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THE ^{13}C-N.M.R. SPECTRA AND THE CONFORMATIONS OF HEPTITOLS IN SOLUTION*

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ABSTRACT

The ^{13}C-n.m.r. signals of the heptitols in aqueous solution, and of their acetates in chloroform solution, have been assigned by the use of specifically deuterium-substituted compounds. From these spectra, the preponderant conformation of each heptitol has been determined, particularly by comparisons with the spectra of the homomorphous hexitols. The results are in good agreement with the predictions made, on the basis of theoretical considerations, by J. A. Mills ten years ago.

INTRODUCTION

There has been considerable interest lately in the conformations of alditols. The crystal structures of the hexitols have been determined[2] and their n.m.r. spectra, and those of related acyclic sugar derivatives, have been studied[1,3–6]. These studies have shown that the acyclic polyols and their derivatives assume mainly an extended, zigzag conformation, provided that it has no oxygen atoms with 1,3-parallel interactions. Were such interactions to be present in the planar zigzag form, one (or several) rotation(s) of 120° around carbon–carbon bonds would occur in order to avoid them, resulting in a "bent" or "sickle" conformation[3].

The conformations of heptitols and higher alditols have not yet been studied experimentally, except that of one compound, *meso-glycero-gulo*-heptitol[5,7], and yet, these conformations would show some interesting features. By the study of stereomodels, and from theoretical considerations, Mills[8] concluded that three of the heptitols can have no conformation free from 1,3-parallel interactions. On the basis of his considerations, Mills predicted the most probable conformation for

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each of the ten heptitols. To prove whether these predictions were correct was the aim of the present work.

The coupling constants in the ^{1}H-n.m.r. spectra would serve to establish the conformations, but, in aqueous solutions, most of the ^{1}H signals of alditols overlap and the coupling constants cannot be observed. By augmenting the spectral dispersion by incremental additions of europium or praseodymium salts, Angyal *et al.*[5] and Kieboom *et al.*[6] determined the solution conformation of the hexitols, but extension of this method to the heptitols appeared to be fraught with difficulties. Hence, we used ^{13}C-n.m.r. spectroscopy, having explored the use of this method on the hexitols[1].

DISCUSSION

The ^{13}C-n.m.r. spectra of all of the *meso* heptitols and of one enantiomer of each optically active heptitol were investigated. The spectra were assigned by deuterium labelling, using the same method as applied to the hexitols[1]. In this method, not only the disappearance of the signal of the labelled carbon atom was used as a criterion but also the β-shift of the signals of the adjacent carbon atoms[9]. The positions labelled by deuterium atoms in each heptitol are shown in Table I.

Assignment of the spectra of the *meso* heptitols can be achieved by the reduction of one heptose or heptulose, because it requires only a choice between the C-2,6 and the C-3,5 signals, the others being obvious: the signal of C-1,7 is found at much higher field than the others, and that of C-4 has only half the intensity of the others.

TABLE I

POSITIONS DEUTERIUM-LABELLED IN THE HEPTITOLS[a]

Heptitol	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-7*
D-*glycero*-L-*allo*- (**1**)		A			B		C[b]
D-*glycero*-D-*galacto*- (**2**)		D				E	
D-*glycero*-L-*galacto*- (**3**)		F[c]				E[c]	G
D-*glycero*-D-*gluco*- (**4**)		H				F	
D-*glycero*-L-*gulo*- (**5**)		I				J	
D-*glycero*-D-*manno*- (**6**)		H	B			D	
meso-*glycero*-*allo*- (**7**)	K[b]						
meso-*glycero*-*altro*- (**8**	L	A					
meso-*glycero*-*gulo*- (**9**)		J					
meso-*glycero*-*ido*- (**10**)		I					

[a]A hydrogen atom in the position denoted by a capital letter has been replaced by a deuterium atom by borodeuteride reduction of A, D-*talo*-heptulose; B, D-*altro*-3-heptulose; C, D-*glycero*-D-*altro*-heptono-1,4-lactone; D, D-*manno*-heptulose; E, L-*galacto*-heptulose; F, L-*gulo*-heptulose; G, D-*glycero*-L-*gluco*-heptose; H, D-*altro*-heptulose; I, D-*ido*-heptulose; J, D-*gluco*-heptulose; K, D-*glycero*-D-*allo*-heptono-1,4-lactone; and L, D-*glycero*-L-*altro*-heptose. [b]Both hydrogen atoms were replaced by deuterium atoms. [c]The compound labelled in this position was the enantiomer of the compound named.

