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TOTAL SYNTHESIS OF RACEMIC METHYL 2,3-ANHYDRO-6-DEOXYHEXOPYRANOSIDES

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ABSTRACT

All the stereoisomeric methyl 2,3-anhydro-6-deoxy-DL-hexopyranosides and/or their 4-*O*-acetyl derivatives have been prepared from methyl 2,3,6-trideoxy-DL-hex-2-enopyranosides or their 4-*O*-acetyl derivatives by epoxidation with hydrogen peroxide–benzonitrile. P.m.r. data for the 4-*O*-acetyl derivatives of the unsaturated and anhydro compounds are reported.

INTRODUCTION

Because of their reactivity, anhydro sugars are widely utilized as intermediates in transformations of monosaccharides[1]. Also, they have frequently been obtained in racemic form from non-sugar precursors, in connection with the total synthesis of monosaccharides[2]. We now report the synthesis of all eight stereoisomeric, racemic methyl 2,3-anhydro-6-deoxyhexopyranosides. These compounds are convenient substrates for the synthesis of 6-deoxy sugars, a class of compound widely exemplified in nature, especially amongst antibiotic sugars[3].

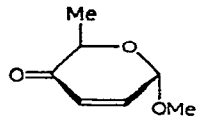
RESULTS AND DISCUSSION

As part of a research project dealing with the total synthesis of monosaccharides, a method for transforming furfuryl alcohol derivatives into methyl 2,3-dideoxy-DL-hex-2-enopyranosid-4-uloses has been developed[4]. For example, 1-(2-furyl)ethanol has been converted into methyl 2,3,6-trideoxy-α-(**1**) and -β-DL-hex-2-enopyranosid-4-ulose (**2**), the reduction of which with lithium aluminium hydride yielded[4] four stereoisomeric methyl 2,3,6-trideoxy-DL-hex-2-enopyranosides (**3**, **9**, **15**, **19**). Compound **3** has been prepared by another route[5]; since the completion of this work, **1**–**3** have been obtained as pure L enantiomers by transformation of L-alanine[6].

Treatment of the ulose **2** with lithium aluminium hydride afforded the stereoisomeric alcohols **15** and **19** in approximately equal amounts, whereas reduction of the ulose **1** was highly stereoselective*, yielding almost exclusively the alcohol **3**.

*Factors exerting an effect on the steric course of the reduction of methyl 2,3-dideoxy-DL-alk-2-enopyranosides with metal hydrides have been discussed[7].

The alcohol **9** was obtained from **3** by inversion of configuration at C-4. The mesylate **5** was treated[8] with sodium benzoate in *N,N*-dimethylformamide at 100° to give, after column chromatography on silica gel, the syrupy benzoate **11** and the crystalline formate **12**. A small amount of the benzoate **6**, in which the configuration at C-4 was retained, was also isolated. It is not clear whether **6** was formed because nucleophilic substitution at C-4 is not stereospecific, or because of the presence of the *α-threo* alcohol **9** in the substrate.



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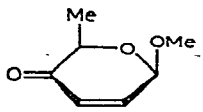

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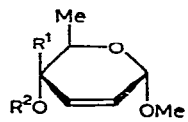
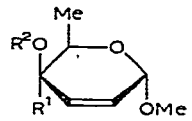
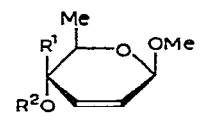


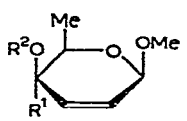
3 $R^1 = H, R^2 = H$ 6 $R^1 = H, R^2 = Bz$
4 $R^1 = H, R^2 = Ac$ 7 $R^1 = D, R^2 = H$
5 $R^1 = H, R^2 = Ms$ 8 $R^1 = D, R^2 = Ac$



9 $R^1 = H, R^2 = H$
10 $R^1 = H, R^2 = Ac$
11 $R^1 = H, R^2 = Bz$
12 $R^1 = H, R^2 = CH(=O)$
13 $R^1 = D, R^2 = H$
14 $R^1 = D, R^2 = Ac$



15 $R^1 = H, R^2 = H$
16 $R^1 = H, R^2 = Ac$
17 $R^1 = D, R^2 = H$
18 $R^1 = D, R^2 = Ac$



19 $R^1 = H, R^2 = H$
20 $R^1 = H, R^2 = Ac$
21 $R^1 = D, R^2 = H$
22 $R^1 = D, R^2 = Ac$

*For the sake of simplicity, all formulae in this paper refer to the D series.

