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LETTERS
TO THE EDITOR

Reaction of Trifluoroacetic Anhydride with 4-Pyridinecarboxylic Acid Hydrazide

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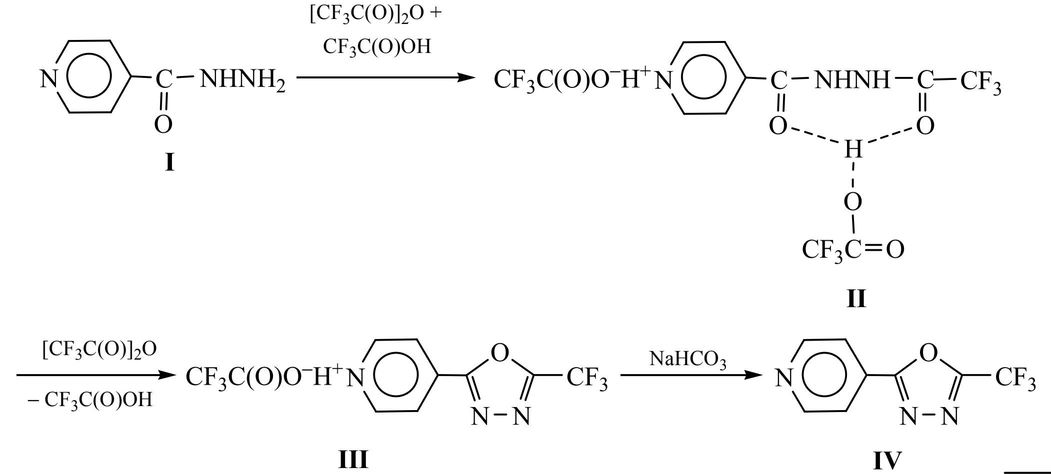
The substituted 1,3,4-oxadiazoles are known to possess a broad spectrum of biological activity and have been suggested as promising antihypertensive drugs and substances with antimicrobial, tuberculocidal action [1]. The approach to the synthesis of the substituted 1,3,4-oxadiazoles via the *N,N'*-diacylhydrazines cyclization under the action of dehydrating agents has been previously described [2].

We found that the reaction of 4-pyridinecarboxylic acid hydrazide **I** with trifluoroacetic anhydride in the presence of trifluoroacetic acid (1:2:1) results in the formation of a complex of trifluoroacetic acid with 4-{[2-(trifluoroacetyl)hydrazinyl]carbonyl}pyridinium trifluoroacetate **II**. The latter reacts with trifluoroacetic anhydride to form 4-[5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyridinium trifluoroacetate **III**. The treatment of salt **III** with aqueous solution of sodium bicarbonate affords 4-[5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyridine **IV**. The structure of 1,3,4-oxadiazole **IV** and intermediate products **II** and **III** was confirmed by the elemental analysis and infrared spectra.



Complex of trifluoroacetic acid with 4-{[2-(trifluoroacetyl)hydrazinyl]carbonyl}pyridinium trifluoroacetate (II). To a stirred suspension of 1.7 g (0.012 mol) of isoniazid in 4 ml of dioxane was added dropwise 2.5 ml of a mixture of trifluoroacetic anhydride with trifluoroacetic acid (1:1) in 4 ml of dioxane. The temperature rose to 58°C. The reaction mixture was kept for 50 min at 50–58°C and cooled to room temperature. The precipitate was filtered off, washed with dioxane and diethyl ether. Yield 4.1 g (76%), mp 118–119°C, soluble in alcohol and water. IR spectrum, ν, cm^{-1}: 1135, 1202 (C_5H_4N), 1644 ($C{=}OCF_3COOH$), 1677, 1756 ($C{=}O^{CF_3\,COOH}$), 3198 (NH), 1971–2165, 2591 (OH). Found N, %: 8.70, 8.85. $C_{12}H_8F_9N_3O_6$. Calculated N, %: N 9.11.

4-[5-(Trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyridinium trifluoroacetate (III). To 2.7 g (0.006 mol) of complex **II** was added by portions 2.16 ml (3.36 g, 0.016 mol) of trifluoroacetic anhydride. The precipitate and the reaction mixture warmed to 40°C. The resulting mixture was maintained in a flask with reflux condenser at 60–100°C for 2.5 h, and then kept in a vacuum of water-jet pump for 0.5 h at 60°C. Yield 87%. Recrystallization from 5 ml of ethanol yields 1.4 g (53%) of salt **III**, mp 141–142°C. IR spectrum, ν, cm^{-1}: 1138, 1200 (C_5H_4N), 1583 (C=N), 1642 ($C{=}O^{CF_3COOH}$), 1988, 2128, 2500 (OH). Found N, %: N 12.65, 12.45. $C_{10}H_5F_6N_3O_3$. Calculated N, %: N 12.76.

4-[5-(Trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyridine (IV). To 7 ml of 5% sodium bicarbonate solution was added in portions 1 g of compound **III**. When the release of carbon dioxide completed the formed precipitate was filtered off, washed with water until neutral pH, and dried in air. Yield 0.5 g (78%), mp 58°C, water insoluble. IR spectrum, ν, cm^{-1}: 1149, 1216 (C_5H_4N), 1587 (C=N). Found N, %: 19.30, 19.10. Calculated, %: N 19.53.

The NMR spectra were recorded on a spectrometer Tesla BS-567A (100 MHz) relative to $(CH_3)_4Si$. The IR spectra were registered on a Specord M-80 instrument.

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