21}H_{20}Br_2O_6$: C, 47.75; H, 3.82; Br, 30.26. Found: C, 47.66; H, 3.73; Br, 31.25.

*Reaction of methyl 2,3:4,6-di-*O*-benzylidene-α-*D*-mannopyranoside* (**5**) *with* N*-bromosuccinimide.* — A suspension of **5** (4.3 g, 11.6 mmol), *N*-bromosuccinimide (4.6 g, 25.9 mmol), and barium carbonate (4.7 g) in carbon tetrachloride (150 ml) was boiled under reflux for 45 min. Standard isolation gave a crude mixture (5.8 g) that was chromatographed on silica gel with eluent *B*. The first fraction afforded a stiff syrup (a mixture of **1**, **2**, and **3**; yield 2.5 g, 37%).

Anal. Calc. for $C_{21}H_{20}Br_2O_6$: C, 47.75; H, 3.82; Br. 30.26. Found: C, 47.34; H, 3.83; Br, 30.92.

The second fraction, compound **4** (50 mg), was obtained as a colorless syrup.

Anal. Calc. for: $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55; Br, 17.18. Found: C, 54.50; H, 4.60; Br, 17.40.

*Methyl 2,3-anhydro-6-bromo-6-deoxy-α-*D*-mannopyranoside* (**6**) *and methyl 3,4-anhydro-6-bromo-6-deoxy-α-*D*-altropyranoside* (**11**). — The foregoing mixture of **1**, **2**, and **3** (1.0 g, 1.9 mmol) was stirred with sodium methoxide (30 ml, 0.2M) for 45 min at room temperature, and then made neutral with Dry Ice. The solution was evaporated, the residue was taken up in ether, and the solution was washed with water. The crude product (330 mg) was chromatographed on silica gel with eluent *B* to give a mixture of **6** + **9** (130 mg) as the first fraction (see earlier).

The second fraction contained pure, syrupy **6** (90 mg), $[\alpha]_D^{20}$ +99.3° (*c* 6.0, methanol).

Anal. Calc. for $C_7H_{11}BrO_4$: C, 35.17; H, 4.64; Br, 33.43. Found: C, 35.92; H, 4.66; Br, 34.10.

The third fraction afforded pure, syrupy **11** (50 mg), $[\alpha]_D^{20}$ +69.4° (*c* 0.8, methanol).

Anal. Calc. for $C_7H_{11}BrO_4$: C, 35.17; H, 4.64; Br, 33.43. Found: C, 35.95; H, 4.69; Br, 34.23.

Rearrangement of **11** *to* **9**. — The rearrangement of **11** (5% solution in 0.2M $NaOCD_3$) was monitored by n.m.r. spectroscopy (90 MHz).

t (*min*)	0	15	35	52	75	105	150	220
11(%)	100	80	60	47	40	25	23	13

Methyl 4-O-acetyl-2,3-anhydro-6-bromo-6-deoxy-α-D-mannopyranoside (**7**). — Compound **6** (40 mg, 0.17 mmol) was acetylated, and the product isolated by standard procedures to give **7** (35 mg, 73%), $[\alpha]_D^{20}$ +48.2° (*c* 0.8, chloroform).

Anal. Calc. for $C_9H_{13}BrO_5$: C, 38.45; H, 4.66; Br, 28.43. Found: C, 38.70; H, 4.70; Br, 28.60.

Methyl 2,3-anhydro-4-O-benzoyl-6-bromo-6-deoxy-α-D-mannopyranoside (**8**). — Epoxide **14** (264 mg, 1.0 mmol) in carbon tetrachloride (15 ml) was treated with *N*-bromosuccinimide (212 mg, 1.2 mmol) in the presence of barium carbonate (300 mg) with vigorous stirring for 40 min at reflux. Standard isolation gave the crude product, which was chromatographed on silica gel with eluent *B*; yield of **8** (100 mg, 29%), $[\alpha]_D^{20}$ +120° (*c* 2.8, dichloromethane).

