The rates of ring flips for Phe and Tyr clearly vary among residues and proteins. Some rings flip very slowly or not at all (< 10 s^{-1}) at a temperature where other rings in the same protein are in the fast exchange limit as described above,[5] because the ^{2}H NMR data of Figures 5 and 6 show that polycrystalline phenylalanine has rapidly flipping rings. With this fast dynamical process found for closely packed crystals[36] and most protein Phe and Tyr residues, it is probable that the cases of immobilized rings are to be regarded as exceptions. The larger temperature factors in the diffraction data for the ring positions of phenylalanine[36] are probably a manifestation of the same small amplitude rapid motions of the ring that reduce the apparent static quadrupole coupling constant at 300 K.

The observation of averaging of second rank tensors for analysis of dynamics works readily for quadrupolar, chemical shift, and dipolar interactions. It can apply to the rings of all the aromatic amino acids, as well as other groups of macromolecules. It is appropriate for supramolecular structures in solution such as DNA-protein complexes or membranes where the overall reorientation rate is slow. It is well suited for the analysis of dynamics of polycrystalline and amorphous solids. When the sample can be prepared with specific isotropic labels, the information surpasses that available from any other source in detail and reliability. The rates of motions can be determined through relaxation measurement on the powder patterns.

Acknowledgment. We thank A. Vega for helpful discussions on the interpretation of ^{2}H NMR spectra. This research is being supported by grants from the National Institutes of Health (GM-24266) and the American Cancer Society (NP-225). C. M.G. is being supported by a Cell and Molecular Biology Training Grant. S.J.O. is a Fellow of the A.P. Sloan Foundation (1980–1982).

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On the Mechanism of Photooxygenation Reactions. Computational Evidence against the Diradical Mechanism of Singlet Oxygen Ene Reactions

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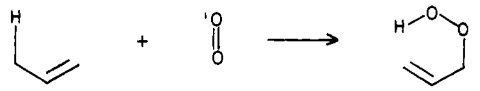
Abstract: Ab initio calculations with the STO-3G basis set and semiempirical MINDO/3 calculations at the unrestricted Hartree–Fock level show that both ab initio and semiempirical techniques predict that 1,4-diradicals formed from singlet oxygen and simple alkenes are more stable than perepoxides. Thus, both techniques now agree that perepoxides are too high in energy to qualify as viable intermediates in singlet oxygen ene reactions, as are zwitterions, for weakly polar alkenes. However, calculations on putative substituted diradical intermediates show that reactions involving such intermediates should be nonstereospecific and show significant regioselectivities. The high stereospecificity and low regioselectivity found experimentally argue strongly against the intermediacy of diradicals in this and related reactions.

The detailed electronic mechanism of singlet oxygen ene reactions with alkenes and enol ethers (Scheme I) continues to be a subject of intense interest and considerable controversy.[1] Experimental evidence has been interpreted both in favor of a perepoxide intermediate or a concerted mechanism. Theory, which should be most useful at predicting structures which cannot be examined experimentally, has cast more confusion on this subject. Dewar and Thiel reported MINDO/3 calculations which indicated that perepoxide intermediates, **1**, are formed from the reaction of simple alkenes and singlet oxygen.[2] Inagaki and Fukui preferred a perepoxide-like complex in the first stage of the reaction.[3] Harding and Goddard reported GVB–CI calculations which indicate that the perepoxide of ethylene is much higher in energy than a 1,4-diradical, **2**, resulting from formation of a single bond between one terminus of ethylene and singlet oxygen.[4] Various regiochemical and stereochemical features were interpreted in terms of biradical intermediates. Additional data, detailed elsewhere,[5] suggested to us that diradical intermediates cannot be formed in singlet oxygen ene reactions. The Harding–Goddard calculations exclude perepoxides as intermediates in singlet oxygen ene reactions and show that the 1,4-diradical is the only possible high-energy intermediate that could be formed in these reactions.

