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SYNTHESIS OF 4-*C*-(1-HYDROXYETHYL) DERIVATIVES FROM BENZYL 2,3-DI-*O*-BENZYL- AND -2,3-*O*-METHYLENE-β-L-*threo*-PENTOPYRANOSID-4-ULOSE, AND THE CORRESPONDING α-D-*xylo*-HEXOPYRANOSID-4-ULOSES*

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ABSTRACT

The title compounds were synthesized by the epoxidation of the corresponding 4-*C*-vinyl derivatives followed by reduction of the epoxy ring (Route *A*), and by osmium tetraoxide oxidation of the corresponding 4-*C*-ethylidene derivatives (Route *C*). Stereoselectivities in the oxidations are discussed on the basis of the chiralities of 1-hydroxyethyl groups as determined by comparison of the products prepared through Routes *A* and *C*.

INTRODUCTION

Oligosaccharide antibiotics, the everninomicins[2], flambamycin[3], and avilamycins[4] of the orthosomycin family, contain three characteristic 2,3-*O*-methylene-aldonolactones having a 4-*C*-(1-hydroxyethyl) or 4-*C*-acetyl group, which are uniquely attached at a terminal position by an orthoester interlinkage[5]. Recently, we communicated the synthesis of 6-deoxy-4-*C*-(hydroxymethyl)-5-*O*-methyl-2,3-*O*-methylene-L-idono-1,4[1]-lactone[6] (in everninomicins B and D) from benzyl 2,3-*O*-methylene-β-L-*threo*-pentopyranosid-4-ulose[7] (**1**) and that of 4-*C*-acetyl-6-deoxy-2,3-*O*-methylene-D-galactono-1,5-lactone[8] (in flambamycin) from benzyl 6-deoxy-2,3-*O*-methylene-α-D-*xylo*-hexopyranosid-4-ulose[7] (**2**), both as the corresponding methyl aldonates. In connection with the foregoing syntheses, a principle for the determination of the chirality of a 1-hydroxyethyl group introduced into benzyl 2,3-di-*O*-benzyl-β-L-*threo*-pentopyranosid-4-ulose, by a combination of synthetic pathways, from the corresponding 4-*C*-vinyl (**4** and **5**) and 4-*C*-ethylidene derivatives (**6**) has been reported[1].

In the present study, 4-*C*-(1-hydroxyethyl) derivatives from **1**, **2**, and benzyl 2,3-di-*O*-benzyl-6-deoxy-α-D-*xylo*-hexopyranosid-4-ulose[7] (**3**) were synthesized by the epoxidation of the corresponding 4-*C*-vinyl derivatives[9], followed by reduction

*Branched-chain Sugars, Part XXVI. For Part XXV, see ref. 1.

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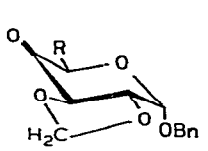
of the epoxy ring (Route *A*), and by osmium tetraoxide oxidation of the corresponding 4-*C*-ethylidene derivatives (Route *C*), and the stereoselectivities in oxidations used in both routes are discussed by use of the aforementioned principle.

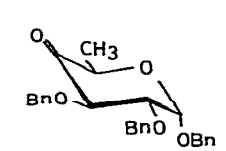
RESULTS AND DISCUSSION

Synthesis of 4-C-ethylidene derivatives. — As the starting materials for examination of the synthesis of 4-*C*-(1-hydroxyethyl) derivatives through Route *C* (shown in the preceding paper[1]), 4-*C*-ethylidene derivatives were synthesized by the Wittig reaction of **1**–**3** with ethyltriphenylphosphonium bromide and butyllithium.



1 R = H
2 R = Me

Bn = $PhCH_2$



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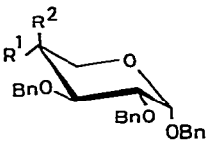
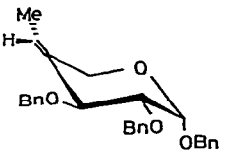
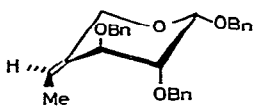


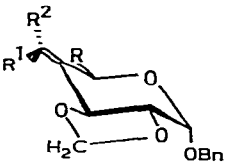
4 R^1 = OH, R^2 = $-CH=CH_2$
5 R^1 = $-CH=CH_2$, R^2 = OH



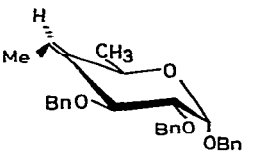
(E)-6



(Z)-6



(E)-7 R = R^1 = H, R^2 = Me
(Z)-7 R = R^2 = H, R^1 = Me
(E)-8 R = R^2 = Me, R^1 = H
(Z)-8 R = R^1 = Me, R^2 = H



(Z)-9

In the cases of **1** and **2**, two geometric isomers [(*E*)- and (*Z*)-**7**, and (*E*)- and (*Z*)-**8**] were respectively obtained, but **3** gave only one isomer [(*Z*)-**9**]. Because the conformational inversion observed in (*Z*)-**6** is impossible in the cases of **7** and **8**, the configurations of these derivatives were at first assigned by comparison of the rotational values shown in Table I, together with those of (*E*)-**6** and (*Z*)-**6**. In general, the (*E*) isomer has a rotational value larger than that of the (*Z*) isomer. In addition, the same trend in the difference of chemical shifts of ring-protons between the (*E*) and (*Z*) isomers of **7** and **8** supports the assignments. The $J_{2,3}$ value of (*Z*)-**9** indicates a $^4C_1$(D) conformation, flattened to avoid the nonbonded interactions around the alkenic function. The foregoing, tentative assignments were confirmed by conversion into the 4-*C*-(1-hydroxyethyl) derivatives as described next.

