I. CONFORMATIONAL PROPERTIES OF CYCLOBUTANES

II. NITROGEN-15 MAGNETIC RESONANCE SPECTROSCOPY

Thesis by

Joseph Buckley Lambert

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TO MARGRET

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The inspiration which guided me ultimately into physical organic chemistry derives almost entirely from four men: Mr. Edwin Nelson and the late Professor Harold Dietrich, who introduced me to chemistry; Professor Gary Griffin and Professor William von E. Doering, who introduced me to research. My debt is particularly great to the first and last of these individuals. Most influential in the basic construction of this thesis, and, indeed, in all future consideration of chemical problems, has been Professor John D. Roberts, with whom it has been a privilege to work. Of the many colleagues who have contributed through discussion to the results described herein, Dr. Gerhard Binsch deserves especial thanks. Fellowships from the Woodrow Wilson Foundation and the National Science Foundation are gratefully acknowledged.

I. CONFORMATIONAL PROPERTIES OF CYCLOBUTANES

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ABSTRACT

The temperature dependence of the geminal fluorine-fluorine chemical-shift differences in a variety of unsymmetrically substituted cyclobutanes has been interpreted in terms of a classical equilibrium between axial and equatorial conformations, for which free-energy differences have been calculated. The absence of this effect for cyclobutenes and cyclobutanones indicates that these systems are nearly planar. The angle of puckering of 1, 1-difluoro-3-phenylcyclobutane has been calculated by the dipole-moment method to be about 27°. The observation of substantial temperature variations of the vicinal hydrogen-fluorine coupling constants is consistent with the presence of an equilibrium between conformers. The magnitude of these couplings as a function of the dihedral angle appears to follow a relationship similar to that described by Karplus for proton-proton coupling constants.

Nitrogen-15 magnetic resonance spectroscopy has been investigated for the first time. The absolute magnitude of the chemical shift and its variation with protonation have been interpreted in terms of the predominance of the paramagnetic term in the shielding expression. A correlation between the energy of the $n \rightarrow \pi^*$ transition and the

magnitude of the chemical shift is considered. An empirical relationship between the hybridization of nitrogen and the coupling between directly bonded nitrogen-15 and hydrogen is derived, and the limitations are discussed. Contributions to the coupling from orbital motion are invoked in order to explain the significant deviation of the coupling in ketimines from the behavior predicted by this relationship. The temperature dependence of the proton spectrum of nitrogen-15-labeled ketimines is interpreted as resulting from a degenerate, bimolecular exchange of the imine protons. Separate geometrical isomers of an imine unsubstituted at nitrogen (s-butylphenylketimine) are observed for the first time.

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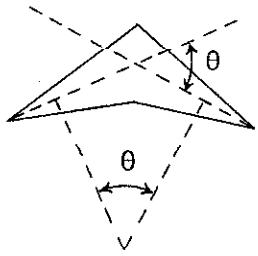
PART I

CONFORMATIONAL PROPERTIES OF CYCLOBUTANES

I. INTRODUCTION

The nonplanar nature of cyclohexane and the resulting axial and equatorial orientation of substituents, although suggested as early as 1890, was not established until the 1920's (1). Conformational properties have been usefully ascribed to the more flexible five- and seven-membered ring systems in terms of the pseudorotation process (2-5). A planar representation, however, has generally been accepted for the four-membered ring systems in spite of a limited number of demonstrations to the contrary. Conceivably, this misconception has arisen because of incorrect conclusions of early workers. The original decision of Wilson (6) that cyclobutane itself is planar was reversed by Dunitz and Schomaker (7), who showed by electron diffraction studies that the molecule has a dihedral angle, θ, of about 20°. The



later infrared-Raman studies of Rathjens, et al. (8), resolved this controversy by establishing the presence of both D_{4h} and D_{2d} cyclobutane molecules. According to the calculations of these authors, a barrier of about 400 $cm.^{-1}$ hinders the out-of-plane bending process. Those molecules in vibrational states below this value will be of D_{2d}

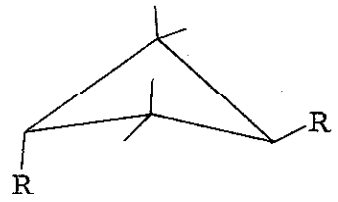
symmetry; the remaining molecules will possess D_{4h} symmetry. The average dihedral angle at any given time is therefore nonzero.

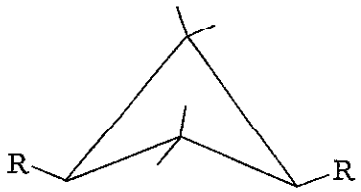
The height of the barrier to inversion should be a sensitive function of the nature of any ring substituent. Nevertheless, Edgell (9) and Claassen (10) concluded from infrared-Raman studies that octafluorocyclobutane is planar. Electron diffraction data, however, again required a molecule of lower symmetry (11). Intensity patterns could best be accounted for by a D_{2d} model with $\theta = 20 \pm 4°$. The description of octachlorocyclobutane by Owen and Hoard (12) similarly included a dihedral angle of 22°, although the X-ray crystallographic data is of questionable significance for molecules in noncrystalline states. Detailed analysis of the microwave spectrum of bromocyclobutane (13) permitted assignment of a dihedral angle of 29° 22' ± 08' to this molecule. Since introduction of a single large substituent increases the dihedral angle, reduction of nonbonded repulsions must contribute substantially to the inversion barrier.

Replacement of a methylene group by a heteroatom, as in trimethylene oxide, would remove two 1, 3 (cross-ring) interactions and four 1, 2 (vicinal) interactions. The barrier to inversion in this oxygen heterocycle was determined by Chan, et al. (14-15), by microwave spectroscopy to be only 35 ± 5 $cm.^{-1}$. Since the lowest vibrational level is about 8 $cm.^{-1}$ above the top of the barrier, the inversion doubling associated with the nonplanarity of cyclobutane (8) does not occur. The microwave spectrum of cyclobutanone (16) was similarly consistent with a planar structure. Reduction of substituent interactions

associated with the introduction of an sp^2 center thus has a substantial effect on the inversion barrier.

On the other extreme of substitution, Lautenschlaeger and Wright (17) have determined the extent of nonplanarity for systems I and II from a careful application of the dipole-moment method.





Ia: R = CN

Ib: R = NC

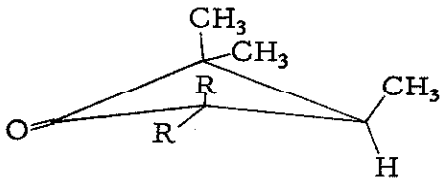
IIa: R = CN

IIb: R = NC

The dihedral angles of the trans isomers were found to be about 24°, whereas the angles for IIa and IIb were approximately 42° and 51°, respectively (benzene solution, 20°). The lowering of the barrier associated with the removal of substituents in trimethylene oxide and cyclobutanone and the increase in the degree of nonplanarity in going from 1,3-trans isomers (I) to 1,3-cis isomers (II) substantiate the view that nonbonded substituent repulsions are the primary cause of ring puckering.

Nonplanarity may arise in highly substituted four-membered rings even if one methylene group has been replaced by an unsubstituted fragment such as the carbonyl group, provided that substituent interactions elsewhere in the molecule are high. By an extension of

the octant rule to four-membered cyclic ketones, Conia and Goré (18-19) have demonstrated that IIIa and IIIb are nonplanar. Although



IIIa: R = H

IIIb: R = Br

the presence of a Cotton effect excludes the planar form, and the sign of the effect determines the orientation of substituents (20), these experiments can give no indication of the degree of nonplanarity. It may actually be rather small (21).

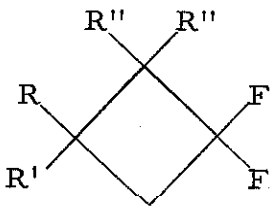
II. THE VARIATION OF CHEMICAL-SHIFT DIFFERENCES WITH TEMPERATURE

The evidence presented thus far indicates that a cyclobutane ring will accommodate a substituent by puckering in such a way as to minimize nonbonded interactions. A deformation of this sort will not increase the strain associated with bond angles and bond lengths, since the changes in these quantities are small. By analogy with the nomenclature of higher ring systems, the position assumed by a substituent in such a deformation may be termed equatorial (IVb), and the

(1)

IVa IVb

corresponding position which arises after the ring-inversion process occurs may be called axial (IVa). The double-well potential barrier for the monosubstituted model IV would be unsymmetrical, the equatorial conformer being of lower energy. The existence of a classical equilibrium of this sort could be established by the temperature dependence of a molecular property which varies with changes in conformational populations. To this end, the chemical-shift difference between nonequivalent geminal fluorine atoms in variously substituted cyclobutanes (V–VIII) was measured as a function of



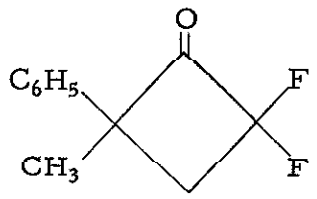
	R	R'	R''
V	C_6H_5	H	H
VI	C_6H_5	H	Cl
VII	Cl	H	Cl
VIII	C_6H_5	Br	H
IX	p-NO_2-C_6H_5	H	H

temperature (22). At a given temperature, the observed chemical-shift difference, δ, is the weighted average of the values for the axial (IVa) and equatorial (IVb) conformers, δ_a and δ_b:

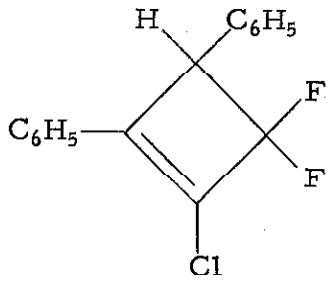
$$\delta = p\delta_b + (1 - p)\delta_a \qquad (2)$$

where p is the temperature-dependent population of the equatorial conformer. Lower temperatures will increase the population of IVb, whereas higher temperatures will bring about an approach to equal populations of both conformations.

The fluorine spectra of compounds V-VIII, X, and XI ac-



X



XI

cordingly were analyzed at -85, -30, 30, 85, and 140° (23).

Compounds V-VIII and XI were examined in 20% carbon disulfide solutions, whereas X was a neat sample. Simultaneous irradiation of the samples at 60.0 Mcps simplified the spectra to the familiar AB pattern by removing hydrogen-fluorine couplings. The chemical shifts and coupling constants were calculated to ± 1 cps from at least fifteen measurements calibrated by the side-band technique. Examination of these data, which are displayed in Table I and Figure 1, reveals a large temperature dependence of the chemical-shift difference between the fluorine atoms of the saturated cyclobutanes V-VIII, a small dependence for the cyclobutanone X, and none at all for the cyclobutene XI. This is the behavior which would be expected of the model depicted by equation 1. The large variation of δ for V-VIII cannot be explained with planar structures. Conversely, the absence of any temperature effect in the spectrum of the cyclobutene XI points toward a completely planar structure. Furthermore, it is indicative that effects not arising from conformational considerations, such as medium effects, are negligible or nullified by cancellation. From the small changes in the spectrum of the cyclobutanone X, no clear-cut decision between models may be made. Deviations from planarity are probably small.

It should be noted that a temperature dependence of the fluorine-fluorine chemical-shift difference does not require two distinct conformations with the associated inversion barrier. The data could also be accommodated by a highly asymmetric potential well which possesses only a single minimum. Increased population of

TABLE I

FLUORINE-FLUORINE CHEMICAL-SHIFT DIFFERENCES AND COUPLING CONSTANTS

V	T, °C	-87	-29	31	87	139
	δ, cps	1093	1039	979	933	908
	J, cps	192	192	195	194	195
VI	T	-84	-30	31	88	141
	δ	635	609	569	543	522
	J	183	182	182	183	184
VII	T	-84	-29	31	88	141
	δ	425	393	358	336	323
	J	187	188	187	187	189
VIII	T	-88	-33	32	83	134
	δ	413	302	225	175	136
	J	196	197	197	199	200
X	T	-79	-31	31	85	139
	δ	116	123	133	135	141
	J	248	250	249	249	250
XI	T	-79	-29	31	85	139
	δ	470	468	472	473	470
	J	192	192	192	194	193

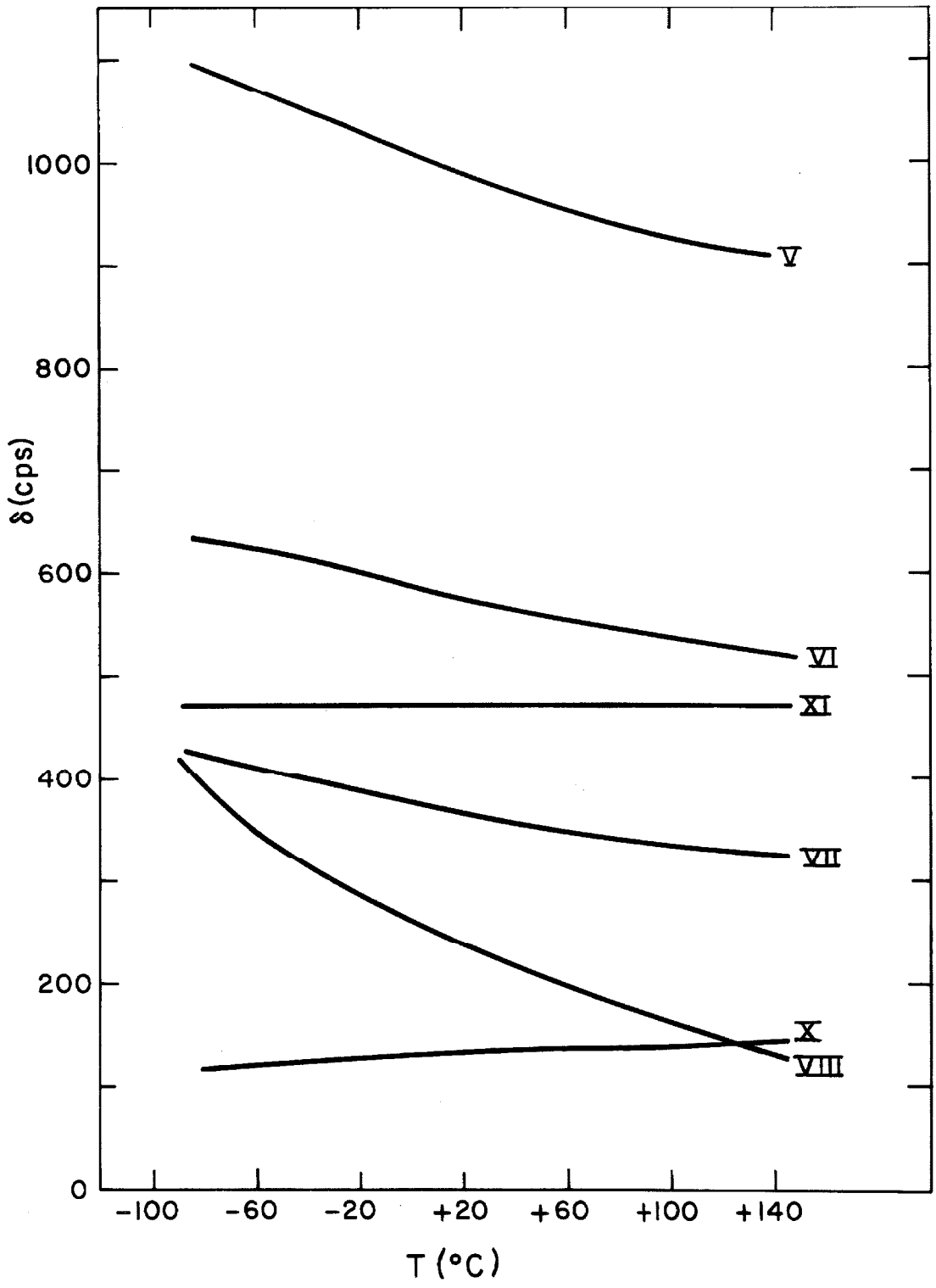


Figure 1. Temperature dependence of chemical-shift differences. Roman numerals refer to the formulas on p. 7.

higher vibrational states at higher temperatures would cause a change in δ as well, although it is doubtful that the magnitude could be as large as that observed here. Since two distinct minima have been demonstrated spectroscopically for cyclobutane (8) and trimethylene oxide (14-15), this model will be accepted for the present study.

Since only a single AB spectrum was observed at low temperatures for compounds V-VIII, the equilibrium represented by equation 1 must be fast on the n.m.r. time scale. The equilibrium constant for the process is:

$$K = \frac{p}{1-p} = e^{-\Delta F/RT} \qquad (3)$$

where ΔF, the free-energy difference between conformers, is negative since the equatorial form IVb is more stable. Solving for p, one obtains:

$$p = \frac{1}{1 + e^{\Delta F/RT}} \qquad (4)$$

Equation 2 may be rearranged to the form:

$$\delta = \delta_a + p(\delta_b - \delta_a) \qquad (5)$$

in which δ is a linear function of p, since δ_a and δ_b are constant for a given molecule. The appropriate value of ΔF is taken as that value which gives the best linear plot of δ vs. p. In order to obtain this

quantity, a Fortran program (Appendix I) was written which calculates the slope and intercept of equation 5 from a least-squares fit of a plot of δ vs. p for steps of 50 cal. in the free-energy difference. The values of ΔF (50 to 4000 cal.) were ordered according to the magnitude of the sum of the squares of the deviations. In all cases, the data converged from both directions to a "best" value of ΔF. It was observed from visual plots that deviations from linearity develop in both directions sufficiently rapidly to warrant placing an error of ± 100 cal. on the magnitude of ΔF. Furthermore, the "best" value of ΔF remains within a 100 cal. range when the input parameters (δ and T) are varied over the range of experimental error. Table II presents the values of the conformational properties obtained in this way.

The bulky phenyl group gives rise to the largest free-energy difference between conformers. The values for V and VI are experimentally the same. Replacement of the phenyl group by the smaller chlorine atom (VI → VII) reduces the value of ΔF by about 0.35 kcal/mole, thereby decreasing the proportion of the equatorial conformer. If two substituents are placed in the 3-position, as in VIII, the free-energy difference becomes rather small. The large variation of δ with temperature for VIII (277 cps) indicates that the increase in nonbonded repulsions accentuates the ring-inversion process, rather than causing the molecule to become more nearly static and planar. This particular situation probably arises because bromine and phenyl are approximately equivalent in size (24).

TABLE II

CONFORMATIONAL PROPERTIES OF SUBSTITUTED CYCLOBUTANES

	V	VI	VII	VIII
ΔF, cal./mole	-950 ± 100	-1100 ± 100	-750 ± 100	-400 ± 100
δ_a, cps	40 ± 50	-60 ± 40	-120 ± 20	-1210 ± 200
δ_b, cps	1175 ± 20	670 ± 10	500 ± 20	960 ± 200
p, 140°	0.761 ± 0.025	0.792	0.713	0.621
p, 85°	0.791	0.823	0.740	0.638
p, 31°	0.828	0.861	0.776	0.659
p, −30°	0.877	0.907	0.825	0.698
p, −85°	0.929	0.949	0.881	0.748

Examination of the theoretical plots of δ vs. p over the extrapolated range of populations (Figure 2) shows that the disubstituted cyclobutane VIII behaves in a totally different manner from the monosubstituted systems V-VII. For the latter group of compounds, the chemical-shift difference approaches a value near zero as the population of the axial conformer approaches unity ($\delta \rightarrow 0$ as $p \rightarrow 0$), whereas at the other extreme ($p \rightarrow 1$), δ_b varies greatly with the nature of the substituents. The values of δ_a and δ_b for VIII, on the other hand, are large and more or less symmetrical with respect to $\delta = 0$. The appearance of Figure 2 suggests that among the axial conformers of V-VII, there is a geometrical similarity which is not shared by the disubstituted molecule VIII. This is reasonable, since the equatorially oriented substituent in the conformer resembling IVa is hydrogen for V-VII, but the axial substituent is a large group such as phenyl. Furthermore, it is significant that the common value of δ_a is close to zero, for this is the value expected if the chemical-shift difference between the fluorine atoms arises principally from the anisotropy of the ring carbon-carbon bonds. McConnell (25) has employed the point-dipole approximation to describe the shieldings of a nucleus by an axially symmetric group such as the carbon-carbon single bond:

$$\sigma_{av.} = \frac{(3 \cos^2 \theta - 1)(\chi_L - \chi_T)}{3 r^3} \qquad (6)$$

where r is the distance from the nucleus to the electrical center of

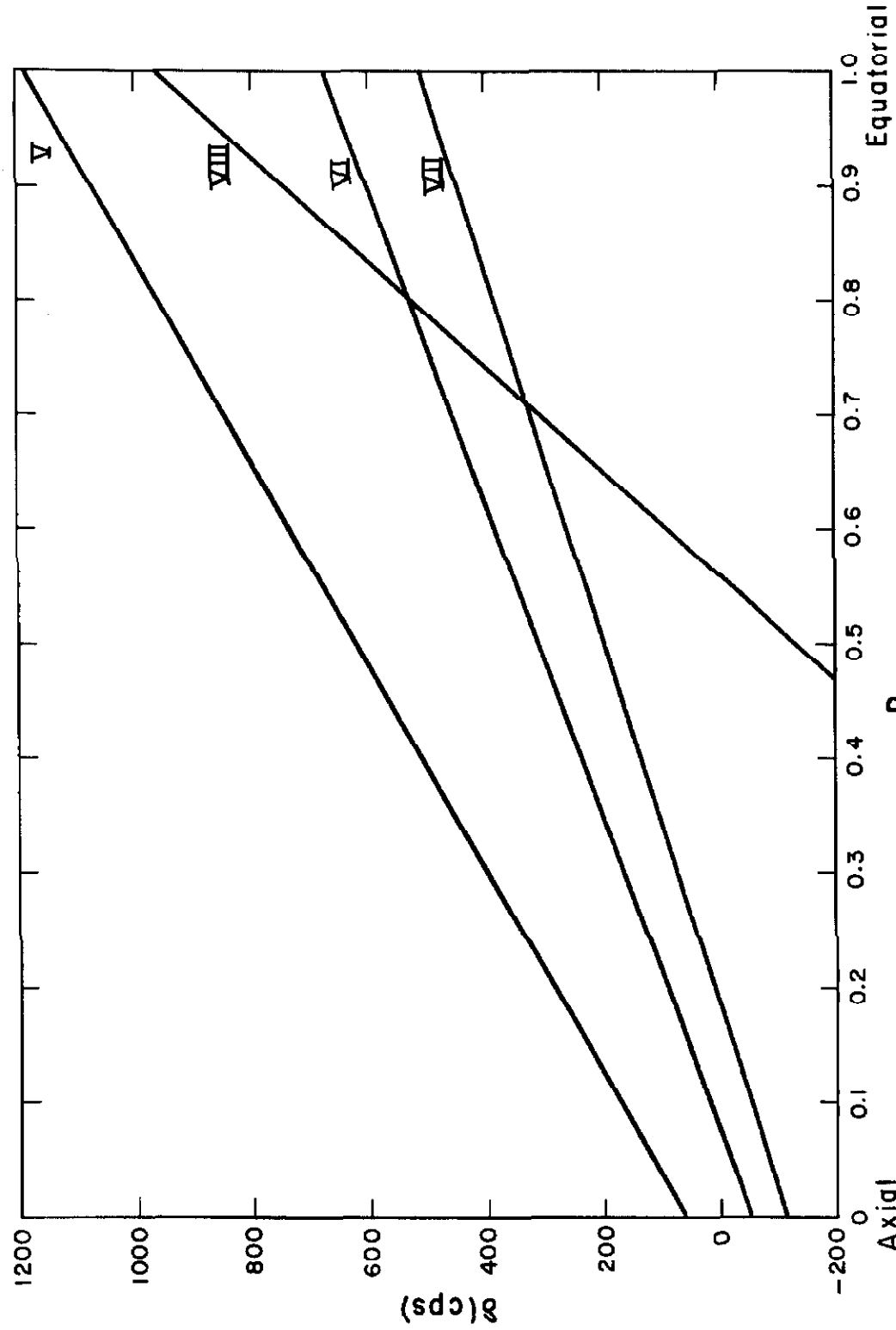
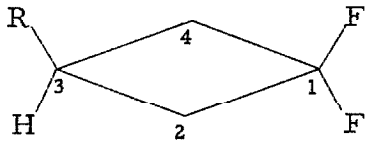
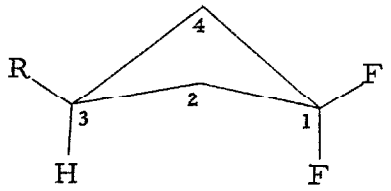


Figure 2. Chemical-shift difference as a function of population. Roman numerals refer to formulas on p. 7.

gravity of the group (the midpoint of the bond), θ is the angle which the vector r makes with the axis of symmetry (the bond), and $\chi_L - \chi_T$ is the difference between the longitudinal and transverse magnetic susceptibilities (a measure of the diamagnetic anisotropy of the group). As in the case of cyclohexane (26), contributions to the shieldings from the 1, 2 and 1, 4 bonds in XII and XIII are the same for both nuclei,



XII

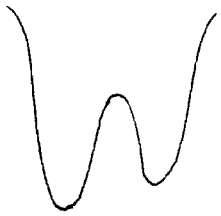


XIII

since r and θ are identical. Although this is also true of the 2, 3 and 3, 4 bonds in XII, these bonds in XIII will shield the two fluorine nuclei to different extents, thus giving rise to a chemical-shift difference. In this description, as in that for cyclohexane (26), it is necessary that the contributions from distant bonds be negligible. Consequently, the freely rotating group R serves only to pucker the ring without contributing directly to δ. This model therefore predicts that only nonplanar cyclobutanes will exhibit magnetically nonequivalent geminal fluorine atoms, provided the only unsymmetrical substitution pattern occurs at the 3-position. This model also suggests that the axial conformer is nearly planar for V-VII, since δ_a is consistently near zero, but that two distinct nonplanar conformers must exist for VIII, since

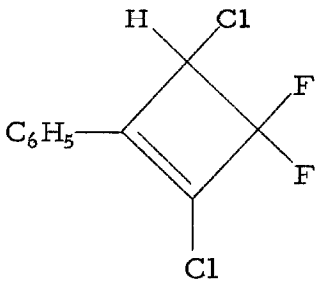
δ_a is large and negative. A planar axial conformer is reasonable for monosubstituted cyclobutanes because 1, 3 cross-ring interactions would increase with the deviations from planarity required of a conformer resembling IVa. The fundamentally different nature of the spectral properties of mono- and disubstituted cyclobutanes probably arises from differences between the shapes of the potential wells.

V-VII

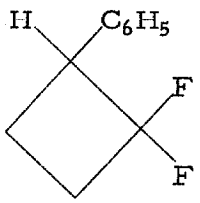


VIII

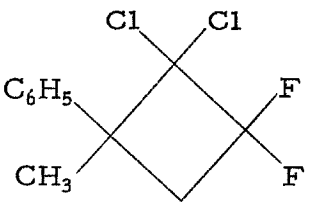
Although the model based on diamagnetic anisotropies as the principal source of the chemical-shift difference explains the general features of Figure 2, there are numerous assumptions inherent in the derivation of equation 6 which militate against its application in a detailed manner to geometrical problems. The magnitude of the effect may be too small to explain the large observed chemical shifts. The magnetic properties of the 2, 3 and 3, 4 bonds need not be constant with substituent changes at the 3- and 4-positions. A more direct test of the contention that a value of δ close to zero implies that θ is also near zero would be to observe the properties of a molecule known to be planar. Evidence cited thus far points to the planarity of cyclobutenes (XI and XIV), but in the two molecules studied, the source of



XIV



XV



XVI

asymmetry has shifted from the 3-position to the 2- or 4-position. Substituents in the 2-position would almost certainly contribute a neighbor-anisotropy effect, and, in fact, the chemical-shift differences (31°) are 472 and 438 cps for XI and XIV, respectively. Similar movement of the phenyl substituent from the 3-position in V to the 2-position in XV raises the chemical-shift difference from 979 to 1778 cps. Thus these cyclobutenes cannot offer a direct test of planarity because unsymmetrical substitution at the 2- or 4-positions introduces rather large chemical-shift effects without necessarily causing substantial nonplanarity. It is also possible that the chemical-shift differences between the fluorines in gem-difluoro substituted cyclobutenes may be appreciably more sensitive to substitution than in cyclobutanes because of hyperconjugation involving the fluorines and the double bonds.

