THE INFLUENCE OF STERIC FACTORS IN DIAZOALKANE–PYRANOSID-2-ULOSE REACTIONS

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ABSTRACT

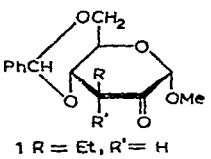
The reactions of diazomethane with methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*arabino*- and -*ribo*-hexopyranosid-2-uloses (**1** and **2**) afford spiro-epoxides preponderantly, whereas the corresponding reactions of **1** and **2** with diazoethane give, exclusively, ring-expansion products. Compound **1** gives, preponderantly, heptoseptanosid-3-uloses with diazoethane and not the expected heptoseptanosid-2-uloses, thereby indicating that the nature of the ring-expansion products is controlled by steric rather than by electronic effects. It is shown that comparisons of pyranosidulose–diazoalkane reactions can provide new information about the stereochemical course of diazoalkane ring-expansion reactions. The reactions of **1** and **2** with diazoethane provide a route to higher sugars containing two R–C–H branch points.

INTRODUCTION

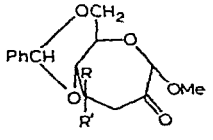
Only a small number of reactions between cyclic sugar ketones and diazoalkanes have been described. Most of the reported examples of this type of reaction concern the addition of diazomethane to 5- or 6-membered, cyclic-sugar ketones with the primary objective of forming spiro-epoxides and, thence, branched-chain, *C*-methyl derivatives by reduction[1] with lithium aluminium hydride. Some papers have also described ring-expansion reactions with diazomethane[2], and, for example, Horwitz and his co-workers have recently described the reaction of diazomethane and 1,2-*O*-isopropylidene-5-*O*-trityl-α-D-*erythro*-pentofuranos-3-ulose which gives a mixture of spiro-epoxides and ring-expanded products[3]. However, comparatively little is known of the steric course of reactions of cyclic sugar ketones (or indeed of less-complicated cyclic ketones) and diazoalkanes, and the potential utility of diazoalkane–pyranosidulose (or furanosidulose) reactions for the synthesis of higher branched-chain sugars has not been explored. In this paper, we report on the importance of steric effects in cyclic ketone–diazoalkane reactions based on a comparison of the products from the reactions of both diazomethane and diazoethane with methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*arabino*- and -*ribo*-hexopyranosid-2-ulose (**1** and **2**, respectively). Also, the reaction of diazoethane with **1** and **2** provides an example of a method of potential utility for the synthesis of sugars containing two R–C–H branch points.

DISCUSSION

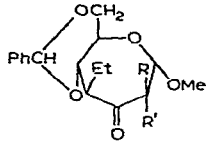
In the preceding paper[4], the reactions of diazomethane with **1** and **2** in ethereal methanol were described. The *arabino*-hexopyranosid-2-ulose derivative (**1**) gave a mixture of the spiro-epoxides methyl 2,2′-anhydro-4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-hydroxymethyl-α-D-mannopyranoside (65%) and -glucopyranoside (8%), together with some of the ring-expanded product methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-α-D-*arabino*-heptoseptanosid-2-ulose (**3**, 18%). Similarly, the *ribo*-hexopyranosid-2-ulose derivative **2** gave a mixture of the spiro-epoxides methyl 2,2′-anhydro-4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-hydroxymethyl-α-D-altropyranoside (25%) and -allopyranoside (40%), together with some of the ring-expanded product methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-α-D-*ribo*-heptoseptanosid-2-ulose (**4**, 12%),



