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Structural and conformational studies of 2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9-one-o-nicotinoyloxime

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ABSTRACT

The title compound crystallizes with the monoclinic cell setting and P2(1)/n space group. The structural compound $C_{26}H_{25}N_3O_2$ exist in a twin-chair conformation with equatorial orientation of the phenyl group. The two phenyl rings attached to the piperidine ring at positions 2 and 4 have equatorial orientation. The angle between the two benzene rings is 48.32(9)°. The crystal structure is further stabilized by C-H...N, C-H...\pi and intramolecular interaction.

Key words: Piperidone, oxime, hydrogen bonding

INTRODUCTION

Oxime esters are serving as important synthetic intermediate, and have been employed as starting materials for both synthetic and medicinal chemistry [1a,b,c]. Tropane, cocaine and granatane (pesudopelletierine) are some azabicyclo types of alkaloids found in pharmacologically and medicinally active drugs[2]. The azabicyclo [3.3.1]nonane is a serotonin 5-HT_3 receptor[3], and also used as anti-Parkinson's[4], local anesthetic[2]. By using the X-ray diffraction method the structure of the above compound is to be discussed. The molecular structure of the title compound is shown in fig.1.

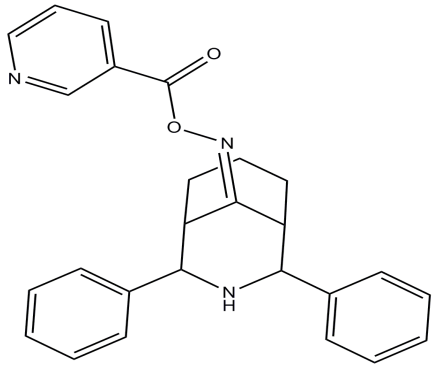

Figure 1

MATERIALS AND METHODS

A mixture of 2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9-one oxime (0.765 g, 2.5 mmol) and nicotinic acid (0.338 g, 2.75 mmol) in dry pyridine (5 mL) was stirred at ambient temperature. $POCl_3$ (0.25 mL, 2.75 mmol) was added drop wise to the reaction mixture and stirring is continued for 40 to 45 min. The progress of the reaction was monitored

by TLC. After completion of the reaction, a saturated solution of $NaHCO_3$ was added portion wise to the reaction mixture and the crude product was thrown out as a precipitate. The crude product was then recrystallized from absolute ethanol to get the pure 2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9-one *O*-nicotinoyl oxime. Yield 0.64 g (78%).The crystal was developed on slow evaporation techniques using absolute ethanol as a solvent.

Intensity Data Collection

X-ray data were collected on a Bruker AXS (Kappa APEX2)[5] CCD area detector using ω and ψ scan mode. A small crystal of size 0.30 × 0.25 × 0.23 mm was chosen and its quality was checked using polarizing microscope. Cell refinement and data reduction were carried out by using APEX2/SAINT-NT [5]. Sets of two standard reflections were monitored for every one hour of exposure during the data collection and there was no noticeable change in the intensity observed. A total of 25944 reflections were collected resulting in 5789 independent reflections of which 3711 had I > 2σ (I), were considered as observed reflections. The intensities were corrected for Lorentz and polarization effects. Absorption corrections were made with **SADABS**[5].

Structure Solution and Refinement

The refinement was carried out by SHELXL-97[6].The positions of the hydrogen atoms bound to the O and C atoms are identified from the difference electron density maps and their distances are geometrically optimized. The H atoms associated with the hydroxyl groups are constrained to a distance of d(O---H) = 0.82\%A; and $U_{iso}(H) = 1.5U_{eq}(O)$. The hydrogen atoms bound to the C atoms are treated as riding atoms, with d(C---H)=0.93 and $U_{iso}(H) = 1.2U_{eq}(C)$ for aromatic,d(C---H)=0.97 and $U_{iso}(H)=1.2Ueq(C)$ for methylene and d(C---H)=0.96 and $U_{iso}(H) =1.5U_{eq}(C)$ for methyl groups.

The ortep diagram is shown in fig 2.

