# Crystal and Molecular Structure of 3-Hydroxy-5-(methylsulphonyl)-4-phenylisothiazole

By Jill L. McVicars, Maureen F. Mackay,* and Michael Davis, Department of Chemistry, La Trobe University, Bundoora, Victoria 3083, Australia

The crystal and molecular structure of the title compound has been determined by X-ray crystallographic analysis from diffractometer data. Crystals are monoclinic, space group $P2_1/c$ with $a = 14.863(4)$, $b = 5.272(1)$, $c = 15.377(5)$ Å, $\beta = 110.49(2)°$, and $Z = 4$. The structure was solved by the heavy-atom method, and refined by full-matrix least-squares to R 0.073 for 1 160 observed terms. The isothiazole ring is planar to within ±0.009 Å, with the C–S 1.715(8), N–S 1.661(7) Å, and N–S–C 93.3(4)°.

THE synthesis of hydroxy-substituted isothiazoles has attracted attention on account of the broad spectrum of biological activity displayed by these compounds and their phosphorus esters.[1] While there are numerous methods [1] for synthesizing 3-hydroxy-isothiazoles (I) reports on the synthesis of the 5-hydroxy-compounds (II) are few.[1,2] The nucleophilic displacement of alkyl-sulphonyl groups from the 3- or 5-positions has previously been investigated as a convenient means of preparation of hydroxy-substituted isothiazoles. Since electron-density calculations indicated preferential nucleophilic

(I) $R^1 = OH, R^2 = R^3 = H$

(II) $R^1 = R^2 = H, R^3 = OH$
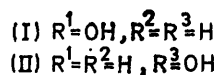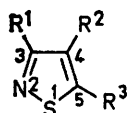
displacement from the 5-position,[3] the isolation of a product from the reaction between aqueous sodium hydroxide and 3,5-bis(methylsulphonyl)-4-phenyliso-thiazole led to a report [4] of the synthesis of 5-hydroxy-3-(methylsulphonyl)-4-phenylisothiazole (III). It now has been found [5] that two products (III) and (IV), each containing a single hydroxy-group, can be isolated from this reaction.

(III) $R^1 = SO_2Me, R^2 = OH$

(IV) $R^1 = OH, R^2 = SO_2Me$
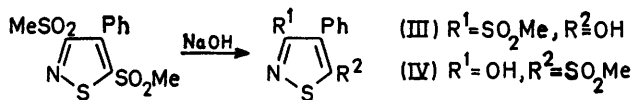
Attempts to differentiate between the two isomers [5] (III) and (IV) by an unequivocal synthesis of the 3-hydroxy-compound (IV) were initially unsuccessful. An X-ray crystal structure determination of the compound previously reported as (III), but now known to be 3-hydroxy-5-(methylsulphonyl)-4-phenylisothiazole (IV), was therefore undertaken. Information concerning the S–N bond, which has been the subject of recent comment,[6] was also sought.

EXPERIMENTAL

The compound now known to be (IV) was prepared as described previously [4] for (III), except that acetic acid was used to acidify the reaction mixture. The product was recrystallized from aqueous ethanol as needles, m.p. 229—230 °C.

Crystal Data.—$C_{10}H_9NO_3S_2$, $M = 255.11$, monoclinic, $a = 14.863(4)$, $b = 5.272(1)$, $c = 15.377(5)$ Å, $\beta = 110.49(2)°$, $U = 1 125.8$ Å^3, $D_m = 1.504(2)$ (by flotation), $Z = 4$, $D_c = 1.505$ g cm^{-3}, $F(000) = 528$. Space group $P2_1/c$. Cu-K_α radiation, $\lambda = 1.541 8$ Å; μ(Cu-K_α) 40.8 cm^{-1}.

Weissenberg photographs established the centrosymmetric space group $P2_1/c$. Accurate unit-cell parameters were determined by a least-squares fit of 2θ values, measured for 25 strong reflections on a four-circle diffractometer with Cu-K_α radiation. Three-dimensional intensity data were recorded on a Rigaku AFC four-circle diffractometer, with graphite-monochromatized Cu-K_α radiation. A crystal with dimensions ca. 0.22 × 0.25 × 0.05 mm^3 was aligned with its b axis approximately parallel to the ϕ axis of the diffractometer. Intensities were recorded by the ω—2θ scan technique with a scan rate of 4° min^{-1} and 10 s stationary background counts. Three reference reflections monitored every 50 reflections showed no significant variation in intensity during data collection. Of the 1 278 non-equivalent terms measured to $2\theta_{max.}$ 130°, 1 160 for which $|F_o| > 3\sigma|F_o|$ were considered observed. Intensities were corrected for Lorentz and polarization factors but not for absorption or extinction. Scattering factors used in the analysis were those given in ref. 7 for carbon, nitrogen, oxygen, and sulphur and in ref. 8 for hydrogen.