Reduction of a heptulose with $NaBD_4$ provides two heptitols, each labelled at a penultimate carbon atom, and thereby provides the assignment of three carbon atoms in each of two heptitols. If the reduction is conducted with all of the heptuloses, all but the C-4 signals of each heptitol will have been assigned. One heptulose was not available, the *allo* isomer; C-6 and C-7 of D-*glycero*-L-*allo*-heptitol (**1**) were assigned by the reductive deuteration of D-*glycero*-D-*altro*-heptono-1,4-lactone, and C-4 and C-5 by the reductive deuteration of D-*altro*-3-heptulose. In most of these instances, it was not necessary to separate the two heptitols formed in each reduction; in the spectrum of the mixture, the signals of each heptitol could be identified by reference to the spectra of the pure alditols. Only in the mixture formed by the reduction of D-*ido*-heptulose did some signals in the spectrum overlap; these heptitols were therefore separated by chromatography on a cation-exchange resin in the Ca^{2+} form[10]. Introduction of deuterium by reduction of hep-

TABLE II

^{13}C CHEMICAL-SHIFT DATA[a] FOR THE HEPTITOLS AND FOR THE HOMOMORPHOUS HEXITOLS

Heptitol	*Hexitol*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*Conformation*[b]
D-*glycero*-L-*allo*- (**1**)		64.0	73.3	73.0	74.25	72.15	72.0	64.45	$_2G^+$
	allitol	63.7	73.5	73.7					
	altritol					72.15	71.8	64.4	
D-*glycero*-D-*galacto*- (**2**)		64.65	71.65	70.65	69.7	70.55	72.3	64.65	*P*
	galactitol	64.5	71.5	70.7					
	mannitol					70.65	72.25	64.6	
D-*glycero*-L-*galacto*- (**3**)		64.5	71.3	70.8	71.4	70.9	74.5	63.7	$_5G^+$
	galactitol	64.5	71.5	70.7					
	glucitol					71.0	74.3	63.85	
D-*glycero*-D-*gluco*- (**4**)		63.8	74.2	71.2	72.85	73.0	73.9	63.45	$_2G^-$, $_5G^+$
	glucitol	63.85	74.3	71.0					
	altritol					72.95	73.95	63.4	
D-*glycero*-L-*gulo*- (**5**)		64.2	72.45	72.2	71.3	73.25	72.6	64.3	$_4G^-$
	glucitol	64.25	72.45	72.6					
	iditol					72.5	73.1	64.1	
D-*glycero*-D-*manno*- (**6**)		64.5	72.15	70.9	71.0	72.85	74.1	63.4	$_5G^+$
	mannitol	64.6	72.25	70.65					
	altritol					72.95	73.95	63.4	
meso-*glycero*-*allo*- (**7**)		63.9	73.4	73.7	73.95				$_2G^-$, $_5G^+$
	allitol	63.7	73.5	73.7					
meso-*glycero*-*altro*- (**8**)		64.4	72.0	72.7	72.5				*P*
	altritol	64.4	71.8	72.15					
meso-*glycero*-*gulo*- (**9**)		64.0	72.6	74.3	69.8				$\begin{cases} P; {}_2G^-, {}_3G^-; \\ {}_2G^+, {}_3G^+ \end{cases}$
	glucitol	64.25	72.45	72.6					
meso-*glycero*-*ido*- (**10**)		64.0	73.2	72.3	72.9				$\begin{cases} {}_2G^-, {}_4G^-; \\ {}_2G^+, {}_4G^+ \end{cases}$
	iditol	64.1	73.1	72.5					

[a]In p.p.m. downfield from external Me_4Si, for solutions in deuterium oxide. [b]*P* = planar zigzag.

