lithium in hexane (Foote Mineral Co.), 41 ml of 1.6 *M* solution, 65 mmol, was added dropwise. The reaction mixture was stirred at −10° for 30 min, and then 10.2 g (65 mmol) of trimethylchlorogermane in an equal volume of diethyl ether was added dropwise at a rate such that the temperature was kept at about −10°. The reaction mixture was stirred at room temperature overnight and heated at reflux for 1 hr. The mixture then was hydrolyzed with saturated ammonium chloride solution and the organic phase was evaporated at reduced pressure. The residual solid was recrystallized twice from hexane to give 12.9 g of the desired product, mp 96–98°.

1-Trimethylsilyl-2-trimethylgermylbenzene. A 200-ml, three-necked flask equipped with a mechanical stirrer, a pressure-equalizing addition funnel, and a reflux condenser topped with an argon inlet tube was charged with 3.0 g (130 mg-atoms) of sodium and 50 ml of dry toluene. The mixture was heated to reflux while being stirred vigorously. To the resulting molten sodium suspension was added dropwise a mixture of 9.4 g (51 mmol) of *o*-chlorophenyltrimethylsilane and 7.0 g (46 mmol) of trimethylchlorogermane. The reaction mixture was heated at reflux for 2 hr. While it was still warm, the mixture was filtered through a glass wool plug under nitrogen. The solid thus separated was washed with toluene. The combined filtrate and washings were hydrolyzed carefully with saturated NH_4Cl and the organic phase was dried and distilled to give 4.2 g (33%) of the desired product. Glc examination of the distillate indicated 95% purity, and an analytical sample was obtained *via* glc (20% Carbowax 20M on Chromosorb P at 175°). (This yield is not typical; usually lower yields were obtained for compounds prepared by this procedure.)

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Hexahydrotetrazine Conformations. The Effect of Substituents

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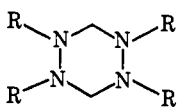
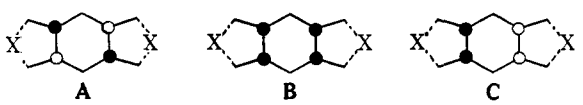
Abstract: The low-temperature nmr spectra of several symmetrically substituted tetraalkylhexahydrotetrazines are presented; at low temperatures both nitrogen inversion and (in most cases) ring flipping are slow on the nmr time scale. Substituents on the 1,2 and 4,5 nitrogens included $-(CH_2)_3-$; $-(CH_2)_4$; $-CH_2CH{=}CHCH_2-$; Me,Me; and Et,Et. These compounds are shown to assume one of four different conformations at the hexahydrotetrazine ring, depending upon substituents. In only one case was more than one conformation observed by nmr; the Et,Et compound was (very approximately) an 85:15 mixture of two conformations at −90°. Significant differences in the chemical shifts observed for methylene groups attached to hydrazine and amino nitrogen are demonstrated, and very different anisotropic effects are shown to result from interaction with gauche and anti hydrazines.

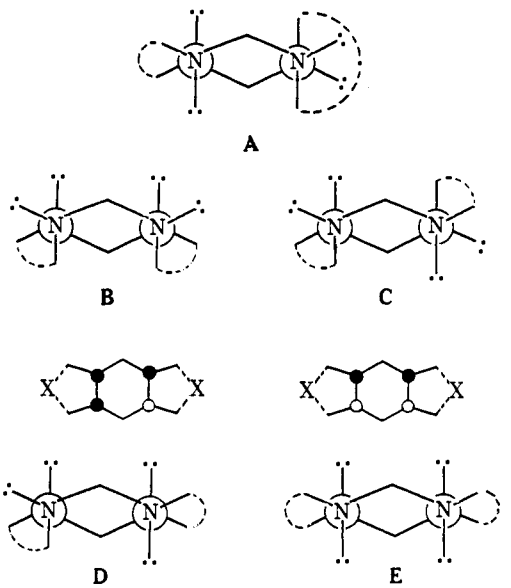
The conformational analysis of hydrazines has been rather intensively studied since the realization that lone-pair interaction causes nitrogen inversion to be slow on the nmr time scale at accessible temperatures.[1] Although the conformations involved are sometimes clear, a controversy has arisen about the conformation of 1,2,4,5-tetramethylhexahydrotetrazine (**1**). Anderson and Roberts[2] found that both the methylene and methyl nmr singlets of **1** split up at low temperatures into an AB quartet and two singlets, respectively. Of the five fundamentally different conformations (**A**–**E**), three have the proper symmetry for the 1:1 methyl absorptions, but **1B** can be ruled out because of



