Syntheses of Some Substituted Heterocyclic Compounds from Propargyl Cyanide and Methylpropargyl Cyanide*[1]

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It has been well established that α, β-unsaturated nitriles condense with the nucleophilic reagents such as hydrazine derivatives and hydroxylamine to give heterocyclic compounds substituted by an amino group.[1] The first step of this cyclization reaction is the Michael addition of the nucleophiles to the α, β-unsaturated nitriles.

We wish to report that the reactions of β, γ-unsaturated nitriles such as propargyl cyanide with nucleophiles, *i. e.*, hydroxylamine and phenylhydrazine led also to heterocyclic compounds substituted by an amino group. However, it was found that the different type of heterocyclic compounds were produced from propargyl cyanide (I) and methylpropargyl cyanide (V). A typical example of the reaction was carried out as follows: a mixture of 2.0 g of I, 2.2 g of hydroxylamine hydrochloride and 0.7 g of sodium in 20 m*l* of methanol was refluxed for 10 hr. After reaction the solvent was removed. Distillation of the residue under reduced pressure gave a pale yellow liquid, bp 120—140°C/1 mmHg which was solidified by cooling and after recrystallization from ligroin afforded the pure methylisoxazole (III), mp 80—81°C. Compound III thus obtained was identified with the authentic sample synthesized from β-iminobutyronitrile and hydroxylamine by the mixed melting point and infrared spectrum. Similar treatment of I with phenylhydrazine

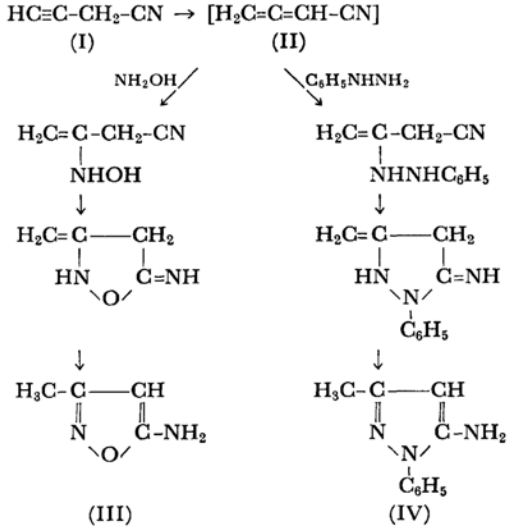

Chart 1

afforded 5-amino-3-methyl-1-phenylpyrazole (IV), mp 110—111°C (from carbon tetrachloride) in 50% yield. These cyclization reactions would be rationalized in terms of the reaction scheme outlined in Chart 1.

In the first step, I was converted to the allen type compound II, then, the nucleophiles attacked to form the heterocyclic compounds.

However, when methylpropargyl cyanide (V)*[2] was treated hydroxylamine by a similar way, 3-amino-5-ethylisoxazole (VI), mp 70—72°C, was obtained in 50% yield. By comparison of the melting points and the infrared spectra, VI was identified with the authentic sample.[2] This cyclization reaction of V may be interpreted as outlined in chart II. The reaction seems to proceed through the first attack of hydroxylamine toward the nitrile group.

The difference of the chemical behaviors of I and V for the nucleophilic attack can not be explained at present.

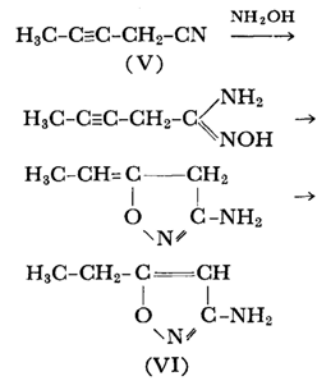

Chart II

The scope and mechanisms of the reported reactions are under investigation.

*1 This constitutes Part V of a series entitled "Studies on the Syntheses of Heterocyclic Compounds."

*2 Methylpropargyl cyanide was prepared by the reaction of methylpropargyl bromide[3] with cuprous cyanide in 75% yield.

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2) Shionogi and Co., Ltd., Brit. Pat. 875458 Sept. 21 (1964); *Chem. Abstr.*, **56**, 8720 (1962).

3) K. E. Schulte and K. P. Reiss, *Chem. Ber.*, **87**, 964 (1954).