

Structure of 2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine–5,5-Diethylbarbituric Acid (1:1)

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Abstract. $C_{14}H_{18}N_4O_3 \cdot C_8H_{12}N_2O_3$, $M_r = 474.5$, monoclinic, $C2/c$, $a = 12.509$ (10), $b = 16.532$ (7), $c = 22.627$ (29) Å, $\beta = 94.56$ (13)°, $U = 4664.4$ Å³, $D_x = 1.352$, D_m (*n*-hexane/ CCl_4) = 1.349 Mg m⁻³, $Z = 8$, $\mu = 0.965$ mm⁻¹, $F(000) = 2016$, Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å. Full-matrix least-squares refinement resulted in a final conventional R index of 0.073 for 3660 observed reflections. 2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine (DTMBP) and 5,5-diethylbarbituric acid (DBA) are alternately linked by hydrogen bonds to form an endless chain in the **b** direction.

Introduction. DTMBP is an antifolate drug and DBA is a hypnotic drug. This investigation was undertaken as part of a series of structural studies of molecular complexes between different drugs. Single crystals (m.p. 497 K) of the title compound were grown from a solution of equimolar quantities of DTMBP and DBA in ethanol–acetone by slow evaporation of the solvent. Lattice constants were calculated by least squares from the diffractometrically determined θ values of 20 reflections. Intensity measurements were performed on a computer-controlled single-crystal diffractometer (Rigaku AFC-5, graphite-monochromated Cu $K\alpha$ radiation, ω – 2θ scan) up to $2\theta = 145^\circ$ using a crystal with dimensions 0.3 × 0.3 × 0.5 mm. A total of 3660 independent structure factors [$F_o \geq 3.0\sigma(F_o)$] were observed and used in this analysis. The phase problem was solved by direct methods using *MULTAN* 78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978); the E map computed with the set of best consistency (COMBOM = 3.0000) revealed 33 of 34 non-hydrogen atoms. The one remaining atom [C(14)] was located after a Fourier synthesis.

Table 1. Positional parameters and equivalent isotropic thermal parameters (Hamilton, 1959), with e.s.d.'s in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>	B_{eq} (Å ²)
DTMBP				
N(1)	0.0839 (3)	0.1806 (2)	0.6917 (1)	3.26
C(1)	0.1459 (3)	0.2263 (2)	0.7294 (1)	2.89
N(2)	0.1468 (2)	0.3077 (2)	0.7300 (1)	2.89
C(2)	0.0803 (3)	0.3454 (2)	0.6889 (1)	2.94
C(3)	0.0112 (3)	0.3024 (2)	0.6474 (1)	2.98
C(4)	0.0174 (3)	0.2201 (2)	0.6519 (2)	3.19
N(3)	0.2119 (3)	0.1883 (2)	0.7694 (2)	4.25
N(4)	0.0827 (3)	0.4265 (2)	0.6890 (1)	4.07
C(5)	−0.0646 (3)	0.3429 (2)	0.6019 (2)	3.48
C(6)	−0.0173 (3)	0.3684 (2)	0.5446 (1)	2.92
C(7)	−0.0879 (3)	0.3918 (2)	0.4971 (2)	3.33
C(8)	−0.0501 (3)	0.4146 (2)	0.4441 (2)	3.41
C(9)	0.0606 (3)	0.4135 (2)	0.4371 (2)	3.40
C(10)	0.1298 (3)	0.3921 (2)	0.4845 (2)	3.66
C(11)	0.0913 (3)	0.3685 (2)	0.5381 (2)	3.53
O(1)	−0.1123 (2)	0.4395 (2)	0.3954 (1)	4.25
O(2)	0.0980 (3)	0.4416 (2)	0.3848 (1)	4.42
O(3)	0.2400 (2)	0.3976 (2)	0.4828 (1)	5.74
C(12)	−0.2262 (4)	0.4420 (3)	0.3997 (2)	5.00
C(13)	0.0754 (4)	0.3887 (3)	0.3339 (2)	5.50
C(14)	0.2904 (4)	0.3472 (4)	0.4435 (3)	7.48
DBA				
C(15)	0.3700 (3)	0.3517 (2)	0.8491 (2)	3.48
C(16)	0.3192 (3)	0.4758 (2)	0.7958 (2)	3.29
C(17)	0.4647 (3)	0.4851 (2)	0.8729 (2)	3.49
C(18)	0.4494 (3)	0.3973 (2)	0.8906 (2)	3.25
N(5)	0.3060 (3)	0.3950 (2)	0.8085 (1)	3.44
N(6)	0.3997 (3)	0.5161 (2)	0.8272 (1)	3.59
O(4)	0.3599 (3)	0.2790 (2)	0.8518 (1)	5.53
O(5)	0.2625 (2)	0.5082 (2)	0.7564 (1)	4.31
O(6)	0.5323 (2)	0.5273 (2)	0.8991 (1)	4.87
C(19)	0.4005 (4)	0.4033 (3)	0.9527 (2)	4.48
C(20)	0.3841 (4)	0.3221 (3)	0.9834 (2)	5.46
C(21)	0.5581 (3)	0.3542 (3)	0.8953 (2)	4.24
C(22)	0.6109 (5)	0.3510 (3)	0.8372 (3)	6.51

