TO MY PARENTS

THE PHOTOCHEMISTRY OF SOME

N-ACYLPHTHALIMIDES

By

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DECLARATION

I, the undersigned, declare that this thesis represents the sole work of the author.

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N. T. McSWEENEY.

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ABSTRACT

The photochemistry of N- alkylphthalimides has been extensively studied while to date no work has been published on N-acylphthtalimides. We were interested in the photochemical reactions of a range of N-acylphthalimides with toluene and cyclohexene.

N-acetylphthalimide, N-acetyl-3,4,5,6-tetrachlorophthalimide and N-benzoyl-3,4,5,6-tetrachlorophthalimide were found to behave photochemically like the carbonyl group of simple ketone systems by undergoing what appeared to be hydrogen abstraction at the "in-ring" carbonyl group of the excited phthalimide and recombination with the resultant benzyl radical to yeild the respective carbinols as the major products. N-Benzoylphthalimide when irradiated in toluene produced a novel spirolactone as the major product. We proposed the mechanism for its formation as involving a pinacol intermediate. The spirolactone formation may involve electron transfer from toluene to the excited N-benzoylphthalimide whereas hydrogen abstraction may be the primary photoprocess on irradiation of the other studied N-acylphthalimides.

Irradiation of N-benzoylphthalimide, N-acetylphthalimide and N-acetyl-3,4,5,6-tetrachlorophthalimide in the presence of cyclohexene resulted in 1,4-cycloaddition of the cyclohexene to the aromatic ring of the phthalimide as the major photoprocess. X-Ray crystallography showed the 1,4-cycloadduct from the irradiation of N-benzoylphthalimide in the presence of cyclohexene as the exo, trans 1,4-cycloadduct. The exo, trans 1,4-cycloadducts were also the major products on irradiation of N-acetylphthalimide and N-acetyl-3,4,5,6-tetrachlorophthalimide in the presence of cyclohexene. Minor products obtained on irradiation of N-acylphthalimides in the presence of cyclohexene included a carbinol by photoaddition of cyclohexene to the "in ring" carbonyl group of N-acetylphthalimide and a novel photoproducts which can formally be seen as insertion of cyclohexene between the two "in ring" carbonyl groups of N-acetyl-3,4,5,6-tetrachlorophthalimide with elimination of acetamide.

Abbreviations used in this thesis

NAP	N- Acetylphthalimide
NATCP	N-Acetyl-3,4,5,6-tetrachlorophthalimide
NBTCP	N-Benzoyl-3,4,5,6-tetrachlorophthalimide
NBP	N-Benzoylphthalimide
NMP	N-Methylphthalimide
TCPN	3,4,5,6-tetrachlorophthalonitrile
THF	Tetrahydrofuran

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CHAPTER 1

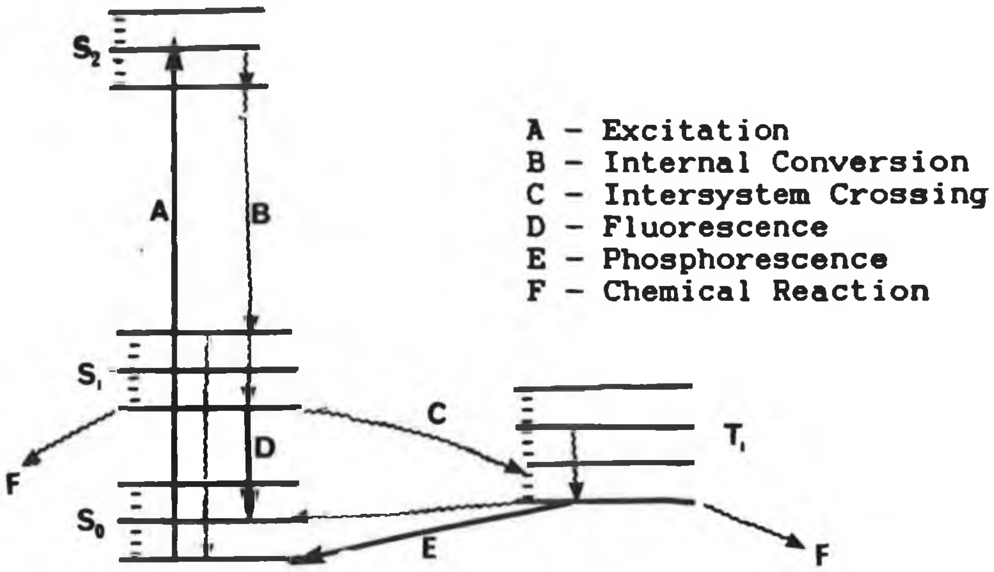
INTRODUCTION

Photochemistry is the study of the physical and chemical changes which occur in molecules on absorption of ultra-violet or visible light.

The electronic excitations of compounds require quanta of energy which correspond to wavelengths of electromagnetic radiation lying in the ultra-violet or, less frequently, the visible region of the spectrum. When a molecule absorbs a photon of the appropiate energy, one of its electrons is promoted to an orbital of higher energy. The resulting molecule may then take part in a reaction while in this or an alternative excited state.

Molecules possess many excited states. The first-formed excited state generally gives up its extra vibrational energy to other bonds in the molecule and falls to the lowest vibrational level of this state.

The time required for this process is very short, about 10^{-13} seconds, the time required for a single vibration. In the next step, this electronic excited state gives up more energy to other vibrational modes in the molecule or in collisions with solvent and becomes an excited vibrational level of the lowest excited state,S_1. This excited vibrational state again gives up vibrational energy until it reaches the lowest vibrational level of S_1. The change from the higher excited states to the lowest excited state (S_1) is called internal conversion and takes about 10^{-11} seconds. The majority of photochemical reactions take place from S_1 (lowest excited singlet) and T_1 (lowest excited triplet) states. The lifetime of the S_1 state in its lowest vibrational level is about 10^{-8} – 10^{-7} seconds and during this lifetime one of four possibilities can occur. These alternatives are discussed[1,2] below with the aid of a Jablonski diagram (scheme 1.1).



Scheme 1.1

Scheme 1.1 Jablonski Diagram. Non-radiative processes are shown as wavy lines.

(1) S_1 can emit a photon and undergo an electronic transition to the ground state, a process called fluorescence. Because the excited state has lost energy before fluorescence occurs, the fluorescence photon has less energy than the original excitation photon and thus

has a longer wavelength.

(2) S_1 can give up energy to other vibrations or to solvent and become an excited vibrational state of the ground state, S_0. This is an internal conversion and is a non-radiative process. The excited vibrational level again gives up energy to its environment until it achieves an equilibrium distribution with the lowest vibrational level. The nett result of all these changes is the conversion of the original light quantum into heat.

(3) S_1 can undergo intersystem crossing to the triplet state, T_1. A triplet state is one in which one electron spin has been changed so that the molecule has two electrons that cannot pair. The lowest triplet state is usually of higher energy than the ground state. Nevertheless T_1 is of lower energy than S_1. Electrons with the same spin tend to stay apart because of the Pauli Principle. As a result, the electrostatic energy of electron repulsion is less than in comparable singlet states. The T_1 state itself can undergo internal conversion, intersystem crossing, photochemical reaction or emit a photon in a process know as phosphorescence. Because phosphorescence is spin-forbidden it is a low-probability event and is usually only seen at low temperatures.

(4) A chemical reaction can take place. The radiative lifetimes of excited singlet states (i.e. the time-lag before return to the ground state) are very short (10^{-6} – 10^{-9}

seconds), so that chemical reactions occurring via these species, despite their high energy, are comparatively uncommon. Conversion into the triplet state occurs with an efficiency which varies widely with the structure of the molecule; for benzophenone, for example, it is a highly efficient process whereas for alkenes it is not. The lifetimes of 'triplets' are relatively long (> ca. 10^{-4} seconds for species containing relatively light atoms) so that the probability of the triplet taking part in a chemical reaction is much higher than for a singlet. Normally the amount of energy necessary to make a transition depends mostly on the nature of the two orbitals involved and much less on the rest of the molecule. Therefore, a simple functional group such as the C=C bond always absorbs in the same general region of the spectrum. A group that causes absorption is called a chromophore. For most organic molecules there are consequently four types of electronic excitation:

(i) (σ,σ^*). Alkanes, which have no n or π electrons, can be excited only in this way.

(ii) (n,σ^*). Alcohols, amines, ethers etc can also be excited in this manner.

(iii) (π,π^*). This pathway is open to alkenes as well as to carbonyl compounds, aromatics etc.

(iv) (n,π^*) Carbonyl compounds etc can undergo this promotion as well as the other three.

The four excitation types are listed in what is normally the order of decreasing energy.

Of the four excitation types listed above, the (π,π^*) and (n,π^*) are far more important in organic photochemistry than the other two. Compounds containing carbonyl groups can be excited in both ways, giving rise to at least two peaks in the UV absorption spectrum. These are often easy to distinguish because (π,π^*) transitions are found further toward the far UV and are generally much more intense [ε for (π,π^*) is usually about 100 to 10,000 compared with ε= 10 to 1,000 for (n,π^*)].

The properties of excited states are not easy to measure because of their generally short lifetimes and low concentrations, but enough work has been done for it to be known that they often differ from the ground state in geometry, dipole moment and acid or base strength. For example acetylene, which is linear in the ground state, has a trans-geometry with approximately sp^2 carbons in the $^1(\pi,\pi^*)$ state.[3] Similarly the $^1(\pi,\pi^*)$ and the $^3(\pi,\pi^*)$ states of ethylene have a perpendicular and not a planar geometry,[4] and the $^1(n,\pi^*)$ and $^3(n,\pi^*)$ states of formaldehyde are both pyramidal.[5] Triplet states tend to stabilize themselves by distortion which relieves interaction between the unpaired electrons. Obviously if the geometry is different, the dipole moment will probably differ also and the change in geometry and electron distribution often results in a change in acid or base strength. For example, the S_1 state of 2-naphthol is a much stronger acid (pKa 3.1) than the ground state (S_0) of the same molecule (pKa 9.5)[6]. Photochemical reactions can be classified into three overall types:

(A) Direct Photoreactions

$$M \xrightarrow{hv} M^{*} \longrightarrow P$$

$*$ = an excited singlet or triplet state.
P = Product

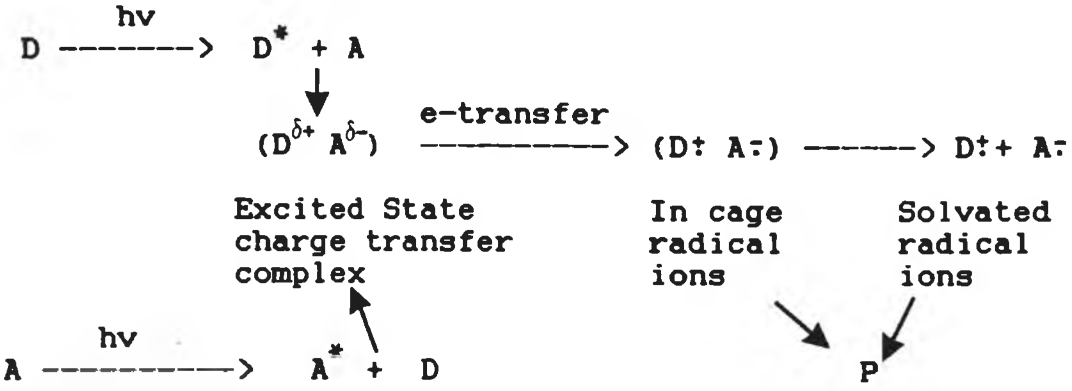
(B) Photosensitized Reactions

$$D \xrightarrow{hv} D^{*}$$

$$D^{*} + A \longrightarrow D + A^{*} \longrightarrow D + P$$

D = Donor molecule
A = Acceptor molecule

(C) Electron - Transfer Photoreactions.



The synthetic potential of the third type of reaction has only been understood relatively recently and is based on the fact that excited states are both better oxidizers and reducers than their ground state counterparts. Irradiation of an electron donor (D) - electron acceptor (A) system can lead to the formation of radical cation-radical anion pairs and subsequent ground state processes may lead to reaction products. In general the feasibility of producing radical ions via photoinduced electron transfer can be predicted using Weller's equation[7] :

$$\Delta G = 23.06\left[E_D^{ox} - E_A^{red}\right] - E_{excit} - C$$

ΔG = free energy for electron transfer.

E_D^{ox} = oxidation potential of the donor molecule.

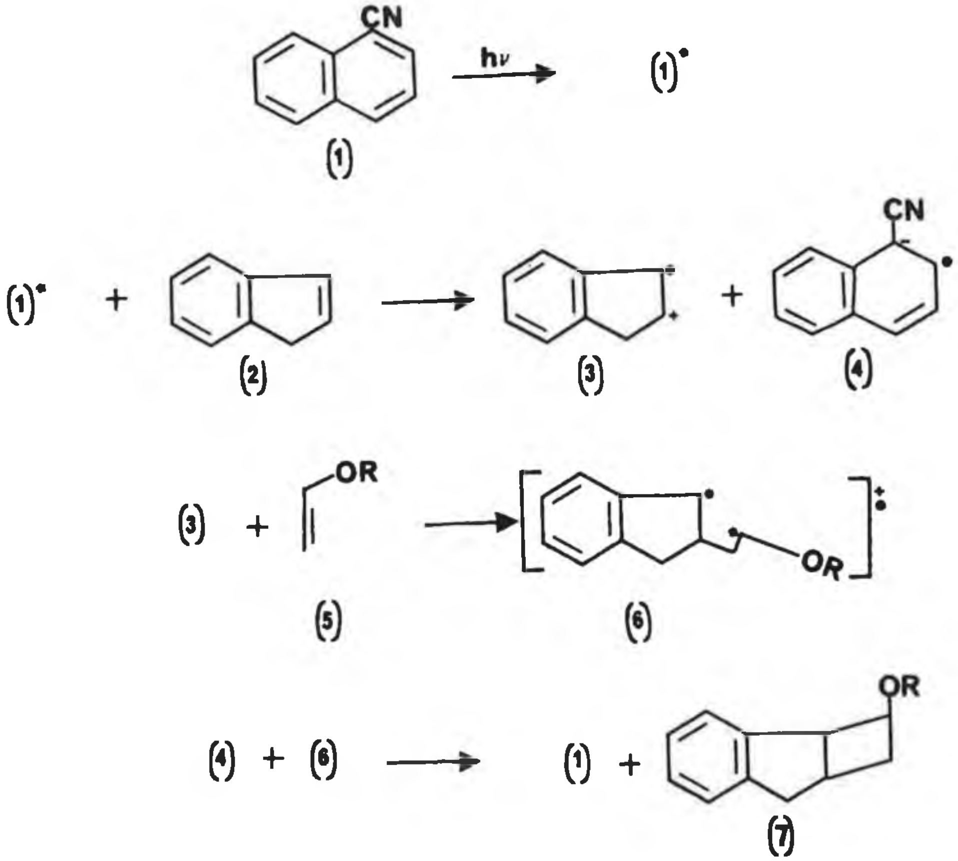
E_A^{red} = reduction potential of the acceptor molecule.

E_{excit} = singlet excitation energy of either the donor or acceptor depending on which is excited.

C = coulombic attraction term.

If the energy stored in the excited species is higher than the energy stored in the radical ion pair (calculated from the oxidation and reduction potentials of the donor and acceptor respectively), the electron transfer becomes exothermic and proceeds at a diffusion-controlled rate. Such electron transfer reactions may be induced by excitation of either the donor or the acceptor. Since the energy content of a radical ion pair, solvated by a polar solvent, is substantially lower than that in a non-polar solvent, photoreactions via separated radical ions are generally observed in polar solvents. Reverse electron transfer between radical ion pairs, leading to the ground state of both molecules, is an unfortunate energy-wasting step responsible for the low quantum yields in many electron transfer reactions.

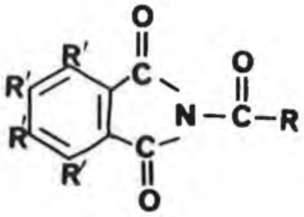
An example of an electron transfer reaction is the (2 + 2) cycloadditions of aromatic ethylenes. On irradiation in acetonitrile, indene(2) and alkyl vinyl ethers(5) in the presence of 1-naphthonitrile(1) yielded the (2 + 2) cycloadduct(7) (scheme 1.2). In the absence of alkyl vinyl ethers, (2 + 2) cyclodimers of indene are formed. This reaction is sensitized by 1-napthonitrile via initial electron abstraction which is later reversed.[8]



Scheme 1.2

The work reported in this thesis concerns the photochemical behaviour of some N-acylphthalimides, both chlorinated (11) and (12) and non-chlorinated (8) - (10) , with donor molecules such as cyclohexene, toluene and propan-2-ol.

(8) R = Me, R'= H
(9) R = Ph, R'= H
(10) R = o-tolyl, R'= H
(11) R = Me, R'= Cl
(12) R = Ph, R'= Cl



Scheme 1.3

As the main chromophores involved in these reactions are the carbonyl and aromatic groups, the remainder of this chapter deals with the general photochemistry of these particular chromophores. Chapter two is concerned with, in more detail, the photochemistry of imides particularly phthalimides.

1.1 Photochemistry of the Carbonyl Group

Perhaps the most widely studied class of compounds, historically and today, is that containing the carbonyl chromophore. This ever-growing interest is inspired by both experimental and theoretical considerations. Thus for example, the absorption spectra of most carbonyl compounds fall into the experimentally readily accessible region of the ultra-violet where quartz has high transmission and mercury arcs produce strong line emission spectra.

1.1.1. Spectra and Excited States

Aliphatic ketones and aldehydes show a weak (ε ~10-30$dm^3mol^{-1}cm^{-1}$) UV absorption band in the 280-300nm region, corresponding to the symmetry and overlap forbidden (n,π^*) transition. Strong absorption occurs in the vacuum ultra-violet region and there are bands centred around 195, 170 and 155nm in the spectrum of saturated aliphatic ketones. The last of these corresponds to the (π,π^*) transition. The lowest energy excited states for these compounds are undoubtedly the (n,π^*) singlet and triplet states, and these are responsible for the observed photochemistry.

The energy difference between the (n,π^*) singlet and triplet states is comparatively small and thus the rate constant for intersystem crossing to the triplet state is very high. Many photoreactions of the carbonyl group occur from the $^3(n,\pi^*)$ state.

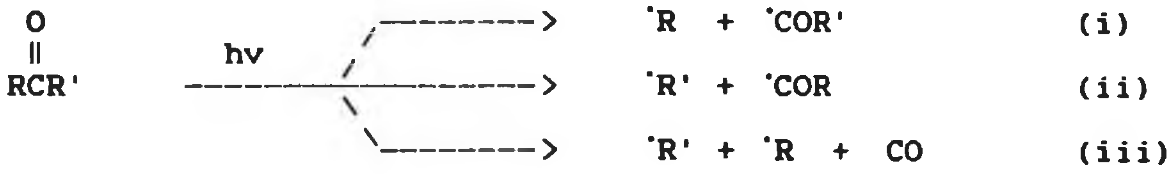
The major difference from the photochemical point of view between saturated and unsaturated carbonyl compounds is that for the unsaturated compounds the (n,π^*) states are not always the lowest in energy (due to delocalization of the individual π and π^* bands). For some, the lowest triplet state is definitely (π,π^*) in nature (e.g. acylnaphthalenes) and for others the (n,π^*) and (π,π^*) triplet states are very close in energy (e.g. p-methoxyphenyl ketones). Because of the difference in the reaction of (n,π^*) and (π,π^*) states, this has a profound effect on the observed photochemistry.

1.1.2 Photoreactions of the Carbonyl Group

The (n,π^*) excited state of a carbonyl compound does not have such an electron-deficiency near the carbon atom as does the ground state, because an electron is transferred in the excitation process from a non-bonding orbital localized mainly on oxygen to an antibonding orbital which covers both carbon and oxygen nuclei. This makes nucleophilic attack at the carbon atom a relatively unimportant reaction for the excited state. Instead the outstanding feature of the electron distribution in the (n,π^*) state of a carbonyl compound is the unpaired electron in a p-type orbital on oxygen.

(a) <u>α- Cleavage Reactions (Norrish type I processes)</u>

One of the most common photoreactions of ketones is α-cleavage to give two radicals (scheme 1.4). When the two α- bonds are not identical, it is the weaker bond which breaks preferentially, forming the more stable radicals. As the energy of the absorbed quantum increases, the selectivity between the two processes [(i) and (ii)] decreases markedly.



Scheme 1.4

Depending on the energy of the absorbed quantum, various fractions of the acyl radicals (RC˙O and R'C˙O) are vibrationally 'hot' and may decompose rapidly into an alkyl radical and carbon monoxide in an early vibration following the primary act [scheme 1.4 (iii)]. The stability of equilibrated acyl radicals, RC˙O and R'C˙O depends markedly upon temperature, with virtually complete dissociation of acetyl radicals at temperatures above 120^0C. Other simple acyl radicals are less stable than acetyl and the quantum yield of carbon monoxide formation approaches unity at correspondingly lower temperatures.

In addition to the simple α-cleavage process, aliphatic aldehydes exhibit a different primary process in which a molecular elimination of carbon monoxide occurs. Acetaldehyde (13) irradiated in the gas phase with 334nm radiation gives largely hydrogen atoms and acetyl radicals (Scheme 1.5) through the triplet (n,π^*) state, but when irradiated with 254 nm radiation the primary products are mainly methane and carbon monoxide by reaction through the (n,π^*) singlet state. It is thought that the molecular elimination pathway is concerted or nearly so, with formation of the C_α- H bond occurring at the same time as, or very shortly after, cleavage of the C(=O)-H[9] bond.

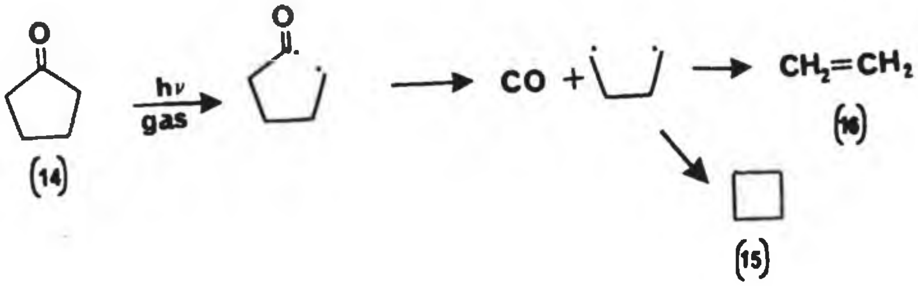
$$CH_3CH{=}O\ (13)\ \xrightarrow{h\nu\ (334nm)}\ H^{\cdot}\ +\ CH_3{-}\dot{C}{=}O$$

$$(13)\ \xrightarrow{h\nu\ (254nm)}\ CH_4\ +\ CO$$

Scheme 1.5

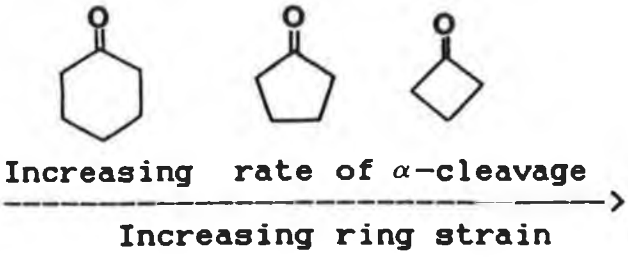
Product formation by the α-cleavage process for acylic ketones is not a major reaction in solution at room temperature. This is because the initially formed radicals are produced in a 'cage' of solvent molecules, and a major secondary process is recombination to reform ground state starting material.

Cyclic ketones undergo α-cleavage to give biradical species on photolysis in gas or solution phase. The biradicals can then recombine to give starting material or can fragment to lose carbon monoxide, e.g. cyclopentanone (14) leads to hydrocarbon products (15) and (16) (scheme 1.6).[10] For these cyclic systems, the reactivity pattern of ring opening follows that expected for the relief of ring strain (scheme 1.7).



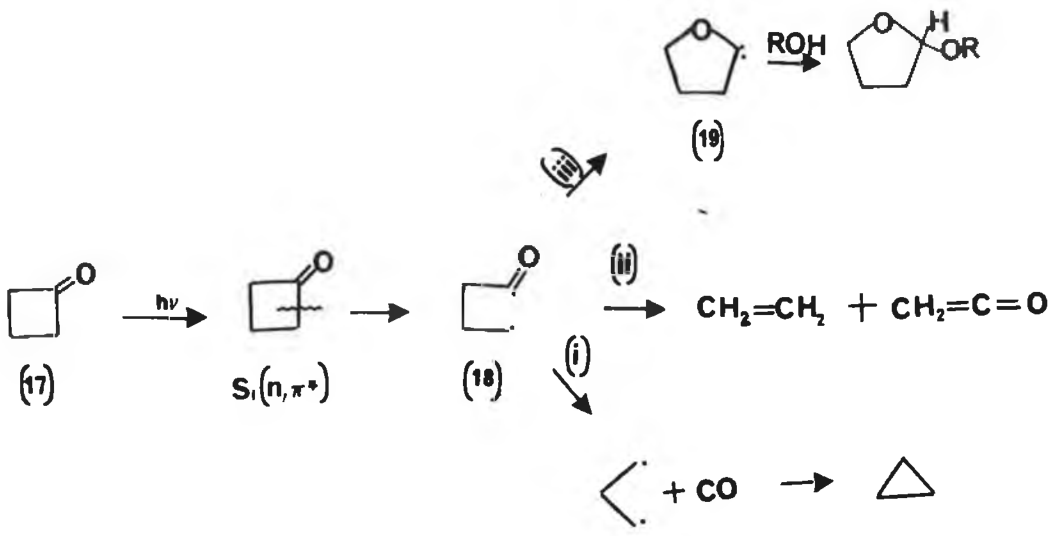
Scheme 1.6

In contrast to other alkanones, cyclobutanones (17) undergo efficient α-cleavage from S_1 (n,π^*) to produce a singlet 1,4-acyl-alkyl diradical (18). The reactions generally resulting from this diradical are



Scheme 1.7

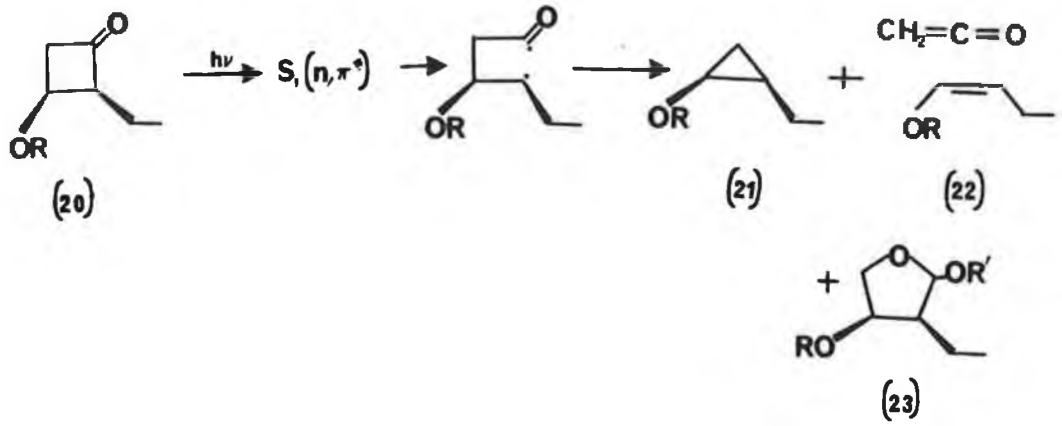
(i) decarbonylation (ii) cycloelimination, and (iii) oxacarbene formation.[11] The oxacarbene intermediate (19) has been trapped by alcohols (scheme 1.8).



Scheme 1.8.

Another important difference between cyclobutanone photochemistry and that of larger cyclanones is the observation of stereospecificity in formation of reaction products. For example, the ethyl alkoxy cyclobutanone (20) undergoes sterospecific decarbonylation to yield (21), cycloelimination to yield (22), and oxacarbene formation to yield (23) (scheme 1.9).[12]

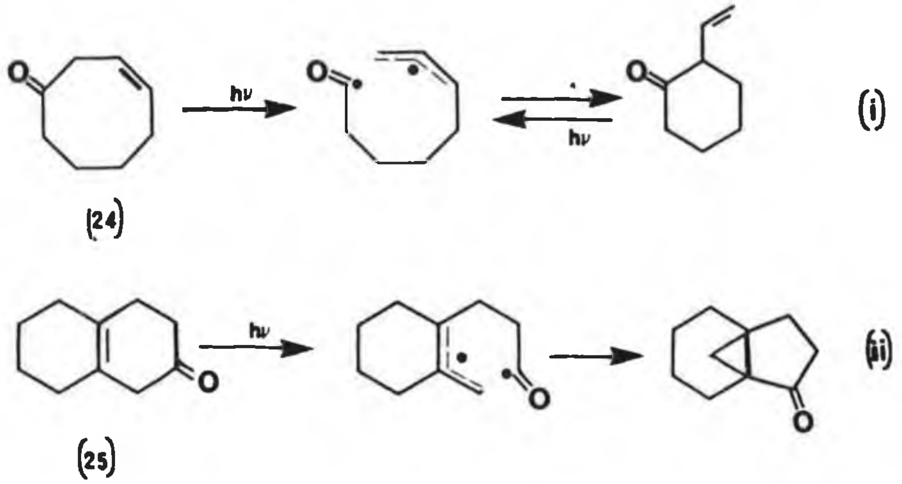
β,γ -Unsaturation in a carbonyl compound promotes α-cleavage, formally at least because of allylic stabilization of the radical produced.



Scheme 1.9

Two modes of overall reaction are observed. The first involves a 1,3-acyl shift resulting in the formation of an isomeric β,γ-unsaturated compound, as with cyclooct-3-enone (24) [scheme 1.10 (i)].[13]

The second mode of reaction involves a ring closure leading to cyclopropyl ketone, as with (25) [scheme 1.10 (ii)]. It seems that this enone reacts via the lowest triplet excited state.[13]

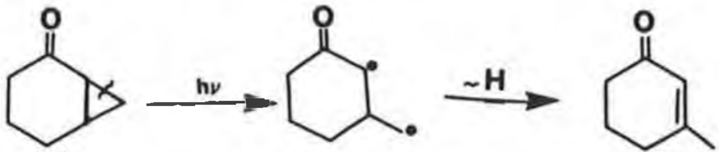


Scheme 1.10

(b) β-Cleavage Reactions

The (n,π*) states of conjugated cyclopropyl and epoxyketones commonly undergo homolytic cleavage of a β-bond. This reaction, in contrast to α-cleavage, appears to be initiated by overlap of the π* orbital with the σ*orbital associated with the bond undergoing rupture. In general, if two β-bonds are potentially available for cleavage, the bond capable of best overlap with the orbital is cleaved preferentially,[14] for example (26) -> (27).

Outside of the β-cleavage reactions of small rings, only a few examples of the cleavage of other groups are known. Among the better documented examples are the photoinduced β-eliminations of a sulphonyloxy group[15] and of acetoxy groups[16].

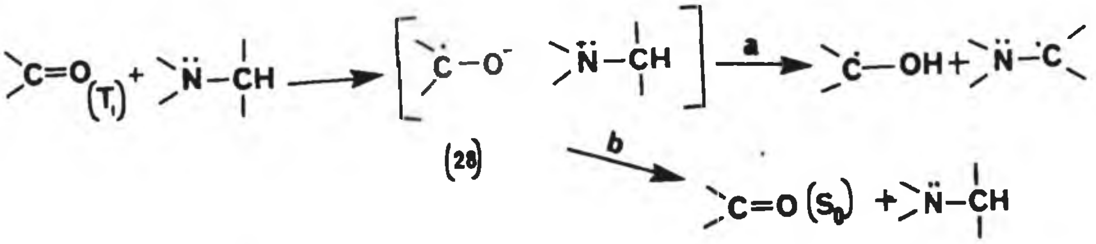

(26)

(27)

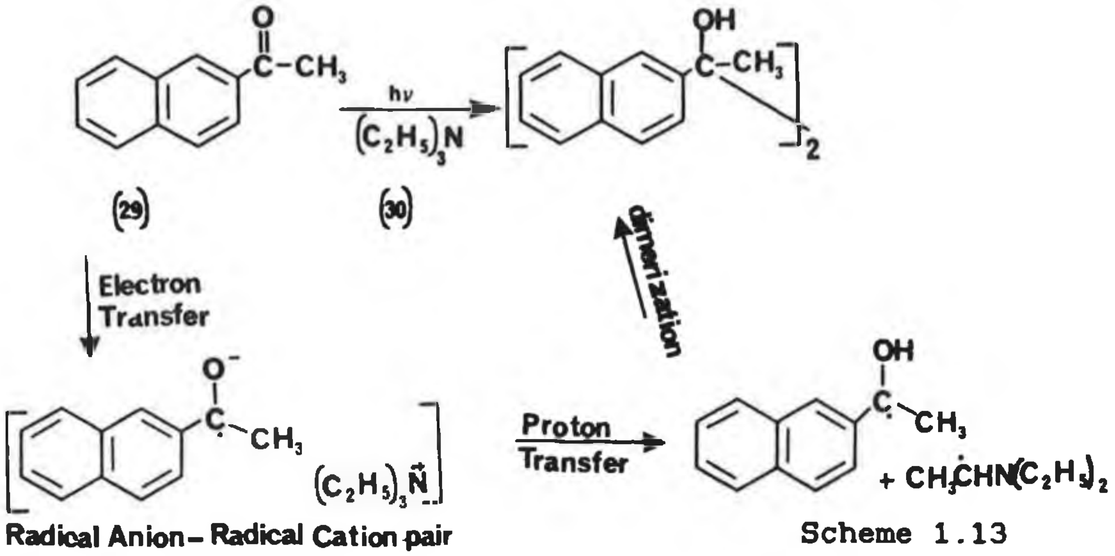
Scheme 1.11

(c) Hydrogen Abstraction

Photoreduction of carbonyl compounds is one of the best known of photoreactions, and in its initial step the mechanism involves either transfer of an electron or hydrogen atom to the oxygen atom of the carbonyl excited state from a donor molecule which may be solvent, an added reagent or a ground state molecule of reactant. For electron transfer to take place, the donor molecule must have a low ionization potential (~9eV). For example, electron transfer occurs between excited carbonyl compounds and amines or sulfides but not with alcohols. These reactions take place by initial electron transfer from the donor to the excited carbonyl compound to form a radical anion-radical cation pair (28). This is followed by transfer of an α-hydrogen and formation of radicals (path a) or by back-electron transfer to regenerate the starting materials, (path b) (scheme 1.12). For example, the photoreduction of 2-acetylnaphthalene (29) by triethylamine (30)[17] is an example of an electron transfer reaction (scheme 1.13).

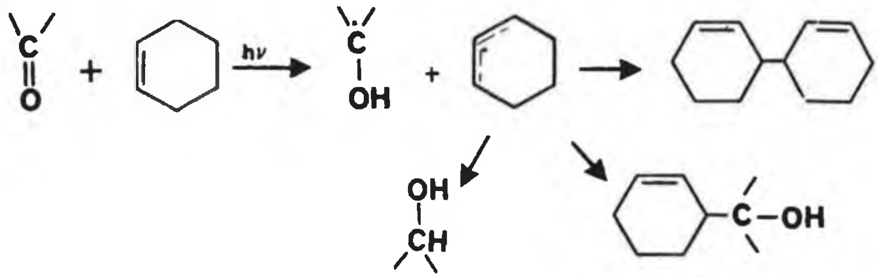


Scheme 1.12



Scheme 1.13

An example of a hydrogen abstraction reaction is that between acetone and cyclohexene[18] (scheme 1.14).

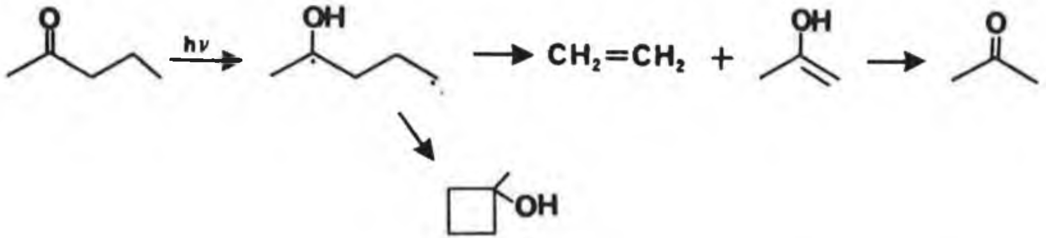


Scheme 1.14

The favoured route for secondary reaction depends on the structure of the radical entities, on the concentration of reagents, on the hydrogen donor power of the reducing agent, and on the temperature.

The excited state responsible for the hydrogen abstraction reactions of ketones is the (n,π^*) triplet state. The singlet state is too short-lived to undergo efficient intermolecular reaction.

Photolysis of carbonyl compounds with an accessible γ-hydrogen atom can give products by a mechanism generally referred to as the 'Norrish type 2' process. The mechanism involves initial γ-hydrogen abstraction (usually via a six membered transition state) to form the biradical which can undergo cyclization or cleavage (scheme 1.15).

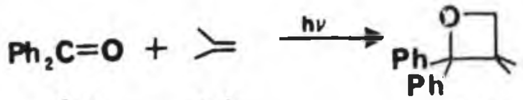


Scheme 1.15

In general the most favourable intramolecular hydrogen abstraction involves a six-membered cyclic transition state in the abstraction step, but in some systems there are factors which make abstraction from other positions an important process.

(d) <u>Photocycloaddition (Oxetane Formation)</u>

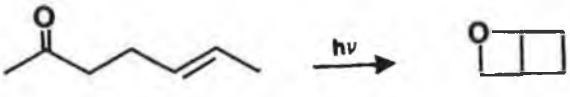
On photolysis in the presence of alkenes, dienes or alkynes, carbonyl compounds undergo cycloadditon reactions to give 4-membered ring oxygen hetrocycles.[19] For example benzophenone (32) with isobutene (33) gives a high yield of an oxetane (34). The reaction can



(32) (33) (34)

Scheme 1.16

occur in an intramolecular manner if the functional groups are suitably oriented, as with acyclic γ, δ-unsaturated ketones[20] (35). These reactions generally proceed from an attack of an (n,π^*) state of the carbonyl compound on an unsaturated substrate. Concerted cycloaddition reactions of (n,π^*) states are unlikely because of the difficulty of obtaining proper cyclic overlap in the transition state. As a result, (2 + 2) photocycloadditions of (n,π^*) states are generally expected to proceed via diradical intermediates.



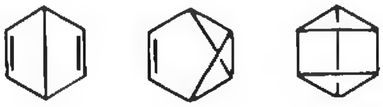
(35)

Scheme 1.17

1.3 The Aromatic Chromophore

1.3.1 Photoisomerizations of Aromatic Systems

Monocyclic aromatic systems undergo remarkable photochemical rearrangements. There are three valence isomers of benzene, i.e. compounds that can be formally derived from benzene by simple reorganization of π- and σ-bonds. These are Dewar benzene (36), benzvalene (37), and prismane (38).



(36) (37) (38)

Scheme 1.18

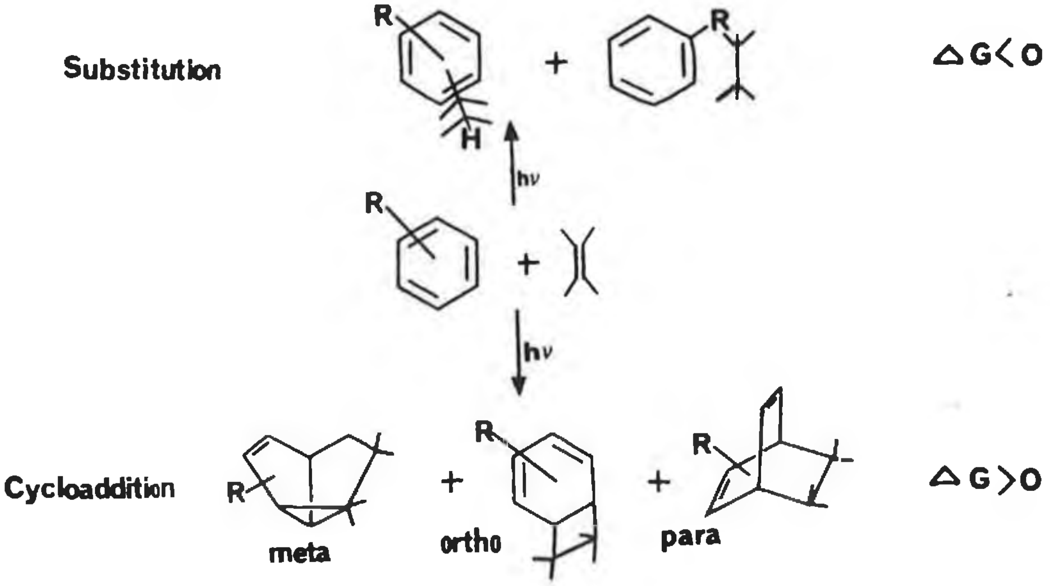
Prismanes are not produced directly from photoexcited benzenes, but result from secondary (2+2) intramolecular cycloaddition of Dewar benzenes. All of the photoisomerizations generally involve singlet states and not triplet states. Excitation of the S_2 state of benzene leads to the formation of Dewar benzene and benzvalene, but excitation of the S_1 state of benzene yields only benzvalene.[21]

1.3.2 Photosubstitution Reactions of Arenes with Alkenes

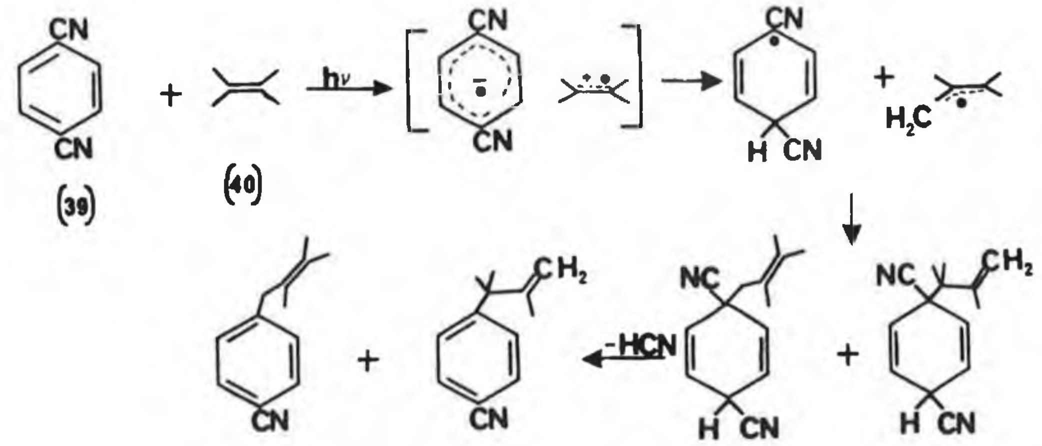
The photoreactions of arenes with alkenes has been investigated for a long time starting from the early discoveries of the ortho[22-24] and the meta cycloadditions.[25,26] Different mechanisms have been proposed, especially for the meta cycloaddition,[27] but only the one involving an exciplex provides a rationalization which is sufficiently in accordance with the experimental evidence. Intermediates of this type have been proposed earlier by Ferree[28] and Srinivasan.[29]

In photoreactions of arenes with alkenes the mode of reaction strongly depends on the free enthalpies (ΔG) of electron transfer for the arene-alkene system. Substitution is preferred if the electron transfer becomes exergonic i.e. if $\Delta G < 0$ according to the Weller equation. When $\Delta G > 0$ cycloaddition products are preferred (scheme 1.19).[30,31]

Formation of substitution products can be rationalized by a mechanism involving initial electron transfer yielding radical cation-radical anion pairs. The final products are formed from these intermediates in a sequential reaction process, first by transfer of an ionic group and then by coupling of the resulting radical pairs. The reaction of 1,4-dicyanobenzene (39) with 2,3-dimethylbut-2-ene (40) exemplifies this mechanism (scheme 1.20).[32] Other examples include 1-cyanonaphthalene - 2,3-dimethylbut-2-ene,[33] 1-cyanonaphthalene - indene,[34] and 9-cyanophenanthrene - 2,3 dimethylbut-2-ene.[35]

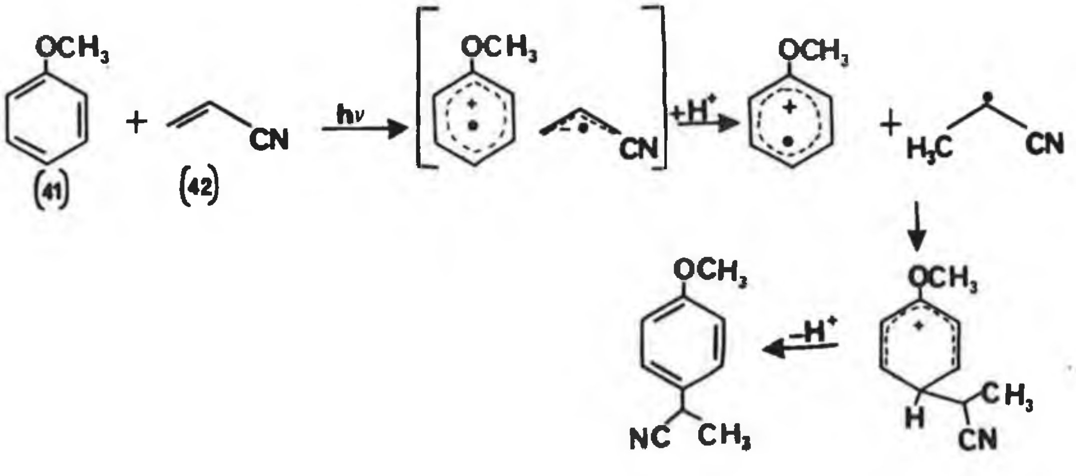


Scheme 1.19



Scheme 1.20

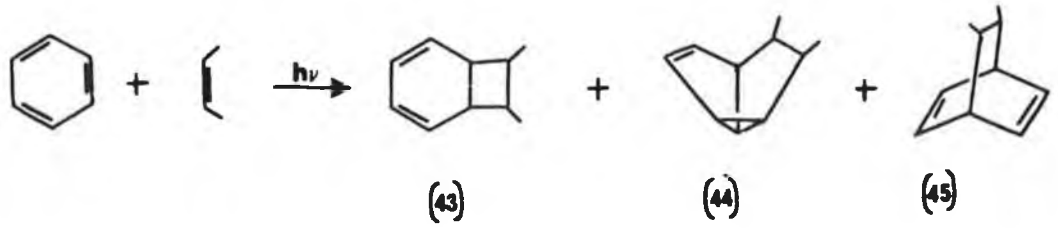
All these systems have in common that the calculated ΔG values are close to zero or even negative, which promotes electron transfer processes. Donor-arenes and acceptor-alkenes also form substitution products upon photolysis provided that $\Delta G < 0$ or that ΔG is at least only slightly positive, for example the photoreaction of methoxybenzene (41) with acrylonitrile (42) in the presence of a proton donor (scheme 1.21).[36]



Scheme 1.21

3.3.3 Photocycloaddition Reaction of Arenes with Olefins

The irradiation of mixtures of arenes and alkenes can give rise to a rich diversity of products, formally obtained by adding the alkene across the 1,2-, 1,3- or 1,4- positions of the aromatic ring. For example irradiation of a benzene and but-2-ene mixture yielded 1,2-(43), 1,3-(44) and 1,4-(45) cycloadducts (scheme 1.22).[37]



Scheme 1.22

Mattay[38] rationalized the preferred mode of cycloaddition as depending on the free energy of electron transfer (ΔG, calculated according to the Weller equation). The free enthalpies (ΔG) were correlated, depending on whether benzene acted as acceptor (upper part of scheme 1.23) or donor (lower part).

Based on the measured redox potentials of a series of olefins Mattay arrived at the following conclusions:

(i) olefins of both poor electron-donor and acceptor abilities preferentially yield metacycloadducts in photoreactions with benzene, i.e. if $\Delta G > 1.4$-1.6eV;

(ii) all other olefins mainly undergo ortho-cycloadditions.

