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Crystal structure of 3-hydroxy-4-cyano-5-methylthiopyrazole, $C_5H_5N_3OS$

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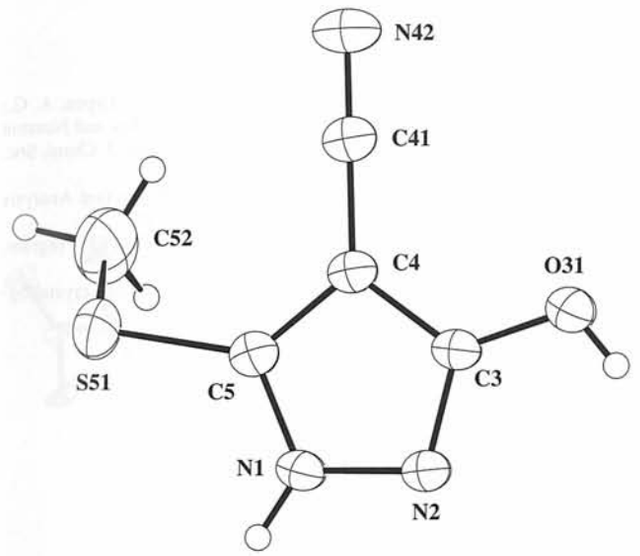

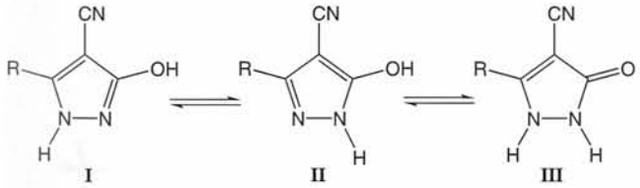

Abstract

$C_5H_5N_3OS$, monoclinic, $P12_1/c1$ (No. 14), $a = 4.5136(2)$ Å, $b = 13.5364(6)$ Å, $c = 11.4552(5)$ Å, $\beta = 92.821(2)°$, $V = 699.0$ Å^3, $Z = 4$, $R_{gt}(F) = 0.047$, $wR_{ref}(F^2) = 0.145$, $T = 298$ K.

Source of material

A mixture of methyl-2-cyano-3,3-bis(methylthio)acrylate [1] (0.5 g, 2.3 mmol) and hydrazine hydrate (0.23 g, 0.46 mmol) in methanol (5 ml) was refluxed for 20 min. After evaporation of the solvent, the residue was recristallized from methanol to give pale yellow needles of the title compound (0.28 g, 1.8 mmol, yield 78%). Crystals suitable for X-ray diffraction were obtained by slow evaporation of an EtOH solution.

Experimental details

The methyl H atoms were placed in calculated positions and refined using a riding atom model with d(C—H) = 0.96 Å and U_{iso} = 1.5 U_{eq} (parent atom). The O- and N-bonded H atoms were refined without constraints. A single orientation parameter was refined for the methyl group.

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Discussion

The title compound was synthesized within a project aimed at finding new, more effective, antimalarial drugs ([2] and references therein), but was found to have low activity in vitro against *Plasmodium falciparum* (IC_{50} = 0.0056 M). In solution, the *enol* (**I** and **II**) and *keto* (**III**) forms of the title compound can exist in tautomeric equilibrium (bottom figure; R = –SMe). In fact, Gompper and Töpfl, who prepared this compound 40 years ago, reported it as a pyrazolone [3]. Moreover, in a previous study of a similar compound (R = *p*-NHC_6H_4OMe), we found that in the solid state the molecules were entirely in the *keto* form [4].

The results of the present work indicate that the title compound is in the *enol* form. The bond length pattern of the five-membered ring, the C—O distance, the positions of the H atoms and the hydrogen-bonding scheme are all consistent with form **I**. In addition, the *endo*- and *exo*cyclic bond angles follow all the empirical rules found by Bonati and Bovio for pyrazole derivatives [5].

All bond lengths are in good agreement with the standard values tabulated [6]. The molecules are linked by a three-dimensional network of hydrogen bonds: O–H···N_{ring} (connecting pairs of centrosymmetrically-related molecules), d(O31···N2^{i}) = 2.712(2) Å (i: $-x+1, -y, -z$), and N–H···N_{cyano}, d(N1···N42^{ii}) = 2.901(2) Å (ii: $x+1, -y+0.5, z-0.5$). See deposited CIF file for more details. Without considering the methyl group (C52), the molecule is essentially planar [max. dev. from the ring mean plane: 0.078(3) Å for S51].

Table 1. Data collection and handling.

