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SYNTHESIS AND CRYSTAL STRUCTURE OF 3,5-DICYANO-2,6-DIETHYLTHIOPYRIDINE

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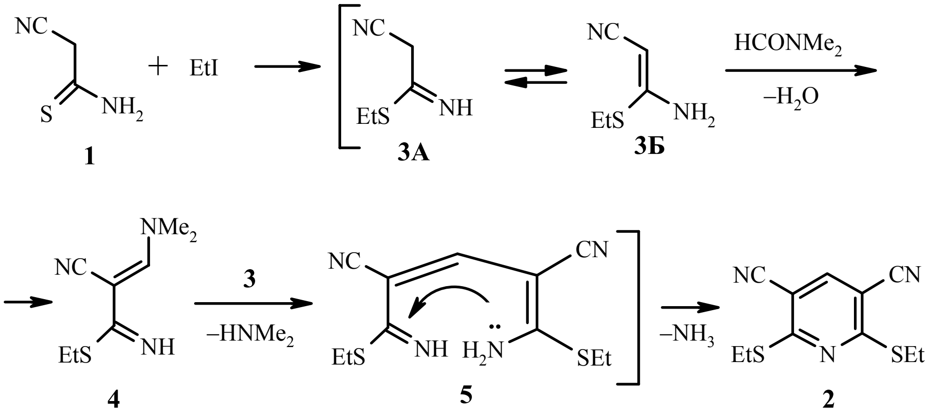
3,5-Dicyano-2,6-diethylthiopyridine has been synthesized by the alkylation of cyanothioacetamide with ethyl iodide in DMF and its molecular and crystal structures have been investigated.

Keywords: 3,5-dicyano-2,6-diethylthiopyridine, cyanothioacetamide, ethyl iodide, alkylation, X-ray structural analysis.

In the Michael synthesis of 3-cyanopyridine-2(1H)-thione derivatives cyanothioacetamide is successfully used as a CH-acid component [1-6]. In addition, only two studies are known, devoted to the preparation of substituted 4-oxoquinazolines, on its alkylation and use in organic synthesis of the corresponding S-alkylimidothioesterates both in the free state [7] and *in situ* [8].

In the present work it has been shown for the first time that the alkylation of cyanothioacetamide (**1**) with ethyl iodide in DMF at 18°C leads to 3,5-dicyano-2,6-diethylthiopyridine (**2**). The reaction pathway probably includes the formation of imine **3A**, capable of prototropic amino–imino tautomerism with enamine **3B**. Under the reaction conditions the latter condenses with DMF to give the corresponding enaminoimine **4**, interacting further with compound **3** according to Michael or by a type of nucleophilic vinyl substitution [9]. The resulting product **5** is converted into substituted pyridine **2** as a result of cyclocondensation [10].

The structure of compound **2** was confirmed by X-ray analysis. Two symmetrically independent molecules **A** and **B** are observed in the crystal of this pyridine (Table 1, Fig. 1).



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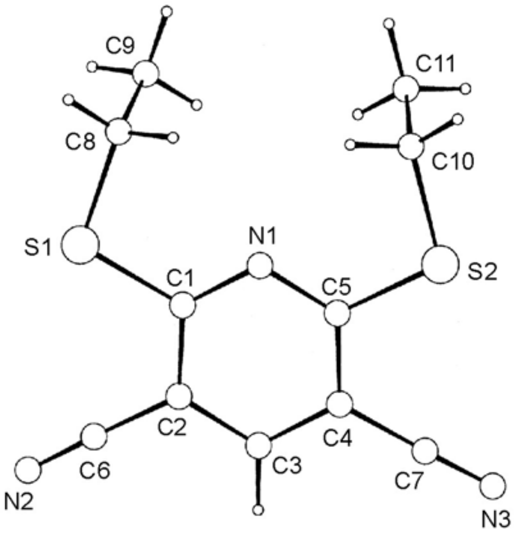

Fig. 1. General shape of the **2A** molecule with numbering of the atoms.

