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Part I N-acylindole 2+2 Photocycloaddition Reactions Part Ii Enone 2+2 Photocycloaddition Reactions

David J. Hastings

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PART I

N-ACYLINDOLE 2+2 PHOTOCYCLOADDITION REACTIONS

PART II

ENONE 2+2 PHOTOCYCLOADDITION REACTIONS

by

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Submitted in partial fulfilment
of the requirements for the degree of
Doctor of Philosophy

Faculty of Graduate Studies
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ABSTRACT

PART I

Ultra-violet irradiation of N-acylindoles in the presence of alkenes results in the formation of 2+2 photocycloadducts containing a cyclobutane ring derived from the bonding of the alkene termini to the 2 and 3-positions of the indole. The reaction proceeds *via* the triplet excited state of the N-acylindole with a quantum yield of product formation which is much less than that of the quantum yield for intersystem crossing. The reaction's inefficiency is explained by the existence of 1,4-biradical intermediates which can undergo cleavage to yield ground state starting materials in competition with ring closure to give the observed photocycloadducts. Part I of this thesis describes evidence for the existence of the 1,4-biradical intermediates and for their structures. The cycloadducts obtained from N-acylindoles and flexible alkenes show mixed stereochemistries which is indicative of a 1,4-biradical intermediate. The structures of the products formed by rearrangement of the biradical generated from the photocycloaddition of N-benzoylindole with vinylcyclopropane indicate that the initial site of bonding between the indole and the alkene is at the 2-position of the indole moiety. The products observed from this reaction along with those from the photocycloaddition of N-benzoylindole with 1,6-heptadiene allow the lifetimes of the biradicals to be "clocked" at approximately 100 ns. The finding that initial bonding of the alkene is to the 2-position of the indole is confirmed by trapping studies in which

hydrogen selenide (H_2Se) was used as a hydrogen donor to intercept the 1,4-biradical intermediate. These studies also indicate that the 2-position of the indole becomes bonded to that end of the alkene less able to support a radical centre. This can be used to rationalize and predict the regiochemistry of the cycloaddition reaction with non-symmetrical alkenes.

PART II

The possible factors governing the regioselectivity of the 2+2 photocycloaddition reaction of enones with alkenes are discussed in Part II of this thesis. A study was conducted aimed at determining whether the regioselectivity of the photochemical reaction between cyclopentenone and ethyl vinyl ether is governed by the relative rates of formation of the isomeric 1,4-biradical intermediates or by the proportions with which these intermediates partition between cycloadducts and starting materials. It is shown that the rate constants for formation of the biradical intermediates and proportions with which they partition to products cannot be determined using steady state kinetic analysis. The generation of the 1,4-biradicals implicated in the 2+2 photocycloaddition reaction by independent routes is discussed. A route for the generation of models of the 1,4-biradicals generated in the photocycloaddition reaction of cyclopentenone with ethyl vinyl ether was examined. The model study indicated that the isomeric 1,4-biradicals partition to products with similar efficiencies.

The relative rate constants for formation of the 1,4-biradical intermediates in the reaction of cyclopentenone with ethyl vinyl ether were determined by trapping the biradicals with H_2Se. The structures of the trapped biradicals indicate that initial bonding occurs to a similar extent at both the α and β-positions of the enone. The bonding occurs to that terminus of the alkene less able to support a radical centre. This result suggests that the regioselectivity of the photocycloaddition reaction of enones with alkenes is not dependent on the rate of interaction of different orientations of the alkene with the excited state enone (Corey-de Mayo mechanism), but rather on the efficiencies with which the intermediate biradicals proceed to products in competition with reversion to ground state starting materials.

This work is dedicated to my loving parents

Don and Georgina

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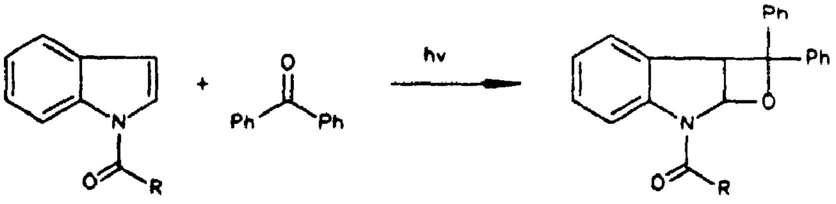
N-ACYLINDOLE 2+2 PHOTOCYCLOADDITION REACTIONS

CHAPTER 1

INTRODUCTION

1.1 PHOTOCHEMICAL CYCLOADDITION REACTIONS OF N-CARBONYL SUBSTITUTED INDOLES

The first part of this thesis will describe work carried out on the photochemical cycloaddition reactions of N-acylindoles with alkenes. This chapter will review the literature describing the photochemical and photophysical properties of N-carbonyl substituted indoles. In the first report of N-carbonylindole cycloaddition photochemistry Julian and Foster found that p-chlorobenzoylindole, 1a, irradiated in the presence of benzophenone yielded the corresponding oxetane 2a with high regioselectivity (1). The reaction also yielded oxetanes when an N-acetyl group was substituted for the benzoyl group as shown by the cycloaddition of benzophenone to 1b to yield cycloadduct 2b (2).



1a,b

2a,b

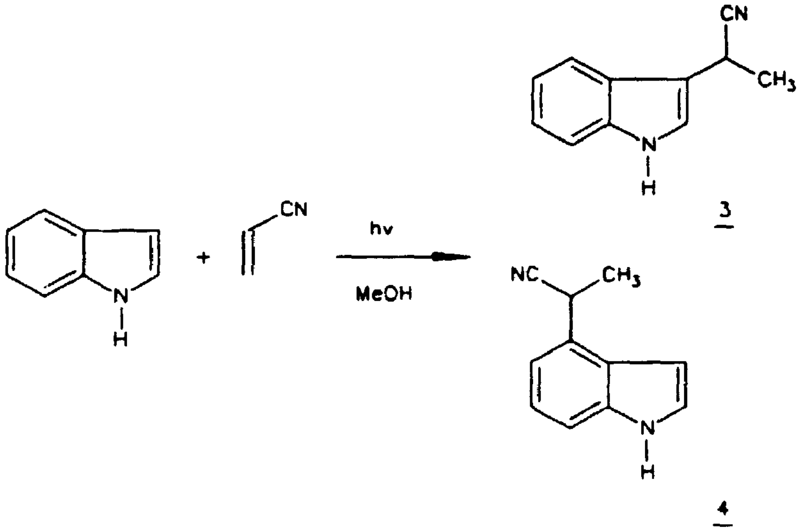
1a R=p–Cl–Ph

2a R=CH_3

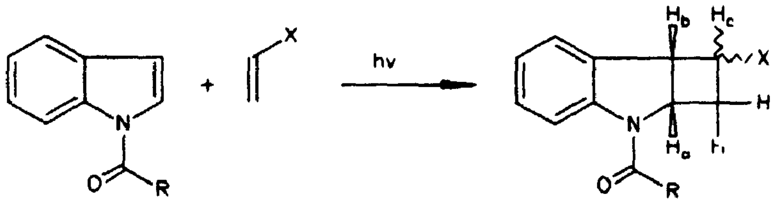
Reactions of this type are also characteristic of the photochemistry of other aromatic heterocycles such as furans (3) and 2,5-dimethylthiophene. Thiophene, pyrrole, oxazole, isoxazole, and indole itself do not however undergo such cycloadditions (4). Their failure to undergo photochemical cycloaddition may be due to several reasons. For example, it is possible that the excited state ketone is quenched by the non-bonded electrons on the heteroatom of some of these compounds; however it is more likely that the lack of reactivity of some of these heterocycles is a reflection of greater resonance energy in the heterocyclic π-system. In the case of indole the presence of an electron withdrawing group on the nitrogen atom may cause the compound to become photoreactive by delocalizing the electron pair on the nitrogen atom into the N-substituent. This would serve to make them less available for construction of the aromatic system. Thus the molecule is less delocalised and the double bond in the C2-C3 position of the indole becomes less aromatic and more alkene-like in character.

It has also been shown that carbonyl compounds such as acetophenone, benzaldehyde and propionaldehyde do not yield oxetane adducts when irradiated with N-acylindoles, whereas benzoylformamide and methylbenzoyl formate do give oxetanes. This reactivity, or lack thereof, correlates with the triplet energies of the carbonyl compounds and suggests that only those with triplet energies of less than 68 kcal/mol can add to the acyl indole. It would seem, therefore, that it is the triplet carbonyl compound which adds to the ground state indole and that any carbonyl compound with a higher triplet energy is quenched by the indole derivative so that no cycloaddition occurs.

Indole itself appears to be quite unreactive photochemically and does not form cycloadducts when irradiated in the presence of carbonyl compounds or alkenes (vide infra). However, if an alkene which is a good acceptor is used in a sufficiently polar solvent then indole can be induced to undergo a photochemical reaction involving electron transfer. Thus, Sato reported that 3-(2-cyanoethyl)indole, 3, and 4-(2-cyanoethyl)indole, 4, are formed when indole or is irradiated with acrylonitrile in methanol (5). Analogous products are formed by irradiation of N-methylindole with acrylonitrile.



In addition to examining the photochemical addition of carbonyl compounds to N-acylindoles, Julian & Foster also irradiated N-benzoylindole, 5, and p-chloro-N-benzoylindole, 1a, with various mono-substituted ethenes and obtained *exo* and *endo* cyclobutane products such as 6 (6).



1a R=p-Cl-Ph

5 R=Ph

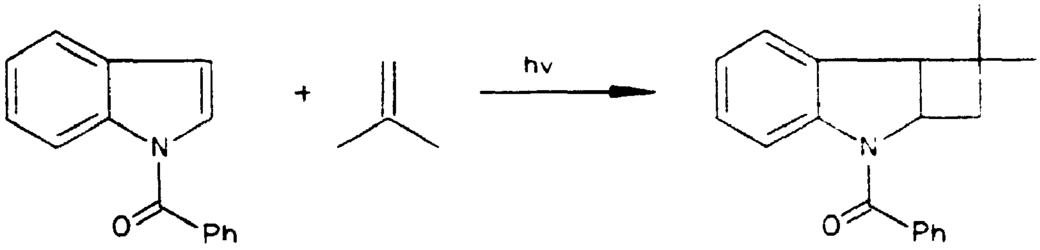
$X = CO_2Me, CO_2H$

Ac, OAc, OEt

6 R=Ph, X=CN

It was noted that with all the mono-substituted alkenes examined the reaction showed preferred regiochemistry in which the olefin substituent is oriented in a head-to-tail arrangement[1]. The preferred adduct stereochemistry was found to be *exo* in which the adjacent methine protons H_b and H_c in 6 are *trans* to each other. The reaction showed no change in efficiency or product distribution when the N-aroylindole was irradiated directly or under sensitized conditions (acetophenone). However, irradiation of indole or N-methylindole with the same olefins under direct or sensitized conditions gave no photocycloaddition products. This suggests as with the addition of carbonyl compounds that the acyl substituent is critical to cycloaddition. This has recently been demonstrated to be general for a series of N-carbonylindoles which have been synthesized and shown to undergo photochemical cycloaddition with cyclopentene (7).

Julian and Foster reported that irradiation of 5 with isobutane yielded 7 only, while acrylonitrile, acrylamide and ethyl vinyl ether also added to 5 yielding the corresponding head-to-head *endo* and *exo*-adducts (6).



7

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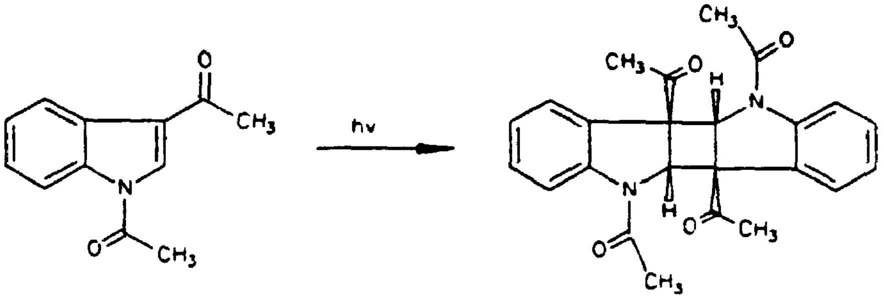
[1] In this nomenclature, derived from that commonly used in enone cycloaddition photochemistry, the "head" of the indole molecule is the Nitrogen, while the "head" of the alkene is the substituent X.

In a competitive irradiation of 5 with acrylonitrile and ethyl vinyl ether only the cyanocyclobutane products were formed suggesting that photoaddition is more efficient with olefins possessing electron withdrawing substituents. It was suggested, based on the evidence of sensitization experiments, that the photocycloaddition involves a triplet excited state of the indole derivative. Support for this was obtained by showing that the triplet quencher naphthalene inhibited the formation of cycloaddition products from 1a and alkenes (6).

Hino and coworkers (8) reported that when 1,3-diacetylindole, 8, was irradiated in various solvents the product formed had structure 9 resulting from 2+2 dimerisation[2].



8 9

The photodimer shown was the only isomer isolated. The reaction outcome was independent of solvent and irradiation conditions (direct or sensitised). Product 9 was isolated by precipitation from ethanol and its molecular structure was determined by X-ray analysis. It has also been reported that analogous photodimerizations occur with indene, benzofuran and benzothiophene 1,1-dioxide

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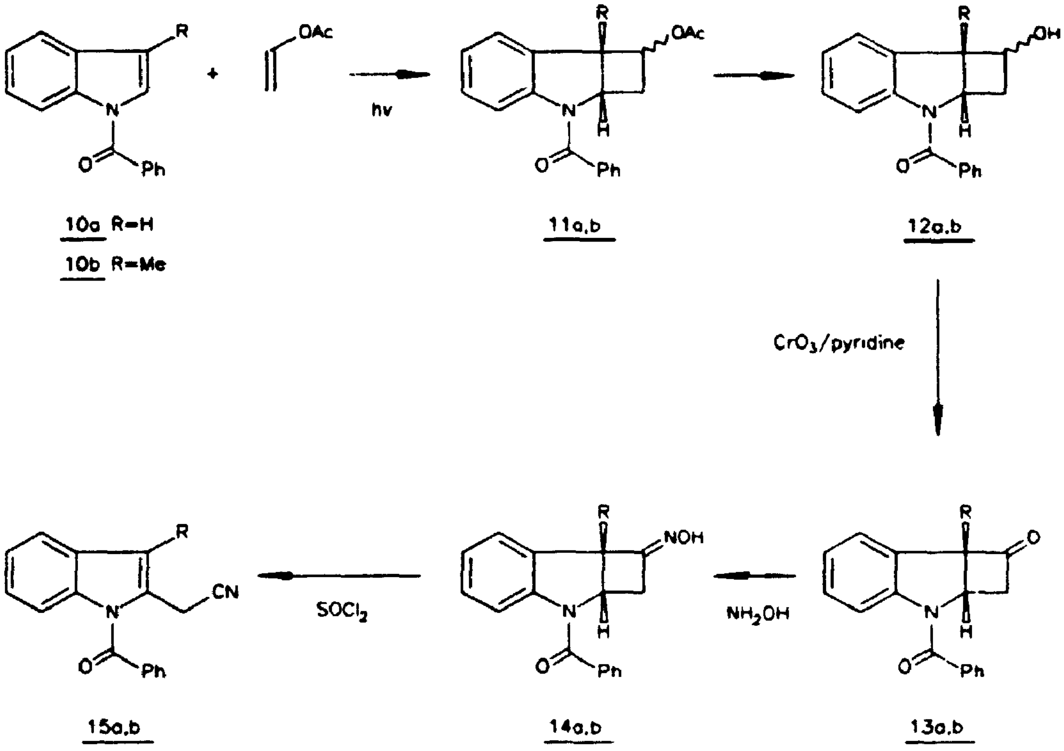
[2] The designation of this reaction as a 2+2 cycloaddition is not meant to imply that it is a concerted reaction. The usage is based upon that commonly applied in enone cycloaddition chemistry where the designation 2+2 is used to indicate a reaction between two pi-bonds forming a cyclobutane ring, albeit non-concertedly via a triplet excited state.

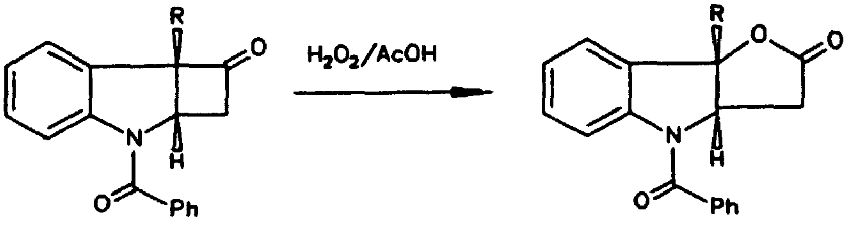
under both direct and sensitized conditions (9).

The synthetic utility of the photochemical cycloaddition reaction of N-acylindoles with alkenes has been explored by Ikeda and coworkers (11). They have shown that the benzoyl-2-cyanomethylindoles 15a and 15b can be synthesized by the route shown in Scheme 1.

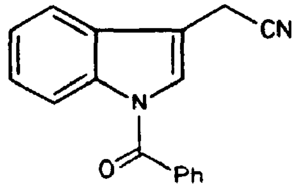
Scheme 1



In this scheme acetophenone sensitized benzene solutions of 10a and 10b in the presence of a large excess of vinyl acetate gave cycloaddition products 11a and 11b, respectively, which after alkaline hydrolysis gave alcohols 12a and 12b in excellent yield. Oxidation with chromium trioxide-pyridine complex gave cyclobutanones 13a and 13b. The structures of these compounds were deduced from their spectral data and by subsequent Baeyer-Villiger oxidation of the cyclobutanones to the corresponding γ-lactones 16a and 16b.



13a,b 16a,b



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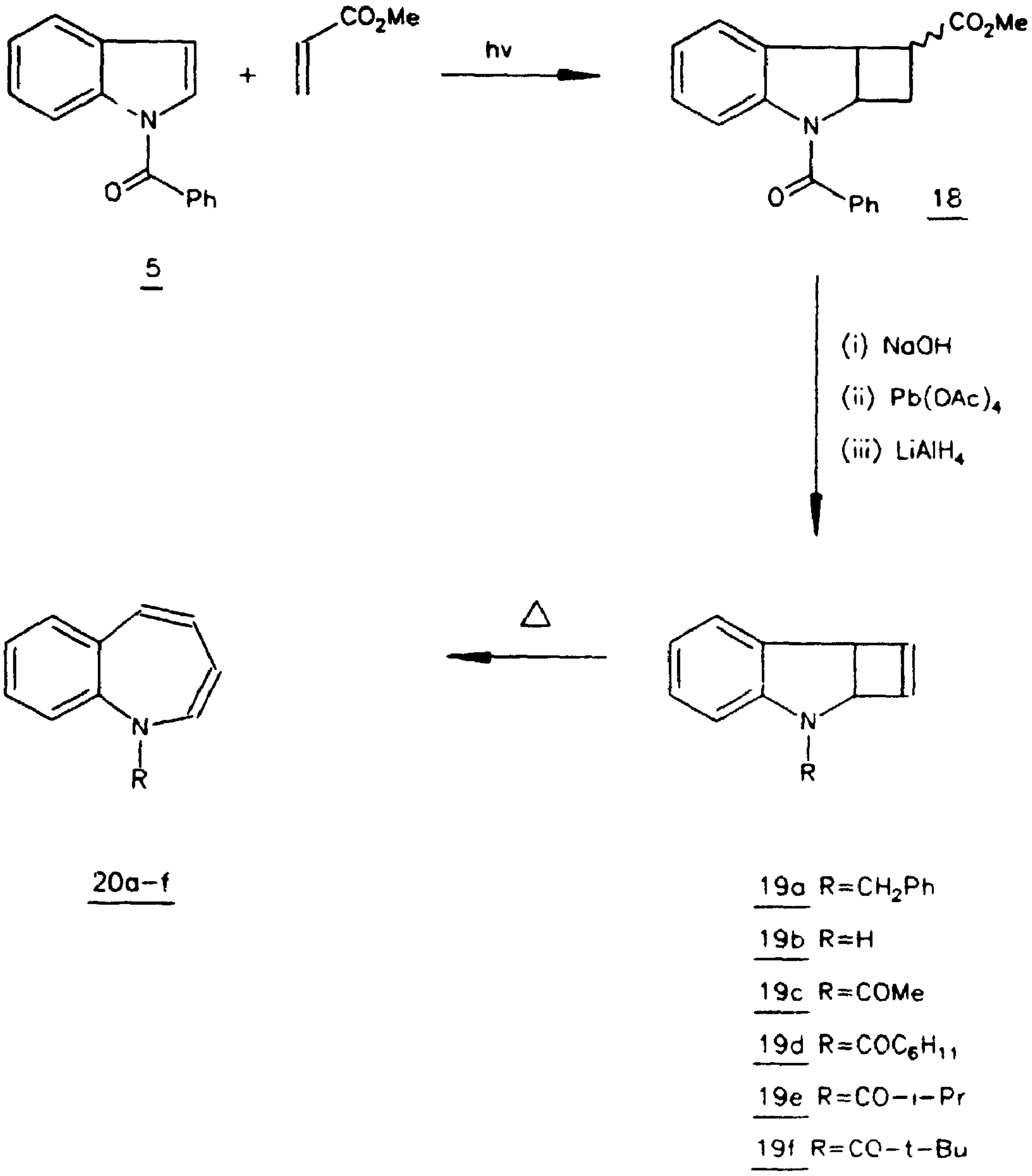
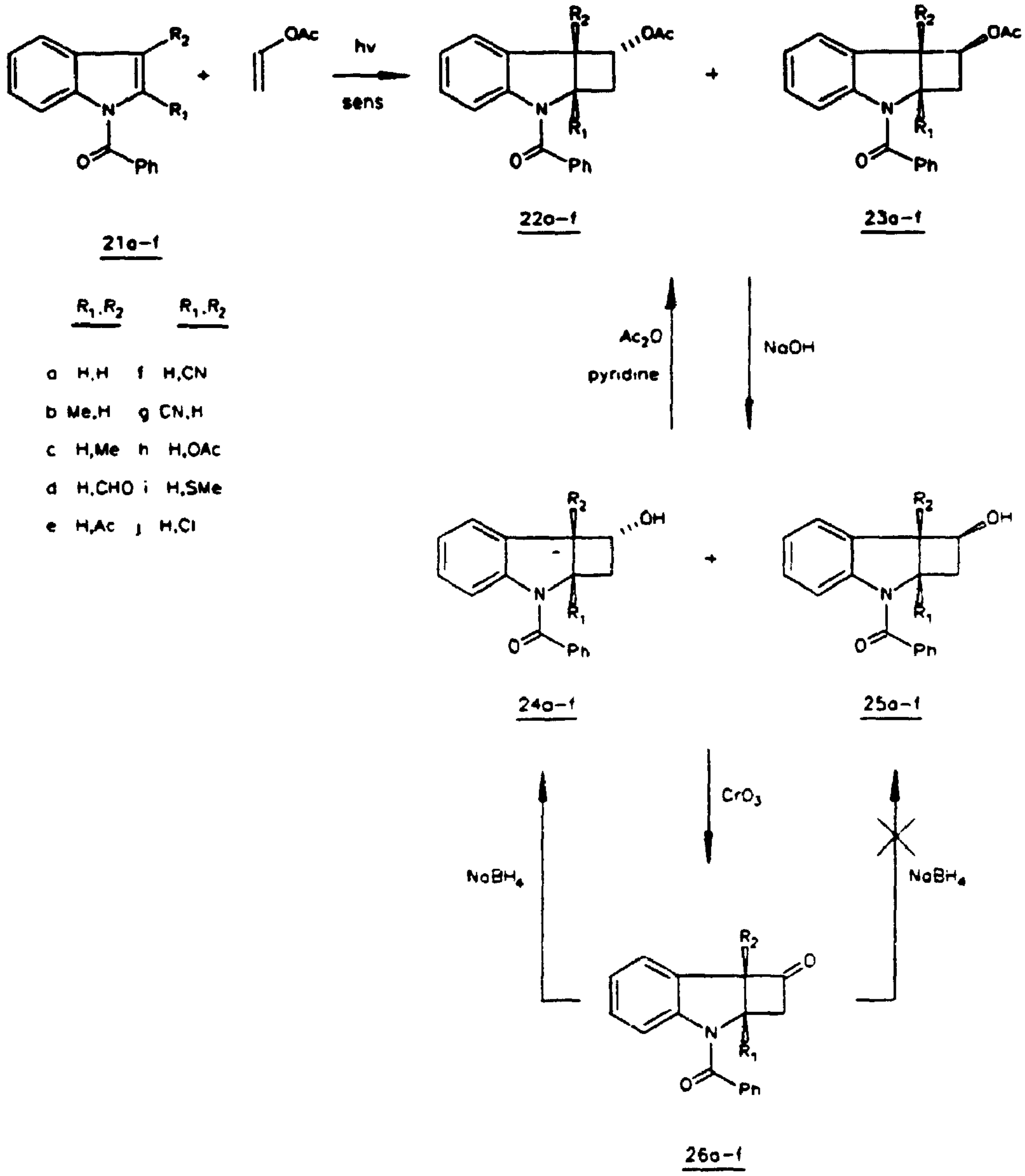
Treatment of the oximes 14a and 14b with thionyl chloride in dimethylformamide yielded 2-cyanomethyl-N-benzoylindoles 15a and 15b. Had the photochemical cycloaddition proceeded with head-to-head regiochemistry, the product from 10a would have been 3-cyanomethyl-N-benzoylindole 17. This was independently synthesised from indole-3-acetonitrile and benzoyl chloride and shown to be different from the product isolated, 15a. The same workers used the cycloadduct derived from N-benzoylindole and methyl acrylate as the precursor to 1H-1-benzazepines as shown in Scheme 2 (12). The mixture of stereoisomers with structure 18 was subjected to alkaline hydrolysis; subsequent oxidative decarboxylation with lead tetraacetate gave 3-benzoyl-2a,7b-dihydrocyclo[*b*]indole and treatment of this with lithium aluminium hydride at room temperature yielded

19a and unsubstituted 2a,7b-dihydrocyclo[*b*] indole 19b. The indole moiety was then substituted with various acyl substituents to yield indoles 19c-f. When these dihydrocyclo[*b*]indoles were heated to 270°C they underwent rearrangement to 1H-1-benzazepines, 20a-f.

Scheme 2



Ikeda et al. also investigated the regioselectivity and stereoselectivity of the 2+2 photocycloaddition of various N-benzoylindoles with methyl acrylate and vinyl acetate (13).

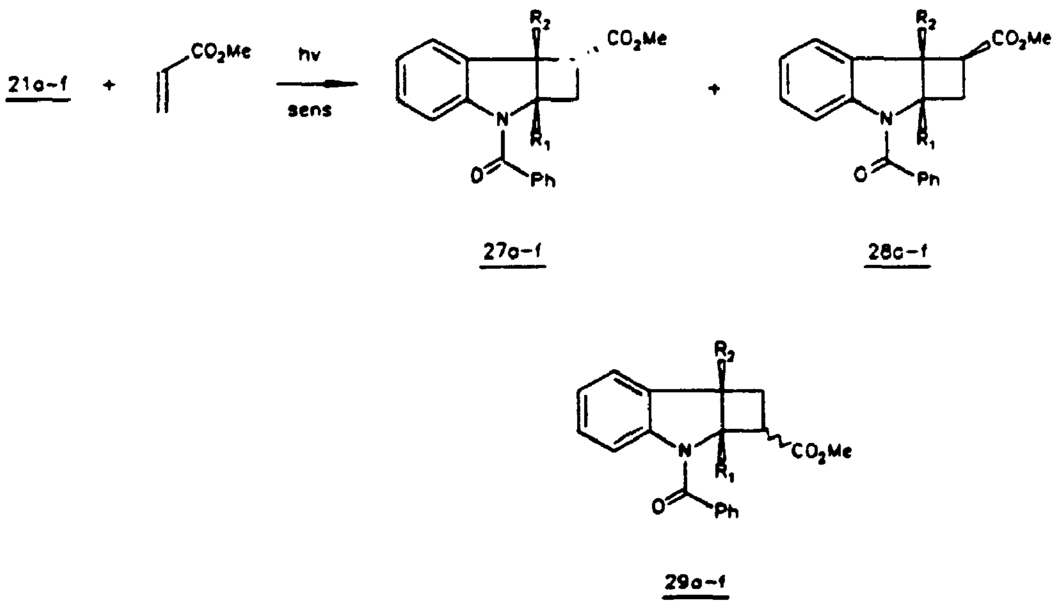


	R$_1$,R$_2$		R$_1$,R$_2$
a	H,H	f	H,CN
b	Me,H	g	CN,H
c	H,Me	h	H,OAc
d	H,CHO	i	H,SMe
e	H,Ac	j	H,Cl

When vinyl acetate was irradiated with the indoles, 21a-f, regioselective formation of adducts 22a-f and 23a-f resulted. Comparable amounts of the *exo*-isomer and *endo*-isomer were present in the reaction mixture. Isolation of these adducts were effected by alkaline hydrolysis to alcohols 24a-f and 25a-f followed by chromatographic separation and reacetylation. The structures of the acetates were elucidated by ^{1}H-nmr spectroscopy and by oxidation of the alcohols to cyclobutanones 26a-f. Treatment of both alcohols 24a-f and 25a-f with chromium (VI) oxide yielded a single cyclobutanone, 26a-f, whose treatment with sodium borohydride would yield alcohol isomer 24a-f only, a result of hydride attack on the less hindered *exo*-face.

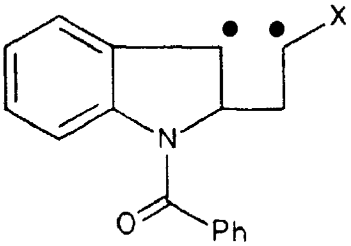
Irradiation of compounds 21a and 21d-f with methyl acrylate gave a mixture of three isomers. Isolation and characterization of these products revealed that the *exo*-isomer 27a-f was the major product and that regioisomers 29a-f were minor.

Scheme 3



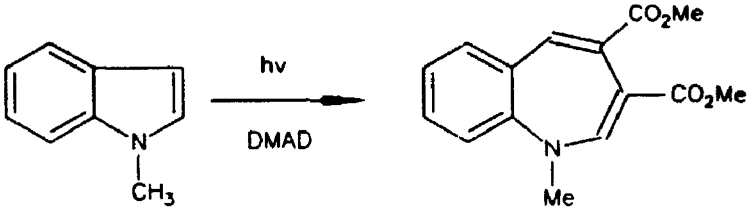
Despite an abundance of ^{1}H-nmr spectroscopic evidence the authors had to rely on chemical manipulation in order to prove the structure since assignment of stereochemistry on the basis of nmr coupling constants proved to be too ambiguous.

From the results described above it can be concluded that the photochemical cycloaddition reaction of N-acylindoles with alkenes proceeds in moderate yields and with high regioselectivity and, in some cases, high stereoselectivity. This type of regioselectivity is similar to that observed when olefins are added to other aromatic heterocycles such as 2-quinolones (14), 1-isoquinolones (15), coumarins (16), indenes(17), and thianapthene 1,1-dioxides (18). In these cases a single regioisomer is formed irrespective of the type of olefin. This contrasts dramatically with the photocycloaddition reaction of olefins with α,β-unsaturated ketones where the regiochemistry is dependent on olefin structure. Ikeda has proposed that the reaction regiochemistry can be rationalised if it is assumed that the product is formed via a 1,4-biradical intermediate in which the 2-position of the indole has become bonded to that end of the alkene least able to support a radical. Such a radical would have structure 30.



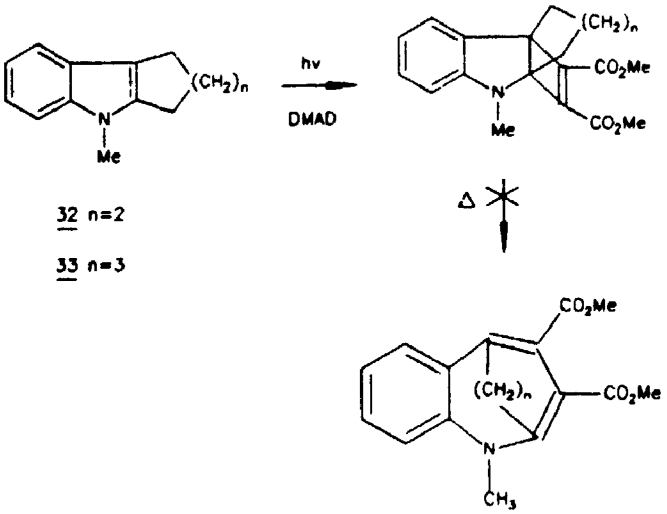
30

Neckers and coworkers (19) have shown that indoles need not possess an N-acyl moiety in order to undergo photochemical cycloaddition reactions if the reacting partner is an alkyne. Thus irradiation of N-methylindole with dimethylacetylenedicarboxylate (DMAD) resulted in the direct formation of N-methyl-3,4-dicarbomethoxybenzoazapine 31.



31

The reaction is thought to be a $\pi^2s + \pi^2s$ cycloaddition process followed by a thermal cyclobutene ring opening at room temperatu To prevent the ring opening the N-alkylindole was ring-fused at the C-2 and C-3 positions as in compounds 32 and 33. Irradiation with DMAD then yielded the cyclobutene adducts which were stable with respect to ring opening.

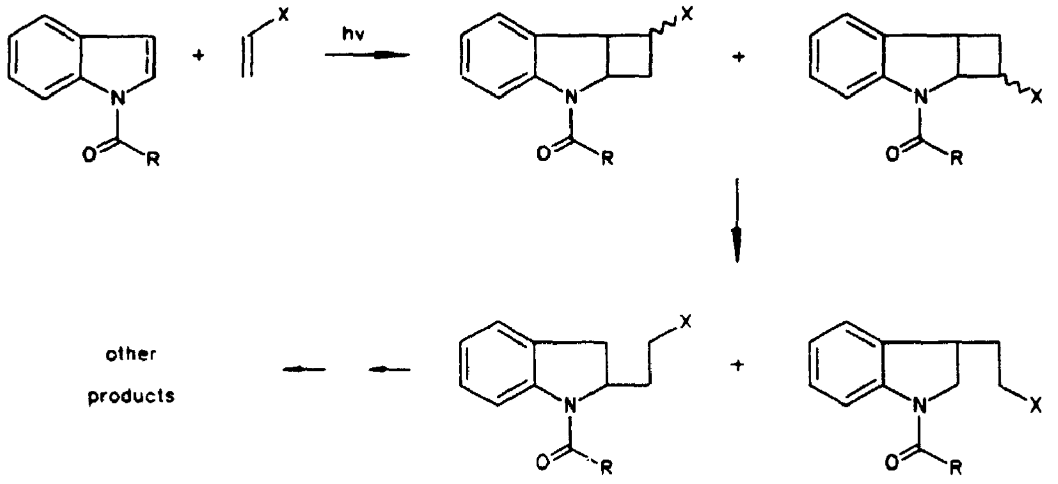


32 n=2

33 n=3

The 2+2 photochemical cycloaddition reaction of N-derivatized indoles with olefins suggests a potential route to 2- and 3-substituted indolines and, following oxidation, indoles. Thus formation of the cyclobutane ring could be followed by selective cleavage to yield indoline products which in turn could be oxidized to synthetically useful indoles as shown in Scheme 4.

Scheme 4



Because of this potential synthetic utility, a better understanding of the mechanism and the factors which govern quantum efficiency, regioselectivity, and stereoselectivity of the photocycloaddition reaction is desirable. The work described in part of this thesis was designed to achieve this understanding.

1.2 SPECTROSCOPIC PROPERTIES OF N-ACYLINDOLES

In most organic solvents indole shows principal absorption maxima at *circa* 225 nm (ϵ = 2.5 X 10^4) and 270 nm (ϵ = 6 X 10^3); vibrational structure is observed and their positions are somewhat sensitive to polarity. The appearance of the absorption spectrum of indole is very characteristic and is often used to identify the presence of indole chromophores in alkaloids. The absorption spectrum arising from the indole ring of tryptophan, a naturally occurring amino acid, is also quite characteristic and the longest wavelength bands in the spectra of many proteins are largely the result of their tryptophan content (20).

The absorption spectra of N-acylindoles are quite different from that of indole. N-Benzoylindole exhibits two characteristic absorption bands in the ultraviolet spectrum, an intense band around the 250 nm region (ϵ = 2.5 X 10^4) and a second weaker band in the 303 nm region (ϵ = 8 X 10^3) (Figure 1). N-Carboethoxyindole, 34, shows a similar absorption spectrum (Figure 2) with the weaker band absorbing at slightly lower wavelength, 292 nm region, presumably because it is less highly conjugated than N-benzoylindole. The spectra show no little vibrational structure. It is the excitation of the weaker, longer wavelength band of N-acylindoles which has been used in the photochemical cycloaddition reactions in which a medium pressure mercury vapour lamp has been employed (1). It has been shown (21) that changing the polarity of the solvent yields no changes in the wavelengths of the absorption maxima of N-benzoylindoles and this suggests that the absorption maxima do not correspond to a simple $n \rightarrow \pi^*$ transition localized on the carbonyl group.

Figure 1: U V spectra of Indole and $\underline{5}$ in n-hexane

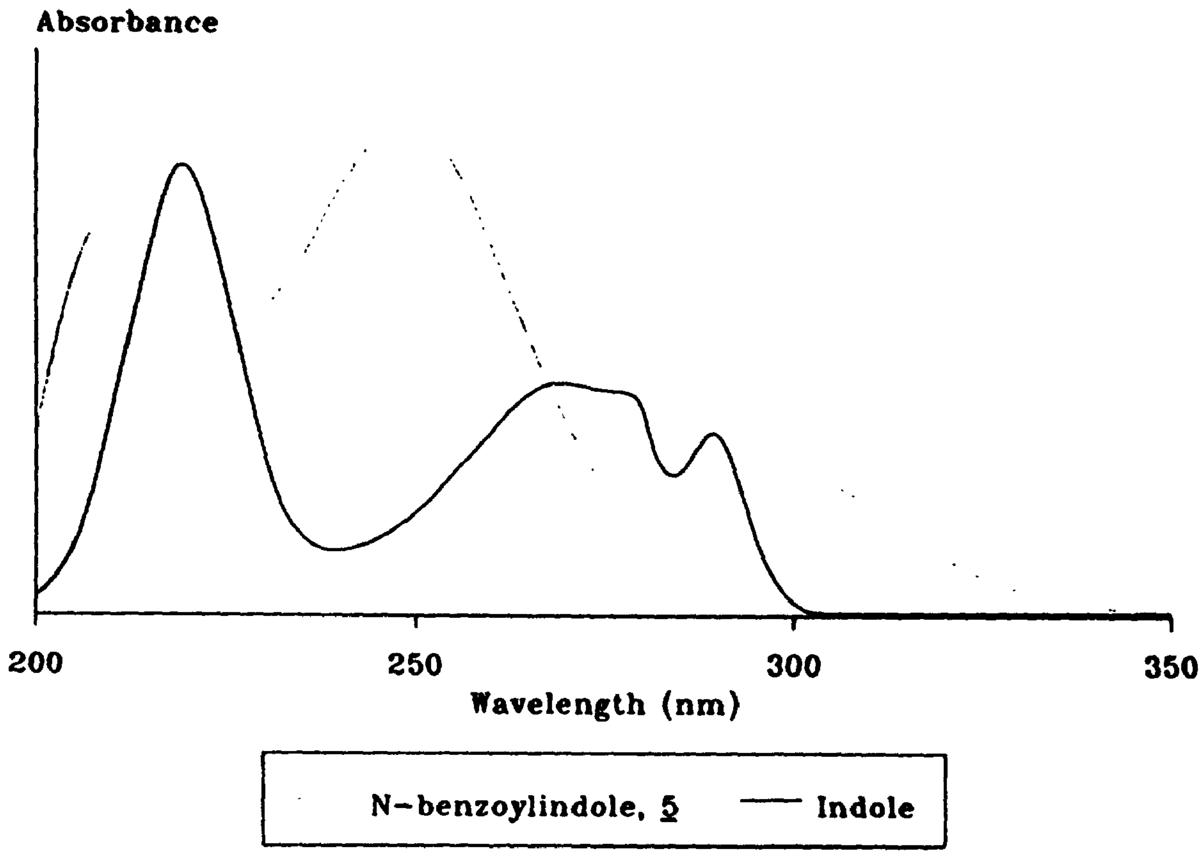
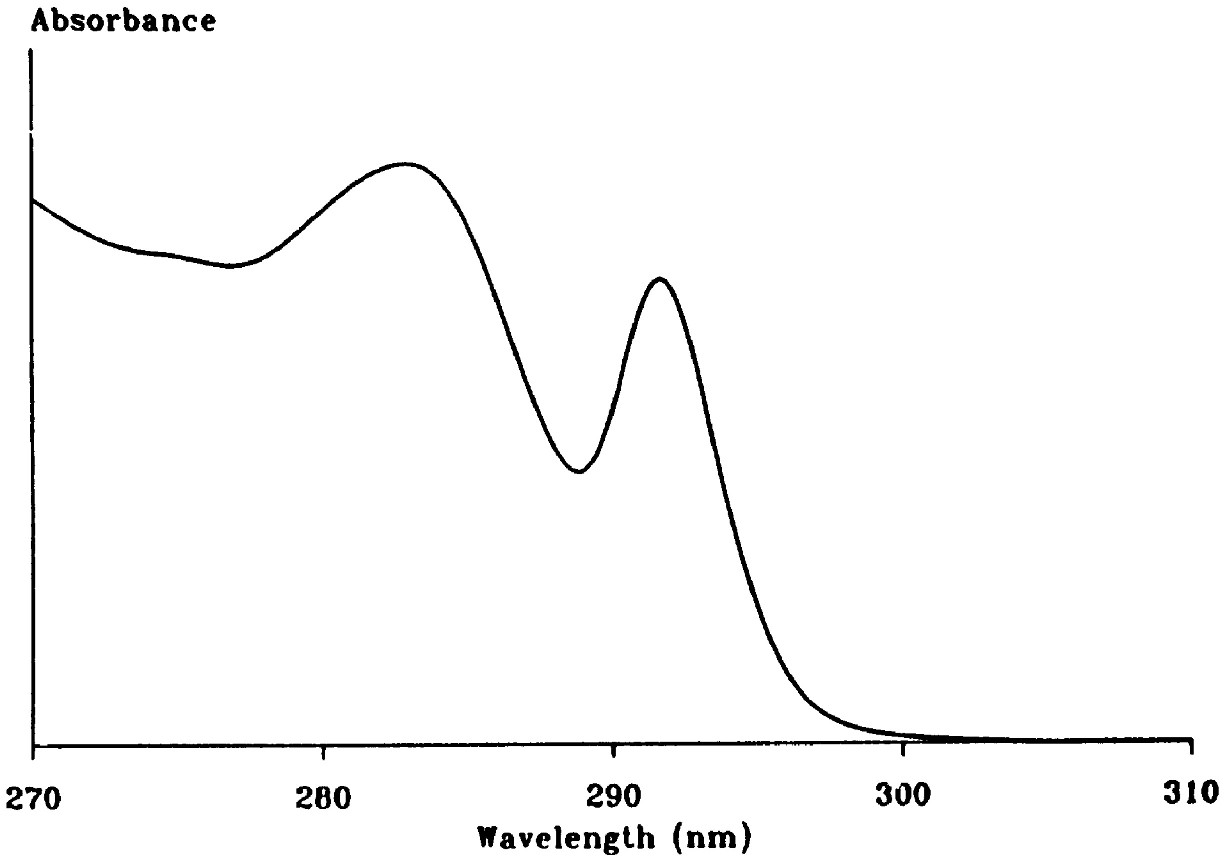


Figure 2: U V spectrum of 34
in n-hexane

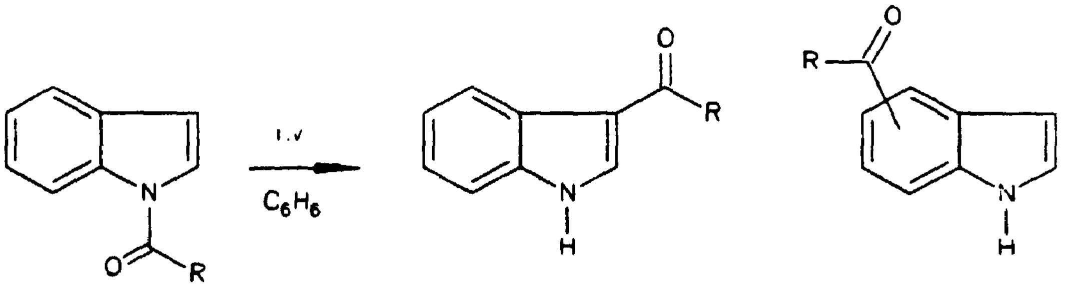


1.3 MECHANISTIC ASPECTS OF 2+2 PHOTOCYCLOADDITION

Several pathways can be envisaged for deactivation of the excited state of N-acylindoles to the ground state. These pathways could reasonably include;

- **(i) rearrangement of the N-acylindole via the photo-Fries reaction.**
- **(ii) cycloaddition reactions, either to the C2-C3 double bond or to the carbonyl group to yield 1:1 adducts. This could, in principle, occur from either the singlet or the triplet excited state.**
- **(iii) radiative decay to ground state.**
- (iv) non-radiative decay to the ground state.
- (v) dimerization by reaction of the excited state with a ground state N-acylindole molecule.

Oldroyd and Weedon have reported (22) that both N-benzoylindole, 5, and N-carboethoxyindole, 34, undergo a photo-Fries rearrangement in which cleavage of the N-acyl fragment is followed by recombination to give a nuclear substituted indole (23).



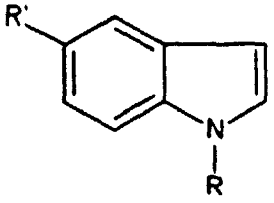
5 R=Ph

33 R=OEt

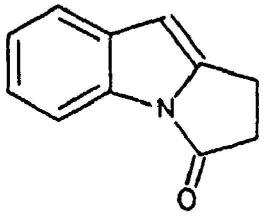
The efficiency of the rearrangement was found to be solvent and wavelength dependent and it is believed that the cleavage necessary for rearrangement was occurring from an upper excited state or from an upper vibrational level of a lowest excited state. It could not be determined whether the reaction was occurring from a singlet or triplet excited state.

As mentioned above Hino (8) has observed photochemical dimerization of 1,3-diacetylindoles; however it has been shown that N-benzoylindole does not dimerize, even though some evidence of inefficient quenching of the triplet excited state of 5 has been observed (24,25). It has recently been found that N-carboethoxyindole, 34, forms a photodimer, very inefficiently, by addition of the 2,3-double bond of an excited indole to the same bond of a ground state partner (10).

The early work of the groups of Julian (6) and Ikeda (13) on the photochemical addition of alkenes to N-aroylindoles yielded little information about the mechanism, beyond the fact that at least part of the products were formed from the indole triplet excited state. In 1987 Disanayaka and Weedon (21) produced the first two papers reporting the results of an investigation of the photophysical and photochemical properties of N-benzoylindoles 5, 34-40. Their photophysical studies revealed that various N-benzoylindoles did not fluoresce normally but instead emitted light at an unusually long wavelength. The fluorescence emission occurred between 400 nm and 600 nm and its position was determined to be solvent dependent and also dependent on the nature of the aroyl substituent conjugated with the indole system. It was concluded that this emission was occurring from a singlet charge transfer excited state in which electron density had moved in the excited state from the indole moiety to the aroyl moiety.



	R'	R
5	H	C_6H_5CO
34	H	EtOCO
35	H	p-MeO-C_6H_5CO
36	H	MeCO
37	H	p-NO_2-C_6H_5CO
38	OMe	C_6H_5CO



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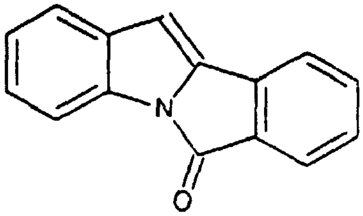
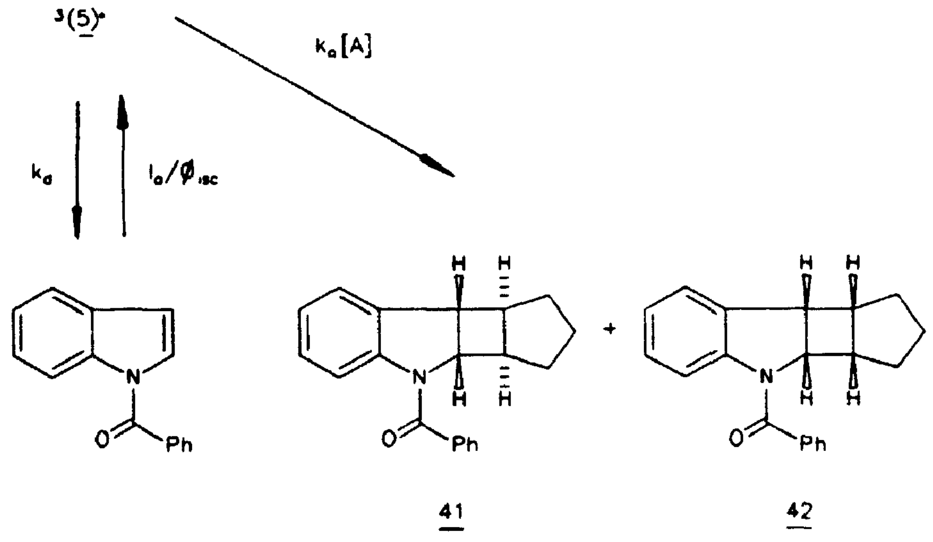


40

Such a state only occurred with aroylindoles; thus N-acylindoles such as N-carboethoxyindole and N-acetylindole did not show any such fluorescence. It was also determined that this charge transfer state was not quenched by the addition of cyclopentene and therefore is not involved in the cycloaddition reaction with alkenes. Other photophysical studies with N-benzoylindole revealed the first singlet excited state energy to be 95 kcal/mol while the lower energy charge transfer state was found to have a fluorescence lifetime of *ca.* 0.5 ns. Phosphorescence measurements at 77°K yielded a relaxed triplet excited state energy of 68 kcal/mol.

Disanayaka and Weedon's studies of the mechanism of the 2+2 photocycloaddition reaction between N-benzoylindole, 5, and cyclopentene revealed two pieces of conflicting data (25). The efficiency of population of the triplet excited state is given by the quantum yield of intersystem crossing, ϕ_{isc}, and was determined by Disanayaka and Weedon using the triplet counting procedure to be 0.39 in benzene. A triplet lifetime of 2.8 $X10^{-8}$ s was also obtained from the triplet counting procedure. If the formation of cycloadducts is assumed to proceed exclusively from interaction of the N-acylindole triplet excited state with ground state alkene, then the pathway shown in Scheme 5 can be envisaged. Application of the steady state approximation to Scheme 5 yields Equation 1, where k_a is the rate constant for quenching of triplet excited state 5 by an alkene, k_d is the rate constant for the deactivation processes of the triplet excited state of 5, ϕ_{isc} is the quantum yield of intersystem crossing of the singlet excited state of 5 to the triplet excited state of 5, and [A] is the concentration of the adding alkene. At high alkene concentration $k_d << k_a[A]$ and Equation 1 equates the quantum yield of product formation to that of ϕ_{isc} (Equation 1).

Scheme 5



(equation 1) $$\phi = \frac{k_a[A]\phi_{isc}}{k_a[A] + k_d}$$

Equation 1 also predicts a linear relationship between $1/\phi$ and $1/[A]$ as shown in equation 2. This equation predicts that a plot of $1/\phi$ verses $1/[A]$ should have an intercept if $1/\phi_{isc}$ corresponding to the limiting quantum yield at "infinite" alkene concentration.

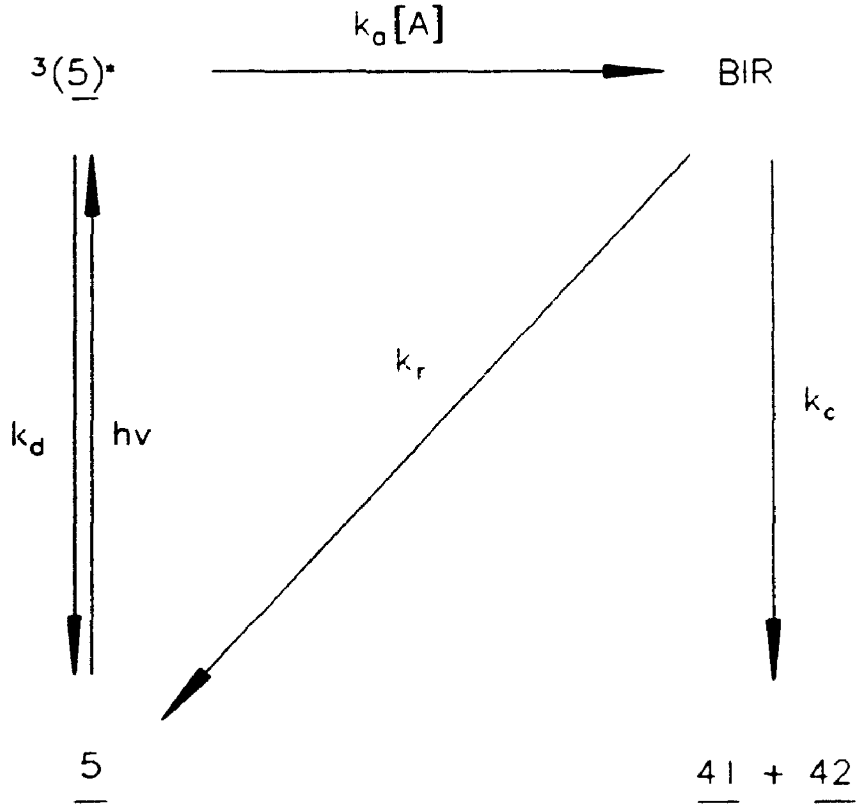
(equation 2) $$\phi^{-1} = \frac{1}{\phi_{isc}} + \left[\frac{k_d}{k_a[A]\phi_{isc}}\right]$$

Disanayaka and Weedon found that a double reciprocal plot does indeed yield a linear relationship. However the experimental intercept yielded a value of ϕ_{isc} of 0.061 which is far different from the value of 0.39 they determined by the triplet counting procedure. The authors concluded from this that interception of the triplet excited state of the indole by the alkene must produce an intermediate which can collapse to ground state starting materials in competition with proceeding to products.

A similar situation has been shown to exist for the 2+2 photochemical cycloaddition reactions between alkenes with 2-cyclopentenones and 2-cyclohexenones (26). In these cases it has been shown that a biradical intermediate is involved along the reaction pathway and that this intermediate accounts for the low quantum yield of product formation, compared to the quantum yield of intersystem crossing, at high alkene concentration.

This led Disanayaka and Weedon to propose the mechanism for the indole photocycloaddition shown in Scheme 6. This mechanism proposes a biradical intermediate formed from the triplet excited state of the indole derivative by interaction with the ground state olefin. This biradical intermediate is proposed to have two fates; it can either undergo cleavage to give back the starting indole derivative and olefin, or it can close to yield cyclobutane products. Both of these processes occur following spin inversion in the triplet 1,4-biradical intermediate. Application of steady state analysis to Scheme 6 yields Equations 3 and 4. The latter predicts a linear relationship between $1/\phi$ and $1/[A]$.

Scheme 6



(equation 3) $$\phi = \left[\frac{k_c}{k_r + k_c}\right]\left[\frac{k_a[A]\phi_{isc}}{k_a[A] + k_d}\right]$$

(equation 4) $$\phi^{-1} = \frac{1}{\phi_{isc}}\left[\frac{k_c}{k_r + k_c}\right]^{-1}\left[1 + \frac{k_d}{k_a[A]}\right]$$

The experimental data was re-interpreted in terms of these relationships. Combining the intercept from the experimental plot of $1/\phi$ verses $1/[A]$ with the value for $\phi_{isc}=0.39$ obtained from triplet counting a value for $k_c/(k_c+k_r)$ of 0.16 ± 0.02 was determined. This means that 16% of the biradicals formed close to give products and the other 84% revert back to starting materials.

The objective of the work described in Part I of this thesis was designed to provide additional evidence for the presence of the biradical intermediate(s) and to deduce their structures and their lifetimes.

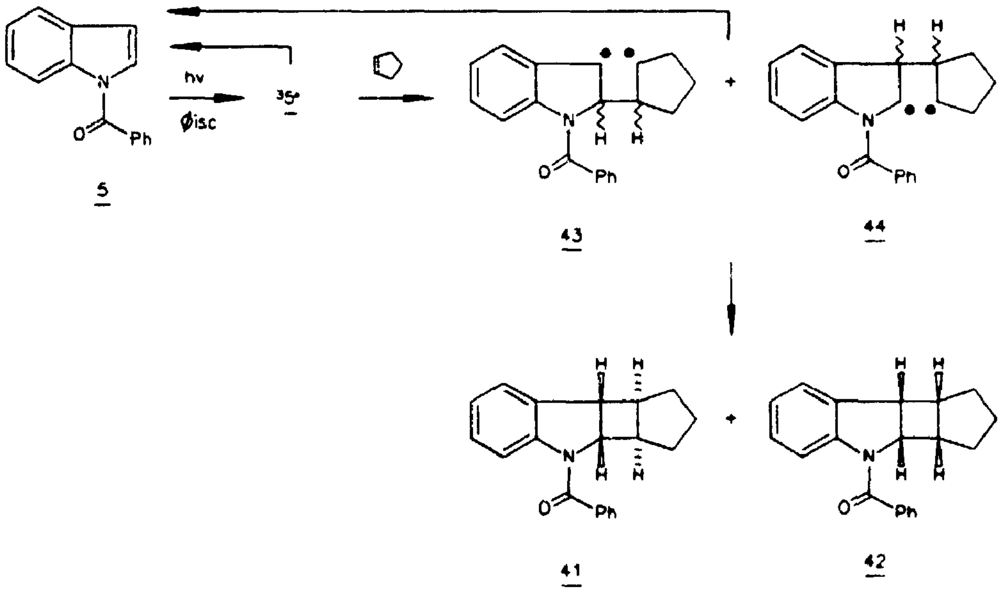
CHAPTER 2

PHOTOCYCLOADDITION REACTIONS OF N-BENZOYLINDOLE AND N-CARBOETHOXYINDOLE WITH OLEFINS

2.1 BIRADICAL INTERMEDIATES

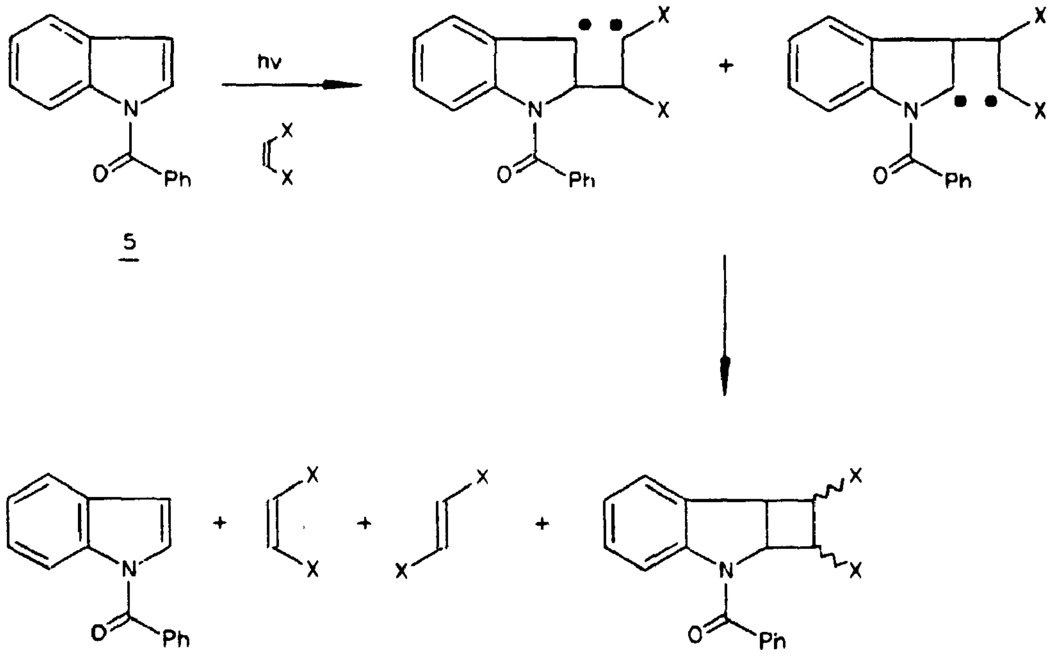
In the previous chapter kinetic evidence for the intermediacy of triplet 1,4-biradicals in the photochemical cycloaddition reaction of N-benzoylindole with alkenes was presented. For the reaction of N-benzoylindole with cyclopentene there are two possible structures for the intermediate biradical. These are structures 43 and 44, and each of these can be formed as a mixture of stereoisomers as shown in Scheme 7.

Scheme 7



If triplet 1,4-biradicals of the type 43 and 44 are indeed intermediates in this reaction and if, as the kinetic evidence indicates, they do revert to the ground state starting materials in competition with product formation, then use of a suitable 1,2-disubstituted olefin as the alkene partner in the photochemical cycloaddition reaction could allow for the detection of the reversion process by observation of geometrical isomerisation of unconsumed alkene. The possibility is illustrated in Scheme 8; this type of alkene photoisomerisation, in which the alkene is never in the excited state is called Schenk isomerisation.

Scheme 8



X = CH_3
X = $CH_2CH_2CH_3$

In addition to the isomerisation of unreacted alkene, if the putative biradical intermediates in Scheme 8 are sufficiently long lived, so that any memory of the alkene stereochemistry is lost, then the stereochemistry of the cyclobutane adducts will be mixed. Alternatively, if no biradical intermediates are formed, or if they are too short lived for conformational relaxation, then different products might be expected depending on the geometrical isomer of the alkene used, and no isomerized alkene would be seen in the reaction mixture.

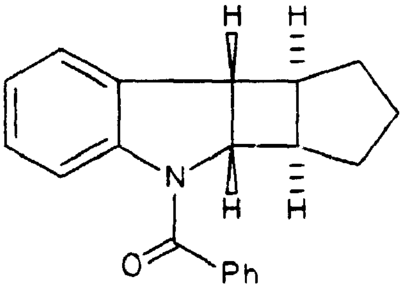
This chapter reports the results of an investigation in which N-acylindoles have been irradiated in the presence of cyclic and acyclic 1,2-dialkyl substituted ethylenes and the stereochemistry of the products examined. These results are then discussed in terms of the postulated biradical species.

2.2 STRUCTURE AND STEREOCHEMISTRY OF CYCLOADDITION PRODUCTS

The addition of a 1,2-disubstituted ethylene to an N-acylindole leads to the formation of four chiral centres. The maximum number of stereoisomers which can be produced is however reduced by the presence of a cyclobutane-cyclopentane ring fusion which is expected to be *cis* as was shown as in Scheme 7. Consequently if the two substituents on the ethylene are the same (so that no possibility of regioisomerism exists) then the photoaddition is expected to produce four enantiomeric pairs of diastereomers. The major analytical problem in this work was to detect, separate and assign the stereochemistries of these diastereomers.

Several groups have examined the use of nmr-spectroscopy for the stereochemical assignment of substituted cyclobutane rings (27-37). The use of ^{1}H-^{1}H coupling constants for the hydrogens of the cyclobutane ring has met with some success but ambiguities can be caused by the conformational mobility of the puckered cyclobutane ring (35-37). Recently it has been shown that nuclear Overhauser effects between cyclobutane ring hydrogens or substituents can lead to stereochemical assignments (27,28), however this has not been demonstrated to be a general method.

Because of these problems of stereochemical assignment the first alkene examined in this work was cyclopentene. It was anticipated that with this alkene only the two enantiomeric pairs of diastereomers represented by structures 41 and 42 would be formed since the sizes of the rings fused to the cyclobutane would preclude the formation of products in which the hydrogens on adjacent ring fusion carbons could be *trans*.



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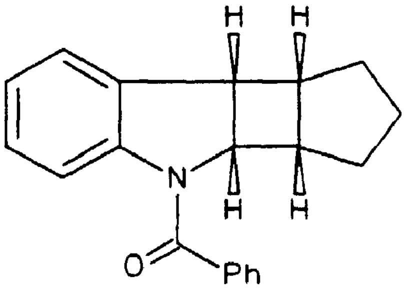


41

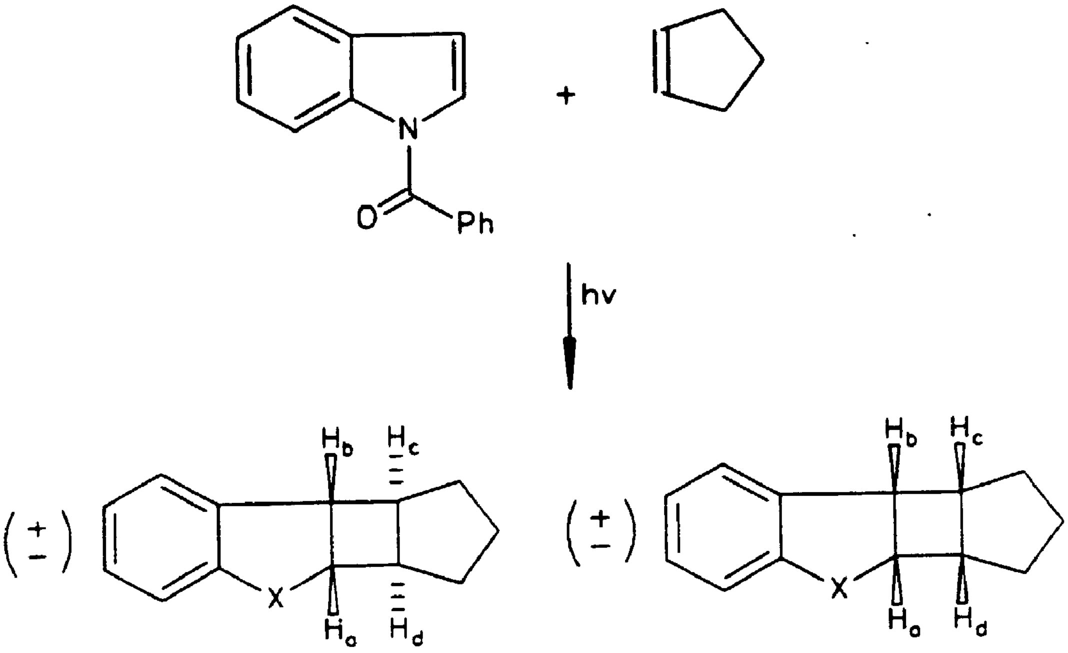
42

It was hoped that the spectroscopic characteristics of the cyclopentene adducts could then be used as models for the deduction of the stereochemistry of adducts from other alkenes.

2.2.1 Irradiation of N-Benzoylindole and N-Carboethoxyindole with Cyclopentene

Both gas chromatography (g.c.) and thin layer chromatography (t.l.c.) indicated the formation of a single major product and a minor product when a benzene solution of N-benzoylindole, 5, and cyclopentene was irradiated with ultraviolet light under conditions such that only 36 was excited. The minor product was indentified as N-carboethoxyindole, 34. Following work-up and removal of the unconsumed starting material, the ^{1}H-nmr and ^{13}C-nmr spectra of the product suggested the presence of two compounds in a 2:1 ratio. The major component was highly crystalline and this allowed its separation from the minor component which was subsequently isolated from the mother liquors as an oil. The mass spectra of the isolated products indicated them to be adducts of 5 and cyclopentene, and the ^{1}H-nmr spectra were consistent with the expected structures of 41 and 42 (Scheme 9). In particular the cyclobutane methine protons were clearly visible; for the major isomer they appeared at 3.94, 3.32, 2.84, and 2.66 ppm and these were assigned to protons H_a, H_b, H_c, and H_d, respectively. These assignments are based partly upon the positions calculated using additive chemical shift correlations, and partly on the appearance of the signals and their coupling relationships as deduced from spin-spin decoupling experiments and 2-dimensional homonuclear correlation experiments. The signal assigned to H_a appeared as a broad singlet and its splitting by H_b and H_d was unresolved. This lack of resolution is ascribed to slow rotation of the adjacent N-benzoyl group. However, the signal assigned to H_b appeared as a doublet of doublets with $J=7.5$ and 2.9 Hz.

