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# SYNTHESIS AND CRYSTAL STRUCTURE OF 3-ETHOXYCARBONYL-4,6-DIPHENYL-3,4-DIHYDROPYRIDINE-2(1H)-THIONE

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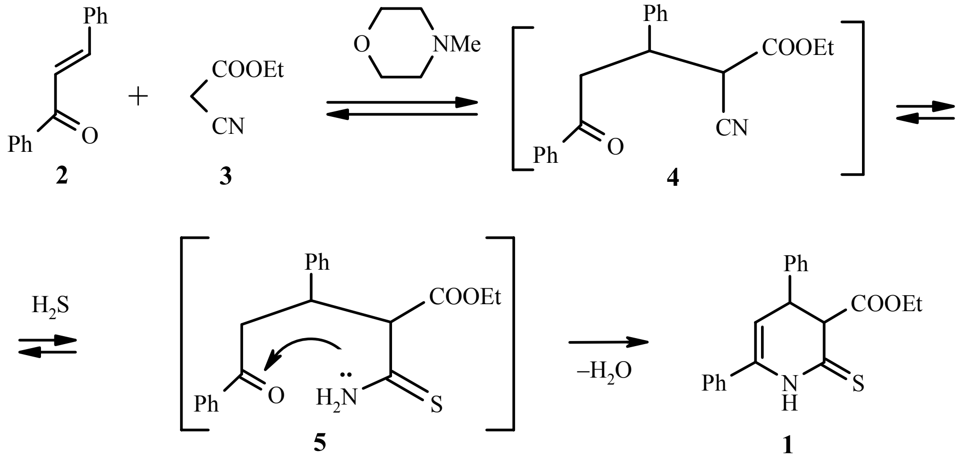
*3-Ethoxycarbonyl-4,6-diphenyl-3,4-dihydropyridine-2(1H)-thione was synthesized by the interaction of benzylideneacetophenone with cyanoacetic ester and hydrogen sulfide. Its structure was investigated by X-ray structural analysis.*

**Keywords:** benzylideneacetophenone, 3-ethoxycarbonyl-4,6-diphenyl-3,4-dihydropyridine-2(1H)-thione, cyanoacetic ester, X-ray structural analysis.

Condensation of 1,3-diaryl-2-propen-1-ones with cyanoacetic ester catalyzed by ammonium acetate leads to 4,6-diaryl-3-cyanopyridine-2(1H)-ones [1-4]. We have discovered that in this reaction the use of N-methylmorpholine as catalyst and bubbling hydrogen sulfide through the reaction mixture enabled 3-ethoxycarbonyl-4,6-diphenyl-3,4-dihydropyridine-2(1H)-thione (**1**) to be obtained. We note that the analogous methyl ester, 3-methoxycarbonyl-4,6-diphenyl-3,4-dihydropyridine-2(1H)-thione, was recently obtained on condensing benzylideneacetophenone (chalcone) with thiocarbamoylacetic acid methyl ester in the presence of piperidine [5].

The reaction route probably includes Michael addition of cyanoacetic ester **3** to 1,3-diphenyl-3-propen-1-one (**2**) with the formation of adduct **4**. Addition of hydrogen sulfide to the cyano group then follows, leading to thioamide **5**. This regioselective intramolecular cyclocondensation is the final stage of the reaction forming dihydropyridinethione **1**.



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The structure of compound **1** was established by X-ray structural analysis (Fig. 1 and Table 1).

The central six-membered heterocycle $N_{(1)}C_{(1,3\text{-}6)}$ is markedly nonplanar (the deviation of atoms from the mean square planarity reaches 0.31 Å) and has a conformation intermediate between *half-boat* and *half-chair* (modified Cremer–Pople parameters [6] $S$, $\theta$, and $\psi$ were 0.64, 47.8°, and 18.7° respectively). The $N_{(1)}$ atom is characterized by a plane-trigonal configuration of bonds (within the limits of experimental error the sum of the valence angles was 360°). The $N_{(1)}$–$C_{(1)}$ bond of 1.336(2) and the $N_{(1)}$–$C_{(3)}$ bond of 1.415(2) Å are shortened somewhat in comparison with the value of 1.45 Å for pure single $N(sp^2)$–$C(sp^2)$ bonds [7], which is probably caused by $p$-$\pi$-conjugation between the unshared electron pair of the $N_{(1)}$ atom and the $C_{(1)}$=$S_{(1)}$ and $C_{(3)}$=$C_{(4)}$ double bonds. In reality, the molecular conformation is fully in favor of such interactions (torsion angles $C_{(3)}$–$N_{(1)}$–$C_{(1)}$–$S_{(1)}$ and $C_{(1)}$–$N_{(1)}$–$C_{(3)}$–$C_{(4)}$ are 171.7 and -12.1°).

