Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-[2-Hydroxyimino-2-(3-methyl-3-phenylcyclobutyl)ethyl]isoindole-1,3-dione

Namık Özdemir,[a] Muharrem Dinçer,[a]* Ibrahim Yılmaz[b] and Alaaddin Çukurovalı[b]

[a]Ondokuz Mayıs University, Arts and Sciences Faculty, Department of Physics, 55139 Samsun, Turkey, and [b]Fırat University, Arts and Sciences Faculty, Department of Chemistry, 23119 Elazığ, Turkey

Correspondence e-mail: mdincer@omu.edu.tr

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.054
wR factor = 0.134
Data-to-parameter ratio = 10.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

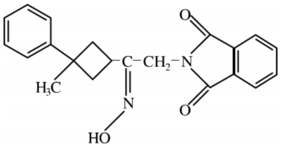
© 2004 International Union of Crystallography
Printed in Great Britain – all rights reserved

Received 4 December 2003
Accepted 18 December 2003
Online 24 December 2003

The molecules of the title compound, $C_{21}H_{20}N_2O_3$, are linked by O—H···O and C—H···N hydrogen bonds, and by π–π interactions. The cyclobutane ring is puckered, with a dihedral angle of 11.55 (3)° between the two planes. The phenyl ring shows positional disorder.

Comment

3-Substituted cyclobutane carboxylic acid derivatives exhibit anti-inflammatory and antidepressant activities (Dehmlow & Schmidt, 1990), and also liquid crystal properties (Coghi *et al.*, 1976). Phthalimide derivatives exhibit anticancer activities, with current and potential applications including erythema nodosum leprosum, renal cell carcinoma, Kaposi's sarcoma, and other cancers (Sampaio *et al.*, 1993; Eisen *et al.*, 2000). Oximes show geometric isomerism due to the double bond between the N and C atoms (Mixich & Thiele, 1979; Migrdichian, 1957). Because of the great differences in physical, chemical and biological properties of the geometric isomers, determination of the configuration of the isomers is important (Mathison *et al.*, 1989). Oximes and oxime ethers have also a broad pharmacological activity spectrum, encompassing antifungal, antibacterial, antidepressant and insecticidal activities, as well as activity as a nerve-gas antidote, depending on the pharmacophoric group of the molecule (Polak, 1982; Balsamo *et al.*, 1990; Holan *et al.*, 1984; Forman, 1964). Taking into account these important features of the cyclobutane, phthalimide and oxime groups, we have undertaken the X-ray diffraction study of the title compound, (I), which contains all three groups.



(I)

A view of the title compound with the atom-labelling scheme is shown in Fig. 1. The crystal structure of (I) can be described as being built from essentially planar fragments, *viz.* a cyclobutane ring (C1–C4), a phthalimide group (O1/O2/N1/C5–C12), an oxime group (C14/N2/O3), a phenyl ring (C16–C21) and a four-atom bridge (C1/C14/C13/N1) linking the cyclobutane ring with the phthalimide group. The maximum deviation of the phthalimide group from planarity is 0.0239 (18) Å. Although close to planar, the cyclobutane ring is slightly puckered. The C4/C1/C2 plane forms a dihedral angle of 11.55 (3)° with the C2/C3/C4 plane. The mean plane

DOI: 10.1107/S1600536803029246

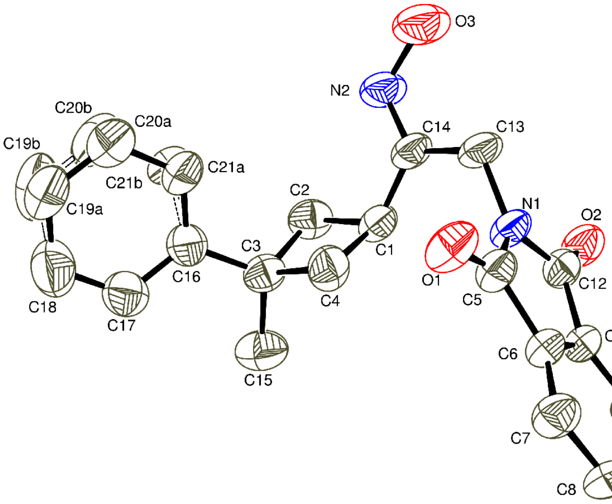


Figure 1
An *ORTEP*-3 (Farrugia, 1997) drawing of the title compound, (I), showing the atomic numbering scheme. Displacement ellipsoids of non-H atoms are drawn at the 50% probability level. The two disordered components are represented with full and dashed lines. H atoms have been omitted for clarity.

