

Photo-Oxidation of α -Keto-Carboxylic
Acids and Related Compounds

by

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A Thesis submitted for the Degree of
DOCTOR OF PHILOSOPHY
in the
Faculty of Science
of the
University of Leicester

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*Dedicated to my Parents,
Janet and David*

To My Parents
When I was young
and learning to dream,
you were always there -
you listened and encouraged
me to follow
my dreams ...

You helped me to become
all that I am.
Because you believed in me
I learned to believe
in myself.
Thank you for everything.

- Linda DuPuy Moore

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*"Well we all shine on, like the moon and
the stars and the sun"*

John Lennon 1940-1980

STATEMENT

The experimental work in this thesis has been carried out by the author in the Department of Chemistry at the University of Leicester, between October 1977 and September 1979, and in the Department of Chemistry at The City University, London, between October 1979 and September 1980. The work has not been presented and is not being presented for any other degree.

A handwritten signature in cursive script that reads "Dean Goodwin". The signature is written in dark ink and is positioned above the typed name.

DEAN GOODWIN
April 1983

Some of this work has been previously published, as follows:

1. The Question of the Rôle of Singlet Oxygen in the Dye-Sensitized Photo-Oxygenation of α -Oxo-Carboxylic Acids.
R. S. Davidson, D. Goodwin and G. Smith, J.C.S. Chem. Commun., 463, (1979).
2. The Direct Photo-Oxidative Decarboxylation of α -Oxo-Carboxylic Acids.
R. S. Davidson, D. Goodwin and G. Turnock, Tetrahedron Letters, 4943, (1980).
3. The Mechanism of the Photoinduced Decarboxylation of Pyruvic Acid.
R. S. Davidson, D. Goodwin and P. Fournier de Violet, Chem. Phys. Letters, 78, 471, (1981).
4. The Mechanism of the Norrish Type II Reaction of α -Keto-Carboxylic Acids and Esters.
R. S. Davidson, D. Goodwin and P. Fournier de Violet, Tetrahedron Letters, 2485, (1981).
5. The Mechanism of the Photoinduced Fragmentation of Alkyl Pyruvates.
R. S. Davidson and D. Goodwin, J.C.S. Perkin Trans. II, 993, (1982).
6. Photo-Induced Electron Transfer Reactions - Pitfalls and Opportunities.
R. A. Beecroft, R. S. Davidson, D. Goodwin and J. E. Pratt, Pure Appl. Chem., 54, 1605, (1982).
7. The Rôle of Electron Transfer Processes in the Photoinduced Decarboxylation of α -Oxo-Carboxylic Acids.
R. S. Davidson and D. Goodwin, J.C.S. Perkin Trans. II, 1559, (1982).
8. The Mechanism of the Direct Photo-Oxidative Decarboxylation of α -Oxo-Carboxylic Esters.
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9. The Rôle of Electron Transfer Processes in the Photoinduced Decarboxylation of Alkyl Pyruvates.
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2. Chemical Society Photochemical Group Meeting, 9 January, 1980, U.M.I.S.T., Manchester, England.
3. The City University Photochemistry Group and The Royal Society of Chemistry Photochemistry Group - Joint Meeting, 3 April, 1981, The City University, London, England.
4. IX I.U.P.A.C. International Symposium on Photochemistry, 25-30 July, 1982, University of Pau, Pau, France.

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CHAPTER 1

SELECTED ASPECTS OF PHOTOCHEMISTRY AND
PHOTOCHEMICAL REACTIONS

*"Imagine there's no heaven
It's easy if you try
No hell below us
Above us only sky
Imagine all the people
Living for today*"

John Lennon 1940 - 1980

SELECTED ASPECTS OF PHOTOCHEMISTRY AND PHOTOCHEMICAL REACTIONS

Preface

Photochemistry, the study of light mediated chemical processes, encompasses many inter-related areas in chemistry and biology. One of the most important and elegant photochemical reactions is that of photosynthesis, the evolution of which led to the existence of life on earth, and it is this process on which all life ultimately depends.

With man's continual consumption of vast quantities of raw materials as sources of energy, we are rapidly exhausting the reserves of these raw materials at rates which Nature cannot replenish in the short term. As a consequence, we are looking to new areas which will supply man's energy needs in the future. One of these areas, which is receiving much attention of late, is the investigations into the possible ways of harnessing solar energy, in the hope that by mimicking photosynthesis we could offset the use of raw materials for some of our energy requirements.

There has been a rapid and extensive expansion of the study of photochemical processes over the last three decades, and the development of sophisticated instrumentation has enabled many fundamental photo-reactions to be probed and their mechanisms elucidated. Let us hope that similar innovations in photochemical research continue, which will not only quench our thirst for knowledge, but also lead to developments in the number of ways which photochemical reactions can be used to man's advantage.

The first section of this chapter discusses some of the basic principles of photochemistry. This thesis concerns the photochemical reactions, in particular photo-oxidation, of α -keto-carboxylic acids and their ester derivatives, some of which are naturally occurring 1,2-di-

ketones. Therefore, the photochemistry of carbonyl, and some α -dicarbonyl, compounds is briefly surveyed in the second section, whilst the final section of this chapter deals with photo-oxidation processes.

1.1 GENERAL ASPECTS OF PHOTOCHEMISTRY

Numerous textbooks have covered the subject of photochemistry in great detail, for example the publications by Calvert and Pitts,¹ Barltrop and Coyle,² Cowan and Drisko,³ and Turro⁴ provide excellent reviews of the topic. The material in the following section is therefore only a basic introduction dealing with the creation of excited states and their photophysical parameters.

1.1(i) ELECTRONIC TRANSITIONS IN ORGANIC MOLECULES

When an organic molecule absorbs a photon of light, an electron is promoted from the ground state to an upper excited state, from either a filled or partially filled orbital within the molecule. The electronic transitions that can occur within organic molecules can be of the type $\sigma \rightarrow \sigma^*$, $n \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$, depending upon the energy of the photon absorbed and the class of compound irradiated. As depicted in Figure 1.1, the transitions $\sigma \rightarrow \sigma^*$ and $n \rightarrow \sigma^*$ require the greatest amount of energy and are associated with wavelengths in the far-ultraviolet region of the electromagnetic spectrum ($\lambda < 200$ nm) and as such are of limited significance in organic photochemistry. The $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions (Figure 1.1), requiring less energy, occur in easily accessible regions of the electromagnetic spectrum ($\lambda > 200$ nm) and are responsible for the majority of organic photochemical reactions. With reference to carbonyl compounds the $n \rightarrow \pi^*$ transition is favoured energetically over the $\pi \rightarrow \pi^*$ transition and for this reason n, π^* singlet and triplet states are important in the majority of photochemical reactions of carbonyl compounds.⁵

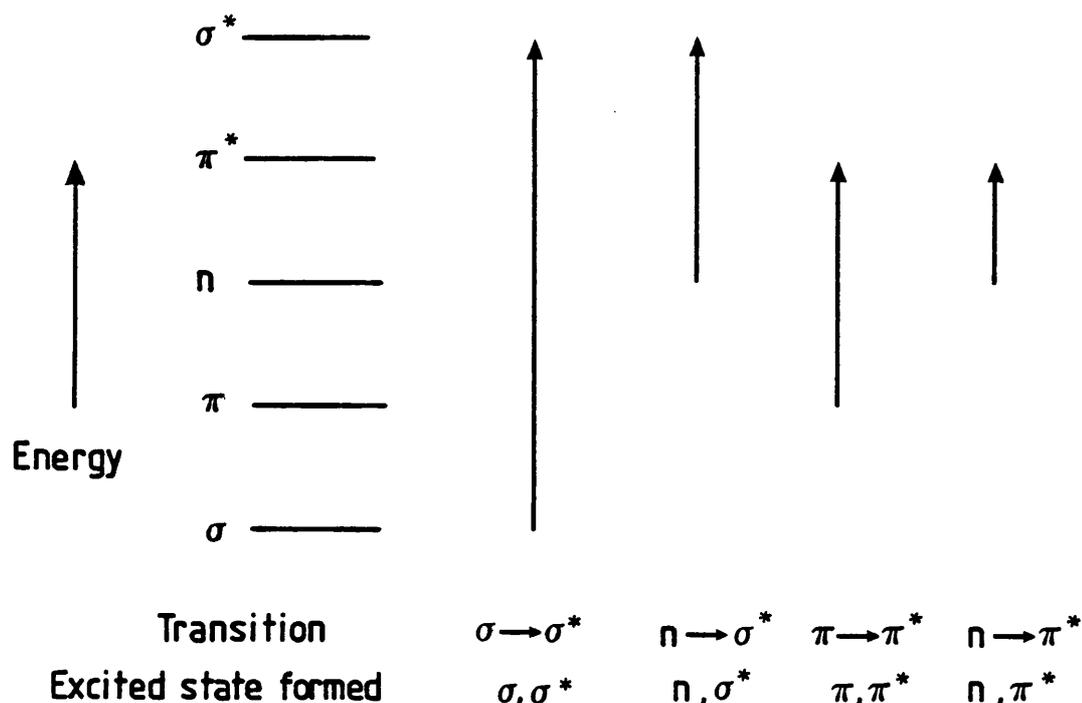


FIGURE 1.1

The electronic excitation processes in organic molecules
 (where n = non-bonding orbital; σ and π = bonding orbitals;
 σ^* and π^* = anti-bonding orbitals)

1.1(ii) PHOTOPHYSICAL PROCESSES OF THE EXCITED STATE

Most organic molecules have ground states in which both the electrons are spin paired and are designated as singlet (S_0) states. Upon absorption of a photon, an electron is promoted to a higher energy level of the same multiplicity, for example, S_1 , S_2 or S_n where n denotes the n^{th} level of the singlet state. The energy level to which the electron is initially promoted is dependent upon the energy of the photon absorbed. Each energy level has sub-divisional vibrational energy levels associated with it and the electron rapidly relaxes from an upper vibrational level to the lowest vibrational level within the electronic state by vibrational cascade, the excess energy being lost to the surroundings by intermolecular collisions.

Internal conversion then ensues, whereby the electron undergoes a radiationless passage from the lowest vibrational level of an upper

electronic state to a higher vibrational level of a lower excited state, via this iso-energetic process, for example $S_2 \rightarrow S_1$.

Upon reaching the lowest vibrational level of the S_1 state, a number of processes can occur. The molecule may:-

- (a) undergo internal conversion and vibrational cascade to the ground state (S_0), losing energy to the surroundings as heat.
 - (b) spontaneously emit a photon of light and return to its ground state (S_0) by a rapid ($\sim 10^{-9}$ s) radiative process known as fluorescence.
 - (c) chemically react with, or transfer its electronic energy, to another molecule, or react intramolecularly producing new chemical species.
- or (d) undergo intersystem crossing to the lower energy triplet state, involving the normally forbidden process of spin inversion of an electron.

If intersystem crossing occurs, the molecule relaxes to the lowest vibrational level of the lower triplet state (T_1) by vibrational cascade and internal conversion. The molecule can then undergo similar processes from the triplet state (T_1) as those described for the singlet state (S_1) above. For example, radiationless conversion to the ground state (S_0) and/or intra- or bimolecular chemical reactions can occur. A quantum of light may be emitted in relaxation to the ground state (S_0), in a relatively slow ($10^{-3} - 10^{-1}$ s) radiative process, similar to (b) above, known as phosphorescence. Phosphorescence is a much longer-lived process than fluorescence as it involves the spin inversion of an electron. Due to the forbidden nature of this process, triplet states are usually more stable in comparison to singlet states and have longer lifetimes.

Although chemical reaction can occur from both the singlet and triplet states, as a consequence of the differences in the excited state lifetimes, chemical reactions more commonly proceed from the triplet state.

The photophysical processes involved in the interconversion of excited states can be conveniently represented by a diagram similar to that first used by Jablonski⁶ as shown in Figure 1.2.

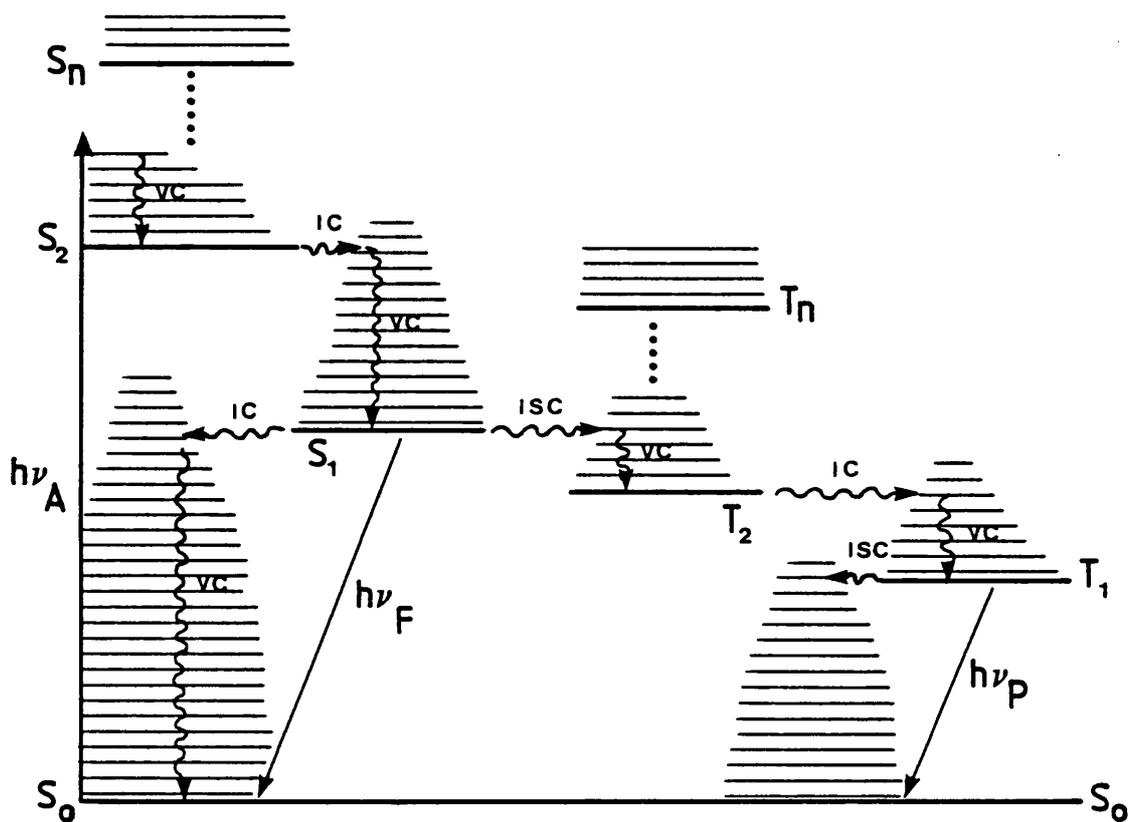


FIGURE 1.2

Modified Jablonski diagram showing some of the radiative ($\rightarrow h\nu_A$ = Absorption; $h\nu_F$ = Fluorescence; $h\nu_p$ = Phosphorescence) and non-radiative (\rightsquigarrow VC = Vibrational cascade; IC = Internal conversion; ISC = Intersystem crossing) processes available to molecules.

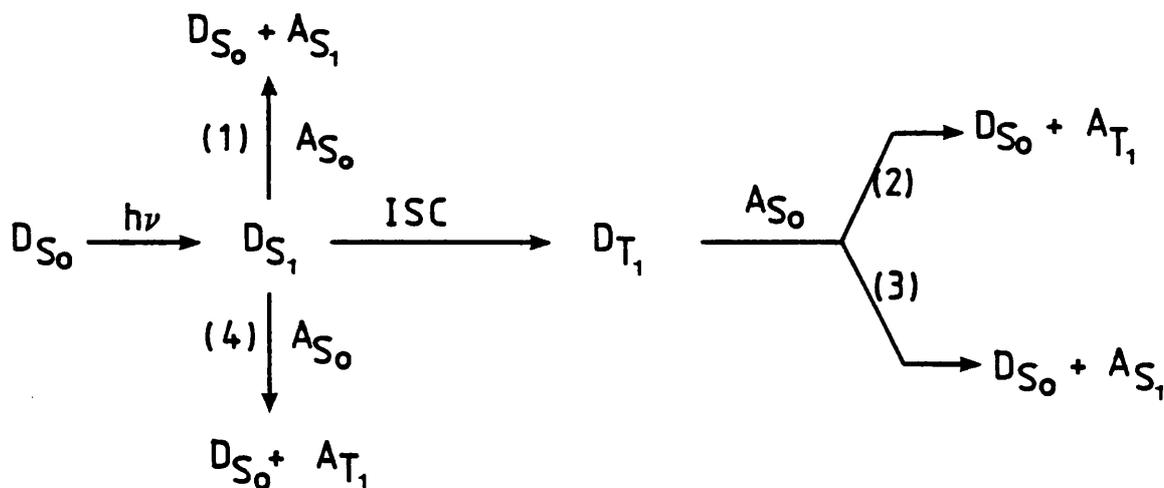
1.1(iii) SENSITIZATION AND QUENCHING BY ENERGY TRANSFER

An excited molecule in either the singlet or triplet state may be deactivated by transfer of energy to another molecule having lower lying singlet or triplet energy levels, the excited molecule returning to the

ground state whilst the other molecule is elevated to a higher energy state. The excited molecule can be referred to as the donor (D), the other molecule being the acceptor (A) and the energy transfer process can be summarised simply by Equation 1.1.



The overall process can be considered as either the donor molecule sensitizing the formation of an excited state of the acceptor, or as the acceptor molecule quenching the excited state of the donor. Thus, the donor molecule can be regarded as a photosensitizer and the acceptor molecule can be regarded as a quencher. The acceptor molecule can quench either the singlet or triplet state of the donor and result in the sensitization of the acceptor molecule to either its singlet or triplet state, as outlined in Scheme 1.1.

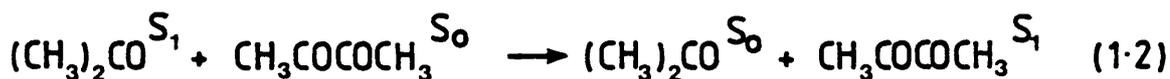


Scheme 1.1

Scheme 1.1 shows four important types of energy transfer processes as follows:-

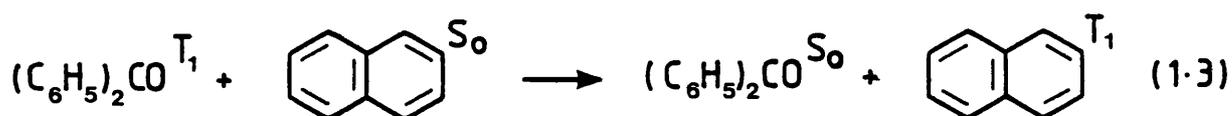
(1) Singlet-Singlet energy transfer: This takes place over relatively long distances and gives rise to an excited singlet state of the acceptor as a result of energy transfer from the donor's excited singlet state.

Thus, if there is sufficient overlap of the emission spectrum of the donor and the absorption spectrum of the acceptor, the donor fluorescence is quenched and acceptor fluorescence is sensitized. An example of singlet-singlet energy transfer is the sensitization of biacetyl fluorescence by energy transfer from singlet state acetone, in cyclohexane⁷ solution, (Equation 1.2).



Donor Acceptor

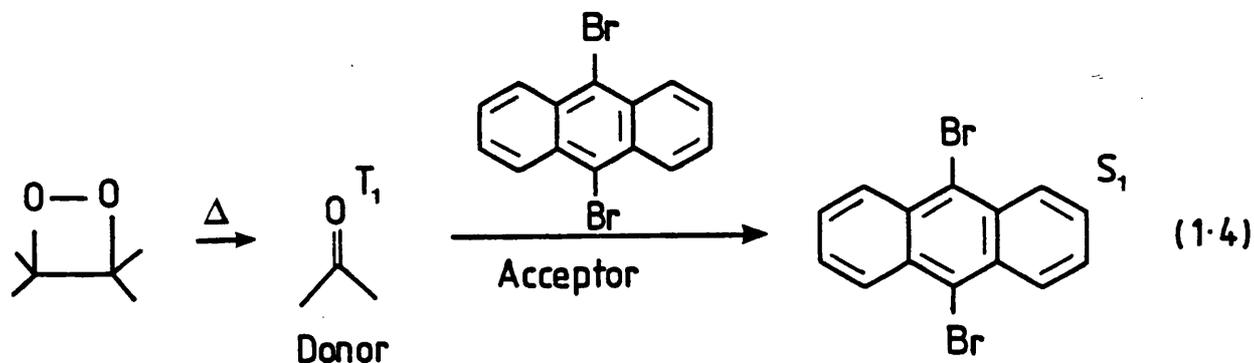
(2) Triplet-Triplet energy transfer: In this case an excited donor in its triplet state produces an excited acceptor in its triplet state. As the lifetime of the triplet state is longer than that of the singlet state, the greater the probability that the donor's triplet state will participate in energy transfer processes compared to the singlet state. Indeed, triplet-triplet energy transfer is the most common and most important type of energy transfer in organic photochemistry, as exemplified by the sensitization of triplet naphthalene by triplet benzophenone, in benzene⁸ solution, (Equation 1.3).



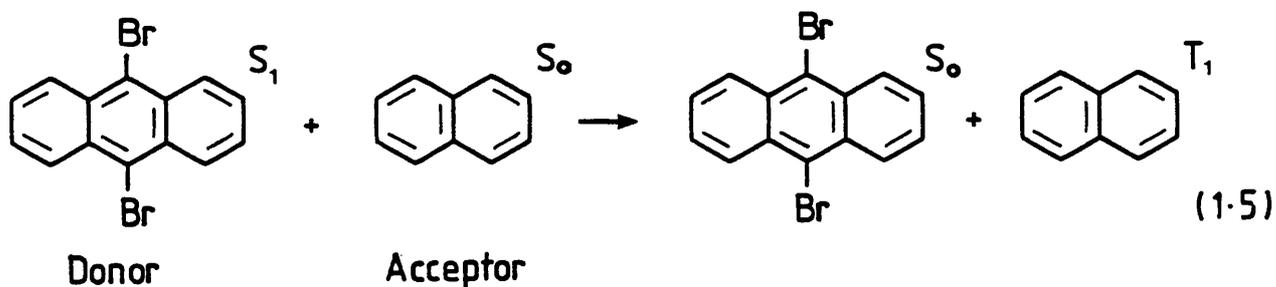
Donor Acceptor

(3) Triplet-Singlet energy transfer: In solution, energy transfer from a triplet donor to an acceptor to give the excited singlet state of the acceptor is relatively rare, however triplet-singlet energy transfer from thermally produced triplet acetone to appropriate acceptors, such as 9,10-dibromoanthracene, has been observed.⁹ In this case, which utilises a chemiluminescence technique, the thermolysis of tetramethyl-

1,2-dioxetane yields triplet acetone which undergoes triplet-singlet energy transfer to 9,10-dibromoanthracene to give the singlet state of the anthracene derivative,⁹ (Equation 1.4).

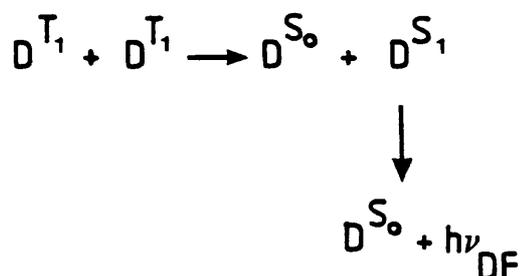
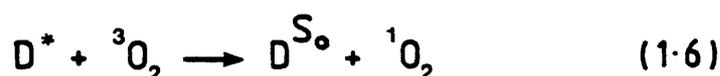


(4) Singlet-Triplet energy transfer: This is the rarest of the four energy transfer processes and involves an excited singlet donor and ground state singlet acceptor to produce an excited triplet acceptor. For example, the fluorescence of 9,10-dibromoanthracene is quenched by naphthalene, in toluene solution, to give triplet naphthalene,¹⁰ (Equation 1.5).



Oxygen is an efficient quencher of the excited states of organic molecules and often gives rise to the formation of oxygen molecules in the excited singlet state, (Equation 1.6). The formation of singlet oxygen by this process is discussed further in Chapter 1.3.

If the concentration of the donor molecule is high, then a bimolecular self-quenching process can result. An example of such self-quenching is triplet-triplet annihilation, whereby deactivation of two donor molecules, both in their excited triplet state, occurs giving rise to a donor molecule in an excited singlet state and a donor molecule in the ground state. Systems which are subject to quenching via triplet-triplet annihilation often show delayed fluorescence which emanates from the donor molecule that is generated in its excited singlet state, as shown in Scheme 1.2. Triplet-triplet annihilation has been observed for anthracene and naphthalene in n-hexane solutions, biacetyl in benzene solutions and benzophenone in freon, for example.¹¹



(where $h\nu_{DF}$ = delayed fluorescence)

Scheme 1.2

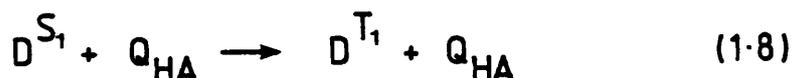
Concentration quenching can also lead to deactivation of the singlet state characterised by a decrease in fluorescence intensity with increasing amounts of the compound under investigation. The fluorescence quenching which is observed in such cases results from interaction of a molecule in its excited singlet state with a molecule of the same species in its ground state to produce an excited dimer or excimer, (Equation

1.7). For example, pyrene fluorescence is progressively quenched as the concentration of pyrene in the solution is increased and this is accompanied by the growth of a broad structureless emission band, corresponding to the pyrene excimer, at longer wavelength than the pyrene fluorescence.¹²



1.1(iv) HEAVY ATOM EFFECTS

Intersystem crossing to the triplet state of an aromatic hydrocarbon is enhanced by the presence of halogens, or other heavy atoms, and a reduction in the fluorescence quantum yield of the molecule is observed, (Equation 1.8).



(where Q_{HA} = heavy atom quencher)

There are two ways by which a halogen can enhance intersystem crossing and quench the fluorescence of an aromatic molecule. Firstly, if the heavy atom is incorporated into a molecule of the aromatic hydrocarbon it can quench intramolecularly. For example, substitution of hydrogen by halogens at the 1-position of naphthalene reduces the fluorescence quantum yield and increases the phosphorescence quantum yield,¹³ (Table 1.1).

Secondly, if the heavy atom is present in the environment of the aromatic hydrocarbon it can quench intermolecularly. For example Xenon, when administered into a solution of an aromatic hydrocarbon, such as anthracene or naphthalene, has been shown to quench the fluorescence and enhance the rate of triplet formation of the molecule.¹⁴ Similar inter-

molecular quenching effects are observed from the quantum yields of fluorescence and phosphorescence of aromatic hydrocarbons in different halogenated solvents as exemplified by the study of naphthalene in halogenated propanes,¹⁵ (Table 1.2).

TABLE 1.1¹³

| Compound | Quantum Yields ^(a) | |
|---------------------|-------------------------------|-----------------|
| | Fluorescence | Phosphorescence |
| Naphthalene | 0.55 | 0.055 |
| 1-Chloronaphthalene | 0.058 | 0.3 |
| 1-Bromonaphthalene | 0.0016 | 0.27 |
| 1-Iodonaphthalene | <0.0005 | 0.38 |

(a) Data for rigid solution at 77 K

TABLE 1.2¹⁵

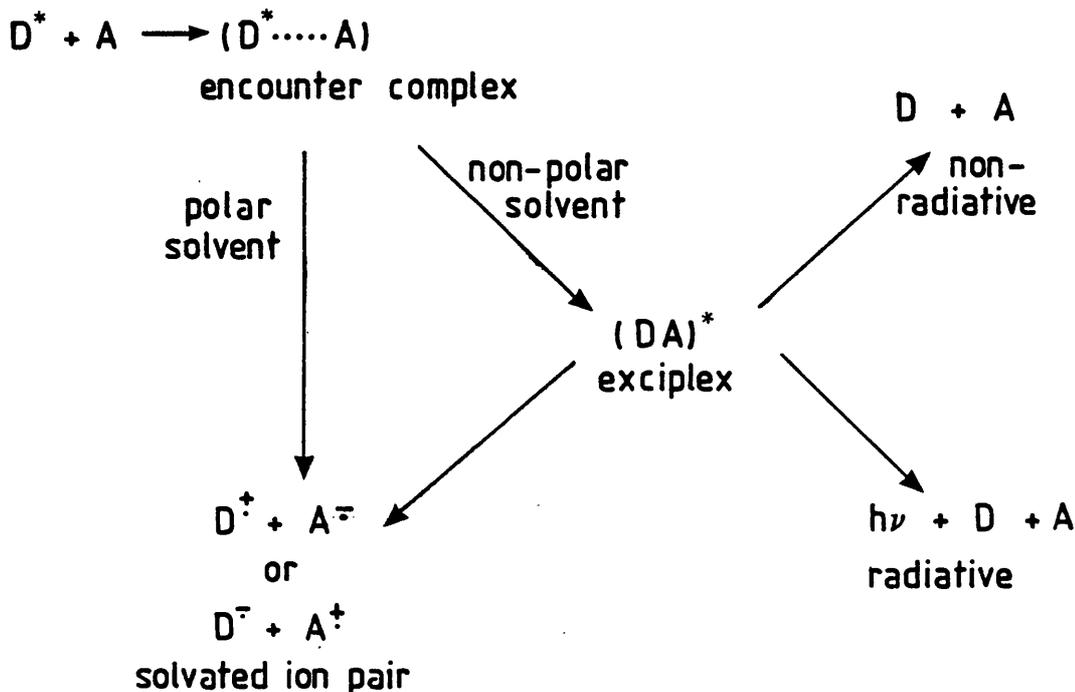
| Solvent | Naphthalene Quantum Yields ^(a) | |
|------------------|---|-----------------|
| | Fluorescence | Phosphorescence |
| Ethanol/Methanol | 0.55 | 0.055 |
| 1-Chloropropane | 0.44 | 0.08 |
| 1-Bromopropane | 0.13 | 0.24 |
| 1-Iodopropane | 0.026 | 0.35 |

(a) Data for rigid solution at 77 K

1.1 (v) QUENCHING VIA ELECTRON TRANSFER

That quenching of excited states of organic molecules can occur via electron transfer processes is well documented,¹⁶ however doubt exists as to the exact nature of the intermediate species involved, which could be an exciplex or an encounter complex. Complete electron transfer occurs in polar solvents leading to the formation of solvent separated

radical ion pairs. In non-polar solvents incomplete electron transfer may occur to form an intermolecular charge-transfer complex in an excited state (termed an exciplex), which may relax by either a radiative or non-radiative process. The parameters for the above mechanisms of electron transfer quenching are summarised in Scheme 1.3.



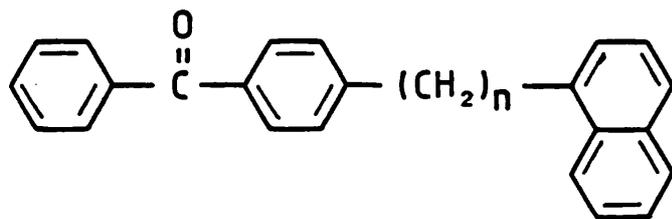
Scheme 1.3

The first example of exciplex emission was the finding of new structureless fluorescent bands in the spectrum of perylene quenched by aromatic amines in non-polar solvents.¹⁷ Radical ion formation has been observed in the reactions of various singlet state aromatic hydrocarbons with amines in aprotic polar solvents which give rise to hydrocarbon radical anions and amine radical cations.¹⁸

1.1(vi) INTRAMOLECULAR ENERGY TRANSFER

Energy transfer can also take place between different chromophores within the same molecule, and is termed intramolecular energy transfer. For example, both singlet and triplet energy transfer have been studied

in the compound below.^{19,20}



(where $n = 1, 2, 3$)

Using an excitation wavelength of 313 nm the naphthalene moiety is promoted to its singlet state. Singlet energy transfer to the benzophenone moiety then proceeds with high efficiency ($n = 1$, 98%; $n = 2$, 80%; $n = 3$, 94%). Intersystem crossing ensues, with unit efficiency, forming the benzophenone triplet which then undergoes triplet energy transfer to naphthalene ($n = 1, 2, 3$, 100%) to yield the naphthalene triplet which, if in a low temperature glass, undergoes phosphorescence. Using an excitation wavelength of 366 nm starts the above process at the benzophenone singlet state.

1.1(vii) UTILISATION OF SENSITIZATION AND QUENCHING STUDIES

Sensitization and quenching are two important photochemical techniques which can be used to probe and elucidate the excited state from which a photochemical reaction occurs. For example, photosensitization can create excited states which may be difficult to obtain by direct irradiation and often provides a route to products which otherwise could not be derived from direct photolysis of a compound. Quenching studies can be used to determine relative rates of photochemical reactions in addition to revealing the excited state from which the reaction occurs.

The kinetics of photochemical quenching are described by the Stern-Volmer equation²¹ below, (Equation 1.9). This equation can be applied to many types of quenching studies including fluorescence, phosphorescence

$$\frac{\Phi_0}{\Phi_q} = 1 + k_q \tau [Q] \quad (1.9)$$

where Φ_0 = quantum yield in the absence of quencher

Φ_q = quantum yield in the presence of quencher at a concentration $[Q]$

k_q = quenching rate constant

and τ = lifetime of the excited state in the absence of quencher.

and product quenching experiments. By representing the data graphically, in the form of a Stern-Volmer plot, a great deal of information regarding the quenching process can be obtained. A plot of Φ_0/Φ_q versus $[Q]$, under ideal conditions, will result in a straight line with an intercept at 1 and a gradient = $k_q\tau$ and if one of these values is known (either k_q or τ) then the other can be calculated.

It should be pointed out that there are several important factors which need to be taken into consideration in the design of an effective quenching experiment. For example, the incident radiation should not directly excite the quencher molecules, and if a product quenching investigation is to be performed it is desirable to use low conversion rates (<10% photochemical reaction) to ensure that any possible interference of the quenching process by reaction products is minimised.

In summary, the greater the difference between the triplet energies of the sensitizer and quencher molecules, the more efficient is the sensitization, or quenching, process. The triplet energies of some commonly used triplet sensitizers and quenchers are given in Table 1.3.²²

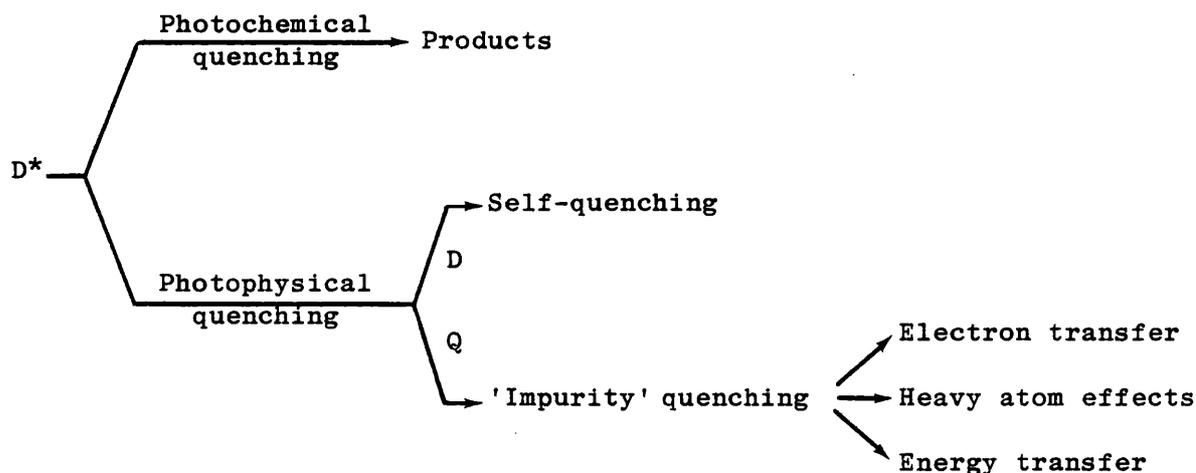
1.1(viii) SUMMARY

Some of the basic principles involving the creation and deactivation of excited states of organic molecules have been discussed. Scheme 1.4

TABLE 1.3²²

| Compound | E _T (kcal/mole) |
|---------------------|----------------------------|
| Acetone | ~78 |
| Xanthone | 74 |
| Benzophenone | 69 |
| Anthraquinone | 62 |
| Naphthalene | 61 |
| Cyclopentadiene | 58 |
| Biacetyl | 55 |
| Cyclohexa-1,3-diene | 53 |
| Pyrene | 49 |
| Anthracene | 47 |
| Perylene | ~35 |
| Tetracene | ~29 |
| Oxygen | ~23 |

summarises the possible quenching mechanisms which can occur for an excited molecule.²³



SCHEME 1.4²³

The process of photophysical quenching, which does not lead to new ground state products, can be sub-divided into self-quenching, where the quenching molecule is D, and 'impurity' quenching where the quenching molecule is another chemical compound Q. Impurity quenching can be further classified into electron transfer, heavy atom and energy transfer processes for example. Photochemical quenching leading to the formation

of products encompasses the whole of organic photochemistry and is discussed in relation to carbonyl compounds in the next section.

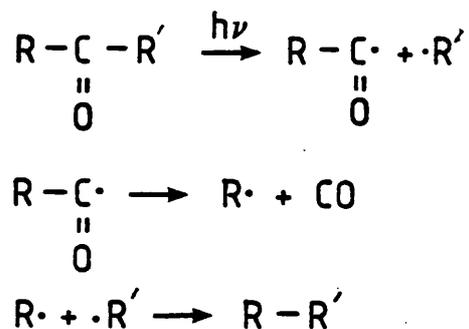
1.2 PHOTOCHEMICAL REACTIONS OF CARBONYL COMPOUNDS

In addition to the previously described processes which are available for deactivation of excited molecules, photochemical reaction, leading to the formation of new chemical compounds, may also occur. The photochemistry of carbonyl⁵ and α -dicarbonyl compounds^{24,25} have been reviewed and the following section serves as a resumé which highlights some of the important characteristic reactions of carbonyl compounds when irradiated in degassed solution. The effect of oxygen upon such reactions is discussed in the final part of this section.

1.2(i) α -CLEAVAGE

Cleavage of the carbon-carbon bond α to the carbonyl portion of a molecule is referred to as α -cleavage or Norrish Type I cleavage.

The primary photochemical process involves a simple cleavage into free radicals, followed by secondary reactions which include decarbonylation of the acyl radical and subsequent radical recombination as outlined in Scheme 1.5.



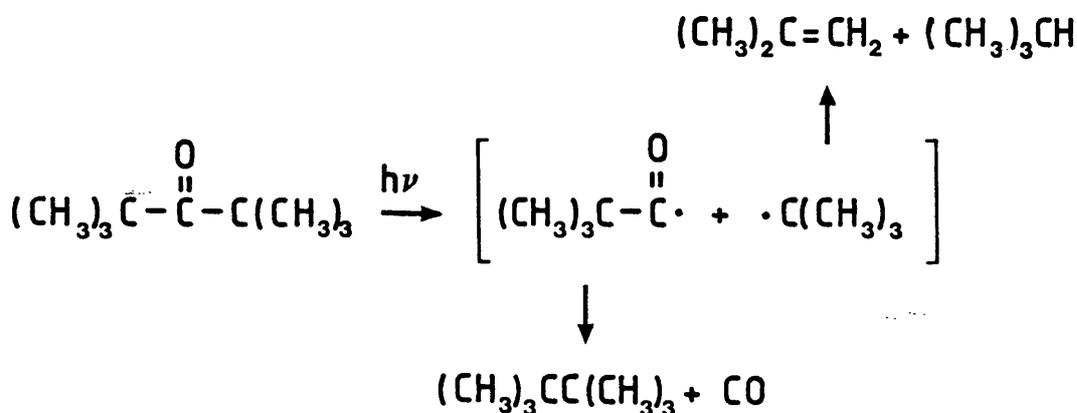
(where, for example, R = alkyl or aryl;
R' = -H or alkyl)

Scheme 1.5

The above Scheme 1.5 is general for many carbonyl compounds and the cleavage reaction can occur from both the excited singlet and triplet

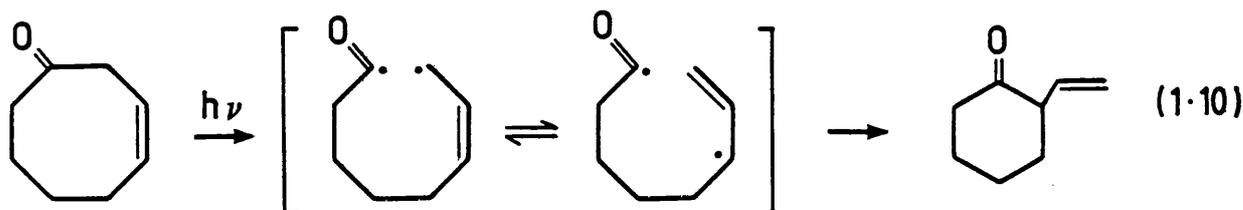
states.

Irradiation of di-*t*-butyl ketone in pentane solution produces several products derived from an initial α -cleavage reaction,²⁶ (Scheme 1.6).



Scheme 1.6

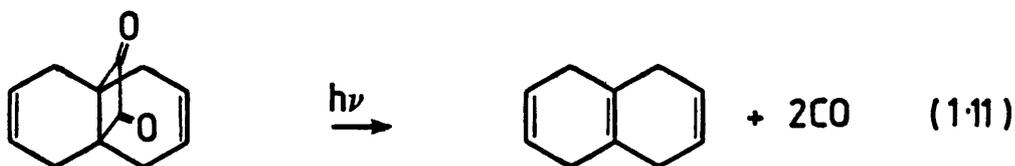
In some cases, molecular rearrangement can occur without decarbonylation. For example, cyclic β,γ -unsaturated ketones undergo photochemical rearrangement, via a mechanism suggested to involve α -cleavage followed by rearrangement of the radical so produced, to yield β,γ -unsaturated ketones possessing exocyclic olefinic linkages,²⁷ (Equation 1.10).



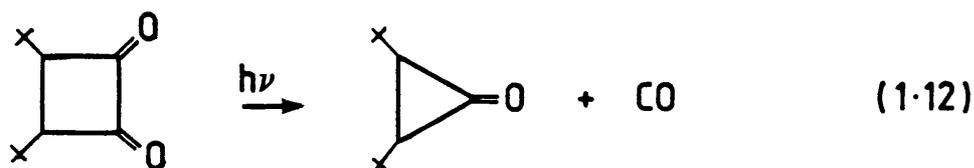
With reference to α -dicarbonyl compounds, such as biacetyl and benzil, cleavage of the carbon-carbon bond between the two carbonyl groups is highly inefficient in aprotic solvents due to the fact that deactivation is much faster than bond cleavage. However, product studies have been carried out on several highly strained α -diketones and although no mechanistic evaluations were performed the formation of products can be rationalised by initial α -cleavage followed by decarbonylation.^{28,29}

For example, the highly strained [4.4.2]propella-3,8-diene-11,12-dione undergoes decarbonylation upon irradiation in various solvents,²⁸

(Equation 1.11), and 3,4-di-*t*-butylcyclobutanedione yields di-*t*-butyl-



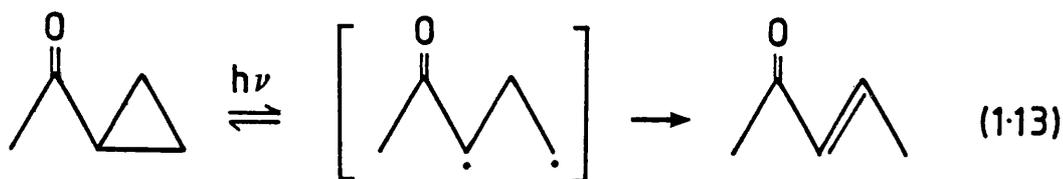
cyclopropanone and carbon monoxide upon photolysis,²⁹ (Equation 1.12).



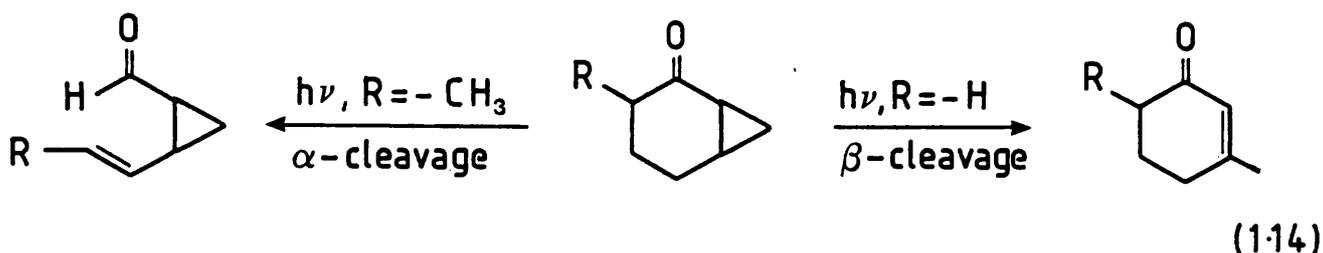
1.2(ii) β -CLEAVAGE

Although β -cleavage is not formally a Type I process it does bear close similarity to α -cleavage. β -Cleavage is observed in compounds with relatively weak C_α - C_β bonds and results in the homolytic cleavage of this bond, as exemplified by cyclopropyl ketones^{30,31} and α,β -epoxyketones.³²

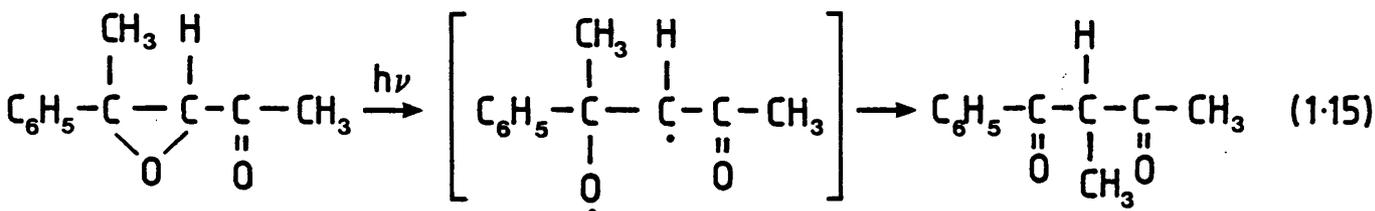
The first report of a β -cleavage process was the formation of methylpropenyl ketone from methylcyclopropyl ketone,³⁰ (Equation 1.13).



The mode of bond cleavage which predominates, either α - or β -cleavage, is sensitive to alkyl substitution³¹ as shown in Equation 1.14.



α,β -Epoxyketones undergo β -cleavage to yield 1,3-diketones via methyl group migration,³² (Equation 1.15).

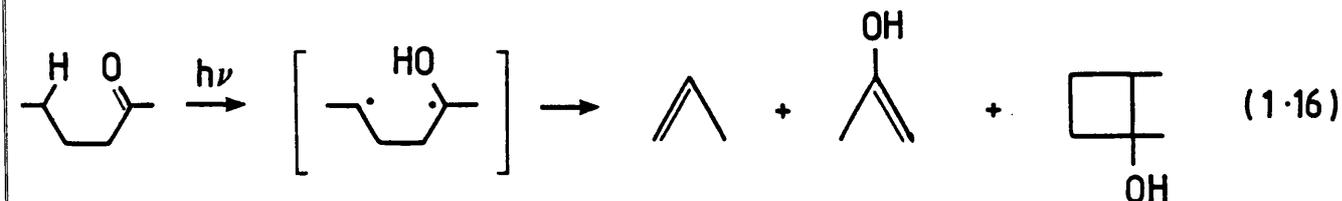


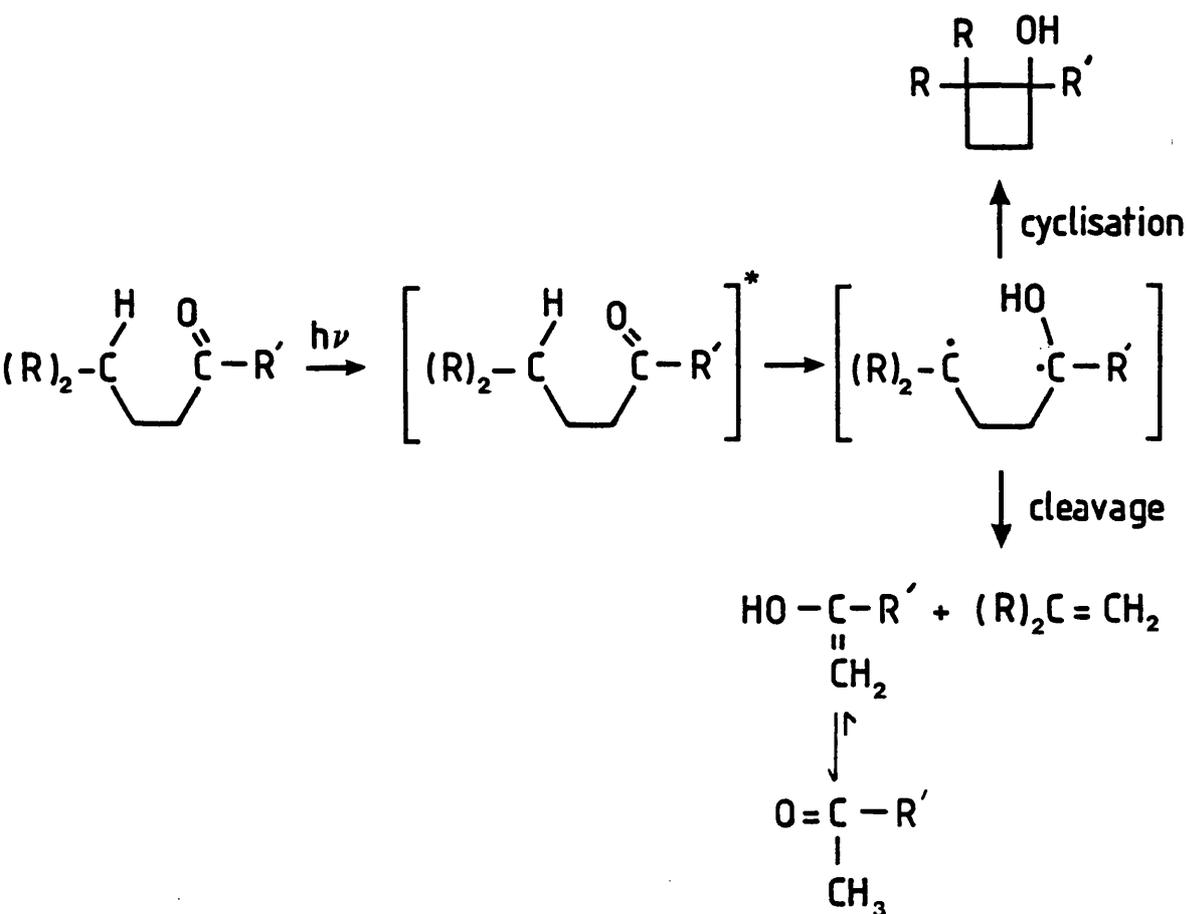
1.2(iii) INTRAMOLECULAR HYDROGEN ATOM ABSTRACTION

Irradiation of carbonyl compounds containing γ -hydrogen atoms, in addition to Norrish Type I cleavage products, yields products which can be explained by a mechanism involving an intramolecular hydrogen abstraction reaction, often referred to as a Norrish Type II process. The products of such a fragmentation reaction are an alkene, a carbonyl compound initially formed as the enol tautomer and often a cyclobutanol derivative. A diradical species is the common intermediate for the formation of the products with the cyclisation pathway being a minor process in some cases. A general mechanism for the Norrish Type II process is shown in Scheme 1.7.

A wide variety of carbonyl compounds fragment via a Norrish Type II process, including aliphatic ketones and long chain aliphatic α -diketones. The reaction can proceed from either the excited singlet or triplet state, or both excited states may contribute to the fragmentation reaction.

The fragmentation of hexan-2-one serves as an example of the Norrish Type II process,³³ (Equation 1.16).

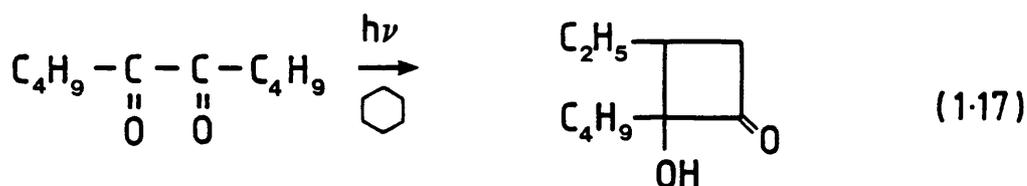




(where, for example, R and R' = -H and/or alkyl)

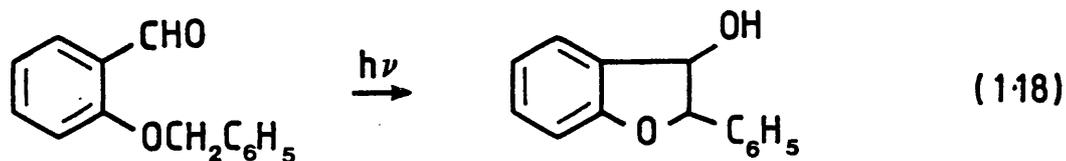
Scheme 1.7

With respect to α -diketones cyclisation, to yield cyclobutanone derivatives, is often favoured over fragmentation to give other products, (a finding which may be due to the greater stability of the intermediate radicals derived from α -diketones), as exemplified by the reaction of 5,6-decanedione in cyclohexane solution yielding 2-butyl-3-ethyl-2-hydroxycyclobutanone,³⁴ (Equation 1.17).



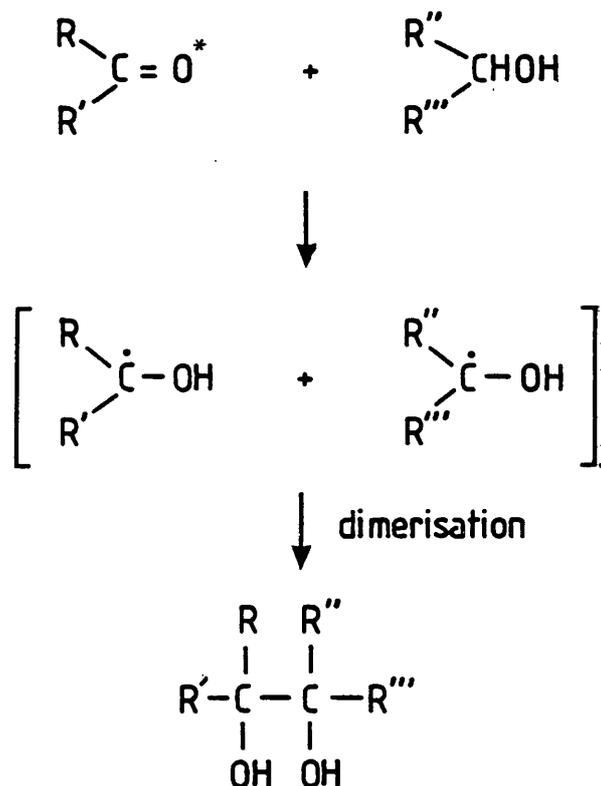
It should be noted that carbonyl compounds which lack a hydrogen atom in the γ -position often give products formed by hydrogen abstraction from

another position as shown by the reaction of o-benzoyloxybenzaldehyde to yield 2-phenyl-3-hydroxy-2,3-dihydrobenzofuran,³⁵ (Equation 1.18).



1.2 (iv) INTERMOLECULAR HYDROGEN ATOM ABSTRACTION

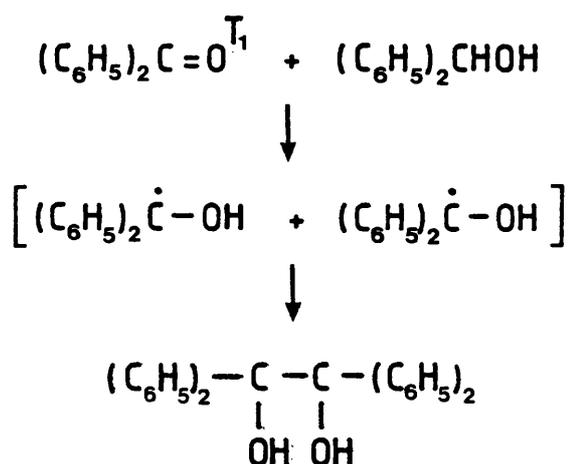
A widely studied reaction is that of the photoreduction of an excited carbonyl compound in the presence of molecules with easily abstractable hydrogen atoms, for example alcohols. A generalised mechanism for the process, which involves radical formation and subsequent dimerisation, is shown in Scheme 1.8.



(where R, R', R'' and R''' = alkyl and/or aryl)

Scheme 1.8

An example of such a photoreduction reaction, which is often used as a standard in quantum yield determinations,³⁶ is that of the photolysis of benzophenone in the presence of benzhydrol leading to the formation of benzpinacol via the dimerisation of the resulting ketyl radicals,³⁷ (Scheme 1.9).

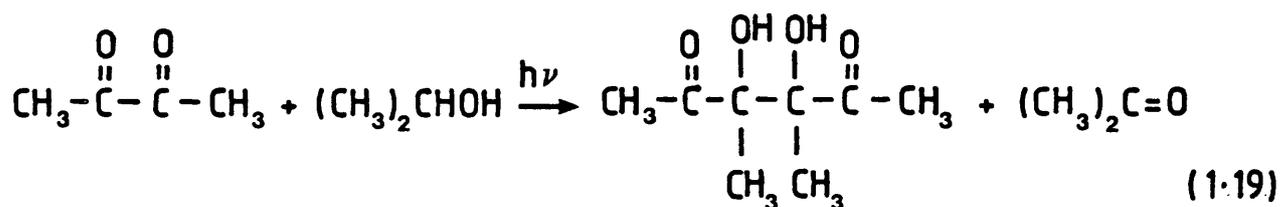


Scheme 1.9

As benzophenone undergoes intersystem crossing with high efficiency, photoreduction is observed only from the triplet state of benzophenone. A similar photoreduction reaction occurs when benzophenone is irradiated in isopropanol solution.³⁸

The photoreduction of biacetyl has been studied in a number of solvents containing abstractable hydrogen atoms³⁹ and the reaction mechanisms in each case can be rationalised on the basis of initial hydrogen abstraction from the solvent by excited biacetyl, followed by reaction of the radicals so formed, as opposed to a mechanism involving α -cleavage. Although biacetyl does not undergo intersystem crossing with as high an efficiency as benzophenone, the triplet state of biacetyl may well be involved in the hydrogen abstraction process. Thus, the irradiation of biacetyl in isopropanol solution gives acetone and a nearly quantitative yield of a mixture of diastereomeric pinacols in approximately equal amounts,³⁹

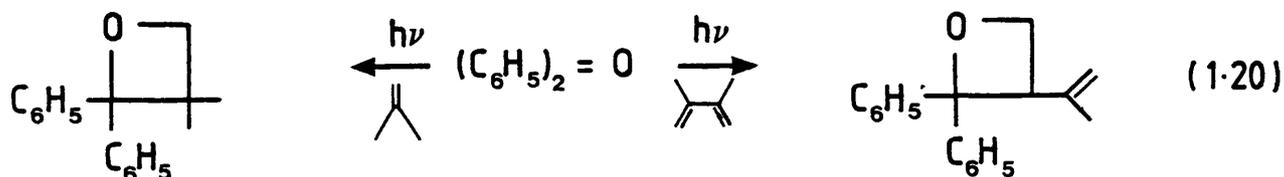
(Equation 1.19).



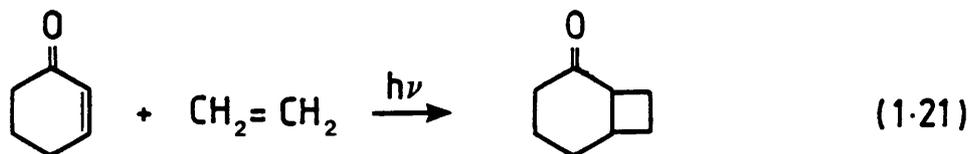
Similarly, when benzil is irradiated in cyclohexane solution a complex mixture of products including benzaldehyde, phenylcyclohexyl ketone, benzoin benzoate and benzoin are obtained via a mechanism suggested to involve initial hydrogen atom abstraction from cyclohexane by excited state benzil.⁴⁰

1.2(v) PHOTOCYCLOADDITION REACTIONS

The irradiation of carbonyl compounds in the presence of alkenes generally leads to oxetanes as photocycloaddition products. For example, benzophenone undergoes photocycloaddition reactions with alkenes⁴¹ and conjugated dienes⁴² to yield oxetanes, (Equation 1.20).

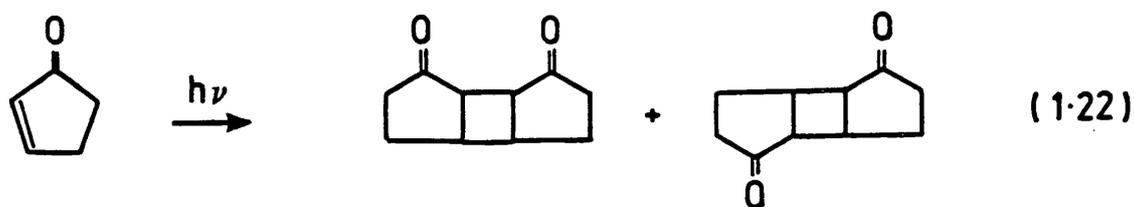


Analogous reactions have also been observed for cyclic ketones, for example, cyclohexenone undergoes a photochemical [2+2] cycloaddition reaction with ethene to give bicyclo[4.2.0]octanone,⁴³ (Equation 1.21).

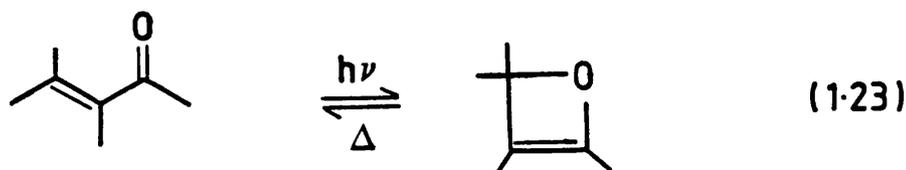


Cyclopentenone upon irradiation yields products of photocyclodimerisation,⁴⁴ (Equation 1.22).

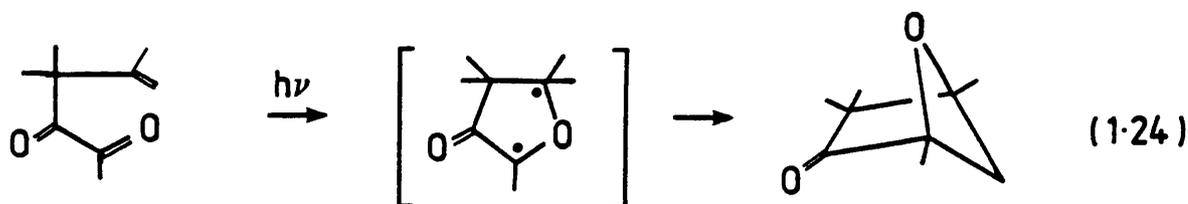
Intramolecular oxetane formation via an intramolecular photocyclo-



addition reaction has been observed for α,β -unsaturated ketones,⁴⁵
 (Equation 1.23).



Similar intramolecular oxetane formation occurs with certain α -
 dicarbonyl compounds⁴⁶ as shown in Equation 1.24.



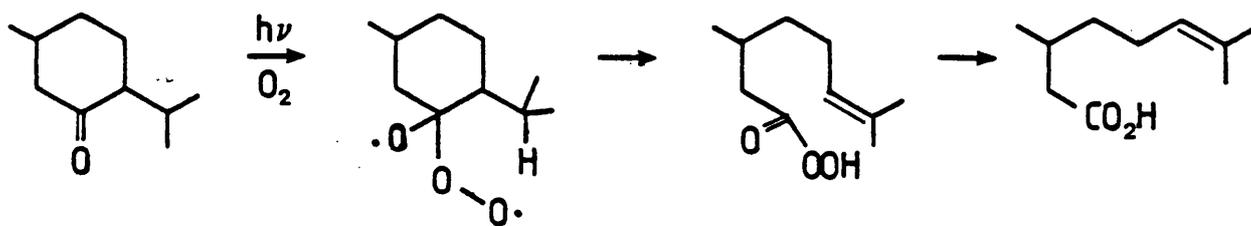
Although biacetyl does not form cycloaddition products upon irradiation
 in the presence of alkenes,^{39,47} the α -diketone, benzil, has been found to
 undergo oxetane formation when photolysed in the presence of vinylene
 carbonate.⁴⁸

1.2(vi) REACTIONS IN THE PRESENCE OF OXYGEN

The effect of oxygen upon the photochemical reactions of carbonyl and
 α -dicarbonyl compounds has not been as extensively investigated as the
 reactions under degassed conditions. The mechanistic details of the
 reactions performed in the presence of oxygen are, in many cases, obscure
 and are exemplified by the following photolyses.

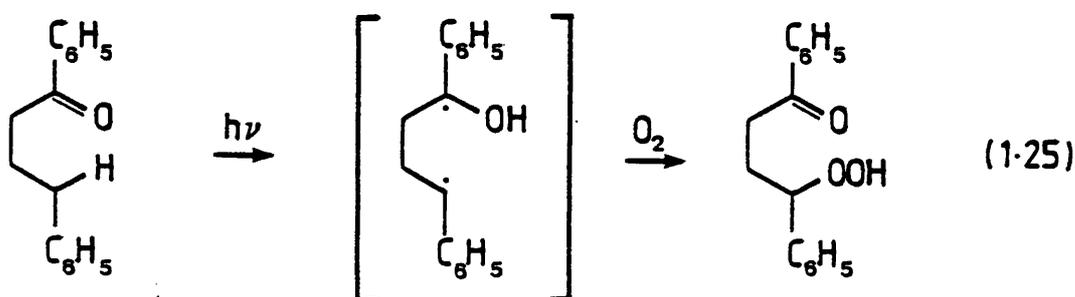
On irradiation in oxygen saturated solution, the cyclic ketone,
 menthone, yields an unsaturated acid⁴⁸ via the mechanism suggested in
 Scheme 1.10.

Oxygen has been used to trap the 1,4-diradicals produced in the



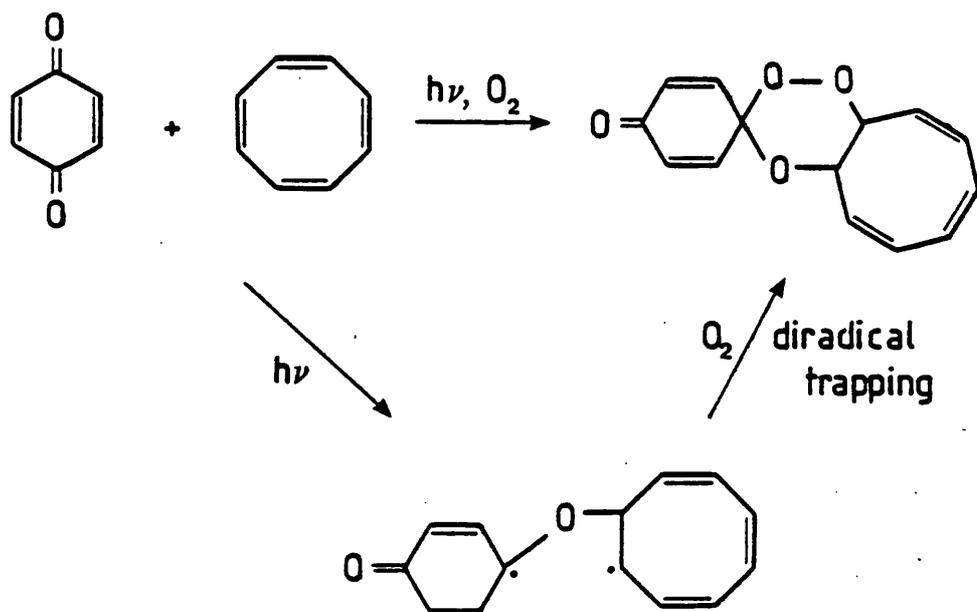
Scheme 1.10

Norrish Type II reaction of carbonyl compounds. For example, the 1,4-diradical produced in the Type II reaction of γ -phenylbutyrophenone has been intercepted by oxygen to yield a hydroperoxide,⁴⁹ (Equation 1.25).



That the hydroperoxide results from trapping of the 1,4-diradical and not from reaction of oxygen with the triplet state of γ -phenylbutyrophenone can be confirmed by kinetic studies utilising laser flash photolysis.⁴⁹ The interaction of oxygen with radicals derived from long-lived carbonyl triplets is less readily observable as triplet quenching by oxygen may affect the radical forming reaction. Attempts to trap the radical intermediates derived from the intermolecular addition of ketones to various substrates with oxygen have been largely unsuccessful. However, oxygen has been found to intercept the diradical formed in the photocycloaddition of benzoquinone to cyclooctatetraene,⁵⁰ (Scheme 1.11).

Tetramethylcyclobutadione yields several products, including tetramethylcyclopropanone, corresponding to loss of carbon monoxide under degassed conditions.^{51,52} The presence of oxygen in the reaction mixture drastically changes the course of the reaction with acetone, carbon monoxide, carbon dioxide and tetramethylethylene oxide being produced.^{51,52}



Scheme 1-11

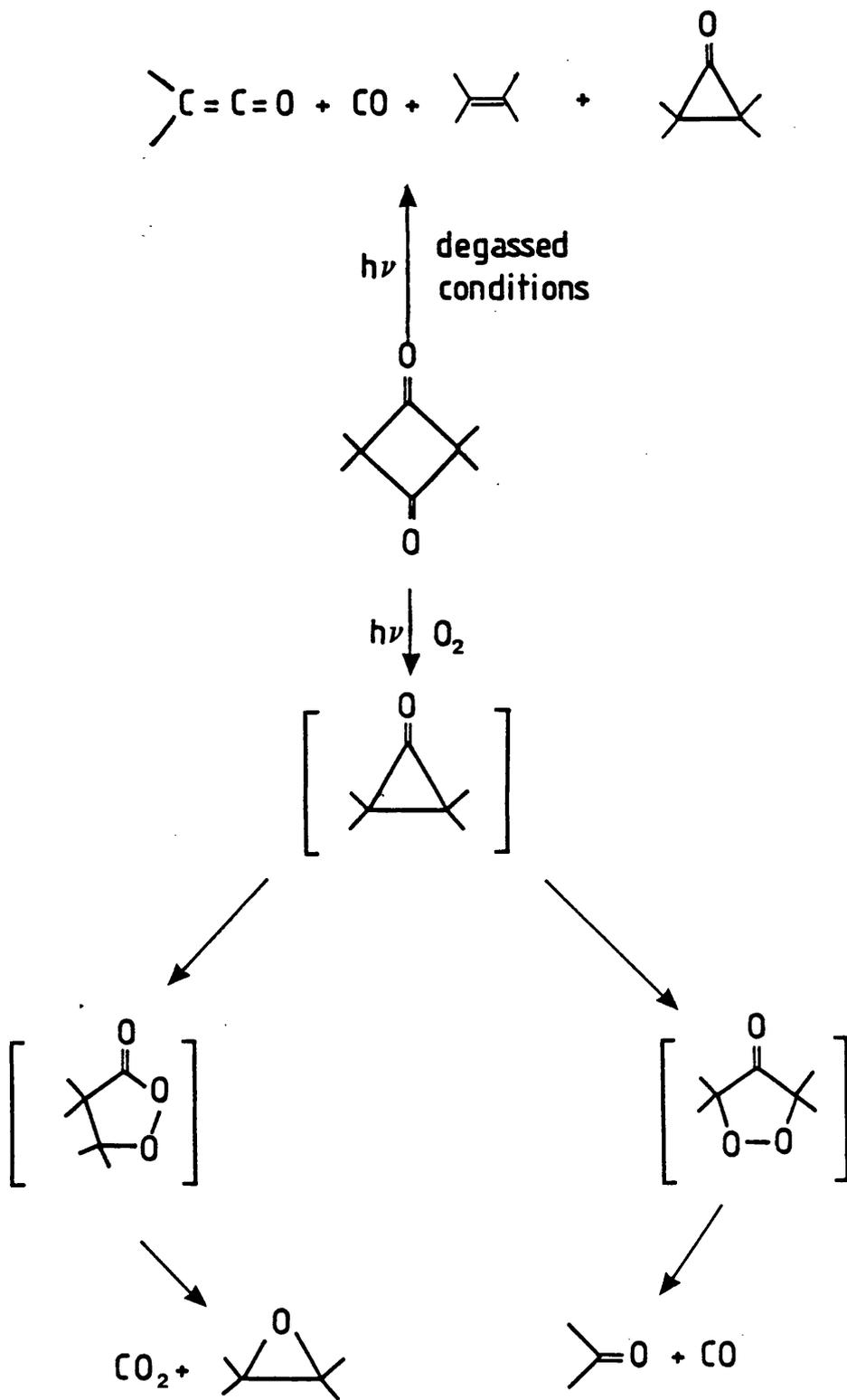
Presumably tetramethylcyclopropanone is initially produced which undergoes addition with oxygen to yield the observed products, as shown in Scheme 1.12.

In conclusion, it is of interest to note that α -dicarbonyl compounds upon irradiation in oxygenated solutions containing various alkenes have been found to sensitize the epoxidation of the alkene.⁵³ For example, irradiation of tetramethylethylene in oxygenated benzene solutions containing either biacetyl or benzil leads to the epoxidation of the alkene,⁵³ (Equation 1.26).



1.2(vii) SUMMARY

Carbonyl and α -dicarbonyl compounds are capable of undergoing a wide variety of photochemical reactions in solution which lead to the formation of new chemical compounds. In some cases, direct cleavage occurs to yield



Scheme 1-12

radicals which undergo further reaction to give the observed products.

Mechanisms involving hydrogen atom abstraction are also important in the

photochemical reactions of carbonyl compounds and can be inter- or intramolecular in nature. When possible internal hydrogen atom abstraction is generally preferred over hydrogen abstraction from the solvent. In the presence of suitable substrates, cycloaddition reactions are observed. The presence of oxygen markedly affects the course of the reactions.

1.3 MECHANISMS OF PHOTOCHEMICAL OXIDATION REACTIONS

Preface

Molecular oxygen is a powerful oxidising species which can undergo reaction with a wide variety of organic substrates. In aerobic organisms the reactivity of oxygen, with biological molecules, is subject to finite control by the organism's metabolism in order to prevent oxygen reacting indiscriminately with the numerous molecules necessary for the maintenance of life. As the ground state of oxygen is a triplet it is prevented from reacting with the wealth of singlet ground state organic compounds by a spin barrier. The highly reactive excited states of oxygen are however singlets and it is only by controlling this triplet-singlet barrier that the requirements for the continued maintenance of life can be attained.

1.3(i) INTRODUCTION

The electronic configuration of molecular oxygen was first interpreted by Mulliken⁵⁴ who predicted three states for the oxygen molecule, spectroscopically denoted as $^3\Sigma_g^-$, $^1\Delta_g$ and $^1\Sigma_g^+$ respectively. The outermost pair of the electrons in the molecule are located in the two highest occupied molecular orbitals. These orbitals are degenerate and the electrons have their spins parallel which makes the ground state a triplet ($^3\Sigma_g^-$) and accounts for the paramagnetic properties exhibited by ground state molecular oxygen. Mulliken⁵⁴ suggested that two other arrangements of these two outermost electrons are possible and should give rise to two low-lying singlet states ($^1\Delta_g$ and $^1\Sigma_g^+$), which were both later identified by spectroscopic studies. The spectroscopic observation of the $^1\Sigma_g^+$ state, 37.5 kcal above the ground state, was reported by Childs and Mecke.⁵⁵ Later, Ellis and Kneser⁵⁶ and Herzberg⁵⁷ independently

reported the observation of the ${}^1\Delta_g$ state, 22.5 kcal above the ground state. These two low-lying states were classified as singlets as a consequence of their outer electron pairs having anti-parallel spins. Thus, the first excited singlet state of molecular oxygen (${}^1\Delta_g$) has the two electrons with anti-parallel spin in one orbital, whilst the second excited singlet state (${}^1\Sigma_g^+$) has the two electrons also with anti-parallel spin, but in this case each of the electrons occupies one of the degenerate orbitals. These electronic configurations of molecular oxygen are shown schematically in Figure 1.3.

| <u>Molecular oxygen</u> | <u>Occupancy of the highest orbitals</u> | <u>Energy difference with the ground state</u> |
|---|--|--|
| Second excited state (${}^1\Sigma_g^+$) | \uparrow \downarrow | 37.5 kcal/mole |
| First excited state (${}^1\Delta_g$) | $\uparrow\downarrow$ --- | 22.5 kcal/mole |
| Ground state (${}^3\Sigma_g^-$) | \uparrow \uparrow | |

FIGURE 1.3

That singlet molecular oxygen was the active intermediate in oxidations performed in the presence of a dye, light and oxygen (or air) was first proposed by Kautsky and de Bruijn⁵⁸ in 1931. Earlier reports of oxidation reactions in the presence of a dye, light and oxygen had appeared⁵⁹⁻⁶¹ although the mechanisms of these photo-oxidations were uncertain and none invoked free singlet molecular oxygen as the reactive species.

Kautsky and co-workers⁶² later reported that if the dye and the substrate were physically separated on silica gel supports, photo-oxidation could still occur. It was proposed⁶² that the reactive singlet state of oxygen responsible for bringing about oxidation was the ${}^1\Sigma_g^+$ state and in a gaseous form diffused from the dye/silica particles to undergo reaction

with substrate/silica particles. Gaffron⁶³ subsequently found that dyes with energies of less than 37.5 kcal/mole could sensitize photo-oxidation reactions and this, together with the spectroscopic observations of the $^1\Delta_g$ state of oxygen,^{56,57} led Kautsky to revise his mechanism to include the first excited singlet state of molecular oxygen.^{64,65}

In retrospect it seems surprising, in spite of Kautsky's elegant experiments, that his deductions did not convince his contemporaries and were generally ignored in favour of a moloxide mechanism proposed initially by Schönberg.⁶⁶ The moloxide mechanism, which involves the formation of an unstable sensitizer-oxygen complex capable of transferring oxygen to an acceptor molecule, was later supported by Schenck⁶⁷ and became the generally accepted mechanism for photo-oxidation reactions, in total disregard to any involvement of singlet oxygen.

The participation of singlet oxygen in photo-oxidation reactions, discovered in the 1930's by Kautsky, was later 're-discovered' in the early 1960's by several groups who found that singlet oxygen, produced by chemical methods, could oxidise a variety of organic substrates to give products similar to those obtained from dye-sensitized photo-oxygenations. In 1964, Foote and Wexler reported that oxidation with singlet oxygen produced by the peroxide-hypochlorite reaction⁶⁸ gave rise to identical products to those formed in the analogous dye-sensitized reaction.⁶⁹ At the same time Corey and Taylor⁷⁰ reported similar observations using singlet oxygen generated by electrical discharge. Although these experiments⁶⁸⁻⁷⁰ did not provide unambiguous evidence for the intermediacy of singlet oxygen in photo-oxygenation reactions, they did however substantiate Kautsky's original proposal and provide the basis for the rapid expansion of investigations into the chemistry of singlet oxygen which has subsequently followed.

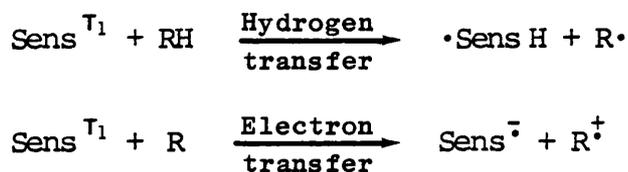
In the gaseous form the radiative lifetime of the $^1\Delta_g$ state of oxygen is around 45 minutes^{71,72} and that of the $^1\Sigma_g^+$ state is around 7 seconds.^{55,73} Due to intermolecular collisions these lifetimes are dramatically reduced in solution and are estimated at around 10^{-3} and 10^{-9} seconds for the $^1\Delta_g$ and $^1\Sigma_g^+$ states of oxygen respectively.⁷⁴ It is now appreciated⁷⁴ that in solution the $^1\Sigma_g^+$ state rapidly relaxes to the $^1\Delta_g$ state by collisional quenching interactions and as such reactions of the $^1\Sigma_g^+$ state in solution are uncertain. Presently the reactive intermediate in solution phase photo-oxidations is considered to be the first excited singlet state ($^1\Delta_g$) of molecular oxygen and hereafter singlet oxygen or 1O_2 refers to the $^1\Delta_g$ state of oxygen unless otherwise mentioned.

Since the work carried out in the early 1960's⁶⁸⁻⁷⁰ much has been learnt regarding the properties and chemistry of singlet oxygen in relation to its interaction with a vast number of other molecules, the reports of which have been abundant in the literature. Many excellent reviews have also appeared.^{75(a)-(1)} The following sections summarise some of the more important aspects of the properties of singlet oxygen and do not represent an exhaustive critique of the reports constantly appearing in the current literature.

1.3(ii) TYPE I AND TYPE II PROCESSES

Photo-oxidation reactions can be defined as those in which a substrate, A, under the action of light, in the presence of molecular oxygen is transformed into the addition product, AO_2 . It is necessary to distinguish between the two mechanisms which can be responsible for such photo-oxidation reactions, classified as Type I and Type II processes respectively.

Type I processes involve the participation of radicals in the oxidation reaction. The radicals can be produced by either hydrogen or electron transfer from a reducing substrate (RH or R) to a triplet sensitizer, (Scheme 1.13).



SCHEME 1.13

The interaction of oxygen with the radicals so produced (Scheme 1.13) then brings about the oxidation of the substrate in which the superoxide radical anion (O_2^{\ominus}) or its conjugate acid ($\text{HO}_2\cdot$) may participate. Hydrogen peroxide, produced by the disproportionation of $\text{HO}_2\cdot$, may also be involved.

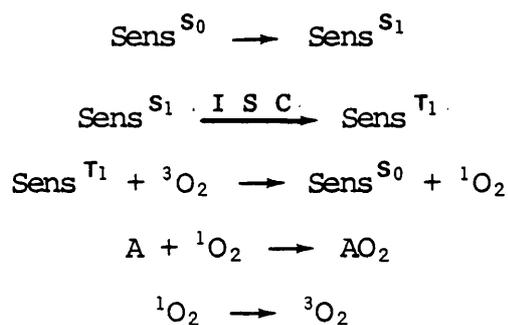
The chemistry of Type I processes is often very complex due to the number of possible pathways open for reaction and the mechanisms of these reactions require careful experimental scrutiny utilising techniques such as flash spectroscopy or chemical trapping to probe the radical intermediates.

The Type II process, which is not radical in nature, involves the intermediacy of singlet oxygen which undergoes direct reaction with a substrate to give the oxidation products. There are a number of ways in which singlet oxygen can be produced and these, together with the characteristic chemical reactions of singlet oxygen, are discussed in later sections.

1.3(iii) METHODS OF GENERATION OF SINGLET OXYGEN

(a) Energy Transfer

Singlet oxygen can be conveniently produced by energy transfer from the excited state of a sensitizer, usually in its triplet state, to ground state oxygen. The sensitizer is first excited to its singlet state, via irradiation with light and can then undergo intersystem crossing, to give the triplet state of the sensitizer, or return to its ground state. The triplet sensitizer so produced can then undergo energy transfer to ground state molecular oxygen to yield singlet oxygen which, in turn, can react with a substrate (A) or return to its ground state, as summarised in Scheme 1.14 and Figure 1.4.



SCHEME 1.14

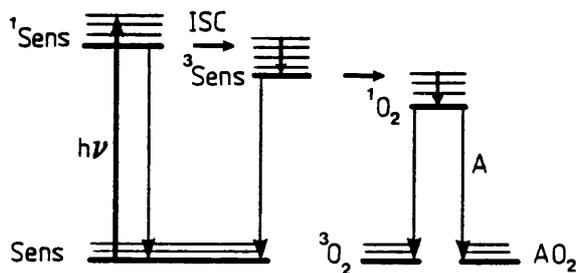
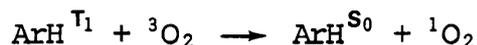


Fig. 1.4

It should be noted that in some cases of self-sensitized photo-peroxidations of aromatic hydrocarbons, singlet oxygen formation has been

observed as a result of quenching of the excited singlet state of the aromatic hydrocarbon.^{76,77} Indeed, the highly fluorescent aromatic hydrocarbon rubrene was reported to lead to singlet oxygen production with quantum yields in excess of unity via the following mechanism,^{76,77} (Scheme 1.15).



(where ArH = Aromatic hydrocarbon)

SCHEME 1.15

Many of the sensitizers used in photo-oxygenation reactions have high rates of intersystem crossing (with resulting high triplet yields) and absorb light in easily accessible regions of the electromagnetic spectrum thus enabling easy generation of triplet sensitizer. The triplet energy of the sensitizer is an important factor in producing excited state oxygen, for sensitizers having triplet energies between 22 and 38 kcal/mole will generate only ${}^1\Delta_g\text{O}_2$ whereas sensitizers having triplet energies in the region 38-45 kcal/mole can produce both ${}^1\Delta_g\text{O}_2$ and ${}^1\Sigma_g^+\text{O}_2$. Dyes such as Rose Bengal ($E_T = 40$ kcal/mole), Tetraphenylporphyrin ($E_T = 34$ kcal/mole) and Methylene Blue ($E_T = 34$ kcal/mole) are commonly used as sensitizers, but their main disadvantage is that they are difficult to remove from the product mixture. However, this problem has now been overcome by the use of insoluble polymer-bound dyes which can be easily removed by filtration after irradiation. The first example of a heterogeneous sensitizer was described by Blossey and co-workers.⁷⁸

Other problems associated with using dyes as sensitizers for singlet oxygen production include dye photobleaching, interaction of dye with substrate and/or products and solubility of dye in the reaction solvent.

(b) Electrical Discharge

The first report of the production of singlet oxygen by passing a stream of oxygen through an electric discharge was that by Foner and Hudson⁷⁹ in 1956. These authors⁷⁹ estimate between 10-20% singlet oxygen in the effluent stream. Production of singlet oxygen by this technique was later utilised by Corey and Taylor⁷⁰ who bubbled the effluent stream through solutions of organic substrates in order to bring about oxygenation.

The development of powerful radio and microwave generators eliminates the necessity for internal electrodes in the discharge process, since radiation of these types can penetrate the walls of the glass vessels and directly excite oxygen molecules in the gas stream. The use of microwave discharge to produce singlet oxygen is now favoured over radiofrequency generation. The microwave generators operate at 2450 MHz, a frequency which does not interfere with other electrical equipment and can be localised and directed using waveguides.

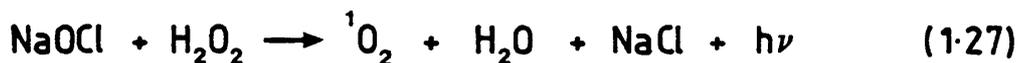
The main disadvantage of using singlet oxygen generated by the above discharge methods is that other species of oxygen, which have powerful oxidising properties, are also produced. Therefore careful control of the effluent gas is required in order to remove the ozone, atomic oxygen and the small amounts of $^1\Sigma_g^+O_2$ thus formed.

(c) Chemical Methods for Singlet Oxygen Production

Singlet oxygen can be generated by a number of chemical methods, some examples of which are given below.

(1) Peroxide Decomposition

The reaction of sodium hypochlorite with hydrogen peroxide leads to the formation of singlet oxygen, (Equation 1.27).



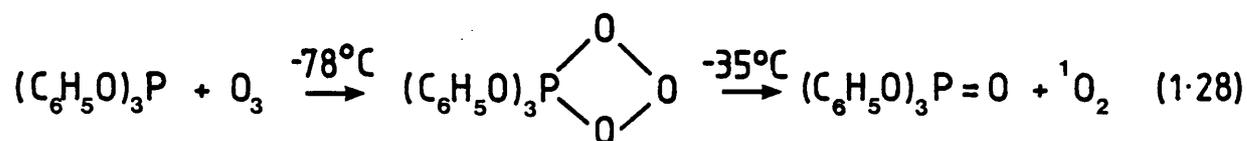
The observation of a weak red chemiluminescence was first observed by Mallet⁸⁰ in 1927 and later confirmed by Seliger⁸¹ in 1960. Khan and Kasha,⁸² in 1963, attributed the chemiluminescence to emission from electronically excited molecular oxygen and subsequently⁸³ identified ${}^1\Delta_g\text{O}_2$ as the species involved. The initial report by Khan and Kasha⁸² invoking singlet oxygen production in the above system prompted Foote and Wexler⁶⁸ to utilise this method of singlet oxygen generation in the oxygenation of various organic substrates.

