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SHORT COMMUNICATIONS

Synthesis and Unusual Reaction of Piperidinium 3-Cyano-5-ethoxycarbonyl-4-(1*H*-indol-3-yl)-6-methyl-1,4-dihydropyridine-2-thiolate with Glacial Acetic Acid

V. D. Dyachenko and A. D. Dyachenko

Taras Shevchenko National Pedagogical University, ul. Oboronnaya 2, Lugansk, 91011 Ukraine
e-mail: dvd_lug@online.lg.ua

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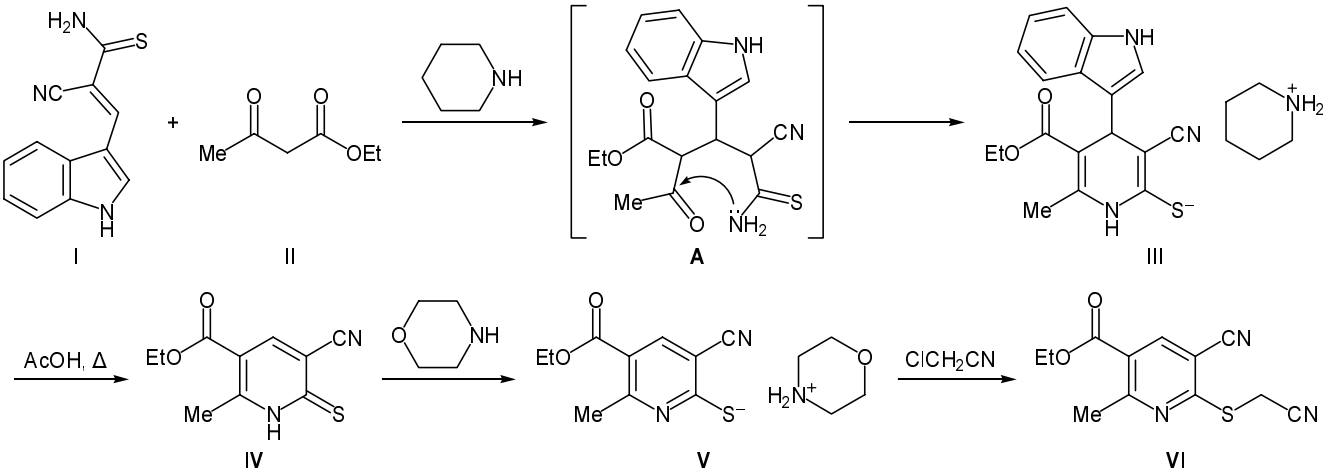
Functionally substituted ammonium 1,4-dihydropyridine-2-thiolates in acid medium undergo protonation at the sulfur atom, followed by dehydrogenation to give the corresponding pyridine-2(1*H*)-thiones [1]. We were the first to reveal that the reaction of 2-cyano-3-(1*H*-indol-3-yl)prop-2-enethioamide (**I**) with ethyl acetoacetate (**II**) at 20°C in anhydrous ethanol in the presence of an equimolar amount of piperidine follows the Michael addition pattern with formation of adduct **A** which undergoes chemoselective cyclocondensation to piperidinium 3-cyano-5-ethoxycarbonyl-4-(1*H*-indol-3-yl)-6-methyl-1,4-dihydropyridine-2-thiolate (**III**). Heating of the latter for a short time in boiling glacial acetic acid leads to ethyl 5-cyano-2-methyl-6-thioxo-1,6-dihydropyridine-3-carboxylate (**IV**) which was prepared previously by condensation of cyanothioacetamide with ethyl 2-dimethylaminomethylidene-3-oxobutanoate [2].

Compound **IV** reacted with morpholine in anhydrous ethanol to produce the corresponding morpholinium salt **V**, and S-alkylation of the latter with 2-chloroacetonitrile gave sulfide **VI**. An oxygen-containing analog of **IV**, ethyl 5-cyano-2-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate, is known to exhibit ionotropic activity [3]; therefore, studies in the series of functionalized pyridine-2(1*H*)-thiones having no substituent on C^4 seem to be promising.

2-Cyano-3-(1*H*-indol-3-yl)prop-2-enethioamide (I) was synthesized by the procedure described in [4]. Yield 1.63 g (72%), yellow powder, mp 174–176°C (from EtOH). IR spectrum, ν, cm^{-1}: 3314 (NH_2), 2212 (C≡N). ^{1}H NMR spectrum, δ, ppm: 7.28 m (2H, 5-H, 6-H), 7.55 d (1H, 4-H, J = 8.70 Hz), 7.96 d (1H, 7-H, J = 9.00 Hz), 8.55 br.s (2H, 2-H, 3-CH), 9.35 br.s and 9.66 br.s (1H each, NH_2), 12.42 br.s (1H, NH). Found, %: C 63.22; H 4.08; N 18.21. M 227. $C_{12}H_9N_3S$. Calculated, %: C 63.41; H 3.99; N 18.49. M 227.29.

