Sugar Equilibria. Observation of a Septanose Anomer

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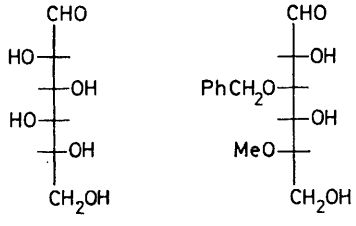
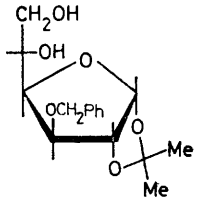
Summary D-Idose at equilibrium in aqueous solution at 37 °C contains 1·6% of a septanose anomer in addition to the furanose and pyranose anomers.

THE aldohexoses in aqueous solution exist as mixtures dominated by the two pyranose anomers,[1] with the furanose anomers[1,2] present to a lesser extent. The free aldehyde forms are also present,[3] but have been shown to constitute only between 0·002 and 0·2% of the mixtures at 20 °C. No quantitative information was previously available about any of the other possible constituents of these mixtures, such as dimers, hydrated aldehydes (aldehydrols), as well as other possible cyclic hemiacetals. In this report, we show for the first time, that, for at least one aldohexose, idose (**1**), an anomer of a cyclic hemiacetal with seven atoms in the ring, a septanose, is present in the equilibrium mixture to a significant extent.





The ^{13}C n.m.r. spectrum of a D-idose solution (3M) was recorded in D_2O at 37 °C under conditions† where integrated intensities are a reliable measure of the concentrations of the individual isomers present. Five peaks were observed in the region where the carbon atoms at the anomeric centre absorb and the four most intense signals could be readily assigned to the appropriate pyranose and furanose anomers by comparison of their intensities with the known concentrations of these isomers previously measured by ^1H n.m.r. spectroscopy.[1] The fifth signal, which had an intensity corresponding to 1·6% of the total sugar, was assigned to a septanose anomer on the basis of the following evidence. An L-idose derivative, 3-*O*-benzyl-5-*O*-methyl-L-idose (**2**) was synthesized from the known[4] 3-*O*-benzyl-1,2-*O*-isopropylidene-L-idofuranose (**3**) as follows: O–6 of (**3**) was blocked with a trityl group, O–5 was methylated, the trityl group was removed with 80% aqueous acetic acid, and then the *O*-isopropylidene group was hydrolysed with 0·1 N sulphuric acid in tetrahydrofuran–water (1 : 1) at 60 °C for 7 h. The product (**2**) was purified by column chromatography on silica gel with ethyl acetate as eluent. Since this derivative (**2**) has the OH group on C-5 blocked, it cannot form pyranose rings. In the anomeric region of its ^{13}C n.m.r. spectrum in D_2O, there were three signals which corresponded extremely closely in chemical shift to the signals observed for the anomeric carbons of the two furanose anomers and the other signal for (**1**) (see Table). Chemical shift effects on the anomeric carbon of (**2**) arising from the relatively distant substituents would be expected to be small.[5] Alkylation of hydroxy-groups is known[6] not to alter substituent *A* values substantially and therefore the two substituents on (**2**) would not be expected to alter the position of any equilibrium to a great extent. The observed intensity ratios of the α-furanose signal to the 'other signal' were 7·7 : 1 for D-idose (**1**) and 7·9 : 1 for (**2**) and of the β-furanose signal to the 'other signal' were 9·5 : 1 for (**1**) and 9·0 : 1 for (**2**). The close correspondence of chemical shifts in (**1**) and (**2**) and the similarity of the concentration ratios to the furanose anomers in (**1**) and (**2**) clearly show that the 'other signal' can be assigned to a single type of isomer in equilibrium with the furanoses.‡ Assignment of these 'other signals'

TABLE. ^{13}C N.m.r. spectral results in D_2O at 37 °C

Sample	Pyranose α	Pyranose β	Furanose α	Furanose β	Septanose
Chemical shifts[a]					
(**1**)[b]	93·25	94·32	102·67	96·47	98·53
(**2**)[c]			103·20	96·78	98·58
Percentage compositions[d]					
(**1**)[b]	37·9	32·9	12·3	15·2	1·6
(**2**)[c]			44·2	50·2	5·6

[a] Measured with respect to 5% dioxan as internal standard and referred to Me_4Si by adding 67·40 p.p.m. [b] 3 M solution. [c] 1·2 M solution. [d] Taken from the relative intensities of the ^{13}C n.m.r. peaks measured by a planimeter.

