INTRODUCTION
1. INTRODUCTION

The presence of partial double bond character at N-C bond in amides and N-N bond in nitrosamines (Figure 1) due to an extensive delocalisation of the lone pair of electrons on nitrogen with C=O and N=O groups, respectively, has been well documented.\textsuperscript{1-4} The appearance of two separate methyl resonances in the room temperature \textsuperscript{1}H NMR spectra of dimethylformamide (1)\textsuperscript{1a,c} and dimethylnitrosamine (2)\textsuperscript{1b} and the coalescence of the signals on raising the temperature indicated that a barrier to rotation about the N-C/N-N bond exists at room temperature which shows clearly that the average plane of the N-CO/N-NO function must be coplanar with the C1-N-C2 plane. The rotational barrier due to the partial double bond character at N-C bond of dimethylformamide\textsuperscript{1a} is 87 kJ mol\textsuperscript{-1} and that of dimethylnitrosamine\textsuperscript{1b,2} is 95 kJ mol\textsuperscript{-1}.

The attachment of electron withdrawing groups like NO, COR, etc., (indicated commonly as X=Y, Figure 2) at nitrogen of a 2,6-disubstituted piperidine ring has been reported to exert major changes in the ring conformation and the orientation of the substituents.\textsuperscript{5-25} It has been shown that the orientation of the -X=Y groups in these molecules can be either coplanar (A) or perpendicular (B) with reference to the C2-N1-C6 plane (Figure 3). The conformational change is attributed to the involvement of lone pair of electrons on nitrogen in conjugation with the -X=Y function. The conjugation creates a partial double bond
Figure 1. Resonance stabilization leading to partial double bond character in amides and nitrosoamines.

R, R¹, R² = alkyl or aryl
Figure 2. Delocalisation along N-X=Y function

Figure 3. Orientations of the -X=Y group
Figure 4. Allylic strain

R = alkyl or aryl

X = Y

3. COCH₃
4. NO
character at N-X (Figure 2) bond and leads to a restricted rotation around this bond which in turn results in the magnetic nonequivalence of the ring carbons and the attached protons. The change of hybridisation of the nitrogen from $^3sp$ to $^2sp$ is possible only in the coplanar orientation (A) of the $-X=Y$ function with reference to C2-N1-C6 plane due to the gain in the resonance energy through delocalisation. The substituents at the equatorial positions alpha to the nitrogen exhibit a severe nonbonded interaction with the coplanar N-X=Y function which is termed as Allylic strain or $A^{1,3}$-strain (Figure 4). In each of the cases of N-acetyl- & N-nitroso-cis-2,6-dimethylpiperidines (3 & 4), the preferred conformation was found to be the one with axial methyl groups in spite of the 1,3-diaxial interaction between the methyl groups. Since the delocalisation energies of the N-X=Y functions (62-95 kJ mol$^{-1}$) in N-substituted-2,6-dimethylpiperidines (X=Y are -NO, -COCH$_3$, -CHO, etc.) are much larger than 1,3-diaxial CH$_3$/CH$_3$ interaction energy (14.6 kJ mol$^{-1}$), these molecules, in general, prefer conformations with diaxial methyl groups.

Lunazzi et al. have carried out detailed stereochemical studies on piperidines, 2,6-dimethylpiperidine(DMP) and 2,2,6,6-tetramethylpiperidine (TMP) containing various -X=Y substituents at nitrogen end. They have shown that the orientations of the -X=Y groups in N-nitrosopiperidines, N-acylpiperidines were coplanar with reference to C2-N1-C6 plane regardless of the number of methyl groups on C2 and C6 of the ring using $^{13}$C NMR.
Figure 5. Paulsen and Todt's amide anisotropy model
data to distinguish A from B. In the coplanar conformation (A),
the C2 & C6 as well as C3 & C5 carbons were anisochronous,
whereas in the perpendicular conformation (B), the C2 & C6 and C3
& C5 carbons became isochronous. In compounds with a coplanar
-X=Y group the rotational barrier was lowered upon increasing the
bulkiness of the -X=Y group as seen in the cases of N-acyl-
cis-2,6-dimethylpiperidines (-COMe=57.3, -COPh=52.8,
-CO-t-Bu=51.1 kJ mol⁻¹).⁵d,⁶

On the basis of ¹³C NMR studies it was shown that the
α-carbon syn to the carbonyl/nitroso oxygen atom is more shielded
relative to the other α-carbon with an anti disposition due to
greater steric compression at the syn carbon.⁸,²⁷⁻³³

The magnetic nonequivalence of the α-protons was explained
by Paulsen and Todt.³⁴ They developed a model for the
anisotropic effect of the amide group which can also be extended
to other N-X=Y systems.

