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Conformational Studies of Some *t*(4)-Acetoxy-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidines Using ^{1}H NMR Spectra. Evidence for Contribution of Boat Forms with a Substituent in the Flagpole Position

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The NOESY spectrum and vicinal coupling constants of *t*(4)-acetoxy-3,3-dimethyl-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine suggest that the compound adopts a chair conformation with axial phenyl groups. The vicinal coupling constants of *t*(4)-acetoxy-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine could be accounted for by an equilibrium mixture of the chair conformation with axial phenyl groups and a boat conformation with one phenyl group in the flagpole position. The vicinal coupling constants suggest that in the case of *t*(4)-acetoxy-*t*(3)-methyl-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine another boat conformation with the acetoxyl group in the flagpole position also makes some contribution and *t*(4)-acetoxy-*t*(3),*t*(5)-dimethyl-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine exists largely in a boat conformation with the acetoxyl group in the flagpole position. The flattened chair conformation, proposed earlier for the piperidine ring in *N*-acetylsolasodine, has been shown to be incorrect and a boat conformation without allylic strain is assigned. The earlier interpretation of spectral results on *N*-nitroso-2α-methyldecahydroquinoline is also re-examined. © **1997 by John Wiley & Sons, Ltd.**

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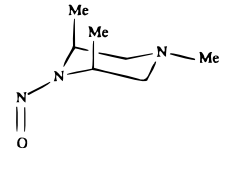
INTRODUCTION

Saturated six-membered ring compounds normally adopt chair conformations with equatorial orientations of the majority of the substituents. However, such a conformation is not favoured if allylic strain[1] is introduced by endo- or exocyclic double bonds on unsaturated substituents. Thus, the vicinal coupling constants (4.8 and 1.2 Hz; 4.4 and 1.2 Hz) of 1,*r*(3),*c*(5)-trimethyl-4-nitrosopiperazine (**1**) are consistent only with the axial orientations of the 3- and 5-methyl groups[2a] (*r* is used to denote the substituent with respect to which the orientations of the other substituents are defined; *c* denotes a substituent *cis* to the reference substituent and letter *t* denotes a substituent *trans* to the reference substituent). A boat conformation has been assigned to the transoid form of 1,4-dinitroso-*r*(2),*t*(3),*c*(5),*t*(6)tetramethylpiperazine (**2**) based on the vicinal coupling constants.[2b] Form the ^{13}C NMR spectrum it has been found that *N*-nitroso-2α-methyl-*trans*-decahydroquinoline (**3**) exists in two forms in the ratio 3:1. A boat conformation has been proposed for the piperidine ring in both forms.[3] In this study[3] the conformations have not been characterized using vicinal coupling constants.



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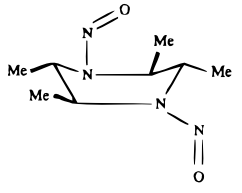

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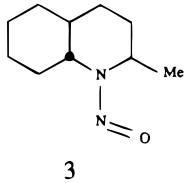

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If the alternative chair conformation without allylic strain contains more axial substituents, boat forms without allylic strain and many substituents in quasi-equatorial positions may be preferred. Hence, it is of interest to investigate *N*-acetyl and *N*-nitroso derivatives of piperidines with many substituents in the ring. Ravindran *et al.*[4] have studied a number of *N*-nitroso-2,6-diphenylpiperidine derivatives (**4**) using ^{1}H and ^{13}C NMR spectra and have suggested that the phenyl groups are equatorial in **4**. However, in that study the vicinal coupling constants were not analysed in detail. The reported vicinal coupling constants are not consistent with chair conformations with equatorial phenyl groups. Indeed, these compounds have been reinvestigated recently by Gdaniec *et al.*[5] using x-ray crystallography and the MM2 method in addition to ^{1}H and ^{13}C NMR spectroscopy. Many compounds have been shown to adopt boat or chair conformations with axial phenyl groups in the solid state. Based on the variation of the vicinal coupling constants with solvent and temperature, it has been suggested that in solution some

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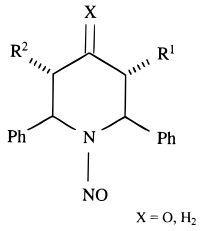

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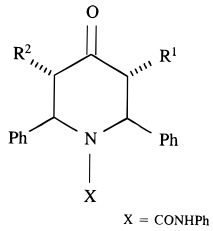

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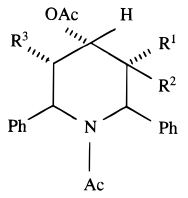


6; $R^1=R^2=Me$; $R^3=H$

7; $R^1=R^2=R^3=H$

8; $R^1=Me$; $R^2=R^3=H$

9; $R^1=R^3=Me$; $R^2=H$

6 - 9

compounds exist as mixtures of two or three conformations. Even in this study the vicinal coupling constants have not been analysed in great detail.

