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FRONTIER MOLECULAR ORBITAL BASIS FOR THE STRUCTURALLY DEPENDENT REGIOSPECIFIC REACTIONS OF SINGLET ($^1\Delta_g$) OXYGEN WITH POLYOLEFINS

Leo A. Paquette* and Dennis C. Liotta
Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210
A. D. Baker*
Department of Chemistry, Queens College of C.U.N.Y., Flushing, New York 11367

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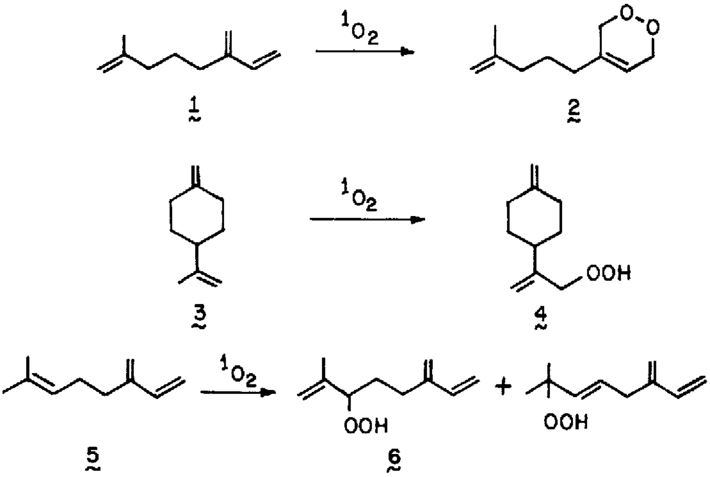
Sensitized photooxygenation plays a utilitarian role in organic synthesis as the result of singlet ($^1\Delta_g$) oxygen's ability to effect clean allylic hydroperoxidation of alkenes and efficient endoperoxidation of 1,3-dienes.[1] Recent years have seen major attention directed toward a more precise definition of the mechanisms of these reactions.[2] In this paper we present observations of a new type which combine to provide a quantitative basis for the regiospecificity of $^1O_2$ reactivity in molecules containing two or more differing reactive sites. The present treatment, which is independent of mechanistic detail, should facilitate the premeditated design of experiments where site-specific oxygenation is desired.

In general terms, the reactivities of various π systems toward $^1O_2$ appear to follow the order: 1,3-diene > isopropylidene > endocyclic trisubstituted olefin > endocyclic disubstituted olefin > isopropenyl > exomethylene. This qualitative ranking which is exemplified by the behavior of α-myrcene (1)[3] and psi-limonene (3)[4] has been attributed to the nucleophilic idiosyncrasies of a mildly electrophilic reagent.[1a] However, exceptions to this ranking are known, as witnessed for example in the case of β-myrcene (5) which is attacked exclusively as its isolated double bond,[3] and have remained a source of some consternation.

When viewed from the frontier molecular orbital viewpoint whose development has been pioneered by Fukui,[5] the regiospecificity exhibited by 5 is not anomalous. Under the terms of this approximative treatment, the separations between the HOMO's and LUMO's of the pair of reactants and the orbital coefficients on the carbon atoms representing the reaction sites have a direct quantitative bearing on the energies of the competing transition states.[6] From the ionization potential (-11.09 eV)[7] and electron affinity (-0.43 eV) data[8] reported for oxygen, it is clear that the influence of HOMO_{O_2}-$\mathrm{LUMO}_{\mathrm{alkene}}$ and HOMO_{O_2}-$\mathrm{LUMO}_{\mathrm{diene}}$ interactions need not be considered further since they are comparatively weak.[9] The important criteria



then become the coefficients of the sp^2-hybridized carbons in the various segments of the polyolefinic substrate and the relative magnitudes of the HOMO$_\pi$-LUMO$_{O_2}$ gaps. This relationship is expressed mathematically in equation 1 where $C_{HO}^{\pi 1}$ and $C_{HO}^{\pi n}$ represent the coefficients

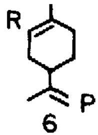
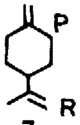
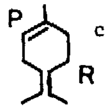
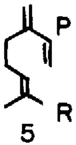
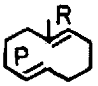
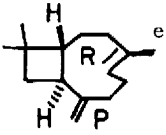
$$\Delta E = \frac{C_{HO}^{\pi 1} \bullet C_{LU}^{o1} + C_{HO}^{\pi n} \bullet C_{LU}^{o2}}{E_{HO}^{\pi} - E_{LU}^{o}} \qquad (1)$$

at carbon 1 and the nth carbon (C-2 for olefin; C-4 for diene) of the π system and C_{LU}^{o} represents the coefficients on the two oxygen atoms in their lowest vacant orbital. By application of Koopmans' theorem,[10] ionization potentials (I.P.) can be directly equated to the negatives of the orbital energies (E), thereby permitting such information to be obtained directly by photoelectron spectroscopic measurement.

