Nitroxides. XL. Stereospecificity of Sign and Magnitude of Long-Range Proton Hyperfine Splitting Constants in Bicyclic Nitroxides

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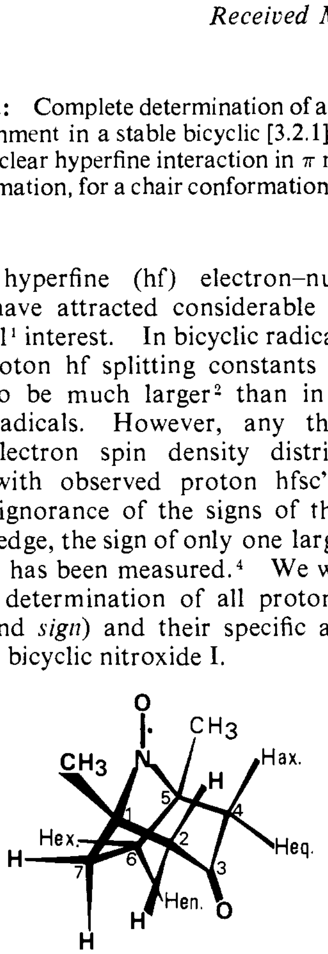
Abstract: Complete determination of all proton hyperfine splitting constants in magnitude and sign and their specific assignment in a stable bicyclic [3.2.1] nitroxide are presented. Theoretical methods to study long-range (γ protons) nuclear hyperfine interaction in π radicals are tested. A good fit is obtained with a MO method in the INDO approximation, for a chair conformation of six-membered ring and an axial nitroxide group.

Long-range hyperfine (hf) electron–nucleus interactions have attracted considerable experimental and theoretical[1] interest. In bicyclic radicals especially, long-range proton hf splitting constants (hfsc's) have been found to be much larger[2] than in aliphatic or monocyclic radicals. However, any theoretical estimates of electron spin density distributions and correlations with observed proton hfsc's have been restricted by ignorance of the signs of these hfsc's.[2,3] To our knowledge, the sign of only one large long-range hfsc (+3.8 G) has been measured.[4] We wish to report the complete determination of all proton hfsc values (magnitude and *sign*) and their specific assignment in the new stable bicyclic nitroxide I.



I

Nitroxide I (1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-one 8-oxyl) has been prepared[5] by phosphotungstic acid–hydrogen peroxide oxidation of the parent amine, obtained by a Schöpf–Robinson reaction. The electron spin resonance (esr) spectrum of a 2×10^{-3} *M* solution of I in lithium chloride saturated water is interpreted as resulting from the interaction of the unpaired electron with one nitrogen nucleus (a_N = 19.5 G) and two groups of equivalent protons (a_H = 2.5 and 1.1 G). Selective deuteration of the $-CH_2-CO-CH_2-$ group[6] shows that the larger hfsc (2.5 G) can be assigned to the equatorial (eq) protons attached to the C-2 and C-4 positions and the smaller hfsc (1.1 G) to the axial (ax) protons attached to the same carbons. Evidence for other small hfsc's exists, but these are easily measured by nuclear magnetic resonance (nmr) (see references cited in ref 1b). A well-resolved 100-MHz nmr spectrum is obtained for a 7 *M* solution of I in deuteriochloroform. At higher and lower fields two broad peaks are observed ($\Delta H \sim 2000$ Hz), whose paramagnetic shifts ($\Delta H_p = +97.5$ and -172.5 ppm relative to tetramethylsilane (TMS) giving respectively $a_H = -1.3$ and $+2.3$ G) are consistent with the two large hfsc's obtained from the esr spectrum (a_H = 1.1 and 2.5 G). The differences in magnitude between the esr and nmr data may be ascribed to solvent effects.[7] At small chemical shifts, there are three narrow peaks ($\Delta H \sim 500$ MHz) (intensity ratio 1:1:3), assigned to the two pairs of protons attached to C-6 and C-7 positions ($\Delta H_p = +11$ and $+22.1$ ppm relative to TMS, giving $a_H = -0.15$ and -0.30 G, respectively) and to the six methyl protons ($\Delta H_p = +32.7$ ppm relative to TMS, giving $a_H = -0.44$ G). We have made no attempt to distinguish between the endo (en) and exo (ex) (C-6, C-7) protons, since their hfsc's are of the same sign and order of magnitude, in contrast with the hfsc's of the equatorial and axial (C-2, C-4) protons.

