# Cyanothioacetamide in the synthesis of spiro-fused hydrogenated quinolinethiones

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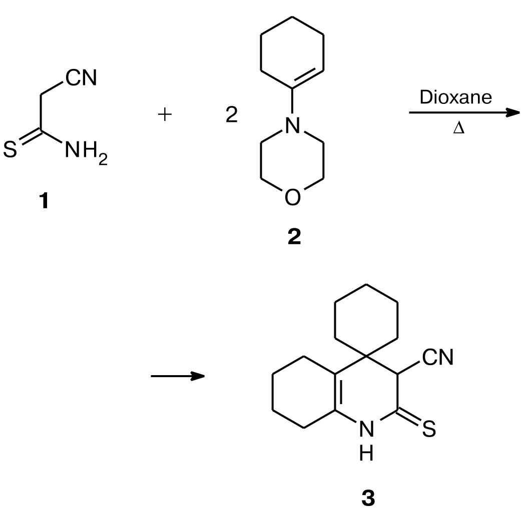
The reaction of cyanothioacetamide with a twofold molar excess of 1-(4-morpholino)cyclohexene in dry dioxane afforded previously unknown 3-cyano-4-cyclohexanespiro-1,2,3,4,5,6,7,8-octahydroquinoline-2-thione. Its structure was established by X-ray diffraction analysis and IR and $^1$H NMR spectroscopy.

**Key words:** cyanothioacetamide, 1-(4-morpholino)cyclohexene, spiroquinolinethione, X-ray diffraction analysis.

Cyanothioacetamide (**1**) is widely and successfully used as a simple and readily accessible reagent in the synthesis of partially hydrogenated pyridinethiones, including spiro-fused derivatives.[1] However, data on the use of **1** in the synthesis of derivatives of spiro-fused quinolinethiones, which are promising biologically active compounds, are lacking in the literature. For this purpose, we have earlier used[2] the reaction of dimedone with a rather complex derivative of **1**, *viz.*, cyclohexylidenecyanothioacetamide.

We found that refluxing of amide **1** with a twofold molar amount of 1-(4-morpholino)cyclohexene (**2**) afforded previously unknown 3-cyano-4-cyclohexane-spiro-1,2,3,4,5,6,7,8-octahydroquinoline-2-thione (**3**) (Scheme 1). The aim of our further investigation is to study the synthetic potential of this reaction and elucidate its mechanism.

**Scheme 1**



The structure of compound **3** was established by X-ray diffraction analysis. The overall view of molecule **3** is shown in Fig. 1. The principal bond lengths/Å and bond angles/deg are as follows: S(1)—C(1), 1.662(4); N(1)—C(1), 1.335(5); N(1)—C(5), 1.416(4); C(1)—C(2), 1.513(5); C(2)—C(3), 1.561(5); C(3)—C(4), 1.530(5); C(4)—C(5), 1.334(5); N(2)—C(15), 1.138(6); C(1)—N(1)—C(5), 124.7(3); N(1)—C(1)—C(2), 114.5(3); C(1)—C(2)—C(3), 111.7(3); C(2)—C(3)—C(4), 106.7(3); C(3)—C(4)—C(5), 119.5(3), N(1)—C(5)—C(4) 120.1(3). The N(1) atom has a planar-trigonal configuration to within the experimental error (sum of the bond angles at this atom is 359.2°). The molecular conformation allows the efficient conjugation between the lone electron pair of this atom and the π systems of the C(1)=S(1) and C(4)=C(5) double bonds. The S(1)—C(1)—N(1)—C(5) and C(1)—N(1)—C(5)—C(4) torsion angles are −178.7 and 17.4°, respectively. The N(1)—C(1) (1.335(5) Å) and N(1)—C(5) (1.416(4) Å) bonds are noticeably shortened

