C2—C1—C6	121.9 (4)	C3—O2—C4	116.0 (4)
C2—C1—C1^i	122.8 (4)	O2—C4—C5	107.4 (3)
C6—C1—C1^i	115.4 (4)	C1—C6—O3	124.2 (3)
C1—C2—C3	121.7 (4)	C1—C6—O4	109.5 (4)
C2—C3—O1	125.9 (2)	O3—C6—O4	126.3 (2)
C2—C3—O2	109.4 (4)	C6—O4—C7	115.2 (4)
O1—C3—O2	124.6 (3)	O4—C7—C8	109.0 (5)

C6—C1—C2—C3	−1.1 (7)
C1^i—C1—C2—C3	180.0 (4)
C2—C1—C6—O3	−97.4 (6)
C2—C1—C6—O4	85.4 (5)
C1^i—C1—C6—O3	81.6 (6)
C1^i—C1—C6—O4	−95.7 (4)
C2—C1—C1^i—C2^i	180.0 (4)
C2—C1—C1^i—C6^i	−1.0 (6)
C1—C2—C3—O1	8.7 (8)
C1—C2—C3—O2	−169.6 (4)
C2—C3—O2—C4	−177.6 (4)
O1—C3—O2—C4	4.2 (7)
C3—O2—C4—C5	−165.3 (4)
C1—C6—O4—C7	179.1 (4)
O3—C6—O4—C7	1.9 (7)
C6—O4—C7—C8	−165.9 (5)

Symmetry code: (i) $-x, -y, -z$.

The $\Delta f'$ and $\Delta f''$ components of anomalous dispersion were included in the calculations for non-H atoms (Cromer, 1974). F_o data were collected at the Research Center for Protein Engineering, Institute for Protein Research, Osaka University, Japan. All calculations were carried out on an NEC ACOS S3700 computer at the Research Center for Protein Engineering.

Data collection: Rigaku software. Cell refinement: Rigaku software. Data reduction: Rigaku software. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *ANYBLK* (Imoto, 1990). Molecular graphics: *ORTEP*II (Johnson, 1976).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: TA1105). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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10-(*N*-Carboxymethylcarbamoyl)-3,7-bis-(dimethylamino)phenothiazine (CCAP)–Ethanol (1/1), $C_{19}H_{22}N_4O_3S.C_2H_6O$

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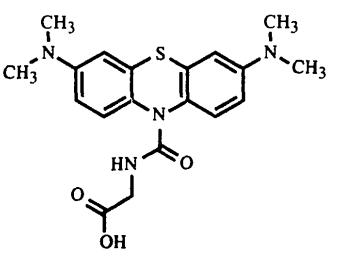
Abstract

In the title molecule, [3,7-bis(dimethylamino)phenothiazin-10-yl]-*N*-carbamoylacetic acid–ethanol (1/1), the phenothiazine ring adopts a boat conformation, with the S and N atoms occupying the bow and stern positions, respectively. The dihedral angle between the two phenyl rings is 131 (1)°. The system of conjugation in the molecule is remarkably different from that in methylene blue.

Comment

10-(*N*-Carboxymethylcarbamoyl)-3,7-bis(dimethylamino)phenothiazine (CCAP) is one of the functional dyes which have applications in clinical diagnostics. For example, it is used to measure the activity of lipase being converted in the presence of peroxidase and hydrogen peroxide to methylene blue. Effective conversion is essential for sensitive and accurate diagnosis. To understand the relationship between the efficiency of conversion and the molecular stereochemistry, the structure of CCAP has been determined as it ethanol solvate.



