

252. The Hydroperoxidation of Olefins by Singlet Oxygen. Validity of the Zwitterionic Peroxide Model

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Summary

The regioselectivity of the hydroperoxidation of tetrasubstituted olefins by singlet oxygen is rationalized in terms of the zwitterionic peroxide model.

The mechanism of the reaction of singlet oxygen with monoolefins to give hydroperoxides, despite the accumulation of much data over the years, still awaits complete definition [1]. New findings have now emerged which permit a more detailed interpretation of the reaction. The chief of these, to our mind, are: 1) the pronounced effect of solvent and substituents on the reaction course [2-4], 2) the dichotomy of hydroperoxidation and dioxetane formation as a function of solvent polarity [5-11], 3) the selectivity of isotope partitioning in hexadeuteriated tetramethylethylenes [12] [13] and 4) the *syn* regioselectivity observed for trisubstituted olefins [14-19].

We believe that these phenomena can be generally accommodated by the zwitterionic (ZI) [20] model. The model is based on the consideration that oxygen adds to an olefin *via* a two-part transition state which may possess a trough where an intermediate could lie (Fig. 1). Bond formation at the end vinyl atom C(1) is rate-determining and precedes hydrogen-abstraction at C(3). The resulting transition state is polarized to an extent which depends on the nature of the substituents and the medium [21] [22]. A zwitterion would be favored by a π -donor substituent at

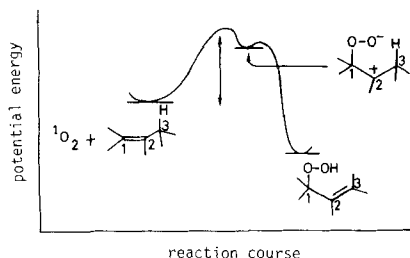
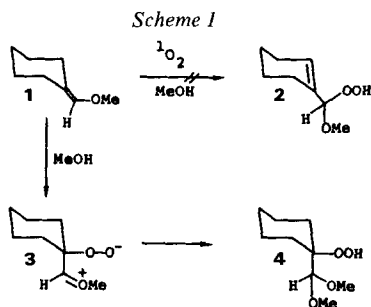


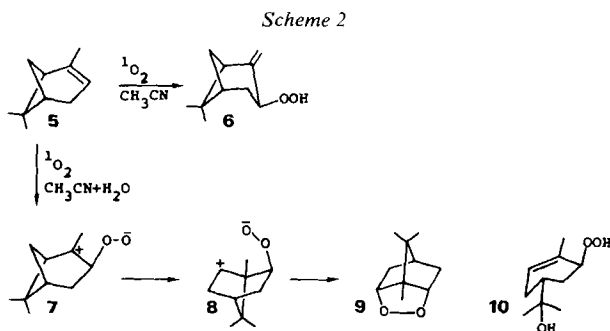
Figure. Hypothetical potential energy profile for the hydroperoxidation of an olefin by singlet oxygen



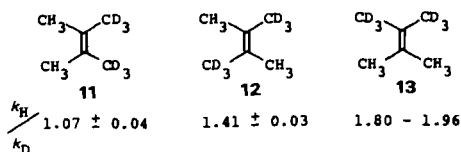
C(2) and by polar solvents. If an external proton is available and captured, then a rearrangeable cation could form. Abstraction of an internal proton is more demanding and depends on the configurational and conformational changes required to achieve propinquity with the hyperconjugated H-atom.

This model is confirmed by the marked effect solvent alcohol has on the photooxygenation of methoxymethylidenecyclohexane (1) [11]. Hydroperoxidation to 2 is suppressed and the intermediate zwitterion 3 leading to dioxetane is captured to give the corresponding alkoxy derivative 4 (Scheme 1). More strikingly, α -pinene (5, Scheme 2) which, on reaction with singlet oxygen in acetonitrile normally [23] gives the expected hydroperoxide 6, rearranges in aqueous conditions *via* cationic intermediates, 7 and 8, to *endo*-epidioxybornane 9 and hydroperoxymenhenol 10 [2].