Thus, simultaneous interpretation of the esr and nmr spectra of I allows complete determination and assignment of all proton hfsc's in the bicyclic radical I (Table I) and clearly demonstrates the strong dependence (both in magnitude and sign) of γ proton hfsc's on their spatial position. The experimental results thus obtained provide a valuable test of theoretical methods used to study long-range nuclear hf interactions in π radicals. Since no structure determination is available for radical I, we assume that its geometry is similar to that of pseudotropine.[8,9] Two angular parameters,

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(1) See, for instance, the following, and references cited therein: (a) J. P. N. Bailey and R. M. Golding, *Mol. Phys.*, **12**, 49 (1967); (b) Z. Luz, *J. Chem. Phys.*, **48**, 4186 (1968); (c) M. Barfield, *J. Phys. Chem.*, **74**, 621 (1970).

(2) (a) G. A. Russel and R. G. Keske, *J. Amer. Chem. Soc.*, **92**, 4458 (1970); (b) S. F. Nelsen and B. N. Trost, *Tetrahedron Lett.*, 5737 (1966); (c) D. Kosman and L. M. Stock, *J. Amer. Chem. Soc.*, **91**, 2011 (1969); (d) P. J. Krusic, J. R. Jesson, and J. K. Kochi, *ibid.*, **91**, 4566 (1969); (e) J. Gloux, M. Guglielmi, and H. Lemaire, *Mol. Phys.*, **17**, 425 (1969); (f) L. Bonazzola and R. Marx, *ibid.*, **19**, 405 (1970); (g) P. Bakuzis, J. K. Kochi, and P. J. Krusic, *J. Amer. Chem. Soc.*, **92**, 1430 (1970); (h) S. F. Nelsen and P. J. Hintz, *ibid.*, **92**, 6215 (1970).

(3) G. R. Underwood and R. S. Givens, *ibid.*, **90**, 3713 (1968).

(4) H. Lemaire, A. Rassat, and P. Rey, *Chem. Phys. Lett.*, **2**, 573 (1968).

(5) J. Ronzaud and A. Rassat, Brevet Français EN 7001865, Jan 20, 1970.

(6) *Cf.* T. T. Tidwell, *J. Amer. Chem. Soc.*, **92**, 1448 (1970), and references cited therein.

(7) Such solvent effects are well documented on nitrogen hfsc in nitroxides: R. Briere, H. Lemaire, and A. Rassat, *Bull. Soc. Chim. Fr.*, 3273 (1965).

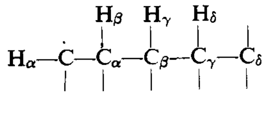
(8) H. Schenk, C. H. MacGillavry, S. Skolnik, and J. Laan, *Acta Crystallogr.*, **23**, 423 (1967).

