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Distribution of pyranose and furanose forms of 6-deoxyheptoses in water solution

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Abstract

On the basis of ^{1}H and ^{13}C NMR spectroscopy studies, the proportion of pyranose and furanose forms of 6-deoxyheptoses in water solution was determined. Water solution of 6-deoxyheptoses contains all possible furanose and pyranose forms (except 6-deoxy-*gluco*-heptose for which only pyranose was found), although pyranose is dominant. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: 6-Deoxyheptoses; NMR spectroscopy; Cyclic forms; Distribution

1. Introduction

Naturally occurring 6-deoxyheptoses are rare components of bacterial lipopolysaccharides (LPS). From the 16 possible stereoisomers of 6-deoxyheptoses, five have been found in LPS in both pyranose and furanose forms.[1,2] The first deoxyheptose, 6-deoxy-D-*manno*-heptose, was isolated from LPS of *Yersinia pseudotuberculosis* Group IIA by Lindberg's group.[3] The same compound was found in LPS of *Yersinia pseudotuberculosis* Group IA[4] and *Pseudomonas pseudomallei*.[5] 6-Deoxy-D-*altro*-heptose is a component of LPS' of *Eubacterium saburreum* strain L49,[6] strain O-2,[7,8] and *Campylobacter jejuni*, serotypes O:36 and O:23.[9–11] Recently, 6-deoxy-D-*altro*-heptose was identified as a part of LPS of *Campylobacter jejuni*, serotype O:41.[12] LPS of *Campylobacter coli* and *C. jejuni* contain 6-deoxy-D-*talo*-heptose.[2,13] 6-Deoxy-L-*galacto*-heptose and 6-deoxy-L-*gulo*-heptose are components of LPS of two strains of *Campylobacter lari*.[2,14–16] Most of the reported synthetic approaches are based on chain elongation at the C-5 and C-6 positions of pentoses and hexoses, respectively.[1,17–21]

For identification and recognition of configuration of monosaccharides isolated from natural sources, physicochemical properties (e.g., full NMR data, optical rotation, composition of solutions) must be known. The proportions of the furanose and pyranose forms of aldohexoses and aldoheptoses at equilibrium in water solution are well known. Plentiful literature data were collected and published by Angyal in 1984 and updated in 1991.[22,23] By comparison, composition of 6-deoxyheptoses in solution has never been investigated, except our recent study for

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6-deoxy-D-*altro*-heptose.[12] Similarly, determination of NMR signals of 6-deoxyheptoses have never been described in details in contrast with fully substituted monosaccharides.[24]

2. Results and discussion

In this paper, we report the determination of proportion of pyranosidic and furanosidic forms of 6-deoxyheptoses on the basis of ^{1}H

Table 1
The composition (%) of 6-deoxy-heptoses and some aldohexoses and aldoheptoses in D_2O (at 303 K unless otherwise indicated)

Form		%		%		%		%
α*f*	6-deoxy-D-*allo*-heptose (**1**)	3.3	allose [a22]	3.5			D-*glycero*-D-*allo*-heptose [b22]	5.0
β*f*		5.5		5.0				7.0
α*p*		11.6		14.0				14.0
β*p*		79.6		77.5				74.0
α*f*	6-deoxy-D-*altro*-heptose (**2**)	14.1	altrose [b22]	17.0	6-deoxy-D-altrose[12]	15.4	D-*glycero*-L-*altro*-heptose [b22]	17.0
β*f*		10.1		13.0		12.8		13.0
α*p*		32.3		27.0		33.3		29.0
β*p*		43.4		43.0		38.5		41.0
α*f*	6-deoxy-D-*gluco*-heptose (**3**)		glucose [c23]	0.14	6-deoxyglucose [d22]		D-*glycero*-L-*gluco*-heptose [b22]	
β*f*				0.15				
α*p*		25.0		38.8		36.0		43
β*p*		75.0		60.9		64.0		57
α*f*	6-deoxy-D-*manno*-heptose (**4**)	2.4	mannose [e23]		6-deoxymannose [d22]		D-*glycero*-L-*manno*-heptose [b22]	
β*f*		<0.5						
α*p*		45.2		68.0		60.0		70.0
β*p*		52.4		32.0		40.0		30.0
α*f*	6-deoxy-L-*gulo*-heptose (**5**)	<1	gulose [b22]				D-*glycero*-D-*gulo*-heptose [b22]	2.0
β*f*		<1		3.0				3.0
α*p*		10.3		16.0				15.0
β*p*		88.7		81.0				80.0
α*f*	6-deoxy-L-*ido*-heptose (**6**)	4.9	idose[23]	13.5			D-*glycero*-D-*ido*-heptose[23]	8.7
β*f*		6.4		16.5				15.5
α*p*		54.2		35.9				24.4
β*p*		34.5		33.4				50.8
α*f*	6-deoxy-D-*galacto*-heptose (**7**)	<1	galactose [a22]	2.5	6-deoxygalactose [a22]	~5	D-*glycero*-D-*galacto*-heptose [b22]	2.0
β*f*		<1		3.5				3.0
α*p*		25.4		30.0		28.0		28.0
β*p*		73.6		64.0		67.0		67.0
α*f*	6-deoxy-L-*talo*-heptose (**8**)	7.7	talose [f23]	18.5	6-deoxytalose[22]	16.0	D-*glycero*-L-*talo*-heptose [b22]	22.0
β*f*		7.7		11.6		11.0		15.0
α*p*		51.5		41.0		44.0		33.0
β*p*		33.1		29.0		28.0		30.0

