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Crystal structure of 2,6-diphenyl-3-methyl-*N*-nitrosopiperidin-4-one

T. Hemalatha, S. Nagarajan *

Department of Chemistry, Annamalai University, Annamalainagar, India

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ABSTRACT

The structure of the 2,6-diphenyl-3-methyl-*N*-nitrosopiperidin-4-one ($C_{18}H_{18}N_2O_2$) has been investigated in solution and in the solid state by IR, NMR and X-ray methods. The crystal belongs to the monoclinic space group $P21/n$ with a = 7.7134(6), b = 14.7754(14), c = 27.321(3) Å and β = 94.617(3)°. In crystal structure, the piperidine ring adopts a boat conformation with a slight distortion. One of the phenyl groups is in axial orientation, while the other phenyl and methyl groups are in equatorial orientations.

1. Introduction

Nitrogen based heterocyclic compounds are very important in the field of medicinal chemistry. Compounds including 2,6-disubstituted derivatives have been reported as tranquillizers and posses hypotensive activity as well as bactericidal, fungicidal and herbicidal activities. The nitroso group introduced at the nitrogen atom profoundly affects the biological activity and conformation of the piperidone ring and the orientation of substituents [1–3]. Many nitrosoamines are known to possess antitumour activity and are used as antitumour agents or antibiotics.

The preferred conformation of all the piperidine and piperidone precursors has been shown to be the chair conformation with a slight flattening or distortion of the ring depending upon the position and size of the substituents [4]. The introduction of nitroso group at the nitrogen position is known to exert a large influence on the conformation of the piperidine ring and orientation of the ring substituents [5]. In this investigation, we report here the crystal structure of 2,6-diphenyl-3-methyl-*N*-nitrosopiperidin-4-one (NOMPO).

2. Results and discussion

The 4-piperidone is prepared from benzaldehyde, ethyl methyl ketone and ammonium acetate in ethanol. 2,6-Diphenyl-3-methyl-*N*-nitrosopiperidin-4-one (Fig. 1) was obtained by nitrosation using sodium nitrite [6]. In the *N*-nitroso compounds the partial double bond character between two nitrogen atoms results in hindered rotation around the N–N bond in *N*-nitroso group. Due to the restricted rotation of N···N···O bond, the *N*-nitrosopiperidones are unsymmetrical and exist in *syn* and *anti* forms (Fig. 2).

The ^{1}H NMR spectrum shows two sets of signals corresponding to *syn* and *anti* isomers. The two forms arise due to the restricted rotation of planar N···N···O group around C_2–N–C_6 plane. These two sets of signals are selectively separated with the help of NMR peak integration values. The signals with high integration values correspond to *anti* isomer and those with low integration values correspond to *syn* isomer. In *syn* form, the nitroso group experiences steric interference with ring protons. Hence the energy of *syn* form is higher, thus leading to smaller populations and thus low integration values are obtained in ^{1}H NMR spectrum. On the other hand, in *anti* form, the nitroso group is far from the ring protons, here there is no pseudoallelic strain between the heteroconjugate group (N···N···O) and the *anti* side proton. Hence the energy of *anti* form is lower, thus leading to higher populations and thus higher integration values are obtained in ^{1}H NMR spectrum.

The crystal structure shows the bond lengths and bond angles of the molecule, the values are in agreement with the values reported for 3,5-dimethyl-2,6-diphenylpiperidin-4-one oxime and other related structures [7–10]. The carbonyl oxygen bond length (C═O) 1.213(3) Å is comparable with the average value of 1.218(3) Å reported elsewhere [11,12]. As expected, it is known from the conformation angles and least-square planes that the piperidine ring adopts a distorted boat conformation. C2 and C5 atoms deviate in the same direction from the best plane of the piperidine rings N1, C1, C3 and C4 in contrast to the parent piperidone (without nitroso group).

The methyl group in the third position is in the equatorial position. The corresponding torsion angle is (N1–C1–C2–C18) 166.6°(2). The phenyl rings at C5 in axial and C1 in the equatorial

* Corresponding author. Tel.: +91 94430 46272.
E-mail address: nagarajan.au@gmail.com (S. Nagarajan).

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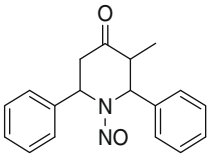

Fig. 1. 2,6-Diphenyl-3-methyl-*N*-nitrosopiperidin-4-one.

