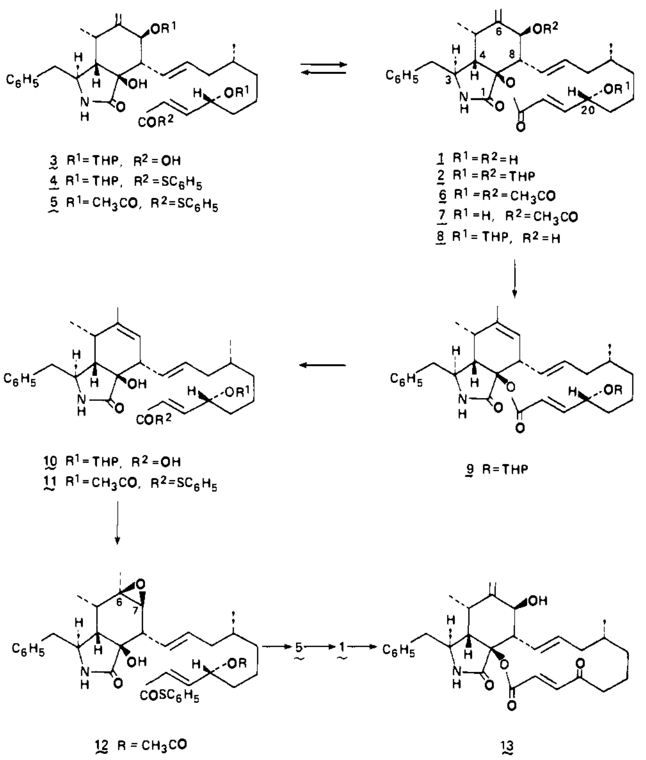
Scheme I



treatment (aqueous CH_3CO_2H) of **4** and then acetylation afforded the diacetate–thiol ester (**5**). A stirred mixture of 16 mg of **5** and 27 mg of Na_2HPO_4 and 22 mg of $AgCF_3CO_2$[11] in 8 mL of benzene was heated at reflux for 2 h under an argon atmosphere. Upon the usual workup there was isolated 4.8 mg (36%) of the cyclized product (**6**), which afforded **1** upon mild alkaline hydrolysis. Identification of these products obtained by cyclization was established in the standard fashion.

Partial hydrolysis of **6** proceeded efficiently to afford monoacetate **7** (in >70%), which after the protection (THP) of the liberated hydroxy group was converted into the hydroxy compound (**8**). Treatment of **8** with methanesulfonyl chloride followed by sodium cyanoborohydride effected reductive migration of the double bond, and the resulting Δ^6 compound (**9**) upon alkaline hydrolysis was converted into the corresponding seco acid (**10**). The preparation of the benzenethiol ester of **10** and then conversion of the 20-*O*-THP into the 20-*O*-acetate (**11**) proceeded well in a manner analogous to that described for **5** (vide supra). Treatment of **11** with *tert*-butyl hydroperoxide and vanadyl acetylacetonate (Sharpless' procedure)[12] provided the 6,7-epoxide (**12**) (in 50 ~ 60% based on consumed **11**), which was subsequently transformed into **5** upon acid treatment[13] (2 N HCl in 50% aqueous acetone for 18 h), followed by acetylation. The Ag(I)-assisted lactonization of **5** in the manner described above completes a conversion of **10** into **1**. The latter compound has already been reported to provide cytochalasin A (**13**) upon oxidation with MnO_2.[14,15]

Utility of **10** as a relay compound in the synthesis of **1** and **13** is evident. The stereochemistry of the tetrahydroisoindole moiety of **10** is such that a Diels–Alder reaction of two appropriately functionalized components would directly lead to the construction of the system. In fact, Auerbach and Weinreb have recently demonstrated that the reaction indeed proceeds in this predictable manner.[16] Thus dissection of **10** into three synthetic units now constitutes a rational synthetic scheme.

Acknowledgment. The authors are grateful to Drs. D. C. Aldridge and W. B. Turner for a generous gift of cytochalasin B and their unpublished data, and to the National Research Council of Canada for financial support.

Supplementary Material Available: A listing of spectral data for the cytochalasin derivatives (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) S. Masamune, S. Kamata, and W. Schilling, *J. Am. Chem. Soc.*, **97**, 3515 (1975).