(9) The remaining chosen parameters are: $d(N\!\!-\!\!\!-\!O) = 1.3$ Å;[10] $d(C\!=\!O) = 1.22$ Å; $d(C\!-\!H) = 1.1$ Å. The following assumptions were also made: the HCH angles are 109°, the NCH planes bisect the

Table I. Experimental and Calculated Proton[a] Hfsc's of Radical I

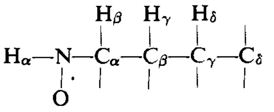
		H(C-2, C-4)		H(C-6, C-7)	
	CH_3(C-1, C-5)	Ax	Eq	Ex	En
Hfsc, G, exptl	−0.44	−1.3	+2.3	−0.15	−0.30
Hfsc, G, calcd[b]	−0.57	−1.33	−1.99	$-0.47(\gamma) + 0.14(\delta) = -0.33$	$-1.13(\gamma) + 0.14(\delta) = -0.9$
Hfsc, G, calcd[c]	+0.73	+1.07	+0.30	$+0.84(\gamma) + 0.12(\delta) = +0.96$	$+0.18(\gamma) + 0.12(\delta) = +0.3$

[a] All hydrogens are γ to the nitroxide group, following the convention for labeling α, β, γ, δ shown in i for carbon radicals and in ii for nitroxide radicals. [b] Using Luz's equations.[b] [c] Using Barfield's equations.[1c]



$$\mathrm{H_\alpha{-}\dot{C}{-}\overset{H_\beta}{C_\alpha}{-}\overset{H_\gamma}{C_\beta}{-}\overset{H_\delta}{C_\gamma}{-}C_\delta}$$

i



$$\mathrm{H_\alpha{-}\underset{\dot{O}}{N}{-}\overset{H_\beta}{C_\alpha}{-}\overset{H_\gamma}{C_\beta}{-}\overset{H_\delta}{C_\gamma}{-}C_\delta}$$

ii

φ and ψ, are introduced (Figure 1) to account for conformational effects.

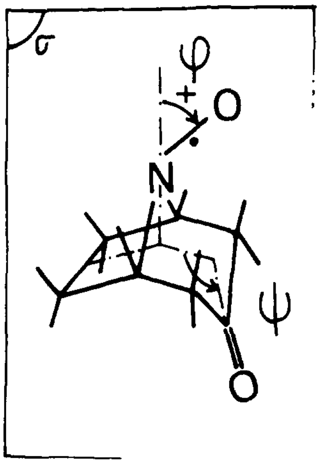


Figure 1. Structural parameters for nitroxide II.

Luz[1b] has given a valence bond (VB) treatment of spin densities in an aliphatic hydrocarbon radical fragment. With approximations appropriate to saturated models, he has calculated semiempirically γ and δ hfsc's, assuming free rotation about all the C–C bonds. Using these numerical values, γ and δ hfsc's for rigid fragments are given by

$$\begin{aligned} a_{\mathrm{H}\gamma}\,(\mathrm{G}) &= -1.14 \cos^2 \theta_\beta{}^{\mathrm{C}} - 0.88 \cos^2 \theta_\gamma{}^{\mathrm{H}} \\ a_{\mathrm{H}\delta}\,(\mathrm{G}) &= +1.35 \cos^2 \theta_\beta{}^{\mathrm{C}} \cos^2 \theta_\delta{}^{\mathrm{H}} \end{aligned} \qquad (1)$$

where $\theta_\beta{}^{\mathrm{C}}$ is the angle between the free-electron π orbital and the $(\dot{C}C_\alpha C_\beta)$ plane, $\theta_\gamma{}^{\mathrm{H}}$ is the angle between the $(\dot{C}C_\alpha C_\beta)$ and the $(C_\alpha C_\beta H_\gamma)$ planes, and $\theta_\delta{}^{\mathrm{H}}$ is the angle between the $(C_\alpha C_\beta C_\gamma)$ and the $(C_\beta C_\gamma H_\delta)$ planes. We have applied these equations to the analogous hypothetical carbon radical (Figure 2) with a planar radical center ($\varphi = 0°$) and a perfect chair conformation, for the six-membered ring ($\psi = 120°$). For the C-6 and C-7 proton hfsc's, both γ and δ contributions must be considered, since two "paths" are available for spin polarization propagation along the bonds. As shown in Table I, Luz's equations give good agreement in relative magnitude and sign for the endo, exo (C-6, C-7), methyl (C-1, C-5), and axial (C-2, C-4) protons, but are unable to rationalize the large positive hfsc of the γ equatorial (C-2, C-4) protons. However, Luz considered only spin polarization into successive localized bonds as contributing to the overall spin density. As a result, his method is incapable of predicting positive γ hfc's irrespective of the geometry assumed by the radical.

