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Rotational equilibria in boat conformations of *N*-acyl-*r*-2,*c*-6-di(2-hetero-aryl)piperidin-4-ones using NMR spectra and semiempirical MO calculations

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Four *N*-acyl-*r*-2,*c*-6-di(2-heteroaryl)piperidin-4-ones **3-6** have been prepared and their conformational preferences examined using ^{1}H and ^{13}C NMR spectral studies and semiempirical MO calculations. Solution state conformational studies on the compounds **3-6** by ^{1}H and ^{13}C NMR spectral methods indicated the preference for the boat conformation with coplanar orientation of *N*-acyl groups. The energy barrier for N-C rotation in **3** has been found to be 58.4 kJ mol^{-1} using variable temperature ^{1}H NMR spectral studies. The semiempirical MO calculations, using AM1 method, also suggested the preference of boat conformation for the *N*-acyl derivatives **3-6**.

Keywords: *N*-acyl-*r*-2,*c*-6-di(2-heteroaryl)piperidin-4-one, NMR spectra, semiempirical MO calculation, boat conformation, *N*-acetyl, *N*-benzoyl, *N*-phenylcarbamoyl

The influence of various *N*-acyl functions (*e.g.* CHO, COMe, COPh, CONHPh, COOEt, *etc*.) on the conformational preferences of *r*-2,*c*-6-diarylpiperidines have been extensively studied[1]. All of these compounds were found to prefer non-chair conformations with coplanar orientations of *N*-acyl functions. Due to the delocalization of nitrogen lone-pair into C=O function the N-C bond exhibits a partial double bond character which results in an equilibrium between *syn* and *anti* rotamers (**Figure 1**). The energy barriers ($\Delta G^{\#}$) for N-C rotation have been estimated for a number of selected compounds and are found to depend on the nature of *N*-acyl functions (*e.g.* $\Delta G^{\#}$ for CHO 66-72 kJ mol^{-1}; for COMe 58-63 kJ mol^{-1} ; for COOEt 47-51 kJ mol^{-1}, *etc*). In all the cases $A^{1,3}$-strain[2] was found to be a major factor in determining the preferred conformation of the piperidine ring. In order to study the effect of heteroaryl substituents, thienyl and furyl, on the conformational preferences and energy barrier for N-C rotation, four new *N*-acylpiperidin-4-ones have now been prepared[1] (**Scheme I**) *viz*., *N*-acetyl-*r*-2,*c*-6-di(2-heteroaryl)-*t*-3,*t*-5-dimethylpiperidin-4-ones **3** and **4**, *N*-phenyl-carbamoyl-*r*-2, *c*-6-di(2-furyl)-*t*-3, *t*-5-dimethylpiperi-din-4-one **5** and *N*-benzoyl-*r*-2,*c*-6-di(2-thienyl)-*t*-3, *t*-5-dimethylpiperidin-4-one **6**. The preferred conformation of the *N*-acyl derivatives **3-6** was analyzed using high resolution ^{1}H and ^{13}C NMR spectra. In addition the dynamic ^{1}H NMR spectral studies were carried out on **3** to estimate the N-C rotational barrier.

N-Acetyl-*r*-2, *c*-6-di(2-heteroaryl)-*t*-3, *t*-5-dimethyl-piperidin-4-ones 3 and 4

Unlike *N*-nitrosopiperidin-4-ones **7** (Ref. 3) and *N*-formylpiperidin **8** (Ref. 1a), the *N*-acetylpiperidin-4-ones **3** and **4** exhibited single NMR absorptions for each of the protons and carbons in their ^{1}H and ^{13}C NMR spectra at RT (**Table I**). However, broad signals obtained for benzylic protons of **3** and **4** at δ 5.30 and 5.46, respectively, and benzylic carbons (δ 55.3 for **3** and 57.9 for **4**) indicated the existence of a conformational equilibrium in these *N*-acetylpiperidin-4-ones **3** and **4** also. The broadening might have resulted from the coalescence of signals corresponding to the individual conformers involved in the rotational equilibrium with coplanar orientation of *N*-acetyl functions.

The existence of two co-planar orientations of acetyl function (*syn* and *anti*) is due to the restricted rotation of the N1-C(O) bond which arises due to the partial double bond character created by the delocalisation of nitrogen lone pair on the carbonyl π cloud. This was, in turn, confirmed by the dynamic ^{1}H NMR spectral studies[4].

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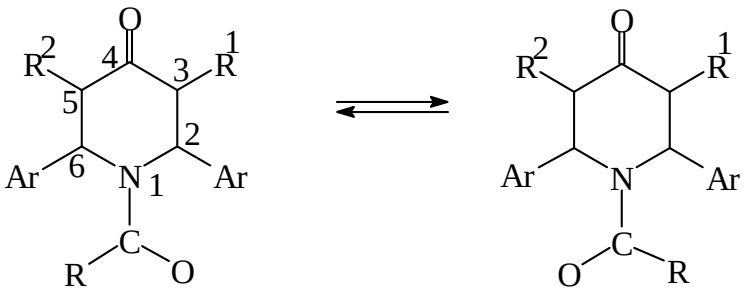
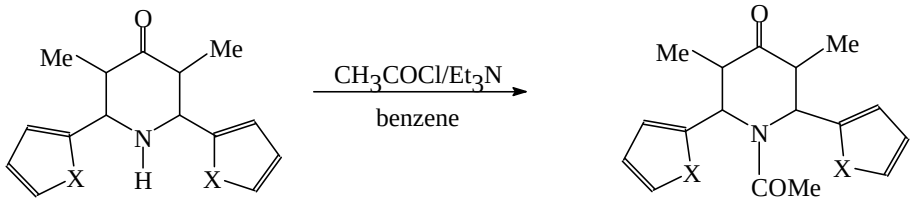