Synthesis of 4-C-(1-hydroxyethyl) derivatives. — Before the synthesis of 4-*C*-(1-hydroxyethyl) derivatives from 4-*C*-vinyl derivatives (**10**, **11**, **16**, **17**, and **22**), the 4-*O*-benzyl derivatives of **11** and **17** were synthesized, in view of the synthesis of

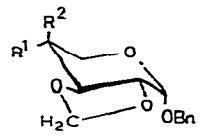
TABLE I

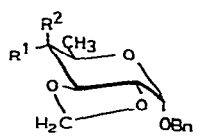
YIELDS AND PHYSICAL CONSTANTS OF 4-*C*-ETHYLIDENE DERIVATIVES

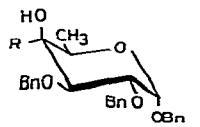
4-C-Ethylidene derivatives[a]	$[\alpha]_D$ *(in $CHCl_3$) (degrees)*	*Chemical shifts (δ, in $CDCl_3$) and coupling constants (Hz) of ^{1}H-n.m.r. spectra*[b]								*Yield (%)*
		H-1 ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3*	*H-5* ($J_{5e,5a}$)	*H-5*	*H-6* ($J_{5,6}$)	*H-4α*[c] ($J_{4\alpha,4\beta}$)	*H-4β*[c]	
(*E*)-6	+225	4.93 d (3.0)	3.53 dd (9.0)	4.35 bd	4.26 bd (13.0)	4.18 bd	—	5.79 bq (7.0)	1.65 bd	22.4
(*Z*)-6	+134	4.79 d (1.5)	3.73 dd (4.0)	3.41 bd	4.31 bd (12.6)	4.06 bd	—	5.78 bq (7.0)	1.64 bd	25
(*E*)-7	+254	5.38 d (3.0)	3.30 dd (9.8)	4.36 bd	4.53 bd (12.0)	3.92 bd	—	5.56 bq (7.0)	1.68 bd	20
(*Z*)-7	+134	5.36 d (3.5)	3.42 dd (10.0)	4.50 bd	4.12 bd (12 5)	3.82 bd	—	5 44 bq (7.0)	1.87 bd	20
(*E*)-8	+245	5 29 d (3.8)	3.33 dd (9.8)	~4.26 m	—	~4.26 m	1.50 d (7.2)	5.88 bq (7.8)	1.77 bd	41
(*Z*)-8	+167	5.28 d (3.8)	3.34 dd (9.8)	4.45 bd	—	4.08 bq	1.23 d (6.7)	5.53 bq (7.1)	1.88 bd	24
(*Z*)-9	+84	5.03 d (3.0)	3.75 dd (6.0)	4.36 bd	—	4.42 q	1.34 d (7.0)	5.66 bq (7.0)	1.70 d	40

[a]These compounds were obtained as syrups. [b]Data on benzyl and 2,3-*O*-methylene protons are omitted. [c]Long-range couplings with ring H-3 and H-5 (<1.5 Hz) were also observed.

methyl 6-deoxy-4-*C*-(hydroxymethyl)-5-*O*-methyl-2,3-*O*-methylene-L-idonate[6]. Reaction of **11** and **17** in *N*,*N*-dimethylformamide with sodium hydride and benzyl chloride gave benzyl 4-*O*-benzyl-2,3-*O*-methylene-4-*C*-vinyl-β-L-arabinopyranoside (**12**) and the corresponding 6-deoxy-α-D-galactopyranoside (**18**) in 89 and 91% yield, respectively.







10 R^1 = OH, R^2 = $-CH=CH_2$

11 R^1 = $-CH=CH_2$, R^2 = OH

12 R^1 = $-CH=CH_2$, R^2 = OBn

(R,S)-**13** R^1 = OH, R^2 = $-CH-CH_2$ (O)

(R,S)-**14** R^1 = $-CH-CH_2$ (O), R^2 = OH

(R,S)-**15** R^1 = $-CH-CH_2$ (O), R^2 = OBn

16 R^1 = OH R^2 = $-CH=CH_2$

17 R^1 = $-CH=CH_2$, R^2 = OH

18 R^1 = $-CH=CH_2$ R^2 = OBn

(R,S)-**19** R^1 = OH R^2 = $-CH-CH_2$ (O)

(R,S)-**20** R^1 = $-CH-CH_2$ (O), R^2 = OH

(R,S)-**21** R^1 = $-CH-CH_2$ (O), R^2 = OBn

22 R = $-CH=CH_2$

(R,S)-**23** R = $-CH-CH_2$ (O)

Bn = $PhCH_2$

Epoxidation of the 4-*C*-vinyl derivatives (**10–12**, **16–18**, and **22**) in 1,2-dichloroethane with *m*-chloroperoxybenzoic acid afforded (*R*,*S*) mixtures of the corresponding 4-*C*-(oxiran-2-yl) derivatives (**13–15**, **19–21**, and **23**) in 40–91% yield. Except for **13** and **20**, the (*R*) and (*S*) isomers could be successfully separated on a column of silica gel. The physical constants and yields of pure isomers are summarized in Table II. In the ^{1}H-n.m.r. parameters, it was noticeable that protons in the oxiran-2-yl group having the (*S*) configuration tend to resonate at lower magnetic field than those of the (*R*) configuration, regardless of the axial and equatorial orientations.

Reduction of the 4-*C*-(oxiran-2-yl) derivatives (**13–15**, **19–21**, and **23**) in oxolane with lithium aluminum hydride gave the corresponding 4-*C*-(1-hydroxyethyl) derivatives (**24–30**) in fairly good yields. In the cases of **13** and **20**, the (*R*,*S*) epimers could be separated after conversion into the 4-*C*-(1-hydroxyethyl) derivatives [(*R*)-**24** and (*S*)-**24**; (*R*)-**27** and (*S*)-**27**], and the ratio of epimers in (*R*,*S*)-**13** and (*R*,*S*)-**20** was estimated from that of those in **24** and **27**, respectively. The yields and physical constants are summarized in Table III. It is characteristic that compounds having an equatorially oriented (*S*)-1-hydroxyethyl group commonly show larger optical rotations than the (*R*) compounds, and this relation is reversed for axial compounds [(*R*,*S*)-**24** and (*R*,*S*)-**25**].