Scheme 9



41 X = NCOPh
42 X = NCOPh

45 X = NCH_2Ph
46 X = NCH_2Ph

47 X = NH
48 X = NH

49 X = CH_2
50 X = CH_2

51 X = NCO_2Et
52 X = NCO_2Et

Molecular models of 41 show that the structure is quite rigid and suggest that with the cyclobutane ring in either of its puckered conformations the dihedral angle between H_b and H_a are close to zero, and between H_b and H_c are close to 90°; in this situation the Karplus equations predict the small and large coupling constants observed.

In the minor photo-adduct the signal assigned to H_a was also an unresolved broadened singlet and was seen at 4.70 ppm; the signal assigned to H_b was a doublet of doublets at 4.05 ppm with coupling constants of 7.5 and 8.0 Hz. The observation of two large coupling constants between H_b and H_a, and H_b and H_c is consistent with the minor photoadduct having structure 42 as judged by the inspection of the dihedral angles between the appropriate hydrogens in a molecular model of 48. The relevant dihedral angles in this case are both close to zero.

In order to support the above assignments attempts were made to remove the benzoyl group from the photoadducts; it was hoped that in the absence of this group the signal assigned to H_a would be resolved so that its coupling constants to H_b and H_d could be measured independently. the benzoyl group was however totally resistant to hydrolysis under both basic and acidic conditions. Eventually it was found that treatment of the photoadducts with lithium aluminium hydride resulted in the formation of a mixture of the N-benzyl derivatives 45 and 56 as well as the products of cleavage, 47 and 48. These compounds were separated by chromatography and their ^{1}H-nmr spectra recorded. As anticipated, the signal assigned to H_a in these compounds was resolved as a doublet of doublets and the coupling constants were consistent with the *cis-anti-cis* stereochemistry in 45 and 47, and the *cis-syn-cis* stereochemistry seen in 46 and 48. The coupling constant data for the cyclobutane methine hydrogens of these compounds are summarised in Table 1.

The above assignments were further tested by a molecular modelling (MM2) calculation to derive the structures of the most stable conformations of 41, 42, 45-48 (38). The dihedral angles between the cyclobutane methine hydrogens in the most stable conformations were then substituted into the appropriate Karplus equation in order to predict the expected coupling constants. For ease of calculation and because the nitrogen parameters necessary for 41, 42, 45-48 were unavailable to us, the indane analogues 49 and 50 were used. The results for 49 and 50 are shown in Table 1 along with the actual coupling constants measured from the ^{1}H-nmr spectra of 41, 42, 45-48. The agreement between the calculated values for 49 and 50 and those measured for compounds 41, 42, 45-48 is qualitatively very good and quantitatively reasonable, and indicates that for these systems the calculation is reliable for deduction of stereochemistry from coupling constant data, even though indane is being used as a model for indoline. It should also be noted that no allowance was made for the effect of an electronegative substituent (the nitrogen atom) on the coupling constants.

The calculated structures of the most stable conformations of 49 and 50 were also used to predict the likely effect of a lanthanide shift reagent (Eu(fod)$_3$) complexed to the nitrogen atom of 47 and 48 on the chemical shifts of the cyclobutane methine hydrogens. The calculated relative shifts of the cyclobutane methine hydrogens were then compared with the observed relative shifts when the shift reagent Eu(fod)$_3$ was added to deutero-chloroform solutions of 47 and 48.

TABLE 1

EXPERIMENTAL AND CALCULATED ^1H-^1H COUPLING CONSTANTS (Hz) FOR CYCLOBUTANE METHINE HYDROGENS IN CYCLOPENTENE AND CYCLOHEXENE ADDUCTS OF N-BENZOYLINDOLE AND N-CARBOETHOXYINDOLE

COMPOUND	J_{ab}	J_{ad}	J_{bc}	J_{cd}
41	7.5	2.9	2.9	7.0
42	7.5	7.7	8.0	8.2
45	7.9	2.5	2.7	6.6
46	9.4	9.0	9.0	6.4
47	7.6	2.5	2.7	7.0
48	9.6	9.0	9.2	8.2
49 (calculated)	7.8	3.6	2.0	8.0
50 (calculated)	7.8	8.1	7.9	8.0
53	7.0	2.5	2.5	7.0
54	8.5	9.0	9.0	9.5
61	8.5	9.3	9.0	9.0
62	8.7	9.3	9.0	9.0
63	8.0	3.0	2.0	8.0
64	6.0	4.0	8.0	7.0
57 (calculated)	7.8	1.9	3.2	7.3
58 (calculated)	7.9	8.2	7.9	8.1
59 (calculated)	7.7	6.8	6.9	6.6
60 (calculated)	7.3	7.2	7.1	8.5

Figure 3: Calculated and observed changes in chemical shift ($\Delta\delta H_x$) of cyclobutane methine protons for 47 upon addition of $Eu(fod)_3$.

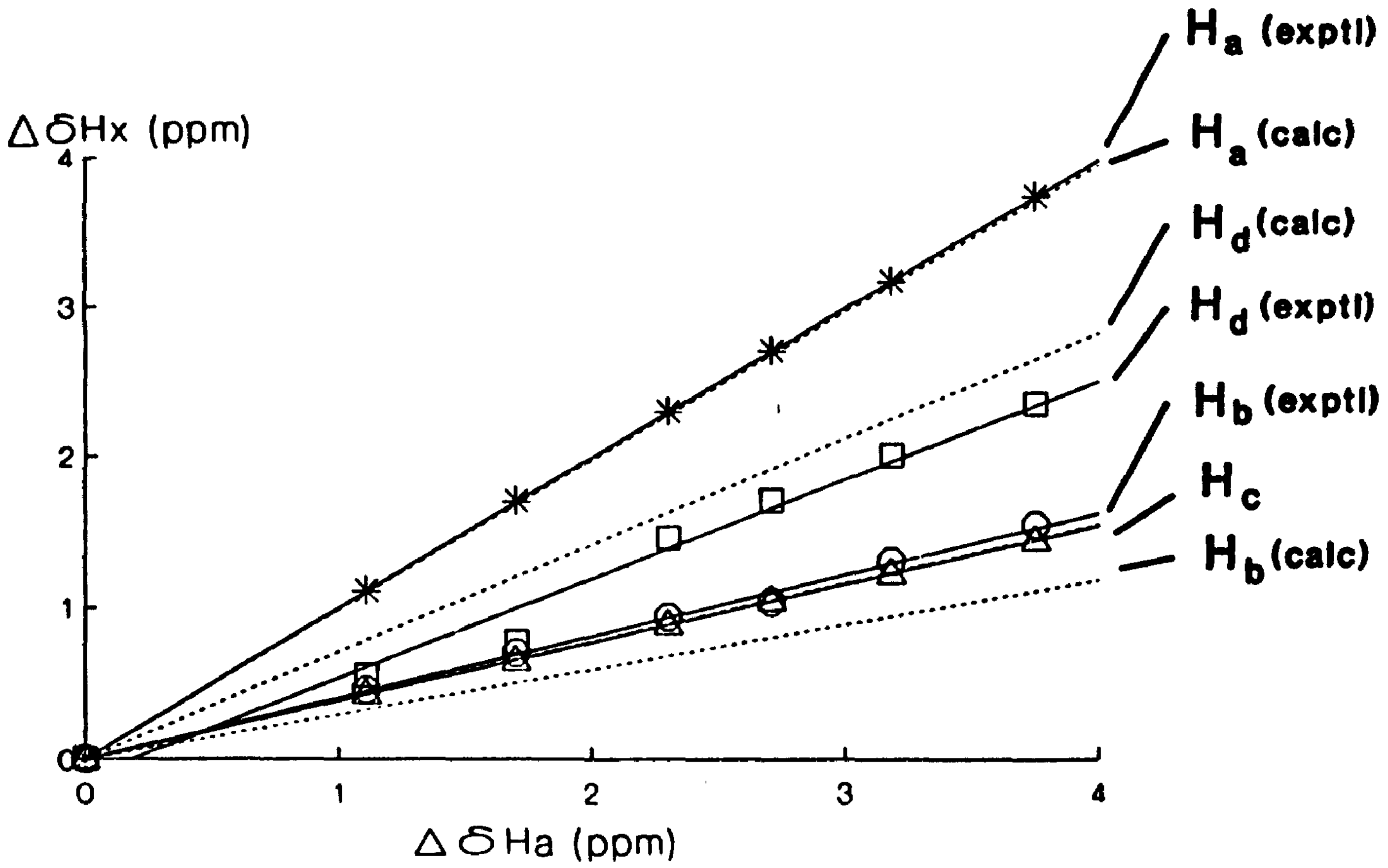
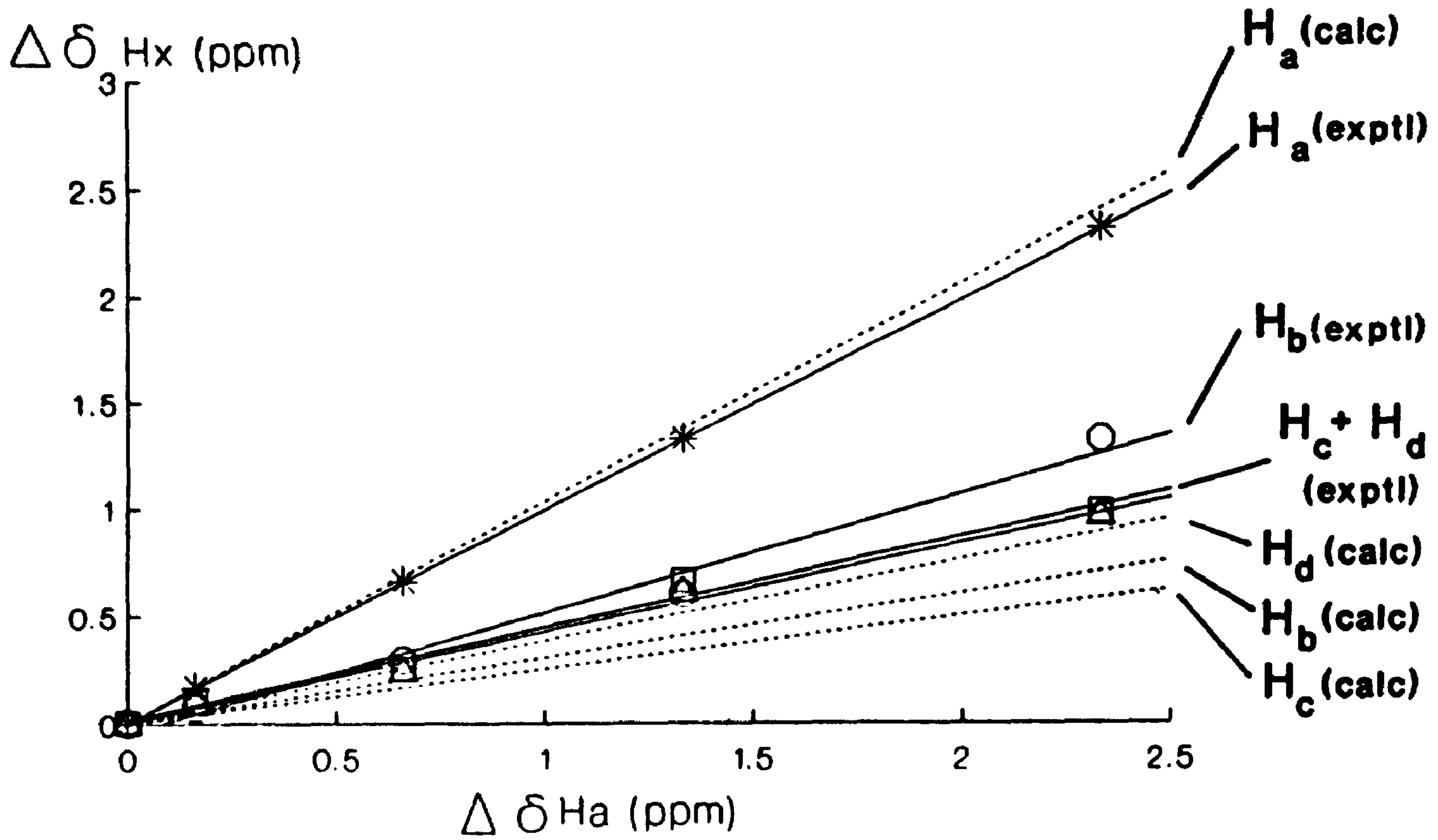


Figure 4: Calculated and observed changes in chemical shift ($\Delta\delta H_x$) of cyclobutane methine protons for <u>48</u> upon addition of $Eu(fod)_3$.



The change in chemical shift of a proton in a rigid molecule induced by a lanthanide shift reagent complexed to a remote Lewis base site in the same molecule is proportional to the magnitude of the pseudocontact interaction between the lanthanide and the proton. The change in chemical shift is given as ΔM whose magnitude is proportional to $1/r^3$, where r is the distance between the lanthanide and the shifted proton. The magnitude of ΔM is also related to the angle, θ, between the line connecting the lanthanide with the shifted proton and the axis of the bond between the lanthanide and the basic site in the molecule, as defined by:

$$\Delta M = (3\cos^2\theta - 1)/r^3$$

Using this relationship for the most stable conformations of 47 and 48, with the assumption that the $Eu(fod)_3$ complex is attached from the less hindered face of the molecule to a tetrahedral nitrogen atom, allows the expected relative changes in chemical shifts of the cyclobutane methine hydrogens to be calculated. These can then be compared with the experimental values. The results of such an experiment for compounds 47 and 48 are shown in Figures 3 and 4 where the experimentally determined Eu induced shifts are expressed relative to the shift observed for H_a, and the calculated values of $(3\cos^2\theta-1)/r^3$ for each cyclobutane methine hydrogen are normalised relative to the value for H_a. The gradients of the lines in Figures 3 and 4 are proportional to ΔM for each hydrogen and these are summarised in Table 2. The experiments in Figures 3 and 4 and Table 2 indicate that for both 47 and 48 the cyclobutane methine closest to the site of Eu complexation (i.e. H_a) is the most greatly shifted. In addition, in 47 H_d is more greatly shifted than H_b and H_c while in 48 H_b, H_c and H_d are shifted to approximately similar extents. The predicted relative shifts for these hydrogens obtained using the calculated most stable conformations follow the same pattern with H_a the most greatly shifted in both compounds H_d more greatly perturbed in 47 only.

For the Eu induced shift experiments it was found convenient to generate the amine adducts 47 and 48 by photochemical cycloaddition of cyclopentene to N-carboethoxyindole, 34, rather than N-benzoylindole, 5. The initially formed adducts 51 and 56 were obtained in a 10:1 ratio and were immediately hydrolysed to 47 and 48 by strong base. This gave the amine adducts in good yield and uncontaminated by their benzylated analogues 45 and 46 which were by-products formed in the removal of the photochemical activating group from the N-benzoylindole photoadducts. It was found necessary to use the free amine adducts 47 and 48 for the lanthanide induced shift study rather than analogues 41, 42, 45 and 46. It was determined that these compounds did not form sufficiently strong complexes to give measurable changes in chemical shift.

TABLE 2

CALCULATED AND OBSERVED RELATIVE LANTHANIDE INDUCED SHIFTS FOR CYCLOBUTANE METHINE HYDROGENS OF N-ACYLINDOLE-CYCLOALKENE PHOTOCHEMICAL ADDUCTS AND THEIR DERIVATIVES

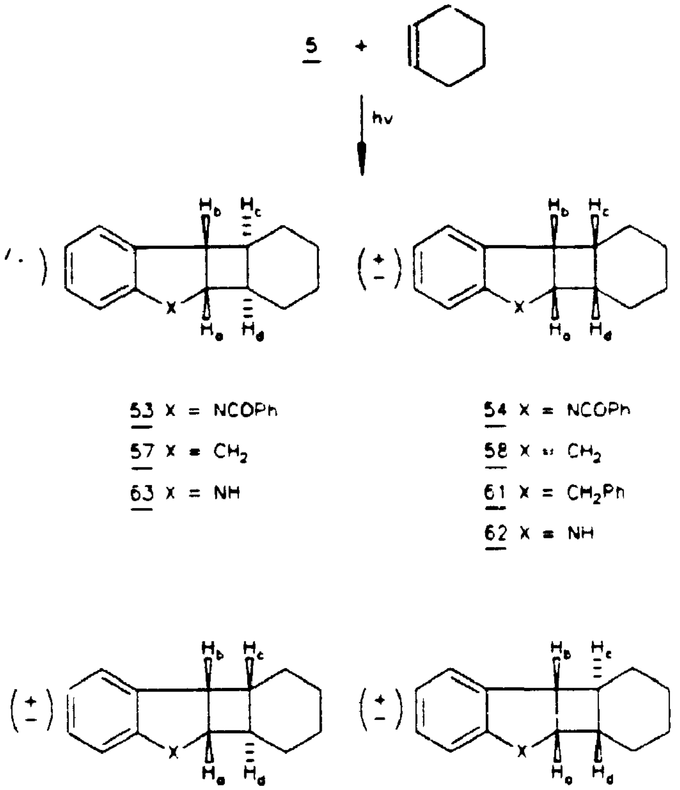
COMPOUND	H_a	H_b	H_c	H_d
47 (calculated)	1	.31	.39	.71
47 (found)	1	.40	.38	.65
48 (calculated)	1	.30	.25	.38
48 (found)	1	.63	.45	.45
63 (calculated)	1	.33	.44	.68
63 (found)	1	.42	.40	.90
62 (calculated)	1	.27	.24	.40
62 (found)	1	.38	.27	.40
65 (calculated)	1	.29	.22	.73
64 (calculated)	1	.40	.61	.34
64 (found)	1	.47	.96	.41

[a] The observed relative lanthanide induced shift data are obtained from the gradients of the lines in the plot of the change in chemical shift of each proton relative to the change in chemical shift of H_a. Examples are shown in figures 3 and 4. The method for derivation of the calculated numbers is described in the text.

2.2.2 Irradiation of N-Benzoylindole and N-Carboethoxyindole with Cyclohexene

The photochemical cycloaddition of cyclohexene to N-benzoylindole could, in principle, yield the four diastereoisomeric pairs of enantiomers represented by 53-56 (Scheme 10).

Scheme 10



53 X = NCOPh
57 X = CH$_2$
63 X = NH

54 X = NCOPh
58 X = CH$_2$
61 X = CH$_2$Ph
62 X = NH

55 X = NCOPh
59 X = CH$_2$
65 X = NH

56 X = NCOPh
60 X = CH$_2$
64 X = NH

In fact when N-benzoylindole was irradiated in the presence of cyclohexene only two products were detected. These compounds were not separable by chromatography but one of them was highly crystalline and could be separated in pure form by recrystallisation. The second product was isolated as an oil contaminated by small amounts of crystalline isomer. The mass spectra of these compounds indicated them to be 1:1 adducts between the indole derivative and cyclohexene and the ^{1}H-nmr and ^{13}C-nmr spectra were consistent with their being cyclobutane adducts analogous to those formed with cyclopentene. Most importantly, the four cyclobutane methine hydrogens were visible for each compound and their coupling constants could be measured. The coupling constants are shown in Table 1 for the crystalline product, 54, and its non-crystalline isomer, 53. The expected coupling constants for the cyclobutane methine hydrogens in the cyclohexene adducts were estimated from the dihedral angles in the most stable conformations of the indane analogues 57-60. These conformations were derived from molecular modelling calculations in the same way as for the cyclopentane analogues 49 and 50. The results are shown in Table 1; they suggest that the non-crystalline isomer is the *cis-anti-cis* stereoisomer 53 because of the small values of J_{ad} and J_{bc} which are predicted for 57 and which were seen in the cyclopentene adduct analogues 41, 45, and 47. However, for the crystalline isomer the estimated and observed coupling constants do not allow determination of stereochemistry. This is because all the coupling constants are predicted to be of similar magnitude in 58, 59, and 60 as those in the crystalline isomer.

As with the cyclopentene cycloadducts, the cyclobutane methine H_a was poorly resolved in the ^1H-nmr spectra of the two cyclohexene adducts and the coupling constants to H_b and H_d could not be seen directly but had to be inferred from the splitting seen in the signals assigned to H_b and H_d. As before, the broadening of the signal for H_a was associated with slow rotation of the N-benzoyl group in these compounds. Treatment of the crystalline adduct with lithium aluminum hydride yielded the N-benzyl derivative, 61, and the free amine, 62, in which the signal ascribed to H_a was resolved. The coupling constants of the cyclobutane methine hydrogens seen in the ^1H-nmr spectra of these two compounds are shown in Table 1 and are similar to those of the parent compound prior to reduction.

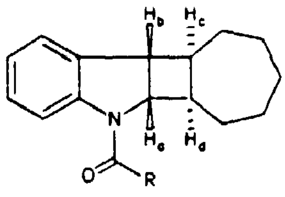
Irradiation of N-carboethoxyindole, 34, with cyclohexene also gave two major products but two minor products were also detected by g.c. Examination of these four compounds by g.c.-mass spectroscopy indicated them to be 1:1 adducts of the indole derivative with the cyclohexene and the ^1H-nmr spectrum of the mixture indicated the presence of the characteristic pattern of methine signals associated with the cyclobutane adducts. Gas chromatography indicated that the products were formed in the ratio 1.1:2:142:100. The product mixture was not separated but was instead hydrolysed to the free amines and separated by chromatography. One of the two major isomers present was identical with the product of reduction of 54 formed from N-benzoylindole (i.e. 65). The ^1H-nmr spectrum of the other major isomer suggested it to be structure 63. This was inferred from the values of the coupling constants between the cyclobutane methine hydrogens and these are listed in Table 1. The *cis-anti-cis* relationship of the hydrogens is indicated by the smaller values of J_{ad} and J_{bc}. This assignment was confirmed by lithium aluminum hydride reduction of 53 which gave the compound identified as 63 (a free amine isomer).

Of the two minor cyclohexene-N-carboethoxyindole cycloadduct isomers present in the original mixture, only one was separated following hydrolysis, the other being inseparable from the major isomers present. This compound was also non-crystalline and the coupling constants for the cyclobutane methine hydrogens are shown in Table 1. Comparison of these with the coupling constants predicted for 58-60 does not allow unambiguous assignment of any one of the possible structures 62, 64, or 65 to this compound.

In order to allow a stereochemical assignment of isomers 54, 56, 62, and 64, and to confirm the identification of the major non-crystalline isomer as 53 the lanthanide induced shift experiment already described for 47 and 48 was performed using the three isolated free amine isomers tentatively assigned to 62, 63, and 64. The relative shifts observed for the cyclobutane methine hydrogens of these three isomers are shown in Table 2 and are compared with those estimated for 62-65 using conformations calculated (MM2) to be the most stable. For the major non-crystalline isomer the shift reagent perturbs H_a and H_d most highly, and H_b and H_c are much less affected; this mirrors the behaviour of the *cis-anti-cis* cyclopentene cycloadduct 47 and confirms the assignment of structure 63 to this isomer based upon coupling constant data. Similarly, comparison of the calculated shifts for the methines of 62, 64, and 65 with those found for the major crystalline and the minor non-crystalline isomers strongly suggests that the former is 62 (H_b, H_c, and H_d all similarly shifted) and that the latter is 64 (H_c more shifted than H_b and H_d). It can also be inferred that neither isomer can be 65 since neither shows the predicted selective shift of H_d.

2.2.3 Irradiation of N-Benzoylindole with Cycloheptene

As with cyclohexene the photochemical cycloaddition of N-benzoylindole to cycloheptene could in principle lead to four pairs of enantiomers related as diastereomers. When the irradiation was performed under the same conditions as for cyclopentene and cyclohexene only two products were detected by g.c. These were formed in a 20:1 ratio and were shown to be 1:1 adducts between 5 and cycloheptene by g.c.-m.s.. The two adducts were separated by chromatography; their 1H-nmr spectra exhibited the characteristic signals associated with the cyclobutane methine protons and confirmed them to be the expected cyclobutane adducts. The minor isomer is assigned as structure 66 which possesses *cis-anti-cis* stereochemistry; this assignment is based upon the observation of coupling constants of 2.5 and 3.0 Hz for J_{ad} and J_{bc}, respectively, which by analogy with the other *cis-anti-cis* stereoisomers in this work is indicative of a *trans* relationship between protons H_a and H_d, and H_b and H_c.



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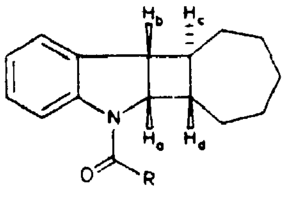

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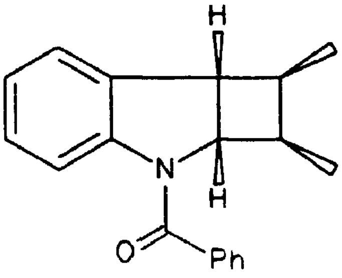
Unlike the other *cis-anti-cis* N-benzoyl substituted adducts 41 and 53, the H_a be measured without removal of the N-benzoyl activating group. This was not the case with the major isomer from the cycloheptene reaction; however the coupling constants for the H_b methine could be discerned and were 9 and 3 Hz. The former of these can be unambiguously assigned to the expected larger *cis* coupling between H_a and H_b so that the latter must correspond to J_{bc}. The small value of 3 Hz is strongly suggestive of a *trans* relationship between H_b and H_c and since the *cis-anti-cis* stereochemistry in 66 has already been assigned to the minor isomer, the major isomer must therefore have the structure 67 which possesses a *trans* cycloheptane-cyclobutane ring fusion.

2.3 IRRADIATION OF N-BENZOYLINDOLE AND N-CARBOETHOXYINDOLE WITH *CIS* AND *TRANS*-2-BUTENE AND 4-OCTENE

Irradiation of N-benzoylindole with *trans*-2-butene gave all four possible diastereomeric 1:1 adducts 68-71 in a ratio 7:21:68:4 as determined by g.c. and g.c.-m.s.. The adducts were separated as a mixture from the other components of the reaction; in the 1H-nmr spectrum of the separated mixture the cyclobutane methines of the two major isomers could be discerned, as could high field doublets corresponding to the methyl substituents on the newly formed cyclobutane rings. The adducts were not further separated. Irradiation of N-benzoylindole with the *cis* isomer of 2-butene gave the same four adducts in almost the same ratio (2:21:74:2); the identity of the products of the two reactions were confirmed by g.c. co-injection and by comparison of the ^{1}H-nmr spectra which were superimposable.

Similar results were obtained with *cis* and *trans*-4-octene. In these cases only three of the four possible diastereoisomeric adducts were present in detectable quantities; these were formed in the ratio 2:49:49 from the *trans* isomer and 10:47:43 from the *cis* isomer.



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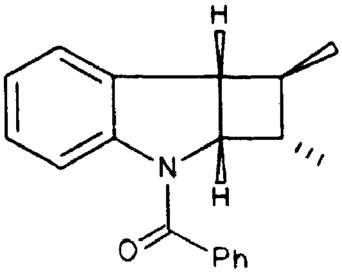

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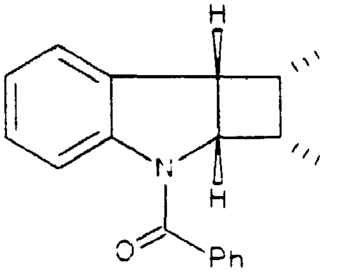

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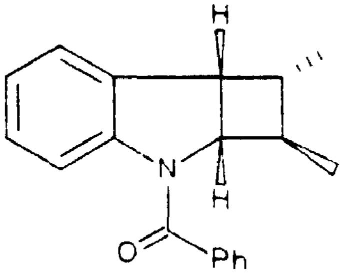

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As with the butene adducts, the cyclobutane methines of the two major octene adducts were clearly visible in the ^{1}H-nmr spectrum of the product mixture.

In the reaction with the octenes the reaction mixture was also examined for the presence of isomerised alkene. No *cis*-4-octene was formed in the irradiation of 5 with *trans*-4-octene. However, in the irradiation of 5 with *cis*-4-octene it was found that the *trans* isomer was formed as the irradiation proceeded. In these experiments the concentration of *cis* alkene was kept very high relative to that of

5 so that the *trans* isomer formed would never build up to a high enough concentration to enable it to react with the excited state of 5; thus the formation of a similar product distribution from both alkenes cannot be attributed to faster reaction of 5 with the *trans* isomer formed during the irradiation.

The formation of *trans*-4-octene during the irradiation of 5 with *cis*-4-octene was quantified at low conversions by measurement of the amount of *trans*-octene produced relative to the amount of light absorbed. The result is shown in Figure 5 and the gradient of this plot yields a value for the quantum yield of formation of the *trans* isomer of 0.074 ± 0.004.

For reasons which will be discussed below the quantum yields of formation of the adducts from both the *cis* and *trans* octenes were also measured as a function of alkene concentration; the results are given in Table 3.

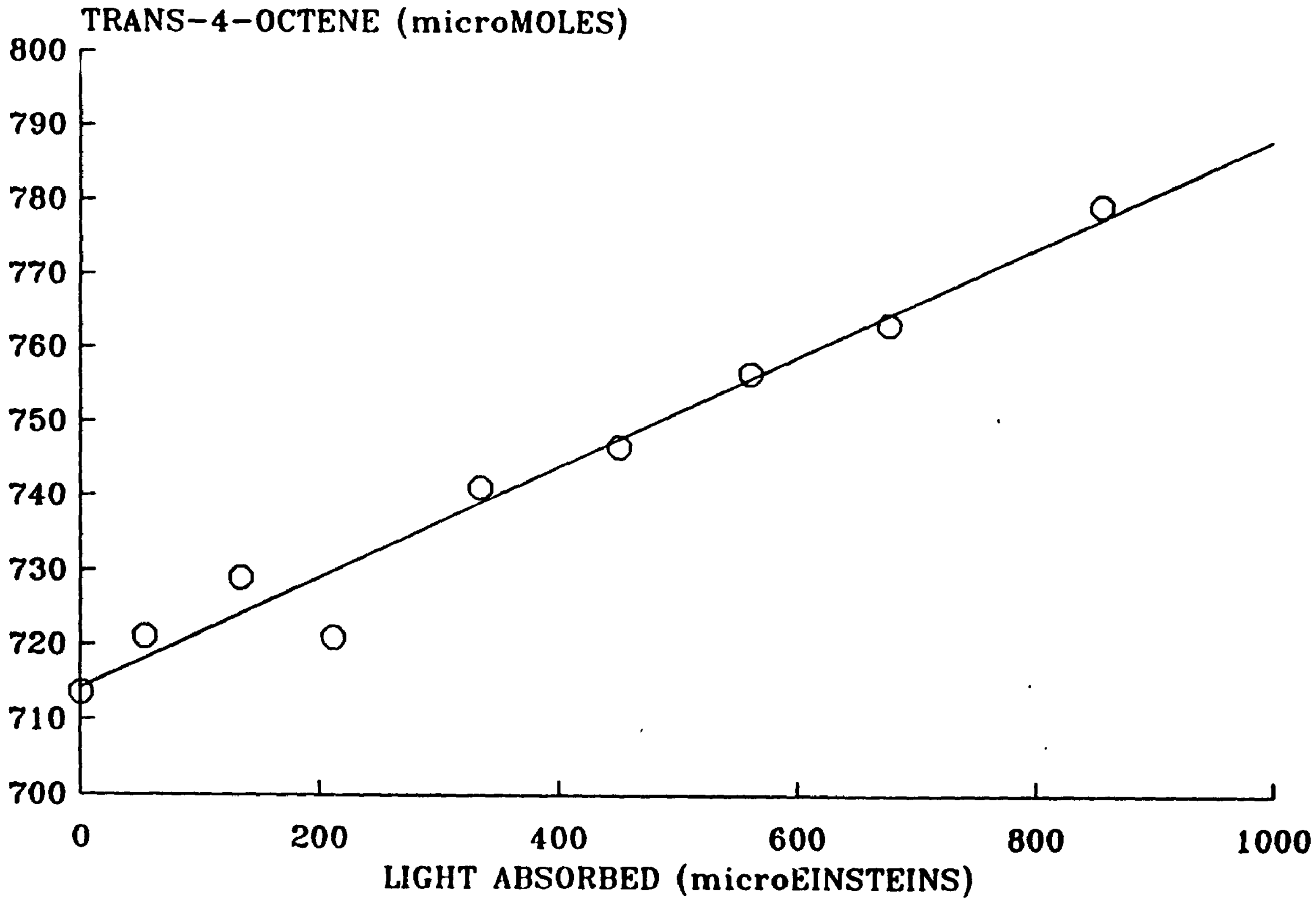
TABLE 3

QUANTUM YIELDS OF PHOTOCHEMICAL CYCLOADDITION OF N-BENZOYLINDOLE, 5, WITH *CIS* AND *TRANS*-4-OCTENE[a]

[*trans*-octene]	[*cis*-octene]	ϕ
2.035 M		0.013
2.379		0.017
2.608		0.018
2.990		0.020
4.060		0.027
5.048		0.033
	4.401 M	0.0039
	2.797	0.0043
	3.210	0.0046
	3.874	0.0048
	4.350	0.0049
	4.931	0.0052

[a] 5 excitation wavelength: 313 nm. Solvent : benzene

Figure 5: Moles of *trans-4*-octene formed on irradiation of 5 (0.018M) with *cis*-4-octene (5.31 M).



2.4 DISCUSSION OF RESULTS

For the reasons outlined in section 2.1, if biradicals are intermediates in the photochemical cycloaddition reactions of N-carbonyl substituted indoles with alkenes and if their lifetimes are long compared with the time required for conformational relaxation then it would be expected that *trans* fused adducts would be obtained from *cis* alkenes and *cis* fused adducts could be obtained from *trans* alkenes. The conclusion of this work is that this is indeed the case. Thus with cyclohexene three of the four possible diastereoisomeric adducts are formed; these are assigned the structures 54, 54 and 56 and of these 56 does not preserve the stereochemistry of the alkene. Similarly with cycloheptene the major product is assigned the structure 67 which has the same stereochemistry as 56, the *trans* fused product formed with cyclohexene, and does not preserve the stereochemistry of the alkene. With the non-cyclic alkenes 2-butene and 4-octene, where both the *cis* and *trans* geometrical isomers of the alkene are available, almost the same distribution of products is obtained from each geometrical isomer. This is consistent with the intermediacy of the biradicals shown in Scheme 8 in which all memory of the alkene stereochemistry can be lost. It should be noted that each of the regioisomeric biradicals shown in Scheme 8 have two new chiral centres; it is not necessarily the case that each geometrical isomer of the alkene would produce the same proportions of the regioisomeric and diastereoisomeric biradicals and it is, in fact, quite surprising that the final distribution of the stereoisomeric cyclobutane adducts is so similar from each alkene geometrical isomer.

In earlier work on the mechanism of photochemical cycloaddition between N-benzoylindole and cyclopentene (25) the quantum yield of adduct formation as a function of alkene concentration was examined and it was shown that the quantum yield varied with alkene concentration as predicted by the relationship shown in Equation 5. This equation was derived assuming the validity of the mechanism shown in Scheme 6.

$$\text{(equation 5)} \qquad \phi^{-1} = \frac{1}{\phi_{isc}} \left[\frac{k_c}{k_r + k_c} \right]^{-1} \left[1 + \frac{k_d}{k_a[A]} \right]$$

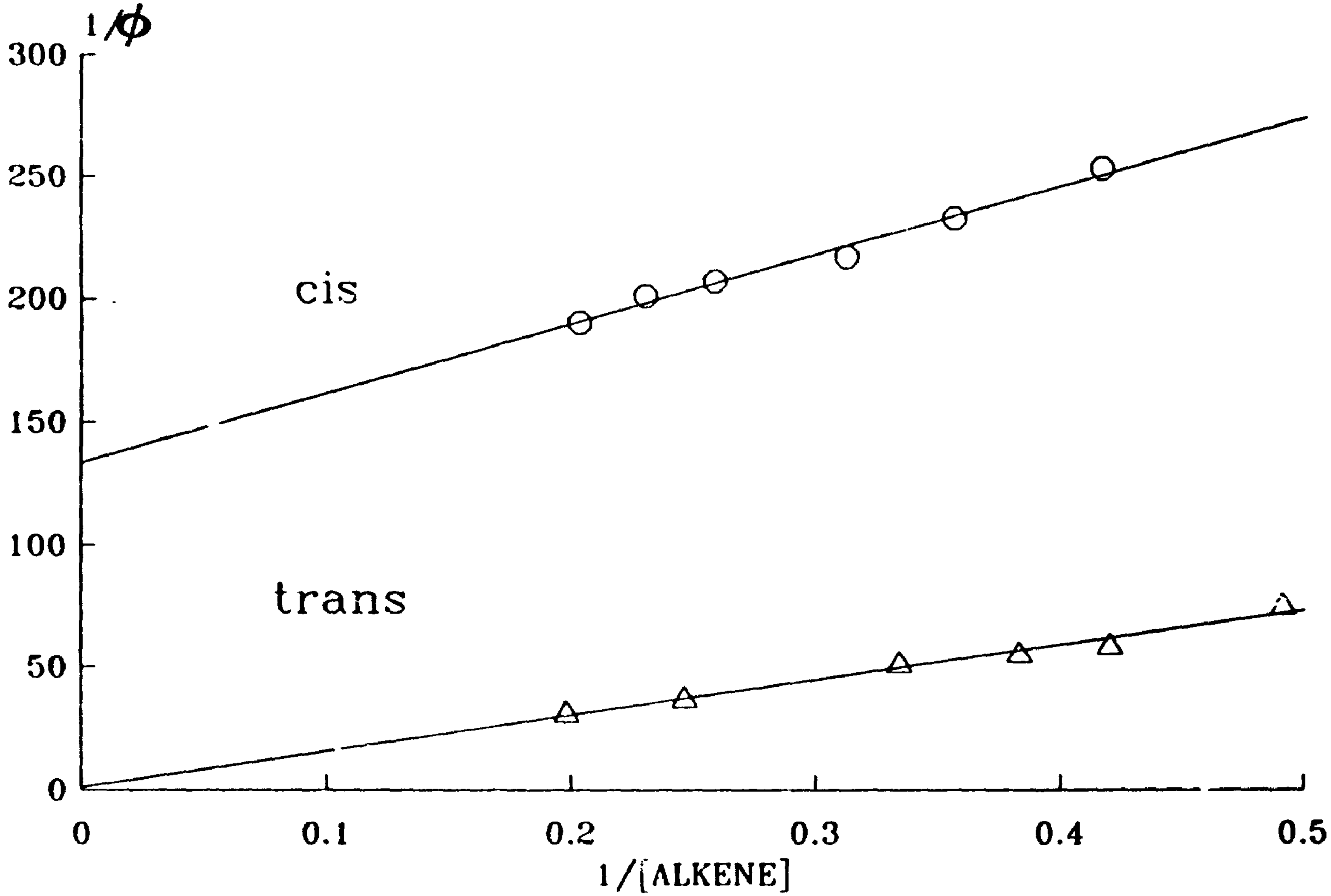
In Equation 5, ϕ is the quantum yield of cycloadduct formation, ϕ_{isc} is the quantum yield of intersystem crossing, k_d is the rate constant for decay of the triplet excited state of 5, [A] is alkene concentration and k_a is the rate constant for reaction of the triplet excited state with alkene. The rate constants k_c and k_r are those for cyclization of the intermediate biradical to product and reversion to starting materials, respectively. Thus the fraction $k_c/(k_c+k_r)$ is the fraction of the biradicals which proceed to the cycloadducts rather than reverting to the ground state starting materials. This treatment is an approximation since it assumes a single biradical intermediate is involved; since stereoisomeric biradicals may well be intermediates, the fraction $k_c/(k_c+k_r)$ and k_a are composites for all the intermediate biradicals. The plot of $1/\phi$ versus 1/[A] can be used to yield values of $k_c/(k_c+k_r)$ and k_a if ϕ_{isc} and k_d are known. For N-benzoylindole, 5, the values of ϕ_{isc} and k_d have been independently determined as 0.39 ± 0.01 and (3.6 ± 0.4) X 10^7 s^{-1}, respectively, using the triplet counting procedure; using these values the quantities $k_c/(k_c+k_r)$ and k_a have been estimated as 0.16 and (4.0 ± 0.8) X 10^6 $M^{-1}s^{-1}$, respectively, for the reaction of 5 with cyclopentene (25). This treatment was applied to the photo-addition of both *cis*- and *trans*-4-octene to 5 and the data shown in Table 3 plotted according to Equation 5 are shown in Figure 6.

For the addition of *cis*-octene to 5 the intercept in Figure 6 yields a value of k_c/k_c+k_r of 0.019 ± 0.001, indicating that only 2% of the intermediate biradicals proceed to cyclobutane adducts and the remainder revert to ground state 5 and alkene. In addition, the intercept indicates that at very high alkene concentration (i.e. when all of the triplet excited states of 5 are intercepted by alkene) the maximum value of ϕ is 0.0075 ± 0.0002. Assuming a value of 3.6 X 10^7 s^{-1} for k_d, combining the intercept of the plot for *cis*-octene with the gradient yields a value of k_a, the rate constant for reaction of the triplet excited state of 5 with *cis*-octene, of (1.7 ± 0.3) X 10^7 $M^{-1}s^{-1}$, which is slightly faster than that observed for the reaction of 5 with cyclopentene.

Formation of *trans*-4-octene when irradiating 5 with *cis*-4-octene is an example of Schenk isomerisation, i.e. a photochemical isomerisation in which the isomerising species itself never attains the excited state. The isomerisation of *cis*-octene to the *trans*-isomer cannot be a result of energy transfer from the triplet excited state of 5 to the alkene since the triplet energy of the latter is higher than that of the indole derivative (25). The quantum yield of Schenk isomerisation for *cis*-octene was determined to be 0.074 ± 0.004; the concentration of the alkene in this experiment was 5.31 M. At this concentration more than 70% of the triplet excited states of **5** are intercepted by the alkene (assuming $k_a = 1.7 \times 10^7$ and $k_d = 3.6 \times 10^7$); since $\phi_{isc} = 0.39$, the maximum quantum yield of Schenk isomerisation possible would be 0.27 if the 98% of the biradicals which do not cyclize to products revert to give only *cis*-octene. The value of 0.074 measured here would appear to indicate that the reverting biradicals prefer to give back *cis*-octene rather than the *trans* isomer. This assumes that no other energy wasting step leading back to starting materials occurs between interception of the triplet excited state by alkene and the formation of the biradical intermediates; such an energy wasting step would be exciplex formation and decay.

For the addition of *trans*-octene to **5** the plot in Figure 6 yields an intercept of 0.9 ± 3. This is indistinguishable from zero and its reciprocal cannot be used to obtain a reliable value of ϕ extrapolated to infinite alkene concentration. However it does allow limits for this value of ϕ to be estimated; the smallest value possible, corresponding to the largest value of the intercept, is 0.26, while the largest is 0.39, the value determined for ϕ_{isc}. This means that between 67% and 100% of the intermediate biradicals formed from the triplet excited state of **5** and *trans*-octene proceed to the product. Using these extreme values of the intercept, the gradient of the plot in Figure 6 can be used to estimate limits on the values possible for k_a, the rate constant for reaction between triplet excited **5** and *trans*-octene. The values are 1×10^6 and 6×10^5 $M^{-1}s^{-1}$, which are substantially slower than those determined for the photoaddition of **5** to cyclopentene and *cis*-octene.

Figure 6: Plot of reciprocal quantum yield of cycloadduct formation against reciprocal of alkene concentration for the 2+2 photocycloaddition reaction of 5 and *cis*- or *trans*-4-octene (5.31 M).



In summary, it can first be said that some products formed from the photochemical addition of cyclic alkenes to N-benzoylindole and N-carboethoxyindole do possess *trans* stereochemistry at the cyclobutane cycloalkane ring fusion. This *trans* stereochemistry must directly result from the closure of a 1,4-biradical intermediate in which the adding cyclic olefin possesses some flexibility which allows for the formation of *trans*-fused cycloadducts from cyclic *cis* starting olefins. If there is to be any mixing of stereochemistry in this case it must be consistent with the intermediacy of a triplet 1,4-biradical intermediate. Secondly we have shown in two cases that the photocycloaddition of N-benzoylindole to different stereoisomeric alkenes (*cis* an *trans*) leads to very similar reaction product mixtures. This could only be the case if the two reactions proceed *via* a common intermediate. The fact that we obtain a mixture of all four stereoisomers from both alkenes as above supports the assertion that the intermediate is a 1,4-biradical. Lastly the evidence of Schenk isomerisation in which *cis*-4-octene is converted to *trans*-4-octene again supports the assertion that the reaction proceeds via a 1,4-biradical intermediate in which most of these biradicals revert back to starting N-benzoylindole and isomerised alkene.

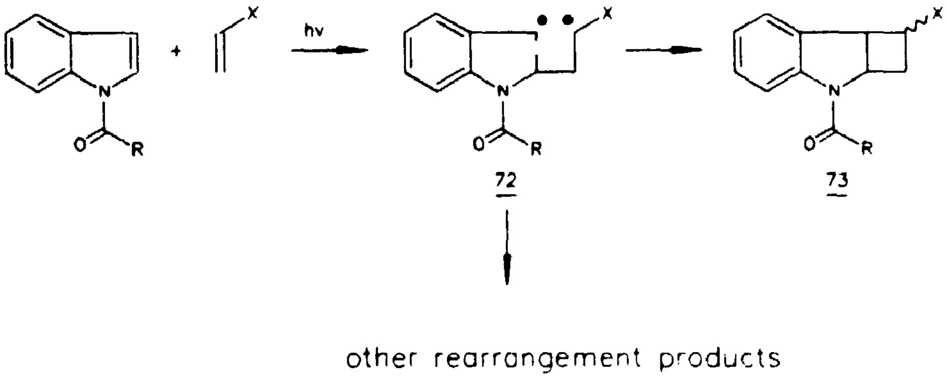
CHAPTER 3

REARRANGEMENTS AND TRAPPING OF 1,4-BIRADICALS FROM PHOTOCYCLOADDITION OF N-BENZOYLINDOLE WITH OLEFINS

3.1 REARRANGEMENT PRECURSORS

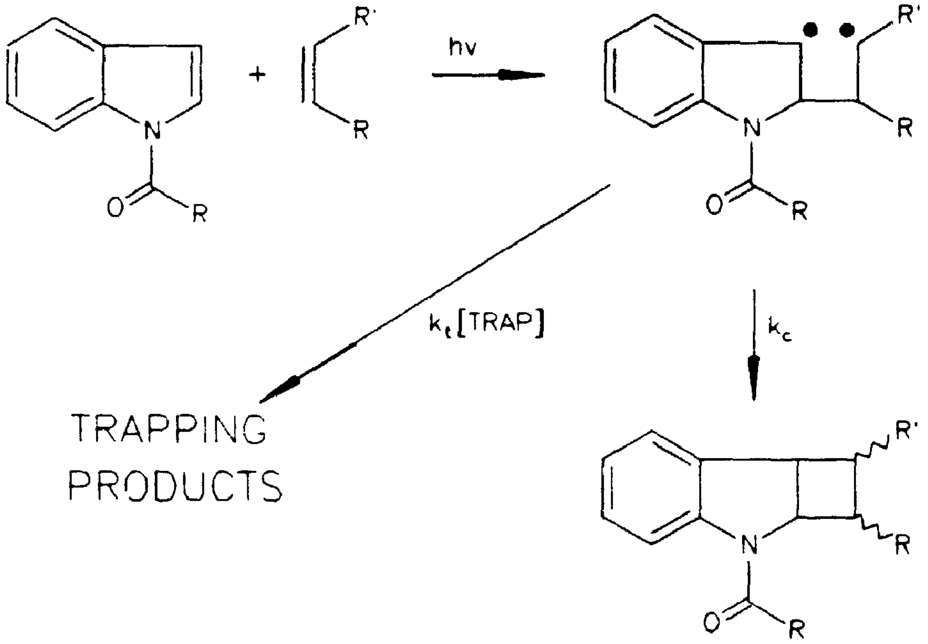
The work described in Chapter 2 of this thesis confirmed the earlier proposal (25) of Disanayaka and Weedon that biradicals are intermediates in the photochemical cycloaddition reaction of N-acylindoles with alkenes. In order to better probe the structures of these biradical intermediates attempts were made to divert them from their normal paths of decay, namely cleavage to starting materials or closure by cyclobutane ring formation. In principle this could be accomplished by modification of the alkene precursor in such a way that the biradical intermediate could rearrange to alternative products (Scheme 11).

Scheme 11



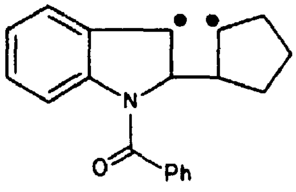
Alternatively a reagent could be added to trap the biradical intermediates (Scheme 12). Elucidation of the reaction products could then yield structural information such as the site of initial bonding between the alkene and the indole. In addition, if the rate of the competing rearrangement reaction indicated in Scheme 11 is known, then the lifetime of the intermediate biradicals can be estimated.

Scheme 12



Reactive radicals decay by several processes which include hydrogen abstraction, addition, disproportionation and coupling. The goal of the work described in this thesis was to exploit one or more of these processes in order to gain information about the 1,4-biradicals implicated in indole-alkene photocycloaddition. Others (40) have utilised these radical reactions to probe the 1,4-biradicals generated in other photochemical reactions. These will be discussed later.

As noted in chapter 2 (Scheme 7) for the reaction of N-benzoylindole with cyclopentene the intermediate biradicals could, in principle, have structures 43 or 44; these correspond to initial bonding of the alkene to the 2-position or the 3-position of the indole derivative, respectively.



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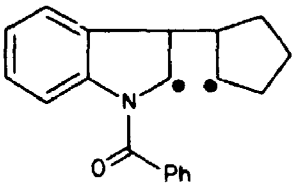

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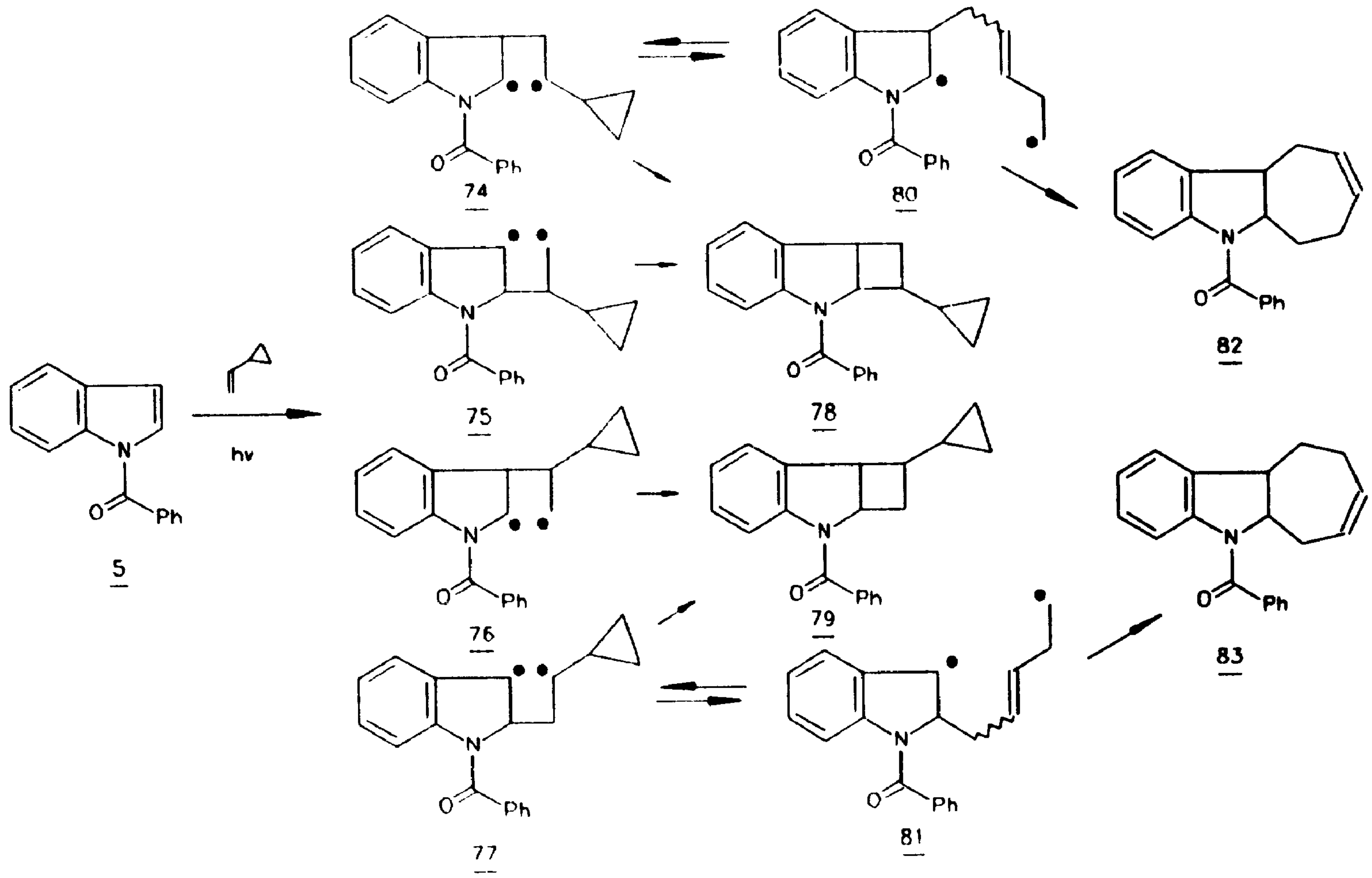
If this reaction were to be performed using alkenes that yield biradicals which can undergo a rearrangement, in competition with ring closure or bond homolysis, to form alternative products, then the rearrangement reaction could be used as a probe of both the structure of the biradical and, if the rate of the rearrangement reaction is known, as a clock to measure its lifetime. Alkenes which fulfil this requirement are tetramethylethylene, 1,6-heptadiene, and vinylcyclopropane.

Scheme 13 shows the anticipated outcome of the reaction between N-benzoylindole and vinylcyclopropane. Interaction of the triplet excited N-benzoylindole with the alkene can, in principle, lead to biradicals 74-77, although 74 and 77 would be expected to dominate over 75 and 76 since the latter pair possess primary radical centres. Biradicals 74 and 75 can cyclize to stereoisomers of 78 while 76 and 77 can close to stereoisomers of 79. The intermediates 74 and 77 contain a cyclopropylalkyl radical which is known (41-44) to ring open rapidly to a homoallylic radical; this would yielding intermediates 80 and 81 respectively.

Scheme 13

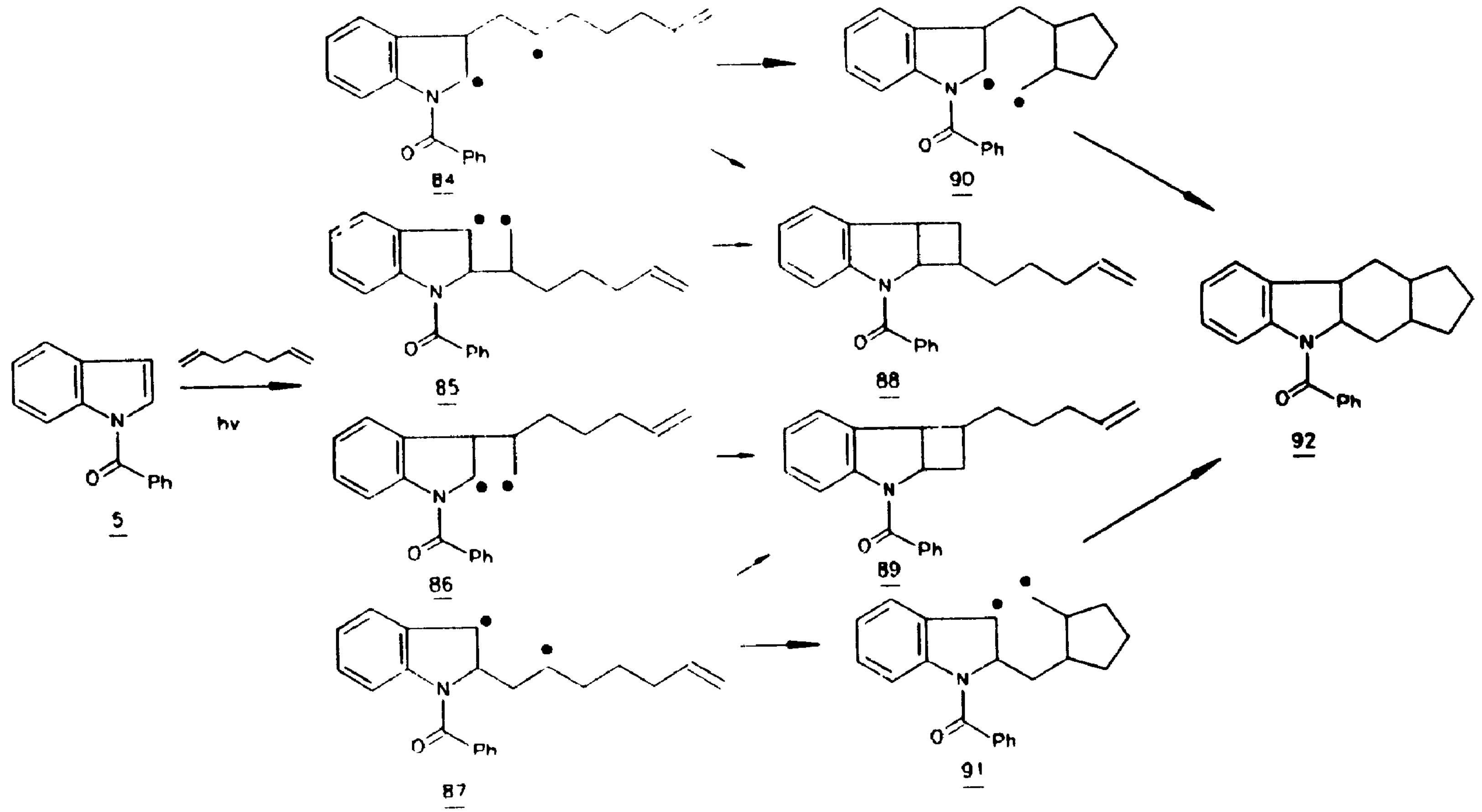


If the double bond geometry is correct in 80 and 81 then they can close to give 82 and 83, respectively. The ring opening is, in principle, reversible but the homoallylic radical is heavily favoured thermodynamically. Since the rate of the rearrangement of the cyclopropylalkyl radical to a homoallylic radical is known (41-44), the quantities of 82 and 83 formed relative to the amounts of 78 and 79 can be used to estimate the lifetimes of 74 and 77. In addition, since 82 only produces 74, and 83 only yields 77, the identity of the products formed yields information about the structures of the intermediate biradicals and the position of the first bond made between the indole and the alkene.

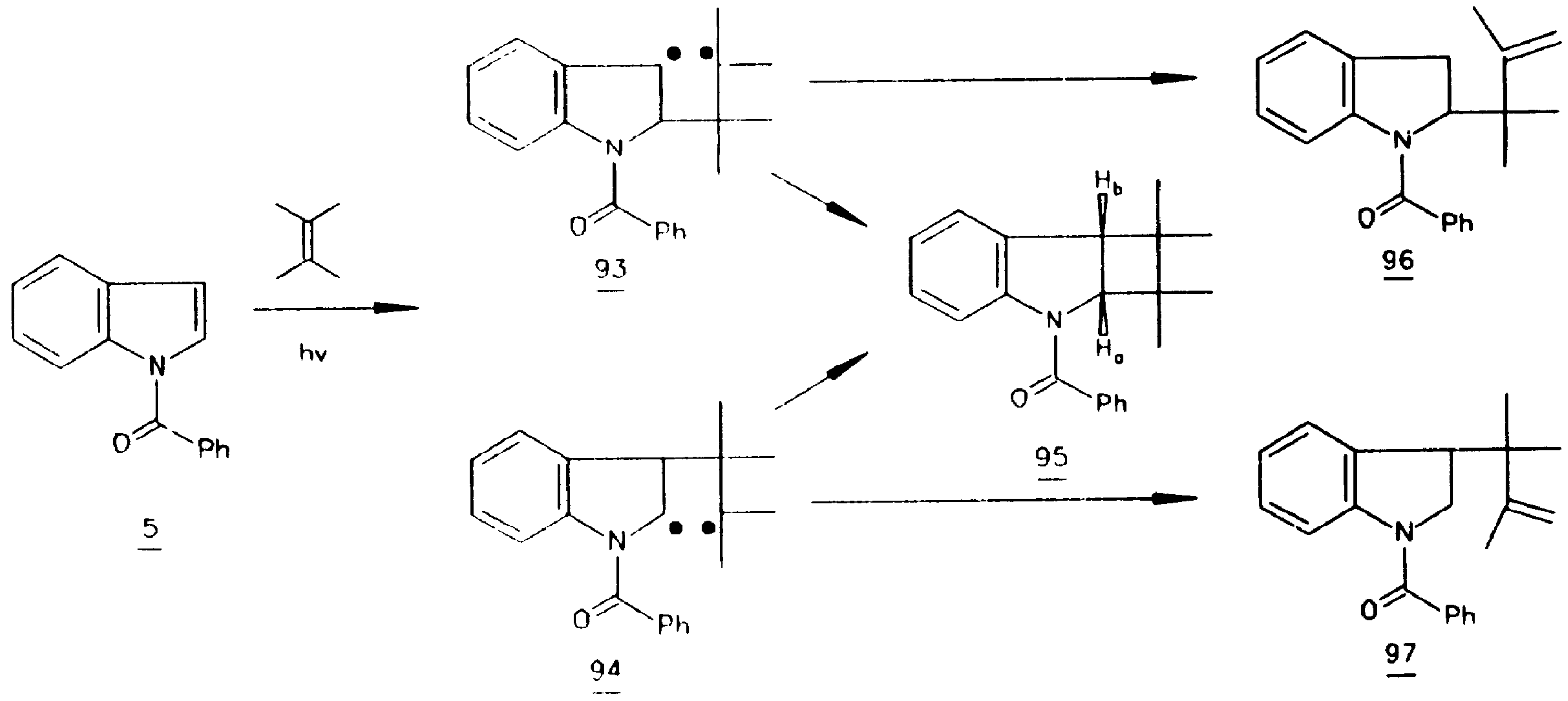
In Scheme 14 the expected outcome of the reaction between N-benzoylindole and 1,6-heptadiene is shown. The expected biradicals are 84-87, although 84 and 87 should dominate since 85 and 86 contain primary radical centres. Cyclization of 84 and 85 gives 88 while cyclization of 86 and 87 gives 89. However, 84 and 87 contain derivatives of 1-hexenyl radicals which can cyclize to cyclopentylmethyl radicals. If this occurs then species 90 and 91 are formed which can proceed to give various stereoisomers of 92. The rate of cyclization of 1-hexenyl radicals to cyclopentylmethyl radicals is known (45) and so the proportions of 88 and 89 relative to 92 formed can be used to define the lifetime of the biradicals 84 and 87.

In Scheme 15, the expected outcome of the reaction between N-benzoylindole and tetramethylethylene is shown. Here only the two biradicals 93 and 94 are possible, and both may cyclize to give 95. This should lead to a single photocycloadduct.

Scheme 14



Scheme 15



However, by analogy with the products obtained in the photochemical 2+2 cycloaddition reaction between 2-cyclohexenones and methyl-substituted (Scheme 16) alkenes (46), it is possible for disproportionation of the 1,4-biradicals to occur so that "ene" products 96 and 97 can be produced. The structures of 96 and 97, if formed, can be used to infer the site of initial bonding between the indole and the alkene. This is further discussed in chapter 3.3 (Scheme 16).

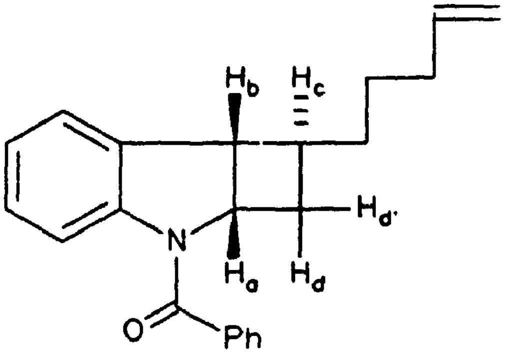
3.2 PHOTOCYCLOADDITION REACTIONS OF N-BENZOYLINDOLE

3.2.1 Irradiation of N-Benzoylindole with Tetramethylethylene

Ultraviolet light irradiation of a benzene solution of N-benzoylindole and tetramethylethylene, under conditions such that 5 absorbed all of the light, gave a single major product which was identified as the 2+2 cycloadduct 95 on the basis of its mass spectrum and ^{1}H-nmr spectrum. In the latter the four methyl groups were seen as the expected high field singlets and the two cyclobutane methine protons were observed at 4.60 and 3.56 ppm, which is characteristic for alkene adducts of N-benzoylindole. The signal at 4.60 ppm was broadened and its splitting pattern unresolved, and is assigned to H_a in 95. As noted in chapter 2, for the adducts this broadening is associated with slow rotation of the N-benzoyl group and has been seen in other N-benzoylindole adducts and characterised by variable temperature nmr spectroscopy (47,48). The signal at 3.56 ppm was a doublet coupled to H_a and is therefore assigned to H_b. The coupling constant of 8 Hz is typical of the *cis* fused indole-cyclobutane ring system. Inspection of the reaction mixture by ^{1}H-nmr spectroscopy or coupled gas chromatography mass spectroscopy (g.c.-m.s.) revealed no evidence for the presence of products with the structures 96 or 97.

3.2.2 Irradiation of N-Benzoylindole with 1,6-Heptadiene

Ultraviolet light irradiation of a benzene solution of N-benzoylindole and 1,6-heptadiene under conditions such that only 5 absorbed light gave one major and three very minor products in a ratio of 0.3:99.4:0.2:0.1 as indicated by g.c. Analysis by g.c.-m.s. indicated that all four products were 1:1 adducts of 5 and the diene. The four compounds were not separable by preparative liquid chromatography; however, the minor components were present in such small amount that they were not discernable in the ^{1}H-nmr spectrum of the chromatographed mixture and so did not interfere with the assignment of structure 89a to the major isomer by ^{1}H-nmr spectroscopy. This structure is based upon the observation of the expected aromatic signals as well as signals corresponding to the pentenyl side chain and cyclobutane protons. The regiochemistry and stereochemistry was determined by analysis of the coupling pattern of the cyclobutane protons. Decoupling of the H_a resonance, which appeared at 4.60 ppm and showed characteristic broadening by the adjacent N-benzoyl group, caused a 2 proton multiplet at 2.52 ppm to collapse to an AB quartet. The multiplet at 2.52 ppm is therefore assigned to H_d and $H_{d'}$, which establishes the regiochemistry of the photoadduct. Proton H_b was seen at 3.58 ppm as a double doublet coupled to H_a (J=8 Hz) and H_c (J=2 Hz). Small vicinal coupling constants between protons on cyclobutane rings in indole-alkene adducts have been found indicative of a *trans* relationship so that the value of J_{bc} found suggests the stereochemistry shown in 89a, corresponding to exo addition of the alkene to 5.

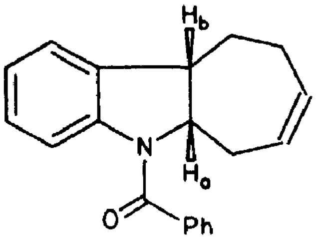


89a

The coupling constants between H_{cd} and $H_{cd'}$ upon irradiation of H_a were quite small (approximately 1 Hz) and thus were not well resolved. Hydrogenation of the mixture of cycloadducts resulted in reduction of three of them to give new products in the ratio 0.3:99.5:0.2 which were shown by g.c.-m.s. to have increased in mass by two units. The third minor product (0.1% of the mixture) was unchanged. Based upon this evidence, two of the minor photoaddition products possess a single double bond and so may be diastereoisomers of 89a or 90. The failure of the third minor component to undergo hydrogenation indicates it to be saturated; consequently it is possible that it may be a stereoisomer of the expected rearrangement product 92.

