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Carbohydrate Research 263 (1994) 1–11

CARBOHYDRATE RESEARCH

The composition of reducing sugars in dimethyl sulfoxide solution

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Received 20 December 1993; accepted in revised form 25 April 1994

Abstract

The composition of aldohexoses, aldopentoses, and hexuloses has been determined by ^{13}C NMR spectroscopy in dimethyl sulfoxide (Me_2SO) solution. While some of the sugars have almost the same composition as in aqueous solution, others (particularly fructose, galactose, and talose) have compositions which are very different. There seems to be no obvious explanation for this behaviour.

Keywords: Reducing sugars, composition in Me_2SO

1. Introduction

One hundred years after Emil Fischer established the configuration of D-glucose, and after the appearance of thousands of research papers, the behaviour of the monosaccharides appears to be well understood. Yet from time to time instances arise when the behaviour is surprising and not readily explained. Naturally, most phenomena have been studied using D-glucose and it has been assumed that other aldoses would behave in a similar way. Occasionally, their behaviour is very different, for no obvious reasons. In this paper, and in two others to follow, such an occurrence is described.

The composition of reducing sugars in aqueous solution has been extensively studied and is well documented [1,2]. However, in other solvents only fragmentary data are available. Kuhn and Grassner [3] were the first to realize that the solution composition of sugars may vary considerably with the solvent. They stated that D-fructose in *N*,*N*-dimethylformamide exists in furanose forms to the extent of ~ 80%. In the early days of NMR, Mackie and Perlin [4] were the first to study systematically the composition of sugars in Me_2SO; however, with the spectrometers then available, they could not always separate the signals of the α and β isomers and obtained only approximate pyranose : furanose ratios. They pointed

SSDI 0008-6215(94)00148-9

Table 1
Composition of some sugars in water and in Me_2SO, and free energy differences $\Delta\Delta G^0$ (kJ mol^{-1})

Sugar	T (°C)	Solvent [a]	α-P	β-P	α-F	β-F	Ref.	$\Delta\Delta G^0$ (α:β-P)	$\Delta\Delta G^0$ (t:c-F)	$\Delta\Delta G^0$ (F:P)
arabino Configuration										
Galactose	27	w	30.2	63.8	~2	4.3	tw [b]	1.0	~0.5	5.1
	27	D	28	39	9	24	tw			
2-deoxy-	31	w	40	44	8	8	1	0.5		0.5
	27	D	43	38	8	11	tw			
3-deoxy-	27	w	21	55	4	20	tw	0.7	1.5	1.9
	27	D	20	40	4	36	tw			
6-deoxy-	27	w	30	67	1	2	tw	1.1	~1.1	5.9
	27	D	31	44	6	19	tw			
Altrose	22	w	27	43	17	13	1	−0.5	2.5	2.1
	27	D	17	33	39	11	tw			
Arabinose	27	w	62	29	5.2	3.6 [c]	tw	1.2 [d]	2.1	4.7
	27	D	33.9	26.1	30.9	9.1	tw			
Fructose	27	w	2.5	71.7	5.4	20.4	9	4.0	1.1	4.5
	27	D	4.8	27.0	20.1	48.1	8			
1-deoxy-	37	w	4	80	6	9.5 [e]	1	1.4	1.7	4.7
	27	D	4.5	51.5	23.5	18.5	2			
1-*O*-methyl-	20	w		61	9	30	2		0	4.5
	30	D		20	18	61	2			
3-*O*-methyl-	20	w	3.1	51.0	11.8	34.1	2	2.2	1.5	3.4
	20	D	3	20	30	47	8			
galacto-Heptulose	22	w	78		16	6	1		1.2	4.3
	20	D	38		38	23	2			
ribo Configuration										
Allose	31	w	14	77.5	3.5	5	1	0.1	2.3	1.4
	27	D	13.5	72.5	3	11	tw			
Talose	27	w	40	29	19	12	tw	3.8	2.5	−0.5
	27	D	63	10	22	5	tw			
6-deoxy-	30	w	44	28	16	11	1	3.9	2.9	−0.6
	27	D	68	9	19	4	tw			
Ribose	27	w	24	53	8	14	11	−0.9	1.6	0.5
	27	D	18	56	6	20	11			
2-*C*-hydroxymethyl- (hamamelose)	23	w	12	21	38	29	1	0.7	0.2	−0.2
		D	15	20	35	30	1			
Psicose	27	w	22	24	39	15	1	0	0.3	−0.4
	27	D	24	26	34.5	15	tw			
altro-3-Heptulose	30	w	11	16	55.5	17.5	1	1.2	0	−0.7
	30	D	16.5	15	50.5	16.5 [e]	1			
lyxo Configuration										
Mannose	27	w	67.4	32.6			10	3.4		
		D	89	11			tw			
6-deoxy-	44	w	60	40			1	3.7		
		D	87	13			1			
Lyxose	31	w	70	28	1.5	0.5	1	2.7		
		D	88	12			1			

