INTERACTION OF 2-AMINODIPYRIDO[1,2-a:3',2'-d]IMIDAZOLE WITH DNA. I. STRUCTURE OF THE MODIFIED NUCLEIC ACID BASE AND INITIAL CHEMICAL EVENT CAUSED BY THE MUTAGEN

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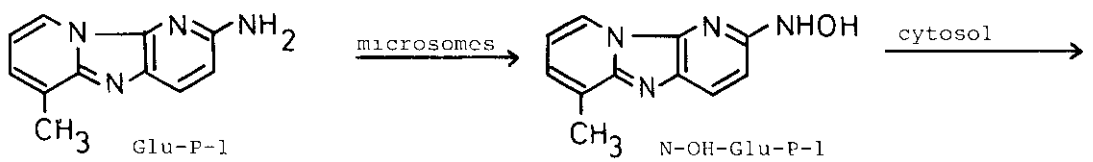
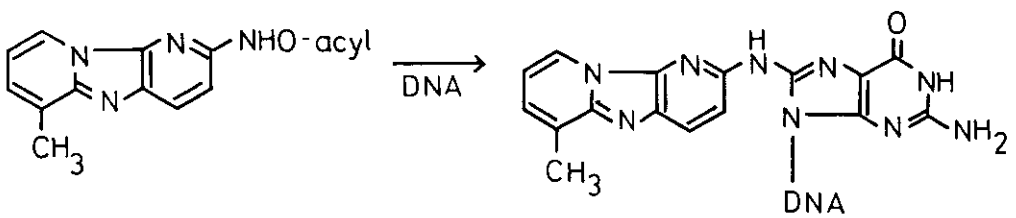
2-Aminodipyrido[1,2-a:3',2'-d]imidazole (Glu-P-2) and 2-amino-6-methyldipyrido[1,2-a:3',2'-d]imidazole (Glu-P-1) are potent muta-carcinogens isolated from a pyrolysate of L-glutamic acid. Glu-P's are metabolically activated to the corresponding hydroxylamines (N-OH-Glu-P's) in vivo and in vitro. N-OH-Glu-P's are the proximate form of Glu-P's. The ultimate form of Glu-P's are O-acylated derivatives of N-OH-Glu-P's. O-Acetylated N-OH-Glu-P-1, which is a model compound of an ultimate form of Glu-P-1, reacted with DNA covalently. The structure of the modified nucleic acid base was determined as 2-(C^8-guanyl)amino-1-methyldipyrido-[1,2-a:3',2'-d]imidazole (Gua-Glu-P-1) which was also identified as a modified nucleic acid base isolated from DNA of the rats treated with Glu-P-1.



Glu-P-1 N-OH-Glu-P-1



Gua-Glu-P-1-DNA