(2) (a) S. Masamune, C. U. Kim, K. E. Wilson, G. O. Spessard, P. E. Georghiou, and G. S. Bates, *J. Am. Chem. Soc.*, **97**, 3512 (1975); (b) S. Masamune, H. Yamamoto, S. Kamata, and A. Fukuzawa, *ibid.*, **97**, 3513 (1975).

(3) Selenol esters appeared to be a likely choice for a more reactive species than the thiol ester owing to the comparatively weak bonding between carbon and selenium. Accordingly, several alkane- and areneselenol esters of cyclohexanecarboxylic acid, prepared in excellent yields by several methods,[17] were tested. However, *O*-ester formation utilizing metal cations which are inert to the C=C bond (e.g., Ag(I), Cu(I)), were rather discouraging, and we have concluded at this time that selenol esters do not offer any advantages for this purpose over thiol esters, although ample room is still left for further investigation.

(4) For instance, Hg(II) reacts with electron-rich, activated double bonds (oxymercuration) more readily than with a thiol ester, and, if this is the case, another thiophilic metal cation must be used.

(5) The Saville rules (*Angew. Chem., Int. Ed. Engl.*, **6**, 928 (1967)) derived from Pearson's hard-soft acids and bases (HSAB) principle (R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **89**, 1827 (1967)) have been used as a guide in selecting appropriate pairs of reactive species, although the words "hard" and "soft" are interpreted in a sense broader than and modified from that originally defined. Note that intermediate I involves a hard–hard pair (RCO^+ and OH) and a soft-soft pair (SR and Hg(II)). For a review, see T.-L. Ho, *Chem. Rev.*, **75**, 1 (1975). Cf. R. Gompper and H.-U. Wagner, *Angew. Chem., Int. Ed. Engl.*, **15**, 321 (1976).

(6) For a recent review, see M. Binder and Ch. Tamm, *Angew. Chem., Int. Ed. Engl.*, **12**, 370 (1973).

(7) Compound **1** with or without the protection of the hydroxy groups reacts instantaneously with mercury(II) salts. The other lactonization methods tested in our hands without success follow. (a) The "double activation" method: E. J. Corey and K. C. Nicolaou, *J. Am. Chem. Soc.*, **96**, 5614 (1974). (b) A modification of the method in 7a: H. Gerlach and A. Thalmann, *Helv. Chim. Acta*, **57**, 2661 (1974). For the application of Gerlach's method to cytochalasin B, see D. Scherling, I. Csendes, and Ch. Tamm, *ibid.*, **59**, 914 (1976).

(8) Designated as "authentic" macrolides in ref 2a and include the compounds originally defined as macrolides (R. B. Woodward, *Angew. Chem.*, **69**, 50 (1957)). For a classification of this entire family, see S. Masamune, G. S. Bates, and J. W. Corcoran, *Angew. Chem., Int. Ed. Engl.*, in press.

(9) The yield of each step is higher than 90%, unless otherwise specified in the text.

(10) S. Masamune, S. Kamata, J. Daikur, Y. Sugihara, and G. S. Bates, *Can. J. Chem.*, **53**, 3693 (1975). Also see G. S. Bates, J. Diakur, and S. Masamune, *Tetrahedron Lett.*, 4423 (1976).

(11) Neither $AgBF_4$ nor $AgCF_3SO_3$ effected the lactonization.

(12) K. B. Sharpless and R. C. Michaelson, *J. Am. Chem. Soc.*, **95**, 6136 (1973).

(13) D. C. Aldridge, B. F. Burrows, and W. B. Turner, *J. Chem. Soc., Chem. Commun.*, 148 (1972); D. C. Aldridge, D. Greatbanks, and W. B. Turner, *ibid.*, 551 (1973); G. Büchi, Y. Kitaura, S.-S. Yuan, H. E. Wright, J. Clardy, A. L. Demain, T. Glinsukon, N. Hunt, and G. N. Wogan, *J. Am. Chem. Soc.*, **95**, 5423 (1973).

(14) D. C. Aldridge, J. J. Armstrong, R. N. Speake, and W. B. Turner, *J. Chem. Soc. C*, 1667 (1967).

(15) Spectral data of all the compounds described in this note appear in the microfilm edition of the journal and experimental details will be available on request.

(16) J. Auerbach and S. M. Weinreb, *J. Org. Chem.*, **40**, 3311 (1975).

