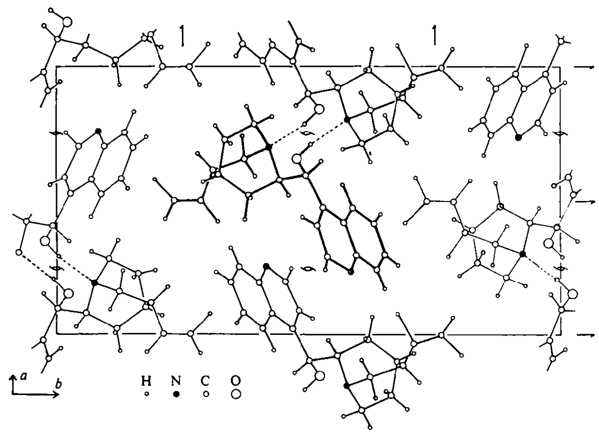


Fig. 2. A view down **c** showing the packing of the molecules.

is the necessary condition for antimalarial activity in *Cinchona* alkaloids (Oleksyn & Lebioda, 1980).

The packing of the molecules (Fig. 2) is very similar to that in cinchonine (Oleksyn, Lebioda & Ciechanowicz-Rutkowska, 1979). The intermolecular hydrogen bonds give rise to chains of molecules along alternate screw axes parallel to **c**. Within a chain each molecule interacts with two others through hydrogen bonds: O(12)–H(O12)···N(1$^{i}$), N(1)···H(O12$^{ii}$)–O(12$^{ii}$), where (i) = $\frac{3}{2} - x, 1 - y, z + \frac{1}{2}$; (ii) = $\frac{3}{2} - x, 1 - y, z - \frac{1}{2}$. The bond length is 2·76 (5) Å, and the angle N(1)···H(O12)–O(12) is 170(3)°.

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# Structure of 2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine–1,2-Benzisothiazol-3(2*H*)-one 1,1-Dioxide (1:1) Monohydrate

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**Abstract.** $C_{14}H_{18}N_4O_3.C_7H_5NO_3S.H_2O$, $M_r$ = 491·5, triclinic, $P\bar{1}$, $a$ = 9·152 (9), $b$ = 11·487 (6), $c$ = 12·674 (9) Å, $\alpha$ = 89·81 (5), $\beta$ = 103·97 (7), $\gamma$ = 113·95 (6)°, $U$ = 1174·9 Å$^3$, $D_x$ = 1·390, $D_m$ ($n$-heptane/$CCl_4$) = 1·397 Mg m$^{-3}$, $Z$ = 2, $\mu$ = 0·210 mm$^{-1}$, $F$(000) = 516, Mo $K\alpha$ radiation, $\lambda$ = 0·71069 Å. The final $R$ value was 0·082 for 4486 observed reflections. It is highly probable that N(1) of 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine (DTMBP) is protonated by an H atom released from N(5) of 1,2-benzisothiazol-3(2$H$)-one 1,1-dioxide ($o$-sulfobenzoimide, OSBI).

**Introduction.** DTMBP is used as an antifolate drug and OSBI as an artificial sweetener. The crystallographic investigation of the title compound was undertaken as part of our structural study of molecular complexes between different drugs. A single crystal for X-ray studies was obtained by slow evaporation of an aqueous solution containing equimolar amounts of DTMBP and OSBI. The crystal system was determined by oscillation and Weissenberg photographs. Intensity data of 5400 unique reflections were collected on a Syntex $R3$ computer-controlled diffractometer using an $\omega$-scan technique with monochromated Mo $K\alpha$ radiation in the range of $2\theta \leq 55°$ from a crystal 1·0 × 1·1 × 1·0 mm, 4486 of which were retained as observed [$I_o \geq 1·96\sigma(I_o)$], and were corrected for Lorentz and polarization factors but not for absorption. The structure was solved by the direct method using *MULTAN* 78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). The first $E$ synthesis revealed all the molecular positions, except C(14) of the DTMBP part. The structure was refined by full-matrix

