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ANOMERIC STEREOCONTROL IN ADDITION REACTIONS TO HEXOSE-DERIVED DIHYDROPYRANONES*

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ABSTRACT

The outcome of base-catalysed *O*- and *C*-nucleophile additions to the carbonyl group of benzoylated 4-deoxy-D-*glycero*-hex-3-enopyranosid-2-ulose (**1**) depends on the conditions used. With methanol/sodium iodide, methanol/sodium methoxide (traces), or methylmagnesium iodide/ether, the addition is followed by benzoyl migration, providing 4-deoxy-D-hexos-3-uloses with an acetal-blocked C-2 carbonyl (**8**), or a C-2 methyl branch (**11**). Under more basic conditions in more polar solvents (potassium carbonate/methyl sulfoxide), the addition→acyl migration sequence is preceded by elimination of benzoic acid to give the 4-benzyloxy-2-methoxy-6-methylene-2*H*-pyran-3-ones of (2*S*)- (**14**) and (2*R*)-configuration (**18**), from which (*S*,*S*)-3-benzoyloxy-2,3-dimethoxy-6-methyldihydropyran-4-one (**15**) and the enantiomeric (*R*,*R*)-analogs **19**–**21** are obtained in enantiomerically pure form. Each of these carbonyl addition reactions is stereocontrolled by the vicinal anomeric substituent, the nucleophile entering exclusively from the side opposite thereto. Structural and configurational assignments are based on ^{1}H- and ^{13}C-n.m.r. data, on the fact that enantiomers are obtained from enolones epimeric at the anomeric centre (**13**→**15**, **9**→**19**), and on an X-ray structural analysis of **19**, which adopts a $^{2}S\leftrightarrow{}^{2}H_{3}$-type conformation with an essentially antiparallel disposition of the newly entered alkoxy group and the anomeric substituent.

INTRODUCTION

Hexose-derived dihydropyranones of type **1**, which are now readily accessible[2,3], are useful and versatile chiral building-blocks that have suitable functional groups and two chiral centres. They may be incorporated intact into a target molecule or used to direct the stereochemical outcome of addition reactions to the carbonyl and/or enol ester groups[2,4]. Similar potential in synthesis is associated with pyranoid systems of types **2** and **3**, which possess a unique array of three or four differently functionalised carbonyl groups and, due to their structural and configu-

*Sugar Enolones, Part XXI. For Part XX, see ref. 1.

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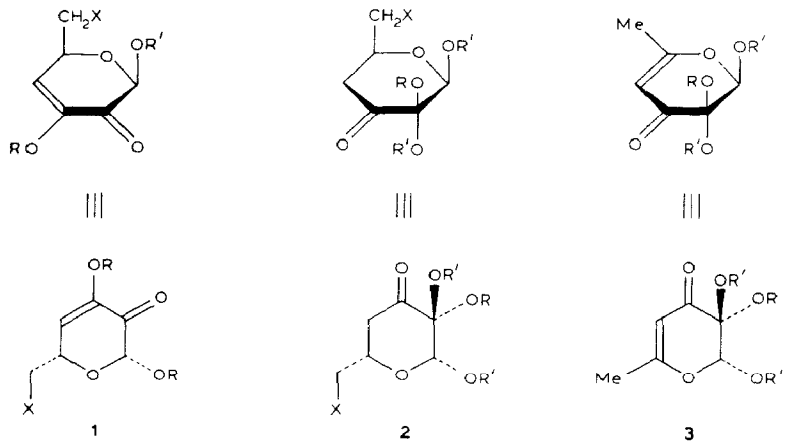

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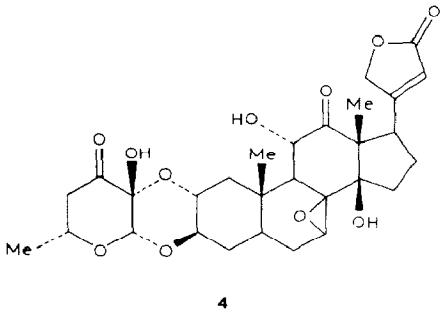
R = Acyl , R′ = Alkyl , X = H,OAcyl



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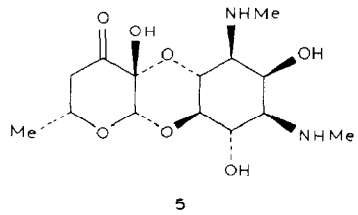

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rational relationships to the sugar portion of the *Asclepiadaceae* cardenolides, labriformidine[5] (**4**) and uscharidine[6], and the antibiotic spectinomycin[7] (**5**), are of particular value for the construction of these products in enantiomerically pure form.

We now report facile preparations* of dihydropyranones of types **2** and **3** from enolone esters **1**.

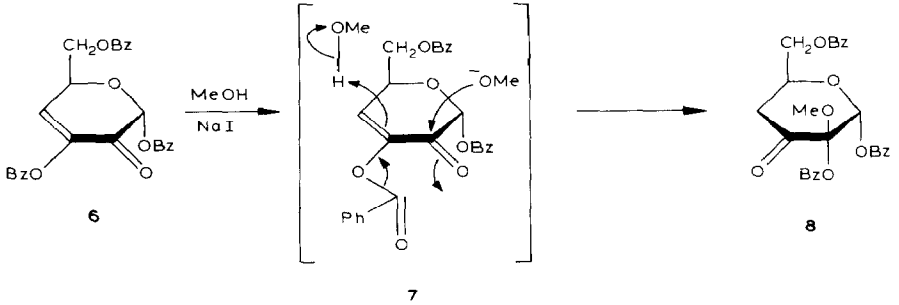
RESULTS AND DISCUSSION

The stereoselectivity associated with addition reactions of pyranoid enolone esters of type **1** is noteworthy. For example, hydride addition to the β-D-enolone **9**, when effected with sodium borohydride in methanol, affords the 4-deoxy-β-D-*lyxo*-hexoside as the major component[9], which becomes the exclusive product when L-Selectride (lithium tri-*sec*-butylborohydride) is used[10]. With zinc borohydride, only

*For a preliminary account of portions of this work, see ref 8.

saturation of the free carbonyl function occurs and *C*-branching with alkyl-lithium reagents (carbonyl addition) or lithium dialkyl cuprates (conjugate addition) also proceeds with high stereoselectiviy[4,11]. Alcohols also add regiospecifically to the carbonyl function of the enolone esters, yielding compounds of type **2** by direct addition and acyl migration, or of type **3**, when preceeded by β-elimination, depending on the basic conditions used.