In the crystal the molecules of compound **1** form endless chains due to intermolecular hydrogen bonds $N_{(1)}$–$H_{(1)}\cdots O_{(1)}$ of moderate stability (Fig. 2). The main geometric parameters of these chains are $N_{(1)}$–$H_{(1)}$ 0.91(2), $N_{(1)}\cdots O_{(1)}$ 2.890(2), $O_{(1)}\cdots H_{(1)}$ 2.01(2) Å, $N_{(1)}H_{(1)}O_{(1)}$ 161.4(1.3)°. The mean statistical value of the N···O distance for hydrogen bonds of the N–H···O type is 2.89 Å [8].

TABLE 1. Main Bond Lengths ($d$) and Valence Angles ($\omega$) in the Compound **1** Molecule

| Bond | $d$, Å | Angle | $\omega$, deg. |
|---|---|---|---|
| $S_{(1)}$–$C_{(1)}$ | 1.647(2) | $C_{(7)}$–$O_{(2)}$–$C_{(8)}$ | 116.96(18) |
| $O_{(1)}$–$C_{(7)}$ | 1.197(2) | $C_{(1)}$–$N_{(1)}$–$C_{(3)}$ | 124.62(16) |
| $O_{(2)}$–$C_{(7)}$ | 1.325(2) | $N_{(1)}$–$C_{(1)}$–$C_{(6)}$ | 113.88(16) |
| $O_{(2)}$–$C_{(8)}$ | 1.459(3) | $N_{(1)}$–$C_{(3)}$–$C_{(4)}$ | 119.77(16) |
| $N_{(1)}$–$C_{(1)}$ | 1.336(2) | $N_{(1)}$–$C_{(3)}$–$C_{(16)}$ | 115.48(16) |
| $N_{(1)}$–$C_{(3)}$ | 1.415(2) | $C_{(4)}$–$C_{(3)}$–$C_{(16)}$ | 124.68(17) |
| $C_{(1)}$–$C_{(6)}$ | 1.513(3) | $C_{(3)}$–$C_{(4)}$–$C_{(5)}$ | 121.25(16) |
| $C_{(3)}$–$C_{(4)}$ | 1.328(3) | $C_{(4)}$–$C_{(5)}$–$C_{(6)}$ | 107.78(16) |
| $C_{(4)}$–$C_{(5)}$ | 1.501(3) | $C_{(1)}$–$C_{(6)}$–$C_{(5)}$ | 111.89(15) |
| $C_{(5)}$–$C_{(6)}$ | 1.545(3) | | |

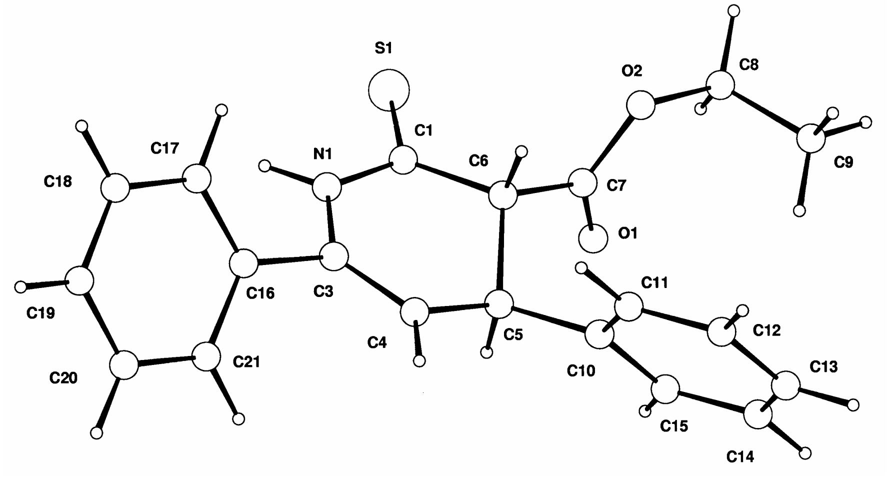

Fig. 1. Overall form of the molecule of **1** with numbering of atoms.

