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THE MECHANISM OF THE HYDROLYSIS OF N-ARYL GLUCOSYLAMINES

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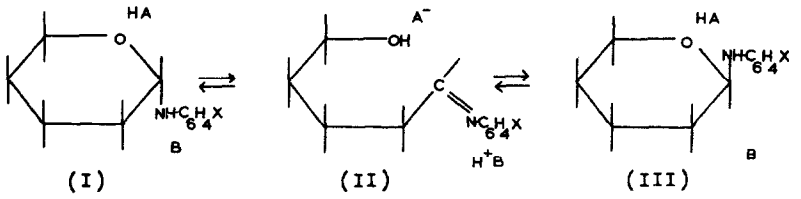
The mechanism of hydrolysis of glucosylamines has been studied fragmentarily by several groups.[1] Generally, compounds of undetermined structure were used and frequently the reactions were not well defined since only changes in optical rotation were measured. We now report a detailed investigation of the mechanism of hydrolysis of the N-aryl D-glucosylamines (I and III), the determination of whose structure is the subject of the preceding communication. The hydrolyses of all the glucosylamines were preceded by a rapid anomerisation to a mixture of about 10% α- and 90% β-forms. This was shown by following the change in optical rotation and determining the concentration of free amine spectrophotometrically. Although this anomerisation must involve an acyclic form, this cannot be present at an appreciable concentration since the reaction shows good first-order behaviour and the measured rate constants, starting from either the α- or the β-form, are equal. The anomerisation shows buffer catalysis and presumably involves a mechanism [scheme (1)] similar to that of the mutarotation of glucose,

although the exact timing of the proton transfers is unknown.

Scheme (1)

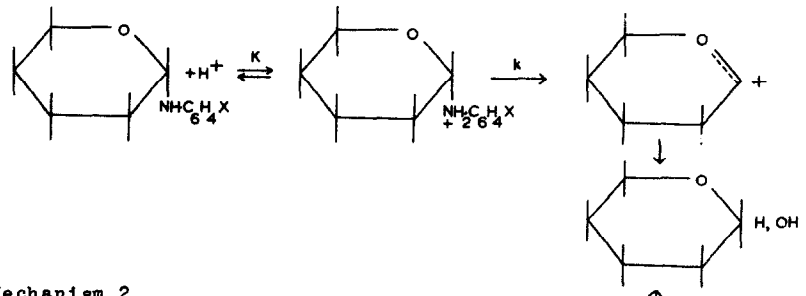


(I) (II) (III)

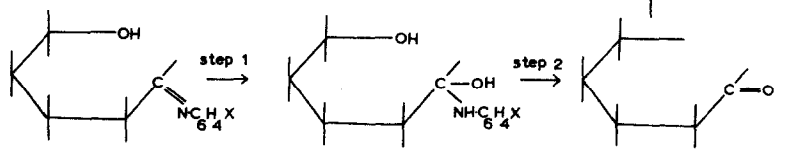
X = H, p-Me, p-NO_2, p-COOH, p-CF_3, p-OH and o-COOH.

Thus when studying the acid catalysed hydrolysis it is always an interconverting mixture of isomers that is being studied. This hydrolysis could be envisaged as either the hydrolysis of the cyclic forms (Mechanism 1) or of the acyclic Schiff base form (Mechanism 2).[2] This reaction shows general acid catalysis

Mechanism 1



Mechanism 2



and this excludes Mechanism 1, but is clearly consistent with

Mechanism 2, since general acid catalysis in the hydrolysis of Schiff bases is well established,[3] and has recently been shown to involve the kinetically equivalent specific acid/general base catalysis.[4]

The effect of substituents on the rate also supports Mechanism 2. A small effect would be expected for Mechanism 1 since the electronic requirements of the pre-equilibrium proton transfer and the slow heterolysis are in opposite senses. With Mechanism 2, for which $k_{obs.} = k[\text{Schiff base}]$, the effect of substituents on k, the rate constant for the hydrolysis of the Schiff base form, should only be small,[3] but the concentration of the Schiff base form should be strongly substituent dependent since resonance interactions between the nitrogen and the aryl ring, present in the acyclic forms, are lost in the Schiff base form. The observed ρ value in 0.5M $HClO_4$ of -2 therefore supports Mechanism 2. The pH-rate profiles of all the hydrolyses show sharp maxima, the position of which moves to higher acidities with decreasing basicity of the amine. This is readily explicable as resulting from a change in the rate determining step of the hydrolysis of the Schiff base form from attack by water or hydroxide ion (step 1 in Mechanism 2) to decomposition of a carbinolamine intermediate (step 2 in Mechanism 2). (Cf. ref.4).

The composition of the glucose formed in the hydrolysis of the p-tolyl and p-hydroxyphenyl compounds can be determined since conditions (pH1.2 -1.3) can be found under which the rates of hydrolysis are faster than the mutarotation of glucose. For both reactions this was found to be 62±5% α-D-glucose and 38±5% β-D-glucose. This corresponds closely to the mixture expected

from the ring closure of aldehydo-glucose (64±2% α and 36±2% β) as calculated from the rate constants for these reactions, determined polarographically.[5]

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1 See G.P.Ellis and J.Honeyman, Advanc. Carbohyd. Chem., 10, 104 (1955).

2 See G.W.Kenner in The Chemistry and Biology of the Purines, J. and A. Churchill Ltd., 1957, p.312.

3 Cf. A.V.Willi and R.E.Robertson, Canad. J. Chem., 31, 361 (1953).
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5 J.M.Los, L.B.Simpson and K.Wiesner, J. Amer. Chem. Soc., 78, 1565 (1956).