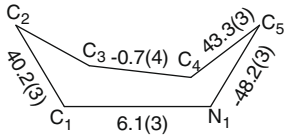

Fig. 3. The conformational angles (°) of the piperidine ring.

position (Fig. 4) with their torsion angles C3–C4–C5–C12 and C3–C2–C1–C6 being equaled to −83.2(3)° and 166.5(2)°, respectively. The piperidine ring system offers a wide variety of conformational flexibility such as chair, boat and twist conformations [13,14]. However, the chair or slightly distorted chair conformation has been found to be the most favoured [15,16]. The conformational angle (°) of the piperidine ring is shown in Fig. 3.

A literature survey on the conformation of 2,6-dialkyl-*N*-nitrosopiperidines and related compounds suggested two possibilities for the conformation of *N*-nitroso-2,6-diphenylpiperidine, in which the phenyl group might have occupied the axial positions when the nitroso group is coplanar to the best plane of the piperidine ring (I). The phenyl ring could occupy the equatorial positions and the nitroso group would then have to adopt a perpendicular orientation to avoid steric interaction (II). The 2,6-diphenyl-3-methyl-*N*-nitrosopiperidin-4-one falls in neither category I nor II but forms a unique conformation with axial and equatorial substituted phenyl groups.

Due to delocalization of lone pair of electrons of nitrogen atom with hetero π-electron system of the carbonyl and nitroso groups, a partial double bond character at the N–C and N–N bonds is developed. This double bond character restricts the N–C and N–N free rotation resulting in two different orientations [17,18] namely, planar and perpendicular (*syn* and *anti*) with respect to the best plane of the piperidine ring, irrespective of the nature and size of substituents at second and sixth positions [19–22].

The ORTEP of the molecule is shown in Fig. 4 and powder XRD of NOMPO is shown in Fig. 5. Packing of the molecules viewed along *b*-axis and *c*-axis is shown in Figs. 6 and 7, respectively.

2,6-Diphenyl-3-methyl-*N*-nitrosopiperidin-4-one, the nitroso group is oriented *syn* to the C1 (C1–N1–N2–O1) = −3.7(4)°) and *anti* to the C5 (C5–N1–N2–O2 = −176.2(2)°) atoms of the piperidine ring. This can be termed as a *syn–anti* conformation of the nitroso group. In this study, the torsion angles, asymmetry parameters and least-square planes show that the piperidine ring adopts a boat conformation with a slight distortion.

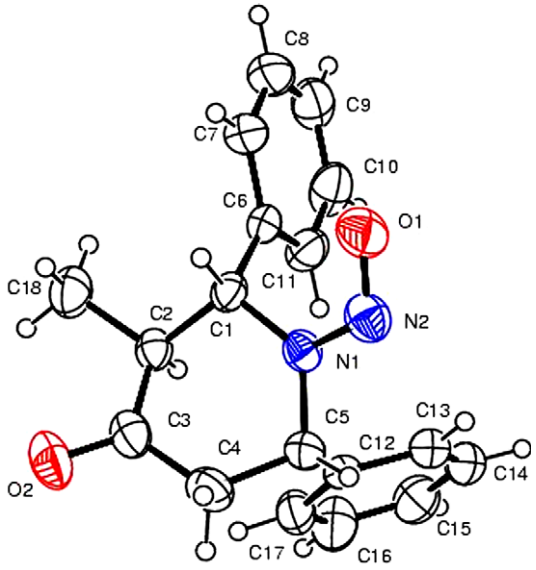

Fig. 4. ORTEP of the molecule.

3. Experimental

IR spectrum was recorded with AVATAR 330 FT-IR spectrometer using KBr pellet. The frequencies corresponding to the functional groups are assigned. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz instrument in $CDCl_3$ solution with TMS as an internal standard.

3.1. Crystal structure determination and refinement

The compound is crystallized in ethanol by slow evaporation method at room temperature. The intensity data were collected on a Bruker AXS (Kappa Apex II) X-ray diffractometer, equipped

