Quinolines from Oxime O-Acetates

A Thesis Presented for the Degree of Doctor of Philosophy

By

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At

School of Chemical Sciences

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August 2004

To Mam, Dad, Anna and Lavelle.

Declaration

I, the undersigned, hereby declare that this thesis, which I now submit for assessment on the programme of study leading to the award of Ph.D., represents the sole work of the author and has not taken from work of others save and to the extent that such work has been cited and acknowledged within the text.

Ray Tully

Table of Contents

Abstract

The photochemistry of a number of arylidenecyclopentanone oxime O-acetates has been investigated Irradiation in methanol leads to initial E-Z geometrical isomerisation and ultimately to the formation of nitrogen containing heterocycles, via a 6π-electron photocyclisation process, followed by an elimination

The scope of the reactions has been extended by investigation of substrates incorporating a range of electron-donating aryl substituents The photocyclisations of 2-(4-dimethylaminobenzylidene)-, 2-(4-hydroxy-benzylidene)-, 2-(4-acetoxybenzylidene) and 2-(2,5-dimethoxybenzylidene) cyclopentanone oxime O-acetates and 2-(4-aminobenzylidene) cyclopentanone oxime were investigated

Substitutents in the 3-position of the aryl system may potentially result in cyclisation at either the 2- or 6-positions of the aryl group In practice cyclisation has been found to be highly regioselective The range of regioselective reactions has been extended by substitution in the aryl 3-position with t-butyl, hydroxy, acetoxy, dimethylamino and amino groups The regioselectivity of the cyclisation reaction has also been investigated with a number of disubstituted aryl groups

An oxime O-acetate derivative of phenothiazine, underwent cyclisation as did 2-(3-phenyl-allylidene)cyclopentanone oxime O-acetate

The leaving group in these cyclisation reactions is oxygen-based A preliminary investigation into a small number of nitrogen-based leaving groups was carried out

Semi-empirical calculations were carried out on a number of 3-substituted oxime O-acetates to investigate the reasons for the observed regioselectivities during photocyclisation

Acknowledgements

I would firstly like to thank my supervisor Prof Albert Pratt for his patience, supervision, advice and encouragement throughout my time at DCU I would also like to thank him sincerely for giving me the opportunity to do this work and for his good humour throughout it all

I would also like to thank the technical staff of the school of chemical sciences for their time and advice, especially Mick, Damian, Maurice and Ambrose I am also very grateful to Veronica and Ann for their help whenever needed Also a special mention to Vinny

Thanks also to Dr Dermot Brougham, Dr Paddy Kane and Noel O'Boyle for their assistance with HyperChem

Special thanks go to my fellow postgrads, past and present for keeping me sane and giving me good advice (well sometimes anyway) I would particularly like to thank, Dugs, Johnny, Darren, Tommy, Neil, Rob, Nameer, Shane, John, Kev, Ian, Moss, Steve, Dave, Ger, Frankie, the two Noels, Dec, Ben and Colm (thanks for all the chemistry tips), Mairead, Lorraine, Andrea, Cathal, Ji-Feng, Yang, Peter, Rachel, Claire, Stephania, Paula, the two Fionas, Marco, Adrian and Bill If I have forgotten anyone, I apologise Thanks everyone for all the nights out and all the laughs

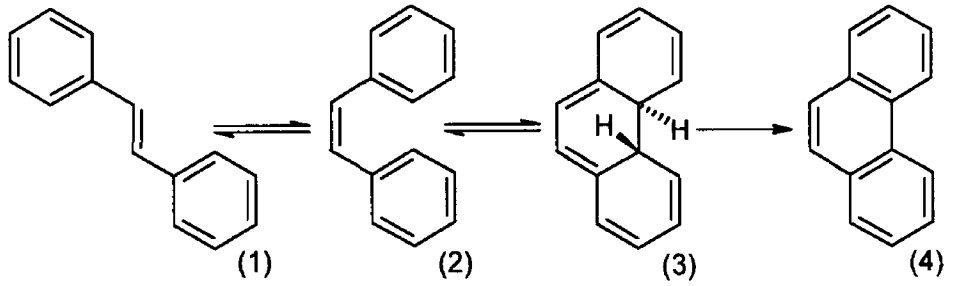
I would like to thank my family and friends for their encouragement and the friendship over the years Especially my Mam, Dad and little sister Anna Thanks for all your support and understanding

Last and by no means least, the lovely moolady and love of my life, Lavelle Thanks for pushing me all the way and always giving me the encouragement I needed to get the job done I would not be here without you

1. The Photocyclisation of 6π-Electron Systems

1 1 6π-Electron Cyclisation

The formation of 6π polycyclic systems by intramolecular photocyclisations is a common process for many different types of aromatic compounds and is a reaction that has been used as a key step in a variety of synthetic pathways In 1934 Smakula observed that a compound having λ_{max} 247 nm was formed from the irradiation of a solution of cis-stilbene (2) [1] Lewis, Magel and Lipkin found that a yellow substance was formed immediately upon irradiation of cis-stilbene, but only slowly from trans-stilbene (1) [2] This suggested the formation of a secondary product directly from cis-stilbene However, it was not until 1950 that the compound having λ_{max} 247 nm was identified as phenanthrene (4) by Parker and Spoerri [3] As phenanthrene is colourless, its presence could not account for the yellow colour observed [2] Buckles confirmed the formation of phenanthrene which he obtained in good yields [4]



(1) (2) (3) (4)

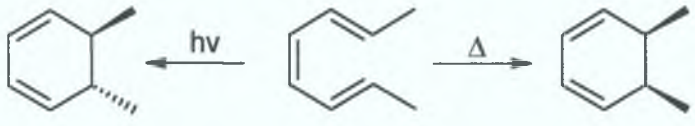
In olefins the singlet (π-π*) excited state cyclisation of stilbene to dihydrophenanthrene (3) and the subsequent formation of phenanthrene is a well documented process [4 5] The allylic hydrogens of the dihydrophenanthrene are susceptible to abstraction by a suitable oxidant, in this case O_2 or I_2 The reaction fails to produce phenanthrene in a nitrogen atmosphere with the careful exclusion of oxygen, suggesting dihydrophenanthrene undergoes ring opening to regenerate cis-stilbene

The photocyclisation of stilbenes may be considered to be analogous to that of a 1,3,5-triene system According to a series of rules formulated by Woodward and Hoffmann, a pericyclic reaction can take place only if the symmetry of all reactant molecular orbitals is the same as the symmetry of the product molecular orbitals The lobes of reactant molecular orbitals must be of

the correct algebraic sign for bonding overlap to occur in the transition state leading to the product.

If the orbital symmetries of both reactant and product match up, or correlate, the reaction is said to be symmetry allowed, likewise if they don't correlate, the reaction is symmetry disallowed. The Woodward-Hoffmann rules for pericyclic reactions require an analysis of all reactant and product molecular orbitals. A simplified version, the frontier orbital approach, in which we need consider only the two molecular orbitals called the frontier orbitals, was developed.

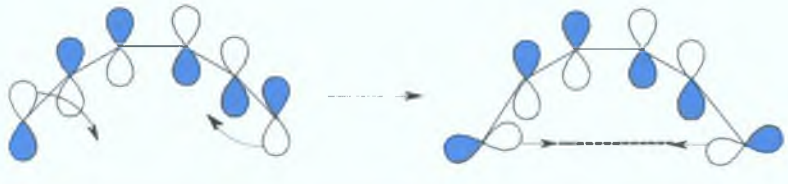
According to the frontier orbital theory, the stereochemistry of an electrocyclic reaction is determined by the symmetry of the polyene's Highest Occupied Molecular Orbital (HOMO). For thermal ring openings and closings, the ground state electronic configuration is used to identify the HOMO.



Scheme 1

For example (2E,4Z,6E)-octatriene involves three π-bonds (scheme 1). Therefore there are altogether six π-orbitals, three bonding and three anti-bonding. The highest energy bonding orbital is the HOMO, Ψ_3 (scheme 2).

In the HOMO orbital (ψ_3), a disrotatory movement is required for ring closure



In the HOMO* orbital (ψ_4), a conrotatory movement is required for ring closure

Scheme 2

To form the new σ-bond on cyclisation in the ground state, the orbital lobes on the terminal atoms must each rotate through 90^0 in opposite directions (a disrotatory movement) This disrotatory cyclisation is exactly what is observed in the thermal cyclisation of 2,4,6-octatnene The 2E,4Z,6E isomer yields the cis product, 5,6-dimethyl-1,3-cyclohexadiene

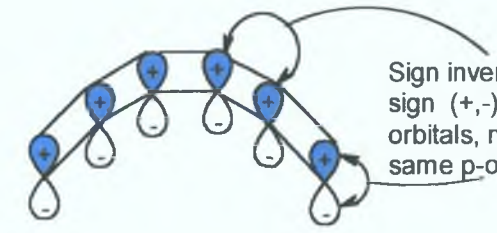
However when in the excited state, an electron is promoted from the ground state HOMO, Ψ_3, into the ground state Lowest Unoccupied Molecular Orbital (LUMO), Ψ_4 In the excited state, the LUMO is now occupied and in theory is therefore the HOMO* The star indicates that the HOMO* is in fact the LUMO from the ground state It can be seen from scheme 2 that in this state, a conrotatory movement is required for overlap of orbital lobes which are in phase This conrotatory cyclisation is exactly what is observed in the photocyclisation of 2,4,6-octatnene The 2E,4Z,6E isomer yields the trans product, 5,6-dimethyl-1,3-cyclohexadiene

The cyclisation of stilbenes (1) may also be considered to be a 6π electron cyclisation, analogous to that of hexatnene The structure which cyclised to form the ring involves three π-bonds (scheme 2) Therefore there are altogether six π-orbitals, three bonding and three anti-bonding The highest energy bonding orbital is the HOMO, Ψ_3 To form the C-C bond on cyclisation in the ground state, the orbital lobes on the terminal atoms (in this case on the carbon atoms position 2 on either phenyl nng) must each rotate through 90^0 in opposite directions (a disrotatory movement)

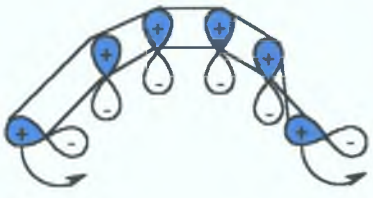
However when in the excited state, an electron is promoted into the LUMO, Ψ_4 It can be seen from scheme 2 that in this state, a conrotatory movement is required for overlap of orbital lobes which are in phase Therefore, cyclisation probably proceeds via a conrotatory movement of the terminal atom orbitals

An alternative approach to predicting the mode of photochemical electrocyclisation is the Aromatic Transition State approach or the Mobius-Huckel method In this method the orbital symmetry rules are related to the Huckel aromaticity rule Huckel's rule states that a cyclic system of electrons is aromatic when it consists of 4n + 2 π-electrons, and are therefore more stable than their non-cyclic counterparts, whereas those with 4n π-electrons

are less stable and are antiaromatic. In applying the orbital symmetry principle to electrocyclisation processes we are not concerned with ground states, but



Sign inversions are differences in sign (+,-) between neighbouring orbitals, not between lobes of the same p-orbital.



A conrotatory movement is predicted to be favourable because in the excited state there must be an odd number of sign inversions (in this case 1) for a Mobius system.

Scheme 3

with transition states. In using this method we do not examine the molecular orbitals themselves, but rather the p-orbitals before they overlap to form the molecular orbitals. Such a set of p-orbitals is called a basis set. The basis set for the "triene" portion of the molecule (2E,4Z,6E)-octatriene is shown in scheme 3.

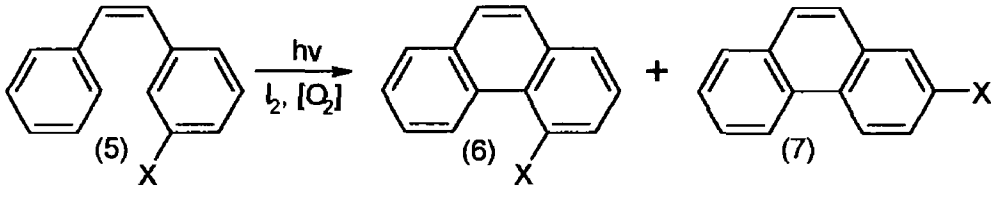
Analysis of the cyclic transition states of concerted reactions is in terms of their "aromatic" and "antiaromatic" nature. Those that are "aromatic" are allowed processes and those that are "antiaromatic" are forbidden processes. The transition state is drawn, one having an even number of sign inversions (such as zero), is called a Hückel system, whereas one having an odd number of sign inversions is called a Möbius system. A Hückel system is aromatic when there are 4n + 2 π-electrons and antiaromatic when there are 4n π-electrons. A Möbius system is aromatic when there are 4n π-electrons and antiaromatic when there are 4n + 2 π-electrons. Thermal pericyclic reactions occur via aromatic transition states, while photochemical pericyclic reactions occur via antiaromatic transition states.

In the ground state for a Hückel system, a thermal pericyclic reaction is allowed only if the total number of participating π-electrons is 4n + 2. A photochemical (excited state) reaction of this type is forbidden for a Hückel

system but is allowed for a Mobius system Therefore for 6π-electron ring closure of (2E,4Z,6E)-octatriene by the conrotatory mode, the system is of the Mobius type Therefore it is antiaromatic and according to the Mobius-Huckel rule this is predicted to be favorable

1 2 Stilbene Photocyclisation

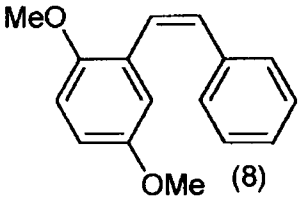
Mallory and his co-workers have studied the synthetic potential of the photocyclodehydrogenation reaction of substituted stilbenes to give phenanthrenes in good yield [5-8] They found that the most satisfactory conditions for preparative scale conversions involved the irradiation of the stilbene analogue and iodine dissolved in cylcohexane under an air atmosphere When oxygen was excluded, so that iodine was the only oxidant present, the time required for the conversion of the stilbene was not altered significantly but the yield of phenanthrene was decreased Chloranil and selenium were also found to be useful oxidants Yields were generally in the 60-85% range Successful conversions were achieved with stilbenes bearing fluoro, chloro, bromo, methoxy, methyl, trifluoromethyl, phenyl and carboxyl substituents but the method failed for stilbenes having nitro, acetyl or dimethylamino substituents Iodo substituents were found to be lost owing to the ready photolysis of the carbon-iodine bond Mallory and Mallory[9] have



X = Me, Cl or CF_3

also reported the photocyclisations of some meta-substituted stilbenes (5) leading to the formation of 2- and 4-substituted phenanthrenes (6) and (7) The isomer ratios of the photocyclisation gave product ratios near unity with the yield of (7) found to be in slight excess

The photocyclisation of 2,5-dimethoxystilbene (8) in hexane to 1,4-dimethoxyphenanthrene in 71% yield has been reported [10] Kitamura and co-



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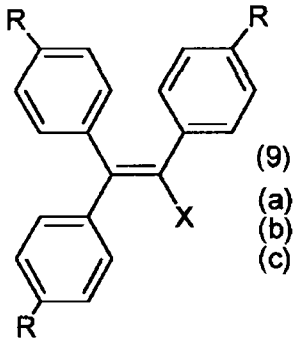
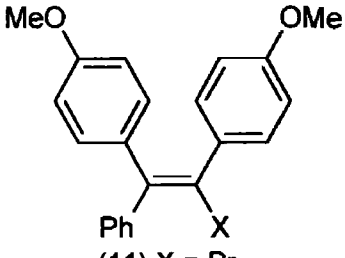
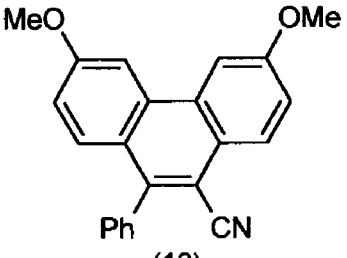


(9) + (10)
(a) R = H
(b) R = Me
(c) R = OMe

workers[11] have reported the irradiation of triarylvinyl bromides (9a-c, X = Br) in methanol to give the vinyl ethers (10a-c, X = OMe) and the corresponding phenanthrenes The yield of the phenanthrenes was around 20% with the vinyl ether being the main product of the reaction In a similar reaction the photocyclisation of the vinyl bromide (11, X = Br), in acetonitnle with excess potassium cyanide, led to formation of (12, X = CN) and the phenanthrene (13) in 35% yield [12] The photocyclisation of 2,3-diphenylacrylic acid (14) was carned out in methanol leading to moderate yields of 9-phenanthrene-carboxylic acid [13]



(11) X = Br
(12) X = CN



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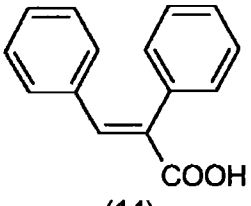
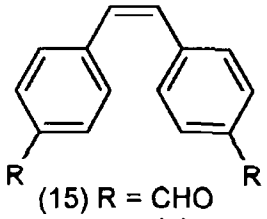
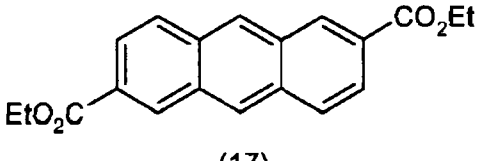


(14)

The failure of the photocyclisation-oxidation reaction of acetylstilbenes to acetylphenanthrenes is well known and has been rationalised in terms of the intervention of the (n-π*) excited states of the carbonyl group [7] In contrast



(15) R = CHO
(16) R = CO_2Et

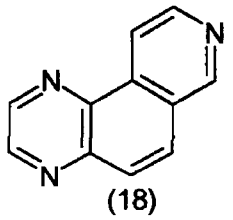


(17)

to this previous failure the photocyclisation of the closely related 4,4'-stilbenedicarbaldehyde (15) to 3,6-phenanthrenedicarbaldehyde has been reported[14] in 40% yield

In a similar reaction the photocyclisation of 4,4'-diethoxycarbonylstilbene (16) to the analogous phenanthrene, has been reported,[15] accompanied by formation of 2,6-diethoxycarbonylanthracene (17) The ratio of the phenanthrene analogue of (16) to (17) was 4 1 The authors tentatively proposed[15] a mechanism for the formation of the anthracene (17), in which cyclisation takes place from a triplet-excited state In the triplet state the ethylenic double bond is weakened and the molecule can revert to a transoid conformation

Several examples of azaphenanthrene formation by photocyclisation of stilbenes have been reported [16-18] In one study,[16] 2-(β-arylvinyl)pyrazines were the substrates, and a typical product was the pyridoquinoxaline (18) 1,4,5,8-Tetra-azaphenanthrene (19) was formed from 1,2-bis(pyrazyl)-ethylene [17] Interestingly, oxygen was used to oxidise the dihydro-intermediate, iodine being unsuitable because it complexes strongly with the starting material and enhances intersystem crossing Perkampus and Bluhm[18] have reported the photocyclisation of the six isomeric trans-styryldiazines to give the corresponding diazaphenanthrenes (20)



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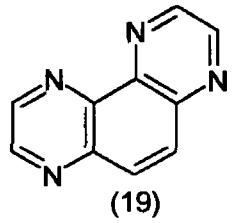

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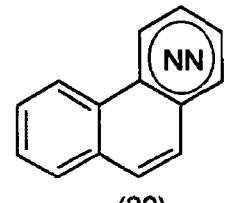
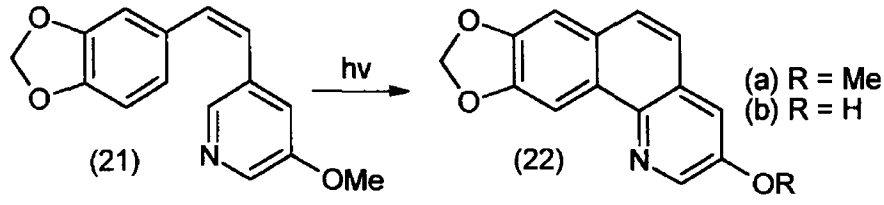
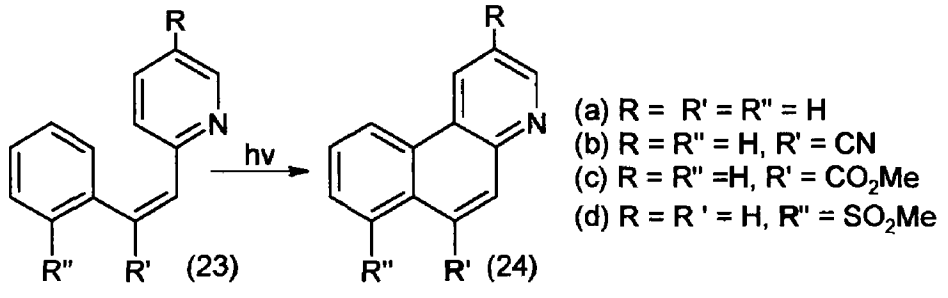


(20)

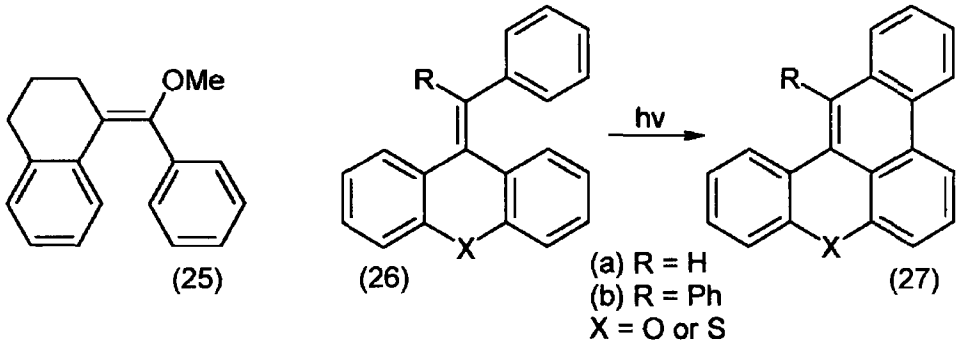
The synthesis of natural products often involves a key photochemical step Toddaquinoline (22b), an alkaloid from Toddalia asiatica, has been synthesised by Harrowven and co-workers,[19] by irradiation of the azastilbene (21) in cyclohexane, giving the toddaquinoline methyl ether (22a) as a minor component in a 20% yield Demethylation to yield the phenol (22b) has proved difficult and provided toddaquinoline in only low yields



The photochemical behaviour of a series of 2-stilbazole derivatives was investigated as part of a synthesis of various alkaloids [20] The 2-stilbazoles (23a-c) photocyclised in various solvents to yield the corresponding benzo[f]quinolines (24a-c) t-Butyl alcohol was found to be the solvent of choice In a similar reaction the photosynthesis of the sulphur containing benzo[f]quinoline (24d) from the equivalent 2-stilbazole (23d) has been achieved [21] Various other sulphur containing benzo[f]quinolines have also been synthesised

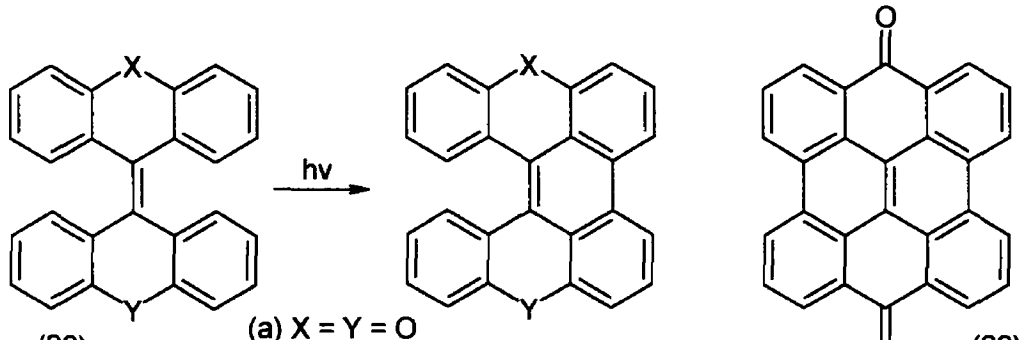


Naturally, rigidly held stilbene moieties yield phenanthrene derivatives on irradiation Kitamura and co-workers[22] have reported the photocyclisation of the stilbene analogue (25) in methanol to yield 9-methoxy-1,10-propano-phenanthrene in 44% yield The photocyclisation of 9-benzylidenexanthenes



and 9-benzylidenethioxanthenes (26a,b, X = O or S) yields compounds (27a,b, X = O or S) from both sunlight and u v irradiation [23]

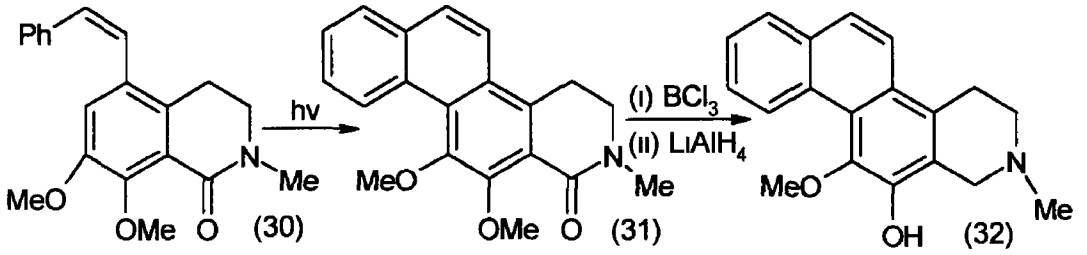
Schonberg and Junghans[24] reported the photocyclisation of the bixanthenes (28a-c) The compounds only undergo a single photocyclisation Similarly the compounds (28d,e) undergo only a single photocyclisation [25,26] The authors conclude that the central unsaturation should be olefinic for photocyclisation to occur Without this structural feature the electronic distribution in the excited state may be such that there is not sufficient electron availability at the two ortho positions between which the new bond would be expected to form The exception to this behaviour is in the bianthrone system (28f) Both bianthrone[27] and substituted bianthrones[28-30] have been reported to undergo two successive oxidative photocyclisations to give naphthodianthrones (29) The reasons for this anomalous character of bianthrones were not given



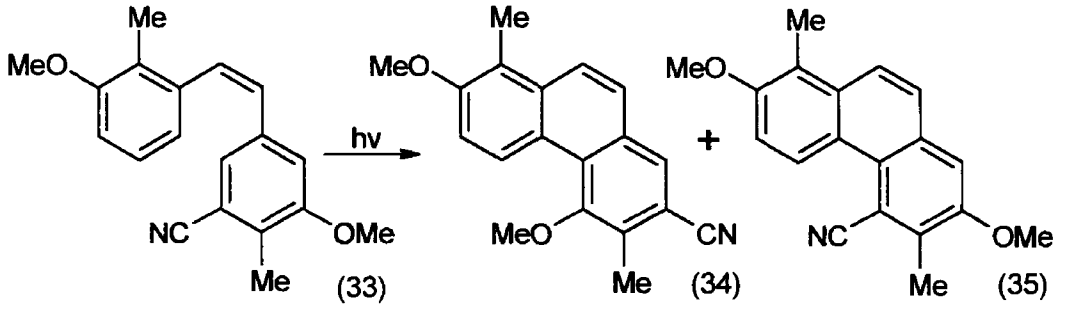
(28) (29)

(a) X = Y = O
(b) X = O, Y = S
(c) X = Y = S
(d) X = CO, Y = O
(e) X = CO, Y = S
(f) X = Y = CO

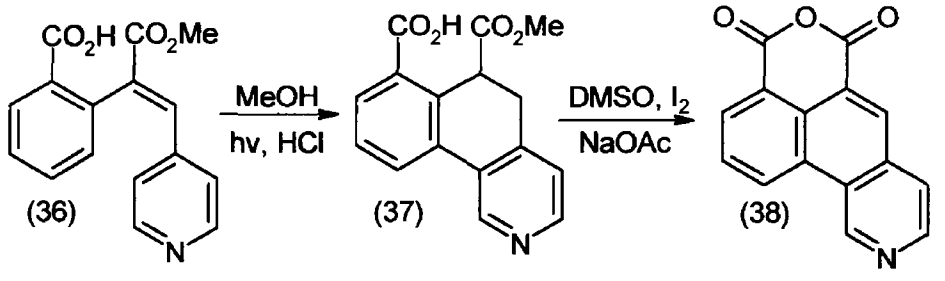
A key step in the total synthesis of the 1,2,3,4-tetrahydronaphtho[2,1-f]isoquinoline annoretine (32), a naturally occurring alkaloid, is a stilbene-like photocyclisation reaction [31] Benzophenanthridine alkaloids, of which annoretine is a member, are used as antibacterial and anti-tumoral drugs The 5-styrylisoquinoline (30) was photocyclised to yield the naphthoisoquinoline (31), which was then converted to the annoretine (32)



A total synthesis of Juncusol, a cytotoxic constituent of the needlerush *Juncus roemerianus*, has been reported [32] The photocyclisation of the cyanostilbene (33) in benzene yielded two regioisomeric phenanthrenes (34) and (35) in a 7 1 ratio Unfortunately the major photoproduct was the unwanted isomer (34) The 7 1 ratio of photocyclisation isomers (34) and (35) from the cyanostilbene (33) was unexpected Studies have shown that the isomer ratios from meta-substituted stilbenes are usually of the order 1 1 to 2 1, and are relatively insensitive to the electron donor or acceptor properties of the substituent(s) [9]



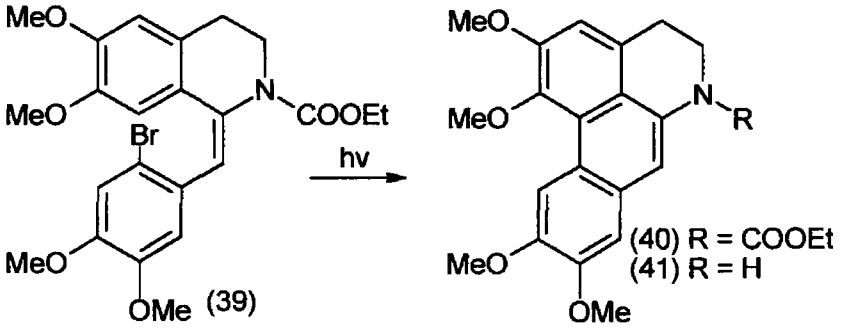
A key step in the synthesis of the azaphenanthroic anhydride (38) is a stilbene like photocyclisation [33] The photolysis of the azastilbene (36) yielded the dihydroazaphenanthrene (37), which when heated in DMSO with iodine



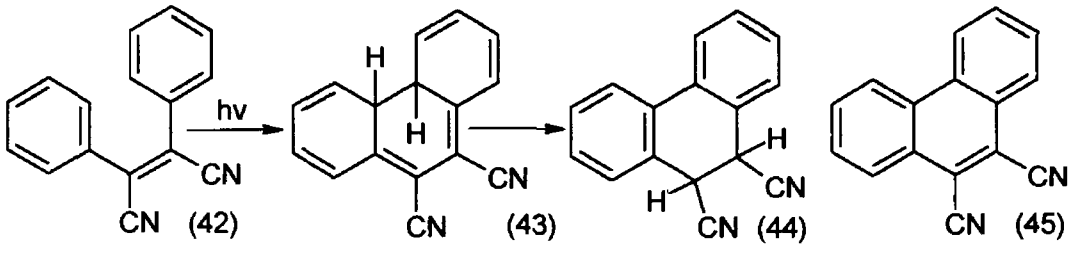
furnished 6-aza-1,10-phenanthroic anhydride (38) The anhydride is a key intermediate in the synthesis of an unsymmetrical bis-imide antitumour agent

Gupta and Bhakuni have reported[34] the synthesis of dehydronorglaucine, an aporphine alkaloid isolated from different plant sources Nonoxidative photocyclisation of bromostilbene (39) furnished N-ethoxycarbonyldehydronorglaucine (40) which on treatment with ethanolic hydrochloric acid afforded dehydronorglaucine (41)

Sargent and Timmons[35] have reported the photocyclisation of 9,10-dicyanostilbene (42) in chloroform to yield the expected phenanthrene-9,10-dicarbonitrile (45) They also isolated the 9,10-dihydrophenanthrenene (44) in small amounts They proposed that the dihydrophenanthrene (44) is a