Anal. Calc. for $C_{14}H_{15}BrO_5$: C, 49.00; H, 4.11; Br, 23.29. Found: C, 49.35; H, 4.12; Br, 24.10.

Methyl 2,4-di-O-acetyl-3,6-dibromo-3,6-dideoxy-α-D-mannopyranoside (**10**). — The first fraction (130 mg) from the isolation of **6**, **9**, and **11** was acetylated and processed by routine methods. The colorless oil (150 mg) was chromatographed on silica gel with eluent *B*. The first fraction (**10**, 16 mg, 77%) had $[\alpha]_D^{20}$ +28.6° (*c* 1.2, chloroform).

Anal. Calc. for $C_{21}H_{16}Br_2O_6$: C, 37.70; H, 3.99; Br, 39.56. Found: C, 37.81; H, 4.06; Br, 40.05.

The second fraction (**7**) weighed 110 mg (77%).

Methyl 2-O-acetyl-3,4-anhydro-6-bromo-6-deoxy-α-D-altropyranoside (**12**). — Epoxide **11** (50 mg, 0.21 mmol) was acetylated and the product processed by standard methods. Compound **12** (40 mg, 68%) was recrystallized from ether–hexane, m.p. 71–72°, $[\alpha]_D^{20}$ +56.1° (*c* 0.6, chloroform).

Anal. Calc. for $C_9H_{13}BrO_5$: C, 38.45; H, 4.66; Br, 28.43. Found: C, 39.01; H, 4.78; Br, 29.64.

Methyl 2,3:4,6-di-O-benzylidene-α-D-allopyranoside (**22**). — Compound **21** (2.4 g, 8.5 mmol) dissolved in dry pyridine (125 ml) was treated with α,α-dichlorotoluene (5 ml, 40 mmol) with stirring for 6 h at reflux. The deep-red suspension was filtered, the residue washed with toluene, and the solution evaporated to a solid red mass, which was dissolved in chloroform and filtered through silica gel with solvent *A*. Evaporation of the effluent gave yellow crystals, which were recrystallized from dichloromethane–ether to give **22** (1.7 g, 54%) as colorless needles, m.p. 176–179°, $[\alpha]_D^{20}$ +101° (*c* 1.0, chloroform).

Anal. Calc. for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 68.20; H, 6.01.

Reaction of methyl 2,3:4,6-di-O-benzylidene-α-D-allopyranoside (**22**) *with N-bromosuccinimide.* — Compound **22** (1.8 g, 4.86 mmol) in carbon tetrachloride (100 ml) was refluxed with *N*-bromosuccinimide (1.92 g, 10.8 mmol) and barium carbonate (2 g) for 1 h. Standard isolation gave the crude product (2.5 g), which was chromatographed on silica gel with eluent *B*; yield of a mixture of compound **23** and **24** 1.44 g (60%).

Anal. Calc. for $C_{21}H_{20}Br_2O_6$: C, 47.75; H, 3.82; Br, 30.26. Found: C, 47.76; H, 3.81; Br, 30.27.

Methyl 2,3-anhydro-6-bromo-6-deoxy-α-D-allopyranoside (**27**) *and methyl 3,6-dibromo-3,6-dideoxy-α-D-glucopyranoside* (**29**). — The foregoing mixture (800 mg, 1.52 mmol) was treated with ammonia-saturated methanol (35 ml) for 4 days at 0°. Evaporation gave a syrup that was chromatographed on silica gel with eluent D. The first fraction (**29**, 50 mg, 10%) had m.p. 83.5–85°, $[\alpha]_D^{20}$ +103.2° (*c* 0.67, chloroform).

Anal. Calc. for $C_7H_{12}Br_2O_4$: C, 26.27; H, 3.78; Br, 49.95. Found: C, 26.42; H, 3.81; Br, 49.19.

The second fraction (**27**, 90 mg, 38%) had m.p. 89–91°, $[\alpha]_D^{20}$ +106.9° (*c* 0.79, chloroform).