The formation of *O*-formyl derivatives when *N,N*-dimethylformamide was used as solvent under conditions analogous to those used herein has previously been noted[9]. The *threo* configuration of **11** and **12** followed from the values (2.7 and 2.4 Hz) of $J_{4,5}$; methanolysis of each ester yielded methyl 2,3,6-trideoxy-α-DL-*threo*-hex-2-enopyranoside (**9**), which was identical with the minor product formed on reduction of the ulose **1**.

Reduction of **1** and **2** with lithium aluminium deuteride, and inversion of configuration on C-4 in the alcohol **7**, as described above, afforded C-4-deuterated compounds **7**, **13**, **17**, and **21**. The deuterated compounds and their *O*-acetyl derivatives, **8**, **14**, **18**, and **22**, gave ^{1}H-n.m.r. spectra which were sufficiently simple to yield coupling constants by first-order analysis. Comparison with the ^{1}H-n.m.r. data for non-deuterated compounds permitted assignment of some otherwise inaccessible coupling-constants in the latter compounds.

*Methyl 2,3-anhydro-6-deoxy-*DL*-hexopyranosides.* — The anhydro compounds were obtained from stereoisomeric methyl 2,3,6-trideoxy-DL-hex-2-enopyranosides

TABLE I

^{1}H-N.M.R. CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (Hz) FOR METHYL 2,3,6-TRIDEOXY-DL-HEX-2-ENOPYRANOSIDES (100 MHz, C_6D_6)

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*Me*	*OMe*	*OAc*	$J_{1,2}$	$J_{1,3}$	$J_{1,4}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$	$J_{5,Me}$	
3	4.61	5.50	5.76	3.70		1.29	3.24	—	2.1	~0.5	[e]	10.5	[e]	[e]	[e]	~6	2.70 (OH)
4[a]	4.71	5.71		5.13	3.98	1.18	3.25	1.78	2.2	~0.5	~1	[e]	~1	~1	9.5	6.5	
6[b]	4.88	5.80	5.96	5.30	4.10	1.31	3.49	[c]	2.2	~0.5	1.6	10.4	1.7	1.6	9.5	6.5	
7	4.66	5.55	5.85	—	3.75	1.37	3.29	—	2.6	~0.5	—	10.5	—	—	—	6.5	3.40 (OH)
8	4.64	5.56	5.84	—	4.00	1.20	3.24	1.70	2.2	~0.5	—	10.2	—	—	—	6.2	
9	4.62	5.62	5.90	3.27	3.97	1.25	3.25	—	3.0	<0.5	0	10.0	0	5.3	2.3	6.5	2.25 (OH), $J_{4,OH}$ 2 Hz
10[a]	4.71	5.56–6.10		4.82	4.07	1.13	3.19	1.70	2.4	<0.5	0	[e]	0	4.6	2.6	6.6	
11[b]	4.92	6.02	6.19	5.11	4.27	1.32	3.48	[c]	2.7	<0.5	0	10.2	0	5.1	2.7	6.8	
12	4.74	5.82	5.99	4.86	4.07	1.14	3.24	[d]	2.6	<0.5	0	10.2	0	4.8	2.4	6.7	
13	4.63	5.62	5.90	—	3.97	1.25	3.26	—	3.0	<0.5	—	10.0	—	—	—	6.7	2.0 (OH)
14	4.70	5.75	5.94	—	4.06	1.17	3.24	1.75	2.8	<0.5	—	10.2	—	—	—	6.7	
15	4.87	5.58	5.80	3.72	3.50	1.32	3.32	—	1.3	1.4	1.9	10.2	1.1	2.1	7.5	6.4	3.14 (OH)
16	4.96	5.78	5.98	5.12	3.85	1.24	3.36	1.75	~0.5	~0.5	~2.0	[e]	~1	~1	6.2	6.7	
17	4.86	5.59	5.75	—	3.50	1.25	3.25	—	1.3	1.4	—	10.2	—	—	—	6.4	2.31 (OH)
18	4.83	5.65	5.78	—	3.77	1.23	3.28	1.70	~0.5	~0.5	—	[e]	—	—	—	6.6	
19	4.72	5.65	5.98	3.35–3.55		1.30	3.37	—	1.7	1.5	1.3	10.2	~0	4.2	[e]	6.5	3.08 (OH)
20	4.84	5.81	5.97	4.97	3.58	1.18	3.39	1.74	<0.5	~0.7	1.9	10.5	0	4.0	3.0	6.5	
21	4.72	5.62	5.92	—	3.42	1.29	3.36	—	1.7	1.5	—	10.2	—	—	—	6.4	2.65 (OH)
22	4.74	5.71	5.85	—	3.55	1.16	3.35	1.77	<0.5	~0.5	—	10.4	—	—	—	6.6	

