

Synthesis of Ketofuranosides by Epoxidation-Ring Closure of Enol Ethers

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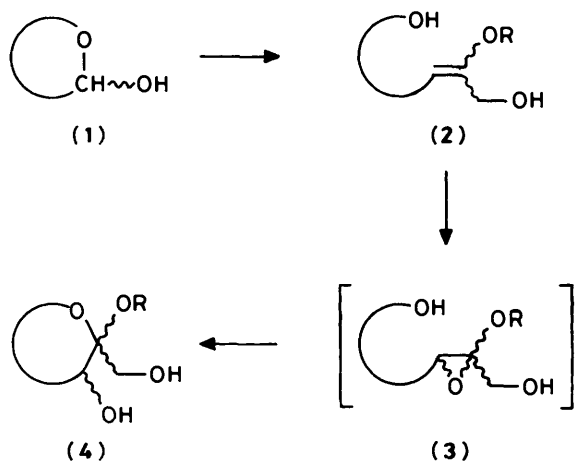
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Z- and *E*-Hydroxy enol ethers, obtained from aldoses, either by an elimination reaction followed by a reduction or by a Wittig-Horner reaction, have been epoxidized using *m*-chloroperbenzoic acid or the Sharpless' procedure to afford ketofuranosides. The stereochemistry of both the epoxidation and the subsequent cyclization are discussed.

The synthesis of complex ketofuranosides has been little studied. Traditional methods of glycosylation generally give low yields and poor stereoselectivity,¹ the only exception, to our knowledge, being a synthesis of 6-*O*- α -D-fructofuranosylglycosides by glycosylation of 6-*O*-trityl derivatives of aldohexoses with thio-ortho esters derived from D-fructose, which proceeds in good yields and high stereoselectivity.² This procedure, however, cannot afford the β anomer.

With the aim of finding a more general and versatile method to ketofuranosides, we tried a different approach and we now present our results. Our approach follows a scheme we previously used³ in the preparation of aldohexopyranosides, which involves the formation of the appropriate enol ether (2) from an aldose (1) followed by epoxidation to produce (4) through the spontaneous cyclization of the intermediate epoxide (3) (see Scheme 1).



The simple enol ethers (*Z*-) or (*E*-)2,4,6-tri-*O*-benzyl-3-deoxy-D-*erythro*-hex-2-enitols (9a) and (10a) were both obtained in pure form from the commercially available 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose by treatment with NaBH₄, according to Rao and Perlin.⁴ A more complex *Z*-enol ether (9c), precursor of psico- or fructo-furanosyl disaccharides, was prepared according to Scheme 2. Acetylation of the enol ether (9a) to (5) followed by ozonolysis afforded 2,4-di-*O*-benzyl-3-*O*-acetyl-D-erythrose (6) in which the protection of the 3-OH group avoids the formation of semiacetalic dimers and leaves the aldehyde group free for the next step. Compound (6) was condensed with the phosphono-acetate (7)⁵ by a Wittig-Horner

reaction⁵ using KH as base. The obtained *Z*-enoate (8)† was then reduced with DIBAH to give the desired enol ether (9c).

The epoxidation of the synthesized enol ethers (Scheme 3) was performed either with MCPBA or through the Sharpless' procedure.⁶

The MCPBA epoxidation occurred easily owing to the electron-rich nature of the enol ether double bond. The same was not true with the Sharpless reaction, probably owing to the presence of several oxygens which could complex titanium and decrease the reactivity.

The above procedures afforded furanosides (15)–(18) in moderate (Sharpless) to good yields (MCPBA); in all cases mixtures of products were obtained and careful separation by chromatography furnished the pure compounds. The obtained results are summarized in Table 1.

During the epoxidation-ring closure reaction two new stereogenic centres, C-2 and C-3, are formed whose configuration had to be assigned. This was a quite difficult problem and was initially solved for the benzyl furanosides (15a)–(18a).

