

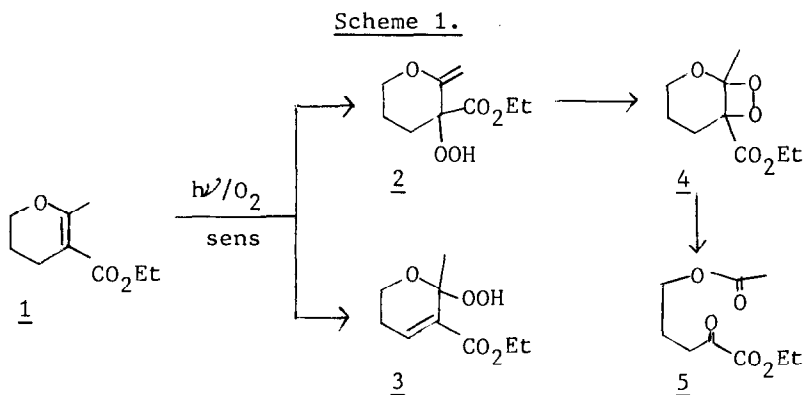
SENSITIZED PHOTOOXYGENATION. II.¹
SOLVENT EFFECTS IN THE REACTION OF SINGLET OXYGEN WITH
3,4-DIHYDRO-6-METHYL-2H-PYRAN-5-CARBOXYLIC ACID ETHYL ESTER

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SUMMARY Photooxygenation of the title compound exhibits an extraordinary solvent effect on the distribution of the ene-products, with the unconjugated hydroperoxide being formed preferentially in polar solvents.

We have recently reported on the sensitized photooxygenation of 3,4-dihydro-6-methyl-2H-pyran-5-carboxylic acid ethyl ester (1) in benzene, as shown in Scheme 1.² Only allylic hydroperoxides (ene-mode) are formed as stable, primary products. Hydroperoxide 2 transforms to the dioxetane mode cleavage product 5 via the intermediacy of dioxetane 4. This represents the first direct evidence supporting Farmer's proposal for Hock-cleavage since 1942.³ In this communication, we would like to report our findings on the extraordinary solvent effects of this ene-mode reaction.



Photooxygenation of 1 was investigated in five solvents: benzene, carbon tetrachloride, chloroform, methylene chloride and acetonitrile.⁴ The reaction mixture (substrate, 0.3M; sensitizer, 10^{-4} M) was irradiated with a 500 W tungsten-halogen lamp, operated at 180 volts. Oxygen was bubbled continuously through the solution. Hydroperoxide 2 and 3 were isolated by column chromatography in high yields.⁵ The results are summarized in Table 1.

Table 1. Solvent Effect on Product Distribution.

Solvent	Sensitizer	<u>2</u> %	<u>3</u> %	<u>2/3</u>	ϵ^a
C ₆ H ₆	TPP	10	90	0.11 ^b	2.3
CCl ₄	TPP	15	85	0.18	2.2
CHCl ₃	TPP	45	55	0.82 ^b	4.8
CH ₂ Cl ₂	TPP	50	50	1.00	9.1
CH ₃ CN	MB	65	35	1.86 ^b	37.5

^aDielectric constant, from "Handbook of Chemistry and Physics"; R. C. Weast, ed.; CRC, 1971, E-43.

^bSimilar ratio (by NMR) was found for deuterated solvents.

Photooxygenation of enol ethers having available allylic hydrogens may furnish both allylic hydroperoxides (ene-mode) and dioxetane (cycloaddition) as primary products,⁶ the ratio of which is highly solvent dependent. Solvent effects are normally attributed to the competition between the two modes of addition: polar solvents favor the dioxetane-mode,^{7,8} while ene-mode reaction is little affected.⁹ When changing the solvent from benzene to acetonitrile, the ratio of dioxetane/ene varied over a 59-fold range for 3,4-dihydro-2H-pyran,¹⁰ and 25-fold for 4-methyl-3,4-dihydro-2H-pyran.⁷ In our case, for substrate 1, only ene-mode reaction occurred, irrespective of the polarity of the solvent. The product distribution showed a preference for hydroperoxide 2 as the polarity of the solvent increased. Taking into consideration that 2 finally transformed to dioxetane 4, we obtained a "dioxetane/ene" (2/3) ratio change of 17-fold in going from benzene to acetonitrile. This serves as a rare example showing parallel solvent effect for the ene-mode and dioxetane-mode reactions, both favoring "dioxetane" product in polar solvents.