(17) Preparation of alkane- and areneselenol esters: (1) reaction of cyclohexanecarboxylic acid with either benzeneselenenyl chloride or diphenyl diselenide in the presence of tri-*n*-octylphosphine, (2) reaction of cyclohexanecarboxylic acid chloride or imidazolide with the Tl(I) salt of benzeneselenoxide or butaneselenoxide, and (3) reaction of cyclohexanecarboxylic acid diethylphosphoric acid anhydride with the above salt.

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Bent Bonds in the Bridgehead Triptycyl Radical

Sir:

Magnetic resonance experiments have provided most of the present information of the geometry of reactive free radicals and carbenes.[1] A particularly powerful technique involves determining the hyperfine splitting of the atom with an unshared valence. The isotropic and anisotropic components of

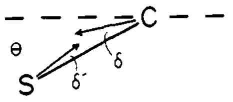

Figure 1. C is the bridgehead atom; S, one of the α substituents. The dashed line, from which θ is measured, is perpendicular to the molecular symmetry axis, which is vertical in the page. Arrows denote directions of the hybrid orbitals involved in the C-S bond.

this hfs yield s and p orbital spin densities at the atom, which may be compared with values estimated for various hypothetical geometries. A simple theoretical approach uses these spin densities to define the hybridization of the singly occupied atomic orbital and determines the local geometry by atomic orbital orthogonality *on the assumption that the bonds are not bent,* that is, that each bonding hybrid orbital points toward the nucleus bound.[2] Here we present evidence that the bonds from the trivalent carbon of the bridgehead triptycyl radical are strongly bent. We suspect that such bending is important in all radicals and carbenes in which straight bonds are not required by symmetry.[3]

In studying pairs of bulky free radicals in organic crystals we have photolyzed single crystals of the chloroform solvate of ditriptoyl peroxide at low temperature in the EPR spectrometer.[4,7] The dominant spectral features are doublets assigned to various arrangements of the triptycyl-triptycyl radical pair. A weak signal assigned to the triptycyl-triptoyloxy pair was observed after brief irradiation at 8 K, but at 9.5 K it decayed, perhaps by decarboxylation, with a half-life of ~10 min.

The spectrum of a crystal which had been irradiated for 4 min at 103-113 K and then warmed to 173 K showed only the fine structure doublets of the most stable triptycyl-triptycyl radical pair, trapped in two symmetry-related crystal sites. Values of the doublet splitting in 100 crystal orientations were fit to first order[6] by a zero-field splitting tensor giving a root mean square (rms) deviation of 7 G (2% of the maximum splitting). The D and E parameters were 0.0450 (4) and 0.0003 (1) cm^{-1}, respectively. This D corresponds to an average spin-spin distance of 5.58 Å. The g factor was 2.0024 (2) and was isotropic within this error. Peak-to-peak line width of the signals varied from 4 to 6 G, presumably because of the anisotropy of unresolved hfs. The signal showed no decay in 5 h at −100 °C, but decayed rapidly at −73 °C.

Increasing the spectrometer gain revealed satellite doublets flanking each of the peaks. The amplitude of each satellite was about 0.9% of the parent, supporting their assignment to splitting by two nearly equivalent ^{13}C nuclei in natural abundance.[8] The peak-to-peak width of the satellites was similar to that of the parent and did not vary more dramatically with crystal orientation; thus the hfs tensors of the two ^{13}C's are effectively coincident. A tensor was fit to first order to 162 measured hyperfine splittings giving an rms error of 2.2 G (3% of the maximum splitting). The principal values of the tensor were 75.3, 38.2, and 35.9 G. The eigenvector with 75.3 G splitting was 4.9° from the eigenvector for the largest zero-field splitting, suggesting that the radical orbitals are nearly colinear. These values correspond to an isotropic ^{13}C hfs of 99.8 G with an anisotropic contribution of $2\boldsymbol{B} = 51$ G for the isolated triptycyl radical. This implies 9.0% 2s spin density and 77% 2p spin density on the radical carbon.[9]