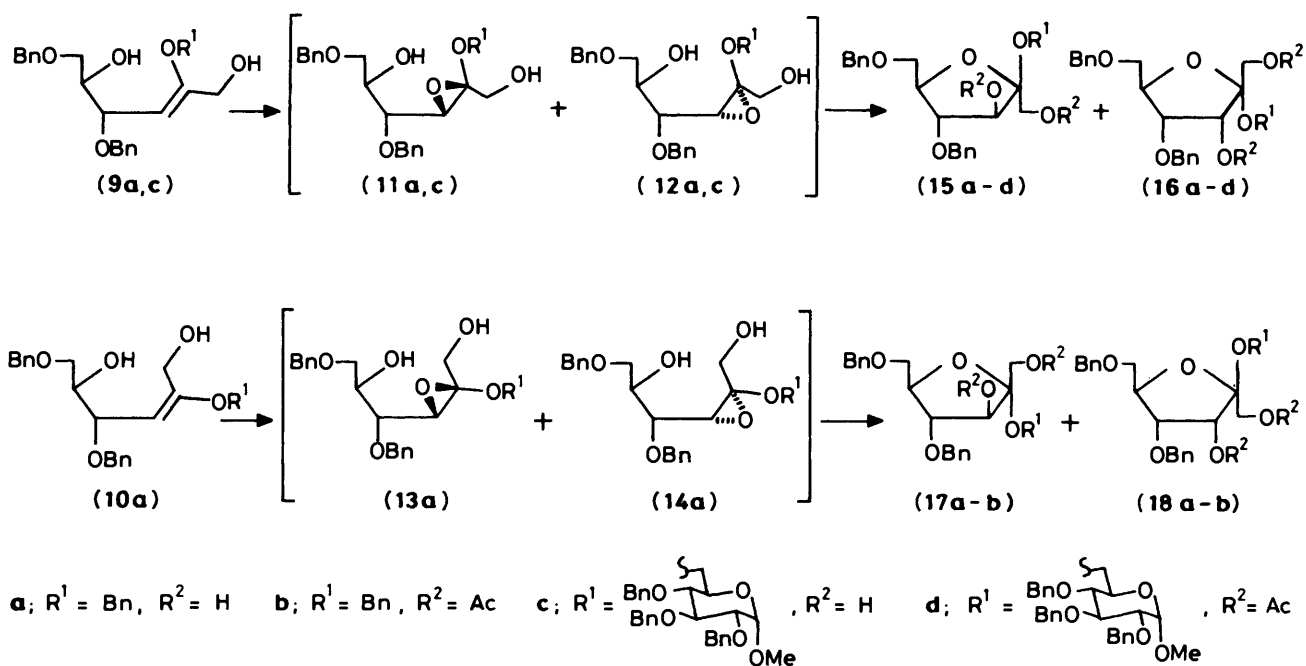
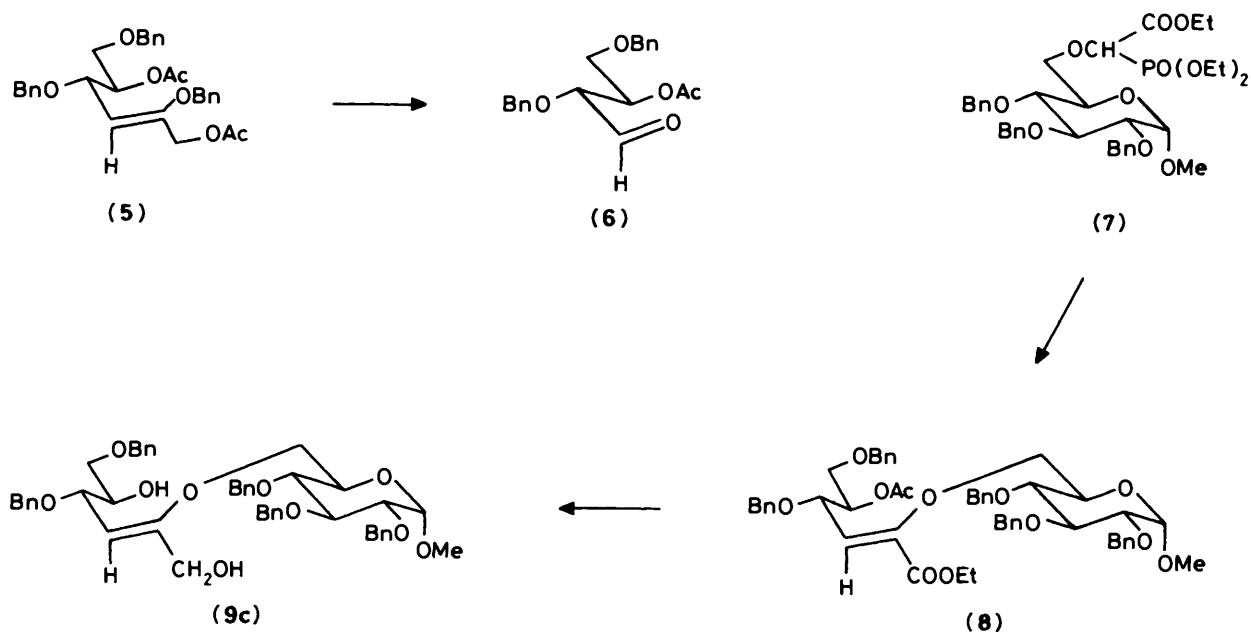
Since it is known that in five-membered rings it is difficult to determine the configurations of the stereocentres from the ¹H n.m.r. vicinal coupling constants between the ring protons, we made an attempt to determine first the configuration of C-3 using the n.o.e. technique. However, n.o.e. experiments carried out on the acetylated derivatives (15b)–(18b) by irradiation of 3-H (Table 2) did not allow unambiguous assignments.

The C-3 configuration of the benzyl furanosides (15a)–(18a) was, therefore, determined by chemical correlation with authentic samples of D-fructose and D-psicose. The compounds (15a) and (17a) gave D-fructose by catalytic hydrogenolysis of the benzyl groups, while (16a) and (18a) gave D-psicose.

The absolute configuration at C-2 of the benzyl ketofuranosides was deduced from its relative configuration with respect to C-3, determined by ¹³C n.m.r. spectroscopy. In fact, literature data⁷ show that in psico- or fructo-furanosides, the anomeric carbon atom resonates at 103–105 p.p.m. when O-2 and O-3 are *cis* oriented (α -psico and β -fructo derivatives) while the same carbon atom resonates at 107–109 p.p.m. when they are *trans* oriented (β -psico and α -fructo configuration). The values observed in our case, shown in Table 3 allow assignment of the anomeric configurations to the benzyl ketofuranosides (15a)–(18a).

The structure of the ketofuranosyl disaccharides (15c) and (16c) was then determined by comparison of their ¹H n.m.r.