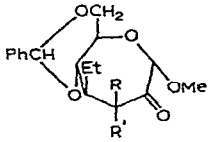
1 R = Et, R′ = H
2 R = H, R′ = Et



3 R = Et, R′ = H
4 R = H, R′ = Et



5 R = Me, R′ = H
6 R = H, R′ = Me



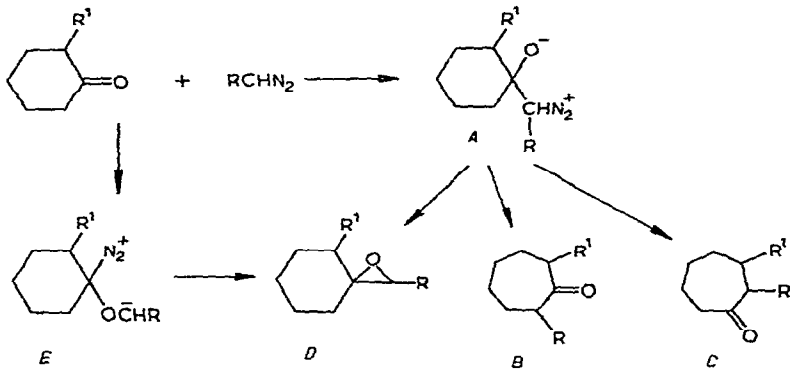
7 R = H, R′ = Me
8 R = Me, R′ = H

The fact that C-4 in **3** and **4** has the same configuration as C-3 in **1** and **2**, respectively, confirms previous assumptions (based on analogy with other 1,2-nucleophilic displacement reactions) that the migrating centre in diazomethane ring-expansion reactions retains its configuration[5].

The reaction of diazoethane and the *arabino*-hexopyranosid-2-ulose **1** in ethereal methanol, in contrast to the corresponding diazomethane reaction, afforded no spiro-epoxides but only the *manno*- and *gluco*-heptoseptanosid-3-uloses (**5** and **6**, respectively) and the *gluco*-heptoseptanosid-2-ulose derivative **7**. Similarly, the reaction between diazoethane and the *ribo*-hexopyranosid-2-ulose (**2**) afforded compounds that were very tentatively identified as the *allo*- and *altro*-heptoseptanosid-2-uloses (**12** and **13**) and the *allo*-heptoseptanosid-3-ulose **14**, but no spiro-epoxides. In the subsequent discussion, it is suggested that stereochemical factors account for the gross differences in behaviour between the diazomethane and diazoethane reactions and provide an explanation of the precise nature of the products formed in the diazoethane reactions; similar explanations of other ring expansions have been published (*e.g.* ref. 6).

Reactions between diazoalkanes and ketones are usually regarded as proceeding *via* charge-separated intermediates (such as *A*, Scheme 1) which then undergo 1,2-nucleophilic rearrangements[7] to give products such as *B*, *C*, and *D*. The long-established view is that the spiro-epoxide *D*, as well as the ring-expansion products *B* and *C*, is formed from the same charge-separated intermediate *A*. However, it has been suggested recently that epoxides are not formed only from intermediates such as *A*, but that they might be formed more readily from intermediates such as *E*, and that

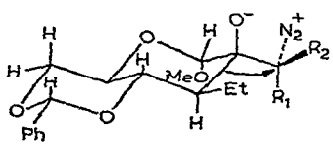
whether or not *A* or *E* is the preferred intermediate might depend on the reaction conditions[8]. In the following discussion, it is assumed that, since diazomethane reactions giving spiro-epoxides were carried out under essentially identical conditions as reactions with diazoethane which did not give spiro-epoxides, both reactions proceeded via the charge-separated intermediate *A*.



SCHEME 1

The first stage in the reaction between diazoalkanes and cyclic ketones, as illustrated in Scheme 1, is usually considered to be a nucleophilic addition of the diazoalkane from the least-hindered side of the cyclic ketone to from a zwitterionic intermediate. Since equatorial addition of diazoethane to **1** is clearly favoured, as indicated by the preponderance of the spiro-epoxide having the *manno* configuration, and in the absence of evidence to the contrary for diazoethane, this common zwitterionic intermediate may be depicted as **9**, **10**, or **11**. The second stage of the reaction is the nucleophilic displacement of nitrogen by oxygen or by the electrons of a C–C bond. Since nucleophilic displacement reactions are favoured by a transition state in which both the nucleophile and the leaving group adopt a *trans*-coplanar relationship, the favoured orientation for epoxide formation must be **10** ($R_1 = R_2 = H$) and the intermediate leading to the ring-expanded **3** must be **9** ($R_1 = R_2 = H$).