The chiralities of the 4-*C*-(1-hydroxyethyl) groups in the aforementioned **24–27** and **30** were determined by comparison of the products obtained by osmium tetraoxide oxidation of the 4-*C*-ethylidene derivatives (**7–9**). As expected, the oxidation of (*E*)-**7** and (*Z*)-**7** gave the pair (*R*)-**24** and (*S*)-**26**, and another pair, (*S*)-**24**

TABLE II

YIELDS AND PHYSICAL CONSTANTS OF 4-*C*-(OXIRAN-2-YL) DERIVATIVES

4-C-(Oxiran-2-yl) derivatives[a]	$[\alpha]_D$ *(in $CHCl_3$) (degrees)*	*Chemical shifts (δ, in $CDCl_3$) and coupling constants (Hz) of ^1H-n.m.r. spectra*[b]							*Yield (%)*
		H-1 ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3*	*H-5* ($J_{5e,5a}$)	*H-5* ($J_{5,6}$)	*H-6*	*H-4α and H-4β (J in the ABC system)*	
(*R*)-**14**	+182	5.36 d (2.0)	3.85 dd (9.8)	3.68 d	3.68 d (13.0)	3.64 d	—	2.98 dd, 2.89 dd, 2.71 dd (2.4, 3.7, 5.1)	16.6
(*S*)-**14**	+183	5.39 d (1.8)	3.86 dd (9.0)	3.96 d	3.68 d (12.0)	3.64 d	—	3.00 dd, 2.96 dd, 2.80 dd (2.8, 3.7, 5.4)	74.5
(*R*)-**19**	+149	5.03 d (3.2)	3.72 dd (10.2)	4.04 d	—	3.82 q (7.0)	1.13 d	3.20 dd, 2.86 dd, 2.75 dd (3.0, 4.0, 5.5)	20.1
(*S*)-**19**	+143	5.29 d (4.0)	3.55 dd (10.3)	4.10 d	—	3.75 q (7.0)	1.19 d	3.30 q, 2.88 q, 2.85 t (3.0, 4.0, 4.0)	39.1
(*R*)-**23**	+82.0	4.96 d (3.0)	4.06 dd (10.0)	3.89 d	—	4.02 q (6.5)	1.45 d	2.71 dd, 2.36 dd, 2.24 dd (2.8, 4.0, 5.6)	39.9
(*S*)-**23**	+91.3	4.87 d (4.0)	3.79 dd (10.5)	4.02 d	—	3.98 q (7.0)	1.16 d	2.86 dd, 2.8–2.6 m (3.0, 6.4)	27.7
(*R*)-**15**	+115	5.39 d (2.0)	4.10–3.98 m		3.95 d (12.2)	3.58 d	—	3.16 dd, 2.90 dd, 2.79 dd (3.0, 4.0, 5.0)	30.2
(*S*)-**15**	+115	5.34 d (2.6)	4.00 dd (10.0)	3.93 d	3.78 d (12.5)	3.66 d	—	3.11 dd, 3.04 dd, 2.83 dd (2.9, 4.2, 5.0)	31.1
(*R*)-**21**	+80.0	5.30 d (3.0)	4.00 dd (10.0)	3.76 d	—	3.66 d (6.8)	1.30 d	3.14t, 2.86–2.70 m (3 4)	28.9
(*S*)-**21**	+73.0	5.30 d (2.0)	3.99 dd (10.0)	3.93 d	—	3.95 q (6.5)	1.38 d	3.29 dd, 3.00 dd, 2.94 dd (3.0, 4.0, 5.3)	57.6

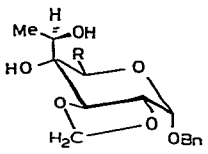
[a]All compounds were obtained as syrups. [b]Data on *O*-benzyl, 2,3-*O*-methylene, and hydroxyl protons are abbreviated.

TABLE III

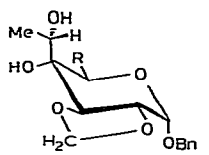
YIELDS AND PHYSICAL CONSTANTS OF 4-C-(1-HYDROXYETHYL) DERIVATIVES

4-C-(1-Hydroxyethyl)[a] *derivatives*	$[\alpha]_D$ *(in $CHCl_3$) (degrees)*	*Chemical shifts (δ, in $CDCl_3$) and coupling constants (Hz) in ^1H-n.m.r. spectra*[b]								*Yield*[c] *(%)*
		H-1 ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3*	*H-5e* ($J_{5e,5a}$)	*H-5a*	*H-6* ($J_{5,6}$)	*H-4α*	*H-4β* ($J_{4\alpha,4\beta}$)	
(*R*)-**24**	+172	5.29 d (3.7)	3.61 dd (10.1)	4.10 d	3.56 s			4.36 q	1.29 d (6.2)	20
(*S*)-**24**	+154	5.26 d (3.7)	3.45 dd (10.0)	4.10 d	3.83 d (11.5)	3.33 d		4.05 q	1.41 d (6.2)	37
(*R*)-**26**	+141	5.36 bs (~ 1.0)	3.84 d (10.0)	3.95 d	3.53 d (12.1)	3.49 d		3.92 q	1.15 d (6.3)	75
(*S*)-**26**	+176	5.35 bs (~ 1.0)	3.82 d (10.0)	3.92 d	3.68 d (13.8)	3.58 d		3.69 q	1.31 d (6.0)	80
(*R*)-**25**	+169	5.22 d (3.0)	3.94 dd (10.0)	4.02 d		3.77 q	1.20 d (7.0)	4.23 q	1.35 d (6.0)	88
(*S*)-**25**	+121	5.22 d (3.5)	3.67 dd (11.0)	4.06 d		3.74 q	1.17 d (7.0)	4.02 q	1.38 d (7.0)	86
(*R*)-**27**	+138	5.32 d (2.0)	4.00 dd (10.0)	3.96 d		3.62 q	1.11 d (6.2)	3.62 q	1.24 d (6.2)	60
(*S*)-**27**	+150	5.29 d (3.0)	3.92 dd (10.0)	4.05 d		4.00 q	1.32 d (6.2)	3.94 q	1.24 d (6.2)	30
(*R*)-**30**	+20.7	4.90 d (3.4)	4.12 dd (10.0)	4.44 d		3.78 q	1.22 d (6.4)	3.69 q	1.30 d (7.0)	62
(*S*)-**30**	+64.3	4.91 d (3.4)	4.12 dd (9.7)	4.26 d		3.80 q	1.10 d (6.6)	3.60 q	1.18 d (6.6)	50
(*R*)-**29**	+103	5.30 d (3.0)	3.95 dd (10.0)	4.10 d		4.54 q	1.26 d (6.7)	3.84 q	1.26 d (6.7)	98
(*S*)-**29**	+124	5.29 d (3.5)	4.02 dd (10.4)	4.22 d		4.17 q	1.26 d (7.0)	3.76 q	1.14 d (7.0)	89

