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# (6*R**,16*R**)-9,14-Dihydro-6-methyl-6,16-methano-6*H*,16*H*-[2,4]benzothiazepino[3,4-*d*][1,3,5]benzoxadiazocine hydrobromide dimethylformamide hemisolvate

**Viktor Kettmann* and Jan Svetlik**

Faculty of Pharmacy, Comenius University, Odbojarov 10, Bratislava, Slovak Republic 83232
Correspondence e-mail: kettmann@fpharm.uniba.sk

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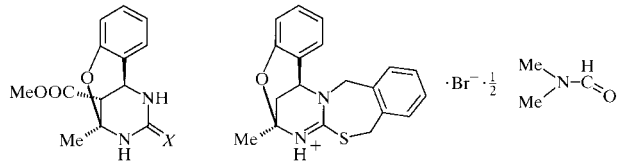
The title compound, $C_{19}H_{19}N_2OS^+\cdot Br^-\cdot 0.5C_3H_7NO$, is an oxygen-bridged phenylpyrimidine derivative in which the heterocyclic ring is protonated, the positive charge being dispersed over both of the N atoms. Both molecules in the asymmetric unit exist in an identical conformation, which consists of a central planar portion with the two terminal phenyl rings protruding from the same side of the plane. One of the independent molecules forms a strong hydrogen bond with the bromide anion, while the other is hydrogen bonded to the dimethylformamide solvent molecule.

## Comment

In recent years, the importance of the Biginelli pyrimidine synthesis (Kappe, 1993) has considerably increased, especially since the discovery that certain 3,4-dihydro-2(1*H*)-pyrimidone derivatives represent a valuable alternative to classical 1,4-dihydropyridine (DHP) calcium-channel blockers (Atwal *et al.*, 1991). Following the above methodology we have described a route to the oxygen-bridged pyrimidines (I*a*) and (I*b*) (Svetlik *et al.*, 1991). The solid-state geometries of (I*a*) and its *N*-acetyl derivative were investigated in order to obtain a better insight into the conformational requirements of the DHP receptor (Kettmann & Svetlik, 1996, 1997; Kettmann *et al.*, 1996). In addition, thioxoester (I*a*) was found to be a useful building block for the construction of conformationally restricted polycyclic systems (Svetlik *et al.*, 1991). Quite recently, we have employed pyrimidinethione (I*a*) in the cyclization reaction with 1,2-bis(bromomethyl)benzene to prepare the corresponding benzothiazepine heterocycle incorporating the fundamental O-bridged pyrimidine skeleton, and the structure of the product, the title compound, (II), has been established by spectroscopic methods (Svetlik & Liptaj, 1999). A careful inspection of Dreiding models, along with NOESY (nuclear Overhauser effect spectroscopy) and *AM*1 (Svetlik & Liptaj, 1999) calculations, allowed us to postulate the molecular conformation of this compound. To confirm the postulated stereochemical model, a single-crystal X-ray analysis of (II) was undertaken and the results are presented here.



(I*a*) $X$ = S
(I*b*) $X$ = O

(II)

As can be seen in Fig. 1, the asymmetric unit of (I) consists of two protonated molecules (*A* and *B*), two bromide anions and one dimethylformamide molecule. The two independent cations are identical; the corresponding bonding and torsional parameters agree to within 4$\sigma$. As shown in Table 1, the protonation causes extensive conjugation in the central part of the molecule: the formal single bond C9—N19 and the formal double bond C9═N8 are comparable to within experimental error. Moreover, the sum of the valence angles around atom N19 is close to 360°, indicating that the state of hybridization of this atom is $sp^2$. These data are consistent with $\pi$-electron delocalization from N19 into the protonated atom N8, leading to dispersion of the positive charge over both N atoms of the pyrimidine ring. The conjugation is extended to the S atom, as indicated by the non-equivalence of the two C—S bond distances (Table 1); while S10—C11 is essentially a single bond, the C9—S10 distances of 1.715 (8) (molecule *A*) and 1.742 (9) Å (molecule *B*) correspond to a bond order of *ca* 1.5 (Khan *et al.*, 1988), assuming values of 1.81 and 1.61 Å for single S—C and double S═C bond lengths, respectively. As a result of this conjugation, atoms C7, N8, C9, S10, C11, C18, N19 and C20 in the central part of the molecule are essentially coplanar [r.m.s. 0.077 (8) and 0.058 (8) Å in molecules *A* and *B*, respectively].

