The Conformational Analysis of Saturated Heterocycles. Part LXI.[1] 1,2,4,5-Tetra-alkylhexahydro-1,2,4,5-tetrazines[2] and Polycyclic Analogues

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Variable temperature n.m.r., together with vibrational spectroscopy and dipole moments, allow definition of conformational equilibria of substituted hexahydro-1,2,4,5-tetrazines. The tetramethyl derivative (1) exists as a rapidly interconverting mixture of monoaxial (1Z) 70% and noncentrosymmetric diaxial (1W) 30%. The tetraethyl derivative (2) exists as rapidly interconverting (2Z) 33% and (2W) 2% together with the centrosymmetric diaxial (2X) 65%. The bicyclic dimethyl derivative (5) closely resembles (1). The tricyclic unsaturated compound (4) exists as the monoaxial (4Z) 67%, the centrosymmetric diaxial (4X) 20%, and the tetraequatorial (4Y) 13%. The tricyclic saturated compound (6) exists mainly in the tetraequatorial conformer (6Y).

OUR work on the conformational analysis of saturated heterocycles such as hexahydropyrimidines [3,4] and hexahydro-*s*-triazines [4,5] led us naturally to consider analogous conformational equilibria in hexahydro-1,2,4,5-tetrazines. We were therefore particularly interested in the variable-temperature n.m.r. work of Anderson and Roberts [6] which they interpreted as indicating that tetramethylhexahydrotetrazine (1) exists predominantly in a single conformation possessing two axial and two equatorial methyl groups. They considered the three possibilities [(1V), (1W), (1X)] and rejected (1V) on steric grounds: the distinction between (1W) and (1X) was less important for their conclusions and they did not detail the reasons which led them to choose (1X). However, our previous work [7-9] indicated that conformer (1W) should be preferred to (1X); moreover, we considered it likely that several conformations of the tetramethyl derivative (1) should be significantly populated. The two conformers (1W) and (1X) differ in that (1X) has a centre of symmetry; we therefore applied dipole moments and vibrational spectroscopy to the problem in addition to reinvestigating the low temperature n.m.r. spectrum. In 1970, we published a preliminary note,[2a] showing that tetramethylhexahydrotetrazine (1) possessed an appreciable dipole moment, and could not therefore exist mainly in conformation (1X). At that time we interpreted our results in terms of essentially complete existence in conformation (1W). Concurrent work in our laboratory on nitrogen inversion barriers in tetra-alkylhydrazines [7] indicated that this interpretation could be oversimplified; we extended our investigation to the tetraethyl derivative (2) and the polycyclic compounds (3), (5), and (6).

Nelsen and Hintz [10] reinvestigated the low temperature n.m.r. spectra of (1) and (2) and compared them with (3) and (6) as models. They alleged that the tetramethyl compound (1) existed in conformation (1X), whereas the tetraethyl derivative existed mainly as (2W) together with some 15% of (2X). They ascribed [10] the measured [2] dipole moment of (1) to impurities in our sample. However, their work contains, as we shall show, fundamental errors of assignment and interpretation which vitiate their conclusions.

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[1] Part LX, L. Angiolini, I. D. Blackburne, R. A. Y. Jones, and A. R. Katritzky, *Gazzetta*, in the press.

[2] For preliminary communications see (*a*) R. A. Y. Jones, A. R. Katritzky, and A. C. Richards, *Chem. Comm.*, 1969, 708; (*b*) R. A. Y. Jones, A. R. Katritzky, A. R. Martin, D. L. Ostercamp, A. C. Richards, and J. M. Sullivan, *J. Amer. Chem. Soc.*, 1974, **96**, 5761.

[3] R. A. Y. Jones, A. R. Katritzky, and M. Snarey, *J. Chem. Soc.* (*B*), 1970, 131.

[4] P. J. Halls, R. A. Y. Jones, A. R. Katritzky, M. Snarey, and D. L. Trepanier, *J. Chem. Soc.* (*B*), 1971, 1320.

[5] R. A. Y. Jones, A. R. Katritzky, and M. Snarey, *J. Chem. Soc.* (*B*), 1970, 135.

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

[7] R. A. Y. Jones, A. R. Katritzky, D. L. Ostercamp, K. A. F. Record, and A. C. Richards, *J.C.S. Perkin II*, 1972, 34.

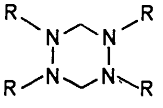
[8] R. A. Y. Jones, A. R. Katritzky, D. L. Ostercamp, K. A. F. Record, and A. C. Richards, *Chem. Comm.*, 1971, 644.

[9] R. A. Y. Jones, A. R. Katritzky, K. A. F. Record, and R. Scattergood, *J. C.S. Perkin II*. 1974, 406.

[10] S. F. Nelsen and P. J. Hintz, *J. Amer. Chem. Soc.*, 1972, **94**, 3138.

Baddeley[11] has also suggested that conformer (1X) should be preferred over (1W), on semi-theoretical grounds, but his comments relate mainly to electronic interactions in the N–C–N fragments and cannot be regarded as conclusive in a system in which so many other interactions, both electronic and steric, are involved.