Recently, Krishnakumar and Krishnapillay[6] have investigated the conformations of several *N*-phenylcarbamoylpiperidin-4-ones (**5**) using IR, ^{1}H NMR and ^{13}C NMR data. For two compounds a sofa conformation and for three other compounds a twist-boat conformation were proposed. However, the variation in the vicinal coupling constants with substituents strongly suggests an equilibrium between at least two different boat conformations in two cases. The analysis of the vicinal coupling constants needs reconsideration.

The analysis of the conformations of **4** and **5** from the vicinal coupling constants seems difficult because it has only been possible to extract the vicinal coupling constants between α- and β-protons. Furthermore, the spectra are complicated by the presence of *E* and *Z* forms in the derivatives of unsymmetric piperidin-4-ones.

We felt that an investigation of *N*-acetylpiperidines (**6–9**) might of interest. We have introduced an acetoxyl substituent at C-4 *trans* to the phenyl groups so as to obtain well resolved signals for all the heterocyclic ring protons and to measure all the vicinal coupling constants more precisely. The vicinal coupling constants of **6–9** were determined from ^{1}H NMR spectra in $CDCl_3$. For **7**, the vicinal coupling constants were determined also in DMSO-d_6. For **6**, a NOESY spectrum was also recorded. The conformation of the piperidine ring in *N*-acetylsolasodine was re-examined in the light of the reported vicinal coupling constants.[7] The conformations proposed for **3** were re-examined.

EXPERIMENTAL

Materials

A mixture of the appropriate 4-hydroxypiperidine[8] and acetic anhydride in a molar ratio of 1:5 in dry pyridine was refluxed for 8–10 h and then poured into ice–water. The product was recrystallized several times from dilute alcohol to a constant melting point and its purity was checked by TLC. The observed melting points were 146 (**6**), 118 (**7**), 115 (**8**) and 110 °C (**9**). The compounds were characterized by IR, ^{1}H NMR and ^{13}C NMR spectra. The IR spectra showed two strong bands in the carbonyl stretching region, one around 1640 cm^{-1} for the amide carbonyl and the other around 1730 cm^{-1} for the ester carbonyl (from the acetoxy group). NMR spectra showed the compounds to be free of any other impurity.

Spectra

^{1}H NMR (270 MHz) spectra were recorded on a Bruker WH-270 NMR spectrometer operating at 6.35 T. Samples were prepared by dissolving 50 mg of the material in about 0.5 ml of $CDCl_3$ containing 1% TMS. Ten FIDS were accumulated for each sample and the number of data points was 16 K. The phase-sensitive NOESY spectrum was performed using the standard pulse sequences employing the TPPI method to obtain pure absorption mode spectra. The mixing time for the NOESY experiment was chosen as 800 ms and the number of data points was 1 K.

RESULTS AND DISCUSSION

Analysis of spectra

For **7**, **8** and **9**, the signals for the heterocyclic ring protons could be assigned based on their multiplicities and positions. However, for **6**, the signals due to H-4 and H-6 could be assigned only from its NOESY spectrum, shown in Fig. 1. For **6**, **7** and **8**, the difference between the chemical shifts of the methylene protons is greater than 100 Hz so that the vicinal coupling constants could be determined by first-order analysis. The observed chemical shifts and vicinal coupling constants are given in Table 1.

Possible conformations of 6–9

Seven conformations are considered for compounds **6–9**. In the chair conformation **A** with equatorial phenyl groups there is severe allylic strain. This allylic strain is relieved in the alternative chair conformation **B** with axial phenyl groups and in boat conformations **C**, **E** and **G**. In boat conformations **D** and **F** the phenyl group at the bowsprit position experiences allylic strain. For **7** and **9** conformations **C** and **E** are identical and conformations **D** and **F** are identical. (The conformations of any compound are designated with the number for the compound and the letter for the corresponding conformation. Thus, the conformations of **6** are designated **6A**, **6B**, **6C**, **6D**, **6E**, **6F** and **6G**.)

