The Structure of Cyclopropane and Cyclobutane from Proton Nuclear Magnetic Resonance in a Nematic Solvent

Sir:

In this note we report structure determinations for cyclopropane and cyclobutane from their nmr spectra in a liquid crystal (nematic) solvent.[1-3]

The proton nmr spectra were recorded on a modified Varian HR-60 spectrometer. The nematic solvent used was *p,p'*-di-*n*-hexyloxyazoxybenzene. The cyclopropane sample had a solute–solvent mole ratio of about 1:3 and was run at 75°; the corresponding figures for cyclobutane are 1:2.5 and 80°. The top trace in Figure 1 shows an experimental spectrum for cyclopropane. This trace was made in a single pass. A greatly improved signal to noise ratio was obtained by digitally averaging up to 5000 passes. In such spectra it was possible to clearly identify lines due to molecules bearing one ^{13}C nucleus[4] in natural isotopic abundance.

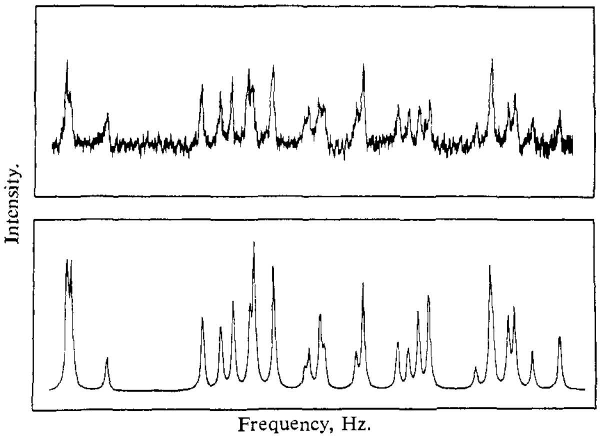

Figure 1. Top: Experimental proton nmr spectrum of cyclopropane in *p,p'*-di-*n*-hexyloxyazoxybenzene at 75°. The full spectrum is symmetrical about a point to the left of the figure. The line at the left of the spectrum is 441 Hz from this center, the line at the right 1020 Hz from it. Except for the mirror half of the spectrum, there are no other strong lines. Bottom: Computer simulation of the spectrum with the parameters given in the text.

We employ the spin Hamiltonian used by Snyder[3] to analyze, simulate, and interpret the observed spectra. In addition to the familiar Zeeman terms and indirect spin–spin couplings, J_{ij}, this Hamiltonian contains the direct dipole–dipole couplings D_{ij}, which provide the major interactions in the anisotropic nematic solvent. For the highly symmetric molecules under considerations, it can be shown[3] that the direct couplings are related to the molecular structure through the equation

$$D_{ij}^{\text{dir}} = \frac{-\gamma_i\gamma_j\hbar C_{3z^2-r^2}}{\pi\sqrt{5}}\left\langle \frac{z_{ij}^2 - \frac{1}{2}(x_{ij}^2 + y_{ij}^2)}{r_{ij}^5} \right\rangle_{\text{av}} \qquad (1)$$

where $r_{ij} = (x_{ij}, y_{ij}, z_{ij})$ is the vector connecting the *i*th and the *j*th nuclei, the coordinates *x*, *y*, and *z* being referred to a molecule-fixed coordinate system with its *z*-axis parallel to the symmetry axis; $C_{3z^2-r^2}$ is the motional constant characterizing the anisotropy of the molecular tumbling; and γ_i is the magnetogyric ratio of the *i*th nucleus. The average must be taken over the vibrations of the molecule.

Our basic method of analysis consisted of assuming an equilibrium geometry and a motional constant, calculating the D_{ij}^{dir} from eq 1, and then computing a theoretical spectrum by diagonalizing the Hamiltonian. The assumed parameters were then varied until a fit between experimental and computed spectra was obtained. This procedure was convenient because for these highly symmetrical molecules some line positions are independent of the J_{ij}. Thus we could determine the J_{ij} later to complete the spectrum fit.

One should note that a uniform scaling of all distances does not affect the D_{ij}^{dir} if $C_{3z^2-r^2}$ is scaled by the cube of that factor. Therefore only relative internuclear distances can be determined from these nmr spectra.

Two approximations made in the above interpretations should be mentioned. (1) We have neglected possible contributions to D_{ij} from anisotropic indirect spin–spin couplings.[5] We believe these contributions to be negligibly small for proton–proton couplings, and probably still negligible for H–^{13}C couplings. (2) In using eq 1 we did not average over the molecular vibrations. One effect of this neglect will be that no choice of geometry and motional constant will give a set of D_{ij} identical with those derived from the experimental spectrum. In the present work, the discrepancy in the D_{ij}, which we shall indicate by D_{ij}^{pseudo}, is very small, but probably significant. Since there are many ways to assign the D_{ij}^{pseudo} to the several nuclear pairs, there are several slightly different geometries which can fit the spectrum. We give our choice for cyclopropane and cyclobutane together with the corresponding D_{ij}^{pseudo}.