The photoreactions of olefins with donor-substituted benzenes show similar trends of the mode selectivities as described for benzene itself. The only difference is that ortho-cycloadditions with donor olefins are only observed with those of extremely small oxidation potentials.[38]

(A) 1,3-Photoadditions to Benzenes

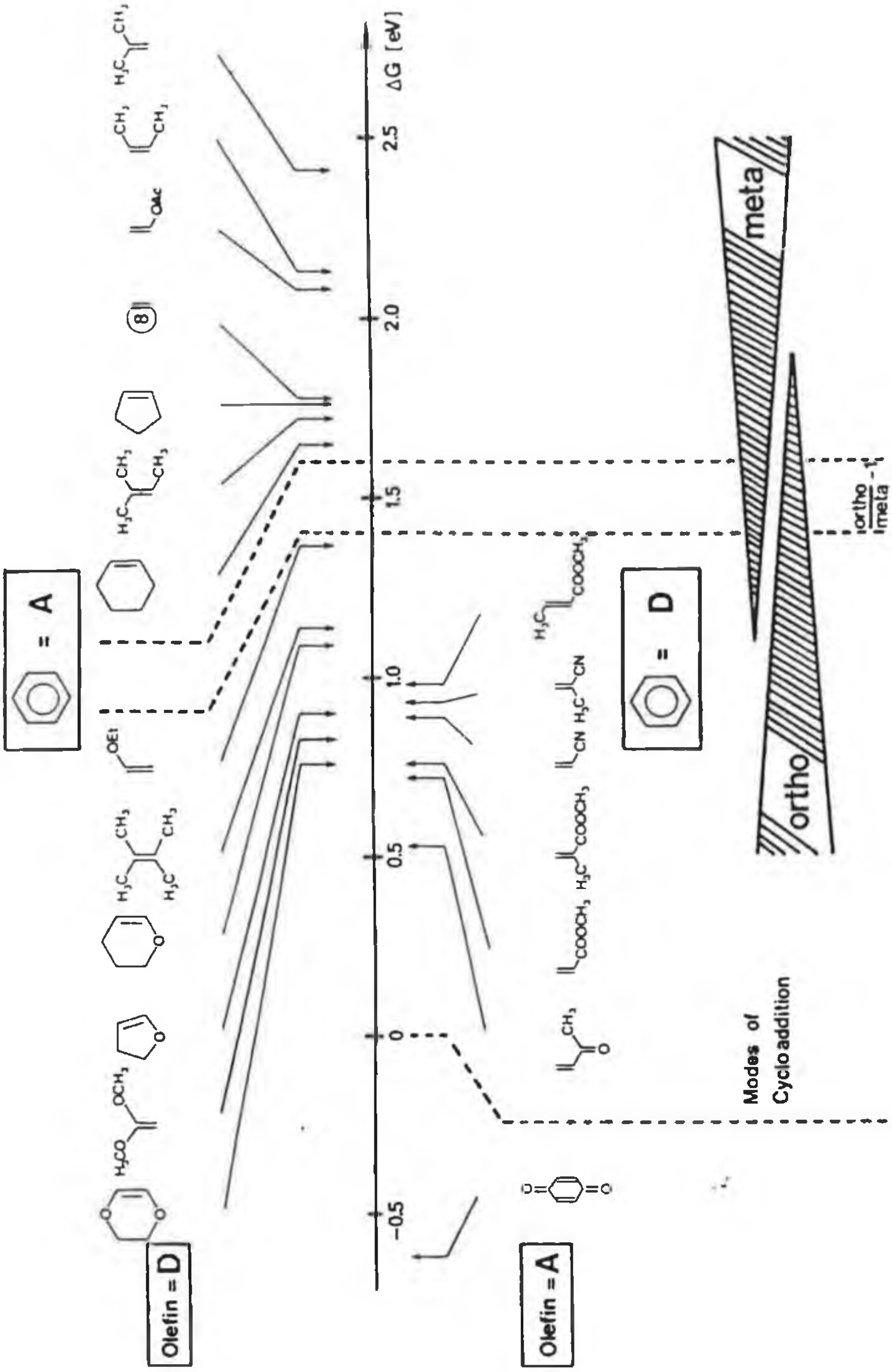
Most simple ethylenic compounds, both cyclic and acyclic, have been observed to undergo 1,3-cycloaddition to benzene as the most efficient mode of reaction.[37] The stereochemistry of the ethylene is preserved in the product, however, the relative amounts of the exo and endo isomers depend upon the ethylene, although the endo isomer predominates in many cases.

On inspection of all the meta cycloadditions of the substituted benzenes, anisole and its derivatives, toluene and its derivatives, benzonitrile, methyl benzoate, trifluorotoluene, and fluorobenzene, Mattay[39] observed the following trends:

(i) donor (D) substituents are always placed in position 1 of the meta adduct; in particular, alkoxy has priority over alkyl;

(ii) acceptor (A) substituents are generally located in positions 3 or 5 of the product.

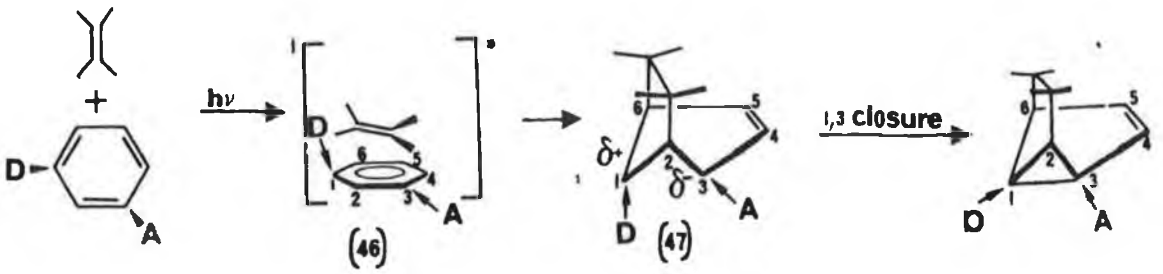
The origin of these features can be explained on the basis of a dipolar intermediate, (47) in scheme 1.24. The assumption of such an intermediate is in accordance with the exciplex mechanism since it can be shown from kinetic studies that an exciplex (46) is a necessary but not a direct precursor of the products.[40] Although zwitterions of this type have not been observed, work by Mattay[39] implies their existence.



D = Donor   A = Acceptor

Scheme 1.23

Correlation of Reaction Modes with Free Enthalpies of Electron Transfer in Photoreactions of Benzene with Olefins



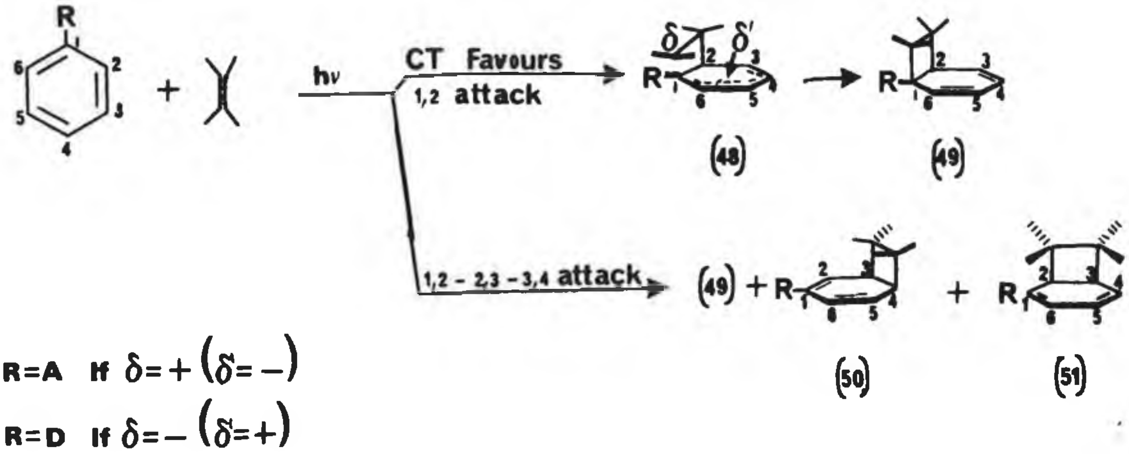
Scheme 1.24

The alkene adds across the 2,6-position of the arene because donor groups can stabilize positive charge while acceptor groups can stabilize negative charge (scheme 1.24).

(B) 1,2-Photoadditions to Benzenes

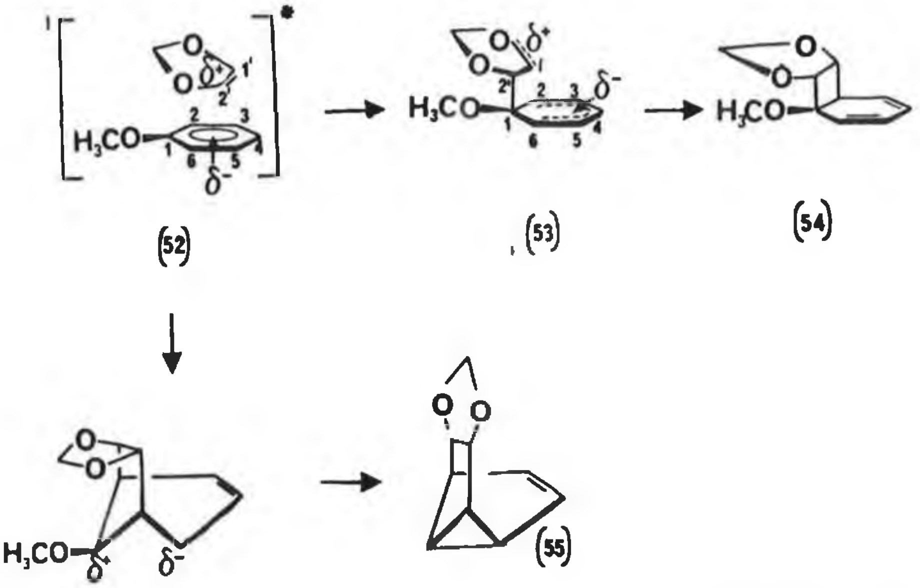
Many ethylenic compounds give minor proportions of 1,2-cycloadducts with benzenes in comparison with the 1,3-cycloadducts, though in some cases the 1,2-cycloadduct predominates.

Despite the generally lower regioselectivities of the ortho-cycloadditions in comparison with the meta mode, the selectivities between 1,2-, and 2,3- and 3,4- attack of the alkene on the arene depend on the degree of charge transfer in the intermediates i.e. the regioselectivity is high (low) if ΔG for electron transfer is relatively low (high). Scheme 1.25 demonstrates that in the former case, 1-substituted ortho adducts (49) are preferentially formed (especially if a substituent R in (48) stabilizes charges (±) in position 1), whereas in the latter case, mixtures of regioisomers (49),(50) and (51) are obtained. The formation of (49) may be rationalized analogously to that of the meta adduct formed in scheme 1.24 simply by assuming stepwise bond formation as shown in the case of the photoaddition of 1,3-dioxole to anisole[41] (scheme 1.26). Here an exciplex with a polarization as shown in (52) may be the precursor of a meta-adduct (55) and the ortho-adduct (54). The methoxy substituent is located at position 1 of the intermediate (53). Rotation around the C1-C2'bond in (53) plays a minor role since the endo isomer is formed in only small amounts.



Scheme 1.25

Other examples of ortho-addition include benzonitrile -[42] olefin systems and trifluorotoluene-1,3 dioxole systems. All these systems have in common that ΔG generally does not range above about 0.5eV, indicating a relatively high degree of charge transfer in the exciplex intermediate.[31] This is in accordance with increasing regioselectivity of the ortho-cycloddition with increasing solvent polarity.

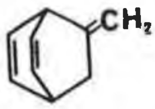


Scheme 1.26

(C) 1,4-Photoadditions to Benzenes

Cycloadducts of the para-type are only formed in some special examples such as in Yang's cycloaddition of benzenoid aromatic hydrocarbons to dienes.[43] Other example include additions of aromatic hydrocarbons to furans[44,45] and allenes.[46] Simple olefins also occasionally form para-cycloadducts with benzene and its substituted derivatives.

An example of 1,4-addition forming the major product (56) was from the irradiation of propa-1,2-diene in benzene.[47]



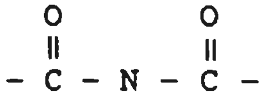
(56)

Scheme 1.27

CHAPTER 2

THE PHOTOCHEMISTRY OF IMIDES

An imide consists of a cross conjugated carbonyl system involving a nitrogen (scheme 2.1).



$$-\overset{O}{\overset{\|}{C}}-N-\overset{O}{\overset{\|}{C}}-$$

Scheme 2.1

2.1. Spectra and Excited States

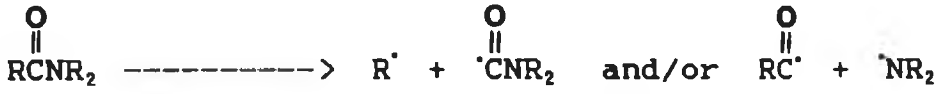
The aliphatic imides show a strong (π,π^*) absorption band in the region of 205-210nm (ε ~12,000) and this absorption is broadened to 190-215nm (ε ~13,000) in cyclic imides. The cyclic aliphatic imide spectra show a shoulder at around 240nm which is assigned to the (n,π^*) transition due to its solvent dependence and extinction co-efficient (ε=150).[48] The open chain imides show a tail which extends out to 280nm and often show points of inflection in the region of 250nm and 230nm.

For phthalimides the absorption spectra show a strong (π,π^*) band at 220nm and a shoulder at 295nm attributed to a (n,π^*) transition. The phthalimides exhibit a strong phosphorescence emission which is due to $T_1(\pi,\pi^*)$.[49,50]

The lowest singlet excited state in phthalimides is assigned as (n,π^*) in character[49,50] and it has been suggested that the fluorescent state is the second excited (π,π^*) singlet state.[49] Coyle[49] has suggested that the (n,π^*) and (π,π^*) states are very close energetically and there may be mixing of these states.

2.2. Aliphatic Imides

The photochemistry of the imide moiety is best compared to that of the related amides and ketones. Investigation of the photochemistry of simple aliphatic amides[51-55] led to the conclusion that the major process involved was the α-cleavage (type I) process via either C(O)-N or C-C(O) cleavage (scheme 2.2). The β-cleavage (type II) process in amides is at best a minor process although it is the dominant one in the corresponding straight chain ketones and esters.

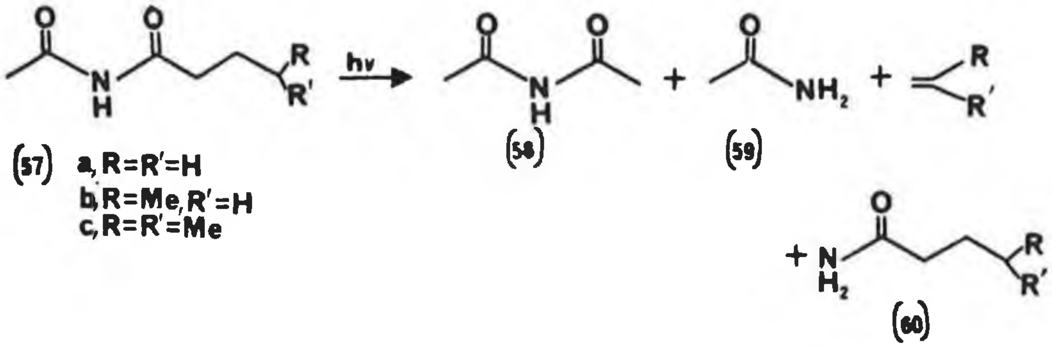


$$R\overset{O}{\overset{\|}{C}}NR_2 \longrightarrow R^{\bullet} + {}^{\bullet}\overset{O}{\overset{\|}{C}}NR_2 \quad \text{and/or} \quad R\overset{O}{\overset{\|}{C}}{}^{\bullet} + {}^{\bullet}NR_2$$

Scheme 2.2

These reactivity differences can be explained by the fact that type II processes occur most efficiently when the reactive carbonyl (n,π^*) state is electrophilic.[56] The ether oxygen in esters has two effects: it withdraws electron density through the σ-bond framework making the carbonyl oxygen electron deficient and it is a π-electron donor which would tend to make the carbonyl oxygen electron rich. Since σ-withdrawal is more efficient than π-donation for oxygen, the net result is an electrophilic (n,π^*) state and reactivity in the type II process. The situation with amides is exactly the opposite, π-donation from nitrogen is more efficient then σ-withdrawal and the amides are predicted to have nucleophilic (n,π^*) states and to be non-reactive in type II processes. Simple resonance theory suggests that the addition of a second carbonyl group on nitrogen should distribute the nitrogen electron pair making the imide carbonyls less nucleophilic and therefore more reactive in type II processes than amides, as is observed for aliphatic and aromatic imides.

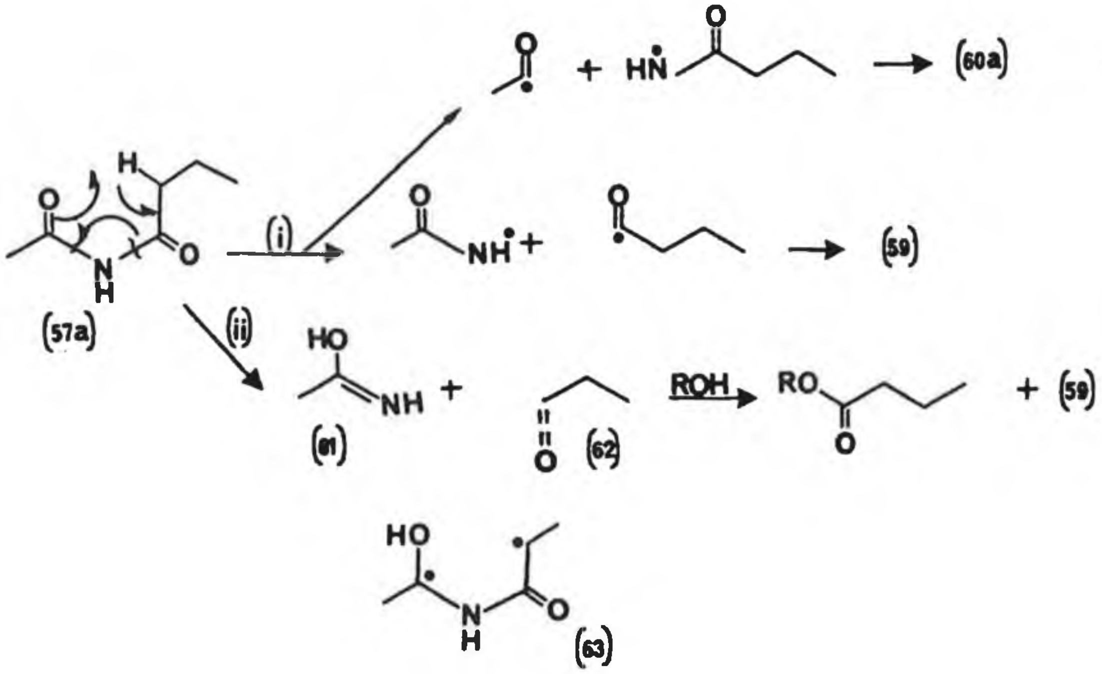
The photochemistry of a series of aliphatic imides has been studied in 1,4-dioxan and alcohol solvents and in all cases the amides (59) and (60), the presumed α-cleavage products, and diacetamide (58), from the β-cleavage, were observed (scheme 2.3).



Scheme 2.3

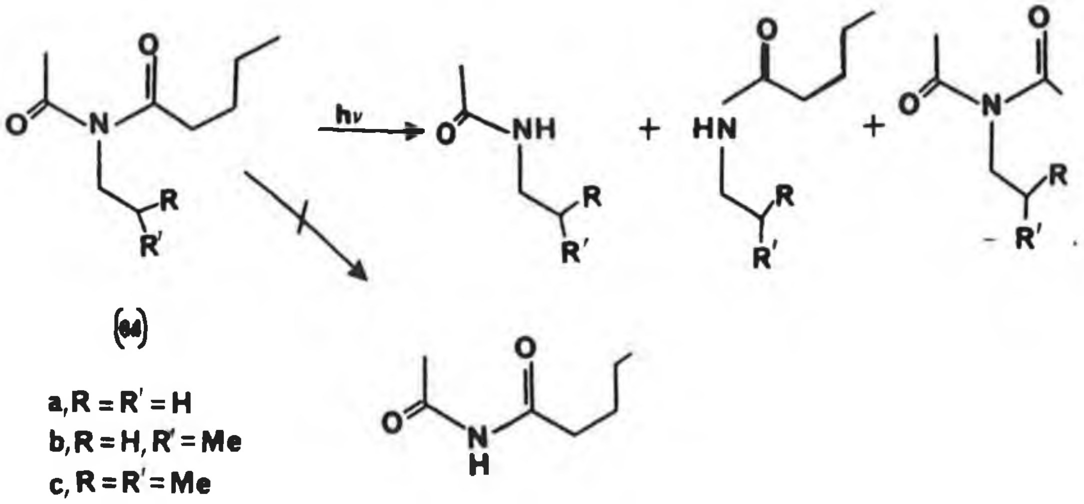
It was shown however, that the 'α-cleavage' products were formed via two routes, the expected α-cleavage followed by hydrogen abstraction from solvent [scheme 2.4(i)], and a novel type II process across the imide moiety affording the enol of the amide (61) and a ketene (62) which was trapped by the alcohol solvent [scheme 2.4 (ii)].[57] This type II process involving hydrogen abstraction α to an sp^2 hybridized centre is unprecedented in carbonyl photochemistry.
In the usual case, the intermediate biradical (63) prefers to close to the cyclobutane rather than undergo

β-cleavage since one of the radical centres is allylic.



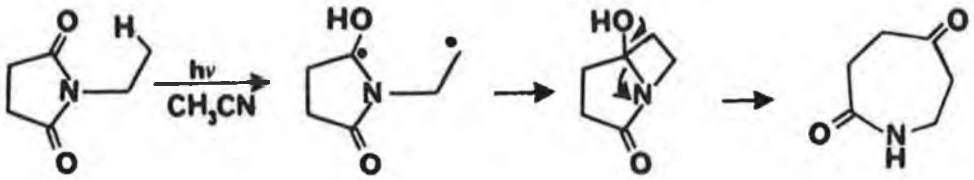
Scheme 2.4

N-Alkyl imides (64) show a similar reaction profile except that α-cleavage products predominate over the type II process since the stability of the incipient radical is greater due to the alkyl substitution on nitrogen (scheme 2.5). No type II process is observed from the N-alkyl substituent even when the abstractable hydrogen is tertiary (64c).



Scheme 2.5

Alicylic imides undergo a different series of photochemical reactions which the open chain aliphatic imides do not exhibit. N-Alkylated cyclic imides (65) undergo a rather efficient hydrogen abstraction from the γ-postion of the N-alkyl group to give the radical (66) which affords the azepinedione (68) via the azacyclobutane (67)[48] (scheme 2.6). For the example above (65), and all aliphatic cyclic imides, biradical closure is the dominant process but, is accompanied by 20-30% of the type II cleavage product.

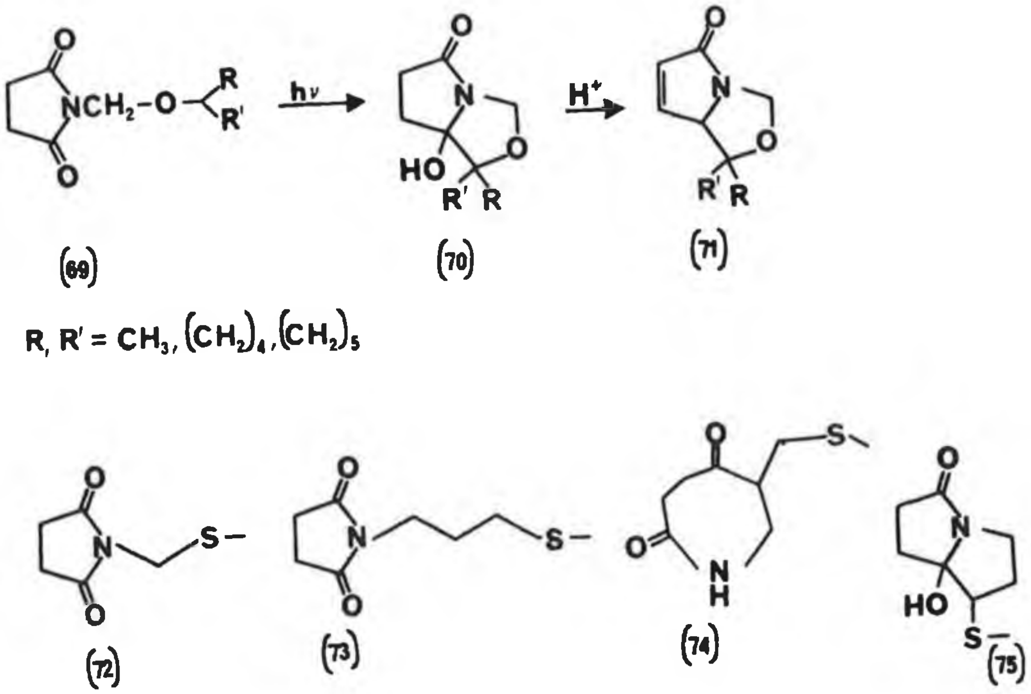


(65) (66) (67) (68)

Scheme 2.6

When an oxygen atom is appropriately placed in the N-alkyl chain to block the γ-position (69), hydrogen abstraction takes place to give the 5,5-ring fused system (70) in yields of 41-75%. Compounds (70) undergo acid catalysed dehydration to (71).[58] By contrast the sulphur analogue (72) is unreactive and (73) affords (74) and (75) in less than 10% yield each[58] (scheme 2.7).

The first example of α-cleavage in cyclic imides was the formation of (78)[59] presumably via hydrogen transfer in (79), (the biradical from α-cleavage of the type II elimination product) in addition to the expected products (76) and (77) (scheme 2.8). The C-C(O) α-cleavage is the

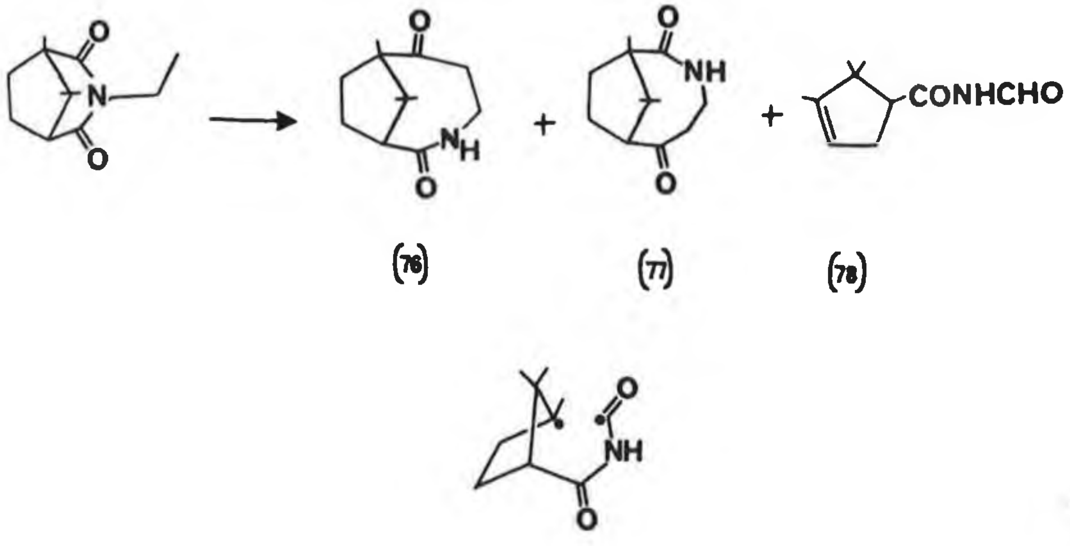


(69) (70) (71)

(72) (73) (74) (75)

Scheme 2.7

prevalent process in cyclic systems whereas C(O)-N cleavage dominates in open chain systems. The C-C(O) cleavage process is efficient in cyclic imides only when the incipient carbon radical is secondary or tertiary.[60,61]

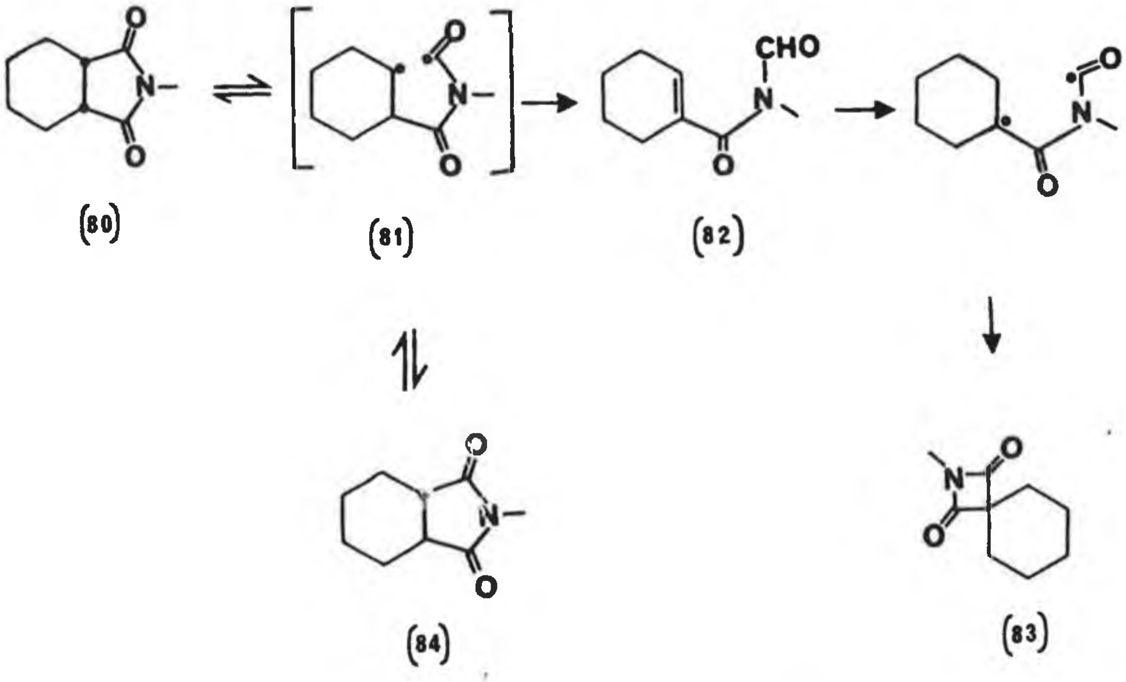


(76) (77) (78)

(79)

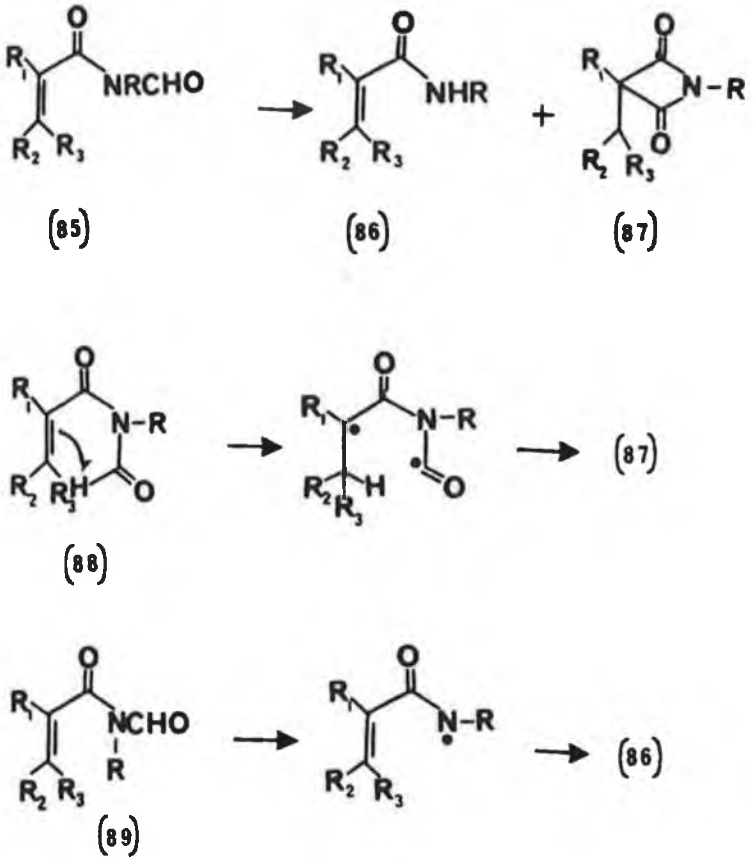
Scheme 2.8

On irradiation of the imide (80) the ene-formimide (82), the azetidinedione (83) and trans-isomer (84) were formed (scheme 2.9). The mechanism was formulated as involving initial α-cleavage to the biradical (81) followed by intramolecular hydrogen abstraction to the ene-formimide (82). The (82) to (83) conversion was demonstrated independently and is similar to conversions observed in ketone systems.[62] Kanaoka[60] has determined that the reactivity of the ene-formimide is very dependent on the substitution pattern. When R=H in (85) the major products are the unsaturated amides (86) from C(O)-N α-cleavage as observed in other aliphatic imides, whereas azetidinedione formation (87) dominates when R=CH_3 (scheme 2.10). The authors believe that the explanation for the difference can be found in the conformations of the ene-formimide. The intramolecular hydrogen transfer involves a six-membered transition state. This state is only formed when R is a bulky group i.e. (88). When R=H the conformer represented by (89) should be more stable. The azetidine-2,4-diones (90) are themselves



Scheme 2.9

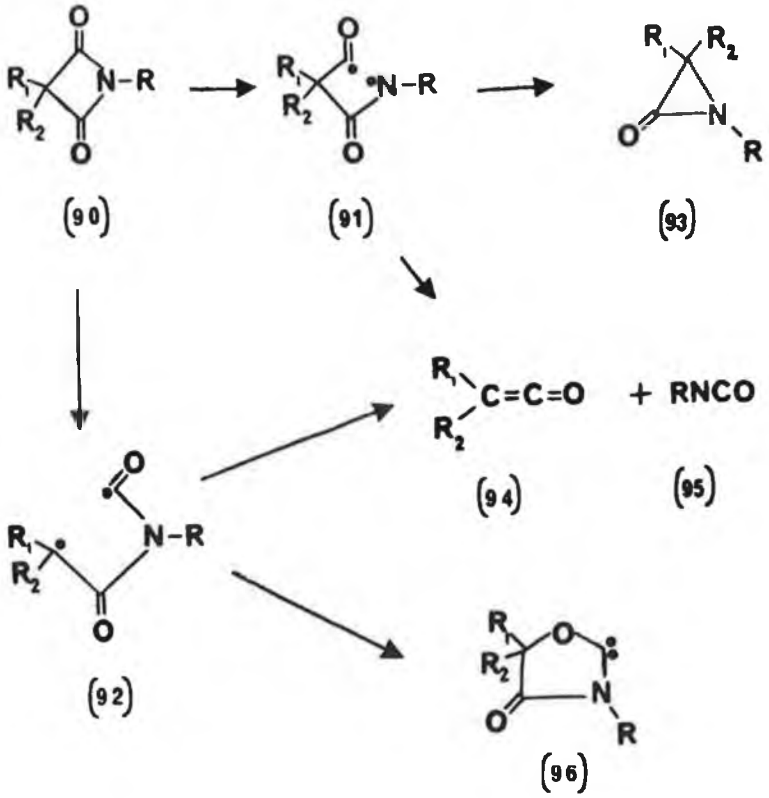
photochemically active, undergoing α-cleavage to biradicals (91) and (92). The biradical (91) can then cleave to the ketone - isocyanate (94) and (95) or undergo loss of CO to the aziridinone (93).



Scheme 2.10

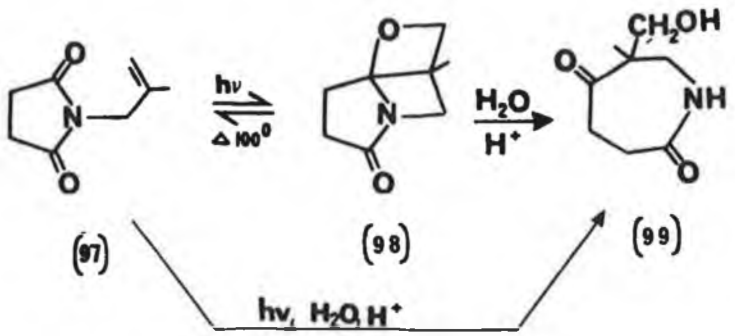
The biradical (92) can also cleave to the isocyanate (95) and ketene (94) as well as undergoing rearrangement to the carbene (96) which can be trapped by alcohol (scheme 2.11). The authors concluded that the route through (91) was favoured when $R=C_6H_5$ and the one through (92) favoured when R was alkyl or H.[62]

Irradiation of a series of aliphatic cyclic imides in the presence of alkenes afforded the corresponding oxetanes in good yield[63-66] whereas attempts to carry out this reaction with the open chain analogue have been fruitless.



Scheme 2.11

The reaction can occur intramolecularly to give tricyclic products such as (98) from (97) which can conveniently be converted to (99) with acid (scheme 2.12) Usually the oxetane cannot be isolated, presumably reverting to starting material; but irradiation in acidic alcoholic solvents gave products which could be rationalized as arising from oxetanes i.e (99) from (98).



Scheme 2.12

2.3 Phthalimides

In N-substituted phthalimides (100) the carbonyl groups as part of a strained five membered ring system are activated. The rigid geometrical arrangement of the polar groups allows for effective intramolecular interaction between the carbonyl and certain side chain groups whereby the symmetrical structure and the presence of two equally reactive carbonyl groups increases the probability of such interaction by a factor of two.

(100)

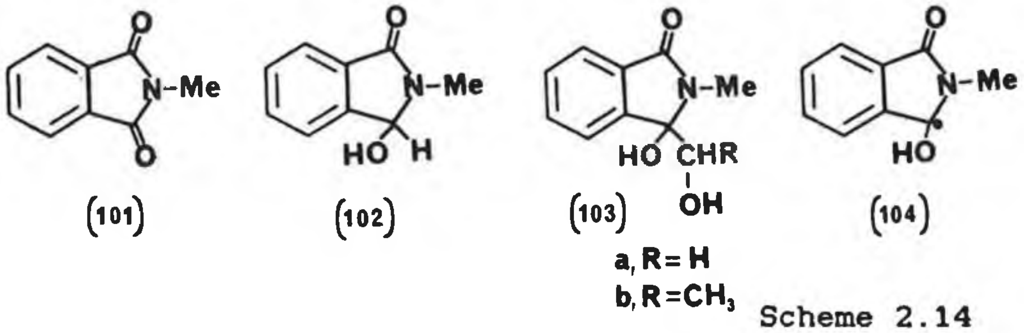
Scheme 2.13

Phthalimides undergo virtually all of the major photochemical reactions known for the aliphatic imides and several unique reactions as well. The photoreactivity of phthalimides is nearly always associated with the carbonyl site.

2.3.1 Photoreduction Reactions

Compounds containing a carbonyl chromophore, upon irradiation in solvents having readily abstractable hydrogen undergo photoreduction as one of the most common reactions.

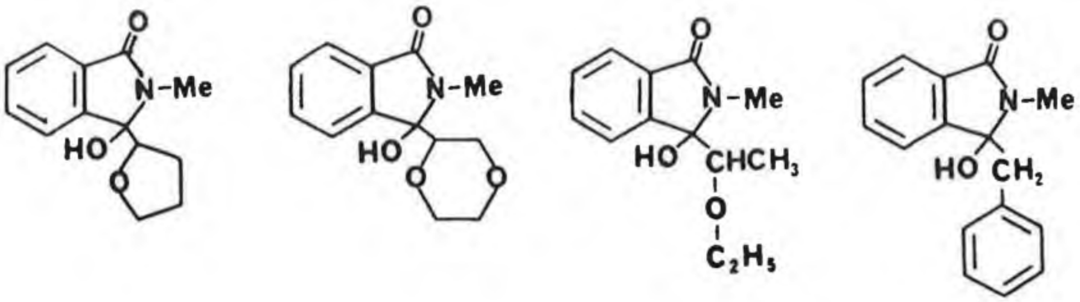
When N-methylphthalimide (NMP) (101) was irradiated in methanol or ethanol as solvent, the dihydroproduct (102) with one imide carbonyl group reduced was isolated in 30-40% yield accompanied by (103) (20-40%) resulting from the addition of the alcohol to the imide carbonyl.[67] The formation of the hydroxyalkyl derivatives instead of the corresponding ether derivatives suggests that a free-radical mechanism is operative in the addition process. This type of addition shows the resemblance between phthalimides and other carbonyl systems already discussed. The authors suggest the reaction proceeds via initial hydrogen abstraction to give the semi-pinacol radical (104). This is followed either by a second hydrogen abstraction to give (102) or coupling with the solvent - derived radical to give the photoaddition



Scheme 2.14

product (103). When tetrahydrofuran was employed as solvent the dihydroproduct (102) (11%) and the addition product (105) (20%) were isolated.[68] Irradiation in 1,4-dioxan, diethylether and toluene[69] afforded the expected addition products (106), (107), and (108) respectively.

Amines are known to be highly efficient photoreducing agents. Irradiation of N-methylphthalimide (NMP) in the amine (109) led to photoreduction to give



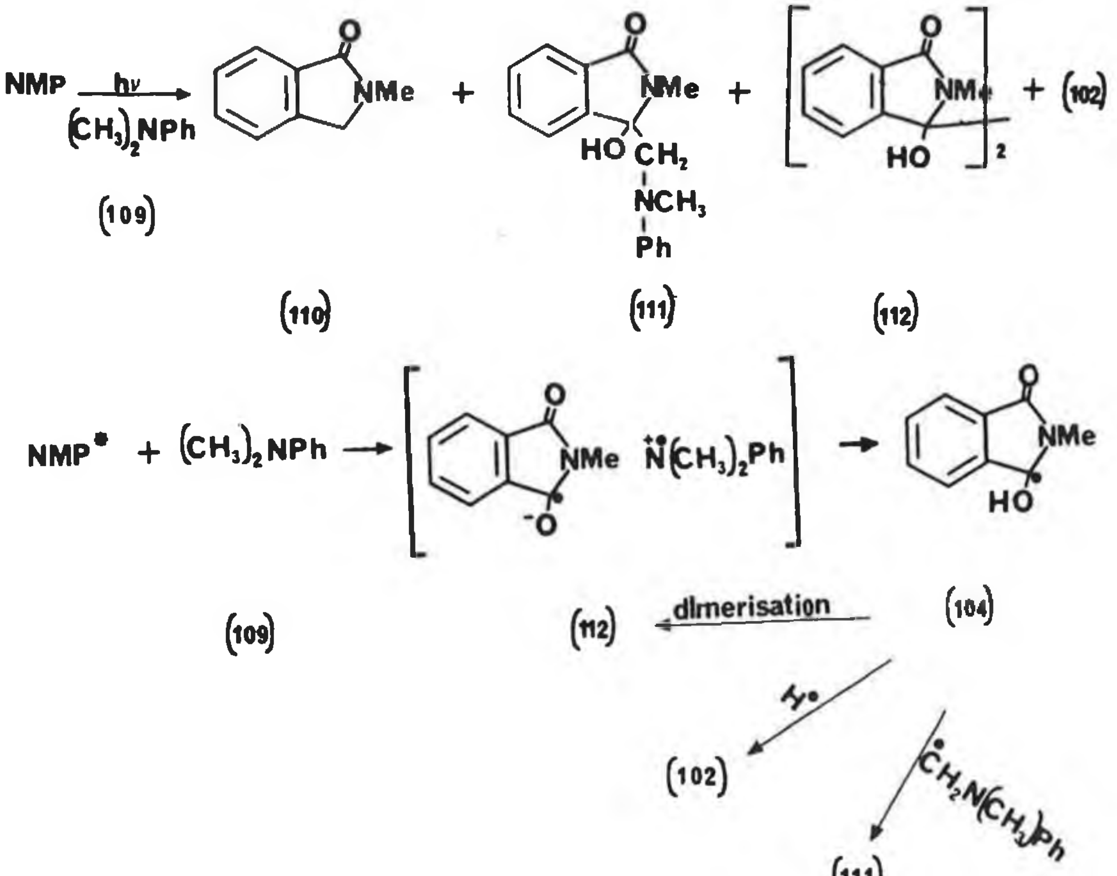
(105) (106) (107) (108)

Scheme 2.15

N-methylphthalimidine (110),[69] a highly reduced product which is not found in the reduction with alcohols. The amino carbinol (111) and pinacol (112) were also formed. Photoreduction of ketone triplet states by amines is known to proceed generally by way of electron transfer.[17] The authors suggest an analogous mechanism for the photoreaction of N-methylphthalimide with (109), that is initial electron transfer followed by proton transfer and radical coupling to give the observed products (scheme 2.16). The pinacol (112) is generally formed in amine mediated photo-reductions. In contrast no pinacol formation has been detected in the photoreduction of NMP by alcohols.

However, intramolecular pinacol formation was observed with N-methylenebisphthalimides (113 a-c) when irradiated in an alcohol solvent such as propan-2-ol.[70]

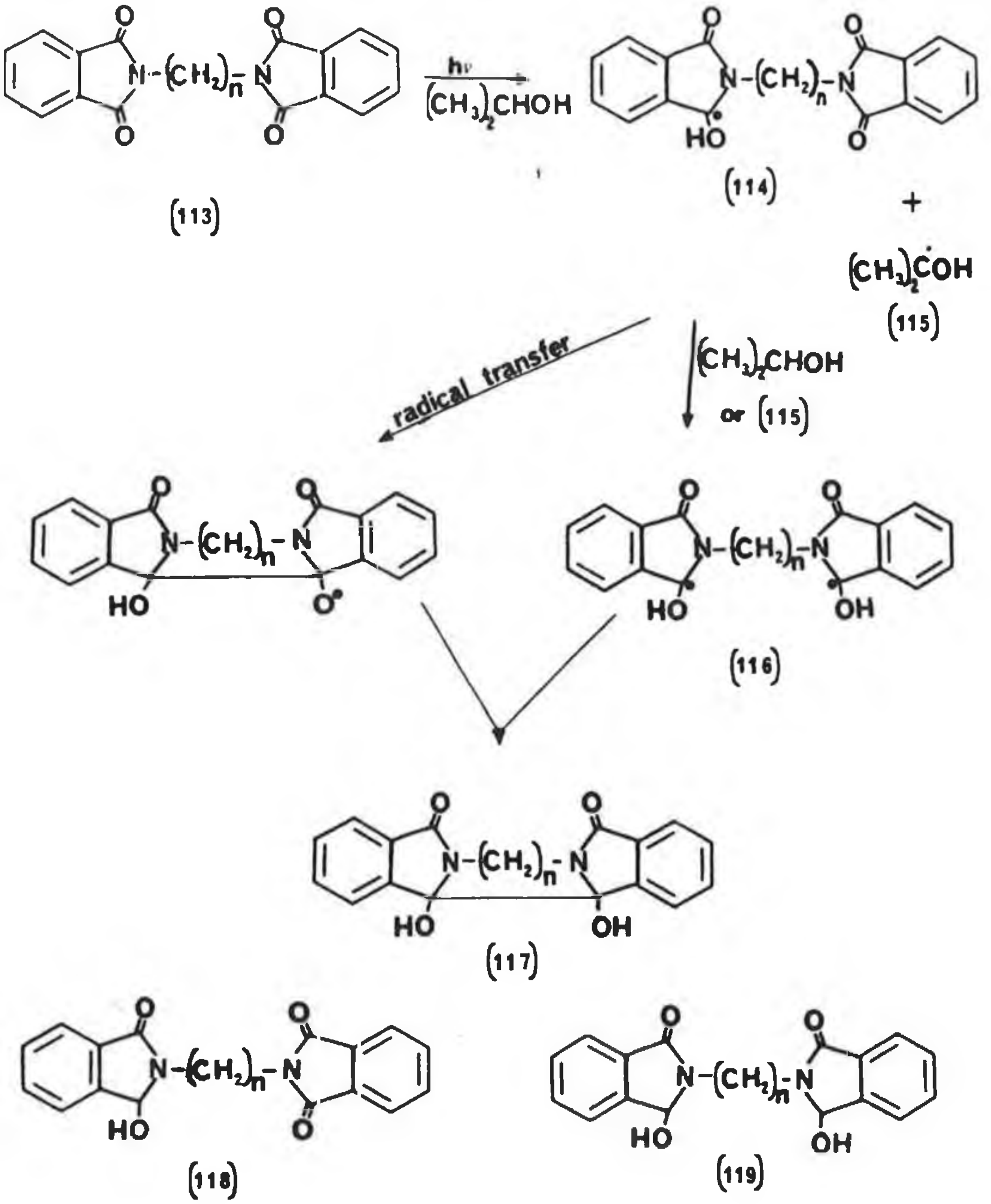
Compounds (113 d-e) in which the two phthalimide moieties were separated by four or more methylene groups did not afford the coupling product, giving only the reduced products (118) and (119). By analogy to the benzpinacol formation from benzophenone, formation of the cyclized products (117 a–c) can be rationalized on the basis of initial hydrogen abstraction by the imide carbonyl from propan-2-ol giving the radicals (114) and (115). These radicals are probably in a cage and radical transfer occurs to give the di-ketyl radical (116) which closes to the observed product (117) (scheme 2.17).



