The Conformations of Tetra- and Hexahydropyridazines. Slow Ring Inversion and Slow Nitrogen Inversion[1a]

J. Edgar Anderson[1b]

Contribution from the Institut de Chimie, Université de Strasbourg,[1c]
Gates and Crellin Laboratories of Chemistry, California Institute of Technology,[1d]
and Department of Chemistry, University College, London, W.C.1, England.[1e]
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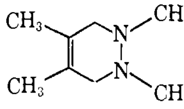
Abstract: The proton nmr spectra of several tetra- and hexahydropyridazines have been studied as a function of temperature. At low temperatures **1**, **12**, and **19** show two distinct regions where coalescences occur, indicating that both ring inversion and nitrogen inversion have become slow on the nmr time scale. It is concluded that the preferred conformations of these three compounds have one N-methyl group equatorial and one axial. The barrier to ring inversion is smaller than the barrier to nitrogen inversion. All other compounds studied show only one region of signal coalescence. In the case of **13** and **14**, these correspond to nitrogen inversion. **15** appears to prefer a conformation with both N-methyl groups equatorial. The implications of these differences of conformational behavior are discussed.

Variations with temperature of the proton nmr spectra of some tetra- and hexahydropyridazines have been reported recently.[2] Thus, 1,2,4,5-tetramethyltetrahydropyridazine (**1**) has an nmr spectrum at room temperature comprising three singlets of relative intensities 2:3:3. From low to high field, these three signals correspond to the methylene groups, the N-methyl groups, and the methyl groups attached to the double bond, respectively. In the spectrum taken at −44°, the signal of the methylene group is an AB quartet while the other signals are as at room temperature. It was concluded that, as the temperature is lowered, either ring inversion or nitrogen inversion becomes slow on the nmr time scale, but it was not possible to decide between these possibilities from the available evidence.



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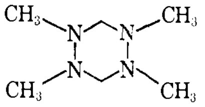

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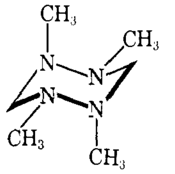

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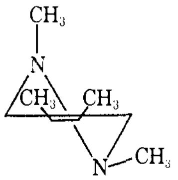
More recently, it has been shown[3] that 1,2,4,5-tetramethylhexahydrotetrazine (**2**) has **3** as its preferred conformation, and that, at −87°, both ring inversion and nitrogen inversion are slow on the nmr time scale.

Obvious similarities between **2** and the tetra- and hexahydropyridazines have prompted an extension of the original study of the latter compounds. In particular it was hoped that by taking spectra at temperatures considerably below −60° (the lower limit at the time of the earlier work), we might observe the slowing of the second possible process, and thence draw more definite conclusions on the conformations and conformational mobility of these compounds.

Conformational Considerations. There is much to be gained from a careful consideration of the possible conformations of a molecule such as **1**. The preferred conformation may be **4** with one N-methyl group axial and the other equatorial, as suggested by what is known of the conformation of **2**. Other conformations which deserve consideration are **5**, with two equatorial N-methyl groups, and **6**, with two axial N-methyl groups.



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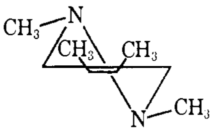

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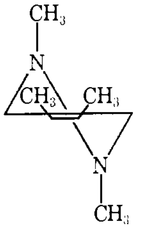

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In the case of **4**, the possible conformational processes are summarized in Figure 1 while those for **5** and **6** are summarized in Figure 2. In Figure 2, the "unequal" signals predicted when both processes are slow would arise from **5** and **6**, although there may be very little of one of these forms present, in which case only one singlet and one AB quartet would be observed. By contrast, in Figure 1, the two signals, predicted for each group when both processes are slow, come from one single molecule, and not from two different molecules, as is the case in Figure 2, so these signals will be of equal intensity.

In considering that the conformation **4** with one N-methyl group axial, may be the most stable, we are allowing in effect that the conformation of the hydrazine system may be more important than the conformation

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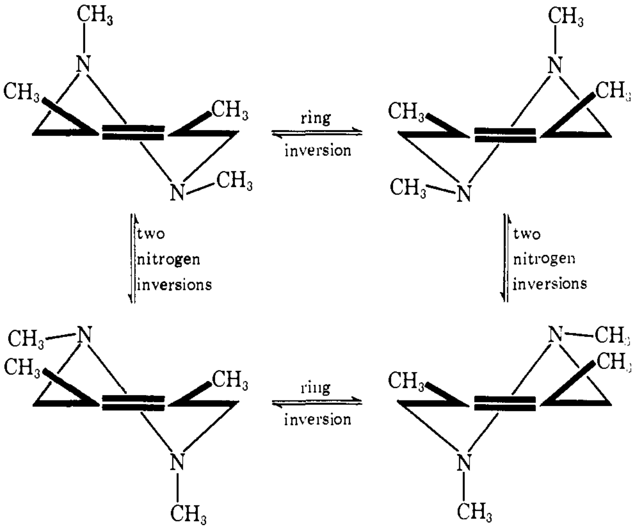
[1] (a) Supported in part by the National Science Foundation; (b) Salters' Fellow, Université de Strasbourg, 1964–1966. Harkness Fellow of the Commonwealth Fund of New York, California Institute of Technology, 1966–1968; Ramsay Fellow, University College, 1968–1970; (c) laboratory associated with the Centre National de la Recherche Scientifique; (d) Contribution No. 3874; (e) to where correspondence should be addressed.

