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REGIOSELECTIVE REACTION OF SINGLET OXYGEN WITH *CIS*-ALKENES

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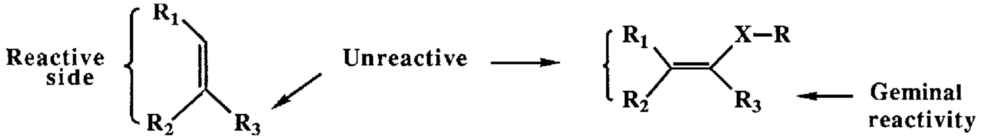
Abstract: The reaction of singlet oxygen with *cis* olefins is regioselective and shows a general preference for hydrogen abstraction on the larger alkyl group of the double bond.

The stereochemistry of photosensitized oxidations has received considerable attention the last few years. For example, singlet oxygen reacts stereospecifically[1] with olefins and shows side selectivity with enol ethers[2] or trisubstituted alkenes[3], where hydrogen abstraction occurs on the more crowded side of the double bond (scheme I). Furthermore the reaction of singlet oxygen with α,β–unsaturated carbonyl[4] or carboxyl[5] compounds or with other systems[6] shows strong geminal regioselectivity (scheme I).



R_1 = Alkyl, OCH_3

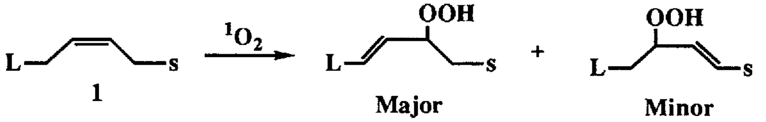
$X = -\overset{\overset{O}{\parallel}}{C}-$, R = Alkyl, H, OCH_3, OH

$X = -CH_2-$, R = halides, sulfones, sulfides

Scheme I

To explain the regioselectivity and reactivity of the s-*cis* α,β–unsaturated carbonyl compounds, Ensley and coworkers[4] proposed a trioxene intermediate which can only be formed with the s-*cis* conformation, but not with the s-*trans*. However, Foote and coworkers reported[7] recently that reactivity and geminal regioselectivity occurs even with α,β–unsaturated cycloketones whose configuration is exclusively the s-*trans*. They proposed the intermediacy either of a polar perepoxide or zwitterion-like intermediate.

We report here a new type of regioselective reaction of singlet oxygen with *cis*-olefins[8]. This reaction shows an unexpected preferential abstraction of the allylic hydrogens on the larger alkyl group of the double bond.



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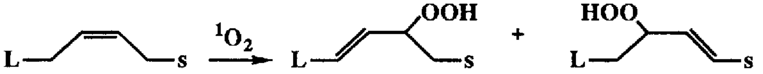
L = large, s = small

These results are summarized in Table I.

Table I. Regioselective Reaction[a] of Singlet Oxygen with *cis*-Alkenes[b].



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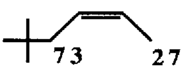

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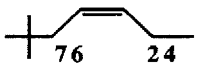

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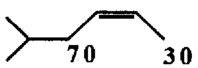

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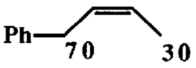

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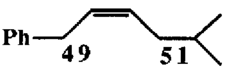

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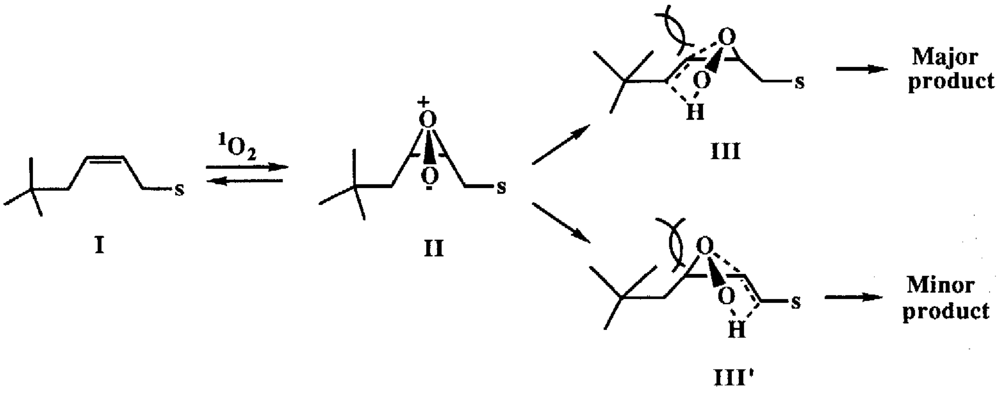
[a] Product ratio was determined by ^1H NMR integration of the proper peaks. Numbers below substances represent percent of hydrogen abstraction. [b] Mixture, 90-96% *cis*, 10-4% *trans*; however, the *trans* isomer is about 20 times less reactive than the *cis*.

As seen from Table I, the *ene* reaction of *cis*-alkenes of the general type **1** shows a consistent regioselectivity for double bond formation closer to the larger group. For example, when L (larger group) is *tert*-butyl and s (smaller group) is hydrogen or methyl, compounds **2** and **3**, the preferential abstraction of hydrogen adjacent to the *tert*-butyl group is greater than 73%. As the size of the s group becomes larger, the regioselectivity towards the *tert*-butyl or phenyl group decreases. This is demonstrated with substrate **5**, where the preferential hydrogen abstraction is only slightly higher on the *tert*-butyl side. Similarly, compounds **7** and **8** also give as the major isomer the product with the double bond on the side of the phenyl group. When **L** and s are phenyl and isopropyl respectively, compound **9**, competition for the two allylic sides leads to nearly equal hydrogen abstraction from the two methylene sides. This result indicates further that non-bonding interactions play a more important role than conjugation with the π system of the phenyl ring in the transition state of this reaction. Formation of a perepoxide intermediate, Scheme II, best accommodates these results.



Scheme II

In the transition state leading to the major product (III), the non-bonding interactions involving the large (*tert*-butyl) group are smaller than those of the transition state (III') leading to the minor product. Since transition state (III) is expected to have lower energy than (III'), the C-O bond next to the larger substituent should be weakened more than the other C-O bond next to the smaller group. Although the results may also be rationalized by the intermediacy of zwitterions, we prefer the perepoxide intermediacy. Such an intermediate in the *ene* reaction of singlet oxygen with alkenes has found ample support from stereoisotopic studies[1,9], analysis of the activation parameters[10], and theoretical calculations[11].

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8. Structures and isomeric purities were determined by ^{1}H NMR, IR and GC. Alkenes were prepared by Wittig reaction and purified by preparative GC. The photooxidations were carried out at -78°C in Freon-11 (alkenes **2**, **3**, **4** and **6**), or at 0°C in carbon tetrachloride (alkenes **5**, **7**, **8**, **9** and **10**) with tetraphenyl porphyrine as sensitizer. A 650-W tungsten-halogen lamp was used for these experiments. Analyses were carried out by direct NMR examination of the hydroperoxides immediately after reaction. Reduction of hydroperoxides with triphenyl phosphine is then followed by NMR and GC examination of the alcohols.

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