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THE SELECTIVE SYNTHESIS OF PYRAZOLES

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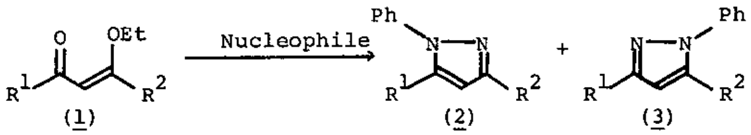
It has been reported on the synthetic utility and medicinal activity of pyrazoles and their derivatives. We already clarified the fact that hydroxylamine had the nature of the anbident nucleophile, and prepared the unsymmetric isoxazoles by the use of this property. N-substituted hydrazine was also expected to have the similar property. Therefor, we attempted the selective synthesis of unsymmetric N-substituted pyrazoles from N-substituted hydrazines with enonos.

When the mixture of phenylhydrazine and β-substituted enones (1) in methanol was heated for 12 h, N-phenylpyrazole (2) was mainly obtained. On the other hand, the reaction of enones with phenylhydrazine hydrochloride or phrnylhydrazine in the presence of sodium hydride gave pyrazole (3). From these sesults, in the nutral condition, phenylated nitrogen of phenylhydrazine preferentially attacked β-carbon of enones. On the contrary, In the acidic or basic conditions, the nucleophilicity of hydrazine was on the non-phenylated nitrogen atom.

Further, the preparation of N-methylpyrazoles and N-substituted pyrazolones was carried out in the same conditions.



R^1	R^2	Nucleophile	Yield	Ratio
Ph	Me	$PhNHNH_2$	84%	74 : 26
Ph	Me	$PhNHNH_2 \cdot HCl$	81%	14 : 83
Ph	Me	$Ph\bar{N}NH_2$	76%	4 : 96