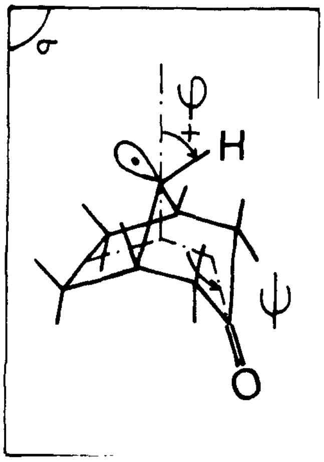


Figure 2. Structural parameters for the hypothetical carbon radical corresponding to nitroxide II.

Barfield,[1c] with a similar VB description of the aliphatic radical fragment, used an alternative theoretical formalism involving a great variety of spin polarization mechanisms and proposed semiempirical polynomials to evaluate γ and δ hfsc's.

$$\begin{aligned} a_{\mathrm{H}}\,(\mathrm{G}) = {} & 1.65 \cos^2 \theta_\beta{}^{\mathrm{C}} - 0.84 \cos^4 \theta_\beta{}^{\mathrm{C}} + \\ & 2.62K(\theta_\gamma{}^{\mathrm{H}}) - 0.68 \cos^2 \theta_\beta{}^{\mathrm{C}}[K(\theta_\gamma{}^{\mathrm{H}} + 120) + \\ & K(\theta_\gamma{}^{\mathrm{H}} - 120)] + 0.15[\cos^2 (\theta_\beta{}^{\mathrm{C}} + 120)K(\theta_\gamma{}^{\mathrm{H}} + \\ & 120) + \cos^2 (\theta_\beta{}^{\mathrm{H}} - 120)K(\theta_\gamma{}^{\mathrm{H}} - 120)] + 0.17 \\ = {} & -8.42K(\theta_\delta{}^{\mathrm{H}}) \cos^2 \theta_\beta{}^{\mathrm{C}} \end{aligned} \qquad (2)$$

where $\theta_\beta{}^{\mathrm{C}}$, $\theta_\gamma{}^{\mathrm{H}}$, and $\theta_\delta{}^{\mathrm{H}}$ have the same significance as in eq 1 and are measured in a clockwise direction. $K(\theta) = -0.287 \cos^2 \theta + 0.016 \cos \theta + 0.015$. When applied in the same manner as above, Barfield's formulas give values (Table I) which are not comparable to experimental values. All calculated hfsc's are positive and the equatorial (C-2, C-4) proton hfsc is too small. Similar results have been found for another monocyclic nitroxide:[11] Barfield's equations do not reproduce experimental values, while Luz's equations give reasonable evaluations for long-range negative γ and positive δ hfsc's. As mentioned above, Luz takes into account

opposing CCC angles, and the exo and endo or axial and equatorial protons are symmetrically disposed with respect to the CCC planes.

(10) A. Capiomont, B. Chion, and J. Lajzerowicz, *Acta Crystallogr.*, in press.

(11) R. Briere, H. Lemaire, A. Rassat, and J. J. Dunand, *Bull. Soc. Chim. Fr.*, 4220 (1970).

