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THE 2,3-DIAZABICYCLO[2.2.1]HEPTYL RING SYSTEM. IV. CASES OF CONFORMATIONAL EXCHANGE PROCESSES.

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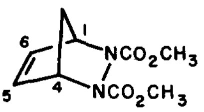
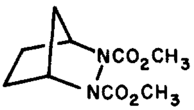
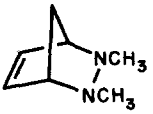
2,3-Diazabicyclo[2.2.1]heptyl ring compounds are of much theoretical interest in a variety of areas because of the fundamental nature of the structure. As a part of a program of research with this system we have been investigating conformational exchange processes by the nuclear magnetic resonance method. Recent reports concerning the conformational changes of the structurally related 1,2,3,6-tetrahydropyridazine system (1-5) prompt us to describe some of the results of our study of I-IV.



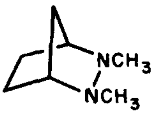
I



II



III



IV

The room temperature n.m.r. spectra of I-IV are consistent with expectations and show the correct numbers and kinds of protons for the respective structures. This is illustrated in FIG. 1a for III. When the temperature is lowered striking changes in the spectra occur. In the case of III, the single sharp absorption of the methyl protons broadens as the temperature decreases and finally separates into two sharp peaks of equal intensity (3 H each). The single peaks for the bridgehead protons (1 and 4) and the vinyl protons (5 and 6) also broaden and become two peaks as the temperature lowers. A low temperature spectrum of III is shown in FIG. 1b. Entirely analogous results were found for the methyl and bridgehead protons

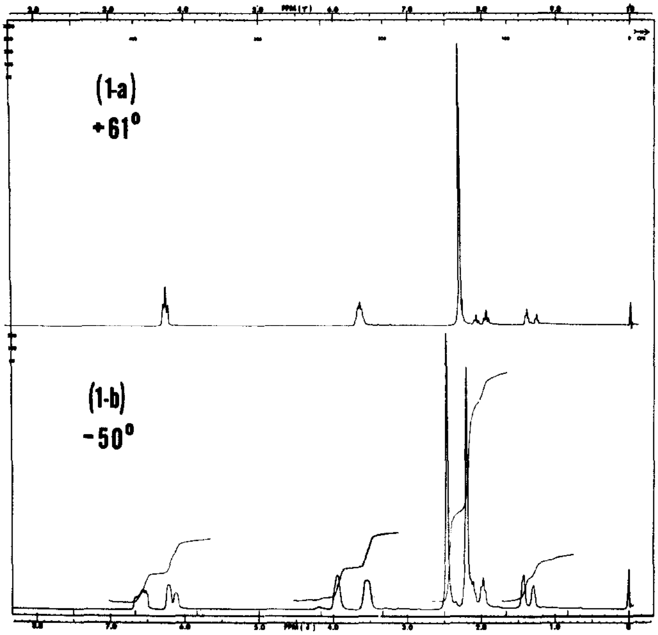


FIG. 1

NMR Spectra of III at 60 Mc (neat)

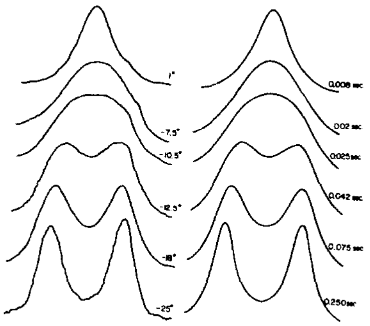


FIG. 2

Calculated and Experimental Spectra of the Bridgehead Protons for I in $CDCl_3$(ν_A-ν_B=19.8 c.p.s., J_{AB}=0 c.p.s., T_2=0.051 sec./radian) of IV and the bridgehead protons of I and II. In the latter two cases the CH_3O signal also splits into two absorptions of _ca._ 2-3 c.p.s. separation at temperatures in the region of -30 to -40°. It is very interesting that, in contrast with III, the vinyl protons of I do not separate into two peaks at temperatures down to -60°. However, some line broadening is observed at lower temperatures. Table I lists the pertinent coalesence temperatures (T_c) and the lowest temperature measurement of ν_A-ν_B data for I, II and IV.

Exchange rates were estimated with the aid of theoretical spectra having τ values (mean half-life) calculated with a Fortran IV program based on the density matrix formulation of Alexander (6). For each case τ was varied until the theoretical spectra were superimposable on the experimental spectra. A set of such spectra for I is shown in Fig. 2. Arrhenius plots of log $(1/\tau)$ _vs._ $1/T \times 10^3$ afforded estimates of E_a. For IV, E_a values were estimated from both methyl and bridgehead (1 and 4) proton signals. This set of values was only in fair agreement.* Some of the results are included in Table I.

The change of spectra with temperature for III and IV may be ascribed to the methyl groups exchanging between _endo_ and _exo_ conformations as a consequence of double inversion at the nitrogen atoms. For the upper temperature, exchange occurs so rapidly that the spectrum shows only averaged signals. At lower temperatures the inversion process is slow enough that a given set of protons (CH_3, 1-4, etc.) exhibit differing chemical shifts as a result of the asymmetric environment. The lowest temperature spectra suggest that the _trans_ conformation V is preferred and the more stable. This is indicated by the excellent integrated intensity relationships of the proton sets. It is highly probably that the spectra would

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*At the present time we have no explanation for the difference in E_a values. We are examining the point further.