syn *anti*

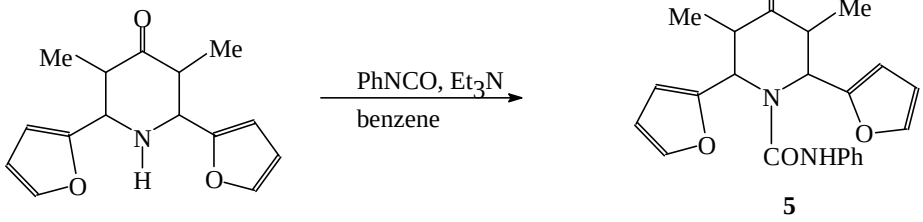
R = H, Me, OEt, Ph, NHPh

R^1, R^2 = H, Me, Et, *i*-Pr

Figure 1



1 X = O **3**
2 X = S **4**



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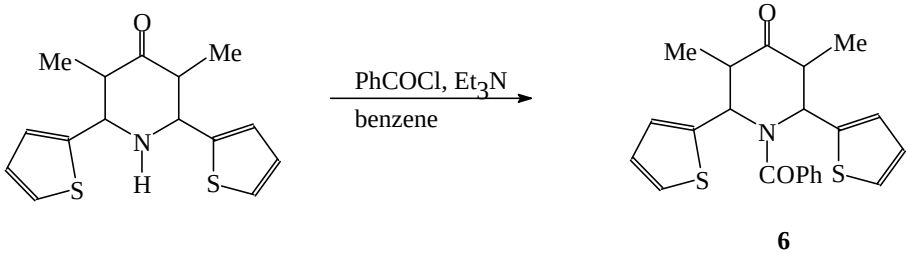

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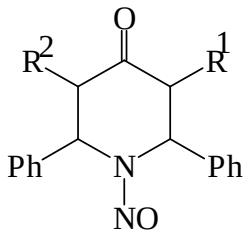
Scheme I

Table I — Spectral characterisation data of compounds **3-6**

Compd	^{1}H NMR($CDCl_3$, δ, ppm)	^{13}C NMR($CDCl_3$, δ, ppm)	MS (M^+)
3	1.15 (d, Me at C3 & C5) 2.2 (s, COMe), 3.25 (m, H3 & H5-ax), 5.30 (s, br, H2 & H6), 6.26-7.27 (aromatic)	14.2 (Me at C3 & C5), 22.1 (Me of COMe), 44.8 (C3 & C5), 55.3 (C2 & C6), 107.7-153.2 (aromatic), 171.1 (COMe), 210.2 (C4)	301
4	1.14 (d, Me at C3 & C5) 2.2(s, COMe), 3.27 (m, H3 & H5-ax), 5.46 (s, br, H2 & H6), 6.91-7.27 (aromatic)	14.4 (Me at C3 & C5), 22.7 (Me of COMe), 47.1 (C3 & C5), 57.9 (C2 & C6), 125.6-144.8 (aromatic), 171.6 (COMe), 209.7 (C4)	333
5	1.20 (d, Me at C3 & C5) 3.27 (m, H3 & H5-ax), 5.36 (d, *J* = 6.2 Hz, H2, & H6), 6.2 9 (d, *J* = 3.2 Hz, H2 & H6), 6.98 (s, NHPh), 7.00-7.37 (aromatic)	14.1 (Me at C3 & C5), 45.1 (C3 & C5), 55.2 (C2 & C6), 107.8-142.2 (aromatic), 153.9 (CONHPh) 210 (C4)	378
6	1.23 (d, Me at C3 & C5) 1.29 (d, Me at C3 & C5) 3.27 (m, H3 & H5-ax), 5.15 & 6.13 (s, br, H2 & H6), 6.72-7.46 (aromatic)	12.0, 16.0 (Me at C3 & C5), 45.9, 48.1 (C3 & C5), 56.8 59.5 (C2 & C6), 125.7-144.9 (aromatic), 172.5 (COPh), 210.6 (C4)	395



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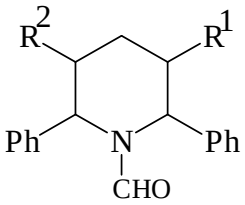
R^1, R^2 = H, Me, Et, *i*-Pr



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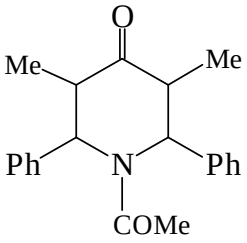
R^1, R^2 = H, Me, Et, *i*-Pr



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Dynamic ^{1}H NMR spectra

The dynamics of restricted N-C rotation for the compound **3** was followed by variable temperature ^{1}H NMR spectral studies at low temperature (0° to –30°C, **Chart 1**). At 10°C, two broad signals appeared around δ 4.9 and δ 5.6. Further decrease in temperature to –35°C resolved the benzylic proton resonances into two separate doublets at δ 5.63 and δ 5.02, corresponding to *syn* and *anti* rotamers. The intensity of both the doublets was observed to be the same indicating the equal population of the two rotamers (*viz.*, *syn* and *anti* with respect to C2 carbon). The energy barrier for the interconversion of one rotamer to the other was evaluated to be 58.4 kJ mol^{-1} from the dynamic ^{1}H NMR studies (**Chart 1**) using modified Eyring equation[4].