Fortunately our own work now allows an unambiguous interpretation of the experimental data in terms of the conformational analysis of (1) and (2) which confirms the main conclusions of our earlier work.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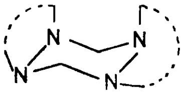
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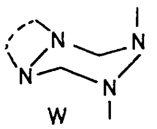
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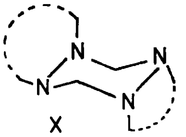
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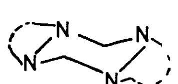
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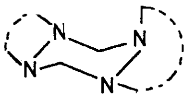
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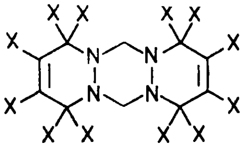
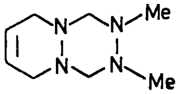

(3) X = H
(4) X = D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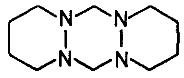
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EXPERIMENTAL

Preparation of Compounds.—The following were prepared by the literature methods indicated: 1,2,4,5-tetramethylhexahydro-1,2,4,5-tetrazine (1),[12] m.p. 9—12° (sealed capillary), b.p. 58—60° at 11 mmHg (lit.,[12] 58—60° at 11 mmHg); 1,2,4,5-tetraethylhexahydro-1,2,4,5-tetrazine (2),[10] m.p. 19—21°, b.p. 95—97° at 9 mmHg (lit.,[10] 165—169° at 100 mmHg); 6*H*,13*H*-1,4,8,11-tetrahydrodipyridazino[1,2-*a* : 1′,2′-*d*]-*s*-tetrazine (3),[10] m.p. 151° (lit.,[10] 151—152·5°); 6*H*,13*H*-octahydrodipyridazino[1,2-*a* : 1′,2′-*d*]-*s*-tetrazine (6),[13] m.p. 170—171° (lit.,[13] 168—169°).

The deuteriated compound (4), prepared by adaptation of the known route to (3) using perdeuterio-1,3-butadiene,[14] had m.p. 153—153·5°. The deuteriated intermediates diethyl 3,3,4,5,6,6-hexadeuterio-1,2,3,6-tetrahydropyridazine-1,2-dicarboxylate and 3,3,4,5,6,6-hexadeuterio-1,2,3,6-tetrahydropyridazine were characterized by n.m.r. spectroscopy.

2,3-*Dimethyl*-1,2,3,4,6,9-*hexahydropyridazino*[1,2-a]-s-*tetrazine* (5).—1,2-Dimethylhydrazine dihydrochloride (5·32 g, 0·04 mol) was added to NaOH (3·0 g, 0·075 mol) in water (50 ml) at 20°. To this was added crude 1,2,3,6-tetrahydropyridazine, obtained by hydrolysis of diethyl 1,2,3,6-tetrahydropyridazine-1,2-dicarboxylate (9·12 g, 0·04 mol) according to the literature procedure.[15] Aqueous formaldehyde (4 ml, 37%) was added and the mixture was stirred for 10 h at 25°. The water and unchanged formaldehyde were removed *in vacuo* and the residue was taken up in $CHCl_3$ (100 ml). The solution was extracted with saturated Na_2CO_3 solution (100 ml), filtered through anhydrous K_2CO_3, and evaporated. The residue was distilled *in vacuo*. Compound (1) was removed as a low boiling fraction (b.p. 50—60° at 18 mmHg). The desired pyridazinotetrazine (5) solidified in the condenser, b.p. 80—103° at 18 mmHg. It was purified further by vacuum sublimation and recrystallized from cyclohexane to give *prisms* (238 mg, 3·5%), m.p. 83—84° (Found: C, 56·5; H, 9·5; N, 32·6. $C_8H_{16}N_4$ requires C, 57·1; H, 9·6; N, 33·3%).

Physical Measurements.—The dipole moments were measured in cyclohexane at 25° by the standard technique;[16] results are recorded in Tables 1 and 2. I.r. spectra of the neat solid and liquid samples between NaCl plates were recorded with a Perkin-Elmer model 125 spectrophotometer at spectral slit widths of *ca.* 1·2 cm^{-1}, using an RIIK variable temperature cell VLT-2. The Raman spectrum of the liquid sample was recorded on a Spex 1401 double monochromator with a 6328 He–Ne laser. Scattering from the sample placed in a cylindrical holder was viewed perpendicularly to the laser beam by the monochromator. Spectral slit width was *ca.* 13 cm^{-1}. I.r. and Raman spectral data are recorded in Table 3. The n.m.r. spectra were measured with Varian HA100 and HR220 spectrometers in $CDCl_3$–$CFCl_3$ solution.

RESULTS AND DISCUSSION

We concur with Anderson and Roberts[6] in neglecting conformation (V) and all other conformers possessing *syn*-1,3-diaxial methyl groups (*cf.* the discussion of

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[11] G. Baddeley, *Tetrahedron Letters*, 1973, 1645.

[12] E. Schmitz, *Annalen*, 1960, **635**, 73.

[13] H. R. Snyder, jun., and J. G. Nichels, *J. Org. Chem.*, 1963, **28**, 1144.

[14] D. Craig and R. B. Fowler, *J. Org. Chem.*, 1961, **26**, 713.