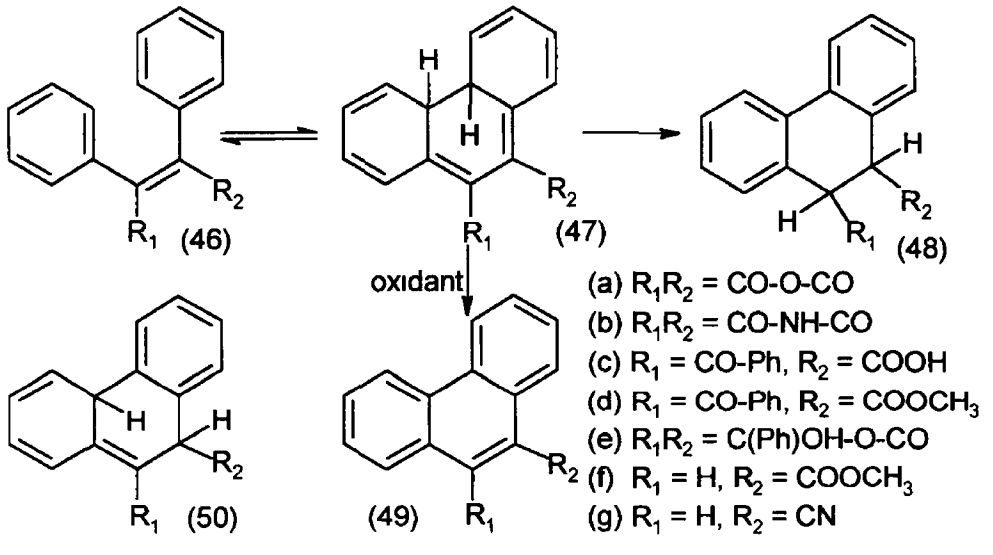
rearrangement product of photolysis intermediate (43) Irradiation of the dicyanostilbene (42), as a suspension in water gave phenanthrene-9,10-dicarbonitrile (45) and (44) in yields of 22% and 60% respectively [36] The



dependence of the efficiency of the light-induced cyclisation of dicyanostilbene (42) on pH has led to the suggestion of ionic intermediates [37] 9,10-Dicyano-9,10-dihydrophenanthrene (44) was formed below pH~4,

whereas the amount of 9,10-dicyanophenanthrene (45) increases with pH increase

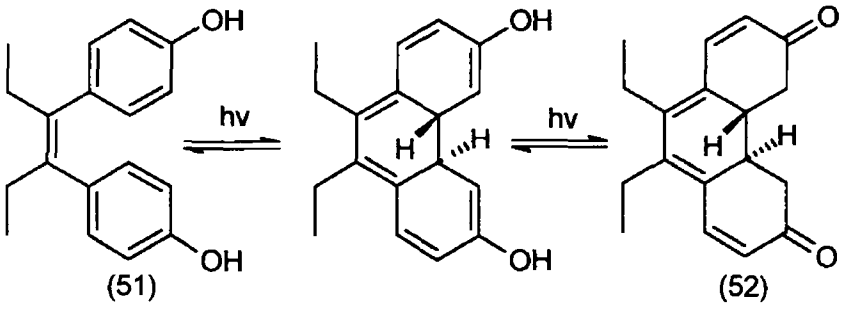
In a few cases it was found that irradiation of a stilbene in the absence of an oxidant yielded a 9,10-dihydrophenanthrene The cyclisation of stilbenes (46a-b) which possess two electron-withdrawing substituents on the double bond yield the products (48a-b) on irradiation under nonoxidative conditions [38] In 1970 Rio and Hardy[39] obtained the 9,10-dihydrophenanthrenes (48c-e) on irradiation of the stilbenes (46c-e) in various alcohols or in a mixture of water-pyridine as the solvent, even when the irradiation was carried out in the presence of oxygen Performing the reaction in D_2O-pyridine showed that the hydrogens at C_9 and C_{10} in the products were derived from the solvent They suggested a mechanism wherein prototropic shifts are responsible for the isomerisation of the 4a,4b-dihydrophenanthrene (47c-e) to the corresponding 9,10-dihydrophenanthrene (48c-e) They proposed that compounds with only one electron-withdrawing substituent on the olefinic bond might not be expected to give 9,10-dihydrophenanthrenes



However in 1971 Srinivasan and Hsu[40] reported the first example of a photocyclisation wherein a stilbene derivative (46f) having only one electron-withdrawing substituent on the olefinic bond gave a 9,10-dihydrophenanthrene (48f) as the product The authors suggested[40] a radical mechanism for the photoreaction, which does not proceed via the 4a,4b-

dihydrophenanthrene intermediate (47f) Laarhoven and co-workers[41] have reported the photocyclisation of (46g) in methanol At neutral pH no (48g) was formed At pH 3 (48g) could be isolated, even in the presence of oxygen Laarhoven[41] has reinvestigated the photocyclisation of (46f) The mechanism has shown the 4a,4b-dihydrophenanthrene (47f) denvative is an intermediate In protic solvent this intermediate undergoes a prototropic shift leading to a 4a,9-dihydrophenanthrene denvative (50f) This product was then converted to the end product (48f) by a radical process

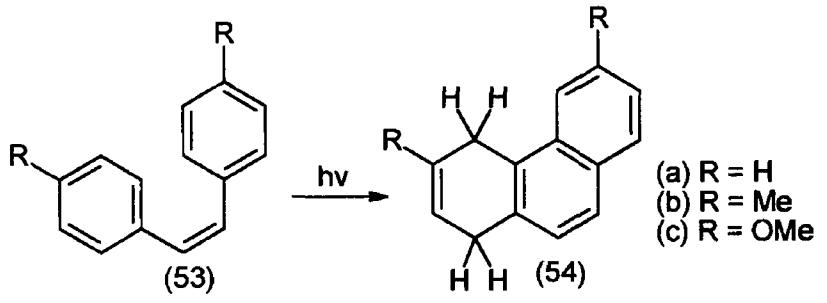
Although the photooxidative cyclisation of stilbenes to phenanthrenes is a reaction of remarkable generality and synthetic utility, the definitive mechanistic studies have been thwarted by the extreme instability of the proposed intermediate dihydrophenanthrenes Isolation has proved very difficult because of rapid oxidative hydrogen abstraction to phenanthrenes or reverse ring opening to starting stilbenes Doyle and co-workers[42-43] have reported the isolation of a stable dihydrophenanthrene intermediate (52), obtained upon irradiation of diethylstilbestrol (51) Stabilisation of this dihydrophenanthrene was conferred by a unique self-trapping double enol/keto tautomerism NMR analysis confirmed the trans stereochemistry of the inner 4a, 4b hydrogens Cuppen and Laarhoven[44] have provided chemical proof of the trans configuration of (52) The dihydrophenanthrene (52) was ozonolysed to yield the expected tetracarboxylic acid The unambiguous establishment of the trans configuration of (52) proves that the cyclisation of (51) proceeds in the first excited state and not from a vibrationally excited ground state



(51) (52)

The photocyclisations of stilbenes in propylamine has been reported [45] This reaction proves to be a facile synthetic route to 1,4-dihydro-

phenanthrenes, compounds which are usually difficult to obtain by other preparative methods Irradiation of the stilbenes (53a-c) led to the formation of

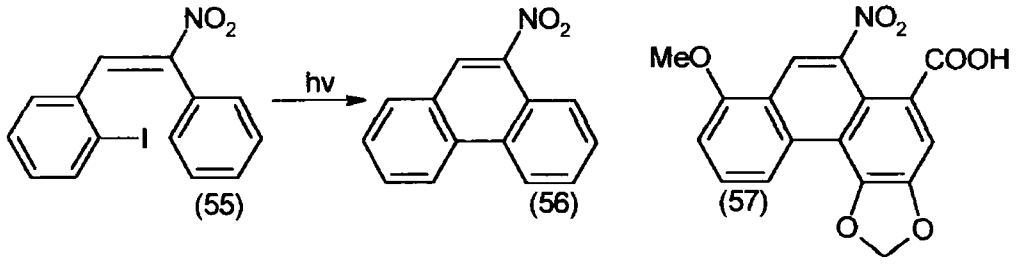


the 1,4-dihydrophenanthrenes (54a-c) in ~70% yields The expected phenanthrene was only found in minor yields Use of π-acceptors such as chloranil and tetracyanoethylene improved the rate of the reaction and the punty of the products obtained [46] Improved yields were also reported when iodine and propylene oxide in the absence of air were used The propylene oxide prevents hydrogen iodide from photoreducing double bonds The absence of air prevents photooxidative side reactions [47]

1 3 Ortho Substituted Stilbenes

Substitution at the ortho or 2-position of the stilbene can be used to promote or inhibit cyclisation at that position Wood and Mallory reported previously that stilbenes bearing nitro substituents failed to undergo photochemical conversion to the corresponding phenanthrenes [8]

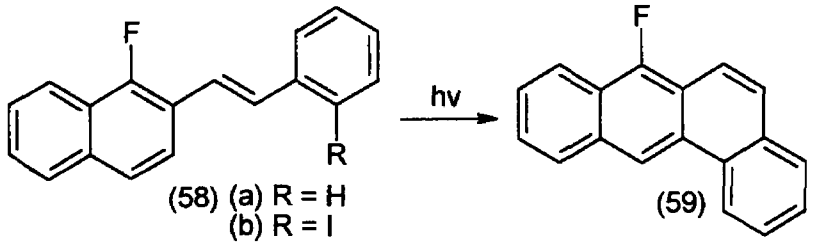
A publication by Kupchan and Wormser investigates the photolysis of α-nitro-2-iodo-cis-stilbene (55) [48] Photolysis of (55) gave a 40% yield of 9-nitrophenanthrene (56) The authors suggested[48] it was highly unlikely that



the photocyclisation of 2-iodostilbene proceeds via a similar intermediate to that of stilbene, i e via the dihydrophenanthrene intermediate α-Nitro-cis-

stilbene failed to yield any corresponding phenanthrene in the presence of added iodine or dissolved oxygen They suggested the photocyclisation of the 2-iodostilbene proceeds via a free-radical pathway with loss of hydrogen iodide The same authors also reported[48] the synthesis of aristolochic acid I (57), a tumour inhibitor found naturally in plants The synthesis was based on the photochemical reaction of the 2-iodostilbene (55) shown above

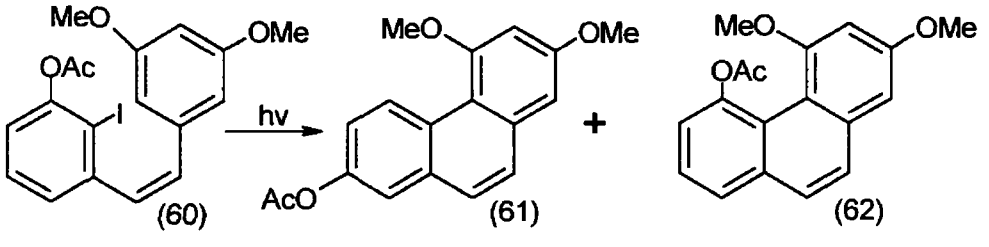
The synthesis of the benz[a]anthracene (59) was expected when the 1-position of 2-styrylnaphthalene was blocked as in (58a) However (58a) did not yield (59) but was only photoisomerised to the cis-isomer However the 2-iodo substituted ethylene (58b) yielded the desired photoproduct (59) [49]



(58) (a) R = H
(b) R = I

(59)

Letcher and Wong[50] further investigated the photochemical cyclisation of 2-iodostilbenes 3-Acetoxy-2-iodo-3',5'-dimethoxystilbene (60) was irradiated in the absence of free iodine and gave both the 7-acetoxy- (61) and the 5-acetoxyphenanthrene (62) in 80% and 20% yield respectively If the reaction involves initial homolytic cleavage followed by cyclisation at the radical site only the 5-acetoxy derivative (62) would be expected The 2-iodo group does not promote cyclisation at the iodine-beanng carbon atom, but



(60)

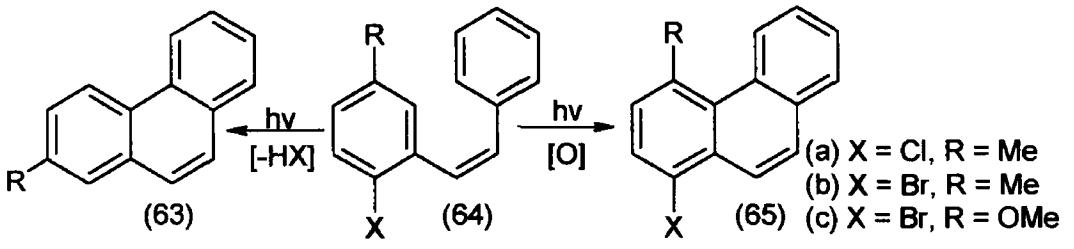
(61)

(62)

actually appears to inhibit cyclisation at this centre Therefore the iodo group cannot be employed to direct cyclisation selectively to the iodine bearing carbon unless the non-iodo-substituted stilbene itself does not undergo

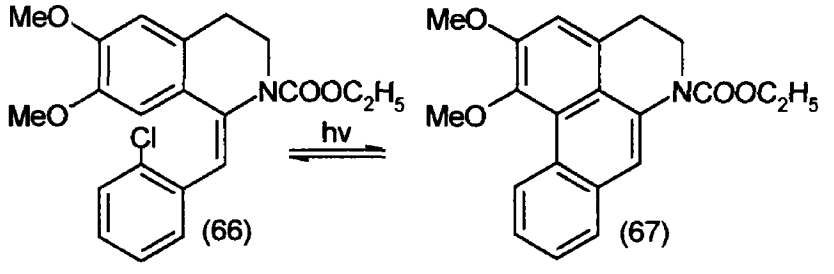
cyclisation The authors assume that the liberated iodine was employed in an oxidative photocyclisation to give the observed major product

Olsen and Pruett[51] reported the use of o-halostilbenes for regiochemical control in the photolysis of stilbenes with meta substituents

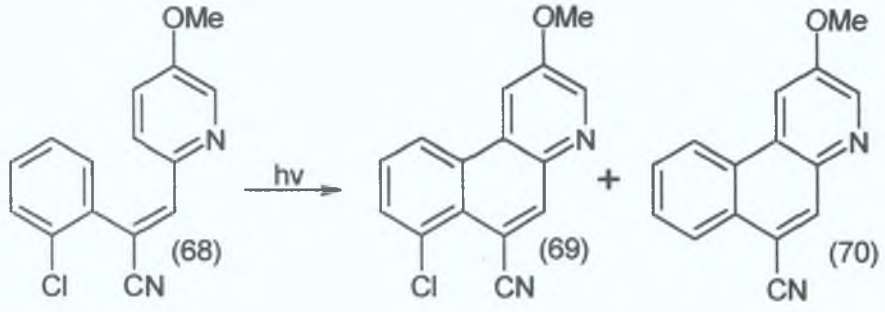


These generally photocyclise with little selectivity giving mixtures of 2- and 4-substituted phenanthrenes Compounds (64a-c) were cyclised under both oxidative and non-oxidative conditions Under oxidative conditions the products (65a-c) were the major photoproducts of the reaction whereas under non-oxidative conditions the major photoproducts (63a-c) were furnished

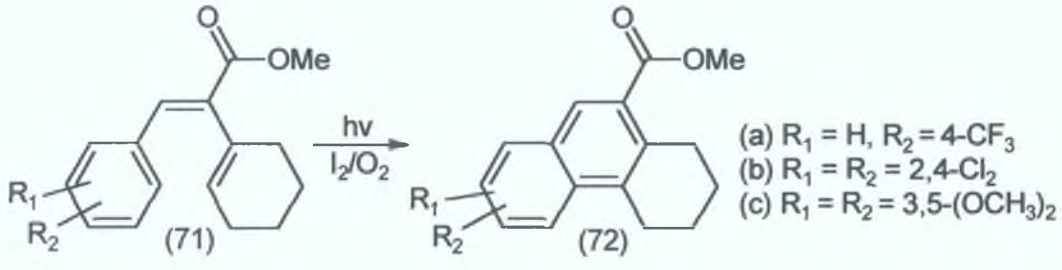
A key step in the synthesis of nuciferine, an aporphine alkaloid, is the non-oxidative photocyclisation of the 2-chlorostilbene analogue (66) followed by loss of hydrogen chloride to yield the dehydronornuciferine (67) [52]



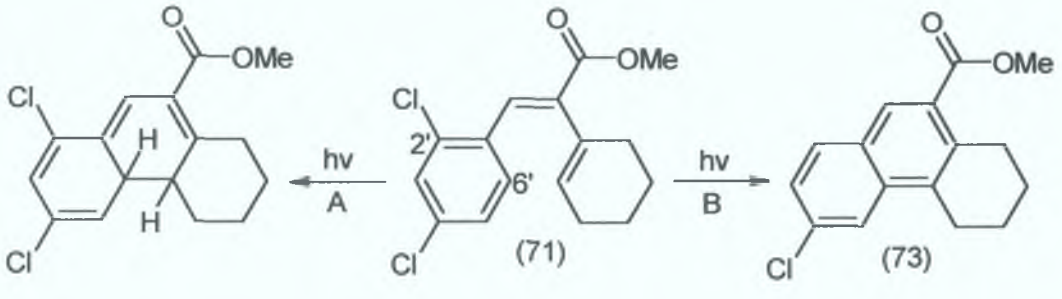
The photochemical behaviour of a series of 2-stilbazole derivatives has been reported as part of a synthetic scheme leading to the ergoline ring system of ergot alkaloids [53] Irradiation of the 2-stilbazole (68) in t-butyl alcohol under oxidative conditions led to photoproducts (69) and (70) in a 2 1 ratio The formation of (70) corresponds to loss of hydrogen chloride



The photocyclisation of α-(1-cyclohexenyl)cinnamic esters (71a-c) has been investigated by Srinivasan and co-workers.[54] Under oxidative conditions 5,6,7,8-tetrahydrophenanthrenes (72a-c) were formed in good yields. Under anaerobic conditions hexahydrophenanthrenes were formed from (71a) and (71c) respectively, whereas the dichlorocinnamate (71b) forms the monochlorotetrahydrophenanthrene (73). The authors concluded[54] that the

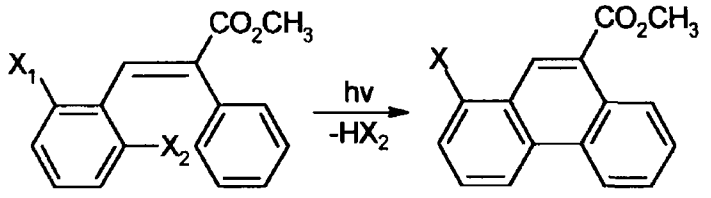


formation of (73) can be ascribed to initial photocyclisation at C-2' followed by subsequent elimination of hydrogen chloride (reaction B). Cyclisation at C-6' (reaction A) would lead to the formation of a hexahydrophenanthrene.



The photochemical conversion of 2,6-dihalo substituted methyl α-phenylcinnamates has been reported.[55] Phenylcinnamates and their derivatives are known antifungal and antibacterial agents. Dihalophenyl-

cinnamates (74a-c) were irradiated to form methyl 1-halo-9-phenanthroates (75) and (76) following dehydrohalogenation of the intermediate (74a) and (74b) formed (75) and (76) respectively On irradiation (74c) formed a mixture of the phenanthroates (75) and (76) in a ratio of 85 15 A less favourable ring-

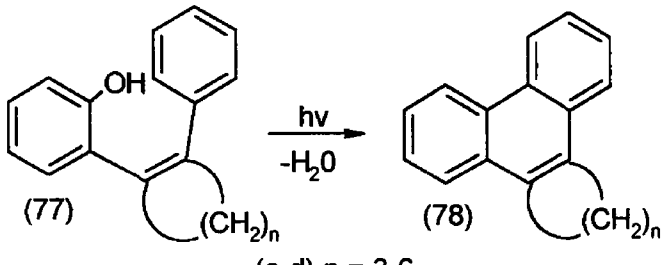


(74) (a) $X_1 = X_2 = Cl$
(b) $X_1 = X_2 = F$
(c) $X_1 = Cl$, $X_2 = F$

(75) X = Cl
(76) X = F

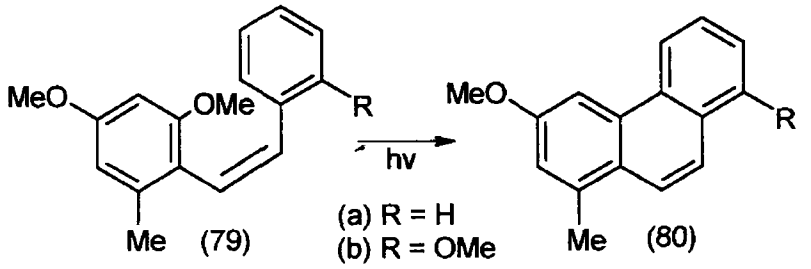
closure at the chloro substituent compared to that at the fluoro substituent might be due to steric effects

Eberbach and Hensle[56] have reported the photocyclisation of o-hydroxy stilbenes (77a-d) to phenanthrenes (78a-d) following loss of water, with yields of 20-50% The yield of phenanthrene decreased with increasing value for n

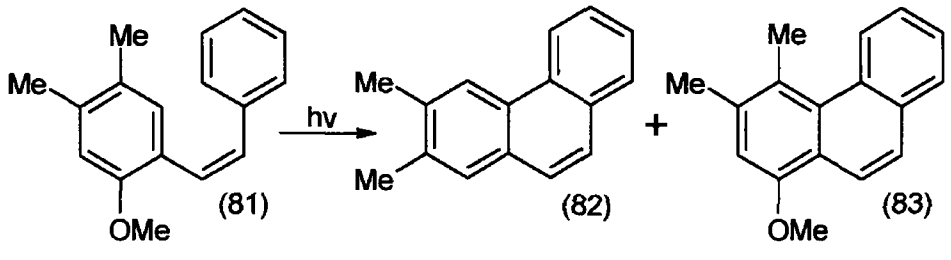


(a-d) n = 3-6

2-Methoxystilbenes undergo photocyclisation under non-oxidative conditions to yield phenanthrenes by loss of the methoxy group [57] Previously Wood and Mallory[8] had reported that the u v irradiation of 2-methoxystilbene under oxidative conditions gave a detectable amount of phenanthrene which could not be isolated, the major product being 1-methoxyphenanthrene More recently Giles and Sargent[57] repeated this experiment in deoxygenated cyclohexane under nitrogen and found that the major photoproduct was phenanthrene in 58% yield following elimination of methanol



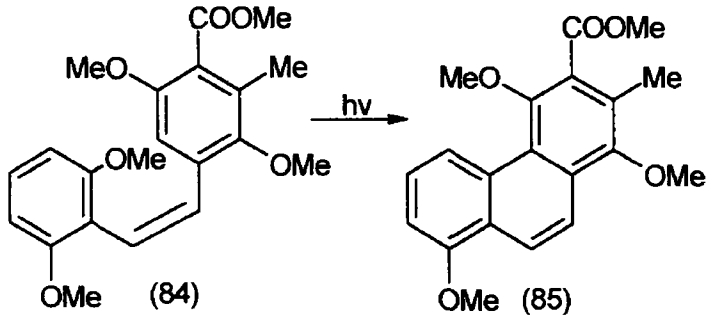
Giles and Sargent[58] have also reported the photocyclisation of the stilbene analogues (79a,b), under non-oxidative conditions, where cyclisation can potentially proceed by loss of either methanol or methane In both cases the phenanthrenes (80a,b) isolated involved loss of methanol Cyclisation of 2-methylstilbenes with expulsion of a methyl group is an oxidative process[62] whereas the photocyclisation of 2-methoxystilbenes is an non-oxidative process



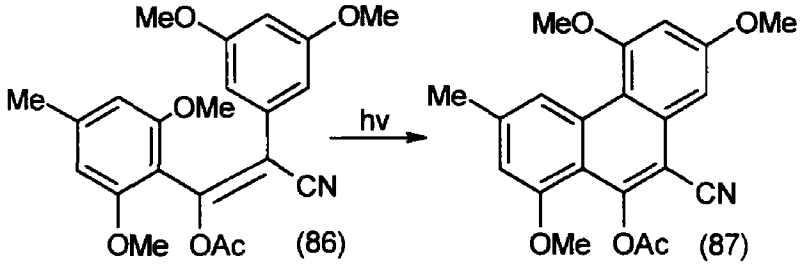
Marvell and co-workers[59] have reported the photocyclisation of 2-methoxy-4,5-dimethylstilbene (81) under both oxidative and non-oxidative conditions Under non-oxidative conditions the only photoproduct was 2,3-dimethylphenanthrene (82) while under oxidative conditions a 1 1 ratio of (82) and the 1-methoxy-3,4-dimethylphenanthrene (83) was formed

A key step in the synthesis of the mould metabolite piloquinone, a naturally occurring phenanthrene-9,10-quinone, involves the photocyclisation of the stilbene (84) [60]

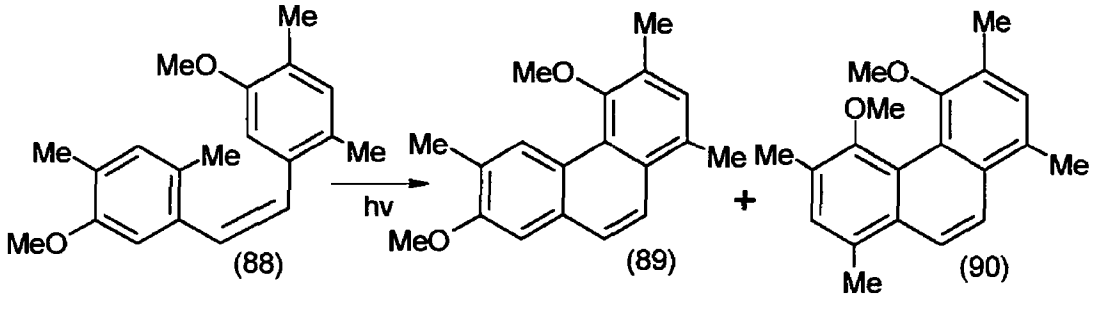
Upon photocyclisation loss of methanol lead to the required phenanthrene (85) The photocyclisation of the 2-methoxystilbene (86) has



been reported [61] The resulting phenanthrene (87) is a key intermediate in the synthesis of the fungal metabolite mollisin

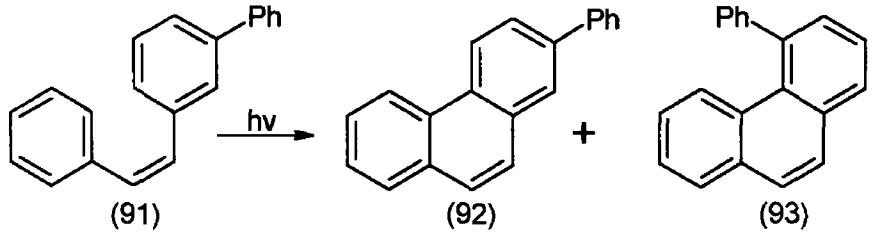


Newman and Chung[62] have reported the photocyclisation of the dimethoxytetramethylstilbene (88) Under oxidative conditions the main product of the photoreaction was the phenanthrene (89), formed by loss of a methyl group The phenanthrene (90) was formed in minor amounts The small amount of (90) formed was thought to be because of steric factors



The reduced loss of methyl groups during the photocyclisation of 2-methylstilbenes in the presence of amines has been reported by Lapouyade and co-workers [63] The use of amine solvent under oxygen-free conditions forces the reaction to follow an ionic pathway rather than the radical pathway usually invoked in the oxidative process The authors speculate[63] that the loss

of a methyl anion was unlikely, so that the reversibility of the cyclisation and of the protonation of the intermediate should favour the non-demethylated compound

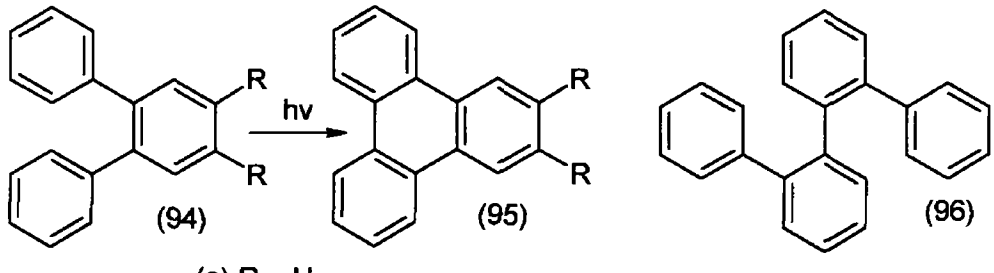


(91) (92) (93)

Cyclisation of 3-phenylstilbene (91) led to a mixture of compounds,[64] 2- (92) and 4-phenylphenanthrene (93) being formed in an almost 3 2 ratio The reason for the lower yield of (93) was thought to be steric

1 4 Cis Stilbenes

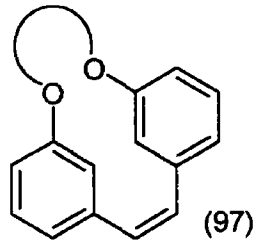
In compounds where the stilbene moiety was held in a cis configuration, by virtue of the molecular structure, their photocyclisation was generally an efficient process The photochemical formation of triphenylene (95a), in near quantitative yield, from o-terphenyl (94a) in the presence of iodine has been reported [65] Bushby and Hardy[66] have reported the photocyclisation of the dimethoxyterphenyl (94b) to dimethoxytriphenylene (95b) in 72% yield The same paper also reported[66] on the photocyclisation of various hexa-substituted o-terphenyls Sato and co-workers[67] have reported the double photocyclisation of 2,2'-diphenyl-biphenyl (96) to give dibenzo[fg,op]-naphthacene in 57% conversion



(94) (95) (96)

(a) R = H
(b) R = OMe

A new procedure for the synthesis of phenanthrenes with oxygen substitution at positions 4 and 5 has been developed [68] Photocyclisation of the cyclophane (97) led to the formation of the corresponding phenanthrene



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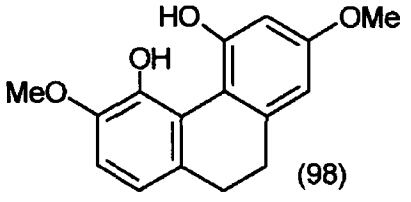
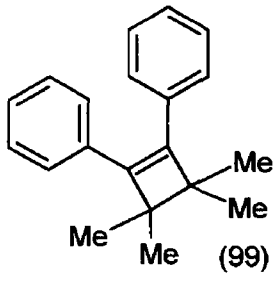


(98)

Removal of the cyclophane yielded the 4,5-O,O-disubstituted phenanthrene This method has been used in the total synthesis of Cannithrene II (98), a phenolic dihydrophenanthrene extracted from the leaves of the Cannabis sativa

The photocyclisation of 1,2-diphenyltetramethylcyclobutene (99) was investigated [69] Irradiation in acetonitnle led to the analogous phenanthrene in nearly quantitative yields In a similar reaction the 1,2-di-phenylcyclobutene (100) cyclised to the corresponding phenanthrene [70]

The key step in the synthesis of Tylophorine is the photocyclisation of septicene (101) in dichloromethane to furnish Tylophonne, the denved phenanthrene derivative, in 43% yield [71] The formation of phenanthro[9,10-c]isocoumarins (104a,b) was observed in an investigation primarily designed



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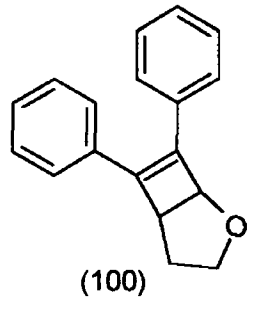

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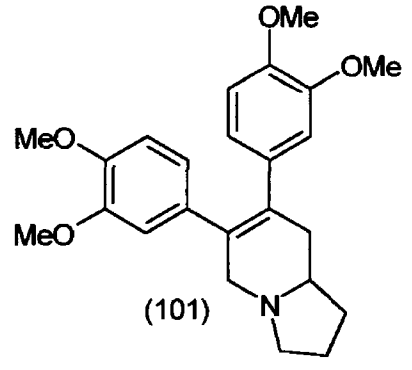
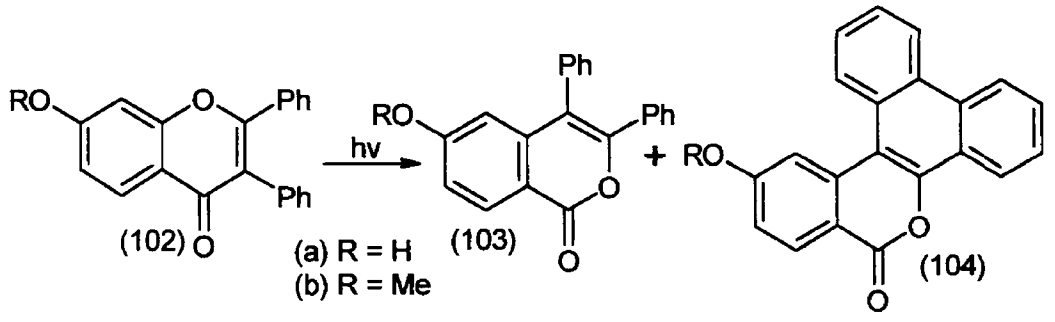
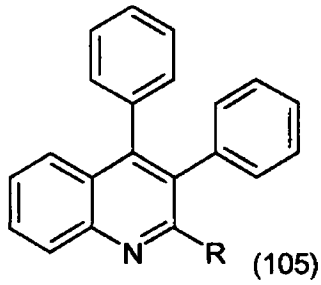


(101)

to study the photorearrangement of isoflavones (102a,b) to isocoumarins (103a,b) [72] When the reaction was carried out in the presence of iodine, phenanthro-[9,10-c]isocoumarins were afforded as the major photoproduct

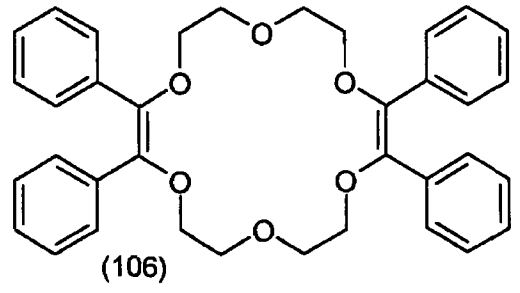


Diphenyl substituted six-membered heterocycles can also undergo stilbene-like cyclisation as seen in the reaction of 2-substituted-3,4-diphenylquinolines (105) to the corresponding phenanthrenes [73] The photochemistry of the unsaturated crown ether (106) has been reported [74] When (106) was irradiated in benzene with catalytic amounts of iodine and oxygen bubbling through the solution the diphenanthrene derivative was obtained as the sole crown ether in 50-60% yield