1.1 Paulsen and Todt's model

A theoretical explanation for the magnetic anisotropy of the
amide group was given by Paulsen and Todt.³⁴ They proposed a
large diamagnetism (shielding) in conical regions extending above
and below the plane of the C=O group while the regions in the
plane of the C=O group are paramagnetic (deshielding, Figure 5).
The two regions are distinguished in the model (Figure 5): the
"plane region", in the plane of the amide group with the
positions AA' and DD' in which A experiences greater shielding
than A' and the "out-of-plane region" (shielding region) in which
the C and C' positions are opposed, with position C' being shielded more strongly than C. The positions EE' are equivalent to CC'. In the case of N,N-dimethylamides, the protons of the methyl group cis to oxygen resonate at higher field than those trans to oxygen.

1.2 Dynamic NMR studies

The energy of activation required for the interconversion between rotamers is a measure of the barrier to rotation about the N-X bond. Moreover, it is a measure of the extent of delocalisation and the N-X double bond character. The barriers to interconversion between the syn and anti rotamers of several N-X=Y systems have been extensively investigated by dynamic NMR spectral studies.

In the case of two equally populated rotamers, the energy barrier for N-X rotation ($\Delta G^\#$) is evaluated using Eyring equation (Eqn.1)

$$\Delta G^\# = 4.57 T_C \left[ 9.97 + \log T_C/8\delta \right] \text{cal mol}^{-1} \text{ cal mol}^{-1} \text{ Eqn. 1}$$

where the \( \Delta G^\# \) is the free energy of activation

\( T_C \) is the coalescence temperature

\( \delta \) is the chemical shift difference in Hz at \( T_C \).

Shanon-Atidi and Bar-Eli have derived a modified Eyring equation for the calculation of the energy barrier for interconversion between the rotamers with unequal populations (Eqn.2 and Eqn. 3).
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\[ \Delta G_{AB}^\# = 4.57 \, T_C \, [ \, 10.62 + \log \frac{X}{2\pi(1-\Delta p)} + \log \frac{T_C}{8\gamma} \, ] \, \text{cal} \, \text{mol}^{-1} \]

\[ \Delta G_{BA}^\# = 4.57 \, T_C \, [ \, 10.62 + \log \frac{X}{2\pi(1+\Delta p)} + \log \frac{T_C}{8\gamma} \, ] \, \text{cal} \, \text{mol}^{-1} \]

\[ \text{Eqn. 2} \]

\[ \text{Eqn. 3} \]

where,

\( \Delta G^\# \) is the free energy of activation

\( T_C \) is the coalescence temperature

\( 8\gamma \) is the chemical shift difference in Hz at \( T_C \)

\( \Delta p \) is the population difference between the rotamers

\( X \) is the value defined by

\[ p = \left[ \frac{X^2 - 2}{3} \right]^{3/2} \cdot \frac{1}{X} \]

\( \Delta G_{AB}^\# \) and \( \Delta G_{BA}^\# \) are the free energy barriers for the interconversion of rotamer A to B and B to A, respectively.

In order to study the effect of the introduction of nitroso group at N1 position containing \( \alpha \)-equatorial phenyl substituents in terms of orientation of the \( \alpha \)-equatorial substituents and the preferred conformations of the piperidine ring, extensive stereochemical analysis has been carried out on \( \text{N-nitroso-cis-} \) 2,6-diphenylpiperidin-4-ones in our laboratory. In addition, the stereochemistry of unsymmetrical \( \text{N-nitrosopiperidin-4-ones with various substituents at C3 & C5 positions has also been studied.} \)