Table 1 (continued)

Sugar	T (°C)	Solvent [a]	α-P	β-P	α-F	β-F	Ref.	$\Delta\Delta G^0$ (α:β-P)	$\Delta\Delta G^0$ (t:c-F)	$\Delta\Delta G^0$ (F:P)
Gulose	22	w	16	81		3	1	−0.2		~2.6
	27	D	14	78	3	5	tw			
D-*glycero*-D-*gulo*-Heptose	27	w	11	89			tw	−0.3		
	27	D	9.8	90.2			tw			
Tagatose	27	w	79	16	1	4	1	−0.2	3.3	0.8
	27	D	76.0	17.2	3.5	3.2	tw			
xylo Configuration										
Glucose	27	w	36.9	63.1			tw	0.7		
	27	D	43.5	56.5			11			
Xylose	31	w	36.5	63	<1		1	0.5		
	27	D	40	57	~1	~1.5	t			

[a] w, Water; D, Me_2SO.
[b] tw, This work.
[c] The data given in Ref. 1 are wrong. On the basis of 100 MHz spectra, it was assumed that the signal of the β-furanose form coincides with that of the α-furanose. In fact, it is slightly downfield from the β-pyranose signal (J.D. Stevens, personal communications).
[d] In arabinose, in contrast to the other aldoses listed, the α-pyranose has an equatorial, and the β anomer and axial OH-1. Hence the figure refers to the β:α, not the α:β, ratio.
[e] Not counting the *keto* form.

out that sugars which had the *arabino* configuration of hydroxyl groups on the pyranose ring showed particularly large variations between different solvents. Fructose was later studied in much detail by Dais and Perlin [5,6].

In an effort to obtain a clearer picture, we determined the composition of some other sugars in Me_2SO. Galactose, which has the same configuration of hydroxyl groups in the ring as fructose, also showed a great increase in the proportions of the furanose forms on changing the solvent to Me_2SO but the proportion of the α-pyranose form also increased whereas that of the analogous β-pyranose form of fructose decreased. Another ketose, psicose, was found to have practically the same composition in the two solvents. It was then decided to extend the investigation to other sugars.

2. Results

Composition data in Me_2SO were available for many sugars [1,2] but there were numerous gaps. By the use of ^{13}C NMR spectroscopy [7] we have extended the data to include all of the aldohexoses, aldopentoses, and hexuloses, and a few other relevant compounds. Idose was omitted because in solution it presents a conformational mixture which would make any interpretation difficult. Sorbose was excluded because only the α-pyranose form is present in solution in significant amounts (besides 2% in aqueous solution and — as now shown — 2.5% in Me_2SO solution of the α-furanose). To avoid any variations caused by the different

entropies and enthalpies of the various forms of different sugars, all comparisons were made at the same temperature (27°C) as far as possible. Thanks to the efforts of Lichtenthaler and co-workers [8,9], data are available on numerous derivatives of fructose; only a few of these are listed here because the others provide no additional information on the composition. The compounds were grouped according to the configuration of the hydroxyl groups in the pyranose ring as *arabino*, *ribo*, *lyxo*, *and xylo*. The results are shown in Table 1.

At a time when fewer data were known, it was stated [1,2] that the $\alpha:\beta$ pyranose ratio is higher in solvents other than water, and that there is also a higher proportion of furanoses. It can now be seen that this statement is not always correct: it is valid for most of the *arabino* compounds but not for most of the *ribo* isomers.