(105)

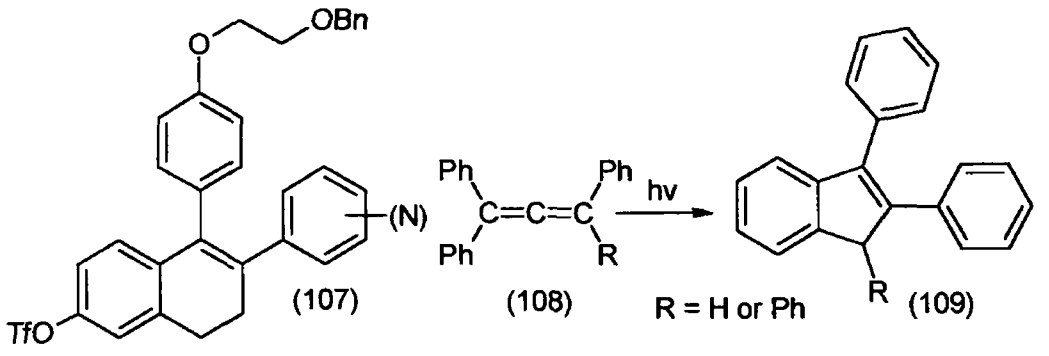
R = Me or Ph



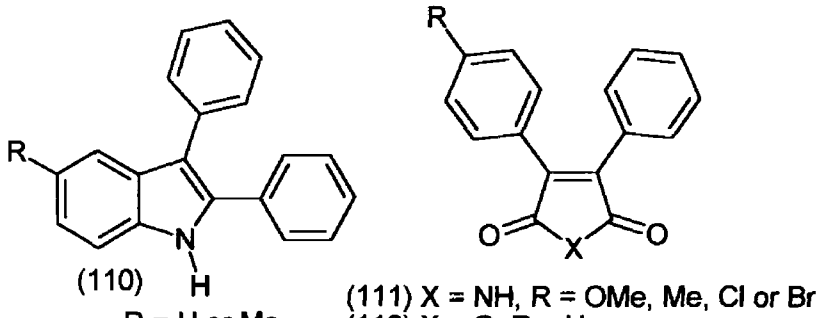
(106)

A key step in the development of fluorescent probes used in elucidating receptor structure and function for the estrogen receptor, is a stilbene-like photocyclisation [75] Irradiation of the stilbazoles (107) in cyclohexane yielded the four analogous azaphenanthrenes in good yields The formation of phenanthrene derivatives was observed in an investigation primarily designed to study the photochemistry of cumulenes (108) [76,77] Upon irradiation the cumulenes rearranged to the stilbene (109) which cyclised to the corresponding phenanthrene derivative

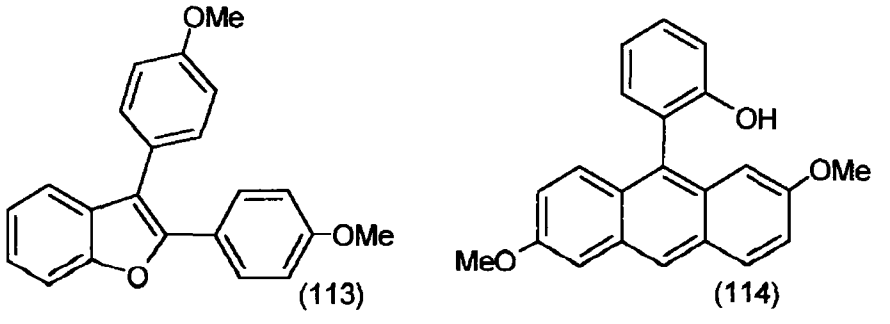
The irradiation of 2,3-diphenylindoles (110) produced the analogous dibenzo-carbazoles [78] The reactions were carried out in acetic acid and yields



were improved when iodine was added to the reaction The photocyclisation was carried out with several other substituted indoles The irradiation of the diphenylmaleimides (111) gave the phenanthrene derivative in excellent yields [79] The reaction was also carried out on several other substituted diphenylmaleimides Diphenyl substituted maleic anhydrides (112) have been shown to undergo cyclisation, in the presence of oxygen and iodine, to the analogous phenanthrene [80]

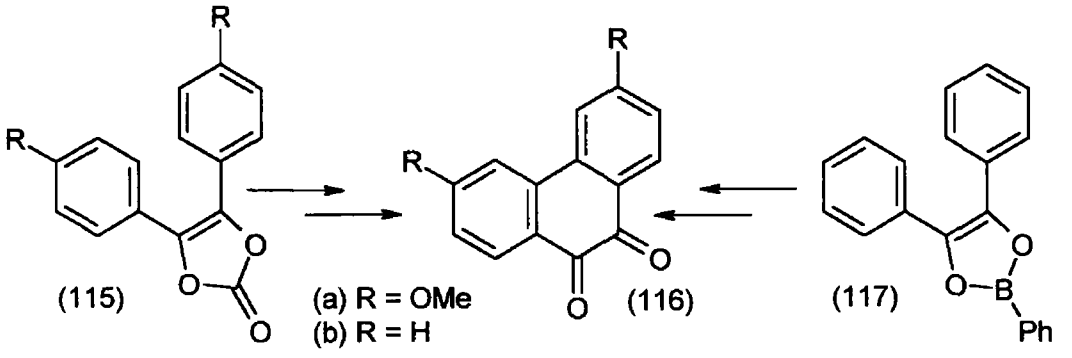


Photolysis of 2,3-bis-(p-methoxyphenyl)benzofuran (113) in benzene under nitrogen yielded beside the expected phenanthrene derivative, the novel rearranged anthracene (114) [81] Irradiation under nitrogen led to a 4 1

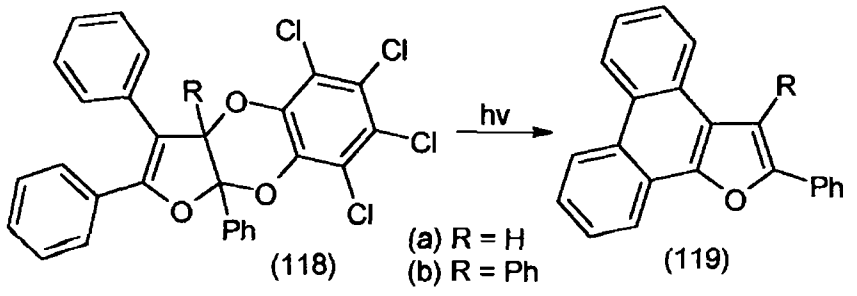


ratio of anthracene to phenanthrene When the reaction was carried out in the presence of air, anthracene formation was completely suppressed Evidence for the formation of the anthracene suggested an intersystem crossing to a reactive triplet state that underwent rearrangement

The synthesis of 9,10-phenanthrenequinones (116a,b) by photocyclisation has been reported by two groups [82,83] Lantos[82] reported the photocyclisation of the stilbene derivative (115a) in cyclohexane in good yields The facile conversion of the corresponding phenanthrene into 9,10-phenanthrenequinone (116a) was carried out in refluxing acetic acid In the second method,[83] reaction of benzoin with phenylboric acid gave the triphenyldioxoborole (117), which on irradiation in benzene, readily gave the 9,10-phenanthrenequinone (116b) in 54% yield

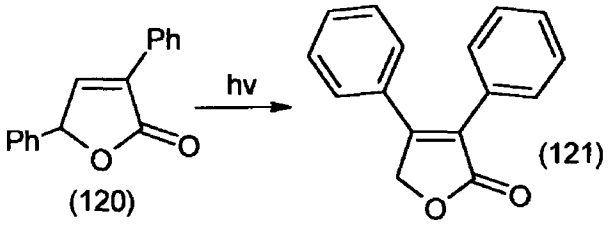


Tri- and tetraphenylfuran did not give the expected phenanthrene on photolysis, but underwent decomposition However on treatment with tetrachloro-1,2-benzoquinone, adducts (118a,b) are formed which undergo photocyclisation in propan-2-ol to give excellent yields of the 2-phenyl (119a) and 2,3-diphenylphenanthro[9,10-b]furans (119b) respectively, with elimination of the benzoquinone moiety [84] The electronic effects which prevent

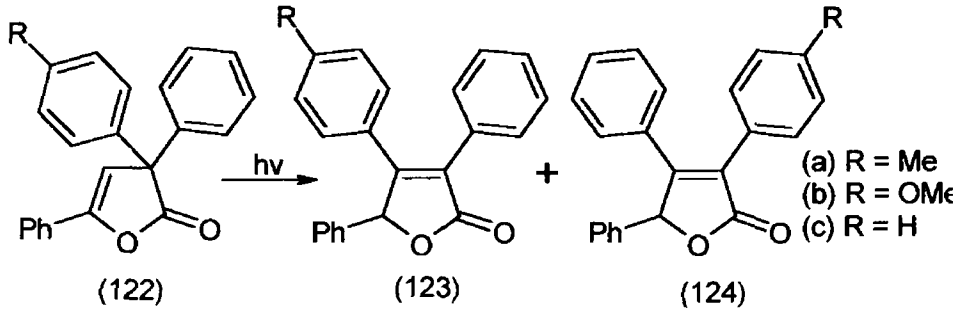


cyclisation in the parent molecules are circumvented The reaction has also been investigated with various substituents on the phenyl rings [85]

As part of an investigation into the photochemical rearrangements of furanones, phenanthrene like compounds were formed [86] Irradiation of the furanone (120) in benzene led to the rearranged product (121) and subsequent formation of the corresponding phenanthro[9,10-c]furanone

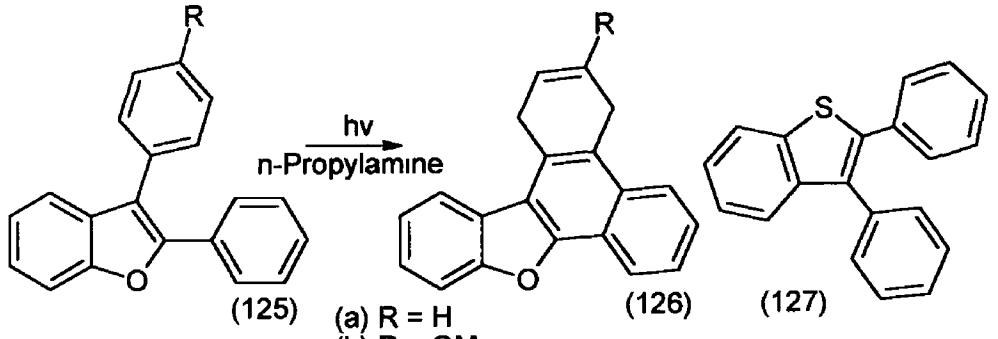


George and co-workers[87 88] have also reported the photorearrangement of 3,3,5-triaryl-2(3H)-furanones to 3,4,5-tnaryl-2(5H)-furanones and subsequent stilbene cyclisation The tnaryl-2(3H)-furanones (122a,b) on photocyclisation in benzene, with acetone as sensitiser, yielded two isomers (123a,b) and (124a,b) in a 3 2 ratio for (a) and a 2 3 ratio for (b) along with the related phenanthrofuranones in the same ratios [87] Photorearrangement of the furanone (122c) to (123c) also led to the phenanthrofuranone derivative [88] The photocyclisation was also observed for several other substituted furanones



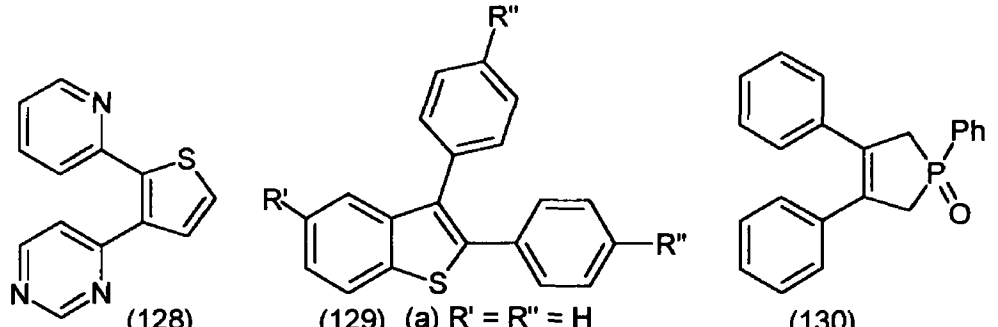
Couture and co-workers[89 90] have reported the photocyclisation of benzo[b]furans and their analogues When the 2,3-diphenylbenzo[b]furans (125a,b) were irradiated in methanol they were converted into the corresponding benzo[b]phenanthro[9,10-d]furans in good yields Upon

irradiation in n-propylamine under nitrogen the major photoproducts were found to be the dihydro derivatives (126a,b) The photocyclisation of the benzothiophene (127) to the derived phenanthrene derivative has been reported in moderate yield [91]



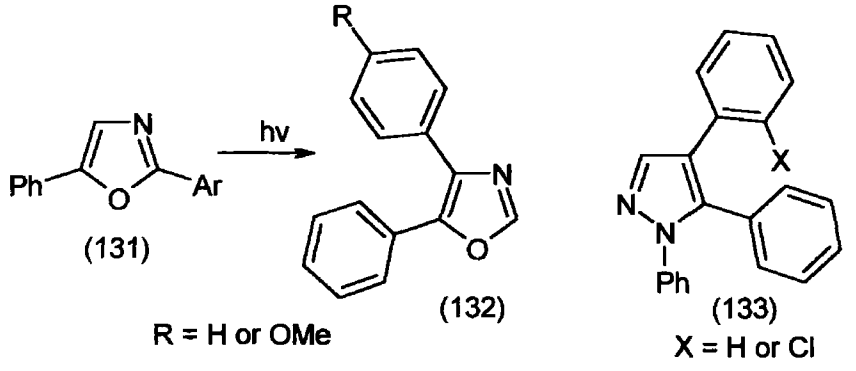
(125) (a) R = H (b) R = OMe (126) (127)

The photocyclisation of the thienostilbenes (128) has been reported [92] The reaction took place in water and yielded the corresponding thieno[3,2-e]pyndo[2,3-g]quinazoline The photochemical behaviour of several benzo-[b]thiophenes (129a-c) has been reported [93] Cyclisation of the thiophenes in cyclohexane in the presence of iodine led to the formation of the analogous phenanthro(9,10-d)benzo[b]thiophene in almost quantitative yields A key step in the construction of large-ring phosphorus compounds is the photocyclisation of the triphenyl-3-phospholene oxide (130) [94] The reaction was carried out in benzene with oxygen and iodine present and gave the corresponding phenanthrene in 56% yield



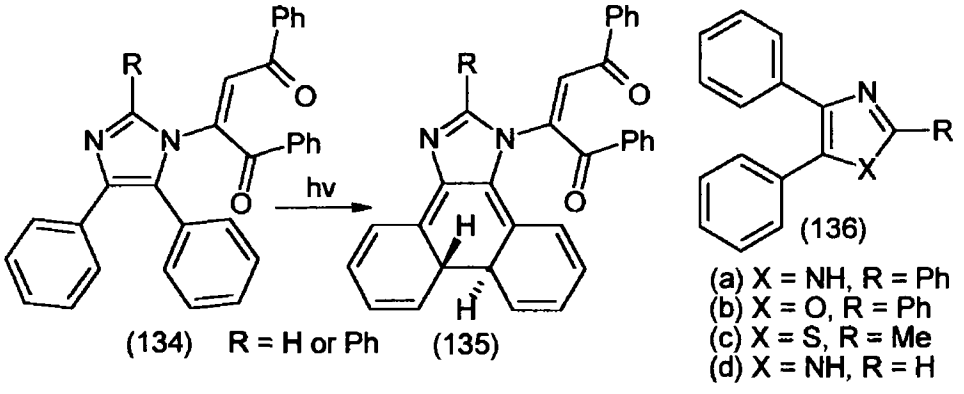
(128) (129) (a) R' = R'' = H (b) R' = Me, R'' = H (c) R' = H, R'' = Me (130)

Phenanthrenes have been found from the photorearrangements of phenyloxazoles [95] Irradiation in benzene led to photorearrangement of the 2,5-diaryloxazoles (131) to 4,5-diaryloxazoles (132) which are stilbene derivatives, and undergo photocyclisation to the corresponding



phenanthro[9,10-d]oxazoles Photocyclisation of 1,4,5-triphenylpyrazoles (133), under nitrogen in the presence of iodine, afforded the analogous 1-phenyl-1H-phenanthro[9,10-c]pyrazole [96] In the absence of iodine only starting material was recovered

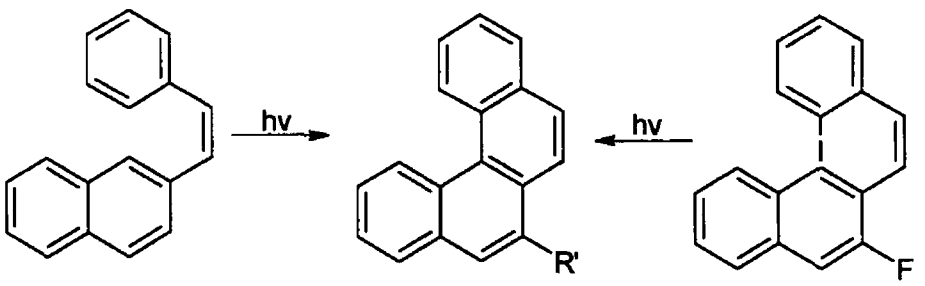
Irradiation of the imidazolyethylene (134) in benzene gave a mixture of the dihydrophenanthroimidazoyl derivatives (135) and the expected phenanthroimidazolyl derivatives as well as a number of isomers [97] A publication has appeared in which the photolysis of triphenylimidazole (136a) has been carried out leading to the formation of the analogous 2-phenyl-9,10-phenanthroimidazole [98] The photolysis of 4,5-diphenyl-oxazoles, -thiazoles and –imidazoles (136b-d) has been reported [99] The reactions were carried out



in ethanol with good yields of the corresponding phenanthro[9,10-d]-heterocyclic system

1 5 Benzostilbenes

The photocyclisation of β-naphthylstyrene (137) has been reported [100] Two modes of cyclisation are possible leading to either benzo-[c]phenanthrene or benz[a]anthracene In fact (137) gave only

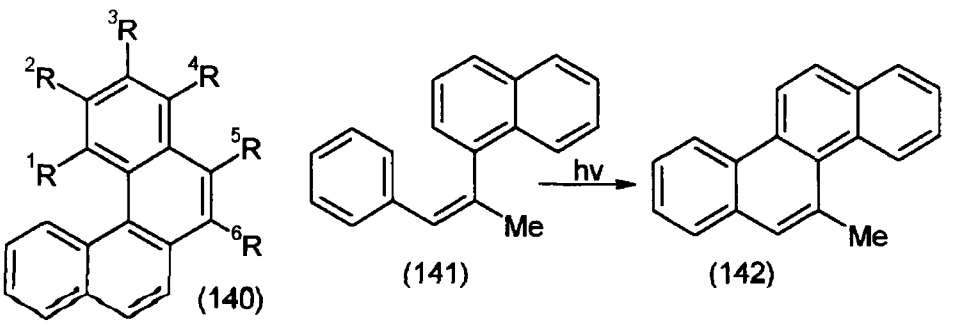


(137) (138) (139)

(a) R' = H
(b) R' = F

benzo[c]phenanthrene (138a) 6-Fluorobenzo[c]phenanthrene (138b) was synthesised by photocyclisation of the 1-β-naphthyl-2-phenylethylene (139), giving (138b) in greater than 90% yield [101]

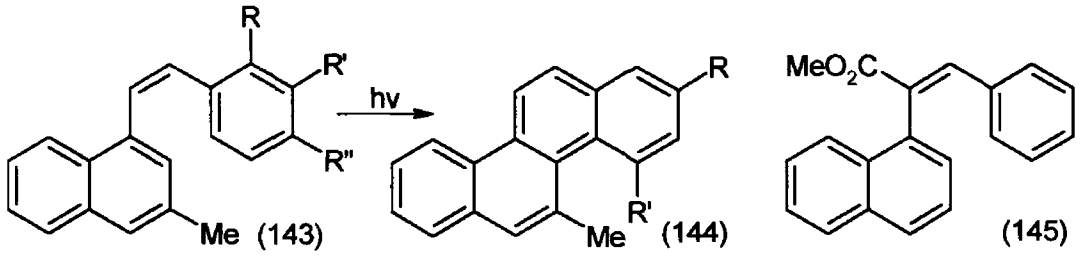
A number of papers have reported the synthesis of various alkylchrysenes [102-105] Nagel and co-workers have reported their investigation into the photocyclisation of various monomethylnaphthylstyrenes [102] The six isomeric monomethylphenanthrenes (140) were prepared in yields ranging from 66 to 89% Methylated chrysenes contribute to the tumour initiation and complete carcinogenic activity of tobacco smoke and have also been detected in coal-liquefaction products The synthesis of 5-methyl-chrysene (142) has



(140) (141) (142)

been reported by two groups [102,103] In both cases cyclisation of the naphthylstyrene (141) led to 5-methylchyrsene in moderate yields

Amin and co-workers[104] have synthesised various methoxy-5-methyl-chrysenes Photocyclisation of the naphthylstyrenes (143a,c) gave the analogous methoxy-5-methylchyrsene Photolysis of (143b) led to two products, 2-methoxy-5-methylchrysene (144a) and 4-methoxy-5-methyl-chrysene (144b) The paper also described[104] the synthesis of various other

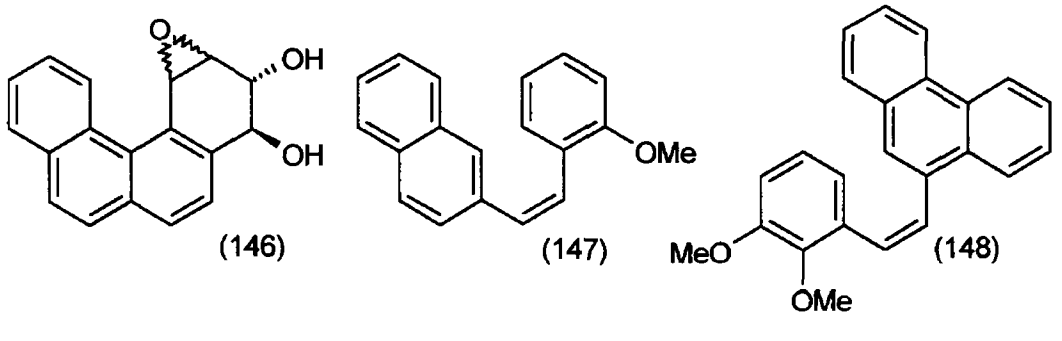


(a) R = OMe, R' = R'' = H
(b) R' = OMe, R = R'' = H
(c) R'' = OMe, R = R' = H

(a) R = OMe, R' = H
(b) R = H, R' = OMe

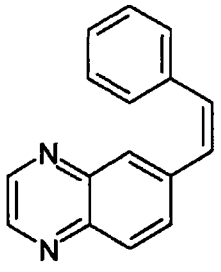
methoxy-5-methylchrysenes and their conversion into 5-methylchrysenols An improved photochemical synthesis of 5-methylchrysene has been reported [105] Photolysis of 2-naphthalene-1-yl-3-phenyl-acrylic acid methyl ester (145) to 5-carbo-methoxychrysene proceeded cleanly in 60% yield with subsequent conversion to 5-methylchrysene proving facile

A key intermediate in the synthesis of the highly carcinogenic benzo[c]phenanthrene-3,4-diol-1,2-epoxide (146) is 4-methoxybenzo[c]-phenanthrene,[106] obtained by photolysis of the olefin (147) in benzene The oxidative photocyclisation of the 1,2-diarylethylene (148) is a key step in the synthesis of the diol epoxide metabolites of the carcinogenic polycyclic



aromatic hydrocarbon benzo[g]-chrysene [107] Photocyclisation of dilute solutions of (148) in benzene with propylene oxide led to yields of around 85% of the corresponding dimethoxybenzo[g]chrysene

The photocyclisation reactions of aza derivatives of 2-styrylnapthalene have been reported [108] The azanaphthalene (149) was found to cyclise to the analogous naphtha[1,2-f]quinoxaline Loader and Timmons[109] have reported



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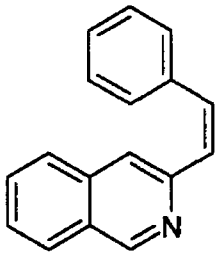

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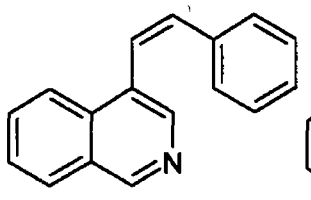

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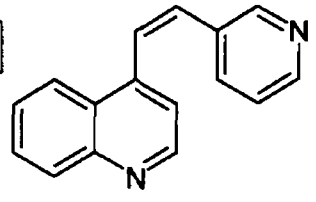
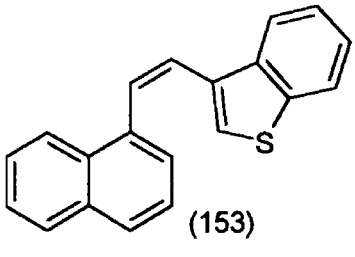


(152)

the photocyclodehydrogenation of some styrylquinolines and styryl-isoquinoline Irradiation of dilute solutions of 3-styrylisoquinoline (150), 4-styrylisoquinoline (151), and the 4-styrylquinoline (152) gave the expected benzo[a]- and benzo[c]phenanthridine, and benzo[2,8-c]phenanthroline respectively

The photocyclisation of benzothienyl napthylethylenes has been reported [110] Irradiation of the diaryl ethylene (153) yielded the expected thia-analogue of benzo[c]chrysene Surprisingly the cyclisation of the ethylene (154) led to cyclisation at the unsubstituted β-position of the naphthalene, even though the adjacent α carbon atom was free, to yield the anthracene derivative (155) No reasons for this unusual photocyclisation were given



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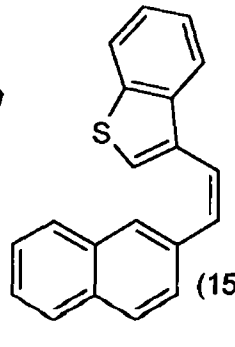

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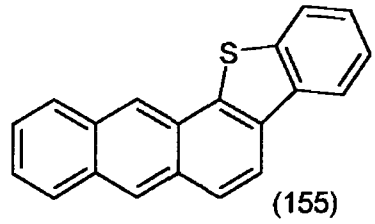
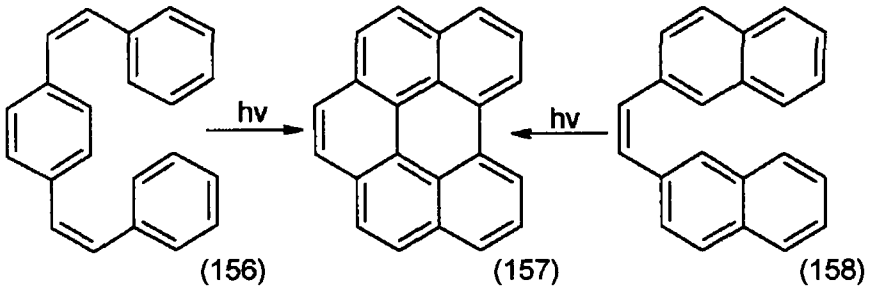


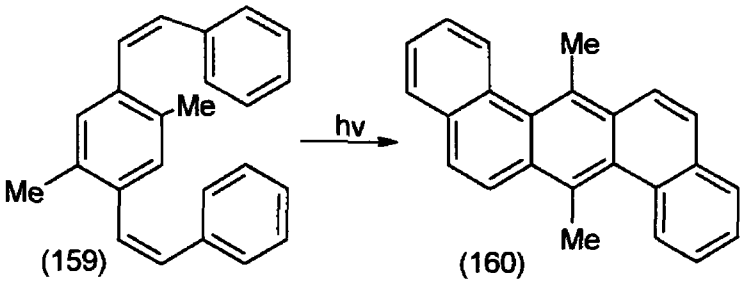
(155)

Irradiation of 1,4-distyrylbenzene (156) in methanol or benzene led to the formation of benzo[c,d,e]perylene (157) in small amounts [111] Benzo[c,d,e]perylene was also synthesised from 1,2-di-(2-naphthyl)ethylene (158) [112]

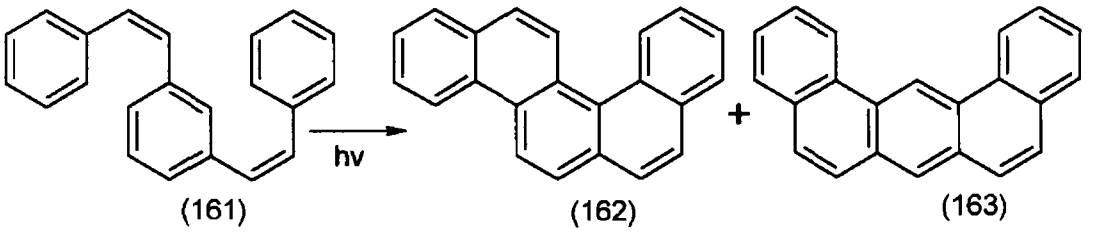


When the 2- and 5-positions of the distyrylbenzene are blocked, formation of dibenz[a,h]anthracenes occurs [113] Irradiation of 2,5-distyryl-p-xylene (159) yielded the anthracene (160) in 23% yield

Morgan and co-workers have investigated the photocyclisation of 1,3-distyrylbenzene (161) [114] Two main photoproducts were found, the expected benzo[c]chrysene (162) and dibenzo[a,j]anthracene (163) in a ratio of 3 1

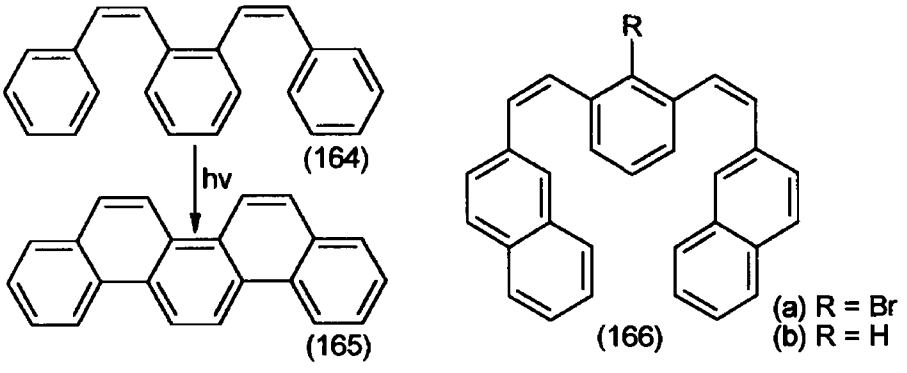


Dietz and Scholz also reported the cyclisation of 1,3-distyrylbenzene (161) [115] They only found the benzo[c]chrysene (162) and did not isolate



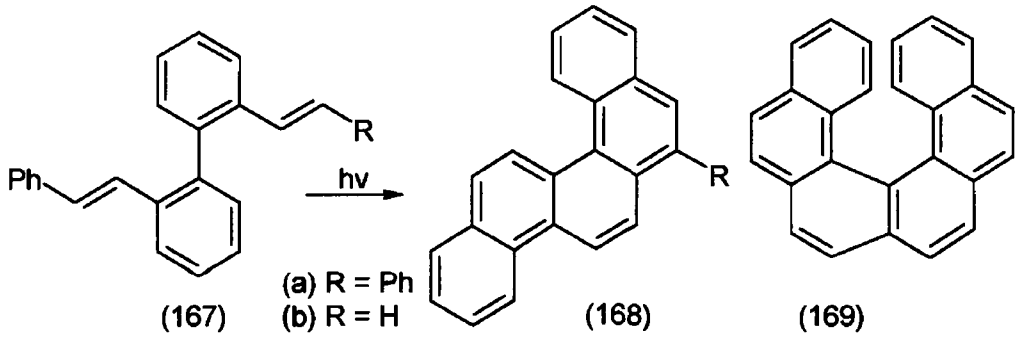
dibenzo[a,j]-anthracene (163) The same paper also reported[115] the cyclisation of 1,2-distyrylbenzene (164) to yield picene (165)

Cyclisation of the bromobenzene (166a) yielded the corresponding bromodinaphth[1,2-a 2',1-j]anthracene in 62% yield [116] It was reasoned that



the bromine substituent in (166a), by blocking any competing ring closure, played a crucial regiochemical role in the directing of the double stilbene-like photocyclisation toward the formation of dinaphth[1,2-a 2',1-j]anthracene Mallory and co-workers,[117] intrigued by the novel use of bromine as a blocking group investigated the cyclisation of (166b) in xylene, in the presence of iodine and oxygen Dinaphth[1,2-a 2',1-j]anthracene was obtained in 75% yield, implying that the bromine substituent in (166a) does not serve as a blocking group in the photochemical transformation of (166a) to dinaphth[1,2-a 2',1-j]anthracene