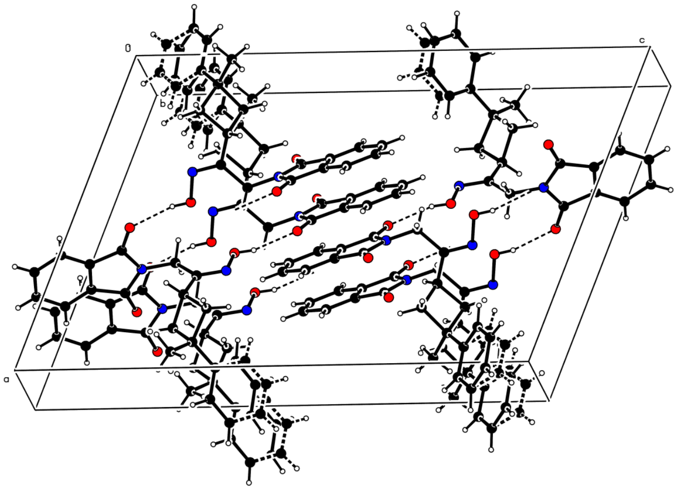


Figure 2
PLATON plot (Spek, 1997) illustrating the hydrogen-bonding network and the stacking of molecules. The two disordered components are represented with full and dashed lines.

of the cyclobutane ring forms a dihedral angle of 71.55 (10)° with the mean plane of the phthalimide group. The C1—C14—C13—N1 torsion angle is 3.9 (4)° and the plane of the four-atom bridge is almost perpendicular to the plane of the phthalimide group, with a dihedral angle of 83.15 (9)°. However, the plane of these four atoms is twisted by 57.56 (13)° out of the mean plane of the cyclobutane ring.

The bond lengths and angles found for both the cyclobutane ring and the phthalimide group are close to those reported in the literature (Zhu *et al.*, 2001; Swenson *et al.*, 1997). The dihedral angle between the plane of the oxime moiety and the phthalimide group is 82.23 (14)°, indicating that these two planes are almost perpendicular to each other, while the plane of the oxime moiety forms a dihedral angle of 57.06 (20)° with the mean plane of the cyclobutane ring.

Two types of intermolecular hydrogen bonds, O—H···O and C—H···N, are observed in the structure (Table 2). In the first of these intermolecular interactions, atom O3 acts as donor to the symmetry-related O2 at $(1 - x, \frac{1}{2} + y, \frac{1}{2} - z)$ [2.814 (3) Å]. In the second type, atom C9 acts as hydrogen-bond donor to the symmetry-related N2 at $(x, \frac{3}{2} - y, \frac{1}{2} + z)$ [3.522 (4) Å]. Hydrogen bonds in the structure link molecules into infinite chains. The crystal structure is also stabilized by π–π stacking interactions between the N1/C5/C6/C11/C12 and C6–C11 rings [symmetry code: (iii) $1 - x, 2 - y, 1 - z$]. The distance between the centroids of these rings is 3.9987 (17) Å.

Experimental

To a solution of 1.471 g (10 mmol) of phthalimide in 20 ml of absolute ethanol, a solution of 2.225 g (10 mmol) of 1-phenyl-1-methyl-3-(2-chloro-1-oxoethyl)cyclobutane, which was synthesized according to the literature method of Akhmedov *et al.* (1991), in 20 ml of absolute ethanol was added dropwise at 333–343 K with continuous stirring and with monitoring of the course of the reaction by IR. Since monitoring of the CH_2—Cl group of 1-phenyl-1-methyl-3-(2-chloro-1-oxoethyl)cyclobutane or the N—H group of phthalimide is easy, it is also easy to determine the reaction time. When the reaction was finished, 0.33 g (10 mmol) of NH_2OH was added and the resulting solution refluxed for a further 2 h. After cooling to room temperature, water (30 ml) was added to the mixture and it was extracted with ether (3 × 40 ml). The combined extracts were washed several times with water and dried (Na_2SO_4). The solvent was evaporated to give crude (I). The product was crystallized from aqueous ethanol (1:3). Yield and melting point of the substance are 82% and 410 K, respectively.

Crystal data

$C_{21}H_{20}N_2O_3$
$M_r = 348.39$
Monoclinic, $P2_1/c$
$a = 14.6497$ (14) Å
$b = 5.6976$ (3) Å
$c = 21.965$ (2) Å
$\beta = 109.095$ (7)°
$V = 1732.5$ (3) Å^3
$Z = 4$
$D_x = 1.336$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 9229 reflections
$\theta = 1.5$–29.6°
$\mu = 0.09$ mm^{-1}
$T = 293$ (2) K
Plate, colourless
0.80 × 0.34 × 0.08 mm

Data collection

Stoe IPDS-2 diffractometer
φ scans
Absorption correction: none
5446 measured reflections
2824 independent reflections
1590 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.071$
$\theta_{\rm max} = 25.0°$
$h = -17 \rightarrow 16$
$k = -6 \rightarrow 6$
$l = -18 \rightarrow 26$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.055$
$wR(F^2) = 0.134$
$S = 1.01$
2824 reflections
264 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0555P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.001$
$\Delta\rho_{\rm max} = 0.19$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.18$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0115 (19)

Table 1
Selected geometric parameters (Å, °).