† The configuration of the double bond was deduced from the chemical shift of the vinylic proton;⁵ the *E* isomer could not be detected in the reaction mixture.



spectra with those of the benzylfuranosides (**15a**)—(**18a**). The signals of the furanosidic moiety of the acetylated disaccharides (**15d**) and (**16d**) showed the same chemical shift and the same coupling pattern as the corresponding signals of respectively the furanosides (**15b**) and (**16b**), and allowed assignment of the structure of the β -fructofuranosyl derivative to (**15c**) and α -psicofuranosyl derivative to (**16c**). The assignment was also confirmed by their n.o.e. and the ^{13}C values.

The overall stereochemistry of the epoxidation-cyclization process results from three factors: (1) the *E/Z* configuration of

the double bond; (2) the stereoselectivity of the epoxidation reaction; and (3) the stereospecificity of the formation of the furanosidic ring.

The stereochemistry of the epoxidation reaction can be inferred from the stereochemistry at C-3 of the ketofuranosides formed since the configuration of this stereocentre does not change during the spontaneous cyclization. In our case it depended on the reagent.

Epoxidation with MCPBA (entries 1, 2, and 3) gave preferentially the psicofuranosides, which are formed by

Table 1.

Entry	Enol ether	Double bond geometry	Epoxidizing agent	Products	Proportions ^a	Yield (%) ^b
1	(9a)	Z	MCPBA	(15a) + (16a) + (18a)	15:69:16	98
2	(10a)	E	MCPBA	(17a) + (18a)	30:70	94
3	(9c)	Z	MCPBA	(15c) + (16c)	30:70	81
4	(9a)	Z	AE[D-(-)-DIPT]	(15a) + (16a) + (18a)	17:31:52	68
5	(10a)	E	AE[D-(-)-DIPT]	(17a) + (18a)	10:90	71
6	(9a)	Z	AE[L-(+)-DIPT]	(15a) + (16a) + (18a)	67:13:20	66
7	(10a)	E	AE[L-(+)-DIPT]	(17a) + (18a)	5:95	64
8	(9c)	Z	AE[D-(-)-DIPT]	(15c) + (16c)	85:15	65
9	(9c)	Z	AE[L-(+)-DIPT]	(15c) + (16c)	75:25	63

^a Determined by h.p.l.c. ^b Isolated products.

Table 2. N.O.e. experiments

Compound	(15b)	(16b)	(17b)	(18b)	(15d)	(16d)
N.O.e. ^a (%)	—	8.6	3.7	5.5	—	6.0

^a Generated in 4-H (or 4'-H) by irradiation of 3-H (or 3'-H).

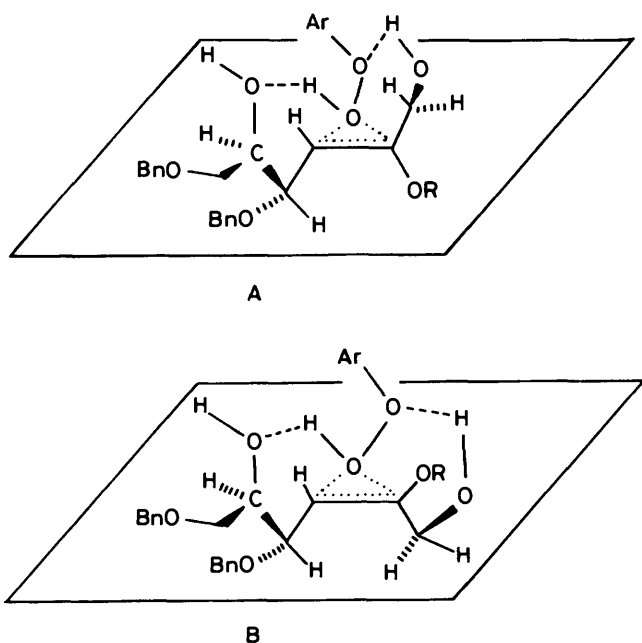


Figure.

cyclization of the 3*R* intermediate epoxides. The ratio between the psico and the fructo configuration is not strongly modified by the geometry of the double bond or the nature of the substituent at the vinylic oxygen.

The preferential formation of the 3*R* epoxides (11a,c) and (13a) can be explained according to the observations of Kishi⁸ on the co-operative effect by a hydroxy group and an ether or an alcohol oxygen in directing the steric course of epoxidation with a peracid. The most preferred conformation of *Z* and *E* enol ethers in the transition state would be respectively A and B (Figure): the hydrogen at C-4 is in the plane of the double bond, and MCPBA could be complexed by two hydrogen bonds.

In the Sharpless reaction the steric course of the epoxidation was more complex and sometimes unexpected (see for example entries 5/7 and 8/9 in which use of enantiomeric tartrates leads in each case to the same predominant product). This was probably due to the contemporaneous presence in the substrate

Table 3. ¹³C Chemical shifts of the anomeric carbon of the furanosidic ring

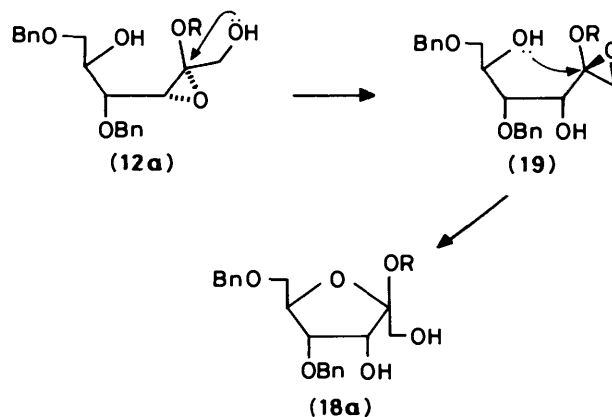
Compound	(15a)	(16a)	(17a)	(18a)	(15c)	(16c)
Chemical shift (p.p.m.)	104.6	105.1	109.0	109.3	104.4	104.8

of several ether oxygens and of a secondary homoallylic hydroxy group bound to a stereogenic carbon atom, which can, in certain cases, counteract the effect of the primary allylic hydroxy group-tartrate system.