1.3 Stereochemistry of \( \text{N-Nitrosopiperidines} \)

Though all the parent piperidines 5a-f, 6a-f & 7a-d preferred chair conformations with equatorial
Figure 6. Conformational equilibrium between syn and anti rotamers of N-nitrosopiperidin-4-ones. 8a-f, 9a-f and 10a-d
phenyl groups the N-nitroso-cis-2,6-diphenylpiperidin-4-ones 8a-f & 9a-f and N-nitroso-cis-2,6-diphenylpiperidines 10a-d were found to prefer twist-boat conformations with quasi-axial or quasi-equatorial phenyl groups. The appearance of two signals for each benzylic protons and carbons in the $^1H$ & $^{13}C$ NMR spectra, respectively, indicated the coplanar orientation of the nitroso function with reference to the C2-N1-C6 plane of the piperidine ring with significant hindrance for rotation at N-N bond. Due to hindered rotation around N-N bond these nitroso derivatives (8a-f, 9a-f & 10a-d) exist in an equilibrium between syn rotamer (nitroso oxygen being cis to C2) and anti rotamer (nitroso oxygen being trans to C2) at room temperature (Figure 6). The $^1H$ NMR spectrum of N-nitroso-cis-2,6-diphenylpiperidin-4-one (8a) showed two triplets for the benzylic protons at C2 & C6 for the syn and anti configurations with coupling constants of 7.2 and 5.4 Hz, respectively, indicating a non-chair conformation. The dihedral angles, estimated using DAERM (Dihedral Angle Estimation by Ratio Method), were used to decide the preferred conformations of the ring.

Jeyaraman and Ravindran determined the energy barriers for the N-N bond rotation using dynamic $^1H$ NMR studies for the compounds 8a, 8e, 8f & 10a and the barriers were found to be 80.8, 80.0, 77.0 & 75.8 kJ mol$^{-1}$, respectively. The lower rotational barrier for N-nitrosopiperidine 10a over the N-nitrosopiperidin-4-one 8a has been explained on the basis of the ground state destabilisation of N-nitrosopiperidines due to the
Figure 7. Crystal structure of 8d

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increased flattening at the C3-C2-N1-C6-C5 part of the ring. Interestingly, the X-ray crystal structure of 3-isopropyl-N-nitroso-\(r\)-2,6-diphenylpiperidin-4-one 8d showed a chair conformation in which all the substituents occupy axial orientations (Figure 7). Polansky et al. also examined a number of N-nitrosopiperidines including the piperidines containing fluoro substituents at the \(\alpha\)-phenyl rings and predicted the conformations to be perfect boat in a few cases by X-ray and molecular mechanics methods. \(^{58}\)

1.4 Stereochemistry of N-Nitrosohexahydrodiazepin-5-ones

In order to understand the effect of introduction of nitroso group on the conformational preferences of azacyclic seven membered rings containing \(\alpha\)-equatorial phenyl groups, the stereochemical studies on N-nitrosohexahydrodiazepin-5-ones 12a-e were also carried out in our laboratory.

The parent hexahydrodiazepin-5-ones 11a-e \(^{59-61}\) (11a-e) were found to adopt chair conformations with equatorial orientations of both the phenyl and alkyl substituents in the seven membered ring on the basis of IR, \(^1\)H and \(^{13}\)C NMR spectra and X-ray crystallography. \(^{59,61}\) These diazepin-5-ones showed vicinal diaxial coupling constants of 8-9 and 10-11 Hz for the benzylic hydrogens at C2 and C7, respectively. The cis coupling constant of 0 Hz observed for the H7 axial protons with H6 equatorial protons in the diazepinones 11a-e indicated a dihedral angle of 90°.
Figure 8. Conformational equilibrium involving syn and anti rotamers of N-nitrosohexahydrazepin-5-ones 12a-e
The N-nitrosohexahydrodiazepinones 12a-e derived from 11a-e were shown to prefer flattened boat conformations (Figure 8). The phenyl groups at the α-carbons preferred pseudo-axial orientations while the alkyl groups at the β-carbons were shown to prefer equatorial positions. In each case two major rotamers were found to be in equilibrium at room temperature involving syn and anti orientations of the coplanar (with reference to C2-N1-C7 plane) nitroso group. The α-protons were found to fall in the plane of the nitroso group. The signal due to the α-carbons syn to the nitroso group was found to be shielded by about 11-15 ppm compared to that of the parent hexahydrodiazepin-5-one. On the basis of the single crystal X-ray crystallographic studies, the geometry around the amine-nitrogen was found to be planar which was consistent with the sp^2 hybridisation arising out of extensive delocalisation of the lone pair of electrons on nitrogen over the nitroso group and the solid state conformations of the N-nitrosohexahydrodiazepines 12a-e were found to be similar to those predicted in the solution state.

