Brief Communications

Synthesis and structure of 6-amino-3,5-dicyano-4-heptylpyridine-2(1*H*)-thione

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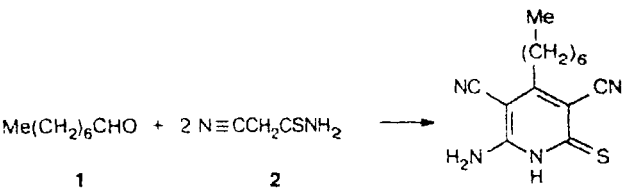
Condensation of caprylic aldehyde with cyanothioacetamide taken in a ratio of 1 : 2 affords 6-amino-3,5-dicyano-4-heptylpyridine-2(1*H*)-thione. The structure of the thione was studied by X-ray structural analysis.

Key words: caprylic aldehyde, cyanothioacetamide, reaction; 3,5-dicyanopyridine-2(1*H*)-thione, X-ray structural analysis.

Functionally substituted 3-cyanopyridine-2(1*H*)-chalcogenones are convenient synthons for preparing biologically active compounds.[1–3] Their lipophilicity is of great importance in the search for new biologically active compounds. With the aim of increasing the solubility of 3-cyanopyridine-2(1*H*)-ones (thiones and selenones), procedures have been developed for the preparation of 6-(adamantyl-1)- [4–8] and 6-pentyl(pentenyl)-substituted derivatives.[9,10] Recently,[11,12] we have developed a convenient method for the preparation of 4-alkyl-6-amino-3,5-dicyano-4*H*-thiopyrans by condensation of aliphatic aldehydes with malononitrile and cyanothioacetamide.

In this work, we used an alternative approach to the synthesis of 6-amino-3,5-dicyano-4-heptylpyridine-2(1*H*)-thione (**3**) based on the condensation of caprylic aldehyde (**1**) with two moles of cyanothioacetamide (**2**) in ethanol in the presence of excess *N*-methylmorpholine at 20 °C, which makes it possible to increase the yield of compound **3** from 30 to 85%.



We carried out an X-ray structural analysis of thione **3**. The overall view of molecule **3** is shown in Fig. 1.

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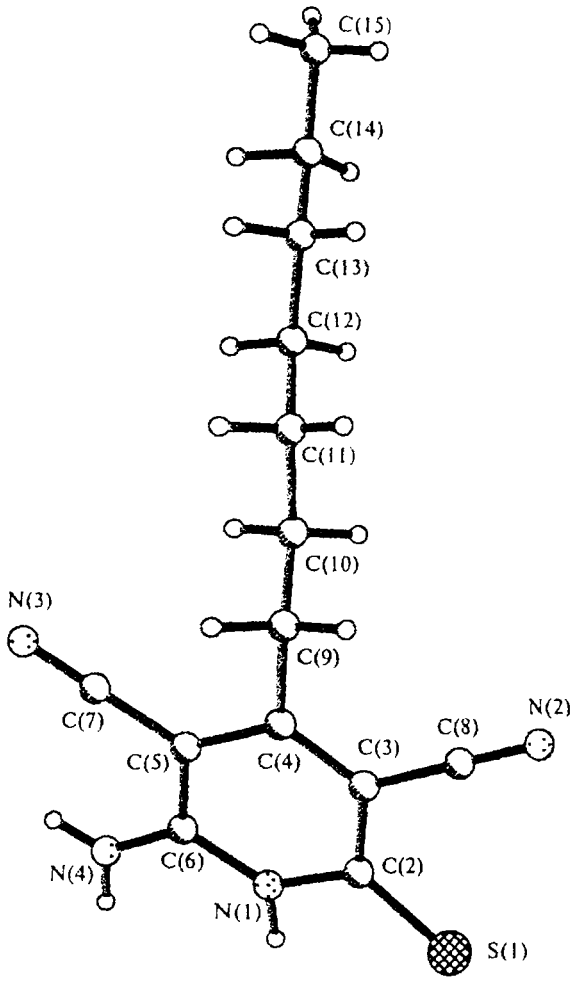

Fig. 1. Overall view of molecule 3 (the solvate ethanol molecules are omitted).

The bond lengths and bond angles are given in Tables 1 and 2, respectively.

As in the case of the related compounds studied previously,[13,14] the heterocycle in thione **3** is planar to within ±0.011 Å. This structure is favorable to conjugation between the ring and the substituents (CN, NH_2, and S), which is indicative of a substantial redistribution of the bond lengths both over the ring and among the ring and the corresponding fragment. The other geometric parameters of the compounds have standard values.[15]

In the crystals, molecules **3** are linked to solvate EtOH molecules (crystals were grown from ethanol) through the following intermolecular hydrogen bonds: N(1)—H(1)...O(1) (2 − *x*, −*y*, 1 − *z*) [N(1)...O(1), 2.80(1) Å; N(1)—H(1), 0.99(5) Å; H(1)...O(1), 1.98(5) Å; the N(1)—H(1)...O(1) angle is 139(5)°], N(4)—H(42)...O(1) (2 − *x*, −*y*, 1 − *z*) [N(4)...O(1), 3.01(1) Å; N(4)—H(42), 0.94(5) Å; H(42)...O(1), 2.30(5) Å; the N(4)—H(42)...O(1) angle is 132(5)°].