The problem of solubility, due to the large amounts of water involved, is the main disadvantage in the use of the hypochlorite-peroxide method for singlet oxygen production.

In an attempt to alleviate the solvent limitations of the reaction, McKeown and Waters⁸⁴ developed a two-phase system in which bromine replaced the sodium hypochlorite. In this way singlet oxygen formed in the lower aqueous phase, via the reaction of hydrogen peroxide and bromine, rises up through the upper organic layer containing the substrate. However, it should be pointed out that side reactions, due to bromine, provide a drawback to this method.

(2) Triphenylphosphite Ozonide Decomposition

Murray and Kaplan⁸⁵ found that when ozone is passed through a solution of triphenylphosphite at -78°C an adduct, triphenylphosphite ozonide, is formed. Upon warming the solution to -35°C the adduct decomposes to yield singlet oxygen and triphenylphosphate, (Equation 1.28). The singlet oxygen so produced can then be used to oxygenate various substrates.⁸⁵



The production of singlet oxygen in the above reaction was initially questioned by Bartlett and Mendenhall⁸⁶ who found that the adduct triphenylphosphite ozonide could undergo direct reaction with several alkenes and thus may be acting as an oxygen transfer agent as opposed to a progenitor of free singlet oxygen. However, the observation of the characteristic absorptions due to singlet oxygen by Wasserman and co-workers,⁸⁷ when the oxygen evolved from the decomposition of solid triphenylphosphite ozonide was passed into the cavity of an E.S.R. spectrometer in the gas phase, point to the involvement of free singlet oxygen in the above reaction.

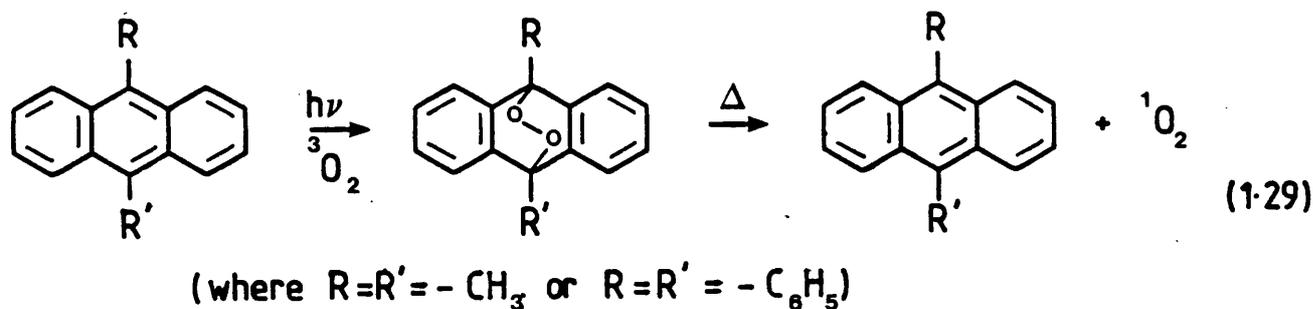
Apart from solvent restrictions the use of this method for singlet oxygen production is severely hampered by the instability of the triphenylphosphite ozonide adduct.

(3) Thermal Decomposition of Transannular Peroxides of Aromatic Hydrocarbons

The reversible addition of oxygen to an aromatic hydrocarbon was first reported by Moureu and co-workers⁶⁰ in 1926. These authors⁶⁰ found that rubrene, when exposed to sunlight in aerated benzene solution, formed a colourless solution from which a crystalline peroxide was isolable. Upon heating, the peroxide regenerated the red hydrocarbon with the concomitant evolution of oxygen.

In 1967, Wasserman and Scheffer⁸⁸ showed that the thermal decomposition of the endoperoxides of 9,10-dimethyl- and 9,10-diphenylanthracene led to the regeneration of the aromatic hydrocarbon and the release of singlet oxygen which could be trapped by acceptors in solution, (Equation 1.29).

The utilisation of this procedure necessitates heating the acceptor and the peroxide under reflux in an organic solvent and, as a consequence of the relatively high temperature requirements and long time for



peroxide decomposition, may cause problems with some acceptors.

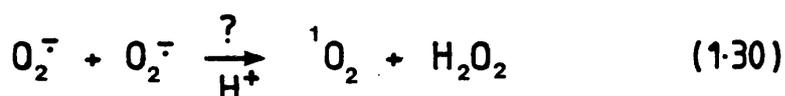
(4) Other Methods of Singlet Oxygen Generation

In 1968, Howard and Ingold⁸⁹ reported that oxidation of *s*-butylhydroperoxide, by Ce^{4+} , led to singlet oxygen formation. Although this finding⁸⁹ was later confirmed spectroscopically by Nakano and co-workers⁹⁰ this method for singlet oxygen production is not very useful preparatively.

Peters and co-workers⁹¹ have reported that potassium perchromate, upon aqueous decomposition, generates singlet oxygen although competitive oxidative processes impair the usefulness of this system as a source of singlet oxygen.

The suggestion by Khan⁹² in 1970 that the superoxide radical anion, produced from the decomposition of potassium superoxide in dimethylsulphoxide solution, could undergo dismutation to yield singlet oxygen gave rise to much discussion due to the obvious implications in many biological systems. Some workers supported this proposal, for example Mayeda and Bard⁹³ reported that superoxide, generated electrochemically, could oxidise the known singlet oxygen acceptor 1,3-diphenylisobenzofuran. However, Barlow and co-workers⁹⁴ found that the enzymes ribonuclease and lysozyme were not inactivated when subjected to γ -radiolysis and as such suggested that singlet oxygen is not formed from either $HO_2\cdot$ or $O_2^{\cdot-}$, which are the only two radical species present under the experimental conditions employed.

The view that dismutation of superoxide does not lead to singlet oxygen production was supported by Foote and co-workers⁹⁵ who found that <0.2% of singlet oxygen is produced from the dismutation reaction. In their⁹⁵ study the oxidation of cholesterol (supported on microbeads) was investigated using superoxide generated from the decomposition of tetramethylammonium superoxide in dimethylsulphoxide solution. More recently, Khan⁹⁶ has reported direct spectroscopic evidence, to substantiate his earlier proposal,⁹² that singlet oxygen is produced from the reaction of potassium superoxide with water. At present there is, therefore, a certain amount of speculation as to whether dismutation of the superoxide radical anion in fact produces singlet oxygen (Equation 1.30) and a definite answer has yet to be provided.

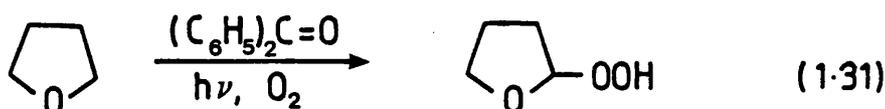


1.3(iv) PHOTO-OXIDATION VIA THE TYPE I PROCESS

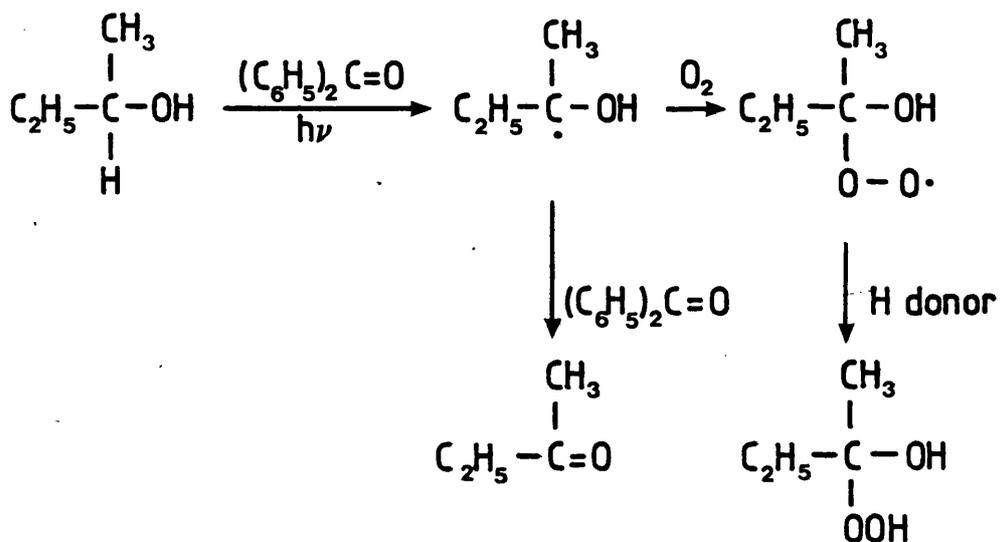
Several photo-oxidation reactions have been shown to involve the intermediacy of radicals and as such can be classified as occurring via Type I processes, as described by the following examples.

The photo-oxidation of alcohols sensitized by ketones, such as benzophenone, proceed via a radical mechanism⁹⁷ yielding hydroxyhydroperoxides or ketones depending upon the reaction conditions, (Scheme 1.16).

Hydroperoxides are formed in the analogous reaction of ethers,⁹⁷ (Equation 1.31).

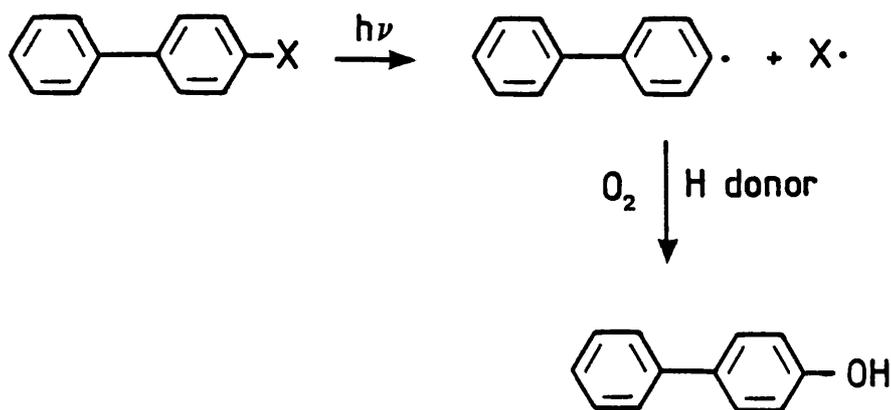


Halogenated biphenyls irradiated in the presence of oxygen lead to the



Scheme 1.16

production of phenols as a result of fission of the carbon-halogen bond and radical scavenging by oxygen,⁹⁸ (Scheme 1.17).

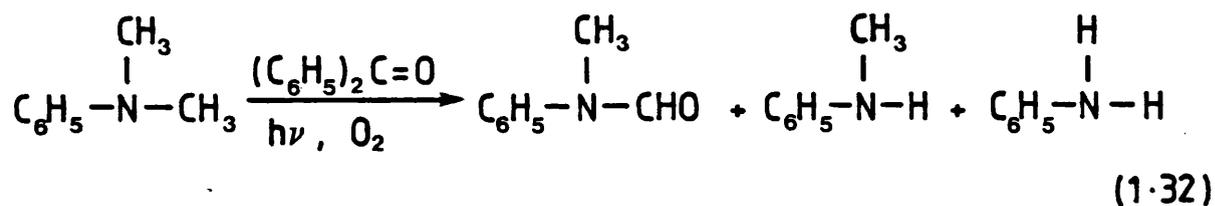


(where X = halogen)

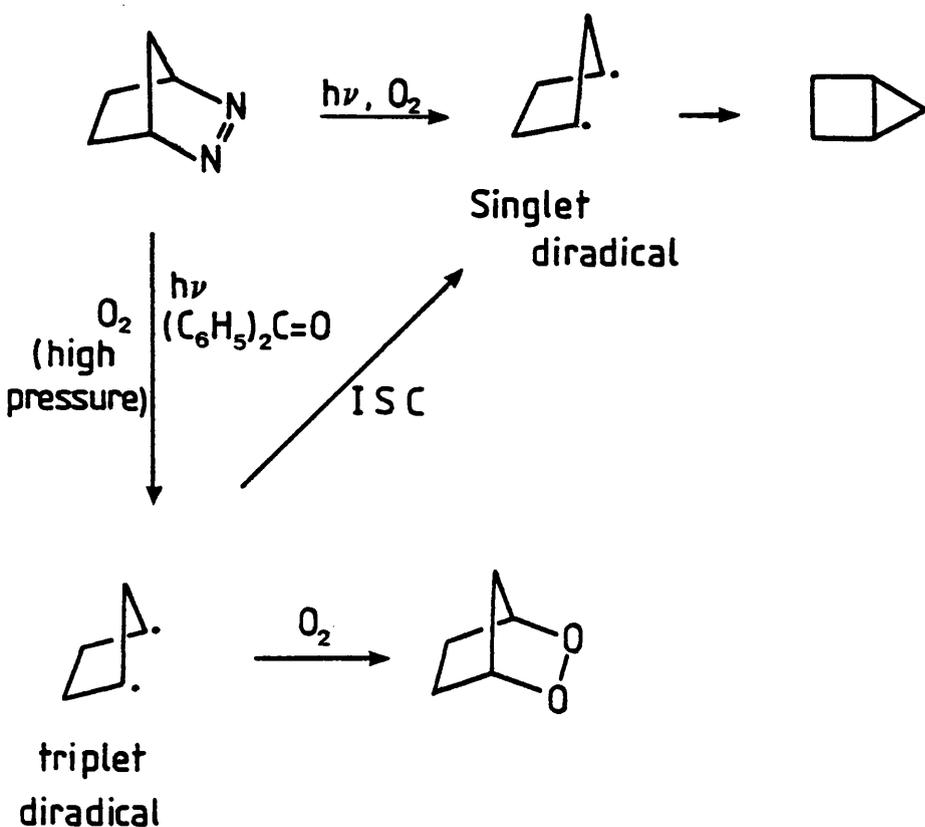
Scheme 1.17

The photo-oxidation of amines, such as N,N-dimethylaniline, by benzophenone has been shown to occur by a mechanism involving radical intermediates⁹⁹ as opposed to singlet oxygen, (Equation 1.32).

The direct photolysis of azo-compounds in the presence of oxygen leads to the formation of products resulting from ring closure of a singlet diradical which is not intercepted by oxygen.¹⁰⁰ However, if



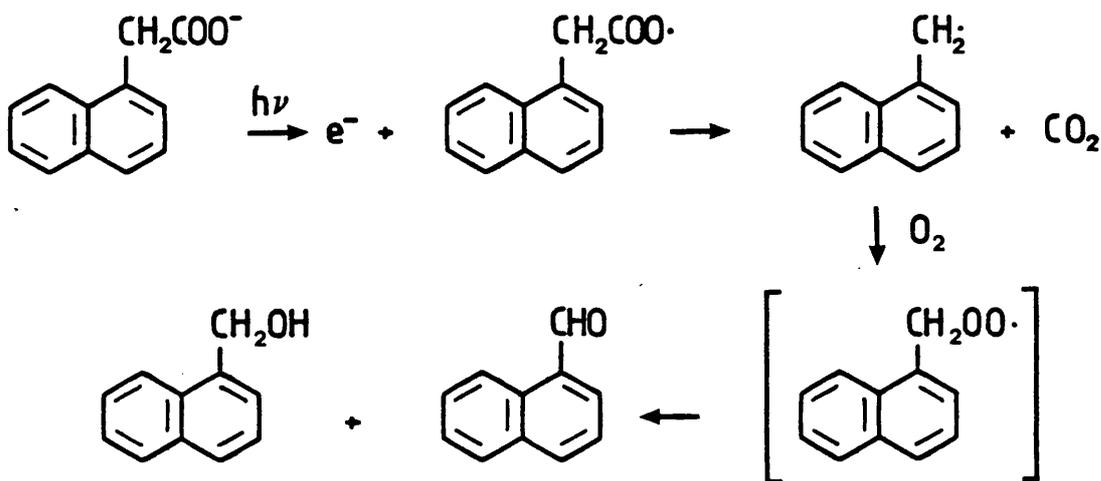
the reaction is performed in the presence of benzophenone and oxygen, sensitization of a triplet diradical occurs and oxygenation products are obtained as a result of interception of the triplet diradical by oxygen,¹⁰⁰ (Scheme 1.18).



Scheme 1.18

Irradiation of 1-naphthylacetates in the presence of oxygen leads to decarboxylation and the formation of 1-naphthylmethanol and 1-naphthaldehyde.¹⁰¹ The mechanism is suggested to involve electron ejection and radical formation with the interception of the radicals by oxygen yielding the observed products,¹⁰¹ (Scheme 1.19).

Similar mechanisms involving electron transfer and radical scavenging



(where e^- = electron)

Scheme 1-19

by oxygen have been proposed for the decarboxylation of various carboxylic acids sensitized by carbonyl compounds and quinoxalines.¹⁰²

The interception of the 1,4-diradicals (formed in intramolecular hydrogen abstraction reactions) by oxygen also exemplifies oxygenation via a Type I process,⁴⁹ (Equation 1.25).

Several of the above examples are unimolecular in nature inasmuch as the direct irradiation of the substrate, in the presence of oxygen, is employed to investigate the photo-oxidative mechanism. However, in cases where a sensitizer is used then these bimolecular reactions usually involve hydrogen atom abstraction from the substrate by the sensitizer. Many of the sensitizers used are dyes and as such are also capable of producing singlet oxygen which may make it difficult to distinguish between Type I and Type II processes in these cases. This problem is discussed in more detail later.

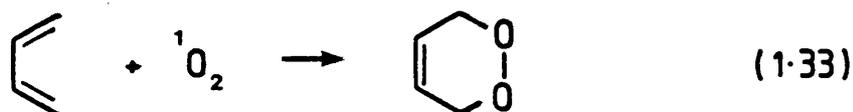
1.3(v) PHOTO-OXIDATION VIA THE TYPE II PROCESS

Singlet oxygen has been suggested to be involved in many photo-oxygenation reactions of organic molecules. The following section high-

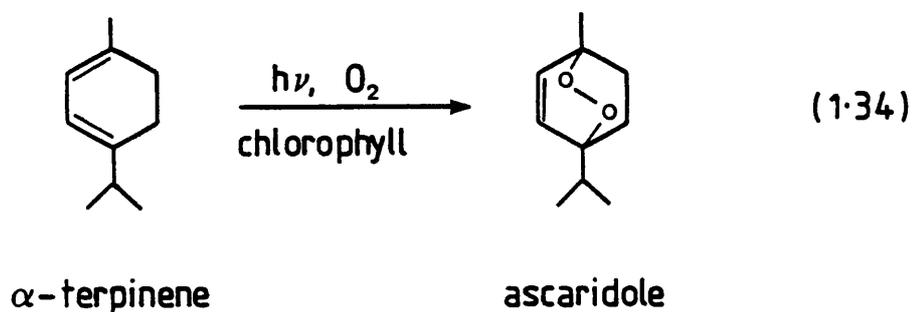
lights the three main types of chemical reaction that singlet oxygen undergoes, citing several well-defined examples of each type of reaction.

(a) 1,4-Addition Reactions

Singlet oxygen may react as a dienophile to give Diels-Alder addition products. This 1,4-cycloaddition reaction of singlet oxygen with a conjugated diene results in the formation of endoperoxides, (Equation 1.33).

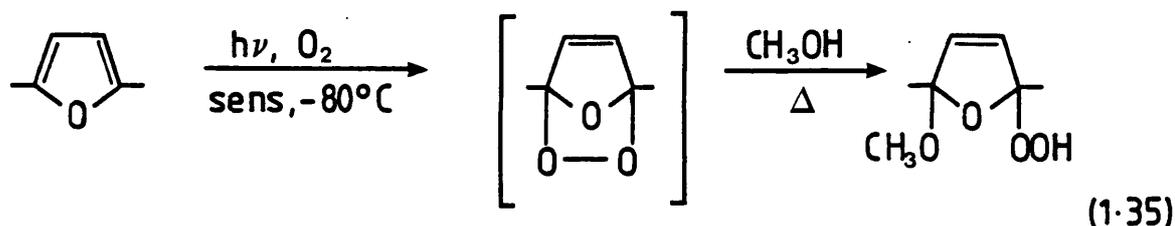


In 1944, Schenck and Ziegler¹⁰³ reported the first dye-sensitized photo-oxygenation of a simple 1,3-diene, α -terpinene to yield ascaridole, a natural product being the active constituent of chenopodium oil, (Equation 1.34). Ascaridole is an endoperoxide formed in plants by the chlorophyll sensitized photo-oxidation of α -terpinene.

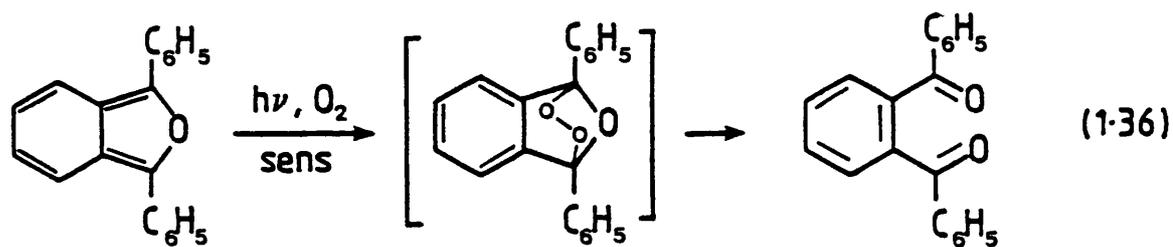


Other examples of 1,4-cycloaddition reactions are shown in Equations 1.35-1.37. The endoperoxides produced in each case, via the initial reaction of singlet oxygen and the diene, are often unstable and rearrange to other products.

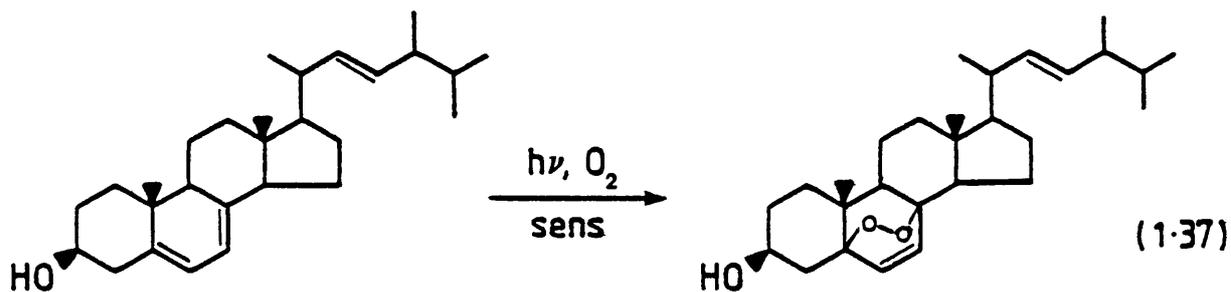
2,5-Dimethylfuran^{68,69}



1,3-Diphenylisobenzofuran¹⁰⁴

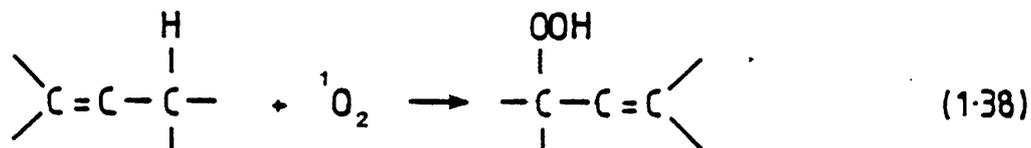


Ergosterol⁶¹



(b) The Ene Reaction

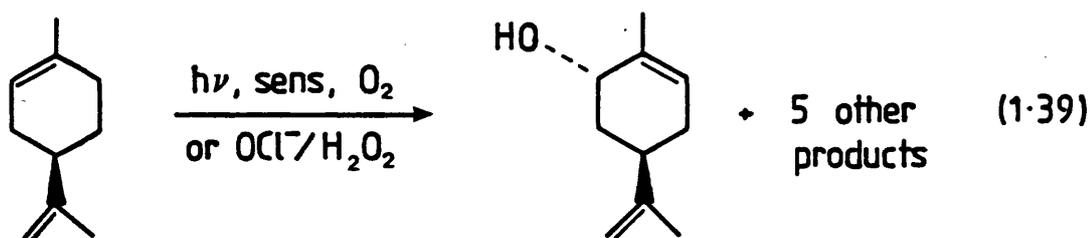
This reaction is the addition of singlet oxygen to an alkene bearing allylic hydrogen atoms with the formation of an allylic hydroperoxide accompanied by an allylic shift of the double bond, (Equation 1.38).



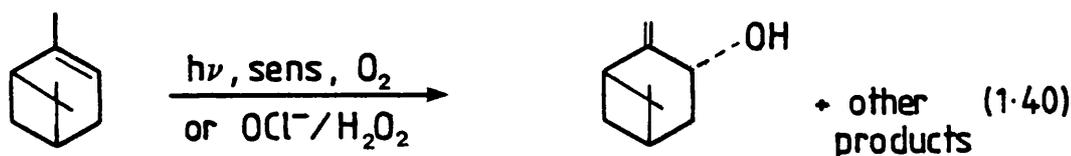
The allylic hydroperoxides thus formed can be easily reduced to the corresponding allylic alcohols and this provides a means of introducing an allylic oxygen function into a molecule, with the simultaneous rearrangement of the double bond. The first report of reactions of this type was that by Schenck and co-workers¹⁰⁵ in 1953 when studying the dye-sensitized photo-oxygenation of alkyl substituted alkenes.

The ene reaction has been shown to occur with limonene both under dye-sensitized conditions¹⁰⁶ and using singlet oxygen generated from the hypochlorite-peroxide system¹⁰⁷ to give the same product distribution in

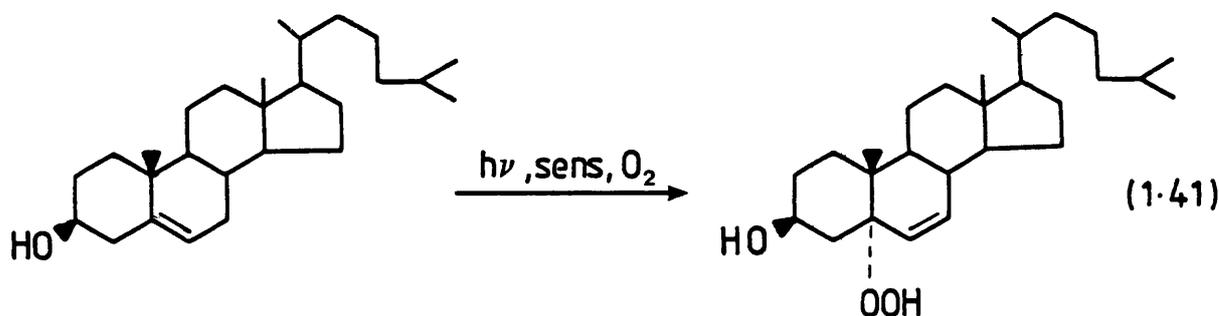
each case. Six hydroperoxides are formed, by attack of singlet oxygen upon the endocyclic double bond, which can be reduced to the corresponding alcohols. Interestingly, the alcohols formed were found to be optically active when using optically active limonene^{106,107} (Equation 1.39) and therefore a mechanism involving free radical intermediates can be excluded as the alcohol is not produced in a racemic form.



Similarly, identical products have been obtained from both the dye-sensitized¹⁰⁸ and hypochlorite-peroxide¹⁰⁷ induced oxidation of α -pinene, (Equation 1.40).

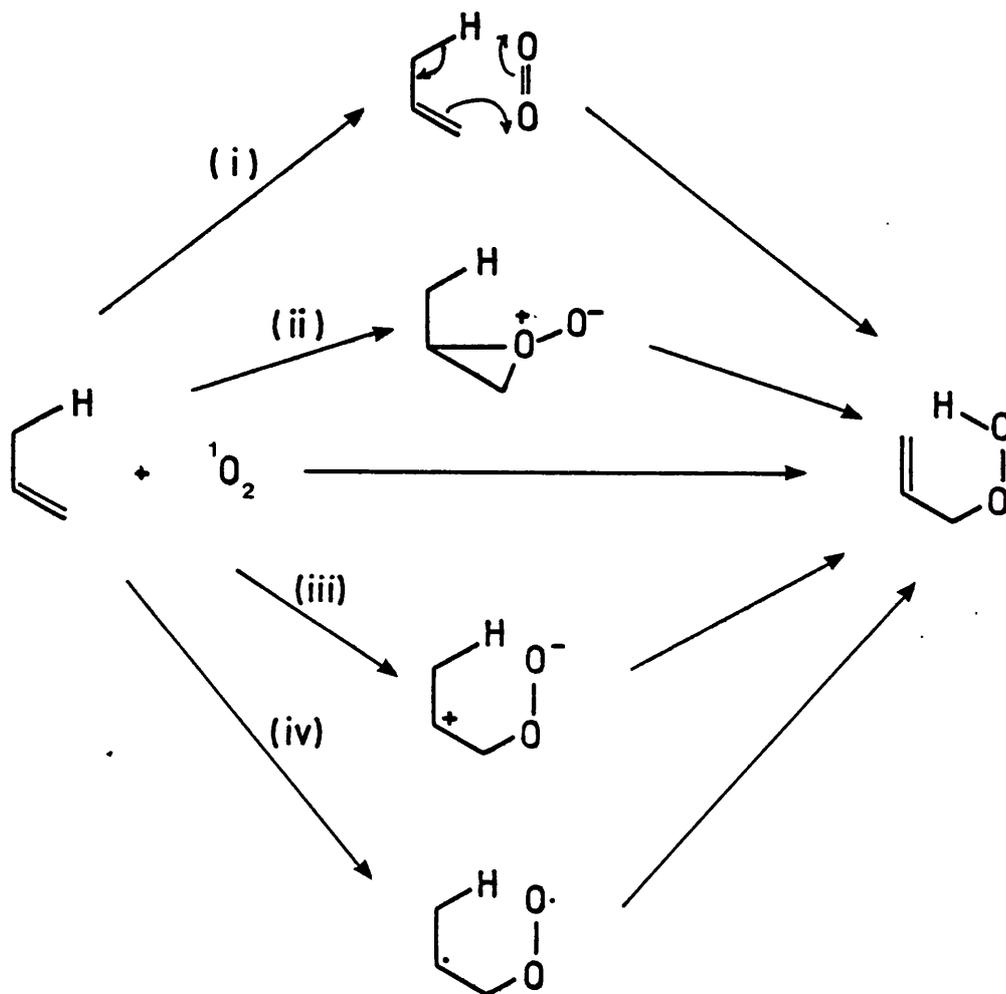


The dye-sensitized photo-oxygenation of cholesterol giving rise to the allylic hydroperoxide, 3- β -hydroxy-5 α -cholest-6-ene-5-hydroperoxide, is another example of the ene reaction of singlet oxygen,¹⁰⁹ (Equation 1.41).



The ene reaction has been the subject of major interest and controversy for many years, the chief mechanistic problem being whether or not the reaction is concerted. Scheme 1.20 summarises the possible mechanisms

which may be involved in the ene reaction. A concerted reaction would involve a six-membered transition state typical of the classical ene reaction [route (i)]. Intermediates which may be possible in a non-concerted reaction are a perepoxide [route (ii)], a zwitterion [route (iii)] or a diradical [route (iv)].



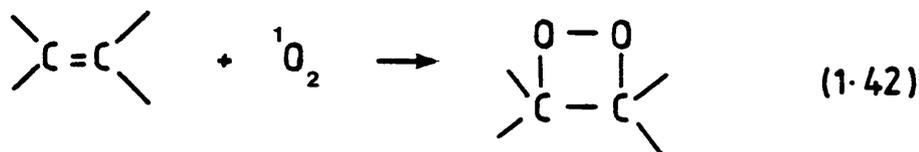
Scheme 1-20

At present it is difficult to draw definite mechanistic conclusions from the vast volume of literature which appears on this subject. There is no rigorous proof available that the ene reaction with singlet oxygen is concerted. At the same time there is also no need to postulate such intermediates as perepoxides, for example, although calculations appear

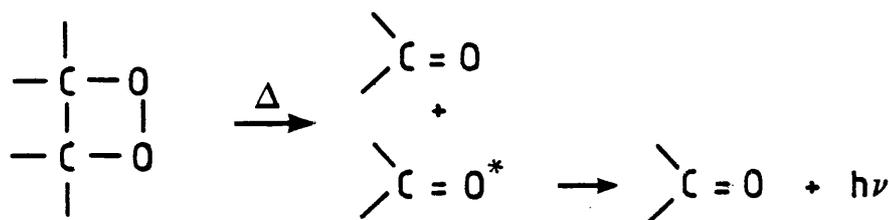
to favour such intermediates. Conversely, the majority of experimental results can be explained by assuming a concerted reaction, whereas the assumptions of peroxide intermediates are not compatible in all experimental reports. However the current interpretations given in the literature are usually based on the assumption that an intermediate is involved. This topic has been the subject of a detailed review¹¹⁰ and an exhaustive critique is not within the scope of this section.

(c) 1,2-Addition Reactions

Under certain conditions singlet oxygen can undergo 2 + 2 cycloaddition reactions with alkenes to yield 1,2-dioxetanes, (Equation 1.42).



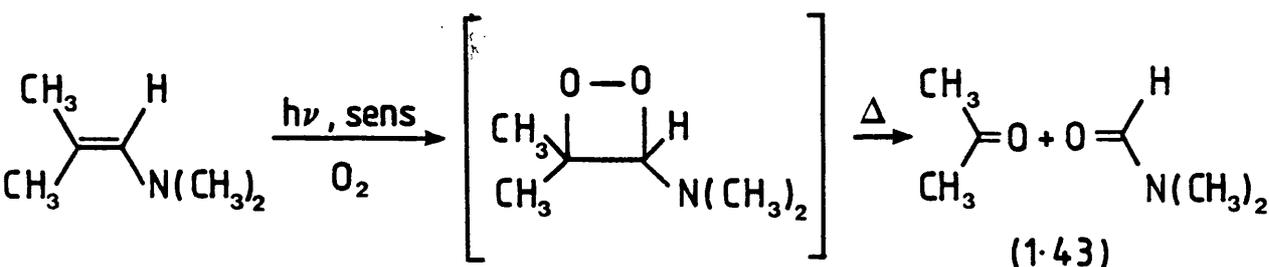
The 1,2-dioxetanes thus formed are often isolable and upon warming cleave to give two carbonyl compounds, one of which is in its ground state and one is in an electronically excited state, the latter carbonyl fragment may undergo deactivation with the emission of light,¹¹¹ (Scheme 1.21).



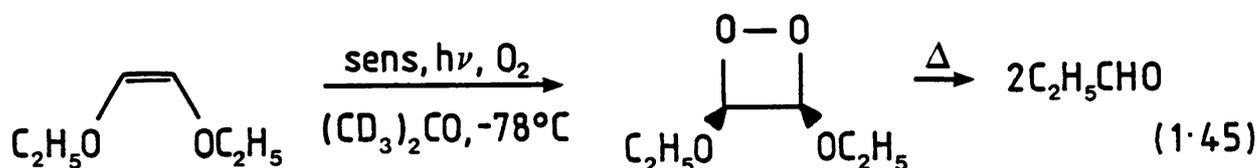
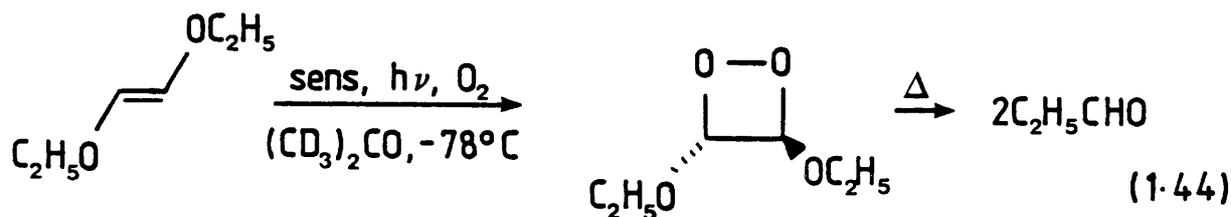
Scheme 1.21

Dioxetane formation with singlet oxygen occurs only with alkenes that bear no allylic hydrogen atoms (or that have the allylic hydrogen attached to the bridgehead carbon atom) and is markedly susceptible to substituent effects. If structurally allowed the ene reaction almost always takes precedence over 1,2-dioxetane formation.

Foote and Lin¹¹² reported that enamines, upon photo-oxygenation, form two carbonyl products arising from an intermediate dioxetane derived from initial singlet oxygen attack upon the enamine. Foote and co-workers¹¹³ later showed that the intermediate dioxetane is monomeric only when the reaction is carried out at low temperatures and high dilution. An example of such an enamine reaction is given in Equation 1.43.



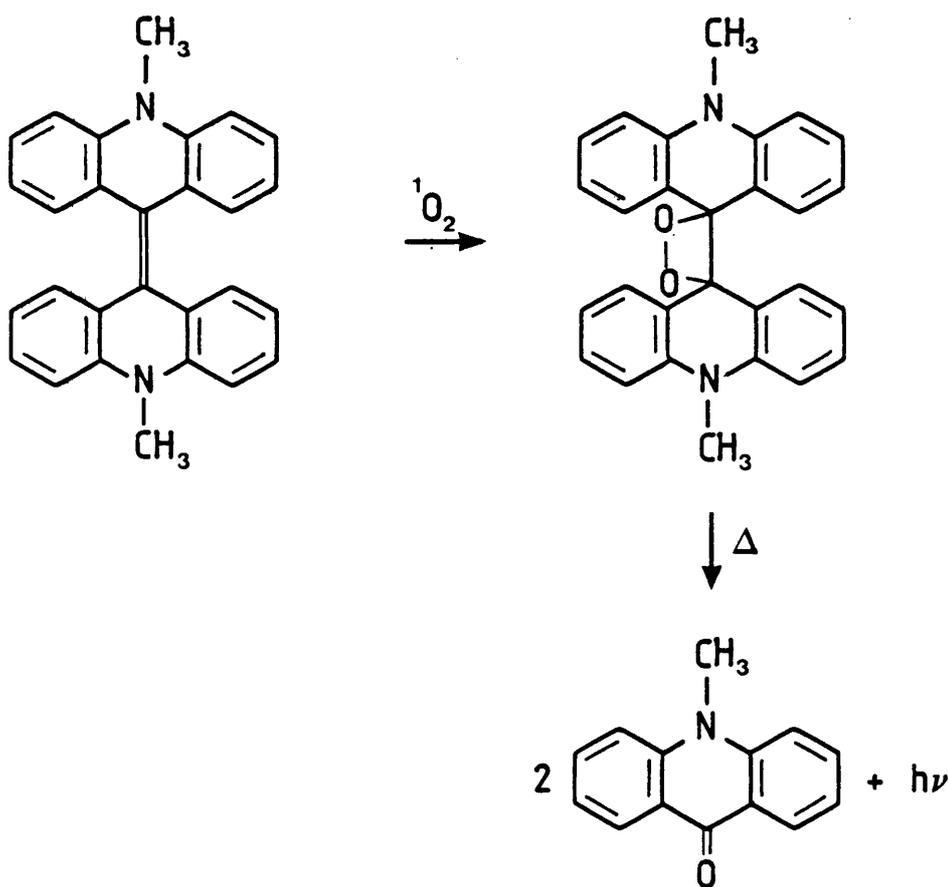
Bartlett and Schaap¹¹⁴ first reported the preparation of 1,2-dioxetanes from the dye-sensitized photo-oxygenation of cis- and trans- diethoxyethenes in acetone-d₆ solution at -78°C. The dioxetanes produced in each case underwent cleavage to yield two carbonyl compounds upon heating, (Equations 1.44 and 1.45).



There are numerous reports in the literature relating to 1,2-dioxetane formation for a wide variety of alkenes upon reaction with singlet oxygen and this subject has been comprehensively reviewed.¹¹⁵ The interest in

1,2-dioxetane formation was no doubt stimulated by the suggestion of McCapra¹¹¹ that dioxetanes may be important intermediates in many chemical and bioluminescent reactions.

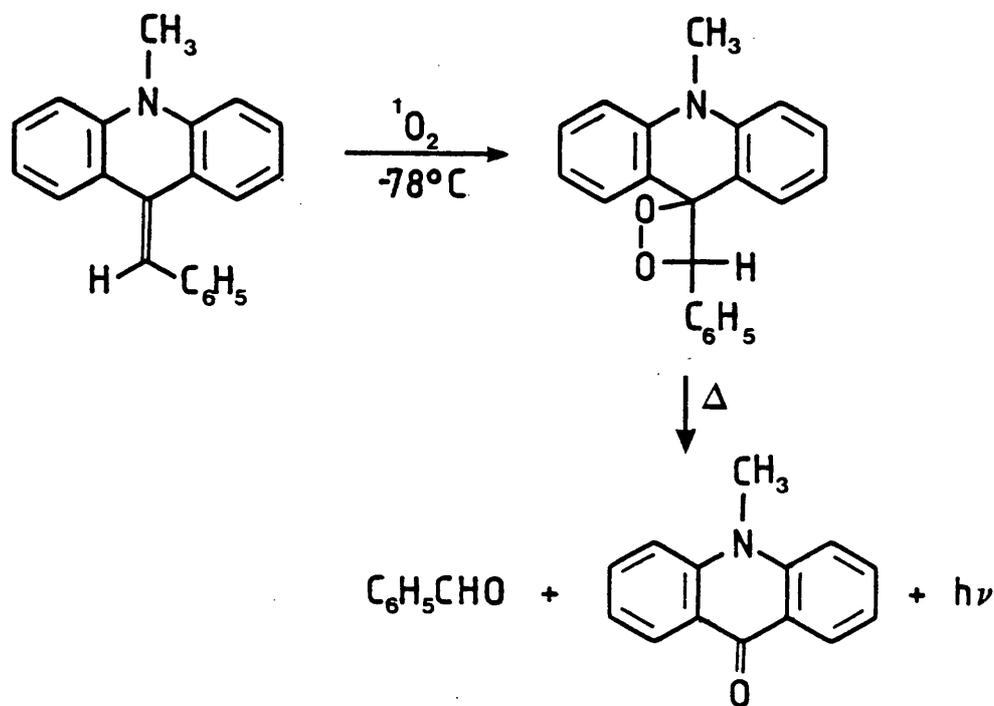
McCapra and Hann¹¹⁶ were the first to recognise that vinylogous enamines should react with singlet oxygen in a manner similar to enamines.^{112,113} Singlet oxygen generated by the thermal decomposition of triphenylphosphite ozonide, the hypochlorite-peroxide system or by an electrical discharge was found to cleave 10,10'-dimethyl-9,9'-biacridylidene to N-methylacridone.¹¹⁶ The reaction was suggested to involve a dioxetane intermediate which upon thermolysis yielded N-methylacridone, accompanied by chemiluminescence, (Scheme 1.22).¹¹⁶



Scheme 1.22

Subsequently a similar vinylogous enamine system was studied by McCapra and co-workers.¹¹⁷ A low temperature spectroscopic investigation

revealed the intermediacy of a dioxetane species which cleaved upon warming to give benzaldehyde and N-methylacridone in its excited singlet state, the latter giving rise to intense chemiluminescence, (Scheme 1.23).¹¹⁷



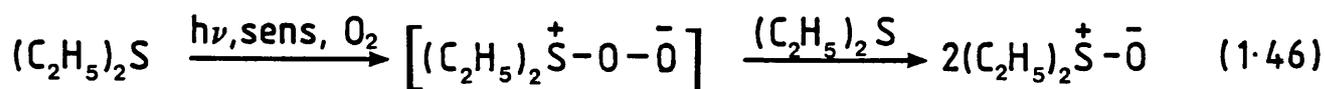
Scheme 1.23

(d) Other Examples of Singlet Oxygen Reactions

Sulphides¹¹⁸

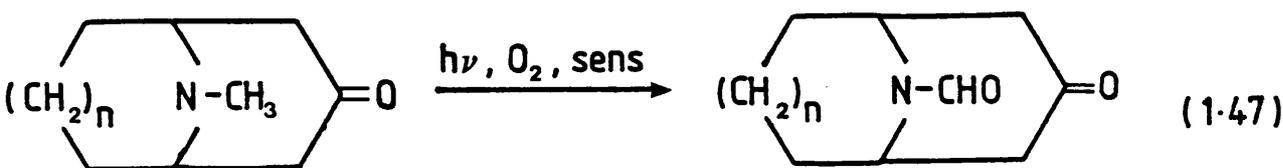
The dye-sensitized oxidation of sulphides produces sulphoxides.

Foot and Peters¹¹⁸ have shown the participation of singlet oxygen and have reported that two sulphide molecules are oxidised for each oxygen molecule used. The authors have detected an intermediate persulphoxide species, by trapping and kinetic experiments, with compounds such as diethyl sulphide,¹¹⁸ (Equation 1.46).



Amines¹¹⁹

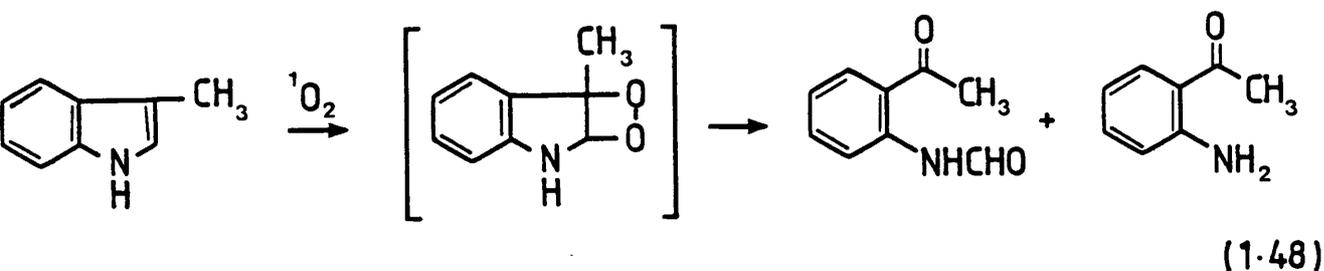
Fisch and co-workers¹¹⁹ reported that the dye-sensitized photo-oxygenation of the amines, tropinone and pseudopelletierine, led to demethylation and also suggested the involvement of singlet oxygen, (Equation 1.47). The implication of singlet oxygen in the above reaction has been challenged,⁹⁹ but a later publication¹²⁰ supports a singlet oxygen mediated reaction.



(where $n=0$ = tropinone ; $n=1$ = pseudopelletierine)

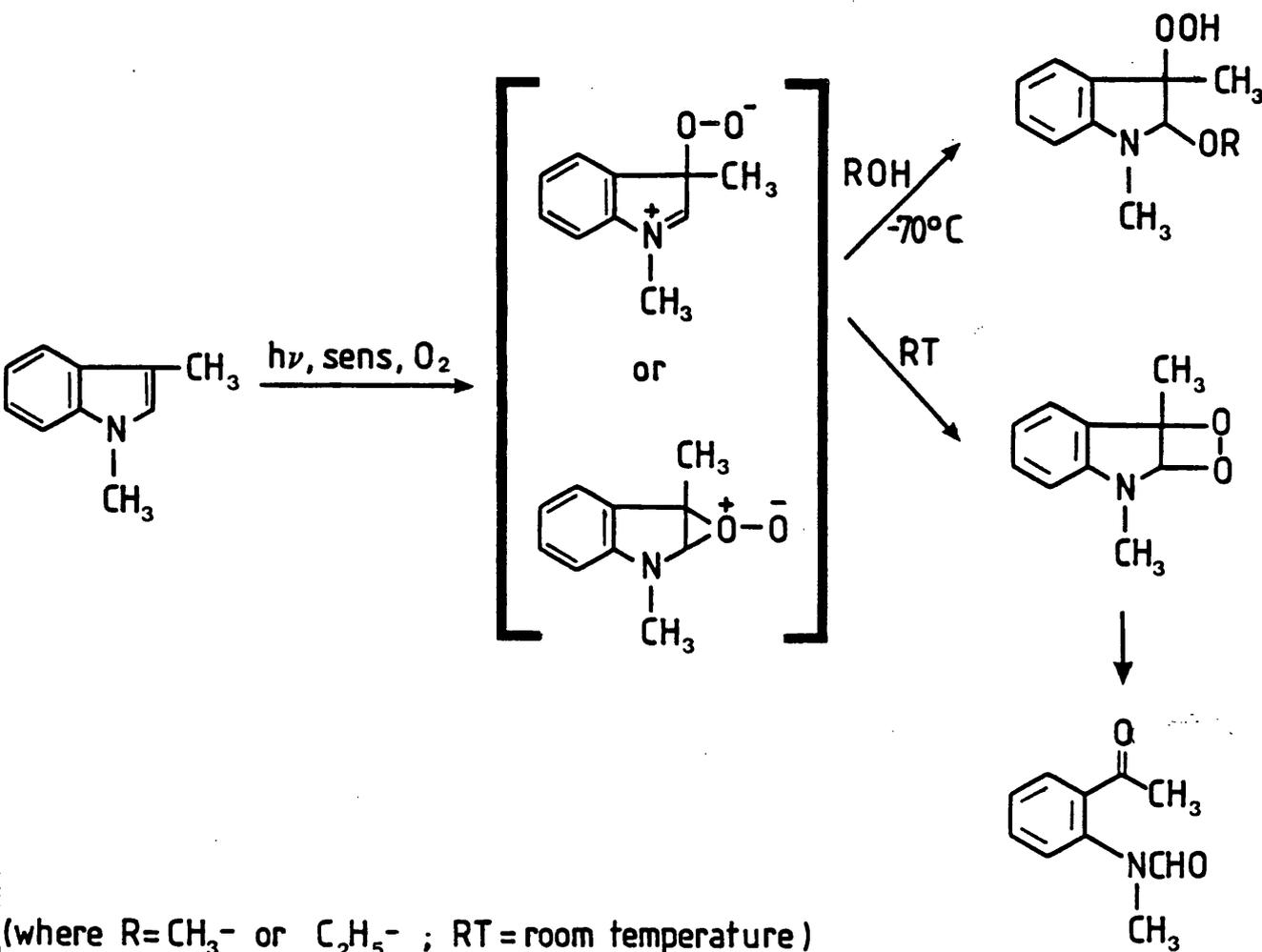
Indoles^{121, 122}

Evans¹²¹ has reported that 3-methylindole undergoes singlet oxygenation, either by dye-sensitization or the hypochlorite-peroxide system, to give o-formamidoacetophenone and o-aminoacetophenone, (Equation 1.48).



Saito and co-workers¹²² have recently implicated peroxidic intermediates in the dye-sensitized photo-oxygenation of 1,3-dimethylindole. When the reaction is carried out in alcoholic solution at -70°C a hydroperoxide is produced, whereas if the reaction is performed at room temperature a formyl derivative is exclusively formed. The initial intermediate is suggested to be a polar peroxide, either a zwitterion or a peroxide, capable of undergoing an efficient addition reaction with

alcohols to give the corresponding hydroperoxide,¹²² (Scheme 1.24).

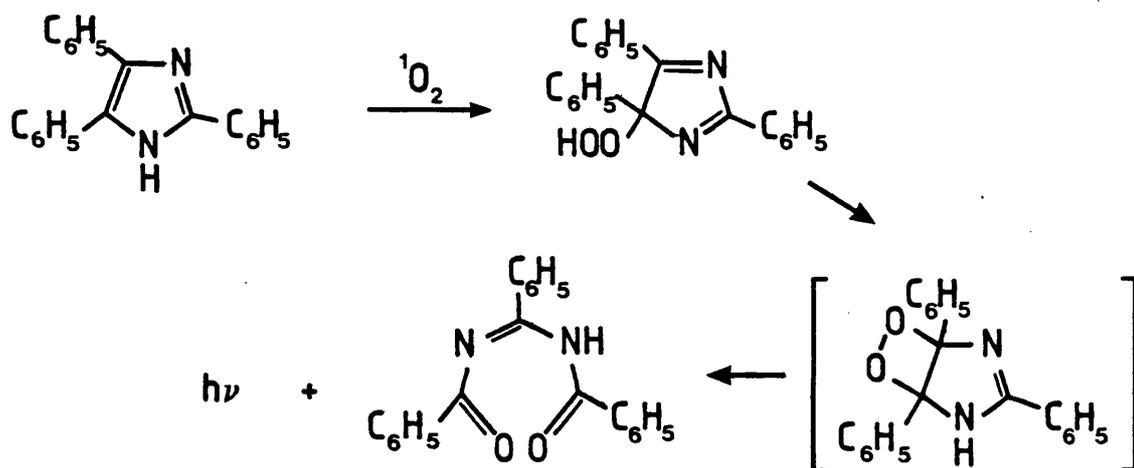


Scheme 1.24

2,4,5-Triphenylimidazole^{123,124}

Singlet oxygenation of 2,4,5-triphenylimidazole (lophine) proceeds via a hydroperoxide intermediate which undergoes decomposition, with accompanying chemiluminescence, via a dioxetane,^{123,124} (Scheme 1.25).

Other substituted imidazoles are also known to react with singlet oxygen.¹²⁵



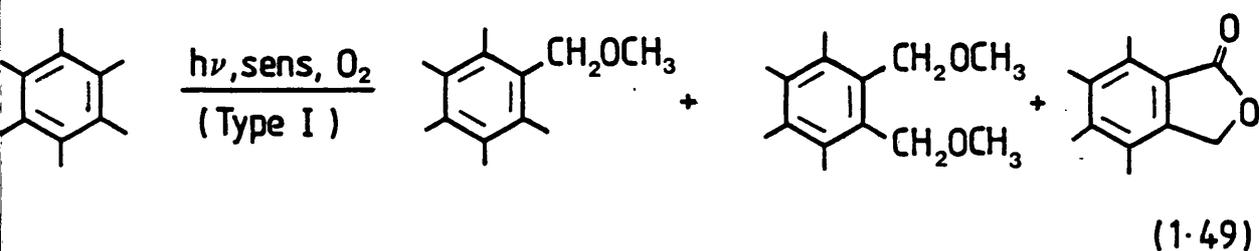
Scheme 1-25

1.3(vi) DETERMINING THE MECHANISM OF A PHOTO-OXIDATION REACTION

When dyes are used as sensitizers in photo-oxygenation reactions there is the possibility that both Type I (radical) and Type II (singlet oxygen) processes can operate and this often leads to difficulties in assessing the mechanism of a photo-oxidation reaction. If the production of radicals by a Type I process can be observed, for example by E.S.R. spectroscopy, C.I.D.N.P. or flash photolysis, then the interception of the radicals by oxygen can be evaluated and rate constants for the reaction determined. When studying direct photo-oxidation reactions it is beneficial to know the photophysical parameters of the compound under investigation in order to assess if the compound is a likely progenitor of singlet oxygen. For compounds which can undergo efficient photo-induced electron transfer reactions there is also the possibility that the superoxide radical anion may be a participating species in the oxidation mechanism. The following section highlights some of the methods which can be used to aid the elucidation of the mechanism of a given photo-oxidation process.

(a) Competing Type I and Type II processes

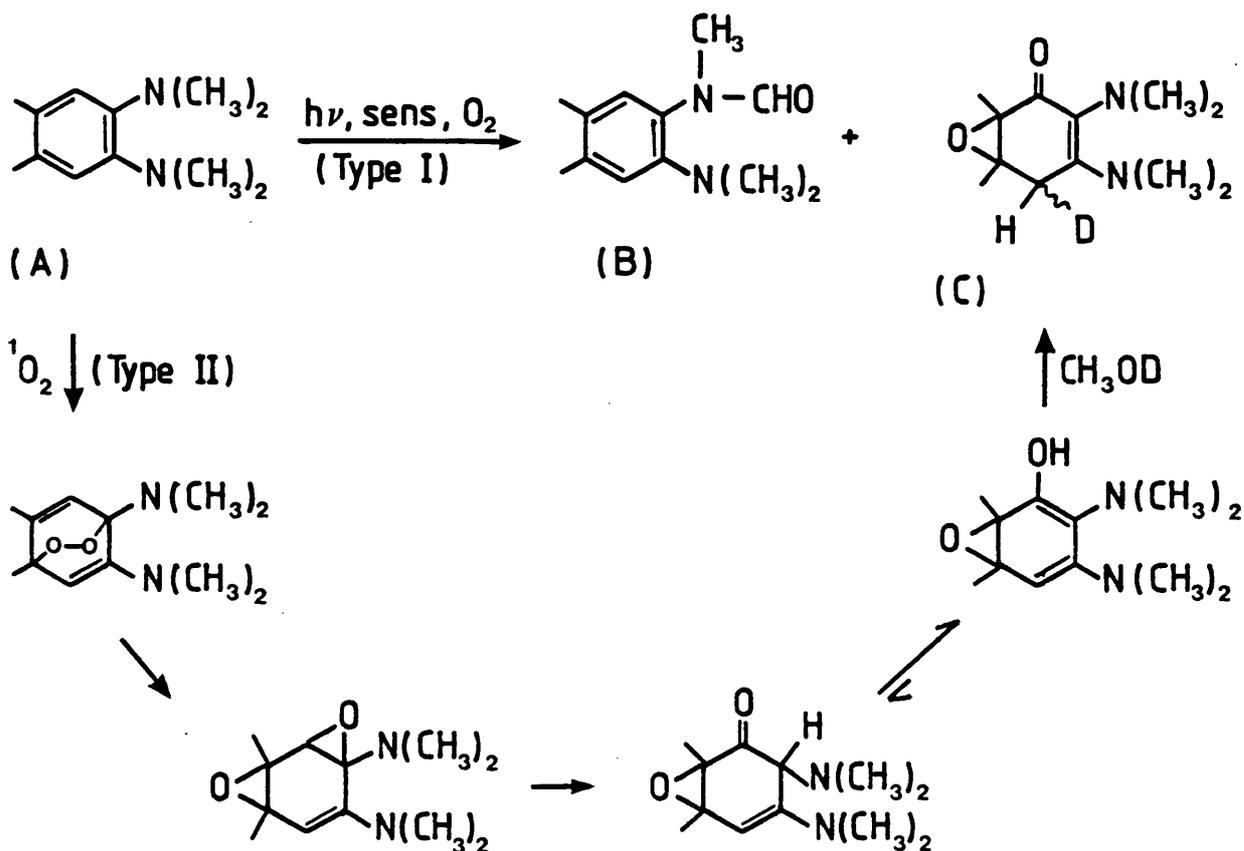
The photo-oxygenation of aromatic hydrocarbons in which benzylic C-H groups are oxidised has recently been reviewed¹²⁶ and a Type I mechanism invoked in order to account for the observed products. For example, Wasserman and co-workers¹²⁷ have reported that the Methylene Blue sensitized photo-oxygenation of hexamethylbenzene proceeds via a mechanism which appears to be exclusively due to a Type I process, (Equation 1.49).



Other reports have appeared which show that both Type I and Type II processes can occur for a given photo-oxidation reaction, the relative extent of each are dependent upon several factors and selected examples are given below.

Saito and co-workers¹²⁸ have shown that the dye-sensitized photo-oxygenation of 4,5-bis-(N,N-dimethylamino)-o-xylene (compound A in Scheme 1.26) can occur simultaneously by both Type I and Type II processes. The formation of the two products (compounds B and C in Scheme 1.26) was found to be highly dependent upon both sensitizer and solvent, with the addition of singlet oxygen quenchers inhibiting the formation of product C but having no effect upon the production of compound B. It was suggested¹²⁸ that product C arises via a Type II singlet oxygen mediated route whereas compound B results from a Type I radical process as outlined in Scheme 1.26.

Davidson and Trethewey¹²⁹ have studied the dye-sensitized photo-oxygenation of the aliphatic amine triethylamine in various solvents

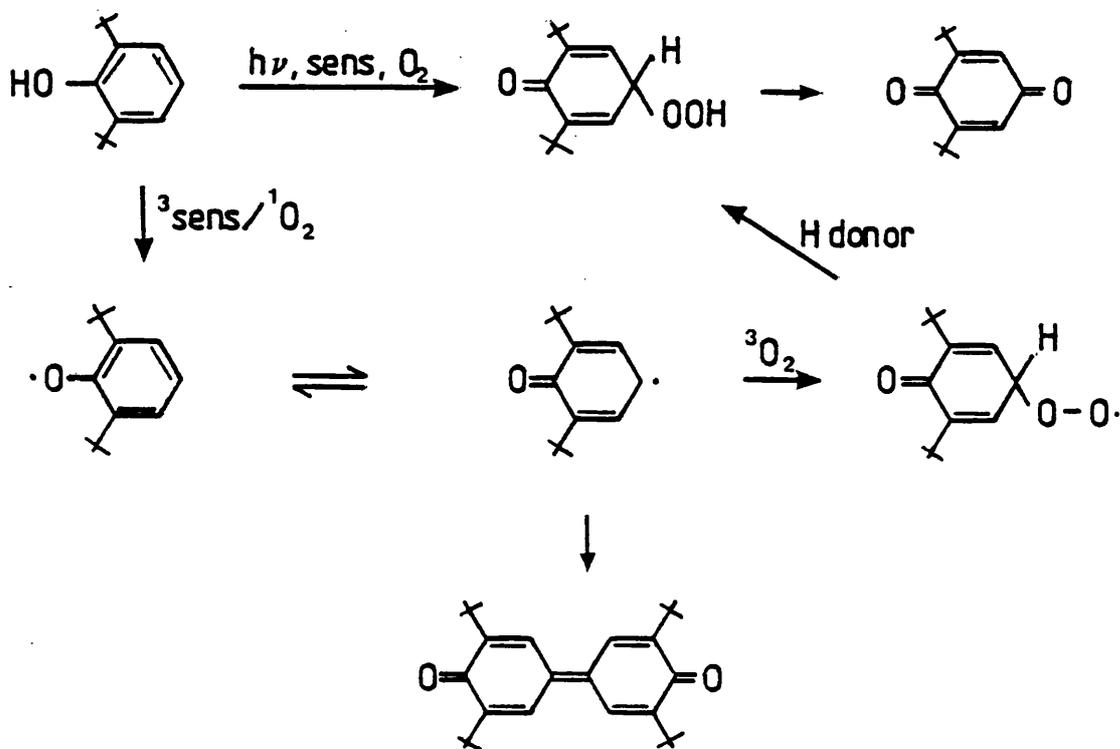


Scheme 1:26

using different sensitizers. It was found,¹²⁹ by utilising solvent isotope effects, that the oxidation reaction could occur by both singlet oxygen and radical processes with the amine concentration determining the extent to which each pathway proceeded. At high amine concentrations a Type I process predominates and at lower amine concentrations reaction via a Type II process becomes important. The reaction was also found to be markedly dependent upon solvent, oxygen concentration and sensitizer.

Matsuura and co-workers¹³⁰ have also shown that both Type I and Type II mechanisms can occur under one set of conditions in their study of the dye-sensitized photo-oxygenation of 2,6-di-*t*-butylphenol. The products found with singlet oxygenation can often be the same as those obtained in radical oxygenations. The hydroperoxide intermediate, isolable only under very mild conditions, is capable of secondary reaction. In

addition, products of phenoxy radical coupling are also found and the overall reaction, involving both Type I and Type II mechanisms, can be summarised as in Scheme 1.27.



Scheme 1.27

It is clear from the examples cited above that careful mechanistic analysis is required in order to correctly assign the mechanism for a given photo-oxygenation reaction. Indeed this is often an extremely difficult task. Use of spectroscopic methods may be used to study the radicals derived from a Type I process and these radicals may be trapped chemically. Oxygen concentration dependence provides another method for interrogation of the reaction mechanism. In systems where the reaction borderline is particularly delicate the use of several different techniques may have to be utilised in a thorough mechanistic study of the oxidation process.

Strong evidence in favour of a singlet oxygen mediated reaction comes from the finding that the product distribution from a dye-sensitized reaction⁶⁸ is the same as that for the analogous reaction carried out using singlet oxygen generated by, for example, the hypochlorite-peroxide system.⁶⁹ However, as the products of both Type I and Type II reactions may be the same¹³⁰ it is necessary to evaluate all experimental results very carefully.

(b) Quenching of Singlet Oxygen

Several types of compound have been found to physically deactivate, or quench, singlet oxygen without undergoing any appreciable chemical reaction. Compounds which possess this capability include tertiary amines such as 1,4-diazabicyclo-[2.2.2]-octane (DABCO),¹³¹ azide ions¹³² and β -carotene.¹³³ Utilisation of these quenchers has been extremely useful in mechanistic studies where the inhibition of a photo-oxygenation reaction, by inclusion of the quencher in the reaction medium, has been taken as good evidence for the intermediacy of singlet oxygen.

However these compounds, which are capable of quenching singlet oxygen, have also been found to be efficient quenchers of the singlet and triplet states of dyes.¹³⁴ Thus any retardation which is observed upon addition of a singlet oxygen quencher to a photo-oxidation reaction may well be due, to some extent, to quenching of the photo-sensitizer. It is therefore imperative to use low concentrations of the quencher in order to eliminate any sensitizer-quencher interaction. A recent publication by Davidson and Pratt¹³⁵ has shown that dyes may also act as quenchers of singlet oxygen which again necessitates using low concentrations (in this case, of the photo-sensitizer) when carrying out kinetic investigations of dye-sensitized photo-oxygenation reactions.

(c) Determination of the Lifetime of Singlet Oxygen and Reactivity Parameters

In steady state experiments, usually carried out at a constant oxygen concentration by bubbling oxygen through a solution of an acceptor A, singlet oxygen can either undergo deactivation to the ground state (Equation 1.50) or react with the acceptor to form the oxidation product (Equation 1.51). Under these steady state conditions Equation 1.52 holds.



$$\Phi_{\text{AO}_2} = \Phi_{{}^1\text{O}_2} \frac{k_r[\text{A}]}{k_d + k_r[\text{A}]} \quad (1.52)$$

where:- k_d = rate constant for the natural decay of singlet oxygen,
 k_r = rate constant for reaction of singlet oxygen with acceptor A,
 Φ_{AO_2} = quantum yield for product formation,
 $\Phi_{{}^1\text{O}_2}$ = quantum yield for singlet oxygen production,
and $[\text{A}]$ = concentration of acceptor A.

The reactivity of an acceptor with singlet oxygen can be expressed as a ratio of the rate constants k_d/k_r (or β -values) obtained experimentally from the slope/intercept plots of $1/\Phi_{\text{AO}_2}$ versus $1/[\text{A}]$. Therefore steady state techniques only allow the determination of rate constants for reaction of acceptor A with singlet oxygen relative to the rate constant for the natural deactivation of singlet oxygen under a particular set of experimental conditions. However, the results of such experiments have greatly contributed to an understanding of the factors which influence the reactivity of singlet oxygen with a variety of acceptor molecules. The use of steady state techniques to gain information relating to singlet oxygen reactivity were severely hampered by the lack of knowledge of the

variation in lifetime of singlet oxygen with solvent. By utilising time-resolved techniques the lifetime and reactivity parameters of singlet oxygen in various solvents have been further elucidated.

Adams and Wilkinson¹³⁶ and Merkel and Kearns¹³⁷ have developed methods for probing the reactivity of a variety of substrates with singlet oxygen. In this procedure^{136,137} an oxygenated solution of Methylene Blue was excited by a pulse of light from a Q-switched ruby laser. The concentration and rate of decay of the singlet oxygen so produced can be determined by following the time-resolved bleaching of 1,3-diphenylisobenzofuran (DPBF) monitored at 415 nm. (It is known that DPBF reacts efficiently with singlet oxygen¹⁰⁴ as previously shown in Equation 1.36.) The rate of decay of singlet oxygen has been shown to be independent of the sensitizer employed.¹³⁶ As the rate constant for reaction of DPBF with singlet oxygen is known the lifetime of singlet oxygen in the particular solvent can be calculated.¹³⁸ In order to determine the rate constant for the reaction of a given compound with singlet oxygen, a known amount of the compound under investigation is added to the sensitizer-DPBF mixture and its effect upon the rate of decay of singlet oxygen evaluated.

The use of the above technique has enabled the absolute rate constants for interaction of singlet oxygen with many compounds, which are soluble in organic solvents, to be determined. An excellent compilation of such data has recently been published.¹³⁹

The lifetime of singlet oxygen has been found to be highly solvent dependent and of particular interest are the observations that the lifetime is often significantly greater in deuteriated compared with non-deuteriated solvents.¹⁴⁰ Thus if a reaction involves singlet oxygen a change from a non-deuteriated to a deuteriated solvent could be expected

to cause an increase in the rate of photo-oxidation. The utilisation of such solvent isotope effects provides a powerful means of identification of singlet oxygen in many photo-oxygenation reactions. However, in order to observe the maximal solvent isotope effect the concentration of the acceptor A has to be carefully selected in order to ensure that the condition $k_d \gg k_r[A]$ is met.¹⁴¹ With regard to ascribing the observation of a solvent isotope effect as being due to the participation of singlet oxygen in a reaction it should be added, as a cautionary note, that this may be due to a variation in the photophysical properties of the sensitizer with change in solvent composition.¹⁴¹

A recent advance in determining the lifetime of singlet oxygen in solution has been achieved by Peters and Rodgers¹⁴² who used direct time-resolved measurements of the luminescence from the ${}^1\Delta_g \rightarrow {}^3\Sigma_g^-$ transition of oxygen at 1270 nm in several solvents. This technique has subsequently been used by several groups to determine the lifetime of singlet oxygen in a wide range of solvents¹⁴³⁻¹⁴⁵ and Table 1.4 gives several examples of the values thus obtained.

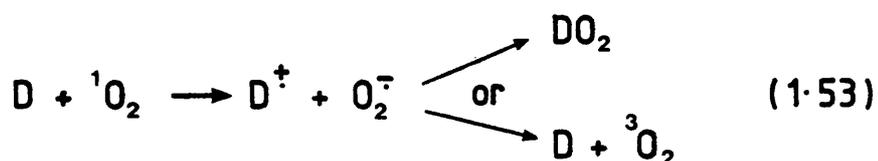
TABLE 1.4

| Solvent | Lifetime of Singlet Oxygen (μ s) |
|-----------------------------------|---------------------------------------|
| H ₂ O | 2(a) |
| D ₂ O | 68.1±2.5(b) |
| C ₆ H ₆ | 26.7±1.3(b) |
| C ₆ D ₆ | 550±11(b) |
| CH ₃ CN | 54.4±1.3(b) |
| CD ₃ CN | 600±33(b) |
| CH ₃ COCH ₃ | 46.5±2.0(b) |
| CD ₃ COCD ₃ | 690±20(b) |
| CH ₂ Cl ₂ | 100(c) |
| CCl ₄ | 900(c) |
| CHCl ₃ | 160±6(d) |
| CDCl ₃ | 3600±150(d) |

(a) Reference 140; (b) Reference 144;
(c) Reference 143; (d) Reference 145.

(d) Photo-Oxidations involving Electron Transfer Reactions

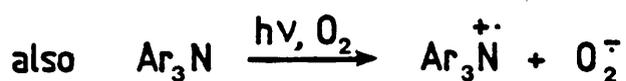
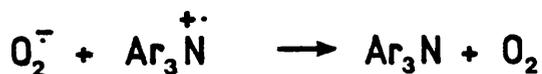
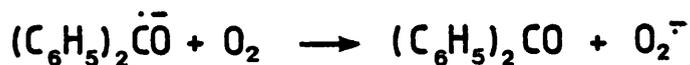
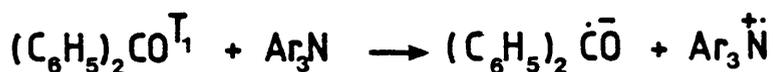
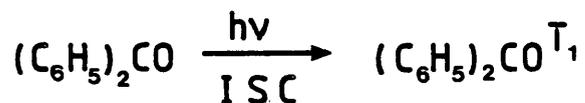
A number of electron rich compounds, for example enamines, have been shown to react with singlet oxygen in a different way from less electron rich compounds.¹¹² It has been suggested by Foote and co-workers¹¹³ that these reactions may proceed by way of electron transfer from the electron rich molecule (D) to singlet oxygen, to give a radical cation-oxygen ion pair or charge-transfer complex ($D^{\cdot+} O_2^{\cdot-}$). The recombination of the ion pair could react either to give the product (DO_2) or undergo back electron transfer to quench singlet oxygen as shown in Equation 1.53.



It has been shown¹⁴⁶ that tetramethylphenylenediamine (TMPD) undergoes a one-electron transfer to singlet oxygen to yield the superoxide anion and the radical cation of TMPD via the mechanism shown in Equation 1.53. Such electron transfer reactions should be quenched by the addition of known singlet oxygen quenchers to the reaction mixture.

That compounds can undergo electron transfer reactions to ground state molecular oxygen under direct, or sensitized, irradiation conditions was first realised by Davidson and co-workers.¹⁴⁷ It was found¹⁴⁷ that flash photolysis of nitrogen-flushed acetonitrile solutions of tri-p-tolylamine containing benzophenone, produced the amine radical cation and the radical anion of the ketone. When oxygenated solutions of either the amine alone or amine plus benzophenone were flash-photolysed, only the radical cation of the amine was observed. The lifetime and concentration of the amine radical cation was increased as the concentration of either oxygen or benzophenone was increased. A mechanism involving the formation of the superoxide radical anion was proposed to account for the above

observations and is shown in Scheme 1.28.

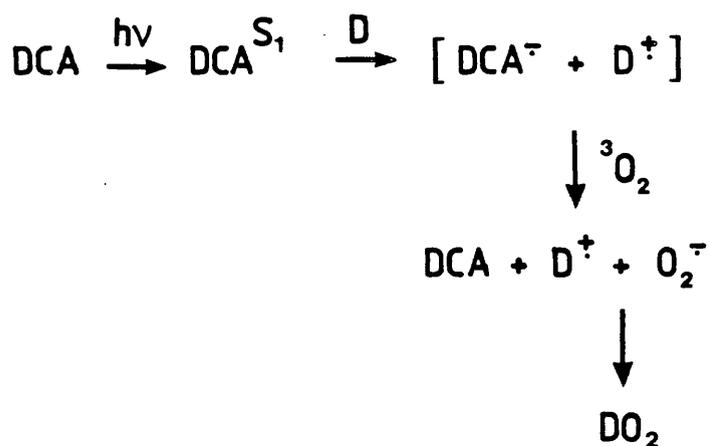


(where Ar_3N = tri-*p*-tolylamine)

Scheme 1.28

Subsequently a similar electron transfer process has been suggested by Foote and co-workers¹⁴⁸ to account for the photo-oxygenation of alkenes and sulphides sensitized by 9,10-dicyanoanthracene (DCA). The DCA sensitized photo-oxygenation of substrates such as tetraphenylethylene, trans-stilbene and diphenylsulphide was investigated in oxygenated acetonitrile solution.¹⁴⁸ A mechanism involving electron transfer, rather than singlet oxygen, was invoked. It was suggested that the singlet state of DCA abstracts an electron from the substrate (D) to produce the substrate radical cation and the DCA radical anion. The reduced DCA is re-oxidised by ground state oxygen to produce the superoxide radical anion, which then undergoes reaction with the substrate radical cation to give the observed product (DO_2) as shown in Scheme 1.29.

In photo-oxygenation reactions involving electron transfer, having mechanisms as shown in Schemes 1.28 and 1.29, it should be possible to observe the radicals produced by spectroscopic means. Also such reactions



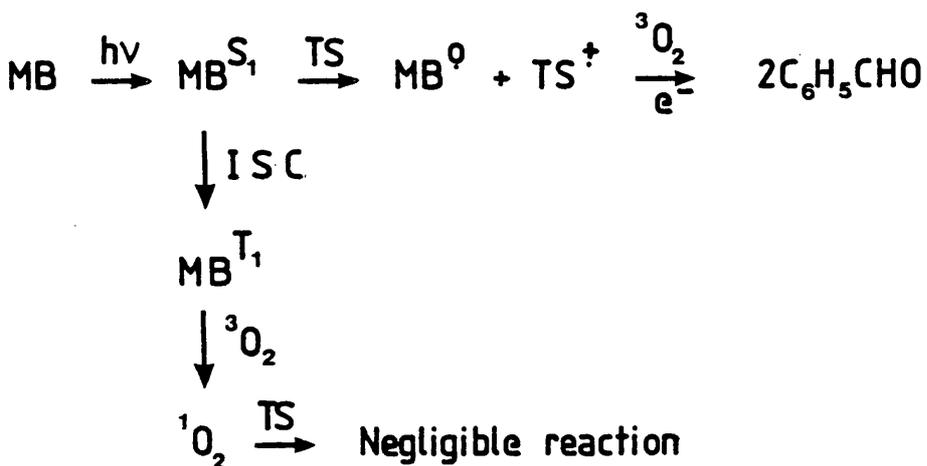
Scheme 1.29

should not be affected by the addition of singlet oxygen quenchers nor should solvent isotope effects be observed.

Recently evidence has been provided by Schaap and co-workers¹⁴⁹ to substantiate the rôle of electron transfer processes in photo-oxygenation reactions involving DCA as the sensitizer. The radical anion of DCA was identified by e.s.r. spectroscopy and the intermediate dioxetane produced for tetraphenylethylene was characterised by n.m.r. and chemiluminescence studies.¹⁴⁹

It has recently been suggested by Foote and co-workers¹⁵⁰ that the major pathway for the Methylene Blue sensitized photo-oxygenation of trans-stilbene does not involve singlet oxygen. By analogy to the DCA mechanism (Scheme 1.29) it was postulated that the Methylene Blue (MB) sensitized photo-oxygenation of trans-stilbene (TS) also goes via an electron transfer process (Scheme 1.30), although the exact mechanism of benzaldehyde formation from MB[•] and TS⁺ was not established.¹⁵⁰

The above report¹⁵⁰ re-emphasises the point that dye-sensitized photo-oxygenations cannot automatically be interpreted as singlet oxygen reactions, especially when the reactions are very slow or when high substrate concentrations are used^{129,134,141} as this may lead to the intervention of radical processes.



Scheme 1.30

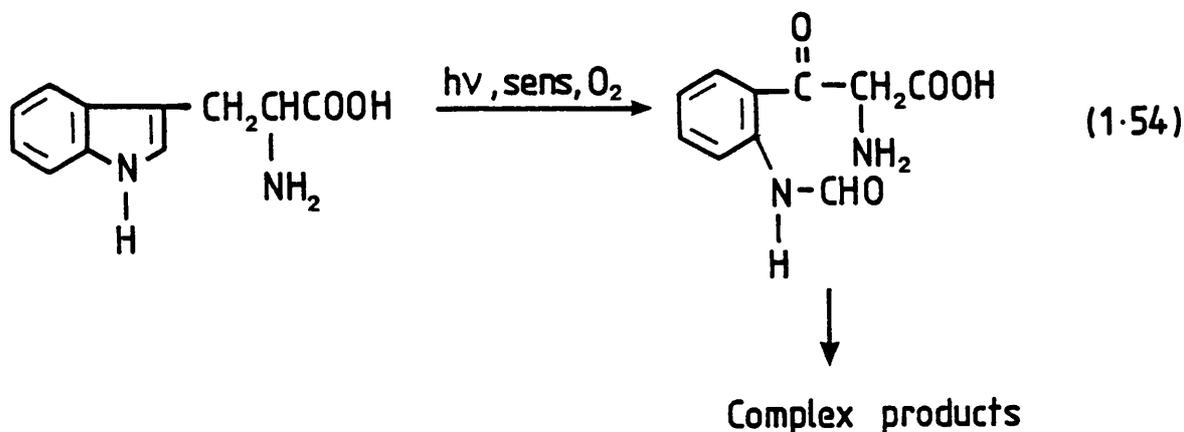
Also of relevance are the findings that some dyes, in addition to being progenitors of singlet oxygen, can also bring about the formation of the superoxide radical anion, albeit to a small extent. Eosin¹⁵¹ has been estimated to yield ~1% O₂^{•-} and Rose Bengal,¹⁵² either in solution or bound to a polymer, has also been shown to yield O₂^{•-}. Little is known regarding the chemical products resulting from electron transfer from dye to oxygen, although dye bleaching is often associated with this reaction and the products arising due to the latter phenomenon may well quench singlet oxygen.

The formation of superoxide radicals from the irradiation of aerated aqueous suspensions of cadmium sulphide has been observed by e.s.r. spectroscopy.¹⁵³ The addition of dyes, such as Rhodamine B or Methylene Blue, to the reaction mixture containing the semiconductor leads to N-dealkylation of the dyes via a mechanism suggested to involve the radical cation of the dye and the superoxide radical anion.¹⁵³ The use of semiconductors as sensitizers for photo-oxygenation reactions may provide a method for investigating the reactions of the superoxide radical anion with certain substrates.

1.3(vii) BIOLOGICAL IMPLICATIONS OF SINGLET OXYGEN

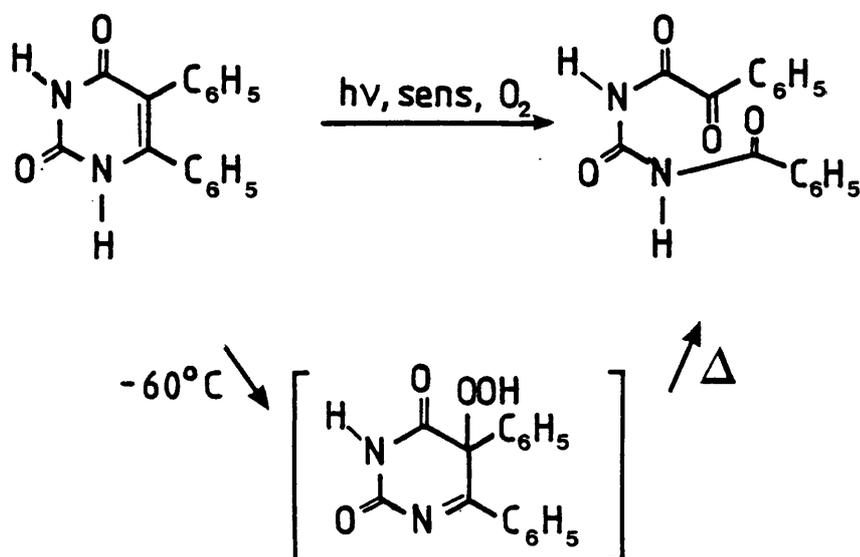
The damaging effects that sensitizing dyes, light and oxygen have upon biological systems, referred to as photodynamic action, have been known for some time. These detrimental effects include, for example, membrane damage, mutagenesis, interference with metabolism and reproduction, all of which can be lethal to the organism concerned. Photodynamic action is not solely confined to lower organisms in the Animal and Plant Kingdoms as evidence of its effects are also apparent in higher species. An excellent review article covering this topic has appeared¹⁵⁴ and some representative examples of the possible rôle that singlet oxygen may play in biological systems and its interaction with bio-molecules are given below.

The photo-oxidation of certain amino acids, in particular histidine, methionine, tyrosine and tryptophan is shown to occur via mechanisms involving singlet oxygen, although in some instances, depending upon the conditions, both Type I and Type II processes may operate.¹⁵⁴ For example, the photo-oxygenation of tryptophan gives a complex mixture of products, with N-formylkynurenine being reported as being the primary product which subsequently undergoes secondary reactions,¹²² (Equation 1.54).



The photochemical inactivation of certain enzymes, for example lysozyme and papain, has been attributed to singlet oxygen attack upon the tryptophyl residues of these proteins.⁷⁵⁽¹⁾

Nucleic acid derivatives have been shown to undergo photo-oxidation processes, although the primary products are poorly known due to their tendency to undergo further reactions and often only products of extensive degradation are isolated.¹⁵⁴ However, Foote and Vickers¹⁵⁵ have detected, using low temperature n.m.r. spectroscopy, the unstable intermediate formed in the photo-oxidation of diphenyluracil, which upon warming breaks down to the cleavage product, (Scheme 1.31).



Scheme 1.31

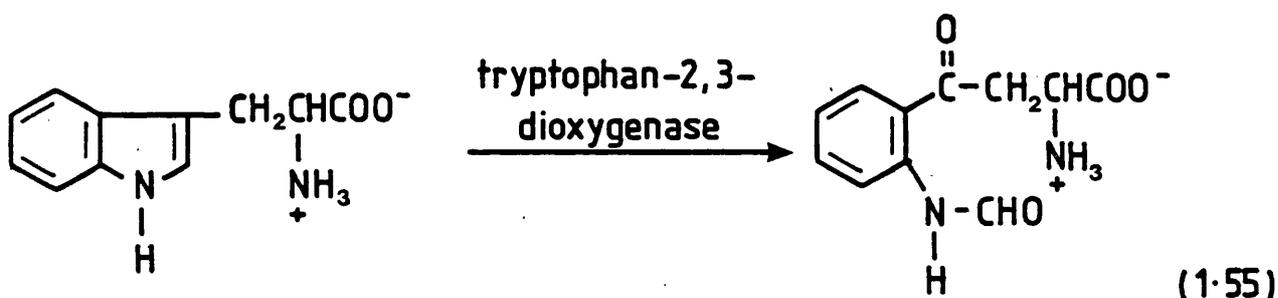
Lipid oxidation is probably the cause of the membrane damage associated with photodynamic action, although the products of such reactions have not been identified in all cases.^{75(f)} An important example of lipid peroxidation is that of the photo-oxidation of cholesterol in porphyrin erythrocytes.^{75(f)(1)} Erythropoietic protoporphyria (EPP) is a disorder which is brought on in susceptible patients by exposure to sunlight and results in edema, erythema and lesions. The oral administration of β -

carotene, a known singlet oxygen quencher, greatly diminishes the photosensitivity of EPP patients. The red blood cells of EPP patients, which contain large amounts of free protoporphyrin, are haemolysed upon irradiation with visible light via the photo-oxidation of membrane components. The photo-oxidation product of cholesterol (see Equation 1.41) has been identified and it is concluded that the singlet oxygen mediated photo-oxidation of cholesterol leads eventually to the breakdown of erythrocyte membranes in EPP patients.

A photodynamic approach has been used in the treatment of neonatal jaundice which is a common problem among newborn, in particular premature, infants.¹⁵⁴ Neonatal jaundice is caused by a lack of glucuronyltransferase, an enzyme which catalyses the conversion of the lipid-soluble pigment bilirubin to the water-soluble conjugate with glucuronic acid. If allowed to go unchecked bilirubin accumulates in the skin and brain resulting in brain damage. By irradiating the infant with light, the bilirubin in the skin is bleached to form products which can be excreted and thus prevents brain damage. It is thought that such phototherapy depends upon the ability of singlet oxygen to photo-oxidatively degrade the pigment bilirubin. Although no conclusive proof has yet been forwarded to substantiate such an hypothesis, the exact mechanism which is operative in vivo has yet to be established.

There are several enzyme systems that mediate oxidative reactions in vivo which resemble singlet oxygen chemistry quite closely. For example, tryptophan-2,3-dioxygenase catalyses the oxidation of tryptophan to N-formyl-L-kynurenine (Equation 1.55), a reaction which bears close similarity to the dye-sensitized photo-oxygenation of tryptophan, (Equation 1.54).

At first sight it may be surmised that singlet oxygen might be involved



in the enzymic reaction (Equation 1.55). Indeed it has been suggested that free singlet oxygen is generated in biological oxidations catalysed by mono- and dioxygenase systems and that it is this species, singlet oxygen, which ultimately transforms the substrate into oxidation products.¹⁵⁶ However, further investigations have failed to show that singlet oxygen is produced in such systems⁷⁵⁽¹⁾ and currently it can be viewed that singlet oxygen does not have a major rôle in oxidase activity.

In all of the biological photo-oxidations examined to date, the intermediacy of singlet oxygen has not been directly demonstrated. Evidence for its participation relies on (a) the correlation of oxidation products with those of established singlet oxygen reactions; (b) the apparent solvent isotope effects which are observed in reactions utilising deuterated solvents and (c) the retardation of the rate of photo-oxygenation by known singlet oxygen quenchers. Only by continued research, in the area of biological photo-oxidation, will it be fully established if free singlet oxygen plays a part in any biological system.

