STUDIES ON 1-PHENYL-1H-PYRAZOLO[3,4-d]PYRIMIDINE DERIVATIVES.

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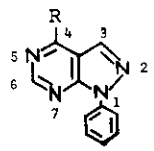
In order to synthesize the antitumoral pyrazolo[3,4-d]pyrimidines, 4-(p-tolylsulfonyl)-1-phenyl-1H-pyrazolo[3,4-d]pyrimidine(I), 1-phenyl-1H-pyrazolo[3,4-d]pyrimidine-4-carbonitrile(II) and 1-phenyl-1H-pyrazolo[3,4-d]pyrimidine-4-carboxylic acid(III) were synthesized, and the synthetic methods of thier derivatives were investigated.

(I) p-Tolylsulfonyl group at the 4-position of I underwent nucleophilic substitution. Especially, the substitution with carbanion(Nu^-= active methylene compounds or ketones in the presence of $NaNH_2$ in benzene) introduced the carbon chains, in good yield, to the 4-position of 1-phenyl-1H-pyrazolo[3,4-d]pyrimidine ring.

(2) Application of nucleophile(NuH or Nu^-) to II resulted in two kinds of reaction; the nucleophilic substitution with replacement of the cyano group(A) and the nucleophilic addition to the cyano group(B). The reaction A occured with hydroxide ion, alkoxide ion, amine, hydrazine and carbanion(active methylene compounds or ketones in the presence of $NaNH_2$ in DMF). The reaction B gave the derivatives of III. For example, NH_2-OH gave amidoxime(V).

(3) III was decarboxylated smoothly in heating and gave 1-phenyl-1H-pyrazolo-[3,4-d]pyrimidine. Decarboxylation of III in carbonyl compounds underwent Hammick reaction and gave carbinol derivatives(VI) or 1-phenyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl ketones(VII). III is one of the few carboxylic acids which undergo Hammick reaction.



-R : $-SO_2-C_6H_4-CH_3$ I

$-CN$ II

$-C(=O)-OH$ III

-Nu IV

$-C(=N-OH)-NH_2$ V

$-CH(-R)-OH$ VI

$-C(=O)-R$ VII