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SHORT COMMUNICATIONS

Mild and Effective Synthesis of Morpholinium 3-Cyano-4-methyl-6-oxo-1,6-dihydropyridine-2-thiolate

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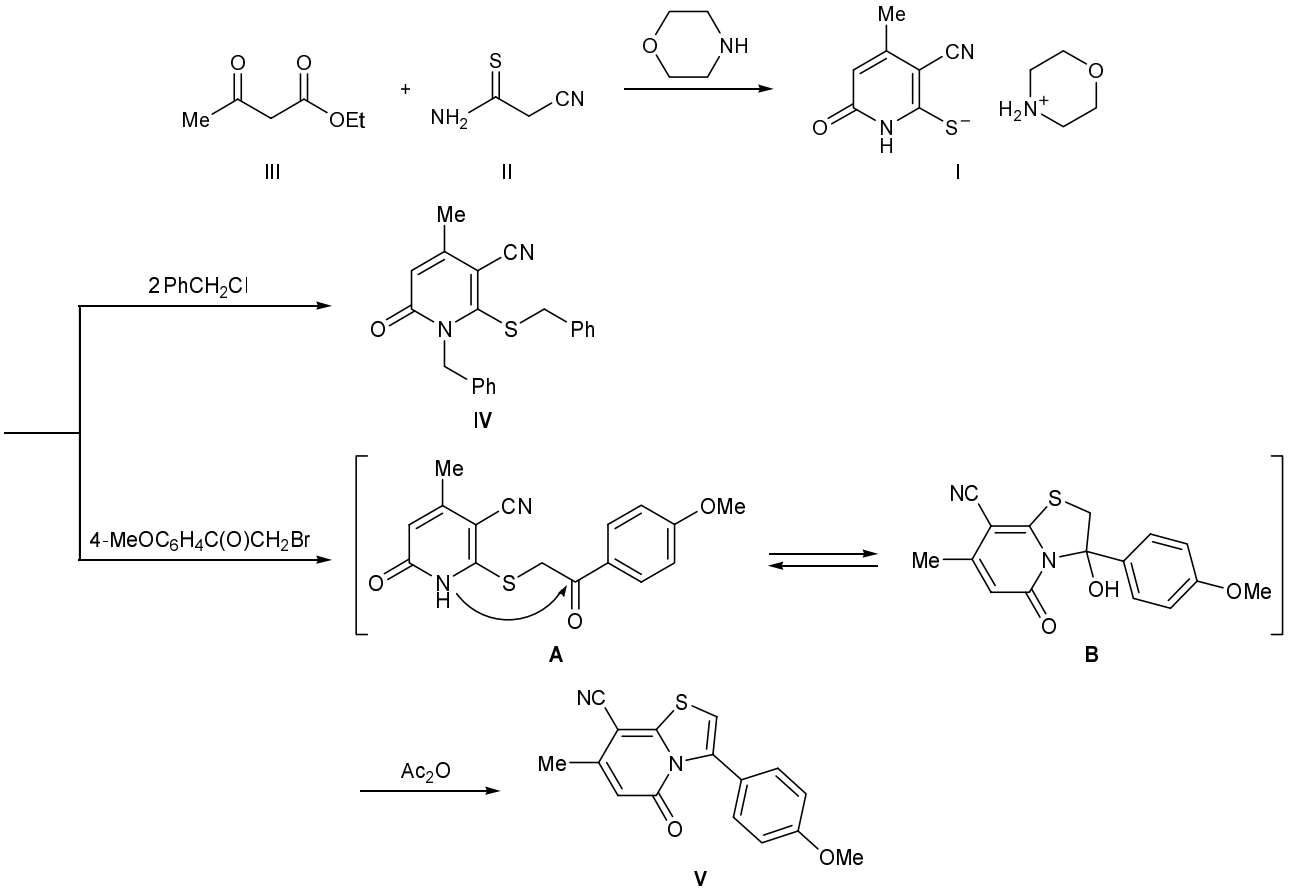
Morpholinium 3-cyano-4-methyl-6-oxo-1,6-dihydropyridine-2-thiolate (**I**) was synthesized previously by condensation of cyanothioacetamide (**II**) with ethyl 4-morpholinobut-2-enoate in ethanol at 20°C in the absence of a catalyst [1]. 6-Hydroxy-4-methyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile was obtained by condensation of ethyl acetoacetate (**III**) with compound **II** in pyridine at 160°C in the presence of 2-(diethylamino)ethanol [2].

