

Structure of 4-Methyl-5-[2-(2-pyrazinyl)vinyl]-3H-1,2-dithiole-3-thione*†

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Abstract. $C_{10}H_8N_2S_3$, $M_r = 252.380$, monoclinic, $P2_1/c$, $a = 9.5215$ (7), $b = 10.0001$ (8), $c = 11.862$ (1) Å, $\beta = 98.190$ (8)°, $V = 1117.9$ (2) Å³, $Z = 4$, $D_m = 1.50$ (1), $D_x = 1.499$ g cm⁻³, $\lambda(\text{Cu } K\alpha_1) = 1.54056$ Å, $\mu = 55.45$ cm⁻¹, $F(000) = 520$, $T = 296$ (1) K. Final $R(F) = 0.031$ for 1861 observed counter data with $F_o^2 \geq 2\sigma(F_o^2)$. The molecule is composed of a pyrazine ring and a five-membered heterocyclic ring linked together through a vinylene group. The length of the C=C bond for the vinylene group is 1.325 (3) Å. Other bond lengths and angles agree with those found in oltipraz and other analogous compounds containing dithiolethione rings. E.s.d.'s of bond lengths and angles involving C and N atoms are of the order of 0.003 Å and 0.2°, respectively. The six- and five-membered rings are each essentially planar to within 0.005 Å; the vinylene carbons and the carbons bonded to them are coplanar to within 0.015 Å; the molecule as a whole has a roughly planar configuration. The angle between the plane normals of the two end rings is 11.54 (5)°.

Introduction. Oltipraz, 4-methyl-5-(2-pyrazinyl)-3H-1,2-dithiole-3-thione, is a slowly acting antischistosomal drug. Structurally this drug is composed of a pyrazine ring and a methylthiolethione ring joined directly through a C—C bond. In reporting the oltipraz activity, Bueding, Dolan & Leroy (1982) pointed out that antischistosomal activity has rather stringent structural requirements. Replacement of the thione S atom by an O atom (Wei, 1985a) abolishes activity. When the methyl group is removed from the dithiolethione ring and the latter is connected directly either to a *p*-methoxyphenyl ring (Wang, Lin & Wei, 1985) or to a phenyl ring (Wei, 1986) it also loses antischistosomal activity. The present paper reports a new type of structure that can be considered to be derived by connecting the methylthiolethione ring and the pyrazine ring of oltipraz by a vinylene group. The

presence of the vinylene group renders this compound inactive (Bueding, Dolan & Leroy, 1982).

Experimental. Diamond-shaped dark maroon crystals grown at 257 K from a solution of 1:1 mixture of toluene and chloroform. Crystal density determined by flotation in mixtures of bromobenzene and xylene. Space group and approximate unit-cell parameters established from Weissenberg and precession photographs. Data from a crystal of dimensions 0.31 × 0.30 × 0.15 mm mounted on a Picker four-circle diffractometer. Lattice parameters refined by least-squares method from angle measurements of 12 strong reflections in the 2θ range 85–100° (Busing, Ellison, Levy, King & Roseberry, 1968). Intensity data collected by θ - 2θ step scans to $2\theta_{\max} = 134$ °. Ranges of h, k, l : -11 to 11, 0 to 11, 0 to 14, respectively. One standard measured for every 40 reflections: variation < 0.8%. Absorption corrections based on an azimuthal scan of reflection 004. Ratio of min. to max. transmission factors 0.72. Of the 1974 unique nonzero reflections, 113 reflections with $F_o^2 < 2\sigma(F_o^2)$ excluded from final least-squares refinement, in which no extinction corrections were applied. Maximum mosaic spread of the crystal specimen estimated to be 0.4°. The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). H atoms located from a difference-Fourier map [using the program *ORFFP3* (Levy, 1977)] and included in final least-squares refinement with the program *ORXFLS4* (Busing, Martin & Levy, 1962). The function minimized was $\sum w |F_o^2 - sF_c^2|^2$, where the weights w are reciprocals of variances $\sigma^2(F_o^2)$, which were estimated from the empirical equation

$$\sigma^2(F_o^2) = A^2 s^2 \{ [G + (t_G/t_B)^2 B] + 0.0036 [G - (t_G/t_B) B]^2 \} / (Lp)^2,$$

where A = correction factor on the intensity for absorption, s = scale factor on the intensity, G = gross count, B = background count, t_G/t_B = ratio of gross intensity and background, and Lp = Lorentz-polarization factor. Scattering factors were from Cromer & Waber (1974); anomalous-dispersion corrections for S ($f' = 0.110$, $f'' = 0.120$) from Cromer (1974). $\Delta x_i/\sigma$ for all nonhydrogen atoms < 0.01, $(\Delta x_i/\sigma)_{\max}$ for H parameters = 0.02. Final $R(F)$, $R(F^2)$, $wR(F^2)$ and S : 0.031, 0.065, 0.089 and 1.327, respectively. The

