Letters to the Editor

First multicomponent synthesis of tricyclic hydrogenated pyridines

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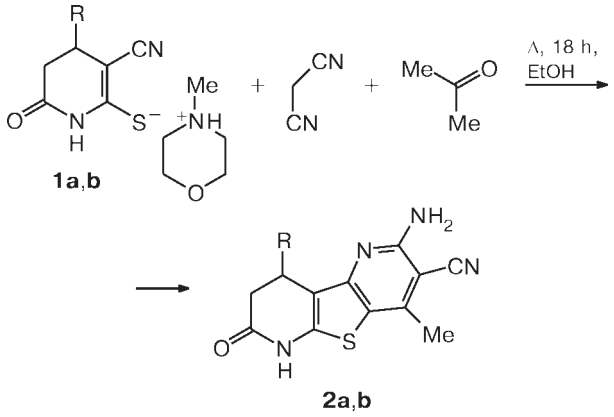
The only known method for the synthesis of tricyclic hydrogenated pyridines is the reaction of piperidinium 3-cyano-1,4-dihydropyridine-2-thiolates with difficultly accessible alkylating agents such as 2-bromo-1-(4-bromophenyl)ethylidenemalononitrile and *N*-cyanochloroacetamidine.[1]

We found that a multicomponent reaction of *N*-methylmorpholinium tetrahydropyridine-6-thiolates **1a**,**b** [2] with malononitrile and acetone affords the corresponding thienodipyridines **2a**,**b**.



R = 2-ClC$_6$H$_4$ (**a**); 2,3-(MeO)$_2$C$_6$H$_3$ (**b**)

The structure of compound **2a** was unambiguously determined by X-ray diffraction analysis (Fig. 1, Table 1). The bicyclic S(1)N(2)C(4—10) system is planar (the atoms deviate from the mean-square plane by no more than 0.033 Å; the dihedral angle between the five- and six-membered rings is only 2.2°). At the same time, the N(1)C(1—5) ring is essentially non-planar and has the half-boat conformation (the Cramer—Pople modified parameters[3] S, θ, and ψ are 0.61, 52.0, and 25.1°, respectively). The N(1) and N(3) atoms have a planar trigonal bond configuration (the sum of the bond angles at these atoms is 360° within the experimental error). Bond lengths and angles in **2a** have standard values.[4]

In crystal, the molecules of compound **2a** are united into infinite chains through the O(2)—H(2)...N(2), N(1)—H(1)...O(2), and N(3)—H(3)...O(1) hydrogen bonds involving the solvation EtOH molecules (Fig. 2). Their main geometrical parameters (bond lengths and angles): O(2)...N(2), N(2)...H(2), and O(2)—H(2) are 2.801(7), 1.77(8), and 1.04(8) Å, respectively, O(2)—H(2)—N(2) 169(4)°; O(2)...N(1), O(2)...H(1), and N(1)—H(1) are 2.733(8), 1.93(8), and 0.84(6) Å, respectively, O(2)—H(1)—N(1) 158(4)°; O(1)...N(3), O(1)...H(3), and N(3)—H(3) are 2.952(5), 2.28(5), and 0.77(4) Å, respectively, O(1)—H(3)—N(3) 147(3)°.

The study of the reaction mechanism is in progress.

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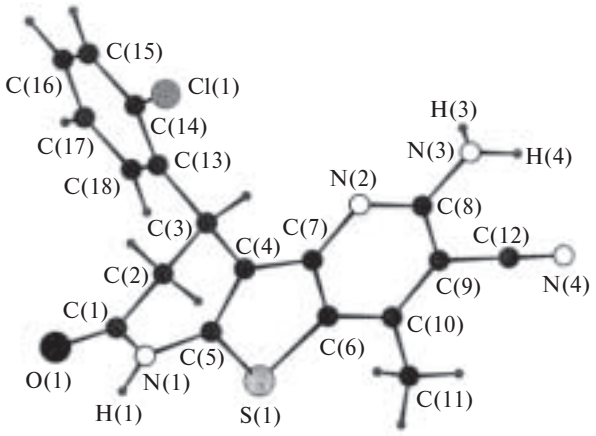

Fig. 1. General view of molecule **2a**.

