*Data collection*

Rigaku AFC-5*R* diffractometer
$\omega$–$2\theta$ scans
Absorption correction: $\psi$ scans (North *et al.*, 1968)
$T_{\min} = 0.661$, $T_{\max} = 0.947$
3541 measured reflections
1736 independent reflections
1341 reflections with $I > 2\sigma(I)$
$R_{\text{int}} = 0.035$
$\theta_{\max} = 70°$
$h = -5 \rightarrow 8$
$k = 0 \rightarrow 39$
$l = -3 \rightarrow 6$
3 standard reflections every 150 reflections intensity decay: 3.8%

*Refinement*

Refinement on *F*
$R = 0.05$
$wR = 0.070$
$S = 1.380$
1341 reflections
118 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o) + 0.00141|F_o|^2]$
$(\Delta/\sigma)_{\max} = 0.0004$
$\Delta\rho_{\max} = 0.15$ e Å$^{-3}$
$\Delta\rho_{\min} = -0.25$ e Å$^{-3}$
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

| | | | |
|---|---|---|---|
| O1—C1 | 1.417 (3) | C5—C6 | 1.519 (3) |
| O2—C11 | 1.421 (3) | C6—C7 | 1.512 (3) |
| C1—C2 | 1.502 (3) | C7—C8 | 1.511 (3) |
| C2—C3 | 1.517 (3) | C8—C9 | 1.516 (3) |
| C3—C4 | 1.518 (3) | C9—C10 | 1.511 (3) |
| C4—C5 | 1.508 (3) | C10—C11 | 1.500 (3) |
| O1—C1—C2 | 112.7 (2) | C6—C7—C8 | 113.6 (2) |
| C1—C2—C3 | 114.6 (2) | C7—C8—C9 | 115.1 (2) |
| C2—C3—C4 | 112.7 (2) | C8—C9—C10 | 112.8 (2) |
| C3—C4—C5 | 114.7 (2) | C9—C10—C11 | 114.4 (2) |
| C4—C5—C6 | 113.7 (2) | O2—C11—C10 | 109.0 (2) |
| C5—C6—C7 | 114.8 (2) | | |
| O1—C1—C2—C3 | −63.3 (3) | O2—C11—C10—C9 | 179.3 (2) |

Table 2. *Hydrogen-bonding geometry (Å, °)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O2—H2O···O1$^{\text{i}}$ | 0.96 | 1.76 | 2.710 (2) | 172.0 |
| O1—H1O···O2$^{\text{ii}}$ | 0.97 | 1.81 | 2.775 (3) | 173.9 |

Symmetry codes: (i) $2 - x, \frac{1}{2} + y, -\frac{1}{2} - z$; (ii) $\frac{3}{2} - x, 1 - y, z - \frac{1}{2}$.

All non-H atoms were refined anisotropically by full-matrix least-squares methods. All H atoms including hydroxyl H atoms were fixed in idealized positions.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1992). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1995). Program(s) used to solve structure: *SAPI91* (Fan, 1991). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

The authors wish to express their gratitude to Miss T. Miyazaki for synthesizing 1,11-undecanediol. This study was partially supported by the Science Research Fund from the Promotion and Mutual Aid Corporation for Private Schools of Japan.

---

Supplementary data for this paper are available from the IUCr electronic archives (Reference: OB1004). Services for accessing these data are described at the back of the journal.

