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TETRA-*O*-BENZOYL-2-HALOHEXOPYRANOSYL HALIDES: PREPARATION, ASSIGNMENT OF CONFIGURATION, AND HYDROLYSIS TO ENOLONES*

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ABSTRACT

Addition of bromine to 1,5-anhydro-tetra-*O*-benzoylhex-1-enitol **1** in tetrachloromethane yields 2-bromohexosyl bromide derivatives having the *β*-D-*gluco* (**2**), α-D-*manno* (**3**), and α-D-*gluco* configurations (**4**) in 6:3:1 ratios, *i.e.*, *cis*-addition preponderates. Chlorination of **1** exclusively affords *cis*-adducts **5** and **6**, their proportion varying with the solvent (~4:1 in toluene and ~2:1 in tetrachloromethane). Evidence for the structure and configuration of these dihalides is presented, and the stereochemistry at C-2 in the α-D-*manno* dichloride **6** is proved by X-ray crystal structure analysis. The configurations of the *manno* isomers **3** and **6** were determined from chiroptical properties. The *β*-D-*gluco*-dibromide **2** is hydrolyzed to the tetra-*O*-benzoyl-α-D-hexosulose **10** on contact with silica gel, but the α-D-*manno* isomer **3** requires silver nitrate–acetone for conversion into the respective *β*-hexosulose **11**, and the α-D-*gluco*-dibromide is hydrolyzed only with boiling silver perchlorate–acetone.

INTRODUCTION

The halogenation of glycal esters was investigated by E. Fischer[2] and, as a result of recent interest[3–7] in this synthetically useful reaction, the steric and stereoelectronic factors are now understood[8]. The halogenation of 2-hydroxyglycal esters was studied by Maurer[9–13] and the addition products, only occasionally obtained in crystalline form[10,12–14], were mainly used for the preparation of various ulose and kojic acid derivatives. Information on the steric course of the halogen addition to 2-hydroxyglycal esters followed[15,16] from the isolation and configurational assignment of two 1,2-dichlorides after chlorination of the 2-hydroxyglycal tetrabenzoate **1**. However, due to the presence of a tertiary carbon atom in the products, absolute proof of configuration was not obtained. Such proof, *inter alia*, is now reported as a result of a detailed investigation of the addition of bromine and chlorine to **1**.

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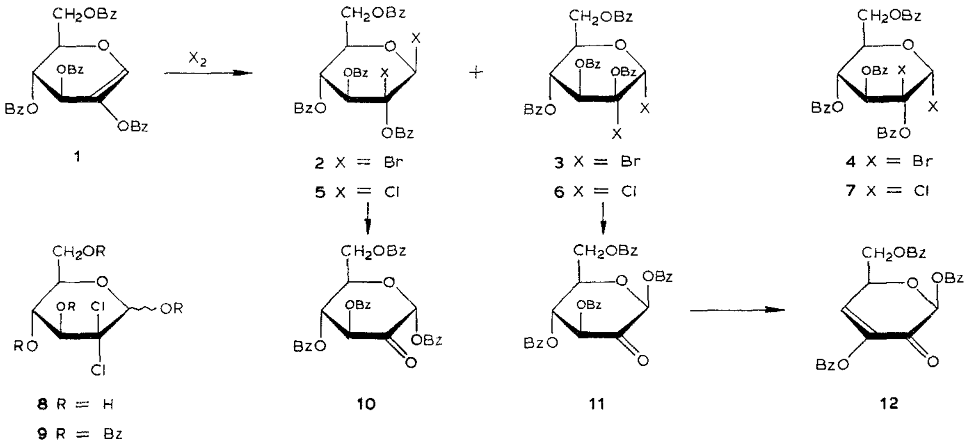
*Sugar Enolones: Part VI. For Part V, see Ref. 1.

RESULTS AND DISCUSSION

Preparation and hydrolysis of 2,3,4,6-tetra-O-benzoyl-1,2-dihalohexoses

On bromination of 1,5-anhydro-2,3,4,6-tetra-*O*-benzoyl-D-*arabino*-hex-1-enitol (**1**) in tetrachloromethane, a ~6:3:1 mixture of β-D-*gluco* (**2**), α-D-*manno* (**3**), and α-D-*gluco* dibromides (**4**) was obtained, based on t.l.c. and p.m.r. data. The β-D-*gluco* compound **2** was highly sensitive towards hydrolysis, and partial conversion into the osulose **10** occurred on contact with silica gel, *e.g.*, during t.l.c. Thus, column chromatography of the dibromide mixture on silica gel gave **2** (6–28%, depending on speed of elution) and substantial amounts of **10** (up to 41%), whereas the α-dibromides **3** and **4** were isolable in yields of 24 and 6%, respectively, without being affected by hydrolysis.



The β-D-*gluco*-dibromide **2** was quantitatively converted into the α-anomer **4** in boiling tetrachloromethane containing titanium tetrabromide, whereas **4** and the α-D-*manno* isomer **3** were recovered unchanged when exposed to the same conditions. The facile β→α-anomerization of **2** suggests that **4** present in the bromination mixture was formed *via* **2**, rather than by *trans*-addition to **1**. However, on exposure of **2** to the conditions of bromination, no α-anomer **4** was detectable by t.l.c. Thus, whereas **1** undergoes mainly *cis*-addition of bromine, in which attack from above the plane of the pyranose ring is favoured (2:1), ~10% of *trans*-addition occurs to give the α-D-*gluco* isomer **4**.

Chlorination of **1** yielded only *cis* adducts, with the β-D-*gluco*-dichloride **5** preponderating over the α-D-*manno* isomer **6**. With tetrachloromethane as reaction solvent[16], the product ratio was ~2:1, whereas, in benzene or toluene, a ratio of ~4:1 was observed. Even when carefully dried solvents were used, the formation of some α-hexosulose **10** was observed (t.l.c.), presumably by hydrolysis of the precursor of **5**, *i.e.*, a 2-chloro-1,2-benzoxonium chloride intermediate[1,16], since the dichlorides are remarkably resistant to hydrolysis.

In view of these intermediates, the formation of 2,2-geminally substituted compounds of type **9** is a possibility on chlorination of **1**. However, their formation was unambiguously excluded by the non-identity of **5** or **6** with the α- or β-tetrabenzoates (**9α** and **9β**) obtained by benzoylation of 2,2-dichloro-2-deoxy-D-*arabino*-hexose[17] (**8**). Since one of the principal modes of mass-spectral fragmentation begins with excision of the C-1 substituent, **5** and **6** always show $M-35$ peaks with the isotopic ratio of 3:1 (loss of chloride), whereas the two anomers **9** give $M-121$ peaks with the isotopic ratio 3:2 owing to loss of the 1-benzoyloxy group.