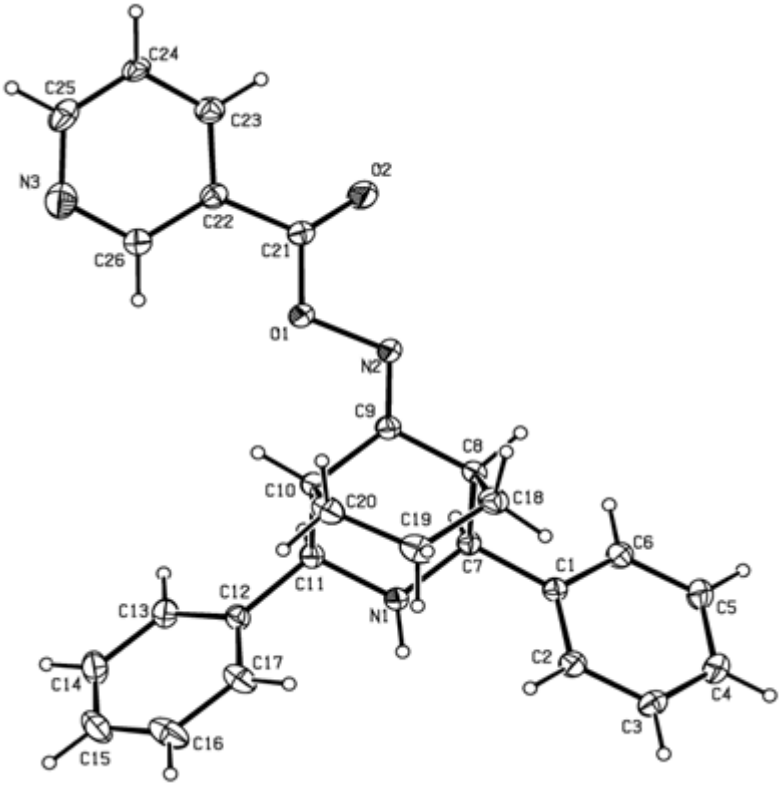

Figure 1

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The weighting scheme [13] adopted during the final cycle of refinement is

w=1/[\s^2^(Fo^2^)+(0.0603P)^2^+0.1935P] .,

where P=(Fo^2^+2Fc^2^)/3'

The geometric calculations were performed using the PARST[7,8,] and PLATON [9].

RESULTS AND DISCUSSION

In the title compound, the cyclohexanone ring deviates from an ideal chair with total puckering amplitude QT = 0.5633°. and the piperidine ring is closer to an ideal chair ,QT = 0.6077°.The piperidine ring (C7/C8/C9/C10/C11/N1)exists in a chair conformation with the puckering amplitude Q=0.6077(15) Å , theta =2.14(13)°, and phi=163(4)°.Also the ring (C8/C9/C10/C18/C19/C20) exists in a twin chair conformation with the puckering amplitude Q= 0.5638(16)Å, theta=166.11(17)° and phi=250.0(7)°[10]. The torsional angles of C9/C10/C11/C12 and C1/C6/ C7/ C8 are 177.91(11)° and -97.24(14)° respectively. The piperidine ring makes the dihedral angle of 55.99(8)°and 76.33(8)° with the phenyl rings respectively. The angle between the two phenyl rings is 48.32(9) °.

The bond distances and bond angles in the title compound agree very well with the corresponding values reported in closely related compound[11,12].

The crystal structure of the compound is stabilized by N-H...N, C-H...N, C-H...\pi and intramolecular interaction. where cg2 is the centroid of (C25/C24/C23/C22/C26/N3) and cg5 is the centroid of (C12/C13/C14/C15/C16/C17) respectively. In the crystal ,the intramolecular intraction form infinite one dimensional chain along (0 0 1) direction shown in Fig3.