However, these authors could not exclude the possibility that these reactions are concerted, or if two-step involve only a low-energy charge-transfer-complex-type intermediate. This intermediate must have the symmetry properties required to explain stereoselective isotope effects, but could proceed over a low-energy barrier with concerted formation of the CO and OH bonds and breaking of the CH bond. In this paper, we report some intermediate computational steps taken on the pathway to an eventual full and reliable potential energy surface for the singlet oxygen ene reaction. Our results show the following.

Scheme I



(1) The apparent discrepancy between the Dewar–Thiel MINDO/3 prediction[2] of the formation of a perepoxide,[3] **1**, from $^{1}O_2$ and ethylene and the Harding–Goddard GVB–CI prediction[4] of a diradical intermediate, **2**, for the same reaction is removed

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(1) Frimer, A. A. *Chem. Rev.* **1979**, *79*, 359. Stephenson, L. M. *Tetrahedron Lett.* **1980**, 1005. Schulte-Elte, K. H.; Rautenstrauch, V. *J. Am. Chem. Soc.* **1980**, *102*, 1738 and references therein.

(2) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1975**, *97*, 3978.

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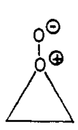
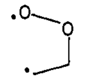
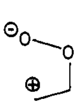
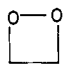
(4) Harding, L. B.; Goddard, W. A., III *J. Am. Chem. Soc.* **1977**, *99*, 4520.

(5) (a) Houk, K. N.; Williams, J. C.; Mitchell, P. A.; Yamaguchi, K. *J. Am. Chem. Soc.* **1981**, *103*, 949. (b) Yamaguchi, K.; Fueno, T.; Saito, I.; Matsuura, T.; Houk, K. N. *Tetrahedron Lett.* **1981**, 749.


1


2


3


4

when the more appropriate unrestricted MINDO/3 (UM3)[6a] and STO-36 (U3G)[6b] techniques are used; therefore, semiempirical and ab initio molecular orbital and ab initio valence bond calculations predict that perepoxides or zwitterions, **3**, are not involved in ene reactions or dioxetane formation with simple alkenes. Previous MINDO/3 calculations on the reaction of singlet oxygen with ethylene did not evaluate the energy of **2** since a restricted closed-shell technqiue was used.[2] In an earlier paper, we have shown that the least-motion $[{}_{\pi}2_s + {}_{\pi}2_s]$ process involving singlet oxygen and ethylene necessarily involves a singlet diradical path.[7] In spite of the Harding–Goddard criticisms of such a treatment,[8,9] these authors came to the same conclusion.

(2) Additional computational and experimental evidence taken in conjunction imply that diradical intermediates cannot be formed in singlet oxygen ene reactions. We show that (i) the Markovnikov directing effect is discernible for the 1,4-peroxy diradicals as in the case of other addition reactions—this is in contradiction to the observed low regioselectivity for ene reactions, and (ii) the barriers to rotation about the C–C single bonds in putative diradical intermediates in the singlet oxygen ene reactions would be too low to account for the stereospecificity observed in these reactions.[10] This provides strong evidence for the concerted mechanism[11] of these ene reactions, and further weakens arguments used to support diradical intermediate mechanisms in related stereospecific cycloadditions.[12] At most, the diradical may represent, in an oversimplified way, the major bonding patterns of a concerted transition state.

Results and Discussion

For intermediates which differ from stable closed-shell molecules by the formal cleavage of one single bond, open-shell (unrestricted) Hartree–Fock (HF) calculations are superior to closed-shell (restricted) HF In UHF calculations, each electron occupies a unique orbital, and the overestimate of zwitterionic character which plagues RHF solutions for such species is avoided. Indeed, the UHF solutions obtained by using the MINDO/3 and STO-3G methods agree remarkably well with the GVB–CI and thermochemical calculations reported by Harding and Goddard.

