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FORMATION OF A BICYCLIC ADDUCT UPON RECYCLIZATION OF PYRIMIDINIUM SALTS

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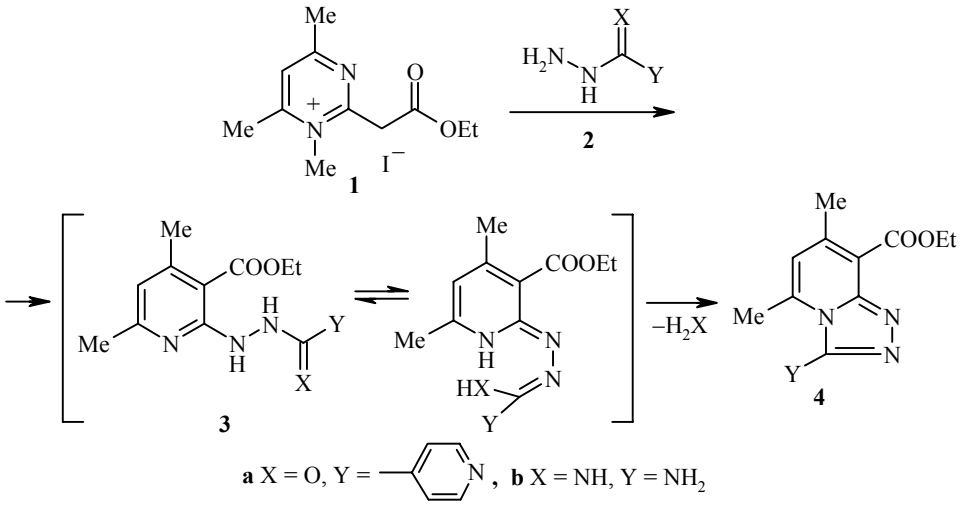
It is known that the action of primary amines on 1,2-dialkylpyrimidinium salts leads to their conversion in the Kost–Sagitullin rearrangement to substituted 2-alkylaminopyridines [1]. In later work [2-4], we showed that the product of "rearrangement with transamination" with introduction of a fragment of the nucleophilic reagent at $C_{(2)}$ in the reformed ring was obtained in addition to the product of the ordinary rearrangement upon the introduction of amines with a different substituent than at the quaternized pyrimidine nitrogen atom.

We have studied the behaviour of 2-ethoxycarbonylmethyl-1,4,6-trimethylpyrimidinium iodide (**1**) upon the action of the hydrazide of isonicotinic acid (Isoniazide **2a**) and aminoguanidine (**2b**) containing a hydrazine fragment.

In both cases, unusual rearrangement products were isolated, namely, 1,2,4-triazolo[4,3-*a*]pyridines **4a** and **4b** obtained due to cyclocondensation of the products of "rearrangement with transamination".



The ^{1}H NMR spectrum of **4a** shows both signals for protons of pyridine reagent **2a** and signals for most of the protons of the rearrangement product (ester and methyl groups and characteristic signal for pyridine 5-H), which indicates rearrangement with incorporation of a fragment of the reagent into the transformation product. The spectrum of the compound isolated after the reaction of salt **1** with aminoguanidine also has a form

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characteristic for a rearrangement product. However, the lack of the NMR signals for the two hydrazinic protons and the lack of accord of the mass of the molecular ion (in the mass spectrum of the compounds studied) with the mass of the expected products **3a** and **3b** and the coincidence of the molecular masses of **3a** and **3b** to the masses of **4a** and **4b** indicate the formation of bicyclic products.

We note that 2-ethoxycarbonylmethyl-4,6-dimethylpyrimidine (**5**) was also isolated in the reaction with isoniazide in addition to the above-mentioned bicyclic compounds. In the reaction with aminoguanidine, the product of the normal rearrangement, namely, 3-ethoxycarbonyl-4,6-dimethyl-2-methylaminopyridine (**6**) was isolated along with pyrimidine **5**.