Scheme 2.16

Alternative mechanisms include:

(i) the formation of a doubly excited bismethylenephthalimide (i.e. two carbonyls on different moieties excited) which undergo hydrogen abstraction to give the diketyl biradical (116) which couples to yield a pinacol;



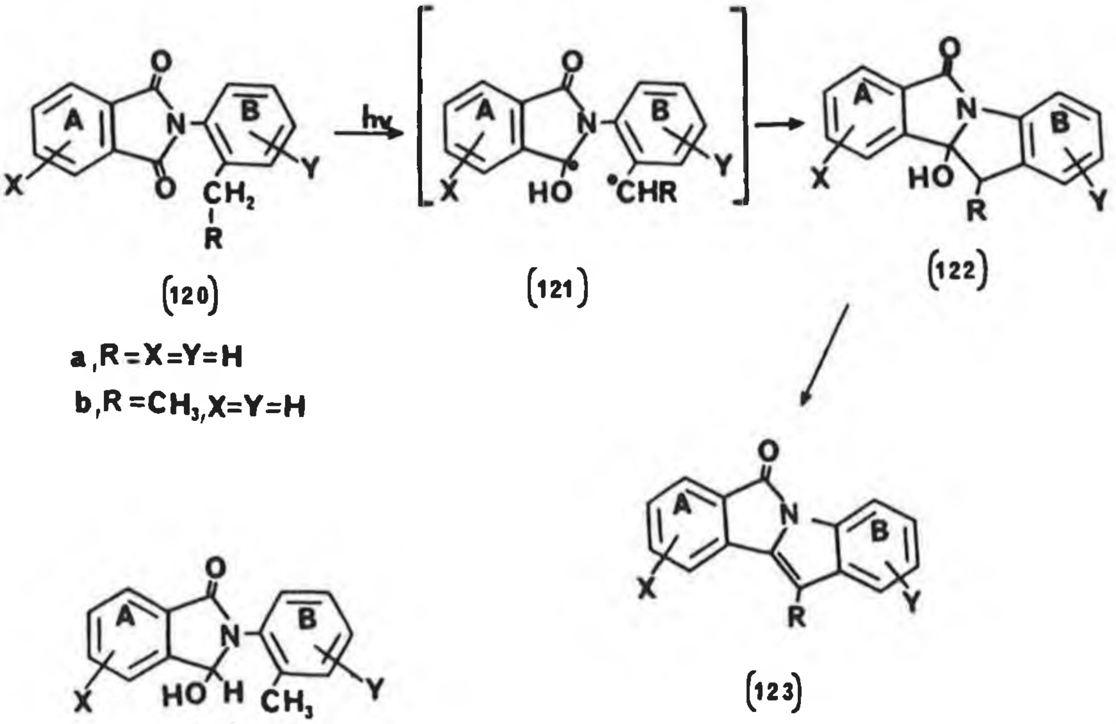
a:n=1 b:n=2 c:n=3 d:n=4 e:n=5 Scheme 2.17

(ii) excitation of the ketyl radical (114) which abstracts a hydrogen to give (116) and then couples to give a pinacol.

Both these alternative processes would be of low probability since they involve excitation of short lived species which are present in low concentration i.e. an excited state in (i) and a radical in (ii).

2.3.2 Photocyclization Reactions of Phthalimides

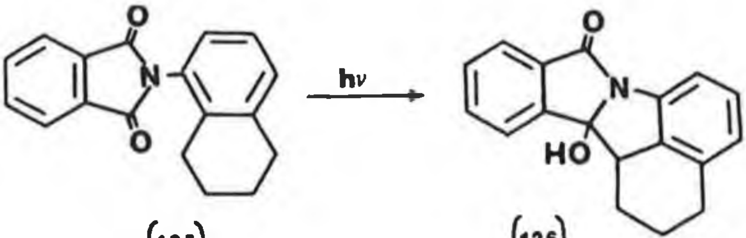
Participation of imides in photocyclization was first observed with the conversion of (120a) to (122a) and (123a) (scheme 2.18).[67] Irradiation of (120a) in ethanol, in addition to the reduced product (124:20%) gave (122a) and (123a). The homologue (120b) gave rise to the cyclized homologue (122b) and (123b). The cyclization of (120) is significantly quenched in the presence of isoprene, suggestive of an excited triplet intermediate. The reaction involves intramolecular hydrogen abstraction by the excited imide carbonyl to give a biradical intermediate (121) followed by coupling to yield (122). Product (123) is readily formed by dehydration of (122).



(124)

Scheme 2.18

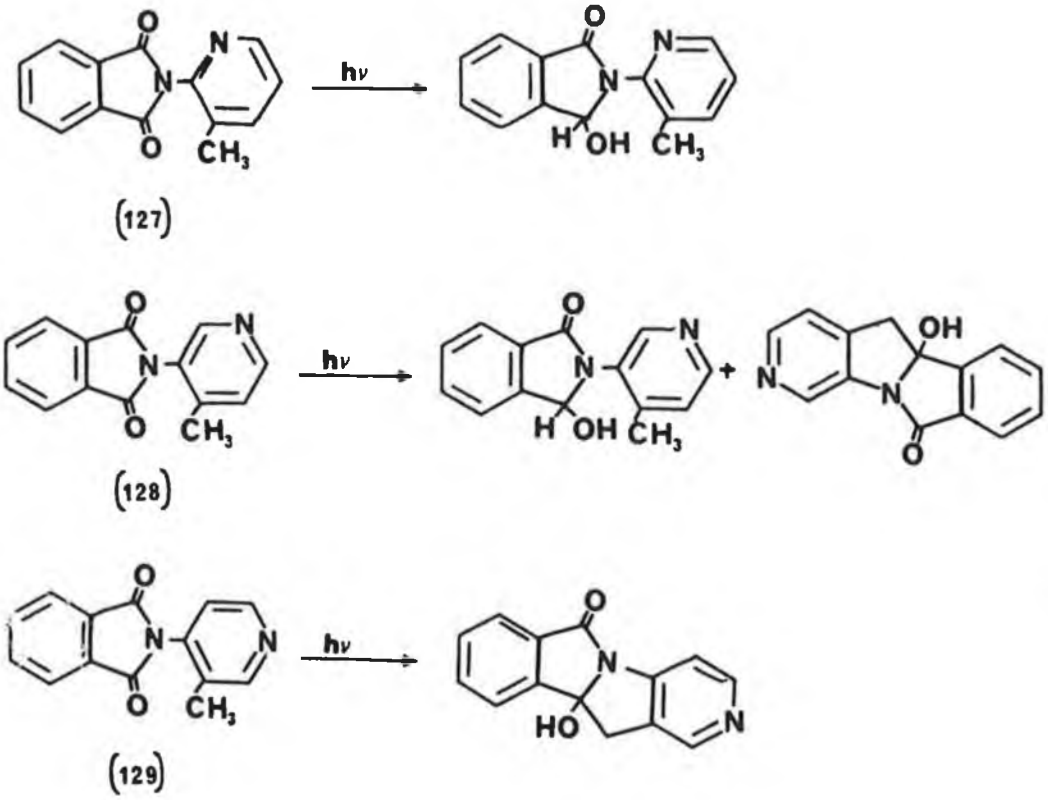
Photolysis of a series of N-o-tolylphthalimides (120) possessing various substituents on the A or B rings were examined in t-butyl alcohol or acetone.[71] Whereas photolysis of imides with an electron-withdrawing group such as nitrile and methoxycarbonyl on the A ring afforded the cyclized product (122) the presence of electron donating substituents such as methoxyl and dimethylamino inhibited this cyclization.[71] By contrast, imides possessing either an electron-withdrawing or -donating group on the B ring smoothly underwent cyclization to the isoindoloindole derivative (122). These results seem consistent with the postulated intermediacy of a biradical (121). While substituent Y influences the stability of the benzyl radical, substituent X must exhibit a direct effect on the reactivity of the excited carbonyl. The lack of reactivity associated with donor substitution on the A ring results from an inversion of (n,π^*) and (π,π^*) states. Triplet (π,π^*) states are generally less reactive than their (n,π^*) counterparts in hydrogen abstraction reactions in ketones.[56] As an example of a variation of the substrate structure, replacement of an alkyl group of (120) by an acyclic methylene moiety led to a new pentacylic ring system (126) (scheme 2.19) on irradiation of (125).[72]



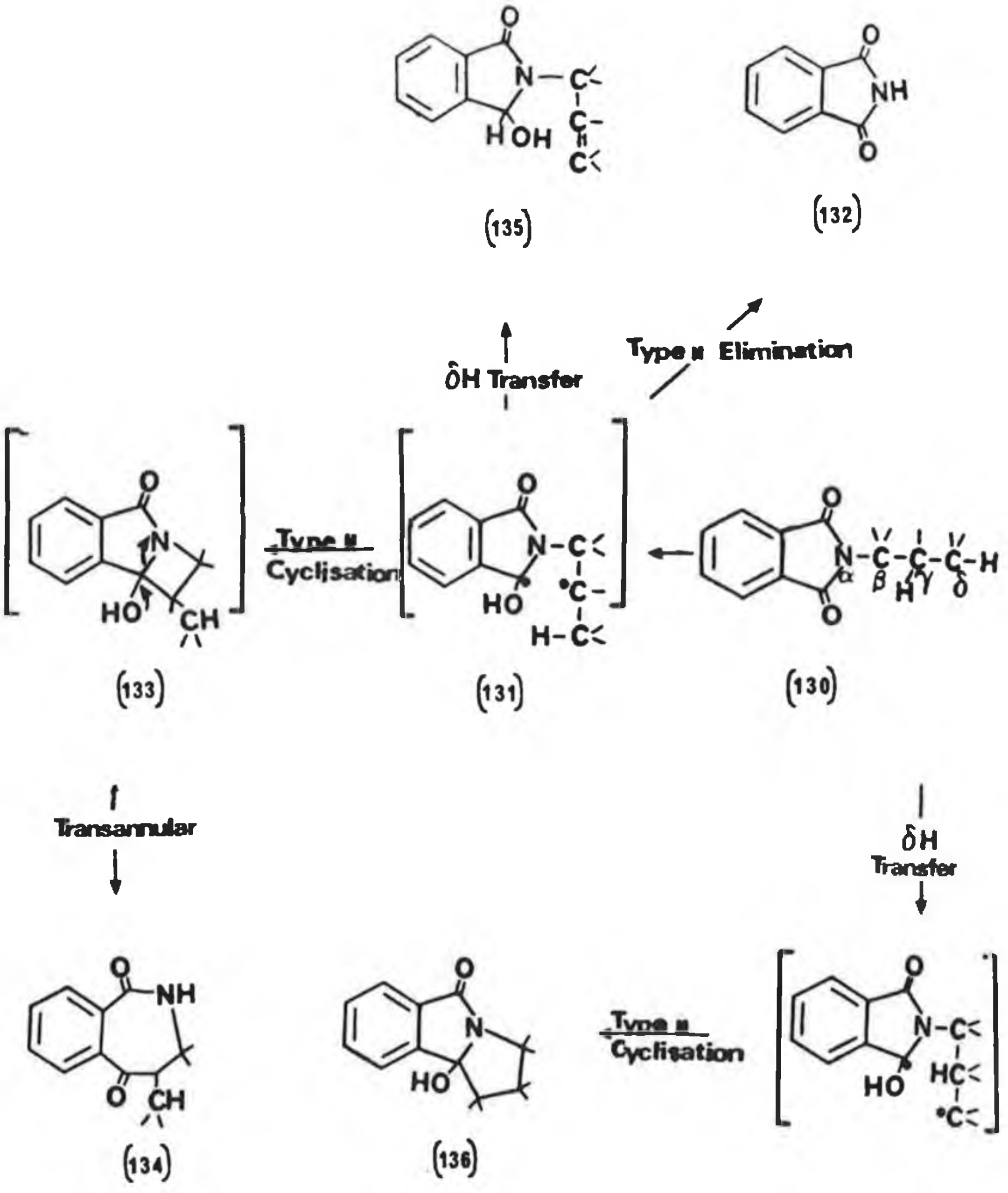
(125) (126) Scheme 2.19

Photoreactions of phthalimides in which the B ring is a heteroaromatic ring system were also studied. Below in scheme 2.20 can be seen some of the products derived from the photolysis of three methyl substituted N-pyridylphthalimides (127), (128) and (129).[73] The reason for the reluctance of (127) to cyclize is unknown. Perhaps interaction between the lone pair of the pyridyl nitrogen and the imide carbonyl group would disturb the planarity of the molecule which is necessary for smooth cyclization to occur.

The photochemical behaviour of a series of N-alkylphthalimides (130) which have γ- and δ-hydrogens were examined in several solvents.[74] As shown in scheme 2.21 the results were best rationalized by strictly formal analogy with the Norrish type II processes established in ketonic systems. The substrate (130) in which the nitrogen atom is regarded as the α-atom in relation to the imide carbonyl, undergoes initial



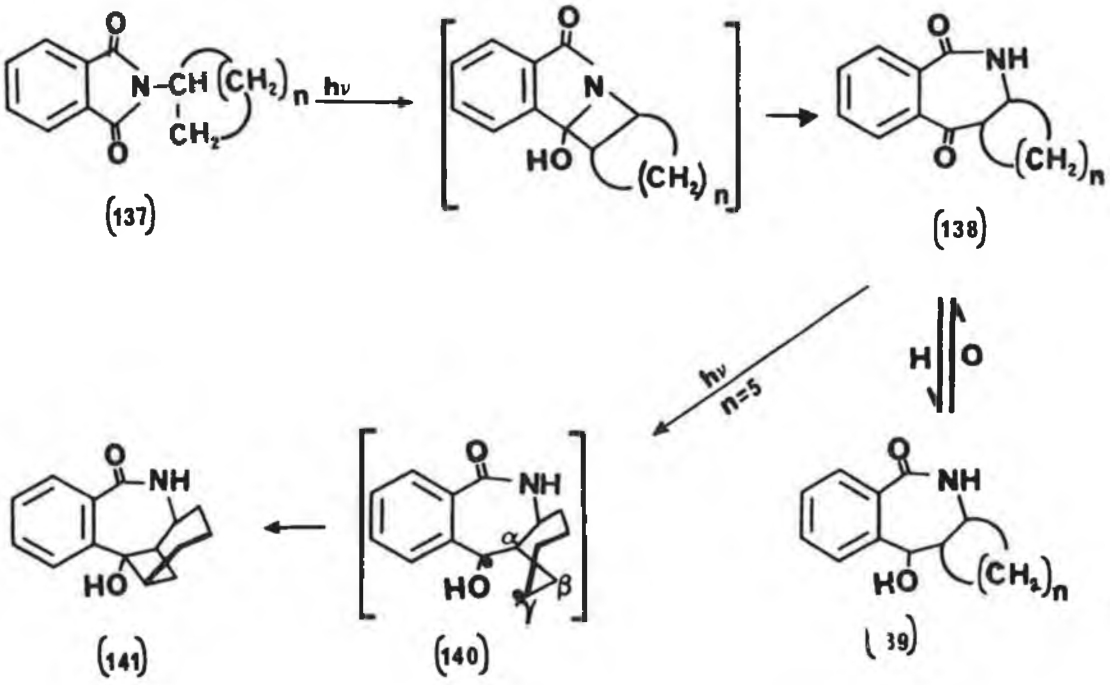
Scheme 2.20



Scheme 2.21

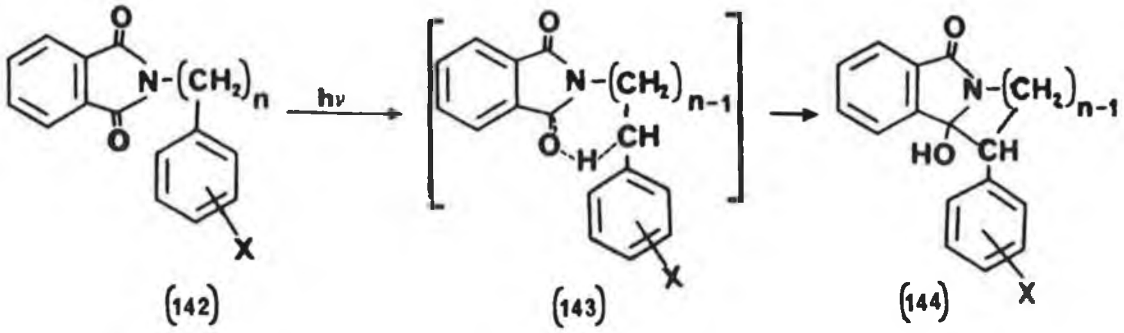
γ-hydrogen abstraction to form a biradical (131) followed either by type II elimination to give phthalimide (132) and an alkene or by type II cyclization to an azacyclobutanol (133). This azacyclobutanol, presumably due to ring strain, undergoes a transannular ring opening leading to a benzazepinone lactam (134). Alternatively, in some of the biradicals with δ-hydrogens, a competing δ-hydrogen transfer takes place with concomitant formation of an unsaturated product (135). With a substrate (130) having a δ-hydrogen a minor process can occur involving type II cyclization resulting in the product (136).

One interesting feature of type II cyclizations is the behaviour of N-alicylic phthalimides.[75] Photolysis of N-cyclopentyl- and N-cyclohexyl-phthalimides (137:n=3,4) in ethanol mainly gave azepinones (138), the normal cyclization products, accompanied by their reduced products (139). However cycloheptyl compound (137:n=5) afforded a novel bridged cyclobutane system (141). The formation of (141) is perfectly consistent with the general pattern (scheme 2.21) as amplified in scheme 2.22; at the benzazepinone stage (138:n=5), it is again the γ-hydrogen which is abstracted, and the cyclobutanol (141) is formed via biradical (140).



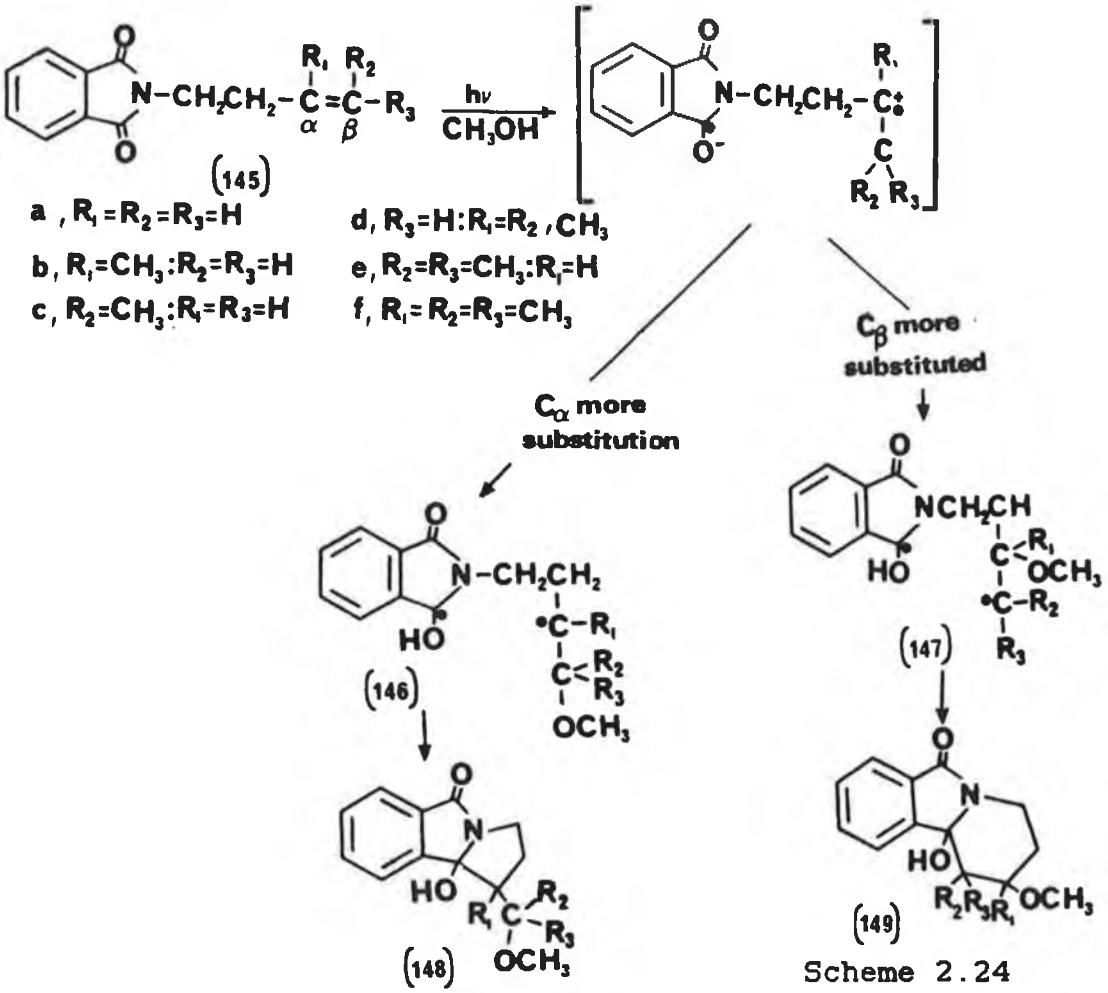
Scheme 2.22

Attempts to subject N-(aralkyl)phthalimides (142) to cyclization uncovered some interesting new aspects of the photochemistry of bichromic systems.[76] In the photolysis of (142:n=3-6) in acetonitrile, the yield of (144) was maximised at n=4, i.e. when the usually unfavourable eight-membered transition state (143:n=4) could be formed (scheme 2.23). Apparently the 7- and 6- membered analogues of (143) formed with relatively less ease. In addition, electron donating substituents X, such as methyl and methoxyl, distinctly promoted the reaction. Since the phthalimide moiety is a good electron acceptor and therefore, capable of forming charge transfer complexes with electron donors, it is possible that cyclization is a result of enhanced hydrogen abstraction from the methylene which is held in close proximity to the excited imide carbonyl through intramolecular complex formation. The involvement of such a charge transfer complex was consistent with a weak charge transfer absorption band in the ultraviolet absorption spectrum of an ethanol solution of (142),(n=4 ; X=p-CH_3O).[78]



Scheme 2.23

Phthalimides (145) with olefin chains also undergo photocyclisation by a mechanism involving electron transfer. For example irradiatiion of N-3-alkenylphthalimides (145; a-f) in methanol resulted in the formation of the pyrroloisoindolones (148)[79] and pyridoisoindolones (149). With (145a), (145b) and (145d) only (148) was formed, whereas for (145c) and (145f) a mixture of the two was obtained (scheme 2.24).

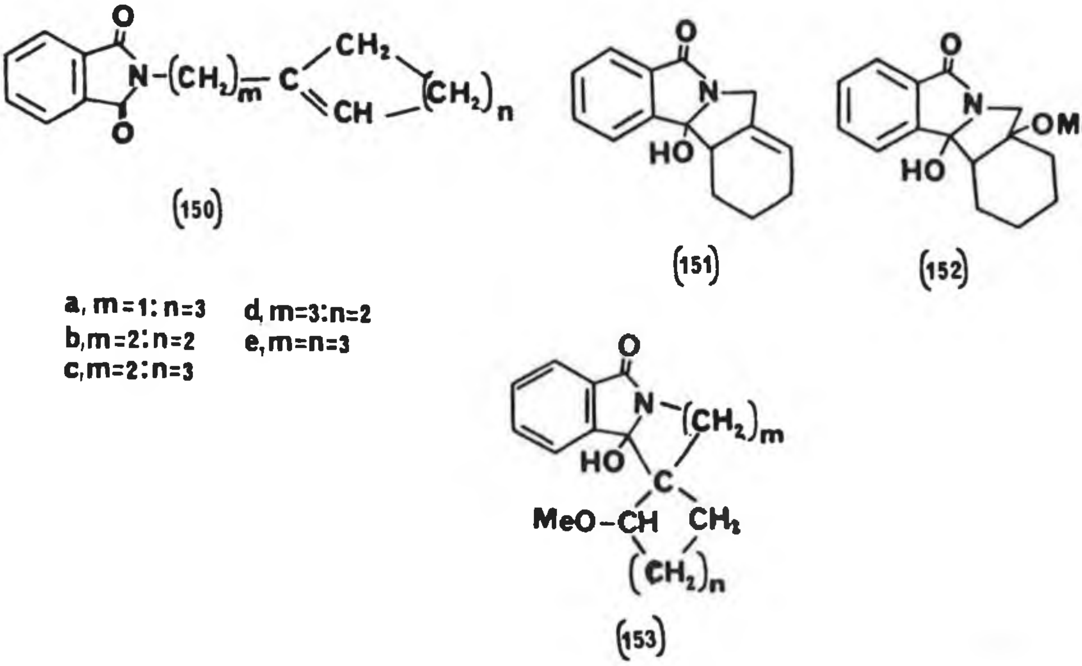


Scheme 2.24

The authors suggest that the pathway consists of electron transfer from the double bond in the side chain to the imide followed by anti-Markownikoff addition of methanol, forming the more stabilized biradical intermediate among the two possible ones. With the substrate in which the α-carbon is more substituted the biradical (146) is formed and this gives rise to the products (148a,b,d) while with that having the β-carbon more substituted the biradical is (147) leading to (149e) (see scheme 2.24). When the α

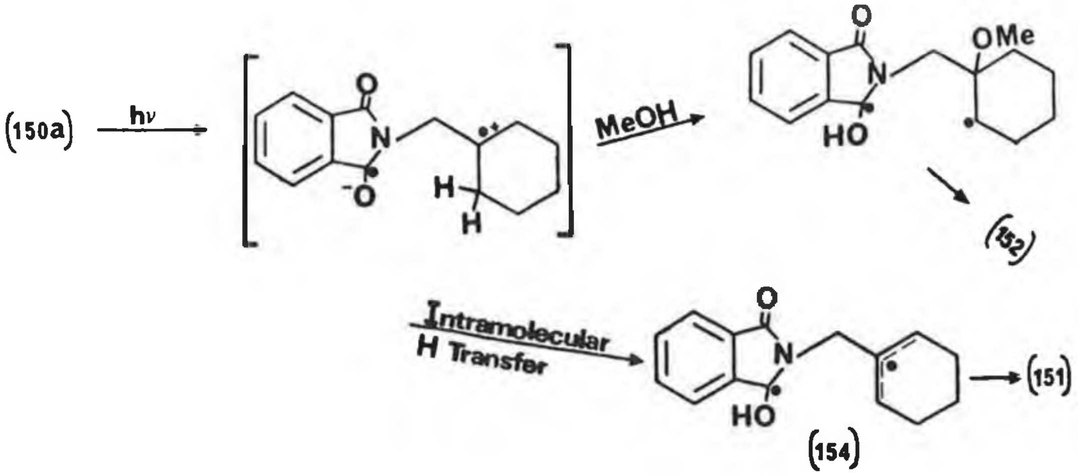
and β-carbon atoms are equally substituted as in (145c) and (145f) both products (148) and (149) are formed.

Kanaoka and co-workers also studied the photochemistry of N-cycloalkenylphthalimides (150) in methanol.[80,81] Photolysis of (150b-e) proceeded to give the cyclized spiro compounds (153b-e) respectively. The mechanism, as for the straight chain N-alkenylphthalimides (145), involved electron transfer followed by addition of methanol forming the more stable biradical. Irradiation of (150a) in methanol afforded two products whose structures were assigned as (151) and (152) (scheme 2.25).



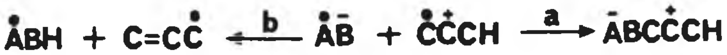
Scheme 2.25

Presumably with the substrate (150a), in which an allylic hydrogen is relatively close to the imide carbonyl, a competing intramolecular proton transfer becomes possible, leading to the biradical (154) which closed to (151) (scheme 2.26).



Scheme 2.26

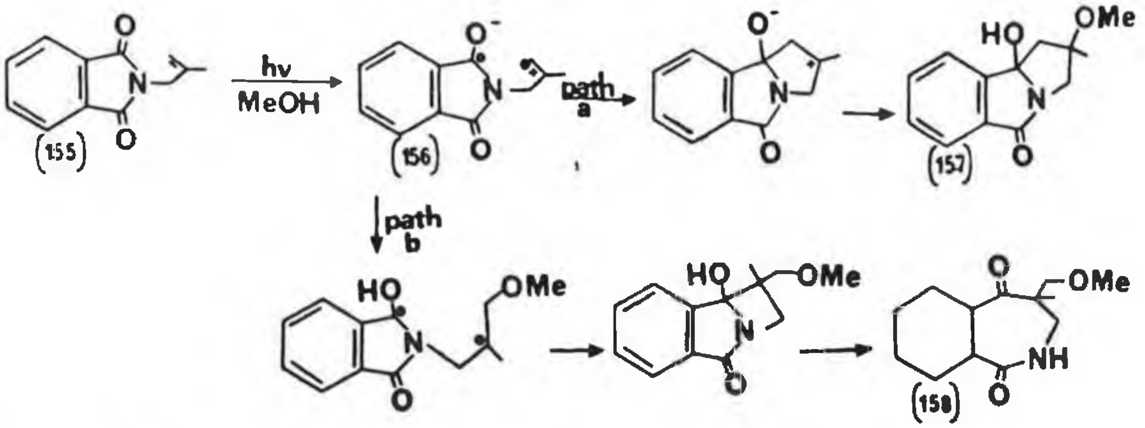
Mazzocchi and co-workers[82] showed that radical-radical coupling of radical anion-radical cation pairs (scheme 2.27) can occur prior to proton transfer [scheme 2.27 path (a)]. Irradiation of N-(2-methyl prop-2-enyl) phthalimide (155) in methanol yielded the expected anti-Markownikoff product (158) as well as (157) (scheme 2.28). The formation of (157) can only be rationalized by radical-radical coupling of (156) prior to the addition of methanol.



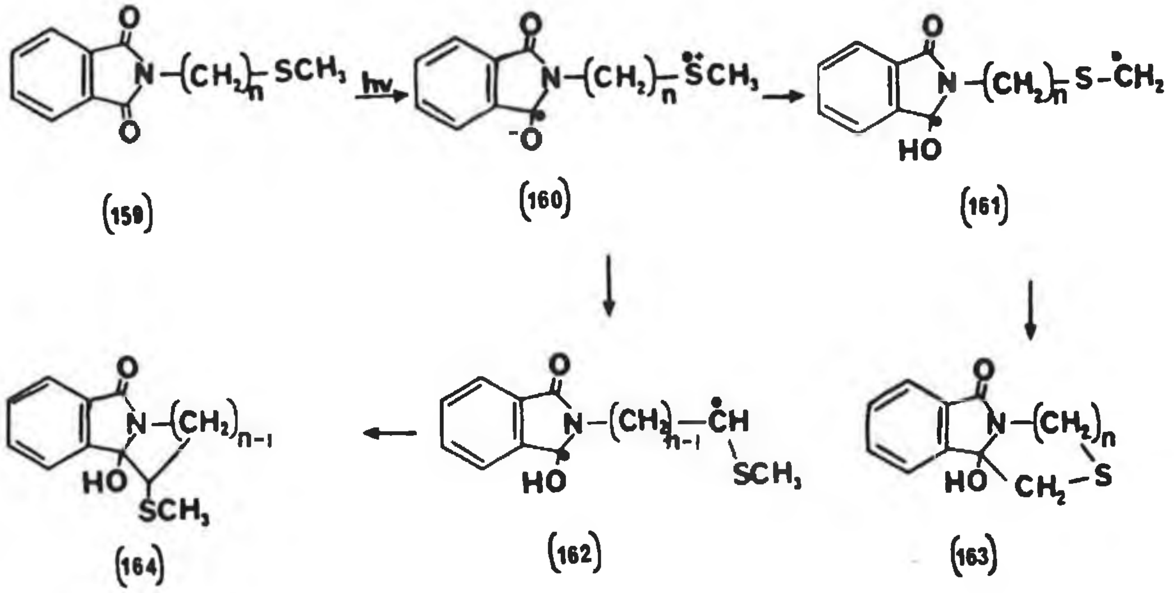
$$\overset{\bullet}{A}BH + C{=}C\overset{\bullet}{C} \xleftarrow{b} \overset{\bullet}{A}\overset{-}{B} + \overset{\bullet}{C}\overset{+}{C}CH \xrightarrow{a} \overset{-}{A}BC\overset{+}{\dot{C}}CH$$

Scheme 2.27

Photocyclization reactions also occur for phthalimides containing heteroatoms in their N-alkyl side chain. For example Kanaoka and co-workers found that N-substituted phthalimides (159) possessing a terminal sulfide function in their side chain underwent unusually facile photocyclization to give azathiacyclols (163) as the major product and (164) as the minor product.[83] The reaction is remarkably efficient giving rings of up to 16 members when n=12, as a result of C-C bond formation between the imide



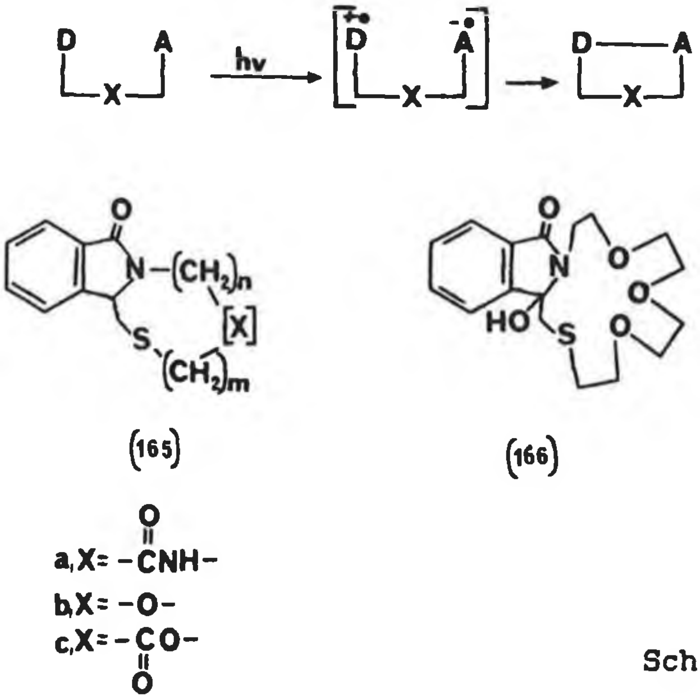
Scheme 2.28



Scheme 2.29

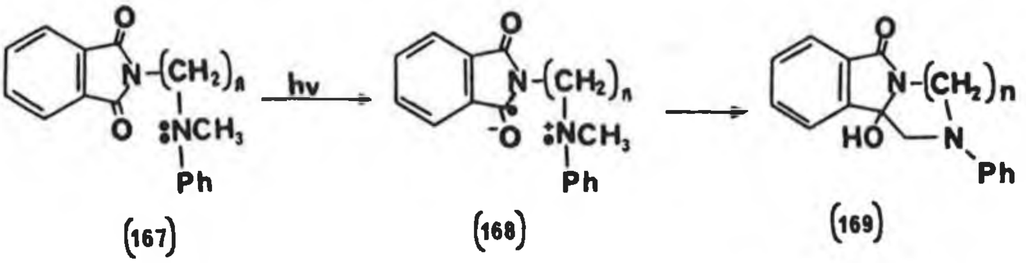
carbonyl and the terminal methylthio group.[84] In a flexible system such as (159), the medium and large rings are formed with unusual facility and regioselectivity. In view of the fact that relative efficiencies of cyclization do not vary much in going to large rings, there seems no critical limitation to the size of macrocycle to be constructed. The mechanism for the reaction can be explained in terms of formation of an electron transfer intermediate (160) which[77] affords the biradicals (161) and (162) following proton transfer. Closure of the biradicals leads to (163) and (164). The fact that the quantum yield for the formation of the 10-membered ring is of the order of 0.07,[50] significantly larger than those reported for the alkyl phthalimides which proceed through a six-membered transition state, points to the existence of some kind of intramolecular charge transfer complex in the ground or excited state which holds the sulphur in proximity to the reactive carbonyl group.

This type of reaction was extended to the general synthesis of macrocycles such as (165) on the basis of remote regioselective photocyclization of a 'pair system' (see scheme 2.30) which consists of, in this case, a phthalimide group as the acceptor and the methylthio group as the donor. With this particular pair of functional groups, macrocycles containing amides (165a),[84-86] ethers (165b),[87] and esters (165c)[85,88] have been synthesised.



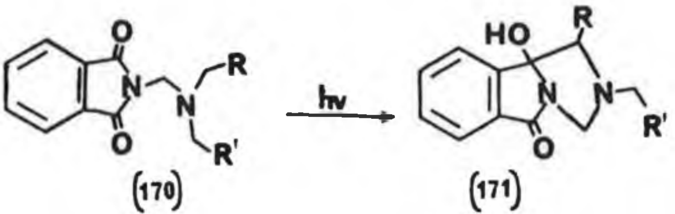
Scheme 2.30

Macrocycles can be obtained with more than one of the functional groups (X) present e.g. the polyether analogue (166).[89] These remote photocyclizations can also take place with nitrogen in the side chain. The Kanaoka group reported the cyclization of a series of compounds (167) with nitrogen in the alkyl substituent with n varying from 1-12 resulting in the formation of new ring systems containing between 5 and 16 members.[90] The reaction proceeds through the intermediacy of the intramolecular electron transfer generated radical anion-radical cation (168) which undergoes proton transfer to yield a biradical which subsequently closes to (169) (scheme 2.31).



Scheme 2.31

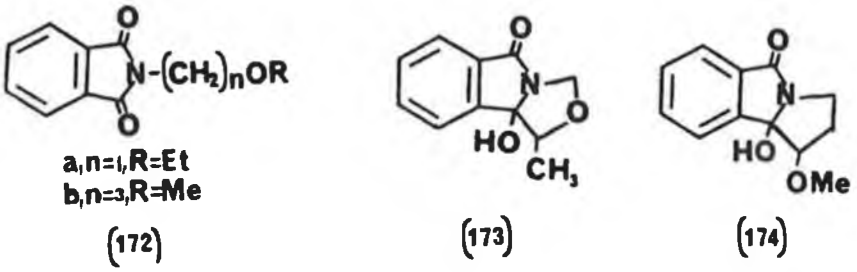
Coyle and co-workers[91-93] have shown that Mannich bases (170) also undergo cyclization by a similar mechanism to yield (171) (scheme 2.32).



Scheme 2.32

Photocyclizations of the phthalimide derivatives (172) with oxygen in the side chain have also been reported.[94]

Irradiation of (172a) and (172b) gave the products of δ-hydrogen abstraction (173) and (174) respectively. The mechanism for this reaction does not involve electron transfer as entropy factors do not favour a charge transfer complex between the carbonyl and alkoxy group. Instead the authors suggest that the driving force for δ-hydrogen abstraction through a seven membered transition state may be due to favourable geometry effects.

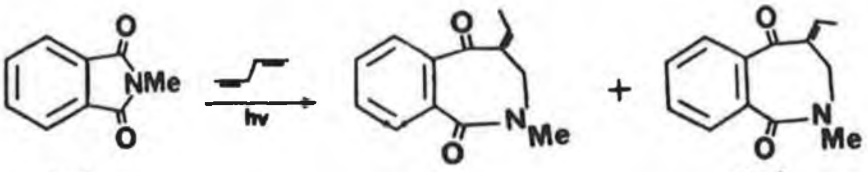


Scheme 2.33

2.3.3 Reaction of Phthalimides with Alkenes

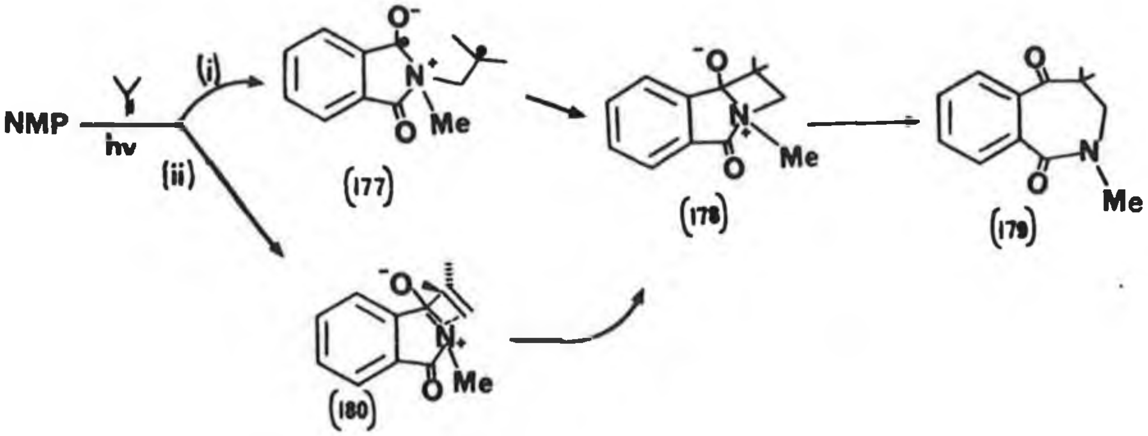
In the course of studying the quenching of type II processes in N-alkylphthalimides, Mazzocchi and co-workers observed that the dienes used as triplet quenchers were reacting with the phthalimides.[95] Further investigation led to the observation that an unprecedented addition of the diene to the C(O)-N bond was occurring to afford benzazepinediones. The reaction is efficient, with the conversion of N-methylphthalimide (101) to the benzazepinediones (175) and (176) (scheme 2.34) occurring in 93% yield. The reaction is general in that it takes place with dienes,[95] alkenes,[63,64,96] vinyl ethers,[97] and vinyl esters.

The reaction has also been found to be regioselective with respect to the direction of addition of the alkene component, the more substituted carbon of the original alkene appearing adjacent to the carbonyl in the final product.


(101) (175) (176)

Scheme 2.34

Two mechanisms have been considered to account for benzazepinedione formation.[98] The first involves addition of the alkene [scheme 2.35 (i)] to give a zwitterionic biradical (177) which could then close to give a dipolar bicyclic intermediate (178) and which subsequently reopens to give the observed benzazepinedione (179). The second mechanism considered is a concerted addition of the alkene to the C(O)-N bond (which has substantial double bond character), possibly via an oriented exciplex (180), to give the dipolar intermediate (178) directly [scheme 2.35 (ii)].



(177) (178) (179) (180)

Scheme 2.35

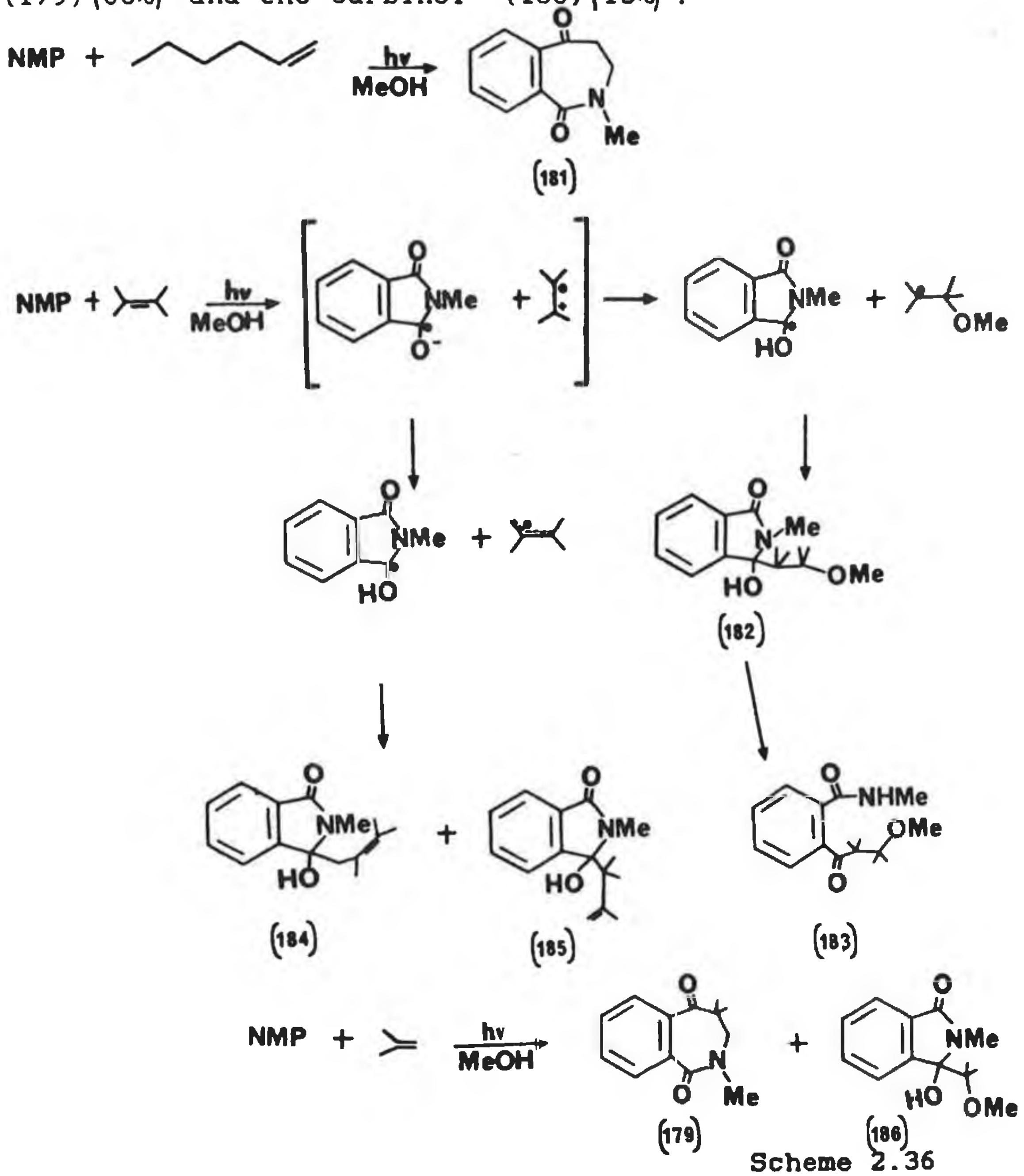
If the reaction were taking place via the biradical mechanism then addition of the alkene would only be stereospecific provided ring closure of the biradical was faster than bond rotation (with subsequent loss of stereochemistry). For example, if the lifetime of the biradical is long with respect to molecular rotation (about C-C bond from the alkene) then addition of cis-but-2-ene to NMP would give both the cis and trans-benzazepinediones. However if the reaction were taking place by the concerted mechanism addition of cis-but-2-ene would give only the cis-benzazepinedione product.

Experiments at low conversion and with excess alkene (to ensure little cis-trans isomerization of the alkene) suggest that addition of cis-but-2-ene gives only the trans-benzazepinedione i.e. that the reaction is stereospecific as well as regiospecific.[98] The concerted mechanism is therefore the preferred one, although a biradical mechanism in which ring closure is faster than bond rotation cannot be ruled out.

Mazzocchi and co-workers[99,100] observed that those alkenes with low ionization potentials did not undergo benzazepinedione formation and suggested that electron transfer might be a competing process. This suggestion was substantiated[99] by examination of the free energy values (ΔG) for electron transfer between a variety of alkenes and N-methylphthalimide, calculated using the Weller equation. Benzazepinedione formation was only observed in those cases where ΔG was positive, photoreduction products from an electron transfer mechanism being obtained from those alkenes for which ΔG was negative.

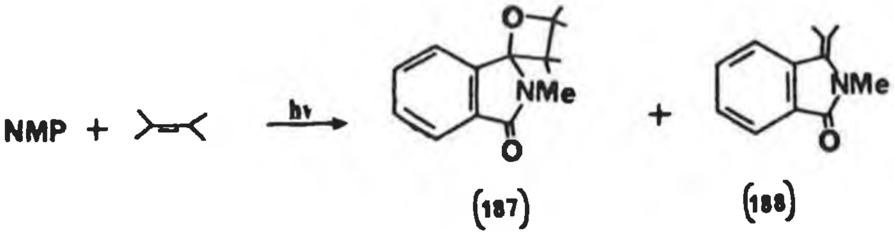
Evidence for this competing electron transfer process was obtained by studying the photochemistry of N-methylphthalimide and alkenes in methanol as solvent.[101] Maruyama[102] had shown that the intramolecular radical anion-radical cation pair of N-alkenylphthalimides are very effectively trapped by alcohol solvents. Thus it was expected that those alkenes which underwent efficient electron transfer to NMP (ΔG negative) should afford only solvent-trapped products. On the other hand, those alkenes whose interaction with NMP resulted in positive ΔG values should only afford benzazepinediones. The results obtained agreed with these observations.[101]

Irradiation of a solution of NMP and hex-1-ene in methanol gave only the benzazepinedione (181) as predicted from the large calculated positive ΔG value (11.2 kcal mol^{-1}). Under similar conditions 2,3-dimethylbut-2-ene afforded (183), which must arise from opening of the carbinolamide (182), along with photoreduction products (184) and (185). No benzazepinediones were observed in accordance with the large negative value of ΔG (-12.7 kcal mol^{-1}). In cases where small positive ΔG values are predicted for the alkene-NMP pairs, both benzazepinediones and photoreduced products were observed. For example irradiation of NMP with 2-methylpropene in methanol yielded the benzazepinedione (179) (60%) and the carbinol (186) (15%).[101]



Scheme 2.36

Irradiation of phthalimides in the presence of alkenes has also been reported to yield oxetanes.[96,103-105] For example irradiation of acetonitrile solutions of 2,3-dimethylbut-2-ene and N-methylphthalimide resulted in the formation of a number of products, including the oxetane (187) and its decomposition product (188).[103,106] Quenching (fluorene) and sensitization (indan-1-one) studies on the 2,3-dimethylbut-2-ene reaction established that the reaction occurs through the triplet excited state of NMP. The authors[107] suggest that intersystem crossing must compete with electron transfer. Thus at high alkene concentrations electron transfer quenching dominates intersystem crossing and no triplet products were observed.