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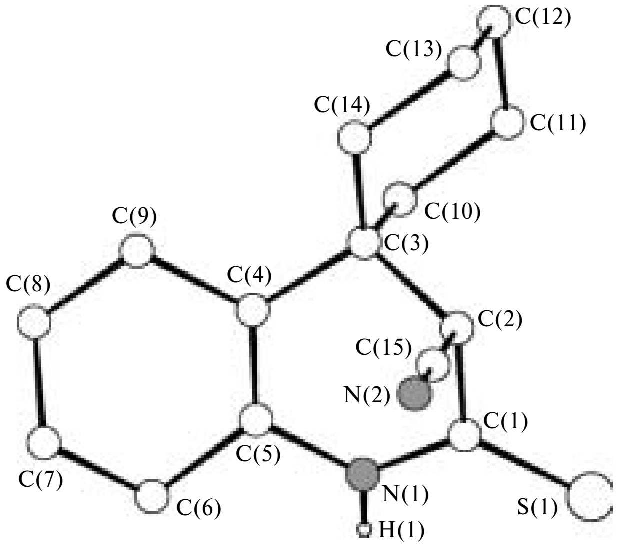

**Fig. 1.** Overall view of molecule **3**.

compared to the standard N(sp$^2$)—C(sp$^2$) single bond (1.45 Å).[3] The N(1)—C(1)—C(2)—C(3)—C(4)—C(5) and C(4)—C(5)—C(6)—C(7)—C(8)—C(9) rings adopt half-boat conformations (modified Cremer—Pople parameters[4] for these rings are $S = 0.66$ and 0.60, $\theta = 52.1°$ and 36.2°, $\Psi = 27.8°$ and 23.18°, respectively). The C(3)—C(10)—C(11)—C(12)—C(13)—C(14) cyclohexane system adopts a chair conformation ($S = 1.12$, $\theta = 1.2°$, $\Psi = 20.0°$). In the crystals of compound **3**, the molecules are linked in centrosymmetrical dimers through the intermolecular N(1)—H(1)...S(1) hydrogen bonds (N(1)—H(1), 0.85(4) Å; N(1)...S(1), 3.357(4) Å; S(1)...H(3), 2.53(3) Å; N(1)—H(1)—S(1), 165(2)°) (Fig. 2).

## Experimental

The $^1$H NMR spectra were recorded on a Gemini 200 instrument (200 MHz) in DMSO-d$_6$ with Me$_4$Si as the internal standard. The IR spectra were measured on an IKS-29 spectrophotometer in Nujol mulls. Elemental analysis was carried out on a Perkin—Elmer C,H,N-analyzer instrument. The course of the reaction and the purity of thione **3** were monitored by TLC on Silufol UV-254 plates in the 3 : 5 acetone—hexane system; visualization was carried out with iodine vapor. The melting point was measured on a Kofler stage.

**3-Cyano-4-cyclohexanespiro-1,2,3,4,5,6,7,8-octahydroquinoline-2-thione (3).** A mixture of cyanothioacetamide (**1**) (2.5 g, 25 mmol) and 1-(4-morpholino)cyclohexene (**2**) (8.2 mL, 50 mmol) in dioxane (28 mL) predried over KOH was refluxed for 20 h. The reaction mixture was treated with water. After 24 h, the solution was decanted to obtain a resinous residue, to which EtOH (5 mL) cooled to −5 °C was added. Then the reaction mixture was kept in a refrigerator at 8 °C for 1 h. The precipitate that formed was filtered off, washed with cooled EtOH, and dried at 60 °C. Quinolinethione **3** was obtained as pale-yellow crystals in a yield of 0.78 g (12%), m.p. 192—193 °C. Found (%): C, 69.31; H, 7.77; N, 10.84. $C_{15}H_{20}N_2S$. Calculated (%): C, 69.19; H, 7.74; N, 10.76. IR, ν/cm$^{-1}$: 3520—3290 (NH); 2238 (CN). $^1$H NMR, δ: 1.25—1.67 and 2.05—2.15 (both m, 18 H, (CH$_2$)$_9$); 4.21 (s, 1 H, C(3)H); 11.58 (s, 1 H, NH).