3.2.3 Irradiation of N-Benzoylindole with Vinylcyclopropane

Ultra-violet light irradiation of a benzene solution of N-benzoylindole and vinylcyclopropane gave a mixture of three 1:1 adducts in the ratio 5:31:64, as determined by g.c., g.c.-m.s. and ^{1}H-nmr spectroscopy. The adducts comprising 64% and 31% of the mixture were separated in pure form by preparative liquid chromatography and were assigned structures 83 and 79a, respectively.



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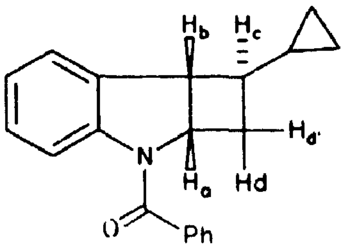


79a

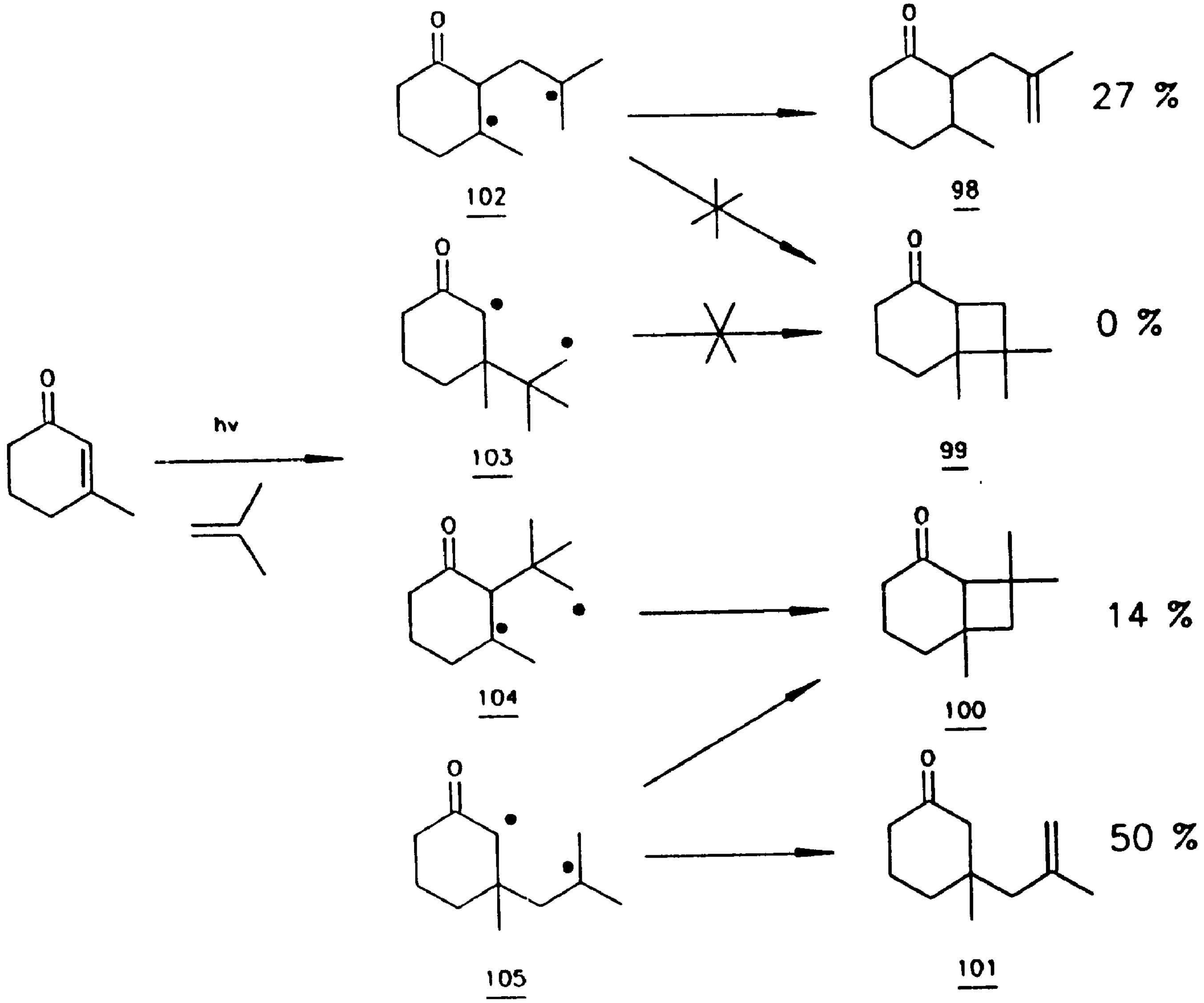
The structure of 83 was assigned on the basis of the appearance of its ^{1}H-nmr spectrum. In the spectrum H_a appears at 4.9 ppm and H_b at 3.7 ppm. As in other adducts of 5 and alkenes the signal assigned to H_a exhibited broadening attributed to slow rotation of the N-benzoyl substituent. Irradiation of H_a resulted in partial decoupling of a methylene multiplet at 2.40 ppm which in turn was also decoupled by irradiation of the two olefinic protons which appeared superimposed on one another at 5.6 ppm. Irradiation of H_b resulted in decoupling of a methylene multiplet at 2.0 ppm; however, the latter was not affected by irradiation of the olefinic protons. This pattern allows unambiguous assignment of structure 83 and rules out the alternative, 82. The value of J_{ab} was 8 Hz which suggests *cis* ring fusion stereochemistry in 83. The structure of 79a was also deduced from the ^{1}H-nmr spectrum. The mono-substituted cyclopropyl group gave rise to a characteristic pattern of signals consisting of a methine multiplet at 0.86 ppm, and methylene multiplets at 0.52 and 0.14 ppm. For the cyclobutane protons a broad signal at 4.60 ppm assigned to H_a was coupled to signals at 3.70 (assigned to H_b) and 2.50 and 2.20 ppm (H_d and $H_{d'}$), while H_b was weakly coupled to a signal at 1.95 ppm (H_c). This pattern is consistent with the regiochemistry in 79a but not for its regioisomer 78 (scheme 13). The *trans* relationship of H_b and H_c shown in 79a is assigned on the basis of the small value of J_{bc} and corresponds to *exo* addition of the alkene to the indole. A *cis* arrangement of H_b and H_c would lead to a coupling constant of the order of 8 Hz as observed for J_{ab}.

The minor component of the mixture (i.e. that comprising 5% of the adducts) was not isolated in sufficiently pure form to allow characterization. However, the presence of cyclopropyl protons in the ^{1}H-nmr spectrum of the impure material suggest that it is either the stereoisomer of 79a or one of the stereoisomers of the regioisomer 78.

3.3 DISCUSSION OF RESULTS

The isolation of 95 as the exclusive product in the irradiation of N-benzoylindole with tetramethylethylene implies that disproportionation of the putative biradicals 93 and 94 to give products 96 and 97 is slower than their alternative fates which are closure to 95 or reversion to 5 and the alkene. Since 96 and 97 are not products, irradiation of 5 with tetramethylethylene yields no information about the point of initial bonding between the alkene and the indole. With vinylcyclopropane the major product, 83, accounts for 64% of the adducts and must have its origins in the biradicals 81 and 77 (scheme 13); thus it can be concluded that for this product the first bond formed between the indole and the alkene is to the 2-position of the indole. In addition, the second most prevalent product, 79a, accounting for 31% of the adducts, must have its origins in either biradical 76 or biradical 77. The addition of radicals to mono-substituted alkenes results in bonding to the less hindered alkene terminus and the formation of a secondary radical at a much faster rate than bonding to the more substituted alkene terminus and formation of primary radicals (49); thus if radicals are accepted as satisfactory models for the triplet excited state of the N-benzoylindole, then it can be argued that the biradical 77 should be formed preferentially over biradical 76 and therefore that the addition of vinylcyclopropane to 5 to give 79a also proceeds by initial bonding between the alkene and the 2-position of the indole. The argument that the regiochemistry of addition of radicals to alkenes is a good model for the expected orientation of addition of triplet excited states to alkenes is supported by the outcome of the addition of 2-methylpropene to triplet excited 2-cyclohexenones (50) as outlined previously by Rudolph and Weedon (51). In addition to cyclobutanes, reactions of this type yield substantial quantities of products derived from the intramolecular disproportionation of the intermediate biradicals. For example, the photochemical reaction between 3-methylcyclohexenone and 2-methylpropene (50a-c) (Scheme 16) gives 98-101 in the yields shown. These must be formed from the biradicals 102-105, with 98 derived exclusively from 102, and 101 exclusively from 105. Of the isolated products, at most 14% (i.e. 100) can have their origin in a biradical resulting from addition of the enone triplet excited state to the more substituted end of the alkene (i.e. 104).

Scheme 16



The rate constant for rearrangement of secondary cyclopropylalkyl radicals to the corresponding open chain homoallylic radical has been estimated (44) to be 2 X 10^7 s^{-1}. Using this value for the rearrangement of biradical 77 to biradical 81 and assuming that formation of 79a is proceeding exclusively from biradical 77 and hence competitively with rearrangement, the sum of the rate constants for closure of 77 to 79a and reversion of 77 to 5 plus alkene can be estimated to be of the order of 1 X 10^7 s^{-1}. This translates into a biradical lifetime of 100 ns for 77.

The product of addition of 1,6-heptadiene to 5, compound 89a, can be formed from closure of either of biradicals 86 or 87; using the same arguments as above, formation of 89a *via* 87 is likely to be the favoured pathway. Thus the isolation of 89a as the almost exclusive product of addition suggests that with this alkene also, the position of initial bonding of the alkene is to the 2-position of the indole. In addition, the fact that 89a accounts for more that 99% of the adducts formed from 5 and 1,6-heptadiene, and the fact that compounds with structure 92 form at most 0.1% of the adduct mixture, indicate that closure of biradical 87 to 89a is 100 to 1000 times faster than rearrangement of 87 to 91. The rate constant for the latter rearrangement can be estimated from the rate constant measured (45) for closure of hexenyl radical to cyclopentylmethyl radical, which is 1 X 10^5 s^{-1}. This leads to a rate constant for closure of 87 of 10^7-10^8 s^{-1} which is similar to that estimated above using vinylcyclopropane as the radical clock precursor.

The value of 100 ns estimated for the lifetime of the 1,4-biradical produced in the cycloaddition of N-benzoylindole to vinylcyclopropane is similar to the lifetimes reported for other 1,4-biradicals such as those generated *via* the Norrish Type II reaction (40,52), the 2+2 photocycloaddition reaction between cyclic enones and olefins (51), and the Paternò-Büchi reaction (52,53). The general similarity reflects the fact that the lifetimes of these biradicals at room temperature largely depend on the rate of intersystem crossing from the triplet biradical to the singlet biradical, and not so much on the structural effects in the biradical (54). For synthetic purposes it is attractive to consider the possibility of trapping the 1,4-biradical intermediates in these indole cycloaddition reactions. The biradical lifetimes estimated here suggest that for this to be successful, species capable of reacting with radical centres with rate constants of the order of 10^8 $M^{-1}s^{-1}$ would be required.

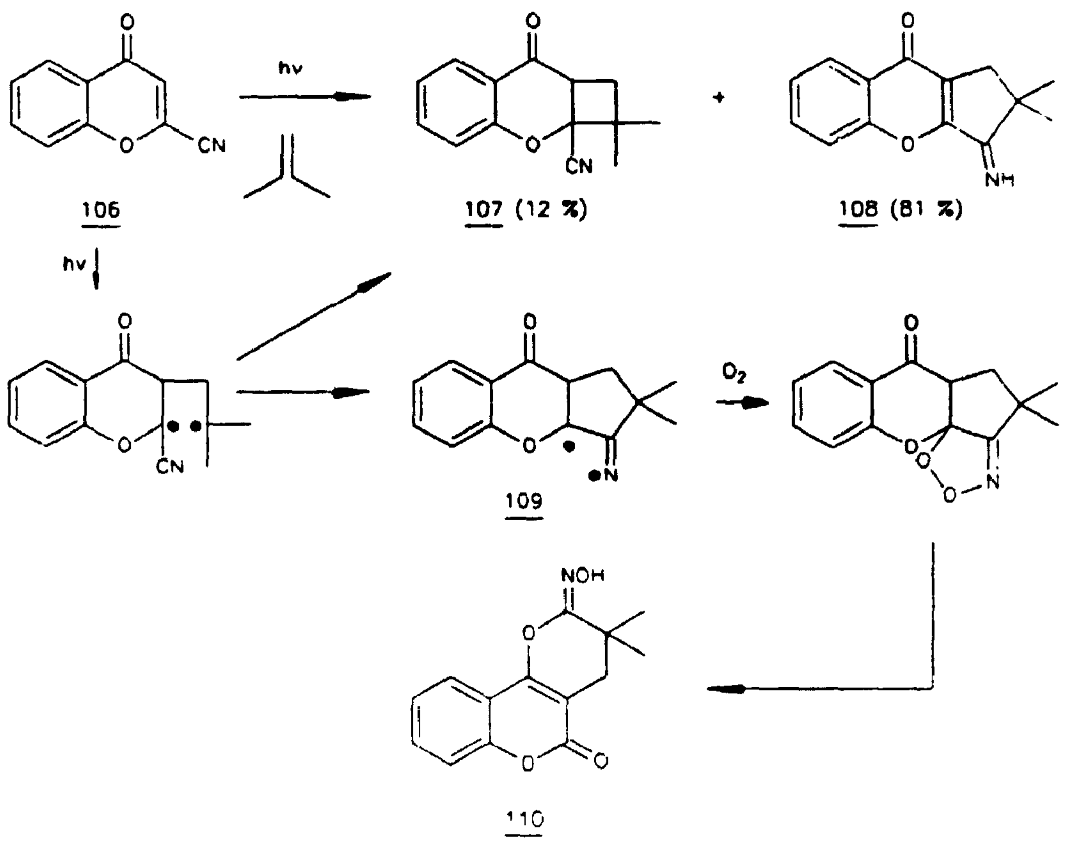
The conclusion that adduct formation between triplet excited 5 and alkenes occurs *via* initial bonding between one terminus of the alkene and the 2-position of 5 can be used to rationalise the generally observed regiochemistry of addition of mono-substituted alkenes to 5. As noted in the Introduction, the addition is normally regioselective and does not depend upon the nature of the alkene substituent. This is in contrast to the situation found for photochemical cycloaddition of alkenes to cyclic enones, where the regiochemistry is apparently governed by the polarity of the group attached to the alkene (46). With the indole system the regiochemistry can be understood and predicted if it is assumed that initial bonding occurs between the 2-position of the indole and the terminus of the alkene less able to stabilise a radical centre. One way of examining this is to intercept all the biradical intermediates formed and deduce the point of initial bond formation from the products produced.

3.4 TRAPPING OF 1,4-BIRADICAL INTERMEDIATES

3.4.1 Previous Trapping Studies

At the time of writing there are no known examples of trapping 1,4-biradicals formed from the 2+2 photocycloaddition of N-acylindoles with olefins. Nor are there any examples of detection of these intermediates by spectroscopic methods. However, many reactions have been reported in which 1,4-biradicals are generated photochemically and then trapped to yield other products. These reactions include Paternò-Büchi reactions (55), Norrish Type I and Type II reactions (55), and 2+2 photocycloaddition reactions of some enones (56).

Adam has reviewed the use of triplet oxygen in trapping biradicals (56a,b) and Saito has reported several interesting examples of the use of oxygen to divert cyanoenones from their normal pathway of photocycloaddition reaction with 2-methylpropene (56c). Cyanoenone 106 affords both 2+2 and 2+3 phototadducts, 107 and 108 with olefins. In the presence of O_2 the 2+3 adduct, 108, is totally suppressed and product 110 is formed in its place. However, the formation of the 2+2 photoadduct is unaffected by oxygen. It is proposed that the 1,4-biradical, 109 is intercepted to form the peroxide which in turn rearranges to yield 110. This would seem to indicate that the 1,4-biradical is too short lived to be trapped and that atomic oxygen-catalyzed spin inversion leading to the singlet biradical and subsequent closure occurs to the exclusion of trapping. Saito's work provides an excellent example of the rational use of oxygen trapping as a probe in the study of competing photochemical processes.

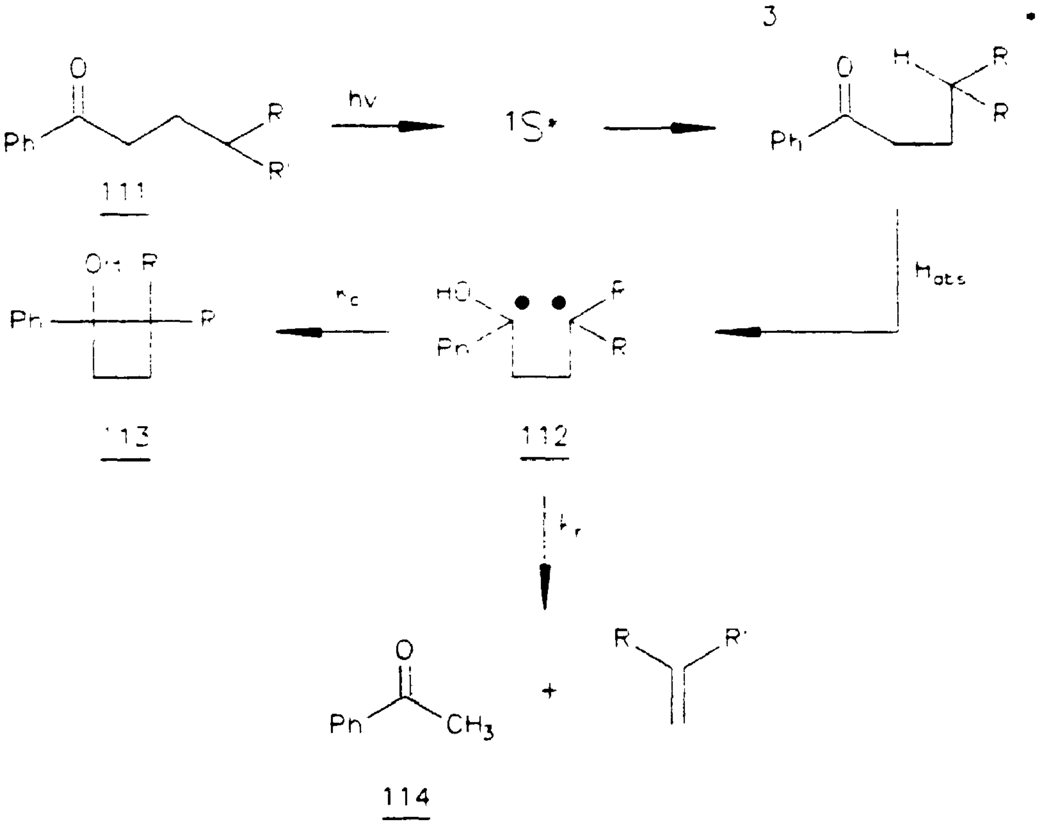


Caldwell and Creed (57) examined the possibility of trapping of biradicals formed during the photocycloaddition of dimethyl fumarate with phenanthrene using oxygen as the trap. No trapped products were observed; instead they discovered only a slight increase in cyclobutanes, which they attribute to O_2-catalyzed intersystem crossing of the biradical.

Although there are many examples (58) of intramolecular trapping of 1,4-biradicals formed from 2+2 photocycloadditions (by use of intramolecular biradical rearrangements as discussed above), there appear to be no known examples in which 1,4-biradicals generated by this reaction have been trapped intermolecularly. There do exist, however, many examples of intermolecular trapping of 1,4-biradicals generated from the Norrish Type II reaction (55).

In these reactions (scheme 17) a ketone such as 111, is photochemically excited ($n \rightarrow \pi^*$) to yield its singlet excited state. This excited state undergoes intersystem crossing to give the triplet excited state of the ketone which can abstract a hydrogen from the γ-carbon. The result is a triplet biradical such as 112. The 1,4-biradical can then follow the typical paths of ring closure to give 113 or fragmentation to yield acetophenone, 114, and alkene.

Scheme 17

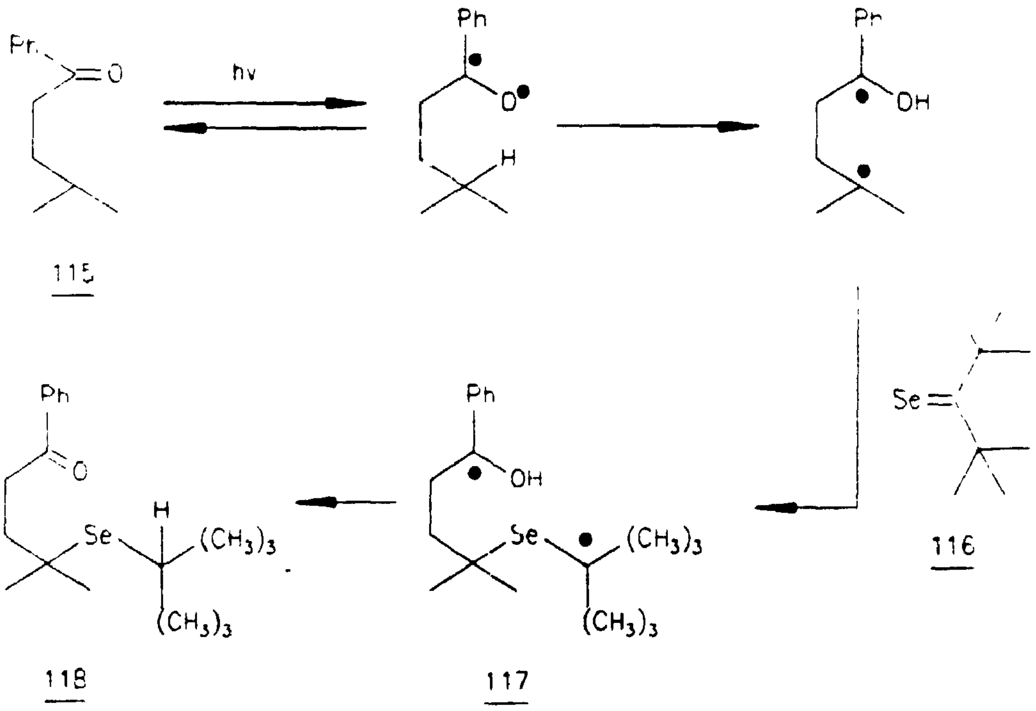


3.4.2 Trapping of Norrish Type II Biradicals

It has been reported (59) that Norrish Type II 1,4-biradicals can be intercepted by olefins although in very poor yields. The result is usually polymer formation which renders this method not very useful.

Scaiano and coworkers (60) have shown di-tert-butyl selenoketone, 116, to be an effective trapping agent for Type II biradicals. Reactions of this kind can proceed with quantum yields up to 0.21 and with rate constants as high as 7 X 10^8 $M^{-1}s^{-1}$.

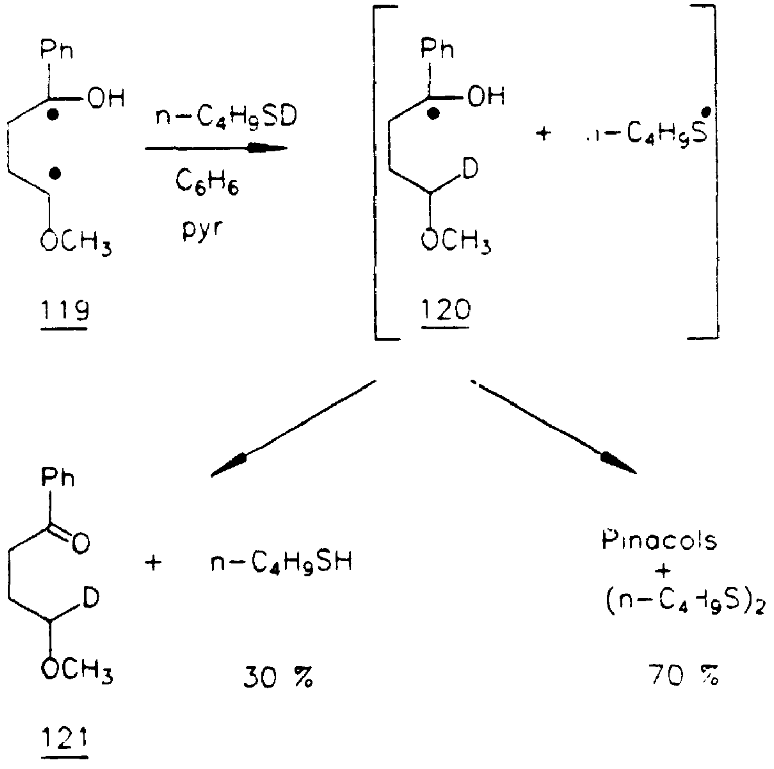
Scheme 18



In this case (scheme 18) the initial trapping step occurs at the biradical alkyl terminus and the trapping is terminated by an intramolecular hydrogen transfer to yield the selenide 118 as opposed to the product of cyclization of the biradical. The proposed trapping scheme was deduced by the identification of the trapping product 118, derived from γ-methylvalerophenone, 115. The shortcoming of this trapping agent is that the selenoketone, 116, is also a diffusion controlled triplet quencher. Fortunately the selenoketone is not consumed in the quenching process but its quenching ability reduces the efficiency of the trapping reaction.

Another method of 1,4-biradical trapping has been demonstrated by Wagner and coworkers (61,62) in which Type II biradicals are intercepted through reaction of alkyl thiols at the biradical alkyl terminus (scheme 19).

Scheme 19

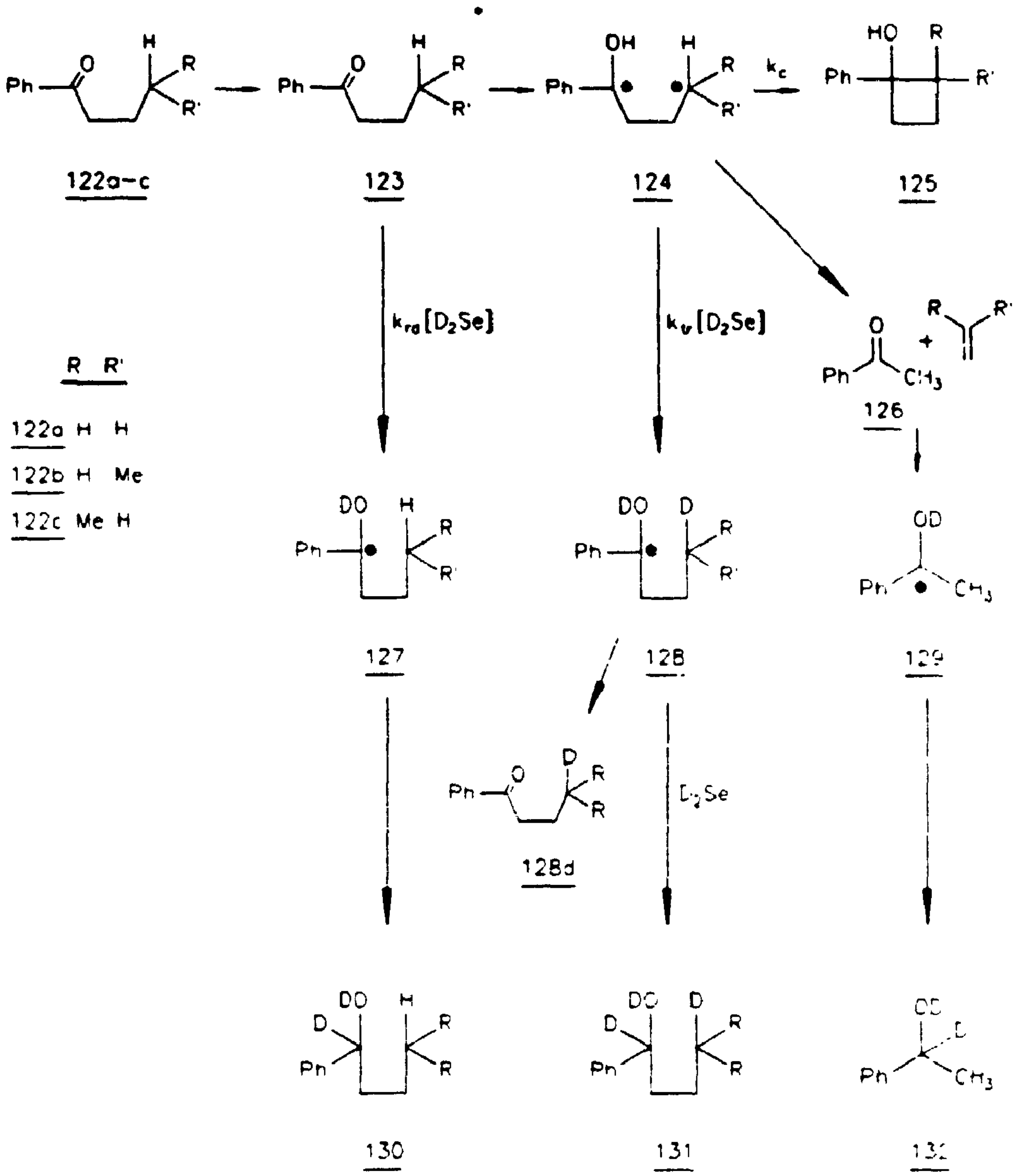


In order to show that the thiol was intercepting the biradical and not the triplet excited state of the carbonyl deuterium incorporation studies were carried out. The use of deuterated thiols gave the ketyl radical, 120, which can undergo either disproportionation with the thiyl radical in the solvent cage to regenerate the starting ketone deuterated in the γ position, or, upon leaving the solvent cage, dimerize to a mixture of pinacols. The trapping rate constant has been estimated by using the known rate constant for the reaction of mono-radicals with tin hydrides (*ca.* 10^6 $M^{-1}s^{-1}$) as a clock. This leads to a biradical lifetimes of approximately 10^{-6} s. More recently, the trapping reaction has been reexamined by direct observation of the ketyl radical by flash photolysis (63) and the rate constant for abstraction from n-$C_8H_{17}SH$ was determined to be 1 X 10^7 $M^{-1}s^{-1}$.

Hydrogen bromide has also been observed to quench Norrish Type II 1,4-biradicals in the gas phase (64). Although the trapping products were never identified they are also presumed to be derived from hydrogen abstraction by the γ-radical terminus. Inspection of the examples in the literature indicate that the most effective and clean trapping reagents are those which readily donate hydrogen atoms to the biradical intermediate. Thus reagents which possess weak bonds to hydrogen and yet do not react with the starting material(s) would be preferable.

In 1987 Kambe and coworkers (65) reported the use of hydrogen selenide and deuterium selenide to quench the 1,4-biradical intermediates formed from Norrish Type II reaction in the photolysis of butyrophenone derivatives, 122. (scheme 20).

Scheme 20



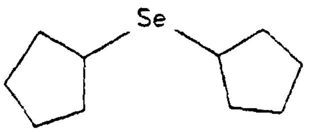
It is well known that photolysis of butyrophenones, 122, in methanol yields Type II products 125 and 126 *via* 1,4-biradical intermediate 124 with a total quantum yield of 1.0 (66). When 122a-c was irradiated in the presence of D_2Se, the formation of Type II products was greatly suppressed and alcohol 131 was obtained as the major product in which deuterium was incorporated. Scheme 20 describes all the possible paths which are taken by the intermediates. It has been shown (67,68) that the triplet excited state 123 can be reduced in the presence of H_2Se or D_2Se to yield intermediates such as 127 which affords alcohols 130. However the major process involves formation of the 1,4-biradical and subsequent hydrogen transfer to yield radical intermediate 128 rather than homolytic cleavage or ring closure to yield 126 and 125. The intermediate 128 has two fates; disproportionation to yield 128d or hydrogen abstraction to yield the fully trapped biradical product 131.

Perhaps one of the major advantages that this method of trapping has over the other methods described is the ease of product identification. It is also superior in that the trapping agent is easily removed and that the byproduct of the trapping process is selenium metal. Based on the known values of 1,4-biradical lifetimes, it was estimated that the rate constant for trapping of 124 by H_2Se was approximately $2 \times 10^8\ M^{-1}s^{-1}$. This value is quite large in comparison with the reported rate constants of carbon radicals with thiols (61-63,69,70) and tin hydrides (61-63,71). Using the biradical lifetimes of between 10^{-7} and 10^{-8} seconds estimated earlier in this chapter for 1,4-biradicals formed from N-benzoylindole-alkene photocycloaddition, it would appear that H_2Se could be employed to trap these short lived intermediates.

3.4.3 Irradiation of N-Benzoylindole in the presence of Cyclopentene and Hydrogen Selenide

A method similar to that reported by Kambe and Sonoda (65) was applied to the photochemical cycloaddition reaction of N-benzoylindole with cyclopentene. The concentration of H_2Se prior to irradiation was measured by ^{1}H-nmr and found to be approximately 0.5 M. Irradiation of a benzene solution of N-benzoylindole with cyclopentene led to the formation of the expected stereoisomers 41 and 42 which were described previously in this chapter. When an identical solution containing H_2Se was irradiated in parallel with the solution containing no H_2Se, g.c. indicated the formation of four new products in a ratio of 0.9:1:1:0.25. The last two peaks possessed g.c. retention times similar to that of the 2+2 cycloadducts 41 and 42. G.c. analysis of unirradiated solutions of 5 and cyclopentene treated with H_2Se showed no change in the starting materials and no formation of products. G.c. co-injection of the reaction mixture with authentic samples of 2+2 cycloadducts, 41 and 42 indicated that none of the new products were cycloadducts. Thus cycloadduct formation had been completely quenched and the four new products result from diversion of the normal reaction pathway by the H_2Se. Relative rates of reaction were determined by g.c. analysis. In the absence of added H_2Se the reaction showed 11% conversion of the starting N-benzoylindole to products after 45 minutes irradiation, whereas the solution containing H_2Se gave only 0.45% conversion of the indole derivative to products. Column chromatography allowed separation of the starting material from the products; subsequent separation of the products by preparative t.l.c. gave 4 pure characterizable fractions. The structures assigned to these products are 133-136 and are shown also in scheme 21 (chapter 3.5).

The product with the shortest g.c. retention time was identified as 133 by mass spectrometry and ^{1}H-nmr spectroscopy. Evident in the mass spectrum was a characteristic isotopic distribution in the parent ion, m/e 218, arising from the presence of a single selenium atom. The mass of the molecular ion is therefore indicative of a product containing two cyclopentyl rings and a selenium atom. Fragments of m/e 69 were also observed and are consistent with the presence of cyclopentyl groups. In the ^{1}H-nmr spectrum a methine quintet shifted downfield to 3.24 ppm confirmed the assignment of compound 133.



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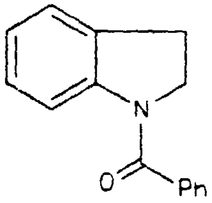

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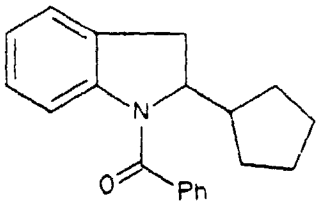

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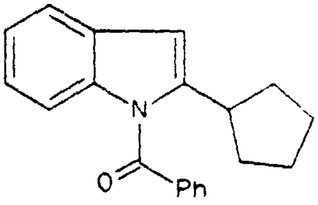

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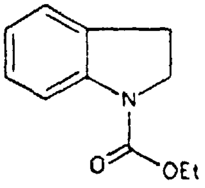
The second most volatile peak in the g.c. was identified as N-benzoylindoline, 134. Thus the parent ion in the mass spectrum had increased by 2 mass units from that seen for N-benzoylindole and the fragmentation pattern generated from the parent ion indicated homolytic cleavage of the benzoyl group to yield an indolinyl ion. The ^{1}H-nmr spectrum confirmed the assignment of structure 134 by exhibiting two coupled methylene signals at 4.05 and 3.10 ppm.

The third peak in the g.c. was assigned to the trapped biradical product 135. Mass spectrometry gave the expected parent ion with m/e 291 and the fragmentation pattern yielded mass ions of 222 and 105 indicative of N-benzoylindolinyl and benzoyl ions respectively, derived from cyclopentyl or benzyl scission in 135. The ^{1}H-nmr of the product exhibited a broad triplet at 4.76 ppm which was assigned to the methine proton next to the indoline nitrogen. This was coupled to three other single proton signals at 3.28, 2.75, and 2.20 ppm. Decoupling experiments determined that the protons at 3.28 and 2.75 ppm were coupled with a large vicinal coupling constant of 16 Hz. These signals were therefore attributed to the methylene protons on the indoline moiety and the remaining signal at 2.20 ppm was assigned to the cyclopentyl methine. Decoupling of the aliphatic region perturbed only the methine signal at 2.20 ppm which sharpened to a doublet. All the above information allowed for unambiguous assignment of structure 135.

The fourth and least volatile product peak in the g.c. was assigned to the 2-substituted indole 136 Mass spectrometry showed this compound to fragment quite differently from that of 135. The molecular ion had m/e 289, the same as 2+2 cycloadducts 41 and 42, but yielded no fragment m/e 221 indicative of the retro 2+2 cleavage commonly seen for these adducts in the mass spectrometer. A benzoyl ion fragment m/e 105 was present suggesting that this compound was an addition product of N-benzoylindole and cyclopentene. The ^{1}H-nmr spectrum showed typical aromatic signals for the indole moiety (and not for an indoline) and aliphatic methylene signals indicative of a cyclopentane ring. No cyclobutane signals were present. A methine quintet at 3.48 ppm suggested that the cyclopentane ring was attached to an unsaturated quaternary carbon. A singlet at 6.45 ppm could be assigned to the methine at the 3-position on the indole ring; other substituted indoles and N-benzoylindole itself normally show the 3-position proton a *ca.* 6.5 ppm split into a doublet by the adjacent protons in the 2-position. This and the absence of the proton in the 2-position at *circa* 7.0 ppm allowed for assignment of the structure as 2-cyclopentyl-N-benzoylindole 136.

A similar trapping reaction was carried out by irradiation of N-carboethoxyindole, 34, in the presence of cyclopentene and hydrogen selenide. This reaction also showed total quenching of 2+2 photocycloadduct formation. Compound 133 and three other products which were identified by gc.-m.s. as having molecular ions of m/e 191, 259, and 257 were formed. This is indicative of the formation of 137, 138, and 139.



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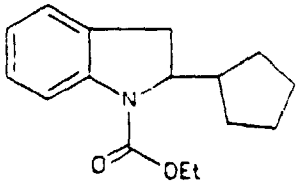

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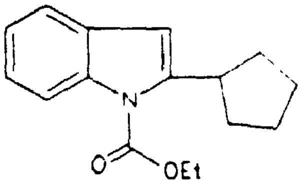

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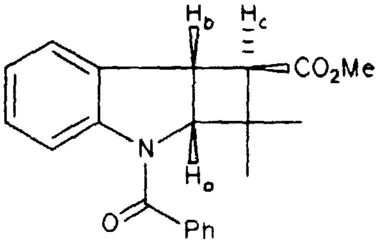
Compared to the reaction of N-benzoylindole, this reaction appeared to be quite inefficient. Even after 80 hours of irradiation, compound 138 and 139 only accounted for *ca.* 4% of the total products while product 133 accounted for *ca.* 30% of the mixture, thus the reaction mixture was not characterized any further.

3.4.4 Irradiation of N-Benzoylindole and 3,3-Dimethylacrylic Acid Methyl Ester with Hydrogen Selenide

Ultraviolet irradiation of 5 in benzene with 3,3-dimethylacrylic acid methyl ester, 140, yielded four new products as detected by g.c. in a ratio in order of increasing retention time of 5:38:45:13. G.c-m.s. showed all four products to have a parent molecular ion m/e 335 indicative of 1:1 adducts of 5 and 140 Since none of these products had been characterized previously, the mixture was chromatographed by preparative t.l.c. to yield three fractions. The first fraction contained the second peak in the g.c. and was assigned to structure 141.



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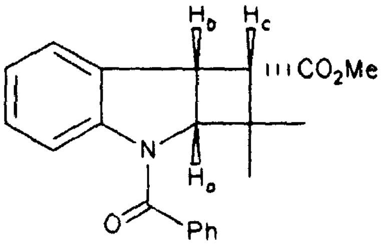

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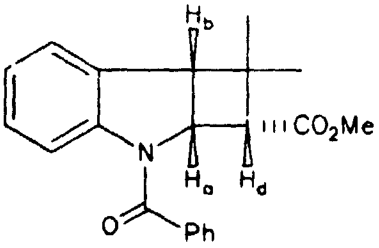

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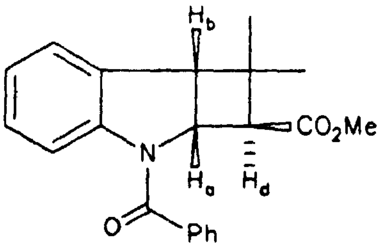


143

Thus the methine proton H_b at 4.21 ppm appeared as a doublet of doublets with coupling constants of 8 and 4 Hz coupled to H_a and H_c respectively. The relatively small coupling constant between H_b and H_c suggested their relationship to be *trans*. Methine proton H_a at 4.92 ppm appeared as a broad doublet and is coupled only to H_b since it is adjacent to the carbon bearing the two methyl groups.

The second fraction contained a mixture of the third and fourth g.c. products in a ratio of 4:1 respectively. Further chromatography showed the two isomers to be inseparable by this technique. In the ^{1}H-nmr spectrum of this mixture of adducts only the cyclobutane protons for the major isomer could be discerned clearly. Thus the structure of the minor adduct could not be assigned. For the major isomer methine proton H_b (3.65 ppm) appeared as a doublet and H_a (4.90 ppm) as a doublet of doublets. This allows assignment of regiochemistry and suggests structure 142 or 143. The coupling constant between H_a and H_d was found to be 6 Hz by decoupling experiments; as discussed below, this does not allow for unambiguous assignment of stereochemistry and does not distinguish between 142 and 143.

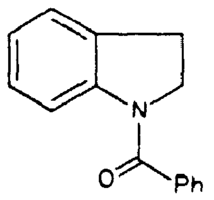
The third fraction contained the first (minor) g.c. adduct and was found to be a stereoisomer of the major compound present in fraction 2. Thus it has structure 142 or 143. The regiochemistry, as before, was based on the appearance of the signal at 3.68 ppm assigned to H_b; this appeared as a doublet coupled only to H_a (4.92 ppm) and is therefore adjacent to the carbon bearing the two methyl groups.

Decoupling experiments showed H_a to be coupled to H_d (2.94 ppm) which appeared as a doublet of doublets with coupling constants of 6 and 0.5 Hz. The first coupling constant arises from coupling with H_a and the latter is due to a long range coupling with H_b. It should be noted that although regiochemistry in this adduct has been established the stereochemistry is again ambiguous. Trends have shown that with other adducts (table 1) if two vicinal protons, specifically H_b and H_c, on different moieties of the photocycloadduct are *cis* then the stereochemistry is reflected by a large (8-10 Hz) coupling constant. Alternatively, if they are *trans* a small (2.5-3 Hz) coupling constant arises. Unfortunately this trend does not seem to allow for the stereochemical assignment between H_a and H_d protons as measured coupling constants for some adducts (table 1) range between 3.5 and 6.6 Hz. Thus a J_{ad} of 6 Hz for the above adducts 142 and 143 does not allow for a stereochemical assignment.

It was believed that the stereochemical relationships of all four methine cyclobutane protons could be elucidated by measuring any nuclear Overhauser effects (nOe) on decoupling. Attempts were made to observe nOe's by recording the coupled and single proton decoupled 200 MHz ^{1}H-nmr spectra and subtracting the two spectra to yield possible differential nOe's. Unfortunately the experiment gave ambiguous results. Problems associated with selective irradiation, due to the proximity of the cyclobutane protons, and detection of nOe, due to proton signals which were nearly isochronous, yielded ambiguous spectra and thus this method of stereochemical elucidation was abandoned for ^{1}H-^{1}H decoupling experiments which yielded cyclobutane methine coupling constants.

Ultraviolet irradiation of a benzene solution of 5 and 3,3-dimethylacrylic acid methyl ester, 140, in the presence of hydrogen selenide yielded three new products by g.c. in a ratio of 1:1:1, the latter two products possessing retention times slightly shorter than those of the 2+2 photocycloadducts.. G.c. and g.c-m.s. confirmed that none of these products were the 2+2 cycloadducts of 5 and 140 produced by the parallel, untreated reaction in which H_2Se was absent. Unirradiated solutions of 5 and 140 containing H_2Se showed no change by g.c. and by ^{1}H-nmr spectroscopy. G.c. comparison of reactions performed in the presence and absence of H_2Se showed 13% conversion of starting 5 to cycloadducts in the absence of H_2Se and 0.9% conversion to the 3 new products in the presence of H_2Se, after 60 minutes irradiation. The three new products were separated by column chromatography. yielding three fractions.

The first of the products off the chromatography column contained the second most volatile g.c. product and was identified as compound 145a.



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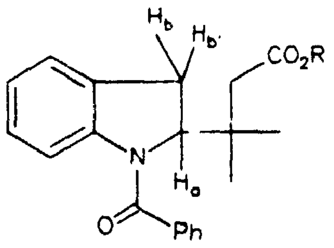
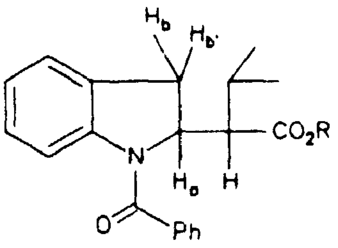


145a,b



146a,b

a R=Me, b R=H

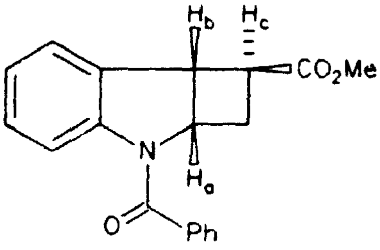
Mass spectrometry indicated a molecular ion of m/e 337; this suggests a 1:1 adduct of 5 and 140 with two additional hydrogens. The fragmentation pattern was similar to that of 135 in parent ion fragments to yield an ion with m/e 222, which corresponds to an N-benzoylindolinyl fragment. ^{1}H-Nmr spectroscopy revealed a broad signal assigned to H_a at 5.05 ppm; decoupling experiments showed that this was coupled to the methylene protons assigned to H_b at 3.19 ppm; the multiplicity of this signal was obscured by the presence of a broad methoxy singlet at 3.10 ppm. The two methyl groups appeared as a singlet at *circa* 1.0 ppm, indicating that they are attached to a saturated quaternary carbon. A methylene singlet at 2.0 ppm was assigned to the protons adjacent to the methyl ester. The conclusion that the alkene derived side chain of 145a is attached to the 2-position of the indoline rather than the 3-position is based upon the chemical shift of H_a, and upon the fact that it shows the characteristic broadening arising from slow rotation of the benzoyl group. In order to resolve the methylene H_b signal at 3.19 ppm, compound 145a was subjected to base hydrolysis to yield the corresponding acid 145b. M.s. yielded a molecular ion m/e of 323 indicative of an acid product of ester hydrolysis. The ^{1}H-nmr spectrum showed signals similar to that of 145a except for the absence of the methoxy signal at 3.1 ppm. The H_b methylene signal was resolved as a doublet of an AB quartet coupled to a downfield signal (H_a) at 4.25 ppm.

The second fraction off the chromatography column contained the first g.c. component and possessed a retention time identical to that previously isolated N-benzoylindoline, 134. G.c.-m.s. and g.c. coinjection with an authentic sample of 134 confirmed this. The ^{1}H-nmr spectrum was also identical to that of 134.

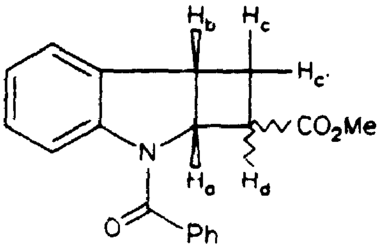
The third fraction off the chromatography column contained the least volatile component of the reaction mixture, as identified by g.c., and was identified as 146a. Thus the mass spectrum established a molecular ion of m/e 337 indicative of a 1:1 adduct of 5 and 140 plus two hydrogens atoms. The fragmentation pattern was similar to that of 145a and 135 in that the parent ion fragmented to yield an ion with m/e 222, which corresponds to an N-benzoylindolinyl fragment. ^{1}H-Nmr spectroscopy indicated that only one diastereomer of 146a was present. The signal assigned to H_a (5.25 ppm) appeared as a doublet of doublet of doublets (J=8, 4.5, and 2 Hz). Proton H_a was coupled to the methylene H_b protons (3.63 ppm), and another proton at 2.56 ppm, a doublet of doublets, which was assigned to the α-proton of the methyl ester; the multiplicity of the H_b signal was obscured by the presence of a methoxy singlet at 3.50 ppm. A septet of doublets at 2.07 ppm was assigned to the methine proton on the carbon bearing the two methyl groups. The methyl groups appeared at 1.07 and 0.9 as doublets (J=6 Hz) and this is a result of the methyl groups being diastereotopic. In order to resolve the methylene H_b signal at 3.63 ppm, compound 146a was subjected to base hydrolysis to yield the corresponding acid 146b. M.s. yielded a molecular ion m/e of 323 indicative of an acid product of ester hydrolysis. The ^{1}H-nmr spectrum showed signals similar to that of 146a except for the absence of the methoxy signal at 3.5 ppm. The H_b methylene signal was resolved as a doublet of an AB quartet coupled to a downfield signal (H_a) at 4.24 ppm. This allowed for an unambiguous assignment of the ester precursor to 146b as 146a.

3.4.5 Irradiation of N-Benzoylindole and Methyl acrylate in the Absence and Presence of Hydrogen Selenide

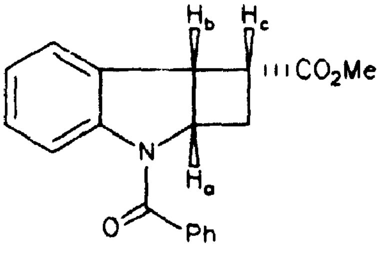
Ultra-violet irradiation of 5 in benzene with methyl acrylate yielded four new products as detected by g.c. in a ratio of 0.5:1.48:5.06:1. Ikeda (13) previously reported finding only three photochemical products in this reaction. G.c-m.s. showed all four products to have a parent molecular ion with m/e 307 indicative of 1:1 adducts of 5 and methyl acrylate. It was decided to characterize these products in order to establish the regioisomeric ratio and to determine if the assignments were consistent with those reported in the literature.



147



148



149

After removal of solvent the major isomer, as indicated by g.c., crystallized out and was identified as 147. The ^{1}H-nmr spectrum showed the typical broad signal at 4.79 ppm, due to slow rotation of the benzoyl group, and this was assigned to H_a. Decoupling experiments showed this signal to be coupled to one signal at 4.18 ppm which appeared as a doublet of doublets ($J=8$ and 2.5 Hz). This signal was assigned to H_b whose coupling pattern suggests that H_b is coupled to two protons. Decoupling of H_b showed it to be coupled to H_a (4.79 ppm) and another proton, H_c (3.12 ppm). The stereochemical relationship was based on the coupling pattern of H_b. The doublet of doublets, which is typified in cycloadduct 41, showed small coupling between H_b and H_c and is indicative of a *trans* arrangement in the cyclobutane ring.

The rest of the mixture was chromatographed by preparative t.l.c. to yield three fractions. The first (least polar) fraction was found by g.c.-m.s. and ^{1}H-nmr to contain cycloadduct 147. This was confirmed by g.c. coinjection with an authentic sample of 147.

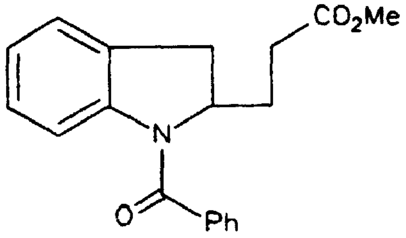
The second fraction was mostly one compound although g.c. indicated the presence of a small amount of 147. The major component was assigned structure 148. Regiochemical assignment was based on the multiplicity of H_b (3.96 ppm), which appeared as a doublet of doublets of doublets. Decoupling experiments showed H_b was coupled not only to H_a (broad signal at 4.89 ppm) but to two other protons, H_c (2.52 ppm) and $H_{c'}$ (2.25 ppm). Proton H_d (3.41 ppm) appeared as a multiplet whose coupling constant, J_{ad}, could not be determined. Thus the compound was assigned to one of the two stereoisomers of 148.

The third (most polar) fraction was shown by g.c. to contain the least volatile cycloadduct of the reaction mixture as the major component with small amounts (12%) of 147 and 148. This isomer was identified as 149. The regiochemistry was assigned on the basis of decoupling experiments which showed H_a (broad signal at 4.55 ppm) coupled to H_b (4.36 ppm) and two other protons H_d and $H_{d'}$ (2.75-2.50 ppm). The stereochemical assignment was based on the two large coupling constants of 8 and 8.5 Hz seen for coupling of H_b to H_a and H_c between respectively. This is indicative of a *cis* relationship between H_b and H_c as was illustrated with cycloadducts 42 and 54.

The fourth, and smallest component of the reaction mixture could not be separated but was contained in the third isolated fraction as shown by g.c. and ^{1}H-nmr spectroscopy. This isomer was assumed to have the regiochemistry shown in 148 and to be a stereoisomer of the component already assigned to this structure since it was the only isomer unaccounted for. The above assignments are all consistent with the literature assignments (13).

Ultra-violet irradiation of a benzene solution of 5 and methyl acrylate in the presence of hydrogen selenide yielded three new products by g.c. in a ratio of 2.31:0.40:1.74 in addition to N-benzoylindoline, 134, and the four 2+2 photoadducts 147-149. The presence of the latter products was confirmed by g.c-m.s. and g.c. coinjection with authentic samples. The ratio of adducts 147-149 differed from that of the typical isomeric ratio obtained from photoreactions performed in the absence of H_2Se. The ratio of the four cycloadducts was 1.4:1:8.68:1 in the presence of H_2Se and 1:3:10:2 in the absence of H_2Se. Unirradiated solutions of 5 and methyl acrylate in the presence of H_2Se showed no change by g.c. and by ^{1}H-nmr spectroscopy. Relative rates of reaction in the presence and absence of H_2Se, as determined by g.c. after 1 hour, were 16% and 0.4% conversion of 5, respectively. Attempts to completely quench the formation of 147-149 by using the highest attainable concentration of H_2Se (0.6 M) proved unsuccessful.

Attempted isolation of the new photoproducts formed in the presence of H_2Se was unsuccessful. All fractions isolated by column chromatography, preparative t.l.c. or H.P.L.C. were found to be heavily contaminated by the 2+2 photocycloadducts 147-149. G.c-m.s. did provide some information as to the nature of the new products however. The two major products possessed molecular ions with m/e 309. This is equivalent to the addition of methyl acrylate to 5 along with the addition of two hydrogens. The fragmentation patterns were very similar to those of the trapping products 145a and 146a; thus ions of m/e 222, the N-benzoylindolinyl moiety, and m/e 105, the benzoyl fragment were observed.



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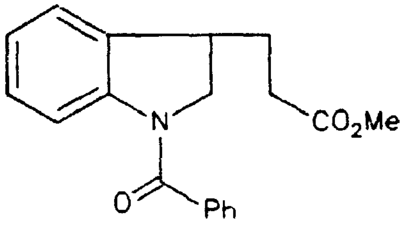

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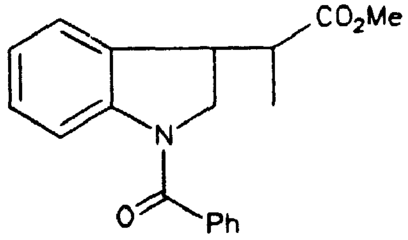

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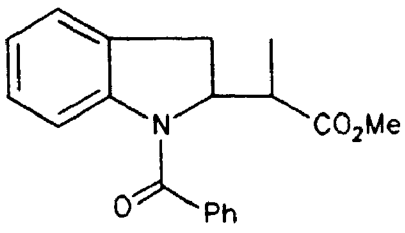
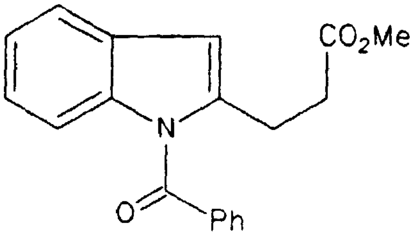


153

These compounds may therefore be the products of trapping, 150-153. The minor product present in the reaction mixture possessed a molecular ion with m/e 307. This is indicative of a 1:1 adduct of 5 and methyl acrylate; however the g.c. retention time of this product was much shorter than that for the 2+2 photocycloadducts characterized previously and could not therefore be 147-149.

The fragmentation pattern of this compound was very similar to that of 2-cyclopentyl-N-benzoylindole, 136, in that major fragments with m/e 105 and 77 and a very minor fragment with m/e 221 (1%) were observed. This is suggestive of structure 154 or 155. Because of the separation problems the characterization of these products was not carried any further.



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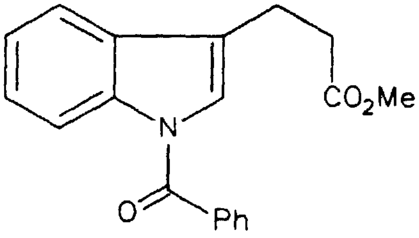

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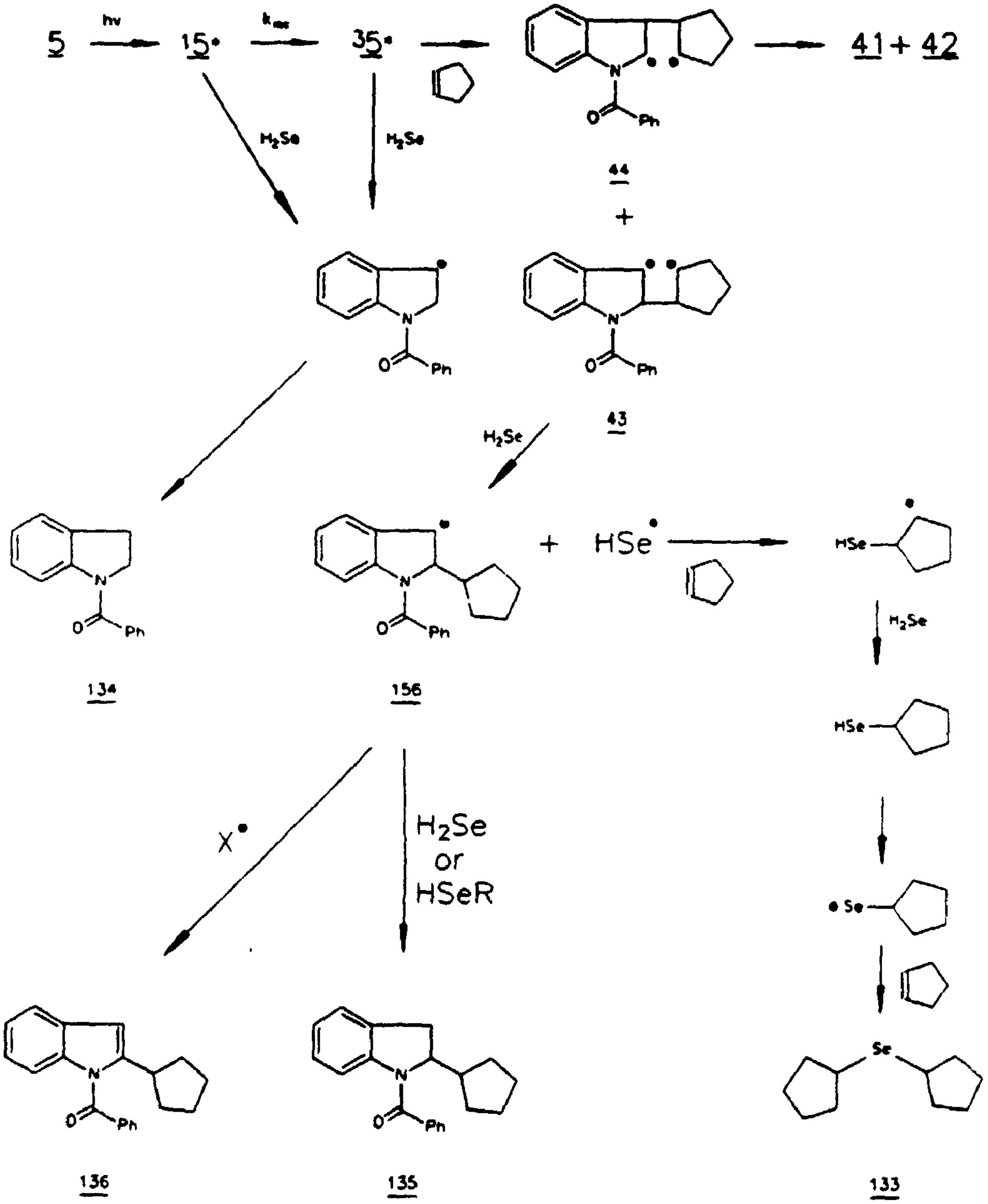
3.5 DISCUSSION OF TRAPPING STUDIES

In order to trap successfully any biradicals produced from the 2+2 photocycloaddition of N-acylindoles and olefins the trapping method must adhere to a number of conditions. These include a fast rate of reaction of the trapping reagent with the 1,4-biradicals, ease of identification of trapping products, absence of dark reaction products and of secondary photochemistry, and ease of removal of unused trapping reagent. Only when these conditions are met can accurate statements with regards to the nature of the 1,4-biradical intermediates be made.

Any successful trapping must start with biradical intermediates which are long lived enough to react with the trapping reagent. Chapter 2 described the rearrangement of the biradical generated from N-benzoylindole and vinylcyclopropane. The lifetime of the biradical intermediate involved was estimated to be *circa* 100 ns. Thus to trap this biradical the trapping reagent must react with a rate constant of at least 10^7 $M^{-1}s^{-1}$. Consequently the reagent chosen in this work was hydrogen selenide, H_2Se, since it has been shown that this is one of the few species which can react with radicals at a sufficiently fast rate. Hydrogen selenide is easily prepared by hydrolysis of aluminum selenide, Al_2Se_3, and has been reported (66) to react with radicals with a rate constant on the order of 10^8 $m^{-1}s^{-1}$. The previous work indicated that the byproduct of biradical trapping was selenium metal which could be removed by filtration. In this work the products of trapping would be simple 2 and 3-substituted indolines, a result of hydrogen atom donation to each of the radical centres in the proposed biradical intermediates. Thus the first trapping experiments of 1,4-biradicals from the 2+2 photocycloaddition of N-benzoylindole with olefins were carried out using H_2Se.

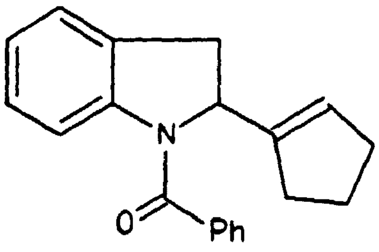
Literature reports suggest that H_2Se is relatively inert to olefins bearing alkyl substituents (72). Thus the first reaction attempted was irradiation of N-benzoylindole, 5, and cyclopentene in the presence of H_2Se. ^{1}H-Nmr studies demonstrated that both 5 and cyclopentene do not reaction with H_2Se under dark conditions. It was also shown that cyclopentene does not react with H_2Se under the conditions of photolysis. Irradiation of 5 with cyclopentene and H_2Se resulted in the formation of products shown in scheme 21.

Scheme 21



The absence of cycloadducts 41 and 42 demonstrates clearly that the cycloaddition reaction is quenched and that products 135 and 136 are a direct result of interception of biradical 43 and not 44.

The first step in the trapping reaction would seem to involve donation of a hydrogen atom to the less stable, more reactive cyclopentyl radical centre rather than the more stable benzylic radical centre generating intermediate 156. This intermediate then accepts another hydrogen from H_2Se or other donating source leading to the major indoline product 135. Intermediate 156 disproportionates with H_2Se to yield the minor product, the 2-substituted indole 136. It is this product which leads to the conclusion about the site of initial trapping since initial reaction at the benzylic terminus would, after disproportionation, lead to totally different products, 157 or 158.



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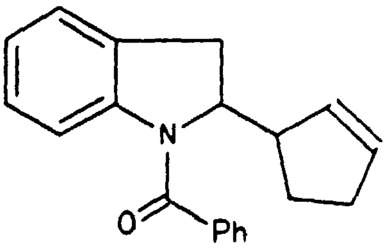


158

Byproducts 133 and 134 are also accounted for in scheme 21. Product 133 was identified as dicyclopentylselenide. This is a reasonable product to expect since the HSe· radicals formed by hydrogen donation to the 1,4-biradical could easily add to the cyclopentene present in high concentration. The resulting selenol, 137, like H_2Se is an excellent hydrogen donor (72) and may assist in quenching the biradical 43 or benzylic radical intermediate 156. This would produce the cyclopentyl selenyl radical which could react with another molecule of cyclopentene to yield 133. In addition, once HSe· is formed in the system conditions for a radical chain reaction are initiated for the production of the cyclopentanyl selenol.

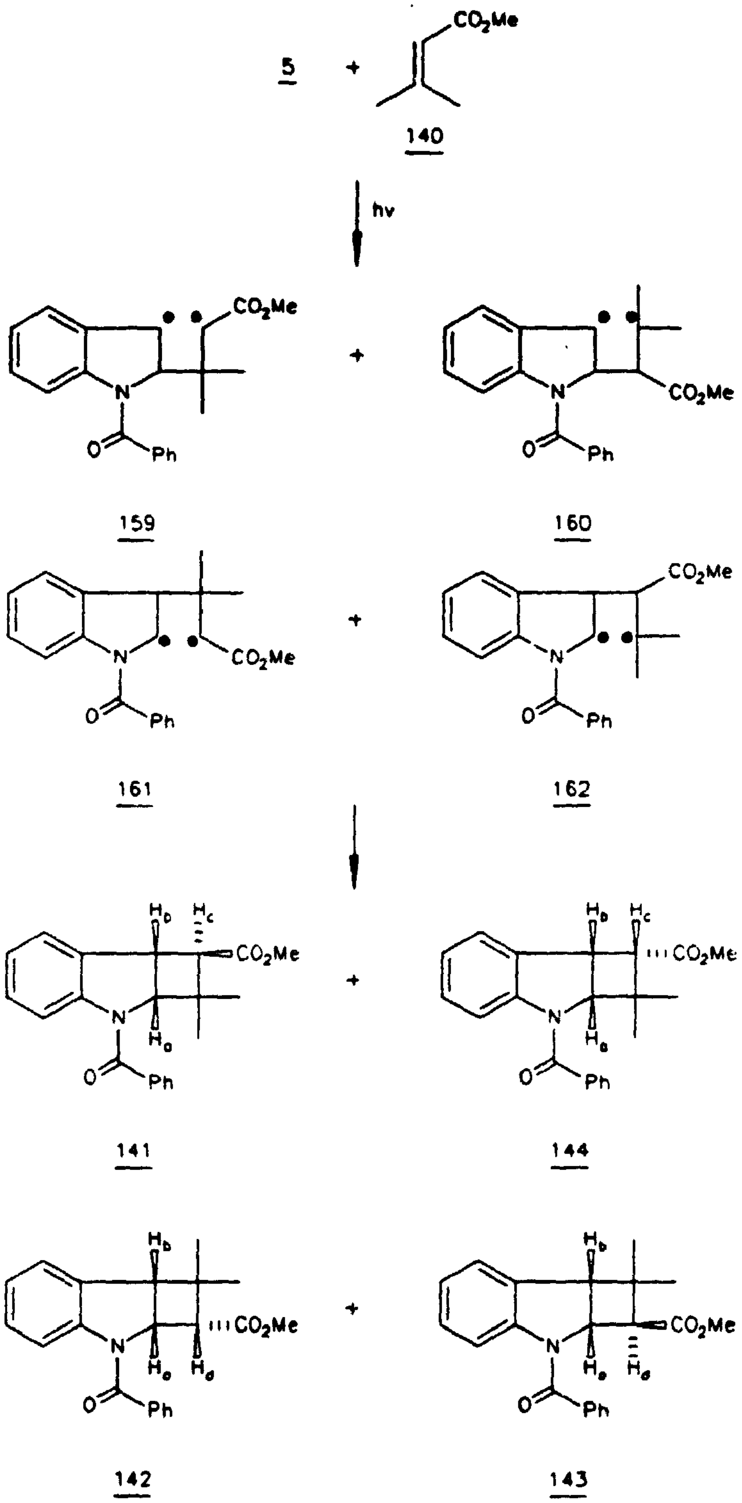
Product 134 was identified as N-benzoylindoline and is presumably a result of quenching of the triplet excited state of 5. This was verified by photolysis of 5 in the presence of hydrogen selenide only; as anticipated, this resulted in the formation of 134. This reaction may partly contribute to the inefficiency of the trapping reaction. Comparison of the relative rate of trapping with the 2+2 cycloaddition reaction shows that the trapping reaction proceeds at a much slower rate (*ca.* 20 times slower). Since the formation small quantities of 134 cannot account for the large inefficiency of trapping it is suggested that the hydrogen selenide is for the most part quenching the triplet excited N-benzoylindole *via* energy transfer or *via* heavy atom induced intersystem crossing. This problem also appeared in the photolysis of N-carboethoxyindole, 34, with cyclopentene and H_2Se; in this case product formation seemed even more inefficient.