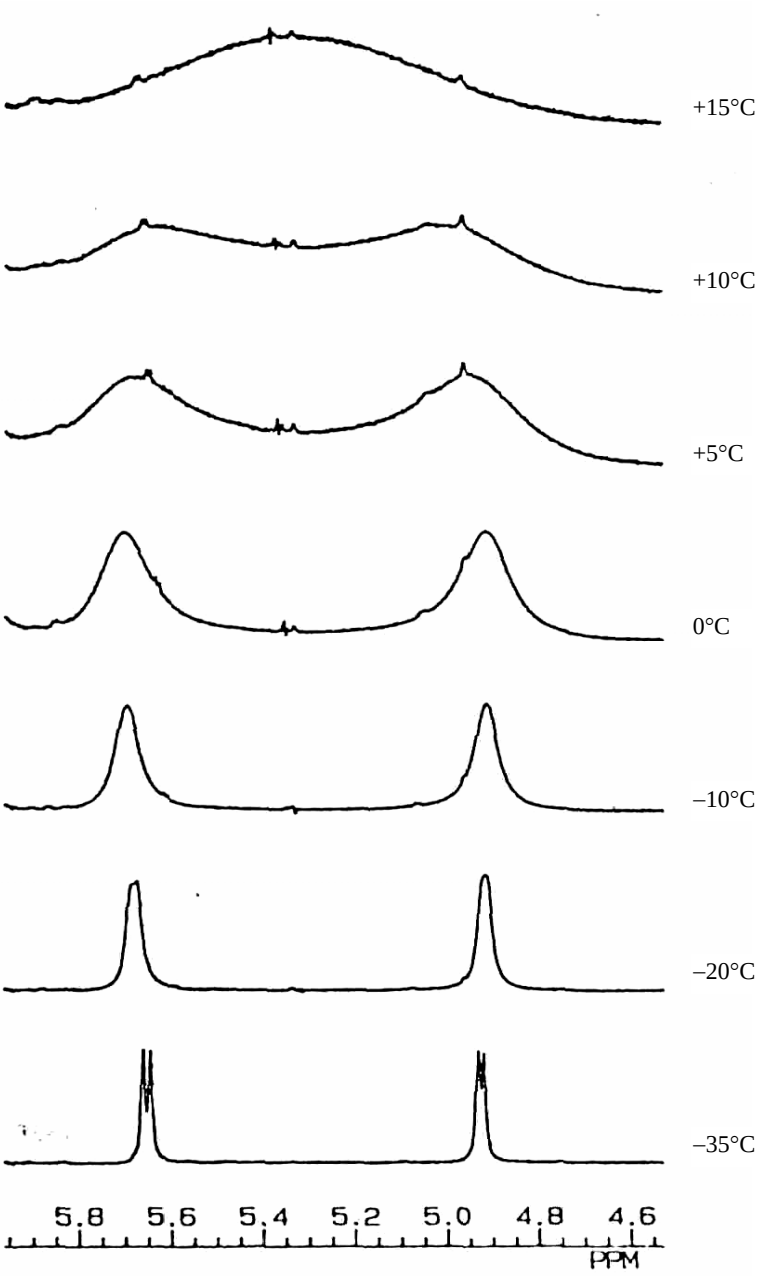


Chart 1 — Dynamic ^{1}H NMR spectrum of **3**

The N-C rotational barrier of *N*-acetyl-*r*-2,*c*-6-di(2-furyl)-*t*-3,*t*-5-dimethylpiperidin-4-one (**3,** 58.4 kJ mol^{-1}) was compared with the N-N rotational barrier of the corresponding *N*-nitroso analog (80.5 kJ mol^{-1})[5] and found to be less by ~22.1 kJ mol^{-1}. It could be due to (i) the destabilisation of the ground state in *N*-acetyl compound as a result of additional $A^{1,3}$-strain between methyl group of acetyl function and the α-aryl group, or (ii) the destabilisation of transition state in *N*-nitroso compounds due to the additional lone-pair repulsions. Hence, to cross-over the barrier higher rotational energy is required for N-N rotation. In addition, both the *N*-acetyl-*r*-2,*c*-6-di(2-furyl)-*t*-3,*t*-5-dimethylpiperidin-4-one (**3,** 58.4 kJ mol^{-1}) and *N*-acetyl-*r*-2,*c*-6-diphenyl-*t*-3,*t*-5-dimethylpiperidin-4-one (**9,** 58.1 kJ mol^{-1}) were found to have almost the same rotational barriers.