1, R = Me
8, R = Et



A B C



A B C D E

(1) J. E. Anderson, *J. Amer. Chem. Soc.*, **91**, 6374 (1969), and references therein.
(2) J. E. Anderson and J. D. Roberts, *ibid.*, **90**, 4186 (1968).

Table I. Low-Temperature Nmr Spectra of Some Hexahydrotetrazines

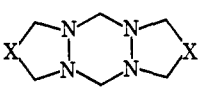
	T, °C	NCH_2N signals A	NCH_2N signals B	J_{AB}	$\Delta\delta$	NCH_2C signals A	NCH_2C signals B	J_{AB}	$\Delta\delta$	Other signals	Conformation
2[a]	20	6.00 (d), 2 H	6.74 (d), 2 H	9	0.76	6.89 (q), 4 H	7.50 (q), 4 H	7.5	0.61	7.94 (quint), 4 H	**E**
3[a]	−10	6.45 (d), 2 H	6.95 (d), 2 H	9	0.50	7.22 (d), 4 H	7.61 (m), 4 H	11	0.39	8.35 (m), 8 H	**E**
4[a]	−50	5.31 (d), 1 H	6.84,[b] 1 H	11	1.53	5.59 (m), 1 H				4.25 (br s), 4 H	**D**
		6.19 (d), 1 H	6.57 (d), 1 H	10	0.38	5.85 (br d, B), 1 H					
						6.15 (m), 2 H					
						6.75–7.10 (m), 4 H					
5b[a,c]	−60					6.87 (m), 4 H	7.11 (m), 4 H		0.24	7.52–8.15 (m), 4 H	Cis
6[a]	0					7.15 (d), 4 H	7.68 (m), 4 H	11	0.53	8.34 (m), 8 H	Trans
1[a]	−50	6.05 (d), 2 H	6.67 (d), 2 H	12	0.64	7.25 (s), 6 H	7.63 (s), 6 H		0.38		**C**
8[d]	−90[e]	5.19 (d), 2 H	6.89 (d), 2 H	14	1.70	6.86 (q), 4 H	7.31 (q), 4 H	7	0.45	8.99 (br t, 7), 2 H	**A**
8[d]	−90[f]	6.10 (d), 2 H	6.59 (d), 2 H	13	0.49	Obscured by major isomers					**C**

[a] In $CDCl_3$. [b] Located by decoupling since upfield signal is obscured by two NCH_2C protons; shift ±*ca.* 5 Hz. [c] In deuteriopyridine $\Delta\delta$ for NCH_2C was 0.39, and for CCH_2, 0.24. [d] In CH_2Cl_2; low enough temperature could not be reached in $CDCl_3$. At room temperature solvent shifts were less than 3 Hz (100 MHz) for all peaks. [e] Major isomer (*ca.* 85%). [f] Minor isomer (*ca.* 15%).