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Table 1. *Positional parameters and equivalent isotropic thermal parameters with e.s.d.'s in parentheses*

| | $x$ | $y$ | $z$ | $B_{eq}$ (Å$^2$)* |
|---|---|---|---|---|
| DTMBP | | | | |
| N(1) | 0·5194 (4) | 0·3188 (3) | 0·0544 (3) | 3·95 |
| C(1) | 0·6638 (4) | 0·4254 (4) | 0·0718 (3) | 3·67 |
| N(2) | 0·7879 (4) | 0·4287 (3) | 0·0327 (3) | 3·58 |
| C(2) | 0·7644 (4) | 0·3257 (4) | −0·0305 (3) | 3·44 |
| C(3) | 0·6088 (4) | 0·2112 (4) | −0·0585 (3) | 3·54 |
| C(4) | 0·4915 (5) | 0·2130 (4) | −0·0116 (3) | 3·88 |
| N(3) | 0·6792 (4) | 0·5294 (4) | 0·1312 (3) | 4·70 |
| N(4) | 0·8904 (4) | 0·3326 (3) | −0·0689 (3) | 4·09 |
| C(5) | 0·5761 (5) | 0·1008 (4) | −0·1394 (3) | 4·17 |
| C(6) | 0·5659 (5) | 0·1428 (4) | −0·2548 (3) | 3·93 |
| C(7) | 0·6728 (5) | 0·1335 (4) | −0·3122 (3) | 4·15 |
| C(8) | 0·6682 (5) | 0·1782 (4) | −0·4155 (3) | 4·38 |
| C(9) | 0·5587 (5) | 0·2323 (4) | −0·4602 (3) | 4·50 |
| C(10) | 0·4500 (6) | 0·2381 (5) | −0·4032 (4) | 4·96 |
| C(11) | 0·4526 (5) | 0·1933 (5) | −0·3005 (3) | 4·81 |
| O(1) | 0·7693 (4) | 0·1753 (4) | −0·4780 (3) | 6·13 |
| O(2) | 0·5710 (4) | 0·2898 (3) | −0·5552 (3) | 5·71 |
| O(3) | 0·3390 (6) | 0·2868 (5) | −0·4526 (3) | 8·52 |
| C(12) | 0·8741 (9) | 0·1114 (8) | −0·4427 (6) | 8·86 |
| C(13) | 0·4481 (8) | 0·2161 (7) | −0·6516 (4) | 7·36 |
| C(14) | 0·3273 (15) | 0·3840 (11) | −0·4091 (10) | 14·98 |
| OSBI | | | | |
| S | −0·0177 (1) | 0·1266 (1) | 0·16072 (9) | 4·52 |
| N(5) | 0·1459 (5) | 0·2105 (4) | 0·1208 (3) | 4·75 |
| O(4) | −0·1609 (4) | 0·0702 (3) | 0·0692 (3) | 5·93 |
| O(5) | 0·0099 (5) | 0·0357 (3) | 0·2340 (3) | 6·31 |
| C(15) | 0·1449 (5) | 0·4827 (4) | 0·2790 (3) | 4·39 |
| C(16) | 0·0355 (7) | 0·4863 (5) | 0·3375 (4) | 5·35 |
| C(17) | −0·1019 (7) | 0·3747 (6) | 0·3427 (4) | 5·69 |
| C(18) | −0·1330 (6) | 0·2559 (5) | 0·2917 (4) | 5·13 |
| C(19) | −0·0218 (5) | 0·2552 (4) | 0·2345 (3) | 3·83 |
| C(20) | 0·1136 (4) | 0·3648 (4) | 0·2285 (3) | 3·52 |
| C(21) | 0·2112 (5) | 0·3342 (5) | 0·1618 (3) | 4·10 |
| O(6) | 0·3408 (4) | 0·4176 (4) | 0·1474 (3) | 5·53 |
| Water | | | | |
| O(7) | 0·0894 (4) | 0·2065 (3) | −0·1192 (3) | 5·22 |

