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CHEMISTRY OF SINGLET OXYGEN

III. PRODUCT SELECTIVITY[1]

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The well-known dye-photosensitized autoxidations of olefins and dienoid compounds have been postulated to proceed through an intermediate adduct (·Sens-O-O·) of excited sensitizer and oxygen which reacts with acceptor (A), to give the product peroxide (AO_2).[3] Excited singlet molecular oxygen (produced by reaction of H_2O_2 and sodium hypochlorite[1a] or by radio-frequency discharge[4]) gives products which are very similar to those of the photooxidations. Energy transfer from triplet sensitizer to oxygen to produce singlet molecular oxygen as the reaction intermediate (originally suggested by Kautsky[5] and, more recently, by Sharp[6]) was shown to be an alternate mechanism for the photooxidations which is consistent with the available evidence.[1a]

$$^3\text{Sens} + {}^3O_2 \longrightarrow \text{Sens} + {}^1O_2$$

$$^1O_2 + A \longrightarrow AO_2$$

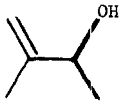
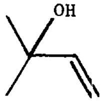
In this study we report a detailed comparison of the product distributions from oxidation of several olefins both by the photochemical reaction and with reagents which produce singlet oxygen, and show that the two reactions give product distributions which are indistinguishable. The photooxidations were carried out in a water-cooled immersion irradiation apparatus using a Sylvania DXY incandescent lamp, with Rose Bengal as sensitizer. The singlet oxygen oxidations were carried out by dropwise addition of aqueous hypochlorite solution to a solution containing the olefin to be oxidized and excess H_2O_2. Inhibitors were added as indicated.

In the workup of both types of reaction, peroxides in the crude reaction mixture were reduced by adding excess $NaBH_4$[7]; after reduction was complete, water was added and the products were extracted. The dried solutions were analyzed by gas chromatography. All major products were collected from the gas chromatograph and characterized by infrared and nuclear magnetic resonance spectroscopy; the spectra were consistent in all cases with the structures previously assigned to the photooxidation products.

The product distributions from 2-methyl-2-butene and limonene are summarized in Tables 1 and 2. The product distributions from the two oxidations are identical within experimental error, and agree well with those reported for the photooxidations.[8,9]

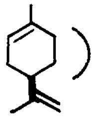
TABLE 1

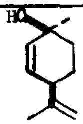
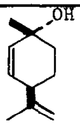
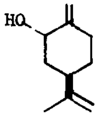
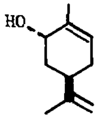
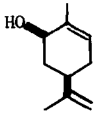
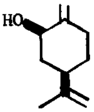
Products of Oxidation of 2-Methyl-2-butene[a]

Products	Per Cent in Reaction Mixture[b]	
	Photosensitized Autoxidation[c,d]	Singlet Oxygen $(Ca(OCl)_2 + H_2O_2)$[d]
 OH	51	48
 OH	49	52

a) In methanol.
b) After reduction.
c) Reported distribution 46 and 54%, respectively.[8]
d) Products with unshifted (trisubstituted) double bonds were absent.

TABLE 2

Products from Oxidation of (+)- Limonene[a] ()

Product	Per Cent in Reaction Mixture[b]	
	Photosensitized Autoxidation[c,d]	Singlet Oxygen (NaOCl + H_2O_2)[d,e]
	31	34
	11	9
	21	18
	10	9
	3	7
	25	24

a) In 1:1 t-butanol methanol.

b) After reduction.

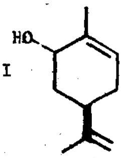
c) A very similar product distribution was reported from photosensitized autoxidation; free radical oxidation gives a drastically different product mixture.[9]

d) Products with unshifted double bonds were not found.

e) $Ca(OCl)_2$ + H_2O_2 with added 2,6-di-t-butyl phenol gave a virtually identical product distribution.

A further sensitive characterization of the stereoselectivity of singlet oxygen is provided by the optical activity of the trans-carveol (I), one of the alcohols which is produced by reduction of the hydroperoxide mixture formed on oxidation of limonene (see Table 2). If the reaction proceeded by initial hydrogen abstraction from limonene to give the allylic free radical (II), I would be

I



II

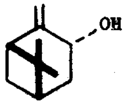
racemic.[8,9] Trans-carveol (I) was isolated gas-chromatographically from the $Ca(OCl)_2/H_2O_2$ oxidation of (+)- limonene,[10] and found to have $[\alpha]_D^{24} = -131°$ ($CHCl_3$, c = 0.04).[11] For comparison, I, isolated gas chromatographically from the photooxidation, had $[\alpha]_D^{24} = -141°$ ($CHCl_3$, c = 0.08).[13] Again, singlet oxygen displays a stereospecificity nearly identical with that of the reactive intermediate in the photosensitized autoxidations.

Recently a study of the oxidation of α-pinene reported that the product distribution from $NaOCl/H_2O_2$ oxidation was completely different from that of photosensitized oxidation, and closely resembled that of free radical oxidation.[8] α-Pinene is an extremely unreactive acceptor for both the photooxidation and the hypochlorite-H_2O_2 oxidation as shown by the fact that both photochemical quantum yield and singlet oxygen utilization are less than 0.5%, and it seemed possible that side reactions can compete with the singlet oxygen reaction in this case. We have reinvestigated the oxidation of this substrate, and this suggestion is dramatically confirmed. In the presence of free radical inhibitors, such as 2,6-di-t-butyl phenol, the product distribution becomes very similar to that from photooxidation; the products from various conditions are summarized in Table 3.

