

A Single Crystal X-Ray Diffraction Analysis of 1,9-Dihydro[1]benzothiopyrano[4,3-c]pyrazole 5,5-Dioxide

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The structure of 1,4-dihydro[1]benzothiopyrano[4,3-c]pyrazole 5,5-dioxide was determined by single crystal x-ray diffraction. The molecule crystallizes in space group $P2_1/c$ with $a = 13.4378(6)$, $b = 5.5938(3)$, $c = 12.9837(6)$ Å, and $\beta = 103.831^\circ$. The final R value is 0.083. Surprisingly, the tautomer with N(2)-H exists in the crystal with the pyrazole ring being planar. The entire system is not planar as the benzene ring is rotated about C(9a) and C(9b) with respect to the pyrazole ring. In the crystal structure the pyrazole exists as hydrogen-bonded dimers with two molecules related by a center of symmetry.

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The structures of pyrazoles, pyrazalones, and related compounds are of interest because of a variety of medicinal properties (1) as well as of theoretical significance regarding tautomerism which can exist in solution (2) and has been examined to a limited extent by pmr analysis (3).

A stereoview of a single molecule of 1 is shown in Fig. 1, bond distance and numbering scheme in Fig. 2 and bond angles in Fig. 3. The two S-O bond distances in the sulfone group show a small but significant difference. Such differences have been observed in other sulfone containing compounds (4) and can be attributed to the fact that oxygen atoms have different chemical environments. The bond lengths of the two S-C bonds are not

significantly different even though one involves an sp^3 -hybridized atom, C(4), while the other involves an sp^2 -hybridized atom, C(5a). The conformation of the sulfone ring can best be described as a twisted half-chair having internal torsion angles of $3a-4 = -34.6^\circ$, $4-5 = 47.5^\circ$, $5-5a = -47.8^\circ$, $5a-9a = 8.1^\circ$, $9a-9b = 15.5^\circ$, and $9b-3a = 0.2^\circ$. The pyrazole ring is planar having an average deviation of 0.002 Å from the least-squares plane (Table I) passing through the five atoms. The general shape of the molecule is easily described with respect to

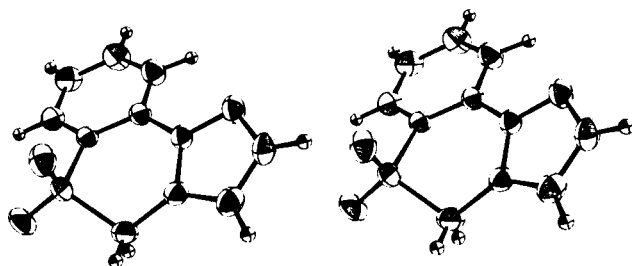
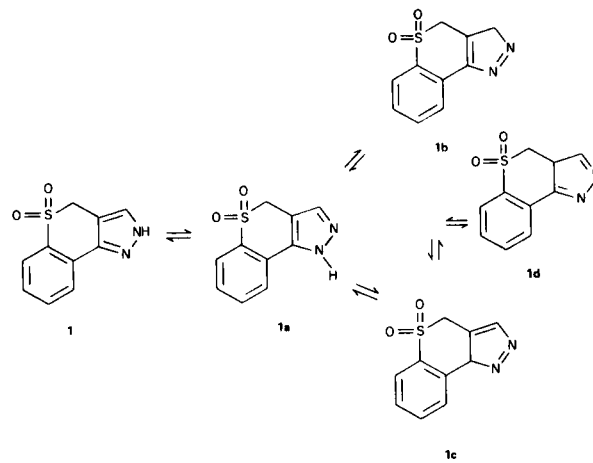


Fig. 1. Stereoview of a single molecule (7).



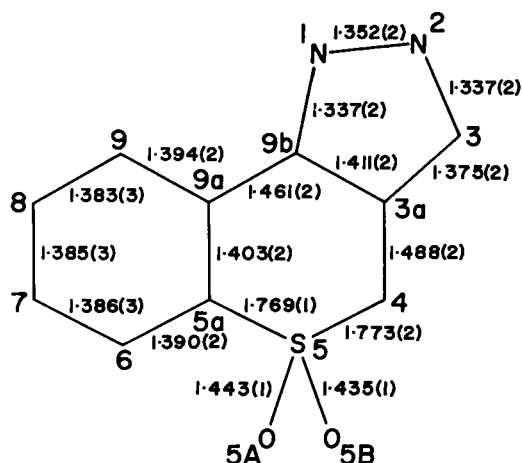


Fig. 2. Bond distances and numbering scheme.