TABLE III

^{13}C CHEMICAL-SHIFT DATA[a] FOR THE HEPTITOL ACETATES

Acetate of heptitol	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*
D-*glycero*-L-*allo*-	61.9	69.55	69.6	68.8	69.15	68.3	62.1
D-*glycero*-D-*galacto*-	62.3	67.8	67.65	66.75	67.4	68.2	61.95
D-*glycero*-L-*galacto*-	62.3	67.85	68.2	67.55	67.8	69.75	62.1
D-*glycero*-D-*gluco*-	61.7	68.85	69.2	70.35	68.6	69.4	61.5
D-*glycero*-L-*gulo*-	61.5	68.8	68.4	68.2	69.0	68.85	61.9
D-*glycero*-D-*manno*-	61.8	68.2	67.65	67.9	68.7	70.1	61.5
meso-glycero-allo-	61.8	69.7	69.4	69.6			
meso-glycero-altro-	62.15	68.7	69.6	68.5			
meso-glycero-gulo-	61.5	68.95	69.2	68.6			
meso-glycero-ido-	61.7	69.2	68.8	68.4			

[a]In p.p.m. downfield from internal Me_4Si, for solutions in deuteriochloroform.

tuloses does not provide information on the signals of C-4; the signal which remained unassigned was allotted to this carbon atom, except for D-*glycero*-L-*allo*- and D-*glycero*-D-*manno*-heptitol, where the reduction of D-*altro*-3-heptulose provided this information.

The assignments thus derived are shown in Table II. The reduction mixtures were all acetylated, and the products provided the assignments for the heptitol acetates, shown in Table III. In order to see the β-effects clearly, each heptose and heptulose was also reduced with $NaBH_4$, and n.m.r. spectra were run on the mixture of the deuterated and nondeuterated products. Thus, from the reduction of each sugar, six ^{13}C-n.m.r. spectra were obtained, as detailed for the hexitols in an earlier publication[1]. After having been separated from each other, the reduction products of D-*ido*-heptulose (D-*glycero*-L-*gulo*- and *meso-glycero-ido*-heptitol) gave spectra in which the β-effect could be recognized without the need to record the spectra of mixtures of labelled and non-labelled compounds.

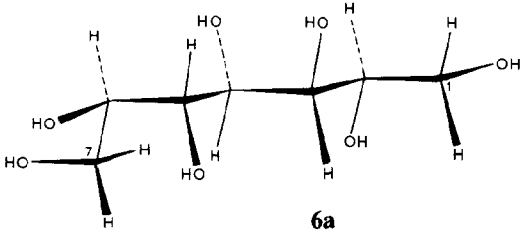
The preponderant conformation of each heptitol was deduced from its ^{13}C-n.m.r. spectrum. Our study of the spectra of the hexitols[1] provided two empirical criteria for the recognition of sickle forms. When an *erythro-erythro* sequence in an alditol is changed by rotation into a sickle form, the signals of the three carbon atoms in the sequence move downfield by ~2 p.p.m.; when a *threo-threo* sequence is similarly treated, the signals of the two outer carbon atoms move downfield. The signal of the terminal carbon atom moves upfield by ~0.7 p.p.m. on rotating the adjacent bond between carbon atoms bearing *threo* hydroxyl groups; if their relationship is *erythro*, the shift is ~1 p.p.m. Useful information on the conformation of heptitols was also obtained from the chemical shift of C-4, as detailed later.

More useful still, for the determination of the conformation of heptitols, is a comparison of their spectra with those of the hexitols. Such application of the concept of homomorphology has already been made by Defaye, Horton and co-workers[4] in the case of aldohexose dimethyl acetals and diethyl dithioacetals. Each hep-