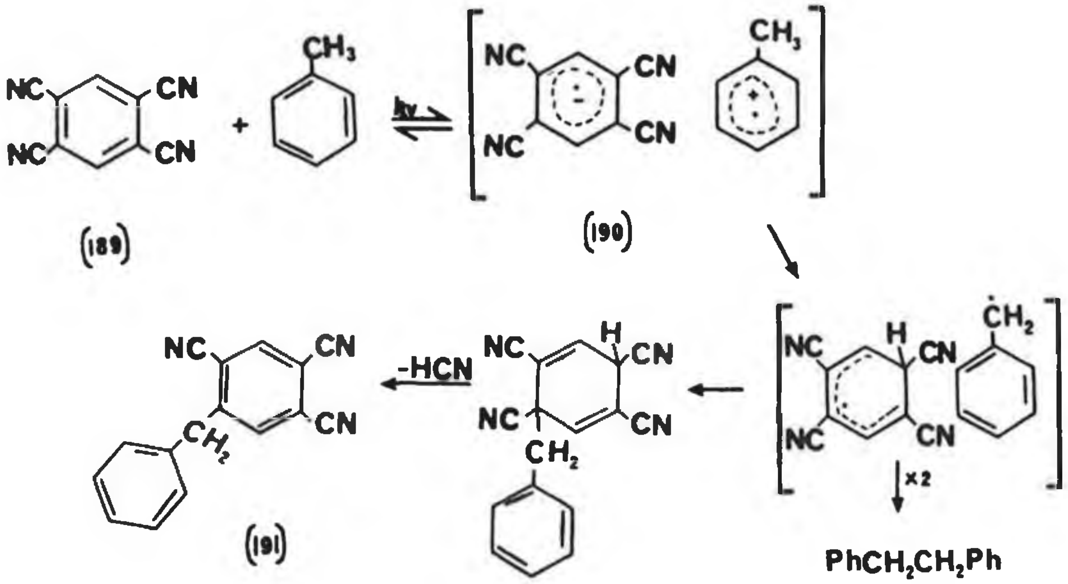
Scheme 2.37

CHAPTER 3

An area of growing interest in organic photochemistry involves the use of light to induce an electron transfer from a donor (D) to an acceptor (A) molecule (photochemical electron transfer) and subsequent product formation from the resulting radical ions.

$$A + D \xrightarrow{hv} A^{\bullet -} + D^{\bullet +} \longrightarrow \text{Products}$$

One such reaction involves the transfer of an electron to the electron deficient tetracyanobenzene (189) on irradiation in the presence of a potential electron donating compound such as toluene (scheme 3.1).[108]

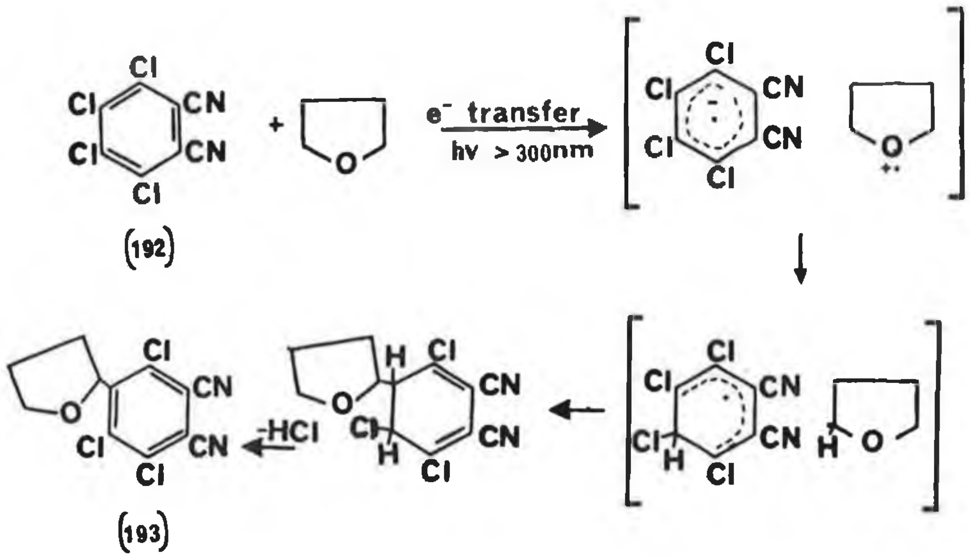


Scheme 3.1

The reaction is believed to take place via electron transfer from toluene to the tetracyanobenzene (189), to give a radical cation-radical anion pair (190). This is followed by proton transfer, radical coupling and elimination of hydrogen cyanide to give the observed product (191). Similar electron transfer reactions were

observed[109-113] with other electron-deficient aromatic compounds such as 3,4,5,6-tetrachlorophthalonitrile (TCPN) (192). This compound as well as being an electron acceptor, also contains chlorine as an effective leaving group. It might therefore be expected that, following initial electron transfer from a donor molecule, a chlorine can be replaced by the donor moiety.
In fact TCPN undergoes a variety of substitution reactions when irradiated in the presence of ethers (diethylether,[109] tetrahydrofuran,[109] methoxybenzene,[110] dimethoxybenzene[110]), aromatic hydrocarbons (anthracene, phenanthrene,[111] naphthalene)[112] and amines (diethylamine)[113] to give products in which a chlorine has been replaced by the donor moiety. In all these cases a mechanism involving initial electron transfer from the donor molecule to the TCPN has been suggested to account for the observed reaction. For example, it has been proposed that the photochemical reaction of tetrahydrofuran (THF) with TCPN proceeds via initial electron transfer from tetrahydrofuran to TCPN[109] to give a radical cation-radical anion pair (scheme 3.2). This is followed by proton transfer from the radical cation to the radical anion, radical coupling and then elimination of hydrogen chloride to give the observed product (193).

The photochemical behaviour of N-methyl-3,4,5,6-tetrachlorophthalimide (194) in tetrahydrofuran was studied by Khan[114] to determine whether an imide could replace the cyano moieties as electron



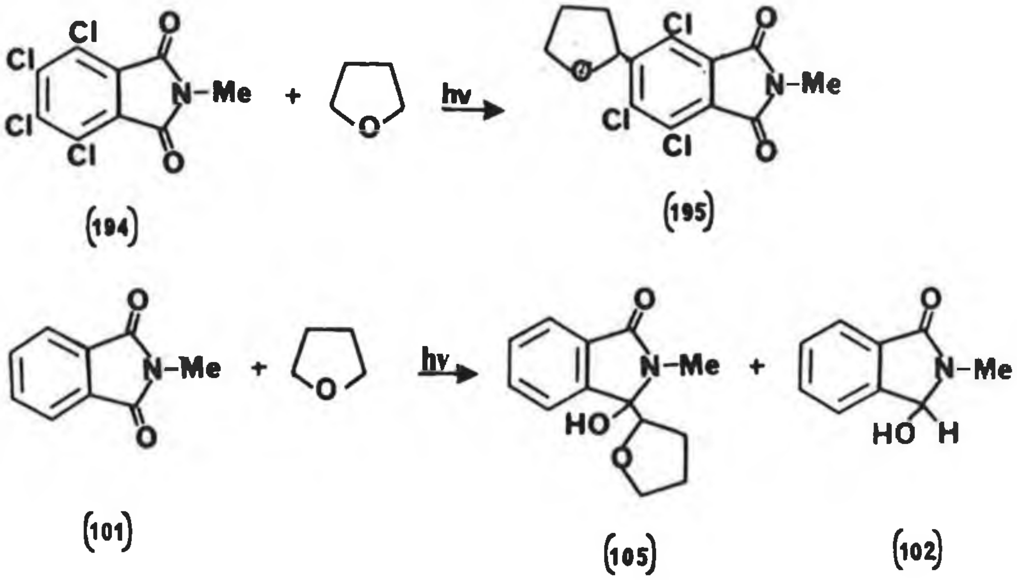
Scheme 3.2

withdrawing groups and whether N-methyl-3,4,5,6-tetrachlorophthalimide would yield products derived from chlorine substitution, or behave as a phthalimide to give photoaddition at the carbonyl group.

Irradiation of N-methyl-3,4,5,6,-tetrachlorophthalimide (194) in tetrahydrofuran gave a product (195) in which a chlorine atom had been replaced by the ether moiety[114] (scheme 3.3). A mechanism involving initial electron transfer from the donor molecule to the electron deficient aryl halide, followed by radical coupling and elimination of hydrogen chloride has again been proposed to account for the observed reactivity.

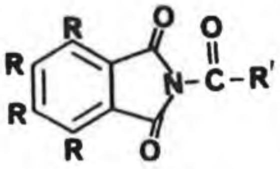
The photochemistry of the N-methyltetrachlorophthalimide (194) is in direct contrast to that of the corresponding non-chlorinated phthalimide (101). Irradiation of N-methylphthalimide (101) in tetrahydrofuran gave a diasteriomeric mixture of the photoaddition product (105), together with the photoreduced product (102)(scheme 3.3) analogous to products expected for the photochemistry of simple ketonic systems.

It was, therefore, decided to study the photochemical behaviour of N-acylphthalimides, (8) and (9) and their chloro derivatives, (11) and (12) in the presence of electron rich compounds to see what effect this perturbation of the imide chromophore would have on the photochemistry of the system.



Scheme 3.3

(8) R = H, R' = Me
(9) R = H, R' = Ph
(11) R = Cl, R' = Me
(12) R = Cl, R' = Ph

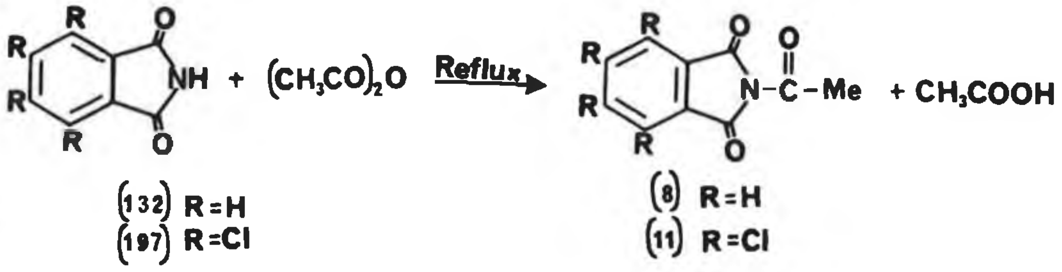


Scheme 3.4

3.1 Preparation of N-Acylphthalimides

(A) N-Acetylphthalimide (8)

N-Acetylphthalimide (8) was prepared by heating phthalimide (132) under reflux in a large excess of acetic anhydride (scheme 3.5). The N-acetylphthalimide was isolated by removing approximately half of the acetic anhydride by distillation, and allowing the product to precipitate on cooling to room temperature over twelve hours. On recrystallisation from ethanol white crystals of N-acetylphthalimide (8), (50%), m.p. 134-135°C (lit.[115] 134-135°C) were obtained.



Scheme 3.5

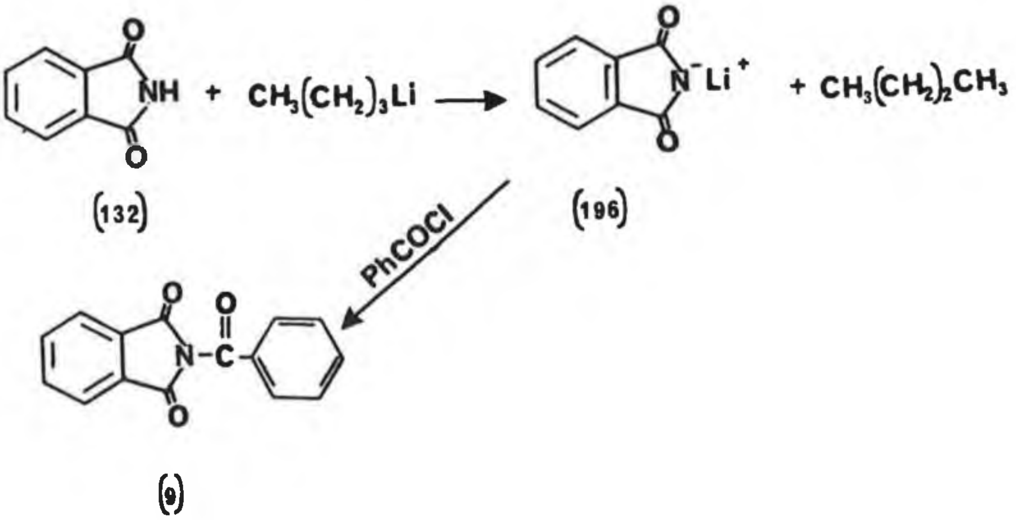
(B) N-Benzoylphthalimide (9)

N-Benzoylphthalimide (9) was readily prepared by the benzoylation of phthalimide with benzoyl chloride in the presence of pyridine.[115] Recrystallisation from ethanol gave white crystals of N-benzoylphthalimide (61%) m.p. 166-167°C (lit.[115] 166-167°C).

N-Benzoylphthalimide was also prepared by another route. This entailed preparing the lithium salt of phthalimide

(196) by reacting n-butyllithium with phthalimide in tetrahydrofuran and benzoylating the resulting phthalimide salt with benzoyl chloride (scheme 3.6).[116] Recrystallisation of the resulting product from ethanol gave white crystals of N-benzoylphthalimide (50%, m.p. 166-167°C).

The former route was preferred for the preparation of N-benzoylphthalimide as it was less laborious, gave a higher yield and required more convenient starting materials. The only advantage of the latter route was that it was a quicker reaction. Both routes are commonly used for the acylation of amides in organic chemistry.



Scheme 3.6

(C) N-Acetyl 3,4,5,6-tetrachlorophthalimide (11)

A detailed study of the literature revealed that the synthesis of N-acetyl-3,4,5,6-tetrachlorophthalimide (11) has never been reported. The N-acetyltetrachlorophthalimide (11) was prepared by a route similar to that used for the synthesis of N-acetylphthalimide (scheme 3.5). The process involved heating tetrachlorophthalimide (197) under reflux in acetic anhydride for eight hours. Recrystallisation of the isolated product from a chloroform-ethanol mixture (1:1 v/v) yielded yellow plates of N-acetyl-3,4,5,6-tetrachlorophthalimide (56%, m.p. 198-199°C). The elemental microanalysis agreed with the molecular formula $C_{10}H_3Cl_4NO_3$. Its infra-red spectrum showed many similarities to that of N-acetylphthalimide. The ^1H nmr spectrum showed a singlet at δ 2.67 (methyl group), similar to that of the methyl group (δ 2.61) in N-acetylphthalimide. The ^{13}C nmr spectrum showed signals at 167.9, 160.9 (carbonyl carbons), 141.8, 131.0, 126.6 (aromatic carbons) and 27.0 (methyl carbon) also consitent with the assigned structure.

(D) N-Benzoyl-3,4,5,6-tetrachlorophthalimide (12)

As with the synthesis of N-acetyl-3,4,5,6-tetrachlorophthalimide, the synthesis of N-benzoyl-3,4,5,6-tetrachlorophthalimide (12) has never been reported in the literature.

Initially the synthesis of N-benzoyl-3,4,5,6-tetrachlorophthalimide (12) was attempted by a method similar to one of those used for N-benzoylphthalimide. This procedure involved adding one equivalent of n-butyllithium to a solution of tetrachlorophthalimide and treating the resulting mixture with benzoyl chloride. This procedure was tried a number of times, and on each occasion the starting material (tetrachlorophthalimide) was recovered, with only a small amount (~2%) of N-benzoy-3,4,5,6-tetrachlorophthalimide (12) being formed.

An alternative procedure, reaction of tetrachlorophthalimide (197) with benzoyl chloride in the presence of pyridine proved successful with N-benzoyl-3,4,5,6-tetrachlorophthalimide (50%, m.p. 211-212°C) being isolated as yellow plates after recrystallisation from a chloroform-ethanol mixture (1:1 v/v). The elemental microanalysis agreed with the molecular formula $C_{15}H_5Cl_4NO_3$. The infra-red spectrum showed strong bands at 1730 and $1705cm^{-1}$ (C=O). The ^1H nmr spectrum showed a multiplet between $\delta 8.1$ and $\delta 7.4$ (aromatic hydrogens) consistent with the assigned structure.

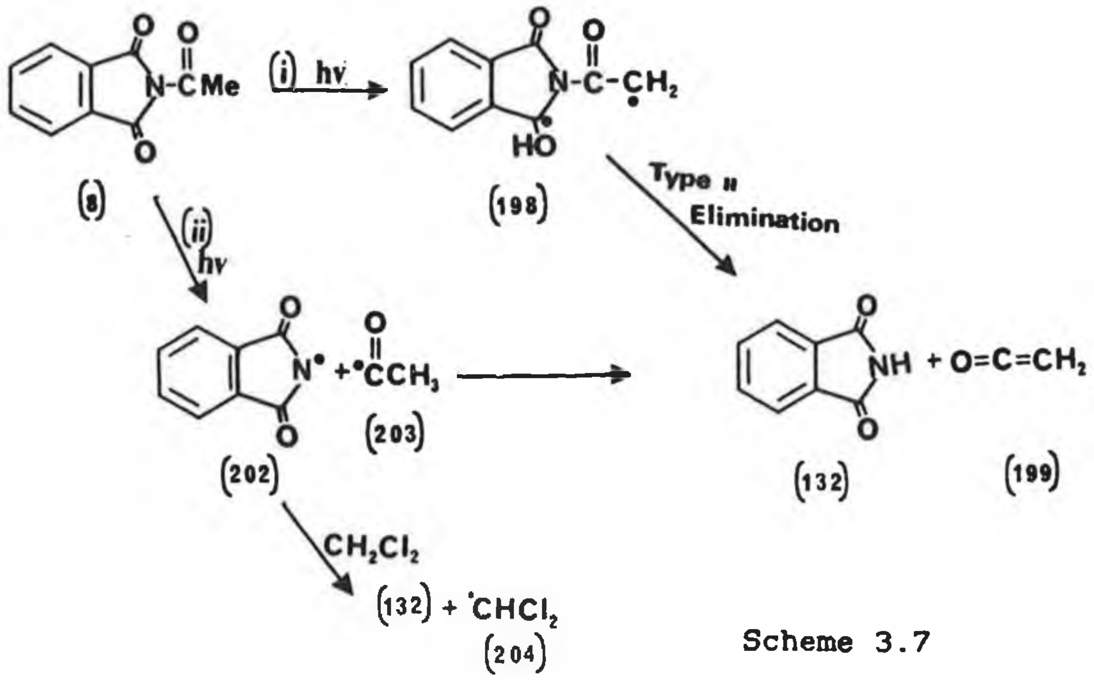
3.2 The Photochemical Reactivity of N-Acetylphthalimide (8) in Acetonitrile and Dichloromethane

When N-acetylphthalimide (8) was irradiated in the 'non hydrogen donating' solvent, acetonitrile, through Pyrex, no product formation was observed by thin layer chromatography (TLC) analysis and most of the starting material (95%) was recovered.

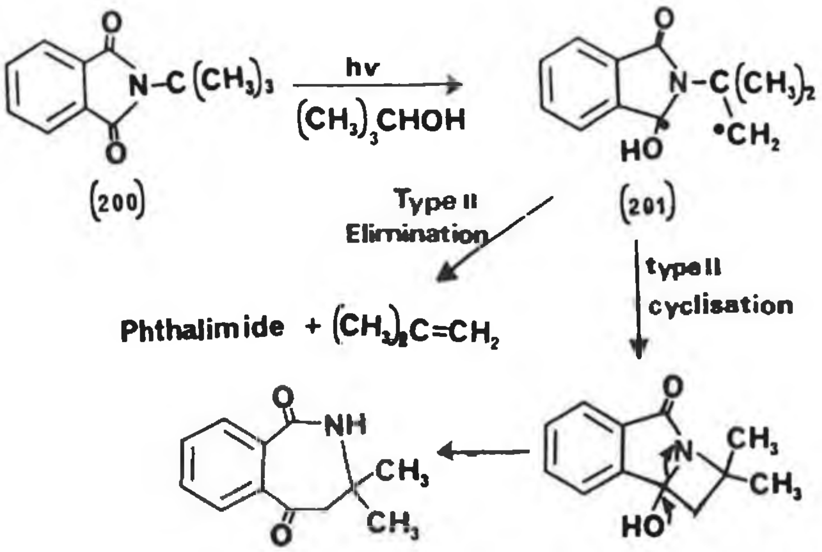
On irradiation of N-acetylphthalimide in another 'non hydrogen donating solvent', dichloromethane, through Pyrex, a single product was seen to form slowly (TLC observation). It was isolated and identified as phthalimide (132) (70% yield based on consumed N-acetylphthalimide) on comparison of its infra-red spectrum with that of an authentic sample.

Two mechanisms have been proposed to explain these observations. The first involves initial intramolecular γ-hydrogen abstraction by the excited N-acetylphthalimide to yield (198) followed by type II elimination to yield phthalimide (132) and ketene (199) [scheme 3.7 (i)].

N-Alkylphthalimides are known to undergo this type of reaction. For example irradiation of N-t-butylphthalimide (200) in t-butyl alcohol yielded phthalimide as one of its photoproducts by type II elimination of the intramolecularly formed biradical (201)[74] (scheme 3.8).



Scheme 3.7



Scheme 3.8

An alternative mechanism for the formation of phthalimide from the irradiation of N-acetylphthalimide in dichloromethane may involve α-cleavage of the excited phthalimide to give the radicals (202) and (203) followed by disproportionation to yield phthalimide (132) and ketene (199). Alternatively hydrogen abstraction from the solvent dichloromethane by (202) to give phthalimide and (204) [scheme 3.7 (ii)]. This mechanism may also be described as a β-cleavage of the excited N-acetylphthalimide with respect to the 'in ring' imide carbonyl group.

The formation of phthalimide on irradiation of N-acetylphthalimide in dichloromethane but not on irradiation in acetonitrile may suggest that in the more polar acetonitrile there may be a different lowest energy excited state. The (π,π^*) and (n,π^*) states, of phthalimides are known to be very close energetically.[49]

It was decided to study the photochemical behaviour of N-acetylphthalimide in a solvent containing a readily abstractable hydrogen atom, tetrahydrofuran, since it was of interest, to compare the photochemistry of N-acylphthalimides with that of N-alkylphthalimides in this solvent.

3.3 Irradiation of N-Acetylphthalimide (8) and N-Acetyl-3,4,5,6-tetrachlorophthalimide in Tetrahydrofuran

Kanaoka and co-workers showed that when N-methylphthalimide was irradiated in tetrahydrofuran[68] the addition product (105) was obtained as well as the reduced product (102) (scheme 3.9). A mechanism involving hydrogen abstraction followed by radical coupling has been proposed to account for the observed product (105).

(105) (102)

Scheme 3.9

N-Acetylphthalimide (8) might possibly be expected to react in a manner similiar to N-methylphthalimide when irradiated in tetrahydrofuran.

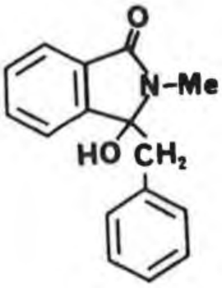
When N-acetylphthalimide was irradiated in tetrahydrofuran through Pyrex two additional spots was observed on TLC. The products eluted marginally behind the starting material. Repeated attempts to isolate the products by chromatographic separation proved unsuccessful.

Irradiation of N-acetyl-3,4,5,6-tetrachlorophthalimide (11) (NATCP) in tetrahydrofuran gave three photoproducts (TLC observation). These also could not be isolated even after prolonged chromatography.

It was therefore, decided to study the photochemical behaviour of N-acetylphthalimide in a different solvent containing a readily abstractable hydrogen atom, toluene.

3.4 The Photochemical Reaction of N-Acetylphthalimide (8) with Toluene

The irradiation of N-methylphthalimide (101) in toluene[69] gave products similar to those formed on irradiation in tetrahydrofuran, that is photoaddition of the solvent (toluene) to give the carbinol (108). Again a mechanism involving hydrogen abstraction followed by radical coupling has been proposed to account for the observed product (108).[69]



(108)

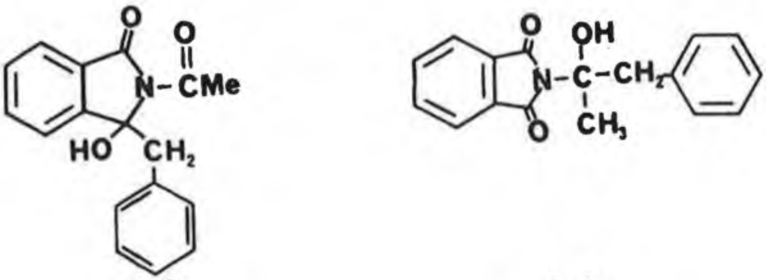
Scheme 3.10

When N-acetylphthalimide (8) was irradiated in toluene through Pyrex two additional spots were observed on TLC.

Chromatographic separation of the reaction mixture led to the isolation of the two products, (A) and (B).

Products (A) was a minor product (4%) which eluted marginally before the major product (B). This minor product was identified as phthalimide by comparison of its infra-red spectrum with that of an authentic sample.

The major product (B) (45%, m.p. 96-98°C) eluted marginally before the starting material. Its infra-red spectrum showed hydroxyl (3457cm^{-1}) and carbonyl (1742, 1657cm^{-1}) absorption bands. The microanalytical results were consistent with a 1:1 toluene/N-acetylphthalimide adduct. The ^{1}H nmr spectrum showed a nine hydrogen multiplet between δ7.76 and 6.59 consistent with the presence of phthalimide and phenyl rings, a one hydrogen singlet (δ5.20) due to a hydroxyl group, two one-proton doublets (δ 3.86 and 3.55, J ~13.2Hz) due to a methylene group, and a three hydrogen singlet (δ2.62) consistent with the presence of a methyl group. This data is consistent with product (B) being one of the carbinols (205) or (206).



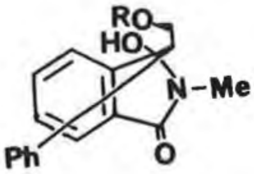
(206)

(205)

Scheme 3.11

The non-equivalence of the two methylene hydrogen atoms can be explained by the fact that they are diastereotopic in both carbinols (205) and (206) , i.e. they are on a carbon attached to a chiral centre. The chemical shift for the methyl group in product (B) (δ 2.62) is very similar to that of the starting material, N-acetylphthalimide (δ 2.61), suggestive of product (B) being the carbinol (206). If product (B) were the carbinol (205) a much greater change in chemical shift might be expected for the methyl group.

Another notable feature of the ^{1}H nmr spectrum was the considerable shielding of the two aromatic protons observed at δ 6.6. Maruyama and co-workers have observed the the ^{1}H nmr spectrum for the alcohol (207) also showed considerable shielding for two of the aromatic hydrogens (δ 6.5–6.3)[105]. They explained this phenomenon by anisotropic shielding effects from the eclipsing benzene rings. The structures of the carbinols (206) and (207) are very similar, so the upfield shift of the two aromatic protons observed at δ 6.6 for product (B) could be explained by anisotropic shielding effects from the eclipsing aromatic phthalimide moiety if (206) was the structure of product (B). This observation provides further evidence for assigning the carbinol structure (206) to product (B).



(207)

Scheme 3.12

Product (B) was confirmed as the carbinol (206) on analysis of its ^{13}C nmr spectrum. Two signals (173.9, 166.1) corresponding to two non-equivalent carbonyl groups were present. If (205) had been the major product only one signal in the carbonyl absorption region would have been expected. Also present were ten non-equivalent aromatic carbons (table 1), whereas only seven would be expected for structure (205).

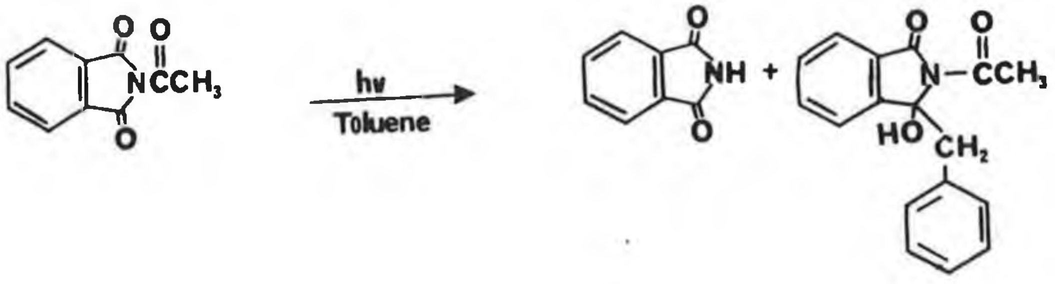
Table 1: ^{13}C nmr spectral data for the major product (206) obtained on irradiation of N-acetylphthalimide in toluene.

δ/ppm	Assignment	δ/ppm	Assignment
173.9	Carbonyl	128.1	Aromatic
166.1	Carbonyl	127.2	Aromatic
145.6	Aromatic	124.6	Aromatic
134.6	Aromatic	123.0	Aromatic
134.2	Aromatic	93.1	C–OH
130.3	Aromatic	45.4	Me
129.6	Aromatic	26.0	CH_2
129.5	Aromatic		

Attempts were made to synthesize the carbinol (206) by a Grignard reaction involving reaction of benzyl magnesium chloride ($PhCH_2MgCl$) with N-acetylphthalimide in tetrahydrofuran. The result was a mixture of two products, neither of which was the carbinol (206) (see chapter five).

In summary, irradiation of N-acetylphthalimide (8) in toluene led to the formation of two products, phthalimide

(132) and the carbinol (206) (scheme 3.13).



(8) (132) (206)

Scheme 3.13

Phthalimide is probably formed by initial γ-hydrogen abstraction by the excited N-acetylphthalimide to yield (197) [see scheme 3.7(i)] followed by type II elimination. The mechanism for this type of reaction has already been discussed (pages 69-70) for the formation of phthalimide on irradiation of N-acetylphthalimide in dichloromethane.

The mechanism for the formation of the carbinol (206) is discussed later (pages 79-82).

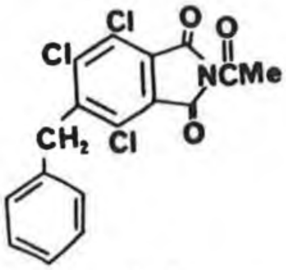
3.5 The Photochemical Reaction of N-Acetyl-3,4,5,6 tetrachlorophthalimide (11) with Toluene

When a solution of N-acetyl-3,4,5,6-tetrachlorophthalimide (NATCP) (11) in toluene was irradiated through Pyrex three additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to the isolation of the major product (78%, m.p. 142-144°C). Further chromatography failed to isolate either of the two minor products which were present in low amounts. The infra-red spectrum of the product isolated showed strong bands at

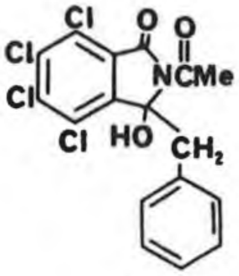
3460 and 1747cm^{-1}, consistent with the presence of hydroxyl and carbonyl groups respectively. The microanalytical results were consistent with a 1:1 toluene/NATCP adduct as was the mass spectrum (molecular ion at m/e 418). This data ruled out the chlorine substituted compound (208) as the major product. The major product was assigned the carbinol structure (209) on analysis of its ^{1}H and ^{13}C nmr spectral data. The ^{1}H nmr spectrum was similar to that of the photoadduct (206) obtained on irradiation of N-acetylphthalimide in toluene, with the exception that the signals due to the aromatic hydrogens of the phthalimide moiety were absent.

The spectrum displayed a multiplet between δ7.14 and δ6.63 (5H, phenyl), a singlet at δ5.15 (OH), two doublets (δ4.00 and 3.91, J~13.7Hz) due to non-equivalent methylene hydrogens and a singlet at δ2.65 corresponding to the methyl group.

The ^{13}C nmr spectrum was also consistent with the assigned structure (209) (table 2).



(208)



(209)

Scheme 3.14

TABLE 2 Data from ^{13}C nmr spectrum of major product (209) obtained on irradiation of N-acetyl-3,4,5,6-tetrachlorophthalimide (11) in toluene.

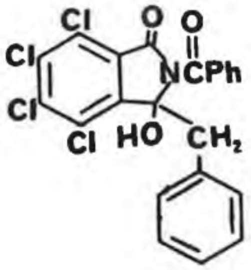
δ/ppm	Assignment	δ/ppm	Assignment
173.5	Carbonyl	128.6	Aromatic
161.5	Carbonyl	128.4	Aromatic
		127.3	Aromatic
141.6	Aromatic	126.4	Aromatic
139.5	Aromatic		
136.4	Aromatic	92.7	C–OH
133.6	Aromatic	41.0	Me
130.6	Aromatic	26.4	CH_2
128.9	Aromatic		

The mechanism for formation of the carbinol (209) is discussed later (pages 79-82).

3.6 The Photochemical Reaction of N-benzoyl-3,4,5,6 tetrachlorophthalimide (12) with Toluene

When a solution of N-benzoyl-3,4,5,6-tetrachlorophthalimide (12) (NBTCP) in toluene was irradiated through Pyrex, five additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to isolation of the major product (31%, m.p. 158-160°C). The minor products were present in very small amounts and it did not prove possible to isolate them.

The infra-red spectrum of the major product revealed absorptions at 3462 (OH) and at 1753 and 1657cm^{-1} (C=O). The ^1H nmr spectrum exhibited an aromatic multiplet (δ 7.59-6.77), an OH singlet (δ 5.56), and two doublets (δ 4.31, 3.91, J=14.3Hz) due to the two methylene hydrogen atoms being non-equivalent. The elemental analysis results were consistent with the product being a 1:1 N-benzoyl-3,4,5,6-tetrachlorophthalimide/toluene adduct. The ^{13}C nmr spectrum showed the presence of two non-equivalent carbonyl groups (δ172.5, 160.9) as well as eleven non-equivalent aromatic absorptions (table 3). Also present were signals due to the methylene carbon (δ40.9) and the hydroxyl-bearing carbon (δ93.3). This data was consistent with the assignment of carbinol structure (210) to this photoproduct.



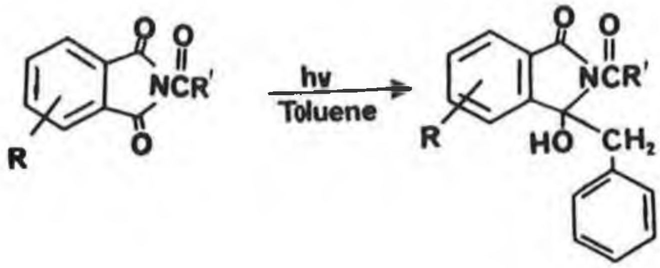
(210)

Scheme 3.15

TABLE 3 Data from ^{13}C nmr spectrum of major product (210) obtained on irradiation of N-benzoyl-3,4,5,6-tetrachlorophthalimide (12) in toluene.

δ/PPM	ASSIGNMENT	δ/PPM	ASSIGNMENT
172.5	Carbonyl	129.4	Aromatic
160.9	Carbonyl	129.2	Aromatic
132.2	Aromatic	128.7	Aromatic
141.9	Aromatic	127.9	Aromatic
133.8	Aromatic	127.8	Aromatic
133.7	Aromatic		
131.2	Aromatic	93.3	C-OH
129.6	Aromatic	40.9	CH_2

Irradiation of the N-acylphthalimides, N-acetylphthalimide (NAP) (8), N-acetyl-3,4,5,6-tetrachlorophthalimide (NATCP) (11) and N-benzoyl-3,4,5,6-tetrachlorophthalimide (NBTCP) (12) in toluene gave the carbinols (206), (209) and (210) respectively as the major photoproducts (scheme 3.16). Two different primary photochemical processes were considered for the production of these carbinols, a hydrogen abstraction mechanism [scheme 3.17 (i)] and an electron transfer mechanism [scheme 3.17 (ii)].

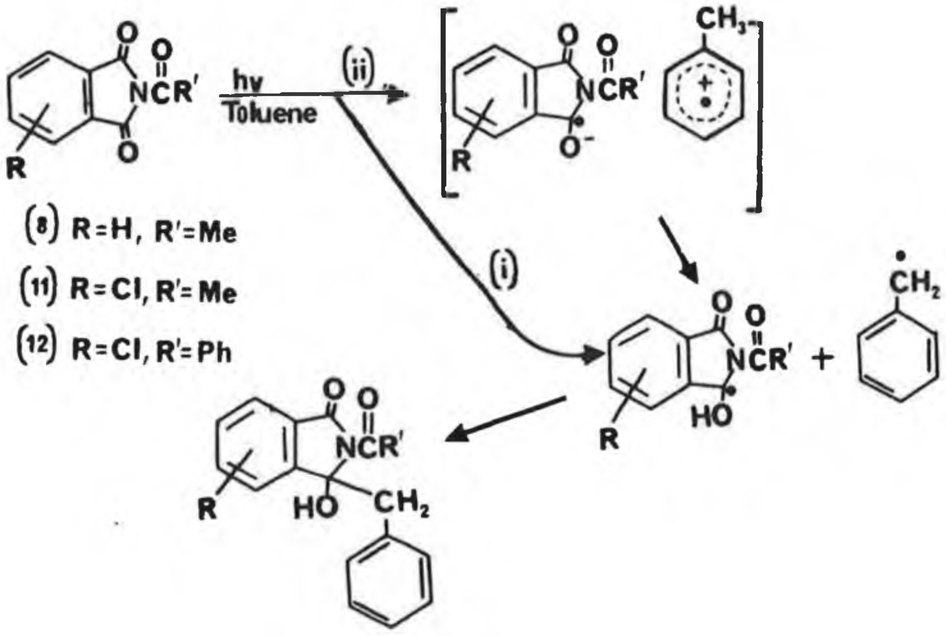


(8) R=H, R'=Me
(11) R=Cl, R'=Me
(12) R=Cl, R'=Ph

(206) R=H, R'=Me
(209) R=Cl, R'=Me
(210) R=Cl, R'=Ph

Scheme 3.16

N-methylphthalimide (101) when irradiated in toluene[69] produced a carbinol (see page 39) by a primary photoprocess suggested by the author as involving hydrogen abstraction from toluene by the $^3(n,\pi^*)$ excited state of the



(8) R=H, R'=Me
(11) R=Cl, R'=Me
(12) R=Cl, R'=Ph

(206) R=H, R'=Me
(209) R=Cl, R'=Me
(210) R=Cl, R'=Ph

Scheme 3.17

phthalimide, although no evidence for this has yet been produced. The suggestion was probably made because simple ketones are known to undergo hydrogen abstraction from their (n,π^*) state. By analogy it is possible that the acylphthalimides (8), (11) and (12) when irradiated in toluene also undergo hydrogen abstraction as the primary photoprocess [scheme 3.17 (i)].

The feasibility of electron transfer being the primary photoprocess on irradiation of the N-acylphthalimides (8), (11) and (12) in toluene can be predicted using the Weller equation[7] (see page 7). Unfortunately the reduction

Weller eqn. $$\Delta G = 23.06\left[E_{D}^{ox} - E_{A}^{red}\right] - E_{excit} - C$$

potentials of the N-acylphthalimides (8),(10) and (11) are not available. However, the reduction potentials of N-methylphthalimide (101)[105] and N-methyl-3,4,5,6-tetrachlorophthalimide (194)[112] are known and the calculated ΔG values for photochemical electron transfer with toluene (see table 4) were negative, therefore, predicting that photoinitiated electron transfer should be spontaneous, provided the excited state of the phthalimide was the singlet state. Electron transfer processes are known to occur for N-methylphthalimide-alkene systems from the singlet excited state of the phthalimide.[106] The singlet excitation energy and reduction potentials of NAP (8) and NATCP (11) would be anticipated to be similar to those of N-methylphthalimide (101) and its chloro derivative (194) respectively. This would result in the ΔG values for the N-acylphthalimides (8), (11) and (12) - toluene systems being negative, making electron transfer a possible primary photoprocess [scheme 3.17 (ii)].

TABLE 4 Showing the reduction potentials, singlet excitation energies and ΔG (electron transfer) for NMP-, NMTCP-toluene systems.

	E^{red} V	E /kcal mol^{-1}	ΔG/kcal mol^{-1}
NMP (101)	-1.36	80.0	-7.7
NMTCP (194)	-1.10	81.0	-14.7

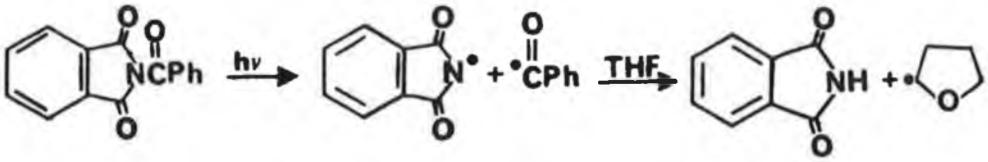
NOTE: oxidation potential of toluene 1.83 V[30]
NMP : N-methylphthalimide (101)
NMTCP: N-methyl-3,4,5,6-tetrachlorophthalimide (194)

As already outlined, irradiation of the acylphthalimides NAP (8), NATCP (11) and NBTCP (12) in toluene leads to products derived by reaction at the 'in ring' and not the 'out of ring' carbonyl group. An explanation for this may be that the location of the excitation energy which determines which carbonyl is photoreduced is more heavily associated with the 'in ring' carbonyl group.

3.7 The Photochemical Reaction of N-Benzoylphthalimide (9) with Tetrahydrofuran

When N-benzoylphthalimide (9) was irradiated through Pyrex in tetrahydrofuran, three additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to the isolation of a very small amount of one of the products. Attempts to isolate the other products by further chromatography proved unsuccessful. The product isolated was identified as phthalimide on comparison of its infra-red spectrum with that of an authentic sample.

Phthalimide from this reaction is probably formed by cleavage of the excited N-benzoylphthalimide to form the radicals (202) and (211) followed by hydrogen abstraction from tetrahydrofuran by the radical (202) to yield phthalimide (scheme 3.18).



(9) (202) (211) (132)

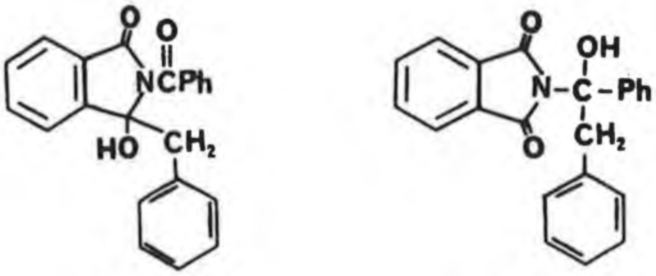
Scheme 3.18

The major products from the irradiation of N-benzoylphthalimide in tetrahydrofuran could not be isolated and attention was then turned to the photochemical behaviour of N-benzoylphthalimide in another solvent containing a readily abstractable hydrogen, toluene.

3.8 The Photochemical Reaction of N-Benzoylphthalimide (9) with Toluene.

When N-benzoylphthalimide (9) was irradiated in toluene through Pyrex three additional spots were observed on TLC. These corresponded to one major and two minor products. Chromatographic separation of the reaction mixture led to the isolation of the major product, which eluted marginally behind the starting material. The minor products were present in very small amounts and were not isolated.

The major product (50%, m.p. 220-222°C) showed no absorption in the 4,000-3,000cm^{-1} region of the infra-red spectrum, showing the absence of a hydroxyl group. This ruled out either carbinol (212) or (213) as the major product. The infra-red spectrum also showed strong absorption in the carbonyl region (1745, 1703 and 1668cm^{-1}). The ^{1}H nmr spectrum showed the absence of aliphatic hydrogen, evidence that the major product did not incorporate a methyl or methylene group derived from toluene. Only aromatic hydrogens (δ7.95-7.43) were observed.



(212) (213)

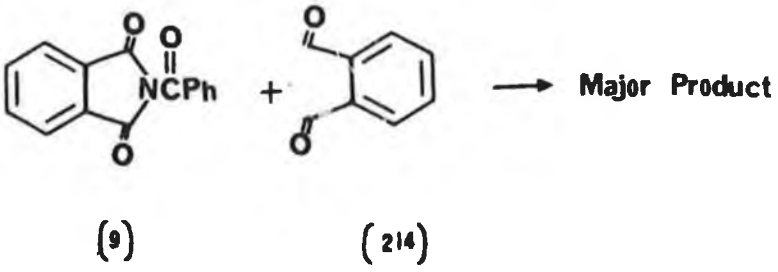
Scheme 3.19

The mass-spectrum of the product indicated a molecular weight of 383 in agreement with the elemental microanalysis and consistent with a molecular formula $C_{23}H_{13}NO_5$. The ^{13}C nmr spectrum (table 5) showed the presence of four non-equivalent carbonyl groups, sixteen non-equivalent aromatic carbons and a single upfield carbon. These results suggest that the product consisted of either the dimerization of two N-benzoylphthalimide molecules followed by loss of some fragment or else addition of N-benzoylphthalimide to some fragment derived from N-benzoylphthalimide.

TABLE 5: Data from the ^{13}C nmr spectrum of the major product obtained on irradiation of N-benzoylphthalimide in toluene.

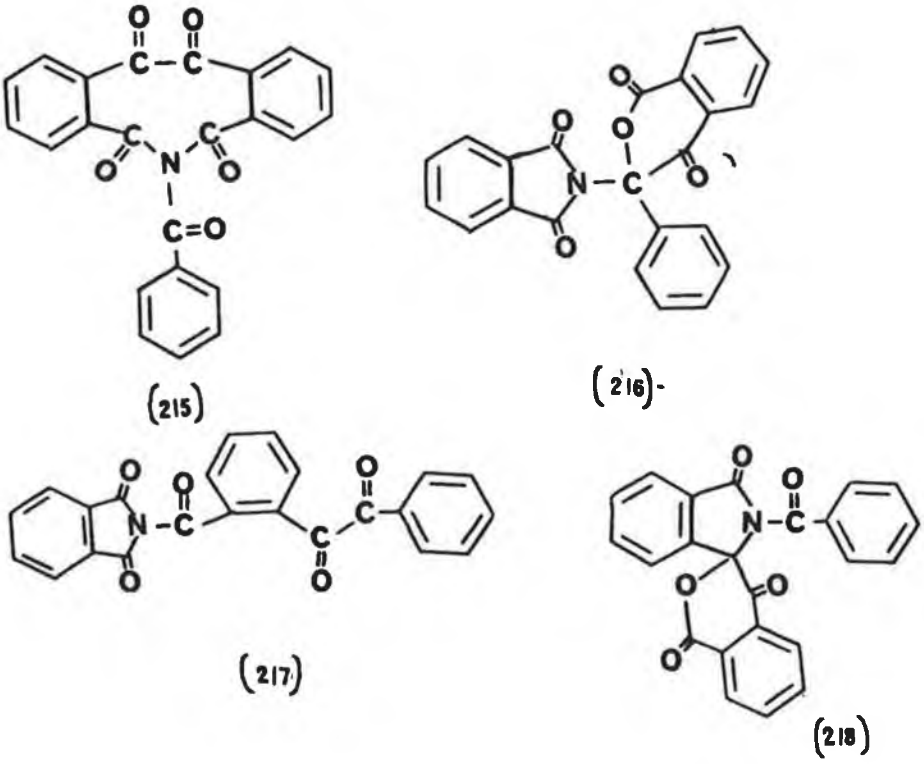
δ/ppm	Assignment	δ/ppm	Assignment
184.7	Carbonyl	132.0	Aromatic
169.0	Carbonyl	131.2	Aromatic
164.3	Carbonyl	131.0	Aromatic
160.2	Carbonyl	129.8	Aromatic
		129.6	Aromatic
141.2	Aromatic	128.1	Aromatic
136.0	Aromatic	128.0	Aromatic
135.3	Aromatic	126.4	Aromatic
135.2	Aromatic	126.0	Aromatic
133.0	Aromatic	121.9	Aromatic
132.5	Aromatic		
		94.8	Spiro-carbon

N-Benzoylphthalimide has a molecular formula of $C_{15}H_9NO_3$ and as such would require the addition of $C_8H_4O_2$ to provide the required molecular formula. Dimerization of N-benzoylphthalimide followed by loss of C_7H_5NO (i.e. a PhCON unit) would also give the required molecular formula. The major product therefore, might be visualised in terms of the addition of N-benzoylphthalimide to the fragment (214) (scheme 3.20).



Scheme 3.20

Structures derived from the addition of (214) across either of the aromatic rings of (9) were ruled out because this would have resulted in loss of aromaticity of the participating ring leading to the formation of vinylic and aliphatic protons and carbons, at variance with the ^1H and ^{13}C nmr observations. Structure (215) from the addition of fragment (214) across the 'in ring' N-C(O) bond, could also be readily ruled out since it should exhibit ten non-equivalent aromatic carbons and three non-equivalent carbonyl groups rather than the four carbonyl and sixteen non-equivalent aromatic carbons observed (see table 5). In addition the signal at δ94.3 would also not have been observed.

