Nicolaou, K. C., Dai, W.-M. & Guy, R. K. (1994). *Angew. Chem. Int. Ed. Engl.* **33**, 15–44; *Angew. Chem.* **106**, 38–69.
Sheldrick, G. M. (1991). *SHELXTL/PC. XMOL. Interactive Molecular Graphics Program for Display of Crystal Structures.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1997*a*). *SHELXL97. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXS97. Program for the Solution of Crystal Structures.* University of Göttingen, Germany.
Stoe & Cie (1996). *XRED. Data Reduction Program.* Version 1.07. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1997). *STADI4. Diffractometer Control Program.* Version 1.06. Stoe & Cie, Darmstadt, Germany.
Wani, M. C., Taylor, H. L., Wall, M. E., Coggon, P. & McPhail, A. T. (1971). *J. Am. Chem. Soc.* **93**, 2325–2357.

Acta Cryst. (1999). **C55**, 1943–1945

2,6-Dimethylspiro[1-oxa-2,5-diazabicyclo[3.3.0]octane-3,1′-cyclohexane]-4,6-dione

Damon R. Billodeaux,[a] Frank R. Fronczek[a] and Yaşar Dürüst[b]

[a]*Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803-1804, USA, and* [b]*Department of Chemistry, Kocaeli University, TR-41300, Izmit, Turkey. E-mail: fronz@chxray1.chem.lsu.edu*

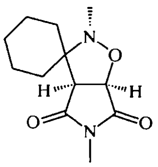
(*Received 29 June 1999; accepted 26 July 1999*)

Abstract

The title compound, $C_{12}H_{18}N_2O_3$, contains two fused five-membered rings; a nearly planar pyrrolidine ring, with a maximum deviation of 0.0352 (11) Å, and an oxazolidine ring in an envelope conformation. The average C=O distance of the pyrrolidine ketone groups is 1.210 (2) Å. The N—O distance in the oxadiazoline ring is 1.458 (2) Å. The structure contains a spiro-cyclohexane group in a chair conformation.

Comment

The 1,3-dipolar cycloaddition of nitrones to different unsaturated systems has been the subject of extensive investigation since this method can be used to synthesize many heterocyclic compounds of great pharmaceutical importance, such as indolizine, quinolizine and indole alkaloids. A literature search revealed that few examples of cycloadditions of nitrones to reactive dipolarophiles, such as *N*-methyl- and *N*-phenylmaleimides, have appeared (Padwa, 1984; Torssel, 1988; Grünanger & Vita-Finzi, 1991; Cordero *et al.*, 1989, 1990; Brandi *et al.*, 1992; Goti, 1996). For this reason, the title cycloadduct, (I), was synthesized and its structure determined. Details of the synthesis, chemistry and spectroscopy of (I) have been published elsewhere (Dürüst *et al.*, 1999).



(I)

The structure of (I) contains two fused five-membered rings, *i.e.* a 1,2-oxazolidine and an *N*-methylpyrrolidine ring (Fig. 1). The pyrrolidine ring system is nearly planar, with a maximum deviation of 0.0352 (11) Å for the C5 atom. The C=O bond lengths of the ketone groups are 1.210 (3) Å for C7=O9 and 1.210 (2) Å for C5=O10. The O9 atom is essentially coplanar with the ring, deviating by only 0.015 (3) Å, while O10 deviates by 0.102 (3) Å from the best-fit plane. The C16 *N*-methyl group has an N—C distance of 1.454 (3) Å and lies 0.061 (4) Å from the best plane.

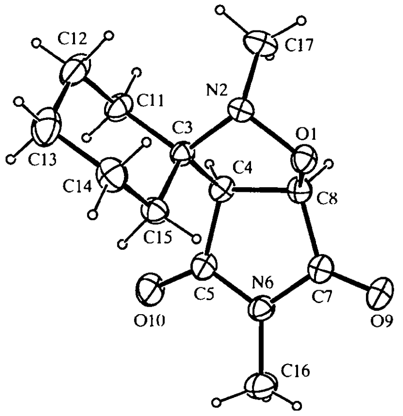


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of (I) with ellipsoids at the 50% probability level.