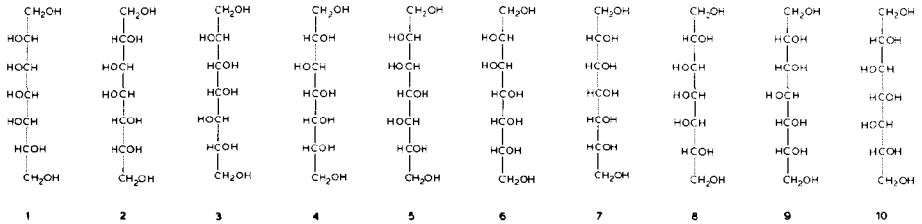
titol can be imagined as being built from two overlapping hexitols, the chiral centers C-2 to C-5 being part of one, and those of C-3 to C-6, of the other. Extension of a hexitol chain by a seventh carbon atom will not affect the ^{13}C-n.m.r. signals of C-1, C-2, and C-3; they will therefore have the same chemical shifts as those of the homologous hexitols, *provided that they are in the same conformation.* Rotation around the C-5–C-6 bond will not affect the signals of C-1, C-2, and C-3; rotation around the C-4–C-5 bond will, however, alter the position of the C-3 signal, and only those of C-1 and C-2 will coincide for the heptitol and for the hexitol. By the use of this test, it is therefore possible to decide for each half of a heptitol whether it is in the same conformation as the homologous hexitol. The conformations of all of the hexitols in aqueous solution are known[5,6].

In Table II, the chemical shifts of each heptitol are juxtaposed with those of the two homomorphous hexitols.

Heptitols with "favorable" conformations. — The only heptitol that can assume the planar, zigzag conformation without 1,3-parallel interactions is D-*glycero*-D-*galacto*-heptitol (**2**). Table I shows satisfactory agreement (within 0.2 p.p.m.) between its chemical shifts and those of galactitol and mannitol, which are also in planar, zigzag conformations. Similar close agreement in the case of D-*glycero*-D-*manno*-heptitol (**6**) shows that there is a sickle at the end homologous with altritol (which is in a sickle form), but that the rest of the chain is zigzag, as in mannitol. The conformation is therefore $_5G^+$ (**6a**) (that is, the sickle form derived from the zigzag form by a 120° counterclockwise rotation of the remote atom around the C-5–C-6 bond; for definition of this terminology, see ref. 11; Mills[8] designated this conformation 5*U*). D-*glycero*-L-*galacto*-Heptitol (**3**), a homolog of glucitol, is clearly in the $_5G^+$ conformation. D-*glycero*-D-*gluco*-Heptitol (**4**) is seen to combine the sickle forms of glucitol and altritol, and is found in the $_2G^-$, $_5G^+$ double sickle form (2*K*,5*U* in Mills's notation).



6a



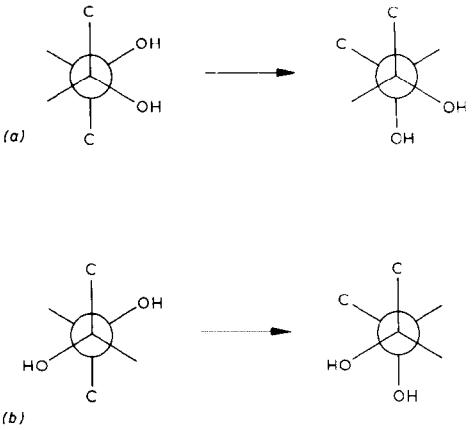
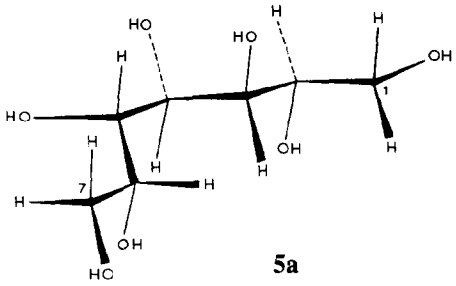


Fig. 1. The *gauche* interactions in the *P* and *G* forms of (*a*) a *threo*-diol and (*b*) an *erythro*-diol.

Comparison of the spectra of these heptitols with that of glucitol leads to an interesting conclusion concerning the conformation of the latter. D-Glucitol can assume two conformations free from 1,3-parallel interactions: ${}_2G^-$ and ${}_3G^+$, ${}_4G^+$. The former has been shown to be the preponderant form in solution, but the question remains as to how much of the latter is present in equilibrium. The ${}_3G^+$, ${}_4G^+$ form of D-*glycero*-D-*gluco*-heptitol and the ${}_3G^-$, ${}_4G^-$ form of D-*glycero*-L-*galacto*-heptitol (which contains an L-glucitol subunit) would have a 1,3-parallel interaction and would therefore not be significantly populated. The close correspondence between the chemical shifts of these heptitols and those of glucitol indicate that, for D-glucitol, also, the proportion of the ${}_3G^+$, ${}_4G^+$ form is insignificant.