CCAP

The molecule as a whole (Fig. 1) has a butterfly form, as is also found in 3,7-bis(dimethylamino)-10-(*N*-methylcarbamoyl)phenothiazine (MCDP) (Fujii, Hirayama & Miike, 1993). The angles at the N10 atom in the phenothiazine ring sum to 359.4 (5)°, indicating an almost planar coordination at this atom. The N10—C11 and N12—C11 bond distances of 1.376 (3) and 1.352 (4) Å, respectively, suggest that rupture of the former N—C bond, an essential step in the production of the blue coloration, may be relatively easy. The amino moiety of the carbamoyl group is almost parallel to the phenothiazine ring and the carboxy group is nearly coplanar with the carbamoyl group. The sums of the bond angles around the N3 and N7 atoms are 360.0 (5) and 359.1 (5)°, respectively, but the terminal dimethylamino groups are not coplanar with their attached phenyl rings. Bond distances and angles in the molecule are within the expected ranges. Although the geometric parameters in the conjugated system are quite different from those in methylene blue pentahydrate (Marr & Stewart, 1973) and methylene blue thiocyanate (Kahn-Harari, Ballard & Norris, 1973), they are similar to those in MCDP.

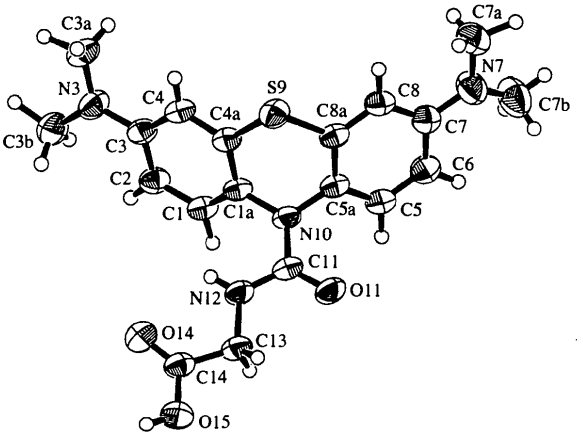


Fig. 1. *ORTEP*II drawing (Johnson, 1976) of the title molecule representing heavy atoms as 50% ellipsoids and H atoms as spheres of arbitrary radii.

In the crystal, two intermolecular hydrogen bonds of type O—H···O [O15···O1*S*(2 − *x*, −*y*, −*z*) 2.599 (4) Å and O15—H15···O1*S* 159 (6)°; O1*S*···O11 2.721 (3) Å and O1*S*—H1*S*···O11 166 (4)°] are observed between the CCAP and ethanol molecules.

Experimental

The title crystals were grown from an ethanol solution at 281 (5) K. A crystal sealed in a glass capillary was used for the diffraction experiments.

Crystal data

$C_{19}H_{22}N_4O_3S.C_2H_6O$
M_r = 432.54
Triclinic
$P\bar{1}$
a = 9.842 (4) Å
b = 15.775 (2) Å
c = 7.382 (1) Å
α = 100.04 (1)°
β = 95.75 (2)°
γ = 79.02 (2)°
V = 1105.4 (5) Å^3
Z = 2
D_x = 1.30 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 30–35°
μ = 1.590 mm^{-1}
T = 293 (5) K
Prism
0.6 × 0.5 × 0.3 mm
Blue

Data collection

Enraf–Nonius Turbo-CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
4847 measured reflections
4480 independent reflections
3599 observed reflections [$F > 3\sigma(F)$]

R_{int} = 0.087
θ_{max} = 74°
$h = -12 \rightarrow 12$
$k = -19 \rightarrow 19$
$l = 0 \rightarrow 9$
3 standard reflections monitored every 30 reflections
intensity decay: 4.95%

Refinement

Refinement on F
R = 0.065
wR = 0.087
S = 2.76
3599 reflections
384 parameters
H atoms were refined isotropically
Weighting scheme based on measured e.s.d.'s; $w = 1/[\sigma(F)^2]$