The cyclobutanone X was judged to be nearly planar, and in this molecule unsymmetrical substitution is restricted to the 3-position. In fact, replacement of the gem-dichloro group in XVI by an oxo group in X lowers δ (31°) from 430 to 133 cps. The chemical-

shift difference in X therefore supports the neglect of anisotropic properties of 3-substituents and indicates that a small value of δ corresponds to small average deviations from planarity. Since, for cases V-VII, the values of δ_a are close to zero, equation 5 reduces approximately to:

$$\delta(T) = p(T)\delta_b \tag{7}$$

where the temperature dependencies have been recognized explicitly. If the average angle of puckering is a weighted average of the angles associated with the frozen conformers, then:

$$\theta = p\theta_b + (1 - p)\theta_a \tag{8}$$

or,

$$\theta = \theta_a + p(\theta_b - \theta_a) \tag{9}$$

which reduces to:

$$\theta(t) = p(T)\theta_b \tag{10}$$

when the axial conformer has a planar configuration. Since the conditions on equations 7 and 10 coincide, the equations may be manipulated simultaneously. Thus:

$$\Delta\theta = \frac{\theta(T)}{\delta(T)} = \frac{p(T)\theta_b}{p(T)\delta_b} = \frac{\theta_b}{\delta_b} = \text{constant} \tag{11}$$

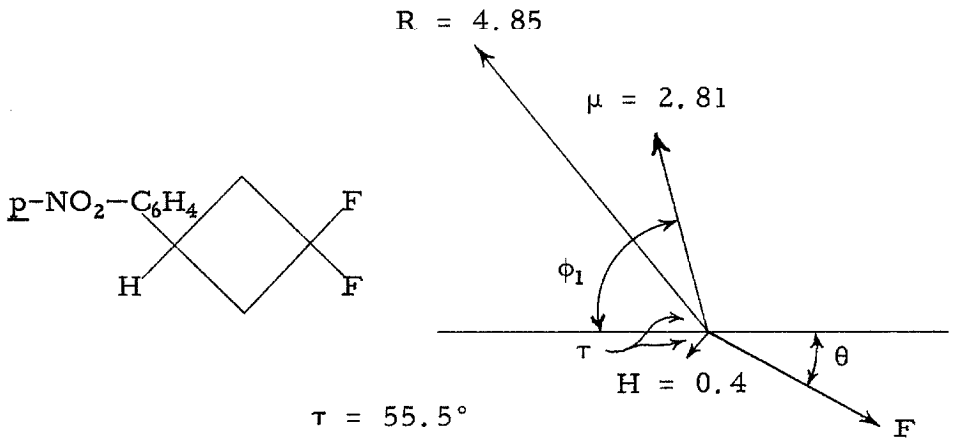
Equation 11 states that for any given temperature, the quotient of the dihedral angle and the chemical-shift difference is constant to a crude

first approximation. Thus a single determination of θ will serve to define the average geometry of the molecule at all temperatures. The magnitude of the chemical-shift difference will reflect the degree of nonplanarity directly.

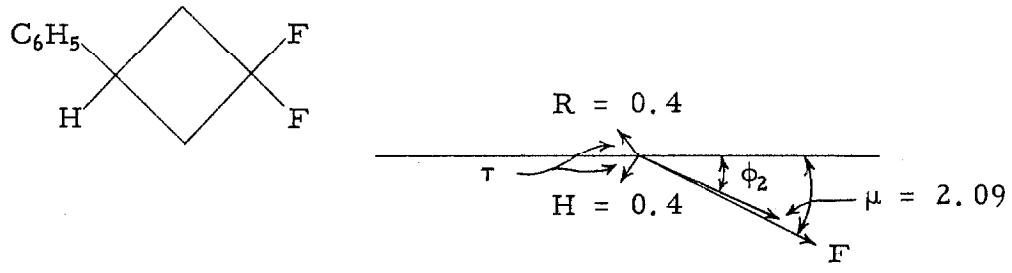
III. DIPOLE-MOMENT CALCULATIONS

The method of dipole moments was used to determine the geometry of 1, 1-difluoro-3-phenylcyclobutane (V) and 1, 1-difluoro-3-p-nitrophenylcyclobutane (IX). The projection of the substituent moments on the plane which passes through carbon atoms 1 and 3 and the substituents on these atoms, is given below for the predominant equatorial isomer (all vectors have been translated to the center of the molecule):

IX:

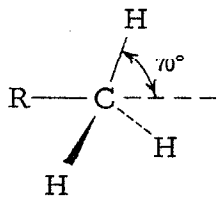


V:



where θ is the angle of puckering, μ is the molecular dipole moment, ϕ_1 and ϕ_2 are the angles between μ and the axis for IX and V, respectively, H is the C—H bond moment, F is the CF_2 group moment, and R is the C—R group moment. The R—C—H and F—C—F angles were taken to be 111°, in accordance with the values of the corresponding angles in bromocyclobutane (13). The assumption that θ is the same for both compounds derives not only from the small change in substituent size, but also from the observed identity of the chemical-shift differences between the fluorine atoms of the two compounds. From the previous discussion, this observation alone would suffice to prove the assertion that the compounds have the same angle of puckering.

The dipole moments of V and IX were measured to be 2.09 and 2.81 ± 0.02 D, respectively, in benzene solutions at 27.5°. The C—H bond moment was taken to be 0.4 D, with hydrogen negative with respect to carbon, in accordance with the evidence presented by Coulson, Wheland, and others (27). This is not a critical decision, although the convention must be maintained throughout the analysis. The C-p-NO_2—C_6H_4 group moment was derived from the dipole moment of p-nitrotoluene in benzene, 4.45 D. The remaining quantities, θ, ϕ_1, ϕ_2, and F, must be calculated from the four simultaneous equations



$$4.45 = R - 3H\cos(70°)$$

$$R = 4.45 + 3 \times 0.4 \times 0.333 = 4.85 \text{ D}$$

derived from the projection drawings of IX and V. The object of including system V was to obviate an independent designation of the value for F. Thus, for IX;

$$2.81\cos(\phi_1) = 4.85\cos(55.5°) + 0.4\cos(55.5°) - F\cos(\theta) - 0.462 + 0.462\cos(\theta) \quad (12)$$

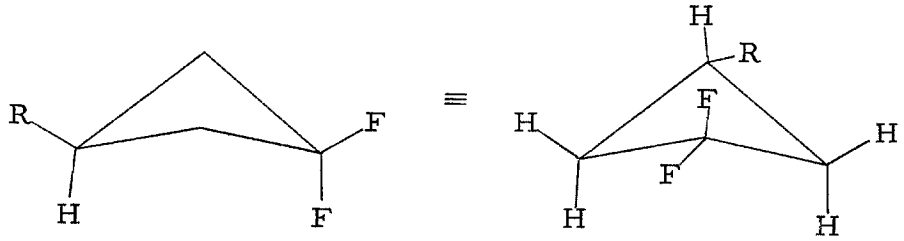
$$2.81\sin(\phi_1) = 4.85\sin(55.5°) - 0.4\sin(55.5°) - F\sin(\theta) + 0.462\sin(\theta) \quad (13)$$

and for V:

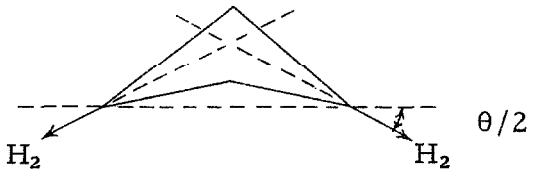
$$2.09\cos(\phi_2) = F\cos(\theta) - 0.4\cos(55.5°) - 0.4\cos(55.5°) + 0.462 - 0.462\cos(\theta) \quad (14)$$

$$2.09\sin(\phi_2) = F\sin(\theta) + 0.4\sin(55.5°) - 0.4\sin(55.5°) - 0.462\sin(\theta) \quad (15)$$

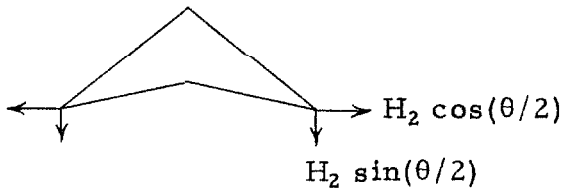
The last two terms in equations 12 and 14 and the last term in equations 13 and 15 arise from contributions from the methylene hydrogens. These small corrections are necessary in order to maintain a consistent convention for the hydrogen dipole. To see how these terms were obtained, one performs two rotations on the geometry of structure IV:



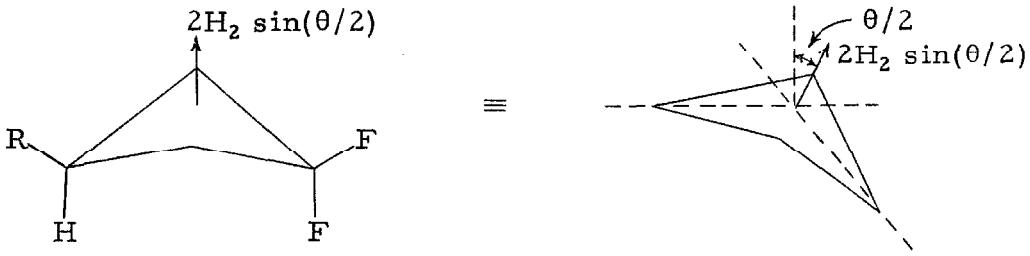
Each geminal hydrogen pair may be represented by a single vector H_2 which makes an angle of $\theta/2$ with the horizontal axis, where θ is defined as before.



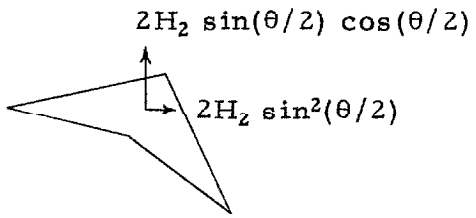
These vectors may be resolved into their vertical and horizontal components, the latter portions of which cancel.



The sine components may be translated to the center of the molecule and added vectorially. When the molecule is returned to the original position and rotated by an angle $\theta/2$ about the C_2-C_4 axis,



the position becomes identical to that in the projection drawings, and the vector must only be further resolved into horizontal and vertical components,



which may be simplified by well-known trigonometric identities:

$$2H_2 \sin(\theta/2) \cos(\theta/2) = H_2 \sin(\theta) \quad (16)$$

$$2H_2 \sin^2(\theta/2) = H_2 - H_2 \cos(\theta) \quad (17)$$

The value of H_2, which is the sum of two vectors of magnitude 0.4 separated by 111°, is 0.462. The right sides of equations 16 and 17 supply the final terms in equations 12-15.

The angle of puckering was found by an iterative procedure which consisted of solving equations 12 and 13 for ϕ_1 and θ, with F taken, as a first approximation, to be the value derived from the dipole moment of methyl fluoride. The resulting value of θ was used in equations 14 and 15 to solve for ϕ_2 and a new value of F. The procedure converged after only two sets of calculations. The unique set of solutions is:

$\theta = 26°45' \pm 40'$ $\qquad$ $\phi_1 = 76°30' \pm 40'$

$F = 2.54 \pm 0.01$ D $\qquad$ $\phi_2 = 26°40' \pm 40'$

The validity of the solution was checked by construction. The listed errors are those which arise from the experimental error in the dipole-moment measurements, and do not include extensive systematic errors inherent in the dipole–moment method itself. The calculative procedure was designed to minimize such errors. The two polar groups in V are on opposite sides of the molecule, so mutual polarization is minimized. The results are independent of the choice of convention for the C–H bond moment, a source of considerable controversy in the literature (27). If the calculations are repeated, with the convention reversed, i.e., with carbon the negative end of the dipole, identical results are obtained. These computations require re-evaluation of the C–R and CF_2 group moments. Thus,

$C\text{-}\underline{p}\text{-}NO_2\text{–}C_6H_4 = 4.05$ D $\qquad F = 1.63$ D $\qquad \theta = 26°35'$

Similarly, if the C–H moment is taken to be zero,

$C\text{-}\underline{p}\text{-}NO_2\text{–}C_6H_4 = 4.45$ D $\qquad F = 2.09$ D $\qquad \theta = 26°30'$

Contributions to the observed moment from solvent effects prevent the results from being considered as absolute. If the study were repeated in several solvents, more nearly absolute numbers could be obtained. The geometrical representation is another source of systematic error. The measured dipole moment is the root-mean-

square of the moments of all the species in solution. To interpret the chemical-shift data, we have assumed the presence of two distinct species, but to calculate θ from the dipole-moment data, only one species, with an average geometry similar to IVb, was taken into account. Since at 27.5°, there is about 83% equatorial conformer present, this approximation is not completely unsatisfactory. A correction, however, may be made for the 17% of axial conformer if its geometry is assumed to be planar. The dipole moment of the equatorial conformer may be computed from the measured molecular moment and the moment of the axial conformer calculated from an assumed planar model. Substitution of the moment of the equatorial conformer for the molecular moment in equations 12-15 will yield θ_b, rather than θ, as the solution. The value of θ is then obtained by correction for the conformer population according to equation 10. The resulting value of θ, 29.1°, represents an average geometry. The small difference between this value and the solution obtained with the assumption of a single geometry probably represents a more realistic approximation to the error. Thus the angle of puckering is 27 ± 3°. This value in conjunction with equation 11 permits an evaluation of the angular gradient, Δθ, to be made from the data at 27.5°:

$$\Delta\theta = \frac{27^\circ}{985 \text{ cps}} = 0.027^\circ/\text{cps}$$

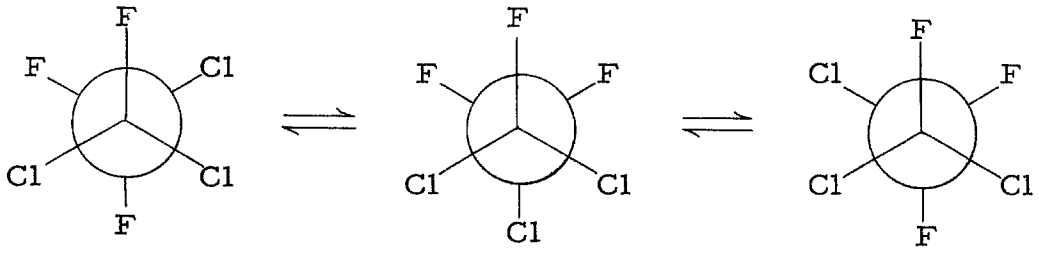
To the extent that the numerous approximations permit further elaboration, this value of Δθ should serve to define the average

geometry of V (IX) at all temperatures. Thus:

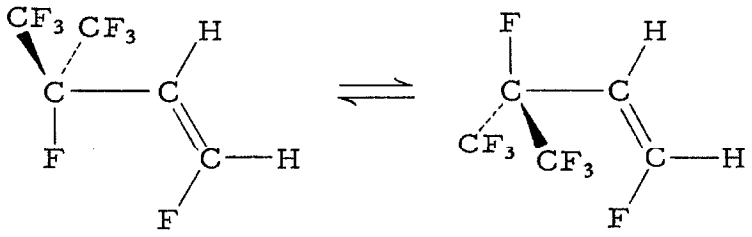
$$\theta(T) = 0.027\ \delta(T)$$

IV. THE DEPENDENCE OF VICINAL COUPLING CONSTANTS ON TEMPERATURE

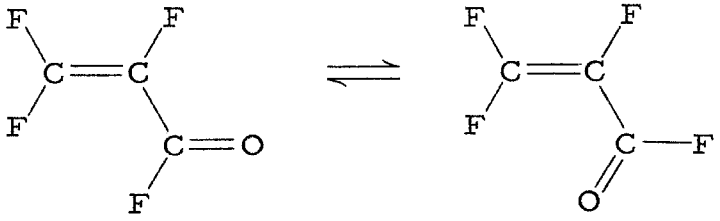
The n. m. r. method discussed thus far provides a clear demonstration of the presence or absence of nonplanarity in difluorocyclobutanes, and the dipole-moment method furnishes a reasonably accurate indication of the degree of puckering. The model of interconverting conformers was adopted by analogy with the properties of cyclohexane systems, but the size of the barrier is such that the model is more closely related to that of rapidly interconverting ethane rotamers. The model is valid provided that the conformers form ideal solutions with each other and have the same entropy and heat capacity over the observed temperature range. When this is the case, the observed molecular properties are weighted averages of the properties of the individual conformers (equations 5 and 8). Changes in the populations with temperature will therefore bring about changes in observables such as the chemical-shift differences. Although the conformational properties of cyclobutanes were derived entirely from temperature-dependent fluorine-fluorine chemical-shift differences, there should be discernible changes in the vicinal hydrogen-fluorine coupling constants as well. Such behavior has been noted extensively



in studies of the equilibria among rotamers of substituted ethanes (28-31), for hydrogen-hydrogen, hydrogen-fluorine, and fluorine-fluorine couplings, as well as in less general rotational equilibria (32-34). Small temperature variations have, however, been observed



(19)



(20)

(21)

for fluorine-fluorine couplings in systems which are incapable of rotational isomerism, such as XVII and XVIII. The torsional oscil-

CF_3CFCl_2 $CF_3CF_2CO_2H$

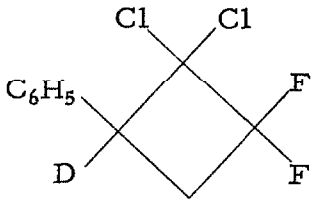
XVII XVIII

lations which give rise to these changes appear to be less important for hydrogen-hydrogen and hydrogen-fluorine couplings (35). Thus,

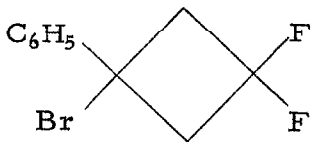
in system 19, couplings between nuclei which are attached to the conformationally rigid double bond exhibit temperature variations which are negligibly small in comparison to the changes in the couplings between the vinyl protons and nuclei in the perfluoroisopropyl substituent.

If it is true that the large variations in the fluorine-fluorine chemical-shift differences are due to conformational changes rather than torsional oscillations, then substantial variations should also be observable in the vicinal hydrogen-fluorine coupling constants, to which torsional oscillations appear to contribute negligibly. Observation of such variations would also comprise one of the first examples of temperature-dependent coupling constants other than in rotational equilibria (36).

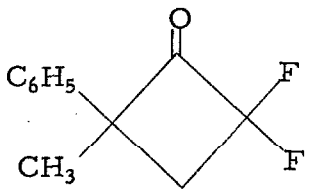
The complete analysis of the hydrogen-fluorine spectra of the ring nuclei of four of the cyclobutanes considered in the previous study (VIa, VIII, X, and XVI) was carried out at -50, 30, and 100° (see



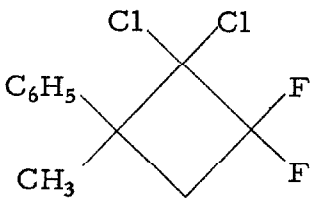
VIa



VIII

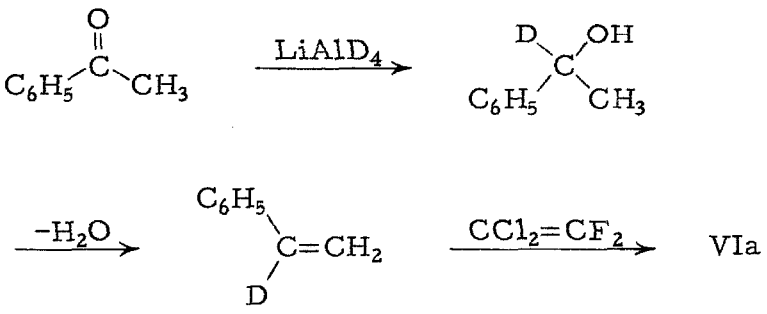


X



XVI

Appendix II). In no case was the spectrum first order. The analysis of the ABXY systems in the spectra of X and XVI was carried out in a straightforward manner by the method of Swalen and Reilly (37). The ABCXY spectrum of VI proved to be intractable because the protons were very closely coupled. A deuterium atom was therefore placed in the 3-position by means of the following reaction sequence:



Irradiation of VIa at the deuterium frequency reduced the spectrum to an ABXY pattern which was amenable to analysis by the Swalen-Reilly procedure. The deceptively simple A_2B_2XY spectrum for VIII could only be analyzed by trial and error with the Wiberg program (38). Agreement between calculated and observed spectra was as good as with the other systems, however. For all cases, observed line positions were obtained with an accuracy of ± 0.05 cps from the average of at least four upfield and four downfield scans of both the proton and the fluorine spectra.

The ring-proton spectrum of VIa at 100° and the calculated spectra for all three temperatures are given in Figure 3 (39). The calculated fluorine spectra are presented in Figure 4. Since the observed spacings are not a direct measure of the couplings, the

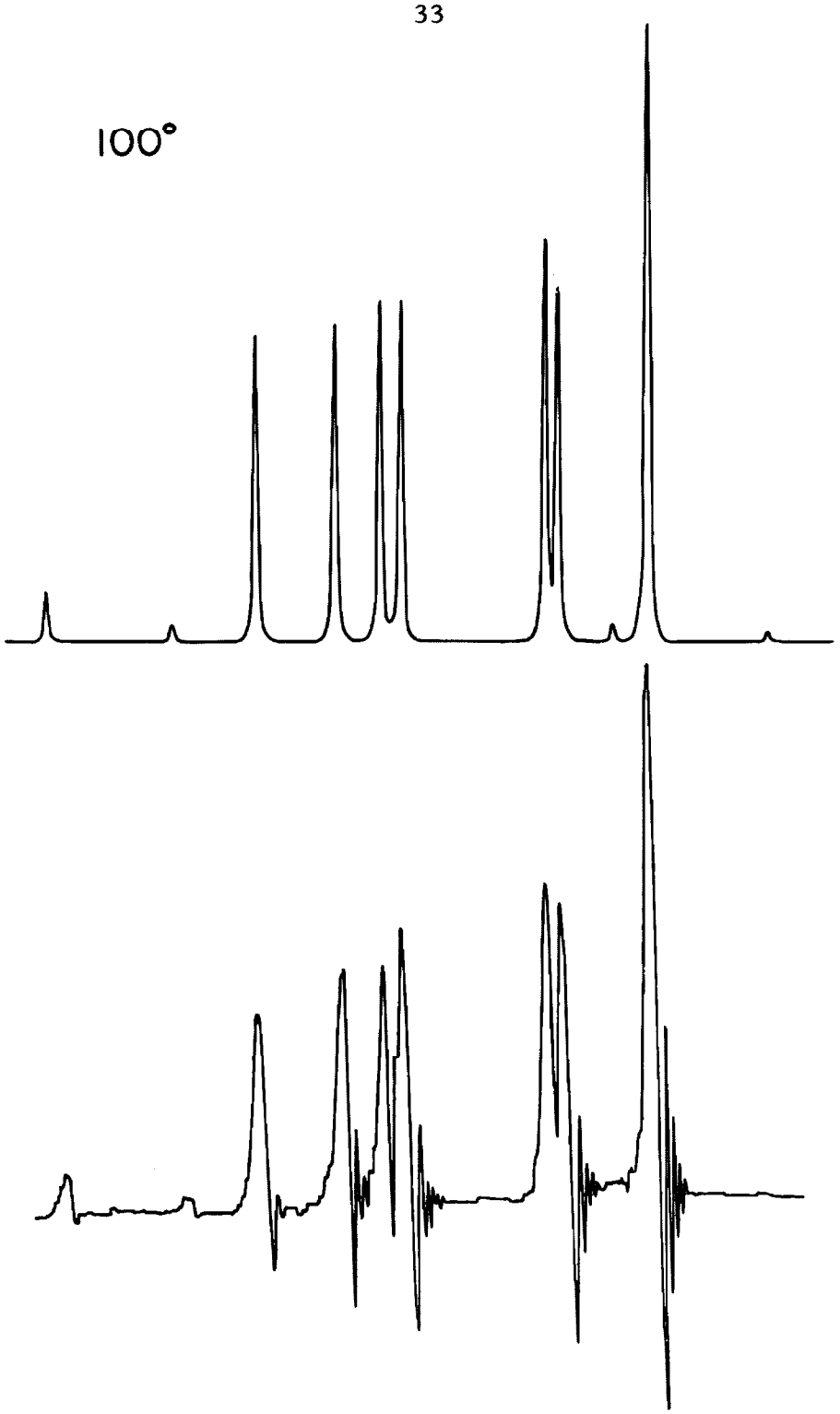


Figure 3. Calculated and experimental 60-Mcps proton spectrum of 1, 1-difluoro-2, 2-dichloro-3-deuterio-3-phenylcyclobutane (VIa), with simultaneous irradiation at the deuterium frequency.

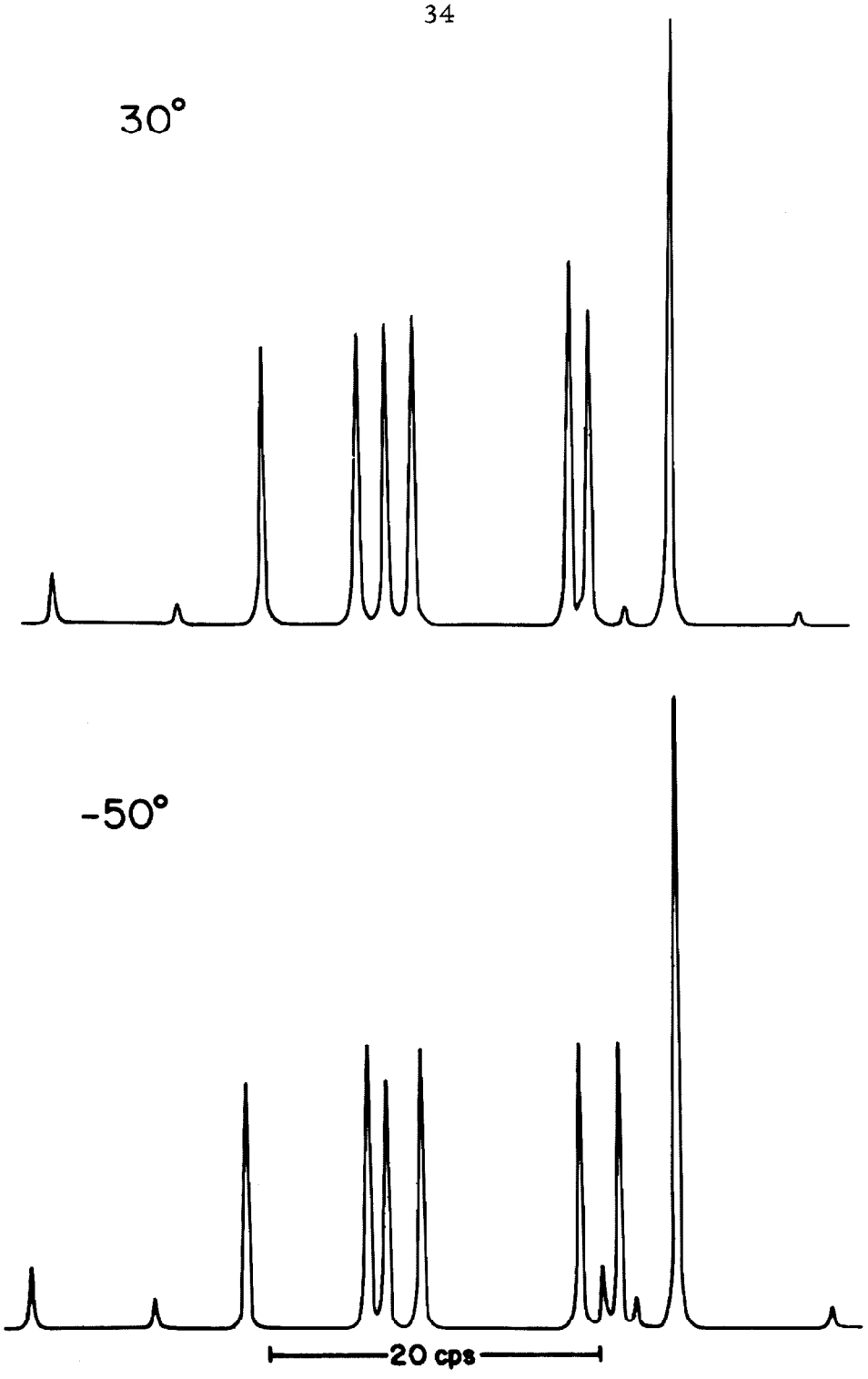


Figure 3. (Continued).

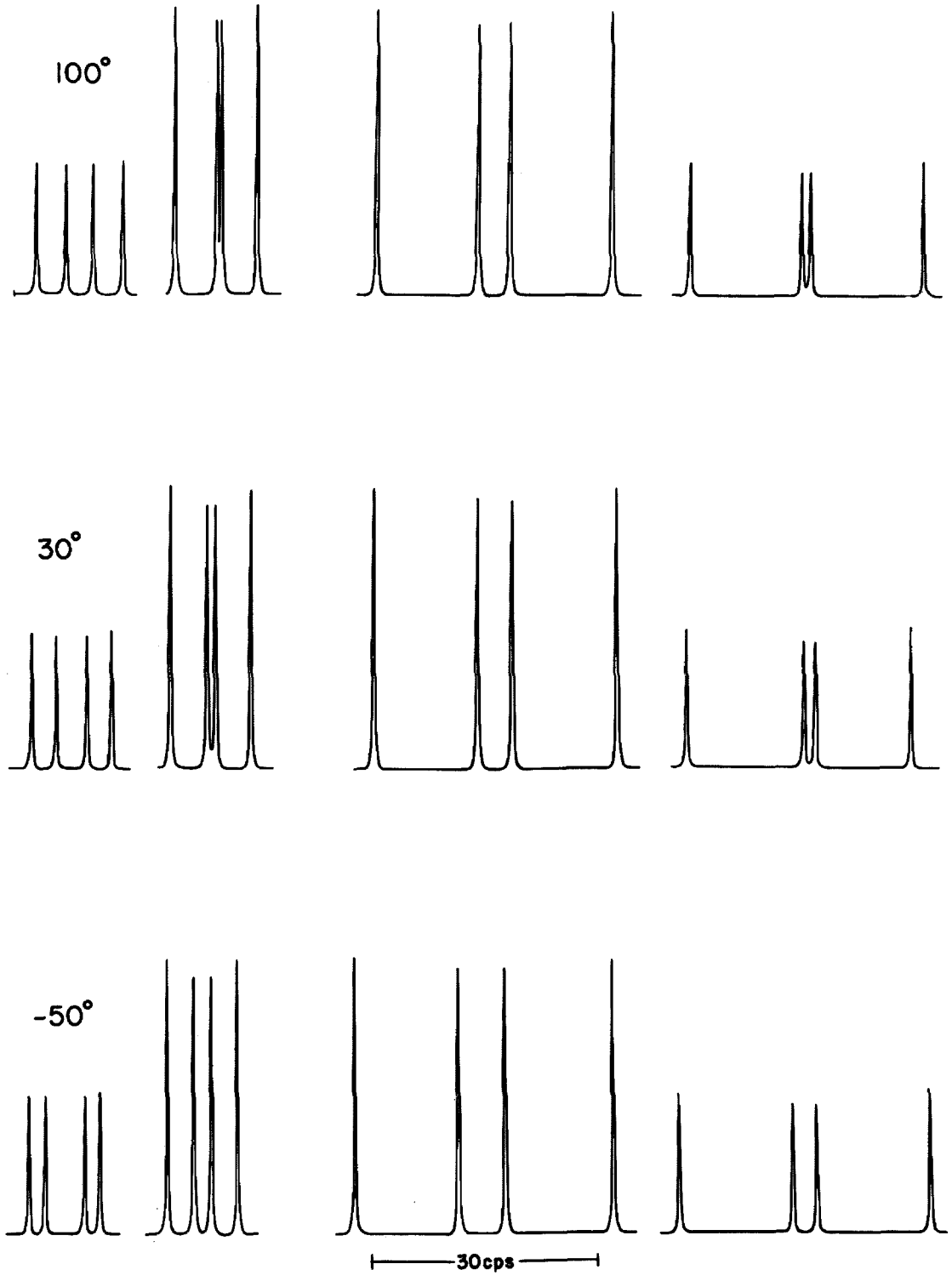


Figure 4. Calculated 56.4-Mcps fluorine spectrum of 1, 1-difluoro-2, 2-dichloro-3-deuterio-3-phenylcyclobutane (VIa).

complete analysis is necessary in order to detect small changes in the coupling constants. Nevertheless, even qualitative examination of the spectra shows severe perturbations in peak positions with temperature. Particularly noticeable in the proton spectrum are the increase in the distance between the 8-14 and 2-8 transitions (the fifth and sixth from the left among the more intense peaks) and the exchange of relative positions of the 6-13 and 10-15 transitions (second and third peaks from the left) as the temperature is lowered (see Appendix II). Similar changes occur in the fluorine spectra (Figure 4).