[15] E. W. Bittner and J. T. Gerig, *J. Amer. Chem. Soc.*, 1972, **94**, 913.

[16] R. A. Y. Jones, A. R. Katritzky, P. G. Lehman, K. A. F. Record, and B. B. Shapiro, *J. Chem. Soc.* (*B*), 1971, 1302.

TABLE 1

Dielectric and specific volume measurements [a] in cyclohexane at 25°

(i) 1,2,4,5-Tetramethylhexahydro-1,2,4,5-tetrazine

10^6w	$10^6(\varepsilon_{12} - \varepsilon_1)$	$10^6(v_1 - v_{12})$
563	884	114
2524	3423	553
4212	5426	894
5497	7565	1213

(ii) 1,2,4,5-Tetraethylhexahydro-1,2,4,5-tetrazine

10^6w	$10^6(\varepsilon_{12} - \varepsilon_1)$	$10^6(v_1 - v_{12})$
2210	1125	415
4184	2183	769
5667	2931	1040
7763	4006	1420

[a] w = Weight fraction of solute, ε = dielectric constant, v = specific volume. The suffixes 1 and 12 refer to solvent and solution respectively.

TABLE 2

Dipole moments in cyclohexane at 25°

	$d\varepsilon/dw$	dv/dw	${}_TP_{2\infty}$	${}_EP$	μ/D
(i) 1,2,4,5-Tetramethylhexahydro-1,2,4,5-tetrazine	$1{\cdot}34 \pm 0{\cdot}04$	$-0{\cdot}219 \pm 0{\cdot}004$	85·55	41·82	$1{\cdot}46 \pm 0{\cdot}02$
(ii) 1,2,4,5-Tetraethylhexahydro-1,2,4,5-tetrazine	$0{\cdot}517 \pm 0{\cdot}003$	$-0{\cdot}183 \pm 0{\cdot}001$	81·03	59·99	$1{\cdot}01 \pm 0{\cdot}01$

TABLE 3

Comparison of i.r. frequencies and Raman displacements for tetramethyl- and tetraethyl-hexahydrotetrazines (1) and (2) (cm^{-1})

Tetramethyl (1)		Tetraethyl (2)	
I.r.	Raman	I.r.	Raman
712		694	
	738		707
755		724	726
772	775	748	
895	892	804	806
918	915	838	
935	935	854	856
972	975		866 [a]
991	990 [a]		908
1025	1026		951
1073 [a]	1073 [a]	962	
1080	1080	990	
1115			996 [a]
1137	1136		1006
1170		1014	
1177 [a]	1180	1024	
1199	1202		1034
1240	1242	1068	1067
1312	1317		1075
1354 [a]		1090	1090
1361	1359	1124	
1401	1402 [a]	1152	
1419	1422 [a]		1169
1436	1438 [a]	1180	1187
1446		1210	1224
	1455	1270	
1462			1280
	1469 [a]		1305
		1320	
		1356	1358
		1375	1378
		1442	1442
			1456
		1465	
			1476

[a] Shoulder.

diaxial conformations of 1,3-dimethylhexahydropyrimidine [3]). However it is necessary to consider the possibility of significant contributions from conformers Y and Z, which possess four and three equatorial methyl groups respectively, in addition to conformers W and X.

Variable Temperature N.m.r. Study of Tricyclic Compounds (3) *and* (4).—Whereas the mono- (1) and (2) and bi-cyclic (5) compounds could reasonably exist in four conformations (W, X, Y, and Z), the tricyclic analogues (3) and (4) cannot adopt form W which would require a *trans*-diaxial ring fusion.

The room temperature n.m.r. spectrum of (3) is ill-defined because of proximity to coalescence temperature, but at +70° the expected three singlets are seen at τ 6·76, 6·42, and 5·61 for the outer ring methylenes, central ring methylenes, and vinyl hydrogens, respectively.

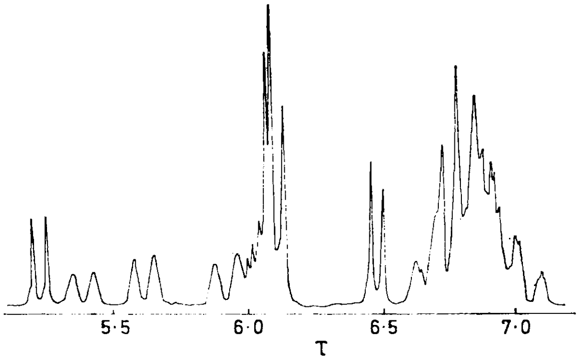

FIGURE 1 The n.m.r. spectrum (220 MHz) of (3) [in $CDCl_3$–$CFCl_3$ (80 : 20)] at −30°

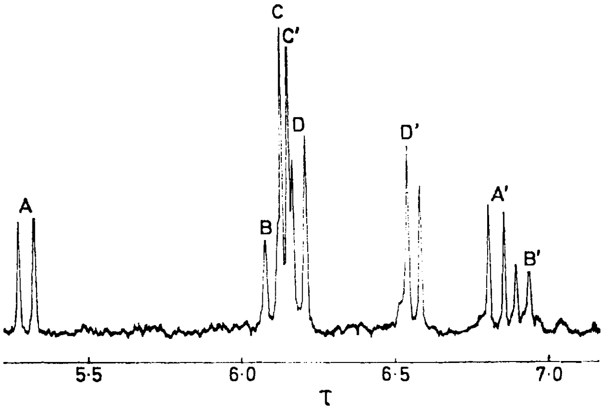

FIGURE 2 The n.m.r. spectrum (220 MHz) of (4) [in $CDCl_3$–$CFCl_3$ (80 : 20)] at −33°