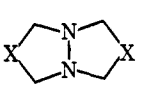
the 1,3-diaxial methyl interaction which **1A** and **1C** lack (as well as the fact that there should be four different NCH_2N hydrogens instead of the two observed). Anderson and Roberts stated a preference for **1C** on the grounds that it has "identical interactions between the members of each pair of vicinal *N*-methyl groups." A dipole moment study by Jones, Katritzky, and Richards[3] gave a value of 1.45 D for **1**, impossible for **1C**, which is centrosymmetric. These authors therefore favor **1A** as the observed conformation, for their estimated dipole moment for **1A** was close to the observed value. They also pointed out that **1A** should be sterically more favorable than **1C**, as there is one less skew butane interaction. On the other hand, **1C** has both hydrazine 1,2 interactions of the gauche type (lone-pair–lone-pair dihedral angle about 60°), whereas one such interaction for **1A** is of the less stable anti type (dihedral angle about 180°); **1C** is electronically preferred. Since the dipole moment study is quite difficult to run on such unstable compounds (any trace of either acid or hydrolysis products would lead to high values for the measured dipole moment), we believed that the question of which conformer really corresponds to that of **1** was still open. Since we desired a series of hydrazines of known conformation for oxidation studies, we have applied low-temperature nmr to several cyclic hexahydrotetrazine derivatives and wish to report our results, which not only establish the low-temperature solution conformation of **1**, but also show that the nmr spectra for **1A** and **1C** would be very different because of hitherto unrecognized differences in the anisotropic effects of gauche and anti hydrazines.

Results and Discussion

Tricyclic Hexahydrotetrazines. The low-temperature nmr spectra of the tricyclic bishydrazines **2–4**



2, X = CH_2
3, X = CH_2CH_2
4, X = CH=CH



5a, X = CMe_2
5b, X = CH_2
6, X = CH_2CH_2

(Table I) allow identification of their conformations on the basis of symmetry arguments. Cooling **2** gives a spectrum showing only a single AB quartet for the NCH_2N hydrogens, while heating causes coalescence to only three types of magnetically nonequivalent hydrogens, as expected. The CCH_2C pattern shows no variation with temperature throughout the broadening and sharpening phenomena observed for the other hydrogens. The symmetry properties of the five possible conformations **A–E** in terms of numbers of magnetically nonequivalent hydrogens appear in Table II. Both **B** and **C** have central rings which can easily undergo flipping, which might well not be frozen at accessible temperatures, so entries are also included for these processes. Only conformations **E** and **B** (flipping) are consistent with the numbers of nonequivalent hydrogens observed for the *N*-methylene protons, but **B** (flipping) may be eliminated as a possibility using two sound arguments. First, it is inconceivable to us that conformation **B** could be more stable than **C**, because the important electronic interactions are the same in both (two gauche hydrazines), but **B** has severe steric destabilization. Secondly, **B** (flipping) does not have the required C_2 axis making all four CCH_2C hydrogens identical as observed. We have an excellent model for what would be expected for the chemical shift difference of such hydrogens in a hypothetical **2B** (flipping) in the nmr spectrum of 1,5-diazabicyclo[3.3.0]octane (**5**), which demonstrates that the chemical shifts for these two types of hydrogens would be detectably different in **2B** (flipping).

Table II. Number of Equivalent Hydrogens for Tricyclic Hexahydrotetrazines **2–4**

Conformation	NCH_2N	NCH_2C
A[a]	4	4,4
B	1,1,1,1	2,2,2,2
C	2,2	2,2,2,2
D	1,1,1,1	1,1,1,1,1,1,1,1
E	2,2	4,4
B(flipping)	2,2	4,4
C(flipping)	4	4,4

[a] The center ring must be a twist boat in these tricyclic compounds.

Compound **3** gave completely analogous variable-temperature behavior and even chemical shifts to **2**, and we therefore confidently assign its low-temperature conformation as **3E**. The symmetry arguments presented above are obviously only valid if it is really true

(3) R. A. Y. Jones, A. R. Katritzky, and A. C. Richards, *Chem. Commun.*, 708 (1969).

that nonequivalent NCH_2 protons would occur at detectably different chemical shifts. For this reason, the spectrum of **4** is important. All four NCH_2N hydrogens occur at different chemical shifts, and two of the NCH_2C absorptions are resolved from all other peaks as well. Although the other NCH_2N hydrogens appear as overlapping multiplets, there would be no danger of interpreting even these signals as being caused by equivalent hydrogens. Only **4D** has the lack of symmetry required by the nmr spectrum. We assert that the wide variation in chemical shifts for the NCH_2 absorptions of **4** gives greater confidence to the symmetry arguments used for the structures of **2** and **3**.