The spectra of the ring protons of VIII (Figure 5) exhibit a temperature dependence which is most obvious in the tendency of the two central peaks to coalesce as the temperature is increased and in the development of additional fine structure in the second and fourth peaks as the temperature is decreased.

The analysis of the spectrum of XVI has been discussed previously (40). The spectral parameters, however, were improved considerably by the use of the iterative method (37). Only small changes in the appearance of the spectrum occurred with temperature variations. Analysis of the spectrum of the cyclobutanone X was not possible at low temperatures because of viscosity broadening which obscured fine structure. The spectrum of the ring protons at 100° was completely identical to that at room temperature (Figure 6) (41).

Table III presents the results of these analyses. In each case, the subscripts 1 and 2 refer to fluorine nuclei and 3 and 4 to hydrogen nuclei; the lower number in each pair refers to the nucleus resonating

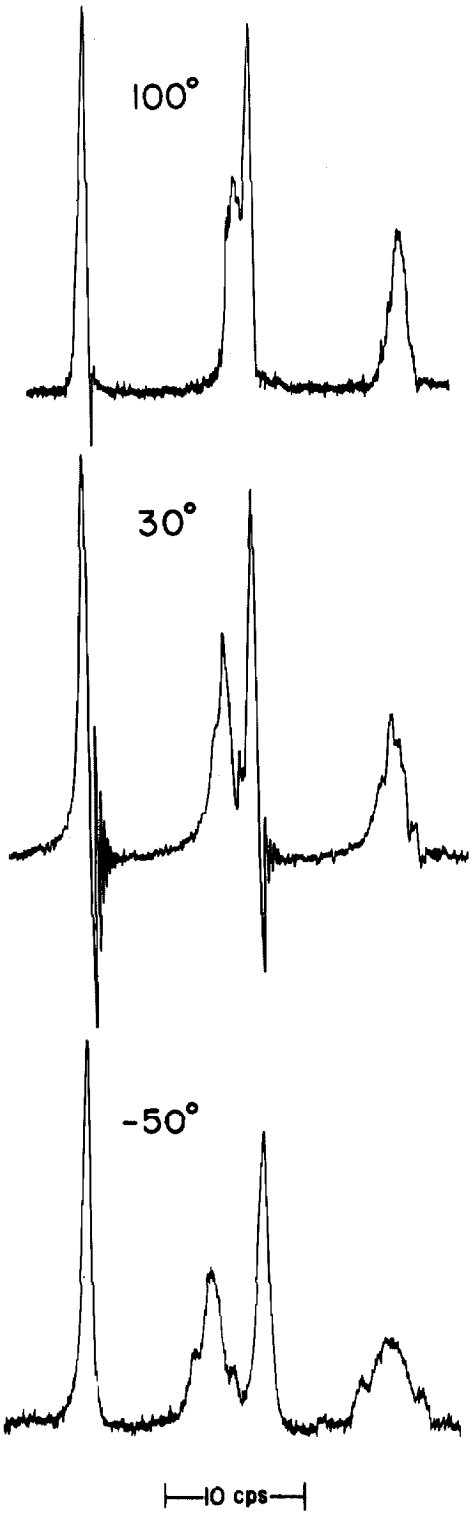


Figure 5. Proton spectrum of 1, 1-difluoro-3-bromo-3-phenylcyclobutane (VIII) at 60 Mcps.

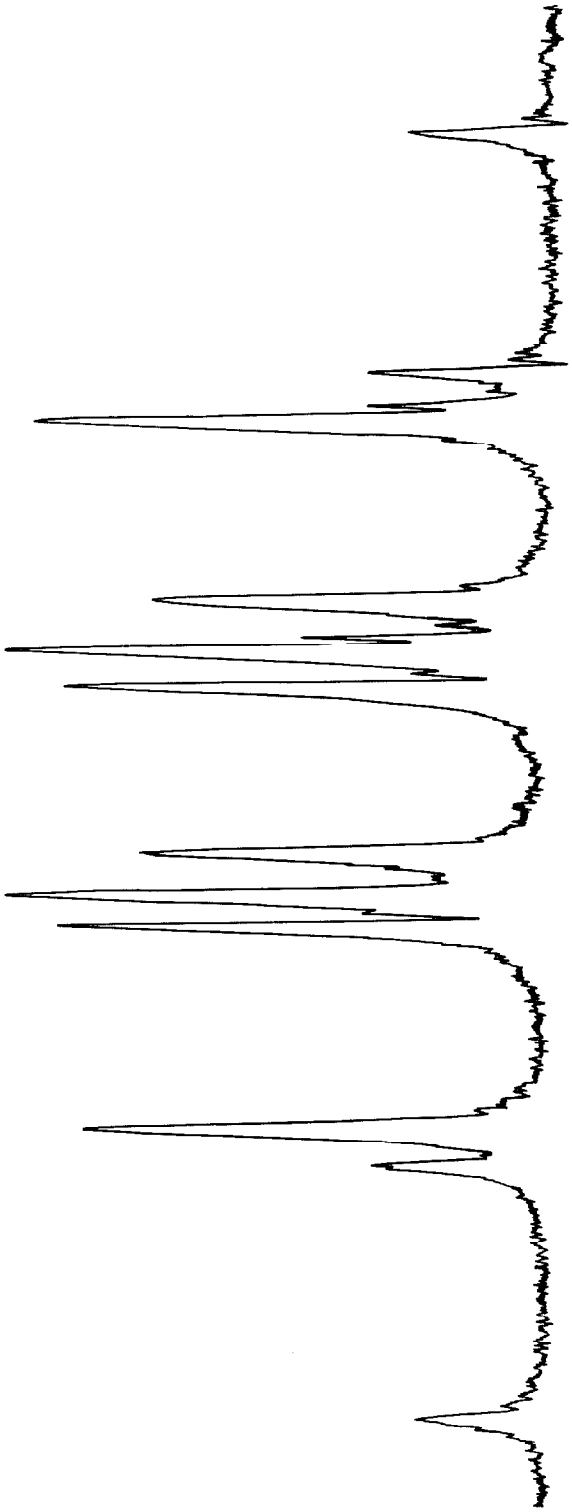


Figure 6. Proton spectrum of 1, 1-difluoro-3-methyl-3-phenylcyclobutanone-2 (X) at 60 Mcps.

TABLE III

TEMPERATURE VARIATION OF VICINAL HYDROGEN-FLUORINE COUPLING CONSTANTS IN CYCLOBUTANES

		δ_{34}[a]	J_{13}	J_{14}	J_{23}	J_{24}
VIa	-50°	8.88	8.18	0.73	21.89	12.77
	30	6.07	8.57	1.75	20.52	12.59
	100	5.23	8.76	2.46	20.08	12.18
VIII	-50	1.10	7.80	9.95	13.10	13.05
	30	0.75	8.90	10.60	12.52	12.45
	100	0.55	9.55	10.85	11.90	11.85
XVI	-50	29.50	8.69	0.64	21.22	13.65
	30	32.92	8.79	0.91	21.02	13.93
	100	35.35	8.89	1.34	20.40	13.63
X	30	19.87	10.97	15.09	16.17	10.28
	100	20.10	10.79	14.87	16.15	10.34

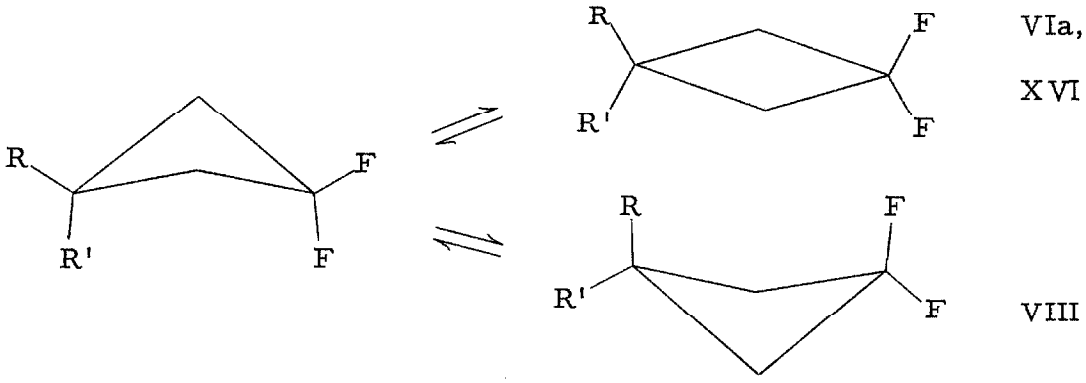
[a]All units are in cps.

at lower field. The geminal fluorine-fluorine chemical-shift difference, δ_{12}, and coupling constant, J_{12}, are listed in Table I. The calculations were fairly insensitive to the geminal proton-proton coupling, J_{34}, and to the cross-ring couplings in VIII. The former was typically about -13 cps, and the latter were effectively zero. The accuracy of the spectral parameters was ±0.1 cps for VIII and X, and slightly better than this value for VIa and XVI.

The largest temperature variation of the fluorine-fluorine chemical-shift difference, δ_{12}, was observed in the case of VIII (Table I), followed in magnitude by VIa, with XVI showing only a small dependence (42), and X almost none at all. These phenomena are paralleled by the effects on vicinal coupling constants and proton-proton chemical shift differences recorded in Table III. The data are adequately interpreted in terms of a classical equilibrium between conformations. The magnitude of the variations are as large as those observed in equilibria among rotamers of substituted ethanes. Since data are lacking to substantiate any contributions to the temperature variation of hydrogen-fluorine coupling constants from torsional oscillations, it is reasonable to neglect the phenomenon in this study.

The absence of a measurable effect in X again suggests that the cyclobutanone must be nearly planar. Although XVI shows only small temperature variations, the values of the coupling constants are strikingly similar to those of VIa. The geometry of the species which comprise the equilibrium for XVI must resemble the geometry of VIa more closely than that of VIII. This may reflect a greater

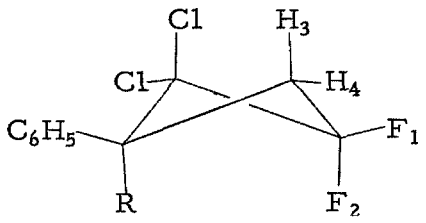
difference in "size" between phenyl and methyl than between phenyl and bromine (24). If the methyl group is significantly "smaller" than bromine, it may well act like hydrogen in having an axial conformation which is almost planar.



VIa, XVI

VIII

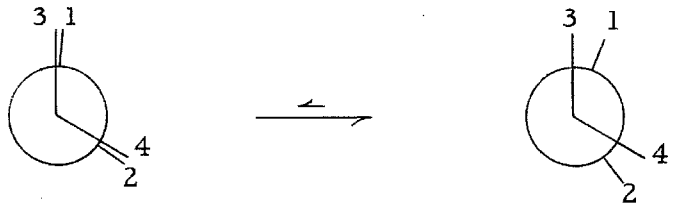
Takahashi and co-workers (40) have synthesized XVI with deuterium placed on the 4-carbon atom. Provided the cycloaddition reaction is stereospecific, they were able to show that the low-field proton (3) is cis to the phenyl group. If the trans hydrogen-fluorine coupling is larger than the cis coupling, as is the case with vicinal hydrogen-hydrogen couplings, then J_{23} is the coupling constant between trans-oriented nuclei, and fluorine 2 must be trans to the phenyl group. The same assignment will be used for VIa on the basis of the similarity of the coupling parameters.



VIa: R = D

XVI: R = CH_3

To clarify this point, Newman projections may be drawn for the planar axial and nonplanar equatorial conformations of VIa (and probably XVI):

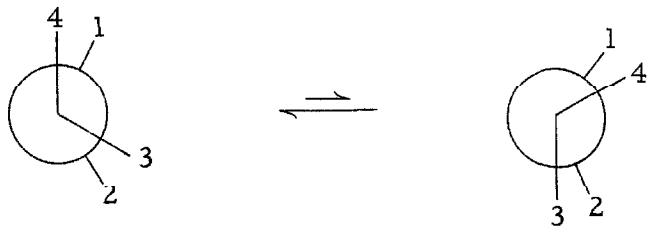


XIXa XIXb

If the relationship between hydrogen-fluorine couplings and dihedral angles is similar to that described by Karplus (43-44) for hydrogen-hydrogen couplings, then one would expect that J_{23} (axial-axial) would be large, J_{14} (equatorial-equatorial) would be small, and J_{13} and J_{24} would be intermediate in magnitude, since the equatorial conformer XIXb predominates. This is precisely the behavior which is recorded in Table III for both VIa and XVI. For the planar geometry (XIXa), however, nucleus 1 bears the same relationship to nucleus 4 as 2 does

to 3. As the population of this conformer increases with temperature, J_{23} should therefore decrease and J_{14} should increase, as a result of the appropriate changes in the dihedral angles. The smaller changes in J_{13} and J_{24} are expected from consideration of the range of dihedral angles involved.

Compound VIII was described as existing in two distinct non-planar conformations of similar energies:



XXa XXb

J_{24} and J_{13} in this representation are averages of large axial-axial and small equatorial-equatorial couplings. Therefore, they are intermediate in magnitude with respect to the analogous couplings (J_{14} and J_{23}) in VIa and XVI. Since J_{24} decreases with temperature, it must represent the axial-axial coupling in the preferred conformer (XXa). The remaining two coupling constants, J_{14} and J_{23}, correspond to the less sensitive axial-equatorial couplings in VIa and XVI (J_{13} and J_{24}), and are therefore intermediate in value. An unambiguous assignment of steric relationships cannot be made on the evidence at hand, since interchanging nuclei 3 and 4 would not alter the interpretation. J_{13} was taken as the equatorial-equatorial coupling, rather than J_{14},

because it is smaller and displays a slightly more pronounced temperature variation.

The coupling constants in the cyclobutanone X, like those of VIII, have intermediate values which fall within a 5 cps range. The molecules, however, are fundamentally different, since X is probably statically planar, but VIII is in dynamic equilibrium between nonplanar conformations. Conia and co-workers (45) have analyzed the first-order spectra of several substituted cyclobutanones. They find that 21 vicinal hydrogen-hydrogen couplings fall in the range 6.4 to 9.7 cps. The similarity of these couplings is in contrast to the wide range of hydrogen-fluorine couplings for cyclobutanes known to be nonplanar, e.g., VIa. Without a temperature study, it is impossible to differentiate between static and dynamic nonplanarity from the magnitudes of the couplings alone. The deviations from a planar configuration, by analogy with the behavior of X, are probably small for these systems also.

Analysis of both the magnitude and temperature dependence of the vicinal coupling constants substantiates the conformational model described in the previous sections. Cyclobutanones and cyclobutenes are statically planar unless there are severe perturbations from substituents in the former case. Cyclobutanes substituted at one position with two groups of equivalent size exist in two distinct nonplanar conformers. When there is only one substituent, or if the second substituent is small, the second conformer is probably planar. The dependence of the hydrogen-fluorine coupling constants on the dihedral

angle appears to be similar to the behavior described by Karplus for hydrogen-hydrogen couplings.

V. EXPERIMENTAL

Melting points and boiling points are uncorrected. Melting points were measured on either the Büchi or the Hershberg apparatus. Infrared spectra were recorded on the Beckman Infrared Spectrometer, Model IR-7. Ultraviolet spectra were obtained with a Cary Recording Spectrometer, Model 11M. Gas-liquid partition chromatography experiments were performed on the Perkin-Elmer Vapor Fractometers, Models 154-C and 800. Elementary analyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Michigan.

Proton magnetic resonance spectra were measured at room temperature on the Varian Associates Model A-60 and V-4300B spectrometers operated at 60.0 Mcps and 14,100 gauss. The latter instrument was used for variable-temperature experiments (46). All heteronuclear double-resonance experiments were accomplished with the Nuclear Magnetic Resonance Specialties Model SD-60 spin decoupler. Fluorine magnetic resonance spectra were measured on the V-4300B spectrometer operated at 56.4 Mcps; nitrogen-15 magnetic resonance spectra were obtained at 6.08 Mcps (vide infra). Calibration was effected by the sideband technique with the use of the Hewlett-Packard Model 200AB audio oscillator and Model 521-C frequency counter (47).

1,1-Difluoro-2,2-dichloro-3-phenylcyclobutane. — Into a 200-ml. heavy-walled glass ampoule were placed 30 g. (0.288 mole) of styrene and 45 g. (0.338 mole) of 1,1-dichloro-2,2-difluoroethylene,

b.p. 19-20° (Columbia Organic Chemicals). The ampoule was sealed and heated in a furnace at 130° for 24 hrs. The slightly viscous, light brown liquid which resulted was distilled at reduced pressure through a 25-cm. Vigreux column to give 49.7 g. (0.210 mole, 72.9%) of 1, 1-difluoro-2, 2-dichloro-3-phenylcyclobutane, b.p. 75-77° (5 mm.).

1, 1-Difluoro-3-phenylcyclobutane. — To a cooled solution of 14 g. (0.250 mole) of potassium hydroxide and 45 ml. of reagent methanol in a citrate bottle was added 46 g. (0.194 mole) of 1, 1-difluoro-2, 2-dichloro-3-phenylcyclobutane slowly with swirling. After 1.5 g. of 10% palladium-on-charcoal catalyst had been added, the mixture was hydrogenated on a medium-pressure Parr apparatus. After 2 hrs., 13 g. (0.232 mole) of additional potassium hydroxide was added and hydrogenation was continued for 3 hrs. The total uptake of hydrogen was 32 p.s.i. The mixture was filtered through a Büchner funnel to remove the catalyst and other precipitates, and the resulting solution was poured into 200 ml. of distilled water. The layers were separated, and the aqueous portion was extracted with diethyl ether six times. The combined organic portions were dried over magnesium sulfate. The drying agent was removed by filtration and the ether by distillation at atmospheric pressure. The residue was distilled to give 26.7 g. (0.159 mole, 82.0%) of 1, 1-difluoro-3-phenylcyclobutane, b.p. 99-102° (40 mm.). Gas chromatography showed that the distillate was at least 97% pure.

1, 1-Difluoro-3-p-nitrophenylcyclobutane. — Into a 500-ml. three-necked round-bottomed flask equipped with a dropping funnel

were placed 140 ml. of concentrated nitric acid and 120 ml. of concentrated sulfuric acid. The temperature was lowered to 10°, and 60 g. (0.357 mole) of 1, 1-difluoro-3-phenylcyclobutane was added with stirring at such a rate that the temperature did not exceed 15°. After an hour, the temperature was raised to 35° for 10 min. The solution was cooled and poured into 220 ml. of an ice-water mixture. The layers were separated and the aqueous portion was extracted six times with diethyl ether. The combined organic portions were extracted five times with 15% aqueous potassium hydroxide. The basic aqueous extract was neutralized and extracted four times with ether. All organic portions were combined and dried over magnesium sulfate. After the drying agent was removed by filtration and the ether by distillation at atmospheric pressure, the residue, upon flash distillation at 0.5 mm., gave 30 g. (0.141 mole, 39.5%) of a yellow oil. The product was fractionally recrystallized in several steps from methanol to remove small amounts of impurities. In this manner, 15.3 g. (0.072 mole) of white needles, m.p. 37.3-39.7°, were obtained free of all impurities according to thin layer chromatography. The n.m.r. spectrum contained an $(AB)_2$ pattern in the aromatic region, characteristic of <u>para</u> substitution, and the infrared spectrum exhibited bands at 1540 and 1349 $cm.^{-1}$, characteristic of antisymmetric and symmetric stretching modes of the nitro group.

<u>Anal.</u> Calcd. for $C_{10}H_9F_2NO_2$: C, 56.33; H, 4.26; F, 17.82; N, 6.57.

Found: C, 56.10; H, 4.13; F, 17.81; N, 6.56.

1, 1-Difluoro-3-bromo-3-phenylcyclobutane. — To a 200-ml. three-necked round-bottomed flask equipped with a reflux condenser were added 10.6 g. (0.0596 mole) of N-bromosuccinimide (NBS), 10 g. (0.0595 mole) of 1, 1-difluoro-3-phenylcyclobutane, 50 ml. of carbon tetrachloride, and about 200 mg. of dibenzoyl peroxide. The NBS had been freshly recrystallized from water. Total consumption of the NBS was signaled after the mixture had refluxed for 3 hrs. by the absence of any solid at the bottom of the flask. The solution was cooled, and the solid was removed by filtration. After the carbon tetrachloride was removed by distillation (28°, 5 mm.), the residue was distilled to give 11.28 g. (0.0456 mole, 76.5%) of 1, 1-difluoro-3-bromo-3-phenylcyclobutane, b.p. 70-75° (1 mm.). The temperature should not be allowed to exceed 100°, since decomposition of the product occurs readily.

α-Methylbenzyl-α-D Alcohol. — To a solution of 0.5 g. (0.0119 mole) of lithium aluminum deuteride in 95 ml. of diethyl ether contained in a 200-ml. three-necked round-bottomed flask equipped with a reflux condenser and a dropping funnel was added 5 g. (0.0416 mole) of acetophenone in 20 ml. of anhydrous ether in a dropwise manner. After the solution had been stirred for 1 hr., the complex was destroyed with 4 ml. of distilled water. The mixture was poured into 75 ml. of 1 N hydrochloric acid and stirred until no solid remained. The layers were separated, the aqueous portion was extracted four times with ether, and the combined organic portions were dried over magnesium sulfate. After the drying agent was removed by filtration

and the ether by distillation, the product was distilled to give 4.66 g. (0.0378 mole, 90.9%) of α-methylbenzyl-α-D alcohol, b.p. 65° (2 mm.). The n.m.r. spectrum showed the label to be located specifically in the alpha position.

Styrene-α-D. — α-Methylbenzyl-α-D alcohol (4.65 g., 0.0378 mole), containing about 10 mg. of p-toluenesulfonic acid as catalyst and 10 mg. of picric acid as polymerization inhibitor, was heated in a 50-ml. round-bottomed flask at a temperature of 160° and a pressure of 100 mm. Styrene-α-D codistilled with water over the range 40 to 80° into a flask which contained about 10 mg. of picric acid. When the distillation was nearly complete, the distillate was taken up in diethyl ether, the layers were separated, and the organic portion was dried over magnesium sulfate. The solution was filtered to remove the drying agent, and the ether was removed from the filtrate by distillation. The residue was distilled to give 3.31 g. (0.0315 mole, 83.3%) of styrene-α-D, b.p. 64° (60 mm.). The specificity of the label was assured by the n.m.r. spectrum, which lacked a resonance for the alpha proton.

1,1-Difluoro-2,2-dichloro-3-deuterio-3-phenylcyclobutane. — The synthesis was achieved in the same manner as that of the unlabeled material (vide supra), with stereospecific placement of the deuterium from styrene-α-D in the 3-position of the adduct.

1,1-Difluoro-2,2,3-trichlorocyclobutane. — A sample of this material was obtained from the work of Dr. E. F. Kiefer (48).

1, 1-Difluoro-2, 2-dichloro-3-methyl-3-phenylcyclobutane. — A sample of this material was obtained from the work of Mr. M. Takahashi (49).

1, 1-Difluoro-2-chloro-3, 4-diphenylcyclobutene-2. — A sample of this material was obtained from the work of Dr. K. Nagarajan (50).

1, 1-Difluoro-2-phenylcyclobutane. — A sample of this material was obtained from the work of Dr. S. L. Manatt (51).

1, 1-Difluoro-3-methyl-3-phenylcyclobutanone-2. — A sample of this material was kindly supplied by Dr. D. C. England of the Central Research Department of the DuPont Company.

Dipole-Moment Measurements. — For the purpose of measuring dielectric constants, an apparatus which operates according to the heterodyne-beat method was constructed after the model of Jen-Yuan Chien (52). Four modifications were made from the original circuit: (1) the B^+ (250 v.) line and the line to the heaters (6.3 v.) were fused; (2) a switch was placed between P_1 and P_2 so that only one cell would operate at a time; (3) a 100 μμf capacitor was placed in series with both the dielectric cell and the standard capacitor in order to lower the capacitance of the former cell to within the range of the instrument; (4) only the 500-kc. crystal and associated circuitry were used. Twenty-nine gage "bondeze" wire #1 for the inductance coils was supplied by Phelps Dodge Copper Products Corporation, Los Angeles. All other components are standard items. The detailed operation procedure has been described elsewhere (53). The standard condenser was a General Radio Type 722-D Precision Capacitor

(Cambridge, Massachusetts). The dielectric cell and pycnometer have been described previously (54-55). Voltages to the apparatus were obtained from a Heathkit Variable Voltage Regulated Power Supply Model PS-3. Molar polarizations were calculated from the slopes of plots of solute mole fraction as a function of the density and of the dielectric constant of dilute benzene solutions (56). Molar refractions were calculated directly from the index of refraction if the solute was a liquid. For solids, this quantity was obtained from the index of refraction of the solvent, together with refractive index increment measurements of dilute solutions (57). The difference between the molar polarization and the molar refraction gave the orientation polarization at infinite dilution, from which the dipole moment was calculated. The accompanying tables present the data for the compounds studied. Since the value of the dipole moment of the nitro compound was extremely important, the measurements were duplicated on a different heterodyne apparatus (58). This data gave a value of 2.84 D. As a further check, both sets of dielectric-constant data were combined with refractive index increment measurements and analyzed according to the method of Guggenheim (59), which avoids the direct measurement of the molar refraction. In this manner, values of 2.83 D and 2.79 D were obtained. Thus, all four methods are in excellent agreement.

TABLE IV

MOLE FRACTIONS, DENSITIES, AND DIELECTRIC CONSTANTS IN BENZENE AT 27.5°

f_2	d_{12}	ϵ_{12}
1, 1-Difluoro-3-p-nitrophenylcyclobutane (A)		
0.00000	0.87050	(2.274)
0.01089	0.87907	2.3952
0.02108	0.88706	2.5077
0.03091	0.89445	2.6164
0.03882	0.90054	2.6975
1, 1-Difluoro-3-phenylcyclobutane (B)		
0.006699	0.87305	2.3150
0.01478	0.87626	2.3605
0.02063	0.87859	2.3990
0.02749	0.88127	2.4394

TABLE V

MOLAR REFRACTIONS, POLARIZATIONS, AND DIPOLE MOMENTS

Compound	MR_D	$P_2^0(27.5°)$	μ(Debye)
A[a]	51.29[d]	210.08	2.80[c]
B[b]	43.36[e]	132.34	2.09

[a] 1, 1-Difluoro-3-p-nitrophenylcyclobutane.

[b] 1, 1-Difluoro-3-phenylcyclobutane.

[c] This quantity was checked in the manner described in the text.

[d] Obtained from measurements on solutions of A.

[e] Obtained from direct measurements on the liquid.