We assume that the equilibrium geometry of cyclopropane has D_{3h} symmetry with the electron diffraction[6] C–C bond length of 1.510 A. Then the observed spectra fit calculated ones for a 1.123-A C–H bond length and an HCH angle of 114.4°. The corresponding electron diffraction values are 1.089 ± 0.003 A and 115.1 ± 1.0°.[6] We also find $J_{cis} = +9.5$, $J_{trans} = +5.5$, $J_{\text{CH}} = +162$, $D_{trans}^{\text{pseudo}} = -1.2$ Hz, and $C_{3z^2-r^2} = -0.06102$. The constants produce the calculated spectrum in Figure 1.

The cyclobutane spectrum can only be reproduced if we assume that it interconverts rapidly between two nonplanar equilibrium conformations having D_{2d} symmetry. From the absence of noticeable line broadening from this cause, the lifetime in a conformation is estimated to be less than 10^{-6} sec. Adopting an electron diffraction C–C bond length of 1.548 A,[7] we fit our spectra with a C–H bond length of 1.171 A, an HCH angle of 108.5°, a dihedral angle of 35°, and a tilt of the methylene group of 2.5° in a direction which carries axial protons on the same side of the ring away from each other. We are forced by the limited information in our spectra to assume that all C–H bond lengths are equal. The electron diffraction studies[7] give a C–H length of 1.092 ± 0.010 A. Earlier electron diffraction studies gave a dihedral angle of 20° (+10°, −20°).[8] We also obtain $J_{cis} = +10.4$, $J_{trans} = +4.9$, $J_{\text{CH}} = +136$, $J_{cis'} \simeq 0$, $J_{trans'}$

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(1) G. Englert and A. Saupe, *Z. Naturforsch.*, **19a**, 172 (1964).
(2) A. Saupe, *ibid.*, **19a**, 161 (1964).
(3) L. C. Snyder, *J. Chem. Phys.*, **43**, 4041 (1965).
(4) L. C. Snyder and S. Meiboom, *ibid.*, **44**, 4057 (1966).
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(6) O. Bastiansen, F. N. Fritsch, and K. Hedberg, *Acta Cryst.*, **17**, 538 (1964).
(7) A. Almenningen, O. Bastiansen, and P. N. Skancke, *Acta Chem. Scand.*, **15**, 711 (1961).
(8) J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952).

$\simeq 0$, $D_{cis}^{\text{pseudo}} = +1.7$, and $D_{trans'}^{\text{pseudo}} = -3.7$ Hz. The primed interactions are across the cyclobutane ring. We find $C_{3z^2-r^2} = -0.08939$, which corresponds to the ring of carbon atoms tending to be parallel to the applied field direction, as in cyclopropane.

We believe that large methylene rocking motions are the source of our D_{ij}^{pseudo} and the relatively large C–H bond lengths we have found.

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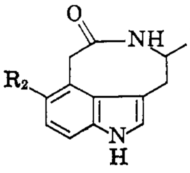
Received December 30, 1966

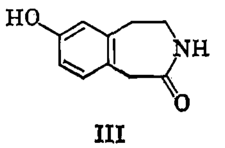
Photolysis of N-Chloroacetyl-O-methyl-L-tyrosine to an Azaazulene

Sir:

The photocyclization of N-chloroacetyl-L-tryptophan provides an easy access to tricyclic indoles of type I.[1] This general and useful preparative method has been applied to other aromatic amino acids and pharmacodynamic amines. For instance, N-chloroacetyl-5-methoxytryptamine gave *dehydromelatonin* (II),[2] and N-chloroacetyl-*m*-tyramine gave 7-hydroxy-1,2,4,5-tetrahydro-3H,3-benzazepin-3-one (III) in 70% yield.[3]



I, R_1 = COOH; R_2 = H
II, R_1 = H; R_2 = OCH_3



III

In all these cases the original chromophore was not changed in the process of photocyclization.