The oxazolidine system, by contrast, is a puckered ring. The ring has an envelope conformation with the N2 atom in the flap position and puckering parameters Q = 0.403 Å and φ = 215.85° (Cremer & Pople, 1975). The endocyclic torsion angle around C3—N2 is −40.1 (2)° and around N2—O1 is 42.6 (2)°. The N—O bond distance in the ring is 1.458 (2) Å (N2—O1), which compares well with similar distances in previously reported structures (Grigg *et al.*, 1993; van Eijk *et al.*, 1988). The C17 *N*-methyl group has a C—N distance of 1.464 (3) Å and, along with the H atoms at C8 and C4, lies on the convex side of the bicyclic system, which also occurs in similar compounds (Grigg *et al.*, 1993).

The structure contains a spiro-cyclohexane group at C3. The C—C distances in the ring range from 1.523 (3) (C14—C15) to 1.538 (3) Å (C3—C15) and the C—C—C bond angles in the ring range from 110.6 (2) (C13—C12—C11) to 112.64 (2)° (C3—C11—C12).

The most significant intermolecular contact is of the C—H···O type [C4···O9^{i} 3.344 (4) Å; symmetry code: (i) $x-1$, y, z] and is almost linear, with a 168° angle about the idealized H-atom position. These contacts form chains along the a axis.

Experimental

A solution of *N*-methylcyclohexylideneamine *N*-oxide and *N*-methylmaleimide in benzene was refluxed for 4 h. The reaction was monitored by thin-layer chromatography. After evaporation of the solvent, the crude material was subjected to flash column chromatography (ethyl acetate–petroleum ether, 1:1). The eluted crude product was recrystallized from benzene/*n*-hexane to give crystals of the title compound with a melting point of 400–401 K.

Crystal data

$C_{12}H_{18}N_2O_3$
$M_r = 238.28$
Orthorhombic
$P2_12_12_1$
$a = 6.2452\ (5)$ Å
$b = 7.8690\ (6)$ Å
$c = 24.1510\ (14)$ Å
$V = 1186.9\ (1)$ Å^3
$Z = 4$
$D_x = 1.334$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 25 reflections
$\theta = 21.6$–$44.1°$
$\mu = 0.792$ mm^{-1}
$T = 297$ K
Plate
0.38 × 0.28 × 0.10 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
$T_{\min} = 0.775$, $T_{\max} = 0.924$
1444 measured reflections
1444 independent reflections

1377 reflections with $I > 2\sigma(I)$
$\theta_{\max} = 75°$
$h = 0 \rightarrow 7$
$k = -9 \rightarrow 0$
$l = -30 \rightarrow 0$
3 standard reflections frequency: 120 min intensity decay: 3.9%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.106$
$S = 1.063$
1444 reflections
155 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0738P)^2 + 0.0956P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.21$ e Å^{-3}
$\Delta\rho_{\min} = -0.16$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0164 (16)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

O1—N2	1.458 (2)	N2—C17	1.464 (3)
O1—C8	1.451 (2)	N6—C5	1.396 (3)
O9—C7	1.210 (3)	N6—C7	1.375 (2)
O10—C5	1.210 (2)	N6—C16	1.454 (3)
N2—C3	1.483 (2)		
C8—O1—N2	106.42 (14)	O10—C5—N6	123.7 (2)
O1—N2—C3	102.55 (12)	O9—C7—N6	125.1 (2)
O1—N2—C17	106.73 (14)	O1—C8—C4	106.31 (14)
N2—C3—C4	102.73 (14)		
C8—O1—N2—C3	42.57 (15)	C4—C3—C11—C12	179.83 (17)
O1—N2—C3—C4	−40.09 (16)	C3—C11—C12—C13	−56.2 (3)
C17—N2—C3—C4	75.48 (18)	C11—C12—C13—C14	56.4 (3)
N2—C3—C4—C8	23.94 (18)	C12—C13—C14—C15	−57.2 (3)
C16—N6—C7—O9	0.4 (3)	C13—C14—C15—C3	56.8 (2)
N2—O1—C8—C4	−26.77 (17)	C11—C3—C15—C14	−54.7 (2)
C5—C4—C8—O1	−119.30 (15)		

Refinement of the Flack (1983) parameter yielded a value of 0.6 (3). Due to the lack of significant anomalous scattering, the absolute configuration of the crystal was not determined.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1993). Cell refinement: *CAD*-4 *EXPRESS*. Data reduction: *XCAD*4 (Harms & Wocadlo, 1996). 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).