The structure was refined by full-matrix least-squares calculations with parameters grouped in three blocks including anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the H atoms to yield $R = 0.073$. Extinction corrections were applied (Zachariassen, 1967) with the isotropic mode. The H atoms of C(13), C(14) and C(20) were not clearly seen in the difference synthesis. Neutral-atom scattering factors were obtained from *International Tables for X-ray Crystallography* (1974). Positional parameters are in Table 1.*

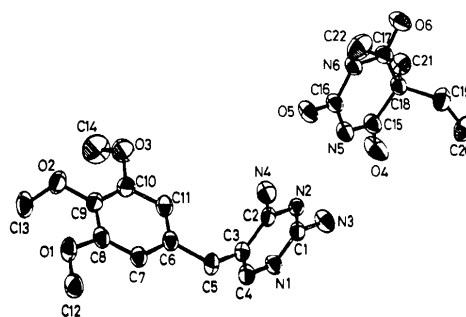


Fig. 1. Molecular structure of the title compound.

Discussion. Fig. 1 shows the structure of the title compound. Table 2 lists bond distances and valence

* Lists of structure factors, anisotropic thermal parameters and H-atom positional parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36831 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Bond distances (Å) and bond angles (°), with *e.s.d.*'s in parentheses

DTMBP			
N(1)—C(1)	1.340 (4)	C(6)—C(11)	1.378 (5)
N(1)—C(4)	1.345 (5)	C(7)—C(8)	1.376 (7)
C(1)—N(2)	1.346 (5)	C(8)—C(9)	1.406 (6)
C(1)—N(3)	1.333 (5)	C(8)—O(1)	1.361 (5)
N(2)—C(2)	1.350 (4)	C(9)—C(10)	1.370 (6)
C(2)—C(3)	1.416 (5)	C(9)—O(2)	1.387 (5)
C(2)—N(4)	1.341 (5)	C(10)—C(11)	1.396 (7)
C(3)—C(4)	1.366 (5)	C(10)—O(3)	1.385 (5)
C(3)—C(5)	1.501 (5)	O(1)—C(12)	1.436 (6)
C(5)—C(6)	1.527 (6)	O(2)—C(13)	1.456 (6)
C(6)—C(7)	1.391 (5)	O(3)—C(14)	1.404 (7)
C(1)—N(1)—C(4)	116.6 (3)	C(7)—C(6)—C(11)	119.2 (3)
N(1)—C(1)—N(2)	125.0 (3)	C(6)—C(7)—C(8)	120.6 (4)
N(1)—C(1)—N(3)	117.6 (3)	C(7)—C(8)—C(9)	120.3 (4)
N(2)—C(1)—N(3)	117.4 (3)	C(7)—C(8)—O(1)	125.1 (3)
C(1)—N(2)—C(2)	116.8 (3)	C(9)—C(8)—O(1)	114.7 (4)
N(2)—C(2)—C(3)	122.4 (3)	C(8)—C(9)—C(10)	118.8 (4)
N(2)—C(2)—N(4)	116.6 (3)	C(8)—C(9)—O(2)	119.6 (4)
C(3)—C(2)—N(4)	121.0 (3)	C(10)—C(9)—O(2)	121.3 (4)
C(2)—C(3)—C(4)	115.0 (3)	C(9)—C(10)—C(11)	120.8 (4)
C(2)—C(3)—C(5)	123.4 (3)	C(9)—C(10)—O(3)	122.0 (4)
C(4)—C(3)—C(5)	121.6 (3)	C(11)—C(10)—O(3)	117.1 (4)
N(1)—C(4)—C(3)	124.2 (3)	C(6)—C(11)—C(10)	120.3 (4)
C(3)—C(5)—C(6)	116.1 (3)	C(8)—O(1)—C(12)	117.4 (3)