When the energy barrier for N-C rotation in *N*-formyl-*r*-2, *c*-6-diphenyl-*t*-3, *t*-5-dimethylpiperidin-4-one (72.5 kJ mol^{-1})[1a,c] was compared with that of the *N*-

acetylpiperidin-4-one **3** (58.4 kJ mol^{-1}), the former was found to be higher than the latter by 14.1 kJ mol^{-1}. This may be due to the (i) destabilizing steric interaction between coplanar methyl group and α-aryl groups leading to increase in energy level of the ground state, (ii) steric effect of methyl group in acetyl function over the C2 carbon and (iii) electron releasing nature of methyl group in the acetyl function since the introduction of electron releasing groups at amide nitrogen results in the reduction of rotational barrier. Hammaker *et al*.[6] reported the N-C rotational barrier of *N*,*N*-diethylformamide and *N*,*N*-diethylacetamide as 85.3 kJ mol^{-1} and 70.7 kJ mol^{-1}, respectively. The former differs from the latter by 14.6 kJ mol^{-1} which is almost equivalent to the difference between the barriers of *N*-formyl-*r*-2,*c*-6-diphenyl-*t*-3,*t*-5-dimethylpiperidin-4-one and *N*-acetylpiperidin-4-one **3**.

Preferred Conformations

Although α and β protons were deshielded by 1.5±0.2 ppm and 0.5 ppm, in the *N*-acetylpiperidin-4-ones **3** and **4,** compared to the parent amines **1** and **2**, respectively, the extent of deshielding is larger for the proton signals *syn* to acetyl function than the *anti*. This observation reveals the "in-plane" orientation for α-*syn* protons than the α-*anti* protons and the deshielding effect could be explained by invoking the Paulsen and Todt's model for amide anisotropy[7].

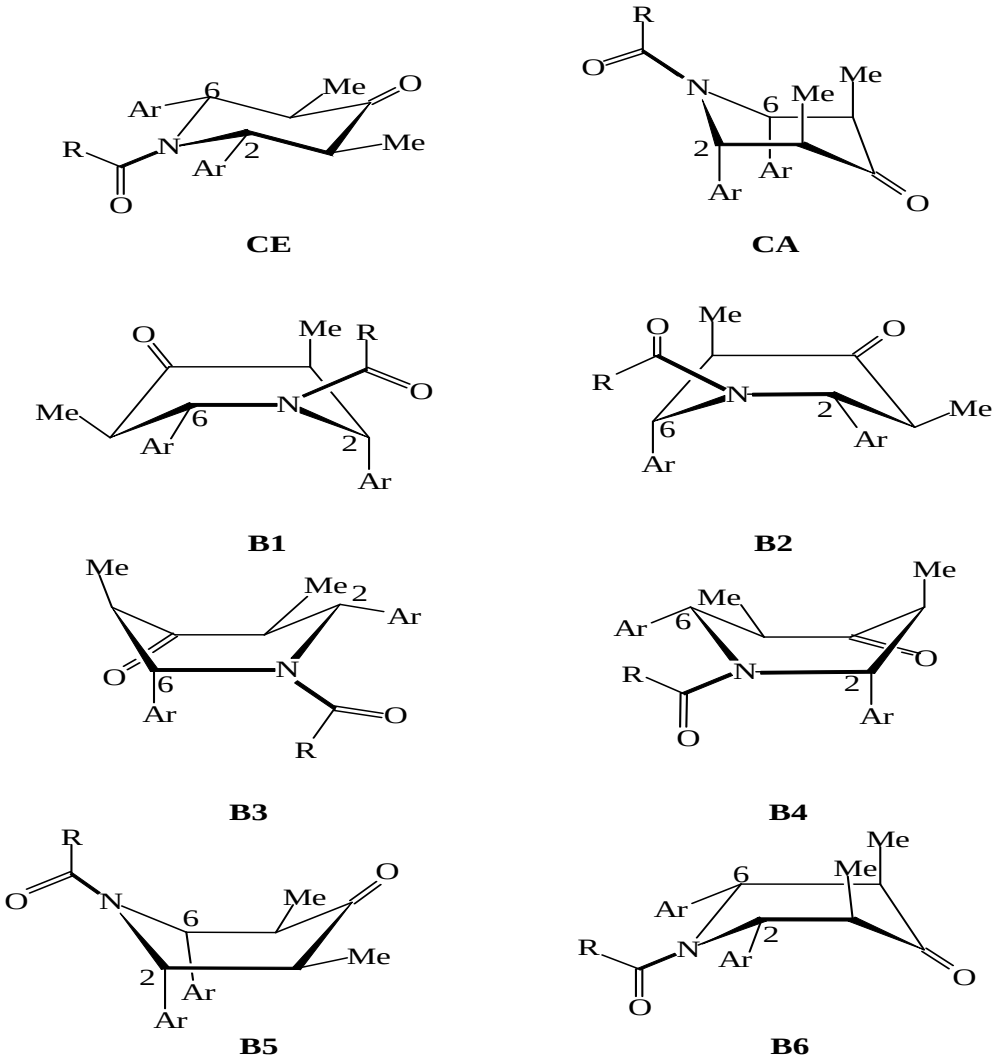


Figure 2 — Possible conformations for *N*-acyl-*r*-2,*c*-6-di(2-heteroaryl)piperidin-4-ones **3-6**

At -35°C the well resolved signals at δ 5.65 (H2-*syn*) and δ 4.93 (H2-*anti*) in the ^{1}H NMR spectrum of *N*-acetylpiperidin-4-one **3** showed the coupling constants of J_{H2-H3}= 6.3 Hz and J_{H5-H6}= 4.9 Hz (The identification of *syn* and *anti* signals was achieved with the help of ASIS[8] (Aromatic Solvent Induced Shift Method) ^{1}H NMR spectrum. The signal (δ 4.93) which experienced large upfield shift in ASIS ^{1}H NMR spectrum was considered as *anti* compared to *syn*.