The stereochemical outcome of allylic strains at two locations of a ring was estimated in N,N'-dinitroso-cis-2,7-diphenylhexahydro-1,4-diazepin-5-ones 13a-c. On the basis of a combination of multipulse experiments (HOHAHA, NOE, etc.,) and variable temperature NMR spectra recorded from -50° to +120°C, it was shown that hexahydro-3-isopropyl-1,4-dinitroso-cis-2,7-diphenyl-1H-1,4-diazepine (13b) exists as an equilibrium
Figure 9. Equilibrium between the major and minor forms of dinitroso compounds 13a-c

Figure 10. Rotational equilibrium in the major isomers of the dinitroso compounds 13a-c
mixture of two sets of conformations (Figure 9), a major set consisting of four rotamers and a minor set consisting of possibly four rotamers resulting from two parallel dynamic processes viz., the restricted N-N rotations at two N-N(O) bonds and the pseudorotations of the seven membered ring. While the pseudorotation was found to bring about the interconversion within a pair of twist-chair conformations of the hexahydrodiazepine ring, the restricted rotation at N-N bond made each twist-chair conformation to exist as an equilibrium mixture of four rotameric states containing different relative orientations of the two nitroso groups viz., \textit{syn-anti}, \textit{syn-syn}, \textit{anti-syn} and \textit{anti-anti} (Figure 10). The relative conformational dispositions of the alkyl groups and various protons in 13a-c were determined from the NOE experiments.\textsuperscript{59b,63}

In all the three dinitroso compounds, among the two sets of twist-chair conformers, the major rotamers (95\%) were shown to have the alkyl group at C3 axially oriented while the minor rotamers were considered to have equatorial alkyl groups. On the other hand, the alkyl group at C6 of the 3,6-dimethyl derivative was shown to be in equatorial orientation in all the conformations. In the major conformer, the phenyl groups at C2 and C7 were shown to be in pseudoaxial and equatorial positions, respectively.\textsuperscript{59b,63}

The X-ray crystallographic studies on the 3-isopropyl derivative 13b revealed that the dinitroso compound adopts partially twisted chair conformation with equatorial orientation
14a Ph CO
   b Ph CH₂
   c p-anisyl CO
   d p-anisyl CH₂

15a CO  H
   b CO  NO
   c CH₂ NO

16a Ph CO
   b Ph CH₂
   c p-anisyl CO
   d o-anisyl CH₂

17a CO
   b CH₂
of the isopropyl as well as the phenyl substituents. This conformation was analogous to one of the conformers in the minor set (5%) indicating that it was the minor conformer that crystallized preferentially.

1.5 Conformational Preferences of N-Nitroso-3-azabicyclo[3.3.1]-nonanes and N,N'-Dinitroso-3,7-diazabicyclo[3.3.1]nonanes

The nitrogen of the N-nitroso-cis-2,6-diphenylpiperidines 8-10 was shown to possess sp² character with the C2-N1-C6 bond angle close to 120° indicated by crystal structure data. The strain due to the expansion of C2-N1-C6 angle can be alleviated by the contraction of C3-N1-C6 angle. But in the case of N-nitroso derivatives of 3-azabicyclo[3.3.1]nonanes such a contraction is not allowed since the 3,5-dialkyl components are part of a ring. These compounds were, therefore, expected to exist either in chair-boat conformation or the nitroso group may adopt an unusual perpendicular orientation. In order to determine the effect of 3,5-diaxial alkyl part of the ring on the energy barrier for rotation of N-NO bond and the preferred conformation of the bicyclic ring, conformational analysis on N-nitroso-cis-2,4-diaryl-3-azabicyclo[3.3.1]nonanes 14a-d and N-nitroso- & N,N'-dinitroso-3,7-diazabicyclo[3.3.1]nonanes 15a-c was also carried out in our laboratory. The parent 3-azabicyclo[3.3.1]nonanes 16a-d adopt a twin-chair conformation while the 3,7-diazabicyclo[3.3.1]nonanes 17a-b were shown to prefer chair-boat conformation with equatorial phenyl groups.
Figure 11. Rotational equilibrium in N-nitrosopiperidin-4-one oximes 18a-d
The N-nitroso-2,4-diaryl-3-azabicyclo[3.3.1]nonanes\textsuperscript{14a-d} were found to prefer twin-chair conformations with phenyl groups at the equatorial orientations\textsuperscript{38a,66} while N-nitroso- & N,N'-dinitroso-\textsuperscript{t}2,\textsuperscript{c}4,\textsuperscript{t}6,\textsuperscript{t}8-tetraphenyl-3,7-diazabicyclo[3.3.1]-nonanes \textsuperscript{15a-c} were shown to adopt twin-chair conformations with two of the phenyl groups occupying axial orientations.\textsuperscript{38a} The energy barriers for the N-NO rotation of N-nitroso-2,4-diaryl-3-azabicyclo[3.3.1]nonanes were found to be low (60-70 kJ mol\textsuperscript{-1}) compared to those of the monocyclic nitrosamines (75-85 kJ mol\textsuperscript{-1}). Moreover, the delocalisation in these rigid bicyclic amines was partial resulting in a slightly nonplanar geometry around nitrogen.\textsuperscript{66} Recent report by Polansky et al. for the similar N-nitroso-3-azabicyclic compounds is in fair agreement with our results.\textsuperscript{79}