APPENDIX I

PROGRAM FOR THE CALCULATION OF FREE-ENERGY DIFFERENCES FOR CYCLOBUTANE CONFORMATIONS

```
$IB JOB            MAP
$IBFTC FED         DECK
C       CALCULATION OF FREE ENERGY DIFFERENCES
C       FOR CYCLOBUTANE CONFORMATIONS
      0DIMENSION DEL(5), T(5), POP(5, 80), P(5), SLOPEM(80),
       BM(80),
      1SDIFM(80), SDIFSM(80), MELTAF(80), DELIIM(80)
     1 READ (5, 2) DEL, T
     2 FORMAT (5F10.0)
       DO 10 MELF = 50, 4000, 50
       L = MELF / 50
       MELTAF(L) = - MELF
       DELF = - MELF
       DO 20 I = 1, 5
       P(I) = 1.0 / (1.0+EXP(DELF/(1.987*T(I))))
    20 POP(I, L) = P(I)
       CALL LEASQR (P, DEL, SLOPE, B, SDIF, SDIFSQ)
       SLOPEM(L) = SLOPE
       BM(L) = B
       SDIFM(L) = SDIF
    10 SDIFSM(L) = SDIFSQ
       DO 80 I = 1, 79
       SDSMIN = SDIFSM(I)
       K = I + 1
       N = I
       DO 70 J = K, 80
       IF(SDSMIN-SDIFSM(J)) 70, 70, 60
    60 SDSMIN = SDIFSM(J)
       N = J
    70 CONTINUE
       EXTRA = MELTAF(I)
       MELTAF(I) = MELTAF(N)
       MELTAF(N) = EXTRA
```

```
      EXTRA = SDIFSM(I)
      SDIFSM(I) = SDSMIN
      SDIFSM(N) = EXTRA
      EXTRA = SLOPEM(I)
      SLOPEM(I) = SLOPEM(N)
      SLOPEM(N) = EXTRA
      EXTRA = BM(I)
      BM(I)  = BM(N)
      BM(N)  = EXTRA
      DELIIM(I) = SLOPEM(I) + BM(I)
      EXTRA = SDIFM(I)
      SDIFM(I) = SDIFM(N)
      SDIFM(N) = EXTRA
      DO 80 J = 1, 5
      EXTRA = POP(J, I)
      POP(J, I) = POP(J, N)
   80 POP(J, N) = EXTRA
      WRITE (6, 15)
   15 FORMAT (25H1       DELTA              TEMP)
      WRITE (6, 14) ((DEL(I), T(I)), I=1, 5)
   14 FORMAT (1HO2F15.2)
      WRITE (6, 11)
   11 FORMAT (43H1CONFORMATIONAL PARAMETERS FOR
      CYCLOBUTANES)
      WRITE (6, 12)
  120FORMAT (///116HODELTAF      SLOPE       DELI
      DELII       POPI
     1POPII       POPIII      POPIV       POPV
      SUMDIF              SUMSQDIF)
     0WRITE (6, 13) ((MELTAF(I), SLOPEM(I), BM(I), DELIIM(I),
     1(POP(J, I), J=1, 5), SDIFM(I), SDIFSM(I)), I=1, 80)
   13 FORMAT (////(1H I6, 3F10.3, 5F10.4, 2E17.5))
      GO TO 1
```

```
        END
$IBFTC LEA      DECK
       SUBROUTINE LEASQR (X, Y, SLOPE, B, SDIF, SDIFSQ)
       DIMENSION X(5), Y(5), CALCY(5), DIF(5)
       SUMX = 0.0
       SUMY = 0.0
       SUMXY = 0.0
       SUMXX = 0.0
       DO 30 J = 1, 5
       SUMX = SUMX + X(J)
       SUMY = SUMY + Y(J)
       SUMXX = SUMXX + X(J)**2
    30 SUMXY = SUMXY + X(J) * Y(J)
       DENOM = SUMX**2 - 5.0 * SUMXX
       SLOPE = (SUMX*SUMY-5.0*SUMXY) / DENOM
       B = (SUMX*SUMXY-SUMY*SUMXX) / DENOM
       DO 40 J = 1, 5
       CALCY(J) = SLOPE * X(J) + B
    40 DIF(J) = Y(J) - CALCY(J)
       SDIF = 0.0
       SDIFSQ = 0.0
       DO 50 J = 1, 5
       SDIF = SDIF + ABS(DIF(J))
    50 SDIFSQ = SDIFSQ + DIF(J)**2
       RETURN
        END
$DATA
       FIRST CARD FIVE VALUES OF DELTA IN FIELDS OF TEN
       SECOND CARD FIVE VALUES OF TEMP IN FIELDS OF TEN
$ENDJOB
```

APPENDIX II

TRANSITION FREQUENCIES FOR CALCULATED CYCLOBUTANE SPECTRA

TABLE VI*

1, 1-DIFLUORO-2, 2-DICHLORO-3-DEUTERIO-3-PHENYLCYCLOBUTANE, -50°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	0.06	-0.06
9-12	2.18	2.12	0.06
10-13	7.59	7.44	0.15
3- 6	9.40	9.50	-0.10
11-14	183.00	183.08	-0.08
4- 7	186.76	186.65	0.11
5- 8	188.86	188.95	-0.09
1- 2	192.52	192.51	0.01
14-16	636.00	636.01	-0.01
7-12	649.99	649.97	0.02
8-13	656.13	656.17	-0.04
2- 6	670.13	670.15	-0.02
11-15	819.00	819.03	-0.03
4- 9	834.58	834.50	0.08
5-10	837.74	837.68	0.06
1- 3	853.11	853.17	-0.06
6-12	8986.87	8986.92	-0.06
3- 9	8994.40	8994.29	0.11
13-16	9000.00	8999.93	0.07
10-15	9007.19	9007.32	-0.13
6-13	9008.49	9008.44	0.05
3-10	9010.48	9010.50	-0.02
8-14	9020.10	9020.10	0.00
2- 8	9022.44	9022.42	0.02
5-11	9025.98	9025.97	0.01
1- 5	9025.98	9025.98	0.00
		Av.	0.05

*The first fluorine transition is arbitrarily set at 0.0 cps; the first strong proton transition is arbitrarily set at 9000.00 cps. Increasing numbers represent increasing field.

TABLE VII

1, 1-DIFLUORO-2, 2-DICHLORO-3-DEUTERIO-3-PHENYLCYCLOBUTANE, 30°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	-0.07	0.07
9-12	3.25	3.28	-0.03
10-13	7.55	7.46	0.09
3- 6	10.72	10.80	-0.08
11-14	183.00	182.99	0.01
4- 7	187.81	187.88	-0.07
5- 8	189.10	188.97	0.13
1- 2	193.73	193.85	-0.12
14-16	587.20	587.35	-0.15
7-12	601.24	601.32	-0.08
8-13	606.06	605.93	0.13
2- 6	619.96	619.91	0.05
11-15	770.15	770.41	-0.26
4- 9	785.90	785.92	-0.02
5-10	787.74	787.44	0.30
1- 3	803.00	802.97	0.03
6-12	8987.16	8987.16	0.00
3- 9	8994.83	8994.68	0.15
13-16	9000.00	8999.93	0.07
6-13	9005.67	9005.70	-0.03
(2- 7)	9005.67	9005.75	-0.08
10-15	9007.65	9007.46	0.19
3-10	9009.25	9009.03	0.22
(12-16)	9018.45	9018.46	-0.01
8-14	9018.45	9018.51	-0.06
2- 8	9019.49	9019.68	-0.19
5-11	9024.44	9024.49	-0.05
1- 5	9024.44	9024.56	-0.12
		Av.	0.10

TABLE VIII

1, 1-DIFLUORO-2, 2-DICHLORO-3-DEUTERIO-3-PHENYLCYCLOBUTANE, 100°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	-0.05	0.05
9-12	4.16	4.05	0.11
10-13	7.70	7.66	0.04
3- 6	11.73	11.75	-0.02
11-14	183.00	183.00	0.00
4- 7	188.66	188.60	0.06
5- 8	189.03	189.21	-0.18
1- 2	194.73	194.80	-0.07
14-16	553.70	553.71	-0.01
7-12	567.47	567.46	0.01
8-13	571.44	571.63	-0.19
2- 6	585.40	585.40	0.00
11-15	736.70	736.76	-0.06
4- 9	752.04	752.01	0.03
5-10	753.44	753.19	0.25
1- 3	768.40	768.45	-0.05
6-12	8986.87	8987.03	-0.16
3- 9	8994.94	8994.73	0.21
13-16	9000.00	9000.05	-0.05
6-13	9005.04	9004.96	0.08
10-15	9007.77	9007.75	0.02
3-10	9009.03	9009.06	-0.03
8-14	9017.95	9017.97	-0.02
2- 8	9018.76	9018.73	0.03
5-11	9024.24	9024.18	0.06
1- 5	9024.24	9024.32	-0.08
		Av.	0.07

TABLE IX

1, 1-DIFLUORO-2, 2-DICHLORO-3-METHYL-3-PHENYLCYCLOBUTANE, -50°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	-0.03	0.03
9-12	1.48	1.37	0.11
10-13	8.69	8.89	-0.20
3- 6	10.32	10.26	0.06
11-14	185.00	184.97	0.03
4- 7	186.48	186.53	-0.05
5- 8	193.69	193.73	-0.04
1- 2	195.32	195.26	0.06
14-16	474.09	474.25	-0.16
7-12	487.76	487.64	0.12
8-13	494.72	494.74	-0.02
2- 6	508.23	508.16	0.07
11-15	659.09	659.25	-0.16
4- 9	672.76	672.80	-0.04
5-10	679.72	679.59	0.13
1- 3	693.23	693.16	0.07
6-12	9000.00	8999.97	0.03
3- 9	9008.89	9008.87	0.02
13-16	9012.67	9012.55	0.12
2- 7	9020.38	9020.49	-0.11
10-15	9021.54	9021.46	0.08
1- 4	9029.29	9029.23	0.06
8-14	9032.88	9033.04	-0.16
6-13	9039.40	9039.35	0.05
3-10	9040.78	9040.73	0.05
5-11	9041.77	9041.80	-0.03
12-16	9052.08	9051.93	0.15
2- 8	9052.77	9052.77	0.00
9-15	9053.30	9053.33	-0.03
1- 5	9054.20	9054.30	-0.10
7-14	9065.30	9065.32	-0.02
4-11	9066.76	9066.87	-0.11
		Av.	0.08

TABLE X

1, 1-DIFLUORO-2, 2-DICHLORO-3-METHYL-3-PHENYLCYCLOBUTANE, 30°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	0.10	-0.10
9-12	1.91	1.79	0.12
10-13	9.12	9.17	-0.05
3- 6	10.80	10.84	-0.04
11-14	186.20	186.26	-0.06
4- 7	188.11	188.07	0.04
5- 8	195.32	195.22	0.10
1- 2	197.00	197.00	0.00
14-16	457.39	457.47	-0.08
7-12	471.11	471.06	0.05
8-13	477.83	477.76	0.07
2- 6	491.41	491.38	0.03
11-15	643.59	643.63	-0.04
4- 9	657.31	657.33	-0.02
5-10	664.03	663.82	0.21
1- 3	677.31	677.54	-0.23
6-12	9000.00	8999.98	0.02
3- 9	9009.08	9009.03	0.05
13-16	9013.04	9013.01	0.03
2- 7	9020.38	9020.30	0.08
10-15	9022.06	9022.08	-0.02
1- 4	9029.32	9029.24	0.08
8-14	9033.18	9033.31	-0.13
5-11	9042.16	9042.27	-0.11
6-13	9042.38	9042.43	-0.05
3-10	9043.98	9044.10	-0.12
12-16	9055.50	9055.46	0.04
2- 8	9056.08	9056.04	0.04
9-15	9057.12	9057.15	-0.03
1- 5	9057.72	9057.82	-0.10
7-14	9069.14	9069.05	0.09
4-11	9070.98	9070.85	0.13
		Av.	0.07

TABLE XI

1, 1-DIFLUORO-2, 2-DICHLORO-3-METHYL-3-PHENYLCYCLOBUTANE, 100°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	0.01	-0.01
9-12	2.27	2.10	0.17
10-13	9.15	9.23	-0.08
3- 6	11.16	11.29	-0.13
11-14	187.00	186.99	0.01
4- 7	189.27	189.16	0.11
5- 8	196.15	196.12	0.03
1- 2	198.16	198.27	-0.11
14-16	445.33	445.29	0.04
7-12	458.56	458.54	0.02
8-13	465.05	465.00	0.05
2- 6	478.23	478.28	-0.05
11-15	632.33	632.27	0.06
4- 9	645.56	645.60	-0.04
5-10	652.05	651.90	0.15
1- 3	665.03	665.26	-0.23
6-12	9000.00	8999.96	0.04
3- 9	9009.16	9009.15	0.01
13-16	9012.76	9012.90	-0.14
2- 7	9019.57	9019.70	-0.13
10-15	9022.13	9022.11	0.02
1- 4	9029.00	9028.80	0.20
8-14	9032.55	9032.60	-0.05
5-11	9041.80	9041.74	0.06
6-13	9044.19	9044.40	-0.21
3-10	9046.26	9046.46	-0.20
12-16	9057.40	9057.33	0.07
2- 8	9057.83	9057.68	0.15
9-15	9059.47	9059.42	0.05
1- 5	9059.98	9059.82	0.16
7-14	9070.61	9070.58	0.03
4-11	9072.72	9072.76	-0.04
		Av.	0.09

TABLE XII

1,1-DIFLUORO-3-METHYL-
3-PHENYLCYCLOBUTANONE-2, 30°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	-0.09	0.09
10-13	12.35	12.38	-0.03
9-12	13.49	13.58	-0.09
3- 6	26.11	26.08	0.03
11-14	249.00	248.91	0.09
5- 8	261.35	261.41	-0.06
4- 7	262.49	262.55	-0.06
1- 2	275.11	275.08	0.03
14-16	281.35	281.41	-0.06
7-12	293.20	293.32	-0.12
8-13	295.98	295.89	0.09
2- 6	307.86	307.76	0.10
11-15	530.35	530.41	-0.06
4- 9	542.20	542.29	-0.09
5-10	544.98	544.92	0.06
1- 3	556.86	556.76	0.10
6-12	9000.00	8999.92	0.08
3- 9	9012.58	9012.43	0.15
2- 7	9014.26	9014.37	-0.11
13-16	9014.58	9014.47	0.11
6-13	9025.32	9025.28	0.04
1- 4	9026.60	9026.90	-0.30
10-15	9026.94	9026.94	0.00
8-14	9028.84	9028.95	-0.11
2- 8	9037.20	9037.15	0.05
3-10	9039.06	9038.97	0.09
12-16	9039.78	9039.82	-0.04
5-11	9041.62	9041.44	0.18
1- 5	9050.82	9050.82	0.00
7-14	9051.60	9051.73	-0.13
9-15	9053.38	9053.49	-0.11
4-11	9065.46	9065.36	0.10
		Av.	0.09

TABLE XIII

1,1-DIFLUORO-3-METHYL-
3-PHENYLCYCLOBUTANONE-2, 100°

Transition	Obs. Freq., cps	Calc. Freq., cps	O - C
15-16	0.00	-0.05	0.05
10-13	12.31	12.23	0.08
9-12	13.45	13.51	-0.06
3- 6	25.75	25.82	-0.07
11-14	249.00	248.95	0.05
5- 8	261.31	261.27	0.04
4- 7	262.45	262.47	-0.02
1- 2	274.75	274.82	-0.07
14-16	284.03	284.10	-0.07
7-12	295.93	295.94	-0.01
8-13	298.55	298.56	-0.01
2- 6	310.46	310.37	0.09
11-15	533.03	533.10	-0.07
4- 9	544.93	544.91	0.02
5-10	547.55	547.59	-0.04
1- 3	559.46	559.37	0.09
6-12	9000.00	8999.94	0.06
3- 9	9012.19	9012.26	-0.07
13-16	9014.33	9014.20	0.13
6-13	9025.34	9025.29	0.05
10-15	9026.48	9026.48	0.00
8-14	9028.45	9028.66	-0.21
2- 8	9036.91	9037.11	-0.20
3-10	9038.92	9038.88	0.04
12-16	9039.51	9039.55	-0.04
5-11	9041.04	9040.98	0.06
1- 5	9050.75	9050.66	0.09
7-14	9051.37	9051.40	-0.03
9-15	9053.25	9053.11	0.14
4-11	9064.87	9064.92	-0.05
		Av.	0.07

PART II

NITROGEN-15 MAGNETIC RESONANCE SPECTROSCOPY

I. INTRODUCTION

Experimental consideration of the magnetic resonance properties of nitrogen has generally been confined to the naturally abundant isotope of mass number 14 (60-64). This choice arose more from expediency than from desirability, since nitrogen-14 possesses an electric quadrupole moment. The mechanism of relaxation associated with the interaction between the quadrupole moment and electric-field gradients at the nucleus causes serious broadening of resonance signals (65). The structural chemist interested in nitrogen magnetic resonance spectroscopy is thus restricted to experiments based almost entirely on chemical-shift measurements, since most of the fine structure is washed out by these relaxation effects (66-70). If the nitrogen nucleus is located in a symmetric environment, however, the diminished magnitude of the electric-field gradient permits the observation of spin-spin splittings (71). The quadrupole interaction has undesirable consequences in the proton spectrum as well. Rather than the 1:1:1 triplet expected from interaction of a proton with a nitrogen nucleus of spin 1, the resonance signals typically range from a sharp singlet (cyanamide) to a peak broadened almost beyond the limits of detectability (pyrrole).

All relaxation problems associated with the quadrupole interaction would be eliminated if nitrogen-15 were substituted for the abundant isotope. Although this isotope is stable and possesses a spin of $\frac{1}{2}$, it suffers from low natural abundance (0.365%) and low

sensitivity (1.04×10^{-3} that of proton at constant field). These drawbacks have been sufficient until recently (72-73) to prevent the utilization of nitrogen-15 in n.m.r. spectroscopy. Resonance signals may be obtained at 6.08 Mcps and 14,100 gauss with samples synthetically enriched in nitrogen-15. Effects from rather long relaxation times may be mitigated under favorable circumstances by addition of a paramagnetic material. In this way, high-resolution conditions (Figure 7) permit observation of fine structure in the nitrogen spectrum, and the proton spectrum of nitrogenous compounds is free of complications arising from the quadrupole interaction.

Figure 7. Nitrogen-15 resonance of nitric-^{15}N acid, 8.57 M.

II. CHEMICAL SHIFTS

Electronic shielding of the nucleus from an applied magnetic field gives rise to the chemical shift (74). This effect has been artificially divided into a diamagnetic and a second-order paramagnetic part (75). The diamagnetic (Lamb) shielding arises from rotation of the entire electronic structure of the molecule around the nucleus at the Larmor frequency. The paramagnetic shielding arises from changes in the electronic wave function produced by the external field, as represented by mixing of the ground state with excited states. This term, which effectively allows for hindrance to free rotation of the electron cloud by the nuclear field, increases with deviations from idealized symmetry, i.e., increased orbital angular momentum. Since the p electrons are of primary importance in describing the electronic structure of nitrogen compounds, the paramagnetic shielding term would be expected to be the dominant contributor to the chemical shift. The magnetic properties of fluorine-19, as described by the calculations of Saika and Slichter on F_2 and HF (76), confirm the predominance of the paramagnetic term for this nucleus. Whereas the paramagnetic contribution is at a minimum for the fluoride ion, the contribution for the axially symmetric fluorine molecule is given by:

$$\Delta\sigma = -\frac{2}{3}\left(\frac{e\hbar}{mc}\right)^2 \left\langle\frac{1}{r^3}\right\rangle \frac{1}{\Delta E} \qquad (22)$$

where $\langle 1/r^3 \rangle$ is averaged over the 2p electrons and ΔE is the electronic excitation energy. The shift is thus to lower field. Since paramagnetic screening is inversely proportional to ΔE, unsaturated molecules should resonate at lower field than saturated molecules, which possess higher excited states. Holder and Klein (61) and Schmidt, Brown, and Williams (62) have described nitrogen-14 chemical shifts in terms of this model, which appears to be fairly general.

Table XIV lists the nitrogen-15 chemical shifts measured thus far. For the spherically symmetrical ammonium ion, the paramagnetic term is at a minimum. Since the electronic structure closely resembles that of a noble gas, which possesses zero angular momentum, the resonance occurs at extremely high field. Ammonia and methylamine resonate at an even higher field because of the shielding effect of the unshared electron pair (77).

When the nitrogen atom is involved in a multiple bond, the presence of low-lying electronic excited states brings about a substantial increase in the paramagnetic term (equation 22). The largest contribution to ΔE appears to come from the $n \rightarrow \pi^*$ transition (78-79). Thus, resonance occurs at increasingly lower field as $\Delta E(n \rightarrow \pi^*)$ decreases in the series: aniline, benzamide, benzonitrile, benzophenoneimine (diphenylketimine), and trans-azobenzene (Figure 8). Qualitative consideration of the excitations available to the lone pair serves as an indication of the magnitude of the screening anisotropy. Molecules in which oxygen is bonded directly to nitrogen will be considered in detail later.

TABLE XIV

NITROGEN-15 CHEMICAL SHIFTS

	Solvent	Chemical shift (ppm downfield)[a]
Ammonia (anhydrous)	None	0
Methylamine[b]	None	2
Ammonium chloride	Water	24
Methylammonium chloride	Water	28
Glycine, pH 6[c]	Water	31
β-Chloroethylamine hydrochloride	Water	34
Anilinium iodide	Water	51
Anilinium tetrafluoroborate	Water	53
Anilinium chloride	Water	55
Aniline	None	59
Urea[c]	DMSO	82
Methyl isothiocyanate[b]	None	93
Hydrazobenzene	DMF	96
Benzamide	Acetone	100
Acetamide[b]	Water	113
Acetanilide	Acetone	135
Diphenylketimine hydrochloride	SO_2	168
Acetonitrile[b]	None	245
Benzonitrile	None	259
Potassium cyanide	Water	279
2, 4-Dichloropyrimidine[c]	$CDCl_3$	290 (av.)
Diphenylketimine	Pentane	308
Benzal methylamine[b]	None	325
trans-Azoxybenzene	Ether	324
		328
Conjugate acid of trans-azobenzene	Acid[d]	360

Table XIV (Continued)

	Solvent	Chemical shift (ppm downfield)[a]
Nitric acid, 8.57 M	Water	367
Nitrobenzene	None	372
trans-Azobenzene	Ether	510
n-Butyl nitrite	None	572
Sodium nitrite	Water	608
Nitrosobenzene	Ether	913

[a]Determined to a precision of about ± 1%.

[b]Measured by Dr. G. Binsch.

[c]Measured by Dr. B. W. Roberts.

[d]65% concentrated sulfuric acid, 20% ethanol, 15% water.

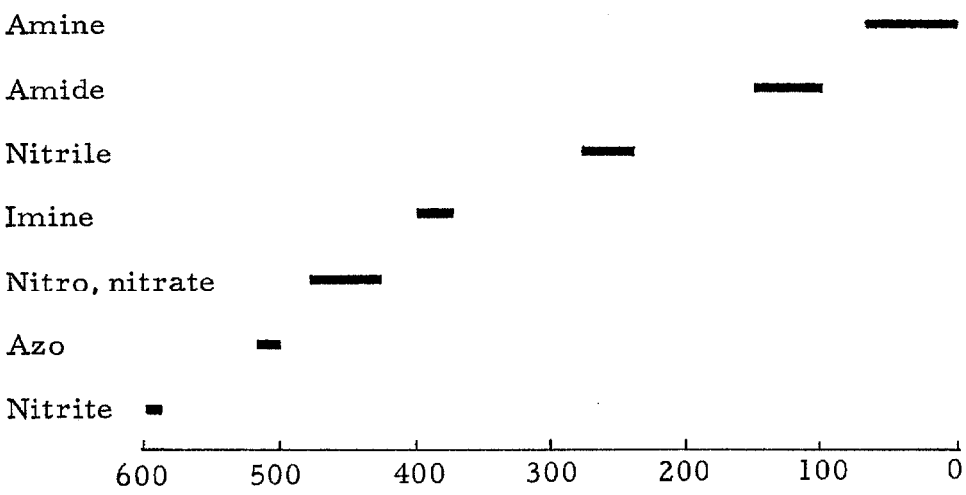


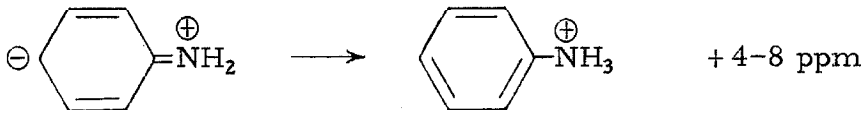
Figure 8. Nitrogen-15 chemical shifts of functional groups.

The effect of protonation serves to illustrate the principles developed in the previous paragraphs. Protonation of nitrogen can produce upfield (trans-azobenzene) and downfield (ammonia) shifts, or it can have almost no effect (aniline). Provided the paramagnetic contribution is small, the normal shift would be to lower field, since protonation removes the shielding of the unshared electron pair. This situation obtains with unconjugated amines such as ammonia and methylamine:

$$NH_3 \longrightarrow NH_4^+ \qquad -24 \text{ ppm}$$

$$CH_3NH_2 \longrightarrow CH_3NH_3^+ \qquad -26 \text{ ppm}$$

In aromatic amines, conjugation of the lone pair with the aromatic ring substantially reduces the shielding from the nonbonding electrons (XXI). Therefore, aniline comes into resonance considerably downfield from the aliphatic amines. This reduction in shielding of the lone pair almost nullifies any effect which protonation would have on the chemical shift. The 20 ppm disparity between the resonances

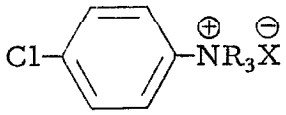


+4–8 ppm

XXI

of the anilinium and methylammonium ions must arise from inductive and magnetic anisotropy effects of the phenyl ring.

Fraenkel (80) has explained the anomalous proton spectra of the p-chloroanilinium salts in terms of ion-pair formation. Although the ortho and meta protons of the iodide salt produce distinct resonances, the ring protons of the chloride and perchlorate salts collectively give rise to single sharp peaks. Ion-pair formation (XXII) in the latter cases, Fraenkel claims, results in cancellation by the



XXII

gegenion (chloride or perchlorate) of the effect which the N^+ entity has on the charge distribution of the ring. The two centers of charge in the ion pair, as conceived by Fraenkel, are not separated by intervening solvent molecules. For the salt of the larger iodide ion, however, ion pairs do not form, and the charge center on nitrogen brings about the usual perturbations on the charge distribution in the aromatic ring. If ion-pair formation is indeed important in aqueous solutions of anilinium salts, the contiguous gegenion may affect the shielding of the nitrogen atom in such a way as to cancel the effect of the positive charge. This may be offered as an alternative explanation of the small effect which protonation has on the chemical shift of aniline. The chemical shifts of the chloride, tetrafluoroborate, and iodide salts of aniline were measured and found to be rather similar (Table XIV). If ion pairs are formed, the presence of the gegenion has a negligible effect on the chemical shift. Otherwise, the iodide

salt would have been shifted with respect to the other salts. The absence of a large effect of protonation on the chemical shift of aniline is best explained by the conjugative mechanism discussed above.

The treatment thus far has applied only to protonation of nitrogen nuclei for which the paramagnetic term is small. The large paramagnetic shift of multiply bonded systems has been associated with a small mean electronic excitation energy. Protonation of such compounds will increase the excitation energy by means of a significant enhancement of the energy of the $n \rightarrow \pi^*$ transitions. As a result, the protonated compounds should resonate at higher fields than the corresponding neutral species. Data in Tables XIV and XV show that the upfield shift with protonation exceeds 100 ppm for cases in which the paramagnetic term is quite large. Thus, as a general rule, the farther downfield the resonance of the neutral species, the larger the upfield shift with protonation. This is a corollary of the dominance of the paramagnetic term in determining the chemical shift (81). These changes are reflected in the electronic spectra of the compounds. The $n \rightarrow \pi^*$ transition of trans-azobenzene shifts from 420 to 300 mμ with protonation (82). The upfield shift of trans-azoxybenzene with respect to trans-azobenzene may also be associated with a higher energy $n \rightarrow \pi^*$ transition. Judging from the position of the nitrogen-15 chemical shift, the $n_N \rightarrow \pi^*$ transition of trans-azoxybenzene should occur near 300 mμ.

The structure of the conjugate acid of trans-azobenzene has been the source of some controversy (83). The single sharp peak in

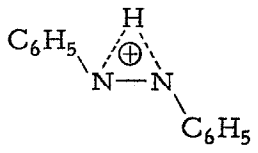
TABLE XV

EFFECT OF PROTONATION
ON NITROGEN CHEMICAL SHIFTS

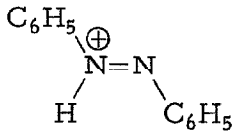
	Shift (ppm)	Change with protonation (ppm)
Pyridine[a]	302	+123
Diphenylketimine	308	+140
trans-Azobenzene	510	+150

[a]Reference 78.

the nitrogen-15 spectrum unfortunately fails to differentiate between structures XXIII and XXIV. Intermolecular exchange must be fast in



XXIII



XXIV

either case in order to bring about the equivalence of the nitrogen-15 nuclei. Intramolecular exchange must not be important if XXIV obtains, because the trans species would first have to isomerize to the cis form. Gerson, et al. (84), have shown that the isomeric identity of the azo compound is retained in the protonated form.