When the enolone esters **6** or **9** are treated with such bases as pyridine and piperidine–chloroform at room temperature, or heated with sodium acetate–acetic anhydride, the γ-pyrone system is elaborated in the form of kojic acid or allomaltol derivatives[12,13]. However, when a methanolic solution of **6** was stirred at ambient temperature with either sodium iodide (12 h) or with catalytic amounts of sodium hydroxide (15 min), conversion into another tribenzoate occurred, which, on the basis of n.m.r. and optical rotational data (see below), was shown to be the hexos-3-ulose **8**. This transformation is readily accounted for by base-catalysed addition of methanol to the carbonyl group in **6** from the sterically, as well as electronically, more favorable β-face (*i.e.*, opposite to the anomeric substituent) and 3→2-benzoyl migration (see **7**) with liberation of the carbonyl group at position 3.



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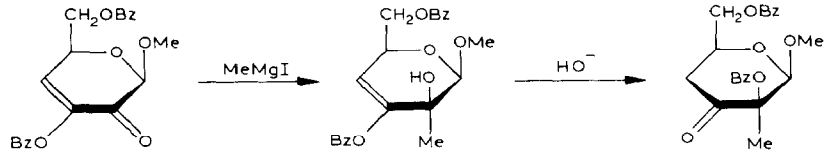

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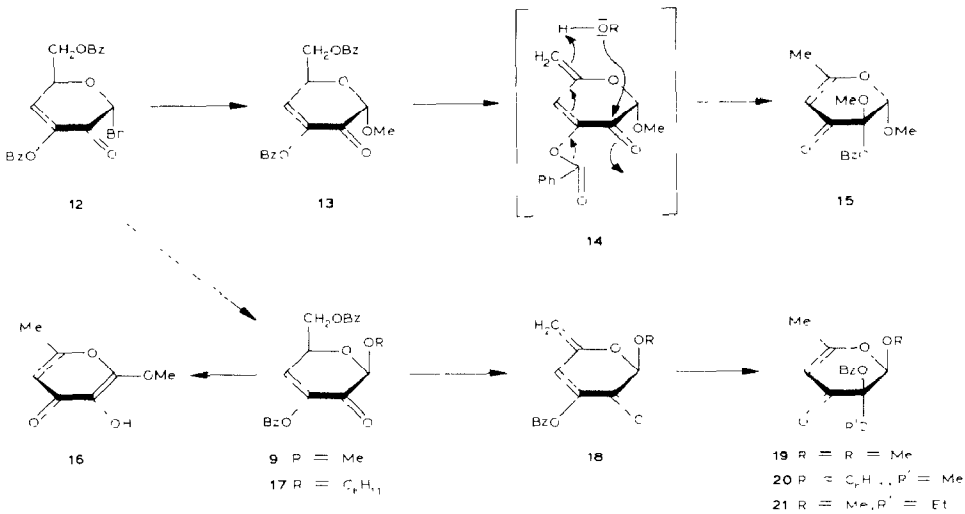
This process appears to be generally applicable, as was shown with enolone esters[14] derived from 6-deoxyhexoses. The addition of *C*-nucleophiles follows a similar course. Thus, reaction of **9** with methylmagnesium iodide in ether at −78°, followed by treatment with catalytic amounts of base, afforded 71% of the crystalline 4-deoxy-2-*C*-methylhexosid-3-ulose derivative **11**. The intermediate enol ester **10** could be isolated (55% yield), characterised unequivocally, and converted into **11** on exposure to traces of alkali.

When enolone esters (*e.g.*, **9, 13,** and **17**) were subjected to more basic conditions in polar solvents (*e.g.*, potassium carbonate in methyl sulfoxide), the main reaction was not carbonyl addition but elimination of the terminal benzoyloxy group to afford the dienolone intermediates **14** and **18**, respectively. In the presence of an alcohol, these products undergo addition of RO^- to the carbonyl group, benzoyl group migration, and protonation at the exocyclic double bond (see **14**). As expected from the steric course of the conversions **6**→**8** and **9**→**11**, the addition of alkoxide was stereocontrolled by the vicinal chiral centre, *i.e.*, attack occurs exclusively at the face opposite to the anomeric substituent. Accordingly, the products formed from **9** and **13** on treatment with methanol–potassium carbonate–methyl sulfoxide, namely, the dihydropyranones **15** (*S,S*) and **19** (*R,R*), are enantiomers (see Experimental).



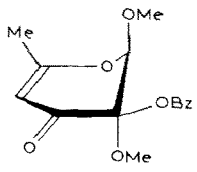
The yields of **15** and **19–21** were not optimised, but were in the range 70–80%, indicating highly stereoselective, if not stereospecific, reactions. The mechanistic interpretation was corroborated by the high yield (79%) of the crystalline (2*R*)-dienolone **18** (R = Me) obtained on treatment of the β-D-enolone ester **9** with tetrabutylammonium acetate–acetone, and by the fact that exposure of **18** to methanol or ethanol under slightly basic conditions gave the *R,R*-dihydropyranones **19** and **21**, respectively. When the alcohol was replaced by water, **9** and **18** in the presence of potassium carbonate–methyl sulfoxide gave methoxyallomaltol (**16**), since the half-acylketal corresponding to **19** (R′ = H), as expected, is unstable and yields the γ-pyrone system by loss of benzoic acid.