1.6 Stereochemistry of Oximes and Semicarbazones of N-nitrosopiperidin-4-ones

The influence of two competing A\textsuperscript{1,3} strain factors (at C1 and C4 positions) over the conformational preferences of piperidine ring systems, such as N-nitroso-\textsuperscript{t}2,\textsuperscript{c}6-diphenylpiperidin-4-one oximes \textsuperscript{18a-d} and semicarbazones of N-nitroso-\textsuperscript{t}2,\textsuperscript{c}6-diphenylpiperidin-4-ones \textsuperscript{18e-h} has been studied by Jeyaraman and Vijayalakshmi.\textsuperscript{80} These compounds were shown to prefer twist-boat conformations with an equilibrium involving coplanar syn and anti orientations of the nitroso function (Figure 11). The preferred conformation of 3,5-dimethyl-N-nitrosopiperidin-4-one oxime (18d) obtained through X-ray
Figure 12. Chair and boat forms of dinitrotetrahydrobenzodiazepines 19a-c
crystallography was similar to the preferred twist-boat conformation in the solution state.

1.7 N,N'-Dinitrosotetrahydrobenzodiazepines

The stereochemical influences of the nitroso groups on the preferred conformations of dinitrosotetrahydrobenzodiazepines (19a-c) was studied by Jeyaraman and Senthilkumar.\textsuperscript{59b} The parent benzodiazepines 20a-c are known to adopt a chair conformation\textsuperscript{81–82} while the dinitrosotetrahydrobenzodiazepines 19a–c were found to exist as a mixture of two conformers (Figure 12), the major conformer being in chair conformation while the minor in boat form and the nitroso groups preferring endo-endo orientations in both the conformers.\textsuperscript{59b}

Since the other N-X=Y functions such as -CHO & -COR also induce similar conformational changes, the effect of stereodynamics of piperidines containing those functions has also been studied and compared with that of the corresponding N-nitrosamines.

1.8 Stereoselectivity in the formation of Spiromonothioketals

It was shown that the N-acetyl- & N-benzoyl-cis-2,6-diphenylpiperidine-4-ones 21-22 exist in non-chair conformations on the basis of \textsuperscript{1}H & \textsuperscript{13}C NMR spectral data, molecular mechanics calculations and X-ray crystallographic studies.\textsuperscript{83}

The influence of N-substituents viz., methyl and acetyl groups on the selectivity of formation of spiromonothioketals from r-2,6-diphenylpiperidin-4-ones 23a-j\textsuperscript{84} was studied by
X = H or Me;  R = H or alkyl

Figure 13. Predominant isomer of 23a-h

Figure 14. Conformational equilibrium between *syn* and *anti* rotamers of *N*-formylpiperidines 24a-j
Jeyaraman and Sujatha and the results were consistent with the prediction of Cieplak's model. When the nitrogen site was free or substituted by methyl group the predominant isomer was the one with the oxygen atom of the spiro ring in the axial orientation with respect to the piperidine ring (Figure 13). In the case of N-acetyl piperidin-4-ones 23i-j the reversal in the selectivity of formation of monothioketals was observed and the predominant isomer was the one with sulfur atom in the axial position.\textsuperscript{84}

1.9 Stereochemistry of N-formyl piperidines

Jeyaraman and Thenmozhiyal found that the N-formyl piperidines 24a-j prefer flattened boat conformations with coplanar orientations of N-C=O function resulting in the conformational equilibrium between syn and anti rotamers (Figure 14).\textsuperscript{39a} The aryl groups at C2 and C6 positions were found to adopt quasi-axial orientations. The other N-acyl piperidin-4-ones 24k-m\textsuperscript{39a} were also found to adopt a conformation similar to that of N-formyl piperidines.