Compounds in which oxygen is attached directly to nitrogen present a more complicated situation, because the possibility arises of contributions to the mean electronic excitation energy from orbitals on oxygen. Chemical shift and electronic absorption data are presented in Table XVI for a series of "oxynitrogen" compounds. s-Butyl nitrate appears to bear the same relationship to the nitrate ion as n-butyl nitrite does to the nitrite ion. In both cases the ester resonates at slightly higher field, and the observed ester n → π* transition is at a slightly lower wavelength. One is tempted to extend the analogy to nitrobenzene and nitrosobenzene. In both cases the alkoxy group of the ester is simply replaced by a phenyl group. The structural analogy, however, does not carry over to the absorption or magnetic resonance spectra. The electronic structures of the various

TABLE XVI

CHEMICAL SHIFTS AND ABSORPTION MAXIMA OF OXYNITROGEN COMPOUNDS

	λ_{max} ($n \rightarrow \pi^*$), mμ	Chemical shift, ppm
s-Butyl nitrate	270[a] (n_O)	337[b]
Nitrate ion	300[c] (n_O)	367
Nitrobenzene	330[d] (n_O, ?)	372
n-Butyl nitrite	356[e] (n_N)	572
Nitrite ion	380[f] (n_N)	608
	300 (n_O)	
Nitrosobenzene	755[d] (n_N)	913

[a]H. E. Ungnade and R. A. Smiley, J. Org. Chem., 21, 993 (1956).

[b]M. Witanowski, private communication on nitrogen-14 data.

[c]H. M. McConnell, J. Chem. Phys., 20, 700 (1952).

[d]J. N. Murrell, "The Electronic Spectra of Organic Molecules," John Wiley and Sons, Inc., New York, 1963, pp. 186 f.

[e]R. N. Haszeldine and J. Jander, J. Chem. Soc., 1954, 691.

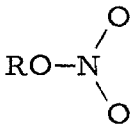
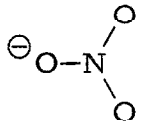
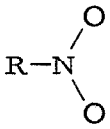
[f]W. G. Trawick and W. H. Eberhardt, J. Chem. Phys., 22, 1462 (1954).

oxynitrogen prototype structures are depicted in Table XVII. Whereas the nitro compound and the nitrates all have $n_O \rightarrow \pi^*$ transitions near 300 mμ, there is a difference of 400 mμ between the absorptions of the nitrites and the nitroso compound. This situation arises because the nonbonding orbital, which is located on the nitrogen atom for the nitroso-nitrite series, is strongly influenced by N-substituents. For the nitro-nitrate series on the other hand, the nonbonding orbitals involved in the transitions of interest are on the oxygen atoms, and hence are less affected by N-substitutents. Because of the similarity of the energies of the $n_O \rightarrow \pi^*$ transitions in the latter series, the resonance position of nitrobenzene is rather close to those of the nitrates. Since the $n_N \rightarrow \pi^*$ transition of nitrosobenzene is of much lower energy than those of the nitrites, the paramagnetic term is immensely increased, and the resonance position is at a considerably lower field (913 ppm below ammonia) (85). The chemical shift of nitrosobenzene was rather insensitive to dilution and changes of solvent (chloroform, 905 ppm; methanol, 908 ppm; ether, 913 ppm), so no information concerning the monomer-dimer equilibrium could be obtained.

The foregoing discussion has attempted to correlate the chemical shift with the energy of the $n \rightarrow \pi^*$ absorption. For the nitro-nitrate series, the transition in question is from a nonbonding orbital on oxygen to a molecular orbital, whereas in the nitroso-nitrite series there is also a nonbonding orbital on nitrogen. It is reasonable that in the latter cases the $n_N \rightarrow \pi^*$ transitions would contribute more

TABLE XVII

ELECTRONIC STRUCTURE OF OXYNITROGEN COMPOUNDS

	s	N(n)	N(p)	O(p)	O(n)
	8	—	2	4	10
	6	—	2	3	12
	8	—	2	4	10
RO–N=O	6	2	1	3	6
$^{\ominus}$O–N=O	4	2	2	2	8
R–N=O	4	2	1	1	4

effectively to the mean electronic excitation energy, ΔE. Thus the nitrites have a substantially larger paramagnetic shift than the nitrates, even though the $n \rightarrow \pi^*$ transitions (n_O or n_N) occur within a range of 100 mμ. Conversely, the large difference between the shifts of the nitrates and the nitrites substantiates the assignment of the longer wavelength absorption (356 to 380 mμ) in the nitrites to the $n_N \rightarrow \pi^*$ transition. If the absorption resulted from an $n_O \rightarrow \pi^*$ transition, the nitrogen-15 resonance positions should have been much closer to those of the nitrates because of the similarity in the position of the absorption maxima. The $n_N \rightarrow \pi^*$ transition must have a significant effect on the oxygen chemical shift also, since the nitrite ion resonance occurs about 260 ppm below that of the nitrate ion (86-87), even though the $n_O \rightarrow \pi^*$ transitions are quite similar in both cases.

These correlations could thus be used (1) to assign ultraviolet absorption bands from observation of nitrogen-15 chemical shifts; and (2) to predict the location of resonances from ultraviolet data. The former possibility has been applied to trans-azoxybenzene, and the latter has been realized in the case of nitrosobenzene. Both possibilities must rely heavily on the availability of data from analogous compounds. As a result, the correlation probably has more explanatory than predictive power.

III. COUPLING CONSTANTS

Ramsay (88-89) has described electron-coupled nuclear spin-spin interactions in terms of three distinct mechanisms: (1) the nuclear spin-electron orbital interaction; (2) the electron-nuclear dipole-dipole interaction; and (3) the Fermi contact interaction. In the orbital term (1), the magnetic moment of one nucleus induces orbital electronic currents which give rise to magnetic fields at a second nucleus. The dipole-dipole interaction (2) between the electron cloud and one nucleus produces a magnetic field at a second nucleus by polarization of electron spins. Since the point "r = 0" is excluded from any such dipole-dipole interaction, there remains the interaction between a nuclear moment and that portion of the electron cloud located at the nucleus, the Fermi contact interaction (3). This interaction, which can only involve electrons in s-orbitals, since p-orbitals vanish at r = 0, also gives rise to magnetic fields at a second nucleus by electron spin polarization.

The early calculations by Ramsay of proton couplings, and later work of Karplus and Grant (90) and O'Reilly (91), have justified neglecting the first two terms. The coupling of protons with other nuclei therefore must derive principally from the contact term. The Hamiltonian for the interaction between the nuclear and electron dipoles is thus given by equation 23 (92):

$$\mathcal{H} = \frac{16\,\pi\beta\hbar}{3} \sum_{k} \sum_{N} \gamma_N \delta(r_{kN})\, \underset{\sim}{S}_k \cdot \underset{\sim}{I}_N \qquad (23)$$

where the index k refers to electron spins, N refers to the nuclei involved, and $\delta(r_{kN})$ selects the value $r_{kN} = 0$ in any integration over electronic coordinates. The corresponding second-order perturbation energy is proportional to the scalar product of the nuclear spin vectors (92):

$$E_{12} = hJ_{12} \underset{\sim}{I}_1 \cdot \underset{\sim}{I}_2 \tag{24}$$

where J_{12} is the spin-spin coupling constant. If the triplet excitation energies which arise in the perturbation calculation may be represented by a single effective value, and if only one electron pair is involved in the coupling interaction, the expression for the coupling constant reduces to:

$$J_{12} = \left(\frac{8}{3}\beta\gamma\right)^2 \frac{h}{\Delta E} (0|\delta_{1N}\,\delta_{2N'}|0) \tag{25}$$

where the operator $\delta_{1N}\delta_{2N'}$ measures the probability that electron 1 is on nucleus N when electron 2 is on nucleus N'. According to the molecular orbital representation of McConnell (93), the wave function ψ is described as a linear combination of the wave functions associated with the individual nuclei, which in turn are linear combinations of atomic orbitals:

$$\psi = c_1\,\phi(1) + c_2\,\phi(2) \tag{26}$$

where $\phi(1) = (1 + \lambda_1^2)^{-1/2}\,[s(1) + \lambda_1\,p(1)]$

and $\phi(2) = (1 + \lambda_2^2)^{-1/2}\,[s(2) + \lambda_2\,p(2)]$

Substitution of equation 26 into equation 25 yields the following relationship:

$$J_{12} = J_0 s_1 s_2 \qquad (27)$$

where $s_i = \frac{100}{(1 + \lambda_i^2)^{1/2}}$ is the per cent s-character of the orbital from the ith nucleus involved in the bond under consideration.

The derivation of equation 27 has been sketched out in order to delineate the approximations inherent in any linear relationship between s-character and coupling constants ("J-s relationship"), namely, (1) the complete predominance of the contact term; (2) the presence of perfect pairing in a two-center orbital; (3) the neglect of overlap (not explicitly pointed out above); and (4) the validity of the use of a mean triplet excitation energy, ΔE, which remains constant throughout a given series (94-95).

Despite the serious limitations placed on equation 27 by these assumptions, correlation of hybridization with coupling constants has seen wide usage, with particular success for the coupling between carbon-13 and directly bonded protons. Muller and Pritchard (96) and Shoolery (97) first established the existence of such a relationship (equation 28) (98):

$$s_C = 0.20\ J_{^{13}CH} \qquad (28)$$

The empirical success of the relationship between s_C and $J_{^{13}CH}$ has not been realized in other systems. The extensive work of Frei and Bernstein (99) on directly bonded carbon-13-carbon-13 couplings

yielded a relationship of only limited value:

$$s_C\, s_C = 17.4\, J_{^{13}C^{13}C} + 59.8 \qquad (29)$$

No simple relationship is apparent between $J_{^{13}CF}$ and hybridization of carbon and fluorine (100-101). Karabatsos and Orzech (102) have pointed out inadequacies even in the carbon-13-hydrogen relationship. Furthermore, the hybridization predicted by $J_{^{13}CH} = 382$ cps for the dimethylcarbonium ion is far from the value expected for a trigonal carbon atom (103).

Since the greatest success was obtained with couplings between carbon-13 and hydrogen, an extension to the couplings of other first-row elements with hydrogen was considered. Of these nuclei, only nitrogen-15 possesses a spin of $\frac{1}{2}$ and forms compounds embracing a wide range of hybridizations. A correlation such as equation 28, involving nitrogen, could offer a direct experimental choice among the various theories of hybridization. Pauling's contention (104) that nitrogen forms predominantly p-type sigma bonds is opposed by those who suggest that the bonding orbitals are more nearly sp^3 or else that hybridization is primarily a function of the bond angles (105-107). The discrepancy between predicted hybridizations permits a differentiation by means of a correlation such as equation 28. Previous studies of couplings between nitrogen-14 and hydrogen were limited because of the quadrupole interaction (66). Studies of nitrogen-15-hydrogen couplings were limited by the availability of the isotope (108-113). Table XVIII displays the couplings measured in the present

TABLE XVIII

DIRECTLY BONDED NITROGEN-15-HYDROGEN COUPLING CONSTANTS

		Solvent	Method	$\lvert J_{^{15}NH} \rvert$[a], cps	s_N[b]
1	$(C_6H_5)_2C{=}NH$	Pentane	c	51.2 ± 0.4	33.3
2	NH_3[d]	None	c	61.2 ± 0.9	—
3	NH_4Cl	Water	c, e	73.2	25.0
4	CH_3NH_3Cl[f]	Water	c, e	75.6	25.0
5	$HO_2CCH_2NH_3Cl$[g]	Water	c, e	77.0	25.0
6	$\underline{H}_2NCONHCON\underline{H}_2$	DMSO	h	88.4 ± 1.0	32.0
7	H_2NCONH_2[g]	DMSO	c, e	89 ± 1	32.0
8	CH_3CONH_2	Water	c, e	89 ± 2	32.0
9	H_2NCN	DMSO	h	89.4 ± 1.0	32.0
10	$C_6H_5NHNHC_6H_5$	DMF	c, e	90.5	—
11	Pyridinium ion	H_2SO_4	i	90.5 ± 1.0	33.3
12	$C_6H_5NHCOCH_3$	Acetone	c, e, h	90.9	—
13	$C_6H_5NHCSNHCH_3$	Ethanol	c, e	91.2	—
14	1-Methylcytosine[j]	SO_2	c	92.0	—
15	$HCONH_2$[k]	None	c	92.0[l]	—
				88.0[m]	
16	$(C_6H_5)_2C{=}NH_2Cl$	SO_2	c	92.6 ± 0.4	33.3
17	Phthalimide	DMSO	c	93.0 ± 0.8	—
18	$CH_3CONHCH_2CO_2H$	DMSO	c	94.5	—

Table XVIII (Continued)

[a]The average deviation is about 0.2 cps unless otherwise indicated.

[b]These values are used for the plot in Figure 9.

[c]Obtained from the proton spectrum of the nitrogen-15 compound.

[d]Reference 113.

[e]Obtained from the nitrogen-15 spectrum.

[f]Measured by Dr. G. Binsch.

[g]Measured by Dr. B. W. Roberts.

[h]From the nitrogen-15 satellites of the proton spectrum of the unlabeled compound by computer averaging.

[i]By calculation from the ^{14}N—H splitting in the proton spectrum.

[j]Reference 111.

[k]Reference 109.

[l]Coupling to the proton trans to the carbonyl group.

[m]Coupling to the proton cis to the carbonyl group.

study (114), as well as a few values from other sources.

A qualitative examination of the relationship between couplings (column 5) and s-character (column 6) suggests that a linear correlation involving compounds 2-18 is conceivable (115). Unequivocal assignments of hybridization may be made in only three cases, there being no doubt that the ammonium ion (3) is sp^3-hybridized and the pyridinium (11) and diphenylketiminium (16) ions are sp^2-hybridized. The two points supplied by the ammonium ion (s = 25%, J = 73.2 cps) and the diphenylketiminium ion (s = 33.3%, J = 92.6 cps) (116) define a straight line which is illustrated in Figure 9. Equation 30 is the mathematical representation of this linear relationship. A number of

$$s_N = 0.43\, J_{^{15}NH} - 6 \qquad (30)$$

compounds for which tentative hybridization assignments may be made (4, 5, 6-9, 11) are included on the plot. The close agreement between the reasonable hybridizations listed in column 6 of Table XVIII and those predicted by equation 30 lends credence to the validity of the J-s relationship for nitrogen-15. Thus the coupling constant of other ammonium compounds (4-5) are consistent with sp^3-hybridization as computed from equation 30. The couplings of compounds 6-18 fall in a narrow range between 88 and 94 cps, corresponding to s-characters of 31-34%. Small variations among the members of the group may arise from differences in bond lengths, although this factor apparently is not important in the carbon-13-hydrogen relationship. After some consequences of this J-s correlation have been explored, the

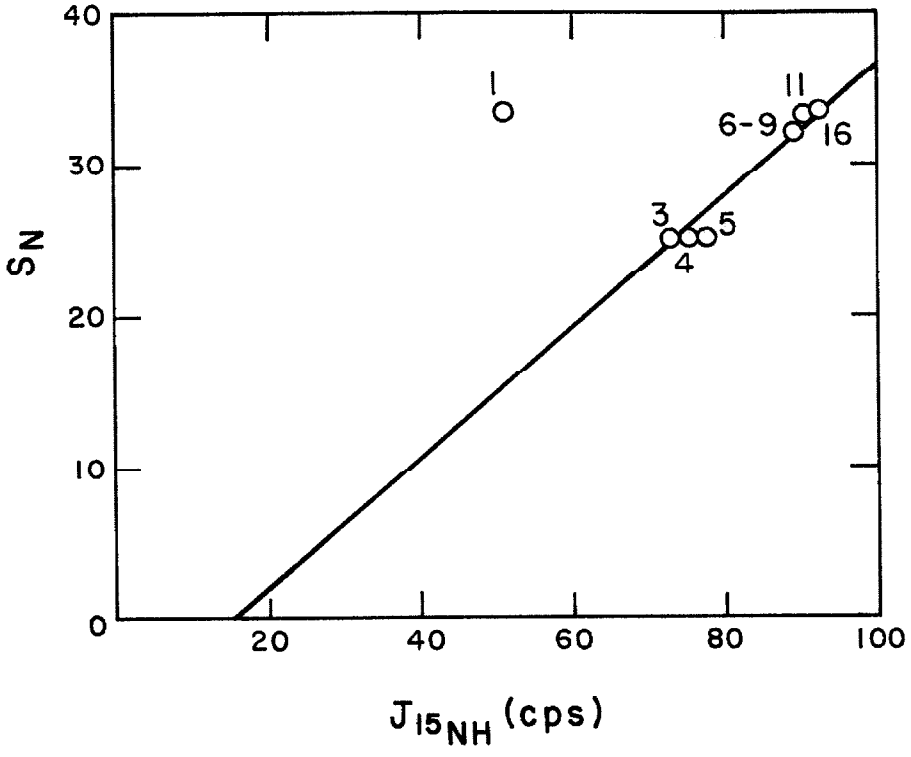


Figure 9. The J-s relationship for nitrogen-15 and hydrogen.

deviations, in particular that of diphenylketimine (1), will be discussed in detail.

The hybridization of the nitrogen atom in ammonia offers the most general platform for discussion. Pauling (104) describes the orbitals as being almost completely p-hybridized, with deviations from 90° taken as perturbations on this model. If the bonds to hydrogen involve p-orbitals, then the lone pair must occupy an s-orbital, distributed symmetrically about the nucleus. A semi-empirical calculation (104) from the s-p promotion energy and the N—H bond energy upholds this contention by predicting an s-character of 4.8% for the nitrogen orbitals to hydrogen. Bader (117) has used the concept of the binding region to strengthen the claim for p-hybridization. He reconciles the observed interbond angle of 107.3° (104, 107) with the supposed orthogonal geometry of p-orbitals by invoking the concept of bent bonds.

If the bond angles accurately reflect the interorbital angles, the conditions of normalization and orthogonality give rise to a simple relationship between bond angles and hybridization. If the bonds in question are equivalent and separated by an angle θ, then (107):

$$s = \frac{100 \cos\theta}{\cos\theta - 1} \qquad (31)$$

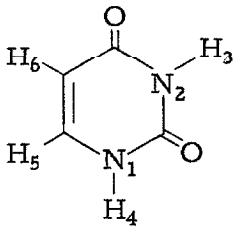
The s-value calculated for ammonia (θ = 107.3°) from this equation is 22.9%, corresponding to hybridization close to sp^3. This calculation is fallacious, however, if the bonds are significantly bent. Certain

molecules, furthermore, take exception to the orthogonality rules. In methylene chloride, for example, both the HCH and ClCCl bond angles are close to 112°.

Coulson (118) has argued that pure p-hybridization cannot account for the large difference between the dipole moment of NH_3 (1.51 D) and that of NF_3 (0.2 D) (119). The moment of a directed lone pair, i.e., one which is partially p-hybridized, would compensate for that of the three fluorine atoms in the latter molecule, resulting in a very small molecular dipole moment. It could be argued, however, that this evidence speaks only for the hybridization of nitrogen trifluoride.

Although the artifice of bent bonds compromises the calculation of hybridizations from bond angles, it will have no effect on J-s relationships, since the contact interaction will always be a valid measure of s-character. The observed nitrogen-15-hydrogen coupling in ammonia is 61.2 ± 0.9 cps (113). The per cent s-character predicted by equation 30 is therefore 19.9 ± 0.4. Thus the hybridization predicted by the nitrogen-15-hydrogen coupling is in substantial disagreement with the theory of bent p-hybridized bonds, which predicts a zero coupling. Since the hybridizations computed from equations 30 and 31 are in good accord, it is doubtful that the bonding orbitals in ammonia are extensively bent.

Although the J-s correlation for nitrogen-15 is quite satisfactory for the majority of cases, it fails to a varying degree for a few compounds. Uracil-$^{15}N_2$ (XXV) (120) is one such contrary case.

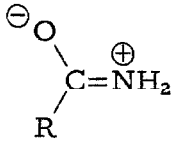


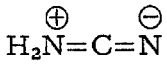
XXV

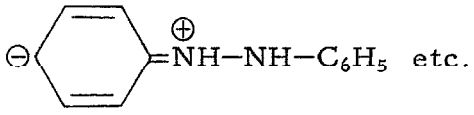
The two directly bonded nitrogen-15-hydrogen couplings were found to be 91 and 97 ± 2 cps. The larger coupling was identified as J_{14} because it involves the hydrogen atom (H_4) which exhibits an ortho coupling of 5.8 cps to H_5. The largest coupling of the other proton (assigned to be H_3) is 1.8 cps, presumably a meta coupling. Thus the coupling of nitrogen conjugated with two carbonyl groups (N_2) is about 6 cps less than that of nitrogen conjugated with a single carbonyl group (N_1). Unless the double bond creates a special effect, the coupling appears to decrease with the amount of s-character. Similarly, the coupling is smaller for the doubly conjugated phthalimide (93.0 cps) than for the singly conjugated acetylglycine (94.5 cps). Finally, the coupling of hydrazobenzene (90.5 cps) is anomalously large unless the conjugative effect of the aromatic ring is more pronounced than expected.

These discrepancies are small, however, compared to that of diphenylketimine (1). Although the s-character is presumably close to 33.3%, the coupling is only 51.2 cps, the smallest value observed. According to equation 30, this would correspond to 15.6% s-character. Since this low s-value is unreasonable, it is more likely that a second factor is operative which makes a contribution of opposite sign to the

coupling constant. Pople (121) has found by calculation that contributions from the nuclear spin-electron orbital interaction are large if the screening constant for either of the coupling nuclei is highly anisotropic. The paramagnetic term in the shielding expression, the magnitude of which is determined by this anisotropy, is the dominant factor in nitrogen-15 chemical shifts (vide supra). The very large downfield nitrogen-15 chemical shift of diphenylketimine suggests that orbital contributions may become important for the coupling in this molecule. The anisotropy which enhances the orbital contribution may intuitively be associated with a low-lying $n \rightarrow \pi^*$ transition. In all other compounds in Table IX, except the aliphatic amines, of course, a canonical structure may be written with positive charge on nitrogen:





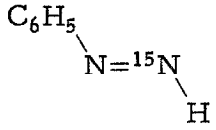


Partial or complete bonding of the lone pair in this manner would raise the energy of the $n \rightarrow \pi^*$ transition. Therefore, the ketimine is uniquely suited for orbital contributions.

In order to test whether the anomalous coupling could be an artifact of the particular system under consideration, a second imine, s-butylphenylketimine-^{15}N, was studied. Since the couplings in this molecule ($J_{^{15}NH}$ = 50.8 cps) were observed to be almost identical to that in diphenylketimine-^{15}N, the anomaly must be a general property

of the electronic make-up of the ketimine system.

It is particularly significant that $J_{^{15}NH}$ for the protonated form of diphenylketimine (16) is quite close to the couplings in all other conjugated, nearly sp^2 systems. Since the molecular framework is the same for (1) and (16), the anomalous coupling of (1) cannot arise from a π-contribution. The "normal" coupling of the protonated form indicates that the orbital contribution is no longer important. The screening constant must therefore be less anisotropic, and the paramagnetic term correspondingly smaller. On this basis, a large upfield shift with protonation would be predicted for the nitrogen resonance. As was discussed previously, the protonated imine resonates 168 ppm downfield from ammonia, a shift of 140 ppm with respect to the imine itself (122). A second corollary to the predominance of the paramagnetic term therefore states that couplings to nitrogen-15 nuclei with large downfield shifts are not necessarily determined exclusively by the Fermi contact interaction. Thus the absolute values of the chemical shift are interrelated in a predictable manner with their changes on protonation and with the apparent deviations from the linear J-s correlation. The extremely low-field resonance of the azo group suggests that $J_{^{15}NH}$ for a system such as phenyldiimide (XXVI) should not be determined by the contact term alone.



XXVI

Binsch has carried out a parallel investigation of nitrogen-15-carbon-13 couplings. These couplings, which are uniformly small because of the small gyromagnetic ratios of both nuclei (123), are listed in Table XIX. By assigning reasonable values to the carbon and nitrogen hybridization parameters, he has produced a linear J-s correlation which is illustrated in Figure 10. Compounds 2, 4-8 are correlated roughly by the equation:

$$s_N s_C = 80 J_{^{15}N^{13}C} \quad (32)$$

but compounds 1, 3, and 9 deviate substantially. Again, the couplings in these three systems are smaller than would be predicted from consideration of the contact term alone. Since the nitrogen-15 resonances for these compounds occur at particularly low fields (Table XIV), the deviations probably arise from orbital contributions associated with low-lying excited states. As was the case with diphenylketimine, canonical structures of acetonitrile and benzalmethylamine cannot be written in which the lone pair is involved in partial double bonding.

Orbital contributions may also explain anomalies in other coupling systems. Juan and Gutowsky (124) have reported that carbon-13-hydrogen couplings, calculated for substituted ethylenes from additivity relationships, are systematically about 7 cps below the observed values. Lynden-Bell and Sheppard (125) have found the carbon-13-carbon-13 couplings in ethane, ethylene, and acetylene to be 34.6, 67.6, and 171.5 cps, respectively. In these cases, increased unsaturation enhances the coupling constant beyond values expected from

TABLE XIX

DIRECTLY BONDED CARBON-13-NITROGEN-15 COUPLING CONSTANTS

		$\lvert J_{^{13}C^{15}N} \rvert$, cps
1	$C_6H_5CH={}^{15}N{}^{13}CH_3$	<3
2	$^{13}CH_3{}^{15}NH_2$	7 ± 1
3	$C_6H_5{}^{13}CH={}^{15}NCH_3$	7.1 ± 0.3
4	$^{13}CH_3{}^{15}NH_3Cl$	<8
5	$C_6H_5{}^{15}NH(^{13}CO)CH_3$	13.0 ± 1.5
6	$^{13}CH_3{}^{15}N=C=S$	13.4 ± 0.2
7	$C_6H_5NH(CS)^{15}NH^{13}CH_3$	<15
8	$CH_3(^{13}CO)^{15}NH_2$	<15
9	$CH_3{}^{13}C\equiv{}^{15}N$	17.5 ± 0.2

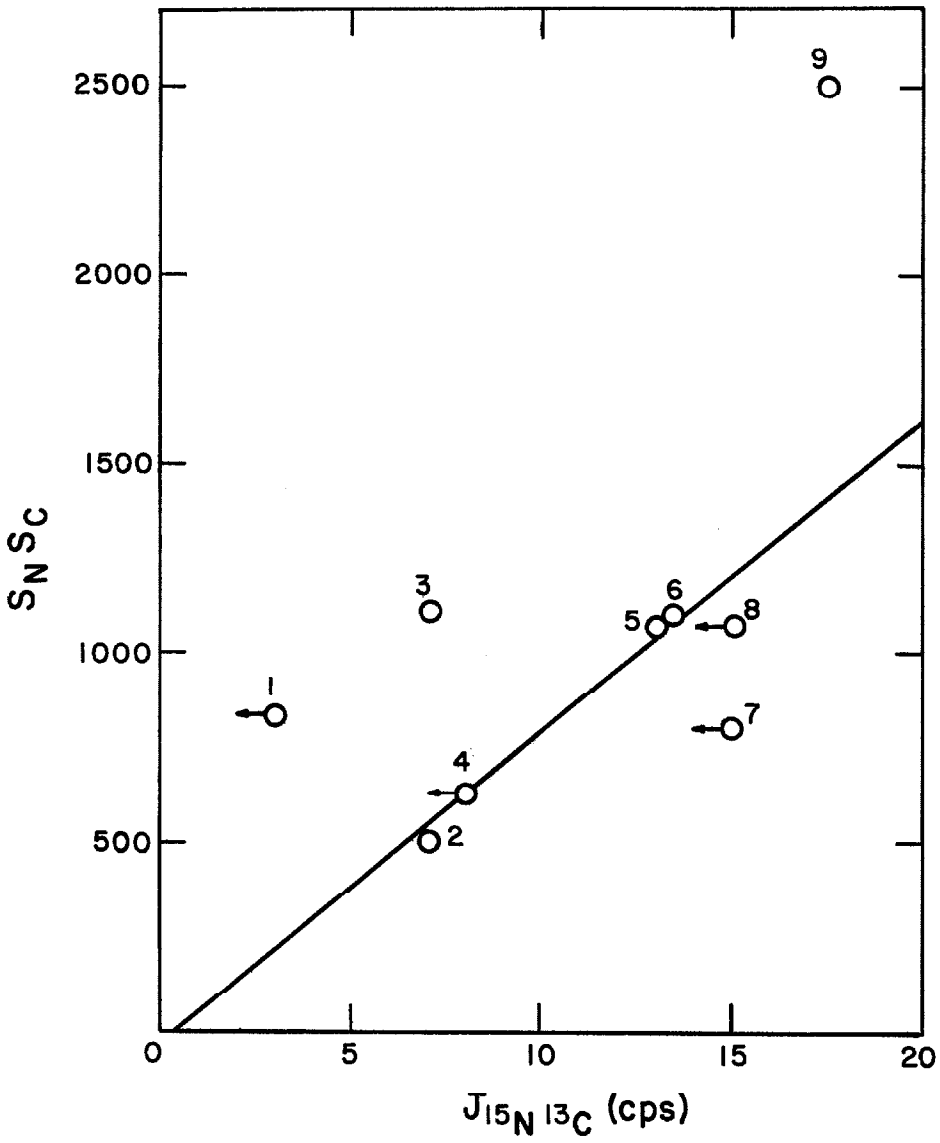


Figure 10. The J-s relationship for carbon-13 and nitrogen-15.

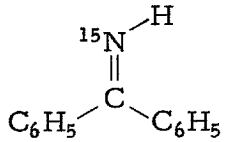
exclusive consideration of the contact term. Furthermore, couplings across double and triple bonds correlated least well with the relationship developed by Frei and Bernstein (99).

In conclusion, it is felt that extreme caution must be exercised in utilizing any J-s correlation for assignment of hybridization. Even in the most favorable case, i.e., one bond couplings involving hydrogen, it has been demonstrated that serious deviations from the linear relationship occur. Each particular case should be examined as to the validity of the assumptions before the coupling constant should be used as a measure of the hybridization.

