Crystal Structure of *N*-Methyl-3-*t*-isopropyl-*r*-2,*c*-6-diphenylpiperidin-4-one

N. SAMPATH,* S. ARAVINDHAN,* M. N. PONNUSWAMY,*† and M. NETHAJI**

*Department of Crystallography and Biophysics, University of Madras,
Guindy Campus, Chennai 600 025, India

**Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560 012, India

N-Methyl-3-*t*-isopropyl-*r*-2,*c*-6-diphenylpiperidin-4-one (NMIDPPO), crystallizes in monoclinic space group $P2_1/c$ with $a = 16.666(6)$, $b = 12.349(5)$, $c = 18.778(7)$ Å; $\beta = 111.74(1)^\circ$, $V = 3590(2)$ Å³, $Z = 8$, $D_{\text{cal}} = 1.138$ Mg/m³. The structure was solved by direct methods and refined by full-matrix least-squares procedures to a final R -value of 0.0556 for 5078 observed reflections. There are two crystallographically independent molecules in the asymmetric unit. The piperidine rings in both molecules adopt the *chair* conformation with the planar phenyl rings substituted equatorially at the 2,6 positions. The C-H...O type of intermolecular hydrogen bonds and C-H... π weak interactions stabilize the molecules in the unit cell in addition to the van der Waals forces.

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Piperidine derivatives are found to possess many pharmacological activities, such as antihistaminic,¹ oral anaesthetics, narcotic analgesic and postganglionic parasympathetic agonists and to form an essential part of the molecular structure of important drugs. Particularly, 2,6-disubstituted piperidine derivatives are used clinically to prevent post-operative vomiting, to speed up gastric emptying before anaesthesia and to correct a variety of disturbances of gastrointestinal functions, hypotensive activity,² as well as bactericidal, fungicidal and herbicidal activities. Many piperidine derivatives also form the skeleton of several alkaloids. As a part of our ongoing studies concerning piperidine derivatives, the crystal structure of the title compound (Fig. 1) was analyzed in order to establish the molecular structure and stereochemistry.

The title compound was prepared by a Mannich condensation reaction using benzaldehyde (2 mol), ammonium acetate (1 mol) and 2-methylpentane-4-one (1 mol) in ethanol, and was then heated on a hot plate to the boiling range. The reacting product, 3-isopropyl-2,6-diphenylpiperidin-4-one was treated with CH₃I in the presence of K₂CO₃ into dry acetone, and stirred for 5 h at 0°C. The reaction mixture was poured into crushed ice, and a white precipitate was recrystallized using methanol.

The crystal structure and other experimental details are given in Table 1. The structure was solved by direct methods and

refined on F^2 by full-matrix least-squares procedures to a final R -value of 0.0556. All of the hydrogen atoms were located from the difference Fourier procedure and refined isotropically. The atomic coordinates along with their equivalent isotropic displacement factors for non-hydrogen atoms are presented in Table 2.

There are two molecules in the asymmetric unit (A and B). It is interesting to note that the molecular structures of A and B are almost in the same conformation, and the RMS-fit reveals a

Fig. 1 Chemical diagram of NMIDPPO.

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† To whom correspondence should be addressed.

E-mail: mnpsy2004@yahoo.com

Table 1 Crystal and experimental data

CCDC No.	CCDC 247429
Empirical formula	C ₂₁ H ₂₅ NO
Formula weight	307.42
Measurement Temperature	293(2)K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group, Z	$P2_1/c$, 8
Unit cell dimensions	
a	16.666(6) Å
b	12.349(5) Å
c	18.778(7) Å
β	111.74(1)°
Volume	3590(2) Å ³
D_x	1.138 Mg/m ³
Absorption coefficient	0.069 mm ⁻¹
θ_{max}	27.22° with Mo K_α
Reflections/unique	27630/7406 [$R_{\text{int}} = 0.0293$]
No. of reflections observed ($I \geq 2\sigma(I)$)	5078
Final R	0.0556
$(\Delta\sigma)_{\text{max}}$	0.000
Measurement	Siemens SMART CCD Area Detector
Program system	SHELX
Structure determination	Direct methods
Largest diff. peak and hole	0.395 and -0.291 e Å ⁻³
Refinement method	full-matrix least-squares on F^2

Table 2 Atomic coordinates ($\text{\AA} \times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) involving non-hydrogen atoms.