[a]60-MHz spectrum. [b]In $CDCl_3$. [c]Aromatic protons at 7.2–7.6 (3 H) and 7.9–8.2 (2 H). [d]CHO δ 7.83, $J_{4,CHO}$ −1.3, $J_{5,CHO}$ 0.7 Hz (*cf.* Ref. 22). [e]Could not be obtained from the spectrum.

and/or their 4-*O*-acetyl derivatives by epoxidation with benzonitrile and 30% hydrogen peroxide, in the presence of sodium hydrogen carbonate[10]; the 4-*O*-acetyl derivatives were deacetylated during epoxidation. The epoxides were isolated after acetylation and chromatography. The α anomers of the unsubstituted 2,3-anhydro compounds were obtained from their 4-*O*-acetyl derivatives by Zemplén deacetylation[11]. The yields and ratios of the anhydro sugars are recorded in Table II.

TABLE II

EPOXIDATION OF METHYL 2,3,6-TRIDEOXY-DL-HEX-2-ENOPYRANOSIDES

Substrate	*Overall yield*[a] (%)	*Products*	*Ratios*[b]
3	70	**24**	60
		26	40
4	66	**24**	29
		26	71
9	65	**28**	33
		30	67
10	62	**28**	68
		30	32
15	43	**32**	51
		34	49
19	60	**38**	100
20	52	**36**	46
		38	54

[a]Yields calculated for chromatographically separated, analytically pure 4-*O*-acetyl derivatives. [b]These ratios correspond approximately (according to t.l.c.) to the ratios of crude expoxidation products.

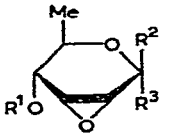
The anhydro compounds and/or their 4-*O*-acetyl derivatives gave analytical and spectral data consistent with their structures (Table III). The i.r. spectra contained epoxide bands in the range of 750–950 cm^{-1}. In the ^{1}H-n.m.r. spectra, the disappearance of vinyl signals (δ 5.50–6.0) was associated with the appearance of signals (δ 2.8–3.6) characteristic of protons attached to an oxirane ring. It is well-established[10,12–14] that the $J_{1,2}$ and $J_{3,4}$ values in 2,3-anhydro sugars are ~2.5 and 2–5 Hz, respectively, for *cis* protons, and ~0 Hz for *trans* protons. The configuration of the oxirane ring in the 2,3-anhydro compounds was assigned on this basis. Moreover, **25** and **27** exhibited ^{1}H-n.m.r. data consistent with those reported[13] for the corresponding D enantiomers.

In the reaction of hydrogen peroxide and benzonitrile with olefins, iminoperoxy acid is believed to be the epoxidizing agent[15]. The stereochemistry of epoxidation of the double bond with this peroxy acid is influenced by the allylic substituents in a manner similar to that for carboxylic peroxy acids. Thus, a bulky substituent deflects oxirane-ring formation to the obverse side of the double bond, whereas, because of hydrogen-bonding effects, a hydroxyl group promotes the introduction of the oxirane