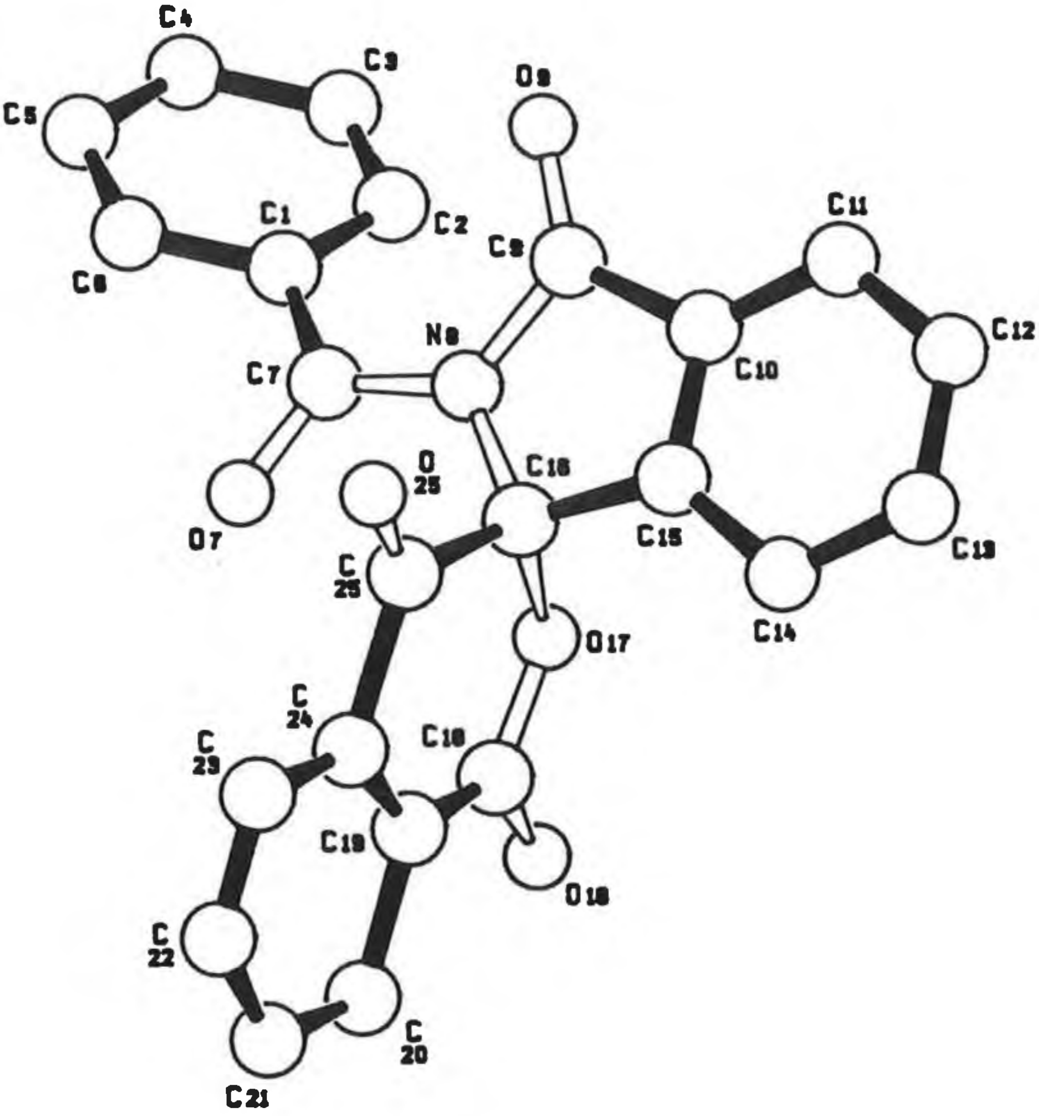

(215) (216) (217) (218)

Scheme 3.21

The lactone (216) and phthalimide (217) which can be formally visualised as addition of (214) across the 'out of ring' carbonyl group and across the 'out of ring' N-C(O) bond respectively were also ruled out for similar reasons. However, lactone (218), formally visualised as the addition of (214) across the 'in ring' carbonyl group is the only structure derived from (9) and (214) which agreed with all the spectroscopic data collected for the photoproduct. The structure was confirmed as the lactone (218) by x-ray crystallographic analysis. A projection of structure (218) as obtained from x-ray techniques is presented in scheme 3.22. Hydrogen atoms are omitted for clarity. The bond lengths, atomic coordinates and bond angles as obtained by x-ray techniques are listed in tables 6, 7 and 7A respectively.

TABLE 6: Bond lengths for the major product (218) obtained on irradiation of N-benzoylphthalimide in toluene as obtained by x-ray techniques.

Atom A	Atom B	Distance (Å)	Atom A	Atom B	Distance (Å)
C1	C2	1.411	C13	C14	1.374
C1	C6	1.400	C14	C15	1.416
C1	C7	1.477	C15	C16	1.479
C2	C3	1.376	C16	O17	1.586
C3	C4	1.422	C16	C25	1.537
C4	C5	1.405	C17	C18	1.313
C5	C6	1.390	C18	C19	1.348
C7	N8	1.388	C18	O18	1.278
C7	O7	1.239	C19	C20	1.541
N8	C9	1.429	C19	C24	1.348
N8	C16	1.411	C20	C21	1.447
C9	C10	1.494	C21	C22	1.343
C9	O9	1.223	C22	C23	1.311
C10	C11	1.389	C23	C24	1.338
C10	C15	1.371	C24	C25	1.612
C11	C12	1.373	O25	C25	1.079
C12	C13	1.409			



Scheme 3.22. The lactone (218).

TABLE 7. Atomic coordinates for the major product (218) obtained on irradiation of N-benzoylphthalimide in toluene as obtained by x-ray techniques.

CELL 11.040 11.782 15.557 90.000 117.310 90.000

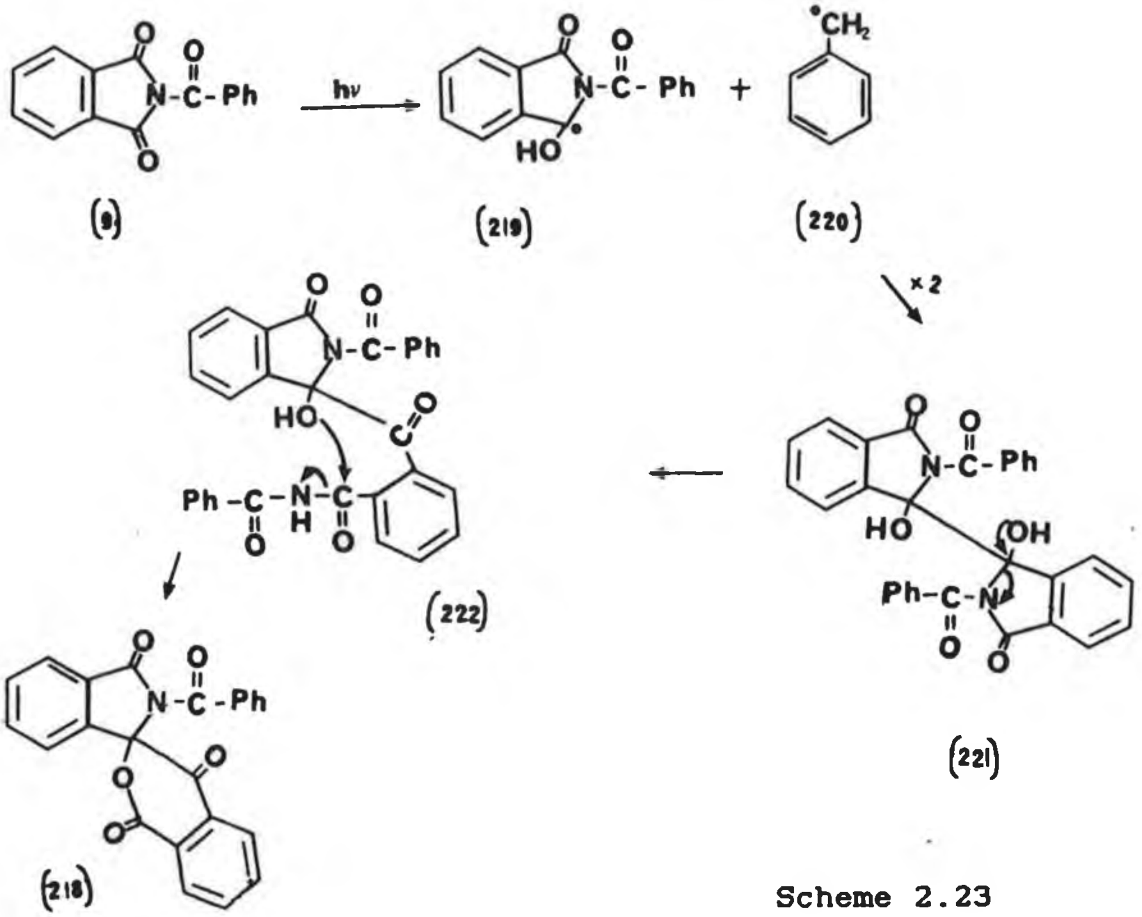
Atom	X	Y	Z
C1	0.81346	0.02557	0.56810
C2	0.72091	-0.03004	0.59313
C3	0.76377	-0.12010	0.65654
C4	0.90225	-0.15514	0.69672
C5	0.99479	-0.09663	0.67408
C6	0.95014	-0.00797	0.60776
C7	0.77277	0.11608	0.49443
N8	0.66767	0.19150	0.47778
C9	0.62239	0.23123	0.54503
C10	0.50842	0.31164	0.48931
C11	0.41848	0.36384	0.51654
C12	0.31775	0.42983	0.44823
C13	0.30739	0.44183	0.35495
C14	0.39873	0.39322	0.32871
C15	0.50170	0.32495	0.39967
C16	0.60372	0.25200	0.38990
O17	0.52642	0.15754	0.31094
C18	0.53633	0.16149	0.23007
C19	0.61706	0.23159	0.21060
C20	0.60956	0.21114	0.11045
C21	0.70213	0.28853	0.09806
C22	0.78899	0.35659	0.16878
C23	0.79610	0.37389	0.25425
C24	0.70857	0.30818	0.26899
O25	0.77230	0.37972	0.42740
O7	0.81992	0.12032	0.43597
O9	0.67158	0.20577	0.63068
O18	0.45951	0.08419	0.17385
C25	0.70896	0.32031	0.37233

TABLE 7A: Bond angles for the major product (218) obtained on irradiation of N-benzoylphthalimide in toluene as obtained by x-ray techniques

Atom A	Atom B	Atom C	Angles (ABC)	Atom A	Atom B	Atom C	Angles (ABC)
C2	C1	C6	121.20	C10	C15	C16	110.47
C2	C1	C7	123.28	C14	C15	C16	128.80
C6	C1	C7	115.38	N8	C16	C15	103.08
C1	C2	C3	120.10	N8	C16	017	104.38
C2	C3	C4	119.06	N8	C16	C25	110.72
C3	C4	C5	120.42	C15	C16	017	108.84
C4	C5	C6	120.26	C15	C16	C25	112.77
C1	C6	C5	118.87	017	C16	C25	114.31
C1	C7	N8	122.53	C16	017	C18	117.76
C1	C7	07	121.21	017	C18	C19	126.28
N8	C7	07	115.72	017	C18	018	108.04
C7	N8	C9	128.03	C19	C18	018	125.64
C7	N8	C16	120.54	C18	C19	C20	113.40
C9	N8	C16	110.87	C18	C19	C24	128.84
N8	C9	C10	105.50	C20	C19	C24	117.51
N8	C9	09	125.97	C19	C20	C21	108.82
C10	C9	09	128.49	C20	C21	C22	123.33
C9	C10	C11	129.31	C21	C22	C23	127.68
C9	C10	C15	107.51	C22	C23	C24	111.84
C11	C10	C15	123.15	C19	C24	C23	130.45
C10	C11	C12	116.94	C19	C24	C25	112.93
C11	C12	C13	120.52	C23	C24	C25	116.62
C12	C13	C14	122.68	C16	C25	C24	118.32
C13	C14	C15	116.17	C16	C25	025	117.77
C10	C15	C14	120.48	C24	C25	025	123.63

The formation of spirolactone structure (218) is unique in phthalimide photochemistry. The mechanism for its formation might involve hydrogen abstraction by the excited N-benzoylphthalimide from toluene to give the radicals (219) and (220). Instead of these radicals combining, (219) may undergo dimerization to give the pinacol (221). The pinacol could then readily undergo ring opening to afford (222). Intramolecular nucleophilic attack by the hydroxyl group on the acyclic imide carbonyl group would result in ring closure, with formation of the observed product (218) and the elimination of benzamide (scheme 3.23).

TLC failed to show the presence of any benzamide in the final photolysis mixture. This however, is not conclusive evidence that benzamide was not formed, since, if formed, it may have undergone photodestruction under the reaction conditions which involved prolonged irradiation.

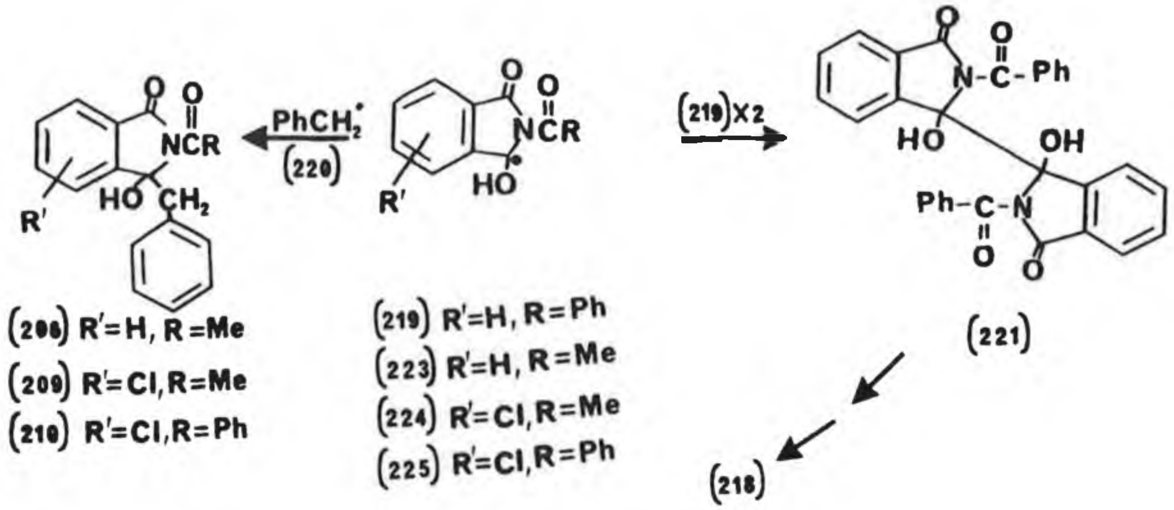


Scheme 2.23

Tentative evidence consistent with formation of a labile intermediate such as (221) or (222) was obtained. During photolysis early TLC observations of the photolysis mixture indicated formation of a product which had a lower r_f value than that of the lactone (218). On further irradiation this spot slowly diminished in relative intensity while the spot due to the lactone (218) appeared and increased in relative intensity. Attempts to isolate this probable intermediate by chromatographic separation of the reaction mixture proved unsuccessful. During attempted separation the concentration of the 'intermediate' diminished rapidly until none could be observed by TLC analysis and only the lactone (218) was present.

Pertinent to the suggested mechanism (scheme 3.23) for formation of the lactone (218) are the following observations;
(i) irradiation of N-benzoylphthalimide in a non-photoreducing solvent such as acetonitrile failed to produce any photoproducts, consistent with the necessity of a reduction step to initiate the reaction process leading to the lactone (218) and
(ii) irradiation of N-benzoylphthalimide through Pyrex in dichloromethane containing propan-2-ol led to the formation and isolation of the lactone (218) as the major product, again consistent with the necessity for a reduction step.

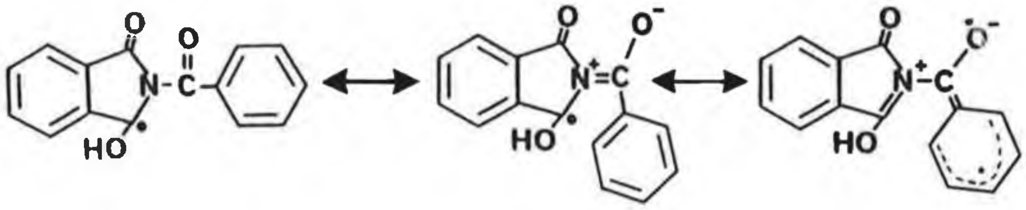
Why N-acetylphthalimide (NAP) (8), N-acetyl-3,4,5,6-tetrachlorophthalimide (NATCP) (11) and N-benzoyl-3,4,5,6-tetrachlorophthalimide (NBTCP) (12) should behave so differently from N-benzoylphthalimide (NBP) (9) in their excited state reactions with toluene is not yet clear. The primary photochemical process for all systems might at first sight seem to be the same, involving initial hydrogen abstraction by the excited N-acylphthalimide to give the radicals (219), (223), (224), and (225) (scheme 3.24). The subsequent process for the radicals (223), (224) and (225) must involve their coupling with the toluene derived benzyl radical (220) (scheme 3.24). This however is not the case for the N-benzoylphthalimide-derived radical (219) as the lactone (218) is the major photoproduct. Such markedly different behaviour for the N-benzoylphthalimide-derived radical (219) and the radicals (223)-(225) derived from the other N-acylphthalimides studied is difficult to reconcile.



Scheme 3.24

The favoured route for the reaction of any radicals produced by hydrogen donation depends on the structure of the radical entities, on the concentration of reagents, on the hydrogen-donor ability of the reducing agent, and on temperature.

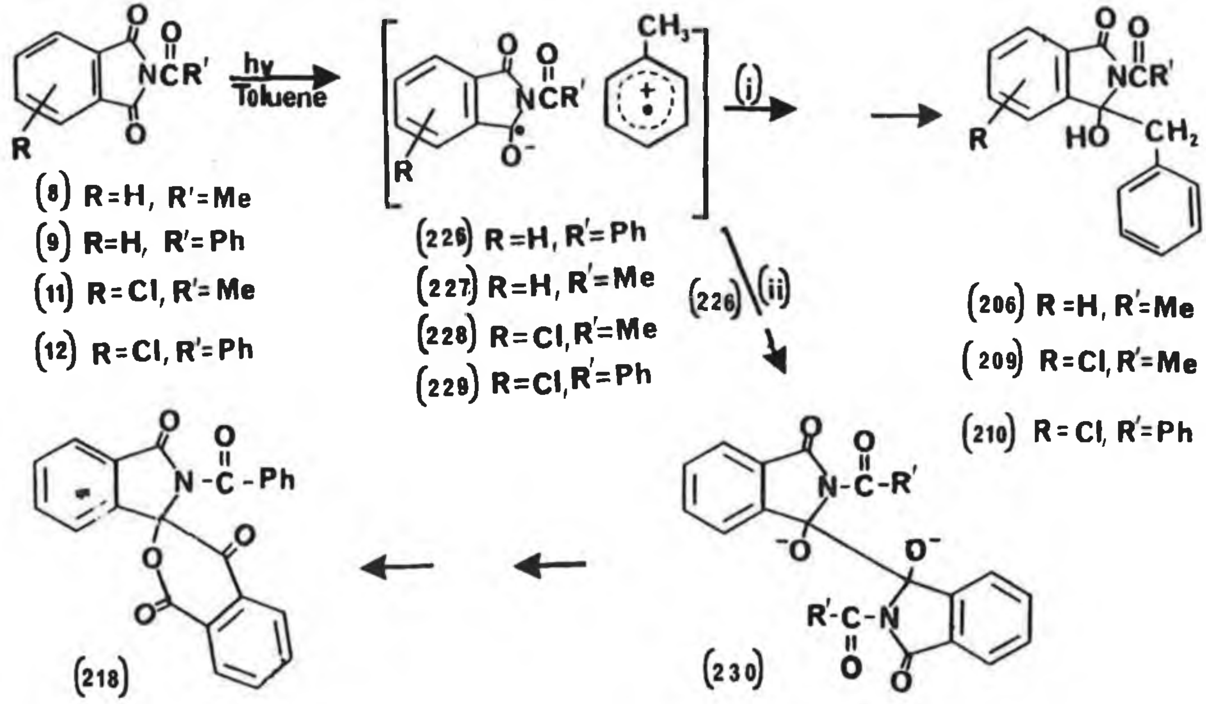
The irradiation of NAP (8), NATCP (11), NBTCP (12) and NBP (9) in toluene were all carried out at the same temperature and at similar concentrations. Assuming an initial hydrogen abstraction process for each, this would therefore, imply that the secondary reaction processes for the two different product types (carbinol and lactone) (see scheme 3.24) are due to subsequent different behaviour by the radical entities. This difference in behaviour may involve the NAP, NATCP and NBTCP derived radicals (223)-(225) and the benzyl radical (220) undergoing reaction within a solvent cage to yield the observed addition products (206), (209) and (210) respectively. On the other hand if the ketyl radical (219) from N-benzoylphthalimide escapes from the cage before coupling with the benzyl radical can occur, dimerization to yield pinacol (221) and subsequently lactone (218), becomes a much more likely process (scheme 3.24). A possible reason why the N-benzoylphthalimide derived radical (219), on the one hand, and the other N-acylphthalimide derived radicals (223)-(225), on the other hand, may behave differently could be due to the N-benzoylphthalimide derived radical being less reactive than the other N-acylphthalimide counterparts [(223)-(225)] and therefore surviving to leave the 'cage'. The radical (219) may be less reactive than (223) and (224) due to increased stabilization by the phenyl group (versus methyl). This stabilisation may be via an increase in resonance delocalization (scheme 3.25), with the odd electron being delocalized into the phenyl ring. This increased stabilization would be expected to prolong its lifetime and therefore give it an increased opportunity to escape from the cage.



Scheme 3.25

The NBTCP derived radical (225) would also be expected to have similar increased stabilization and a more prolonged lifetime than the radicals (223) and (224) but because of chlorine substitution on the phthalimide aromatic ring the molecule may be too bulky to enable its escape from the solvent cage during its lifetime.

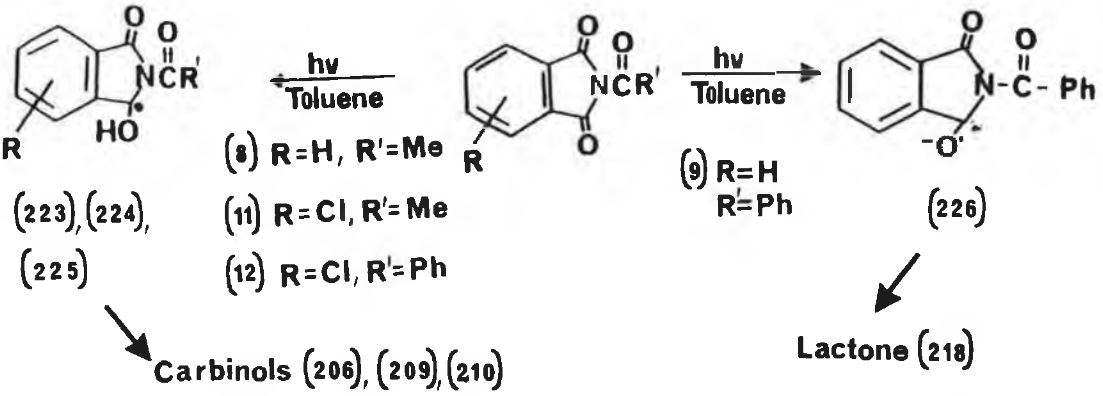
As already discussed on pages 79-82 it is possible that electron transfer is the primary photochemical process for carbinol formation on irradiation of NAP (8), NATCP (9) and NBTCP (12) in toluene (scheme 3.26). By analogy it is also possible that N-benzoylphthalimide (9) undergoes photochemical electron transfer with toluene as a primary photochemical process (scheme 3.26). The difference in behaviour of these radical anions can also be explained by analogy to the postulated different reaction pathways for the ketyl radicals (219) and (223)-(225) (scheme 3.24) i.e. the radical anion (226) escapes from the solvent cage and



Scheme 3.26

dimerizes to give (230) which subsequently gives the lactone (218). The radical anions (227)-(229) remain in the solvent cage reacting to give the carbinols (206), (209) and (210) respectively (scheme 3.26).

Another explanation for the different photochemical behaviour of NAP (8), NATCP (11) and NBTCP (12), on the one hand, with that of N-benzoylphthalimide (NBP) (9), on the other, may be that excited NBP initially undergoes electron transfer while the primary photoprocess for the other N-acylphthalimides is hydrogen abstraction. The radical anion (226) may then escape from the solvent cage, dimerize and subsequently lead to the lactone (218), whereas the ketyl radicals (223), (224) and (225) may remain in the solvent cage where they combine with the benzyl radical to yield carbinols (scheme 3.27).



Scheme 3.27

Support for this postulated explanation comes from N-alkylphthalimide photochemistry. It has been reported that when N-alkylphthalimides were irradiated in the presence of alcohols,[67] ethers[68] and alkylbenzenes[69] the expected reduced and addition products were obtained (see pages 38-39), but no pinacol formation was observed. The authors suggested a primary photoprocess involving hydrogen abstraction for these reactions. When amines however are used as the donor molecules pinacol formation has been observed.[69] Phthalimides irradiated in the presence of amines undergo a primary photoprocess which is suggested as involving electron transfer followed by a subsequent proton transfer from the amine radical cation (see pages 39-40).

Electron transfer and hydrogen abstraction processes are favoured by decreasing ionization potential of the hydrogen - or electron-donor. However, electron transfer processes are more sensitive to small changes in the substrate molecule than are hydrogen abstraction processes. Changing from an N-acetyl substituted phthalimide (8) to an N-benzoyl substituted phthalimide (9) may be sufficient to change the primary photoprocess from hydrogen abstraction to electron transfer.

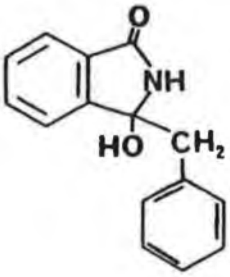
Irradiation of N-benzoylphthalimide in both toluene and propan-2-ol resulted in the lactone (218) being produced. Toluene is well established as both a hydrogen atom donor and an electron donor. While alcohols are good hydrogen atom donors their involvement in electron transfer reactions is very rare. Symons,[117] however, has shown using electron spin resonance evidence that methanol can undergo electron transfer under certain conditions and this may perhaps be true of propan-2-ol.

Irradiation of N-alkyl[69] and N-acylphthalimides in toluene lead to photoproducts. However, the photochemical behaviour of phthalimide (132) with toluene has never been published. It was, therefore, decided to irradiate phthalimide in toluene to see what photoproducts, if any, were formed.

3.9 The Photochemical Reaction of Phthalimide (132) with Toluene

Phthalimide (132) is only sparingly soluble in toluene. When a saturated solution of phthalimide in toluene was irradiated through Pyrex, TLC showed the appearance of one additional spot. Chromatographic separation of the reaction mixture led to the isolation of this product (80%). Its infra-red spectrum showed a sharp peak (3200cm^{-1}) protruding from a broader peak, consistent with the presence of an OH, or NH, or both groups. Also present were strong bands at 1695 and 1669cm^{-1} consistent with the presence of a carbonyl group.

The product was identified as the carbinol (231) following comparison of its infra-red spectrum and TLC with that of an authentic sample.

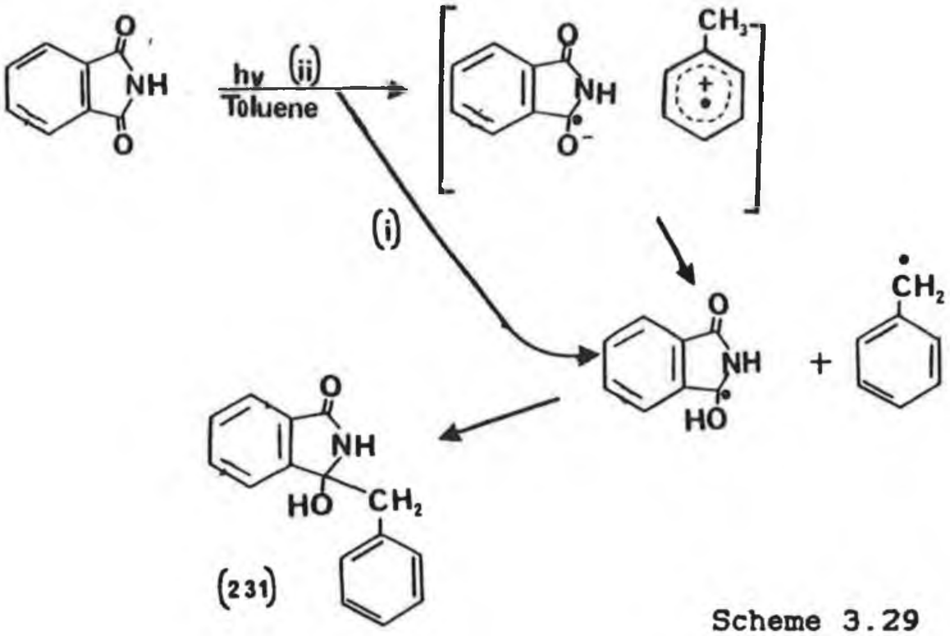


(231)

Scheme 3.28

The authentic sample was prepared by Grignard reaction of benzyl magnesium chloride with phthalimide (132) (see chapter five).

As for the carbinols (206), (209) and (210) produced on irradiation of NAP (8), NATCP (11) and NBTCP (12) respectively in toluene, the proposed mechanism for the formation of (231) involves either hydrogen abstraction [scheme 3.29 (i)] or electron transfer [scheme 3.29 (ii)] of the excited phthalimide from toluene as the primary photoprocess (scheme 3.29).

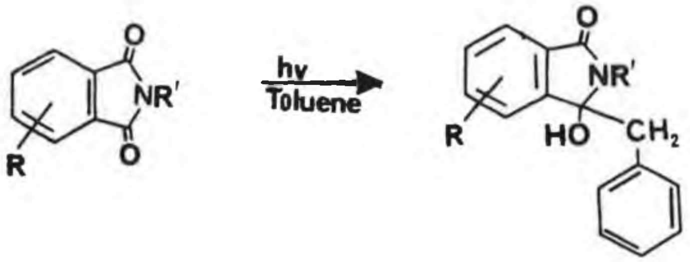


Scheme 3.29

3.10 Conclusions

Irradiation of NAP (8), NATCP (11) and NBTCP (12) in toluene gave carbinols (206), (209) and (210) respectively, analogous to the photochemical behaviour of N-methylphthalimide (101) in toluene.[69]

Two different primary photochemical processes were considered for the production of these carbinols, a hydrogen abstraction mechanism and an electron transfer mechanism.

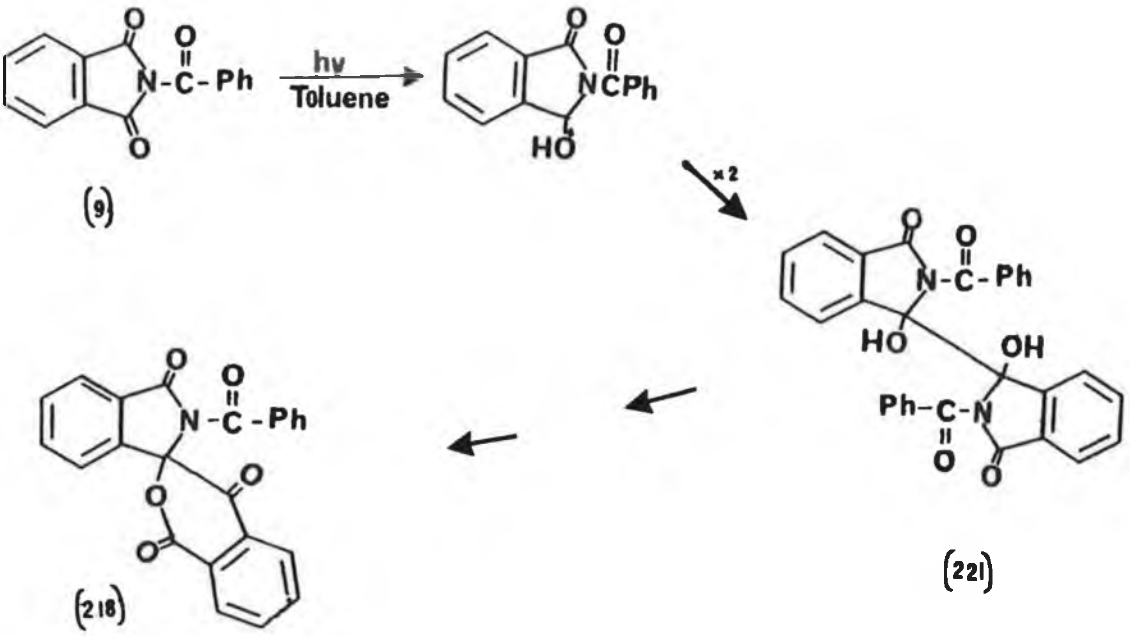


(108) R=H, R'=Me
(206) R=H, R'=Acetyl
(209) R=Cl, R'=Acetyl
(210) R=Cl, R'=Benzoyl

Scheme 3.30

The feasibility of electron transfer being the primary photoprocess was predicted by calculating ΔG (electron transfer) using the Weller equation^{7} (see page 82) for N-methylphthalimide- and N-methyl-3,4,5,6-tetrachlorophthalimide-toluene systems. Both of these systems gave negative ΔG values (-7.7 and -14.7 kcal mol^{-1} respectively) provided the excited state of the phthalimide was the singlet state. The singlet excitation energy and reduction potentials of NAP (8) and NATCP (11) would be anticipated to be similar to those of N-methylphthalimide (101) and N-methyl-3,4,5,6-tetrachlorophthalimide (194) respectively resulting in negative ΔG (electron transfer) values making electron transfer a possible primary photoprocess.

Irradiation of N-benzoylphthalimide (9) in toluene gave the lactone (218) as the major product by a postulated mechanism involving the pinacol (221) as an intermediate (scheme 3.31).



Scheme 3.31

As for the formation of the carbinols (206), (209) and (210) two different primary photochemical processes were considered, a hydrogen abstraction mechanism and an electron transfer mechanism. Why NAP (8), NATCP (11) and NBTCP (12) should behave so differently from NBP (9) in their excited state reactions with toluene is not yet clear. The following explanations were suggested:

(i) the four N-acylphthalimides undergo hydrogen abstraction from toluene as the primary photoprocess. The ketyl radicals obtained from NAP (8), NATCP (11) and NBTCP (12) combine with the benzyl radical in a solvent cage to give the observed carbinols. The NBP derived ketyl radical however, escapes from the solvent cage and undergoes dimerization to form the pinacol (221) which subsequently gives the lactone (218);

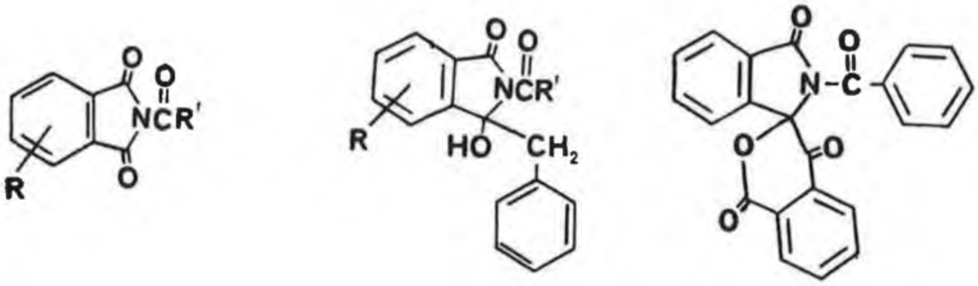
(ii) the four N-acylphthalimides undergo electron transfer as the primary photoprocess. The radical anions derived from NAP (8), NATCP (11) and NBTCP (12) remain in a solvent cage and subsequently yield the respective carbinols whereas the radical anion derived from NBP (9) escapes the solvent cage, dimerizes and subsequently forms the lactone (218);

(iii) the carbinol forming N-acylphthalimides undergo hydrogen abstraction whereas N-benzoylphthalimide (9) undergoes electron transfer as the primary photoprocess. The radical anion derived from NBP escapes the solvent cage and subsequently yields the lactone (218). The ketyl radicals derived from NAP, NATCP and NBTCP however do not escape the solvent cage and subsequently form the respective carbinols.

CHAPTER 4

In the last chapter it was reported that the N-acylphthalimides (8), (11) and (12) yielded the carbinols (206), (209) and (210) respectively as the major product on irradiation in toluene. This type of reaction is common to the phthalimide system in general, having been previously reported for N-alkylphthalimides.[69] N-Benzoylphthalimide (9) was an exception, forming the spirolactone (218) as the major product.

It was of interest to see how these same N-acylphthalimides would behave when irradiated in the presence of an alkene such as cyclohexene.



(218)

(8) R = H, R'= Me
(9) R = H, R'= Ph
(11) R = Cl, R'= Me
(12) R = Cl, R'= Ph

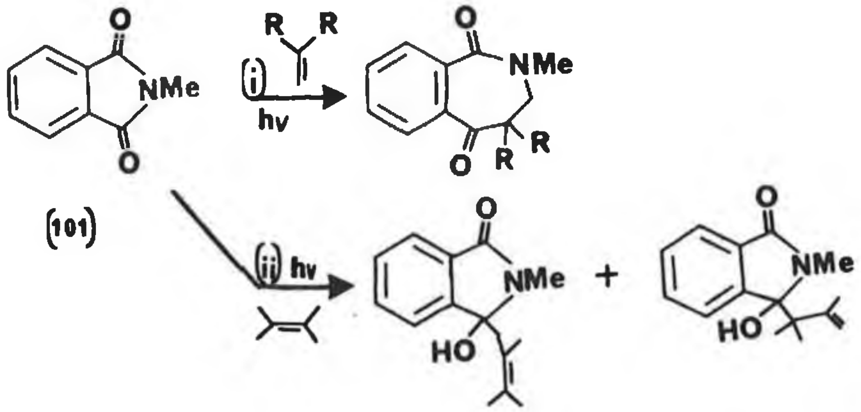
(206) R = H, R'= Me
(209) R = Cl, R'= Me
(210) R = Cl, R'= Ph

Scheme 4.1

The photochemical reactions of phthalimides and alkenes have been extensively studied (see chapter two for review of this topic). In summary the photochemistry is characterized by two major processes:

(i) the addition of the alkene to the C(O)-N bond, resulting in the formation of a ring expanded benzazepinedione[63,64,95,96,97] [scheme 4.2 (i)],

(ii) a photoreduction reaction, for example photoreduction of N-methylphthalimide (101) by 2,3-dimethyl-but-2-ene[106] [scheme 4.2 (ii)].



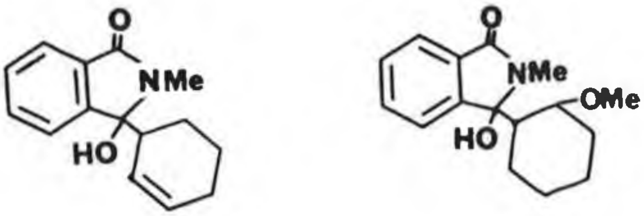
Scheme 4.2

Benzazepinedione formation occurs by $\pi^2 + \sigma^2$ concerted addition of the alkene to the C(O)-N bond of the excited imide. This $\pi^2 + \sigma^2$ addition occurs where ΔG for electron transfer from the alkene to the excited phthalimide is positive. When ΔG is negative, electron transfer effectively competes with $\pi^2 + \sigma^2$ addition and photoreduced phthalimides are observed[101] e.g. scheme 4.2 (ii).

4.1 The Photochemical Reaction of N-Benzoylphthalimide (9) with Cyclohexene

Kanaoka and co-workers first reported the photochemical reaction of a phthalimide with cyclohexene.[68] They found that irradiation of N-methylphthalimide and cyclohexene in acetonitrile gave the photoreduced product (232) as the only product. This result was confirmed on separate occasions by the Mazzocchi[101] and Maruyama[105] groups.

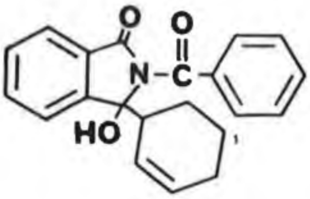
It was initially reported that the photoreduced product (232) arises by direct hydrogen abstraction via the N-methylphthalimide (n,π^*) triplet state. However, careful examination of the literature on this subject made it apparent that there was a distinct lack of experimental evidence to support these conclusions. Maruyama and co-workers showed that the photoreduction of N-methylphthalimide (101) by cyclohexene was occuring by initial electron transfer, by trapping of the radical cation-radical anion pair with methanol to form a diastereomeric mixture of (233),(27%).[105] Also formed from this reaction was a diastereomeric mixture of (232).



(232) (233)

Scheme 4.3

Irradiation of N-benzoylphthalimide (NBP) (9) in toluene or in the presence of propan-2-ol yielded the spirolactone (218), a product whose structural type has not previously been encountered in phthalimide photochemistry. Irradiation of N-benzoylphthalimide (NBP) (9) in the presence of cyclohexene, which contains a readily abstractable allylic hydrogen as well as a potential electron donating double bond, might well be expected to also give rise to the lactone (218). An alternative photoreaction of NBP with cyclohexene may be photoreduction to yield (234).



(234)

Scheme 4.4

When a solution of NBP (9) (0.038 M) and cyclohexene (0.797 M) in dichloromethane was irradiated through Pyrex, three additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to the isolation of the major product (80%, m.p. 138-140°C). The two other products were present in very small amounts and were not isolated. The microanalytical results showed a molecular formula of $C_{21}H_{19}NO_3$, consistent with a 1:1 NBP/cyclohexene adduct and confirmed by the presence of a molecular ion peak at m/e 333 in the mass spectrum. The infra-red spectrum showed strong bands at 2929, 1717 and 1694cm^{-1} consistent with the presence of a cyclohexane derived moiety and carbonyl groups. No absorbance was present between 4000 and 3000cm^{-1}, indicating the absence of a hydroxyl group and thus ruling out the photoadduct structure (234). The ^{1}H nmr spectrum showed a ten hydrogen multiplet between δ2.10 and 1.11 consistent with the presence of the cyclohexane ring. The spectrum also showed the replacement of the normal AA' BB' pattern for the aromatic phthalimide hydrogens by what appeared to be three olefinic protons and an aliphatic proton (see table 9). These observations suggest addition of the alkene across the aromatic ring of the phthalimide moiety. The five proton multiplet in the region δ7.89-7.47 corresponds to a phenyl group. This multiplet had the same profile as the corresponding portion of the ^{1}H nmr spectrum of NBP (9), consistent with formation of the product by reaction at the phthalimide benzo group rather than the benoyl group.

TABLE 9. Spectral data obtained from the ^{1}H nmr spectrum of the major product (243a) obtained on irradiation of NBP in the presence of cyclohexene.

δ(ppm)	Assignment	Multiplicity	Integration	Coupling Constants
7.89-7.47	Benzoyl	m	5	-
7.10	H_a Vinyl	d	1	J=6Hz
6.82	H_b Vinyl	d,d	1	J=6Hz, 7Hz
6.16	H_c Vinyl	d	1	J=7Hz
3.76	H_d Allylic	t	1	J=6Hz
2.10-1.11	Cyclohexene derived	m	10	-

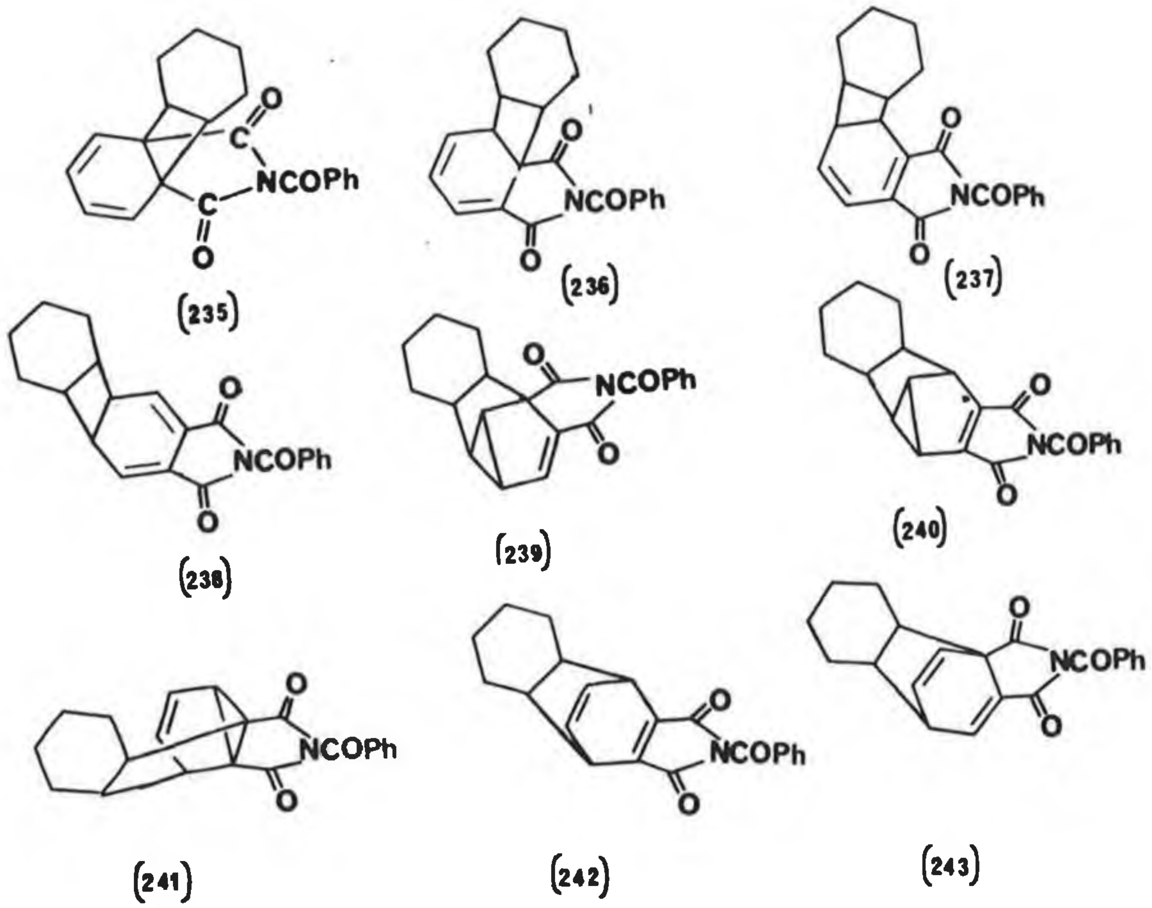
The ^{13}C nmr spectrum of the major product (Table 10), showed a total of nineteen peaks, consistent with an unsymmetrical addition of cyclohexene to NBP. There are eight peaks between δ27.4 and 56.2. These can be assigned to the six carbons of the cyclohexane moiety and the two bridgehead carbons from the original aromatic ring in the NBP molecule. The ^{13}C nmr spectrum also showed three peaks at δ173.0, 157.1 and 162.3, assigned to three non-equivalent carbonyl carbons, and eight peaks between δ143.3 and 123.5, assigned to sp^2 alkene and aromatic carbons.

TABLE 10. Spectral data from the ^{13}C nmr spectrum of the major product (243a) obtained on irradiation of NBP in the presence of cyclohexene.

δ(ppm)	Assignment	δ(ppm)	Assignment
173.0			
167.1	Carbonyl		
162.3		56.2	
		52.5	
143.3		50.7	Aliphatic
141.7		45.7	
137.3	Vinyl + Aromatic	32.7	
134.8		30.2	
131.9		27.7	
130.4		27.4	
128.8			
123.5			

Ignoring stereoisomers, there are nine possible structural adducts arising from the addition of cyclohexene across the benzo group of NBP. They are: four 1,2-adducts (235)-(238) three 1,3-adducts (239)-(241), and two 1,4-adducts (242)-(243). The data from the ^{13}C and ^{1}H nmr spectra eliminated the symmetrical 1,2- and 1,4- addition products, (235), (238) and (242). Nineteen peaks were observed in the ^{13}C nmr spectrum whereas only twelve would be expected for these symmetrical adducts providing cis addition occurred. More might be expected if trans addition occurred. However, the ^{1}H nmr spectrum showed three vinylic protons present in the product whereas only two would be expected for structures (237) and (238) and four for (235). Similarly, 1,2-adduct structure (237) may be eliminated since it should also only show the presence of two vinylic hydrogens and two allylic hydrogens. The 1,3-adducts (239)-(241) were also ruled out as possible structures because:

(i) only one vinylic proton would be expected for (239)



Scheme 4.5

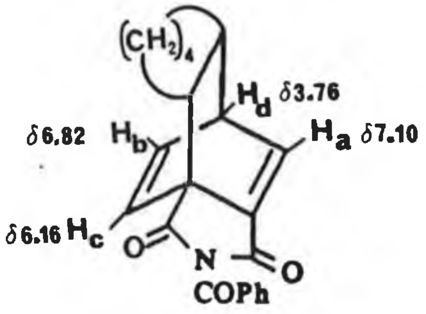
whereas three were observed in the ^{1}H nmr spectrum. Also only six peaks between δ150–120 would be expected in the ^{13}C nmr spectrum instead of the eight observed;

(ii) no vinylic protons would be expected in the ^{1}H nmr spectrum for structure (240). Also only six peaks between δ150–120 would be expected in the ^{13}C nmr;

(iii) for structure (241) only two vinylic protons would be expected from the ^{1}H nmr spectrum and six peaks between δ150–120 from the ^{13}C nmr spectrum.

The structures (236) and (243) were both consistent with the data obtained from the ^{13}C nmr spectrum (table 10).

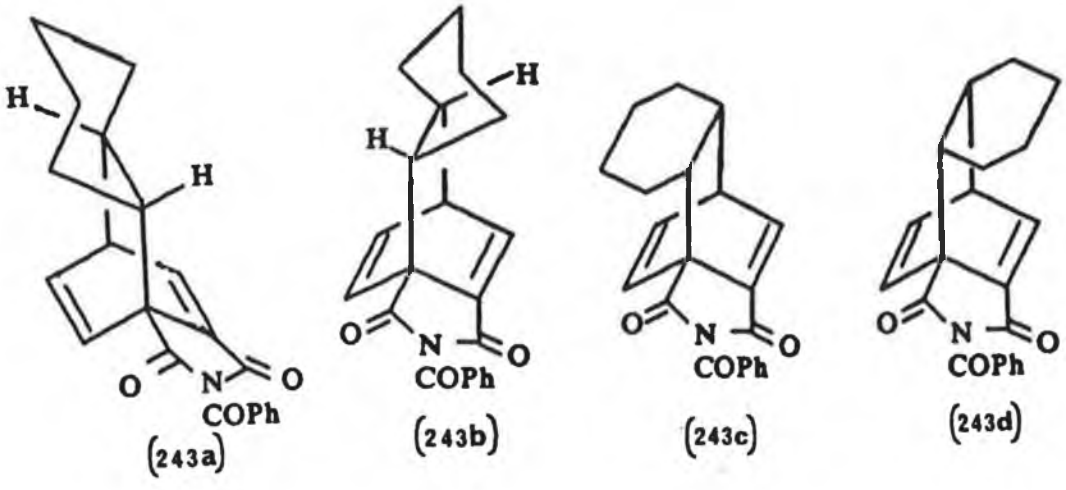
Both structures were also consistent with the chemical shifts and integrations of the signals obtained from the ^1H nmr spectrum (table 9) of the product. However, analysis of the multiplicities of the vinylic protons (table 9) permitted a distinction to be made between structures (236) and (243). Structure (236) would be expected to exhibit two doublet of doublets and one doublet absorption for its vinylic protons whereas for structure (243) one doublet of doublet and two doublet absorptions would be expected, consistent with the data obtained. The photoproduct was therefore assigned the 1,4-adduct structure (243) (scheme 4.6).