* $B_{eq}$ defined according to Hamilton (1959).

least-squares calculations with parameters grouped in two blocks including anisotropic temperature factors for the non-H atoms to yield $R = 0·082$. Extinction corrections were applied (Zachariasen, 1967) with the isotropic mode. Anomalous dispersion for S was taken into account in the structure-factor calculation. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Positional parameters are shown in Table 1.*

* Lists of structure factors and anisotropic parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36677 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

**Discussion.** The stereostructure is presented in Fig. 1. Table 2 lists bond distances and angles. Table 3 contains some best planes and deviations of the atoms from them. In the DTMBP part, bond lengths N(1)—C(1) 1·357 (4) and N(1)—C(4) 1·376 (6) Å are significantly longer than the values obtained in DTMBP (Koetzle & Williams, 1976): N(1)—C(1) 1·343 (1), N(1)—C(4) 1·343 (1) Å, and the bond angle C(1)—N(1)—C(4) 120·8 (4)° is larger than 115·46 (5)° of Koetzle & Williams, suggesting that the H atom from OSBI is attached to N(1). The dihedral angle between planes (1) and (2) is 87·5 (1)°.

Table 4 gives the torsion angles. Angles $\varphi_1$ and $\varphi_2$ are −67·5 (4) and 122·1 (4)° respectively. The three $CH_3O$— groups, which belong to the phenyl group (plane 2), have a wide range of free rotation about each torsion angle. O(2) deviates from plane (2) by

Table 2. *Bond distances* (Å) *and bond angles* (°)

E.s.d.'s are given in parentheses.

