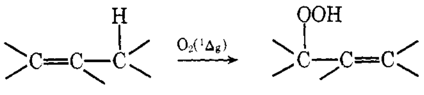
Transition State Geometry in Hydroperoxidation of Monoolefins with Singlet Oxygen[1]

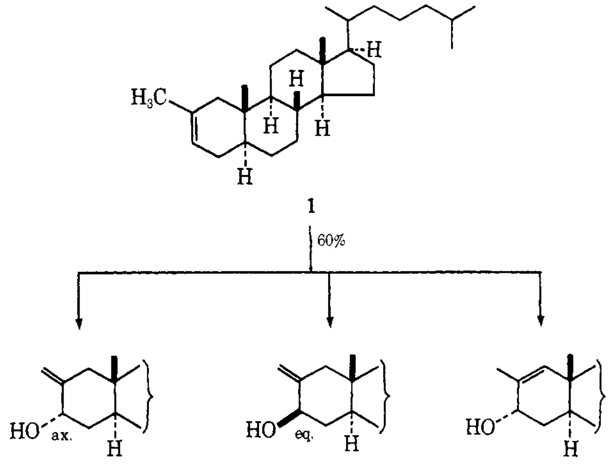
Sir:

Singlet oxygen is of interest for its synthetic, mechanistic, biological, environmental, and theoretical aspects.[2] Much information on its chemical behavior has come from studies on the allylic hydroperoxidation of monoolefins, a reaction believed to proceed by a cyclic ene mechanism with little ionic character.[3] This ene reaction involves considerable change in substrate geometry, and an important mechanistic goal is to define the extent of these changes in the transition state.[4] Such knowledge is necessary for prediction of product ratios, particularly in ring systems where steric effects can be pronounced and where stereoelectronic factors can govern the ease of cleavage and formation of allylic bonds.[5] We now present stereochemical and isotope effect evidence that the transition state resembles the starting olefin and that there is no strong inherent preference for creation of an axial type C–O bond over an equatorial type. Therefore the frequent predominance of axial hydroperoxides as primary products[2a,b,g,6] is largely a consequence of the cis, cyclic mechanism, in which abstraction of axial C–H is favored because of its better orientation for cyclic transfer.



Our chemical approach utilized steroids **1** and **5** in which ring-inversion ambiguities are precluded and in which the allylic CH$_3$'s have conformationally mobile hydrogens that can adopt optimum, or at least equivalent,[7] alignment above or below the olefinic plane. Consequently, ratios of epimeric products that arise from abstraction of methyl hydrogens reveal factors that influence formation of the C–O bond. Initially, attacks from above and below the π-olefinic unit are stereoelectronically (but not necessarily sterically) equivalent, and differences in allylic overlap develop only as the geometry approaches that of the product, in which the C–O becomes either axial or equatorial. Therefore, the degree of stereoelectronic control (*i.e.*, preference for axial C–O) reflects how far the transition state geometry lies along the reaction coordinate.[5]

We photooxygenated **1** and **5** in pyridine at *ca.* 35° with hematoporphyrin and reduced the hydroperoxide mixture to alcohols, which were assayed by combinations of infrared, nmr, and polarimetric methods.[8] Olefin **1** gave three alcohols (**2**, **3**, and **4**) in the ratio 57:13:30, and olefin **5** gave two alcohols (**6** and **7**) in the ratio 70:30.[9] The slight preference (*ca.* 4.4:1) for **2** (axial OH) over **3** (equatorial OH) shows the relative unimportance of stereoelectronic control in C–O formation.[10] The absence of the epimer of **7** in the oxidation of **5** strengthens this conclusion because it shows that a single 1,3 interaction with the angular methyl group at C-10 completely overrides any stereoelectronic factors.[10]



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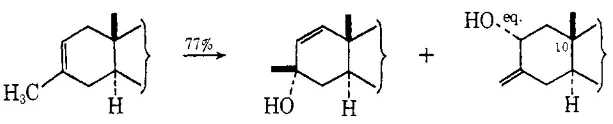
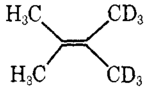
2 (57%) **3** (13%) **4** (30%)



5 **6** (70%) **7** (30%)

Information on the cleavage of the C–H was obtained from studies of deuterium isotope effects. In oxygenation of **8**, **9**, and **10** (the latter two as mixtures of cis and trans isomers), the competition between H and D abstraction is intramolecular, and the mass spectral d_6/d_5 ratios of derived alcohols provide k_H/k_D.[11]



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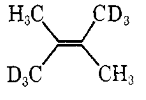

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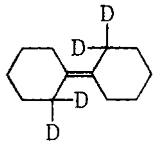

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(1) Supported by the National Institutes of Health, Grant GM 09693.