As Table I reveals, the 2-substituted 1,3-butadiene moieties in α- (1) and β-myrcene (5) have nearly identical I.P.'s of ~ 8.6 eV as expected.[11] For 1, this band is the HOMO since the isolated π bond exhibits its maximum at 9.13 eV (compare 2-methylpentene, 9.07 eV).[12] In contrast, the trisubstituted nature of the nonconjugated double bond in 5 raises its energy to 8.48 eV so that orbital crossover takes place and it becomes the HOMO site. This effect is directly correlatable with the regiospecificity of $^1O_2$ attack.

An entirely comparable situation operates within the limonene (6)—α-terpinolene (7) pair. Here the endocyclic double bond present in both structures exhibits an IP of 8.6 eV. Its level of alkyl substitution causes the isopropenyl group in 6 (9.05 eV) to be lower in energy, a fate shared by the exo-methylene group in β-caryophyllene (9) for the same reasons. In contrast, the HOMO of 7 is localized in its external fully alkylated double bond (8.27 eV).

Table I. Correlation Between Ionization Potentials of Polyolefins and Regiospecificity of Attack by Singlet ($^1\Delta_g$) Oxygen.[a]

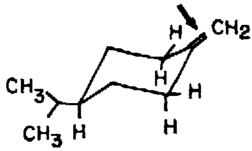
Hydrocarbon	Ionization potentials (eV)		Hydrocarbon	Ionization potentials (eV)	
	Reactive center (R)	Passive center (P)		Reactive center (R)	Passive center (P)
 R P 1	8.6_3	9.1_3	 R P 6[b]	8.6_0	9.0_5
 P R 3	9.1_0	8.9_5	 P R 7[c]	8.2_7	8.6_3
 P R 5	8.4_8	8.6_8	 R P 8[d]	7.8_5	9.6
			 H R H P 9[e]	8.7_0	9.1_5

[a] All spectra were obtained on a Perkin Elmer PS 18 photoelectron spectrometer using the He I excitation line and calibration was effected using He Iα (21.2 eV) and He Iβ (23.1 eV) on methyl iodide, xenon, argon, and nitrogen. [b] K. Gollnick, T. Franken, G. Schade, and G. Dorhofer, Ann. N.Y. Acad. Sci., 171, 89 (1970). [c] See reference 4. [d] S.-K. Chung and A. I. Scott, J. Org. Chem., 40, 1652 (1975). [e] K. H. Schulte-Elte and G. Ohloff, Helv. Chim. Acta, 51, 494 (1968).

Bischof and Heilbronner have previously shown the π bands of trans,trans-1,6-cyclodecadiene to be somewhat anomalous (8.05, 9.75 eV) because of prevailing transannular interactions.[13] The additional C_1 methyl group in 8 seemingly little perturbs the through-space phenomenon, but does give rise to an expected increase in the C_1C_2 π orbital energy (0.2 eV).

The above discussion tacitly assumes the $E^{\pi}_{HO} - E^{O}_{LU}$ gaps to be the major factor in determining regiospecificity. Actually, a common assumption is that the relevant orbital coefficients do not vary sufficiently within a given series of compounds to be of significance.[6] While we fully agree that this supposition likely presents no major difficulties when a group of similar reactions are being considered, the comparison of different types of reaction (e.g., the ene process and (4+2) cycloaddition) should be made with caution, particularly when the energy separations are known to be small. We believe the present correlation to be successful because olefin and diene coefficients are not greatly dissimilar.[14] It is all the more remarkable in that the diene moieties in 1 and 5 probably do not exist in the cisoid forms demanded of the transition state for (4+2) cycloaddition.

Since the model utilized herein measures reactivity only in terms of the electronic properties of the isolated reactants, steric effects which are known to play a deleterious role in $^1O_2$ chemistry[1] can be expected to cause major discrepancies. The behavior of psi-limonene (3) is a case in point. In light of the proximity of its ionization potentials, the assignments in Table I are best regarded as tentative. Notwithstanding, 3 like 10 (which is completely unreactive to $^1O_2$)[4] and 11 (which reacts to give 12)[4] finds it sterically impossible to experience allylic hydroperoxidation toward the ring. This is because kinetically preferred axial attack (compare $LiAlH_4$ reduction[15] and methylenation with $(CH_3)_2S{=}CH_2$[16] of 4-tert-butylcyclohexanone) does not result in access to an in-plane allylic hydrogen. Since a comparable steric barrier does not surround the isopropenyl group, this center is oxygenated exclusively in 3.[17]



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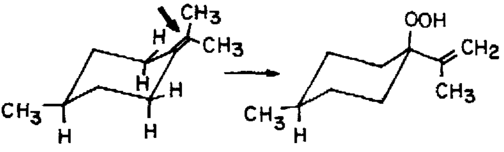

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FOOTNOTES AND REFERENCES

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(9) Reactive olefins and dienes usually has I.P.'s less than 9.5 eV, while their E.A.'s are estimated to be between 0 and -2 eV.

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