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1-(3-Methyl-3-phenylcyclobutyl)-2-(piperidin-1-yl)ethanone oxime

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.008 Å
R factor = 0.046
wR factor = 0.122
Data-to-parameter ratio = 5.3

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

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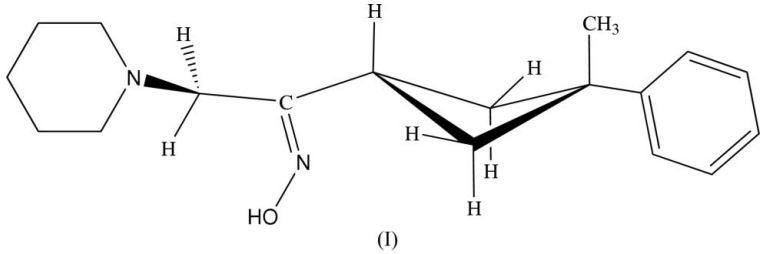
The asymmetric unit of the title compound, $C_{18}H_{26}N_2O$, contains two molecules. In both molecules, the oxime group has an *E* configuration and the piperidine ring adopts a chair conformation. Intramolecular C—H···O and intermolecular O—H···N hydrogen bonds are observed in the crystal structure.

Comment

3-Substituted cyclobutanecarboxylic acid derivatives exhibit anti-inflammatory and antidepressant activities (Dehmlow & Schmidt, 1990), and also liquid crystal properties (Coghi *et al.*, 1976). Owing to their unique biological properties, piperidines have been target molecules in organic synthesis (Weintraub *et al.*, 2003). In recent years, polyhydroxylated piperidine alkaloids have attracted much attention because some of them have the ability to act as selective glycosidase inhibitors (Stutz, 1999). Oximes show geometric isomerism due to the double bond between the N and C atoms (Mixich & Thiele, 1979; Migrdichian, 1957). As there are significant differences in the physical, chemical and biological properties of these geometric isomers, the determination of the configuration of the isomers is important (Mathison *et al.*, 1989). Oximes and oxime ethers also have a broad pharmacological activity spectrum, encompassing antifungal, antibacterial, antidepressant and insecticidal activities, as well as activity as nerve-gas antidotes, depending on the pharmacophoric group of the molecule (Polak, 1982; Balsamo *et al.*, 1990; Holan *et al.*, 1984; Forman, 1964). The oxime group (C=N—OH) possesses stronger hydrogen-bonding capabilities than the alcohol, phenol or carboxylic acid group (Marsman *et al.*, 1999). Hydrogen bonding plays a key role in molecular recognition in chemical engineering (Bertolasi *et al.*, 1982; Gilli *et al.*, 1983; Hökelek *et al.*, 2001). As part of our ongoing study of the relationship between the structures of cyclobutane and oxime derivatives, a crystal structure determination of the title compound, (I), has been undertaken and the results are presented here.



(I)

Previously we have reported the crystal structures of similar compounds, *viz.* 2-[2-hydroxyimino-2-(3-methyl-3-phenyl-

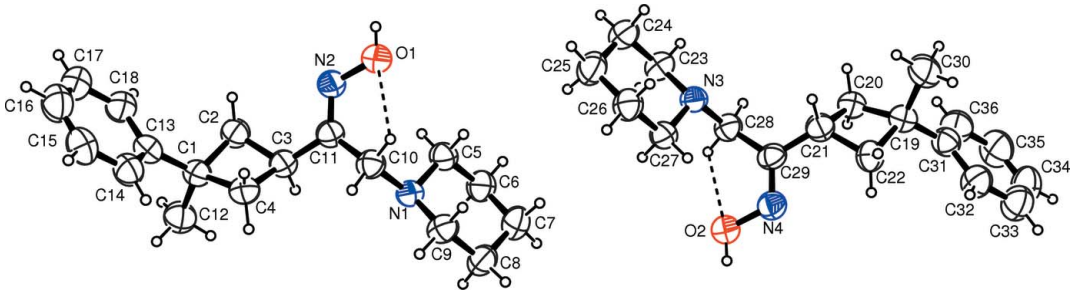


Figure 1
ORTEP3 (Farrugia, 1997) plot of the two independent molecules of (I), showing 30% probability displacement ellipsoids and the atomic numbering scheme. Dashed lines represent intramolecular C—H···O hydrogen bonds.