In the present work, the condensation of compounds **III** and **II** in ethanol at room temperature in the presence of an equimolar amount of morpholine was shown for the first time to give salt **I** in quantitative yield. The proposed procedure requires no preliminary preparation of the corresponding enamine from ethyl acetoacetate and heating of the reaction mixture.

The alkylation of pyridinethiolate **I** with 2 equiv of benzyl chloride in DMF in the presence of a base gave



substituted 1,2-dihydropyridin-2-one **IV** which is a promising intermediate product in the synthesis of azo dyes [3]. Treatment of salt **I** with 4-methoxyphenacyl bromide, followed by heating of the product in boiling acetic anhydride resulted in formation of substituted thiazolopyridinone **V** as potential peptidomimetic [4]. Presumably, the reaction involves formation of sulfide **A** and hydroxy-substituted thiazolopyridine **B**.

Morpholinium 3-cyano-4-methyl-6-oxo-1,6-dihydropyridine-2-thiolate (I). Morpholine, 0.87 ml (10 mmol), was added under stirring at 20°C to a suspension of 1.0 g (10 mmol) of cyanothioacetamide (**II**) in 20 ml of ethanol. The mixture was stirred for 5 min until it became homogeneous, 1.28 ml (10 mmol) of ethyl acetoacetate (**III**) was added, and the mixture was stirred for 10 min and was left to stand for 24 h. The precipitate was filtered off and washed with ethanol and hexane. Yield 2.0 g (78%), white powder, mp 224–226°C; published data [1]: mp 226–228°C. Mass spectrum, m/z (I_{rel}, %): 166 (78) $[M + 1]^+$ (anionic fragment), 138(49), 133 (25), 122 (14), 110 (15), 105 (32), 87 (36) $[M - 1]^+$ (cationic fragment), 83 (14), 78 (59), 70 (11), 63 (14), 57 (100), 51 (33).

1-Benzyl-2-benzylsulfanyl-4-methyl-6-oxo-1,6-dihydropyridine-3-carbonitrile (IV). Salt **I**, 2.53 g (10 mmol), was dissolved in 15 ml of DMF, 5.6 ml (10 mmol) of 10% aqueous potassium hydroxide and 2.3 ml (20 mmol) of benzyl chloride were added in succession at room temperature, and the mixture was stirred for 3 h, diluted with an equal volume of water, and left to stand for 48 h. The precipitate was filtered off and washed with water, ethanol, and hexane. Yield 2.28 g (66%), colorless needles, mp 73–74°C (from AcOH). IR spectrum, ν, cm^{-1}: 2204 (C≡N), 1695 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.43 s (3H, Me), 4.44 s (2H, SCH_2), 5.38 s (2H, NCH_2), 6.51 s (1H, 5-H), 7.15–7.36 m (10H, H_{arom}). Found, %: C 72.60; H 5.06; N 7.88. $C_{21}H_{18}N_2OS$. Calculated, %: C 72.81; H 5.24; N 8.09.

3-(4-Methoxyphenyl)-7-methyl-5-oxo-4,5-dihydrothiazolo[3,2-*a*]pyridine-8-carbonitrile (V). A mixture of 2.53 g (10 mmol) of compound **I** and 2.29 g (10 mmol) of 4-methoxyphenacyl bromide in 15 ml of DMF was stirred for 2 h at 20°C. It was then diluted with an equal volume of water and was left to stand for 24 h. The precipitate was filtered off, washed with water, ethanol, and hexane, dried in air, and heated in 15 ml of acetic anhydride for 2 h under reflux. The mixture was filtered while hot through a folded paper filter, and the filtrate was left to stand for 48 h. The precipitate was filtered off and washed with diethyl ether. Yield 2.4 g (81%), yellow cotton-like material, mp 229–230°C (from AcOH). IR spectrum, ν, cm^{-1}: 2206 (C≡N), 1694 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 3.89 s (3H, MeO), 5.99 s (1H, 2-H), 6.85 d and 7.24 d (2H each, C_6H_4, J = 8.82 Hz), 7.17 s (1H, 6-H). Found, %: C 64.68; H 3.91; N 9.29. $C_{16}H_{12}N_2O_2S$. Calculated, %: C 64.85; H 4.08; N 9.45. M 296.348.

The IR spectra were recorded on an IKS-40 spectrophotometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Varian Mercury-400 instrument (400.397 MHz) from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectrum of salt **I** (70 eV) was obtained on a Kratos MS-890 spectrometer with direct sample admission into the ion source.

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