1,2-Diaminoethyl- and 1,3-diaminopropyl-derivatives of aldoses and their tautomerism

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2-Aminoethylimines and 3-aminopropylimines of aldoses have been synthesized and their structure in solutions has been investigated by ^{13}C NMR spectroscopy. 2-Aminoethylimines usually exist as pyranoses, 3-aminopropylimines are the corresponding piperimidines while ring–ring interconversion between pyranose and piperimidine tautomers takes place in some cases.

The presence of one molecule of a single polar double bond (C=O, C=N, *etc.*) and two nucleophilic centres (OH, NH groups, *etc.*) or *vice versa* makes interaction between them possible which may result in ring–chain–ring tautomeric equilibria that can be regarded as a superposition of two ring–chain equilibria. Over the past fifteen years, a number of studies aimed at investigating this problem resulted in the discovery of a series of ring–chain–ring tautomeric systems.[1–3]

Nitrogen derivatives of saccharides containing an additional nucleophilic centre in the imine fragment of their molecules can be considered as suitable objects for molecular design in this field (C=N bond and two nucleophilic centres – OH group and this additional centre). In particular, a three component equilibrium involving two cyclic forms, 2,3-dihydro-1,3,4-thiadiazole and pyranose, and a linear one, the hydrazone tautomer, has been observed for glucose thiobenzoylhydrazone with an additional SH group.[4,5] The ring–chain–ring tautomerism between hexahydro-1,2,4,5-tetrazine-3-thione, thiocarbonohydrazone and tetrahydropyrane takes place for galactose and glucose thiocarbonohydrazones containing an additional NH_2 group.[5,6]

In theory, the occurrence of similar properties would be expected for the products of equimolar interaction of monoses with 1,2-diaminoethane and 1,3-diaminopropane possessing β(γ)-amino groups active in intramolecular cyclizations. It is known that monoalkylidene 1,2-diaminoethyl and 1,3-diaminopropyl derivatives of aliphatic aldehydes exist in the form of corresponding imidazolidines[7] and piperimidines.[8,9]

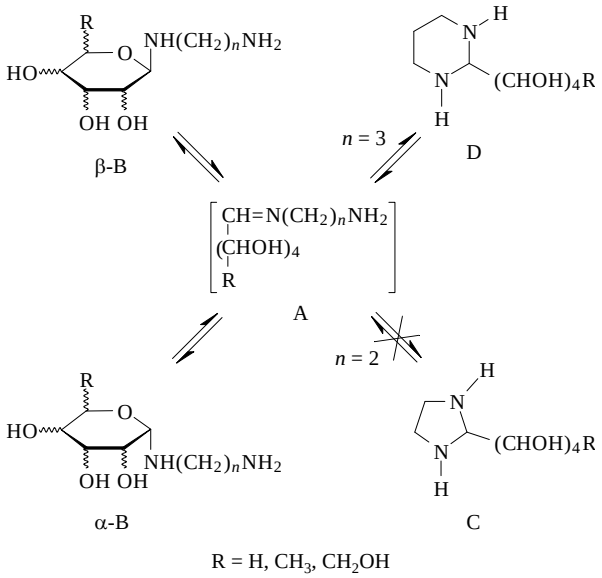
The purpose of this study was to obtain hitherto unknown monoalkylidene derivatives of aldoses with 1,2-diaminoethane and 1,3-diaminopropane[†] and to investigate their structure by ^{13}C NMR spectroscopy.

The data on the chemical shifts of the carbon atoms of the pyranose forms of *N*-substituted aldose hydrazones,[4–6] on the one hand, and those of the imidazolidine[7] or piperimidine ring,[8,9] on the other hand, have served as criteria for structure interpretation.

In particular, the linear form A could be easily detected by the appearance of a C=N carbon signal at 145–160 ppm in the ^{13}C NMR spectra.[4–6]

The anomer carbon atom signal for the pyranose form B of the nitrogen monose derivatives is situated in the 87–91 ppm interval (O,N-environment). Almost complete coincidence of the carbon atom signals of the saccharide fragment of these forms with the literature data on the derivatives of appropriate monoses was observed.[4–6]

At the same time the carbon ^{2}C atom signal for the imidazolidine C[7] or piperimidine D[8,9] tautomer should be shifted to the upfield region (65–70 ppm, N,N-environment).



Scheme 1

The positions of two other signals of carbon ring atoms (C-4,6 and C-5) for form D agree with the known data.[8,9]

On the basis of the data listed in Table 1, the following conclusions were drawn:

– the linear tautomer form A was found in neither case;

– the cyclic imidazolidine form C was not formed for 2-aminoethylimines **1**;

– as regards 3-aminopropylimines **2**, the piperimidine form D usually predominates;

– the anomeric equilibrium α-B ⇄ β-B takes place for pyranose forms (compounds **1**, **2b**,**c**,**e**);

– the three-component ring–ring tautomerism α-B ⇄ β-B ⇄ D was observed for some 3-aminopropylimines (compounds **2b**,**c**,**e**).