The trapping products 135 and 136 are derived from 43. Since these are the only two products of biradical trapping it can be concluded that initial bonding of the cyclopentene to the excited state indole must occur exclusively at the 2-position, rather than at the 3-position, which would lead to 44.

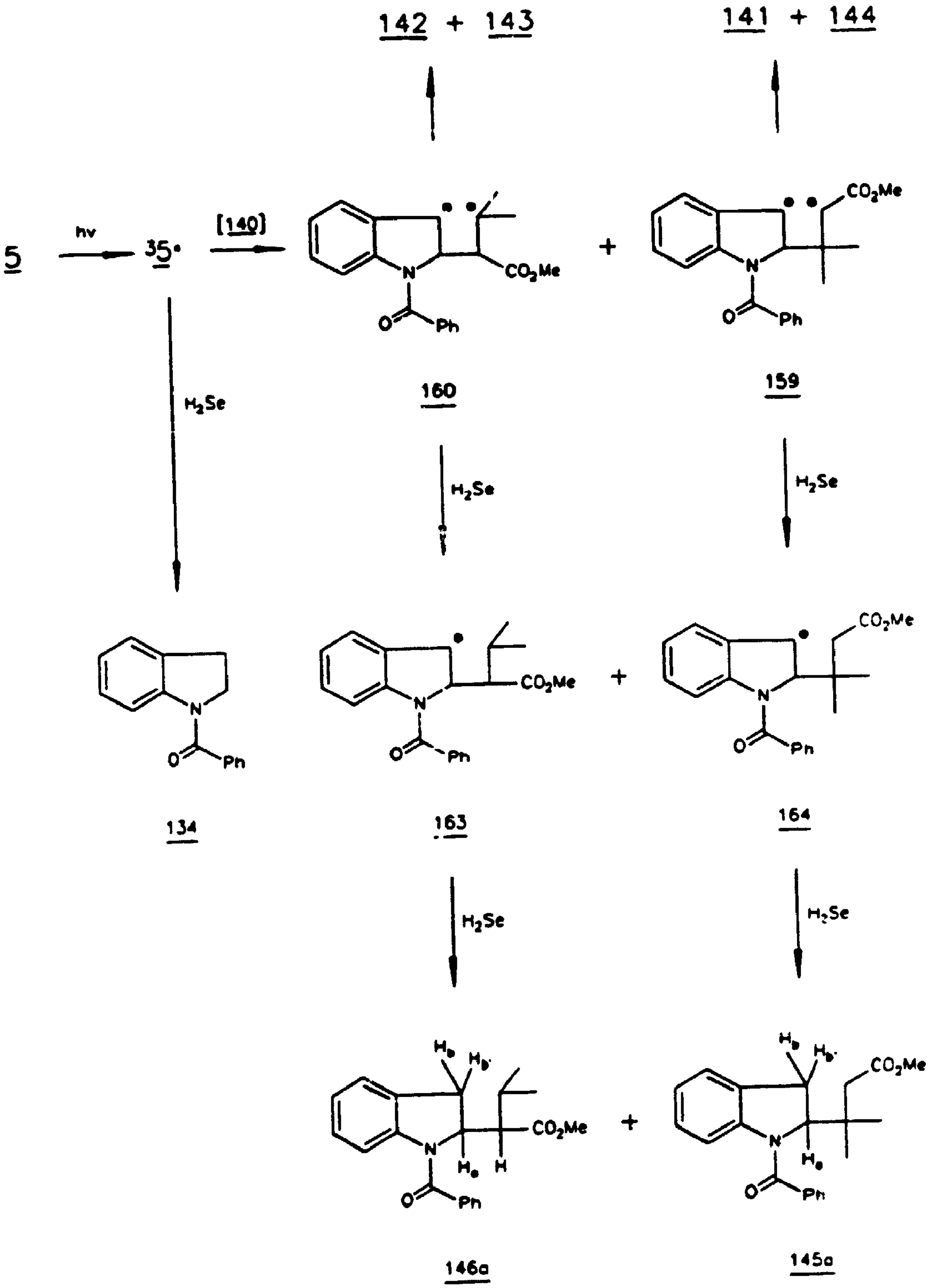
These findings that photocycloaddition of 5 and cyclopentene proceeds through intermediate 43 exclusively demonstrates a preference for bonding to the indole 2-position and formation of a benzylic radical centre rather than bonding to the 3-position and formation of an amino alkyl radical. In order to probe this preference further an asymmetric olefin which yields a mixture of regioisomers under 2+2 photocycloaddition conditions was substituted for cyclopentene. Using an asymmetric olefin which gives mixed regiochemistry demands the presence of a minimum of 2 biradical intermediates which would be trapped by the hydrogen selenide. The olefin chosen was 3,3-dimethyl acrylic acid methyl ester, 140.

Irradiation of 5 with 140 yielded four products as shown in scheme 22. The regioisomeric ratio of 141 + 144 to 143 + 142 was estimated to be close to 1:1. The 1,4-biradical intermediates 159-162 represent the structures of the possible precursors to the cycloaddition products and as with cyclopentene (scheme 21) allow for the possibility of initial bond formation at the 2 or 3-position. The results of irradiation of 5 with 140 in the presence of H_2Se are depicted in scheme 23. In this reaction N-benzoylindoline, 134, was formed along with trapping products 145a and 146a in a ratio of 1:1. The latter two products can only be formed from biradicals 159 and 160, which from the product ratio of 146a to 145a would be present in equal amounts. Exclusive formation of 146a and 145a demonstrates, as in the reaction for cyclopentene, that initial bond formation must be at the 2-position and it is proposed by analogy that radicals 163 and 164 are the intermediates formed on initial quenching of 159 and 160. The fact that only one diastereomer of 146a is seen in the trapping reaction and the two stereoisomers 142 and 143 are formed in the 2+2 photocycloaddition suggests that a single diastereoisomeric 1,4-biradical is formed and leads to these products.

Scheme 22


5
+
CO2Me
140
hν
CO2Me
159
+
CO2Me
160
CO2Me
161
+
CO2Me
162
Hb
Hc
CO2Me
Ha
141
+
Hb
Hc
CO2Me
Ha
144
Hb
CO2Me
Ha
Hd
142
+
Hb
CO2Me
Ha
Hd
143
N
O
Ph

Scheme 23

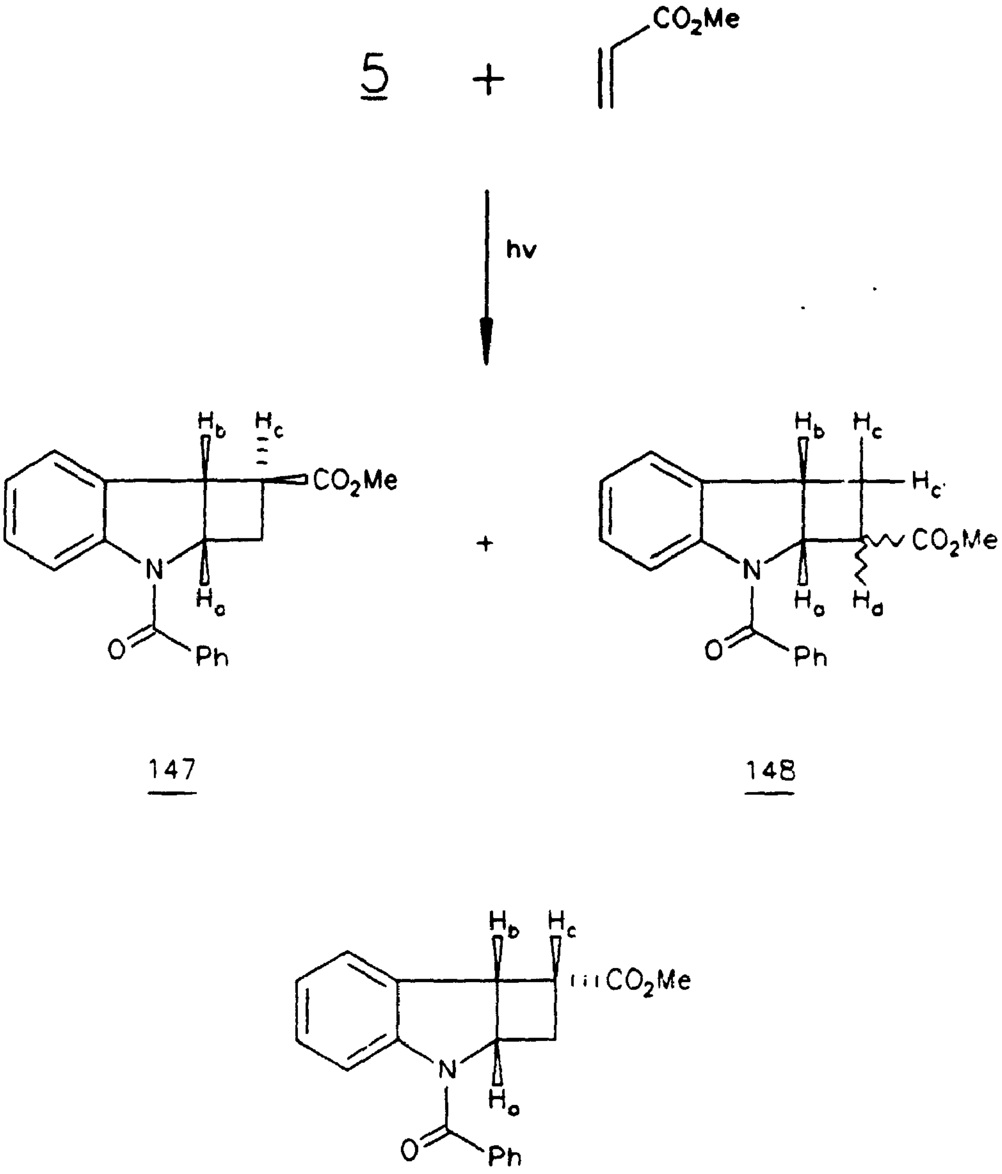

142 + 143
141 + 144
5
hv
35•
[140]
CO₂Me
Ph
+
160
159
H₂Se
134
163
164
146a
145a
Hb
Hb'
Ha
H
N
O

If two diastereomeric biradicals led to the two stereoisomeric cycloadducts then a diastereomeric trapping product should have been detected. Formation of biradical intermediate 160 rather than 161 suggests that the formation of the benzylic radical centre is preferred. However, although 160 also possesses a tertiary radical centre on the alkene derived portion of the biradical; this is more stable than the secondary radical centre in the alkene derived portion of the biradical of 161 and it could be argued that this is responsible for the preferential formation of 142 over 143. However, intermediate 159 is preferred over 162 since only the former is trapped by H_2Se thus formation of the biradical by initial bonding of the alkene to the indole 2-position is preferred regardless of the nature of the alkene terminus.

It was then decided to examine a mono-substituted olefin known in the literature to react yielding a mixture of regioisomers and therefore invoking the need for a minimum of two 1,4-biradicals along the reaction pathway. The 3,3-dimethyl acrylic acid methyl ester was thus replaced with methyl acrylate. Scheme 24 shows the products of photocycloaddition of 5 and methyl acrylate and Scheme 25 depicts the putative intermediates for the cycloaddition reaction and trapping reaction. The 2+2 photocycloaddition reaction between 5 and methyl acrylate had been previously studied by Ikeda (13) and, although our studies revealed four isomers as opposed to three previously described, the assigned structures were consistent with the literature and yielded a regioisomeric ratio for 147 + 149 to 148 of 3:1. If the reaction does involve exclusive initial bond formation at the indole 2-position, as in the previous cycloaddition reactions, then biradical 160, precursor to product 148, must be formed. This would suggest that formation of a benzylic radical centre by initial bonding to the indole 2-position is preferred even if the alkene derived radical terminus is primary.

As previously described (section 3.4.5), irradiation of 5 with methyl acrylate in the presence of hydrogen selenide yielded a mixture of cycloadducts, indoline 134, and three suspected trapping products. Unfortunately the reaction products could not be isolated and no conclusion can be drawn about the structures of the intermediate biradicals. The failure of H_2Se to trap all the biradical intermediates, so that the product mixture contained considerable quantities of cycloadducts, is, however informative. What this indicates is that methyl acrylate derived biradicals are short-lived (and therefore change incompletely trapped) than those derived from methyl dimethylacrylate. In addition, the ratio of cycloadduct regioisomers changed from 3:1 (147 + 149 : 148) in the absence of H_2Se to 4:1 in the presence of H_2Se. Also the ratio of the stereoisomers of each regioisomer was altered drastically by the presence of H_2Se. This suggests that the isomeric biradicals possess different lifetimes, and so are trapped with different efficiencies.

Scheme 24

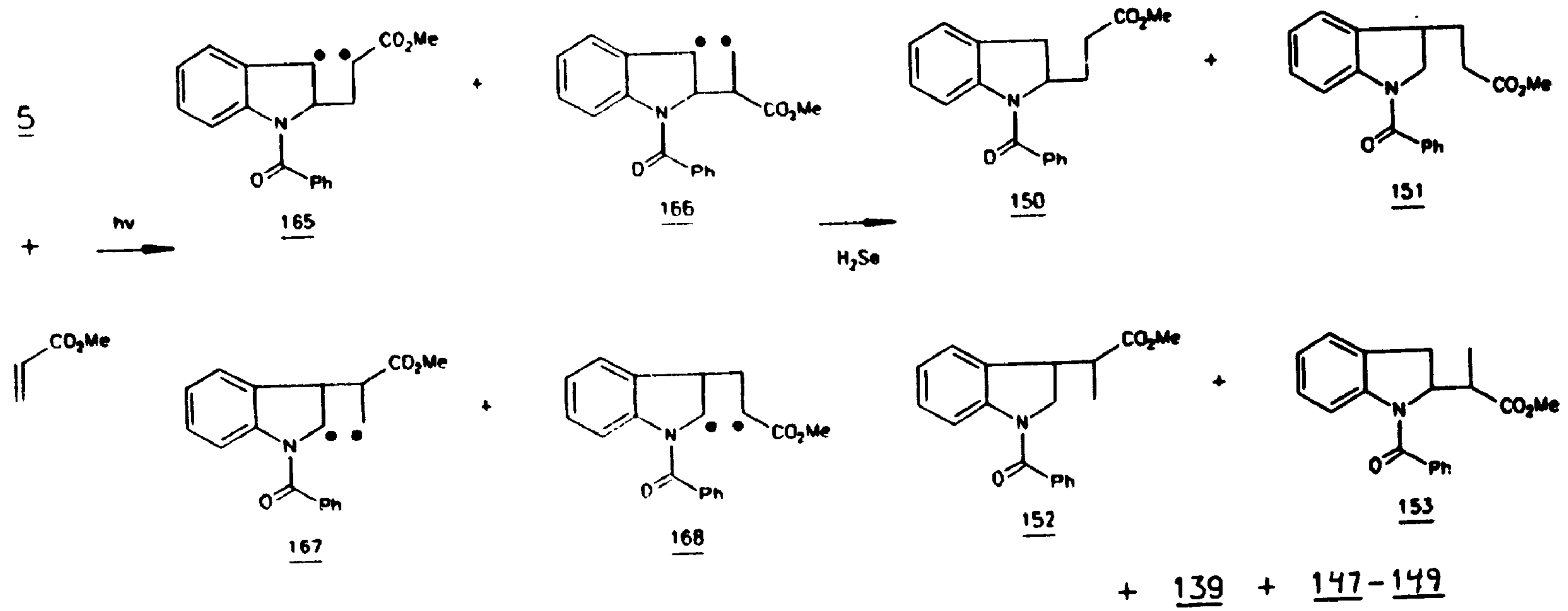


147

148

149

Scheme 25



In conclusion it has been shown that in the 2+2 photocycloaddition reaction between N-benzoylindole and olefins a single 1,4-biradical intermediate exists along the reaction pathway with an estimated lifetime of 100 ns. When the biradical is capable of undergoing a rearrangement, as opposed to cyclobutane formation, the products indicate that they were derived from an intermediate in which initial bonding between the alkene and the N-substituted indole occurs at the 2-position of the indole moiety. Thus the intermediate is one which always possesses a benzylic radical centre regardless of the alkene used. This assertion was supported by hydrogen selenide trapping experiments in which the 1,4-biradical intermediates for most reactions could be intercepted by the donation of hydrogen atoms to the radical centres. The products from these experiments yielded 2-substituted indoles and indolines exclusively which indicates that the site of initial bond formation on the indole moiety is the 2-position.

CHAPTER 4

EXPERIMENTAL

Melting points and boiling points are uncorrected. Melting points were determined on a Koffler hot stage melting point apparatus. I.R. spectra were recorded with IBM System 9000 FT-IR spectrometer. Ultra-violet absorption spectra were recorded on a Hewlett-Packard 8450A diode array spectrophotometer or a Shimadzu UV160 spectrophotometer. All ^{1}H-nmr spectra were recorded at 200 MHz on either a Varian XL-200 nmr spectrometer or a Varian gemini 200 MHz nmr spectrometer. All ^{13}C-nmr spectra were recorded at 75 MHz using a Varian XL-300 nmr spectrometer. Methyl, methylene, methine and quaternary signals were identified by comparing the fully decoupled spectra with the APT spectrum (73). The chemical shifts are given in parts per million (ppm) downfield from tetramethylsilane in δ units and coupling constants are given in cycles per second (Hz). The data is reported as chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, quin=quintuplet, m=multiplet, dd=doublet of doublets, ddd=doublet of doublet of doublets), coupling constants, and number of protons.

Gas-liquid chromatography (g.c.) analyses were performed using a Varian 2400 gas chromatograph equipped with a flame detector, Megabore DB-1 (15 m), and a Hewlett Packard 3390A integrator, or using a Hewlett Packard HP5880 gas chromatograph equipped with either a DB-1 (30 m) or a DB-5 (30 m) capillary column. G.c.-m.s. analyses were performed using a Finnigan-MAT 8230 mass spectrometer coupled to a Varian 3400 gas chromatograph equipped with a DB-5 (30m) capillary column. High performance liquid chromatography (H.P.L.C.) was performed using a Waters automatic gradient controller with dual Waters model 510 pumps and a Waters 490 programable multiwavelength detector. The column used was a Varian normal phase silica semi-preparative steel column and fractions were collected with a Gilson 201 collector. Quantum yield determinations were performed using a PTI Quantacount apparatus equipped with a 100 Watt high pressure Hg lamp.

Reagent grade solvents were used for all large scale reactions. Spectrophotometric grade solvents were used for all irradiations. Tetrahydrofuran was freshly distilled before use from sodium and benzophenone. Anhydrous ethyl ether was BDH anhydrous grade and was used without further purification. All anhydrous reactions were performed under a dry nitrogen atmosphere with all glassware being dried overnight in a drying oven at 150°C prior to use. Assembly of the dry reaction apparatus was conducted under a flow of dry nitrogen. The drying agents were either potassium carbonate (K_2CO_3) or sodium sulphate (Na_2SO_4) and were BDH reagent grade.

General Procedure for Preparation of Cycloadducts

All preparative irradiations (gram scale) were carried out in a preparative irradiation well into which was immersed a 450 W Hanovia medium pressure mercury lamp housed in a water cooled quartz jacket. The lamp was filtered with a Pyrex sleeve to ensure that only wavelengths greater than 300 nm were transmitted to the reaction solution. Solutions of N-benzoylindole, 5, or N-carboethoxyindole, 34, ([5]>10^{-4} M) and alkene ([alkene]>0.05 M) were prepared in benzene previously purged with nitrogen. The solutions were flushed with nitrogen and sealed with a rubber septum. The solutions were stirred during irradiation. Smaller scale irradiations (milligram scale) were prepared similarly in a Pyrex tube and irradiated in front of a 450 W medium pressure mercury lamp house in a water cooled Pyrex jacket.

Preparation of N-benzoylindole 5

To a stirred suspension of indole (5 g, 0.043 Mol), powdered NaOH (5 g, 0.125 Mol) and $(Bu)_4NBr$ (0.2 g) in dry methylene chloride (150 mL) was added a solution of benzoyl chloride (9.25 g, 0.88 Mol) in methylene chloride (25 mL) over 15 minutes. During addition, the reaction was cooled with ice. After 1.5 hours, H_2O (50 mL) was added and was extracted (3 X 50 mL) with CH_2Cl_2. The extracts were dried (K_2CO_3) and solvent removed to yield a red oil which was crystallized from ether/hexanes to yield 8.6 g (91%) of 5 as white crystals, mp 63-64°C; lit. (2) 57-58°C.

Preparation of N-carboethoxyindole 34

Indole (12 g, 0.1025 Mol), powdered NaOH (10 g), $(Bu)_4NBr$ (0.5 g) and CH_2Cl_2 (150 mL) were stirred together and ethylchloroformate (12.5 g, 0.115 Mol) was added dropwise with ice cooling. After stirring for 1.5 hours the reaction mixture was worked up as for 5 to give a red oil which was distilled to yield

13.7 g (72%) of 34 as a clear pale yellow liquid; bp 133°C at 3 mm of Hg; lit.(74) 142-144°C at 16 mm of Hg; ^{1}H-nmr δ ($CDCl_3$) 8.20 (m, 1H), 7.6-7.0 (m, 4H), 6.55 (d, 1H), 4.43 (q, 2H), 1.38 (t, 3H).

Irradiation of N-benzoylindole with cyclopentene

As described in the general procedure, a solution of N-benzoylindole (1.626 g, 7.36 mMol) was irradiated with cyclopentene (7.8 g, 111.5 mMol) in 300 mL of benzene for 89 hours. Removal of the benzene and unreacted alkene under reduced pressure afforded 2.13 g of a brown oil. The oil was purified by column chromatography (silica gel, 30% ether/70% hexanes) to yield unreacted N-benzoylindole (0.53 g) and a yellow oil (o.49 g) in which crystals formed. The white crystals were washed with hexanes to yield 0.3 g of *cis-anti-cis* photoadduct 41, mp 123-126°C, ^{1}H-nmr δ($CDCl_3$) 8.30 (broad s, 1H), 7.44 (m, 5H), 7.4-7.0 (m, 3H), 3.94 (broad s, 1H), 3.32 (dd, J=7.5, 2.9 Hz, 1H), 2.84 (m, 1H), 2.66 (m, 1H), 1.80 (m, 2H), 1.62 (m, 2H), 1.31 (m, 2H), m/e(%) M^+=289(4.1), 221(46), 105(100), 77(20), calc. m/e=289.14666 (found 289.14654), ^{13}C NMR δ 25.4, 30.9, 32.4 (CH_2), 45.1, 46.2, 47.9, 63.7 (CH), 110.5, 118.3, 124.7, 126.4, 126.8, 127.6, 128.3, 128.4, 130.0, 137.5 ppm (aromatic C), 193.8 (quaternary C=O).

The remaining mother liquor was evaporated to yield 0.18 g of yellow oil determined to be mainly *cis-syn-cis* photoadduct 42, ^{1}H-nmr, δ($CDCl_3$) 8.30 (broad s, 1H), 7.44 (m, 5H), 7.4-7.0 (m, 3H), 4.70 (broad s, 1H), 4.05 (broad dd, J=7.5, 8.0 Hz, 1H), 3.08 (broad m, 2H), 1.80 (m, 2H), 1.62 (m, 2H), 1.31 (m, 2H), calc. m/e=289.14666 (found 289.14656), ^{13}C-nmr δ 27.1, 27.9, 28.9 (CH_2), 42.2, 43.4, 45.5, 61.7 (CH), 110.5, 118.3, 125.7, 126.4, 126.8, 127.3, 128.3, 128.4, 130.5, 137.5 ppm (aromatic C), 195.0 (quaternary C=O).

Reduction of N-benzoylindole-cyclopentene adducts 41 and 42

A sample (570 mg, 1.97 mMol) of the irradiation products obtained from irradiation of N-benzoylindole and cyclopentene which had been partially purified to remove unreacted N-benzoylindole was dissolved in dry ether (25 mL) and reduced with excess lithium aluminium hydride (121 mg, 318 mMol). After one hour the reaction was quenched by slow addition of water (50 mL) and the reaction mixture was extracted (3 X 50 mL) with ether. The ether extracts were washed with water, dried (K_2CO_3), and solvent removed to yield 534 mg of a green oil. T.l.c. (30% ether/70% hexanes) revealed the oil to be a mixture of three compounds with R_f 0.49, 0.63, and 0.70. The green oil was chromatographed on a column of silica gel (15% ether/85% hexanes) to yield 3 fractions. After removal of eluent the last fraction yielded 99 mg of light pink crystals of secondary amine 47, recrystallized from MeOH/H_2O, mp 95-96.5°C, ^{1}H-nmr δ($CDCl_3$) 7.00 (m, 2H), 6.68 (m, 2H), 3.94 (s, 1H), 3.72 (dd, J=7.5, 2.5 Hz, 1H), 3.33 (dd, J=7.6, 2.5 Hz, 1H), 2.68 (m, 2H), 1.78 (m, 4H), 1.48 ppm (m, 2H), ^{13}C-nmr δ 25.6, 31.8, 32.6 (CH_2), 47.2, 47.3, 49.1, 60.8 (CH), 109.9, 118.8, 124.4, 127.3 (aromatic CH), 134.1, 151.5 (quaternary C), ms m/e(%) M^+=185(19), 117(100), 90(33), calc. m/e=185.120449 (found 185.12049).

The second fraction yielded a red oil (50 mg) which crystallized from MeOH/H_2O to afford white crystals of secondary amine 48, mp 90-92°C, ^{1}H-nmr δ($CDCl_3$) 6.93 (m, 2H), 6.62 (m, 2H), 4.81 (s, 1H), 4.42 (dd, J=9.6, 9.0 Hz, 1H), 4.14 (dd, J=9.6, 9.2 Hz, 1H), 3.08 (m, 2H), 1.9-1.1 ppm (m, 6H), ^{13}C-nmr δ 26.6, 28.4, 28.8 (CH_2), 42.6, 45.0, 56.4 (CH), 109.1, 117.8, 126.0, 127.2 (aromatic CH), 130.0, 154.0 ppm (quaternary C), ms m/e(%) M^+=185(15), 117(100), 90(30), calc. m/e=185.120449 (found 185.120992).

The third fraction afforded 254 mg of a brown oil. A portion (60 mg) was chromatographed on preparative tlc plates (100% hexanes) to yield two bands. The first band gave 21 mg of a solid which was recrystallized from ether/hexanes affording white crystals of *cis-syn-cis* benzyl products 46, mp 57-58.5°C, ^{1}H-nmr δ($CDCl_3$) 7.22 (m, 5H), 6.91 (m, 2H), 6.55 (m, 1H), 6.32 (d, J=4 Hz, 1H), 4.31 (AB q, J=16 Hz, 2H), 4.30 (dd, J=9.4, 9.0 Hz, 1H), 4.11 (dd, J=9.4, 9.0 Hz, 1H), 3.01 (m, 2H), 1.71 (m, 2H), 1.40 ppm (m,4H), ^{13}C-nmr δ 27.8, 28.4, 28.7 (CH_2), 42.2, 43.4, 45.5, 62.0 (CH), 51.3 (benzyl CH_2), 105.4, 115.7, 125.8, 126.7, 127.3, 127.4, 128.2 (aromatic CH), 129.5, 138.6, 154.7 ppm (quaternary C), ms m/e(%) 275(3.4), 207(93), 91(100), calc. m/e=275.167399 (found 275.167344).

The second band yielded 14.4 mg of crystals recrystallized from ether/MeOH afforded *cis-anti-cis* benzyl product 45, mp 52-55°C, ^{1}H-nmr δ($CDCl_3$) 7.17 (m, 5H), 7.00 (m, 2H), 6.58 (m, 5H), 6.36 (d, J=4 Hz, 1H), 4.33 (AB q, J=15 Hz, 2H), 3.62 (dd, J=7.6, 2.5 Hz, 1H), 3.29 (dd, J=7.6, 2.7 Hz, 1H), 2.80 (d of t, J=7.0, 2.7 Hz, 1H), 2.68 (d of t, J=7.0, 2.5 Hz, 1H), 1.9-1.2 ppm (m, 6H), ^{13}C-nmr δ 25.4, 31.5, 32.6 (CH_2), 45.2, 45.3, 46.3, 65.6 (CH), 49.8 (benzyl CH_2), 105.5, 116.5, 124.1, 126.8, 127.44, 127.46, 128.22 (aromatic CH), 133.8, 138.6, 152.3 ppm (quaternary C), ms m/e(%) 275(9.2), 207(100), 91(96), calc. m/e=275.167399 (found 275.167344).

Irradiation of N-carboethoxyindole, 34, with cyclopentene

N-carboethoxyindole (2.87 g, 15.2 mMol) in 300 mL of benzene was irradiated in the presence of cyclopentene (16.25 g, 239 mMol) for 65 hours. The benzene was removed to yield 3.58 g of brown oil. G.c. analysis of the oil indicated *ca.* 30% conversion to 3 new products in a ratio of 1:1.24:6.34. G.c.-m.s. revealed parent ions for the three products to be m/e 189, 257 and 257 respectively. The first of these is isomeric with 34 and the latter two correspond to the adducts 51 and 52 produced from 34 with cyclopentene. A portion (300 mg) of the crude irradiation product was chromatographed on preparative tlc plates (silica gel, 50% ether/50% hexanes) and yielded three bands which were analyzed by g.c.-m.s.. The first band (166 mg) contained a mixture of N-carboethoxyindole and the two adducts 51 and 52 both of which had m/e(%) 257(3.0), 189(100), 73(32), indicative of 1:1 adducts. The second band was identified as indole, g.c-m.s., m/e $M^+ = 117$, and confirmed by coinjection. The third band (7.5 mg) was identified as 3-carboethoxyindole, mp 122-124°C (lit. mp 124°C), ^1H-nmr $\delta(CDCl_3)$ 8.68 (broad s, N-H), 8.18 (m, 1H), 7.93 (d, J=3 Hz, 1H), 7.30 (m, 3H), 4.40 (q, J=7 Hz, 2H), 1.40 ppm (t, J=7 Hz, 3H).

Hydrolysis and Decarboxylation of Photochemical Adducts 51 and 52

A sample (1.66 g) of the crude product obtained from irradiation of N-carboethoxyindole with cyclopentene was hydrolysed by refluxing in 25 mL of $MeOH/H_2O$ (2:1) saturated with KOH for three hours. The reaction was cooled and acidified with conc HCl, then refluxed for 20 minutes. The reaction mixture was cooled and extracted (5 X 50 mL) with ether. The extracts were combined and extracted (5 X 50 mL) with 10% HCl. The acid extracts were combined and washed with ether and then CH_2Cl_2 to remove any remaining indole. The acid extracts were then made basic with saturated NaOH and extracted (7 X 50 mL) into CH_2Cl_2. The organic extracts were washed with water, dried (Na_2SO_4) and solvent removed to afford 212 mg of white solid. G.c.-m.s. showed two peaks with m/e 185 in a ratio of 1:10. Isolation by column chromatography yielded 18 mg of indoline <u>48</u> (previously described), confirmed by g.c. coinjection and mp 90-91°C (MeOH/H_2O), and 190 mg of indoline <u>47</u> (previously described), confirmed by g.c. coinjection and mp 94-95°C (MeOH/H_2O). All spectral data were identical to the authentic samples.

<u>Irradiation of N-benzoylindole with cyclohexene</u>

N-Benzoylindole (2.54 g, 0.0115 Mol) was irradiated in 300 mL of benzene containing cyclohexene (8.5 g, 0.104 Mol) for 48 hours. The solution was filtered and solvent removed to yield 3.78 g of brown oil which was purified on a silica gel column (eluent 20% ether/80% hexanes) to give unreacted N-benzoylindole (1.28 g) and cycloadducts (0.95 g) which appeared as crystals in a yellow oil. Crystallization from CH_2Cl_2/ethyl acetate afforded 0.3 g of white crystals identified as *cis-syn-cis* adduct <u>54</u>, mp 170-171°C, ^{1}H-nmr δ($CDCl_3$) 8.28 (broad d, J=4 Hz, 1H), 7.44 (m, 5H), 7.20 (m, 3H), 4.72 (broad 2, 1H), 4.00 (dd, J=8.5, 9.0 Hz, 1H), 2.78 (broad s, 2H), 1.9-0.9 ppm (m, 8H), ^{13}C-nmr δ 20.9, 21.3, 22.2, 22.4 (CH2), 32.7, 38.8, 45.3, 61.0 (CH), 118.4, 124.2, 126.1, 127.1, 127.9, 128.3, 130.2 (aromatic CH), 134.6, 137.2, 146.6, 169.0, 205.7 ppm (quaternary C), m/e(%) 303(0.55), 221(26), 105(100), calc. m/e=303.162314 (found 303.162570).

The mother liquor (0.7 g) remained as an oil and was identified as mainly *cis-anti-cis* adduct 53, ^{1}H-nmr δ(CDCl$_3$) 8.28 (broad d, J=4 Hz, 1H), 7.44 (m, 5H), 7.20 (m, 3H), 4.63 (broad s, 1H), 3.56 (dd, J=7.7, 2.5 Hz,1H), 2.60 (m, 1H), 2.11 (m, 1H), 2.00 (m, 2H), 1.9-1.0 ppm (m, 6H), ^{13}C-nmr δ 21.2, 21.6, 22.0, 22.3 (CH2), 37.6, 39.8, 46.7, 63.7 (CH), 117.8, 126.0, 127.0, 129.3, 139.1, 134.0, 135.4, 136.3, 142.8, 144.7 (aromatic C), 197.2 ppm (quaternary C=O).

Reduction of *cis-syn-cis* Adduct 54

Adduct 54 (106 mg, 0.37 mMol) was treated with lithium aluminium hydride (50 mg) in 15 mL of dry ether for 3 hours. After quenching with water the reaction mixture was extracted (3 X 20 mL) with ether, the extracts washed with water, dried and solvent removed to yield 81.5 mg of yellow oil which t.l.c. showed to contain two components. These were separated as oils by preparative t.l.c..

The first of these (40.6 mg) was identified as amine 61, m/e(%) 289(3.5), 207 (100), 91(75), calc. m/e=289.183049 (found 289.183068), ^{1}H-nmr δ(CDCl$_3$) 7.61 (m, 1H), 7.15 (m, 5H), 7.00 (m, 1H), 6.59 (m, 1H), 6.38 (d, J=4 Hz, 1H), 4.38 (AB q, J=20 Hz, 2H), 4.36 (dd, J=8.5, 9.2 Hz, 1H), 4.06 (dd, J=8.5, 9.0 Hz, 1H), 2.78 (m, 1H), 2.66 (m, 1H), 1.50 (m, 4H), 1.24 ppm (m, 4H), ^{13}C-nmr δ 21.1, 21.3, 21.9, 22.6 (CH2), 34.6, 39.3, 45.4, 63.4 (CH), 51.2 (benzyl CH2), 105.4, 116.3, 125.6, 126.9, 127.6, 127.2, 128.4, 128.8, 131.2, 138.8 ppm (aromatic C).

The second component (9.2 mg) was identified as secondary amine 62, m/e(%) 199(2), 117(100), 90(30), calc. m/e=199.136099 (found 199.136103), ^{1}H-nmr δ(CDCl$_3$) 8.14 (broad s, 1H), 7.20-7.00 (m, 3H), 4.21 (broad s, 1H), 4.12 (s, N-H), 3.80 (ddd, J=8.7, 9.0, 1.0 Hz, 1H), 2.78 (m, 2H), 2.2-1.6 ppm (m, 8H),

^{13}C-nmr δ 25.2, 26.4, 32.0, 32.7 (CH2), 34.3, 39.7, 44.6, 52.4 (CH), 111.3, 119.4, 119.7, 121.32, 121.6, 122.2 ppm (aromatic CH).

Irradiation of N-carboethoxyindole with cyclohexene

N-Carboethoxyindole (2.2 g, 0.01 Mol) was irradiated in 300 mL of benzene and cyclohexene (15 g, 0.183 Mol) for 48 hours. Removal of the benzene afforded 3.55 g of brown oil. g.c. analysis revealed 5 new products in a ratio of 1:1.1:2:142:100. The most minor peak showed m/e=189 by g.c.-m.s. and coinjection with authentic sample confirmed this product to be 3-carboethoxyindole. The other 4 peaks all possessed parent ions of m/e=271 indicative of 1:1 photoadducts between 34 and cyclohexene. Characterization of these compounds was not carried any further.

Hydrolysis and decarboxylation of Photoadducts from Irradiation of N-Carboethoxyindole with Cyclohexene

A sample (6 g) of the crude mixture of products from irradiation of N-carboethoxyindole with cyclohexene was hydrolysed in 75 mL of MeOH/H_2O (2:1) saturated with KOH by refluxing for 3 hours. The reaction mixture was then acidified (conc HCl) and refluxed another 20 minutes. After cooling the reaction mixture was washed sequentially with ether and CH_2Cl_2 and made basic by addition of aqueous NaOH. The basified solution was then extracted with CH_2Cl_2. The organic extracts were washed with H_2O, dried (Na_2SO_4), and solvent removed to yield 4.14 g of brown oil. G.c. revealed 3 peaks with ratios of 1:17:14. The major portion of the oil (4 g) was then chromatographed (silica gel column, 10% ether/90% hexanes) to yield 3 fractions. The first fraction (67 mg) afforded yellow crystals identified as secondary amine 64, mp 69-72°C (ether/hexanes), m/e(%) 199(7.5), 156(9), 117(100), calc. m/e=199.13601 (found 199.13562), ^{1}H-nmr δ($CDCl_3$) 6.97 (m, 2H), 6.63 (m, 2H), 4,58 (dd, J=6, 4 Hz, 1H), 3.98 (broad s, N-H), 3.66 (dd, J=8, 6 Hz, 1H), 2.20-1.90 (m, 2H), 1.90-0.80 ppm (m, 8H).

The second fraction (0.93 g) was isolated as an oil and identified as secondary amine 62, m/e(%) 199(31), 156(51), 117(100), calc. m/e=199.13601 (found 199.13582), ^{1}H-nmr δ($CDCl_3$) 7.0 (m, 2H), 6.63 (m, 2H), 4.42 (dd, J=8, 8 Hz, 1H), 4.04 (dd, J=8, 8 Hz, 1H), 3.88 (broad s, N-H), 2.80 (m, 1H), 2.60 (m, 1H), 2.3-0.8 ppm (m, 8H).

The third fraction (0.64 g) was isolated as a brown solid. Recrystallization from ether/hexanes afforded crystals of secondary amine 66, mp 73-75°C, m/e(%) 199(25), 156(48), 117(100), calc. m/e=199.13601 (found 199.13562), ^{1}H-nmr δ($CDCl_3$) 7.1 (m, 2H), 6.74 (m, 2H), 4.18 (dd, J=8, 4 Hz, 1H), 3.65 (broad s, NH), 3.60 (dd,J=8, 2 Hz, 1H), 2.8-2.25 (m, 2H), 2.25-1.00 ppm (m, 8H).

Irradiation of N-benzoylindole with cycloheptene

N-Benzoylindole (1.94 g, 8.79 mMol) was irradiated in 300 mL of benzene with cycloheptene (8.7 g, 90.5 mMol) for 22 hours. Removal of benzene afforded 2.5 g of brown oil. G.c. analysis showed approximately 40 % conversion of the N-benzoylindole to products in a ratio of 1:21:0.05. The oil was hydrolysed to remove unreacted 5 by stirring in 125 mL of $MeOH/H_2O$ (2:1) saturated with NaOH at 25°C for 3 hours. The mixture was extracted with ether and solvent removed to yield 1.1 g of brown oil. The oil was then steam distilled to remove remaining indole and the aqueous stillpot extracted with ether to give 0.7 g of yellow oil. T.l.c. showed two components R_f 0.15 and 0.10 (silica gel, 30% ether/70% hexanes). The oil (122 mg) was chromatographed by preparative t.l.c. (silica gel,40% ether/60% hexanes) and yielded two bands. The first band (5 mg) afforded an oily film and was assigned to structure 66, m/e(%) 317(4), 221(100), 105(14), calc. m/e=317.177984 (found 317.178169), ^{1}H-nmr δ($CDCl_3$) 8.25 (m, 1H), 7.80-7.45 (m, 5H), 7.31 (m, 2H), 7.15 (d, J=4 Hz, 1H), 4.13 (dd, J=8, 2.5 Hz, 1H), 3.59 (dd, J=8, 3 Hz, 1H), 2.8-2.35 (m, 2H), 2.2-1.2 ppm (m, 10H).

The second band (95 mg) yielded an oil assigned to structure 67, m/e(%) 317(0.25), 221(34), 117(100), calc. m/e=317.177984 (found 317.1778534), ^{1}H-nmr δ($CDCl_3$) 8.28 (broad s, 1H), 7.44 (m, 5H), 7.30-6.90 (m, 4H), 4.43 (broad s, 1H), 3.46 (dd, J=9, 3 Hz, 1H), 2.54 (broad m, 1H), 2.42 (m, 1H), 2.0-1.0 ppm (m, 10H).

Irradiation of N-benzoylindole with *cis*-2-butene

A solution of *cis*-2-butene in benzene was prepared by condensing *cis*-2-butene (5 mL) into benzene (5 mL) previously purged with nitrogen. To this was added N-benzoylindole (192 mg, 0.87 mMol) and the solution was irradiated for 60 hours. G.c. revealed 4 products in a ratio of 7:21:68:4. G.c.-m.s. confirmed that the products were 1:1 cycloadducts of 5 all with parent ion m/e 277. First g.c. product m/e(%) 277(1.7), 221(57), 105(100), second g.c. product m/e 277(2.0), 221(59), 105(100), 77(25), third g.c. product 277(1.7), 221(60), 105(100), 77(25), fourth g.c. product m/e 277(2.0), 221(60), 105(100), 77(25).

A sample of the reaction mixture was partially chromatographed to give a mixture of the four adducts. The ^{1}H-nmr spectrum of the mixture of adducts yielded a broad singlet at 4.3 ppm and was assigned to superimposed signals corresponding to H_a in all the stereoisomers. Similarly, multiplets in the range 2.7-1.9 ppm were assigned to H_c and H_d of all the isomers present. The signal assigned to H_b of the most prevalent isomer was seen as a doublet of doublets at 3.97 ppm, J=8 and 3 Hz. That corresponding to H_b of the second most prevalent isomer was seen at 3.48 ppm as a triplet, J=8 Hz. The methyl substituents of both major isomers were seen as overlapping doublets at 1.16 and 0.92 ppm, J=6 Hz.

Irradiation of N-benzoylindole with *trans*-2-butene

A solution of *trans*-2-butene in benzene was prepared by condensing *trans*-2-butene (5 mL) into benzene (5 mL) previously purged with nitrogen. To this solution was added N-benzoylindole (199 mg, 0.9 Mol); the reaction solution was sealed via septum, and irradiated for 44 hours. G.c. revealed formation of 4 products in a ratio of 2.1:21:74:1.1:. The four products were confirmed by g.c. coinjection to be the same as the irradiation products obtained from N-benzoylindole and *cis*-2-butene. First g.c. product m/e(%) 277(1.7), 221(57), 105(100), 77(23), second product m/e 277(3), 221(58), 105(100), 77(23), third product m/e 277(3), 221(58), 105(100), 77(24), fourth product m/e 277(3), 221(60), 105(100), 77(24). The ^{1}H-nmr spectrum of the mixture of adducts following their separation from starting material and byproducts by chromatography was identical with that of the mixture of the adducts obtained from the irradiation of **5** with the *cis*-alkene.

Preparation of *cis*-4-octene

A sample of 4-octyne (12.2 g, 0.11 Mol) was hydrogenated at one atmosphere using Lindlar's catalyst (0.8 g) and quinoline (10 mL) in pentane (300 mL) until g.c. analysis indicated 100% conversion of the octyne. The pentane mixture was filtered, washed with 10% HCl and H_2O and dried over anhydrous Na_2SO_4. Removal of solvent via fractional distillation and subsequent distillation yielded 8.1 g (67%) of *cis*-4-octene (94% pure by ^{1}H-nmr analysis), bp 122°C, ^{1}H-nmr δ($CHCl_3$) 5.36 (m 2H), 2.02 (q, J=4 Hz, 4H), 1.38 (m, 4H), 0.92 ppm (t, J=4 Hz, 6H), ^{13}C-nmr δ 129.9, 29.5, 23.1, 13.9 ppm.

Irradiation of N-benzoylindole with *trans*-4-octene

A solution of N-benzoylindole (1 g, 4.5 mMol) in benzene (20 mL) containing *trans*-4-octene (9 g, 80 mMol) was irradiated for 311 hours. Removal of benzene yielded 1.18 g of brown oil; g.c. indicated 3 products in a ratio of 1:32:32 and 36% conversion of **5**. The oil was chromatographed (silica gel, 5% ether/95% hexanes) to remove N-benzoylindole and gave 394 mg of yellow oil. G.c.-m.s. of the oil showed three products all with parent ions of m/e 333 indicative of 1:1 photoadducts of **5** and octene. First g.c. product m/e(%) 333(0.81), 221(78), 105(100), second product m/e 333(1.7), 221(80), 105(100), third product m/e 333(1.1), 221(82), 105(100). In the ^{1}H-nmr spectrum of the mixture a broad singlet at 4.42 ppm was assigned to H_a of both major isomers. Signals between 2.6 and 1.9 ppm were assigned to H_c and H_d of both major isomers also. A signal at 4.03 (t, J= 8 Hz) was assigned to H_b of one of the major isomers and a signal at 3.54 ppm (dd, J=8, 4 Hz) was assigned to H_b of the second major isomer.

Irradiation of N-benzoylindole with *cis*-4-octene

N-Benzoylindole (2.0 g, 0.01 Mol) was irradiated in benzene (60 mL) with *cis*-4-octene (11.0 g, 0.09 Mol) for 400 hours. Removal of benzene afforded 2.14 g of brown oil which contained three products (7% conversion) by g.c. analysis in a ratio of 1:5:5 with retention times equivalent to those of the N-benzoylindole-*trans*-4-octene irradiation products (confirmed by coinjection). The oil was chromatographed (silica gel, 5% ether/95% hexanes) to yield unreacted N-benzoylindole and 0.51 g of yellow oil. G.c.-m.s. of the oil showed three products all with parent ions of m/e 333 indicative of 1:1 photoadducts. First g.c. product m/e(%) 333(1.1), 221(78), 105(100), second product m/e 333(1.5), 221(75), 105(100), third product m/e 333(1.5), 221(79), 105(100). The ^{1}H-nmr spectrum of the mixture of adducts was identical with that of the products of 5 with *trans*-octene.

Schenk Isomerization Studies

Solutions (5.00 mL) of N-benzoylindole (19.6 mg, 0.0886 mMol) in benzene containing either *cis*-4-octene (3.03 g, 0.0266 Mol) or *trans*-4-octene (2.8 g, 0.026 Mol) were prepared and samples (3.00 mL) were irradiated with 313 ± 2 nm light from a 100 W high pressure mercury lamp. The light intensity was determined by actinometry (74) with azoxybenzene. The amount of isomerized alkene was determined by g.c. (10 injections) with methylcyclohexane as a calibrated internal standard.

The results for the addition of *cis*-4-octene to 5 are given in table 4 in which the amount of light absorbed is given in μEinsteins and the increase in [*trans*-4-octene] is given as the change in moles of *trans*-4-octene due to the 6% *trans*-4-octene impurity in the starting *cis*-4-octene. Conversion of the *cis*-4-octene to *trans*-4-octene was kept below 5% over a 10 hour irradiation period to ensure that the *cis*-4-octene was the adding alkene. The results are also shown in figure 5 (chapter 2).

TABLE 4

AMOUNT OF *TRANS*-4-OCTENE FORMED ON IRRADIATION OF 5 WITH *CIS*-4-OCTENE

Light Absorbed (μEinsteins)	Δ[*trans*-4-octene] (μMol)
0	7.13
53	7.21
133	7.29
211	7.21
334	7.41
450	7.47
560	7.57
676	7.63
855	7.79

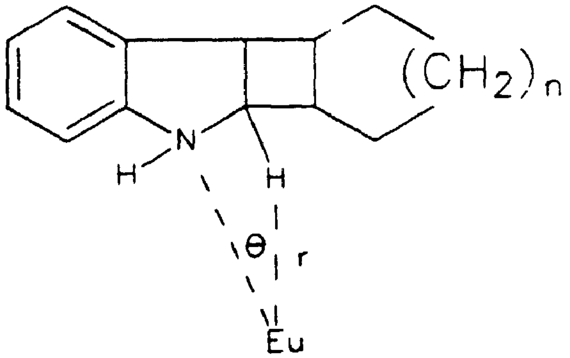
For the addition of *trans*-4-octene (99.9% pure) to 5 no isomerized *cis*-4-octene was detected after 100 hours of irradiating and 18% conversion of 5 to 2+2 photocycloadducts.

MM2 Model Studies

Indane models 49, 50, 57-60 were designed and the coordinates of the atoms approximated from molecular models. These coordinates were entered into a Computer Assisted Design (CAD) program, called Chemcad (38), using a XT type computer. The coordinates were optimized via MM2 calculations. Optimized coordinates were used to determine dihedral angles and intra-atomic distances. Predicted changes in chemical shifts due to $Eu(fod)_3$ treatment were determined using the formula:

$$\Delta\delta = K(3\cos^2\theta - 1)/r^3$$

where r is the distance from the complexing lanthanide to the shifting proton, H_a-H_d, θ is the angle between the Eu-N bond (length approximated at 2.7 A°) and the line between Eu and the shifting proton (as determined by MM2 calculation), and K is a proportionality constant.



The predicted changes in the chemical shift of the methine cyclobutane protons for each isomer are expressed as the change in chemical shift relative to the change in chemical shift for H_a. The results are shown in Table 2 (chapter 2) and further illustrated in Figures 3 and 4.

The observed changes in chemical shift for the methine cyclobutane protons of the amine adducts 47, 48, 62, 63 and 64 were induced by small (5 mg) stepwise additions of $Eu(fod)_3$. After each addition of $Eu(fod)_3$ to an amine adduct (*ca.* 50 mg) a 200 MHz ^{1}H-nmr spectrum was recorded and the absolute change in the chemical shift for each methine proton was measured as the difference in chemical shift from its original (no $Eu(fod)_3$) chemical shift for each proton. The change in chemical shifts, $\Delta\delta$, were plotted as a function of the change in chemical shift of H_a ($\Delta\delta H_a$). The plots for amine adducts 47 and 48 are shown in Figures 3 and 4. The slopes of these lines yielded the observed relative changes in chemical shift for each methine cyclobutane proton of each amine adduct and are given in Table 2.

Preparation of Vinylcyclopropane

Cyclopropyl methyl ketone was prepared from acid hydrolysis of α-acetyl-γ-butyrolactone and was converted to its tosylhydrazone by literature procedures (51). A suspension of sodamide in liquid ammonia was prepared by dissolution of sodium (3.5 g, 152.2 mMol) in liquid ammonia (100 mL) containing ferric nitrate (0.2 g). Decalin (100 mL) was added and the ammonia was allowed to evaporate. The tosylhydrazone of cyclopropyl methyl ketone (5.2 g, 21 mMol) was added and the mixture was heated to 190°C. The colourless liquid which distilled out of the reaction mixture was cooled using an efficient dry ice condenser and redistilled (bp. *ca.* 40°C) to yield a mixture of vinyl cyclopropane and 1-methylcyclobutene (1.0 g, 70 %) in a ratio of 95:5 as determined by ^{1}H-nmr spectroscopy. For vinyl cyclopropane: ^{1}H-nmr δ($CDCl_3$) 0.38 (m, 2H), 0.68 (m, 2H), 1.38 (m, 1H), 4.76 (dd, J=10, 2 Hz, 1H), 4.97 (dd, J=17, 2 Hz, 1H), 5.25 ppm (ddd, J=17, 10, 2 Hz, 1H); ^{13}C-nmr 6.67, 14.76, 111.5, 142.6 ppm. For 1-methylcyclobutene: ^{1}H-nmr δ($CDCl_3$) 1.64 (m, 3H), 2.27 (m, 2H), 2.36 (m, 2H), 5.55 ppm (m, 1H); ^{13}C-nmr 16.88, 26.47, 32.67, 146.5 ppm.

Irradiation of N-Benzoylindole with Tetramethylethylene

N-Benzoylindole (26 mg, 0.118 mMol) and tetramethylethylene (0.8 g, 9.5 mMol) were dissolved in benzene (2 mL), purged with nitrogen and sealed with a septum cap. This solution was irradiated with Pyrex/water filtered light and the reaction progress was monitored by g.c.. After 87 hours g.c. indicated that a single product had formed in 61 % yield. G.c.-m.s. showed the product peak to possess a molecular ion, M^+, m/e=305 indicative of 1:1 adducts of 5 with tetramethylethylene. The solvents were removed *in vacuo* and preparative t.l.c. (silica gel, 25% ether/75% hexanes) was performed on the irradiation mixture (40 mg). Two bands were isolated and characterized. The first band (15 mg) was identified as N-benzoylindole, 5, and this was verified by g.c. coinjection as well as ^{1}H-nmr spectroscopy. The second band yielded 20 mg of an oily solid and was identified as 95, ^{1}H-nmr δ ($CDCl_3$) 8.36 (broad s, 1H), 7.45 (m, 5H), 7.08 (m, 3H), 4.60 (broad s, 1H), 3.56 (d, J=8.0 Hz, 1H), 1.61 (s, 3H), 1.20 (broad s, 3H), 0.81 (s, 3H), 0.79 (s, 3H), m/e(%) M^+=305(1.0), 221(44), 105(100), 77(28), calculated M^+=305.17794 (found 305.1777).

Irradiation of N-Benzoylindole with 1,6-heptadiene

A solution of N-benzoylindole (53.1 mg, 0.24 mMol) and 1,6-heptadiene (124.4 mg, 1.28 mMol) in benzene (6 mL) was deoxygenated by purging with nitrogen and irradiated at room temperature using water and Pyrex filtered light from a medium pressure mercury lamp for 68 hours at which time g.c. indicated *ca.* 75% conversion of the N-benzoylindole. Four products were observed in relative amounts (in order of increasing retention times) of 0.3:99.6:0.2:0.1. G.c.-m.s. indicated all four products to be 1:1 adducts of N-benzoylindole and 1,6-heptadiene (M^+=317). The solvent was removed under reduced pressure to yield a yellow oil (60.3 mg) which was chromatographed on preparative tlc plates (silica gel) doubly eluted with 30% ether/70% hexanes to give 2 fractions. The least polar fraction was identified as N-benzoylindole (12 mg) and the second fraction (47 mg) was identified as predominantly (99 %) cycloadduct 89a, ^{1}H-nmr δ($CDCl_3$) 8.26 (broad s, 1H), 7.44 (m, 5H), 7.16 (m, 3H), 5.79 (m, 1H), 4.98 (m, 2H), 4.60 (broad s, 1H), 3.58 (broad d, J=8, 2 Hz, 1H), 2.52 (m, J=12, 1-2 Hz, 2H), 2.26 (m, J=1-2 Hz, 1H), 2.08 ppm (m, 6H), g.c.-m.s. calculated M^+=317.17796 (found 317.1781), m/e(%) 317(3), 221(40), 105(100). The other three adducts were undetectable by ^{1}H-nmr; however, g.c.-m.s. gave mass spectral data in order of increasing retention times; first minor product m/e(%) M^+=317(1.0), 221(49), 105(100); second minor product M^+=317(6.0), 221(4), 105(57), 91(100); Third minor product m/e(%) 317 (M^+, 21), 221 (6), 105(96), 91(100). This fraction was then dissolved in benzene (2 mL) and hydrogenated over PtO_2 at 1 atmosphere for 1 hour. G.c. showed 4 product peaks with retention times slightly slower than that of the starting mixture. G.c. coinjection confirmed that 3 new products had formed in a % ratio of 0.3:99:0.2 and that the one minor (0.1%) product remained unchanged. G.c.-m.s. showed that the new products have parent ions $M^+=319$ indicative of hydrogenation products and the unchanged minor product with $M^+=317$.

Irradiation of N-benzoylindole with Vinylcyclopropane

N-Benzoylindole (1.0 g, 4.5 mMol) was dissolved in benzene (4 mL) and purged with nitrogen. To this solution vinylcyclopropane (2.2 mL, 1.54 g, 22.6 mMol) was added, the solution was sealed with a septum cap and irradiated at room temperature using water and Pyrex filtered light from a medium pressure mercury lamp for 122 hours at which time g.c. indicated approximately 10% conversion of the N-benzoylindole. The g.c. indicated that 7 products were formed. Removal of the solvent gave 0.8 g of a yellow oil which was not characterized further. This crude irradiation mixture was hydrolysed with 5 mL of concentrated KOH in methanol/H_2O (3:1 by vol) to remove unreacted 5. The hydrolysed mixture was extracted into (50 mL) ether, dried (Na_2SO_4), and solvent removed to yield 352 mg of yellow oil. G.c. showed the 7 unreacted products still intact and conversion of the N-benzoylindole to indole (confirmed by coinjection). The oil was steam distilled for 45 minutes after which the stillpot was extracted (4 X 50 mL) with ether, dried (Na_2SO_4), and solvent removed to give 130 mg of an oily brown solid. G.c. indicated 5 major products in a ratio of 7:15:4:24:50 accounting for 99% of the total products, and 2 minor peaks accounting for less than 1%. G.c.-m.s. showed all peaks to possess a parent ion $M^+ = 289$, consistent with the formation of 1:1 adducts of 5 and vinylcyclopropane.

This mixture of 5 adducts (35 mg) was then separated by H.P.L.C. (eluent 25% diethyl ether/75% n-hexane at 1.5 mL/min, $\lambda_{det} = 320$ nm) using a normal phase silica semi-preparative steel column to yield three product containing fractions which were analyzed by g.c., g.c.-m.s., and ^{1}H-nmr spectroscopy. Fractions are described in order of increasing retention times. Fraction 1 yielded 3.5 mg of a colourless oil which by g.c. showed 3 peaks with retention times identical to the first three peaks in the starting mixture. G.c.-m.s. revealed all three peaks to have M^+ with m/e 289. The ^{1}H-nmr spectrum of the mixture indicated that the two major components were adducts of N-benzoylindole and 1-methylcyclobutene, the latter being a contaminant in the vinylcyclopropane. The third component in the mixture showed cyclopropyl signals at 0.50 and 0.86 ppm and was tentatively assigned to isomer 78 or 79. G.c.-m.s. yielded molecular ions for each compound of $M^+ = 289.1462$, $M^+ = 289.1456$, and $M^+ = 289.1462$ (calculated $M^+ = 289.1466$ for all three compounds).

Fraction 2 yielded 2.1 mg of a clear colourless oil which g.c. showed to be a single species (99% pure). This was identified as 79a. g.c.-m.s. gave $M^+ = 289$, m/e(%) 289(2), 221(20), 105(100). ^{1}H-nmr δ($CDCl_3$) 7.5-6.7 (m, 9H), 4.60 (broad s, 1H), 3.70 (broad dd, J=8, 2.5 Hz, 1H), 2.50 (m, 1H), 2.2 (m, 2H), 1.7 (m, 1H), 0.98 (m, 1H), 0.51 (dd, J= 9, 2 Hz, 2H), 0.20 ppm (dd, J=9, 1-2 Hz, 2H). This structure was also confirmed by ^{1}H-^{1}H decoupling experiments.

The last (third) fraction yielded 10 mgs of an oily solid whose g.c. indicated to be the major product of the mixture (50% of mixture). G.c.-m.s. gave

M^+ =289.1462 (calc. 289.1466). ^{1}H-nmr δ($CDCl_3$) 7.5-6.7 (m, 9H), 5.6 (broad, 2H), 4.88 (broad s, 1H), 3.71 (m, 1H), 2.7-1.7 ppm (3 multiplets, 6H). The structure was assigned to 83 and confirmed by ^{1}H-^{1}H decoupling experiments.

Preparation of Hydrogen Selenide

Hydrogen selenide, H_2Se, was prepared under nitrogen by slow addition of distilled water (20-30 mL) to freshly prepared aluminum selenide (1-2 g), Al_2Se_3 (76). The gas was condensed (acetone/dry ice) directly into the irradiation vessel or bubbled through the irradiation solution to saturation. Aluminum selenide was prepared according to literature procedures (77). Pure, dry aluminum powder (6 g) was ground together with dry selenium metal powder (10 g). Half of this mixture was transferred a thick walled porcelain crucible in a fumehood and the mixture was ignited with a small burning magnesium strip. The reaction was immediately covered (asbestos wire gauze) and small amounts (1 g) of the Al/Se mixture were added every ten seconds to the burning reaction followed by covering until all the unreacted mixture was consumed. The covered reaction was allowed to cool (45 min.) and then the crude Al_2Se_3 was removed and crushed with a mortar and pestle into small grey chunks. The Al_2Se_3 was transferred into a vial and stored in a desiccator until needed.

Irradiation of N-Benzoylindole-cyclopentene with Hydrogen Selenide

N-Benzoylindole, 5 (0.52 g, 2.34 mMol), was dissolved in benzene (5 mL) and purged with nitrogen. This solution was then purged for 15 minutes with hydrogen selenide under nitrogen. A small portion of this solution was dissolved in $CDCl_3$ and the 200 MHz ^{1}H-nmr spectrum was recorded. The signal due to hydrogen selenide could be seen at *ca.* -1.2 ppm and was integrated against the total number of protons for 5. This allowed for an estimation the H_2Se concentration to be *ca.* 0.5 M. To the main benzene solution cyclopentene (5 mL, 5.7 M) was added. A small aliquot was taken as a dark reaction control and the remainder was irradiated for 13.5 hours. An identical solution was prepared without the addition of H_2Se and irradiated along side the treated solution.

G.c analysis of the dark reaction showed no conversion of the starting materials. Analysis by g.c. of the untreated irradiation performed in the absence of H_2Se showed typical product formation as described previously for the irradiation of N-benzoylindole-cyclopentene. The g.c. ratio of the cycloadducts to 5 was 1:1 after 1 hour. G.c. analysis of the mixture obtained by irradiation of the solution containing H_2Se showed no formation of cycloadducts but indicated the formation of 4 products in a g.c. ratio of 0.9:1:1:0.25; accounting for 50% conversion (based on uncalibrated g.c. ratios) of the starting N-benzoylindole had occurred. The irradiation solution was washed with saturated sodium bicarbonate solution (to remove unreacted H_2Se) and distilled water. The organic layer was then dried (Na_2SO_4) and solvent removed *in vacuo* to yield 0.6 g of a cloudy red oil (some Se present). The components of this oil were separated by preparative t.l.c. (30% ether/70% hexanes) to yield five fractions.

The first fraction (140.9 mg) corresponding to the most volatile g.c. product was identified as 133, m/e(%) M^+=218(10), 152(46), 69(100) and had M^+=218.057592, calc. 218.057375. ^{1}H-nmr $\delta(CDCl_3)$ 3.24 (quin, 2H), 2.06 (m, 4H), 1.80 ppm (m, 12H).

The second fraction (2 mg) corresponding to the second most volatile g.c. product was identified as <u>136</u>, m/e(%) M^+=289(26), 105(100), 78(32) and had M^+=289.14640, calc. 289.146664. ^{1}H-nmr δ($CDCl_3$) 7.70 (d, J=8 Hz, 1H), 7.61-7.30 (m, 5H), 7.05 (t, J=8 Hz, 1H), 6.87 (t, J=8 Hz, 1H), 6.65 (d, J=8 Hz, 1H), 6.45 (s, 1H), 3.48 (quin, J=8 Hz, 1H), 2.03 (m, 2H), 1.61 ppm (m, 6H). The structure was confirmed by a 2-dimensional homonuclear correlation experiment.

The third fraction (122 mg) corresponding to the least volatile g.c. product was identified as starting indole, <u>5</u> (previously characterized), and confirmed by g.c. coinjection with authentic sample of <u>5</u>.

The fourth fraction (54.3 mg) was identified as <u>135</u>, m/e(%) M^+=291(4), 221(32), 105(100), 78(35) and had M^+=291.16399, calc. 291.162314. ^{1}H-nmr δ($CDCl_3$) 8.20 (broad s, 1H), 7.8-6.8 (m, 8H), 6.26 (m, 1H), 4.76 (broad t, J=8 Hz, 1H), 3.20 (ddd, J=16, 8, 2 Hz, 1H), 2.75 (dd, J= 16, 2 Hz, 1H), 2.20 (broad m, 1H), 1.90-0.80 ppm (broad m, 8H). The structure was confirmed by ^{1}H-^{1}H decoupling experiments.

The fifth fraction (30.9 mg) was identified as <u>134</u>, m/e(%) M^+=223(42), 105(100), 77(44) and has a M^+=223.09951, calc. 23.09971. ^{1}H-nmr δ($CDCl_3$) 7.5 (m, 5H), 7.2-6.8 (m, 4H), 4.05 (t, J=8.8 Hz, 2H), 3.10 ppm (t, J=8.8 Hz, 2H). This structure was confirmed by ^{1}H-^{1}H decoupling experiments.

<u>Preparation of 3,3-Dimethylacrylic Acid Dimethyl ester, 140</u>

A solution of 3-methylbutenoic acid (60 g, 0.6 Mol) and toluenesulfonic acid (0.5 g) in methanol was refluxed for 24 hours. The reaction was then diluted with diethyl ether (1 L) and washed with a saturated solution of sodium bicarbonate.

The ether extracts were washed with distilled water and dried ($MgSO_4$), and solvent removed to yield 60 g (88%) of crude ester. The ester was fractionally distilled to yield 58 g of pure (99.9 % by g.c. analysis) ester 140, bp 60°C (40 mm of Hg), lit. bp 72-74°C (50 mm Hg), ^{1}H-nmr δ($CDCl_3$) 5.55 (m, 1H), 3.55 (s, 3H), 2.06 (s, 3H), 1.77 ppm (s, 3H).

Irradiation of N-Benzoylindole with 3,3-Dimethylacrylic acid methyl ester

A solution of N-benzoylindole (250 mg, 1.13 mMol) with 3,3-dimethylacrylic acid methyl ester, 140, (3.5 g, 30.7 mMol, 6.1 M) in benzene (5 mL, N_2 purged) was prepared and irradiated for 78 hours. The reaction was followed by g.c. and showed growth of four products whose g.c. ratio of 4.6:37.7:45.2;13.1 remained unchanged with product formation. The above irradiation time led to a g.c. conversion of 78% g.c-m.s. of the irradiation solution gave molecular parent ions for all four products of m/e=335 indicative of 1:1 photoadducts. The solvent was removed *in vacuo* to yield 251 mg of a yellow oil. A small portion (100 mgs) of this oil was chromatographed using preparative t.l.c. (30% ether/70% hexanes) to three fractions.