Bicyclic Hydrazines. The low-temperature nmr spectra of **5b** and **6** offer a useful contrast to those of **2** and **3**, for the conformations of the former two are clearly different. Klintzinger, Lehn, and Wagner[4] showed that **5a** is cis fused (though equilibrating so that there are only two types of NCH_2 hydrogens) because the methyl signal freezes out to 1:1 singlets. At 100 MHz, the spectrum of **5b** is sufficiently spread out to allow analysis, and different chemical shifts are easily observed for the "X" hydrogens. The nmr pattern of the methylene group of **5b** is qualitatively different from that of **2**, which is as expected since one is attached to a cis-fused hydrazine and the other to a trans-fused one. From the great similarity of the nmr spectra of **3** and **6**, we argue that they must both have the same sort of hydrazine, and hence must both be trans fused. If **6** were in an equilibrating cis-fused conformation, which would also give the observed symmetry, both types of NCH_2C protons would spend half their time in equatorial positions, and half in axial positions, which would be expected to lower their $\Delta\delta$ over that for **3E**, which cannot be equilibrating. This effect is observed in comparing **2** with **5b** and surely would have been if **3** and **6** had had different conformations.

Steric and Electronic Effects on Hydrazine Conformations. The principal conformations (the only observed ones, in fact) for **2** and **3** are **2E** and **3E**, which minimize steric interactions, but maximize electronic ones. Not only are there two anti 1,2-lone-pair interactions, but also two 1,3-diaxial lone-pair interactions; **3E** is a double violator of the "rabbit ear effect."[5] This effect cannot be of very great importance energetically, at least for hexahydrotetrazine rings. The conformational balance is delicate, however, and removal of a pair of 1,3-diaxial interactions by going from **3** to **4** causes a change in geometry, to the unsymmetrical conformation **4D**, which represents a compromise between destabilizing steric and electronic effects. It is interesting to note that the identically substituted halves of the molecule end up in different geometries, and also that one "rabbit ear effect" violation remains.

Effect of Geometry on Chemical Shift. The wide variations in chemical shift for *N*-methylene protons in **2–6** are of particular interest, as the known conformations should allow these compounds to be used as models in other cases. The most surprising effect is the low $\Delta\delta$ (chemical shift difference $\tau_a - \tau_e$ for axial and equatorial hydrogens on one CH_2 group; $\Delta\delta$ is positive for axial more shielded than equatorial) values observed for methylenes attached to hydrazines. Whereas $\Delta\delta$ (C_2) in *N*-methylpiperidine[6] is 1.02, a considerable enhancement over the 0.57 observed at C_4, we only observe 0.53 for $\Delta\delta$ of **6**. Although it could be argued that a substantial deformation from cyclohexane-like geometry was somehow responsible for this low value, we do not believe that such is the explanation.

As will be justified more completely in a subsequent publication,[7] we believe that there is a strong through-space deshielding effect for a proton held near the backside of an amino nitrogen, but that this effect is reversed for piperidines by the well-established through-bond trans diaxial shielding effect, leading to the positive $\Delta\delta$'s observed for NCH_2 six-ring protons. In an anti six-ring hydrazine (*i.e.*, diequatorial *N*-alkyl substituents), however, there are two additional effects to be considered. First, the 1,3 through-space nitrogen lone-pair–H (axial) interaction is shielding, which by itself would make $\Delta\delta$ more positive. The second factor to consider is that the energy splitting of the lone-pair orbitals is very substantially increased by electronic lone-pair–lone-pair interaction, which should lower the effectiveness of through bond mixing, since it will raise the difference in energy between the highest occupied lone-pair orbital and that of the C–H bond. That $\Delta\delta(NCH_2C)$ is still positive for **3** and **6** is assured by the splitting pattern observed; the downfield hydrogen signal appears as a doublet, and the upfield one as a broad singlet, which requires that they are H_e and H_a, respectively. The chemical shift raising and lowering effects are shown experimentally to almost cancel for a trans–anti hydrazine in a six-membered ring, leading to small, positive $\Delta\delta$ values. Although this is a purely qualitative explanation, we find it attractive, because the interaction of a CH_2 group with two trans–anti hydrazines in the same six-membered ring clearly does not lead to large $\Delta\delta$ values, as is shown by the small $\Delta\delta$ observed at the NCH_2N protons of **3**, which is only slightly larger than that at the NCH_2C protons. This is in great contrast to the geometrically similar interaction of a CH_2 group with one and two amino nitrogens,[8] where $\Delta\delta$ is substantially increased.