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CHAPTER 2

PHOTOCHEMICAL REACTIONS OF α -KEITO-CARBOXYLIC ACIDS

*"Imagine there's no countries
It isn't hard to do
Nothing to kill or die for
And no religion too
Imagine all the people
Living life in peace"*

John Lennon 1940 - 1980

PHOTOCHEMICAL REACTIONS OF α -KETO-CARBOXYLIC ACIDS

INTRODUCTION

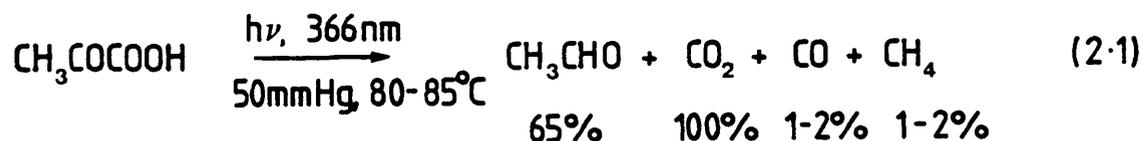
Preface

The following sections contain a review of the literature pertaining to both the direct (Section 2.1) and the dye-sensitized (Section 2.2) photochemical reactions of α -keto-carboxylic acids. The mechanisms suggested to be involved in these reactions are discussed.

2.1 DIRECT IRRADIATION OF α -KETO-CARBOXYLIC ACIDS

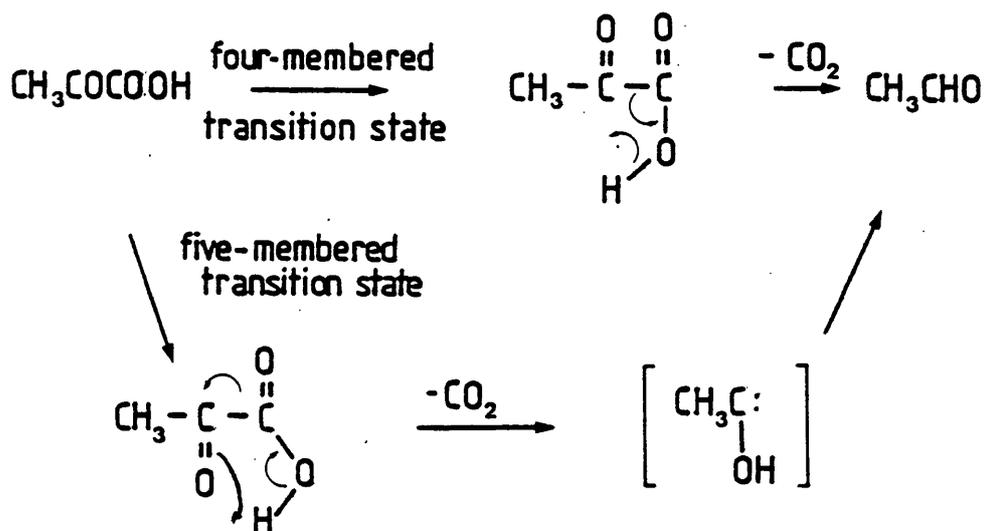
2.1(i) PYRUVIC ACID

Vesley and Leemakers¹ have shown that irradiation of pyruvic acid, in the vapour phase, leads to an extremely efficient photodecomposition having a quantum yield close to unity. Carbon dioxide is produced quantitatively, the other major product being acetaldehyde, with the minor formation of both carbon monoxide and methane, (Equation 2.1).



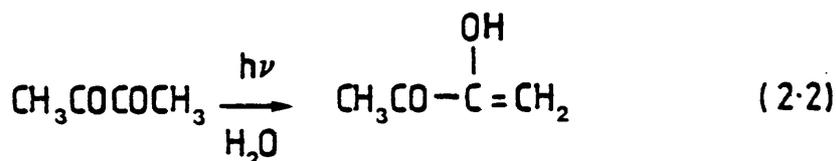
The mechanism of the primary photochemical process was postulated as being a concerted decarboxylation, involving either a four- or five-membered transition state, rather than a free radical reaction, in order to account for the observed photoproduct acetaldehyde, (Scheme 2.1).

Photodecomposition via the four-membered transition state does have an analogy to the photo-enolisation of biacetyl in aqueous solution, as described by Lemaire,² in which the enol arises by an internal hydrogen abstraction reaction from a highly strained four-membered transition



Scheme 2.1

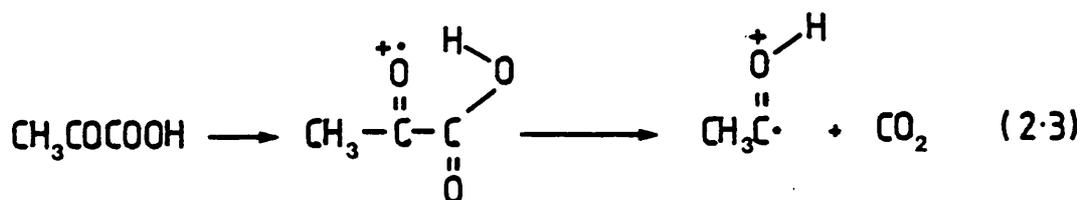
configuration in the triplet state, (Equation 2.2).



However, Vesley and Leermakers¹ favour a mechanism involving a five-membered transition state, with the intermediacy of a hydroxy carbene because (i) this configuration of the transition state is probably that of the ground state (for maximum hydrogen bonding), thus little rearrangement need take place in the excited state to get to the transition state; and (ii) by analogy to the Norrish Type II process,³ hydrogen is initially becoming bonded to oxygen rather than carbon. The finding that nitrogen, oxygen or ethylene, (at pressures up to 50 mm of Hg) had no effect on the reaction,¹ indicates that the reaction must be very fast and thus may involve an upper excited singlet or triplet state.

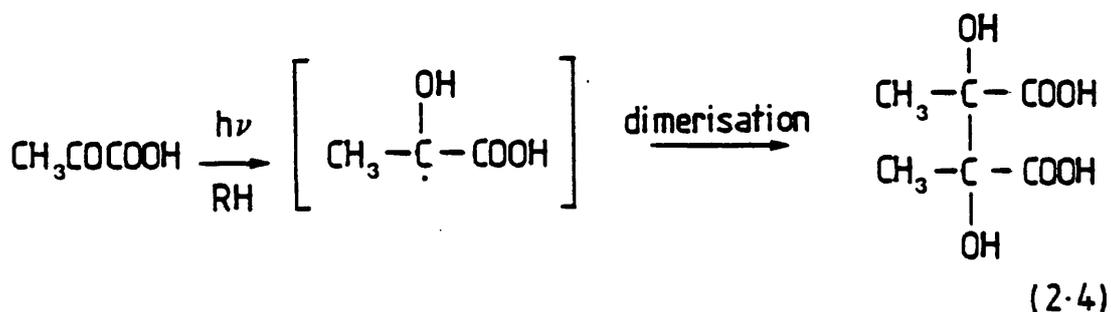
Turro and co-workers⁴ have provided evidence to support the mechanism involving the five-membered transition state, as proposed above, by the observation of a $\text{C}_2\text{H}_4\text{O}$ peak in the mass spectral breakdown of pyruvic

acid, (Equation 2.3).



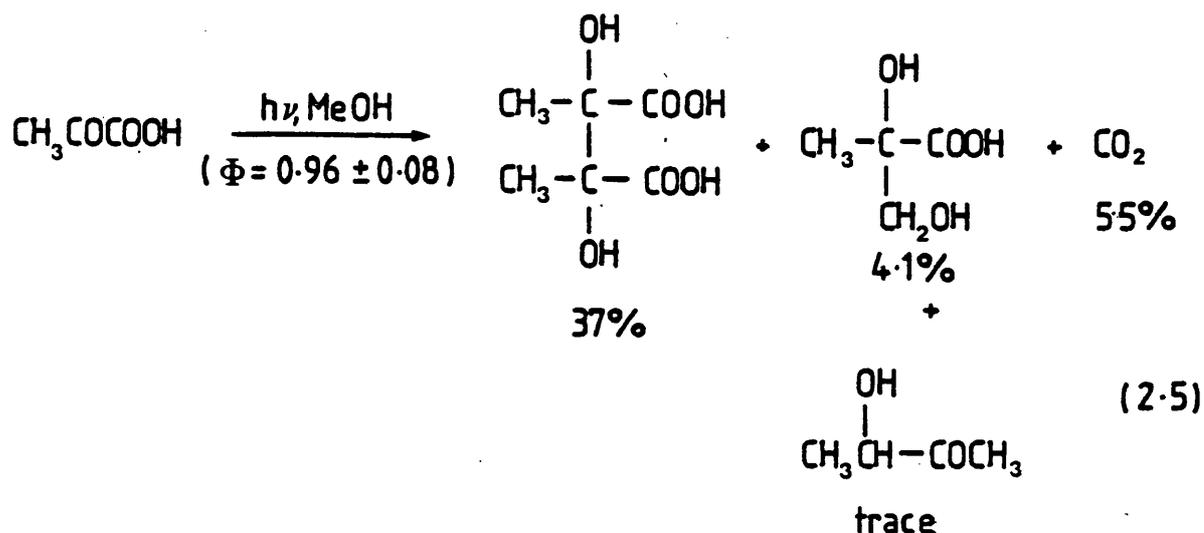
Pyruvic acid undergoes an entirely different series of photoreactions in solution, when compared to those encountered in the vapour state, as exemplified by the following literature reports, all of which refer to photoreaction under deoxygenated conditions.

Leermakers and Vesley,^{5,6} and Kendall and Leermakers,⁷ have shown that in hydrogen donating solvents such as isopropanol, methanol, t-butanol, chloroform or diethyl ether, pyruvic acid is photoreduced with high efficiency to yield dimethyltartaric acid via the dimerisation of an intermediate ketyl radical, (Equation 2.4).



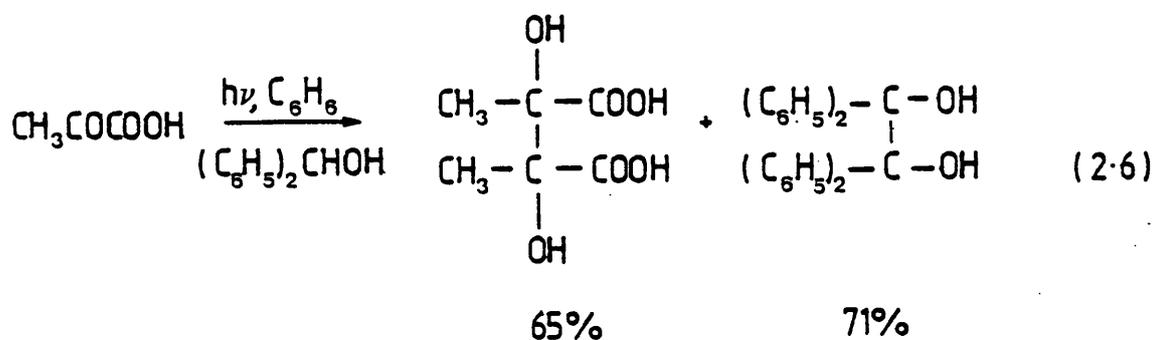
Using electron spin resonance spectroscopy, Fujisawa and co-workers⁸ have observed the intermediate ketyl radical from the photolysis of pyruvic acid in isopropanol. Several other reports have appeared which confirm the existence of such a radical in these systems.⁹

When methanol⁶ was utilised as solvent for irradiation of pyruvic acid, in addition to the formation of dimethyltartaric acid other photo-products are observed, namely a solvent adduct 2-methyl-2,3-dihydroxypropanoic acid, carbon dioxide and small amounts of acetoin, (Equation 2.5).

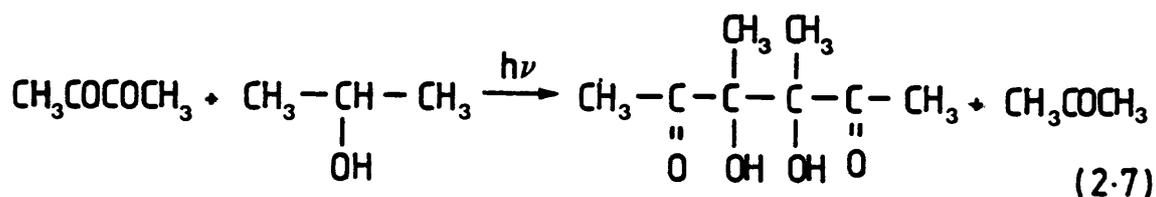


The quantum yield for the production of carbon dioxide was found to be highly solvent dependent.⁶ Leermakers and Vesley^{5,6} made no attempt to isolate any solvent dimer (which is presumably present in reactions utilising hydrogen donating solvents), or any other solvent adducts, apart from the 2-methyl-2,3-dihydroxypropanoic acid formed when methanol was the medium for reaction.

Pyruvic acid was found to be photochemically inert when irradiated in benzene solution,^{5,6} and this was attributed to the absence of abstractable hydrogen atoms in this solvent. However, the addition of benzhydrol,⁶ a good hydrogen donor,¹⁰ to benzene solutions of pyruvic acid, brought about the photoreduction of the latter to dimethyltartaric acid and the formation of benzpinacol in relatively high yield, (Equation 2.6).



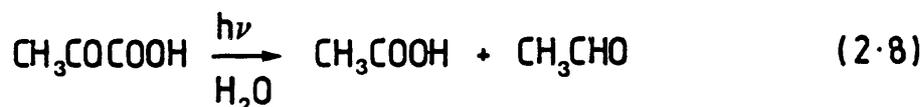
Monroe¹¹ has suggested the photoreduction of pyruvic acid to be entirely analogous to that observed for biacetyl. For example, Bentrude and Darnall,¹² and Urry and Trecker¹³ have shown that irradiation of biacetyl in isopropanol gives acetone, plus a nearly quantitative yield of a mixture of diastereomeric pinacols in approximately equal amounts, (Equation 2.7).



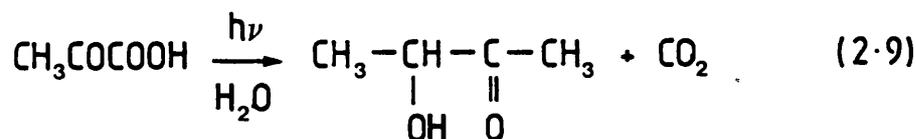
98%

It is clear, from the above reports,^{5,6,7} that photoreduction is an extremely important pathway for the decomposition of pyruvic acid in hydrogen donating solvents. However, the photoreaction of pyruvic acid in aqueous solution is far more intriguing and leads to a remarkable transformation, the mechanism of which is obscure.¹⁴

Lieben and co-workers¹⁵ reported that an aqueous solution of pyruvic acid decomposed upon irradiation to give acetaldehyde and possibly acetic acid, (Equation 2.8).



This finding¹⁵ conflicts with the result obtained by Dirscherl,^{16,17} who claimed that the products of the aqueous photodecomposition of pyruvic acid were acetoin and carbon dioxide, (Equation 2.9).



to an extreme difference in the solvation of pyruvic acid in benzene and in water.¹⁴

Kendall and Leermakers⁷ have shown that the photoreduction of pyruvic acid in solvents containing abstractable hydrogen atoms is quenched by 1,3-pentadiene, a poor singlet but good triplet quencher,¹⁸ and have invoked the participation of the triplet state in the reaction. This is in accord with the previously reported spectroscopic data for pyruvic acid,⁶ which shows two near-ultraviolet absorption maxima; an n- π^* band in the 300-350 nm region with low, and solvent dependent, extinction coefficients showing a blue shift in polar solvents, (Table 2.1); and a π - π^* band which occurs at 200 nm in water with an extinction coefficient of 2100.

TABLE 2.1⁶

| Solvent | n- π^* λ_{\max} (nm) | ϵ |
|-------------------------------|----------------------------------|------------|
| Water | 321.2 | 11.3 |
| Methanol | 325 | 4.55 |
| Chloroform | 337.5 | 11.5 |
| Diethyl ether | 342.5 | 14.7 |
| Benzene | 358.5 | 18.9 |
| Acetonitrile ²¹ | 337 | 16.9 |
| Deuterium oxide ²¹ | 324 | — |

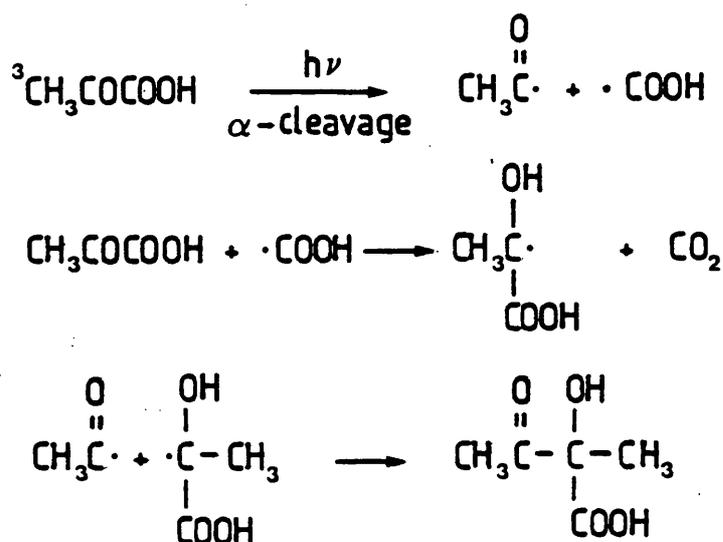
The emission spectrum of pyruvic acid, in an ethanol glass at 77 K, shows two well defined phosphorescence bands; the 0-0 band at 423 nm and the 0-1 band at 455 nm, the former corresponding to a triplet energy of 68 Kcal. As the phosphorescence was found to be more intense than that observed for benzophenone, which has a quantum yield of 0.8,¹⁹ it was suggested that pyruvic acid undergoes intersystem crossing with a high

degree of efficiency, possibly equal to unity, and as such the excited $n-\pi^*$ triplet state was designated responsible for photochemical reaction.

Gibson and Turnbull²⁰ have since reported the quantum yield of phosphorescence of pyruvic acid, in ethanol glass at 77 K, to be 0.18, as determined relative to benzophenone, and propose that the photochemistry of pyruvic acid proceeds from the lowest excited singlet state. Therefore the triplet yield of pyruvic acid is not known with any degree of certainty.

Closs and Miller²¹ have studied the mechanism for both the photoreduction and photodecarboxylation of pyruvic acid utilising the technique of CIDNP. Naphthalene was found to efficiently quench the photoreduction of pyruvic acid by ethanol in acetonitrile solution, reaffirming the involvement of the excited triplet state of pyruvic acid in hydrogen transfer reactions.^{6,7} Photoreduction of triplet pyruvic acid by both isopropanol and acetaldehyde in acetonitrile solution was also observed.²¹ It was suggested that photodecarboxylation of pyruvic acid in water and other non-reducing polar solvents, occurred from the excited triplet state of the acid and a mechanism, initiated via unimolecular scission of the carbonyl-carboxy bond, was postulated, (Scheme 2.3). The carboxy radicals so produced in this Type 1 reaction rapidly reduce ground state pyruvic acid, and a radical coupling reaction follows to yield 2-hydroxy-2-methyl-acetoacetic acid as the product. The triplet state was deemed responsible for the reaction as addition of naphthalene quenched the formation of 2-hydroxy-2-methyl-acetoacetic acid.

It is known that 2-hydroxy-2-methyl-acetoacetic acid undergoes rapid acid-catalysed hydrolysis to give acetoin.²² Closs and Miller²¹ found 2-hydroxy-2-methyl-acetoacetic acid to be photochemically inert in acetonitrile (under the experimental conditions employed in their CIDNP

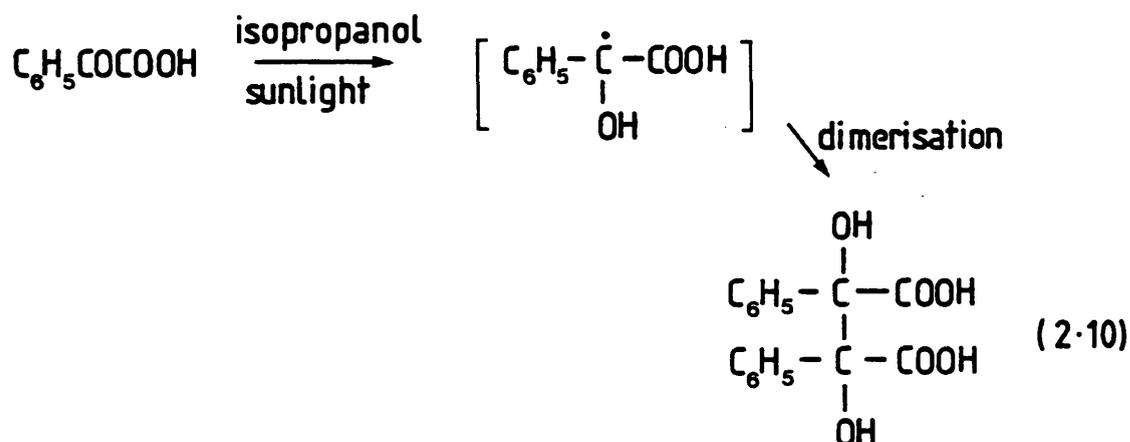


Scheme 2.3

study) and suggested that acetoin is not a primary photoproduct of pyruvic acid in aqueous solution, but arises from the facile hydrolysis of 2-hydroxy-2-methyl-acetoacetic acid, which was found to be the primary photoproduct in all solvents. This result may offer an explanation as to why acetoin is not formed in other photolyses of pyruvic acid apart from those employing water as solvent.^{5,6,16,17} If acetoin does arise from 2-hydroxy-2-methyl-acetoacetic acid in aqueous solution, and should the latter prove to be photochemically inert in other non-reducing solvents, as it is in acetonitrile,²¹ then the photodecomposition of pyruvic acid in such solvents would effectively yield 2-hydroxy-2-methyl-acetoacetic acid as the product, rather than acetoin. However, the above mechanism implies that when benzene is utilised as solvent, 2-hydroxy-2-methyl-acetoacetic acid should be formed; but Closs and Miller²¹ also found pyruvic acid to be photochemically inert in this solvent.^{5,6}

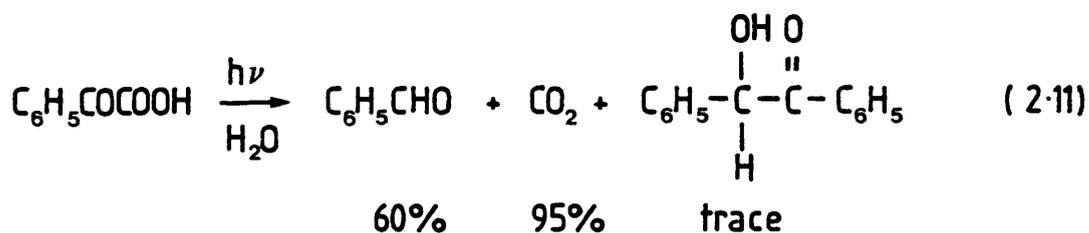
2.1(ii) PHENYLGLYOXYLIC ACID

Schönberg and co-workers²³ have reported that phenylglyoxylic acid is photoreduced to diphenyltartaric acid in isopropanol, via an intermediate ketyl radical, (Equation 2.10).



Fujisawa and co-workers⁸ have observed the intermediate ketyl radical in an electron spin resonance study of phenylglyoxylic acid.

Leermakers and Vesley⁶ have shown that phenylglyoxylic acid, upon irradiation in water, gives benzaldehyde and carbon dioxide as the major products, with only trace amounts of benzoin being detected, (Equation 2.11).



Although the photoreduction of phenylglyoxylic acid²³ is similar to that reported for pyruvic acid,⁵⁻⁷ the aqueous photodecomposition of the two α -keto-carboxylic acids is different; benzaldehyde being the principal product from phenylglyoxylic acid,⁶ whereas the main isolable product from pyruvic acid is acetoin.⁶ The observation of benzaldehyde

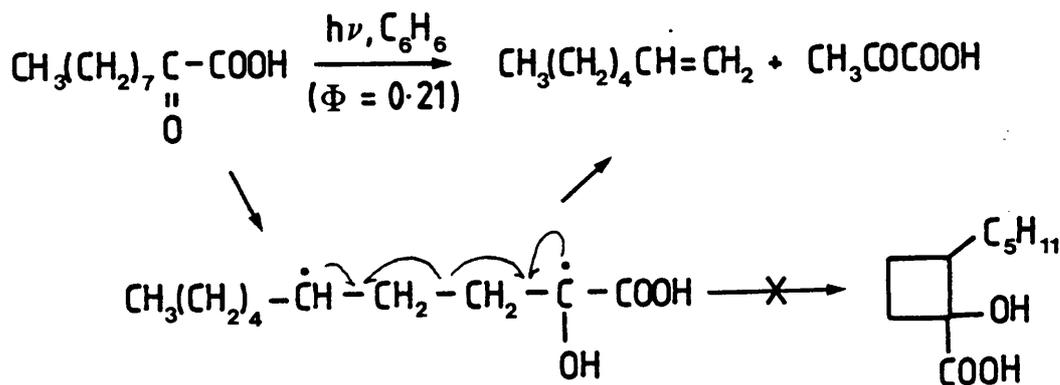
in the former reaction could be rationalised on the basis of homolytic loss of carbon dioxide with subsequent recombination of the benzoyl radical and a hydrogen atom. However, such a cage mechanism will not account for the formation of acetoin from pyruvic acid in the latter reaction.

From spectroscopic studies⁶ the excited state responsible for the photodecomposition of phenylglyoxylic acid has been ascribed to the triplet. Similar to pyruvic acid, phenylglyoxylic acid shows two near-ultraviolet absorption bands; an $n-\pi^*$ band at 337.5 nm in water ($\epsilon = 48$) and at 376 nm in benzene ($\epsilon = 77$), and a $\pi-\pi^*$ transition at 262.5 nm in water ($\epsilon = 9530$). The emission spectrum, in ethanol glass at 77 K, shows the 0-0 band at 470.5 nm, corresponding to a triplet energy of 60.8 Kcal, and the 0-1 band at 510 nm. The quantum yield of phosphorescence for phenylglyoxylic acid is reported to be close to unity,⁶ and hence the triplet state of the acid has been designated responsible for photo-reaction.

2.1(iii) LONG CHAIN α -KETO-CARBOXYLIC ACIDS

Evans and Leemakers²⁴ have shown that irradiation of α -keto-decanoic acid in benzene solution affords hept-1-ene and pyruvic acid via a Norrish Type II³ elimination, (Scheme 2.4).

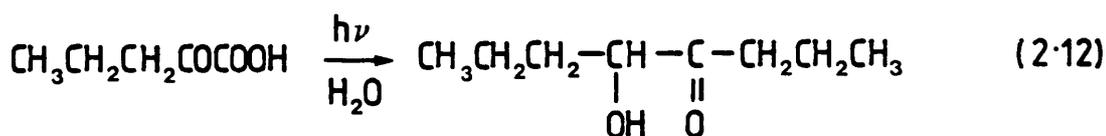
Unlike the long chain α -diketones,^{13,25} α -keto-decanoic acid does not form cyclobutanol derivatives when irradiated in benzene solution. Surprisingly, the reaction was suggested to occur from the triplet manifold with no singlet contribution, as quenching with cyclohexa-1,3-diene gave a linear Stern-Volmer plot in which the quantum yield for elimination of hept-1-ene did not level out, even at very high concentrations of quencher.²⁴ This is in direct contrast to aliphatic ketones



Scheme 2.4

which undergo Norrish Type II reactions and show between 10-40% unquenchable photoelimination from the singlet state.²⁶

In an earlier report by Dirscherl,¹⁷ α -keto-pentanoic acid produced butyrolin when irradiated in aqueous solution, (Equation 2.12).



30-40%

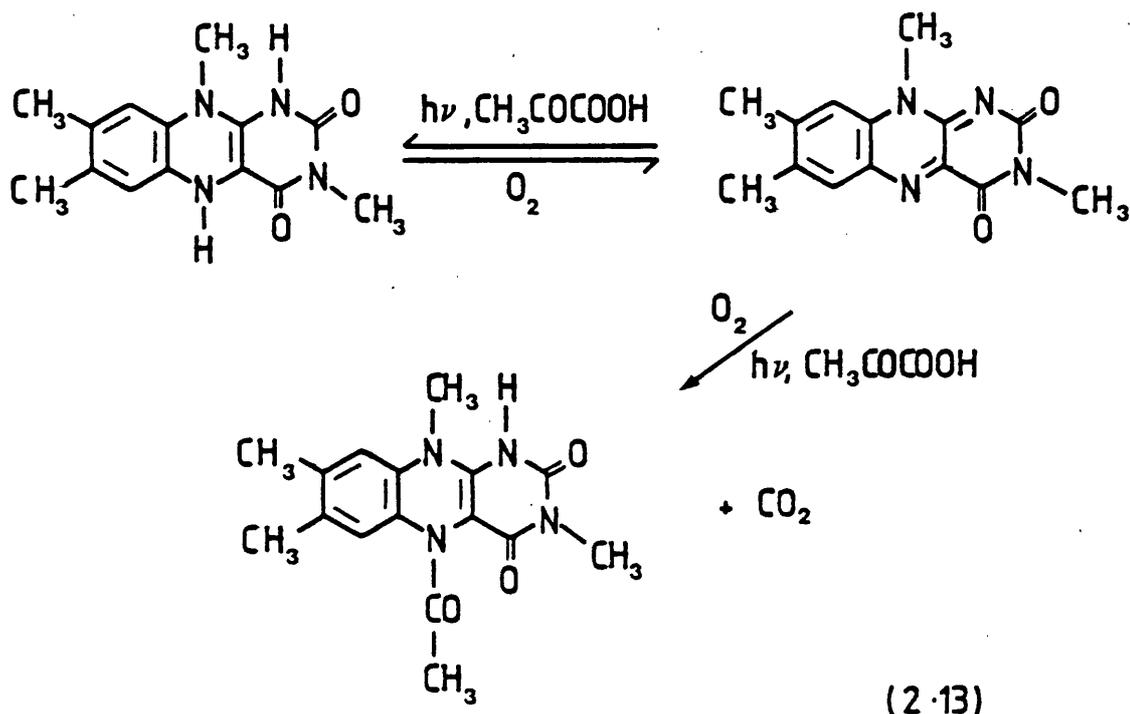
The low yield of butyrolin may have been due to a competing Norrish Type II photoelimination.

2.2 DYE-SENSITIZED PHOTO-OXYGENATION OF α -KETO-CARBOXYLIC ACIDS

De Kok and Veeger²⁷ reported the effect of light on flavoproteins in the presence of α -keto-carboxylic acids. The formation of a species, detected by absorption spectroscopy, and suggested to arise via an addition reaction between the flavoprotein and α -keto-carboxylic acid was observed. The rate of formation of the species was found to be very slow in the dark but greatly enhanced by illumination at wavelengths below 500 nm. L-Amino-acid oxidase irradiated in the presence of α -keto-

isovaleric acid produced a species having a shoulder at 375 nm, maxima at 385 and 485 nm and absorption above 540 nm. Similar light induced reactions occurred with other flavoproteins, for example when D-amino-acid oxidase is irradiated in the presence of pyruvic acid it gives rise to a product having absorptions at 380 nm, a shoulder at 400 nm, a maximum at 490 nm and absorption above 540 nm. When the latter reaction was carried out using light of 320 nm, i.e. the substrate $n-\pi^*$ transition being excited, an electron transfer from pyruvate to flavoquinone took place resulting in the formation of flavosemiquinone anion, which was stable under the anaerobic conditions of fixation to the protein. Alternatively, if the reaction is performed using light of 390 nm (which excites the flavin system) in the presence of isotopically labelled [3- 14 C]-pyruvate, the thin layer chromatogram of the reaction mixture showed that the radioactivity was associated with the flavin, supporting the hypothesis of an irreversible addition compound.²⁷ The authors did not find any evidence for adduct formation on replacing the flavoprotein with free flavocoenzymes.

Later, Brustlein and Hemmerich²⁸ found that aqueous solutions of 3-methyllumiflavin containing pyruvic acid, or its salts, gave an addition compound upon irradiation. Under anaerobic conditions a reversible photoreduction occurred, which was suppressed under aerobic conditions and a slower irreversible photoreduction (with decarboxylation of the pyruvic acid) ensued and finally became quantitative forming an adduct, 3-methyl-5-acetyl-1,5-dihydroflavin, which was isolated from the reaction mixture, (Equation 2.13). In order to account for the above observations, two mechanisms were proposed; one involved a 'hydride' transfer (i.e. transfer of a proton and two electrons in one step) from the pyruvic acid to the flavin, whilst the second involved group transfer with concerted



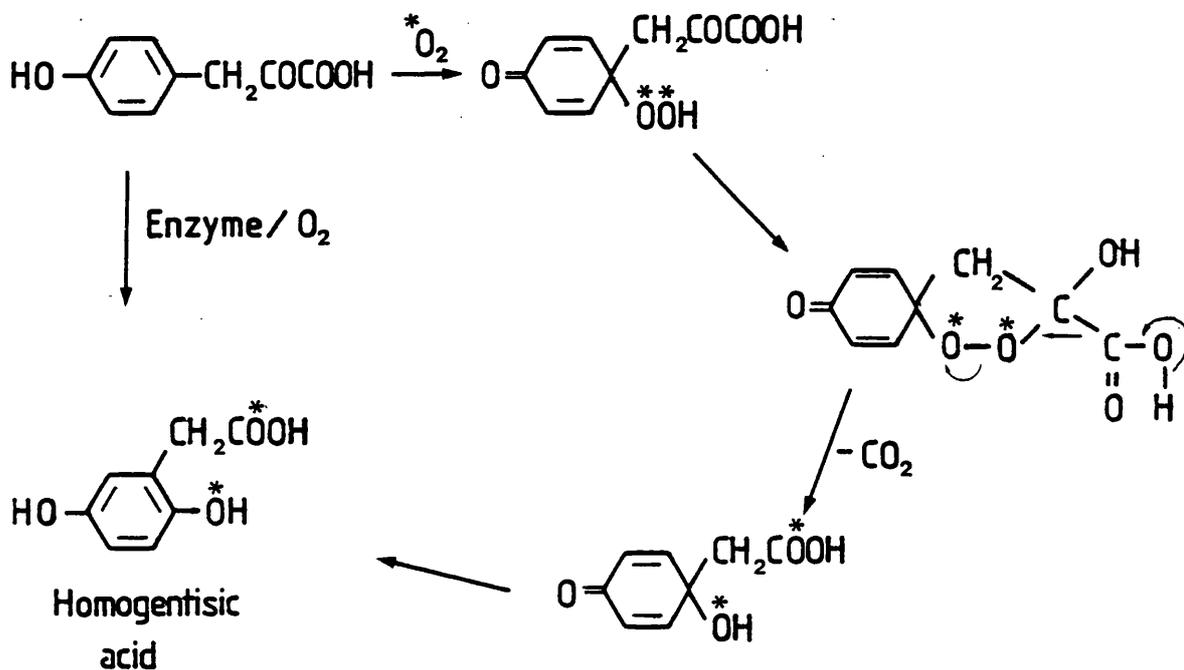
loss of carbon dioxide. The feasibility of the above mechanisms was not explored.

Breslow²⁹ observed that pyruvic acid in the absence of oxygen, underwent a photo-decarboxylation reaction when irradiated in the presence of thiamine, and proposed that the mechanism involved the initial formation of an addition product which subsequently decarboxylated.

The formation of a thiamine - pyruvate adduct, possibly of an ion-pair nature, was later confirmed by Gibson and Turnbull,²⁰ although these authors were unable to detect any photochemical decarboxylation of pyruvic acid in a system sensitized by thiamine.

Recently, the non-enzymic photo-oxidation of p-hydroxyphenylpyruvic acid has been studied^{30, 31} as a model for the action of p-hydroxyphenylpyruvic acid dioxygenase, which catalyses the conversion of p-hydroxyphenylpyruvic acid into homogentisic acid.³² Lindblad and co-workers³³ have shown that atmospheric oxygen is incorporated into both the hydroxy moiety and the carboxyl group of homogentisic acid. These authors³³

postulate a mechanism involving nucleophilic attack of the hydroperoxy group of the intermediate hydroperoxide, on the keto group of the side chain. The cyclic peroxide thus formed is converted, via a decarboxylation reaction, into the quinol intermediate which undergoes migration of the side chain to the ortho position by a mechanism analogous to that of the NIH shift,³⁴ to yield homogentisic acid, (Scheme 2.5). A similar mechanism was first suggested by Goodwin and Witkop.³⁵



Scheme 2.5

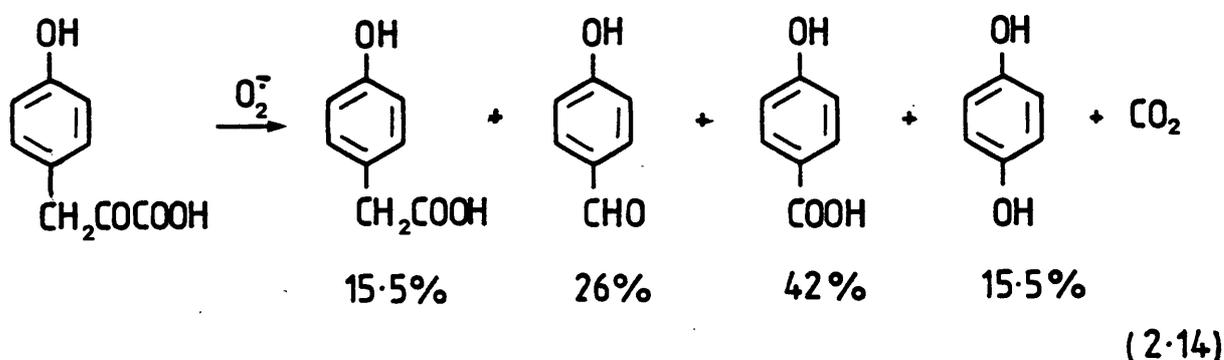
Saito and co-workers³⁰ have studied the dye-sensitized photo-oxygenation of both the enol and keto forms of p-hydroxyphenylpyruvic acid. The Methylene Blue sensitized photo-oxygenation of the enol form in methanol resulted in the rapid consumption of an equimolar amount of oxygen and the formation of p-hydroxybenzaldehyde and oxalic acid. Rose Bengal sensitized photo-oxygenation of the keto form in phosphate-buffer (pH 7.0) gave three products; the quinol intermediate, p-hydroxybenzaldehyde and

p-hydroxyphenylacetic acid in 18, 12 and 15% yields respectively. At a pH greater than 12 the quinol intermediate was converted into homogentisic acid. Thus when the photo-oxygenated mixture was made alkaline, without further isolation of the intermediate quinol, homogentisic acid was obtained in greater than 25% yield, based on the amount of reacted keto form of p-hydroxyphenylpyruvic acid, as outlined in Scheme 2.6.

A mechanism involving singlet oxygen was invoked³⁰ from the observation that the addition of known singlet oxygen quenchers, DABCO and sodium azide, led to a decrease in the rate of photo-oxygenation of p-hydroxyphenylpyruvic acid. The rate of disappearance of the keto form of p-hydroxyphenylpyruvic acid was found to increase six-fold in going from water to deuterium oxide and this also was attributed to the participation of singlet oxygen.³⁰ Thus it was suggested, from the quenching studies and the solvent isotope enhancement, that a large proportion of the photo-oxygenation of the keto form of p-hydroxyphenylpyruvic acid leading to the quinol intermediate was a singlet oxygen mediated reaction. However, the possibility that a radical process involving triplet sensitizer may also be operating could not be rigorously excluded.³⁰ Whether free singlet oxygen participates in the enzymic reaction is still unclear, but the results show that the mode of oxidation of p-hydroxyphenylpyruvic acid catalysed by the enzyme,³³ is very similar to that observed in the dye-sensitized reaction,³⁰ and the latter provides chemical support for the proposed mechanism of the enzymic reaction.

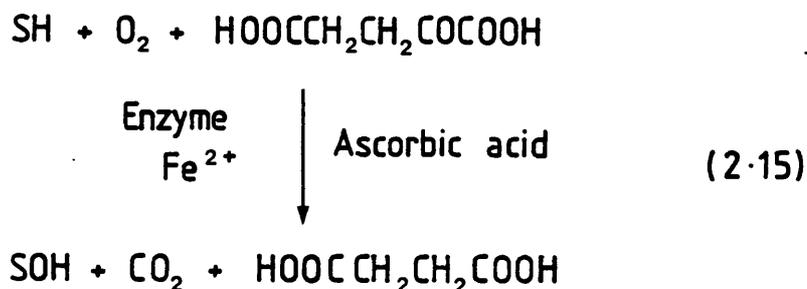
The one-electron reduction of oxygen is also a possible way in which oxygenases might activate oxygen for reaction with organic substrates.³⁶ The superoxide anion is invoked in the mechanism for the hydroxylation of organic substrates by the liver-microsomal-P450 system.³⁷ Accordingly, Jefford and Cadby³¹ have studied the reaction of p-hydroxyphenylpyruvic

acid with potassium superoxide in dimethylsulphoxide, and report the production of carbon dioxide and the p-hydroxy derivatives of phenylacetic acid, benzaldehyde, benzoic acid and phenol, (Equation 2.14).

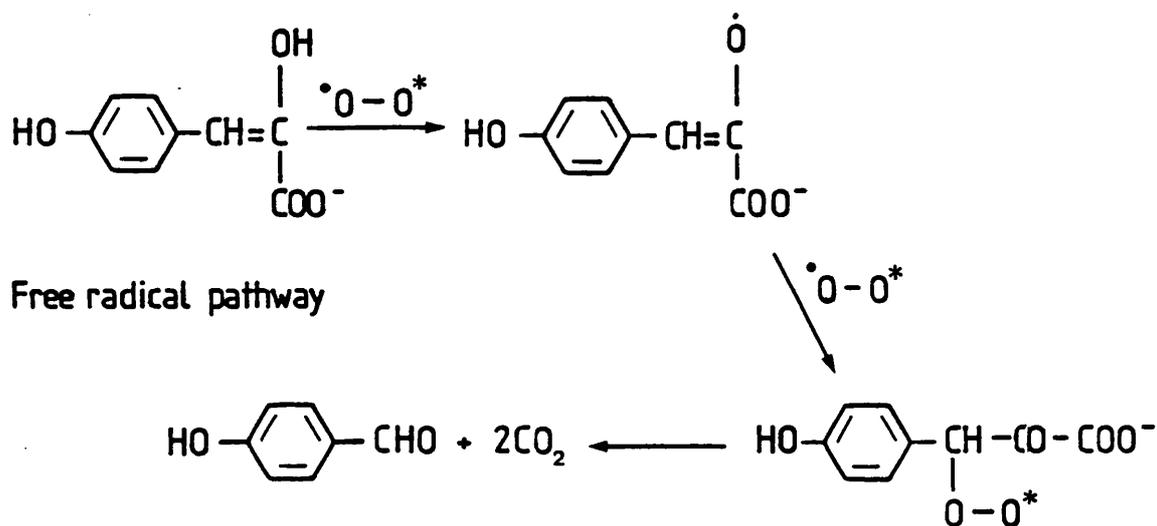
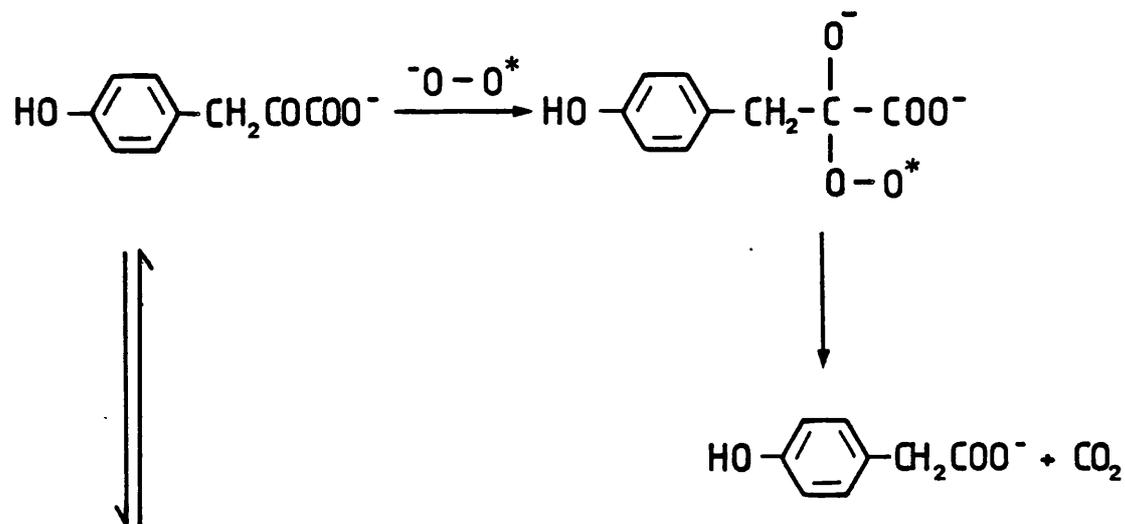


The absence of homogentisic acid in the product mixture means that this reaction is not a model for the enzymic process.³³ Jefford and Cadby³¹ propose that the products arise by two pathways involving dioxygen species behaving as radical and/or nucleophilic reagents, (Scheme 2.7a), the benzoic acid and phenol derivatives being produced by the further oxidation of p-hydroxybenzaldehyde, (Scheme 2.7b).

An important class of mono-oxygenases are those which require α -keto-glutaric acid as a cofactor.³⁸ Biological oxidation is catalysed by the metalloenzyme so that hydroxylation of a substrate (SH) is effected by half a mole of molecular oxygen while the other half is taken up by α -keto-glutaric acid which acts as a reductant, (Equation 2.15). The details of the general scheme are presently not known.³⁹



Nucleophilic pathway

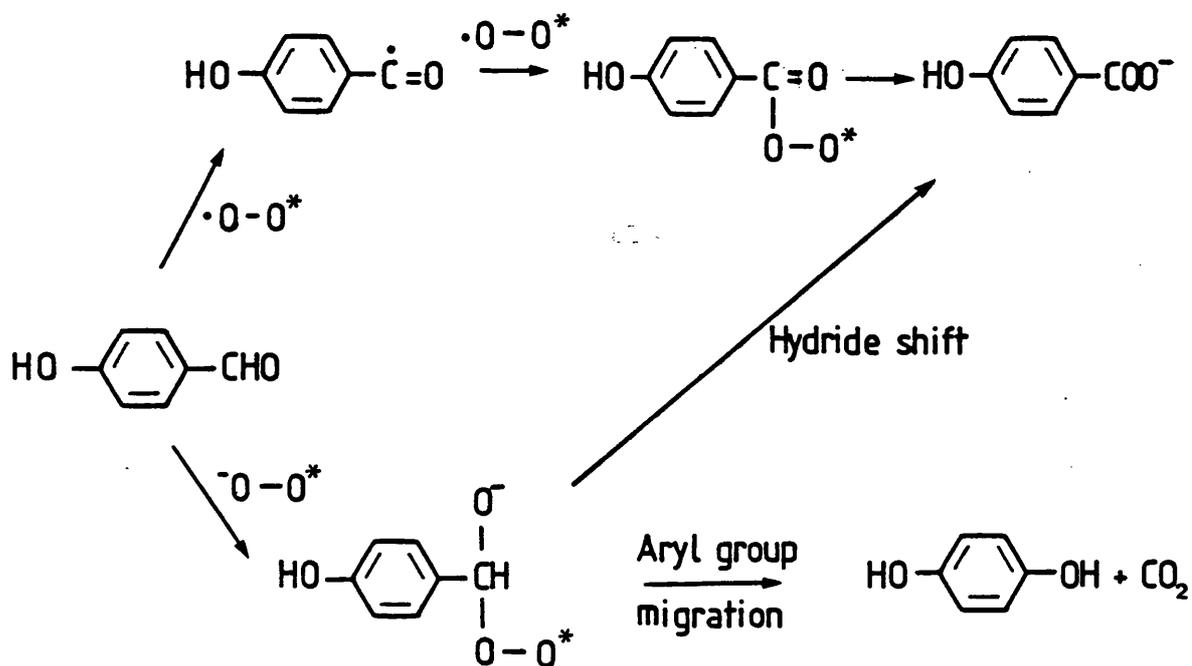


(where $-\text{O}^* = -\text{O}^\cdot, -\text{O}^-$ or $-\text{OH}$)

Scheme 2.7a

It has been suggested by Hamilton⁴⁰ that α -keto-glutaric acid is converted by oxygen to per-succinic acid which subsequently brings about the oxidation of the substrate, (Equation 2.16). Direct reaction between singlet α -keto-glutaric acid and triplet molecular oxygen is spin forbidden and thus cannot take place, and the rôle of transition

Free radical pathway

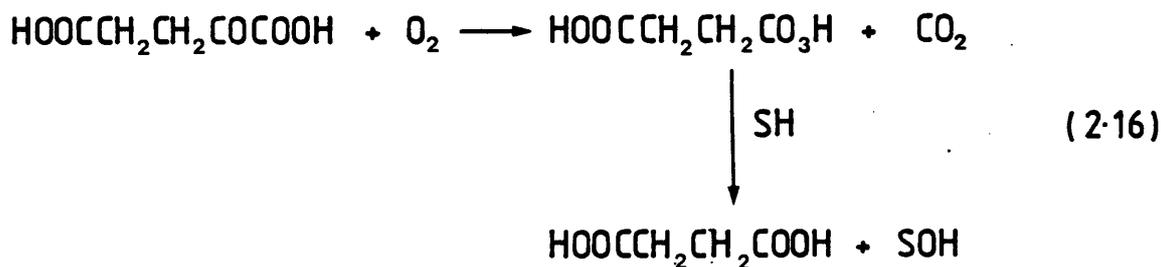


Nucleophilic pathway

(where $-\text{O}^* = -\text{O}^\cdot, -\text{O}^-$ or $-\text{OH}$)

Scheme 2.7b

metal complexation has been implied in order to render molecular oxygen acceptable to the α -keto-carboxylic acid function.⁴⁰



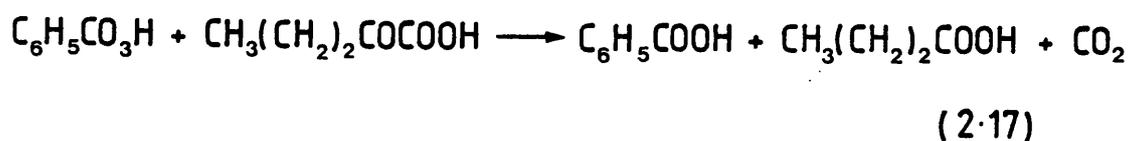
Jefford and co-workers⁴¹ have studied the reaction of singlet oxygen towards α -keto-carboxylic acids in order to determine the plausibility of the above hypothesis.⁴⁰ Both oxidative decarboxylation and peroxy acid formation occurred when a variety of α -keto-carboxylic acids were

irradiated in oxygenated acetonitrile solutions containing the dye Methylene Blue,⁴¹ (Table 2.2).

TABLE 2.2

| α -Keto-carboxylic acid | Photolysis time (h) | % CO ₂ evolved | Products (%) |
|--|---------------------|---------------------------|---|
| HOOC(CH ₂) ₂ COCOOH | 19 | 45 | HOOC(CH ₂) ₂ COOH (45) |
| CH ₃ (CH ₂) ₃ COCOOH | 40 | 51 | CH ₃ (CH ₂) ₂ COOH (45) |
| HOOCCH ₂ COCOOH | 19 | 32 | HOOCCH ₂ COOH (60) |
| C ₆ H ₅ -COCOOH | 19 | 0 | none |
| t-Bu-COCOOH | 23 | 100 | t-Bu-COOH (95) |

The participation of singlet oxygen was inferred in these reactions from the observation that light, oxygen and dye are all essential for the reaction to occur. However, the addition of DABCO did not quench the reactions, but in fact accelerated them, and the progressive addition of β -carotene slowed up, but did not halt the reactions. Although the colouration of starch-iodide paper pointed to the formation of per-acids, their isolation was not possible, and the authors⁴¹ suggest that as fast as the per-acid was formed, it was decomposed by further reaction with the parent α -keto-carboxylic acid. The evidence for this assumption comes from the finding that instantaneous decarboxylation of α -keto-valeric acid to butyric acid occurred after equimolar mixing with per-benzoic acid, (Equation 2.17).



Davidson⁴² subsequently found that the decarboxylation of α -keto-glutaric acid, and its anion, could be sensitized by Methylene Blue and other dyes such as Rose Bengal, in the absence of oxygen. In some cases the presence of oxygen led to a retardation of the decarboxylation reaction, and in others to the production of greater than one mole of carbon dioxide per mole of α -keto-glutaric acid consumed, (Table 2.3).

TABLE 2.3

| State of acid | Solvent | Yield (%) of CO ₂ | | | |
|-----------------|---------------------------|------------------------------|----------------|----------------|----------------|
| | | Methylene Blue | | Rose Bengal | |
| | | N ₂ | O ₂ | N ₂ | O ₂ |
| Free | Methanol | 25.5 | 31.5 | | |
| Free | Acetonitrile | | 59 | | |
| Pyridinium salt | Methanol/ Pyridine | 33 | 58 | 100 | 84 |
| Pyridinium salt | Acetonitrile/ Pyridine | none | 120 | 72 | 200 |

These results (Table 2.3) established that a reaction pathway exists in the dye-sensitized decarboxylation of α -keto-carboxylic acids which does not involve singlet oxygen. The alternative route for decarboxylation clearly involves the attack by an excited state of the dye (suggested to be the triplet⁴²) upon the α -keto-carboxylic acid. The previous observation⁴¹ that addition of β -carotene retards the decarboxylation may be due to its quenching action on either singlet oxygen or the excited singlet and triplet states of the dye.^{42,43} It was noted⁴² that in oxygenated solution there is the possibility that two mechanisms could be operating, i.e. attack of both singlet oxygen and triplet dye upon the α -keto-carboxylic acid. Melnick⁴⁴ later argued against a dye-acid inter-

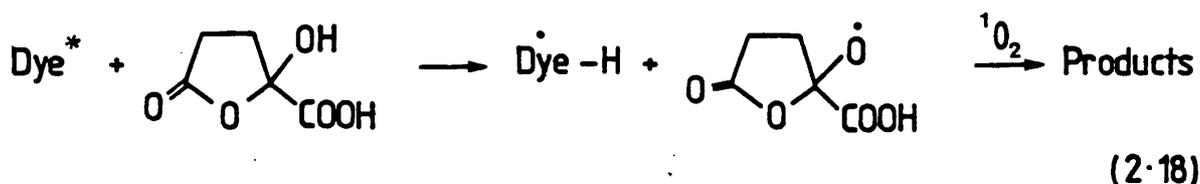
action suggesting that decarboxylation in methanolic solution (Table 2.3) could be due to metal ion impurities which exhibit catalytic activity.⁴⁵

Davidson's proposal⁴² of a dye-acid interaction and the finding that more than one mole of carbon dioxide was evolved, were later confirmed by Jefford and co-workers⁴⁶ in a study of the Rose Bengal sensitized decarboxylation of a number of α -keto-carboxylic acids in acetonitrile/pyridine solution. The authors⁴⁶ found that the photo-excited dye alone brought about decarboxylation, but when oxygen was present, extra decarboxylation occurred (Table 2.4), which again⁴¹ was attributed to the involvement of singlet oxygen on the basis of a solvent isotope effect of 3.63 ± 0.46 in deuterium oxide as compared to water.

TABLE 2.4

| α -Keto-carboxylic acid | Yield (%) of CO ₂ | | Products under oxygen |
|--------------------------------|------------------------------|----------------|---|
| | N ₂ | O ₂ | |
| α -Keto-glutaric acid | 90 | 125 | Succinic acid, Hydroxypropionic acid, Malic acid, Oxalic acid |
| Pyruvic acid | 5 | 50 | Acetic acid |
| α -Keto-butyric acid | 3 | 100 | Propionic acid |
| α -Keto-valeric acid | 7 | 75 | Butyric acid |

To account for the high yields of carbon dioxide, and the other products formed from α -keto-glutaric acid (Table 2.4), it was suggested that this acid exists as a lactol tautomer that is preferentially oxidised by the dye, to give the lactol radical, which reacts to give the observed products, (Equation 2.18).



Further evidence⁴⁶ supporting the dye-acid interaction⁴² comes from the observation that when the acid and dye are immobilised on solid supports, decarboxylation was moderate under oxygen (27%) and non-existent under nitrogen. The latter finding confirms that contact between sensitizer and acid is necessary for part of the photoreaction.

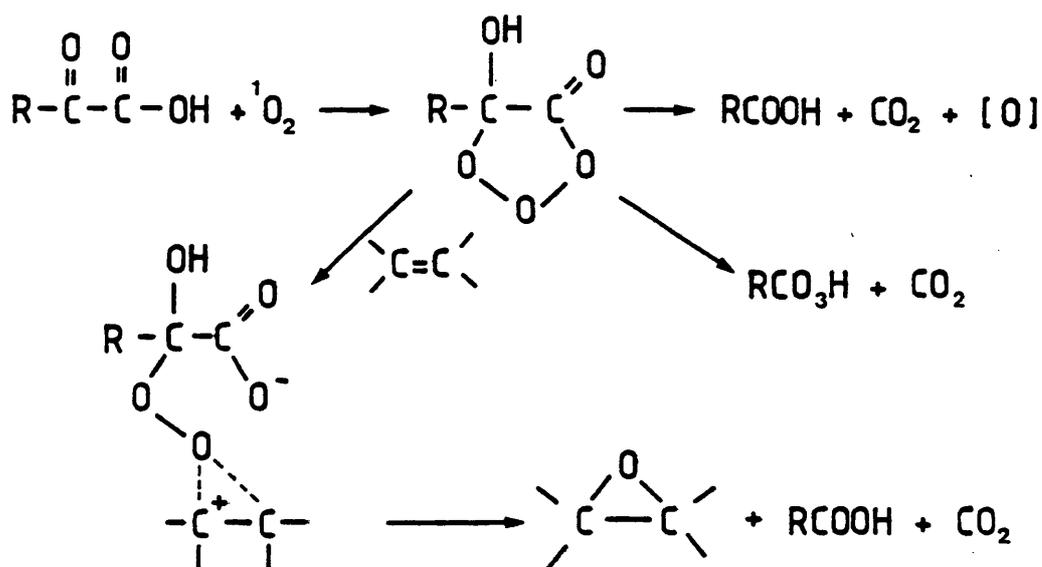
Moriarty and co-workers⁴⁷ have studied the reaction of α-keto-glutaric acid with singlet oxygen generated by the triphenyl phosphite-ozone reaction and microwave discharge. In each case the yields of carbon dioxide and succinic acid were similar, and this was taken as evidence for the participation of singlet oxygen in the dye-sensitized photo-oxygenation of α-keto-glutaric acid, (Table 2.5). An interesting observation in the latter reaction was that the addition of an alkene to the reaction mixture led to the formation of the alkene epoxide, (Table 2.5).

The per-acid formed under the reaction conditions did not bring about the epoxidation of the alkene, and a mechanism involving the formation of a trioxalane intermediate which transfers oxygen to the alkene was postulated, (Scheme 2.9). The authors⁴⁷ describe this mechanism as being analogous to what may generally occur in the enzymic activation of molecular oxygen, in α-keto-glutarate-dependent oxygenases. The relationship between the singlet oxygen reaction with α-keto-glutaric acid, and the enzyme reaction, is that in each case the α-keto-carboxylic acid is the intermediate dioxygen acceptor.

Sawaki and Ogata⁴⁸ have recently confirmed that the dye-sensitized photo-oxygenation of α-keto-acids leads to the epoxidation of alkenes,

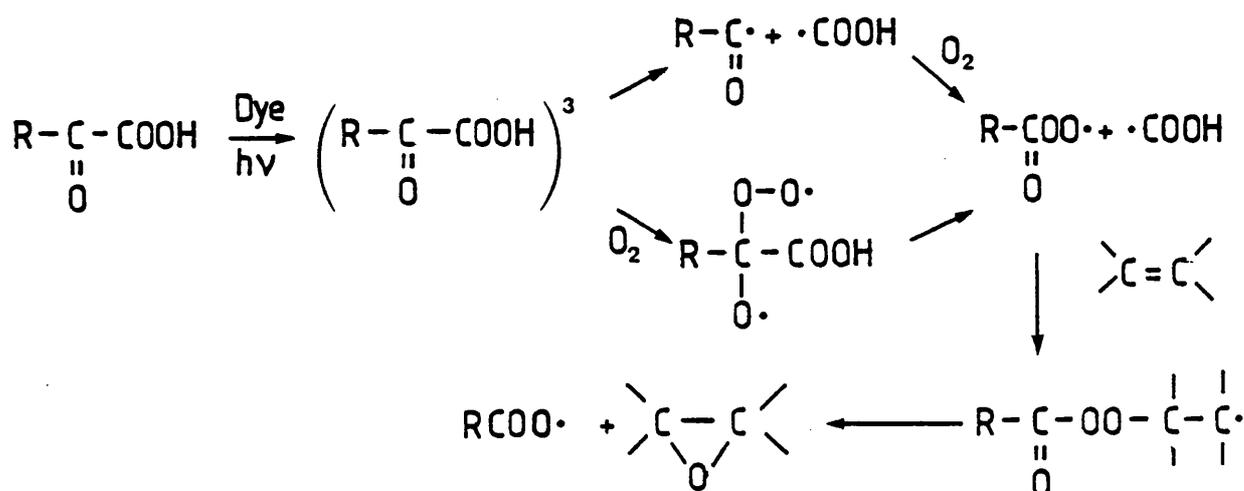
TABLE 2.5

| ¹ O ₂ source | Temp. °C | Alkene | CO ₂ (%) | Succinic Acid (%) | Alkene Epoxide (%) |
|---|----------|--------------------|---------------------|-------------------|--------------------|
| (C ₆ H ₅ O) ₃ P-O ₃ | - 24 | - | 24 | 24 | - |
| Microwave discharge | 25 | - | 26 | 30 | - |
| Dye MeOH O ₂ hv | 25 | Tetracyanoethylene | 15 | 18 | 15 |
| Dye MeOH O ₂ hv | -100 | Cyclohexene | 26 | 21 | 18 |
| Dye MeOH O ₂ hv | -100 | Styrene | 23 | 22 | 19 |
| Dye MeOH O ₂ hv | -100 | trans-stilbene | 24 | 24 | 14 |



Scheme 2.9

but have questioned the rôle of the previously suggested trioxalane intermediate.⁴⁶ The epoxidation of α -methylstyrene was found to occur in the Methylene Blue sensitized photo-oxygenation of phenylglyoxylic acid in acetonitrile solution.⁴⁸ A reaction proceeding by way of photochemical α -cleavage leading to the formation of an acylperoxy radical, which can effectively transfer an atom of oxygen to the alkene, was favoured, (Scheme 2.10).



Scheme 2.10

Evidence for the above mechanism (Scheme 2.10) comes from the finding that the relative reactivities of the alkene with the acylperoxy radicals derived from the decomposition of the α -keto-carboxylic acid were similar to those for epoxidation with benzoin (i.e. $\text{PhCO}_3\cdot$), and quite different from those for per-acid epoxidation.⁴⁸

It is clear that the results obtained from in vitro, i.e. dye-sensitized studies of α -keto-carboxylic acids, require careful rationalisation when being used as models for the in vivo or enzymic processes, as the dye-sensitized reactions alone are subject to much conjecture.

Summary

The direct and dye-sensitized photochemical reactions of α -keto-carboxylic acids have been reviewed and the mechanisms involved in the reactions have been discussed.

RESULTS AND DISCUSSION

Object of investigation

A study of the photo-induced decarboxylation of pyruvic acid, and other α -keto-carboxylic acids, was performed under deoxygenated conditions (Sections 2.3 and 2.4), in order to re-evaluate the mechanism involved in their photodecomposition. The effect of oxygen upon the solution phase photo-decarboxylation of α -keto-carboxylic acids has not previously been studied, and was the subject of an investigation, (Section 2.5).

Dye-sensitized photo-oxygenations of α -keto-carboxylic acids were carried out to establish whether singlet oxygen plays a significant rôle in these reactions, (Section 2.6.1). The effect of oxygen concentration upon the dye-sensitized reactions was also studied, (Section 2.6.2).

2.3 DIRECT PHOTO-INDUCED DECARBOXYLATION OF α -KETO-CARBOXYLIC ACIDS IN DEOXYGENATED SOLUTION

2.3(i) DECARBOXYLATION STUDIES

The photo-induced decarboxylation of pyruvic acid was found to be highly solvent dependent and occurred in solvents, such as methanol, which are capable of reducing triplet carbonyl compounds; higher yields of carbon dioxide being obtained when employing polar solvents, (Table 2.6).

Similar reactions were found to occur for a variety of α -keto-carboxylic acids both in methanol and acetonitrile solutions, the yields of carbon dioxide are given in Table 2.7.

The aqueous photo-induced decarboxylation of pyruvic acid was found to be pH dependent (Table 2.8). When the reaction was carried out either

TABLE 2.6

Yields of carbon dioxide from the direct irradiation^(a) of pyruvic acid (10^{-2} M) under nitrogen, in various solvents

| Solvent | Yield (%) of carbon dioxide |
|--------------------|-----------------------------|
| Acetone | 15.4 |
| Acetonitrile | 15.0 |
| Benzene | 4.0 |
| t-Butanol | 7.3 |
| Chloroform | 6.7 |
| Dimethylformamide | 10.2 |
| Dimethylsulphoxide | 4.0 |
| Dioxan | 15.2 |
| Ethanol | 7.1 |
| Methanol | 15.0 |
| Water | 52.0 |

(a) 3h irradiation

TABLE 2.7

Yields of carbon dioxide from the direct irradiation of α -keto-carboxylic acids under nitrogen (A) in methanol and (B) in acetonitrile

| α -Keto-carboxylic acid (10^{-2} M) | Yield (%) of carbon dioxide | | | |
|--|-----------------------------|------|------------------|------|
| | (A) Methanol | | (B) Acetonitrile | |
| | 6h | 20h | 6h | 20h |
| Pyruvic acid | 23.6 | 32.9 | 52.8 | 100 |
| α -Keto-butyric acid | 19.9 | 26.4 | 69.9 | 100 |
| α -Keto-glutaric acid | 13.2 | 19.3 | 76.8 | 100 |
| 3,3-Dimethyl-2-keto-butyric acid | 12.8 | 41.3 | 40.8 | 62.7 |
| α -Keto-valeric acid | 15.0 | 22.8 | 10.0 | 43.3 |
| α -Keto-pimelic acid | 8.9 | 33.7 | 28.4 | 66.6 |

in ammonia solution or in acetonitrile containing t-butylamine (4:1 v/v), carbon dioxide was not evolved even after prolonged irradiation times.

TABLE 2.8

The effect of pH upon the yield of carbon dioxide from the direct irradiation^(a) of aqueous pyruvic acid solutions (10^{-1} M) under argon

| pH | Yield (%) of carbon dioxide |
|---------|-----------------------------|
| 0.9(b) | 21.0 |
| 1.85(c) | 31.4 |
| 6.3(d) | 3.4 |
| 9.4(d) | <1.0 |

- (a) 1.5h irradiation
- (b) adjusted with concentrated sulphuric acid
- (c) pH of stock solution
- (d) adjusted with triethylamine

The yields of carbon dioxide from acetonitrile solutions of pyruvic acid were increased by the addition of water (9:1 v/v), (Table 2.9).

TABLE 2.9

The effect of water upon the yields of carbon dioxide from the direct irradiation^(a) of acetonitrile solutions of pyruvic acid, under argon

| Pyruvic acid concentration (M) | Solvent | Yield (%) of carbon dioxide |
|--------------------------------|--------------------|-----------------------------|
| 10^{-1} | Acetonitrile | 16.0 |
| 10^{-1} | Acetonitrile/Water | 32.1 |
| 10^{-2} | Acetonitrile | 16.8 |
| 10^{-2} | Acetonitrile/Water | 35.3 |

- (a) 6h irradiation

The addition of pyridine greatly enhanced the production of carbon dioxide from benzene solutions of pyruvic acid, whereas only a slight enhancement was observed when the reaction was carried out in acetonitrile, (Table 2.10).

TABLE 2.10

The effect of added pyridine ($10^{-1}M$) upon the yields of carbon dioxide from the direct irradiation^(a) of benzene and acetonitrile solutions of pyruvic acid ($10^{-1}M$), under argon

| Solvent | Yield (%) of carbon dioxide | Enhancement |
|-----------------------|-----------------------------|-------------|
| Benzene | 1.6 | } 17.2 × |
| Benzene/Pyridine | 27.5 | |
| Acetonitrile | 25.5 | } 1.3 × |
| Acetonitrile/Pyridine | 33.1 | |

(a) 9h irradiation

A most striking finding was that the addition of methyl viologen to an aqueous acetonitrile-pyridine solution of pyruvic acid, upon irradiation, increased the yield of carbon dioxide, (Table 2.11), and led to the production of reduced methyl viologen, as characterised by its absorption spectrum,⁴⁹ (Fig. 2.1).

Enhanced yields of carbon dioxide were also obtained from acetonitrile solutions of pyruvic acid irradiated in the presence of various electron acceptors, (Table 2.12).

Similarly, pyridine and 1-cyanonaphthalene increased the yield of carbon dioxide from irradiation of α -keto-glutaric acid in acetonitrile, (Table 2.13).

TABLE 2.11

The effect of methyl viologen (10^{-2} M) upon the yield of carbon dioxide from the direct irradiation^(a) of pyruvic acid (10^{-2} M) in acetonitrile/pyridine/water (8:1:1 v/v), under argon

| Conditions | Yield (%) of carbon dioxide |
|-------------------------|-----------------------------|
| Methyl viologen absent | 10.4 |
| Methyl viologen present | 20.3 |

(a) 1h irradiation

TABLE 2.12

Yields of carbon dioxide from the direct irradiation^(a) of pyruvic acid (10^{-2} M) in acetonitrile, under argon, in the presence of electron acceptors (10^{-2} M)

| Electron acceptor | Yield (%) of carbon dioxide |
|---------------------------------------|-----------------------------|
| None | 16.8 |
| Pyrene | 18.5 |
| Dichlorodicyanoquinone | 20.9 |
| 1-Cyanonaphthalene ^(b) | 28.0 |
| Tetracyanoethylene | 37.6 |
| 9,10-Dicyanoanthracene ^(c) | 43.0 |

(a) 4h irradiation

(b) 6h irradiation

(c) OD = 1.0 at 370 nm

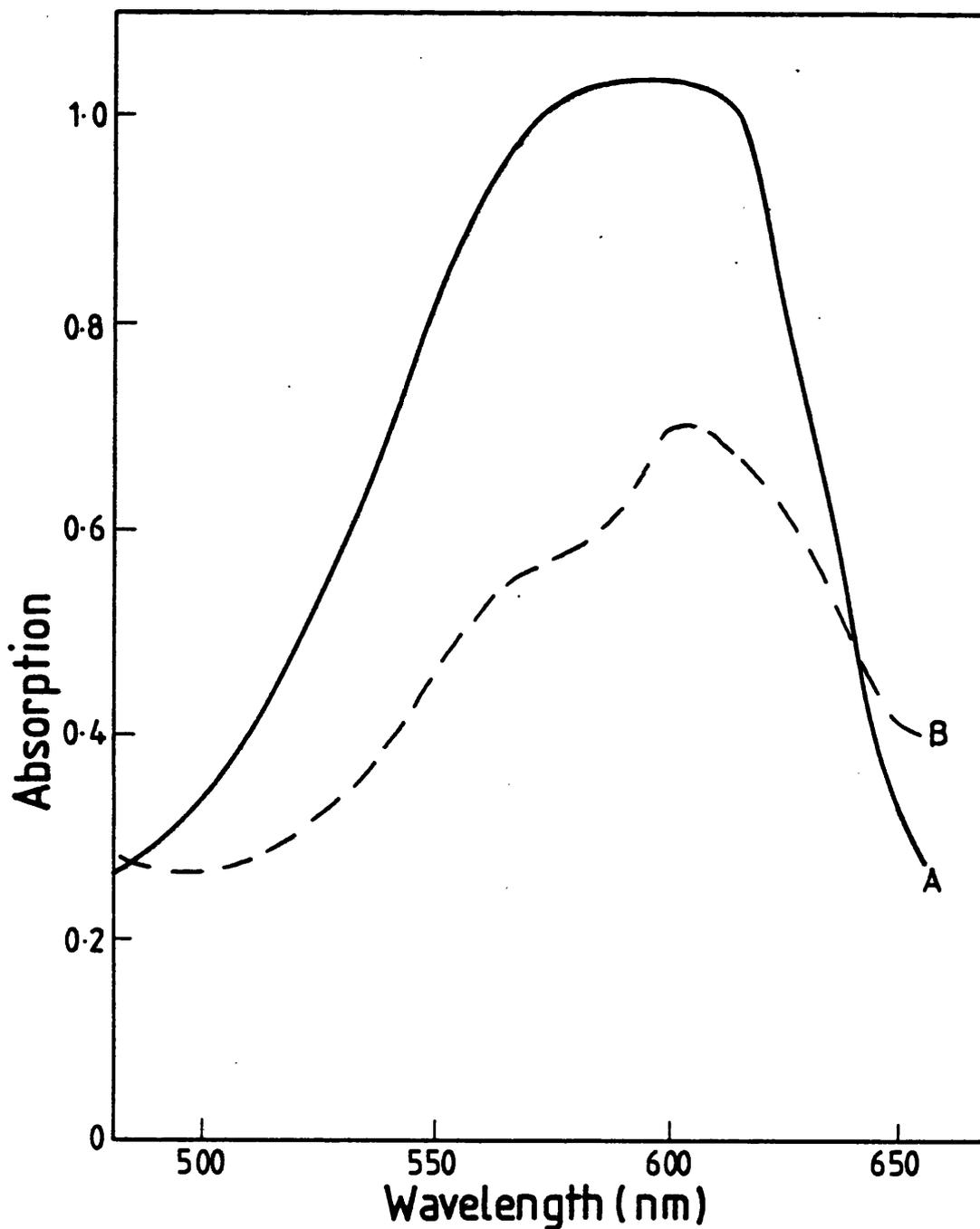


FIG. 2.1

Absorption spectrum of reduced methyl viologen produced from (A) 5-minute irradiation of pyruvic acid (5×10^{-2} M) in acetonitrile/water/pyridine (8:1:1 v/v) solution containing methyl viologen (10^{-2} M) under argon, and (B) 30-minute irradiation of pyruvic acid (5×10^{-2} M) in acetonitrile/water (9:1 v/v) solution containing methyl viologen (10^{-2} M) under argon.

TABLE 2.13

Yields of carbon dioxide from the direct irradiation^(a) of α -keto-glutaric acid (10^{-2} M) in acetonitrile, and acetonitrile-pyridine solution (4:1 v/v) containing 1-cyanonaphthalene (10^{-2} M) under argon

| Conditions | Yield (%) of carbon dioxide |
|--|-----------------------------|
| Acetonitrile | 11.8 |
| Acetonitrile/Pyridine | 37.8 |
| Acetonitrile/Pyridine/1-Cyanonaphthalene | 52.8 |

(a) 6h irradiation

2.3(ii) FLUORESCENCE QUENCHING STUDIES

α -Keto-glutaric acid and pyruvic acid were found to quench the fluorescence of aromatic hydrocarbons in degassed solution, (Table 2.14). Methyl viologen, an efficient electron acceptor, also led to quenching of aromatic hydrocarbon fluorescence.

2.3(iii) FLASH PHOTOLYSIS STUDIES⁵⁰

Flash photolysis of solutions of pyruvic acid in benzene, acetonitrile and water produced transients having a broad absorption band centred around 690-700 nm, (Fig. 2.2). The lifetimes of these transients for 10^{-1} M solutions of pyruvic acid were found to be 68 ± 4 , 100 ± 8 and 74 ± 4 ns respectively. The lifetimes are concentration dependent and for acetonitrile solutions the self-quenching rate constant was evaluated as $\approx 2 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$. Extrapolation to zero concentration gave a lifetime for the transient of 500 ns. Furthermore, the addition of pyridine suppressed the self-quenching reaction, as evidenced by the increased lifetime (≈ 150 ns) of the transient, from pyruvic acid, in benzene solution.

TABLE 2.14

Quenching of the fluorescence of aromatic hydrocarbons by α -keto-glutaric acid, pyruvic acid and methyl viologen

| Aromatic Hydrocarbon | Quencher | Solvent | $K_{sv} \times 10^2$ |
|-------------------------|------------------------------|---------------------|----------------------|
| 1-Cyanonaphthalene | Pyruvic acid | Benzene | 1.88 |
| 1-Cyanonaphthalene | Pyruvic acid | Acetonitrile | 1.85 |
| 1-Cyanonaphthalene | Methyl viologen | Acetonitrile/water* | 11.46 |
| 2,6-Dimethylnaphthalene | Pyruvic acid | Benzene | 5 |
| 2,6-Dimethylnaphthalene | Pyruvic acid | Acetonitrile | 4.85 |
| 2,6-Dimethylnaphthalene | Pyruvic acid | Acetonitrile/water* | 3.3 |
| 2,6-Dimethylnaphthalene | Methyl viologen | Acetonitrile/water* | 43.45 |
| 9-Cyanoanthracene | α -Keto-glutaric acid | Acetonitrile | 7.2 |
| 9-Cyanoanthracene | Methyl viologen | Acetonitrile/water* | 4.12 |
| 9-Methylanthracene | α -Keto-glutaric acid | Acetonitrile | 43.5 |

* (9:1 v/v)

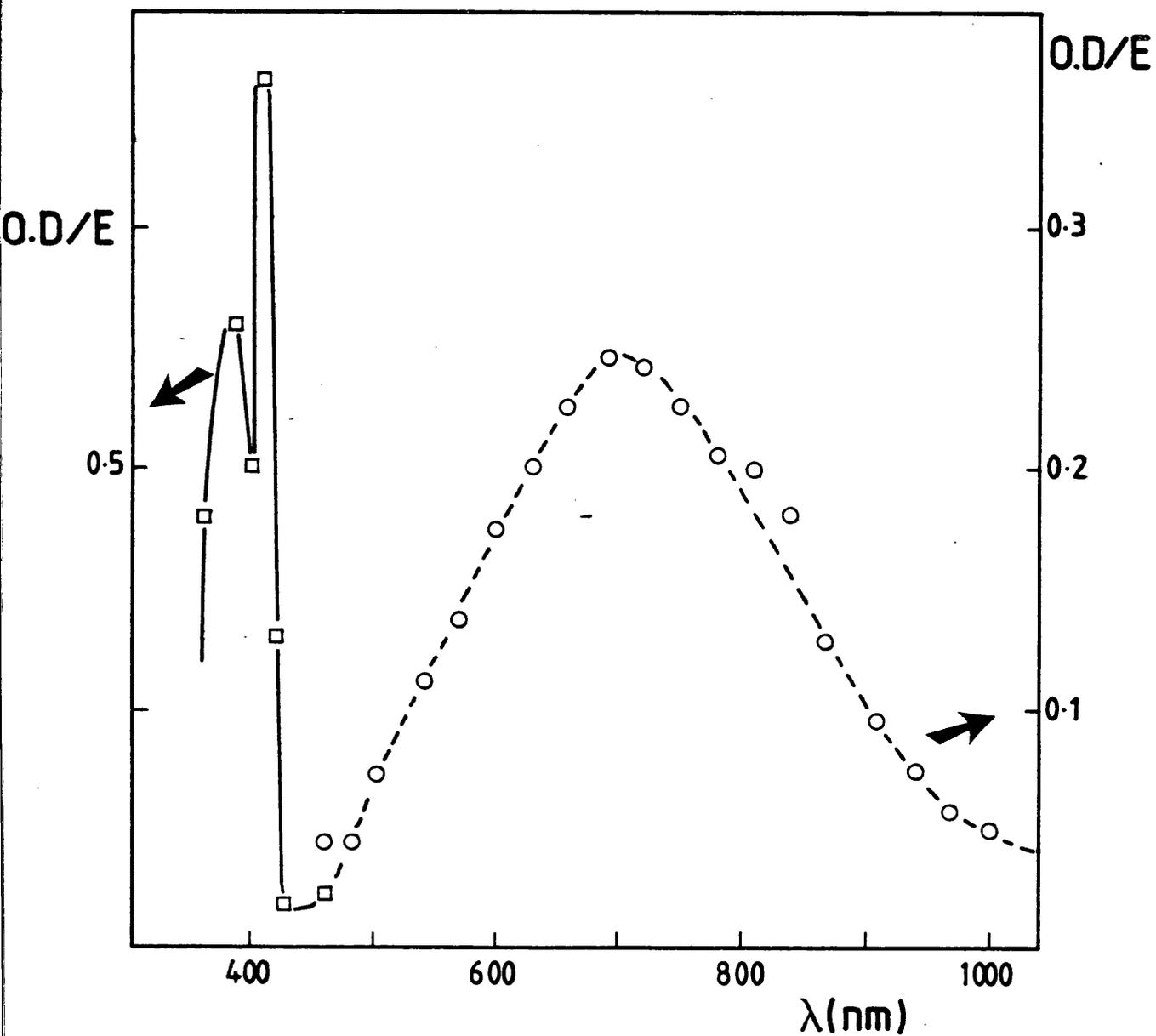


FIG. 2.2

Triplet-triplet transient absorption spectra of pyruvic acid in acetonitrile (○). Triplet naphthalene produced by energy transfer from triplet pyruvic acid (□).

The transients are quenched by oxygen and naphthalene, (Das and co-workers⁵¹ have evaluated the rate constant for quenching by 1-methylnaphthalene in aqueous acetonitrile as $5.6 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$). The quenching by naphthalene is accompanied by the appearance of triplet-triplet absorption spectrum of naphthalene, (Fig. 2.2). From this observation and also the fact that the transient derived from pyruvic acid is produced during the laser flash, the transients are assigned as being due to triplet pyruvic acid.

The quantum yields for formation of triplet pyruvic acid were determined by using naphthalene as the triplet counter, and were found to be 0.88, 0.65 and 0.22 for acetonitrile, benzene and water solutions respectively. The value obtained for water as solvent matches that previously obtained from phosphorescence measurements.²⁰

The flash photolysis results confirm the report by Closs and Miller²¹ that naphthalene behaves as a triplet quencher of pyruvic acid, but surprisingly the triplet naphthalene produced in this way has a very short lifetime ($\approx 145 \text{ ns}$). Thus triplet naphthalene appears to be deactivated by pyruvic acid. Since naphthalene quenches pyruvic acid at close to the diffusion-controlled rate, and also from the observation that at times when the naphthalene triplet-triplet absorption is clearly visible, there is little or no absorption due to triplet pyruvic acid (Fig. 2.3), it is considered that the short lifetime of triplet naphthalene cannot be due to reverse energy transfer from triplet naphthalene to pyruvic acid. It is proposed that triplet naphthalene is being deactivated by electron transfer to pyruvic acid. This view is supported by the finding that the flash photolysis of deoxygenated acetonitrile solutions of pyruvic acid containing naphthalene produces species absorbing between 450 and 900 nm, (Fig. 2.4). These species are

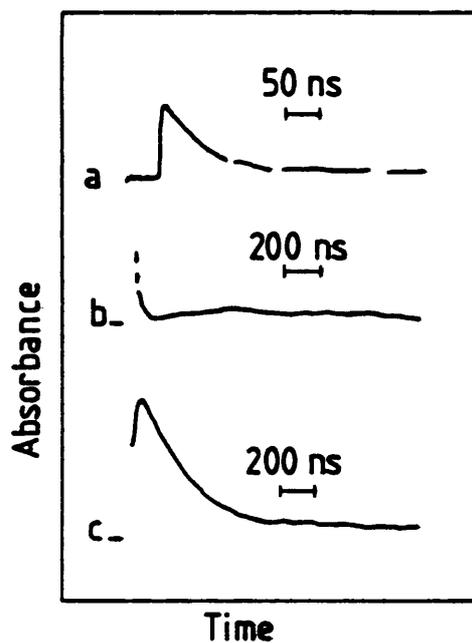


FIG. 2.3

- (a) Decay of triplet pyruvic acid in deoxygenated acetonitrile monitored at 650 nm.
- (b) Decay of triplet pyruvic acid in deoxygenated acetonitrile solution containing 5×10^{-2} M of naphthalene monitored at 650 nm.
- (c) Decay of triplet naphthalene monitored at 415 nm produced by energy transfer from triplet pyruvic acid.

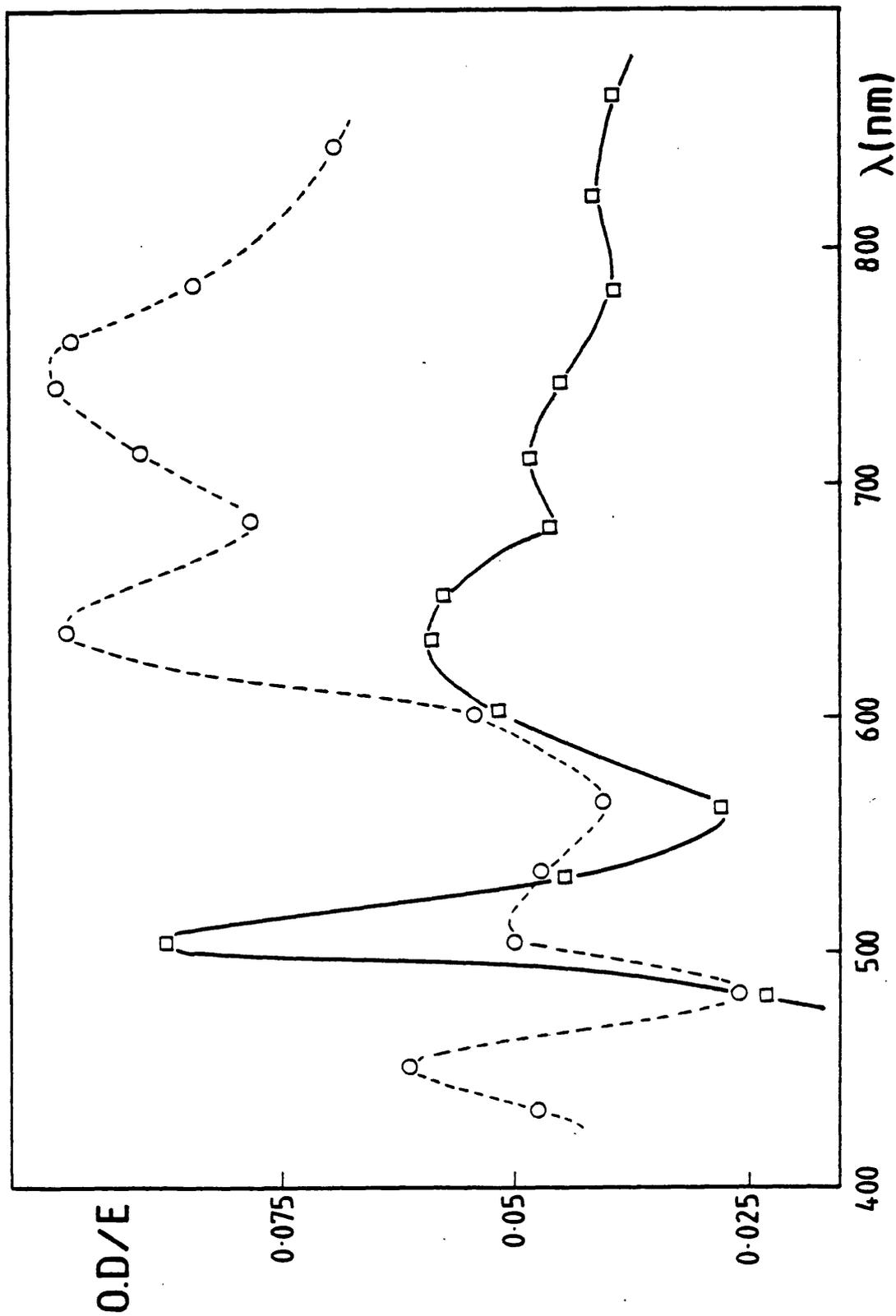
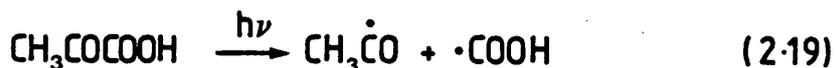


FIG. 2.4
 Absorption spectra of transients formed by the laser flash photolysis of an acetonitrile solution of pyruvic acid containing naphthalene at 200 ns (O) and 700 ns (\square) delay time.

in hydrogen donating solvents⁷ and photo-induced decarboxylation in both hydrogen and non-hydrogen donating solvents.^{5,6} The excited state responsible for decarboxylation has been assigned by some to the triplet^{5,6,21} and others to the singlet.²⁰ On the basis of CIDNP studies,²¹ carbon dioxide production has been suggested to arise via a Type 1 process, (Equation 2.19).