Notwithstanding the conviction conveyed by these examples, difficulties of interpretation have been experienced regarding the apparently puzzling, yet informative, isotope effects observed with certain tetrasubstituted ethylenes [12] [13] and 4-methyl-2,3-dihydro- γ -pyran [8]. Accordingly, we judge the moment opportune to provide clarification with the aid of the ZI model [20]. The (*Z*)- (11), (*E*)- (12) and geminal (13) dimethyldi(trideuteriomethyl)ethylenes constitute a test case (Scheme 3). Photooxygenation gives the expected hydroperoxides, in which ^1H - or ^2H -abstraction is characteristically partitioned (Scheme 3). By way of explanation [24] [25], the Fukui secondary orbital interaction model has been recently resurrected. A molecule of oxygen is supposed to initially attack all ethylenes in exactly



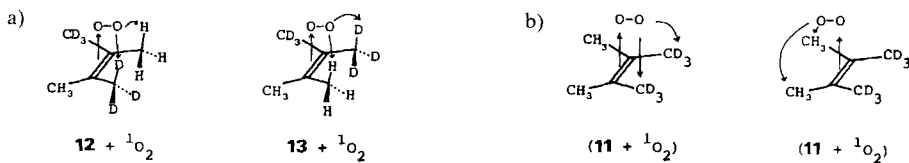
Scheme 3



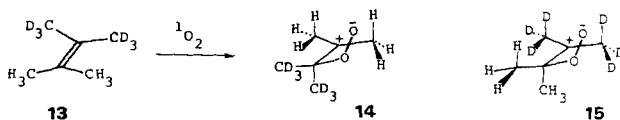
the same way, having equal chances of achieving a complex of C_s symmetry where the first and second O-atom lie evenly between the vinyl and allylic C-atoms, respectively. Abstraction is then thought to compete between the terminal O-atom and the pair of *cis*-disposed allylic groups as reflected by the isotope effect. This scheme is qualitatively plausible for **12** and **13**, although it does not account for the magnitude of the k_H/k_D values which should be the same (Scheme 3 and 4a). Moreover, it is implausible for **11** where the two possible Fukui complexes are not likely to have the same stabilities in view of the different energies of hyperconjugation conferred by methyl and trideuteriomethyl groups (Scheme 4b) [26]. In fact, it is just this hyperconjugative difference, in our opinion, which lies at the root of isotope partitioning.

As conformational factors are negligible for olefins tetrasubstituted by similar groups, it is the ease of formation of the C, O-bond which controls isotope selectivity. The partitioning observed between the ends of the geminal isomer **13** is explained by zwitterion **14** being favored over **15** (Scheme 5). An important feature is that C(1) at which oxygen attack occurs becomes tetrahedral, while C(2) retains its trigonal geometry throughout the process. This means that as the zwitterion progressively forms, an antiperiplanar arrangement of (*E*)-methyl substituents is preselected at the expense of the other pair. A molecule of oxygen can attack the (*E*)-olefin **12** either to preserve an (*E*)-arrangement of two methyl groups, as in **16**, or alternatively two trideuteriomethyl groups, as in **17** (Scheme 6). Better hyperconjugation is achieved for two (*E*)-antiperiplanar methyl groups (**16**) than for two

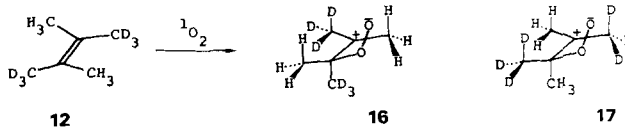
Scheme 4



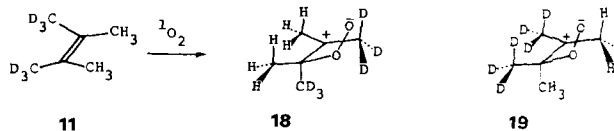
Scheme 5



Scheme 6



Scheme 7






deuteriomethyl groups (**17**). For the (*Z*)-isomer **11**, no great electronic distinction is realized as the pair of zwitterions possess similar arrangements of (*Z*)-methyl and trideuteriomethyl groups (**18** vs. **19**), hence an isotope effect close to unity is seen (Scheme 7).