In *N*-acetylpiperidin-4-one **3** the coupling constants obtained for the benzylic doublets at δ 5.65 and 4.93 were found to be smaller compared to that of the parent compound **1** ($J_{H2-H3} = J_{H5-H6}$ = 10.2 Hz). The decrease of vicinal coupling constants by 3.9 Hz in *syn* rotamer and 5.3 Hz in *anti* rotamer revealed the decrease in the corresponding dihedral angles H2-C2-C3-H3 (ϕ_{trans}) and H6-C6-C5-H5 (ϕ_{trans}). The decrease of these dihedral angles may be attributed to the flattening of C2-N1-C6 end due to the introduction of acetyl function at nitrogen. Due to the delocalisation of nitrogen lone pair on the carbonyl π cloud of the acetyl function, the N-C bond gained partial double bond character and leading to a flattening at nitrogen end. The various possible conformations for the *N*-acyl-*r*-2,*c*-6-di(2-heteroaryl)-*t*-3,*t*-5-dimethylpiperidin-4-ones **3-6** are presented in **Figure 2**. The observed vicinal coupling constants (two different *J* values, 4.9 and 6.3 Hz) and presence of only two signals for C2 and C6 protons of *syn* and *anti* rotamers of **3** and **4** at low temperatures could be well explained by considering an equilibrium between the two boat conformations **B1** and **B2 (Figure 3)**. The alpha (C2 and C6) and beta (C3 and C5) carbons of *N*-acetylpiperidin-4-one **3** were shielded by 5.0±1.0 ppm compared to those of the parent compound **1** and the shielding of *syn* alpha carbon was ascribed to the gamma eclipsing interaction between N1-C2/N1-C6 bond with C-O bond[9]. The shielding of β carbons was attributed to the *gamma anti effect*[10] induced at the β carbon by the N-C bond. In addition, the absence of Bohlmann bands around 2850 cm^{-1}, in the IR spectra, indicated the involvement of lone pair in N-C=O conjugation which is possible only when the acetyl carbonyl is coplanar to the dynamically averaged plane of the piperidine ring[11]. The compound **4** also showed the observations similar to that of **3**.

The non-bonded allylic interaction ($A^{1,3}$-strain) between the coplanar *N*-acetyl function and the alpha equatorial substituents would force the latter to occupy axial orientation (**Figure 3**). In order to get rid of the two opposing destabilising factors (*viz*., $A^{1,3}$-strain and 1,3-diaxial interaction) the substituents *syn* to carbonyl group preferred to occupy axial orientations (**B1** and **B2**).

Thus, the preferred conformational equilibrium in the *N*-acetylpiperidin-4-ones **3** and **4** was considered to be between the boat conformations **B1** and **B2** (**Figure 3**). The *N*-acetyl function is coplanar to the dynamically averaged plane of the piperidine ring exhibiting the rotational equilibrium between the *syn* and *anti* orientations.

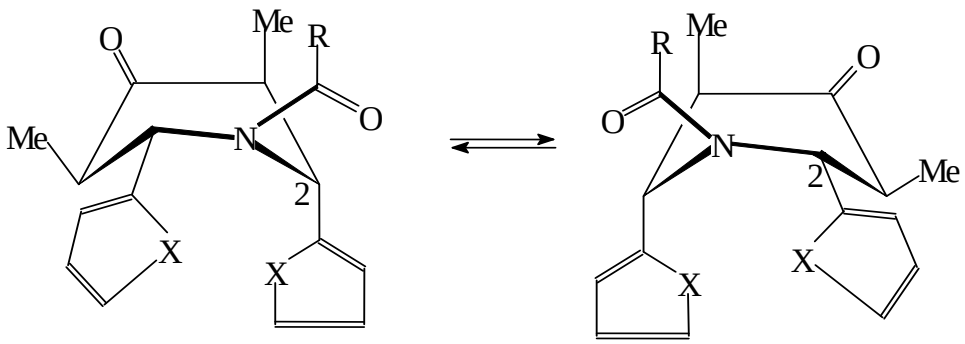
N-Phenylcarbamoyl-*r*-2,*c*-6-di(2-furyl)-*t*-3,*t*-5-dimethylpiperidin-4-one, 5

The analysis of ^{1}H and ^{13}C NMR spectra showed isochronous NMR spectral resonances for each of the protons and carbons suggesting two possibilities *viz*., (i) a perpendicular orientation of the phenylcarbamoyl group (with respect to the averaged plane of the piperidine ring making the molecule symmetric) or (ii) a coplanar orientation of phenylcarbamoyl group with a very low N-C rotational barrier.