This leads to a stereoselectivity lower than those generally observed in this type of reactions and, most importantly, to lack of predictivity about the steric outcome of the reaction.

The stereospecificity of the epoxide opening can be inferred from the relative stereochemistry at C-2 and C-3 in the furanosidic ring. Two products are expected, from a given configuration of the double bond, by stereospecific cyclization of the intermediate 3*R* and 3*S* epoxides. So, *E* enol ethers should lead to β-psico- and α-fructo-furanosides, while *Z* enol ethers should lead to β-fructo and α-psico-furanosides (Scheme 2).

This proved true for all the compounds examined both in the MCPBA and in the Sharpless experiments, except for the 3*R* epoxide (12a) (entries 1, 4, and 6). In fact, in these cases a substantial amount of β-psicofuranoside was formed, beside the expected α-psico and β-fructo-furanoside. The 2*S*,3*R* epoxide was opened, therefore, in a non-stereospecific way. This lack of stereospecificity could be attributed to a partial transposition of the epoxidic ring⁹ to the 1, 2 positions with inversion of configuration at C-2, followed by opening of the new epoxide (19) with a second inversion at C-2 to give the β-psico compound (18a) (Scheme 4).



Scheme 4.

In conclusion, the synthesis of ketofuranosides by epoxidation-ring closure of the appropriate enol ethers proceeds in moderate to good yields and with good stereoselectivity. From the point of view of the stereochemical outcome, MCPBA offers a better predictivity than the Sharpless method.

Experimental

N.m.r. spectra were recorded for solutions in deuteriochloroform with tetramethylsilane as internal standard on Bruker WP 80 (80 MHz) and Varian Associates XL 200 (200 MHz) spectrometers.

Optical rotations were determined on a Perkin-Elmer 241 polarimeter in chloroform solution. T.l.c. was performed on Merck 60 F-254 (0.25 mm thickness) silica gel plates and detected by u.v. light or by 50% aqueous H₂SO₄ spray followed by heating at 110 °C for 5 min. Column chromatography was performed on Merck 60 silica gel (70–230 mesh). Flash chromatography was performed on Woelm 0–63 silica gel (<230 mesh). High pressure liquid chromatography (h.p.l.c.) was performed on a Varian LC 5020 instrument equipped with a 254 nm u.v. detector. MCPBA refers to *m*-chloroperbenzoic acid (85%), TBHP refers to a 3.4M solution of *t*-butyl hydroperoxide in toluene,¹⁰ DIPT refers to di-isopropyl tartrate, DIBAH refers to a 1.2M solution of di-isobutyl-aluminium hydride in toluene, AcOEt refers to ethyl acetate.

2,4-Di-O-benzyl-3-O-acetyl-D-erythrose (6).—The diacetyl hexenitol (**5**)⁴ (550 mg) was dissolved in dry dichloromethane (60 ml). Ozone was bubbled through the solution cooled at –78 °C, until the appearance of a light blue colour. Nitrogen was then bubbled through to eliminate the excess of ozone and triphenylphosphine (290 mg) was added. The mixture was stirred for 15 min at –78 °C and 1 h at room temperature. The solvent was then removed under reduced pressure and the resulting crude reaction mixture chromatographed (SiO₂, hexane–AcOEt, 8:2) to afford the title compound (330 mg, 91%) as an oil, $[\alpha]_D^{20} + 10.5^\circ$ (*c* 1.0 in CHCl₃); δ_H (80 MHz) 2.05 (3 H, s, Ac), 3.63 and 3.69 (2 H, AB part of an ABX system, $J_{3,4A}$ 5.5 Hz, $J_{3,4B}$ 5.5 Hz, $J_{4A,4B}$ 10.2 Hz, 4-H_A and 4-H_B), 4.03 (1 H, dd, $J_{1,2}$ 1.6 Hz, $J_{2,3}$ 4.5 Hz, 2-H), 4.4–4.8 (4 H, 1 s and 1ABq, CH₂Ph), 5.35 (1 H, ddd, $J_{2,3}$ 4.5 Hz, $J_{3,4A}$ 5.5 Hz, $J_{3,4B}$ 5.5 Hz, 3-H), 7.1–7.4 (10 H, m, Ph), and 9.60 (1 H, d, $J_{1,2}$ 1.6 Hz, 1-H) (Found: C, 70.4; H, 6.8. C₂₀H₂₂O₅ requires C, 70.1; H, 6.5%).

