ONE STAGE SYNTHESIS OF NITROGEN-HETEROCYCLES USING NITRILES UNDER HIGH PRESSURE

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Many nitrogen-heterocycles are synthesised by the use of imidates and amidines, and these reagents are usually supplied as chloride salts by somewhat troublesome way. In liquid phase the equiliblium nitrile + alcohol ⟷ imidate or nitrile + ammonia ⟷ amidine is shifted to the right by compression.[1),2)] When a lower alcohol such as methanol or a mixture of alcohol and ammonia is employed, the concentration of imidate or amidine in the above mentioned systems becomes sufficiently high for a synthetic application under the pressure of more than 2,000 kg/cm² in the absence of hydrogen halide.

When amidoximes, Schiff bases(or mixtures of ammonia and ketones or aldehides), α,β-unsaturated ketons and β-ketoesters were respectively kept with nitriles at 40-140°C and 2.000-8,000 kg/cm² in the presence of methanol and/or ammonia, 3,5-disubstituted 1,2,4-oxadiazoles, 1,2,4,6-tetrasubstituted dihydro-1,3,5-triazines, 2,4,4,6-tetrasubstituted dihydropyrimidines and 2,6-disubstituted 4-pyrimidones (these substituents were alkyl, aryl, and heterocyclic groups and hydrogen) were produced in fair yields. Of these products the dihydro compounds were apt to dehydrogenated under the conditions they were produced. A mixture of two kinds nitriles in methanol gives a mixture of randomly substituted 1,3,5-triazines at 9,150 kg/cm².[3)] Hydrogen cyanide is unsuitable for this co-trimerization because of its easily polymerizable nature. Then, formimidate, formamidine, 1,3,5-triazine, formate, and orthoformate were respectively treated with acetonitrile in the presence or absence of ammonia to form 2,4-dimethyl-1,3,5-triazine predominantry and a minute 2-methyl- and 2,4,6-trimethyl-1,3,5-triazine followed by rapid rearrangement to 4-amino-2-methyl-, 4-amino-, and 4-amino-2,6-dimethylpyrimidine in situ. 4-Amino-2-methylpyrimidine may be remarkable as a new intermediate for the synthesis of Vitamine B_1.

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