These data will be discussed under three headings: (*1*) The variation of the $\alpha:\beta$ pyranose ratio; (*2*) the variation of the *trans*:*cis* furanose ratio; and (*3*) the variation of the furanose:pyranose ratio on changing the solvent from water to Me_2SO. The best way to compare these data is by looking at the variation of the differences between the free energies of each form with the change of solvents; this variation will be designated as $\Delta\Delta G^\circ$ [1]. The $\Delta\Delta G^\circ$ figures have been rounded to the nearest 0.1 kJ mol^{-1}; their uncertainty is probably greater than that value. There are in some cases considerable differences between data given by different authors: for example, for D-fructose (for which there are many data [5,6,8–10]), the composition data differ in some instances by more than 3%. Some choice of figures given in Table 1 are arbitrary. Where data were available for several temperatures, we quote a number for 27°C, arrived at by interpolation.

$\alpha:\beta$-Pyranose ratios.—Dais and Perlin [5] have noted that sugars having the *arabino* configuration show an increase in the $\alpha:\beta$ ratio when changing the solvent from water to Me_2SO. This also applies to the *xylo* series. The increase is small ($\Delta\Delta G^\circ(\alpha:\beta\text{-P}) \sim 1$ kJ mol^{-1}) and there are quite a few exceptions. Thus talose (and its 6-deoxy derivative) is outstanding in showing a very large change (~ 4 kJ mol^{-1}), and aldoses with the *lyxo* configuration also have a large, though somewhat smaller, ratio (~ 3.5 kJ mol^{-1}). On the other hand, aldoses with the *ribo* configuration, and also gulose and altrose, show no increase, or even a decrease of the $\alpha:\beta$ ratio. Ribose is a special case because the β-pyranose is a conformational mixture; the proportions of the two chair forms are known [11], $\Delta\Delta G^\circ$ is -0.8 kJ mol^{-1} but if the proportion of the α anomer is compared with only the component of the β isomer which has the same conformation ($^4C_1$), it is close to 0 kJ mol^{-1}.

The ketoses are not included in this summary. The α- and β-pyranose forms of the aldoses have the same conformation and the energy differences between them are caused only by the difference in the configuration of C-1. By contrast, in both

[1] As an example of the calculations: for glucopyranoses in water, the $\alpha:\beta$ ratio of 36.9:63.1 corresponds to a free energy difference of 1.33 kJ mol^{-1}; in Me_2SO, the $\alpha:\beta$ ratio of 43.5:56.5 corresponds to 0.65 kJ mol^{-1}. The difference between these figures, characterizing the change from aqueous to Me_2SO solution, is $\Delta\Delta G^\circ(\alpha:\beta\text{-P})$ 0.68 kJ mol^{-1}.

pyranose forms of the ketoses, OH-1 is axial and the ring conformations are different; no general correlation can be expected. For fructose, 1-deoxyfructose, and several substituted fructose derivatives (1-*O*-, 3-*O*-, 4-*O*-, and 5-*O*-α-D-glucopyranosyl-D-fructoses [8]), $\Delta\Delta G°$ is 2–4 kJ mol^{-1}. By contrast, for psicose and tagatose it is very small.

trans : cis-*Furanose ratio*.—The ratio between the anomer in which O-1 and O-2 are *trans* and the one in which they are *cis* increases on changing the solvent to Me_2SO, $\Delta\Delta G°(t : c\text{-F})$ being 1.2–2.0 kJ mol^{-1}. The *trans* anomer, which is usually the predominant one in aqueous solution, becomes even more predominant in Me_2SO. Even in the case of fructose, where the β-(*cis*)-furanose becomes the major form in Me_2SO solution, the α-furanose increases to a greater extent then the β anomer. However, $\Delta\Delta G°$ is very small for psicose, *altro*-3-heptulose and 4-*O*-D-glucopyranosyl-D-fructose [8]. For sugars of the *xylo* and *lyxo* configuration, the proportion of furanoses being very small and reliable data are not available; when figures are given as 1 or 2%, they are unsuitable for calculating $\Delta\Delta G°$ values.

Furanose : pyranose ratios.—Compounds with *arabino* configurations show a very large increase in the proportion of furanoses, $\Delta\Delta G°$ being of the order of 4 kJ mol^{-1}. This applies also to the ketoses. When the configuration is *ribo*, $\Delta\Delta G°$ is much smaller ($\sim$ 1 kJ mol^{-1}) and it is negative for psicose and talose. The two sugars of the *lyxo* configuration for which data are available (gulose and tagatose) show a small increase.