Mills pointed out[8] that not all sickle forms are equally disfavored. When the C-2–C-3 bond in D-glucitol is rotated to produce the ${}_2G^-$ sickle form, the original three *gauche* interactions along this bond (2C/O, O/O) change into two *gauche* interactions (C/C, O/O) (see Fig. 1); although C/C is the strongest of these interactions, the change in free energy resulting from this rotation would be quite small. Mills did not regard this C–C *gauche* conformation (which he designated *MU*) as unfavorable. Such a "favorable" sickle form can be obtained only by rotation around the C–C bond of a *threo*-diol, and only one of the two possible rotations produces it. When the substituents at the end of the bond are *erythro*, rotation gives a conformation having three *gauche* interactions (C/C, C/O, O/O), whereas originally there were only two (2C/O); an "unfavorable" sickle form is produced (see Fig. 1). This is the case when the C-4–C-5 bond in D-glucitol is rotated; hence, the ${}_3G^+$, ${}_4G^+$ form is unfavorable.

By contrast, both possible conformations of D-iditol, ${}_3G^-$ and ${}_2G^+$, ${}_4G^+$, have only "favorable" C–C *gauche* arrangements; this hexitol has been found to occur as a mixture of these two conformers[1,12]. However, the chemical shifts of D-*glycero*-L-*gulo*-heptitol (**5**) do not coincide with those of iditol, one of its homologs. The heptitol can have only one favorable conformation free from 1,3-parallel in-

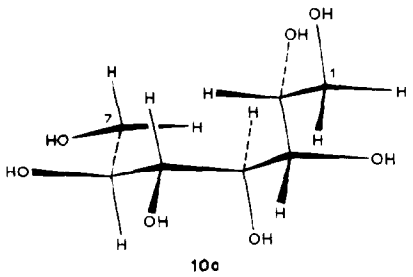


5a

teractions: the $_4G^-$ form (**5a**), homologous to the $_3G^-$ form of D-iditol. That this is indeed the preponderant conformation is indicated by the high δ values of C-1 and C-7, which show that the C-1–C-4 and the C-4–C-7 fragments are planar. The chemical shifts of C-5, C-6, and C-7 therefore correspond to those of the $_3G^-$ form of D-iditol, whereas those actually observed for D-iditol are average values of the $_3G^-$ and the $_2G^+$, $_4G^+$ forms.

It is appropriate now to consider *meso-glycero-ido*-heptitol (**10**). Its chemical shifts correspond closely with those of iditol. However, the n.m.r. spectra of *meso* heptitols give less information than those of the chiral ones, because each signal, except that of C-4, is the average of two signals, which will be magnetically equivalent only if the preponderant conformation itself is symmetrical. This is not always the case. The ^{13}C signals of *meso-glycero-ido*-heptitol correspond with those of iditol; but in solution, iditol, as already discussed, consists of a mixture of two conformations, and its chemical shifts are average values of the two. It appears that the heptitol has the $_3G^-$ conformation of D-iditol at one end and the $_2G^-$ conformation of L-iditol at the other. The resulting $_2G^+$, $_4G^+$ conformation (**10a**), and its enantiomer $_2G^-$, $_4G^-$, are the only possible conformations without 1,3-parallel interactions. In solution, the heptitol is a rapidly interconverting mixture of enantiomers.