Enol ethers (9a,c) and (10a).—The simple enol ethers (**9a**) and (**10a**) were prepared according to the method of Rao and Perlin.⁴ The *Z*-enol ether (**9c**) was synthesized according to Sinay's procedure⁵ by reaction of the phosphonoacetate (**7**) $[\alpha]_D^{20} + 21.5^\circ$ (*c* 1.0 in CHCl₃), δ_H (80 MHz) 1.0–1.6 (9 H, m, OCH₂CH₃), 3.33 and 3.35 (3 H, 2 s, OCH₃), with the protected erythrose (**15**) but using KH instead of NaH as base. Chromatography (SiO₂, hexane–AcOEt, 75:25) afforded the methyl (6-O-[(3'S,4'R)-4'-acetoxy-3',5'-dibenzyloxy-1'-ethoxy-carbonylpent-1-1'(Z)-enyl]-2,3,4-tri-O-benzyl- α -D-glucopyranoside (**8**) (44% unoptimized yield) as an oil, R_F (hexane–AcOEt, 7:3) 0.38, $[\alpha]_D^{20} + 33^\circ$ (*c* 1.0 in CHCl₃); δ_H (80 MHz) 1.28 (3 H, t, OCH₂CH₃), 2.01 (3 H, s, Ac), 3.25 (3 H, s, OCH₃), 3.30–5.15 (22 H, m, 1-H, 2-H, 3-H, 4-H, 5-H, 6-H₂, 4'-H, 6'-H₂, OCH₂CH₃ and CH₂Ph), 5.15–5.42 (1 H, m, 5'-H), 6.10 (1 H, d, $J_{3,4}$ 9.6 Hz, 3'-H), and 7.0–7.6 (25 H, m, Ph) (Found: C, 71.1; H, 6.9. C₅₂H₅₈O₁₂ requires C, 71.4; H, 6.6%).

A solution of the enol ether (**8**) (200 mg, 0.24 mmol) in dry diethyl ether (4 ml) was cooled to –78 °C and DIBAH (1 ml) was added. The mixture was stirred at –78 °C for 2 h after which the reaction was quenched with methanol (0.5 ml). After 1 h Celite (0.5 g) was added and after further 15 min sodium sulphate (0.5 g). The reaction mixture was filtered through a

Celite pad, the filtrate evaporated under reduced pressure, and the residue chromatographed on SiO₂ using hexane–AcOEt (3:7) and to give methyl 6-O-[(3'S,4'R)-3',5'-dibenzyloxy-4'-hydroxy-1'-hydroxymethylpent-1'(Z)-enyl]-2,3,4-tri-O-benzyl- α -D-glucopyranoside (**9c**) (81%) as an oil, R_F (hexane–AcOEt 3:7) 0.40, $[\alpha]_D^{20} + 16^\circ$ (*c* 0.8 in CHCl₃); δ_H (200 MHz) 3.32 (3 H, s, OCH₃), 3.50 (1 H, dd, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9 Hz, 2-H), 3.51 (1-H, dd, $J_{5,6A}$ 2.5 Hz, $J_{6A,6B}$ 10 Hz, 6'-H_A), 3.52 (1 H, t, $J_{3,4} = J_{4,5}$ 9 Hz, 4-H), 3.58 (1 H, dd, $J_{5,6B}$ 3.5 Hz, $J_{6A,6B}$ 10 Hz, 6'-H_B), 3.77 (1 H, dt, $J_{4,5}$ 9 Hz, $J_{5,6}$ 3 Hz, 5-H), 3.78–3.89 (1 H, m, 5'-H), 3.97 (1 H, t, $J_{2,3} = J_{3,4}$ 9 Hz, 3-H), 4.02 (2 H, d, $J_{5,6}$ 3 Hz, 6-H₂), 4.12 (2 H, br s, 1'-H₂), 4.46 (1 H, dd, $J_{3,4}$ 9.5 Hz, $J_{4,5}$ 6 Hz, 4'-H), 4.59 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), 4.84 (1 H, d, $J_{3,4}$ 9.5 Hz, 3'-H), 4.3–5.0 (10 H, 1 s and 4 ABq, CH₂Ph), and 7.1–7.4 (25 H, m, Ph) (Found: C, 72.7; H, 7.1. C₄₈H₅₄O₁₀ requires C, 72.9; H, 6.9%).

General Procedure for MCPBA Epoxidation.—In a typical procedure a solution of the appropriate *E* or *Z* enol ether (0.2 mmol) in dichloromethane (5 ml) was cooled to 0 °C.

Na₂HPO₄ (0.02 mmol) and MCPBA (45 mg, 10% molar excess) were added and the solution was left at 0 °C until the starting material disappeared (t.l.c. hexane–AcOEt, 1:1). After 3–6 h 5% aqueous FeSO₄ (2 ml) was added and the mixture was stirred at room temperature over 30 min. The mixture was extracted with dichloromethane and the organic phase was washed with saturated aqueous NaHCO₃ and water, dried (Na₂SO₄), and evaporated under reduced pressure. The furanosides were carefully separated by chromatography on SiO₂ as follows: (**17a**) and (**18a**), obtained from (**10a**), were separated using hexane–AcOEt (6:4) as eluant; (**18a**) was isolated from the reaction mixture obtained from (**9a**) using the same eluant, but (**15a**) and (**16a**) were eluted together and separated by a second chromatography using toluene–acetone (85:15). Finally, compounds (**15c**) and (**16c**) were separated by flash chromatography using benzene–AcOEt (6:4) as eluant. The relative ratios of the diastereoisomeric glycosides were determined by h.p.l.c. on Merck Hibar LiChrosorb Si-60, 25 cm × 4 mm column, flow rate 1.2 ml/min, hexane–ethyl acetate (1:1) as solvent.

