

Structure of 8-Amino-7-bromo-3,4-dihydro-3-methyl-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one

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Abstract. $C_8H_{10}BrN_3OS$, $M_r = 276.15$, triclinic, $P\bar{1}$, $a = 7.564$ (1), $b = 10.747$ (1), $c = 13.322$ (2) Å, $\alpha = 91.68$ (1), $\beta = 101.02$ (2), $\gamma = 102.63$ (1)°, $V = 1034.4$ Å³, $Z = 4$, $D_x = 1.77$ g cm⁻³, $\lambda(\text{Mo } K\alpha) = 0.7107$ Å, $\mu = 40.3$ cm⁻¹, $F(000) = 552$, $T = 293$ K, $R = 0.039$ for 2572 unique reflections with $I > 2\sigma(I)$. The compound crystallizes in racemic form with two crystallographically independent molecules in the unit cell. Both molecules are statistically disordered over two alternative half-chair conformations of the thiazine rings. The occupancy factors of the major sites are 0.782 and 0.685. There are no significant differences between the dimensions of the two molecules, whose loss of crystallographic equivalence appears to be a result of their different hydrogen-bonding networks.

Introduction. In a previous paper (Pecorari, Rinaldi, Costantino, Provvisionato, Cermelli & Portolani, 1991) the synthesis and the biological activity of some pyrimido[2,1-*b*][1,3]thiazine derivatives were described. The title compound was obtained by reacting 6-amino-2-thiouracil with (\pm)-1-bromo-3-chloro-2-methylpropane and subsequent bromination in glacial acetic acid. The molecule was tested, together with other polyheterocyclic compounds, for antibacterial, antimycotic and antiviral activity on a number of bacterial and mycotic strains, and viruses, showing moderate activity against *Candida albicans*.

Experimental. Colourless air-stable plate crystals, grown by slow evaporation at room temperature from dimethylformamide/ether solution, dimensions $0.33 \times 0.25 \times 0.12$ mm. Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Mo $K\alpha$ radiation. 25 ($7 \leq \theta \leq 17^\circ$) reflections for cell-parameter determination; $\omega/2\theta$ scan, scan width ($1.1 + 0.35 \tan \theta$)°; two standard reflections (223 and 14 $\bar{3}$)

measured at 2 h intervals showed no significant intensity decay; 5426 reflections measured in the range $2 \leq \theta \leq 28^\circ$, $-10 \leq h \leq 10$, $-14 \leq k \leq 14$, $0 \leq l \leq 17$; 2810 with $I > 2\sigma(I)$, 2572 unique ($R_{\text{int}} = 0.012$) used for structure determination; intensities corrected for Lorentz–polarization effects and for absorption based on empirical ψ scan ($0.855 \leq T \leq 0.999$). Structure solved by conventional Patterson and Fourier methods, and refined by full-matrix least squares on F (SHELX76; Sheldrick, 1976). During refinement, anomalously large thermal parameters and residual peaks in ΔF maps showed evidence of statistical disorder, as a result of two C atoms in each independent molecule having two alternative positions. Least-squares refinement of their occupancy factors led to the values of 0.782 and 0.685 which were then held fixed. All non-H atoms were refined anisotropically, except the C atoms at minor sites. H atoms were placed in calculated positions at a bond distance of 1.0 Å, except the aminic protons and one hydrogen of each methyl group with major occupancy, which were placed as fixed contributors at their observed positions. Their temperature factors were set 1.0 Å² higher than the B_{eq} of the bonded atoms. 271 parameters varied. $R = 0.039$, $wR = 0.041$, $S = 0.95$, $w = 0.93/(\sigma^2 F + 0.00162 F^2)$, max. $\Delta/\sigma = 0.03$, $-0.53 \leq \Delta\rho \leq 0.70$ e Å⁻³ (near Br atoms). No correction for secondary extinction. Complex neutral atom scattering factors from SHELX76 (Sheldrick, 1976). Major calculations carried out on a VAX 6310 computer.