The differences in the reaction of **1** with diazomethane and diazoethane may possibly be explained, at least in part, by postulating that the transition state **10**, when $R_1 = Me$, $R_2 = H$ or $R_1 = H$, and $R_2 = Me$, is less favourable than transition states **9** and **11**. When $R_1 = Me$ in **10**, there is obviously a strong, non-bonded interaction with the C-3 ethyl substituent, but it is less clear why conformation **10**



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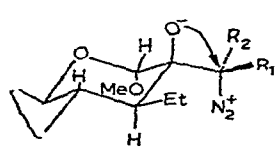

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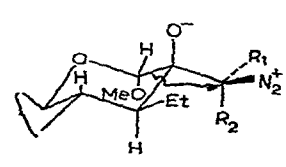

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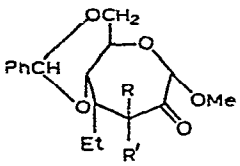
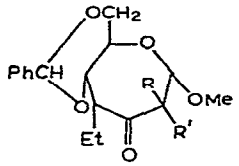


12 R = H, R' = Me
13 R = Me, R' = H



14 R = H, R' = Me
15 R = Me, R' = H

should be less favourable than **9** or **11** when $R_1 = H$ and $R_2 = Me$. It must be postulated that even the introduction of a 1,3-diaxial CH_3–H interaction results in a sufficient energy increase in the transition state **10** to cause a change to other conformations. The validity of this argument is difficult to assess, however, since energy values for non-bonded interactions with $-CH_2N_2^+$ are not available.

An alternative, and perhaps more probable, general explanation for the differences in the diazomethane and diazoethane reactions is that, whereas epoxide formation from diazomethane only results in the eclipsing of C–H and C–C bonds, epoxide formation from diazoethane would result in the more unfavourable eclipsing of C–C bonds. Thus, for diazoethane reactions, resistance to epoxide formation would be encountered during the actual elimination step rather than by resistance to the assumption of the preferred conformation for elimination of N_2^+.

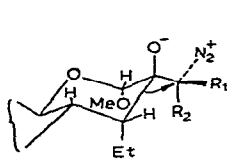
Similar stereochemical arguments may be used to explain the gross differences in the reactions of diazomethane and diazoethane with **2**. However, for these reactions, the transition states arising from both axial and equatorial addition must be considered, since, with diazomethane, **2** afforded appreciable quantities of spiro-epoxides having the *allo* and *altro* configurations.

For the reaction of diazoethane and **1**, the formation of the heptoseptanosid-3-uloses (**5** and **6**) and the heptoseptanosid-2-ulose (**7**) from the charge-separated intermediate resulting from equatorial addition of diazoethane can be explained by a consideration of the four transition states represented by **9** and **11**. The most unfavourable intermediate is **9** ($R_1 = H$, $R_2 = Me$), where there is a strong, non-bonded interaction between the methyl and 3-*C*-ethyl groups, and it is this intermediate that would lead to **8**. If the initial reaction between **1** and diazoethane gave an axial addition product, a consideration of the possible transition states for this charge-separated intermediate suggests that **6** and **7** would be the favoured products and that little **5** or **8** would be formed. The presence of an appreciable quantity (36%) of **5** as a reaction product is therefore indirect evidence that equatorial addition of diazoethane to **1** occurs preponderantly. These results indicate that the nature of the products formed in diazoalkane ring-expansion depends on both the initial direction of addition of the diazoalkane to the carbonyl group and on the presence, or otherwise, of non-bonded interactions that control the ease with which the zwitterionic intermediate can take up the conformation necessary for ring expansion.