## References

Fan, H.-F. (1991). *SAPI91. Structure Analysis Programs with Intelligent Control.* Rigaku Corporation, Tokyo, Japan.
Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Kobayashi, H. & Nakamura, N. (1995). *Cryst. Res. Technol.* **30**, 495–500.
Kobayashi, H., Yamamoto, T. & Nakamura, N. (1995). *Cryst. Res. Technol.* **30**, 375–380.
Kuple, S., Seidei, I., Szulzewsky, K., Steger, U. & Steger, E. (1981). *Cryst. Res. Technol.* **16**, 349–356.
Molecular Structure Corporation (1992). *MSC/AFC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Molecular Structure Corporation (1995). *TEXSAN. Single Crystal Structure Analysis Software*. Version 1.7. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Nakamura, N. & Setodoi, S. (1997). *Acta Cryst.* C**53**, 1883–1885.
Nakamura, N., Tanihara, Y. & Takayama, T. (1997). *Acta Cryst.* C**53**, 253–255.
Nakamura, N. & Yamamoto, T. (1994). *Acta Cryst.* C**50**, 946–948.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.
Seto, T. (1962). *Mem. Coll. Sci. Univ. Kyoto Ser. A*, **30**, 89–107.
Watanabe, A. (1961). *Bull. Chem. Soc. Jpn*, **34**, 1728–1734.

---

*Acta Cryst.* (1999). C**55**, 791–794

# Tautomerism in a 2,4-dichlorobenzenesulfonamide derived from 2-amino-4-(2,5-dimethoxyphenyl)thiazole

PIERRE BEUCHET,[a] JEAN-MICHEL LÉGER,[b] MARTINE VARACHE-LEMBÈGE[a] AND ALAIN NUHRICH[a]

[a]*Laboratoire de Pharmacie Chimique et Chimie Thérapeutique, UFR des Sciences Pharmaceutiques, 3 place de la Victoire, 33076 Bordeaux CEDEX, France, and* [b]*Laboratoire de Chimie Analytique, UFR des Sciences Pharmaceutiques, 3 place de la Victoire, 33076 Bordeaux CEDEX, France. E-mail: pbeuchet@rockefeller.univ-lyon1.fr*

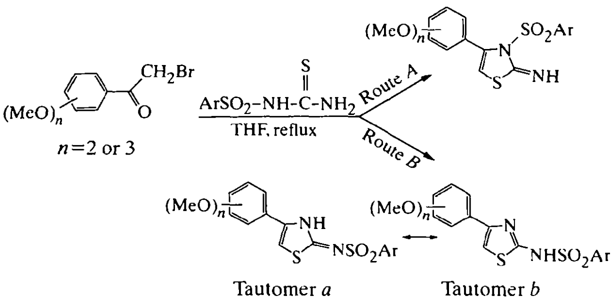
(*Received 19 October 1998; accepted 18 December 1998*)

## Abstract

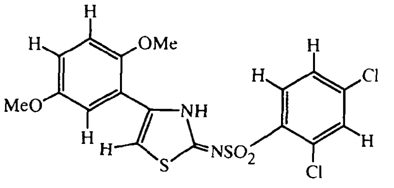
2,4-Dichloro-*N*-[2,3-dihydro-4-(2,5-dimethoxyphenyl)thiazol-2-ylidene]benzenesulfonamide, $C_{17}H_{14}Cl_2N_2O_4S_2$, crystallizes in space group $P\bar{1}$ with two independent molecules. The structural parameters do not indicate a tautomeric equilibrium but a single imino form. The main differences between the two crystalline forms lie in the intramolecular hydrogen bonding and the relative orientation of the methoxy groups. Attractive intermolecular interactions occur and are responsible for the crystalline cohesion.

## Comment

With the objective of designing potential antifungal agents, we have focused our efforts on the preparation of new thiazole derivatives incorporating both an arylsulfonamide moiety and a polyoxygenated phenyl group (Beuchet *et al.*, 1999). These compounds were obtained by the Hantzsch condensation between an $\alpha$-bromoketone and an appropriate arylsulfonyl thiourea, according to the scheme below.