(243)

Scheme 4.6

The product, to which 1,4-cycloadduct structure (243) has been assigned, could be one of four stereoisomers, the exo, trans- (243a), endo, trans- (243b), exo, cis- (243c) or endo, cis- (243d) (scheme 4.7).



(243a) (243b) (243c) (243d)

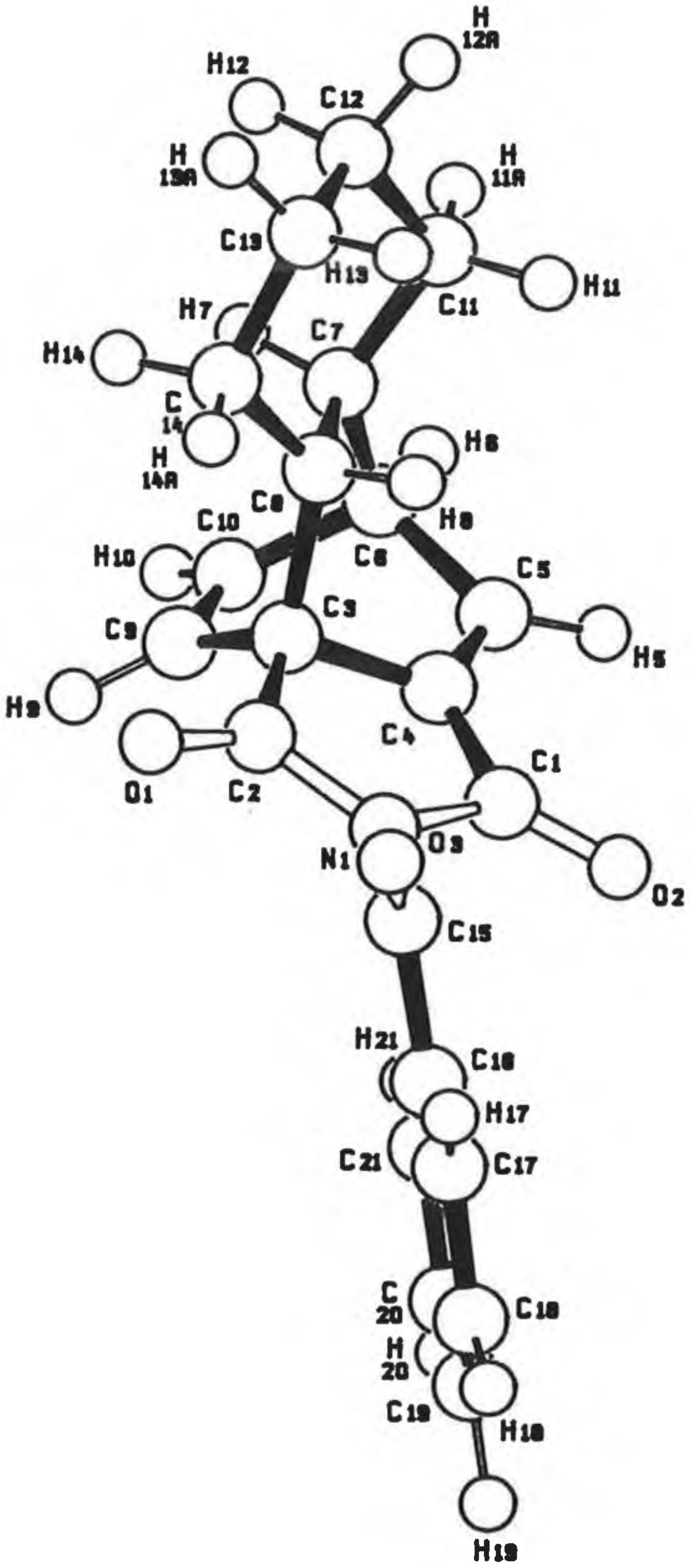
Scheme 4.7

X-Ray structure determination proved conclusively that the 1,4-cycloadduct (243) isolated from the irradiation of N-benzoylphthalimide in the presence of cyclohexene was the trans-isomer (243a). A projection of the structure (243a) is presented in scheme 4.8. The bond lengths, atomic coordinates and bond angles are listed in tables 11, 12 and 13 respectively.

The mechanism for the formation of (243a) is discussed in section 4.5.

TABLE 11. Bond lengths for the exo, trans-1,4-cycloadduct (243a) as obtained by x-ray techniques.

Atom A	Atom B	Distance (Å)	Atom A	Atom B	Distance (Å)
O 1	C 2	1.197	C16	C21	1.390
N 1	C 1	1.434	C 3	C 9	1.503
N 1	C 2	1.403	C 3	C 4	1.507
N 1	C15	1.444	C 3	C 8	1.584
O 2	C 1	1.195	C17	C18	1.391
O 3	C15	1.195	C 7	C 6	1.599
C 1	C 4	1.463	C 7	C11	1.502
C 2	C 3	1.508	C 7	C 8	1.510
C10	C 6	1.323	C 6	C 5	1.512
C10	C 9	1.326	C 4	C 5	1.335
C19	C18	1.371	C20	C21	1.390
C19	C20	1.361	C11	C12	1.527
C16	C17	1.377	C 8	C14	1.504
C16	C15	1.481	C12	C13	1.519
C14	C13	1.526			



Scheme 4.8 The exo, trans-1,4-cycloadduct (243a).

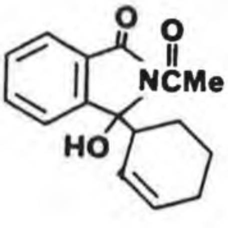
TABLE 13. Bond angles for the exo, trans-1,4-cycloadduct (243a) as obtained by x-ray techniques.

Atom A	Atom B	Atom C	Angles (ABC)	Atom A	Atom B	Atom C	Angles (ABC)
N 1	C 2	O 1	124.5	C 3	C 2	O 1	127.7
C 2	N 1	C 1	113.7	C15	N 1	C 1	124.4
O 2	C 1	N 1	124.1	C 4	C 1	N 1	104.4
C15	N 1	C 2	121.3	C 3	C 2	N 1	107.8
O 3	C15	N 1	118.1	C16	C15	N 1	118.0
C 4	C 1	O 2	131.5	C16	C15	O 3	123.8
C 3	C 4	C 1	110.7	C 5	C 4	C 1	133.4
C 9	C 3	C 2	118.5	C 4	C 3	C 2	103.4
C 8	C 3	C 2	114.0	C 9	C10	C 6	114.6
C 7	C 6	C10	99.7	C 5	C 6	C10	109.1
C 3	C 9	C10	113.2	C20	C19	C18	120.2
C17	C18	C19	120.7	C21	C20	C19	120.2
C15	C16	C17	117.7	C21	C16	C17	119.9
C18	C17	C16	119.3	C21	C16	C15	122.4
C20	C21	C16	119.7	C 4	C 3	C 9	108.6
C 8	C 3	C 9	109.4	C 8	C 3	C 4	101.2
C 5	C 4	C 3	115.7	C 7	C 8	C 3	107.6
C14	C 8	C 3	123.7	C11	C 7	C 6	121.1
C 8	C 7	C 6	108.5	C 5	C 6	C 7	109.3
C 8	C 7	C11	110.2	C11	C12	C 7	107.1
C14	C 8	C 7	109.9	C 4	C 5	C 6	111.8
C13	C12	C11	114.2	C13	C14	C 8	107.8
C14	C13	C12	114.2				

4.2 The Photochemical Reaction of N-Acetylphthalimide with Cyclohexene

When a solution of N-acetylphthalimide (8) (NAP) (0.088 M) and cyclohexene (1.760 M) in dichloromethane was irradiated through Pyrex, two additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to the isolation of two products.

The minor product (4%, m.p. 114-116°C), eluted marginally before the major product. The infra-red spectrum of the minor product showed strong bands at 3416, (OH), 1733 (C=O) and 1670cm^{-1} (C=C). The infra-red spectrum also contained relatively strong absorption at 2926cm^{-1} (aliphatic CH) consistent with the presence of a cyclohexene derived ring in the product. The data obtained from the infra-red spectrum suggests that the minor product may be the carbinol (244). Assignment of the structure (244) to the minor photoproduct was supported by analysis of its ^{1}H nmr spectrum. The spectrum contained



(244)

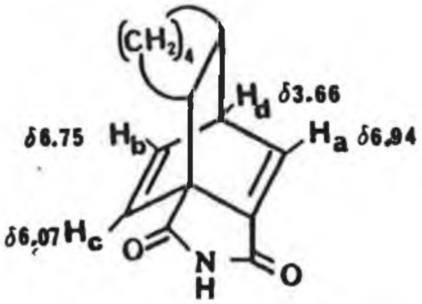
Scheme 4.9

a four-hydrogen multiplet due to the aromatic protons (δ7.9-7.5), two one-hydrogen multiplets at δ6.2 and δ5.9 consistent with the presence of two vinyl protons, and a one proton singlet (δ5.0) due to the hydroxyl group. Also present were a one-hydrogen multiplet (δ3.6), a three hydrogen singlet (δ2.7) and a six-hydrogen multiplet (δ2.0-1.3) due to methine, methyl and methylene groups respectively.

The major product (60% , m.p. 162-164°C) eluted marginally behind the minor product (244) and before the starting material, N-acetylphthalimide. The microanalytical results suggested a molecular formula $C_{14}H_{15}NO_2$.
The mass spectrum yielded a molecular ion at m/e 229 consistent with the molecular formula which corresponds to a 1:1 NAP/cyclohexene adduct minus CH_2O. The infra-red spectrum showed strong bands at 3179 (NH), 3062 (aromatic

CH) 2927 and 2856 (aliphatic CH) 1756 and 1709cm^{-1} (C=O). Also present was a band at 1645cm^{-1} consistent with the presence of C=C groups. The ^{1}H nmr spectrum showed a broad signal at δ8.84 consistent with the presence of an NH group. The spectrum also showed the replacement of the normal AA'BB' pattern for the aromatic hydrogens of a phthalimide by what appeared to be three olefinic protons (see table 14). Also present was one allylic hydrogen at δ3.66, and a ten hydrogen multiplet between δ2.00 and 1.80. Absent from the spectrum however was a three hydrogen singlet, evidence for the absence of an acetyl group from the product. This major product would seem to formally arise from addition of the cyclohexene across the aromatic moiety of phthalimide. Ignoring stereoisomers there are nine possible structural adducts arising from such an addition. These isomers are analogous to those shown in scheme 4.5 for the addition of cyclohexene to NBP.

The 1,4-adduct (245) (scheme 4.10) was the only structure consistent with the ^{1}H and ^{13}C nmr data obtained for the major product (tables 14 and 15). The explanations for ruling out the other eight isomers are the same as those used to eliminate isomers (235)-(242) as the product isolated from irradiation of NBP in the presence of cyclohexene (pages 108-110).



(245)

Scheme 4.10

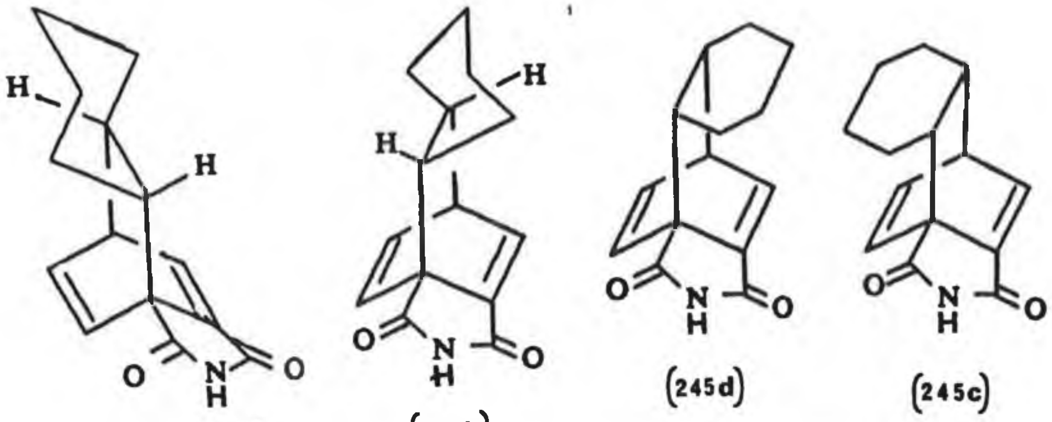
Table 14. ^1H nmr spectral data of major product (245) and exo, trans 1,4-cycloadduct (243a).

Assignment	Multiplicity	Integration	Coupling Constant	(245) δ/ppm	(243a) δ/ppm
NH	s	1	–	8.84	
Vinylic H_a	d	1	J=6Hz	6.94	7.10
Vinylic H_b	d,d	1	J=6,7Hz	6.75	6.82
Vinylic H_c	d	1	J=7Hz	6.07	6.16
Allylic H_d	t	1	J=6Hz	3.66	3.76
Cyclohexene derived	m	10	–	2.00	1.80

Table 15. ^{13}C nmr spectral data of major product (245) and exo, trans 1,4-cycloadduct (243a).

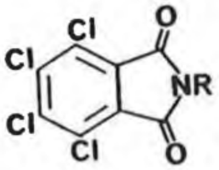
Assignment	δ/ppm (245)	δ/ppm (243a)
Carbonyl	175.9 165.3	173.0 167.2 162.3
Vinyl C,s	145.3 141.5 134.9 123.6	143.3 141.7 137.3 123.6
Bridgehead C,s	56.6 51.9 51.0 45.4	56.5 52.5 50.7 45.7
CH_2	32.7 30.2 27.7 27.5	32.7 30.2 27.7 27.4

The remarkable similarities between the spectral data (^1H and ^{13}C nmr, tables 14 and 15) for (243a) and the cycloadduct (245) obtained on irradiation of NAP in the presence of cyclohexene strongly suggests that, of the four possible stereoisomers of general stucture (245) (scheme 4.11), stereostructure (245a) is the most appropiate to be assigned to the isolated 1,4-adduct (245).


(245a) (245b) (245d) (245c)

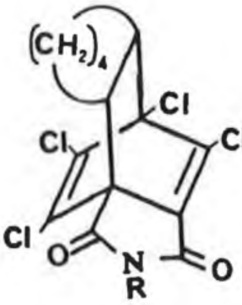
Scheme 4.11

Consideration of results from previous work[112] concerning the 1,4-addition of cyclohexene to N-methyl and N-ethyl-3,4,5,6-tetrachlorophthalimide, (194) and (246) respectively, adds further weight to the assignment of the exo, trans stereochemistry (245a) to product (245), as detailed in the following discussion.


(246) R= Et
(194) R=Me

Scheme 4.12

Grimley[112] has shown that irradiation of N-methyl-3,4,5,6-tetrachlorophthalimide (194) in the presence of cyclohexene with acetonitrile as solvent led to the formation of two products represented by the general structure (247). Irradiation of N-ethyl-3,4,5,6-tetrachlorophthalimide under the same conditions resulted in two products of the general structure (248).

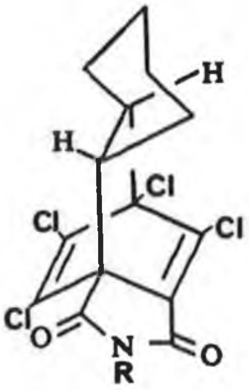


(247) R=Me

(248) R=Et

Scheme 4.13

Spectroscopic data[112] (^{1}H and ^{13}C nmr, ir and mass spectra) failed to elucidate the precise stereochemistry of these four products. Recently x-ray crystallography has confirmed the major and minor product from the irradiation of N-ethyl-3,4,5,6-tetrachlorophthalimide in the presence of cyclohexene as the trans-isomers (248b) and (248a) respectively. A projection of (248b) and (248a) as obtained by x-ray techniques is presented in schemes 4.15 and 4.16.

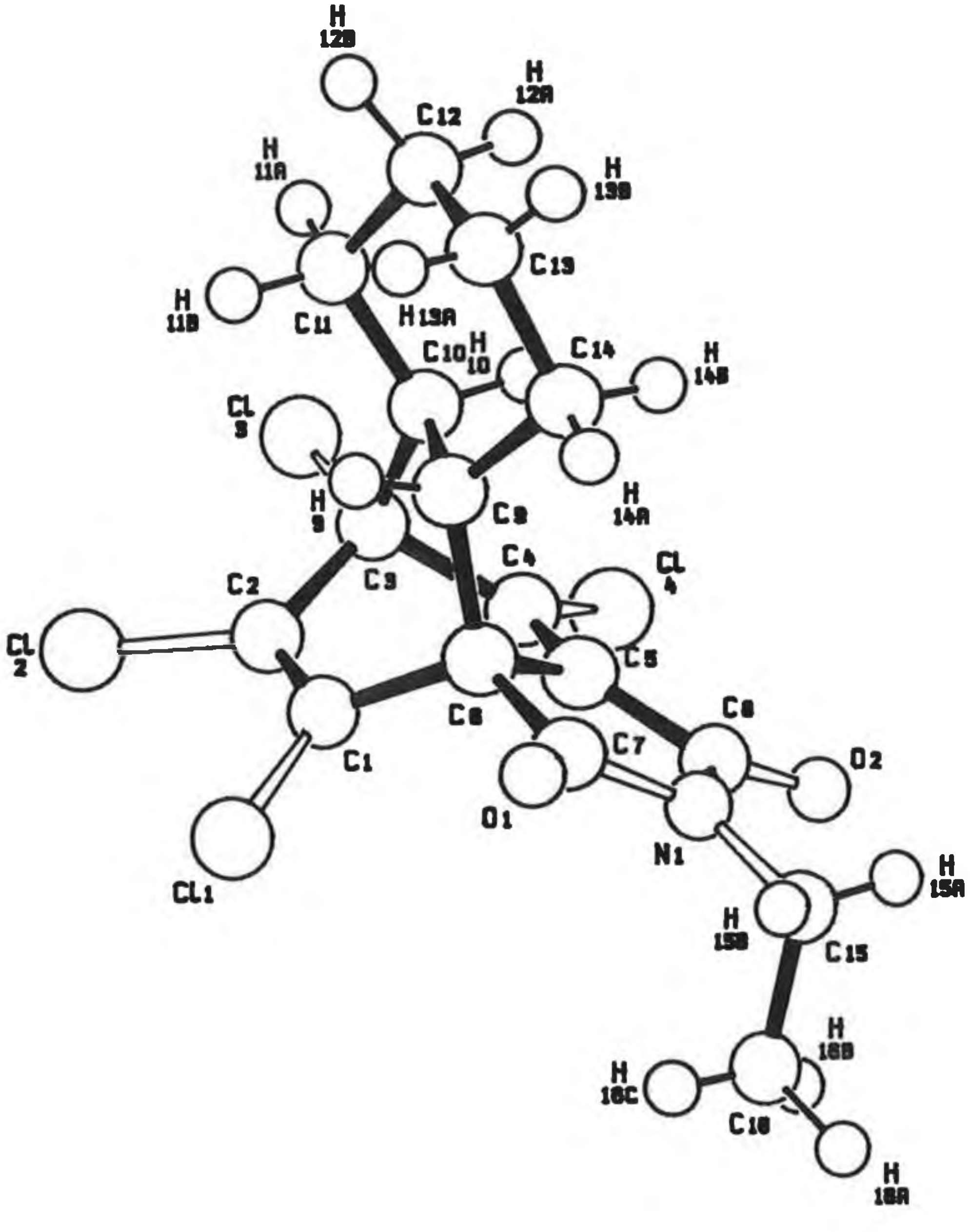


(247b) R=Me

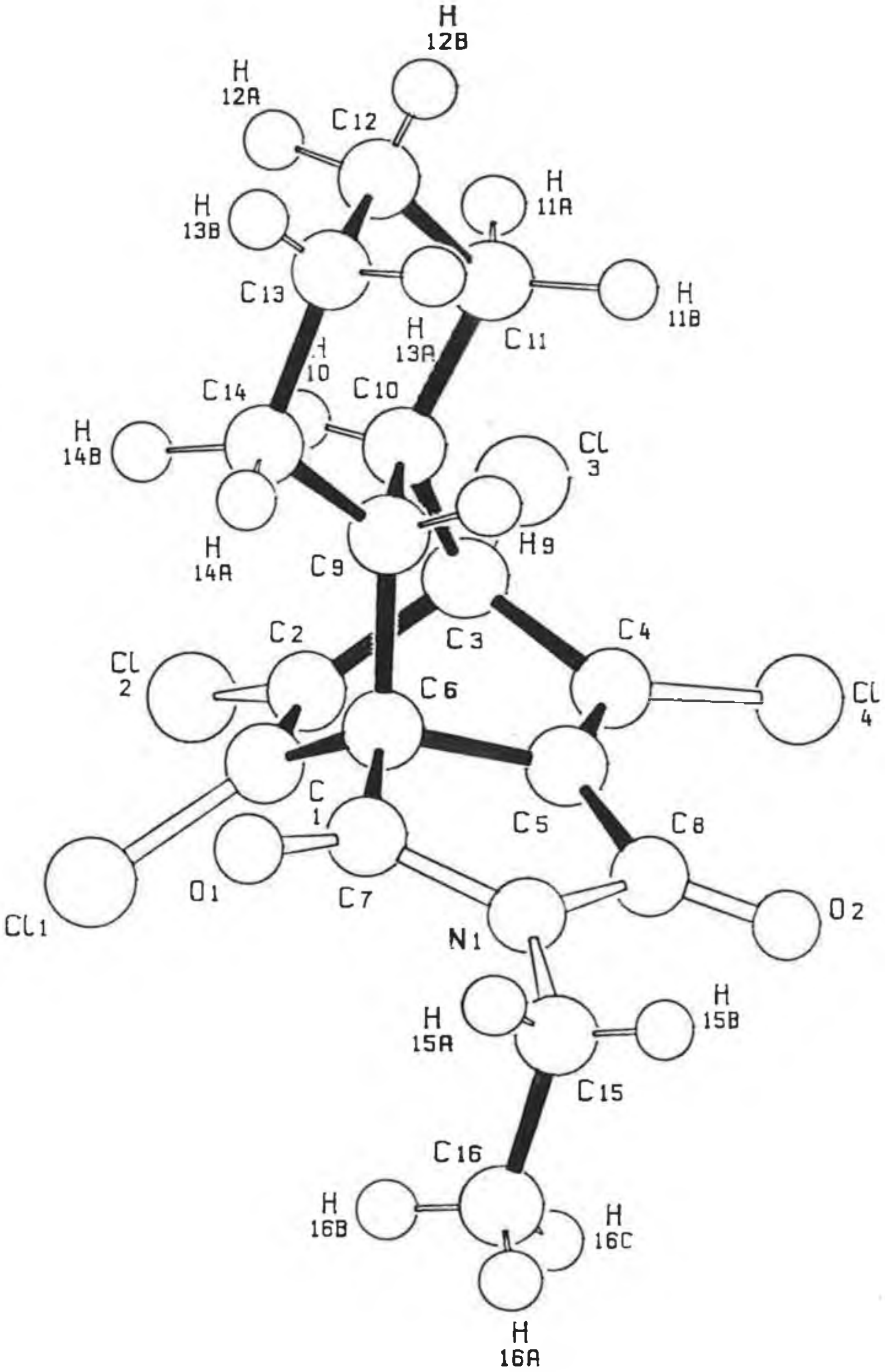
(248b) R=Et

Scheme 4.14

Table 16 lists some of the data obtained from the ^{13}C nmr spectra of (i) (248b), (ii) (248b)
obtained on irradiation of N-ethyl-3,4,5,6-tetrachlorophthalimide in the presence of cyclohexene, in addition to (iii) the major and (iv) the minor isomers represented by the general structure (247) obtained on irradiation of N-methyl-3,4,5,6-tetrachlorophthalimide in



Scheme 4.15 The endo, trans-1,4-cycloadduct (248b).



Scheme 4.15a The exo, trans-1,4-cycloadduct (248a)

the presence of cyclohexene.

Table 16. Some of the ^{13}C nmr spectral data for the trans-isomers (248b) and (248a) and two isomers represented by the general structure (247).

Assignment	δ (248b)	δ (248a)	δ Major isomer(247)	δ Minor isomer(247)
Carbonyl	168.3	168.1	168.6	169.0
	162.2	161.5	162.5	162.5
Vinylic C's	147.0	139.0	147.2	140.0
	133.0	138.5	132.9	137.5
	129.1	135.1	129.1	135.8
	125.6	123.5	125.5	125.5
Bridgehead C's	78.3	78.5	78.3	79.6
	58.4	58.7	58.6	59.5
	57.3	57.9	57.3	59.1
	51.7	53.4	51.8	53.2
CH_2	29.3	29.2	29.3	30.8
	28.7	27.0	28.9	29.6
	27.0	27.0	26.9	27.8
	26.6	26.9	26.6	27.6

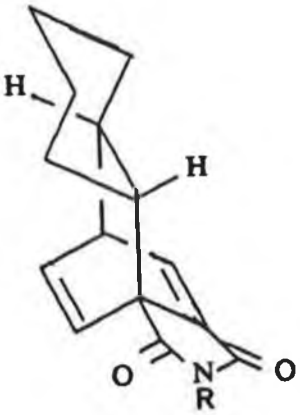
Table 16 shows:

(i) significant differences in the chemical shifts for the two isomers of (248), especially for the vinylic carbons; similar differences are evident for the two isomers of (247), and

(ii) remarkable similarities between the ^{13}C nmr data for (248b) and the major isomer of (247), the chemical shifts for these two products being so similar that the biggest difference for any one carbon in 0.3ppm.

These observations suggest that the major product from the irradiation of N-methyl-3,4,5,6-tetrachlorophthalimide in the presence of cyclohexene was the endo, trans-isomer

(247b). Futher evidence for this was found on studying the ^{1}H nmr signals due to the cyclohexene derived moiety of the minor and major isomers represented by structures (247) and (248). This region (δ2.2–0.9) for the two isolated isomers represented by structure (247) revealed obvious differences in profile; similar differences were evident for the two isolated isomers of (248). These differences arise from the different stereochemistries of the cyclohexane derived moiety in each isomer pair. However, this region (δ2.2–0.9) for the two major isomers represented by structures (247) and (248) were very similar also arguing in favour of their having identical stereochemistry. Comparison of the ^{1}H nmr spectra of (243a) and the 1,4-cycloadduct (245) showed that the regions between δ2.2 and δ0.9 were very similar for the two compounds. This lends added weight to the assignment of exo, trans structure (245a) to the primary 1,4-cycloadduct obtained on irradiation of NAP (8) in the presence of cyclohexene.

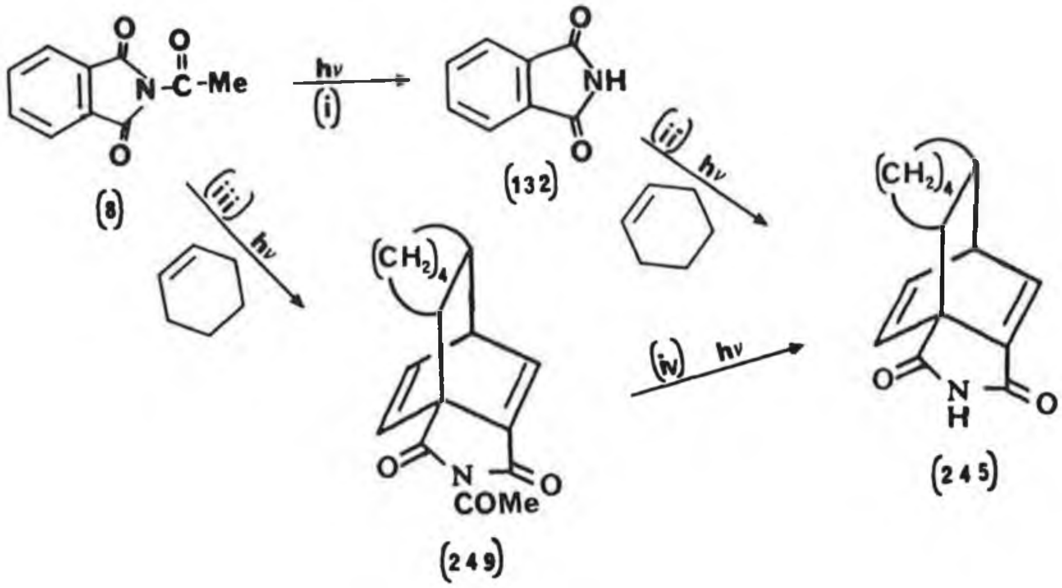


(243a) R=COPh
(245a) R=H
(249a) R=COMe

Scheme 4.16

The product (245a) is believed to be produced by a secondary rapid deacetylation of (249a), believed to be the primary photoproduct (scheme 4.17). Irradiation

(35hrs) of NAP (8) (1.37g) in dichloromethane (300ml) yielded 30mgs of phthalimide. Irradiation of NAP in the presence of cyclohexene under otherwise similar conditions gave 80mgs of the 1,4-cycloadduct (245). These observations suggest that whilst deacetylation of NAP [scheme 4.17 (i)] followed by cycloaddition of cyclohexene to the resulting phthalimide [scheme 4.17 (ii)] is possible, it is a highly unlikely route for the formation of the cycloadduct (245).



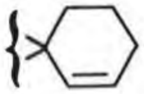
Scheme 4.17

Irradiation of NBP (9) and NAP (8) in the presence of cyclohexene gave isomerically pure 1,4-cycloadducts of the general structure (243) and (245) respectively. However, irradiation of phthalimide (132) in the presence of cyclohexene (discussed later in section 4.4) led to the isolation of a mixture of three stereoisomers of the general structure represented by (245). This lends added weight to deacetylation [scheme 4.17 (iv)] subsequent to cycloaddition [scheme 4.17 (iii)].

4.3 The Photochemical Reaction of N-Acetyl-3,4,5,6-tetrachlorophthalimide (11) with Cyclohexene.

When a solution of N-acetyl-3,4,5,6-tetrachlorophthalimide (NATCP) (11) (0.031M) and cyclohexene (0.642M) in dichloromethane was irradiated through Pyrex, three additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to the isolation of the major and one of the minor products. Repeated chromatography failed to isolate the other minor product.

The minor product isolated (5%, m.p. 128-131°C) eluted marginally before the non-isolated minor product. It's infra-red spectrum showed strong bands at 2938 (aliphatic CH), 1749 (C=O) and 1533cm^{-1} (C=C). The ^{1}H nmr spectrum showed one hydrogen signals at δ6.28 (d,t; J=9.9Hz, J=7.7Hz) and δ5.29 (d, J= 9.9Hz) as well as a six hydrogen multiplet between δ2.22 and δ1.26. These observations are consistent with the cyclohexene derived moiety (250) (scheme 4.18) present in the minor product.



(250)

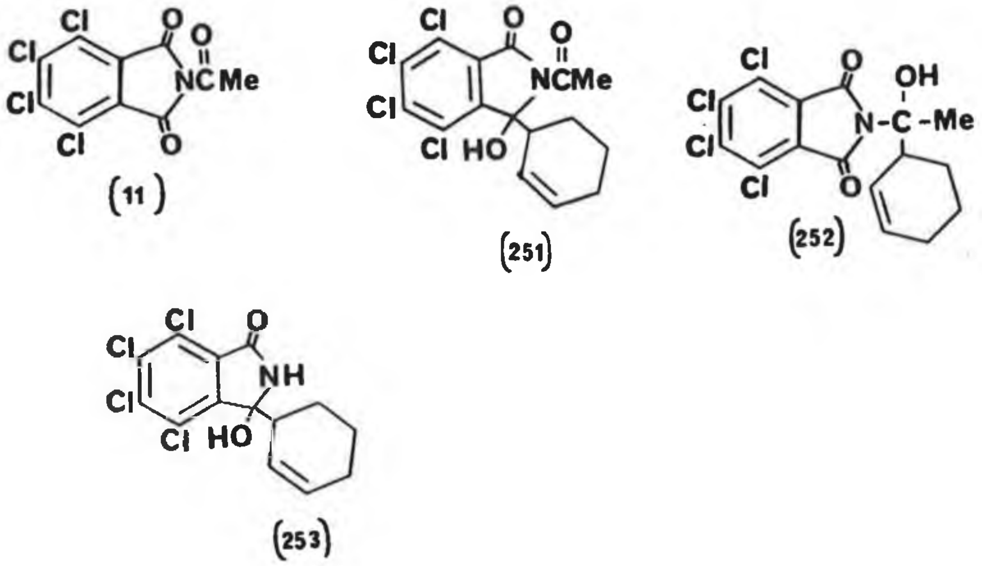
Scheme 4.18

The observations also rule out the minor product as arising from 1,2-, 1,3-, or 1,4- addition of the cyclohexene across the aromatic moiety of the NATCP (11) as no signals would be expected between δ7 and 5.

The carbinols (251)-(253) were also ruled out as possible structures for the minor product because:

(i) no bands were observed in the infra-red spectrum corresponding to NH or OH groups, and

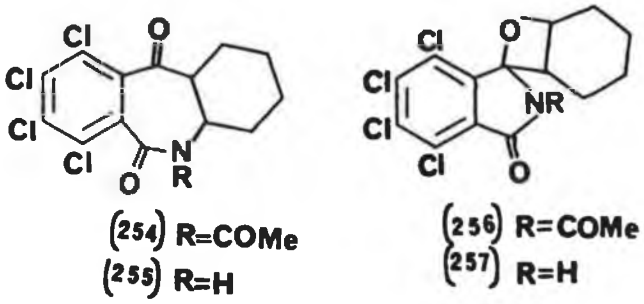
(ii) no signals were observed in the ^{1}H nmr spectrum corresponding to OH, NH or methyl groups.



(11) (251) (252) (253)

Scheme 4.19

Benzazepinediones (254) and (255), and the oxetanes (256) and (257) were also ruled out as possible structures for the minor product based on the ^{1}H nmr and infra-red spectral



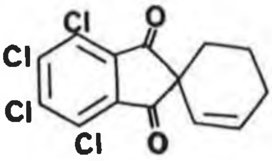
(254) R=COMe
(255) R=H
(256) R=COMe
(257) R=H

Scheme 4.20

data. The ^{1}H nmr spectum showed a six hydrogen multiplet between δ3 and 1 whereas a multiplet corresponding to a greater number of hydrogens would be expected for the structures (254)-(257). The ^{1}H nmr spectrum also showed one proton signals at δ6.3 and 5.3 again inconsistent with structures (254)-(257). The absence of a signal corresponding to a methyl group in the ^{1}H nmr spectrum and a NH group in the infra-red spectrum was futher evidence for ruling out structures (254)-(257).

Data obtained from the ^{13}C nmr spectrum of the minor product can be seen in table 17. Analysis of the DEPT (distortionless enhancement by polarization transfer) spectrum permitted elucidation of the numbers of hydrogens bonded to each different carbon. The DEPT analysis showed primary and tertiary carbons as peaks above the baseline, while secondary carbons showed as signals below the baseline. Quaternary carbons showed no signals on DEPT analysis. Using the DEPT observations and the chemical shifts for the different carbons present, it was possible to make assignments to each of the signals present in the ^{13}C nmr spectrum (table 17).

The infra-red, ^{1}H nmr and ^{13}C nmr data were consistent with (258) as the minor product. X-Ray diffraction analysis proved conclusively that the minor product was (258). A projection of the structure (258) is presented in scheme 4.22. Hydrogen atoms are omitted for clarity. The bond lengths, atomic coordinates and bond angles are listed in tables 18, 19 and 20 respectively.



(258)

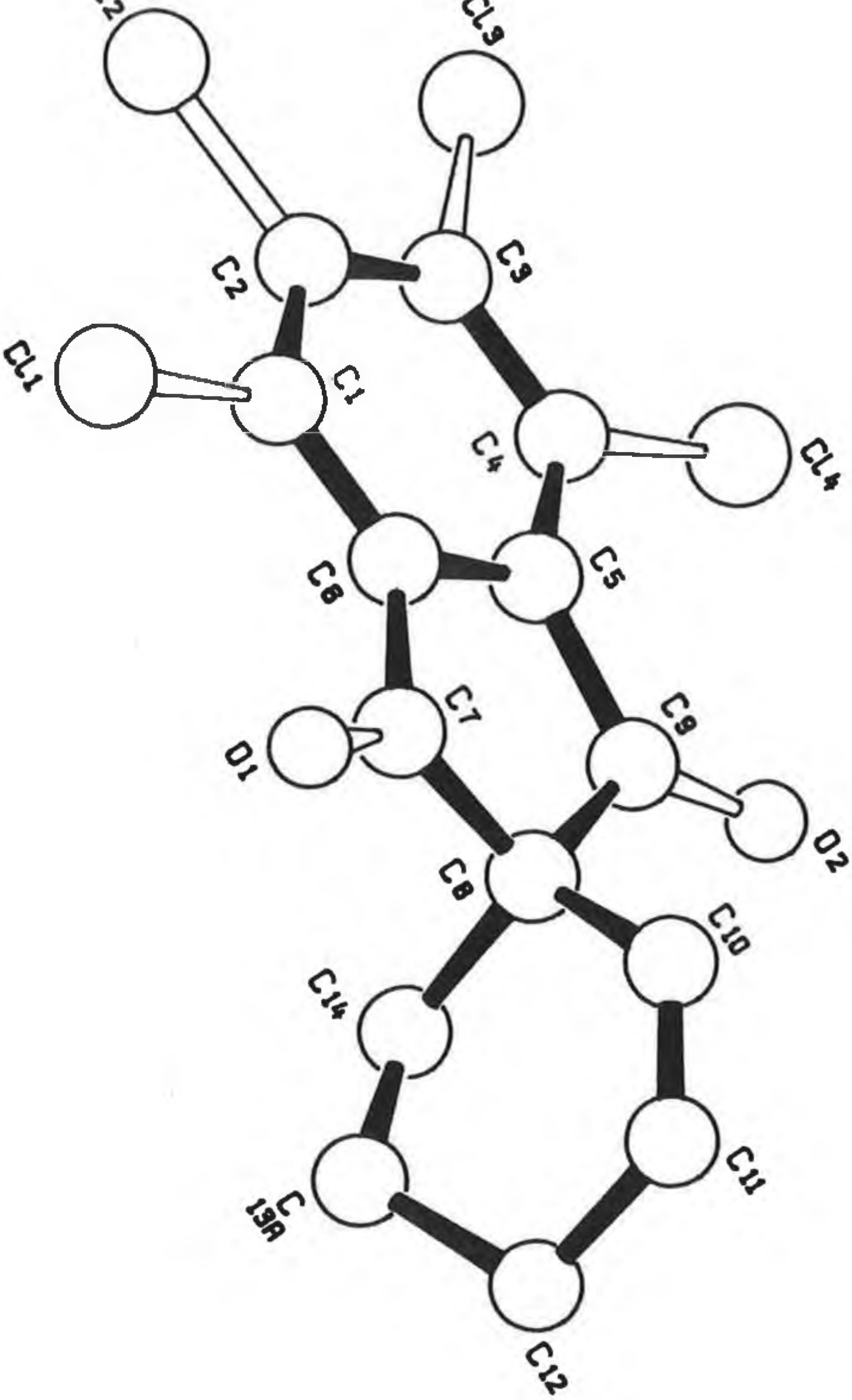
Scheme 4.21

TABLE 17. ^{13}C nmr spectral data for the minor product (258) obtained on irradiation of NATCP (11) in the presence of cyclohexene.

δ /ppm	$-CH_n$: n=	Assignment
197.1	0	C=O
142.0	0	C=C
135.6	0	C=C
135.1	1 or 3	-CH=C
131.1	0	C=C
119.8	1 or 3	-CH=C
56.7	0	C
28.7	2	CH
23.9	2	CH
17.7	2	CH

TABLE 18. Bond lengths for (258) as obtained by x-ray techniques.

Atom A	Atom B	Distance (Å)	Atom A	Atom B	Distance (Å)
C4	C14	1.725	C13b	C13a	0.961
C1	C6	1.396	C3	C111	1.708
C5	C6	1.383	C7	C6	1.501
C8	C9	1.523	O2	C9	1.208
C2	C3	1.392	C5	C9	1.493
C2	C1	1.372	C4	C3	1.392
C8	C7	1.521	C7	O1	1.201
C14	C8	1.569	C10	C8	1.511
C4	C5	1.379	C10	C11	1.301
C13a	C12	1.584	C11	C12	1.497
C13a	C14	1.333	C13b	C12	1.497
			C13b	C14	1.378



Scheme 4.22 The photoproduct (258)

TABLE 19. Atomic coordinates for the photoproduct (258) as obtained by x-ray techniques.

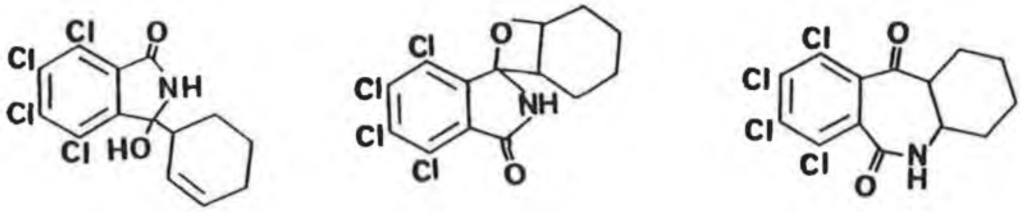
ATOM	X	Y	Z
Cl1	.4245	.2720	.0658
Cl2	.2670	.3988	-.1356
Cl3	.6880	.5475	-.3419
Cl4	.3988	.5342	-.3377
C6	.6265	.3485	-.0541
C9	.8228	.3959	-.1311
C3	.4860	.4652	-.2282
O2	.9013	.4411	-.1918
C1	.4964	.3463	-.0493
C2	.4280	.4033	-.1373
O1	.7023	.2471	.1235
C7	.7231	.2945	.0285
C8	.8499	.3112	.0297
C10	.9488	.3495	.0625
C5	.6846	.4104	-.1438
C12	1.0763	.1792	.0404
C14	.8872	.1991	-.0920
C4	.6159	.4689	-.2311
C11	1.0477	.2915	.0907
C13a	.9539	.1289	-.0222
C13b	1.0086	.1622	-.0809

TABLE 20. Bond angles for (258) as obtained by x-ray techniques

Atom A	Atom B	Atom C	Angles (ABC)	Atom A	Atom B	Atom C	Angles (ABC)
C7	C6	C1	130.2	C5	C6	C1	120.0
C5	C6	C7	109.7	C8	C9	O2	124.8
C5	C9	O2	126.6	C5	C9	C8	108.5
C2	C3	C13	120.4	C4	C3	C13	120.0
C4	C3	C2	119.6	C6	C1	C11	119.8
C2	C1	C11	121.3	C2	C1	C6	118.9
C3	C2	C12	119.0	C1	C2	C12	119.7
C1	C2	C3	121.3	O1	C7	C6	125.3
C8	C7	C6	107.8	C8	C7	O1	126.9
C7	C8	C9	103.2	C10	C8	C9	112.7
C10	C8	C7	112.8	C14	C8	C9	108.7
C14	C8	C7	107.4	C14	C8	C10	111.5
C11	C10	C8	122.9	C9	C5	C6	109.4
C4	C5	C6	121.0	C4	C5	C9	129.5
C13a	C12	C11	109.2	C13b	C12	C11	110.0
C13b	C12	C13a	36.2	C13a	C14	C8	116.5
C13b	C14	C8	119.4	C13b	C14	C13a	41.5
C3	C4	C14	119.7	C5	C4	C14	121.1
C5	C4	C3	119.1	C12	C11	C10	125.3
C14	C13a	C12	115.1	C13b	C13a	C12	67.0
C13b	C13a	C14	71.7	C14	C13b	C12	118.0
C13a	C13b	C12	76.8	C13a	C13b	C14	66.8

The major product (14.5%, m.p. 151-152°C) eluted marginally behind the starting material. Its infra-red spectrum showed bands at 3201 (NH), 2938 (aliphatic CH) and 1706cm^{-1} (C=O). Its ^{1}H nmr spectrum showed a broad singlet at δ 8.35 and a multiplet between δ 2.4 and δ 0.8. The ^{13}C nmr spectrum (table 21) showed peaks corresponding to two non-equivalent carbonyl groups, four non-equivalent vinylic or aromatic carbons and eight non-equivalent aliphatic carbons. The presence of a signal in the infra-red spectrum consistent with the presence of a NH group, and the absence of a three hydrogen signal at δ 2.7 corresponding to a methyl group in the ^{1}H nmr spectrum showed that this product did not contain an acetyl group. The spectral data suggests it to be a deacetylated 1:1 NATCP/cyclohexene adduct.

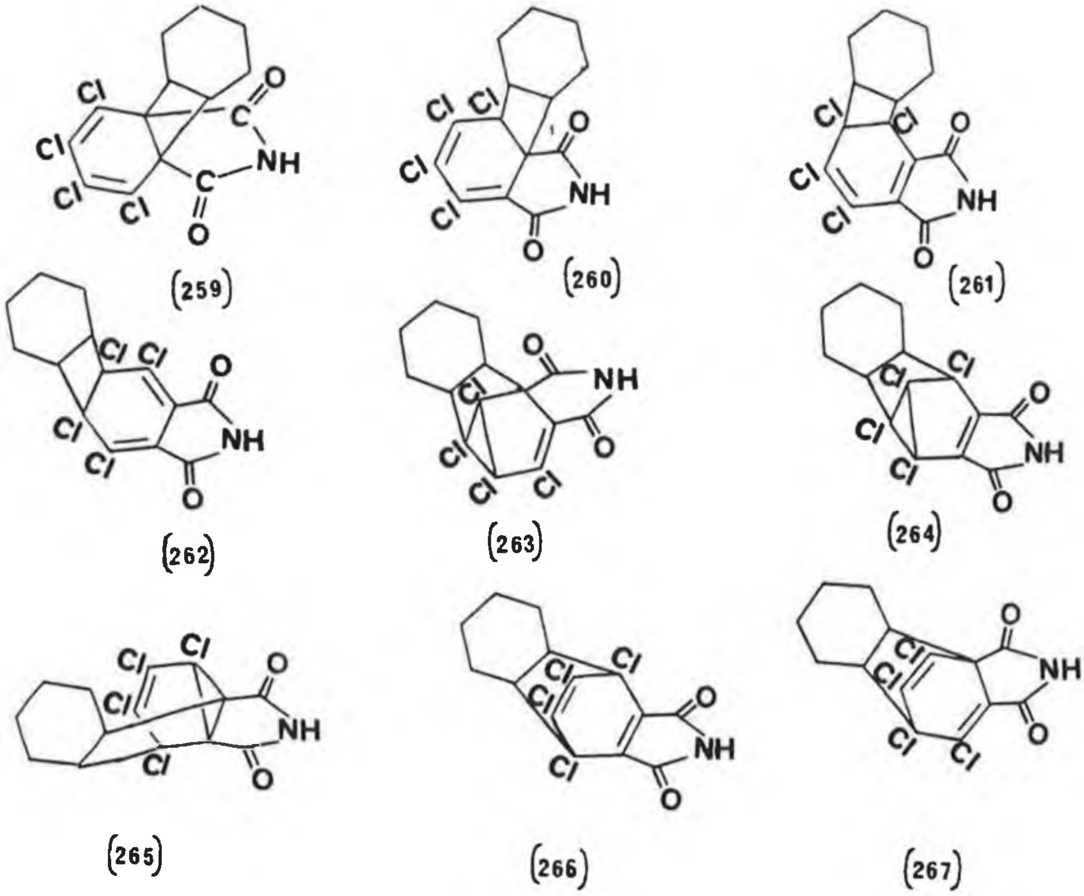
The carbinol (253), benzazepinedione (255) and oxetane (257) were all ruled out as possible structures for the major product based on ^{1}H and ^{13}C nmr spectral data. The absence of any vinylic protons in the ^{1}H nmr spectrum ruled out the carbinol (253). The ^{13}C nmr spectrum showed the presence of four non-equivalent aromatic or vinylic carbons and eight non-equivalent aliphatic carbons, inconsistent with the benzazepinedione (255) or oxetane (257). It is however consistent with a structure arising from the addition of cyclohexene across the benzo group of tetrachlorophthalimide or across the benzo group of NATCP followed by deacetylation.