[a] At 304 K.
[b] At 295 K.
[c] At 300 K.
[d] At 317 K.
[e] At 294 K.
[f] At 301 K.

Table 2
^{1}H chemical shifts (ppm) and coupling constants (Hz) for 6-deoxy-heptoses in D_2O at 303 K

	Form	H-1 $J_{1,2}$	H-2 $J_{2,3}$	H-3 $J_{3,4}$	H-4 $J_{4,5}$	H-5 $J_{5,6}$ $J_{5,6'}$	H-6 $J_{6,6'}$ $J_{6,7}$	H-6' $J_{6',7}$ $J_{6',7'}$	H-7 $J_{7,7'}$	H-7' $J_{7',6}$
6-deoxy-D-*allo*-heptose (**1**)	α*p*	5.09 3.8	3.71 3.3	4.12 3.1	3.46 9.6	4.03 2.7 9.5	2.07 14.8 7.5	1.68 4.7 5.1	3.72	3.72
	β*p*	4.85 8.3	3.41 3.2	4.14 3.1	3.46 9.9	3.80 2.6 9.3	2.03 15.1 7.6	1.64 4.7 5.8	3.75 11.3	3.73 7.6
	α*f*	5.36 4.3	4.05 6.0	4.17 3.5	4.03 4.2	3.88	1.94	1.80	3.72	3.72
	β*f*	5.22 1.9	3.96 4.9	4.33 5.6	3.85 5.6	3.89	1.82	1.70	3.74	3.74
6-deoxy-D-*altro*-heptose (**2**)	α*p*	4.88 5.0	3.73 7.2	3.91 3.5	3.79 5.5	4.11 4.5 7.9	1.90 14.1 8.1	1.87 5.0 5.0	~3.75 $J_{7,7'}$ 12.7 $J_{7',6}$ 8.1	
	β*p*	5.08 <2	3.82 4.0	4.05 3.3	3.66 9.7	3.82 2.9 9.7	2.03 14.5 7.6	1.72 5.6 5.6	~3.75 $J_{7,7'}$ 12.7 $J_{7',6}$ 7.6	
	α*f*	5.24 2.6	4.02 3.5	4.13 5.0	4.01 5.0	3.94	1.85	1.70	~3.75	
	β*f*	5.28 4.6	4.07 7.1	4.21 6.7	3.73 7.0	3.88	1.88	1.68	~3.75	
6-deoxy-D-*gluco*-heptose (**3**)	α*p*	5.18 3.8	3.53 9.8	3.67 9.6	3.22 9.7	3.87 2.7 9.7	2.09 14.7 6.9	1.66 4.7 8.3	3.75 11.1	3.69 6.4
	β*p*	4.61 8.0	3.24 9.6	3.44 9.6	3.24 9.6	3.47 2.6 9.6	2.09 14.7 6.9	1.66 4.7 8.2	3.75 11.1	3.71 5.6
6-deoxy-D-*manno*-heptose (**4**)	α*p*	5.12 1.5	3.94 3.3	3.80 9.6	3.51 9.6	3.84 2.7 9.6	2.09 14.8 7.5	1.71 5.3 6.2	3.75 11.0	3.70 7.5
	β*p*	4.85 <1	3.92 3.5	3.61 9.5	3.44 9.5	3.37 2.6 9.5	2.09 14.8	1.71	3.75	3.74
	α*f*	4.95 4.5	4.14 4.6	4.34 2.9	3.96 8.2	4.01 2.9 8.9	1.97 14.8 7.1	1.72	3.73	3.70 7.1
6-deoxy-L-*gulo*-heptose (**5**)	α*p*	5.13 3.8	3.89 3.6	4.01 3.6	3.80 1.4	4.33 9.0 4.6	1.85 14.5	1.77	3.74	3.70
	β*p*	4.85 8.4	3.59 3.7	4.08 3.7	3.68 <1	4.05 9.0 4.6	1.88 14.5 5.7	1.76 7.2 7.2	3.74	3.70 5.7
6-deoxy-L-*ido*-heptose (**6**)	α*p*	4.87 6.6	3.38 8.1	3.67 8.1	3.76 5.4	4.20 9.7 4.6	1.88 14.6	1.84	3.76 11.1	3.71
	β*p*	5.05 1.2	3.67 3.3 $J_{2,4}$ 1.5	4.10 3.3	3.52 1.5	4.06 4.5 7.4	1.97 14.6	1.80	3.76 11.1	3.74
	α*f*	5.21 1.2	4.11	4.19	4.06	4.06	1.84 14.4	1.72	3.74	3.74
	β*f*	5.44 4.3	4.15 4.6	4.29 5.0	4.11 4.1	3.96 4.1 5.0	1.79	1.74	3.75	3.70

