

## SYNTHESIS OF 3-CYANO-6-METHYL-5,6,7,8-TETRAHYDRO-1,6-NAPHTHYRIDINE-2(1H)-THIONE

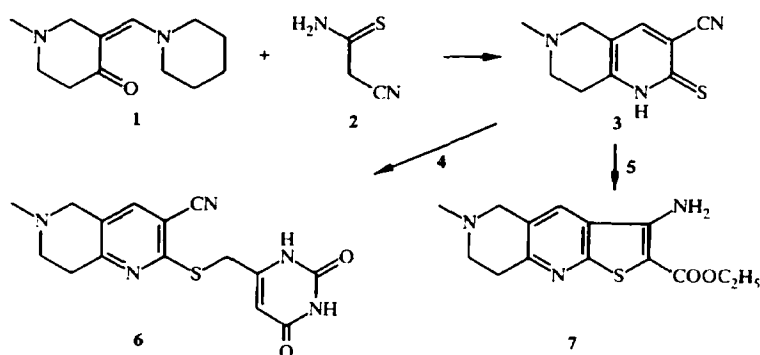
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In spite of the high biological activity of the derivatives of 1,6-naphthyridines and their partially hydrogenated analogs, there is little information on their synthesis based on derivatives of cyanoacetic acid [1, 2].

We studied for the first time the reaction of 1-methyl-3-(1-piperidinomethylene)-4-piperidone (**1**) with cyanothioacetamide (**2**) under the mild conditions of acid catalysis, leading to 1,6-naphthyridine **3**.

The structure of compound **3** was confirmed by the spectral data and chemical transformations. The alkylation of **3** by 6-chloromethyluracil (**4**) and ethyl chloroacetate (**5**) in an alkaline medium led to the formation of sulfide **6**, and in the case of ester **5** the product **7** from cyclization in the Thorpe–Ziegler reaction was isolated [3].



**3-Cyano-6-methyl-5,6,7,8-tetrahydro-1,6-naphthyridine-2(1H)-thione (3).** Yield 1.1 g (54%); mp 254–256°C (DMF). IR spectrum (vaseline oil): 2221 ( $\nu$  CN), 3386 ( $\nu$  NH<sub>2</sub>). <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>), ppm: 13.88 (1H, br. s, NH); 7.89 (1H, s, C<sub>4a</sub>, of naphthyridine); 3.29 (2H, s, CH<sub>2</sub>); 2.77 (2H, m, CH<sub>2</sub>); 2.60 (2H, s, CH<sub>2</sub>); 2.32 (3H, s, CH<sub>3</sub>). Found, %: C 58.29; H 4.79; N 20.61; S 15.26. C<sub>10</sub>H<sub>11</sub>N<sub>2</sub>S. Calculated, %: C 58.51; H 4.91; N 20.46; S 15.39.

**3-Cyano-2-(2,4-dihydroxy-1,2,3,4-tetrahydro-6-pyrimidinylmethylthio)-6-methyl-5,6,7,8-tetrahydro-1,6-naphthyridine (6).** Yield 2.96 g (90%); mp >300°C (DMF). IR spectrum (vaseline oil): 3250, 3190, 3140 ( $\nu$  NH), 2210 (CN), 1662 ( $\nu$  C=C). <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>), ppm: 11.05 (2H, br. s, C<sub>4a</sub>, of naphthyridine); 5.52 (1H, s, 5-H of uracil); 4.17 (2H, s, CH<sub>2</sub>); 3.35 (2H, s, CH<sub>2</sub>); 2.94 (2H, m, CH<sub>2</sub>); 2.71 (2H, s, CH<sub>2</sub>); 2.36 (3H, s, CH<sub>3</sub>). Found, %: C 54.44; H 4.55; N 21.042; S 9.926. C<sub>15</sub>H<sub>17</sub>N<sub>5</sub>O<sub>2</sub>S. Calculated, %: C 54.77; H 4.48; N 21.26; S 9.73.

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**3-Amino-2-ethoxycarbonyl-6-methyl-5,6,7,8-tetrahydrothieno[2,3-*b*]-1,6-naphthyridine (7).** Yield 2.64 g (95%); mp 232-234°C (ethanol). IR spectrum (vaseline oil): 3245 ( $\nu$  NH<sub>2</sub>), 1720 ( $\nu$  C=O). <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>), ppm: 8.20 (1H, s, C<sub>4</sub>, of naphthyridine); 7.72 (2H, br. s, NH<sub>2</sub>); 4.27 (2H, q, CH<sub>2</sub>CH<sub>3</sub>); 3.61 (2H, s, CH<sub>2</sub>); 3.01 (2H, m, CH<sub>2</sub>); 2.73 (2H, m, CH<sub>2</sub>); 2.39 (3H, s, CH<sub>3</sub>); 1.29 (3H, t, CH<sub>3</sub>). Found, %: C 57.44; H 5.86; N 14.32; S 11.36. C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S. Calculated, %: C 56.09; H 5.79; N 15.09; S 11.51.

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