Conformational and Configurational Equilibria of the Eight D-Aldopentopyranose Tetra-acetates

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Summary The conformational equilibria of the eight D-aldopentopyranose tetra-acetates in perdeuterioacetone were measured by n.m.r. spectroscopy.

WE report measurement of the conformational equilibria in solution of the eight peracetylated D-aldopentopyranose sugars (I—VIII); these represent all of the different stereochemical arrangements possible for a 2,3,4,5-tetra-acetoxytetrahydropyran [the eight L-enantiomorphs of (I—VIII) would give identical equilibrium data].

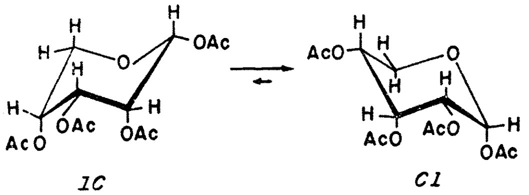
For each of the sugar acetates (I—VIII) in perdeuterioacetone at room temperature, the n.m.r. spectral method of averaging of spin coupling was used to determine the proportions of the 1*C*(D) and *C*1(D) conformers, and hence the equilibrium constant K and free energy ΔG^0 values for the 1*C*(D) $\rightleftharpoons$ *C*1(D) equilibria, by procedures already detailed[1] for compounds (II) and (VI). Deuteriochloroform was used as solvent with compound (III) in order to obtain an easily interpreted spectrum, and all spectra were measured at 100 MHz. The results are presented in Table 1.

TABLE 1

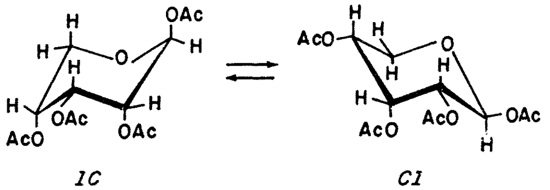
Conformational equilibria of D-*aldopentopyranose tetra-acetates in perdeuterioacetone*

Compound	Configuration	Temperature	Coupling constants, [a]Hz. $J_{1,2}$	$J_{4,5}$	$J_{4,5'}$	Equilibrium constant $K = C1/1C$	$\Delta G^{\ddagger}$, kcal.mole^{-1}, for $1C$(D) $\rightleftharpoons$ $C1$(D)
(I)	α-D-*ribo*	28°	3·7	9·1	4·6	4·0	$-0{\cdot}83 \pm 0{\cdot}36$
(II)	β-D-*ribo*	20°	4·8(8·0)[b]	3·3	5·8	1·2	$-0{\cdot}11 \pm 0{\cdot}09$
(III)[c]	α-D-*arabino*	28°	6·3(7·5)	3·5	1·8	0·23	$+0{\cdot}87 \pm 0{\cdot}36$
(IV)	β-D-*arabino*	28°	2·7	1·2	1·8(1·5)	0·03	$+2{\cdot}1 \pm 0{\cdot}4$
(V)	α-D-*xylo*	28°	3·5(3·5)	5·4(5·4)	11·0(11·0)	>50[d]	$> -2{\cdot}5$
(VI)	β-D-*xylo*	25°	6·9(8·1)	4·7	8·6(10·5)	4·0	$-0{\cdot}82 \pm 0{\cdot}14$
(VII)	α-D-*lyxo*	28°	2·9	4·3	8·6	2·9	$-0{\cdot}63 \pm 0{\cdot}28$
(VIII)	β-D-*lyxo*	28°	2·0	3·1	5·3	0·67	$+0{\cdot}24 \pm 0{\cdot}29$

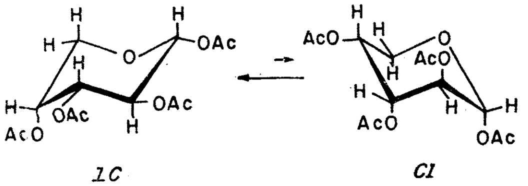
[a] Values in parentheses are limiting values observed at low temperature (~−85°). The C-5 proton resonating at lower field is designated 5-H, that resonating at higher field is designated 5-H′. [b] $J_{1a,2a}$. [c] In $CDCl_3$. [d] Almost exclusively $C1$(D) at 28°.