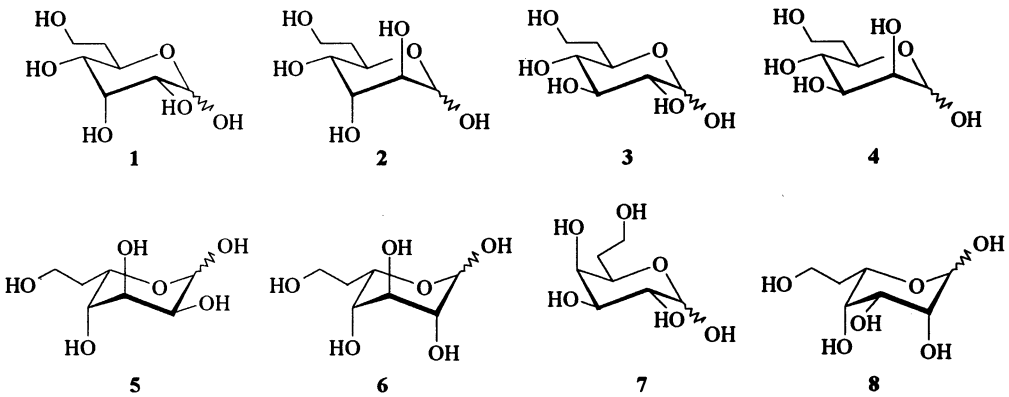
Table 2 (*Continued*)

	Form	H-1 $J_{1,2}$	H-2 $J_{2,3}$	H-3 $J_{3,4}$	H-4 $J_{4,5}$	H-5 $J_{5,6}$ $J_{5,6'}$	H-6 $J_{6,6'}$ $J_{6,7}$	H-6' $J_{6',7}$ $J_{6',7'}$	H-7 $J_{7,7'}$	H-7' $J_{7',6}$
6-deoxy-D-*galacto*-heptose (**7**)	α*p*	5.19 4.0	3.75	3.83	3.83 1.5	4.13 9.0 5.0	1.83 14.5	1.78	3.70	3.66
	β*p*	4.53 7.9	3.44 9.9	3.62 3.5	3.77 1.5	3.72 9.0 4.8	1.89 14.2 5.7	1.77 7.1 7.1	3.70 11.2	3.66 5.7
6-deoxy-L-*talo*-heptose (**8**)	α*p*	5.20 1.2	3.77 3.3	3.90 3.3	3.80 1.5 4.7	4.12 9.2	1.94 14.3	1.80	3.72 11.1	3.69
	β*p*	4.75 <1	3.86 3.2	3.75 3.2	3.69 <1	3.63 9.0 4.6	1.96 14.3	1.81	3.72 11.1	3.69
	α*f*	5.21 1.8	3.96 5.1	4.24 5.3	3.79	3.81	1.84 14.4	1.72	3.74	3.74
	β*f*	5.34 4.1	4.07 5.8	4.11 <1	3.97 4.7	3.78	1.94	1.76	3.73	3.73