3. Discussion

These results are not readily explained. Looking at fructose, which displays great increases in the α : β-pyranose and the furanose : pyranose ratios, one would be tempted to attribute both to the same cause, namely, a sharp reduction of the proportion of the β-pyranose form. However, the two phenomena are not related. Galactose shows a great increase of the furanose forms but only a small change of the α : β-P ratio. On the other hand, talose shows a great increase in the α : β-P ratio but very little change in F : P. Hence the three changes will be discussed separately.

α : β-Pyranose ratios.—An explanation of such changes has been attempted by invoking a theory [12], based on the proposals by Kabayama and Patterson [13], that pyranose forms are stabilized in aqueous solution by better accommodation into the water structure, stabilization being greater for equatorial than for axial hydroxyl groups. This theory has been expanded by Suggett [14] and Bociek and Franks [15]. From the data now presented, however, it appears that the water structure is not fully responsible for the changes occurring when another solvent replaces water. If the equatorial hydroxyl group of the β-pyranoses is stabilized, by better fit into the water structure, compared to the axial hydroxyl group of the α-anomer, the effect of changing the solvent — and thereby losing the stabilization — should be the same for all aldoses. In fact there are significant differences. The results of Dais and Perlin [5] show that when an equal volume of Me_2SO is added

to an aqueous solution of fructose, the β-pyranose content drops from 62.5 to only 51.5%, whereas the value in Me_2SO is 27.5% (at ~30°C). Surely, such a dilution of water would leave very little of the crystalline structure, yet much of the stablization of the β anomer still persists.

A more plausible explanation for the undoubted stabilization of equatorial hydroxyl groups in water lies in the consideration of the extent of hydration. All hydroxyl groups are hydrated in aqueous solution [16]. However, equatorial hydroxyl groups can act both as hydrogen donors and hydrogen acceptors, while axial ones only as donors [17]. Accepting a hydrogen bond by an axial hydroxyl group would force its hydrogen atom into an inward orientation, a conformation highly unstable. Hence equatorial hydroxyl groups are more stabilized by hydrogen bonding with water than are axial ones. This effect will operate, proportionally, even when diluted with another solvent. On the other hand, Me_2SO can bond with a hydroxyl group only by acting as an acceptor; hence the difference between axial and equatorial groups will disappear, and the proportion of the axial anomer becomes comparatively greater. This is probably the reason for the small increase found for many aldoses. In the case of allose and ribose, where no increase is observed, it is counterbalanced by reduced interaction between the axial O-1 and O-3 atoms in the α anomer. In water the hydroxyl groups are effectively larger, owing to their extensive hydration by water, than in Me_2SO.

The greater increase in the proportion of the α-pyranose form, as observed for talose and mannose, occurs only if O-2 is axial. However, if both O-2 and O-3 are axial (e.g., altrose), there is no increase in the α-content. Probably the interaction between the axial O-1 and O-3 prevents this, as mentioned in the preceding paragraph. It is not clear why an axial O-2 should favour high α-pyranose levels in Me_2SO. Maybe solvation of an axial anomeric hydroxyl group is easier when it is distant from O-2.

In Me_2SO solution, talose has a hydrogen bond between O-2 and O-4. The presence of cooperative hydrogen bonds [18] in sugars has been studied by NMR spectroscopy of partially deuterated hydroxyl protons [19]. By this technique it was found that such hydrogen bonds occur in α-mannopyranose and in α-talopyranose in Me_2SO solution [20]. They would stabilize the α anomer but similar stabilization should occur in the β anomer too. Moreover, such cooperative hydrogen bonds have also been found in the Me_2SO solutions of α-glucopyranose [19] but not in that of α-galactopyranose. They therefore do not seem to offer any explanation for the compositions in Me_2SO.