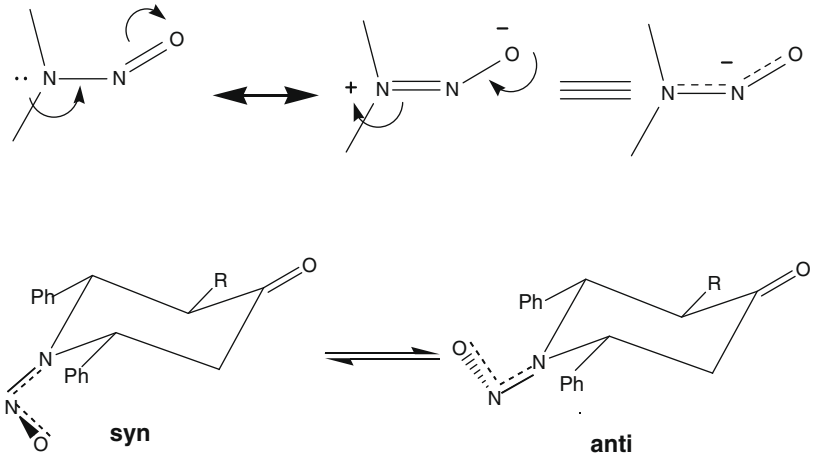

Fig. 2. N–NO partial double bond character: *syn* and *anti* forms.

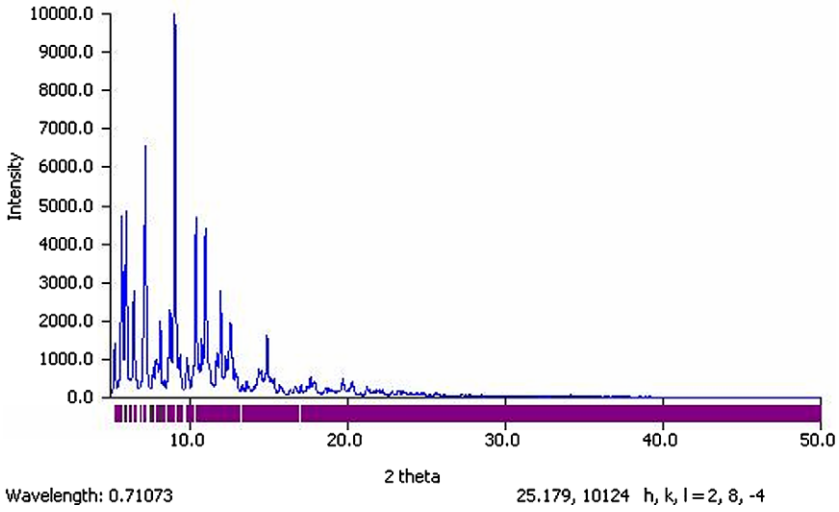

Fig. 5. Powder XRD of the molecule.

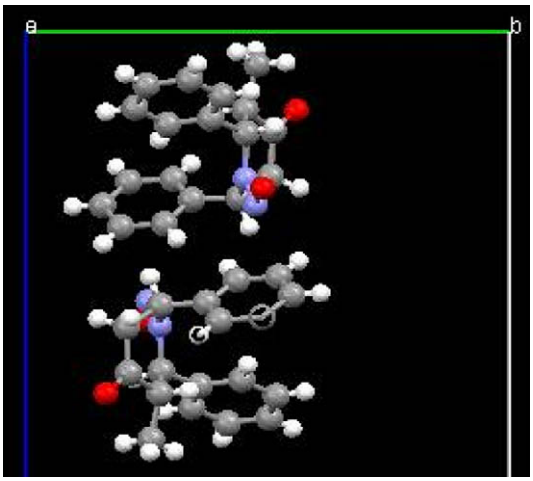

Fig. 6. Packing of NOMPO along *b*-axis.

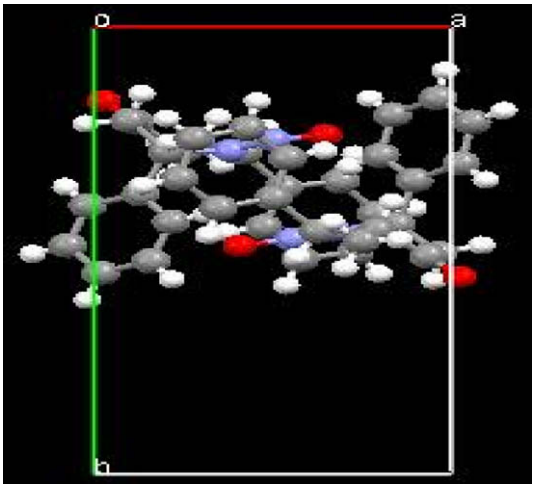

Fig. 7. Packing of NOMPO along *c*-axis.

with a graphite monochromated Mo Kα radiation (λ = 0.71073 Å). The crystal structure of NOMPO was solved and refined by full matrix least squares on F^2 with Wingx software package utilizing SHELXS-97 and SHELXL-97 modules. Molecular graphics was performed by ORTEP 3 and mercury. The plot for the structures was created with DIAMOND software. The crystal data and structure refinement detail of 2,6-diphenyl-3-methyl-*N*-nitrosopiperidin-4-one are given in Table 1. The atomic coordinates of non-hydrogen atoms with their equivalent displacement parameters are given in Table 2. The table in the supplementary material lists the bond length, bond angles and some selected torsion angles of interest.

