Acta Crystallographica Section E
Structure Reports
Online

ISSN 1600-5368

2,6-Bis(2-methoxyphenyl)-1-nitroso-3,5-diphenylpiperidin-4-one

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Key indicators

Single-crystal X-ray study
T = 105 K
Mean σ(C–C) = 0.002 Å
R factor = 0.035
wR factor = 0.098
Data-to-parameter ratio = 18.7

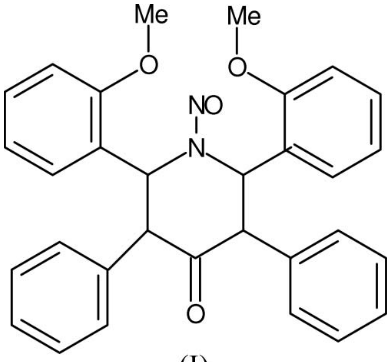
For details of how these key indicators were automatically derived from the article, see
http://journals.iucr.org/e.

Received 9 August 2005
Accepted 19 August 2005
Online 27 August 2005

The piperidone ring in the title compound, $C_{31}H_{28}N_2O_4$, adopts the usual twist–boat conformation. The configurations of the aryl rings at the 2- and 3-positions are equatorial and those at the 5- and 6-positions are axial. The crystal structure is characterized by C—H···O and C—H···N hydrogen bonds between centrosymmetrically related pairs of molecules. In addition, there is an intramolecular C—H···O hydrogen bond and a weak C—H···π interaction. No significant aryl–aryl interactions were observed.

Comment

Piperidinones belong to an important class of heterocycles which are found to possess a variety of biological activities, including cytotoxic and anticancer properties (Dimmock *et al.*, 1990, 2001). Derivatives of piperidinones have also attracted wide attention from chemists and biologists due to their predicted mode of interaction with cellular thiols, having little or no affinity for the hydroxy and amino groups found in nucleic acids (Baluja *et al.*, 1964; Mutus *et al.*, 1989). Moreover, precise X-ray crystallographic investigations of the molecular and crystal structures of symmetrically shaped molecules are expected to provide insights into the nature and strength of the competition between inter- and intramolecular forces and their role in effecting symmetry carry-over from the free state to the solid. The observed symmetry of a molecule in the solid state is often found to be reduced compared with that observed in the free state, as molecules tend to pack as closely as possible upon crystallization (Kitaigorodskii, 1973). As a consequence, a variety of intermolecular interactions are observed among molecules within crystal structures, of which hydrogen-bonded interactions play a vital role. In order to characterize the complex interaction picture within the crystal structure, it would be suitable to attribute, to begin with, a



(I)

doi:10.1107/S1600536805026553

direct relationship between the complexity of these interactions and the ratio of the number of acceptors to donors. In this context, we have undertaken single-crystal X-ray investigations of a series of piperidinone derivatives and this paper deals with a precise description of the title compound, (I), namely, 2,6-bis(2-methylphenyl)-1-nitroso-3,5-diphenylpiperidin-4-one (PIP3). Recently, we have elucidated the crystal structures of 2,6-bis(4-methoxyphenyl)-1-nitroso-3,5-diphenylpiperidin-4-one (PIP1; Natarajan *et al.*, 2005) and 2,6-bis(2-methylphenyl)-1-nitroso-3,5-diphenylpiperidin-4-one (PIP2; Suresh *et al.*, 2005).

The molecular structure of compound (I) is illustrated in Fig. 1. The piperidinone ring adopts a twist–boat conformation, as observed in PIP1 and PIP2. Atoms C2 and C5 deviate by 0.556 (1) and 0.547 (1) Å, respectively, from the least-squares plane defined by the other atoms (N1, C3, C4 and C6). These values are 0.592 (2) and 0.492 (2) Å, respectively, for PIP1 and 0.627 (1) and 0.560 (1) Å, respectively, for PIP2. The twist–boat conformation is also evident from the values observed for the torsion angles of the piperidinone ring (Table 1). The nitroso O atom is *syn* to the neighbouring equatorial methylphenyl at C6 [O1—N2—N1—C6 = 5.2 (1)°], as observed in PIP1 [5.3 (2)°] and PIP2 [−5.7 (2)°]. The configurations of the aryl rings at the 2- and 3-positions [equatorial, C21—C2—C3—C31 − 59.23 (1)°] and those at the 5- and 6-positions [axial, C51—C5—C6—C61 = 157.10 (9)°] differ significantly from those observed in PIP1 and PIP2 (the aryl rings at the 2- and 3-positions are axially oriented and those at the 5- and 6-positions are equatorially oriented). Thus, the structure of (I) provides a good example of how substitution effects can significantly effect conformational changes in molecules.

The observations made in the present study concerning the conformation of the title compound, (I), are in accord with the results of ^{1}H NMR studies of piperidinone in solution (Alex Raja & Perumal, 2004) and establish that compound (I) adopts the same conformation in both solution and the solid state.

The crystal structure of (I) is characterized by C—H···O and C—H···N hydrogen bonds between centrosymmetrically related pairs of molecules (Table 2, Fig.2). A relatively stronger intramolecular C—H···O hydrogen bond [C66—H66···O3 = 176 °] is observed, which presumably plays a role in effecting significant differences in the conformation of the molecule in (I) compared with those observed in compounds PIP1 and PIP2. In addition, a weak C27—H27···π interaction is observed, involving the 2-methoxyphenyl ring and with H···π = 2.72 Å and an angle of 141°. No significant aryl–aryl interactions were observed.