[2] J. E. Anderson and J. M. Lehn, *Bull. Soc. Chim. Fr.*, 2402 (1966).

[3] J. E. Anderson and J. D. Roberts, *J. Amer. Chem. Soc.*, **90**, 4186 (1968).



	N-Methyl signal	Methylene group signal
Fast ring and nitrogen inversion	Singlet	Singlet
Slow ring inversion and fast nitrogen inversion	Singlet	AB quartet
Fast ring inversion and slow nitrogen inversion	Singlet	AB quartet
Slow ring and nitrogen inversion	1:1 doublet	Two equal intensity AB quartets

Figure 1. Predicted nmr spectra of **1** in various conformational situations on the assumption that the most stable conformation is **4**.

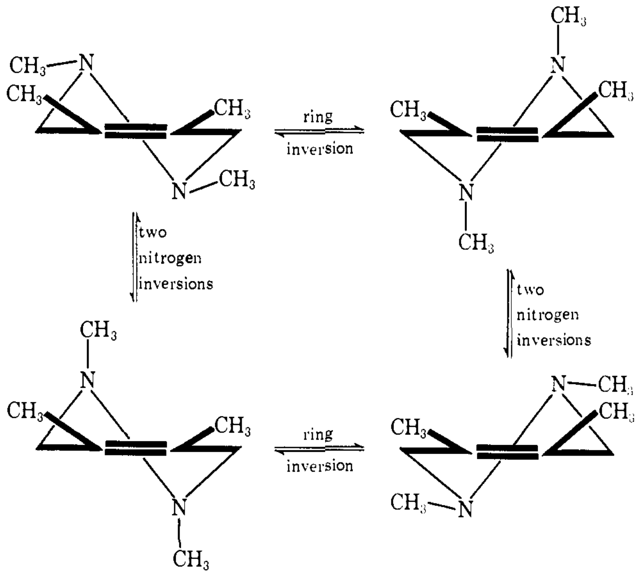
("axial" or "equatorial") with respect to the rest of the ring.

We have assumed here that the two nitrogens invert in one single process. If the two nitrogen inversions actually take place independently of each other, a more complex system comprising all the conformations in Figures 1 and 2 would be more correct. However, in all the work reported, there is no evidence of the simultaneous occurrence of forms with equivalent (**5** and **6**) and nonequivalent (**4**) N-methyls so that the more simple diagrams of Figures 1 and 2 appear to suffice.

For each of the other compounds considered in this paper it is possible to draw similar diagrams and to predict possible spectral changes. Comparison of experimentally observed changes with these predictions allows conclusions to be drawn about the conformations these various molecules prefer to adopt.

There is some information in the literature which has a bearing on the present work. The preferred conformation of hydrazine has a dihedral angle of 90–95°.[4] The conformation preferred by hydrazine with four alkyl substituents may be somewhat different from this to accommodate steric interactions, but presumably the dihedral angle will still be close to 90°. An examination of molecular models suggests that the dihedral angle in **4** is slightly less than 90°, in **6** it is substantially less than 90°, while that in **5**, about 180°, is considerably greater. Thus, considered only in terms of the hydrazine moiety, **4** with one axial and one equatorial methyl group is most favored.

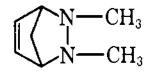
In only one case has the barrier to inversion of an acyclic tetraalkylhydrazine been measured, Anderson, Griffith, and Roberts[5] finding a barrier of 6.8 kcal/mol to inversion of the nitrogen bearing the benzyl group in benzyltrimethylhydrazine.



	N-Methyl signal	Methylene group signal
Fast ring and nitrogen inversion	Singlet	Singlet
Slow ring inversion and fast nitrogen inversion	Singlet	AB quartet
Fast ring inversion and slow nitrogen inversion	Singlet	AB quartet
Slow ring and nitrogen inversion	Two singlets of unequal intensities	Two AB quartets of unequal intensities

Figure 2. Predicted nmr spectra of **1** in various conformational situations on the assumption that the most stable conformation is **5** or **6**.