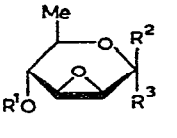
TABLE III

PHYSICAL AND ANALYTICAL DATA FOR ANHYDROHEXOPYRANOSIDES

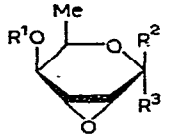
Compound	*M.p.* (*degrees*)	*B.p.* (*degrees/torr*)	*I.r.* ν_{max} (cm^{-1})	*Elemental analysis*				
				Formula	*Found* (%)		*Calc.* (%)	
					C	*H*	*C*	*H*
23	79–80.5	—	3400 (OH), 1245, 900, 870 (epoxide)	$C_7H_{12}O_4$	52.6	7.4	52.5	7.6
24	87–90	—	1740, 1250 (OAc), 905, 880 (epoxide)	$C_9H_{14}O_5$	53.8	7.1	53.5	7.0
25	—	100/0.2	3500 (OH), 1240, 850, 805 (epoxide)	$C_7H_{12}O_4$	52.8	7.7	52.5	7.6
26	44–45	—	1740, 1235 (OAc), 850, 805 (epoxide)	$C_9H_{14}O_5$	53.6	6.9	53.5	7.0
27	—	110/0.2	3500 (OH), 1245, 850, 825 (epoxide)	$C_7H_{12}O_4$	52.7	7.8	52.5	7.6
28	52.5–55	100/0.4	1750, 1230 (OAc), 900, 855 (epoxide)	$C_9H_{14}O_5$	53.3	6.9	53.5	7.0
29	79–80.5	—	3550 (OH), 900, 860 (epoxide)	$C_7H_{12}O_4$	52.6	7.6	52.5	7.6
30	92–93.5	—	1730, 1240 (OAc), 860, 780 (epoxide)	$C_9H_{14}O_5$	53.4	6.8	53.5	7.0
32	70–71.5	—	1740, 1240 (OAc), 840, 795 (epoxide)	$C_9H_{14}O_5$	53.3	6.9	53.5	7.0
34	—	130/0.35	1740, 1235 (OAc), 890, 820 (epoxide)	$C_9H_{14}O_5$	53.6	7.0	53.5	7.0
36	—	105/0.6	1740, 1230 (OAc), 820, 770 (epoxide)	$C_9H_{14}O_5$	53.3	6.8	53.5	7.0
38	94–96	—	1730, 1240 (OAc), 890, 800 (epoxide)	$C_9H_{14}O_5$	53.3	6.8	53.5	7.0



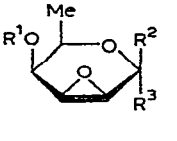
23 $R^1 = R^2 = H, R^3 = OMe$
24 $R^1 = Ac, R^2 = H, R^3 = OMe$
31 $R^1 = R^3 = H, R^2 = OMe$
32 $R^1 = Ac, R^2 = OMe, R^3 = H$



25 $R^1 = R^2 = H, R^3 = OMe$
26 $R^1 = Ac, R^2 = H, R^3 = OMe$
33 $R^1 = R^3 = H, R^2 = OMe$
34 $R^1 = Ac, R^2 = OMe, R^3 = H$



27 $R^1 = R^2 = H, R^3 = OMe$
28 $R^1 = Ac, R^2 = H, R^3 = OMe$
35 $R^1 = R^3 = H, R^2 = OMe$
36 $R^1 = Ac, R^2 = OMe, R^3 = H$



29 $R^1 = R^2 = H, R^3 = OMe$
30 $R^1 = Ac, R^2 = H, R^3 = OMe$
37 $R^1 = R^3 = H, R^2 = OMe$
38 $R^1 = Ac, R^2 = OMe, R^3 = H$

ring on the same side of the double bond. A methoxyl group has a directing effect analogous to, though weaker than, that of a hydroxyl group[16]. The steric course of the epoxidation of methyl 2,3-anhydro-6-deoxy-DL-hexopyranosides, described herein, can be qualitatively rationalized on the basis of the foregoing effects.

Epoxidation of **3** and **9** leads mainly to the *α-allo* (**23**) and *α-talo* (**29**) epoxides, respectively, with the oxirane ring *cis* to the vicinal hydroxyl group. For the 4-*O*-acetyl derivatives **4** and **10**, the stereoselectivity is reversed and the main products are the *α-manno* (**26**) and *α-gulo* (**28**) epoxides, respectively. The competing effects of hydroxyl and methoxyl groups is evident in the epoxidation of **15** which gave similar amounts of the epoxides **32** and **34**. However, the alcohol **19** gave exclusively the *β-talo* epoxide **37**, presumably because of the combined directing-influence of hydroxyl and methoxyl groups, whereas the *O*-acetyl derivative **20** afforded similar amounts of the epoxides **36** and **38**.

The stereoselectivity of iminoperoxy acid as epoxidizing reagent (*cf.* Table II) appears to be lower than that of, for example, 3-chloroperoxybenzoic acid[17]. However the possibility of controlling, at least to some extent, the steric course of epoxidation of 2,3-unsaturated sugars with hydrogen peroxide and benzonitrile makes this method a convenient one for the direct preparation of anhydro compounds from unsaturated precursors.