The situation is obviously altered considerably by interaction with a cis hydrazine, since $\Delta\delta$ values for the two different NCH_2N methylenes in **4D** are δ 0.38 and 1.53. The chemical shifts in Table I show that the large $\Delta\delta$ arises not by a shielding, but mostly by a deshielding effect, for one of the four protons occurs 0.8 ppm below the other three, or any of the $N–CH_2N$ protons of **2** and **3**. Since experimentally a trans hydrazine does not deshield hydrogens attached to it very effectively, the choice of the low-field proton of **4** seems clear; it can only be H_A' in **4D**, which is held upon the side away from the cis-fused hydrazine, that is, on its deshielding side.[9] We cannot, unfortunately, yet prove that the deshielded proton is an

(4) J. P. Klintzinger, J. M. Lehn, and J. Wagner, *Chem. Commun.*, 206 (1967).

(5) R. O. Hutchins, L. D. Kopp, and E. L. Eliel, *J. Amer. Chem. Soc.*, 90, 7174 (1968).

(6) J. B. Lambert, R. G. Keske, R. E. Carhart, and A. P. Jovanovich, *ibid.*, 89, 3761 (1967).

(7) S. F. Nelsen and P. J. Hintz, to be submitted for publication.

(8) F. G. Riddell and D. A. R. Williams, *Tetrahedron Lett.*, 2073 (1971).

(9) We have ignored the anisotropic effects of the vinyl groups in this qualitative explanation. The major effect will be upon H_a' but it appears from models that shielding would be expected.

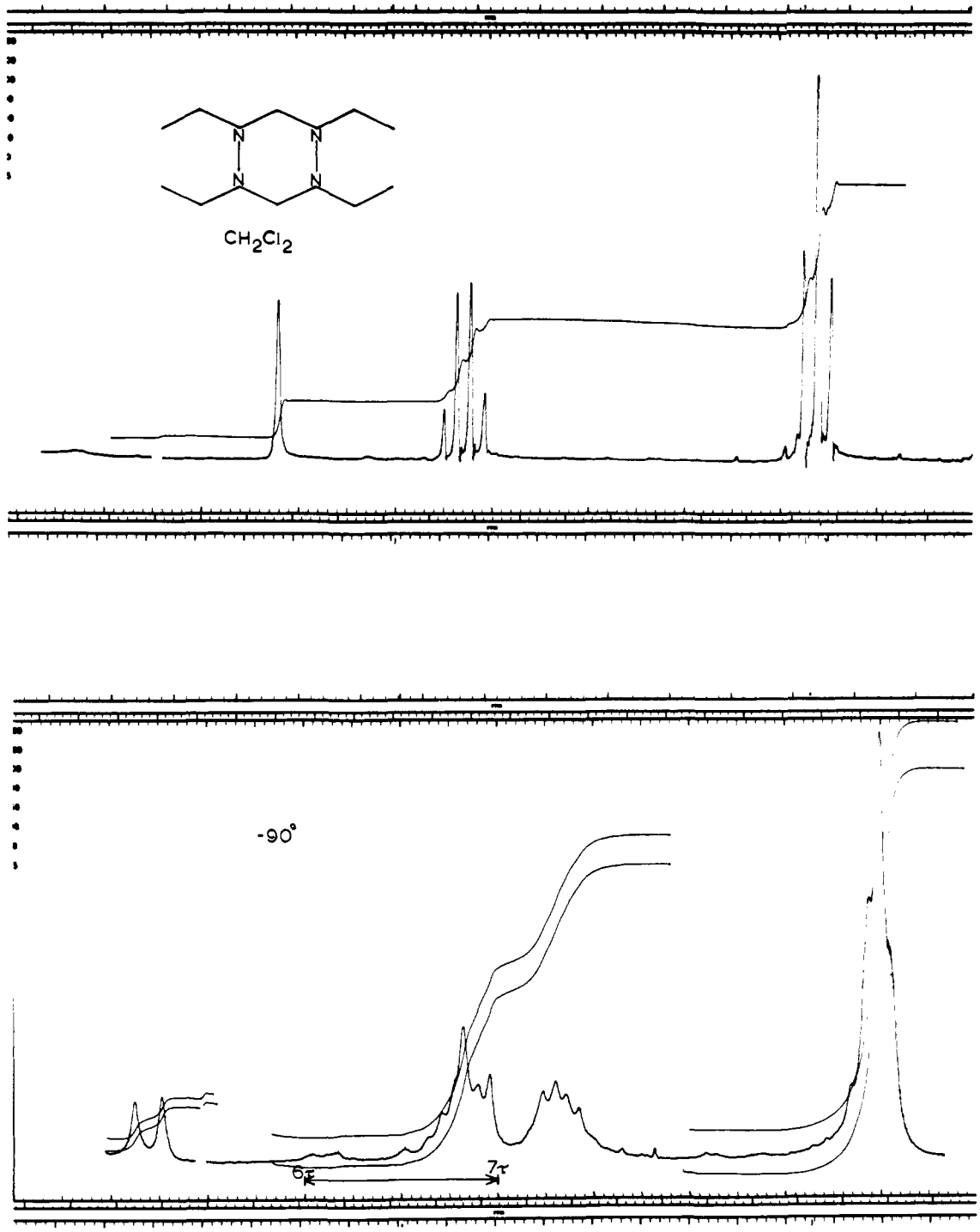
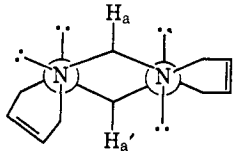
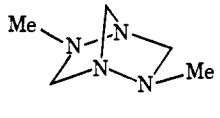