$(\Delta/\sigma)_{max}$ = 0.65
$\Delta\rho_{max}$ = 0.49 e Å^{-3}
$\Delta\rho_{min}$ = −0.46 e Å^{-3}
Extinction correction: Zachariasen (1968), type 2
Extinction coefficient: 306 (2)
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
S9	0.68453 (7)	0.39613 (4)	0.7214 (1)	0.0557 (2)
O11	0.8403 (2)	0.0973 (1)	0.5430 (3)	0.0587 (6)
O14	1.1445 (3)	0.1832 (2)	0.1592 (4)	0.0893 (9)
O15	1.1404 (3)	0.0480 (2)	0.0173 (3)	0.0777 (8)
N3	1.1321 (3)	0.5249 (2)	0.7456 (4)	0.0610 (7)
N7	0.4774 (3)	0.2660 (2)	1.2052 (4)	0.0736 (9)
N10	0.8823 (2)	0.2288 (1)	0.6953 (3)	0.0482 (6)
N12	0.9853 (3)	0.1646 (1)	0.4240 (3)	0.0529 (6)
C1*a*	0.9488 (3)	0.3033 (2)	0.7112 (4)	0.0452 (6)
C1	1.0913 (3)	0.2963 (2)	0.7264 (4)	0.0506 (7)
C2	1.1529 (3)	0.3690 (2)	0.7356 (4)	0.0520 (7)
C3*b*	1.2781 (4)	0.5155 (2)	0.7266 (6)	0.071 (1)
C3	1.0713 (3)	0.4529 (2)	0.7399 (4)	0.0483 (7)
C3*a*	1.0494 (4)	0.6118 (2)	0.7685 (5)	0.0627 (9)
C4	0.9274 (3)	0.4600 (2)	0.7404 (4)	0.0495 (7)
C4*a*	0.8671 (3)	0.3863 (2)	0.7235 (3)	0.0458 (6)
C5	0.7786 (3)	0.1718 (2)	0.9295 (4)	0.0508 (7)
C5*a*	0.7790 (3)	0.2354 (2)	0.8231 (4)	0.0464 (6)
C6	0.6806 (3)	0.1819 (2)	1.0555 (4)	0.0547 (8)

C7	0.5774 (3)	0.2572 (2)	1.0810 (4)	0.0520 (7)
C7*a*	0.3688 (5)	0.3401 (3)	1.2234 (7)	0.081 (1)
C7*b*	0.4928 (6)	0.2102 (4)	1.3414 (8)	0.095 (1)
C8	0.5794 (3)	0.3218 (2)	0.9750 (4)	0.0498 (7)
C8*a*	0.6795 (3)	0.3112 (2)	0.8478 (4)	0.0465 (6)
C11	0.8993 (3)	0.1598 (2)	0.5522 (4)	0.0466 (6)
C13	1.0210 (3)	0.0919 (2)	0.2802 (4)	0.0507 (7)
C14	1.1094 (3)	0.1141 (2)	0.1484 (4)	0.0546 (8)
O1*S*	0.7711 (3)	−0.0426 (2)	0.3052 (4)	0.0938 (10)
C1*S*	0.6581 (5)	−0.0591 (3)	0.3788 (7)	0.094 (1)
C2*S*	0.5669 (6)	−0.1010 (5)	0.2389 (9)	0.129 (2)