1.10 Sterechemistry of N-Formylhexahydrodiazepin-5-ones

Similar to N-nitrosohexahydrodiazepines 12a-e, the N-formyl hexahydro-1,4-diazepin-5-ones 25a-e were shown to prefer flattened boat conformations (Figure 15).\textsuperscript{59b} The phenyl groups at the α-positions are in pseudo-axial orientations while the alkyl groups at the β-carbons prefer equatorial positions.
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<td>CH&lt;sub&gt;2&lt;/sub&gt; CHO</td>
</tr>
<tr>
<td>k 2-thienyl</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>H</td>
<td>CO COMe</td>
</tr>
<tr>
<td>l 2-furyl</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>H</td>
<td>CO COMe</td>
</tr>
<tr>
<td>m 2-furyl</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>H</td>
<td>CO CONHPh</td>
</tr>
</tbody>
</table>

Figure 15. Conformational equilibrium between <em>syn</em> and <em>anti</em> rotamers of N-formylhexahydrodiazepines 25a-e.

<em>syn</em> and <em>anti</em> rotamers of N-formylhexahydrodiazepines 25a-e.
1.11 Stereochemistry of Carbamates

Though the hindered rotation at N-C(0) bonds in the N,N-dimethylcarbamates (26a) was reported much earlier \(^{85}\) (in the year 1965 by Lustig et al.) not much work has been done, to our knowledge, on the stereodynamics of carbamates of piperidine and related systems, \(^{4a,9,31a,86-89}\) in spite of its importance as intermediates in organic synthesis \(^{90-98}\). Many carbamates are used as insecticides and pesticides \(^{99}\). The energy barriers \((\Delta G^\#)\) for the N-C rotation in the case of carbamates 26b-26h were found to be 63 \(^{86}\), 62 \(^{87}\), 63 \(^{89}\), 49 \(^{31a}\), 66 \(^{88}\), 66 \(^{88}\), 67 \(^{88}\) kJ mol\(^{-1}\), respectively. These barriers are lower than those observed for N-nitroso, N-formyl & N-acetyl systems \(^{1-4,31a}\) and the lower barriers in carbamates were considered to be due to a slight decrease in C-N bond order caused by the inductive effect of the electronegative OR group \(^{86}\). The preferred conformations of the carbamates of 4-methyl-4-phenylpipecolic acids 26i-26j were found to be the one with diaxial Ph/Me & COOH groups and their preference was explained on the basis of the A\(^{1,3}\)-Strain \(^9\).

1.12 Scope of the present work

Review of the literature indicated that the conformational preferences of azacycles are largely decided by the magnitude of the resonance energy caused by the delocalisation of nitrogen lone pair in N-N=O, N-C=O. In addition, the relative magnitudes of the other destabilizing interactions such as A\(^{1,3}\)-Strain, torsional strain in the rings, and 1,3-diaxial strain are the deciding factors. Hence, with a view to studying the relative
$26a \quad X = \text{Me, Et, t-Bu}$

$26b$

$26c$

$R = \text{long chain hydrocarbon}$

$26d$

$26e$

$26f$

$26g$

$26h$

$26i \quad \text{cis}$

$26j \quad \text{trans}$

$R = \text{t-Bu}$
influences of these factors over the azacyclic six & seven membered rings, certain N-ethoxycarbonylpiperidines, N-ethoxycarbonyl- & N,N'-diethoxycarbonylhexahydrodiazepines, N-acetylazabicyclononane, N-acyldiazabicyclononanes, N-acyl- & N,N'-diacetyl tetrahydrobenzodiazepines were synthesized and their stereochemistry was studied with the help of $^1$H & $^{13}$C NMR data, HETCOR, COSY, NOE spectral techniques and X-ray crystal structure determination. In addition, the stereochemistry of 4-cyano-4-N-phenylaminopiperidines was studied.