The almost exclusive formation of *cis*-adducts from **1** can be attributed to the intermediate formation of 2-halobenzoxonium ions. However, the factors governing the ratios of *cis*-adducts, *i.e.*, the 2:1 to 4:1 preponderance of halogen attack from above the plane of the pyranose ring, is less easily rationalized. In halogenations of tri-*O*-acetyl-D-glucal, attack from the lower side of the ring is favoured (by 9:1 to 5:1 for chlorine addition in tetrachloromethane[5]). However, on chlorination of 1,5-anhydro-2,3,4-tri-*O*-benzoyl-6-deoxy-D-hex-1-enitol, *i.e.*, **1** lacking BzO-6, the steric course is the reverse of that for **1**, yielding a 1:3 mixture of the 6-deoxy-β-D-*gluco*- and α-D-*rhamno*-dichlorides[18]. Clearly, more data are needed to explain these steric preferences.

Of the 1,2-dihalo sugars **2**–**6**, the most easily hydrolysed is the β-D-*gluco*-dibromide **2** (see above). On treatment of **2** with silver carbonate in aqueous acetone at room temperature, hydrolysis was complete within 15 min to give 1,3,5,6-tetra-*O*-benzoyl-α-D-*arabino*-hexosulose (**10**, 73%). Of the α-dibromides **3** and **4**, the *manno* isomer **3** is more readily hydrolyzed, *e.g.*, on exposure to silver nitrate–aqueous acetone for 6 h, quantitative conversion occurs into a ~5:1 mixture of the β-hexosulose **11** and the β-enolone **12**, from which **11** was isolated in 36% yield. For the isolation of **12**, it was advantageous to convert **11** → **12** by brief treatment with boiling, moist benzene in the presence of sodium hydrogen carbonate followed by chromatography on cellulose, as silica gel caused partial conversion of **12** into dibenzoylkojic acid.

The α-*gluco*-dibromide **4** was stable towards silver carbonate–aqueous acetone (15 h, 56°), and yielded a mixture of **11** and **12** only on treatment with boiling, moist acetone in the presence of silver perchlorate and silver carbonate. Treatment with silver perchlorate–silver carbonate in moist acetone at ambient temperature gradually converted the β-*gluco*-dichloride **5** into the α-hexosulose **10**, whereas the α-*manno* isomer **6** was unaffected; at boiling temperature, however, this reagent slowly hydrolyzed **6** to yield a mixture of **11** and **12**, the latter being the major product after 8 h.

On the basis of these results, the stability of the dihalo sugars **2**–**6** towards hydrolysis in the presence of silver salts follows the sequence: α-*manno*-dichloride (**6**) > α-*gluco*-dibromide (**4**) > β-*gluco*-dichloride (**5**) > α-*manno*-dibromide (**3**) > β-*gluco*-dibromide (**2**). The α-*gluco*-dichloride **7** was not included in the hydrolytic experiments but may be placed at the beginning on the basis of analogy with the stabilities of the dibromides (**4** > **3** > **2**).

Exploratory experiments indicate the same reactivity scale for solvolysis reactions.

Configurational assignments

Some conclusions about configurational relationships may be drawn from the reactivities of the dihalides **2**–**6**. The titanium tetrabromide-induced β→α-anomerization **2**→**4** indicates identical configuration at C-2, but the stability of **3** indicates it to be an α anomer and thus the C-2 epimer of **4**. A 1,2-diaxial arrangement of the two bromine substituents should be the most stable towards hydrolysis due to a minimum of dipole–dipole interactions; therefore, **4** may be assigned the α-D-*gluco* configuration, with those for **2** (β anomer) and **3** (C-2 epimer of **4**) following correspondingly. Although these conclusions are correct, they do not unequivocally establish the configuration at C-2.

Lundt and Pedersen[16] have deduced the configuration of the dichlorides **5**–**7** by comparing their ^{1}H- and ^{13}C-n.m.r. spectral data with those for structural analogues of known stereochemistry. The p.m.r. data for the dibromides **2**–**4**, which correspond closely with those for **5**–**7** (*cf.* Table I), particularly the chemical shifts for the H-1 singlet, allow the same configurational assignments but still do not provide absolute proof of the stereochemistry at the tertiary carbon atom.

TABLE I

P.M.R.[a] DATA FOR THE ISOMERIC 2,3,4,6-TETRA-*O*-BENZOYL-2-HALO-D-HEXOPYRANOSYL HALIDES

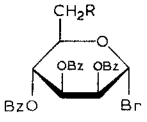
Compound	*H-1* (*s*)	*H-3* (*d*)	*H-4* (*dd*)	*H-5*[b]	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$
β-D-*gluco*-Dibromide (**2**)	7.03	6.52	6.10	4.38	9.0	9.0	2.0	6.5
β-D-*gluco*-Dichloride (**5**)[c]	7.0	6.69	6.02	4.42	9.2	9.6	3.4	4.6
α-D-*manno*-Dibromide (**3**)	>7.33[d]	6.62	6.18	4.79	9.5	10.0	2.0	4.0
α-D-*manno*-Dichloride (**6**)[c]	7.50	6.48	6.17	4.82	9.4	10.2	2.8	3.8
α-D-*gluco*-Dibromide (**4**)	>7.33[d]	6.25	6.32	4.74	7.5	7.0	2.0	4.0
α-D-*gluco*-Dichloride (**7**)[c]	7.36	6.55	6.17	4.78	9.6	10.0	2.8	4.6

[a]In $CDCl_3$: δ scale. [b]X-Part of an ABX-type set of signals; the AB portion for the H-6,6′ appears around δ 4.6 ±0.1. [c]Data from Ref. 2. [d]Hidden by the signals of the aromatic protons. [e]Nicely resolved octet; 6-Me at δ 1.30.

Proof was provided by application of the exciton chirality method[20] to the 1,2-dihalides. Tri-*O*-benzoylpyranoses[21,22] display very intense, Davydov-split Cotton effects of which the sign and magnitude of the first (around 235 nm) agree with the net chirality of the benzoate groups, as composed of all 1,2- and 1,3-interactions between the aromatic chromophores. Only where there are opposing interactions of the benzoate groups is one c.d. maximum of small intensity obtained.