Compound **7**, a bicyclic hydrazine with no possibility for ring inversion, exists as an equilibrium mixture of forms **8** and **9**, and has a barrier to nitrogen inversion of 14.5 kcal/mol.[6,7] In **2** the barrier to nitrogen inversion is at least 11.7 kcal/mol.[3] Compound **10** exists as an equilibrium mixture of **11** and its enantiomeric form.[8]



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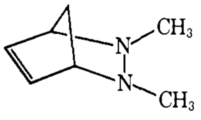

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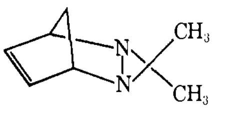

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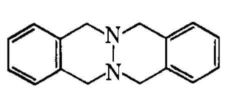

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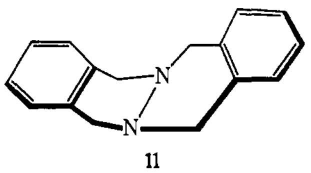

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Ring inversion and nitrogen inversion are both slow on the nmr time scale at −53°, and the barrier to nitrogen inversion is 12.4 kcal/mol. If we accept benzyltrimeth-

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[4] A recent summary of experimental and theoretical evidence is given in A. Veillard, *Theor. Chim. Acta*, **5**, 413 (1966).

[5] J. E. Anderson, D. L. Griffith, and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 6371 (1969).

[6] J. E. Anderson and J. M. Lehn, *ibid.*, **89**, 81 (1967).

[7] E. L. Allred, C. L. Anderson, R. L. Miller, and A. L. Johnson, *Tetrahedron Lett.*, 525 (1967).

[8] B. Junge and H. A. Staab, *ibid.*, 709 (1967).

Table I. Coalescence Temperatures (T_c) and Free Energies of Activation ($\Delta G^{\ddagger}{}_{T_c}$) for Inversion Processes Involving Tetra- and Hexahydropyridazines

		CF_2Cl_2 soln		CD_3OD soln		$CDCl_3$ soln[a]	
Compd	Signal	T_c, °C	$\Delta G^{\ddagger}{}_{T_c}$, kcal/mol	T_c, °C	$\Delta G^{\ddagger}{}_{T_c}$, kcal/mol	T_c, °C	$\Delta G^{\ddagger}{}_{T_c}$, kcal/mol
1	N-CH_2	−14.5	12.3[b]	−13	12.4[b]	−12	12.4[b]
	N-CH_3	−111.5	8.2[c]	−92	9.5[c]		
19	N-CH_2	−11	12.4[b]	−16	12.2[b]		
	N-CH_2	−100[d]	8.3[c,d]	−87[d]	9.1[c]		
12	N-CH_2	−20	12.0[b]	−15	12.3[b]		
	N-CH_3	−109	8.5[c]	[e]	[e]		
13	N-CH_3	−35	12.0[b]	−33	12.3[b]		
	C-CH_3			−41	11.7[b]		
14	N-CH_3	−1	13.3[b]			+1	13.4[b]
15	N-CH_2	−30	11.6	−20	12.1		
20	N-CH_2	−25	11.9	−12	12.5		
16	N-CH_3	−46.5	12.5	−48	12.3	−44	12.3
	C-CH_3	−31	12.4	−39	12.0	−35	12.4
17	N-CH_3	[f]	[f]	−46.5	11.7		
	C-CH_3	−39	11.5	−36.5	11.6		
18	N-CH_3					−44	11.1

[a] From ref 2, adjusted where necessary for transmission coefficient of $^1/_2$. [b] Process concluded to be nitrogen inversion (see text). [c] Process concluded to be ring inversion (see text). [d] From a computer fit so that values given are not exactly T_c, but a temperature close to T_c at which matching experimental and calculated spectra were obtained. [e] Not observed by the lowest temperatures attainable. [f] Peaks remain a singlet to lowest temperatures. This is probably due to a coincidence of chemical shifts.

ylhydrazine through its acyclic nature to be of less relevance to the compounds studied here than the cyclic hydrazines **2**, **7**, and **10**,[9] then the barrier to nitrogen inversion that we would expect to find for **1** is between 11 and 15 kcal/mol.

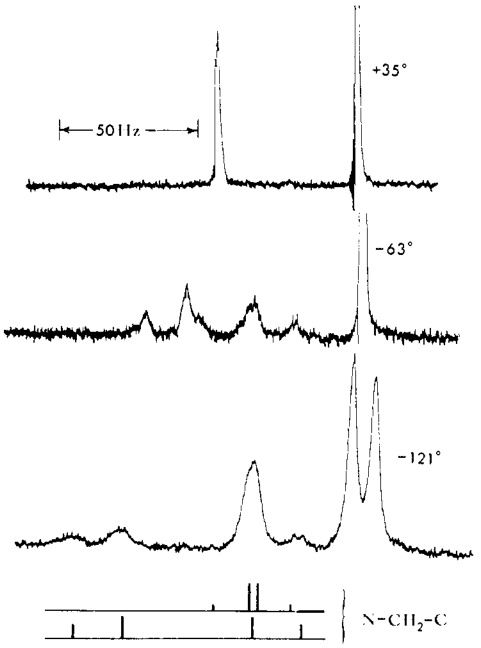

Figure 3. Proton nmr spectra of 1,2-dimethyl-Δ^4-tetrahydropyridazine (**12**) at several temperatures. Only the N-methyl and N-methylene resonances are shown. The resonance assignments which account for the two superimposed N-CH_2-C AB quartets at −121° are indicated at the bottom of the figure.

