THE 1H-NMR SPECTRA AND THE CONFORMATION
OF 1,6-ANHYDRO-β-D-HEXOPYRANOSES AND THEIR TRIACETATES

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The 1H-NMR spectra of 1,6-anhydro-β-D-hexopyranoses and their triacetates, measured in hexadeuteriodimethyl sulfoxide or deuteriochloroform, confirmed the existence of these compounds in $^1C_4(D)$ conformations, with the pyranose ring partly planarized in dependence on the configuration of the substituents in positions $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$. The effects of the substituents on the chemical shifts and the adjusted relationship for the dependence of vicinal coupling constants on the torsion angle are discussed in detail from the point of view of the determination of the configuration and the conformation of 1,6-anhydro-β-D-hexopyranoses and their derivatives. The 1H-NMR spectra of triacetates were also measured in the presence of the lanthanide shift reagent, tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione) europium (III) [Eu . . (FOD)₃].

In a number of papers dealing with 1,6-anhydrohexopyranoses the 1H-NMR spectroscopy was used for structural proofs and to obtain stereochemical information (for a review see ref.[1]). 1,6-Anhydro-β-D-hexopyranoses have a 6,8-dioxabicyclo-[3.2.1]octane skeleton and therefore represent systems with considerably restricted sterical flexibility. Their pyranose ring can assume only two basic types of conformation: the chair conformation $^1C_4$ (D) and the boat conformation $B_{0,3}$ (D). Heyns and Weyer[2] studied the 1H-NMR spectra of 1,6-anhydro-β-D-hexopyranoses in water and formulated some rules for the chemical shifts of their protons. In a number of other papers there is a scattering of 1H-NMR data of some derivatives of 1,6-an-hydrohexopyranoses, which were however often obtained under different conditions and with differing precision. Therefore in this paper we summarize the results of our own measurements of the 1H-NMR spectra of complete series of 1,6-anhydro--β-D-hexopyranoses (*Ia* — *VIIIa*) in hexadeuteriodimethyl sulfoxide and their acetates (*Ib* — *VIIIb*) in deuteriochloroform, and we also discuss the parameters of the spectra predominantly from the point of view of the spacial arrangement of these molecules.

Chemical Shifts

The values of the chemical shifts of individual protons of 1,6-anhydro-β-D-hexo-pyranoses the molecules of which contain several magnetically anisotropic groups (structurally identical at the same positions, but spacially oriented in different ways) are the result of the effect of a series of electronic and geometric factors. Their interpretation in the conformational sense is very difficult, and if made on a semi-quantitative level, it would require the separation of the effects of the substituents in the positions $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$ of model substances, such as 1,6-anhydro-2,3,4--trideoxy-β-D-*glycero*-hexopyranose and its monohydroxy or monoacetoxy deriva-tives. Therefore we shall limit ourselves to the characterization of the chemical shifts

TABLE I

^{1}H-NMR Parameters of 1,6-Anhydro-β-D-hexopyranoses in Hexadeuteriodimethyl Sulfoxide

Compound	Chemical shifts, δ						
	H-1	H-2	H-3	H-4	H-5	H-6en	H-6ex
Ia	5·18	3·21	3·44	3·33	4·36	3·92	3·52
IIa	5·14	3·51	3·69	3·82	4·20[a]	4·21[a]	3·40
IIIa	5·30	3·45 — 3·66[a]			4·48	3·71	3·57
IVa	5·22	3·54[a]	3·39[a]	3·62	4·24	3·87[a]	3·43[a]
Va	5·14	3·51[a]	3·68[b]	3·65[b]	4·34	4·06	3·51[a]
VIa	5·10	3·42[a]	3·94	3·68	4·19	4·32	3·45[a]
VIIa	5·11	3·34	3·46[a]	3·66[a]	4·44	3·63[b]	3·53[b]
VIIIa	5·10	3·19[b]	3·29[b]	3·49	4·26	3·89	3·52

Compound	Coupling constants, Hz						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6en}$	$J_{5,6ex}$	$J_{6,6}$
Ia	1·4	2·6	2·8	1·8	1·2	5·9	−7·1
IIa	1·5	1·4	5·2	4·2	0·9	5·6	−7·1
IIIa	2·3	c	c	2·7	1·0	5·8	−7·9
IVa	2·3	4·7	9·0	4·0	0·8	5·1	−7·6
Va	2·0	5·4	c	1·8	1·1	6·0	−7·1
VIa	1·9	5·0	4·7	4·1	0·8	5·3	−6·8
VIIa	1·5	8·8	3·9	2·2	1·0	5·3	−8·0
VIIIa	1·5	7·9	7·9	4·1	0·8	5·2	−7·5

[a] A partial overlapping of the signals; [b] the position of the signals was determined with a lower precision (±0·03 ppm); [c] the values of the parameters were not obtained.

of protons of 1,6-anhydro-β-D-hexopyranoses and their triacetates and to the formulation of some more general rules on the effect of the position and the orientation of the substituents, similarly as described for the solutions of aldopentoses and aldohexoses[3] and 1,6-anhydro-β-D-hexopyranoses[2] in water. The ^{1}H-NMR parameters of the triols and triacetates $I - VIII$ are listed in Tables I and II.
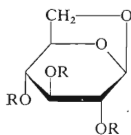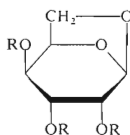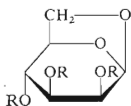

D-*gluco*
Ia, R = H
Ib, R = Ac
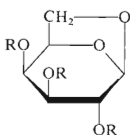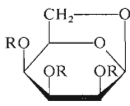
D-*galacto*
IIa, R = H
IIb, R = Ac
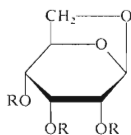
D-*allo*
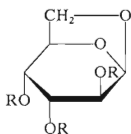*IIIa*, R = H
IIIb, R = Ac

