CYCLIC STRUCTURE OF THE $\beta(\gamma)$ -HYDROXY-(MERCAPTO)ALKYLIMINES OF ALDOSES

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In solutions in DMSO-d₆, the products from the condensation of ethanolamine and 1,2- and 1,3aminopropanols with aldoses are mixtures of the α - and β -pyranose forms, whereas the β -mercaptoethylimines of aldoses have the 1,3-thiazolidine structure. Glucose β -mercaptoethylimine is characterized by ring – chain tautomerism involving the α -pyranose and diastereomeric 1,3-thiazolidine tautomers.

Certain functionally substituted nitrogen derivatives of monosaccharides are able to exhibit ring-chain tautomerism. They include the thiosemicarbazones, thioacylhydrazones, and 3-aminopropylimines of aldoses and the thiosemicarbazones of fructose [1-4]. In the light of data on the susceptibility of the imines of 1,2- and 1,3-amino alcohols and $\beta(\gamma)$ -mercaptoalkylimines to ring-chain transformations [5], we turned to a study of the products from the condensation of typical aldoses with ethanolamine and 1,2- and 1,3-aminopropanols and also with β -mercaptoethylamine [compounds (I-X), Table 1]. Individual representatives of these substances were described earlier [6, 7], but no rigorous evidence for their structures was given.



We found that, irrespective of the distance between the amino and alcohol groups and the branching of the carbon chain (the introduction of substituents into the link usually favors the cyclic tautomer [5]), the amino alcohol derivatives (I-V) do not exhibit the ability to exist in the likely 1,3-oxazolidine (1,3-oxazine) tautomeric form. In solutions in DMSO-d₆ (other solvents were unsuitable on account of the low solubility) these substances represented anomeric mixtures of the α - and β -pyranose forms (α -B and β -B, respectively, in the scheme and Table 2). The structures were assigned on the basis of the almost complete agreement of the signals of the carbohydrate part of the molecule of these substances with authentic published data on the carbon spectra of the anomeric forms of aldoses and their imino derivatives [1-4, 8]. The signals of the C₍₁₎ atom for these substances lie in the region of 86-91 ppm, typical of the nitrogen N-glycosides of aldopyranoses [1-4].

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Com- pound	Empirical formula	Found, % Calculated, %			mp, °C	z	Y	Carbohydrate	eld, %
		с	н	Я					Ϋ́ι
I	C8H17NO6	<u>43,2</u> 43,4	7,5 7,7	<u>6,4</u> 6,3	Oil	0	CH ₂ CH ₂	Glucose	86
11	C8H17NO6	<u>43,3</u> 43,4	<u>7,7</u> 7,7	<u>6,5</u> 6,3	Oil	0	CH ₂ CH ₂	Mannose	92
ш	C9H19NO6	<u>45,4</u> 45,6	<u>7,9</u> 8,1	<u>6,0</u> 5,9	Glass	0	CH ₂ CH ₂ CH ₂	Glucose	76
IV	C9H19NO6	<u>45,5</u> 45,6	<u>8,1</u> 8,1	<u>6,0</u> 5,9	120	0	CH ₂ CH ₂ CH ₂	Mannose	85
v	C9H19NO6	<u>45,6</u> 45,6	<u>8,0</u> 8,1	<u>6,0</u> 5,9	Glass	0	CH(CH ₃)CH ₂	Mannose	82
vı	C7H15NO4S	<u>40,2</u> 40,2	<u>7,3</u> 7,2	<u>6,8</u> 6,7	133	S	CH ₂ CH ₂	Arabinose	84
VII	C8H17NO4S	<u>43,1</u> 43,0	<u>7,6</u> 7,7	<u>6,2</u> 6,8	150	S	CH ₂ CH ₂	Rhamnose	88
VIII	C8H17NO5S	<u>40,3</u> 40,2	<u>7,2</u> 7,2	<u>5,8</u> 5,8	123	S	CH ₂ CH ₂	Glucose	73
IX	C8H17NO5S	<u>40,2</u> 40,2	<u>7,2</u> 7,2	<u>5,9</u> 5,8	179	S	CH ₂ CH ₂	Mannose	89
x	C8H17NO5S	<u>40,2</u> 40,2	<u>7,1</u> 7,2	<u>5,9</u> 5,8	159	S	CH ₂ CH ₂	Galactose	73

TABLE 1. Characteristics of Compounds (I-X)