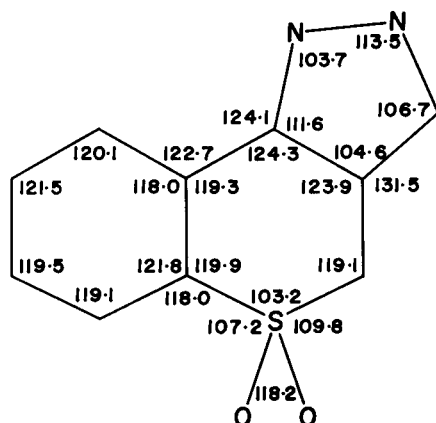
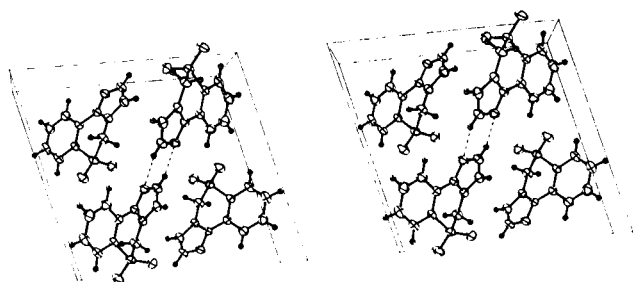


Fig. 3. Bond angles. Standard deviations range from 0.1 to 0.2°. Additional bond angles are C(4)-S(5)-O(5)A = 108.4° and C(5a)-S(5)-O(5)B = 109.0°.

Fig. 4. Packing diagram illustrating hydrogen bonding. Direction of axes are $a \rightarrow b \nearrow c \uparrow$.

this least-squares plane. In the benzene ring atoms C(8) and C(9) are below the plane and atoms C(5a) and C(6) are above the plane indicating that the benzene ring is twisted

about the C(9a)-C(9b) bond with respect to the pyrazole ring. The sulfur atom is farthest removed (excluding O(5)A and O(5)B) from the plane. The bond S(5)-O(5)A is generally perpendicular to the plane of the molecule while the bond S(5)-O(5)B is approximately in the plane. Although the molecule may exist in at least five tautomeric forms in solution (5), only tautomer 1 is found in the solid state. This is shown by the fact that the parameters of the hydrogen atom, attached to N(2), refines to normal values, resulting in the following bond length and bond angles, N(2)-H(2): 0.84(3) Å; H(2)-N(2)-N(1): 124(2)° and H(2)-N(2)-C(3): 122(2)°. In addition, the final thermal parameter of H(2) is normal, 6.3(6) Å², compared to an average of 5.2 Å² for all hydrogen atoms. Finally no residual peak is found in the final, or earlier difference Fourier, which can be associated with an atom attached to N(1). A survey of the literature reveals the occurrence of both tautomers in pyrazoles (6), with 1a likely to be preferred. This was initially considered because of the suspected energy advantage of an endocyclic double bond in the major resonance form of tautomer 1a. Considering just the major resonance structure for each tautomer, one expects for tautomer 1 C(3a)-C(3) to be shorter than C(3a)-C(9b) and C(3)-N(2) to be longer than C(9b)-N(1), with the reverse to be true for tautomer 1a. In the present structure C(3a)-C(9b) is indeed longer than C(3a)-C(3), but the distances C(9b)-N(1) and C(3)-N(2) are equal. A possible explanation for the presence of a tautomer 1 rather than 1a in the crystal is the predicted occurrence of an unfavorable contact for a hydrogen atom attached to N(1) for tautomer 1a, with H(9) attached to C(9), with a calculated value of 2.27 Å, slightly less than the sum of the van der Waals radii.

Table I

Least-squares Plane Through the Pyrazole Ring.
The Equation of the Plane is $8.786x - 3.249y - 8.143z = 0.141$
where x, y and z are Fractional Coordinates.