D-*gulo*
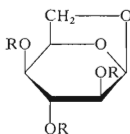*IVa*, R = H
IVb, R = Ac

D-*manno*
Va, R = H
Vb, R = Ac

D-*talo*
VIa, R = H
VIb, R = Ac

D-*altro*
VIIa, R = H
VIIb, R = Ac

D-*ido*
VIIIa, R = H
VIIIb, R = Ac

The anomeric protons H-1 are in the lowest magnetic field, with the exception of H-3 in triacetate *VIb*. In triols they occur within a narrow range of 0·20 ppm and in triacetates even within a mere 0·09 ppm range. The comparison of pairs of the $C_{(2)}$-epimers shows that the 2α-OH* derivatives have H-1 at a lower field ($\delta = 5·14 - 5·30$) than the corresponding 2β-OH derivatives ($\delta = 5·10 - 5·14$), averagely by 0·10 ppm. The effect of the orientation of the OH groups on more remote carbons $C_{(3)}$ and $C_{(4)}$ is weaker. In triacetates the effect of the orientation of the $C_{(2)}$—OAc group on H-1 is negligible, and the effect of $C_{(3)}$ and $C_{(4)}$ substituents is more characteristic (Table III). A similarly narrow range of chemical shifts is also observed for the proton H-5. For triols it is 0·29 ppm ($\delta = 4·19 - 4·26$ in 4β-OH and $\delta = 4·34$

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* In order to simplify the interpretation of the spectra we use the α, β symbols to indicate the configuration of the hydroxy and the acetoxy groups. The substituents in the *endo* position (closer to the 1,6-anhydro bonds) are indicated by β, and the substituents in the *exo* position by α.

to 4·48 in 4α-OH derivatives), while the 4α-OH epimer has H-5 averagely by 0·18 ppm downfield in comparison with the 4β-OH epimer. For triacetates the H-5 proton is in the 0·20 ppm range ($\delta = 4·47 - 4·61$ in 4β-OAc and $\delta = 4·61 - 4·67$ in 4α-OAc derivatives) with an average deshielding effect of 0·10 ppm for the 4α-OH in relation to the 4β-OH epimer. The effect of the orientation of the OH and the OAc group on $C_{(3)}$ is less (0·09 or 0·08 ppm, respectively) and on $C_{(2)}$ it is negligible (Table III).

The hydrogens H-6en and H-6ex do not change their configuration either. The proton H-6ex, oriented outside the bicyclic system, is little sensitive — as expected — to the changes in the configurations of the substituents in the positions $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$ and it appears in the 0·17 ppm range ($\delta = 3·40 - 3·57$) for triols and 0·15 ppm ($\delta = 3·71 - 3·86$) for triacetates. The proton H-6en reacts much more sensitively to these changes. We observed it in the 0·58 ppm range ($\delta = 3·63 - 4·21$) in the case of triols and the 0·54 ppm range ($\delta = 3·94 - 4·48$) in the case of triacetates. The non-equivalence of the protons of the $C_{(6)}$—H_2 group is thus very variable in both series (0·10 to 0·81 ppm). It is most pronounced in triols *IIa* and *VIa* (0·81 and 0·77 ppm) and their triacetates *IIb* and *VIb* (0·61 and 0·57 ppm), *i.e.* in both series in substances with β-oriented substituents in the positions $C_{(3)}$ and $C_{(4)}$. In contrast to this the smallest internal shift is observed in the case of $C_{(6)}$-protons of triols *IIIa* and *VIIa* (0·14 and 0·10 ppm) and their acetates *IIIb* and *VIIb* (0·13 and 0·14 ppm), *i.e.* in derivatives with α-oriented substituents on $C_{(3)}$ and $C_{(4)}$. The last mentioned values are comparable with the value 0·17 ppm found for 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hexopyranose[4] where the chemical shifts of the $C_{(6)}$-

TABLE II

^{1}H-NMR Parameters of Triacetates of 1,6-Anhydro-β-D-hexopyranoses in Deuteriochloroform

Com- pound	Chemical shifts, δ								
	H-1	H-2	H-3	H-4	H-5	H-6en	H-6ex	2-OAc	3-OAc
Ib	5·44	4·59[b]	4·85	4·64[b]	4·61[b]	4·09	3·79	2·16	2·10
Ib[c]	5·41	4·70	5·02	4·51	4·21	3·56	3·27	1·57	1·50
IIb	5·41	4·74	5·23[d]	5·23[d]	4·47	4·33	3·72	2·13	2·13
IIIb	5·50	5·09[d]	5·26	5·14[d]	4·68	3·94	3·81	2·15	1·99
IVb	5·43	5·22[d]	5·22[d]	5·22[d]	4·61	4·10	3·71	2·13	1·99
Vb	5·43	5·00	5·27	4·82	4·62	4·25	3·86	2·05	2·14
VIb	5·41	4·92	5·69	5·17	4·49[b]	4·48[b]	3·81	2·03[e]	2·15
VIIb	5·49	5·01	5·22[d]	5·28[d]	4·66	3·97	3·83	2·09	2·00
VIIIb	5·45	4·84	5·34	5·08	4·60	4·17	3·79	2·06	2·02
VIIIb[f]	5·45	4·74	5·16	4·95	4·71	4·05	3·70	2·01	1·97

[a] The assignment of the signals of the acetoxy groups was done according to refs[7,8]; [b] partial overlapping of the signals; [c] parameters from the spectrum of compound *Ib* in deuteriobenzene; [d] the position of the signals was determined with a lower accuracy ($\pm 0·03$ ppm); [e] the assignment

-protons are not perturbed by the presence of substituents. The comparison of groups of four epimeric pairs at $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$ shows that in the triols and the triacetates the highest effect on the shift of the H-6en proton is exerted by the orientation of the $C_{(3)}$-substituent (the deshielding effect of the substituent β in comparison with α is 0·35 or 0·24 ppm, respectively), the orientation of the $C_{(4)}$-substituent has a little weaker effect (0·24 or 0·21 ppm, resp.), while the effect of the orientation of the $C_{(2)}$-substituent (Table III) is weakest and not very characteristic. A pronounced deshielding effect of the β-oriented $C_{(3)}$-substituent can be explained by the van der Waals interactions[5,6] of the two axial substituents on $C_{(3)}$ and $C_{(5)}$, in agreement with the decrease of the strength of the effect when the hydroxyl group is substituted by the acetoxy group.