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Table 1. Positional and isotropic thermal parameters

The equivalent isotropic temperature factors for non-H atoms were calculated from the corresponding anisotropic thermal parameters and unit-cell parameters by the relation $B_{eq} = \frac{1}{3}(\beta_{11}a^2 + \beta_{22}b^2 + \beta_{33}c^2 + 2\beta_{13}accos\beta)$ (Hamilton, 1959).

| | x | y | z | B_{eq} or $B(\text{\AA}^2)$ |
|--------|-------------|--------------|-------------|-------------------------------|
| S(1) | 0.11141 (4) | 0.10067 (4) | 0.16380 (3) | 3.36 (2) |
| S(2) | 0.03528 (5) | -0.07954 (4) | 0.21020 (4) | 3.55 (2) |
| S(3) | 0.08125 (6) | -0.34176 (4) | 0.11404 (5) | 4.47 (2) |
| N(1) | 0.4328 (2) | 0.2700 (2) | -0.1456 (1) | 3.82 (4) |
| N(2) | 0.4071 (2) | 0.5483 (2) | -0.1500 (1) | 4.33 (5) |
| C(1) | 0.3527 (2) | 0.3342 (2) | -0.0786 (1) | 3.11 (4) |
| C(2) | 0.3406 (2) | 0.4724 (2) | -0.0820 (2) | 3.82 (5) |
| C(3) | 0.4872 (2) | 0.4835 (2) | -0.2147 (2) | 4.43 (6) |
| C(4) | 0.4994 (2) | 0.3463 (2) | -0.2126 (2) | 4.42 (6) |
| C(5) | 0.2758 (2) | 0.2540 (2) | -0.0041 (1) | 3.32 (4) |
| C(6) | 0.2755 (2) | 0.1216 (2) | -0.0066 (1) | 3.37 (4) |
| C(7) | 0.1108 (2) | -0.1777 (2) | 0.1149 (1) | 3.24 (4) |
| C(8) | 0.1918 (2) | -0.1038 (2) | 0.0430 (1) | 3.14 (4) |
| C(9) | 0.1992 (2) | 0.0317 (2) | 0.0596 (1) | 3.08 (4) |
| C(10) | 0.2600 (2) | -0.1752 (2) | -0.0447 (2) | 4.16 (6) |
| H(2)* | 0.279 (3) | 0.520 (3) | -0.029 (2) | 5.9 (6) |
| H(3) | 0.538 (3) | 0.524 (3) | -0.264 (2) | 5.6 (6) |
| H(4) | 0.550 (3) | 0.304 (3) | -0.256 (2) | 5.2 (5) |
| H(5) | 0.220 (2) | 0.306 (2) | 0.048 (2) | 3.8 (4) |
| H(6) | 0.325 (2) | 0.084 (2) | -0.057 (2) | 3.4 (4) |
| H(10a) | 0.249 (4) | -0.130 (3) | -0.110 (3) | 8.8 (9) |
| H(10b) | 0.205 (4) | -0.243 (3) | -0.068 (3) | 8.4 (8) |
| H(10c) | 0.346 (4) | -0.196 (3) | -0.018 (2) | 7.7 (8) |

* H atoms are numbered according to the C atoms to which they are attached.

data-to-variable ratio was 10.88. With all 1974 unique nonzero reflections included, $R(F) = 0.033$; subsequent $\Delta\rho$ excursions $< 0.32 \text{ e \AA}^{-3}$.

Discussion. Positional parameters and isotropic temperature factors (or their equivalents) are listed in Table 1.*†

The molecule is depicted in Fig. 1, in which bond lengths and angles, calculated with the program ORFF4 (Busing, Martin & Levy, 1964), are also given. All figures were prepared with the program ORTEPII (Johnson, 1976). The vinylene group is connected to the six-membered ring and the five-membered ring through bonds C(5)–C(1) and C(6)–C(9), both of which are shorter than the single-bond C–C length of 1.544 Å because they are in a conjugated system, as in the inter-ring bond in oltipraz (Wei, 1983). The double-bond character of C(5)–C(6) is evidenced by the length of 1.325 (3) Å. Interior angles at N atoms less than 120° and at C atoms larger than 120°, characteristic of a pyrazine ring and pointed

* Lists of structure factors, anisotropic thermal parameters and equations of best molecular planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43287 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

† The e.s.d.'s are given in parentheses in all tables and in the text. The digits in parentheses correspond to the least-significant digits of the parameters.