Figure 1. Room-temperature and −90° nmr spectra of 1,2,4,5-tetraethylhexahydrotetrazine (**8**) in methylene chloride.

axial one, but do have precedent for axial hydrogens appearing below equatorial ones in amines; $\Delta\delta$(**3**) is −0.86 for both 1,5-diazabicyclo[3.2.1]octane and 1,5-diazabicyclo[3.3.1]nonane.[7]



4D



7

Although the "special" τ 5.31 NCH_2N hydrogen of **4D** is surprisingly deshielded compared to **2** or **3**, it is not when compared with those of **7**, another tetraalkylhexahydrotetrazine, but one without the rather special trans-anti hydrazine bridges of **2** and **3**. The three types of NCH_2 hydrogens of **7** appear at δ 3.92, 4.06 (AB quartet, $\Delta\delta$ = 0.14), and 5.24 (singlet). The nmr spectrum of **7** is temperature invariant, as expected if the bis-exo methyl conformation shown predominates greatly. Since **7** (which is in a distorted **B**-type of conformation) lacks both through-space and through-bond shielding alignments, the through-space backside deshielding effects of the approximately gauche cross-ring cis hydrazine groups dominate, substantially deshielding all three types of NCH_2N hydrogens in comparison to **2** or **3**.

Table III

Compd	Mp or bp (mm), °C	Analysis or exact mass					
		Calculated, %			Found, %		
		C	H	N	C	H	N
2	131–132	57.10	9.59	33.31	57.10	9.61	33.34
4	151–152.5	62.46	8.39	29.15	62.44	8.40	29.18
7	86–87 (25)		128.1062			128.1062	
8	165–169 (100)		200.2001			200.1983	