TABLE 1. Principal Bond Lengths (*d*) and Valence Angles (ω) in the **2A** and **2B** Molecules

Bond	*d*, Å		Angle	ω, deg.	
	2A	**2B**		**2A**	**2B**
$S_{(1)}$–$C_{(1)}$	1.745(3)	1.748(3)	$C_{(1)}$–$S_{(1)}$–$C_{(8)}$	102.61(14)	103.62(16)
$S_{(1)}$–$C_{(8)}$	1.809(3)	1.802(4)	$C_{(5)}$–$S_{(2)}$–$C_{(10)}$	103.49(15)	103.23(15)
$S_{(2)}$–$C_{(5)}$	1.749(3)	1.747(3)	$C_{(1)}$–$N_{(1)}$–$C_{(5)}$	119.2(2)	118.3(3)
$S_{(2)}$–$C_{(10)}$	1.810(3)	1.812(4)	$N_{(1)}$–$C_{(1)}$–$C_{(2)}$	121.9(2)	122.9(2)
$N_{(1)}$–$C_{(1)}$	1.334(4)	1.342(4)	$C_{(1)}$–$C_{(2)}$–$C_{(3)}$	118.9(3)	118.6 (3)
$N_{(1)}$–$C_{(5)}$	1.336(3)	1.342(4)	$C_{(2)}$–$C_{(3)}$–$C_{(4)}$	118.8(3)	118.9(3)
$C_{(1)}$–$C_{(2)}$	1.413(4)	1.404(4)	$C_{(3)}$–$C_{(4)}$–$C_{(5)}$	118.8(3)	119.2(2)
$C_{(2)}$–$C_{(3)}$	1.389(4)	1.386(4)	$N_{(1)}$–$C_{(5)}$–$C_{(4)}$	122.4(2)	122.1(3)
$C_{(3)}$–$C_{(4)}$	1.388(4)	1.386(4)			
$C_{(4)}$–$C_{(5)}$	1.408(4)	1.408(4)			

The pyridine ring in the **2A** and **2B** molecules is planar (the deviation of atoms from mean square planarity did not exceed 0.007 and 0.003 Å respectively). The $S_{(1)}$ and $S_{(2)}$ atoms emerge on the same side of the ring plane (by 0.030 and 0.039 Å in the **2A** molecule and 0.046 and 0.020 Å in the **2B** molecule). The ethyl substituents therefore have an almost orthogonal orientation relative to the pyridine ring by virtue of the steric conditions. The torsion angles $C_{(1)}$–$S_{(1)}$–$C_{(8)}$–$C_{(9)}$ and $C_{(5)}$–$S_{(2)}$–$C_{(10)}$–$C_{(11)}$ amount to 83.4 and -80.6° (**2A** molecule) and 84.1 and -80.4° (**2B** molecule). The geometric parameters in the groupings $C_{(1)}$–$S_{(1)}$–$C_{(9)}$ and $C_{(5)}$–$S_{(2)}$–$C_{(10)}$ are close to the corresponding parameters found in the Ph–S–Me molecule [S–C(sp^2) 1.749(4), S–C(sp^3) 1.803(4) Å, CSC 105.6(7)°] [11]. In the crystals of compound **2** the molecules are packed in such a manner that all the pyridine rings are parallel to one another (the dihedral angle between the pyridine systems of the **2A** and **2B** molecules was only 1.0°) and form a pseudo dimer of an **AA** and **BB** type (Fig. 2) with the corresponding distances between the pyridine rings of the dimeric pairs of 3.40 and 3,45 Å (which probably indicates the possibility of a π–π stacking interaction [12]). In each dimeric pair the ethyl substituents are directed to the side opposite to the center of gravity, thereby sterically hindering the formation of a stacked ordering in the crystal.