The purchase of the diffractometer was made possible by a National Science Foundation chemical instrumentation grant, which we gratefully acknowledge. Improvements to the LSU X-ray Crystallography Facility were supported by grant No. LEQSF(1996–97)-ENH-TR-10, administered by the Louisiana Board of Regents. DRB wishes to acknowledge the Chancellor's Student Aid Fund which made this structure determination possible.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1097). Services for accessing these data are described at the back of the journal.

References

Brandi, A., Dürüst, Y., Cordero, F. M. & De Sarlo, F. (1992). *J. Org. Chem.* **57**, 5666–5670.

Cordero, F. M., Brandi, A., Querci, C., Goti, A., De Sarlo, F. & Guarna, A. (1990). *J. Org. Chem.* **55**, 1762–1767.

Cordero, F. M., Goti, A., De Sarlo, F., Guarna, A. & Brandi, A. (1989). *Tetrahedron*, **45**, 5917–5924.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Dürüst, Y., Döndaş, H. A. & Özkoru, N. (1999). *Heterocycl. Commun.* **5**, 173–177.

Eijk, P. J. S. S. van, Verboom, W., van Veggel, F., Reinhoudt, D. & Harkema, S. (1988). *Rec. Trav. Chim. Pays-Bas*, **107**, 142–148.

Enraf–Nonius (1993). *CAD*-4 *EXPRESS*. Version 1.1. Enraf–Nonius, Delft, The Netherlands.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Goti, A. (1996). *Tetrahedron*, **52**, 9187–9192.

Grigg, R., Hadjisoteriou, M., Kennewell, P., Markandu, J. & Thornton-Pett, M. (1993). *J. Chem. Soc. Chem. Commun.* pp. 1340–1343.

Grünanger, P. & Vita-Finzi, P. (1991). *Isoxazoles*, pp. 686–725. New York: Wiley Interscience.

Harms, K. & Wocadlo, S. (1996). *XCAD*4. *Program for the Lp Correction of Nonius Four-Circle Diffractometer Data.* University of Marburg, Germany.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

Padwa, A. (1984). In *1,3-Dipolar Cycloaddition Chemistry*. New York: Wiley Interscience.

Sheldrick, G. M. (1990). *Acta Čryst.* A**46**, 467–473.

Sheldrick, G. M. (1997). *SHELXL97. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.

Torssel, K. B. G. (1988). In *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis.* New York: VCH Publishers.

Acta Cryst. (1999). C**55**, 1945–1947

7-Chloro-(*R*)-3-[1-(cyclohexyl)ethylamino]-4*H*-1,2,4-benzothiadiazine 1,1-dioxide and 7-chloro-(*S*)-3-[1-(cyclohexyl)ethylamino]-4*H*-1,2,4-benzothiadiazine 1,1-dioxide

Léon Dupont,[a] Pascal de Tullio,[b] Smail Khelili,[b] Fabian Somers,[b] Jacques Delarge[b] and Bernard Pirotte[b]

[a]*Unité de Cristallographie, Institut de Physique B5, Université de Liège, Allée du 6 août, 17, B-4000 Liège, Belgium, and* [b]*Service de Chimie Pharmaceutique, Institut de Pharmacie B36, Université de Liège, Avenue de l'Hôpital, 1, B-4000 Liège, Belgium. E-mail: leon.dupont@ulg.ac.be*

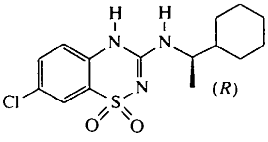
(*Received 29 June 1999; accepted 23 July 1999*)

Abstract

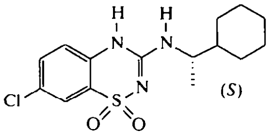
3-Alkylamino-4*H*-1,2,4-benzothiadiazine 1,1-dioxides structurally related to diazoxide are expected to present a pharmacological profile of potassium-channel openers. The influence on biological activity of the absolute configuration of the title compounds, both $C_{15}H_{20}ClN_3O_2S$, is being studied. The crystallographic results confirm the enantiomeric characterization of each compound.

