SYNTHESIS OF 1-(2-OXO-2-ARYLETHYL)-3-ARYLCARBAMOYLPYRIDINIUM BROMIDES

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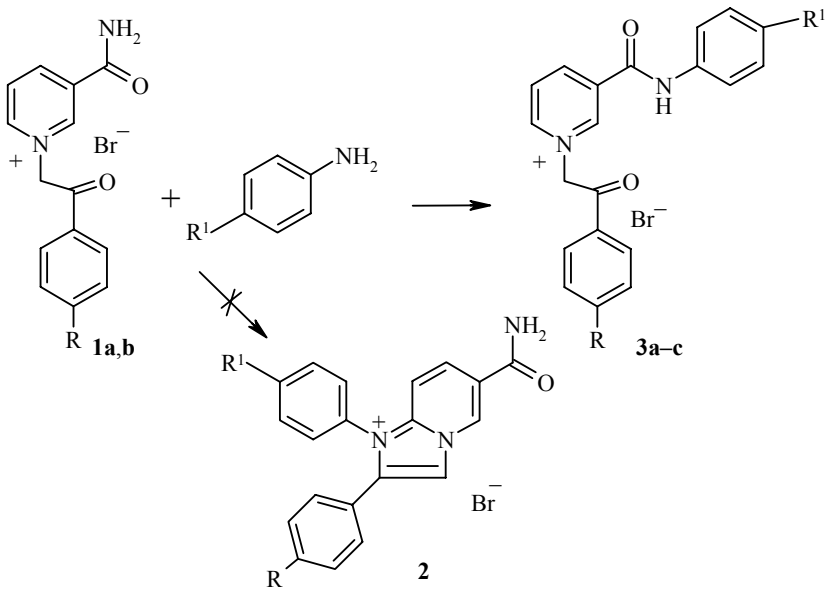
Pyridine derivatives have a broad spectrum of biological action and exhibit antitubercular [1], antimicrobial [2, 3], fungicidal, and pesticidal activity [4].

Since quaternary salts, obtained by alkylation of quinoline by substituted phenacyl bromides, when fused with a two-fold excess of aromatic amine followed by treatment with 45% hydrobromic acid yield the corresponding imidazo[1,2-*a*]quinolinium salts [5], we attempted to carry out the analogous reaction based on nicotinamide. We also hypothesized that the presence of an electron-acceptor substituent in the position 3 of the system would promote the reaction.



1 a R = H, **b** R = Br; **3 a** R = H, R^1 = OMe, **b** R = H, **c** R = Br, R^1 = OMe

We obtained the starting 1-phenacylnicotinamide bromides **1a,b** by the method in [6]. Note that in the cited paper, the reaction product of nicotinamide and phenacyl bromide is assigned a structure corresponding to alkylation at the amide nitrogen atom. The ^{1}H NMR spectroscopy data suggest that the reaction occurs at the

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ring nitrogen atom. Thus the methylene group of compound **1a** appears as a two-proton singlet in the 6.59 ppm region, while the protons from the amide group appear as two broadened singlets at 8.19 ppm and 8.65 ppm respectively. If the structure indicated in [6] were realized, then the methylene group should appear in the ^{1}H NMR spectrum as a two-proton doublet, while the proton from the amide group should appear as a one-proton triplet. The melting point of the compound **1a** that we obtained practically coincides with the literature value (222-223°C for the sample we obtained, and 224°C according to [6]).

The ^{1}H NMR spectra of the products of fusion of pyridinium salts **1** with anilines and also elemental analysis data indicate that instead of the proposed formation of imidazo[1,2-*a*]pyridinium salts **2**, transamidation in the quaternary salt **1** occurs to a substituted aniline moiety, with formation of 3-arylcarbamoyl-1-(2-oxo-2-arylethyl)pyridinium bromides **3**.

When nicotinamide was fused with substituted anilines, we did not observe the transamidation reaction.

3-(4-Methoxyphenylcarbamoyl)-1-(2-oxo-2-phenylethyl)pyridinium Bromide (3a). A mixture of of compound **1a** (3.21 g, 0.01 mol), *p*-anisidine (2.46 g, 0.02 mol) and acetic acid (1 ml) was heated on an oil bath under reflux at a temperature of 150°C for 3 h. After cooling, the reaction mixture was ground with 45% hydrobromic acid (20 ml) and poured into water. The crystallized precipitate was filtered out, washed with water until it tested neutral, and dried. Yield 2.22 g (52%); mp 215°C (EtOH–DMF). ^{1}H NMR spectrum (300 MHz, DMSO-d_6/TMS), δ, ppm (*J*, Hz): 3.77 (3H, s, OCH_3); 6.61 (2H, s, CO$\underline{CH_2}$); 7.01 and 7.71 (4H, two d, *J* = 8.7, C_6H_4); 7.65-8.08 (5H, m, C_6H_5); 8.47 (1H, m, 5-H_{Py}); 9.23 (1H, d, *J* = 5.7, 6-H_{Py}); 9.31 (1H, d, *J* = 8.4, 4-H_{Py}); 9.65 (1H, s, 2-H_{Py}); 10.9 (1H, s, NH). Found, %: Br 18.5; N 6.41. $C_{21}H_{19}BrN_2O_3$. Calculated, %: Br 18.7; N 6.56.

1-(2-Oxo-2-phenylethyl)-3-phenylcarbamoylpyridinium Bromide (3b) was obtained as for compound **3a** from compound **1a** (0.01 mol) and aniline (20 mmol). Yield 1.74 g (44%); mp 231°C (EtOH–DMF). ^{1}H NMR spectrum (300 MHz, DMSO-d_6/TMS), δ, ppm (*J*, Hz): 6.62 (2H, s, CO$\underline{CH_2}$); 7.19-8.08 (10H, m, Ar); 8.46 (1H, m, 5-H_{Py}); 9.19 (1H, d, *J* = 5.7, 6-H_{Py}); 9.29 (1H, d, *J* = 8.1, 4-H_{Py}); 9.64 (1H, s, 2-H_{Py}); 11.0 (1H, s, NH). Found, %: Br 19.9; N 7.31. $C_{20}H_{17}BrN_2O_2$. Calculated, %: Br 20.1; N 7.05.

3-(4-Methoxyphenylcarbamoyl)-1-[2-oxo-2-(4-bromophenyl)ethyl]pyridinium Bromide (3c) was obtained as for compound **3a**. Yield 2.33 g (46%); mp 250°C (EtOH–DMF). ^{1}H NMR spectrum (300 MHz, DMSO-d_6/TMS), δ, ppm (*J*, Hz): 3.77 (3H, s, OCH_3); 6.60 (2H, s, CO$\underline{CH_2}$); 6.97 and 7.70 (4H, two d, *J* = 8.4, C_6H_4); 7.88-8.04 (4H, two d, *J* = 8.7, C_6H_4); 8.44 (1H, m, 5-H_{Py}); 9.18 (1H, d, *J* = 6.0, 6-H_{Py}); 9.28 (1H, d, *J* = 7.8, 4-H_{Py}); 9.63 (1H, s, 2-H_{Py}); 10.9 (1H, s, NH). Found, %: Br 31.3; N 5.34. $C_{21}H_{18}Br_2N_2O_3$. Calculated, %: Br 31.6; N 5.53.

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