O1—C5	1.197 (3)	C1—C14	1.475 (4)
O2—C12	1.208 (3)	C1—C2	1.538 (3)
O3—N2	1.408 (3)	C1—C4	1.549 (4)
N1—C12	1.384 (3)	C2—C3	1.553 (4)
N1—C5	1.397 (4)	C3—C16	1.517 (4)
N1—C13	1.458 (3)	C3—C15	1.525 (4)
N2—C14	1.266 (4)	C3—C4	1.560 (3)
C12—N1—C5	111.8 (2)	C2—C3—C4	88.32 (19)
C12—N1—C13	124.5 (2)	C1—C4—C3	90.3 (2)
C5—N1—C13	123.3 (2)	O1—C5—N1	124.9 (3)
C14—N2—O3	111.1 (2)	O1—C5—C6	129.2 (3)
C14—C1—C2	118.6 (3)	N1—C5—C6	105.9 (2)
C14—C1—C4	115.1 (2)	O2—C12—N1	125.4 (3)
C2—C1—C4	89.24 (18)	O2—C12—C11	128.7 (3)
C1—C2—C3	91.0 (2)	N1—C12—C11	105.9 (2)
C16—C3—C15	113.4 (2)	N1—C13—C14	114.3 (2)
C16—C3—C2	116.5 (2)	N2—C14—C1	119.0 (2)
C15—C3—C2	111.9 (2)	N2—C14—C13	120.3 (2)
C16—C3—C4	113.1 (2)	C1—C14—C13	120.6 (3)
C15—C3—C4	111.2 (3)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O2^{i}	0.82	2.01	2.814 (3)	165
C9—H9···N2^{ii}	0.93	2.59	3.522 (4)	176

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

H atoms were positioned geometrically and treated using a riding model, fixing the bond lengths at 0.82 Å for atom O3, at 0.93 Å for both the phthalimide group and the phenyl ring, at 0.96 Å for the methyl group, at 0.97 Å for atom C2, C4 and C13, and at 0.98 Å for atom C1. The displacement parameters of the H atoms were constrained as $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}$ ($1.5U_{\rm eq}$ for methyl) of the carrier atom. Three of the six atoms of the phenyl ring are disordered with a nearly statistical distribution over two sites [0.52 (3)/0.48 (3)].

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED*32 (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III *for Windows* (Farrugia, 1997) and *PLATON* (Spek, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

References

Akhmedov, M. A., Sardarov, I. K., Akhmedov, I. M., Kostikov, R. R., Kisin, A. V. & Babaev, N. M. (1991). *Zh. Org. Khim.* **27**, 1434.

Balsamo, A., Macchia, B., Martinelli, A., Orlandini, E., Rossello, A., Macchia, F., Bocelli, G. & Domiano, P. (1990). *Eur. J. Med. Chem.* **25**, 227–233.

Coghi, L., Lanfredi, A. M. M. & Tiripicchio, A. (1976). *J. Chem. Soc. Perkin Trans.* 2, pp. 1808–1810.

Dehmlow, E. V. & Schmidt, S. (1990). *Liebigs Ann. Chem.* p. 411

Eisen, T., Boshoff, C., Mak, I., Sapunar, F., Vaughan, M. M., Pyle, L., Johnston, S. R., Ahern, R., Smith, I. E. & Gore, M. E. (2000). *Br. J. Cancer*, **82**, 812–817.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.

Forman, S. E. (1964). *J. Org. Chem.* **29**, 3323–3327.

Holan, G., Johnson, W. M. P., Rihs, K. & Virgona, C. T. (1984). *Pest. Sci.* **15**, 361–368.

Mathison, I. W., Solomons, W. E., Morgan, P. H. & Tidwell, R. R. (1989). *Structural Features and Pharmacologic Activity*, edited by W. O. Foye, *Principals of Medicinal Chemistry*, pp. 49–77. Philadelphia: Lea and Febiger.

Migrdichian, V. (1957). *Organic Synthesis, Open-Chain Saturated Compounds*, pp. 703–707. New York: Reinhold.

Mixich, G. V. & Thiele, K. (1979). *Arzneim. Forsch.* (*Drug Res.*), **29**, 1510–1513.

Polak, A. (1982). *Arzneim. Forsch.* (*Drug Res.*), **32**, 17–24.

Sampaio, E. P., Kaplan, G., Miranda, A., Nery, J. A., Miguel, C. P., Viana, S. M. & Sarno, E. N. (1993). *J. Infect. Dis.* **168**, 408–414.

Sheldrick, G. M. (1990). *SHELXS*86. University of Göttingen, Germany.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Spek, A. L. (1997). *PLATON*. University of Utrecht, The Netherlands.

Stoe & Cie (2002). *X-AREA* (Version 1.18) and *X-RED*32 (Version 1.04). Stoe & Cie, Darmstadt, Germany.

Swenson, D. C., Yamamoto, M. & Burton, D. J. (1997). *Acta Cryst.* C**53**, 1445–1447.

Zhu, Y., Zhang, H., Maguire, J. A. & Hosmane, N. S. (2001). *Inorg. Chem. Commun.* **4**, 447–449.