and D. E. Ryono, *ibid.*, **98**, 1900 (1976).
(68) E. Holler, J. A. Rupley, and G. P. Hess, *Biochemistry*, **14**, 2377 (1975).
(69) F. W. Dahlquist, T. Rand-Meir, and M. A. Raftery, *Biochemistry*, **8**, 4214 (1969).
(70) The hydrolysis of four substituted phenyl disaccharides gives a value of ρ = 1.2 [G. Lowe, G. Sheppard, M. L. Sinnott, and A. Williams, *Biochem. J.*, **104**, 893 (1967)]; however, it is likely that at least the 2,4-dinitrophenolate leaving group leaves without protonation.

Electronic Structure, Aromatic Character, and Chemical Reactivity of *o*-Quinonoidal Heterocycles

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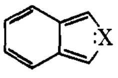
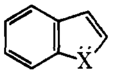
Abstract: The electronic structure of *o*-quinonoidal heterocycles is discussed in the light of NMR data which indicate (a) bond fixation in the carbocyclic ring and (b) insensitivity of the electron distribution in the carbocyclic ring to the nature of the heteroatom. A structural representation is proposed in which the π systems of *o*-quinonoidal heterocycles consist of contiguous but noninteracting butadiene and six-electron monocyclic systems. The structure reconciles their coexistent aromaticity and chemical reactivity.

Introduction

The contrast between the extreme chemical reactivity of the *o*-quinonoidal heterocycles **1** and the unreactivity of their stable Kekule counterparts **2** is intriguing, insofar as they differ only in the placement of the heteroatom, yet all contain a bicyclic 10 π electron array.[2] While it is tempting to regard them as basically *o*-xylylene derivatives, attribution of their reactivity simply to their polyenic or *o*-quinonoidal character seems inconsistent with the results of recent experimental and theoretical investigations, which indicate the heteroatom lone pairs of **1** to be strongly coupled into the π systems.[3] Moreover, isoindole (**1a**), isobenzofuran (**1b**), and isothianaphthene (**1c**) have been calculated to possess substantial resonance energies[4] (albeit less than in the corresponding Kekule compounds), a prediction verified indirectly for **1a** by our observation that isoindolenine (**3**) is converted smoothly, spontaneously, and irreversibly into **1a**, even at −40 °C.[5]

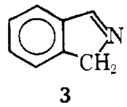


1



2

a, X = NH
b, X = O
c, X = S
d, X = Se



3

If the *o*-quinonoidal heterocycles are, in fact, "aromatic" in the sense of possessing substantial resonance energies, a question arises whether the aromaticity is global, extending over the entire π system, or whether it derives primarily from only one ring.[6] We posed this question for isoindole in our previous paper,[5] but were unable to choose between the alternatives using data for isoindole alone. We now return to the discussion of this point, using NMR coupling constant data and theoretical analyses for compounds **1a–d**, and propose **4** as the structural representation which best depicts their structures and reconciles their aromaticity and chemical reactivity.

4

Results and Discussion

Despite their superficial structural similarity, the heterocycles **1** display a wide range of stabilities, from the relatively stable isothianaphthene (**1c**) to the ephemeral isobenzofuran (**1b**). We sought evidence for a structural basis of these pronounced stability differences, using the NMR spectra of isoindole (**1a**), isobenzofuran (**1b**), isothianaphthene (**1c**), and benzo[*c*]selenophene (**1d**).[7] Aromatic systems generally exhibit bond length averaging, while systems which display pronounced bond length alternation invariably lack significant resonance stabilization,[8] a fact which has been employed in connection with allylic coupling constant data to establish the nonaromaticity of 2-pyrones.[9] We felt that the vicinal proton couplings in the carbocyclic rings of **1a–d** could similarly serve as an index of electron delocalization or localization, since the heteroatoms are sufficiently far removed as to influence the couplings only by their effects on the π-electron distribution.