These highly stereoselective reactions emphasise the value of pyranoid sugar enolones as chiral synthons. Their potential for the construction of uscharidine-type cardiac glycosides (*e.g.*, **4**) and of spectinomycin-type antibiotics has already been exploited, resulting in an elegant total synthesis of (+)-spectinomycin (**5**) from L-

glucose[15], of analogues thereof[16], and of (+)-spectinomycin from D-glucose-derived enolone esters[17]. Analogous applications to steroidal aglycones having a *trans*-diol grouping in a ring A are being investigated.

Structural and configurational assignments. — The presence of a CH_2-CH-CH_2-system in the tetrahydropyranones **8** and **11**, for the protons at C-5 to C-7, was indicated by the ^{1}H-n.m.r. signals and the coupling patterns. The signals for the anomeric protons were singlets. The configurations at the tertiary centres in **8** and **11** were inferred from the mechanistic considerations noted above, from the $[\alpha]_D$ values (+16.5° and −96.5°, respectively), and, unequivocally, from X-ray crystallography of **11**[18], the pyranoid ring adopting a slightly flattened $^4C_1$ conformation with a torsional angle between the methoxy and tertiary benzoyloxy groups of 59.6°.

The dihydropyranones **15** and **19–21** exhibit λ_{max} at 233 and 267 nm typical for 1,3-enolones, and the ^{1}H- and ^{13}C-n.m.r. data are fully consistent with the structures assigned. Configurational information was derived from the facts that the chiral integrity at the anomeric centre is not affected in the rearrangements **13**→**15** and **9**→**19**, and that formation of the new chiral centre is essentially stereospecific since **15** and **19** are enantiomers. Mechanistically, such a course can be understood only in terms of rigid stereoanomeric control, which necessitates *trans*-disposition of the anomeric and tertiary alkoxy groups, and, hence, *S,S*-configuration for **15** and *R,R*-chirality for **19**.



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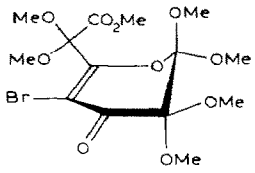

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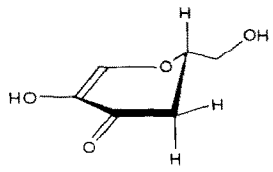

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This conclusion was confirmed by an X-ray crystal-structure analysis of the *R,R*-dihydropyranone **19** (Fig. 1), which demonstrated the vicinal methoxy groups to be *trans* with a torsional angle deviating from antiparallel by only 7°. The bond lengths and the bond angles (Fig. 2) are in the expected ranges[19], as is the glycosidic torsion angle (−65.8° for O-1–C-2/O-2–C-21, *cf.* Table I) which is only slightly smaller than that usually found for β-D-glycosides. The pyranoid ring adopts a sofa conformation (^2S), with all atoms except C-2 coplanar, which is somewhat distorted towards a $^2H_3$ half-chair. This is indicated by the torsional angles in Table I, the largest deviation from a five-atom plane being 6.7° for C-3, and by the least-squares plane parameters calculated for the two planes corresponding to the ^2S (plane I in Table II) and $^2H_3$ conformations (plane II).

Comparison of the conformational features of **19** with those of the two related dihydropyranones **22**[21] and **23**[22] reveals some analogies. The ring-puckering is most

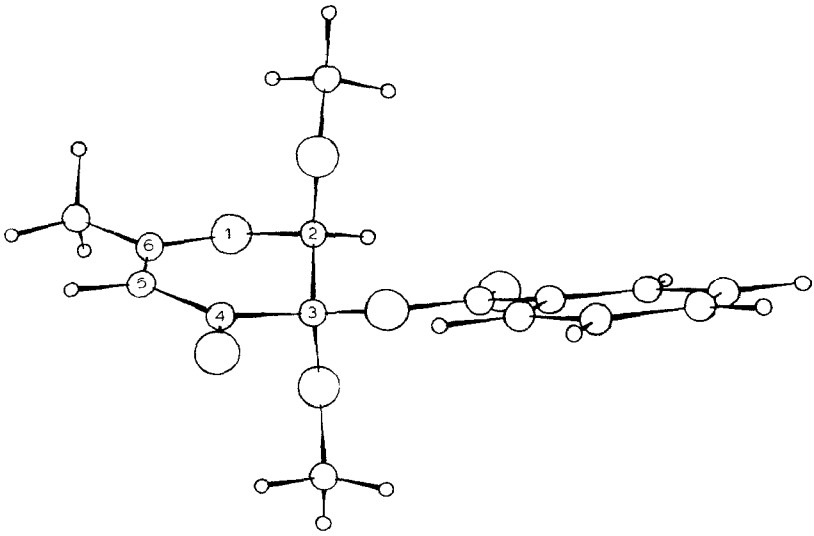

Fig. 1. Perspective view[20] of the molecular structure of (2*R*,3*R*)-3-benzoyloxy-2,3-dihydro-2,3-dimethoxy-6-methyl-4*H*-pyran-4-one (**19**). The pyranoid atoms have been numbered; for complete numbering, see Fig. 2.