These empirical rules should be applicable to the tetra-*O*-benzoyl-1,2-dihalohexoses **2**–**7** after accounting for the additional 1,3-interaction between BzO-4 and

BzO-6. For compounds of the *manno* configuration, having a net tribenzoate chirality of −3 (see Fig. 1A), the contribution of BzO-6 is positive, since 2,3,4,6-tetra-*O*-benzoyl-α-D-mannosyl bromide (**13**) exhibits a less intense, negative Cotton effect at 238 nm ($\Delta\varepsilon - 35.1$, *cf.* Table II) than the respective 6-deoxy analogue **14** ($\Delta\varepsilon - 48.1$). This situation is not surprising, as BzO-6 should preferentially adopt a conformation gauche to BzO-4 as well as to the ring oxygen (Fig. 1B). For the *manno*-1,2-dihalides, c.d. curves very similar to that of **13** would be expected, and are, in fact, observed for the dibromide **3** and the dichloride **6** (see Fig. 2 and Table II), thereby confirming the configurations.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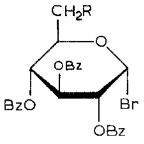
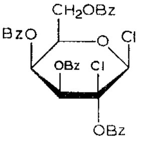
14 R = H


15 R = OBz
16 R = H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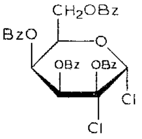
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For *gluco* isomers having a net tribenzoate chirality of zero, interpretation of Cotton effects is more complex. For example, tri-*O*-benzoyl-6-deoxy-α-D-glucopyranosyl bromide (**16**) exhibits three extrema, the one at 232 nm being negative ($\Delta\varepsilon - 5.2$, *cf.* Table II), whereas positive Cotton effects are observed[22] for methyl tri-*O*-benzoyl-6-deoxy-α-D-glucopyranoside ($\Delta\varepsilon + 4.4$ at 237 nm) and for tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (**15**) (+8.4 at 235 nm, *cf.* Fig. 1). Moreover, the *gluco*-1,2-dihalotetrabenzoates **2**, **4**, **5**, and **7** show three extrema (Table II), with that at ~233 nm being negative, but with considerably higher intensities for the β anomers **2** and **5**. Thus, on the basis of a comparison of the c.d. curves of the α-D-*manno*-dichloride **6** and the alternative isomer (**5**) obtained from **1** (*cf.* Fig. 2), either the β-D-*gluco* or β-D-*manno* configuration may be deduced for this product*.

The perbenzoates of *galacto* configuration have a net tribenzoate chirality of +3 (see Fig. 1A), so that the c.d. curves should be approximate mirror images of those for the respective *manno* isomers, since BzO-6 should preferentially adopt a conformation gauche to that on C-4 (Fig. 1B) and have a negative chirality contribution. This view is borne out by the chiroptical properties of tetra-*O*-benzoyl-2-chloro-β-D-galactopyranosyl chloride** (**17**), the amplitude for the first Cotton effect comparing favourably with those observed for the respective *manno* analogues **13** and **6**.

For the 1,2-dichloro-*talo*-isomer **18**, in which the individual chirality contributions cancel out (Fig. 1A), except for the 4,6-interaction, four c.d. extrema with

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*In our preliminary report[15], based on considerably less comparative data, the c.d. curve for **5** was interpreted as indicating the β-D-*manno* configuration.

Compounds **17 and **18** were kindly provided by Dr. Inge Lundt (Technical University of Denmark, Lyngby).

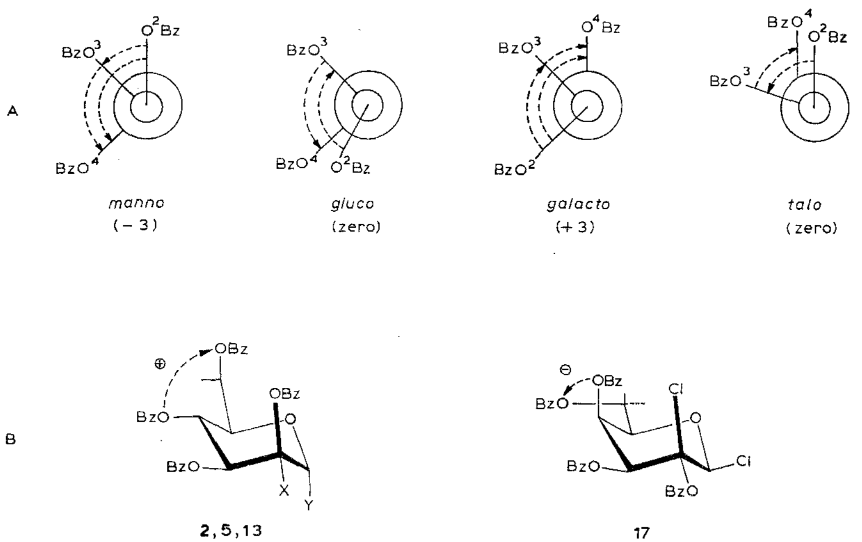

Fig. 1. (A) Net tribenzoate chiralities of per-*O*-benzoylhexopyranosyl halides of *manno*, *gluco*, *galacto*, and *talo* configuration, neglecting the chirality contribution from interaction between C-4 and C-6 benzoyloxy groups. (B) Apparent contributions of 4,6-interactions to overall chirality in *manno* and *galacto* isomers.

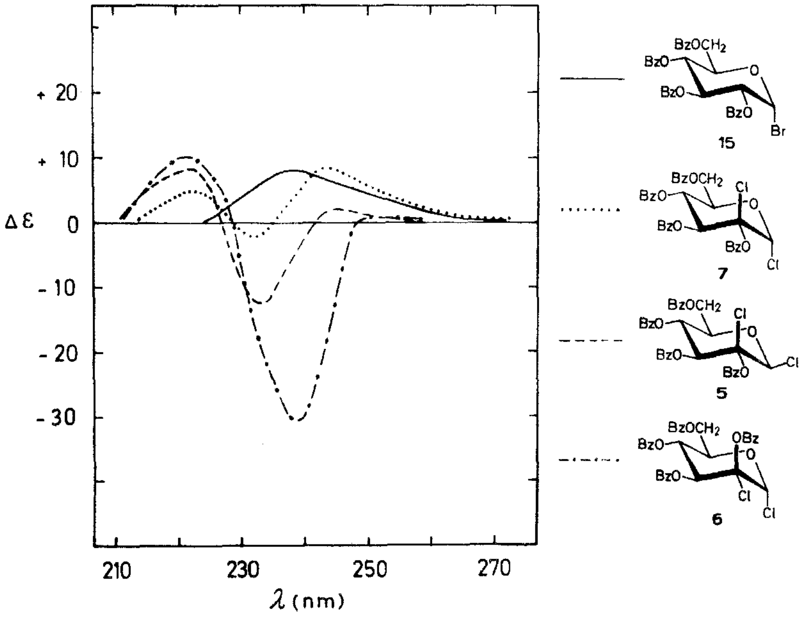

Fig. 2. Comparative c.d. spectra (iso-octane solution) of 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (**15**, solid line) and of the 2-chloro analogues **5**–**7** (broken lines).