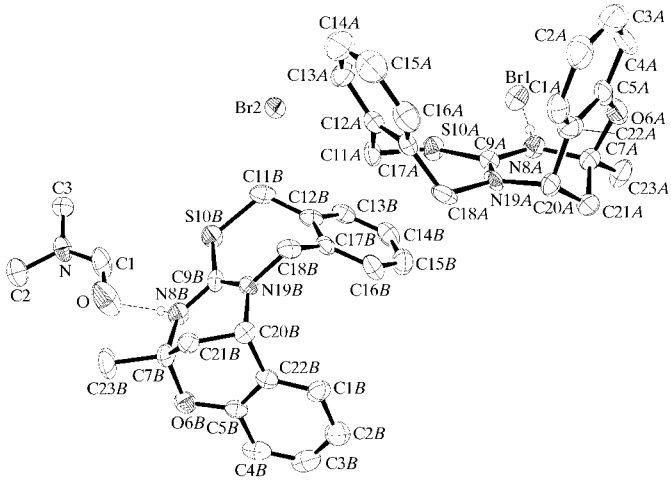



**Figure 1**
A view of both molecules of the asymmetric unit of (II) with the atom-numbering scheme. Displacement ellipsoids are shown at the 35% probability level and for clarity only the polar H atoms are shown.

As noted above, it is of interest to compare the conformation of the O-bridged phenylpyrimidine moiety with that found in compounds of type (I) containing this molecular fragment and possessing calcium-channel blocking activity. Calculation of the least-squares planes has shown that the conformation of the pyrimidine ring is intermediate between the C20,C21-half-chair and the C21-envelope form: atoms C20 and C21 are displaced by 0.238 (11) and −0.606 (12) Å, respectively (molecule *A*), and by −0.168 (11) and 0.629 (13) Å, respectively (molecule *B*) from the least-squares plane of the remaining four atoms. Due to the pseudoaxial orientation of the O-bridged phenyl ring, the ring is fixed in an approximately perpendicular orientation with respect to the mean plane of the pyrimidine ring. Similar features for the phenylpyrimidine moiety have also been observed in compounds of type (I) (Kettmann & Svetlik, 1996, 1997). With regard to the conformation of the seven-membered ring, the ring consists of two approximately planar segments, C11/S10/C9/N19/C18 and C11/C12/C17/C18, folded about the C11···C18 line in such a manner that both phenyl rings point to the same side of the central molecular plane.

The positive charge of the protonated molecules is neutralized by the bromide anions, but only one (Br1) forms a hydrogen bond with N8*A*$^+$—H [N8*A*—H···Br1: N—H 0.86, H···Br 2.43 and N···Br 3.285 (7) Å, and N—H···Br 170°]. The other Br$^-$ ion is situated between molecules *A* and *B*, where it makes short contacts with their C atoms. The protonated atom N8 of molecule *B* donates a hydrogen bond to the O atom of the dimethylformamide solvent molecule [N8*B*—H···O: N—H 0.86, H···O 1.94 and N···O 2.769 (10) Å, and N—H···O 161°].

## Experimental

Compound (II) was prepared by refluxing methyl (2*R**,6*R**,11*S**)-3,4,5,6-tetrahydro-2-methyl-2,6-methano-4-thioxo-2*H*-[1,3,5]benzoxadiazocine-11-carboxylate, (I*a*) (Svetlik *et al.*, 1991), and 1,2-bis(bromomethyl)benzene in dimethylformamide (DMF), as described by Svetlik & Liptaj (1999). For the X-ray analysis, the product was recrystallized from DMF–EtOH (1:1).