Discussion. Atomic coordinates are reported in Table 1, and selected bond lengths and angles in Table 2.†

† Lists of structure factors, anisotropic thermal parameters for non-H atoms, positional and thermal parameters for H atoms, complete bond distances and bond angles, selected least-squares planes, and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54371 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. Final fractional coordinates and equivalent isotropic thermal parameters (\AA^2)
$$B_{eq} = (1/3) \sum_i \sum_j B_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

| | x | y | z | B_{eq} |
|--------|-------------|-------------|-------------|----------|
| S(1) | 0.9944 (2) | 0.8324 (1) | 0.0742 (1) | 4.49 (6) |
| C(1) | 0.8104 (8) | 0.9082 (5) | 0.0875 (5) | 5.5 (3) |
| C(2a)* | 0.6711 (9) | 0.8365 (5) | 0.1429 (6) | 3.2 (3) |
| C(2b) | 0.648 (5) | 0.831 (3) | 0.079 (3) | 5.4 (7) |
| C(3a) | 0.513 (1) | 0.9009 (8) | 0.1440 (9) | 5.0 (4) |
| C(3b) | 0.502 (5) | 0.903 (3) | 0.097 (2) | 3.5 (7) |
| C(4) | 0.5986 (7) | 0.7021 (5) | 0.0999 (5) | 4.8 (3) |
| N(1) | 0.7409 (5) | 0.6259 (3) | 0.1095 (3) | 2.7 (1) |
| C(5) | 0.9174 (6) | 0.6745 (4) | 0.1002 (3) | 2.8 (2) |
| N(2) | 1.0463 (5) | 0.6101 (3) | 0.1097 (3) | 2.8 (1) |
| C(6) | 1.0013 (6) | 0.4852 (4) | 0.1308 (3) | 2.7 (2) |
| N(3) | 1.1391 (5) | 0.4237 (4) | 0.1417 (3) | 3.7 (2) |
| C(7) | 0.8257 (6) | 0.4300 (4) | 0.1416 (3) | 2.8 (2) |
| Br(1) | 0.76600 (7) | 0.25938 (5) | 0.17715 (5) | 4.31 (2) |
| C(8) | 0.6850 (6) | 0.4981 (4) | 0.1326 (3) | 2.9 (2) |
| O(1) | 0.5254 (4) | 0.4555 (3) | 0.1435 (3) | 3.9 (1) |
| S(2) | 0.0844 (3) | 0.4047 (2) | 0.6193 (1) | 6.45 (8) |
| C(9) | -0.140 (1) | 0.3218 (9) | 0.6352 (6) | 9.4 (5) |
| C(10c) | -0.255 (1) | 0.2419 (8) | 0.5491 (7) | 4.4 (4) |
| C(10d) | -0.206 (3) | 0.206 (2) | 0.597 (2) | 4.7 (4) |
| C(11c) | -0.439 (2) | 0.171 (1) | 0.573 (1) | 6.3 (6) |
| C(11d) | -0.407 (4) | 0.150 (3) | 0.606 (2) | 5.0 (6) |
| C(12) | -0.1746 (9) | 0.1553 (6) | 0.4976 (5) | 5.8 (3) |
| N(4) | 0.0009 (6) | 0.2151 (4) | 0.4656 (3) | 3.9 (2) |
| C(13) | 0.1182 (8) | 0.3243 (5) | 0.5111 (4) | 4.2 (2) |
| N(5) | 0.2690 (6) | 0.3801 (4) | 0.4811 (3) | 4.1 (2) |
| C(14) | 0.3111 (7) | 0.3267 (5) | 0.3977 (4) | 3.8 (2) |
| N(6) | 0.4646 (6) | 0.3920 (5) | 0.3695 (3) | 5.0 (2) |
| C(15) | 0.2044 (7) | 0.2136 (5) | 0.3497 (4) | 3.5 (2) |
| Br(2) | 0.27120 (8) | 0.13367 (5) | 0.23993 (4) | 4.99 (3) |
| C(16) | 0.0420 (7) | 0.1488 (5) | 0.3815 (4) | 3.8 (2) |
| O(2) | -0.0620 (6) | 0.0487 (4) | 0.3441 (3) | 5.0 (2) |

* The occupancy factors of the atoms labelled *a*, *b*, *c* and *d* are 0.782, 0.218, 0.685 and 0.315, respectively.