TABLE II

C.D. DATA FOR PERBENZOYLATED HEXOPYRANOSYL HALIDES

Configuration	*Anomeric substituent*	*$\Delta\varepsilon$ in iso-octane (nm)*		
α-D-*manno* (**13**)	Br	+18.1 (222)	−35.1 (238)	—
6-Deoxy-α-D-*manno* (**14**)	Br	+10.3 (221)	−48.1 (238)	—
2-Chloro-α-D-*manno* (**6**)	Cl	+13.0 (223)	−34.8 (238)	—
2-Bromo-α-D-*manno* (**3**)	Br	+15.7 (222)	−33.5 (237)	—
α-D-*gluco* (**15**)	Br	—	+8.4 (235)	—
6-Deoxy-α-D-*gluco* (**16**)	Br	+3.6 (221)	−5.2 (232)	+4.9 (243)
2-Chloro-α-D-*gluco* (**7**)	Cl	+4.8 (222)	−1.5 (232)	+8.3 (243)
2-Bromo-α-D-*gluco* (**4**)	Br	+4.6 (221)	−3.4 (233)	+8.9 (243)
2-Chloro-β-D-*gluco* (**5**)	Cl	+10.8 (221)	−12.6 (233)	+2.1 (244)
2-Bromo-β-D-*gluco* (**2**)	Br	+9.8 (221)	−10.2 (233)	+0.9 (243)
2-Chloro-β-D-*galacto* (**17**)	Cl	−8.2 (222)	+29.7 (237)	—
2-Chloro-α-D-*talo* (**18**)	Cl	−2.6 (221)	−7.5 (228)	+6.0 (245) −2.8 (282)

relatively low amplitudes are observed. In conclusion, the foregoing chiroptical data indicate that the exciton chirality method, which has been claimed to be one of the most reliable optical methods for studies of absolute configuration[23], is unambiguous only when applied to systems with substantial, very high overall chiralities of benzoyl chromophores, *i.e.*, very intense, exciton-split Cotton effects.

Finally, the configurational conclusions noted above were confirmed by an X-ray crystal structure analysis of the α-D-*manno*-dichloride **6** (Fig. 3), which clearly revealed a *cis*-arrangement (1 ax, 2 eq) of the chlorine substituents and BzO-2 axial. The pyranose ring, as evidenced by torsional angles of 50.2–59.6° (Table III), was in the expected $^4C_1$ conformation, and the O-5–C-1 bond was shortened to 1.38 Å (Fig. 4), as anticipated for α anomers. The C-2–Cl-2 bond length of 1.78 Å is practically identical with the mean value for the paraffinic C–Cl bond[24] (1.79 Å), whereas the C-1–Cl-1 bond is slightly lengthened to 1.81 Å, as expected for axially oriented chlorine[25,26]. The slight distortion at C-4, as indicated by the dihedral angles H-3/H-4 and H-4/H-5 being only 164.8° and 160.2°, was presumably caused by nonbonded repulsions between Cl-2 and BzO-3 and BzO-4, rather than by a direct effect of the 2-benzoyloxy function.

Inspection of the ester group conformations in the crystal structure of **6** is of relevance to the applicability of the exciton chirality method, which requires the electric transition moment of the benzoyl group to be approximately parallel to the alcoholic C–O bond[20]. The ester groups are almost planar within the fragment R–O–CO–Ph, *i.e.*, the bonds R–O and $C–C_6H_5$ are nearly antiparallel, deviating from 180° by angles of 8.7° (C-2), 4.3° (C-3), 9.1° (C-4), and 3.2° (C-6) only (see Table III). Furthermore, BzO-6 is oriented gauche to the ring oxygen as well as to the C-4 substituent. The fact that this orientation of BzO-6 had to be assumed for

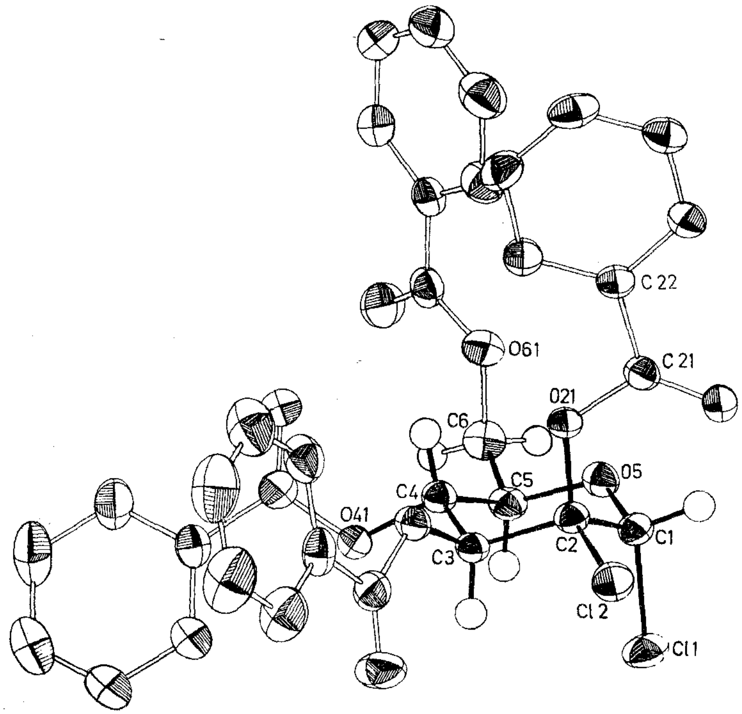

Fig. 3. An ORTEP drawing of 2,3,4,6-tetra-*O*-benzoyl-2-chloro-D-mannopyranosyl chloride (**6**), showing thermal ellipsoids and partial atomic numbering (for complete numbering, see Fig. 4). Hydrogen atoms of benzene rings have been omitted.

TABLE III

SELECTED TORSIONAL ANGLES IN **6**

Pyranose ring			
C-1–C-2/C-3–C-4	−53.9°	C-6–O-61/C-61–C-62	+176.8°
C-2–C-3/C-4–C-5	+51.5°	C-6–O-61/C-61–C-62	−3.4°
C-3–C-4/C-5–O-5	−50.2°	O-62–C-61/C-62–C-63	−1.4°
C-4–C-5/O-5–C-1	+55.9°		
C-5–O-5/C-1–C-2	−59.6°	*Ring substituents*	
O-5–C-1/C-2–C-3	+57.5°	Cl-1–C-1/C-2–Cl-2	+55.9°
		Cl-1–C-1/C-2–O-21	−178.4°
Benzoyl substituents		H-1–C-1/C-2–O-21	+60.9°
C-2–O-21/C-21–C-22	−171.3°	H-1–C-1/C-2–Cl-2	−61.6°
C-2–O-21/C-21–O-22	+8.0°	Cl-2–C-2/C-3–H-3	−54.1°
O-22–C-21/C-22–C-23	−172.5°	Cl-2–C-2/C-3–O-31	+64.9°
C-3–O-31/C-31–C-32	+175.7°	O-21–C-2/C-3–O-31	−52.8°
C-3–O-31/C-31–O-32	−3.1°	H-3–C-3/C-4–H-4	+164.8°
O-32–C-31/C-32–C-33	−172.3°	O-31–C-3/C-4–O-41	−72.8°
C-4–O-41/C-41–C-42	−170.9°	H-4–C-4/C-5–H-5	−160.2°
C-4–O-41/C-41–O-42	+10.4°	H-4–C-4/C-5–C-6	−44.4°
O-42–C-41/C-42–C-43	+9.6°	C-4–C-5/C-6–O-61	+57.9°
		C-4–C-5/C-6–H-61	−65.1°
		C-4–C-5/C-6–H-62	+171.2°

