Tetrahedron Letters Vol. 21, pp 1005 - 1008
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0040-4039/80/0308-1005$02.00/0

THE MECHANISM OF THE SINGLET OXYGEN ENE REACTION

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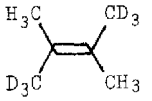
Summary: A complex between singlet oxygen and olefins is proposed in which frontier orbital interactions between the oxygen and both the olefin π orbitals and C-H bonds are important. Formation of this complex is proposed to dominate the chemistry of this reaction and is shown to be consistent with the available data.

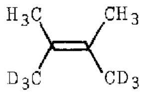
Although research into the nature of the singlet oxygen olefin reaction now spans a period of about fifty years,[1] no general agreement on the characteristics of the reaction mechanism exists. Several significant new findings are summarized here and are incorporated into a new view of this reaction.

1. The reaction is stereospecific, occurring in a suprafacial manner with respect to the ene unit. This result has been confirmed for one cyclic,[2a] and many di-[3c] and trisubstituted[2b] acyclic olefins.

2. The deuterium isotope effect, never very large in this reaction,[3a-d] *is dependent on the relative placement of the competing groups.*[3d] Most convincing here are the data for the *cis* and *trans* tetramethylethylene-d_6 isomers.

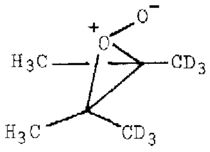


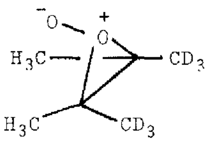
$k_H/k_D = 1.41 \pm 0.03$

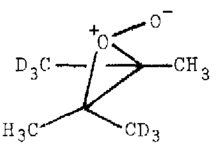


$k_H/k_D = 1.07 \pm 0.04$

These results show that groups with *cis* relationships are competitive, while groups with geminal and/or trans relationships are not. Traditional reasoning applied to these experiments would appear to demand an intermediate in the reaction with rather substantial stereochemical constraints. A perepoxide, irreversibly formed, and which does not undergo pyramidal inversion

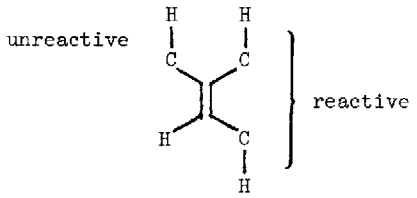






before hydrogen abstraction, is satisfactory to explain *this result*,[3d] but perhaps not others.

3. The reactions of singlet oxygen show an unusual preference for hydrogen abstraction on the disubstituted side of trisubstituted olefins,[4] and for *cis* disubstituted olefins over *trans*.[1a]

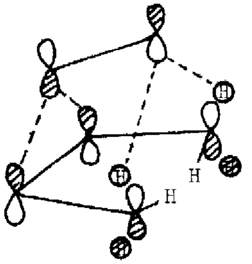


In the absence of gross conformational effects, this result is general with a variety of substituents; e.g., phenyl, alkyl, cycloalkyl, and methoxy. Steric arguments would make the prediction that reactivity[4] would be highest on the least crowded side for both the perepoxide and the concerted reaction.

4. Calculations of Goddard and Harding[5] show (GVB-CI level) that ethylene perepoxide has a higher enthalpy of formation than the known activation enthalpy for the reaction of propylene and singlet oxygen. This calculation appears to be reliable, specifically since high accuracy in the calculation of similar *known* heats of formation (i.e., ethylene oxide) has been demonstrated. The extension of this conclusion to more highly substituted systems has been argued to be sound.

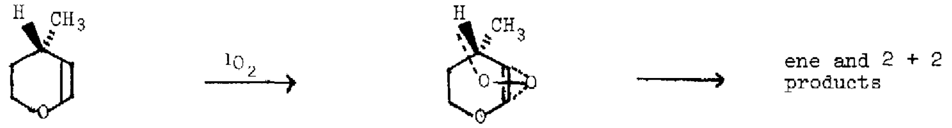
Thus, an interesting dichotomy exists. Intermediates with the structural characteristics of perepoxides are required by isotope effect data and stereochemical experiments. On the other hand, the unusual regioselectivity in the trisubstituted olefins does not lend itself to obvious explanation by a perepoxide or other traditional mechanisms. Calculations also suggest that perepoxides are inappropriate descriptions. Other orientational effects support dipolar intermediates,[6] but such intermediates completely fail to rationalize the recent isotope effect data, and thus cannot be generally applicable.[7]

The low activation energies in this reaction, as in many other photochemical reactions, suggest that orientation preferences in a π or charge transfer complex might determine many characteristics of the reaction. Frontier molecular orbital thoery provides valuable insight here. The strongly electrophilic nature of singlet oxygen suggests that the HOMO-olefin LUMO-oxygen interaction might be particularly dominant in this case. The olefin HOMO for a system like 2-butene has contributions from both the olefin π and the $-CH_3$ pseudo π orbitals,[8] creating



an orbital array similar to Ψ_3 for butadiene. With the LUMO oxygen π^*-like, it is clear that satisfactory frontier orbital overlap is achieved in a complex of C_s symmetry.[9] If the attractive forces in such a complex are sufficiently strong, one has the operational equivalent of the perepoxide, creating a satisfactory rationalization of the isotope effect data which implicate *cis* competition only. This interaction would be expected to be stronger in cis-2-butene than in trans, where only one alkyl carbon π orbital can be involved at one time, and thus provides clear explanation of the trisubstituted olefin data. The effect would remain substantial for a variety of substituent types, and would be expected to be even more important for $-O-CH_3$ groups, where high lying n-orbitals can participate. The methoxy group appears to be a strong cis director, an effect which has been variously rationalized previously.[5,10,11]

Bartlett and co-workers[12] have proposed a similar complex, a crisscross O_2-olefin complex to rationalize isotope effect data for the enol ether below. Bartlett's work, and ours, provides strong evidence for a non-least-motion pathway in the ene reactions (and in Bartlett's case for 2 + 2 cycloaddition as well). Our present proposal modifies the Bartlett intermediate by providing greater structural detail and by providing an orbital basis. Our proposal represents an equally satisfactory rationalization of the data from Bartlett's lab.



To be an effective explanation of the singlet oxygen reaction, this complex must be formed essentially irreversibly.[13] This implies that activation energies for the steps which follow, C-O bond formation and C-H bond breaking, must be of similarly low activation energy. This provides a reasonable explanation for the uncharacteristically low isotope effects found in this ene reaction.[14]

A complex such as that proposed here provides a coherent rationalization of the recent results in this area (listed earlier) and does not conflict with previously established work in this field. The details of this reaction which follow complex formation remain interesting. For example, the complex could relax to a perepoxide, could move smoothly into the bond-making and bond-breaking events, or could form dipolar intermediates in special cases.[7] The very low activation barriers required for the following reactions suggest that the surface may be more amenable to theoretical than experimental approaches at this point. The explanation proposed here and the recent associated data clearly suggest that future sophisticated calculations in this field can be profitably carried out only on systems at least as complex as 2-butene.

Acknowledgement: This work was supported by the National Science Foundation through Grant CHE 78-21153. The author is grateful to Notre Dame College of Ohio for considerable hospitality during stays in Cleveland.

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(Received in USA 8 November 1979)