The barriers to ring inversion of cyclohexene and cyclohexane, the parent ring systems of **1** and its saturated analog, are distinctly different, being 5.4 kcal/mol[10] and 10.3 kcal/mol,[11] respectively, while the barrier to ring inversion of **2** is 11.7 kcal/mol.[3]

Results

The details of the spectral measurements are given in the Experimental Section; we give here only an outline of the significant changes of spectra observed for **1** and **12** to **20**. The solvents were dichlorodifluoromethane or perdeuteriomethanol. Earlier[2] the solvent was deuteriochloroform, but this solvent freezes around −70°, so it was not used for this work.

As mentioned earlier,[2] on cooling **1** to −44°, the slightly broadened singlet absorption of the methylene hydrogens becomes an AB quartet, while other absorptions are essentially unchanged. At lower temperatures additional changes are observed. The N-methyl peak broadens and splits below −111.5° (for a CF_2Cl_2 solution) to a 1:1 doublet, the components of which have relative chemical shift 0.18 ppm (10.5 Hz at 60 MHz). At the same time the AB quartet from the methylene hydrogens changes markedly, and at −118° appears as four broad lines which we conclude are two overlapping AB quartets, one of which has very similar A and B chemical shifts. These changes are almost identical with those of **12** which are shown in Figure 3. The free energies of activation for the processes involved have been calculated at the respective coalescence temperatures and are listed along with those of the other compounds studied in Table I. For **1** in CF_2Cl_2 solution the barriers are $\Delta G^{\ddagger}{}_{-14.5}$ = 12.3 kcal/mol for the high-temperature process (from the collapse of the AB quartet) and $\Delta G^{\ddagger}{}_{-111.5}$ = 8.2 kcal/mol for the low-temperature process (from the collapse of the N-Me doublet). At −118°, the N-CH_3 signals and methylene signals of **1** almost overlap, so **19** was prepared and studied. With this substance, the changes in the methylene signals can be followed without interference, and they confirm the interpretation for changes of the spectrum of **1**. A computer fit to these changes in terms of two AB quartets coalescing to one AB quartet gave a free energy of activation for the low-temperature process of 8.3 kcal/mol at about −100°.

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(9) See ref 5 for a detailed discussion of this point.

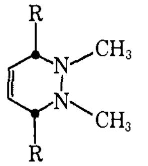
(10) F. A. L. Anet and M. Z. Haq, *J. Amer. Chem. Soc.*, **87**, 3147 (1965).

(11) F. A. L. Anet and A. J. R. Bourn, *ibid.*, **89**, 760 (1967), and earlier references therein.

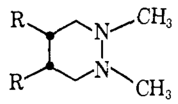
Table II. Proton Chemical Shift and Coupling Data of Relevant Nmr Signals at Ambient and Low[a] Temperatures of Tetra- and Hexahydropyridazines[b,c] in Dichlorodifluoromethane

	Low	$N\text{-}CH_3$		$N\text{-}CH_2$ or $N\text{-}CH$		$C\text{-}CH_3$	
Compd	temp, °C[a]	Ambient	Low[a]	Ambient	Low[a]	Ambient	Low[a]
12	−63	2.36 s	2.30 s	3.13 d (J = 0.9)	3.11 bq (δ_{AB} 34.0, J_{AB} = 16.0)		
1	−45	2.29 s	2.21 s	3.00 bs	2.93 bq (δ_{AB} ∼37.5, J_{AB} ∼ 14.1)	1.59 bs	1.58 bs
19	−40			2.96 s	2.86 q (δ_{AB} 39.6, J_{AB} = 15.0)	1.59 s	1.54 bs
13	−52	2.39 s	2.31 d (δ 9.8)	2.94 m	2.89 m	1.16 d (J = 6.55)	1.16 d,d (δ 9.2, J_1 = 6.75, J_2 = 6.46)
14	−35	2.40 s	2.35 d (δ 27.4)	4.05 d (J = 1.2)	3.96 bm		
15	−70	2.33 s	2.24 s	2.59 m	2.38 bq (δ_{AB} ∼ 30, J_{AB} ∼ 11.3)		
20	−75			2.56 m	2.48 bq (δ_{AB} 22.6, J_{AB} = 10.5)		
16	−51	2.29 s	2.37 d (δ 0.9)	2.37 m	2.54 m	0.89 d	0.94 d,d (δ 7.6)
17	−78	2.38 s	2.39 d	2.74 m	2.72 m	1.09 d (J = 6.5)	1.09 d,d (δ 20.7, J_1 = 6.75, J_2 = 6.2)

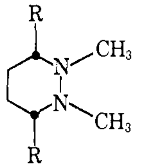
[a] "Low" temperature is suitably below the *first* coalescence to give reasonably sharp lines. [b] Chemical shifts of main lines or averages of groups of lines are in ppm downfield from tetramethylsilane. Relative chemical shifts of signals in multiplets are in Hz at 60 MHz. All couplings (J) are in Hz. [c] The code for descriptions of lines is: s = singlet, d = doublet, q = quartet, m = multiplet, b = broad.



