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NEW CASCADE SYNTHESIS OF PYRIDO[2',3':4,5]THIENO-[2,3-*b*]PYRIDINE DERIVATIVES

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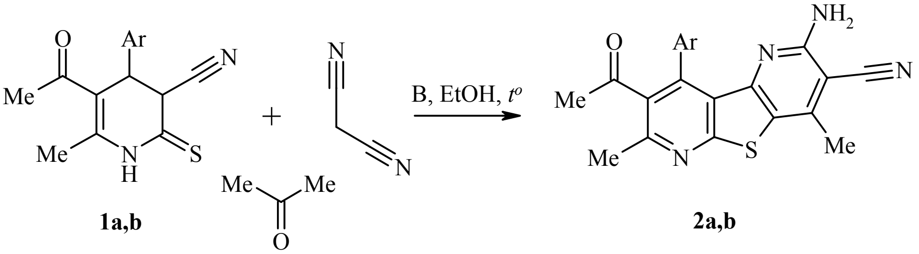
In previous work [1-5], we showed that the triple cyclocondensation of partially hydrogenated 3-cyano-2-pyridinethiolates with acetone and malononitrile leads to the formation of derivatives of pyrido[2',3':4,5]thieno[2,3-*b*]pyridine. The mechanism of this unusual reaction involves the oxidation of the starting thiolates by atmospheric oxygen to give bis(2-pyridyl) disulfides, subsequent nucleophilic cleavage of the S–S bond by the isopropylidenemalononitrile anion, and cascade heterocyclization [6]. As a rule, the partially hydrogenated pyridine system remains unchanged during the reaction although, in some cases, the formation of oxidation products was noted [4, 5]. In a continuation of our investigation, we decided to study the behavior of readily available 5-acetyl-4-aryl-3-cyano-6-methyl-3,4-dihydropyridine-2(1H)-thiones **1a** and **1b** [7-11] under conditions for cyclocondensation with acetone and malononitrile.



B = N-methylmorpholine; **a** Ar = 2-ClC_6H_4; **b** Ar = 4-$O_2NC_6H_4$

We have found that dipyridothiophene derivatives are also formed during this reaction but, in contrast to other tetrahydropyridine derivatives [1-3], cyclocondensation in this case is accompanied by aromatization of the tetrahydropyridine ring. The structure of dipyridothiophenes **2a** and **2b** was supported by the spectroscopic data. We should also note that these products have a highly pronounced blue-green UV photoluminescence.

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The ^1H NMR spectra were taken on a Varian Gemini 200 spectrometer at 200 MHz in DMSO-d_6 with TMS as the internal standard. The IR spectra were taken on an IKS-29 spectrometer for vaseline mulls.

Dipyridothiophenes 2a,b. N-Methylmorpholine (1 ml, 9 mmol) was added to a mixture of corresponding thiolactam **1a**,**b** (8 mmol), malononitrile (0.8 g, 12 mmol), and acetone (5.9 ml, 80 mmol) in ethanol (30 ml), heated at reflux for 15 h with stirring, and left for 72 h at ~20°C. The crystalline product was separated and recrystallized from the indicated solvent.

8-Acetyl-2-amino-9-(2-chlorophenyl)-4,7-dimethylpyrido[2',3':4,5]thieno[2,3-*b*]pyridine-3-carbonitrile- (2a) was obtained in 36% yield as yellow crystals; mp 340-342°C (dec., DMF). IR spectrum, ν, cm^{-1}: 1695 (C=O); 2213 (C≡N); 3345, 3450 (NH_2). ^1H NMR spectrum, δ, ppm: 7.56-7.19 (4H, m, Ar); 5.94 (2H, br. s, NH_2); 2.62 and 2.61 (3H each, both s, 4-CH_3 and 7-CH_3); 2.14 (3H, s, C(O)CH_3). Found, %: C 61.60; H 3.74; N 13.87. $C_{21}H_{15}ClN_4OS$. Calculated, %: C 61.99; H 3.72; N 13.77.

8-Acetyl-2-amino-4,7-dimethyl-9-(4-nitrophenyl)pyrido[2',3':4,5]thieno[2,3-*b*]pyridine-8-carbonitrile (2b) was obtained in 20% yield; mp 310-313°C (dec., 4:1 AcOH–DMF). IR spectrum, ν, cm^{-1}: 1698 (C=O); 2218 (C≡N); 3360, 3450 (NH_2). ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 8.26 (2H, d, $^3J = 8.6$, H-3, H-5 Ar); 7.48 (2H, d, $^3J = 8.6$, H-2, H-6 Ar); 6.28 (2H, br. s, NH_2); 2.59 and 2.57 (3H each, both s, 4-CH_3 and 7-CH_3); 2.09 (3H, s, C(O)CH_3). Found, %: C 60.04; H 3.63; N 16.83. $C_{21}H_{15}N_5O_3S$. Calculated, %: C 60.42; H 3.62; N 16.76.

REFERENCES

1. V. V. Dotsenko, S. G. Krivokolysko, V. P. Litvinov, and A. N. Chernega, *Izv. Akad. Nauk, Ser. Khim.*, 339 (2002).
2. V. V. Dotsenko, S. G. Krivokolysko, A. N. Chernega, and V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 918 (2003).
3. V. V. Dotsenko, S. G. Krivokolysko, and V. P. Litvinov, in: *Abstracts of International Conference on the Chemistry of Nitrogen-Containing Heterocycles CNCH-2003*, Kharkov, Ukraine, p. 48.
4. V. V. Dotsenko, S. G. Krivokolysko, and V. P. Litvinov, *Mendeleev Commun.*, **13,** 267 (2003).
5. V. V. Dotsenko, S. G. Krivokolysko, and V. P. Litvinov, *Vestn. Moskovsk. Gos. Univ., Ser. 2, Khim.*, **46**, No. 5, 304 (2005).
6. V. V. Dotsenko, S. G. Krivokolysko, and V. P. Litvinov, *Mendeleev Commun.*, **14,** 30 (2004).
7. A. A. Krauze, Yu. E. Pelcher, Z. A. Kalme, and G. Ya. Dubur, *Khim. Geterotsikl. Soedin.*, 1694 (1984). [*Chem. Heterocycl. Comp.*, **20**, 1400 (1984)].
8. Yu. A. Sharanin, L. A. Rodinovskaya, V. P. Litvinov, V. K. Promonenkov, V. Yu. Mortikov, and A. M. Shestopalov, *Zh. Org. Khim.*, **21**, 683 (1985).
9. A. A. Krauze, R. O. Vitolinya, M. R. Romanova, and G. Ya. Dubur, *Khim.-Farm. Zh.*, **22**, 955 (1988).
10. F. A. Attaby, S. M. Eldin, W. M. Bassyouni, and M. A. A. Elneairy, *Phosphorus, Sulfur, Silicon, Relat. Elem.*, **119**, 1 (1996).
11. A. Krauze and G. Duburs, *Khim. Geterotsikl. Soedin.*, 794 (2000). [*Chem. Heterocycl. Comp.*, **36**, 693 (2000)].