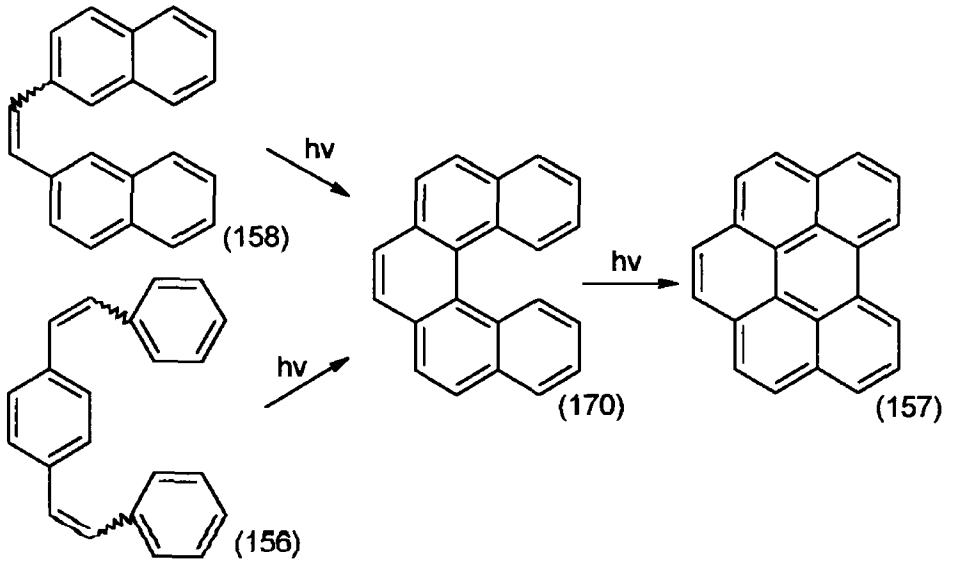
The photochemistry of the 2,2'-divinylbiphenyls (167a,b) has been investigated [118 119] Irradiation under nitrogen, in the presence of iodine, led to the corresponding benzo[c]chrysene (168a,b) as the sole photoproduct in each case



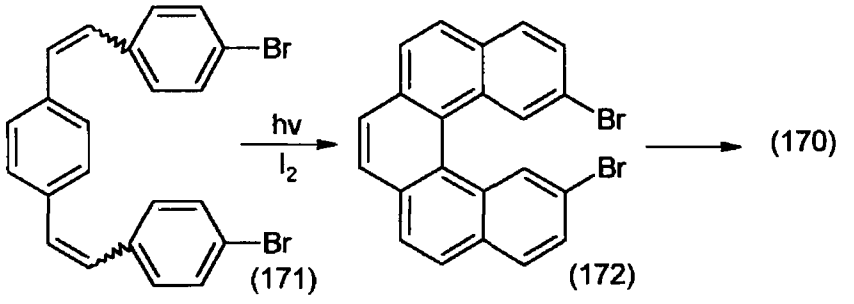
1 6 Helicene Formation

"Helicene" is the name introduced by Newman in 1955, to describe the benzologues of phenanthrene in which the extra ortho-condensed rings give rise to a cylindrical helix The pioneering work of Newman[120] in the synthesis and resolution of [6]helicene (169) opened the way to the study of a new class of synthetic molecules The helicenes are charactensed by a helical structure made up of ortho-condensed aromatic rings, by the presence of a powerful inherently chiral chromophore, and by the possibility of interactions between overlapping aromatic rings The scientific interest raised by these compounds is due to the unique combination of these three properties in a single molecule In the case of all benzene-helicenes, a frequently used nomenclature indicates the number of rings present in a compound by an Arabic numeral preceding the name "helicene" Thus compound (169), phenanthro[3,4-c]phenanthrene, is called [6]helicene Multiplying affixes can also designate the number of all types of rings Compound (169) is also called hexahelicene

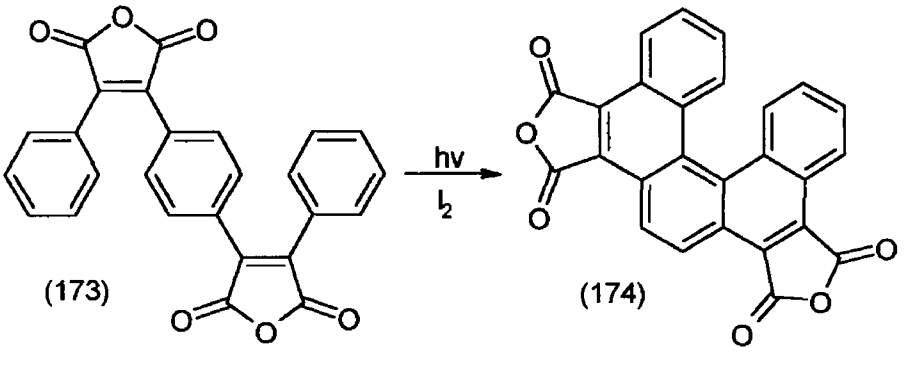
Although [5]helicene (170) can in pnnciple be obtained by oxidative photocyclisation of either 1,2-di-(2-naphthyl)ethylene (158)[100 112] or p-distyrylbenzene (156),[111 115] the rate at which the [5]helicene (170) then continues to photocyclise to benzo[g,h,i]perylene (157) makes it very difficult to prepare useful quantities in this way



A publication by Liu and Katz reported the synthesis of [5]helicenes from the dibromide of p-distyrylbenzene [121] 4,4'-Dibromodistyrylbenzene (171) was photocyclised in benzene to yield the dibromo[5]helicene (172) The bromines were then removed using butyl lithium to yield [5]helicene (170) The bromines protected the ortho carbons in the dibromo[5]helicene (172), preventing further reaction from occurring The bromines also enhanced the photocyclisation process for (171)

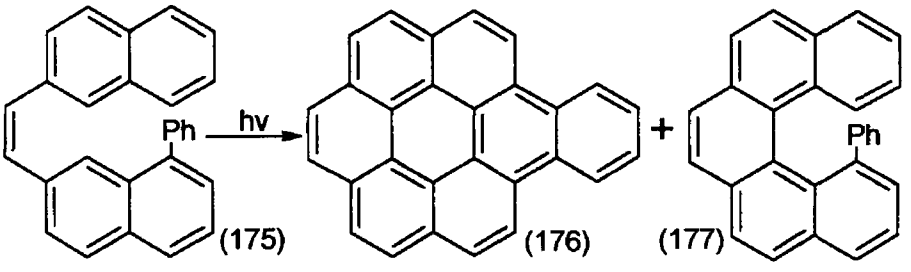


Fnmer and co-workers[122] have reported the synthesis of [5]helicene dianhydride (174) on the oxidative photocyclisation of 1,4-phenylenebis(phenylmaleic anhydride) (173) The [5]helicene dianhydride (174) is not cyclised further to the corresponding benzoperylene The explanation given for the diffenng behaviour of [5]helicene and (174) is that in



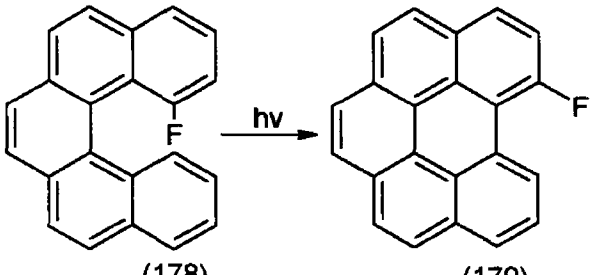
the HOMO of both there is an antibonding interaction between the two intenor bonding carbons But in the case of [5]helicene, however, while the corresponding LUMO orbital has a sizeable bonding interaction, there is no such interaction in the LUMO of (174) [The frontier orbital approach to cyclisation of 6π-electron hexatriene systems is discussed in section 1 1]

The photodehydrocyclisation of the naphthylethylene (175) gives rise to benzo[a]coronene (176) as the major photoproduct [123] Benzo[a]coronene was formed from the monocyclisation product 10-phenylnaphtho[1,2-a]anthracene (177), which was found in minor amounts Formation of (177) is accompanied by migration of the phenyl group followed by a second cyclisation to the benzo[a]coronene



(175) (176) (177)

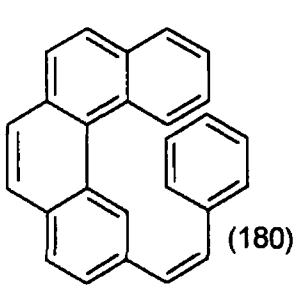
Mallory and Mallory[124] noted an unusual fluonne atom rearrangement in the photocyclisation of 1-fluoro[5]helicenes Cyclisation of 1-fluoro-[5]helicene (178) led to the formation of 8-fluorobenzo[g,h,i]perylene (179), through an inter-ring fluonne atom migration Photoelimination of HF to give benzo[g,h,i]perylene also occurs as a competing process The rearrangement pathway predominates when the irradiation was carried out at 0°C in the presence of air or iodine The elimination pathway predominates at higher temperatures or in the absence of either oxygen or iodine



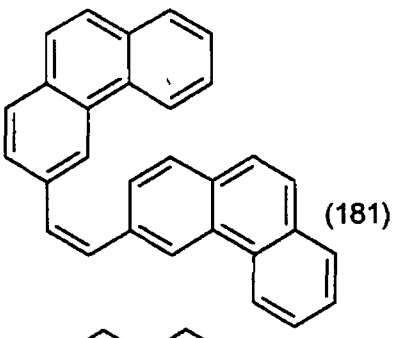
(178) (179)

The photosynthesis of [6-9]helicenes have been reported by two groups [125 126] Laarhoven and co-workers[125] have synthesised [6-9]helicene from 2-styrylbenzo[c]phenanthrene (180), 1,2-di(3-phenanthryl)ethylene (181), 1-(3-phenanthryl)-2-(2-benzo[c]phenanthryl)ethylene (182) and 1,2-di(2-

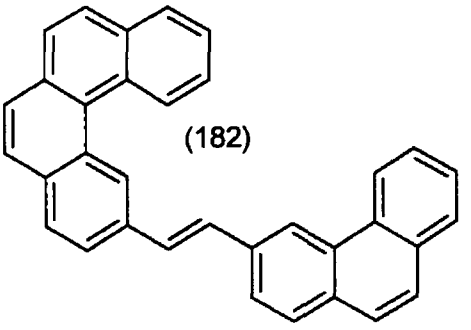
benzo[c]-phenanthryl)ethylene (183) respectively in yields varying from 50-80% Kagan and co-workers[126] have reported the synthesis of [8] and [9]helicene from the same starting materials used by Laarhoven[125] above The



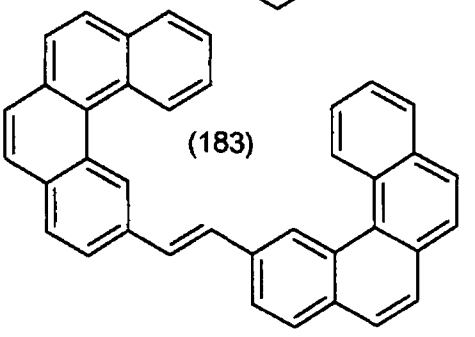
(180)



(181)



(182)

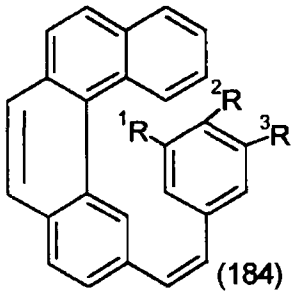


(183)

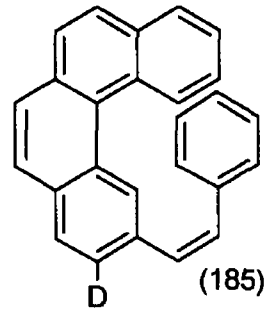
photochemistry was carried out with circularly polansed light Octahelicene prepared in 80% yield, showed a very high specific rotation $[\alpha]_D = 21 \pm 1°$ The (+)- and (-)-antipodes are obtained respectively with left and right circularly polansed light The synthesis of optically active hexahelicene has also been carried out with polansed light [127] The specific rotation of hexahelicene was found to be much smaller, $[\alpha]_D = (\pm)\ 7°$

A number of alkyl substituted hexahelicene derivatives have been synthesised by photodehydrocyclisation of the corresponding ethylenes (184a-d) [128] Substitution at the 2- and 3-positions revealed little change in the conformation of the helix in hexahelicene Substitution at the 1-postion, especially with larger substituents, caused either bending of the alkyl residue introduced or torsion of the substituted ring

Synthesis of helicenes gives rise to isomeric polycyclic aromatic systems that are highly ambiguous and difficult to charactense by NMR Martin and Schurter[129] have determined the chemical structure of helicenes



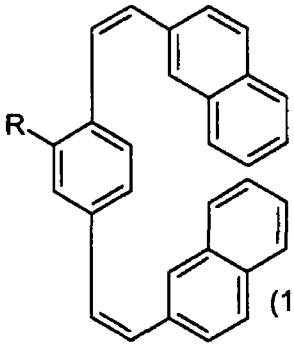
(184) (a) ^{1}R = Me, ^{2}R = ^{3}R = H
(b) ^{2}R = Me, ^{1}R = ^{3}R = H
(c) ^{1}R = ^{3}R = Me, ^{2}R = H
(d) ^{1}R = ^{3}R = tBu, ^{2}R = H



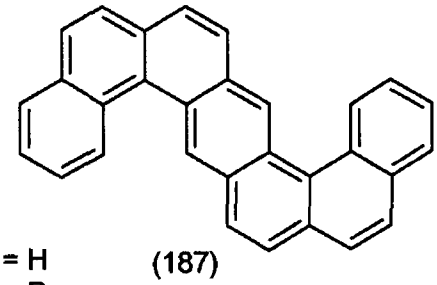
(185)

by deuterium labelling Cyclisation of the ethylene (185) was carried out in benzene to yield corresponding hexahelicene-7-d in 87% yield

Although the cyclisation of (186a) led to [7]helicene it also gave an equal amount of (187) [130] Introduction of a bromine atom to the benzene ring as in (186b), directed the photocyclisation to give the helical product in 75% yield with only minor amounts of its planar isomer The bromine was removed easily to yield [7]helicene in excellent yields

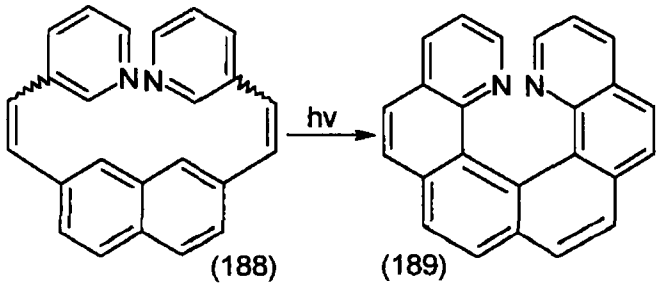


(186) (a) R = H
(b) R = Br

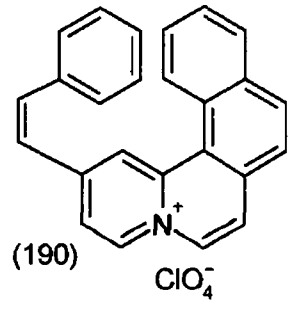


(187)

1,16-Diaza[6]helicene (189) was of interest to define the scope and limitation of "proton sponge" properties [131] Repulsive lone-pair interaction of the two closely neighbouring nitrogen atoms and the release of this strain on monoprotonation leads to a strong N H N hydrogen bond Cyclisation of the



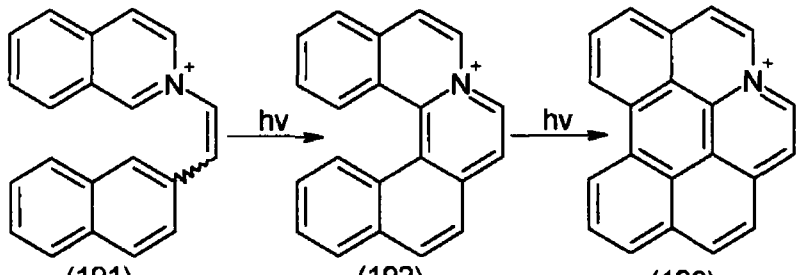
(188) (189)



(190)

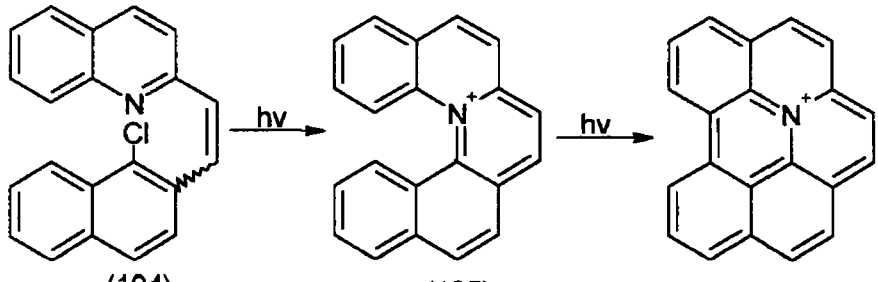
naphthalene (188) yielded (189) in minor amounts along with various other isomers The synthesis of the azonia derivative of hexahelicene has been described [132] The azonia salt (190) was photocyclised in methanol in the presence of iodine to afford 4a-azonia-phenanthro[3,4-c]phenanthrene perchlorate in 13% yield

Arai and co-workers have reported the synthesis of azonia derivatives of [5]helicene [133] Photocyclisation of dinaphthylethylene (158) yielded mostly benzoperylene (157) with only minor amounts of [5]helicene being isolated Similarly, the azonia derivative, 2-[2-(2-naphthyl)vinyl]isoquinoline (191), when



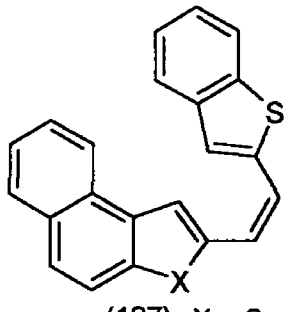
(191) (192) (193)

oxidatively photocyclised, yielded the azoniabenzo[ghi]perylene salt (193) selectively This implies that the [5]helicene (192) was easily photocyclised to yield (193) In contrast 2-[2-(1-chloro-2-naphthyl)vinyl]quinoline (194) when irradiated in acetonitrile, gave the [5]helicene derivative, 14b-azonia[5]helicene (195), as the major product with only minor amounts of the azoniabenzoperylene (196) being formed The authors concluded[133] that the photocyclisation of (194) to afford the azonia[5]helicene (195) was faster than the following oxidative photocyclisation to afford the benzoperylene (196) and therefore azonia[5]helicene could be isolated

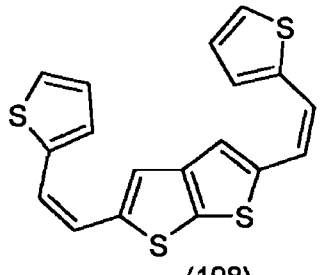


(194) (195) (196)

The synthesis of a number of heterohelicenes has been reported [134] Photocyclisation of the 1,2-di(hetaryl)ethenes (197) yielded the derived helicene derivatives benzo[d]naphtha[1,2-d']benzo[1,2-b 4,3-b']dithiophene and 1-benzothieno[3,2-e]naphtha[2,1-b]benzofuran in yields of 73% and 40% respectively The paper also reported[134] the synthesis of a number of other penta-, hexa- and heptaheterohelicenes The synthesis of hetero[6]helicenes has been reported by Dopper and co-workers [135] Cyclisation of the 1,2-di(hetaryl)ethene (198) led to the corresponding [6]helicene in 51% yield A number of other hetero[6]helicenes were also photosynthesised



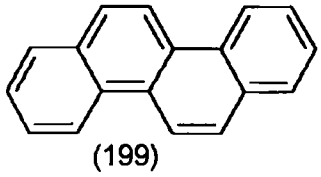
(197) X = S or O



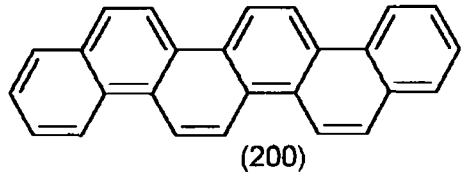
(198)

1 7 Phenacene Formation

Mallory and co-workers have proposed the name phenacenes for the family of polycyclic aromatic compounds having fused benzene rings in an extended phenanthrene-like structural motif [136] Chrysene or [4]phenacene (199) and fulminene or [6]phenacene (200) are examples of [n]phenacenes No reports of any phenacene systems with seven or more rings had appeared prior to the synthesis of [7]phenacene by Mallory et al [136] This could be ascribed to solubility problems, which increase severely with n as a consequence of the highly favourable crystal packing interactions that are expected for molecules of this shape The authors proposed[136] the synthesisof 2,13-di-t-butyl[7]phenacene (202), incorporating alkyl substituents along the polycyclic framework leading to a significant decrease in the

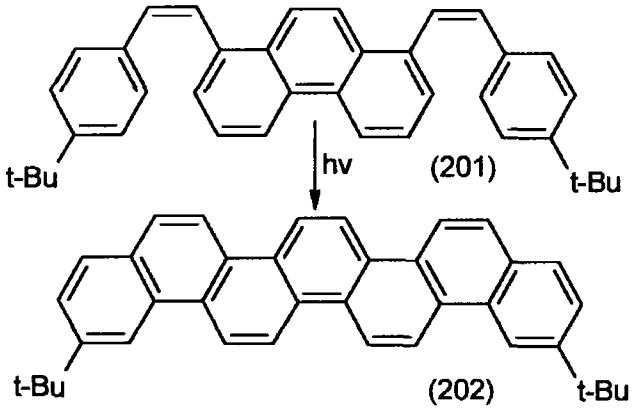


(199)

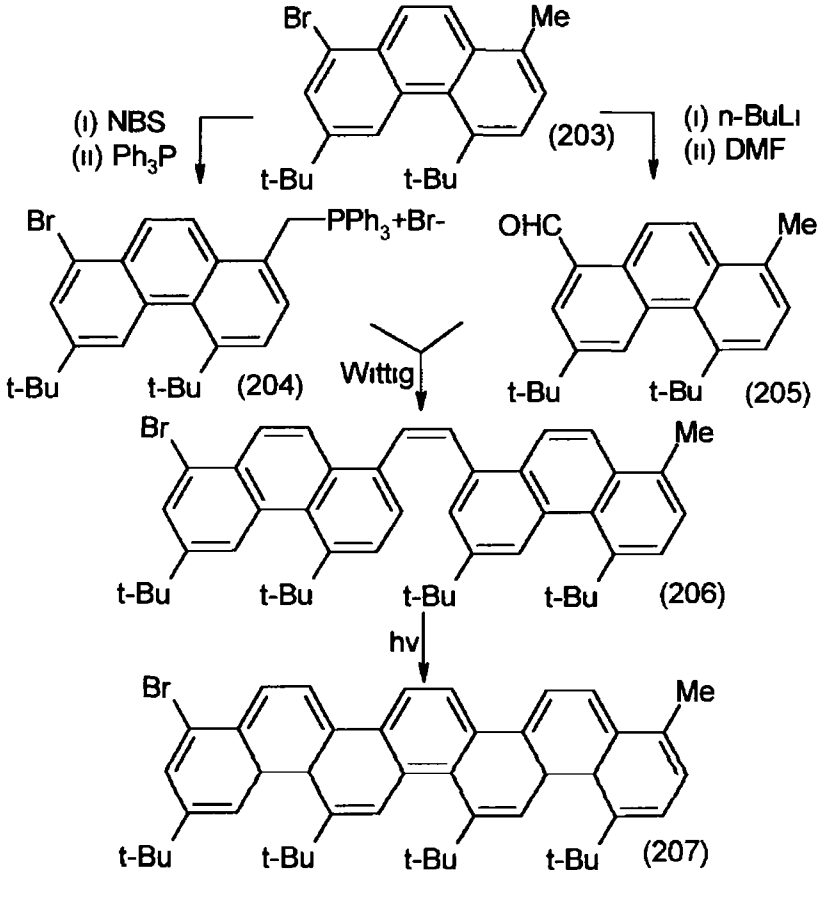


(200)

magnitude of the normal crystal packing interactions Oxidative photocyclisation of (201) led to the formation of the [7]phenacene (202) The melting point of the t-butyl denvative (202) was almost 300°C lower than that of the parent phenacene



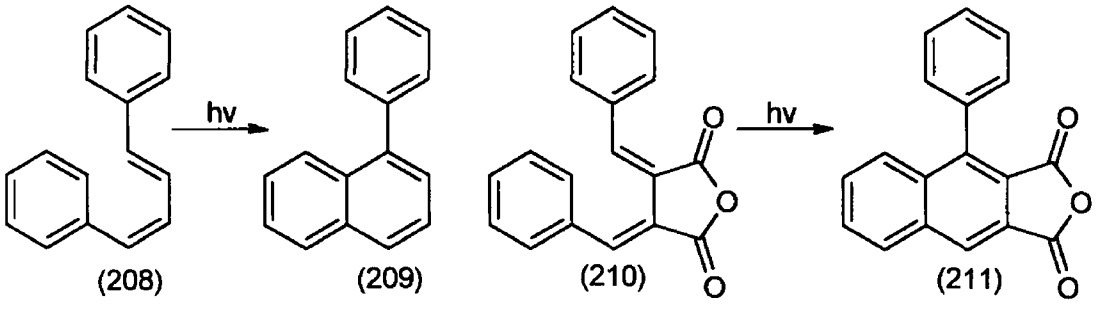
Mallory and co-workers[137] have also reported on the synthesis of [n]phenacenes with dramatically large values of n, in the hope these compounds might possess properties that could make them potentially



interesting and useful in materials science The phenacene (203) was reacted first with n-bromosuccinimide and then triphenylphosphine to give the corresponding phosphonium salt (204) In a parallel reaction (203) was reacted with n-butyl-lithium and then DMF to yield the aldehyde (205) A Wittig reaction yielded the stilbene derivative (206) which was photocyclised to the [7]phenacene (207) in an overall yield of 47% In principle, with two additional iterations [7]phenacene could be transformed into the corresponding [15]phenacene and [31]phenacene denvatives, respectively

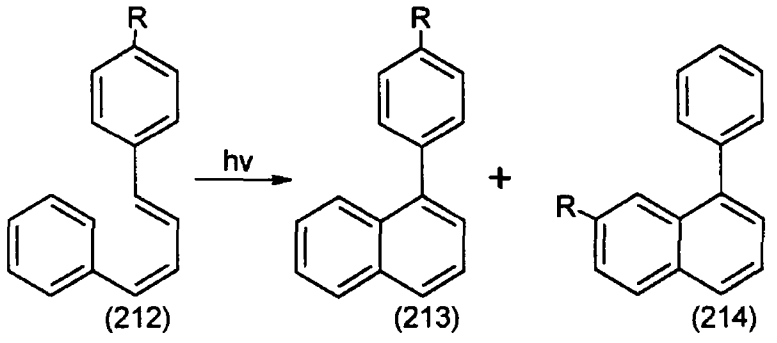
1 8 Aryl Polyenes

A similar stilbene-like photocyclisation occurs when 1,4-diaryl-1,3-butadienes are irradiated in benzene or ether solution, in the presence of oxygen or iodine, to yield 1-phenylnaphthalenes Fonken[138] reported the photocyclisation of 1,4-diphenylbutadiene (208) to yield 1-phenylnaphthalene (209) In an analogous reaction Stobbe[139] photocyclised dibenzalsuccinic anhydride (210) to give 1-phenylnaphthalene-2,3-dicarboxylic acid anhydride (211)

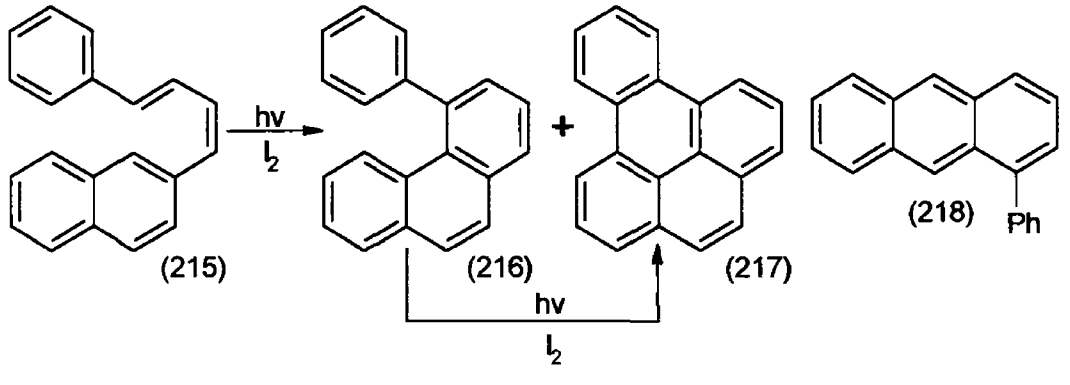


(208) (209) (210) (211)

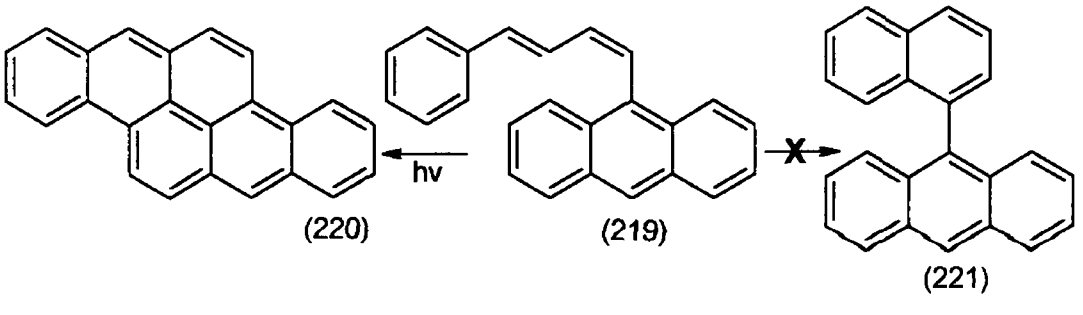
Leznoff and Hayward[140] have reported the photocyclisation of substituted 1,4-diaryl-1,3-butadienes (212) The photoreaction yielded two products, the naphthalenes (213) and (214) The photocyclisation of 1-(β-naphthyl)-4-phenyl-1,3-butadiene (215) has also been reported [141] When irradiated in benzene a mixture of products was obtained, 4-phenylphenanthrene (216) and 1,2-benzopyrene (217) The benzopyrene arose from a subsequent photochemical reaction of the first formed



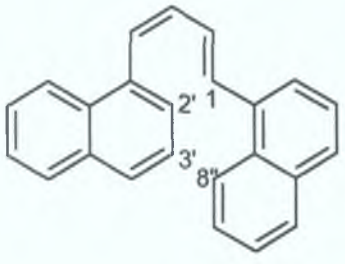
phenylphenanthrene The other monomeric product 1-phenylanthracene (218) does not result from the cyclisation The authors suggested[141] that the photocyclisation of (215) occurs to the 1-position of the naphthalene nucleus to give (216), rather than to the 3-position to give (218), as the free valence index at the 1-position of naphthalene was greater than that at the 3-position



The authors also carried out[141] the photocyclisation of the 1,3-butadiene (219) to 3,4,8,9-dibenzopyrene (220) and not the expected 9-(α-naphthyl)-anthracene (221) The photocyclisation was thought to proceed via 10π electron cyclisation to produce the intermediate [10]annulene which itself photocyclised to form the dibenzopyrene

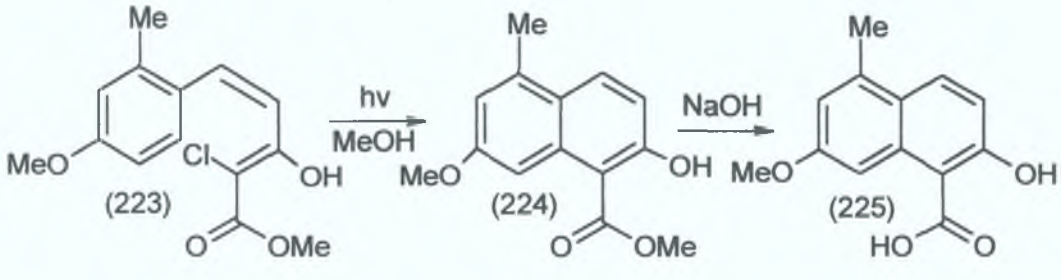


Leznoff and co-workers have also looked at the photocyclisation of various dinaphthyl-1,3-butadienes.[142] The cyclisation of 1,4-di-(α-naphthyl)-1,3-butadiene (222) led to photocyclisation at the 1,2' positions where the sum of the free valence indices was greater than unity. Cyclisation does not occur at the 3',8" positions where the free valence indices was less than unity.



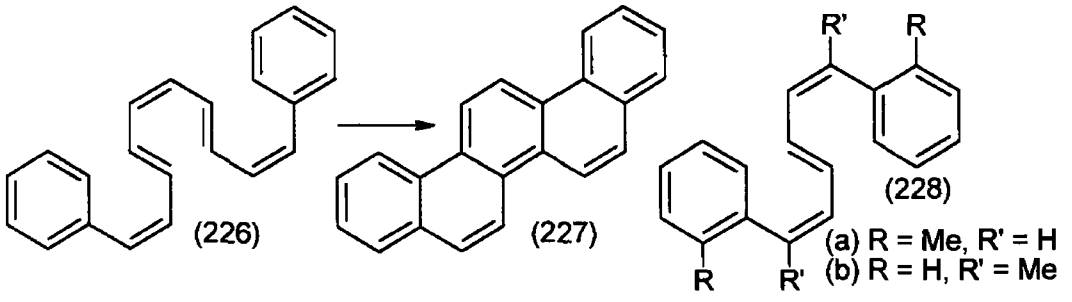
(222)

Myers and co-workers[143] have reported a synthesis of the naphthoic acid component of the neocarzinostatin chromophore, a key part of the natural chromoprotein antitumour agent neocarzinostatin, featuring a key photo-cyclisation step. Irradiation of a deoxygenated methanolic solution of (223) produced the methyl ester (224). Saponification of the methyl ester with sodium hydroxide afforded the substituted naphthoic acid (225). The photointermediate (224) is formed after rapid elimination of hydrogen chloride from (223).