We analyzed the NMR spectra of isoindole and benzo[*c*]selenophene using the program LAOCN3[10] and Tables I and II, respectively, summarize vicinal coupling constant data for the carbocyclic rings of **1a–d** and for several isoindoles of widely varying stabilities. The most striking feature of these data is the near constancy of the vicinal couplings J_{45} and J_{56}, with only the benzo[*c*]selenophenes deviating appreciably. Moreover, the ratio J_{56}/J_{45} (= J_{ratio}), proposed by Crews et al.[11] as a measure of the degree of electron delocalization in butadienic fragments, is nearly invariant, at 0.72 ± 0.02, for all members of both series, including the deviant benzo[*c*]selenophene, and shows no correlation with either reactivity or calculated indices of resonance stabilization. If J_{ratio} is indeed a valid measure of electron localization or delocalization, the data indicate the electron distributions in the carbocyclic rings to be insensitive to perturbations in the five-membered rings. The value of J_{ratio} is also significantly less than in the Kekule series (ca. 0.9),[12] indicative of at least some residual butadienic character in the carbocyclic rings. As we pointed out previously,[5] this latter observation is, in principle, consistent

Table I. Influence of Heteroatoms on the Vicinal Proton Couplings of *o*-Quinonoid Heterocycles (**1**)[a]

	Heteroatom			
Coupling	NH[b]	O[c]	S[c]	Se[b,d]
J_{56}, Hz	6.29	6.22	6.35	6.79
J_{45}, Hz	8.49	8.52	8.64	9.16
J_{ratio}[e]	0.74	0.70	0.72	0.74

[a] The standard numbering system is used. [b] This work. [c] Reference 3a. [d] A spectrum of benzo[*c*]selenophene was kindly provided by Professor M. P. Cava. [e] J_{56}/J_{45}.

Table II. Influence of Substitution in the Pyrryl Ring on the Vicinal Couplings in Isoindole

	Isoindole (**1a**)[a]	*N*-Methyl[b]	1,3-Diphenyl[c]
J_{56}, Hz	6.29	6.28	6.39
J_{45}, Hz	8.49	8.60	8.63
J_{ratio}	0.74	0.73	0.74

[a] This work. [b] Reference 3b. [c] Reference 11.

Table III. Annelation Energies of Kekule and *o*-Quinonoidal Heterocycles[a] (kcal/mol)

X	**1**	**2**
NH	3.2	15.6
O	0.8	18.7
S	2.8	18.8
CH=CH	20	20

[a] Derived from data given in ref 4b (X = NH, O), 4c (X = S), and 8a (CH=CH).

with either structure **4**, in which electron localization is confined to the carbocyclic ring, or one in which the *o*-quinonoidal heterocycles are true 10 π electron aromatic systems, with their low resonance energies accounted for by slight bond alternation extending over the entire bicyclic π system. However, the constancy of J_{ratio} for systems of such widely varying stabilities seems consistent only with structure **4**, in which the π systems of the heterocycles **1** are depicted as containing contiguous, but energetically noninteracting, butadiene and six-electron heterocyclic π systems. These conclusions are supported by further analysis of these data and of published theoretical calculations.

Analysis of SCF Calculations. Theoretical studies by Dewar et al.[4b,c] are consistent with the structure **4**. The Dewar resonance energy (DRE) of butadiene is zero,[13] so that the difference between the calculated DRE's of a heterocycle (**1** or **2**) and of the corresponding five-membered heterocycle **5** affords a measure of the stabilization (the annelation energy, AE) which results from interaction of the butadiene and six-electron heterocyclic π systems. The relevant data, given in Table III, show the AE's for the Kekule series (**2a–c**) to range from 15 to 19 kcal/mol, comparing favorably with the naphthalene AE of 20 kcal/mol.[13] In contrast, the *o*-quinonoid heterocycles **2a–c** have nearly negligible AE's (1–3 kcal/mol), indicating formation of the second ring to afford little additional stabilization.

5

Structure **4** appears also to require the bond lengths in the carbocyclic ring to be essentially those of acyclic polyenes, while the bond lengths in the five-membered ring should be the same as those in the monocycles **5**. Dewar's calculated bond lengths support this expectation (Table IV). In contrast, the bond lengths in the carbocyclic rings of the Kekule series (**2a–c**) correspond closely to those of naphthalene (Table V). It should be noted, however, that application of the Cooper–Manatt vicinal coupling constant–bond length equation[4] to derive carbon–carbon bond lengths for the 4,5 and 5,6 bonds of *N*-methylisoindole has led to values which resemble those of naphthalene more than those of butadiene.[3b]

Table IV. Bond Lengths in Isoindole. Comparison of Calculated and Predicted Values (Å)

	Calcd	Predicted	
Bond	length[a]	Localized[b]	Delocalized[c]
12	1.384	1.383	1.383
18	1.370	1.371	1.371
45	1.357	1.345	1.365
56	1.448	1.464	1.404
49	1.456	1.464	1.425
89	1.440	1.440	1.393
Average deviation		0.006	0.022

[a] Bond lengths calculated by Dewar et al.[4b] using a modified Pople-type SCF method. [b] Assumed to consist of a pyrrole ring and a carbocyclic ring with polyenic single and double bonds (structure **4**). [c] Assumed to consist of a pyrrole ring and a naphthalenoid carbocyclic ring.