The values of the chemical shifts of the protons H-2, H-3 and H-4 the configuration of which changes in the series of diastereoisomers appear in broader ranges: for H-2 it is 0·35 or 0·63 ppm, for H-3 it is 0·65 or 0·84 ppm, and for H-4 it is 0·49 or 0·64 in triols or triacetates, respectively. In the classification of these protons into axial and equatorial (if a chair form is assumed for the pyranose ring) the values of the effects of the substituents on the vicinal $C_{(b)}$ carbon or the more remote $C_{(γ)}$ carbon can be expressed by the comparison of epimeric pairs as the differences of the shifts of the proton with the substituent in an axial and an equatorial position (Table III). The observed average values of these effects differ for triols and triacetates, and — with the exception of the effect of the $C_{(3)}$-OAc group on the neighbouring axial proton — they are quite characteristic. The relatively broad ranges of some chemical

TABLE II
(*Continued*)

4-OAc[a]	Compound	Coupling constants, Hz						
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6en}$	$J_{5,6ex}$	$J_{6,6}$
2·13	Ib^g	—	—	—	—	—	—	—
1·53	Ib^c	1·3	2·2	2·3	1·6	1·0	5·9	−7·9
2·02	IIb	1·4[h]	1·4[h]	5·3[h]	4·4[h]	0·7	5·3	−7·7
2·17	$IIIb$	2·4	4·7	4·8	2·4	0·9	5·7	−8·5
2·06	IVb	2·2[h]	4·7[h]	9·7[h]	3·9[h]	0·6	4·9	−8·2
2·16	Vb	1·95	5·6	1·8	1·6	1·1	6·0	−8·0
2·06[e]	VIb	1·9	5·0	4·7	4·3	0·7[h]	5·3	−7·7
2·15	$VIIb$	1·5	9·3[h]	4·4[h]	2·2[h]	0·9	5·9	−8·5
2·08	$VIIIb$	1·7	8·2	8·8	4·4	0·7	5·1	−8·2
2·01	$VIIIb^f$	1·8	8·4	8·8	4·1	0·7	5·2	−8·4

can be exchanged; [f] the parameters from the spectrum of compound *VIIIb* in hexadeuteriodimethyl sulfoxide; [g] the parameters could not be obtained; [h] the values *J* were obtained after addition of Eu(FOD)₃.

TABLE III

The Effect of Orientation of the Substituents in the Positions 2, 3 and 4 on the Chemical Shifts of Protons

Proton	Substituent R in the position	$\Delta\delta_H = \delta_H(R_{ax}) - \delta_H(R_{eq})$		Number of epimeric pairs
		average value	range	
		1,6-Anhydro-β-D-hexopyranoses		
H-1	$C_{(2)}$—OH	0·10	(0·04 to 0·19)	4
	$C_{(3)}$—OH	−0·04[a]	(−0·12 to 0·03)	4
	$C_{(4)}$—OH	0·04	(0·01 to 0·08)	4
H-2, H-3, H-4	$C_{(\beta)}$—OH	0·16	(0·10 to 0·20)	6
(axial)	$C_{(\gamma)}$—OH	0·13	(0·09 to 0·15)	4
H-2, H-3, H-4	$C_{(\beta)}$—OH	−0·17 (−0·25)[b]	(−0·01 to −0·26)	6
(equatorial)	$C_{(\gamma)}$—OH	−0·31	(−0·30 to −0·32)	2
H-5	$C_{(4)}$—OH	0·18	(0·15 to 0·24)	4
	$C_{(3)}$—OH	−0·08	(−0·04 to −0·12)	4
	$C_{(2)}$—OH	0·01[a]	(−0·02 to 0·04)	4
H-6en	$C_{(4)}$—OH	−0·24	(−0·16 to −0·29)	4
	$C_{(3)}$—OH	0·35	(0·21 to 0·43)	4
	$C_{(2)}$—OH	−0·05[a]	(−0·14 to 0·08)	4
H-6ex	$C_{(4)}$—OH	0·08	(0·01 to 0·12)	4
	$C_{(3)}$—OH	−0·05	(−0·02 to −0·07)	4
	$C_{(2)}$—OH	−0·02[a]	(−0·09 to 0·04)	4
		Triacetates of 1,6-anhydro-β-D-hexopyranoses		
H-1	$C_{(2)}$—OAc	0·00[a]	(−0·02 to 0·01)	4
	$C_{(3)}$—OAc	−0·05	(−0·06 to −0·02)	4
	$C_{(4)}$—OAc	0·04	(0·02 to 0·07)	4
H-2, H-3, H-4	$C_{(\beta)}$—OAc	0·00[a]	(−0·12 to 0·09)	4
(axial)	$C_{(\gamma)}$—OAc	0·10	(0·06 to 0·17)	8
H-2, H-3, H-4	$C_{(\beta)}$—OAc	−0·45	(−0·50 to −0·38)	8
(equatorial)	$C_{(\gamma)}$—OAc	−0·15	(−0·18 to −0·13)	8
H-5	$C_{(4)}$—OAc	0·10	(0·06 to 0·14)	4
	$C_{(3)}$—OAc	−0·09	(−0·14 to −0·04)	4
	$C_{(2)}$—OAc	0·00[a]	(−0·02 to 0·02)	4
H-6en	$C_{(4)}$—OAc	−0·21	(−0·23 to −0·16)	4
	$C_{(3)}$—OAc	0·24	(0·15 to 0·31)	4
	$C_{(2)}$—OAc	−0·10	(−0·16 to −0·03)	4
H-6ex	$C_{(4)}$—OAc	0·07	(0·04 to 0·10)	4
	$C_{(3)}$—OAc	0·01[a]	(−0·02 to 0·03)	4
	$C_{(2)}$—OAc	−0·07	(−0·09 to −0·02)	4

[a] The value is not characteristic — both the values with a (+) and a (−) sign were found; [b] a typical value is −0·25 ppm (the low value −0·01 ppm is an exception distorting the average value).

shift values of protons are evidently caused both by mutual interactions of substituents and by their interactions with the bicyclic 1,6-anhydroskeleton. This leads to different conformations of the substituents themselves in individual diastereoisomers or also to more or less distinct deformations of the chair conformation of the pyranose ring.