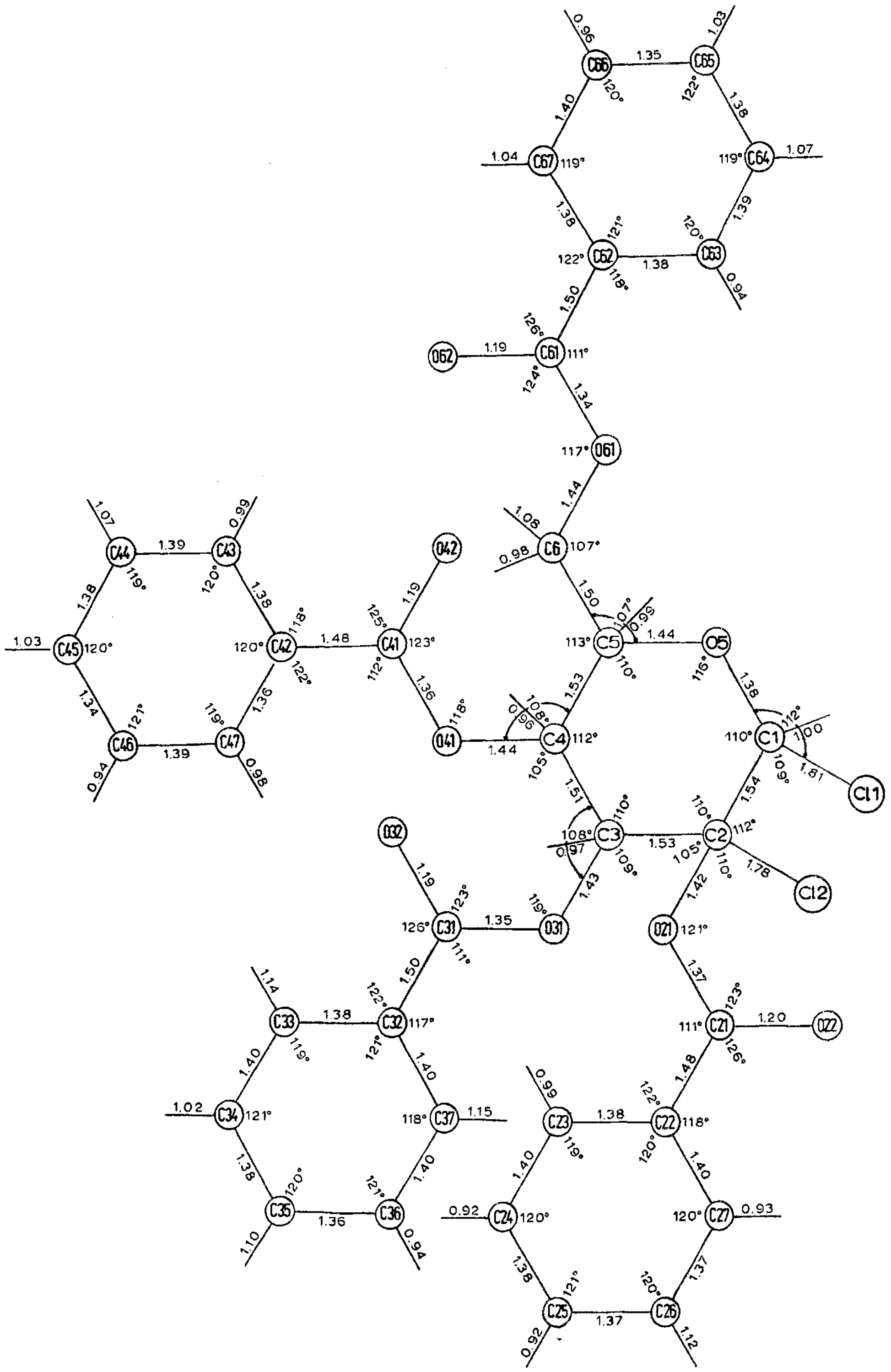

Fig. 4. Bond distances (Å) and bond angles (deg.) in 6. Standard deviations are within 0.01 Å and 0.8°, respectively. Additional C-2 angles: Cl-2–C-2–C-3 = 109°; O-21–C-2–C-1 = 110°.

iso-octane solutions of **3**, **6**, and **13** on the basis of their chiroptical properties, not only stresses the applicability of the exciton chirality method to systems with appreciable overall chiralities, but clearly demonstrates the high correspondence of conformations in the crystalline state and in solution for the pyranose ring and for benzoyl ester groups.

EXPERIMENTAL

Melting points were determined on a Bock Monoskop and are uncorrected. Spectral measurements were effected with Perkin–Elmer 125 (i.r.), Perkin–Elmer 141 (rotations), Jasco J-20 (c.d.), Varian A-60A and XL-100 (^{1}H- and ^{13}C-n.m.r.), and Varian CH 4B (*m/e*) instruments. Reactions were monitored, and purity of products ascertained, by t.l.c. on silica gel F_{254} plastic sheets (Merck) with *A*, carbon tetrachloride–ethyl acetate (10:1); *B*, cyclohexane–ethyl acetate (5:1); *C*, chloroform–dichloromethane (1:1); and visualization with u.v. light, iodine vapour, or charring with sulphuric acid. P.l.c. was performed on 1.5-mm layers of Kieselgel PF_{254} (Merck), and column chromatography on Kieselgel 60 (70–230 mesh, Merck).

*Bromination of 1,5-anhydro-tetra-*O*-benzoyl-*D-arabino-*hex-1-enitol* (**1**). — To a solution of **1** (1.16 g, 2 mmol) in anhydrous carbon tetrachloride (20 ml) was added an excess of bromine at 0°. The solution was kept for 15 min at 0° and then for 15 min at room temperature. The solvent was evaporated *in vacuo* followed by addition of carbon tetrachloride and re-evaporation. This procedure was thrice repeated to give a nearly colourless syrup (1.6 g) of a ~2:1 mixture of the β-D-*gluco*-dibromide **2** (R_F 0.30, solvent *A*) and α-D-*manno*-dibromide **3** (R_F 0.35), together with 5–10% of the α-D-*gluco* isomer **4** (R_F 0.41) and hexosulose **10** (R_F 0.03). Elution of the mixture from a column (30 × 25 cm) of silica gel with cyclohexane–ethyl acetate (10:1) gave **2**, but considerable hydrolysis to **10** occurred during chromatography, the column becoming deep orange in colour.