Table 1. Bond lengths (*d*) in molecule 3

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(2)	1.676(5)	C(4)—C(9)	1.527(7)
N(1)—C(2)	1.375(6)	C(5)—C(6)	1.419(7)
N(1)—C(6)	1.342(6)	C(5)—C(7)	1.429(8)
N(2)—C(8)	1.144(8)	C(9)—C(10)	1.507(8)
N(3)—C(7)	1.144(8)	C(10)—C(11)	1.511(8)
N(4)—C(6)	1.315(7)	C(11)—C(12)	1.47(1)
C(2)—C(3)	1.425(7)	C(12)—C(13)	1.48(1)
C(3)—C(4)	1.379(7)	C(13)—C(14)	1.39(2)
C(3)—C(8)	1.433(8)	C(14)—C(15)	1.38(2)
C(4)—C(5)	1.396(7)		

Table 2. Bond angles (ω) in molecule 3

Angle	ω/deg	Angle	ω/deg
C(2)—N(1)—C(6)	127.1(4)	N(1)—C(6)—N(4)	119.3(5)
S(1)—C(2)—N(1)	119.4(4)	N(1)—C(6)—C(5)	116.8(4)
S(1)—C(2)—C(3)	125.8(4)	N(4)—C(6)—C(5)	124.0(5)
N(1)—C(2)—C(3)	114.8(4)	N(3)—C(7)—C(5)	178.3(6)
C(2)—C(3)—C(4)	121.4(4)	N(2)—C(8)—C(3)	179.2(6)
C(2)—C(3)—C(8)	117.6(4)	C(4)—C(9)—C(10)	112.0(4)
C(4)—C(3)—C(8)	121.1(5)	C(9)—C(10)—C(11)	113.7(5)
C(3)—C(4)—C(5)	119.9(4)	C(10)—C(11)—C(12)	115.7(6)
C(3)—C(4)—C(9)	122.1(5)	C(11)—C(12)—C(13)	118.2(7)
C(5)—C(4)—C(9)	118.0(5)	C(12)—C(13)—C(14)	121.6(9)
C(4)—C(5)—C(6)	119.9(5)	C(13)—C(14)—C(15)	125.4(11)
C(4)—C(5)—C(7)	121.6(5)	O(1)—C(16)—C(17)	145.4(19)
C(6)—C(5)—C(7)	118.5(5)		

Experimental

IR spectra were recorded on an IKS-29 spectrophotometer in Nujol mulls. The identities of the compounds were monitored by TLC on Silufol UV-254 plates in an acetone—hexane system (3 : 5).

6-Amino-3,5-dicyano-4-heptylpyridine-2(1*H*)-thione (3). A suspension of caprylic aldehyde (**1**) (10 mmol), cyanothioacetamide (**2**) (20 mmol), and *N*-methylmorpholine (20 mmol) was stirred for 20 min (intense elimination of hydrogen sulfide was observed). The homogeneous reaction mixture was kept for 24 h, and then diluted with a 10% aqueous HCl solution until the pH became 4. The precipitate was filtered off and washed with ethanol and hexane. Thione **3** was obtained in a yield of 2.3 g (85%), m.p. 210—212 °C. IR, ν/cm^{-1}: 3300 (NH_2); 2200 (CN); 1648 (δNH_2). Based on the data of elemental analysis and the ^{1}H NMR spectra, thione **3** is identical to the product of the recyclization of 2,6-diamino-3,5-dicyano-4-heptyl-4*H*-thiopyran.[12]

X-ray structural analysis of compound 3. Crystals of **3** are monoclinic, at 20 °C *a* = 10.389(4) Å, *b* = 16.468(6) Å, *c* = 11.098(4) Å, β = 98.42(3)°, *V* = 1878(2) Å^3, d_{calc} = 1.417 g cm^{-3}, *Z* = 4, space group *P*2/*n*. The unit cell parameters and intensities of 3309 independent reflections were measured on an automated four-circle Siemens P3/PC diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ-scanning technique to θ_{max} = 26°). The structure was solved by the direct method, which revealed all nonhydrogen atoms, and refined by the full-matrix least-squares method

Table 3. Atomic coordinates ($\times 10^4$) in the structure of 3

Atom	x	y	z
S(1)	7980(1)	−589(1)	9600(1)
O(1)	10360(6)	-1840(3)	2970(4)
N(1)	9505(4)	−266(2)	7958(4)
N(2)	7424(5)	1573(3)	10372(5)
N(3)	11138(5)	1859(3)	5715(5)
N(4)	10855(4)	−243(3)	6498(4)
C(2)	8756(4)	46(3)	8772(4)
C(3)	8717(4)	911(3)	8819(4)
C(4)	9351(5)	1382(3)	8064(5)
C(5)	10066(5)	1012(3)	7243(4)
C(6)	10170(4)	154(3)	7214(4)
C(7)	10678(5)	1477(3)	6400(5)
C(8)	7995(5)	1274(3)	9685(5)
C(9)	9336(5)	2308(3)	8114(5)
C(10)	10582(6)	2646(3)	8796(6)
C(11)	10642(7)	3563(4)	8802(7)
C(12)	11872(8)	3918(4)	9385(8)
C(13)	11947(10)	4808(6)	9527(11)
C(14)	13058(12)	5188(6)	10126(14)
C(15)	13212(13)	6014(10)	10295(16)
C(16)	9897(20)	2587(7)	2713(11)
C(17)	10155(9)	3236(5)	2572(8)

with anisotropic temperature factors for all nonhydrogen atoms using 1808 reflections with $I > 4\sigma(I)$. The H(1), H(41), and H(42) atoms were revealed from the difference Fourier maps. The positions of the other hydrogen atoms were calculated geometrically (the hydrogen atom of the OH group was not located). Because of the high thermal parameters, the H atoms were included in the refinement with the fixed positional and thermal parameters ($U = 0.08$ Å^2). The final values of the R factors were as follows: $R = 0.067$, $R_w = 0.067$ ($S = 1.1212$). All calculations were carried out using the SHELXTL PLUS program[16] (the PC Version). The coordinates of nonhydrogen atoms are given in Table 3.

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