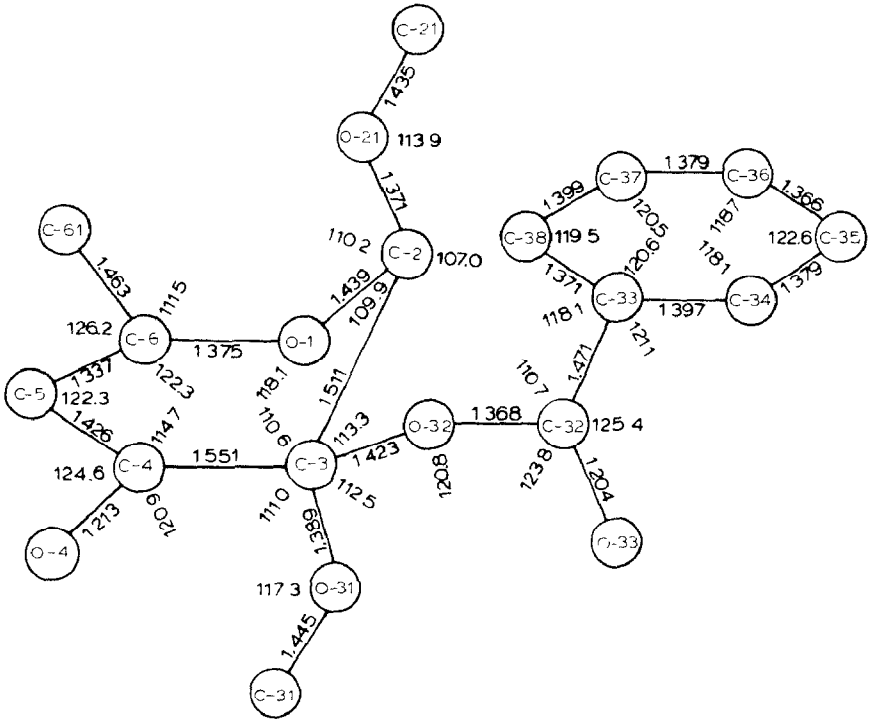

Fig. 2. Bond distances (Å) and bond angles (degrees) for **19**. Standard deviations are within 0.01 Å and 0.8°, respectively. Additional C-3 angles: C-2–C-3–O-31 = 106.3°; C-4–C-3–O-32 = 103.1°.

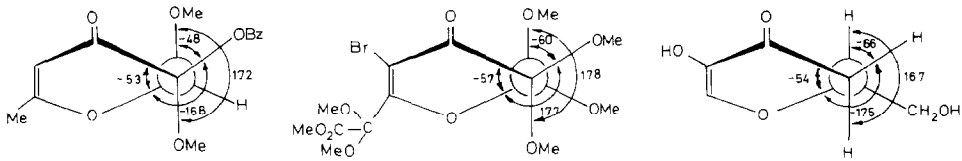

Fig. 3. Newman projections along the C-3→C-2-bond with torsional angles (degrees) from the X-ray data.

TABLE I

SELECTED TORSIONAL ANGLES (DEGREES) IN DIHYDROPYRANONES **19**, **22**[21], AND **23**[22]

Ring substituents in **19**		*Pyranoid ring*	**19**	**22**	**23**
O-1–C-2/O-21–C-21	−65.8	O-1–C-2/C-3–C-4	−52.6	−57	−54
O-1–C-2/C-3–O-32	−167.9	C-2–C-3/C-4–C-5	+34.4	+38	+30
O-21–C-2/C-3–O-31	−172.3	C-3–C-4/C-5–C-6	−6.7	−4	+2
O-21–C-2/C-3–O-32	−48.2	C-4–C-5/C-6–O-1	−2.8	−9	−11
C-21–O-21/C-2–C-3	174.7	C-5–C-6/O-1–C-2	−18.3	−15	−16
C-31–O-31/C-3–O-32	+178.3	C-6–O-1/C-2–C-3	+46.3	+47	+48
C-4–C-5/C-6–C-61	+175.8	O-4–C-4/C-5–C-6	180.0	175	—

TABLE II

LEAST-SQUARES PLANES FOR DIHYDROPYRANONES **19**, **22**[21], AND **23**[22]

Deviations (Å) of atoms from least-squares planes						
Atom	*Plane I* (^{2}S)			*Plane II* ($^2H_3$)		
	19	**22**	**23**	**19**	**22**	**23**
C-6	−0.046[a]	−0.07[a]	0.061[a]	−0.011[a]	−0.03[a]	0.042[a]
C-5	−0.016[a]	0.00[a]	−0.023[a]	0.011[a]	0.03[a]	−0.040[a]
C-4	+0.062[a]	0.07[a]	−0.021[a]	−0.005[a]	−0.01[a]	0.018[a]
C-3	−0.055[a]	−0.06[a]	0.032[a]	−0.215	−0.25	0.123
C-2	0.588	0.65	−0.630	0.446	0.48	−0.551
O-1	0.054[a]	0.07[a]	−0.047[a]	0.005[a]	0.02[a]	−0.020[a]
O-4	0.103	0.22	−0.003	0.026	0.14	0.041
Coefficients of equations for planes[b]						
m	−3.983	12.84	−3.384	−4.393	12.49	−2.411
n	6.451	0.18	11.067	6.285	0.98	11.377
r	−0.481	−3.32	−2.698	−1.170	−3.48	−2.412
s	2.263	3.03	3.067	3.354	2.75	3.156

[a]Atoms defining the plane. [b]mx + ny + rz = s.

pronounced in the most highly substituted compound (**22**), the torsional angles having near-ideal values of 175–178° and 57–60° (*cf.* Fig. 3 and Table I) and the pyranoid ring adopting a $^2S\leftrightarrow{}^2H_3$ conformation similar to those of **19** and **23**, in which the ring is somewhat flatter and the torsional angles for the substituents somewhat more distorted. Inspection of the data in Tables I and II suggests that, in the 2,3-dihydropyranones, C-2 is related to the more-or-less coplanar arrangement of the other ring atoms in such a way that the alkyl substituents are brought into a pseudo-equatorial position (as in **23**), whereas alkoxy moieties, due to the operation of dipolar interactions corresponding to the anomeric effect, may adopt pseudo-axial orientations. With increasing number and bulk of the ring substituents, the half-chair character of the $^2S\leftrightarrow{}^2H_3$ conformation increases. Thus, the conformational features of 2,3-dihydropyranones are very similar to those observed for their 2,6-dihydropyran-3-one analogues[23,24].