There is, as expected, little delocalization of the spin in this radical. To a good approximation the singly occupied orbital is an $\text{sp}^{8.6}$ hybrid on the bridgehead carbon.[10] By atomic orbital orthogonality the singly occupied hybrid must make an angle of about 102.5° with each of the three bonding atomic orbitals of the bridgehead carbon. In view of recent evidence that the *tert*-butyl radical is nearly tetrahedral[11] such flattening would be remarkable, especially since the constraints of the triptycene skeleton should oppose it.[12] Trigonal geometry of the benzo groups in triptycene would require an angle θ (Figure 1) of 30° between the bridgehead bonds and the plane normal to the molecular threefold symmetry axis, but tetrahedral geometry at the bridgehead would require 19.5°. X-ray studies of triptycene and numerous derivatives have given values near 23° for θ.[13] In these cases accommodation is reached with 7° distortion of the exocyclic bond angles from the benzo rings and and 3.5° distortion of the tetrahedral angles at the bridgehead carbon *in the direction opposite to flattening.*[14] Bridgehead ^{13}C-H coupling constants of triptycene (145 Hz)[17] and of barrelene (140 Hz)[18] suggest smaller distortions from tetrahedral geometry of 1.3 and 1.0°, respectively. In triptycene the angle δ between the hybrid orbital of the bridgehead carbon and the internuclear vector is 2.2° and δ' is 4.3°.[16] The bonds to the bridgehead carbon of triptycene itself are thus bent, since at neither nucleus does the atomic orbital hybrid point toward the other nucleus. Apparently the corresponding bonds in the triptycyl radical are even more strongly bent. If the nuclear geometry is that of the parent hydrocarbon, δ is 10.1°. If the bridgehead carbon moves in along the threefold axis by 0.1 Å, as has been suggested in other bridgehead radicals,[19] δ is reduced to 6.6°, but δ' increases from 6.2 to 7.9°.[16]

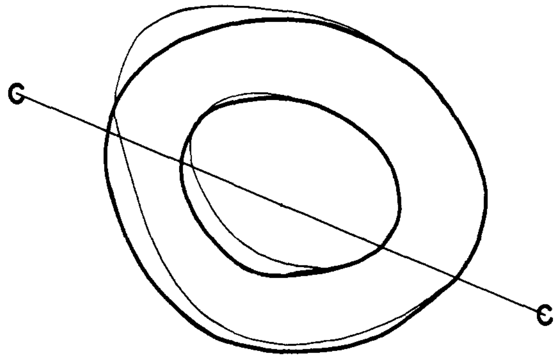

Figure 2. Electron deformation density contours (0.02 and 0.03 e/Å^3) for the bridgehead C-C bond of barrelene (heavy contours) and barrelenyl (light contours) as calculated by INDO. The bridgehead carbon is at the upper left.

INDO calculations[20] of barrelenyl radical, as a model for triptycyl, indicate that changing θ from 23 to 19° by the 0.1-Å motion of the bridgehead carbon is favorable by 13 kcal/mol. The calculated 2s and 2p spin densities on the bridgehead carbon are 0.15 and 0.70 with θ = 23° and 0.10 and 0.73 with θ = 19°. While the latter figures are in reasonable agreement with our observations, their significance is questionable, since INDO spin densities are empirically related to ^{13}C hfs constants, and barrelenyl may be an inadequate model for triptycyl. Transforming the INDO MOs to localized orbitals could confirm the lack of orbital following,[21] but it is more convincing to demonstrate the calculated bond bending by plotting the deformation density (total INDO electron density less the contribution of spherical atoms) in the region of the bridgehead bond.[22] Figure 2 compares the deformation density in the bridgehead C-C bond of barrelene (heavy contours) with that in the corresponding bond of the bridgehead radical (light contours). Although the scale and overall bending of both bonds may be artifacts of the calculation method, the greater bending near the radical center is striking and probably realistic.

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Anderson, Mr. Lawrence Rissman, and Mr. Michael Vary for help with this work.