Table V. Bond Lengths in Indole. Comparison of Calculated and Predicted Values (Å)

	Calcd	Predicted	
Bond	length[a]	Localized[b]	Delocalized[c]
12	1.398	1.383	1.383
23	1.353	1.371	1.371
39	1.453	1.440	1.440
49	1.412	1.464	1.425
45	1.384	1.345	1.365
56	1.408	1.464	1.404
67	1.385	1.345	1.365
78	1.410	1.464	1.425
18	1.401	1.383	1.383
89	1.397	1.371	1.371
Average deviation		0.033	0.0150

[a] Bond lengths calculated by Dewar et al.[4b] using a modified Pople-type SCF method. [b] Assumed to consist of a pyrrole ring and a carbocyclic ring with alternating polyenic single and double bonds. [c] Assumed to consist of a pyrrole ring and a naphthalenoid carbocyclic ring.

J_{ratio} as a Measure of Electron Delocalization. The major difficulty posed by structure **4** is that the value of J_{ratio} (0.72 ± 0.02) seems too large for a polyenic π system (for instance, $J_{\text{ratio}} = 0.52$ for 1,3-cyclohexadiene[11,14]) an observation which we noted elsewhere.[5] This judgement, however, derives alike from the choice of model compounds to define J_{ratio} for localized systems (i.e., 1,3-cyclohexadiene) and from the implication that electron delocalization necessarily implies resonance stabilization. Dewar[8a] has demonstrated the incorrectness of the latter assertion for systems such as acyclic polyenes and others which exhibit electron delocalization while lacking resonance stabilization. The former point led us to a consideration of models.

In attempting to assess the significance of J_{ratio}, we felt that 1,3-cyclohexadiene, in which the double bonds occur at the termini of the conjugated system, might be less appropriate as a model for the formal butadienic fragment in **1** than, for example, the 3,4 and 4,5 bonds of 1,3,5,7-octatetraene, which occur in the interior of a conjugated, indisputably nonaromatic, compound. Unfortunately, the relevant vicinal coupling con-

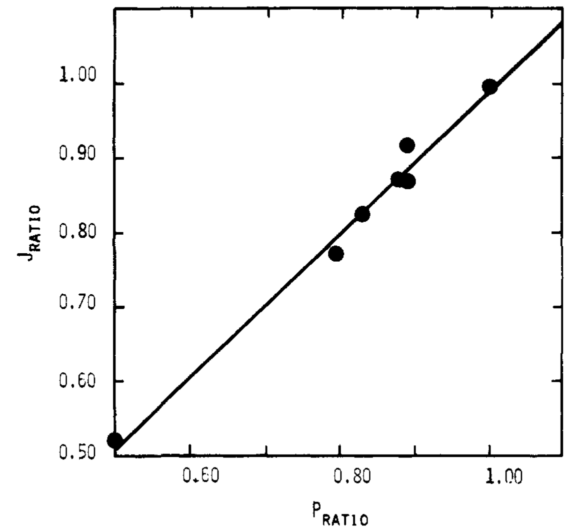
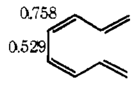


Figure 1. Linear correlation between J_{ratio} and P_{ratio}. $J_{\text{ratio}} = 0.954P_{\text{ratio}} + 0.037$ (correlation coefficient 0.992).

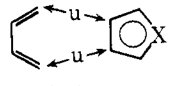
stant data for an appropriate conformation, such as **6**, are not directly accessible. Their ratio, however, can be derived from π bond order data. In Figure 1 are plotted ratios of vicinal coupling constants $(J_{\text{ratio}})^{15}$ vs. ratios of π bond orders $(P_{\text{ratio}})^{16}$ for a series of hydrocarbons containing formally cisoid butadienic fragments, and it is clear that an excellent linear correlation results.[17] This correlation allows an estimate of J_{ratio} to be made for the interior bonds of 1,3,5,7-octatetraene in conformation **6**. Significantly, while P_{ratio} for 1,3-butadiene is 0.50, the corresponding ratio for the 3,4 and 4,5 bonds in **6** (0.70) leads to a prediction for J_{ratio} of 0.71, very close to the value of 0.72 observed in the *o*-quinonoidal heterocycles **1**.[18] Structure **4**, therefore, is consistent with all the available data.