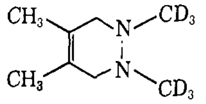
12, R = H
13, R = CH_3
14, R = C_6H_5



15, R = H
16, R = CH_3



17, R = H
18, R = C_6H_5



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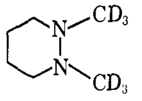

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Only one other compound studied showed evidence of slowing of two conformational processes as found for **1**, the rather similar **12**. The changes are analogous to those found for **1** and are shown in Figure 3. The barriers for CF_2Cl_2 solution were $\Delta G^{\ddagger}_{-20}$ = 12.0 kcal/mol for the high-temperature process and $\Delta G^{\ddagger}_{-109}$ = 8.5 kcal/mol for the low-temperature process.

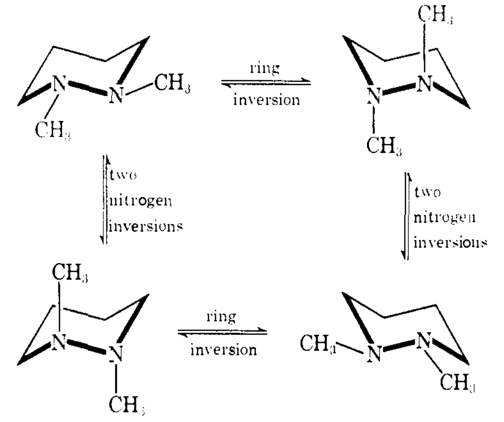
The two N-methyl signals observed at lowest temperatures for **2** and **12** are of equal intensity, so it is unlikely that they arise from two different forms, but rather correspond to single conformations in which the two methyl groups are different. Since there is no unsymmetrical substitution on the ring, this can only mean that the preferred conformation of **1** and **12** is like **4**, with one N-methyl group axial and one equatorial.

The other compounds studied show only one set of changes in the nmr spectrum which occur above −50° at the lowest (see Table II). The lowest temperatures attained were −150° in CF_2Cl_2 solution and about −120° in deuteriomethanol solution.

Compound **15** is particularly important, for in it, unlike **13**, **14**, **16**, **17**, and **18**, there are no extraneous substituent interactions, but relative to **12** there are additional 1,3 interactions arising from the saturation of the double bond. The torsional interactions will also be different, but in comparison with 1,3 interactions the differences will be small. The N-methylene signal of **15** splits to an AB quartet (broadened due to further coupling) below −30° and remains unchanged thereafter to −150°. The N-methyl signal is a singlet even at −150°. Since these signals are close in the spectrum, the deuterated compound **20** was prepared and examined. The N-methylene signal, which in **1** and **12** shows marked changes as the low-temperatures process becomes slow, shows no change below −30°, in line with the results for **15**. The possibility that, by chance at low temperatures, two AB quartets for the N-methylene and two singlets for the N-methyls overlap can be excluded.

Discussion

In summary, the observed results are that while **1**, **12**, and **19** show nmr evidence of slowing of two conformational processes, the evidence for **15** and **20** suggests slowing of only one conformational process. This conclusion must be qualified to the extent that in the case of **15** and **20** two equilibration processes, ring and nitrogen inversion, *should* be taking place, the results implying therefore that one of these equilibria is too far on one



	N-Methyl signal	N-Methylene signal
Fast ring and nitrogen inversion	Singlet	Singlet
Slow ring inversion and fast nitrogen inversion	Singlet	AB quartet
Slow nitrogen inversion and fast ring inversion	Singlet	AB quartet
Slow ring and nitrogen inversion	Two singlets in different amounts	Two AB quartets in different amounts

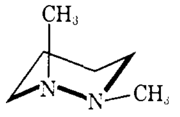
Figure 4. Predicted nmr spectra of **15** in various conformational situations on the assumption that the most stable conformation is **22** and neglecting all couplings of the —CH_2–N groups to the directly attached C–CH_2–C groups.