Molecule A					Molecule B				
Atom	x	y	z	U_{eq}	x	y	z	U_{eq}	
N1	8652(1)	-1983(1)	4306(1)	49(1)	8108(1)	871(1)	6654(1)	43(1)	
C2	7741(1)	-1759(1)	4190(1)	46(1)	7164(1)	901(1)	6462(1)	41(1)	
C3	7263(1)	-2765(2)	4338(1)	48(1)	6933(1)	1122(2)	7177(1)	43(1)	
C4	7794(1)	-3329(2)	5067(1)	65(1)	7431(1)	369(2)	7825(1)	53(1)	
C5	8721(1)	-3487(2)	5177(2)	67(1)	8366(1)	272(2)	7967(1)	57(1)	
C6	9127(1)	-2416(2)	5078(1)	54(1)	8526(1)	37(1)	7231(1)	46(1)	
C7	7262(1)	-1341(2)	3384(1)	53(1)	6748(1)	1753(1)	5853(1)	41(1)	
C8	6864(1)	-336(2)	3253(2)	74(1)	6128(1)	1482(2)	5148(1)	51(1)	
C9	6408(2)	13(3)	2507(3)	105(1)	5748(1)	2272(2)	4604(1)	62(1)	
C10	6344(2)	-619(5)	1902(2)	120(2)	5983(1)	3338(2)	4751(1)	61(1)	
C11	6733(2)	-1601(4)	2018(2)	104(1)	6605(1)	3619(2)	5446(1)	58(1)	
C12	7195(2)	-1967(3)	2759(1)	75(1)	6981(1)	2831(2)	5992(1)	49(1)	
C13	10079(1)	-2561(2)	5234(1)	55(1)	9490(1)	-32(1)	7426(1)	47(1)	
C14	10690(2)	-2015(2)	5829(1)	67(1)	9992(1)	880(2)	7541(1)	66(1)	
C15	11563(2)	-2149(2)	5982(2)	83(1)	10875(1)	808(2)	7757(1)	71(1)	
C16	11833(2)	-2825(3)	5543(2)	85(1)	11271(1)	-173(2)	7871(1)	65(1)	
C17	11240(2)	-3375(2)	4954(2)	86(1)	10786(2)	-1085(2)	7767(2)	84(1)	
C18	10367(2)	-3250(2)	4796(2)	74(1)	9897(1)	-1016(2)	7541(2)	73(1)	
C19	6330(1)	-2520(2)	4248(1)	53(1)	5954(1)	1156(2)	6992(1)	57(1)	
C20	5796(2)	-3547(2)	4179(2)	83(1)	5741(2)	1617(3)	7651(2)	78(1)	
C21	6246(2)	-1763(3)	4850(2)	80(1)	5507(2)	76(3)	6723(2)	89(1)	
C22	9058(2)	-967(2)	4205(2)	72(1)	8278(2)	644(2)	5956(1)	66(1)	
O23	7508(1)	-3636(2)	5538(1)	113(1)	7109(1)	-117(1)	8206(1)	88(1)	

$$U_{\text{eq}} = (1/3) \sum_i \sum_j U_{ij} (a_i^* a_j^*) (a_i a_j).$$

Fig. 2 Perspective view of the molecules (A and B) showing the thermal ellipsoids drawn at the 30% probability level.