† ^{13}C N.m.r. spectra were measured on a Varian CFT-20 spectrometer using 66° pulses and 1·5 s pulse intervals. For a discussion of intensity measurements on sugars by ^{13}C n.m.r. spectroscopy see ref. 2. Agreement on percentage concentrations for the constituents of D-idose between present results at 37 °C (septanose anomer removed) and an average of the 31 and 44° ^1H n.m.r. results (ref. 1) was within 1% for every constituent.

‡ A common impurity is extremely unlikely since (**1**) was synthesized from D-glucose by an entirely different method (H. Paulsen, in 'Methods in Carbohydrate Chemistry,' eds. R. L. Whistler and D. Horton, Academic Press, New York, 1972, vol. 6, pp. 142–149) than (**2**). For (**1**), the only possible impurity is D-glucopyranose and in its ^{13}C n.m.r. spectrum in deuterium oxide the chemical shifts exhibited for C–1 by its anomers were 96·8 and 93·0 p.p.m. (ref. 5, p. 461), clearly different than the shift of the 'other signal'.

to a septanose anomer follows from the observed chemical shifts; of the other reasonable possibilities, the aldehydrol would exhibit a signal in the region 90–93 p.p.m.§ and the aldehyde would have a peak at *ca.* 200 p.p.m.

This observation of a septanose anomer in the equilibrium mixture of idose is initially somewhat surprising in view of the extensive previous studies[1,2] of aldohexoses by ^{1}H n.m.r. spectroscopy without such an observation. However in ^{1}H n.m.r. spectra, the signals of the anomeric protons cover a relatively small region of the spectrum and small signals could easily be missed because of overlapping. Indeed, 220 MHz ^{1}H n.m.r. spectra of neither (**1**) nor (**2**) showed obvious additional peaks in their anomeric region. If any sugar were to have measurable septanose isomers, idose is the most likely candidate since with respect to glucose it has extremely unstable pyranose anomers[7] and probably has relatively unstable furanose anomers because both of these anomers have destabilizing 1,2-*cis* interactions[7] between O–3 and C-5. In contrast, α-idoseptanose has 4 of its 14 twist-chair (TC) conformations¶ with all equatorial substituents, and β-idoseptanose has 2 such TC conformations; most other aldohexoseptanoses have no all-equatorial conformations (β-galacto-, gluco-, and gulo-septanose each have two), and no sugar has both anomers with some. As a result, the septanose anomers of idose are probably more stable than those of other sugars and this together with the relatively unstable nature of the other cyclic hemiacetals of idose explains the observation of the septanose anomer.

We gratefully acknowledge financial support from the National Research Council of Canada.

(*Received*, 19*th July* 1978; *Com.* 774.)

§ The aldehydrols and the septanose anomers of five 2,3,4,5-tetra-*O*-methylaldohexoses exhibit ^{13}C n.m.r. shifts in deuterium oxide in the range 90·4–91·3 p.p.m. and 93·2–98·4 p.p.m., respectively (D. B. Tulshian and T. B. Grindley, unpublished results). C–1 would be expected to have a slightly larger (0–4 p.p.m.) downfield shift when O–2 was not methylated.

¶ The TC conformation is the most stable oxepan conformation (D. F. Bocian and H. L. Strauss, *J. Amer. Chem. Soc.*, 1977, **99**, 2876).

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