UNUSUAL BEHAVIOR OF ACETOACETIC ESTER IN CONDENSATION WITH 2-AMINOPYRIDINE PERCHLORATE

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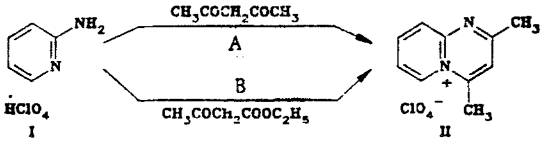
The cyclization of 2-aminopyridine perchlorates (e.g., I) with β-dicarbonyl compounds and β-chlorovinylketones [1] resulting in the formation of pyrido[1,2-*a*]pyrimidines of type II (route A) has been described. β-Ketoesters have not been used in this synthesis although a multitude of examples of their use (and of malonic ester) in the synthesis of pyrido[1,2-*a*]pyrimidones via condensation with 2-aminopyridines are known [2].



Condensation of acetoacetic ester with 2-aminopyridine perchlorate gave compound II (route B) (also formed by reaction with acetylacetone) which has not previously been reported in the literature known to us. The unusual behavior of the β-ketoesters lies in the fact that they have a four carbon aliphatic chain but give condensation products formed by β-diketones with five carbons in the basic chain.

In our opinion explanation of the experimental facts must involve the generation of an acylating species from the β-ketoester under the action of the perchlorate behaving as a Lewis acid. The C-acylated ketoester formed subsequently undergoes ketonic splitting to give a β-diketone which reacts with the amidine component I to give compound II. It is possible that the reaction product has a catalytic effect on the process since addition of 0.5% of β-diketone (based on ketoester) gave rise to a nonstoichiometric increase in yield and reaction rate.

It is more likely that first stage formation of a Schiff base with 2-aminopyridine occurs with subsequent conversion, as discussed above, involving this substrate.

The reaction was carried out both with excess (3-5 fold) β-ketoester at 120-140°C and also in refluxing alcohol for 4-12 h to give II (44-65%) with mp 225-227°C. PMR Spectrum ($DMSO-D_6$): 2.83 (s, 3H, $4-CH_3$), 3.00 (s, 3H, $2-CH_3$), 8.08 (s, 1H, 3-H), 8.12 (m, $J_{8,9} = 8.7$; $J_{7,8} = 7.2$, $J_{6,8} = 1.6$ Hz, 1H, 8-H), 8.43 (dd, $J_{7,9} = 1.3$ Hz, 1H, 9-H), 8.61 (m, $J_{6,7} = 6.9$ Hz, 1H, 7-H), 9.23 (dd, 1H, 6-H). According to [3] the melting point is 221-222°C.

Elemental analysis confirmed the given structure.

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