It appears that these compositions will not be fully understood until more detailed knowledge becomes available on the solvation of sugars by Me_2SO.

trans : cis-*Furanose ratios.*—Little is known about the way furanoses are solvated by water but it is safe to assume that, like pyranoses, they are extensively solvated. Even less is known about the solvation of furanoses by Me_2SO. However, Me_2SO is a much larger molecule than water, and it may be assumed that solvation will not be complete if hydroxyl groups are very close to each other. Since *cis* hydroxyl groups in furanoses are not completely staggered, they may be hydrogen bonded to Me_2SO to a lesser extent than *trans* hydroxyl groups. Molecular mechanics (MM2

force-field) calculations show that the most stable conformation of three *cis* hydroxyl groups on a five-membered ring is unfavourable for hydrogen bonding to Me_2SO; the change to a favourable conformation requires 19 kJ mol^{-1} of energy [2]. This may explain the universal increase in the *trans* : *cis* ratio in Me_2SO, compared to that in water. When there is a *cis* interaction in each of the anomers (psicose, *altro*-3-heptulose, hamamelose), there is little change in the *trans* : *cis* ratio.

In the case of fructose, the composition versus solvent molarity graph published by Dais and Perlin [5] for the α-furanose shows evidence for the existence of an intramolecular hydrogen bond (an initial increase, followed by decrease, on gradual addition of water to the solution in Me_2SO). This increase is due to a strengthening of a hydrogen bond by formation of a cooperative hydrogen bond with a water molecule. This is reminiscent of a case illustrated by Lemieux and Pavia [22] in which gradual addition of Me_2SO to a solution in ethylene dichloride produced such a maximum. In fructofuranose, the cooperative bond requires a hydrogen donor: water, but not Me_2SO, can fulfill this function. (Perlin's graph is scaled to mole fractions whereas Lemieux's is to percentage by volume. The latter scale shows the effect much better.)

Furanose : *pyranose ratios.*—Conventional wisdom has it that the furanoses increase on changing the solvent because the pyranoses are loosing the stabilization conferred on them by the solvent water. If so, this is not the whole explanation.

Calculations [23] show that the hydrophilicities (a measure of the extent of hydration) of galactose, altrose, and allose are closely similar, yet galactose shows a great increase in the proportion of furanoses, altrose a small one, and allose even less. Talose, which has the lowest hydrophilicity, shows a decrease of the furanoses. What is not taken into account here is the solvation of the furanose forms, about which little is known. Because none of the bonds are fully staggered, each hydroxyl group will have a close neighbour, even if it is only a hydrogen atom. It is likely therefore that double hydration (being both donor and acceptor) would occur less frequently than in the pyranoses. In Me_2SO, where only one hydrogen bond can occur on each hydroxyl group, there is probably little difference between the solvation of pyranoses and furanoses, provided that the furanose hydroxyl groups do not hinder each other. It is significant that large increases in the furanose forms occur only if the configuration is *arabino*, all substituents being *trans*; when it is *lyxo* or *ribo*, there is no substantial increase. In psicose, *altro*-3-heptulose and hamamelose, both furanoses have *cis* substituents on the anomeric and the neighbouring carbon atoms and all three show a decrease in the F : P ratio. The 2,3-di-*O*-methyl derivatives of arabinose, galactose and altrose

[2] It is worth noting that in the crystal structure of coriose (D-*altro*-3-heptulose), in which there are three *cis* hydroxyl groups on a furanose ring, the central one acts only as hydrogen donor whereas all the other hydroxyl groups are both donors and acceptors of hydrogen bonds [21].