The products (**15a**)–(**18a**) were deprotected by catalytic hydrogenation (Pd/C 5%, 1 atm, EtOH) to give the free ketohexoses. These were compared with authentic samples of D-fructose and D-psicose¹¹ by t.l.c. and gas chromatography, as propylsilyl derivatives,¹² to determine the stereochemistry at C-3. In fact, t.l.c. of D-fructose showed a spot at R_F 0.37 while the R_F of D-psicose was 0.43 (SiO₂, CH₃CN–H₂O, 8:2). Moreover, gas chromatography (Carbowax 20 M, carrier gas N₂, carrier pressure 1.4 atm, oven temp. 150 °C) showed only a peak with R_i of 25.7 min when D-fructose was analyzed. In the case of D-psicose 4 peaks were detected at R_i 23.3, 25.6, 27.6 and 31.2 min.

General Procedure for the Sharpless Asymmetric Epoxidation.⁶—A 10 ml flask equipped with a magnetic stir bar was oven dried and then fitted with a septum cap and flushed with nitrogen. The flask was charged with dry CH₂Cl₂ (2 ml) and cooled to –23 °C. Ti(OiPr)₄ (68 μ l, 0.23 mmol) and DIPT (60 μ l, 0.29 mmol) were added *via* a syringe and the mixture was stirred for 5 min.

The appropriate enol ether (0.23 mmol) dissolved in dry CH₂Cl₂ (1 ml) and TBHP (0.28 ml, 0.95 mmol, 4 equiv) were then finally added. The reaction was monitored by t.l.c. (hexane–AcOEt, 1:1) until the starting material disappeared. The mixture was then diluted with diethyl ether (1.5 ml) and saturated aqueous Na₂SO₄ (0.1 ml) added. After 2 h the mixture was filtered through a Celite pad and the filtrate evaporated under reduced pressure. The following compounds were prepared by both methods.

Benzyl 4,6-di-O-benzyl-β-D-fructofuranoside (15a), as an oil, R_F (toluene-acetone) 0.36, $[\alpha]_D^{20} + 15^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz) 3.49 (1 H, dd, $J_{5,6A}$ 6.5 Hz, $J_{6A,6B}$ 10 Hz, 6- H_A), 3.56 (1 H, dd, $J_{5,6B}$ 4 Hz, $J_{6A,6B}$ 10 Hz, 6- H_B), 3.71 and 3.77 (2 H, ABq, $J_{1A,1B}$ 12 Hz, 1- H_A and 1- H_B), 3.96 (1 H, t, $J_{3,4} = J_{4,5}$ 6.5 Hz, 4-H), 4.10–4.22 (1 H, m, 5-H), 4.41 (1 H, d, $J_{3,4}$ 6.5 Hz, 3-H), 4.44–4.86 (6 H, 3 ABq, CH_2Ph), and 7.1–7.4 (15 H, m, Ph) (Found: C, 71.8; H, 6.8. $\text{C}_{27}\text{H}_{30}\text{O}_6$ requires C, 72.0; H, 6.7%).

Benzyl 4,6-di-O-benzyl-α-D-psicofuranoside (16a), as an oil, R_F (toluene-acetone, 8:2) 0.40, $[\alpha]_D^{20} + 38^\circ$ (c 1.1 in CHCl_3); δ_H (200 MHz) 3.43 (1 H, dd, $J_{5,6A}$ 3.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_A), 3.56 (1 H, dd, $J_{5,6B}$ 3.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_B), 3.71 and 3.79 (2 H, ABq, $J_{1A,1B}$ 11.5 Hz, 1- H_2), 3.95 (1 H, dd, $J_{3,4}$ 6.5 Hz, $J_{4,5}$ 3 Hz, 4-H), 4.24 (1 H, q, Hz, 5-H), 4.36 (1 H, d, $J_{3,4}$ 6.5 Hz, 3-H), 4.4–4.9 (6 H, 3 ABq, CH_2Ph), and 7.2–7.5 (15 H, m, Ph) (Found: C, 71.9; H, 6.8%).

Benzyl 4,6-di-O-benzyl-α-D-fructofuranoside (17a), as an oil, R_F (hexane-AcOEt, 1:1) 0.44, $[\alpha]_D^{20} + 42^\circ$ (c 0.5 in CHCl_3); δ_H (200 MHz) 3.56 (1 H, dd, $J_{5,6A}$ 3 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_A), 3.73 (1 H, dd, $J_{5,6B}$ 2.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_B), 3.78 and 3.83 (2 H, ABq, $J_{1A,1B}$ 12 Hz, 1- H_2), 4.03 (1 H, dd, $J_{3,4}$ 3.5 Hz, $J_{4,5}$ 5.5 Hz, 4-H), 4.21 (1 H, ddd, $J_{4,5}$ 5.5 Hz, $J_{5,6A}$ 3 Hz, $J_{5,6B}$ 2.5 Hz, 5-H), 4.38 (1 H, d, $J_{3,4}$ 3.5 Hz, 3-H), 4.48–4.79 (6 H, 1 s and 2 ABq, CH_2Ph), and 7.2–7.5 (15 H, m, Ph) (Found: C, 71.7; H, 6.9%).