***t*(4)-Acetoxy-3,3-dimethyl-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine (6).** From the NOESY spectrum of **6** (Fig. 1) it is inferred that H-2 shows an NOE with the protons of both methyl groups at C-3 (signals 1 and 2). In the ^{1}H NMR spectrum of **6** there are two double doublets at 5.65 and 5.75 ppm. The proton appearing at 5.65 ppm shows an NOE with one of the methyl groups at C-3 (signal 3). Therefore, this resonance is assigned to H-4 and the signal appearing at 5.75 ppm is due to H-6. The

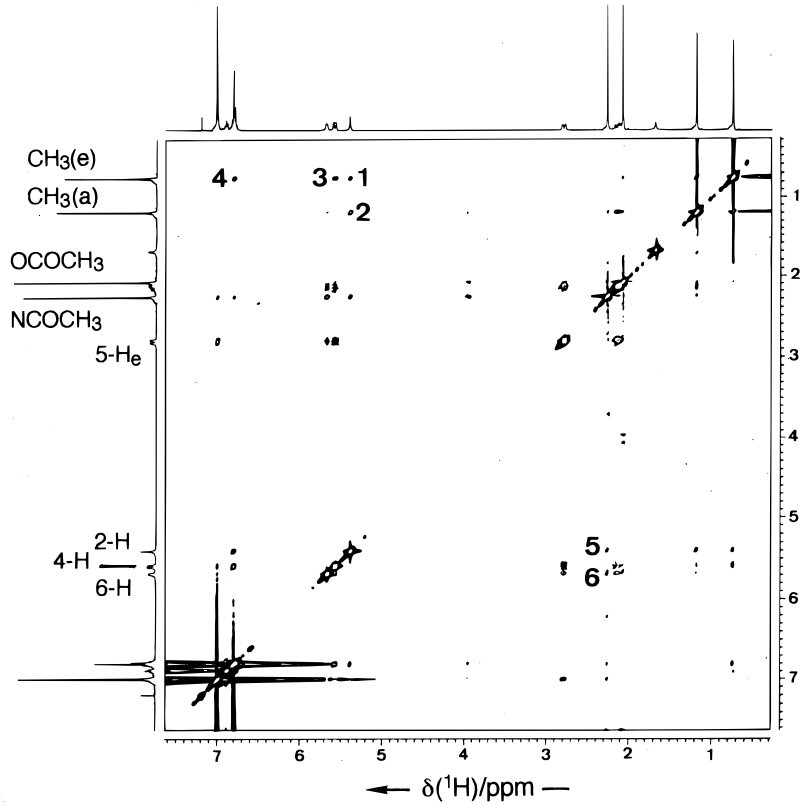


Figure 1. 270 MHz phase-sensitive ^{1}H NOESY spectrum of **6**.

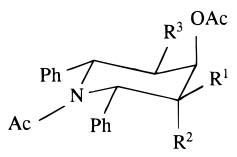
vicinal coupling constants of H-4 are characteristic of J_{aa} and J_{ae}, respectively, while the vicinal coupling constants of H-6 are characteristic of J_{ee} and J_{ea}, respectively. Indeed, of the two methylene protons, that with a coupling of 4.4 Hz with H-4 has a coupling of 2.2 Hz with H-6. All these observations show that **6** exists in the chair conformation **6B** with the following vicinal coupling constants: $J_{4a,\,5a} = 11.8$, $J_{4a,\,5e} = 4.4$ Hz and $J_{5a,\,6e} = 6.6$, $J_{5e,\,6e} = 2.2$ Hz. It is also interesting that the methyl protons, having NOEs with H-2 and H-4, have NOEs with one set of aromatic protons (signal 4) whereas the other methyl protons do not show an NOE with the aromatic protons. This also suggests conformation **6B** for **6**. Since the 3-methyl groups cannot have much influence on the vicinal coupling constants it may be assumed that the vicinal coupling constants in **7B** and **8B** will have the same values as in **6B**. The value of $J_{5a,\,6e}$ is three times that of $J_{5e,\,6e}$ although the torsional angle between the protons should be close to 60° in both cases. However, similar observations have been made. For example, in **10** the value of $J_{4e,\,5a}$ is 5.2 Hz whereas $J_{4e,\,5e}$ is only 1.8 Hz.[9]