EXPERIMENTAL

General methods. — Melting points were determined on a Bock Monoskop instrument and are uncorrected. Spectral measurements were effected with Perkin–Elmer 141 (rotations), Jasco J-20 (c.d.), Perkin–Elmer 125 (i.r.), Varian XL 100 (^{1}H-n.m.r., 100 MHz), Bruker WM 300 (300 MHz), and Varian MAT 311 A (m.s.) instruments. T.l.c. was performed on Kieselgel 60 F_{254} (Merck), and was used to monitor the reactions and to ascertain the purity of the products; *A*, dichloromethane–ethyl acetate (19:1); *B*, benzene–ethyl acetate (9:1), *C*, chloroform–methanol (15:1), detection with u.v. light or by charring with sulfuric acid. Column chromatography was performed on Kieselgel 60 (70–230 mesh, Merck).

(2R,3S,6S)-2,3-Dibenzoyloxy-6-benzoyloxymethyl-3-methoxytetrahydropyran-4-one (**8**). — To a solution of (2*R*,6*S*)-2,4-dibenzoyloxy-6-benzoyloxymethyl-2*H*-pyran-3(6*H*)-one[3,13]* (**6**; 2.36 g, 5.0 mmol) and sodium iodide (0.75 g, 5 mmol) in methanol (250 mL) was added molecular sieve (3 Å, 500 mg) to exclude moisture. The mixture was stirred at ambient temperature overnight, filtered, and concentrated under reduced pressure, and a solution of residue in dichloromethane (100 mL) was washed with water, dried (Na_2SO_4), and concentrated. The residue was crystallised from acetone–hexane to yield **8** (2.15 g, 85%), m.p. 151–152°, $[\alpha]_D^{20}$ +16.9° (*c* 1.2, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (300 MHz), δ 8.1–7.3 (m, 15 H, 3 Ph), 7.22 (s, 1 H, H-2), 4.67 (m, 1 H, H-6), 4.53 and 4.48 (m, 2 H, AB portion of ABX system, H-7,7′), 3.54 (s, 3 H, OMe), 3.31 and 2.79 (2 dd, each 1 H, H-5*a*,5*e*); $J_{5e,5a}$ 13.6, $J_{5e,6}$ 2.8, $J_{5a,6}$ 11.6, $J_{6,7}$ 3.9, $J_{6,7'}$ 5.2, and $J_{7,7'}$ 11.8 Hz; ^{13}C (75.5 MHz), δ 195.48 (s, C-4), 166.03, 163.78, and 163.61 (3 s, 3 benzoyl C=O), 93.99 (d, C-2), 99.37 (s, C-3), 70.50 (d, C-6), 65.42 (t, C-7), 52.17 (q, OMe), and

*Carbohydrate nomenclature used previously[13]: 1,3,6-tri-*O*-benzoyl-4-deoxy-α-D-*glycero*-hex-3-enopyranos-2-ulose (**6**) and methyl 3,6-di-*O*-benzoyl-4-deoxy-β-D-*glycero*-hex-3-enopyranosid-2-ulose (**9**)

42.26 (t, C-5). F.d.-mass spectrum (12 mA): *m/z* 504 (M^+), 399 (M^+ − Bz), and 383 (M^+ − BzO).

Anal. Calc. for $C_{28}H_{24}O_9$: C, 66.66; H, 4.80. Found: C, 66.64; H, 4.63.

The conversion **6**→**8** may also be accomplished by stirring at room temperature for 15 min a methanolic suspension of **6** (2.0 g in 40 mL) after the addition of a catalytic amount of 2M sodium hydroxide (40 μL, 0.08 mol). Although complete dissolution did not occur at any stage, the reaction was quantitative (t.l.c.). Filtration and washing with cold methanol gave **8** (1.90 g, 89%) identical with the product described above.

(2R,3S,6S)-4-Benzoyloxy-6-benzoyloxymethyl-3-hydroxy-2-methoxy-3-methyl-2,3-dihydro-6H-pyran (**10**). — To a solution of (2*R*,6*S*)-4-benzoyloxy-6-benzoyloxymethyl-2-methoxy-2*H*-pyran-3(6*H*)-one[3,13]* (**9**; 2.0 g, 5.2 mmol) in ether (400 mL) at −78° was introduced portionwise during 30 min methylmagnesium iodide (10 mL of a freshly prepared ethereal solution, containing ~1.5 mmol of reagent per mL). T.l.c. (solvent *A*) then revealed **10** (R_F 0.28, major product) and three minor components of R_F 0.22 (C-3 epimer of **10**), 0.48 (**11**), and 0.53 (C-3 epimer of **11**). The mixture was poured into M ammonium chloride (400 mL) and stirred for 15 min. The organic phase was separated and the aqueous phase was extracted with ether (2 × 100 mL). The combined ether solutions were washed with water (100 mL), dried (Na_2SO_4), and concentrated. The crystalline residue was recrystallised from ether to give **10** (1.1 g, 55%), m.p. 112–114°, $[\alpha]_D^{20}$ −64° (*c* 0.7, chloroform). ^{1}H-N.m.r. data (100 MHz, $CDCl_3$): δ 8.2–7.2 (m, 10 H, 2 Ph), 5.78 (d, 1 H, H-5), 4.76 (dt, 1 H, H-6), 4.7–4.4 (m, 2 H, H-7,7′), 4.57 (s, 1 H, H-2), 3.61 (s, 3 H, OMe), 2.75 (s, 1 H, OH), and 1.42 (s, 3 H, Me); $J_{5,6}$ 2.4 and $J_{6,7}$ 6.0 Hz.

Anal. Calc. for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.26; H, 5.50.