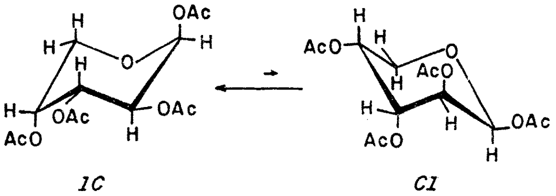
α-D-*ribo* (I)



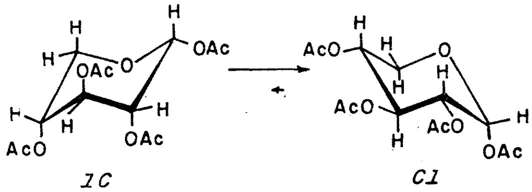
β-D-*ribo* (II)



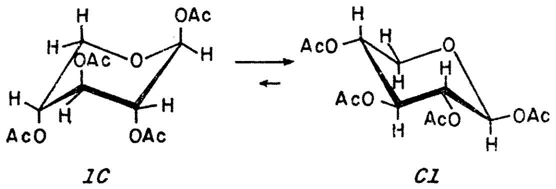
α-D-*arabino* (III)



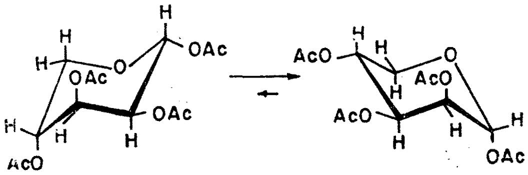
β-D-*arabino* (IV)



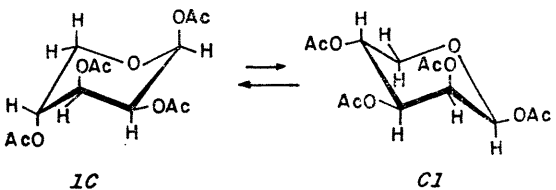
α-D-*xylo* (V)



β-D-*xylo* (VI)



α-D-*lyxo* (VII)



β-D-*lyxo* (VIII)

Analysis of the signals of 4-H and the two protons at C-5, as ABX spin-systems, gave $J_{4,5}$ and $J_{4,5'}$ values for (I—VIII) that represent weighted time-averages for the two chair conformers in rapid equilibrium. Conformational populations at room temperature were determined from the observed coupling of 4-H with the *trans*-disposed proton at C-5, taken in conjunction with values for $J_{4eq,5eq}$ and $J_{4ax,5ax}$ that had been obtained from model compounds. The $J_{4,5'}$ value for α-D-xylopyranose tetra-acetate (V) was 11·0 Hz., and $J_{2,3}$ was 9·7 Hz. These values remained unchanged as the temperature was lowered to −50° and it was concluded that (V) was essentially all in the $C1$(D) conformation; a value of 11·0 ± 0·5 Hz. was, accordingly, taken as the magnitude of $J_{4ax,5ax}$ for each compound. For the β-D-*arabino*-derivative (IV) the $J_{4a,5'}$ value (1·8 Hz) decreased to a lower limit of 1·5 Hz. at −25°, and the value 1·5 ± 0·5 Hz. was used throughout as the magnitude of $J_{4eq,5eq}$. An uncertainty of ±0·2 Hz. was used with the time-averaged couplings measured directly, and from the conformational populations determined from the coupling data, the equilibrium constants and free-energy values (at room temperature) given in Table 1 were calculated. In the case of (II), (III), (VI), and (VII), where 1-H and 2-H are *trans*-disposed, the conformational populations could also be measured from the time-averaged $J_{1,2}$ values, in conjunction with the values of 8·0 ± 0·5 Hz. for $J_{1ax,2ax}$ and 1·0 ± 0·5 Hz. for $J_{1eq,2eq}$, as used in measurements already reported[1,2] for (II) and (VI); the results for all four compounds accord well with the values obtained by the first method.