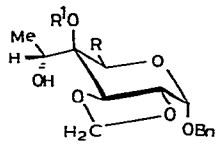
[a]Most of these compounds were obtained as syrups, except for (*R*)-**24** (m.p. 104–107°) and (*S*)-**26** (m.p. 152–154°). [b]Data on *O*-benzyl, 2,3-*O*-methylene, and hydroxyl protons are omitted. [c]Yields of (*R*)-**24** and (*S*)-**24**, and of (*R*)-**27** and (*S*)-**27**, are those from inseparable mixtures of (*R,S*)-**13** and (*R,S*)-**20**, respectively.



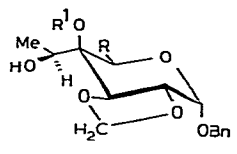
(*R*)-24 R = H
(*R*)-25 R = Me



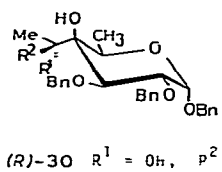
(*S*)-24 R = H
(*S*)-25 R = Me



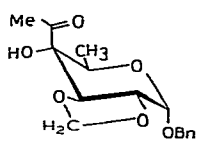
(*R*)-26 R = R^1 = H
(*R*)-27 R = Me, R^1 = H
(*R*)-28 R = H, R^1 = Bn
(*R*)-29 R = Me R^1 = Bn



(*S*) 26 R = R^1 = H
(*S*) 27 R = Me R^1 = H
(*S*) 28 R = H R^1 = Bn
(*S*) 29 R = Me R^1 = Bn



(*R*)-30 R^1 = OH, R^2 = H
(*S*)-30 R^1 = H R^2 = OH



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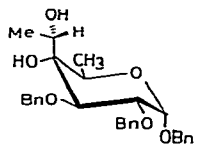

32

Bn = $PhCH_2$

and (*R*)-**26**, respectively. However, similar oxidation of (*E*)-**8** and (*Z*)-**8** gave only (*R*)-**25** and (*S*)-**25**, respectively, together with a small amount of peroxidized product, benzyl 4-*C*-acetyl-6-deoxy-2,3-*O*-methylene-α-D-glucopyranoside (**31**). Therefore, the formation of (*S*)-**25** and (*R*)-**27** from (*E*)-**8**, and that of (*R*)-**25** and (*S*)-**27** from (*Z*)-**8** by successive epoxidation and alkaline opening of the *spiro*-epoxides (Route *B* in the preceding paper[1]) were ascertained, without isolation of the intermediary *spiro*-epoxides. The structure of **31** was ascertained by an independent synthesis, *i.e.*, the oxidation of a mixture of (*R*)-**25** and (*S*)-**25** with *N*-chlorosuccinimide and dimethyl sulfide[10].

In the case of (*Z*)-**9**, oxidation with osmium tetraoxide gave (*R*)-**30** as a minor product, together with benzyl 2,3-di-*O*-benzyl-6-deoxy-4-*C*-[(*S*)-1-hydroxyethyl]-α-D-glucopyranoside (**32**). Thus, the (*R*) and (*S*) configurations of the 4-*C*-(1-hydroxyethyl) groups in **24**–**27** and **30**, and also the (*E*) and (*Z*) configurations of **7**–**9**, were established. In the cases of (*R*)-**28** and (*S*)-**28**, their configurations were ascertained in an intermediary step to methyl 6-deoxy-4-*C*-(hydroxymethyl)-5-*O*-methyl-2,3-*O*-methylene-L-idonate[6], by comparison with the compounds from (*R*)-**26** and (*S*)-**26**. The configurations of (*R*)-**29** and (*S*)-**29** were deduced only from the n.m.r. spectra of the precursors, (*R*)-**21** and (*S*)-**21**, already mentioned. From these facts, the configurations of the epoxides (**14**, **15**, **19**, and **23**) were also determined unambiguously.

*Stereoselectivities in the oxidation of 4-*C*-vinyl and 4-*C*-ethylidene derivatives.* — The epoxidation of 4-*C*-vinyl derivatives with *m*-chloroperoxybenzoic acid, and the oxidation of 4-*C*-ethylidene derivatives with osmium tetraoxide, were the key steps used to determine the chiralities in the branch, and at the branching carbon atom, of the 4-*C*-(1-hydroxyethyl) derivatives. The stereoselectivities in the two reactions are, respectively, summarized in Tables IV and V.