Lanthanide Shift Reagent in Triacetates of 1,6-Anhydro-β-D-hexapyranoses

Although the majority of the 1,6-anhydropyranoses investigated affords at a 100 MHz frequency "pseudo first-order spectra", in some cases a partial overlapping of some protons takes place, which makes the obtaining of the parameters of the spectrum more difficult, especially of $^3J_{H,H}$. While in triols in hexadeuteriodimethyl sulfoxide the parameters were determined in such cases with less accuracy, or were not obtained at all (Table I), in the case of triacetates well soluble in deuteriochloroform the measurement in the presence of tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octane-dione)europium (III) was applied. This permitted a better separation of some signals. At the same time it was observed whether more pronounced changes of other coupling constants do take place, which would indicate conformational changes in the molecule. Since the changes of these coupling constants were generally less than 0·2 Hz, we considered it as acceptable for further conformational analysis. In order to enable the evaluation of the use of the shift reagent the measurement with the europium shift reagent was carried out for all triacetates. The observed downfield induced shifts (Table IV) were referred to the most mobile hydrogen of the given compound, which is always one of the protons on the carbon atoms carrying the acetoxy groups.

TABLE IV

The Values of the Relative Induced Shifts of Protons of the Triacetates of 1,6-Anhydro-β-D-hexo-pyranoses in the Presence of Eu(FOD)$_3$, Referred to the Proton with the Greatest Mobility

Compound	H-1	H-2	H-3	H-4	H-5	H-6en	H-6ex	2-OAc	3-OAc	4-OAc[a]
Ib	0·36	0·78	1·00	0·75	0·32	0·26	0·19	0·29	0·28	0·26
IIb	0·44	0·95	1·00	0·53	0·31	0·35	0·25	0·31	0·31	0·26
IIIb	0·61	0·95	0·85	1·00	0·47	0·38	0·34	0·47[b]	0·37	0·56[b]
IVb	0·66	1·00	0·94	0·84	0·61	0·58	0·53	0·33	0·39	0·49
Vb	0·38	0·62	1·00	0·86	0·52	0·24	0·17	0·29	0·26	0·40
VIb	0·51	0·71	1·00	0·72	0·45	0·39	0·27	0·36[b]	0·32	0·37[b]
VIIb	0·61	0·85	0·81	1·00	0·39	0·28	0·15	0·53	0·47	0·50
VIIIb	0·72	0·99	0·89	1·00	0·61	0·48	0·31	0·58	0·31	0·56

[a] The assignment of the acetoxy groups was carried out according to refs[7,8]; [b] the assignment can be exchanged.

In chair conformation this hydrogen is bound equatorially, with the exception of compound *VIIIb* which does not contain an equatorial proton; if more equatorial protons are present in the molecule, then their mobility decreases in the order H-3 > H-4 ≧ H-2. The protons on etherically bonded carbon atoms have generally lower $\Delta\delta_{rel.}$ values and their mobility usually decreases in the following order: H-1 > H-5 > H-6en > H-6ex. The methyl protons of the acetoxyl group — the assignment of which was done according to ref.[7,8] — have comparable and mostly mutually slightly differing values of induced shifts.

The studied series of triacetates represents polyfunctional substrates with five groups, of which three are conformationally mobile, and which are capable of forming approximately equally strong complexes with Eu(FOD)$_3$. This represents a serious difficulty in the interpretation of the induced shifts from the point of view of geometric parameters, and therefore one cannot expect to obtain reliable conformational information in this manner.

Vicinal Coupling Constants

During the conformational studies of organic compounds the relationship between the vicinal coupling constant ($^3J_{H,H}$) and the torsion angle of the coupling protons (ϕ), proposed for the first time by Karplus[9,10] in the general approximate form $^3J = A + B \cos \phi + C \cos 2\phi$, is of special importance. However the vicinal coupling constants also depend[10] on the electronegativities of the substituents, bond lengths and valence angles $\theta = \measuredangle$ HCC′ and $\theta' = \measuredangle$ CC′H in the fragment H—C—C′—H. Therefore the relatively best results are obtained on applying the relationship $^3J = f(\phi)$ in structurally very similar compounds where the torsion angle of the protons is a dominant variable and the coefficients A, B and C are adjusted directly for a given structural system; undoubtedly 1,6-anhydro-β-D-hexapyranoses represent such a set of compounds. For the adjustment of the coefficients model substances are usually employed for which geometric parameters have been obtained (and thus the torsion angles of protons as well) by diffraction analysis in the solid or gaseous phase, or rigid substances the models of which permit a sufficiently accurate evaluation of the torsion angles and from the ^{1}H-NMR spectra of which the corresponding ^3J values are accessible.