Benzyl 4,6-di-O-benzyl-β-D-psicofuranoside (18a), as an oil, R_F (hexane-AcOEt 1:1) 0.35, $[\alpha]_D^{20} + 7^\circ$ (c 1.1 in CHCl_3); δ_H (200 MHz) 3.48 (1 H, dd, $J_{5,6A}$ 5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_A), 3.60 (1 H, dd, $J_{5,6B}$ 3.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_B), 3.85 and 3.91 (2 H, ABq, $J_{1A,1B}$ 12 Hz, 1- H_2), 4.18 (1 H, d, $J_{3,4}$ 4 Hz, 3-H), 4.22–4.36 (2 H, m, 4-H and 5-H), 4.46–4.66 (6 H, 1 and 2 ABq, CH_2Ph), and 7.1–7.4 (15 H, m, Ph) (Found: C, 71.6; H, 7.0%).

Benzyl 1,3-di-O-acetyl-4,6-di-O-benzyl-β-D-fructofuranoside (15b), as an oil, R_F (hexane-AcOEt, 7:3) 0.43, $[\alpha]_D^{20} - 23^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz) 2.01 and 2.07 (6 H, 2 s, Ac), 3.54 (1 H, dd, $J_{5,6A}$ 5 Hz, $J_{6A,6B}$ 10 Hz, 6- H_A), 3.64 (1 H, dd, $J_{5,6B}$ 4 Hz, $J_{6A,6B}$ 10 Hz, 6- H_B), 4.08–4.22 (1 H, m, 5-H), 4.22 and 4.28 (2 H, ABq, $J_{1A,1B}$ 11.5 Hz, 1- H_2), 4.34 (1 H, t, $J_{3,4}$ 7 Hz, $J_{4,5}$ 7 Hz, 4-H), 4.4–4.7 (6 H, 1 s and 2 ABq, CH_2Ph), 5.51 (1 H, d, $J_{3,4}$ 7 Hz, 3-H), 7.1–7.4 (15 H, m, Ph) (Found: C, 69.2; H, 6.7. $\text{C}_{31}\text{H}_{34}\text{O}_8$ requires C, 69.7; H, 6.4%).

Benzyl 1,3-di-O-acetyl-4,6-di-O-benzyl-α-D-psicofuranoside (16b), as an oil, R_F (hexane-AcOEt, 7:3) 0.42, $[\alpha]_D^{20} + 31.5^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz) 1.93 and 2.09 (6 H, 2 s, Ac), 3.45 (1 H, dd, $J_{5,6A}$ 4 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_A), 3.56 (1 H, dd, $J_{5,6B}$ 3.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_B), 4.15 (1 H, t, $J_{3,4}$ 6.5, $J_{4,5}$ 6.5 Hz, 4-H), 4.16 and 4.33 (2 H, ABq, $J_{1A,1B}$ 12 Hz, 1- H_A and 1- H_B), 4.1–4.3 (1 H, m, 5-H), 4.4–4.9 (6 H, 3 ABq, CH_2Ph), 5.20 (1 H, d, $J_{3,4}$ 6.5 Hz, 3-H), and 7.1–7.4 (15 H, m, Ph) (Found: C, 69.4; H, 6.4%).

Benzyl 1,3-di-O-acetyl-4,6-di-O-benzyl-α-D-fructofuranoside (17b), as an oil, R_F (hexane-AcOEt, 7:3) 0.48, $[\alpha]_D^{20} + 78^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz) 1.99 and 2.01 (6 H, 2 s, Ac), 3.58 (2 H, d, $J_{5,6}$ 5 Hz, 6- H_2), 3.83 (1 H, dd, $J_{3,4}$ 1.5 Hz, $J_{4,5}$ 5 Hz, 4-H), 4.19 (1 H, d, $J_{1A,1B}$ 12 Hz, 1- H_A), 4.25 (1 H, q, $J_{4,5} = J_{5,6}$ 5 Hz, 5-H), 4.4–4.9 (7 H, m, 1- H_B and CH_2Ph), 5.42 (1 H, d, $J_{3,4}$ 1.5 Hz, 3-H), and 7.2–7.5 (15 H, m, Ph) (Found: C, 69.2; H, 6.8%).

Benzyl 1,3-di-O-acetyl-4,6-di-O-benzyl-β-D-psicofuranoside (18b), as an oil, R_F (hexane-AcOEt, 7:3) 0.47, $[\alpha]_D^{20} + 16^\circ$ (c 0.8 in CHCl_3); δ_H (200 MHz) 2.02 and 2.12 (6 H, 2 s, Ac), 3.41 (1 H, dd, $J_{5,6A}$ 5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_A), 3.62 (1 H, $J_{5,6B}$ 2.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_B), 4.2–4.3 (1 H, m, 5-H), 4.33 (1 H, dd, $J_{3,4}$ 4 Hz, $J_{4,5}$ 8 Hz, 4-H), 4.2–4.7 (8 H, 4 ABq, CH_2OAc and CH_2Ph), 5.47 (1 H, d, $J_{3,4}$ 4 Hz, 3-H), and 7.1–7.4 (15 H, m, Ph) (Found: C, 69.3; H, 6.5%).