The first fraction (18.1 mg) corresponding to the second most abundant isomer was identified as 141, m/e(%) M^+=335(1.0), 221(45), 105(100), 77(28) and had M^+=335.1498, calc. 335.15213. ^{1}H-nmr δ($CDCl_3$) 8.30 (broad s, 1H), 7.5-7.0 (m, 8H), 4.69 (broad d, J=8.0 Hz, 1H), 4.21 (dd, J=8, 4 Hz, 1H), 3.67 (s, 3H), 2.75 (d, J=4 Hz, 1H), 1.1 (s, 3H), 0.9 ppm (broad s, 3H). This structure was confirmed by ^{1}H-^{1}H decoupling experiments.

The second fraction (25.6 mg), corresponding to the major isomer, was identified as 143, m/e(%) M^+=335(1.3), 221(30), 105(100), 77(30) and had M^+=335.1523, calc. 335.15213. ^{1}H-nmr δ($CDCl_3$) 8.15 (broad s, 1H), 7.5-7.0 (m, 8H), 4.90 (t or dd, J=8, 6 Hz, 1H), 3.65 (d, J=8 1H), 3.45 (s, 3H), 2.91 (dd, J=6, 1 Hz, 1H), 1.2 (s, 3H), 1.0 ppm (s, 3H). This structure was confirmed by ^{1}H-^{1}H decoupling. experiments. The fourth isomer was unisolatable and tentatively assigned to 145.

The third fraction (3.5 mg), corresponding to the minor adduct, was identified as 142, m/e(%) M^+=335(1.5), 221(42), 105(100), 77(30) and had M^+=335.1525, calc. 335.15213. ^{1}H-nmr δ($CDCl_3$) 8.05 (broad s, 1H), 7.6-7.0 (m, 8H), 4.92 (broad s, 1H), 3.68 (d, J=8.0 Hz, 1H), 3.55 (s, 3H), 2.94 (dd, J=6,0.5 Hz, 1H), 1.70 (broad s, 3H), 1.49 ppm (s, 3H). This structure was confirmed by ^{1}H-^{1}H decoupling experiments. The most minor isomer was contained in small (<5%) amounts in each fraction and could not be isolated in high purity.

Irradiation of N-benzoylindole and 3,3-Dimethylacrylic acid methyl ester with Hydrogen Selenide

N-Benzoylindole, 5 (1.3 g, 5.9 mMol), was dissolved in benzene (25 mL) and purged with nitrogen. This solution was then purged for 15 minutes with hydrogen selenide under nitrogen. A small portion of this solution was dissolved in $CDCl_3$ and the 200 MHz ^{1}H-nmr spectrum was recorded. The signal due to hydrogen selenide could be seen at *ca.* -1.2 ppm and was integrated against the total number of protons for 5. This allowed for an estimation of the H_2Se

concentration to be *ca.* 0.52 M. To the bulk of the solution was added 3,3-dimethylacrylic acid methyl ester (15 g, 0.144 Mol, 3.6 M). A small aliquot was taken as a dark reaction control and the rest of the solution was irradiated for 48 hours. An identical solution was prepared without the addition of H_2Se and irradiated along side the treated solution. It showed a 40% g.c. conversion (uncalibrated) of 5 to the 2+2 photocycloadducts previously described.

G.c analysis of the dark reaction showed no change from the starting materials and analysis of the irradiation performed in the absence of H_2Se showed typical product formation as described previously. G.c. analysis of the irradiation mixture treated with H_2Se indicated no formation of cycloadducts and showed formation of 3 products in a g.c. ratio of 1:1:1, accounting for 31% conversion of the starting N-benzoylindole, as determined by uncalibrated g.c. ratios, after 48 hours. The irradiated solution was washed with saturated aqueous sodium bicarbonate solution (to remove unreacted H_2Se) and then distilled water. The organic layer was dried (Na_2SO_4) and solvent removed *in vacuo* to yield 1.5 g of a yellow oil. The oil was applied to a silica gel (60-200 mesh) column and eluted with 15%/ether/85% hexanes. Fractions were collected, analyzed by g.c., combined, and characterized.

The first set of fractions (650 mg) was identified as starting indole, 5 (previously characterized), and confirmed by g.c. coinjection with authentic sample of 5. The second set of fractions (90 mg) was identified as 145a, m/e(%) M^+=337(7.6), 222(26), 105(100), 77(26) and had M^+=337.16699, calc. 337.167782. ^{1}H-nmr δ($CDCl_3$) 7.5 (m, 5H), 7.2-6.8 (m, 4H), 5.05 (broad t, 1H), 3.19 (m, 2H), 3.10 (s, 3H), 2.0 (broad s, 2H), 1.0-0.8 ppm (broad s, 6H). This structure was confirmed by ^1H-^1H decoupling experiments. A sample of 145a (36 mg, 0.11 mMol) was refluxed in 5mL MeOH/H_2O (3:1) containing KOH (2g) for 20 minutes after which 5 mL of distilled water was added and the basic mixture washed (2 X 10 mL) with CH_2Cl_2. The aqueous layer was then acidified (conc. H_2SO_4) to pH 4 and the cloudy mixture was extracted (3 X 10 mL) with CH_2Cl_2. The organic extracts were dried ($MgSO_4$) and solvent removed to yield 26.2 mg of a pink oily solid identified as 145b, m/e(%) M^+=323(2.6), 221(10), 118(100) 105(44), 77(15) and had M^+=323.15222, calc. 323.15214. ^1H-nmr δ($CDCl_3$) 9.15 (broad s, 1H), 8.15 (m, 1H), 7.7-6.8 (m, 8H), 4.25 (ddd, J=8,4,4 Hz, 1H), 3.10 (d of q, J=16(AB q),4 Hz, 2H), 2.15 (s, 2H), 1.1 ppm (s, 6H). This structure was confirmed by ^1H-^1H decoupling experiments.

The third set of fractions (170 mg) was identified as N-benzoylindoline, 134, and was previously characterized. The structure was confirmed by g.c.-m.s., ^1H-nmr, and coinjection with authentic sample of 134. The fourth set of fractions (133 mg) was identified as 146a, m/e(%) M^+=337(9.0), 222(24), 105(100), 77(22) and had M^+=337.16791, calc. 337.167782. ^1H-nmr δ($CDCl_3$) 7.5 (m, 5H), 7.3-6.75 (m, 4H), 5.25 (ddd, J=8.2, 4.6, 2.3 Hz, 1H), 3.63 (m, 2H), 3.50 (s, 3H), 2.56 (dd, J=4, 2 Hz, 1H), 2.07 (d of sept, J=6, 0.5 Hz, 1H), 1.05 (d, J=6 Hz, 3H), 0.9 ppm (d, J=6 Hz, 3H). This structure was confirmed by ^1H-^1H decoupling. experiments. A sample of 146a (45 mg, 0.13 mMol) was refluxed in 5mL MeOH/H_2O (3:1) containing KOH (2g) for 20 minutes after which 5 mL of distilled water was added and the basic mixture washed (2 X 10 mL) with CH_2Cl_2. The aqueous layer was then acidified (conc. H_2SO_4) to pH 4 and the cloudy mixture was extracted (3 X 10 mL) with CH_2Cl_2. The organic extracts were dried ($MgSO_4$) and solvent removed to yield 20.1 mg of a pink oily solid identified as 146b, m/e(%) M^+=323(1.6), 221(15), 118(100) 105(40), 77(22) and had M^+=323.15224, calc. 323.15214. ^{1}H-nmr δ($CDCl_3$) 9.37 (broad s, 1H), 8.15 (m, 1H), 7.7-6.8 (m, 8H), 4.24 (ddd, J=8,4,4 Hz, 1H), 3.05 (dd, J=16(AB),4 Hz, 2H), 2.55 (dd, J=4, 2 Hz, 2H), 2.10 (d of sept, J=6, 2 Hz, 1H), 1.15 (d, J=6 Hz, 3H), 1.05 ppm (d, J=6 Hz, 3H). This structure was confirmed by ^{1}H-^{1}H decoupling experiments.

Irradiation of N-Benzoylindole with Methylacrylate

The procedure of Ikeda (12) was repeated; 5 (2 g, 9.0 mMol) was irradiated in 300 mL of benzene (N_2 purged) containing methylacrylate (20 g, 232 mMol, 0.77 M) for 2 hours after which the solvent was removed to yield 3.0 g of a yellow oil. G.c. showed approximately a 1:1 ratio of 5 to four products in a ratio of 6:18:63:12. One of the products crystallized out of the oil and after recrystallization from ethyl acetate and hexanes yielded 720 mg of crystalline compound 147, mp 122-124°C, lit. mp 123-124°C (13), m/e(%) M^+=307(5), 221(32), 105(100), 77(28) and had M^+=307.12104, calc. 30712082, ^{1}H-nmr δ($CDCl_3$) 8.21 (broad s, 1H), 7.6-7.4 (m, 5H), 7.30 (m, 2H), 7.15 (d, 1H), 4.79 (broad s, 1H), 4.18 (dd, J=8, 2.5 Hz, 1H), 3.74 (s, 3H), 3.12 (m, 1H), 2.75-2.55 ppm (m, 2H). A small sample (200 mg) of the oil was chromatographed by preparative t.l.c. (silica gel, 15% ether/85% hexanes) to yield 3 fractions which were analyzed by g.c..

The first fraction (27.3 mg) contained the major and second major components of the reaction mixture in a ratio of 35:1. ^{1}H-nmr spectroscopy of this fraction identified the major component as 147, previously described. G.c. coinjection with crystalline 147 confirmed that this was the *endo*-isomer. The structure was also confirmed by ^1H-^1H decoupling. experiments.

The second fraction (113.4 mg) contained some (20%) of 147 as seen by g.c. and ^1H-nmr spectroscopy but the major component which corresponded to the second major component of the reaction mixture was identified as 148, m/e(%) M^+=307(10), 221(40), 105(100), 77(25) and had M^+=307.12098, calc. 30712082, ^1H-nmr δ($CDCl_3$) 8.20 (broad s, 1H), 7.6-7.4 (m, 5H), 7.35 (m, 2H), 7.12 (d, 1H), 4.89 (broad dd, 1H), 3.96 (ddd, J=10, 8, 2 Hz, 1H), 3.55 (s, 3H), 3.41 (m, 1H), 2.52 ppm (m, 1H), 2.25(ddd, J=16, 8, 3 Hz, 1H). The stiucture was also confirmed by ^1H-^1H decoupling. experiments.

The third fraction (24.2 mg) contained a mixture of all four components of the reaction mixture in a ratio of 1:1:1:5 as seen by g.c. and ^1H-nmr spectroscopy. The major species present, which corresponded to the third major component of the reaction mixture, was identified as 149, m/e(%) M^+=307(13), 221(42), 105(100), 77(29) and had M^+=307.12114, calc. 30712082, ^1H-nmr δ($CDCl_3$) 8.20 (broad s, 1H), 7.5-7.3 (m, 5H), 7.30 (m, 2H), 7.15 (m, 1H), 4.55 (broad s, 1H), 3.36 (dd, J=8.5, 8 Hz, 1H), 3.65 (s, 3H), 2.86 (m, 1H), 2.75-2.50 ppm (m, 2H). The structure was also confirmed by ^1H-^1H decoupling. experiments.

Irradiation of N-Benzoylindole and Methylacrylate with Hydrogen Selenide

N-Benzoylindole, 5 (0.512 g, 2.32 mMol), was dissolved in benzene (10 mL) and purged with nitrogen. This solution was then purged for 15 minutes at 12°C with hydrogen selenide. A small portion of this solution was dissolved in $CDCl_3$

and the 200 MHz ^{1}H-nmr spectrum was recorded. The signal due to hydrogen selenide could be seen at *ca.* -1.2 ppm and was integrated against the total number of protons for 5. This allowed for an estimation the H_2Se concentration to be *ca.* 0.6 M. To the bulk of the solution was added methylacrylate (4.78 g, 57 mMol, 3.7 M). A small aliquot was taken as a dark reaction control and the rest of the solution was irradiated for 23 hours. An identical solution was prepared without the addition of H_2Se and irradiated along side the treated solution.

G.c analysis of the dark reaction showed unchanged starting materials and analysis of the irradiation performed in the absence of H_2Se showed the same mixture of adducts as obtained for 5 and methylacrylate previously. G.c. analysis of the mixture obtained from the irradiation performed in the presence of H_2Se showed formation of 8 products in a ratio of 1.6:2.3:0.4:1.7:1.4:1:8.7:1; the last four products possessing g.c. retention times identical to those of the four cycloadducts produced in the photoreaction without H_2Se. G.c. coinjection with an authentic mixture of cycloadducts of 5 and methylacrylate confirmed that there were cycloadducts in the photolysis mixture. The irradiated solution was washed with saturated sodium bicarbonate solution (to remove unreacted H_2Se) and distilled water. The organic layer was then dried (Na_2SO_4) and solvent removed *in vacuo* to yield 0.6 g of a yellow oil.

The mixture was first examined by g.c-m.s.. The first peak possessed a g.c. retention identical to that of N-benzoylindoline, 134. G.c. coinjection confirmed that this product was 134, m/e(%) M^+=223(7), 105(100), 77(23). The second peak gave the following g.c.-m.s. spectral pattern, m/e(%) M^+=309(14), 222(22), 105(100), 77(30). The third peak gave the following g.c.-m.s. spectral pattern, m/e(%) M^+=307(8), 202(12), 105(100) 77(38). The fourth peak gave a g.c.-m.s. spectral pattern identical to that of the second peak, m/e(%) M^+=307(8), 202(12), 105(100) 77(38). G.c components 5-8 were previously described as photocycloadducts of 5 and methylacrylate.

The oil was then applied to a silica gel (60-200 mesh) column and eluted with 15%/ether/85% hexanes. Fractions were collected, analyzed by g.c., combined, and characterized. All fractions were shown by g.c. and ^{1}H-nmr to contain large amounts (50%-70%) of cycloadducts 147-149 and thus could not be characterized fully. All attempts (preparative t.l.c., H.P.L.C.) to isolate any of the components of the mixture resulted in mixtures containing mostly cycloadducts as above. This mixture thus was not characterized further.

PART II

ENONE 2+2 PHOTOCYCLOADDITION REACTIONS

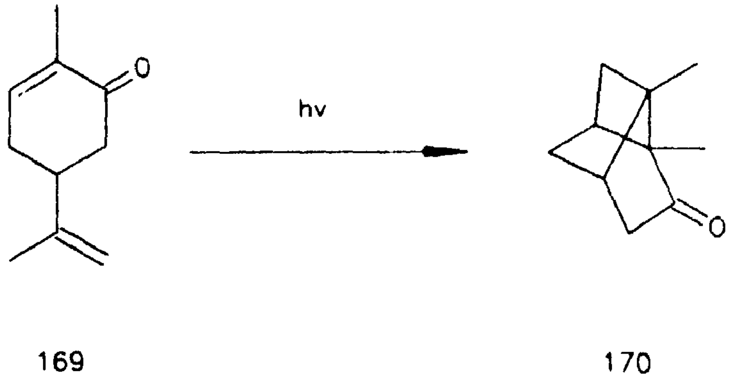
CHAPTER 5

INTRODUCTION

5.1 INTRODUCTION

As mentioned in previous chapters, α,β-unsaturated ketones (hereinafter referred to as enones) also undergo photoannelation with alkenes to give cyclobutanes. The reaction is also referred to as enone 2+2 photocycloaddition and in the case where cyclobutane formation results from reaction between enolized diketones and olefins it is often called the de Mayo reaction. This part of the thesis deals with certain mechanistic aspects of the enone 2+2 photocycloaddition reaction.

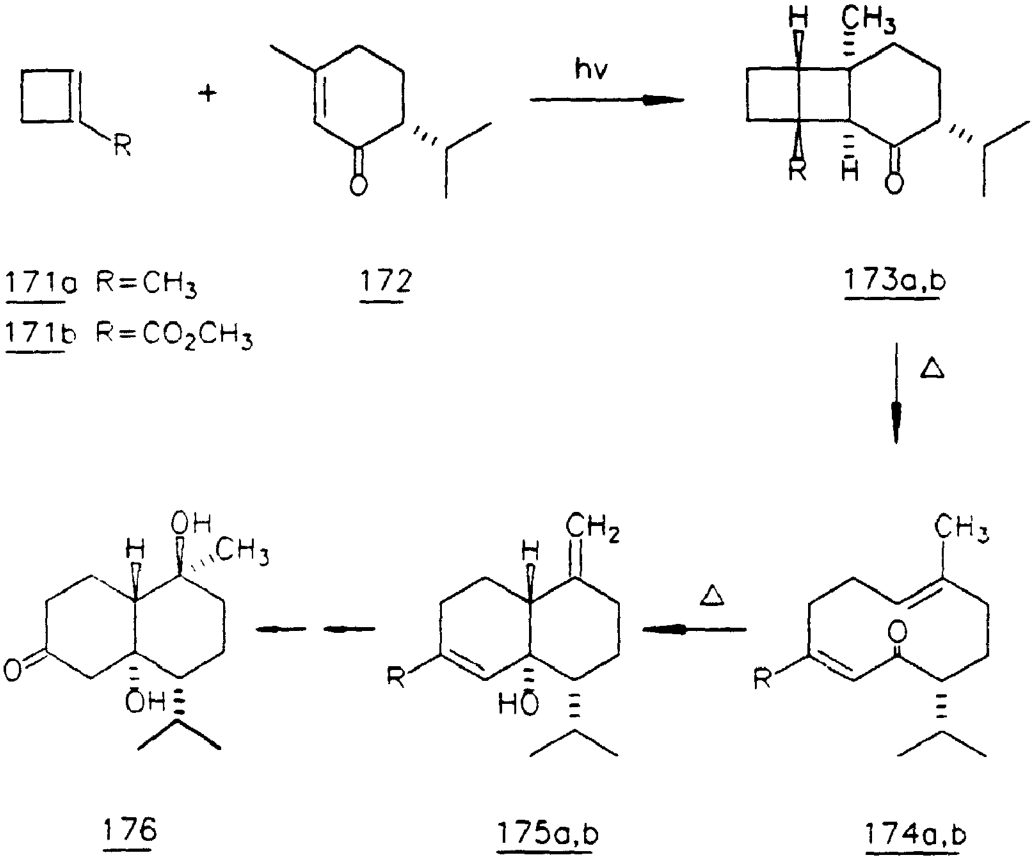
The reaction was reported as early as 1908 when Ciamician published the fact that carvone, 169, rearranged when exposed to light to yield carvone-camphor, 170, (78). Although the reaction received little attention at that time, in the 1960's the groups of de Mayo, Corey, Eaton and others began to investigate the reaction mechanism and potential utility for organic synthesis (77-79).



169 170

One of the more common ways in which this reaction has been exploited is for the preparation of various sesquiterpenes. An example reported by Williams and co-workers (82) is shown in scheme 26.

Scheme 26

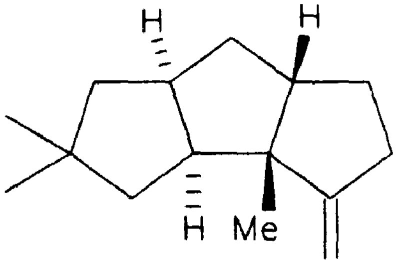


Irradiation of (-)-piperitone, 172, in the presence of substituted cyclobutenes yielded the tricyclo[4.4.0.0]decane photoadducts 173a,b. Flash vacuum pyrolysis of 173b afforded *trans*-1(10)-*cis*-4-germacrene 174b; however, thermolysis of 173b in a sealed tube at 210°C gave the *trans*-decalin ester 175b and it was shown that

174b was an intermediate for the conversion of 173b to 175b. Product 175b was then subjected to various functional group interconversions to yield the cadinane sesquiterpene (+)-isocalamendiol, 176b.

Recently, Disanayaka and Weedon described a sequence which allows the preparation of the tricyclo[6.3.0.0]undecane skeleton found in a number of physiologically active fungal metabolites such as hirsutene, 177 (83). The sequence involves the preparation of a bicyclo-[6.3.0]-undecane-2,6-dione by the photocycloaddition of an enolized cyclohexane-1,3-dione to a substituted cyclopentene (an example of the de Mayo reaction), followed by intramolecular reductive coupling of the dione with a low valence titanium compound (Scheme 27).

In this reaction, as in the reaction shown in Scheme 26, the alkene can add to the enone with either of two orientations to give a mixture of regioisomers. After reductive coupling the hirsutene skeleton, with the desired regiochemistry, was obtained with a yield of 57%. Functional group interconversion completed the formal synthesis of (±)-hirsutene by yielding norketone 178 obtained by ozonolysis of hirsutene, 177.



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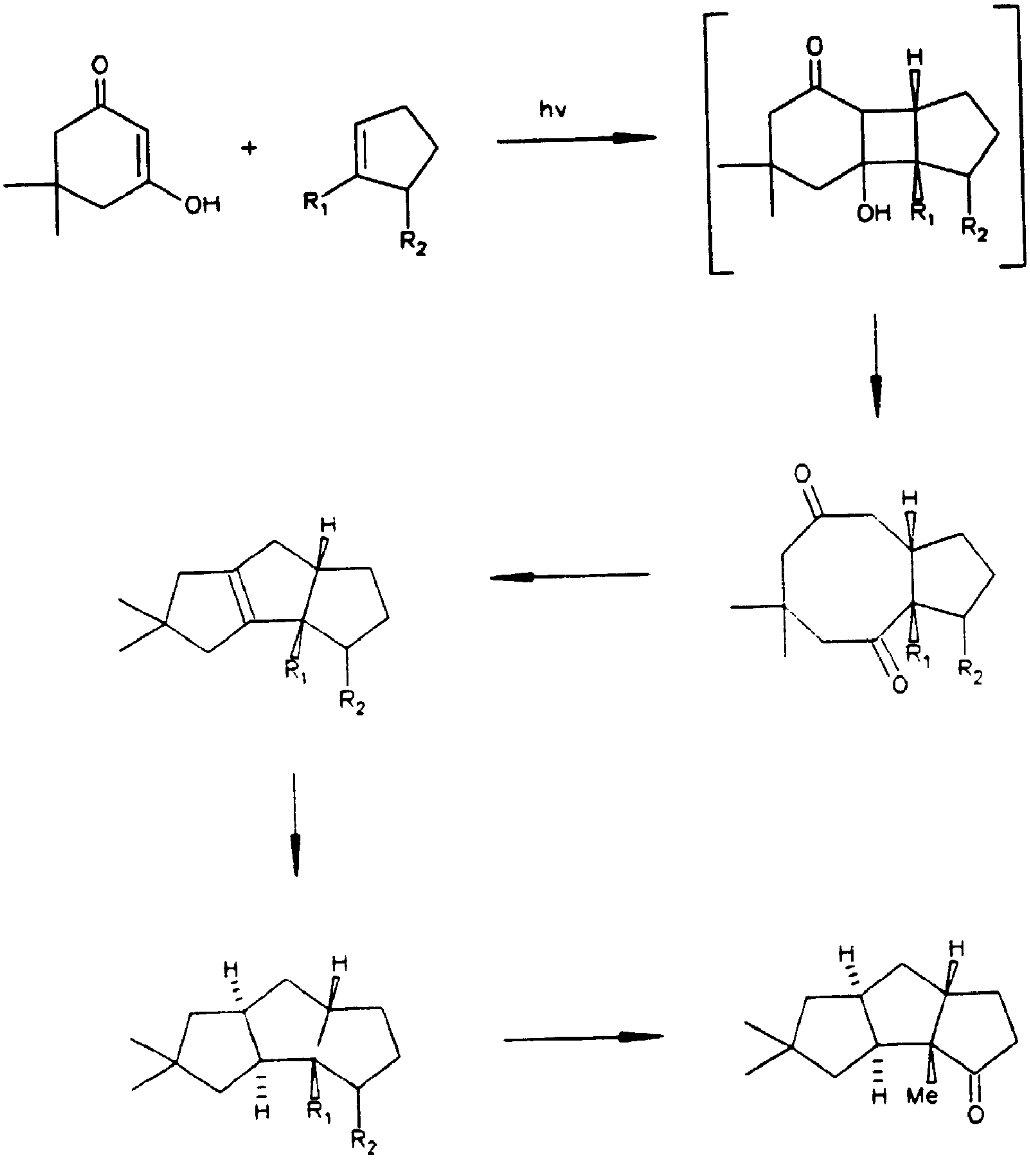
Scheme 27



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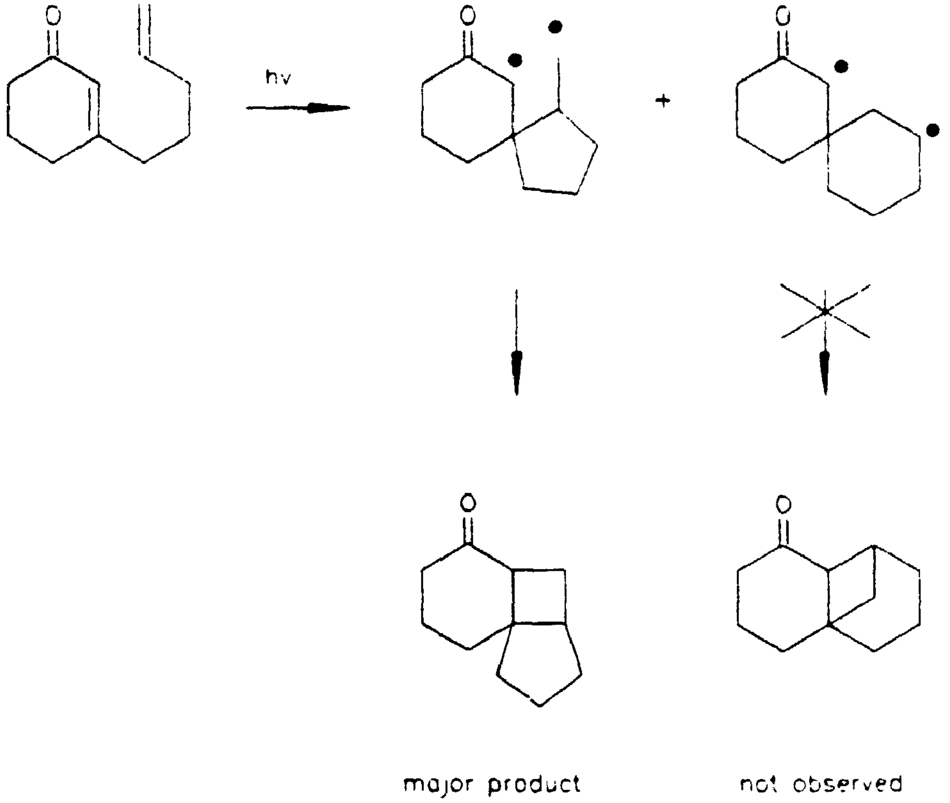
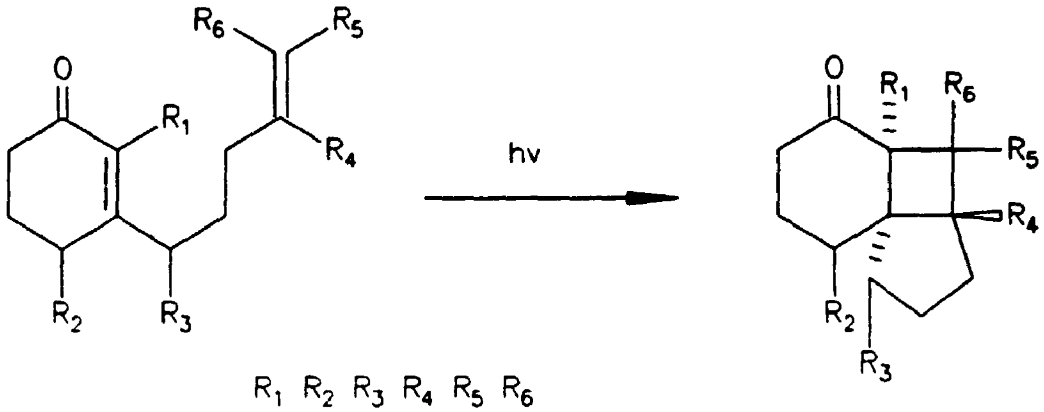
Many examples have also been reported of intramolecular 2+2 photochemical cycloadditions (84) such as that reported by Ciamician for the rearrangement of carvone. Unlike the intermolecular photocycloaddition, the intramolecular reaction does not normally yield mixtures of regioisomers. This regioselectivity is generally attributed to the "rule of five" (85) for compounds in which the enone and alkene carbon-carbon double bonds are 1,5 to each other (*ie.* separated by two atoms) or 1,6 to each other (*ie.* separated by three atoms). The rule generally stated is that the major regioisomeric product is derived from the biradical intermediate in which a five-membered ring has been formed. An example of the rule is given in scheme 28.

Scheme 28



This type of 2+2 cycloaddition has been used in the synthesis of many natural products such as the isocomenes <u>179a,b</u> (86).



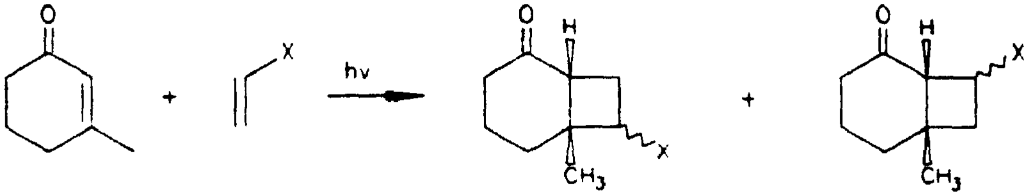
	R_1	R_2	R_3	R_4	R_5	R_6
<u>179a</u>	Me	Me	H	Me	H	H
<u>179b</u>	H	Me	H	Me	H	H .

The many synthetic uses of both inter and intramolecular photocycloaddition reactions of enones with alkenes have been reviewed (40a,46,87,88).

5.2 Mechanistic Aspects of 2+2 Photocycloaddition Reactions

For many photochemical reactions between enones and olefins there appears to be a preference to form one regioisomer over another. The reactions also show some stereoselectivity. Understanding the factors which govern the regioselectivity is, of course, very important if the reaction is to be used to its full potential in organic synthesis. It has been observed that olefins bearing an electron donating-group, such as an alkoxy group as in ethyl vinyl ether, <u>180</u>, prefer to form adducts with cycloalkenones in which the ketone function and ethoxy group are in a "head-to-tail" arrangement. The minor isomers are stereoisomers of the "head-to-head" arrangement (80). These products are illustrated in scheme 29. The early work in this area (80) also suggested that alkenes with electron-withdrawing substituents (*eg.* acrylonitrile, methyl acrylate) favour the formation of "head-to-head" adducts.

Scheme 29



180 X=OEt

181 X=CN

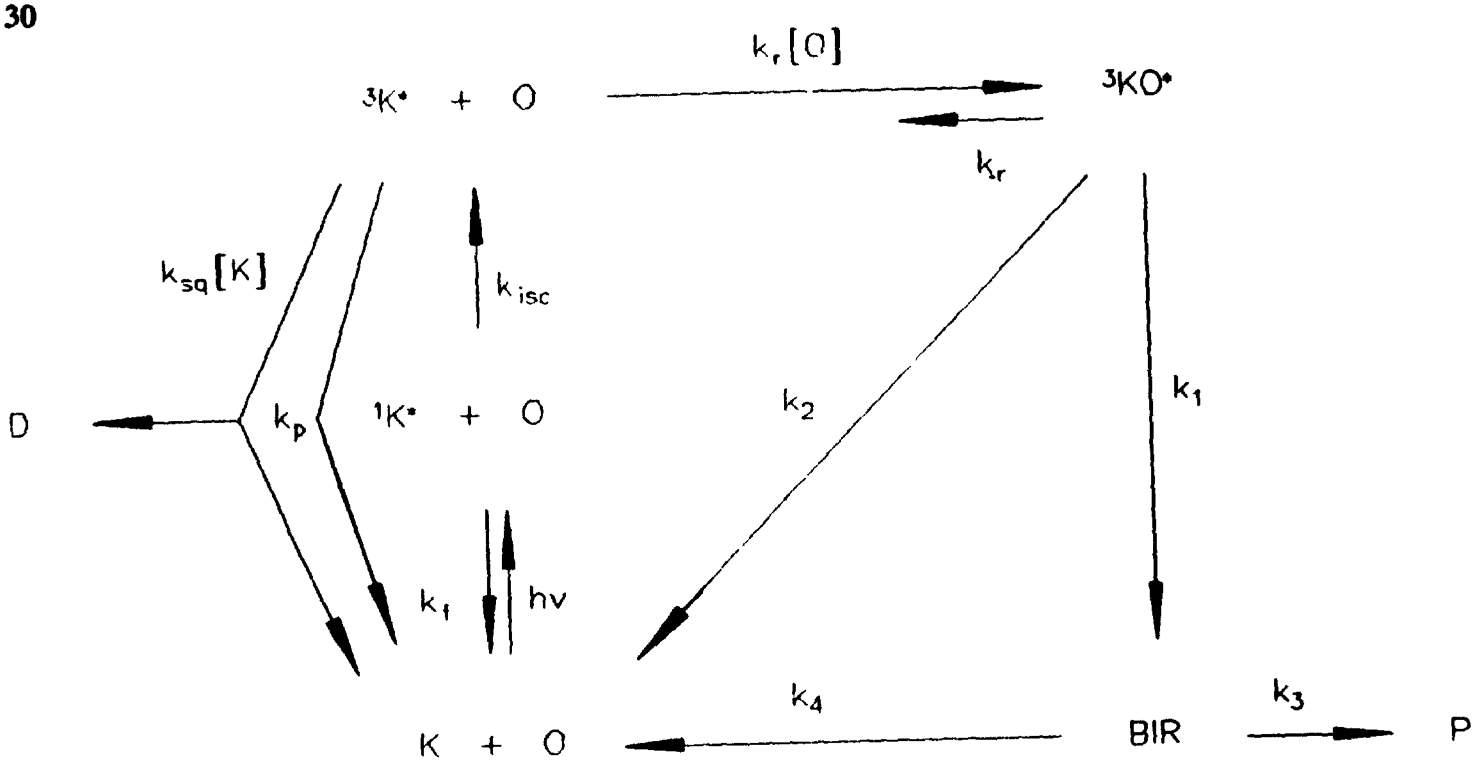
head-to-tail

head-to-head

Various mechanisms have been proposed to explain the regioselectivity of the reaction. A commonly accepted mechanism for enone photoannelation is based upon a rationalization developed by Corey and elaborated in detail by de Mayo (26,89). The mechanism is shown in scheme 30 and will be discussed below.

The photochemical reaction is initiated by absorption of light by the enone which yields its singlet excited state. In acyclic enones radiationless decay to the ground state *via* efficient *cis-trans* isomerization competes with intersystem crossing to the triplet excited state, while with less flexible five and six membered cyclic enones intersystem crossing is the dominant fate of the singlet excited state (90).

Scheme 30



K=enone

O=olefin

$^1K^*$=singlet excited state of enone

$^3K^*$=triplet excited state of enone

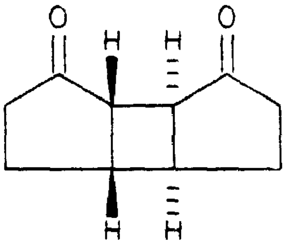
BIR=biradical

$^3KO^*$=triplet exciplex

D=enone dimer

P=enone-olefin product

Consequently the quantum efficiencies for triplet excited state formation are quite high for cyclic enones and in the case of cyclopentenones approach unity (90). The triplet excited state possesses a lifetime of approximately 10^{-8} s for cyclopentenone and 10^{-9} s for cyclohexenone (88,91). These lifetimes are long enough for bimolecular reactions with other species in solution, including ground state enone. Interception of the triplet excited state by ground state enone affords 2+2 photodimers 182 and 183, characterized as "head-to-head" and "head-to-tail" (92).



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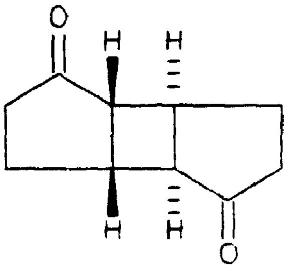

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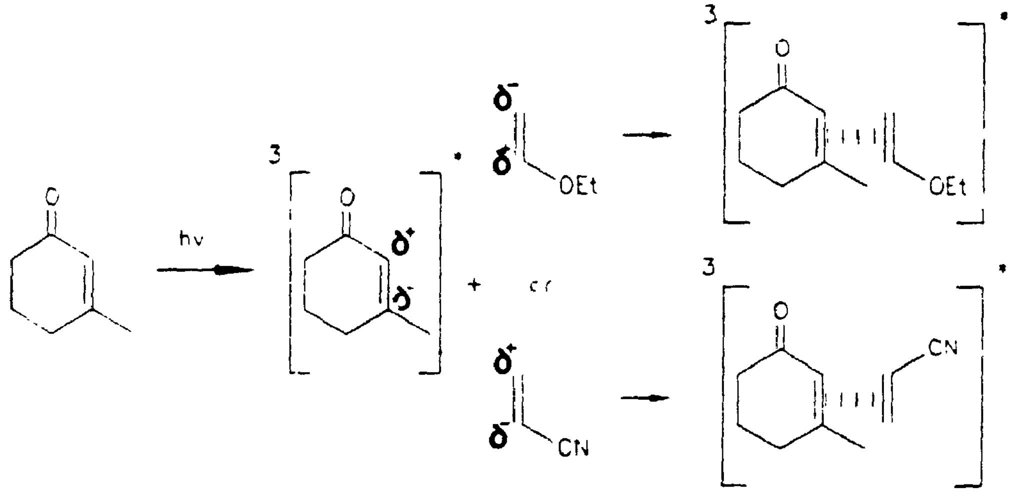
In the presence of olefin, the triplet excited state can also be intercepted to give adducts, provided the triplet energy of alkene is above that of the enone. In order to explain the different regioselectivity observed in the addition of electron-rich and electron-poor alkenes to enones Corey proposed that a π-complex is formed between the alkene and the excited enone (50a). In this complex it is proposed that the dipoles of the alkene and the excited enone align to maximize electrostatic attraction. The polarization of the excited enone is presumed to be opposite to that in the ground state. This reversal arises if the triplet excited state enone is an $n \rightarrow \pi^*$ state whose charge distribution is such that the ß-carbon is negative relative to the α-carbon because of movement of the electron density from the carbonyl oxygen into the π-system. This was supported by calculations made by the extended Hückel method (93). The π-complex (*ie.* the species $^3KO^*$ in scheme 30) proposed by Corey was suggested to be an acceptor-donor complex, or exciplex, by de Mayo. In scheme 31 the excited state complexes for the reaction with an electron-poor or an electron-rich alkene are shown; it is the alignment in these complexes which is presumed to lead to head-to-head regioselectivity for electron-poor alkenes such as acrylonitrile, and head-to-tail regiochemistry for electron-rich alkenes such a ethyl vinyl ether.

Scheme 31

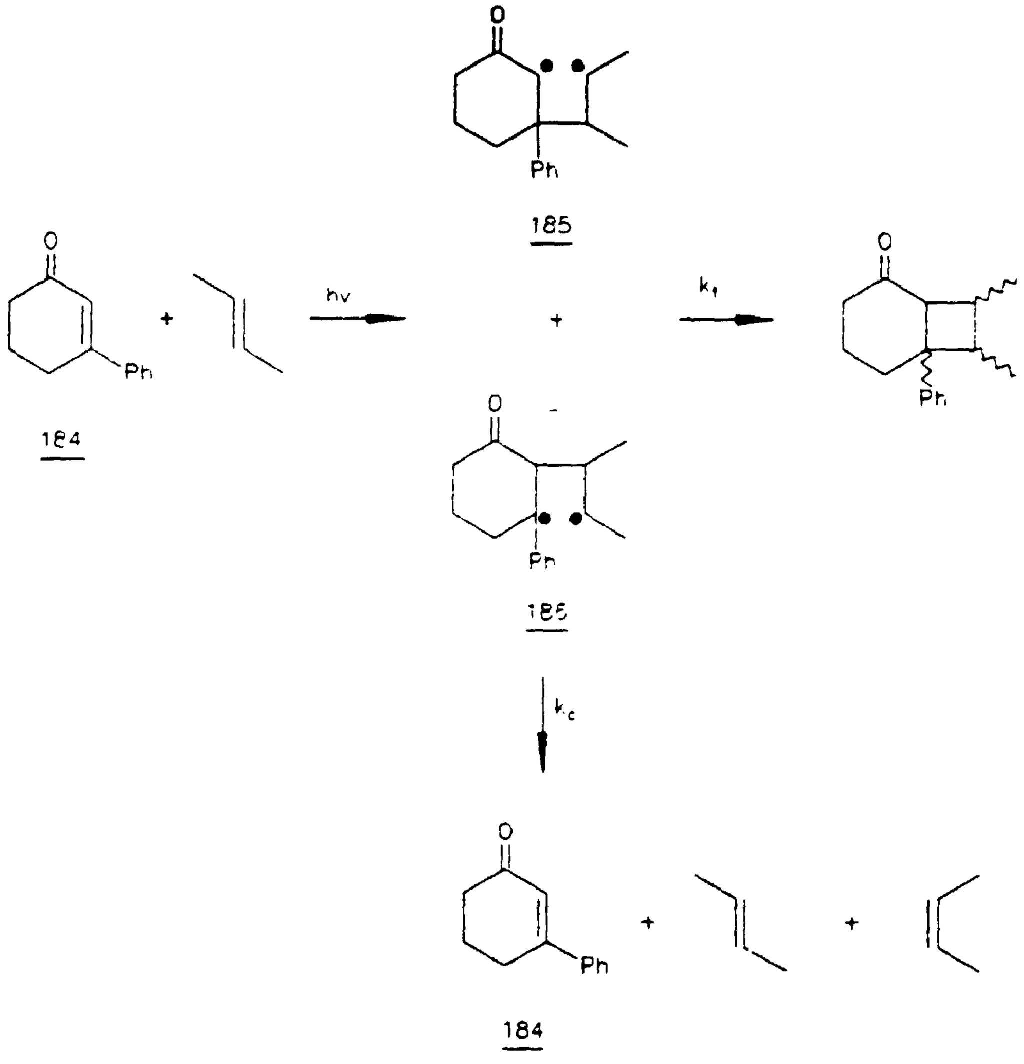


de Mayo used steady state kinetic methods to examine the reaction of simple alkenes with excited cyclopentenones and cyclohexenones (26). He concluded that the triplet excited enones react with the alkenes with rate constants of the order of 10^8 $M^{-1}s^{-1}$. Since this is several orders of magnitude faster than the reaction of radicals with alkenes, and since it was assumed that triplet excited states should have similar properties and reactivity to radicals, it was proposed that the fast rate of reaction between excited enones and alkenes was due to the formation of the excited complex, or exciplex, which then collapsed to a triplet 1,4-biradical intermediate (BIR in Scheme 30).

The formation of the triplet 1,4-biradical was also proposed to account for the inefficiency of the photochemical cycloaddition reaction. As noted above, the major fate of excited enones is intersystem crossing to the triplet excited state which is then intercepted by alkene. At sufficiently high alkene concentration all the excited states should be intercepted and hence yield adducts. In fact, the measured quantum yields of product formation at very high alkene concentration were far less than unity. This can be explained if the biradical intermediates formed can either close to give products or undergo cleavage back to starting materials. Measurements of quantum yields of cycloaddition extrapolated to infinite alkene concentration have shown that in some situations on the order of 80% of the biradicals appear to revert to the ground state starting materials (26).

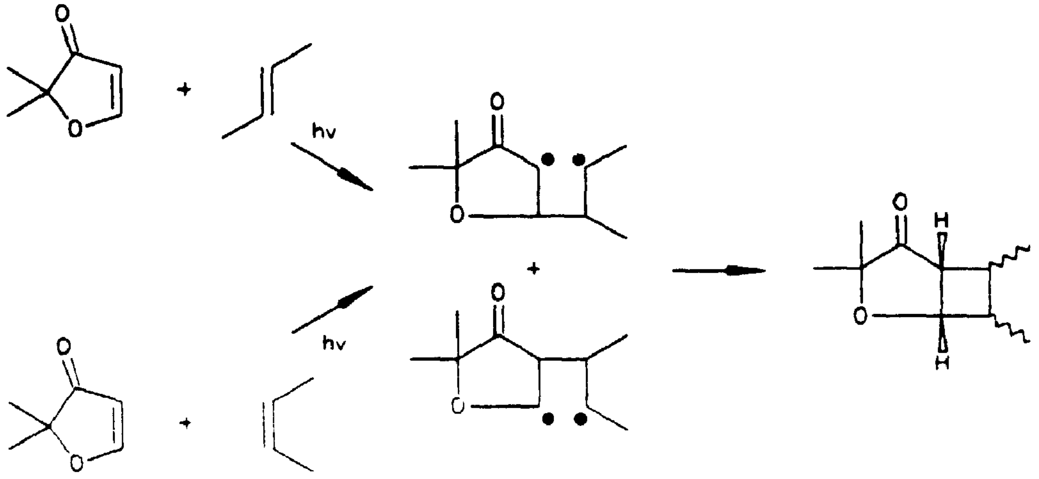
Evidence for the existence of the 1,4-biradical intermediate is quite convincing. The products of addition of olefins to enones show that a freely rotating 1,4-biradical intermediate must exist along the reaction pathway. This is illustrated by an example reported by McCullough et al (94) in Scheme 32. It was shown that irradiation of 3-phenylcyclohexenone, 184, in the presence of *trans*-2-butene led to a mixture of stereoisomeric cyclobutanes. Examination of the unconverted starting material revealed the presence of isomerized olefin. This must occur *via* biradicals 185 or 186 which have a long enough lifetime to allow rotational equilibration around the olefinic double bond. Closure then yields the stereoisomeric cyclobutane products, while cleavage regenerates ground state enone plus a mixture of alkene geometrical isomers. This mechanism of alkene isomerization is commonly referred to as Schenk isomerization (3,95).

Scheme 32



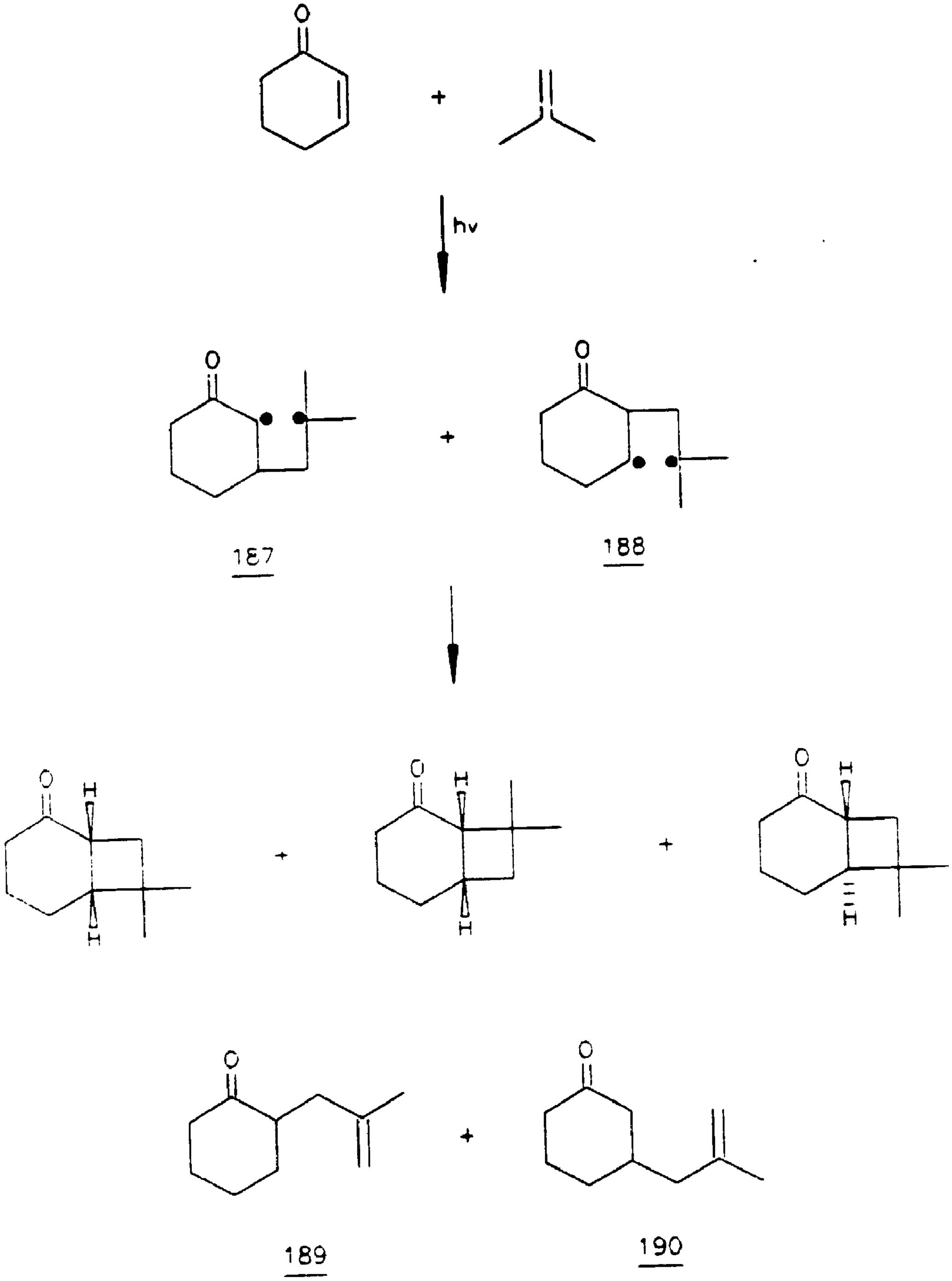
Similarly, addition of *cis* or *trans*-2-butenes to excited enones has led to similar mixtures of stereoisomers as shown in scheme 33 (78,94).

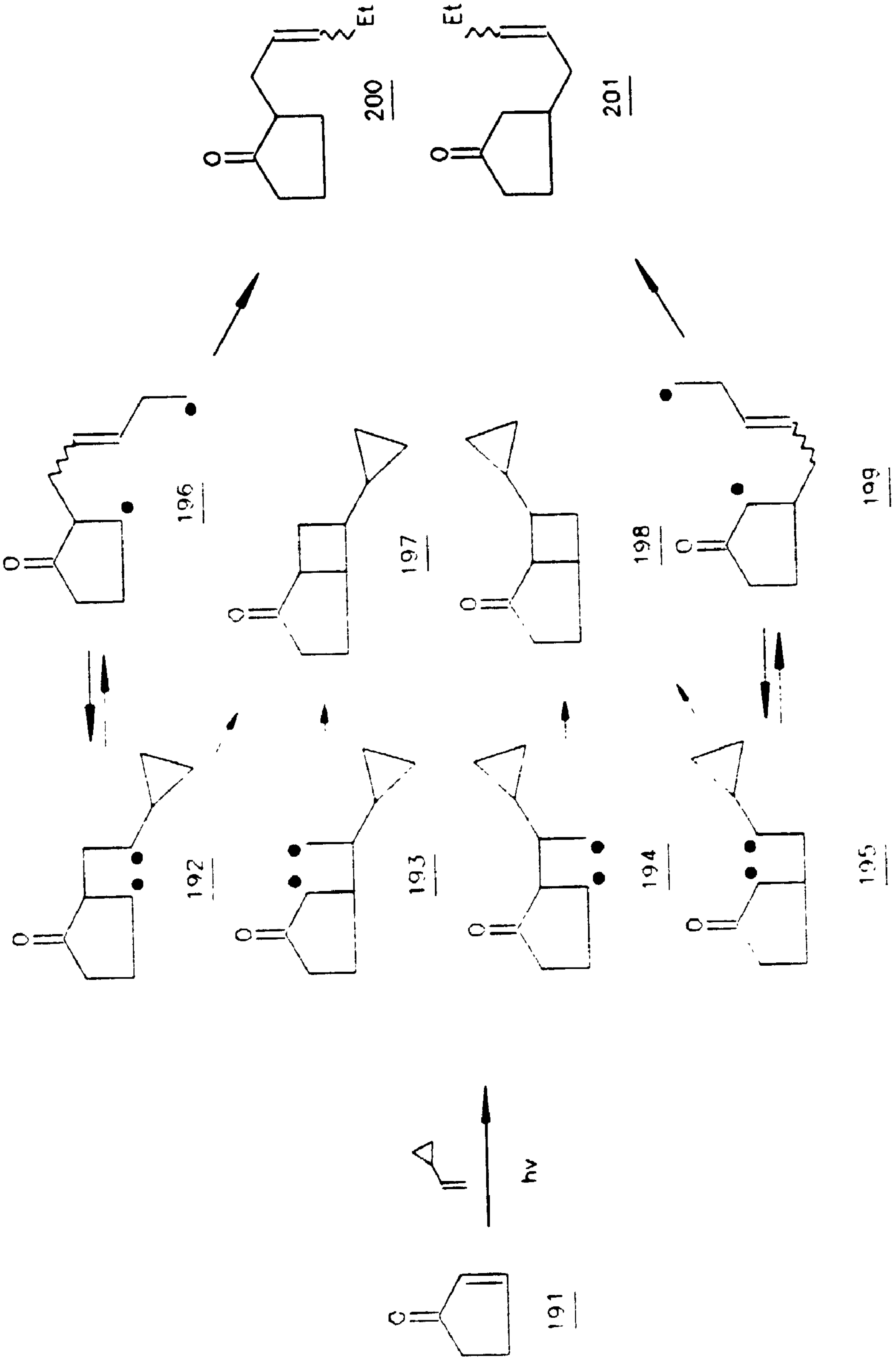
Scheme 33



Further evidence for the intermediacy of biradicals in enone-alkene photocycloaddition is the observation of intramolecular disproportionation products. This has been observed by Corey (80a) in the addition of 2-methylpropene to cyclohexenones (scheme 34). The olefinic or "ene" products 189 and 190 are formed by intramolecular hydrogen abstraction in the biradical intermediates 187 and 188. Product 189 must derive from intermediate 188 and similarly 190 from 187. These products therefore suggest that initial bonding between the alkene and the excited enone may be at either the α or β position of the enone (50c). Other evidence has been presented to suggest that for some alkenes the first bond is formed to the β position of the enone (96a,97). The question of the site of initial bonding and of the biradical lifetimes was recently re-examined by Rudolph and Weedon (51). In their work cyclopentenone, 191, was irradiated with olefins which produced biradicals capable of intramolecular rearrangements (schemes 35 and 36).

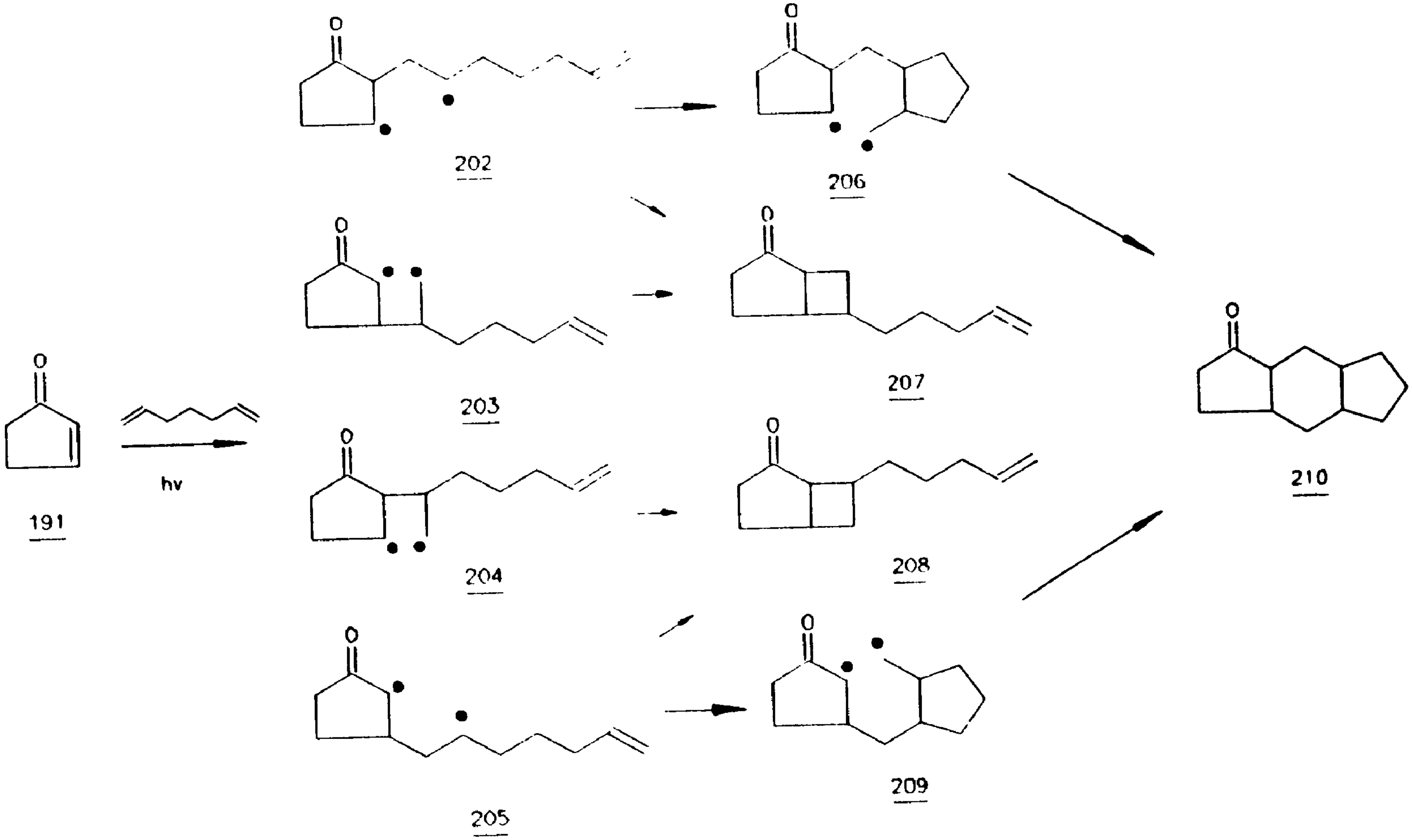
Scheme 34





Scheme 35

Scheme 36



Irradiation of 191 with vinylcyclopropane yielded products 197 and 198 and 200 and 201 in a 4:1 ratio. Products 200 and 201 are derived from intermediates 196 and 199 which are in turn derived from cyclopropyl ring opening of 1,4-biradical intermediates 192 and 195. Thus the isolation of 200 and 201 indicates that initial bonding between the excited enone and the alkene occurs at both the enone α and β positions.

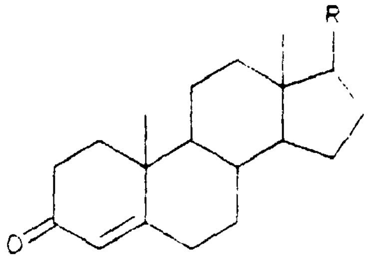
Irradiation of 191 with 1,6-heptadiene yielded products 207 and 208 only, and none of the potential rearrangement product 210. Rate constants have been measured for the ring opening of the cyclopropylalkyl radicals (*eg.* 192→196 or 195→199) and ring closure of 1-hexenyl radicals (*eg.* 205→209 or 202→206). Using these rearrangements as "radical clocks" it was estimated that the lifetimes of the biradical intermediates were of the order of 50 ns.

5.3 Exciplex Formation and 1,4-Biradicals

As mentioned earlier, the existence of a triplet exciplex as an intermediate in the photocycloaddition of alkenes to enones was proposed to explain the reaction regioselectivity and the observed reaction rates as determined by steady state kinetics. However, no direct evidence has ever been reported for the existence of an exciplex in this system and its intermediacy has remained controversial. Indeed, several arguments can be presented to show that it is not necessary to invoke an exciplex as an intermediate in this reaction. For example, the original proposal by Corey, that the reaction regioselectivity reflects the orientation in a complex between the excited enone and the alkene, overlooks the fact that various biradical precursors to each regioisomer may proceed to products (as opposed to reverting to starting materials) with different efficiencies.

Thus the ratio of head-to-head and head-to-tail isomers may not necessarily reflect the initial orientation in a π complex, even if it is formed.

The exciplex argument is also based on the assumption that the triplet excited state of the enone is an $n\rightarrow\pi^*$ state and that the excited state dipole is the reverse of that in the ground state. Although the electronic configurations of the lowest triplet state of all cyclohexenones have not been determined, studies of steroidal enones 211 and 212 have suggested that the lowest triplet excited state is $\pi\rightarrow\pi^*$ in nature and that the $n\rightarrow\pi^*$ triplet is a few kcal/mol higher in energy (98). Later studies have also claimed to show that the reactive state in the enone-olefin photocycloaddition is the $\pi\rightarrow\pi^*$ triplet state of the enone. While there is some reverse polarization of charge in the $\pi\rightarrow\pi^*$ state, the charge distribution is not as extreme as it would be for the $n\rightarrow\pi^*$ excited state enone (99).



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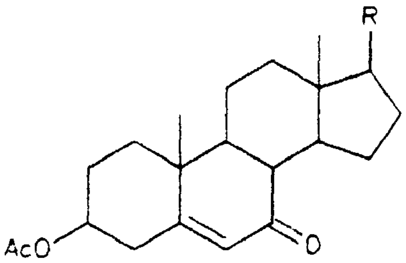

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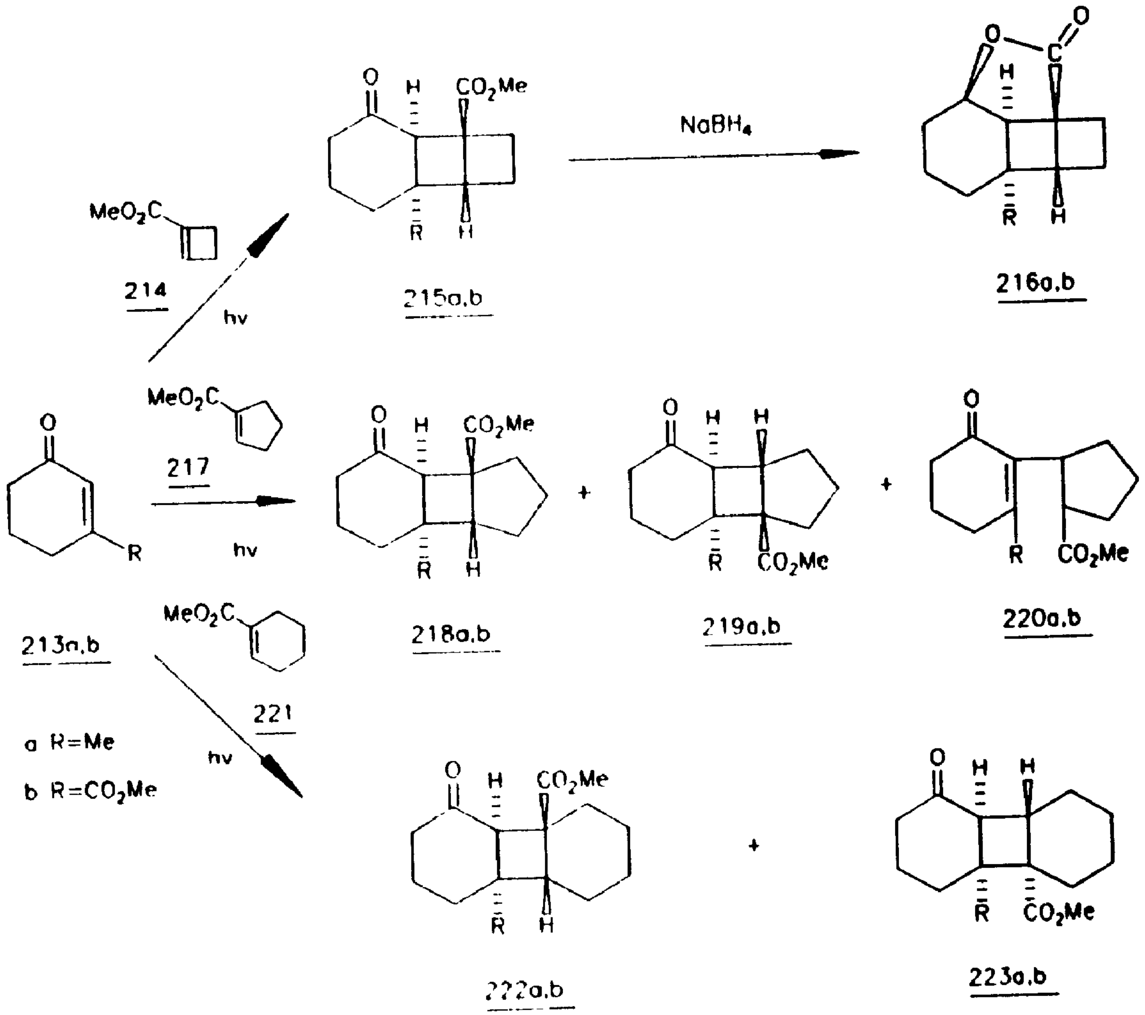
A success of the exciplex argument was that it correctly predicted the different regiochemical outcome of the reaction with electron-poor and electron-rich alkenes. However in recent years several examples have come to light in which electron-poor alkenes added with the "wrong" regioselectivity so that the head-to-tail regioisomer is favoured as the major product.