TABLE IV

STEREOSELECTIVITIES IN THE EPOXIDATION OF 4-*C*-VINYL DERIVATIVES WITH *m*-CHLOROPEROXYBENZOIC ACID

Equatorial 4-C-vinyl derivatives	*4-C-(Oxiran-2-yl) derivatives*				*Axial 4-C-vinyl derivatives*	*4-C-(Oxiran-2-yl) derivatives*			
		Ratio of R:S		*Yield (%)*			*Ratio of R:S*		*Yield (%)*
5		1:14		68	**4**		1:1.2[a]		91
11	(*R*)-**14**	1:4.5	(*S*)-**14**	91	**10**	(*R*)-**13**	1:1 9[a]	(*S*)-**13**	64
12	(*R*)-**15**	1:1	(*S*)-**15**	61	**16**	(*R*)-**19**	1:2	(*S*)-**19**	59
17	(*R*)-**20**	2:1	(*S*)-**20**	46					
18	(*R*)-**21**	2:1	(*S*)-**21**	89					
22	(*R*)-**23**	1.5:1[a]	(*S*)-**23**	68					

[a]The ratio was determined after conversion into the corresponding 4-*C*-(1-hydroxyethyl) derivatives.

In the case of the epoxidation of methyl 4,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hexopyranoside, Brimacombe *et al.*[11] introduced a 2,3-*O*-isopropylidene group to control the orientation of the vinyl group, and obtained the corresponding (*S*)-oxiran-2-yl derivative preponderantly (in the ratio of 3:1). Similar epoxidation of methyl 2,3-anhydro-6-deoxy-4-*C*-vinyl-α-D-gulopyranoside in the $^{O}H_{5}$ conformation gave[12] the (*S*)- and (*R*)-epoxides in the ratio of 5.9:1. Thus, a vicinal, *cis*-fused ring encourages the approach of a peroxy acid to the alkenic bond oriented to the opposite side of the pyranose ring from the direction of the tertiary hydroxyl group.

Comparison of the results for **11** and **12**, and for **17** and **18**, indicates that the effect of the free 4-hydroxyl group is not decisive, as in the *cis*-epoxidation of cyclohexenols[14]. However, the results in Table IV indicate that equatorial 4-*C*-vinyl groups in pentose derivatives and in hexose derivatives gave preferentially the (*S*)- and (*R*)-(oxiran-2-yl) groups, respectively, but that the axial 4-*C*-vinyl derivatives

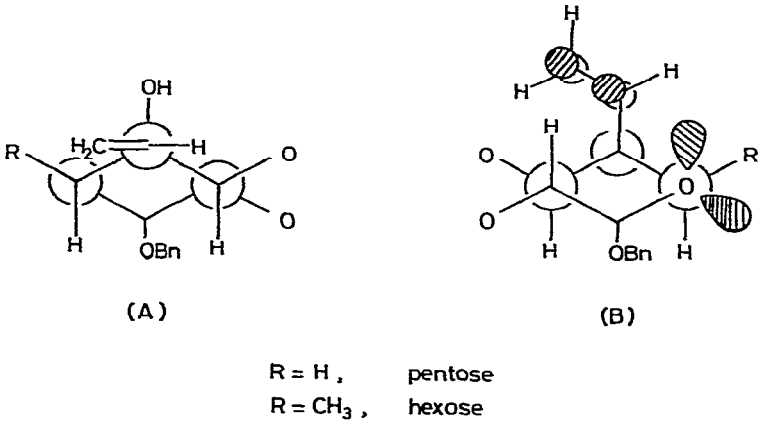

Fig. 1. Böeseken projections of 4-*C*-vinyl derivatives. [(A) equatorial, (B) axial attachment.]

TABLE V

STEREOSELECTIVITIES IN THE OXIDATION OF 4-*C*-ETHYLIDENE DERIVATIVES WITH OSMIUM TETRAOXIDE

4-C-Ethylidene derivatives	*4-C-(1-Hydroxyethyl) derivatives*			
		Axial:equatorial attack		*Yield (%)*
(*E*)-**6**	(*S*)	1 4 8	(*R*)	93
(*Z*)-**6**[a]	(*S*)	1.7:1	(*R*)	45
(*E*)-**7**	(*S*)-**26**	1.12	(*R*)-**24**	86
(*Z*)-**7**	(*R*)-**26**	1:7.8	(*S*)-**24**	90
(*E*)-**8**		0:1	(*R*)-**25**	73
(*Z*)-**8**		0:1	(*S*)-**25**	73
(*Z*)-**9**	(*R*)-**30**	1:13	(*S*)-**32**	75

[a]This compound exists in the $^1C_4$ conformation.

gave (*S*)-epoxides, regardless of whether they were pentose or hexose derivatives. These results may be explained by the deduction that the orientation of an equatorial vinyl group, shown in (A) of Fig. 1, is preferable because of the nonbonded interactions in the case of pentosides (but not of hexosides) and that the axial orientation shown in (B) is commonly preferable, owing to the electrostatic repulsion between the electrons of the ring-oxygen atom and the vinyl group. Recently, there has been considerable interest in the difference in stereoselectivities, and in assigning the optimum orientations for epoxidation of acyclic allylic alcohols with *tert*-butyl hydroperoxide catalyzed by Vd(V) and Mo(VI), and with *m*-chloroperoxybenzoic acid[13]. The application of metal-catalyzed epoxidation may induce much enhancement of the difference in the aforementioned stereoselectivities.

In the osmium tetraoxide oxidation of the 4-*C*-ethylidene derivatives, the (*E*) and (*Z*) isomers gave mainly the axially oriented (*R*)- and (*S*)-(1-hydroxyethyl) derivatives, respectively, due to the equatorial attack of the reagent[14]. The sole exceptional result, for (*Z*)-**6**, may be attributed to the balance of the steric hindrance between the axial substituents at C-2 and C-3 in the $^1C_4$ conformation. The remarkable selectivities in the case of hexose derivatives reflect the large steric requirement for the complex-formation in the transition state of this oxidation.