| | | | |
|---|---|---|---|
| DTMBP | | | |
| N(1)—C(1) | 1·357 (4) | C(6)—C(11) | 1·394 (8) |
| N(1)—C(4) | 1·376 (6) | C(7)—C(8) | 1·402 (6) |
| C(1)—N(2) | 1·332 (6) | C(8)—C(9) | 1·393 (7) |
| C(1)—N(3) | 1·353 (7) | C(8)—O(1) | 1·365 (7) |
| N(2)—C(2) | 1·343 (6) | C(9)—C(10) | 1·385 (8) |
| C(2)—C(3) | 1·457 (5) | C(9)—O(2) | 1·378 (6) |
| C(2)—N(4) | 1·330 (6) | C(10)—C(11) | 1·396 (7) |
| C(3)—C(4) | 1·354 (7) | C(10)—O(3) | 1·374 (9) |
| C(3)—C(5) | 1·517 (6) | O(1)—C(12) | 1·422 (11) |
| C(5)—C(6) | 1·532 (6) | O(2)—C(13) | 1·430 (6) |
| C(6)—C(7) | 1·388 (7) | O(3)—C(14) | 1·301 (16) |
| C(1)—N(1)—C(4) | 120·8 (4) | C(7)—C(6)—C(11) | 120·3 (4) |
| N(1)—C(1)—N(2) | 121·7 (4) | C(6)—C(7)—C(8) | 119·3 (5) |
| N(1)—C(1)—N(3) | 117·9 (4) | C(7)—C(8)—C(9) | 120·7 (5) |
| N(2)—C(1)—N(3) | 120·4 (3) | C(7)—C(8)—O(1) | 124·0 (5) |
| C(1)—N(2)—C(2) | 118·5 (3) | C(9)—C(8)—O(1) | 115·3 (4) |
| N(2)—C(2)—C(3) | 122·8 (4) | C(8)—C(9)—C(10) | 119·4 (4) |
| N(2)—C(2)—N(4) | 116·9 (3) | C(8)—C(9)—O(2) | 119·3 (4) |
| C(3)—C(2)—N(4) | 120·3 (4) | C(10)—C(9)—O(2) | 121·0 (5) |
| C(2)—C(3)—C(4) | 115·2 (4) | C(9)—C(10)—C(11) | 120·5 (5) |
| C(2)—C(3)—C(5) | 122·7 (4) | C(9)—C(10)—O(3) | 117·4 (5) |
| C(4)—C(3)—C(5) | 122·1 (3) | C(11)—C(10)—O(3) | 122·0 (5) |
| N(1)—C(4)—C(3) | 121·0 (3) | C(6)—C(11)—C(10) | 119·8 (5) |
| C(3)—C(5)—C(6) | 110·2 (4) | C(8)—O(1)—C(12) | 118·7 (5) |
| C(5)—C(6)—C(7) | 119·7 (4) | C(9)—O(2)—C(13) | 115·0 (4) |
| C(5)—C(6)—C(11) | 119·9 (4) | C(10)—O(3)—C(14) | 123·7 (6) |
| OSBI | | | |
| S—N(5) | 1·618 (5) | C(16)—C(17) | 1·400 (7) |
| S—O(4) | 1·437 (4) | C(17)—C(18) | 1·401 (9) |
| S—O(5) | 1·453 (4) | C(18)—C(19) | 1·387 (8) |
| S—C(19) | 1·769 (5) | C(19)—C(20) | 1·380 (5) |
| N(5)—C(21) | 1·346 (7) | C(20)—C(21) | 1·503 (7) |
| C(15)—C(16) | 1·395 (9) | C(21)—O(6) | 1·240 (5) |
| C(15)—C(20) | 1·389 (7) | | |
| N(5)—S—O(4) | 111·1 (2) | C(17)—C(18)—C(19) | 116·4 (4) |
| N(5)—S—O(5) | 111·5 (3) | S—C(19)—C(18) | 130·0 (3) |
| N(5)—S—C(19) | 96·6 (2) | S—C(19)—C(20) | 107·7 (4) |
| O(4)—S—O(5) | 114·2 (2) | C(18)—C(19)—C(20) | 122·3 (4) |
| O(4)—S—C(19) | 111·7 (2) | C(15)—C(20)—C(19) | 121·4 (4) |
| O(5)—S—C(19) | 110·5 (2) | C(15)—C(20)—C(21) | 128·4 (4) |
| S—N(5)—C(21) | 111·2 (4) | C(19)—C(20)—C(21) | 110·2 (4) |
| C(16)—C(15)—C(20) | 117·6 (4) | N(5)—C(21)—C(20) | 114·2 (4) |
| C(15)—C(16)—C(17) | 120·6 (5) | N(5)—C(21)—O(6) | 124·1 (5) |
| C(16)—C(17)—C(18) | 121·7 (6) | C(20)—C(21)—O(6) | 121·6 (5) |

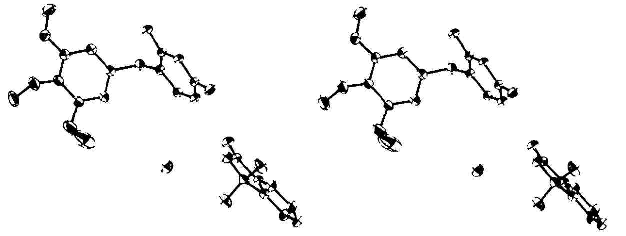

Fig. 1. Stereoscopic drawing of the title compound.

Table 3. *Least-squares planes and deviations* (Å) *of atoms from them*

The planes are expressed by $lx + my + nz = d$ in Å.