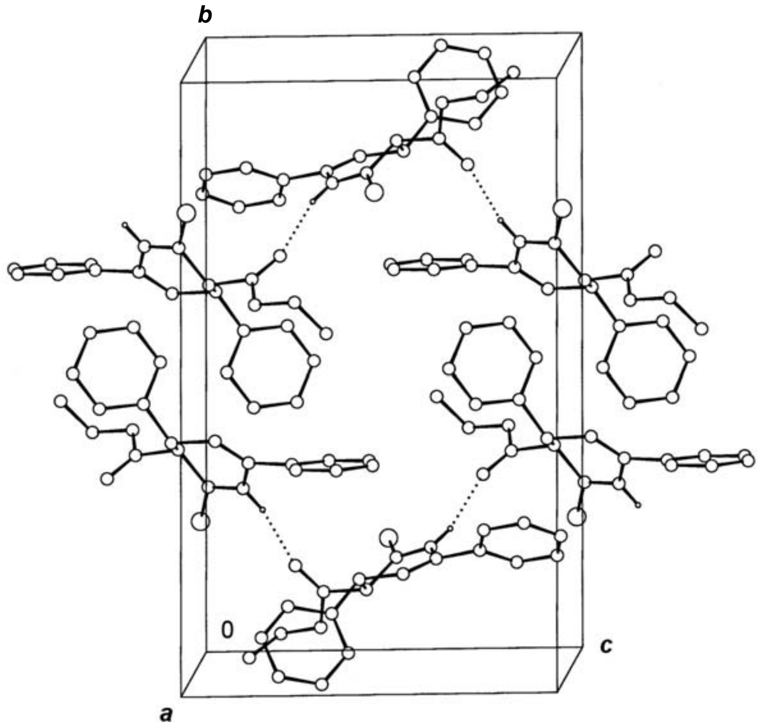

Fig. 2. Crystal packing of compound **1** (dotted lines denote intermolecular hydrogen bonds).

## EXPERIMENTAL

**X-ray Structural Investigation** of a monocrystal of dihydropyridine **1** with linear dimensions 0.25 × 0.38 × 0.47 mm was carried out at room temperature on an Enraf-Nonius CAD-4 automatic four-circle diffractometer (CuK$\alpha$ radiation, relative scanning rate $2\theta/\omega = 1.2$, $\theta_{max} = 60°$, segment of sphere $0 \leq h \leq 9$, $0 \leq k \leq 21$, $-12 \leq l \leq 12$). Overall 3027 reflections were collected, of which 2717 were symmetrically independent ($R_{int}$ = 0.017). Crystals of compound **1** were monoclinic, $a$ = 8.316(7), $b$ = 19.329(9), $c$ = 11.655(11) Å; $\beta$ = 99.25(6)°; $V$ = 1849.1(x) Å$^3$; M = 347.43; $Z$ = 4; $d_{calc}$ = 1.25 g/cm$^3$; $\mu$ = 16.1 cm$^{-1}$; $F$(000) = 715.0; space group $P2_1/c$. The structure was solved by the direct method and refined by the method of least squares in a full matrix anisotropic approach using the CRYSTALS set of programs [9]. In the refinement 2358 reflections with $I > 3(I)$ were used (221 parameters being refined, number of reflections per parameter 10.7). All the hydrogen atoms were revealed by an electron density difference synthesis and included in the refinement with fixed positional and thermal parameters (only atom $H_{(1)}$, participating in the formation of a hydrogen bond, was refined isotropically). Calculation of the absorption in the crystal was carried out with the aid of the azimuthal scanning method of [10]. In the refining the weighting factor method of Chebyshev [11] was used with parameters 3.34, -0.28, 2.62, -0.54, and 0.56. The final values for the reliability factors were $R$ = 0.039 and $R_W$ = 0.043, $GOF$ = 1.109. The residual electron density from the Fourier difference series was 0.21 and -0.26 e/Å$^3$. The coordinates of the non-hydrogen atoms may be obtained from the author.

The IR spectrum of the synthesized compound **1** was recorded on a 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. The melting point was determined on a Kofler block. A check on the course of reaction was effected by TLC (Silufol UV-254, acetone–hexane, 3:5, visualization with iodine vapor).

**3-Ethoxycarbonyl-4,6-diphenyl-3,4-dihydropyridine-2(1H)-thione (1).** N-Methylmorpholine (3 drops) was added to a mixture of chalcone **2** (4.16 g, 20 mmol) and cyanoacetic ester **3** (2.13 ml, 20 mmol) in absolute ethanol (25 ml). The mixture was stirred for 0.5 h. Hydrogen sulfide was then bubbled through the reaction mixture for 1 h, and the mixture was then stored in the refrigerator. After 1 day the solid formed was filtered off, washed with ethanol, and with hexane. Dihydropyridine **1** (3.89 g, 62%) was obtained as yellow crystals; mp 133°C (EtOH). IR spectrum, ν, $cm^{-1}$: 3266 (NH), 1730 (C=O). $^1H$ NMR spectrum, δ, ppm, (*J*, Hz): 1.07 (3H, t, $J = 6.9$, $CH_3$); 4.08 (1H, d, $J = 4.8$, $C_{(3)}H$); 4.02 (2H, q, $J = 6.9$, $CH_2$); 4.05 (1H, m, $C_{(4)}H$); 5.86 (1H, d, $J = 4.8$, $C_{(5)}H$); 2.23-7.56 (10H, m, $2C_6H_5$); 11.97 (1H, br. s, NH). Found, %: C 69.14; H 5.87; N 4.62. $C_{18}H_{19}NO_2S$. Calculated, %: C 68.98; H 6.11; N 4.47.

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