Assuming conformers X—Z are all present, the low temperature spectrum of (3) should show four AB quartets for the central ring methylenes (one each from X and Y, and two from Z) and seven AB quartets for the outer ring methylenes (one from Y, two from X, and four from Z).* Figure 1 shows the 220 MHz spectrum of the methylene region of (3) at −30°. It can be seen, not surprisingly, that considerable overlap occurs, but doublet portions of two AB quartets stand out at τ 5·30 and 6·57. Nelsen and Hintz [10] studied a 100 MHz spectrum of (3) and assigned these quartets

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* There is only very small coupling between vinyl hydrogens and adjacent methylenes, as reported by Bittner and Gerig [15] for this ring system.

to the four central ring methylene protons of conformer Z, which they assert is the only conformer present. We reject this interpretation on the following grounds: (i) the areas of these two doublets are not, as Nelsen and Hintz allege, equal, which shows that they must come from different conformers and (ii) the total area of the two doublets represents only 1·1 protons, whereas they should represent 2 protons if derived from the central ring methylene protons of the only conformer present.

TABLE 4

Low temperature n.m.r. data[a] and conformational assignments for N–CH_2–N signals of hexahydrotetrazines

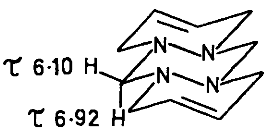
Compound	Chemical shifts (τ)		Δ_{ae}	J_{gem}/Hz	Relative areas	Conformer assignment
(1)[b]	6·03	6·67	0·64	12·0		W $\rightleftharpoons$ Z; Scheme 1, Set III
(2)[b]	5·12	6·8[c]	1·7	14·0	80	X; Scheme 1, Set II
	6·07	6·38	0·31	12·0	20	W $\leftrightharpoons$ Z; Scheme 1, Set III
(4)	6·11	6·19	0·08	11·5	33	Z; 8
	6·19	6·56	0·37	9·5	33	Z; 8
	5·29	6·83	1·54	11·5	20	X; 9
	6·10	6·92	0·82	9·5	13	Y; 7
(5)	5·96	6·53	0·57	12·5		W $\rightleftharpoons$ Z; Scheme 2, Set V
(6)	6·45	6·95	0·50	9·5		Y

[a] 220 MHz unless otherwise stated. [b] 100 MHz spectrum. [c] Partly obscured by N–CH_2–C peak.

TABLE 5

Self-consistent assignments of chemical shifts (τ) in compound (4)

Assignment	Y	Z	X
A	*e* 6·10	*e* 6·19, *e′* 6·56	*e* 6·83
	a 6·92	*a* 6·11, *a′* 6·19	*a* 5·29
B	*e* 6·10	*e* 6·56, *e′* 6·19	*e* 6·83
	a 6·92	*a* 6·19, *a′* 6·11	*a* 5·29
C	*e* 6·92	*e* 6·19, *e′* 6·11	*e* 5·29
	a 6·10	*a* 6·56, *a′* 6·19	*a* 6·83
D	*e* 6·92	*e* 6·11, *e′* 6·19	*e* 5·29
	a 6·10	*a* 6·19, *a′* 6·56	*a* 6·83
E	*e* 5·29	*e* 6·19, *e′* 6·11	*e* 6·92
	a 6·83	*a* 6·56, *a′* 6·19	*a* 6·10
F	*e* 5·29	*e* 6·11, *e′* 6·19	*e* 6·92
	a 6·83	*a* 6·19, *a′* 6·56	*a* 6·10
G	*e* 6·83	*e* 6·19, *e′* 6·56	*e* 6·10
	a 5·29	*a* 6·11, *a′* 6·19	*a* 6·92
H	*e* 6·83	*e* 6·56, *e′* 6·19	*e* 6·10
	a 5·29	*a* 6·19, *a′* 6·11	*a* 6·92



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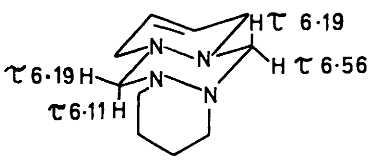

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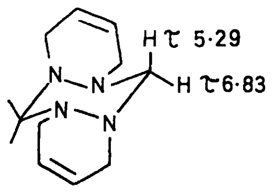