The quantum yield for carbon dioxide production has been shown to be highly solvent dependent.⁶ The Type 1 reaction is normally insensitive to solvent unless the solvent perturbs the relative energies of the excited states. Since this is probably not the case, it would appear that carbon dioxide production does not occur via a simple Type 1 process.

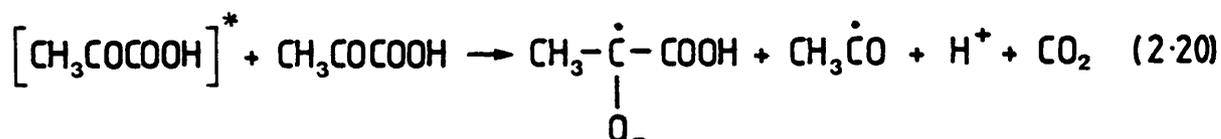
The results reported confirm the decarboxylation of pyruvic acid (Table 2.6) to be highly solvent dependent. Similar results were also obtained from other α -keto-carboxylic acids, (Table 2.7).

A comparison of the quantum yields for triplet production from pyruvic acid with carbon dioxide yield (Table 2.6) shows that the decarboxylation reaction is unrelated to the triplet yield. If the Type 1 reaction is an important mechanism of radiationless decay for triplet pyruvic acid, the triplet lifetime in water should be found to be considerably less than that in benzene. This rationalisation assumes that the lack of carbon dioxide in benzene is not due to geminate radical combination. Such a process should not be significantly more efficient in benzene compared with water because of the similarity in their viscosities (0.649 and 1.002 cP respectively⁵⁴). However, the triplet lifetime of pyruvic acid in water and benzene was found to be similar.

From the laser flash photolysis study it can be seen (Figs. 2.2, 2.3

and 2.4) that triplet pyruvic acid is quenched by naphthalene, forming triplet naphthalene, which subsequently undergoes an electron transfer reaction with ground state pyruvic acid leading to the production of naphthalene radical cation and pyruvate radical anion, (Scheme 2.11).

To account for the effect of solvent upon the yields of carbon dioxide it is proposed⁵⁵ that the photo-induced decarboxylation reaction occurs via electron transfer from an excited state of pyruvic acid, or its anion, to another molecule of pyruvic acid, (Equation 2.20). It is conceivable that a similar electron transfer reaction occurs for other α -keto-carboxylic acids, (Table 2.7).



This reaction will, of course, be favoured by the use of polar solvents. The lack of reaction in benzene can be ascribed to the low polarity of the solvent, and to the almost negligible concentration of pyruvate anion. The addition of small amounts of pyridine should facilitate the decarboxylation reaction (by forming some pyruvate anion which is capable of reducing another molecule of pyruvic acid), and this was found to be the case, (Table 2.10). There is also the possibility that pyridine could act as a polar environment to aid electron transfer.^{56,57} From the flash photolysis study, pyridine was found to suppress the self-quenching reaction of pyruvic acid, and as such could lead to increased decarboxylation.

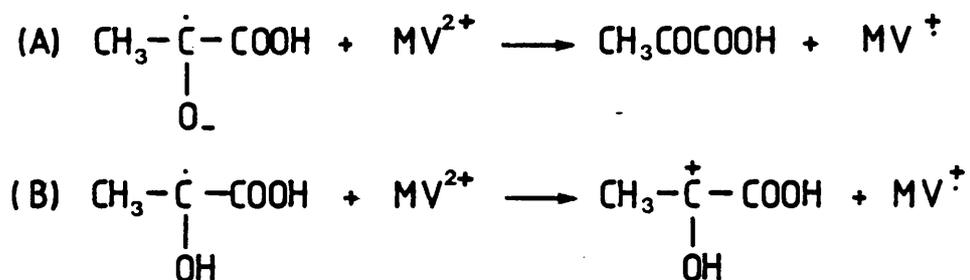
Pyridine is not unique in being able to enhance the decarboxylation reaction; water was also capable of increasing the yields of carbon dioxide, (Tables 2.6 and 2.9), presumably by the liberation of some pyruvate anion, (Equation 2.21).



From the above results it can be seen that decarboxylation is increased when small amounts of pyruvate anion are produced in the solution. However, the decarboxylation of pyruvic acid showed a marked pH dependence, (Table 2.8), becoming inefficient under alkaline conditions. This shows that when pyruvic acid exists mostly in its anionic form the electron transfer reaction (Equation 2.20) cannot take place as there are fewer pyruvic acid molecules which are capable of being reduced, and hence carbon dioxide production ceases.

The finding that both water and pyridine⁵⁵ catalyse the decarboxylation of pyruvic acid, and the observation of a pH dependency upon the latter reaction, have been confirmed in a subsequent publication.⁴⁸

The formation of reduced methyl viologen (MV^\cdot , Fig. 2.1) is attributable to electron transfer from a reduced species [(A) and/or (B)] of pyruvic acid, (Scheme 2.12).

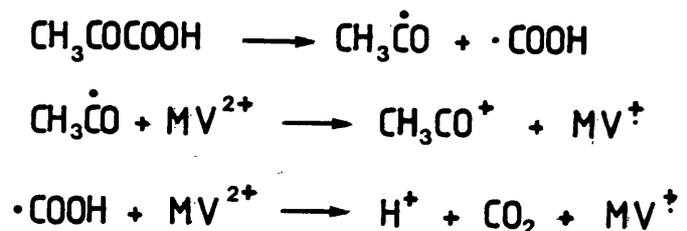


Scheme 2.12

From the laser flash photolysis study it was found that reduced methyl viologen is not produced by direct reaction of methyl viologen (10^{-2} M) with an excited state of pyruvic acid (10^{-1} M), which reflects the higher concentration of the pyruvic acid and its ability to accept an electron.

Unfortunately the observation of the formation of reduced methyl viologen is not unequivocal evidence for the formation of (A) and (B) in

the photoreactions of pyruvic acid. It is possible to rationalise the formation of reduced methyl viologen via a Type 1 mechanism, (Equation 2.19). This requires that species such as $\text{CH}_3\dot{\text{C}}\text{O}$ and $\cdot\text{COOH}$ are sufficiently long-lived in solution to undergo bimolecular reactions, and that these radicals do not efficiently react with each other to give acetaldehyde and carbon dioxide, (Scheme 2.13).

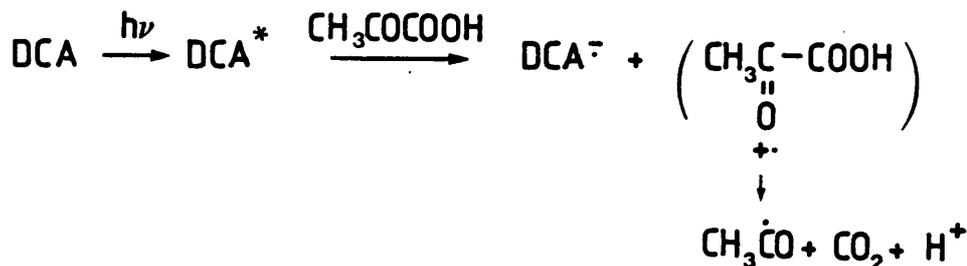


Scheme 2.13

It is noteworthy that the photochemically unreactive t-butyl-pyruvate was capable of forming reduced methyl viologen when irradiated in degassed solutions containing methyl viologen, (see Chapter 3).

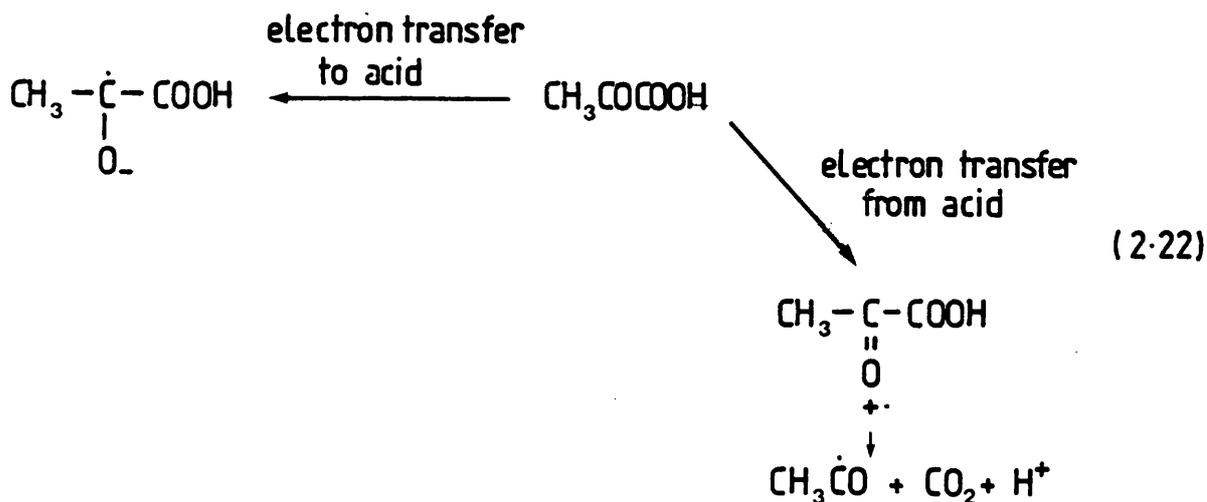
According to the postulated mechanism (Equation 2.20) it should be possible to sensitize the photo-induced decarboxylation of pyruvic acid by irradiation in the presence of electron acceptors. This hypothesis was confirmed (Tables 2.11 and 2.12) and the results obtained lend credence to the electron transfer mechanism. Addition of methyl viologen to aqueous acetonitrile-pyridine solutions of pyruvic acid sensitized the photo-induced decarboxylation (Table 2.11), which indicates that electron transfer from the pyruvate anion of pyridinium pyruvate to methyl viologen is effective in carbon dioxide production. Table 2.12 shows that known electron acceptors can sensitize the decarboxylation of pyruvic acid. Compounds such as 9,10-dicyanoanthracene (DCA) have been shown to take part in electron transfer reactions,⁵⁸ and a mechanism involving electron transfer from pyruvic acid to the electron acceptor,

e.g. DCA, would account for the sensitization process, (Scheme 2.14).



Scheme 2.14

That the fluorescence of aromatic hydrocarbons can be quenched by α -keto carboxylic acids suggests that an energy transfer process is occurring, although an electron transfer contribution to the quenching cannot be ruled out.⁵⁹ α -Keto-carboxylic acids have been shown to undergo electrochemical reduction,⁶⁰ so there is the possibility that electron transfer to the α -keto-carboxylic acid may be a competing process for reaction with relatively weak electron acceptors. This reaction would lead to inefficient decarboxylation whereas electron transfer from the acid to the electron acceptor will result in efficient decarboxylation, (Equation 2.22).



Summary

From laser flash photolysis and decarboxylation studies, it is

proposed that the photo-induced decarboxylation of α -keto-carboxylic acids such as pyruvic acid occurs via electron transfer from an excited to ground state molecule. That electron acceptors sensitize the photo-induced decarboxylation reaction lends credence to the proposed electron transfer mechanism.

2.4 THE EFFECT OF TRIPLET QUENCHERS UPON THE PHOTO-INDUCED
DECARBOXYLATION OF α -KETO-CARBOXYLIC ACIDS

As the excited state responsible for the decarboxylation reaction has been assigned to both the singlet²⁰ and triplet,^{5,6,21} the following investigation was performed in an attempt to elucidate the exact nature of the excited state responsible for photoreaction.

2.4(i) INITIAL QUENCHING STUDIES

The yields of carbon dioxide from the irradiation of a variety of α -keto-carboxylic acids in methanol and acetonitrile solutions containing naphthalene are shown in Table 2.14.

TABLE 2.14

Yields of carbon dioxide from the direct irradiation of α -keto-carboxylic acids under nitrogen in (A) methanol and (B) acetonitrile solutions containing naphthalene (0.5×10^{-4} M)

| α -Keto-carboxylic acid (10^{-2} M) | Yield (%) of carbon dioxide | | | |
|--|-----------------------------|------|------------------------|------|
| | (A) Methanol/Naph. | | (B) Acetonitrile/Naph. | |
| | 6h | 20h | 6h | 20h |
| Pyruvic acid | 23.6 | 32.9 | 43.1 | 86.3 |
| α -Keto-butyrac acid | 16.2 | 22.3 | 50.0 | 84.5 |
| α -Keto-glutaric acid | 18.3 | 22.3 | 53.6 | 84.1 |
| 3,3-Dimethyl-2-keto-butyrac acid | 16.5 | 52.2 | 63.4 | 98.3 |
| α -Keto-valeric acid | 19.3 | 29.2 | 29.2 | 69.0 |
| α -Keto-pimelic acid | 20.7 | 48.7 | 41.4 | 84.5 |

By comparison to the yields of carbon dioxide in the absence of naphthalene (Table 2.7), it can be seen that the addition of naphthalene to the solutions in some cases quenched the carbon dioxide production, and

in other cases led to enhanced yields of carbon dioxide. The latter observation is surprising and further experiments were performed on individual α -keto-carboxylic acids in order to ascertain the mechanism by which naphthalene can enhance the carbon dioxide production. In these experiments all the incident light led to excitation of the $n-\pi^*$ transition of the α -keto-carboxylic acids.

2.4(ii) PYRUVIC ACID

The photo-induced decomposition of pyruvic acid was monitored by ^1H n.m.r. spectroscopy in deuterated acetonitrile and deuterated benzene solutions (Fig. 2.5). Irradiation of pyruvic acid in deuterated acetonitrile solution led to the rapid consumption of the acid, and the addition of naphthalene was seen to markedly retard the rate of disappearance of pyruvic acid. This suggests that the triplet state of pyruvic acid is being deactivated by naphthalene and hence slowing down its photodecomposition. However, the rate of photodecomposition in deuterated benzene was exceedingly slow, and the addition of naphthalene brought about an increase in the rate of disappearance of the acid, (Fig. 2.5). The photodecomposition of pyruvic acid in benzene has previously been shown to be inefficient^{5,6,21,55} and these results are confirmed.

The effect of added triplet quenchers, naphthalene and myrcene, upon the quantum yield for carbon dioxide production was studied in acetonitrile and benzene solutions and the results shown in Figure 2.6. The effect of cyclohexa-1,3-diene upon the reaction was studied in benzene solution and the results shown in Figure 2.7. As can be seen, quenching occurred but with varying efficiency. Since the triplet lifetime of pyruvic acid is known,⁵⁵ the slope of the Stern-Volmer plot can be calculated if it is assumed that energy transfer occurs at the diffusional

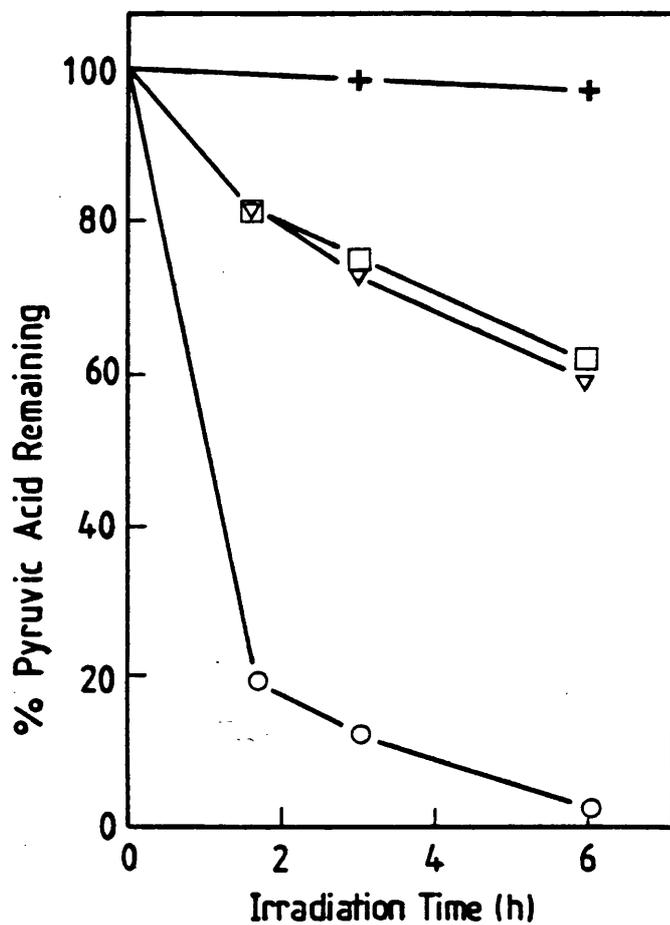


FIG. 2.5

Irradiation of pyruvic acid (10^{-1} M) in (a) deuterated acetonitrile solution (○), (b) deuterated acetonitrile solution containing naphthalene (10^{-2} M, ▽), (c) deuterated benzene solution (+), and (d) deuterated benzene solution containing naphthalene (10^{-2} M, □), under nitrogen.

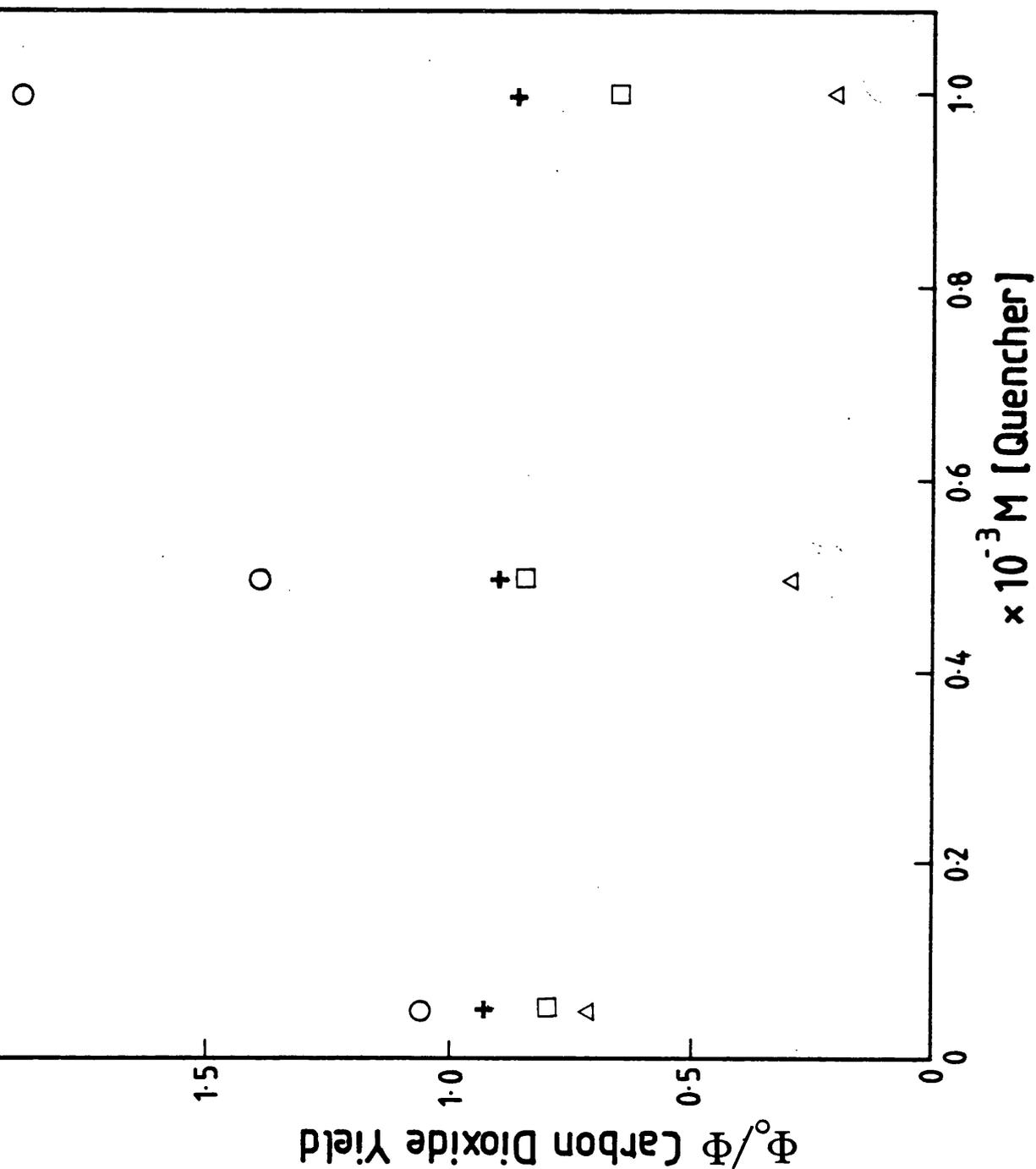
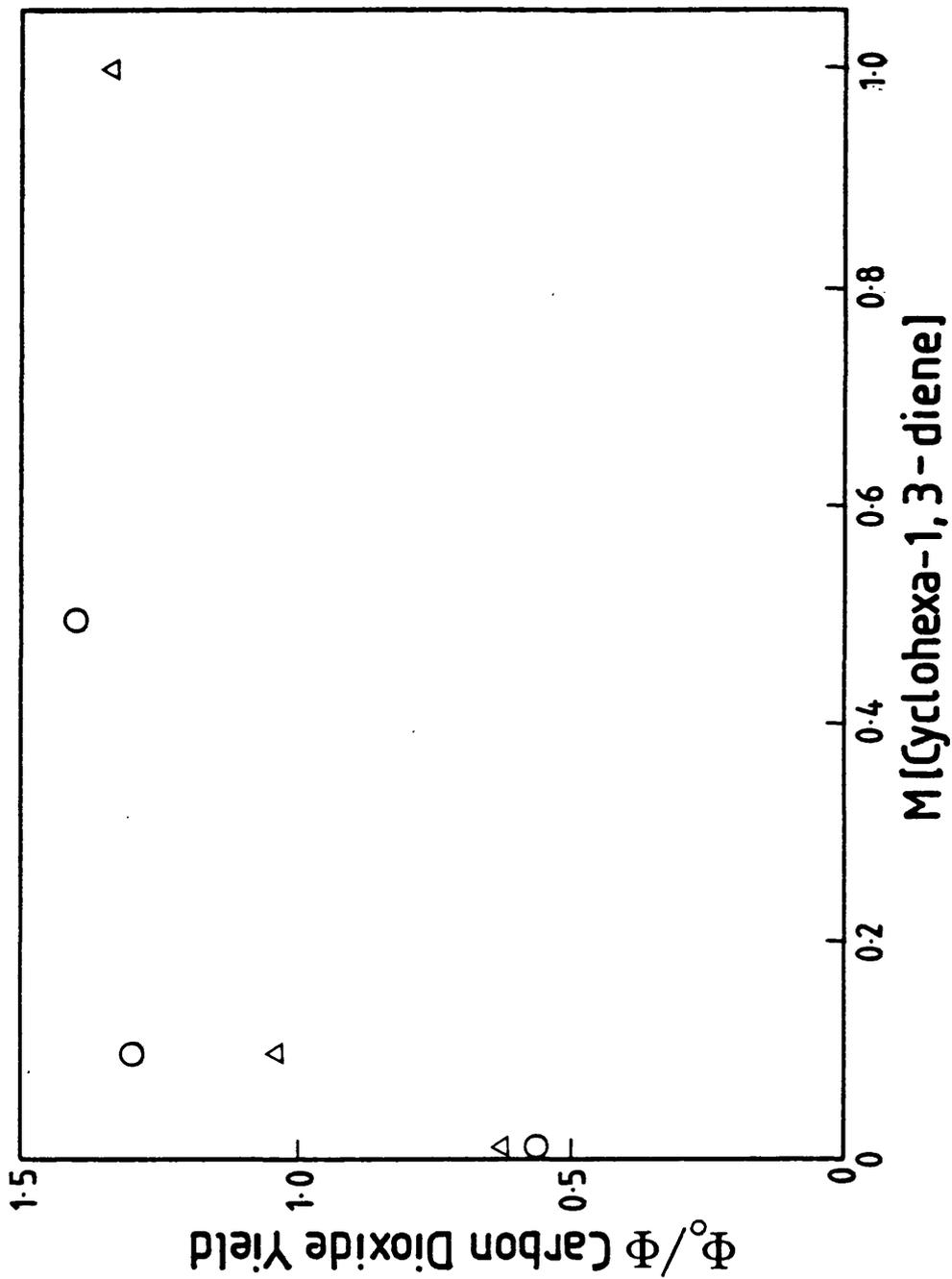


FIG. 2.6

Quantum yields for carbon dioxide production from 9h irradiation of pyruvic acid (2×10^{-2} M) in the presence of varying amounts of quencher, (a) naphthalene in acetonitrile solution (O), (b) naphthalene in benzene solution (Δ), (c) myrcene in acetonitrile solution (+), and (d) myrcene in benzene solution (\square), under nitrogen.

FIG. 2.7

Quantum yields for carbon dioxide production from 9h irradiation of (a) α -keto-octanoic acid (2×10^{-2} M, O) and (b) pyruvic acid (2×10^{-2} M, Δ), in benzene solutions containing cyclohexa-1,3-diene, under argon.



controlled limit of $3 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$, and for acetonitrile gives a K_{SV} value of 3000, and for benzene a K_{SV} value of 2240. 1-Methylnaphthalene has previously been shown to quench pyruvic acid with a quenching constant of $5.6 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ which is close to the diffusional controlled limit.⁵¹ The observed slope of the Stern-Volmer plots (Figs. 2.6 and 2.7) give a K_{SV} value of 850 for naphthalene quenching in acetonitrile and a K_{SV} value of 3.3 for cyclohexa-1,3-diene quenching in benzene. From these results it is apparent that the quenchers are not quenching at the diffusional controlled limit or else the quenchers are quenching triplet production but enhancing carbon dioxide production via some other route. The effect of the added quenchers upon the disappearance of α -keto-carboxylic acids was evaluated by monitoring the decrease in the absorption of the acid at 350 nm, and comparing this to the decrease observed in the absence of quencher. The results are shown in Table 2.15, and in some cases the quencher retarded, and in others accelerated the decomposition of pyruvic acid. The ^1H n.m.r. observation that naphthalene accelerates the decomposition in benzene (Fig. 2.6) was confirmed by the absorption spectroscopic studies, (Table 2.15).

Naphthalene is not unique in being able to assist the decarboxylation of pyruvic acid, and several other aromatic hydrocarbons were found to behave in the same way, (Table 2.16). That these compounds can aid the carbon dioxide production is shown by the results utilising benzene as solvent.

2.4(iii) OTHER α -KETO-CARBOXYLIC ACIDS

The effect of added quencher upon the quantum yield for carbon dioxide production was investigated using other α -keto-carboxylic acids.

Naphthalene and myrcene led to quenching of carbon dioxide production.

TABLE 2.15

The effect of added quenchers upon the photodecomposition of α -keto-carboxylic acids (2×10^{-2} M) monitored by following the decrease in the absorption of the acid at 350 nm in the presence and absence of quencher, under nitrogen

| α -Keto-carboxylic acid | Solvent | Quencher | Observation |
|--------------------------------|--------------|---------------------|--------------------|
| α -Keto-glutaric acid | Acetonitrile | Naphthalene | Retardation |
| α -Keto-glutaric acid | Acetonitrile | Myrcene | Retardation |
| Pyruvic acid | Acetonitrile | Naphthalene | Retardation |
| Pyruvic acid | Acetonitrile | Myrcene | Little effect |
| Pyruvic acid | Benzene | Naphthalene | Acceleration |
| Pyruvic acid | Benzene | Myrcene | Acceleration |
| Pyruvic acid | Benzene | Cyclohexa-1,3-diene | Acceleration |
| α -Keto-octanoic acid | Acetonitrile | Naphthalene | Slight retardation |
| α -Keto-octanoic acid | Acetonitrile | Myrcene | Slight retardation |
| α -Keto-octanoic acid | Benzene | Naphthalene | Little effect |
| α -Keto-octanoic acid | Benzene | Myrcene | Little effect |
| α -Keto-octanoic acid | Benzene | Cyclohexa-1,3-diene | Acceleration |

TABLE 2.16

Yields of carbon dioxide from irradiation^(a) of pyruvic acid (10^{-1} M) (A) in benzene solution and (B) in acetonitrile solution containing various aromatic hydrocarbons (10^{-2} M), under argon

| Aromatic hydrocarbon (10^{-2} M) | Yield (%) of carbon dioxide | |
|--|-----------------------------|------------------|
| | (A) Benzene | (B) Acetonitrile |
| None | 2.2 | 16.0 |
| Naphthalene | 19.9 | 1.9 |
| 2-Methylnaphthalene | 21.9 | 2.2 |
| 2,3-Dimethylnaphthalene | 32.3 | 5.9 |
| 2,6-Dimethylnaphthalene | 34.5 | 7.3 |
| Phenanthrene | 19.7 | 6.8 |

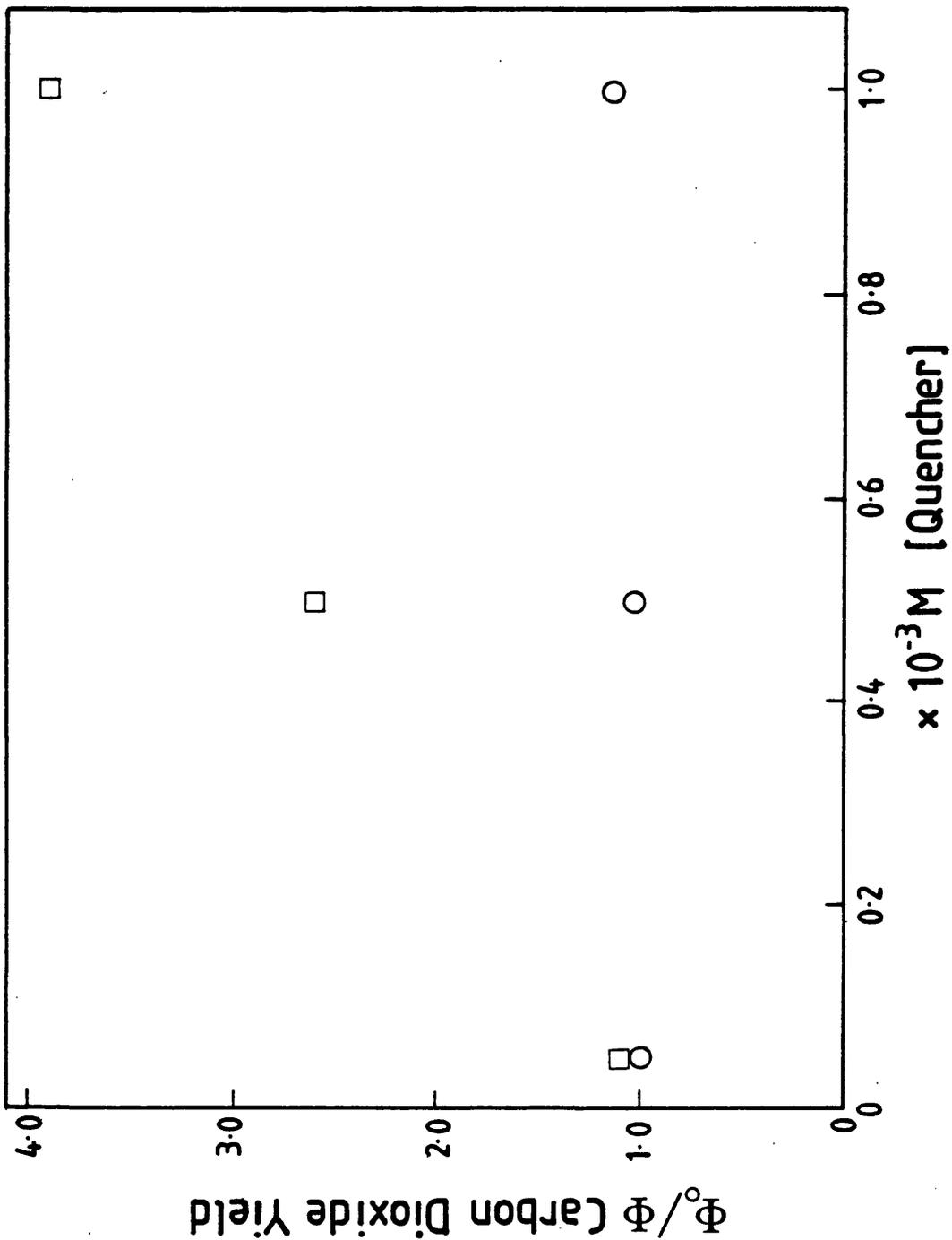
(a) 6h irradiation

from α -keto-glutaric acid in acetonitrile solution (Fig. 2.8) and also retarded the consumption of the acid, (Table 2.15). This indicates that the triplet state of α -keto-glutaric acid is being deactivated by the quenchers and hence retarding the decarboxylation reaction. Due to solubility problems the effect of these quenchers upon α -keto-glutaric acid in benzene solution could not be assessed.

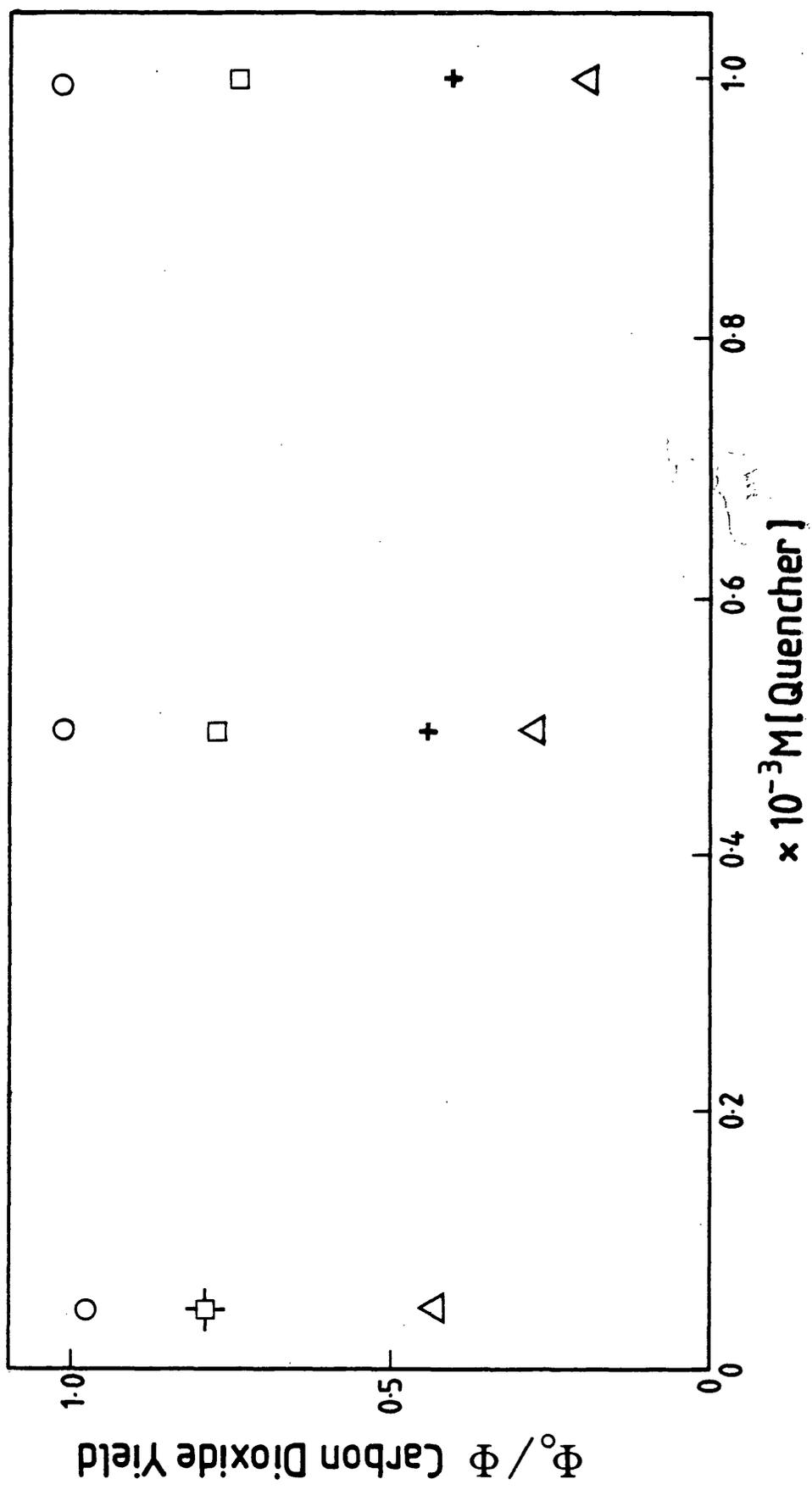
It is known that α -keto-carboxylic acids capable of undergoing the Type II fragmentation reaction, e.g. α -keto-octanoic acid, react from the excited singlet state.⁶¹ However, naphthalene and myrcene were found to have a marked effect upon the quantum yield of carbon dioxide production from α -keto-octanoic acid in acetonitrile and benzene solutions (Fig. 2.9), and little effect upon the decomposition of the acid, (Table 2.15). Cyclohexa-1,3-diene was found to accelerate the decomposition of α -keto-octanoic acid in benzene solution (Table 2.15), but the effect on the quantum yield of carbon dioxide production was dependent upon the concentration of cyclohexa-1,3-diene, (Fig. 2.6). At high concentrations it

FIG. 2.8

Quantum yields for carbon dioxide production from 9h irradiation of α -keto-glutaric acid (2×10^{-2} M), (a) in acetonitrile solution containing naphthalene (\square), and (b) in acetonitrile solution containing myrcene (O), under nitrogen.



Quantum yields for carbon dioxide production from 15h irradiation of α -keto-octanoic acid (2×10^{-2} M) in the presence of varying amounts of quencher, (a) naphthalene in acetonitrile solution (O), (b) naphthalene in benzene solution (Δ), (c) myrcene in acetonitrile solution (+), and (d) myrcene in benzene solution (\square), under nitrogen.



led to quenching of the carbon dioxide production. α -Keto-octanoic acid undergoes the Type II reaction leading to the formation of pent-1-ene and pyruvic acid from the excited singlet state.⁶¹ The enhanced carbon dioxide yields obtained from α -keto-octanoic acid could arise from the reaction of naphthalene with the triplet state of the acid, or from reaction of triplet pyruvic acid formed from the Type II fragmentation of α -keto-octanoic acid. However, if carbon dioxide was arising from the pyruvic acid produced via the Type II reaction, one would expect to observe a marked quenching of the quantum yield for carbon dioxide production by naphthalene in acetonitrile solutions of α -keto-octanoic acid, as is observed for pyruvic acid itself, (Fig. 2.6). As this is not the case for naphthalene quenching of α -keto-octanoic acid in acetonitrile solution, it seems that the enhanced carbon dioxide yields are due to naphthalene interacting with the starting acid and not the pyruvic acid that is produced via the Type II reaction.

The quantum yields for disappearance of α -keto-valeric acid in acetonitrile solution as shown in Figure 2.10, were obtained by following the decrease in absorption of the acid at 350 nm in the presence of varying amounts of naphthalene. The carbon dioxide yield was found to be highly dependent on the naphthalene concentration, and in each case gave a higher yield than in the absence of naphthalene, the enhancement being most prominent at low naphthalene concentrations, (Fig. 2.10). It would appear that α -keto-valeric acid can react by processes other than the Type II reaction from its singlet state, and the addition of naphthalene to solutions of this acid quenches some of the former processes. The carbon dioxide yields may be perturbed by pyruvic acid which is formed via the Type II reaction of α -keto-valeric acid.

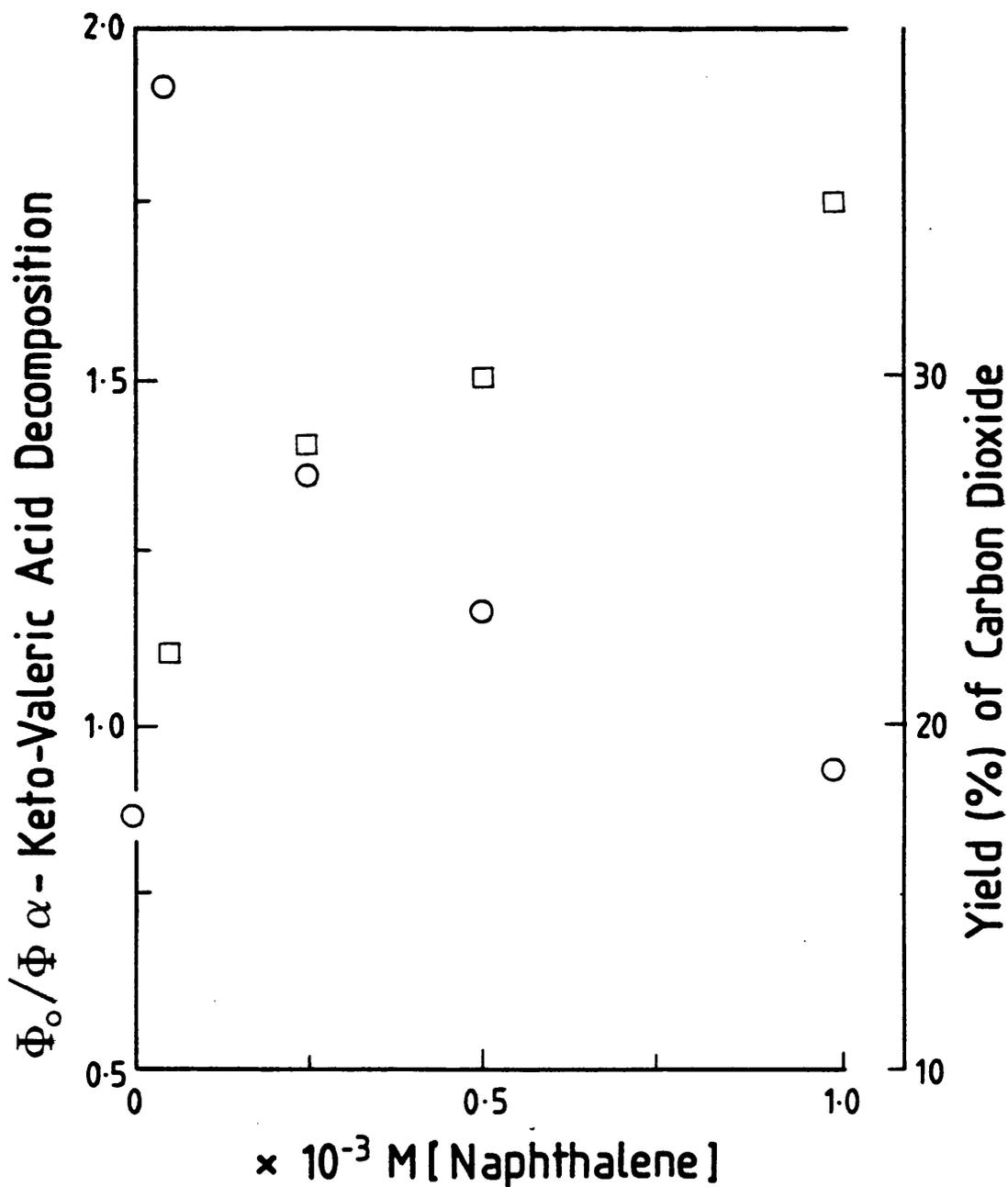
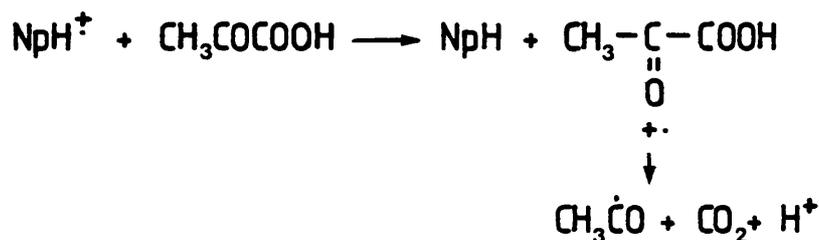


FIG. 2.10

Yields of carbon dioxide production (○) and quantum yields of decomposition of α -keto-valeric acid (10^{-2} M □) from 4.5h irradiation in acetonitrile solutions containing varying amounts of naphthalene, under nitrogen.

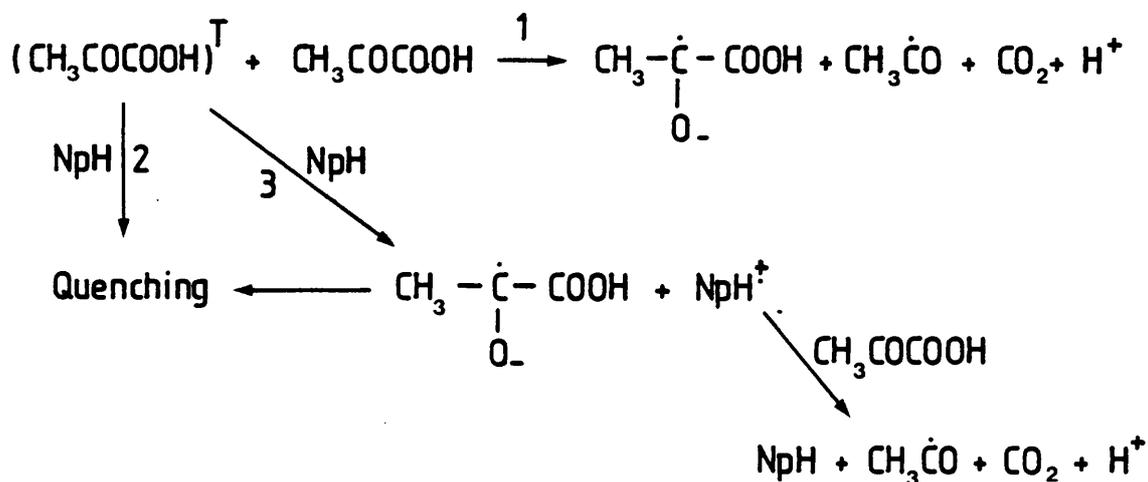
2.4(iv) THE MECHANISM OF DECARBOXYLATION

It has previously been shown⁵⁵ that triplet pyruvic acid is quenched by naphthalene forming triplet naphthalene which reacts with pyruvic acid to give the naphthalene radical cation. It is conceivable that the naphthalene radical cations could react with pyruvic acid to produce carbon dioxide, (Scheme 2.15).



Scheme 2.15

In order to rationalise the effect of solvent upon the sensitization of carbon dioxide production and the rate of photodecomposition of pyruvic acid by quenchers such as naphthalene, the following mechanism is proposed, (Scheme 2.16).



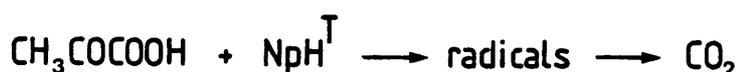
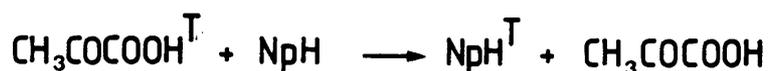
Scheme 2.16

In acetonitrile solution photodecomposition of pyruvic acid leading to carbon dioxide production via route 1 is relatively efficient. In the presence of naphthalene the triplet pyruvic acid can be physically quenched via route 2 which will reduce the carbon dioxide yield. There

is also the possibility that quenching of triplet pyruvic acid by naphthalene will lead to the formation of radical ions via route 3 and this could result in the enhancement of carbon dioxide production. However, no overall enhancement of carbon dioxide will be observed due to the fact that reaction via route 1 is efficient and the addition of naphthalene to acetonitrile solution simply suppresses this reaction by the combined effects of routes 2 and 3.

In benzene solution the photodecomposition of pyruvic acid leading to carbon dioxide production via route 1 is very inefficient and gives rise to extremely low yields of carbon dioxide. In the presence of naphthalene, quenching of triplet pyruvic acid can occur via route 2 and could lead to reduced carbon dioxide yields. As the carbon dioxide yields are enhanced by naphthalene, the contribution of route 2 may be small, and quenching of triplet pyruvic acid leading to the formation of radicals via route 3 important. This could result in increased yields of carbon dioxide by the subsequent reaction of naphthalene radical cations with pyruvic acid molecules. Thus in benzene solution the addition of naphthalene enhances the carbon dioxide yield by route 3, as reactions by route 1 (and/or route 2) are unfavourable for carbon dioxide production.

The balance between quenching of triplet pyruvic acid by naphthalene leading to triplet naphthalene, and the subsequent reaction of triplet naphthalene to give radical formation (and hence carbon dioxide production) will determine the quantum yield of carbon dioxide, i.e.



Therefore in retrospect the carbon dioxide yields, and rate of photo-decomposition, are not particularly good guides as to the efficiency of

quenching, since a number of triplet aromatic hydrocarbons sensitize carbon dioxide formation, (Table 2.16).

The mechanism described in Scheme 2.16 can be used to account for the quenching effects noted with other α -keto-carboxylic acids and quenchers.

That the triplet state of the α -keto-carboxylic acids are involved is shown by the ability of naphthalene to quench the carbon dioxide production from acetonitrile solutions of pyruvic and α -keto-glutaric acids.

The ability of myrcene to quench the decomposition and decarboxylation of the α -keto-carboxylic acids will be dependent upon the relative efficiency with which this quencher deactivates triplet production giving rise to radical formation, i.e. a partitioning effect between the two reactions will be operative.

Cyclohexa-1,3-diene undergoes [2+2] cycloaddition reactions with pyruvic acid and α -keto-octanoic acid,^{62,63} and the occurrence of this reaction would account for the observed quenching of carbon dioxide production and the accelerating effect that this compound exerts on the disappearance of the acids. At high concentrations of cyclohexa-1,3-diene, photo-addition can occur by reaction of the diene with the excited singlet state of the acids,⁶⁴ which accounts for the difference in the K_{gy} value observed for reaction with pyruvic acid. A further consequence of the occurrence of the cycloaddition reaction of the excited singlet state of the acid is that the triplet yield of the acid will be reduced, and consequently the carbon dioxide yield also. At low concentrations of cyclohexa-1,3-diene, carbon dioxide production is enhanced by reaction of the diene triplet with the acid giving rise to radical formation (via route 3). This explains the results obtained with pyruvic and α -keto-octanoic acids in the presence of cyclohexa-1,3-diene.

These results, showing that addition of what should be a quencher for

a reaction can lead to enhanced product formation via a sensitization process are not unique. It has previously been reported⁶⁵ that if interaction of an excited state with "quencher" leads to product formation, rather than to other modes of decay, then "negative" Stern-Volmer plots will be obtained. Such Stern-Volmer plots have been observed for piperylene quenching of acetone sensitized reactions of trans-crotylchloride,⁶⁵ and for piperylene quenching of acetone sensitized rearrangement of norbornadiene to quadricyclene.⁶⁶ These results^{65,66} are discussed in terms of the "quencher" in effect acting as "sensitizer" of product formation.

The mechanism proposed in Scheme 2.16 is similar to that proposed to account for the acceleration by azulene of reduction of dyes by allylthiourea.⁶⁷ Irradiation of thionine in the presence of allylthiourea produces the reduced form of thionine, leucothionine. The addition of the quencher azulene was found to dramatically increase the rate of the reduction process. Azulene was found to react with thionine to produce radicals, via an electron transfer process, which subsequently undergo reaction with the allylthiourea and give rise to increased amounts of leucothionine.⁶⁷

Summary

The addition of triplet quenchers to solutions of α -keto-carboxylic acids can enhance the photo-induced decarboxylation reaction, and this is proposed to occur via interaction of quencher with the triplet state of the acid leading to radical formation, and the subsequent reaction of quencher radical cation with another molecule of α -keto-carboxylic acid. The results show that the previously held view that the addition of a quencher should retard product formation does not hold in all cases, as other processes may be operative which can lead to an actual sensitization of product formation.

2.5 THE DIRECT AND SENSITIZED PHOTO-OXIDATIVE DECARBOXYLATION OF α -KETO-CARBOXYLIC ACIDS

2.5(i) DIRECT PHOTO-OXIDATIVE DECARBOXYLATION

Pyruvic acid was found to undergo direct photo-oxidative decarboxylation in a wide variety of oxygenated solutions, (Table 2.17).

TABLE 2.17

Yields of carbon dioxide from the direct irradiation^(a) of pyruvic acid (10^{-2} M) under oxygen, in various solvents

| Solvent | Yield (%) of carbon dioxide |
|--------------------|-----------------------------|
| Acetone | 101 |
| Acetonitrile | 73.1 |
| Benzene | 46.5 ^(b) |
| t-Butanol | 76.3 |
| Chloroform | 52.4 |
| Dimethylformamide | 85.3 |
| Dimethylsulphoxide | 15.0 |
| Dioxan | 18.0 |
| Ethanol | 23.6 |
| Methanol | 32.5 ^(b) |
| Water | 62.1 |

(a) 3h irradiation

(b) 6h irradiation

The yield of carbon dioxide is clearly highly dependent upon the type of solvent, (Table 2.17). Other α -keto-carboxylic acids also yielded carbon dioxide on irradiation in acetonitrile and methanol. In the latter solvent photoreduction of the α -keto-carboxylic acid can also occur,⁷ (Table 2.18).

The addition of small amounts of pyridine enhanced the decarboxylation of oxygenated benzene solutions of pyruvic acid, with only a slight

TABLE 2.18

Yields of carbon dioxide from the direct irradiation of α -keto-carboxylic acids (10^{-2} M) under oxygen (A) in methanol and (B) in acetonitrile

| α -Keto-carboxylic acid (10^{-2} M) | Yield (%) of carbon dioxide | | | |
|--|-----------------------------|------|------------------|-------|
| | (A) Methanol | | (B) Acetonitrile | |
| | 6h | 20h | 6h | 20h |
| Pyruvic acid | 32.5 | 57.9 | 141.3 | 160.0 |
| α -Keto-butyric acid | 41.4 | 61.2 | 148.6 | 156.4 |
| α -Keto-glutaric acid | 52.4 | 72.7 | 123.0 | 140.5 |
| 3,3-Dimethyl-2-keto-butyric acid | 32.9 | 61.3 | 145.6 | 189.0 |
| α -Keto-valeric acid | 45.3 | 78.4 | 112.9 | 154.5 |
| α -Keto-pimelic acid | 46.5 | 94.8 | 98.9 | 133.8 |

TABLE 2.19

The effect of added pyridine (10^{-1} M) upon the yields of carbon dioxide from the direct irradiation^(a) of benzene and acetonitrile solutions of pyruvic acid (10^{-1} M) under oxygen

| Solvent | Yield (%) of carbon dioxide | Enhancement |
|-----------------------|-----------------------------|-------------|
| Benzene | 14.1 | } 3.4 x |
| Benzene/Pyridine | 48.1 | |
| Acetonitrile | 39.9 | } 1.3 x |
| Acetonitrile/Pyridine | 50.4 | |

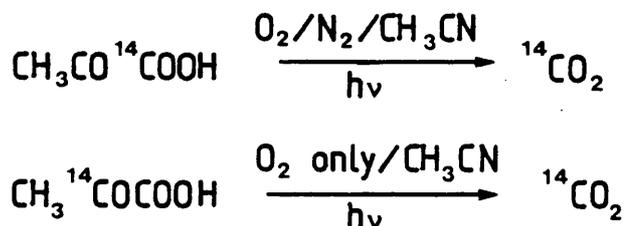
(a) 9h irradiation

enhancement being observed for similar acetonitrile solutions, (Table 2.19).

Thus the presence of some pyruvate anions of pyridinium pyruvate

facilitates the decarboxylation in oxygenated solution, albeit to a lesser extent than in degassed benzene solutions (Table 2.10). This gives an indication as to the efficiency of carbon dioxide production from α -keto-carboxylic acids under oxygen, which after long irradiation periods yields greater than one mole of carbon dioxide per mole of α -keto-carboxylic acid consumed, (Table 2.18).

It seemed reasonable to assume that under oxygen the first mole of carbon dioxide is derived from the carboxyl group, whilst the second mole arises from the carbonyl group of the α -keto-carboxylic acid. To verify this hypothesis, isotopically labelled pyruvic acids were employed,⁶⁸ (Table 2.20). It was found that 1- ^{14}C -pyruvic acid produced labelled carbon dioxide in the presence and absence of oxygen, whereas irradiation of 2- ^{14}C -pyruvic acid gave rise to labelled carbon dioxide under oxygen, with only negligible amounts being detected under nitrogen, from acetonitrile solutions of the acids, i.e:



The second mole of carbon dioxide obtained under oxygen, could well be derived from per-acetic acid, as per-acids are known to be intermediates in the dye-sensitized photo-oxygenation of α -keto-carboxylic acids.^{41,47} Indeed per-acetic acid⁶⁹ was found to undergo photo-induced decarboxylation under the irradiation conditions employed, (Table 2.21).

The rôle that singlet oxygen may play in the direct photo-oxidative decarboxylation of α -keto-carboxylic acids was evaluated by measuring the rate of carbon dioxide production in deuterated and non-deuterated solvents, for both pyruvic and α -keto-glutaric acids. The solvent

Assay of labelled carbon dioxide produced from 5h irradiation of acetonitrile solutions of labelled pyruvic acid under oxygen and nitrogen

| | Counts per minute (a) |
|--|-----------------------|
| <u>1-[¹⁴C]-PYRUVIC ACID</u> | |
| Reaction mixtures [†] | |
| (1) Initially | 2948 |
| (2) After irradiation under O ₂ | 507 |
| (3) After irradiation under N ₂ | 2037 |
| Carbon dioxide traps [‡] | |
| (1) Irradiation under oxygen - Trap 1 | 10,126 |
| - Trap 2 | 190 |
| (2) Irradiation under nitrogen - Trap 1 | 3991 |
| - Trap 2 | 58 |
| <u>2-[¹⁴C]-PYRUVIC ACID</u> | |
| Reaction mixtures [†] | |
| (1) Initially | 4910 |
| (2) After irradiation under O ₂ | 4283 |
| (3) After irradiation under N ₂ | 5063(b) |
| Carbon dioxide traps [‡] | |
| (1) Irradiation under oxygen - Trap 1 | 2267 |
| - Trap 2 | 51 |
| (2) Irradiation under nitrogen - Trap 1 | 175 |
| Trap 2 | 25 |

(a) Values are a mean of three readings, uncorrected for background.

(b) Higher than initial reading due to evaporation of solvent during flushing to remove carbon dioxide.

[†] 0.01 ml assayed in toluene based scintillant.

[‡] Reaction mixtures were flushed after irradiation, the carbon dioxide produced being trapped by passing exit gases through two Dreschel bottles containing 0.1 M KOH. 0.2 ml of each KOH solution being assayed in a toluene-Triton X-100 scintillant.

TABLE 2.22

Solvent isotope effect upon the yield of carbon dioxide from the direct irradiation (a)
of α -keto-carboxylic acids (10^{-2} M) in oxygenated solution

| α -Keto-carboxylic acid 10^{-2} M | Solvent | Yield (%) of carbon dioxide | Isotope Effect |
|---|---|--------------------------------|-------------------|
| Pyruvic acid | Deuteriochloroform | 76.8 | 1.4 |
| Pyruvic acid | Chloroform | 54.8 | |
| α -Keto-glutaric acid | Acetonitrile/D ₂ O (1:24 %v) | 66.6 | 1.2 |
| α -Keto-glutaric acid | Acetonitrile/H ₂ O (1:24 %v) | 54.8 | |

(a) 3h irradiation

TABLE 2.21

Yields of carbon dioxide from irradiation^(a) of acetonitrile solutions containing per-acetic acid (0.032 M) under oxygen and argon

| Conditions | Yield (%) of carbon dioxide |
|------------|-----------------------------|
| Oxygen | 14.7 |
| Argon | 20.7 |

(a) 9h irradiation

isotope effects obtained in each case were small, (Table 2.22).

α -Keto-octanoic acid, which is capable of undergoing the Type II reaction, gave good yields of both pent-1-ene and carbon dioxide under oxygen, (Table 2.23). That both oxygen and naphthalene had little effect on the yield of pent-1-ene produced from the Type II fragmentation of α -keto-octanoic acid would suggest that the Type II reaction occurs from the singlet state⁶¹ and not the triplet state as previously reported.²⁴

TABLE 2.23

Yields of pent-1-ene and carbon dioxide from irradiation^(a) of α -keto-octanoic acid (5×10^{-2} M) in benzene solution under oxygen and under argon

| Conditions | % Pent-1-ene | % Carbon dioxide |
|-----------------------------|--------------|------------------|
| Argon purged | 46 | 14.6 |
| Argon purged ^(b) | 45 | 15.0 |
| Oxygen purged | 38 | 69.9 |

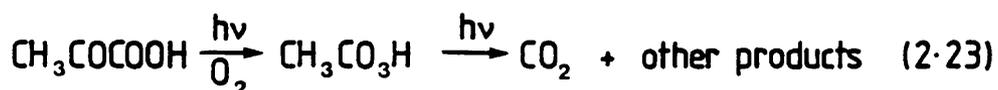
(a) 18h irradiation

(b) containing naphthalene (1×10^{-3} M)

2.5(ii) DISCUSSION

In studies on the dye-sensitized photo-oxygenation of α -keto-carboxylic acids it was found that, in many cases, more than one mole of carbon dioxide was liberated from one mole of the α -keto-carboxylic acid.^{42,46} The results presented in Table 2.18 show that in the direct photo-induced decarboxylation of α -keto-carboxylic acids under oxygen, a similar situation arises, i.e. more than one mole of carbon dioxide is produced. From the studies utilising isotopically labelled pyruvic acids (Table 2.20) it is clear that photo-oxidative decarboxylation occurs from both the C-1 (carboxyl) and C-2 (carbonyl) positions of the α -keto-carboxylic acid.

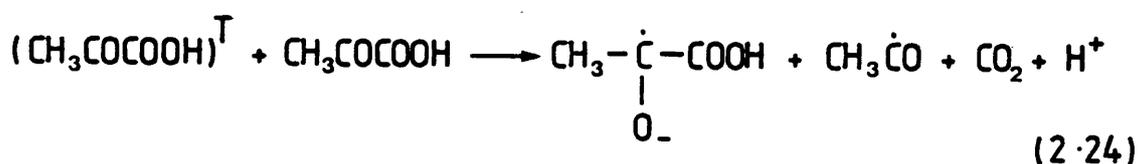
Per-acids have been reported to be intermediates in the dye-sensitized photo-oxygenation reaction of α -keto-carboxylic acids,^{41,47} and it is proposed that the second mole of carbon dioxide (from the C-2 carbonyl position) is produced via a per-acid intermediate; per-acetic acid in the case of pyruvic acid, (Equation 2.23)



That per-acetic acid undergoes photo-induced decarboxylation under the irradiation conditions employed was verified, (Table 2.21). The per-acetic acid may also undergo sensitized decarboxylation in which the pyruvic acid acts as sensitizer. It is known⁷⁰ that per-acetic acid gives carbon dioxide on direct irradiation in the absence of oxygen, and this was confirmed, (Table 2.21). The per-acids so produced could also undergo a Baeyer-Villiger reaction, but from the yields of carbon dioxide obtained (Table 2.18) this appears to be a minor route for reactions carried out under oxygen.

The inevitable question arose as to whether singlet oxygen is involved in the photo-oxidative decarboxylation process. From the small solvent isotope effects observed (Table 2.22), [if these are, in fact, true solvent isotope effects], the difference in rate indicates that little, if any, of the decarboxylation occurs via singlet oxygen. However, there is a fallacy in this argument in that very small solvent isotope effects would be observed if the α -keto-carboxylic acid generated singlet oxygen and immediately reacted with it, i.e. the reaction with singlet oxygen did not involve a diffusional process. Previous measurements⁷¹ of the rate constants for reaction of singlet oxygen with α -keto-carboxylic acids suggest that because of their extremely low values, a large solvent isotope effect should have been observed if singlet oxygen was involved.

The photo-induced decarboxylation of pyruvic acid in deoxygenated solution does not involve a Type I cleavage but occurs via a bimolecular electron transfer process,⁵⁵ (Equation 2.24).



In the presence of oxygen at a concentration approximately that of the acid, electron transfer to oxygen could also occur, (Equation 2.25).



The acetyl radicals generated in these processes (Equations 2.24 and 2.25) can be scavenged by oxygen to give per-acetic acid. The pyruvate radical anion should be oxidised by oxygen to give the superoxide anion, and the latter species may well participate in the photo-oxidative degradation.³¹ It is also possible that per-acetic acid may suffer further degradation by reduction with an electron derived from either the

sensitized by a variety of aromatic hydrocarbons, as shown in Table 2.24. In each case irradiation led to the excitation of the aromatic hydrocarbon, which absorbed greater than 95% of the incident light. In some cases, the yields of carbon dioxide in the presence of the sensitizer were lower than those obtained in the direct irradiation. However, as the aromatic hydrocarbon absorbed all the incident light the carbon dioxide must be arising via a sensitization process. Sensitization was found to occur when compounds that can act as electron acceptors, e.g. 9,10-dicyanoanthracene were used, and also by using compounds that are capable of undergoing hydrogen abstraction reactions, e.g. acridine.

The direct photo-oxidative decarboxylation of α -keto-carboxylic acids has been suggested to involve an electron transfer mechanism.⁷³ The finding that electron acceptors can sensitize the decarboxylation reaction lends credence to the reported mechanism.⁷³ The efficiency of the decarboxylation reaction in the presence of sensitizer may, in some cases, be less than that for the direct reaction. This would account for the lower carbon dioxide yields obtained with sensitizers such as 1-cyanonaphthalene. A diffusional process may be occurring between the excited sensitizer and α -keto-carboxylic acid molecules, i.e. the sensitizer molecules have to migrate to form exciplexes with the α -keto-carboxylic acid. Such a diffusion process could also lead to an apparent reduction in the carbon dioxide yield when compared to the direct reaction, in which the α -keto-carboxylic acids could break down in situ. As previously discussed electron transfer from the sensitizer to the α -keto-carboxylic acid could be a competing process and lead to a reduction in the amount of carbon dioxide produced when compared to the relatively efficient direct photo-oxidative decarboxylation.

The following mechanism is proposed (Scheme 2.17) in order to account

Yields of carbon dioxide from irradiation of α -keto-carboxylic acids (10^{-2} M) in acetonitrile solution, containing various aromatic hydrocarbons (10^{-2} M), under oxygen

| α -Keto-carboxylic acid (10^{-2} M) | Aromatic hydrocarbon (10^{-2} M) | Irradiation Time (h) | Yield (%) of carbon dioxide |
|--|--|-------------------------|--------------------------------|
| Pyruvic acid | None | 3 | 73.1 |
| Pyruvic acid | 1-Cyanonaphthalene | 3 | 42.6 |
| Pyruvic acid | Acridine | 3 | 109.0 |
| Pyruvic acid | Acridine (a) | 3 | 21.5 |
| Pyruvic acid | 9,10-Dicyanoanthracene (b) | 4 | 61.9 |
| Pyruvic acid | None | 4 | 76.8 |
| α -Keto-valeric acid | None | 6 | 112.9 |
| α -Keto-valeric acid | 1-Cyanonaphthalene | 4 | 39.6 |
| α -Keto-valeric acid | 9-Cyanoanthracene | 4 | 98.3 |
| α -Keto-valeric acid | 9-Nitroanthracene | 21 | 114.1 |
| α -Keto-valeric acid | Acridine | 4 | 126.9 |
| α -Keto-valeric acid | Phenazine | 4 | 56.2 |
| α -Keto-valeric acid | None | 5.5 | 125.8 |
| 3,3-Dimethyl-2-keto-butyric acid | 1-Cyanonaphthalene | 4 | 97 |
| 3,3-Dimethyl-2-keto-butyric acid | 9-Cyanoanthracene | 4 | 125.4 |
| 3,3-Dimethyl-2-keto-butyric acid | 9-Nitroanthracene | 4 | 29.9 |
| 3,3-Dimethyl-2-keto-butyric acid | Acridine | 4 | 129.4 |
| 3,3-Dimethyl-2-keto-butyric acid | Phenazine | 4 | 103.6 |

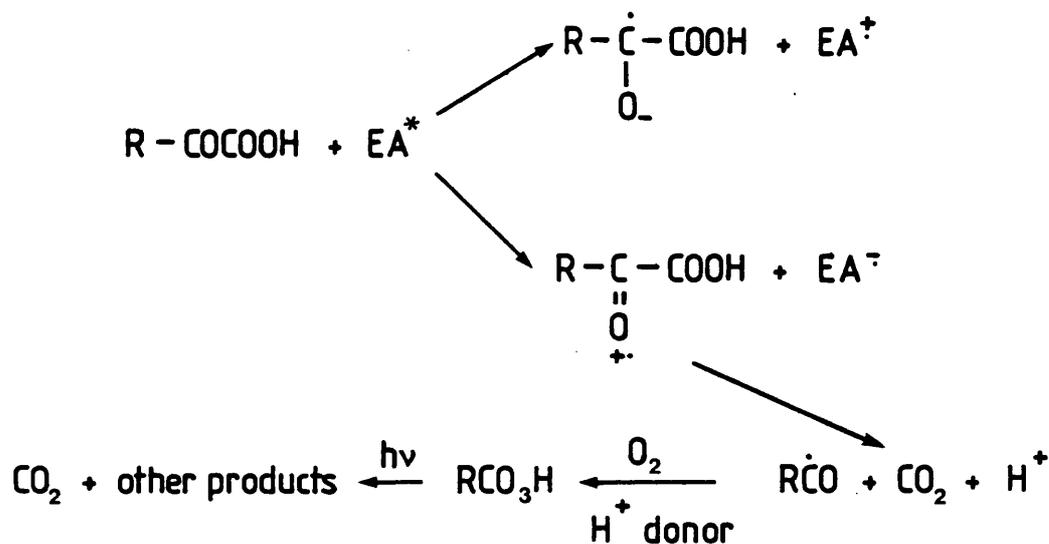
TABLE 2.24 (Continued)

| α -Keto-carboxylic acid (10^{-2} M) | Aromatic hydrocarbon (10^{-2} M) | Irradiation Time (h) | Yield (%) of carbon dioxide |
|--|--|-------------------------|--------------------------------|
| Phenylpyruvic acid | None | 17 | 143.1 |
| Phenylpyruvic acid | 1-Cyanonaphthalene | 17 | 178.2 |
| Phenylpyruvic acid | 9-Cyanoanthracene | 17 | 156.4 |
| Phenylpyruvic acid | 9-Nitroanthracene | 17 | 198.9 |
| Phenylpyruvic acid | Acridine | 17 | 161.9 |
| Phenylpyruvic acid | Phenazine | 17 | 166.0 |
| α -Keto-glutaric acid | None | 21.5 | 145.2 |
| α -Keto-glutaric acid | 1-Cyanonaphthalene | 23 | 147.2 |
| α -Keto-glutaric acid | 9-Cyanoanthracene | 23 | 158.4 |
| α -Keto-glutaric acid | 9-Nitroanthracene | 23 | 128.9 |
| α -Keto-glutaric acid | Phenazine | 18 | 84.3 |
| α -Keto-glutaric acid | Acridine | 6 | 132.9 |
| α -Keto-glutaric acid | None | 6 | 91.2 |

(a) In acetonitrile/pyridine solution (4:1 v/v)

(b) OD = 1.0 at 370 nm.

for the sensitization of carbon dioxide production via electron acceptors, (EA).



Scheme 2.17

Superoxide anion, formed by electron transfer from either the pyruvate radical anion or electron acceptor radical anion, may also be participating in the reaction.

As previously stated a sensitization process must be occurring as irradiation initially leads to the formation of excited sensitizer molecules.

Sensitization by compounds that can take part in hydrogen abstraction processes has been further investigated by using acridine as sensitizer.

2.5(iv) ACRIDINE SENSITIZED PHOTO-OXIDATIVE DECARBOXYLATION

Acridine was found to sensitize the photo-oxidative decarboxylation of various α -keto-carboxylic acids, (Table 2.24). The addition of pyridine to acetonitrile solutions of pyruvic acid containing acridine effectively reduced the yield of carbon dioxide, (Table 2.24).

The addition of increasing amounts of pyruvic acid to acetonitrile

solution of acridine led to the formation of a highly fluorescent species, the intensity of which increased with increasing pyruvic acid concentration, (Fig. 2.11). It is suggested that the fluorescent species is the protonated form of acridine. A similar fluorescent species was also observed when dilute hydrochloric acid was added to acetonitrile solutions of acridine, and its intensity was found to decrease markedly upon the addition of pyridine, (Fig. 2.12). It would therefore appear that protonation of acridine by pyruvic acid to form acridinium pyruvate, is a pre-requisite for decarboxylation of such systems, and the addition of pyridine decreases the amount of protonated acridine, by a competing process forming pyridinium pyruvate, and leads to a decrease in the yield of carbon dioxide. In the latter case the acridine would merely be acting as a light filter.

The addition of acridine to acetonitrile solutions of α -keto-valeric acid led, upon irradiation, to the production of greater than one mole of carbon dioxide under oxygen, and to one mole of carbon dioxide from similar irradiations under argon, (Table 2.25). In each case the yields of carbon dioxide are higher in the presence of acridine, than in the direct irradiations.

TABLE 2.25

Yields of carbon dioxide from irradiation of α -keto-valeric acid (10^{-2} M), (A) in acetonitrile solution and (B) in acetonitrile solution containing acridine (10^{-2} M), under oxygen and argon

| Conditions | Yield (%) of carbon dioxide | | | |
|------------|-----------------------------|-------|---------------------------|-------|
| | (A) Acetonitrile | | (B) Acetonitrile/Acridine | |
| | 9h | 20h | 9h | 20h |
| Argon | 16.7 | 24.4 | 100 | 100 |
| Oxygen | 98.7 | 112.7 | 142.5 | 180.3 |

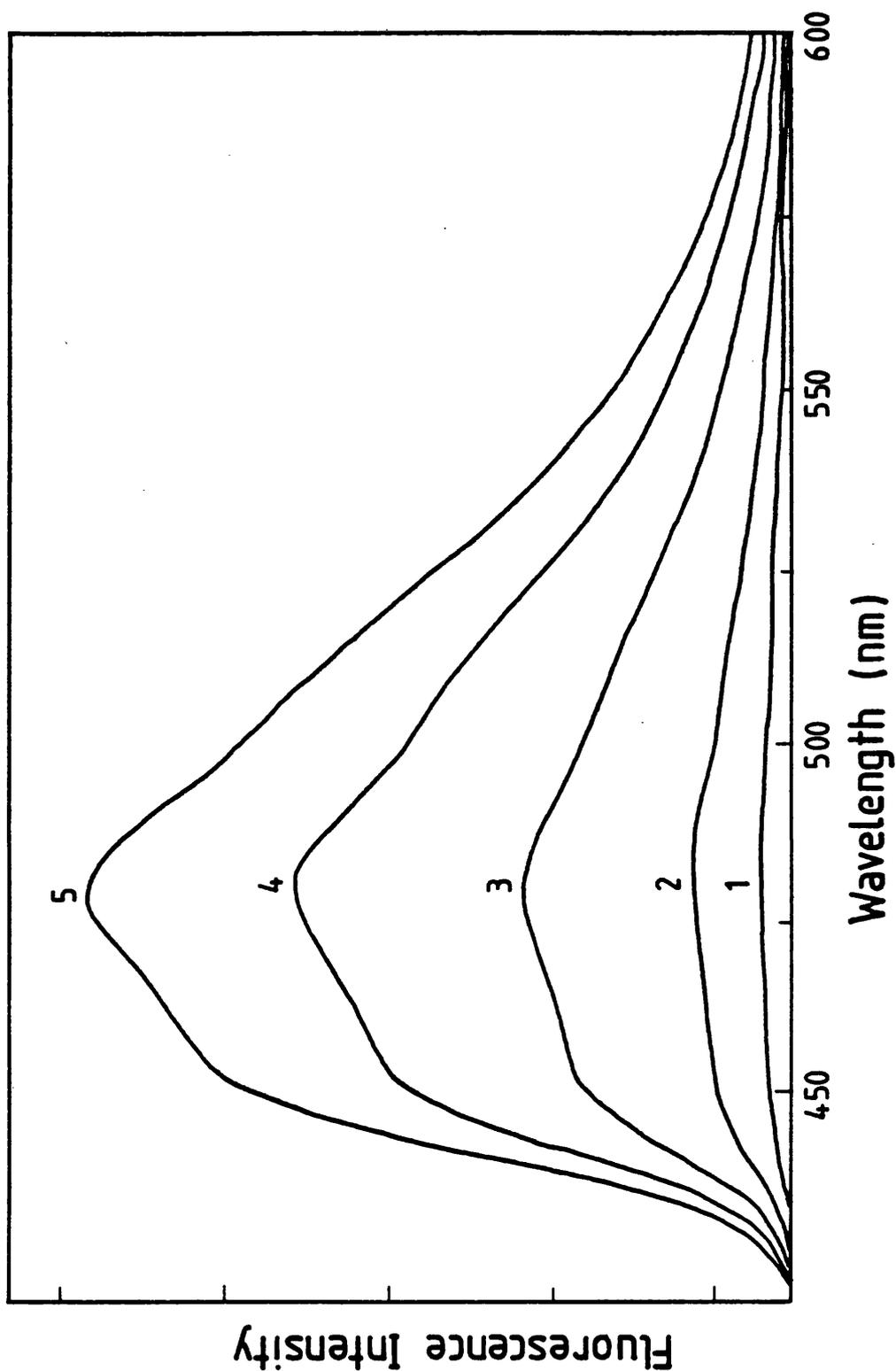
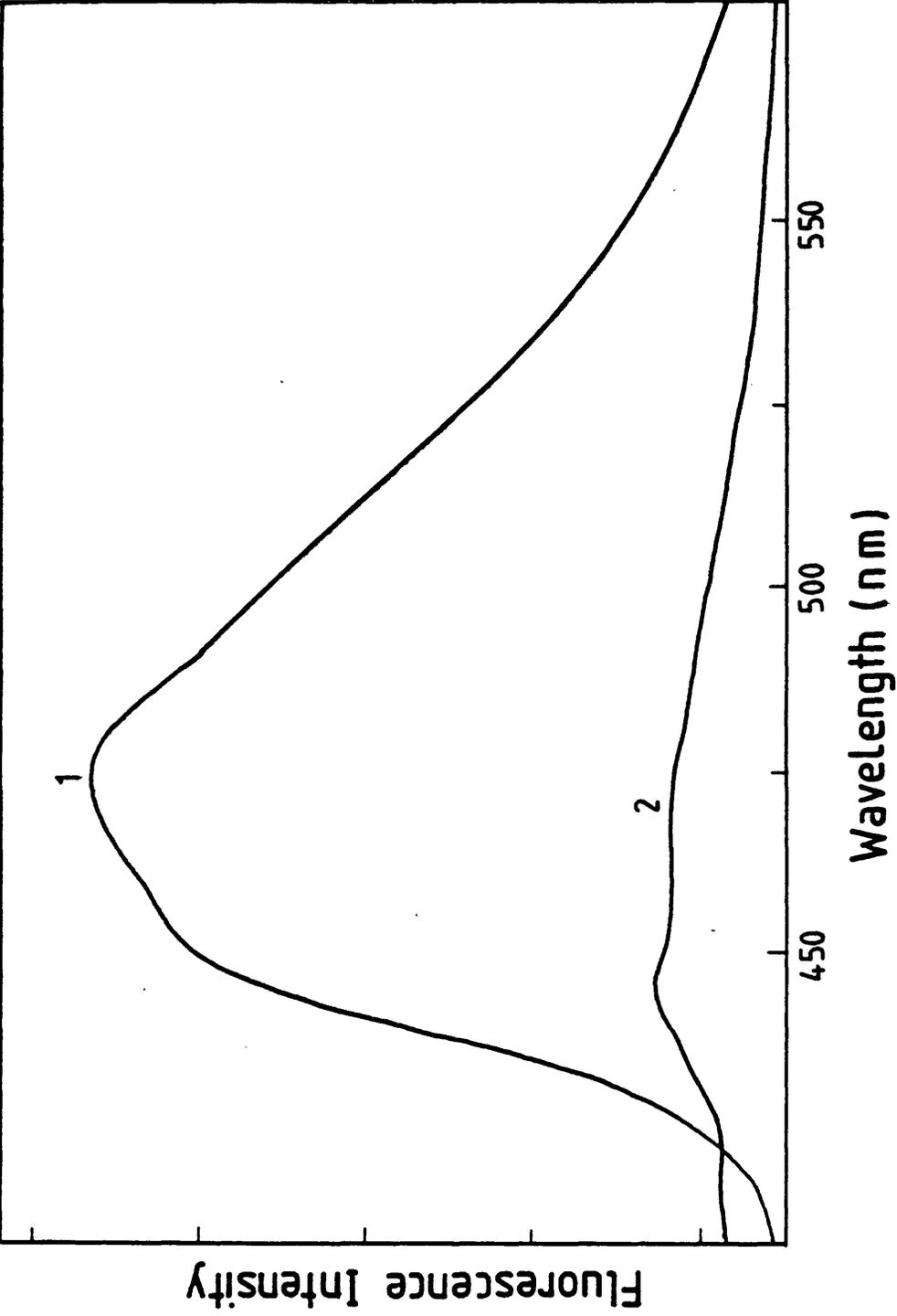


FIG. 2.11

Fluorescence spectra of acridinium ion produced in acetonitrile solutions of acridine, excited at 392 nm, by the presence of varying amounts of pyruvic acid (1) 5×10^{-3} M, (2) 1×10^{-2} M, (3) 1.5×10^{-2} M, (4) 2×10^{-2} M and (5) 3×10^{-2} M. [No fluorescence was observed for neat acridine solution.]

Fluorescence spectra of acridinium ion produced in acetonitrile solutions of acridine excited at 392 nm (1) containing dilute hydrochloric acid (~0.02 M) and (2) as in (1) but with added pyridine (~0.2 M).



An interesting observation is seen in the acridine sensitized photo-oxidative decarboxylation of α -keto-glutaric and α -keto-pimelic acids, (Table 2.26). In both cases prolonged irradiation led to the production of greater than two moles of carbon dioxide from each acid. Similar irradiations under argon led to the production of greater than one mole of carbon dioxide in each case. Again the yields of carbon dioxide are substantially higher in the presence of acridine when compared to the yields obtained from the direct irradiation.

α -Keto-glutaric and α -keto-pimelic acids both contain a second carboxylic acid group, and it would appear that the third mole of carbon dioxide produced from irradiation of such acids under oxygen may originate from this second or distant carboxylic acid group. Accordingly investigations were carried out on the parent dicarboxylic acids, namely glutaric and pimelic acids, in order to ascertain if the acridine sensitized photo-decarboxylation of such acids would lead to the production of greater than one mole of carbon dioxide, which would indicate that carbon dioxide can arise from both the carboxylic acid functions. As can be seen from Table 2.27, acridine was found to sensitize the production of greater than one mole of carbon dioxide from irradiation of acetonitrile solutions of glutaric and pimelic acids, under oxygen and argon. No decarboxylation occurred in the absence of acridine.

The above results (Table 2.27) show that the acridine sensitized decarboxylation of dicarboxylic acids leads to the production of carbon dioxide from both carboxylic acid groups.

2.5(v) DISCUSSION

The mechanism whereby acridine can sensitize greater than two moles of carbon dioxide production is particularly intriguing. It has

TABLE 2.26

Yields of carbon dioxide from irradiation of α -keto-glutaric acid and α -keto-pimelic acid (10^{-2} M respectively), (A) in acetonitrile solution and (B) in acetonitrile solution containing acridine (10^{-2} M), under oxygen and argon

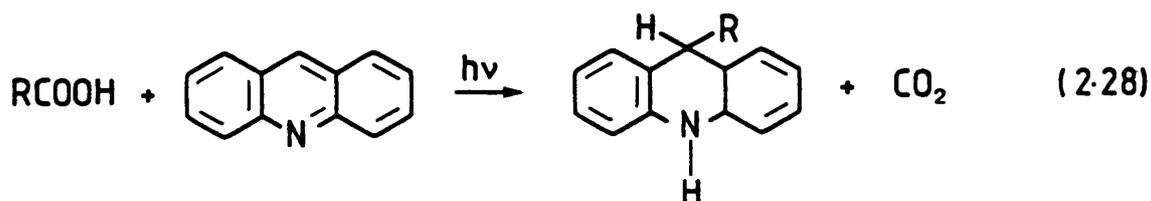
| α -keto-carboxylic acid (10^{-2} M) | Conditions | Yield (%) of carbon dioxide | | | |
|--|------------|-----------------------------|-------|---------------------------|-------|
| | | (A) Acetonitrile | | (B) Acetonitrile/Acridine | |
| | | 9h | 20h | 9h | 20h |
| α -keto-glutaric acid | Argon | 19.9 | 28.8 | 104.4 | 119.0 |
| α -keto-glutaric acid | Oxygen | 104.0 | 113.3 | 168.1 | 215.6 |
| α -keto-pimelic acid | Argon | 12.6 | 17.9 | 130.0 | 152.4 |
| α -keto-pimelic acid | Oxygen | 85.3 | 111.3 | 192.5 | 254.2 |

TABLE 2.27

Yields of carbon dioxide from irradiation of glutaric and pimelic acids (10^{-2} M respectively) in acetonitrile solution containing acridine (10^{-2} M), (A) under argon and (B) under oxygen

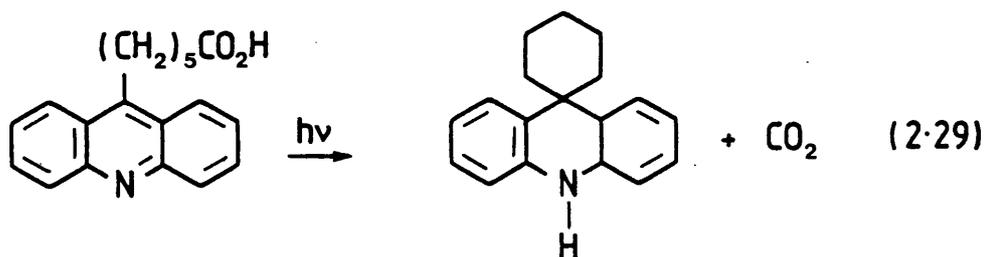
| Dicarboxylic acid (10^{-2} M) | Yield (%) of carbon dioxide | | | |
|-------------------------------------|-----------------------------|-------|------------|-------|
| | (A) Argon | | (B) Oxygen | |
| | 9h | 20h | 9h | 20h |
| Glutaric acid | 92.6 | 125.9 | 110.5 | 159.9 |
| Pimelic acid | 84.1 | 117.4 | 111.7 | 164.5 |

previously been reported⁷⁴ that carboxylic acids are decarboxylated when irradiated in the presence of acridine, with the formation of addition products, (Equation 2.28).