6

Aromaticity of *o*-Quinonoidal Heterocycles. Whereas the electronic structures of **1** are usually discussed in terms of the interaction of the heteroatom lone pair with an *o*-xylylene π system, structure **4** emphasizes the interaction between the π systems of butadiene and the monocycles **5**. Such an approach facilitates comparison of the reactivities of the bicyclic compounds and their monocyclic analogues.

The union of butadiene and monocyclic π systems to give the *o*-quinonoidal π systems can be studied using perturbation theory applied to Hückel molecular orbitals.[19] An orbital correlation diagram for isoindole, constructed using first- and second-order energy corrections, is shown in Figure 2. The heteroatom parameters used were $\alpha_N = \alpha + \beta$ and $\beta_{CN} = \beta$.[20] Two principal types of interactions can be distinguished.



A first-order interaction occurs between the degenerate HOMO's of butadiene and pyrrole, resulting in a reduction of the HOMO-LUMO energy gap, leading to a low first ionization potential and the observed long-wavelength absorption maximum. No energy stabilization results from this interaction, however. Moreover, since the HOMO's are antisymmetric with respect to the symmetry plane $\sigma_v(y)$, the interaction energy is independent of the heteroatom. To the extent that reactivity is governed by the frontier orbitals, all the *o*-quinonoidal heterocycles **1** should exhibit similar reactivities.[22]

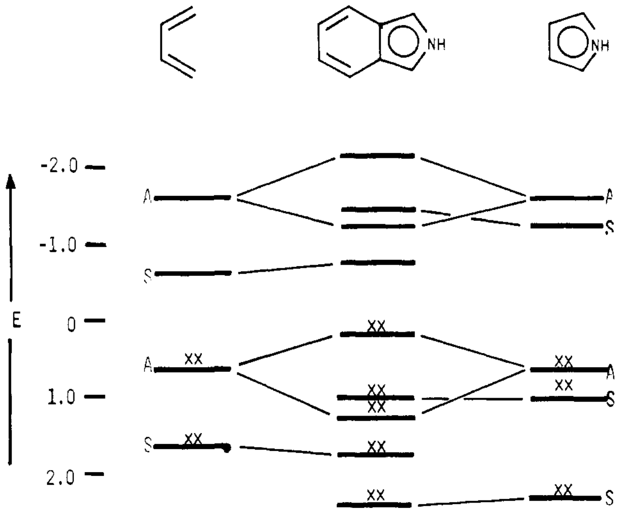


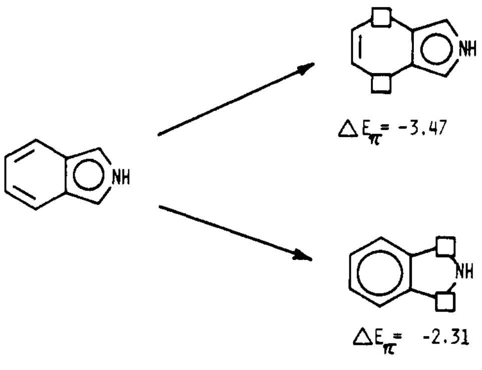
Figure 2. Orbital interaction diagram for formation of the isoindole π system by union of butadiene and pyrrole.

Second-order interactions lead to a slight lowering of the energies of the lowest occupied (symmetric) MO's of both butadiene and the monocycle, and these interactions, which depend upon the nature of the heteroatom, account for the annelation energies. The "aromaticities" of the heterocycles **1** should be essentially those of the corresponding five-membered heterocycles.

Reactivity of the Heterocycles. To explain satisfactorily the chemical behavior of **2**, structure **4** must account for both their enhanced reactivity toward dienophiles and the preferential occurrence of Diels-Alder reactions in the heterocyclic rings. The following discussion is specific for isoindole, but analogous treatments for **2b-d** give qualitatively similar results.