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To eliminate the problem of overlap between central and outer ring methylenes in (3), we studied compound (4), in which all outer ring protons are replaced by deuterium. Figure 2 shows the 220 MHz spectrum of (4) at −33°. Although some overlap occurs in the region τ 6·1—6·2, the expected four AB quartets can be readily seen. Chemical shifts, geminal coupling constants, Δ_{ae} values, relative areas, and conformational assignments are listed in Table 4. The interpretation is as follows: conformer Z should show two AB quartets of equal area since given types (axial or equatorial) of protons are not equivalent. The AB quartets at τ 6·11, 6·19 and 6·19, 6·56 do show equal areas and can therefore readily be assigned to conformer Z. Each of the remaining two conformers X and Y should show a single AB quartet since given types (axial or equatorial) of protons within each are equivalent. The assignment of these structures to the remaining two AB quartets together with the assignment of chemical shifts to individual protons is shown in structures (7)—(9). These assignments are based on three criteria. (a) The primary requirement of self-consistency in the effects of moving a lone pair from the axial to the equatorial position as the conformation is changed from (7) to (8) and from (8) to (9) limits the assignments to eight possibilities (A—H; Table 5: the corresponding induced shifts are listed in Table 6). (b) Moving a lone pair from axial to equatorial deshields rather than shields both α-axial and β-axial[17] protons. This eliminates assignments C, D, G, and H. (c) The expectation that the orientation of the nitrogen lone pair will have a smaller influence on the shifts of the remote β-equatorial protons than on the β-axial or α-equatorial protons eliminates assignments B—G. This leaves A as the preferred assignment [*cf.* (7)—(9)], in which the

TABLE 6

Differential shifts (Δτ)[a] induced by moving a nitrogen lone-pair from axial to equatorial, from assignments in Table 5

Proton Assignment	α-*eq*	α-*ax*	β-*eq*	β-*ax*
A (preferred)	+0·55	−0·78	−0·18	−0·85
B	+0·18	−0·85	+0·55	−0·78
C	−0·85	+0·18	−0·78	+0·55
D	−0·78	+0·55	−0·85	+0·18
E	+0·78	−0·55	+0·85	−0·18
F	+0·85	−0·18	+0·78	−0·55
G	−0·18	+0·85	−0·55	+0·78
H	−0·55	+0·78	−0·18	+0·85

[a] 0·18 and 0·55 Values are ±0·09; 0·78 and 0·85 values are ±0·05.

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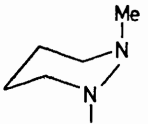
[17] *Cf.* H. Booth and J. H. Little, *Tetrahedron*, 1967, **23**, 291.

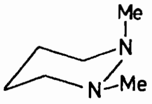
movement of an axial lone pair to equatorial has the following effects on the various CH proton shifts: *α-eq*, +0·46 to 0·64; *β-eq*, +0·09 to +0·27; *α-ax*, −0·73 to −0·82; *β-ax*, −0·81 to −0·90 p.p.m. Part of these shifts will be due to the anisotropy of the carbon–carbon double bonds, but the maximum contribution from this source [18] does not exceed 0·1 p.p.m.

It should be noted that the arguments below, based on differential chemical shifts between geminal axial and equatorial protons (Δ_{ae}), are not altered at all if the correct assignment should actually be B, C, or D instead of A, as we suggest (and in fact B represents the only reasonably possible alternative). If E, F, G, or H should be the correct assignment the major consequence for our conclusions would be to interchange our assignments of conformers X and Y. The n.m.r. spectra of the saturated tricyclic compound (6) precludes this alternative (see below) and thus confirms our original assignment. In fact, the keystone of our argument is the small Δ_{ae} values (*ca.* 0·1 and 0·4 p.p.m.) for both CH_2 groups of the unsymmetrical conformer Z (8). There can be no doubt on this score, and in the misinterpretation of this lies one of the fundamental errors in Nelsen and Hintz's reasoning.[10]

Prediction of Expected Low Temperature N.m.r. Spectra of Mono- and Bi-cyclic Hexahydrotetrazines.—Considerable work in this laboratory [8,9,19] has clarified the conformational equilibria of tetralkylhydrazines, and has shown that inversions at nitrogen which do not involve substituents passing [such as (10) $\rightleftharpoons$ (11)] are of low energy (*ca.* 8 kcal mol^{-1}) compared with those [*e.g.* (11) $\rightleftharpoons$ (12)] in which substituents do pass (*ca.* 11 kcal mol^{-1}).



(10)



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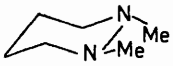
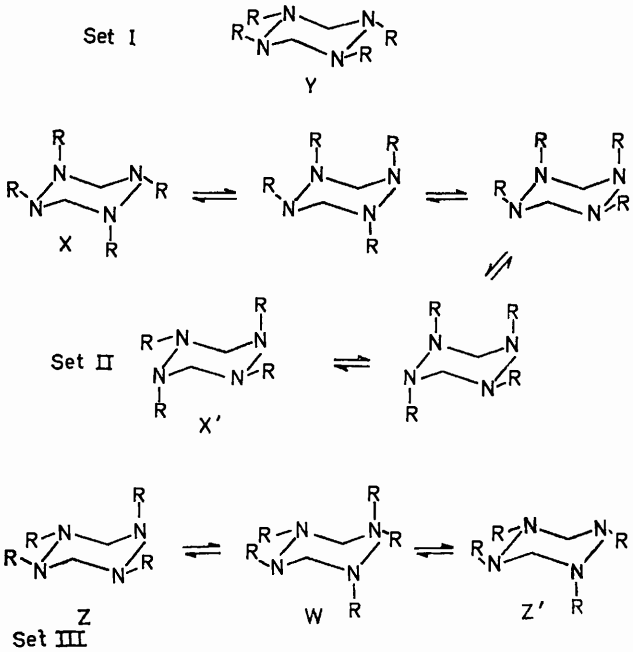