It is apparent from these results that serious side reactions (apparently free radical in nature) can compete with the H_2O_2/hypochlorite reaction when the

TABLE 3

Products from Oxidation of α-pinene ()

Conditions	Per Cent in Reaction Mixture[a]	
		Other Products[b]
Photosensitized Autoxidation	93[c]	7
Free Radical Oxidation[8]	14	86
NaOCl + H_2O_2 Ref. 8	9 - 12	88 - 91
Present Study[d]	35	65
$Ca(OCl)_2 + H_2O_2$[d]	43	57
$Ca(OCl)_2 + H_2O_2$[d,e] + 2,6-di-t-butyl phenol	85	15

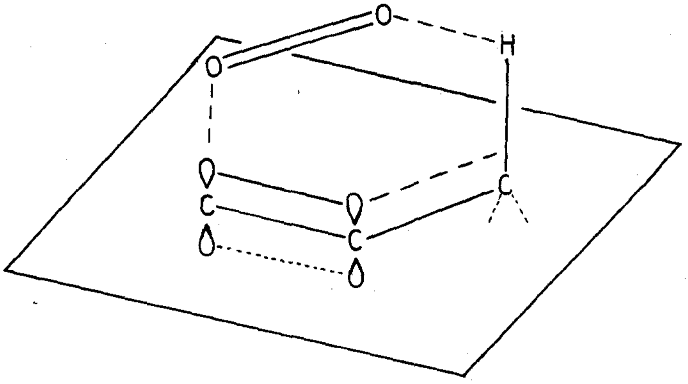
a) After reduction.
b) Not all identified.
c) Ref. 8 reports 94%.
d) At -20°; the study in Ref. 8 was presumably done at room temperature.
e) Addition of other free radical inhibitors gave similar results.

olefin acceptor is unreactive. It is interesting to note that the reactivity of acceptors is extraordinarily sensitive to structure in both photosensitized autoxidation[8,14] and hypochlorite/H_2O_2 oxidation[15], trialkylated olefins being in general around 100 times less reactive than tetraalkylated and dialkylated olefins being still less reactive. It is for this reason that the disubstituted double bond in limonene is unreactive in both reactions. This unreactivity of many olefins which are less than tetraalkylated sets an important limitation on the synthetic utility of the hypochlorite/H_2O_2 oxidation, since very large excesses of reagents are required for only modest conversions of unreactive olefins: most of the singlet oxygen decays to ground-state oxygen and escapes from the solution unless a reactive acceptor is present. Corresponding limitations are not present in the photochemical reaction, because even if the quantum yield is low, conversions can be made high by increasing the length of irradiation.

It is apparent from the results of this and previous[1a,4] work that singlet oxygen displays a chemistry identical to that of the intermediate in the photosensitized autoxidations. Gollnick and Schenck have recently reformulated the hypothetical ·Sens-O-O· intermediate as a charge-transfer complex between excited sensitizer and oxygen.[8] We cannot rule out the possibility rigorously that a sensitizer-oxygen complex is the reactive intermediate, but our results require that <u>sensitizer exert no steric influence whatever on the oxygen</u>, since otherwise one should have expected to see differences in product distribution and stereochemistry; there appears to be no convincing evidence which requires <u>any</u> participation of sensitizer in the transition state for oxygen transfer.[1a]

The photosensitized autoxidation of olefins has been shown by extensive stereochemical studies to proceed by a cycloaddition mechanism, as shown below with[8,9,16] or without[16] the oxygen complexed with sensitizer. As complexing appears unlikely, the reactions of singlet oxygen can be visualized as those of a reactive dienophile, which undergoes the "ene" reaction[17] with suitable olefins, and the

Diels-Alder reaction with dienes.



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3. (a) G. O. Schenck, Naturwiss., 35, 28 (1948); (b) ibid., 40, 205, 229 (1953); (c) G. O. Schenck and E. Koch, Z. Elektrochem., 64, 170 (1960); (d) E. J. Bowen, in "Advances in Photochemistry", Vol. 1, W. A. Noyes, G. S. Hammond, and J. N. Pitts, Jr., Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 23, and references therein cited.

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5. H. Kautsky, Biochem. Z., 291, 271 (1937), and earlier papers.

6. D. B. Sharp, Abstracts, 138th Meeting of the American Chemical Society, New York, N. Y., Sept. 1960, p. 79P.

7. Occasionally, addition of dry $NaBH_4$ to the reaction mixtures caused fires or small vapor explosions; addition in aqueous solution proceeds without incident.

8. K. Gollnick and G. O. Schenck, Pure and Appl. Chem., 9, 507 (1964).

9. G. O. Schenck, K. Gollnick, G. Buchwald, S. Schroeter, and G. Ohloff, *Ann.*, **674**, 93 (1964).

10. The limonene used had $[\alpha]_D^{26}$ = +122.7° (that used in ref. 9 had $[\alpha]_D^{20}$ = +122.4°). In this reaction, 2,6-di-*t*-butyl phenol was added; the overall product distribution was essentially identical to that reported in Table 2 for a run using NaOCl + H_2O_2 with no inhibitor, but uninhibited runs gave products with lower rotations. The epimeric *cis*-carveol could not be isolated in sufficient quantity to permit measurement of its rotation.

11. Rotations were measured in $CHCl_3$ on milligram quantities using a Cary 60 spectropolarimeter. The reported rotation for pure I as a *neat liquid* is $[\alpha]_D^{22}$ = -213.8°[9]; $[\alpha]_D^{22}$ = +213°, for the enantiomer.[12]

12. R. G. Johnston and J. Read, *J. Chem. Soc.*, 233 (1934).

13. This product was reported to be optically active,[9] but rotations were measured on derivatives which had been purified by repeated recrystallization, so that optical purity is uncertain.

14. K. Kopecky and H. Reich, *Can. J. Chem.*, **43**, 2265 (1965). We are grateful to Dr. Kopecky for a prepublication copy of this manuscript.

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