The methyl protons of the *N*-acetyl group of **6** showed NOEs with H-2 and H-6 (signals 5 and 6), suggesting the existence of two rotamers arising due to the restricted rotation of the *N*-acetyl group. However, only an average ^{1}H NMR spectrum was obtained. Hence the two rotamers undergo interconversion at a faster rate on NMR time-scale. However, in the cases of **4** and **10** the two rotamers undergo interconversion slowly so that independent spectra are obtained for the two rotamers at room temperature. This can be explained as follows: the barriers to rotation about the C—N bond in *N*-acetylpiperidines[10] are lower than those in the corresponding *N*-nitrosopiperidines.[11] Compound **10** has no allylic strain in the chair conformation whereas in the conformation **6B** of **6** there is a 1,3-diaxial interaction between the two phenyl groups. Thus, the ground-state conformation of **6** is more strained than that of **10**. However, **6** can adopt conformation **6A** in

Table 1. Chemical shifts (ppm) and vicinal coupling constants (Hz)[a] for protons of the piperidine ring in 6–9

Compound	H-2	H-4	H-6	Methylene protons	Methine proton
6	5.47	5.68 (11.8, 4.4)	5.75 (2.2, 6.6)	2.21, 2.87	—
7	5.74 (4.4, 5.9)	5.52 (8.0, 6.0)	As H-2	1.96, 2.72	—
7[b]	5.72 (4.0, 6.2)	5.43 (8.8, 4.9)	As H-2	1.93, 2.60	—
8	5.15 (5.6)	5.59 (8.6, 6.1)	6.02 (2.7, 7.3)	2.20, 2.78	2.67 (4.7)[c]
9	5.10 (7.4)	5.65 (4.2)	As H-2	—	2.65 (4.2)[c]

[a] Vicinal coupling constants are given in parentheses.
[b] Values in DMSO-d_6.
[c] Coupling constant with H-4.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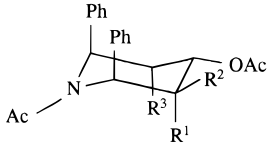
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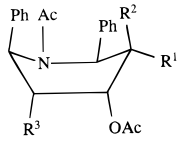
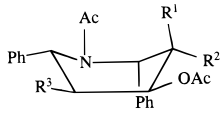

C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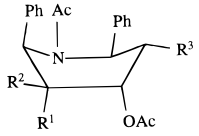
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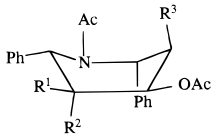
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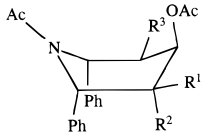
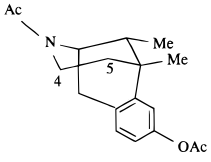
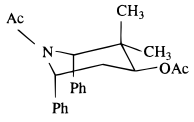
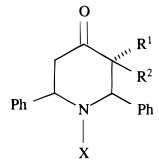

G

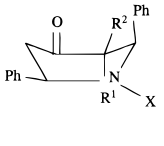
the transition state, since the *N*-acetyl group will be perpendicular to the CNC plane in the transition state. Thus, the transition states for **6** and **10** do not differ much in their internal strains. Hence the barrier to rotation is less in **6** than in **10**.

However, from an x-ray crystallographic study, *N*-nitroso-3,3-dimethyl-*r*(2),*c*(6)-diphenylpiperidin-4-one (**11**) has been shown to adopt a boat conformation (**11C**) in the solid state.[5] The analogous conformation **6E** of **6** is apparently destabilized by an Me···OAc eclipsing interaction.


10


6B





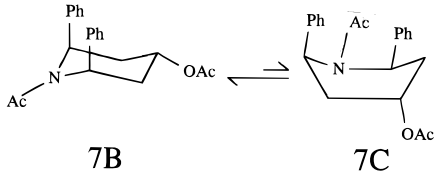
11	11C	X=NO; R^1=R^2=Me
12	12C	X=CONHPh; R^1=i-Pr; R^2=H
13	13C	X=CONHPh; R^1=Et; R^2=H