The broadening of benzylic proton signals in the ^{1}H NMR spectrum at -40°C indicated the dynamic equilibrium between two coplanar orientations of the phenylcarbamoyl function with very low barrier for N-C rotation. The dynamic equilibrium between two perpendicular orientations through nitrogen inversion could not be observed at this temperature since the process of nitrogen inversion of *N*-acetylpiperidine[12] ring itself was observed as 23 kJ mol^{-1} and the introduction of an electron withdrawing group (phenylcarbamoyl group in this case) at nitrogen would result in further decrease of the barrier.

Increase in the bulkiness of the substituents destabilises planar ground state rather than the perpendicular transition state leading to a lowering of the rotational barrier[13]. As evidenced from the broadening of benzylic signals, dynamic equilibrium between *syn* and *anti* rotamers occurred only below –40°C. In the case of *N*-acetylpiperidin-4-ones **3** and **4,** the broadening of α-proton signals was observed at RT. Thus, the extent of delocalisation around N-C-O linkage was expectd to be relatively less in *N*-phenylcarbamoylpiperidin-4-one **5** compared to its *N*-acetyl analog **3** and it may be due to the extended conjugation through Ph-NH linkage of the phenylcarbamoyl function.

The shielding of alpha carbons by ~ 6.0 ppm in the *N*-phenylcarbamoyl compound **5** compared to those of



B1 **B2**

syn *anti*

	X	R
3	**O**	**Me**
4	**S**	**Me**
5	**O**	**NHPh**
6	**S**	**Ph**

Figure 3 — Conformational equilibrium in *N*-acetyl-*r*-2,*c*-6-di(2-heteroaryl)piperidin-4-ones **3-6**

the parent **1** supported the coplanar orientation of phenylcarbamoyl group. The shielding of α-carbons in this case too could arise due to the bond eclipsing interaction between N1-C2/N1-C6 bond and the coplanar C-O bond of the phenylcarbamoyl moiety.

In *N*-phenylcarbamoylpiperidin-4-one **5** the α-protons (H2 and H6) were deshielded by 1.55 ppm compared to those of the parent piperidin-4-one **1** indicating the orientation within the deshielding cone of the *N*-CONHPh moiety.

If the preferred conformation of *N*-phenylcarbamoylpiperidin-4-one **5** was chair (similar to the parent piperidin-4-one **1**) with equatorial substituents (**CE**), the observed diaxial vicinal coupling constant (J_{H2-H3} and J_{H5-H6}) should be around 10-12 Hz. The vicinal coupling constant was, however, found to be 6.2 and 3.2 Hz for J_{H2-H3} and J_{H5-H6}. Hence, the dihedral angles H2-C2-C3-H3 and H5-C5-C6-H6, were lowered from 180°. Thus, it could be stated that the resonanace energy gained by the delocalisation of nitrogen lone pair over the carbonyl π-cloud was retained by the deformation in the ring conformation.

From these observations, similar to compounds **3** and **4**, it could be concluded that the *N*-phenylcarbamoyl-*r*-2, *c*-6-di(2-furyl)-*t*-3, *t*-5-dimethyl-piperidin-4-one, **5,** prefers a conformational equilibrium between boat conformations **B1** and **B2** with coplanar orientation of -CONHPh group (**Figure 3**).

N-Benzoyl-*r*-2, *c*-6-di(2-thienyl)-*t*-3, *t*-5-dimethyl-piperidin-4-one, 6

The ^{1}H NMR spectrum of the *N*-benzoylpiperidin-4-one **6** showed two broad signals at δ 5.15 and 6.13 corresponding to benzylic protons (H2 and H6) (**Table I**). The ^{13}C NMR spectrum also showed two NMR absorptions for each carbon (**Table I**) and the signals were found to be broad. The broadening of NMR signals at RT suggested the dynamic equilibrium between the two coplanar orientations of *N*-benzoyl function *viz*., *syn* and *anti* with respect to C2. The equilibrium in this compound **6** was due to the delocalisation of lone pair of electrons with the carbonyl group of the benzoyl moiety. The partial double bond character thus created along N-C bond resulted in the restricted rotation leading to the existence of the two orientations (*syn* and *anti*).

Since the doubling of benzylic proton and carbon signals was observed at RT itself, it could be predicted that the rotational barrier for N-C rotation in *N*-benzoylpiperidin-4-one **6** would be higher than *N*-phenylcarbamoylpiperidin-4-one **5**. The diffcrences in the rate of N-C rotation might be due to the increased bulkiness of acyl function in *N*-phenylcarbamoyl compound compared to *N*-acetyl and *N*-benzoyl compounds. This would result in the destabilisation of the ground state to a greater extent compared to *N*-acetyl and *N*-benzoyl groups and therefore, the barrier for N-C rotation becomes lower.

The introduction of benzoyl group at ring nitrogen leads to the deshielding of ring protons compared to their parent compound **2**. The benzylic protons were deshielded by 1.41 and 2.18 ppm. This indicates that the orientation of benzylic protons were forced to be in the deshielding cone of the N-COPh function due to the flattening at the nitrogen end.