Among 1,6-anhydro-β-D-hexopyranoses only the crystal structure of 1,6-anhydro--β-D-glucopyranose (*Ia*) has been determined so far, for which a flattened chair conformation $^1C_4$(D) has been found by X-ray diffraction analysis[11]. The torsion angles H—C—C—H of the pyranose ring calculated from it are unfortunately in a very narrow range, 26° ($\measuredangle$ H-1/H-2 = 62·1°, $\measuredangle$ H-2/H-3 = 78·2°, $\measuredangle$ H-3/H-4 = = 88·2°, $\measuredangle$ H-4/H-5 = 71·3°). In addition to this a comparison with the experimental values of ^3J either indicates different torsion angles of the substance in solution or distinct differences in further geometric parameters (bond lengths, valence

angles), that distort the results of the relation $^3J = f(\phi)$, similarly as in a number of other cases (*cf.* for example ref.[12]). Since the diffraction data proved to be useless for the adjustment of the parameters we chose the following approach. From the literature[13,14] it follows that the approximate relationship $^3J = f(\phi)$ should be extended at least by the fourth term of the series, *i.e.* to $^3J = A + B \cos \phi + C \cos 2\phi + D \cos 3\phi$. Further, for the determination of the parameters A, B, C and D for a given structural fragment, it is indispensable to know the extreme values of the function, *i.e.* $^3J_{trans}$ ($\phi = 180°$), $^3J_{cis}$ ($\phi = 0°$) and the lowest value of ^3J. Since sufficiently precise geometric parameters with corresponding ^{1}H-NMR data for the tetrahydropyrane system are not known, we used cyclohexane as the starting model. The values $^3J_{ax,ax} = 13.12$, $^3J_{ax,eq} = 3.65$ and $^3J_{eq,eq} = 2.96$ Hz were obtained[15] by the analyses of the ^{1}H-NMR spectra of octadeuteriocyclohexane at $-100°$C. The electron diffraction of gaseous cyclohexane showed[16,17] a moderately flattened chair conformation with the torsion angle C—C—C—C approximately 56°, which, for the angle H—C—H 118° leads to torsion angles of approximately 174°, 56° and 62° for $^3J_{ax,ax}$, $^3J_{ax,eq}$ and $^3J_{eq,eq}$, respectively. The value $J = 13.12$ Hz was used for the evaluation of J_{trans} ($\phi = 180°$) = 13.2 Hz. For J_{cis} ($\phi = 0°$) the value 9.6 Hz was selected on the basis of ^3J found for *exo*-protons in 1,2,3,4,7,7-hexafluorobicyclo-[2,2,1]hept-2,3-ene with an enforced boat conformation of the cyclohexane ring and an approximately eclipsed arrangement of the protons ($\theta \sim 0°$), and on the basis of similar values in further rigid polycyclic systems[18]. In agreement with the VB theory[9,10] a minimum value of ^3J is supposed for the angle 90° and its value was estimated to be 0.5 Hz. From the mentioned extreme values of ^3J the following values of the parameters were obtained for cyclohexane: A = 5.95, B = -1.35, C = 5.45 and D = -0.45.* The application of the function $^3J = f(\phi)$ to the 1,6-anhydro--β-D-hexapyranoses studied by us requires corrections for the electronegativities of the substituents (the effect of the differences in the bond lengths and the valence angles HCC is disregarded). The correction for electronegativity was carried out in the usual manner[19] using the relationship $^3J_{cor} = {}^3J \cdot (1 - k \sum_i \Delta E_i)$, where $k = 0.1$ and $\sum_i \Delta E_i$ is the sum of the differences of electronegativities of the first atom of each substituent of the given fragment and the hydrogen (or carbon) with respect to the cyclohexane fragment C—CH$_2$—CH$_2$—C, using Pauling's values for electronegativities $E_H = 2.1$, $E_C = 2.5$ and $E_0 = 3.5$.

In Table V the torsion angles H—C—C—H (obtained with Dreiding models and rounded up to 5°) for 1,6-anhydro-β-D-hexopyranoses $I-VIII$ are given, both for the chair $^1C_4$, boat $B_{0.3}$ and planar (envelope) E_0 conformation. In consequence of

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* The relation $J = f(\theta)$ with these coefficients gives for $J(\theta = 56°)$ the value 3.59 Hz and for $J(\theta = 62°)$ the value 2.72 Hz, which are in very good accord with experimental values for $J_{ax,eq}$ and $J_{eq,eq}$ in cyclohexane[15].

the pseudosymmetry of 6,8-dioxabicyclo[3.2.1]octane system (if the difference between the atom $O_{(6)}$ and the methylene group of the 1·6-anhydride bond is disregarded) its molecule has its plane of "symmetry" passing through the carbon atom $C_{(3)}$, oxygen $O_{(5)}$ and the centre of the $C_{(6)}$—$O_{(6)}$ bond and also identical values of the torsion angles of the protons H-1/H-2, H-4/H-5, and H-2/H-3, H-3/H-4. Using the relationship $^3J = f(\phi)$, corrected for electronegativity, theoretical values of $^3J_{H,H}$ of the compounds $I - VIII$ in individual conformations were calculated and they are listed in Table VI. From Tables V and VI it can be seen that the chair or boat form can be distinguished on the basis of ^3J between the protons H-1/H-2 and H-4//H-5 the torsion angles of which are sufficiently different for the two conformations. The use of $J_{2,3}$ for this purpose can fail in compounds III, IV, V and VI, and the use of $J_{3,4}$ in compounds II, III, VI and VII, where the torsion angle values are identical in both conformations. A comparison of the experimental values $J_{1,2}$ and $J_{4,5}$ with the theoretical ones shows that the chair conformation $^1C_4(D)$ of the pyranose ring is evidently preferred in the whole series. However, it can be destabilized to a greater or smaller extent by sterical mutual interactions of the substituents in the positions 2, 3 and 4, or by the interaction with the 1,6-anhydro-bridge. Thus, for example, in compounds I, II, V and VI, when in chair conformation, a destabilizing effect of 1,3-diaxial interactions in positions 1 and 5 with the axial substituent in the position 3 can be expected. This effect, leading to a preference of the boat conformation $B_{0,3}$, was observed in 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose[20]. Since, however,

TABLE V

Torsion Angles H—C—C—H in the Chair (C), Envelope (E) and Boat (B) Conformation in 1,6--Anhydro-β-D-hexopyranoses, Obtained from Dreiding Models and Rounded up to 5°

The torsion angles between the protons H-5/H-6 are constant within the whole series of diastereoisomers and they are little sensitive even to a change in the conformation of the pyranose ring: H-5/H-6-en = 100° (C) and 90° (B); H-5/H-6ex = 20° (C) and 30° (B).