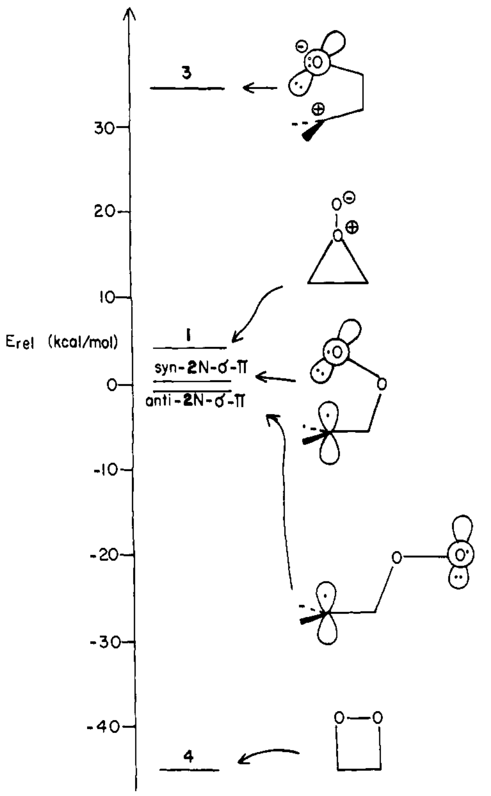
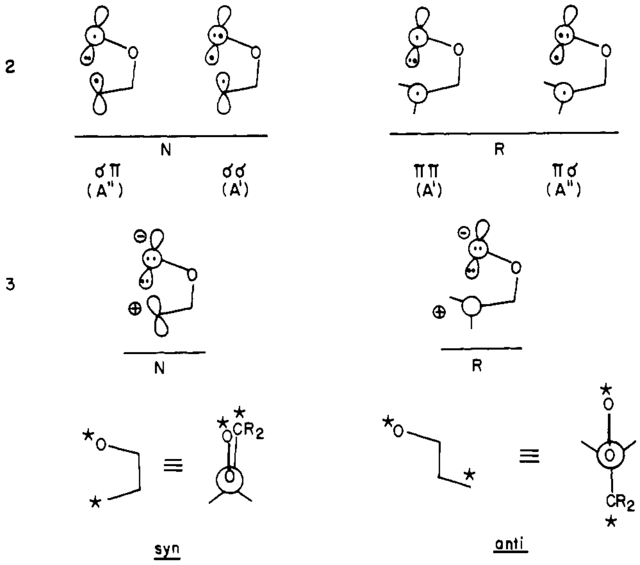


Figure 1. Energies and configurations of potential intermediates in the reaction of singlet oxygen with ethylene.

Scheme II



On the other hand, UMINDO/3 calculations may overestimate the stability of radical and diradical species relative to closed-shell species.[6a] Although it has apparently not been documented, this overestimate of diradical stability may be shared by GVB–CI calculations, as well.

As discussed by Harding and Goddard, when one bond is formed between oxygen and ethylene, there are various ways to alot electrons to the resulting orbitals. Scheme II depicts these for the syn conformations of a potential diyl intermediate. The first two drawings depict diradicals formed by attack of oxygen such that the ethylene moiety retains its local symmetry. That is, no rotation has occurred about the CC bond. These will be referred to as **2N**, where N stands for a nonrotated ethylene moiety. Of the two possible diradical configurations, the $\sigma\pi$ is that which correlates with (has the same symmetry as) the configurations of ground-state ethylene plus ${}^1\Delta_g$ oxygen, while the $\sigma\sigma$ state

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(6) (a) Dewar, M. J. S.; Olivella, S., Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 5650. (b) The IMS version of the program GAUSSIAN/70 was used.

(7) (a) Yamaguchi, K.; Fueno, T.; Fukutome, H. *Chem. Phys. Lett.* **1973**, *22*, 466. (b) Yamaguchi, K.; Yabushita, S.; Fueno, T. *Chem. Phys. Lett.* **1981**, *78*, 572.

(8) Harding, L. B.; Goddard, W. A., III *J. Am. Chem. Soc.* **1980**, *102*, 439.

(9) Recently Harding and Goddard[8] discussed the orbital-phase continuity problem for $\sigma\pi$-diradical **2**. For open-shell states such as those for **2**, the orbital-phase continuities of the singly occupied MO's (SOMO), i.e., σ and π MOs, should be discussed as in the case of free-radical reactions: Yamaguchi, K. *Chem. Phys.* **1977**, *25*, 215.