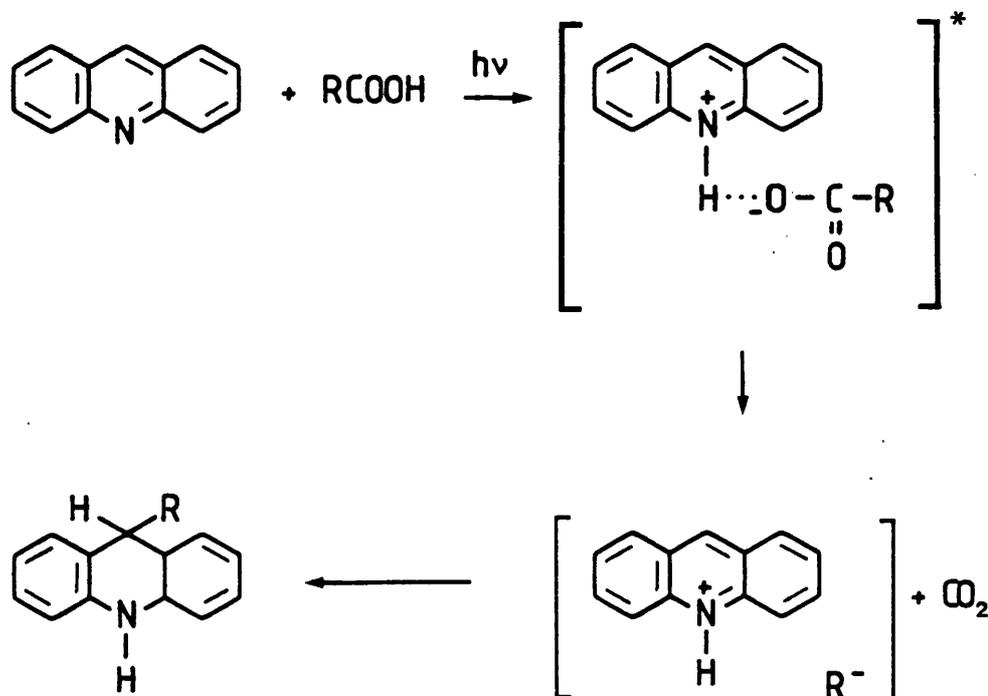
(where $R = \text{Me}, t\text{-Bu}, \text{PhCH}_2$)

Intramolecular decarboxylation was also found to occur,⁷⁴ (Equation 2.29).



The mechanism was interpreted in terms of an acid-base equilibrium. Acridine is known to be weakly basic in its ground state, but shows a marked enhancement of basicity in its first excited singlet state.⁷⁵ Thus it was suggested⁷⁴ that acridine upon irradiation, probably via its singlet state, captured the hydroxyl proton from the carboxylic acid and

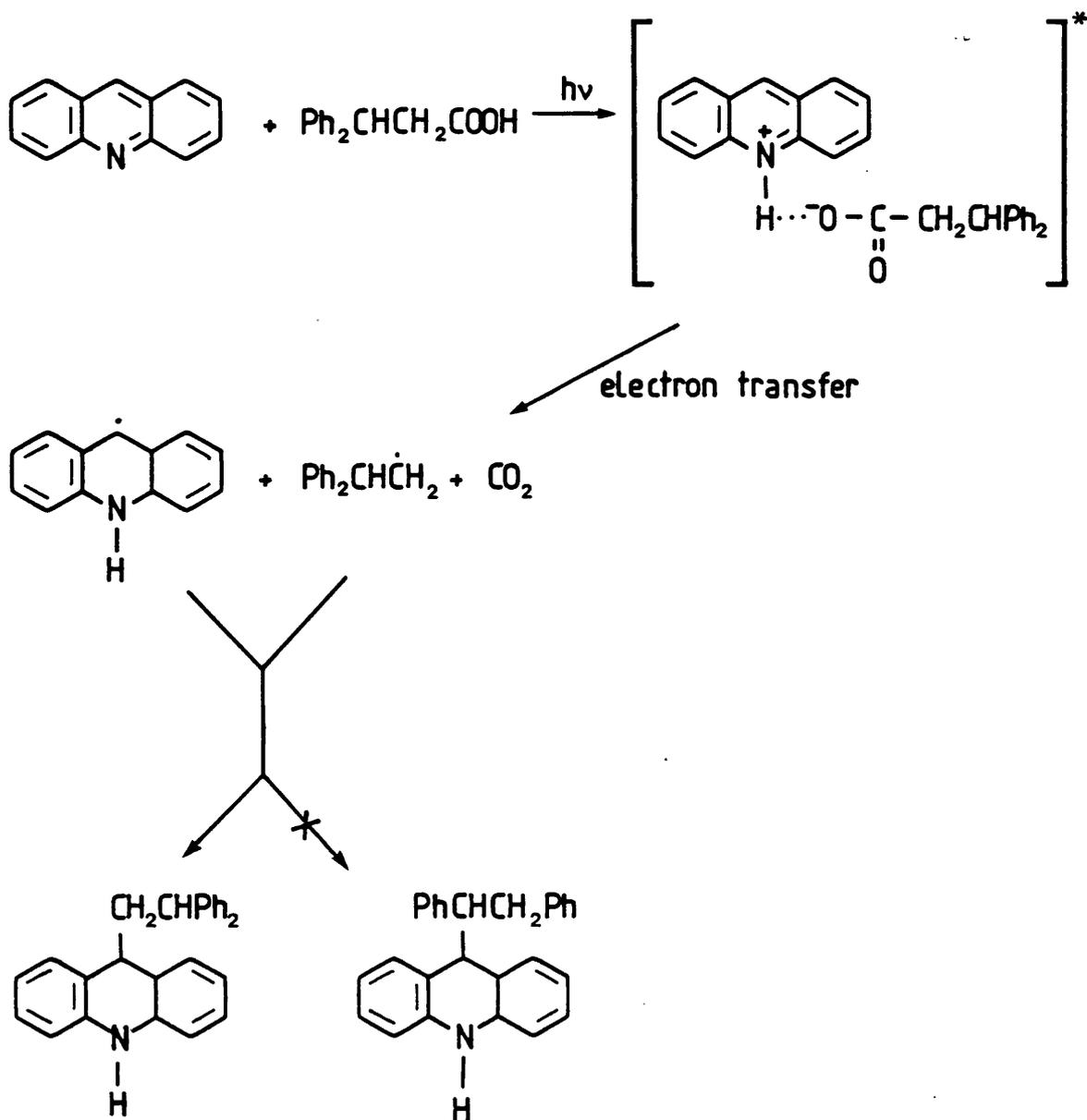
formed an excited complex of acridinium and carboxylate ions, the subsequent decarboxylation of which produced an ion-pair whose combination gave the addition product, (Scheme 2.18).



Scheme 2.18

The authors⁷⁴ considered an alternative mechanism involving radicals, whereby proton transfer was followed by electron ejection from the carboxylate ion to the acridinium ion; the alkoxy radicals so generated would lose carbon dioxide and combination of the radicals, produced within a solvent cage, would give the addition product. The finding that the decarboxylation of 2,2-diphenylpropionic acid did not lead to products of phenyl migration (Scheme 2.19) which would be expected to occur if a 2,2-diphenylmethyl radical was involved, led the authors⁷⁴ to favour an ionic mechanism. However, the lack of product arising from phenyl migration may be due to an extremely efficient radical recombination process.

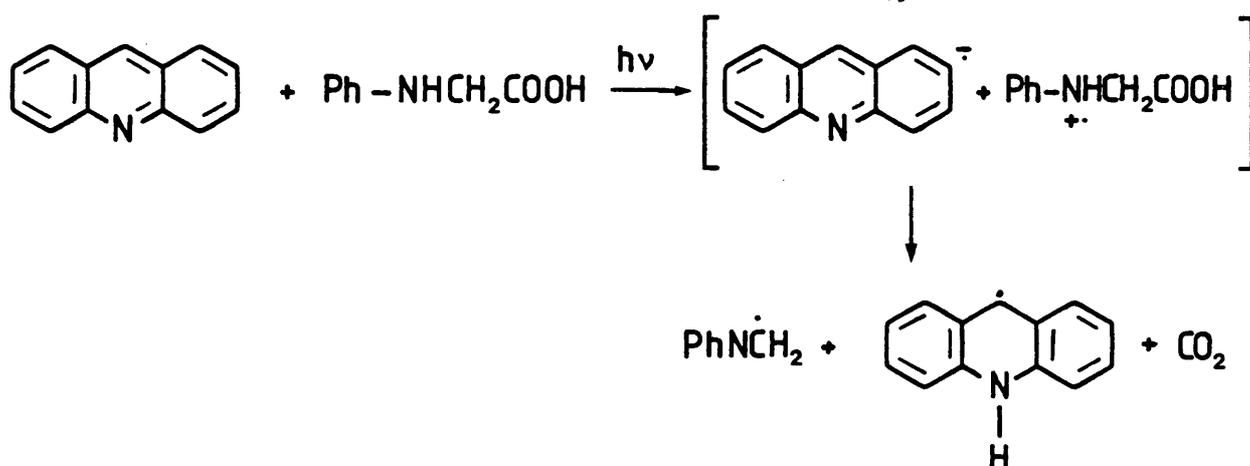
It has previously been suggested⁷⁶ that the decarboxylation of



Scheme 2-19

carboxylic acids such as N-phenylglycine with acridine as sensitizer, occur via an electron transfer process from the acid to the excited sensitizer, the resulting exciplex can then react, with the production of carbon dioxide, and radical formation, (Scheme 2.20).

These authors⁷⁶ show that the acridine sensitized decarboxylation of mono-carboxylic acids does not produce more than one mole of carbon dioxide, as would be expected.

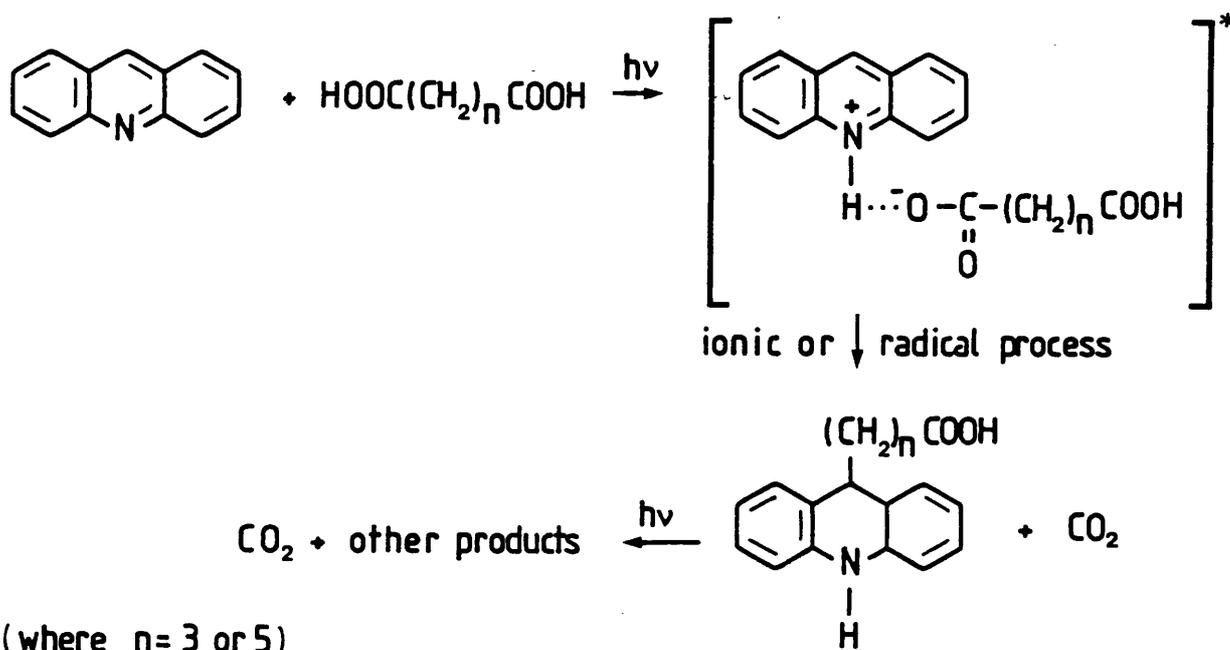


Scheme 2.20

As strong fluorescence was observed from acridine in the presence of pyruvic acid, (Fig. 2.11), it is probable that the decarboxylation reaction occurs via the α -keto-carboxylic acids protonating the highly basic and fluorescent $^1\pi\pi^*$ state of acridine. Pyridine diminished the intensity of the fluorescent species and also led to lower carbon dioxide yields, (Fig. 2.12 and Table 2.24), as a result of reducing the amount of the protonated acridine, in a competitive reaction with pyruvic acid.

From the carbon dioxide yields of the parent dicarboxylic acids (pimelic and glutaric) it can be seen that greater than one mole of carbon dioxide is produced, both under oxygen and argon, which implies that decarboxylation occurs from both carboxylic acid groups, (Table 2.27). It is possible for this to occur by initial hydrogen abstraction from one of the carboxyl groups followed by either ionic or radical (involving electron transfer) reaction leading to decarboxylation. Recombination of the species produced would give the acridine addition product which could then undergo an intramolecular decarboxylation, from the second carboxyl group, and hence give rise to the production of the second mole of carbon dioxide, (Scheme 2.21).

In the case of the α -keto-carboxylic acids it is possible that an

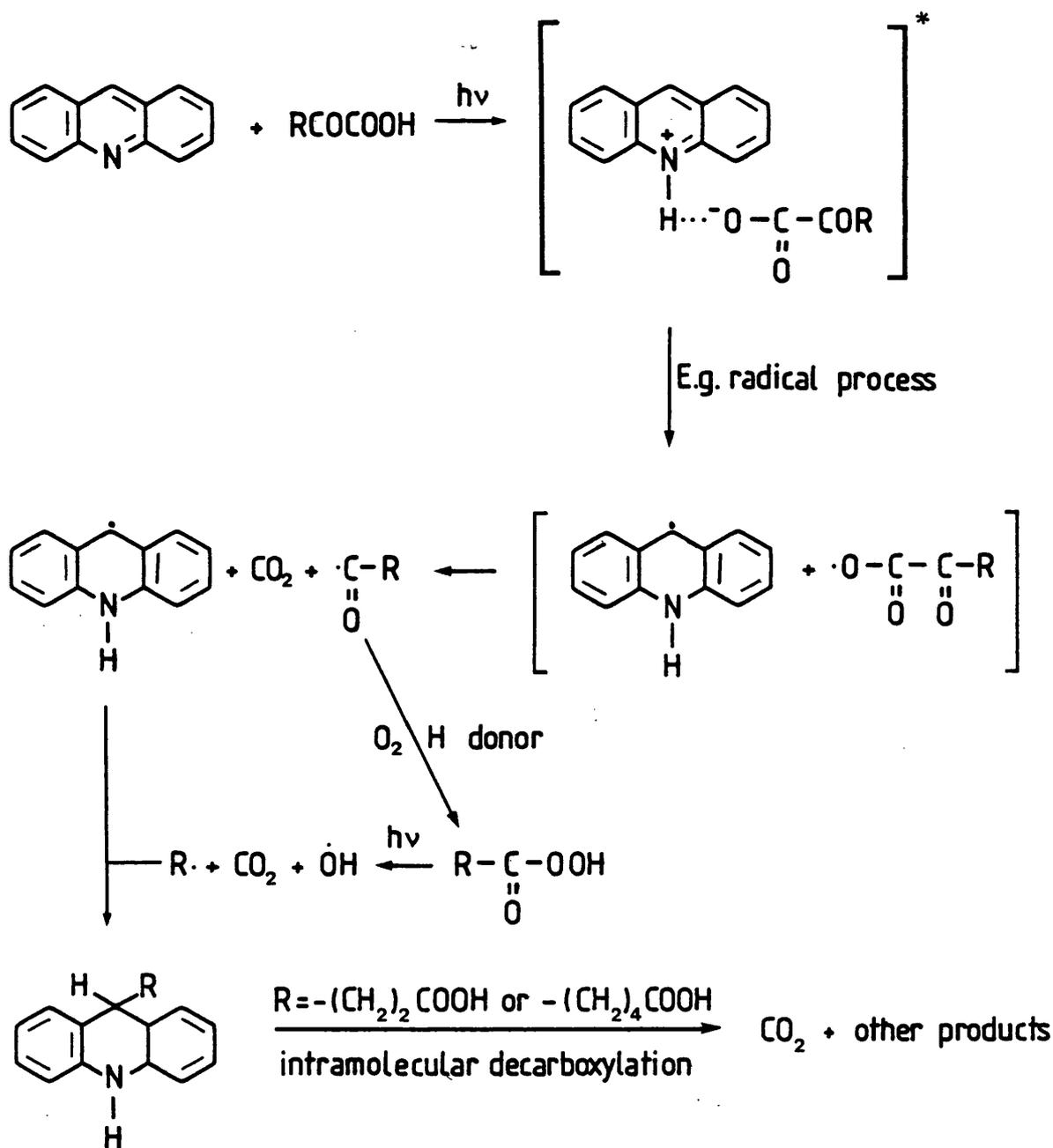


Scheme 2.21

electron transfer process to the acridinium ion causing decarboxylation and radical formation could occur. The acyl radicals produced from initial decarboxylation of the α -keto-carboxylic acid could be intercepted by oxygen to form per-acids which subsequently undergo decarboxylation to give the second mole of carbon dioxide. Radical recombination would lead to an acridine addition product, which could give rise to the third mole of carbon dioxide via intramolecular decarboxylation, (Scheme 2.22). Alternatively, a mechanism involving an ionic process may be in operation. Unfortunately, time did not allow a closer evaluation of the mechanism. Utilising 5- ^{14}C - α -keto-glutaric acid would verify the production of carbon dioxide from the "distant" carboxyl group, and a thorough product study may elucidate the reaction mechanism which is involved

Summary

Decarboxylation of α -keto-carboxylic acids in oxygenated solution can be sensitized by electron acceptors, in accord with the postulated mechanism for photo-oxidative decarboxylation. The reaction can also be



Scheme 2-22

sensitized by compounds capable of undergoing hydrogen abstraction reactions. In the case of acridine the decarboxylation involves the $^1\pi\pi^*$ state of the sensitizer, and when the structure of the α -keto-carboxylic acid is appropriate, greater than two moles of carbon dioxide can be produced.

2.6 DYE-SENSITIZED PHOTO-OXYGENATION OF α -KETO-CARBOXYLIC ACIDS

2.6.1 THE RÔLE OF SINGLET OXYGEN

Previous reports^{41,46,47} have suggested that singlet oxygen is involved in the dye-sensitized photo-oxygenation of α -keto-carboxylic acids. However these findings have been subject to speculation,⁴² and the following experiments were performed to assess the rôle that singlet oxygen may have in these reactions.

2.6.1(i) DECARBOXYLATION STUDIES

α -Keto-carboxylic acids were found to undergo decarboxylation when irradiated in the presence of a variety of sensitizing dyes, (Table 2.28). It has previously been reported^{42,46} that in many cases greater than one mole of carbon dioxide is produced per mole of α -keto-carboxylic acid, and the results shown in Table 2.28 confirm this. The second mole of carbon dioxide has been suggested to arise from the breakdown of per-acid intermediates in these reactions.^{41,46} The yields of carbon dioxide from acetonitrile/pyridine solution compared to E.D.T.A. distilled acetonitrile /pyridine solution are similar (Table 2.28) and therefore the enhanced yields of carbon dioxide would not appear to be arising from metal ion impurities as previously claimed.⁴⁴ Further experiments were performed to evaluate if singlet oxygen is involved in these reactions.

2.6.1(ii) SOLVENT ISOTOPE EFFECTS

The lifetime of singlet oxygen is appreciably longer in deuterium oxide than in water,⁷⁷ therefore if the photo-oxygenation reaction is carried out in each solvent, the participation of singlet oxygen should be evidenced by a solvent isotope effect.

Yields of carbon dioxide from irradiation of α -keto-carboxylic acids in the presence of various sensitizers

| α -keto-carboxylic acid | Concentration (M) | Sensitizer (a) | Solvent (b) | Filter (c) | Irradiation Time (h) | Yield (%) of carbon dioxide |
|----------------------------------|--------------------|----------------|---------------------------|------------|----------------------|-----------------------------|
| α -Keto-glutaric acid | 8×10^{-3} | Rose Bengal | Methanol/water/pyridine | A | 6 | 22 |
| α -Keto-glutaric acid | 8×10^{-3} | Rose Bengal | Methanol/water/pyridine | A | 13 | 61 |
| α -Keto-glutaric acid | 1×10^{-2} | Rose Bengal | Methanol/pyridine | A | 18 | 62.1 |
| α -Keto-glutaric acid | 1×10^{-2} | Rose Bengal | Acetonitrile/pyridine | A | 18 | 121.0 |
| α -Keto-glutaric acid | 1×10^{-2} | Rose Bengal | Acetonitrile/pyridine (d) | A | 18 | 119.4 |
| α -Keto-glutaric acid | 2×10^{-2} | Rose Bengal | Methanol/pyridine | A | 6 | 20.1 |
| α -Keto-glutaric acid | 2×10^{-2} | Rose Bengal | Methanol/pyridine | A | 20 | 74.1 |
| α -Keto-glutaric acid | 2×10^{-2} | Rose Bengal | Acetonitrile/pyridine | A | 20 | 125.4 |
| α -Keto-glutaric acid | 1×10^{-2} | Alloxazine | Acetonitrile | B | 21 | 89.3 |
| α -Keto-glutaric acid | 1×10^{-2} | Riboflavin | Acetonitrile | B | 18 | 79.7 |
| Phenylpyruvic acid | 1×10^{-2} | Rose Bengal | Methanol/pyridine | A | 21 | 88.5 |
| Phenylpyruvic acid | 1×10^{-2} | Rose Bengal | Acetonitrile/pyridine | A | 18 | 124.9 |
| Phenylpyruvic acid | 1×10^{-2} | Rose Bengal | Methanol/water/pyridine | A | 4 | 37.5 |
| Phenylpyruvic acid | 1×10^{-2} | Rose Bengal | Methanol/water/pyridine | A | 7.5 | 70.3 |
| Phenylpyruvic acid | 1×10^{-2} | Alloxazine | Acetonitrile | B | 6 | 82.2 |
| Phenylpyruvic acid | 1×10^{-2} | Riboflavin | Acetonitrile | B | 18 | 133 |
| 3,3-Dimethyl-2-keto-butyric acid | 1×10^{-2} | Rose Bengal | Acetonitrile/pyridine | A | 21 | 31 |
| 3,3-Dimethyl-2-keto-butyric acid | 1×10^{-2} | Riboflavin | Acetonitrile | B | 17 | 98.2 |
| 3,3-Dimethyl-2-keto-butyric acid | 1×10^{-2} | Alloxazine | Acetonitrile | B | 6 | 69.5 |
| α -Keto-butyric acid | 1×10^{-2} | Rose Bengal | Acetonitrile | A | 18 | 45.2 |
| Pyruvic acid | 1×10^{-2} | Rose Bengal | Acetonitrile | A | 18 | 21.1 |

(a) Rose Bengal/Riboflavin concentration = 0.02 g/25 ml; Alloxazine = 10^{-2} M.

(b) Acetonitrile/pyridine and methanol/pyridine = 4:1 v/v respectively; Methanol/water/pyridine = 2:2:1 v/v.

(c) Filter solution A = 2% potassium chromate; Filter solution B = saturated sodium nitrate; (both aqueous solutions).

(d) Distilled from E.D.T.A. prior to use.

The rate of photo-oxygenation of a number of α -keto-carboxylic acids were monitored by following their rate of consumption by polarography⁷⁸ in both deuterium oxide and water, and the results are shown in Table 2.29. It is readily seen that the reactions display a remarkably small solvent isotope effect, and for oxidation of α -keto-glutaric acid by Rose Bengal the magnitude of the effect is not markedly dependent upon the concentration of the α -keto-carboxylic acid.

2.6.1(iii) LASER FLASH PHOTOLYSIS STUDY⁷⁹

The rates of reaction of α -keto-carboxylic acids with singlet oxygen were measured using the method developed by Wilkinson⁸⁰ and Kearns⁸¹ in which the α -keto-carboxylic acids compete for singlet oxygen with 1,3-diphenylisobenzofuran. The results are shown in Table 2.30. Laser flash photolysis of aerated methanolic solutions of Methylene Blue containing the α -keto-carboxylic acids show the presence of a transient produced by reaction of the triplet dye with the acid. The transient appears to be the same as that observed by Kayser and Young,⁸² i.e. a radical derived from a Methylene Blue molecule. Analysis of the kinetics gave the rate constants for reaction of the dye with the α -keto-carboxylic acids and these are shown in Table 2.30. The rate constants given in Table 2.30 demonstrate that the acids react with triplet dye far more efficiently than with singlet oxygen.

2.6.1(iv) DISCUSSION

Previous evidence for the participation of singlet oxygen in the dye-sensitized photo-oxygenation of α -keto-carboxylic acids is:- (a) the reactions are slowed down by the addition of β -carotene⁴¹ (a known quencher of singlet oxygen, but also a quencher of the excited singlet

TABLE 2.29

Solvent isotope effect upon the dye-sensitized photo-oxidation of α -keto-carboxylic acids (a)

| α -Keto-carboxylic acid (Concentration/M) | Dye (Concentration/M) | Rate in H ₂ O /mol min ⁻¹ | Rate in D ₂ O /mol min ⁻¹ | Isotope Effect Rate D ₂ O/Rate H ₂ O |
|--|--|--|--|---|
| α -Keto-glutaric acid (1×10^{-4}) | Rose Bengal (2×10^{-6}) | 0.152 ± 0.012 $\times 10^{-6}$ | 0.169 ± 0.024 $\times 10^{-6}$ | 1.17 ± 0.21 |
| α -Keto-glutaric acid (1×10^{-4}) | Methylene Blue (2×10^{-6}) | 0.122 ± 0.024 $\times 10^{-6}$ | 0.187 ± 0.034 $\times 10^{-6}$ | 1.65 ± 0.60 |
| α -Keto-glutaric acid (2×10^{-2}) | Rose Bengal (1×10^{-3}) | 0.158 ± 0.011 $\times 10^{-4}$ | 0.247 ± 0.079 $\times 10^{-4}$ | 1.61 ± 0.61 |
| Phenylpyruvic acid (1×10^{-4}) | Rose Bengal (2×10^{-6}) | 0.204 ± 0.02 $\times 10^{-6}$ | 0.205 ± 0.051 $\times 10^{-6}$ | 1.04 ± 0.35 |
| Phenylpyruvic acid (1×10^{-4}) | Methylene Blue (2×10^{-6}) | 0.179 ± 0.015 $\times 10^{-6}$ | 0.212 ± 0.008 $\times 10^{-6}$ | 1.2 ± 0.15 |

(a) The reported results are the mean of four determinations and all have been subjected to least squares analysis.

TABLE 2.30⁷⁹

Rate constants for reaction of α -keto-carboxylic acids with singlet oxygen and Methylene Blue in aerated methanolic solutions^(a)

| α -Keto-carboxylic acid | Singlet oxygen $k_q/\ell \text{ mol}^{-1} \text{ s}^{-1}$ | Methylene Blue $k_q/\ell \text{ mol}^{-1} \text{ s}^{-1}$ |
|----------------------------------|--|--|
| Phenylpyruvic acid | $<7 \times 10^6$ (b) | 3×10^8 |
| α -Keto-glutaric acid | $3-4 \times 10^6$ | 6.5×10^8 |
| 3,3-Dimethyl-2-keto-butyric acid | ca. 1×10^6 | 4.5×10^8 |

- (a) The solutions were flash photolysed ($\lambda = 694 \text{ nm}$) using 15 ns, 1 J single pulses from a Q-switched ruby laser
- (b) The formation of transient species absorbing at the monitoring wavelength of 410 nm made it difficult to measure the bleaching of the 1,3-diphenylisobenzofuran. Thus the acid concentration was kept as low as possible but this introduces large errors and, therefore, only an upper limit for this rate constant can be given.

and triplet state of dyes⁴³), and (b) the observation of an apparent solvent isotope effect.^{30,46} Decarboxylation has been shown to occur in the dye-sensitized photo-reactions of α -keto-carboxylic acids in the absence of oxygen,^{42,46} and therefore the possibility exists that in the photo-oxygenation reactions, decarboxylation can arise by more than one mechanism. Using solvent isotope effects and also studying the ability of the α -keto-carboxylic acids to quench singlet oxygen (by laser flash photolysis investigations), enabled the rôle of singlet oxygen in the photo-oxygenation reactions to be ascertained.

From the laser flash photolysis study (Table 2.30) it is clear that the α -keto-carboxylic acids react far more efficiently with triplet dye than with singlet oxygen. The availability of the rate constants shown in Table 2.30 enable meaningful solvent isotope studies to be carried out and

analysed.⁸³

If singlet oxygen is solely responsible for oxidation the kinetics of the reaction will be described by equation 2.30.⁸³

$$-d[\text{Acid}]/dt = I \phi_T k_q [\text{Acid}] / (k_d + k_q [\text{Acid}]) \quad \dots (2.30)$$

where: I = Light intensity,

ϕ_T = Triplet yield of dye,

k_d = Unimolecular decay constant for singlet oxygen.

Since the k_q values for the α -keto-carboxylic acids are so low, the use of a low concentration of the acid, e.g. 1×10^{-4} M, will mean that the rate of reaction is largely controlled by k_d . Thus the rate of reaction should be considerably higher in deuterium oxide ($k_d = 5 \times 10^4 \text{ s}^{-1}$)⁸⁴ than for water ($k_d = 5 \times 10^5 \text{ s}^{-1}$).⁸⁵ [More recently a $k_d = 3 \times 10^4 \text{ s}^{-1}$ has been reported for deuterium oxide.⁸⁶]

From the observed solvent isotope effects shown in Table 2.29, it can be concluded that either singlet oxygen is not involved in the reaction or else the oxidation is occurring predominantly by the dye- α -keto-carboxylic acid interaction and this is swamping the contribution made by the singlet oxygen reaction. From equation 2.31⁸³ and the results shown in Table 2.30 it is possible to calculate that the isotope effects for phenylpyruvic acid, α -keto-glutaric acid and 3,3-dimethyl-2-ketobutyric acid should be 1.4, 2.0 and 1.4 respectively, provided that N_t and N_o are either unity or of a similar magnitude.

$$\frac{-d[\text{Acid}]}{dt} = \frac{N_t I \phi_T k_r [\text{Acid}]}{(k_{d_1} + k_{O_2} [^3O_2] + k_r [\text{Acid}])} + \frac{N_o I \phi_T k_{O_2} [^3O_2] k_q [\text{Acid}]}{(k_{d_1} + k_{O_2} [^3O_2] + k_r [\text{Acid}])(k_d + k_q [\text{Acid}])} \quad \dots (2.31)$$

where: I = Light intensity,

- Φ_T = Quantum yields of triplets for sensitizer,
 k_d = Unimolecular decay constant for singlet oxygen,
 k_{d1} = Unimolecular decay constant for the triplet dye,
 k_{O_2} = Bimolecular rate constant for quenching of dye triplets by oxygen,
 $[^3O_2]$ = Concentration of oxygen in solution,
 N_t = Fraction of triplet dye - acid collisions which result in chemical reactions,
 N_o = Fraction of singlet oxygen - acid collisions which result in chemical reaction.

The fact that the measured isotope effects are smaller than the calculated values may indicate that $N_o < N_t$. The fact that the observed values for a particular α -keto-carboxylic acid apparently vary with the sensitizer used is probably a reflection of the fact that the isotope effect falls within the limits of experimental reproducibility. The previously reported, small solvent isotope effects vary considerably in the range 1-2 and therefore the results cannot be taken as evidence for the participation of singlet oxygen.

Summary

The results reported here show that singlet oxygen plays little, if any, rôle in the Rose Bengal and Methylene Blue sensitized photo-oxygenation of α -keto-carboxylic acids. The dye - acid interaction is obviously an important reaction, but the fact that some of the reaction may occur via an intermediate such as the superoxide anion⁴⁷ cannot be ruled out. The finding that singlet oxygen is not involved in the dye-sensitized photo-oxygenation of α -keto-carboxylic acids⁷¹ has subsequently been confirmed in a later publication.⁴⁸

2.6.2 EFFECT OF OXYGEN CONCENTRATION UPON THE DYE-SENSITIZED PHOTO-OXIDATIVE DECARBOXYLATION OF α -KETO-CARBOXYLIC ACIDS

2.6.2(i) DECARBOXYLATION STUDIES

Earlier reports^{42,46} suggested that decarboxylation occurs when the reactions are carried out under nitrogen, i.e. in the absence of oxygen, and these findings prompted an investigation of the effect of oxygen concentration upon the dye-sensitized decarboxylation of α -keto-carboxylic acids.

Reactions were therefore performed by continually flushing the α -keto-carboxylic acid/dye solutions with the following gases, throughout the duration of the irradiation, at a flow rate of approximately 10 ml/min:- argon (zero oxygen concentration), pure oxygen, air, nitrogen (OFN) and nitrogen (commercial grade), [the latter two gases having oxygen concentrations of approximately 0.001 and a maximum of 0.5% respectively]. The dye used in each experiment was Rose Bengal obtained from B.D.H. Chemical Co. Ltd. Tables 2.31 and 2.32 show the yields of carbon dioxide obtained from α -keto-glutaric and pyruvic acids respectively, in both acetonitrile/pyridine and methanol/pyridine solutions. The rate of oxygen flushing on the yield of carbon dioxide was studied in acetonitrile/pyridine solutions of α -keto-glutaric acid (Table 2.31) and as can be seen a faster flow rate of gas leads to a dramatic increase in decarboxylation. The yields of carbon dioxide production from the α -keto-carboxylic acids under different oxygen concentrations were found to be in the order of air > oxygen > argon > nitrogen in each case.

The yield of carbon dioxide from methanol/pyridine solutions of α -keto-glutaric acid, sensitized by Rose Bengal from Eastman-Kodak Ltd., was studied under different oxygen concentrations and the results shown in Table 2.33. From these results (Table 2.33) it is apparent that the

TABLE 2.31

Yields of carbon dioxide from irradiation of α -keto-glutaric acid (2×10^{-2} M) sensitized by Rose Bengal (a) under different oxygen concentrations (A) in methanol/pyridine solution and (B) in acetonitrile/pyridine solution

| Conditions | Yields (%) of carbon dioxide | | | |
|-----------------------|------------------------------|-------|-------------------------------|---------------------------|
| | (A) Methanol/pyridine (b) | | (B) Acetonitrile/pyridine (b) | |
| | 6h | 20h | 6h | 20h |
| Argon | 9.8 | 42.7 | 9.1 | 37.4 |
| Oxygen | 11.5 | 51.3 | 11.7 [17.3] ^c | 54.0 [116.3] ^c |
| Air | 20.3 | 105.9 | 22.1 | 113.4 |
| Nitrogen (OFN) | 6.2 | 17.9 | 5.8 | 22.2 |
| Nitrogen (Commercial) | 6.4 | 20.6 | 6.7 | 29.2 |

(a) Concentration = 0.02 g/25ml

(b) Methanol/pyridine and acetonitrile/pyridine both 4:1 v/v

(c) Rate of oxygen flushing = 20 ml/min.

TABLE 2.32

Yields of carbon dioxide from irradiation of pyruvic acid (2×10^{-2} M) sensitized by Rose Bengal (a) under different oxygen concentrations (A) in methanol/pyridine solution and (B) in acetonitrile/pyridine solution

| Conditions | Yields (%) of carbon dioxide | | | |
|-----------------------|------------------------------|------|-------------------------------|------|
| | (A) Methanol/pyridine (b) | | (B) Acetonitrile/pyridine (b) | |
| | 6h | 20h | 6h | 20h |
| Argon | 9.7 | 28.1 | 12.2 | 39.6 |
| Oxygen | 6.8 | 28.5 | 17.7 | 63.9 |
| Air | 12.4 | 58.7 | 34.5 | 98.9 |
| Nitrogen (OFN) | 7.5 | 20.0 | 8.1 | 24.3 |
| Nitrogen (Commercial) | 7.1 | 20.0 | — | — |

(a) Concentration = 0.02 g/25ml

(b) Methanol/pyridine and acetonitrile/pyridine both 4:1 v/v

TABLE 2.33

Yields of carbon dioxide from irradiation of α -keto-glutaric acid (2×10^{-2} M) sensitized by Rose Bengal^(a) (Eastman-Kodak) under different oxygen concentrations in methanol/pyridine solution

| Conditions | Yields (%) of carbon dioxide | |
|-----------------------|----------------------------------|------|
| | Methanol/pyridine ^(b) | |
| | 6h | 20h |
| Argon | 11.9 | 33.0 |
| Oxygen | 11.7 | 45.8 |
| Air | 19.2 | 75.5 |
| Nitrogen (OFN) | 10.0 | 26.2 |
| Nitrogen (Commercial) | 8.4 | 24.3 |

(a) Concentration = 0.02 g/25ml

(b) Methanol/pyridine 4:1 v/v

source of Rose Bengal is an important factor in determining the overall production of carbon dioxide, as Rose Bengal from Eastman-Kodak Ltd.

(Table 2.33) gave differing values from those obtained when using Rose Bengal supplied from B.D.H. Chemical Co. Ltd. (Table 2.31), under similar irradiation conditions.

In each of the dye-sensitized decarboxylation reactions carried out in this section, the α -keto-carboxylic acid-dye solutions were irradiated through a potassium chromate filter (2% aqueous solution), to ensure that only the dye absorbed the incident light. From the results obtained it is clear that the yield of carbon dioxide is highly dependent upon (i) the oxygen concentration, (ii) the source of the sensitizer and (iii) the flow rate at which the gas is flushed through the reaction mixtures.

2.6.2(ii) DISCUSSION

That α -keto-carboxylic acids decarboxylate when irradiated in the

absence of oxygen^{42,46} was confirmed, although the yields of carbon dioxide reported here (Tables 2.31, 2.32 and 2.33) are substantially lower than those previously reported under anaerobic conditions.⁴² However it later became apparent that the high carbon dioxide yields⁴² probably arose due to leakage of air into the systems studied,⁸⁷ and as this was not the case in the results reported herein, accounts for the difference in the two sets of data. Therefore, although not as high as previously anticipated,⁴² the yields of carbon dioxide obtained here are a more accurate representation of the anaerobic decarboxylation of α -keto-carboxylic acids, and confirm that carbon dioxide is produced even in the absence of oxygen,^{42,46} substantiating the claim that a dye-acid interaction^{42,71} is responsible for at least part of the decarboxylation reaction.

The observation of an oxygen concentration dependency upon the decarboxylation reaction can be rationalised by reference to Scheme 2.23, which shows the possible reaction pathways for the dye-sensitized decomposition of α -keto-carboxylic acids.

The formation of triplet excited dye (path 1) is a pre-requisite for all subsequent reactions.

The triplet dye could undergo an energy transfer process with ground state oxygen to produce singlet oxygen (path 2), which could further react with the α -keto-carboxylic acid to give products via path 3. However, singlet oxygen has previously been shown not to be involved to a significant extent, if at all, in the dye-sensitized photo-oxygenation reaction of α -keto-carboxylic acids,^{48,71} and therefore paths 2 and 3 can be excluded from further discussion.

It is known that α -keto-carboxylic acids react with the triplet state of dyes,⁷¹ and hence this could result in a radical process occurring via

Also the small amounts of oxygen in the nitrogen, although low, could quench the triplet state of the dye and effect the efficiency of the reaction by path 4, i.e. becoming less efficient than under argon and hence having lower carbon dioxide yields (Tables 2.31, 2.32 and 2.33) for this reason.

When the reaction is performed under air paths 4, 5 and 6 could all lead to decarboxylation. The higher concentration of oxygen in air, as compared to nitrogen, will lead to efficient scavenging of acyl radicals which are formed in path 4b, and give rise to more than one mole of carbon dioxide through the intermediate per-acids produced in path 5. Superoxide formation will also be more efficient at this higher oxygen concentration (path 6), and may lead to decarboxylation. Obviously more triplet dye will be quenched at the higher oxygen concentration but this is counteracted by efficient radical scavenging by paths 5 and 6.

Quenching of triplet dye becomes marked when the reactions are carried out in pure oxygen, i.e. 100% concentration, and reduces the efficiency of reaction via path 4 and hence decreased yields of carbon dioxide are obtained under oxygen as compared to air, as less radicals are produced that can be effectively scavenged by oxygen.

Oxygen concentration studies have previously been carried out on photo-oxygenation reactions.^{88,89} In the dye-sensitized oxidation of amines⁸⁸ it has been shown that a reaction involving only singlet oxygen is insensitive to change in oxygen concentration, unless extremely low concentrations of oxygen are employed. However a rate enhancement or retardation by decrease in oxygen concentration, e.g. reaction under pure oxygen as compared to air, may indicate a radical pathway. From this study⁸⁸ it was observed that both singlet oxygen and radical pathways are operative in the dye-sensitized oxidation of amines. It was also noted⁸⁸

that for high conversion of starting material to products, an acceleration should be observed under lower oxygen concentrations, i.e. oxygen compared to air, if reaction is via a radical pathway, and this was found to be the case in the results reported here.

The rate of the dye-sensitized photo-oxygenation of tetramethylethylene has been shown to be similar under oxygen and air,⁸⁹ as would be expected for a reaction involving only singlet oxygen.⁸⁸ However an oxygen dependency was found to exist for the dye-sensitized photo-oxygenation of trans-stilbene, and was explained on the basis of the involvement of an electron transfer process, rather than the participation of singlet oxygen,⁸⁹ in the reaction.

The finding of an oxygen dependency upon the dye-sensitized photo-oxygenation of α -keto-carboxylic acids (Tables 2.31, 2.32 and 2.33), provides further evidence to support the previously reported observations^{48,71} that the reaction does not involve singlet oxygen and that a dye-acid interaction with radical intermediates is operative, as shown in Scheme 2.23.

Differences in the photo-physical properties of Rose Bengal obtained from various sources has been observed,⁹⁰ and would account for the yields of carbon dioxide obtained from B.D.H. Chemical Co. Ltd. (Table 2.31) and Eastman-Kodak Ltd. (Table 2.33) Rose Bengals respectively, in the dye-sensitized photo-oxygenation of α -keto-glutaric acid. The above observation, together with the finding that the yield of carbon dioxide is dependent upon the rate of flushing of oxygen through the solutions (Table 2.31), shows that careful evaluation is required when comparing the results obtained from different laboratories, as a variation in results may arise by overlooking these points.

Summary

The yields of carbon dioxide from the dye-sensitized photo-oxygenation of α -keto-carboxylic acids are dependent upon (i) the oxygen concentration, (ii) the source of the sensitizing dye, and (iii) the flow rate of oxygen. The results support a mechanism involving dye - acid interaction leading to radical formation rather than a singlet oxygen mediated reaction.

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CHAPTER 3

PHOTOCHEMICAL REACTIONS OF α -KETO-CARBOXYLIC
ESTERS

*"Imagine no possessions
I wonder if you can
No need for greed or hunger
A brotherhood of man
Imagine all the people
Sharing all the world*

*You may say I'm a dreamer
But I'm not the only one
I hope someday you'll join us
And the world will be as one"*

John Lennon 1940-1980

PHOTOCHEMICAL REACTIONS OF α -KETO-CARBOXYLIC ESTERS

INTRODUCTION

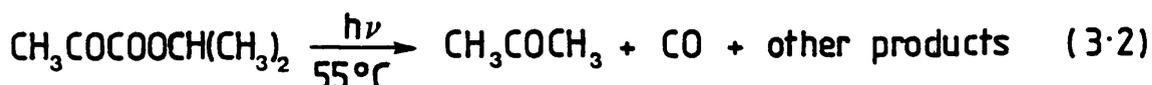
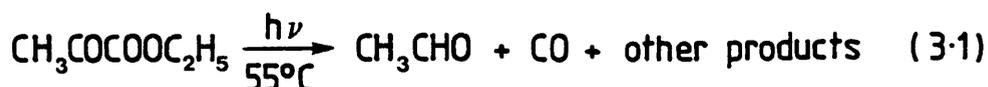
Preface

The following sections contain a review of the literature pertaining to the photochemical reactions of α -keto-carboxylic esters, both under direct and dye-sensitized conditions. The mechanisms suggested to be involved in these reactions are discussed.

3.1 DIRECT IRRADIATION OF α -KETO-CARBOXYLIC ESTERS

3.1 (i) PYRUVATES AND PHENYLGLYOXYLATES

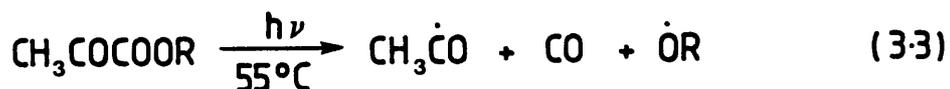
Leermakers and co-workers¹ studied the vapour phase decomposition of ethyl and isopropyl pyruvates. In both cases complex mixtures of products were obtained. The principal products from the photolysis of ethyl pyruvate were acetaldehyde and carbon monoxide respectively (Equation 3.1), whereas irradiation of isopropyl pyruvate produces mainly acetone and carbon monoxide, (Equation 3.2).



The yield of acetaldehyde from the photolysis of ethyl pyruvate was found to decrease after long irradiation times,¹ presumably due to secondary reactions. Also, modest pressures of oxygen did not significantly affect the efficiency, or the course, of the photodecomposition of isopropyl pyruvate.¹

The mechanism of the vapour phase photodecomposition of ethyl and isopropyl pyruvates is thought to initially involve radical formation from

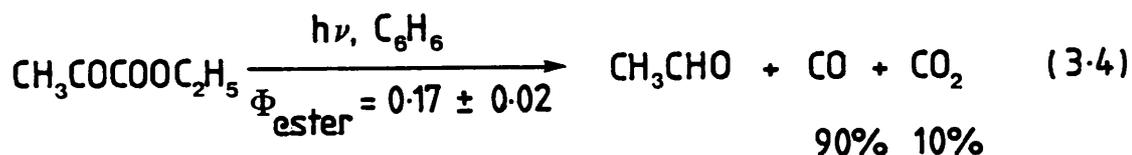
the carbon-carbon bond cleavage,¹ as shown in Equation 3.3.



(where R = ethyl or isopropyl)

The mechanism of the photochemical reactions of α -keto-carboxylic esters in oxygen-free solution is not well understood and subject to much conjecture.^{2,3} These reactions are highly dependent upon irradiation conditions, such as the nature of the solvent employed, and are described below.

Hammond and co-workers⁴ reported that irradiation of ethyl pyruvate in benzene solution yields acetaldehyde, carbon monoxide and small amounts of carbon dioxide as the only isolable products, (Equation 3.4).

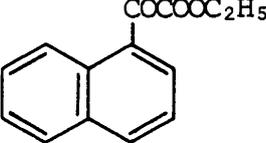


The triplet state of ethyl pyruvate was deemed responsible for the photodegradation due to the finding (i) of a weak blue phosphorescence (in ether-pentane-alcohol glass at 77°K) and (ii) that benzophenone sensitized the photodecomposition, as evidenced by an increase in the quantum yield for ethyl pyruvate disappearance, from 0.17 to 0.32 in the presence of the ketone.

Leermakers and co-workers⁵ studied the photodecomposition of a series of α -keto-carboxylic esters, in benzene solution, in an attempt to elucidate the mechanism of the primary photochemical process leading to fragmentation, and their findings are summarised in Table 3.1.

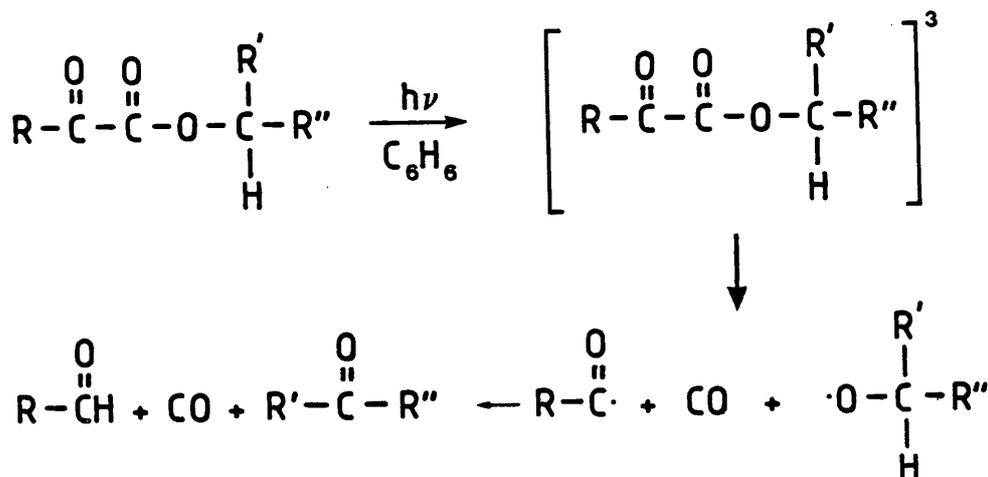
These authors⁵ argued that if hydrogen abstraction was the primary photochemical step, then deuterium incorporation at the appropriate

TABLE 3.1⁵

| α -Keto-carboxylic ester | Products (%) | Φ Ester photodecomposition |
|--|---|---------------------------------|
| $\text{CH}_3\text{COCOCH}_3$ | CH_3CHO (20) CH_2O (8) CO (65) | 0.15 ± 0.02 |
| $\text{CH}_3\text{COCOOC}_2\text{H}_5$ | CH_3CHO (60) CO (80) | 0.17 |
| $\text{CH}_3\text{COCOCH}(\text{CH}_3)_2$ | CH_3CHO (15) CH_3COCH_3 (83) CO (50) | 0.18 ± 0.01 |
| $\text{CH}_3\text{COCOCD}(\text{CH}_3)_2$ | Not reported | 0.19 ± 0.02 |
| $\text{C}_6\text{H}_5\text{COCOOC}_2\text{H}_5$ | $\text{C}_6\text{H}_5\text{CHO}$ (30) CH_3CHO (25) CO (30) | 0.056 ± 0.005 |
|  | Not reported | <0.01 |

position of the isopropyl pyruvate should result in a decrease in the quantum yield for ester disappearance. However, the quantum yield for the disappearance of isopropyl pyruvate was found to be insensitive to deuterium substitution ($\Phi_{\text{H}} = 0.18 \pm 0.01$; $\Phi_{\text{D}} = 0.19 \pm 0.02$; Table 3.1), and a mechanism involving photodecarbonylation in the primary process, leaving caged acyl and alkoxy radicals which can disproportionate to give the observed photoproducts, was suggested, (Scheme 3.1).

In accord with the previous findings by Hammond and co-workers,⁴ the reactive state was ascribed as being the triplet, based on the observations of phosphorescence from ethyl pyruvate (in ether-pentane-alcohol glass at 77°K) and isopropyl pyruvate (in ethanol glass at 77°K) corresponding to triplet energies of 65.0 Kcal and 64.5 Kcal respectively.⁵



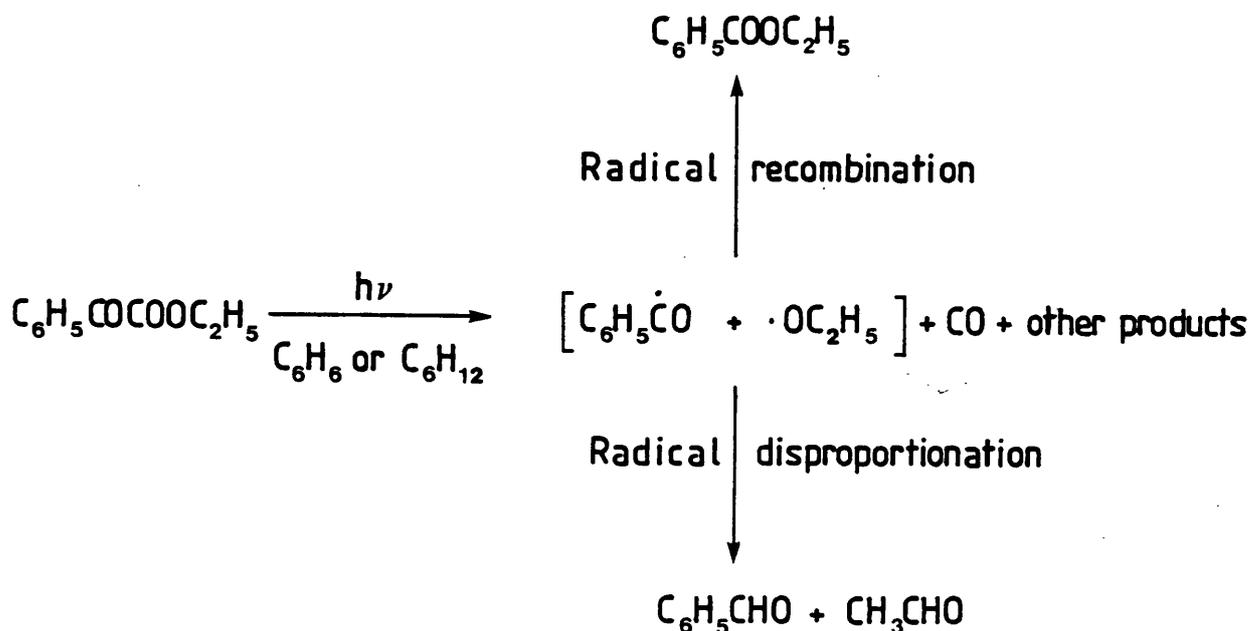
(where R = alkyl or aryl; R' and R'' = alkyl and/or hydrogen)

Scheme 3.1

Leermakers and co-workers⁵ suggested that the low quantum yield for disappearance of ethyl- α -naphthylglyoxylate may be due to the fact that its triplet state is so low lying that the ester does not possess enough energy to undergo carbon-carbon bond cleavage, although this finding can be equally well explained⁶ on the basis of the low reactivity of naphthyl ketones in hydrogen abstraction reactions.⁷ It was also noted by Neckers³ that as all of the pyruvate esters decompose with the same efficiency, (Table 3.1), this may indicate that the hydrogen abstraction reaction is very exothermic and so rapid that no isotope effect would be expected, even if a hydrogen abstraction step did occur.

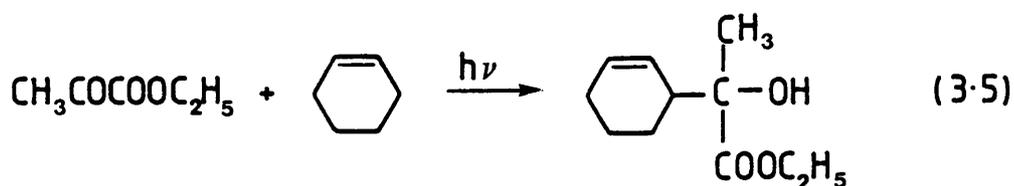
Further evidence to support a radical cleavage mechanism, similar to that proposed by Leermakers and co-workers,⁵ (Scheme 3.1), comes from the results obtained by Tominaga and co-workers⁸ when studying the photo-decomposition of ethyl phenylglyoxylate in benzene and cyclohexane solutions. In addition to the finding of carbon monoxide, benzaldehyde and acetaldehyde in the complex mixture of products, the observation of ethyl benzoate was highlighted.⁸ Thus it would appear that carbon-carbon

bond cleavage can occur leading to direct decarbonylation and the acyl and alkoxy radicals thus produced can undergo subsequent recombination to yield ethyl benzoate, or disproportionate to yield benzaldehyde and acetaldehyde, as outlined in Scheme 3.2.



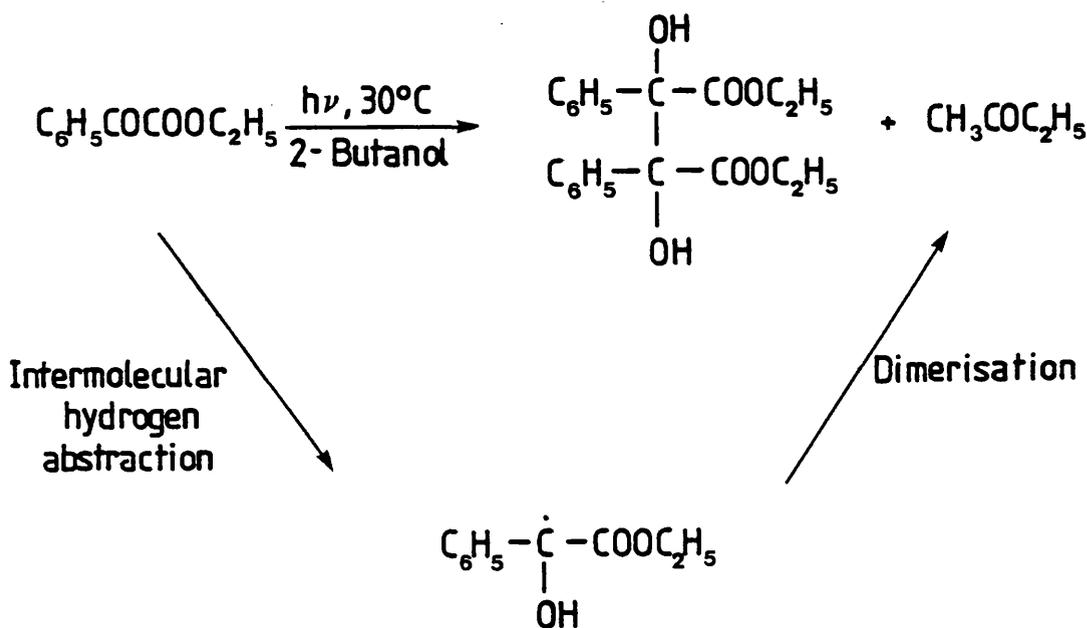
Scheme 3.2

Jolly and De Mayo⁹ have shown that ethyl pyruvate upon irradiation in cyclohexene solution undergoes a solvent addition reaction. A mechanism involving initial hydrogen abstraction from cyclohexene by the triplet ester, followed by a radical coupling process, would account for the formation of the hydroxy-ester so observed, (Equation 3.5).



Further studies^{10,11} have been carried out to investigate the photo-reduction reactions of α -keto-carboxylic esters in appropriate hydrogen donating solvents.

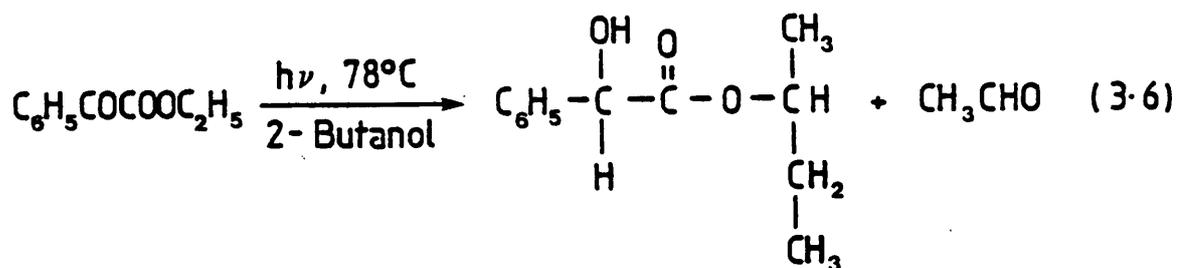
Huysen and Neckers¹⁰ studied the reactions of a series of alkyl esters of phenylglyoxylic acid in various alcohol solutions, and a marked temperature dependency upon the course of the reactions was found to exist. At lower temperatures reductive dimerisation appears to be an important process, exemplified by the reaction of ethyl phenylglyoxylate in 2-butanol. The major products are diethyl- α,α' -diphenyltartrate and 2-butanone, which indicate that the primary process is an intermolecular hydrogen abstraction, with subsequent radical dimerisation yielding diethyl- α,α' -diphenyltartrate, (Scheme 3.3).



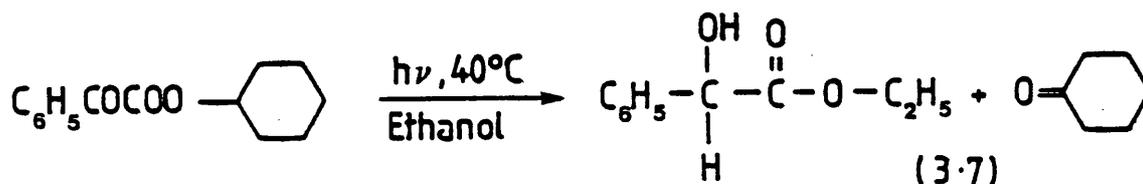
Scheme 3.3

At higher temperatures the reaction takes a completely different route, with 2-butyl mandelate and acetaldehyde being the major products from irradiation of ethyl phenylglyoxylate in 2-butanol, which suggests that an intramolecular hydrogen abstraction process is operative, (Equation 3.6).

Similarly, ethyl mandelate and cyclohexanone are the major products



from irradiation of cyclohexyl phenylglyoxylate in ethanol solution at 40°C, (Equation 3.7).



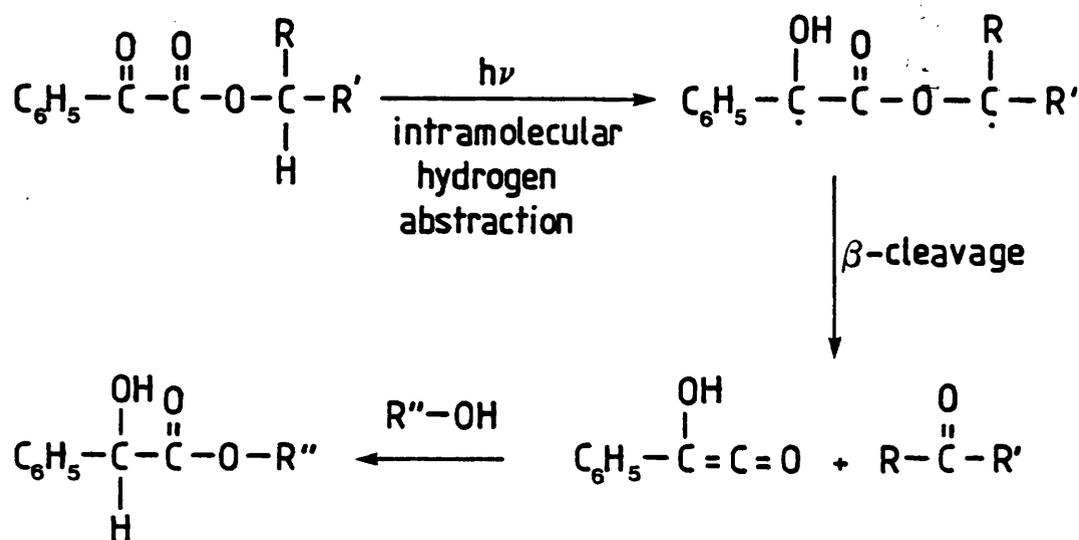
Huyser and Neckers¹⁰ found the reaction at elevated temperature to be general for a series of alkyl esters of phenylglyoxylic acid, in each case the phenylglyoxylate being reduced to the mandelate ester of the solvent alcohol, and the alcohol moiety of the phenylglyoxylate being oxidised. These results¹⁰ are summarised in Table 3.2.

TABLE 3.2¹⁰

Photochemical reactions of alkyl phenylglyoxylates in alcoholic solution at 78°C

| Alkyl phenylglyoxylate | Solvent alcohol | Products |
|------------------------|-------------------|---|
| Ethyl | Cyclohexanol | Cyclohexyl mandelate, acetaldehyde |
| Ethyl | <i>l</i> -Menthol | <i>l</i> -Menthyl mandelate, acetaldehyde |
| 2-Propyl | Ethanol | Ethyl mandelate, acetone |
| 2-Hexyl | Ethanol | Ethyl mandelate, 2-hexanone |
| 2-Octyl | Ethanol | Ethyl mandelate, 2-octanone |
| 2-Octyl | 2-Butanol | 2-Butyl mandelate, 2-octanone |

The mechanism Huyser and Neckers¹⁰ proposed in order to account for the formation of the mandelate esters involves initial hydrogen abstraction to yield a diradical that undergoes β -cleavage giving a hydroxy ketene which then reacts with the solvent alcohol to produce the appropriate mandelate ester, as outlined in Scheme 3.4.



(where, for example, R and R' = alkyl and/or hydrogen;
R'' = ethyl or 2-butyl)

Scheme 3.4

To account for the temperature effect upon the course of the reaction, the authors¹⁰ suggest that at lower temperatures the rate of intramolecular hydrogen abstraction is slower than that of intermolecular hydrogen abstraction, and dimeric products result. However, at higher temperatures a marked increase in the rate of the slower reaction, namely intramolecular hydrogen abstraction, ensues favouring the formation of the mandelate ester.

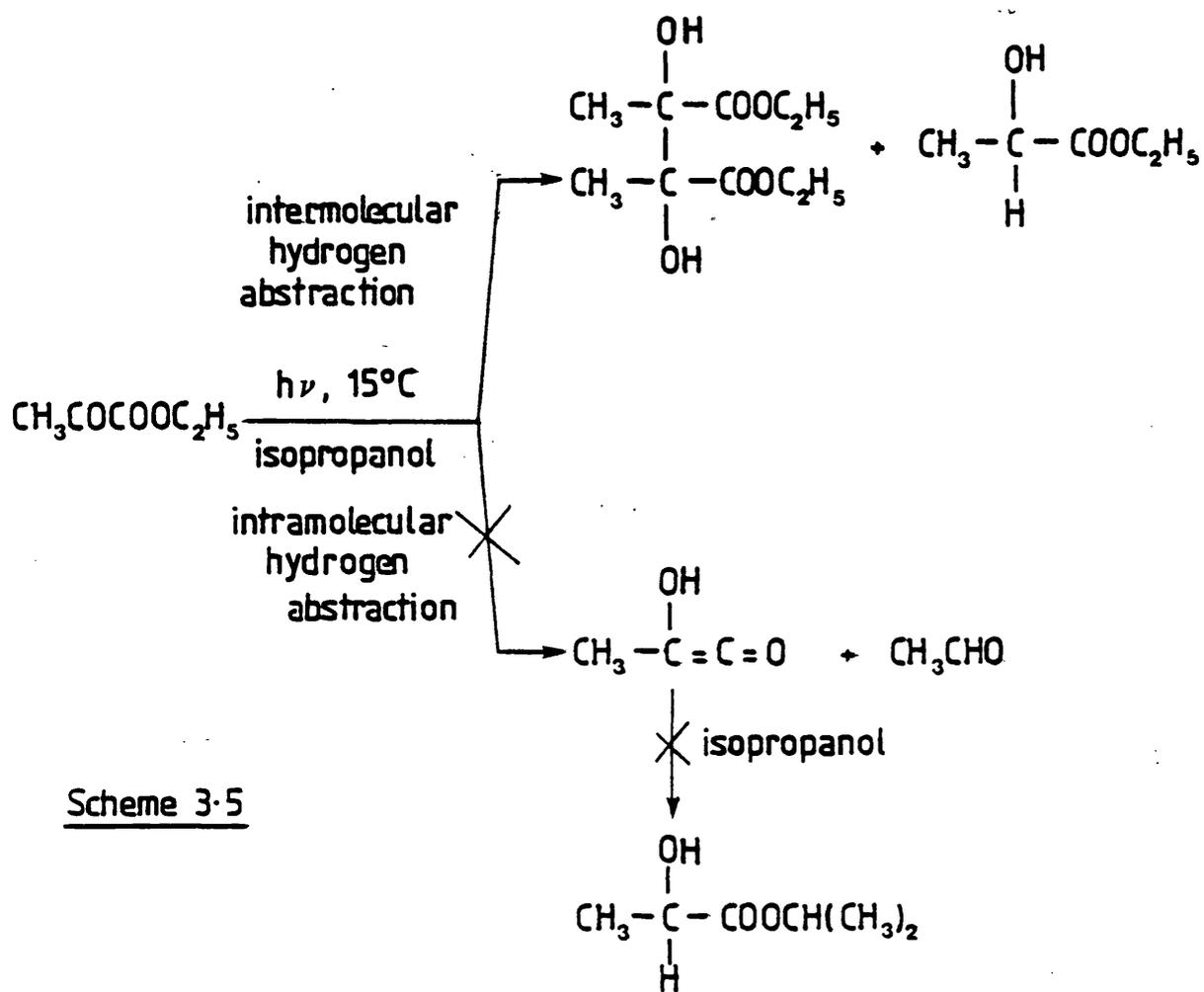
Monroe⁶ subsequently questioned the existence of the hydroxy ketene as an intermediate in these reactions on the basis that phenylglyoxal, the keto form of the hydroxy ketene, was not an observed reaction product as

may be expected. However, it is possible that the rate of reaction of the hydroxy ketene with the solvent alcohol, yielding the mandelate ester, is much faster than the rate of tautomerisation which would yield the phenylglyoxal, and this may explain the absence of the latter in the product mixture.

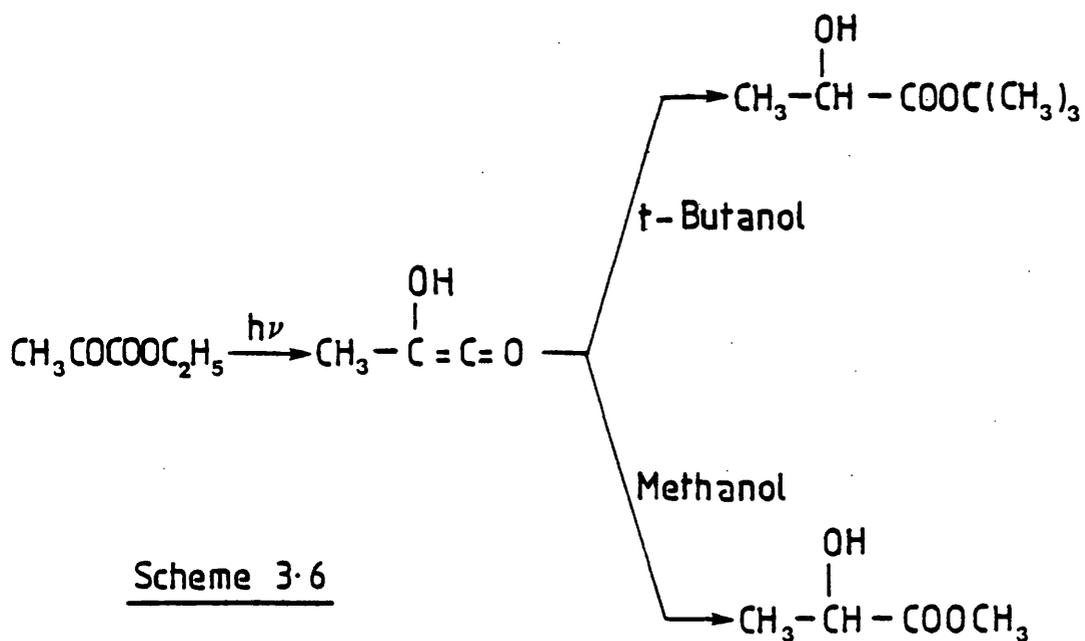
In an attempt to trap the hydroxy ketene formed in the intramolecular hydrogen abstraction process, as proposed by Huyser and Neckers,¹⁰ Yang and Morduchowitz¹¹ studied the reaction of ethyl pyruvate in isopropanol. No trapping product (i.e. isopropyl lactate) was isolated, indicating that intramolecular hydrogen abstraction may not be occurring in isopropanol, and the observed products, dimethyltartrate and small amounts of ethyl lactate, result presumably from intermolecular hydrogen abstraction from the solvent alcohol, with subsequent radical dimerisation, (Scheme 3.5).

It should be noted, however, that the temperature used in the above reaction by Yang and Morduchowitz¹¹ was low (15°C), and the dimeric product which they observed is in accord with the findings of Huyser and Neckers¹⁰ that reductive dimerisation is an important process for photodecomposition of α -keto-carboxylic esters at reduced temperatures.

More recently, evidence for the existence of hydroxy ketene intermediates in the photolysis of α -keto-carboxylic esters has been forwarded by DeBergalis,¹² who isolated esters of lactic acid from pyruvates when irradiated in alcoholic solvents. Thus the photolysis of ethyl pyruvate in *t*-butanol led to the formation of *t*-butyl lactate. Similarly, when methanol was used as solvent for the reaction, methyl lactate was produced. DeBergalis¹² suggested that these esters, *t*-butyl and methyl lactate, arise from the reaction of the hydroxy ketene, produced by intramolecular hydrogen abstraction, with the solvent alcohol, as shown in



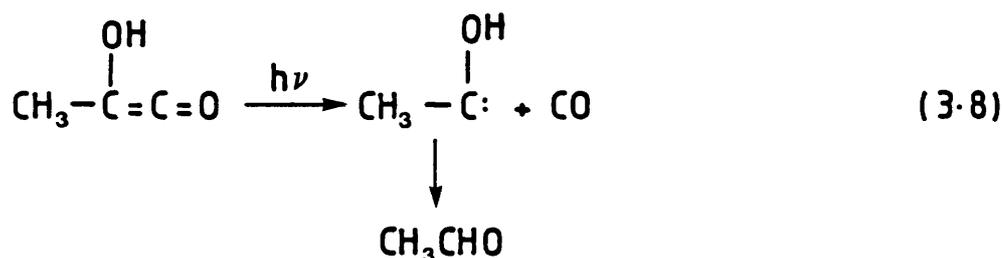
Scheme 3-5



Scheme 3-6

Scheme 3.6.

To account for the formation of acetaldehyde and carbon monoxide from irradiation of ethyl pyruvate, as observed in previous investigations,^{4,5} DeBergalis¹² proposes that the methyl hydroxy ketene, produced by intramolecular hydrogen abstraction, would undergo photolytic decarbonylation to yield methyl hydroxy carbene which would subsequently rearrange to form acetaldehyde, (Equation 3.8).

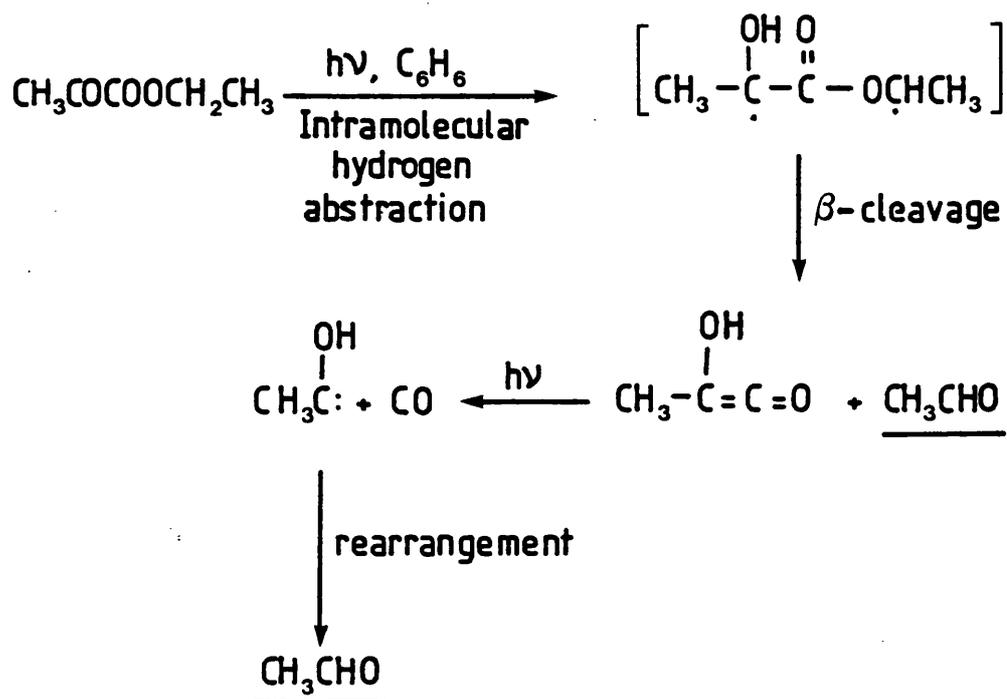


Yang and Morduchowitz¹¹ have previously suggested that ethyl pyruvate upon photolysis in benzene solution produces carbon monoxide and a two molar equivalent of acetaldehyde, (Equation 3.9).



Using the proposal put forward by DeBergalis¹² (Equation 3.8) it is possible to rationalise the formation of two moles of acetaldehyde as observed by Yang and Morduchowitz,¹¹ in the photodecomposition of ethyl pyruvate in benzene solution. The first mole of acetaldehyde could arise from the β -cleavage of the diradical formed by initial intramolecular hydrogen abstraction, and the second mole of acetaldehyde could be produced by the further photolytic decarbonylation of the methyl hydroxy ketene, by rearrangement of the methyl hydroxy carbene so produced, (Scheme 3.7).

The intermediacy of methyl hydroxy carbene in the gas phase photolysis



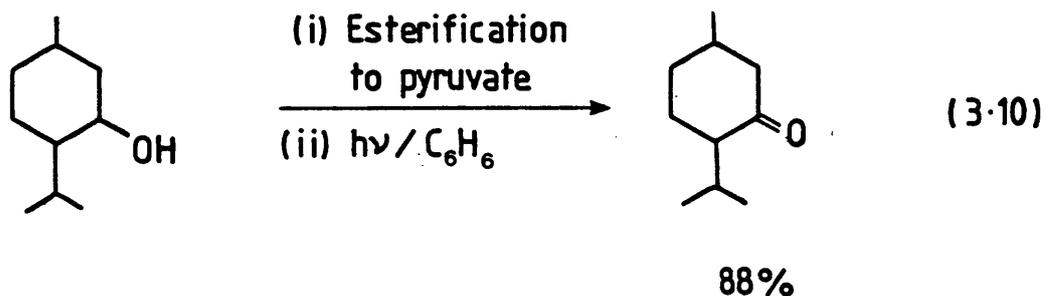
Scheme 3.7

of pyruvic acid has been proposed by Vesley and Leenmakers,¹³ and its existence has been supported by Turro and co-workers¹⁴ who observed a C₂H₄O fragment in the mass spectral breakdown of pyruvic acid. Leenmakers and Vesley¹⁵ also invoked the intermediacy of methyl hydroxy carbene in the aqueous photodecomposition of pyruvic acid, although this claim was later shown to be unfounded by Closs and Miller,¹⁶ who could find no evidence for its existence when studying the same reaction utilising the technique of CIDNP. As yet there is no evidence which disclaims the suggested existence of methyl hydroxy carbene in the gas, or non-aqueous, phase photodecomposition of pyruvic acid or alkyl pyruvates.

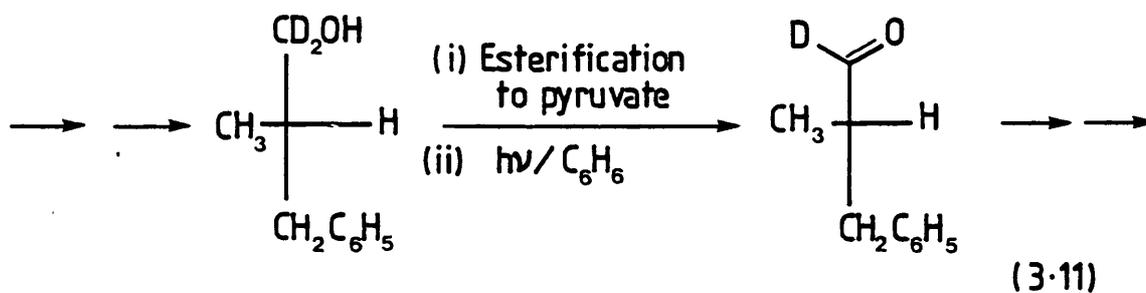
It is apparent from the work cited herein that the mechanism of photodecomposition of α -keto-carboxylic esters is not known with any degree of certainty and is worthy of further investigation.

Binkley¹⁷ has exploited the fact that irradiation of alkyl pyruvates gives high yields of carbonyl compounds by utilising pyruvate photo-

fragmentation as a synthetic tool in the oxidation of sensitive alcohols to the corresponding carbonyl derivative. Thus the pyruvate esters of a series of alcohols were prepared and irradiated in benzene solution to give excellent yields of the desired carbonyl compound. The conversion of menthol to menthone is an example of this synthetic pathway, (Equation 3.10).



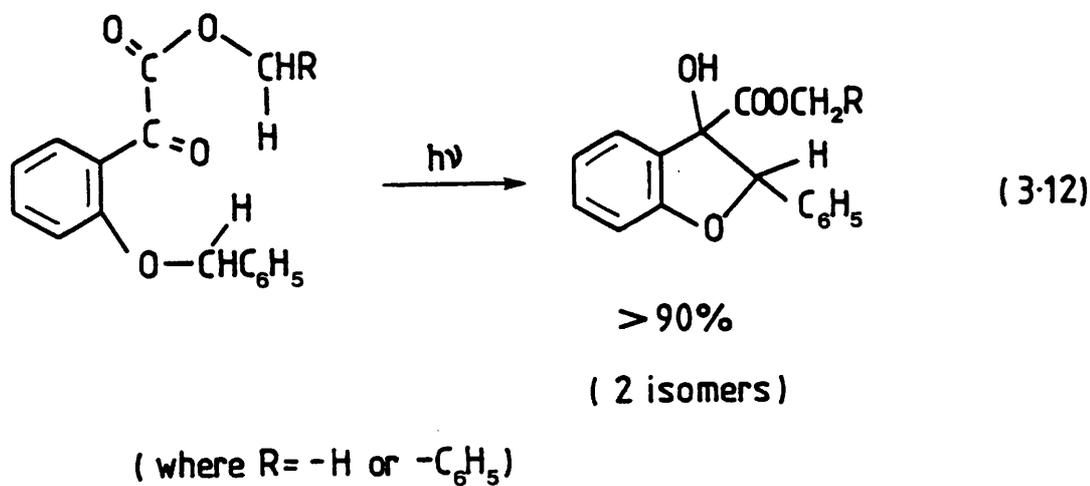
Pyruvate photo-fragmentation has also been used in part of a reaction sequence in the preparation of compounds containing chiral methyl groups adjacent to an asymmetric centre, as shown in the recent synthesis of (3R, 4S)- and (3R, 4R)-[4-²H, ³H]valine, by Townsend and co-workers,¹⁸ (Equation 3.11).



3.1(ii) OTHER α -KETO-CARBOXYLIC ESTERS

Pappas and co-workers^{19,20} have investigated the photochemical reactions of methyl- and benzyl-o-benzyloxyphenylglyoxylates and have established that intramolecular cyclisation occurs to afford an isomeric mixture of products in high yield, (Equation 3.12). The initial process in the cyclisation mechanism is that of intramolecular hydrogen abstrac-

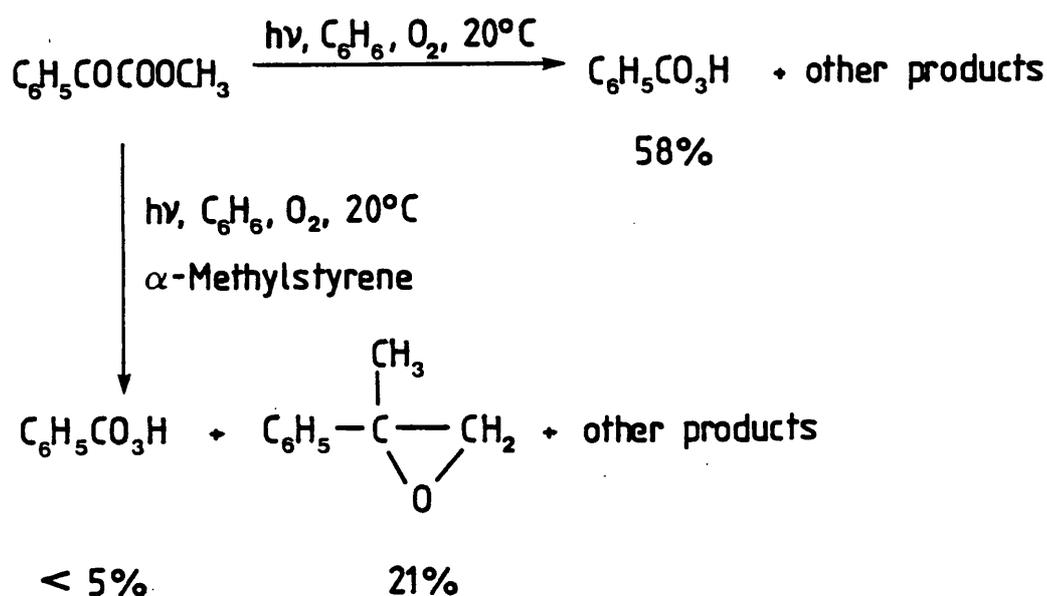
tion, however this abstraction occurs at the benzyl ether carbon via a seven-membered cyclic transition state in preference to the alkoxy ester carbon via a six-membered ring. This observation may be due to the fact that intramolecular hydrogen abstraction from the six-membered transition state is reversible, whereas this may not be the case for abstraction from the seven-membered state which results in trapping the observed photoproducts. The results of quenching and sensitization studies, using naphthalene and benzophenone respectively, define the reactive intermediate as the triplet state.^{19,20}



Apart from the work by Pappas and co-workers,^{19,20} above, there are no other literature reports pertaining to the photochemistry of α -keto-carboxylic esters with available abstractable hydrogen atoms on the ketone side of the molecule, i.e. long chain α -keto-carboxylic esters such as alkyl- α -keto-octanates for example. However, work of a similar nature has been carried out on analogous α -keto-carboxylic acids, [see Chapter 2.1(iii)], in which Evans and Leermakers²¹ found that α -keto-decanoic acid, upon irradiation, produced hept-1-ene and pyruvic acid via an intramolecular hydrogen abstraction (or Norrish Type II) reaction. It remains to be seen whether the esters of long chain α -keto-carboxylic acids are capable of undergoing such reactions.

3.1(iii) EFFECT OF OXYGEN UPON DIRECT IRRADIATION

Sawaki and Ogata²² have recently reported the effect of oxygen upon the direct irradiation of methyl phenylglyoxylate in benzene solution, the major product of the reaction being per-benzoic acid. Per-acid formation is suggested to occur in an analogous manner to that which these authors²² have proposed for the photo-oxygenation of phenylglyoxylic acid (see Chapter 2.2), namely via a mechanism involving photochemical α -cleavage, followed by radical scavenging by oxygen to yield per-benzoic acid. Interestingly, if methyl phenylglyoxylate is irradiated in the presence of α -methylstyrene, then the per-benzoic acid transfers an atom of oxygen to the alkene to yield an epoxide, (Scheme 3.8).



Scheme 3.8

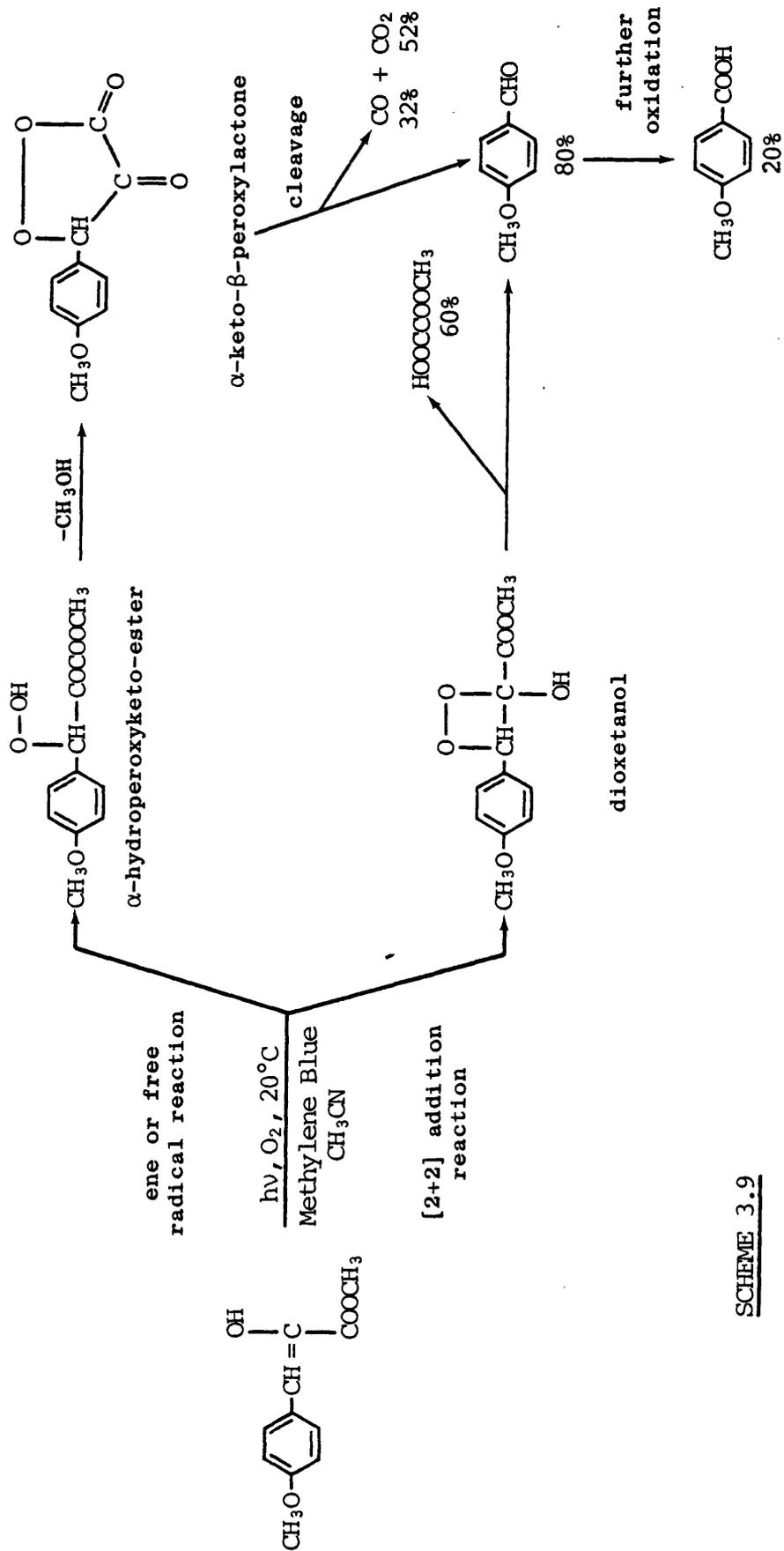
Apart from the above study by Sawaki and Ogata,²² showing that methyl phenylglyoxylate when irradiated in the presence of an alkene in oxygenated benzene solution leads to epoxide formation, no other reports have appeared relating to the rôle that oxygen may play in the direct photo-oxidation of other α -keto-carboxylic esters.