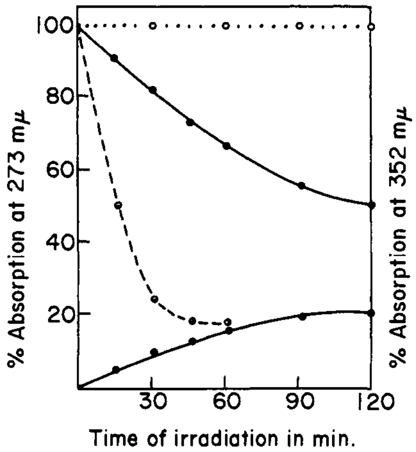


Figure 1. Disappearance of chromophore on irradiation in neutral aqueous solution. Control: N-acetyl-L-tyrosine (-○-○-○-); N-chloroacetyl-L-tyrosine (-◒-◒-◒); O-methyl-N-chloroacetyl-L-tyrosine (—●—●—●).

By contrast, the phenolic chromophore of N-chloroacetyl-L-tyrosine on irradiation in aqueous solution (N_2) disappeared rapidly ($t_{1/2}$ = 1.2 min, Figure 1), presumably by formation of secondary products from an unstable intermediate such as a spirocyclohexadienone.[4]

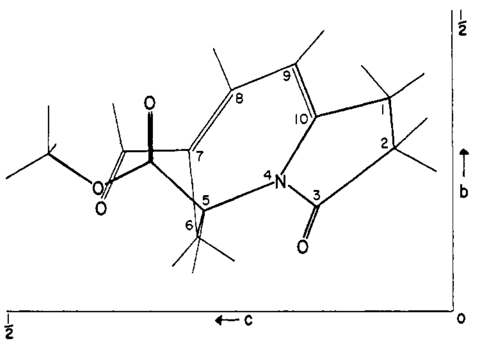


Figure 2. Spatial arrangement of atoms in L-5-carbomethoxy-7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-*a*]azepin-3-one (IV).

Irradiation of the homologous O-methyl-N-chloroacetyl-L-tyrosine not only led to slower disappearance of the anisole chromophore but also to the concomitant appearance of a compound with λ_{max} 352 mμ (Figure 1). This compound has now been isolated as a yellow crystalline powder (mp 225° dec) and characterized as its methyl ester, pale yellow needles, mp 145°. Mass spectrometry confirmed the composition of this ester as $C_{12}H_{13}NO_4$.

An X-ray diffraction analysis of a single crystal of $C_{12}H_{13}NO_4$ was made using three-dimensional intensity data which were collected with the equiinclination, multiple-film Weissenberg technique. The material crystallized in the orthorhombic system, space group $P2_12_12_1$, with cell parameters a = 7.17 A, b = 10.08 A, and c = 15.99 A (all ±0.02 A). Phases for the strong and moderately strong reflections were determined directly from the experimental intensities by the symbolic addition procedure[5] for noncentrosymmetric crystals. The atoms in the molecule were located and identified in a three-dimensional density mass computed with the reflections for which phases had been determined. Hydrogen atoms were located on a difference map. The coordinates and anisotropic thermal parameters for each atom were subjected to a least-squares refinement resulting in a final agreement factor of 7.8%. In this way structure IV was deduced with the spatial arrangement indicated in Figure 2.[6] Except for C(6), the carbon and nitrogen atoms in the two rings are nearly coplanar. The ester group is roughly parallel to the aldehyde group.

Nmr and mass spectrometry confirmed this structure (X).[7] The strongest peak (176) next to the parent peak (221 or 235) results from loss of CO_2 or $COOCH_3$. Loss of the aldehyde as CHO (29) gives a significant base peak at 148.

This unusual photolysis of an aromatic ring system is probably initiated by homolysis of the C–Cl bond followed by *ortho* substitution, addition of a Cl (or HO) radical (V → VI), or hydrolysis of the allylic chloride (see Chart I). Hydrolysis of the vinyl ether might lead to VII, which by retroaldol cleavage would lead to the nine-membered ring VIII. Transannular condensation and (vinylogous) β elimination of the carbinolamide

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[1] O. Yonemitsu, P. Cerutti, and B. Witkop, *J. Am. Chem. Soc.*, 88, 3941 (1966).

[2] T. Kobayashi and B. Witkop, unpublished results.

[3] M. Chaykovsky, C. M. Foltz, and B. Witkop, unpublished results.

[4] *Cf.* L. Farber and L. A. Cohen, *Biochemistry*, 5, 1027 (1966). In contrast to these rapid photocyclizations (*under nitrogen*), the slow photooxidation of tyrosine opens up the phenolic ring to aliphatic amino acids: P. G. Gordon, W. A. Jerram, and R. B. Johns, *Biochem. Biophys. Res. Commun.*, 23, 269 (1966).

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[6] I. L. Karle, J. Karle, and J. Estlin, in preparation.

[7] This ring system of a hydrogenated azaazulene was first described by L. A. Cohen and B. Witkop, *J. Am. Chem. Soc.*, 77, 6595 (1955).