(2R,3R,6S)-3-Benzoyloxy-6-benzoyloxymethyl-2-methoxy-3-methyltetrahydropyran-4-one (**11**, *methyl 2,6-di-O-benzoyl-4-deoxy-2-C-methyl-β-*D*-threo-hexopyranosid-3-ulose)*. — To a solution of **10** (400 mg, 1 mmol) in acetone (20 mL) was added 25mM sodium hydroxide (1 mL). The mixture was kept for 30 min at ambient temperature, diluted with ether (50 mL), and washed with water (2 × 30 mL). The aqueous phase was extracted with ether (20 mL), and the combined ether solutions were dried (Na_2SO_4) and concentrated under reduced pressure. Trituration of the residue with ether gave **11** (370 mg, 92%) as prisms, m.p. 129–131°, $[\alpha]_D^{20}$ −96.5° (*c* 0.8, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (300 MHz), δ 8.2–7.2 (m, 10 H, 2 Ph), 4.49 and 4.45 (m, 2 H, AB portion of ABX system, H-7,7′), 4.27 (s, 1 H, H-2), 3.98 (m, 1 H, H-6), 3.66 (s, 3 H, OMe), 2.92 (dd, 1 H, H-5*a*), 2.53 (dd, 1 H, H-5*e*), and 1.60 (s, 3 H, Me); $J_{5a,5e}$ 12.6, $J_{5a,6}$ 11.6, $J_{5e,6}$ 2.8, $J_{6,7}$ 4.1, $J_{6,7'}$ 5.2, and $J_{7,7'}$ 11.8 Hz; ^{13}C (75.5 MHz), δ 201.70 (s, C-4), 165.98 and 165.71 (2 s, 2 benzoyl C=O), 106.10 (d, C-2), 84.67 (s, C-3), 71.21 (d, C-6), 65.81 (t, C-7), 58.20 (q, OMe), 41.28 (t, C-5), and 14.59 (q, Me). F.d.-mass spectrum (10 mA): *m/z* 300 $(M + H)^+$ and 398 (M^+).

Anal. Calc. for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.30; H, 5.60.

(2S,3S)-3-Benzoyloxy-2,3-dihydro-2,3-dimethoxy-6-methyl-4H-pyran-4-one (**15**). — A mixture of (2*S*,6*S*)-4-benzoyloxy-6-benzoyloxymethyl-2-methoxy-2*H*-pyran-3(6*H*)-one[13,25]* (**13**; 765 mg, 2 mmol), potassium carbonate (320 mg, 2.3 mmol), methyl sulfoxide (12 mL), and methanol (3 mL) was stirred overnight at room temperature, and then processed as described below for conversion of **9** into enantiomeric **19**, to give **15** (405 mg, 69%), m.p. 106–107°, $[\alpha]_D^{19}$ +264° (*c* 1, chloroform). The ^{1}H-n.m.r., u.v., i.r., and m.s. data were identical with those of **19**. C.d. data (methanol): $\Delta\varepsilon$ −1.7 (229 nm), +6.9 (260), +1.0 (290), and +2.3 (319).

Anal. Calc. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.71; H, 5.54.

3-Hydroxy-2-methoxy-6-methyl-4H-pyran-4-one (**16**, *6-methoxyallomaltol*). — A mixture of the β-D-enolone **9** (200 mg, 0.52 mmol), or its α-anomer **13**, methyl sulfoxide (2 mL), water (0.4 mL), and potassium carbonate (80 mg) was stirred for 12 h, and then diluted with chloroform (30 mL) and water (20 mL). The organic phase was dried (Na_2SO_4) and concentrated to afford a brownish syrup, consisting of **16** (R_F 0.45, solvent *C*) and two minor components (R_F 0.56 and 0.36). Purification by elution from a short column of silica gel with chloroform–methanol (50 : 1) and recrystallisation of the product from ethanol gave **16** (52 mg, 67%) as needles, m.p. 169°; lit.[13] m.p. 169°. The ^{1}H-n.m.r. data and intense violet color on detection with ferric chloride solution corresponded with previous[12] findings.

(2R,6S)-4-Benzoyloxy-6-benzoyloxymethyl-2-cyclohexyloxy-2H-pyran-3(6H)-one (**17**). — To a stirred suspension of cyclohexanol (1.1 mL, 11 mmol), dichloromethane (30 mL), silver carbonate (2.8 g, 10 mmol), and molecular sieve (3 Å) was added (2*R*,6*S*)-4-benzoyloxy-6-benzoyloxymethyl-2-bromo-2*H*-pyran-3-(6*H*)-one[13,*] (**12**; 5.3 g, 10 mmol) in dichloromethane (20 mL). Stirring at room temperature was continued for 15 h, and the mixture was then filtered, washed with water (2 × 30 mL), dried (Na_2SO_4), and concentrated to dryness. The residue was recrystallised from methanol (200 mL) to give **17** (3.6 g, 81%), as colorless needles, m.p. 141.5–142°, $[\alpha]_D^{20}$ −116° (*c* 0.8, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (300 MHz), δ 8.2–7.4 (m, 10 H, 2 Ph), 6.91 (d, 1 H, H-5), 5.24 (s, 1 H, H-2), 5.08 (dt, 1 H, H-6), 4.76 and 4.76 (2 d, each 1 H, H-7,7'), 3.84 (m, 1 H, cyclohexyl CH), and 2.1–1.2 (m, 10 H, cyclohexyl CH_2); $J_{5,6}$ 3.5, $J_{6,7}$ 6.4, $J_{6,7'}$ 6.9, $J_{7,7'}$ 11.0 Hz; ^{13}C, δ 183.07 (s, C-3), 166.06 and 163.81 (2 s, benzoyl C=O), 142.23 (d, C-4), 134–128 (C-5 and 2 C_6H_5), 96.97 (d, C-2), 78.03 (d, cyclohexyl CH), 70.99 (s, C-6), 66.50 (q, C-7), 33.13, 31.56, 25.52, 24.07, and 23.73 (cyclohexyl CH_2). F.d.-mass spectrum (12 mA): *m/z* 450 (100%, M^+).

Anal. Calc. for $C_{26}H_{26}O_7$: C, 69.32; H, 5.82. Found: C, 69.30; H, 5.77.