Conformation of methyl 2,3-anhydro-6-deoxyhexopyranosides. — The pyranoid ring in 2,3-anhydropyranosides adopts a half-chair form, and, for mobile systems, the preferred conformation in solution is that in which the substituent on C-5 is equatorial[14]. Analysis of the ^{1}H-n.m.r. spectra of a number of methyl 2,3- and 3,4-anhydro-6-deoxypyranosides has confirmed the above conclusion[18]. The ^{1}H-n.m.r. data of the stereoisomeric methyl 4-*O*-acetyl-2,3-anhydro-6-deoxyhexopyranosides

TABLE IV

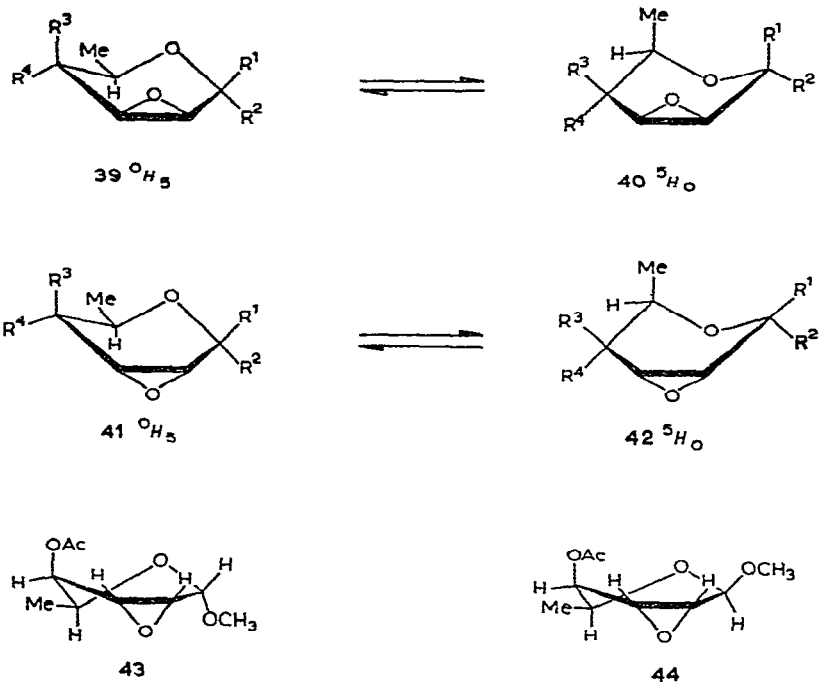
100-MHz ^{1}H-N.M.R. DATA FOR METHYL 4-*O*-ACETYL-2,3-ANHYDRO-6-DEOXYHEXOPYRANOSIDES

Compound	*Solvent*	*Chemical shifts (δ)*								*Coupling constants (Hz)*				
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*Me*	*OMe*	*OAc*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
24	$CDCl_3$	4.82	3.49		4.75	3.91	1.15	3.45	2.13	2.6	[a]	1.4	9.5	6.3
	C_6D_6	4.38	2.96	3.19	4.73	4.06	1.07	3.16	1.63	3.0	4.2	1.5	9.7	6.4
26	$CDCl_3$	4.81	3.02	3.14	4.58	3.58	1.16	3.44	2.10	0	3.4	0	9.9	6.4
	C_6D_6	4.60	2.80	2.96	4.72	3.68	1.05	3.08	1.64	0	3.3	0	9.8	6.2
28	$CDCl_3$	4.90	3.34		5.04	4.03	1.11	3.45	2.15	2.4	[a]	[a]	2.0	6.5
	C_6D_6	4.60	2.98	3.08	4.96	4.0	0.98	3.23	1.78	3.2	3.8	2.5	1.5	6.7
30	$CDCl_3$	4.85	3.07	3.59	4.81	3.98	1.14	3.42	2.16	0	3.7	5.3	3.4	6.7
	C_6D_6	4.61	2.78	3.35	4.49	3.70	1.05	3.12	1.78	0	3.2	5.2	3.2	6.7
32	$CDCl_3$	4.68	3.31	3.44	4.84	3.54	1.19	3.50	2.10	0[b]	4.2	1.9	9.5	6.4
	C_6D_6	4.50	3.14	3.20	4.82	3.52	1.09	3.27	1.71	0	4.5	1.7	9.5	6.2
34	$CDCl_3$	4.79	3.15		4.59	3.39	1.22	3.51	2.10	~0.8	[a]	0	9.2	6.3
	C_6D_6	4.46	2.80	2.90	4.64	3.21	1.12	3.34	1.74	~0.8	3.8	0	8.7	6.3
36	$CDCl_3$	4.74	3.26	3.38	5.11	3.72	1.17	3.63	2.20	~1.0	3.8	2.3	2.0	7.0
	C_6D_6	4.61	3.12		5.04	3.55	1.02	3.37	1.76	~1.0	[a]	~2	2.0	6.7
38	$CDCl_3$	4.73	3.23	3.60	4.85	3.69	1.22	3.60	2.21	~0.5	3.9	5.0	3.5	6.6
	C_6D_6	4.35	2.84	3.30	4.53	3.21	1.11	3.39	1.81	~0.5	3.8	4.8	3.5	6.5