3.2 DYE-SENSITIZED PHOTO-OXYGENATION OF α -KETO-CARBOXYLIC ESTERS

Although α -keto-carboxylic acids have been the subject of numerous dye-sensitized photo-oxygenation investigations, (see Chapter 2.2), their ester counterparts have received little interrogation. However, photo-oxygenation studies have been performed on the enol tautomers of phenyl pyruvate ester derivatives.^{23,24}

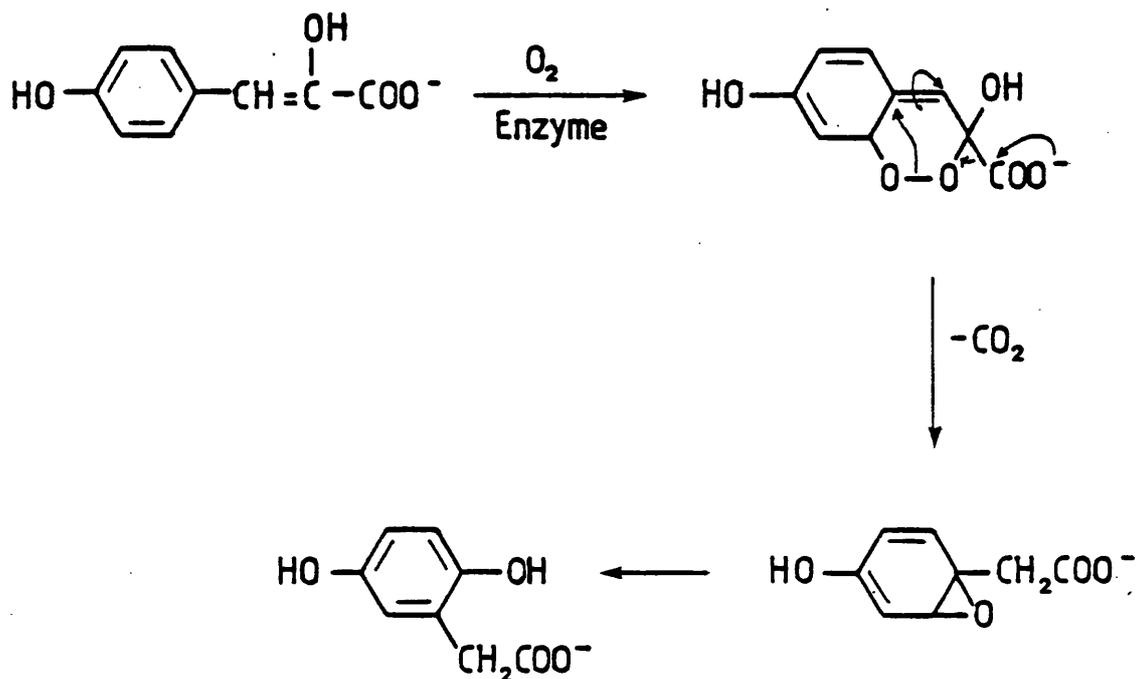
Jefford and co-workers²³ have described the photo-oxygenation of the enol form of the ester methyl-p-methoxyphenyl pyruvate. A singlet oxygen mechanism was suggested to operate in the Methylene Blue sensitized reaction in acetonitrile solution, and the intermediacy of an α -keto- β -peroxylactone and a dioxetanol were invoked in order to account for the formation of the observed photoproducts. [No definitive evidence was put forward to confirm the participation of singlet oxygen, and none of the proposed intermediates could be isolated.] It is possible to envisage that the α -hydroperoxyketo-ester could be produced by either an ene-type, or free radical, reaction of singlet oxygen upon methyl-p-methoxyphenyl pyruvate. The α -hydroperoxyketo-ester so produced would then have to lose methanol in order to undergo rearrangement to the desired α -keto- β -peroxylactone intermediate. The latter would undergo rapid cleavage to yield the products p-methoxybenzaldehyde, carbon monoxide and carbon dioxide. p-Methoxybenzoic acid would then arise from the further oxidation of p-methoxybenzaldehyde. A [2+2] addition reaction of singlet oxygen upon methyl-p-methoxyphenyl pyruvate, would account for the dioxetanol formation, and the subsequent cleavage of which yields the products p-methoxybenzaldehyde and monomethyl oxalate.

The proposed reaction pathway, showing the intermediate α -keto- β -peroxylactone, previously unknown as a stable entity, is summarised in Scheme 3.9.



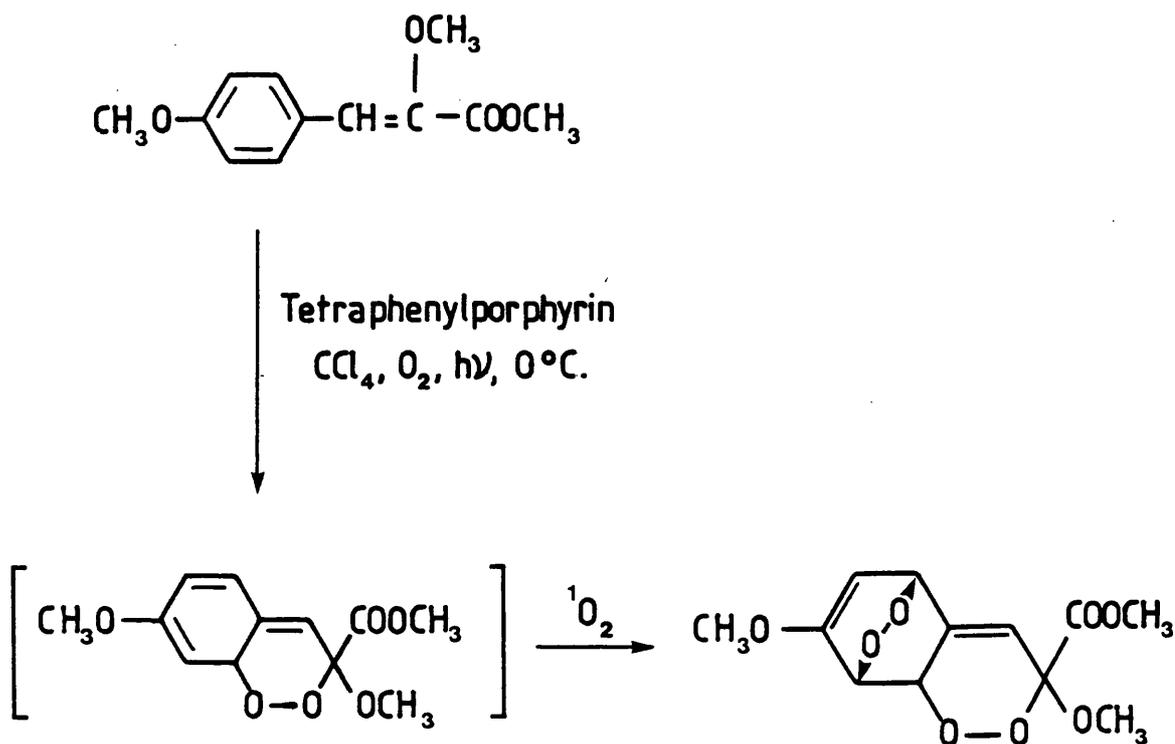
SCHEME 3.9

Kotsuki and co-workers²⁴ have carried out a similar study to that outlined above,²³ in an attempt to obtain chemical support for the mechanism proposed by Matsuura,²⁵ of the enzymatic conversion of p-hydroxyphenyl pyruvic acid into homogentisic acid. Matsuura²⁵ suggests a mechanism involving 1,4-addition of molecular oxygen to the enol tautomer of p-hydroxyphenyl pyruvate, as described in Scheme 3.10.



Scheme 3-10

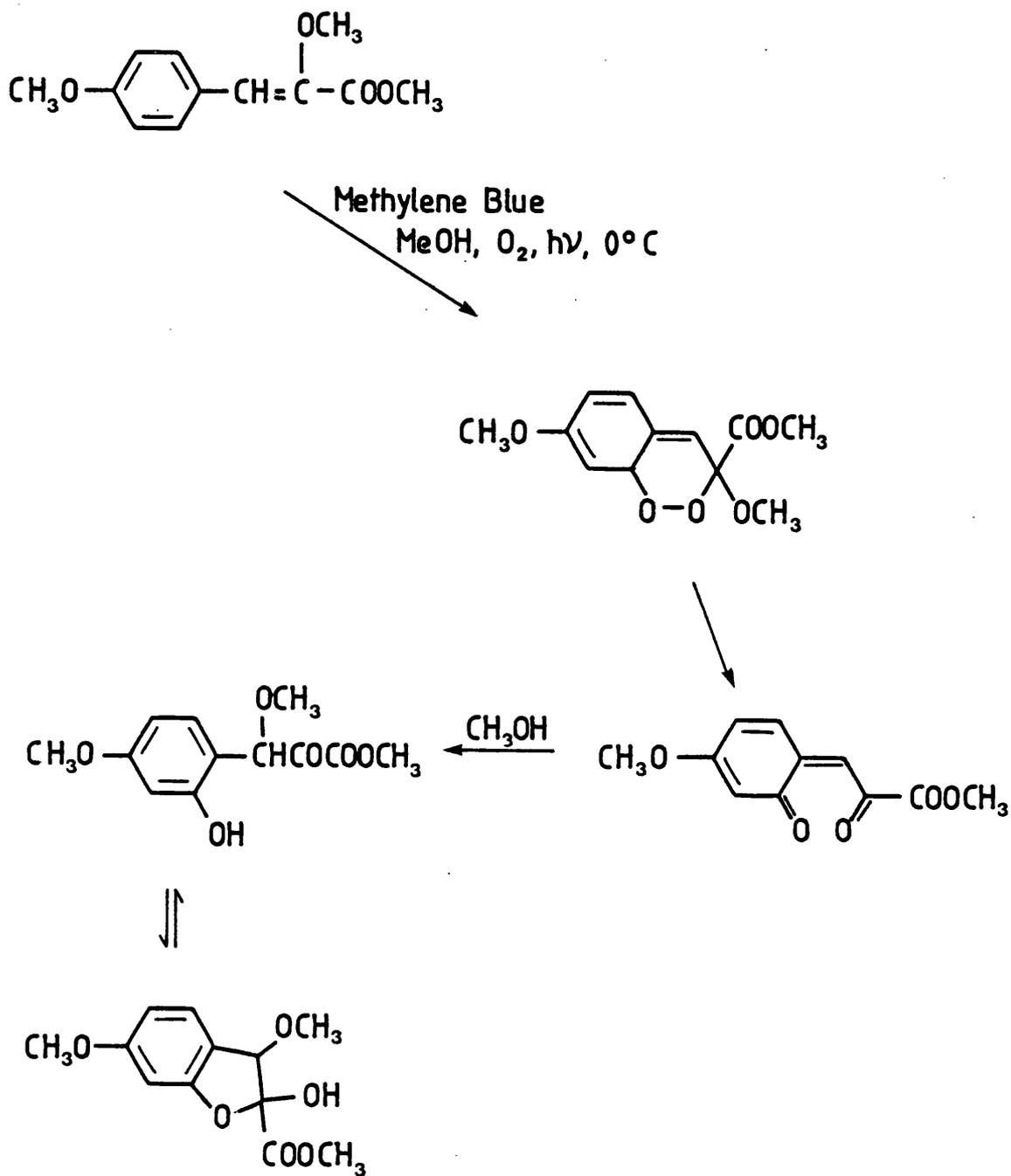
In their study, Kotsuki and co-workers²⁴ confirmed that p-methoxybenzaldehyde and monomethyl oxalate are produced in the Methylene Blue sensitized photo-oxygenation of methyl-p-methoxyphenyl pyruvate, as reported by Jefford and co-workers.²³ In addition it was also demonstrated that if the enol group was protected, for example by methyl substitution, then the pyruvate ester undergoes a 1,4-addition with singlet oxygen to yield a diendoperoxide, (Scheme 3.11). Low temperature photo-oxygenations in aprotic solvents were performed in an attempt to isolate the monoendoperoxide, but these proved unsuccessful.



Scheme 3.11

When the above reaction was performed using methanol as solvent, diendoperoxides are not observed, the isolated products being an equilibrated mixture of hydroxylated derivatives, as shown in Scheme 3.12.

The above work (Scheme 3.11) by Kotsuki and co-workers,²⁴ shows that the enol tautomer of methyl-p-methoxyphenyl pyruvate is capable of undergoing a 1,4-addition with singlet oxygen, under certain conditions and when the enol group is protected. The reaction pathway observed in methanol, (Scheme 3.12), is quite different from the enzyme reaction inasmuch as the chemical reaction results in meta- rather than para-hydroxylation, as is observed under enzymic conditions. The authors²⁴ suggest that the result obtained in the aprotic solvent (Scheme 3.11), showing 1,4-addition and diendoperoxide formation, does offer some chemical support for the mechanism proposed by Matsuura²⁵ (Scheme 3.10)



Scheme 3.12

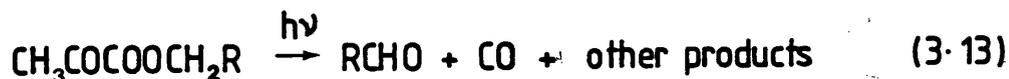
for the enzymic reaction.

To date there are no reports describing the dye-sensitized photo-oxygenation of the keto-tautomer of α -keto-carboxylic esters, as investigations have been confined solely to the enol tautomers, as described above.^{23,24}

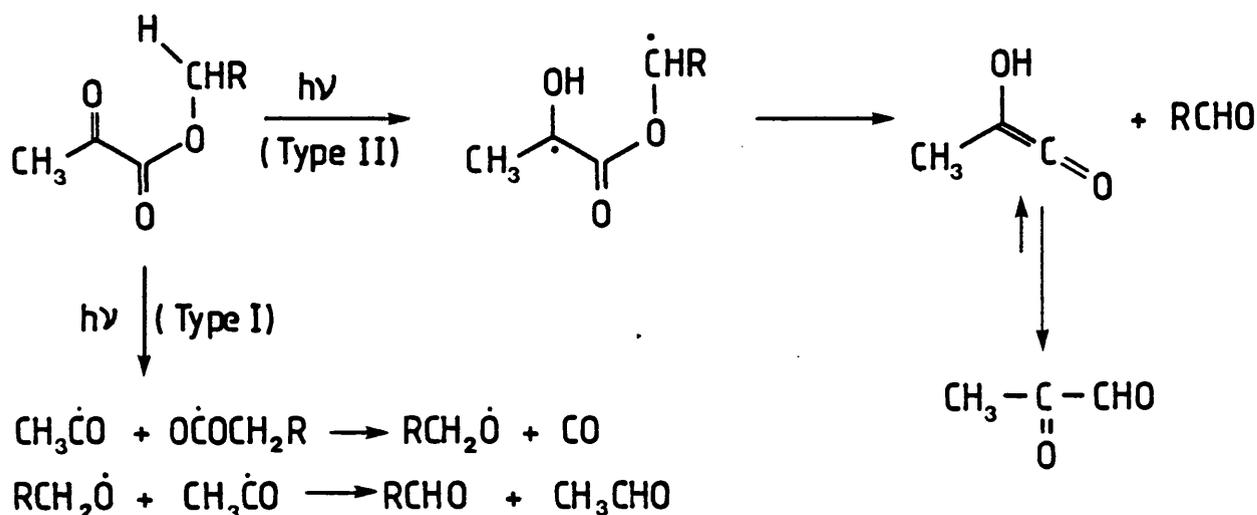
3.3 THE DIRECT PHOTO-INDUCED FRAGMENTATION OF ALKYL PYRUVATES

3.3(i) OBJECT OF INVESTIGATION

Alkyl pyruvates have been shown to undergo photo-induced fragmentation in the absence of oxygen,^{5,17} (Equation 3.13).



The mechanism by which this fragmentation reaction occurs has not been clearly established and two different mechanisms have been proposed to account for the observed oxidation of the alkyl group, and are labelled Type I⁵ and Type II^{12,26} because of their analogy to the fragmentation reaction of ketones, (Scheme 3.13).



Scheme 3.13

It has been clearly established that the fragmentation of methyl, ethyl and isopropyl pyruvates leads to carbon monoxide production.⁵ The oxidation of the alkyl group (RCH_2) to give carbonyl compounds has been shown to occur in good yield and can be used as part of a sequence of reactions to transform primary and secondary alcohols into carbonyl compounds.¹⁷ Although no direct evidence exists to confirm the inter-

mediacy of a hydroxy ketene in the fragmentation process, the observations that the use of alcohols as solvents for the reaction leads to the formation of esters of mandelic acid from phenylglyoxylates¹⁰ (Scheme 3.4; Table 3.2) and lactic acid from pyruvates¹² (Scheme 3.6), lends credence to their suggested formation, (i.e. via a Type II reaction). However, the finding that a number of alkyl pyruvates produce acetaldehyde favours the Type I mechanism if the isolated products are primary photochemical products.⁵

The following investigations are aimed at identifying the mechanism by which the photo-induced fragmentation reaction occurs.

3.3(ii) PHOTOLYSIS OF ALKYL PYRUVATES MONITORED BY ¹H N.M.R. SPECTROSCOPY

The decomposition of alkyl pyruvates and the formation of the observed photo-products were evaluated by following the reactions by ¹H n.m.r. spectroscopy, in both deuterated acetonitrile and deuterated benzene solutions, under degassed conditions. Samples were therefore irradiated in n.m.r. tubes for known periods of time and their spectra recorded on cessation of illumination. In this way the formation of formaldehyde, acetaldehyde, acetone and benzaldehyde from the degradation of methyl, ethyl, isopropyl/2-deuterioisopropyl and benzyl pyruvates respectively, were investigated and the results shown in Figures 3.1-3.5, and Table 3.3. From these results the rates of photo-induced decomposition of the alkyl pyruvates and the rates of formation of carbonyl compound were determined and are shown in Table 3.4.

The addition of a triplet quencher (naphthalene) to the reaction mixture slowed up both the rate of disappearance of the alkyl pyruvate and the rate of formation of the carbonyl compound in each case, (Table 3.4). Further quenching experiments were performed using varying concen-

FIG. 3.1

Photolysis of methyl pyruvate (0.1 M) in degassed solution

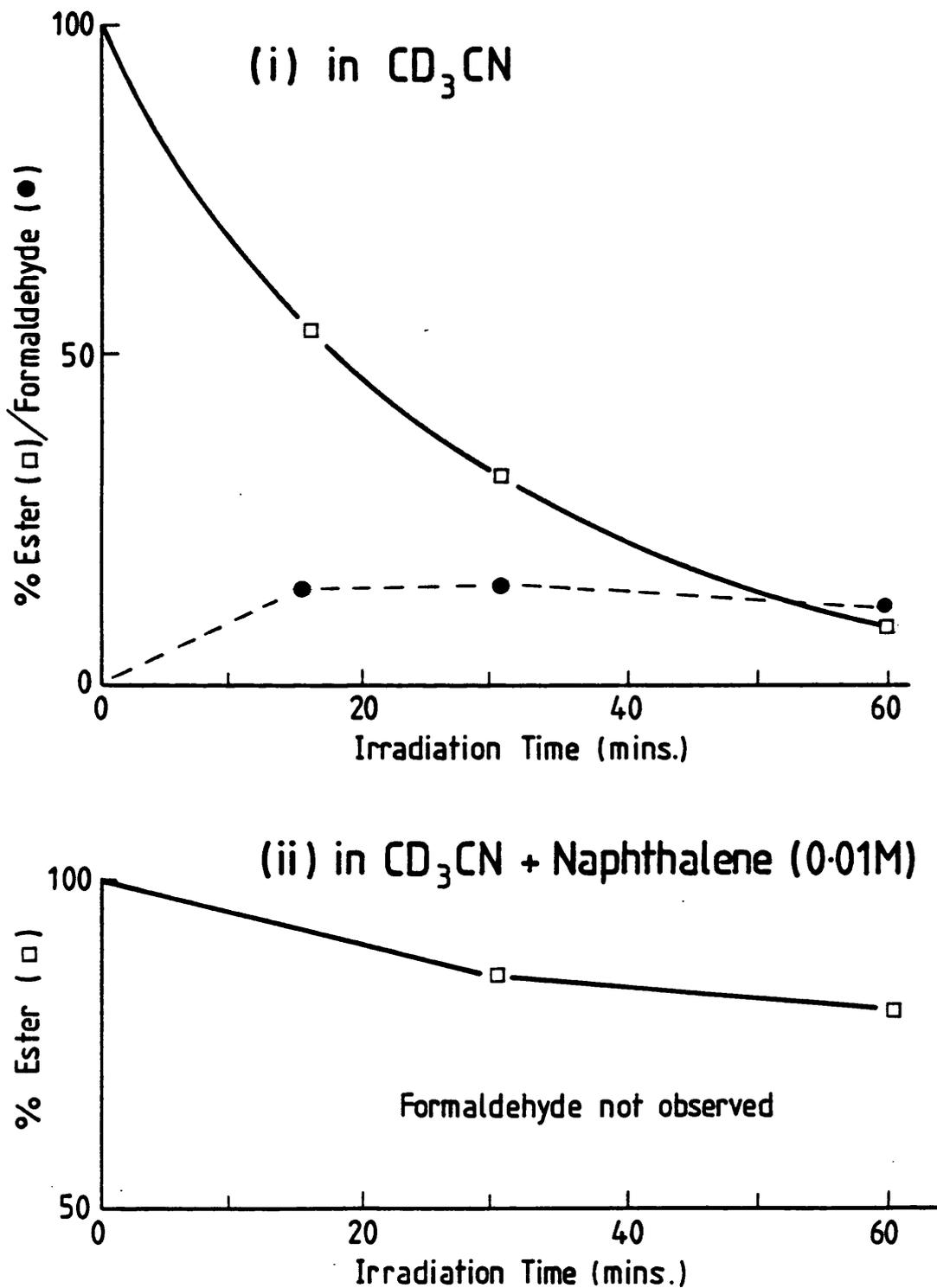
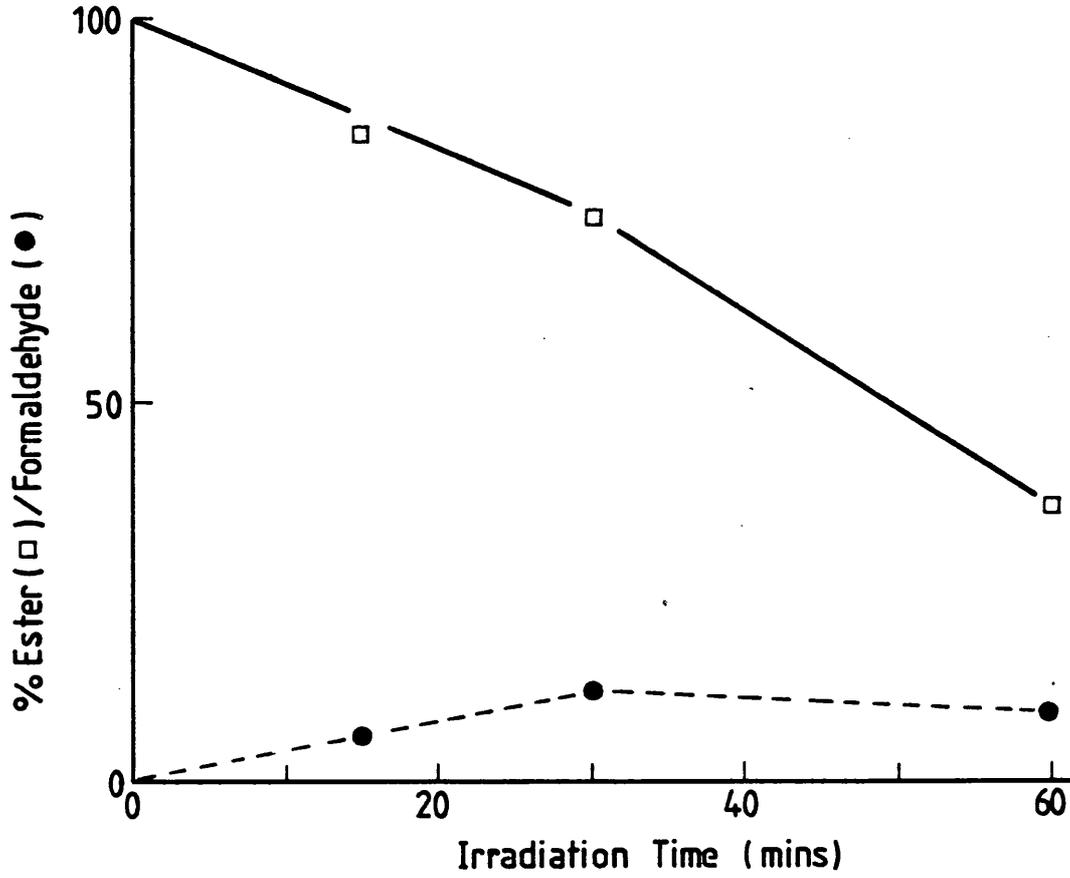


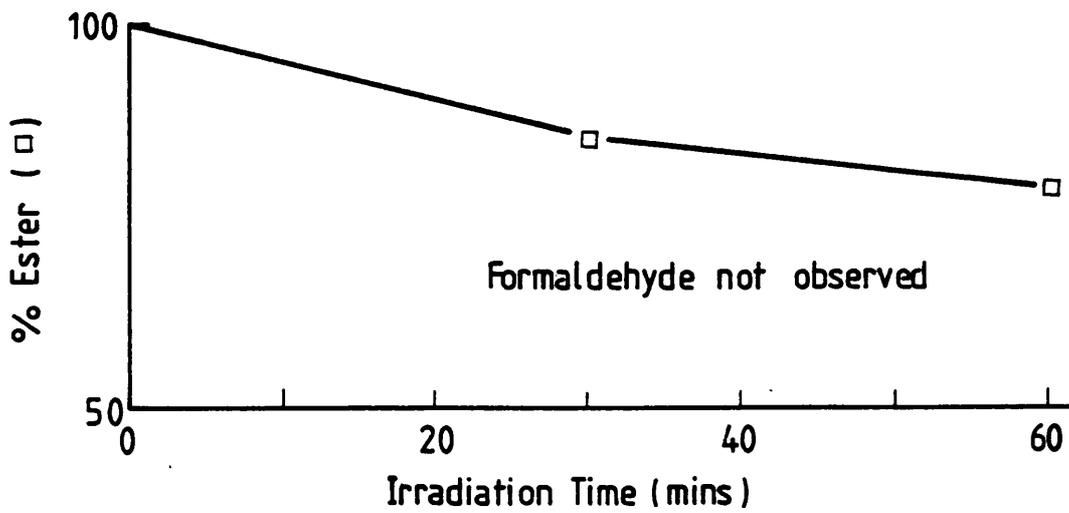
FIG. 3.1

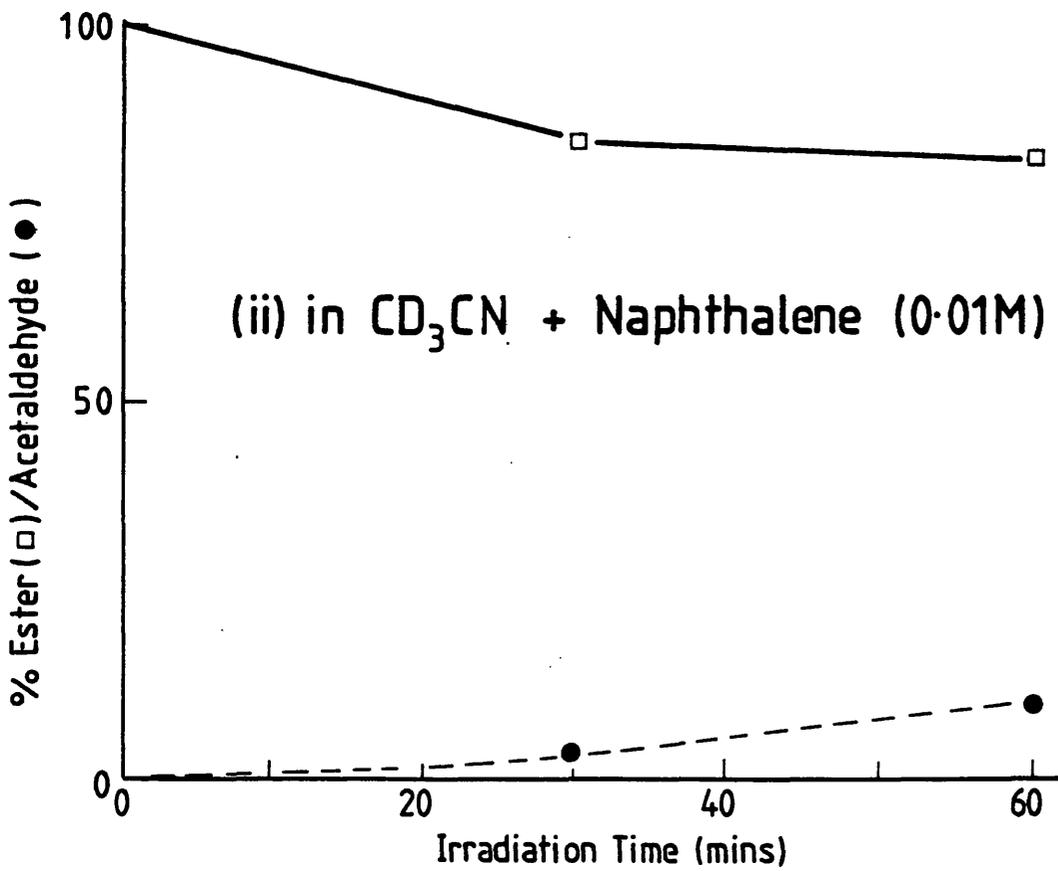
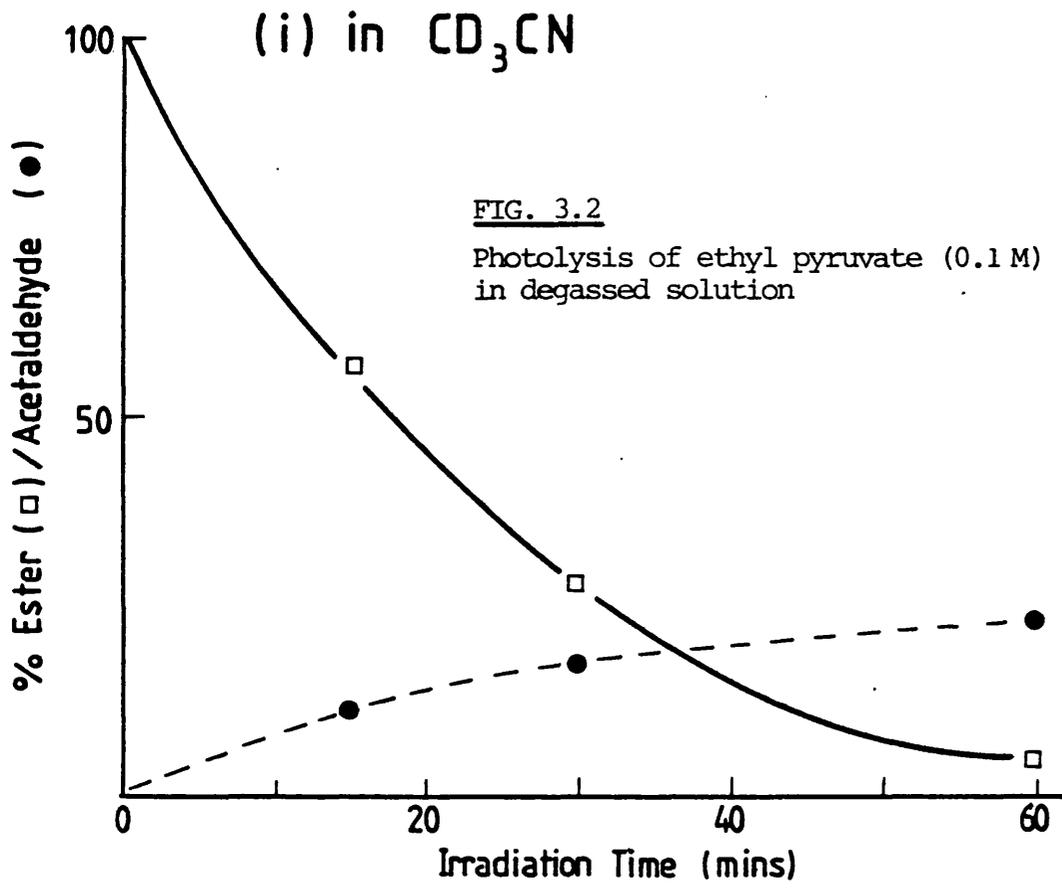
Photolysis of methyl pyruvate (0.1 M)
in degassed solution

(iii) in C_6D_6



(iv) in C_6D_6 + Naphthalene (0.01M)





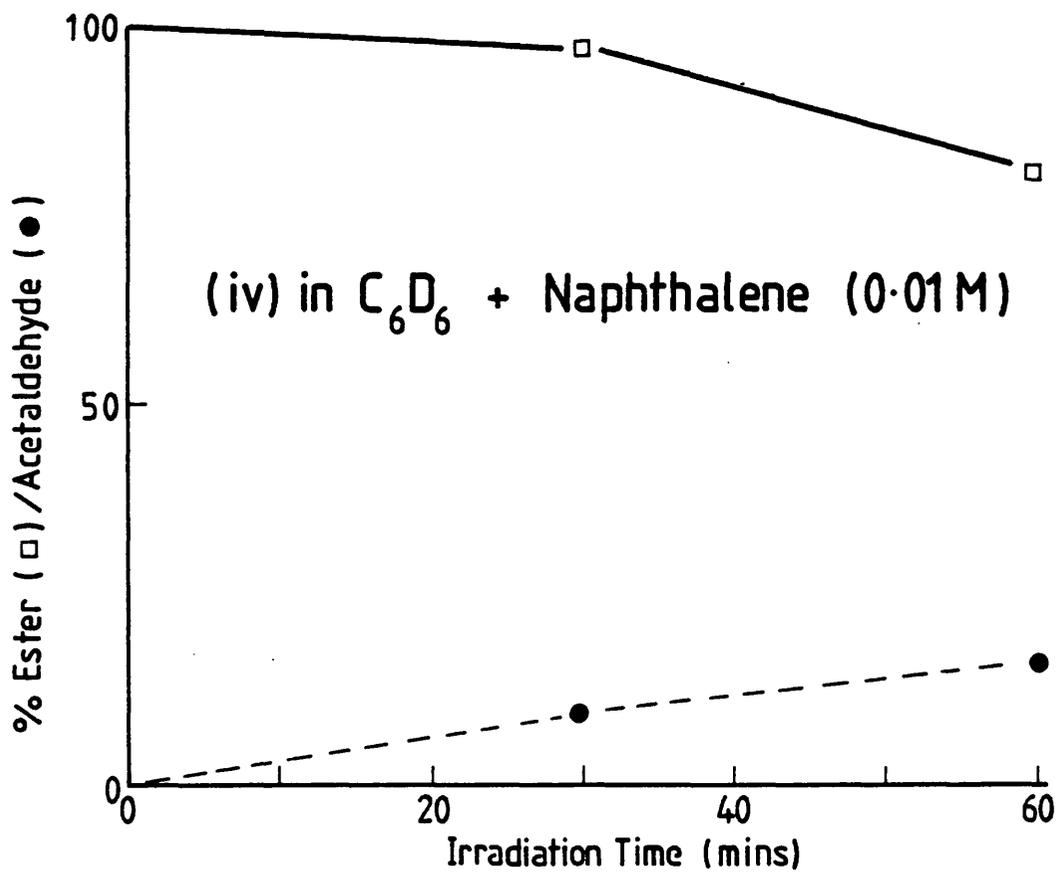
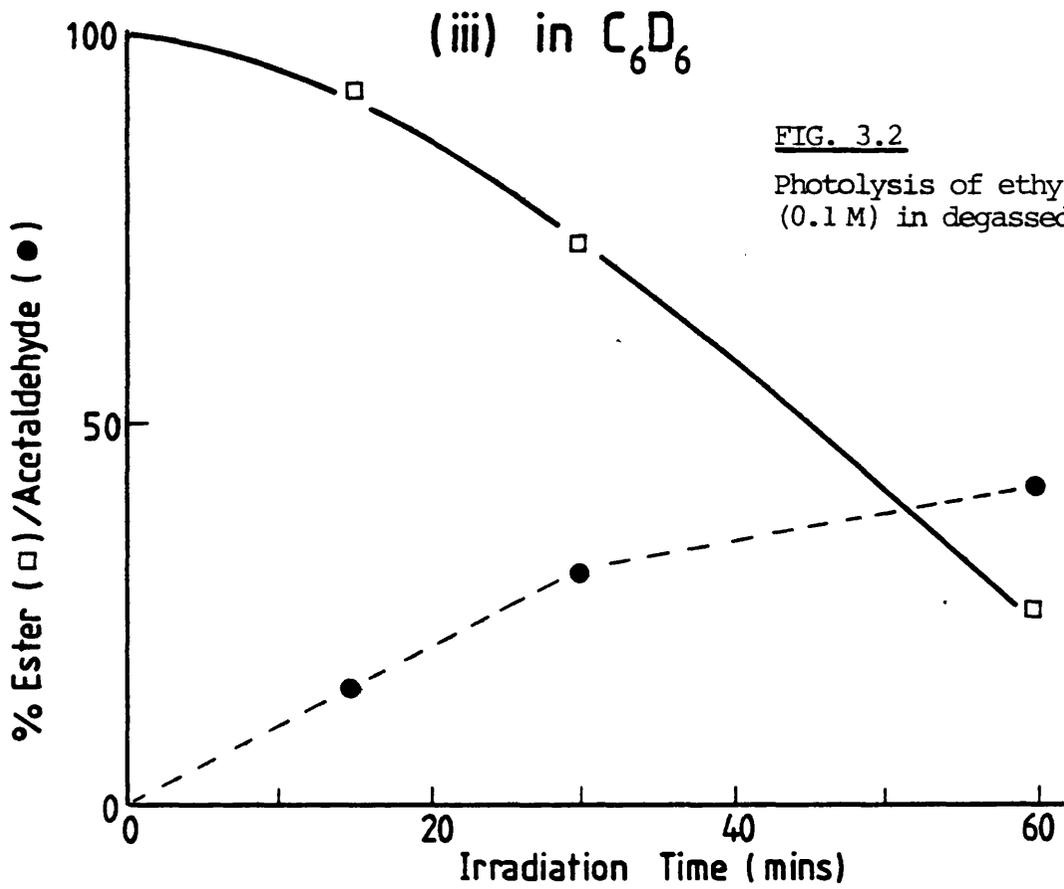
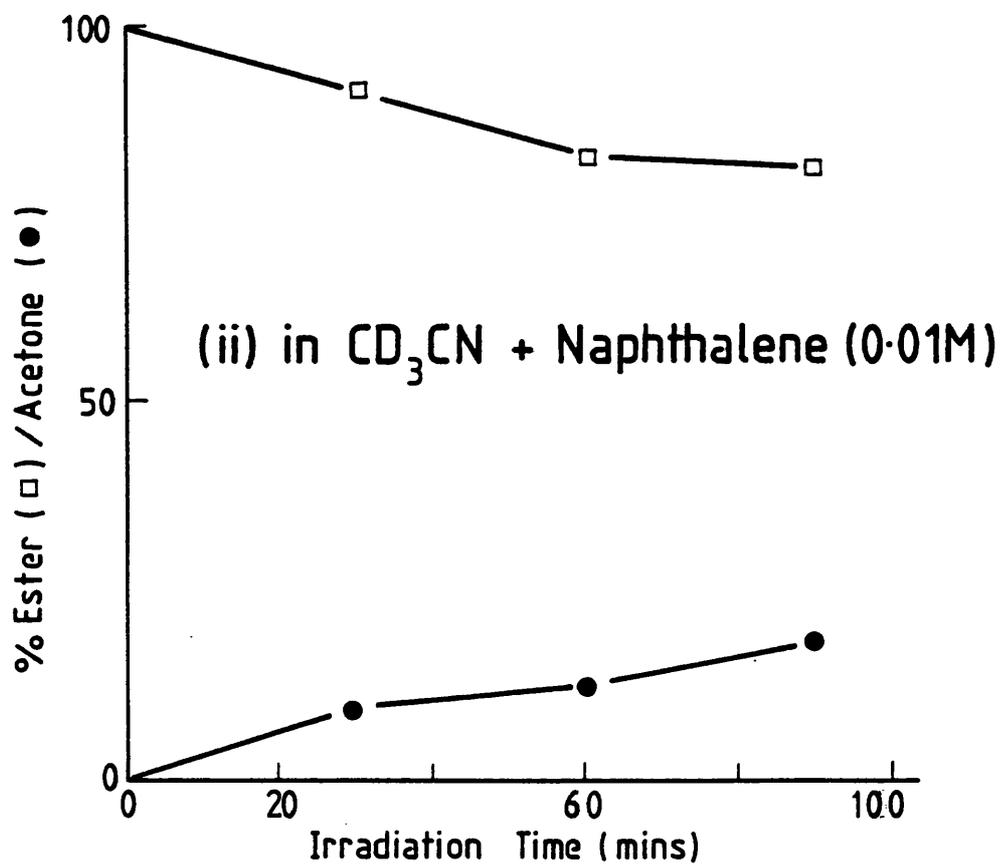
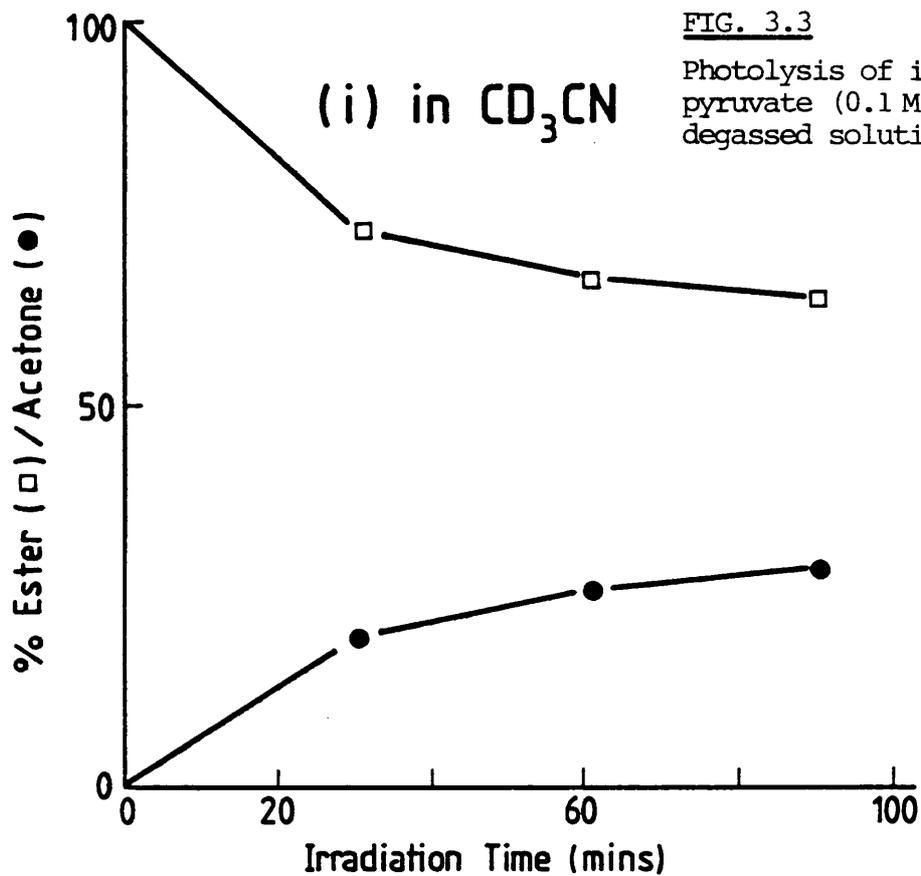


FIG. 3.3

Photolysis of isopropyl pyruvate (0.1 M) in degassed solution



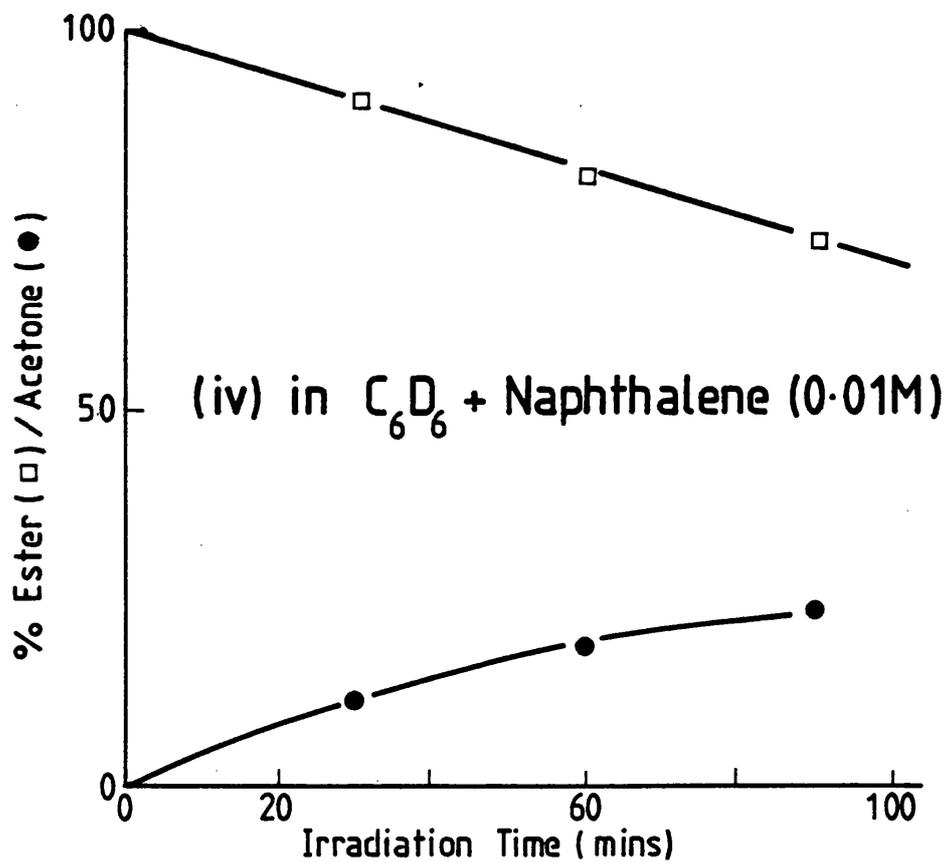
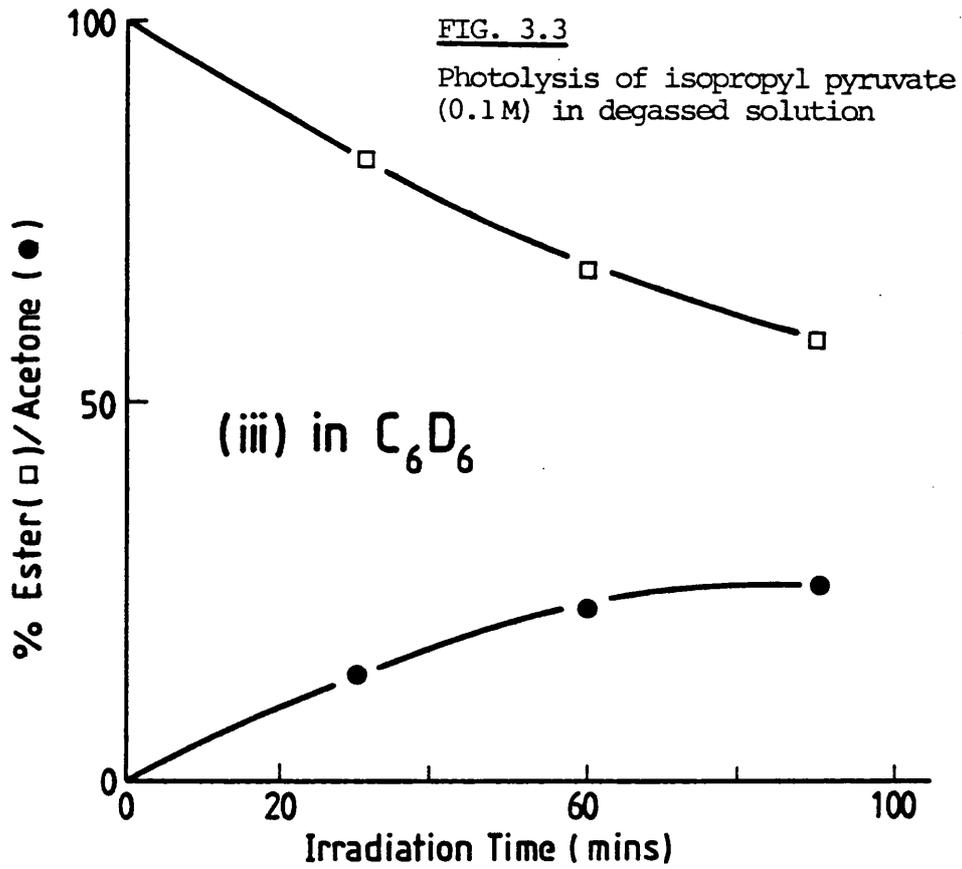


FIG. 3.4

Photolysis of 2-deuterioisopropyl pyruvate (0.1 M) in degassed solution

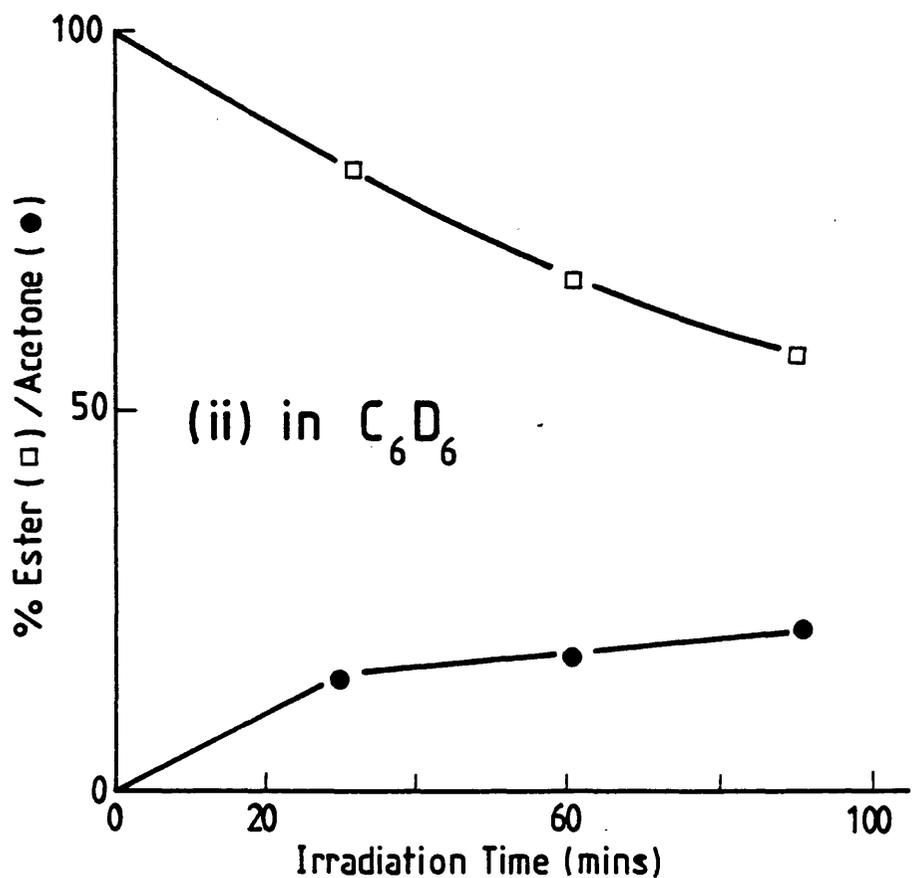
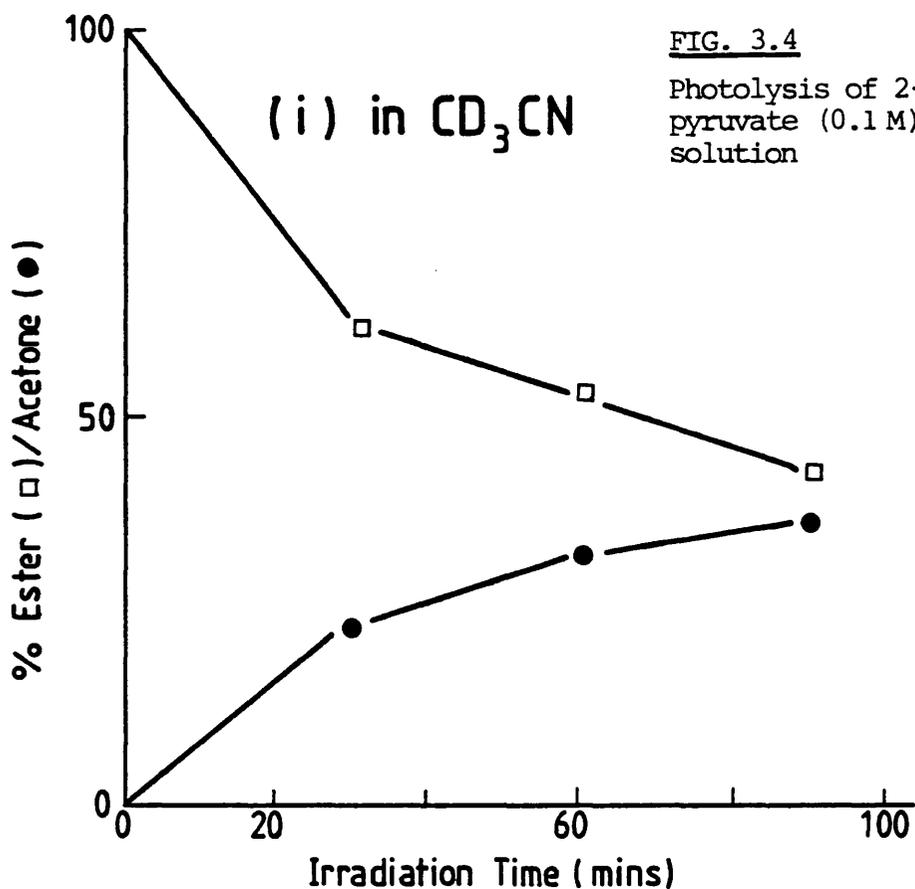


FIG. 3.5

Photolysis of benzylpyruvate (0.1 M) in degassed solution

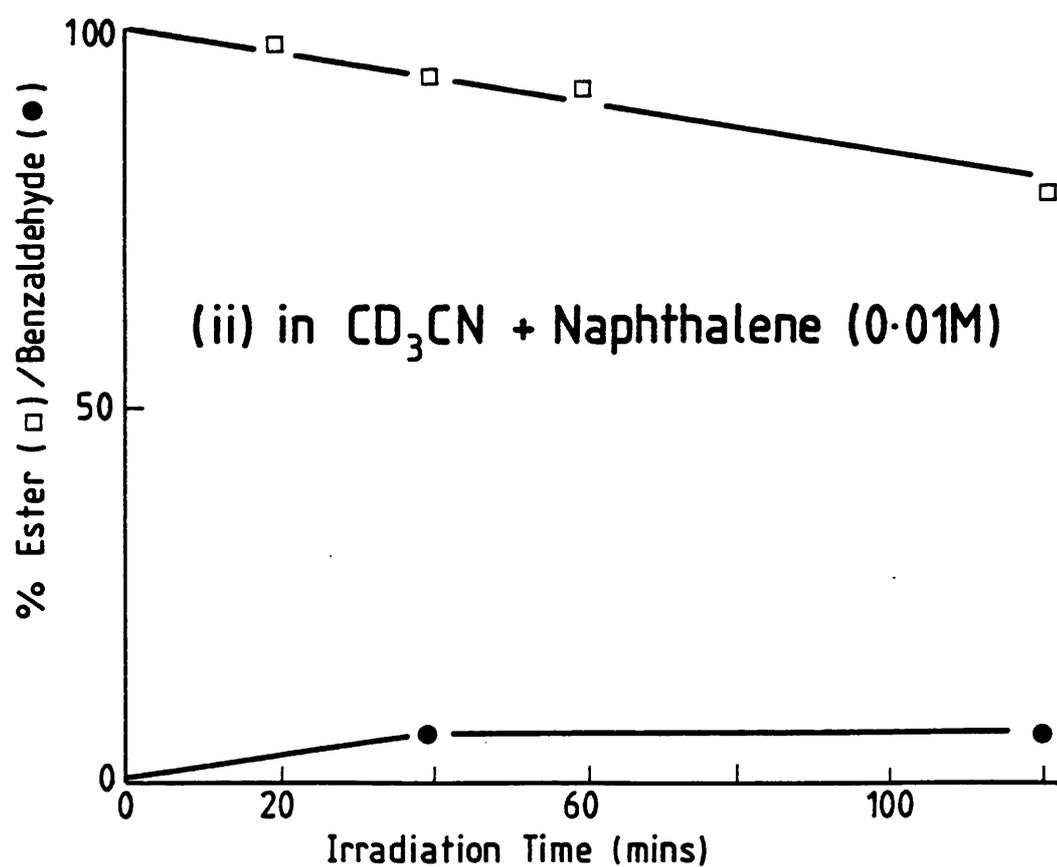
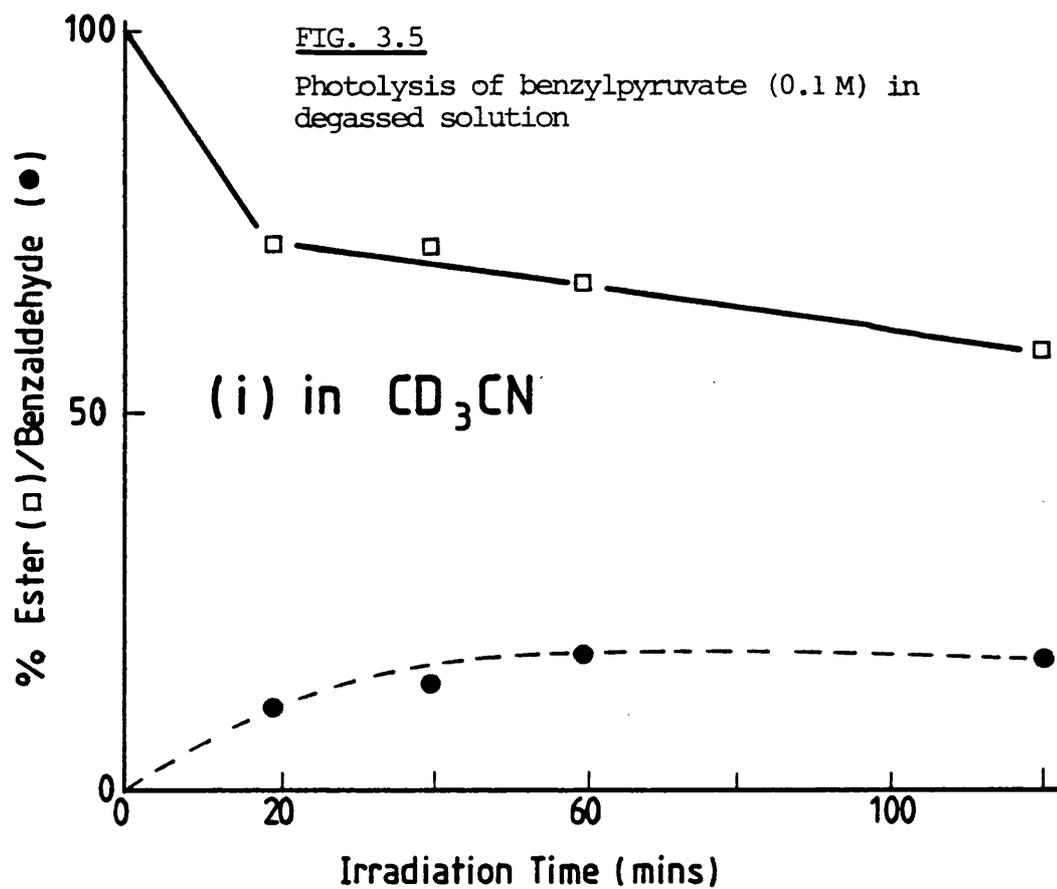


TABLE 3.3

The photolysis of alkyl pyruvates (0.1M), (A) in degassed solution and (B) in degassed solution containing naphthalene (0.01M), showing the amounts of ester remaining (%) and of carbonyl compound produced (%) after various irradiation times "t" (mins)

| Pyruvate Ester (0.1M) | Solvent | A | | | | | | B | | | | | |
|--------------------------|-------------------------------|---------------------|------|------|---------------------------------|------|------|---------------------|------|------|---------------------------------|------|------|
| | | Ester Remaining (%) | | | Carbonyl Compound Produced (%)† | | | Ester Remaining (%) | | | Carbonyl Compound Produced (%)† | | |
| | | t=15 | t=30 | t=60 | t=15 | t=30 | t=60 | t=15 | t=30 | t=60 | t=15 | t=30 | t=60 |
| Methyl | CD ₃ CN | 54 | 33 | 8 | 15 | 16 | 11.5 | - | 86 | 81 | -* | -* | -* |
| Methyl | C ₆ D ₆ | 86 | 74 | 36 | 7 | 12 | 9 | - | 85 | 78 | -* | -* | -* |
| Ethyl | CD ₃ CN | 57 | 29 | 5 | 12 | 18 | 24 | - | 76 | 73 | - | 4.5 | 11 |
| Ethyl | C ₆ D ₆ | 92 | 73 | 25 | 15 | 30 | 41 | - | 97 | 80 | - | 9 | 15 |
| Isopropyl | CD ₃ CN | t=30 | t=60 | t=90 | t=30 | t=60 | t=90 | t=30 | t=60 | t=90 | t=30 | t=60 | t=90 |
| Isopropyl | C ₆ D ₆ | 73 | 67 | 65 | 20 | 26 | 29 | 93 | 84 | 82 | 10 | 13.5 | 18 |
| 2-Deuterioisopropyl | CD ₃ CN | 82.5 | 67 | 58 | 15 | 23 | 26 | 91 | 80 | 72 | 11 | 19 | 24 |
| 2-Deuterioisopropyl | C ₆ D ₆ | 82 | 67 | 58 | 15 | 18 | 22 | - | - | - | - | - | - |
| Benzyl | CD ₃ CN | t=20 | t=40 | t=60 | t=20 | t=40 | t=60 | t=20 | t=40 | t=60 | t=20 | t=40 | t=60 |
| | | - | 72 | 68 | 12 | 14 | 19 | 98.5 | 94 | 92 | - | 6.7 | 6.6 |

* no carbonyl compound observed

† from the alkyl portion of the ester

TABLE 3.4

Rate[†] of photo-induced decomposition of alkyl pyruvates and rate of formation of carbonyl compound in deuterated benzene and deuterated acetonitrile (a) directly and (b) in the presence of triplet quencher (naphthalene)

| Pyruvate Ester (0.1M) | Solvent | Rate of Ester Decomposition ($\times 10^{-6}$ mole min^{-1}) | | Rate of Formation of Carbonyl Compound ($\times 10^{-6}$ mole min^{-1}) [‡] | |
|--------------------------|-------------------------------|--|-------|---|-------|
| | | a | b | a | b |
| Methyl | CD ₃ CN | 1.66 | 0.24 | 0.48 | -* |
| Methyl | C ₆ D ₆ | 0.43 | 0.25 | 0.23 | -* |
| Ethyl | CD ₃ CN | 1.29 | 0.25 | 0.4 | 0.07 |
| Ethyl | C ₆ D ₆ | 0.63 | 0.18 | 0.34 | 0.13 |
| Isopropyl | CD ₃ CN | 0.46 | 0.15 | 0.39 | 0.12 |
| Isopropyl | C ₆ D ₆ | 0.3 | 0.16 | 0.29 | 0.15 |
| 2-Deuterioisopropyl | CD ₃ CN | 0.64 | - | 0.4 | - |
| 2-Deuterioisopropyl | C ₆ D ₆ | 0.305 | - | 0.26 | - |
| Benzyl | CD ₃ CN | 0.72 | 0.083 | 0.31 | 0.077 |

[†] Rates refer to the first 10% decomposition of the pyruvate

[‡] From alkyl portion of the ester

* No carbonyl compound observed

(a) rate in neat solvent; (b) rate with added naphthalene (0.01M)

trations of naphthalene in deuterated acetonitrile solutions of methyl, ethyl, isopropyl and benzyl pyruvates and the resulting Stern-Volmer plots are shown in Figures 3.6 - 3.9 respectively. As can be seen, the Stern-Volmer plots deviated from linearity and therefore meaningful quenching rate constants could not be obtained.

In each of the reactions studied, the rate of disappearance of the alkyl pyruvate, and the rate of formation of the carbonyl compound produced, was found to be faster in deuterated acetonitrile solution, (Table 3.4). It was also found that irradiation of methyl pyruvate solutions containing acetaldehyde leads to consumption of the added aldehyde, (Table 3.5). The rate of consumption of acetaldehyde is faster in deuterated acetonitrile solution than in deuterated benzene solution, (Table 3.5) and in the presence of naphthalene, the rate of acetaldehyde consumption is negligible in both solvents. This result indicates that the triplet methyl pyruvate is being reduced by the acetaldehyde, which accounts for the consumption of the aldehyde.

TABLE 3.5

Consumption of acetaldehyde (0.1M) upon irradiation^(a) of deuterated acetonitrile and deuterated benzene solutions containing methyl pyruvate (0.1M)

| Solvent | % Acetaldehyde consumed |
|-------------------------------|-------------------------|
| CD ₃ CN | 48 |
| C ₆ D ₆ | 29 |

(a) 20 minute irradiation

Methyl glyoxal, the keto-tautomer of methyl hydroxy ketene, was found to undergo photo-decomposition in deuterated benzene solution, (10% decomposition after 20 minute irradiation of a 0.1M solution of methyl

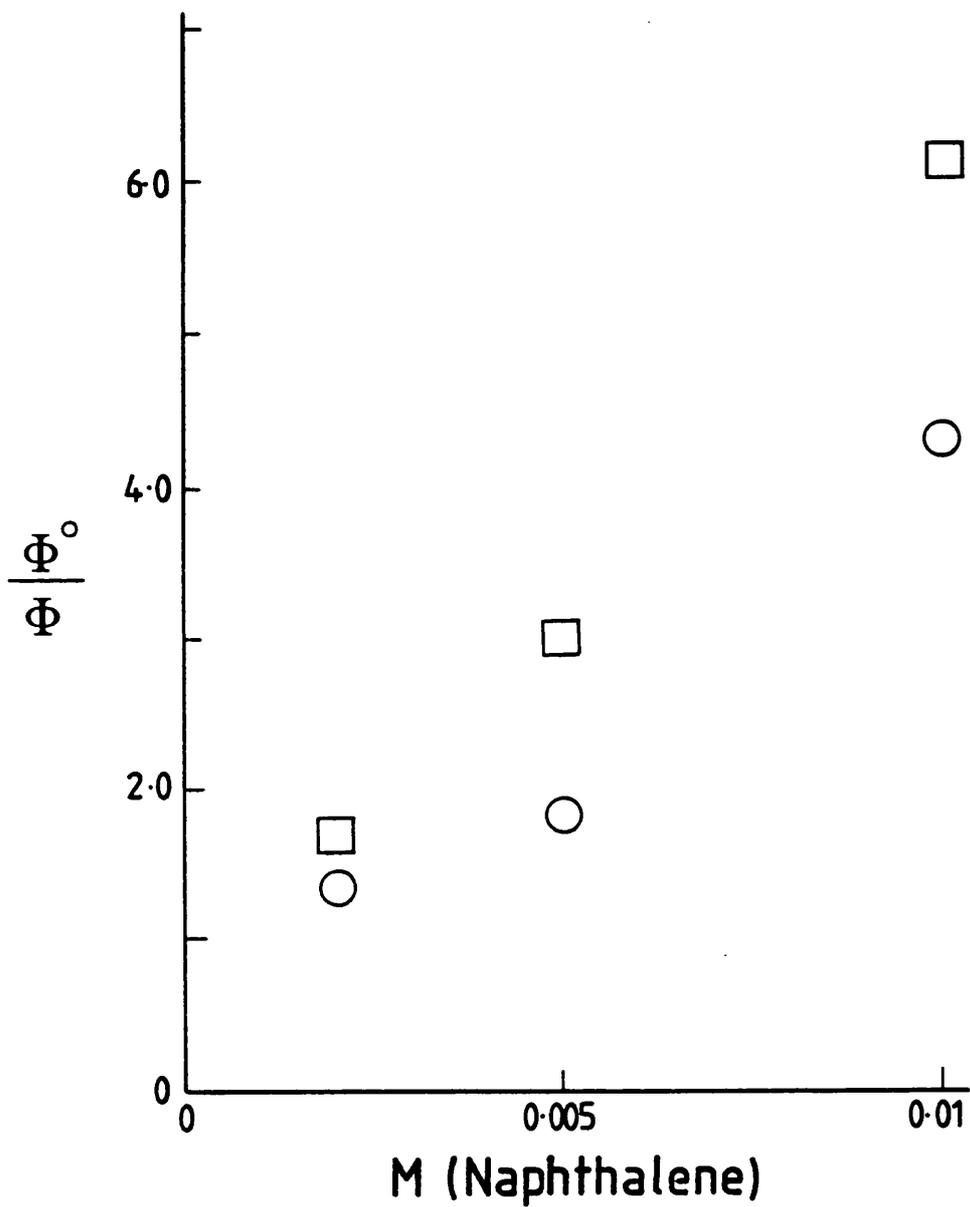


FIG. 3.6

Stern-Volmer plot of the quenching of methyl pyruvate (0.1 M, □) disappearance, and formaldehyde formation (○) by naphthalene in deuterated acetonitrile. [Irradiation time = 30 mins.]

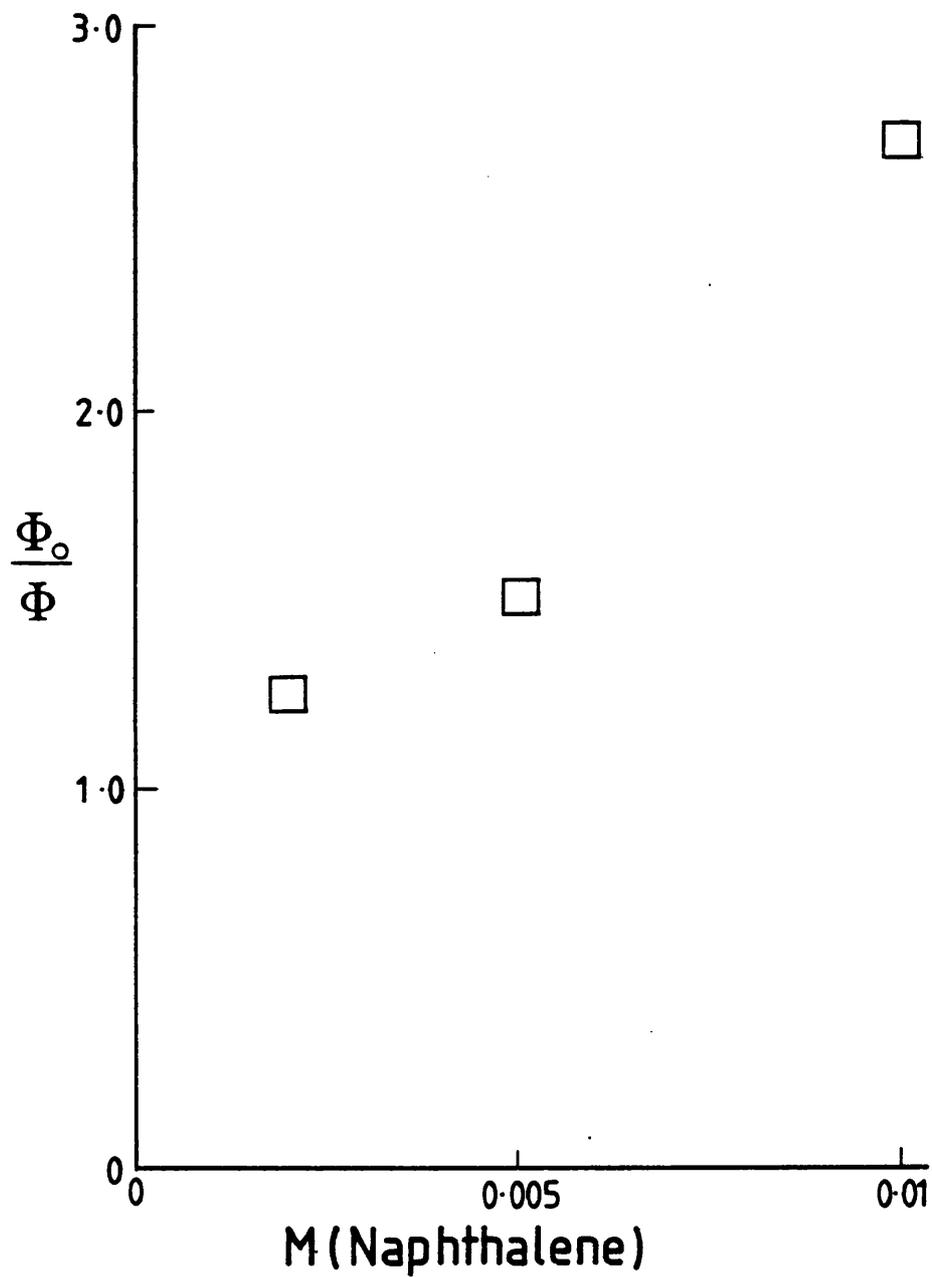


FIG. 3.7

Stern-Volmer plot of the quenching of ethyl pyruvate (0.1M, \square) disappearance by naphthalene in deuterated acetonitrile. [Irradiation time = 30 mins.]

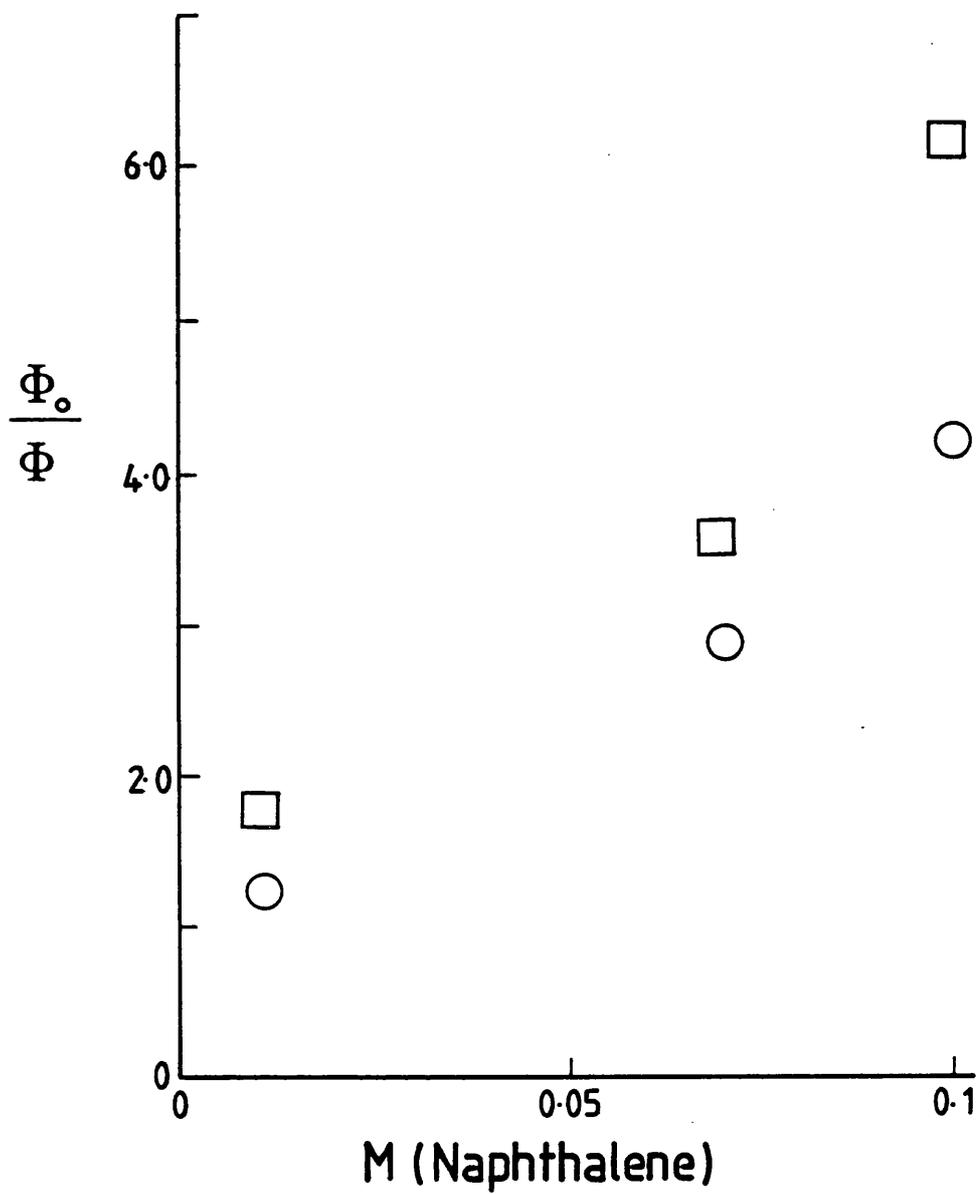


FIG. 3.8

Stern-Volmer plot of the quenching of isopropylpyruvate (0.1M, □) disappearance and acetone formation (○) by naphthalene in deuterated acetonitrile. [Irradiation time = 90 mins.]

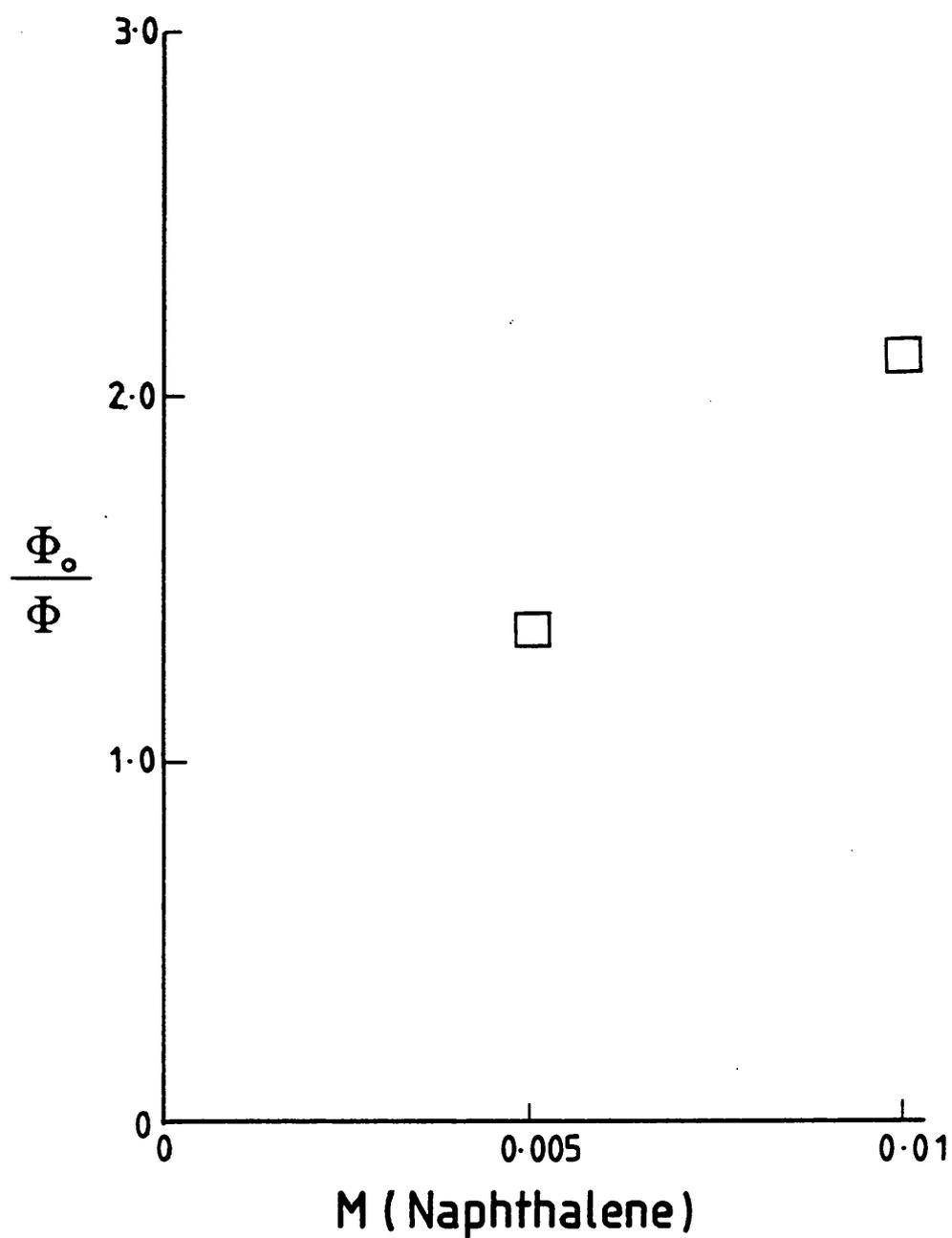


FIG. 3.9

Stern-Volmer plot of the quenching of benzyl pyruvate (0.1M, \square) disappearance by naphthalene in deuterated acetonitrile. [Irradiation time = 60 mins.]

glyoxal).

Most strikingly, t-butyl pyruvate was found to be photochemically inert under the reaction conditions employed.

3.3(iii) TRIPLET LIFETIME MEASUREMENTS OF ALKYL PYRUVATES

The triplet lifetimes of alkyl pyruvates in deoxygenated acetonitrile solution were determined by laser flash photolysis. The triplet decays obtained from the esters are shown in Fig. 3.10. That the transient observed is the triplet state was shown by the fact that all of the esters gave a species having the same absorption spectrum ($\lambda_{\max} \sim 685$ nm in acetonitrile) which decayed with first order kinetics (Figures 3.11 - 3.16) and was quenched by triplet quenchers such as oxygen and naphthalene. The resulting triplet lifetimes are given in Table 3.6, and the photo-stable t-butyl pyruvate is seen to have a much longer lifetime than those of the reactive esters.

TABLE 3.6

Triplet lifetimes and rate constants obtained from laser flash photolysis of alkyl pyruvates in deoxygenated acetonitrile solution, monitored at 685 nm

| Pyruvate Ester | τ (ns) | $\Sigma k_d + k_r$ ($\times 10^7 \text{ s}^{-1}$) | k_r ($\times 10^7 \text{ s}^{-1}$) |
|---------------------|-------------|--|---|
| Methyl | 70 | 1.43 | 1.24 |
| Ethyl | 60 | 1.68 | 1.49 |
| Isopropyl | 66 | 1.52 | 1.33 |
| 2-Deuterioisopropyl | 69 | 1.44 | 1.25 |
| Benzyl | 74 | 1.36 | 1.17 |
| t-Butyl | 521 | 0.192 | - |

FIG. 3.10

Decay of triplet alkyl pyruvates in deoxygenated acetonitrile solution monitored at 685 nm.
(a) methyl pyruvate, (b) ethyl pyruvate, (c) isopropyl pyruvate, (d) 2-deuterioisopropyl pyruvate,
(e) benzyl pyruvate and (f) t-butyl pyruvate.

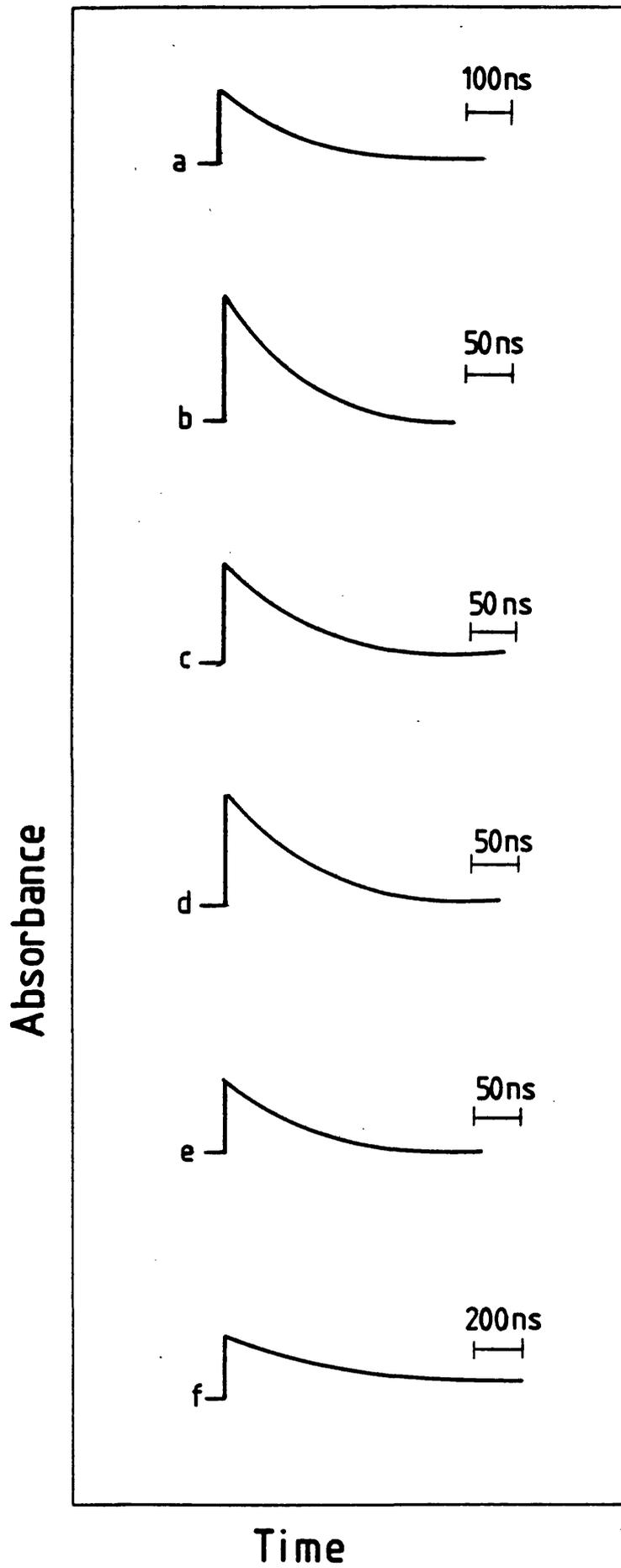


FIG. 3.11

Plot of \log_{10} O.D. v time for decay of transient produced from laser flash photolysis of methyl pyruvate, monitored at 685 nm, showing first-order decay kinetics, where $k_d = \text{gradient} \times 2.3026$.