Methyl 6-O-(4,6-di-O-benzyl-β-D-fructofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (15c), as an oil, R_F (benzene-AcOEt, 6:4) 0.40, $[\alpha]_D^{20} + 4^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz)

3.30 (3 H, s, OCH_3), 3.91 (1 H, t, $J_{3,4} = J_{4,5}$ 6 Hz, 4'-H), 3.97 (1 H, t, $J_{2,3} = J_{3,4}$ 9 Hz, 3-H), 3.32–4.24 (10 H, m, 2-H, 4-H, 5-H, 6- H_2 , 1'- H_2 , 5'-H, and 6'- H_2), 4.31 (1 H, d, $J_{3,4}$ 6 Hz, 3'-H), 4.55 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), 4.36–5.02 (10 H, 5 ABq, CH_2Ph), and 7.1–7.4 (25 H, m, Ph) (Found: C, 71.1; H, 7.0. $\text{C}_{48}\text{H}_{54}\text{O}_{11}$ requires C, 71.5; H, 6.7%).

Methyl 6-O-(4,6-di-O-benzyl-α-D-psicofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (16c), as an oil, R_F (benzene-AcOEt, 6:4) 0.35, $[\alpha]_D^{20} + 49^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz) 3.33 (3 H, s, OCH_3), 3.4–3.6 (4 H, m, 2-H, 4-H and 6'- H_2), 3.62–3.86 (5 H, m, 5-H, 6- H_2 and 1'- H_2), 3.91 (1 H, dd, $J_{3,4}$ 6.5 Hz, $J_{4,5}$ 3.5 Hz, 4'-H), 3.96 (1 H, t, $J_{2,3} = J_{3,4}$ 9 Hz, 3-H), 4.13 (1 H, q, J 3.5 Hz, 5'-H), 4.24 (1 H, d, $J_{3,4}$ 6.5 Hz, 3'-H), 4.36–5.04 (11 H, m, 1-H and CH_2Ph), and 7.2–7.5 (25 H, m, Ph) (Found: C, 71.2; H, 6.8%).

Methyl 6-O-(1,3-di-O-acetyl-4,6-di-O-benzyl-β-D-fructofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (15d), as an oil, R_F (hexane-AcOEt, 7:3) 0.37, $[\alpha]_D^{20} - 3^\circ$ (c 0.8 in CHCl_3); δ_H (200 MHz) 1.98 and 1.99 (6 H, 2 s, Ac), 3.31 (3 H, s, OCH_3), 3.46 (1 H, t, $J_{3,4} = J_{4,5}$ 9.5 Hz, 4-H), 3.48 (1 H, dd, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.5 Hz, 2-H), 3.62 (2 H, d, $J_{5,6}$ 5 Hz, 6'- H_2), 3.64–3.90 (3 H, m, 5-H and 6- H_2), 3.93 (1 H, t, $J_{2,3} = J_{3,4}$ 9.5 Hz, 3-H), 4.09 (1 H, dt, $J_{4,5}$ 7.5 Hz, $J_{5,6}$ 5 Hz, 5'-H), 4.17 and 4.21 (2 H, ABq, $J_{1A,1B}$ 11.5 Hz, 1'- H_2), 4.24 (1 H, t, $J_{3,4} = J_{4,5}$ 7.5 Hz, 4'-H), 4.51 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), 4.4–5.0 (10 H, 1 s and 4 ABq, CH_2Ph), 5.42 (1 H, d, $J_{3,4}$ 7.5 Hz, 3'-H), 7.1–7.4 (25 H, m, Ph) (Found: C, 69.6; H, 6.7. $\text{C}_{52}\text{H}_{58}\text{O}_{13}$ requires C, 70.1; H, 6.6%).

Methyl 6-O-(1,3-di-O-acetyl-4,6-di-O-benzyl-α-D-psicofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (16d), as an oil, R_F (hexane-AcOEt, 7:3) 0.30, $[\alpha]_D^{20} + 42^\circ$ (c 1.0 in CHCl_3); δ_H (200 MHz) 1.89 and 2.03 (6 H, 2 s, Ac), 3.32 (3 H, s, OCH_3), 3.38 (1 H, dd, $J_{5,6A}$ 3.5 Hz, $J_{6A,6B}$ 11 Hz, 6'- H_A), 3.45 (1 H, dd, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 10 Hz, 2-H), 3.49 (1 H, dd, $J_{5,6B}$ 3 Hz, $J_{6A,6B}$ 11 Hz, 6'- H_B), 3.50 (1 H, t, $J_{3,4} = J_{4,5}$ 10 Hz, 4-H), 3.66–3.76 (1 H, m, 5-H), 3.79 (1 H, dd, $J_{5,6A}$ 2 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_A), 3.90 (1 H, dd, $J_{5,6B}$ 4.5 Hz, $J_{6A,6B}$ 10.5 Hz, 6- H_B), 3.97 (1 H, t, $J_{2,3} = J_{3,4}$ 9.5 Hz, 3-H), 4.09 (1 H, t, $J_{3,4} = J_{4,5}$ 6 Hz, 4'-H), 4.04 and 4.28 (2 H, ABq, $J_{1A,1B}$ 12 Hz, 1'- H_2), 4.1–4.2 (1 H, m, 5'-H), 4.56 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), 4.32–5.00 (10 H, 5 ABq, CH_2Ph), 5.20 (1 H, d, $J_{3,4}$ 6 Hz, 3'-H), and 7.1–7.4 (25 H, m, Ph) (Found: C, 69.8; H, 6.8%).

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Received 21st March 1988; Paper 8/481