EXPERIMENTAL

General methods. — Evaporations were conducted under diminished pressure. Melting points were determined with a Mel-Temp melting-point apparatus and are uncorrected. Optical rotations were measured in chloroform, unless otherwise stated, with a Carl Zeiss LEP-Al or a JASCO DIP-4 polarimeter, using a 0.5-dm tube. N.m.r. spectra were recorded with a JEOL JNM PS-100 spectrometer for solutions in chloroform-*d* containing tetramethylsilane as the internal reference-standard.

Synthesis of 4-C-ethylidene derivatives (**7–9**). — The 4-*C*-ethylidene derivatives were generally synthesized as follows. To a solution of ethyltriphenylphosphonium bromide (1.5 equimolar with respect to the 4-ulose) in ether (80 mL) was added a 10% solution of butyllithium (1.4 equimolar with respect to the 4-ulose) in hexane, with stirring, under an argon atmosphere. After stirring for 1 h, a solution of the 4-ulose (1.4 mmol) in ether was added to the orange-colored mixture, and the mixture was kept for 1 h at room temperature, poured into water, and extracted with ether. The usual processing of the extract, and separation of the products on a column of silica gel with hexane–ethyl acetate (20:1 → 6:1), gave pure products. Thus, (*E*)-**7** and (*Z*)-**7** were each obtained from **1** in 20% yield.

Anal. Calc. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found for (*E*)-**7**: C, 68.43; H, 6.70; and for (*Z*)-**7**: C, 68.27: H, 6.94.

(*E*)-**8** and (*Z*)-**8** were obtained from **2** in 41 and 24% yield, respectively.

Anal. Calc. for $C_{16}H_{20}O_4$: C, 69.54: H. 7.30. Found for (*E*)-**8**: C, 69.86; H, 7.55; and for (*Z*)-**8**: C, 69.66; H, 7.25.

Only (*Z*)-**9** was obtained from **3**, in 40% yield.

Anal. Calc. for $C_{29}H_{32}O_4$: C, 78.35; H. 7.26. Found: C, 78.50; H, 7.40.

*Benzyl 4-O-benzyl-2,3-O-methylene-4-C-vinyl-β-*L*-arabinopyranoside* (**12**) *and the corresponding 6-deoxy-α-*D*-galactopyranoside* (**18**). — To a suspension of **11** (1.7 g, 6.1 mmol) and sodium hydride (50%; 380 mg, 7.9 mmol) in anhydrous *N*,*N*-dimethylformamide (5 mL) was added, dropwise, benzyl chloride (1.02 g, 8 mmol), and the resulting mixture was stirred for 2 h at room temperature, poured into ice–water, and then extracted with chloroform. The usual processing of the extract, and purification of the product on a column of silica gel with 15:1 hexane–ethyl acetate, gave pure **12** as a syrup (2.0 g) in 89% yield; $[\alpha]_D$ +101° (*c* 1.8); n.m.r.: δ 7.5–7.1 (m, 10 H, 2 Ph), 5.86 (dd, 1 H, J_{trans} 17.0, J_{cis} 9.8 Hz, H-4α), 5.58 and 5.45 (each dd, 2 H, J_{gem} 1.9 Hz, H-4β,4β'), 5.37 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1), 5.12 and 5.06 (ABq, 2 H, *J* 1.0 Hz, OCH_2O), 4.76, 4.71, 4.65, and 4.64 (2 ABq, 4 H, *J* 12.0 and 13.0 Hz, 2 CH_2Ph), 4.12 (d, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 4.03 (dd, 1 H, H-2), and 3.68 and 3.50 (ABq, 2 H, *J* 13.0 Hz, H-5*e*,5*a*).

Anal. Calc. for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 71.94; H, 6.40.

Similar treatment of **17** (1.8 g, 6.2 mmol) afforded **18** as a syrup (2.15 g) in 91% yield; $[\alpha]_D$ +70.0° (*c* 5.6).

Anal. Calc. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 71.84; H, 6.98.

Epoxidation of 4-C-vinyl derivatives. — The 4-*C*-(oxiran-2-yl) derivatives were generally synthesized as follows. To a solution of the 4-*C*-vinyl derivative (3 mmol) in 1,2-dichloroethane (10 mL) was added *m*-chloroperoxybenzoic acid (3 equiv.) at room temperature, or under reflux. After the reaction was complete, the mixture was diluted with 1,2-dichloroethane, washed successively with sodium sulfite solution (10%), sodium hydroxide solution, and water, dried, and evaporated. Separation of the residual syrup on a column of silica gel with 5.1 benzene–acetone, or hexane–ethyl acetate (3 → 7:1) usually gave two syrupy 4αepimers. The yields and physical constants of the pure isomers are summarized in Table II.

The reaction of **10** (0.1 g, 0.36 mmol) for 8 h at room temperature gave a mixture of (*R*)-**13** and (*S*)-**13** as a syrup (96 mg, 91 % yield) that could not be separated However, similar reaction of **11** gave (*R*)-**14** (16.6%) and (*S*)-**14** (74 5%), using 5:1 benzene–acetone as the eluant.

Anal. Calc. for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17. Found for (*R*)-**14**: C, 60.98; H, 6.30; and for (*S*)-**14**: C, 61.58; H, 6.44.

The reaction of **16** (89 mg, 0.31 mmol) overnight at 50°, and separation of the product with 3:1 hexane–ethyl acetate, gave (*R*)-**19** (19 mg, 20.1%) and (*S*)-**19** (37 mg, 39.1%), but that of **17** (0.5 g, 1.7 mmol) under reflux overnight gave an inseparable mixture (245 mg, 46.1%) of (*R*)-**20** and (*S*)-**20** (2:1 hexane–ethyl acetate) and unchanged **17** (120 mg, 24%).

Anal. Calc. for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found for (*R*)-**19**: C, 62.76; H, 6.40; for (*S*)-**19**: C, 61.96; H, 6.53; and for (*R,S*)-**20**: C, 61.86; H, 6 71.