Table 2. Selected bond distances (\AA) and bond angles ($^\circ$)

| | | | |
|-----------------|-----------|-------------------|-----------|
| C(1)—S(1) | 1.792 (6) | C(9)—S(2) | 1.793 (8) |
| C(5)—S(1) | 1.737 (4) | C(13)—S(2) | 1.748 (5) |
| C(5)—N(1) | 1.354 (5) | C(13)—N(4) | 1.353 (6) |
| C(8)—N(1) | 1.407 (5) | C(16)—N(4) | 1.429 (6) |
| N(2)—C(5) | 1.304 (5) | N(5)—C(13) | 1.308 (7) |
| C(6)—N(2) | 1.361 (5) | C(14)—N(5) | 1.357 (6) |
| N(3)—C(6) | 1.340 (5) | N(6)—C(14) | 1.344 (6) |
| Br(1)—C(7) | 1.887 (4) | Br(2)—C(15) | 1.879 (5) |
| O(1)—C(8) | 1.231 (5) | O(2)—C(16) | 1.214 (6) |
| C(5)—S(1)—C(1) | 105.1 (2) | C(13)—S(2)—C(9) | 103.9 (3) |
| C(5)—N(1)—C(4) | 123.2 (4) | C(13)—N(4)—C(12) | 124.1 (4) |
| C(8)—N(1)—C(4) | 116.2 (3) | C(16)—N(4)—C(12) | 115.6 (4) |
| C(8)—N(1)—C(5) | 120.6 (3) | C(16)—N(4)—C(13) | 120.3 (4) |
| N(1)—C(5)—S(1) | 122.4 (3) | N(4)—C(13)—S(2) | 122.8 (4) |
| N(2)—C(5)—S(1) | 113.1 (3) | N(5)—C(13)—S(2) | 112.6 (4) |
| N(2)—C(5)—N(1) | 124.5 (4) | N(5)—C(13)—N(4) | 124.6 (4) |
| C(6)—N(2)—C(5) | 118.0 (3) | C(14)—N(5)—C(13) | 118.4 (4) |
| N(3)—C(6)—N(2) | 115.8 (4) | N(6)—C(14)—N(5) | 114.8 (4) |
| C(7)—C(6)—N(2) | 120.6 (4) | C(15)—C(14)—N(5) | 120.9 (5) |
| C(7)—C(6)—N(3) | 123.6 (4) | C(15)—C(14)—N(6) | 124.3 (5) |
| Br(1)—C(7)—C(6) | 120.6 (3) | Br(2)—C(15)—C(14) | 121.0 (4) |
| C(8)—C(7)—C(6) | 122.3 (4) | C(16)—C(15)—C(14) | 122.3 (5) |
| C(8)—C(7)—Br(1) | 116.9 (3) | C(16)—C(15)—Br(2) | 116.7 (4) |
| C(7)—C(8)—N(1) | 113.9 (4) | C(15)—C(16)—N(4) | 113.4 (4) |
| O(1)—C(8)—N(1) | 120.2 (4) | O(2)—C(16)—N(4) | 119.2 (5) |
| O(1)—C(8)—C(7) | 125.9 (4) | O(2)—C(16)—C(15) | 127.4 (5) |

The structure is built up of two crystallographically independent molecules, one of which is shown in Fig. 1. The molecule contains one optically active centre [C(2)], but the crystal is racemic. Both molecules are affected, to different extents, by disorder arising from two alternative half-chair conformations of the six-membered thiazine ring. The out-of-plane C-ring

atoms [C(2) and C(10)] and their equatorially bonded methyl groups [C(3) and C(11)] are distributed over two positions, related by an approximate mirror plane, on which lie all other non-H atoms. The same type of disorder was observed for 8-amino-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one (Antolini & Pecorari, 1991). The presence of a bulky methyl group does not prevent the coexistence, even in one crystalline phase, of two conformers for this ring system. There are no significant differences between the dimensions of the two independent molecules. Bond distances and angles are typical (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987), and similar to those observed in the above-cited parent derivative (Antolini & Pecorari, 1991). The main difference between the independent molecules is in their hydrogen-bonding networks (Fig. 2). One molecule is bonded in linear chains, parallel to *a*, through one strong N(3)—H...O(1) interaction [N...O = 2.862 (5), H...O = 2.05 \AA , \angle N—H...O = 146°]. The second molecule forms dimeric units through two weaker centrosymmetrically related N(6)—H...N(5) hydrogen bonds [N...N = 3.169 (6), H...N = 2.17 \AA , \angle N—H...N = 159°]. This weakening of hydrogen-bond interactions could explain the larger thermal motion in the second molecule.