The chemical shift of C-4. — Armed with a knowledge of the preponderant conformations of the heptitols, the chemical shifts of C-4 in their spectra can now be discussed. In the spectrum of D-*glycero*-D-*galacto*-heptitol (**2**), the signal of C-4 is at higher field (69.7 p.p.m.) than any other signal of any heptitol, except those of the terminal carbon atoms. This reflects the presence of *two* H//O interactions



10a

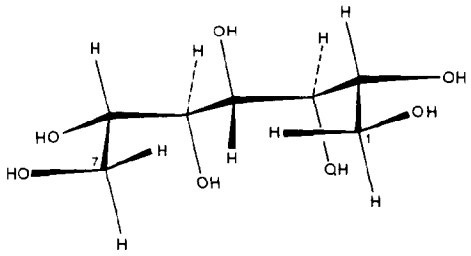
(with O-2 and O-6). The signal of C-4 in D-*glycero*-D-*manno*- and D-*glycero*-L-*galacto*-heptitol is at lower field (71.0 and 71.4 p.p.m.), because now there is one H//O and one H//C interaction; the latter is less shielding than the former[13]. In D-*glycero*-D-*gluco*-heptitol, C-4 has two H//C interactions, and the signal is farther downfield, at 72.9 p.p.m. In D-*glycero*-L-*gulo*-heptitol, C-4 has two H//O interactions, but is part of a C–C *gauche* bond (which is deshielding); the signal is at δ 71.3. Finally, in *meso-glycero-ido*-heptitol, C-4 is affected by one H//O and one H//C interaction, and is involved in a *gauche* bond; its signal is at δ 72.9. All of these assignments are seen to fall into a logical pattern.

Heptitols having unfavorable conformations. — In these cases, comparison of the spectra with those of hexitols is of limited value, because these heptitols have conformational features that are not found in the hexitols.

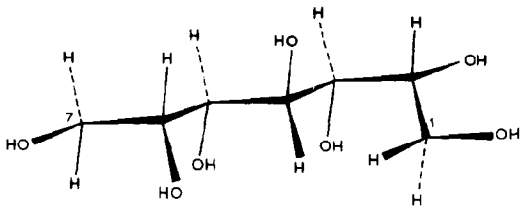
The conformation of *meso-glycero-gulo*-heptitol (**9**) has been studied before. In the crystalline state, it assumes the ${}_2G^-, {}_3G^-$ and the enantiomorphous ${}_2G^+, {}_3G^+$ conformation[7]. The *gauche* arrangement of the C-2–C-3 bond is of the "unfavorable" type, and hence, this conformation is comparable in energy content to the planar one, which contains a 1,3-parallel interaction between two hydroxyl groups. From the study of its ^{1}H-n.m.r. spectrum and from its considerable ability to complex with cations, it was concluded that its aqueous solution contains a substantial proportion of the planar, zigzag form[5]. Interpretation of its ^{13}C-n.m.r. spectrum is again hampered by its *meso* nature, each signal representing two carbon atoms; no quantitative conclusions can be derived. The chemical shift of C-1,7 is intermediate between that expected for the planar and for the double-sickle form (C-4–C-7 planar, O-2 and O-3 *gauche*). The position of the C-4 signal at very high field is compatible only with the planar form (two H//O interactions); in the double-sickle form, C-4 is part of a *gauche* bond and would be at lower field. The high value of the chemical shift of C-3, on the other hand, suggests a *gauche* bond. The ^{13}C-n.m.r. spectrum therefore merely confirms the conclusion[5] that the planar and the double-sickle forms are both present in substantial proportions.

The remaining three heptitols all have 1,3-parallel interactions in any of their possible conformations. Mills[8] defined the circumstances under which such a condition would occur: no alditol having a sequence of three consecutive centers of *ribo* configuration that is separated from each end of the alditol chain by at least one asymmetric center can avoid having some 1,3-parallel interaction.

meso-glycero-altro-Heptitol (**8**), in the planar zigzag form, has no unfavorable interaction other than the one between O-3 and O-5. This appears to be the preponderant conformation; agreement of the chemical shifts of C-1 and C-2 with those of altritol indicates that there is no *gauche* bond at C-2–C-3. Rotation around the C-3–C-4 bond, to relieve the 1,3-parallel interaction, would create an unfavorable *gauche* arrangement, as well as new 1,3-parallel interaction between O-2 and O-4. The δ value of C-3, somewhat higher than for altritol, probably indicates that there is a small proportion of this sickle form, and of its enantiomer, present in solution. The signal of C-4 is at considerably lower field than expected



7a



1a

(two H//O interactions). This is probably due to its being located between two carbon atoms carrying hydroxyl groups in 1,3-parallel arrangement; such neighboring is known to cause anomalous, chemical shifts[14].