The reaction of **22** (230 mg, 0.5 mmol) under reflux for 6 days, followed by separation of the products with 7:1 hexane–ethyl acetate, gave (*R*)-**23** (100 mg, 42%) and (*S*)-**23** (66 mg, 28%), together with unchanged **22** (26 mg, 11%).

Anal. Calc. for $C_{29}H_{32}O_6$: C, 73.09; H, 6.77. Found for (*S*)-**23**: C, 72.68; H, 6.58; and for (*R*)-**23**: C, 72.81; H, 6.71.

Reaction of **12** and **18** for 2 days at 80–90°, and separation of the products with 3:1 hexane–ethyl acetate, gave (*R*)- and (*S*)-**15** (30.2 and 31.1 % yield), and (*R*)- and (*S*)-**21**, respectively.

Anal. Calc. for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found for (*R*)-**15**: C. 68.50; H, 6.25; and for (*S*)-**15**: C, 68.45; H, 6.13.

Anal. Calc. for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found for (*R*)-**21**: C, 68.85; H, 6.45; and for (*S*)-**21**: C, 68.98; H, 6.22.

Synthesis of 4-C-(1-hydroxyethyl) derivatives (**24–30**) *by reduction of the corresponding 4-C-(oxiran-2-yl) derivatives.* — The conversion of 4-*C*-(oxiran-2-yl) derivatives into the corresponding 4-*C*-(1-hydroxyethyl) derivatives was generally performed as follows. A suspension of the 4-*C*-(oxiran-2-yl) derivative (0.4 mmol) and lithium aluminum hydride (1.3 equiv.) in anhydrous oxolane (8 mL) was stirred for 2 h at room temperature, and small amounts of ethyl acetate and water were then added to the mixture. The precipitates formed were filtered off, the filtrate was evaporated, and the residue extracted with chloroform. The usual processing of the extract, and purification or separation of the products on a column of silica gel, gave the pure 4-*C*-(1-hydroxyethyl) derivatives, usually as syrups, except for benzyl 4-*C*-[(*R*)-1-hydroxyethyl]-2,3-*O*-methylene-α-D-xylopyranoside [(*R*)-**24**, m.p. 104–107°] and benzyl 4-*C*-[(*S*)-1-hydroxyethyl]-2,3-*O*-methylene-β-L-arabinopyranoside [(*S*)-**26**, m.p. 152–154°]. The yields and some physical constants of the pure derivatives are summarized in Table III.

Reaction of a mixture of (*R,S*)-**13** (80 mg, 0.27 mmol), and separation of the products on a column of silica gel with 2:1 hexane–ethyl acetate, gave (*R*)-**24** (16 mg, 19.9%) and (*S*)-**24** (30 mg, 37.2%) Similarly, (*R*)-**26** and (*S*)-**26** were obtained from (*R*)-**14** and (*S*)-**14**, respectively.

Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found for (*R*)-**24**: C, 61.20; H, 6.45; for (*S*)-**24**: C, 61.25; H, 6.68; for (*R*)-**26**: C, 60.92; H, 6.81; and for (*S*)-**26**: C, 60.66; H, 6.76.

Similar reduction of mixture (*R*,*S*)-**20** (200 mg, 0.65 mmol), and the usual separation of the products, gave benzyl 6-deoxy-4-*C*-[(*R*)-1-hydroxyethyl]- [(*R*)-**27**] and 4-*C*-[(*S*)-1-hydroxyethyl]-2,3-*O*-methylene-α-D-galactopyranoside [(*S*)-**27**] in 60.6 (122 mg) and 30.8% (62 mg) yield, respectively. In a similar way, (*R*)-**25** and (*S*)-**25**, having the D-*gluco* configuration, were obtained from (*R*)-**19** and (*S*)-**19**, respectively.

Anal. Calc. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found for (*R*)-**25**: C, 61.45; H, 7.00; for (*S*)-**25**: C, 61.67; H, 7.21; for (*R*)-**27**: C, 62.46; H, 7.41; and for (*S*)-**27**: C, 62.24; H, 7.31.

Benzyl 2,3-di-*O*-benzyl-6-deoxy-4-*C*-[(*R*)-1-hydroxyethyl]-α-D-galactopyranoside [(*R*)-**30**] and its 4α-epimer [(*S*)-**30**] were obtained from (*R*)-**23** and (*S*)-**23**, respectively.

Anal. Calc. for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found for (*R*)-**30**: C, 72.48; H, 7.20; and for (*S*)-**30**: C, 72.36; H, 7.15.

The 4-*O*-benzyl derivatives [(*R*)-**28** and (*S*)-**28**] of (*R*)-**26** and (*S*)-**26** were obtained from (*R*)-**22** and (*S*)-**22**, respectively. However, these compounds were characterized *after* conversion into the corresponding 4-*C*-(1-methoxyethyl) derivatives[6].

Benzyl 4-*O*-benzyl-6-deoxy-4-*C*-[(*R*)-1-hydroxyethyl]-2,3-*O*-methylene-α-D-galactopyranoside [(*R*)-**29**] and its 4α-epimer [(*S*)-**29**] were, respectively, obtained as syrups from (*R*)-**21** and (*S*)-**21**, in quantitative yield.

Anal. Calc. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found for (*R*)-**29**: C, 68.85; H, 7.00; and for (*S*)-**29**: C, 69.25; H, 6.88.

Oxidation of 4-C-ethylidenes derivatives (**7**–**9**) *with osmium tetraoxide.* — The direct conversion of the 4-*C*-ethylidene derivatives (**7**–**9**) into the corresponding 4-*C*-(1-hydroxyethyl) derivatives was generally conducted as follows. To a mixed solution of 4-methylmorpholine *N*-oxide dihydrate (1.1 equimol) in 5:2 acetone–water (7 mL) and a catalytic amount of osmium tetraoxide (0.05 equimol) in *tert*-butanol (1 mL) was added a solution of the 4-*C*-vinyl derivative (0.4 mmol) in acetone, and the resulting solution was stirred overnight at room temperature. After the reaction was complete, hydrogen sulfide was bubbled into the mixture, the precipitates formed were filtered off, the filtrate was evaporated, and the residue was extracted with chloroform. The usual processing of the extract, and separation of the products by preparative t.l.c., gave the corresponding 4-*C*-(1-hydroxyethyl) derivative.