Table 2
^{13}C Chemical shifts in Me_2SO solutions

Sugar	Chemical shifts (ppm)					
	C-1	C-2	C-3	C-4	C-5	C-6
Allose						
α-furanose	97.8	73.6		85.2	70.7	63.6
β-furanose	103.7	77.2	74.3	84.0	71.9	63.8
α-pyranose	94.8	68.8	73.8	68.0	68.5	62.0
β-pyranose	95.3	72.3 [a]	72.2 [a]	68.7	75.3	62.5
Altrose						
α-furanose	102.4	82.9	76.8	83.6	72.4	63.0
β-furanose	96.3	77.9	75.4	83.1	73.0	63.2
α-pyranose	94.8	70.5	70.0	64.8	71.6	61.7
β-pyranose	92.2	71.7	71.6	65.0	74.8	62.3
Galactose						
α-furanose	95.7	77.8	74.9	81.6	71.3	63.0
β-furanose	102.1	81.7	76.5	82.9	70.9	63.3
α-pyranose	93.0	69.2 [a]	69.4 [a]	69.9 [a]	70.8	61.0
β-pyranose	97.9	72.5	73.9	68.7	75.4	61.0
2-Deoxygalactose						
α-furanose	97.62	43.04	71.65 [d]	83.65	71.17 [d]	63.41
β-furanose	97.75	43.56	71.37 [d]	85.64	71.01 [d]	63.59
α-pyranose	91.32	34.20	65.00 [a]	67.99 [a]	71.01	61.42
β-pyranose	94.44	37.11	68.61 [c]	66.69 [c]	75.74	61.33
3-Deoxygalactose [b]						
α-furanose	95.3 (96.9)	73.5 (76.0)	32.0 (33.0)	76.6 (78.8)	71.9 (72.6)	(64.6)
β-furanose	103.0 (104.0)	75.3 (77.0)	34.5 (35.4) [a]	77.4 (79.7)	73.4 (75.0)	63.3 (64.7)
α-pyranose	92.4 (93.4)	63.9 (65.2) [c]	34.5 (34.4) [a]	65.7 (67.7) [c]	70.3 (71.6)	61.5 (63.2)
β-pyranose	99.9 (100.2)	66.8 (68.4)	39.2 (39.1)	65.4 (67.6)	78.6 (80.0)	61.5 (63.1)
6-Deoxygalactose [b]						
α-furanose	95.7 (96.7)	78.0	75.5 (74.6)	86.0 (86.6)	67.7 (70.6)	20.2 (20.4)
β-furanose	102.0 (102.7)	83.3 (83.6)	77.2 (78.3)	86.0 (87.8)	66.5 (66.6)	20.1 (20.0)
α-pyranose	92.9 (94.0)	66.8 (69.9) [a]	69.9 (71.1) [a]	65.5 (67.8) [a]	72.2 (73.7)	17.0 (17.6)
β-pyranose	97.6 (98.1)	71.6 (73.2) [c]	72.2 (73.6) [c]	70.0 (72.3)	74.0 (74.8)	17.1 (17.6)
Gulose						
α-furanose	102.4	82.9	76.8	83.6	72.4	63.0
β-furanose	96.3	77.9	75.4	83.1	73.0	63.2
α-pyranose	94.8	70.5	70.0	64.8	71.6	61.7
β-pyranose	92.2	71.7	71.6	65.0	74.8	62.3
Talose						
α-furanose	101.6	75.9	70.6	82.1	71.3	63.4
β-furanose	94.9		70.9 [d]	82.5		63.2
α-pyranose	95.1	71.4	65.5	70.2	72.5	61.0
β-pyranose	94.9	73.1	69.0 [a]	69.1 [a]	76.1	60.6
6-Deoxytalose						
α-furanose	101.40	76.09	71.09	86.16	67.68	20.13
β-furanose	96.48	70.70 [a]	71.48 [a]	86.65	66.64	18.86
α-pyranose	95.01	71.80	65.55	73.10	66.22	17.12
β-pyranose	94.68	72.60 [c]	69.20	72.60	71.80 [c]	17.00
Arabinose						
α-furanose	102.2	83.1 [a]	77.0	83.4 [a]	62.0	
β-furanose	96.1	77.6	75.5	83.0	63.5	
α-pyranose	97.6	72.1	73.0	67.9	65.4	
β-pyranose	93.1	69.6 [c]	69.5 [c]	67.9 [c]	62.9	

Table 2 (continued)

Sugar	Chemical shifts (ppm)					
	C-1	C-2	C-3	C-4	C-5	C-6
Xylose						
α-furanose	96.4	75.6 [a]		79.2 [c]	60.7	
β-furanose	103.1	75.9 [a]		81.7 [c]	60.9	
α-pyranose	92.9	72.7	73.6	70.6	61.9	
β-pyranose	98.1	75.1	77.1	70.2	66.1	
Psicose [e]						
α-furanose	64.1	103.8		71.5	83.5	62.1
β-furanose	63.3	106.0		71.8	83.9	63.4
α-pyranose	64.0 [a]	98.3 [c]		73.1	66.9	58.8
β-pyranose	64.4 [a]	98.5 [c]		65.5 [a]	70.3	64.8 [d]
Tagatose						
α-furanose	105.6		78.2	74.2	79.8	
β-furanose	103.5			71.8	80.7	61.4
α-pyranose	98.6	65.0	71.0	72.0	70.2	63.3
β-pyranose	99.5	63.8	64.6	72.6	70.5	60.4