(253) (257) (255)

Scheme 4.23

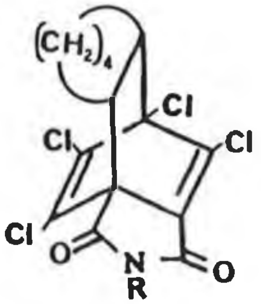
Ignoring stereoisomers, there are nine possible structural adducts arising from the addition of cyclohexene across the benzo group of tetrachlorophthalimide (259)-(267). Comparison of the ^{13}C nmr spectral data of this product with that of (248a) (table 21) obtained on irradiation of N-ethyl-3,4,5,6-tetrachlorophthalimide in the presence of cyclohexene suggests that the product is the 1,4-cycloadduct (267). Indeed the ^{13}C nmr spectral data (table 21) for (267) and (248a) are so similar it suggests that they are stereochemically identical.



Scheme 4.24

TABLE 21. ^{13}C nmr spectral data for the major product (267) obtained on irradiation of NATCP in the presence of cyclohexene and (248a).

Assignment	δ/ppm (267)	δ/ppm (248a)
Carbonyl	168.0	168.1
	161.0	161.5
Vinylic	139.1	139.0
	138.8	138.5
	135.3	135.1
	123.1	123.5
Aliphatic	78.5	78.5
	58.8	58.7
	58.2	57.9
	53.4	53.4
	29.1	29.2
	29.0	
	26.9	27.0
	26.8	26.9



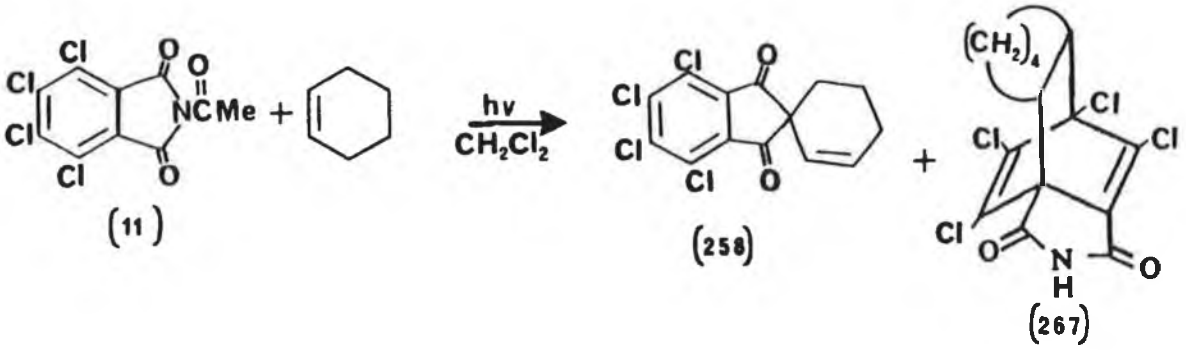
(248) R=Et

(267) R=H

Scheme 4.25

Comparison of the ^{1}H nmr spectra of (267) and (248b) showed that the regions between δ 2.5–0.8 were very similar for the two compounds, lending added weight to the suggestion that the two compounds have the same stereochemistry.

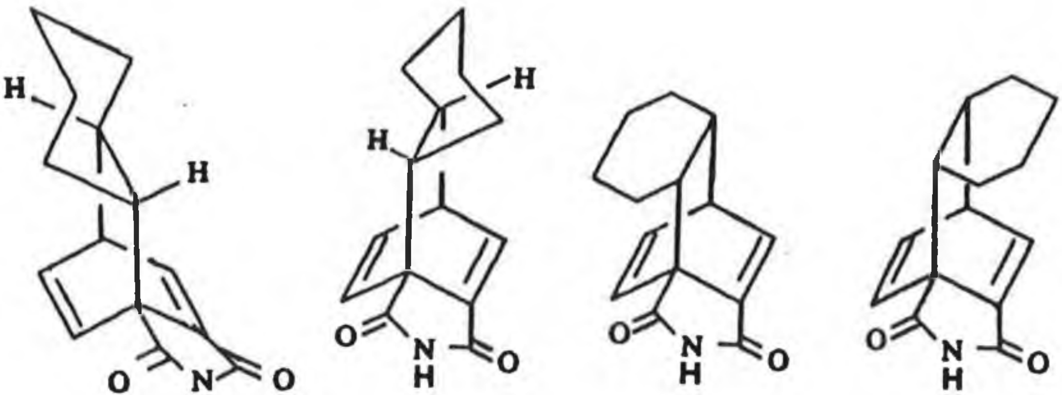
In summary, irradiation of NATCP (11) and cyclohexene in dichloromethane led to the isolation of two products (258) and (267) (scheme 4.26). The mechanism for the formation of these products is discussed later (section 4.5).



Scheme 4.26

4.4 The Photochemical Reaction of Phthalimide with Cyclohexene

Phthalimide is very insoluble in dichloromethane and so acetonitrile was used as co-solvent to ensure its dissolution during this part of the investigation. When a solution of phthalimide (0.038M) and cyclohexene (0.958M) in a acetonitrile/dichloromethane mixture was irradiated through Pyrex three additional spots were observed on TLC. Chromatographic separation of the reaction mixture led to the isolation of the major fraction. The two minor fractions were not isolated, being present in only trace amounts. The major fraction (26%, m.p. 128-131°C) eluted marginally behind the starting material, phthalimide. Its microanalysis was consistent with a 1:1 adduct of cyclohexene and phthalimide. Its infra-red spectrum showed strong bands at 3179 (NH), 2927 (aliphatic CH), 1759, 1707 (C=O) and 1227cm^{-1}. The mass spectrum was also consistent with the presence of a 1:1 phthalimide/cyclohexene adduct (M^+ 229). The ^{1}H nmr spectrum showed a ten hydrogen multiplet between δ 2.0 and 1.0 consistent with the presence of the cylohexene derived ring. The spectrum also showed the replacement of the normal AA' BB' pattern for the aromatic phthalimide hydrogens by what appeared to be vinylic and aliphatic protons. These vinylic and aliphatic protons existed as complex multiplets, inconsistent with the product being a single pure isomer. Integration showed the ratio of vinylic protons (δ7.7-6.0) to aliphatic protons (δ3.8-3.7) as 3:1, consistent with the presence of a number of the four possible stereoisomers of the 1,4-cycloadduct (245) (scheme 4.27).



(245a) (245b) (245c) (245d)

Scheme 4.27

Careful study of the ^1H nmr spectrum confirmed the presence in the mixture of the same isomeric 1,4-cycloadduct (245) as obtained on irradiation of NAP in the presence of cyclohexene, and for which the trans-structure (245a) has being suggested. Comparison of the signals in the vinylic region of the spectrum showed a significantly higher integration for the signals from this isomer. Trans-isomer (245a) was therefore the major isomer present in the mixture [1.0:1.2 (245a); other isomers represented by general structure (245)], calculated from ^1H nmr spectrum. Futher evidence for the presence of the trans-isomer (245a) was obtained from the ^{13}C nmr spectrum of the isolated fraction. This showed the presence of peaks with chemical shifts identical to all the peaks observed for the trans-isomers (245a) obtained on the irradiation of NAP in the presence of cyclohexene. The ^{13}C nmr spectrum consisted of at least thirty-seven peaks (table 22), showing that the major fraction contained at least three isomers.

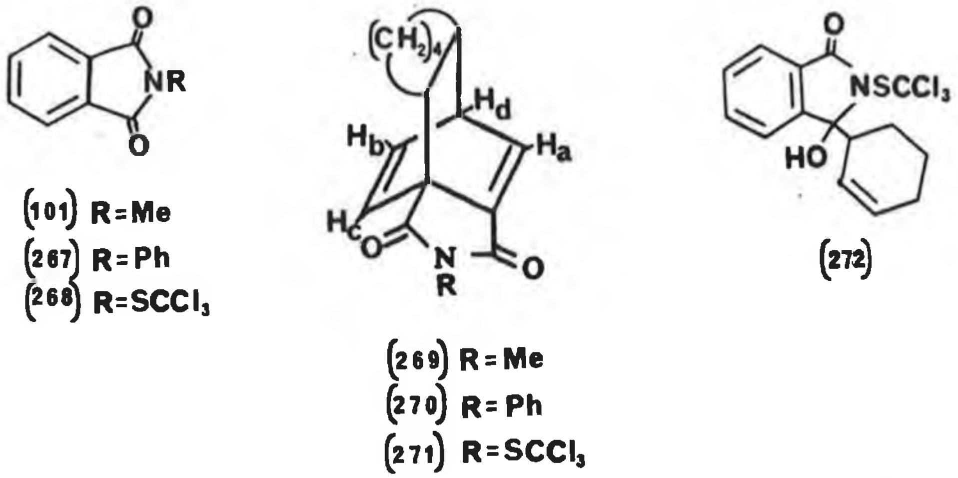
The ^1H nmr spectrum of the major fraction also showed other vinylic signals present which had chemical shifts,

TABLE 22. ^{13}C nmr spectral data of the major fraction obtained on irradiation of phthalimide in the presence of cyclohexene.

Assignment	δ/ppm	Assignment	δ/ppm
	176.4		56.8
(245a)	176.0		56.6
Carbonyl	166.5	(245a)	51.9
(245a)	165.4	(245a)	51.1
			50.4
	145.7		48.3
(245a)	145.4		45.9
(245a)	141.5	(245a)	45.4
	139.6		45.2
	137.8	Saturated	41.1
(245a)	134.9		39.3
	134.2	(245a)	32.7
Vinylic	134.0	(245a)	30.3
	130.7		29.3
	127.8		27.8
(245a)	123.6	(245a)	27.6
		(245a)	27.5
			27.3
			26.2
			22.7
			19.9
			19.8

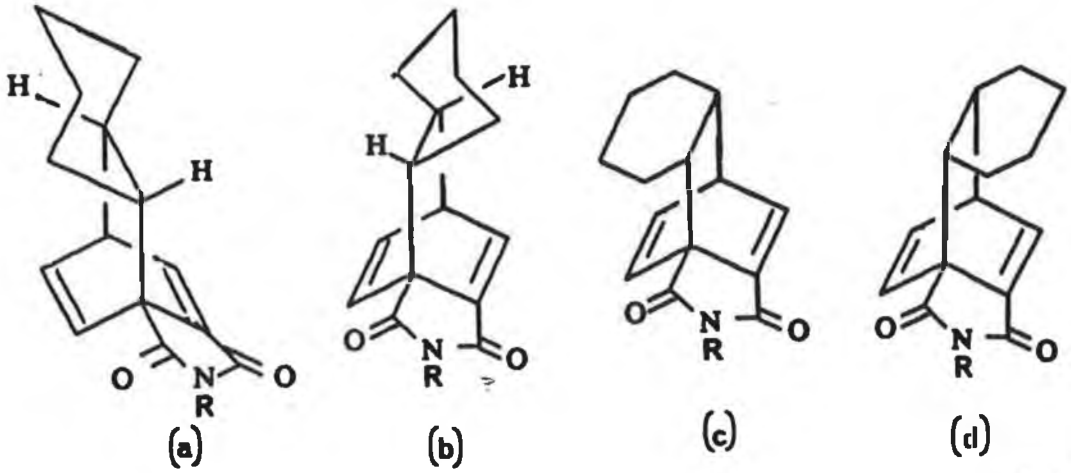
multiplicities and coupling constants similar to those obtained from a mixture of three stereoisomers of the 1,4-cycloadduct represented by structures (269) and (270) obtained by Schwack on irradiation of N-methylphthalimide (101) and N-phenylphthalimide (267) respectively in cyclohexene.[118]

Schwack[118] showed the major product from the irradiation of N-(trichloromethylthio)phthalimide (268) in cyclohexene to be the carbinol (272) (80%). The 1,4-cycloadduct (271) was a minor product (11%) but was found to be isomerically pure. The evidence for paracycloaddition was obtained by ^{1}H nmr analysis. Schwack observed, instead of the AA'BB' in the aromatic region three vinylic protons,



Scheme 4.28

i.e. δ 7.2 (d, J=6Hz, H_a), δ6.82 (dd, J=6Hz, 7Hz, H_b) and 6.15 (d, J=7Hz, H_c). It was shown from decoupling experiments that two of these protons were vicinal (H_b and H_c) and separated from the third (H_a) by H_d at δ3.81 (t, J=6Hz). From the three possible modes of addition (1,2-, 1,3-, 1,4-), only the 1,4-adduct was consistent with the observed pattern of three vinyl protons. Schwack assigned the 1,4-cycloadduct (271) as the exo, cis-isomer (271c) based on ^{1}H nmr studies of the isomeric mixtures of the 1,4-cycloadducts (269) and (270) obtained on irradiation of N-methylphthalimide and N-phenylphthalimide respectively in cyclohexene. The adducts (269) and (270) were major products and GC and HPLC analysis showed each to consist of three isomers. Schwack also assigned the exo, cis-isomer, (269c) and (270c), as the major stereo-isomer in the isomeric mixture of the 1,4-cycloadducts represented by the general structures (269) and (270) respectively. Below in table 23 can be seen the ^{1}H nmr spectral data for the 1,4-cycloadduct represented by the general structure (269). The table shows how the chemical shifts, multiplicities and coupling constants differ for each vinylic proton in each of the stereo-isomers. Analogous differences were observed for the isomeric mixture represented by the general structure (270).



(269) R=Me: (270) R=Ph: (271) R=SCCl$_3$

Scheme 4.29

Table 23. Some of the ^{1}H nmr spectral data from the isomeric mixture of the 1,4-cycloadduct represented by the general structure (269).

assig-nment	Major isomer		Minor Isomer A		Minor Isomer B	
	δ (ppm)	Coupling Const. (Hz)	δ (ppm)	Coupling Const. (Hz)	δ (ppm)	Coupling Const. (Hz)
H_a	6.92	d; 6	7.51	d; 6	7.16	d,d;6,0.8
H_b	6.77	d,d; 6,7	6.08	d,d; 6,7	6.40	m; 2H
H_c	6.07	d,t; 7,1	6.80	d,d;7,1.5		
H_d	3.65	t; 6	3.67	t; 6	3.77	m

Comparison of the ^{13}C nmr and ^{1}H nmr spectral data for (271) with that for stereo-isomer (243a) of known structure, suggests that the adduct (271) is not the exo, cis-isomer (271c) but rather the exo, trans-isomer (271a).

As can be seen from tables 24 and 25 the ^{13}C nmr and ^{1}H nmr spectral data for the adducts (243a) and (271) are remarkably similar. By analogy the major 1,4-cycloadduct isomer obtained on irradiation of N-methylphthalimide and N-phenylphthalimide in cyclohexene were the exo, trans-adducts (269a) and (270a) respectively.

TABLE 24. ^{1}H nmr spectral data for the protons H_a-H_d for 1,4-cycloadducts (243c) and (271).

Assignment	multiplicity	Integration	δ (ppm) (243a)	δ (ppm) (271)	Coupling Const. (243a)	Coupling Const. (271)
H_a	d	1	7.10	7.20	6Hz	6Hz
H_b	t	1	3.76	3.81	6Hz	6Hz
H_c	d	1	6.82	6.82	6, 7Hz	6, 7Hz
H_d	t	1	6.16	6.15	7Hz	7Hz

TABLE 25. Some of the ^{13}C nmr spectral data for (243c) and (271).

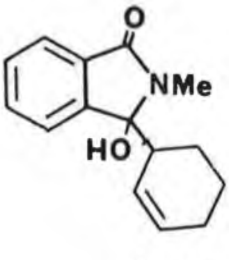
Assignment	δ (ppm)(243a)	δ (ppm)(271)	$\Delta\delta$
Aliphatic	27.4 27.7 30.2 32.7 45.7 50.7 52.5 56.5	27.4 27.6 30.2 32.7 45.8 50.6 52.9 56.4	0.0 0.1 0.0 0.0 0.1 0.1 0.4 0.2
Vinylic	123.6 137.3 141.7 143.3	123.4 138.3 141.4 142.7	0.2 1.0 0.3 0.6

To summarize, irradiation of phthalimide in the presence of cyclohexene led to the isolation of a mixture of three stereo-isomers of the 1,4-cycloadduct (245). The major isomer in the mixture was assigned the exo, trans-1,4-cycloadduct structure (245a). The other two stereo-isomers in the mixture were not identified.

The mechanism for the formation of the 1,4-cycloadduct (245) is discussed in section 4.5.

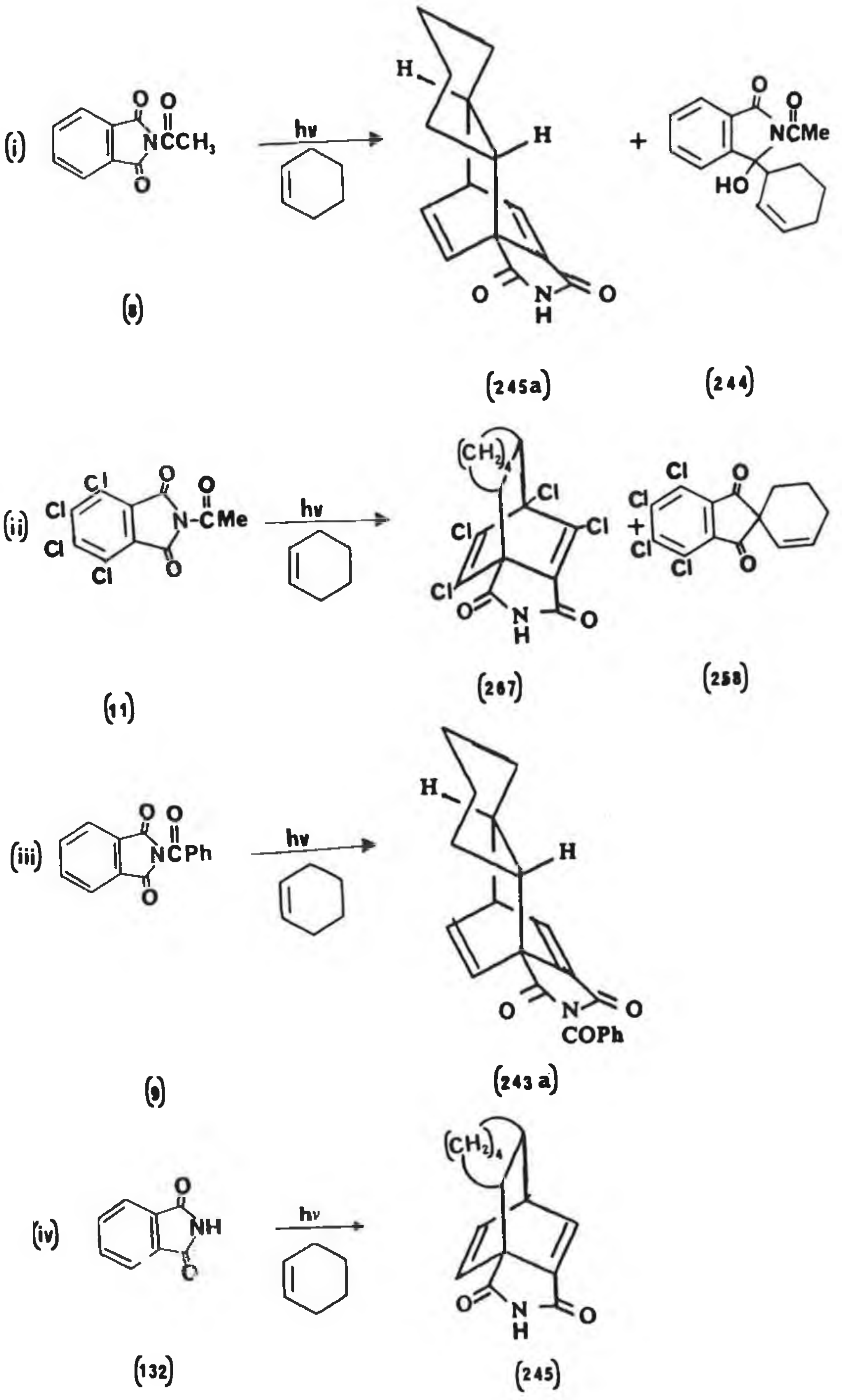
4.5 Discussion

Irradiation of NAP (8) in the presence of cyclohexene led to the isolation of two products (244) and (245) [scheme 4.30 (i)]. Carbinol formation on irradiation of N-alkylphthalimides in the presence of cyclohexene is well established.[68, 101, 105] Maruyama showed that the formation of the carbinol (232) on irradiation of N-methylphthalimide and cyclohexene in acetonitrile was ocurring by initial electron transfer via the (π,π^*) singlet state.[105] The carbinol (244) is probably formed by a similar process, i.e electron transfer to the excited N-acetylphthalimide followed by proton transfer and radical coupling (scheme 4.32).

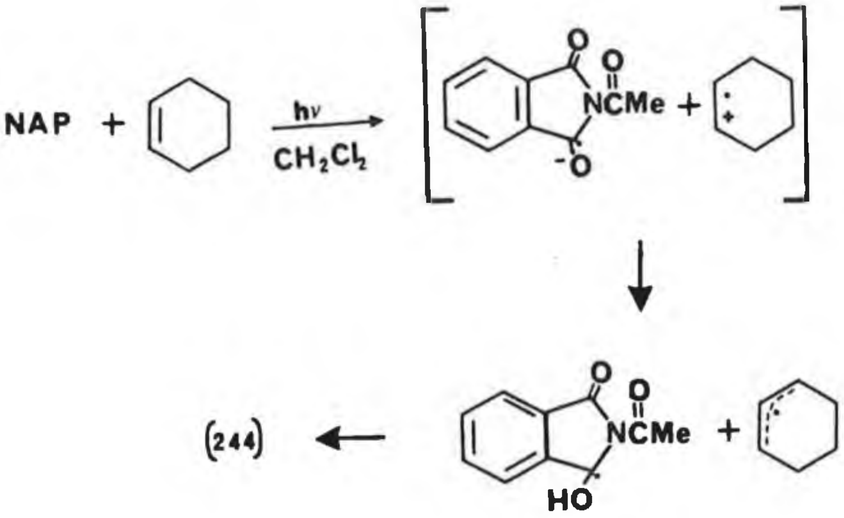


(232)

Scheme 4.31


(i)
NCCH3
hν
H
H
+
NCMe
HO
(8)
(245a)
(244)
(ii)
Cl
N-CMe
hν
(CH2)4
Cl
+
(11)
(267)
(258)
(iii)
NCPh
hν
H
H
COPh
(9)
(243 a)
(iv)
NH
hν
(CH2)4
(132)
(245)

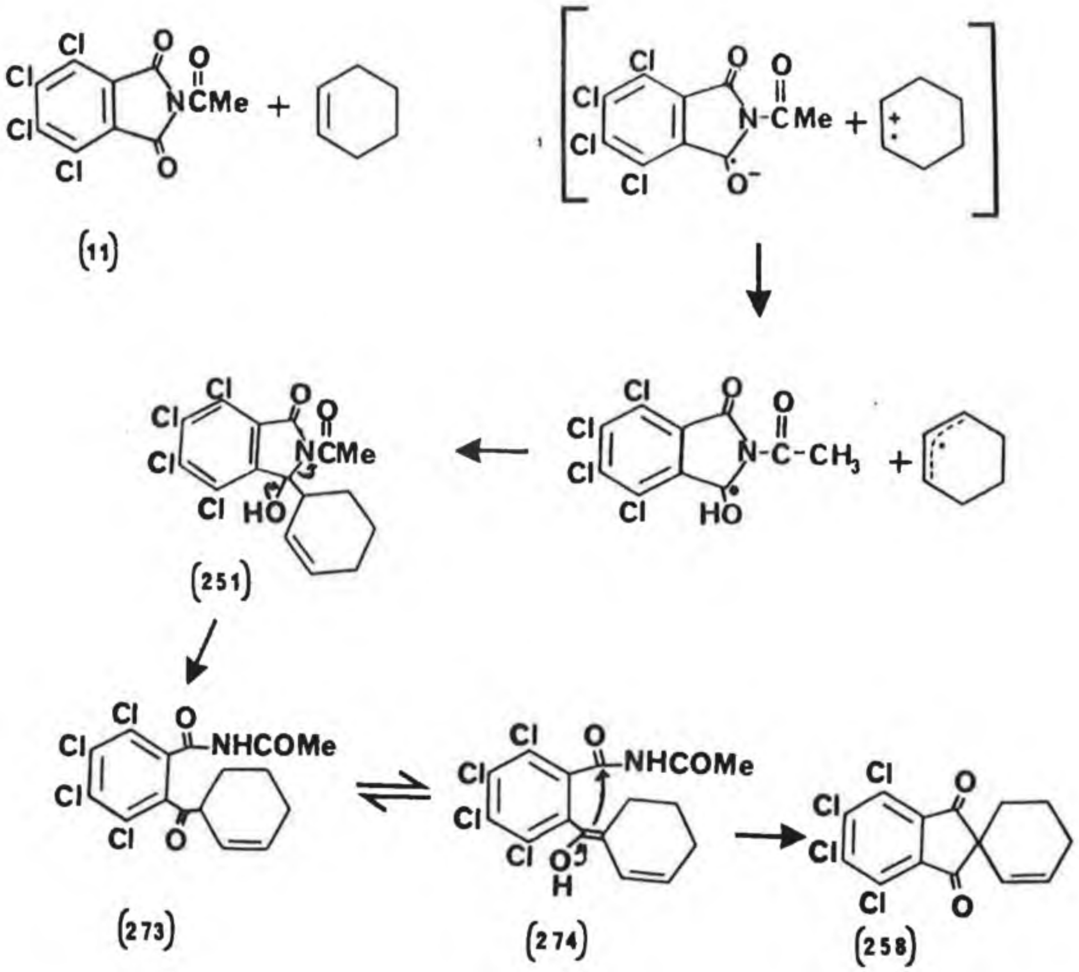
Scheme 4.30



Scheme 4.32

Irradiation of NATCP (11) in the presence of cyclohexene also led to the isolation of two products [scheme 4.30 (ii)], one of which was also a 1,4-cycloadduct, (267). The minor product (258) is unique in phthalimide photochemistry. Its formation might involve the carbinol (251) as an intermediate. The carbinol (251) may be formed by a similar process to the formation of the carbinol (232), i.e., electron transfer to the excited NATCP (11) followed by proton transfer and radical coupling (scheme 4.33). The carbinol (251) could then readily undergo ring opening to afford unsaturated ketone (273). Intramolecular nucleophilic attack by the enol (274) at the imide carbonyl would result in ring closure, with formation of the observed product (258) and the elimination of acetamide (scheme 4.33).

In competition with formation of (244) and (258) is 1,4-cycloaddition leading to (245) and (267) respectively [scheme 4.30 (i) and (ii)]. Coyle has shown the (n,π^*) and



Scheme 4.33

(π,π^*) states for some N-substituted phthalimides to be very close energetically. It is therefore possible that the (n,π^*) and (π,π^*) states for NAP (8) and NATCP (11) are also very close energetically. A number of possibilities arise for formation of the two different kinds of product [(258) and carbinol (244) versus 1,4-cyloadduct (267) and (245)] ;

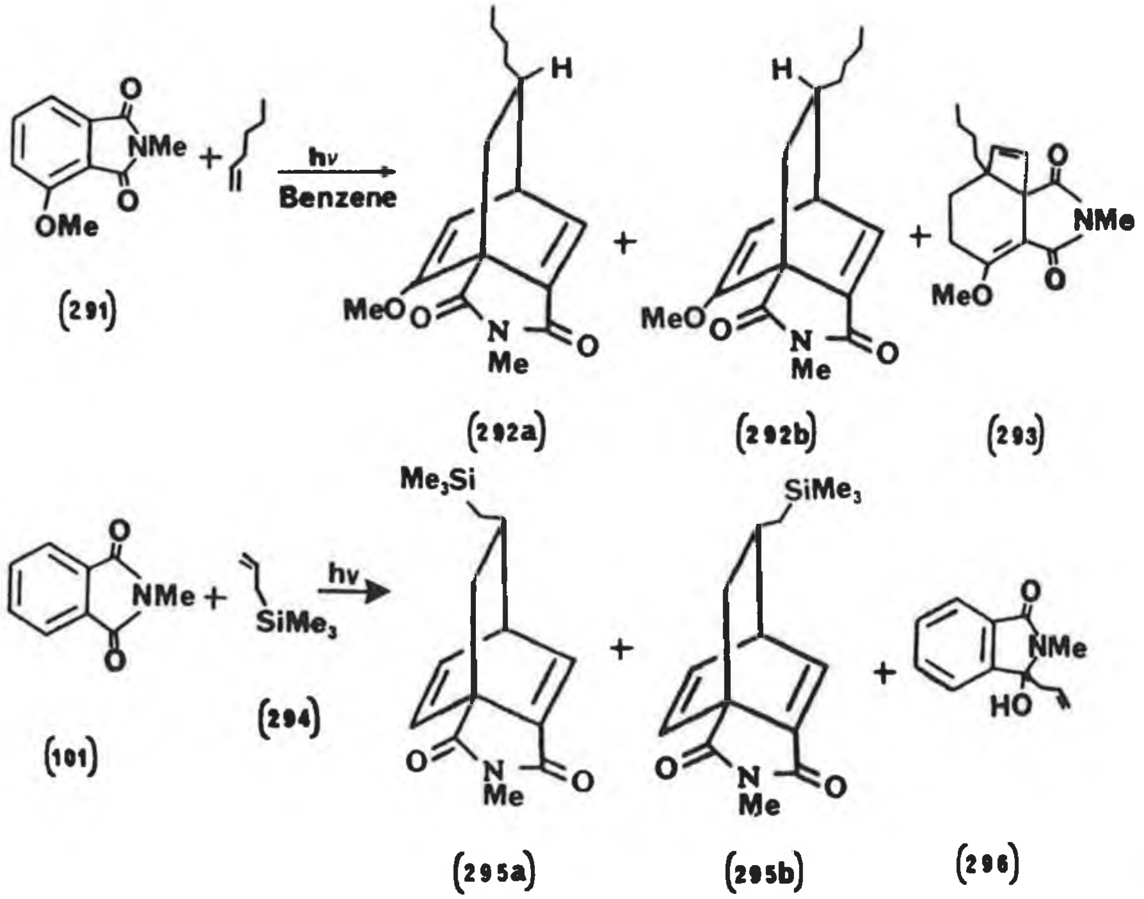
(i) formation of (258) and the carbinol (244) may originate from a (π,π^*) excited state and cycloaddition from an (n,π^*) state;

(ii) formation of one product type may be occurring from a singlet state and the other from a triplet state, and

(iii) both product types may arise from the same excited state.

Recent work by Suau[121] and Kubo[122] yielded 1,4-cycloadducts on irradiation of phthalimides in the presence of alkenes. Suau[121] and coworkers obtained the cycloadducts (292a) and (292b) on irradiation of 3-methoxy-N-methylphthalimide (291) in the presence of n-hexene (scheme 4.33a). Also obtained from the reaction was (293), probably formed by initial 1,2-cycloaddition.

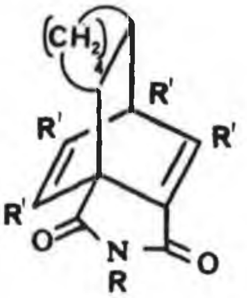
Kubo[122] and coworkers isolated (295a), (295b) and (296) on irradiation of N-methylphthalimide in the presence of allyltrimethylsilane (294). On examination of the



Scheme 4.33a

concentration effect of (294) on the yields of the photoproducts, Kubo showed the yields of (295a) and (295b) decreased and that of (296) increased on increasing the concentration of (294). On the other hand, isomer ratios of (295a) and (295b) remained almost constant throughout the examined concentration of (294). The results indicated that the carbinol (296) arose from the relatively short-lived singlet excited state of (101), and (295a) and (295b) from the triplet excited state, since a marked decrease of yields of photoproducts derived from the triplet excited state of (101) with increasing concentration of the alkene have been reported.[106, 107]

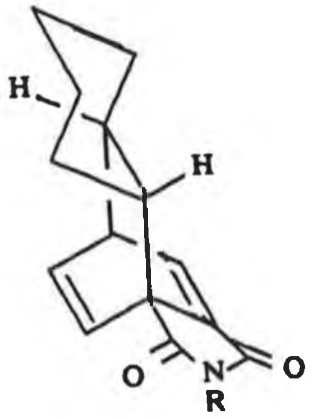
Irradiation of NAP (8), NBP (9), NATCP (11) and phthalimide (132) in the presence of cyclohexene led to the 1,4-cycloadducts (245), (243), (267) and (245) respectively as the major photoproducts. The 1,4-cycloadducts obtained on irradiation of NBP (9) and NAP (8) in the presence of cyclohexene were assigned the exo, trans 1,4-cycloadduct structures (243a) and (245a) respectively. The stereochemistry of the 1,4-cycloadduct obtained on photolysis of NATCP (11) in the presence of cyclohexene is currently unknown, while phthalimide and cyclohexene photoreacted to give a mixture of three stereoisomers of the 1,4-cycloadduct represented by structure (245), with



(243) R' = H, R = COPh
(245) R' = R = H
(267) R' = Cl, R = H

Scheme 4.34

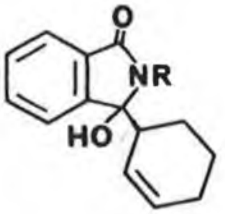
the exo, trans-1,4-cycloadduct (245a) being the major stereoisomer in the mixture.



(243a) R=COPh
(245a) R=H

Scheme 4.35

If initial electron transfer were occurring on irradiation of N-benzoylphthalimide (NBP) (9) and cyclohexene in dichloromethane the carbinol (212) might be expected as a product, by a mechanism similar to that for formation of the carbinol (232) on irradiation of N-methylphthalimide in the presence cyclohexene. The failure to isolate (212) or a derivative suggests,



(212) R = COPh
(232) R = Me

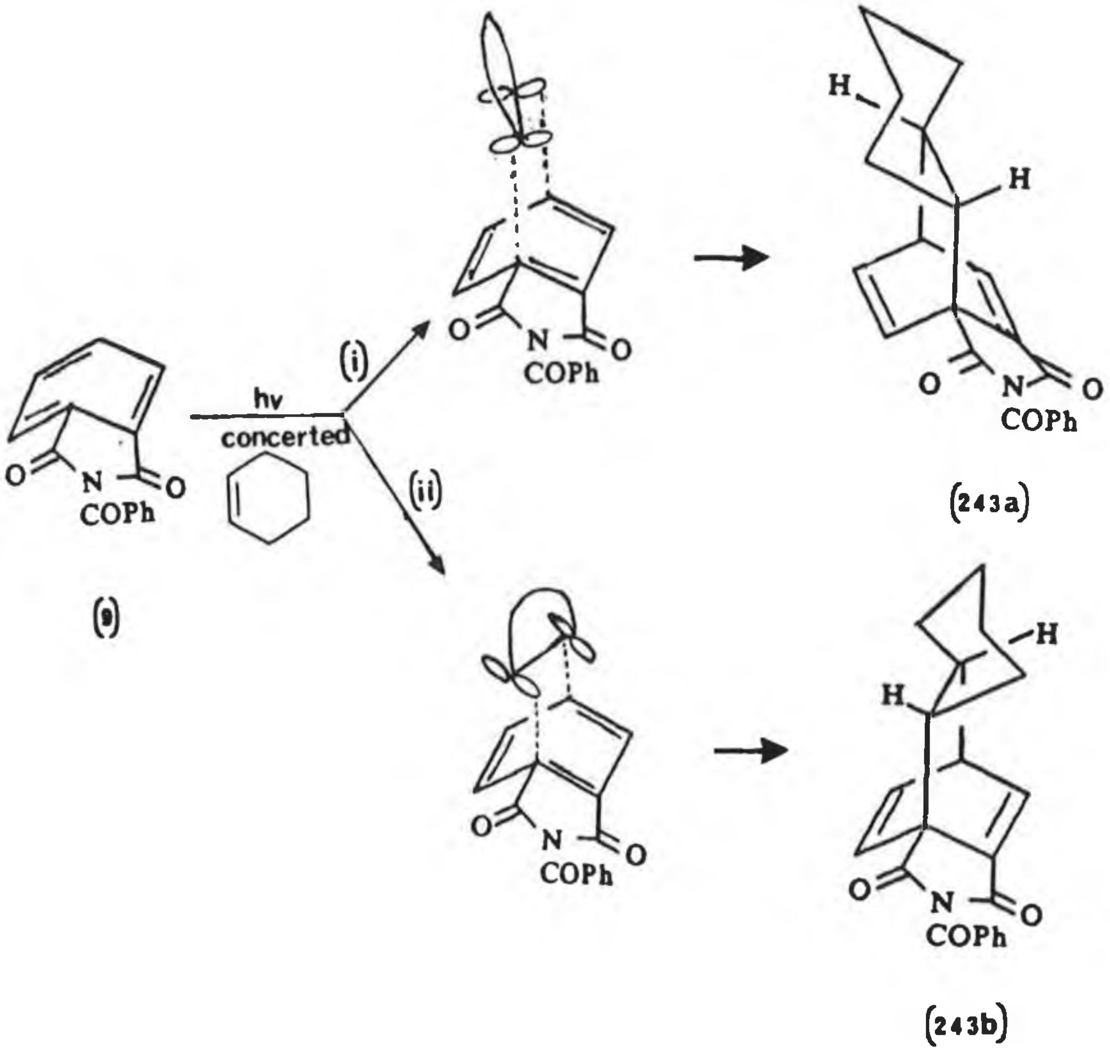
Scheme 4.36

though does not conclusively prove, that radical ion pair formation is not occurring to any great extent, and that an alternative process may be involved. This other process may be either ;

(i) a concerted addition of the cyclohexene to the NBP, i.e with both new σ-bonds in (243a) being formed simultaneously or

(ii) a stepwise addition, i.e. with the σ-bonds being formed sequentially and involving either a zwitterionic or diradical intermediate.

If a concerted process is involved, addition of the phthalimide to the ends of the alkene π-system must be antarafacial (scheme 4.37) if the observed trans-isomer (243a) is to be produced. The cyclohexene may in principle approach the phthalimide in either of two different orientations [scheme 4.37 (i) or (ii)] to give one of the two possible trans-isomers (243a) or (243b) respectively.

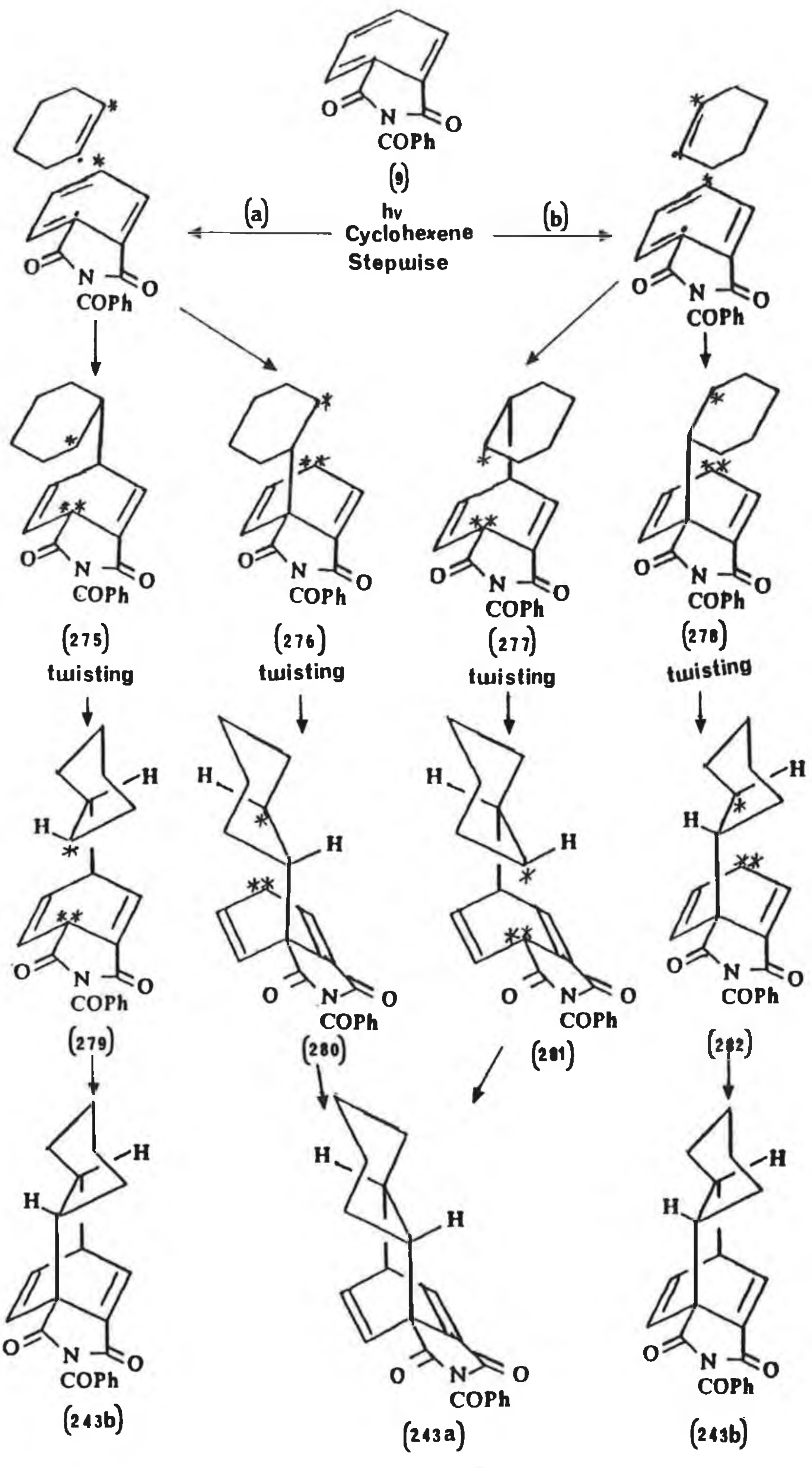


Scheme 4.37

X-Ray crystallography showed the 1,4-cycloadduct to be the trans-isomer (243a). If (243a) were to be formed by a concerted antarafacial process the orientation of the cyclohexene with respect to the excited phthalimide in the transistion state would have to be as shown in [scheme 4.37 (i)].

The 1,4-trans concerted addition of ethylene to benzene is symmetry allowed from the S_1 and S_2 excited states of benzene[119]. The carbonyl groups in the phthalimide unit of NBP do not strongly perturb the symmetry of the carbon π-orbitals of the benzene ring in the phthalimide moiety and as such the trans-1,4-addition of cyclohexene to NBP to yield (243a) is symmetry allowed as a concerted process.

Alternatively, a stepwise addition of cyclohexene to NBP may involve two possible orientations of approach of the cyclohexene to the excited NBP molecule [scheme 4.38 (a) and (b)]. The bond first formed between the cyclohexene and the excited NBP molecule for both orientations of approach may (i) involve the tertiary aromatic carbon as in (275) and (277) (back bond first), or (ii) involve the quaternary aromatic carbon as in (276) and (278) (front bond first) (scheme 4.38).
These intermediates [(275)-(278)] must then undergo rotation around the carbon - carbon bond of the former vinylic moiety of the cyclohexene to give (279)-(282) respectively if trans-1,4-addition products are to be obtained. These can then undergo ring closure to yield the exo, trans-1,4-adduct (243a) and/or the endo, trans-1,4-adduct (243b) (scheme 4.38).



$*$ = +, − or ·

$**$ = + − or ·

Scheme 4.38

The irradiation of NBP (9) in the presence of cyclohexene gave the exo, trans-1,4-cycloadduct (243a) as sole product, ruling out participation of (275), (278), (279) and (282) in the reaction pathway. This means that if a stepwise process is involved in the formation of (243a) then the cyclohexene approaches the excited NBP molecule (i) as shown in scheme 4.38 (a) followed by 'front bond' formation to give (276), bond rotation and finally ring closure, and/or

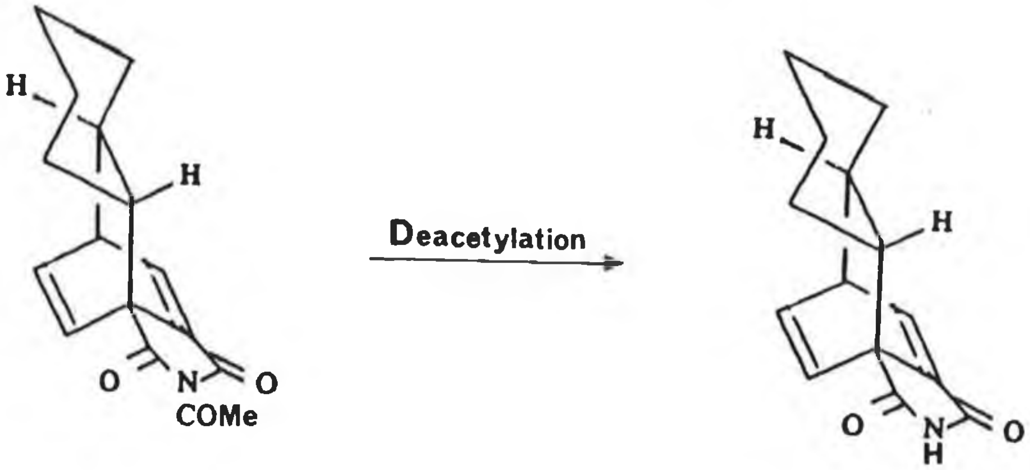
(ii) as shown in scheme 4.38 (b) followed by 'back bond' formation to give (277), bond rotation and finally ring closure.

The intermediates (276) and (277) may possibly exist as diradicals or zwitterions. If zwitterions are involved then the positive or negative charge may be associated with the cyclohexene derived moiety or the phthalimide derived moiety. However, association of the negative charge with the phthalimide derived moiety would seem preferable because of the possibility of involvement of the carbonyl groups in its stabilisation. Whether (276) or (277) is preferred is difficult to decide based on the data available. However (276) would seem to provide for greater delocalisation of negative charge (or radical centres) and may perhaps on balance be more favoured.

The trans-adduct is formed rather than the cis adduct because bond rotation to relieve ring strain followed by formation of the second bond produces the more thermodynamically stable cyclohexane chair conformation in which the trans alkyl groups on the adjacent carbons of the cyclohexane ring are both in the more favoured equatorial positions.

Information about the stereochemical details of 1,4-addition of an alkene to N-benzoylphthalimide (9) might be obtainable from an investigation of cis- and trans-but-2-enes as addends. A concerted antarafacial addition process would lead to a different stereochemical outcome from each alkene. On the other hand, a stepwise addition permitting free rotation around the alkene 2,3-bond in the intermediate(s) formed, would be expected to lead to common products from the two alkenes.

By analogy to (243a), the exo, trans-1,4-cycloadduct (245a) obtained on irradiation of NAP (8) in the presence of cyclohexene may also involve either a concerted or stepwise addition of cyclohexene to the excited phthalimide to give initially (246a). Deacetylation would subsequently yield the observed product, (245a) (scheme 4.39).



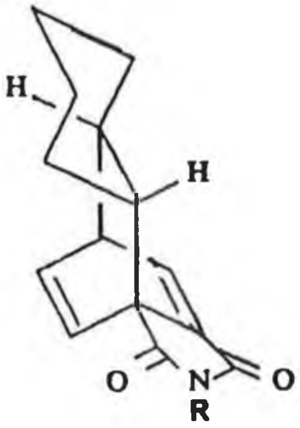
(246a)

(245a)

Scheme 4.39

The irradiation of phthalimide in the presence of cyclohexene led to the formation of three stereo-isomers of the 1,4-cycloadduct represented by structure (245). This is in direct contrast to NBP (9), NAP (8) and NATCP (11) which photoreacted with cyclohexene to give only the exo, trans-1,4-cycloadduct. This lends added weight to deacetylation subsequent to cycloaddition in the formation of (245a) from the irradiation of NAP (8) in the presence of cyclohexene.

Alternative concerted and stepwise processes have been considered for the formation of the 1,4-cycloadducts (243a) and (245a) obtained from NBP and NAP respectively. A stepwise mechanism seems the more likely process on consideration of the summary tabulated in table 26.



(243a) R=COPh

(245a) R=H

Scheme 4.40

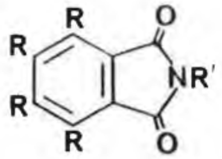
The table shows that when phthalimide (132), N-methylphthalimide (101) and N-phenylphthalimide (263) were irradiated in the presence of cyclohexene three stereoisomers of the respective 1,4-cycloadducts were formed. This would suggest a stepwise and not a concerted mechanism as being operative.

For those phthalimides (8), (9) and (264), for which only a single stereochemically pure 1,4-cycloadduct was obtained (table 26), it may be that the N-substituent through its arrangement in space and/or its electronic effect favours attack of the cyclohexene on the excited phthalimide from one orientation only.

Most phthalimides in table 26 when irradiated in the presence of cyclohexene produced the exo trans-1,4-cycloadduct as the major stereo-isomer. N-Methyl- (194) and N-ethyl-3,4,5,6-tetrachlorophthalimide (246) however gave the endo, trans-1,4-cycloadduct as the major stereo-isomer. This suggests that the chlorine substituents also play a role in determining the stereochemical outcome of the 1,4-cycloaddition.

TABLE 26. Number of 1,4-cycloadducts formed on irradiation of various phthalimides in the presence of cyclohexene.

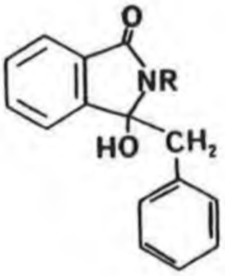
	R	R'	No. of 1,4 Adducts	Major Stereoisomer
(132)	H	H	3	exo, trans
(8)	H	COMe	1	exo, trans
(9)	H	COPh	1	exo, trans
(264)	H	$SCCl_3$	1	exo, trans
(101)	H	Me	3	exo, trans
(263)	H	Ph	3	exo, trans
(194)	Cl	Me	2	endo, trans
(246)	Cl	Et	2	endo, trans
(11)	Cl	COMe	1	?