Concentration of the fastest moving fraction afforded a syrup (100 mg) which was subjected to rechromatography to give 2,3,4,6-tetra-*O*-benzoyl-2-bromo-α-D-glucopyranosyl bromide (**4**; 85 mg, 6%) as a chromatographically homogeneous syrup, $[\alpha]_D^{28}$ +22° (*c* 1, chloroform). For p.m.r. data, see Table I.

Anal. Calc. for $C_{34}H_{26}Br_2O_9$: C, 55.28; H, 3.52. Found: C, 55.44; H, 3.56.

The second fraction, consisting of **3** with small proportions of **2** and **4**, was concentrated to dryness. Trituration of the residue with ethyl acetate–pentane gave 2,3,4,6-tetra-*O*-benzoyl-2-bromo-α-D-mannopyranosyl bromide (**3**), and recrystallization from the same solvents gave platelets (360 mg, 24%), m.p. 143–144°, $[\alpha]_D^{33}$ +69° (*c* 1, chloroform). For p.m.r. data, see Table I.

Anal. Found: C, 55.27; H, 3.77.

The third fraction, containing **2** and a small proportion of **3**, was concentrated, and the residue was subjected to rechromatography to yield 2,3,4,6-tetra-*O*-benzoyl-2-bromo-β-D-glucopyranosyl bromide (**2**; 75 mg, 5%) as a chromatographically homogeneous syrup, $[\alpha]_D^{33}$ +29° (*c* 0.5, chloroform).

Anal. Found: C, 55.30; H, 3.59.

A better yield (28%) of **2** was obtained by using less material on a smaller column (2 x 15 cm), and fast elution with hexane–ethyl acetate (9:1).

Subsequent elution with cyclohexane–ethyl acetate (2:1) gave 1,3,4,6-tetra-*O*-benzoyl-α-D-*arabino*-hexopyranosulose (**10**; 487 mg, 41%) as a syrup, $[\alpha]_D^{28}$ +38° (*c* 1, chloroform); lit.[19] +37.1° (*c* 1.1, chloroform). The p.m.r. data corresponded with those reported[19].

Anomerizations with titanium tetrabromide. — To a solution of the crude mixture of dibromides, obtained on bromination of **1** (580 mg, 1 mmol), in tetrachloromethane (20 ml), titanium tetrabromide (370 mg) was added and the mixture was boiled under reflux for 3 h. The mixture, which was now devoid of **2** and contained **4** and **3** (ratio ~3:1) together with **10** (t.l.c., solvent *A*), was poured into ice–water. The precipitate was collected, washed successively with water, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and concentrated *in vacuo*. The syrupy residue was eluted from silica gel with cyclohexane–ethyl acetate (5:1) to give, first, syrupy **4** (310 mg, 42%), and then **3** (85 mg, 11%), m.p. 143–144°.

After treatment of the β-D-*gluco*-dibromide **2** with titanium tetrabromide in tetrachloromethane (3-h reflux), only the α-D-*gluco* anomer **4** was detectable by t.l.c. (solvent *A*). The α-D-*manno*-dibromide **3** was unaffected by similar treatment, and 85% was reisolated.

2,3,4,6-Tetra-O-benzoyl-2-chloro-α-D-mannopyranosyl chloride (**6**). — Dry chlorine was passed through a solution of **1** (5.8 g, 10 mmol) in toluene[15] (150 ml) at 5–10° until a greenish-yellow colour persisted (5 min). Excess of chlorine was removed with nitrogen, and the solution was concentrated *in vacuo*. Ether was evaporated several times from the amorphous residue (6.6 g) which comprised a ~1:4 mixture of **6** (R_F 0.70, solvent *B*) and the β-D-*gluco* isomer **5** (R_F 0.58). Crystallization from methanol gave **6** (1.1 g, 17%), m.p. 156–158°, $[\alpha]_D^{20}$ +10° (*c* 1, chloroform), +44° (*c* 2, pyridine); lit.[13] m.p. 156°, $[\alpha]_D$ +10.3° (*c* 0.25, chloroform). The p.m.r. data (Table I) correlated well with those reported[16]. C.d. data (MeOH): $\Delta\varepsilon$ −31.1 (242 nm) and +13.5 (225).

The crystals of **6** were monoclinic, space group C2, with 4 molecules per unit cell of dimensions a = 17.91 ±0.01, b = 11.87 ±0.01, c = 16.51 ±0.01 Å, β = 112.7 ±0.1°. An automatic 4-circle diffractometer (STADI-4) was used with CuKα radiation to measure 7050 reflexes (h01–h71). After data reductions, including averaging of symmetry-related reflexions, 3400 remained and were used for structure determination by direct methods, *i.e.*, the SHEL-X programme[27] which also allowed full-matrix least-squares refinement of the provisional parameters, and by difference Fourier maps. Structure refinement (all but the hydrogen atoms were treated anisotropically) converged at R = 0.044. The final positional and thermal parameters are listed in Tables IV and V. The bond distances and bond angles are given in Fig. 4, and torsional angles in Table III. The thermal motions of the atoms were calculated and plotted by the ORTEP[28] programme to yield Fig. 3.

TABLE IV

ATOM POSITIONS AND THERMAL PARAMETERS FOR 2,3,4,6-TETRA-*O*-BENZOYL-2-CHLORO-α-D-MANNOPYRANOSYL CHLORIDE[a] (6)