(2) For reviews see: (a) K. Gollnick, *Advan. Photochem.*, **6**, 1 (1968); (b) C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968); (c) C. S. Foote, *Science*, **162**, 963 (1968); (d) T. Wilson and J. W. Hastings, "Photophysiology," Vol. V, A. C. Giese, Ed., Academic Press, New York, N. Y., 1970, p 49; (e) I. R. Politzer, G. W. Griffen, and J. L. Laseter, *Chem.-Biol. Interactions*, **3**, 73 (1971); (f) D. R. Kearns, *Chem. Rev.*, **71**, 395 (1971); (g) R. W. Denny and A. Nickon, *Org. React.*, in press.

(3) A different mechanism has been proposed by W. Fenical, D. R. Kearns, and P. Radlick (*J. Amer. Chem. Soc.*, **91**, 3396, 7771 (1969)) but some of their interpretations have been questioned (C. S. Foote, T. T. Fujimoto, and Y. C. Chang, *Tetrahedron Lett.*, 45 (1972); K. Gollnick, D. Haisch, and G. Schade, *J. Amer. Chem. Soc.*, **94**, 1747 (1972)) and modified (N. Hasty, P. B. Merkel, P. Radlick, and D. R. Kearns, *Tetrahedron Lett.*, 49 (1972)).

(4) H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 556 (1969).

(5) (a) G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, **82**, 1512 (1960); (b) G. Stork and J. Tsuji, *ibid.*, **83**, 2783 (1961); (c) H. O. House and H. W. Thompson, *J. Org. Chem.*, **28**, 360 (1963); (d) M. J. T. Robinson, *Tetrahedron*, **21**, 2475 (1965); (e) G. Subrahmanyam, S. K. Malhotra, and H. J. Ringold, *J. Amer. Chem. Soc.*, **88**, 1332 (1966).

(6) (a) A. Nickon and J. F. Bagli, *ibid.*, **81**, 6330 (1959); (b) A. Nickon and W. L. Mendelson, *Can. J. Chem.*, **43**, 1419 (1965); (c) A. Nickon, N. Schwartz, J. B. DiGiorgio, and D. A. Widdowson, *J. Org. Chem.*, **30**, 1711 (1965).

(7) The equivalence should also hold for the lowest energy CH$_3$ conformer. D. R. Herschbach and L. C. Krishner, *J. Chem. Phys.*, **28**, 728 (1958).

(8) With the exception of **2**, all allylic alcohols were identified by comparison with authentic samples.

(9) Of the six alcohols possible from **1** and from **5**, three from each substrate were not expected on the basis of known stereochemical restrictions.[6]

(10) Contrast strong axial preferences in other reactions involving allylic bonds, even in opposition to marked steric hindrance.[5]

(11) Details regarding syntheses, *d* assays, controls, etc., will be reported in full elsewhere.

Table I summarizes the results and reveals consistently low, positive k_H/k_D values under a variety of experimental conditions.[12] Low primary isotope effects (*cf.* Table I) for linear H transfer reactions are expected when the hydrogen in the activated complex is much more tightly bound to one atom than to the other.[13,14] This condition is met in the oxygenation transition state if the C–H bond is either weakened very little or is nearly broken,[15] and only the former possibility is compatible with our C–O stereochemical findings.

Table I. Deuterium Isotope Effects in Singlet Oxygen Reactions by Intramolecular Competition (20–35°)[a]

Substrate	Generation of singlet O_2	Solvent	k_H/k_D
8	Seven sensitizers[b]	CH_3OH	1.80–1.96[c]
8	Methylene Blue	Pyridine	1.85
8	Two sensitizers[d]	Benzene	1.78–1.81
8	NaOCl, H_2O_2	$CH_3OH–H_2O$	2.37–2.42
9	Two sensitizers[e]	CH_3OH	1.28–1.43[c]
9	NaOCl, H_2O_2	$CH_3OH–H_2O$	1.76–1.77
10	Rose Bengal	CH_3OH	1.18–1.20[c]

[a] 2,4,6-Tri-*tert*-butylphenol was added as a radical inhibitor in most cases. [b] Methylene Blue, hematoporphyrin, Rose Bengal, Erythrosine B, Eosine Y, fluorescein, and riboflavin. [c] Assay by nmr gave k_H/k_D values that were *ca.* 0.1 lower for **9** and **10** and 0.4 lower for **8**. Similar values have been obtained by K. R. Kopecky, J. H. Van de Sande, and C. Mumford (*Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **16**, No. 4, A65 (1971)) in their nmr studies of isotope effects. [d] Zinc tetraphenylporphin and 1,8-dinaphthalenethiophene. [e] Methylene Blue and Rose Bengal.