Table 1. Selected bond lengths (*d*) and angles (ω) in molecule **2a**

Bond	*d*/Å	Angle	ω/deg
Cl(1)—C(14)	1.738(4)	C(5)—S(1)—C(6)	89.60(1)
S(1)—C(5)	1.724(4)	C(1)—N(1)—C(5)	120.9(4)
S(1)—C(6)	1.743(4)	C(7)—N(2)—C(8)	116.6(3)
O(1)—C(1)	1.221(5)	N(1)—C(1)—C(2)	116.4(4)
N(1)—C(1)	1.361(6)	C(1)—C(2)—C(3)	113.5(4)
N(1)—C(5)	1.384(5)	C(2)—C(3)—C(4)	107.6(3)
N(2)—C(7)	1.363(5)	C(3)—C(4)—C(5)	119.3(4)
N(2)—C(8)	1.337(5)	C(5)—C(4)—C(7)	110.5(4)
N(3)—C(8)	1.353(5)	S(1)—C(5)—C(4)	115.3(3)
N(4)—C(12)	1.139(5)	N(1)—C(5)—C(4)	123.4(4)
C(1)—C(2)	1.508(6)	S(1)—C(6)—C(7)	111.8(3)
C(2)—C(3)	1.543(6)	C(7)—C(6)—C(10)	121.5(4)
C(3)—C(4)	1.503(5)	N(2)—C(7)—C(6)	122.8(4)
C(4)—C(5)	1.362(5)	C(4)—C(7)—C(6)	112.8(3)
C(4)—C(7)	1.424(6)	N(2)—C(8)—C(9)	122.2(4)
C(6)—C(7)	1.397(5)	C(8)—C(9)—C(10)	121.3(4)
C(6)—C(10)	1.375(6)	C(10)—C(9)—C(12)	120.0(4)
C(8)—C(9)	1.417(5)	C(6)—C(10)—C(9)	115.5(4)
C(9)—C(10)	1.390(6)	N(4)—C(12)—C(9)	179.2(5)

^{1}H NMR spectra were recorded on a Gemini 200 instrument (200 MHz) in DMSO-d_6 with Me_4Si as the internal standard. IR spectra were recorded on an IKS-29 spectrophotometer (Nujol). Elemental analyses were carried out on a Perkin—Elmer C,H,N-analyser instrument. The reaction course was monitored, and the purity of the compounds obtained was checked, by TLC on Silufol UV-254 plates in acetone—hexane (3 : 5); spots were visualized with iodine vapor. The melting points were determined on a Kofler stage.

Synthesis of tetrahydropyridothienopyridines 2a,b (general procedure). A solution of salt **1a** or **1b** (8.2 mmol), malononitrile (0.81 g, 12.3 mmol), and acetone (6 mL, 82 mmol) in 35 mL of EtOH was refluxed for 18 h. The reaction mixture was kept at ~20 °C for 24 h, and the crystalline product was filtered off, washed three times with EtOH, and recrystallized from an appropriate solvent.

2-Amino-9-(2-chlorophenyl)-3-cyano-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (2a).

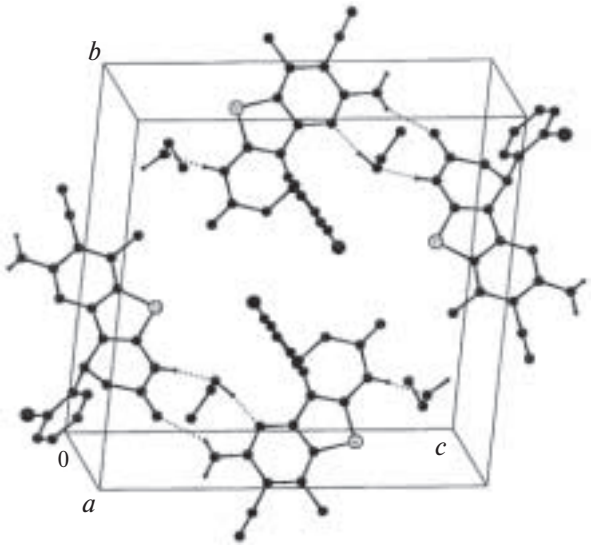

Fig. 2. Crystal packing of compound **2a · EtOH** (the intermolecular hydrogen bonds are shown in dotted line).

Yield 37%, m.p. 283—285 °C (from AcOH—EtOH, 3 : 2). Found (%): C, 58.91; H, 3.57; N, 15.24. $C_{18}H_{13}ClN_4OS$. Calculated (%): C, 58.62; H, 3.55; N, 15.19. IR, ν/cm^{-1}: 3465, 3320—3100 (NH, NH_2); 2211 (CN); 1689 (C=O). ^{1}H NMR, δ: 2.54 (s, 3 H, Me); 2.70, 3.13 (both m, each 1 H, C(8)H_2); 4.84 (br.d, 1 H, H(9), ^3J = 7.6 Hz); 6.28 (br.s, 2 H, NH_2); 6.67, 7.11—7.28, 7.47 (three m, 4 H, Ar); 11.15 (s, 1 H, NH).

2-Amino-3-cyano-9-(2,3-dimethoxyphenyl)-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (2b). Yield 36%, m.p. 332—334 °C (from AcOH). Found (%): C, 61.05; H, 4.63; N, 14.26. $C_{20}H_{18}N_4O_3S$. Calculated (%): C, 60.90; H, 4.60; N, 14.20. IR, ν/cm^{-1}: 3470, 3340, 3262 (NH, NH_2); 2206, 2187 sh (CN); 1689 (C=O). ^{1}H NMR, δ: 2.47 (s, 3 H, Me); 2.97—3.10 (m, 2 H, C(8)H_2); 3.80, 3.89 (both s, each 3 H, 2 MeO); 4.73 (br.d, 1 H, H(9), ^3J = 8.0 Hz); 6.08 (br.s, 2 H, NH_2); 6.27, 6.79 (both m, 3 H, Ar); 10.96 (s, 1 H, NH).

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