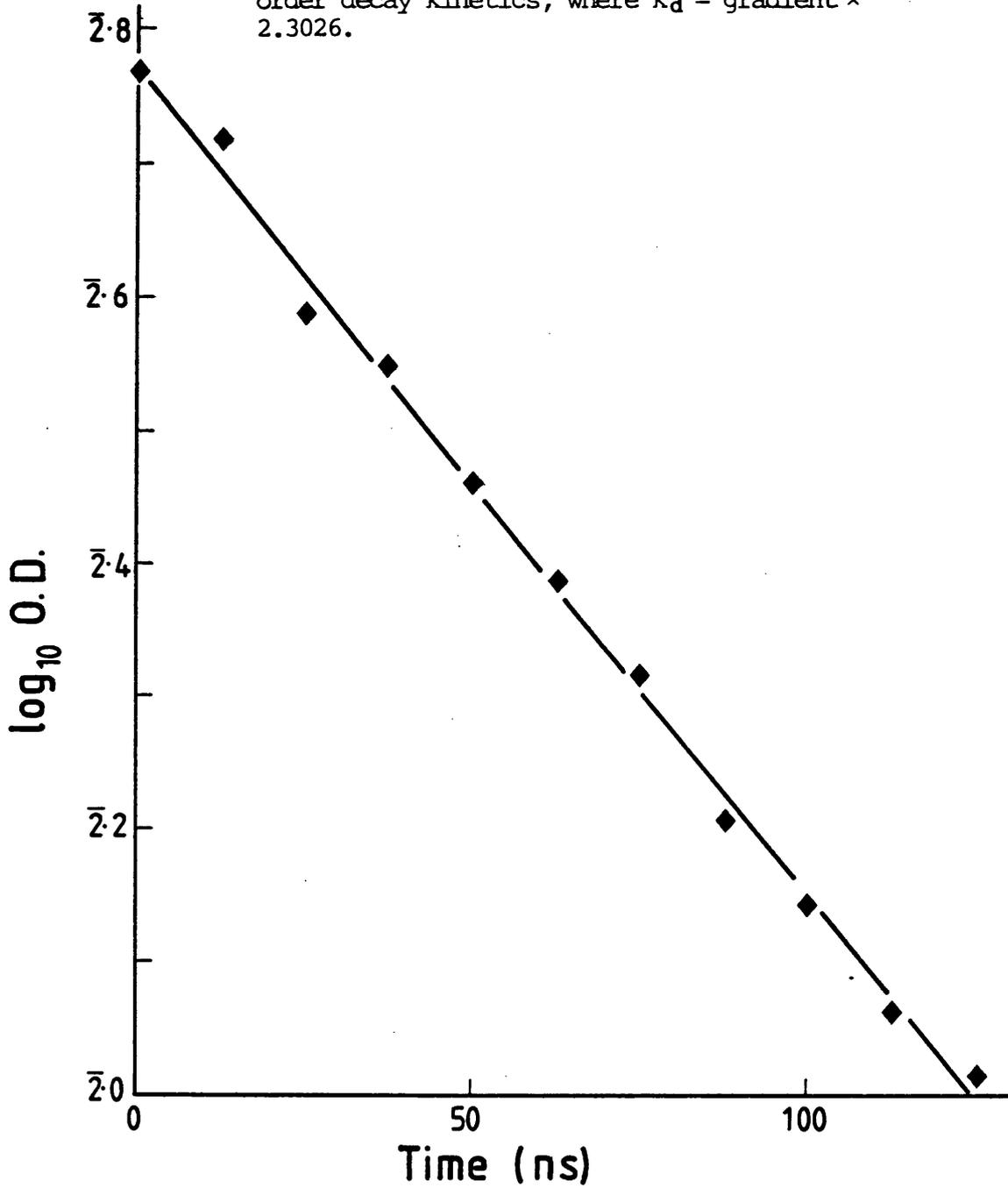


FIG. 3.12

Plot of \log_{10} O.D. v time for decay of transient produced from laser flash photolysis of ethyl pyruvate, monitored at 685 nm, showing first-order decay kinetics, where $k_d = \text{gradient} \times 2.3026$.

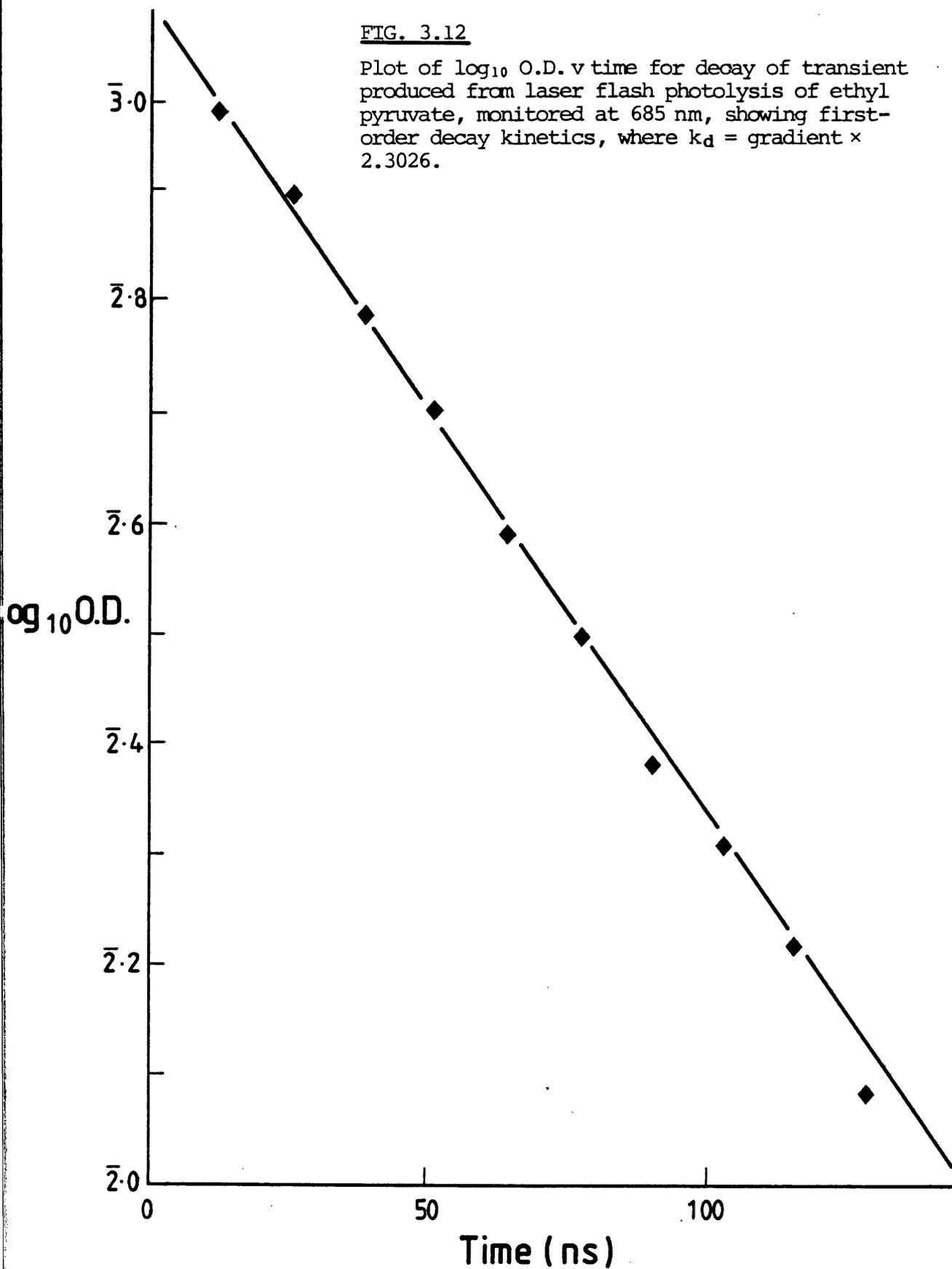


FIG. 3.13

Plot of \log_{10} O.D. v time for decay of transient produced from laser flash photolysis of isopropyl pyruvate monitored at 685 nm, showing first-order decay kinetics, where $k_d = \text{gradient} \times 2.3026$.

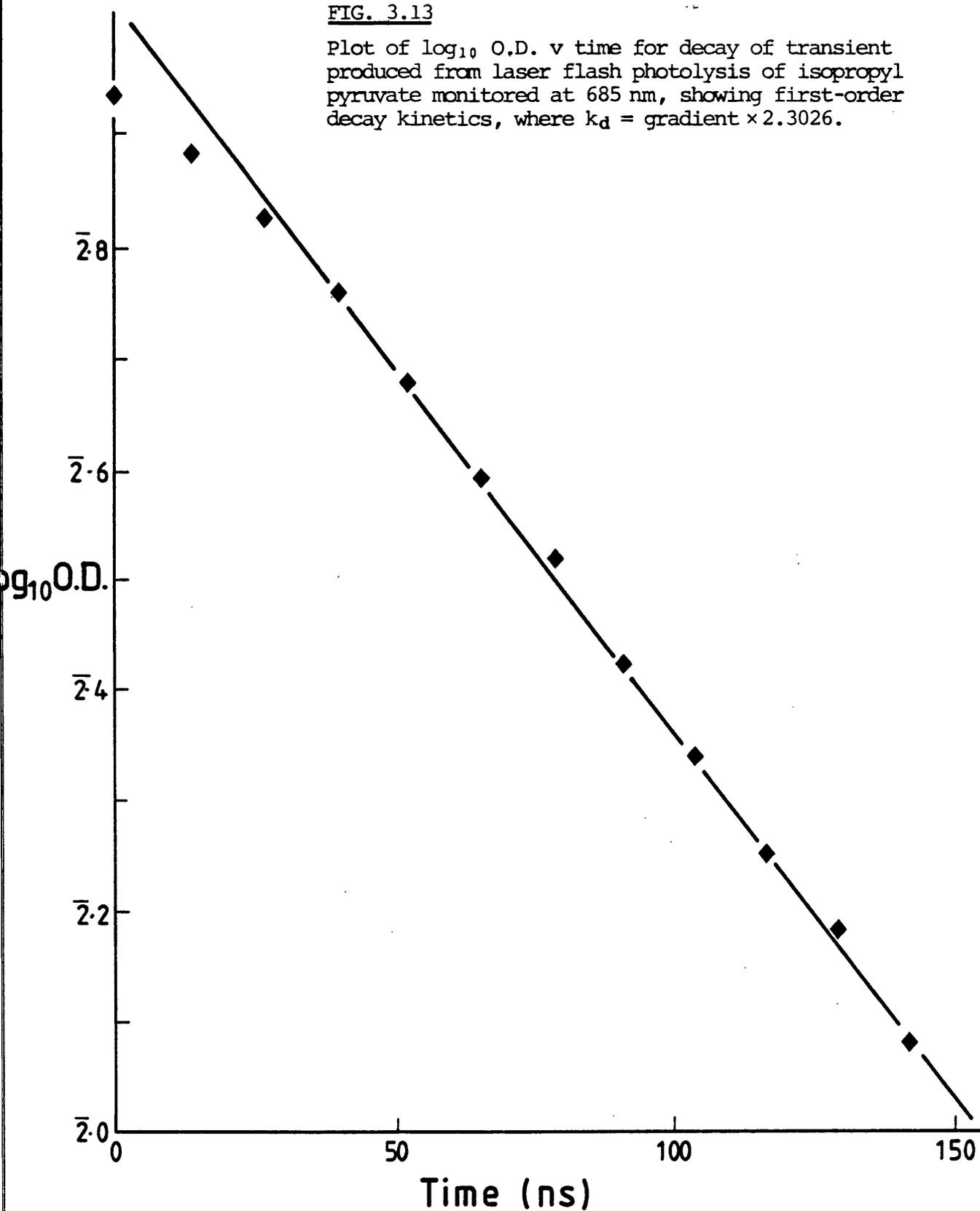


FIG. 3.14

Plot of \log_{10} O.D. v time for decay of transient produced from laser flash photolysis of 2-deuterioisopropyl pyruvate, monitored at 685 nm, showing first-order decay kinetics, where $k_d = \text{gradient} \times 2.3026$.

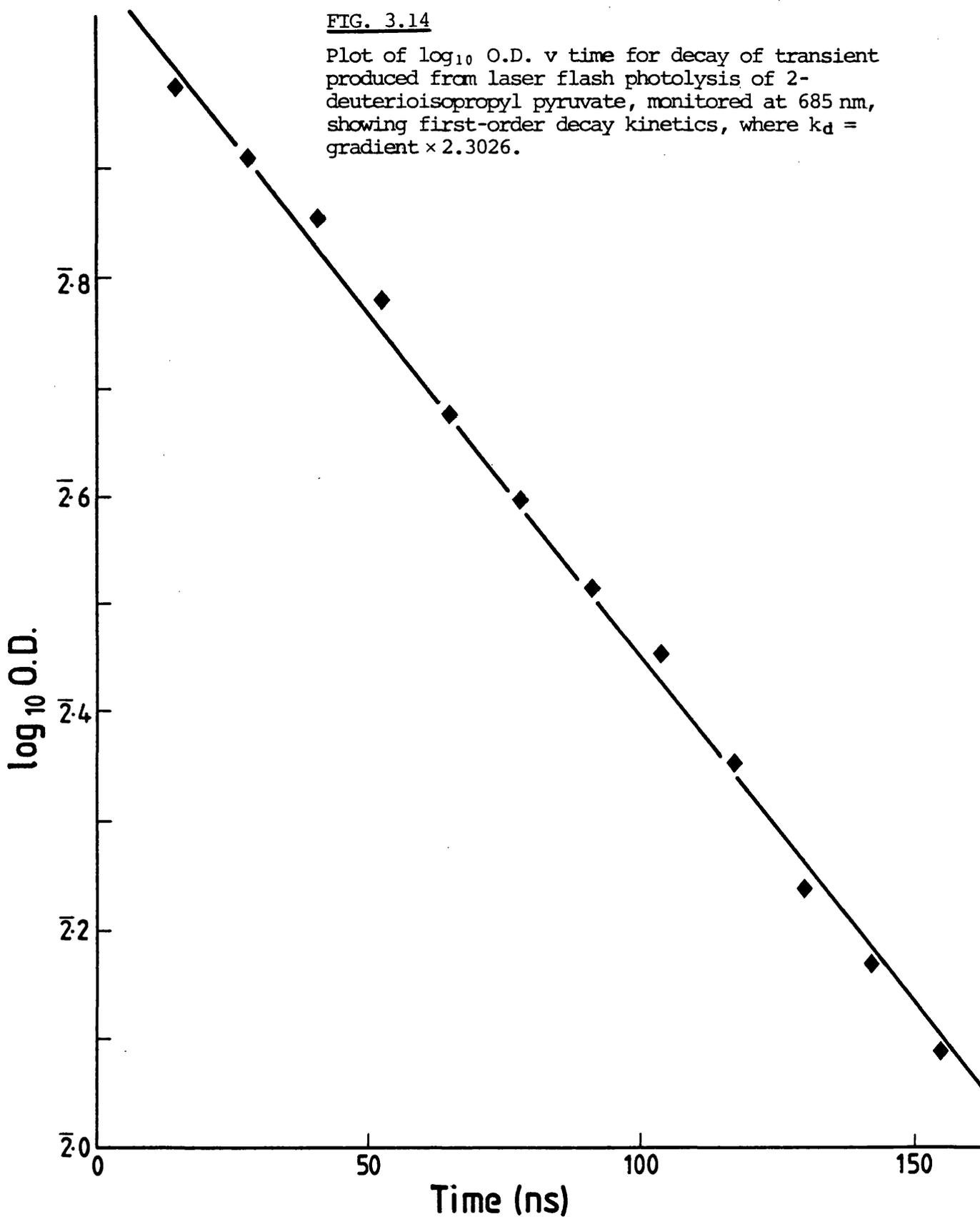


FIG. 3,15

Plot of \log_{10} O.D. v time for decay of transient produced from laser flash photolysis of benzyl pyruvate, monitored at 685 nm, showing first-order decay kinetics, where $k_d = \text{gradient} \times 2.3026$.

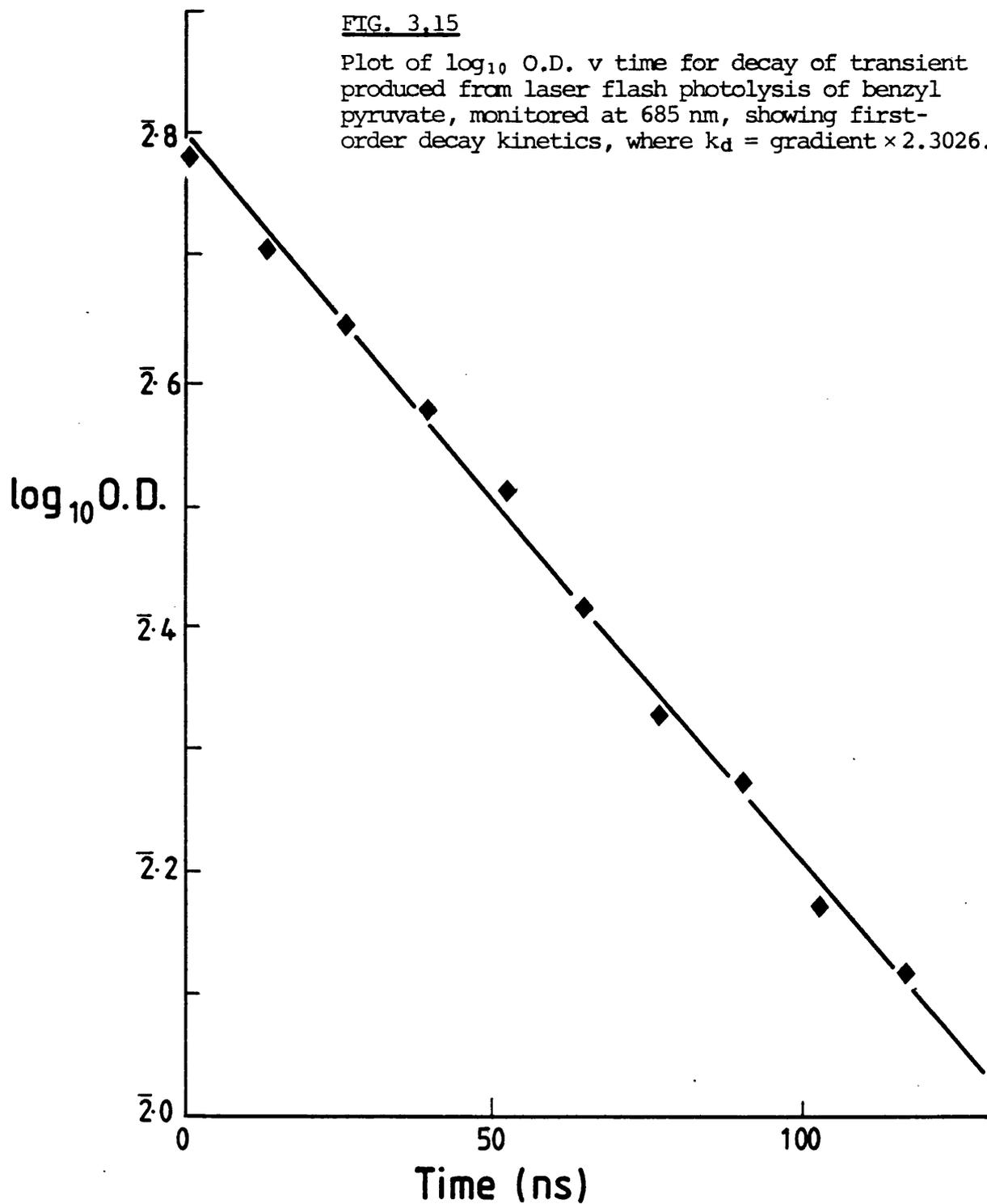
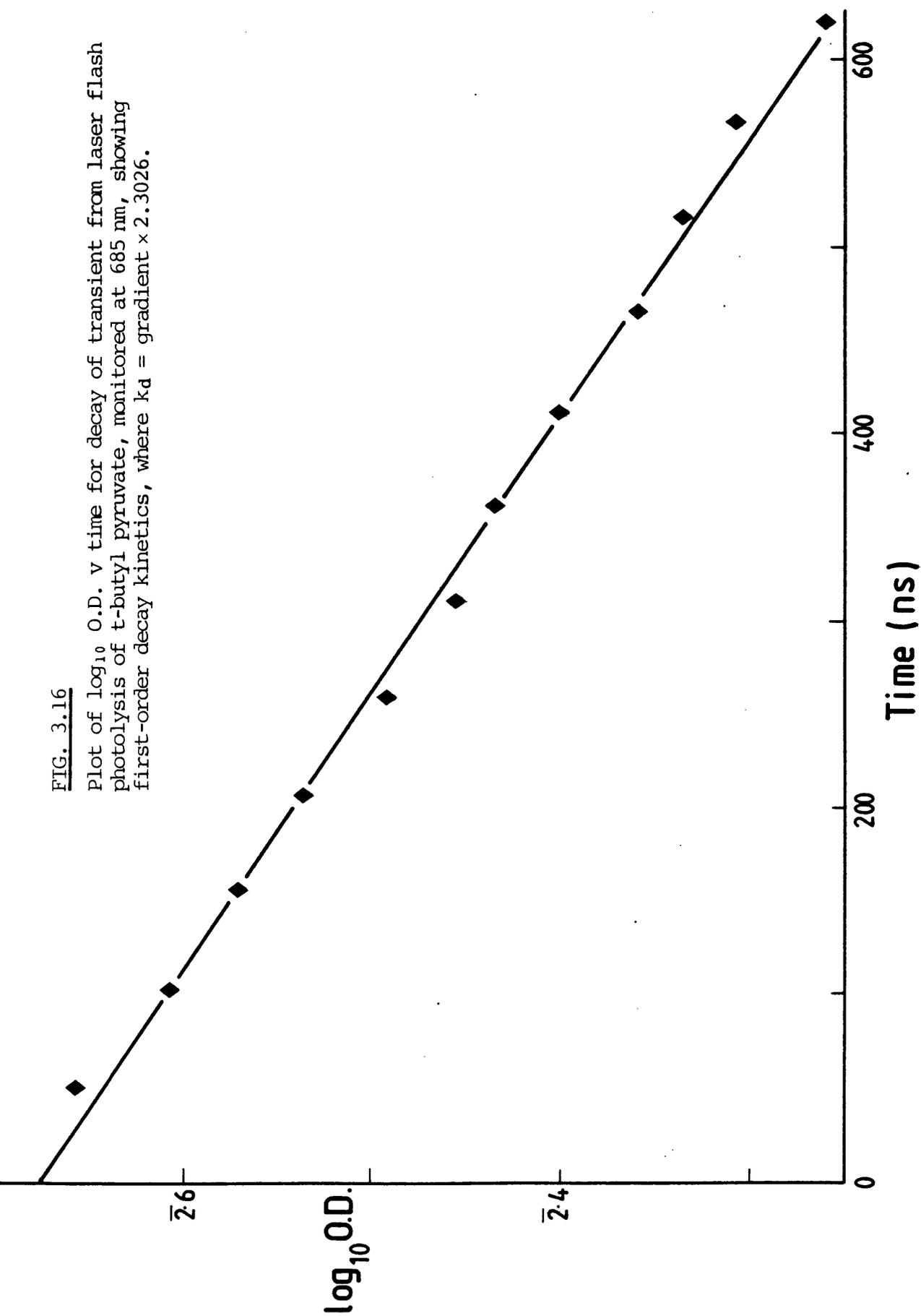


FIG. 3.16

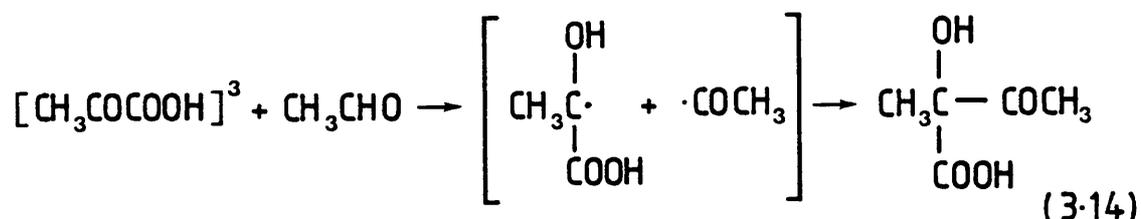
Plot of \log_{10} O.D. v time for decay of transient from laser flash photolysis of t-butyl pyruvate, monitored at 685 nm, showing first-order decay kinetics, where $k_d = \text{gradient} \times 2.3026$.



3.3(iv) DISCUSSION OF THE RESULTS AND FRAGMENTATION MECHANISM

From the results obtained by following the reactions by n.m.r. spectroscopy, it is apparent that the fragmentation of methyl pyruvate to give formaldehyde is a minor pathway for the destruction of this ester. The yield of formaldehyde based on the amount of methyl pyruvate consumed is very small (~12%: Table 3.3, CD₃CN/t=60 mins.). In contrast, isopropyl pyruvate gives acetone in almost quantitative yield, (Table 3.3). Thus it can be concluded that the fragmentation of alkyl pyruvates to give carbonyl compounds from the alkyl portion of the molecule is not the only way by which these esters are consumed, and that favourability of this reaction increases as the degree of substitution of the alkyl group is increased.

It is known that acetaldehyde reacts with triplet pyruvic acid¹⁶ (Equation 3.14) and therefore the possibility arises that the aldehydes formed from the methyl, ethyl and benzyl pyruvates are consumed by reaction with the parent esters.



This probably accounts for the fact that the methyl pyruvate is consumed far more rapidly than isopropyl pyruvate. The yield of carbonyl compound produced in the fragmentation reaction, based on the amount of alkyl pyruvate used is higher when benzene is used as solvent, and the success of the previously described preparative reactions is no doubt due, in part, to the use of benzene as solvent.¹⁷ The fact that the rates of disappearance of the alkyl pyruvates are slower in benzene than acetonitrile suggests that side reactions, such as reduction are

suppressed in this solvent. This view is substantiated by the finding that the rate of consumption of acetaldehyde, when irradiated in the presence of methyl pyruvate, is slower in benzene than acetonitrile, (Table 3.5).

The quenching of the fragmentation reaction of alkyl pyruvates, and of product formation, by naphthalene demonstrates that the triplet state of the alkyl pyruvate is involved in these reactions. It has previously been shown,²⁷ by the use of laser flash photolysis, that naphthalene quenches the triplet states of alkyl pyruvates by energy transfer. Das, Encinas and Scaiano²⁸ have determined, using the same technique, the rate constants for the quenching process and found them to be close to diffusion controlled. The results reported herein substantiate the earlier claim,⁴ which was based on benzophenone sensitization studies, that the triplet state of the alkyl pyruvate is responsible for the fragmentation process.

As previously stated the lack of linearity of the Stern-Volmer plots (Figs. 3.6 - 3.9) precluded the extraction of reliable values for rate constants. A problem encountered in making these measurements was that in order to obtain measurable amounts of the consumption of the alkyl pyruvate and formation of the products, greater than 10% conversion of the starting material had to be allowed. Therefore the accumulation of products which may either react (e.g. aldehydes) with the triplet ester, or sensitize the formation of the triplet ester (e.g. acetone will sensitize the formation of triplet isopropyl pyruvate) may well make a simple kinetic analysis of the disappearance of the alkyl pyruvate invalid.

If the curvature is real, it could indicate that the naphthalene is quenching more than one excited state of the alkyl pyruvate, e.g. the

singlet and triplet state. However, it has been shown²⁷ that naphthalene does not quench the short-lived excited singlet state of α -keto-carboxylic esters, and this is not surprising when one considers that the excited singlet state of naphthalene is of higher energy than that of the α -keto-carboxylic ester.

Another factor which may well account for the non-linearity of the Stern-Volmer plots is the occurrence of ground state association of the alkyl pyruvate and the naphthalene. Association of this type would lead to a "static" contribution to the quenching process, and to an overall increase in the efficiency of the quenching process. If drastic assumptions are made in order to obtain slopes from the Stern-Volmer plots (e.g. use only the portion of the graph which covers low concentrations of naphthalene) and consider the triplet quenching process to be truly diffusional, then using a quenching rate constant of $\sim 1 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ the calculated triplet lifetime of methyl pyruvate is $\sim 40 \text{ ns}$ and for isopropyl pyruvate it is $\sim 4 \text{ ns}$. These values are far shorter than the values obtained by laser flash photolysis. The laser flash photolysis experiments give a direct measure of the triplet lifetimes for the alkyl pyruvates, (Table 3.6), and for methyl and isopropyl pyruvates are 70 and 66 ns respectively, which are far shorter than the triplet lifetime obtained for the unreactive t-butyl pyruvate which was evaluated to be 521 ns.

Using the method developed by Dalton and Turro²⁹ for determining the rate constants for the Type II reaction of alkanones, it should be possible to use the triplet lifetime of the photostable t-butyl pyruvate to determine the rate constants for reaction of the other esters. The triplet lifetime (τ) of the t-butyl pyruvate is given by Equation 3.15:-

$$\tau = \frac{1}{\sum k_d} \quad (3.15)$$

(where k_d is the sum of the various unimolecular decay processes, e.g. radiationless to the ground state, but not including a term for chemical reaction).

By substituting the triplet lifetime of the t-butyl pyruvate (521 ns) into Equation 3.15 gives a Σk_d value for this unreactive ester of $0.192 \times 10^7 \text{ s}^{-1}$.

The triplet lifetime (τ') of the reactive alkyl pyruvates is given by Equation 3.16:-

$$\tau' = \frac{1}{\Sigma k_d + k_r} \quad (3.16)$$

(where Σk_d is as above and k_r is the rate constant for the Type II reaction of the reactive alkyl pyruvate).

Using the Σk_d value for the unreactive t-butyl pyruvate obtained from Equation 3.15 ($0.192 \times 10^7 \text{ s}^{-1}$), together with the value of the triplet lifetime (τ') for each of the reactive alkyl pyruvates (as determined by laser flash photolysis) and substituting them into Equation 3.16 gives the k_r values for the Type II reaction of the reactive alkyl pyruvates, (Table 3.6).

Use of the above equations gives k_r values for the methyl and ethyl pyruvates as being $1.2 \times 10^7 \text{ s}^{-1}$ and $1.5 \times 10^7 \text{ s}^{-1}$ respectively. The slightly higher reactivity of the ethyl pyruvate is to be anticipated since the abstractable hydrogen atom of the ethyl group is secondary whereas in the methyl group it is primary. However, this rationale predicts that the isopropyl pyruvate should have a higher rate constant than the ethyl pyruvate and this is not found to be the case since the triplet lifetimes of the ethyl and isopropyl pyruvate esters are similar. If the rate constant for reaction of the ethyl pyruvate had been particularly high, e.g. $\sim 10^{10} \text{ s}^{-1}$ this finding would not have been too

surprising since a slight change in C-H bond strength should hardly effect the free energy change for a reaction with such a rate constant. Another puzzling feature is that the triplet lifetimes and quantum yields for photoreaction of the isopropyl and 2-deuterioisopropyl pyruvates are very similar. The finding that deuteration has a slight negative primary kinetic isotope effect upon the photoreactivity (Table 3.6) is in agreement with the results reported by Leemakers.⁵ The lack of a positive kinetic isotope effect upon the reactivity of the isopropyl pyruvate and the similarity of reactivity between ethyl and isopropyl pyruvates suggests that the Type II reaction has a very low energy of activation.²⁹ Certainly the entropy of activation should be almost negligible due to the conformations adopted by the ground state of the esters. The trans-trans arrangement of the two carbonyl groups³⁰ means that even for the least favourable conformation (with regard to reaction) only rotation about the oxygen-carbon bond of the oxygen-alkoxy group is necessary to give the ester the correct conformation for the Type II reaction, (Fig. 3.17[a]).

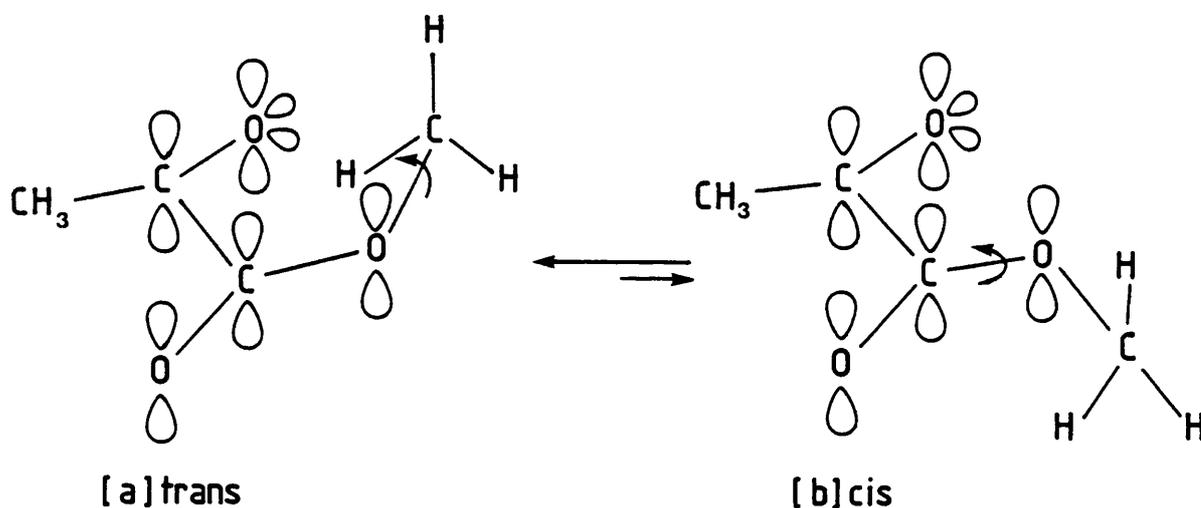


Fig. 3.17

This favourable conformation effect should reduce the energy of activation and one would anticipate a high rate constant for these reactions. It is therefore difficult to reconcile the low rate constants

for the reactions with the absence of a primary kinetic isotope effect. A similar paradox has been encountered by Coulson and Yang³¹ in a study of the photochemistry of hexan-2-one, where it was found that replacement of the appropriate hydrogen by deuterium led to a slight increase in the quantum yield for the Type II reaction. More surprisingly, the deuterium substitution altered the relative amount of Type II reaction occurring from the excited singlet and triplet states.

Although the parameters for the fragmentation of the alkyl pyruvates have not been fully quantified, the results reported herein support the view that the reaction occurs via the Type II process from the excited triplet state.

The finding that the alkyl pyruvates fragment via the Type II process prompts the question as to how the carbon monoxide is produced in these reactions. It has been suggested that this is a secondary product and is derived from methyl glyoxal,¹² (Equation 3.8). However, a thorough search of the n.m.r. spectra did not reveal any formation of methyl glyoxal, which in a separate experiment was, in fact, found to be unstable under the irradiation conditions employed. Apart from the ethyl pyruvate, acetaldehyde, which is the expected product from a Type I process, was not formed, and therefore the eventual fate of the CH₃CO- portion of the alkyl pyruvates is unclear.

Summary

The finding that t-butyl pyruvate is photochemically unreactive and has a much longer triplet lifetime than methyl, ethyl, isopropyl, 2-deuterioisopropyl and benzyl pyruvates, together with triplet quenching studies, shows that alkyl pyruvates fragment from the triplet state via a Type II and not a Type I process. That alkyl pyruvates do not fragment via a Type I process is consistent with the finding that pyruvic acid does

not fragment in this way and shows that photolytic cleavage of the bond linking the carbonyl groups in 1,2-dicarbonyl compounds is an unfavourable process.

3.4 THE DIRECT PHOTO-INDUCED DECARBOXYLATION OF ALKYL PYRUVATES

Object of investigation

The only report pertaining to the photo-induced decarboxylation of α -keto-carboxylic esters is that by Hammond and co-workers⁴ who have shown that ethyl pyruvate produces carbon dioxide upon irradiation in degassed benzene solution. It has previously been demonstrated that alkyl pyruvates undergo photo-fragmentation via a Type II mechanism (Chapter 3.3), and therefore the possibility of carbon dioxide production from esters of this type is particularly intriguing. The aim of the experiments reported in this section is to investigate the decarboxylation reaction of alkyl pyruvates, and the mechanism by which this process occurs.

3.4(i) INITIAL DECARBOXYLATION STUDIES

Carbon dioxide production was found to occur for several alkyl pyruvates in degassed solution, albeit to a small extent, (Table 3.7). That ethyl pyruvate undergoes decarboxylation⁴ is confirmed, (Table 3.7). The yields of carbon dioxide and hexaldehyde from irradiation of n-hexyl pyruvate, in degassed acetonitrile solution, are shown in Table 3.8.

3.4(ii) PHOTOLYSIS IN THE PRESENCE OF METHYL VIOLOGEN

It has previously been reported that α -keto-carboxylic acids, such as pyruvic acid, undergo decarboxylation via an electron transfer mechanism,³² therefore the possibility arises that α -keto-carboxylic esters may undergo analogous reactions. In order to ascertain whether alkyl pyruvates are capable of undergoing photo-induced electron transfer reactions, irradiations of several esters were performed in the presence of methyl viologen, (MV^{2+}). In each case, the blue coloured species,

TABLE 3.7

Yields of carbon dioxide from the direct irradiation^(a) of alkyl pyruvates (10^{-2} M) in degassed solution

| Alkyl pyruvate (10^{-2} M) | Solvent | Yield (%) of carbon dioxide |
|-------------------------------|--|-----------------------------|
| Methyl pyruvate | Benzene | 5.3 |
| Methyl pyruvate | Acetonitrile | 7 |
| Methyl pyruvate | Acetonitrile/water ^(b) | 12 |
| Ethyl pyruvate | Acetonitrile | 9 |
| Isopropyl pyruvate | Acetonitrile | 11 |
| t-Butyl pyruvate | Acetonitrile | 0 |
| t-Butyl pyruvate | Benzene | 0 |
| t-Butyl pyruvate | Acetonitrile/pyridine/water ^(c) | 0 |

(a) 6h irradiation

(b) (9:1 v/v)

(c) (8:1:1 v/v)

TABLE 3.8

Yields of carbon dioxide and hexaldehyde from the direct irradiation^(a) of n-hexyl pyruvate (5×10^{-2} M) in degassed acetonitrile solution

| Product | Yield (%) |
|----------------------------|-----------|
| Carbon dioxide | 7 |
| Hexaldehyde ^(b) | 30 |

(a) 3h irradiation

(b) determined by g.l.c.

reduced methyl viologen ($MV^{\bullet+}$) characterised by its absorption spectrum, was rapidly produced. Figure 3.18 shows the production of reduced methyl viologen from the 1 minute irradiation of degassed acetonitrile/water (9:1 v/v) solutions of methyl, ethyl, isopropyl and t-butyl pyruvates respectively, and Figure 3.19 shows the results obtained when the same reactions were performed in degassed acetonitrile/pyridine/water (8:1:1 v/v) solutions. The yield of reduced methyl viologen was shown to increase with increasing irradiation time (Fig. 3.20). On cessation of illumination the absorption band due to reduced methyl viologen was observed to decline with time, which may indicate that a reversible back electron transfer reaction is operative, (Fig. 3.21). Since the colour due to reduced methyl viologen was subject to fading, the absorption values obtained in Figs. 3.18 - 3.20 cannot be used quantitatively, but clearly indicate the production of reduced methyl viologen in the reactions.

It is interesting to note that t-butyl pyruvate, which has previously been shown to be photostable (Chapter 3.3) and did not lead to carbon dioxide production upon direct irradiation (Table 3.7), was capable of producing reduced methyl viologen when irradiated in the presence of methyl viologen.

Control experiments in the absence of the alkyl pyruvates did not give rise to reduced methyl viologen, and confirm that the reduced methyl viologen is produced via an electron transfer reaction from the alkyl pyruvate to the parent methyl viologen, as shown in Equation 3.17.

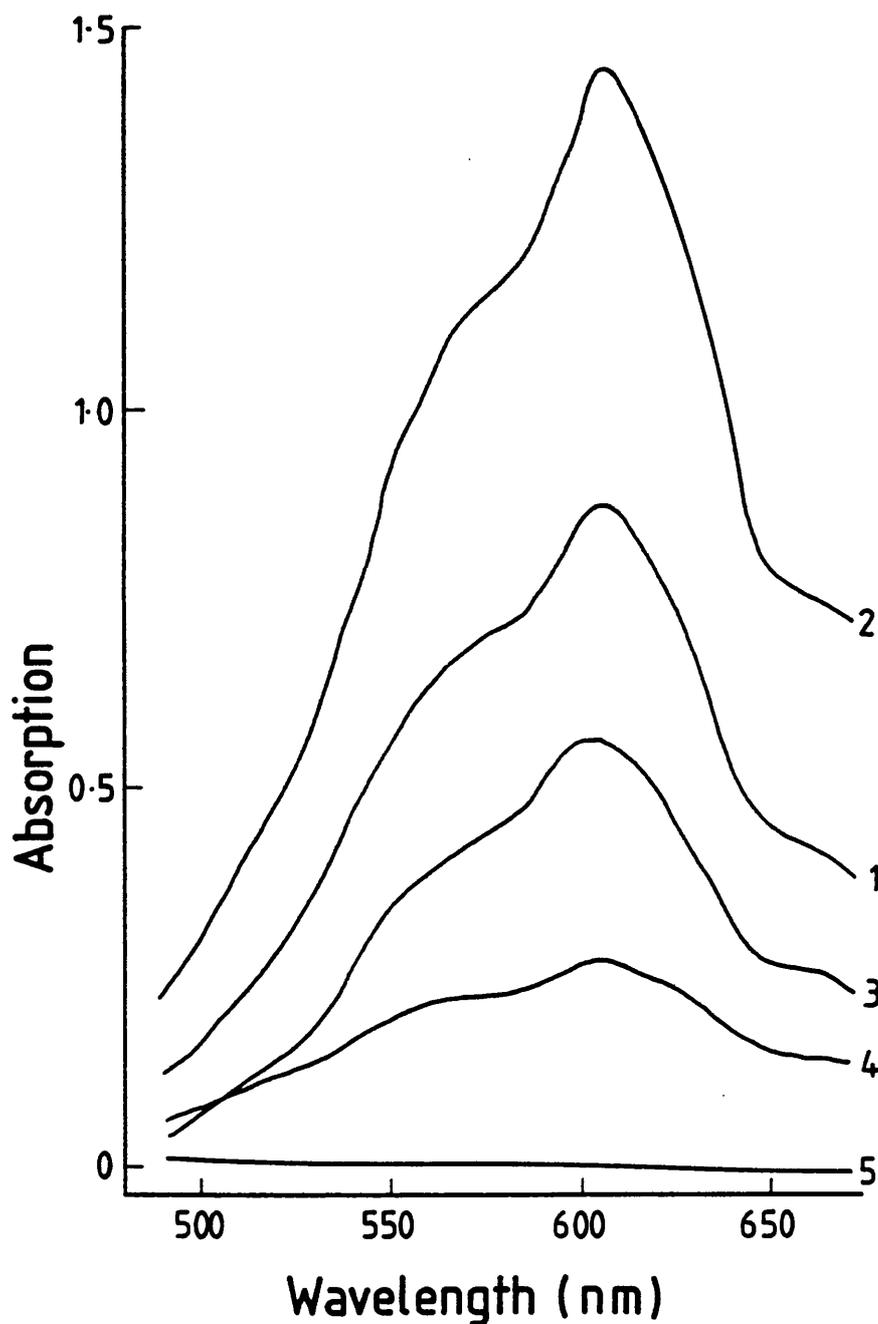


Methyl pyruvate has been shown, by a laser flash photolysis study,³³ to have a triplet-triplet absorption spectrum similar to that of pyruvic

FIG. 3.18

Production of reduced methyl viologen from 1 minute irradiation of α -keto-carboxylic esters (5×10^{-2} M) in degassed acetonitrile/water (9:1 v/v) solution containing methyl viologen (10^{-2} M).

(1) methyl pyruvate, (2) ethyl pyruvate, (3) isopropyl pyruvate, (4) t-butyl pyruvate and (5) shows the absorption of each solution prior to irradiation.



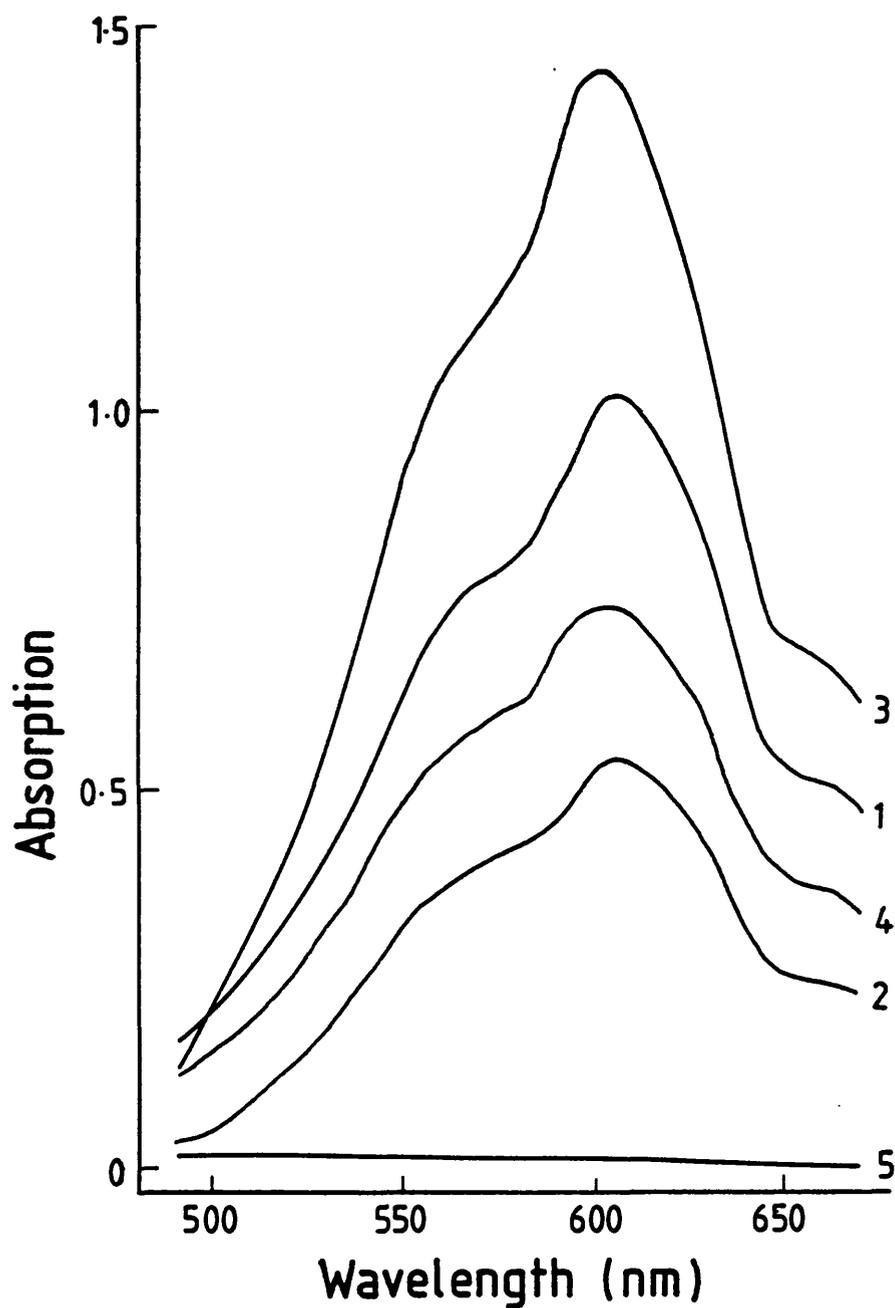


FIG. 3.19

Production of reduced methyl viologen from 1 minute irradiation of α -keto-carboxylic esters (5×10^{-2} M) in degassed acetonitrile/pyridine/water (8:1:1 v/v) solution containing methyl viologen (10^{-2} M). (1) methyl pyruvate, (2) ethyl pyruvate, (3) isopropyl pyruvate, (4) t-butyl pyruvate and (5) shows the absorption of each solution prior to irradiation.

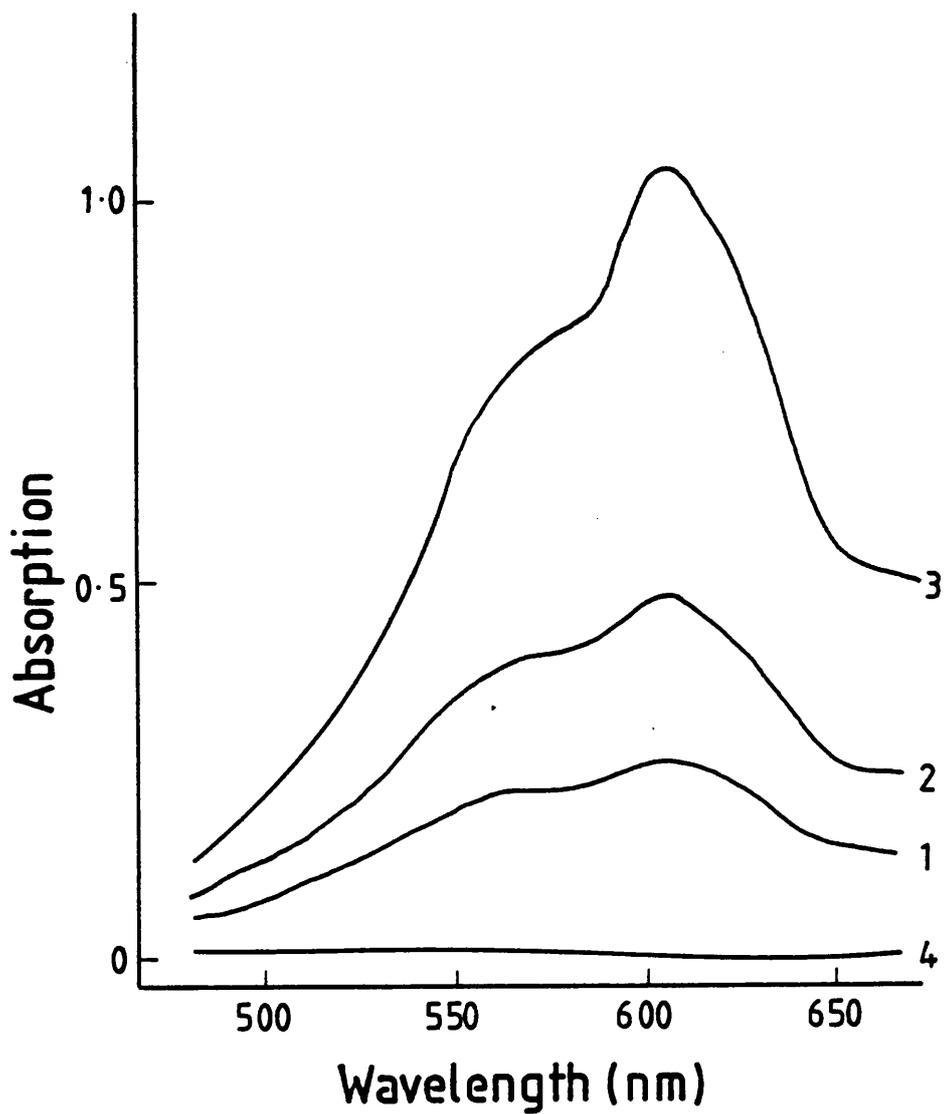


FIG. 3.20

Production of reduced methyl viologen from irradiation of t-butyl pyruvate (5×10^{-2} M) in degassed acetonitrile/water (9:1 v/v) solution containing methyl viologen (10^{-2} M), (1) 1 minute irradiation, (2) 2 minutes irradiation, (3) 3 minutes irradiation and (4) shows the absorption of the solution prior to irradiation.

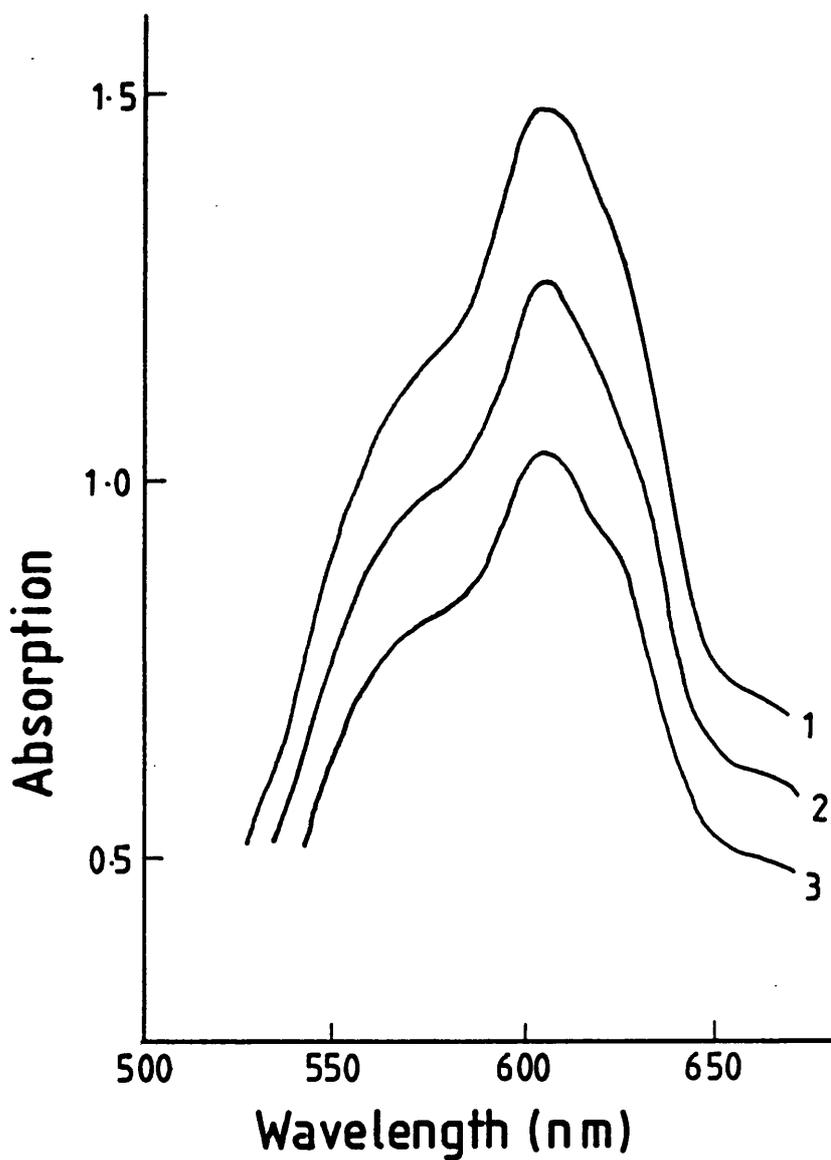


FIG. 3.21

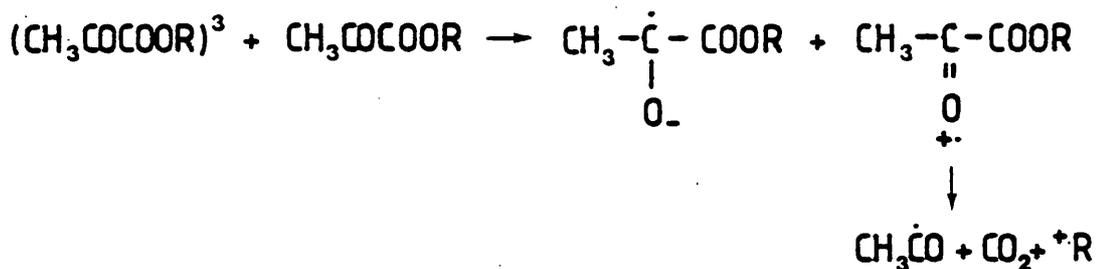
Decay of reduced methyl viologen.

- (1) initial production of reduced methyl viologen from 1 minute irradiation of isopropyl pyruvate (5×10^{-2} M) in acetonitrile/pyridine/water (8:1:1 v/v) solution containing methyl viologen (10^{-2} M),
- (2) after standing for $2\frac{1}{2}$ minutes after irradiation and
- (3) after standing for 5 minutes after irradiation.

acid.^{28,32} That the transient produced is that of triplet methyl pyruvate is illustrated by the observation that the triplet quenchers naphthalene and oxygen reduce the lifetime of the transient. The triplet lifetime of methyl pyruvate was found to be concentration dependent, having a self-quenching rate constant = $2 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$, and at methyl pyruvate concentrations of $5 \times 10^{-2} \text{ M}$ in acetonitrile solution the lifetime was found to be 140 ns. The addition of methyl viologen to an aqueous acetonitrile (1:9 v/v) solution of methyl pyruvate led, upon flash photolysis, to the production of reduced methyl viologen. A similar observation has been noted in the analogous reaction of pyruvic acid.³² The addition of methyl viologen had little effect upon the fluorescence and triplet lifetimes of methyl pyruvate, thus the reduced methyl viologen is not predominantly produced by the reaction of methyl viologen with the excited states of methyl pyruvate.

3.4(iii) DISCUSSION

Several alkyl pyruvates have been found to undergo direct photo-induced decarboxylation in degassed solution, (Table 3.7). From the yields of carbon dioxide obtained (Reference 4 and Table 3.7) it appears that decarboxylation is a minor pathway for the degradation of these esters. The observation of reduced methyl viologen production (Figs. 3.18 - 3.21) clearly demonstrates that alkyl pyruvates are capable of undergoing electron transfer reactions, and therefore it is possible that the carbon dioxide could arise from a bimolecular electron transfer reaction from the excited triplet state of the alkyl pyruvate to a molecule of alkyl pyruvate in its ground state, (Scheme 3.14). This mechanism, analogous to that proposed to account for the direct photo-induced decarboxylation of pyruvic acid,³² could account for the concentration dependence of the



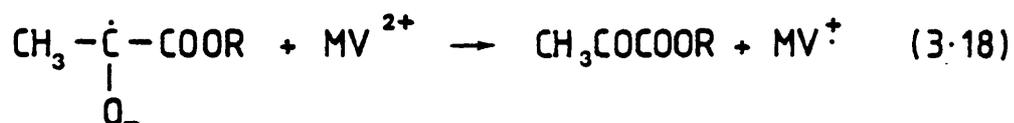
(where R = CH₃-, C₂H₅-, or (CH₃)₂CH-)

Scheme 3-14

lifetime of triplet methyl pyruvate.

The triplet state of the alkyl pyruvates is suggested to be involved in the reaction since naphthalene has been shown, by a laser flash photolysis study,³³ to quench triplet methyl pyruvate, and the Type II photo-fragmentation has been shown to occur from the triplet state of alkyl pyruvates, (Chapter 3.3). This suggestion is also in accord with the proposal by Hammond and co-workers⁴ that ethyl pyruvate undergoes decarboxylation from the triplet state.

The formation of reduced methyl viologen can be attributed to electron transfer from a reduced species of the alkyl pyruvate to methyl viologen, as exemplified in Equation 3.18.



(where R = CH₃-, C₂H₅-, (CH₃)₂CH- or (CH₃)₃C-)

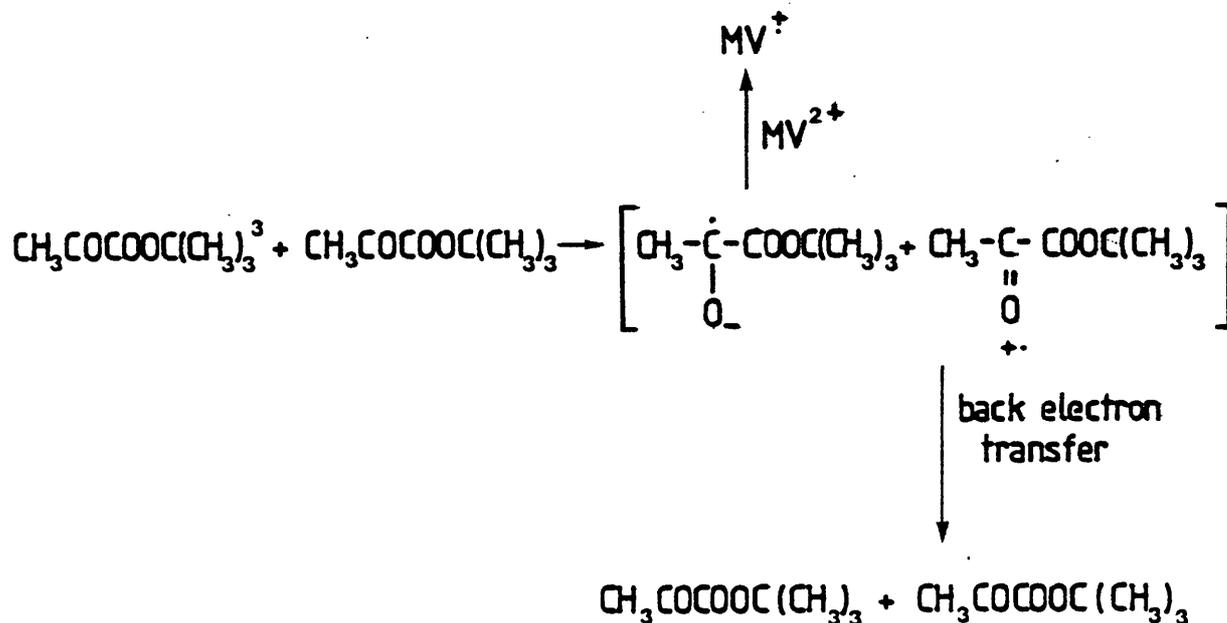
The laser flash photolysis study of methyl pyruvate has shown that the fluorescence and triplet lifetimes of this ester are little affected by the presence of methyl viologen, and as such suggests that the formation of reduced methyl viologen does not arise from reaction of methyl viologen

with an excited state of methyl pyruvate.

The bimolecular electron transfer process, leading to decarboxylation, as proposed in Scheme 3.14, will be in direct competition with the Type II fragmentation reaction for the photo-degradation of the alkyl pyruvates, and this could account for the finding that the fragmentation of methyl pyruvate to give formaldehyde is a minor pathway for the destruction of this ester, (Chapter 3.3). n-Hexyl pyruvate, upon irradiation in degassed acetonitrile solution, was found to be capable of undergoing both decarboxylation (via the proposed bimolecular electron transfer process) and the Type II fragmentation reaction (leading to hexaldehyde production). This result, shown in Table 3.8, confirms that both pathways can occur simultaneously and are in competition for the degradation of the alkyl pyruvate. However, the reported yields of hexaldehyde, in Table 3.8, may be artificially low due to the possibility of its consumption in a reduction reaction with triplet n-hexyl pyruvate.

The t-butyl pyruvate has been shown to be photostable (Chapter 3.3) and did not lead to carbon dioxide production upon direct irradiation. The t-butyl pyruvate does not fragment via a Type I reaction and cannot fragment via a Type II process, (Chapter 3.3). However, t-butyl pyruvate was found to produce reduced methyl viologen when irradiated in the presence of methyl viologen, and the mechanism of this reaction is particularly complicated. As the t-butyl pyruvate is photostable upon direct irradiation, it could be considered that any bimolecular electron transfer which takes place may be accompanied by an efficient back electron transfer reaction, leading to the formation of ground state t-butyl pyruvate, as opposed to decarboxylation, hence conferring photostability upon this ester, (Scheme 3.15). In the presence of methyl viologen, the production of reduced methyl viologen (by electron transfer

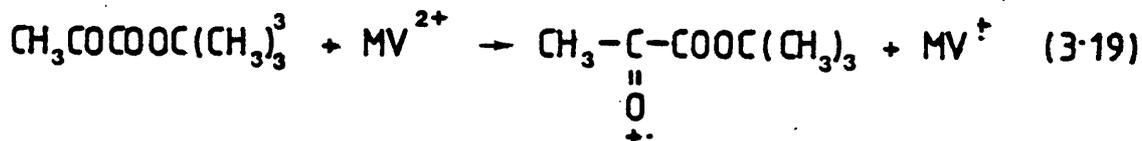
from the reduced form of t-butyl pyruvate to methyl viologen) will be in direct competition with the back electron transfer reaction if a mechanism as shown in Scheme 3.15 is operative.



Scheme 3-15

Alternatively, the bimolecular electron transfer reaction of t-butyl pyruvate could be very inefficient and may not occur to any appreciable extent. Indeed, the triplet lifetime of t-butyl pyruvate has been shown to be considerably longer than those for other alkyl pyruvates, (Chapter 3.3), and the bulky t-butyl groups of this ester could lead to steric hindrance, making electron transfer from the triplet to a ground state molecule of the ester an unfavourable process. Das³⁴ has recently demonstrated that aromatic carbonyl compounds undergo electron transfer reactions from the carbonyl triplet state, to methyl viologen, with the concomitant formation of reduced methyl viologen.³⁴ Thus the possibility exists, for the long-lived triplet t-butyl pyruvate, that a similar reaction could ensue in the presence of methyl viologen. The reduced

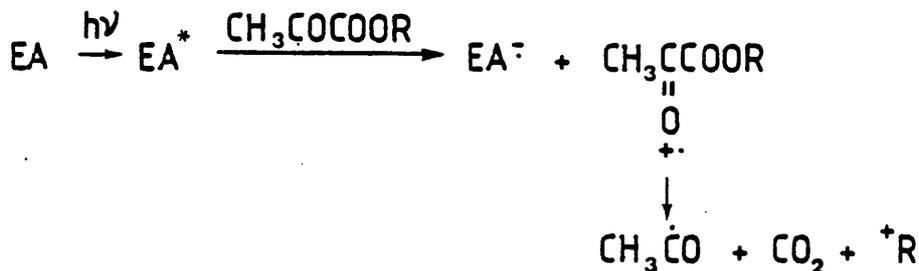
methyl viologen in this case could arise from electron transfer from the triplet t-butyl pyruvate to methyl viologen, giving the radical cation of the ester, (Equation 3.19).



3.4(iv) DECARBOXYLATION IN THE PRESENCE OF ELECTRON ACCEPTORS

If the bimolecular electron transfer reaction is to be considered feasible for the direct photo-induced decarboxylation of alkyl pyruvates (Scheme 3.14) it should be possible to enhance the carbon dioxide production by irradiation of alkyl pyruvates in the presence of electron acceptors. Accordingly, irradiations of degassed solutions of alkyl pyruvates in the presence of various electron acceptors were performed and the yields of carbon dioxide thus obtained are given in Table 3.9.

As can be seen from this Table, the addition of electron acceptors was found to sensitize the decarboxylation reaction. A mechanism involving electron transfer from the alkyl pyruvate to the electron acceptor is envisaged as being accountable for the sensitization process, (Scheme 3.16).



(where EA = electron acceptor, and R = alkyl group)

Scheme 3-16

TABLE 3.9

Yields of carbon dioxide from the irradiation (a) of alkyl pyruvates (10^{-2} M) in degassed solution, in the presence of electron acceptors (10^{-2} M)

| Alkyl pyruvate (10^{-2} M) | Electron acceptor (10^{-2} M) | Solvent | Yield (%) of carbon dioxide |
|----------------------------------|-------------------------------------|--------------|--------------------------------|
| Methyl pyruvate | Dichlorodicyanobenzoquinone | Acetonitrile | 11.8 |
| Methyl pyruvate | Tetracyanoethylene | Acetonitrile | 12.8 |
| Methyl pyruvate | 1-Cyanonaphthalene | Acetonitrile | 15.2 |
| Methyl pyruvate | 1-Cyanonaphthalene | Benzene | 21.5 |
| Methyl pyruvate | 9,10-Dicyanoanthracene (b) | Acetonitrile | 11.6 |
| Isopropyl pyruvate | 1-Cyanonaphthalene | Acetonitrile | 23.6 |
| t-Butyl pyruvate | 1-Cyanonaphthalene | Acetonitrile | 14.6 |
| t-Butyl pyruvate | 9,10-Dicyanoanthracene (b) | Acetonitrile | 7.7 |
| t-Butyl pyruvate | 1-Cyanonaphthalene | Benzene | 10.4 |

(a) 6h irradiation

(b) OD = 1.0 at 370 nm

Higher yields of carbon dioxide were envisaged for the sensitized decarboxylation of t-butyl pyruvate, when compared to the other alkyl pyruvates, due to the greater stability of the t-butyl cation over the cations produced from the other esters. However, as can be seen in Table 3.9, the yields of carbon dioxide from t-butyl pyruvate were in some cases lower than those obtained from the methyl and isopropyl pyruvates which were similarly investigated.

It is of interest to note that the addition of methyl viologen to degassed solutions of methyl and t-butyl pyruvates led to enhanced carbon dioxide yields, (Table 3.10), together with the formation of reduced methyl viologen.

TABLE 3.10

Yields of carbon dioxide from the direct irradiation^(a) of alkyl pyruvates (10^{-2} M) in degassed solutions containing methyl viologen (10^{-2} M)

| Alkyl pyruvate (10^{-2} M) | Solvent | Yield (%) of carbon dioxide |
|----------------------------------|---|--------------------------------|
| Methyl pyruvate | Acetonitrile/water (9:1 v/v) | 19 |
| t-Butyl pyruvate | Acetonitrile/pyridine/water (8:1:1 v/v) | 11.4 |

(a) 6h irradiation

The above result also lends credence to the involvement of an electron transfer reaction in the decarboxylation of alkyl pyruvates. The enhanced carbon dioxide yields in the presence of methyl viologen result from the subsequent fragmentation of the ester radical cation produced in each case, and for the t-butyl pyruvate can be explained by the mechanisms shown in Scheme 3.15 and/or Equation 3.19. Methyl viologen does not undergo any

appreciable reaction with the excited states of methyl pyruvate, and the mechanisms shown in Scheme 3.14 and Equation 3.18 can be used to explain the enhanced carbon dioxide yields from this system. This latter result further substantiates the proposed bimolecular electron transfer reaction.

Further evidence to support an electron transfer reaction in the photo-induced decarboxylation of alkyl pyruvates comes from the finding that irradiation of methyl pyruvate, in degassed acetonitrile and benzene solutions containing various aromatic hydrocarbons, leads to enhanced yields of carbon dioxide, (Table 3.11).

TABLE 3.11

Yields of carbon dioxide from irradiation^(a) of methyl pyruvate (10^{-2} M) (A) in benzene and (B) in acetonitrile solution containing various aromatic hydrocarbons (10^{-2} M), under degassed conditions

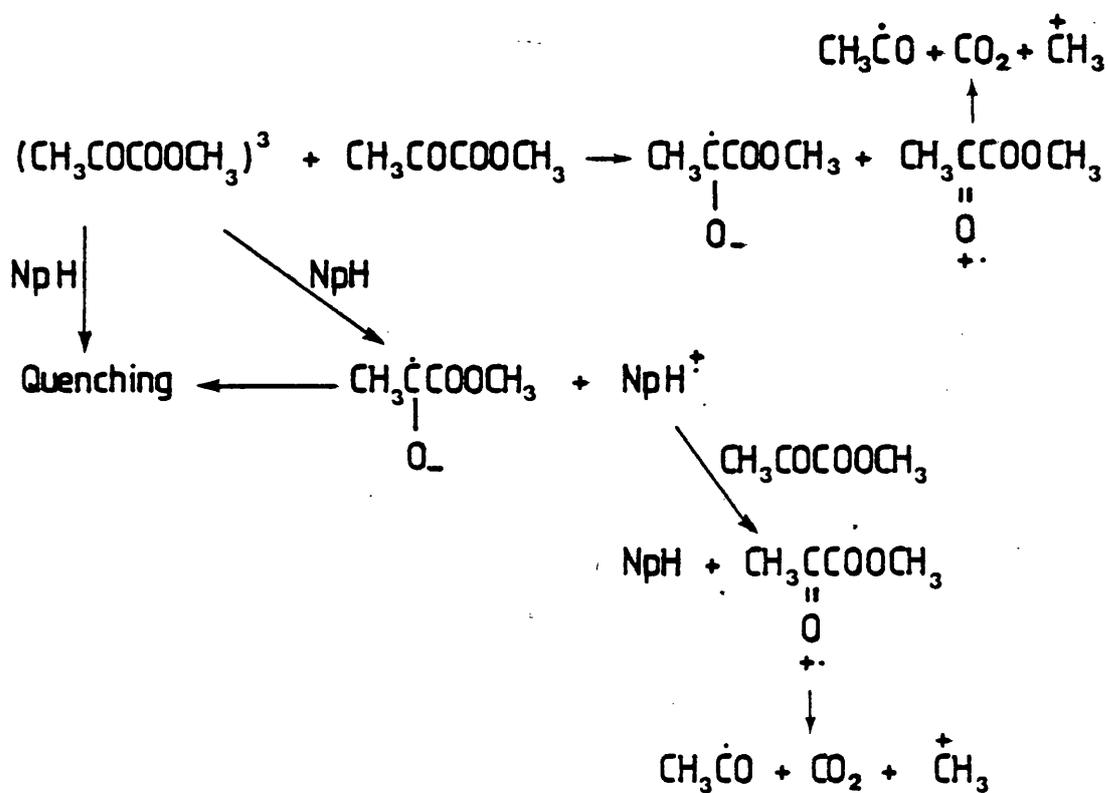
| Aromatic hydrocarbon (10^{-2} M) | Yield (%) of carbon dioxide | |
|--|-----------------------------|------------------|
| | (A) Benzene | (B) Acetonitrile |
| None | 5.3 | 7 |
| Naphthalene | 10.4 | 12 |
| 2,6-Dimethylnaphthalene | 7.1 | 17.5 |
| 9,10-Dimethylanthracene | 13.4 | 22.3 |
| Biphenyl | 11.4 | 20.9 |
| Phenanthrene | 11.6 | 11.8 |
| Pyrene | - (b) | 10.2 |

(a) 6h irradiation

(b) not measured

A similar observation has been encountered in analogous reactions of pyruvic acid (Chapter 2.4), and the same mechanism can be used to explain the enhanced carbon dioxide yields from methyl pyruvate when irradiated in the presence of aromatic compounds, such as naphthalene.

It has been shown, by laser flash photolysis,³³ that naphthalene quenches the triplet state of methyl pyruvate, and it is possible that in the quenching process some electron transfer could take place resulting in the formation of reduced methyl pyruvate and the naphthalene radical cation. The further reaction of the naphthalene radical cation with ground state methyl pyruvate would explain the enhanced yields of carbon dioxide observed in this system, as described in Scheme 3.17. A similar rationale can be used to account for the sensitization of carbon dioxide production observed with the other aromatic hydrocarbons.



Scheme 3-17

Summary

That alkyl pyruvates are capable of undergoing decarboxylation via a bimolecular electron transfer process is consistent with the finding that pyruvic acid produces carbon dioxide via an analogous mechanism. The

decarboxylation reaction of alkyl pyruvates appears to be a minor route for photoreaction, indeed the decarboxylation reaction will be in competition with the Type II reaction for fragmentation of these esters. That electron acceptors can sensitize carbon dioxide production further validates the involvement of a bimolecular electron transfer process in the direct decarboxylation of alkyl pyruvates. The irradiation of methyl pyruvate in the presence of aromatic hydrocarbons also gives rise to enhanced carbon dioxide yields via a mechanism suggested to involve electron transfer.

3.5 THE DIRECT PHOTO-OXIDATIVE DECARBOXYLATION OF α -KETO-CARBOXYLIC ESTERS

Object of investigation

The only report pertaining to the effect of oxygen upon the photo-reactions of α -keto-carboxylic esters in solution, is that referring to the epoxidation of α -methylstyrene by methyl phenylglyoxylate.²² The aim of this investigation is to elucidate the rôle of oxygen in the direct photo-oxidative decarboxylation of α -keto-carboxylic esters.

3.5(i) DECARBOXYLATION STUDIES

A wide variety of α -keto-carboxylic esters were found to undergo direct photo-oxidative decarboxylation in oxygenated acetonitrile and benzene solutions, (Table 3.12).

TABLE 3.12

Yields of carbon dioxide from the direct irradiation^(a) of α -keto-carboxylic esters (10^{-2} M) under oxygen (A) in acetonitrile and (B) in benzene solutions

| α -Keto-carboxylic ester (10^{-2} M) | Yield (%) of carbon dioxide | |
|---|-----------------------------|-------------|
| | (A) Acetonitrile | (B) Benzene |
| Methyl pyruvate | 37 | 34 |
| Ethyl pyruvate | 63 | 54 |
| Isopropyl pyruvate | 46 | 23 |
| n-Butyl pyruvate | 20 | 19 |
| t-Butyl pyruvate | 58 | 47 |
| n-Hexyl pyruvate | 35 | 33 |
| Benzyl pyruvate | 33 | 23 |
| Ethylbenzoylformate | 16 | 18 |
| 2-(1-naphthyl)ethyl pyruvate | 15 | 18.5 |
| 2-(2-naphthyl)ethyl pyruvate | 21 | 11 |
| 2-(2-naphthyl)ethyl- α -keto-octanoate | 17 | 17 |

(a) 3h irradiation

The rates of carbon dioxide production from the irradiation of methyl pyruvate in oxygenated acetonitrile and oxygenated benzene solutions are shown in Fig. 3.22.

Rather surprisingly, t-butyl pyruvate, which has been shown to be photostable under degassed conditions (Chapter 3.3 and 3.4), was found to undergo efficient photo-oxidative decarboxylation (Table 3.12), and the rates of carbon dioxide production for this ester, in oxygenated acetonitrile and oxygenated benzene solutions are shown in Fig. 3.23.

Table 3.13 shows the yields of carbon dioxide and hexaldehyde from the direct photo-oxidation of n-hexyl pyruvate in oxygenated acetonitrile solution.

TABLE 3.13

Yields of carbon dioxide and hexaldehyde from the direct irradiation^(a) of n-hexyl pyruvate (5×10^{-2} M) in oxygenated acetonitrile solution

| Product | Yield (%) |
|----------------------------|-----------|
| Carbon dioxide | 35 |
| Hexaldehyde ^(b) | 45 |

(a) 3h irradiation

(b) determined by g.l.c.

The addition of 9,10-dicyanoanthracene to oxygenated acetonitrile solutions of methyl pyruvate was found to lead to decarboxylation, (Table 3.14). Although the yield of carbon dioxide is not as high as under direct irradiation conditions, sensitization must be occurring since the 9,10-dicyanoanthracene absorbed all the incident light.

The effect of solvent deuteration upon the yields of carbon dioxide from irradiation of oxygenated solutions of methyl and ethyl pyruvates

FIG. 3.22

Rates of carbon dioxide production from irradiation of methyl pyruvate (10^{-2} M), (a) in oxygenated acetonitrile solution (\square) and (b) oxygenated benzene solution (\blacktriangle).

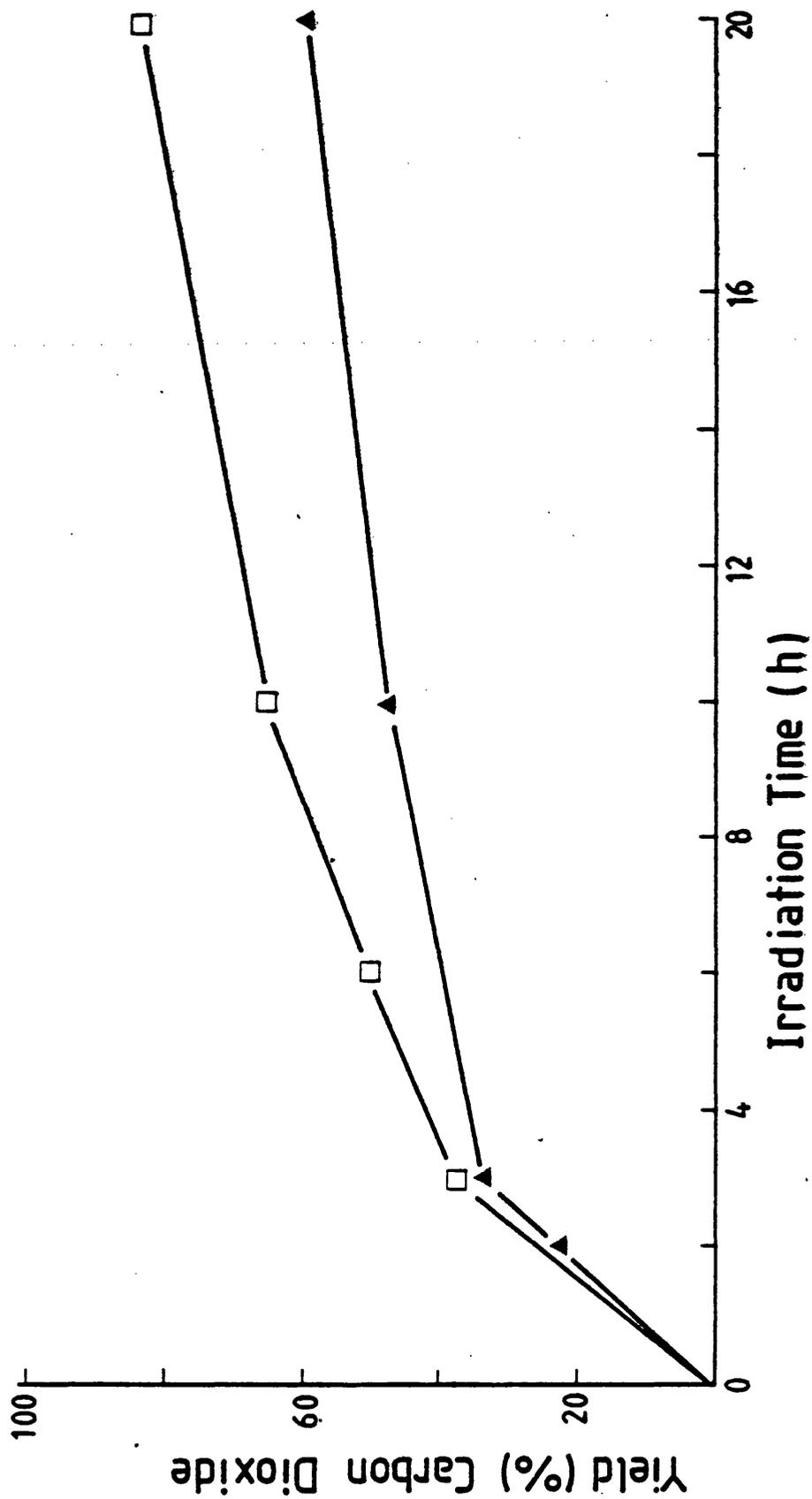


FIG. 3.23

Rates of carbon dioxide production from irradiation of t-butyl pyruvate (10^{-2} M), (a) in oxygenated acetonitrile solution (\square), and (b) in oxygenated benzene solution (\blacktriangle).

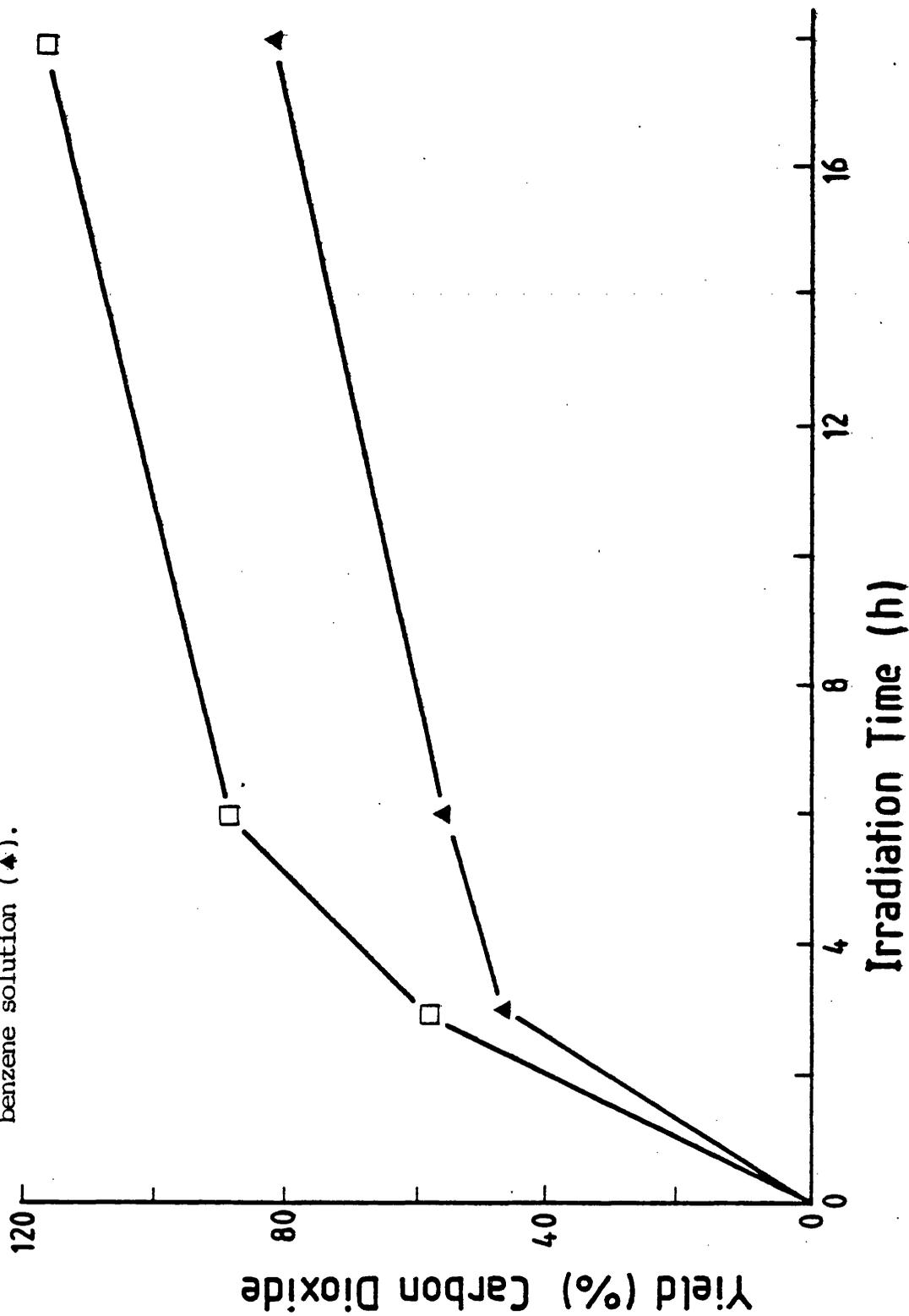


TABLE 3.14

Yields of carbon dioxide from the irradiation^(a) of methyl pyruvate (10^{-2} M) in oxygenated acetonitrile solution containing 9,10-dicyanoanthracene^(b)

| Conditions | Yield (%) of carbon dioxide |
|--------------------------------|-----------------------------|
| 9,10-dicyanoanthracene absent | 50 |
| 9,10-dicyanoanthracene present | 38 |

(a) 6h irradiation

(b) OD = 1.0 at 370 nm

was investigated and the results shown in Table 3.15. As can be seen no appreciable solvent isotope effect exists for the carbon dioxide formation.

TABLE 3.15

Solvent isotope effect upon the yield of carbon dioxide from the direct irradiation^(a) of α -keto-carboxylic esters (10^{-2} M) in oxygenated solution

| α -Keto-carboxylic ester (10^{-2} M) | Solvent | Yield (%) of carbon dioxide | Isotope Effect |
|--|--------------------|-----------------------------|----------------|
| Methyl pyruvate | Deuteriochloroform | 52 | 1.48 |
| Methyl pyruvate | Chloroform | 35 | |
| Ethyl pyruvate | Deuterium oxide | 15.4 | 0.94 |
| Ethyl pyruvate | Water | 16.3 | |

(a) 5h irradiation

3.5(ii) DISCUSSION

Alkyl pyruvates have been shown to undergo direct photo-induced decarboxylation via a bimolecular electron transfer process under degassed conditions, (Chapter 3.4). In the presence of oxygen the yields of carbon dioxide are dramatically increased, and therefore the mechanism of the

interaction of oxygen and α -keto-carboxylic ester leading to carbon dioxide production, is of particular interest.

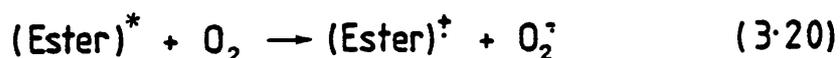
It has previously been suggested that the photo-epoxidation of α -methylstyrene by methyl phenylglyoxylate proceeds by initial α -cleavage of the ester, followed by radical scavenging by oxygen leading to epoxidation via per-acid intermediates.²² However, it is now appreciated that alkyl pyruvates, and presumably other α -keto-carboxylic esters, do not fragment via a Type I reaction involving α -cleavage, but via a Type II reaction involving hydrogen atom abstraction, (Chapter 3.3). Thus, the epoxidation reaction cannot involve the interaction of oxygen with radicals produced via α -cleavage of the α -keto-carboxylic ester.