Table II. Experimental Hfsc's (G) in Radicals I and II

	N	H(C-1, C-5)	CH_3(C-1, C-5)	H(C-2, C-4) Ax	H(C-2, C-4) Eq	H(C-6, C-7) Ex	H(C-6, C-7) En
Radical I	19.5		−0.44	−1.3	+2.3	−0.15	−0.3
Radical II	20	5.75		1.25	2.5	0.1	0.2

only through-bond spin polarization contributions to the long-range hfsc's. In our opinion, existence of the large *positive* γ equatorial proton hfsc is evidence for substantial and very stereoselective electron delocalization in the bicyclic nitroxide I.[12]

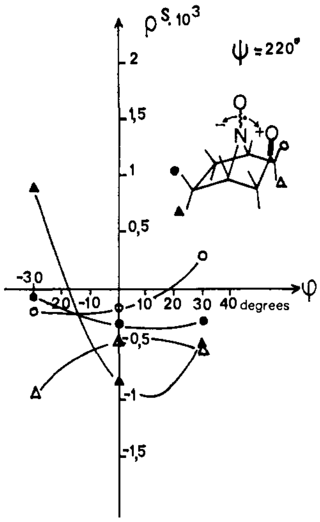
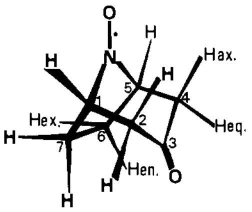


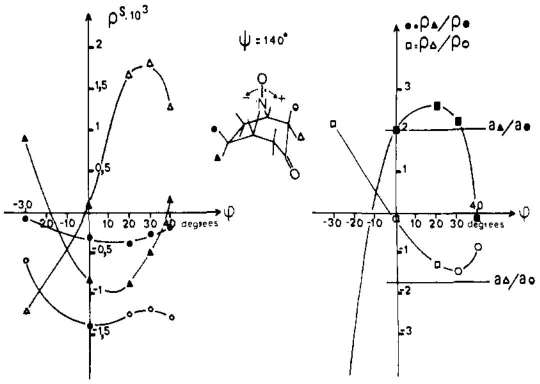
Figure 3. INDO spin densities at endo (▲), exo (●), equatorial (△), and axial (○) protons as a function of the NO conformation for a boat conformation of the six-membered ring.

From this viewpoint, molecular orbital (MO) methods for open-shell systems[13,14] are well suited to rationalize electron delocalization. Recently, two applications of the SCF–MO–INDO method have been reported for two bicyclic radicals.[2d–g] Because of computer memory limitations, we have carried out INDO calculations[15] for the smaller nitroxide II (8-azabicyclo[3.2.1]octan-3-one 8-oxyl). This radical has been obtained by oxidation of nortropinone.[5]



II

Its well-resolved esr spectrum (2×10^{-3} *M* solution in lithium chloride saturated water) is interpreted as follows: $a_N = 20.25$, $a_H\,(2\ H) = 5.75$, $a_H\,(2\ H) = 2.5$, $a_H\,(2\ H) = 1.25$, $a_H\,(2\ H) \sim 0.2$, $a_H\,(2\ H) \sim 0.1$ G. By selective deuteration of the $-CH_2-CO-CH_2-$group[6] we have assigned an hfsc of 2.5 G to the equatorial (C-2, C-4) protons and an hfsc of 1.25 G to the axial (C-2, C-4) protons. By comparison with radical I, the 5.75-G splitting is attributed to bridgehead (C-1, C-2) protons and the small hfsc to exo and endo (C-6, C-7) protons. Unfortunately, this radical is very insoluble (giving a diamagnetic yellow solid[16]), preventing the observation of its nmr spectrum. Because of the similarity of the absolute values of all γ-proton and nitrogen hfsc's (Table II) and because bridgehead substitution is not expected to change the conformation of the radical,[10] it is reasonable to assume the same signs for the γ-proton hfsc's in II as in I. As pointed out by Pople and Beveridge,[13] calculated spin density in the "S" atomic orbital centered on one nucleus ($\rho^S{}_n$) can be compared with the measured hfsc (a_n) of the same nucleus if the ratio of these two quantities is known. Although there are some difficulties in the determination of this ratio, it is certain that its sign is positive for ^1H and ^{14}N. In order to be free from this constant, we have chosen to compare the *signs* of the spin densities with the *signs* of the hfsc's and if necessary the *ratio* of spin densities on two protons attached to the same carbon atom to the ratio of corresponding hfsc's as a function of the two structural parameters φ and ψ. The results of these calculations are reported in Figures 3–5.