(10) Stephenson et al. (Stephenson, L. M.; McClure, D. E.; Sysak, P. K. *J. Am. Chem. Soc.* **1973**, *95*, 7888) report stereospecificity in acetone, but not in methanol. In the later solvent, a competing radical chain autoxidation occurs: Orfanopoulos, M.; Stephenson, L. M. *J. Am. Chem. Soc.* **1980**, *102*, 1417. Gollnick, K.; Kuhn, H. J. In "Singlet Oxygen"; Wasserman, H. H.; Murray, R. W.; Ed.; Academic Press: New York, 1979; p 323.

(11) One-stage[18] and two-stage[19] concerted mechanisms have been suggested. See also Woodward and Katz (Woodward, R. B.; Katz, T. J. *Tetrahedron* **1959**, *5*, 70) for the classic proposal of a two-stage concerted cycloaddition mechanism.

(12) Firestone, R. A. *Tetrahedron* **1977**, *33*, 3009.

(13) The detailed discussions of the UHF solutions resulting from the triplet instabilities of the RHF solutions are given in: Yamaguchi, K.; Yabushita, S.; Fueno, T.; Kato, S.; and Moroduma, K. *Chem. Phys. Lett.* **1980**, *70*, 27.

(14) (a) Caramella, P.; Gandour, R. W.; Hall, J. A.; Deville, C. G.; Houk, K. N. *J. Am. Chem. Soc.* **1977**, *385*. (b) Yamaguchi, K; Nishio, A.; Yabushita, S.; Fueno, T. *Chem. Lett.* **1977**, 1479. (c) Yamaguchi, K.; Nishio, A.; Yabushita, S.; Fueno, T. *Chem. Phys. Lett.* **1978**, *53*, 109.

(15) The ab initio (STO-3G) energy gradient was calculated by using the IMS ab initio package: Kato, S.; Morokuma, K. *Chem. Phys. Lett.* **1979**, *65*, 19.

Table I. Relative Stabilities of Potential Intermediates in the Reaction of Singlet Oxygen with Ethylene, According to the UMINDO/3 (UM3) and UHF STO-3G (U3G) Methods (kcal/mol)

intermediates	UM3	U3G	GVB[4]
perepoxide (1)	3.5	58.4	7.5
$\sigma\pi$ diradical (*anti*-2N-$\sigma\pi$)	−0.8	−2.4	
$\sigma\pi$ diradical (*syn*-2N-$\sigma\pi$)	0.0[a]	0.0[b]	0.0
zwitterion (3)	34.5		
dioxetane (4)	−46.0	−24.3	−45.9

[a] −931.1775 eV. [b] −224.7189 au.

correlates with the ground state of dioxetane. Rotation about the CC bond is also possible, and upon 90° rotation about the CC bond, the "rotated" diradicals **2R** are formed. Again, two configurations are possible for this geometry. Various zwitterion states are also possible, but **3N** and **3R** should be energetically much preferred over the zwitterions with positive oxygen and negative carbon.

Each of these diyl intermediates may exist in a variety of conformations. We shall discuss the two extremes, the anti, which should be preferred for steric and torsional reasons, and the syn, which would be preferred if there were either direct orbital overlap between half-occupied orbitals on C and O or strong electrostatic attraction between the two termini.

We shall first describe the nonrotated species **2N**. The energies of the UM3 solutions[7,13] for the various **2N** species and of the restricted MINDO/3 (RM3) solutions for the closed-shell states of perepoxide, **1**, zwitterion, **3**, and dioxetane, **4**, are given in Figure 1. Full geometry optimizations at the semiempirical (UM3) and ab initio (U3G) levels were performed by using an energy gradient technique.[14,15] These results indicate that **1**, *anti*-**2N**-$\sigma\pi$, and the dioxetane **4** are true local energy minima, and thus qualify as possible intermediates in the reaction of oxygen with ethylene or simple alkenes. The syn singlet diradical, *syn*-**2N**-$\sigma\sigma$, smoothly cyclizes into **4** without activation, and the syn $\sigma\pi$ diradical, *syn*-**2N**-$\sigma\pi$ corresponds to the transition state for the internal rotation about the C–O bond. By RM3, **3** dissociates into ethylene and singlet oxygen without activation, so that the geometry of *syn*-**2N**-$\sigma\pi$ was used for the calculations on **3**. The relative stabilities among these intermediates **1**–**4** are summarized in Table I, where the GVB–CI plus thermochemical results are also listed.[4]