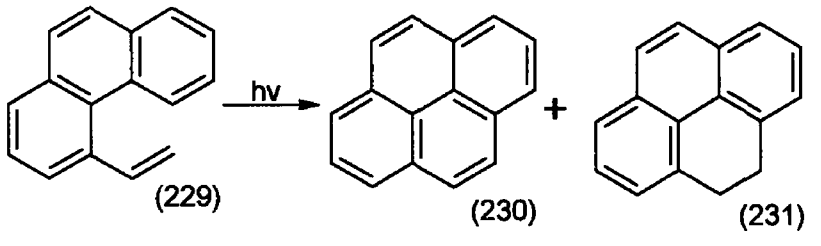


The photocyclisation of some highly conjugated diphenyl polyenes has been investigated.[144] The photocyclisation of the diphenyl-decapentene (226) led to a sole monomeric product, picene (227) in very poor yields.

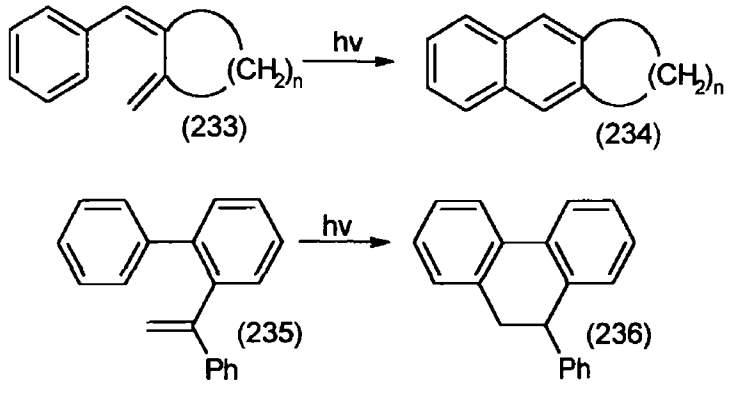
Carruthers and co-workers have reported the photocyclisation of 1,6-diarylhexa-1,3,5-trienes.[145,146] Photocyclisation of the diarylhexa-1,3,5-trienes



(228a,b) led to 1,7- and 6,12-dimethylchrysene, respectively Photocyclisation of the 4-vinylphenanthrene (229) in benzene under aerobic conditions led to the formation of pyrene (230) and the rearrangement product, 4,5-dihydropyrene (231) [147]

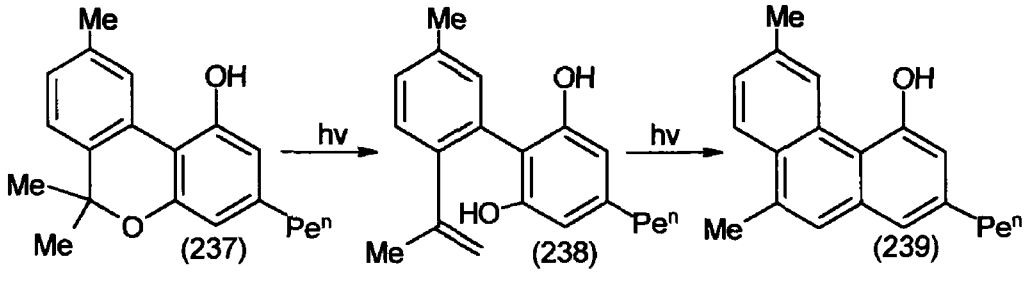


Photoannulations to naphthalenes have been investigated by Olsen and co-workers [148] Irradiation of (233) in benzene yielded the cyclised product (234) The photocyclisation has been shown to proceed via the triplet state, with enhanced yields on irradiation in the presence of a triplet sensitiser, such as benzophenone Successful cyclisations occur from ring sizes of n = 3 to n = 6

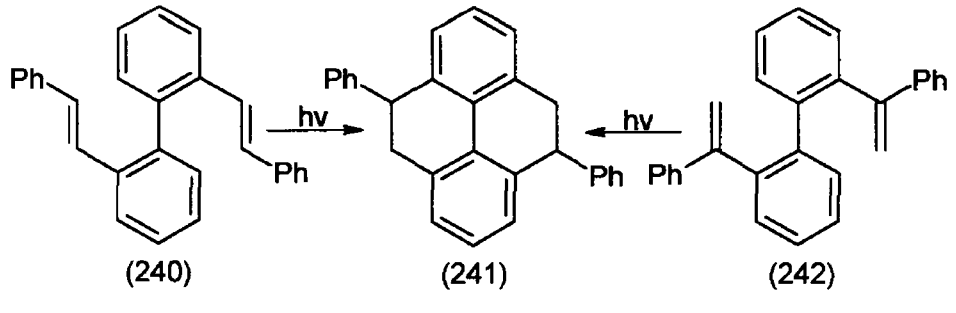


Photocyclisation of the 1,1-diarylethylene (235) in a degassed solution of cyclohexane led to a single photoproduct, the dihydrophenanthrene (236), in excellent yields [149] When the reaction was carried out under oxygen with iodine present 9-phenylphenanthrenene was obtained as the sole product in 80% yield

The photochemical reactivity of the cannabis constituent cannabinol (237) has been reported,[150] leading to isomeric diol (238) which underwent cyclisation to the 4-hydroxyphenanthrene (239)

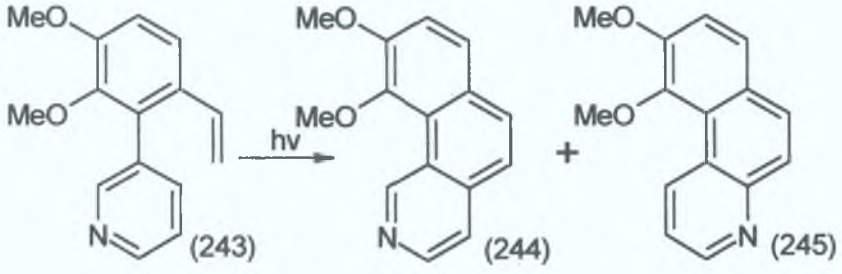


The synthesis of tetrahydro-4,9-diphenylpyrene (241) has been reported by two groups[151 152] Laarhoven and Cuppen irradiated 2,2'-distyrylbiphenyl (240) and obtained (241) as the thermodynamically controlled photoproduct [151] Padwa and Mazzu have photocyclised the diphenyl-2,2'-divinylbiphenyl (242) to yield (241) as the exclusive photoproduct [152] The authors presumed[152] the photocyclisation of 2,2'-divinylbiphenyl derivatives proceeds by a mechanism which involves an initial stilbene-phenanthrene type cyclisation followed by a 1,5-sigmatropic hydrogen shift



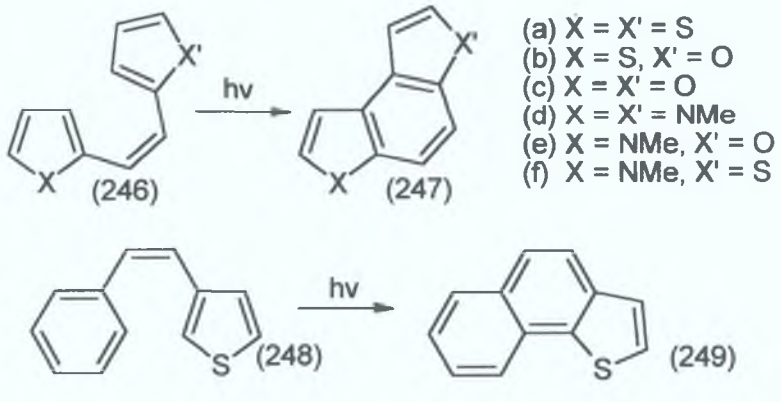
A novel photosynthesis of azaphenanthrenes has been reported [153] Photocyclisation of the biphenyl (243) in the presence of iodine and oxygen,

led to a 1:1 ratio of the azaphenanthrenes (244) and (245) in an overall yield of 73%.



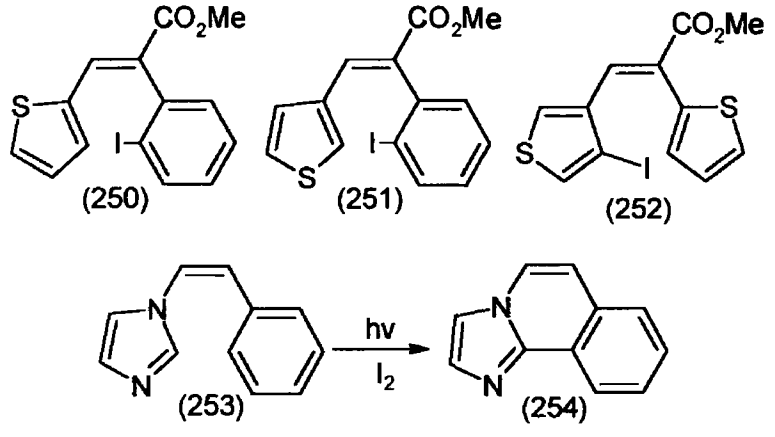
1.9 5-Membered Heterocyclic Stilbene-like Cyclisations

Photochemically induced cyclisations of some furyl- and thienylethenes has been reported by Kellogg and co-workers.[154] The irradiation of the ethenes (246a-c) were carried out in benzene or ethanol with iodine or cupric chloride present forming the corresponding phenanthrene analogues (247a-c) in good yields. A catalytic amount of palladium has been shown to improve product yields in the photocyclisation of heterocyclic analogues of stilbene to the corresponding phenanthrene-like systems.[155] Cyclisation of (246d-f) led to formation of the analogous phenanthrene (247d-f) in yields of 85%. Various other systems were investigated. Song and co-workers have reported the oxidative photocyclisation of 3-styrylthiophene (248) in cyclohexane to give naphtho[1,2-b]thiophene (249) in greater than 95% yield.[156]

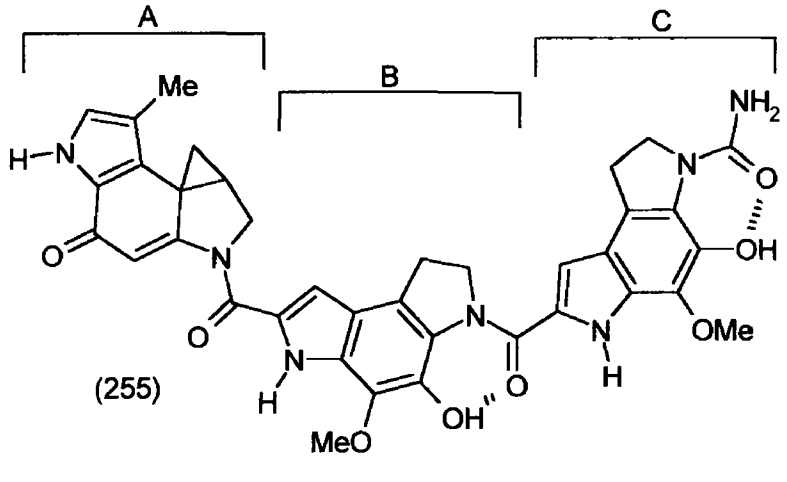


The photochemical cyclisation of some iodophenyl- (250) and iodothienyl-acrylates (251) and (252) leading to the corresponding naphtha-thiophene and benzodithiophene carboxylates respectively has been

reported [157] The authors suggested[157] that the intermediate in these cyclisations is likely to be a dihydro-derivative, which suffers dehydrogenation, rather than an aryl radical which effects an intramolecular substitution Photocyclisation of 1-styryl-imidazole (253) in methanol yields imidazo[2,1-a]isoquinoline (254) [158]

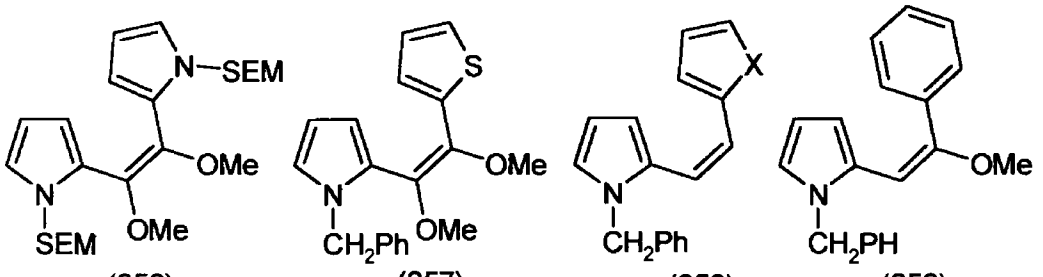


Cava and co-workers[159-162] have reported a number of papers that discuss the photocyclisation strategy for the synthesis of antitumour agent CC-1065 (255) and its analogues The synthesis of modified B and C units has been of most interest Cyclisation of the enediol dimethyl ether (256) yielded the phenanthrene analogue in 82% yield [159] Replacement of the pyrrole rings with thiophene and furan congeners has been reported [160 161]



The heterocycles (257) and (258) were photocyclised in excellent yields in acetonitrile in the presence of palladium Cava and Drost have also reported

the modification of unit A in the hope of obtaining less toxic analogues of (255) [162] Replacement of the pyrrole ring of the A unit with a benzene has been carried out Photocyclisation of the stilbene (259) led to the analogous benzindole in 98% yield



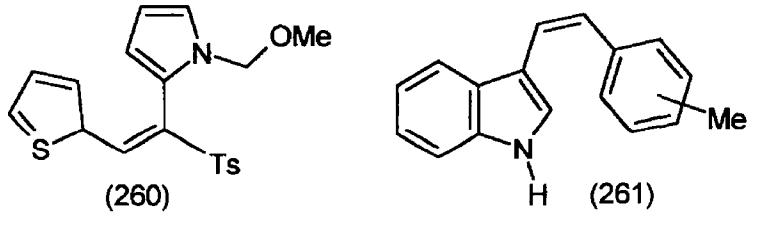
(256) (257) (258) (259)

SEM = $(Me)_3SiCH_2CH_2OCH_2$-

X = S or O

The photocyclisation of 1-tosyl-1,2-diarylethenes has been reported by Antelo and co-workers [163] The sulfonyl stilbenoid (260) was irradiated in ethanol to yield the corresponding tosylphenanthrenoid Several of these phenanthrenoids have been synthesised with a variety of substituents

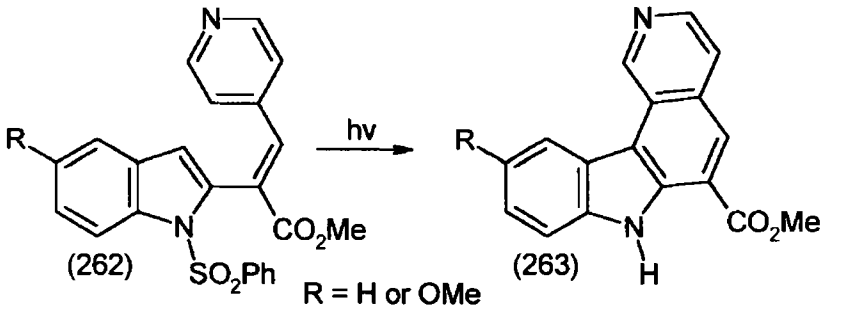
Carruthers and Evans[164] have reported the synthesis of 1-, 2-, 3- and 4-methyl-11H-benzo[a]carbazoles Irradiation of o-, m-, and p-methylstyryl-indoles (261) in benzene gave the corresponding methyl carbazole in low yields

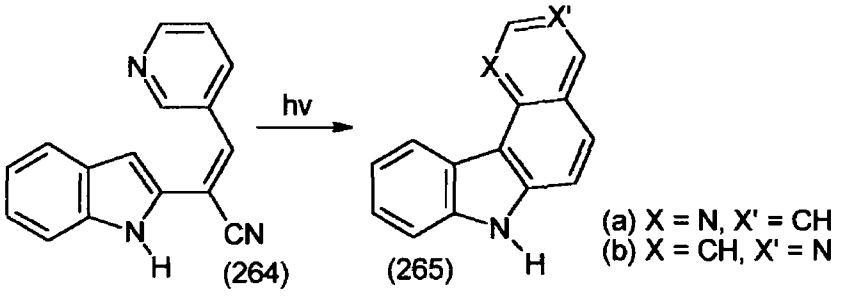


(260) (261)

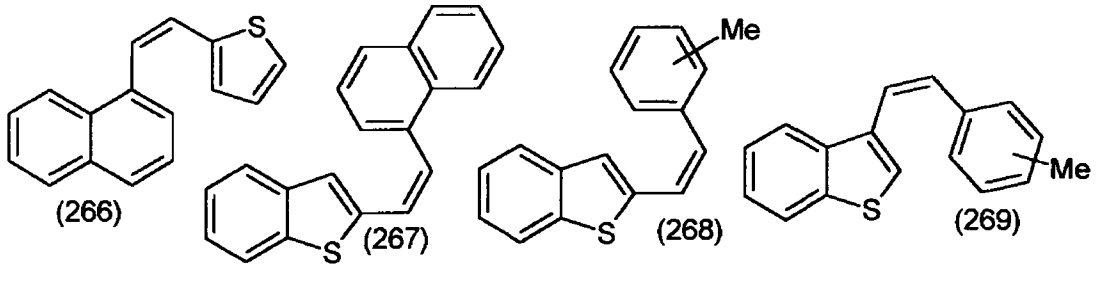
A key step in the synthesis of ellipticine, an alkaloid that exhibits antitumour activity, is an oxidative photocyclisation of the olefins (262), in methanol, to furnish the pyndo[4,3-c]carbazoles (263) in moderate yields [165]

A key step in the synthesis of Aspidosperma alkaloids involves an oxidative photocyclisation,[166] involving the nitrile (264) with formation of two products, (265a) and (265b), in 5% and 30% yield, respectively

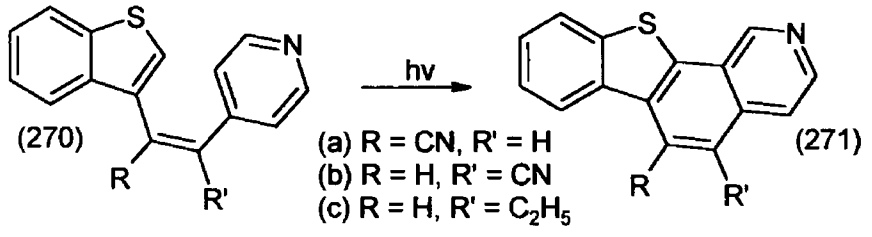




Castle and co-workers[167-170] have reported the synthesis of a number of sulphur containing heterocycles Photocyclisation of the 2-naphthyl-vinylthiophene (266) led to phenanthro[2,1-b]thiophene in 88% yield [167] Photocyclisation of the olefin (267) yielded the corresponding benzo[b]phenanthro[1,2-d]thiophene [168] The synthesis of all of the monomethyl isomers of benzo[b]naphtha[1,2-d]thiophene[169] and benzo[b]naphtha[2,1-d]thiophene[170] have been reported Cyclisation of the o-, m- and p-methyl olefin (268) led to formation of the 1-, 2-, 3- and 4-methyl isomers of benzo[b]naphtha[1,2-d]thiophene [169] In similar reactions photocyclisation of the methyl olefins (269) led to formation of the 1-, 2-, 3- and 4-methyl isomers of benzo[b]naphtha[2,1-d]thiophene [170]

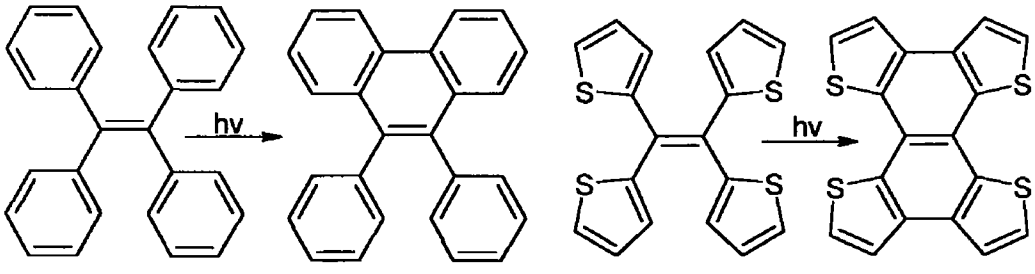


The photochemical behaviour of a series of benzo[b]thiophene derivatives was investigated [171] Photolysis of the olefins (270a-c) yielded the corresponding isoquinolines (271a-c) in moderate yields



It has been reported by Mallory and co-workers[7] that tetra-phenylethylene (272) was converted photochemically to 9,10-diphenyl-phenanthrene (273) but a second nng closure does not occur even on prolonged irradiation The authors conclude that the central unsaturation should be olefinic for photocyclisation to occur Without this structural feature the electronic distribution in the excited state may be such that there was not sufficient electron availability at the two ortho positions between which the new bond would be expected to form

In the diphenylphenanthrene (273) the excitation in the excited singlet state was probably confined largely to the phenanthrene system with little involvement of the two-phenyl groups In an analogous reaction the photocyclisation of the ethene (274) was found to yield the tetrathienonaphthalene (275) [172] The enhanced reactivity of the thienyl substituent over that of phenyl could be viewed as a reflection of the fact that only five atoms are sharing the π electrons of the aromatic sextet

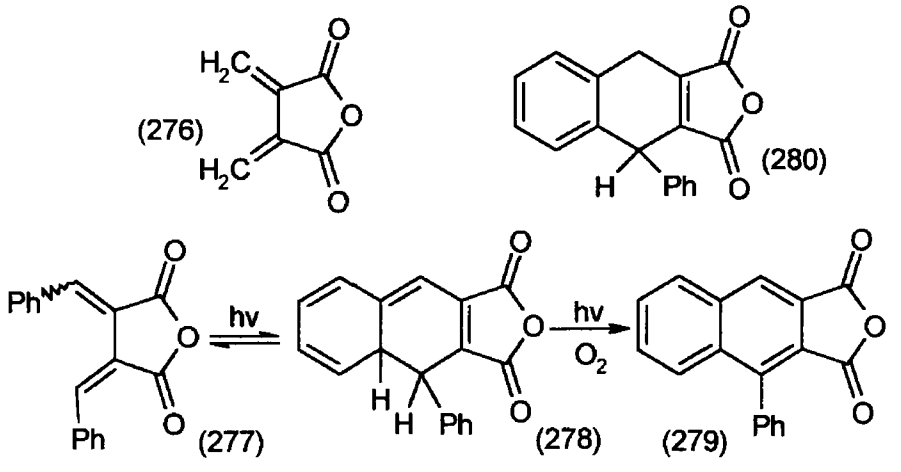


(272) (273) (274) (275)

1.10 Photochromism

Photochromism is defined as a reversible change in a chemical species between two forms having different absorption spectra Organic compounds that possess photochromic properties have attracted a significant amount of attention from the viewpoint of using them as optical memory media

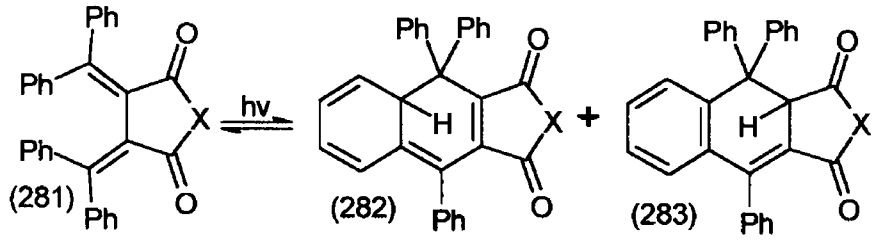
In 1905, Stobbe gave the name fulgides to derivatives of dimethylene-succinic anhydride (276) and showed that, if one of the substituents was phenyl, the compound was photochromic [173] Santiago and Becker[174] have



investigated the photocyclisation of the diphenylfulgide (277) At low temperatures, irradiation of (277) led to EZ isomerisation about the carbon/carbon double bond, and a deepening of the colour, thought to be brought about by the formation of the dihydro compound (278) When the reaction was carried out in the presence of oxygen the naphthalene (279) was furnished A reinvestigation of the photochemistry of bis(benzylidene)succinic anhydride (277) by Heller and co-workers[175] showed that the dihydro-intermediate was actually the 1,4-dihydronaphthalene (280)

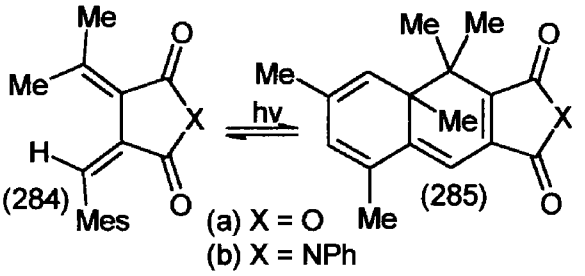
Heller has coined the name fulgimide for the novel class of compounds obtained by substitution of hydrogen in dimethylenesuccinimide [176] When the pentaphenylfulgimide (281a) was irradiated at 366 nm the colour of the solution changed rapidly from yellow to red The red compound was assigned as the dihydro compound (282a) On prolonged irradiation, the solution became colourless and the dihydronaphthalene (283a) was obtained

Compound (283a) was formed by a 1,5-shift of hydrogen in the photochrome (282a)



(a) X = N-Ph
(b) X = O

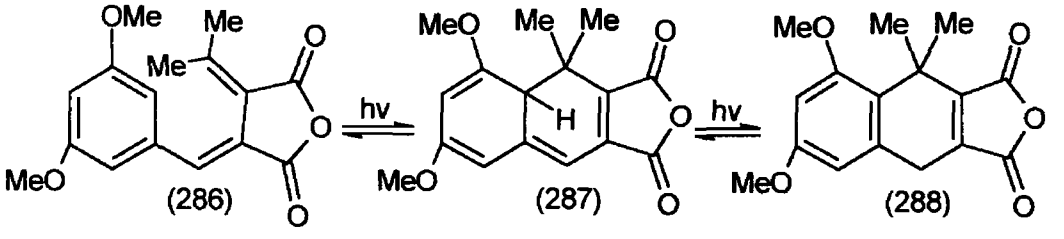
The photochemical reactions of photochromic benzylidene-(diphenylmethylene)succinic anhydnde have been reported [177] Irradiation of (281b) at 366 nm led to the 1,8a-dihydro compound (282b) Prolonged irradiation led to a 1,5-hydrogen shift to give the dihydronaphthalene (283b) 2-Isopropylidene-3-(mesitylmethylene)succinic anhydnde (284a) and phenylimide (284b) on irradiation, led to a fatigue free photochromic



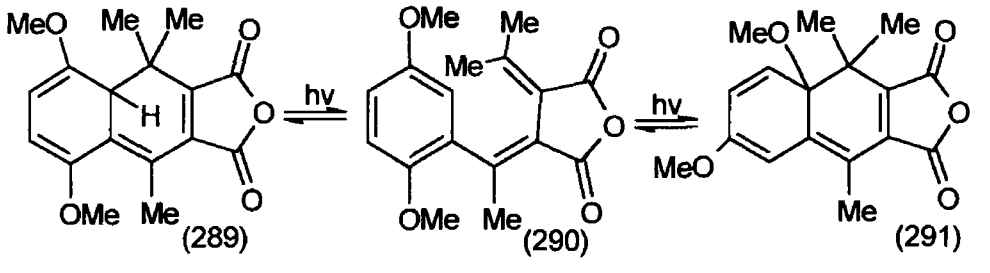
systems [178] On irradiation (284a,b) produced the 1,8a-dihydronaphthalene intermediate (285a,b) as the sole product respectively On irradiation with white light, (284a,b) were reformed The methyl substituents in (284a,b) prevent a 1,5 shift in the 1,8a-dihydro compound Further the allowed thermal disrotatory ring opening reaction did not occur until 160°C

The yellow 3,5-dimethoxybenzylidene succinic anhydride (286) undergoes reversible photochemical ring closure to form deep blue solvatochromic 6,8-dimethoxy-1,8a-dihydronaphthalene (287) which does not undergo a 1,5-H shift at ambient temperatures but rather a photochemical 1,7-H shift to yield the colourless 1,4-dihydronaphthalene (288) [179] Solvato-

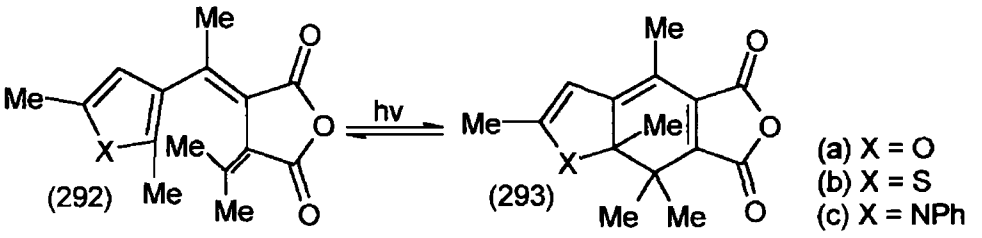
chromism is the solvent dependence of the position and intensity of absorption bands



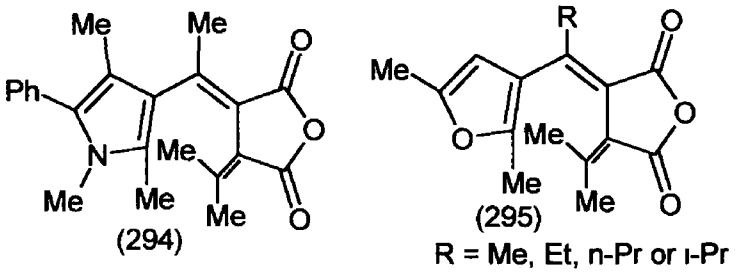
The (2,5-dimethoxyphenyl)ethylidenesuccinic anhydride (290) undergoes two competing ring closure processes on irradiation at 366 nm [180] One involves photocyclisation onto the unsubstituted ortho position of the 2,5-dimethoxyphenyl group to produce a blue 8-methoxy-1,8a-dihydro-naphthalene (289) which is thermally unstable and reverts back to the fulgide (290) at ambient temperatures The other involves ring closure onto the 2-position of the 2,5-dimethoxyphenyl group to form a red 1,8a-dihydronaphthalene (291) which is thermally stable in the dark



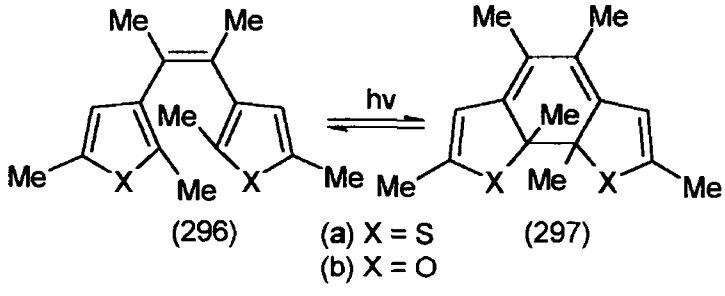
Heller[181-183] has also reported a number of photochromic heterocyclic fulgides The 2,5-dimethyl-3-furyl- and 2,5-dimethyl-3-thienyl-ethylidene(iso-propylidene)succinic anhydrides (292a,b) undergo conrotatory ring-closure to the deep red 7,7a-dihydropentamethylbenzofuran and the purple dihydrobenzothiophene anhydrides (293a,b) respectively in near quantitative yield on irradiation at 366 nm in a wide range of common organic solvents [181 182] The 1-phenyl-3-pyrryl succinic anhydnde (292c) behaved in an analogous manner to both (292a,b) forming the deep blue (293c) Wintgens and co-workers[184] have reported the use of the fulgide (292a) as an actinometer for one- and two-laser expenments



Yu and co-workers[185] have reported the synthesis of a number of pyrryl fulgides One example, the fulgide (294), on irradiation at 360 nm, formed the corresponding 7,7a-dihydroindole derivative, which showed absorption up to λ 720 nm Quantum yields of photoreactions of furylfulgides (295), with various alkyl groups were measured [186] E-Z isomerisation was greatly suppressed and the cyclisation was accelerated when the alkyl group became bulkier