DTMBP

Plane (1): $-0{\cdot}1524x + 0{\cdot}5720y - 0{\cdot}8060z = -0{\cdot}1581$

N(1) −0·020 (4), C(1) 0·027 (4), N(2) −0·008 (4), C(2) −0·016 (4), C(3) 0·022 (4), C(4) −0·005 (4), N(3)* 0·105 (4), N(4)* −0·041 (4), C(5)* 0·162 (4)

Plane (2): $-0{\cdot}5848x - 0{\cdot}6871y - 0{\cdot}4311z = -1{\cdot}5838$

C(6) −0·012 (6), C(7) 0·004 (6), C(8) 0·008 (6), C(9) −0·013 (6), C(10) 0·005 (7), C(11) 0·008 (6), C(5)* −0·091 (6), O(1)* 0·005 (5), O(2)* −0·177 (5), O(3)* 0·046 (7)

OSBI

Plane (3): $-0{\cdot}3482x + 0{\cdot}4432y - 0{\cdot}8260z = -0{\cdot}6944$

S −0·015 (1), N(5) 0·023 (5), C(15) 0·002 (5), C(16) −0·003 (7), C(17) 0·008 (7), C(18) 0·001 (6), C(19) 0·000 (5), C(20) −0·005 (5), C(21) −0·011 (5), O(4)* 1·168 (4), O(5)* −1·257 (5), O(6)* 0·048 (5)

* Atoms not included in the plane calculations.

0·177 (5) Å. In the OSBI part, the observed S—N(5) distance 1·618 (5) Å is appreciably shorter than the 1·663 (2) Å found by Bart (1968) and the 1·663 (4) Å found by Okaya (1969) for OSBI not in a molecular complex. On the other hand, the angle S—N(5)—C(21) of 111·2 (4)° is significantly smaller than 115·0 (2)° found by Bart and 115·1° found by Okaya. These results strongly suggest that the H was released from N(5) of OSBI. Plane (3) is nonplanar [S and N(5) have large deviations]. Fig. 2 depicts the hydrogen bonds. The DTMBP molecules are in a dimeric arrangement by virtue of centrosymmetrically related hydrogen bonds between N(4) and N(2). O(7)(water) participates in four hydrogen bonds. The noteworthy contacts between DTMBP (*A*) and OSBI (*B*) are N(1)···O(6) 2·792 (7) and N(3)···O(6) 2·891 (6) Å. Although the positions of H atoms were not confirmed on a difference Fourier synthesis, it is highly probable that the H atom released from the OSBI is transferred to N(1) of the pyrimidine ring, and that the water molecule contributes to the stabilization of this crystal.

Table 4. *Torsion angles* (°)

| | | Present work | Koetzle & Williams (1976) |
|---|---|---|---|
| $\varphi_1$ | C(2)—C(3)—C(5)—C(6) | −67·5 (4) | −89·4 (1) |
| $\varphi_2$ | C(3)—C(5)—C(6)—C(7) | 122·1 (4) | 153·3 (1) |
| | C(7)—C(8)—O(1)—C(12) | 6·9 (5) | −4·9 (1) |
| | C(8)—C(9)—O(2)—C(13) | 103·6 (3) | −101·0 (1) |
| | C(9)—C(10)—O(3)—C(14) | −123·1 (6) | −172·3 (1) |

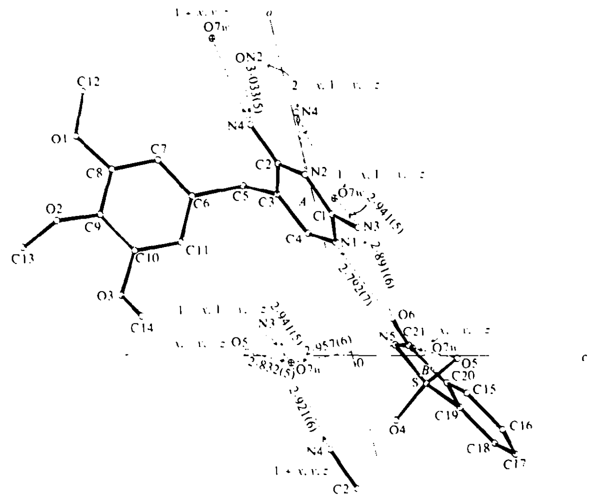

Fig. 2. Intermolecular hydrogen bonds. *A*: DTMBP; *B*: OSBI.

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