Atom	Distance (Å)	Atom	Distance (Å)
*N(1)	0.002	C(7)	-0.040
*N(2)	0.000	C(8)	-0.350
*C(3)	-0.002	C(9)	-0.349
*C(3a)	0.003	C(9a)	-0.011
C(4)	-0.003	*C(9b)	-0.003
S(5)	0.935	O(5)A	2.315
C(5a)	0.314	O(5)B	0.634
C(6)	0.296		

* Indicates those atoms which were included in the calculation of the least-squares plane.

Table II

Positional Parameters ($\times 10^4$) and Thermal Parameters ($\times 10^4$) for S, N, O and C Atoms. ThermalParameters are of the Form $\exp(-2\pi^2(h^2a^*2U_{11}+k^2b^*2U_{22}+\ell^2c^*2U_{33}+2hka^*b^*U_{12}+2h\ell a^*c^*U_{13}+2k\ell b^*c^*U_{23}))$.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	4030(1) (a)	393(3)	4016(1)	337(6)	449(8)	310(6)	-43(6)	-18(5)	-9(6)
N(2)	4739(1)	2139(3)	4086(1)	310(6)	498(8)	360(7)	-69(6)	-44(5)	-65(6)
C(3)	4537(1)	3655(3)	3266(1)	336(8)	404(9)	435(9)	-74(6)	32(7)	-51(6)
C(3a)	3640(1)	2894(3)	2596(1)	308(7)	302(7)	359(7)	-5(5)	35(6)	-27(6)
C(4)	3037(1)	3858(3)	1568(1)	398(8)	306(8)	427(9)	-16(6)	9(7)	57(6)
S(5)	2458.4(3)	1451.1(7)	752.0(3)	332(2)	368(2)	287(2)	38(1)	-12(1)	35(1)
C(5a)	1910(1)	-282(3)	1614(1)	267(6)	283(7)	329(7)	33(5)	4(5)	11(5)
C(6)	1018(1)	-1543(3)	1177(1)	282(7)	388(8)	431(9)	29(6)	-69(6)	-6(7)
C(7)	636(1)	-3125(3)	1810(2)	291(7)	457(9)	596(11)	-66(6)	-11(7)	11(8)
C(8)	1150(1)	-3420(4)	2862(2)	407(9)	537(10)	535(10)	-126(8)	88(8)	86(8)
C(9)	2031(1)	-2145(3)	3302(1)	406(9)	488(10)	364(8)	-76(7)	26(7)	60(7)
C(9a)	2430(1)	-548(3)	2681(1)	279(6)	320(7)	318(6)	-1(5)	16(5)	2(6)
C(9b)	3352(1)	866(3)	3102(1)	282(6)	346(7)	281(6)	0(6)	11(5)	-16(6)
O(5)A	3257(1)	29(3)	486(1)	428(6)	564(7)	378(6)	91(6)	98(5)	-43(6)
O(5)B	1656(1)	2338(3)	-98(1)	458(7)	559(8)	386(6)	38(6)	-106(5)	149(6)

(a) Standard deviation for the last digit is in parenthesis.

Table III

Positional Parameters ($\times 10^3$) and Isotropic Thermal Parameters (\AA^2) for Hydrogen Atoms

	x	y	z	B
H(2)	525(2)	203(5)	460(2)	6.3(6)
H(3)	498(2)	486(4)	325(2)	5.2(5)
H(4)A	348(2)	465(4)	116(2)	5.4(5)
H(4)B	250(2)	481(3)	161(2)	4.5(5)
H(6)	73(2)	-134(4)	47(2)	4.0(5)
H(7)	1(2)	-398(4)	154(2)	4.8(5)
H(8)	90(2)	-444(4)	330(2)	6.2(6)
H(9)	237(2)	-228(4)	401(2)	5.3(5)

In the crystal structure the compound exists as hydrogen bonded dimers in which the two molecules are related by a center of symmetry. A packing diagram is shown in Fig. 4 in which the dimer is illustrated. The N(1) ... H(2)'-N(2)' hydrogen bond has dimensions as follows: N(1) ... N(2)' = 2.978 Å, N(1) ... H(2)' = 2.37 Å and N(2)-H(2) = 0.84 Å. The N(1) ... H(2)'-N(2)' angle of 130° is directly related to the unfavorable geometry required by dimer formation in this system and the hydrogen bond is in fact quite weak. The position of N(2)' and H(2)' are transformed by 1-x, -y, 1-z.

