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

J. Suresh,[a] V. P. Alex Raja,[b] S. Natarajan,[c] S. Perumal,[b] A. Mostad[d] and R. V. Krishnakumar[e]*

[a]Department of Physics, The Madura College, Madurai 625 011, India, [b]School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India, [c]Department of Physics, Madurai Kamaraj University, Madurai 625 021, India, [d]Department of Chemistry, University of Oslo, PO Box 1033, Blindern, N-0315 Oslo 3, Norway, and [e]Department of Physics, Thiagarajar College, Madurai 625 009, India

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

Key indicators

Single-crystal X-ray study
T = 105 K
Mean σ(C–C) = 0.002 Å
R factor = 0.034
wR factor = 0.098
Data-to-parameter ratio = 18.9

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

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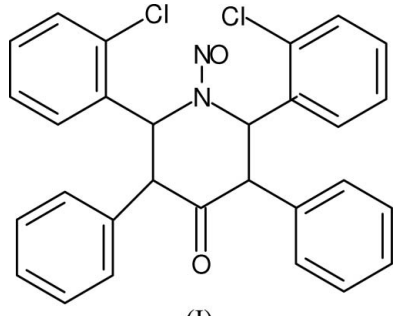
In the title compound, $C_{29}H_{22}Cl_2N_2O_2$, the piperidinone ring adopts its usual twist–boat conformation. The crystal packing is stabilized by a three-dimensional network of C—H···O hydrogen bonds involving the nitroso and carbonyl O atoms. No significant C—H···π, π–π and Cl···Cl interactions are observed but there are weak Cl···Cl interactions.

Comment

The piperidine ring is a distinct structural feature of a variety of alkaloid natural products and drug candidates. Watson *et al.* (2000) observed that during the past decade there were thousands of piperidine compounds mentioned in clinical and preclinical studies. Piperidinones, though relatively less prominent, have also been regarded as precursors of a host of biologically active compounds and natural alkaloids, prior to their conversion to piperidines. This paper reports the structure of the title compound, (I), a nitroso-piperidinone derivative, namely 2,6-bis(2-chloroyphenyl)-1-nitroso-3,5-diphenylpiperidin-4-one. Many nitroso–amines are carcinogenic (Magee *et al.*, 1976) and certain *N*-nitroso–ureas are antitumour agents and antibiotics (Durand, 1989; Fujimoto *et al.*, 1991). Combining these groups together may therefore lead to many useful biologically active compounds. In addition to their possible biological significance, accurate X-ray crystallographic investigations on a variety of nitroso–piperidinone derivatives with various substituted phenyl rings at the 2-, 3-, 5- and 6-positions have been carried out in our laboratory with the aim of obtaining some information on the effect of substituents on the conformation of individual molecules and also on the crystal-packing features of these compounds.



(I)

Recently, in our laboratory, we have elucidated the crystal structures of a few nitroso–piperidinones with varying substituted phenyl rings at the 2- and 6-positions and unsubstituted phenyl rings at the 3- and 5-positions, namely the 4-methoxy (PIP1; Natarajan *et al.*, 2005), 2-methyl (PIP2;

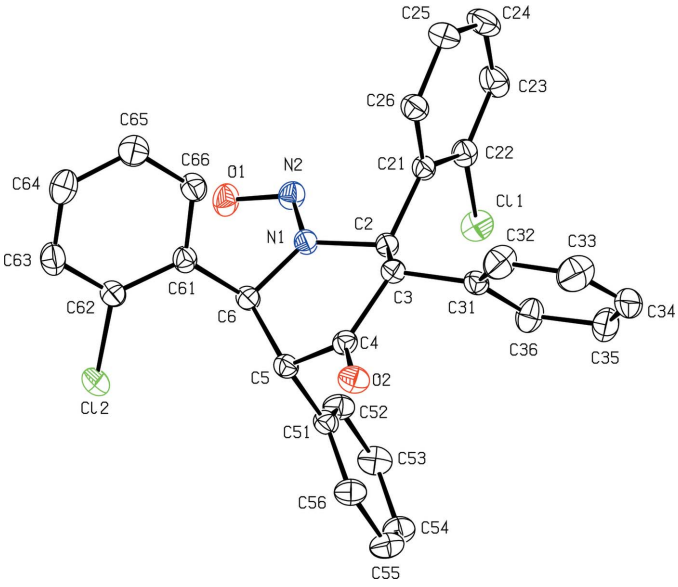


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms have been omitted for clarity.

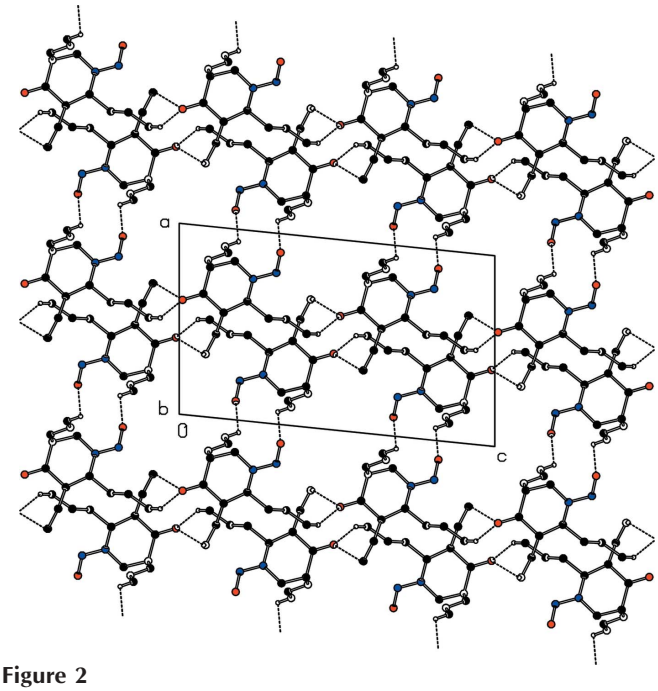


Figure 2
A view along the *b* axis of the three-dimensional network of hydrogen bonding (dashed lines) within the crystal structure. H atoms which do not take part in hydrogen bonding have been omitted for clarity.