value of $0.177 \text{ \AA}$. ZORTEP plots of the molecules are shown in Fig. 2. A study of the torsion angles, asymmetric parameters and least-squares plane calculations³ reveals that the piperidine rings adopt the *chair* conformation.⁴ The atoms C2 and C5 deviate by $-0.617(2)$ and $0.666(2) \text{ \AA}$ and $0.653(2)$ and $-0.630(2) \text{ \AA}$ in molecules A and B respectively, from the best plane of the other atoms (N1, C3, C4 and C6) in the piperidine

Table 3 Possible hydrogen bonds

D-H...A	(D-H) $\text{\AA}$	(D...A) $\text{\AA}$	(H...A) $\text{\AA}$	$\angle(\text{D-H...A})^\circ$
C20A-H44...O23A ⁱ	1.027(2)	3.034(3)	2.414(6)	118(2)
C21A-H42...O23A ⁱ	0.951(1)	3.071(4)	2.480(2)	120(2)
C20B-H21...O23B ⁱ	0.960(3)	3.017(4)	2.450(1)	118(2)
C21B-H47...O23B ⁱ	0.981(1)	3.071(3)	2.396(1)	117(2)
C3A-H9...O23B ⁱⁱ	0.942(2)	3.319(3)	2.396(1)	166(2)
C20A-H37...O23B ⁱⁱⁱ	0.992(6)	3.715(5)	2.881(8)	142(3)
C11B-H19...O23A ⁱⁱⁱ	0.990(3)	3.687(3)	2.726(4)	164(2)
C16B-H25...Cg1 ^{iv}	0.939	3.938	3.252	131.6
C16A-H33...Cg2 ^v	0.971	3.892	3.159	133.6
C5B-H17...Cg3 ^{vi}	0.985	3.811	3.004	139.8

Equivalent positions: (i) x, y, z ; (ii) $x, -y - 1/2, z - 1/2$; (iii) $x, y + 1, z$; (iv) $-x, 1/2 + y, 1/2 - z$; (v) $-x, -1/2 + y, 1/2 - z$; (vi) $-x, 1 - y, -z$. Cg is the centroid of the benzene ring: Cg1 = C7A through C12A; Cg2 = C7B through C12B; Cg3 = C13A through C18A

ring. The piperidine rings in molecules A and B are oriented at an angle of $42.8(1)^\circ$ with each other.

The planar phenyl rings substituted at the 2,6 positions⁴ adopt an equatorial orientation to the piperidine ring, which is evidenced from the torsion angles [(C4-C5-C6-C13=) $176.7(2)$ and $179.1(2)^\circ$ and (C4-C3-C2-C7=) $169.4(2)$ and $-172.8(1)^\circ$ for molecules A and B, respectively]. The phenyl rings (C7 through C12) are oriented at angles of $89.9(1)$ and $89.1(3)^\circ$ and the phenyl rings (C13 through C18) are oriented at angles of $75.3(1)$ and $61.9(1)^\circ$ from the plane of the piperidine ring, respectively, for molecules A and B.

The isopropyl group is substituted equatorially⁴ [(C5-C4-C3-C19=) $-175.5(2)$ and $175.6(2)^\circ$; (N1-C2-C3-C19=) $177.8(2)$ and $-179.9(2)^\circ$ for A and B, respectively]. The N atoms in the piperidine ring of both molecules show sp^3 hybridization, which can be seen from the angles around N1A and N1B (329.2° and 329.9°). The *N*-methyl groups take an equatorial orientation to the best plane of the piperidine ring, which are seen from the torsion angles [C22-N1-C2-C3=] $-176.2(1)$ and $179.2(2)^\circ$ and [C22-N1-C6-C5=] $-178.5(2)$ and $179.1(2)^\circ$ for the molecules A and B.

The molecules are packed in a discrete fashion and are stabilized by the C-H...O type of intra and intermolecular hydrogen bonds. Interestingly, three C-H... π weak interactions⁵ stabilize the molecules in the unit cell. The details of the hydrogen bondings are given in Table 3.

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