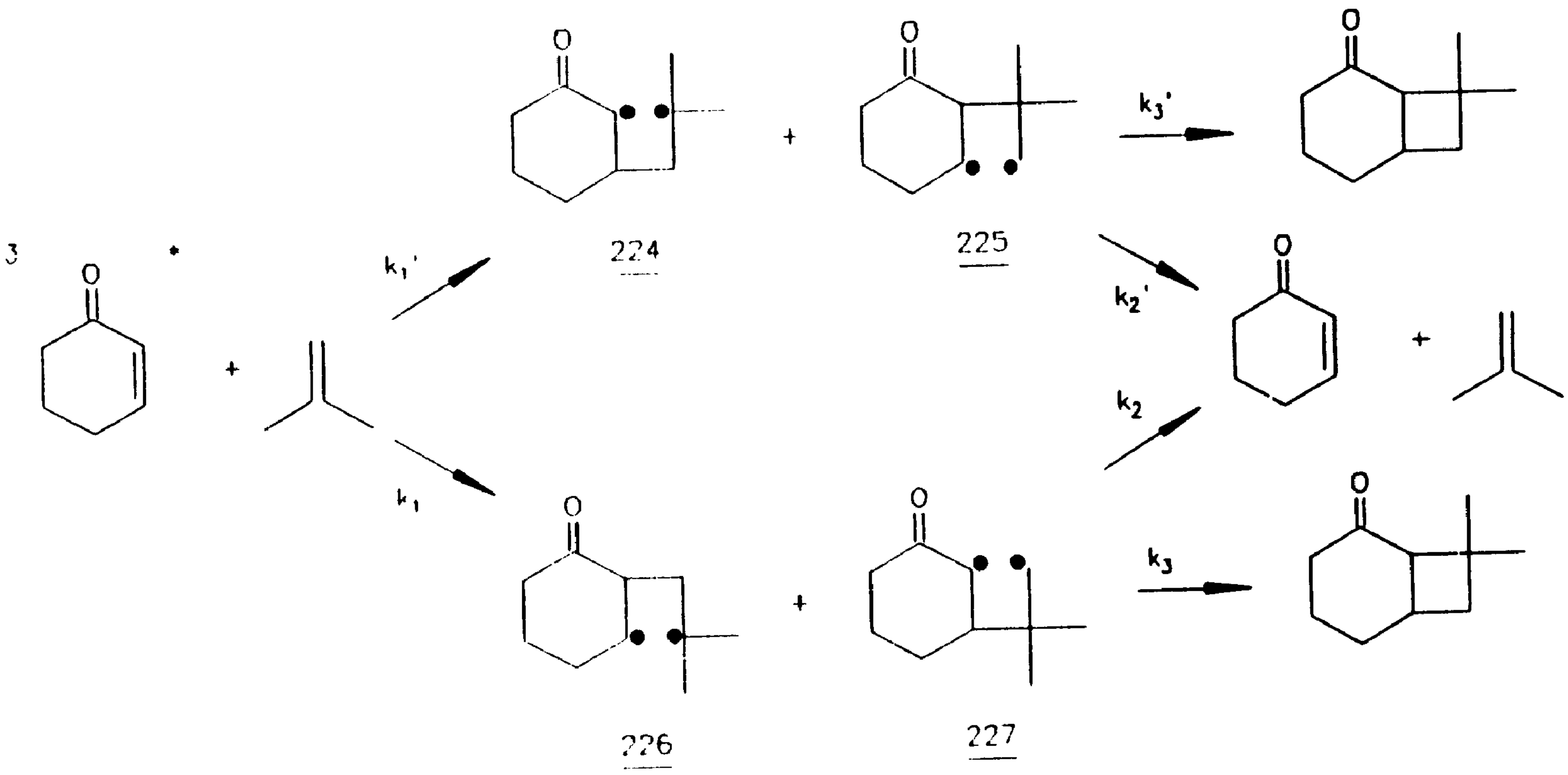
Scheme 37


MeO$_2$C
214
hv
NaBH$_4$
215a,b
216a,b
MeO$_2$C
217
hv
213a,b
a R=Me
b R=CO$_2$Me
218a,b
219a,b
220a,b
MeO$_2$C
221
hv
222a,b
223a,b
H
CO$_2$Me
R
O

This has been reported most recently by Lange and coworkers (100) who found a gradual reversal of regioselectivity in the photoaddition of cyclohexenone to cycloalkene esters of increasing ring size (scheme 37). It was shown that irradiation of 213a,b in the presence of cycloalkene ester 214 yielded cyclobutane product 215a,b, confirmed by sodium borohydride reduction to 216a,b. This is as would be predicted from the oriented π complex or exciplex. However, as the cycloalkene ring is expanded to a five membered ring (*ie.* olefin 217), the regioselectivity is lost (approximately 1:1 ratio of head-to-head and head-to-tail isomers). Changing to olefin 221 almost completely reversed the regioselectivity and isomer 223a,b dominated in a 90:10 ratio over 222a,b. Since the polarization of 214, 217, and 221 should be very similar, the results are not consistent with Corey's dipolar interaction hypothesis. A similar result has been observed by Tada and Nieda who also examined the reaction of 3-substituted cyclohexenones with various cyclic alkene esters (101).

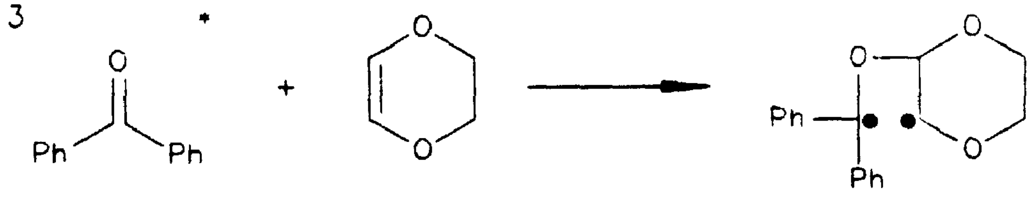
In an early review of the enone-alkene photocycloaddition reaction Bauslaugh (102) proposed that the regiochemistry observed by Corey and co-workers could be explained without the need for exciplexes. Instead, he proposed that the regiochemistry observed resulted from competition between cyclobutane formation and reversion to starting materials in the intermediate biradicals. He also proposed that only the more stable biradicals would be formed as reaction intermediates. Thus for the addition of 2-methylpropene to cyclohexenone it was proposed that 4 biradical intermediates are possible (scheme 38).

Scheme 38



On the basis of radical stability it was argued that the rate of formation of 224 should be greatest and 225 the least. This would tend to reduce the amount of head-to-head regioisomer produced as it must come from 224 or 225. Since 224 is quite stable, it was proposed that it would probably show more reversion to starting enone than other biradicals, although the reason for this proposal is unclear. The corollary of this is that the biradicals 226 and 227 would prefer ring closure and consequently the head-to-tail products would predominate, as observed. Bauslaugh's hypothesis does not require an exciplex intermediate. Unfortunately, like Corey's hypothesis, it contains assumptions which have not been, or cannot be tested. In order to assess the validity of the de Mayo-Corey mechanism or the Bauslaugh mechanism it is necessary to know the quantum yields (and rates) of formation of the isomeric biradical intermediates and also to know how the biradicals partition between products and starting materials (*ie.* k_2/k_3 and k_2'/k_3', Scheme 38).

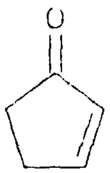
Loutfy and de Mayo (26) studied the dependence of quantum yield of photocycloaddition of cyclopentenone and cyclohexenone with alkenes in the presence and absence of quenchers such as 2,5-dimethyl-2,4-hexadiene. Temperature effects were also examined; for cyclopentenone reacting with cyclohexene, the quantum yield at high alkene concentration, increased from 0.46 at 27°C to 0.72 at -102°C, while for cyclopentenone-cyclopentene it increased in excess of two fold, from 0.23 at 27°C to 0.63 at -71°C. These large changes were attributed to the changes in the fraction of the biradical intermediates giving product rather than to changes in the fractions of enone triplets intercepted by alkene. A steady state kinetic analysis of the quantum yield data was used by de Mayo to extract values for the proportion of the biradicals which revert to starting materials in competition with product formation, and for the rate constant for the reaction between the triplet excited state of the enones and the alkenes. It was the high value of these rate constants (of the order of 10^{8} $M^{-1}s^{-1}$) in comparison with the rates of addition of radicals to alkenes, which were used to argue for the intermediacy of an exciplex in these reactions. In fact, as will be outlined below, the kinetic analysis was flawed and cannot be used to estimate biradical partitioning ratios or rates of formation. In addition, studies by Peters and co-workers on the Paternò-Büchi reaction have shown that formation of 1,4-biradical intermediates are a result of direct attack of triplet excited ketone on the olefin and do not apparently involve charge transfer or formation of an exciplex (103). Thus, it was shown that dioxene, 228, could react with triplet excited state benzophenone with a rate constant, k_r, equal to 5×10^9 $M^{-1}s^{-1}$, and they showed that alkene mediated decay of the triplet excited state was concurrent with biradical formation.



228

Therefore, if an exciplex is involved in this reaction it is extremely short-lived, and shorter-lived than either the ketone triplet excited state or the biradical intermediate.

More recently, Heibel and Schuster (88) have reported, using flash techniques, that structurally constrained enones such as cyclopentenone, 191, 3-methylcyclohexenone, 229 and testosterone acetate, 230, react directly with olefins proceeding to a triplet 1,4-biradical. The rate constants for triplet interception are reported as $4.0X10^{8}$ $M^{-1}s^{-1}$ and $5X10^{6}$ $M^{-1}s^{-1}$ for 191 and 229, respectively, in hexane. Schuster and co-workers have also offered, for more flexible enones, (*ie.* 3,3-dimethylcyclohexenones) the possibility of a twisted enone intermediate, 232, whose existence is currently being tested. Such an intermediate is also said to be involved in the lumiketone rearrangement of 231, (Scheme 39).



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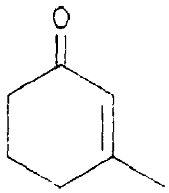

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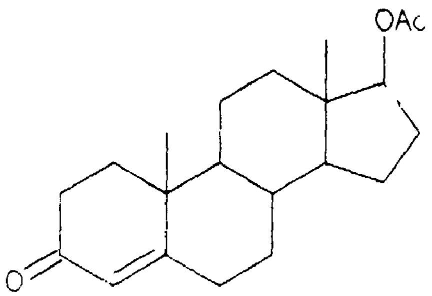

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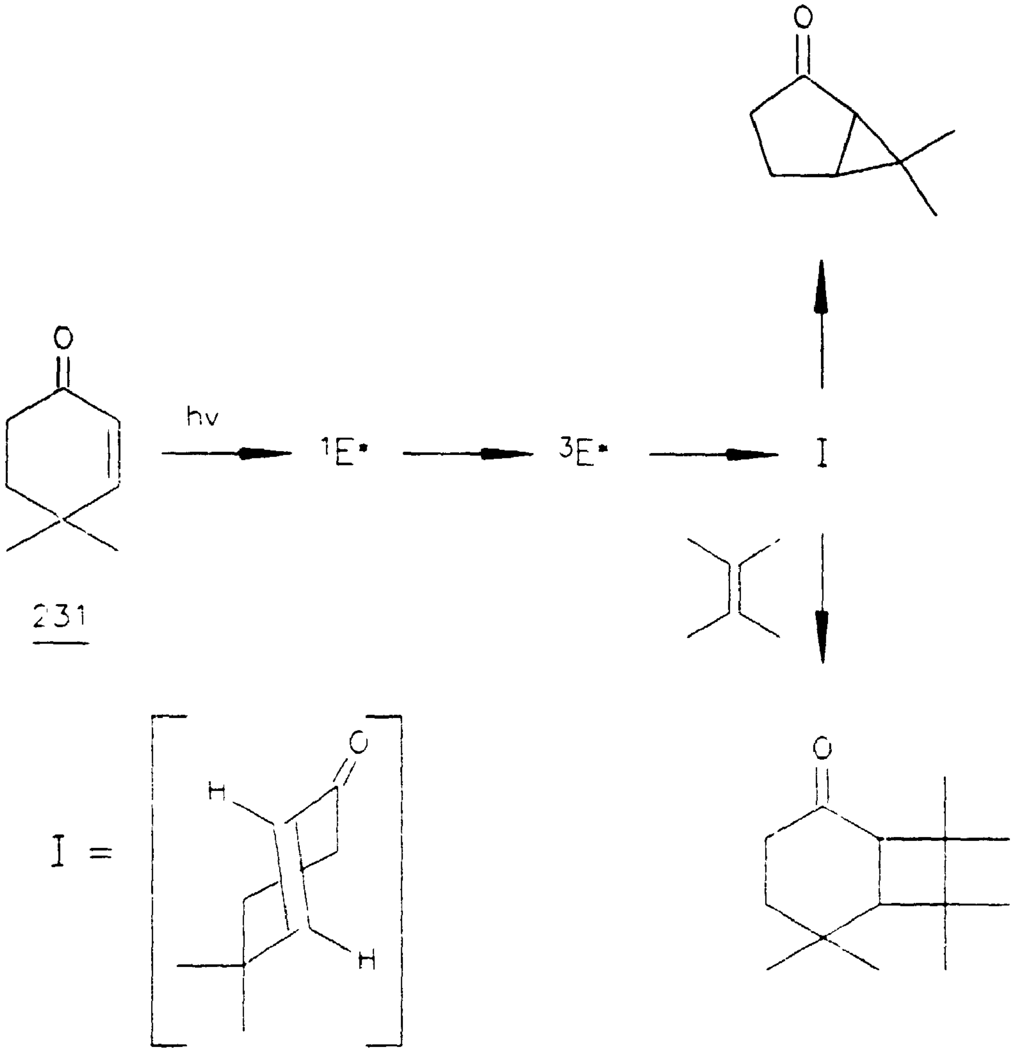
Scheme 39



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5.4 Kinetic Treatment of the 2+2 Photocycloaddition Mechanism

Loutfy and de Mayo (26) have carried out extensive quantitative studies of enone photoannelation. Their application of steady state kinetics to scheme 30 yielded an expression (equation 6) for the quantum yield of product formation.

(equation 6) $$\phi_p = \phi_{isc}\left[\frac{k_3}{k_3 + k_4}\right]\left(\left[\frac{k_1 + k_2}{k_1}\right]\left[\frac{k_d + k_r[O]}{k_r[O]}\right] + \frac{k_d k_{-r}}{k_1 k_r[O]}\right)^{-1}$$

The reciprocal of this yields equation 7

(equation 7) $$\phi_p^{-1} = \frac{1}{P\phi_{isc}}\left(1 + \frac{k_d}{k_r[O]} + \left[\frac{k_d}{k_r[O]} \bullet \frac{k_{-r}}{k_1 + k_2}\right]\right)$$

where

$$P = \left[\frac{k_3}{k_3 + k_4}\right]\left[\frac{k_1}{k_1 + k_2}\right]$$

From equation 7 a plot of reciprocal quantum yield versus reciprocal olefin concentration would, if scheme 30 is valid, yield a straight line with an intercept given by equation 8 and a slope given by equation 9.

intercept,

(equation 8) $$I = \frac{1}{P\phi_{isc}}$$

slope

(equation 9) $$m = \frac{k_d}{P\phi_{isc}\, k_r}\left[1 + \frac{k_{-r}}{k_1 + k_2}\right]$$

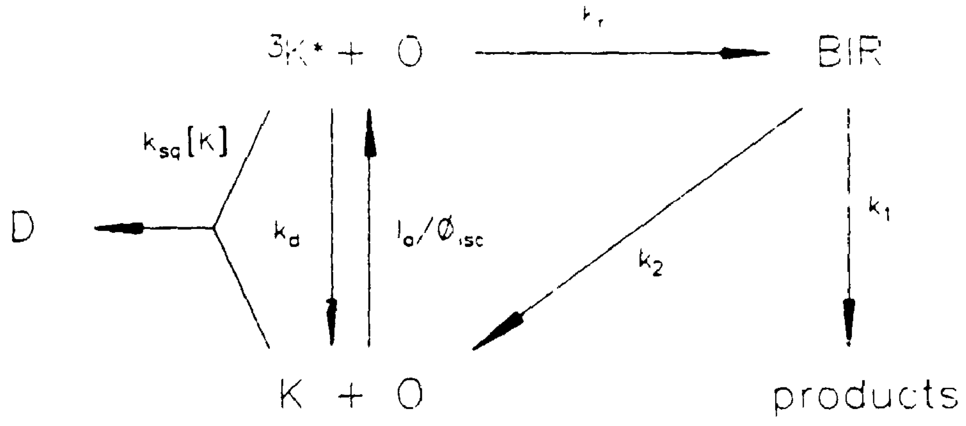
If $k_{-r}/(k_1+k_2)$ is defined as C, then the ratio of the slope to the intercept would yield equation 10.

slope/intercept

$$\text{(equation 10)} \qquad \frac{m}{I} = \frac{k_d}{k_r}\left[1 + C\right]$$

It was shown by using a series of different alkenes that C, which represents the efficiency of reversal of the exciplex to the triplet enone, is likely very small; thus the ratio slope/intercept is equal to k_d/k_r. The data obtained by de Mayo and Loutfy did yield straight lines for various enone-alkene systems and so are consistent with the sequence shown in scheme 30. They were used to estimate values of k_r, the rate constant for exciplex formation. de Mayo's results are, of course, also consistent with a mechanism which excludes the formation of an exciplex. Such a mechanism is given in scheme 40.

Scheme 40



If in this case we apply steady state analysis we derive an expression for the quantum yield of product formation given by Equations 11 and 12.

(equation 11) $$\phi_p = \phi_{isc}\left[\frac{k_1}{k_1 + k_2}\right]\left[1 + \frac{k_d}{k_r[O]}\right]^{-1}$$

(equation 12) $$\phi_p^{-1} = \phi_{isc}^{-1}\left[\frac{k_1 + k_2}{k_1}\right]\left[1 + \frac{k_d}{k_r[O]}\right]$$

Equation 12 also predicts that a plot of $1/\phi_p$ against $1/[O]$ should yield a straight line with slope,

(Equation 13) $$m = \phi_{isc}^{-1}\rho^{-1}(k_d/k_r)$$

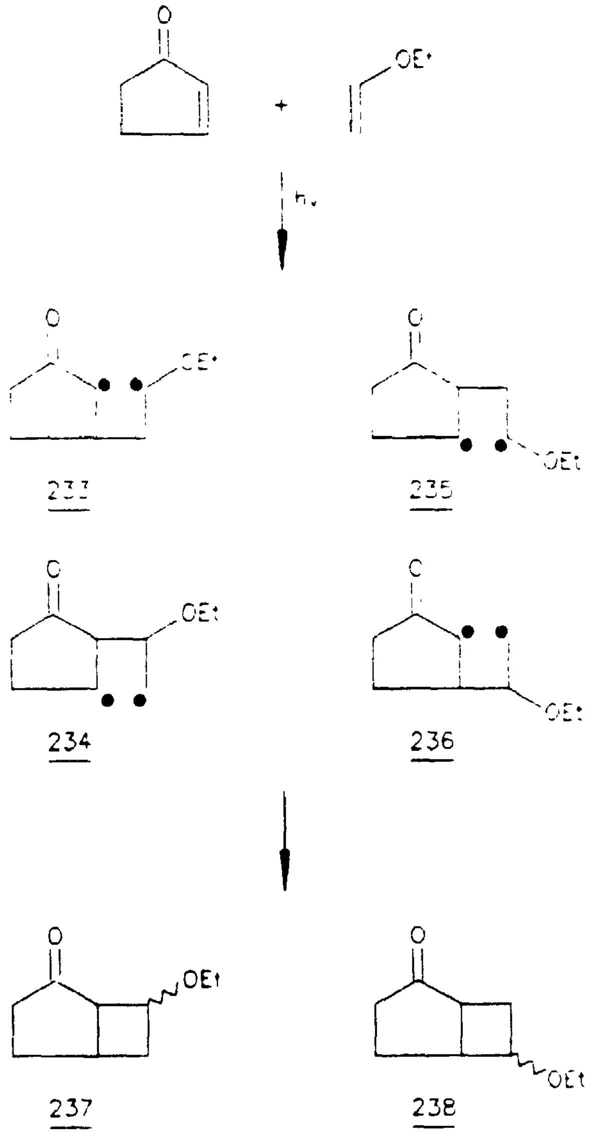
where (Equation 14) $$\rho = k_1/(k_1+k_2)$$

and intercept, $$I = \phi_{isc}^{-1}\rho^{-1}$$

In Equation 13, ρ represents the fraction of biradicals which proceed to products, and k_r represents the rate constant for biradical formation. Thus, de Mayo's results can be used to estimate the rate constant for biradical formation if no exciplex is assumed, and the kinetic analysis of Scheme 40 is correct.

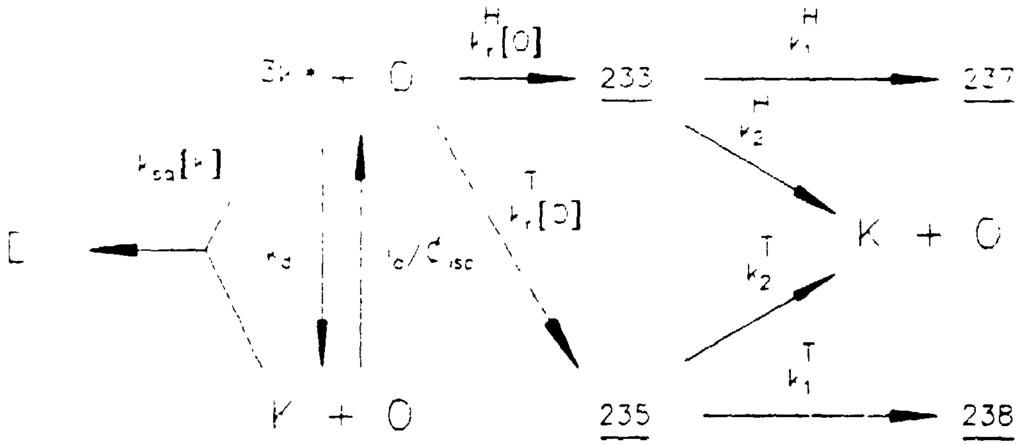
Unfortunately, the kinetic equations derived assuming the validity of schemes 30 or 40 are incorrect since both fail to take into account the fact that there can be, and in some cases must be, a minimum of two biradicals along the reaction pathway. Consider the 2+2 photocycloaddition reaction between cyclopentene and a mono-substituted ethylene (*eg.* ethyl vinyl ether) shown in scheme 41.

Scheme 41



It is known that, ignoring optical isomers, this reaction yields four possible isomeric products, that is, two pairs of regioisomers, 237 and 238. Since these products are derived from biradical intermediates, then they must derive from biradicals 233-236. Product 237 can only be formed from closure of 233 or 234, or both, and similarly 238 can only form from 235 or 236. Thus at least two of the four intermediate biradicals must be involved in order to account for the observed products. The likelihood that biradicals such as 234 and 236 are not involved has been discussed previously (chapter 3.3). Thus scheme 40 can be modified to accommodate biradicals 233 and 235 (scheme 42).

Scheme 42



Application of steady state kinetics for the derivation of the quantum yield of formation of each regioisomer (ϕ_H for 237, ϕ_T for 238) gives quantum yield expressions 15 and 16.

(equation 15) $$\phi_H = \rho^H \bullet \frac{k_r^H \phi_{isc} [O]}{[O][k_r^H + k_r^T] + k_d}$$

(equation 16) $$\phi_T = \rho^T \bullet \frac{k_r^T \phi_{isc} [O]}{[O][k_r^H + k_r^T] + k_d}$$

where

(equation 17) $\rho^H = k_1^H/(k_1^H + k_2^H)$ and $\rho T = k_1^T/(k_1^T + k_2^T)$.

Since $\phi_{isc} = 1.0$ for cyclopentenone,

(equation 18) $$\frac{1}{\phi_H} = \frac{k_d}{\rho^H k_r^H [O]} + \frac{1}{\rho^H \left[\frac{k_r^H}{k_r^H + k_r^T}\right]}$$

(equation 19) $$\frac{1}{\phi_T} = \frac{k_d}{\rho^T k_r^T [O]} + \frac{1}{\rho^T \left[\frac{k_r^H}{k_r^H + k_r^T}\right]}$$

If we plot $1/\phi$ for each regioisomer verses $1/[O]$ we should obtain straight lines with

(Equation 20) slope, $m_H = k_d/(\rho^H k_r^H)$

and

(Equation 21) intercept, $I^H = 1/\rho^H[k_r^H/(k_r^H + k_r^T)]$

for the head-to-head isomer. Similarly for the head-to-tail isomer,

(Equation 22) slope, $m_T = k_d/(\rho^T k_r^T)$

and

(Equation 23) intercept, $I^T = 1/\rho^T[k_r^T/(k_r^H + k_r^T)]$

What these Equations imply is that measurement of quantum yields of product formation as a function of alkene concentration do not allow estimation of the rate constants for biradical formation or the fraction of biradicals which partition to products since the values of ρ and k_r in Equations 20-23 cannot be separated. This dilemma has also been encountered by Wagner who applied steady state kinetics to the photodimerization of cyclopentenone and measured the quantum yield of dimerization as a function of cyclopentenone concentration (91a). In order to obtain information about the rates of biradical formation and about the efficiency of partitioning of the biradical intermediates between starting materials and products alternative methods are required to allow for independent determination of each. Chapter 6 describes an approach designed to allow independent determination of the partitioning efficiencies of the biradical intermediates while chapter 7 describes an approach designed to allow independent determination of the relative rates of formation of the biradical intermediates. In the conclusion to this part of the thesis it will then be shown how separation of these factors allows an assessment to be made as to whether the regiochemistry of enone-alkene cycloaddition depends on the relative rates of formation of the regioisomeric biradical intermediates (which could reflect orientation in an exciplex, or alternatively could reflect the stabilities of the biradicals produced) or whether the regiochemistry depends on the relative efficiencies with which the regioisomeric biradicals partition between products and starting materials.

CHAPTER 6

ENONE 1,4-BIRADICAL PARTITIONING: A MODEL STUDY

6.1 INTRODUCTION

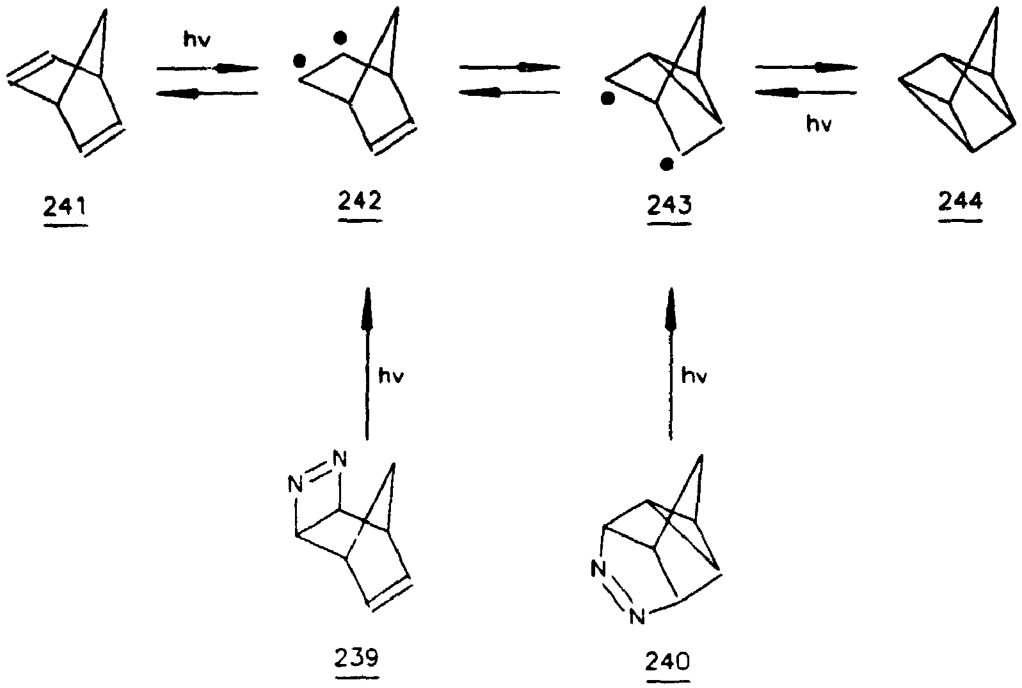
As discussed in chapter 5 it is impossible to extract values for k_r or ρ, as defined by the kinetic treatment of the sequence shown in scheme 42, by measurement of quantum yields of product formation as a function of olefin concentration. In order to gain better insight into the reaction mechanism and to determine whether or not biradical partitioning governs the regioselectivity it is necessary to determine separated values of k_r and ρ for each biradical intermediate by some independent method(s). Our first challenge was to design and synthesize compounds which would be capable of generating separately each of the 1,4-biradicals 233 and 235 independent of the enone 2+2 photochemistry. Once each biradical is generated independently its fate can be determined by monitoring the amounts of cyclopentenone and cyclobutanes formed by biradical cleavage and closure, respectively. The relative amounts of these products directly reflects the relative rates of the two possible fates and therefore the partitioning ratio, ρ, which would be given by

$$\rho = \frac{\text{(moles of cyclobutanes)}}{\text{(moles of cyclopentenone + moles of cyclobutanes)}}$$

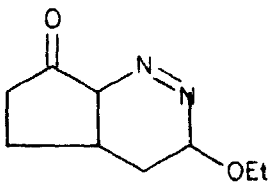
We envisioned three possible routes for the generation of the 1,4-biradicals; two of these involve extrusion of small molecules such as nitrogen or carbon monoxide, from an appropriate precursor, and the third involves an application of the Norrish Type II reaction.

The first of these involved photoextrusion of a nitrogen molecule from a tetrahydropyridazine derivative to generate a 1,4-biradical. Such reactions are well known in the literature and possess synthetic applications. For example, Turro (104) and coworkers have examined the photoextrusion of N_2 from the azo compounds 239 and 240 (Scheme 43) in an effort to generate biradicals 242 and 243 which are capable of cyclization to yield the quadricyclane 244 in competition with rearrangement to 241. The reaction could be sensitized to yield triplet 1,4-biradical intermediates which is essential for the type of biradical intermediates we wished to generate. The literature contains numerous examples of synthetic applications of the photoextrusion of nitrogen and this has been reviewed by Givens (105). Givens also summarized the results of the mechanistic and biradical studies of the nitrogen extrusion reaction of cyclic azoalkanes and noted that certain features consistently appeared. The photoextrusion reaction takes place most readily from rigid cyclic or bicyclic systems and can occur from both singlet or triplet (sensitized) excited states. The initial process is homolysis of one or both C-N bonds to yield a 1,n-biradical intermediate; however, if the cyclic system is flexible then *cis-trans* isomerization of the azo group may dominate the excited state chemistry instead. Formation of the biradical is followed by closure to generate a carbocyclic ring, by fragmentation, or by internal disproportionation to yield an acyclic alkene.

Scheme 43



The partitioning between these pathways is dependant on structural features (ring size, substitution pattern, etc.) and the multiplicity of the biradical and azoalkane precursors. These results suggest that if azo analogues <u>245</u> and <u>246</u> could be synthesized, then they would be viable precursors of the biradicals <u>233</u> and <u>235</u>.



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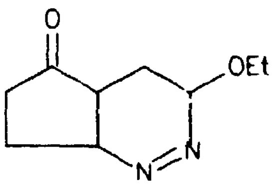
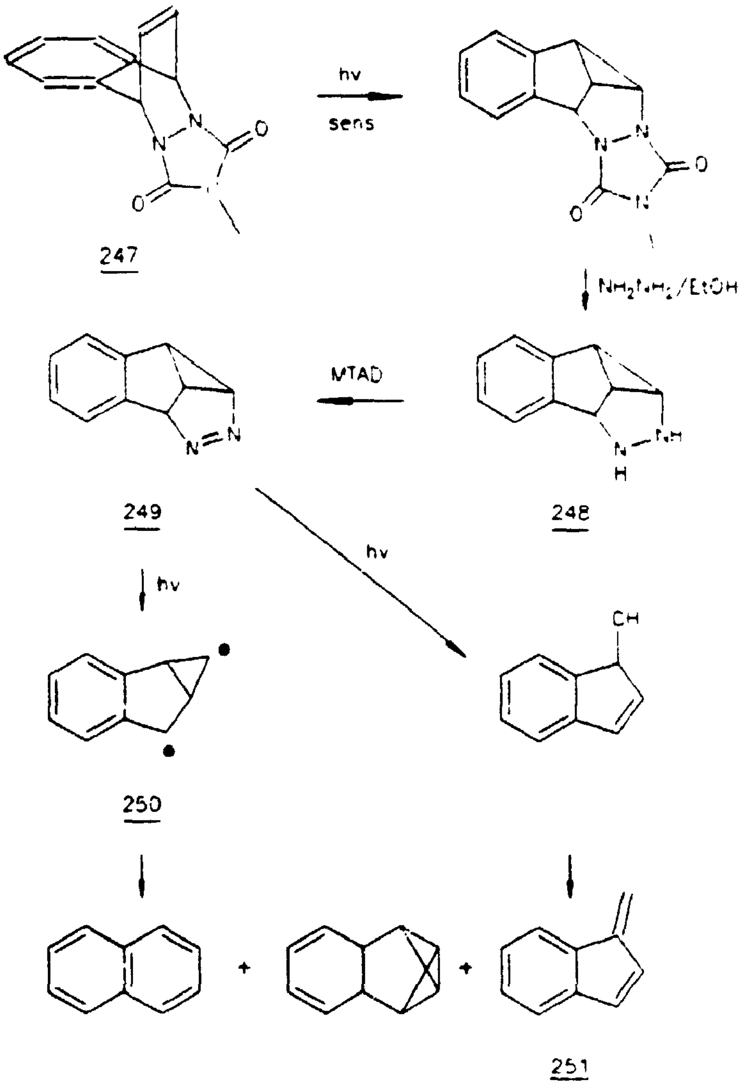


246

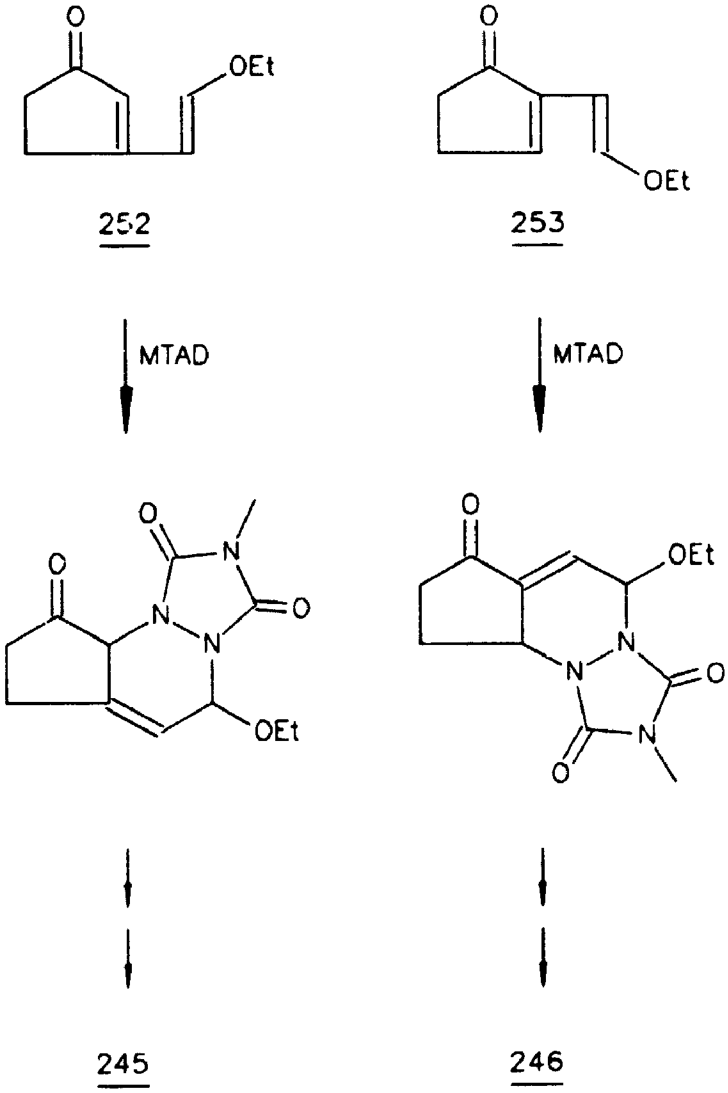
Recent work by Kjell and Sheridan (105) suggest a pathway for the synthesis of 245 and 246. They were able to generate a precursor to the benzoprefulvene biradical, 250, and indenylmethylene, 251, by synthesizing diazo compound 249 by oxidation of hydrazine 248 which was generated by deprotection of the photochemically rearranged Diels-Alder product 247 obtained from naphthalene and 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) (scheme 44).

Scheme 44



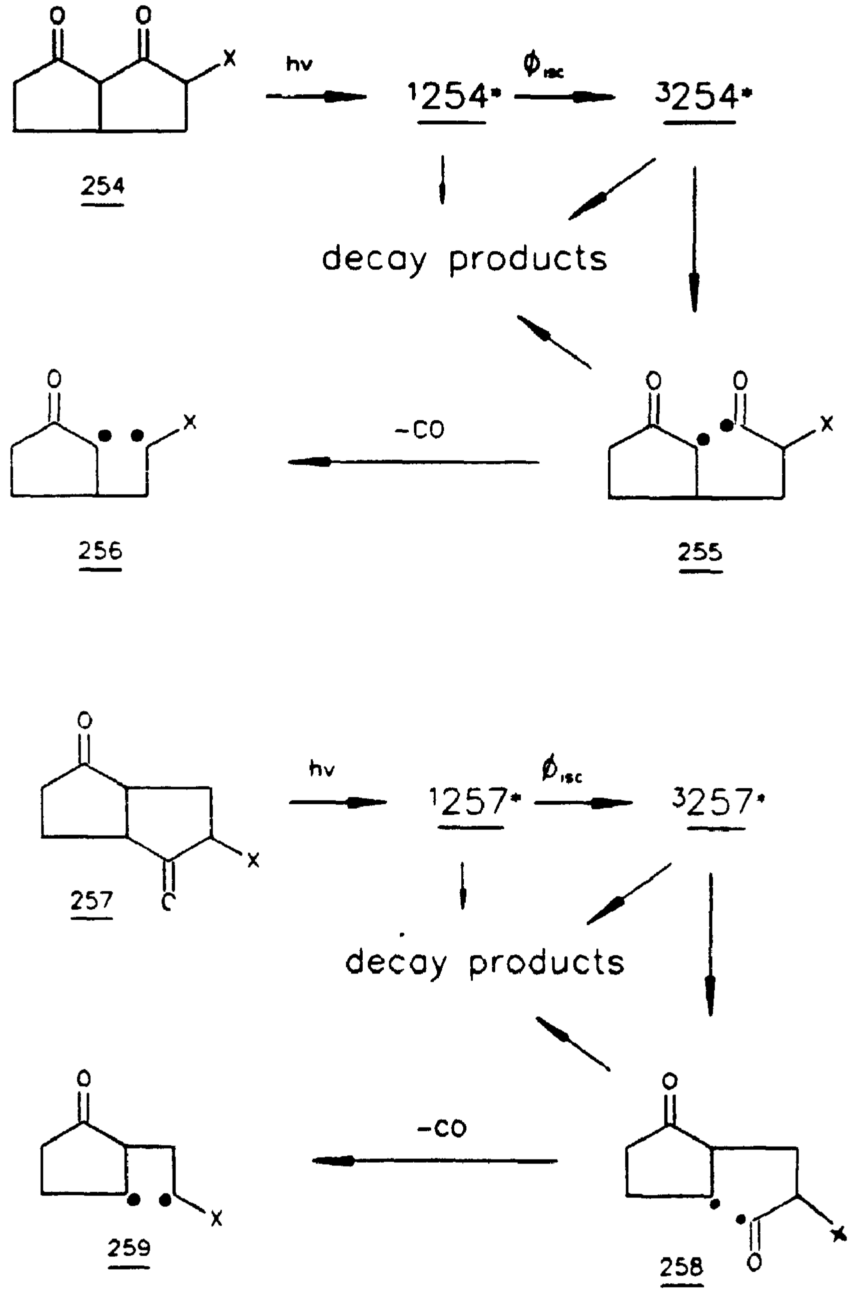
Using a similar route, it might also be possible to synthesize 245 and 246 by a Diels-Alder reaction of the appropriate substrates 252 and 253 (Scheme 45). However, in view of the rather lengthy synthetic effort which would be required to bring such a route to fruition, it was decided not to explore this pathway for independent generation of biradicals 233 and 235.

Scheme 45



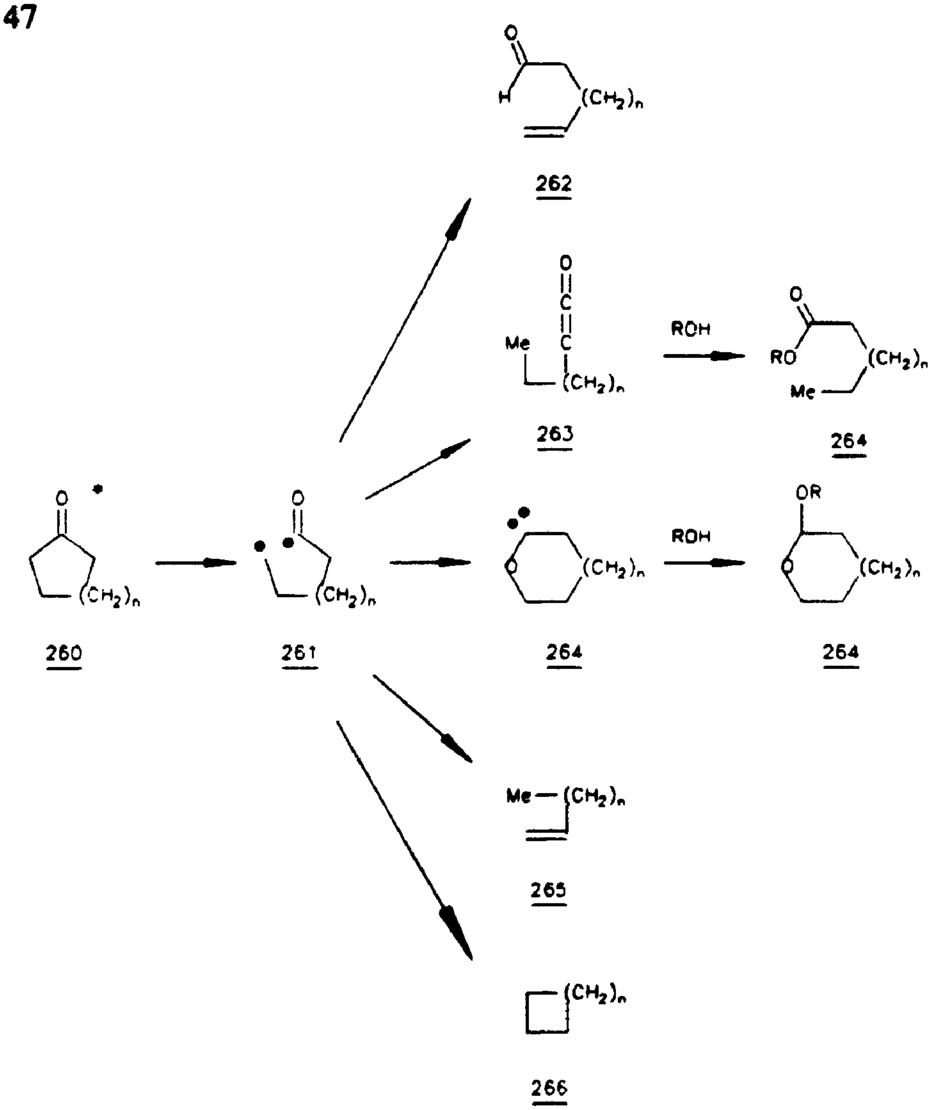
A second possible route to the biradicals involves extrusion of carbon monoxide from a biradical generated via a Norrish Type I cleavage of an excited state bicyclooctanedione (scheme 46).

Scheme 46



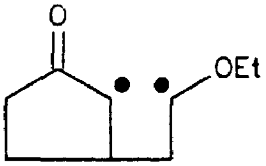
Norrish Type I α-cleavage of diones 254 and 257 would yield biradicals 255 and 258 respectively. Once these intermediates are formed they possess a number of fates analogous to the photochemical decomposition of cyclic aliphatic ketones (107) shown in scheme 47. One of these fates includes loss of carbon monoxide through homolytic cleavage to yield 1,4-biradicals 256 and 259. Once formed the biradicals may then partition to yield cyclobutanes or cleave to yield olefin and cyclopentenone.

Scheme 47



The photoextrusion of carbon monoxide from cyclic ketones is one of the earliest recorded and most well studied extrusion reactions. It has been the subject of several reviews (105-108) which have surveyed both the mechanistic details and synthetic applications. The "decay products" indicated in scheme 46 result from fates analogous to those shown for biradical 261 in scheme 47. The degree to which each pathway is followed is dependant upon a number of variables (ring size, substituents, temperature, and photolysis conditions). Although these other processes may dominate over the formation of the 1,4-biradicals 256 and 259 this is not of any consequence as long as some of these biradicals are formed. This approach to the independent generation of 1,4-biradicals implicated in enone-alkene photocycloaddition was not investigated in great detail as part of the work described in this thesis. It is, however, being examined by other workers in our laboratory.

The third approach to biradical generation involves the generation of 1,4-biradicals 267 and 268 which we envisioned would model the behaviour of biradicals 233 and 235.



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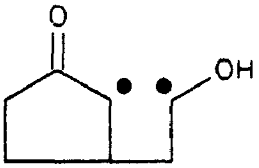

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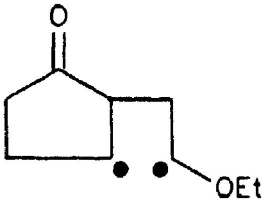
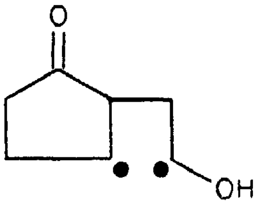
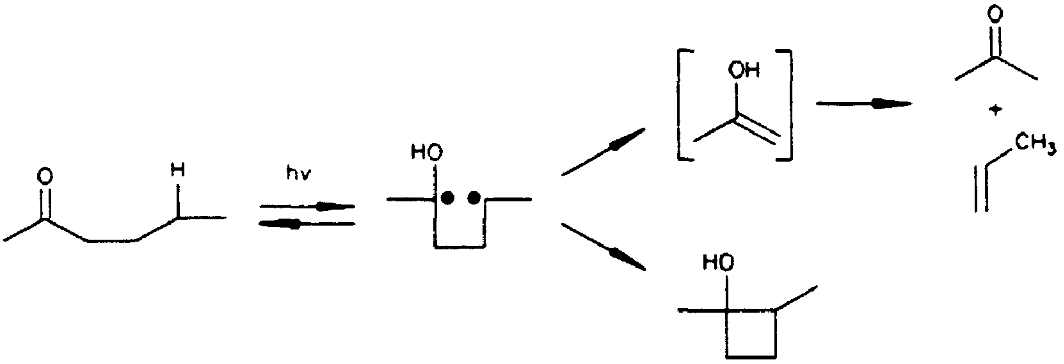


235



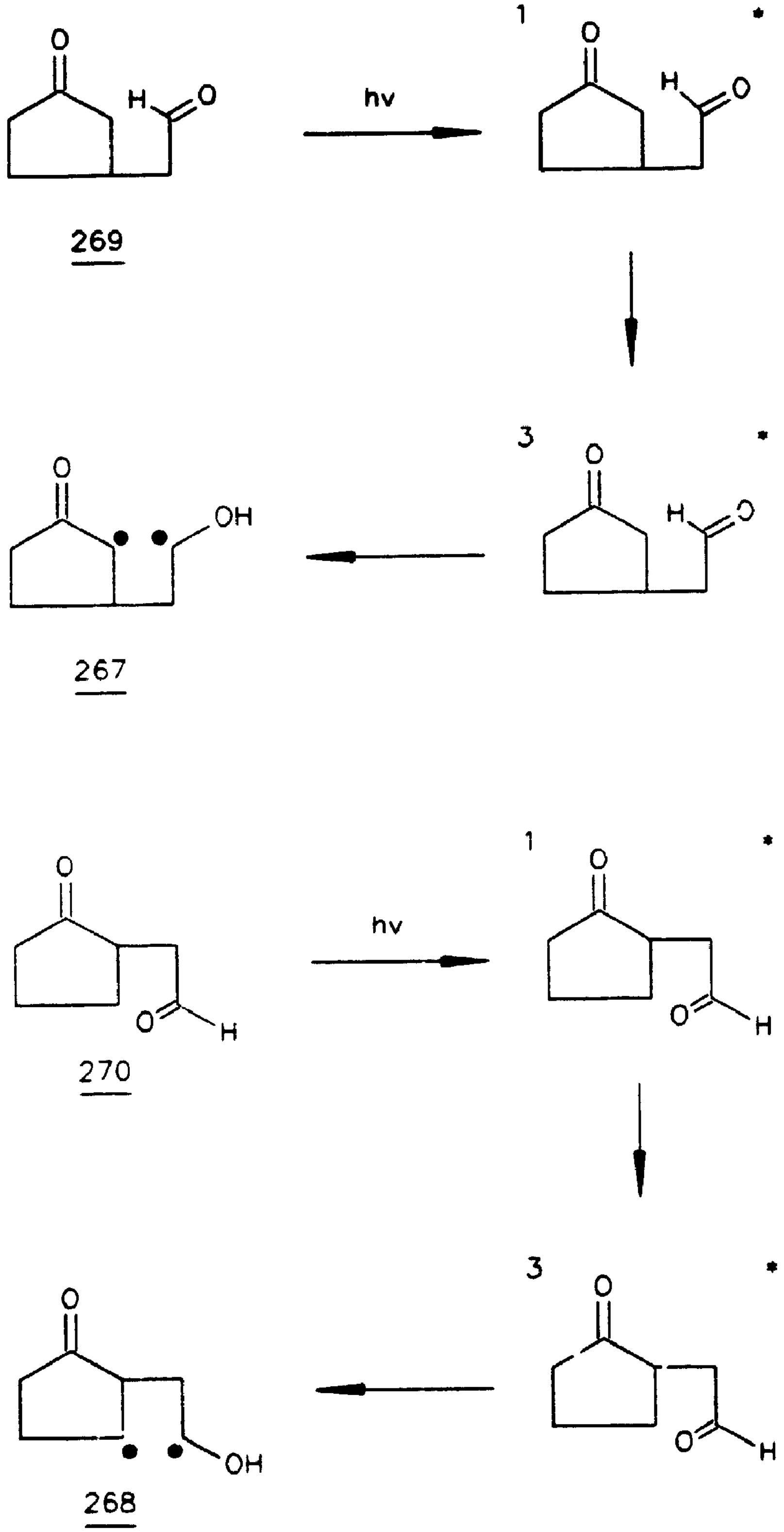
268

The latter biradicals are the anticipated intermediates in the photocycloaddition with ethyl vinyl ether to cyclopentenone. Intermediates 267 and 268 can be generated by an intramolecular hydrogen abstraction (Norrish Type II reaction) of the triplet excited state of the corresponding isomeric aldehydes 269 and 270, respectively (scheme 48). Norrish Type II reactions have also been extensively studied and have been reviewed (109).



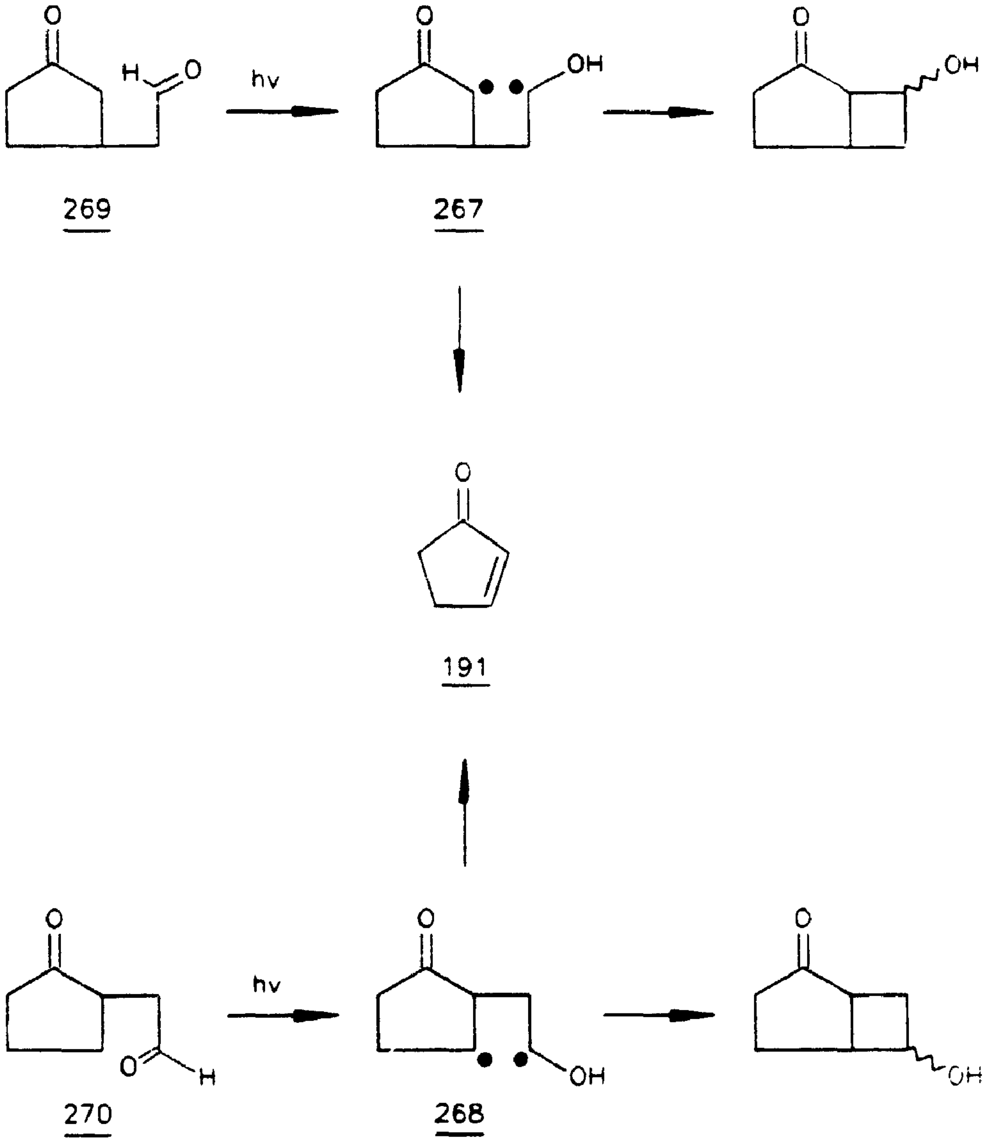
Excitation of carbonyl compounds with a γ-hydrogen results in characteristic 1,5-hydrogen transfer to yield a 1,4-biradical similar to the biradicals formed from photocycloaddition reactions. The Norrish Type II derived biradical can undergo cleavage or cyclization. In addition it can undergo back hydrogen transfer to yield the ground state starting material, although this can be suppressed by the use of solvents capable of hydrogen bonding (110). In the case of aldehydes 269 and 270 there are two independent chromophores present which can absorb light with similar molar extinction coefficients in the 300 nm region. Thus 269 and 271 are open to competition from photochemical processes originating from the excited states of the ketone functions present.

Scheme 48



This is not of any consequence as long as none of these other processes lead to cyclopentenone or cyclobutanols resulting from the decay of the Type II derived biradicals. Once the desired biradicals have formed then their fates can be determined by measuring the relative quantities of cyclopentenone and cyclobutanols formed (scheme 49).

Scheme 49



The major portion of this chapter is devoted to a description of the results of an examination of this third approach to the independent generation of 1,4-biradicals implicated in enone-alkene photocycloaddition. A minor portion of this chapter is devoted to a description of a study of the photolysis of bicyclo[3.3.0]octane-2,8-dione whose aim was to determine if the molecule is a viable precursor to the biradical obtained by photocycloaddition of ethene to cyclopentenone.

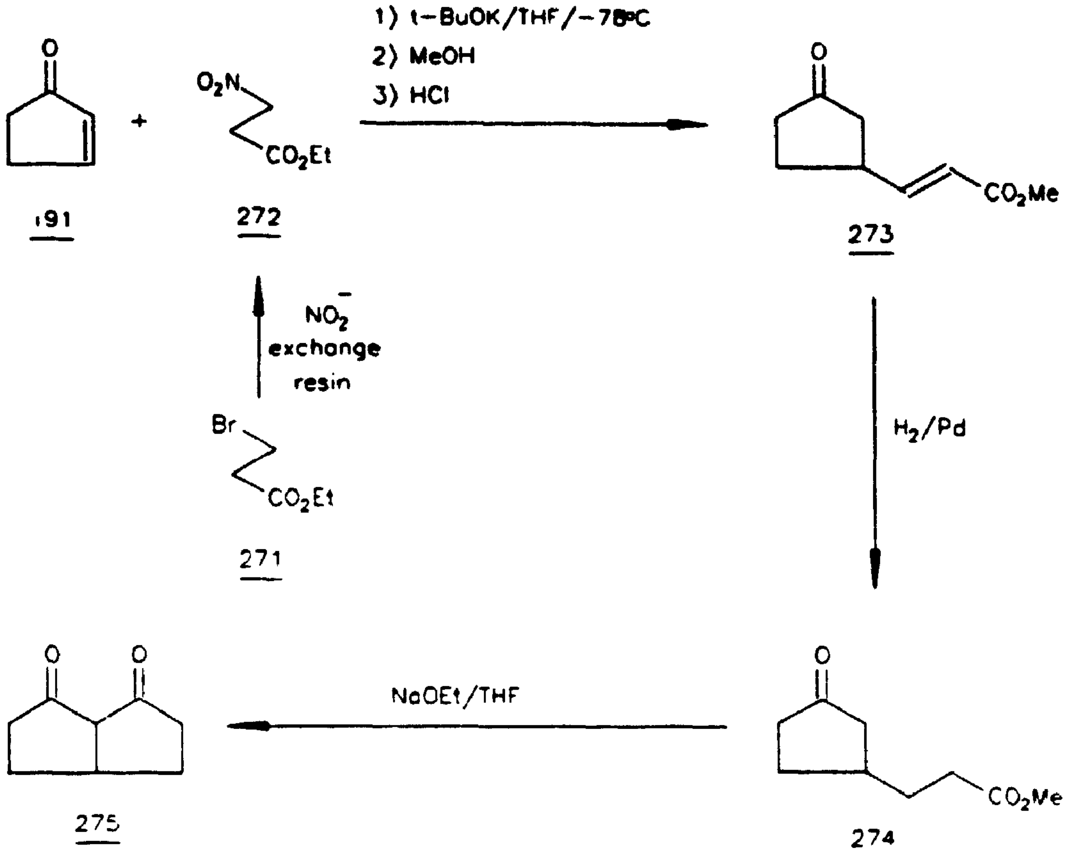
If biradicals 267 and 268 can be independently generated and their fates determined, then this will yield information about the likely fates of 233 and 235. In particular, it will be possible to infer the relative efficiencies with which each biradical proceeds to cycloadducts rather than reverting to starting materials. These can then be compared with the regiochemical outcome of the photocycloaddition reaction of cyclopentenone and ethyl vinyl ether; this comparison will yield information about the amounts of each biradical formed in the photocycloaddition reaction and hence about their relative rates of formation.

6.2 Synthesis and Photolysis of Bicyclo[3.3.0]octane-2,8-dione

6.2.1 Synthesis

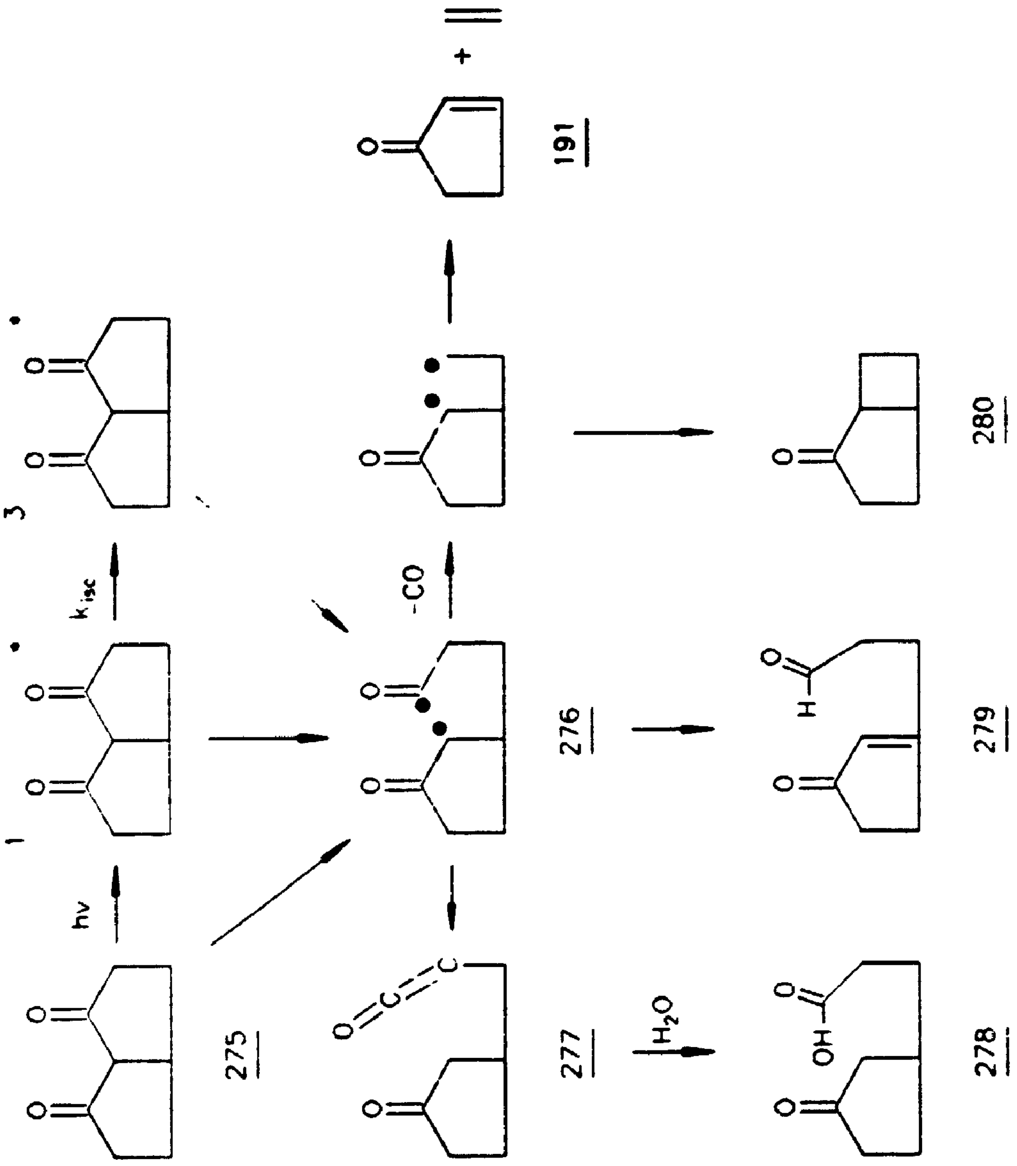
Bicyclooctanedione 275 was prepared as outlined in scheme 50 using a modification of the method of Eaton (111) and Duthaler (112). Nitropropionate 272 was prepared by reacting bromoester 271 with a nitrite charged anion exchange resin. Addition of 3-nitropropionate 272 to cyclopentenone 191 followed by hydrogenation of the resulting acrylate 273 gave 274 in an overall yield of 78%. Treatment of 274 with sodium ethoxide in THF resulted in an intramolecular Claisen condensation to yield dione 275 in an overall yield of 55%.

Scheme 50



6.2.2 Photolysis

Irradiation of dione 275 was performed in benzene with a drop of distilled water added to prevent any build up of ketene 277 (scheme 51). Photolysis led to the disappearance of starting dione and formation of a single major product with a slightly shorter g.c. retention time. No evidence was observed for the formation of cyclopentenone or the cyclobutane product 280, which had previously been prepared by irradiation of cyclopentenone with ethene. G.c.-m.s. indicated that the new product possessed a molecular ion m/e 138.



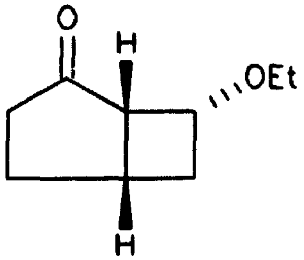
Scheme 51

This is the same as the starting material and suggests that it was not a product of any decarbonylation process. The irradiation was allowed to continue in order to accumulate the product for nmr analysis. An ^{1}H-nmr spectrum was obtained of a reaction mixture containing the new product and starting material in a ratio of 3:1. It showed a low field signal at 9.75 ppm which can be assigned to the aldehyde proton of 279. The corresponding olefinic proton was also present at 5.82 ppm and gave small allylic coupling constants of 0.5 Hz. This, along with the m.s. data allowed for assignment of structure 279 to the product.

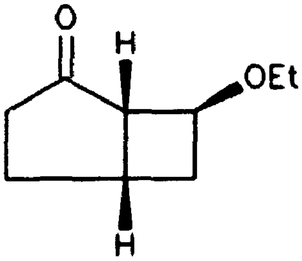
The photolysis was repeated under sensitized conditions (benzene solvent/quartz tube/low pressure Hg vapour lamp) and at elevated temperatures (sealed tube 70°C). The results were very similar; the single major product was again 279.

6.3 Irradiation of Cyclopentenone with Ethyl Vinyl Ether

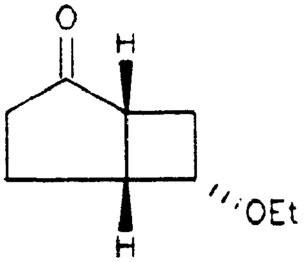
In order to supply the necessary data for comparison, the regiochemical outcome of the reaction of cyclopentenone with ethyl vinyl ether was examined in detail and the results compared with these previously published by other groups (113). When cyclopentenone, prepared by the method of Mihelich (114), was photolyzed in the presence of ethyl vinyl ether (20 fold excess) clean conversion to 4 separable products in a ratio of 9.9:17.6:29.9:42.6 was observed. This is as one would expect as the cyclobutane-cyclopentane ring fusion is always *cis* (80) and the isomers produced would be head-to-head (HH) or head-to-tail (HT) and *endo* or *exo*, 281-284.



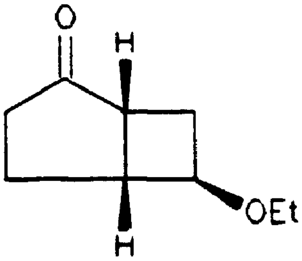
281



282



283



284

Coupled gas chromatography-chemical ionization mass spectrometry (g.c-c.i.m.s.) yielded molecular ions of m/e 155 for each product, indicative of 1:1 photoadducts. The ^{1}H-nmr spectrum of the reaction mixture exhibited methylene quartet signals in the 3.6 ppm region along with methyl signals as triplets between 1.4 and 1.1 ppm. Between these regions were various multiplets due to the cyclopentanone and cyclobutane protons. The nmr and mass spectral data clearly suggested that these products were indeed 2+2 cycloadducts of cyclopentenone and ethyl vinyl ether. No cyclopentenone dimers were present.

The isolation of these photoadducts was not undertaken. Their stereochemistry and regiochemistry were probed by the method of Vandewalle (113a) using chemical ionization mass spectrometry (c.i.m.s.) to study each compound as it eluted from the gas chromatograph. This technique has also been used to determine the structures of the photodimers of cyclopentenone, cyclohexenone, and indenone (115). The regioisomers were readily distinguished by analysis of the c.i.m.s. data. Unlike the head-to-tail isomers, the head-to-head isomers fragment nearly exclusively in a cycloreversion type process in which the cyclopentenone radical cation containing an added hydrogen (m/e 83) is formed as well as the ethyl vinyl ether radical cation containing an added hydrogen. The fragmentation can be rationalized as shown in scheme 52. Compounds 281 and 282 upon chemical ionization yield the quasi-molecular ion 285 which exists in several forms; ion 286 being the most stable with carbenium ion character. Heterolytic cleavage or homolytic cleavage yields ions 287 (m/e 83) and 288 (m/e 73). However when isomers 283 and 284 are ionized the cycloreversion process has a lower probability because of the contribution of form 290 is decreased. In general this leads to a relatively higher abundance of the parent ion for the head-to-tail isomers, and when the fragmentation does occur it results in the loss of a molecule of ethanol to yield ion 292. Table 5 shows the relative intensities of the fragment ions 287 + 288, ion 292, and the parent ion, m/e 155. For head-to-head isomers the value of the ratio of the intensities %(287+288)/%285 is larger than unity while for head-to-tail isomers it is less than unity.