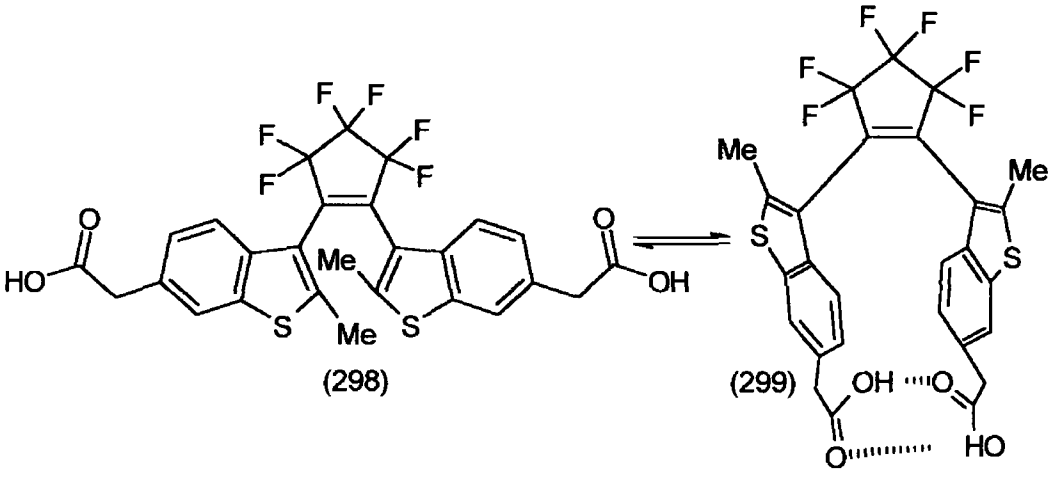


The ultraviolet irradiation (λ 313 nm) of 2,3-bis(2,5-dimethyl-3-thienyl)-2-butene (296a) and 2,3-bis(2,5-dimethyl-3-furyl)-2-butene (296b) led to the formation of a yellow colour [187] The absorption maxima were observed at 431nm for (296a) and at 391 nm for (296b) Exposure of the solutions to visible light (λ>390 nm) led to rapid disappearance of the yellow colour The colour was regenerated by irradiation with 313 nm light The yellow colour is attributed to the ring closed forms (297a,b) Oxygen did not convert the



dihydro form into the aromatic ring The photogenerated ring-closed forms were very stable even at elevated temperature

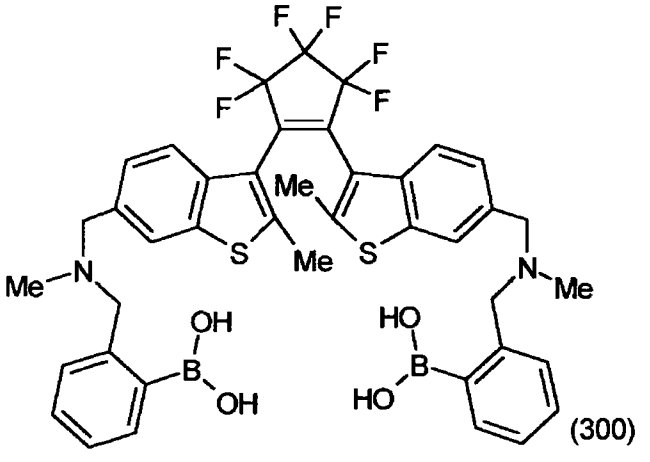
A property that is strongly desired in photochromic molecules is gated photochemical reactivity Gated reactivity is the property that irradiation with any wavelength causes no molecular change, while a photoreaction occurs when another external stimulation, such as an electrical field or chemicals, is present Such threshold reactivity is indispensable for the application to optical memory media Photochromic molecules with a clasp, which undergo photoisomerisation only when the clasp is freed by a switch molecule have been synthesised [188,189] For the thiophene derivative (298) the parallel isomer



(299) exists in cyclohexane, held in place by hydrogen bonding In this conformer photocyclisation is prohibited When ethanol is added to the solution, this intramolecular hydrogen bonding is broken, and photocyclisation takes place [188] Replacement of the carboxyl groups in (298) with mercaptoalkyl groups yields similar results, with the formation of disulphide linkages restraining the molecule in the parallel isomer [189]

Irie and co-workers have reported the synthesis of a novel saccharide tweezers [190] Saccharides have many hydroxy groups which can form esters with boronic acids and the parallel conformer of (300) forms a 1 1 complex with saccharides Photocylisation only occurs from the anti-parallel form and in the presence of saccharides this reaction is halted

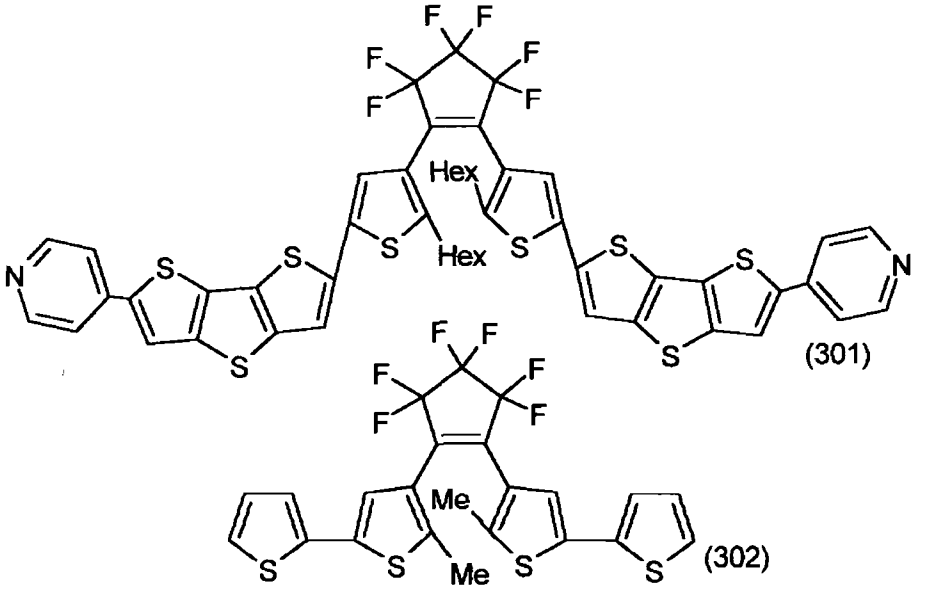
Thiophene oligomers having a dithienylethene structure have been synthesised for use as non-destructive readout for optical memory [191] The thiophene oligomer (301) can be reversibly converted between a nonplanar,



(300)

colourless open form and a planar, coloured closed form in which extended conjugation over the whole molecule was possible Thus properties depending on changes in the π system as well as structural changes may be strongly altered by the form of the system

Thiophene oligomers can also be used as photoswitches [192] The polythiophene rings of (302) are in a twisted conformation in the open ring form and are not in a π-conjugated system After photocyclisation the four double bonds in the closed ring form are conjugated Consequently, the non-

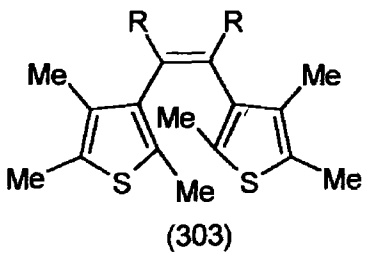


(301)

(302)

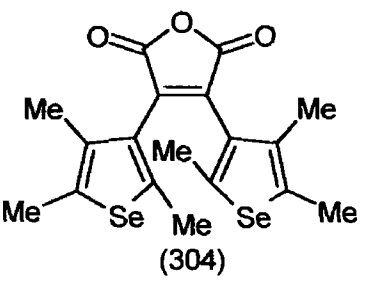
conjugated polythiophene chains of (302) are connected Therefore the thiophene oligomer can be used as an insulating/proconducting photoswitch

In the hope of obtaining highly efficient photochromic compounds a number of modified systems have been developed Increasing the absorption maximum wavelength means conventional laser lights can efficiently induce the reactions of these compounds and is an area of keen investigation Use of dicyano substituents, for example (303a), raised the absorption maximum to 512nm [187] Replacement of the dicyano groups with an acid anhydnde group (303b) led to an absorption maximum at 560 nm [187] The selenophene (304) and indole (305) rings[193] led to absorption maximum in the region of 520 nm and 620 nm respectively



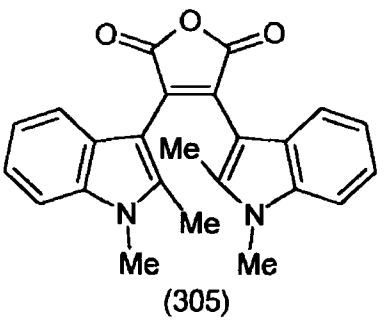
(303)

(a) R = CN
(b) RR = C(O)OC(O)

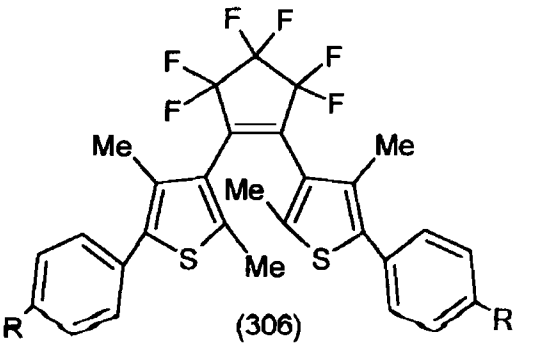


(304)

A number of bis(5-phenylthiophene)perfluorocyclopentenes (306) were synthesised [194] Electron donating substituents, such as methoxy or diethylamino groups, were found to increase the absorption maximum 1,2-Dimethylindolyfulgides (307) were synthesised[195] and electron donating substituents were found to lengthen the absorption maximum of the coloured form and decrease the quantum yields of the photoreactions The coloured



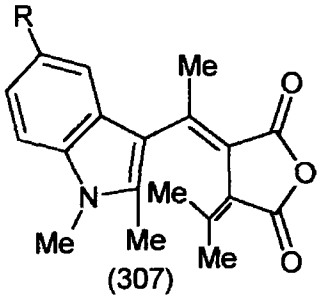
(305)



(306)

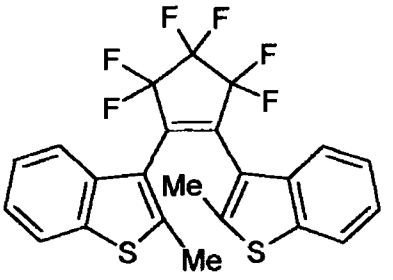
R = H, OMe, $N(C_2H_5)_2$ or CN

form of the dimethylaminoindoly-substituted fulgide (307, R = NMe_2) has an absorption maximum at 673 nm Replacement of the appropriate carbonyl oxygen of the anhydride ring in the fulgide (307) by the powerful electron-withdrawing dicyanomethylene group causes a major shift, (>100 nm), of the absorption band in the corresponding coloured form [196]



(307)

R = H, MeS, MeO or NMe_2

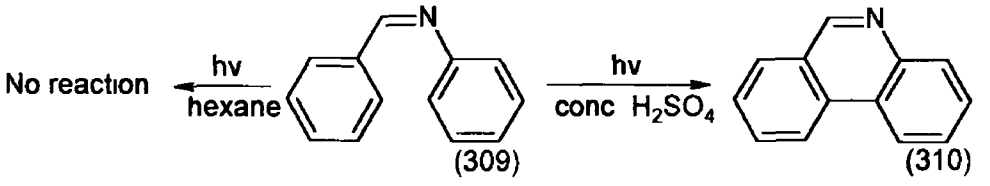


(308)

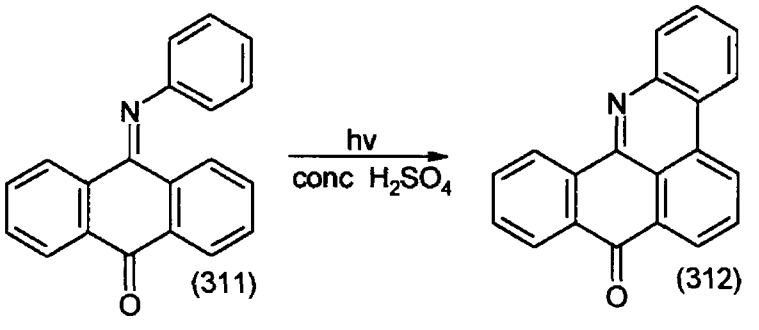
The fatigue resistance, how many times colouration and decolouration cycles can be repeated without permanent product formation is another area of interest Replacement of the methyl on the indolylmethylidene group of (307) with a trifluoromethyl group resulted in remarkably high fatigue resistivity towards the repetition of photochromic reactions and remarkably high resistivity towards the thermal decomposition of the coloured form [197] The acid anhydride group was found to increase the fatigue resistance in both (304) and (305) The use of the perfluro-cycloalkene moiety in both (306) and (308)[198 199] increases the fatigue resistance dramatically and also reduces cis-trans isomerisation, a competing process

1 11 Benzalaniline and Azobenzene Cyclisations

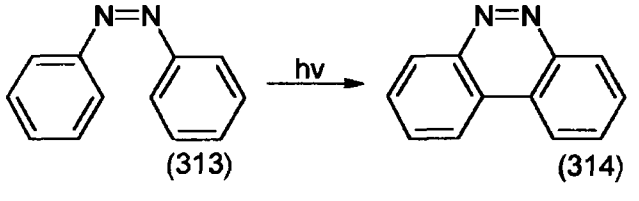
Early experiments demonstrated the absence of reaction on irradiation of the benzalaniline (309) [200 201] It had been shown that the photochemical isomerisation of benzalaniline (309) brings about a photostationary state in which the ratio of cis/trans isomers was extremely small,[7] except at lower temperatures [202 203] By irradiating (309) at lower temperatures, cyclisation to the phenanthridine derivative (310) occured Irradiation in concentrated acid also yielded (310) [201] Thompson and Docter[204] have photocyclised



benzalaniline (309) in dichloromethane, in the presence of boron trifluoride etherate, a Lewis acid In an analogous reaction Scholz and co-workers showed that the anil (311) cyclised to form (312) in the presence of concentrated sulphuric acid [205]



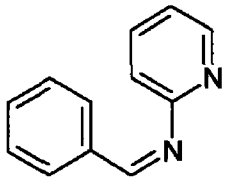
A similar system to that of benzalaniline was that of azobenzene (313) Early experiments showed the absence of reaction on irradiation of azobenzene in both isooctane[206] and glacial acetic acid [200 207] However, the photocyclisation of azobenzene to 9,10-diazaphenanthrene (314) has been reported to occur in an ethanol/sulphuric acid solution [208 209] It has also been observed that azobenzene was photocyclised in glacial acetic acid to which ferric chloride has been added[200] or in non-acidic conditions with the Lewis acid, aluminium chloride, added [210 211]



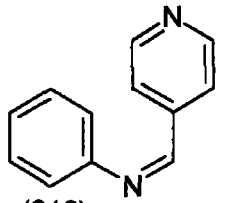
Mallory and co-workers[7] suggested that both benzalaniline and azobenzene fail to undergo cyclisation because the lowest excited singlet

state of each of these stilbene analogues was believed to be of the $n \rightarrow \pi^*$ type, implying that the electronic distributions in this excited state are unfavourable for cyclisation It was suggested that under strong acidic conditions the species actually undergoing cyclisation is a protonated one that has a lowest excited singlet state of the $\pi \rightarrow \pi^*$, rather than the $n \rightarrow \pi^*$ type The observation that benzalaniline and azobenzene are photocyclised in the presence of Lewis acids could conceivably be given a similar interpretation, by assuming that the Lewis acid interacts with the lone pair electrons on the nitrogen(s) Blackburn and Timmons[212] suggested that for azobenzene, $n \rightarrow \pi^*$ excitation results in the $S^1 \rightarrow T^1$ and the radiationless $S^1 \rightarrow S^0$ processes being very efficient, leading to a rapid depopulation of the S^1 level from which photocyclisation is believed to proceed

The photocyclisation of the azastilbenes (315) and (316) led to the corresponding benzo[c]- and benzo[h]naphthyridines [213] A wide variety of naphthyndines were synthesised

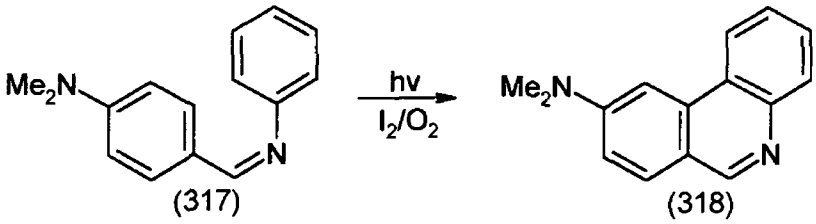


(315)



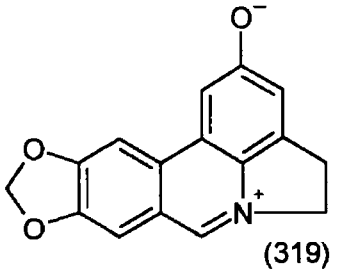
(316)

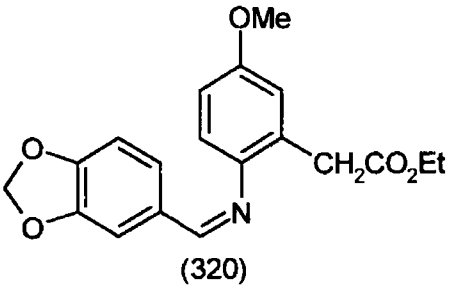
Onaka and co-workers[214] have suggested that the presence of a group which interacts electronically with the benzalaniline system, can facilitate the formation of phenanthridines in a neutral solution containing an oxidant (I_2 or O_2) The benzylideneaniline (317) was oxidatively photocyclised to the phenanthridine (318) in good yields



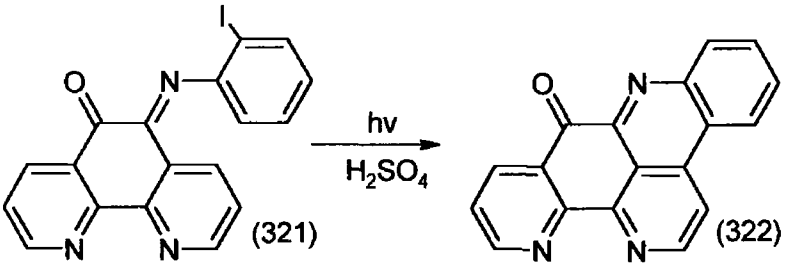
(317) (318)

The authors also reported[214] the synthesis of the methobromide of the phenanthridine alkaloid ungeremine (319) Irradiation of (320) yields the corresponding cyclised product, which on reduction with $LiAlH_4$ and treatment with PBr_3 yields the methobromide salt of (319)

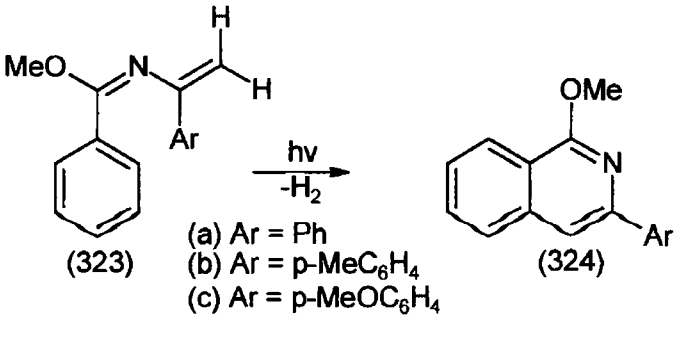

(319)


(320)

In the search for useful syntheses of natural products, photochemistry has played an important role Moody and co-workers[215,216] have reported a synthesis of the pentacyclic marine alkaloid ascididemin from the 1,10-phenanthroline (321) Irradiation took place in sulphuric acid to give ascididemin (322) in an overall yield of 32%

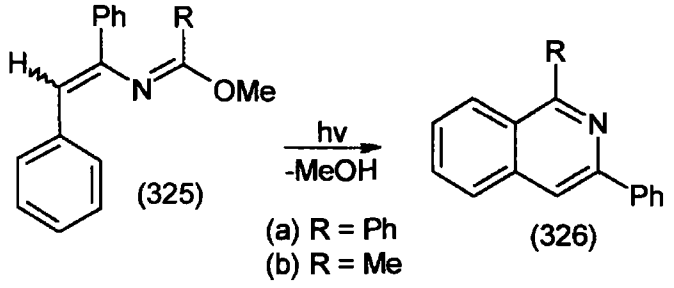

(321) (322)

On irradiation of the 1-methoxy-2-azabuta-1,3-dienes (323a-c) in methanol, photocyclisation to the corresponding isoquinolines (324a-c) occurred in good yields [217]

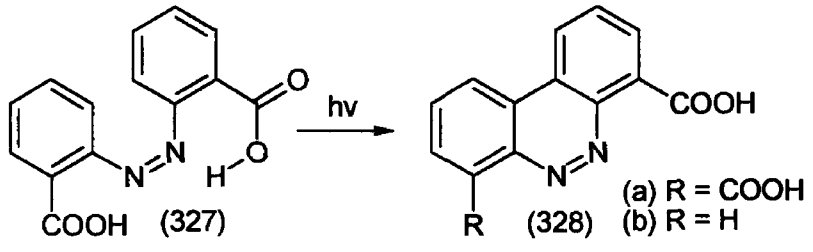

(323) (324)

(a) Ar = Ph
(b) Ar = p-MeC_6H_4
(c) Ar = p-$MeOC_6H_4$

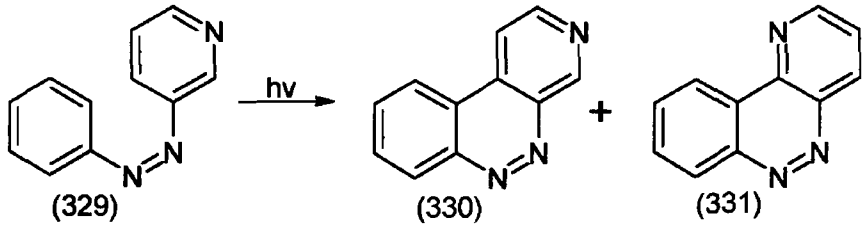
When the 2-azadiene bears a phenyl group at the 4-position, this group became involved in the cyclisation For example 2-aza-1,3-butadienes (325a,b) yielded the corresponding isoquinolines (326a,b), explained by the fact that methanol was easier to eliminate than molecular hydrogen



Irradiation of azobenzene-2,2'-dicarboxylic acid (327) in 1,2-dichloroethane yielded both the benzo[c]cinnoline mono- and dicarboxylic acids (328a,b) in the ratio of 1 2 5 [218] Intramolecular hydrogen-bonding between the carboxyl group and the azo nitrogen facilitated cyclisation

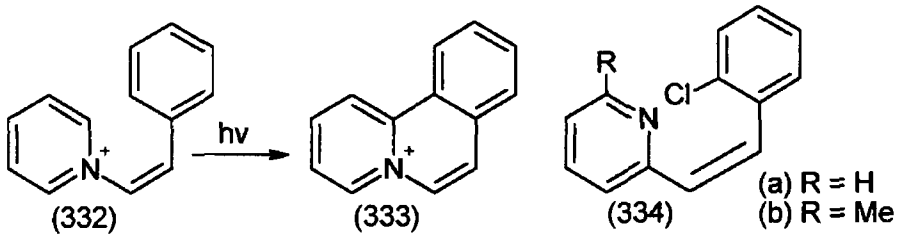


Photolysis of 3-phenylazopyridine (329) in concentrated sulphuric acid furnished 2,9,10-triazaphenanthrene (330) as the main photoproduct in 19% yield [219] The 4,9,10-isomer (331) was obtained in only small amounts

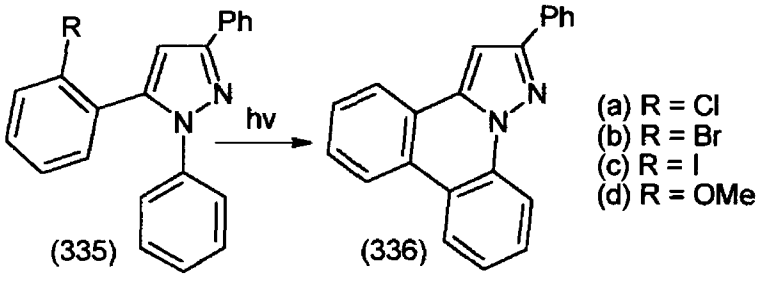


An aerated ethanol solution of 1-styrylpyridinium salt (332) was irradiated to afford the benzo[a]quinolizinium salt (333) in 60% yield[220] and the

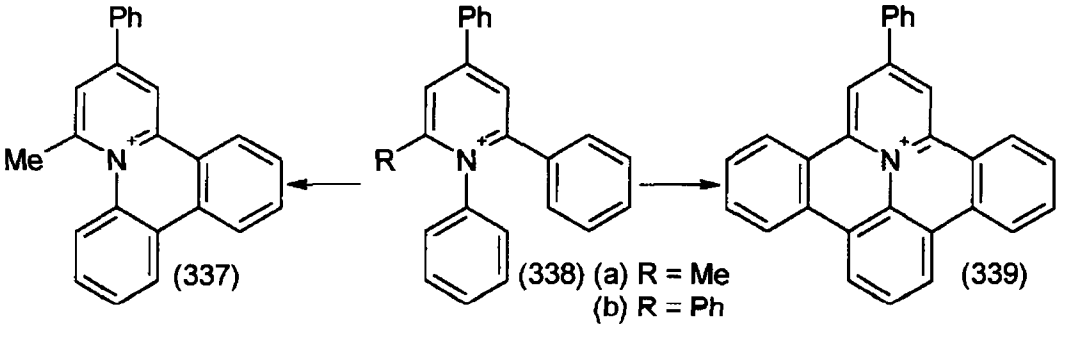
photocyclisation of various styrylisoquinolinium salts was also investigated In a similar reaction the 2-chloro compounds (334a,b) were photocyclised to the corresponding quinolizinium salts in good yields [221]



The photocyclisation of the triphenylpyrazoles (335a-d), to yield the corresponding phenanthrene analogues (336), has been reported [222] The photocyclisation of (335a-c) is thought to proceed via a radical process, while the photocyclisation of (335d) is thought to proceed via a dihydro-phenanthrene intermediate The reaction of the methoxy compound (335d) improved when the polarity of the solvent was increased

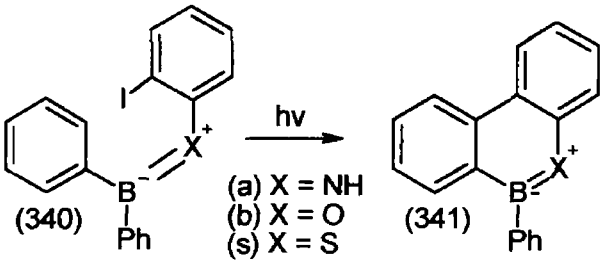


The photocyclisation of 1,2-di- and 1,2,6-triarylpyridinium cations have been reported [223 224] Cyclisation of (338a) furnished the azo compound (337)



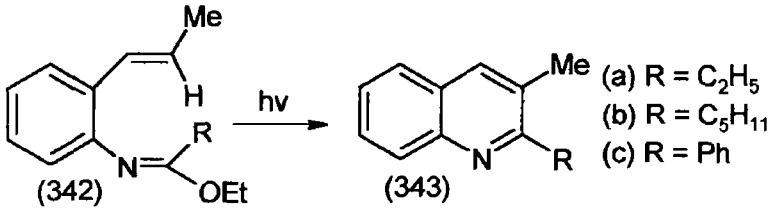
The triphenyl derivative (338b) undergoes two cyclisations to give the fused hexacycle (339) in 85% yield A wide range of hexacycles were synthesised Electron donor groups appear to inhibit the reaction

Photochemical synthesis of the borazaro-, boroxaro- and borathiarophenanthrene (341a-c) from the 2-iodo substituted precursors (340a-c) has been reported [225] Yields were found to be around 85%, except in the case of the boroxaro, which returned yields of 45% and, as with most oxygen heterocycles, photodegradation is a competing process

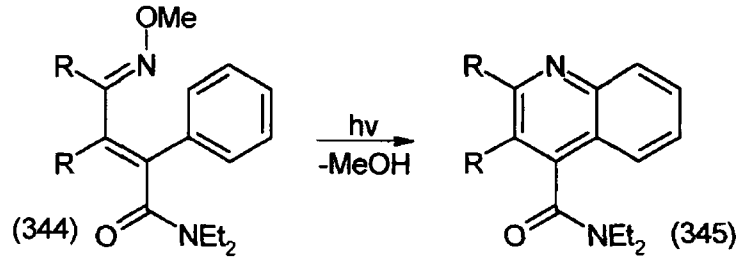


1 12 Quinolines and Isoquinolines

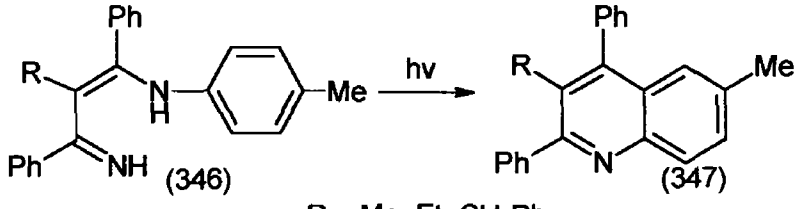
Qiang and Baine have reported the synthesis of quinolines in high yields by the irradiation of imidates [226] The imidates (342a-c) on irradiation in cyclohexane yield the quinolines (343a-c) in high yields, without the formation of any side products Several other of these quinolines have been synthesised with a variety of substituents



The synthesis of quinoline carboxamides from carboxamides has been reported by Elferink and Bos [227] The carboxamide (344) on irradiation yields the quinoline system (345), following initial cyclisation and subsequent elimination of methanol, in 80% yield

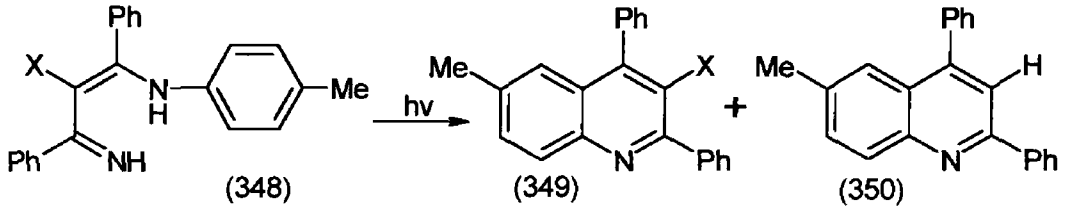


The photocyclisation of a number of 3-amino-2-alkenimines (346) has been reported[228] in various solvents (THF, methanol, diethyl ether, and toluene) to produce the substituted quinolines (347) in good yields Several other quinolines have been synthesised with a variety of substituents



R = Me, Et, CH_2Ph

In a similar reaction the photocyclisation of 3-haloquinolines from 3-amino-2-halo-2-alkenimines has been reported [229] The 2-iodo and 2-bromo alkenimines (348a,b) were irradiated in benzene, yielding a mixture of haloquinolines (349a,b) and dehalogenated quinolines (350) The 2-chloro alkenimine (348c) was irradiated in THF yielding only the haloquinoline (349c) in 95% yield 3-Iodo and 3-bromo quinolines were obtained in 30% and 55% yields respectively

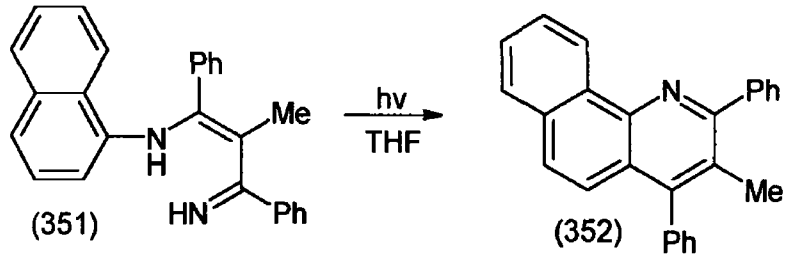


(a) X = I, (b) X = Br, (c) X = Cl

Photocyclisation of 3-(naphthylamino)-2-alkene imines yield substituted benzoquinolines [230] For example irradiation of the alkene imine (351) in THF,

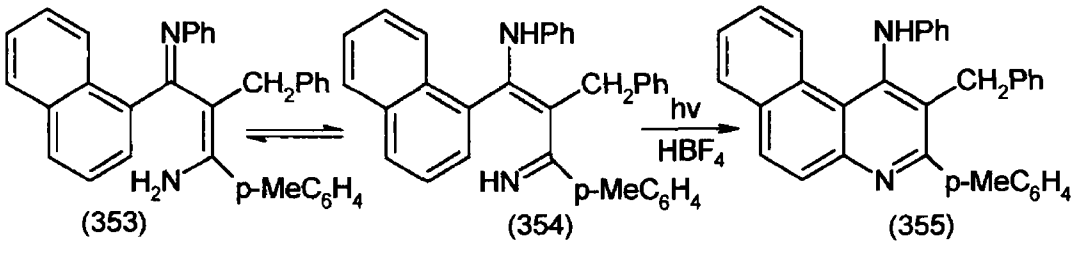
gave the benzo[h]quinoline (352) in 83% yield Several of these benzoquinolines have been synthesised with a variety of substituents

The synthesis of aminobenzoquinolines from the irradiation of 3-amino-2-alkene imines in acid medium has been reported [231] Alkene imines show equilibrium between two tautomers that can both participate in photocyclisation processes, depending on the reaction conditions Irradiation



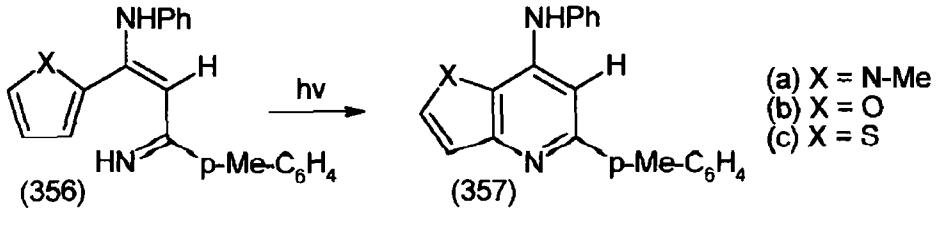
(351) (352)

in the presence of tetrafluoroboric acid leads to the formation of 4-(arylamino)quinolines For example the alkene imine (353) tautomerises to (354) which undergoes photocyclisation in the presence of tetrafluoroboric acid to yield 3-benzyl-4-(phenylamino)benzo[f]quinoline (355) in 40% yield The synthesis was repeated with several different substituents to yield various aminobenzoquinolines