The present X-ray study was undertaken in order to elucidate the cyclization pathway (route *A* or route *B*) and to determine the prominent form in the tautomeric equilibrium (*a* or *b*). The structure determination of the product, (1), obtained from 1-(2,5-dimethoxyphenyl)-2-bromoethanone and *N*-(aminothioxomethyl)-2,4-dichlorobenzenesulfonamide is reported. The main feature lies in the presence of two independent molecules (designated I and II; Fig. 1) contained in each asymmetric unit. The arylsulfonyl group is linked unambiguously to the exocyclic N atom (N12 or N62), thus indicating the cyclization to occur *via* route *B*. A comparison of intramolecular bond lengths and angles (Table 1) found for the five-membered ring indicates certain similarities between the two conformations. Both structures are characterized by the inequality of the two C—S bonds. The distances C9—S10 [1.747 (3) Å] and C59—S60 [1.732 (3) Å] are longer than C11—S10 [1.727 (3) Å] and C61—S60 [1.720 (4) Å]. A similar situation has been encountered with the crystal structures of various benzo- and naphthothiazoles (Fehlmann, 1970; Ekstrand & van der Helm, 1977). According to these reports, we can consider these extended C—S distances in our heterocyclic system as pure single bonds. For both molecules I and II, analysis of C—N distances around C9 and C59 shows that the exocyclic double bond [mean value 1.312 (4) Å] is shorter than its intracyclic counterpart [mean value 1.341 (4) Å]. These data are in agreement with those found for 2-iminothiazole derivatives (Cohen-Addad *et al.*, 1981; Cohen-Addad, 1982; Kalcheva *et al.*, 1993). Furthermore, each of molecules I or II possesses an H atom located near the endocyclic N atom, as shown from the final difference Fourier maps. These observations are indicative of the prominence of the imino tautomer *a* in the crystalline state.



(1)

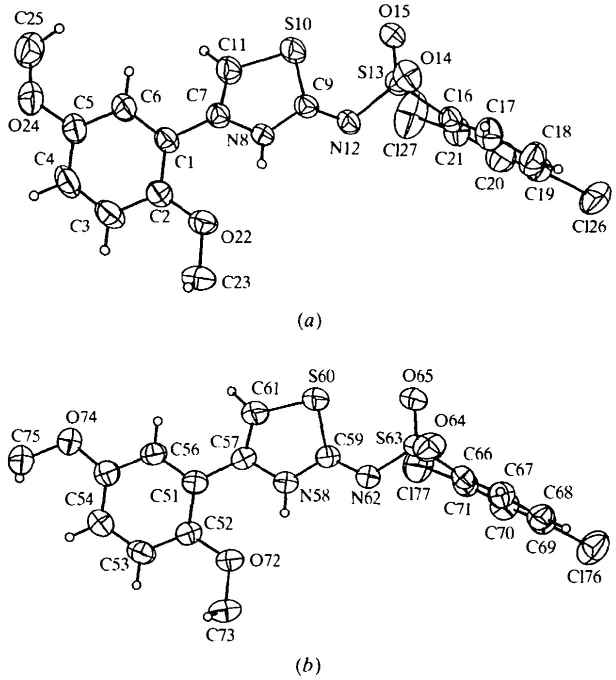


Fig. 1. The molecular structure and atomic numbering scheme of (*a*) molecule I and (*b*) molecule II, showing 50% probability displacement ellipsoids for all non-H atoms. H atoms have been set artificially small.

Inspection of the dihedral angles relative to the dimethoxyphenyl ring reveals some differences between the two molecules. In the first molecule (I), the methoxy groups are on opposite sides of the molecule, whereas they are on the same side in molecule II. It is interesting to note that, in spite of the absence of steric hindrance, the dimethoxyphenyl moiety of molecule I exists with a non-planar conformation, generated by a 36.8 (6)° rotation of the methoxy O24—C25 group around the C5—O24 bond. Some interactions of special interest, including both intramolecular and intermolecular interaction, are given in Table 2. As a main structural feature for molecule II, the O72 atom participates in an intramolecular hydrogen bond with the heterocyclic N—H group. The N58···O72 contact [2.627 (4) Å] falls short of the corresponding van der Waals radii sum by 0.32 Å (Emsley, 1989). On the other hand, in the structure of I, the distance N8···O22 is increased significantly [2.808 (4) Å] and thus indicates a weaker intramolecular interaction than in molecule II. This diversity in the strength of hydrogen bonding reflects the variation in the distribution of angles between the heterocyclic and the aromatic rings. Comparison of torsion angles (Table 1) shows that dimethoxyphenyl and dihydrothiazolyl moieties are less twisted in conformation II [15.0 (1)°] than in conformation I [39.1 (1)°]. Furthermore, a close intramolecular approach is observed between S60 and O65 whose distance [2.723 (4) Å] is shorter than the calculated sum of the van der Waals radii for O and S (3.25 Å; Emsley, 1989). This non-bonding attractive interaction between S and O atoms is in accordance with previously reported data for a benzoylimino-1,3-thiazolidine derivative (Cohen-Addad *et al.*, 1981). The hydrogen bond involving N8 and O14$^{\rm i}$ [symmetry code: (i) $-x$, $1-y$, $1-z$] is among the molecular distances of particular interest given in Table 2. The crystalline cohesion is achieved by numerous van der Waals contacts and also by C—H···O attractive interactions.