The structure was solved by the heavy-atom method. The sulphur-atom sites were derived from an ' unsharpened ' three-dimensional Patterson map. A Fourier synthesis phased on the sulphur contributions to the structure factors revealed the sites of the non-hydrogen atoms apart from the methyl carbon and sulphonyl oxygen atoms; the latter were located on a subsequent difference-Fourier map. Least-squares refinement of all non-hydrogen atoms with individual isotropic temperature factors, yielded R 0.152. The hydrogen atom sites (apart from those of the hydroxy- and methyl-group) were derived from a difference distribution. Final refinement cycles, in which non-hydrogen atoms were given anisotropic temperature factors and the positional parameters of the hydrogen atoms were varied, reduced R to 0.073 for the 1 160 terms; hydrogen atoms were given the same thermal parameters as the atoms to which they were bonded. Ten strong terms which, by comparison with $|F_c|$ values, appeared to be significantly affected by extinction were omitted from the final refinement cycles.

[1] K. R. H. Wooldridge, *Adv. Heterocyclic Chem.*, 1972, **14**, 1.

[2] J. A. Waite and K. R. H. Wooldridge, *Tetrahedron Letters*, 1972, 327.

[3] A. Adams and R. Slack, *J. Chem. Soc.*, 1959, 3061.

[4] M. Davis and J. A. Gordon, *J.C.S. Perkin I*, 1972, 638.

[5] M. Davis, M. C. Dereani, J. L. McVicars, and I. J. Morris, *Austral J. Chem.*, in the press.

[6] G. Kresze, ' Some Aspects of the Sulphur–Nitrogen Double Bond,' in ' Organic Sulphur Chemistry,' ed. C. J. M. Stirling, Butterworths, London, 1975, p. 65.

[7] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

[8] R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 42, 3175.

Least-squares refinements were carried out using ORFLS,[9] the function minimized being $w(|F_o| - |F_c|)^2$ with $w = 1.0$; all Fourier summations were calculated with MUFR3.[10]
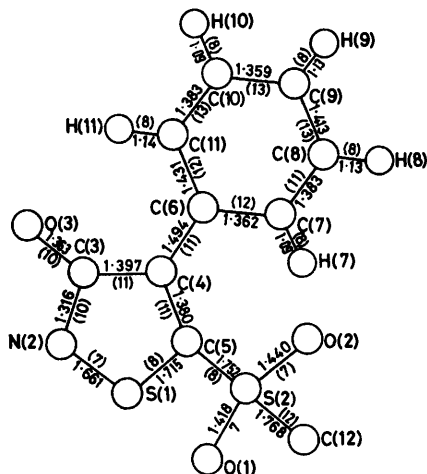

FIGURE 1(a)   Bond lengths with estimated standard deviations in parentheses

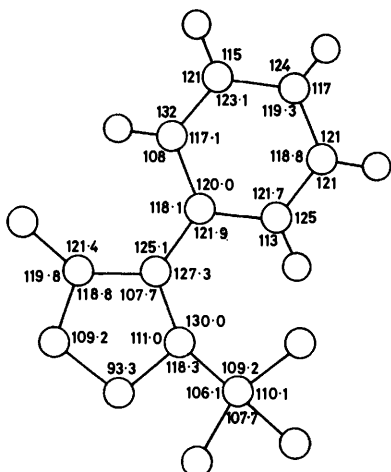

FIGURE 1(b)   Bond angles. The estimated standard deviations for angles subtended at the sulphur atoms are 0.5°, for angles involving hydrogen atoms 4°, and for all other angles the values range from 0.6 to 0.8°
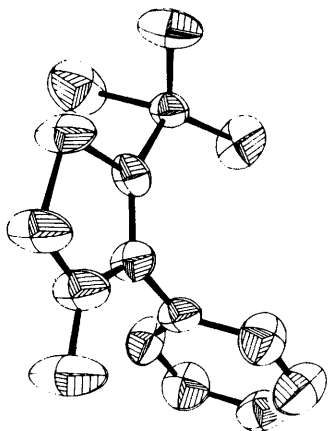

FIGURE 2   A perspective view of the molecule with thermal ellipsoids scaled to 75% probability