[a]Could not be obtained from the spectrum. [b]$J_{1,5}$ 0.9 Hz.

are given in Table IV; the spectra of the unsubstituted anhydro compounds were unsuitable for obtaining ^{1}H-n.m.r. parameters because of the overlapping of signals.

The assignment of the conformational equilibria of the anhydro compounds having the *manno* or *allo* configuration was based on the $J_{4,5}$ values. The highest value (9.9 Hz) was observed for $J_{4,5}$ of **26** (*α-manno*), indicating almost exclusive existence in conformation $^{O}H_5$ (**39**, $R^1 = R^3 = H$, $R^2 = OMe$, $R^4 = OAc$), which is stabilized both by the anomeric effect and the equatorial Me-5. Compounds **24**, **32**, and **34** also exist mainly in the $^{O}H_5$ conformation.



Scheme I

Assuming **26** to be nearly conformationally homogeneous, and a Karplus-type dependence for $J_{4,5}$, then it can be estimated that the conformational equilibria of the *α-allo* (**24**) and *β-allo* (**32**) epoxides contain 2–4% of the ^5H_o conformers **42** ($R^1 = R^3 = H$, $R^2 = OMe$, $R^4 = OAc$ for **24**; $R^2 = R^3 = H$, $R^1 = OMe$, $R^4 = OAc$ for **32**). The proportion of the ^5H_o conformation **40** ($R^2 = R^3 = H$, $R^1 = OMe$, $R^4 = OAc$) for the *β-manno* epoxide **34**, which is stabilized by the anomeric effect, increases to ~8% (14% in C_6D_6).

For the *talo* and *gulo* epoxides, which lack axial–pseudoaxial $J_{4,5}$ coupling, use was made of the $J_{1,2}$ and $J_{3,4}$ values.

From the ^{1}H-n.m.r. data[18] of 2,3-anhydro sugars having rigid conformations, as well as the values obtained from the spectra of the acetates **24**, **26**, **32**, and **34**,

$J_{1,2}$ and $J_{3,4}$ values have been determined for *cis* and *trans* orientations of H-1/H-2 and H-3/H-4 for the conformations $^{\circ}H_5$ and $^{5}H_{o}$: *cis*-$J_{1peq,2}$ 3.1, *cis*-$J_{1pax,2}$ 0.8–1.0, *cis*-$J_{3,4peq}$ 5.4, *cis*-$J_{3,4pax}$ 1.5–1.9, *trans*-$J_{1peq,2}$ 0.6, *trans*-$J_{1pax,2}$ ~0.1, *trans*-$J_{3,4peq}$ 0.4, *trans*-$J_{3,4pax}$ 0 Hz. The high value (5.3 Hz) of $J_{3,4}$ for the α-taloside **30** corresponds to the $^{\circ}H_5$ conformation **39** ($R^1 = R^4 = H$, $R^2 = OMe$, $R^3 = OAc$). The slightly smaller value (5.0 Hz) of $J_{3,4}$ for the β anomer **38**, indicates the presence of ~10% of the $^{5}H_{o}$ form **40** ($R^2 = R^4 = H$, $R^1 = OMe$, $R^3 = OAc$), favoured by the anomeric effect[19].

Contrary to the above results, the $J_{1,2}$ and $J_{3,4}$ values for the α- and β-anhydrogulosides (**28** and **36**) (Table IV) cannot be interpreted in terms of equilibria of $^{\circ}H_5$ and $^{5}H_{o}$ conformations. Assuming the Karplus-type dependence of coupling constants[20,21] for the oxirane-ring protons, the dihedral angles in the gulosides **28** and **36** could be determined.