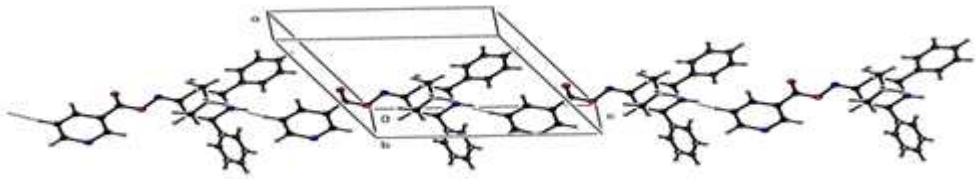

Figure 2

Table :1 Crystal data and structure refinement of the title compound

Cell:	a=10.5208(3)	b=19.6025(6)	c= 11.3596(3)
	α=90.000(0)	$_{\beta}$ = 113.356(1)	$_{\gamma}$= 90.000(0)
Wavelength			0.71073
Temperature			293K
Volume (Å3)			2150.77(10)
Density (g cm-1)			1.40
Crystal system			Monoclinic
Space group			P 21/n
Hall group			-P 2yn
Moiety formula			C26 H25 N3 02
Formula weight			452.4
Abs.coefficient(mm^{-1})			0.104
F(ooo)			927.8
F000'			872.34
No.of reflections			5789
No.of parameters			284
Goof			1.008
Shift/esd max			0.000
Shift/esd mean			0.000
Delta-rho(e Å-3)max			0.237
Delta-rho(e Å-3)min			- 0.186
RI :	0.083	WR2 all	0.131
RI observed: 0.046		WR2 observed	0.112
R merge			0.033
AvI/sig(I)			30.30
h,k,l max : 14,26,10		h,k,l min	-13,-24,-15
Refinement method			Full-matrix least-square on F^2
Data completeness= 0.995			Theta(max)= 29.160

Table 2: Torsional angles of non –hydrogen atoms

Atoms	Angles
C2 C1 C6 C7	179.75(13)
C4 C5 C6 C7	-179.53(12)
C1 C6 C7 N1	26.35(17)
C5 C6 C7 N1	-154.57(12)
C1 C6 C7 C8	-97.24(14)
C5 C6 C7 C8	81.84(14)
N1 C7 C8 C9	58.54(12)
C6 C7 C8 C9	-176.23(10)
C9 C10 C11 C12	177.91(11)
N1 C7 C8 C18	-61.92(14)
C6 C7 C8 C18	63.32(14)
C18 C8 C9 N2	-115.87(13)
C7 C8 C9 N2	119.10(13)
C18 C8 C9 C10	63.58(13)
C7 C8 C9 C10	-61.46(13)
N2 C9 C10 C20	114.47(16)
C8 C9 C10 C20	-64.86(13)
N2 C9 C10 C11	-120.41(16)
C8 C9 C10 C11	60.25(14)
C9 C10 C11 N1	-57.12(13)
C20 C10 C11 N1	61.48(14)
C20 C10 C11 C12	-63.49(15)
N1 C11 C12 C17	-47.38(17)
C10 C11 C12 C17	77.27(16)
N1 C11 C12 C13	131.62(13)
C10 C11 C12 C13	-103.73(15)
C11 C12 C13 C14	178.93(13)
C13 C14 C15 C16	1.4(3)

Table3: Hydrogen bonding geometry (Å, º) (D-donor; A-acceptor; H-hydrogen) for compound

D	H	A	D-H	H..A	D..A	D-H..A	A-site
N1	H1A	N3	0.869	2.3030	3.1446(18)	163.3	1_656
C7	H7	Cg2	0.980	2.8100	3.7888(15)	174	3_556
C20	H20A	Cg2	0.970	2.9500	3.6588(17)	131	4_555
C25	H25	Cg5	0.930	2.7500	3.5806(17)	149	1_454

symmetry code:(i)1+X,Y,1+Z ii)-X,-Y,1-Z iii)1/2+X,1/2-Y,1/2+Z iv) -1+X,Y,-1+Z

CONCLUSION

The title compound adopts a monoclinic cell setting with the standard cell parameters and the piperidine ring adopts the twin- chair conformation. Further the crystal packing was stabilized by intramolecular interaction.

We are doing active research in the area of heterocycles which are acting as potential candidates in medicinal chemistry. The diseases such as Parkinson's disease, Alzicemers are great problems in the western countries. No effective drugs are available to cure them completely. So ongoing research for developing effective drug candidate in this area urge us to do research on heterocycles active for curing them.

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