IV. THE DEGENERATE BIMOLECULAR EXCHANGE OF PROTONS IN KETIMINES

Nuclear magnetic resonance spectroscopy is ideally suited for rate studies of rapidly reversible unimolecular reactions with Arrhenius activation energies between 5 and 20 kcal/mole. Isomerization processes (126-127), ring inversions (128-129), and valence tautomerizations (130-131) have been studied by analysis of the temperature variation of spectral parameters. Reactions of higher order involving proton transfers have also been examined by means of spectral changes as a function of solvent, pH, and solute concentration (132). The rapid rates of proton transfer reactions have generally caused the spectral lineshapes to be temperature insensitive (133). Reversible changes with temperature in the spectra of nitrogen-15 labeled ketimines are interpreted in the following discussion in terms of an intermolecular exchange of protons between nitrogen atoms. Bimolecular reactions have seldom been susceptible to study by this method.

In the absence of exchange, the proton on nitrogen in diphenylketimine-^{15}N (XXVIII) should be a doublet because of coupling with

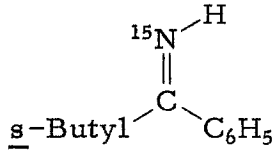


XXVIII

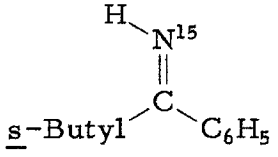
nitrogen-15. At 40°, however, the imine hydrogen resonance varies

from a single sharp peak in carbon disulfide or a broad singlet in carbon tetrachloride and dimethyl sulfoxide, to no observable peak at all in acetonitrile, deuterochloroform, and pentane. The spectrum of the ketimine in 2-5% solutions of the last three solvents was examined to -50°, at which temperature the solutions solidified. Whereas no change occurred over this temperature range for the acetonitrile and deuterochloroform solutions, the expected doublet appeared below 0° in the spectrum of the pentane (134) solution (Figures 11a, b and 12). Under identical conditions of solvent and temperature, the nitrogen-14 compound exhibited a single broad imine resonance which fell midway between the two peaks of the nitrogen-15 compound (Figure 11c). The integrated intensity of the two peaks, furthermore, was 1/10 that of the phenyl peaks. There remains little doubt, therefore, that the doublet resonance ($J_{^{15}NH}$ = 51.2 cps) arises from the imine proton coupled with nitrogen-15.

This same phenomenon was observed at lower temperatures in the spectrum of s-butylphenylketimine-^{15}N (XXIX). At -60°, the imine proton resonance consists of four peaks, which must arise from the two distinct ketimine isomers (XXIXa and b) which are possible in this



XXIXa



XXIXb

unsymmetrical system (Figure 13). The components of each small

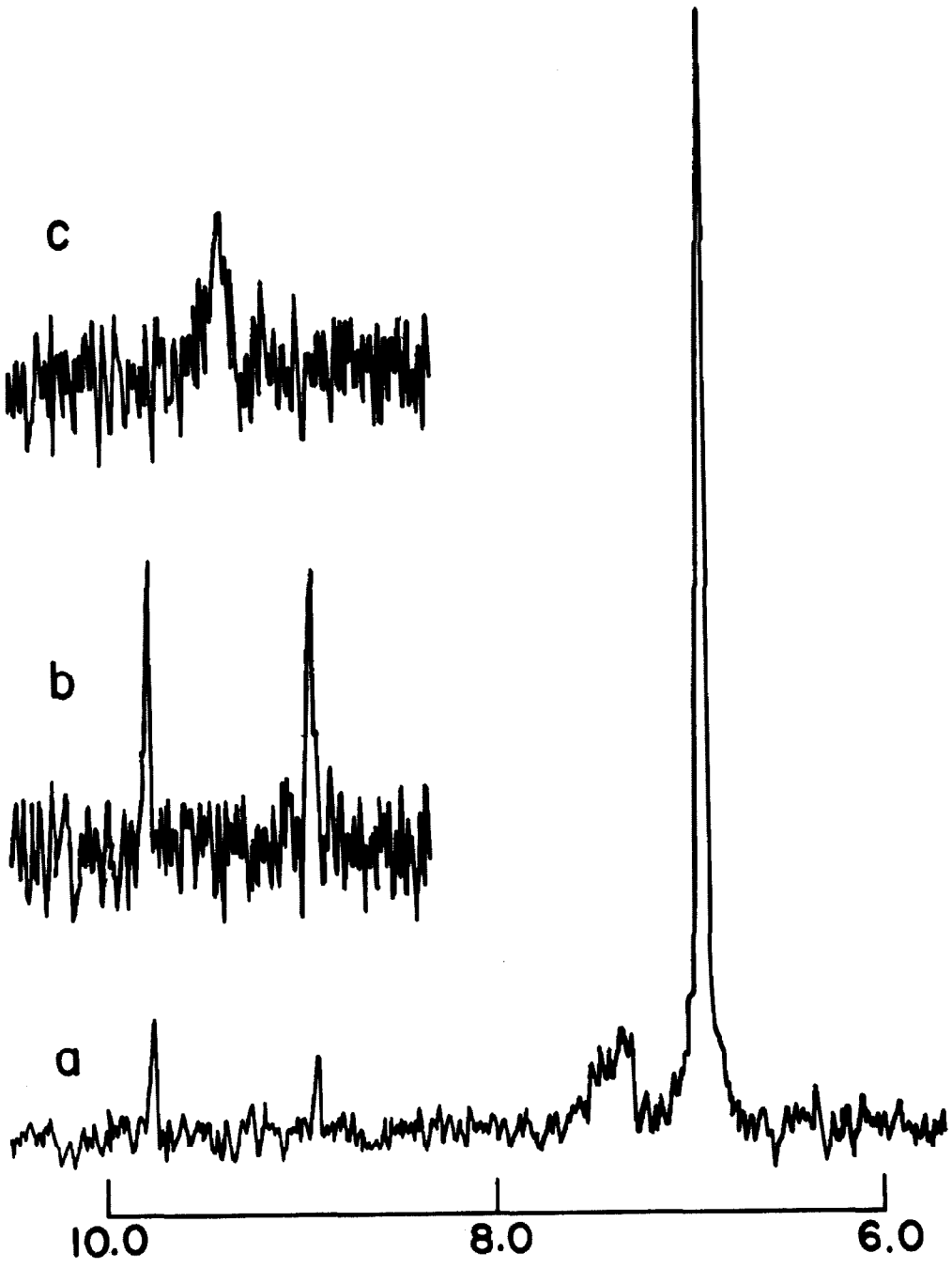


Figure 11. Proton spectrum of diphenylketimine, -40°.

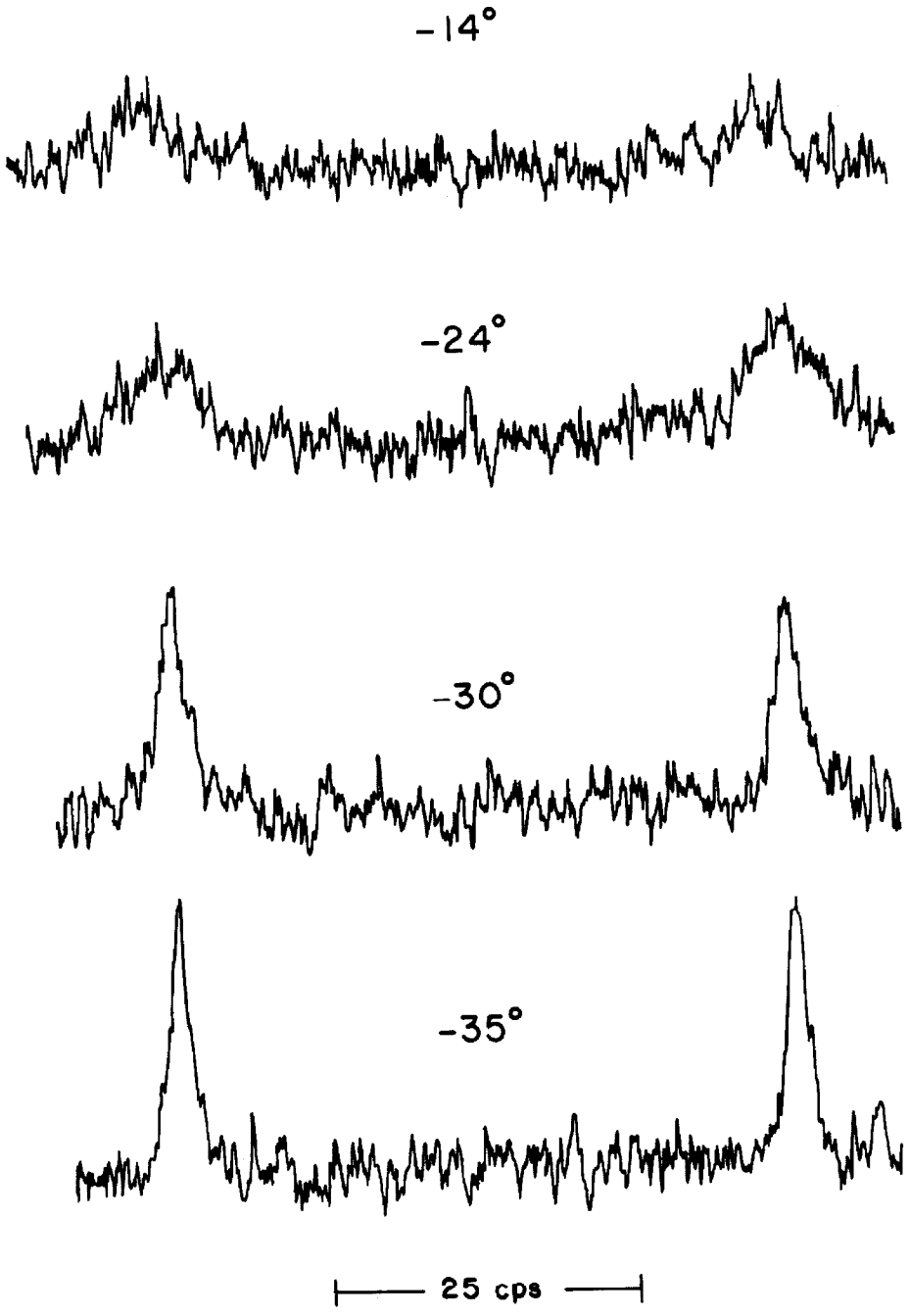


Figure 12. Temperature dependence of the imine proton resonance in diphenylketimine-^{15}N.

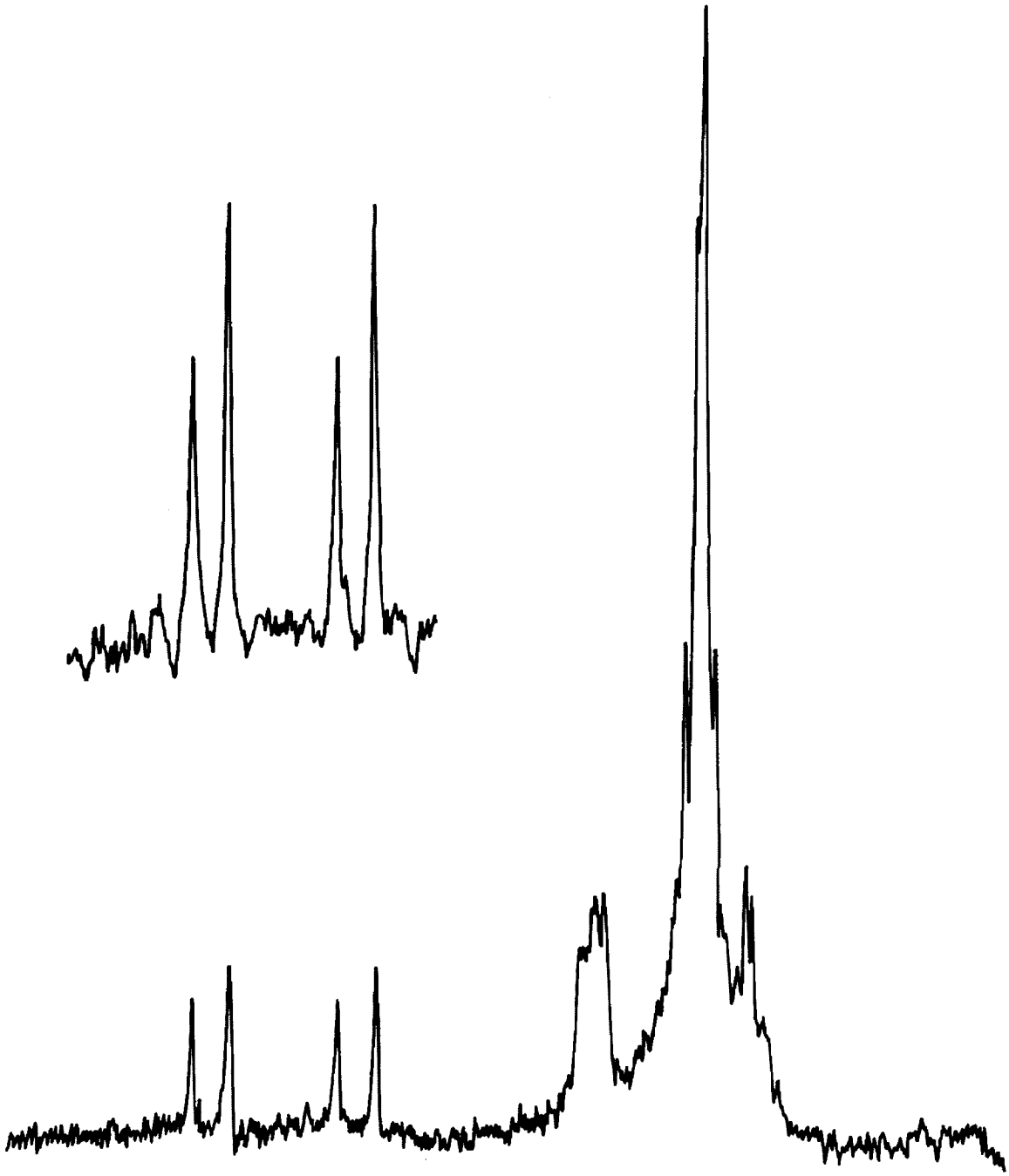


Figure 13. Proton spectrum of s-butylphenylketimine-^{15}N, -60°.

doublet are chemically shifted about 11 cps from each other. The low-field components in each doublet are separated by 50.6 cps, and the high-field components are separated by 50.9 cps. As the temperature of the pentane solution is raised, the components of each doublet broaden and finally coalesce (Figure 14, left side; only one of the doublets is shown). The free-energy difference between isomers was calculated to be 70 cal./mole from the equilibrium constant at -60° (1.5, obtained by electronic integration).

The observation of separate geometric isomers of N-substituted imines has been claimed erroneously in the past (135-136). The actual isolation of both syn and anti forms of a given system was not realized until quite recently (137-138), for the case of N-substituted benzophenone imines. The present observation of separate resonances for the two isomers of s-butylphenylketimine-^{15}N is the first example of cis-trans isomerism about a carbon-nitrogen double bond which is unsubstituted at nitrogen.

The coalescence of the peaks for the two isomers (Figure 14) results from a simple spin-exchange phenomenon. The possible mechanisms of exchange will be discussed in detail for the case of the unsymmetrical imine (XXIX).

$$\text{A} \qquad \text{XXIXa} \rightleftharpoons \text{XXIXb} \tag{33}$$

$$\text{B} \qquad \text{M} + \text{SH} \rightleftharpoons \text{protonation or deprotonation} \tag{34}$$

$$\text{C} \qquad \text{M} + \text{M}' \rightleftharpoons \text{M}' + \text{M} \tag{35}$$

$$\text{D} \qquad \text{D} \rightleftharpoons \text{D}' \tag{36}$$

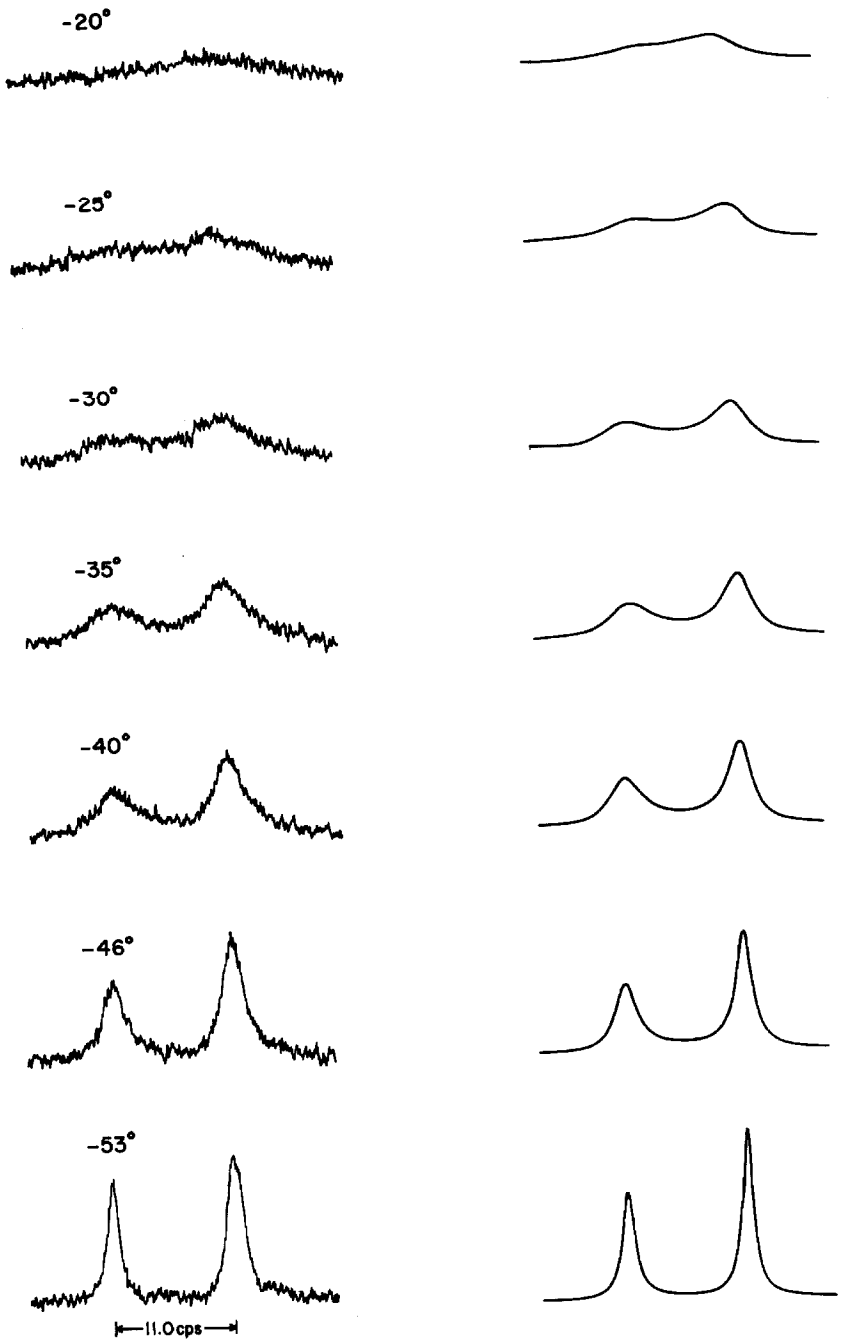
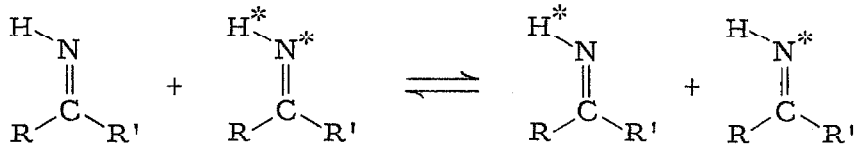


Figure 14. Temperature dependence of the proton spectrum of s-butylphenylketimine-^{15}N.

Mechanism A involves a cis-trans isomerization. Mechanism B involves a proton exchange between monomer and some other species such as water or ammonia. Mechanism C is a special case of B, in which the second species is also monomer. Mechanism D involves a proton exchange within a dimeric structure.

In order to differentiate between the various mechanistic possibilities, the Gutowsky-Holm method (126, 139) was employed to determine mean lifetimes, τ (140), which are related to the reaction rate in a manner to be discussed. Figure 14 compares the calculated spectra with the observed spectra for various temperatures. The molecularity of the reaction must be determined before rates may be calculated from the mean lifetime.

Certain mechanistic possibilities may be eliminated by observing the effect on the mean lifetime of changes in reaction conditions. Addition of water directly to the solution of pentane had no effect on the mean lifetime. The presence of calcium hydride or calcium oxide in the n. m. r. tube had a similarly negligible effect. Mechanism B is thus eliminated, since addition or destruction of the most likely choices for SH, water and ammonia, do not affect the rate. When the concentration of ketimine was varied, however, significant changes in the mean lifetime were indicated by substantial lineshape changes. This excludes as the only mechanism any kind of unimolecular process, such as those represented in mechanisms A and D. Mechanism C therefore best accounts for the experimental details:



Such a pathway is bimolecular and degenerate; not only are both reactants the same, but they are the same as the products.

Although the mechanism has been discussed in terms of a bimolecular process, the actual molecularity remains to be determined. The experimental facts could also be interpreted in terms of a termolecular process. The Gutowsky-Holm-Borčić treatment enables one to determine the mean lifetime, τ, which is simply the reciprocal of the first-order rate constant for a unimolecular process. The relationship is more complicated for reactions of higher order. The integrated form of the rate law given in

$$-\frac{dM}{dt} = kM^n \tag{37}$$

equation 37 is:

$$-\int_{M_0}^{M_0/e} M^{-n}\, dM = \int_0^{\tau} k\, dt$$

For n = 1: $$k\tau = \ln \frac{M_0}{M_0/e} = \ln e = 1$$

In general, for $n \neq 1$:

$$k\tau = -\left[\frac{1}{-n+1} M^{-n+1}\right]_{M_0}^{M_0/e}$$

$$= \frac{1}{1-n}\left[M_0{}^{1-n} - \left(\frac{M_0}{e}\right)^{1-n}\right]$$

$$= M_0{}^{1-n}\left(\frac{1-e^{n-1}}{1-n}\right) \qquad (38)$$

Thus, $$\log \tau = (1-n)\log M_0 - \log k' \qquad (39)$$

where $$\frac{1}{k'} = \frac{1}{k}\left(\frac{1-e^{n-1}}{1-n}\right) = \tau M_0{}^{n-1} \qquad (40)$$

A statistical factor of 2, which arises because two equivalent protons are exchanged in each reaction, is canceled by the spin factor which arises because exchange between nuclei of the same spin is not observed in the n.m.r. experiment (132). Table XX lists the values of the parameters which are used in Figure 15 for the plot of log τ vs. log M_0 according to equation 39. From the slope of this graph, the molecularity was calculated to be about 1.7. Since the error in measuring the values of τ from calculated spectra is at least 10%, and the error in M_0 is large, the line in Figure 15 is deceptively straight, and the result must be judged accordingly. This analysis at least casts serious doubt on the presence of higher order processes. A second-order process is most suitably accommodated by a transition state involving a concerted shift of two protons in a four-membered ring:

TABLE XX

MEAN LIFETIMES AND CONCENTRATIONS

τ, sec.	log τ	M_0, mole/l.	log M_0
0.070	-1.155	0.93	-0.032
0.055	-1.260	1.40	0.146
0.045	-1.347	1.86	0.270
0.040	-1.398	2.33	0.367

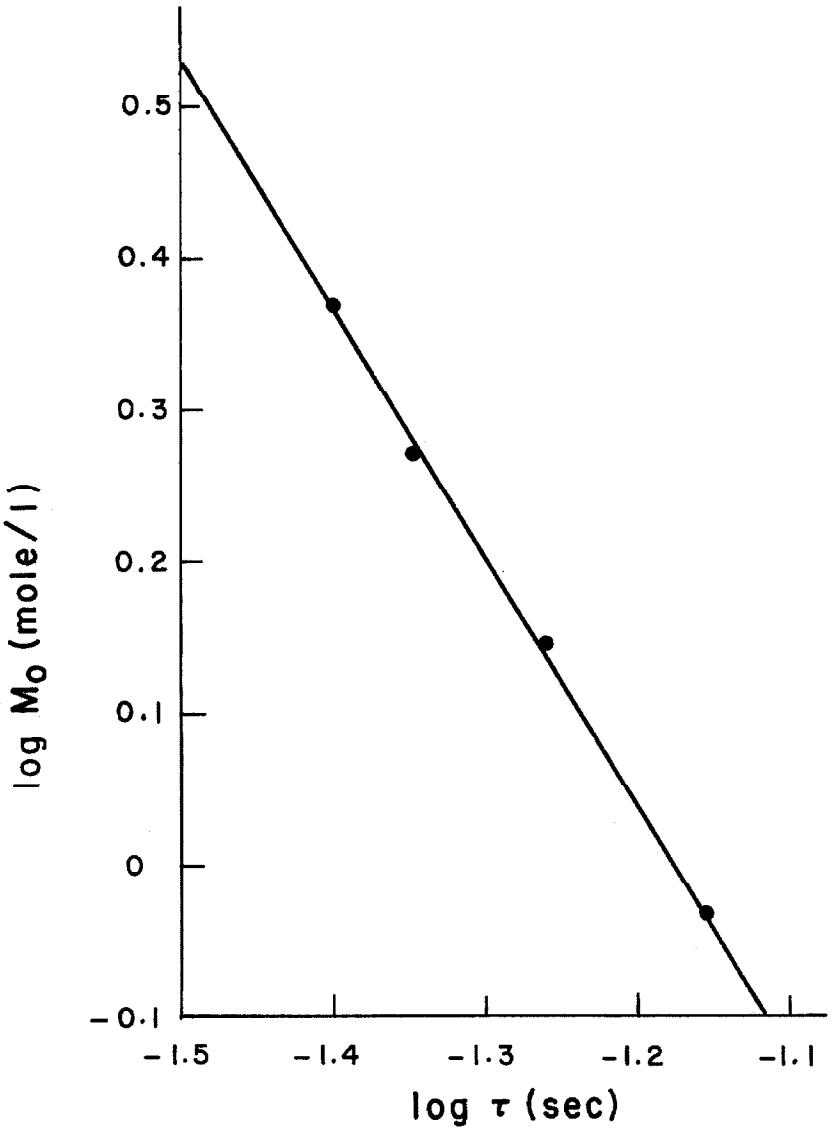
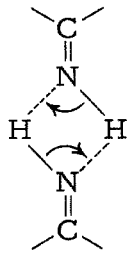


Figure 15. Plot for the determination of the molecularity of the proton exchange reaction of s-butylphenylketimine-^{15}N.



An admixture of a unimolecular process such as mechanism D cannot be excluded.

Arrhenius plots for the exchange reactions of XXVIII and XXIX may be constructed from the rate constants calculated by equation 38 from machine-determined values of τ. The data are displayed in Tables XXI and XXII and in Figures 16 and 17. The activation energy for the degenerate proton exchange in diphenylketimine is thus calculated to be 13.8 ± 2 kcal/mole, and the values for s-butylphenylketimine are 6.5 and 6.6 ± 1 kcal/mole. Two values arise since approach to the transition state can occur from either direction. The smaller value is necessarily associated with the less stable isomer. No imine hydrogen resonance was observed down to -80° for di-n-butylketimine-^{15}N. The activation energy for exchange in systems containing two aliphatic substituents must therefore be less than 5-7 kcal/mole. Sensitivity and solubility problems prevented accurate concentration studies of the proton exchange in XXVIII. It should be noted that the calculation of activation energies is completely independent of both the molecularity and the units of concentration, since changes in these quantities will not affect the slope of the plot. Therefore, the activation parameters are valid, even if the proposed

TABLE XXI

RATE PARAMETERS FOR DIPHENYLKETIMINE-^{15}N

T(°C)	τ, sec.	k, l/mole-sec.	log k
-10	0.03	173	2.24
-14	0.04	130	2.12
-17	0.05	104	2.20
-20	0.08	65	1.81
-23	0.12	43	1.64
-26	0.15	34	1.54

TABLE XXII

RATE PARAMETERS FOR s-BUTYLPHENYLKETIMINE-^{15}N

T(°C)	τ_A	τ_B	k_A	k_B	log k_A	log k_B
-25	0.055	0.077	33.6	24.0	1.526	1.380
-30	0.075	0.106	24.7	17.5	1.393	1.243
-35	0.095	0.135	19.5	13.7	1.290	1.137
-40	0.130	0.186	14.2	9.95	1.152	0.998

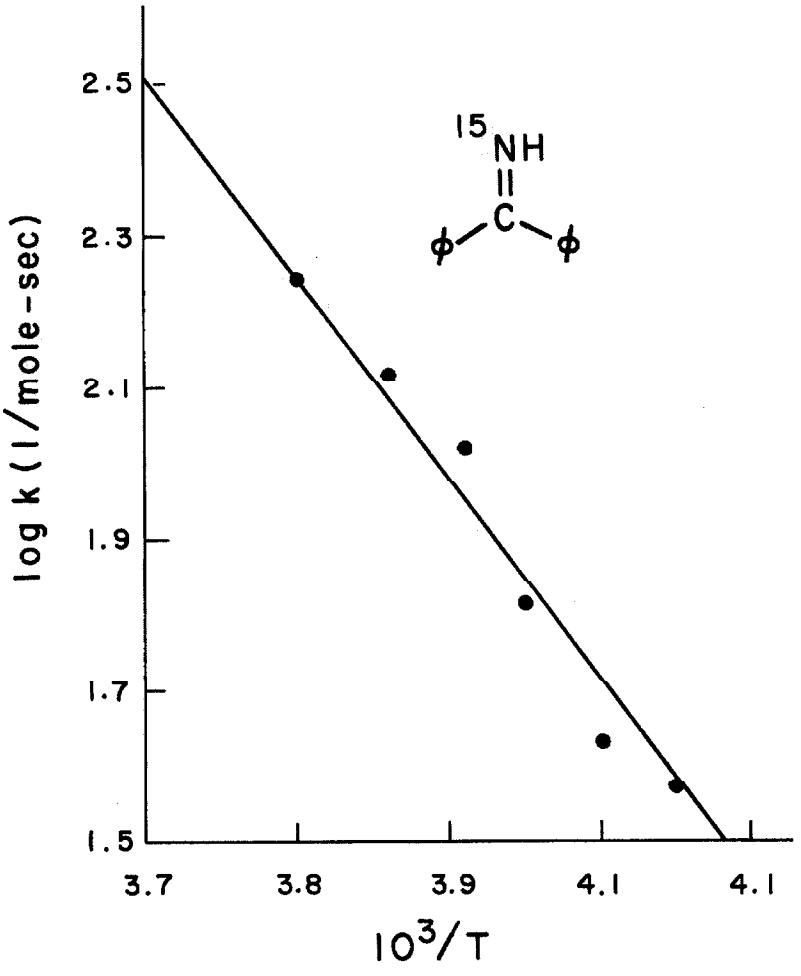


Figure 16. Arrhenius plot for diphenylketimine-^{15}N.