The π-electron activation energy (ΔE_π) of a reaction is defined as the difference between the π-electron energy of the transition state and that of the reactants.[23] For pyrrole, the transition state in a Diels-Alder reaction is reached by excision of carbon atoms 2 and 5 from the π system along with two electrons, leaving an isolated double bond and two electrons localized on nitrogen. For isoindole, two such Diels-Alder reactions are conceivable—in the pyrrole ring and in the carbocyclic ring. Development of the transition states is shown diagrammatically in Scheme I, along with ΔE_π values calculated assuming *complete* lack of interaction between the butadiene and pyrrole π systems. Both π activation energies are predicted to be substantially lower than that of pyrrole itself, indicating greatly enhanced reactivities. Even more strikingly, the activation energy for reaction in the pyrrole ring is *lower* than that for attack in the carbocyclic ring, despite the fact that the latter process involves attack at an isolated butadiene moiety. Attack in the heterocyclic rings of **1** is invariably observed.

Scheme I



The model also provides a convenient rationalization of the reactivity differences in the series of *o*-quinonoidal heterocycles. The activation energy for Diels–Alder reaction can be considered to involve two contributions: an endothermic contribution due to disruption of the π system in the five-membered heterocyclic ring, and an exothermic one due to simultaneous formation of a benzene ring. The degree of cancellation determines the height of the activation barrier. The greater the resonance stabilization of the "parent" five-membered heterocycle, the less reactive should be the bicyclic heterocycle. Thus isobenzofuran, derived from the nonaromatic or weakly aromatic furan (DRE = 1.6 kcal/mol[4b]), is much more reactive than either isothianaphthene or isoindole, both of which are derived from aromatic monocycles (DRE's of 6.5[4c] and 8.4 kcal/mol,[4b] respectively).

Conclusion

On the basis of our experimental results, our perturbation calculations, and our analysis of the published SCF calculations of Dewar et al., we suggest the heterocycles **1** to consist of contiguous but virtually noninteracting π systems, with their aromaticities deriving largely from the five-membered ring and their reactivity stemming from the adjacency of the butadiene moiety. This structural feature allows synchronous disruption of the π system in the heterocyclic ring and formation of a benzene ring during dienophile addition, leading to the observed hyperreactivity.

References and Notes

(1) Taken in part from the Ph.D. Thesis submitted by E.C. to the Graduate School of Arts and Sciences, 1976.

(2) (a) Isoindole: J. D. White and M. E. Mann, *Adv. Heterocycl. Chem.*, **11**, 113 (1969). (b) Isobenzofuran: R. N. Warrener, *J. Am. chem. Soc.*, **93**, 2345 (1971). (c) Isothianaphthene: B. Iddon, *Adv. Heterocycl. Chem.*, **14**, 331 (1972). (d) Benzo[*c*]selenophene: L. E. Saris and M. P. Cava, *J. Am. Chem. Soc.*, **98**, 867 (1976).

(3) (a) M. H. Palmer and S. M. F. Kennedy, *J. Chem. Soc., Perkin Trans. 2*, 81 (1976); (b) W. Rettig and J. Wirz. *Helv. Chim. Acta*, **59**, 1054 (1976).

(4) (a) J. Kopecky, J. Shields, and J. Bornstein, *Tetrahedron Lett.*, 3669 (1967); (b) M. J. S. Dewar, A. J. Harget, N. Trinajstic, and S. D. Worley, *Tetrahedron*, **26**, 4505 (1970); (c) M. J. S. Dewar and N. Trinajstic, *J. Am. Chem. Soc.*, **92**, 1453 (1970); (d) B. A. Hess, L. J. Schaad, and C. W. Holyoke, *Tetrahedron*, **28**, 3657 (1972); (e) B. A. Hess and L. J. Schaad. *Tetrahedron Lett.*, 535 (1977).

(5) E. Chacko, J. Bornstein, and D. J. Sardella, *Tetrahedron Lett.*, 1095 (1977).

(6) This question has been formulated by various authors (e.g., ref 1a. 3a,b, and 5), with Rettig and Wirz[3b] coming closest to our proposed structure.

(7) The 60-MHz NMR spectrum of benzo[*c*]selenophene was graciously supplied by Professor Cava.

(8) (a) M. J. S. Dewar, "Molecular Orbital Theory of Organic Chemistry", McGraw-Hill, New York, N.Y., 1969, Chapter 5; (b) L. Salem, "The Molecular Orbital Theory of Conjugated Systems", W. A. Benjamin, New York, N.Y., 1966, Chapter 8.

(9) D. J. Sardella, T. Holak. and G. Vogel, *Orgn. Mag. Reson.*, **7**, 355 (1975).