***t*(4)-Acetoxy-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine (7).** The observed vicinal coupling constants for H-4 are not characteristic of J_{aa} and J_{ae} and suggest that **7** must exist in solution as an equilibrium mixture of two or more conformations. The observed vicinal coupling constants for the benzylic proton suggest that **7B** should be the major conformation for **7**. Hence the *trans* vicinal coupling for H-4 should be 8.0 Hz. Among the methylene protons, one which has a coupling of 8.0 Hz with H-4 has a coupling of 5.9 Hz with the benzylic proton. Therefore, for the benzylic proton the *trans* and *cis* vicinal couplings are 4.4 and 5.9 Hz, respectively. The observed coupling constants should be the weighted average values of **7B** with the other conformations contributing. Since the vicinal coupling constants in **7B** may be taken as those in **6B**, it follows that in the other conformations contributing to **7**, for the benzylic proton the *trans* vicinal coupling constant should be greater than 4.4 Hz and *cis* vicinal coupling constant should be lower than 5.9 Hz. Also for H-4 the *trans* vicinal coupling constant should be less than 8.0 Hz and the *cis* vicinal coupling constant should be greater than 6.0 Hz. Only conformations **7C** and **7D** meet these requirements.

The probable values for the vicinal coupling constants of **7C** and **7D** were computed using the Karplus equation.[12] The Karplus constants for the —(AcN)CHCH$_2$ segment were calculated from the $J_{4a,\,5a}$ and $J_{4a,\,5e}$ values for **10** using the DAERM method[13] assuming $k_1/k_2 = 0.9$. These values are 13.5 and 12.2 Hz. The Karplus constants for the —CH$_2$CH(OAc) segment were calculated from the $J_{4a,\,5a}$ and $J_{4a,\,5e}$ values of **6** as 12.5 and 11.3 Hz.

We did not use the Altona equation[14] for the following reasons: we have found that in many heterocyclic systems the results obtained using simple Karplus equations[12] do not differ from those obtained using the Altona equation provided that the Karplus constants are computed from the vicinal coupling constants of suitable model compounds using the method of Slessor and Tracey.[13] Indeed, the Altona equation is not satisfactory in some cases.[15] Furthermore, the use of the Altona equation requires electronegativities of complex moieties which are not available.

In **7C** and **7D** the benzylic proton as well as H-4 are in two different environments which are interchanged in the other enantiomers. The vicinal coupling constants should be the average values for the two different environments. On one side the benzylic proton is flanked by the adjacent methylene protons and for this environment the *trans* and *cis* vicinal coupling constants were taken as 2.2 and 6.6 Hz, respectively. On the other side the coupling constants were calculated using the Karplus equation taking the torsional angle between *trans* protons as 180° and that between the *cis* protons as 60°. The calculated *trans* and *cis* vicinal coupling constants for the benzylic proton in **7C** and **7D** are 7.7


7B 7C

and 4.7 Hz, respectively. In **7C** on one side H-4 is flanked by the adjacent methylene protons and for this side the *trans* and *cis* vicinal coupling constants were taken as 2.0 and 6.0 Hz, respectively, in view of the smaller Karplus constants for the —CH_2CH(OAc) segment than for the —CH_2CH(NAc) segment. On the other side the vicinal coupling constants for H-4 were calculated taking the torsional angle between the *trans* protons as 120° and that between the *cis* protons as 0°. The calculated *trans* and *cis* vicinal coupling constants of H-4 in **7C** are 2.4 and 8.5 Hz, respectively. In **7D** these coupling constants were calculated as 6.9 and 7.3 Hz.

Calculations showed that the observed vicinal coupling constants of **7** could be accounted for by an equilibrium mixture of **7B** and **7C** in the ratio 3:2. The calculated vicinal coupling constants for this situation are $J_{trans(\text{benzylic})} = 4.4$ Hz, $J_{cis(\text{benzylic})} = 5.8$ Hz, $J_{trans(\text{H-4})} = 8.0$ Hz and $J_{cis(\text{H-4})} = 6.0$ Hz. These values are in excellent agreement with the observed values.

The confidential limits of the relative populations of **7B** and **7C** could be obtained by considering distortion of **7C** to a reasonable extent. However, for the distorted boat form *cis* vicinal coupling constants could not be computed using the Karplus equation when one proton is flanked by two adjacent methylene protons. Therefore, only *trans* vicinal coupling constants could be used for obtaining the confidential limits for the relative populations of **7B** and **7C**. For this the possible limiting values of either $J^{\text{boat}}_{trans(\text{benzylic})}$ or $J^{\text{boat}}_{trans(\text{H-4})}$ should be computed.

