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NEW TRANSFORMATION OF 2-SUBSTITUTED 5-NITROPYRIMIDINES BY THE ACTION OF THE ENAMINE FORM OF N-METHYLACETONE IMINE

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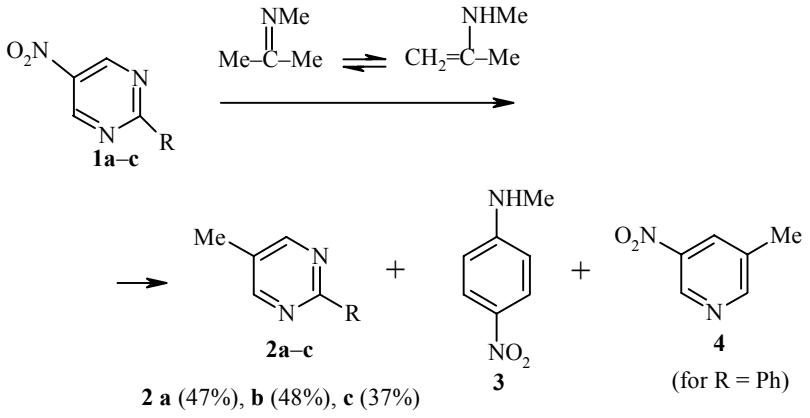
Keywords: 2-amino-5-nitropyrimidine, 2-hydroxy-5-nitropyrimidine, 5-nitro-2-phenylpyrimidine, 2-amino-2-phenylpyrimidine, 2-hydroxy-2-phenylpyrimidine, 5-methyl-2-phenylpyrimidine, N-methylacetone imine, nucleophilic transformations, [2+4] cycloaddition.

Of the many reported nucleophilic transformations of 5-nitropyrimidines, there have only been two examples involving the action of enamines. Shkil and Sagitullin [1] reported the transformation of 5-nitropyrimidine to give the corresponding bicyclic 3-nitropyridine by the action of an enamine of cyclododecanone. Gromov [2] reported the conversion of 5-nitro-2-phenylpyrimidine to give N-alkyl-*p*-nitroanilines in ~30% yield and methylnitropyridine in ~4% yield in aqueous acetone solutions of alkylamines and dialkylamines (the *in situ* formation of enamines may be assumed in this case).

We are the first to report a new direction in the transformation of 2-substituted 5-nitropyrimidines **1a-c** by the action of N-methylacetone imine in DMF at ~20°C leading to formation of 2-substituted 5-methylpyrimidines **2a-c** as the major reaction products.



1, **2 a** R = Ph, **b** R = NH_2, **c** R = OH

Thus, 5 mmol of freshly prepared N-methylacetone imine [6] was added to a solution of 1 mmol nitropyrimidine **1a-c** in 5 ml DMF. Nitropyrimidines **1a-c** were prepared according to known methods [3-5]. The reaction mixture was maintained for 120 h at ~20°C. At the end of the reaction, **2a-c** separated as a

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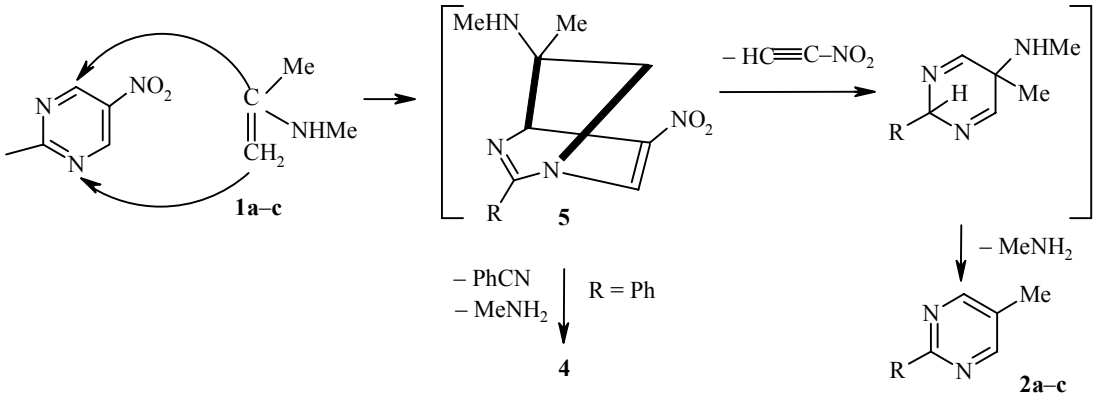
precipitate. In all cases, the mass spectral data and identity of the IR and ^{1}H NMR spectral data with the data reported by various workers [7-9] indicate formation of 2-substituted 5-methylpyrimidines **2a-c**.

We propose the following mechanism for the formation of **2a-c:**



The reaction mixtures were analyzed by GC/MS on a HP GC 689 Plus/MSD HP 5973N system. The analysis indicated formation of **2a, 3,** and **4** in 5:1:0.1 ratio in the case of **1a.** In the case of **1b**, about 50% unreacted starting reagent was recovered, while **2b** and **3** were formed in 5:1 ratio. N-Methyl-*p*-nitroaniline **3**, which was obtained in all cases, probably through the 4,6-*meta*-bonding mechanism proposed by Gromov [2], was identical to the compound described in the literature.

The high content of the tautomeric enamine form of N-methylacetone imine under our conditions [6] probably permits the unusual participation of the electron-rich dienophile in the Diels–Alder reaction with inverted electronic requirements with the electron-deficient azadiene system of 5-nitropyrimidines **1a-c.** The consecutive elimination of nitroacetylene (detected by GC/MS) and, then, methylamine from intermediate bicyclic adduct **5** leads to the formation of 2-substituted 5-methylpyrimidines **2a-c**.

We should note that a different pathway for the decomposition of bicyclic intermediate **5** with the elimination of a stable benzonitrile fragment (also detected by GC/MS) is possible only in the case of nitropyrimidine **1a** (R = Ph). In this case, trace amounts of 3-methyl-5-nitropyridine **4** are specifically formed.

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