side to give measurable spectral changes with temperatures. The same applies in a slightly different way to the compounds **13**, **14**, **16**, **17**, and **18**. One equilibrium will again be very much displaced to one side but now because of the dissymmetry introduced by the substituents in the molecule. Again only one set of spectral changes is expected to be observable. To clarify the point, consider as an analogy the nmr spectrum of *trans*-1,2-dimethylcyclohexane which does not change with temperature.[12] This fact does not require that ring inversion of this compound fails to take place, but only that one conformation, that with the two methyl groups equatorial, is much more stable than the other. The spectrum observed when ring inversion is fast on the nmr time scale is the weighted average of the spectra of the two separate forms, to which the more stable conformation contributes much more than 99%. When ring inversion is slow on the nmr time scale, the spectrum of the less stable form is likely to be of so weak an intensity as to be undetectable, and only the spectrum of the more stable conformation is observed, and this is essentially identical with the fast-exchange spectrum. Thus, no change in the spectrum is observed, but ring inversion can be taking place at ordinary temperatures and can be slow on the nmr time scale at the lower temperatures studied.

We have already indicated our reasons for concluding that the most stable conformation of **1** is **4** (or its enantiomeric form).[13] Let us now assign the respective identities of the two processes taking place in this molecule. The barriers to these processes are 12.3 and 8.2 kcal/mol at the respective coalescence temperature. The high barrier is in line with those found for **2**, **7**, and **10** (11.7–14.5 kcal/mol)[3,6,8] and inconsistent with the barrier to ring inversion of cyclohexene (5.4 kcal/mol).[10] The low barrier is more consistent with the barrier to ring inversion than with the barrier to nitrogen inversion.

For **1** then, it seems reasonable that the process with a high barrier is nitrogen inversion and that with the low barrier is ring inversion. The same conclusions apply directly to **12** and **19**.

In the case of **15** only one set of changes is observed. The barrier to ring inversion should be rather higher than that for **1** since the ring is now saturated (*cf.* cyclohexane and cyclohexene above), so there seems to be no reason why slow ring inversion should not be observed. Likewise, if the conformation of **15** were as in **21**, there is no reason why nitrogen inversion should not be observed. To explain this failure to observe a second process, it is necessary to postulate that the preferred conformation changes to either **22** or **23**. In terms of **22** being the stable conformation (rather than **23**), as presented in Figure 4, both ring and nitrogen inversions are taking place and both are presumably slow at low temperatures, but the form with two axial N-methyl groups is present in such a small amount that only one singlet and one AB quartet can be detected, and only one set of changes in the spectrum is seen as the temperature is lowered. It will be noted further from Figure 4 that the spectra predicted for slow ring inversion–fast nitrogen inversion and for slow nitrogen inversion–fast ring inversion are the same, so that it is not possible to assign the barrier measured for this compound to either of these processes.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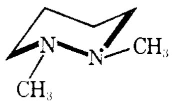
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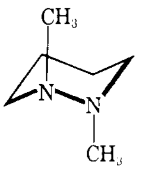
23

We are saying then, by analogy with **1**, that both ring and nitrogen inversion should be slow in **15** at low temperatures. Because we only see one process in **15**, there must be a considerable difference between it and **1**, and this difference is a change to a preferred conformation which has the two N-methyl goups identical, *i.e.*, **22** or **23**.

We can justify the choice of **22** rather than **23** as the stable conformation. In going from the unsaturated compound **10** to the saturated compound **15**, the largest change as far as conformational energy is concerned is the additional 1,3-diaxial nonbonded interactions. If, as seems reasonable, these interactions are the cause of the change in conformation of the N-methyl groups, then the preferred conformation of **15** must be **22** in which these interactions are at a minimum. Nonbonded interactions in **4**, the preferred conformation of **1**, are likely to be small. The axial hydrogen on the same side of the molecule as the axial N-methyl group is

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(12) N. Muller and W. C. Tosch, *J. Chem. Phys.*, 37, 1167 (1962).

(13) A referee has suggested that the "rabbit-ear effect" (R. O. Hutchins, L. Kopp, and E. L. Eliel, *J. Amer. Chem. Soc.*, 90, 7174 (1968)) may also be relevent here, because unfavorable interactions between π electrons of the double bond and the unshared electrons on nitrogen could lead to a preference for an axial N-methyl group. This effect would operate as suggested in **1**, **12**, and **19**, but not in **15** and **20**. This, the "normal conformational preference" of the hydrazine system would be accentuated in **1**, **12**, and **19**, but in **15** and **20**, where this preference is expected to be opposed by steric interactions, the proposed extension of the rabbit-ear effect would not apply.

directed quite markedly outward away from the N-methyl group.

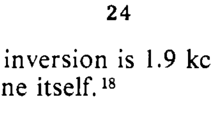
In the case of the substituted compounds **13**, **14**, **16**, **17**, and **18**, the interplay of substituent interactions becomes too complex to allow sure prediction of preferred conformations, and the experimental evidence is too scant to allow much clarification. The preferred conformation of **13**, for example, will be one that strikes a balance amoung the conformational preference of the hydrazine part of the molecule, the various possible torsional (1,2) interactions of the N-methyl and C-methyl groups, and the various 1,3-nonbonded interactions. In a simple case, analysis of coupling constants and chemical shifts might be of some use, but the present molecules have too many anisotropic centers, are too symmetric, and have too many couplings and broadenings due to long-range couplings.