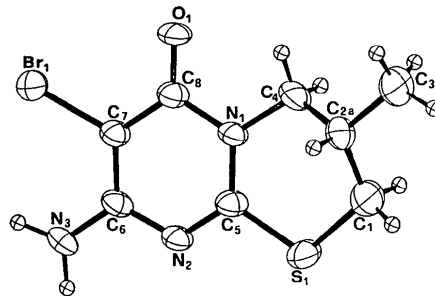


Fig. 1. ORTEP (Johnson, 1965) plot of one of the two crystallographically independent molecules. Ellipsoids for non-H atoms enclose 50% probability.

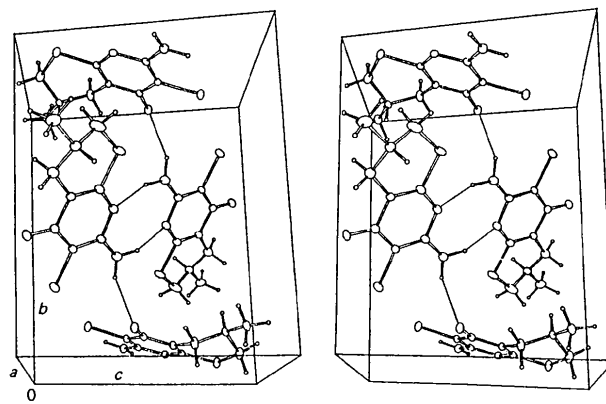


Fig. 2. Stereoview of the unit-cell contents.

Furthermore, the dimeric units act as a bridge between the linear chains, through two weak hydrogen bonds between a carbonyl oxygen and an amino group [$N\cdots O = 3.202$ (7), $H\cdots O = 2.34$ Å, $\angle N-H\cdots O = 150^\circ$].

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Structure of 3-Hydroxy-2-methyl-1,4-benzoquinone 4-Oxime Monohydrate

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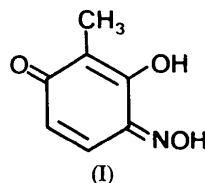
Abstract. (I) C₇H₇NO₃.H₂O, $M_r = 171.15$, monoclinic, $P2_1/c$, $a = 3.931$ (2), $b = 13.741$ (3), $c = 14.214$ (3) Å, $\beta = 92.08$ (2)°, $V = 767.28$ Å³, $Z = 4$, $D_x = 1.482$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0.71069$ Å, $\mu = 0.11$ mm⁻¹, $F(000) = 360$, $T = 295$ K, $R = 0.065$ for 1353 observed unique reflections with $I/\sigma(I) > 3.0$. The molecule is essentially planar. The mean values of the two short and the four long bond distances in the hexagonal ring are 1.327 (18) and 1.449 (12) Å, respectively. In the oxime group the dimensions are C—N 1.284 (6), N—O 1.364 (6) Å and C—N—O 113.8 (4)°, while the phenolic and quinonic C—O bond distances are 1.371 (5) and 1.247 (5) Å, respectively. The crystal structure is stabilized by a network of hydrogen bonds formed between the molecules of the title compound both directly as well as through the solvate water molecules.

Introduction. The structural character of what are frequently referred to as 2- and 4-nitrosophenols has been the subject of discussion for a considerable time and has been investigated using spectroscopic and X-ray crystallographic techniques (Hadzi, 1956;

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Romers & Fischmann, 1960; Bartindale, Crowder & Morley, 1959; Romers, 1964). The X-ray crystallographic studies have demonstrated that invariably they are 1,2- or 1,4-quinone oximic in character and the isolation in two forms in some cases has been shown to be due to the orientation of the N—OH group relative to the C=O group. A predominantly quinone oximic structure has also been established from X-ray crystallographic studies of metal complexes of the deprotonated anionic form (Charalambous, Stoten & Henrick, 1989). A more complex situation exists in the case of the so-called nitrosoresorcinols which have an additional hydroxy group. No structural studies on these compounds have been reported and here we report on the structure of 3-hydroxy-2-methyl-1,4-benzoquinone 4-oxime (I) which exists as a monohydrate.



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Experimental. 3-Hydroxy-2-methyl-1,4-benzoquinone 4-oxime was synthesized by nitrosation of 3-hydroxy-2-methylphenol using amyl nitrite/sodium