Compound	H-1/H-2			H-2/H-3			H-3/H-4			H-4/H·5		
	C	E	B	C	E	B	C	E	B	C	E	B
I	55	80	100	75	120	165	75	120	165	55	80	100
II	55	80	100	75	120	165	45	0	45	65	40	20
III	55	80	100	45	0	45	45	0	45	55	80	100
IV	55	80	100	45	0	45	165	120	75	65	40	20
V	65	40	20	45	0	45	75	120	165	55	80	100
VI	65	40	20	45	0	45	45	0	45	65	40	20
VII	65	40	20	165	120	75	45	0	45	55	80	100
$VIII$	65	40	20	165	120	75	165	120	75	65	40	20

the substituents in positions 2, 3 and 4 are in both series of triols and triacetates identical and have equally oriented dipoles, the dipol–dipol interactions can act in some instances in the opposite direction than sterical interactions. Thus, for example, while the grouping of the three vicinal axial substituents in the positions 2, 3 and 4 is energetically unfavourable from the point of view of steric interactions, the same arrangement with antiparallelly oriented dipoles seems optimal from the point of view of dipole–dipole interactions. A combination of these types of interactions in individual diastereoisomers can result in a more or less distinct flattening of the chair conformation, which should be manifest by corresponding changes in all four vicinal coupling constants of the pyranose ring. Regardless of the accuracy of the actual values of ^3J for idealized non-deformed conformations in Table VII, the measure of planarization of individual diastereoisomers can be estimated from the expected trends of their changes within their series on the basis of a comparison with experimental values of ^3J. In the first approximation the coupling constants $J_{1,2}$ and $J_{4,5}$ are most suitable because they change monotonously during the planarization for all diastereoisomers, and they also enable a direct comparison of substances with equal configurational fragments. According to expectation a planarization of the pyranose ring should lead to a drop of the $J_{1,2}$ values in compounds $I-IV$ and their increase in compounds $V-VIII$, and to a decrease of the values $J_{4,5}$ in compounds I, III, V and VII, and their increase in compounds II, IV, VI and $VIII$ (Table VI). From a comparison with the

TABLE VI

Theoretical Values of $^3J_{H,H}$ in the Chair (C), Envelope (E) and Boat (B) Conformation in 1,6--Anhydro-β-D-hexopyranoses

The values of $^3J_{H,H}$ were obtained from the relationship $J = 5.95 - 1.35 \cos \theta + 5.45 \cos 2\theta - 0.45 \cos 3\theta$, corrected for the electronegativities of the substituents (see the text) for the torsion angles in Table V. The values $J_{5,6}$ are constant within the whole series of diastereoisomers and they are little sensitive even to a change in conformation: $J_{5,6en} = 0.6$ (C) and 0.4 (B), $J_{5,6ex} = 6.6$ (C) and 5.7 (B).

Compound	$J_{1,2}$			$J_{2,3}$			$J_{3,4}$			$J_{4,5}$		
	C	E	B	C	E	B	C	E	B	C	E	B
I	2.3	0.5	0.5	0.9	2.5	8.9	0.9	2.5	8.9	2.7	0.6	0.6
II	2.3	0.5	0.5	0.9	2.5	8.9	3.8	6.9	3.8	1.7	4.4	6.2
III	2.3	0.5	0.5	3.8	6.9	3.8	3.8	6.9	3.8	2.7	0.6	0.6
IV	2.3	0.5	0.5	3.8	6.9	3.8	8.9	2.5	0.9	1.7	4.4	6.2
V	1.4	3.8	5.4	3.8	6.9	3.8	0.9	2.5	8.9	2.7	0.6	0.6
VI	1.4	3.8	5.4	3.8	6.9	3.8	3.8	6.9	3.8	1.7	4.4	6.2
VII	1.4	3.8	5.4	8.9	2.5	0.9	3.8	6.9	3.8	2.7	0.6	0.6
VIII	1.4	3.8	5.4	8.9	2.5	0.9	8.9	2.5	0.9	1.9	4.4	6.2

experimental values of these coupling constants (see Table I and II) it follows that the triols and the triacetates with a 3β-substituent, *i.e.* the compounds *I, II, V* and *VI* are more deformed (planarized) than the compounds with a 3α-substituent, *i.e. III, IV, VII* and *VIII*. This is in agreement with the theoretical conclusions based on the destabilizing effect of steric 1,3-diaxial interactions: while compound *I* has three and the compounds *II, V* and *VI* have two 1,3-diaxial-interactions each, compound *III* has only one and the remaining compounds *IV, VII* and *VIII* have none.

For a more detailed analysis of the conformational behaviour of individual triols and triacetates corresponding torsion angles $\phi(H—C—C—H)$ were calculated from the experimental values of $^3J_{H,H}$ by means of the above derived relation $J = f(\phi)$. Their values, rounded up to 5°, are given in Table VII together with the differences from the values for a regular chair conformation of individual diastereoisomers. From Table VII the following conclusions can be derived: *1*) The triol and the corresponding triacetate assume a very similar conformation in solution (the differences

TABLE VII

Values of the Torsion Angles of Protons in 1,6-Anhydro-β-D-hexopyranoses and Their Acetates

These were determined from experimental values of $^3J_{H,H}$ and the relationship $J = f(\theta)$ (see the text) and rounded up to 5°. The deviations from the angles in chair conformation, given in Table V, are in brackets. The sign $(+)$ means an increase and the sign $(—)$ a decrease of the angle. From the two usually possible values of torsion angles only that one is given which fits into the range of the angles realizable during the conformational change chair-boat (Table V).