Atom	*x/a*	*y/b*	*z/c*	U_{11} ($\times 10^4$)	U_{22} ($\times 10^4$)	U_{33} ($\times 10^4$)	U_{23} ($\times 10^4$)	U_{13} ($\times 10^4$)	U_{12} ($\times 10^4$)
Cl(1)	−0.2894	0.2020	−0.4246	747	751	690	−203	384	128
Cl(2)	−0.3505	0.2424	−0.2670	646	526	630	−21	223	−56
C(1)	−0.3637	0.1100	−0.4094	462	531	413	−68	163	64
C(2)	−0.3492	0.1056	−0.3112	439	457	421	−53	189	21
C(3)	−0.2682	0.0491	−0.2594	366	518	394	−72	186	55
C(4)	−0.2647	−0.0644	−0.2986	397	510	452	−38	172	20
C(5)	−0.2861	−0.0582	−0.3976	432	590	518	−46	263	10
C(6)	−0.2977	−0.1715	0.4407	606	609	556	−14	289	−68
O(5)	−0.3608	−0.0029	−0.4400	478	574	397	−54	152	−22
O(21)	−0.4082	0.0364	−0.2983	379	509	183	−32	196	68
C(21)	−0.4889	0.0638	−0.3348	418	581	446	−42	158	13
O(22)	−0.5150	0.1394	−0.3863	457	694	640	15	163	215
C(22)	−0.5366	−0.0103	−0.3013	474	483	496	−38	256	−12
C(23)	−0.5002	−0.0871	−0.2345	500	695	661	11	261	147
C(24)	−0.5487	−0.1508	−0.2026	733	697	783	0	388	222
C(25)	−0.6317	−0.1373	−0.2387	770	651	951	−144	574	−6
C(26)	−0.6672	−0.0622	−0.3055	496	704	752	−62	319	−41
C(27)	−0.6208	−0.0017	−0.3374	457	595	546	−24	210	−22
O(31)	−0.2618	0.0311	−0.1713	477	611	349	−83	128	24
C(31)	−0.2046	0.0880	−0.1055	652	580	507	−47	100	−1
O(32)	−0.1569	0.1493	−0.1171	969	1090	546	−549	71	57
C(32)	−0.2117	0.0646	−0.0197	709	646	382	156	74	38
C(33)	−0.2628	−0.0178	−0.0114	652	1118	533	75	212	177
C(34)	−0.2649	−0.0368	0.0716	896	1561	618	157	361	251
C(35)	−0.2176	0.0263	0.1429	1441	1379	619	409	436	129
C(36)	−0.1671	0.1061	0.1340	1779	1096	473	71	243	−116
C(37)	−0.1642	0.1297	0.0522	1226	919	554	−31	195	−62
O(41)	−0.1816	−0.1005	−0.2569	380	538	612	6	179	90
C(41)	−0.1688	−0.2049	−0.2206	573	646	586	−34	201	78
O(42)	−0.2189	−0.2728	−0.2321	680	734	1258	−160	63	355
C(42)	−0.0797	−0.2231	−0.1685	567	640	450	84	137	11
C(43)	−0.0541	−0.3308	−0.1407	863	677	712	116	53	−4
C(44)	0.0270	−0.3517	−0.0904	1112	929	794	455	64	10
C(45)	0.0814	−0.2637	−0.0689	675	1301	854	243	129	27
C(46)	0.0557	−0.1590	−0.0961	591	1086	1407	−107	74	260
C(47)	−0.0250	−0.1372	−0.1476	549	812	1009	−16	112	157
O(61)	−0.3611	−0.2277	−0.4227	506	553	622	−50	244	−103
C(61)	−0.3582	−0.3406	−0.4193	515	624	430	32	63	22
O(62)	−0.3089	−0.3953	−0.4339	684	674	1013	117	388	31
C(62)	−0.4248	−0.3861	−0.3950	485	708	455	−30	39	84
C(63)	−0.4315	−0.5017	−0.3907	576	750	1017	32	137	287
C(64)	−0.4940	−0.5480	−0.3717	691	927	1515	−83	155	578
C(65)	−0.5473	−0.4768	−0.3553	576	1404	1181	−114	230	493
C(66)	−0.5405	−0.3639	−0.3581	626	1187	779	−46	271	51
C(67)	−0.4789	−0.3158	−0.3788	586	847	579	−47	196	−27
Largest values of standard deviations:									
Cl	0.0001	0.0001	0.0001	6	7	6	5	5	5
C	0.0004	0.0006	0.0004	68	57	50	41	35	46
O	0.0002	0.0003	0.0002	21	25	24	19	17	19

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[a] The form of the anisotropic temperature factor is $T = \exp[-2\pi^2(U_{11}a^{*2}h^2 + U_{22}b^{*2}k^2 + U_{33}c^{*2}l^2 + 2U_{12}a^*b^*hk + 2U_{13}a^*c^*hl + 2U_{23}b^*c^*kl)]$.

TABLE V

POSITIONAL AND THERMAL PARAMETERS FOR HYDROGEN ATOMS OF **6**[a]

Atom	*x/a*	*y/a*	*z/c*	$U \times 10^4 (\text{Å}^2)$[b]
H(1)	−0.4180	0.1426	−0.4441	368
H(3)	−0.2246	0.0977	−0.2585	368
H(4)	−0.2986	−0.1182	−0.2855	368
H(5)	−0.2403	0.0249	−0.4084	368
H(61)	−0.2470	−0.2142	−0.4195	562
H(62)	−0.3217	−0.1618	−0.5114	562
H(23)	−0.4413	−0.1014	−0.2047	645
H(24)	−0.5239	−0.2010	−0.1583	645
H(25)	−0.6597	−0.1807	−0.2143	645
H(26)	−0.7343	−0.0497	−0.3362	645
H(27)	−0.6447	0.0493	−0.3852	645
H(33)	−0.3033	−0.0717	−0.0683	1305
H(34)	−0.3101	−0.0875	0.0736	1305
H(35)	−0.2217	0.0130	0.2070	1305
H(36)	−0.1278	0.1458	0.1801	1305
H(37)	−0.1077	0.1623	0.0427	1305
H(43)	−0.0959	−0.3863	−0.1430	1150
H(44)	0.0471	−0.4346	−0.0656	1150
H(45)	0.1399	−0.2840	−0.0286	1150
H(46)	0.0848	−0.0934	−0.0975	1150
H(47)	−0.0404	−0.0980	−0.1583	1150
H(63)	−0.3945	−0.5381	−0.4091	1064
H(64)	−0.5003	−0.6366	−0.3656	1064
H(65)	−0.5912	−0.5232	−0.3448	1064
H(66)	−0.5781	−0.3119	−0.3508	1064
H(67)	−0.4762	−0.2296	−0.3881	1064

[a]Largest value for standard deviations: x/a 0.0028; y/b 0.0041; z/c 0.0030; $B \times 10^4$ 82. [b]Common isotropic temperature factors were used for refinement of structurally similar hydrogen atoms.

The above methanolic mother liquor, which was almost devoid of **6** (t.l.c., solvent *B*), was concentrated and ether was evaporated several times from the residue. The product (4.4 g, 68%) was eluted from silica gel to afford 2,3,4,6-tetra-*O*-benzoyl-2-chloro-β-D-glucopyranosyl chloride (**5**; 3.6 g, 59%) as a colourless, amorphous product, m.p. 66–68°, $[\alpha]_D^{25}$ +23° (*c* 1, chloroform); lit.[16] $[\alpha]_D^{25}$ +28° (*c* 3, chloroform). C.d. data (MeOH): $\Delta\varepsilon$ −2.44 (240 nm) and +8.5 (223); (iso-octane) −11.50 (233), and +7.42 (220). The p.m.r. data (Table I) were identical with those reported[16].