Perhaps the result that is most indicative of the importance of steric factors in diazoalkane–cyclic ketone ring-expansion reactions is that, in the diazoethane–**1** reaction, the preponderant products resulted from nucleophilic attack by the C-1–C-2

bond that carries two oxygen atoms at C-1. This bond is much less nucleophilic than the C-2–C-3 bond, and previous evidence had indicated that ring expansion is inhibited[9] for cyclic ketones in which the 2-position carries electronegative substituents. Thus, electronic considerations were outweighed by stereochemical factors and, whereas a heptoseptanosid-2-ulose (**3**) was favoured in the diazomethane ring-expansion of **1**, the corresponding diazoethane reaction gave, preponderantly, heptoseptanosid-3-uloses (**5** and **6**).

The steric course of the reaction of diazoethane and **2** was more difficult to elucidate, because the configuration of the products could not be established with certainty and because appreciable quantities of both the *allo* (40%) and *altro* (25%) spiro-epoxides (the epoxides resulting from axial and equatorial addition of diazomethane, respectively) were formed by reaction of **2** with diazomethane. The latter observation necessitated the assumption that both axial or equatorial addition of diazoethane to **2** could occur. Thus, for ring-expansion reactions, the stereochemistry of the eight possible transition states represented by **16**, **17**, **18**, and **19** were considered. In each case, where $R_1 = H$ and $R_2 = Me$, strongly unfavourable, non-bonded interactions are present, but when $R_1 = Me$ and $R_2 = H$, the stereochemical factors permit the coplanar transition states that are necessary for ring expansion.



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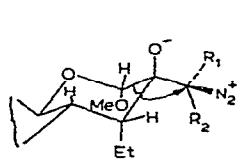

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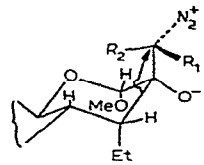

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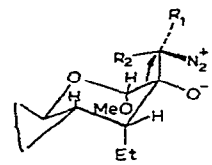


19

There is some evidence that the major products from the reaction of diazoethane and the *ribo*-hexopyranosid-2-ulose **2** were the *allo*-heptoseptanosid-3-ulose **14** (23%) and the *allo*-heptoseptanosid-2-ulose **12** (43%), although these assignments must be considered to be only tentative (see later for structural assignments). It will be seen that the *allo*-heptoseptanosid-3-ulose and the *allo*-heptoseptanosid-2-ulose can be derived from the transition states **19** and **18** ($R_1 = Me$, $R_2 = H$), respectively, which result from axial addition of diazoethane to **2**. The only other product isolated was the *altro*-heptoseptanosid-3-ulose **13**, which can be derived from **16** ($R_1 = Me$, $R_2 = H$); **13** was formed only to a limited extent (4.8%), and it is therefore apparent that axial addition of diazoethane to **2** was preferred to equatorial addition. However, if the major products were the *altro*-heptoseptanosid-3-ulose and *altro*-heptoseptanosid-2-ulose (represented by **13** and **15**, respectively), it will be seen that **13** could be derived from the equatorial-addition intermediate **16** ($R_1 = Me$, $R = H$) and that **15** could result from the equatorial-addition intermediate **17** ($R_1 = Me$, $R = H$). The importance of stereochemical factors in controlling the direction of the addition of diazoalkanes to cyclic ketones is illustrated by the fact that, whereas diazomethane addition to **1** was preponderantly equatorial (65%, *cf.* 8% axial), the corresponding addition to **2** was preponderantly axial (40%, *cf.* 25% equatorial). If small differences in

the nature of the substrate can cause such pronounced differences in the direction of addition of diazomethane to cyclic ketones, it is reasonable to assume that small changes in the diazoalkane may also have a pronounced effect on the steric course of diazoalkane–cyclic ketone reactions, and thus almost exclusively axial (or almost exclusively equatorial) addition of diazoethane to **2** would not be unexpected. On the assumption that **2** exists in a normal-chair conformation, axial-addition intermediates appear to be favoured, since the formation of equatorial-addition intermediates necessitates attack on the carbonyl carbon atom along a pathway between the C-1 and C-3 axial substituents in **2**.