(12)

Application of these concepts to a symmetrical tetra-alkylhexahydrotetrazine indicates that, at temperatures where 'passing inversions' are slow but 'non-passing inversions' are fast, it should exist in four sets, within which each conformer is rapidly interconverting. Three of these sets are shown in Scheme 1; Set IV is the mirror image of Set III. As regards Set II, it should be noted that the interconversion of equivalent conformers X and X′ involves the formation of intermediate conformers which are not significantly populated, though their energies are not so high as to hinder the easy interconversion of X and X′. On the other hand such interconversion is not possible in bicyclic or tricyclic compounds because *trans*-diaxial fused ring intermediates would be invoked. We are assuming that ring interconversions are of high energy: 3,3,6,6-tetramethyl-1,2,4,5-tetraoxan has $\Delta G_{303}^{\ddagger}$ 15 kcal mol^{-1} [20] and the corresponding tetrathian has $\Delta G^{\ddagger}$ 16 ± 1 kcal mol^{-1}.[21]



SCHEME 1 Conformational equilibria of tetra-alkylhexahydro-*s*-tetrazines

The low temperature n.m.r. spectra of Set I should show a single signal for the four R groups and one AB quartet for the ring methylene with ($\tau_{eq} - \tau_{ax}$) *ca.* −0·8 p.p.m. and J_{gem} *ca.* 9·5 Hz [using (7) as a model].

Set II should show a single signal for the four R groups and one AB pattern for the ring methylene with ($\tau_{eq} - \tau_{ax}$) *ca.* +1·5 p.p.m. and J_{gem} *ca.* 11·5 Hz [using (9) as a model].

Sets III and IV are equivalent and should show two signals of equal area for the R groups, one from the vicinal diequatorial pair, and one from the rapidly interconverting *ea–aa–ae* pair, together with one AB pattern for the ring methylenes. The differential chemical shift of this AB pattern will depend on the relative population of conformers W, Z, and Z′. Conformers Z and Z′ will be equally populated; for each the expected ($\tau_{eq} - \tau_{ax}$) is *ca.* $\tfrac{1}{2}(+0{\cdot}4 + 0{\cdot}1) = +0{\cdot}25$ p.p.m. and J_{gem} *ca.* 10·5 Hz [model (8)]. There is no model for conformer W, but each ring CH_2 is α and β to one axial and one equatorial lone pair, just as in conformer X; we thus expect ($\tau_{eq} - \tau_{ax}$) *ca.* +1·5 p.p.m. for conformer W. Hence the AB quartet of equivalent Sets III and IV should have ($\tau_{eq} - \tau_{ax}$) intermediate between *ca.* +0·25 and +1·5 p.p.m. depending on the relative proportions of Z, Z′ : W.

Low Temperature N.m.r. Spectrum of Tetramethylhexahydrotetrazine (1).—The spectrum shows two equal methyl signals together with a single AB quartet with Δ_{ae} 0·64 p.p.m. and J_{gem} 12 Hz (Table 4). This indicates that

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[19] R. A. Y. Jones, A. R. Katritzky, and R. Scattergood, *Chem. Comm.*, 1971, 644.

[20] R. W. Murray, P. R. Story, and M. L. Kaplan, *J. Amer. Chem. Soc.*, 1966, **88**, 526.

[21] C. H. Bushweller, *J. Amer. Chem. Soc.*, 1967, **89**, 5978.

Set III greatly predominates, and further that the ratio Z : W is *ca.* 70 : 30. Nelsen and Hintz's assignment [10] of these signals to conformer X (*i.e.* Set II) was made without the realisation that rapid interconversion of X and X′ would render the four methyl groups equivalent.

Low Temperature N.m.r. Spectrum of Tetraethylhexahydrotetrazine (2).—The spectrum (Figure 3; Table 4) shows two AB patterns for ring methylenes. That of larger area (80%) has Δ_{ae} *ca.* 1·7 p.p.m. and is assigned to Set II, conformer X: the alternative possibility, Set III with conformer W greatly predominating over Z, is excluded by decoupling the CH_3 from the ethyl-CH_2 signal when the latter becomes a single AB pattern (Figure 4). The other ring methylene AB pattern (20%) has Δ_{ae} 0·31 p.p.m. and is assigned to Set III with conformer Z predominating over W (*ca.* 95 : 5). Indirect evidence supporting this assignment comes from the decoupled ethyl signals. These (Figure 4) are in better agreement with *two* AB quartets for the N–CH_2–C groups of the minor component, each comprising *ca.* 10% of the total N–CH_2–C area, rather than with a single signal of 20% area; in other words it indicates that the minor component is unsymmetrical. Nelsen and Hintz [10] assigned the signals of the major conformer to structure W largely on the basis of their erroneous assignment of the tricyclic compound (3). Their assignment of structure X to the minor conformer was made without the benefit of decoupling experiments.

