PREBIOTIC SYNTHESIS OF IMIDAZOLE-4-ACETALDEHYDE, IMIDAZOLE-4-GLYCOL AND IMIDAZOLE-4-ETHANOL

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A wide variety of chemical processes have been used for the synthesis of amino acids from prebiotic molecular precursors under plausible primitive Earth conditions (Miller, 1982). The prebiotic formation of all protein-type amino acids has been demonstrated except for three amino acids: histidine, lysine, and arginine (Weber and Miller, 1981). As a continuation of our work on the prebiotic synthesis of imidazole, 2-methylimidazole, and 4-methylimidazole (Oró et al., 1984), this paper reports the prebiotic synthesis of other imidazoles (Im-4-acetaldehyde, Im-4-glycol, and Im-4-ethanol), which are among the intermediate products in the proposed prebiotic synthetic pathway of histidine.

In one set of experiments (1st Exp.) imidazole-4-glycol and imidazole-4-acetaldehyde were synthesized from an aqueous reaction mixture (pH 5.5) of D-erythrose and formamidine at 80°C for 12 hr. In another set of experiments (2nd Exp.) imidazole-4-ethanol and imidazole-4-glycol were synthesized from an aqueous reaction mixture (pH 6.6) of D-erythrose, ammonia and formaldehyde at 80°C for 12 hr. The products were desalted by Dowex 50, 8X, 100-200 mesh H^+ form, eluting with 2M NH_4OH. The 2M NH_4OH eluants were collected and evaporated to 1.0 ml for analysis. The desalted samples were analyzed by thin layer chromatography using silica gel TLC plates and a basic solvent (n-propanol:30% NH_4OH = 3:1). At least four diazo reagent positive spots were observed on the TLC plates. The imidazole products were further identified by combined HPLC and thermospray mass spectrometry, using a LDC/Milton Roy RPC-18 column (4.6 x 250 mm), a Spectra physics SP8700 solvent delivery system, and a modified Biospec mass spectrometer. A solvent mixture of 0.075 M ammonium formate (pH 5.5):methanol (4:1, v/v) was used for the liquid chromatographic separation preceding mass spectrometry. The results obtained by TLC and HPLC-thermospray-MS are shown in Table 1. The HPLC-MS analytical results definitely show that the erythrose-formamidine reaction produced imidazole-4-acetaldehyde and imidazole-4-glycol and

and the erythrose-ammonia-formaldehyde reaction produced imidazole-4-ethanol and imidazole-4-glycol.

TABLE I

Analysis of Imidazole Derivatives

Exp.	Reactant	Imidazole product	MW	Diazo (TLC)	HPLC (R.T. sec)	LCMS MH^+	Yield % Im/ery
1	erythrose + H_2N-CH=NH	Im-4-acetaldehyde	110	+	291	111	2.5
		Im-4-glycol	128	+	179	129	6.8
2	erythrose + NH_3 + HCHO	Im-4-ethanol	112	+	226	113	13.9
		Im-4=glycol	128	+	182	129	1.8

The imidazole acetaldehyde obtained in the 1st experiment was probably produced by condensation of D-erythrose with formamidine followed by dehydration of the imidazole-4-glycol formed. The imidazole-4-ethanol obtained in the 2nd experiment may have been produced by the condensation of the erythrose dehydration product ($HOC-CO-CH_2-CH_2OH$) with ammonia and formaldehyde. The imidazole-4-acetaldehyde is the immediate prebiotic precursor to histidine by means of the Strecker synthesis. The imidazole-4-ethanol may be converted to imidazole-4-acetaldehyde by some prebiotic dehydrogenation reactions.

This work was supported in part by a NASA Planetary Biology Internship to one of us (C.S.), by NASA Grant NGR 44-005-002 to J.O. and Grant NAGW-20 to S.M.

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