C(5)—C(6)—C(7)	117.9 (3)	C(9)—O(2)—C(13)	114.6 (3)
C(5)—C(6)—C(11)	122.9 (3)	C(10)—O(3)—C(14)	118.5 (3)
DBA			
C(15)—C(18)	1.513 (6)	C(17)—N(6)	1.364 (5)
C(15)—N(5)	1.371 (5)	C(17)—O(6)	1.214 (5)
C(15)—O(4)	1.211 (5)	C(18)—C(19)	1.580 (7)
C(16)—N(5)	1.379 (5)	C(18)—C(21)	1.531 (6)
C(16)—N(6)	1.360 (5)	C(19)—C(20)	1.533 (7)
C(16)—O(5)	1.218 (5)	C(21)—C(22)	1.518 (8)
C(17)—C(18)	1.522 (5)	C(15)—C(18)—C(19)	107.6 (3)
C(18)—C(15)—N(5)	118.4 (3)	C(15)—C(18)—C(21)	110.3 (3)
C(18)—C(15)—O(4)	122.0 (4)	C(17)—C(18)—C(19)	103.9 (3)
N(5)—C(15)—O(4)	119.6 (4)	C(17)—C(18)—C(21)	109.4 (3)
N(5)—C(16)—N(6)	117.5 (3)	C(19)—C(18)—C(21)	111.8 (4)
N(5)—C(16)—O(5)	120.4 (3)	C(15)—N(5)—C(16)	124.9 (3)
N(6)—C(16)—O(5)	122.1 (3)	C(16)—N(6)—C(17)	125.8 (3)
C(18)—C(17)—N(6)	118.6 (3)	C(18)—C(19)—C(20)	115.1 (4)
C(18)—C(17)—O(6)	121.1 (4)	C(18)—C(21)—C(22)	113.6 (4)
N(6)—C(17)—O(6)	120.3 (3)		
C(15)—C(18)—C(17)	113.7 (3)		

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

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

DTMBP

Plane (1)

$$-0.767744x + 0.003668y + 0.640746z = 10.162057$$

N(1) -0.005 (5), C(1) -0.001 (5), N(2) 0.005 (4),
C(2) -0.005 (5), C(3) -0.005 (5), C(4) 0.006 (5), N(3)* -0.004 (5),
N(4)* -0.021 (5), C(5)* 0.009 (5)

Plane (2)

$$-0.033759x - 0.949567y - 0.311741z = -9.576522$$

C(6) 0.004 (6), C(7) -0.002 (6), C(8) -0.007 (6), C(9) 0.013 (6),
C(10) -0.011 (6), C(11) 0.002 (6), C(5)* 0.025 (6),
O(1)* -0.032 (4), O(2)* -0.080 (6), O(3)* -0.132 (4)

DBA

Plane (3)

$$-0.719466x + 0.240296y + 0.651634z = 11.716209$$

C(15) -0.070 (5), C(16) 0.028 (5), C(17) -0.012 (5),
C(18) 0.060 (5), N(5) 0.029 (4), N(6) -0.035 (4),
O(4)* -0.225 (4), O(5)* 0.037 (4), O(6)* -0.034 (4)

Dihedral angles (°)

(1) \wedge (2) 100.21 (5) (1) \wedge (3) 13.89 (15) (2) \wedge (3) 114.02 (15)°

* Atoms not included in the plane calculations.

angles. Table 3 contains selected best planes and deviations of atoms from them and dihedral angles.

The bond lengths and angles in the DTMBP part are in good agreement with those of DTMBP itself (Koetzle & Williams, 1976). Planes (1) and (2) of DTMBP are planar within experimental error.