TABLE 1

Final atom positional parameters ($\times 10^4$, H $\times 10^3$) with estimated standard deviations in parentheses

	x	y	z
S(1)	454(1)	1 379(5)	1 846(1)
S(2)	2 274(1)	−975(4)	3 077(1)
O(1)	1 572(4)	−2 209(13)	3 383(4)
O(2)	3 017(4)	−2 435(13)	2 945(4)
O(3)	1 259(4)	4 193(14)	5(4)
N(2)	346(4)	2 999(16)	888(4)
C(3)	1 167(5)	2 927(19)	742(5)
C(4)	1 937(4)	1 603(17)	1 368(5)
C(5)	1 625(5)	567(16)	2 037(5)
C(6)	2 906(5)	1 323(17)	1 290(4)
C(7)	3 624(5)	3 022(18)	1 682(5)
C(8)	4 515(5)	2 784(19)	1 594(6)
C(9)	4 670(5)	757(19)	1 062(5)
C(10)	3 943(6)	−896(21)	654(6)
C(11)	3 056(6)	−744(19)	753(6)
C(12)	2 772(8)	1 564(24)	3 846(7)
H(7)	339(5)	466(15)	197(5)
H(8)	512(5)	412(16)	198(5)
H(9)	540(5)	63(15)	100(4)
H(10)	404(5)	−210(17)	12(6)
H(11)	232(5)	−153(15)	32(5)

TABLE 2

Intermolecular approach distances (Å) < 3.75 Å

O(1) ⋯ C(12^I)	3.68		C(12) ⋯ C(11^III)	3.57
O(2) ⋯ C(12^I)	3.52		O(1) ⋯ C(11^IV)	3.70
O(2) ⋯ C(7^I)	3.40		O(2) ⋯ C(9^V)	3.37
C(10) ⋯ C(7^I)	3.68		O(2) ⋯ C(8^V)	3.49
C(11) ⋯ C(7^I)	3.57		C(8) ⋯ C(8^V)	3.74
C(10) ⋯ C(8^I)	3.61		C(9) ⋯ C(8^V)	3.72
C(11) ⋯ O(3^I)	3.67		O(3) ⋯ C(3^VI)	3.71
O(1) ⋯ S(1^II)	3.00		O(3) ⋯ N(2^VI)	2.73
O(1) ⋯ N(2^II)	3.41		N(2) ⋯ N(2^VI)	3.32
O(1) ⋯ O(3^III)	3.13		N(2) ⋯ C(3^VI)	3.47
C(12) ⋯ O(3^III)	3.35		C(8) ⋯ C(8^VI)	3.74
C(12) ⋯ C(10^III)	3.55			

Roman numeral superscripts denote the following equivalent positions relative to the reference molecule at x, y, z:

I $x, -1 + y, z$ V $1 - x, -\frac{1}{2} + y, \frac{1}{2} - z$
II $-x, -\frac{1}{2} + y, \frac{1}{2} - z$ VI $-x, 1 - y, -z$
III $x, \frac{1}{2} - y, \frac{1}{2} + z$ VII $1 - x, \frac{1}{2} + y, \frac{1}{2} - z$
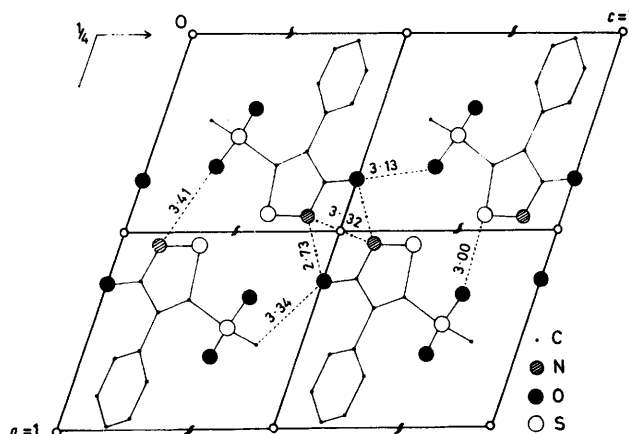IV $x, -\frac{1}{2} - y, \frac{1}{2} + z$

FIGURE 3   The projection of the structure down the b axis

[9] W. R. Busing, K. O. Martin, and H. A. Levy, ORFLS, A Fortran Crystallographic Least-Squares Program, 1963, Report ORNL TM 305, Oak Ridge National Laboratory, Oak Ridge, Tennessee.
[10] J. C. B. White, 1966, MUFR3, A Three-Dimensional Fourier Synthesis Program, University of Melbourne.