Scheme 52

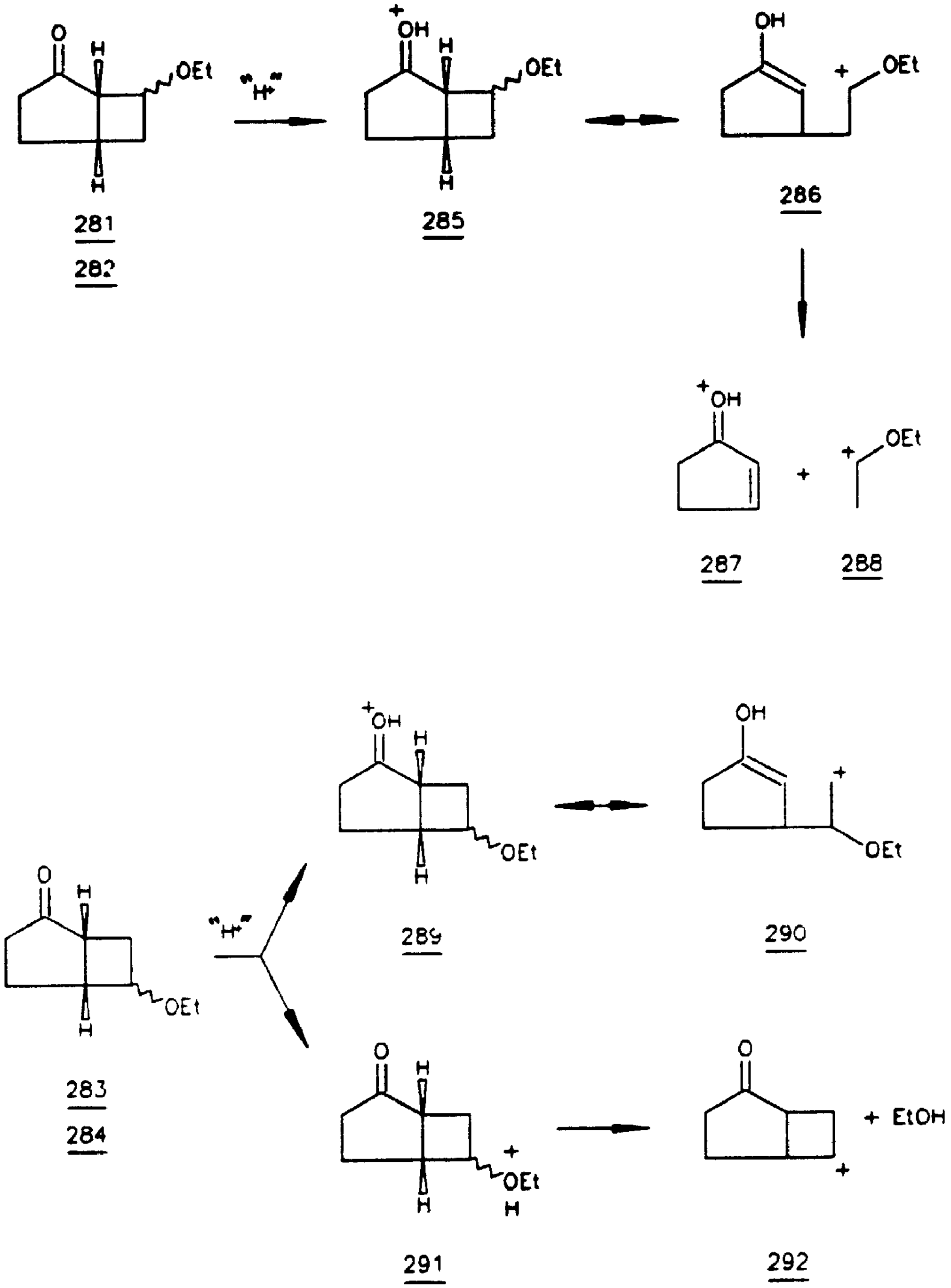

O
H
OEt
H
281
282
"H+"
+OH
H
OEt
H
285
OH
+
OEt
286
+OH
+
+
OEt
287
288
+OH
H
OEt
H
289
OH
+
OEt
290
O
H
OEt
H
283
284
"H+"
O
H
+
OEt
H
H
291
O
+ EtOH
+
292

TABLE 5

MASS FRAGMENT PROPERTIES OF CYCLOPENTENONE-ETHYL VINYL ETHER ISOMERS 281-284

isomer	g.c. % ratio (lit.)[a]	total % of ions m/e 83 + 73[b]	% ion m/e 109[b]	% ion m/e 155[b]	stereochemistry
281	9.9 (8.0)	183 (179)	9 (2)	1.44 (2)	*syn* HH
282	17.6 (11.8)	170 (156)	21 (2)	1.25 (0.5)	*anti* HH
283	29.9 (28.4)	9 (5)	16 (5)	100 (100)	*syn* HT
284	42.6 (51.8)	7.5 (5)	100 (100)	16.0 (35)	*anti* HT

[a] compared literature values (113a) are given in parentheses.
[b] fragment ions are indicative of the following structures shown in scheme 52,

m/e 83 - 287
m/e 73 - 288
m/e 109 - 292
me/ 155 - 285

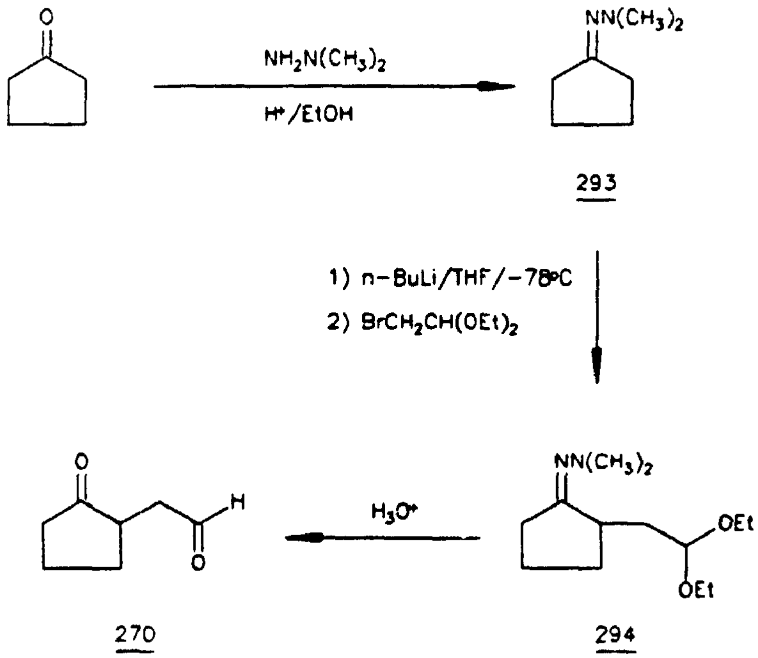
The data given in table 5 correlate well with the data determined by Vandewalle (shown in parentheses); thus the stereoisomers could be assigned to structures 281-284. This led to a regioisomeric ratio for HH:HT of 1:2.64.

6.4 Synthesis and Photolysis of Aldehyde 270

6.4.1 Synthesis

Aldehyde 270 was synthesized according to scheme 53. Cyclopentanone was first protected as the N,N-dimethylhydrazone to give 293 which upon treatment with n-butyl lithium followed by addition of bromoacetaldehyde diethyl acetal yielded the alkylated product 294 in 51% yield from cyclopentanone. Product 294 was then hydrolysed by treatment with a 10% HCl solution; continuous extraction and distillation then gave the desired aldehyde 270 in an overall yield of 25%. The aldehyde was identified from its mass spectrum, which showed a parent ion with m/e 126, and from its ^{1}H-nmr spectrum which showed the expected low field aldehyde signal at 9.66 ppm. The rest of the m.s. and nmr data were consistent with structure 270.

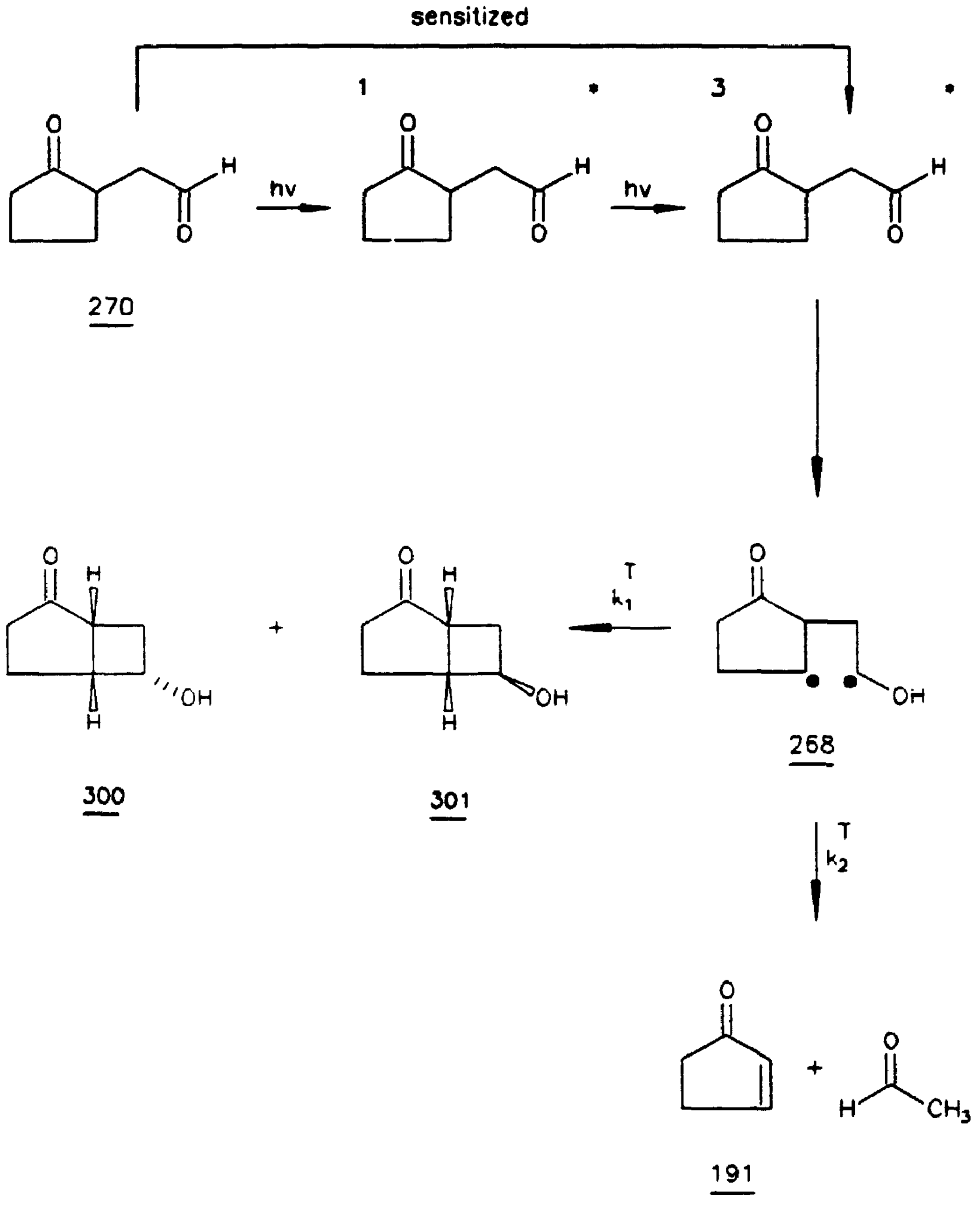
Scheme 53



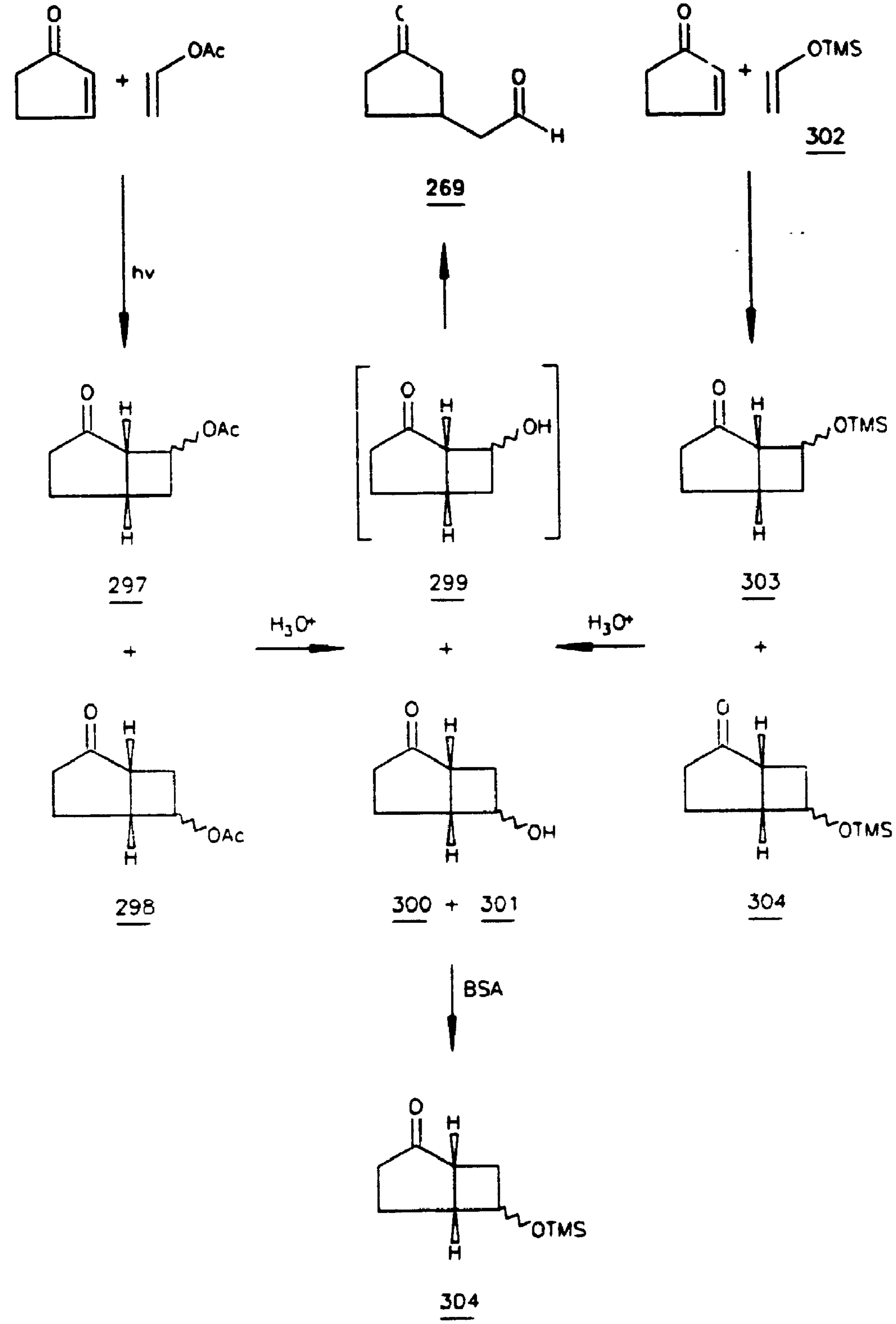
6.4.2 Photolysis

Irradiation of 270 in benzene yielded six detectable products by g.c.; those of interest were, in order of increasing volatility, the first and last two products. The first product was shown by g.c. coinjection and g.c.-m.s. (m/e $M^+ = 82$) to be cyclopentenone. This indicates that biradical 268 is indeed formed and that it undergoes cleavage. The last two g.c. products possessed g.c. retention times close to the starting aldehyde. M.s. revealed that they possessed molecular ions of m/e 126, which is consistent with that expected for cyclobutanols 300 and 301. G.c. products 2-4 could not be identified but their m.s. revealed molecular ions of 162, 174, and 154, respectively. The absence of any ion with m/e 126 suggests that these are not cyclobutanols or products derived from biradical 268. The route to the identified products is shown in Scheme 54. Further evidence for cyclobutanol formation was provided by three experiments. Firstly, the photocycloadducts from cyclopentenone and vinyl acetate (Scheme 55) were synthesized and hydrolysed with acid to yield cyclobutanols 299-301. G.c., g.c.-m.s., and ^{1}H-nmr spectroscopy revealed that only two cyclobutanols were formed and that aldehyde 269 was also produced. This can be attributed to the decomposition of cyclobutanol 299 *via* a retro-aldol reaction to yield 269. Thus we can assign structures 300 and 301 to the two stable cyclobutanols. Cyclobutanols 300 and 301 and aldehyde 269 were also obtained from acid hydrolysis of photocycloadducts 303 and 304 which were produced by irradiation of cyclopentenone with trimethylsiloxyethene, 302.

Scheme 54



Scheme 55


O
OAc
+
O
H
O
OTMS
302
269
hν
O
H
OAc
H
297
O
H
OH
H
299
O
H
OTMS
H
303
H₃O⁺
H₃O⁺
+
+
+
O
H
OAc
H
298
O
H
OH
H
300 + 301
O
H
OTMS
H
304
BSA
O
H
OTMS
H
304

Thirdly, silylation of the hydrolysis products of both cyclopentenone-vinyl acetate and cyclopentenone-302 photoadducts with bis(trimethylsilyl)acetamide, BSA, yielded aldehyde 269, and silylated cyclobutanols 304. G.c. coinjection of the cyclobutanols obtained by hydrolysis of 298 and 304 with the photolysis products of 270 confirmed that the latter were the desired cyclobutanol adducts. The mixture of photolysis products obtained from 270 was also treated with BSA; conversion of the cyclobutanols to the cyclobutane products 304 was confirmed by g.c. and g.c.-m.s..

In order to quantify the amounts of cyclopentenone and cyclobutanols 300 and 301 produced by photolysis of 270, each was calibrated against a decane internal standard by gas chromatography. Cyclopentenone was also calibrated against cyclobutanols 300 and 301. The procedure for calibrations and quantitative analysis is described in the experimental section in chapter 8. The results are given in table 6 where the partitioning ratio is determined by the expression $\rho^T = \text{moles}_{(300+301)}/\text{moles}_{(191+300+301)}$. Some irradiations were performed under sensitizing conditions to ensure that the reaction was proceeding *via* the triplet biradical. The mixed solvent system consisting of methanol/benzene (experiments 6 and 7) was used for two irradiations in order to allow comparison of the results with those obtained in a similar solvent system used in the photolysis of 269. In addition, the solvent system was chosen in order to suppress decay of the Type II biradical back to 269 by back hydrogen atom transfer. The small change in the solvent did not affect the results. The results given in table 6 indicate that for the various irradiation conditions the intermediate biradical partitions between cyclopentenone and cyclobutanols with a constant ratio. The average partitioning ratio was 0.29 ± 0.02 (6%).

TABLE 6

PARTITIONING RATIOS FOR PHOTOLYSIS OF ALDEHYDE 270

Exp. #	Solvent	Irrad. time (hrs)[a]	Ratio 191: 300+301	ρ^T [b]	Stereoisomeric ratio (300:301)
1(dir)[c]	benzene	2.0	2.45 (0.16)[e]	0.29 (0.02)[e]	1:1.80
1(dir)	benzene	4.0	2.56 (0.13)	0.28 (0.01)	1:1.78
1(dir)	benzene	8.0	2.56 (0.20)	0.28 (0.02)	1:1.79
2(dir)	benzene	2.0	2.23 (0.20)	0.31 (0.03)	1:1.68
3(sens)[d]	benzene	8.0	2.56 (0.18)	0.28 (0.02)	1:1.72
4(sens)	benzene	0.167	2.85 (0.11)	0.26 (0.01)	1:1.71
4(sens)	benzene	0.33	2.33 (0.14)	0.30 (0.02)	1:1.70
*5(sens)	benzene	3.0	1.62 (0.11)	0.38 (0.03)	1:1.68
6(dir)	mixed	2.0	2.18 (0.19)	0.32 (0.03)	1:1.73
7(sens)	mixed	0.33	2.33 (0.20)	0.30 (0.03)	1:1.74

[a] all photolyses did not exceed 10% conversion of starting 270. Conversion varied with light source and irradiation vessel. *over irradiated (20% conversion of 270).

[b] ρ^T defined as $k_1/(k_1+k_2)$ according to Scheme 54.

[c] direct (dir) irradiations were performed with a Pyrex filtered medium pressure Hg lamp ($\lambda_{ex}>300$ nm).

[d] sensitized (sens) irradiations were performed in benzene using a low pressure Hg lamp. Mixed solvent - Methanol-d_4/benzene (1:14).

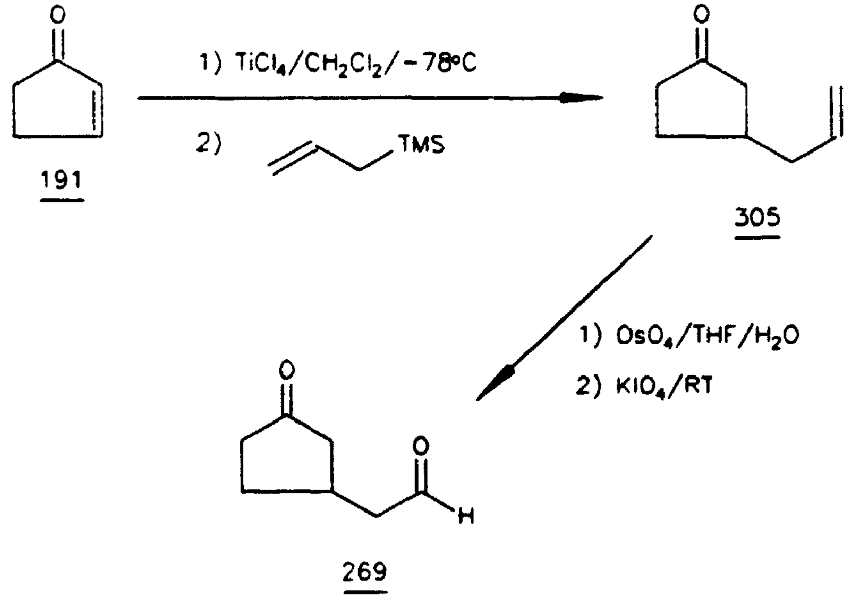
[e] errors given in parentheses are reported as standard deviations for 10 g.c. injections of the photolysis reaction.

6.5 Synthesis and Photolysis of Aldehyde 269

6.5.1 Synthesis

Aldehyde 269 was synthesized according to scheme 56. Conjugate allylation of 2-cyclopentenone with allylsilane 305 (116) was accomplished by the literature method (117) to yield 3-(2-propenyl)cyclopentanone, 305 in a 58% yield. After purification the product was oxidized using a modification of the method of Mori (118); olefin 305 was treated with osmium tetroxide followed by addition of sodium metaperiodate to complete the oxidation and regenerate the catalyst. The overall yield of the aldehyde was 40%. It was identified from its mass spectrum, which showed a parent ion with m/e 126, and from its ^{1}H-nmr spectrum which showed the expected low field aldehyde signal at 9.17 ppm. The rest of the m.s. and nmr data were consistent with structure 269.

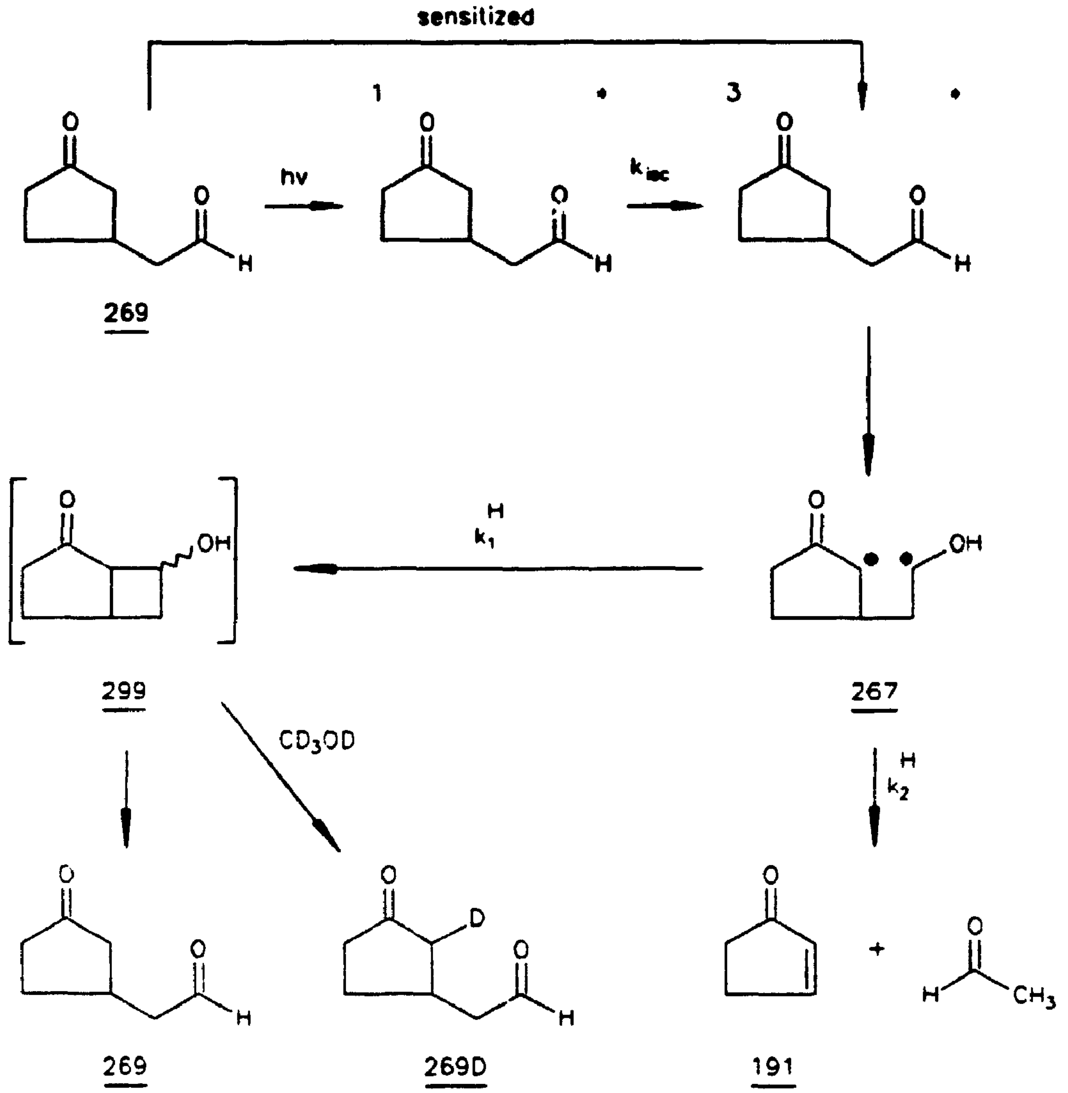
Scheme 56



6.5.2 Photolysis

Irradiation of 269 in benzene yielded three products detectable by g.c. The first (most volatile) product was shown by g.c. coinjection and g.c.-m.s. (m/e $M^+=82$) to be cyclopentenone which indicates that biradical 267 is indeed formed and undergoes cleavage. The last two g.c. products possessed g.c. retention times slightly longer than the starting aldehyde; however, m.s. revealed that they possessed molecular ions of m/e 153 and no ions with m/e 126 (corresponding to the cyclobutanols 299) were present. These last two g.c. products remain unidentified. The route to the cyclopentenone product is shown in scheme 57. Sensitized reactions, in which the solvent benzene was irradiated with a low pressure mercury vapour lamp, showed faster conversion to cyclopentenone and the two unidentified products. It was concluded that the cyclobutanols 299 were probably being formed but were undergoing retro-aldol cleavage back to 269, either spontaneously in the reaction mixture or following injection onto the g.c. In order to determine whether cyclobutanols were being formed and were stable in solution, the ^{1}H-nmr spectrum of a reaction mixture was examined by g.c. and showed a ratio of cyclopentenone to starting material of 1:4.4. The ^{1}H-nmr spectrum contained aliphatic multiplets between 2.5 and 1.0 ppm, the aldehyde peak at 9.19 ppm and cyclopentenone protons at 5.95 and 6.82 ppm. The region between 3.0 and 5.0 ppm remained unchanged and there was no evidence of signals corresponding to the expected cyclobutane protons.

Scheme 57



Attempts were made to trap the cyclobutanols by silylation with trimethylsilyl chloride/triethylamine or with BSA immediately after photolysis. Irradiations were also carried out in the presence of the silylating reagent. It was hoped that this would yield the previously described cycloadducts 303; however under all the conditions examined none of these adducts could be detected. Similar photolyses with aldehyde 270 did yield adducts 304, suggesting that the trapping was viable provided the cyclobutanol has a long enough lifetime to react with the silylating agent.

In order to confirm the presence of the cyclobutanols 299, and to allow their quantification, photolysis of 269 was carried out under direct and sensitized conditions in a solvent system consisting of 14 parts benzene and 1 part methanol-d_4. It was reasoned that this would result in deuterium incorporation into the aldehyde upon retro-aldol opening of cyclobutanol 299 to yield aldehyde 269D (scheme 57). The amount of cyclobutanols formed could then be determined by measurement of the amount of deuterium incorporated into the aldehyde remaining. In order that the amount of deuterium incorporated would correctly reflect the amount of cyclobutanol formed, conversions were kept low to avoid photolysis of deuterated aldehyde. Cyclopentenone produced upon photolysis was shown not to contain deuterium. This provides evidence that the deuterated aldehyde 269D was not photolyzed. The amount of cyclopentenone was also determined and compared with the amount of cyclobutanol formed and hence the biradical partitioning ratio determined by $\rho^{H} = \text{moles}_{299}/\text{moles}_{191+299}$. The absolute amount of aldehyde 269 and cyclopentenone present following irradiation was determined by g.c. relative to a calibrated internal standard, and the amount of deuterium incorporation into the aldehyde was determined by g.c.-m.s.. The results are shown in table 7 and a sample calculation for experiment 5 in the table is given in the Experimental section (chapter 8). The results in table 7 were consistent for the various irradiation conditions and yielded an average partitioning ratio, $\rho^{H} = 0.22 \pm 0.02$ (9%). Anomalous results of $\rho^{H} = 0.67$ and 0.55 obtained in two further experiments (not shown in table 7) were discarded due to the presence of significant amounts of impurities (20%) in the starting aldehyde 269.

TABLE 7

PARTITIONING RATIOS FOR PHOTOLYSIS OF ALDEHYDE 269

Exp. #	Irrad. time (hrs)	mMol[a] 269	% "D" incorp.	mMol 299 (X 10^3)	mMol 191 (X 100)	ρ^H	% conv.[b]
1(dir)	23	0.159[c] (0.006)	4.26[d] (0.69)	6.77 (1.13)	2.325[c] (0.074)	0.23[e] (0.04)	12
2(dir)	6	0.213 (0.014)	3.02 (0.56)	6.43 (1.26)	1.941 (0.080)	0.25 (0.05)	9
3(dir)	4	0.188 (0.002)	6.48 (2.16)	12.20 (4.07)	4.309 (0.116)	0.22 (0.07)	15
4(sens)	0.12	0.207 (0.011)	5.50 (1.76)	11.40 (3.70)	4.420 (0.181)	0.21 (0.07)	4
5(sens)	0.13	0.168 (0.004)	5.27 (1.85)	8.85 (3.11)	3.148 (0.059)	0.22 (0.08)	18
6(sens)	0.13	0.188 (0.020)	4.62 (0.67)	8.69 (1.56)	3.507 (0.247)	0.20 (0.04)	12

[a] amount of 269 measured after photolysis.

[b] amount of 269 lost during photolysis.

[c] determined by g.c., calibrated against internal standard.

[d] determined by g.c./m.s as shown in the Experimental (Chapter 8).

[e] ρ^H defined as $k_1/(k_1+k_2)$ according to scheme 57.

[f] direct (dir) irradiations were performed with a Pyrex filtered medium pressure Hg lamp ($\lambda_{ex} > 300$ nm).

[g] sensitized (sens) irradiations were performed in benzene using a low pressure Hg lamp. Mixed solvent - Methanol-d_4/benzene (1:14).

*All absolute errors are given in parentheses. Error analysis given in Experimental (Chapter 8).

As mentioned earlier in this chapter, for purposes of comparison cyclopentenone and ethyl vinyl ether were irradiated under both direct and sensitized conditions in benzene and in a 1:14 methanol-d_4/benzene solvent using approximately 2% EVE by volume. This was done in order to demonstrate that the effect of changing the solvent polarity upon the cycloaddition reaction and the aldehyde photolysis was similar. The results yielded a regioisomeric HH:HT ratio of 1:3.2 and 1:3.3 in benzene and the mixed solvent, respectively, and stereoisomeric ratios for the HT isomers of 1:1.6 in both solvents.

6.6 Discussion of Results

As noted in the Introduction, generation of the regioisomeric biradicals implicated in enone-alkene cycloaddition by photolysis of azo precursors such as 245 and 246 is attractive. However, because of the synthetic inaccessibility of these compounds it was decided to investigate the two other routes proposed for independent generation of the biradical intermediates. The first of these involved examination of bicyclo[3.3.0]octanedione photochemistry.

Following the successful synthesis of the unsubstituted dione 275 it was photolyzed in order to determine if it would undergo α-cleavage and decarbonylation to generate a 1,4-biradical. However, photolysis of 275 did not lead to cyclopentenone or cyclobutane formation. Even at elevated temperatures, where decarbonylation of the primary biradical would be enhanced (119) decarbonylation did not occur. The major product was 279 which results from intramolecular hydrogen abstraction in the initially produced biradical 276.

The failure of 275 to undergo decarbonylation is presumably derived from the fact that it would result in the formation of a 1,4-biradical possessing a primary radical centre. Givens (105) has pointed out that although photoextrusion is quite efficient for cyclobutanones and does occur for cyclopentanones, the competing intramolecular hydrogen abstraction (to give aldehydes and ketenes) has a lower activation barrier than the carbon-carbon bond scission in the acyl radical. In order to make decarbonylation competitive, dione 275 would have to be substituted (or disubstituted) with radical stabilizing groups as shown for 254 in Scheme 46. This possibility is now under examination in our laboratory (120).

The third route for independent generation of the desired biradicals involved photolysis of aldehydes 269 and 270. The ratio of cyclopentenone to cyclobutanols 300 and 301 formed on photolysis of aldehyde 270 indicates that ρ^T, the fraction of the intermediate biradical 268 which proceeds to cyclobutane product rather than reverting to cyclopentenone, is 0.29 ± 0.02 (7%). Similarly the ratio of cyclopentenone to cyclobutanol 299 formed during the photolysis of aldehyde 269 indicates that ρ^H, the fraction of biradical 267 which proceed to cyclobutane product rather than reverting to cyclopentenone, is 0.23 ± 0.02 (9%). The error given for the partitioning ratio is a result of the statistical treatment used for averaging values with associated error. Each error for ρ^H was deterimined by error propagation and is given in Table 7. The error for the mean ρ^H of 0.02 (9%) seems artificial since the relative errors for each ρ^H ranges from 17% to 33%. Thus it is believed that the error calculated is somewhat low. Nonetheless, this does not affect the conclusion that the two partitioning ratios are similar.

The most important point about these partitioning ratios is that they are similar. If the biradicals 233 and 235 also partition between cyclopentenone and cyclobutanols 299-301 with the same ratios then this implies that the rate of formation of the two biradicals in the photocycloaddition of ethyl vinyl ether to cyclopentenone must be very different in order to explain the fact that the head-to-tail adducts 273 and 274 dominate over the head-to-head adducts 271 and 272 in a ratio of 3:1. This is shown by taking the ratio of equations 15 and 16 (chapter 5) to yield

(equation 24) $$\phi_T/\phi_H = \rho^T k_r^T/\rho^H k_r^H$$

If ϕ_T/ϕ_H is *ca.* 3:1 and ρ^T/ρ^H is 1:1 then it follows that k_r^T/k_r^H would be 3:1. It should be noted that this conclusion rests on at least two assumptions. Firstly, only biradicals 233 and 235 were considered as viable intermediates. However, biradicals 234 and 236 could also contribute to the regioselectivity of the reaction. Secondly, the conclusions drawn require that the biradicals 267 and 268 are good models for the behaviour of biradicals 233 and 235. These points will be addressed further in chapter 7.

CHAPTER 7

TRAPPING OF 1,4-BIRADICALS FROM PHOTOCYCLOADDITION OF CYCLOPENTENONE WITH OLEFINS

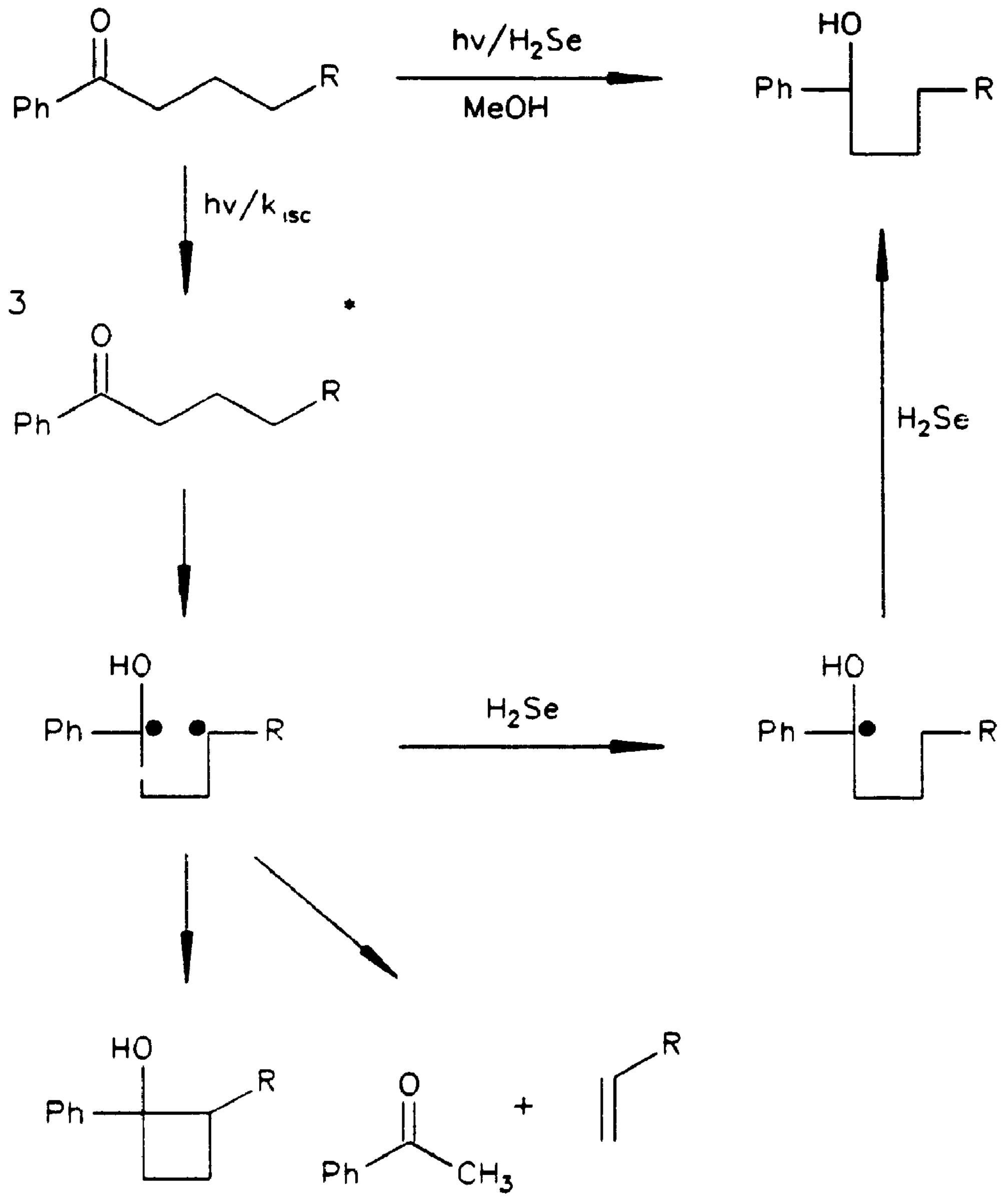
7.1 INTRODUCTION

In chapter 6 it was argued that the formation of regioisomeric 1,4-biradicals with different partitioning ratios could, in principle, be responsible for the regioselectivity of the 2+2 photocycloaddition reaction of cyclopentenone and ethyl vinyl ether. This was based on the assumption that biradicals 233 and 235 (the more stable intermediates) are either the only or major 1,4-biradicals along the reaction pathway, and that the alternative less stable biradicals 234 and 236 are not involved (scheme 40). The alternative explanation for the observed regioselectivity is that the rates of formation (k_r) of these biradical intermediates are different and that the reaction's regiochemistry reflects the relative amounts of the biradicals formed.

This chapter is concerned with the interception of the biradical intermediates by a chemical trap and hence assignment of structures to the 1,4-biradicals present. This does not allow determination of values for k_r^H and k_r^T, the rate constants for formation of the biradicals 233 and 235, respectively. However, it does make it possible to determine the relative rate constants, k_r^H/k_r^T, by quantifying the relative amounts of 1,4-biradical intermediates. This is because if all of the biradicals in the reaction can be intercepted (*i.e.* no cycloadducts formed) then the product ratios of the intercepted biradicals would directly reflect the relative proportions of the biradical precursors and the relative rates of formation of the biradicals.

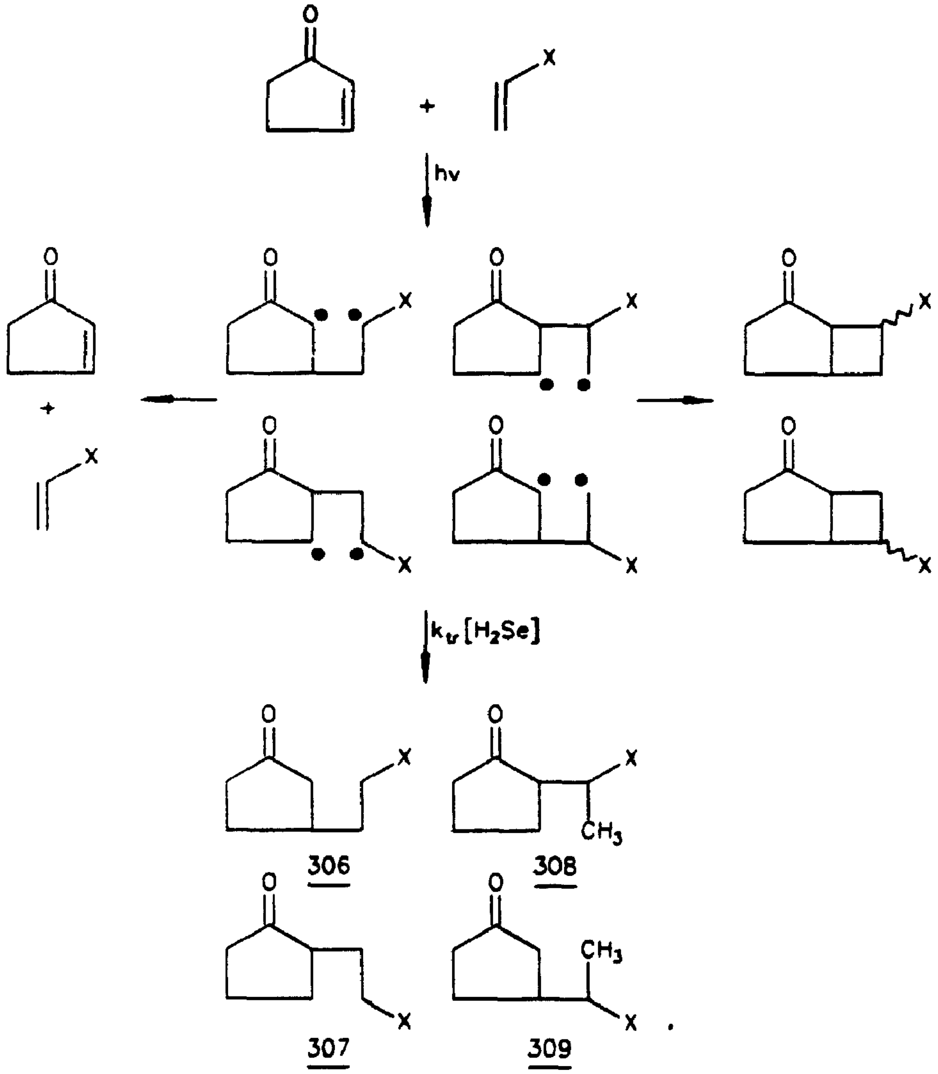
As already noted, Kambe and Sonada (67) have recently shown that short lived 1,4-biradical intermediates can be trapped by the addition of the excellent hydrogen atom donor, hydrogen selenide. This is summarized in scheme 58.

Scheme 58



It has also been shown (chapter 3.4) that this methodology can be applied to trapping 1,4-biradicals generated in the photocycloaddition reaction of N-benzoylindole with various alkenes. These results suggested that such a method would also trap 1,4-biradical intermediates formed in the photocycloaddition reaction of cyclopentenone with alkenes provided the rate of trapping, governed by the value of $k_{tr}[H_2Se]$, is sufficient to compete with other 1,4-biradical fates (scheme 59).

Scheme 59

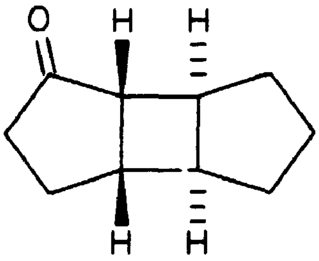


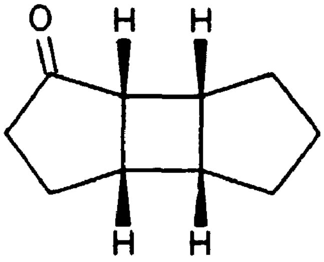
If this is the case then the putative intermediates would lead to products 306-309. If all of the biradicals are completely trapped, then the relative amounts of 306-309 would yield the relative rate constants for formation of the intermediate biradicals.

7.2 Irradiation of Cyclopentenone in the Presence of Cyclopentene and Hydrogen Selenide

First attempts to trap the biradical intermediates formed from the irradiation of cyclopentenone with ethyl vinyl ether with H_2Se failed and resulted in the observation of dark (*i.e.* thermal) products only. Many of these were derived from the reaction of H_2Se with alkene (*vide infra*). Thus it was decided to examine a much simpler case, the reaction between cyclopentenone and cyclopentene.

A method similar to that used for the trapping the biradical intermediates formed in the photocycloaddition of N-benzoylindole with alkenes was applied to the photochemical cycloaddition reaction of 2-cyclopentenone with cyclopentene. Irradiation of cyclopentenone in benzene containing cyclopentene yielded a single new product peak as indicated by g.c. analysis. Inspection of the reaction mixture by g.c.-m.s. indicated that the product peak possessed a molecular ion with m/e 150 indicating that it was a 1:1 adduct of the enone and cyclopentene. de Mayo and others have previously reported the characterization of this photoadduct and have shown it to be a mixture of stereoisomers assigned to structures 311a and 311b (121). The major isomer obtained is the *cis-anti-cis* photoadduct, 311a, and it is accompanied by small amounts of the *cis-syn-cis* adduct, 311b (121c).



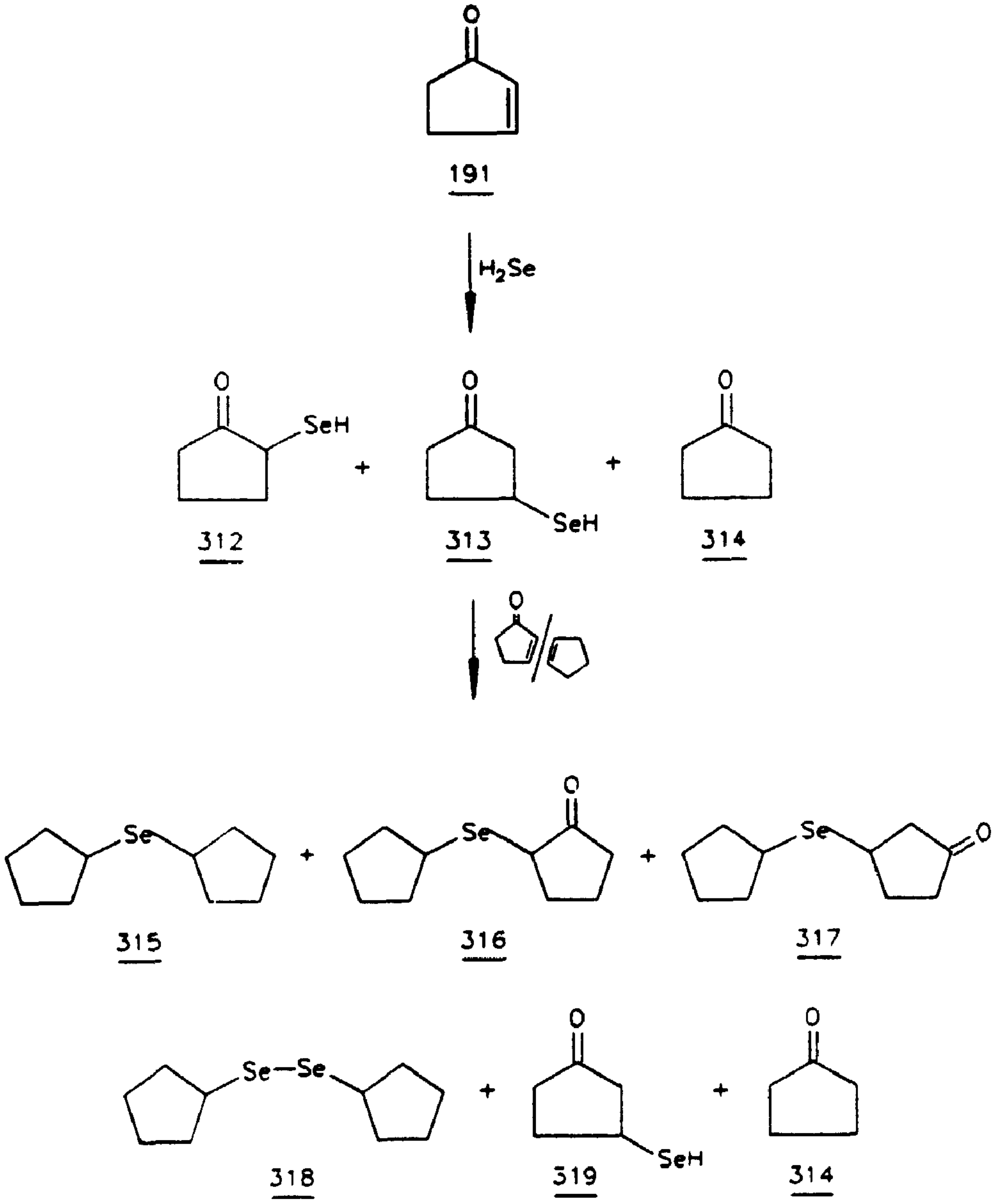


311a 311b

Irradiation of a benzene solution of cyclopentenone and cyclopentene containing H_2Se showed that dark reaction products dominated the reaction mixture. It was then demonstrated that the hydrogen selenide, although unreactive with the alkene, does react thermally with cyclopentenone to yield cyclopentanone and a selenol possessing possible structures 313 or 312 (*vide infra*). In addition, while cyclopentene is unreactive with H_2Se, it was apparently an effective quencher of intermediates generated by the reaction of cyclopentenone with H_2Se. This led to the array of dark reaction products described below and shown in scheme 60. Fortunately the dark reaction products were formed at a relatively slow rate (100% reaction after 24 hours). Thus it was anticipated that if the concentration of cyclopentenone was kept low (but high enough to maintain its absorbance >1) then the photochemical trapping reaction would proceed more rapidiy than the dark reaction. In order to further decrease the amount of dark reaction, irradiation times were kept short and starting materials were removed immediately from the reaction mixture following photolysis.

Irradiation of a benzene solution of cyclopentenone (10^{-2} M) with cyclopentene (5.7 M) yielded the cycloadducts previously discussed but when an identical solution containing H_2Se (0.3 M) was irradiated in a parallel reaction, g.c. showed 51% conversion of cyclopentenone to yield two sets of product peaks.

Scheme 60



One of these set of product peaks was assigned to "dark products" on the basis of dark reaction experiments described above, and the other set was assigned to photochemical products. The ratio of the dark to photochemical products was 1:1 by g.c. and none of the photochemical products possessed retention times equivalent to that of the cyclobutane adduct 311 (confirmed by coinjection). Thus the H_2Se had completely quenched the formation of cycloadducts. The reaction was irradiated for 10 minutes and this was followed by immediate removal of the volatile starting materials by reduced pressure distillation to yield a yellow oil contaminated with a red solid (Se).

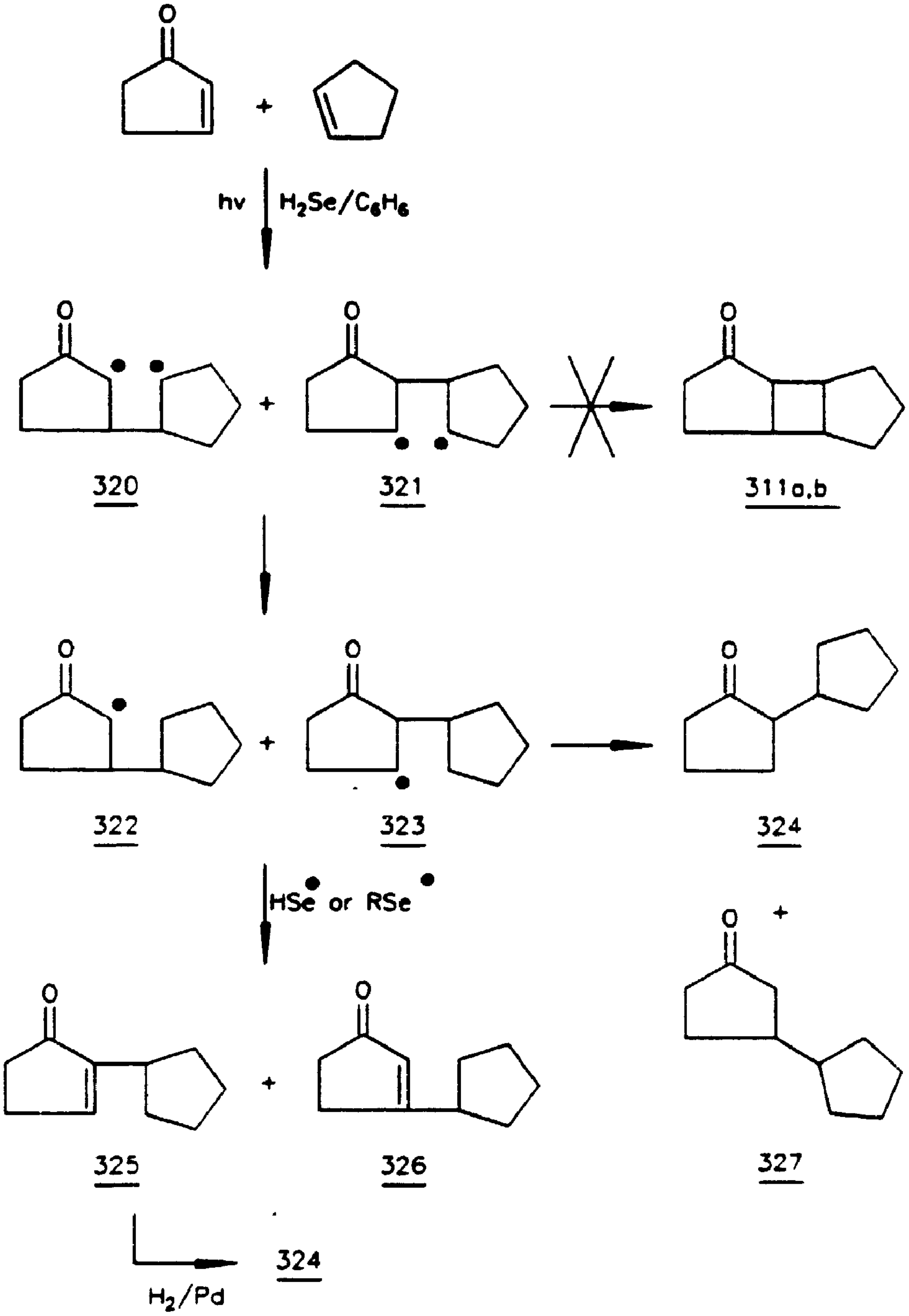
The dark products noted above were those which appeared when a mixture identical to that irradiated was wrapped in aluminum foil and placed along side the irradiated solution. Samples of the dark products for structure determination were obtained by allowing a benzene solution of cyclopentenone to react with H_2Se, and by allowing a benzene solution of cyclopentenone and cyclopentene to react with H_2Se. The first of these dark reactions yielded a clean mixture of selenol 313 or 312 and cyclopentanone, 314 in a g.c. ratio of 12:1. The presence of cyclopentanone in the reaction mixture was easily recognizable from its m.s. ($M^+=84$) and g.c. retention time. G.c-m.s. of the selenol gave a molecular ion m/e(%) 164(49) and showed the expected isotopic distribution for a species containing a single selenium atom. Thus additional molecular ion peaks were seen at 166(9), 162(23) and 161(10). A large fragment in the mass spectrum with m/e 83 indicated the presence of the cyclopentanonyl unit in the selenol. The ^{1}H-nmr spectrum of the reaction mixture containing the selenol as the major product showed a signal at -0.11 ppm indicative of a selenol hydrogen and the expected cyclopentanone multiplets (3.6-1.8 ppm).

The six products resulting from the second dark reaction in which a benzene solution of cyclopentenone and cyclopentene was treated with H_2Se were partially separated by chromatography. The three major products were isolated and identified. The first product was cyclopentanone. The mass spectrum of the second major product indicated a molecular ion of m/e 218 which possessed an isotopic distribution pattern indicative of a species containing a single selenium atom. Fragments with m/e 150 and 69 were suggestive of two cyclopentyl units and thus the product was assigned to structure 315 (scheme 60). The ^{1}H-nmr spectrum was consistent with this symmetrical structure and showed a methine quintet at 3.21 ppm. The mass spectrum of the third major product indicated a molecular ion of m/e 232 which also possessed an isotopic distribution pattern indicative of a species containing one selenium atom. Fragments with m/e 154, 83 and 67 were suggestive of a cyclopentyl and a cyclopentanonyl unit; thus the product was tentatively assigned to structure 316 or its structural isomer 317. The ^{1}H-nmr spectrum contained signals corresponding to cyclopentyl protons (multiplets *circa* 2.4-1.0 ppm) but did not allow for assignment of regiochemistry.

Three minor dark products were also present but were not isolable; however, g.c.-m.s. data did allow for tentative assignments. The first minor product possessed a mass spectrum identical to that of the species from the reaction of H_2Se and cyclopentenone identified as 313 and 312. G.c. coinjection with an authentic sample of the previously isolated selenol showed that these were indeed the same compound. The second minor product possessed a similar mass spectrum to that of the third major dark product and was assigned structure 317 or its structural isomer 316. The third minor product yielded a molecular ion of m/e 298; however, the isotopic distribution pattern was unlike that of the other selenides or selenol 313. The relative abundances of the M-6 to M+4 ions were indicative of a species containing 2 selenium atoms. Fragments with m/e 150 and 69 clearly showed that this product possessed two selenium atoms and two cyclopentyl units and thus it was assigned structure 318.

The three photochemical products were formed in the ratio 3.0:8.2:6.0 and possessed g.c. retention times close to that of the cycloadducts 311. Although chromatography (column and preparative t.l.c.) was unsuccessful in isolating these products, g.c.-m.s. yielded spectra which allowed for reasonable tentative assignments. The first photochemical product possessed a molecular ion with m/e 152 in low abundance. This mass is indicative of a 1:1 photoadduct with two hydrogens added and is consistent with either of the expected structures 324 and 327. No selenium atoms were present. The low abundance of the molecular ion was complimented by an intense fragment with m/e 84(100%). This may arise from a facile McLafferty Type II rearrangement in structure 324 (Scheme 61). Other 2-substituted cyclopentanones show a similar fragmentation pattern (122) which it is not evident in the corresponding 3-substituted cyclopentanones. The second and major photochemical product also possessed a molecular ion with m/e 152(32%). The relative intensity of this peak in the mass spectrum was higher than that for the first photochemical product and no fragment with m/e 84 was observed. Instead a large fragment with m/e 83(100%) was present which corresponds to cleavage of a cyclopentyl group. On this basis the product was assigned to 327. The third product yielded a molecular ion m/e 150 which is indicative of a 1:1 photoadduct of cyclopentenone and cyclopentene; however it possessed a different retention time from that of 311. The product contained no selenium atoms.

Scheme 61



By analogy with the products of H_2Se trapping of biradical intermediates in the photocycloaddition of N-benzoylindole with cyclopentene, this product could result from disproportionation of radicals 322 and 323 with $HSe^{\cdot}$. This would yield 325 or 326. Indeed, upon hydrogenation using a 10% palladium on carbon catalyst the third photochemical product was quantitatively converted to 324. This was confirmed by g.c. coinjection and comparison of the g.c.-m.s. fragmentation pattern. Accordingly the third photochemical product was assigned structure 325. The g.c. ratio of 324 + 325 to 327 was 8.2:9.0.

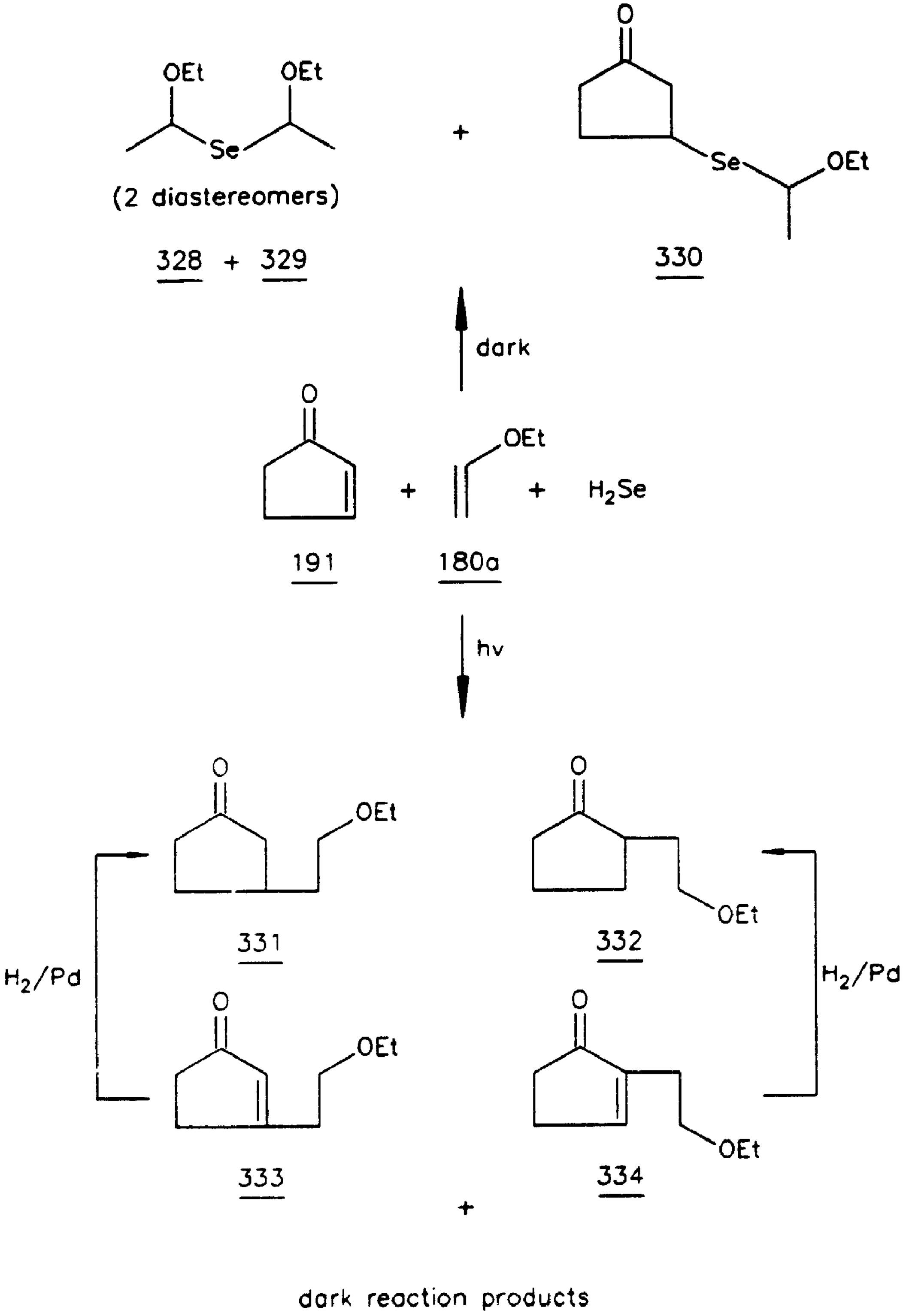
7.3 Irradiation of Cyclopentenone in the Presence of Ethyl Vinyl Ether and Hydrogen Selenide

Ultra-violet light irradiation of a benzene solution of cyclopentenone and ethyl vinyl ether, 180a, in the presence of hydrogen selenide yielded seven new major products (32% conversion) as indicated by g.c. A parallel dark reaction indicated that three of these were dark reaction products and four photochemical; from the original g.c. the ratio of dark to photochemical reaction products was determined as 5:1. The four photochemical products possessed retention times similar to those of the 2+2 photocycloadducts 281-284 and were present in a ratio (in order of decreasing volatility) of 3.2:5.7:3.5:1.0. However, g.c. and g.c-m.s. confirmed that none of these products were 2+2 cycloadducts of 191 and 180a produced in a parallel reaction performed with no H_2Se present. The major dark products were determined by g.c. to be present in a ratio (in order of decreasing volatility) of 1.0:1.0:1.0. These compounds were not isolated but structures were tentatively assigned using g.c.-m.s. data. Two of the dark products had g.c.

retention times similar to those of adducts 281-284. They possessed molecular ions with m/e 226 and contained one selenium atom. Fragments with m/e 181, 153, and 74 were observed for both products and allowed for assignment of the diastereomeric structures 328 and 329 (Scheme 62). The third dark product had a much longer g.c. retention time than those of 281-284 and possessed a molecular ion with m/e 236. It also contained one selenium atom. Fragments of m/e 191, 163, 83, and 74 suggested structure 330 or a related structural isomer.

The four photochemical products were shown to be two pairs of isomers by g.c.-m.s. One pair possessed a molecular ion with m/e 156 and the other pair a molecular ion with m/e 154. Each product was isolated and purified by preparative t.l.c. and characterised by m.s., ^{1}H-nmr and ^{13}C-nmr spectroscopy. The fourth product (longest g.c. retention time), which made up 7.5% of the four products, possessed a molecular ion with m/e 154 indicative of a disproportionation product of one of the biradicals 233-236. The ^{1}H-nmr spectrum suggested structure 333 for this product; thus quartet and triplet signals typical of an ethoxy group (3.45 and 1.15 ppm) were observed as well as a low field triplet at 3.62 ppm. The latter indicates that bonding of the cyclopentenone to the ethyl vinyl ether moiety had occurred at the methylene terminus of the ethyl vinyl ether. Evidence that the alkene had bonded to the 3-position of the cyclopentenone was provided by the observation of an olefinic signal characteristic of the enone 2-position at 5.95 ppm and the absence of the 3-proton at its normal position of *circa* 7-8 ppm. This allowed for unequivocal assignment of structure 333 to the fourth product.

Scheme 62


OEt
OEt
Se
(2 diastereomers)
328 + 329
+
O
Se
OEt
330
dark
O
OEt
+
+
H2Se
191
180a
hν
O
OEt
331
O
OEt
332
H2/Pd
O
OEt
333
O
OEt
334
H2/Pd
+
dark reaction products

Product 3 (third longest retention time) accounted for 25.7% of the four products, and possessed a molecular ion with m/e 154 which is also indicative of a disproportionation product of biradicals 233-236. The ^{1}H-nmr spectrum suggested structure 334 for this product; thus a quartet and a triplet (3.49 and 1.19 ppm) characteristic of an ethoxy group were present and a low field triplet (3.55 ppm) was seen. These indicate that bonding of the cyclopentenone to the ethyl vinyl ether moiety had occurred at the methylene terminus of the alkene. Evidence for bonding to the 2-position of the cyclopentenone was provided by the presence of an olefinic signal at 7.45 ppm and absence of the 2-proton at *circa* 6 ppm. This allowed for unequivocal assignment of structure 334 to the third product.

The first product (shortest g.c. retention time), which made up 24.1% of the four products, possessed a molecular ion with m/e 156 indicative of a trapping product of biradical 233-236. The ^{1}H-nmr spectrum exhibited the typical ethoxy quartet and triplet signals (3.45 and 1.20 ppm) and a low field triplet (3.49 ppm) which indicated that bonding of the cyclopentenone to the ethyl vinyl ether moiety had occurred at the methylene terminus of the alkene. Evidence for the position of bonding to the cyclopentenone could not be deduced from the ^{1}H-nmr spectrum but the m.s. fragmentation pattern yielded a relatively small molecular ion (2.5%) and a base ion with m/e 84. This could arise from a McLafferty Type II rearrangement of a 2-substituted cyclopentanone. This allowed for an assignment of structure 332 to the first product and this was confirmed when it was produced by hydrogenation of the third product which had been assigned unambiguously as structure 334 (confirmed by g.c.-m.s. and g.c. coinjection).