*Crystal data*

$C_{19}H_{19}N_2OS^+\cdot Br^-\cdot 0.5C_3H_7NO$
$M_r$ = 439.89
Monoclinic, $P2_1/c$
$a$ = 18.612 (8) Å
$b$ = 19.807 (9) Å
$c$ = 11.087 (5) Å
$\beta$ = 95.94 (3)°
$V$ = 4065 (3) Å$^3$
$Z$ = 8
$D_x$ = 1.437 Mg m$^{-3}$
$D_m$ = 1.44 (1) Mg m$^{-3}$
$D_m$ measured by flotation in bromoform/*c*-hexane
Mo $K\alpha$ radiation
Cell parameters from 15 reflections
$\theta$ = 10–22°
$\mu$ = 2.141 mm$^{-1}$
$T$ = 293 (2) K
Plate, colourless
0.35 × 0.30 × 0.10 mm

*Data collection*

Syntex $P2_1$ diffractometer
$\theta/2\theta$ scans
Absorption correction: $\psi$ scan (North *et al.*, 1968)
$T_{min}$ = 0.495, $T_{max}$ = 0.810
7534 measured reflections
7166 independent reflections
3573 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.024
$\theta_{max}$ = 25.08°
$h = -22 \rightarrow 0$
$k = 0 \rightarrow 23$
$l = -12 \rightarrow 12$
2 standard reflections
frequency: 100 min
intensity decay: none

**Table 1**
Selected geometric parameters (Å, °).

| | Molecule *A* | Molecule *B* |
|---|---|---|
| C7—N8 | 1.462 (10) | 1.437 (10) |
| N8—C9 | 1.332 (9) | 1.332 (9) |
| C9—N19 | 1.320 (9) | 1.289 (9) |
| C9—S10 | 1.715 (8) | 1.742 (9) |
| S10—C11 | 1.814 (8) | 1.807 (8) |
| C18—N19 | 1.481 (10) | 1.462 (9) |
| N19—C20 | 1.484 (9) | 1.513 (9) |
| | | |
| C9—N8—C7 | 126.3 (7) | 125.7 (7) |
| N19—C9—N8 | 118.1 (7) | 120.8 (8) |
| N19—C9—S10 | 129.8 (6) | 129.0 (7) |
| N8—C9—S10 | 112.1 (7) | 110.2 (6) |
| C9—S10—C11 | 109.6 (4) | 110.4 (4) |
| C9—N19—C18 | 123.0 (7) | 124.5 (7) |
| C9—N19—C20 | 118.9 (6) | 118.2 (7) |
| C18—N19—C20 | 117.8 (7) | 117.2 (6) |
| | | |
| C7—N8—C9—N19 | 10.5 (12) | 7.7 (13) |
| C9—S10—C11—C12 | 47.4 (8) | 50.4 (8) |
| S10—C11—C12—C17 | −72.7 (9) | −66.1 (9) |
| C12—C17—C18—N19 | 74.9 (9) | 79.1 (9) |
| N8—C9—N19—C20 | 2.7 (11) | 1.4 (11) |
| C17—C18—N19—C9 | −62.3 (10) | −64.9 (11) |
| N19—C20—C22—C1 | 87.7 (10) | 27.2 (10) |
| C21—C20—C22—C5 | 23.3 (11) | 89.9 (9) |

*Refinement*

Refinement on $F^2$
$R(F)$ = 0.063
$wR(F^2)$ = 0.157
$S$ = 0.896
7166 reflections
483 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0758P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.39 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.31 e Å$^{-3}$
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0017 (3)

Data collection and cell refinement: $P2_1$ software: data reduction: *XP*21 (Pavelčík, 1987); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1354). Services for accessing these data are described at the back of the journal.

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