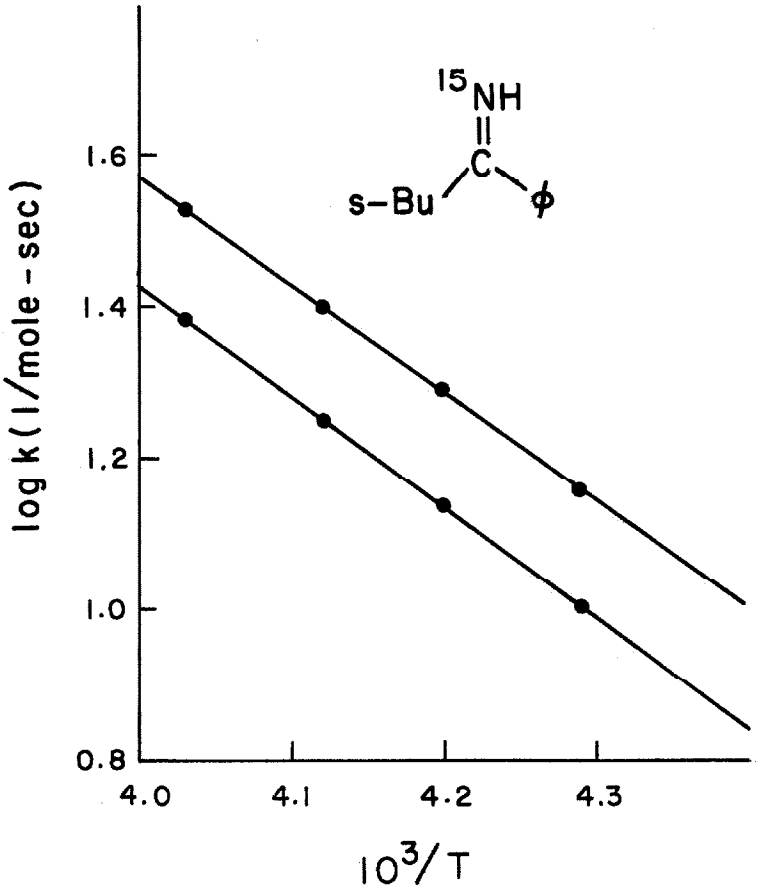


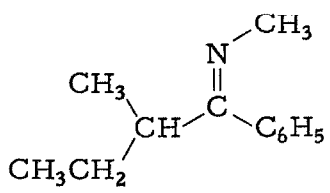
Figure 17. Arrhenius plot for s-butylphenylketimine-^{15}N.

mechanism of spin exchange is incorrect.

An isomerization process such as that depicted by mechanism A has been studied by Andreades (141) for the N-substituted imine XXX. Analysis of the temperature dependence

XXX

of the fluorine spectrum yielded an activation energy of 13 ± 3 kcal/mole. Replacement of the exchangeable imine proton with a methyl group in the ketimine systems investigated in the present work might permit the observation of rotation about nonfluorinated carbon-nitrogen double bonds. Methylamine Schiff bases were therefore made from s-butylphenylketone, n-propylphenylketone, ethylphenylketone, diisopropylketone, and p-chlorobenzophenone. In all cases but the first, the N-methyl resonances consisted of a single sharp peak, indicative of fast exchange, the coincidence of chemical shifts, or the presence of only a single isomer. This is particularly unusual in the case of the methylimine of p-chlorobenzophenone, since Curtin and Hauser (137) reported that the N-methyl resonance consisted of two peaks. The N-methyl resonance of s-butylphenylketone methylimine (XXXI)



XXXI

was a doublet, the components of which were separated by 1 cps. The invariance of the peak separation to a change of field from 14, 100 to 23, 500 gauss (142) identifies the doublet as a coupling, rather than a chemical shift. This is presumably a five-bond coupling between the N-methyl protons and the methinyl proton of the s-butyl group (143). The absence of chemically shifted N-methyl resonances for all members of this series renders impossible the study of isomerization about the carbon-nitrogen double bond by n. m. r. methods (144).

V. EXPERIMENTAL

Nitrogen-15 magnetic resonance spectra were obtained with a Varian V-4300B spectrometer operated at 14,100 gauss. The V-4310C transmitter-receiver unit was operated at 6.08 Mcps (145). A 12-mm. insert equipped with a Wilmad spinner assembly admitted tubes of 9.85 ± 0.05-mm. outside diameter. The sample volume was about 0.4-0.7 ml. In spite of the low sensitivity, spectra of fully labeled materials were routinely obtained in the absorption mode.

Nitrogen-15-hydrogen coupling constants were measured by three different methods. Isotopically labeled materials permitted direct observation of the coupling by proton or nitrogen-15 magnetic resonance spectroscopy. If the N—H resonance consisted of three peaks because of a relatively ineffective quadrupole relaxation, the measured value of $J_{^{14}NH}$ could be converted to $J_{^{15}NH}$. In certain favorable cases, computer-averaging techniques permitted observation of the ^{15}N satellites of the N—H resonance. The 400 channel Mnemotron "CAT" was triggered by an audio-frequency sideband of tetramethylsilane at the beginning of each sweep. Fifty to eighty scans were usually required to define the position of the satellite accurately.

Nitric-^{15}N acid was obtained from Volk Radiochemical Laboratories or from Merck Sharp and Dohme of Canada. The molarity and amount of label varied from sample to sample.

Nitrobenzene-^{15}N. — Concentrated sulfuric acid (3.30 ml.) and 1.95 g. of nitric-^{15}N acid (0.0305 mole, 7 M, 74% ^{15}N) were placed in

a 100-ml. three-necked round-bottomed flask equipped with a reflux condenser and a magnetic stirrer. The solution was cooled to 20°, and 2.9 g. (0.0371 mole) of benzene was added with a pipette. The mixture was heated at 55-60° for 1.75 hrs., cooled, and diluted with 15 ml. of diethyl ether. After the layers were separated, the organic portion was washed once with distilled water, three times with 10% aqueous potassium hydroxide, and once with a saturated aqueous solution of sodium chloride. The combined aqueous portions were extracted three times with ether, and the washing process was repeated on the ether extracts. The ethereal solutions were combined and dried over magnesium sulfate. The drying agent was removed by filtration and the ether by distillation. The residue was distilled to give 3.16 g. (0.0255 mole, 83,6%) of nitrobenzene-^{15}N, b.p. 77-81° (20 mm.).

Aniline-^{15}N. — Nitrobenzene-^{15}N (2.0 g., 1.68 ml., 0.0161 mole) and granulated tin (4.17 g., 0.0351 mole) were placed in a 100-ml. three-necked round-bottomed flask equipped with a reflux condenser, a dropping funnel, and a magnetic stirrer. Concentrated hydrochloric acid (9.16 ml.) was added with stirring at such a rate that effervescence did not occur. The mixture was then heated at 80° for 45 min., i.e., until the odor of nitrobenzene was no longer detectable. The reaction mixture was cooled, and 6.67 g. of sodium hydroxide in 20 ml. of water was added in a dropwise manner. The resulting mixture was steam-distilled. About 40 g. of sodium chloride was added to the distillate, and the saturated solution was

extracted seven times with diethyl ether. The combined organic extracts were dried over potassium carbonate. The solution was filtered to remove the drying agent, and distilled at atmospheric pressure to remove the ether. Distillation of the residue produced 1.134 g. (0.0121 mole, 75.2%) of aniline-^{15}N, b.p., 55-60° (1 mm.).

Acetanilide-^{15}N. — In a 100-ml. round-bottomed flask equipped with a reflux condenser were placed 1.040 g. (0.0110 mole) of aniline-^{15}N, 1 ml. of acetic anhydride, 1.2 ml. of acetic acid, and a trace of zinc dust. The mixture was refluxed for 45 min. and poured with stirring into 30 ml. of distilled water. White crystals formed immediately. The product was isolated on filter paper, washed with cold water, and dried. The yield of acetanilide-^{15}N was 0.93 g. (0.00683 mole, 62.1%).

N,N-Diethylaniline. — Aniline (5.0 g., 0.0537 mole) and triethyl phosphate (6.07 ml., 6.48 g., 0.0356 mole) were placed in a 100-ml. round-bottomed flask equipped with a reflux condenser. The solution was stirred and heated cautiously with a flame until the reaction temperature was sustained by itself. It was then refluxed for 2 hrs., during which time two layers separated. The solution was cooled to 50°, and 4.47 g. of sodium hydroxide in 18 ml. of distilled water was added. The mixture was refluxed for 1 hr. and cooled to room temperature. The layers were separated, and the inorganic portion was washed three times with ether before it solidified. The organic portions were combined and dried over magnesium sulfate. After the drying agent had been removed by filtration, the ether was

removed by distillation. The residue was distilled to give 7.27 g. (0.0487 mole, 90.7%) of N, N-diethylaniline, b.p. 74-5° (5 mm.).

Anilinium-^{15}N Chloride. — Aniline-^{15}N (345 mg.) was treated with 0.55 ml. of concentrated hydrochloric acid in a 30-ml. beaker. The mixture was cooled, and the solid was collected and dried on filter paper. The conversion was quantitative.

Anilinium-^{15}N Tetrafluoroborate. — Anilinium-^{15}N chloride (320 mg.) was dissolved in the minimum amount of distilled water. A concentrated aqueous solution of silver tetrafluoroborate was added dropwise until precipitation was complete. The mixture was filtered twice to remove silver chloride. The clear, yellow solution was used directly for spectral measurements.

Anilinium-^{15}N Iodide. — To 1.4 ml. of 55% hydriodic acid was added 500 mg. of aniline-^{15}N in a dropwise manner. The resulting solid was dried in a desiccator under vacuum for 30 hrs. The yield was quantitative.

Ammonium ^{15}N chloride was obtained from Volk Radiochemical Laboratories or Merck Sharp and Dohme of Canada. The amount of label varied from sample to sample.

Ammonia-^{15}N. — A 10 N solution of sodium hydroxide (5.71 g., 0.143 mole in 14 ml. of water) was placed in a three-necked round-bottomed flask equipped with a dropping funnel, a condenser, and a gas inlet tube for nitrogen. The upper end of the condenser led through two drying tubes containing potassium hydroxide to a 10-ml. flask protected by a calcium chloride drying tube and containing about

2 g. of potassium hydroxide. After nitrogen flow was initiated, the receiver flask was flamed out and immersed in a Dry Ice-acetone mixture. The solution was brought to a gentle reflux, and a concentrated aqueous solution of 3 g. (0.0550 mole) of ammonium-^{15}N chloride was introduced dropwise. Ammonia evolution was spontaneous. The gas was collected in the flask and allowed to stand over potassium hydroxide for 1 hr. The ammonia-^{15}N was then distilled into a 10-mm. n.m.r. tube, which was sealed. The yield, as judged by the volume, appeared to be nearly quantitative.

trans-Azobenzene-$^{15}N_2$. — A 100-ml. three-necked round-bottomed flask was equipped with a mechanical stirrer and a reflux condenser. After 2.5 g. of sodium hydroxide in 5.7 ml. of water, 1.89 g. (0.0152 mole) of nitrobenzene-^{15}N, 2.00 g. (0.0306 mole) of zinc, and 19 ml. of methanol were introduced, stirring was begun, and the mixture was refluxed for 12 hrs. A gray-white precipitate collected on the walls of the flask. The mixture was filtered while hot, and the precipitate was washed free of azobenzene with liberal portions of methanol. The filtrate was neutralized by the careful addition of concentrated hydrochloric acid. The mixture was filtered again to remove the sodium chloride, the precipitate was carefully washed as before, and the methanol was removed by distillation. The residue was cooled in an ice bath, and the crude azobenzene with occluded sodium zincate was isolated on filter paper. To remove the inorganic salts, 6 ml. of 2% hydrochloric acid was added to the solid, and the mixture was heated at 70° with stirring for 5 min. The

mixture was cooled in an ice bath in order to solidify the azobenzene. The product was isolated on filter paper, washed several times with water, and dried in a desiccator. The yield of trans-azobenzene-$^{15}N_2$ was 1.13 g. (0.00613 mole, 80.7%). The ultraviolet absorption spectrum was identical to that reported by Jaffé (82).

Conjugate Acid of trans-Azobenzene-$^{15}N_2$. — trans-Azobenzene-$^{15}N_2$ (850 mg.) was dissolved in 1.2 ml. of a solution containing 65% concentrated sulfuric acid, 20% ethanol, and 15% water (82). The resulting solution was opaque, dark red, and quite viscous. The azobenzene was recovered by dilution of the acid solution with 5 ml. of water. The solid was isolated on filter paper and dried under vacuum to give 810 mg. of trans-azobenzene. The ultraviolet spectrum was identical to that of the starting material.

trans-Azoxybenzene-$^{15}N_2$. — Acetic acid (5 ml.) and 30% hydrogen peroxide (1 ml.) were heated at 55° in a 50-ml. round-bottomed flask with 1.02 g. (0.00554 mole) of trans-azobenzene-$^{15}N_2$. After 8 hrs. and after 20 hrs., 0.5 ml. of 30% hydrogen peroxide was added. The color of the solution changed from deep orange to light yellow. After 24 hrs., the mixture was diluted with 25 ml. of water and extracted six times with 60-70° petroleum ether. The organic extracts were combined and dried over magnesium sulfate. The drying agent was removed by filtration and the volatile solvent was removed by distillation. The product solidified from the solution at 0°. Drying of the solid for 1 hr. in a vacuum desiccator yielded 1.05 g. (0.00524 mole, 94.6%) of trans-azoxybenzene-$^{15}N_2$. The

ultraviolet absorption maxima were identical to those recorded by Maier, et al. (146).

Hydrazobenzene-$^{15}N_2$. — Into a 100-ml. two-necked round-bottomed flask equipped with a reflux condenser were placed 0.987 g. (0.00493 mole) of trans-azoxybenzene-$^{15}N_2$, 5.3 ml. of ethanol, and 1.17 g. of sodium hydroxide in 3 ml. of water. A total of 1.71 g. (0.0262 mole) of zinc was added in small portions to the mechanically stirred solution. The mixture was heated at 100° for 1 hr., i.e., until the color had changed from yellow to red and again to yellow. Ethanol (5 ml.) was added, and the mixture was filtered hot. The solid in the Büchner funnel was washed several times with hot ethanol, and the filtrate was placed in the refrigerator so that all the hydrazobenzene precipitated. The mixture was filtered while cold, and the solid was washed until white with 50% ethanol containing a small amount of sodium bisulfite. The crystals were dried to give 393 mg. (0.00211 mole, 42.8%) of hydrazobenzene-$^{15}N_2$ (white needles, m.p. 121.5-125°, reported 125-126°) (147). Alcohol was removed from the filtrate by distillation. The trans-azobenzene which separated during distillation was collected and dried on filter paper. The yield was 462 mg. (0.0251 mole, 50.9%).

Potassium phthalimide-^{15}N was obtained from Merck Sharp and Dohme of Canada (96.0% ^{15}N).

Phthalimide-^{15}N. — A solution of 1 ml. of concentrated hydrochloric acid in 10 ml. of water was added dropwise at 0° to 1 g. (0.00537 mole) of potassium phthalimide-^{15}N dissolved in the minimum

amount of water. The precipitate was collected and dried on filter paper. The yield of phthalimide-^{15}N was 636 mg. (0.0429 mole, 79.8%).

Benzamide-^{15}N. — A 100-ml. three-necked round-bottomed flask was equipped with an inlet tube for dry nitrogen, a dropping funnel, and a reflux condenser leading through two potassium hydroxide drying tubes to a second flask. The latter 200-ml. round-bottomed flask was equipped with the inlet tube, a mechanical stirrer, and an exit tube which led through a trap to a 10% hydrochloric acid solution. After nitrogen flow was initiated, the second flask was flamed out several times and filled with 4.38 g. (0.0312 mole) of benzoyl chloride and 120 ml. of anhydrous ether. The stirred ether solution was cooled in a Dry Ice-acetone bath, and ammonia was introduced slowly. The ammonia was generated in the first flask by the dropwise addition of 3 g. (0.0550 mole) of concentrated aqueous ammonium-^{15}N chloride to a refluxing solution of 5.7 g. of sodium hydroxide in 14 ml. of water. An hour and a half after evolution of ammonia had ceased, the second flask was warmed to room temperature and allowed to stand for 12 hrs. There was no ammonia trapped in the hydrochloric acid solution. The ether solution was filtered, and the solid was washed with five 18-ml. portions of absolute ethanol. The filtrate was concentrated to incipient crystallization by rotary evaporation, and 75 ml. of benzene was added. The solution was filtered at its boiling point, and the residue was washed with three 35-ml. portions of hot benzene. Two crops of benzamide, totaling

1.582 g., were obtained from this solution. The original solid by-product was washed with acetone. This solution eventually produced an additional 1.428 g. of the product. The total yield of benzamide-^{15}N was 3.010 g. (0.0246 mole, 89.5%), m.p. 122.8-123.2° (reported 121-123°) (148). The excess ammonium chloride (1.58 g.) was recovered quantitatively.

Benzonitrile-^{15}N. — Benzamide-^{15}N (1.582 g., 0.0130 mole) and sodium aluminum chloride (2.50 g., 0.0130 mole) were mixed carefully in a 50-ml. round-bottomed flask equipped with a distillation head. The mixture was heated with a silicone oil bath at 180° until effervescence ceased. Heating was continued with a free flame until distillation of the product was finished. The yield of benzonitrile-^{15}N was 0.995 g. (0.00956 mole, 73.5%).

Diphenylketimine-^{15}N. — Phenyl Grignard reagent was prepared from 3.16 g. (0.0201 mole) of bromobenzene and 0.500 g. (0.0206 mole) of magnesium in 30 ml. of anhydrous ether contained in a 100-ml. three-necked round-bottomed flask equipped with a dropping funnel and a reflux condenser. Benzonitrile-^{15}N (1.87 g., 0.0180 mole) in 10 ml. of anhydrous ether was added dropwise at room temperature, and the mixture was mechanically stirred for 7.5 hrs. The solution was cooled, and 3.61 g. of anhydrous methanol was added carefully at room temperature. The resulting gum was stirred for 30 min. until it became completely crystalline. The slurry was filtered, and the ether and excess methanol were removed by distillation. The residue on distillation gave 2.16 g. (0.0121 mole, 67.2%)

of diphenylketimine-^{15}N, b.p. 120° (1 mm.), n_D^{37} = 1.6088 (149).

s-Butylphenylketimine-^{15}N was prepared for this work by Mr. W. L. Oliver from benzonitrile-^{15}N and the s-butyl Grignard reagent.

Di-n-butylketimine-^{15}N was prepared for this work by Mr. W. L. Oliver from n-butylnitrile-^{15}N and the n-butyl Grignard reagent.

Diphenylketimine-^{15}N Hydrochloride. — A 200-ml. three-necked round-bottomed flask was flamed out and filled with 0.681 g. (0.00380 mole) of diphenylketimine-^{15}N and 80 ml. of diethyl ether which had just been distilled from lithium aluminum hydride. A nitrogen atmosphere was maintained in the flask throughout the reaction. Hydrogen chloride gas was bubbled through a sulfuric acid trap into the ether solution until no more precipitate formed. The solid was isolated by filtration and dried under vacuum in a desiccator. The yield of diphenylketimine-^{15}N hydrochloride was 0.643 g. (0.00298 mole, 78.4%).

s-Butylphenylketone. — A 1-l. three-necked round-bottomed flask equipped with a gas inlet tube, a reflux condenser, and a dropping funnel was flamed out and flushed with argon. Benzonitrile (40 g., 0.388 mole) was added dropwise with stirring to a Grignard reagent formed from 68.5 g. (0.500 mole) of 2-bromobutane and 12.4 g. (0.510 mole) of magnesium in 500 ml. of anhydrous ether. The yellow-gray mixture was refluxed for 12 hrs. After the mixture had cooled to room temperature, 96 g. of methanol was added very slowly with agitation. The precipitate was removed by filtration when

it had become completely crystalline. Methanol (100 ml.) containing 10 ml. of water was added, and the solution was allowed to stand for an hour. The ether and methanol were removed by distillation at atmospheric pressure, and the residue was fractionated at 5 mm. After benzonitrile was removed at 72-3°, two fractions (94-7°, 97-100°) of ketone-ketimine were collected. The mixtures were treated with water until VPC traces showed no ketimine to be present.

N-Methyl-s-butylphenylketimine. — s-Butylphenylketone (5 g.) was placed in a 15-ml. heavy-walled ampoule and degassed three times at 0.1 mm. to remove all traces of ammonia. Methylamine (1 g.), prepared by the addition of potassium hydroxide solution to the stock 40% aqueous solution, was distilled under vacuum into the ampoule, which was sealed at atmospheric pressure and heated at 175° for 3 days. An aqueous layer separated. The tube was opened, the water was removed, and four additional milliliters of amine were distilled under vacuum into the tube, which was again sealed and heated at 175° for 1 day. No further reaction was evident, so the tube was opened and the contents distilled, b.p. 67° (1 mm.). VPC analysis showed the distillate to contain about 60% ketimine and 40% ketone. Pure samples of the former were obtained by preparative vapor phase chromatography.

Potassium cyanide-^{15}N was obtained from Volk Radiochemical Laboratories.

Sodium nitrite-^{15}N was obtained from Volk Radiochemical Laboratories.

n-Butyl Nitrite-^{15}N. — A 50-ml. three-necked round-bottomed flask equipped with a thermometer and a 5 ml. syringe inserted through a syringe stopper was filled with a solution of 2.00 g. (0.0286 mole) of sodium nitrite-^{15}N in 7.87 ml. of water. After the flask was cooled to -1° with an ice-salt bath, a solution of 0.72 ml. of concentrated sulfuric acid, 1.95 g. n-butanol (0.0263 mole), and 0.53 ml. of distilled water was added by means of the syringe below the surface of the liquid in such a way that the temperature did not rise above +1°. During the course of the addition, which took 2 hrs., the flask was shaken constantly by hand. After the mixture had remained at 0° for an hour, the sodium sulfate was removed by filtration, and the layers were separated. The organic product was washed with sodium bicarbonate:sodium chloride:water (1:12.5:50) solution and dried over magnesium sulfate. The yield of n-butyl nitrite-^{15}N was 1.106 g. (0.0106 mole, 40.3%). The infrared spectrum contained no hydroxyl absorptions. The nitrite bands at 1615 (cis) and 1660 cm.$^{-1}$ (trans) confirmed the structure.

Nitrosobenzene-^{15}N. — A mixture of 2.02 g. (1.66 ml., 0.0163 mole) of nitrobenzene-^{15}N and 1 g. of ammonium-^{14}N chloride in 33 ml. of water was placed in a 100-ml. round-bottomed flask equipped with a magnetic stirrer. Zinc (2.5 g., 0.0382 mole) was added in small portions over a 5 min. period. The temperature rose to about 50°. After 20 min., the solution was filtered to remove the zinc oxide, and the precipitate was washed with 20 ml. of boiling water. The filtrate was transferred to a 250-ml. Erlenmeyer flask

and cooled quickly to 0° by the addition of excess ice. Concentrated sulfuric acid (5 ml.), cooled to 0° with about 20 g. of ice, was added quickly with stirring, and a cooled solution of 1.13 g. (0.0379 mole) of sodium dichromate in 4.2 ml. of water was added at once. The solution was filtered and washed with water. The precipitate was placed in a 100-ml. round-bottomed flask with about 20 ml. of water and steam-distilled from an all-glass apparatus. The white solid which condensed in the cooled receiver was collected in a Büchner funnel, crushed, and washed carefully with water. After being dried over calcium chloride, the nitrosobenzene-^{15}N weighed 0.664 g. (0.00614 mole, 37.7%).

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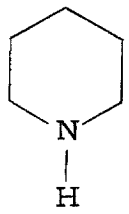
PROPOSITIONS

Proposition I

An experiment is proposed to determine the conformational preference of the nonbonding electron pair on nitrogen in piperidine.

In 1958, Aroney and LeFèvre (1) reported that the sign and magnitude of the molar Kerr constants of piperidine (I), N-methylpiperidine, and morpholine require the electron lone pair to be sterically larger than hydrogen, in fact, about equivalent in size to the methyl group. Moynehan, et al. (2), however, found that seven of the



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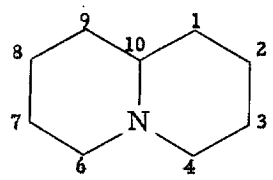
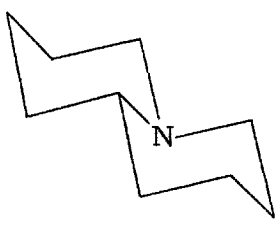
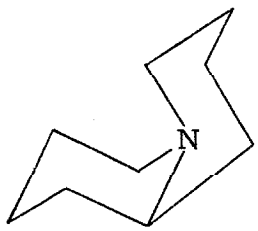


II

1-, 2-, 3-, and 4-methylquinolizidine isomers (II, cis and trans refer to the relative orientation of the 10-hydrogen and the substituent) possess a trans ring juncture, the exception being the trans-4 isomer.



trans



cis

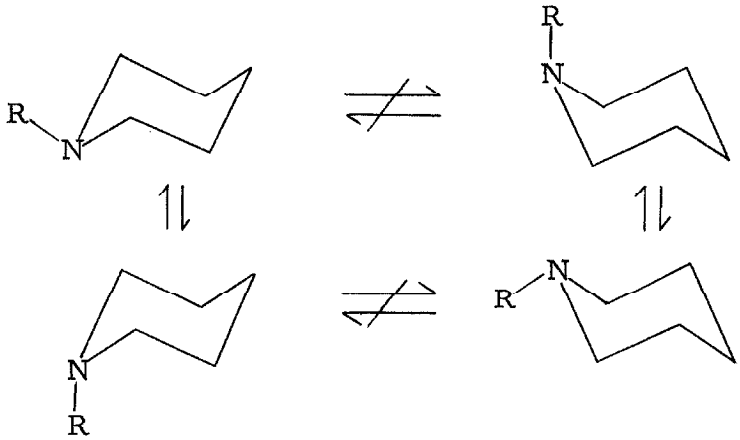
Unlike decalin, quinolizidine is capable of isomerization at the ring juncture because of configurational instability of the bridgehead nitrogen atom. Nonetheless, three of the four possible trans isomers with an axial methyl group (c-1, t-2, c-3) and an axial lone pair do not isomerize to the cis form. In the latter conformation, the methyl group would be equatorial, but the nitrogen atom would have an axial substituent, the lone pair having become equatorial. Similar qualitative evidence in the 3-azabicyclo[3.3.1]nonane system showed that the lone pair preferentially occupies the hindered "inside" position in the chair-chair conformation (3).

Aroney and co-workers (4) strengthened their original contention by new measurements on morpholine and N-methylmorpholine. In contradiction, dipole-moment calculations of Allinger (5) on piperidine and piperazine systems showed that the methyl group is much larger than the electron pair. Clapton (6) tried to rationalize the results of Aroney and LeFèvre in terms of contributions from an equatorial lone pair to other bonding situations in the molecule. At any rate, the dipole-moment calculations present an inconsistent picture because of the uncertainty in the assignment of the various bond moments associated with nitrogen.

It is proposed that this controversy be resolved by the direct observation of the position of the lone pair by n.m.r. spectroscopy. This determination is made possible by the peculiar effect an axial lone pair will have on an anti-coplanar proton. Bohlmann (7) reported that trans-fused quinolizidine derivatives possess a band in the infrared at 2700-2800 $cm.^{-1}$ which arises from hydrogens situated on

carbon atoms adjacent to nitrogen and oriented trans to the lone pair. This observation has since been substantiated in over 100 cases. Hamlow, Okuda, and Nakagawa (8) have shown by decoupling experiments that the axial and equatorial protons on the 4- and 6-positions of quinolizidine are chemically shifted from each other by 0.93 ppm. This may be compared to a chemical-shift difference of 0.48 ppm between the axial and equatorial protons of cyclohexane at low temperatures (9). This enhanced chemical-shift difference in quinolizidine, not present in its protonated form, was attributed to participation of the nonbonding electron pair in a σ^* orbital between C-4 and the axial proton. This situation is most probable when the lone pair and the C_4-H_{ax} bond are anti-coplanar. By examination of various deuterated quinolizidines, Bohlmann and co-workers (10) have supported the existence of a special effect of the lone pair on the chemical shift of an adjacent axial proton, although they showed that certain spectral assignments of the previous workers were incorrect.