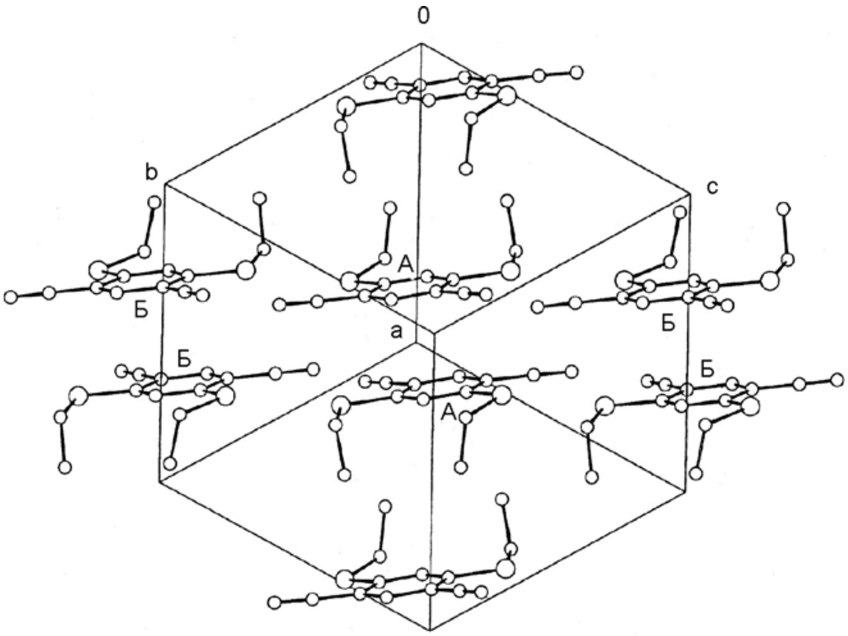

Fig. 2. Fragment of the crystal packing of compound **2**.

EXPERIMENTAL

X-ray Structural Investigation of a Compound 2 Monocrystal of linear dimensions 0.13 × 0.28 × 0.44 mm was carried out at room temperature on an automatic Enraf-Nonius four-circle CAD-4 diffractometer (Mo$K\alpha$ radiation, relative scanning rate $2\theta/\omega = 1.2$, $\theta_{max} = 27°$, segment of sphere $0 \leq h \leq 11$, $-12 \leq k \leq 12$, $-21 \leq l \leq 21$). In all 5805 reflections were taken of which 5442 were symmetrically independent ($R_{int} = 0.01$). The crystals of compound **2** were triclinic, $a = 8.854(1)$, $b = 9.740(1)$, $c = 16.654(3)$ Å; $\alpha = 84.21(1)$, $\beta = 75.15(1)$, $\gamma = 64.17(1)°$; $V = 1249.3(4)$ Å^3; M = 249.35; $Z = 4$; $d_{calc} = 1.32$ g/cm^3; $\mu = 3.84$ cm^{-1}; $F(000) = 520.9$; space group $P2_{1/}n$ (N 2). The structure was solved by the direct method and refined by the least squares method in a full-matrix anisotropic approach using the CRYSTALS set of programs [13]. In the refinement 2685 reflections with $I > 3(I)$ were used (289 parameters being refined, number of reflections per parameter 9.3). All the hydrogen atoms were made apparent from an electron density difference synthesis and were put into the refinement with fixed positional and thermal parameters. Calculation of the absorption in the crystal was carried out with the aid of the azimuthal scanning method of [14]. Chebyshev weighting factors [15] were used in the refinement with parameters 1.50, 1.37, and 1.11. Final values for reliability factors were $R = 0.043$ and $R_w = 0.047$, $GOF = 1.129$. The residual electron density from the Fourier difference series was 0.31 and -0.22 e/Å^3. The coordinates of the non-hydrogen atoms may be obtained from the author.

The IR spectrum of the synthesized compound **2** was recorded on an IKS 29 instrument in nujol. The ^{1}H NMR spectrum was recorded on a Bruker AM 300 (300 MHz) instrument in DMSO-d$_6$, internal standard was TMS. Mass spectra were obtained on a Kratos MS 890 spectrometer (70 eV). Melting points were determined on a Kofler block. A check on the progress of reactions was effected by TLC (Silufol UV 254, acetone–hexane, 3:5, visualizing with iodine vapor).

3,5-Dicyano-2,6-diethylthiopyridine (2). Ethyl iodide (1.61 ml, 20 mmol) was added to a solution of cyanothioacetamide **1** (2.00 g, 20 mmol) in DMF (15 ml) and the mixture was stirred for 5 h. After 48 h the reaction mixture was diluted with water (27 ml). The solid formed was filtered off, washed with water, with ethanol, and with hexane. Pyridine **2** was obtained as colorless needles in a yield of 1.67 g (67%); mp 132°C (ethanol). IR spectrum, ν, cm^{-1}: 2226 (C≡N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.41 (6H, t, *J* = 6.0, $2CH_3$); 3.34 (4H, q, *J* = 6.0, $2CH_2$); 8.49 (1H, s, $C_{(4)}H$). Mass spectrum, *m/z* (I_{rel}, %): 249 (100) $[M]^+$, 234 (15), 221 (44), 220 (58), 216 (43), 206 (32), 188 (79), 160 (38), 133 (24), 89 (49), 82 (26), 69 (37), 59 (51), 45 (77). Found, %: C 53.14; H 4.51; N 16.68. $C_{11}H_{11}N_3S_2$. Calculated, %: C 52.99; H 4.45; N 16.85.

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