## Experimental

Crystals for X-ray structural analysis were grown by recrystallization of the title compound from an acetone–heptane solution.

### *Crystal data*

$C_{17}H_{14}Cl_2N_2O_4S_2$
$M_r = 445.32$
Triclinic
$P\bar{1}$
$a = 12.369\,(1)$ Å
$b = 12.998\,(1)$ Å
$c = 13.390\,(1)$ Å
$\alpha = 63.54\,(1)°$
$\beta = 88.97\,(1)°$
$\gamma = 79.89\,(1)°$
$V = 1892.9\,(3)$ Å$^3$
$Z = 4$
$D_x = 1.568$ Mg m$^{-3}$
$D_m$ not measured

Cu $K\alpha$ radiation
$\lambda = 1.54178$ Å
Cell parameters from 25 reflections
$\theta = 3.64–64.94°$
$\mu = 5.393$ mm$^{-1}$
$T = 296\,(2)$ K
Prism
0.15 × 0.12 × 0.10 mm
White

### *Data collection*

Enraf–Nonius CAD-4 diffractometer
$\omega$–$2\theta$ scans
Absorption correction: $\psi$ scan (North *et al.*, 1968)
$T_{\rm min} = 0.486$, $T_{\rm max} = 0.583$
6620 measured reflections
6303 independent reflections

4512 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.013$
$\theta_{\rm max} = 64.94°$
$h = -14 \rightarrow 14$
$k = 0 \rightarrow 15$
$l = -13 \rightarrow 14$
2 standard reflections
frequency: 90 min
intensity decay: none

### *Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.101$
$S = 1.043$
6303 reflections
488 parameters
H atoms not refined
$w = 1/[\sigma^2(F_o^2) + (0.0782P)^2 + 2.2037P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\rm max} = -0.029$
$\Delta\rho_{\rm max} = 0.318$ e Å$^{-3}$
$\Delta\rho_{\rm min} = -0.301$ e Å$^{-3}$
Extinction correction: *SHELXL*93
Extinction coefficient: 0.0145 (15)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