Examination of literature data[5,6] suggested that the lower limiting value of $J^{\text{boat}}_{trans(\text{benzylic})}$ could be computed from the vicinal coupling constants of *N*-phenylcarbamoyl-*t*(3)-isopropyl-*r*(2),*c*(6)-diphenylpiperidin-4-one (**12**). The reported vicinal coupling constants of **12** are $J_{2,3} = 1.72$ Hz, $J_{5,6(trans)} = 11.97$ Hz and $J_{5,6(cis)} = 5.18$ Hz. However, the reported vicinal coupling constants about the C(5)—C(6) bond are only apparent values and their correct values were computed using second-order analysis as 12.3 and 4.9 Hz, respectively. These coupling constants strongly suggest that **12** exists largely in conformation **12C** in solution. It is also interesting that the x-ray data reported for *N*-phenylcarbamoyl-*t*(3)-ethyl-*r*(2),*c*(6)-diphenylpiperidin-4-one (**13**) are consistent with boat conformation **13C**. A detailed discussion of the coupling constants of **13** and other compounds[6] is outside the scope of this paper.

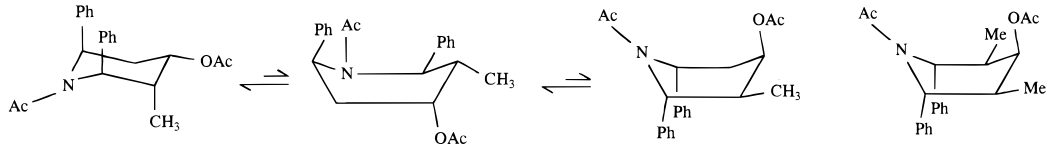
We have found that the vicinal coupling constants in 4-hydroxypiperidines[16] are not much different from those in the corresponding piperidin-4-ones. In both **7** and **12** the functional nature of N-1 is only amide. Hence, the average of the value of $J_{5,6(trans)}$ and $J_{2,3}$ in **12C** may be taken as $J^{\text{boat}}_{trans(\text{benzylic})}$ in **7C**. If an alternative chair conformation makes some contribution to **12** in solution, the average J_{trans} value of **12C** should be higher than the observed value. Therefore, it is obvious that the average J_{trans} value in **12C** should be 7.0 Hz [(12.3 + 1.7)/2] or higher. Taking the lower limiting value of $J^{\text{boat}}_{trans(\text{benzylic})}$ as 7.0 Hz, the minimum possible population of **7B** was calculated as 54%.

The lower limiting value of $J^{\text{boat}}_{trans(\text{H-4})}$ could be computed by considering possible distortions about C(3)—C(4) and C(4)—C(5) bonds. Distortion of the fragment where the torsional angle between the *trans* protons is 120° should only increase the coupling constant. However, increase in the torsional angle between the *trans* protons in the other fragment should decrease the *trans* vicinal coupling constant. Taking the *trans* vicinal coupling in this fragment as 0, the lowest possible $J^{\text{boat}}_{trans(\text{H-4})}$ was computed as 1.4 Hz. From the observed $J_{trans(\text{H-4})}$ value, the maximum possible relative population of **7B** was calculated as 63.5%. The relative population of **7B** may, therefore, be taken as 59 ± 5%. Thus, the lowest energy conformation of **7** should be **7B**. Considering the entropy of mixing for **7C**, the energy difference between **7B** and **7C** should be higher than appears from the relative populations alone.

The vicinal coupling constants of **7** in DMSO-d_6 suggest that **7B** is more populated in DMSO-d_6 than in $CDCl_3$. This is probably due to a decrease in the electrostatic repulsion between the π electrons of the axial phenyl groups of **7B** in the more polar solvent DMSO-d_6.