Torsion angles C(2)—C(3)—C(5)—C(6) and C(3)—C(5)—C(6)—C(7) are 84.3 (4) and 168.0 (3)° respectively, compared to the corresponding angles of -89.4 (1) and 153.3 (1)° found by Koetzle & Williams, and to the values -67.5 (4) and 122.1 (4)° from our previous result for DTMBP-*o*-sulfo benzimidazole (1:1) monohydrate (Shimizu & Nishigaki, 1982). The bond distances and angles of the DBA moiety are in agreement with those of DBA itself (Craven, Vizzini & Rodrigues, 1969). O(4) deviates from plane (3) by

Table 4. Intermolecular hydrogen bonds (distances in Å, angles in degrees)

Donor	Acceptor		
N(6)—H <i>E</i> (ii)	N(1) <i>A</i> (i)	N(6)—H	0.99 (3)
		N(6)···N(1)	2.763 (5)
		H···N(1)	1.78 (3)
		N(6)—H···N(1)	176 (3)
N(3)—H(1) <i>A</i> (i)	O(5) <i>E</i> (ii)	N(3)—H(1)	0.83 (3)
		N(3)···O(5)	3.056 (5)
		H(1)···O(5)	2.24 (3)
		N(3)—H(1)···O(5)	166 (4)
N(3)—H(2) <i>A</i> (i)	O(4) <i>B</i> (i)	N(3)—H(2)	0.95 (4)
		N(3)···O(4)	2.933 (6)
		H(2)···O(4)	2.01 (4)
		N(3)—H(2)···O(4)	165 (4)
N(5)—H <i>B</i> (i)	N(2) <i>A</i> (i)	N(5)—H	0.95 (4)
		N(5)···N(2)	2.940 (5)
		H···N(2)	2.00 (4)
		N(5)—H···N(2)	171 (3)
N(4)—H(1) <i>A</i> (i)	O(5) <i>B</i> (i)	N(4)—H(1)	1.05 (4)
		N(4)···O(5)	2.943 (5)
		H(1)···O(5)	1.91 (4)
		N(4)—H(1)···O(5)	168 (4)

Symmetry code: (i) x, y, z ; (ii) $0.5 - x, -0.5 + y, 1.5 - z$. (*A*) DTMBP. (*B*) and (*E*) DBA.

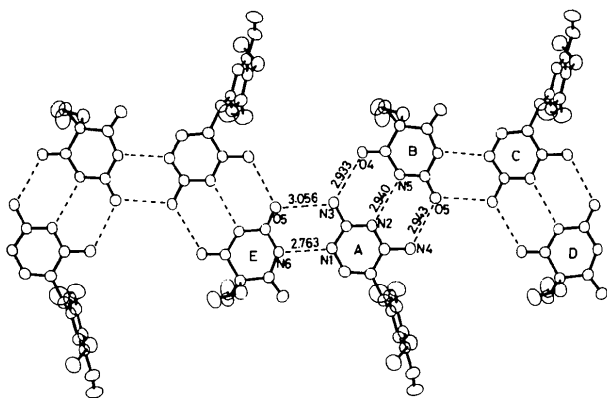


Fig. 2. Packing diagram of the title compound (*A*, *C*: DTMBP; *B*, *D*, *E*: DBA). (Distances are in Å.)

0.225 (4) Å. The angles C(15)—C(18)—C(19)—C(20) and C(15)—C(18)—C(21)—C(22) are 63.3 (3) and 63.4 (4)°, respectively. Table 4 gives the hydrogen-bonding parameters. A packing diagram is shown in Fig. 2. The shortest N(1)···H—N(6) contact between DTMBP(*A*) and DBA(*E*) is 2.763 (5) Å, which is considerably shorter than the sum of the radii, 3.0 Å (Pauling, 1960). O(6) does not participate in any hydrogen bonds. DTMBP molecules have a tendency

to form dimers — as Koetzle & Williams found in DTMBP, and we found in DTMBP-*o*-sulfo-benzo-imide (1:1) monohydrate — via the hydrogen bond N(4)···N(2); DBA molecules also have a tendency to form dimers (NH···C=O), as observed in DBA by Craven *et al.* (1969), and in the DBA-caffeine (2:1) complex by Craven & Gartland (1970).

In the present crystal, however, DTMBP and DBA are alternately linked to form an endless chain (—*A*—*B*—*C*—*D*—) by characteristic hydrogen bonds, which apparently contribute significantly to the stabilization of this crystal; this is probably why its melting point (497 K) is so high. No significant contacts exist between molecules of the same kind (DTMBP···DTMBP, DBA···DBA).

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