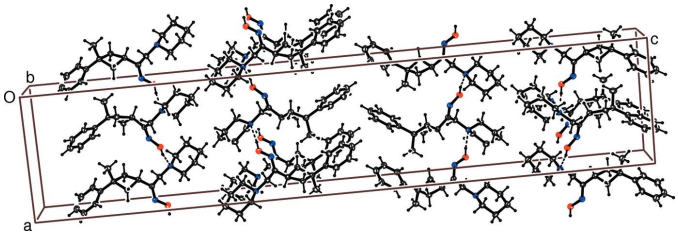


Figure 2
A projection of the crystal structure of (I) approximately along the *b* axis. Dashed lines indicate the O—H···N hydrogen bonds.

cyclobutyl)ethyl]isoindole-1,3-dione, (II) (Özdemir *et al.*, 2004) and 3-[1-hydroxyimino-2-(succinimido)ethyl]1-methyl-1-phenylcyclobutane, (III) (Dinçer *et al.*, 2004). The main aim of the present investigation is to study the differences among the structures of (I), (II) and (III), and also to determine the strength of the hydrogen-bonding capabilities of the oxime group.

The structures of the two independent molecules, *A* (O1/N1/N2/C1–C18) and *B* (O2/N3/N4/C19–C36), of (I) have very similar molecular dimensions (Fig. 1 and Table 1). In the following discussion, values for molecule *B* are quoted in square brackets. In the crystal structure, the phenyl and (piperidin-1-yl)acetaldehyde oxime groups are in *cis* positions with respect to the cyclobutane ring. The four-atom bridge linking the cyclobutane and piperidine rings is not planar, and the Φ_{CC} torsion angle is 82.9 (5)° [−83.3 (5)°], which shows that the conformation about the C—C bond is synclinal.

Although close to being planar, the cyclobutane ring in (I) is more puckered than in (II) and (III), because of the steric hindrance of the substituents. The C4/C1/C2 plane forms a dihedral angle of 25.0 (4)° [25.7 (4)°] with the C2/C3/C4 plane [11.55 (3)° in (II), 19.26 (17)° in (III)]. However, when the bond lengths of the cylobutane ring in (I) are compared with those in (II) and (III), it is seen that there are no significant differences. The piperidine ring adopts a chair conformation, as is evident from the Cremer & Pople (1975) puckering parameters Q = 0.569 (5) Å [0.562 (5) Å], θ = 176.8 (5)° [177.6 (6)°] and φ_2 = 207 (10)° [138 (11)°]. The oxime group has an *E* configuration, with a C3—C11—N2—O1 torsion angle of 178.3 (4)° [−178.4 (4)°]. In (I), the plane of the oxime group is twisted by 45.2 (4)° [46.4 (4)°] out of the mean plane of the cyclobutane ring. The bond lengths and angles of the oxime group in (I) are close to those in (II) and (III).

In each independent molecule, an intramolecular C—H···O interaction generates a five-membered ring (Fig. 1). Atom O1 acts as hydrogen-bond donor to atom N1 of the piperidine ring at ($x + \frac{1}{2}$, $-y$, z). Similiarly, atom O2 acts as hydrogen-bond donor to atom N3 of the piperidine ring at ($x - \frac{1}{2}$, $1 - y$, z). There are no intermolecular π–π and C—H···π interactions in the crystal structure of (I).

Experimental

A solution of 3-(2-chloro-1-oxoethyl)-1-methyl-1-phenylcyclobutane (2.225 g, 10 mmol) and piperidine (1.70 g, 20 mmol) in absolute ethanol (50 ml) was refluxed with continuous stirring. After completion of the reaction, $NH_2OH{\cdot}HCl$ (0.695 g, 10 mmol) was added. The course of both reactions was monitored by IR. The mixture was cooled to room temperature and neutralized with aqueous dilute ammonia (5%) to obtain the target product. It was filtered, washed with copious cold ethanol, recrystallized from ethanol and dried in air (yield 2.29 g, 80%; m.p. 425 K). IR (KBr, ν, cm^{-1}): 3253 (–OH, oxime), 1613 (C═N); ^{1}H NMR ($CDCl_3$, TMS, δ, p.p.m.): 1.26–1.65 (*m*, 6H, $-CH_2-$ piperidine), 1.53 (*s*, 3H, $-CH_3$ on cyclobutane), 2.25–2.60 (*m*, 8H, $-CH_2-$, cyclobutane $-CH_2-$ plus piperidine $-CH_2-$ adjacent to N), 3.22 (*s*, 2H, $-CH_2-$, adjacent to oxime), 3.79 (*q*, 1H, J = 3.67 Hz, >CH–), 7.01–7.35 (m, 5H, aromatics), 10.48 (*s*, 1H, –OH, D_2O exchangeable).