(2R)-4-Benzoyloxy-2-methoxy-6-methylene-2H-pyran-3-one (**18**, *R* = *Me*). — To a solution containing **9**[13] (383 mg, 1 mmol) in dry acetone (10 mL) was added tetrabutylammonium acetate (600 mg, 2 mmol), and the solution was stirred at

*Carbohydrate nomenclature used previously[13]. 3,6-di-*O*-benzoyl-1-bromo-1,4-dideoxy-α-D-*glycero*-hex-3-enopyranos-2-ulose (**12**) and methyl 3,6-di-*O*-benzoyl-4-deoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**13**).

room temperature until reaction was complete (10–15 min; t.l.c., solvent *A*). The yellowish solution was concentrated *in vacuo* at ~25° (bath), and a solution of the residue in chloroform was washed twice with water, dried (Na_2SO_4), and concentrated. The resulting, reddish syrup crystallised on trituration with methanol. Recrystallisation from methanol afforded **18** (205 mg, 79%), as fine needles, m.p. 93–95°, $[\alpha]_D^{22}$ +17.7° (*c* 0.7, chloroform). ^{1}H-N.m.r. data (300 MHz, $CDCl_3$): δ 7.02 (s, 1 H, H-5), 5.17 and 4.92 (2 d, each 1 H, *J* 1.5 Hz, *exo*-CH_2), 5.10 (s, 1 H, H-2), and 3.61 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{12}O_5$: C, 64.61; H, 4.65. Found: C, 64.57; H, 4.60.

(2R,3R)-3-Benzoyloxy-2,3-dihydro-2,3-dimethoxy-6-methyl-4H-pyran-4-one (**19**). — A mixture of **9**[13] (765 mg, 2 mmol), potassium carbonate (320 mg, 2.3 mmol), methyl sulfoxide (12 mL), and methanol (3 mL) was stirred overnight at ambient temperature. T.l.c. (solvent *B*) then indicated the presence of **19** (R_F 0.55) and faint spots at R_F 0.69 and 0.28. The mixture was diluted with chloroform, washed with water, dried (Na_2SO_4), and concentrated to dryness. The resulting syrupy residue was purified by elution from a column (2 × 20 cm) of silica gel with benzene–ethyl acetate (15:1). Concentration of the eluate containing **19** (t.l.c.) and recrystallisation of the residue from chloroform–hexane furnished, in two crops, **19** (450 mg, 77%) as needles, m.p. 106–107°, $[\alpha]_D^{19}$ −263 (*c* 1, chloroform); λ_{max}^{MeOH} 233 (ε 1100) and 267 nm (ε 8500); $\nu_{max}^{CHCl_3}$ 1735 (ester C=O), 1690 (C=O), 1630 (phenyl), and 1605 cm^{-1} (C=C). C.d. data (methanol): +1.6 (228 nm), −6.8 (260), −1.0 (291), and −2.3 (318). N.m.r. data ($CDCl_3$): ^{1}H (100 MHz), δ 8.3–7.3 (m, 5 H, Ph), 6.18 (s, 1 H, H-5), 5.40 (s, 1 H, H-2), 3.51 and 3.38 (2 s, each 3 H, 2 OMe), and 2.06 (s, 3 H, Me-7); ^{13}C, δ 183.33 (C-4), 170.03 (C-6), 164.40 (benzoyl C=O), 133.5–128.5 (Ph), 103.19 and 102.65 (C-2,5), 95.49 (C-3), 57.63 and 52.33 (2 OMe), and 21.09 (C-7). Mass spectra: f.d., *m/z* 292 (100%, M^+); e.i. (70 eV), 292 (0.5%, M^+), 262 (0.47%, $M^+ - CH_2O$), 261 (0.78%, $M^+ - OMe$), 232 (78%, $M^+ - HCOOMe$), 208 (46%), 187 (21%, $M^+ - Bz$), and 105 (base peak, Bz^+).

Anal. Calc. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.66; H, 5.48.

The crystals of **19** were monoclinic, space group $P2_1$, with cell constants a = 9.461 (5), b = 7.117 (5), c = 11.677 (5) Å, β = 86.50 (5)°, V = 784.8 Å^3, Z = 2, D_y = 1.236 g.cm^{-3}, D_0 = 1.24 (2) g.cm^{-3} (flotation), μ(CuKα) = 7.2 cm^{-1}. Intensities were collected on a Stoe two-circle diffractometer (CuKα radiation) equipped with a graphite monochromator; the crystal was oriented along *b*. The 973 symmetry-independent reflections h01–h51 with δ <60° were measured in the δ–2δ scan mode. The data were corrected for background and for Lorentz and polarization factors, but not for absorption. The structure was solved with SHELX-76[26].

Anisotropic refinement of the carbon and oxygen atoms with fixed positions of H atoms converged to an R value of 0.069. None of the positional parameters, listed in Table III, shifted for more than 0.06 σ.

Storage of a solution of enolone **9** in pyridine–methanol (3:1) overnight at room temperature (50 mg in 1 mL) similarly effected its conversion into **19** (R_F 0.55, solvent *A*) with the concomitant formation of minor components at R_F 0.70,