The combined stereochemical and isotope effect results therefore reveal a product-forming transition state in which oxygen, while bonded partially to olefinic carbon and to allylic C–H, has neither much perturbed the olefin geometry nor extensively weakened the C–H bond. Among other things, these findings clarify why thermodynamic stability of the final double bond has little effect on the reaction,[16] why conformational ring inversion (which sometimes must accompany a double bond shift) does not block oxygenation,[6b,c] and why the susceptibility of C–H to abstraction is not inherently related to whether it is primary, secondary, or tertiary.[2,17]

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(12) The slightly greater electron donor effect and slightly smaller size of CD_3 relative to CH_3 could influence the site of attack in the unsymmetrical olefin **8**, but not in **9**. We are currently studying intermolecular isotope effects to probe these points. Note that for a transition state that resembles reactant (*i.e.*, no hybridization change at CD_3) there should be virtually no secondary (*i.e.*, α) isotope effect (A. Streitwieser Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Amer. Chem. Soc.*, **80**, 2326 (1958)).

(13) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961); J. Bigeleisen, *Pure Appl. Chem.*, **8**, 217 (1964); R. A. More O'Ferrall and J. Kouba, *J. Chem. Soc. B*, 985 (1967).

(14) W. A. Pryor and K. G. Kneipp, *J. Amer. Chem. Soc.*, **93**, 5584 (1971).

(15) Bending modes could also be responsible for low isotope effects if the hydrogen has to be transferred *via* a severely angled transition state. However, More O'Ferrall has pointed out that six-membered cyclic transition states are not subject to such constraints, and Kwart and Latimore have presented experimental support for cases of cyclic transfer from oxygen to carbon. R. A. More O'Ferrall, *J. Chem. Soc. B*, 785 (1970); H. Kwart and M. C. Latimore, *J. Amer. Chem. Soc.*, **93**, 3770 (1971).

(16) *E.g.*, caryophyllene is only slightly more reactive than its less strained isomer isocaryophyllene (F. A. Litt and A. Nickon, *Advan. Chem. Ser.*, **No. 77**, 118 (1968)); terminal open-chain olefins and methylene cycloolefins react sluggishly. See ref 2a, b, g and K. R. Kopecky and H. J. Reich, *Can. J. Chem.*, **43**, 2265 (1965). See also behavior of germacrene (T. W. Sam and J. K. Sutherland, *J. Chem. Soc., Chem. Comm.*, 424 (1972)).

(17) Contrast the situation for homolytic cleavage of allylic C–H bonds. W. J. Farrissey, Jr., *J. Org. Chem.*, **29**, 391 (1964), and references cited therein.

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Some Reactions of Ground-State Magnesium Atoms

Sir:

There is no prior literature concerned with the reactions of ground-state atomic magnesium.

High vacuum (~10^{-5} Torr) evaporation of magnesium can be carried out essentially as was done with carbon,[1] from a resistively heated crucible to produce ground-state magnesium (^1S) or by arcing to produce in addition a population rich in metastable[2] excited state (^3P). We report here some reactions which occur on codeposition at liquid nitrogen temperature of ground-state magnesium atoms and a large excess of substrate (>100:1).

The codeposition of magnesium atoms with water at −196° results in greater than 90% yields of H_2 during the codeposition, 1 mol of H_2 per mol of Mg. The same hydrogen yields are obtained in codeposition of magnesium with anhydrous hydrogen bromide.

By contrast, codeposition with ammonia produces H_2 in only 2.4% yield and a bright maroon matrix. On slight warming the maroon is replaced by a briefly transient blue color before becoming colorless. During the warm-up, with pumping, 7–25% of the theoretical H_2 is released. The residue is mainly magnesium, since addition of deuterium oxide releases the hydrogen as greater than 80% D_2, and no NH_3, indicating only minor amounts of Mg–H, Mg–NH_3, or Mg–NH_2 are present. It will be reported elsewhere that excited state magnesium atoms show a different behavior.

Codeposition of magnesium atoms and neopentane produces a colorless matrix which deposits a film of metal on warming.

Alkyl halides codeposited with magnesium atoms produce a black matrix. Warm-up of the black matrices obtained from alkyl and aryl chlorides or bromides results in formation of colorless organomagnesium compounds, unsolvated Grignard reagents. Yields were determined by hydrolysis: *n*-propyl iodide, 76%; isopropyl bromide, 55%; *tert*-butyl bromide, 5%; chlorobenzene, 58%; vinyl bromide, 78% (latter product stable at −78°).

These organomagnesium compounds are not produced at −196°, but instead on warm-up. If the black matrix of *n*-propyl bromide and magnesium is prepared, the evaporation discontinued, and then methyl bromide is deposited on the black matrix, on warm-up methylmagnesium compounds are produced rather than propyl-. Further, if the propylmagnesium compound is

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(1) P. S. Skell, L. D. Wescott, J.-P. Goldstein, and R. R. Engel, *J. Amer. Chem. Soc.*, **87**, 2829 (1965).

(2) C. E. Moore, "Atomic Energy Levels," National Bureau of Standards, Washington, D. C., 1949, p 106.