| | | | |
|---|---|---|---|
| C1—C7 | 1.475 (4) | C51—C57 | 1.473 (5) |
| C7—C11 | 1.336 (4) | C57—C61 | 1.343 (5) |
| C7—N8 | 1.390 (4) | C57—N58 | 1.386 (4) |
| N8—C9 | 1.341 (4) | N58—C59 | 1.341 (4) |
| C9—N12 | 1.313 (4) | C59—N62 | 1.311 (4) |
| C9—S10 | 1.747 (3) | C59—S60 | 1.732 (3) |
| S10—C11 | 1.727 (3) | S60—C61 | 1.720 (4) |
| N12—S13 | 1.591 (3) | N62—S63 | 1.593 (3) |
| S13—O14 | 1.438 (2) | S63—O64 | 1.437 (3) |
| S13—O15 | 1.440 (2) | S63—O65 | 1.441 (3) |
| S13—C16 | 1.775 (3) | S63—C66 | 1.769 (4) |
| C11—C7—N8 | 111.2 (3) | C61—C57—N58 | 109.8 (3) |
| N8—C7—C1 | 122.1 (3) | N58—C57—C51 | 121.9 (3) |
| C9—N8—C7 | 116.8 (2) | C59—N58—C57 | 117.2 (3) |
| N12—C9—N8 | 120.5 (3) | N62—C59—N58 | 120.3 (3) |
| N12—C9—S10 | 131.0 (2) | N62—C59—S60 | 130.9 (3) |
| N8—C9—S10 | 108.5 (2) | N58—C59—S60 | 108.9 (2) |
| C11—S10—C9 | 91.0 (2) | C61—S60—C59 | 90.7 (2) |
| C7—C11—S10 | 112.5 (3) | C57—C61—S60 | 113.3 (3) |
| C9—N12—S13 | 120.8 (2) | C59—N62—S63 | 120.5 (2) |
| O14—S13—O15 | 116.14 (15) | O64—S63—O65 | 116.4 (2) |
| O14—S13—N12 | 108.23 (14) | O64—S63—N62 | 108.8 (2) |
| O15—S13—N12 | 113.59 (14) | O65—S63—N62 | 112.7 (2) |
| O14—S13—C16 | 105.28 (15) | O64—S63—C66 | 105.7 (2) |
| O15—S13—C16 | 108.09 (14) | O65—S63—C66 | 108.0 (2) |
| N12—S13—C16 | 104.56 (14) | N62—S63—C66 | 104.3 (2) |
| C1—C2—O22—C23 | 174.3 (3) | C51—C52—O72—C73 | 172.7 (3) |
| C6—C5—O24—C25 | 36.8 (6) | C54—C55—O74—C75 | −5.7 (5) |

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

Hydrogen bonds

| *D*—H···*A* | *D*···*A* | H···*A* | *D*—H···*A* |
|---|---|---|---|
| N58—H58···O72 | 2.627 (5) | 2.031 (5) | 125.6 (4) |
| N8—H8···O14$^{\rm i}$ | 2.994 (4) | 2.168 (4) | 161.4 (4) |
| N8—H8···O22 | 2.809 (4) | 2.423 (4) | 107.9 (3) |

C—H···O interactions

| C—H···O | C···O | H···O | C—H···O |
|---|---|---|---|
| C11—H11···O64$^{\rm ii}$ | 3.158 (6) | 2.402 (6) | 138.3 (5) |
| C73$^{\rm iii}$—H73C$^{\rm iii}$···O15 | 3.289 (6) | 2.644 (6) | 124.9 (5) |

van der Waals contacts

| | | | |
|---|---|---|---|
| S60···O65 | 2.723 (4) | O64···C11$^{\rm iv}$ | 3.156 (6) |
| O65···Cl77 | 3.210 (4) | Cl26···C23$^{\rm v}$ | 3.554 (6) |
| O14···O22$^{\rm i}$ | 2.962 (4) | S60···C75$^{\rm vi}$ | 3.625 (6) |
| N62···Cl77 | 3.307 (4) | Cl26···Cl26$^{\rm vii}$ | 3.285 (2) |
| C61···Cl27$^{\rm iv}$ | 3.584 (5) | | |

Symmetry codes: (i) $-x, 1-y, 1-z$; (ii) $x, y-1, z$; (iii) $1-x, 1-y, 1-z$; (iv) $x, 1+y, z$; (v) $1+x, y, z$; (iv) $1-x, 2-y, 2-z$; (vii $1-x, 1-y, 2-z$.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *CAD*-4 *Software*. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993).

We thank M. Stephane Larrouture for his participation in the synthetic procedure.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1030). Services for accessing these data are described at the back of the journal.