TABLE III

ATOM POSITIONS AND THERMAL PARAMETERS[a] FOR THE HEAVY ATOMS IN DIHYDROPYRANONE **19**

Atom	$-x/a$	$-y/b$	$-z/c$	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O-1	0.6791(5)	0.1400(16)	1.0738(5)	0.051(3)	0 049(5)	0.063(4)	−0.005(3)	0 002(3)	0.001(3)
C-2	0.6755(7)	0.0472(0)	0.9646(7)	0.039(4)	0.043(6)	0.061(5)	−0.008(4)	−0.003(4)	0.004(4)
C-3	0.7341(8)	0.1757(17)	0.8703(7)	0.055(5)	0.029(6)	0.062(5)	−0.011(4)	−0.009(4)	0 000(4)
C-4	0.8820(8)	0.2509(20)	0.8982(8)	0.048(5)	0.066(8)	0.082(6)	0.004(6)	−0 004(5)	−0.012(5)
O-4	0.9693(6)	0.2928(19)	0.8220(6)	0.063(4)	0.145(8)	0.094(5)	−0.015(6)	0.017(4)	−0.050(5)
C-5	0.8994(8)	0.2826(21)	1.0171(7)	0.051(5)	0.063(7)	0.070(6)	−0.006(5)	−0.005(4)	0.004(5)
C-6	0.8011(9)	0.2326(19)	1.0985(7)	0.068(5)	0.043(7)	0.058(5)	−0.009(5)	−0 012(4)	0.011(5)
C-21	0.7104(11)	−0.2542(20)	1.0407(10)	0.074(6)	0.045(8)	0.111(8)	−0.004(7)	−0.004(6)	−0.005(6)
O-21	0.7598(5)	−0 1097(15)	0.9624(5)	0.040(3)	0.043(4)	0.081(4)	−0.003(3)	0.000(3)	0.004(3)
C-31	0.6673(12)	0.4628(23)	0.7767(10)	0.110(9)	0.076(10)	0.101(8)	0.033(8)	−0.015(7)	0.003(8)
O-31	0.6374(6)	0.3216(16)	0.8637(5)	0.068(4)	0.057(5)	0.075(4)	0.002(4)	−0.006(3)	0.012(4)
C-32	0 6567(9)	−0.0154(19)	0.7139(7)	0.060(5)	0.059(8)	0.061(5)	0.004(5)	−0.010(4)	0.010(5)
O-32	0.7613(5)	0.0827(16)	0.7635(5)	0.047(3)	0.067(6)	0.060(3)	−0.012(3)	−0.004(3)	−0.007(3)
C-33	0.7096(9)	−0.0957(20)	0.6034(7)	0.067(5)	0.058(7)	0.054(5)	−0.006(5)	−0.010(4)	0.000(5)
O-33	0.5393(6)	−0.0366(18)	0.7577(5)	0.055(3)	0 101(7)	0.071(4)	−0.011(5)	−0.002(3)	−0.012(4)
C-34	0.8468(10)	−0.0582(23)	0.5580(8)	0.078(6)	0.088(9)	0.069(6)	−0.004(7)	−0.002(5)	−0.015(7)
C-35	0.8876(12)	−0.1317(24)	0.4519(8)	0.097(8)	0.108(12)	0.075(7)	−0.025(7)	0.005(6)	0.001(8)
C-36	0.7998(14)	−0.2399(25)	0 3907(9)	0.133(11)	0 103(12)	0.075(7)	−0.015(8)	0.000(7)	−0.004(10)
C-37	0.6637(13)	−0.2724(25)	0.4354(9)	0 110(9)	0.122(13)	0.084(8)	−0.031(8)	−0.023(7)	−0 027(9)
C-38	0.6178(11)	−0.1993(22)	0.5425(8)	0 087(7)	0.069(9)	0 084(7)	−0.009(7)	−0 015(6)	−0.011(6)
C-61	0.8054(12)	0.2699(22)	1.2214(8)	0.107(8)	0.086(10)	0 071(6)	−0.016(7)	−0.020(6)	0.008(7)

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

0.38, and 0.0. Processing of the mixture as described above afforded **19** (16 mg, 42%) after recrystallisation from chloroform–hexane.

When the dienolone **18** (R = Me) was stirred with potassium carbonate–methanol–methyl sulfoxide as described for the conversion **9**→**19**, an analogous work-up afforded *R,R*-**19** (82%).

(2R,3R)-3-Benzoyloxy-2-cyclohexyloxy-2,3-dihydro-3-methoxy-6-methyl-4H-pyran-4-one (**20**). — The cyclohexylenolone **17** (900 mg, 2 mmol) was treated with potassium carbonate–methyl sulfoxide (320 mg in 12 mL) in the presence of methanol (3 mL) for 12 h at ambient temperature, followed by work-up as described above for the conversion **9**→**19**, to afford **20** as a syrup (495 mg, 69%), $[\alpha]_D^{20}$ −285° (*c* 0.6, chloroform). N.m.r. data ($CDCl_3$): ^1H (300 MHz), δ 6.36 (s, 1 H, H-2), 5.40 (d, 1 H, H-5), 3.70 (m, 1 H, cyclohexyl CH), 3.88 (s, 3 H, OMe), 2.04 (d, 3 H, $J_{5,7}$ 0.7 Hz, Me-6), and 2.0–1.0 (m, 10 H, cyclohexyl CH_2); ^{13}C, δ 183.78 (s, C-4), 170.25 (s, C-6), 164.50 (s, benzoyl C=O), 133.5–128.5 (Ph), 102.46 and 101.32 (d each, C-2,5), 95.89 (s, C-3), 79.03 (d, cyclohexyl C-1′), 52.34 (q, OMe), 33.3, 31.6, 25.3, 23.7, and 23.5 (t each, cyclohexyl C-2′/C-6′), and 21.30 (q, C-7). F.d.-mass spectrum: *m/z* 360 (100%, M^+).

Anal. Calc. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.67; H, 6.67.

(2R,3R)-3-Benzoyloxy-2,3-dihydro-3-ethoxy-2-methoxy-6-methyl-4H-pyran-4-one (**21**). — Treatment of the β-D-enolone **9** with potassium carbonate–methyl sulfoxide in the presence of ethanol, as described above for **19**, afforded amorphous **21** (73%), $[\alpha]_D^{20}$ −261° (*c* 1, chloroform); λ_{max}^{MeOH} 233 (ε 18,000) and 267 nm (ε 13,000). C.d. data (methanol): Δε +0.8 (226 nm), −7.2 (258), −0.9 (292), and −2.9 (318). ^1H-N.m.r. data (100 MHz, $CDCl_3$): δ 8.3–7.3 (m, 5 H, Ph), 6.20 (s, 1 H, H-5), 5.40 (s, 1 H, H-2), 3.51 (s, 3 H, OMe), 2.07 (s, 3 H, Me-6), and 1.15 (t, 3 H, ethyl Me). F.d.-mass spectrum: *m/z* 306 (M^+).

Anal. Calc. for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.64; H, 5.72.

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