TABLE 2. ^{13}C NMR Spectra of Compounds (I-X) in DMSO-d_6, $\delta,$ ppm

Com- pound	Found, %	C _{carbohydrate}									
		C-1	C-2	C-3	C⊣	C-5	C-6	O,S—CH₂	NCH2		
I	a-B, 38	87,6	72,2	74,2	70,9	71,1	62,0	62,0	48,6		
	β-B, 62	91,3	74,2	78,0	71,1	78,0	62,0	62,0	49,7		
п	α-B, 31	88,7	71,9	71,9	68,0	72,5	61,3	62,3	49,2		
	β - \overline{B} , 69	88,1	71,9	75,2	68,0	78,1	61,9	62,2	48,1		
III	α-B, 22	86,8	71,6	73,7	70,8	70,8	61,3	59,3	43,0		
	β-B, 78	90,7	73,5	77,6	70,6	77,5	61,5	59,3	42,7		
IV	α-B,18	88,3	71,5	71,4	68,0	72,2	61,6	59,6	42,4		
	β-B, 82	87,5	71,6	74,9	67,6	78,0	61,7	59,4	42,4		
v	α-Β, 47	88, <i>5</i>	71,5	71,5	67,5	72,5	61,7	66,3 (CH)	53,5		
	β-B,53	87,7	71,5	75,2	67,5	77,2	61,7	66,6 (CH)	53,5		
VI	C, 57	71,7	71,7	72,3	74,4	63,8		34,4	52,1		
	C', 43	71,7	71,7	72,3	72,7	63,8		34,7	51,3		
VII	C, 70	70,5	74,5	72,4	73,5	66,3	21,0	33,6	51,8		
	C', 30	70,1	74,5	73,4	73,7	66,5	21,0	34,4	52,4		
VIII	β-B,53	90,8	73,7	77,9	71,0	76,9	61,5	40,8	45,1		
	C, 41	71,6	72,5	70,0	71,4	73,7	63,6	34,3	51,9		
	C'.6	71,6	73,6	71,4	72,0	74,3	63,6	34,7	51,7		
IX	C, 66	70,0	72,6	71,1	69,7	74,5	63,8	33,6	51,8		
	C', 34	69,9	73,6	71,3	69,8	74,5	63,8	34,4	52,4		
x	C, 54	70,3	73,0	71,8	70,3	69,7	63,4	34,4	52,1		
	C′, 46	70,3	74,8	72,4	71,0	69,7	63,4	34,7	51,3		

The derivatives of β -mercaptoethylamine (V-X) are constructed differently. The signal of the C₍₁₎ carbon atom for compounds (V-VII, IX, X) is found in the region of 70-72 ppm (Table 2), which indicates that it has the N,S environment [2, 9, 10]. The chemical shifts of the carbon atoms of the carbohydrate part of the molecules almost coincide with authentic data

for the analogous isomers in the case of the derivatives of thiocarbonohydrazine and thiobenzohydrazide [1-3]. Thus, compounds (V-VII, IX, X) exist in the 1,3-thiazolidine form, represented by comparable amounts of the two diastereomeric forms C and C'.

A special situation applies in the case of the β -mercaptoethylimine of glucose (VIII). In solution in DMSO-d₆ this substance represents a tautomeric mixture of three cyclic forms — β -pyranose (β -B) and the diastereomeric 1,3-thiazolidines C and C'. The structure of the first compound was established by comparison of the absorption signals of its carbon atoms with data for the β -pyranose form of glucose β -hydroxyethylimine (I) (Table 2). The other two were identified by means of the signals of the C₍₁₎ carbon atoms, characteristic of the 1,3-thiazolidine and 1,3,4-thiazolidine rings [2, 9, 10].

In the whole series of functionally substituted aldose imines (hydrazones) that we investigated it is possible to see the following relationships. Whereas the tendency to form the cyclic compound is poorly defined in the simplest analogs [the aldimines (aldohydrazones)], the corresponding derivatives of monoses exist in one or the other pyranose (furanose) form. This is the situation with the derivatives of ethanolamine and ethylenediamine [5]. When the linear form in such derivatives is stabilized by p, π conjugation, this form begins to coexist with the pyranose (furanose) tautomer. This effect is typical of the acylhydrazones, semicarbazones, guanylhydrazones, and thiosemicarbazones of aldoses [11].

The respective aldose derivatives exist in a form other than the pyranose (furanose) form in cases where the simplest aldimines (hydrazones) tend to exist in the cyclic tautomeric form [11, 14]. (This occurs with β -mercaptoethylimines that are usually represented by 1,3-thiazolidines [11], with γ -aminopropylimines that exist in the form of hexahydropyrimidines [12], with thiobenzohydrazones that cyclize to the 1,3,4-thiadiazolidine tautomer [9], and with thiocarbonohydrazones that change to a 1,2,4,5-tetrahydrotetrazine ring [13].)

Finally, in some cases it is possible for the competing cyclic forms to coexist, and ring-ring tautomerism then occurs. This effect is observed for glucose thiobenzoylhydrazone [4], glucose and galactose thiocarbonohydrazone [1], and glucose, galactose, and rhamnose 3-aminopropylimine [3].

EXPERIMENTAL

The ¹³C NMR spectra were recorded on a Bruker AC-200 instrument (50, 32 MHz).

Condensation of Aldoses with $\beta(\gamma)$ -Hydroxy-Substituted Amines (I-V). To a solution of 0.01 mole of the amine in 20 ml of methanol we added 0.01 mole of the respective carbohydrate. The mixture was boiled for 3 h. The solvent was removed under vacuum, and the residue was washed with ether (3 × 50 ml) and dried under vacuum and then over phosphorus pentoxide in a desiccator. The characteristics of the obtained compounds (I-V) are given in Table 1.

Condensation of Aldoses with Mercamine (VI-X). To a solution of 0.77 g (0.01 mole) of mercamine in 20 ml of methanol we added 0.01 mole of the respective carbohydrate. The mixture was boiled for 3 h, and the crystals that separated were filtered off, washed with ether, and dried over phosphorus pentoxide in a desiccator. The characteristics of compounds (VI-X) are given in Table 1. The constants of compounds (VIII-X) correspond to the published data [6].

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