(10) LAOCN3; Program 111. Quantum Chemistry Program Exchange; average deviation between experimental and calculated line positions.

(11) P. Crews, R. R. Kintner, and H. C. Padgett, *J. Org. Chem.*, **38**, 4391 (1973).

(12) (a) Indole: P. J. Black and M. L. Heffernan, *Aust. J. Chem.*, **18**, 353 (1968); $J_{\mathrm{ratio}} = 0.92$. (b) Benzothiophene: K. Takahashi, I. Ito, and Y. Matsuki, *Bull. Chem. Soc. Jpn.*, **39**, 2316 (1968); $J_{\mathrm{ratio}} = 0.88$–$1.00$. (c) Benzofuran: no data are available; however, Okuyama and Fueno [*Bull. Chem. Soc. Jpn.*, **47**, 1263 (1974)] report values of 8.1 and 8.4 Hz for J_{45} in 6-methyl- and 6-methoxybenzofuran, respectively, which bracket the value for the corresponding coupling in naphthalene (8.3 Hz).

(13) Reference 8a, p 173 ff.

(14) M. A. Cooper and S. L. Manatt, *J. Am. Chem. Soc.*, **91**, 6325 (1969).

(15) Coupling constants were taken from ref 10 and 13.

(16) π bond orders were taken from (a) C. A. Coulson and A. Streitwieser, "Dictionary of π-Electron Calculations", W. H. Freeman, San Francisco, Calif., 1965; (b) A. Streitwieser and J. I. Brauman, "Supplemental Tables of Molecular Orbital Calculations". Pergamon Press, Elmsford. N.Y., 1965.

(17) A least-squares fit yielded the equation $J_{\mathrm{ratio}} = 0.954P_{\mathrm{ratio}} + 0.037$, with a correlation coefficient of 0.992.

(18) $P_{\mathrm{ratio}} = 0.70$ in *o*-xylylene: C. R. Flynn and J. Michl. *J. Am. Chem. Soc.*, **96**, 3280 (1974).

(19) Reference 8a, Chapter 6.

(20) Calculations were done using wave functions and energies given in ref 16a; the parameters are not the best values suggested by Streitwieser,[21] and no quantitative significance is intended to be attached to the results.

(21) A. Streitwieser, "Molecular Orbital Theory for Organic Chemists", Wiley, New York, N.Y., 1961. Chapter 4.

(22) K. Fukui, *Acc. Chem. Res.*, **4**, 57 (1971), and references cited therein.

(23) Reference 8a, Chapter 8.

Stereochemistry of Cyclopropyl Radicals by Electron Spin Resonance[1]

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Abstract: ESR spectra are examined for cyclopropyl radicals including 1-fluoro analogues and the *exo*-tricyclo[3.2.1.0^{2,4}]octan-3-yl radical in cyclopropane or ethane solutions. The rate of inversion at the pyramidal tervalent carbon atoms of cyclopropyl radicals with an α hydrogen atom is rapid ($k > 8 \times 10^7$ s^{-1}), whereas the pyramidal geometry of 1-fluorocyclopropyl radicals is static on the ESR time scale. The hfsc of the β proton cis to the odd electron orbital is larger than that of the trans β proton. The β-methyl proton hfsc trans to the odd electron orbital is larger than the cis one. The 2,3-*cis*-dimethylcyclopropyl radical is slightly more stable in the structure where the odd electron orbital is trans to the methyl substituents. The stable geometry of 2-bicyclobutyl radical is also discussed.

Fessenden and Schuler[2] have shown on the basis of ESR results that the trigonal carbon atom of the cyclopropyl radical is pyramidal and is undergoing a rapid inversion from one pyramidal form to another. Since then the pyramidal geometry and the configurational stability of cyclopropyl radicals have been a subject of theoretical investigations[3] and of product studies.[4] Molecular orbital calculations[3b,c] predicted conflicting geometrical dependences of β-proton hfsc's for the nonplanar cyclopropyl radical. The β-proton hfsc's arise predominantly from hyperconjugation. To our knowledge, no experimental study has been reported on this subject, although such a study is important in order to understand the stereochemistry of cyclopropyl radicals.

Ando and his co-workers[4a,b] have demonstrated that the geometry of the fluorine atom is retained in the homolytic reduction of *gem*-halogenofluorocyclopropanes with a tin hy-

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