*1,3,4,6-Tetra-*O*-benzoyl-2,2-dichloro-2-deoxy-α-* (**9α**) *and -β-*D-arabino-*hexopyranose* (**9β**). — To a solution of 2,2-dichloro-2-deoxy-D-*arabino*-hexopyranose[17] (**8**; 2 g, 0.75 mmol) in pyridine (30 ml), benzoyl chloride (5 ml) was added gradually with cooling. The mixture was stored at ambient temperature overnight, stirred into ice–water, and extracted with chloroform (2 × 20 ml). The combined extracts were washed with water (2 × 20 ml), dried (Na_2SO_4), and concentrated. The solid residue was washed with methanol (30 ml) and recrystallized from ethanol–ethyl acetate to give **9β** (1.1 g, 23%) as needles, m.p. 209–210°, $[\alpha]_D^{25}$ −16° (*c* 1, chloroform). C.d. data (iso-octane): $\Delta\varepsilon$ −10.2 (235 nm) and +6.8 (220). P.m.r. data ($CDCl_3$): δ 4.52 (m, 3 H, H-5,6,6'), 6.10 (m, 2 H, H-3,4), and 6.38 (s, 1 H, H-1). ^{13}C-N.m.r. data ($CDCl_3$): 94.1 (C-1), 86.2 (C-2), 76.8 and 73.8 (C-3,C-5), 68.3 (C-4), and 62.5 p.p.m. (C-6).

Anal. Calc. for $C_{34}H_{26}Cl_2O_9$: C, 62.87; H, 4.04; Cl, 10.05. Found: C, 62.77; H, 4.00; Cl, 10.19.

From the above methanolic washings, a crystalline product separated. Recrystallisation from ethanol gave **9α** (1.21 g, 25%) as colourless plates, m.p. 176–177°, $[\alpha]_D^{25}$ +37.5° (*c* 1, chloroform). C.d. data (iso-octane): $\Delta\varepsilon$ −9.1 (235 nm) and +8.9 (221). P.m.r. data ($CDCl_3$): δ 4.54 (m, 3 H, H-5,6,6'), 6.03 (t, 1 H, $J_{3,4} = J_{4,5} =$ 9 Hz, H-4), 6.41 (d, 1 H, H-3), 6.76 (s, 1 H, H-1), and 7.3–8.3 (m, 20 H, 4 Ph). ^{13}C-N.m.r. data ($CDCl_3$): 94.8 (C-1), 85.4 (C-2), 74.2 and 71.2 (C-3,C-5), 68.3 (C-4), and 62.2 p.p.m. (C-6).

Anal. Calc. for $C_{34}H_{26}Cl_2O_9$: C, 62.87; H, 4.04; Cl, 10.95. Found: C, 63.28; H, 3.84; Cl, 10.93.

Hydrolysis of dihalides **2**–**6**. — (*a*) A solution (120 mg in 5 ml) of **2** in 9:1 acetone–water was stirred with silver carbonate (100 mg) at ambient temperature. After 20 min, t.l.c. showed the absence of **2**, and the mixture was filtered and concentrated. Fast elution of the residue from a small column of silica gel with cyclohexane–ethyl acetate (2:1) afforded **10** (65 mg, 65%) as a syrup, $[\alpha]_D^{25}$ +37° (*c* 1, chloroform).

(*b*) To a solution of syrupy **5** (650 mg, 1 mmol) in acetone–water (9:1, 30 ml), was added silver carbonate (280 mg, 1 mmol) and silver perchlorate (75 mg). The mixture was stirred at room temperature for 15 h, filtered, and concentrated to give syrupy **10** (350 mg, 73%), $[\alpha]_D^{25}$ +37°, identical (p.m.r. data) with the product obtained in (*a*).

(*c*) To a solution of **3** (740 mg, 1 mmol) in acetone–water (9:1, 50 ml) was added silver carbonate (280 mg, 1 mmol). The mixture was stirred for 6 h at ambient temperature, filtered, and concentrated. The resulting syrup, consisting of **11** and the β-enolone **12** (~15% on the basis of p.m.r. data), crystallised from chloroform–pentane to afford crude **11**. Recrystallisation from the same solvents gave the monohydrate of 1,3,4,6-tetra-*O*-benzoyl-β-D-*arabino*-hexopyranosulose (**11**; 220 mg, 36%), m.p. 112–113°, $[\alpha]_D^{25}$ −8° (*c* 1, chloroform). P.m.r. data ($CDCl_3$): δ 6.16 (s, 1 H, H-1), 5.95 (t, 1 H, $J_{3,4} = J_{4,5} = 9$ Hz, H-4), 5.56 (d, 1 H, H-3), and 4.2–4.8 (m, 3 H, H-5,6,6').

Anal. Calc. for $C_{34}H_{26}O_{10} \cdot H_2O$: C, 66.66; H, 4.61. Found: C, 66.59; H, 4.58. Anhydrous **11** has[19] m.p. 127–129°, $[\alpha]_D^{23}$ −9° (*c* 1, chloroform).

(*d*) Silver carbonate (380 mg) and silver perchlorate (50 mg, washed with benzene and dried over phosphorus pentaoxide) were added to a solution of **6** (785 mg) in acetone (20 ml) containing water (0.2 ml). The mixture was boiled under reflux for 8 h, filtered, and concentrated, and the residue was eluted from a column of cellulose with hexane–ethyl acetate (4:1). Fractions (10 ml) were collected, and fractions 2 and 3 gave the monohydrate of **11** (85 mg, 10%), m.p. 112–113°, identical with the product obtained in (*c*).

(*e*) A mixture of silver carbonate (330 mg, 1.2 mmol) and a solution of **3** (890 mg, 1.2 mmol) in acetone–water (9:1, 60 ml) was stirred for 6 h at room temperature, and then filtered and concentrated. The crude **11**, already containing some enolone **12**, was stirred with benzene (20 ml), water (0.4 ml), and sodium hydrogen carbonate (200 mg) for 1 h at 80°. The mixture was filtered and concentrated, and the syrupy residue (470 mg, 83%) was eluted from a column (25 × 2.5 cm) of cellulose with hexane–ethyl acetate (10:1) to give, from the appropriate fractions, 1,3,6-tri-*O*-benzoyl-4-deoxy-β-D-*glycero*-hex-3-enopyranosulose (**12**; 220 mg, 39%), m.p. 91.5–92°, $[\alpha]_D^{25}$ $-78°$ (*c* 0.5, chloroform); lit.[19] m.p. 103–105°, $[\alpha]_D^{33}$ $-75°$ (*c* 2.3, chloroform). The p.m.r. data correlated well with those reported[19].

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