Two processes are operative in the piperidine system: ring



inversion and inversion of configuration of nitrogen. Observation of the spectrum of the protons adjacent to nitrogen in 3, 3, 5, 5-

tetradeuteropiperidine at -100° will permit identification of the position of the lone pair. At this temperature, ring inversion is slow on the n.m.r. time scale. If the axial orientation of the lone pair obtains, the chemical-shift difference between the axial and equatorial protons on C_2 and C_6 will be enhanced with respect to the value in the corresponding protonated form, or in cyclohexane. On the other hand, there should be no enhancement if the lone pair occupies the equatorial position, which Aroney and LeFèvre have favored. The deuterated piperidine may be obtained by treatment of Y-piperidone with deuterium oxide in the presence of base, followed by the Wolff-Kishner reduction of the ketone.

Slowing of ring inversion has been observed by Reeves and coworkers in perfluoropiperidine (11) and in N, N'-dimethylpiperazine (12). When the inversion process is slowed in 3, 3, 5, 5-tetradeuteropiperidine, the protons in the 2- or 6-position will become nonequivalent, regardless of configurational stability of nitrogen. The resultant chemical-shift difference will then be the weighted average of the values corresponding to the lone pair in an axial or in an equatorial orientation.

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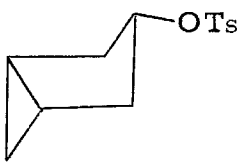
Proposition II

A carbonium ion system is proposed which would permit one to decide whether 1, 3, 5 conjugation can compete successfully with 1, 2, 4 (homoallylic) conjugation.

The phenomenon of charge delocalization between carbon atoms separated by a methylene group has received considerable attention recently. Conjugation among three centers situated 1, 2, 4 with respect to one another (homoallylic resonance) has been useful in explaining the characteristics of several systems, including the cholesteryl (1), endo-5-norbornyl (2), anti-7-norbornenyl (3), and allylcarbinyl (4) cases. Conjugation among three centers situated 1, 3, 5 with respect to one another is a less well-documented phenomenon. Winstein (5) has described studies of the solvolysis of the tosylate derived from cis-3-bicyclo[3. 1. 0]hexanol (I) in terms of a "homoaromatic" cation (II). As evidence for this intermediate, he cited complete scrambling



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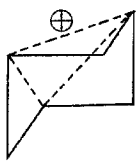
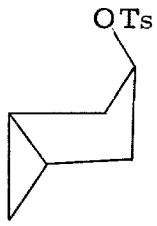


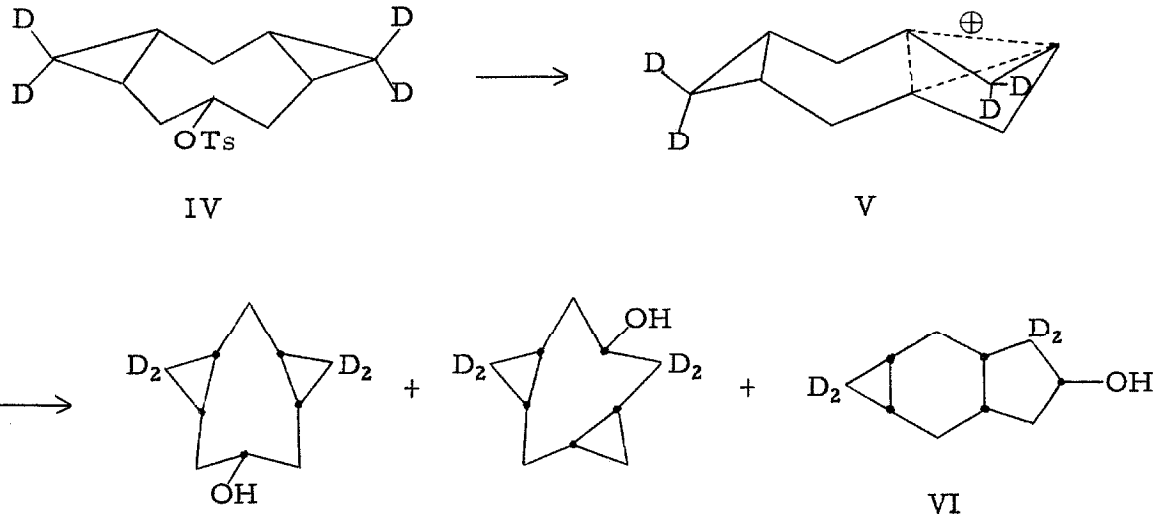
II



III

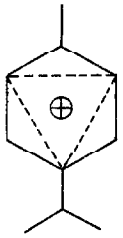
of deuterium among the 1, 3, 5 positions and a rate enhancement of 9. 2 with respect to the solvolysis of the trans tosylate (III). Winstein

generalized the concept to include the "perhomo" derivatives of benzene, the cyclopentadienyl anion, and the tropylium cation. This generality has not been realized in the first case (6). The solvolysis of the tosylate IV, however, is consistent with a 3-center 1, 3, 5 over-

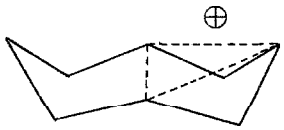


IV V VI

lap in the intervening cation (V). Deuterium scrambling among the secondary cyclopropane positions and formation of the hydrindanol VI are best accounted for in terms of the intermediacy of the trishomocyclopropenyl cation V (7). Corey, however, has questioned the validity of the concept of homoconjugation even in the original system (8). The studies of Norin (9) on the various epimeric thujyl tosylates and of Cope (10) on the cis-3-bicyclo[5. 1. 0]octyl bromobenzenesulfonate system are explicable in terms of cations involving 1, 3, 5 conjugation (VII, VIII). It is also conceivable that 1, 3, 5 conjugation

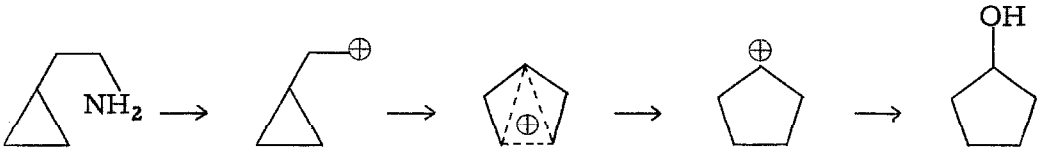


VII



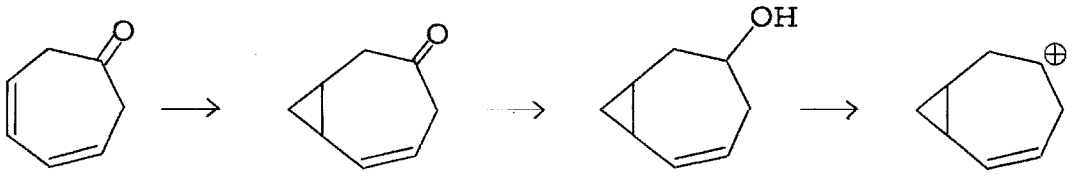
VIII

is involved in part in the deamination of 2-cyclopropylethylamine (IX), since cyclopentanol was found among the products (11).



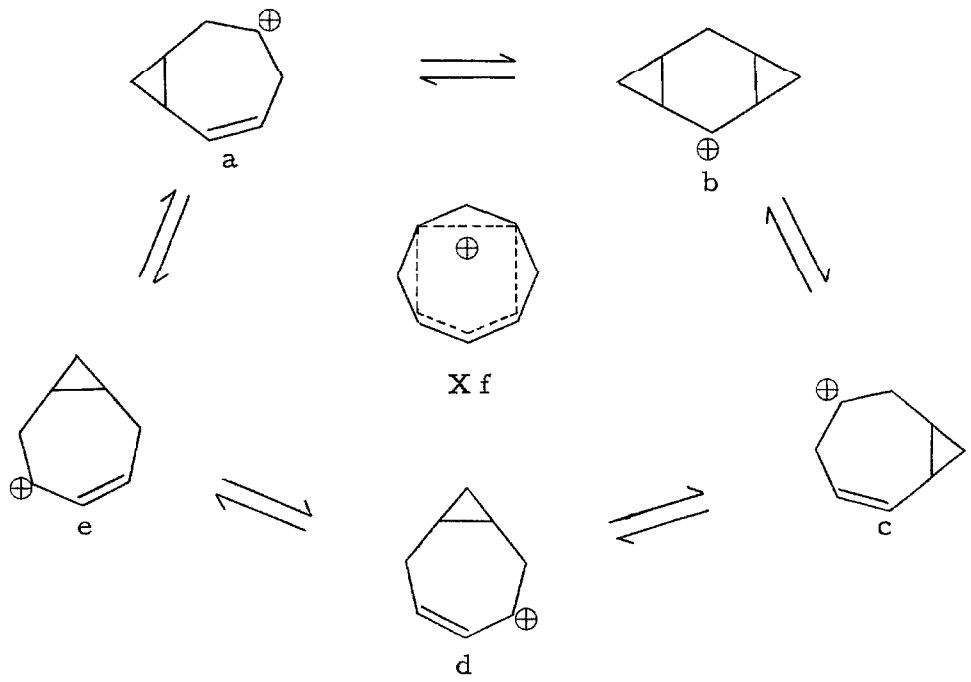
IX

The proposed cation (X) is generated in such a way that the positive charge may be delocalized in both the 1, 2, 4 and the 1, 3, 5 manners:

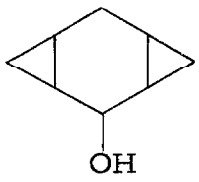


X

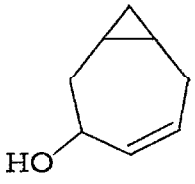
The solvolysis would be undertaken according to the method of Winstein (5). At least five cationic forms may be drawn which illustrate the ability of the system to undergo homoconjugation both with a



double bond and with a cyclopropane ring. Examination of the alcoholic products allows one to ascertain whether 1, 3, 5 conjugation can compete with homoallylic conjugation. The most likely products should be those derived from form b (XI) and from the allylic pair, d and e (XII). Alcohol XI is the product expected from homoallylic



XI

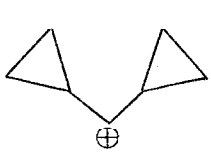


XII

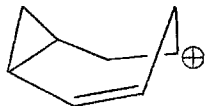
rearrangement, whereas XII would result from 1, 3, 5 rearrangement. Isolation of the latter product should demonstrate that 1, 3, 5 conjugation can compete with 1, 2, 4 conjugation, since it can only result

from one of the processes, a → e or a → b → c → d, both of which require 1, 3, 5 rearrangement. Alcohol XII could not result from a single 1, 2 hydride shift. Under the conditions suggested for the final solvolysis, Winstein did not observe hydride shifts in the process I → II.

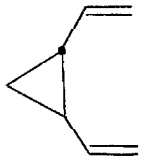
It could be argued that the cationic form b is more stable than the other species, and that form a would immediately be converted to form b without the formation of other products. However, one must be wary of drawing conclusions concerning form b from the dicyclopropylcarbinyl cation XIII. The restrictions in the degrees of freedom involved in bridging the cyclopropane rings and the ease of achieving the cisoid conformation (Xg) should have a significant effect



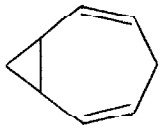
XIII



Xg



XIV



XV

on the delocalization of charge among centers. The dramatic increase in the rate of rearrangement in passing from XIV to XV results from this effect (12).

It is conceivable that the cationic system X could exhibit some stability, as does the homotropylium cation of Pettit (13). The five centers of positive charge can in fact become coplanar rather easily. Placing a deuterium atom at position 1 (5) and observing the amount

of isotopic scrambling between positions 1 and 3 (5 and 7) in the product XII by n. m. r. spectroscopy would more fully demonstrate the extent of equilibration of positions in the carbonium ion. Complete equilibration of positions 1 and 3 (5 and 7) would be a necessary, but not sufficient condition for an intermediate such as Xf.

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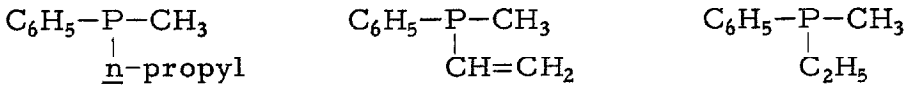
Proposition III

It is proposed to study the inversion of trigonally hybridized phosphorus by high-temperature magnetic resonance methods.

The configurational instability of nonplanar trigonal nitrogen has thus far prevented the resolution of potentially asymmetric tertiary amines into optical antipodes. The inversion process, however, has been studied by n.m.r. spectroscopy in several cases (1-3). In the absence of ring constraints or ponderous substitution, inversion is generally too rapid for observation even by this method.

The recent conversion of optically active quaternary phosphonium salts to optically active tertiary phosphines (4) in three different cases (I-III) established a fundamental difference between the configu-

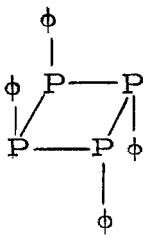


I II III

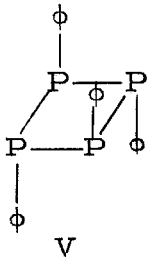
rational stabilities of trigonal phosphorus and nitrogen. Whereas the inversion process in nitrogen is generally too fast for observation by the n.m.r. method, the analogous process in phosphorus may be too slow, in view of the isolation of the optically active species. Two experimental observations lead one to believe that phosphorus inversion may nonetheless be susceptible to study by n.m.r. spectroscopy, provided that the particular case is selected judiciously.

First, the optically active phosphine I racemizes when heated in boiling toluene (111°) for three hours (4). Compound II is even more prone to racemize by thermal means. Processes such as the thermal isomerization of cis-azobenzene, which occur in this temperature range, are generally characterized by activation energies between 20 and 25 kcal/mole, just beyond the range studied by n. m. r. temperature methods.

The second case involves the thermal interconversion of the isomeric tetraphenylcyclotetraphosphines. Henderson and co-workers (5) have described two tetrameric products from the reaction of dichlorophosphine and phenylphosphine. It is here suggested that these isomers probably have structures IV and V, the rings of which may be



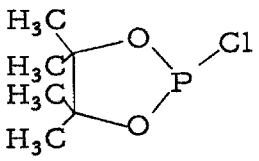
IV



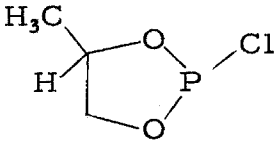
V

puckered. The smooth conversion of the isomer known as B to the A form during sublimation at 153° would therefore result from inversion of configuration of two phosphorus atoms. The temperature of conversion again suggests that the activation energy is just beyond the range susceptible to n. m. r. determination.

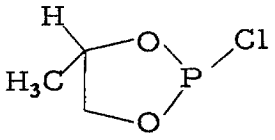
In light of the thermally accessible inducement of inversion of configuration of trigonal phosphorus, it is here proposed that the energetics of the process be studied by n.m.r. spectroscopy. Two specific cases which are likely to exhibit the desired spectral changes will be discussed. Goldwhite (7) has reported that there are two magnetically nonequivalent methyl groups in the dioxaphospholane VI. This is only explicable in terms of slow inversion of configuration of



VI



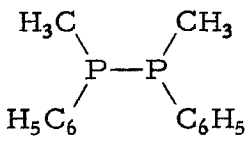
VIIa



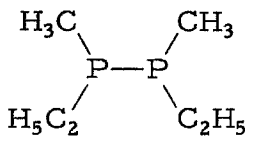
VIIb

phosphorus. Similarly, the methyl resonance of VII consists of two doublets of unequal intensity (1.65:1). The two possible isomers a and b must therefore be interconverting slowly on the n.m.r. time scale. It is proposed to examine the process of phosphorus inversion in these systems by the variation of spectral parameters as the temperature is increased.

Maier (8) has prepared the diphosphines VIII and IX. The



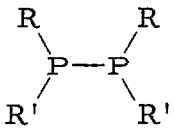
VIII



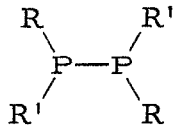
IX

phosphorus-31 spectrum of both compounds consists of a doublet, even

when decoupled from all proton spin-spin interactions. The components of the doublets must therefore represent separate resonances of the two isomers, which might be termed <u>erythro</u> (Xa) and <u>threo</u> (Xb), since each phosphorus atom maintains a tetrahedral configu-



Xa



Xb

ration. The R—R (or S—S) form (b) may be converted to the R—S form (a) by an inversion of phosphorus. It is proposed to study the energetics of this process by the effects of temperature on the n. m. r. spectrum.

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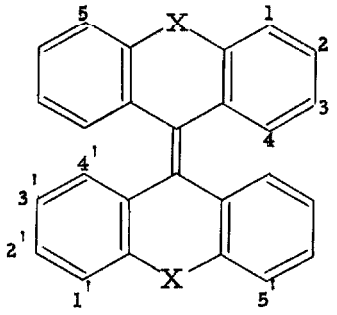
Proposition IV

It is proposed that the nature of the thermochromic modification of compounds similar to bianthrone be studied by the effect the species would have on proton relaxation times. Such a study would differentiate between the conformational equilibrium and the triplet state theories.

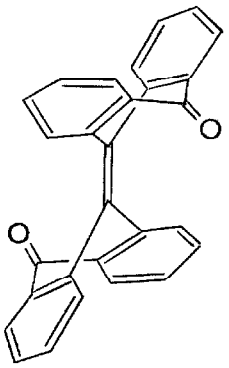
The reversible coloring with temperature (thermochromism) (1) of compounds of the form I has generally been attributed to the shift



Ia: X : C=O Ib: X : O

of an equilibrium between two forms of the same molecule. Ionic species were eliminated by the work of Grubb and Kistiakowsky (2), who showed that the visible absorption spectra of various bianthrone derivatives did not change with solvent polarity. Theilacker (3) ruled out dissociation by observing that Beer's Law holds in the temperature range 76–182°. From a linear relationship between ln (ϵ_{max}) and 1/T, he was able to calculate that the two molecular forms differ in energy by 3.4 kcal/mole (4.9) for Ia (Ib).

The nature of the "ground state" modification has been described by Harnik (4) from an X-ray study of bianthrone (5). An equilibrium between forces of repulsion from 4, 8' overcrowding and distortion of bond angles results in a "doubly bent" conformation (II).



II

The nature of the thermochromic modification has been the source of controversy. Twisting of the central double bond can reduce 4, 8' interactions and allow the formation of a second stable configuration, in which each of the two halves of the molecule is planar. From analogy to the biphenyl case, Harnik (4) judged the barrier separating the two conformations to be about 20 kcal/mole. Other authors (2, 6) have suggested that the thermochromic form is a low-lying triplet state. Hirshberg (7) identified the low-temperature photochromic species with the thermochromic modification, although Kortüm strongly disagreed with this interpretation. Photochromism was absent in the solid state and in rigid media, indicating that the phenomenon involves changes in the atomic, as well as the electronic configuration. The

formation of a triplet was also held to be unlikely by Hirshberg because the frequency factors for the process, without exception, were normal or high. Furthermore, the lifetime of the photochromic form was measured by Kortüm to be about a hundred times as long as the longest known phosphorescence lifetimes.

Hirshberg, Kortüm (10), and others demonstrated that 4, 4'-substituted bianthrones do not exhibit thermochromism. In terms of the conformational equilibrium, the substituted positions must pass each other in the process of conversion to the thermochromic form. The presence of substituents raises the barrier to a level which cannot be attained thermally.

Evidence against the conformational equilibrium theory has come from X-ray diffraction and paramagnetic resonance experiments. Mills and Nyburg (6) claim to have compared the crystal structures of the yellow and the blue-green modifications of dixanthylene (Ib) and found them to be nearly identical. This would argue against a difference in conformation. However, their model was ill-chosen, since Hirshberg (7) calculated that even at 363°K, only 0.04% of the colored modification would be present in this particular compound. Fraenkel (11) reported that the thermochromic form of bianthrone is paramagnetic both in solution and in the solid state. Other workers (12), however, attributed this phenomenon to irreversibly formed decomposition products. Theilacker (13) claimed that similar systems were diamagnetic, but this result is questionable because of the low concentrations used. Hirshberg (14) failed to obtain electron spin resonance signals from the photochromic forms of xanthylideneanthrone and

several bianthrones, although the resonance lines could have been very broad. In contrast to this, Wasserman (15) obtained well-resolved signals with bianthrone in pyridine, although Keller (16) observed only a broad signal at high temperatures.

This wealth of contradictory and inconclusive evidence fails to prove or disprove either theory, although the conformational equilibrium explains more fully many of the observations. If the thermochromic form is a triplet, it should have an observable effect on the n.m.r. spectrum. It is therefore proposed that the temperature dependence of the n.m.r. spectrum of bianthrone be examined in decalin. If both the ground state and the thermochromic modification are diamagnetic, the equilibrium may be represented as follows:

$$D \rightleftharpoons D'$$

The measurements of Theilacker (3) and of Hirshberg (7) have demonstrated that the two forms differ in energy by 3-4 kcal/mole. Thus, at 200°, there should be 1.5-4.2% of the thermochromic species present. If the chemical shift of a proton differs by 100 cps (certainly a liberal estimate) in the two forms, the rate at the coalescence temperature should be (17):

$$k = \sqrt{2}\,\pi\delta = 450 \text{ sec.}^{-1}$$

If the rate is much faster than this, complete averaging will occur, and the spectrum should be well resolved and not change significantly with temperature. If one assumes an activation energy of 20 kcal/mole

and a normal frequency factor (10^{13} sec.$^{-1}$), the rate is calculated to be 15,000 sec.$^{-1}$ at 200°. Thus, if the conformational equilibrium theory is valid, temperature effects should be negligible.

If the thermochromic modification is a triplet, the equilibrium may be represented as follows:

$$D \rightleftharpoons P$$

Equilibria between paramagnetic and diamagnetic species have been investigated by n.m.r. spectroscopy by McConnell and co-workers (Cu^{+}-Cu^{++} and V^{IV}-V^{V}) (18-19) and by Bruce, Norberg, and Weissman (Wurster's blue) (20). These cases, however, are bimolecular, rather than unimolecular, and involve electron transfers, rather than isomerizations. More analogous are the studies of equilibria between diamagnetic planar and paramagnetic tetrahedral complexes of nickel (21-22). Breslow and co-workers (23) have obtained the n.m.r. spectrum of the pentaphenylcyclopentadienyl cation, which possesses a paramagnetic triplet excited state about 450 cal. above the diamagnetic ground state.

The precise effect on line widths and line positions of an increase in the concentration of paramagnetic molecules is a function of lifetimes of both forms and of the nuclear and paramagnetic spin-lattice relaxation times. Unfortunately, none of these quantities have been measured for bianthrone. If the conditions enumerated by McConnell (24) hold, the phenomenon could be explained in terms of a paramagnetic pulse reaction, in which line broadening results from

limitations imposed on proton relaxation times by the lifetime of the diamagnetic species. In this case, broadening would be observed in the spectrum of the solute, but that of the solvent would remain essentially unchanged. Contact shifts may very well be observed. If the paramagnetic dipolar broadening is the dominant effect, solute and solvent peaks will both be affected. Thus, the spectrum of Breslow's cation (23) was severely broadened, even at room temperature, and small effects on the solvent resonances (methylene chloride) were observed. In this case, the paramagnetic excited state is 2-3 kcal. lower than the corresponding state would be in bianthrone. Thus, if the triplet state theory is valid, line broadening of solute and/or solvent resonances would be observed as the temperature is increased.

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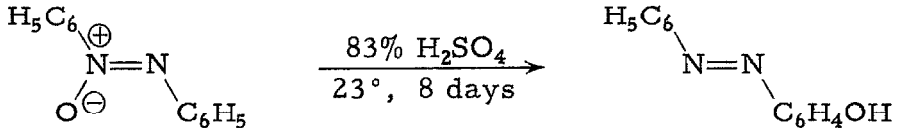
Proposition V

A method is proposed to elucidate the nature of the intermediate involved in the Wallach rearrangement.

Substantial progress was made in the elucidation of the mechanism of the Wallach rearrangement (I → II) when Shemyakin and co-

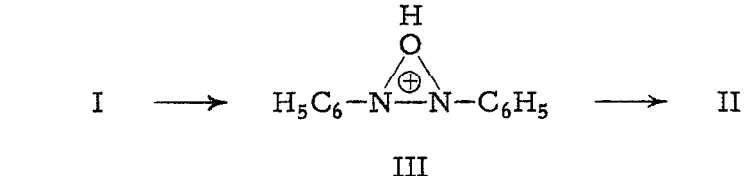


I II

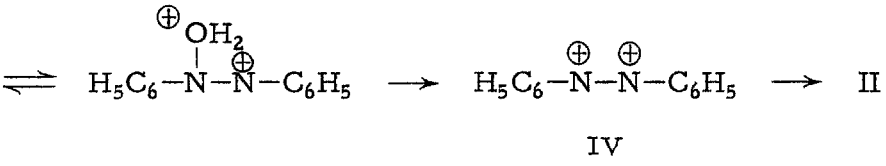
workers (1) ascertained that the rearrangement of trans-azoxybenzene-β-^{15}N yielded a product, trans-p-hydroxyazobenzene, in which the label was scrambled, although the label was intact in unreacted starting material. Upon ultraviolet irradiation or treatment with acetic anhydride, the product, trans-o-hydroxyazobenzene, contained an excess of label on the nitrogen adjacent to the hydroxylated ring. The same group (2) later found that, for systems and conditions for which the ortho rearrangement operates, little incorporation of ^{18}O from the solvent ($H_2S^{18}O_4$) occurred, whereas incorporation was almost complete in the para rearrangement. These results were corroborated by Oae, et al. (3), who carried out the rearrangement with trans-azoxybenzene-^{18}O. It is apparent that the ortho and para rearrangements are fundamentally different, the former involving a predominantly intramolecular mechanism similar to that described by

Fieser and Fieser (4). The mechanism of the intermolecular para rearrangement will be the subject of this proposition.

Under conditions where complete symmetrization of nitrogen occurs (5), two mechanisms have been proposed:

A: 

III

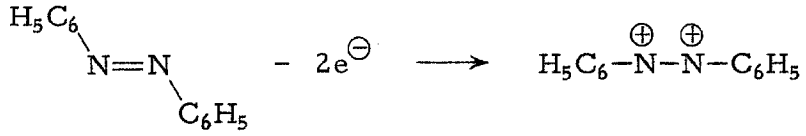
B: 

IV

The transition state in mechanism A would contain a single proton, whereas that in B would contain two. In A, removal of the oxygen on nitrogen follows attack by solvent, whereas in B it precedes attack. Shemyakin has favored mechanism A (6) because iodide ion was found to oxidize the proposed oxazirane intermediate, and because trans-α- and -β-p-nitroazoxybenzene equilibrated under the reaction conditions. Gore (7) and Buncel and Lawton (8), however, have favored mechanism B. The latter workers found that the reaction rate increased by a factor of 40 after protonation of I was complete, according to calculations which assumed that the pKa of trans-azoxybenzene is -5.1. Furthermore, a plot of log(k) vs. ($-H_0$) was not linear. These data are best accommodated by a two-proton mechanism, or a mixture of mechanisms. Shemyakin has criticized mechanism B on the basis that the dipositive cation IV would be a high-energy species. The

justification made by Buncel and Lawton on the basis of Hart's work (9) now appears to be unfounded (10). Thus, in spite of extensive efforts, there has been no direct indication of the nature of the intermediate, although the work of Buncel and Lawton causes one to favor the di-cation IV.

It is proposed to test the existence and intermediacy of IV by electrochemical generation under a variety of conditions. If the product of the Wallach rearrangement of trans-azoxybenzene arises from the two electron oxidation of trans-azobenzene, followed by hydrolysis, then the intermediacy of IV is very likely. Although the



IV

electrochemical reduction of trans-azobenzene has been studied extensively (11) in connection with the benzidine rearrangement, the anodic chemistry has not been examined since 1921, when Fichter and Jaeck (12) electrolyzed 40 g. of trans-azobenzene to give several polyhydroxylated monomeric and dimeric products.

A preliminary potentiostatic experiment using a rotating platinum electrode should be performed in order to determine the half-wave potential. A controlled-potential electrolysis may then be performed on an isolable amount of material, using a platinum gauze electrode. A wide variety of conditions should be employed. A control run to determine the behavior of trans-azoxybenzene should always

be carried out. Water-sulfuric acid mixtures, from 0% acid to acidities at which the rearrangement begins to occur, should be examined, and the oxidation should be carried to varying degrees of completion. It would be of particular interest to attempt to generate the di-cation IV in an inert solvent, possibly dioxane. Under such conditions, the ion may be sufficiently stable to permit direct spectrophotometric investigations. Product analysis could then be performed following quenching in various solvents (13).

Such an electrochemical experiment would give information concerning the intermediate in the Wallach rearrangement, but, as a footnote to this proposition, it should be noted that the experiment does not exclude mechanism A. It is very possible that this mechanism is operative at low acidity, with mechanism B becoming dominant at very high acidity. The relative importance of the various mechanisms might be determined by a more careful study of the rate in terms of the various acidity functions.

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13. The author is deeply appreciative to Mr. Arthur Hubbard, who described the possible electrochemical experiments.