EXPERIMENTAL

A crystal of **1** in the shape of a thick hexagonal plate was obtained from a solution of dilute acetic acid. Preliminary examination of the crystals showed them to be monoclinic space group P2₁/c. The crystal data are: C₁₀H₈N₂O₂S; M = 220.24; monoclinic; a = 13.4378(6); b = 5.5938(3); c = 12.9837(6) Å, β = 103.831(4)°; V = 947.67 Å³; Z = 4; ρ_{obs} = 1.549 g. cm⁻³; ρ_{calc} = 1.543 g. cm⁻³; F(000) = 456; space group P2₁/c; nickel filtered CuKα radiation: λ(CuKα₁) = 1.54051 Å for 2θ-data and λ(CuKα) = 1.54178 Å for intensity data; μ(CuKα) = 27.954 cm⁻¹. The unit cell parameters were determined by least-squares fit of the +2θ and -2θ values of 56 reflections distributed through all octants of reciprocal space. The observed density was measured by flotation in a mixture of carbon tetrachloride and cyclohexane.

A total of 1945 reflections with 2θ ≤ 150° were measured on a Nonius CAD-4 automatic diffractometer using θ-2θ scan techniques. A receiving aperture with a variable width was located 173 mm from the crystal. The width was calculated as (4.0 + 0.4 tan θ) mm while the height was constant at 6 mm. The scan width was adjusted for dispersion and calculated as (1.0 + 0.1 tan θ)°. A maximum of 120s was spent scanning each intensity, of which 2/3 of the time was used for scanning the peak (P) and 1/6 of the time for each of the left and right backgrounds (LB + RB). Less than 120s were used for those intensities in which 50,000 counts could be obtained using a faster scan speed than the normal one of 1°/minute. The total time was divided into two 60s scans. When the counts of the two scans were significantly different, up to three additional scans were made. The unscaled intensity (I) was calculated as I = P - 2(RB + LB).

The intensity of a monitor reflection was measured after every 30 reflections. The monitor showed no significant variation

during the period of data collection. Three orientation control reflections were centered after every 100 reflections. In the event that any of the θ , ϕ , ω or K angles varied from their initial positions by more than 0.1° a new orientation matrix was automatically determined from a list of 11 reflections. There were 101 reflections which could not be distinguished from the background on the basis that the intensity (I) was less than $1.4 T^{1/2}$ [$T = P + 2(LB + RB)$]. These intensities were assigned a value equal to $T^{1/2}$ for the purpose of least-squares refinement. Lorentz, polarization and absorption corrections were applied to the data. For the absorption correction a method (8) using Gaussian integration with 512 sampling points was employed. The transmission coefficient ranged from 0.467 to 0.846. Each structure amplitude was assigned a weight given by $\omega_F = 1/\sigma_F^2$ where σ_F is the standard deviation of the structure amplitude and is defined by:

$$\sigma_F = 1/2 \left[\frac{\sigma^2 + 0.04 (L\nu)^2}{(Lp) (L\nu)} \right]^{1/2}$$

where $\sigma = (T^{1/2})\nu$, ν is the scan speed and Lp is the Lorentz-polarization factor.

The structure was solved using conventional heavy atom techniques. A difference Fourier map was calculated from which the positions of the 8 hydrogen atoms were located. Least-squares refinement (4×4 or 9×9 block diagonal)⁴ using isotropic temperature factors for hydrogen atoms and anisotropic temperature factors for non-hydrogen atoms was terminated when the shifts for all S, O, N and C atoms were less than the corresponding estimated standard deviations. In the final stages of refinement the observed structure factors were corrected for the anomalous dispersion of sulfur (9). The final R value for all 1945 data was 0.038. The least-square calculation minimized the quantity $\sum w_F (kF_o - F_c)^2$. The mean value of $w_F \Delta F^2$ did not vary with either $|F_o|$ or $\sin\theta/\lambda$ thus validating the weighting scheme used (10). Final parameters are given in Table II and Table III and supplementary material (10). The only notable features in the final difference Fourier map were several negative peaks of about $0.35 e \cdot \text{\AA}^{-3}$ around the sulfur atom position. Scattering factors for S, N, O and C atoms and anomalous scattering factors for the S atom were taken from International Table for X-ray Crystallography (11) while those for H atoms were from Stewart, Davidson and Simpson (12).

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