Suresh, Alex Raja *et al.*, 2005) and 2-methoxy (PIP3; Suresh, Krishnakumar *et al.*, 2005) analogues of (I).

The molecular structure of compound (I) is illustrated in Fig. 1. The piperidinone ring adopts a twist–boat conformation, as observed in PIP1, PIP2 and PIP3. Atoms C2 and C5 deviate by 0.529 (2) and 0.499 (2) Å, respectively, from the least-squares plane defined by the other atoms (N1, C3, C4 and C6). The corresponding values are 0.592 (2) and 0.492 (2) Å for PIP1, 0.627 (1) and 0.560 (1) Å for PIP2, and 0.556 (1), 0.547 (1) Å for PIP3. 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 axial chlorophenyl at C6 [C6—N1—N2—O1 = 6.04 (17)°]. The orientation of the nitroso O atom remains relatively unperturbed by the effect of the substituent. The value of this torsion angle is 5.3 (2)° for PIP1, −5.8 (1)° for PIP2 and 5.2 (1)° for PIP3. This may be attributed to the fact that the nitroso O atom encounters large steric effects due to the bulky substituents at the neighbouring 2- and 6-positions of the piperidinone ring. The configuration of the aryl rings at the 2- and 3- (equatorial, C21—C2—C3—C31 = −63.4°) and those at the 5- and 6-positions (axial, C61—C6—C5—C51 = 158.2°) are similar to those observed in PIP3, but are different from those of PIP1 and PIP2 where the aryl rings at the 2- and 3-positions are axially oriented and those at the 5- and 6-positions are equatorially oriented. The observations concerning the conformation of (I) agree well 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.

A sterically favoured short intramolecular distance is observed (H2···Cl1 = 2.544 Å). The crystal packing is stabilized by a three-dimensional network of C—H···O hydrogen bonds in which the nitroso and carbonyl O atoms participate as acceptors (Table 2 and Fig. 2). A weak Cl···Cl contact [Cl1···Cl2^{i} = 3.696 (1) Å; symmetry code: (i) $-x, +y-\frac{1}{2}, -z+\frac{1}{2}$] is also observed. No significant C—H···π or π–π interactions are present. Though the formation of centrosmmetric dimers seems a common feature in the crystal packing of these compounds, the choice between interconnected layers and columns stabilized by van der Waals interactions among them could not be attributed to the change and nature of the substituents.

Experimental

A mixture of 2,6-bis(2-chlorophenyl)-3,5-diphenylpiperidin-4-one (0.75 g, 0.0015 mol) and concentrated HCl (0.4 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 $NaNO_2$ (0.21 g, 0.003 mol) in a 1:1 ethanol–water mixture (15 ml) was added dropwise over a period of 1 h. The 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 sulfate. After removal of the ether, the crude product was recrystallized twice from ethyl acetate to give colourless crystals (yield: 68%, m.p. 493 K).

Crystal data

$C_{29}H_{22}Cl_2N_2O_2$
M_r = 501.39
Monoclinic, $P2_1/c$
a = 10.5812 (3) Å
b = 12.9766 (4) Å
c = 17.5935 (5) Å
β = 95.863 (1)°
V = 2403.09 (12) Å^3
Z = 4
D_x = 1.386 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3344 reflections
θ = 2–23°
μ = 0.30 mm^{-1}
T = 105 (2) K
Block, colourless
0.28 × 0.17 × 0.14 mm

Data collection

Bruker SMART APEX CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 1998)
T_{min} = 0.95, T_{max} = 0.96
30319 measured reflections
5972 independent reflections
5061 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 28.3°
$h = -13 \rightarrow 14$
$k = -17 \rightarrow 17$
$l = -23 \rightarrow 23$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.098
S = 1.05
5972 reflections
316 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0476P)^2 + 1.0027P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.40 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Table 1
Selected torsion angles (°).

C6—N1—N2—O1	6.04 (17)	C4—C3—C2—N1	48.15 (13)
C2—N1—N2—O1	172.10 (10)	C31—C3—C2—C21	−63.41 (13)
C5—C4—C3—C2	−13.35 (15)	C2—N1—C6—C5	−10.19 (16)
C3—C4—C5—C6	−35.20 (15)	C4—C5—C6—N1	46.62 (14)
C6—N1—C2—C3	−37.93 (15)	C51—C5—C6—C61	158.20 (10)

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

D—H···A	D—H	H···A	D···A	D—H···A
C53—H53···O1^{i}	0.93	2.45	3.0470 (17)	122
C32—H32···O2^{ii}	0.93	2.60	3.377 (2)	142
C23—H23···O2^{iii}	0.93	2.50	3.3583 (18)	154

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

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}(H) = 1.2U_{eq}(C).

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); 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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