The second product, accounting for 42.7% of the four products could not be isolated in pure form and was contaminated by the first product. G.c.-m.s. indicated a molecular ion with m/e 156, consistent with a trapping product of biradical 233-36. The ^{1}H-nmr spectrum, although a mixture of products 1 and 2, yielded isochronous ethoxy quartet and triplet signals (3.45 and 1.20 ppm) and a low field triplet (3.49 ppm) which indicated that bonding of the cyclopentenone to the ethyl vinyl ether moiety had occurred at the methylene terminus of the alkene. Evidence for the position of bonding to the cyclopentenone could not be deduced from the ^{1}H-nmr spectrum. However, the m.s. fragmentation pattern contained a relatively large fragment ion with m/e 110(100%), indicative of a cleavage of the ethoxy group, and no ion with m/e 84 which would result from a McLafferty Type II rearrangement. This allowed for an assignment of structure 331 to the second product. This was confirmed by hydrogenation of 333 which yielded the second product (confirmed by g.c-m.s. and g.c. coinjection). The relative (uncalibrated) g.c. ratios of 331+333 to 332+334 was 1.0:1.0. This ratio did not change when purified samples of 331-334 were calibrated against decane.

Following the successful trapping of the 1,4-biradicals implicated in the photocycloaddition of cyclopentenone with ethyl vinyl ether, attempts were made to trap the 1,4-biradicals implicated in the photochemical reaction of cyclopentenone with alkenes bearing electron withdrawing substituents. The alkenes investigated were namely acrylonitrile and methyl acrylate. Irradiation of cyclopentenone with acrylonitrile in the presence of hydrogen selenide resulted in the formation of an insoluble solid which could not be analyzed. It was also shown by a separate experiment in which acrylonitrile was treated with H_2Se that this alkene is quite reactive with H_2Se and forms a similar, apparently polymeric solid to that seen in the previous reaction. This reaction was not pursued any further.

Irradiation of cyclopentenone with methyl acrylate in the presence of H_2Se also led to an insoluble, apparently polymeric solid. It was possible, however, to reduce the amount of polymerization by using relatively low (<0.5 M) concentrations of methyl acrylate. Although this led to reduced polymerization, the photochemical reaction yield was also substantially reduced and dark reaction products dominated the reaction (20:1, dark:photochemical reaction products). This made detection and analysis of the photochemical products by g.c.-m.s. ambiguous and their isolation difficult. Because of time constraints this reaction was not pursued further.

7.4 Discussion of Results

Our work with the H_2Se trapping of short-lived 1,4-biradicals generated in the 2+2 photocycloaddition reaction of N-benzoylindole, 5, with olefins indicated that the biradicals could be intercepted and their structures inferred. It was felt therefore, that the biradicals formed in the enone photocycloaddition reaction with alkenes could also be trapped. In the photochemical reaction of cyclopentenone with cyclopentene and hydrogen selenide the absence of cycloadducts suggested that all of the biradical intermediates had been trapped and hence the ratio of 324 + 325 : 327 reflects the ratio of regioisomeric biradicals formed in the reaction. This ratio was approximately 1:1 and indicates that initial bonding occurs at both 2 and 3-positions of the enone with the same relative rate.

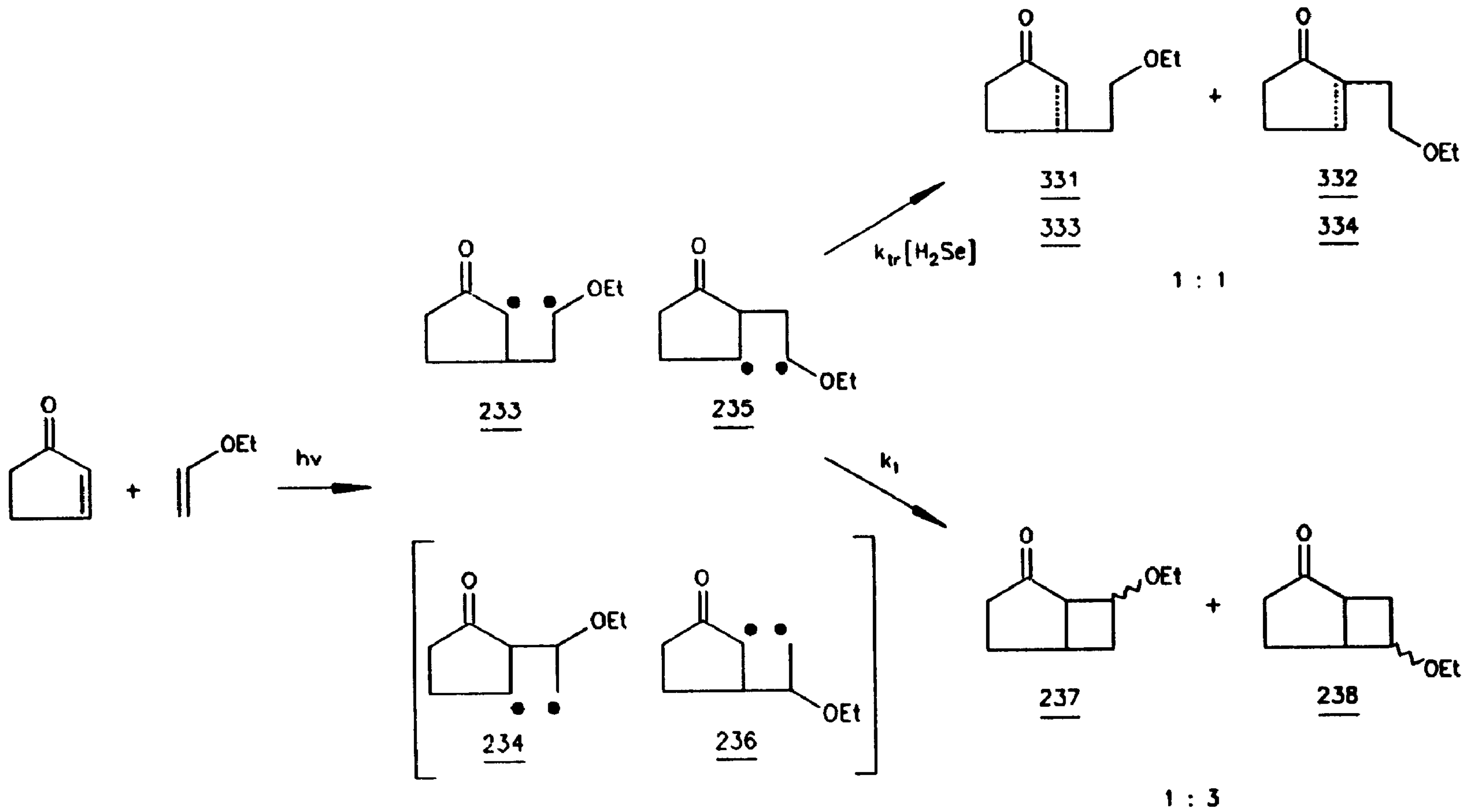
The presence of two regioisomeric biradicals in the reaction of cyclopentenone with vinylcyclopropane has been previously demonstrated by Rudolph and Weedon (51). Their studies showed that the initial site of bonding of the alkene is to both the 2 and 3-positions of the cyclopentenone, although they were unable to accurately quantify their results. Our findings with cyclopentenone allowed for quantification and suggests that the formation of one biradical over the other is not preferred. If this result also applies to the photocycloaddition of cyclopentenone with non-symmetrical alkenes then it suggests that the partitioning of these biradicals between starting materials and products might play a role in determining the relative amounts of each of the regioisomeric products formed. Of course, in the case of the reaction of cyclopentenone with cyclopentene the formation of the regioisomeric biradicals in no way influences the distribution of products since there is no regiochemistry within the product. Cyclopentene is symmetrical and both the *cis-anti-cis* and *cis-syn-cis* stereoisomers can be formed from the appropriate diastereomer of 320 or 321 (Scheme 61). Thus this study with cyclopentene as the alkene rendered no revealing information as to the origin of the regiochemistry of the enone photocycloaddition with alkene, although it did lead to the development of reaction conditions which allowed for the successful trapping of intermediate 1,4-biradicals.

Application of the optimized trapping conditions to the reaction of cyclopentenone with ethyl vinyl ether in the presence of H_2Se resulted in partial suppression of dark reaction products and the formation of four photochemical trapping products. The ratio of the dark to photochemical products was 5:1. The products were isolated and characterized as shown in scheme 62. The dark products were only partially characterized. The photochemical products consisted of two pairs of products, compounds 331-334, derived from biradicals 233 and 235. The ratio of the 2-substituted species, 332 and 334 (scheme 63), to the 3-substituted species, 331 and 333, was approximately 1:1 (10% error).

The structures of the trapped biradicals formed in the photochemical reaction of cyclopentenone with ethyl vinyl ether allows two important conclusions to be drawn. Firstly, that biradicals 233 and 235 are the major, if not the only, contributors to the reaction mechanism and the intermediates 234 and 236 are either present in low amounts or not formed at all. This is consistent with our previous arguments as to the viability of forming intermediates which possess primary radical centres (chapter 6). Knowing that these biradicals are not formed allows prediction of the structures of biradical intermediates in other photocycloaddition reactions. This result also aids in validating the assumption in chapter 6, that aldehydes 269 and 270 lead to the correct regioisomeric biradicals which could model the 1,4-biradicals implicated in enone-alkene photocycloaddition.

Secondly and most importantly, the formation of 331 + 333 and 332 + 334 in a 1:1 ratio indicates that biradicals 233 and 235 are also formed in a 1:1 ratio. Therefore, there is no preference for the site of initial bonding and these two biradicals are formed with similar rate constants. Comparison of this ratio with the ratio of 1:3 observed for the head-to-head and head-to-tail regioisomers 237 and 238 formed when the trapping agent is absent suggests that the preference for formation of the head-to-tail regioisomer, 238, must be due to the difference in the partitioning of 233 and 235 between starting materials and products.

Scheme 63



The conclusions drawn from the trapping studies differ from those drawn from the modelling studies described in chapter 6. The modelling study suggested that the regioisomeric biradicals partition between starting materials and products with similar efficiencies, while the trapping results suggest that they partition with different efficiencies. This contrast suggests that the biradicals generated from the aldehydes in the modelling experiments differ from the 1,4-biradicals generated by the photocycloaddition of cyclopentenone and ethyl vinyl ether with respect to their partition ratios. As stated above, the trapping experiments indicate that the model biradicals do possess the correct structural features (*i.e.* regiochemistry) of the cyclopentenone-ethyl vinyl ether generated biradicalsformed from the irradiation of cyclopentenone with ethyl vinyl ether. However, the fact that the biradicals generated in the model possess a hydroxy substituent, and not an ethoxy substituent, would seem to affect the efficiencies of ring closure and/or cleavage to starting materials. Thus the suitability of the 1,4-biradicals generated from aldehyde photolysis as models for those generated from cyclopentenone and ethyl vinyl ether is questionable.

The second conclusion drawn above has considerable ramifications for the mechanism of the enone 2+2 photocycloaddition reaction. Since there is no preference for the site of initial bonding between cyclopentenone and ethyl vinyl ether and since the two biradicals are formed with similar rate constants, this implies that the electron donating group has no effect on the rate of interaction between the alkene and the excited state enone. This is supported by the work of Lange (100) and Tada (101) in which the regioselectivity of the enone photocycloaddition was drastically altered by changing the alkene ring size of a cyclic olefin bearing a carboxylic ester on the ring. The Corey-de Mayo exciplex would predict the regioselectivity to remain constant. Thus, the failure of exciplex formation to explain product ratios suggests that it is questionable. As noted in chapter 5, the exciplex intermediate in the Corey-de Mayo mechanism was introduced to explain the reaction regiochemistry and the observed high rate constant for reaction of the enone triplet excited state with alkenes. The recent evidence (88,103) that ketone and enone triplets really do react rapidly with alkenes to produce biradicals directly combined with the results of the trapping experiments described here suggest that the exciplex is an unnecessary intermediate and that the regioselectivity of the reaction can be explained by the difference in partitioning of each regioisomeric 1,4-biradical between their respective products and ground state starting materials.

CHAPTER 8

EXPERIMENTAL

Melting points and boiling points are uncorrected. Melting points were determined on a Kofler hot stage melting point apparatus. I.R. spectra were recorded with an IBM System 9000 FT-IR spectrometer. Ultra-violet absorption spectra were recorded on a Hewlett-Packard 8450A diode array spectrophotometer or a Shimadzu UV160 spectrophotometer. All ^{1}H-nmr spectra were recorded at 200 MHz on either a Varian XL-200 nmr spectrometer or a Varian gemini nmr spectrometer. All ^{13}C-nmr spectra were recorded at 75 MHz using a Varian XL-300 nmr spectrometer. Methyl, methylene, methine and quaternary signals were identified by comparing the fully decoupled spectra with the APT spectrum (73). The chemical shifts are given in parts per million (ppm) downfield from tetramethylsilane in δ units and coupling constants are given in cycles per second (Hz). The data are reported in the order chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, quin=quintuplet, m=multiplet, dd=doublet of doublets, ddd=doublet of doublet of doublets), coupling constants, and number of protons.

Gas-liquid chromatography (g.c.) analyses were done using either a Varian 2400 gas chromatograph equipped with an FID detector, Megabore DB-1 (15 m) column, and a Hewlett Packard 3390A integrator, or using a Hewlett Packard HP5880 gas chromatograph equipped with either a DB-1 (30 m) or a DB-5 (30 m) capillary column using an oven temperature profile of 50-250°C at a rate of 10°C/minute. g.c.-m.s. analyses were performed using a Finnigan-MAT 8230 mass spectrometer coupled to a Varian 3400 gas chromatograph equipped with a DB-5 (30m) capillary column. High performance liquid chromatography (H.P.L.C.) was performed using a Waters automatic gradient controller with dual Waters model 510 pumps and a Waters 490 programable multiwavelength detector. The column used was a Varian normal phase silica semi-preparative steel column and fractions were collected with a Gilson 201 collector. Quantum yield determinations were performed using a PTI Quantacount equipped with a 100 Watt high pressure Hg lamp.

Reagent grade solvents were used for all large scale reactions. Spectrophotometric grade solvents were used for all irradiations. Tetrahydrofuran was freshly distilled from sodium and benzophenone before use. Anhydrous diethyl ether was BDH anhydrous grade and was used without further purification. All anhydrous reactions were performed under a dry nitrogen atmosphere with all glassware being dried overnight in a drying oven at 150°C prior to use. Assembly of the reaction apparatus was conducted under a flow of dry nitrogen. The drying agents were either potassium carbonate (K_2CO_3) or sodium sulphate (Na_2SO_4) and were BDH reagents.

General Procedure for Preparation of Cycloadducts

All preparative irradiations (gram scale) were carried out in a preparative irradiation well with a 450 W Hanovia medium pressure mercury lamp housed in a water cooled quartz jacket. The lamp was filtered with a Pyrex sleeve to ensure that only light with wavelengths greater than 300 nm was transmitted. The jacket was then immersed in the solution to be irradiated. Irradiation mixtures of 2-cyclopentenone, 191, ([191]>10^{-4} M) and alkene ([alkene]>0.05 M) were prepared in benzene previously purged with nitrogen. The irradiation solutions were flushed with nitrogen, sealed with a septum and irradiated with stirring. Smaller scale irradiations (milligram scale) were performed by placing a Pyrex tube containing the reaction solution in front of a 400 W medium pressure mercury lamp house in a water cooled Pyrex jacket.

Preparation of 2-Cyclopentenone 191

A method similar to that of Mihelich (115) was used. Cyclopentene (21 g, 0.31 Mol) was dissolved in methylene chloride (300 mL total volume) containing tetratolylporphyrin, TTP, (50 mg), acetic anhydride (30 mL, 0.312 Mol), dimethylaminopyridine, DMAP, (0.8 g, 6.7 mMol), and pyridine (12 mL, 0.15 Mol). The reaction mixture was stirred while oxygen was bubbled through the solution, and irradiated with a 450 W medium pressure mercury vapour immersion lamp. After 4 hours the irradiation was stopped, diluted with 200 mL of methylene chloride and this solution was washed repeatedly with saturated $NaHCO_3$ until the aqueous layer was basic. The organic layer was then washed twice with 10% HCl (200 mL) and the solvent removed to yield 12 g of a dark liquid. The liquid was then fractionally distilled (47-49°C, 30 mm Hg) to yield 10.0 g (40%) of a clear colourless liquid identified as cyclopentenone, 191; ^{1}H-nmr $\delta(CDCl_3)$ 7.65 (m, 1H), 6.04 (m, 1H), 2.40 (m, 2H), 2.15 ppm (m,2H).

Preparation of β-Bromopropionic acid Ethyl Ester 269

β-Bromopropionic acid ethyl ester was prepared by Fischer esterification of the acid. β-Bromopropionic acid (30 g, 0.196 Mol) was dissolved in absolute ethanol (275 g) containing p-toluenesulfonic acid (0.8 g). After refluxing for 1 hour the solution was diluted with diethyl ether (200 mL) and washed with a saturated solution of sodium bicarbonate (2 X 250 mL). The organic portion was then dried (Na_2SO_4) and the solvent removed to yield a clear colourless liquid which was distilled (bp. 90-92°C, 30 mm Hg) *in vacuo* to yield 30.1 g (85%) of the ester 269; ^{1}H-nmr δ($CDCl_3$) 4.21 (q, J=7.0 Hz, 2H), 3.59 (t, J=6 Hz, 2H), 2.90 (t, J=6 Hz, 2H), 1.25 ppm (t, J=7 Hz, 3H).

Preparation of β-Nitropropionic acid Ethyl Ester, 272

Amberlite® (Aldrich) IRA-900 highly basic anion exchange resin was charged with nitrite ions by flushing 90 g of the resin with 500 mL of 2 M NaCl followed by distilled H_2O until chloride failed to elute (tested with $AgNO_3$ solution). The resin was then eluted with 500 mL of 2 M sodium nitrite (120). The resin was washed with distilled water (500 mL), with absolute ethanol (500 mL) and finally with benzene (500 mL). The wet resin was then dried at 40°C under vacuum (3 mm of Hg) for 4 hours.

A portion of the resin (40 g) was added to dry benzene (100mL) and stirred with β-bromopropionic acid ester, 285, (4.2 g, 0.023 Mol) at 60°C for 36 hours. After this time g.c. showed complete conversion of starting ester to a single new product. The resin was filtered off to yield a slightly yellow solution which was distilled slowly through a Vigreux to remove the bulk of the benzene.

The residue was then fractionally distilled to yield 3.1 g (91 %) of a clear colourless fraction (83-88°C at 70 mm Hg) identified as nitroester 272; bp. 160-163°C (lit (120) bp. 162-164°C, ^{1}H-nmr δ($CDCl_3$) 4.61 (t, J=6 Hz, 2H), 4.18 (q, J=7 Hz, 2H), 2.95 (t, J=6 Hz, 2H), 1.25 ppm (t, J=7 Hz, 3H).

Preparation of Unsaturated Ester 273

Nitropropionate ester 286 (1.013 g, 6.84 mMol) was dissolved in dry THF (10mL) under a nitrogen atmosphere and the solution was cooled to -20°C. A THF (10 mL) solution of potassium t-butoxide (0.597 g, 5.1 mMol) was then added at -20°C over 20 minutes. After stirring for another 10 minutes, cyclopentenone (0.610 g, 7.44 mMol) was added over 10 minutes. During the addition the reaction mixture turned to a clear orange colour. The reaction mixture was allowed to warm up to room temperature and after 3 hours absolute ethanol (2 mL) was added and the solution stirred for a further 48 hours. The reaction was then quenched with 10% HCl (50 mL) and the products extracted into ether (50 mL). The ether extracts were dried (Na_2SO_4) and solvent removed to yield 1.06 g (84%) of a clear pale orange liquid. The liquid was further purified by column chromatography (silica gel, 1:1 ether/hexanes) and identified as product 273; ^{1}H-nmr δ(acetone-d_6) 7.05 (dd, J=16, 7 Hz, 1H), 5.91 (d, J=16 Hz, 1H), 4.22 (q, J=7 Hz, 2H), 2.2 (m, 6H), 1.8 (m, 1H), 1.24 ppm (t, J=7 Hz, 3H), m.s. m/e(%) M^+=182(58), 153(74), 109(96), 81(100), calc. 182.094295 (found 182.09345).

Hydrogenation of Unsaturated Ester 273

Ester 273 (0.645 g, 3.5 mMol) was hydrogenated under atmospheric pressure using 10% Pd on carbon catalyst (50 mg) and absolute ethanol as solvent (10 mL). After 2 hours 85 mL of hydrogen had been taken up and g.c. showed complete conversion of starting material to give a new product with a slightly shorter g.c. retention time. The catalyst was filtered off to yield a clear colourless liquid which was taken up in 50 mL of ether and washed with distilled water. The ether layer was dried (Na_2SO_4) and solvent removed to yield 0.600 g (93%) of a colourless oil identified as hydrogenated ester 274; ^{1}H-nmr δ($CDCl_3$) 4.15 (q, J=7 Hz, 2H), 2.2-1.5 (m, 11H), 1.25 ppm (t, J=7 Hz, 3H), m.s. m/e(%) M^+=184(6), 166(12), 139(42), 96(100), 83(95), calc. 184.109945 (found 184.109948).

Preparation of Bicyclo[3.3.0]octane-2,8-dione, 275

A method similar to Eaton (118) was followed using ethyl ester 274. Under a nitrogen atmosphere a 5 mL solution of 274 (0.45 g, 2.5 mMol) in dry ether was added over 35 minutes to a stirred suspension of NaOEt (0.25 g, 3.2 mMol, freshly prepared) in 5 mL of dry ether at 5°C. A creamy precipitate formed and was stirred at 5°C for another 3 hours. The reaction was then quenched by pouring the reaction mixture into 10 mL of an aqueous solution containing KH_2PO_4 (2.0 g). The ether layer was removed and the aqueous portion extracted with methylene chloride after which the organic extracts were combined, washed with saturated $(NH_4)_2SO_4$, and dried over Na_2SO_4. After removal of solvent the resulting pale yellow oil (280 mg) was purified by preparative t.l.c. (eluted once with diethyl ether) to yield 236 mg (70%) of a white crystalline solid identified as diketone 275; mp. 56-60°C (lit(118) mp. 61-62°C), ^{1}H-nmr δ(CDCl$_3$) 3.15 (d of quint, J=8, 4 Hz, 1H), 3.03 (d, J=8 Hz, 1H), 2.5-2.1 (m, 6H), 1.80 ppm (m, 2H), m.s. m/e(%) M^{+}=183(100), 109(40), 83(38), 68(40), calc. 138.06808 (found 138.0676902).

Photolysis of Bicyclo[3.3.0]octane-2,8-dione, 275

A u.v. absorption spectrum of compound 275 was taken in benzene and the molar extinction coefficient at 303 nm was calculated to be 90. A small (10.0 mg) sample of 275 was dissolved in 1 mL of benzene in a Pyrex nmr tube and purged for 5 minutes with nitrogen. A small drop of distilled water was added and the sample was irradiated with a medium pressure mercury vapour lamp. The reaction was followed by g.c. and showed conversion of diketone 275 to a new product which possessed a slightly shorter retention time. During the photolysis there was no evidence of 2-cyclopentenone formation or formation of cyclobutane 280. g.c.-m.s. revealed that the new product possessed a weak molecular ion of m/e=138 consistent with the aldehyde photoproduct 279. After 3 hours the irradiation was stopped and the solvents removed. The residue yielded a 3:1 ratio of product to starting dione and was taken up into CDCl$_3$ which allowed for assignment of the photoproduct to 279; ^{1}H-nmr δ(CDCl$_3$) 9.75 (s, 1H), 5.82 (d, J=0.5 Hz, 1H), 2.65 (m, 2H), 2.51 (m, 2H), 2.4-2.1 ppm (m, 4H), m.s. m/e(%) M^{+}=138(5), 110(78), 78(100), 55(84), calc. 138.06808 (found 138.0677434).

Preparation of Cyclopentanonedimethylhydrazone, 293

Cyclopentanone (10g, 0.119 Mol) and anhydrous dimethylhydrazine (36 g, 0.06 Mol) were refluxed in 40 mL of absolute ethanol for 24 hours after which the resulting dark orange solution was distilled under vacuum (70 mm of Hg) to remove the bulk of the hydrazine and ethanol. The residue was then fractionally distilled (70-73°C fraction at 25 mm Hg) to yield 12.45 g (83%) of a clear colourless liquid identified as 293; ^{1}H-nmr $\delta(CDCl_3)$ 2.26 (s, 6H), 2.38 (m, 4H), 1.75 ppm (m, 4H), m.s. m/e(%) $M^+ = 126(100)$, 111(40), 82(86), 54(56).

Alkylation of Cyclopentanone-DMH, 293, with Bromoacetaldehyde Diethyl acetal

A dry THF (7.5 mL) solution of cyclopentanone-DMH, 293, (3.02 g, 0.024 Mol) was cooled to -78°C under a nitrogen atmosphere and treated with n-butyllithium (10 mL of 2.42 M in hexane, 0.0242 Mol) to form an off white precipitate. To this, bromoacetaldehyde diethylacetal (4.8 g, 0.0243 Mol) in 5 mL of dry THF was added dropwise over 10 minutes, The reaction mixture was stirred for a further 10 minutes at -78°C. The reaction mixture was then allowed to warm up to room temperature and stirred for 20 hours after which it was quenched with an aqueous solution of 10% NH_4OH and saturated NH_4Cl. The mixture was then extracted into ether and the extracts washed with distilled water, dried ($MgSO_4$) and solvent removed to yield 5.77 g of a brown oil. The crude oil was applied to a silica gel column (25% ether/75% hexanes) to yield a major fraction (3.52 g, 61%) as a colourless oil. This was identified as 294; bp. 107-109°C (0.9 mm Hg), ^{1}H-nmr $\delta(CDCl_3)$ 4.70 (t, J=5 Hz, 1H), 3.55 (broad q, J=7 Hz, 4H), 2.45 (s, 6H), 2.3-1.3 (m, 9H), 1.23 ppm (t, J=7 Hz, 6H), m.s. m/e(%) M^+=242(5), 213(12), 197(30), 126(100), 103(54), 96(58), calc. 242.199428 (found 242.199465).

Hydrolysis of Alkylation Product 294

A sample of hydrazone 294 (18 g, 0.074 Mol) was stirred with 150 mL of 10% HCl for 1 hour under nitrogen. The aqueous solution was then extracted with 250 mL of ether for 24 hours using a continuous liquid-liquid extractor. The ether layer was dried (Na_2SO_4) and solvent removed by slow fractional distillation to yield 15.5 g of a clear orange liquid which was fractionally distilled under vacuum to yield 4.5 g (48%) of the aldehyde identified as 270; bp. 105-108°C (15 mm Hg), ^{1}H-nmr $\delta(CDCl_3)$ 9.66 (s, 1H), 2.8-1.9 ppm (m, 9H), ^{13}C-nmr $\delta(CDCl_3)$ 219.2 (quaternary C), 199.9 (CHO) 43.64, 37.12, 29.39, 23.14 (CH_2), 43.57 ppm (CH), m.s. m/e(%) M^+=126(4), 98(40), 84(100), 70(63), calc. 126.06808 (found 126.06765).

Preparation of Allyltrimethylsilane, 305

The grignard reagent from allyl bromide was prepared by reacting magnesium turnings (5 g, 0.21 Mol) in 25 mL of dry ether with allyl bromide (25.2 g, 0.21 Mol). The solution of the grignard reagent was then cooled to 0°C and freshly distilled trimethylsilylchloride (22.5 g, 0.21 Mol) in 25 mL of ether was added dropwise over 1 hour. Upon addition the magnesium salts precipitated out; after 30 minutes of stirring at room temperature the salts were removed by filtration and washed with ether. The organic extracts were then combined, washed with distilled water, dried (Na_2SO_4), and solvent removed by fractional distillation to yield 16 g of a pale yellow liquid residue which was fractionally distilled to yield 13 g (55%) of the allyltrimethylsilane, 305; bp. 85-89°C (lit. (116) bp. 84.9°C at 737 mm Hg), ^{1}H-nmr δ($CDCl_3$) 5.90 (m, 1H), 5.15 (m, 2H), 1.84 (m, 2H), 0.04 ppm (s, 9H), m.s. m/e(%) M^+=114(12), 99(10), 73(100), 59(16).

Conjugate Allylation of Cyclopentenone with Allyltrimethylsilane 305

A methylene chloride (50 mL) solution of 2-cyclopentenone (6.0 g, 0.073 Mol) was cooled to -78°C under a nitrogen atmosphere. To this was added freshly distilled $TiCl_4$ (8 mL, 0.073 Mol) using a syringe. This was performed over a period of 10 minutes and the yellow precipitate which formed was stirred for a further 5 minutes. Allyltrimethylsilane (10.0 g, 0.088 Mol) was then added over 30 minutes during which time the reaction mixture turned dark red. The reaction mixture was stirred at -78°C for 2 hours then warmed to 0°C. 50 mL of ether and 50 mL of distilled water were then added and this caused the reaction mixture to turn green. The aqueous phase was extracted with ether, and the organic phases combined, dried (Na_2SO_4), and solvent removed to yield 13.8 g of a clear colourless liquid. The liquid was fractionally distilled under vacuum to yield 4.71 g (58%) of 99.9% pure 3-(2-propenyl)cyclopentanone, 306; bp. 74-76°C at 15 mm Hg, ^{1}H-nmr δ($CDCl_3$) 5.84 (m, 1H), 5.05 (m, 2H), 2.4-1.2 ppm (m, 9H), m.s. m/e(%) M^+=124(20), 83(40), 67(28), 55(100).

Oxidation of Olefin 306

A sample of 3-(2-propenyl)cyclopentanone, 306, (4.25 g, 0.034 Mol) was dissolved in a 3:1 solution of THF and distilled water. To this solution was added osmium tetroxide (167.7 mg 0.65 mMol); the solution stirred at room temperature for 10 minutes and this was followed by the addition of KIO_4 (40g). After 1 hour of stirring g.c. analysis revealed that all of the starting material had been converted to a single product. The reaction mixture was diluted with 50 mL of ether and 50 mL of distilled water, and the aqueous phase was extracted with ether. The organic extracts were combined, washed with water and dried (Na_2SO_4). The solvent was removed by fractional distillation under nitrogen to yield a clear colourless liquid (3.0 g, 69%), (99% g.c. purity) identified as aldehyde product 269; ^{1}H-nmr $\delta(C_6D_6)$ 9.17 (d, J=1.3 Hz, 1H), 2.5-1.0 ppm (m, 9H), m.s. m/e(%) M^+=126(6), 82(80), 69(28), 55(100), calc.126.06808 (found 126.0678).

Irradiation of Cyclopentenone with Ethyl Vinyl Ether

A benzene solution (5 ml) of cyclopentenone (71.5 mg, 0.8719 mMol) was irradiated with ethyl vinyl ether (1.5 g, 20.83 mMol) for a total of 17.5 hours after which g.c. showed clean conversion (87%) to four product peaks in a ratio of 9.8:17.6:29.9:42.6 (in order of decreasing volatility). During the irradiation the product ratios remained unchanged. The solvent was removed from the reaction mixture and residual cyclopentenone removed by pumping on a vacuum line for 1 hour leaving 70 mg of a colourless oil. The product was taken up into $CDCl_3$ and a ^{1}H-nmr spectrum recorded. This showed cyclobutane protons in the 4.0-1.5 ppm region. Examination of the four cycloadducts by g.c.-m.s. using chemical ionization techniques yielded mass ions for all four peaks of $M^+ = 155$; fragments were also seen at m/e 109, 83, and 73. This is consistent with the formation of 1:1 photocycloadducts of cyclopentenone and ethyl vinyl ether. The relative amounts of each ion fragment for each adduct is given in table 4 and their stereochemical and regiochemical assignments discussed in chapter 6 (section 6.2).

Irradiation of Cyclopentenone with Vinyl acetate

A benzene solution (100 mL) of cyclopentenone (6.0 g, 0.073 Mol) and distilled vinyl acetate (30 g, 0.35 Mol) was irradiated for 39 hours after which g.c. showed 85% conversion of the starting cyclopentenone to 4 products in a ratio of 4.21:1:4.35:1.61. The ratio remained constant during the photolysis. After the irradiation the solvent was removed *in vacuo* to yield 11.3 g of a yellow oil. The oil was fractionally distilled under vacuum to yield 6.5 g (53%) of a clear colourless oil (bp. 102°C at 1mm Hg) which g.c. showed to be the four products in good purity (99%). g.c.-m.s. showed all four peaks to possess weak molecular ions of m/e 168 and fragments 125, 108 and base ion 83 indicative of 1:1 photoadducts. A small portion of this liquid was taken up in $CDCl_3$ and a ^1H-nmr spectrum was recorded which showed aliphatic resonances as multiplets (2.8-2.1 ppm), acetate methyl signals at 2.09, 2.07 (major signals in a 1:1 ratio), 2.08, and 2.06 ppm (minor signals), and low field signals at 5.18 ppm (dd, J=8, 7 Hz, 1H) and 4.90 ppm (dd, J=6, 4 Hz) corresponding to the methine cyclobutane protons bearing the acetate groups of the major isomers. The products were assigned 297 and 298.

Hydrolysis of Cyclopentenone-Vinyl acetate Adducts

A sample (1.3 g) of the photolysis product from the cyclopentenone-vinyl acetate irradiation was dissolved in methanol (20 mL) and to this 2 mL of 2.5 M aqueous NaOH was added. After stirring the reaction mixture for 15 minutes it was acidified to neutral pH with 0.5 M HCl then extracted with ether. The extract was dried ($MgSO_4$) and solvent removed to yield 100 mg of a pale yellow oil. The oil was analyzed by g.c. and g.c.-m.s. It showed that the starting adducts were converted to three products in a 1:1:3 ratio, all with shorter retention times relative to the starting material. G.c.-c.i.m.s. gave mass spectral fragmentation patterns as follows; peak 1, m.s. m/e(%) $M^+=127(40)$, 109(10), 83(100); peak 2, m.s. m/e(%) $M^+=127(91)$, 109(26), 81 (100), 83(77); peak 3, m.s. m/e(%) $M^+=127(30)$, 109(100), 83(49). The liquid was taken up into $CDCl_3$ and a ^1H-nmr spectrum was recorded. It showed aliphatic signals between 3.0 and 1.5 ppm and two sets of two signals to low field. The first set of signals at 4.60 and 4.45 ppm were broad singlets in a ratio of 1:2.6 respectively and disappeared on the addition of D_2O. The second set of signals at 4.30 and 4.05 ppm were broad doublets of doublets (J= 8, 6 Hz) in a ratio of 2.6:1 respectively and were unaffected by addition of D_2O. The mixture also showed a singlet at 9.2 ppm (aldehyde proton) which was equal in intensity to that of the minor OH peak. The cyclobutanol products were tentatively assigned to structures 300 and 301. The g.c. fragmentation pattern of peak 1 was consistent with that of aldehyde 269 and this assignment was confirmed by coinjection with an authentic sample.

Preparation of Trimethylsiloxyalkene, 304

Under a nitrogen atmosphere freshly distilled trimethylsilylchloride (43 g, 0.39 Mol) and triethylamine (50.8 g, 0.50 Mol, distilled from KOH) were added to dimethylformamide (100 mL) at 0°C. Freshly distilled acetaldehyde (47.27 g, 1.07 Mol) was added dropwise over 1.5 hours after which the reaction mixture was refluxed under nitrogen for 24 hours. The flask was then charged with 50 mL of dry xylenes and the resulting brown slurry was distilled. A fraction boiling between 25-95°C was collected (150 mL). This clear colourless distillate was washed with distilled water, ice cold 10% HCl, then saturated $NaHCO_3$. After drying the organic phase (Na_2SO_4) the solution was fractionally distilled to give 28.5 g (23%) of a clear colourless liquid (99% g.c. pure) identified as siloxyalkene 302; bp. 73-76°C, ^{1}H-nmr δ($CDCl_3$) 6.10 (dd, J=13, 6 Hz, 1H), 4.21 (d, J=13 Hz, 1H), 3.95 (d, J=6 Hz, 1H), 0.15 (s, 9H).

Irradiation of Cyclopentenone with Trimethylsiloxyalkene, 302

A benzene (5 mL) solution of cyclopentenone (150 mg, 1.83 mMol) and 302 (2 g, 17.2 mMol) was irradiated for 3 hours after which g.c. showed 54% conversion to 4 products in a ratio of 1:1.7:2.5:5.25. The ratio remained constant during the course of the irradiation. The solvents were then removed to yield 184 mg (50.5%) of a colourless oil which when analyzed by g.c.-m.s. showed all four peaks to have similar mass spectra; m/e(%) M^+=198(6), 183(14), 116(80), 101(100), indicative of 1:1 photoadducts. The mixture was not characterized further and the products were tentatively assigned to structures 303 and 304.

Desilylation of Cyclopentenone-Siloxyalkene Adducts

A small portion of adducts 303-304 (5 mg) was dissolved in 3 mL of 20% HCl and stirred for 30 minutes at 50°C. The reaction mixture was then cooled to room temperature and extracted with 3 mL of ether. The extract was analyzed by g.c. and showed loss of starting material and formation of three products in a g.c. ratio of 1:2:5.1. g.c.-m.s. revealed all three products to possess molecular ion m/e 126. g.c. retention times were identical to those found for the hydrolysis products of the cyclopentenone-vinylacetate cycloadducts. g.c. coinjection confirmed that the products formed were indeed the same as those described above.

Resilylation of Cyclobutanols 301-301

A small sample of hydrolysis products 269 and 301-301 (25 mg), prepared from the hydrolysis of adducts 297 and 300, was dissolved in 0.5 mL of dry benzene and to this bis(trimethylsilyl)acetamide, BSA, (100 mg, 0.49 mMol) was added. The reaction mixture was stirred at 50°C for 5 minutes after which g.c. analysis showed complete conversion of the two cyclobutanols to two products (1:2.7 ratio) whose retention times were identical with the two major cyclopentenone-siloxyalkene photoadducts, 304. No change in the peak assigned to the aldehyde 269 was observed. g.c.-m.s. gave molecular ions m/e 126, 198 and 198 for the three peaks consistent with unreacted aldehyde 269 and silylated cyclobutanols 304, all of which were confirmed by g.c. coinjection with authentic samples. This allowed for assignment of the cyclopentenone-siloxyalkene regioisomers as described in chapter 6.

Photolysis of Aldehyde 270

A benzene solution (1.5 mL) of aldehyde 270 (50 mg) was irradiated in a Pyrex nmr tube with a medium pressure mercury vapour lamp. The photolysis reaction was followed by g.c.; after 5.5% loss of the starting material 6 detectable products could be seen in a g.c. ratio of 9.67:6.53:0.67:0.52:1.88:3.50. The first product peak possessed a g.c. retention time identical to that of cyclopentenone and this assignment was confirmed by coinjection with an authentic sample and by g.c.-m.s. where the mass spectrum was identical to that of cyclopentenone (m/e $M^+ = 82$). The fifth and sixth g.c. peaks had g.c. retention times identical to those of the cyclobutanols 300 and 301. This assignment was confirmed by purifying products of 297-298 hydrolysis 300 and 301 by column chromatography (silica gel, 25% ether/75% hexanes) and coinjecting the photolysis mixture with the purified sample. g.c.-m.s. also yielded molecular ions m/e 126 consistent with cyclobutanol formation. g.c. peaks 2-4 were unidentified, but possessed molecular ions of 162, 174 and 153 respectively.

In order to quantify the amounts of starting aldehyde, cyclopentenone, and cyclobutanol products present in the reaction mixture by g.c. each was calibrated against a decane internal standard. Cyclopentenone was also calibrated against cyclobutanols 300 and 301. The results for the photolyses are shown in table 5 where % conversion of aldehyde and ratio of photolysis products are based on an average value of 10 g.c. injections with errors corresponding to standard deviations. The partitioning ratio, ρ^T, was calculated using the expression $\rho^T = \text{moles}_{300+301}/\text{moles}_{191+300+301}$. Reactions were performed under both direct irradiation conditions (medium pressure Hg vapour lamp/Pyrex filter) and sensitized conditions (low pressure Hg vapour lamp/quartz irradiation vessel). Photolyses exceeding 10% conversion of the starting material were discarded. The value of ρ^T=0.29 is the mean of experiments 1-7 and the error was calculated to be 0.023 using the standard deviations of each ρ^T and entering these values into "gmean02" software program (123).

Photolysis of Aldehyde 269

A benzene solution (1.5 mL) of aldehyde 269 (44 mg) was irradiated in a Pyrex nmr tube with a medium pressure mercury vapour lamp. The photolysis was followed by g.c. and after 2.5 hours approximately 15% of the starting material had reacted to yield 3 detectable photolysis products in a ratio of 1.53:1:6.11. The first product peak possessed a g.c. retention time identical to that of cyclopentenone and this assignment was confirmed by coinjection with an authentic sample and by g.c.-m.s. where the mass spectrum was identical to that of cyclopentenone (m/e M^+=82). The second and third g.c. peaks had g.c. retention times slightly longer than the starting aldehyde. Attempts to characterize these peaks as head to head cyclobutanols 299 by coinjection failed since authentic samples of the cyclobutanols could not be obtained. However, g.c-m.s. of these peaks yielded molecular ions of m/e(%) 153(5) with fragment ions 115(100), 87(74), and 69(33), clearly not indicative of any cyclobutanol. This mixture was not characterized any further.

A second irradiation was performed using aldehyde 269 (40 mg) in 1.5 mL of benzene contained in a quartz nmr tube. The sample was irradiated with a low pressure Hg vapour lamp and the reaction progress was followed by g.c.. After

1 hour it showed 15% conversion of the starting aldehyde 269 to yield a cyclopentenone peak (confirmed by coinjection and g.c.-m.s.) accounting for 9% and 10 new peaks accounting for less than 6% of the converted starting material. Four of these peaks possessed retention times close to that of the solvent and the other six possessed retention times near that of the starting material. g.c.-m.s. did not allow for assignment of molecular ions to these peaks due to problems with sensitivity.

A third irradiation was performed using aldehyde 269 (100 mg) in 1 mL of benzene-d_6 in a quartz nmr tube using a low pressure Hg lamp as the light source. The aldehyde was irradiated for a period of 24 hours and the reaction progress followed by g.c. and 200 MHz ^{1}H-nmr spectroscopy. After 24 hours g.c. showed a ratio of cyclopentenone to starting material of 1:4.4. The ^{1}H-nmr spectrum contained aliphatic multiplets between $\delta = 2.5$ and 1.0 ppm, the aldehyde peak at 9.19 ppm and cyclopentenone protons at 5.95 and 6.82 ppm. The region between 3.0 and 5.0 ppm had remained unchanged and there was no evidence of signals corresponding to cyclobutane or alcohol protons. The mixture was not characterized further.

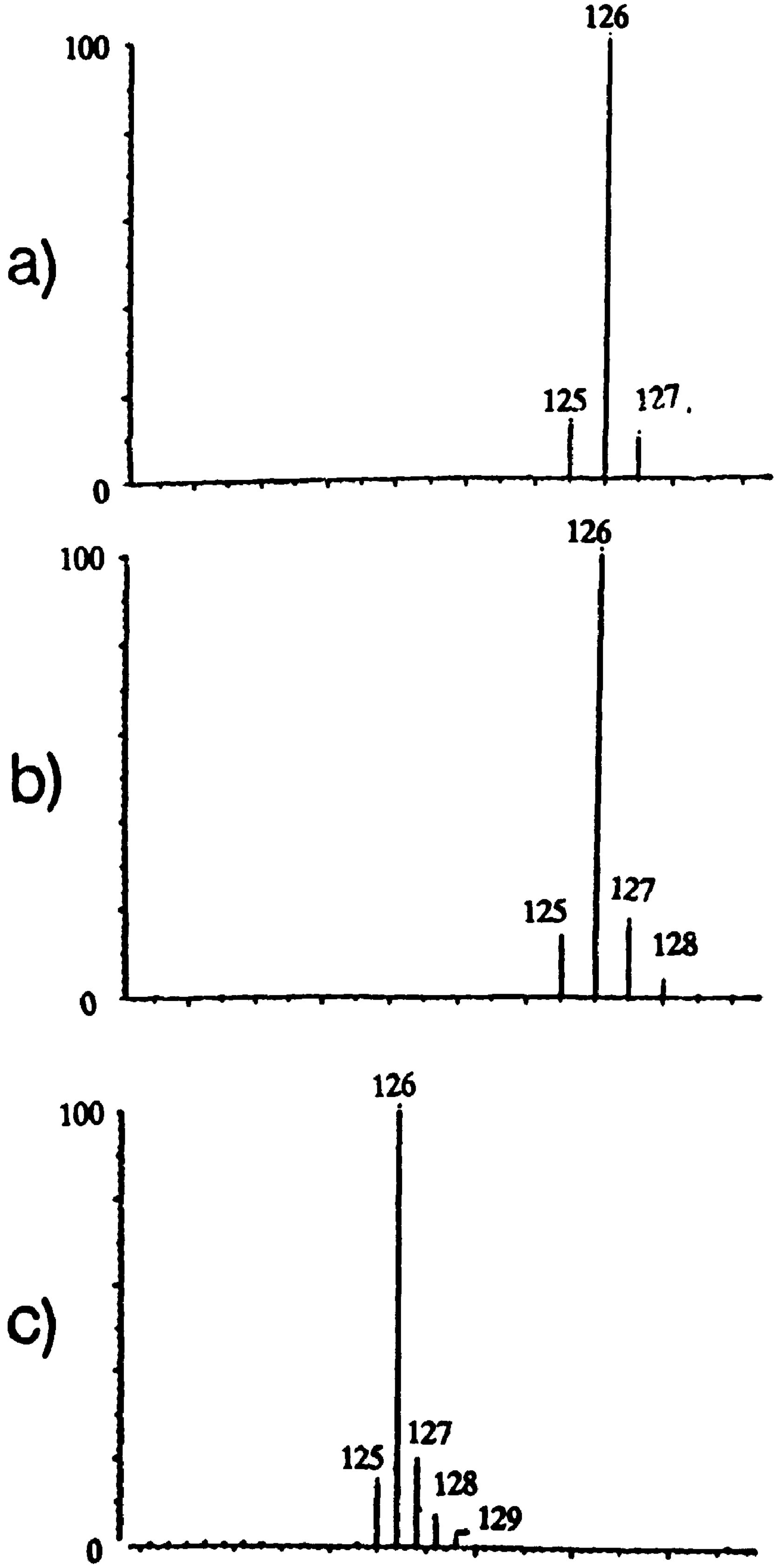
Photolysis of Aldehyde 269 in CD_3OD

Photolyses similar to that using aldehyde 270 were performed using aldehyde 269 (46 mg) in a mixed solution (1.5 mL) of CD_3OD/benzene (1:14 by volume). In order to quantify the starting aldehyde, and cyclopentenone product each was calibrated against a decane internal standard by g.c. Cyclopentenone was also calibrated against the starting aldehyde 269. The amount of head-to-head cyclobutanols formed was based on the percent of deuterium incorporation into the unconverted aldehyde. This was determined by g.c-m.s. analysis in which the ion intensity was measured for the parent ion m/e $M^+ = 126$, as well as the 127(M+1), 128(M+2) and 129(M+3) ions. An example of the mass spectra for the aldehyde before irradiation is given in figure 7a. The parent ion was set as the base ion (100% intensity) and the intensities of the other ions were measured as an average of 10 scans of the g.c. peak with a standard deviation ranging from 6-14 %. However, the observed relative intensities are not indicative of the relative amounts of each isotopic ion from the aldehyde alone. This is due to the presence of an aldehyde fragment with m/e 125 whose own isotopic distribution contributes to the intensities observed. The fragment results from a loss of a hydrogen atom from the aldehyde parent ion (m/e 126). In order to determine the isotopic distribution of the aldehyde parent ion alone it is necessary to determine the contributions of the m/e fragment and deduct those contributions from the observed intensities. The observed data for experiment #5 is given below where each sample was injected three times.

Observed intensities

m/e	125	126	127	128	129
aldehyde 269	15.36	100.00	9.35	0.31	0.31
	15.31	100.00	8.72	0.31	0.31
	15.29	100.00	8.26	0.59	0.29
dark reaction	13.93	100.00	20.23	3.81	0.83
	13.96	100.00	20.53	3.90	0.62
	14.17	100.00	20.42	3.13	0.63
photolysis reaction	15.13	100.00	22.49	7.16	1.23
	15.42	100.00	24.84	8.35	1.07
	15.02	100.00	25.75	8.80	1.93

Figure 7: Mass Spectra for a) 269, b) unirradiated 269 in CD_3OD and c) irradiated 269 in CD_3OD.[a]



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[a] averaged peak intensities for molecular ions M^+, $M^+ + 1$, $M^+ + 2$ and $M^+ + 3$.

It is possible to determine the intensities for m/e 126, 127, 128 and 129 from the aldehyde alone assuming that the isotopic distributions for the aldehyde (m/e 126) and its fragment (m/e 125) are equivalent. If this is the case then the ratio of the two isotopic distributions, n, can be determined (*i.e.* the ratio of the ion intensity due to aldehyde alone (m/e 126) to the ion intensity of the fragment ion (m/e 125)). It can be solved as the fourth order equation,

$$I_1 n^4 - I_2 n^3 + I_3 n^2 - I_4 n + I_5 = 0$$

where I_1, I_2, I_3, I_4 and I_5 are the observed intensities of ions with m/e 125, 126, 127, 128 and 129, respectively. The root to this equation, n, can be approximated using Newton's method and was determined by entering the appropriate coefficients into "Lintek", a basic program designed to solve such equations (125). For example, for observed intensities,

m/e	<u>125</u>	<u>126</u>	<u>127</u>	<u>128</u>	<u>129</u>
	15.02	100.00	25.75	8.80	1.93

n is approximated to be 6.404 thus for the aldehyde only, the ion intensities are

m/e	<u>126</u>	<u>127</u>	<u>128</u>	<u>129</u>
	96.19	24.42	8.50	1.93

These ion intensities were then normalized to give a sum equal to 1.0000. The increase in M+2, M+3, and M+4 due to photolysis was measured by the difference between the ion intensity increase of the irradiated sample (figure 7, spectrum c) and a control sample which was subjected to the same reaction conditions except it was wrapped in aluminum foil (figure 7, spectrum b). The g.c-m.s. analysis was repeated three times to yield an average percent deuterium incorporation. The results of the photolyses are shown in table 7 where the amounts of aldehyde and cyclopentenone photolysis product were based on the mean of 5-10 injections with errors corresponding to standard deviations. The value for ρ^H was determined using $\rho^H = \text{moles}_{\underline{299}}/\text{moles}_{\underline{191}+\underline{299}}$ and the errors associated were calculated according to the literature (124). Reactions were performed under both direct irradiation conditions (medium pressure Hg vapour lamp/Pyrex filter) and sensitized conditions (low pressure Hg vapour lamp/quartz irradiation vessel). Photolyses exceeding 20% conversion of the starting material were not used. The mass spectral data for the peak intensities are given below. Normalized peak intensities are given in parentheses.

G.c.-m.s. before photolysis (no CD_3OD), true ion intensity,

m/e	126	127	128	129
	98.55(0.9089)	9.31(0.0859)	0.26(0.0024)	0.31(0.0028)
	98.65(0.9143)	8.68(0.0804)	0.26(0.0024)	0.31(0.0028)
	98.73(0.9164)	8.18(0.0759)	0.54(0.0051)	0.29(0.0027)

0.9132 ± 0.0039 (normalized average)

G.c.-m.s. of dark reaction (aldehyde 269 + CD_3OD), true ion intensity,

m/e	126	127	128	129
	97.18(0.8005)	19.70(0.1623)	3.69(0.0304)	0.83(0.0068)
	97.13(0.7991)	19.98(0.1644)	3.81(0.0314)	0.62(0.0051)
	97.08(0.8041)	19.98(0.1655)	3.03(0.0252)	0.63(0.0052)

0.8012 ± 0.0026 (normalized average)

G.c.-m.s. of the photolysed aldehyde 269, true ion intensity,

m/e	126	127	128	129
	96.65(0.7656)	21.40(0.1695)	6.97(0.0552)	1.23(0.0097)
	96.23(0.7459)	23.53(0.1824)	8.18(0.0634)	1.07(0.0083)
	96.19(0.7340)	24.42(0.1864)	8.50(0.0649)	1.93(0.0015)

0.7485 ± 0.0159 (normalized average)

from g.c data (calibrated), number of moles 191 = $(3.148 \pm 0.059) \times 10^{-2}$ mMol
number of moles 269 = $(1.678 \pm 0.036) \times 10^{-1}$ mMol

The amount of deuterium incorporated into aldehyde 269 reflects the normalized decrease in the m/e 126 ion which equals the sum of the normalized increases in the M+1, M+2 and M+3 ions. Therefore the amount of "D" incorporated

$$\% \text{"D"} = [0.8012-0.7485 \pm (0.0026+0.0159)] \times 100$$

$$= 5.27 \pm 1.85$$

Thus the moles of 269D = moles of 269 X % "D"

$= (8.85 \pm 3.11) \times 10^{-3}$ mMol

= moles of 299

Thus, $\rho^H = \text{moles}_{\underline{299}}/\text{moles}_{\underline{191}+\underline{299}}$

$= 0.22 \pm 0.08$

The average value for $\rho^H = 0.22$ is the mean for experiments 1-6 and the error was 0.019. This was calculated using the values for each ρ^H and their respective errors and entering them into "gmean02" previously mentioned.

Irradiation of Cyclopentenone with cyclopentene

A solution of cyclopentenone (50 mg, 0.61 mMol) and cyclopentene (0.8 g, 0.012 Mol) in benzene (10 mL) was irradiated for 10 minutes with a medium pressure Hg vapour lamp after which g.c. analysis showed clean conversion (45%) to a single product. g.c.-m.s. of the product peak yielded a molecular ion m/e (%) 150(41) with fragments of 122(49), 108(36), 83(62), and 68(100) indicative of 1:1 adducts of cyclopentenone and cyclopentene. The product was assigned to structures 311a and 311b.

Dark Reaction of Cyclopentenone with Hydrogen Selenide

Cyclopentenone (30 mg, 0.366 mMol) was dissolved in 0.5 mL of $CDCl_3$ in an nmr tube and purged for 10 minutes with nitrogen. Aluminum selenide (0.3 g) was placed in a 2-necked flask, under nitrogen, and distilled water was slowly added dropwise. The flask outlet was adapted to a pipette which was immersed in the cyclopentenone solution. The nitrogen flow was stopped and hydrogen selenide was allowed to bubble through the solution for 15 minutes.

After treating the solution with H_2Se the pipette was removed and the tube immediately capped and wrapped with teflon tape. The reaction was then followed by g.c. and 200 MHz ^1H-nmr and after 24 hours showed clean conversion (50%) to 2 products in a ratio of 1:12. The first and minor product was identified as cyclopentanone, 314, described below, based on g.c.-m.s. $M^+=84$ and g.c. coinjection with an authentic sample.

The second and major peak was tentatively assigned to selenol, 313; ^1H-nmr $\delta(CDCl_3)$ from reaction mixture 83% pure 3.66 (m,2H), 2.44 (dd, J=16, 4 Hz, 2H), 1.91 (m, 1H), 1.80 (m, 2H), -0.11 ppm (d, J=3 hz, 1H), c.i.m.s. (isobutane) m/e(%) 167(9), $M^+=165(49)$, 163(23), 162(10), 83(100), calc. 164.98186 (found 164.98210).

Dark Reaction of Cyclopentenone/Cyclopentene with Hydrogen Selenide

A solution of cyclopentenone (60 mg, 0.73 mMol) and cyclopentene (7 g, 0.103 Mol) in benzene (20 mL) was treated with H_2Se for 15 minutes as described above (1.0 g Al_2Se_3), mixed and allowed to stand over 12 hours. The solution turned yellow and some selenium deposits were evident. The reaction was filtered and analyzed by g.c. This indicated 88% conversion of cyclopentenone to three major product peaks in a ratio of 1:11:28, accounting for 97% of the total products and 3 minor peaks in a ratio of 1:2:1, accounting for the other 3%. The solvent was removed to yield 75 mg of a yellow oil which was chromatographed (preparative t.l.c., silica gel, 25% ether/75% hexanes).

The first band isolated (5 mg) contained the minor of the three major products and was identified as cyclopentanone, 314; ^1H-nmr $\delta(CDCl_3)$ 2.24 (m, 4H), 1.92 ppm (m, 4H), m.s. m/e(%) M^+=84(10), 70(64), 56(100), confirmed by g.c. coinjection with an authentic sample.

The second band (17 mg) contained the second major product and was identified as selenide 315. ^{1}H-nmr $\delta(CDCl_3)$ 3.21 (quint, J=4 Hz, 1H), 2.30 (t, J= 4 Hz, 4H), 2.05 ppm (m, 4H), g.c.-m.s. m/e(%) M^+=218(35, 1 Se atom), 150(46, 1 Se atom), 69(100).

The third band (30 mg) contained the major product and was identified as selenide 317 or structural isomer based on m.s. m/e(%) M^+=232 (28, 1 Se atom), 164(46, 1 Se atom), 83(100), 67(76), ^{1}H-nmr $\delta(CDCl_3)$ 2.41 (broad m, 1H), 2.25 (broad m, 1H), 2.15- 0.9 ppm (m, 14H).

The three minor peaks could not be isolated by chromatography and were contained in small amounts within the bands isolated above. g.c.-m.s. of these products yielded data which allowed for tentative assignments of the minor components. Minor product 1, m/e(%) M^+=164(7, 1 Se atom), 83(100), 55(73), was assigned to selenol 313 and confirmed by g.c. coinjection with an authentic sample. Minor product 2, m/e(%) M^+=232(22, 1 Se atom), 164(41, 1 Se atom), 83(100), 67(76), 55(72), was tentatively assigned to selenide 316 or structural isomer. Minor product 3, m/e(%) M^+=300(3.4, 2 Se atoms), 230(4.4, 2 Se atoms), 150(6.5), 69(96), 67(100), was tentatively assigned to diselenide 318 or structural isomer.

Irradiation of Cyclopentenone/Cyclopentene with Hydrogen Selenide

Benzene (10 mL) was purged with nitrogen for 15 minutes after which H_2Se was bubbled (previously described) through the solvent for a period of 20 minutes (1.1 g Al_2Se_3). Immediately after treating the benzene with H_2Se a solution of cyclopentenone (54.8 mg, 0.668 mMol) in cyclopentene (7.74 g, 0.114 Mol) was added and the resulting solution mixed. Prior to addind the benzene/H_2Se and cyclopentene/cyclopentenone solutions together a small aliquot (0.5 mL) was taken from the latter and was diluted with an equal volume of benzene. This solution was used to monitor the 2+2 photocycloaddition reaction. An aliquot (1 mL) was also taken from the cyclopentenone/cyclopentene/H_2Se solution and wrapped with aluminium foil. This was used to monitor the dark reaction. All three solutions were then placed in front of a medium pressure Hg vapour lamp and irradiated for 10 minutes after which they were analyzed by g.c. and g.c.-m.s.

The solution containing cyclopentenone and cyclopentene showed clean conversion (approx. 50%) to a single product peak identified as <u>311a,b</u>. This was confirmed by g.c. coinjection with irradiation product described previously and by g.c.-m.s.

G.c. analysis of the unirradiated solution containing cyclopentene, cyclopentenone and H_2Se after 45 minutes showed 15% of the cyclopentenone had been converted to three major product peaks. in a ratio of 1:10:30 and accounting for 98% of the total products, and 3 minor peaks accounting for the other 2%. After 12 hours g.c. analysis showed 95% conversion of the cyclopentenone to the above products which are described in the above section.

G.c. analysis of the irradiated H_2Se sample after 30 minutes showed 51% conversion of cyclopentenone to yield two sets of product peaks; those product peaks which were observed in the dark reaction experiment and new peaks which were a result of photolysis. The ratio of the dark to photochemical products was 1:1 by g.c. and none of the photochemical products possessed retention times equivalent to that of the cycloadducts 311a,b (confirmed by coinjection). The dark reaction products were shown by coinjection to be cyclopentanone, 315, 317, 316, and 319 in a ratio of 1:9:4.8:1.3:2 respectively. The three product peaks due to photolysis were formed in a g.c. ratio of 3.0:8.2:6:0 in order of increasing retention times. All three products possessed retention times near that of the 2+2 photocycloadducts, 311a,b. The reaction mixture was filtered and the solvent removed to yield 50 mg of a yellow oil in which the ratio of dark to photochemical products remained unchanged. Chromatography (preparative t.l.c., silica gel, 30% ether/70% hexanes) yielded mixed fractions of photochemical and dark reaction products. The structures of the photochemical products were tentatively assigned and discussed in chapter 7. The assignments were as follows; first peak, minor photochemical product 324, m.s. m/e(%) M^+=152(3), 84(100), 67(18), 55(9); second peak, major photochemical product 327, m.s. m/e(%) M^+=152(32), 83(100), 67(56), 55(47); third peak, second major photochemical product 325, m.s. m/e(%) M^+=150(100), 122(56), 108(58), 67(22), 55(15).

Irradiation of Cyclopentenone and Ethyl Vinyl Ether with Hydrogen Selenide

Benzene (30 mL) was purged with nitrogen for 10 minutes after which H_2Se was bubbled in over a period of 20 minutes (1.3 g Al_2Se_3). Immediately, a solution of cyclopentenone (154.7 mg, 1.9 mMol) in ethyl vinyl ether (18.85 g, 0.26 Mol) was added and the solutions mixed. Prior to mixing the benzene/H_2Se and ethyl vinyl ether solutions a small aliquot (0.5 mL) was taken from the ethyl vinyl ether solution and diluted with and equal volume of benzene. This was used to monitor the 2+2 photocycloaddition reaction. An aliquot was also taken from the cyclopentenone/EVE/H_2Se solution (1 mL) and wrapped with aluminium foil. This was used to monitor the dark reaction. All three solutions were then placed in front of a medium pressure Hg vapour lamp and irradiated for 10 minutes after which all three solutions were analyzed by g.c. and g.c.-m.s.

The solution irradiated in the absence of H_2Se showed clean conversion (approx. 27%) to a four products identified as 281-284 in a g.c. ratio of 1:1.6:3.25:4.6 (regioisomeric ratio of 1:3.12). This was confirmed by g.c. coinjection with the irradiation products described previously and by g.c.-m.s..

G.c. analysis of the unirradiated H_2Se treated sample 40 minutes after mixing showed 50% of the cyclopentenone converted to three major product peaks in a ratio of 1:1:1. g.c.-m.s. of the products yielded molecular ions of m/e 226, 226 and 236 all containing one selenium atom by m.s.. g.c showed these product to grow with time and after 2 hours all the cyclopentenone was consumed. Tentative assignments for these products is discussed in chapter 7.

G.c. analysis of the irradiated H_2Se sample showed 32% conversion of cyclopentenone to yield two sets of product peaks; one set of three product peaks which were described in the dark reaction experiment, and a set of new peaks which were a result of photolysis. The ratio of the dark to photochemical products was 5:1 by g.c. and none of the four photochemical products possessed retention times equivalent to that of 281-284 (confirmed by coinjection). The g.c. ratio of the four photochemical products in order of increasing retention time was 3.23:5.73:3.45:1.00. After photolysis the reaction vessel was immediately adapted to a vacuum pump, with a liquid N_2 trap and solvent and volatiles removed within 5 minutes. This yielded 220 mg of a yellow oil whose g.c. remained unchange from the irradiated solution. The photochemical reaction was repeated twice (183 mg and 220 mg of cyclopentenone) and the irradiation times were extended to 30 minutes. This did not affect the ratios of the photolysis products. Immediately after each photolysis the resulting yellow solution was filtered and solvent removed under high vacuum to prevent further dark reaction. The products from each irradiation were combined to yield 627 mg of a yellow oil. Chromatography (preparative t.l.c., silica gel, 30% ether/70% hexanes) of the oil (365 mg) allowed for separation of the dark reaction products (band 1, 23.9 mg) from the photochemical products (bands 2, 53.2 mg, and 3, 32.5 mg). Band 2 contained a mixture of the first three of the four photochemical products by g.c. analysis and band 3 contained the last two of the four photochemical products. Further preparative t.l.c. (30% ether/70% hexanes) of each band allowed for isolation of the first, third, and fourth products and a mixture of the second and third products. The products were assigned as follows; product 1, 332, 14 mg, ^{1}H-nmr δ($CDCl_3$) 3.49 (t, J=6 Hz, 2H), 3.45 (q, J=7 Hz, 2H), 2.35-2.00 (m, 7H), 1.65 (m, 2H), 1.20 (t, J=7 Hz, 3H), ^{13}C-nmr δ($CDCl_3$) 200.1 (C=O), 68.5, 66.0, 38.0, 29.7, 29.6, 20.8 (CH_2), 46.5 (CH), 15.2 ppm (CH_3), m.s. m/e(%) M^+=156(2.5), 84(100), 73(96), 59(24), calc. 156.11503 (found 156.11492).

Product 3, 334, 5 mg, ^{1}H-nmr δ($CDCl_3$) 7.45 (m, 1H), 3.55 (t, J=8 Hz, 2H). 3.49 (q, J=7 Hz, 2H) 2.58 (m, 2H), 2.45 (t of d, J=8, 2 Hz, 2H), 2.35 (m, 2H), 1.19 ppm (t, J=7 Hz, 3H), ^{13}C-nmr δ($CDCl_3$) 159.3 (C=O), 68.2, 66.0, 34.2, 29.6, 26.5 (CH_2), 34.2 (CH), 15.0 ppm (CH_3), m.s. m/e(%) M^+=154(12), 125(100)

110(25), 98(44) 84(34), 59(75) calc. 154.09938 (found 154.1002).

Product 4, 333, 4 mg, ^{1}H-nmr δ(CDCl$_3$) 5.95 (m, 1H), 3.62 (t, J=8 Hz, 2H), 3.45 (q, J=7 Hz, 2H) 2.61 (m, 2H), 2.45 (broad m, 4H), 2.35 (m, 2H), 1.15 ppm (t, J=7 Hz, 3H), ^{13}C-nmr δ(CDCl$_3$) 159.3 (C=O), 68.2, 66.0, 34.2, 29.6, 26.5 (CH$_2$), 34.2 (CH), 15.0 ppm (CH$_3$), m.s. m/e(%) M$^+$=154(2.5), 126(9), 125(100), 110(25), 59(76) calc. 154.09938 (found 154.1003).

Product 2 could not be isolated pure but was obtained as a mixture of products 2 and 1 (2:1 ratio) and tentatively assigned to 331. ^{1}H-nmr δ(CDCl$_3$) yielded signals isochronous with those given for 336. ^{13}C-nmr δ(CDCl$_3$) 217.1 (C=O), 69.2, 68.7, 34.6, 29.9, 29.8, 21.0 (CH$_2$), 53.7 (CH), 15.4 ppm (CH$_3$) , m.s. m/e(%) M$^+$=156(1.3), 110(100), 83(60) 59(80), calc. 156.11503 (found 156.11494).

Samples of 333 and 334 (1.5 mg) were hydrogenated for 5 minutes over 10% palladium on carbon at atmospheric pressure in methanol (0.5 mL). Each reaction was analyzed by g.c. and g.c.-m.s. Compound 334 underwent clean conversion to yield 332 and this was confirmed by g.c. coinjection with an authentic sample. M.s. showed the molecular ion change from m/e(%) 154 to 156(1.6) consistent with the addition of two hydrogens and yielded fragments 84(100) 73(84) and 55(48). Compound 333 also showed clean conversion to give 331 and this confirmed by coinjection. M.s. yielded a molecular ion m/e(%) 156 and a fragmentation pattern consistent with that of 335, 110(100), 83(74), 59(83).

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