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5-AMINO-1-β-D-RIBOFURANOSYL-4-IMIDAZOLECARBOXAMIDE BY ALKALINE DEGRADATION FROM INOSINE

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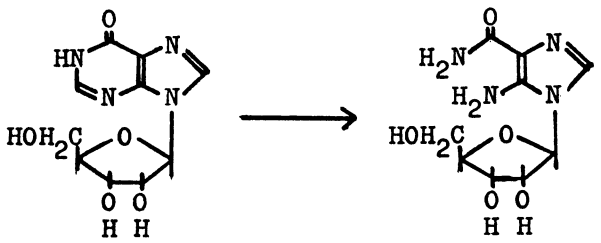
5-Amino-1-β-D-ribofuranosyl-4-imidazolecarboxamide has been obtained from inosine by means of degradation in aqueous alkali over 100°C.

The ring opening reactions of N-substituted inosine, such as N-benzylinosine, N-toluenesulfonyl inosine, and N-methoxymethylinosine, to the corresponding 5-amino-1-β-D-ribofuranosyl-4-imidazole-N-substituted-carboxamides with alkali have been reported by Shaw.[1,2,3] Inosine is known extremely stable to alkali[1,4] and its ring opening reaction has not yet been reported in the literature.

The present author will report the ring opening reaction of inosine to 5-amino-1-β-D-ribofuranosyl-4-imidazolecarboxamide (AICA-riboside) with aqueous alkali.



When inosine was heated in an aqueous alkaline solution in a sealed tube, over 100 °C AICA-riboside was formed in 20-30% yields. This reaction, however, was accompanied with the concurrent hydrolysis of the glycosidic bond to give hypoxanthine and D-ribose.

The yields of AICA-riboside varied with the pH values of the solutions as shown in Fig. 1. The optimum pH for the formation of AICA-riboside is between 9 and 12. The relation between the yield and the reaction period is shown in Fig. 2.

The amount of AICA-riboside in the reaction mixture was determined by paper chromatography with the solvent system, butanol-acetic acid-water (4:1:1). The chromatogram was revealed by ultraviolet light. The spot corresponding to AICA-riboside which was free from any contaminant was cut off together with their appropriate blanks and eluted with 0.1 N HCl, and the absorbance of the eluate was measured at 267 mμ. The authentic standard was used for control.

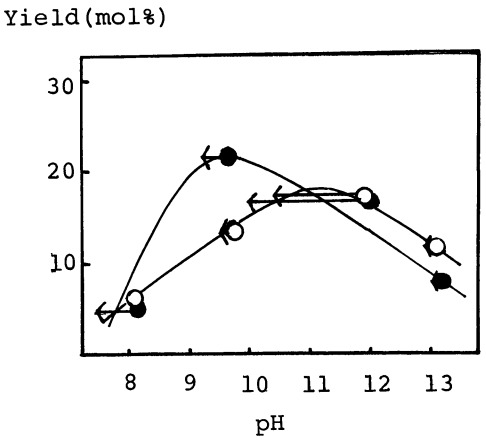


Fig. 1. The pH dependence of AICA-riboside yield.

Three percent(w/v) solutions of inosine with pH adjusted by sodium hydroxide were heated in a seald tube at 120°C for 8 hour(o), and 16 hour(●).
The pH values (at room temp.) of the solutions decreased at the end of the reaction in all the cases (⟵).

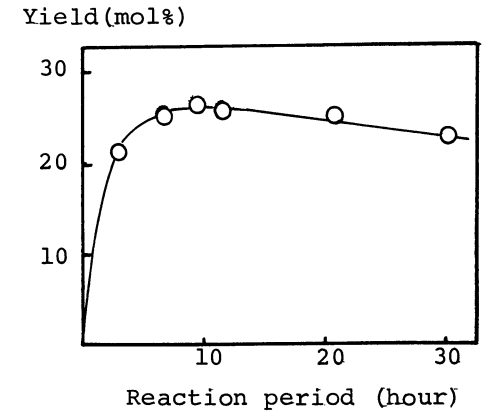


Fig. 2. Dependence of AICA-riboside yield on the reaction period.

A thirty five percent(w/v) solution of inosine (pH 9.6) was prepared by dissolving inosine in an aqueous potassium hydroxide, and heated in a seald tube at 150°C keeping the pH between 10 and 9 by the addition of potassium hydroxide at intervals.

The analytical data of AICA-riboside isolated by column chromatography using Dowex 50W X-8 agreed with those reported by Greenberg and Spilman.[5] The X-ray (Cu K_α) diffraction patterns, which have three intense lines at 18.9, 21.8 and 26.6 degree (2θ), were also used for identification.

References:

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