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

S. Natarajan,[a] R. V. Krishnakumar,[b]* M. Subha Nandhini,[a] V. P. Alex Raja,[c] S. Perumal[c] and K. Ravikumar[d]

[a]School of Physics, Madurai Kamaraj University, Madurai 625 021, India, [b]Department of Physics, Thiagarajar College, Madurai 625 009., India, [c]School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India, and [d]Laboratory of Crystallography, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Correspondence e-mail: mailtorvkk@yahoo.co.in

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.051
wR factor = 0.151
Data-to-parameter ratio = 17.3

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

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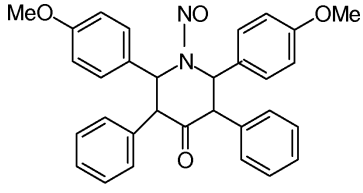
The piperidone ring of the title compound, $C_{31}H_{28}N_2O_4$, adopts a twist boat conformation. The crystal packing is characterized by a layered arrangement of molecules held together by C—H···O hydrogen bonds, in which each of the nitroso and carbonyl O atoms participate. No significant aryl–aryl interactions are observed.

Comment

Piperidones 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). Many nitroso-amines are carcinogenic (Magee *et al.*, 1976). Certain *N*-nitroso-ureas are antitumour agents and antibiotics (Durand, 1989; Fujimoto *et al.*, 1991). Thus, combining these two biologically active moieties together may lead to many useful biologically active compounds. Derivatives of piperidones have attracted wide attention from chemists and also biologists, due to their predicted mode of interaction with cellular thiols, with little or no affinity for the hydroxy and amino groups found in nucleic acids (Baluja *et al.*, 1964; Mutus *et al.*, 1989). Thus, it is possible that the development of these compounds as potential cytotoxic agents may one day lead to drugs devoid of mutagenic and carcinogenic properties (Benvenuto *et al.*, 1993).



(I)

The piperidone ring adopts a twist boat conformation with atoms C2 and C5 deviating by 0.592 (2) and 0.492 (2) Å, respectively, from the least-squares plane defined by the other atoms (N1, C3, C6 and C4). The twist boat conformation is also apparent from the values observed for the torsion angles of the piperidone ring (Table 1). The aryl rings at the 5- and 6-positions of the piperidone ring are equatorially oriented and those at the 2- and 3-positions are axially oriented. The nitroso O atom is *syn* to the neighbouring equatorial methoxyphenyl at C6 [C6—N1—N2—O1 = 5.3 (2)°]. The axial orientation of the methoxyphenyl and phenyl rings at the 2- and 3-positions is defined by the torsion angle C21—C2—C3—C31 [−155.26 (13)°], and that of the equatorial substituents at the 5- and 6-positions by C51—C5—C6—C61 [67.15 (15)°]. Least-squares-plane calculations through all of the aromatic rings reveal that the dihedral angle between the

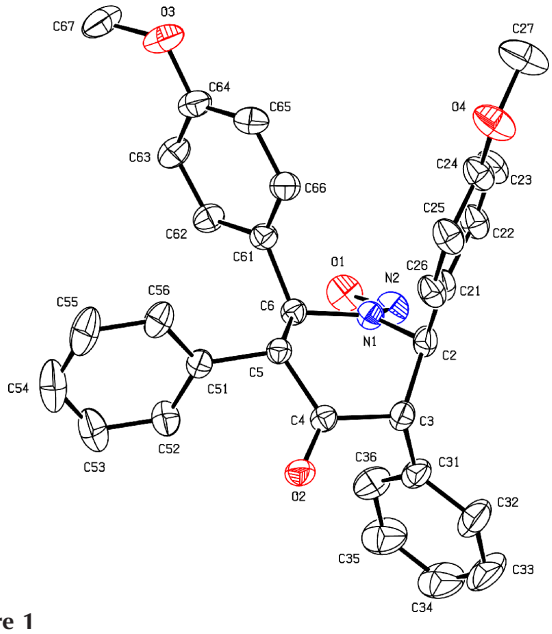


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms have been omitted for clarity.

planes passing through the axially oriented rings at the 2- and 3-positions is 78.9 (1)°, and that between the equatorially oriented rings at the 5- and 6-positions is 50.0 (1)°. This is in accord with the results of ^{1}H NMR studies of piperidone in solution (Alex Raja & Perumal, 2004). Thus the piperidone molecule adopts the same conformation in both solution and solid state.

The title compound, (I), contains several potentially strong acceptors of hydrogen bonds, but only weak (aryl C—H) donors. Thus, it is not surprising that the aggregation of such molecules in the crystal structure is stabilized through C—H···O hydrogen bonds, C···O short contacts and van der Waals interactions. The crystal packing is characterized by a layered arrangement of molecules held together by C—H···O hydrogen bonds, in which each of the nitroso and carbonyl O atoms participate (Fig. 2). These layers run parallel to the (20$\bar{2}$) planes; adjacent layers are cross-linked through methoxy–carbonyl linkages (C67—H67*A*···O2), in addition to van der Waals interactions. No significant aryl–aryl interactions are observed.