Table 3
^{13}C chemical shifts (ppm) of 6-deoxy-heptoses in D_2O at 303 K

	Form	C-1	C-2	C-3	C-4	C-5	C-6	C-7
6-Deoxy-D-*allo*-heptose (**1**)	α*p*	93.7	68.5	72.7	71.2	65.7	34.3	59.4
	β*p*	94.6	72.6	72.3	71.8	71.4	34.8	59.3
	α*f*	97.2	72.3	70.0	87.6	69.1	34.3	59.6
	β*f*	101.7	76.6	71.6	86.2	69.7	35.3	59.6
6-Deoxy-D-*altro*-heptose (**2**)	α*p*	94.4	72.1	71.25	70.6	71.4	33.35	59.35
	β*p*	93.3	71.95	71.7	69.0	71.85	35.25	59.3
	α*f*	102.4	83.0	76.9	87.05	70.0	35.6	59.5
	β*f*	96.5	78.15	75.8	85.15	70.8	35.65	59.55
6-Deoxy-D-*gluco*-heptose (**3**)	α*p*	93.2	73.0	74.1	74.9	69.6	34.7	59.55
	β*p*	97.2	75.6	77.1	74.7	73.9	34.7	59.2
6-Deoxy-D-*manno*-heptose (**4**)	α*p*	95.3	72.0	71.5	71.8	70.5	34.6	59.6
	β*p*	95.0	72.5	74.3	71.6	74.1	34.6	59.4
	α*f*	102.3	78.0	72.4	83.7	67.4	36.8	59.4
6-Deoxy-L-*gulo*-heptose (**5**)	α*p*	94.1	66.1	72.2	72.1	64.5	33.1	59.7
	β*p*	95.1	70.4	72.6	72.5	71.4	33.6	59.6
6-Deoxy-L-*ido*-heptose (**6**)	α*p*	93.75	74.7	73.2	72.4	71.4	29.9	59.4
	β*p*	93.7	71.0	71.1	70.7	72.4	33.8	59.4
	α*f*	103.0	82.0	76.2	85.6	69.0	36.1	59.4
	β*f*	96.9	77.5	76.5	82.0	68.1	36.0	59.4
6-Deoxy-D-*galacto*-heptose (**7**)	α*p*	93.5	69.6	70.6	72.3	68.4	33.8	59.5
	β*p*	97.6	73.1	74.3	71.9	72.8	33.8	59.4
6-Deoxy-L-*talo*-heptose (**8**)	α*p*	95.9	72.6	66.5	71.8	69.0	34.0	59.4
	β*p*	95.3	72.6	69.9	71.6	73.3	33.9	59.3
	α*f*	101.9	76.6	71.8	86.0	71.8	36.1	59.5
	β*f*	97.6	72.2	72.0	86.6	70.0	36.4	59.6

and ^{13}C NMR spectroscopic studies. Data obtained were collected in Table 1 and compared with literature data for hexoses, 6-deoxyhexoses and heptoses. Tables 2 and 3 contain ^{1}H and ^{13}C NMR data for all furanoses and pyranoses detected in mutarotating solutions of 6-deoxyheptoses.



Composition of the solution of 6-deoxy-D-*allo*-heptose (**1**) is very similar with those obtained for allose and D-*glycero*-D-*allo*-heptose. It contains β-pyranose as major components; α-pyranose and furanose were detected as minor ones.

Different results were obtained for 6-deoxy-D-*manno*-heptose (**4**). Both pyranoses were found as major components (β-form as slightly dominated) with a small contribution of α-furanose and traces of β-furanose. Literature data show that furanoses were not detected in solutions of mannose, 6-deoxymannose and D-*glycero*-L-*manno*-heptose, and α-pyranoses were dominating isomers.