(353) (354) (355)

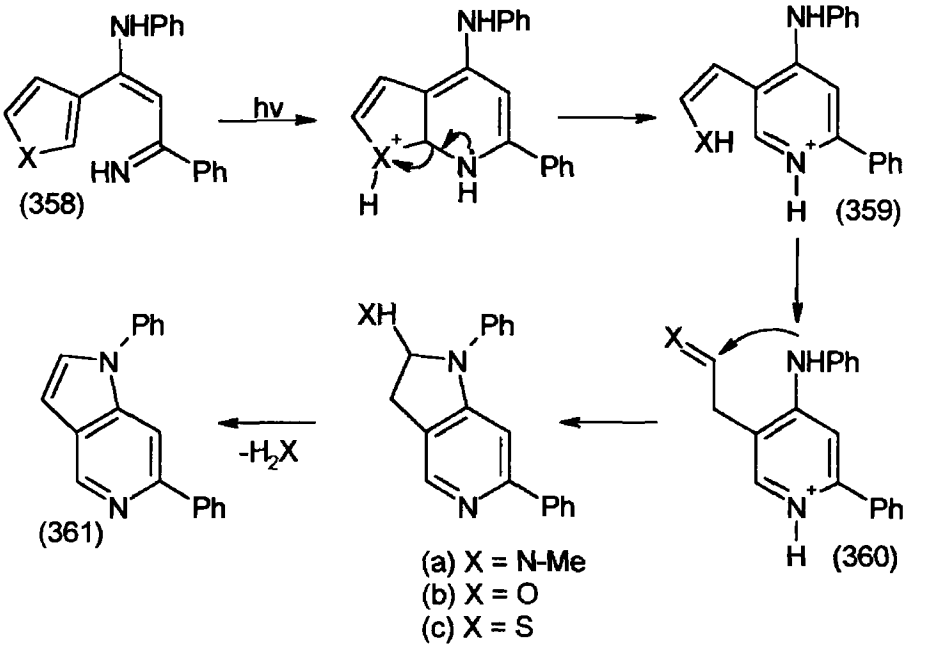
A versatile synthesis of pyrrolo-, furo- and thienopyridines via photocyclisation of 3-amino-2-alkene imines has been reported [232] 2-Pyrrolyl-



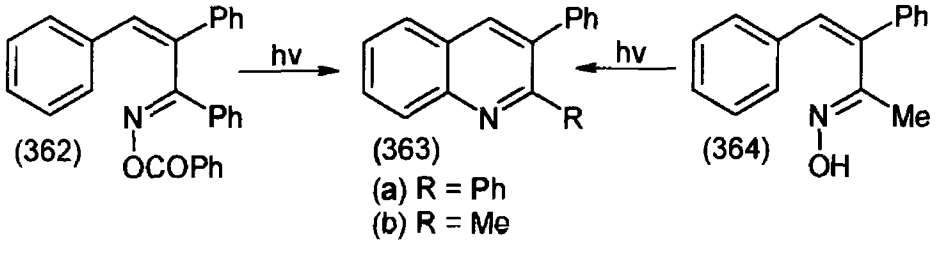
(356) (357)

2-furyl- and 2-thienylalkene imines (356a-c) in methanol with tetrafluoroboric acid yielded the corresponding pyridines (357a-c) in good yields

The photochemical behaviour of the analogous system with a 3-substituted five-membered heterocyclic ring was also investigated [232] These imines (358a-c), in methanol with tetrafluoroboric acid lead to the formation of 1,6-diphenylpyrrolo[3,2-c]pyndine (361) in each case The authors suggested that, after initial six π-electron photocyclisation, ring opening occurs to give the intermediate (359) which undergoes tautomerism to (360), followed by ring closure involving the amino group and final evolution to the corresponding pyrrolo[3,2-c]pyridine (361)

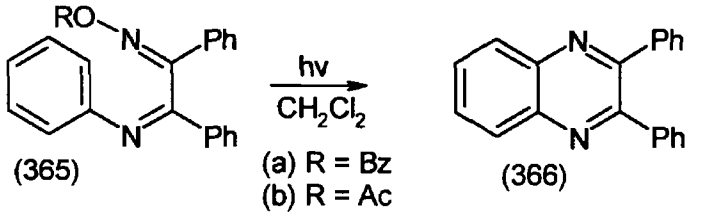


The photocyclisation of azabuta-1,3-dienes has been reported by Armesto and co-workers [233] Diene (362) afforded the corresponding quinoline (363a) in a yield of 43% Several of these quinolines have been synthesised

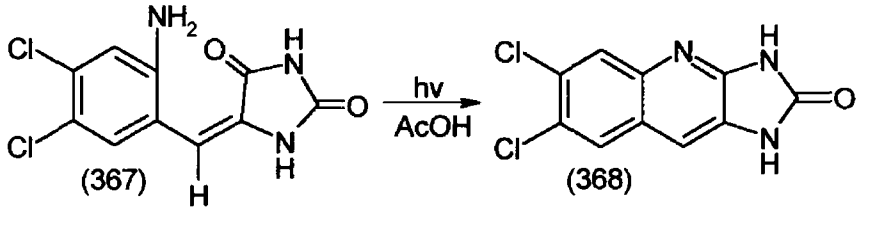


with a variety of substituents In a similar reaction Glinka reported[234] that the oxime (364) was transformed photochemically into the quinoline (363b)

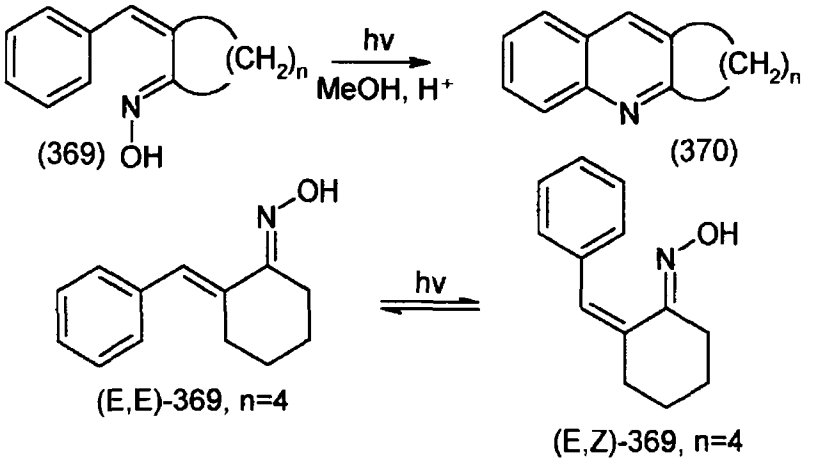
The synthesis of quinoxalines by photocyclisation of diazadienes has also been reported [235] Diazadienes (365a,b) yielded the quinoxalines (366a,b) When the reaction was carried out in acetone the yield of quinoxaline increased suggesting a triplet state was involved



Zhu and co-workers[236] have reported the synthesis of 6, 7-dichloro-imidazo[4,5-b]quinolin-2-one (368), a key intermediate in the synthesis of benzoimidazole nbonucleosides, which have potent and selective activity against human cytomegalovirus (HCMV) Photocyclisation of (367) in acetic acid leads to the formation of the quinolin-2-one (368), in 90% yield

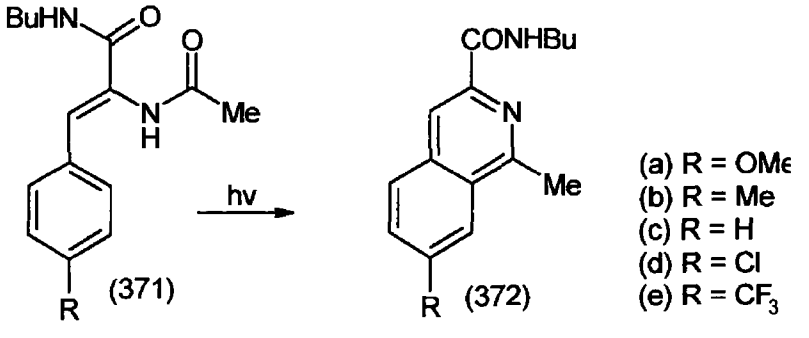


The cyclisation of oxime (369) to the quinoline (370) has been reported by Olsen [237 238] The reaction proceeds for values of n from n=3 to n=6, with the best results in six and seven membered rings, affording yields of 84% and 70% respectively The triplet state behaviour of the oximes E,E- and E,Z-(369, n=4), was studied in benzene using a vanety of sensitisers with different triplet energies Triplet state reactivity was localised almost exclusively in isomerisation at the C=C bond, giving photostationary state mixtures of E,E- and E,Z-isomers Direct irradiation of E,E-(369, n=4) gives isomerisation primarily at the C=N bond, a result which was similar to those which have been described for other α,β-unsaturated oxime derivatives Because triplet

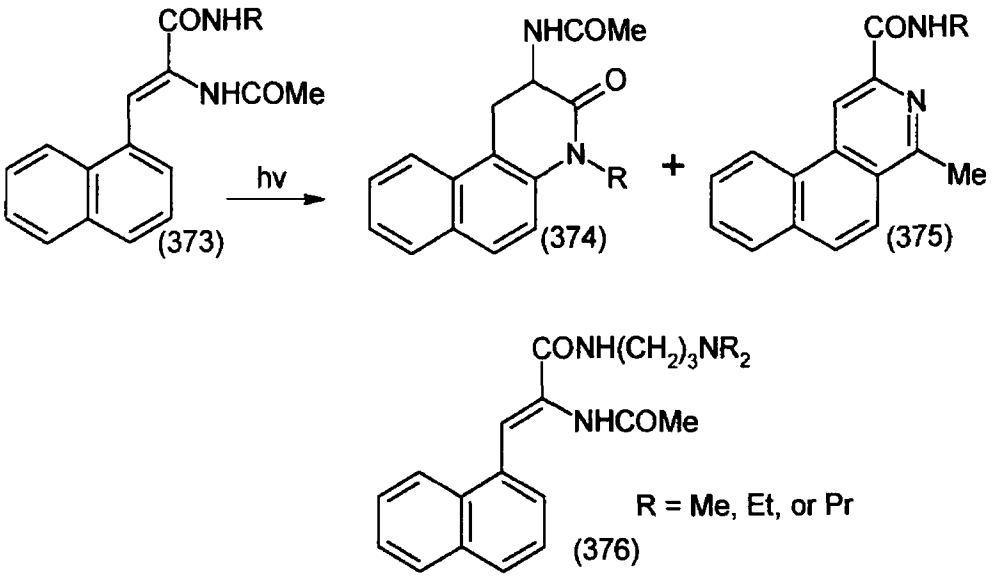


sensitisation experiments give almost exclusive isomerisation about the C=C bond, it is apparent that the cyclisation of the oxime arises from the excited singlet state

The photocyclisation of substituted N-acetyl-α-dehydrophenyalanines (371a-e) in methanol has led to the formation of isoquinoline derivatives (372a-e) in moderate yields [239]



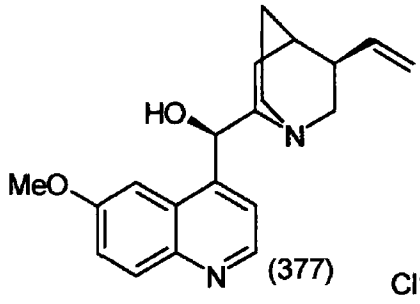
Kubo and co-workers[240 241] have reported the photocyclisation of dehydronapthylalanines to benzoquinolinone and benzoisoquinolines The N-acetyl-α-dehydro(1-naphthyl)alanine (373) on irradiation in methanol gave both 1,2-dihydrobenzo[f]quinolinone (374) and benzo[f]isoquinoline (375) [240] The yields of (375) were improved with increasing bulkiness of the R group In an analogous reaction the α-dehydro(1-naphthyl)alanines (376) yielded both the corresponding quinolinones and isoquinolines in various yields depending on the bulkiness of the alkyl substituent [241]


CONHR
NHCOMe
hv
(373)
NHCOMe
O
N
R
(374)
+
CONHR
N
Me
(375)
CONH(CH2)3NR2
NHCOMe
R = Me, Et, or Pr
(376)

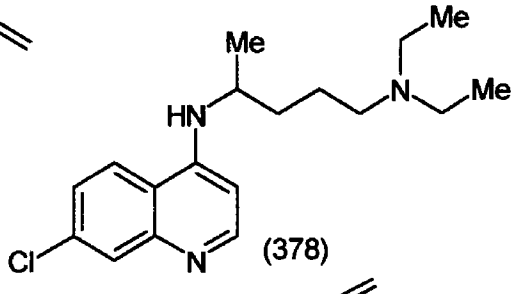
2. Non-Photochemical Syntheses of Quinolines

2.1 Quinolines: Non-Photochemical Synthesis

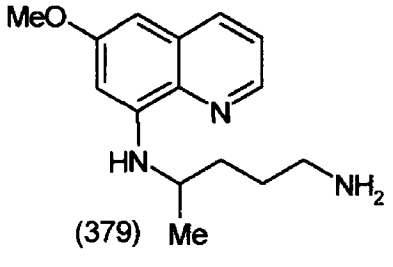
Quinoline derivatives are widely used in the treatment of malaria Malaria is probably the most studied and best understood parasitic disease The most commonly used are quinine (377), the main alkaloid obtained from the bark of the cinchona tree, chloroquine (378), a 4-aminoquinoline, and primaquine (379), an 8-aminoquinoline Quinidine (380) is used as a antiarrhythmic drug A range of non-photochemical methods for the synthesis of quinolines have been devoloped and are briefly reviewed here



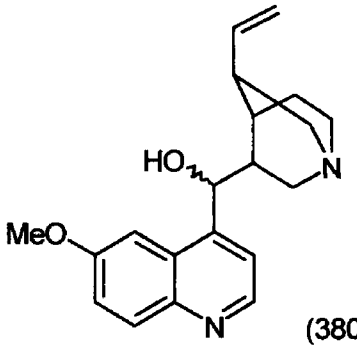
(377)



(378)



(379)

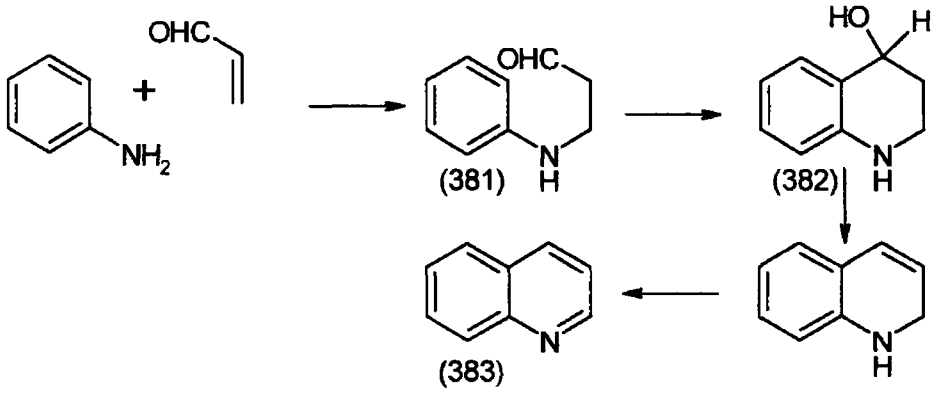


(380)

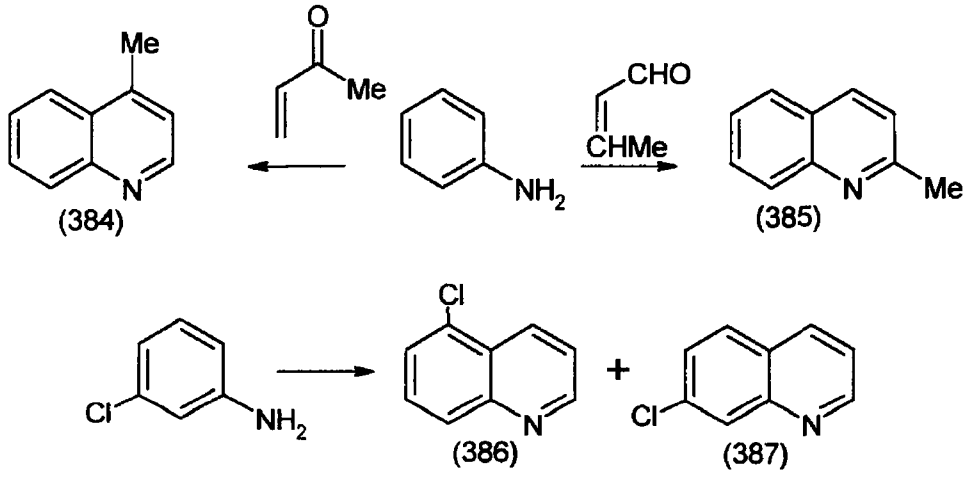
2 2 Skraup Synthesis

The most widely used synthesis of quinoline (383) is that of Skraup, and it can be applied to the synthesis of many derivatives, providing the substituents present are unchanged by the reaction conditions Skraup's original mixture was nitrobenzene, glycerol and concentrated sulphuric acid but he found considerable improvement in yield if aniline was added [242] An oxidising agent, which may be nitrobenzene, stannic chloride, ferric salts, oxygen, or arsenic pentoxide, led to improved yields The initial stages of the reaction are very vigorous, and can be moderated by the presence of some ferrous sulphate Yields are often further improved by the addition of boric acid The glycerol was first converted into acrolein, a Michael addition with aniline gave the aldehyde (381) Cyclisation to a tetrahydroquinoline (382) was then followed by dehydration and oxidation [243] Attempts to prepare

quinoline directly from acrolein have given low yields It appears that the acrolein is polymerised before it can combine with the aniline

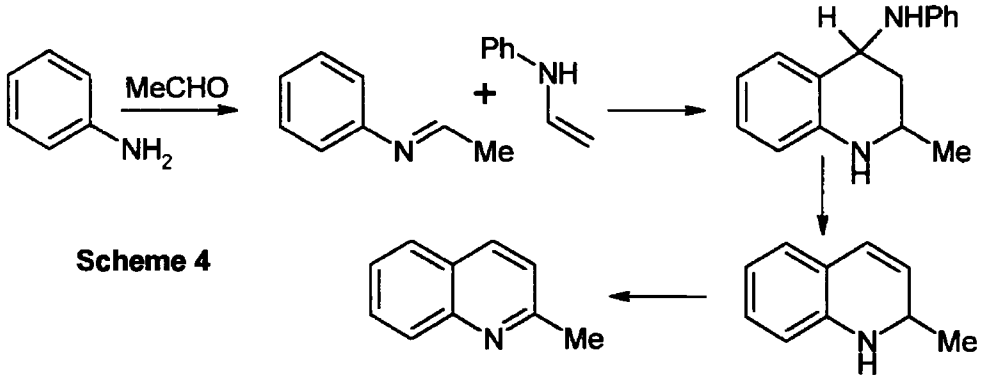


When the glycerol or acrolein is replaced by crotonaldehyde or methyl vinyl ketone, 4- (384) and 2-methylquinolines (385) are furnished respectively If the carbonyl group combined first with the aniline to give a Schiff's base, and this then cyclised onto the benzene ring, the positions of the methyl groups would be reversed



In the case of 3-substituted anilines, cyclisation can occur in two ways Where the 3-substituent is a strongly activating one, such as a methyl, hydroxyl, or methoxy group, only a 7-substituted quinoline is obtained from the reaction With 3-bromo, 3-chloro, or 3-dimethylamino groups both the 5- (386) and 7-substituted quinolines (387) are isolated, with the 7-substituted quinoline (387) as the major product

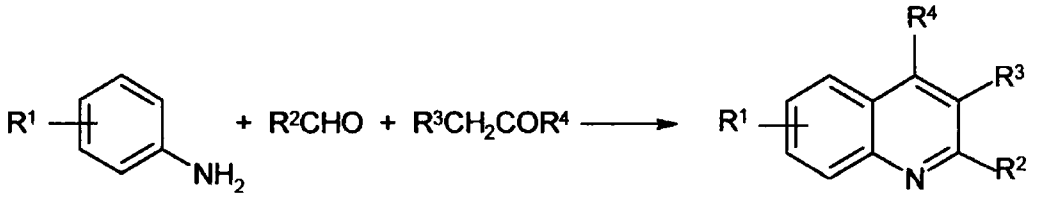
The Doebner-von Miller[244] synthesis is closely related to that of Skraup It consists of heating a primary aromatic amine with an aldehyde in the presence of ethanol and hydrochloric acid (scheme 4) No oxidising agent is used, although iron (III) chloride or arsenic acid is often added



Scheme 4

In practical terms, the major advantage of the Doebner-von Miller and Skraup synthesis is the wide range of o- and p-substituents in the aniline which are tolerant of the acid conditions Thus, 6- and 8-substituted quinolines can be made by the Skraup method where the substituent is an alkyl, aryl, hydroxyl, or carboxyl group, or a halogen In the Doebner-von Miller procedure the same range of substituents can be used to produce 2-, 3-, or 4-alkyl- or aryl-substituted quinolines A few groups are unstable to the acid conditions, especially in the Skraup synthesis For example the cyano group is hydrolysed and the resulting carboxylic acid may decarboxylate As illustrated already the major disadvantage of this synthesis lies in the production of mixtures of 5- and 7-quinolines when meta-substituted arylamines are used

Beyer discovered that a mixture of an aldehyde and a ketone could be used to give 2,4-di- or 2,3,4-tri-substituted quinolines, if the difference in

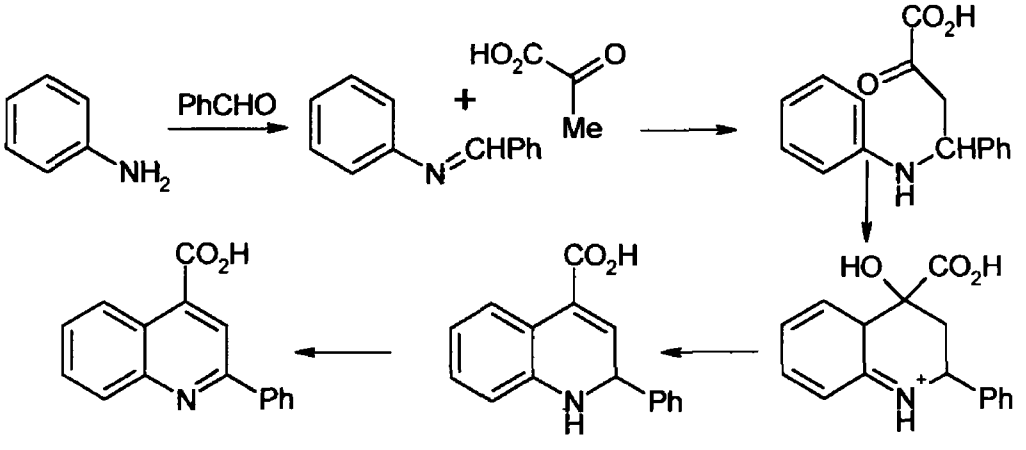


R^2 = H, alkyl or aryl, R^3 = H or alkyl, R^4 = alkyl or aryl

Scheme 5

reactivity was sufficient [245] The commonest carbonyl compounds used are acetone or acetophenone, and formaldehyde is particularly useful, giving quinolines with no substituent in position 2 The general reaction is given above (scheme 5)

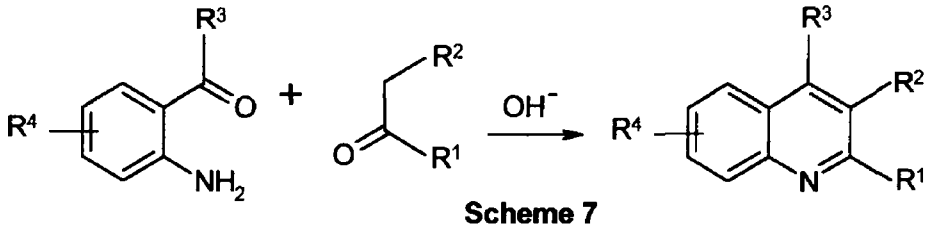
The quinoline-4-carboxylic acid synthesis, originally discovered by Bottinger,[246] but fully developed by Doebner[247], comes from the discovery that pyruvic acid and aniline condensed to give 2-methylquinoline-4-carboxylic acid An aldehyde, pyruvic acid and an aromatic amine boiled in alcoholic solution give 2-substituted quinoline-4-carboxylic acids, which can readily be decarboxylated (scheme 6)



Scheme 6

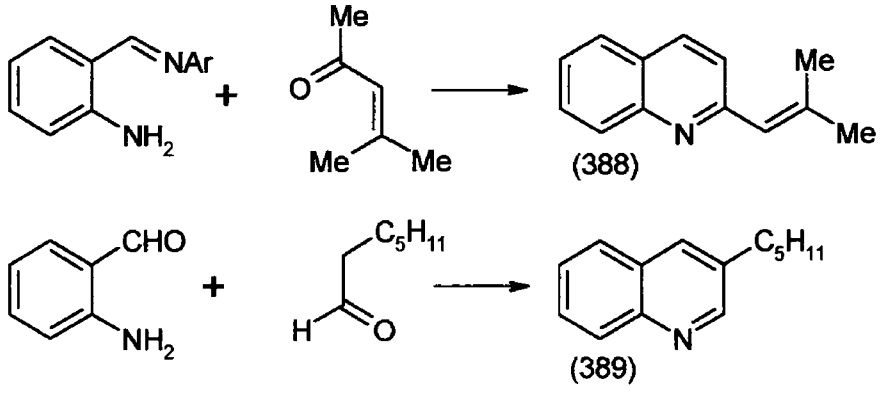
2 3 Friedlander Synthesis

The Friedlander synthesis of quinoline uses o-aminobenzaldehyde or simple ketones, with strongly basic medium [248] The general reaction scheme is illustrated below (scheme 7) The synthesis is weakest when substituents in the benzenoid ring of the quinoline are required

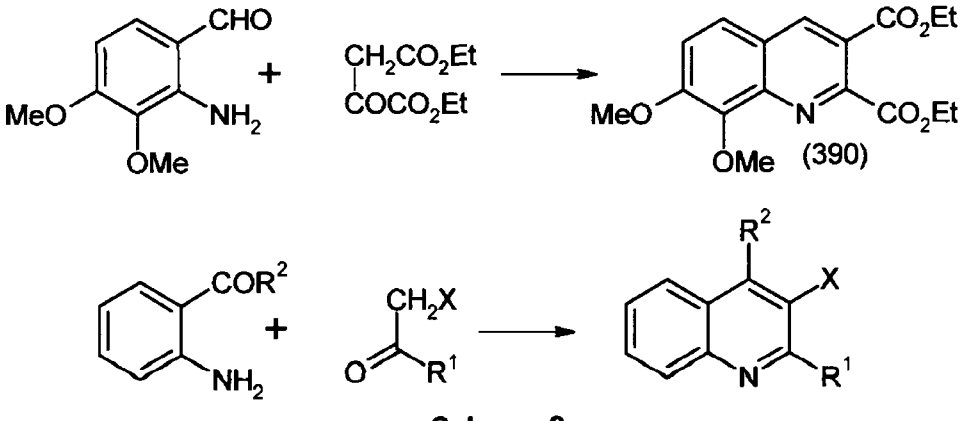


Scheme 7

The range of substituents which can be introduced in position 4 of the quinoline is also small, but the major advantage of the synthesis is in the range of 2- or 3-mono- and 2,3-di-substituted quinolines which can be obtained The o-aminobenzaldehydes are unstable and can often be replaced with advantage by anils 2-Isobutenylquinoline (388) is prepared in this way[249] and another advantage is that a much milder base, piperidine, can be used Aldehydes should give 3-substituted quinolines but many cannot tolerate the strongly basic conditions Long chain aldehydes will react with o-amino-benzaldehyde without a basic catalyst at 180°C to give 3-alkylquinoline,[250] for example heptanal gives 3-pentylquinoline (389)

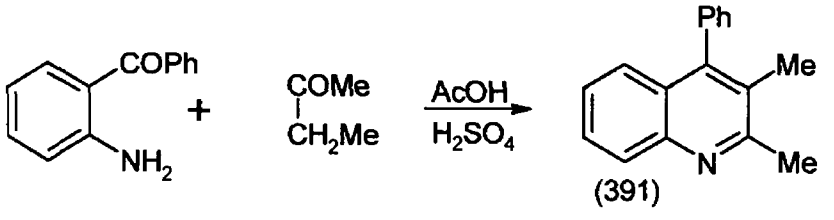


Oxaloacetates give quinoline-2,3-dicarboxylates such as compound (390) in 75% yield [251] Mixtures are obtained generally from ketones with two enolic forms, but if the enolisation in one direction can be enhanced, as in a β-keto ester, a high yield of one component can be obtained Examples of this type are summarised in scheme 8



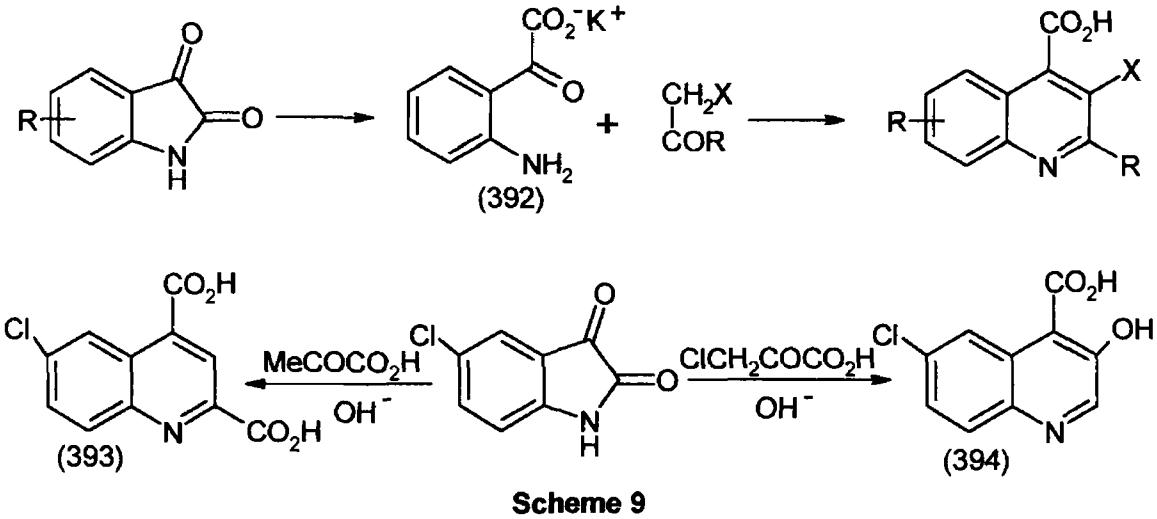
Scheme 8

A major modification of the Friedlander synthesis is the use of acid catalysis, first reported by Clemo and Felton[252] but much developed by Fehnel and by Kempter One of the major advantages of the acid-catalysed procedure is its greater regioselectivity Methyl ethyl ketone is reported to react with o-aminobenzophenone to give of 2,3-dimethyl-4-phenylquinoline (391) [253]



(391)

The most widely used variant on the Friedlander synthesis is that due to Pfitzinger[254] (scheme 9) Isatin in potassium hydroxide solution reacts as potassium isatogenate (392), and hence gives quinoline-4-carboxylic acids The variations in, and the drawbacks to, the Pfitzinger synthesis are largely due to the small number of substituted isatins available, so that only limited variations in benzene ring substituents are possible Most Pfitzinger reactions have used ketones, as aldehydes undergo self condensation, but aldoximes can be used [255] While pyruvic acid gives quinoline-2,4-dicarboxylic acids (393),[256] halopyruvic acids give 3-hydroxyquinoline-4-carboxylic acids (394), with loss of the 2-carbonyl group [257]



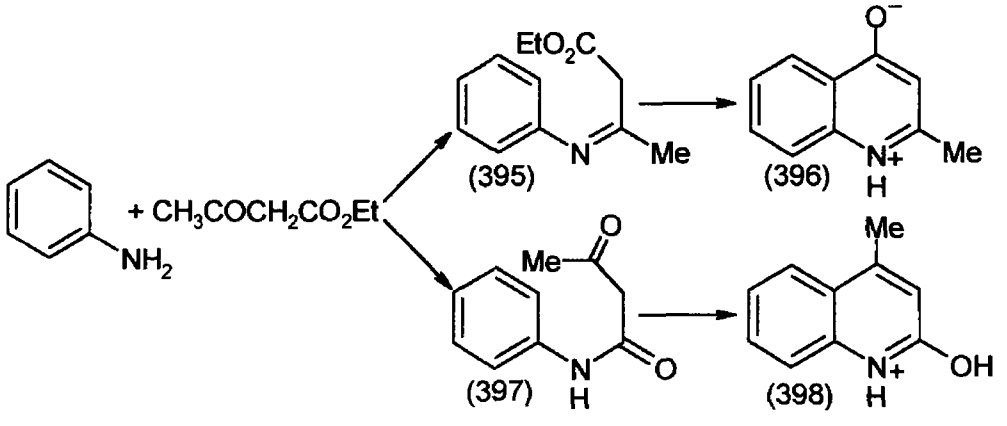
(392)

