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PREPARATION METHOD OF N-METHYLMORPHOLINIUM 3,5-DICYANO-6-OXO-1,4,5,6-TETRAHYDRO-4-SPIRO-4'-(N-METHYLPIPERIDINE)-PYRIDINE-2-THIOLATE AND ITS DERIVATIVES

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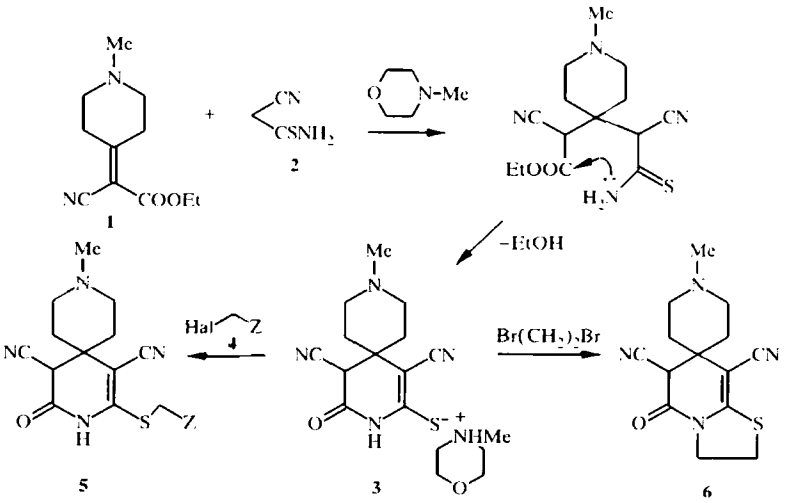
Spiro-substituted pyridine chalcogenones represent a difficultly obtainable class of organic compound, but the prospects of search for medicinal products among them are obvious [1, 2]. By the reaction of N-methylpiperidinyl-4-ylidenecyanoacetic ester (**1**) with cyanothioacetamide (**2**) and N-methylmorpholine we first realized the synthesis of N-methylmorpholinium 3,5-dicyano-6-oxo-1,4,5,6-tetrahydro-4-spiro-4'-(N-methylpiperidine)pyridine-2-thiolate (**3**). Its alkylation by halides **4** and 1,2-dibromoethane was investigated; as a result sulfides **5** and the new heterocyclic system **6** were obtained.



4, **5** a Hal = I, Z = Me; b Hal = Br, Z = $C_{11}H_{23}$

N-Methylmorpholinium 3,5-Dicyano-6-oxo-1,4,5,6-tetrahydro-4-spiro-4'-(N-methylpiperidine)-2-thiolate (3). A mixture of N-methylpiperidin-4-ylidenecyanoacetic ester (**1**) (2.1 g, 10 mmol), cyanothioacetamide (**2**) (1 g, 10 mmol), and N-methylmorpholine (2.02 ml, 20 mmol) in absolute ethanol (15 ml) was stirred at 20°C

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for 1 h. After 24 h the precipitate was filtered off and washed with water and with acetone. Yield 3.4 g (93%); mp 301-303°C. IR spectrum (vaseline oil), cm^{-1}: 2230, 2155 (C≡N), 1710 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 9.32 (1H, br. s, NH); 4.39 (1H, s, 5-H); 3.35 (4H, m, CH_2OCH_2); 3.01 (4H, m, CH_2NCH_2); 2.78 (3H, s, NCH_3); 2.52 (4H, m, CH_2NCH_2); 2.09 (3H, s, NCH_3); 1.91 (4H, m, $(CH_2)_2$). Found, %: C 56.0; H 7.01; N 19.30; S 8.91. $C_{17}H_{23}N_5O_2S$. Calculated, %: C 56.17; H 6.93; N 19.27; S 8.82.

3,5-Dicyano-2-ethylthio-6-oxo-1,4,5,6-tetrahydro-4-spiro-4'-(N-methylpiperidine)pyridine (5a). To a suspension of salt **3** (3.62 g, 10 mmol) in DMF (10 ml) we added 10% potassium hydroxide (5.6 ml, 10 mmol) and then ethyl iodide (0.8 ml, 10 mmol). The mixture was stirred for 4 h and diluted with water (10 ml). The precipitate was filtered off and washed with water, ethanol, and hexane. Yield of compound **5a** 1.3 g (45%); mp 210-211°C (ethanol). IR spectrum, cm^{-1}: 3400 (NH), 2168 (C≡N), 1740 (C=O). ^1H NMR spectrum, δ, ppm: 9.75 (1H, s, NH); 4.59 (1H, s, 5-H); 3.01 (2H, t, SCH_2); 2.55 (4H, m, CH_2NCH_2); 2.29 (3H, s, NMe); 1.78 (4H, m, $(CH_2)_2$); 1.21 (3H, t, CH_3). Found, %: C 57.78; H 6.19; N 19.37; S 11.22. $C_{14}H_{18}N_4OS$. Calculated, %: C 57.91; H 6.25; N 19.29; S 11.04.

3,5-Dicyano-2-dodecanylthio-6-oxo-1,4,5,6-tetrahydro-4-spiro-4'-(N-methylpiperidine)pyridine (5b). The compound was obtained like sulfide **5a** using halide **4b** (2.4 ml, 10 mmol). Yield 1.6 g (38%); mp 185-187°C (ethanol). IR spectrum, cm^{-1}: 3310 (NH), 2192, 2142 (C≡N), 1740 (C=O). ^1H NMR spectrum, δ, ppm: 9.73 (1H, s, NH); 4.48 (1H, s, 5-H); 3.00 (2H, t, SCH_2); 2.60 (4H, m, CH_2NCH_2); 2.23 (3H, s, NMe); 1.75 (4H, m, $(CH_2)_2$); 1.55-0.87 (23H, m, $(CH_2)_{10}CH_3$). Found, %: C 67.13; H 8.76; N 13.09; S 7.34. $C_{24}H_{38}N_4OS$. Calculated, %: C 66.94; H 8.89; N 13.01; S 7.45.

6,8-Dicyano-5-oxo-2,3,6,7-tetrahydro-7-spiro-4'-(N-methylpiperidine-7-thiazolo[3,2-*a*])pyridine (6). The compound was obtained similarly to sulfide **5** using 1,2-dibromoethane (10 mmol). Yield 0.95 g (33%); mp 250-252°C (DMF). IR spectrum, cm^{-1}: 2180 (C≡N), 1690 (C=O). ^1H NMR spectrum, δ, ppm: 4.58 (1H, s, 5-H); 4.19 (2H, m, NCH_2); 3.41 (2H, m, SCH_2); 2.62 (4H, m, CH_2NCH_2); 2.25 (3H, s, NMe); 1.80 (4H, m, $(CH_2)_2$). Found, %: C 58.43; H 5.63; N 19.41; S 11.24. $C_{14}H_{16}N_4OS$. Calculated, %: C 58.31; H 5.59; N 19.43; S 11.12. Mass spectrum, *m/z* (I_{rel}, %): 288 (16) $[M]^+$, 135 (57), 134 (74), 96 (35), 70 (100).

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