No furanose was found in solution of 6-deoxy-D-*gluco*-heptose (**3**), which contained α- and β-pyranoses in only a 1:3 ratio. Similar results were described for 6-deoxyglucose and D-*glycero*-L-*gluco*-heptose whereas solution of glucose contains detectable amount of furanose. Pyranosidic forms of 6-deoxy-D-*gluco*-heptose are strongly favored as having all of its substituents equatorial. A very small amount of furanose was also detected for 6-deoxy-L-*gulo*-heptose (**5**) in which furanose forms have the least favorable all-cis configuration, and 6-deoxy-D-*galacto*-heptose (**7**). For comparison, solutions of glucose, D-*glycero*-D-*gulo*-heptose, galactose, 6-deoxy-D-galactose and D-*glycero*-D-*galacto*-heptose contained considerable amounts of furanose.

A significant amount of furanose was measured for 6-deoxy-L-*ido*-heptose (**6**) and 6-deoxy-L-*talo*-heptose (**8**), although a much higher proportion of furanose in solutions of idose, D-*glycero*-D-*ido*-heptose, talose and 6-deoxytalose was detected. Especially, a solution of D-*glycero*-L-*talo*-heptose contained an extremely high amount of furanosidic forms.

Between all 6-deoxyheptoses studied, the highest proportion of furanose was found for 6-deoxy-D-*altro*-heptose (**2**) at equilibrium. For this sugar, ratio of pyranose and furanose was similar to that described in literature for altrose, 6-deoxyaltrose and D-*glycero*-L-*altro*-heptose. In this case, the content of furanose forms is high because they have the favorable trans–trans arrangement.

Results clearly show that the lack of substituent (hydroxyl group) at C-6 of the heptose chain changes in many cases the equilibrium between pyranose and furanose in comparison with fully substituted analogues. Also, in all cases (except for the ido isomer) removal of O-6 causes a substantial increase in the proportion of β-pyranosidic forms, whereas in most cases, concentration of α-pyranosidic forms decreases. The possible explanation is that the presence of an oxygen atom at C-6 affects the anomeric effect.

3. Experimental

The ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX-500 instrument, for solutions in D_2O (10–20 mg/mL, neutral pH) at 303 K (internal acetone, ^{1}H δ 2.225 ppm and ^{13}C δ 31.45 ppm). All samples were

allowed to equilibrate for 24 h prior to analysis and the equilibrium was checked after 1 week for each sample. A standard Bruker software was used to obtain 2D spectra (COSY, TOCSY, HSQC). Mixing time for TOCSY was 200 ms. Expected accuracy was 0.005 and 0.05 ppm for ^{1}H and ^{13}C NMR signals, respectively. The isomer ratios were determined by integration of anomeric hydrogen signals and/or integration of other well-resolved signals.

6-Deoxyheptoses were prepared from protected pentofuranoses or pentofuranosides and acetyliron complex as we described earlier.[20,21] Four of them were from D series: 6-deoxy-D-*allo*-, -D-*gluco*-, D-*manno*-, and D-*galacto*-heptoses; three from L series: 6-deoxy-L-*gulo*-, -L-*ido*-, and L-*talo*-heptoses. The remaining 6-deoxy-D-*altro*-heptose, which has not been prepared yet, was obtained as described below.

3-O-*Benzyl-6-deoxy*-D-altro-*heptose*.—To a solution of 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-D-*altro*-heptofuranose (156 mg)[20] in THF (5 mL) and water (1 mL) trifluoroacetic acid (10 mL) was added and stirred for 1 h at rt. The solvents were evaporated. Column chromatography (95:5 CH_2Cl_2:MeOH) of the residue gave 3-*O*-benzyl-6-deoxy-D-*altro*-heptose (77 mg, 57%), which was immediately used for the next reaction step.

6-Deoxy-D-altro-*heptose* (**2**).—To a solution of 3-*O*-benzyl-6-deoxy-α,β-D-*altro*-heptose (77 mg) in EtOH (9 mL) and water (1 mL), 10% Pd on charcoal (100 mg) was added and the suspension was hydrogenated overnight. The mixture was filtered through a Celite pad and concentrated to dryness to yield **2** (44 mg, 79%) as a foam.

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