The good agreement between the spectra of allitol and *meso-glycero-allo*-heptitol (**7**) shows that the preponderant conformation of the latter is ${}_2G^-, {}_5G^+$ ($\equiv$ ${}_2G^+, {}_5G^-$) (**7a**), which has a parallel interaction between O-3 and O-5. The C-4 signal is at even lower field than that of the *meso-glycero-altro* isomer; C-4 is affected by two H//C interactions.

Finally, D-*glycero*-L-*allo*-heptitol (**1**) is mainly in the ${}_2G^+$ conformation (**1a**) in which O-3 and O-5 have a parallel interaction but the one between O-2 and O-4 has been relieved by rotation around C-2–C-3. Agreement of the chemical shifts of C-5, C-6, and C-7 with those of altritol indicates that they are in a planar arrangement. The agreement, at the other end of the heptitol, with allitol is less satisfactory, indicating that there may also be some of the ${}_3G^+$ and ${}_3G^-$ forms present; these forms result from rotation, around the C-3–C-4 bond, which relieves both of the 1,3-parallel interactions of the zigzag form but creates a new one between O-2 and C-5, and O-5 and C-2, respectively. The signal of C-4 is at low field (one H//O and one H//C interaction).

The preponderant conformer of each heptitol is shown in Table II. It may be seen that all of Mills's predictions[8] have been verified and vindicated.

Acetates. — The chemical shifts of the heptitol acetates are shown in Table III. As with the hexitol acetates[1], the spectra are less informative than those of the free alditols, and the range of chemical shifts is smaller. A chemical shift greater than 69.0 p.p.m. generally indicates a *gauche* arrangement or the presence of a 1,3-parallel interaction.

In most cases, there is good agreement between the chemical shifts of the heptitol acetates and those of the homomorphous hexitol acetates[1] (which are not shown in Table III). There are substantial disagreements, however, in the case of D-*glycero*-L-*galacto*- and D-*glycero*-D-*gluco*-heptitol.

The peracetates of the alditols do not necessarily have the same conformation in solution as the free alditols. Parallel 1,3-interaction between two acetoxyl groups is much smaller than that between similar hydroxyl groups[15]; hence, conformations containing such an interaction are less unfavorable among the acetates than among the free alditols. Moreover, the acetoxyl groups themselves introduce unfavorable interactions. Those on C-3 and C-4 of the hexitol acetates, and those on C-3, C-4, and C-5 of the heptitol acetates, inevitably have 1,3-parallel interactions unless they are *anti*-periplanar to the acetoxyl groups on both neighboring carbon atoms (in which case, there is such interaction between those two acetoxyl groups). This explains why, whereas allitol is preponderantly in the ${}_2G^-$, ${}_4G^+$ form, at least half of its hexaacetate is found in other conformations that all have 1,3-parallel interactions[12].

As already shown, D-glucitol is preponderantly in the ${}_2G^-$ conformation, but about one-third of its hexaacetate was found[12] to be in the ${}_3G^+$, ${}_4G^-$ form. It appears that the interactions of the acetoxyl groups are less unfavorable in this double-sickle form. For the acetate of D-*glycero*-L-*galacto*-heptitol, the double-sickle form would encounter serious interactions, and is therefore not significantly populated. The n.m.r. signals of the heptitol acetate consequently correspond to the sickle form, whereas those of glucitol acetate are an average of those for the sickle and the double-sickle forms; hence, the discrepancy in the chemical shifts.

The discrepancy of the chemical shifts between the acetates of D-*glycero*-D-*gluco*-heptitol and its homologous hexitols (glucitol and altritol) cannot be explained in the same way, and remains puzzling. Perhaps, the steric requirements of the acetoxyl groups distort the shape of the molecule (expected to be ${}_2G^-$, ${}_5G^+$), or cause it to assume another conformation.