Crystal data

$C_{18}H_{26}N_2O$
M_r = 286.41
Orthorhombic, $Pca2_1$
a = 10.8782 (5) Å
b = 5.8899 (3) Å
c = 53.307 (3) Å
V = 3415.5 (3) Å^3
Z = 8
D_x = 1.114 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 14206 reflections
θ = 1.2–21.5°
μ = 0.07 mm^{-1}
T = 296 K
Prism, colourless
0.64 × 0.45 × 0.13 mm

Data collection

Stoe IPDS-II diffractometer
ω scans
Absorption correction: none
16092 measured reflections
1988 independent reflections
1661 reflections with $I > 2\sigma(I)$
R_{int} = 0.124
θ_{max} = 21.5°
$h = -11 \rightarrow 11$
$k = -6 \rightarrow 6$
$l = -54 \rightarrow 54$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.122
S = 1.06
1988 reflections
374 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0796P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.11 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—N2	1.403 (5)	O2—N4	1.406 (5)
N1—C5	1.460 (6)	N3—C27	1.453 (6)
N1—C9	1.461 (6)	N3—C23	1.452 (6)
N1—C10	1.485 (5)	N3—C28	1.468 (5)
N2—C11	1.271 (6)	N4—C29	1.276 (6)
C1—C12	1.520 (7)	C19—C31	1.497 (7)
C1—C13	1.523 (7)	C19—C30	1.537 (7)
C1—C2	1.543 (7)	C19—C20	1.546 (7)
C1—C4	1.544 (7)	C19—C22	1.548 (7)
C2—C3	1.536 (7)	C20—C21	1.556 (7)
C3—C11	1.493 (7)	C21—C29	1.481 (7)
C3—C4	1.554 (7)	C21—C22	1.524 (7)
C5—N1—C9	110.2 (4)	C27—N3—C23	110.4 (4)
C5—N1—C10	110.8 (3)	C27—N3—C28	111.6 (3)
C9—N1—C10	109.0 (3)	C23—N3—C28	109.7 (4)
C11—N2—O1	112.5 (4)	C29—N4—O2	112.7 (4)
C2—C1—C4	88.0 (4)	C20—C19—C22	87.4 (4)
C3—C2—C1	89.6 (3)	C19—C20—C21	88.8 (4)
C2—C3—C4	87.9 (4)	C22—C21—C20	88.0 (4)
C1—C4—C3	88.9 (4)	C21—C22—C19	89.9 (4)
N1—C10—C11	113.1 (4)	N3—C28—C29	113.5 (4)
N2—C11—C3	116.6 (4)	N4—C29—C21	116.5 (4)
N2—C11—C10	125.4 (4)	N4—C29—C28	124.9 (5)
C3—C11—C10	117.9 (4)	C21—C29—C28	118.5 (4)
C5—N1—C10—C11	67.4 (5)	C27—N3—C28—C29	−67.1 (5)
C9—N1—C10—C11	−171.1 (4)	C23—N3—C28—C29	170.2 (4)
O1—N2—C11—C10	2.0 (7)	O2—N4—C29—C28	−1.2 (6)
C2—C3—C11—N2	−11.7 (7)	C22—C21—C29—N4	7.7 (7)
C4—C3—C11—N2	−116.1 (5)	C20—C21—C29—N4	113.0 (5)
C2—C3—C11—C10	164.9 (4)	C22—C21—C29—C28	−169.8 (4)
C4—C3—C11—C10	60.5 (6)	C20—C21—C29—C28	−64.5 (5)
N1—C10—C11—N2	−100.9 (5)	N3—C28—C29—N4	99.5 (5)
N1—C10—C11—C3	82.9 (5)	N3—C28—C29—C21	−83.3 (5)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C10—H10*A*···O1	0.97	2.30	2.682 (5)	102
C28—H28*B*···O2	0.97	2.30	2.685 (5)	102
O2—H2···N3^{i}	0.82	1.98	2.778 (5)	164
O1—H1···N1^{ii}	0.82	1.97	2.754 (5)	161

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

H atoms were positioned geometrically and treated using a riding model, fixing the bond lengths at 0.82 Å for OH, 0.93 Å for aromatic CH, 0.96 Å for CH_3, 0.97 Å for CH_2, and at 0.98 Å for the CH group. The U_{iso} values were constrained to be $1.5U_{eq}$ of the carrier atom for hydroxyl and methyl H atoms and $1.2U_{eq}$ for the remaining H atoms. The same anisotropic displacement parameters were used for the atoms N2 and C11. Owing to the absence of any significant anomalous scatterers in the molecule, Friedel pairs were merged before the final refinement and the absolute configuration was arbitrarily assigned.

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED32* (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *PLATON* (Spek, 2003).

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