The α- and β-carbons were shielded by 5-7 ppm from parent piperidin-4-one **2**. This shielding of α-carbons was attributed to the gamma eclipsing interaction betweeen N1-C2/N1-C6 bonds with N1-C(O) bond and that of β-carbon is acccounted for by the *gamma anti effect* arising due to N-C(O) carbon of the benzoyl group.

Considering all the above observations the *N*-benzoylpiperidin-4-one **6** has also been found to exist in an equilibrium between the boat conformations **B1** and **B2** (**Figure 3**).

Semiempircal MO calculations

In order to understand the preferred conformation of the piperidine ring as well as the orientation of the acyl groups in the gaseous state, semiempirical molecular orbital calculations were carried out for the *N*-acyl derivatives **3-6** using AM1 method available in MOPAC 6 program[14].

For each *N*-acyl-*r*-2,*c*-6-di(2-heteroaryl)piperidin-4-one **3-6** various possible conformations (**Figure 2**) such as a chair form (**CE**), a flipped chair form (**CA**) and four boat forms (**B1**-**B4**) with C2 and C5 occupying prow and stern positions and two boat forms (**B5** and **B6**) with N1 and C4 occupying stern and prow positions were considered as input structures for the conformational analysis. The optimization of these conformations was done by changing the torsion angle C2-N1-C=O within the possible range in 10° increments and the results are summarized in **Table II**.

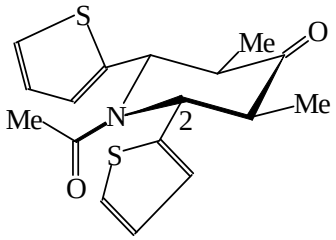
The results obtained by changing the dihedral angle C2-N1-C=O in all the forms indicated that the acyl groups were found to be coplanar with respect to the C2-N1-C6 plane and conformational equilibrium between *syn* rotamer of boat conformations **B1** and *anti* rotamer of boat conformations **B2** for *N*-acyl derivatives **3-6**. AM1 optimized structures for various conformations of **4** are given in **Figure 4** as a representative example.

Conclusion

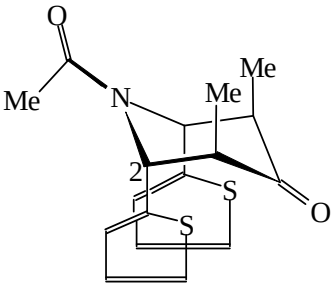
On the basis of the above observations, it was concluded that the NMR spectral studies and semiempirical MO calculations suggested an equilibrium between boat conformations **B1** and **B2** for *N*-acyl-*r*-2,*c*-6-(2-heteroaryl)piperidin-4-ones **3-6** with coplanar orientation of *N*-acyl groups. The energy barrier for N-C rotation in **3** calculated using variable

Table II — Calculated relative heats of formation (kcal mol^{-1}) of various conformations of the *N*-Acyl-*r*-2,*c*-6-di(2-heteroaryl)piperidin-4-ones **3-6** by AM1 method

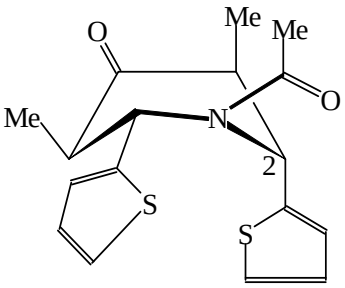
		Relative Heats of Formation (kcal mol^{-1})							
		Conformations							
Compd	Rotamers	CE	CA	B1	B2	B3	B4	B5	B6
3	*syn*		1.94	0.00	1.21	—	—	5.03	
		10.39							13.60
	anti		1.94	1.21	0.00	—	—	5.03	
4	*syn*		2.23	0.00	2.72	—	—	5.49	
		6.42					9.77		11.43
	anti		2.23	2.72	0.00	—		5.49	
5	*syn*		2.33	0.00	2.38	—	—	—	
		7.78							11.68
	anti		2.00	2.38	0.00	—	—	—	
6	*syn*		1.47	0.00	0.32	—	—	—	—
		6.30							
	anti		1.41	0.32	0.00	—	—	—	—



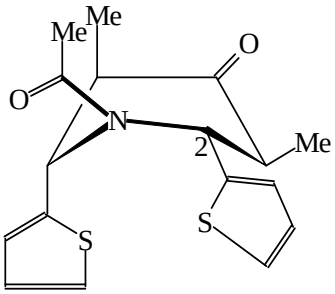
CE



CA



B1



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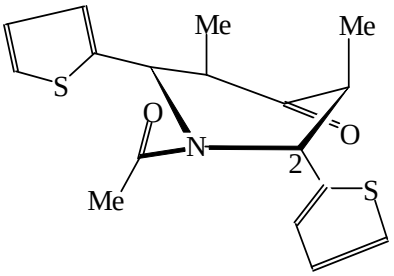

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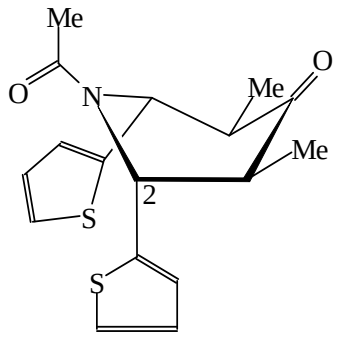
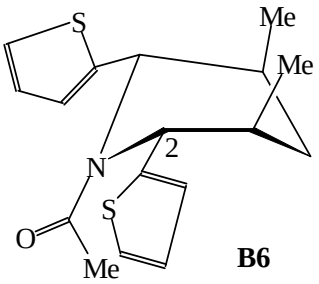


B5



B6

Figure 4

temperature ^{1}H NMR spectral studies was found to be 58.4 kJ mol^{-1}.