Table 2. *Selected geometric parameters (Å, °)*

S9—C4*a*	1.773 (3)	N12—C13	1.436 (3)
S9—C8*a*	1.771 (3)	C1*a*—C1	1.380 (4)
O11—C11	1.225 (3)	C1*a*—C4*a*	1.393 (3)
O14—C14	1.192 (4)	C1—C2	1.385 (4)
O15—C14	1.306 (4)	C2—C3	1.408 (4)
N3—C3*b*	1.434 (4)	C3—C4	1.400 (4)
N3—C3	1.374 (3)	C4—C4*a*	1.384 (4)
N3—C3*a*	1.447 (4)	C5—C5*a*	1.378 (4)
N7—C7	1.383 (4)	C5—C6	1.374 (4)
N7—C7*a*	1.423 (5)	C5*a*—C8*a*	1.392 (4)
N7—C7*b*	1.428 (5)	C6—C7	1.408 (4)
N10—C1*a*	1.432 (3)	C7—C8	1.393 (4)
N10—C5*a*	1.432 (4)	C8—C8*a*	1.396 (4)
N10—C11	1.376 (3)	C13—C14	1.493 (4)
N12—C11	1.352 (4)		
C4*a*—S9—C8*a*	98.5 (1)	S9—C4*a*—C1*a*	118.8 (2)
C3*b*—N3—C3	120.9 (3)	S9—C4*a*—C4	120.5 (2)
C3*b*—N3—C3*a*	118.7 (3)	N10—C5*a*—C5	122.7 (2)
C3—N3—C3*a*	120.4 (3)	N10—C5*a*—C8*a*	118.5 (2)
C7—N7—C7*a*	121.0 (3)	N7—C7—C6	121.1 (3)
C7—N7—C7*b*	121.1 (3)	N7—C7—C8	121.6 (3)
C7*a*—N7—C7*b*	117.0 (3)	S9—C8*a*—C5*a*	119.3 (2)
C1*a*—N10—C5*a*	115.8 (2)	S9—C8*a*—C8	120.1 (2)
C1*a*—N10—C11	123.4 (2)	O11—C11—N10	121.5 (3)
C5*a*—N10—C11	120.2 (2)	O11—C11—N12	122.1 (2)
C11—N12—C13	120.5 (2)	N10—C11—N12	116.4 (2)
N10—C1*a*—C1	122.3 (2)	N12—C13—C14	111.0 (2)
N10—C1*a*—C4*a*	118.9 (2)	O14—C14—O15	124.7 (3)
N3—C3—C2	120.7 (3)	O14—C14—C13	124.8 (3)
N3—C3—C4	121.7 (2)	O15—C14—C13	110.5 (2)
N10—C1*a*—C4*a*—S9	0.7 (3)	C1*a*—N10—C11—N12	0.8 (4)
C3*b*—N3—C3—C2	7.0 (4)	C5*a*—N10—C11—O11	−9.2 (4)
C3*a*—N3—C3—C4	5.4 (4)	O11—C11—N12—C13	−5.9 (4)
N10—C5*a*—C8*a*—S9	−0.1 (3)	C11—N12—C13—C14	176.3 (3)
C7*b*—N7—C7—C6	14.8 (6)	N12—C13—C14—O14	−0.9 (5)
C7*a*—N7—C7—C8	2.8 (5)	N12—C13—C14—O15	−179.5 (3)

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *CAD-4 Software*. Program(s) used to solve structure: *SIR88* (Burla *et al.*, 1989). Program(s) used to refine structure: *TEXSAN LS* (Molecular Structure Corporation, 1992). Molecular graphics: *ORTEP*II (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: MU1269). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Penicillin V Benzhydryl Ester Sulfoxide Monohydrate

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Abstract

Diphenylmethyl 3,3-dimethyl-7-oxo-6-phenoxyacetamido-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4-oxide monohydrate, $C_{29}H_{28}N_2O_6S.H_2O$, assumes an *S* configuration, with the penam moiety (1-azabicyclo-[3.2.0]heptane-7-one) in the open conformation. The conformation of the penam moiety including the 3α-carboxyl and the 6β-acetamido groups is very similar to that of penicillin V benzyl ester sulfoxide [Shin, Kim & Kim (1992). *Acta Cryst.* C**48**, 1449–1451], but the orientations of the terminal phenyl groups at the 6β-position with respect to the central penam moiety are different in the two compounds. The acetamido N9 atom forms an intramolecular three-centred hydrogen bond with the sulfoxide O1 and phenoxy O13 atoms [N9···O1 2.839 (4) and N9···O13 2.554 (4) Å]. The molecules are linked along the *a* axis *via* hydrogen bonds involving water molecules [O1···O*w*···O11].

Comment

Penicillin sulfoxides with protective ester groups are useful as intermediates in the manufacture of therapeutically important cepharosporins and β-lactamase inhibitors (Colvin, 1992). Oxidation of penicillin to its sulfoxide results in the inactive derivative with the *S* configuration. The penam moiety in the sulfoxide derivatives always assumes the open conformation, while that of their parent compounds assumes the closed conformation (Cooper, DeMarco, Cheng & Jones, 1969). An example is the pair, penicillin V benzyl ester