Thus, oxidation of (*E*)-**7** and (*Z*)-**7** (each 100 mg, 0.38 mmol) and columnar separation of the products with 4:1 benzene–acetone gave the pair (*R*)-**24** (90 mg, 79.5%) and (*S*)-**26** (7.5 mg, 6.6%), and another pair, (*S*)-**24** (89.8 mg, 79.5%) and (*R*)-**26** (11.5 mg, 10.2%), respectively.

Similar oxidation of (*E*)-**8** and (*Z*)-**8**, and columnar separation of the products with 1:1 chloroform–ethyl acetate, gave (*R*)-**25** and (*S*)-**25** respectively, both in

73.3% yield, in addition to a small amount (2.2 and 2.1% yield) of the peroxidized product, benzyl 4-*C*-acetyl-6-deoxy-2,3-*O*-methylene-α-D-glucopyranoside (**31**), m.p. 88–89°, $[\alpha]_D$ +152.7° (*c* 2.6); n.m.r.: δ 7.5–7.3 (m, 5 H, Ph), 5.40 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1), 5.10 and 5.05 (ABq, 2 H, *J* 1.0 Hz, OCH_2O), 4.77 and 4.71 (ABq, 2 H, *J* 12.3 Hz, CH_2Ph), 4.24 (s, OH), 4.10 (d, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 3.95 (dd, 1 H, H-2), 3.79 (q, 1 H, $J_{5,6}$ 7.0 Hz, H-5), 2.26 (s, 3 H, Ac), and 1.07 (d, 3 H, H-6).

Anal. Calc. for $C_{16}H_{20}O_6$: C, 62.32; H, 6 54. Found: C, 61.88; H, 6.77.

Compound **31** was also obtained by the oxidation of (*R*,*S*)-**25**, as follows. To a solution of *N*-chlorosuccinimide (2.7 g, 20 mmol) in anhydrous toluene (40 mL) was added dimethyl sulfide (1.26 g, 21 mmol) at 0° under an argon atmosphere. To the resulting solution, cooled to −25°, was added (*R*,*S*)-**25** (2 g, in the ratio of 2:1; 9.1 mmol), and the mixture was stirred for 3 h. The reaction was quenched by addition of triethylamine (1 g), and the mixture poured into ice–water. Extraction of the products with ether, and separation on a column of silica gel with 4:1 benzene–acetone, gave **31** (760 mg, 38.2%) and its 4-*O*-[(methylthio)methyl] derivative (630 mg, 27%); 4-*O*-[(methylthio)methyl]-**31**: syrup, $[\alpha]_D$ +52 3° (*c* 1.0); n.m.r.: δ 7.5–7.3 (m, 5 H, Ph), 5.34 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1), 5.13 and 4.98 (ABq, 2 H, *J* 1.0 Hz, OCH_2O), 4.95 and 4.88 (ABq, 2 H, *J* 11.8 Hz, SCH_2O), 4.70 (s, 2 H, CH_2Ph), 4.41 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.36 (d, 1 H, H-3), 3.83 (q, 1 H, $J_{5,6}$ 7.0 Hz, H-5), 2 25 (s, 3 H, Ac), 2.19 (s, 3 H, SMe), and 1 14 (d, 3 H, H-6).

Anal. Calc. for $C_{18}H_{24}O_6S$: C, 58.68; H, 6.57; S, 8.70. Found: C, 58.12; H, 6.33; S, 8.52.

Similar oxidation of (*Z*)-**9**, and columnar separation of the products with 3:1 hexane–ethyl acetate, gave (*R*)-**30** and **32** in 5.2 and 69.9% yield, respectively.

Compound **32**: syrup, $[\alpha]_D$ +18.5° (*c* 0.8); n.m.r.: δ 7.48–7.18 (m, 15 H, 3 Ph), 5.12–4.45 (m, 6 H, $3CH_2Ph$), 4.81 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.06 (d, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 4.06 (q, 1 H, H-4α), 3.99 (dd, 1 H, H-2), 3.76 (q, 1 H, H-5), 1.32 (d, 3 H, $J_{5,6}$ 7.0 Hz, H-6), and 1.14 (d, 3 H, $J_{4\alpha,4\beta}$ 7.2 Hz, H-4β).

Anal. Calc. for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 72.58; H, 7.03.

Preparation of 4-C-(1-hydroxyethyl) derivatives (**25** *and* **27**) *by successive* spiro *epoxidation and alkaline ring-opening of 4-C-ethylidene derivatives* [(E)-**8** *and* (Z)-**8**].— A solution of (*E*)-**8** (190 mg, 0.69 mmol) and *m*-chloroperoxybenzoic acid (200 mg, 1.16 mmol) in 1,2-dichloroethane (12 mL) was stirred overnight at room temperature, washed successively with sodium sulfite (10%), saturated aqueous sodium hydrogencarbonate, and water, and evaporated, to give a mixture of the corresponding *spiro*-epoxides as a syrup. A solution of the syrup in dimethyl sulfoxide (10 mL) and 2M potassium hydroxide solution (2 mL) was kept overnight at 80–90°, poured into water, and then extracted with ether. The usual processing of the extract, and separation of the products by preparative t.l.c., gave pure (*S*)-**25** and (*R*)-**27** in 5.2 (11 mg) and 9.3% (19.9 mg) yield, respectively.

Similar epoxidation and alkaline ring-opening of (*Z*)-**8** (270 mg, 0.98 mmol), and separation of the products in a flash column with 5:5:1 hexane–ether–pyridine, gave pure (*R*)-**25** and (*S*)-**27** in 9.1 (27.6 mg) and 40% (121.3 mg) yield, respectively.

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