**Single-crystal X-ray diffraction study** of compound **3** of dimensions 0.16×0.34×0.44 mm was carried out on an automated four-circle Enraf—Nonius CAD-4 diffractometer (Mo-Kα radiation, the ratio between the scan rates $2\theta/\omega = 1.2$, $\theta_{max} = 27°$, the segment of the sphere $0 \le h \le 9$, $-10 \le k \le 10$, $-15 \le l \le 15$) at ~20 °C. A total of 3360 reflections were measured of which 3119 reflections were symmetrically independent ($R_{int} = 0.035$). The crystals of compound **3** belong to the triclinic system, $a = 7.615(3)$, $b = 8.188(3)$, $c = 12.057(6)$ Å, $\alpha = 95.30(4)$, $\beta = 93.99(4)$, $\gamma = 106.34(3)°$, $V = 714.7(6)$ Å$^3$, $M = 260.40$, $Z = 2$, $d_{calc} = 1.21$ g cm$^{-1}$, $\mu = 2.02$ cm$^{-1}$, $F(000) = 280.25$,

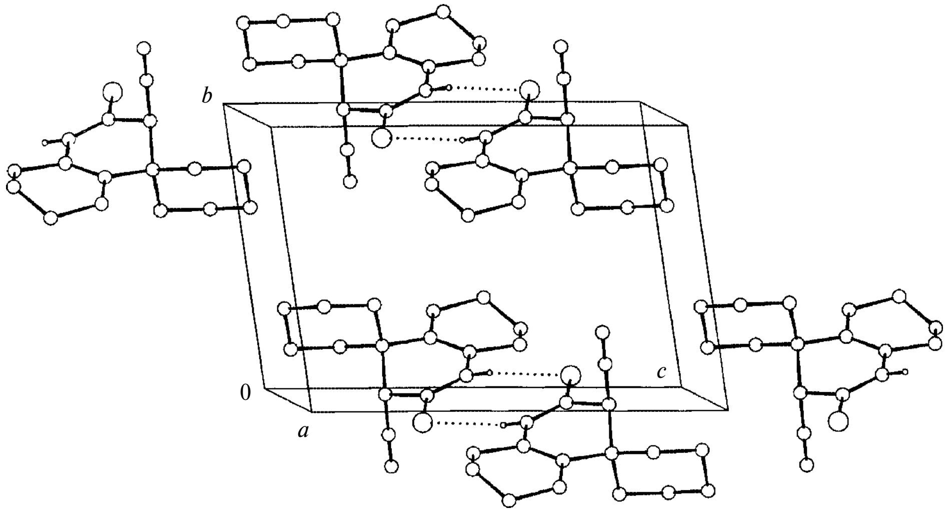

**Fig. 2.** Crystal packing of compound **3** (intermolecular hydrogen bonds are shown by dashed lines).

space group $P\bar{1}$ (N2). The structure was solved by direct methods and refined anisotropically by the full-matrix least-squares method using the CRYSTALS program package.[5] The refinement was carried out based on 1441 reflections with $I > 3(I)$ (167 parameters were refined, 8.6 reflections per parameter). All H atoms were revealed from the difference electron density synthesis and included in the refinement with fixed positional parameters (with the exception of the H(1) atom, which was refined isotropically). The absorption correction was applied according to the azimuthal scanning method.[6] The refinement was carried out using the Chebyshev weighting scheme[7] with the following four parameters: 0.42, –0.31, 0.03, and –0.33. The final reliability factors were as follows: $R = 0.064$ and $R_w = 0.068$, GOF = 1.113. The residual difference Fourier electron densities were 0.42 and –0.36 $e \cdot Å^{-3}$. The coordinates and thermal parameters of the nonhydrogen atoms were deposited with the Cambridge Structural Database.

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