***t*(4)-Acetoxy-*t*(3)-methyl-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine (8).** The vicinal coupling constants about the C(4)—C(5) bond suggest that **8** should exist as a mixture of two or more conformations. The major conformation may be **8B**, **8C**, **8D** or **8F**. If **8B** or **8F** is the major conformation the value of 8.6 Hz must correspond to the *trans* vicinal coupling. On the other hand, if **8C** or **8D** is the major conformation, the value of 8.6 Hz must correspond to **cis** coupling. In **8D** there is allylic strain on one side and also the methyl group is in the flagpole position. Moreover, **7D** does not seem to make any contribution to **7**. Hence **8D** cannot be the major conformation for **8**. In **8F**, the vicinal coupling constant between H-3 and H-4 should be around 10 Hz. The observed vicinal coupling constant between these two protons is only 4.7 Hz and, therefore, **8F** cannot be the major conformation. In **8B** and **8C** for H-6 the *trans* vicinal coupling constant may be taken as 2.2 Hz and the *cis* vicinal coupling constant may be taken as 6.6 Hz. Therefore, among the two vicinal coupling constants observed for H-6 the value of 2.7 Hz must correspond to the *trans* vicinal coupling. The proton at C-5 having a coupling of 2.7 Hz with H-6 has a coupling of 6.1 Hz with H-4. Therefore, among the two vicinal coupling constants about C(4)—C(5) bond the value of 6.1 Hz should correspond to a *cis* vicinal coupling. Hence, it follows that **8B** should be the major conformation. This should be expected based on the following considerations also: compared with **7B**, in **8B** there is one Me···H *syn*-axial interaction. In **8C** there is one Ph–Me *gauche* interaction. These two interactions should be of comparable energy and the energy difference between **7B** and **7C** should be very nearly the same as that between **8B** and **8C**. Further, both **8B** and **8C** exist as pairs of enantiomers whereas in the case of **7** only **7C** exists as a pair of enantiomers.

Since in **8B** the value of $J_{4a,5a}$, $J_{4a,5e}$, $J_{5e,6e}$ and $J_{5a,6e}$ may be taken as those in **6B**, it is obvious that in the next important conformation of **8** among the two vicinal coupling constants about the C(4)—C(5) bond the *trans* coupling constant should be lower than 8.6 Hz and the *cis* vicinal coupling constant should be greater than 6.1 Hz. Although **8C** and **8D** meet these require-



8B 8C 8G 9G

ments, conformation **8D** has already been ruled out based on energy considerations. Furthermore, in **8D** the *trans* vicinal coupling constant for H-6 should be around 12 Hz whereas the vicinal coupling constant for H-2 should be small. In **8C** the situation is the reverse. The observed vicinal coupling constant for H-2 is 5.6 Hz whereas the *trans* vicinal coupling constant for H-6 is only 2.7 Hz. Hence it is obvious that **8C** should be the next important conformation. However, both the vicinal coupling constants for H-6 are slightly higher than those expected for **8B** and **8C**. This cannot be due to some distortion of **8B** and **8C** since such a distortion should decrease one vicinal coupling but increase the other. Hence one more conformation should be present to a small extent. Since this could only be a minor conformation it should have $J_{5,6(trans)}$ value much higher than 2.7 Hz and a $J_{5,6}(cis)$ value much higher than 6.6 Hz. Only conformation **8G** with some distortion about the C(5)–C(6) bond could have such vicinal couplings. Such a distortion in **8G** will decrease the interactions between the axial-like phenyl groups. Detailed calculations showed that the observed vicinal coupling constants could be accounted for by a mixture of 65% of **8B**, 24% of **8C** and 11% of **8G** with a distortion of 15° about the C(2)—C(3) and C(5)—C(6) bonds. The calculated vicinal coupling constants for this possibility are $J_{2,3} = 5.3$ Hz, $J_{4,5(trans)} = 8.6$ Hz, $J_{4,5(cis)} = 6.2$ Hz, $J_{5,6(trans)} = 2.7$ Hz and $J_{5,6(cis)} = 7.1$ Hz. These are in excellent agreement with the observed values. Further, in all these conformations the torsional angle between H-3 and H-4 is around 60° and the observed vicinal coupling constant of 4.7 Hz between these two protons also is consistent with the proposed conformational equilibrium. In view of the good agreement between the calculated and observed vicinal coupling constants, the calculated relative populations should be accurate to within ± 5%.

Since the Ph···Me *gauche* interaction in **8C** is relieved in **8G**, the energy difference between **8C** and **8G** is smaller than that between **7C** and **7G** so that **8G** makes detectable contribution to **8**.