Let us consider therefore the ways in which oxygen could interact with the α -keto-carboxylic esters. There is the possibility, for those esters capable of undergoing the Type II fragmentation reaction, that oxygen could intercept the intermediate 1,4-diradical,³⁵ and give rise to a product which collapses giving carbon dioxide. However, that the yield of hexaldehyde, the Type II fragmentation product, from the irradiation of oxygenated acetonitrile solutions of n-hexyl pyruvate is high, (Table 3.13), would suggest that oxygen does not intercept the 1,4-diradical formed via the Type II process. This is consistent with the finding that oxygen does not intercept the 1,4-diradical formed in the Type II reaction of α -keto-octanoic acid (Chapter 2.5). It should be noted that the yield of hexaldehyde from irradiation of n-hexyl pyruvate is higher under oxygenated (Table 3.13) than under degassed conditions, (Chapter 3.4; Table 3.8). This indicates that the reduction reaction of triplet n-hexyl pyruvate by hexaldehyde is being suppressed under oxygen, presumably the interaction of oxygen with triplet n-hexyl pyruvate reduces the amount of triplet n-hexyl pyruvate available for reduction, and hence a higher yield

of hexaldehyde is observed. That oxygen does not intercept the 1,4-diradical formed by the Type II reaction, together with the finding that good yields of carbon dioxide are obtained from t-butyl pyruvate, (which does not fragment via either a Type I or Type II reaction and is found to be photostable under degassed conditions), would suggest that decarboxylation may arise from a direct reaction between oxygen and α -keto-carboxylic ester. A similar direct reaction between oxygen and the esters capable of fragmenting by a Type II process, would obviously compete with the Type II reaction for degradation of these esters.

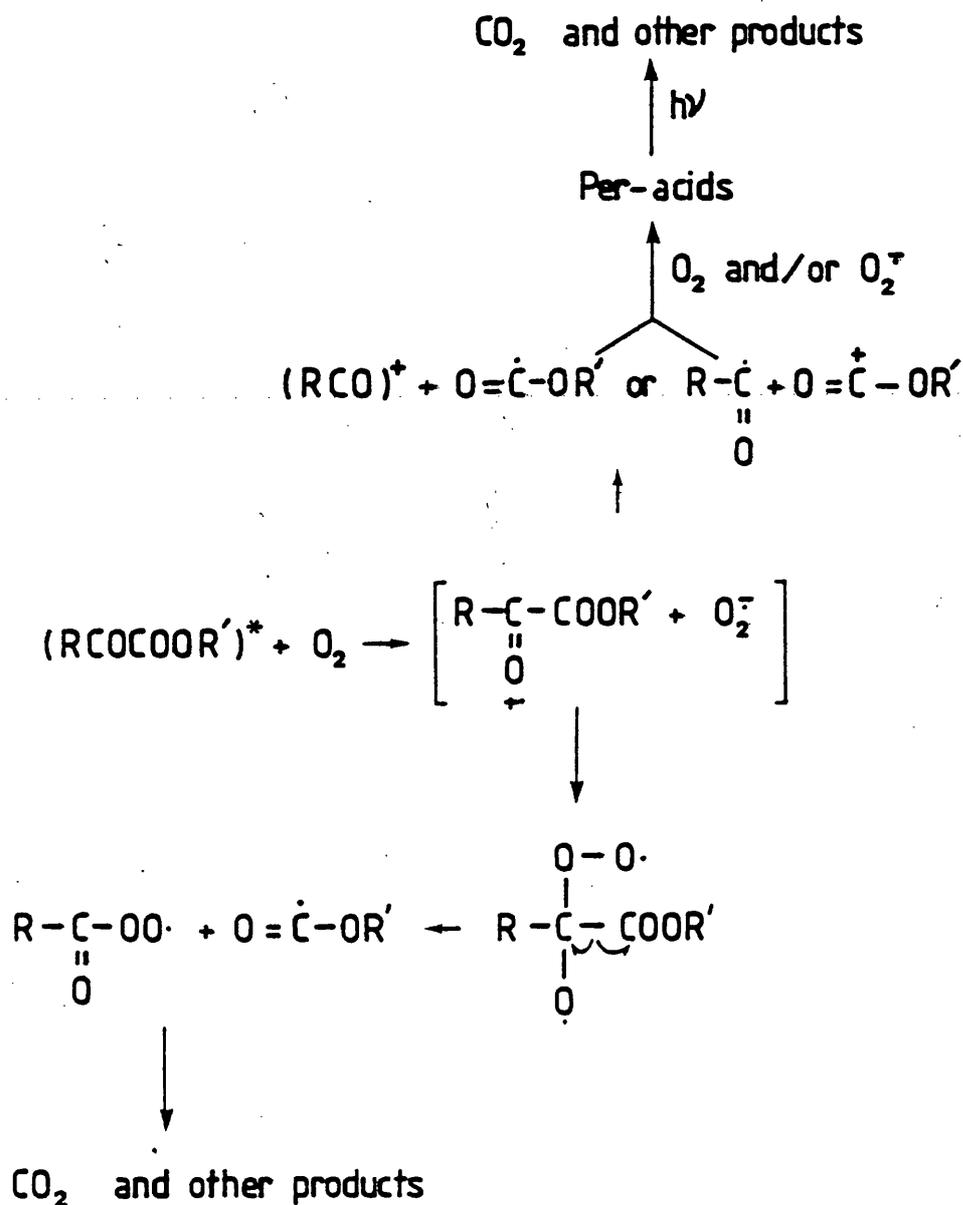
An obvious mechanism for the decarboxylation of α -keto-carboxylic esters in oxygenated solution, would be to suggest the involvement of singlet oxygen, which could be produced by reaction of the triplet ester with oxygen. Any singlet oxygen so produced may react with the α -keto-carboxylic ester to produce carbon dioxide. However, the lack of a solvent isotope effect upon the decarboxylation reaction of methyl and ethyl pyruvates (Table 3.15) indicates that singlet oxygen plays little, if any, rôle in the photo-oxidative decarboxylation of these esters. This rationale assumes that any singlet oxygen reaction would involve a diffusional process.

Alkyl pyruvates have been shown to undergo an electron transfer reaction with methyl viologen to produce reduced methyl viologen, (Chapter 3.4). It is conceivable that in oxygenated solutions, where the oxygen concentration is similar to that of the α -keto-carboxylic ester, electron transfer to oxygen from the ester may occur, (Equation 3.20).



The superoxide anion may then react with the ester radical cation to produce carbon dioxide, and/or the ester radical cation may fragment to

form radicals which could be scavenged by oxygen to form per-oxy species and give rise to carbon dioxide, as shown in Scheme 3.18.



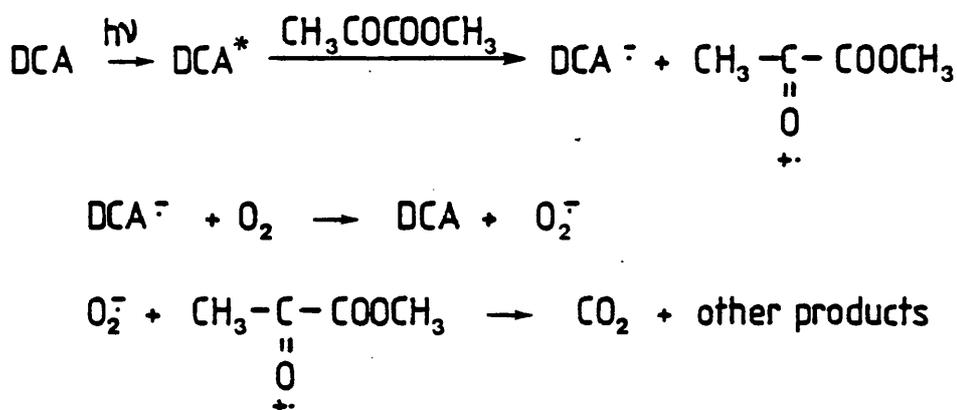
(where R = methyl, phenyl or octyl

and R' = alkyl, benzyl, 2-(1-naphthyl)ethyl or
2-(2-naphthyl)ethyl)

Scheme 3.18

The formation of the per-oxy species, as shown in the above mechanism, would account for the observed epoxidation of alkenes.²² That per-oxy species are produced in the photo-oxidative decarboxylation of α -keto-carboxylic esters is indicated by the observation that t-butyl pyruvate, upon prolonged irradiation in oxygenated acetonitrile solution, leads to greater than one mole of carbon dioxide evolution, (Fig. 3.23). The production of more than one mole of carbon dioxide from the photo-oxidation of pyruvic acid has previously been shown to involve the participation of per-acids, (Chapter 2.5), and therefore the possibility exists that such species could be involved in similar reactions of α -keto-carboxylic esters, as shown in Scheme 3.18. Indeed, that per-acids are produced in the photo-oxidation of α -keto-carboxylic esters has previously been shown by the observation of per-benzoic acid from irradiation of methyl phenylglyoxylate in oxygenated benzene solution.²²

Further evidence to support the mechanism proposed in Scheme 3.18, involving electron transfer from α -keto-carboxylic ester to oxygen, comes from the finding that 9,10-dicyanoanthracene (DCA), a good electron acceptor, can sensitize the decarboxylation of methyl pyruvate in oxygenated acetonitrile solution, Table 3.14. The mechanism by which this sensitization could occur is shown in Scheme 3.19.



Scheme 3.19

It is of interest to note that 2-(2-naphthyl)ethyl pyruvate has been shown, by laser flash photolysis, to undergo reaction with methyl viologen to produce reduced methyl viologen, (Chapter 3.7). The addition of methyl viologen to aqueous acetonitrile solutions of 2-(2-naphthyl)ethyl pyruvate did not affect the fluorescence or triplet lifetimes of the ester, and therefore reduced methyl viologen does not arise from reaction of methyl viologen with an excited state of this ester, (Chapter 3.7). It is conceivable that the naphthyl- α -keto-carboxylic esters could undergo an internal electron transfer reaction upon irradiation, to form a molecule which contains a carbonyl radical anion and a naphthalene radical cation group, (Equation 3.21). The interaction of this latter species, with methyl viologen, will give reduced methyl viologen.



(where R = CH₃- or CH₃(CH₂)₅-, Np = 1- or 2-naphthyl)

The interaction of oxygen with a species such as that formed in Equation 3.21 above, could also be responsible for decarboxylation of esters of this type, (possibly by the formation of the superoxide anion), in addition to the mechanism proposed in Scheme 3.18.

In the study of α -keto-octanoic acid, (Chapter 2.5), high yields of pent-1-ene were obtained both in oxygenated and degassed solutions. The carbon dioxide produced in the above system was suggested to arise from the pyruvic acid produced by the Type II fragmentation of the α -keto-octanoic acid, as opposed to the interception of the 1,4-diradical with oxygen, (Chapter 2.5). Thus, for α -keto-carboxylic esters capable of undergoing a Type II reaction, one cannot rule out the possibility that at least some of the carbon dioxide may arise from the subsequent

decarboxylation of a product of the Type II fragmentation process, via the interaction of oxygen with the latter species. However, that t-butyl pyruvate gives high yields of carbon dioxide when irradiated in oxygenated solution shows that decarboxylation can occur from the direct reaction of the esters with oxygen, (Equation 3.20). As t-butyl pyruvate does not undergo the Type II reaction, the decarboxylation of this ester cannot arise from the interaction of oxygen with a product of the Type II fragmentation process, and further substantiates the mechanism proposed in Scheme 3.18.

In conclusion, carbon dioxide yields in excess of 100% were only obtained from prolonged irradiation of oxygenated acetonitrile solutions of t-butyl pyruvate, (Fig. 3.23). The second mole of carbon dioxide may well arise from the $O=\dot{C}-OR'$ species either by direct decarboxylation, or by interaction with oxygen to form an intermediate which collapses giving carbon dioxide. In contrast to the t-butyl pyruvate, which cannot undergo a Type II reaction, prolonged irradiation of methyl pyruvate, which is capable of fragmentation via the Type II process did not produce high yields (i.e. >1 mole) of carbon dioxide, (Fig. 3.22). Hence, the lower yields of carbon dioxide, obtained from irradiation of oxygenated acetonitrile solutions of methyl pyruvate, can be explained on the basis of competition between the Type II process and the mechanism shown in Scheme 3.18, for the decomposition of this ester.

Summary

The direct photo-oxidative decarboxylation of α -keto-carboxylic esters has been studied, and found to lead to higher yields of carbon dioxide than those reported under degassed conditions. The proposed mechanism for the reaction is suggested to involve an electron transfer reaction from the α -keto-carboxylic ester to oxygen, with carbon dioxide production

arising from either the interaction of the superoxide anion with the ester radical cation, and/or the scavenging, by oxygen, of the radicals produced from the further degradation of the ester radical cation. This electron transfer reaction will be in competition with the Type II reaction for degradation of the esters, and there is the possibility that carbon dioxide may be produced from the reaction of the species generated in the Type II process. The intermediacy of per-acids is invoked, and the mechanism is supported by the observation that the electron acceptor, 9,10-dicyanoanthracene, sensitizes the decarboxylation reaction of methyl pyruvate.

3.6 THE DYE-SENSITIZED PHOTO-OXIDATIVE DECARBOXYLATION OF α -KETO-CARBOXYLIC ESTERS

Object of investigation

Few reports have appeared relating to the dye-sensitized photo-oxidative decarboxylation of α -keto-carboxylic esters, namely the enol tautomers of methyl-p-methoxyphenylpyruvate²³ and a derivative which has the enol group protected by methyl substitution.²⁴ The decarboxylation reaction was shown to be sensitized by dyes such as Methylene Blue^{23,24} and tetraphenylporphyrin.²⁴ The following investigations were performed in order to establish whether other α -keto-carboxylic esters are capable of undergoing similar dye-sensitized photo-oxidative decarboxylation reactions, using a variety of dyes as sensitizers.

3.6(i) DECARBOXYLATION STUDIES

Several α -keto-carboxylic esters were found to produce carbon dioxide upon dye-sensitized photo-oxygenation in acetonitrile/pyridine (4:1 v/v) solution, and the results are shown in Table 3.16.

The decarboxylation reaction of methyl pyruvate, in acetonitrile/pyridine (4:1 v/v) solution, was found to occur using a variety of sensitizers, (Table 3.17). That Methylene Blue^{23,24} and tetraphenylporphyrin²⁴ can lead to decarboxylation is confirmed, (Table 3.17). Carbon dioxide was also obtained from the Methylene Blue sensitized photo-oxygenation of methyl pyruvate in methanol/pyridine (4:1 v/v) solution, (Table 3.17).

The effect of oxygen concentration upon the decarboxylation of methyl pyruvate, sensitized by Rose Bengal, in acetonitrile/pyridine (4:1 v/v) solution was studied and the results shown in Table 3.18. Higher yields of carbon dioxide were obtained when the reaction was performed under

TABLE 3.16

Yields of carbon dioxide from the dye-sensitized photo-oxygenation (a) of α -keto-carboxylic esters (10^{-2} M) in acetonitrile/pyridine (4:1 v/v) solution

| α -Keto-carboxylic ester (10^{-2} M) | Irradiation Time (h) | Yield (%) of carbon dioxide (b) | |
|---|-------------------------|---------------------------------|-----------------|
| | | Methylene Blue (c) | Rose Bengal (c) |
| Methyl pyruvate | 20 | 39 | 54 |
| Ethyl pyruvate | 20 $\frac{1}{2}$ | -* | 37 |
| Ethyl pyruvate | 22 $\frac{1}{2}$ | 21 | -* |
| Isopropyl pyruvate | 18 | 15.5 | 23 |
| n-Butyl pyruvate | 18 | 30 | 34 |
| t-Butyl pyruvate | 18 | 27 | 29 |
| n-Hexyl pyruvate | 18 | 21 | 34 |
| Benzyl pyruvate | 18 | 24.5 | 26 |
| Ethylbenzoylformate | 19 | 14 | 14 |
| 2-(1-naphthyl)ethyl pyruvate | 18 | 28 | 51 |
| 2-(2-naphthyl)ethyl pyruvate | 18 | 29 | 45 |
| 2-(2-naphthyl)ethyl- α -keto-octanoate | 18 | 47 | 43 |

(a) 2% potassium chromate filter solution used.

(b) Negligible amounts of carbon dioxide were obtained from control experiments in the absence of dye.

(c) Dye concentration = 0.02g/25 ml. In each case the dye had been slightly bleached during the course of the irradiation.

* Yield not determined.

TABLE 3.17

Yields of carbon dioxide from the dye-sensitized photo-oxygenation of methyl pyruvate (10^{-2} M) in acetonitrile/pyridine (4:1 v/v) solution

| Sensitizer (a) | Irradiation Time (h) | Filter (b) | Yield (%) of carbon dioxide |
|----------------------|----------------------|------------|-----------------------------|
| Rose Bengal | 20½ | A | 76.3 |
| Methylene Blue | 19 | A | 59.3 |
| Methylene Blue (c) | 19 | A | 36 |
| Rhodamine B | 18 | B | 45 |
| Erythrosin B | 18 | B | 70.3 |
| Tetraphenylporphyrin | 18 | B | 28 |

(a) Rose Bengal/Methylene Blue = 0.02g/25 ml; Rhodamine B/Erythrosin B = 0.02g/50 ml; Tetraphenylporphyrin = OD = 0.8 at 514 nm.

(b) Filter solution A = saturated sodium nitrate; filter solution B = 2% potassium chromate, (both aqueous solutions).

(c) In methanol/pyridine (4:1 v/v) solution.

TABLE 3.18

Yields of carbon dioxide from irradiation^(a) of methyl pyruvate (2×10^{-2} M) in acetonitrile/pyridine (4:1 v/v) solution, sensitized by Rose Bengal^(b) under different oxygen concentrations

| Conditions | Yield (%) of carbon dioxide |
|-----------------------|-----------------------------|
| Argon | 17.4 |
| Oxygen | 27.1 |
| Air | 42.5 |
| Nitrogen (OFN) | 12.0 |
| Nitrogen (Commercial) | 11.4 |

(a) 18h irradiation; 2% potassium chromate filter solution.

(b) Concentration = 0.02g/25 ml.

air than under pure oxygen, (Table 3.18).

The Rose Bengal sensitized photo-oxygenation of n-hexyl pyruvate was studied in a variety of solvents, and the yields of carbon dioxide obtained in each case are shown in Table 3.19. A g.l.c. analysis was carried out on one of the n-hexyl pyruvate solutions, and it was found to contain hexanol as a product, (Table 3.19).

3.6(ii) DISCUSSION

The dye-sensitized photo-oxygenation of α -keto-carboxylic esters was found to lead to carbon dioxide production, (Tables 3.16 - 3.19). The decarboxylation reaction was found to be sensitized by a variety of dyes (Table 3.17), and the reaction was observed to show a marked dependence upon oxygen concentration, (Table 3.18).

It has previously been suggested that the dye-sensitized photo-oxygenation of α -keto-carboxylic esters proceeds via a mechanism involving singlet oxygen,^{23,24} although no concrete evidence was put forward in these studies to substantiate such a claim. From the results reported

TABLE 3.19

Yields of carbon dioxide from the dye-sensitized photo-oxygenation (a)
of n-hexyl pyruvate in various solutions

| n-Hexyl pyruvate concentration | Solvent | Irradiation Time (h) | Yield (%) of carbon dioxide |
|--------------------------------|----------------------------------|----------------------|-----------------------------|
| 5×10^{-2} M | Acetonitrile | 18 | 8 |
| 2×10^{-2} M | Acetonitrile/pyridine (4:1 v/v) | 18 | 17.3 |
| 3.3×10^{-2} M | Acetonitrile/quinoline (4:1 v/v) | 20 | 15 (b) |

(a) Rose Bengal = 0.02g/25 ml; 2% potassium chromate filter solution.

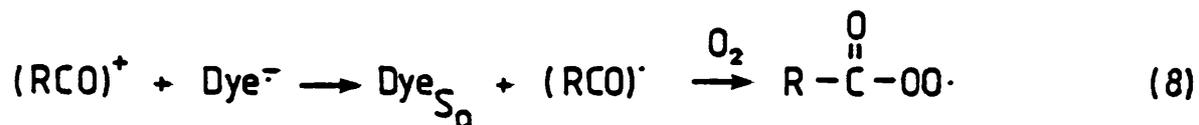
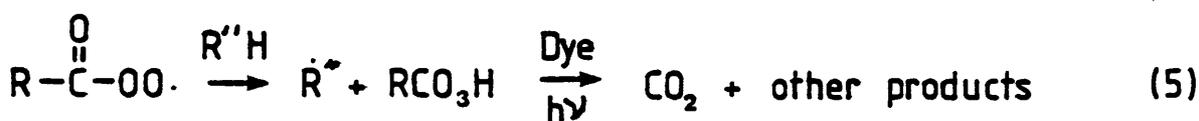
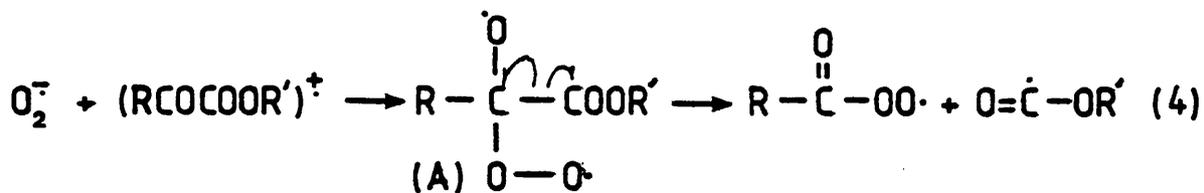
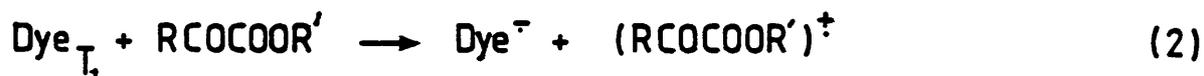
(b) Hexan-1-ol (25%) determined by g.l.c.

herein the participation of singlet oxygen cannot be either definitely invoked or rigorously excluded in the dye-sensitized photo-oxygenation of α -keto-carboxylic esters. Although further studies are required in order to conclusively elucidate the rôle that singlet oxygen may play in these reactions, its participation is considered unlikely because of the observed effect of oxygen concentration.

Reactions which involve singlet oxygen do not show a dependency on oxygen concentration, (Chapter 2.6.2), i.e. the reactions proceed at similar rates both under low and high oxygen concentrations. However, the decarboxylation of methyl pyruvate was shown to be markedly dependent upon oxygen concentration, (Table 3.18), and as such indicates that singlet oxygen is not involved in the decarboxylation reaction. Thus, if singlet oxygen was responsible for the reaction, the yields of carbon dioxide from methyl pyruvate should have been comparable at both low and high oxygen concentrations, and as this was not the case a singlet oxygen mediated reaction is considered improbable. A similar oxygen dependency has been shown to exist in the dye-sensitized photo-oxidative decarboxylation of α -keto-carboxylic acids (Chapter 2.6.2) which are known not to react via a singlet oxygen mechanism.^{22,36}

From this initial decarboxylation study, together with the previous findings that α -keto-carboxylic esters are capable of undergoing electron transfer reactions (Chapter 3.4 and 3.5), the following mechanism is tentatively proposed in order to account for the production of carbon dioxide under dye-sensitized photo-oxygenation conditions, (Scheme 3.20).

The formation of a species such as (A), in the above Scheme 3.20, has been suggested as an intermediate in the direct photo-oxidation reactions of α -keto-carboxylic acids²² and their esters (Chapter 3.5). It is considered feasible that in the dye-sensitized photo-oxygenation of α -



(where R = methyl, phenyl or octyl,

R' = alkyl, benzyl, 2-(1-naphthyl)ethyl or

2-(2-naphthyl)ethyl

and R''H = hydrogen donor)

Scheme 3.20

keto-carboxylic esters a similar species could arise from the reaction shown in Scheme 3.20.

Per-acid intermediates have been shown to be produced in the direct photo-oxidation of α -keto-carboxylic esters,²² and in the dye-sensitized reaction the formation of per-acid species could well account for carbon dioxide production. In fact in separate experiments, per-acetic acid was found to undergo decarboxylation upon dye-sensitized reaction both under

TABLE 3.20

Yields of carbon dioxide from the dye-sensitized reaction^(a) of per-acetic acid (3.2×10^{-2} M) in acetonitrile/pyridine (4:1 v/v) solution

| Conditions | Yield (%) of carbon dioxide |
|--------------|-----------------------------|
| Under argon | 8 |
| Under oxygen | 9 |

(a) Rose Bengal = 0.02g/25 ml; 2% potassium chromate filter solution; 15h irradiation.

degassed and oxygenated conditions, (Table 3.20).

It is possible that the species $O=\dot{C}-O-R'$ could undergo decarboxylation as opposed to decarbonylation as shown in Scheme 3.20. The resulting $\cdot R'$ could then undergo hydrogen atom abstraction to yield $R'H$. However, in the dye-sensitized photo-oxygenation of n-hexyl pyruvate, only hexanol was observed in the irradiated solution, i.e. no hexaldehyde, hexane or hexene appeared, therefore decarbonylation of $O=\dot{C}-O-R'$ with the formation of hexanol from the resulting $\cdot OR'$ radical is favoured over the fragmentation of the species $O=\dot{C}-O-R'$ via decarboxylation. It is also feasible that the $O=\dot{C}-O-R'$ species could be intercepted by oxygen to give rise to an intermediate that could undergo decarboxylation and lead to a second mole of carbon dioxide. However, as the yields of carbon dioxide were never greater than 100% (i.e. 1 mole), the occurrence of such a reaction may be unlikely. That hexanol is produced in the dye-sensitized photo-oxygenation of n-hexyl pyruvate provides further evidence to support the mechanism as proposed in Scheme 3.20.

Such a mechanism (Scheme 3.20) predicts that equivalent amounts of carbon dioxide and hexanol should be formed. However, this was not found to be the case, as the yield of carbon dioxide was 10% lower than the

yield of hexanol, (Table 3.19). This discrepancy could be due to the fact that decarboxylation of per-acetic acid may be less efficient than the reaction leading to hexanol formation. Also any per-acetic acid formed may undergo reactions other than decarboxylation and hence lower the theoretical yield of carbon dioxide as compared to the yield of alcohol.

Obviously further experiments, for example (a) a full product study for each α -keto-carboxylic ester and (b) an investigation into the rôle that singlet oxygen may have, are warranted in order to elucidate the mechanism of the dye-sensitized photo-oxygenation of α -keto-carboxylic esters conclusively.

Summary

α -Keto-carboxylic esters are capable of undergoing dye-sensitized photo-oxygenation leading to carbon dioxide production. In the case of n-hexyl pyruvate, hexanol, in addition to carbon dioxide, was produced. The decarboxylation reaction can be sensitized by a variety of dyes, and the reaction of methyl pyruvate was shown to be dependent upon the oxygen concentration. A mechanism, not involving singlet oxygen, is proposed.

3.7 THE DIRECT PHOTO-INDUCED FRAGMENTATION OF A SERIES OF LONG CHAIN α -KETO-CARBOXYLIC ESTERS

Object of investigation

It has previously been demonstrated that α -keto-decanoic acid undergoes the Type II reaction leading to hept-1-ene and pyruvic acid.²¹ From quenching studies using cyclohexa-1,3-diene, the excited state responsible for the fragmentation process was thought to be the triplet.²¹ α -Keto-octanoic acid has recently been shown to undergo an analogous Type II reaction leading to pent-1-ene formation, and the excited state deemed responsible for the reaction was suggested to be the singlet state, (Chapter 2.5). Experiments are now described which investigate the hitherto unreported Type II fragmentation reaction of α -keto-octanoates, and probe the excited state from which the fragmentation reaction occurs.

3.7(i) PRODUCT STUDIES

α -Keto-octanoic acid, its methyl and 2-(2-naphthyl)ethyl esters were found to undergo the Type II reaction in benzene solution, yielding pent-1-ene, (Table 3.21). The reaction of α -keto-octanoic acid has previously been reported in Chapter 2.5 and is included in the results shown in Table 3.21 for comparison purposes. The Type II reaction of 2-(2-naphthyl)ethyl- α -keto-octanoate was also studied in acetonitrile solution, (Table 3.22). The yields of carbon dioxide produced from the solutions under investigation were also evaluated and are included in Tables 3.21 and 3.22. The Type II fragmentation can also lead to cyclic photo-products via cyclisation of the intermediate 1,4-diradical, however the formation of such products was not investigated for the reported reactions.

The Type II reaction leading to pent-1-ene formation was found to be

TABLE 3.21

Yields of pent-1-ene and carbon dioxide from the direct irradiation (a) of α -keto-octanoic acid and its ester derivatives (5×10^{-2} M) in benzene solutions

| Compound (5×10^{-2} M) | Reaction Conditions | Yields (%) of products | |
|---|---------------------|------------------------|----------------|
| | | Pent-1-ene (b) | Carbon Dioxide |
| α -Keto-octanoic acid | Nitrogen purged (c) | 4 | 9 |
| α -Keto-octanoic acid | Argon purged | 46 | 14.6 |
| α -Keto-octanoic acid | Argon purged (d) | 45 | 15.0 |
| α -Keto-octanoic acid | Oxygen purged | 38 | 69.9 |
| Methyl octanoate | Argon purged | 52 | 2.8 |
| Methyl octanoate | Argon purged (d) | 49 | 2.6 |
| Methyl octanoate | Oxygen purged | 39 | 28 |
| 2-(2-naphthyl)ethyl- α -keto-octanoate | Argon purged | 40 | 12.2 |
| 2-(2-naphthyl)ethyl- α -keto-octanoate | Oxygen purged | 32 | 31.3 |

(a) 18h irradiation

(b) Yield determined by g.l.c. and identified by g.l.c. and GC/MS

(c) Cyclohexa-1,3-diene (1.0 M) added

(d) Naphthalene (1×10^{-3} M) added

TABLE 3.22

Yields of pent-1-ene and carbon dioxide from the direct irradiation^(a) of 2-(2-naphthyl)ethyl- α -keto-octanoate (5×10^{-2} M) in acetonitrile solutions

| Reaction conditions | Yields (%) of products | |
|---------------------|------------------------|----------------|
| | Pent-1-ene | Carbon dioxide |
| Argon purged | 26 | 17.3 |
| Oxygen purged | 24 | 48.7 |

(a) 18h irradiation

relatively insensitive to the presence of triplet quenchers such as oxygen and naphthalene, (Tables 3.21 and 3.22). Interestingly, 2-(2-naphthyl)ethyl- α -keto octanoate, which contains a naphthalene group ideally situated to deactivate the triplet state of the ester by energy transfer, also gave rise to quite high yields of pent-1-ene, (Tables 3.21 and 3.22). In the earlier study of α -keto-decanoic acid by Evans and Leenmakers,²¹ cyclohexa-1,3-diene at concentrations >1.5 M were used to quench the Type II reaction. It was found that cyclohexa-1,3-diene at a concentration of 1.0 M almost totally quenched the formation of pent-1-ene from the Type II reaction of α -keto-octanoic acid in benzene solution, (Table 3.21).

The yield of carbon dioxide from the solutions investigated was found to be markedly increased in the presence of oxygen, with much lower yields being obtained from the same reactions when performed under degassed conditions, (Tables 3.21 and 3.22).

The rate of disappearance of methyl octanoate in degassed deuterated benzene solution was determined by following the reaction by ^1H n.m.r. spectroscopy, and was evaluated to be 0.3×10^{-6} moles/min, [Fig. 3.24(a)]. The addition of the triplet quencher naphthalene had little effect upon the rate of disappearance of methyl octanoate under the same irradiation

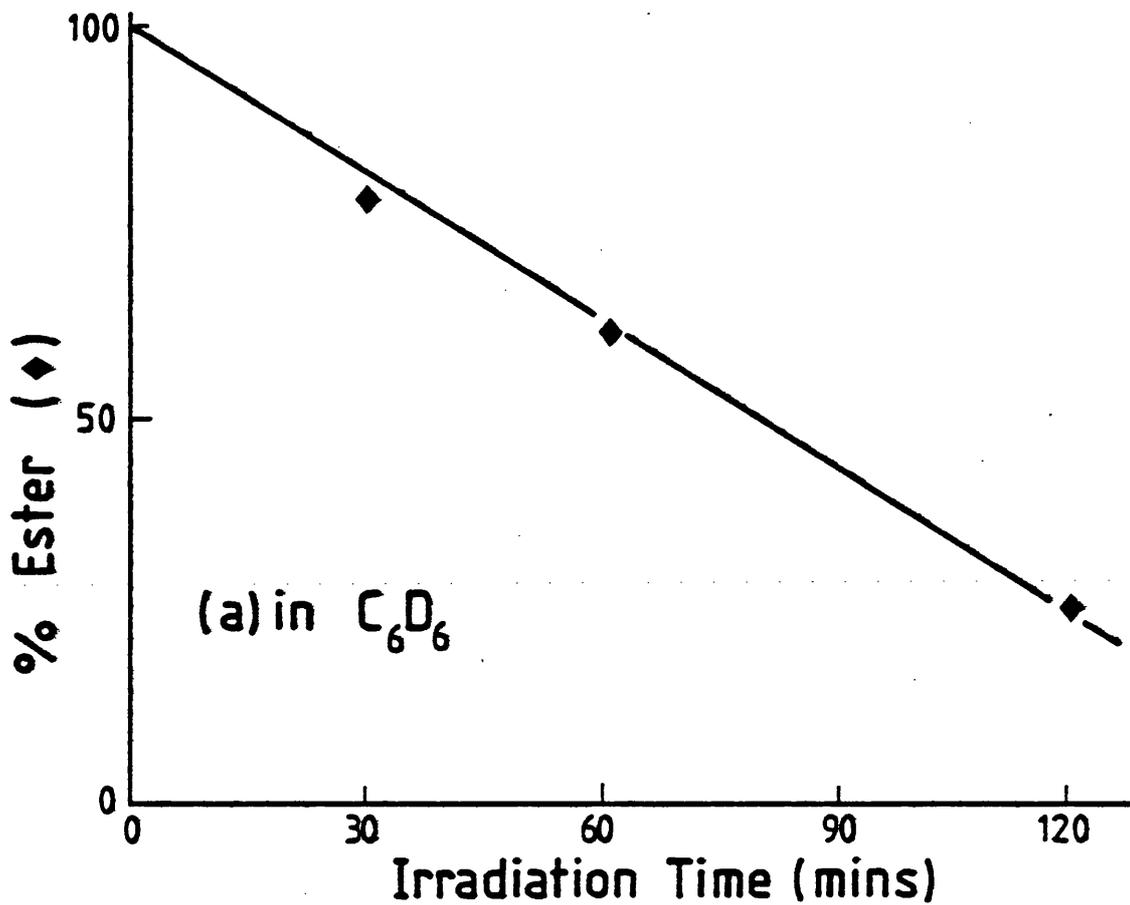
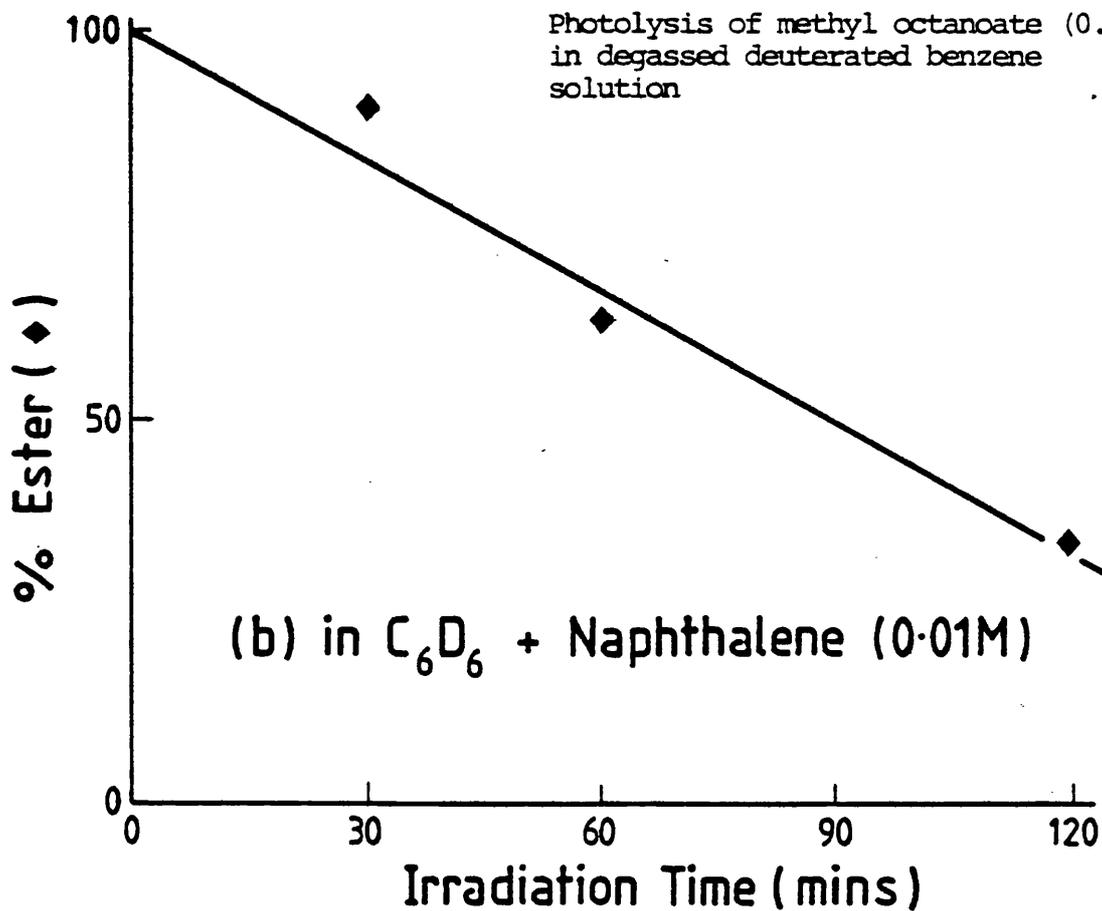


FIG. 3.24

Photolysis of methyl octanoate (0.1 M)
in degassed deuterated benzene
solution



conditions [Fig. 3.24(b)] and was determined as being 0.28×10^{-6} moles/min. In both cases the products of the Type II reaction (methyl pyruvate and pent-1-ene) were observed in the ^1H n.m.r. spectra, although no attempt was made to quantify the yields as methyl pyruvate was observed to undergo secondary photo-reactions.

3.7(ii) LASER FLASH PHOTOLYSIS STUDY³³

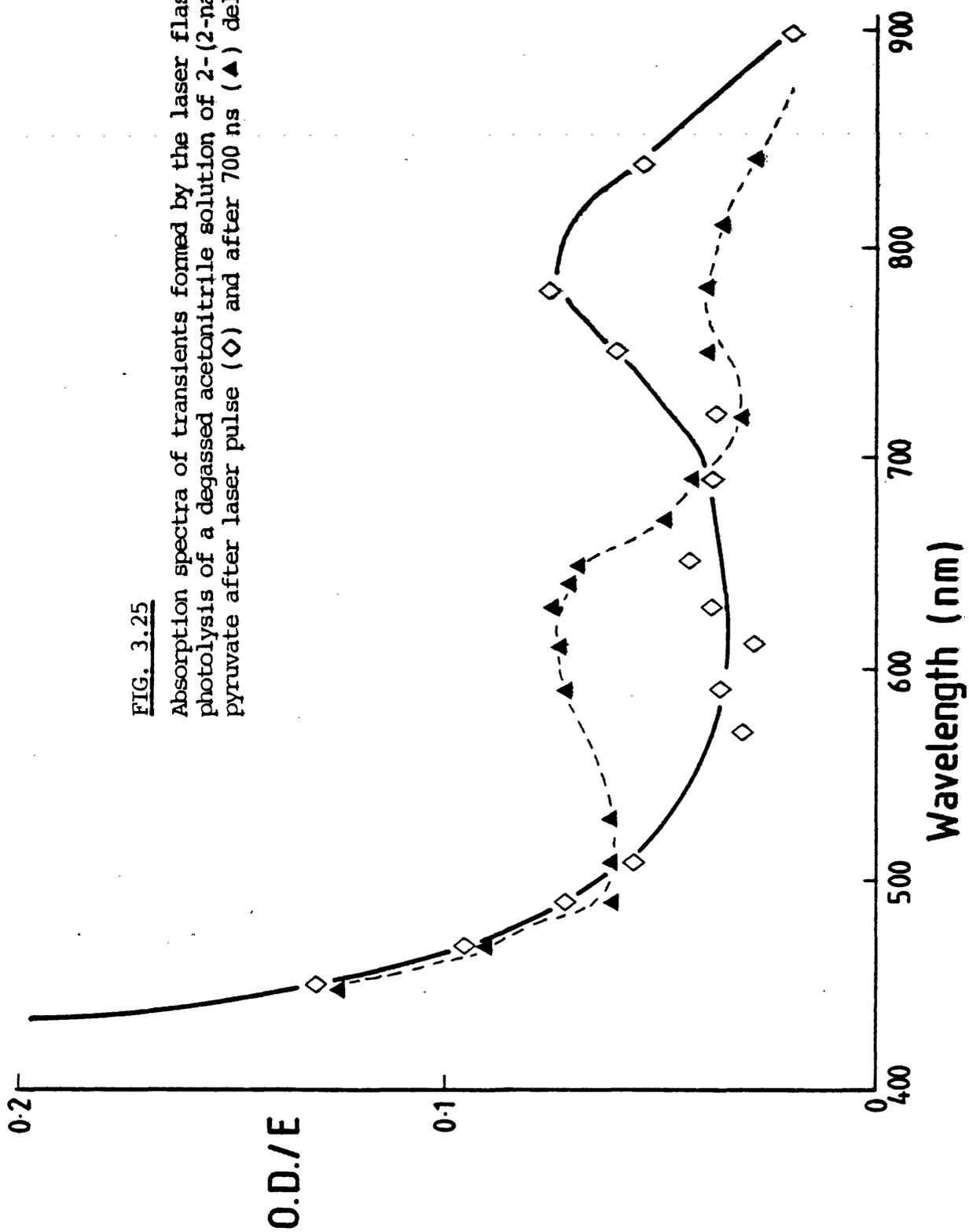
It has been shown, by nanosecond laser flash photolysis (Chapter 3.4), that naphthalene quenches the triplet state of methyl pyruvate. The triplet lifetime of methyl pyruvate was found to be concentration dependent ($k_{sq} = 2 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$) and at concentrations of $5 \times 10^{-2} \text{ M}$ in acetonitrile solution the triplet lifetime was found to be 140 ns, (Chapter 3.4). From this lifetime measurement, the presence of oxygen at a concentration of $8 \times 10^{-3} \text{ M}$ ³⁷ should reduce the yield of pent-1-ene ~20-fold if the triplet state of the ester is responsible for the Type II reaction.

Furthermore, laser flash photolysis of 2-(2-naphthyl)ethyl pyruvate showed that the presence of the naphthalene group leads to almost total quenching of the triplet state of the ester, and this is attended by the formation of triplet naphthalene. Figure 3.25 shows the absorption spectra of the transients produced by laser flash photolysis of 2-(2-naphthyl)ethyl pyruvate. The absorption bands between 600 and 800 nm may be due to the formation of the naphthalene radical cation.³² The triplet naphthalene so produced was found to decay with first-order kinetics and have a lifetime of 770 ns, (Fig. 3.26). Thus the formation of pent-1-ene from 2-(2-naphthyl)ethyl- α -keto-octanoate cannot have arisen from the triplet state of the ester.

The addition of methyl viologen to aqueous acetonitrile solutions

FIG. 3.25

Absorption spectra of transients formed by the laser flash photolysis of a degassed acetonitrile solution of 2-(2-naphthyl)ethyl pyruvate after laser pulse (\diamond) and after 700 ns (\blacktriangle) delay time,



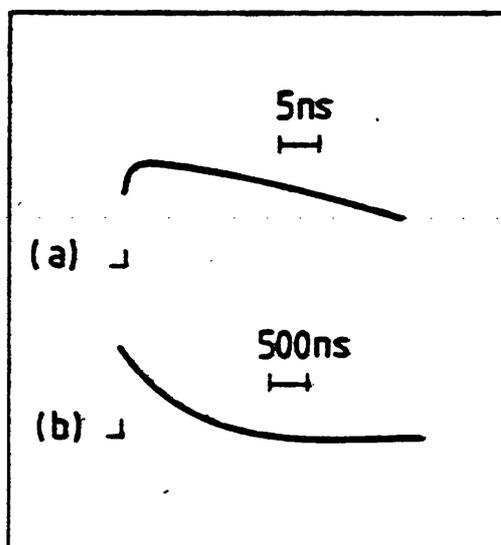


FIG. 3.26

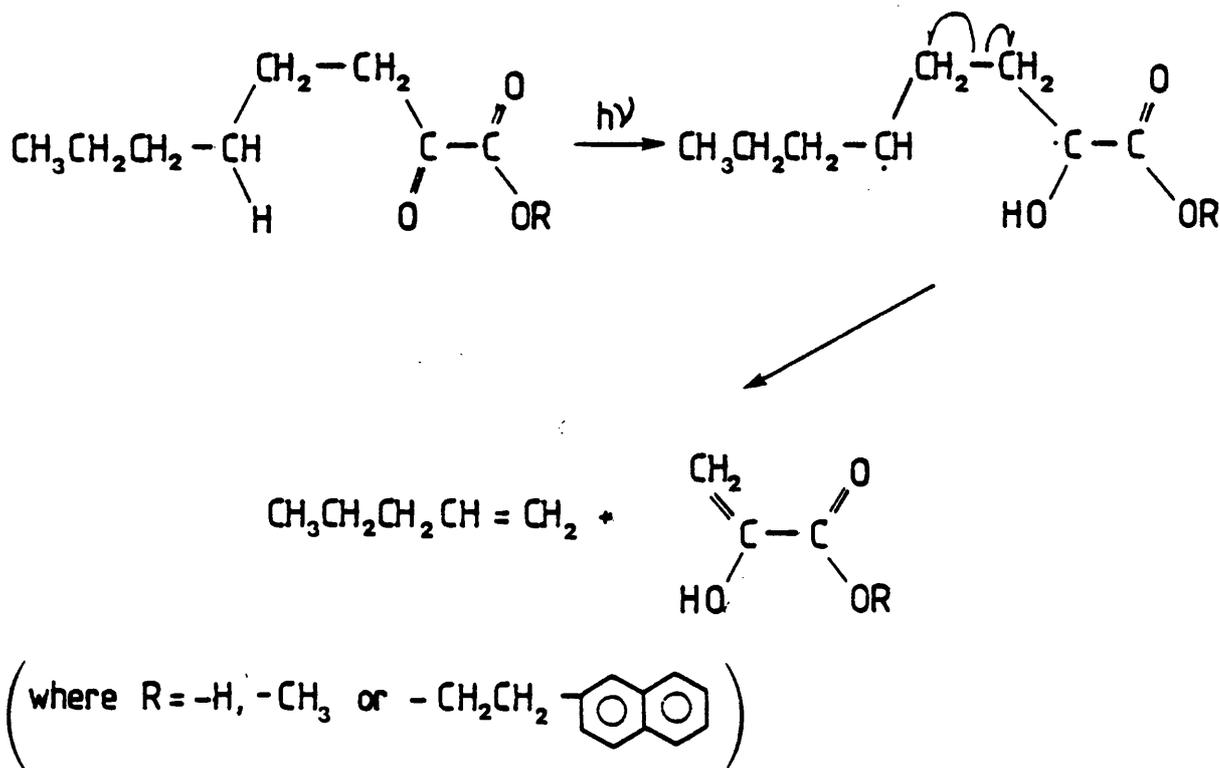
Decay of triplet naphthalene, monitored at 415 nm, produced by energy transfer from the triplet ester function of 2-(2-naphthyl)ethyl pyruvate, in degassed acetonitrile solution.

(a) 5 ns/division, (b) 500 ns/division.

(1:9 v/v) of 2-(2-naphthyl)ethyl pyruvate led, upon flash photolysis, to the production of reduced methyl viologen. The addition of methyl viologen had little effect upon the fluorescence and triplet lifetimes of 2-(2-naphthyl)ethyl pyruvate, and this shows that the reduced methyl viologen is not predominantly produced by reaction of methyl viologen with the excited states of the ester.

3.7(iii) DISCUSSION

Ester derivatives of α -keto-octanoic acid are shown to be capable of undergoing the Type II fragmentation reaction leading to the formation of pent-1-ene, (Tables 3.21 and 3.22), via a mechanism shown in Scheme 3.21.



Scheme 3-21

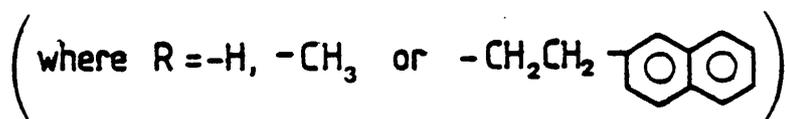
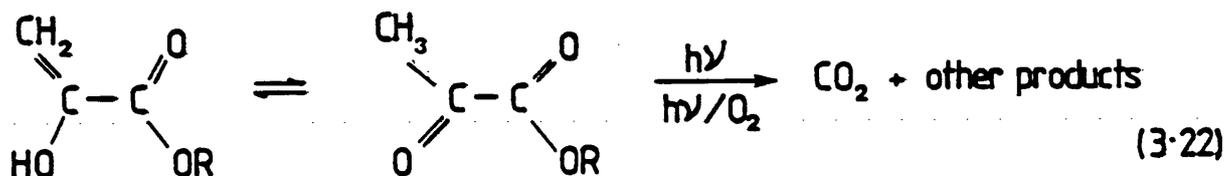
As the yields of pent-1-ene, from irradiation of the α -keto-octanoates, are little affected by the presence of the triplet quenchers oxygen and naphthalene, it can be surmised that the Type II reaction does not occur

from the excited triplet state. This view is further substantiated by the finding that good yields of pent-1-ene are obtained from 2-(2-naphthyl)-ethyl- α -keto-octanoate. Since the naphthalene group in 2-(2-naphthyl)-ethyl pyruvate efficiently quenches the triplet state of its ester group (Fig. 3.25), it is feasible that the triplet state of the ester portion of 2-(2-naphthyl)ethyl- α -keto-octanoate is quenched by the naphthalene group within the molecule. Naphthalene also quenches the triplet state of methyl pyruvate and this is consistent with the observation that triplet pyruvic acid is efficiently quenched by oxygen and naphthalene.³²

It can be concluded that the Type II fragmentation reaction of both α -keto-carboxylic acids, such as α -keto-octanoic acid, and α -keto-carboxylic esters, such as α -keto-octanoates, occurs from the excited singlet state. This view is in direct conflict with that proposed by Evans and Leermakers²¹ who showed that high concentrations of cyclohexa-1,3-diene quench the Type II reaction of α -keto-decanoic acid, and as such invoked the participation of the triplet state. However, it has now been appreciated that the excited singlet states of ketones are quenched by high concentrations of dienes³⁸ including cyclohexa-1,3-diene. It has also been shown that α -keto-carboxylic esters react with alkenes to give [2+2] cycloaddition products,^{39,40} and that the excited singlet state of methyl pyruvate is quenched by cyclohexa-1,3-diene.⁴⁰ Thus it would appear that the quenching observed by Evans and Leermakers²¹ was due to quenching of the excited singlet state.

The question arises as to how carbon dioxide is produced in these systems. As the yields of pent-1-ene are high when the reaction is performed under oxygen, it appears that the oxygen is not interacting with the intermediate 1,4-diradical.³⁵ In all probability the carbon dioxide generated in these systems (Tables 3.21 and 3.22) comes from the

subsequent reaction of the dicarbonyl compound which is produced, together with pent-1-ene, from the Type II fragmentation reaction of the parent molecule (Equation 3.22) via the mechanisms previously described, (Chapters 2.3; 2.5; 3.4 and 3.5), although the reaction of triplet ester with oxygen may also be accountable for part of the decarboxylation reaction, (Chapter 3.5).



Summary

Methyl octanoate and other α -keto-octanoate ester derivatives undergo the Type II fragmentation reaction to give pent-1-ene. From photo-physical measurements, and quenching studies, the Type II reaction of α -keto-carboxylic acids, (contrary to previous claims), and also the previously unreported Type II reaction of α -keto-octanoates, occurs from the excited singlet state. The carbon dioxide produced in these reactions is suggested to arise from a secondary reaction of the dicarbonyl fragment produced in the Type II reaction.

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CHAPTER 4

EXPERIMENTAL

*"Whatever gets you to the light is alright
is alright"*

John Lennon 1940~1980

4.1 INSTRUMENTATION

Fluorescence spectra were recorded using a Perkin-Elmer MPF4 spectrofluorimeter. A Pye-Unicam SP 800 and a Perkin-Elmer 402 spectrophotometer were used to record ultra-violet and visible spectra. Where solutions of known optical density at a specific wavelength were required a Cecil Instruments CE 272 Linear Readout Ultra-violet Spectrophotometer was used to prepare the solutions.

Infrared spectra were recorded, either as Nujol mulls or neat films, using a Perkin-Elmer 237, 257 or 157G grating spectrophotometer.

Proton nuclear magnetic resonance spectra were recorded on a Varian T60 or a Jeol JNM-MH 100 spectrometer. Tetramethylsilane (TMS) was used as the internal standard and deuteriochloroform (CDCl_3) was used as the solvent unless otherwise stated. [The following abbreviations have been used in the spectral interpretations:- s = singlet; d = doublet; t = triplet; q = quartet and m = multiplet.]

Melting points were determined using a Kofler block and are uncorrected. All compounds prepared as oils were distilled, under reduced pressure, using a Büchi Kugel oven. Boiling points are uncorrected.

Mass spectra were recorded by Mr. C. Whitehead using a Kratos MS 30 mass spectrometer (connected to a DS-50-S data system) operated at 70 eV. The molecular ion is given in each case.

Elemental analyses were performed by Mr. P. Hemming using a Carlo Erba Model 1106 Elemental Analyser.

Gas liquid chromatography was carried out using a Perkin-Elmer Sigma 3 gas chromatogram, equipped with a flame ionisation detector, which gave a linear response over the whole range of concentrations used. Products were confirmed by comparison of their retention times with those of

authentic material and also by peak enhancement. Quantitative estimation of the products was carried out by comparing the area of the elution peak for the product, with that for an authentic sample of the product in solutions of known concentrations. Each evaluation was determined from the mean of at least four injections and in all cases the peak areas were reproducible to within $\pm 2\%$. Pent-1-ene was determined using a Perkin-Elmer 5% SE 30 column at 30°C . Hexaldehyde and hexanol were determined using a Perkin-Elmer 10% SE 30 column at 70° and 60°C respectively. In each case the supporting material was Chromosorb W 60-80 mesh and the column dimensions were $8' \times \frac{1}{8}"$.

4.2 REAGENTS AND STARTING MATERIALS

The reagents and starting materials used in the experiments described herein were obtained from the following manufacturers and used as supplied unless otherwise stated.

Aldrich Chemical Co. Ltd.

Acetaldehyde (99%)
Acetonitrile (Gold Label - spectrophotometric grade)
Alloxazine
Benzene (Gold Label - spectrophotometric grade)
Biphenyl (recrystallised from acetonitrile prior to use)
9-Cyanoanthracene
Cyclohexa-1,3-diene (99%)
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (98%)
 α,α -Dichloromethyl methyl ether (97%)
Dimethylformamide (99%)
2,6-Dimethylnaphthalene
Ethylenediaminetetraacetic acid [EDTA] (99%)
Ethyl pyruvate (98%)
n-Hexane (99+%)
1-Hexene (99%)
 α -Keto-butyric acid (99%)
 α -Keto-glutaric acid (99%)
Lithium aluminium deuteride (98% D)
9-Methylanthracene (99%)
Methylglyoxal (40% aqueous solution)
Methyl pyruvate (94%)
Methyl viologen hydrate
9-Nitroanthracene (97%)

Aldrich Chemical Co. Ltd. (continued)

Pyrene
Pyruvic acid (95%)
Quinoline (95%)
Triethylamine (99%)

James Borrough Ltd.

Ethanol (Absolute)

B.D.H. Chemicals Ltd.

Ammonia (0.88 AnalaR)
Barium hydroxide (97%)
Benzyl alcohol (98%)
t-Butanol (AnalaR)
Calcium hydride (99.5%)
Dimethylsulphoxide (98%)
n-Hexanol (distilled over calcium hydride prior to use)
Isopropanol (AnalaR)
Methylene Blue (metal-free)
2-Methylnaphthalene
Molecular sieve: Type 3A and Type 4A (self-indicating)
Naphthalene
Phenanthrene (95%)
Potassium chromate (99%)
Potassium hydroxide pellets
Pyridine (distilled and stored over potassium hydroxide pellets
prior to use)
Rhodamine B
Riboflavin
Rose Bengal

B.O.C. Ltd.

Air (20% oxygen content)
Argon (Research grade <0.0001% oxygen content)
Fluorine (2% in helium)
Helium (Research grade)
Nitrogen - oxygen free (<0.001% oxygen content)
Nitrogen - commercial grade (<0.5% oxygen content)
Oxygen (Research grade)
Xenon (Research grade)

Cambrian Chemical Co. Ltd.

Acetonitrile (AnalaR)

Eastman-Kodak Co. Ltd.

Acridine
9,10-Dicyanoanthracene
Rose Bengal

Ralph N. Emanuel

Benzoylformic acid [phenylglyoxylic acid] (97%)

Ralph N. Emanuel (continued)

1-Cyanonaphthalene
2,3-Dimethylnaphthalene (99%)
Myrcene
Tetracyanoethylene

Fisons Chemical Co. Ltd.

Acetone (AnalaR)
Benzene (AnalaR)
Carbon tetrachloride (AnalaR)
Chloroform (AnalaR)
Ethyl acetate (AnalaR)
Hydrochloric acid (1.18 Sp. Gr.)
Magnesium sulphate (dried)
Methanol (AnalaR)
Sulphuric acid (98%)

Fluka Chemical Co. Ltd.

α -Keto-valeric acid (99%)

Goss Scientific Instruments Ltd.

Acetonitrile-d₃ (99% D)
Benzene-d₆ (99.6% D)
Chloroform-d (99.8% D)
Deuterium oxide (99.8% D)
Tetramethylsilane

Hopkin & Williams Chemical Co. Ltd.

Glutaric acid

Koch-Light Chemicals Ltd.

t-Butylamine
Hexaldehyde (pure)
 α -Keto-pimelic acid (pure)
Pent-1-ene (pure)
Phenazine
Pimelic acid (pure)

May & Baker Chemical Co. Ltd.

n-Butanol
Diethyl ether (dried and stored over sodium wire)
Dioxan
Petroleum ether (40-60°)
Sodium nitrate

Oxford Organic Chemical Co. Ltd.

1,3-Diphenylisobenzofuran (DPBF)

The Radiochemical Centre, Amersham

[1-¹⁴C]-pyruvic acid, sodium salt
[2-¹⁴C]-pyruvic acid, sodium salt

Sigma Chemical Co. Ltd.

Erythrosin B
 α -Keto-octanoic acid (99%)
Phenylpyruvic acid

The author gratefully acknowledges the following individuals for providing the materials stated below:-

Dr. H. A. J. Carless:- Per-acetic acid (6% in glacial acetic acid)

Dr. S. Matlin:- Nitrosomethyl urea

Miss J. E. Pratt:- 2-(1-naphthyl)ethanol and 2-(2-naphthyl)ethanol

Mrs. M. Szpek:- 3,3-Dimethyl-2-keto-butyrac acid and tetraphenyl-porphyrin.

4.3 PREPARATION OF MATERIALS

4.3.1 PREPARATION OF α -KETO-CARBOXYLIC ESTERS

4.3.1(i) PREPARATION OF PYRUVOYL CHLORIDE

The acid chloride of pyruvic acid was prepared using the method described by Ottenheijm and De Man¹ as outlined in Equation 4.1 (where R = CH₃-).



α,α -Dichloromethyl methyl ether (0.06 mole) was added dropwise, with stirring, to pyruvic acid (0.06 mole) under nitrogen at room temperature, with the evolution of hydrogen chloride gas. The mixture was heated at an oil bath temperature of 50°C for 30 minutes. The formation of pyruvoyl chloride was confirmed by n.m.r. spectroscopy and no further purification was undertaken. [It was not necessary to distill the pyruvoyl chloride provided 2 equivalents of pyridine were used in the esterification step.²] A yield of 54% (~0.03 mole) was assumed as obtained previously.¹

4.3.1(ii) PREPARATION OF α -KETO-OCTANOYL CHLORIDE

This compound was prepared by the method given in 4.3.1(i) above

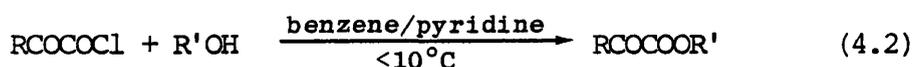
using α -keto-octanoic acid ($R = \text{CH}_3(\text{CH}_2)_5-$ in Equation 4.1) in place of pyruvic acid.

4.3.1(iii) PREPARATION OF BENZOYLFORMYL CHLORIDE

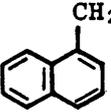
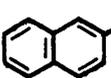
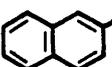
This compound was prepared by the method given in 4.3.1(i) above using benzoylformic acid ($R = \text{C}_6\text{H}_5-$ in Equation 4.1) in place of pyruvic acid.

4.3.1(iv) GENERAL METHOD FOR THE PREPARATION OF α -KETO-CARBOXYLIC ESTERS

The α -keto-carboxylic esters were prepared using the method described by Binkley² as outlined by Equation 4.2 below.



where:-

- (a) $R = \text{CH}_3-$; $R' = (\text{CH}_2)_2\text{CH}-$ = Isopropyl pyruvate
- (b) $R = \text{CH}_3-$; $R' = (\text{CH}_2)_2\text{CD}-$ = 2-Deuterioisopropyl pyruvate
- (c) $R = \text{CH}_3-$; $R' = \text{C}_6\text{H}_5\text{CH}_2-$ = Benzyl pyruvate
- (d) $R = \text{CH}_3-$; $R' = \text{CH}_3(\text{CH}_2)_3-$ = n-Butyl pyruvate
- (e) $R = \text{CH}_3-$; $R' = (\text{CH}_3)_3\text{C}-$ = t-Butyl pyruvate
- (f) $R = \text{CH}_3-$; $R' = \text{CH}_3(\text{CH}_2)_5-$ = n-Hexyl pyruvate
- (g) $R = \text{C}_6\text{H}_5-$; $R' = \text{CH}_3\text{CH}_2-$ = Ethylbenzoylformate
- (h) $R = \text{CH}_3-$; $R' =$  $= 2-(1\text{-Naphthyl})\text{ethyl pyruvate}$
- (i) $R = \text{CH}_3-$; $R' =$  $= 2-(2\text{-Naphthyl})\text{ethyl pyruvate}$
- (j) $R = \text{CH}_3(\text{CH}_2)_5-$; $R' =$  $= 2-(2\text{-Naphthyl})\text{ethyl octanoate}.$

The alcohol to be esterified (0.03 mole) and dry pyridine (0.06 mole) were dissolved in anhydrous benzene solution (100 ml). The appropriate acid chloride (0.03 mole) in anhydrous benzene solution (50 ml) was added dropwise with stirring, under nitrogen. Precipitation of pyridinium

hydrochloride was immediate. The reaction was cooled in an ice bath to keep the temperature below 10°C. When addition of the acid chloride was complete the mixture was allowed to reach room temperature and stirring continued for a further 30 minutes. The pyridinium hydrochloride was removed by filtration and the benzene solution distilled in vacuo to yield the α -keto-carboxylic ester contaminated with pyridinium hydrochloride. The contaminant was removed by shaking the mixture in carbon tetrachloride solution (50 ml), allowing it to stand overnight and then filtering off the insoluble material. The carbon tetrachloride solution was removed in vacuo leaving the uncontaminated α -keto-carboxylic ester, which after further purification by recrystallisation, or in the case of an oil by distillation under reduced pressure, was obtained in >70% yield in each case. The spectral and physical data obtained for each α -keto-carboxylic ester is given below.

(a) Isopropyl pyruvate

B.pt. 58-60°C, 15 mm. (Lit. 62-64°C, 17 mm.³)

Nmr. (CDCl₃) δ = 5.4 (m, 1H); 2.46 (s, 3H); 1.34 (d, 6H).

IR. (Neat film): 2980, 2930, 1725, 1460, 1420, 1375, 1360,
1300, 1270, 1180, 1145, 1100, 1020, 980, 910,
855, 810, 750, 720, 710 cm⁻¹.

(b) 2-Deuterioisopropyl pyruvate

B.pt. 52-53°C, 15 mm. (Lit. 61-62°C, 22 mm.⁴)

Nmr. (CDCl₃) δ = 2.52 (s, 3H); 1.38 (s, 6H).

IR. (Neat film): 2980, 2940, 1780, 1740, 1450, 1370, 1280,
1230, 1180, 1120, 1000, 975, 945, 900,
800, 750 cm⁻¹.

(c) Benzyl pyruvate

B.pt. 110-112°C, 16 mm.

Nmr. (CDCl₃) δ = 7.26 (s, 5H); 5.18 (s, 2H); 2.4 (s, 3H).

IR. (Neat film): 3040, 1730, 1500, 1455, 1420, 1360,
1295, 1265, 1135, 985, 910, 755, 700 cm⁻¹.

(d) n-Butyl pyruvate

B.pt. 85-87°C, 26 mm.

Nmr. (CDCl₃) δ = 4.2 (t, 2H); 2.41 (s, 3H); 1.28 (m, 7H).

IR. (Neat film): 2960, 2870, 1775, 1730, 1655, 1460, 1380,
1250, 1130, 940, 840, 750 cm⁻¹.

(e) t-Butyl pyruvate

B.pt. 45-46°C, 24 mm. (Lit. @ 35°C, 12 mm.³)

Nmr. (CDCl₃) δ = 2.46 (s, 3H); 1.56 (s, 9H).

IR. (Neat film): 1725, 1370, 1315, 1285, 1260, 1135, 975,
835, 745 cm⁻¹.

(f) n-Hexyl pyruvate

B.pt. 104-106°C, 23 mm.

Nmr. (CDCl₃) δ = 4.15 (t, 2H); 2.4 (s, 3H); 1.1 (m, 11H).

IR. (Neat film): 2960, 2920, 2860, 1730, 1470, 1420, 1360,
1300, 1140, 990, 895, 720 cm⁻¹.

(g) Ethylbenzoylformate (Ethyl phenylglyoxylate)

B.pt. 138-140°C, 30 mm. (Lit. 75°C, 1 mm.⁴)

Nmr. (CDCl₃) δ = 7.76 (m, 2H); 7.3 (m, 3H); 4.32 (q, 2H); 1.38 (t, 3H).

IR. (Neat film): 1720, 1675, 1580, 1440, 1295, 1190, 1000, 680 cm⁻¹.

(h) 2-(1-Naphthyl)ethyl pyruvate

White crystals [petroleum ether (40-60°)/ethyl acetate]

M.pt. 50-52°C.

Nmr. (CDCl₃) δ = 8.72 (m, 1H); 8.44 (m, 2H); 8.04 (m, 4H); 4.99 (t, 2H);
3.81 (t, 2H); 2.64 (s, 3H).

IR. (Nujol): 1745, 1730, 1295, 1258, 1135, 950, 800, 760 cm⁻¹.

C₁₅H₁₄O₃ requires C, 74.36; H, 5.82: found C, 73.79; H, 5.75.

Mass spectrum: m/e 242 (m⁺).

(i) 2-(2-Naphthyl)ethyl pyruvate

White crystals [petroleum ether (40-60°)/ethyl acetate]

M.pt. 82-83°C.

Nmr. (CDCl₃) δ = 8.29 (m, 4H); 7.94 (m, 3H); 4.9 (t, 2H); 2.95 (t, 2H);
2.61 (s, 3H).

IR. (Nujol): 1735, 1270, 1150, 960, 827, 752 cm^{-1} .

$\text{C}_{15}\text{H}_{14}\text{O}_3$ requires C, 74.36; H, 5.82: found C, 74.54; H, 5.78.

Mass spectrum: m/e 242 (m^+).

(j) 2-(2-Naphthyl)ethyl octanoate

Waxy solid M.pt. @ 35°C.

Nmr. (CDCl_3) δ = 7.84 (m, 4H); 7.49 (m, 3H); 4.63 (t, 2H);

3.29 (t, 2H); 2.8 (t, 2H); 1.34 (m, 8H); 0.91 (m, 3H).

IR. (Nujol): 1724, 1270, 1124, 1078, 948, 862, 790 cm^{-1} .

$\text{C}_{20}\text{H}_{24}\text{O}_3$ requires C, 76.92; H, 7.69: found C, 74.16; H, 7.8.

Mass spectrum: m/e 312 (m^+).

4.3.1 (v) PREPARATION OF METHYL- α -KETO-OCTANOATE

α -Keto-octanoic acid (1g) was dissolved in a solution of dry ether (3 ml) and cooled in ice. An ethereal solution of diazomethane was added slowly dropwise with stirring until gas evolution ceased and the reaction mixture acquired a pale yellow colour. The solvent was removed in vacuo leaving a pale yellow coloured oil which gave a colourless oil, upon distillation under reduced pressure, in excess of 75% yield.

B.pt. 58-60°C, 12 mm.

Nmr. (CDCl_3) δ = 3.96 (s, 3H); 2.9 (t, 2H); 1.36 (m, 8H);

0.92 (t, 3H).

IR. (Neat film): 2950, 2920, 2855, 1730, 1460, 1435, 1400, 1264, 1122, 1064, 725 cm^{-1} .

$\text{C}_9\text{H}_{16}\text{O}_3$ requires C, 62.78; H, 9.36: found C, 62.75; H, 9.48.

4.3.2 PREPARATION OF 2-DEUTERIOISOPROPANOL

2-Deuterioisopropanol was prepared as previously described.⁴

Lithium aluminium deuteride (1g) was carefully added to a solution of dry ether (100 ml) cooled in ice. Acetone (AnalaR, 8 ml) was slowly added dropwise, with stirring under nitrogen, over a period of 1 hour and the mixture allowed to reflux overnight. After cooling, distilled water was added slowly and the precipitated alumina removed by filtration. The

ethereal solution was dried over magnesium sulphate, filtered and distilled using a fractionating column. The first fraction (ether) was discarded and the second fraction collected yielding the product, 2-deuterioisopropanol, in >35% yield.

B.pt. 80-82°C. (Lit. 80-82°C⁴).

Nmr. (CDCl₃) δ = 2.32 (s, 1H); 1.24 (s, 6H). [The addition of deuterium oxide removed the signal due to the exchangeable -OH proton at 2.32 δ .]

The 2-deuterioisopropanol obtained by the above method was used in the esterification process [4.3.1(iv)] to prepare 2-deuterioisopropyl pyruvate.

4.3.3 PREPARATION OF DIAZOMETHANE

Diazomethane was prepared as previously described.⁵

Potassium hydroxide (4.8g) was dissolved in distilled water (9.7 ml) and added to a solution of ether (35 ml) cooled in ice. Nitrosomethyl urea (3g) was added to the reaction mixture slowly over a period of 1 hour, stirring continuously. The mixture was stirred for a further 5 minutes, whereupon it was decanted and left to stand over potassium hydroxide pellets for 15 minutes. The diazomethane solution was again decanted and left to stand over potassium hydroxide pellets for a further 1 hour before being used in the esterification of α -keto-octanoic acid [4.3.1(iv)].

4.4 PHOTOCHEMICAL REACTORS

All of the photolyses reported in this thesis were performed using one or other of the photochemical reactors described below.

(a) ULTRA-VIOLET REACTOR

This reactor consisted of a circular array of fluorescent lamps having

a maximum emission at 350 nm (16×8W, Sylvania F8T5/BLB). The reactor was also equipped with a tube holder (capacity 8 tubes) which was rotated during all irradiations.

The above reactor was used in all of the photochemical reactions reported in Chapters 2.3, 2.4, 2.5, 3.3, 3.4, 3.5 and 3.7 respectively.

(b) DAYLIGHT REACTOR

This reactor consisted of a circular array of fluorescent daylight lamps (8×20W, Cryselco). The reactor was also equipped with a tube holder (capacity 4 tubes) which held each photolysis tube in place, immersed in a filter solution, during the irradiation.

The above reactor was used in all of the photochemical reactions reported in Chapters 2.6 and 3.6 respectively.

4.5 GAS FLUSHING AND GENERAL IRRADIATION PROCEDURES

Each gas used, to purge the prepared solutions, was first passed through a Dreschel bottle containing saturated barium hydroxide (@ 100 ml) and then through a cylindrical glass tube (1m×2.5 cm) containing activated molecular sieves Type 3A and Type 4A (self-indicating). In this way a stream of dry carbon dioxide-free gas, for example argon, oxygen, etc., was obtained.

The reaction mixtures to be irradiated (25 ml), prepared as per the Figures and Tables in Chapters 2 and 3, were flushed with the appropriate dry carbon dioxide-free gas for 45 minutes in Pyrex photolysis tubes which were then stoppered. The tubes were then irradiated using the appropriate photochemical reactor. After irradiation the yields of carbon dioxide were determined as described in 4.6. In some cases duplicate reaction mixtures were analysed for additional products, for example pent-1-ene, hexaldehyde or n-hexanol as described in 4.7.

In some instances the Pyrex photolysis tubes containing the reaction mixtures were not stoppered but the gas allowed to continually flush through the solution during irradiation. The carbon dioxide produced throughout each irradiation was trapped by passing the exit gases through two Dreschel bottles in series, each containing a saturated solution of aqueous barium hydroxide (@ 100 ml) and the yield determined as described in 4.6. In each case the gas was allowed to purge the reaction mixture for 30 minutes prior to commencement of irradiation and for 1 hour after irradiation, to remove any residual carbon dioxide trapped in solution, at a gas flow rate of 10ml/min.

The results obtained from the experiments performed by continual flushing during irradiation are reported in Tables 2.28, 2.31-2.33, 3.17, 3.18 and 3.20 where 45 ml solutions were used and in Table 2.29 where 10 ml solutions were used respectively.

4.6 DETERMINATION OF CARBON DIOXIDE YIELDS

The various methods for determining the yield of carbon dioxide produced in a photochemical reaction have been reviewed.⁶ A gravimetric method, for the determination of carbon dioxide, was utilised in the work presented in this thesis and has previously been shown to give yields which are reproducible to within $\pm 2\%$. The general method is given below.

After irradiation the yield of carbon dioxide produced in the reaction was determined by the weight of barium carbonate precipitated by slowly flushing each reaction mixture with a stream of dry carbon dioxide-free argon, nitrogen or oxygen (as appropriate) for 2 hours. The exit gases were passed through two Dreschel bottles in series, each containing a saturated solution of aqueous barium hydroxide (@ 100 ml). The barium

carbonate precipitate was quickly filtered off through a pre-weighed sintered glass crucible and washed thoroughly with distilled water. The crucible was then dried in an oven at 100°C, to constant weight, thus affording the yield of carbon dioxide. Care was taken to use an identical procedure for each reaction and to handle the crucible only with tweezers throughout the analysis. After use each crucible was washed repeatedly with dilute hydrochloric acid and distilled water in order to remove the barium carbonate before re-using for other determinations.

The yields of carbon dioxide reported were calculated on the basis of one mole of carbon dioxide being generated per mole of α -keto-carboxylic acid or ester initially present.

The carbon dioxide from the reaction mixtures which were continually flushed throughout the irradiation was analysed as above after each photolysis tube had been purged, for a further 1 hour at the end of irradiation, to ensure that all of the carbon dioxide was removed from the photolysis solution.

The carbon dioxide produced in the reactions of the ^{14}C -labelled pyruvic acids was determined by flushing each solution, after irradiation, for 2 hours with the appropriate gas and passing the exit gases through two Dreschel bottles containing potassium hydroxide (0.1 M, @ 100 ml). The ^{14}C -labelled carbon dioxide produced in each case was assessed by assaying each potassium hydroxide solution (0.2 ml diluted to 1 ml with distilled water) in a toluene-Triton X-100 scintillant (4 ml) and the results reported in Table 2.20.

4.7 DETERMINATION OF PENT-1-ENE, HEXALDEHYDE AND n-HEXANOL

Where it was necessary to determine the yield of pent-1-ene, hexaldehyde or n-hexanol as photolysis products from a reaction mixture,

solutions (25 ml) separate to those used in the corresponding carbon dioxide determinations were prepared. In each case the solutions were subjected to g.l.c. analysis before and after being irradiated in stoppered Pyrex tubes. In this way the yields of the above products were determined as described in 4.1 and reported in Tables 2.23, 3.8, 3.13, 3.19, 3.21 and 3.22 respectively.

4.8 ANALYSIS OF PHOTOLYSES OF ^{14}C -LABELLED PYRUVIC ACIDS

The liquid scintillation counting reported in Table 2.20 was kindly performed by Dr. G. Turnock, Department of Biochemistry, University of Leicester. The reaction mixtures were prepared as described below.

The ^{14}C -labelled pyruvic acid sodium salt was dissolved in distilled water (0.1 ml) and acetonitrile solution (0.9 ml) added. The acetonitrile/water solution of labelled pyruvic acid (0.2 ml) was added to an acetonitrile solution of pyruvic acid (10^{-2} M , 55ml) and left to equilibrate for 1 hour. A sample of the solution (5 ml) was withdrawn and set aside for assay by liquid scintillation counting in order to obtain an initial level of label prior to irradiation. The remaining stock solution (50 ml) was divided into two equal portions and placed in separate Pyrex photolysis tubes, one tube being purged with a stream of dry carbon dioxide and oxygen-free nitrogen and the other with a stream of dry carbon dioxide-free oxygen for 45 minutes and stoppered. After irradiation each tube was flushed with the appropriate gas to remove the labelled carbon dioxide produced in the reaction, which was assayed as described in 4.6. After removal of carbon dioxide a sample of each of the reaction mixtures was extracted (0.01 ml), added to distilled water (1 ml) and assayed in a toluene-based scintillant (4 ml). The results of each assay are reported in Table 2.20.

4.9 ANALYSIS OF PHOTOLYSES BY ^1H N.M.R. SPECTROSCOPY

N.m.r. tubes containing the appropriate α -keto-carboxylic acid or ester solution (0.5 ml) and tetramethylsilane as internal standard, were degassed with a stream of dry carbon dioxide-free argon for 1 minute and stoppered. Quenching experiments were performed by the addition of varying amounts of naphthalene to the prepared solutions prior to degassing. 100 MHz ^1H n.m.r. spectra were recorded prior to and after irradiation. The amount of α -keto-carboxylic acid or ester remaining (and in the case of the alkyl pyruvates the yield of carbonyl compound formed) were evaluated by reference to the ratio of peak heights of the pyruvate methyl singlet (or the methyl ester singlet with reference to methyl- α -keto-octanoate) and the residual proton peaks of the deuterated acetonitrile and deuterated benzene solutions in each case. In this way the disappearance of the α -keto-carboxylic acid or ester and the appearance of photoproducts was determined and the results reported in Figures 2.5, 3.1-3.9 and 3.24 and Tables 3.3-3.5 respectively.

4.10 IRRADIATION IN THE PRESENCE OF METHYL VIOLOGEN

The α -keto-carboxylic acid or ester solutions (3 ml) were prepared as reported in Figures 2.1 and 3.18-3.21 and degassed in quartz cuvettes with a stream of dry carbon dioxide-free argon for 4 minutes. The absorption spectrum was recorded prior to and after illumination in each case. The formation of the blue coloured species reduced methyl viologen (identified by its characteristic absorption spectrum) was observed and the results reported in Figures 2.1 and 3.18-3.21 respectively.

4.11 RATE OF PHOTO-OXYGENATION OF α -KETO-CARBOXYLIC ACIDS MONITORED BY POLAROGRAPHY

The polarographic measurements were kindly performed by Miss H.

Kinghorn, Department of Biochemistry, University of Leicester. The reaction mixtures were prepared as described below.

The solutions containing the appropriate dye and α -keto-carboxylic acid (10.5 ml) were prepared as in Table 2.29. A sample (0.5 ml) was extracted for polarographic analysis prior to photolysis and the remaining reaction mixture (10 ml) irradiated through a potassium chromate filter (2% aqueous) solution, continually flushing each solution with a stream of dry carbon dioxide-free oxygen. Samples (0.5 ml) were extracted for polarographic analysis at 30, 60, 120 and 180 minute time intervals throughout the irradiation. Each extracted sample was diluted 10 times with a 20 mM Tris buffer/10 mM magnesium chloride solution (1:1 \forall) prior to polarographic analysis. In each case the height of the observed peak was measured and compared to the initial peak height of the sample prior to irradiation. In this way the amount of α -keto-carboxylic acid remaining and hence the rate of photo-oxygenation was evaluated and the results reported in Table 2.29. Each of the reported results are the mean of four determinations all of which were subjected to a least squares analysis.

4.12 EFFECT OF QUENCHERS UPON THE RATE OF PHOTODECOMPOSITION OF α -KETO-CARBOXYLIC ACIDS

In each of the Stern-Volmer quenching experiments (Figures 2.6-2.10) reported in Chapter 2.4, in addition to the carbon dioxide determinations, the absorption of the α -keto-carboxylic acid at 350 nm was recorded prior to, and upon cessation of, illumination. From the values obtained for each solution (3 ml), the effect of added quencher upon the rate of α -keto-carboxylic acid photodecomposition was evaluated and the results reported in Table 2.15.

4.13 RECORDING OF FLUORESCENCE SPECTRA AND FLUORESCENCE QUENCHING EXPERIMENTS

Dilute solutions (3 ml) of the compounds under test were made up to have an optical density of 0.1 at the excitation wavelength used for each compound. This was achieved by diluting a more concentrated solution of the fluorescing compound in each case. The excitation wavelengths used for each of the compounds investigated are given in Table 4.1.

TABLE 4.1

| Fluorescing compound | λ_{ex} (nm) |
|-------------------------|---------------------|
| 1-Cyanonaphthalene | 315 |
| 2,6-Dimethylnaphthalene | 295 |
| 9-Cyanoanthracene | 415 |
| 9-Methylanthracene | 390 |
| Acridine | 392 |

Fluorescence spectra were recorded in stoppered quartz spectrofluorimeter cells after initial degassing with a stream of dry carbon dioxide-free argon for 3 minutes. Fluorescence quenching experiments were performed by the addition of varying amounts of the quencher to a solution of the fluorescing compound and the Stern-Volmer quenching constants obtained in each case are reported in Table 2.14.

The fluorescence spectra of the acridinium ion produced by the addition of varying amounts of pyruvic acid or dilute hydrochloric acid to acetonitrile solutions of acridine are shown in Figures 2.11 and 2.12 respectively.

All the solvents used were checked to ensure that they did not fluoresce when irradiated under the same conditions as those used for recording each fluorescence spectra.

4.14 LASER FLASH PHOTOLYSIS EXPERIMENTS

(a) RATE CONSTANTS FOR REACTION OF α -KETO-CARBOXYLIC ACIDS WITH SINGLET OXYGEN AND METHYLENE BLUE

These measurements were made in conjunction with Dr. G. Smith at The Royal Institution of Great Britain, London, using the following method.

The rates of reaction of the α -keto-carboxylic acids with the triplet state of Methylene Blue and with singlet oxygen in air-saturated methanol solutions (5 ml) were determined by laser flash photolysis using 15 ns, 1 J pulses from a Q-switched ruby laser operating at 694 nm.

The reactions of the α -keto-carboxylic acids with the triplet state of Methylene Blue were studied by flashing solutions of different concentrations of each acid (generally $> 5 \times 10^{-3}$ M) in the presence of Methylene Blue, (5×10^{-5} M). The change in absorption at 420 nm resulting from the laser flash was followed and the rate of reaction determined using the procedure described by Kayser and Young.⁷

The reactions of singlet oxygen with the α -keto-carboxylic acids were studied by flashing solutions of Methylene Blue (5×10^{-5} M) in order to generate singlet oxygen and by following the bleaching of 1,3-diphenylisobenzofuran (DPBF, 2×10^{-5} M) at 410 nm. The rate of reaction was determined in the way described by Nilsson and co-workers.⁸ Care was taken in these latter experiments to keep the concentration of the α -keto-carboxylic acid low enough (generally $< 5 \times 10^{-5}$ M) to avoid modification of the observed bleaching of DPBF resulting from competing reaction between the α -keto-carboxylic acid and the triplet state of Methylene Blue. The rate constants determined by the above procedures are reported in Table 2.30.

(b) TRANSIENT ABSORPTION MEASUREMENTS

The transient absorption measurements reported in Chapters 2.3 and 3.7

were made in conjunction with Dr. Ph. Fournier de Violet at the University of Bordeaux, France, using the procedure outlined below.

Transient absorption measurements of the appropriate solutions were made with a laser flash photolysis system. A Q-switched neodymium laser (Quantel Instruments) operating in the third harmonic was used as the excitation source. The light pulses produced by this system are of ~3 ns duration and ~8 mJ. Details of the detection system have previously been described.⁹ The results obtained from these measurements are reported in Figures 2.2-2.4, 3.25 and 3.26 respectively.

(c) TRIPLET LIFETIMES OF ALKYL PYRUVATES

These measurements were made at The City University, London, by the following procedure.

Acetonitrile solutions of the appropriate alkyl pyruvate (3 ml) were made up to have an optical density of 1.0 at 353 nm and degassed by three successive freeze-pump-thaw-shake cycles. Triplet lifetimes were measured using nanosecond laser flash photolysis. An excimer laser (Oxford Instruments) emitting light at an excitation wavelength of 353 nm from a Xe-F gas mixture in helium was the light source. The light pulses produced by this system are of ~23 ns duration and ~114 mJ. A conventional pulsed-Xenon arc lamp detection system with a Hamamatsu (Type R 928) photomultiplier tube was used. The observed transients are reported in Figure 3.10 and were found to decay with first order decay kinetics (Figures 3.11-3.16). The triplet lifetimes and rate constants evaluated by this method are reported in Table 3.6.

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PHOTO-OXYGENATION OF α -KETO-CARBOXYLIC ACIDS AND RELATED COMPOUNDS

Dean Goodwin

A B S T R A C T

Basic photochemistry, the photoreactions of carbonyl compounds and the mechanisms involved in photo-oxygenation reactions are surveyed. The photochemical reactions of α -keto-acids and esters are reviewed.

From photophysical and decarboxylation studies of α -keto-acids and esters in degassed solution, the direct photoinduced decarboxylation reaction is shown to occur via a bimolecular electron transfer reaction as opposed to a Norrish Type I fragmentation. The addition of triplet quenchers enhances the decarboxylation reaction via a mechanism suggested to involve radical processes. The proposed mechanisms are substantiated by using electron acceptors to sensitize decarboxylation.

The finding that t-butyl pyruvate is photostable in degassed solution and has a much longer lifetime than other alkyl pyruvates, together with triplet quenching studies, shows that alkyl pyruvates fragment from the triplet state via a Norrish Type II process.

From photophysical, quenching and product studies in degassed solution, the Norrish Type II reaction of long chain α -keto-acids and esters occurs from the excited singlet state.

α -Keto-acids and esters undergo direct photo-oxidative decarboxylation, leading to higher yields of carbon dioxide than under degassed conditions. Decarboxylation of pyruvic acid occurs from both the C-1 and C-2 positions. Singlet oxygen does not appear to be involved and a mechanism mediated via electron transfer, with per-acid intermediates, is postulated. In accord with the proposed mechanism, the decarboxylation can be sensitized by electron acceptors.

The dye-sensitized photo-oxygenation of α -keto-acids and esters proceeds via a mechanism involving dye-acid/ester interaction rather than a singlet oxygen mediated process. Kinetic studies and solvent isotope effects lend credence to the proposed mechanism.

The reported results confirm that photochemical α -cleavage of the bond linking the carbonyl groups in 1,2-dicarbonyl compounds is an unfavourable process.