It is possible to draw certain conclusions for these unsubstituted cases even though one is ignorant of the preferred conformation. From the analogy with cyclohexene, it is unlikely that the process observed for the unsaturated compounds **13** and **15** is ring inversion, and probable that it is nitrogen inversion.

In the saturated compounds **15**, **16**, **17**, and **18**, it is not possible to tell from the spectrum whether slow ring inversion or nitrogen inversion is responsible for the spectral changes observed. With **12**, **1**, **13**, and **14**, where we can confidently attribute barriers to nitrogen inversion, these turn out to be remarkably similar. Only the diphenyl compound **14** is sensibly different. Clearly, substitution on the ring has relatively little effect on the barrier to nitrogen inversion.

The barrier to ring inversion of **12** is substantially higher than that of its parent cyclohexene (8.2 kcal/mol *vs.* 5.4 kcal/mol).[10] Some contribution to this enhanced barrier is probably derived from the intrinsically greater barrier to rotation about nitrogen–nitrogen and nitrogen–carbon bonds than about carbon–carbon bonds.[4,14] We have discussed elsewhere,[6] in connection with nitrogen inversion of 7, the energy of eclipsing of two methyl groups along a nitrogen–nitrogen bond, and in that case this seemed to amount to 1–2 kcal/mol. The transition state for ring inversion of cyclohexene appears to be a boat conformation or a conformation very close to this.[15–17]

Such conformations require an eclipsing of the two N-methyl groups, so that it seems reasonable to assign some of the increased barrier found for **12** compared with cyclohexene to the N-methyl–N-methyl interaction in the transition state. This assignment is supported by the results for the ring inversion of dimethyl *cis*-cyclohexene-4,5-dicarboxylate (**24**), where the barrier to ring inversion is 1.9 kcal/mol higher than that of cyclohexene itself.[18]



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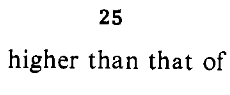

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Table III. Proton Chemical Shift and Coupling Data of Relevant Nmr Signals at Very Low[a] Temperatures of Tetra- and Hexahydropyridazines[b,c] in Dichlorodifluoromethane

Compd	Temp,[a] °C	N–CH$_3$	N–CH$_2$	C–CH$_3$ or =CH
1	−118	2.17d (δ 10.5)	[d]	1.58 bs
12	−120	2.26d (δ 7.8)	2.90 q (small δ_{AB}), 3.28 q (δ_{AB} 57.7, J_{AB} = 16.0)	5.70 bs
19	−125		2.59 q (small δ_{AB}), 2.95 q (δ_{AB} 61.3, J_{AB} = 15.0)	

[a] "Very low" temperature is suitably below the *second* coalescence to give reasonably sharp lines. [b] Chemical shifts of main lines or group lines are in ppm downfield from tetramethylsilane Relative chemical shifts of signals in multiplets are in Hz at 60 MHz. All couplings (J) are in Hz. [c] The code for line description is: s = singlet, d = doublet, q = quartet, b = broad. [d] This signal was obscured by the N–CH$_3$ signals.

The present results shed very little light on the ring inversion of the precursor compounds such as **25**. The barriers in these are around 20 kcal/mol independent of whether the ring is unsaturated or not.[19] It is probable that the greatest contribution to the barrier comes from interaction of the carbomethoxy groups.

We have discussed elsewhere the choice of transmission coefficient in the calculation of barriers to ring inversion of cyclohexenes.[17] The results in Table I for ring inversion of **1**, **12**, and **19** are calculated on the basis of a transmission coefficient of unity in line with Bucourt and Hainaut's calculations.[15] If the mechanism presented by Allinger and coworkers[16] is preferred, the barriers to ring inversion are 0.2 to 0.3 kcal/mol lower than those given in Table I.

For nitrogen inversion, the situation is very similar to that found for the compound 7.[6] Simultaneous inversion of both nitrogen atoms is unlikely, because the energies derived from the distortion of two nitrogen atom configurations and from torsional interaction of the methyl substituents combine to give a much higher barrier than would result from successive but interdependent inversion of the two atoms. The barrier to the complete process is then twofold,[6] and the transmission coefficient is then more correctly to be taken to be one-half.

Some comment on solvent effects seems desirable here. We have shown for 7 that the barrier to nitrogen inversion increases with the polarity of the solvent.[6] On the other hand, that of N,N,O-trimethylhydroxylamine decreases with polarity.[20] Elsewhere we have claimed[21] that the barrier to ring inversion is relatively insensitive to solvent. In the present work, comparison of barriers found in dichlorodifluoromethane and in perdeuteriomethanol solution suggests that ring inversion is more sensitive to the solvent than nitrogen inversion. At this stage, it seems wiser to admit a certain ignorance in the matter of solvent effects and to postpone discussion pending further investigations.