Anal. Calc. for $C_7H_{11}BrO_4$: C, 35.17; H, 4.64; Br, 33.43. Found: C, 35.73; H, 4.73; Br, 33.08.

Methyl 2,4-di-O-acetyl-3,6-dibromo-3,6-dideoxy-α-D-glucopyranoside (**30**). — Conventional acetylation of **29** (50 mg, 0.16 mmol) gave **30** (45 mg, 71%), $[\alpha]_D^{20}$ +81.0° (*c* 0.2, chloroform).

Anal. Calc. for $C_{11}H_{16}Br_2O_6$: C, 37.70; H, 3.99; Br, 39.56. Found: C, 37.91; H, 4.07; Br, 40.01.

Methyl 2,3:4,6-di-O-benzylidene-α-D-glucopyranoside (**32**). — Compound **36** (10 g, 35.4 mmol), dissolved in dry pyridine (300 ml), was refluxed with α,α-dichlorotoluene (22 ml, 177.2 mmol) for 17 h. The mixture was filtered, the filter washed with toluene, and the filtrate evaporated. The red, solid residue was dissolved in chloroform and filtered through silica gel (160 g) with solvent *A* +3% triethylamine. Evaporation of the effluent and recrystallization from chloroform–ether–petroleum ether (b.p. 60–70) gave pure **32**; yield: 4.3 g (33%) (lit.[19] 10%), m.p. 168–174° (lit.[19] 157–161°), $[\alpha]_D^{20}$ +71.6° (*c* 12.0, chloroform), (lit.[19], $[\alpha]_D^{20}$ +55° (*c* 0.3, chloroform)).

Anal. Calc. for $C_{21}H_{22}O_6$: C, 68,10; H, 5.99. Found: C, 68.08, H, 6.01.

Reaction of methyl 2,3:4,6-di-O-benzylidene-α-D-glucopyranoside (**32**) *with N-bromosuccinimide.* — Compound **32** (1.0 g, 2.7 mmol) was treated with *N*-bromosuccinimide (1.1 g, 6.2 mmol) in the presence of barium carbonate (1.2 g) in carbon tetrachloride (100 ml) for 1.5 h under reflux. Standard isolation and subsequent separation by column chromatography with eluent *A* gave, as the first fraction, compound **33** (140 mg, 22%), m.p. 132–133°, $[\alpha]_D^{20}$ +78.5° (*c* 0.4, methanol).

Anal. Calc. for $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55; Br, 17.18. Found: C, 55.03; H, 4.71; Br, 17.40.

The second fraction (**34**, 140 mg, 22%) had $[\alpha]_D^{20}$ +34.4° (*c* 1.0, methanol).

Anal. Calc. for $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55; Br, 17.18. Found: C, 54.22; H, 4.60; Br, 17.40.

Methyl 2,4-di-O-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**33**). — A mixture of **37** (240 mg, 0.62 mmol), *N*-bromosuccinimide (130 mg, 0.73 mmol), and barium carbonate (190 mg) in carbon tetrachloride (10 ml) was refluxed for 1 h. Subsequent, standard isolation gave a crude product, which was resolved by prepara-

tive t.l.c. with eluent *A* to give **33** (72 mg, 25%); crystallized from ether–hexane, m.p. 132–134°, $[\alpha]_D^{20}$ +77.5° (*c*, 0.4, methanol).

Anal. Calc. for $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55; Br, 17.18. Found: C, 54.40; H, 4.64; Br, 17.36.

Methyl 3,4-di-O-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**34**). — A mixture of **38** (180 mg, 0.46 mmol), *N*-bromosuccinimide (100 mg, 0.56 mmol), and barium carbonate (140 mg) in carbon tetrachloride (10 ml) was refluxed for 1 h. Isolation and separation were performed as before; yield, 85 mg (39%); $[\alpha]_D^{20}$ +32.8° (*c* 0.4, methanol).

Anal. Calc. for $C_{21}H_{21}BrO_7$: C, 54.21; H, 4.55; Br, 17.18. Found: C, 54.34; H, 4.66; Br, 17.37.

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