out in the structure of oltipraz (Wei, 1983, and references cited therein), are again observed in this structure. The molecular parameters for the methyl-dithiolethione ring are also similar to those found in analogous compounds: 4-methyl-3H-1,2-dithiole-3-thione (Jeffrey & Shiono, 1959), oltipraz (Wei, 1983), 5-(*p*-methoxyphenyl)-3H-1,2-dithiole-3-thione (Wang, Lin & Wei, 1985), 4-methyl-5-(2-pyrazinyl)-3H-1,2-dithiol-3-one (Wei, 1985a), 3H-1,2-dithiole-3-thione (Wei, 1985b), 4- and 5-phenyl-3H-1,2-dithiole-3-thione (Wei, 1986). In this family of compounds, the S–S bond lengths range from 2.035 to 2.050 Å, with an average value of 2.045 (0.4) Å; and the average C=S bond length is 1.667 (1) Å. These average bond lengths are in fair agreement with those found in xanthane hydride (5-amino-3H-1,2,4-dithiazole-3-thione): 2.052 (4) and 1.650 (9) Å (Stanford, 1963); 2.063 (5) and 1.653 (9) Å (Hordvik, 1963). In the dithiole heterocyclic ring system the angle subtended at S(2) has been found to be invariably greater than the angle subtended at S(1).

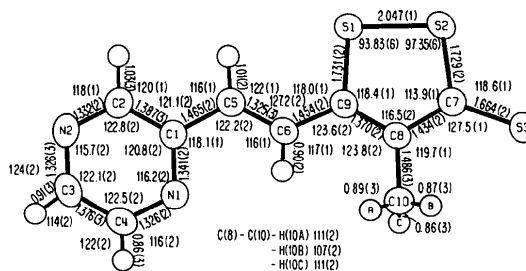


Fig. 1. View of the $C_{10}H_8N_2S_3$ molecule approximately perpendicular to the molecular plane, showing the numbering scheme and also the bond lengths (Å) and bond angles (°) with their e.s.d.'s.

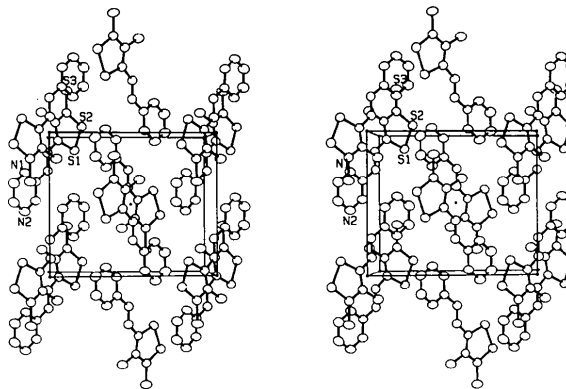


Fig. 2. A stereoscopic view showing the packing viewed along *a*. The axial system is right-handed. For the sake of clarity, H atoms are not included, and only S and N atoms of the reference molecule are labeled. The origin of the unit cell is in the upper left rear corner.

The pyrazine ring and the dithiolethione ring are both essentially planar to within 0.005 Å. The vinylene C atoms and the two C atoms bonded to them are coplanar to within 0.015 Å. This four-C-atom plane is nearly coplanar with the six- and five-membered ring planes, and the molecule as a whole is roughly planar, in sharp contrast with the molecules of 4- and 5-phenyl-3*H*-1,2-dithiole-3-thione (Wei, 1986) in which plane normals of the six- and five-membered rings form angles of 67.40 (9) and 29.36 (8)°, respectively. In the present structure, angles between plane normals for planes of the vinylene group and five- and six-membered rings are 6.2 (1) and 5.4 (1)°, respectively; and that between five- and six-membered rings is 11.54 (5)°.

Fig. 2 shows the [100] projection of the unit cell. The packing of the molecules is assumed to be mainly dictated by van der Waals forces. The closest intermolecular contact between nonhydrogen atoms is 3.392 (2) Å for C...N, and the closest such contact between nonhydrogen and H atoms is 2.71 (3) Å for N...H.

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The Double-Stack Structure of Di(3,4-ethylenedithio-3',4'-dimethyl-2,2',5,5'-tetrathiafulvalenium) Perchlorate,* (DIMET)₂ClO₄

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Abstract. 2C₁₀H₁₀S₆^{1/2+}.ClO₄⁻, *M_r* = 744.62, triclinic, *P* $\bar{1}$, *a* = 7.000 (2), *b* = 7.824 (3), *c* = 27.010 (14) Å,

$\alpha = 88.10$ (4), $\beta = 89.02$ (4), $\gamma = 74.58$ (3)°, *V* = 1425 Å³, *Z* = 2, *D_x* = 1.73 g cm⁻³, λ (Mo *K*α) = 0.7107 Å, $\mu = 10.1$ cm⁻¹, *F*(000) = 762, room temperature, final *R* = 0.063 for 3076 observed independent reflections. Two crystallographically independent

* Alternative nomenclature: di(4,5-ethylenedithio-4',5'-dimethyl-2,2'-bi-1,3-dithiolyliiden)ium perchlorate.