(a) (b)

Figure 4. (a) INDO spin densities at endo (▲), exo (●), equatorial (△), and axial (○) protons as a function of the NO conformation for a chair conformation of the six-membered ring. (b) Ratio of these spin densities for protons on the same carbon atom.

From these data, the following conclusions can be made. s-Orbital spin densities at the endo and exo protons of the five-membered ring are independent of the six-membered ring conformation (Figures 3, 4a, and 5a), while spin densities at axial and equatorial protons are considerably changed both in magnitude

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(12) Using Luz's formalism, this delocalization could be taken into account by a "homohyperconjugative" valence-bond structure: G. A. Russell, G. Holland, K. Y. Chang, and L. H. Zalkow, *Tetrahedron Lett.*, 1955 (1967).

(13) G. Berthier in "Molecular Orbital in Chemistry, Physics and Biology," P.-O. Löwdin and B. Pullman, Ed., Academic Press, New York, N. Y., 1964.

(14) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N. Y., 1970.

(15) We wish to thank the QCPE, Indiana University, for a copy of this program, adapted in this laboratory by M. Plaindoux.

(16) Probably a dimer as in the case of norpseudopelletierine *N*-oxyl.[10]

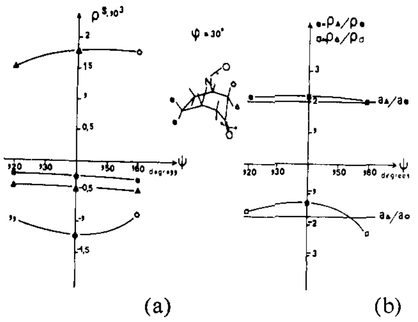

Figure 5. (a) INDO spin densities at endo (▲), exo (●), equatorial (△), and axial (○) protons as a function of the conformation of the six-membered ring for an axial NO group. (b) Ratio of these spin densities for protons on the same carbon atom.

and sign (Figures 3, 4a, and 5a). s-Orbital spin densities at endo and equatorial protons are highly dependent both in magnitude and sign on the >N–O conformation (Figures 3 and 4a) and these protons are directly involved in the empirical W-plan description.[17] A boat conformation (ψ = 220°) for the six-membered ring is consistent with the experimental signs (Figure 3). On the other hand, a chair conformation ($120° < \psi < 160°$) gives positive spin density at equatorial protons only for positive φ (Figure 4a). The best fit is obtained for $\varphi = 30°$ (Figure 4b) and $\psi = 120°$ (Figure 5b).[18] Moreover, this conformation has the lowest INDO calculated energy, and the observed hfsc's are in agreement with the W rule.

It may tentatively be concluded that these two radicals have a six-membered ring in a chair conformation, as in the tropinone series,[19] and predominantly *an axial N–O group.*

Acknowledgment. We wish to thank Y. Ellinger, H. Lemaire, and R. Subra for helpful discussions during this work. We are also indebted to Drs. P. J. Krusic and G. R. Underwood for comments on this paper.

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[17] G. A. Russell in "Radical Ions," E. T. Kaiser and L. Kevan, Ed., Interscience, New York, N. Y., 1968.

[18] If we assume that radical II has the conformation where ψ = 120° and φ = 30°, we can estimate the ratio, r_M, of the hfsc (a_M) to calculated s-orbital spin density ($\rho^S{}_M$) for a given nucleus M: $r_M = a_M/\rho^S{}_M$. It is found that for γ protons, $1000 < r_{H\gamma} < 1500$, for β protons $r_{H\beta} \sim 3000$, and for nitrogen $r_N \sim 800$. The quantities are much larger than those given by Pople: r_H = 539.86 and r_N = 379.34. It is seen that INDO calculations underestimate s-orbital spin densities at γ protons. In our opinion, too much spin density is kept at the two heteroatoms of the "radical center," and this may deserve a new analysis of the N and O INDO parameters for the nitroxide group.