Experimental Section

All the melting points were determined using an electrically heated block with a calibrated thermometer and are uncorrected. Infrared spectra were recorded on Shimadzu IR-435 spectrometer as KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded[1c] on a Jeol GSX - 400 MHz spectrometer in $CDCl_3$ solution using TMS as internal reference. Mass spectra were recorded on a Jeol JMS-D 300 spectrometer operating at 70 eV. The piperidin-4-ones **1** and **2** were prepared by following the reported procedures[5].

Computational details

The AM1 method available in MOPAC 6.1 version was used to perform the calculations on Pentium personal computers. The optimization of the conformations was performed by using an analytic gradient minimization method (BFGS, Precise option). Furthermore, eigenvector (EF option) procedure was used to lower the mean gradient upto values below 0.01 kcal mol^{-1}.

***N*-Acetyl-*r*-2, *c*-6-di(2-furyl)-*t*-3, *t*-5-dimethylpiperidin-4-one**, **3**. To a solution of the piperidin-4-one **1** (0.65 g, 2.5 mmoles) in anhydrous benzene (50 mL) was added triethylamine (1.4 mL, 10 mmoles) and acetic anhydride (1 mL, 10 mmoles). The contents were allowed to reflux on a water bath for 6 hr. The reaction mixture was cooled to RT and washed with sodium bicarbonate solution (10%), water and dried over anhydrous sodium sulphate. Evaporation of the solvent and purification by crystallization from ethanol gave crystals of **3**, yield 0.21 g (28%), m.p. 73-74°C. Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.77; H, 6.31; N, 4.65. Found: C, 67.59; H, 6.26; N, 4.51%.

***N*-Acetyl-*r*-2,*c*-6-di(2-thienyl)-*t*-3, *t*-5-dimethylpiperidin-4-one, 4**. To a solution of the parent piperidin-4-one **2** (0.75 g, 2.5 mmoles) in anhydrous benzene (50 mL) was added triethylamine (1.4 mL, 10 mmoles) and acetic anhydride (1 mL, 10 mmoles). The contents were allowed to reflux on a water bath for 6 hr. The reaction mixture was cooled to RT and washed with sodium bicarbonate solution (10%), water and dried over anhydrous sodium sulphate. Evaporation of the solvent and purification by crystallization from ethanol gave crystals of **4**, yield 0.27 g (33%), m.p.73-74°C. Anal. Calcd. for $C_{17}H_{19}NS_2O_2$: C, 61.26; H, 5.71; N, 4.20; S, 19.21. Found: C, 61.07; H, 5.81; N, 4.12; S, 19.05%.

***N*-Phenylcarbamoyl-*r*-2, *c*-6-di(2-furyl)-*t*-3, *t*-5-dimethylpiperidin-4-one**, **5**. To a solution of the piperidin-4-one **1** (0.65 g, 2.5 mmoles) in anhydrous benzene (50 mL) was added triethylamine (1.4 mL, 10 mmoles) and phenyl isocyanate (0.8 mL, 10 mmoles). The contents were allowed to reflux on a water bath for 2 hr. After the completion of the reaction, the mixture was cooled to RT and passed through a short column of silica gel and the solvent was removed. The residue obtained was purified by recrystallisation from ethanol to get **5,** yield 0.3 g (32%), m.p. 140-41°C. Anal. Calcd. for $C_{22}H_{22}N_2O_4$: C, 69.84; H, 5.82; N, 7.41. Found: C, 70.04; H, 5.92; N, 7.26%.

***N*-Benzoyl-*r*-2, *c*-6-di(2-thienyl)-*t*-3, *t*-5-dimethylpiperidin-4-one**, **6**. To a solution of the piperidin-4-one **2** (0.75 g, 2.5 mmoles) in anhydrous benzene (50 mL) was added triethylamine (1.4 mL, 10 mmoles) and benzoyl chloride (1.2 mL, 10 mmoles). The contents were allowed to reflux on a water bath for 8 hr. The reaction mixture was cooled to RT and poured into water and the organic layer was separated. The aqueous layer was extracted with benzene (4 × 25 mL). The organic layers were combined and washed with several 25 mL portions of 2N solution of HCl followed by water. The combined organic layer was then dried over anhydrous sodium sulphate and concentrated. The solvent was evaporated and the solid obtained was purified by recrystallisation from ethanol to get **6**, yield 0.26 g (29%), m.p. 201-03°C. Anal. Calcd. for $C_{22}H_{21}NS_2O_2$: C, 66.84; H, 5.32; N, 3.54; S, 16.20. Found: C, 66.57; H, 5.45; N, 3.70; S, 16.08%.

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