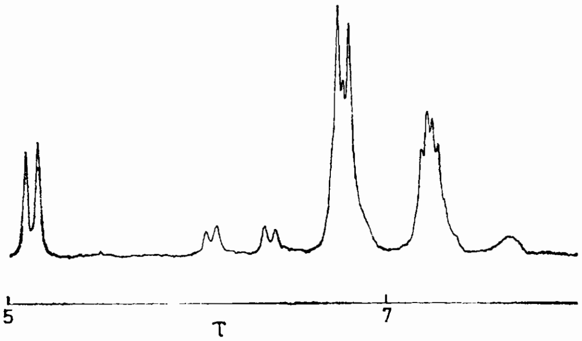


FIGURE 3 The n.m.r. spectrum (220 MHz) of (2) [in $CDCl_3$–$CFCl_3$ (75 : 25)] at −80°

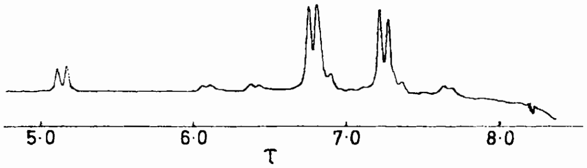
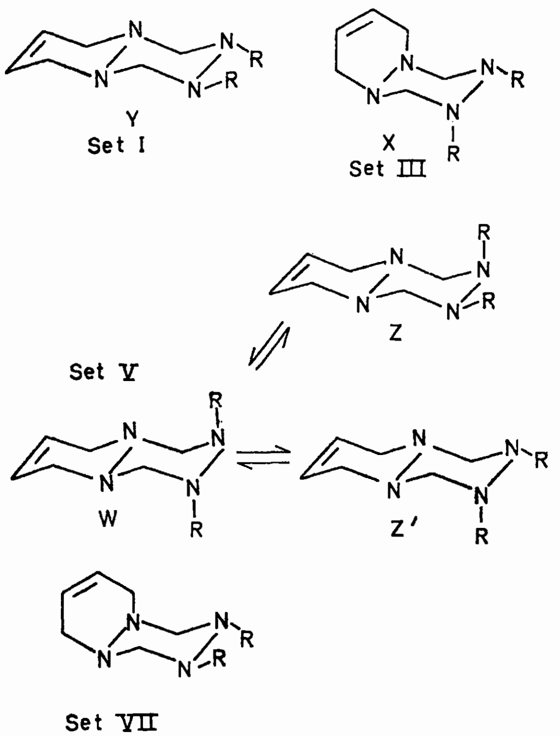


FIGURE 4 The n.m.r. spectrum (220 MHz) of (2) [in $CDCl_3$–$CFCl_3$ 75 : 25)] at −80° decoupled at τ 8·9

Variable Temperature N.m.r. Spectrum of 2,3-*Dimethyl*-1,2,3,4,6,9-*hexahydropyridazino*[1,2-a]-s-*tetrazine* (5). At 25° this compound shows four singlets: methyl (τ 7·3), N–CH_2–C (7·0), N–CH_2–N (6·4), and vinyl (4·3) protons. At −60° (Figure 5; Table 4) a single AB pattern with Δ_{ae} 0·56 p.p.m. and J_{gem} 12·5 Hz is found for N–CH_2–N together with a single *N*-methyl signal and a single AB pattern for N–CH_2–C. This compound can exist in eight sets of conformations, Sets I, III, V, and VII are shown in Scheme 2 and Sets II, IV, VI, and VIII are their respective mirror images. The observed single AB and single *N*-Me signals are consistent only with Set I or V. The Δ_{ae} value (0·56 p.p.m.) points to Set V, with an Z–Z′ : W ratio of *ca.* 75 : 25; the J_{gem} value appears to exclude Set I. The conformational behaviour is thus closely similar to that of the tetramethyl compound.



SCHEME 2 Conformational equilibria of 2,3-dialkyl-1,2,3,4,6,9-hexahydropyridazino[1,2-*a*]-*s*-tetrazine

Variable Temperature N.m.r. Spectrum of 6H,13H-*Octahydrodipyridazino*[1,2-a : 1′,2′-d]-s-*tetrazine* (6).—At room temperature the n.m.r. spectrum of (6) is ill-defined, but at +90° the spectrum consists of broad

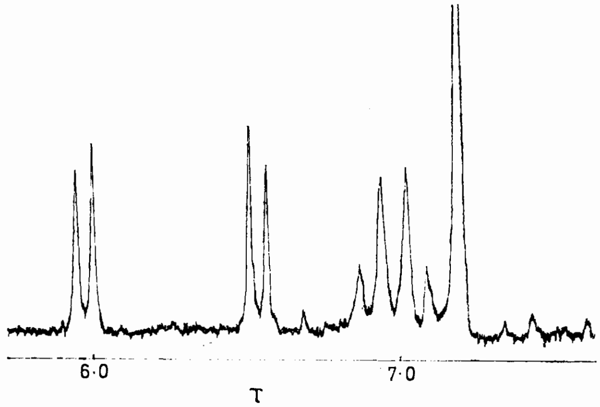


FIGURE 5 The n.m.r. spectrum (220 MHz) of (5) [in $CDCl_3$–$CFCl_3$ (50 : 50)] at −60°

singlets for N–C–CH_2 (τ 8·5) and N–CH_2–C (7·6), and a sharp singlet for N–CH_2–N (6·9).