The non-existence of linear form A for these compounds could be explained by the impossibility of its stabilization through the p,π-conjugative effect, in contrast to aldose hydrazones where ring–chain tautomerism has been really observed.[3]

The absence of the tautomeric interconversion B ⇄ C for ethylenediamine derivatives **1** agrees with the recorded lesser tendency to form five-membered rings in comparison with six-membered ones during intramolecular cyclizations according to Baldwin's rules.[10]

Thus, the polycomponent tautomeric interconversion of heterocyclic derivatives B ⇄ D in a number of selected aldose derivatives is observed between pyranose anomers and the corresponding pyperimidine for 3-aminopropylimines of rhamnose, glucose and galactose (compounds **2b**,**c**,**e**).

From the available data[4–6] one can conclude that propylenediamine derivatives possess the greatest possible

[†] Compounds **1**–**2** were obtained by mixing 0.05 mol of the corresponding diamine with 0.05 mol of the appropriate carbohydrate in 50 ml methanol. After partial removal of solvent *in vacuo* up to 20 ml the separated crystals were filtered, washed with ether and dried *in vacuo* (compounds **1a**,**c** and **2a**,**b**,**d**,**e**). Solvent was removed *in vacuo* and residue washed with ether and dried *in vacuo* (compounds **1b** and **2c**). Compounds **1**–**2** gave satisfactory elemental analyses.

Table 1 Compounds **1** and **2**.

Compound	Carbohydrate	Yield (%)	Mp/°C	Form (%)	^{13}C NMR, δ/ppm[a]							
					C-1	C-2	C-3	C-4	C-5	C-6	N-CH_2	CCH_2C
1 (n = 2)												
a	rhamnose	59	134	α-B (15)	88.7	71.7	71.1	72.7	66.7	18.2	46.1[b]	–
				β-B (85)	87.1	71.7	74.6	72.7	72.5	18.2	45.9[b]	–
b	glucose	69	glass	α-B (20)	87.3	71.9	73.4	70.9	71.3	61.6	45.6, 49.3	–
				β-B (80)	91.1	73.8	77.9	70.7	77.7	61.6	44.6, 48.6	–
c	mannose	83	123	α-B (35)	88.3	71.2	70.9	67.9	72.2	61.8	42.2, 45.4	–
				β-B (65)	87.6	71.6	74.8	67.7	76.7	61.8	44.9, 48.3	–
2 (n = 3)												
a	arabinose	76	114	D (100)	70.7	71.2	72.3	73.6	63.7	–	44.8, 45.0[c]	27.3
b	rhamnose	68	128	α-B (10)	88.5	71.7	71.2	73.8	66.6	18.2	43.3[b]	33.9
				β-B (30)	87.3	71.7	74.6	72.7	72.5	18.2	42.9[b]	33.9
				D (60)	70.5	73.9	71.3	71.7	66.5	21.0	45.0	27.4
c	glucose	76	glass	α-B (5)	87.3	71.9	73.9	70.7	71.2	61.6	39.8, 49.9	33.6
				β-B (45)	90.0	73.7	77.9	69.7	77.7	61.6	39.4, 48.8	33.6
				D (50)	70.0	73.7	69.7	71.2	74.7	64.2	44.4, 45.3[c]	27.1
d	mannose	71	135	D (100)	70.2	71.6	71.3	70.7	72.3	64.1	45.0	27.4
e	galactose	52	105	α-B (5)	90.6	70.8	69.2	70.8	71.2	62.3	43.4[b]	33.1
				β-B (10)	91.4	73.8	74.3	68.6	76.0	60.7	43.9[b]	33.1
				D (85)	70.0	73.8	71.6	70.8	69.5	63.3	44.9, 45.0[c]	27.3

[a]50.33 MHz, [$^2H_6$]DMSO. [b]The second signal is overlapped by the solvent signals. [c]The presence of two signals can be explained by the appearance of diastereoisomers.

tendency to exist in the cyclic form other than pyranose. This tendency is exhibited in the case of thiocarbohydrazide derivatives to a lesser degree and is observed for glucose thiobenzoylhydrazone as well.[4–6] The other known nitrogen derivatives of aldoses do not display this tendency. These facts can serve as a tentative criterion of the relative stability of various tautomeric nitrogen heterocycles and cyclic forms of individual aldoses.

The results obtained call for further research in this field, which should comprise, in particular, the investigation of monose derivatives of aminoalcohols, aminothioles, *o*-phenylenediamine, *etc*.

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