Piperidinium 3-cyano-5-ethoxycarbonyl-6-methyl-4-(1*H*-indol-3-yl)-1,4-dihydropyridine-2-thiolate (III). Piperidine, 1ml (10 mmol), was added to a mix-



ture of 2.27 g (10 mmol) of compound **I** and 1.27 ml (10 mmol) of ethyl acetoacetate (**II**) in 15 ml of anhydrous ethanol under stirring at 20°C. The mixture was stirred for 25 min (until it became homogeneous) and was left to stand for 24 h. The precipitate was filtered off and washed with ethanol and hexane. Yield 3.45 g (81%), yellow powder, mp 177–180°C. IR spectrum, ν, cm^{-1}: 3315 (NH), 2183 (C≡N), 1694 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.02 t (3H, **Me**CH_2, J = 6.17 Hz), 1.48 m (2H, CH_2), 1.54 m (4H, $2CH_2$), 2.13 s (3H, Me), 2.91 t (4H, CH_2NCH_2, J = 4.37 Hz), 3.89 q (2H, CH_2O), 4.58 s (1H, 4-H), 6.78 d (1H, 2'-H, J = 2.03 Hz), 6.84 t (1H, 5'-H, J = 8.72 Hz), 6.99 t (1H, 6'-H), 7.22 d (1H, 4'-H, J = 8.69 Hz), 7.53 d (1H, 7'-H, J = 8.72 Hz), 8.22 br.s (1H, NH), 8.36 br.s (2H, H_2N^+), 10.59 br.s (1H, 1'-H). Found, %: C 64.89; H 6.41; N 12.95. M 425. $C_{23}H_{28}N_4O_2S$. Calculated, %: C 65.07; H 6.65; N 13.19. M 424.569.

Ethyl 5-cyano-2-methyl-6-thioxo-1,6-dihydropyridine-3-carboxylate (IV). A suspension of 4.26 g (10 mmol) of salt **III** in 20 ml of glacial acetic acid was heated to the boiling point and was filtered while hot through a folded filter paper. After 24 h, the precipitate was filtered off and washed with glacial acetic acid and diethyl ether. Yield 1.53 g (69%), yellow crystals, mp 239–241°C; published data [2]: mp 239–240°C. Mass spectrum, m/z (I_{rel}, %): 224 (15) $[M + 2]^+$, 223 (100) $[M + 1]^+$, 207 (14), 195 (9), 176 (7), 138 (12), 121 (17), 99 (18).

Morpholinium 3-cyano-5-ethoxycarbonyl-6-methylpyridine-2-thiolate (V). Morpholine, 0.87 ml (10 mmol), was added under stirring to a suspension of 2.22 g (10 mmol) of pyridinethione **IV** in 15 ml of anhydrous ethanol, and the mixture was stirred for 20 min and left to stand for 24 h. The precipitate was filtered off and washed with anhydrous ethanol and hexane. Yield 2.63 g (85%), yellow powder, mp 208–210°C (sublimes at 140°C). IR spectrum, ν, cm^{-1}: 2202 (C≡N), 1688 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, **Me**CH_2, J = 6.23 Hz), 2.54 s (3H, Me), 3.04 t (4H, CH_2NCH_2, J = 4.44 Hz), 3.73 t (4H, CH_2OCH_2), 4.16 q (2H, CH_2O), 5.68 br.s (2H, H_2N^+), 7.90 s (1H, 4-H). Found, %: C 54.17; H 6.02; N 13.44. M 309. $C_{14}H_{19}N_3O_3S$. Calculated, %: C 54.35; H 6.19; N 13.58. M 309.389.

Ethyl 5-cyano-6-cyanomethylsulfanyl-2-methylpyridine-3-carboxylate (VI) was synthesized according to the procedure described in [5]. Yield 2.30 g (88%), yellow needles, mp 128–129°C (from *i*-PrOH). IR spectrum, ν, cm^{-1}: 2247, 2216 (C≡N); 1691 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.33 t (3H, **Me**CH_2, J = 6.17 Hz), 2.83 s (3H, Me), 4.32 q (2H, CH_2O), 4.42 s (2H, SCH_2), 8.61 s (1H, 4-H). Found, %: C 55.02; H 4.15; N 15.90. M 261. $C_{12}H_{11}N_3O_2S$. Calculated, %: C 55.16; H 4.24; N 16.08. M 261.305.

The IR spectra were recorded on an IKS-40 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were obtained on Bruker WP-100 SY (100 MHz; compounds **V**, **VI**), Bruker AM-300 (300.13 MHz; **I**), and Varian Mercury-400 instruments (400.397 MHz; **III**, **IV**) using TMS as internal reference. The mass spectrum of compound **IV** (70 eV) was recorded on a Hewlett–Packard Chrommas GC–MS system (HP 5890/HP 5972) using HP-5MS column; sample was injected as a solution in CH_2Cl_2.

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