Final atomic parameters together with their estimated standard deviations are given in Table 1. Bond lengths and angles are given in Figure 1. No corrections for thermal effects have been made. A perspective view of the molecule given in Figure 2 has been prepared from the output of the ORTEP program.[11] A projection of the structure as viewed down the b axis appears in Figure 3, while some short inter-molecular approach distances are given in Table 2. Final observed and calculated structure factors and anisotropic thermal parameters are deposited in Supplementary Publication No. SUP 22023 (12 pp., 1 microfiche).*

DISCUSSION

Apart form O(1), O(2), and C(12), the atoms lie almost in two planes (Figure 2). The carbon atoms in the benzene ring and the associated atom C(4) are planar to within ± 0.018 Å, the equation of the plane being $-0.0288X + 0.5690Y - 0.8218Z + 1.2170 = 0$, where X, Y, and Z are orthogonal (Å) co-ordinates. Atoms in the isothiazole ring together with the associated atoms O(3) and C(6) are planar to within ± 0.012 Å; atom S(2) lies 0.207 Å from this plane defined by $-0.1151X - 0.8238Y - 0.5550Z + 2.0286 = 0$. Rotation about the bond C(4)–C(6) results in a dihedral angle between the two planar groups of 89.5° (hydrogen atoms were not included in the calculations).

The bond lengths in the isothiazole ring and the associated bond length, C(3)–O(3), have values that indicate considerable double-bond character. Table 3 gives a comparison of these lengths with some reported values for the respective pure single and double bonds. The value for the short bond, C(3)–N(2), [1.316(10) Å] is comparable to that [1.319(3) Å] for the C–N bond in a 3-hydroxyisoxazole system;[12] the angle subtended at the sulphur atom [N(2)–S(1)–C(5) 93.3°] agrees with other reported values[13] which range from 93 to 100°.

In view of the planarity and dimensions of the isothiazole ring, it would appear that significant charge delocalization is present. Somewhat similar situations also have

TABLE 3

Bond lengths (Å) of the isothiazole ring and some reported values for the respective pure single and double bond lengths

Bond	Present work	Reported values
C–S	1.715 (8)	1.812,[a] 1.554 (4) [b]
N–S	1.661 (7)	1.74, 1.56 [c]
C–C (mean value)	1.389 (11)	1.537 (5), 1.335 (5) [d]
C–N	1.316 (10)	1.472 (5),[d] 1.255 (9),[e] 1.275 (20) [f]
C–O	1.363 (10)	1.426 (5), 1.215 (5) [d]

[a] E. G. Cox and G. A. Jeffrey, *Proc. Roy. Soc.*, 1951, *A*, **207**, 110. [b] A. H. Guenther, *J. Chem. Phys.*, 1959, **31**, 1095. [c] L. Pauling, 'The Nature of the Chemical Bond,' Cornell University Press, Ithaca, New York, 1960, pp. 224, 228. [d] *Chem. Soc. Special Publ.*, No. 18, 1965. [e] M. Nardelli and G. Fava, *Acta Cryst.*, 1962, **15**, 214. [f] K. K. Cheung, D. Melville, K. H. Overton, J. M. Robertson, and G. A. Sim, *J. Chem. Soc. (B)*, 1966, 853.

been noted in a 2,1-benzisothiazole[14] and in a 1,2-benzisothiazole[15] system.

The C–C bonds in the benzene ring have a mean of 1.388 Å (mean deviation 0.020 Å). In the methyl-sulphonyl group, the S(2)–C(5) bond length [1.752(8) Å] is similar to that [1.761(12) Å] for the S–C(Ph) bond in propenyl p-tolyl sulphone.[16] The S(2)–C(12) bond length [1.768(12) Å], and mean S–O [1.429(7) Å] agree with the values for the S–C(Me) [1.765(5) Å] and S–O [1.446(3) Å] in dimethyl sulphone.[17]

The molecular packing in the crystal is illustrated in Figure 3. Intermolecular hydrogen bonds between the hydroxy-group and the nitrogen atom of an adjacent molecule related by a centre of symmetry, link the molecules into dimers. The O(3) $\cdots$ N(2) distance (2.73 Å) is in accord with other reported values.[18] The intermolecular approach distances are normal and closest contacts are listed in Table 2.

[6/2113 *Received, 17th November, 1976*]

* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1975, Index issue.

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[12] L. Brehm and P. Krogsaard-Larsen, *Acta Chem. Scand.*, 1974, **B28**, 625.
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[14] M. Davis, M. F. Mackay, and W. A. Denne, *J.C.S. Perkin II*, 1972, 565.

[15] A. C. Bonamartini, M. Nardelli, C. Palmieri, and C. Pelizzi, *Acta Cryst.*, 1971, **B27**, 1775.
[16] A. H. Klazinga and A. Vos, *Rec. Trav. chim.*, 1973, **92**, 360.
[17] D. A. Langs, J. V. Silverton, and W. M. Bright, *Chem. Comm.*, 1970, 1653.
[18] G. C. Pimental and A. L. McClellan, 'The Hydrogen Bond,' Freeman, San Francisco, 1960, ch. 9.