Comment

3-Alkylamino-4*H*-1,2,4-benzothiadiazine 1,1-dioxides structurally related to diazoxide (Bandoli & Nicolini, 1977) and bearing a short branched hydrocarbon chain in the 3-position have been reported to exhibit myorelaxant properties (de Tullio *et al.*, 1996). Such an effect of the drugs should be attributed to their possible pharmacological profile as potassium-channel openers. In the search of new similar compounds expressing smooth muscle myorelaxant properties, it was of interest to study the influence on biological activity of the stereospecificity associated with the first C atom of the hydrocarbon chain linked to the exocyclic N atom in the 3-position. The (*R*)- and (*S*)-7-chloro-3-[1-(cyclohexyl)ethylamino]-4*H*-1,2,4-benzothiadiazine 1,1-dioxides, (I) and (II), respectively, were prepared from the reaction of 7-chloro-3-methylsulfanyl-4*H*-1,2,4-benzothiadiazine 1,1-dioxide with commercially available (*R*)- and (*S*)-1-(cyclohexyl)ethylamine. The optical purity of the enantiomeric antipodes was determined by a chiral high-pressure liquid chromatography technique as previously described (Khelili *et al.*, 1999).

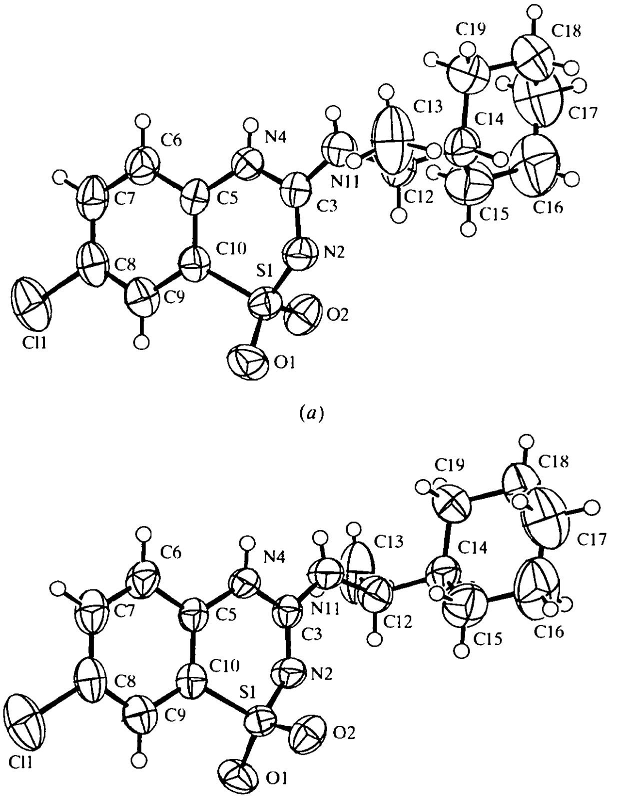


(I)



(II)

For the two compounds, the enantiomeric excess (ee) is larger than 95%. The Flack parameter of the crystal structure confirms the configuration of each enantiomer. The refinements of the inverted structures have been tested. The corresponding Flack parameters have the values of 0.94 (3) and 0.84 (4), respectively. In the two structures the geometrical parameters (cell dimensions,



(*a*)

(*b*)

Fig. 1. Molecular structure with atom-labelling scheme for the (*a*) (*R*)- and (*b*) (*S*)- enantiomers. Displacement ellipsoids are shown at 50% probability levels. H atoms are drawn as small circles of an arbitrary radius.

Acta Crystallographica Section C
ISSN 0108-2701 © 1999