Compound	H-1/H-2	H-2/H-3	H-3/H-4	H-4/H;5	H-5/H-6en	H-5/H-6ex
Ia	65 (+10)	120 (+45)	120 (+45)	65 (+10)	105 (+5)	30 (+10)
Ib	65 (+10)	120 (+45)	120 (+45)	65 (+10)	105 (+5)	30 (+10)
IIa	65 (+10)	110 (+35)	30 (−15)	40 (−25)	105 (+5)	30 (+10)
IIb	65 (+10)	110 (+35)	30 (−15)	40 (−25)	100 (0)	35 (+15)
IIIa	55 (0)	*a*	*a*	55 (0)	105 (+5)	30 (+10)
IIIb	55 (0)	35 (−10)	35 (−10)	55 (0)	105 (+5)	30 (+10)
IVa	55 (0)	35 (−10)	165 (0)	45 (−20)	105 (+5)	35 (+15)
IVb	55 (0)	35 (−10)	180 (+15)	45 (−20)	100 (0)	35 (+15)
Va	60 (−5)	30 (−15)	*a*	65 (+10)	105 (+5)	25 (+5)
Vb	60 (−5)	30 (−15)	115 (+40)	65 (+10)	105 (+5)	25 (+5)
VIa	60 (−5)	35 (−10)	35 (−10)	45 (−20)	105 (+5)	35 (+15)
VIb	60 (−5)	35 (−10)	35 (−10)	40 (−25)	100 (0)	35 (+15)
VIIa	65 (0)	165 (0)	45 (0)	60 (+5)	105 (+5)	35 (+15)
VIIb	65 (0)	170 (+5)	40 (−5)	60 (+5)	105 (+5)	30 (+10)
VIIIa	65 (0)	155 (−10)	155 (−10)	45 (−20)	105 (+5)	35 (+15)
VIIIb	60 (−5)	160 (−5)	165 (0)	40 (−25)	100 (0)	35 (+15)

a The values $^3J_{H,H}$ were not determined.

in torsion angles are usually $\leq 5°$). Hence, the intramolecular hydrogen bonds do not affect the conformation of the molecule to any great extent. *2)* Very small mutual differences of the determined and the theoretical torsion angles in slightly deformed 3α-hydroxy or acetoxy derivatives, especially in compounds *III* and *VII* ($\leq 10°$), show that the derived relation $J = f(\phi)$ is also convenient quantitatively for the system under study within the whole range of angles, and that it can be used for the estimation of the magnitude of the deformation of the molecules of the compounds of this series. *3)* The determined deviations of the torsion angles of protons of the pyranose ring generally have signs identical with the theoretically expected changes of the torsion angles on the planarization of the ring (Table V and VII). This supports the hypothesis that the interactions of the substituents generally lead to a more or less distinct flattening of the pyranose ring. In agreement with the theoretical conclusions compound *I* is most deformed (with the axial substituents on $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$ in chair conformation). However, in contrast to this the least deviations from the idealized chair conformation are not found in compound *VIII* (with equatorial substituents on $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$), evidently in consequence of the unfavourable orientation of the three vicinal dipoles, and maybe even the steric interactions of the 4β-substituent with a $C_{(6)}$-methylene group, but in compound *VII* which differs

TABLE VIII
Long-range Couplings $^4J_{H,H}$ in 1,6-Anhydro-β-D-hexopyranoses in Hexadeuteriodimethyl Sulfoxide, and in Their Acetates in Deuteriochloroform

Compound	$J_{1,3}$	$J_{2,4}$	$J_{3,5}$	$J_{4,6en}$	$J_{4,6ex}$
Ia	1·3	1·1	1·4	0	0
Ib	1·2	0·8	1·5	0	0
IIa	1·4	0	1·4	0	1·0
IIb	1·3	0	1·3	0	0·8
IIIa	0	1·1	0	0	0
IIIb	0	1·0	0	0	0
IVa	0	0	0	0	0·9
IVb	0	0	0	0	0·8
Va	1·4	0	1·6	0	0
Vb	1·4	0·4	1·6	0	0
VIa	1·2	0	1·2	0	1·0
VIb	1·2	0	1·2	0	1·2
VIIa	0	0	0	0	0
VIIb	0	0	0	0	0
VIIIa	0	0	0	0	1·0
VIIIb	0	0	0	0	1·1

from *VIII* just by the configuration on $C_{(4)}$. A pronounced "deformation effect" of the β-substituent is evident from the considerable deviations of the torsion angles H-4/H-5 in compounds *II*, *IV*, *VI* and *VIII*. 4) The protons H-6en and H-6ex are bound to a five-membered ring outside the pyranose ring, and therefore the small changes of the torsion angles H-5/H-6en and H-5/H-6ex — expected from models — cannot be used as criteria for the conformational changes of the pyranose ring. The values of these angles determined from $J_{5,6en}$ and $J_{5,6ex}$ are within the narrow range of 5° or 10°, respectively. Their sum affords an average value of 135° which is in very good agreement with the value 132° (the angle H-5/H-6en is 100° and the angle H-5/H-6ex is 32°) found[11] by X-ray diffraction in levoglucosan *Ia*, and it proves a distinct enlargment of the valence angle H—$C_{(6)}$—H.

