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Synthesis and structural study of *3t*-isopropyl-*2r*,*6c*-diphenyl-4-oxopiperidinium nitrate and N-benzoyl-*3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one oxime

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ABSTRACT

3t-Isopropyl-*2r*,*6c*-diphenyl-4-oxopiperidinium nitrate (**2**) and N-benzoyl-*3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one oxime (**4**) have been synthesized. The crystal structures of **2** and **4** have been determined. ^{1}H NMR, ^{13}C NMR, ^{1}H–^{1}H COSY and HSQC spectra also have been recorded for both the compounds. The piperidine ring in **2** adopts chair conformation in the solid state and in solution. In **4** the configuration about the C=N bond is E. In the solid state the piperidine ring in **4** adopts boat conformation **4B$_2$** with the phenyl group at C-2 in the flagpole position and the phenyl group at C-6 in the boat-equatorial position. The isopropyl group is in the boat-axial position. In solution alternative chair conformation **4CA** with axial phenyl group may contribute to extent of 11% to **4**.

1. Introduction

Structural study of organic molecules involves not only the determination of the various chemical bonds in the molecule but also the determination of the relative positions of the nonbonded atoms in the molecules or the conformation of the molecule. Several conformations may be possible for an organic compound. In case one conformation has significantly low energy than the other conformations, the compound adopts the most stable conformation in the solid state and in solution. However, in cases where two or more conformations have comparable energy, the compound exists as an equilibrium mixture of various conformations in solution. However, in the solid state it should adopt only a single conformation. Thus, it is of interest to investigate the structure of organic compounds in the solid state and in solution. Single crystal X-ray crystallography is used for the determination of structure and conformation in the solid state whereas NMR spectroscopy is used for such a determination in solution. Several conformational studies have been made on *2r*,*6c*-diphenylpiperidine-4-ones and their derivatives [1–8] using NMR spectroscopy. The crystal structure of *3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one (**1**) has been reported [9]. Crystal structures of N-nitroso-*2r*,*6c*-diarylpiperidin-4-one oximes have been reported [10–12].

In the present work the structure of *3t*-isopropyl-*2r*,*6c*-diphenyl-4-oxopiperidinium nitrate (**2**) has been investigated in the solid state and in solution. The objective is to find whether there is a significant change in the conformation of the piperidine ring due to salt formation. Also it is of interest to find the location of the nitrate ion in the crystal.

Though in the conformational study on N-benzoylpiperidine-4-ones [7] N-benzoyl-*3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one **(3)** has been included, in the conformational study on N-acylpiperidin-4-one oxmies [8] the oxime (**4**) of **3** has not been included. In the present work the conformation of N-benzoyl-*3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one oxime (**4**) has been investigated in the solid state and in solution.

2. Experimental

2.1. Physical measurements

NMR measurements were made in DMSO-d6 for **2** and in $CDCl_3$ for **4,** in 5 mm NMR tubes. ^{1}H NMR spectra were recorded on a Bruker 500 NMR spectrometer operating at 500.033 MHz. ^{13}C NMR spectrum was recorded on a Bruker 400 NMR spectrometer operating at 100.644 MHz for **2** and on a Bruker 500 spectrometer at 125.757 MHz for **4**. ^{1}H – ^{1}H COSY and HSQC spectra were recorded on a Bruker DRX 500 NMR spectrometer using standard parameters.

2.2. X-ray crystallography

For **2** and **4** the intensity data were collected at ambient temperature on a BRUKER axis Kappa apex CCD diffractometer using graphite monochromated Mo Kα radiation (λ = 0.71073 Å). The crystallographic data are summarized in Table 1. The structure

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was solved by **SIR 92** [13] and refined by Full matrix least square with **SHELXL-97** [14]. All the non-hydrogen atoms were fixed geometrically.