## References

Beuchet, P., Varache-Lembége, M., Neveu, A., Léger, J.-M., Larrouture, S., Deffieux, G. & Nuhrich, A. (1999). *Eur. J. Med. Chem.* In the press.
Cohen-Addad, C. (1982). *Acta Cryst.* B**38**, 1753–1757.
Cohen-Addad, C., Savariault, J.-M. & Lehmann, M. S. (1981). *Acta Cryst.* B**37**, 1703–1706.
Ekstrand, J. D. & van der Helm, D. (1977). *Acta Cryst.* B**33**, 1012–1016.
Emsley, J. (1989). In *The Elements*. Oxford: Clarendon Press.
Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Fehlmann, M. (1970). *Acta Cryst.* B**26**, 1736–1741.
Kalcheva, V., Tosheva, M. & Hadjieva, P. (1993). *Ann. Chem.* pp. 1319–1322.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

---

*Acta Cryst.* (1999). C**55**, 794–796

# (+)-(2*R*-*cis*)-Dimethyl(10-bromo-2,3,3a,8-tetrahydrodibenz[*c*,*f*]isoxazolo[2,3-*a*]azepin-2-ylmethyl)amine†

Oswald M. Peeters,[a] Norbert M. Blaton,[a] Camiel J. De Ranter[a] and Hans L. De Winter[b]

[a]*Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Faculteit Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium, and* [b]*Theoretical Medicinal Chemistry, Janssen Research Foundation, Turnhoutseweg 30, B-2340 Beerse, Belgium. E-mail: maurice.peeters@farm.kuleuven.ac.be*

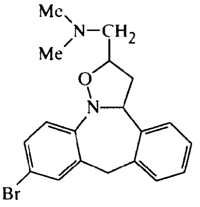
(*Received 7 December 1998; accepted 4 January 1999*)

## Abstract

The title compound, $C_{19}H_{21}BrN_2O$, is a central active serotonin 5-$HT_{2c}$ antagonist with some $H_1$ affinity. The (6,7,6)-tricyclic moiety is asymmetrically folded with a dihedral angle of 124.3 (1)° between the aromatic planes. The fused tetrahydroisoxazole ring adopts a conformation halfway between that of a twist and an envelope.

## Comment

The structure of the title compound, (I), has been determined as part of our studies on serotonin antagonists (Peeters *et al.*, 1995, and references cited therein). The compound is a central active serotonin 5-$HT_{2c}$ antagonist with some $H_1$ affinity. *In vivo* the compound antagonizes anxiety symptoms (Meert, 1998).



(I)

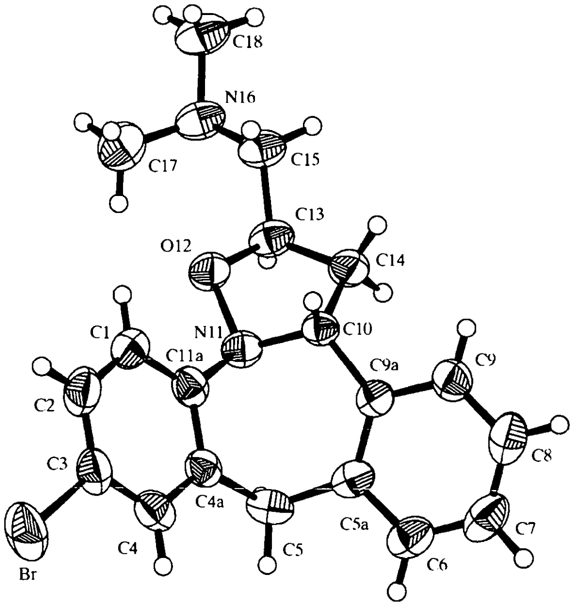


Fig. 1. Perspective view of the title compound with atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

The conformation and the atomic numbering scheme are shown in Fig. 1. The (6,7,6)-tricyclic moiety folds asymmetrically about a line through C5 and N11. The dihedral angle between the least-squares planes of the aromatic rings is 124.3 (1)°. The bond lengths do not show outstanding features. Apart from the endocyclic angles of the seven-membered ring, the bond angles have normal values. The endocyclic angles facing the non-bromo-substituted benzo ring are markedly enlarged. This enlarging and the

---

† Internal code of the Janssen Research Foundation: R110580.