Long-Range Couplings

In rigid cyclic systems non-zero couplings ^4J are often observed. The largest ^4J values are generally found in planar "W"-arrangement. H\C/C\C/H. In pyranoid compounds in chair conformation the values $+0.8$ to $+1.6$ Hz were found for ^4J between two equatorial protons, the values -0.2 to -0.7 Hz between the axial and the equatorial proton, and very rarely non-zero interactions ^4J between two axial protons. This is in agreement with the semiempirical equation $^4J = A \cos^2 \phi_1 \cos^2 \phi_3 - B$, where $A = 2.4$, $B = 0.7$ and ϕ_1, ϕ_3 are the torsion angles H—C—C—C of both interacting protons[21]. In the case of the compounds studied by us totally eight various ^4J coupling constants are observed ($J_{1,3}$, $J_{2,4}$, $J_{3,5}$, $J_{4,6en}$, $J_{4,6ex}$, $J_{1,5}$, $J_{1,6en}$ and $J_{1,6ex}$). Of these only the first five contain an exclusively carbon fragment, which is directly dependent on the configuration of the substituents on $C_{(2)}$, $C_{(3)}$ and $C_{(4)}$, and, hence, on the conformation of the pyranose ring. Their absolute values for triols and triacetates (the sign was not determined) are given in Table VIII. The constants $J_{1,3}$, $J_{2,4}$ and $J_{3,5}$ assume distinctly non-zero values ($\geqq 0.8$ Hz) only in those compounds where both interacting hydrogens are equatorial in chair conformation. In agreement with the above statement the observed ^4J values can be considered as a further confirmation of the existence of the chair conformation in the whole series of 1,6-anhydro-β-D-hexopyranoses. According to expectation of the two constants $J_{4,6}$ only $J_{4,6ex}$ assumes distinctly non-zero values ($0.8 - 1.2$ Hz), and this only in the case of 4β-OR derivatives where the "W" arrangement is realizable. The coupling pathway of the $J_{1,5}$, $J_{1,6en}$ and $J_{1,6ex}$ always contains an ethereal oxygen. While for $J_{1,5}$ a non-zero value was observed ($\leqq 0.2$ Hz) in triol *IIIa* only, non-zero values of $J_{1,6en}$ and $J_{1,6ex}$ (approximately $0.2 - 0.5$ Hz) can be proved by decoupling in all the triols and triacetates investigated, while $J_{1,6ex}$ is as a rule slightly larger than $J_{1,6en}$. The differences between $J_{1,5}$ and $J_{1,6}$ are evidently caused primarily by the different orientation of the protons with respect to free electron pairs of the ether oxygen, and hence also by the variously large

π-contributions to ^4J. The values of ^4J are too small and their dependence on geometrical parameters too complicated for them to be used for quantitative determination of planarization of the pyranose ring.

Geminal Coupling Constants $J_{6en,6ex}$

The value $J_{6en,6ex}$ in the series of 1,6-anhydrohexopyranoses should be affected mainly by the size of the valence angle H—$C_{(6)}$—H, the lengths of the X—H bonds and the orientation of free electron pairs of the ethereal oxygens with respect to the protons of the $C_{(6)}$-methylene group[21]. The values $J_{6,6}$ in Table I and II show a higher absolute value (the sign $J_{6,6}$ is negative) for the acetate than for the triol in each diastereoisomer (by $0.5 - 0.9$ Hz). The measurement of the acetate *VIIIb* in hexadeuteriodimethyl sulfoxide and deuteriochloroform indicates that this difference is not caused by solvent effect. The value of $J_{6,6}$ also depends on the configuration of the $C_{(3)}$-substituent; 3β-substituted derivatives have distinctly lower absolute values of $J_{6,6}$ than their 3α-epimers (by $0.5 - 0.9$ Hz), both for triols and for triacetates. The torsion angles between the protons H-5/H-6en and H-5/H-6ex, determined from the values of $^3J_{5,6}$, do not show such changes as would be utilizable for the interpretation of the differences in $J_{6en,6ex}$ as changes of valence angles of H—$C_{(6)}$—H or as changes in the orientation of the protons on $C_{(6)}$ with respect to ethereal oxygens.

EXPERIMENTAL

All the 1,6-anhydro-β-D-hexopyranoses studied as well as their acetates were prepared in our laboratory using methods described earlier[1,22]. The ¹H-NMR spectra were measured on a spectrometer Varian HA-100 at a 100 MHz frequency and approximately 30°C; the solution contained 20—30 mg of substance in 0·4 ml of solvent. The acetates *Ib— VIIIb* were measured in deuteriochloroform with tetramethylsilane as internal reference. Free 1,6-anhydrohexoses *Ia— VIIIa*, poorly soluble in deuteriochloroform, were measured in hexadeuteriodimethyl sulfoxide with hexamethyldisiloxane (HMDS) as internal reference; the signals of hydroxyl protons were suppressed by addition of deuterated acetic acid. The chemical shifts were corrected with respect to tetramethylsilane ($\delta_{HMDS} = 0.06$ ppm). The signals of individual protons were expanded to a 50 Hz scale, double-resonance experiments were also carried out and the values of the coupling constants were determined with a 0·1 Hz error.

The majority of 1,6-anhydrohexoses and their acetates afforded pseudo first-order spectra at 100 MHz, the lines of which were only slightly distorted. Hence the chemical shifts and the coupling constants were obtained by first-order analysis (second-order effects on J should be smaller than 0·1 Hz). The signals of the protons H-6en and H-6ex are an exception since in relation to the geminal coupling of −7 to − 8 Hz and the vicinal couplings with H-5 they form in some instances a stronger interacting system. Therefore they were analysed as AB-parts of ABX spectra (X = H-5) and the δ values were obtained with a 0·01 ppm accuracy. If a partial overlap of the signals in dimethyl sulfoxide did not permit a sufficiently accurate determination of δ or J, this fact is indicated in the Tables. With acetates the values J were obtained in such cases from the spectra measured in deuteriochloroform after addition of the shift reagent Eu(FOD)₃, *i.e.* tris--(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione) europium (III) at the lowest concentra-

tion that led to a sufficient separation of the signals (molar ratio reagent: substrate was always lower than 0·5). In the measured concentration range the chemical shifts of all protons were a linear function of the added amount of Eu(FOD)$_3$.

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