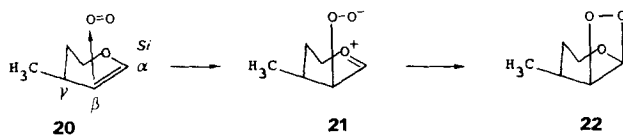
The photo-oxygenation of 4-methyl-2,3-dihydro- γ -pyran (**20**) has received thorough study [8]. Nonetheless, the results are scarcely rationalized by the 'complex criss-cross complex', no matter whether secondary orbital interactions are invoked or not [25]. We believe that elementary conformational considerations, hitherto neglected, and the ZI model provide a satisfactory explanation of the main features of the reaction, *i.e.* 1) the variation of the ratio of dioxetane **22** to hydroperoxide **24** with solvent polarity (Table 1), and 2) the kinetic isotope effects observed for **20** and its α , β and γ -monotritiated derivatives (Table 2).

It is important to remember that **20** exists in a half-chair conformation and that the double bond possesses two diastereoisomeric faces [27]. Consequently, attack by singlet oxygen on the *si*-face to form a quasiaxial bond necessarily occurs at C(β) and generates the zwitterion **21** and thence the dioxetane **22** (Scheme 8). The corresponding transition state entails considerable charge separation and should be favored by polar solvents (Table 1, entry 5). Attack and development of an axial bond on the *re*-face at C(α) engenders little charge separation as no charge stabi-

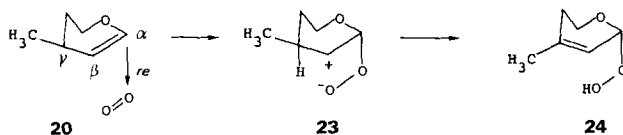
Table 1

 20	 22	+	 24	Ratio 22/24
Solvent				
1) Cyclohexane	13%		87%	0.15
2) Benzene	17		83	0.20
3) Carbon disulfide	40		60	0.67
4) Methanol	60		40	1.50
5) Acetonitrile	84		16	5.25

Scheme 8






Scheme 9



zation to **23** is possible (Scheme 9). Consequently, nonpolar solvents will favor the ene reaction, giving **24** (Table 1, entry 1).

The duality of mechanism implicating either *si*- or *re*-faces also nicely accounts for the kinetic isotope data (Table 2). Photo-oxygenation in acetonitrile gives mainly dioxetane (Scheme 8). The inverse isotope effect observed at C(β) confirms that this atom is undergoing change from trigonal to tetrahedral geometry in the transition state [28]. The negligible effect of the C(α) substituent is in keeping with the dominant formation of the zwitterion (**20** \rightarrow **21**). Nevertheless, the C(γ) substituent is implicated. Some of the C(γ) effect (15%) could be attributed to the 'ene' process (Scheme 9). In fact, for the photo-oxygenation in benzene where hydroperoxidation is predominant (Scheme 9), the C(γ) effect is significantly larger in agreement with the loosening of the C(γ)-bond in the second part of the transition state. The inverse effect at C(β) is correspondingly smaller, perhaps being due to the minor dioxetane mode. Finally, the small but finite inverse effect at C(α) confirms that attack at this side is the primary event for the 'ene'-dominant mode.

Table 2

	$k_{\text{H}}/k_{\text{T}}$ for photo-oxygenation	
	in acetonitrile	in benzene
1)  $[\gamma\text{-}^3\text{H}]\text{-20}$	1.211 ± 0.017	1.335 ± 0.023
2)  $[\beta\text{-}^3\text{H}]\text{-20}$	0.866 ± 0.003	0.908 ± 0.006
3)  $[\alpha\text{-}^3\text{H}]\text{-20}$	1.067 ± 0.010	0.980 ± 0.010

The ZI model proposed here could be construed as being in favor of a relatively late transition state since singlet oxygen is sensitive to the development of an axial bond. The contradiction with evidence favoring an early transition state, namely the unimportance of the development of strain in the product [29] and the low energy of activation [30], may only be apparent. The magnitude of the isotope effects cited (for **11**, **12**, **13** and **20**) are perceptible, but rather small; they would be expected to be bigger if indeed the transition state were later than it is.

In summary, we stress that configurational, conformational and electronic factors, as represented by the ZI model, need to be considered to correctly interpret the regioselectivity of the hydroperoxidation of olefins by singlet oxygen.

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