References and Notes

(1) See J. Kochi in *Adv. Free-Radical Chem.*, **5**, 189 (1975).
(2) (a) C. A. Coulson, "Valence", Oxford University Press, New York, N.Y., 1961, p 193; (b) P. W. Atkins and M. C. R. Symons, "The Structure of Inorganic Radicals", Elsevier, New York, N.Y., 1967, pp 22, 209, 257.
(3) J. M. McBride, *J. Am. Chem. Soc.*, following paper in this issue.
(4) The peroxide was prepared from triptoyl chloride[5a,b] using the urea complex of hydrogen peroxide.[5c] Crystals grown from chloroform solution were monoclinic, space group *Pc* or *P2/c*; $a = 17.84$, $b = 12.80$, $c = 16.63$ Å; $\beta = 105.19°$; $\rho_{obsd} = 1.41$, $\rho_{calcd} = 1.37$ g cm^{-1} for $C_{42}H_{26}O_4 \cdot 2CHCl_3$; $Z = 4$. The equipment was described previously,[6] except that temperature was controlled by Varian 4540 and Air Products Heli-tran LTD-3-110 cryostats.
(5) (a) R. C. Parish and L. M. Stock, *J. Org. Chem.*, **30**, 927 (1965); (b) P. D. Bartlett and F. D. Greene, *J. Am. Chem. Soc.*, **76**, 1088 (1954); (c) D. F. DeTar and L. A. Carpino, *ibid.*, **77**, 6370 (1955).
(6) N. J. Karch, E. T. Koh, B. L. Whitsel, and J. M. McBride, *J. Am. Chem. Soc.*, **97**, 6729 (1975).
(7) Using an Osram HBO-200 w/2 lamp with a $CuSO_4$ filter.
(8) The only previous report of ^{13}C hfs in a bridgehead radical is for 1-adamantyl generated by γ radiolysis of glassy solutions of 1-bromoadamantane. The isotropic (137 G) and anisotropic ($2B = 43$ G) components inferred from poorly resolved shoulders suggested more delocalization (22%) and more s character ($sp^{5.3}$) in the radical orbital than we find for triptycyl: S. P. Misra and M. C. R. Symons, *Tetrahedron Lett.*, 2267 (1973).
(9) Using the 1110- and 33-G constants of J. R. Morton, *Chem. Rev.*, **64**, 453 (1964).
(10) There should be a little less 2s character than in an $sp^{8.6}$ hybrid, because some 2s (and 1s) density arises by spin polarization. Thus the amount of bond bending is probably ~1° greater than we calculate here.
(11) (a) J. B. Lisle, L. F. Williams, and D. E. Wood, *J. Am. Chem. Soc.*, **98**, 227 (1976); (b) P. J. Krusic and P. Meakin, *ibid.*, **98**, 228 (1976).
(12) (a) P. D. Bartlett and L. H. Knox, *J. Am. Chem. Soc.*, **61**, 3184 (1939); (b) P. D. Bartlett and E. S. Lewis, *ibid.*, **72**, 1005 (1950).
(13) (a) K. Anzenhofer and J. J. DeBoer, *Z. Kristallogr.*, **131**, 103 (1970); (b) I. L. Karle and J. A. Estlin, *ibid.*, **128**, 371 (1969); (c) K. J. Palmer and D. H. Templeton, *Acta Crystallogr., Sect. B*, **24**, 1048 (1968); (d) N. Sakabe, K. Sakabe, K. Ozeki-Minakata, and J. Tanaka, *ibid.*, **28**, 3441 (1972); (e) M. Mikami, K. Toriumi, M. Konno, and Y. Saito, *ibid.*, **31**, 2474 (1975); (f) T. Kaneda, N. Sakabe, and J. Tanaka, *Bull. Chem. Soc. Jpn.*, **47**, 1858 (1974).
(14) Greater distortion at the benzo carbon may be due in part to transannular repulsion among the benzo groups;[15] however, this distortion is overestimated, since we assume straight bonds within the benzo rings.[16]
(15) As suggested for barrelene by O. Ermer, *Tetrahedron*, **30**, 3103 (1974).
(16) If rehybridization at the benzo carbon is taken into account by an optimization of overlap calculation,[3] the values of δ' in triptycene, triptycyl ($\theta = 23°$), and triptycyl ($\theta = 19.5°$) are 4.3, 6.2, and 7.9°, respectively.
(17) W. B. Smith and B. A. Shoulders, *J. Phys. Chem.*, **69**, 2022 (1965).
(18) H. E. Zimmerman, G. L. Grunewald, R. M. Paufler, and M. A. Sherwin, *J. Am. Chem. Soc.*, **91**, 2330 (1969).
(19) (a) P. J. Krusic, T. A. Rettig, and P. R. Schleyer, *J. Am. Chem. Soc.*, **94**, 995 (1972); (b) T. Kawamura, M. Matsunaga, T. Yonezawa, *ibid.*, **97**, 3234 (1975); (c) W. C. Danen and R. C. Rickard, *ibid.*, **97**, 2303 (1975); (d) T. Kawamura and T. Yonezawa, *J. Chem. Soc., Chem. Commun.*, 948 (1976).
(20) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory", McGraw-Hill, New York, N.Y., 1970, p 130.
(21) D. M. Schrader and K. Morokuma, *Mol. Phys.*, **21**, 1033 (1971).
(22) See, e.g., P. Coppens, *Angew. Chem.*, **16**, 32 (1977).