[a,c] Values marked with the same letter may need to be interchanged.
[b] Figures in parentheses refer to aqueous solution.
[d] Assignment uncertain.
[e] To simplify the spectrum, psicose labelled with deuterium on C-3 was used; hence no values were obtained for the chemical shifts of the C-3 atoms.

show [4] large increases in $\Delta\Delta G°$ (F:P) and they all have the *arabino* configuration. It is probable that in these cases the methyl groups hinder solvation of the pyranoses. Idose shows an increase in the proportion of the β-pyranose [24]; in this case, three of the hydroxyl groups are axial and therefore are well separated from neighbouring substituents and free to be solvated. The composition was obtained, not in Me_2SO, but in a 1:1 mixture of Me_2SO and acetone, hence these data are not comparable with those shown in the Table.

Dais and Perlin [5] invoked the presence of an intramolecular hydrogen bond between O-2 and O-6 in β-fructofuranose to explain its preponderance in Me_2SO. If such a bond were present, it would also occur in β-psico- and β-lyxo-furanoses which do not show such an increase. Rather, as shown above, there seems to be an intramolecular hydrogen bond in the α-furanose; such a bond may occur in other furanoses too and may contribute to their increased stability.

Numerous data are available on the composition of sugars in pyridine solution [1,2]. They lie between the values in aqueous and in Me_2SO solutions (with the exception of 3-*O*- and 6-*O*-α-D-glucopyranosyl-D-fructose [8]). Apparently the factors responsible for the composition in Me_2SO are also operative in pyridine but to a lesser extent.

Mention should be made here of the composition of D-glucose in water. It has been determined over a wide range of temperature by Franks and co-workers [11] and by Maple and Allerhand [25]. Both sets of data are internally consistent but the α-pyranose content found by Maple and Allerhand is considerably higher, e.g.,

39.0 ± 0.8% versus 34.5 ± 1% at 27°C. It was suggested [2] that the difference may be due to the addition of 11% 1,4-dioxane to the solution used for the recording of the ^{13}C NMR spectra by the latter authors, this being sufficient to cause a significant increase in the $\alpha:\beta$ ratio. The present data show that this is not so. We found 36.9% of the α-pyranose in H_2O (halfway between the above quoted figures) and 36.7% after the addition of 1,4-dioxane. From the optical rotation of the solution equilibrated at 20°C, a value of 36.2% was obtained [26]. To check whether the difference may have been caused by Franks et al. having used D_2O, and Maple and Allerhand H_2O, as solvent, we obtained the ^{13}C NMR spectrum of glucose in D_2O; 38.1% of α-pyranose was found. The explanation for the difference in these results therefore remains unexplained. Maybe the compositions obtained by NMR are less reliable than commonly assumed, different instruments and techniques showing a different bias in the integrations.

4. Experimental

Solutions of the sugars were equilibrated for 2 weeks at ambient temperature (~ 25°C) or 24 h at 60°C, followed by standing for several days before recording the spectra. Broadband ^{1}H-decoupled ^{13}C NMR spectra were recorded with a Bruker AM-500 spectrometer on ~ 0.2 M solutions at 125 MHz at 27°C. Spectra were referenced to the Me_2SO signal at 39.80 ppm, even for aqueous solutions. For integrations, every ^{13}C signal was used [7] unless it overlapped with another signal. The estimated standard deviation is ± 1.0%. To check the reproducibility of the results, a mixture of *myo*-, *chiro*-, and *epi*-inositols in Me_2SO was recorded three times; the composition data agreed within 1%. In some instances, when equilibrium had been reached, a subsequent spectrum gave results differing by less than 1%.

In most cases, the chemical shifts were similar to those recorded in aqueous solutions [27] but occasionally there were considerable differences; hence they are listed in Table 2. All the four tautomeric forms were distinguishable in every spectrum, except that of mannose. There appears to be no correlation between changes in the chemical shifts and changes in the composition on altering the solvent.

Acknowledgments

Our thanks are due to Mrs. H.E.R. Stender for running the numerous NMR spectra and to Professor M.N. Paddon-Row for the molecular mechanics calculations.

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