Monocyclic Hexahydrotetrazines. Armed with the nmr spectra of some model compounds of known geometry, we now turn our attention back to monocyclic examples. To get data directly comparable to our other data, we have obtained the nmr spectrum of **1** as well as its tetraethyl analog **8** in deuteriochloroform (Table I). **8** required much lower temperature to "freeze out" than did **1**, but at −90° an approximately 85:15 mixture of two conformers was observed (see Figure 1). The major conformer was clearly very different from the only conformer present at low temperature for **1**, since it shows $\Delta\delta = 1.70$ for its single NCH_2N AB quartet. The large $\Delta\delta$ results in a wide temperature range for broadening. The only peaks of the minor conformer which are observed unobscured are the NCH_2N peaks, but the agreement in both $\Delta\delta$ and chemical shift causes us to assign the minor conformer as being the same as the only one observed for **1**. Since both **1** and **8** give different major isomers with only two types of ring protons, and two types of methyl or ethyl groups, the nmr symmetry requires that they be conformations **A**, **B**, or **C**. We follow both previous groups in ruling out **B** on the basis of unfavorable 1,3-diaxial alkyl interactions which are not present in **A** or **C**. The major difference between the conformation assumed by **1** and the major conformation of **8** lies in the strong deshielding of one set of NCH_2N protons in the latter. The best candidates for the strongly deshielded protons are the axial protons of **A**, which are held in the deshielding area of the gauche hydrazine. In **C**, which has two gauche hydrazines, the axial protons will be shielded by one, and deshielded by the other. Quite independent of the chemical shift difference argument, subsequent changing from methyl to ethyl substituents causes a change in major conformation; this can only be toward a sterically less hindered conformation. **A** is indeed less hindered than **C**, for it lacks a gauche interaction of two *N*-alkyl substituents that is present in **C** (as Jones, Katritzky, and Richards have pointed out[9]). Thus **1** exists as **1C**, while **8** is an 85:15 mixture of **8A** and **8C** at −90°.

Conclusion

The interplay of electronic and steric destabilization is clearly responsible for the fascinating gyrations through which a hexahydrotetrazine ring goes as substituents are changed. If only the electronic interactions within the hydrazine units are considered for a hexahydrotetrazine, conformations **B** and **C** (each two gauche hydrazines) should be the most stable. Next should come **A** and **D** (one gauche and one anti) and the least stable should be **E** (two anti hydrazines). Since **B** is strongly destabilized by 1,3-dialkyl interactions, an approximation of this conformation can only be postulated by building up a cage structure as in **7** (forcing the hexahydrotetrazine ring into a boat form). For the tetramethyl-substituted compound **1**, only the electronically most stable conformation **1C** was observed at low temperature. With four ethyl substituents, **8A**, electronically less favorable, but lacking one gauche di-*N*-alkyl steric interaction, was present in significantly higher concentration than **8C**. In the tricyclic series, conformation **A** is strongly destabilized (the central ring would have to become a twist boat for the nitrogens to assume the relative configurations shown for **A**), and both **2** and **3** assume the least electronically but most sterically favorable conformation, **E**. The fine balance of effects is well illustrated by the low-temperature conformation of **4** being **4D**, with one axial and three equatorial *N*-alkyl substituents. Simply removing axial hydrogens by introducing the double bonds allows the molecule to assume an electronically more favorable conformation.[10]

In a future publication we shall discuss the nmr spectra of dialkylhexahydropyridazines, which are also in dispute, and are amenable to a similar type of analysis.

Experimental Section

Compounds **1**,[11] **3**,[12] **5b**,[13] **6**,[14] and **9**[11] were prepared according to established literature procedures and had physical constants in accord with those reported. Compounds **2**, **4**, **7**, and **8** were prepared by the condensation of formaldehyde with pyrazolidine,[13] 1,2,3,6-tetrahydropyridazine,[15] 1,4-dimethyl-1,2,4,5-hexahydro-*s*-tetrazine,[16] and diethylhydrazine,[17] respectively. Final purification of compounds **2**, **3**, and **4** was accomplished by repeated recrystallization from petroleum ether while compounds **1**, **5b**, **6**, **8**, and **9** were subjected to vpc through a 5 ft × 0.25 in. XF-1150 silicone fluid column. Compound **7** could only be purified by distillation. The physical constants and analytical data for the previously unreported compounds are seen in Table III.

The nmr spectra were recorded on a Varian Associates HA-100 spectrometer equipped with a V-4343 variable-temperature controller capable of reaching temperatures of +200 to −100°. Temperatures above ambient were calibrated with the hydroxyl shift of ethylene glycol and those below ambient with the hydroxyl shift of methanol.

(10) We thank the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work.

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