Scheme 4.41

CHAPTER FIVE

As already outlined in chapter three, irradiation of phthalimide (132) and N-acetylphthalimide (NAP) (8) in toluene yielded the carbinols (231) and (206) respectively. As part of the identification procedure the attempted synthesis of these carbinols by reaction of Grignard reagent (benzyl magnesium chloride) with phthalimide (section 5.1) and NAP (section 5.2) was carried out.



(231) R=H

(206) R=COMe

Scheme 5.1

5.1 Reaction of Phthalimide (132) with Grignard Reagent (benzyl magnesium chloride)

Phthalimide is known to react with the Grignard reagent phenylmagnesium bromide to yield the carbinol (283)[120] (scheme 5.2).

(132)

(283)

Scheme 5.2

When phthalimide was added to 2.4 molar equivalents of Grignard reagent (benzyl magnesium chloride), TLC showed the formation of one product. Following neutralization with dilute hydrochloric acid and removal of the organic solvents, the product precipitated from solution.

Recrystallisation of the product yielded white crystals (68%, m.p. 154°C). The elemental microanalysis was consistent with addition of a benzyl group to phthalimide. The infra-red spectrum showed strong bands at 3203 (OH, NH), 1686, 1672 (C=O) and 702cm^{-1}, consistent with (231) as the product structure. The ^{1}H nmr spectrum showed a one hydrogen singlet at δ 8.2 (NH), a nine hydrogen multiplet between δ 7.9 and 7.3 (Ar-H), a one hydrogen singlet (δ 6.6, OH), and two one proton doublets (δ 3.4 and 3.1, J 13.6 Hz). The non-equivalence of the two methylene hydrogen atoms can be explained by the fact that they are diastereotopic in the carbinol (231), i.e. they are on a carbon attached to a chiral centre. The ^{13}C nmr spectrum (table 27) showed peaks corresponding to a carbonyl group, ten non-equivalent aromatic carbons and two aliphatic carbons, consistent with the carbinol (231) as the product structure.

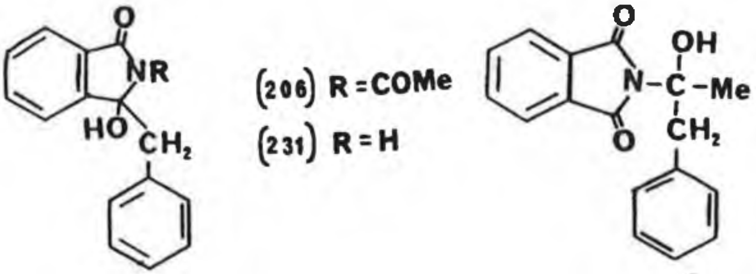
TABLE 27. ^{13}C nmr spectral data for the carbinol (231).

δ/ppm	Assignment	δ/ppm	Assignment
168.9	Carbonyl	128.4	
		127.4	
		123.9	Aromatic
134.9		123.7	
132.8	Aromatic	122.4	
130.7			
130.5		87.7	C-OH
129.8		45.1	CH_2

5.[illegible] Reaction of NAP (8) with Grignard Reagent (benzyl magnesium chloride)

One molar equuivalent of Grignard reagent was cautiously added to NAP (8) dissolved in tetrahydrofuran. After heating under reflux for two hours neutralizing the resulting solution with dilute hydrochloric acid, TLC showed the presence of two products. Neither of the two products had the same rf value as the carbinol (206), obtained on irradiation of NAP (8) in toluene.

Chromatographic separation of the reaction mixture led to the isolation of the major product (20%, m.p. 78-79°C). Its infra-red spectrum showed strong bands at 1760 (C=O) and 973cm^{-1}. The absence of an absorbance in the region 4000-3000cm^{-1} corresponding to a hydroxyl group ruled out the carbinols (206), (231) and (205) as the product structure. The elemental microanalysis results and mass spectrum (M^+236) were consistent with a molecular formula of $C_{15}H_{10}O_3$. The ^1H nmr spectrum showed a nine hydrogen multiplet between δ 7.88 and 7.24 (Ar-H), and a one proton singlet at δ 6.35. The absence of any signals between δ 6 and δ 0 in the ^1H nmr spectrum showed the absence of a methyl group and a methylene moiety derived from toluene in the product structure. The ^{13}C nmr spectrum showed peaks corresponding to one type of carbonyl group (δ 167.0) and seven non-equivalent aromatic and vinylic carbons (δ 145 - 119) (table 28). The spectrum also showed the presence of a signal at δ 107.0. The presence of only nine non-equivalent carbon atoms suggests that the product is symmetrical (elemental microanalysis and mass spectrum have



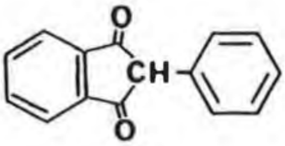
(206) R = COMe

(231) R = H

(205)

Scheme 5.3

shown fifteen carbons present in product). The only structure consistent with all the data collected for the product was the dione (284).



(284)

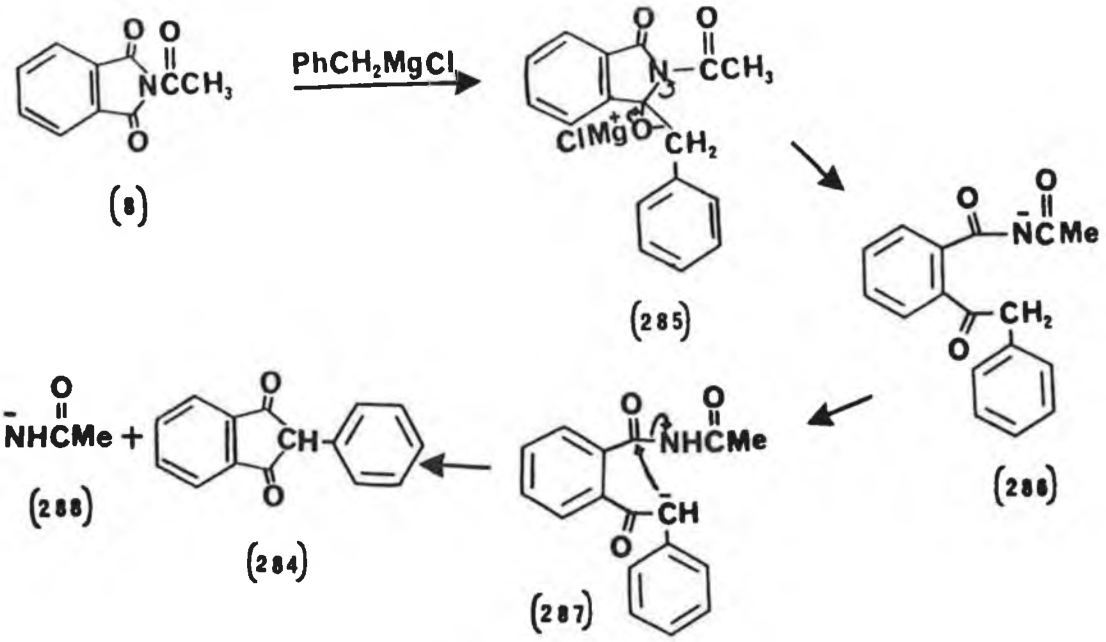
Scheme 5.4

TABLE 28. ^{13}C nmr spectral data for (284).

Assignment	δ/ppm	Assignment	δ/ppm
Carbonyl	167.0		133.0 130.1
Aromatic	144.5 140.5 134.5	Aromatic	125.4 123.2 119.8
		Aliphatic	107.0

A suggested mechanism for the formation of (284) may be as shown in scheme 5.5. N-Acetylphthalimide (8) reacts with the Grignard reagent to form (285) which ring opens to (286). The anion (287) then undergoes ring closure to give the observed product (285).

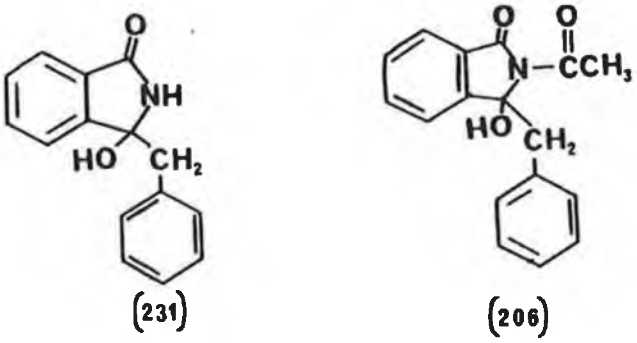
Repeated attempts to isolate the minor product by chromatographic separation proved unsuccessful.



Scheme 5.5

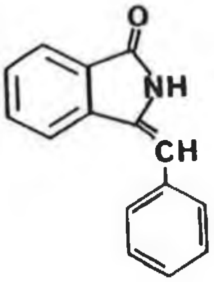
5.3 Reaction of 3-Benzyl-3-hydroxy-isoindol-1-one (231) with Acetyl Chloride

The synthesis of the carbinol (206) was also attempted by another method. This involved adding a one molar equivalent of acetyl chloride to (231) suspended in pyridine. Following stirring of the resulting mixture at room temperature for twenty-four hours TLC showed a single product. On addition of ethanol and cooling (0-5°C) for five hours the product precipitated from solution. Recrystallisation of the product gave yellow crystals (67%, m.p. 172-173°C). The microanalysis results were consistent



Scheme 5.6

with a molecular formula of $C_{15}H_{11}NO$. Its infra-red spectrum showed strong absorbance at 3240 (NH), 1697 (C=O) and 760cm^{-1} The ^1H nmr spectrum showed the presence of a nine aromatic hydogen multiplet between δ7.8 and 7.2 . Also present were one proton singlets at δ 8.7 and 6.5 corresponding to NH and vinylic protons respectively. The absence of a signal corresponding to a methyl group in the ^1H nmr spectrum ruled out the carbinol (206) as the product structure. The data suggests (289) as the product structure. This was confirmed on analysis of its ^{13}C nmr spectrum. It showed



(289)

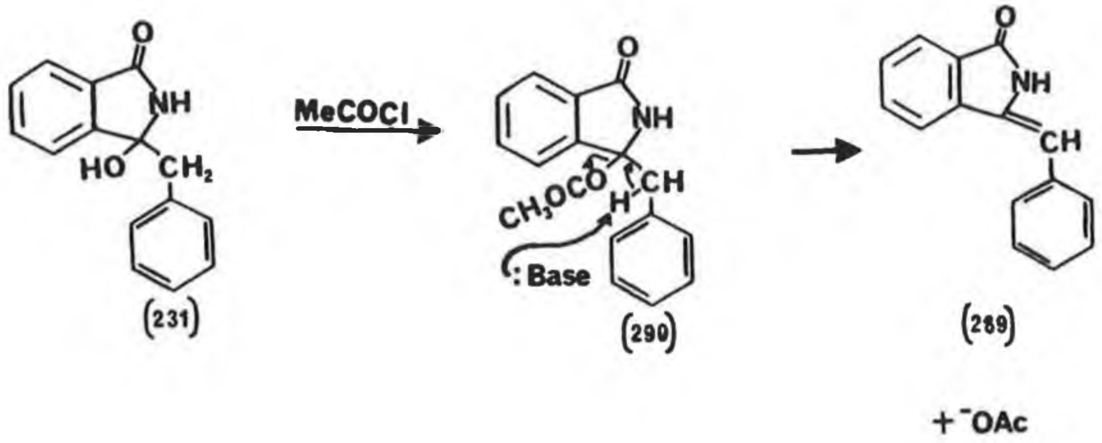
Scheme 5.7

peaks corresponding to a carbonyl group and twelve non-equivalent aromatic and vinylic carbons (table 29) consistent with (289) as the product structure.

TABLE 29. ^{13}C nmr spectral data for (279).

Assignment	δ/ppm	Assignment	δ/ppm
Carbonyl	169.2		128.7
			128.6
	138.2	Aromatic	127.7
Aromatic	134.9	+	126.0
+	133.0	Vinylic	123.5
Vinylic	132.2		119.8
	129.2		106.8

The product (289) is probably formed by initial attack of the acetyl chloride at the hydroxyl group of the phthalimide to give the intermediate (290) which then loses an acetate group.



Scheme 5.8

CHAPTER SIX

EXPERIMENTAL SECTION

General Techniques

Photochemical reactions were carried out in a cylindrical vessel approximately 30cm in length and 8cm in diameter. The vessel was fitted with a water-cooled quartz immersion well containing a 400W medium pressure mercury vapour lamp fitted with a Pyrex filter. All solutions were first degassed by vigorous bubbling with nitrogen then a slow stream of the gas was employed throughout the subsequent reaction period. All solvents used for photochemical reactions were previously dried and distilled: dichloromethane and toluene over anhydrous calcium chloride, tetrahydrofuran over potassium, acetonitrile over anhydrous calcium sulphate and propan-2-ol over calcium oxide.

Separation of crude reaction mixtures was carried out by a preparative scale radial centrifugal thin layer chromatographic method using a Chromatotron (Model 7924 T, Harrison Research, Palo Alto, California). Circular glass plates (24cm in diameter) were covered with silica gel (Merck No 7749, silica gel 60 PF 254 containing calcium sulphate as binder) of layer thickness 1,2 or 4mm.

The crude reaction mixture and solvent were then applied to the centre of the plate which was spinning at a constant rate. The polarity of the solvent was increased slowly over approximately an hour and movement of the resulting concentric bands which formed on the silica was followed using an ultraviolet lamp operating at 254nm. The separated bands were collected as they reached the edge of the plate.

Thin layer chromatography (TLC) was carried out on pieces of aluminium coated with silica gel containing a fluorescent indicator (Riedel-de-Haen, D.C. Karten SIF, layer thickness 0.2mm). After development, plates were examined using an ultra-violet lamp operating at 254nm. Infra-red absorption spectra were recorded using a Perkin Elmer 983G infra-red spectrometer. Solids were examined as potassium bromide discs. Ultra-violet absorption spectra were recorded on a Shimadzu UV240 spectrophotometer. ^{1}H-Nuclear magnetic resonance spectra (60MHz) were recorded on a Perkin Elmer R12B instrument using tetramethylsilane as internal standard. ^{1}H-Nuclear magnetic resonance spectra (270MHz) and ^{13}C-nuclear magnetic resonance spectra (67.80MHz) were recorded by the NMR section, Department of Chemistry, University College, Galway, on a Joel GX270 S.C.M. nmr spectrometer. Unless otherwise stated, reported spectra were recorded at 60MHz. Microanalyses were carried out by the Microanalysis Department, Department of Chemistry, University College, Dublin. Mass spectra were recorded by the Department of Agricultural Chemistry and Soil Science, University College, Dublin on a V.G. Analytical 70S double focussing mass spectrometer and a Finnigan Super Incos 2400 data system. X-Ray diffraction analysis was carried out at Aberdeen University using a Nicolet P3 four-circle diffractometer.

Synthesis of N-Acetylphthalimide (8)

Phthalimide (73.5g, 500mmol) was heated under reflux for six hours in an excess of acetic anhydride (350ml). Approximately half of the acetic anhydride was then removed by distillation and the resulting solution allowed to cool. Isolation of the resulting precipitate by filtration (61.4g, m.p. 133-136°C) followed by recrystallisation from ethanol yielded white crystals of N-acetylphthalimide (47.2g, 50%), m.p. 134-135°C (lit.[115] 134-135°C); λ_{max}(MeCN) 222nm (ε 4.76 X $10^4 dm^3 mol^{-1} cm^{-1}$); $V_{max.}$ 1788 (C=O), 1735 (C=O) and 1291cm^{-1}; δ_H (270MHz, $CDCl_3$), 7.80-7.93 (4H, m, Ar H), 2.61 (3H, s, Me); δ_C ($CDCl_3$), 168.8, 165.3 (carbonyl C's), 135.5, 130.9 124.4 (aromatic C's), 26.8 (Me); (Found: C, 63.6; H, 3.6; N, 7.3. $C_{10} H_7NO_3$ requires C, 63.5; H, 3.7; N, 7.4%).

Synthesis of N-Benzoylphthalimide (9)

(a) Using n-Butyllithium

Phthalimide (7.4g, 50mmol) was dissolved in tetrahydrofuran (75ml) in a 250ml round-bottom flask. A solution of n-butyllithium in hexane (15%; 23.5ml, 55mmol) was slowly added with stirring to the flask by means of a septum and syringe. After thirty minutes the resulting white suspension was treated during a ten minute period with a solution of benzoyl chloride (7.9g, 56mmol) in tetrahydrofuran (50ml) and the contents then heated under reflux for five hours. After cooling the solution was placed in a separating funnel containing water (100ml) and shaken vigorously. The aqueous layer was discarded and the step repeated. Removal of the tetrahydrofuran yielded an 'off-white' solid which after recrystallisation from ethanol gave N-benzoylphthalimide (6.3g, 50%) m.p. 166-167°C (lit[115] 166-167°C); $\lambda_{max.}$(MeCN) 227 (34,422), 217 (ε 32,663dm^{3}mol^{-1}cm^{-1}); $V_{max.}$ 1785, 1728, 1695 (C=O) and 1299cm ; δ_H ($CDCl_3$) 8.0-7.2 (m); δ_C ($CDCl_3$) 167.1, 165.4 (carbonyl C's), 135.4, 134.5, 132.6, 131.4, 130.4, 128.7, 124.5 (aromatic C's); (Found: C, 71.8; H, 3.7; N, 5.8. $C_{15}H_9NO_3$ requires C, 71.7; H, 3.6; N, 5.6%).

(b) Using Pyridine

Phthalimide (21.0g, 143mmol), partially dissolved and suspended in pyridine (70ml) in a round bottom flask was treated gradually with benzoyl chloride (21.0g, 149mmol). During the addition of the mixture stirring was maintained at 0-5°C and a calcium chloride guard tube used. The solution, which became dark red, was left to stir for twenty four hours. Ethanol (80ml) was then added, with stirring, and during the course of ten minutes a white powdery precipitate (30.0g, m.p. 162-166°C) was deposited. Recrystallisation from ethanol gave colourless, gritty prisms of N-benzoylphthalimide (22.0g, 61%), m.p. 166-167°C.

Synthesis of N-Acetyl-3,4,5,6-tetrachlorophthalimide (11)

A solution of tetrachlorophthalimide (20.0g, 70mmol) in acetic anhydride (100ml) was heated under reflux for eight hours. On cooling, a yellow solid precipitated and was isolated by filtration (19.0g, m.p. 193-196°C) and recrystallised from chloroform/ethanol (1:1) to yield yellow plates of N-acetyl-3,4,5,6-tetrachlorophthalimide (11) (12.9g, 56%), m.p. 198-199°C; $\lambda_{max.}$(MeCN) 335 (2,485), 322 (2,355) and 239nm (ε 54,277dm^{3}mol^{-1}cm^{-1}); $V_{max.}$1751(C=O) and 1274 cm^{-1}; δ_H (270MHz, CDCl$_3$), 2.67 (s, Me); δ_C (CDCl$_3$), 167.9, 160.9 (carbonyl C's), 141.8, 131.0, 126.6 (aromatic C's), 27.0 (Me); (Found: C, 36.6; H, 0.9; N, 4.6; Cl, 43.7. $C_{10}H_3NO_3Cl_4$ requires C, 36.7; H, 0.9; N, 4.3, Cl, 43.4%).

Preparation of N-Benzoyl-3,4,5,6-tetrachlorophthalimide(12)

Tetrachlorophthalimide (75.0g, 263mmol), partially dissolved and suspended in pyridine (130ml) in a round-bottom flask was treated gradually with benzoyl chloride (37.0g, 263mmol). During the addition stirring was maintained at 0-5°C and a calcium chloride guard tube used. The solution, which became dark red, was left to stir for twenty four hours. Ethanol (400ml) was then added with stirring, and during the course of ten minutes a yellow powdery precipitate (51.3g, m.p. 206-210°C) was deposited. Recrystallisation from chloroform/ethanol (1:1) gave yellow plates of N-benzoyl-3,4,5,6-tetrachlorophthalimide, (51.2g, 50%), m.p. 211-212°C, $\lambda_{max.}$ (MeCN) 338 (2713), 243 (52,326) and 210nm (ε15,503dm^{3}mol^{-1} cm^{-1}); $V_{max.}$1730, 1705 (C=O),1369 and 1307cm^{-1}; δ_H (CDCl$_3$), 8.1-7.4 (m); (Found: C, 46.5; H, 1.3; N, 3.6; Cl, 36.7. $C_{15}H_5NO_3Cl_4$ requires C, 46.3; H, 1.3; N, 3.6; Cl, 36.5%).

Irradiation of N-Acetylphthalimide (8) in Acetonitrile

N-Acetylphthalimide (1.01g, 5.3mmol) in acetonitrile (300ml) was irradiated through Pyrex for forty hours. TLC showed no product formation. The acetonitrile was removed under vacuum to yield a white solid of N-acetylphthalimide (0.95g), identified by comparison of its infra-red spectrum with that of an authentic sample.

Photolysis of N-Acetylphthalimide (8) in Dichloromethane

N-Acetylphthalimide (1.37g, 7.2mmol) in dichloromethane (300ml) was irradiated through Pyrex for thirty five hours. TLC showed the formation of one product in trace amounts. The dichloromethane was removed under vacuum and the resulting solid shaken with dichloromethane (100ml). The undissolved portion was isolated by filtration and found to be the pure product (50mgs, 70%) by TLC analysis. This product was identified as phthalimide by comparison of its infra-red spectrum with that of an authentic sample. The solution contained no phthalimide (TLC observation). Removal of the solvent under vacuum yielded a white solid (1.28g) identified as N-acetylphthalimide by comparison of its infra-red spectrum with that of an authentic sample.

Irradiation of N-Acetylphthalimide (8) in Tetrahydrofuran

N-Acetylphthalimide (1.20g, 6.3mmol) in tetrahydrofuran (300ml) was irradiated through Pyrex for thirty hours. TLC showed the formation of two products. The tetrahydrofuran was removed under vacuum to give a brown oil. The mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. Repeated attempts to isolate the products from the resulting crude mixture using a Chromatotron proved unsuccessful. The attempted separation consisted of applying the crude mixture to a 4mm plate and using dichloromethane-light petroleum (b.p.40-60°C) (5:95, increased stepwise to 60:40) and ethylacetate-light petroleum (b.p. 40-60°C) (5:95, increased stepwise to 30:70) as eluent.

Irradation of N-Acetyl-3,4,5,6-tetrachlorophthalimide (11) in Tetrahydrofuran

N-Acetyl-3,4,5,6-tetrachlorophthalimide (1.20g, 3.7mmol) in tetrahydrofuran (300ml) was irradiated through Pyrex for ten hours. TLC showed the formation of three products. The tetrahydrofuran was removed under vacuum to give a brown oil. The mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. Repeated attempts to isolate the products from the resulting crude mixture using a Chromatotron proved unsuccessful. The attempted separation consisted of applying the crude mixture to a 4mm plate and using dichloromethane-light petroleum (b.p. 40-60°C) (5:95, increased stepwise to 80:20) and ethylacetate: light petroleum (b.p. 40-60°C) (5:95, increased stepwise to 35:65) as eluent.

Photolysis of N-Acetylphthalimide (8) in Toluene

N-Acetylphthalimide (3.00g, 15.8mmol) in toluene (300ml) was irradiated through Pyrex for thirty hours. TLC showed the formation of two products. The toluene was removed under vacuum to give a brown oil. The mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. The dichloromethane was removed under vacuum and the resulting crude mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of dichloromethane-light petroleum (b.p. 40-60°C) (5:95, increased stepwise to 60:40). This gave in order of recovery from the plate:

(i) phthalimide (12mg, 4%), identified by comparison of its infra-red spectrum with that of an authentic sample;

(ii) 2-acetyl-3-benzyl-3-hydroxyisoindol-1-one (206), a white crystalline solid (254mg, 45%), m.p. 96-98°C (from chloroform-light petroleum, b.p. 90-100°C), $V_{max.}$ 3457 (OH) 1742 (C=O) and 1657cm^{-1}(C=O); δ_H (270MHz, $CDCl_3$) 7.76-6.59 (9H, m, Ar H), 5.20 (1H, s, OH), 3.86 (1H, d, CH_aPh, J 13.2Hz), 3.55 (1H, d, CH_bPh, J 13.2Hz), 2.62 (3H, s, Me); δ_C ($CDCl_3$) 173.9 and 166.1 (carbonyl C's) 145.6, 134.6, 134.2, 130.3, 129.6, 129.5, 128.1, 127.2, 124.6, and 123.0 (aromatic C's), 93.1 (C-OH), 45.4 (Me), 26.0 (CH_2); (Found: C, 72.6; H, 5.3; N, 5.2. $C_{17}H_{15}NO_3$ requires C, 72.9; H, 5.0; N, 5.0%);

(iii) N-acetylphthalimide (2.62g, 13.8mmol), identified by comparison of its infra-red spectrum with that of an authentic sample.

Photolysis of N-Acetyl-3,4,5,6-tetrachlorophthalimide (11) in Toluene

A solution of N-acetyl-3,4,5,6-tetrachlorophthalimide (2.71g, 8.3mmol) in toluene (300ml) was irradiated through Pyrex for eight hours. TLC showed the formation of three products. The toluene was removed under vacuum to give a brown oil. The mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. The dichloromethane was removed under vacuum and the resulting crude mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of dichloromethane: light petroleum (b.p.40-60°C) (5:95 increased stepwise to 70:30).

This gave, in order of recovery for the plate:

(i) 2-acetyl-3-benzyl-3-hydroxy-4,5,6,7-tetrachloroisoindol-1-one (209), a yellow solid (658mg, 78%) m.p. 142-144°C (from chloroform: light petroleum b.p. 90-100°C), V_{max}.3460 (OH) and 1747cm^{-1} (C=O); δ_H (270MHz, $CDCl_3$) 7.14-6.63 (5H, m, Ar H), 5.15 (1H, s, OH), 4.00 (1H, d, CH_aPh, J 13.7Hz), 3.91 (1H, d, CH_bPh, J 13.7Hz), 2.65 (3H, s, Me); δ_C ($CDCl_3$), 173.5, 161.5 (carbonyl C's), 141.6, 139.5, 136.4, 133.6, 130.6, 128.9, 128.6, 128.4, 127.3, 126.4 (aromatic C's), 92.7 (C-OH) 41.0 (Me), 26.4 (CH_2); (Found: C, 49.0; H, 2.5; N, 3.3; Cl, 34.1;. $C_{17}H_{11}NO_3Cl_4$ requires C, 48.7; H, 2.7; N, 3.3; Cl, 33.8%); m/e 418 (M^+<1), 364 (11), 362 (47), 361 (18), 360 (100), 3659 (18), 358 (76), 328 (12), 326 (13), 324 (10), 297 (10), 295 (10), 90 (15), 89 (10), 59 (12), 43 (27%);

(ii) N-acetyl-3,4,5,6-tetrachlorophthalimide (2.05g, 6.3mmol) identified by comparison of its infra-red spectrum with that of an authentic sample;

(iii) mixture of two minor products as a brown oil (55mg).

Photolysis of N-Benzyol-3,4,5,6-tetrachlorophthalimide (12) in Toluene

N-Benzoyl-3,4,5,6-tetrachlorophthalimide (0.98g, 2.5mmol) in toluene (300ml) was irradiated through Pyrex for fourteen hours. TLC showed the formation of five products. The toluene was removed under vacuum to give a brown oil. The mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. The dichloromethane was removed under vacuum and the resulting crude mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of dichloromethane-light petroleum (b.p. 40-60°C) (5:95, increased stepwise to 70:30). This gave, in order of recovery from the plate:

(i) 2-benzoyl-3-benzyl-3-hydroxy-4,5,6,7-tetrachloro-isoindol-1-one (210), a yellow powder (70mg, 31%), m.p. 158-160°C (from chloroform-light petroleum b.p. 90-100°C); $\lambda_{max.}$ (MeCN) 308 (2,382), 265 (12,004), 228 (30,803), 210nm (sh) (ε 23,182dm^{3}mol^{-1}cm^{-1}); $\nu_{max.}$ 3462 (OH), 1753 and 1657 (C=O), 1265 and 1224cm^{-1}; δ_H (270 MHz, $CDCl_3$), 7.59-6.77 (10H, m, Ar H), 5.56 (1H, s, OH), 4.31 (1H, d, CH_aPh, J 14.3Hz), 3.91 (1H, d, CH_bPh, J 14.3Hz); δ_C ($CDCl_3$) 172.5 and 160.9 (carbonyl C's), 141.9, 133.8, 133.7, 132.2, 131.2, 129.6, 129.4, 129.2, 128.7, 127.9 and 127.8 (aromatic C's), 93.3 (C-OH), 40.9 (CH_2); (Found: C, 55.4; H, 2.7; N, 2.9.; Cl, 29.0. $C_{22}H_{13}NO_3Cl_4$ requires C, 54.9; H, 2.7; N, 2.9; Cl, 29.5%);

(ii) N-benzoyl-3,4,5,6-tetrachlorophthalimide (0.80g, 2.1mmol) identified by comparison of its infra-red spectrum with that of a known sample;

(iii) a mixture of four minor products as a brown oil (70mg).

Photolysis of N-Benzoylphthalimide (9) in Tetrahydrofuran

N-Benzoylphthalimide (2.10g, 8.4mmol) in tetrahydrofuran (300ml) was irradiated through Pyrex for thirty hours. TLC showed the formation of three products. The tetrahydrofuran was removed under vacuum to give a yellow solid. The resulting product mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. The dichloromethane was removed under vacuum and the resulting mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of dichloromethane: light petroleum (b.p. 40-60°C) (2.98, increased stepwise to 70:30). This gave in order of recovery from the plate:

(i) phthalimide (20mg), identified by comparison of its infra-red spectrum with that of an authentic sample;

(ii) a mixture (1.95g) of starting material and two other minor products.

Photolysis of N-Benzoylphthalimide (9) in Toluene

N-Benzoylphthalimide (9) (1.51g, 6.0mmol) in toluene (300ml) was irradiated through Pyrex for forty hours. TLC showed the formation of three products. The toluene was removed under vacuum to give a brown oil. The resulting product mixture was filtered through a silica column (10cm X 4cm), using dichloromethane as eluent, in order to remove baseline impurities. The dichloromethane was removed under vacuum and the resulting mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of ethyl acetate and light petroleum (b.p. 40–60°C) (2:98, increased stepwise to 30:70). This gave in order of recovery from the plate:

(i) a mixture of two minor products as an oil (7mg);

(ii) N-benzyolphthalimide (1.26g), identified by comparison of its infra-red spectrum with that of an authentic sample;

(iii) lactone (218), a colourless crystalline solid (95mg, 50%), m.p. 220–222°C (from chloroform: light petroleum, b.p. 90–100°C); $\lambda_{max.}$(MeCN) 305 (3065), 295 (sh) (3,602), 253 (27,586), 218nm (ε 52,874dm^{3}mol^{-1}cm^{-1}); $V_{max.}$1745, 1703, 1668 (C=O), 1286 and 1261cm ;δ_H(270 MHz, $CDCl_3$): 7.95–7.43 (m, Ar H);δ_C($CDCl_3$) 184.7, 169.0, 164.3, 160.2 (carbonyl C's), 141.2, 136.0, 135.3, 135.2, 133.0, 132.5, 132.0, 131.2, 131.0, 129.8, 129.6, 128.1, 128.0, 126.4, 126.0, 121.9, (aromatic C's), 94.8 (spirocarbon); (Found: C, 71.7; H, 3.4; N, 3.6. $C_{23}H_{13}NO_3$ requires C, 72.1; H, 3.4; N, 3.7%); m/e 383 (1), 326 (18), 236 (18), 235 (100), 133 (13), 132 (92), 105 (56), 104 (90), 77 (11), 76 (10%).

Irradiation of N-Benzoylphthalimide (9) in Acetonitrile

N-Benzoylphthalimide (0.50g, 2.0mmol) in acetonitrile (300ml) was irradiated through Pyrex for forty hours. TLC showed no product formation. The acetonitrile was then removed under vacuum to leave a white solid (0.44g) identified as N-benzoylphthalimide by comparison of its infra-red spectrum with that of an authentic sample.

Photolysis of N-Benzoylphthalimide (9) and Isopropan-2-ol in Dichloromethane.

N-Benzoylphthalimide (9) (2.01g, 8.0mmol) in propan-2-ol (150ml) and dichloromethane (150ml) was irradiated through Pyrex for forty hours. TLC showed the formation of two products, one major and one minor. The solvents were removed under vacuum and the reaction mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of dichloromethane and ethylacetate (5:95, increased stepwise to 50:50). This gave, in order of recovery from the plate:

(i) N-benzoylphthalimide (1.80g, 7.2mmol), identified by comparison of its infra-red spectrum with that of an authentic sample;

(ii) lactone (218), (20mg, 14%), identified by comparison of its infra-red spectrum with that of an authentic sample;

(iii) mixture of the lactone and minor product as a brown oil (7mg).

Photolysis of Phthalimide (132) in Toluene

Phthalimide (0.51g, 3.5mmol) in toluene (300ml) was irradiated through Pyrex for forty hours. TLC showed the formation of one product. The toluene was removed under vacuum to leave an 'off white' solid. Toluene (20ml) was added to the solid and after vigorous shaking the undissolved solid (0.32g) was isolated and identified as phthalimide. The solution was concentrated under vacuum and the product mixture separated using a Chromatotron with a 2mm plate. The eluent was a mixture of dichloromethane and light petroleum (b.p. 40-60°C) (5:95, increased stepwise to 60-40). This gave, in order of recovery from the plate:

(i) phthalimide (0.14g, 1.0mmol), identified by comparion of its infra-red spectrum with that of an authentic sample;

(ii) 3-benzoyl-3-hydroxy-isoindol-1-one (231) (65mg, 80%), identified by comparison of its infra-red spectrum with that of an authentic sample.

Photolysis of N-Benzoylphthalimide (9) with Cyclohexene in Dichloromethane

N-Benzoylphthalimide (2.90g, 11.5mmol) and cyclohexene (19.60g, 239.0mmol) in dichloromethane (300ml) were irradiated through Pyrex for forty hours. TLC showed the formation of three products. The solvents were removed under vacuum and the resulting mixture separated using a Chromatotron and a 4mm silica plate. The eluent was a mixture of dichloromethane and light petroleum (b.p. 40-60°C) (2:98 increased stepwise to 60:40). This gave in order of recovery from the plate;

(i) a mixture of minor products as a colourless oil (12mg);

(ii) the exo, trans-isomer of N-benzoyl, tricyclo (4.2.2.0) dodeca-8, 11-diene-9, 10-dicarboximide (243a), a white crystalline solid (160mg, 80%), m.p 138-140°C (from chloroform/light petroleum b.p. 90-100°C), $\lambda_{max.}$ (MeCN) 251 (ε 20,208dm^{3}mol^{-1}cm^{-1}); $\nu_{max.}$ 2929 (aliphatic CH), 1717 and 1694 (C=O), 1297 and 1252cm^{-1}; δ_H (270 MHz, $CDCl_3$) 7.89-7.47 (5H, m, Ar H), 7.10 (1H, d, J 6.0Hz vinylic H), 6.82 (1H, d of d, J 6.0Hz, J 7.0Hz vinylic H), 6.16 (1H, d, J 7.0Hz vinylic H), 3.76 (1H, t, J 6.0Hz), 2.10-1.11 (10H, m, cyclohexane derived moiety); δ_C ($CDCl_3$) 173.0, 167.1, 162.3 (carbonyl C's), 143.3, 141.7, 137.3, 134.8, 131.9, 130.4, 128.8, 123.5 (aromatic and vinylic C's), 56.2, 52.5, 50.7, 45.7, 32.7, 30.2, 27.7 and 27.4 (aliphatic C's); (Found; C, 75.3; H, 5.8; N, 3.9. $C_{21}H_{19}NO_3$ requires C 75.7; H, 5.8; N, 4.2%); m/e 333 (1), 265 (47), 264 (31), 252 (56), 105 (100), 77 (63) and 67 (45%).

Photolysis of N-Acetylphthalimide (8) with Cyclohexene in Dichloromethane

N-Acetylphthalimide (8) (5.00g, 26.4mmol) and cyclohexene (43.4g, 528mmol) in dichloromethane were irradiated through Pyrex for forty hours. TLC showed the formation of two products. The solvents were removed under vacuum and the resulting crude reaction mixture separated using a Chromatotron and a 4mm silica plate. The eluent was a mixture of dichloromethane/light petroleum (b.p. 40-60°C) (5:95 increased stepwise to 70:30). This gave in order of recovery from the plate:

(i) 2-acetyl-3-[2-cyclohexen-1-yl]-3-hydroxy-isoindol-1-one (244), a white crystalline solid (25mg, 4%), m.p. 114-116°C (from light petroleum b.p. 90-100°C), $V_{max.}$ 3416 (OH), 2926 (aliphatic CH), 1733 and 1670cm^{-1} (C=O), 1291 and 1227cm^{-1}; δ_H (270 MHz, CDCl$_3$) 7.7 (4H, m, Ar H), 6.2 (1H, m, vinyl H), 5.9 (1H, m, vinyl H), 5.0 (1H, s, OH), 3.6 (1H, m, allylic H), 2.7 (3H, s, Me), 1.7 (6H, m, CH);

(ii) the exo, trans isomer of tricyclo (4.2.2.0) dodeca-8, 11-diene-9, 10-dicarboximide (245a), a white crystalline solid (317mg, 60%), m.p. 162-164°C (from light petroleum b.p. 90-100°C), $\lambda_{max.}$(MeCN) 217 (ε 8865dm^{3}mol^{-1}cm^{1}); $V_{max.}$ 3179 (NH), 3062 (aromatic CH), 2927, 2856 (aliphatic CH), 1756 and 1709 (C=O), 1645 (C=C), 1335 and 1211cm^{-1}; δ_H(270MHz, CDCl$_3$) 8.84 (1H, s NH), 6.94 (1H, d, J 6.0Hz, vinlyic H), 6.75 (1H, d of d, J 6.0Hz, J 7.1Hz vinylic H), 6.07 (1H, d , J 7.0Hz, vinylic H), 3.66 (1H, t, J 6Hz, allylic H), 2.00-1.08 (10H, m, cyclohexene derived moiety); δ_C(CDCl$_3$) 175.9, 165.3 (carbonyl C's), 145.3, 141.5, 134.9, 123.6 (vinylic C's), 56.6, 51.9, 51.0, 45.4, 32.7, 30.2, 27.7, 27.5 (aliphatic C's); (Found; C, 72.5; H, 6.6; N, 5.9. $C_{14}H_{15}NO_2$ requires C, 73.3; H, 6.6; N, 6.3%); m/e 229 (M^+,2), 161 (100), 148 (82), 82 (42), 67 (79) and 54 (47%);

(iii) N-acetylphthalimide (4.66g, 24.6mmol) identified by comparison of its infra-red spectrum with that of an authentic sample.

Photoylsis of N-Acetyl-3,4,5,6-tetrachlorophthalimide (11) with Cyclohexene in Dichloromethane

N-Acetyl-3,4,5,6-tetrachlorophthalimide (11) (3.08g, 9.4mmol) and cyclohexene (15.80g, 192.7mmol) in dichloromethane (300ml) were irradiated through Pyrex for thirty hours. TLC showed the formation of three products. The solvents were removed under vacuum and the resulting mixture separated using a Chromatotron and a 4mm plate. The eluent was a mixture of dichloromethane and light petroleum (b.p. 40-60°C) (2:98 increased stepwise to 60:40). This gave in order of recovery from the plate:

(i) the dione (258), a yellow crystyalline solid (15mg, 5%), m.p. 128-131°C (from chloroform/light petroleum b.p. 90-100°C), $V_{max.}$ 2938 (aliphatic CH), 1749 (C=O), 1533 (C=C), 1284 and 1207cm^{-1}; δ_H (270MHz, $CDCl_3$) 6.3 (1H, t of d, J 9.9Hz, J 7.7Hz), 5.3 (1H, d, J 9.9Hz) and 2.2-1.3 (6H, m, aliphatic H); δ_C ($CDCl_3$) 197.1 (carbonyl C's) 142.0, 135.6 135.1, 131.1, 119.8 (unsaturated C's), 56.7 (quaternary C), 28.7, 23.9 and 17.7 (aliphatic C's);

(ii) mixture of minor product and starting material as brown oil (25mg);

(iii) N-acetyl-3,4,5,6-tetrachlorophthalimide (11) (2.80g, 8.6mmol), identified by comparison of its infra-red spectrum with that of an authentic sample;

(iv) tricyclo (4.2.2.0) dodeca-8, 11-diene-8,9,10,11-tetrachloro-9, 10-dicarboximide (267), a yellow solid (46mg, 15%), m.p. 151-152°C (from chloroform/light petroleum b.p. 90-100°C), $V_{max.}$ 3201 (NH), 2938 (aliphatic CH), 1706 (C=O) and 1099cm^{-1}; δ_H (270MHz, $CDCl_3$) 8.4 (1H, s, NH) and 2.4-0.8 (10H, m, cyclohexane H); δ_C ($CDCl_3$)

168.0, 161.0 (carbonyl C's) 139.1, 138.8, 135.3, 123.1 (vinylic C's), 78.5, 58.8, 58.2, 53.4, 29.1, 29.0, 26.9 and 26.8 (aliphatic C's).

Photolysis of Phthalimide (132) with Cyclohexene in Acetonitrile/Dichloromethane

Phthalimide (1.69g, 11.5mmol) and cyclohexene (23.6g, 287.3mmol) in a dichloromethane (100ml)- acetonitrile (170ml) mixture was irradiated through Pyrex for thirty hours. TLC showed three extra spots. The solvents were removed under vacuum and the resulting reaction mixture separated using a Chromatotron with a 4mm plate. The eluent was a mixture of dichloromethane-light petroleum (b.p. 40-60°C) (5:95 increased stepwise to 80-20). This gave in order of recovery from the plate;

(i) phthalimide (1.40g, 4.9mmol), identified by comparison of its infra-red spectrum with that of an authentic sample;

(ii) an isomeric mixture of tricyclo (4.2.2.0) dodeca-8, 11-diene-9,10-dicarboximide (245), a white crystalline solid (239mg, 26%), m.p. 128-131° C (from chloroform: light petroleum b.p. 90-100°C), $V_{max.}$ 3179 (NH), 2927 (aliphatic CH), 1759, 1707 (C=O) and 1227cm^{-1}; $\lambda_{max.}$ (MeCN) 222.5 (ε 9,046dm^{3}mol^{-1}cm^{-1}); δ_H (270MHz, $CDCl_3$) 9.0 (1H, s, NH), 7.7-6.0 (3H, m, vinylic H), 3.7 (1H, m allylic H), 2.0-1.0 (10H, m, cyclohexane moiety); δ_C ($CDCl_3$) 176.4, 176.0, 166.5, 165.4 (carbonyl C's), 145.7, 145.4, 141.5, 139.6, 137.8, 134.9, 134.2, 134.0, 130,7, 127.8, 123.6 (vinylic C's), 56.8, 56.6, 51.9, 51.1, 50.4, 48.3, 45.9, 45.4, 45.2, 41.1, 39.3, 32.7, 30.3, 29.3, 27.8, 27.6, 27.5, 27.3, 26.2, 22.7, 19.9 and 19.8 (aliphatic C's); m/e 229 (M^+,1), 161 (100), 148 (78), 82 (43), 67 (84) and 54 (53%).

Preparation of 3-Benzyl-3-hydroxy-isoindol-1-one (231) by a Grignard Reaction

Benzyl chloride (3.54g, 28.0mmol) in diethyl ether (20ml) was slowly added with stirring to magnesium turnings 0.66g, 27.0mmol) in diethyl ether (20ml) under nitrogen. When the addition was complete the reaction mixture was heated under reflux for thirty minutes. Phthalimide (132) (1.63g, 11.mmol) in tetrahydrofuran (65ml) was cautiously added to the Grignard reagent with cooling. When the addition was completed TLC showed no phthalimide present and only one product formed. Following the addition of water (20ml), dilute HCl (20ml) was slowly added with stirring.

The organic solvents were then removed under vacuum. On cooling a white crystalline solid precipitated from solution (2.39g, m.p. 147-150°C). On recrystallisation (chloroform/light petroleum b.p. 90-100°C), it yielded white crystals of 3-benzyl-3-hydroxy-isoindol-1-one (231) (1.80g, 68%) m.p. 154°C; $\lambda_{max.}$(Me CN) 217 (sh)(18,000dm^3mol^{-1} cm^{-1});$V_{max.}$ 3203 (OH, NH), 1686, 1672 (C=O) and 702cm^{-1}; δ_H(270 MHz, $CDCl_3$) 8.2 (1H, s, NH), 7.9-7.3 (9H, m, Ar H), 6.6 (1H, s, OH), 3.4 (1H, d, J 13.6Hz, CH_aPh) and

3.1 (1H, d, J 13.6Hz, CH_bPh);$\delta_C(CDCl_3)$ 168.9 (carbonyl C) 134.9, 132.8, 130.7, 130.5, 129.8, 128.4, 127.4, 123.9, 123.7, 122.4 (aromatic C's), 87.7 (C OH) and 45.1 (CH_2); (Found; C, 74.0; H, 5.4; N, 5.9. $C_{15}H_{13}NO_2$ requires C, 73.5; H, 5.5; N, 5.9%).

Reaction of N-Acetylphthalimide (8) with Grignard Reagent (Benzyl Magnesium Chloride)

Benzyl chloride (1.35g, 10.7mmol) in diethyl ether (20ml) was slowly added with stirring to magnesium turnings (0.26g, 10.6mmol) in diethyl ether (20ml) under nitrogen. When the addition was complete the reaction mixture was heated under reflux for thirty minutes. This mixture was then cautiously added to N-acetylphthalimide (8) (2.00g, 10.6mmol) in tetrahydrofuran (50ml) with cooling. When the addition was completed the reaction mixture was heated under reflux for two hours. On cooling, water (20ml) and dilute hydrochloric acid (2M) (10.8mmol) was added

with stirring. TLC showed three spots present, one with the same rf value as N-acetylphthalimide (8). Neither of the two product spots had the same rf value as the carbinol (206) obtained on irradiation of N-acetylphthalimide (8) in toluene. Following removal of the organic solvents under vacuum a white solid precipitated from solution. TLC showed the solid to consist of the starting material (N-acetylphthalimide) and two products. The mixture was separated using a Chromatotron and a 2mm plate. The eluent was a mixture of dichloromethane:light petroleum (b.p. 40-60°C) (5:95 increased stepwise to 50:50).

This gave in order of recovery from the plate:

(i) 2-Phenylindan-1,3-dione (284), a yellow crystalline solid (250mg, 20%) m.p. 78-79°C (from chloroform/light petroleum 90-100°C), $V_{max.}$ 1760 (C=O) and 973cm^{-1}; δ_H (270MHz, $CDCl_3$) 7.9-7.2 (9H, m, Ar H) and 6.4 (1H, s, vinyl H); δ_C ($CDCl_3$) 167.0 (carbonyl C,s), 144.5, 140.5, 134.5, 133.0, 130.1, 125.4, 123.2, 119.8 (aromatic C,s), 107.0 (aliphatic C,s); (Found: C, 82.1; H, 4.6; O, 14.0. $C_{15}H_{10}O_2$ requires C, 82.1; H, 4.3;,O, 13.7%); m/e 223 (16), 222 (100), 194 (13), 166 (71), 104 (15), 90 (12), 89 (12) and 76 (22%);

(ii) N-acetylphthalimide (8) (1.3g), identified by comparison of its infra-red spectrum with that of an authentic sample;

(iii) an unidentified product, a white crystalline solid (8mg) m.p. 110-111°C (from chloroform/light petroleum 90-100°C), (Found C, 72.9; H, 4.4; N, 6.6%); $V_{max.}$ 1744, 1722, 1369, 1346 and 1303cm^{-1}; δ_H (270MHz, $CDCl_3$) 7.8-6.5 (13H, m, Ar-H), 4.9 (1H, d, J 13.7Hz), 4.1 (1H, d, J 13.7 Hz) and 2.6 (3H, s).

Reaction of 3-Benzyl-3-hydroxy-isoindol-1-one (231) with Acetyl Chloride

Acetyl chloride (0.16g, 2.1 mmol) was added to a solution of 3-benzyl-3-hydroxy-isoindol-1-one (231) (0.50g, 2.1mmol) in pyridine (20ml) and the mixture was stirred at room temperature for twenty four hours. TLC of the resulting mixture showed a single product to have been formed. Following the addition of ethanol (10ml) and cooling (0-5°C) for five hours a yellow solid precipitated from solution. On recrystallisation (from chloroform/light petroleum 90-100°C) it yielded yellow crystals of the benzylidene (289) (0.31g, 67.0%) m.p. 172-173°C, (Found: C, 81.5; H, 4.8; N, 6.7. $C_{15}H_{11}NO$ requires C, 81.4; H, 5.0; N, 6.3%); V_{max} 3240 (NH), 1697 (C=O) and 760cm^{-1}; δ_H (270MHz, $CDCl_3$) 8.7 (1H, s, NH), 7.8-7.2 (9H, m, Ar H) and 6.5 (1H, s, vinyl H); δ_C ($CDCl_3$) 169.2 (carbonyl C), 138.2, 134.9, 133.0, 132.2, 129.2, 128.7, 128.6, 127.7 126.0 123.5, 119.8 and 106.8 (aromatic and vinyl C's).

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