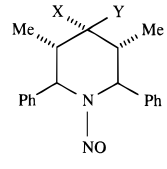
***t*(4)-Acetoxy-*t*(3),*t*(5)-dimethyl-*r*(2),*c*(6)-diphenyl-*N*-acetylpiperidine (9).** The results for **6**, **7** and **8** strongly suggest that only conformations **B**, **C** and **G**, which do not have allylic strain, are important. The observed coupling constants of **9** could then be accounted for only by conformation **9G** with a distortion of 20° about the C(2)—C(3) and C(5)—C(6) bonds. The calculated value for the vicinal coupling constant of the benzylic proton is 7.6 Hz, which is in good agreement with the observed value. In **9G** the torsional angle between H-4 and the adjacent proton (H-3 or H-5) should be around 60°. The calculated torsional angle is 51°. Thus, the preferred conformation of **9** should be **9G**.

In the case of **8** the energies of the conformations increase in the order **8B** < **8C** < **8G**. However, the presence of an additional axial methyl group in **9B** introduces an Me···Me *syn*-axial interaction which increases the energy of this conformation substantially. In **9C** the additional methyl group introduces an Me···OAc eclipsing interaction. In **9G** the additional methyl group does not introduce any interaction. Therefore, **9G** should be the preferred conformation for **9**.

It is of interest to discuss the conformations of *N*-nitroso-4-hydroxypiperidines **14** and **15**. From the vicinal coupling constants it has been shown that **14** adopts the boat conformation **14C** whereas **15** adopts the chair conformation **15A**.[5] Obviously, conformation **15C** is destabilized by an Me···OH eclipsing interaction. However, **9A** is not the preferred conformation of **9**, because in **15A** there is allylic strain in only one side whereas in **9A** there are allylic strains in both the sides.

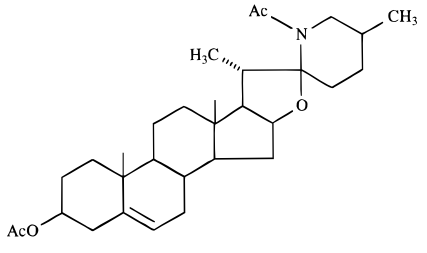
Conformation of the piperidine ring in *N*-acetylsolasodine (16)

The vicinal coupling constants about the C(α)—C(β) bond in **16** are 6.1 and 2.6 Hz.[7] These coupling constants have been interpreted in terms of a flattened chair conformation for the piperidine ring with H—C—C—H torsional angles of 150° and 30°. The calculated vicinal coupling constants for these angles are 9.8 and 8.8 Hz, respectively. Indeed, we have observed similar values for the vicinal coupling constants in one case.[16] Therefore, the conformation proposed for **16** is not correct. The observed vicinal coupling constants could be better accounted for by the boat conformation **16a** without allylic strain. The methine proton (H-3) is flanked

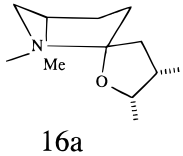


14; X=H; Y=OH

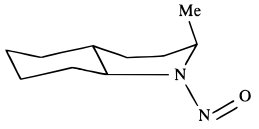
15; X=OH; Y=H



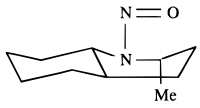
16



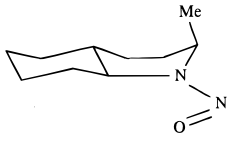
16a



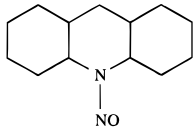
3a



3b



3c



17

between the two adjacent α-protons and both the H—C—C—H torsional angles should be around 60°.

Conformation of *N*-nitroso-2-methyl-*trans*-decahydroquinoline (3)

Conformations **3a** and **3b** have been proposed for the two forms of **3**. In both of these conformations the nitroso group is *syn* to C-2, i.e. both have an *E* configuration. These two conformations should undergo interconversion at a faster rate through a boat–chair–boat conversion. The reported coalescence temperature of 130 °C is not consistent with this possibility. Indeed, the *Z* form of **3** can also exist without allylic strain in conformation **3C**. Therefore, the two forms observed are only *E* and *Z* forms. Of course, *E* can adopt two conformations which undergo interconversion at a faster rate.

It is also interesting that in the case of *N*-nitroso-*trans-syn-trans*-perhydroacridine (**17**)[3] the interconversion between the two equivalent forms occurs at a much faster rate so that even at −30 °C the carbon signals are broad. Indeed, **17** has to exist with all the three rings in the chair conformation and therefore should possess allylic strain. Since the barrier to rotation is less for **17** than for **3**, it is obvious that the conformations of **17** are more strained than those of **3**. This is in agreement with the conclusions reached from this study that boat conformations without allylic strain should be more stable than chair conformations with allylic strain.

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