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2,3,5,8-TETRAHYDROPYRIDO-[3,2-*e*]-1,3-THIAZINES

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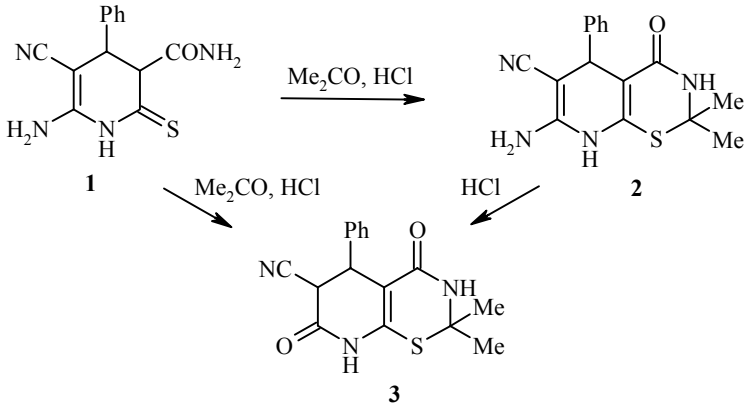
Keywords: 1,4-dihydropyridine-2-thione, 1,3-thiazino[2,3-*e*]pyridine.

We recently described an effective method for obtaining 7H-2,3-dihydrothiazolo[3,2-*a*]pyridines that involved condensation of benzylidene malononitrile, thiocarbamoylacetamide, piperidine, and α-halo ketone [1]. To prove the mechanism of this reaction, we synthesized the intermediate 6-amino-3-carbamoyl-5-cyano-4-phenyl-1,4-dihydropyridine-2-thiolates. By treating them with α-halo ketones, we obtained the indicated thiazolo[3,2-*a*]pyridines in close to quantitative yields. By acidification of the thiolates with an HCl solution in ethanol, we obtained 1,4-dihydropyridine-2-thiones of type **1** [2].



We found that when thione **1** and a twofold excess of hydrochloric acid in acetone were heated until the mixture dissolved and then the solution was neutralized, 7-amino-6-cyano-2,2-dimethyl-4-oxo-5-phenyl-2,3,5,8-tetrahydropyrido[3,2-*e*]-1,3-thiazine (**2**) was formed in 29% yield. When heated for 5 minutes with a ten-fold excess of hydrochloric acid in acetone, the major reaction product (28% yield) is 6-cyano-2,2-dimethyl-4,7-dioxo-5-phenyl-6H-2,3,5,8-tetrahydropyrido[3,2-*e*]-1,3-thiazine (**3**). Compound **2** was converted to **3** in 52% yield. More vigorous treatment of **1** with hydrochloric acid leads to cleavage of 1,4-dihydropyridine-2-thione **1** and formation of an inseparable mixture.

Thus we have obtained 2,3,5,8-tetrahydropyrido[3,2-*e*]-1,3-thiazines for the first time.

7-Amino-6-cyano-2,2-dimethyl-4-oxo-5-phenyl-2,3,5,8-tetrahydropyrido[3,2-*e*]-1,3-thiazine (2). Yield 29%; mp 250-252°C. IR spectrum, ν, cm^{-1}: 3365, 3312, 3210 (NH, NH_2); 2174 (C≡N); 1636 (C=O). ^{1}H NMR spectrum (DMSO-d_6) δ, ppm: 1.40 and 1.60 [6H, s and s, 2-$(Me)_2$]; 4.78 (1H, s, 5-H); 6.07 (2H, s, 7-NH_2); 7.0-7.3 (5H, m, 5-C_6H_5); 8.32 (1H, s, 3-NH); 9.55 (1H, s, 8-NH). Found, %: C 61.20; H 5.19; N 17.60; S 10.35. $C_{16}H_{16}N_4OS$. Calculated, %: C 61.52; H 5.16; N 17.93; S 10.26.

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6-Cyano-2,2-dimethyl-4,7-dioxo-5-phenyl-6H-2,3,5,8-tetrahydropyrido[3,2-*e*]-1,3-thiazine (3). Yield 28%; mp 244-246°C. IR spectrum, ν, cm^{-1}: 3314, 3206 (NH); 2260 (C≡N); 1628, 1722 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm, *J*, Hz: 1.60 and 1.67 [6H, s and s, 2-$(Me)_2$]; 4.50 (1H, d, *J* = 7.22, 6-H); 4.72 (1H, d, *J* = 7.22, 5-H); 6.43 (1H, br. s, 3-NH); 7.3-7.4 (5H, m, 5-C_6H_5); 8.81 (1H, br. s, 8-NH). Found, %: C 60.92; H 4.90; N 13.58; S 10.33. $C_{16}H_{15}N_3O_2S$. Calculated, %: C 61.22; H 4.82; N 13.58; S 10.23.

REFERENCES

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