The ene reaction of singlet oxygen with enol ethers is regioselective. The most crowded side of the double bond is more susceptible to attack (cis effect),¹¹ and oxygen tends to add on the same side as the alkoxy group, with the carbon-oxygen bond forming preferentially at the carbon bearing the alkoxy group.¹² Special regioselectivity has been reported for the photooxygenation of α,β -unsaturated ketones¹³ and esters¹⁴ also. Preferential abstraction of allylic hydrogen geminal to the carboxyl group, forming the conjugated hydroperoxide was observed.¹⁴ The regioselectivity for α,β -unsaturated ketones was independent of solvent.¹³ In the case of ethyl 2-methoxycyclopentene carboxylate (β -alkoxyenoate), only one ene-product, the conjugated hydroperoxide was formed, in accord with the directing effects of both the alkoxy and the carboxyl groups.¹⁵

As an example of a β -alkoxyenoate, substrate 1 was expected to show similar regioselectivity as ethyl 2-methoxycyclopentene carboxylate. The conjugated hydroperoxide 3 should be the preferred product. This was indeed the case in non-polar solvent. But as the solvent polarity increased, there was an increase in the formation of the unconjugated hydroperoxide 2, contrary to the directing effects of both the alkoxy and the carboxyl groups.¹⁶ The significant solvent effect clearly demonstrates that the photooxygenation of 1 follows a different mechanistic pathway from unsaturated ketones and esters.^{13,14}

The relative rate of the reaction was monitored by oxygen consumption from a gas burette. The results are summarized in Table 2.

Table 2. Solvent Effect on Rate of Reaction.

Sens/Solvent	MB/CD ₃ CN	MB/CH ₃ CN	TPP/CH ₂ Cl ₂ [*]	TPP/CCl ₄	TPP/C ₆ D ₆	TPP/C ₆ H ₆
O ₂ Absorbed (cm ³ , ±0.06)	1.50	1.40	0.76	0.60	0.60	0.33
Relative Rate	4.55	4.24	2.30	1.82	1.82	1.00
τ_{1O_2} (μ s) ¹⁷	690	46.5	100 ¹⁸	900 ¹⁸	550	26.7

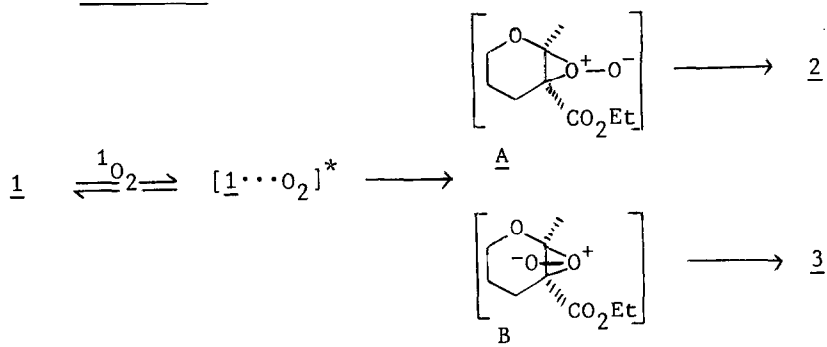
Conditions: [1]=0.3M; [sens]=3x10⁻⁴M; reaction time: 25 minutes.

*MB/CH₂Cl₂ gave similar result.

The rate of the reaction did not correlate with the lifetime of singlet oxygen in the appropriate solvents.^{7,19} In going from benzene to acetonitrile, the total rate increased by a factor of 4. The partial rate²⁰ leading to the formation of hydroperoxide 2 was estimated to increase by 27-fold, while that of hydroperoxide 3 was little affected, when changing the solvent from benzene to acetonitrile.

For discussion purposes, we would like to propose a mechanistic pathway as shown in Scheme 2.^{7,8,21} Singlet oxygen adds reversibly to the double bond to form a complex.²² The complex collapses to form hydroperoxide 2 via a possible intermediacy of perepoxide A (extended form, more polar) and to hydroperoxide 3 via perepoxide B (folded form, less polar). The solvent polarity may affect the process in 2 ways: 1. the partition between the extended (A) and the folded (B) forms; 2. the partition between the 2 pathways, should a somewhat polar intermediate or transition state (zwitterionic-like) be involved in the transformation of A to product. Further work in estimating the dipole moments of A and B, as well as studying the substituent and solvent effects for analogous systems are in progress to clarify the situation.

Scheme 2.



References and Notes

- † Also spelled as Yu-Yi CHEN and Xiao-Guang LIANG, respectively, in China.
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 - Substrate 1 is not soluble in methanol.
 - Purification was carried out immediately following complete consumption of 1. Hydroperoxide 2 was less stable in polar solvents, and may partly rearrange to 4 and 5 if not handled carefully.
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