Experimental

A mixture of 2,6-bis(4-methoxyphenyl)-3,5-diphenylpiperidin-4-one (0.75 g, 2.98 m mol) and concentrated HCl (0.4 ml) was dissolved in a 1:1 ethanol–water mixture (25 ml) kept at 338–343 K. A solution of $NaNO_2$ (0.21 g, 3.0 m mol) in a 1:1 ethanol–water mixture (15 ml) was added dropwise over a period of 1 h to the former solution. 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 diethyl ether layer was dried over anhydrous sodium bisulfate. After removal of diethyl ether, the crude product was recrystallized twice from ethanol to give pale-yellow crystals (yield: 70%; m.p: 476 K).

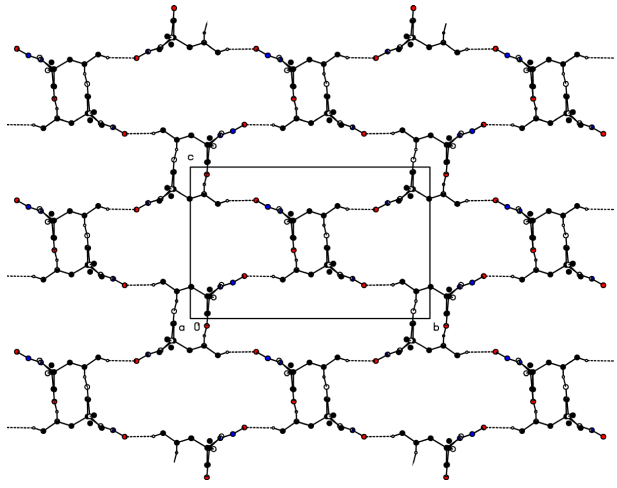


Figure 2
View down the *a* axis, showing the stabilization of layers through C—H···O hydrogen bonds (dashed lines). Aryl rings have been omitted for clarity.

Crystal data

$C_{31}H_{28}N_2O_4$
M_r = 492.55
Monoclinic, $P2_1/n$
a = 10.8364 (8) Å
b = 19.4649 (15) Å
c = 12.6722 (10) Å
β = 103.926 (1)°
V = 2594.4 (3) Å^3
Z = 4
D_x = 1.261 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5412 reflections
θ = 2.2–27.2°
μ = 0.08 mm^{-1}
T = 293 (2) K
Block, yellow
0.28 × 0.22 × 0.16 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.90, T_{max} = 0.99
15 676 measured reflections
5783 independent reflections
4264 reflections with $I > 2\sigma(I)$
R_{int} = 0.021
θ_{max} = 28.0°
$h = -12 \rightarrow 13$
$k = -25 \rightarrow 25$
$l = -16 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.151
S = 1.04
5783 reflections
334 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0796P)^2 + 0.332P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—N2	1.2237 (18)	C2—C3	1.537 (2)
O2—C4	1.2029 (18)	C4—C3	1.521 (2)
N1—N2	1.3265 (17)	C4—C5	1.5219 (19)
N1—C2	1.4709 (18)	C5—C6	1.5492 (19)
C6—N1—N2—O1	5.3 (2)	O2—C4—C5—C51	−13.9 (2)
N2—N1—C2—C21	114.60 (14)	C3—C4—C5—C6	41.55 (17)
C6—N1—C2—C3	53.04 (17)	N2—N1—C6—C61	−77.39 (16)
N1—C2—C21—C26	116.08 (16)	C2—N1—C6—C5	−9.76 (17)
N1—C2—C21—C22	−63.66 (18)	C4—C5—C6—N1	−37.75 (16)
O2—C4—C3—C31	58.73 (18)	N1—C6—C61—C62	119.26 (15)
C5—C4—C3—C2	2.42 (18)	N1—C6—C61—C66	−66.83 (18)
N1—C2—C3—C4	−46.40 (16)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C25—H25···O1^{i}	0.93	2.57	3.467 (2)	163
C26—H26···O2^{ii}	0.93	2.62	3.382 (2)	140
C27—H27A···O1^{iii}	0.96	2.57	3.078 (3)	114
C67—H67A···O2^{iv}	0.96	2.62	3.562 (2)	168

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

H atoms were placed at calculated positions and allowed to ride on their carrier atoms, with C—H = 0.93–0.98 Å and $U_{iso} = 1.2U_{eq}$(C) for CH_2 and CH groups, and $1.5U_{eq}$(C) for CH_3 groups. The data coverage is 97.5% of all independent reflections to $2\theta = 51°$ (a d spacing of 0.825 Å); close examination revealed that all missing reflections lie only in high-angle ($2\theta > 46°$) regions.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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