[19] P. Scheiber, G. Kraiss, and K. Nador, *J. Chem. Soc. B*, 1366 (1970), and references cited therein.

Molecular Structure of Bicyclo[2.1.1]hexane

J. F. Chiang

Contribution from the Department of Chemistry, State University of New York, College at Oneonta, Oneonta, New York 13820. *Received December 19, 1970*

Abstract: The molecular structure of bicyclo[2.1.1]hexane has been determined by gas-phase electron diffraction. The geometry of this bicyclic compound was determined by resolution of the refined radial distribution curve, followed by a least-squares fitting of the calculated intensity curve to that observed. The structural parameters thus determined are as follows: C_1–C_5 = 1.544 ± 0.015, C_1–C_2 = 1.565 ± 0.024, C_2–C_3 = 1.513 ± 0.015, and C–H = 1.112 ± 0.003 Å and the dihedral angle of the four-membered ring is 125.0 ± 2.0°. A comparison of this structure with tricyclo[3.3.0.0^{2,6}]octane has been made in order to check the constancy of some C–C bond lengths.

Several strained polycyclic hydrocarbons have been subjected to structural studies owing to their rigidity and their importance for the discussions of nonbonded interactions, chemical reactivity, and strain energy calculations.[1] Bicyclo[2.1.1]hexane is one of the strained compounds in the series under investigation by the author at this laboratory. It is chosen for this study in order to make a valid, meaningful comparison with the previous determined structure of tricyclo[3.3.0.0^{2,6}]octane,[1b] and to investigate the constancy of the C–C bond length and the puckering in cyclobutane ring. It is also the purpose of this study to report a concise, true structure of this molecule, since an earlier electron diffraction study[2] is not conclusive owing to false assumption in the analysis.

Experimental Section

The sample of bicyclo[2.1.1]hexane was furnished by Dr. F. Uno and Professor J. Meinwald of Cornell University. Sectored electron diffraction photographs were taken with the apparatus at Professor Bauer's laboratory at Cornell University; it has been described elsewhere.[3] Two sets of data were obtained for this compound under the following conditions: 65 kV at a 251.2-mm sample-to-plate distance covered the angular range from q = 10 to 38 Å^{-1}, and 65 kV, 124.1 mm, covered the range q = 26 to 128 Å^{-1} ($q = (40/\lambda) \sin \theta/2$). MgO diffraction patterns were concurrently recorded for scale factors. The scattering patterns were microphotometered with a double-beam Jarrell-Ash microdensitometer interfaced with a digital recorder. The procedure for data reduction and structure analysis has been described in several previous publications.[4] The elastic and inelastic form factors of

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[1] (a) J. F. Chiang, C. F. Wilcox, Jr., and S. H. Bauer, *J. Amer. Chem. Soc.*, 90, 3149 (1968); (b) J. F. Chiang and S. H. Bauer, *Trans. Faraday Soc.*, 64, 2247 (1968).

[2] G. Dallinga and L. H. Toneman, *Recl. Trav. Chim. Pays-Bas*, 86, 171 (1967).

[3] S. H. Bauer and K. Kimura, *J. Phys. Soc. Jap.*, 17, 300 (1962); S. H. Bauer, Electron Diffraction Studies at High Temperatures, Report No. Nonr-401(41), Project No. NR092-504, ARPA Order No. 23-53.

[4] J. L. Hencher and S. H. Bauer, *J. Amer. Chem. Soc.*, 89, 5527 (1967); W. Harshbarger, G. Lee, R. F. Porter, and S. H. Bauer, *Inorg. Chem.*, 8, 1683 (1969).