It must be pointed out, however, that, if the preponderant products from the **2**–diazoethane reaction were, in fact, either of the pairs **12** and **15** or **13** and **14**, it would be necessary to postulate not only that there was considerable steric control of the reaction after the formation of the zwitterionic intermediate but also that equatorial and axial addition products were formed with equal facility and that the formation of the charge-separated intermediate itself was subject to pronounced steric control[6c]. For example, if the preponderant products are **13** and **14**, in order to explain the formation of **13** as the sole product from equatorial addition of diazoethane to **2**, the asymmetric $R_1R_2CN_2^+$ group in the zwitterionic intermediates **16** and **17** can only have the (*S*)-configuration ($R_1 = Me$, $R_2 = H$ in **16**, and $R_2 = Me$, $R_1 = H$ in **17**). With this situation, ring expansion of **16** to **13** is permitted, but ring expansion of **17** is not allowed. Similarly, to account for the fact that **14** is the only product from axial addition of diazoethane on **2**, the $R_1R_2CN_2^+$ centre in **18** and **19** can also only have the (*S*)-configuration ($R_1 = Me$, $R_2 = H$ in **19**, and $R_1 = H$ and $R_2 = Me$ in **18**). With this situation, only ring expansion of **19** to afford **14** is permitted. However, the possibility of such stringent stereochemical control during the addition of diazoethane to cyclic ketones appears unlikely, since, in the reaction of diazoethane with **1**, the $R_1R_2N_2^+C$ centre having the (*R*)-configuration [from which **5** and **7** (47%) were formed] and the (*S*)-configuration [from which **6** (39%) was formed] were produced in closely similar proportions. This conclusion differs from that of Turro and Gagosian[6c] who presented some evidence in favour of "steric approach control". However, the general applicability of their argument is difficult to assess, since no account was taken of interactions between $C–N_2^+$ and other groups.

The above discussion of the reaction between **2** and diazoethane is presented to illustrate some of the stereochemical factors that must be considered if the products from diazoalkane ring-expansion reactions are to be predicted. It is, perhaps, encouraging that the conclusion about the identity of **12** and **14** is the same whether arrived at from a consideration of the influence of stereochemical factors on the reaction pathway or from a consideration of the possible structures of **12** and **14** suggested by n.m.r. data (see below).

Structural assignments of heptoseptanosiduloses

The structural assignments of the heptoseptanosiduloses **3**, **4**, **5**, **6**, and **7** were made on the basis of the first-order n.m.r. parameters, listed in Table I, by appropriate

application of rules that relate chemical-shift data and the magnitude of coupling constants with configuration and conformation[10].

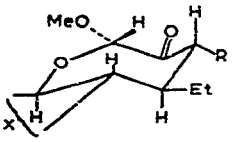
TABLE I

N.M.R. ASSIGNMENTS FOR HEPTOSEPTANOSIDULOSES AND RELATED COMPOUNDS[a]

Compound	*H-1*	*H-2*	*H-3*	*H-3'*	*H-4*	*H-5*	*Coupling constants*
3	4.76	—	2.42	2.73	1.45	—	$J_{3,3'}$ 11, $J_{3,4}$ 2.5, $J_{3',4}$ 11.8
	(4.30	—	[2–2.5]		1.3	3.49	$J_{4,5}$ 9, $J_{5,6}$ 9)[b]
4	4.68	—	2.68	2.98	—	—	$J_{3,3'}$ 12.5, $J_{3,4}$ 6, $J_{3',4}$ 2.8
5	4.2	3.15	—	—	2.72	—	$J_{1,2}$ 8, $J_{4,5}$ 9.8
6	4.43	2.85	—	—	2.6	—	$J_{1,2}$ 1.9, $J_{4,5}$ 9
7	4.78	—	3.0	—	1.8	—	$J_{3,4}$ 9
12	4.62	—	3.2	—	1.95	—	$J_{3,4}$ 2, $J_{4,5}$ 3
13	4.74	—	3.0	—	1.9	—	$J_{3,4}$ 4.7
14	4.58	2.88	—	—	2.65	—	$J_{1,2}$ 1.5, $J_{4,5}$ 4
26	4.67	5.06	—	—	—	—	$J_{1,2}$ 4.2, $J_{2,3}$ 2.4
27	4.59	4.82	—	—	—	—	$J_{1,2}$ 1.8, $J_{2,3}$ 10.2
28	4.58	—	5.2	—	—	3.4	$J_{1,2}$ 4.5, $J_{2,3}$ $J_{3,4}$ 1.5, $J_{4,5}$ 6.8, $J_{5,6}$ 10