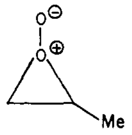
The syn $\sigma\pi$ diradical is more stable than the perepoxide, **1**, by 3.5 and 53 kcal/mol, using the UM3 and U3G methods, respectively. The UM3 result is compatible with the GVB result.[4] The zwitterion, **3**, is highly unstable in the absence of polar substitutents. On the other hand, dioxetane, **4**, is more stable than *syn*-**2N**-$\sigma\pi$ by 46 annd 24 kcal/mol, using the UM3 and U3G methods, respectively. The UM3 and U3G methods overestimate and underestimate the stabilities of the cyclic compounds **1** and **4**, respectively. The former provides rather similar energies to those by GVB–CI and thermochemical estimates.

The electronic structures of lowest singlet state must vary during the course of a $[_{\pi}2_s + {}_{\pi}2_s]$ reaction:

$$({}^1O_2 + C_2H_4)(A'') \rightarrow \mathbf{2}(A'') \rightarrow \mathbf{2}(A') \rightarrow \mathbf{4}(A')$$

The symmetry-forbidden diradical property of the path is in accord with previous work.[7-9,13] Thus there is no discrepancy between the GVB and Hartree–Fock (HF) type MO calculations, as long as UHF calculations are used for calculations on open-shell (diradical) species.[13] The only remaining question is whether the correlation energies will alter the relative stabilities of **1** and **2**.

Full geometry optimizations of the perepoxide, **5**, and the syn $\sigma\pi$ diradicals, **6a** and **7a**, formed by the attack of $^1O_2$ on propene were also performed. The present UM3 calculations indicate that **7a** is more stable than **5** by about 7.9 kcal/mol. Thus the energy difference between the perepoxide and the diradical becomes even larger for the propene reaction than for the ethylene reaction. Therefore the UM3 results are also compatible with the GVB and thermochemical calculations by Harding and Goddard.[8] Harding and Goddard predicted that the $\sigma\pi$ diradical, **7a**, is more stable than **6a** on the basis of thermochemical estimates.[8] However, UM3 calculations predict the reverse tendency, **6a** < **7a**; that is, the Markovnikov effect is observed. In order the confirm this result, we have performed full geometry optimizations of these intermediates at the ab initio STO-3G level. The U3G calculation also showed that **6a** is more stable than **7a** by 1.9 kcal/mol.[16]



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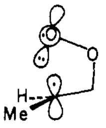
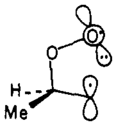
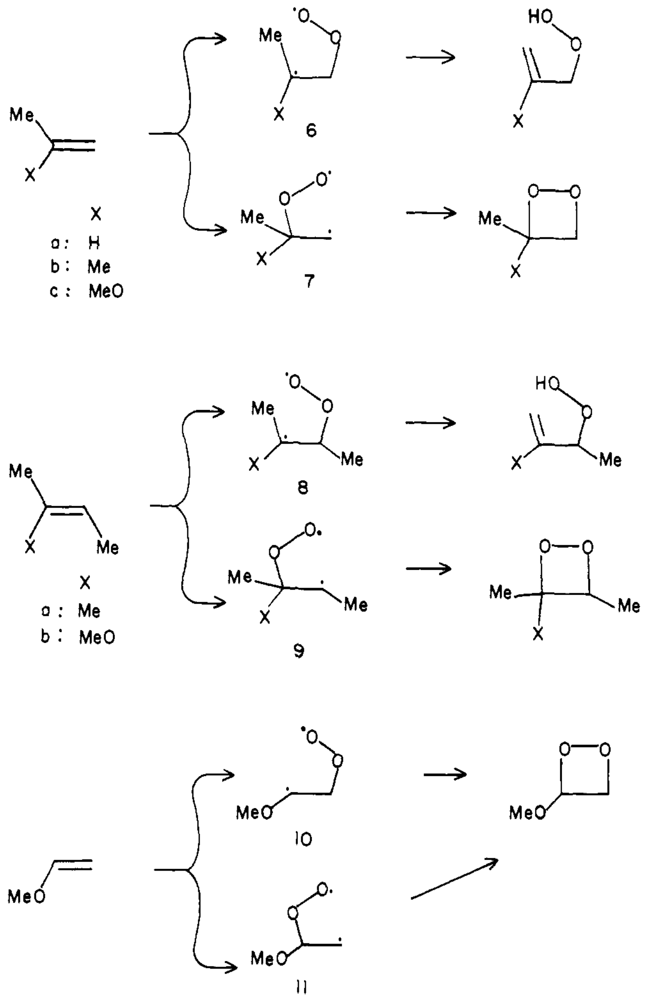