Crystal:	pale yellow prism, size 0.20 × 0.25 × 0.35 mm
Wavelength:	Mo K_α radiation (0.71069 Å)
μ:	3.91 cm^{-1}
Diffractometer, scan mode:	Huber A-8901, $\omega/2\theta$
$2\theta_{max}$:	60°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	2257, 2034
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 1263
$N(param)_{refined}$:	100
Programs:	SHELX-97 [7], ZORTEP [8], WinGX [9]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(1)	4*e*	0.521(6)	0.243(2)	–0.085(3)	0.055(8)
H(31)	4*e*	0.321(7)	–0.023(3)	0.095(3)	0.08(1)
H(521)	4*e*	0.2908	0.5059	0.1678	0.096
H(522)	4*e*	0.5245	0.4202	0.1740	0.096
H(523)	4*e*	0.2116	0.4046	0.2248	0.096

Table 3. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	4*e*	0.4260(4)	0.2183(1)	–0.0338(2)	0.046(1)	0.0282(8)	0.0377(9)	0.0017(7)	0.0236(8)	0.0036(7)
N(2)	4*e*	0.4413(4)	0.1182(1)	–0.0132(2)	0.047(1)	0.0275(8)	0.0394(9)	0.0049(7)	0.0235(8)	0.0023(6)
C(3)	4*e*	0.2661(4)	0.1037(1)	0.0754(2)	0.040(1)	0.0297(9)	0.0318(9)	0.0027(8)	0.0168(8)	0.0019(7)
C(4)	4*e*	0.1377(4)	0.1929(1)	0.1109(2)	0.039(1)	0.0290(9)	0.0313(9)	0.0038(7)	0.0143(8)	–0.0005(7)
C(5)	4*e*	0.2471(4)	0.2650(1)	0.0376(2)	0.041(1)	0.0292(9)	0.0326(9)	0.0041(8)	0.0124(8)	–0.0001(7)
O(31)	4*e*	0.2209(4)	0.0157(1)	0.1222(1)	0.063(1)	0.0279(7)	0.0492(9)	0.0051(7)	0.0328(8)	0.0059(6)
C(41)	4*e*	–0.0552(5)	0.2068(2)	0.2026(2)	0.043(1)	0.035(1)	0.037(1)	0.0049(8)	0.0161(9)	0.0001(8)
N(42)	4*e*	–0.2098(5)	0.2186(2)	0.2782(2)	0.062(1)	0.056(1)	0.045(1)	0.008(1)	0.0295(9)	–0.0013(9)
S(51)	4*e*	0.1764(2)	0.39126(4)	0.02427(5)	0.0697(5)	0.0295(3)	0.0455(4)	0.0112(2)	0.0123(3)	0.0024(2)
C(52)	4*e*	0.3172(7)	0.4357(2)	0.1640(3)	0.093(2)	0.041(1)	0.058(2)	0.002(1)	0.005(2)	–0.009(1)

References

1. Jensen, K. A.; Henriksen, L.: Thioacids and their derivatives. XIV. Reactions of carbon disulfide with active methylene compounds. Acta Chem. Scand. **22** (1968) 1107-1128.
2. Domínguez, J. N.; Charris, J.E.; Capparelli, M.V.; Riggione, F.: Synthesis and Antimalarial Activity of Substituted Pyrazoles Derivatives. Arzneim. Forsch./Drug Res. **52** (2002) 482-488.
3. Gompper, R.; Töpfl, W.: Carboxylic acid derivatives. III. Pyrazoles and isoxazoles from ketene mercaptals. Chem. Ber. **95** (1962) 2881-2884.
4. Capparelli, M. V.; Charris, J. E.; Domínguez, J. N.: 5-(p-anisidino)-4-cyano-2-3-dihydro-3-pyrazolone hemihydrate, $C_{11}H_{10}N_4O_2 \cdot 0.5H_2O$. Acta Crystallogr. C**52** (1996) 447-449.
5. Bonati, F.; Bovio, B.: X-ray crystal structure of bis(4-nitropyrazol-1-yl)-methane, and empirical rules concerning the bond angles in pyrazoles. J. Cryst. Spectrosc. Res. **20** (1990) 233-244.
6. Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R.: Tables of Bond Lengths determined by X-Ray and Neutron Diffraction. Part 1. Bond Lengths in Organic Compounds. J. Chem. Soc. Perkin Trans. II (1987) S1-S19.
7. Sheldrick, G. M.: SHELX-97. Programs for Crystal Structure Analysis (Release 97-2). University of Göttingen, Germany 1997.
8. Zsolnai, L.; Pritzkow, H.: ZORTEP. An interactive ORTEP Program. University of Heidelberg, Germany 1995.
9. Farrugia, L. J.: WinGX suite for small-molecule single-crystal crystallography. J. Appl. Crystallogr. **32** (1999) 837-838.