[a]N.m.r. spectra were measured on a JEOL JNM-4H-100 n.m.r. spectrometer at 100 MHz with deuteriochloroform as solvent and tetramethylsilane as internal standard. Chemical-shift data are expressed as δ values in p.p.m., and coupling constants are in Hz. [b]The figures in parentheses are data obtained from a spectrum for a benzene solution of **3**.

The structures assigned to compounds **3** and **4** were fully consistent with the n.m.r. data. In both compounds, the appearance of H-1 as a low-field singlet when the methylene protons also showed vicinal coupling was consistent only with a carbonyl group at C-2 and a methylene group at C-3 in the heptoseptanosidulose structure. The magnitude of the $J_{3,4}$, $J_{3',4}$, and $J_{4,5}$ coupling constants (2.5, 11.8, and 9 Hz, respectively) in **3** were consistent only with an *arabino*-heptoseptanosid-2-ulose structure, and it therefore followed that **4** had the *ribo* configuration. The coupling constants of **3** did not permit an unequivocal assignment of conformation to the seven-membered ring but were consistent with the chair forms **20** and **21** or the intermediate twist-chair. The precise factors governing the stereochemistry of septanosides are as yet unknown, but it is perhaps significant that the n.m.r. parameters of **3** were consistent with the structures that are favoured if vicinal non-bonded interactions, non-bonded interactions across the ring which are analogous to 1,3-diaxial interactions in six-membered rings, and dipole effects (the anomeric effect and the effect of the carbonyl group at C-2) are considered. It is probable that **4** adopts a conformation similar to **3**, but insufficient coupling constants were obtained to confirm this. Although the geminal $J_{3,3'}$ coupling constant changes from 11 Hz in **3** to 12.5 Hz in **4**, this change does not necessarily reflect any major change in the orientation of the C-2 carbonyl group with respect to the C-3 protons, since small changes in orientation can cause appreciable changes in coupling constants, as has been shown by Barfield and Grant[11].



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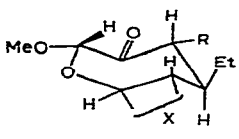
26 R = Me



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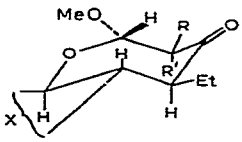
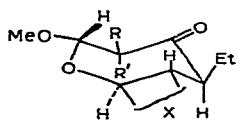
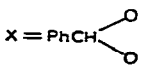
27 R = Me



22 R = Me, R' = H
24 R = H, R' = Me



23 R = Me, R' = H
25 R = H, R' = Me

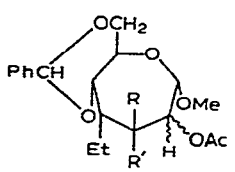


X = PhCH(O)O

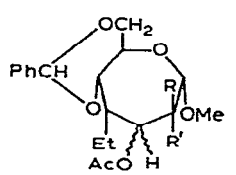
The n.m.r. parameters of compounds **5**, **6**, and **7** clearly indicated that compound **7** was a heptoseptanosid-2-ulose and that compounds **5** and **6** were heptoseptanosid-3-uloses. Thus, in **7**, H-1 and H-4 had chemical shifts similar to those for the corresponding protons in **3**, and also H-1 showed no vicinal coupling. In **5** and **6**, H-1 was at higher field than in **7** and showed vicinal coupling, whereas H-4 was at lower field. Configurational assignments to **5**, **6**, and **7** were made on the basis that the migrating centre in diazoalkane ring-expansions retains its configuration.