EXPERIMENTAL

Materials. — D-*glycero*-L-*allo*-Heptitol and D-*altro*-3-heptulose (coriose[16]) were obtained from an extract of the wood of *Stenocarpus salignus* R. Br. (Proteaceae)[17]; additional amounts of the heptitol were prepared by the reduction of D-*glycero*-D-*altro*-heptono-1,4-lactone[18] with $NaBH_4$. D-*glycero*-D-*galacto*-Heptitol (perseitol) was a commercial product; D-*glycero*-L-*galacto*-, D-*glycero*-L-*gulo*-, *meso*-*glycero*-*allo*-, and *meso*-*glycero*-*altro*-heptitol were respectively obtained by the reduction of D-*glycero*-L-*galacto*-heptose[19] (and also of D-*glycero*-L-*gluco*-heptose[20]), D-*glycero*-D-*ido*-heptono-1,4-lactone[21], D-*glycero*-D-*allo*-heptono-1,4-lactone[18], and D-*glycero*-L-*altro*-heptose[22]; D-*glycero*-D-*gluco*- and *meso*-*glycero*-*ido*-heptitol were prepared by the reduction of L-*gulo*-, D-*altro*-, and D-*ido*-heptuloses (see later). The other heptitols were obtained from the late Dr. J. A. Mills.

D-*manno*-Heptulose was a commercial product: D-*altro*-heptulose (sedoheptulose) was prepared[23] from commercial sedoheptulosan; D-*gluco*-heptulose was synthesized[24] from commercial D-*glycero*-D-*gulo*-heptose; L-*galacto*-, L-*gulo*-, D-*talo*-, and D-*ido*-heptulose were respectively obtained by *Acetobacter suboxydans* oxidation from D-*glycero*-D-*galacto*-, D-*glycero*-D-*gluco*-, D-*glycero*-L-*allo*-, and D-*glycero*-L-*gulo*-heptitol. The oxidations were conducted as described by Pratt *et al.*[24]. Following their instructions, 2,7-anhydro-β-D-*ido*-heptulopyranose was obtained as the sole product from D-*glycero*-L-*gulo*-heptitol; only when the pH was carefully controlled by the addition of disodium hydrogenphosphate to the fermentation mixture, and during the use of ion-exchange resins in subsequent steps, was the heptulose obtained. Apparently, it is readily dehydrated, even under mildly acidic conditions. We had a supply of the anhydride, donated by Dr. N. K. Richtmyer, but attempts to open the anhydro bridge by acetolysis of its tetraacetate[25], as described for sedoheptulosan[23] and for 1,6-anhydro-β-D-idopyranose[26], failed. Under mild conditions, much of the anhydride was recovered; under more vigorous conditions, decomposition set in. *ido*-Heptulose, all forms of which have substantial destabilizing interactions[27], appears to be a rather unstable sugar.

Methods. — Mixtures of heptitols were separated on a column of Dowex 50-W X-4 resin in its calcium form[10], with 4:1 water–methanol as the eluant: D-*glycero*-D-*manno*-heptitol was separated from its D-*glycero*-D-*gluco* isomer; D-*glycero*-L-*gulo*-heptitol from the *meso*-*glycero*-*ido* isomer; D-*glycero*-D-*galacto*-heptitol from the D-*glycero*-L-*galacto* isomer; and D-*glycero*-D-*gluco*-heptitol from the D-*glycero*-L-*galacto* isomer. Of each pair, the first named emerged first from the column. The column was also used to remove traces of glucitol and iditol which derived from the bacterial medium. D-*glycero*-L-*gulo*-Heptitol and *meso*-*glycero*-*gulo*-heptitol could not be separated on the column, either in its calcium or in its lanthanum[28] form.

Aldoses and ketoses were reduced by means of sodium borohydride (and deuteride) in water[29]; the lactones, by use of sodium borohydride and sodium methoxide in methanol[30].

N.m.r. spectra. — The ^{13}C-n.m.r. spectra were first recorded with a Bruker WP-60, Fourier-transform spectrometer; those of the heptitols, for solutions in deuterium oxide, and those of the acetates, for solutions in deuteriochloroform. Spectra of mixtures, particularly of those where the β-effect was to be observed, were recorded with a Varian XL-100 instrument. In a few cases, the spectra were also recorded with a Cameca 250 spectrometer.

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