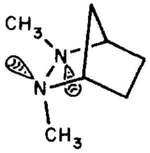
TABLE I

Some Activation Energies and Chemical Shift Differences.[a]

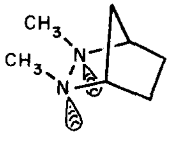
Compound	Solvent	ν_A-ν_B c.p.s.	T_c °C	E_a, kcal.	log A
I	$CDCl_3$	19.8[b]	-10	16.6 ± 0.2[b,c]	15.3
II	$CDCl_3$	14.5[b]	- 7	14.8 ± 0.2[b,c]	13.6
IV	None	6.5[d]	-28	14.6 ± 0.3[c,d]	14.1
		16.4[b]	-17	16.7 ± 0.2[b,c]	15.7
	$CDCl_3$	17.6[b]	-11	16.0 ± 0.3[b,c]	14.9

[a] The n.m.r. spectra were determined in degassed, sealed thin-wall tubes with either a Varian A-60 or A-56/60A instrument fitted with a variable temperature probe. [b] Data for bridgehead (1 and 4) protons. [c] Errors are reported as the root-mean-square error from the least squares line. [d] Data for the methyl protons.

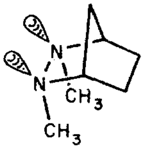
show additional absorptions or at least unequal integration ratios if the cis conformations VI and VII were significant. A favored trans conformation also is consistent with theoretical expectations. Both VI and VII should be higher energy because of eclipsing of the methyl groups and non-bonding electron pairs.*



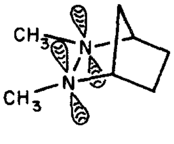
V



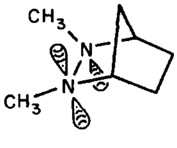
VI



VII



VIII



IX

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[*] The exact magnitude of this is difficult to assess because of the uncertainty of the relative spatial requirements of the methyl group and the lone electron pair (7).

For IV the energy barrier to inversion is significantly greater than for the acyclic structure 1-benzyl-1,2,2-trimethylhydrazine (8). Undoubtedly this is a consequence of substantial angle strain and non-bonded interactions imposed by the rigid bicyclo[2.2.1]heptyl structure.

The details of the mechanism for the double inversion process are of considerable theoretical interest. A process involving two simultaneously planar nitrogens in the transition state (VIII) seems unlikely for at least two reasons. First of all, angle strain will be increased substantially.* Secondly, unshared electron pairs in eclipsed parallel orbitals in close proximity will result in increased electronic repulsion in the transition state. The interaction energy of the cis methyl groups should be small by comparison since the separation is comparable to cis-2-butene (11). On these grounds, a transition state with one planar nitrogen (IX) is favored. This implies a consecutive inversion of the two nitrogen atoms.

Closer inspection of intermediate and low temperature spectra indicates that the above description is an oversimplification for III. For example, the vinyl protons at low temperature (-62°) show strikingly different splitting patterns (FIG. 3). Analysis by computer has allowed for assignment of the low temperature vinyl proton coupling constants and confirms

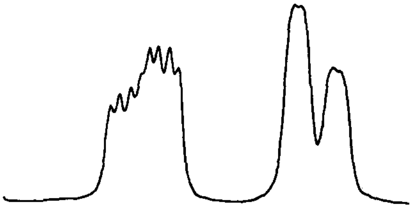

FIG. 3
60 Mc Vinyl Proton Spectra for III at -62° (neat).

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*Internal skeletal angles at $C_1C_2C_3$ for structurally similar norbornane and norbornadiene are reported as 104° and 109°, respectively (9, 10).

a difference in coupling to the bridgehead protons. This is in contrast to the vinyl proton patterns for endo- and exo-5- substituted 2-norbornenes (12, 13). For the latter system couplings between vinyl and bridgehead protons are affected little by a variety of endo- or exo-5-substituents (12). Such observations suggest that for III there is significant interaction between the endo unshared electron pair on nitrogen and the π-electrons of the remote double bond. We will discuss this aspect in a later paper when work now in progress is finished.

There are two possible exchange processes which might account for the n.m.r. spectral temperature dependence of I and II: (i) double nitrogen inversion (2), or (ii) hindered rotation associated with the N-CO_2CH_3 bond (1, 3-5). Structural considerations argue against the latter alternative. If there is appreciable double-bond character in the two N-CO_2CH_3 bonds, the rigid bicyclic structure requires that the two nitrogen atoms be coplanar. This will increase angle strain significantly, especially for I (see the preceding footnote). Coplanar N-CO_2CH_3 groups will also interact strongly. Such effects will be reduced with pyramidal nitrogens. On this basis a nitrogen inversion process seems best. This view is supported by the comparable energy barriers found for the exchange processes of the related structures I, II, and IV.

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