2.3. Synthesis of the compounds

2.3.1. 3t-Isopropyl-2r,6c-diphenylpiperidin-4-one (*1*)

The procedure of Noller and Baliah [15] was followed for preparing **1**. However, ethanol was used as the solvent instead of acetic acid. After recrystallization, the compound melted at 125 °C: lit. [15] mp 125 °C.

2.3.2. 3t-Isopropyl-2r,6c-diphenyl-4-oxopiperidinium nitrate (*2*)

3t-Isopropyl-*2r*,*6c*-diphenylpipridine-4-one (**1**) (0.01 mol) was dissolved in ethanol. An aqueous solution of sodium nitrate (0.01 mol) containing 3 ml of hydrochloric acid was added dropwise with stirring. The stirring was continued for 20 min. The separated solid was filtered and washed with water. It was recrystallized from (1:1) mixture of ethanol and methanol. After recrystallization it melted at 158–160 °C. The colourless crystals of **2** were suitable for X-ray analysis. Anal. Calcd. For $C_{20}H_{24}N_2O_4$: C, 67.41; H, 6.74; N, 7.86; found: C, 67.13; H, 7.97; N, 7.77%.

2.3.3. N-benzoyl-3t-isopropyl-2r,6c-diphenylpiperidin-4-one (*3*)

N-benzoyl-*3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one (**3**) was prepared from **1**, following the procedure of Krishnakumar and Krishnapillay [7].

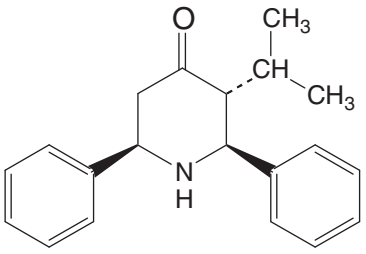
2.3.4. N-benzoyl-3t-isopropyl-2r,6c-diphenylpiperidin-4-one oxime (*4*)

To a solution of **3** (50 mmol) and sodium acetate trihydrate (150 mmol) in boiling ethanol, hydroxylamine hydrochloride (60 mmol) was added. The mixture was heated under reflux for 15 min and poured into water. The separated N-benzoyl-*3t*-isopropyl-*2r*,*6c*-diphenylpiperidin-4-one oxime was recrystallized from ethanol. The compound melted at 188° C.

3. Results and discussion

3.1. Numbering of atoms

The numbering of carbon atoms in **2** and **4** are shown in Fig. 1.The protons are numbered accordingly. Thus, the proton on C-2 is denoted as H-2.



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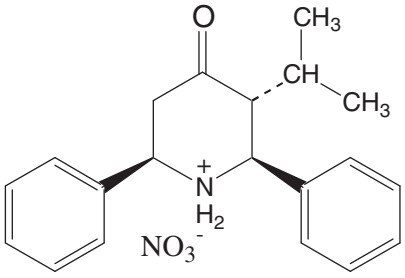

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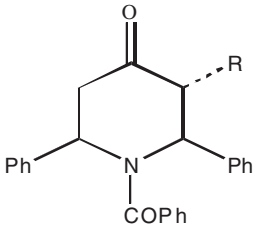

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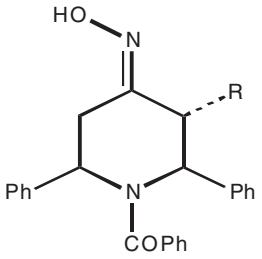
5, R = Et

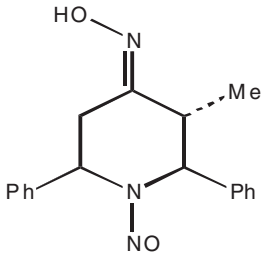


4, R = i-Pr

8, R = H

9, R = Me

10, R = Et



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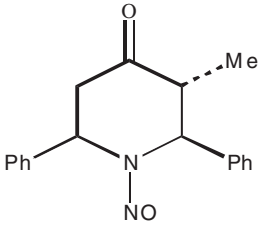

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