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(14) J. Dale, *Tetrahedron*, **22**, 3373 (1966). This summarizes experimentally measured barriers.

(15) R. Bucourt and D. Hainaut, *Bull. Soc. Chim. Fr.*, 4562 (1967).

(16) N. L. Allinger, J. A. Hirsch, M. A. Miller, and T. Tyminski, *J. Amer. Chem. Soc.*, **90**, 5773 (1968).

(17) For a discussion of this see J. E. Anderson and J. D. Roberts, *ibid.*, in press.

(18) C. H. Bushweller, Ph.D. Thesis, University of California, Berkeley, 1966.

(19) J. E. Anderson and J. M. Lehn, *Tetrahedron*, **24**, 137 (1968).

(20) D. L. Griffith and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 4089 (1965).

(21) J. E. Anderson and A. C. Oehlschlager, *Chem. Commun.*, 284 (1968).

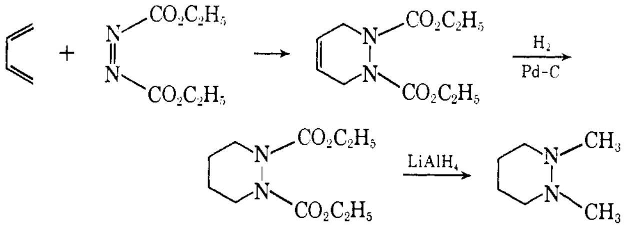
Table IV. Physical Constants and Analytical Data for Tetra- and Hexahydropyridazines

			Anal., %					
			Calcd			Found		
Compd	Bp, °C (mm, Hg)	$n^{20}D$	C	H	N	C	H	N
1	73-75 (98)	1.4772	68.52	11.50	19.98	68.78	11.66	19.66
12	48 (15)	1.4651	64.25	10.76	24.99	64.38	10.76	24.83
13	58 (18)	1.4611	68.52	11.50	19.98	68.09	11.72	20.15
15	38 (18)[a]	1.4569						
16	90-91 (86)	1.4588	67.55	12.76	19.70	67.54	12.61	19.58
17	64-66 (19)	1.4574	67.55	12.76	19.70	67.31	12.50	19.44
18	114 (0.08)[b]	1.5769	81.17	8.32	10.52	81.37	8.22	10.28

[a] Methiodide, mp 245° (lit.[22] mp 248°). [b] Mp ~42°.

Experimental Section

Compounds **1** and **12** through **20** with the exception of **15**[22] have not previously been characterized. Their preparation generally followed the example of eq 1 for synthesis of **15**. Compounds **19** and **20** were prepared using lithium aluminum deuteride in the last step. Table IV summarizes the characteristic data. Compound **14** was unstable and could never be obtained free of the starting diene. Mass spectrometric determination gave a mol wt of 264.1639 (calculated for $C_{18}H_{20}N_2$, 264.1626). The substances were freshly distilled from sodium and sealed in nmr tubes before recording the spectra. Deuteriomethanol was purchased from Diaprep Inc., Atlanta, Ga.



The nmr spectra were recorded on a Varian Associates A56/60A spectrometer at 60-MHz operating frequency. The spectrometer was equipped with a V6040 variable-temperature unit capable of reaching temperatures of −150°. Temperatures down to −80° were calibrated with the hydroxyl shift of methanol. Below this temperature, calibration was achieved by inserting an open dummy tube containing dichlorodifluoromethane and allowing it to equilibrate at identical controller settings. The temperature of the dummy solution was then measured directly by inserting a calibrated thermocouple to the bottom of the tube. Tables II and III contain the significant nmr spectral data.

Free energies of activation were calculated in the usual way[23] from the coalescence of signals. In the case of the low-temperature process of **19** (two AB quartets coalescing to one), a computer program kindly supplied by Professor G. M. Whitesides of the Massachusetts Institute of Technology, based on the equations of Sack,[24] was used. The free energies of activation quoted are considered accurate to ±0.2 kcal/mol.

Acknowledgment. I gratefully acknowledge the facilities provided by Professor G. Ourisson, Strasbourg, and Professor J. D. Roberts, Pasadena, in their laboratories. Early work was done in collaboration with Dr. J. M. Lehn of Strasbourg,[2] and I have had many helpful discussions with him and with Dr. F. G. Riddel of Stirling University, for which I warmly thank them. Professor Roberts made a number of suggestions with regard to the preparation of the final manuscript.

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[22] H. R. Snyder and J. G. Michaels, *J. Org. Chem.*, **28**, 1144 (1963).

[23] L. W. Reeves, *Advan. Phys. Org. Chem.*, **3**, 18 (1965).

[24] R. A. Sack, *Mol. Phys.*, **1**, 163 (1958).