The coupling constants of **5** were consistent with the *manno* configuration, and either of the chair conformations **22** and **23** or the intermediate twist-chair. For compound **6**, the coupling constants were consistent with the *gluco* configuration and similar conformations (**24**, **25**, and the intermediate twist-chair), although the chair conformation **25** appeared unlikely because of a strong interaction between H-6 and the 2-methyl substituent. The large $J_{3,4}$ coupling constant in compound **7** is only consistent with the *gluco* configuration, and again it is probable that chair conformations (*e.g.*, **26** and **27**) are favoured.

Analyses of the n.m.r. parameters of compounds **12**, **13**, and **14**, similar to those described for compounds **5**, **6**, and **7**, indicated that compounds **12** and **13** were heptopyranosid-2-uloses and that compound **14** was a heptoseptanosid-3-ulose. The n.m.r. results did not permit unequivocal configurational assignments to any of these compounds. Consequently, compounds **12**, **13**, and **14** (or **15**) were reduced and acetylated to give **28**, **29**, and **30** (or **31**), respectively; for all three heptoseptanosid-uloses, reduction with lithium aluminium hydride afforded only one product. No definite structural assignments were possible from an analysis of the n.m.r. parameters of the acetylated products. However, by use of molecular models, by application of established conformational principles, and from consideration of all possible configurations and conformations for compounds **12**, **13**, **14**, **15**, **28**, **29**, **30**, and **31**, it appeared probable that the n.m.r. data were most consistent with conformations in which **12** and **14** had the *allo* configuration and **13** the *altro* configuration.



28 R = H, R' = Me
29 R = Me, R' = H



30 R = H, R' = Me
31 R = Me, R' = H

EXPERIMENTAL

General methods and the reactions of methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*arabino*- and -*ribo*-hexopyranosid-2-uloses (**1** and **2**) with diazomethane are described in the preceding paper[4].

Reaction of diazoethane and methyl 4,6-O-benzylidene-3-deoxy-3-C-ethyl-α-D-arabino-hexopyranosid-2-ulose (**1**). — A solution of diazoethane in ether was added to a solution of **1** (2 g) in methanol at room temperature. More diazoethane in ether was added at intervals until a pale-yellow colour persisted. The solution was concentrated and chromatographed over silica gel in acetone–light petroleum (1:19) to give, in order of elution: (*a*) methyl 5,7-*O*-benzylidene-2,4-dideoxy-4-*C*-ethyl-2-*C*-methyl-α-D-*manno*-heptoseptanosid-3-ulose (**5**) (0.75 g, 36%), m.p. 202–203° (from light petroleum), $[\alpha]_D^{26}$ +89.6° (*c* 0.6, chloroform) (Found: C, 67.4; H, 7.7. $C_{18}H_{24}O_5$ calc.: C, 67.5; H, 7.6%); (*b*) methyl 5,7-*O*-benzylidene-2,4-dideoxy-4-*C*-ethyl-2-*C*-methyl-α-D-*gluco*-heptoseptanosid-3-ulose (**6**) (0.82 g, 39%), m.p. 75° (from light petroleum), $[\alpha]_D^{26}$ +191.8° (*c* 6, chloroform) (Found: C, 67.4; H, 7.6. $C_{18}H_{24}O_5$ calc.: C, 67.5; H, 7.6%); (*c*) methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-3-*C*-methyl-α-D-*gluco*-heptoseptanosid-2-ulose (**7**) (0.23 g, 11%), m.p. 143–144° (from light petroleum), $[\alpha]_D^{32}$ +32.3° (*c* 0.4, chloroform) (Found: C, 67.4; H, 7.4. $C_{18}H_{24}O_5$ calc.: C, 67.5; H, 7.6%).