6a



7a

Scheme III



Unrestricted MINDO/3 calculations have also been carried out on a variety of hypothetical substituted diradicals which could be formed by attack of singlet oxygen on alkylethylenes and vinyl ethers, as shown in Scheme III. Table II summarizes the energy differences obtained, along with the energies of the corresponding perepoxides. In most cases, the $\sigma\pi$ diradical is more stable than the $\pi\pi$, and anti species are more stable than the syn. Most importantly, the Markovnikov directing effects are found for these species, in contradiction to thermochemical estimations.[8] Therefore the low or anti-Markovnikov regioselectivities observed for the ene reactions of the trisubstituted ethylenes cannot be rationalized by assuming the diradical intermediates shown in Scheme III. An alternative explanation based upon rotational barriers in alkylethylenes, and a concerted mechanism, has been proposed.[5a]

Finally, we have considered the barriers to rotation which would be expected in diradicals such as **2** and more highly substituted

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(16) Similarly the Markovnikov directing effect is recognized in the case of the addition reaction of O atom (^3P) to propene, being consistent with experimental results: Strausz, O. P.; Gosavi, R. K.; Demare, G. R.; Peter, M. R.; Csimadia, I. G. *Chem. Phys. Lett.* **1980**, *70*, 31.

Table II. Relative Energies (kcal/mol) of Potential Diradical and Perepoxide[a] Intermediates in Reactions of Singlet Oxygen with Electron-Rich Alkenes, According to UM3 Calculations

		$\sigma\pi$			$\pi\pi$	
alkene	intermediate	anti	syn		anti	syn
propene	**6a**	0.0[b]	0.7		−0.4	0.7
	7a	10.1			9.9	
	perepoxide			8.6		
2-methylpropene	**6b**	0.0[c]	1.0		0.9	3.8
	7b	19.9			19.8	
	perepoxide			13.3		
2-methoxypropene	6c	0.0[d]	1.0		3.2	5.7
	7c	22.9			22.9	
	perepoxide			2.13		
2-methyl-2-butene	**8a**	0.0[e]	1.2		0.9	
	9a	9.7			8.8	
	perepoxide			7.2		
2-methoxy-2-butene	**8b**	0.0[f]			5.7	
	9b	12.7			13.3	
	perepoxide			13.8		
methoxyethylene	**10**	0.0[g]	1.0		3.6	8.2
	11	14.9			15.1	
	perepoxide			16.6		

[a] The exocyclic oxygen is syn to the methyl or methoxy groups. [b] −1088.339 eV. [c] −1245.056 eV. [d] −1556.450 eV. [e] −1401.637 eV. [f] −1713.094 eV. [g] −1299.555 eV.

derivatives. The syn and anti forms of the $\sigma\pi$ diradical are eclipsed and staggered about the C–O single bond as illustrated in Scheme II. The former corresponds to the local maximum on the potential surface for the internal rotation of the O_2 group around the C–O bond. The relative energies given in Table II demonstrate the 0.7–3.1 preference of the anti (staggered) over the syn (eclipsed) geometries. Thus, it is unreasonable to assume that the syn $\sigma\pi$ diradical is a plausible intermediate in ene reactions.[8] On the other hand, the anti $\sigma\pi$ diradical might be a true intermediate for the reactions. However, if so, the internal rotations of alkyl and alkoxy groups should be facile, since the bonding interactions between the 1,4-diradical sites are negligible. In order to confirm this point we have performed full geometry optimizations on the $\pi\pi$ diradicals, **2R**-$\pi\pi$, and substituted derivatives. The energy differences between the anti $\sigma\pi$ and $\pi\pi$ diradicals are very small, indicating essentially free rotation of these groups. The situation is similar even for the syn conformers. This implies that the ene reaction between singlet oxygen and a suitable substituted alkene or enol ether would be nonstereospecific if the diradical were an intermediate in these reactions. As mentioned previously,[1,10] stereospecificity has been observed experimentally.