For **28** in C_6D_6, the values $J_{1,2}$ 3.2 and $J_{3,4}$ 2.5 Hz indicate the dihedral angles H-1–C-1/C-2–H-2 and H-3–C-3/C-4–H-4 to be 0° and 60°, respectively, and are consistent with the skew-boat conformation **43**; the ^{1}H-n.m.r. data cited[10] for methyl 4,6-di-*O*-acetyl-2,3-anhydro-α-D-gulopyranoside can be interpreted in a similar manner. Likewise, for the β anomer **36**, the dihedral angles H-1–C-1/C-2–H-2 and H-3–C-3/C-4–H-4 were ~55° and ~50°, consistent with the skew-boat form **44**, in which MeO-1 is pseudo-axial.

Although half-chair forms cannot be ruled out for anhydrogulosides, skew-boat conformations appear to be preponderant.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Bath temperatures are given for boiling points. I.r. spectra were obtained with a Unicam SP-200 spectrometer, using KBr discs for solids and films for liquids. ^{1}H-N.m.r. spectra were measured with a Jeol JNM-4H-100 instrument operating at 100 MHz. For column chromatography, silica gel Schuchardt (100–200 mesh) was used. All reactions and chromatographic separations were monitored by t.l.c. on silica gel G (Merck). Solvents were removed *in vacuo* by rotary evaporation.

Acetylations were carried out with acetic anhydride–pyridine (1:1) at room temperature, followed by the usual work-up. Deacetylations were effected with sodium methoxide in methanol[11].

Epoxidations. — The following general procedure was used. A solution of each 2,3-unsaturated compound (30 mmol) in methanol (10 ml) was stirred with a mixture of benzonitrile (2 ml), 30% hydrogen peroxide (3 ml), and sodium hydrogen carbonate (0.2 g) overnight at room temperature. The mixture was poured into water and extracted with chloroform, the extract was concentrated, and the residue was triturated with ether. Benzamide was removed, the filtrate was concentrated to dryness, the residue was acetylated, and the product was eluted from silica gel (15 g) with light petroleum–ether (85:15). The various products are listed in Tables II and III.

4-C-Deuterated derivatives. — Compounds **7**, **13**, **17**, and **21** were obtained by reduction of **1** or **2** with lithium aluminium deuteride and subsequent chromatography, or by inversion of configuration at C-4 as described for non-deuterated compounds. Each deuterio derivative exhibited a b.p. and t.l.c. mobility identical with those of the corresponding non-deuterated compound. Their ^{1}H-n.m.r. data are given in Table I.

4-O-Benzoyl- (**11**) *and-4-O-formyl* (**12**) *derivatives of methyl 2,3,6-trideoxy-α-*DL-threo-*hex-2-enopyranosides.* — A solution of **3** (1.6 g, 11.1 mmol) in pyridine (20 ml) was treated with mesyl chloride (2.35 g, 20.6 mmol) at 3° for 12 h. Isolation using chloroform yielded **5** (2.2 g, 90%), m.p. 44–47°; ν_{max} 1360, 1190, and 1175 cm^{-1} (SO_2). A mixture of **5** (2.1 g, 9.5 mmol), sodium benzoate (4 g, 28 mmol), and *N,N*-dimethylformamide (100 ml) was stirred for 3 h at 100°, then diluted with benzene, filtered, and concentrated. The residue was eluted from silica gel (60 g) with light petroleum–ethyl acetate (40:1) to give **6** (0.16 g, 8%), b.p. 120°/0.3 torr, ν_{max} 1720 and 1260 cm^{-1} (C=O) (Found: C, 67.5; H, 6.6. $C_{14}H_{16}O_4$ calc.: C, 67.7; H, 6.5%); **11** (0.65 g, 28%), b.p. 100°/0.15 torr, ν_{max} 1720 and 1270 cm^{-1} (C=O) (Found: C, 67.5; H, 6.4. $C_{14}H_{16}O_4$ calc.: C, 67.7; H, 6.5%); and **12** (0.3 g, 18%), m.p. 83–84.5° (from hexane), ν_{max} 1700 and 1160 cm^{-1} (C=O) (Found: C, 56.0; H, 6.9. $C_8H_{12}O_4$ calc.: C, 55.8; H, 7.0%).

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