Experimental

A mixture of 2,6-bis(2-methoxyphenyl)-3,5-diphenylpiperidin-4-one (0.5 g, 0.0014 mol) and concentrated HCl (0.3 ml) was dissolved in a 1:1 ethanol–water mixture (20 ml). The temperature of the solution was kept at 338–343 K and, while stirring, a solution of $NaNO_2$ (0.097 g, 0.0014 mol) in a 1:1 ethanol–water mixture (15 ml) was added dropwise over a period of 1 h. Heating and stirring were continued for another 2 h. The reaction mixture was extracted four times with diethyl ether (100 ml) and the extracts were washed with water several times. The combined ether layer was dried over anhydrous sodium bisulfate. After removal of diethyl ether, the crude product was recrystallized twice from ethyl acetate to give colourless crystals of (I) (yield 64%, m.p. 448 K).

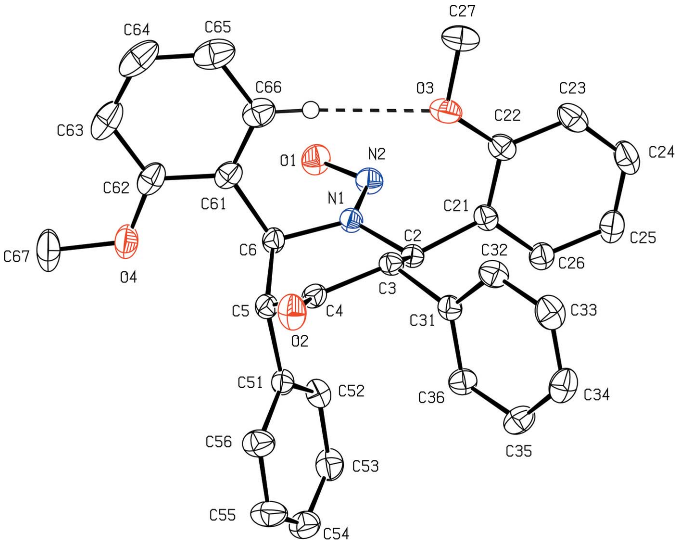


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. The intramolecular hydrogen bond is shown as a dashed line. Carbon-bound H atoms have been omitted for clarity.

Crystal data

$C_{31}H_{28}N_2O_4$
M_r = 492.55
Monoclinic, $P2_1/n$
a = 13.4969 (3) Å
b = 11.7546 (3) Å
c = 16.1467 (4) Å
β = 97.842 (1)°
V = 2537.73 (11) Å^3
Z = 4

D_x = 1.289 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3342 reflections
θ = 2–23°
μ = 0.09 mm^{-1}
T = 105 (2) K
Block, colourless
0.28 × 0.14 × 0.12 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 1998)
$T_{\min}$ = 0.97, $T_{\max}$ = 0.99
39911 measured reflections

6291 independent reflections
5047 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.056
$\theta_{\max}$ = 28.3°
$h = -17 \rightarrow 17$
$k = -15 \rightarrow 15$
$l = -21 \rightarrow 21$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.098
S = 1.06
6291 reflections
337 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0431P)^2 + 0.6373P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max}$ = 0.31 e Å^{-3}
$\Delta\rho_{\min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0018 (5)

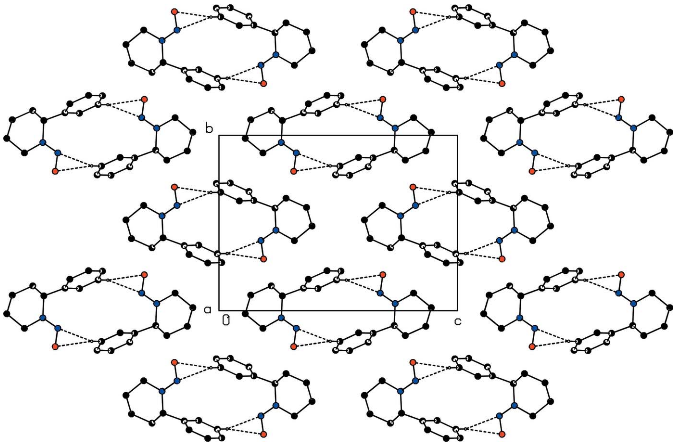


Figure 2
The crystal packing of the molecules of (I), viewed down the *a* axis. H atoms and the aryl rings which do not take part in hydrogen bonding (dashed lines) have been omitted for clarity.

Table 1
Selected geometric parameters (°).

O1—N2—N1—C6	5.17 (13)	C31—C3—C2—C21	−59.26 (11)
O1—N2—N1—C2	171.70 (8)	C2—N1—C6—C5	−5.63 (13)
C2—C3—C4—C5	−7.45 (12)	C3—C4—C5—C6	−41.19 (12)
C6—N1—C2—C3	−42.70 (12)	N1—C6—C5—C4	47.57 (11)
C4—C3—C2—N1	47.65 (11)	C61—C6—C5—C51	157.10 (9)

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

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
C66—H66$\cdots$O3	0.95	2.47	3.4138 (16)	176
C23—H23$\cdots$O1^{i}	0.95	2.59	3.4370 (14)	149
C23—H23$\cdots$N2^{i}	0.95	2.55	3.3796 (14)	146

Symmetry code: (i) $-x, -y+1, -z$.

H atoms were placed in calculated positions and allowed to ride on their carrier atoms, with C—H = 0.93–0.98° and $U_{\rm iso} = 1.2U_{\rm eq}$(C) for CH_2 and CH groups, and $1.5U_{\rm eq}$ for CH_3 groups.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

The authors thank the UGC for the DRS programme. JS thanks the UGC and the management of The Madura College, Madurai, for providing a teacher's fellowship. SP thanks CSIR, New Delhi, for a Major Research Project.

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