The compound was prepared by using the method proposed in our previous research paper [6]. The compound shows strong absorption band at 1654–1714 cm^{-1} which shows the presence of a cyclic ketone. The peaks observed at 1654–1439, 2935 and 1601 cm^{-1} represent aromatic C–C, methyl C–H and N=O, respectively.

^{1}H NMR (400 MHz, $CDCl_3$): *syn* isomer δ (ppm) = 5.24 (d, 10.1 Hz, H-2), 6.06 (t, 6.68 Hz, H-6), 1.15 (d, 7.16 Hz, CH_3); *anti* isomer δ (ppm) = 5.93 (d, 6.24, H-2), 6.39 (dd, 6.82 Hz, 3.54 Hz, H-6),

Table 1
Crystal data and summary of intensity data collection and structure refinement.

Parameters	NOMPO
Empirical formula	$C_{18}H_{18}N_2O_2$
Colour/shape	Colourless/needle
Formula weight	249.34
CCDC deposit No.	715,906
Temperature (K)	293(2)
Crystal system	Monoclinic
Space group	*P*21/*n*
Cell constants	
a (Å)	7.7134(6)
b (Å)	14.7754(14)
c (Å)	27.321(3)
β (°)	94.617(3)
Volume (Å^3)	3103.6(5)
Molecules/cell (2)	8
Calculated density (mg/m^3)	1.260
Absorption coefficient (mm^{-1})	0.083
Crystal size (mm)	0.3 × 0.05 × 0.05
F(0 0 0)	1248
Reflections collected	17,851
Unique reflections	2865
Parameters refined	400
Goodness of fit (F^{o2})	1.157
R_1	0.0414
WR_2	0.1086
ρ_{mm} (e/Å^3)	−0.227
$\rho_{(max)}$ (e/Å^3)	0.272

Table 2
Atomic coordinates ($Å \times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for the non-hydrogen atoms.

Atom	*X*	*Y*	*Z*	*U*(eq)
C1	11,266(3)	434(2)	6196(1)	43(1)
C2	12,922(3)	457(2)	5923(1)	44(1)
C3	14,352(4)	−116(2)	6163(1)	52(1)
C4	14,658(4)	−64(2)	6710(1)	60(1)
C5	13,480(3)	580(2)	6958(1)	48(1)
C6	10,022(3)	1173(2)	6022(1)	45(1)
C7	8489(4)	945(2)	5756(1)	61(1)
C8	7385(4)	1606(4)	5562(1)	79(1)
C9	7787(5)	2501(3)	5631(1)	78(1)
C10	9297(5)	2733(3)	5898(1)	75(1)
C11	10,421(4)	2669(2)	6093(1)	60(1)
C12	13,970(4)	1568(2)	6979(1)	44(1)
C13	13,027(4)	2124(2)	7266(1)	54(1)
C14	13,362(4)	3032(3)	7303(1)	64(1)
C15	14,627(5)	3405(3)	7048(2)	73(1)
C16	15,594(5)	2868(3)	6769(1)	79(1)
C17	15,287(4)	1944(2)	6739(1)	62(1)
C18	12,500(4)	213(2)	5386(1)	67(1)
N1	11,706(3)	435(2)	6731(1)	45(1)
N2	10,537(4)	252(2)	7042(1)	59(1)
O1	9075(3)	100(2)	6846(1)	71(1)
O2	15,256(3)	−599(2)	5930(1)	75(1)

0.9140 (d, 6.72 Hz, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$): *syn* isomer δ (ppm) = 59.6 (C-2), 53.2 (C-6), 14.3 (CH_3); *anti* isomer δ (ppm) = 66.8 (C-2), 62.1 (C-6), 12.1 (CH_3).

4. Conclusion

2,6-Diphenyl-3-methyl-*N*-nitrosopiperidin-4-one crystal is with monoclinic space group. The crystal structure proves that the piperidine ring adopts a boat conformation with a slight distortion rather than the expected chair conformation. One of the phenyl groups in the molecule is in the axial orientation, while the other phenyl and methyl groups are in the equatorial orientations.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2009.10.021.

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