In the case of the β-D-*ribo*-compound (II) it has already been shown[1,2] that, by low-temperature n.m.r. spectroscopy in perdeuterioacetone, it is possible to observe signals of the separate chair conformers because a substantial proportion of the minor conformer is present at −90°, a temperature at which conformational interconversion is slow on the n.m.r. time-scale. A similar "conformational freeze-out" can be observed in the spectrum of the β-D-*lyxo*-derivative (VIII); at +2° the 1-H signal is a narrow doublet at τ 3·93, whereas at −97° separate signals at τ 4·00 and 3·81 are observed. The relative intensities of these signals give, for the 1*C*(D) ⇌ *C*1(D) equilibrium at −97°, a $\Delta G°$ value of −0·14 ± 0·04 kcal.mole^{-1}. From the temperature (−82°) at which the 1-H signals just coalesce into a single, broad peak, it may be calculated[1] that conformational inversion occurs 43 times per sec. at −82°; this corresponds[1] to a $\Delta G^{\ddagger}$ value of 9·6 ± 0·4 kcal. mole^{-1} for the inversion, if the transmission coefficient in the Eyring equation is taken as unity.

The polarity of the solvent does not appear to affect in any regular way the position of the conformational equilibrium; for example, in the case of β-D-ribopyranose tetra-acetate (II) at 28° the $J_{1,2}$ values observed for various solvents were: 5·5 (CCl_4), 4·8 (C_6D_6), 5·1 ($C_6D_5{\cdot}CD_3$), 4·5 ($CDCl_3$), 4·3(C_5D_5N), 4·5 (MeCN), 4·6 [$(CD_3)_2CO$], and 5·2 Hz. [$(CCl_3)_2CO$].

By equilibrating 15% (w/v) solutions of each of the compounds (I—VIII) at 27° in 1 : 1 acetic anhydride–acetic acid, 0·1M in perchloric acid, the αβ anomeric equilibria for the pairs (I) and (II), (III) and (IV), (V) and (VI) and (VII) and (VIII) were established. The compositions of these mixtures were determined by n.m.r. spectroscopy and the equilibrium data are recorded in Table 2. The data are in excellent agreement with literature values[3] (determined by optical rotatory methods) for the first three pairs. The equilibrium constant for the interconversion (VII) ⇌ (VIII), here determined as 0·20 at 27° by approach from both sides of the equilibrium, differs substantially from the value (0·08 at 25°) previously[3] reported.

TABLE 2

Anomeric equilibria of D-*aldopentopyranose tetra-acetates at* 27° *in* 1 : 1 *acetic anhydride–acetic acid,* 0·1M *in perchloric acid*

Anomeric pair	Equilibrium constant, $K = \beta/\alpha$	$\Delta G°$, kcal.mole^{-1}, for α ⇌ β at 27°
Tetra-*O*-acetyl-αβ-D-ribopyranose (I and II)	3·4	−0·73±0·03
Tetra-*O*-acetyl-αβ-D-arabinopyranose (III) and (IV)	5·4	−1·01±0·03
Tetra-*O*-acetyl-αβ-D-xylopyranose (V and VI)	0·23	+0·89±0·03
Tetra-*O*-acetyl-αβ-D-lyxopyranose (VII and VIII)	0·20	+0·98±0·05

The results provide data of value for the quantitative interpretation of steric and electronic effects of multiple acyloxy-substituents on the stability of tetrahydropyran ring-systems.

(*Received, March* 10*th*, 3969; *Com.* 338.)

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