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Overlap and the Prevalence of Banana Bonds in Free Radicals and Carbenes

Sir:

Evidence suggesting bent bonds (lack of orbital following) from the central carbon of numerous organic free radicals and carbenes is scattered through the literature,[1-12] but no one has discussed the generality of this phenomenon or its source. We were surprised to find that this bond bending can be understood semiquantitatively in terms of maximization of orbital overlap. We now believe that substantial distortion should be expected whenever the symmetry of a radical or carbene permits.

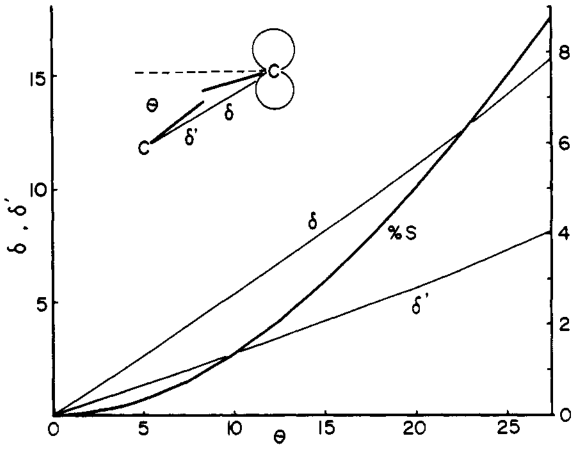

Figure 1. Orbital following in the *tert*-butyl radical calculated by maximization of overlap.

Table I presents the 13 relevant examples known to us of hydrocarbon free radicals and carbenes where internuclear angles and hybridization angles at the functional carbon have been measured, calculated, or estimated. To compare systems with twofold and threefold rotational symmetry, angles from the plane normal to the symmetry axis are reported (see Figure 1 of ref 3) rather than angles among nuclei or between atomic hybrids. In every case but one the bonding hybrids of the central carbon fall short of pointing toward the nuclei to which they bind, and by as much as 16°. Distortion in the *tert*-butyl and vinyl radicals and in methylene (and perhaps in diphenylmethylene) is especially striking, because ring strain could not be responsible for bond bending in these acyclic molecules. The methyl radical, which must have straight bonds in its planar, minimum-energy geometry, shows substantial bond bending as it undergoes out-of-plane distortion.

From the valence-bond viewpoint we say a carbon atom adjusts its hybridization to minimize the molecular energy according to two consideration: (a) it must hold down the valence state promotion energy by maximizing the fraction of the 2s atomic orbital in the occupied hybrids; and (b) it must maximize the strength of the bonds to be formed.[13,14] Although the first consideration is very important with the three valence electrons of a carbocation or the five of a carbanion, it is of little importance when four valence electrons are distributed one to each of the four orthogonal hybrids.[15] For radicals and carbenes valence state promotion energy should be significant only when the bonds are strongly polar.[14] In these species, as in tetravalent carbon, bond strengths dominate hybridization.

Since the earliest discussions of hybridization, orbital overlap has been invoked as a criterion of bond strength.[21] Recently Randić and his collaborators have used overlap maximization at fixed nuclear geometries to determine atomic hybridization in strained-ring hydrocarbons.[20] These hybrids are similar to those resulting from transformations which localize molecular orbitals calculated by ab initio or semiempirical methods, and they correlate even better tha the latter with values measured empirically by such criteria as ^{13}C–H coupling constants.[22]

The ability of an atomic hybrid to overlap depends both on its direction and on its extension. Although it has repeatedly been asserted that sp^3 hybrids give the best overlap,[23] Coulson showed that at normal C–C bonding distances overlap miximized near sp hybridization.[13] In a free radical where one of the central carbon's atomic orbitals is singly occupied and not involved in bonding, the other three hybrids are free to appropriate some or all of its s character. Up to some limit overlap may increase if the greater extension of the bonding hybrids more than compensates for their departure from the internuclear axes. Thus the bonds may bend to maximize overlap.[24]

The δ_{calcd} column of Table I reports the amount of bond