Reaction of diazoethane and methyl 4,6-O-benzylidene-3-deoxy-3-C-ethyl-α-D-ribo-hexopyranosid-2-ulose (**2**). — A solution of crude **2** (obtained by oxidation of methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-altropyranoside with acetic anhydride–methyl sulphoxide) in methanol was treated at room temperature with an excess of an ethereal solution of diazoethane, so that after 24 h a permanent, yellow colour remained. The solution was concentrated, and the residue was chromatographed over silica gel to yield, in order of elution, (*a*) 0.7 g of a mixture of products, none of which contained a *C*-methyl substituent and which probably arose from impurities from the Ac_2O–Me_2SO oxidation; (*b*) methyl 5,7-*O*-benzylidene-2,4-dideoxy-4-*C*-ethyl-2-*C*-methyl-α-D-*allo*-heptoseptanosid-3-ulose (**14**) (0.7 g, 23%), m.p. 112–113°, $[\alpha]_D^{23}$ +204° (*c* 0.8, chloroform) (Found: C, 67.0; H, 7.6. $C_{18}H_{24}O_5$ calc.: C, 67.5; H, 7.6%); (*c*) methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-3-*C*-methyl-α-D-*altro*-heptoseptanosid-2-ulose (**13**) (0.14 g, 4.8%); (*d*) methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-3-*C*-methyl-α-D-*allo*-heptoseptanosid-2-ulose (**12**) (1.3 g, 43%), m.p. 101–102°, $[\alpha]_D^{23}$ −63° (*c* 1, chloroform) (Found: C, 67.2; H, 7.4. $C_{18}H_{24}O_5$ calc.: C, 67.5; H, 7.6%).

Preparation of acetates **28**, **29**, *and* **30** (*or* **31**). — The products of reduction of the heptoseptanosiduloses **12**, **13**, and **14** (*ca.* 0.1 g of each) with lithium aluminium hydride were examined by t.l.c. and shown to be essentially homogeneous. The products were acetylated with acetic anhydride in pyridine overnight at room temperature, and the acetates were examined directly by n.m.r. For all three compounds, no traces of diastereoisomers could be detected.

REFERENCES

1 W. G. OVEREND AND N. R. WILLIAMS, *J. Chem. Soc.*, (1965) 3446; R. J. FERRIER, W. G. OVEREND, G. A. RAFFERTY, H. M. WALL, AND N. R. WILLIAMS, *J. Chem. Soc., C*, (1968) 1091.
2 B. FLAHERTY, W. G. OVEREND, AND N. R. WILLIAMS, *Chem. Commun.*, (1966) 434; S. NAHAR, W. G. OVEREND, AND N. R. WILLIAMS, *Chem. Ind. (London)*, (1967) 2114.
3 J. P. HORWITZ, N. MODY, AND R. GASSER, *J. Org. Chem.*, 35 (1970) 2335.
4 T. D. INCH, G. J. LEWIS, AND N. E. WILLIAMS, *Carbohyd. Res.* 19 (1971) 17.
5 D. J. CRAM, in M. S. Newman (Ed.), *Steric Effects in Organic Chemistry*, Wiley, New York, 1956, Chapter 5.
6 (*a*) N. J. TURRO AND R. B. GAGOSIAN, *Chem. Commun.*, (1969) 949; (*b*) J. A. MARSHALL AND J.J. PARTRIDGE, *J. Org. Chem.*, 33 (1968) 4090; (*c*) N. J. TURRO AND R. B. GAGOSIAN, *J. Amer. Chem. Soc.*, 92 (1970) 2036.
7 C. D. GUTSCHE AND D. REDMORE, *Carbocyclic Ring Expansion Reactions*, Academic Press, New York, 1968, p. 81.
8 G. W. COWELL AND A. LEDWITH, *Quart. Rev. Chem. Soc.*, 24 (1970) 119.
9 Ref. 7, p. 88.
10 T. D. INCH, *Ann. Rev. N.m.r. Spectroscopy*, 2 (1969) 35.
11 M. BARFIELD AND D. M. GRANT, *J. Amer. Chem. Soc.*, 85 (1963) 1899.