The geometries of the terminal carbon radical centers of the $\sigma\pi$ and $\pi\pi$ diradicals are found to be similar to those of corresponding alkyl and alkoxy free radicals, which are known to have very small rotational barriers.[17] The C–O and O–O bond lengths are essentially identical with the corresponding optimized bond lengths of peroxide radicals. Thus the 1,4-diradicals examined here may be regarded simply as the coupled states of two free radicals. The optimized geometries of the diradicals, **7c**, **8b**, and **11**, formed by α attack on enol ethers exhibit a characteristic conformation of the O_2 group with respect to the MeO. Similar conformations are observed for ethanediol-like species. This conformation is characteristic of an "anomeric effect" stabilization.[4,8] In spite of such stabilization, however, the relative stabilities of the diradicals are normal; the more substituted radical is more stable. Thus it seems difficult to regard the anomeric effect as a determining factor of the anti-Markovnikov-type regioselectivities observed for ene reactions, although it plays an important role for conformational stabilizations of methanediol species.

Although both the UM3 and U3G, and GVB calculations predict the greater stability of the $\sigma\pi$ diradical intermediate than the perepoxide intermediate in the case of alkenes and enol ethers, as shown in Tables I and II, they do not prove that ene reactions of these species proceed through a diradical mechanism.[4,8] Indeed, theoretical results described here and experimental results are not compatible with the diradical mechanism.[1,5,10] Although our theoretical evidence is circumstantial rather than direct, we feel that these results exclude all but concerted mechanisms, with simultaneous CO and OH bond making.

Acknowledgment. The ab initio HF (STO-3G) calculations were carried out at the Institute for Molecular Science (Okazaki, Japan). The author (K.Y.) thanks Professor K. Morokuma and Dr. S. Kato for their discussions. Financial support of this research from the National Science Foundation (to KNH) is gratefully acknowledged.

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(17) Krusic, P. J.; Meakin, P.; Jesson, J. P. *J. Phys. Chem.* **1971**, *15*, 3438.

(18) (a) Gollnick, K. *Adv. Photochem.* **1968**, *6*, 1. (b) Foote, C. S. *Pure Appl. Chem.* **1972**, *27*, 635.

(19) Singlet molecular oxygen ($^1O_2$) may simultaneously attack the π bond and the allylic hydrogen in the initial stage of ene reactions as shown in a previous paper: Yamaguchi, K. *Jpn. Chem. Rev.* **1973**, *1*, 292. This model emphasizes the importance of the attack of the C–C double bond instead of the terminal carbon atom as in the case of perepoxide model, but it requires participation of allyl hydrogen for maximizing the allowed orbital interactions.

The Origin of the Pyramidalization of the *tert*-Butyl Radical

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Received November 7, 1980

Abstract: The pyramidal nature of the *tert*-butyl radical is confirmed by ab initio UHF calculations with the 4-31G basis set. Each CH_3–C· bond is predicted to be 22.1° out of the plane of the $\cdot C(CH_3)_2$ group. The calculated barrier to inversion is 1.2 kcal/mol. The transition state for inversion has C_{3h} symmetry, while the energy minimum has C_{3v} symmetry, so that methyl rotation is synchronized with inversion. The pyramidalization of *tert*-butyl simultaneously maximizes hyperconjugative stabilization of the radical, and minimizes torsional interactions between the methyl groups and the radical center.

The geometry of the *tert*-butyl radical has been a matter of considerable dispute during the last decade. Prior to 1972, this species was generally conceded to have a planar carbon skeleton with a low out-of-plane bending force constant, much like the

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