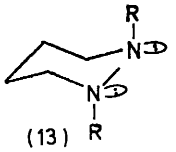
At −33°, *our* 220 MHz study confirmed the finding of Nelsen and Hintz [10] of an AB pattern for N–CH_2–N at τ 6·45 and 6·95 (Table 4). The integration shows that a single conformer predominates. The J_{gem} value (9·5 Hz) indicates that this is the all-equatorial conformer Y, and the Δ_{ae} value (0·50 p.p.m.) is in reasonable agreement. The eight N–CH_2 protons of the pyridazine rings appear as a single AB pattern when decoupled from the adjacent C–CH_2–C protons. This effectively precludes conformer X, because in this system the rapid interconversion of X and X′ (*cf.* Scheme 1, Set II) is prevented by ring fusion and two distinct AB patterns (probably with markedly differing chemical shifts) would be expected.

If our original assignments of chemical shifts in (7) and (9) were reversed (to assignments E—H, Table 5), we should have been led to suggest conformer X for the saturated tricyclic system (6). The fact that this is not found lends further support to our original assignment.

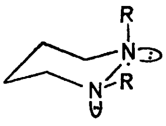
I.r. and Raman Spectra.—Comparison of the liquid phase i.r. and Raman spectra of the tetramethyl (1) and tetraethyl (2) compounds offers additional evidence in favour of the conformational assignments made above. For the centrosymmetric conformers X and Y there should be no absorption coincidences between the i.r. and Raman spectra.[22] Table 3 records the observed i.r. frequencies and Raman displacements for the two compounds over the relatively narrow range of 1500—600 cm^{-1}. No transitions occurred between 1500 cm^{-1} and the CH stretching region, and the use of NaCl plates for the i.r. measurements imposed the lower limit. Nevertheless the region chosen for study is quite rich in both i.r. and Raman transitions. Peak positions were measured to within 2 cm^{-1}; only obvious shoulders are reported. Transitions within 5 cm^{-1} of each other were regarded as coincidences for the i.r. and Raman comparison.

For the tetramethyl compound (1) the data strongly support our contention that non-centrosymmetric conformers predominate: of the 21 Raman bands observed only three lack coincidence in the i.r. By contrast for the tetraethyl compound only eight of the 23 Raman and i.r. bands are coincidental, indicating a considerable contribution from one of the centrosymmetric conformers.

Dipole Moments.—In our earlier work on hexahydropyridazines [7] we assumed, in the absence of any better approximation, that the group moment of a *gauche*-hydrazino-grouping was independent of the actual orientation of the nitrogen substituents, that is, that the moments of (13) and (14) were identical; this is clearly only a crude approximation. In fact the six-membered rings will distort in an attempt to reach the preferred 90° dihedral angle between the lone pairs.[9] Such distortion will be much easier in (13), where it involves flattening of the ring, than in (14), where it would lead to increased pucker. We thus expect the group moment of *ax–ax*-disubstituted hydrazine fragments (as in conformers W) to be less than the previously estimated [7] average value of 1·79 D, and *eq–ax*-fragments (as in conformers Z) to be more. We can set up two simultaneous equations (1) and (2) relating the observed dipole moments of the tetramethyl and tetraethyl compounds to their mole fractions (obtained by extrapolation of the low temperature n.m.r. values from 183 to 298 K, assuming that the only entropy differences between the conformers are statistical) and to the moments of the separate conformers. Since $\mu_X = 0$ by symmetry we can calculate that $\mu_W =$ 1·3 D and $\mu_Z = 1{\cdot}7$ D. These values will be only approximate because (a) we have neglected differences between the moments of *N*-ethyl and *N*-methyl fragments, and (b) the ratios of conformers W : Z are not highly accurate. Nevertheless the values which are obtained are reasonable: allowing for a small opposing moment from the diaxial lone pairs on the opposite side of the ring (which, not being completely symmetrical, will not quite cancel each other) they agree satisfactorily with our previous estimate, and more importantly the value of μ_Z is greater than μ_W as expected. Nelsen and Hintz's suggested conformational assignment [10] requires a zero dipole moment for the tetramethyl compound: the closely similar values we obtained on different occasions, with different operators, for measurements of meticulously purified samples in two different solvents confound this interpretation.



(13)



(14)

$$0{\cdot}57\,\mu_W{}^2 + 0{\cdot}43\,\mu_Z{}^2 = 1{\cdot}46^2 \qquad (1)$$

$$0{\cdot}04\,\mu_W{}^2 + 0{\cdot}34\,\mu_Z{}^2 + 0{\cdot}62\,\mu_X{}^2 = 1{\cdot}01^2 \qquad (2)$$

General Conclusions.—Clearly, the conformational preferences in the tetra-alkylhexahydrotetrazine series are finely balanced. Although we believe that the work now reported has elucidated the equilibria, we do not yet wish to attempt an explanation of the results in energetic terms. Further work is proceeding which we hope will allow rationalization of these fascinating conformational equilibria.

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[3/2474 *Received, 3rd December*, 1973]

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