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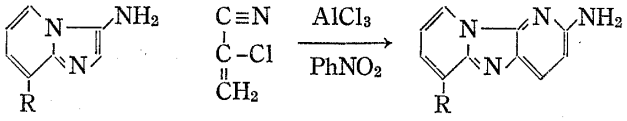
Synthesis of Mutagenic Principles Isolated from L-Glutamic Acid Pyrolysate

Two mutagenic compounds isolated from L-glutamic acid pyrolysate, 2-amino-6-methyldipyrido[1,2-a: 3′,2′-d]imidazol (Glu-P-1), and 2-aminodipyrido[1,2-*a*: 3′2′-*d*]-imidazole (Glu-P-2), were prepared from 3-amino-8-methylimidazo[1,2-*a*]pyridine and 3-aminoimidazo[1,2-*a*]pyridine, respectively.

Keywords——2-aminodipyrido[1,2-*a*: 3′,2′-*d*]imidazole; L-glutamic acid; mutagen; aminopyridine; Glu-P-1; Glu-P-2

The pyrolysis products of L-tryptophan, L-glutamic acid, L-ornitine, and L-serine showed very potent mutagenic activity to *Salmonella typhymurium* strain TA 98.[1] The mutagenic components in L-tryptophan pyrolysate were isolated and their structures were determined.[1,2] Their syntheses were also established.[3,4] Recently two mutagenic components in L-glutamic acid pyrolysate were obtained and their structures were determined as 2-amino-6-methyldipyrido[1,2-*a*: 3′,2′-*d*]imidazole(Glu-P-1) and 2-aminodipyrido[1,2-*a*: 3′,2′-*d*]imidazole (Glu-P-2).[5] In the present communication, we wish to report synthesis of these mutagenic compounds in a very simple way.



R=CH_3 Glu-P-1
R=H Glu-P-2

A mixture of 3-amino-8-methylimidazo[1,2-*a*]pyridine (300 mg) prepared by the method reported by Sugiura[6] and Ohta,[7] 2-chloroacrylonitrile (430 mg, 2.4 eq.), and aluminum trichloride (1.09 g, 4 eq.) in nitrobenzene (10 ml) was heated at 100° for 12 hr. After evaporation of nitrobenzene, water was added and neutral products were removed by benzene. The aqueous solution was basified and extracted by ethyl acetate. The organic layer was evaporated and chromatographed over silica gel to give crude Glu-P-1 (206 mg), which was crystallyzed from methanol–ethyl acetate to give yellow prisms, 130 mg (32% yield), mp 226°. Hydrobromide with a molecule of water, mp 290—292°, was prepared and identified with the isolated sample dried at 60° for 5 hr by infrared (IR), ultraviolet (UV), and nuclear magnetic resonance spectra (NMR). UV and NMR spectra of the hydrobromide were temperature or concentration dependent, probably because of change of dissociation equilliblium of the salt.

Similarly, Glu-P-2 was prepared from 3-aminoimidazo[1,2-*a*]pyridine[6,7] and 2-chloroacrylonitril in a yield of 20—40%. Melting point of hydrobromide was 286—287°. Identification with the isolated hydrobromide was done by IR, NMR and UV spectra. NMR and UV spectra were temperature or concentration dependent.

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A quantity of the compounds is now available for detailed biological experiments. The present and previous[3,4] syntheses may illustrate the usefulness of nitril group in constructing an aminopyridine moiety of heterocyclic compounds.

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