4-Ethoxycarbonyl-5,7-dimethyl-1-(4-pyridyl)-1,2,4-triazolo[4,3-*a*]pyridine (4a). A mixture of salt **1** (0.67 g, 2 mmol) and hydrazide of isonicotinic acid (0.27 g, 2 mmol) was dissolved in absolute ethanol (8 ml) and heated in a sealed glass ampule on a steam bath for 25-30 h. The solvent was distilled off and the residue was washed consecutively with hot hexane, benzene, and hot chloroform. The solvent was removed from the benzene extracts and the residue was separated preparatively on a column packed with silica gel L 5/40 using 3:1 acetone–benzene as the eluent to give 0.2 g (35%) of compound **4a**, R_f 0.63 (3:1 acetone–benzene); mp 153-154°C. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz), δ, ppm (*J*, Hz): 1.3 (3H, t, *J* = 7.1, $OCH_2\underline{CH_3}$); 2.73 (3H, s, 5-CH_3); 2.83 (3H, s, 7-CH_3); 4.37 (2H, q, *J* = 7.1, $O\underline{CH_2}CH_3$); 6.8 (1H, s, 6-H); 7.71 (2H, d, *J* = 6.8, 2'- and 6'-H); 8.71 (2H, d, *J* = 6.8, 3'- and 5'-H). Mass spectrum, *m/z* (I_{rel}, %): 296 (57), 252 (20), 251 (100), 225 (17), 224 (87), 223 (16), 174 (9), 78 (10). Found, %: C 64.59; H 5.21; N 19.17. $C_{16}H_{16}N_4O_2$. Calculated, %: C 64.85; H 5.44; N 18.91.

After cooling of the chloroform solution, 0.15 g (27%) crystals of the iodomethylate of the hydrazide of isonicotinic acid were isolated. Upon cooling of the hexane solution, 0.1 g (25%) **5** was isolated, which proved identical in its melting point, thin-layer chromatography, and NMR spectrum to an authentic sample.

1-Amino-4-ethoxycarbonyl-5,7-dimethyl-1,2,4-triazolo[4,3-*a*]pyridine (4b). A solution of salt **1** (0.67 g, 2 mmol) in ethanol (5 ml) was added to a solution of aminoguanidine obtained by dissolving aminoguanidine nitrate (0.69 g, 5 mmol) in ethanolic sodium ethylate obtained from adding sodium (0.11 g, 5 mmol) to absolute ethanol (5 ml). The mixture was heated in a sealed ampule on a steam bath for 15 h. The solvent was distilled off and the residue was treated with benzene. The solvent was distilled off the benzene extracts and the residue was separated on a column packed with silica gel L 5/40 using 2:1 benzene–acetone as the eluent to give 0.18 g (38%) of compound **4b**, R_f 0.43 (1:2 benzene–acetone); mp 197-198°C. ^{1}H NMR spectrum (DMSO-d_6, 300 MHz), δ, ppm (*J*, Hz): 1.44 (3H, t, *J* = 7.1, $OCH_2\underline{CH_3}$); 2.56 (3H, s, 5-CH_3); 2.63 (3H, s, 7-CH_3); 4.57 (2H, q, *J* = 7.1, $O\underline{CH_2}CH_3$); 4.62 (2H, br. s, NH_2); 6.55 (1H, s, 6-H). Mass spectrum, *m/z* (I_{rel}, %): 234 (63), 205 (9), 190 (9), 189 (66), 188 (76), 163 (19), 162 (100), 161 (10), 160 (24), 119 (24), 118 (13), 78 (10). Found, %: C 56.75; H 6.30; N 23.59. $C_{16}H_{16}N_4O_2$. Calculated, %: C 56.40; H 6.02; N 23.92.

Separation of the mixture also gave 0.08 g (20%) of pyridine **6** and 0.04 g (10%) of ester **5**, which were identical in their thin-layer chromatography and ^{1}H NMR spectra to authentic samples.

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