(393) (394)

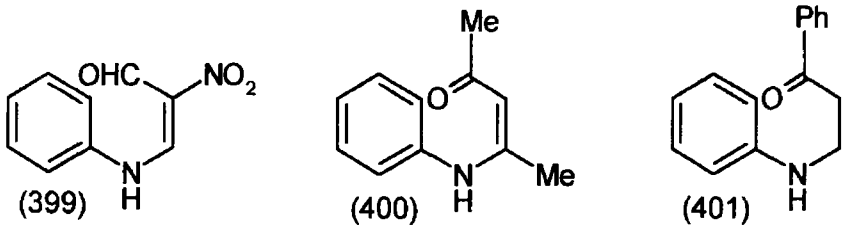
Scheme 9

2 4 Quinolines from Carbonyl Electrophilic Centres

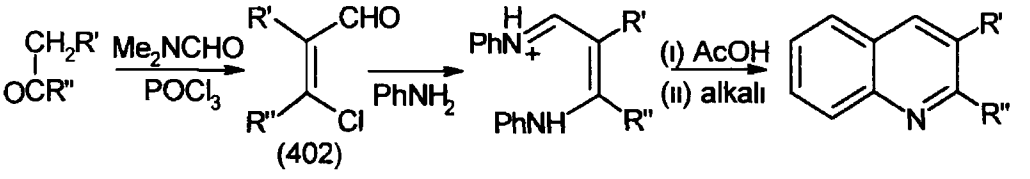
An important group of syntheses use a carbonyl group to generate the electrophilic centre Among these are the named syntheses due to Knorr, Combes and Conrad-Limpach Ethyl acetoacetate combines with aniline in two ways, and the products can be converted to different quinolines Reaction in the cold, or up to about 100°C, gives the anil (395) This cyclises, the Conradt-Limpach synthesis,[258] to the quinolone (396) on being dropped into a hot inert solvent, one of the best being diphenyl-biphenyl ether mixture On boiling ethyl acetoacetate with aniline, the anilide (397) is formed and is cyclised by concentrated sulphunc, the Knorr's synthesis,[259] or polyphosphonc acid to the quinolone (398)



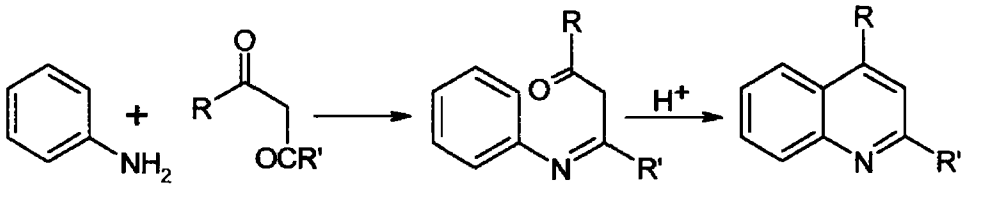
In a similar way the enamines (399) and (400), obtained from aniline with either nitromalondialdehyde[260] or acetylacetone respectively, can be cyclised to the corresponding quinolines by acids Cyclisation of the N-substituted aniline (401) yielded the corresponding quinoline in 25% yield rather than the dihydroquinoline [261]



A most valuable development[262] of this last synthesis consists in converting ketones to corresponding β-chlorovinyl aldehydes (402) and condensing these with aromatic amines Quinolines are obtained in high yield



The Combes synthesis uses the condensation between a β-diketone or β-ketoaldehyde to give an anil, which is cyclised by acid, as in scheme 10 [263] A better procedure for β-ketoaldehydes is to use a mixture of aromatic amine hydrochloride and zinc chloride in addition to the amine and β-dicarbonyl compound [264]

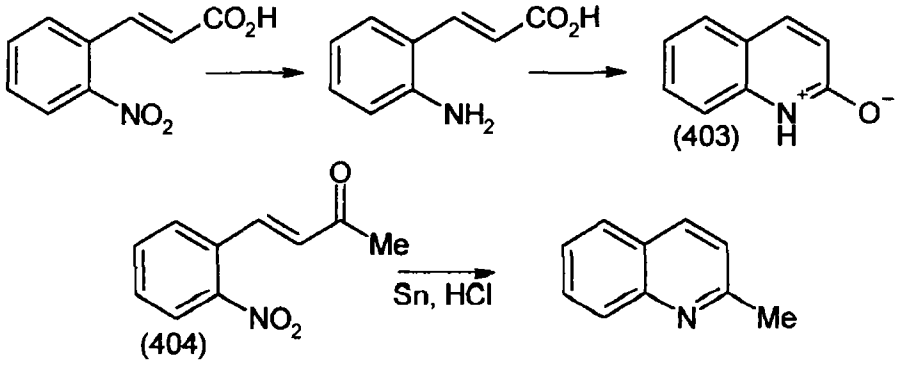


R = alkyl or aryl, R' = H, alkyl, or aryl

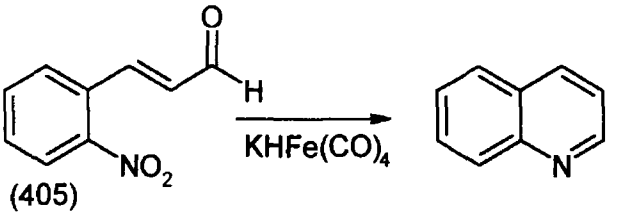
Scheme 10

2 5 Miscellaneous Reactions

A large number of quinolines have been obtained by the cyclisation of the appropriate aniline, often synthesised from the corresponding nitro compound 2-Quinolone (403) was synthesised by this method The 2-nitro compound (404), obtained from 2-nitrobenzaldehyde and acetone, cyclises similarly in acidic reducing conditions [265]

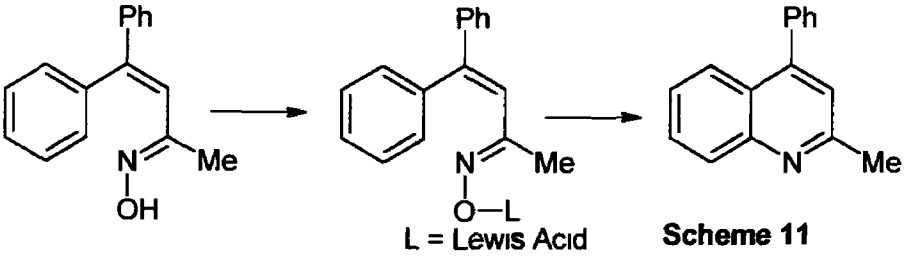


A number of quinoline syntheses involve the reduction of an o-nitrocinnamyl derivative The simplest uses o-nitrocinnamaldehyde Potassium tetracarbonylhydridoferrate reduces (405) to quinoline in quantitative yield [266]



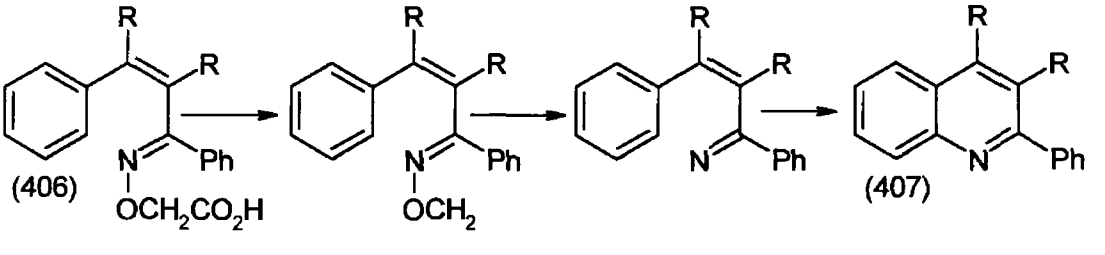
(405)

A number of syntheses of quinolines involve the attack by a reactive nitrogen atom on a benzene ring Electrophilic cyclisation of cinnamaldoximes to give quinolines has been reported using phosphorous pentoxide or alumina (scheme 11) When acetic anhydride was used as the cyclisation solvent it was discovered that oxime esters can be cyclised without Lewis acids, if they have the correct stereochemistry about the double bond [266]



Scheme 11

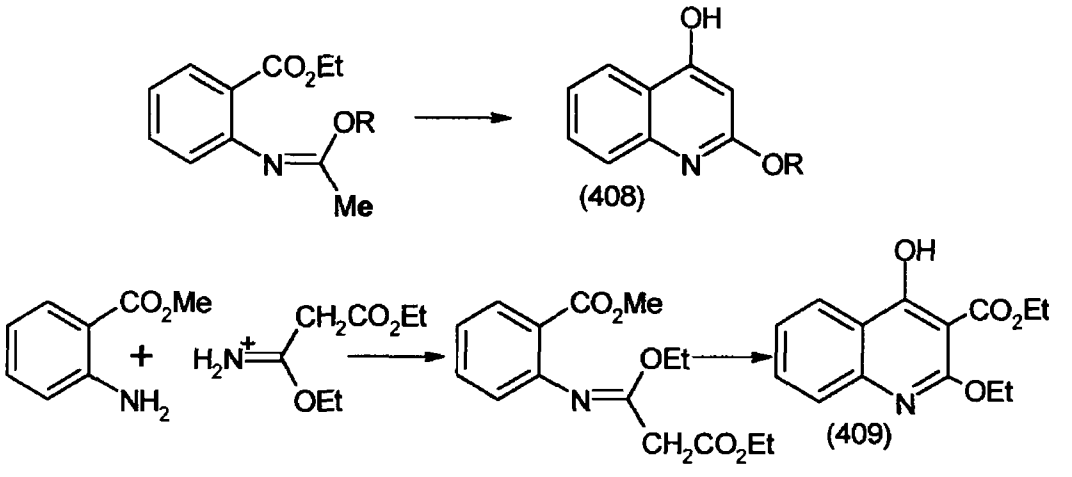
A free radical attack causes the cyclisation in the persulphate oxidation of the oxime derivative (406) to the corresponding quinoline (407) in a yield of 91% [267]



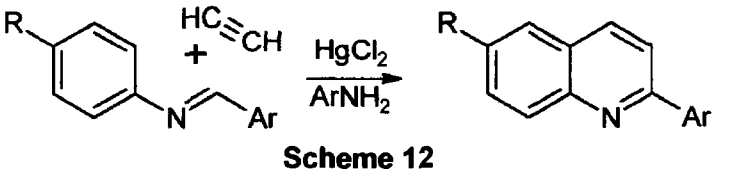
(406) (407)

Quinol-2- and 4-one derivatives are obtained by an intermolecular aldol condensation in the Camps synthesis [268] Extensions of the Camps synthesis

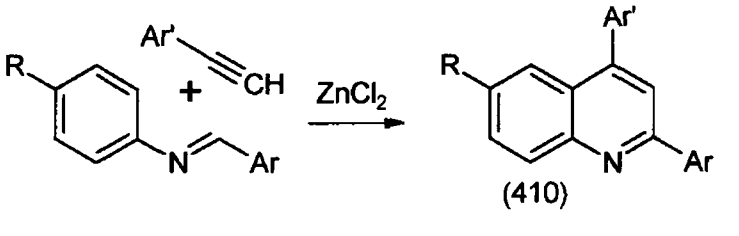
have yielded quinolines Cyclisation can be achieved by heat, as in the preparation of 2-alkoxy-4-hydroxyquinolines (408),[269] or by isopropylamine as in the synthesis of the 3-substituted derivative (409) [270]



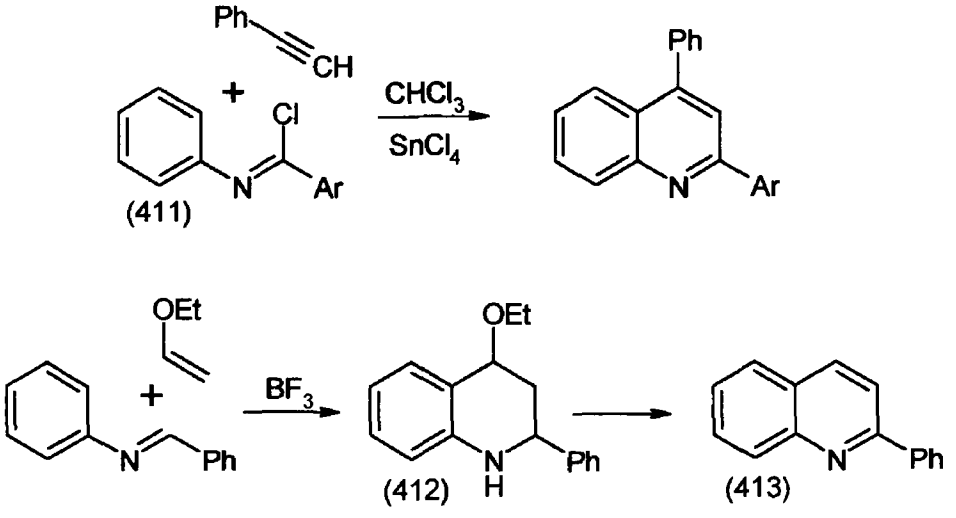
A number of syntheses of quinolines are based on reaction between anils and alkynes, or anils and substituted alkenes Although these are formally [4π + 2π] reactions, most are initiated by salts or by Lewis acids, and are presumably electrophilic substitutions on the benzene ring during the cyclisation step Kozlov and his co-workers have exhaustively examined the reaction between Schiff bases and acetylene, using a wide range of metal salts as catalysts One example is given in scheme 12 [271] Arylalkynes condense with Schiff bases when treated with zinc chloride to give 2,4-diarylquinolines (410) [272]



Scheme 12



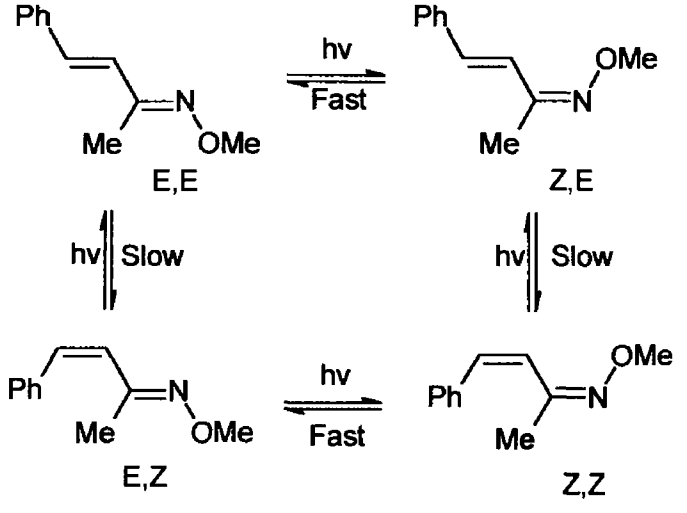
The chloroimines (411) and phenylacetylene, with tin(IV) chloride, can also give good yields of 2-aryl-4-phenylquinolines [273] Most of the cyclisation reactions between anils and alkenes use enol ethers to give, as intermediates or final products, 4-alkytetrahydroquinolines In one version of the synthesis the reaction is catalysed by boron trifluonde or aluminium tribromide A simple example shows the synthesis of 2-phenylquinoline (413) via the intermediate tetrahydroquinoline (412) [274]



3. The Photochemistry of 2-Arylidenecyclopentanone Oxime O-Acetates

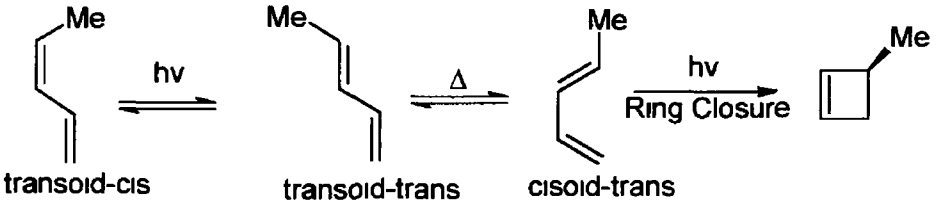
3.1 Introduction

The photochemistry of α,β-unsaturated compounds containing the carbon-nitrogen double bond has been investigated by several authors [226 237 275-279] On irradiation of the conjugated oxime ether E-(E-benzylidenenacetone)oxime O-methyl ether (E,E), Pratt and Majid found that the carbon-nitrogen double bond isomerises more efficiently than the carbon-carbon double bond both under direct and triplet sensitised irradiation (scheme 13) [276]



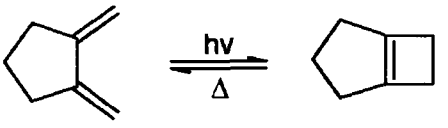
Scheme 13

Buta-1,3-dienes in the transoid conformation fail to undergo electrocyclic ring closure, but in the cisoid conformation electrocyclic ring closure occurs to yield cyclobutenes on irradiation (scheme 14) [280]



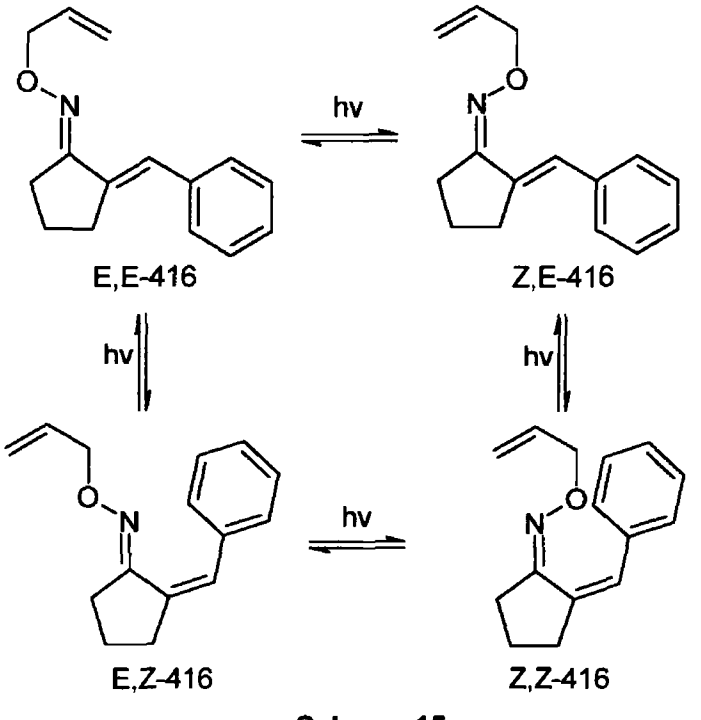
Scheme 14

Constraining the buta-1,3-diene chromophore in the cisoid conformation facilitates the electrocyclisation [281] Thus 1,2-dimethylenecyclopentane (414) yields bicycloheptene (415) in quantitative yield



(414) (415)

It was therefore of interest to study the effects of irradiation on a system containing an α,β-unsaturated carbon-nitrogen double bond constrained in the cisoid conformation by placing a ring system such as that in (414), in the molecule An investigation into such systems was carried out by Austin [282] 2-Benzylidenecyclopentanone oxime O-allyl ether (416) was irradiated in ethyl acetate, resulting in a photostationary state of four geometrical isomers on prolonged irradiation The allyl group remained intact throughout (scheme 15)

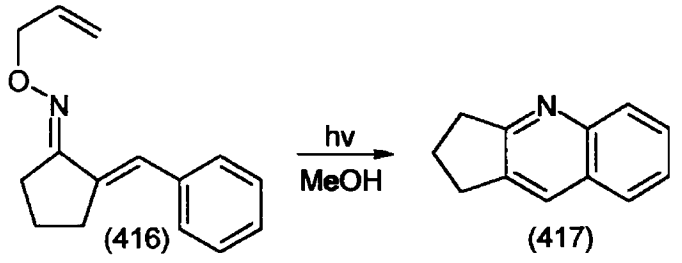


E,E-416 Z,E-416

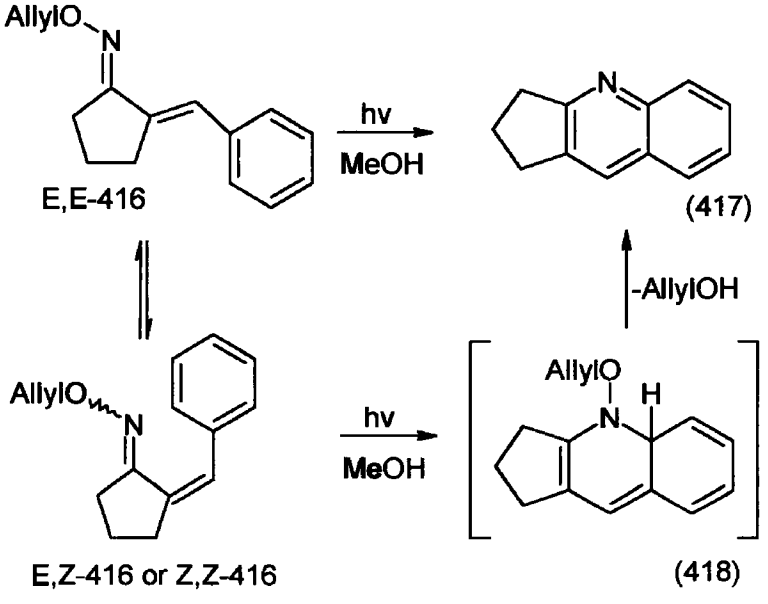
E,Z-416 Z,Z-416

Scheme 15

In methanol however, an additional product was formed After preparative chromatography, the product was isolated and was shown to be the quinoline (417) Formation of (417) on irradiation was accounted for by initial carbon-carbon double bond isomerisation followed by 6π-electrocyclic ring closure of E,Z-(416) or



Z,Z-(416) to the intermediate dihydroaromatic heterocycle (418) followed by spontaneous aromatisation by elimination of allyl alcohol (scheme 16)



Scheme 16

3 2 Mechanism of Reaction

The oxime O-allyl ether (416) was irradiated, with various amounts of isoprene, a triplet quencher, present [282] In each case the photocyclisation reaction proceeded unaffected, giving the quinoline (417) in the same yield Therefore the

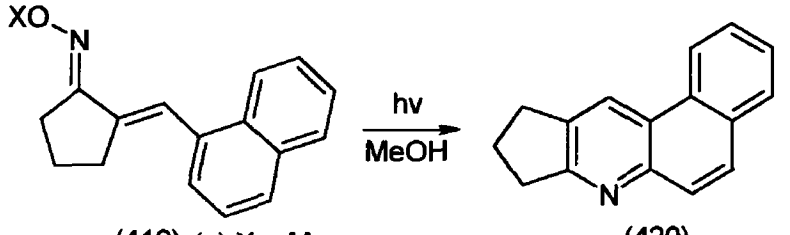
photocyclisation reaction proceeds via a singlet excited state, since product formation is not affected by the presence of a triplet quencher

The photocyclisation of the 2-arylidenecyclopentanone oxime O-allyl ether (416) may be considered to be a 6π electron cyclisation analogous to that of a 1,3,5-triene system, which is discussed in section 1 1

3 3 Scope of the Reaction

Since the allyl group did not participate in the photocyclisation reaction, a series of oxime O-methyl ethers with different aryl substituents was synthesised by Austin[282] and the photochemistry of each investigated

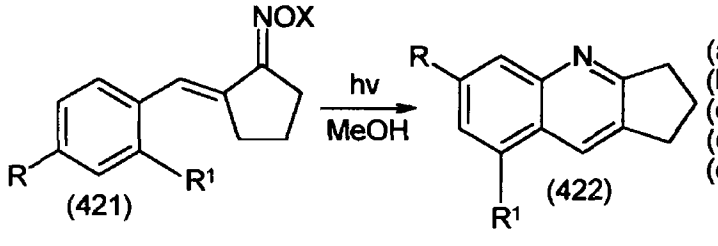
One of the first investigated was 2-(1-naphthylidene)cyclopentanone oxime O-methyl ether (419a) This was irradiated in methanol and the product isolated was the quinoline (420) in 70% yield



(419) (a) X = Me
(b) X = Ac

(420)

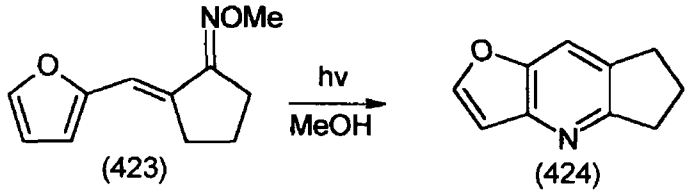
Irradiation of oxime ethers (421a-d) and (423) in methanolic solution also yielded the corresponding cyclised photoproducts (422a-d) and (424), respectively The yields of the methoxy compounds were around 15% higher than for the



(421)

(422)

(a) R = H, R^1 = OMe, X = Me
(b) R = H, R^1 = Me, X = Me
(c) R = OMe, R^1 = H, X = Me
(d) R = Me, R^1 = H, X = Me
(e) R = OMe, R^1 = H, X = Ac

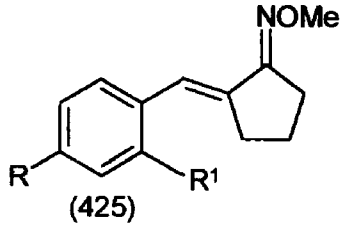


(423) (424)

corresponding methyl compounds Austin concluded[282] that the stronger electron-donating methoxy group enhanced the reaction

Irradiation of the chloro- and nitro-substituted oxime ethers (425a-d) in methanolic solution failed to yield the corresponding cyclised photoproducts, possibly due to intersystem crossing to an unreactive triplet excited state or the intervention of radical processes

(a) R = H, R^1 = NO_2
(b) R = H, R^1 = Cl
(c) R = NO_2, R^1 = H
(d) R = Cl, R^1 = H



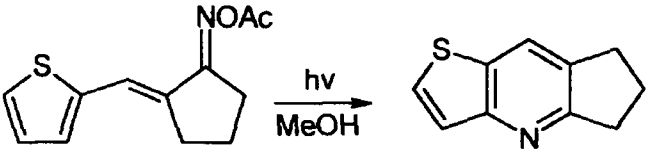
(425)

hv, MeOH → No 6 pi electron cyclisation

The oxime ethers synthesised by Austin were usually isolated as liquids and were therefore inconvenient to handle This, coupled with the fact that dimethyl sulphate, the reagent used for methylation of the oximes, is a hazardous reagent, prompted the synthesis of the corresponding oxime acetates, compounds which are generally crystalline and relatively easier to synthesise in good yields

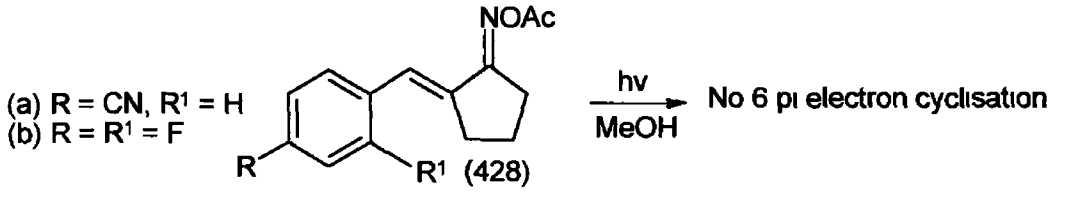
The 2-(1-naphthylidene) oxime O-acetate (419b) and 2-(4-methoxy-benzylidene)cyclopentanone oxime O-acetate (421e) were synthesised by Egan[283] and their photochemistry investigated In both cases cyclisation occurred as for the methyl ethers yielding (420) and (422e) respectively

A number of oxime O-acetates with different aryl substituents were synthesised and the photochemistry of each investigated 2-(2-Thienylidene)-cyclopentanone oxime O-acetate (426) on irradiation in methanol led to the quinoline product (427) in 51% yield [283]



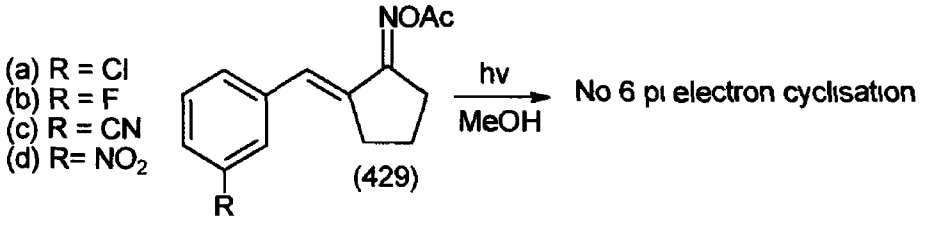
(426) (427)

Irradiation of oxime O-acetates (428a,b) in methanolic solution failed to yield the corresponding cyclised photoproducts [283]



(428)

Similarly irradiation of oxime O-acetates (429a-d) in methanolic solution failed to yield the corresponding cyclised photoproducts [283]

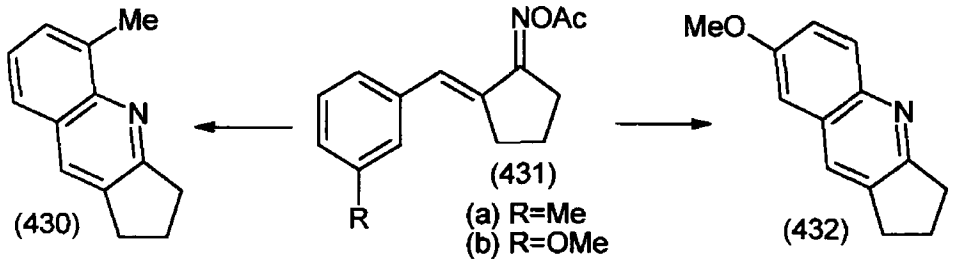


(429)

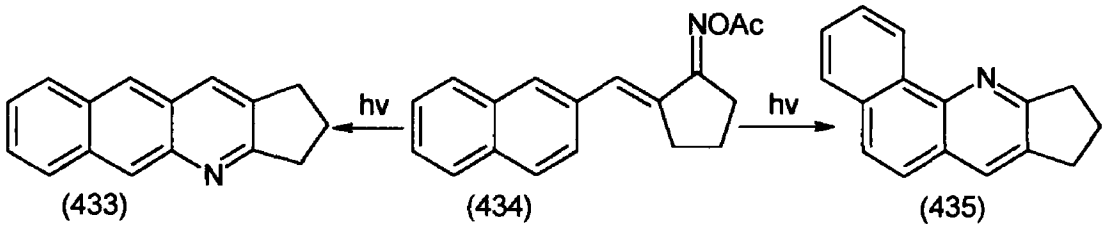
Combining these results with those of Austin,[282] it became clear that, since the oxime substituent plays no part in the cyclisation reaction, the best yields of cyclised product are obtained when the aryl group has substituents which are electron donating or when there is no aryl substituent When the aryl substituent is electron withdrawing smooth cyclisation to yield quinolines is not competitive Although it may have occurred to some minor extent, other decomposition processes competed to produce complex reaction mixtures in all such cases

Some initial investigations into the regioselectivity of these cyclisation reactions were carried out by Egan [283] Substitution at the 3-position of the aromatic ring leads to highly regioselective outcomes Thus compound (431a) yields (430)

as exclusive product, whereas (431b) yields solely the alternative regioisomer (432) [283]



2-(2-Naphthylidene)cyclopentanone oxime O-acetate (434), on irradiation in methanol, can in principle give two products (433) and (435) The sole photoproduct of the reaction was the quinoline (435) [283]

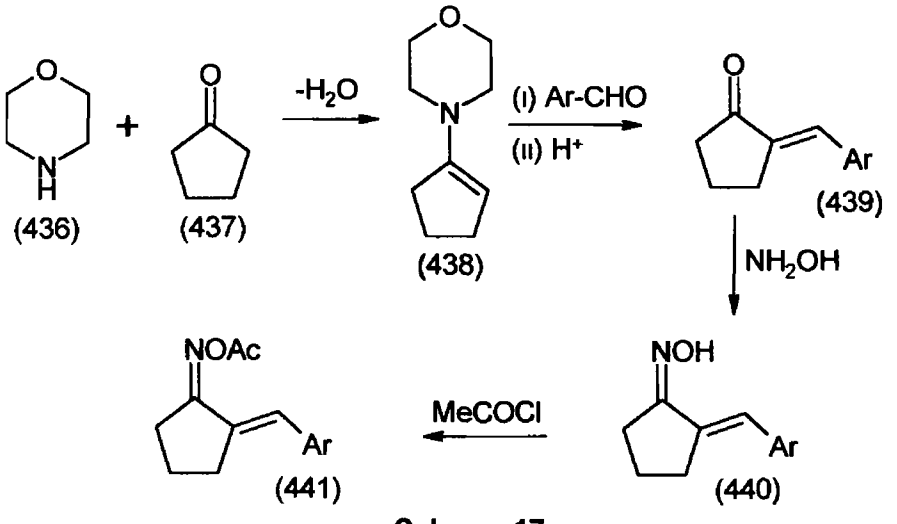


Both Austin[282] and Egan[283] have shown that electron-donating groups facilitate the photocyclisation reaction, while electron-withdrawing groups seem to impede it To broaden the scope of the reactions an investigation of substrates incorporating a range of electron-donating aryl substituents was carried out

3 4 Synthesis

The method for the synthesis of the required oxime O-acetates was based on that developed by Egan [283] The azeotropic reflux of morpholine (436) with cyclopentanone (437) in toluene led to the formation of the morpholine enamine (438), which was reacted, without isolation, with the desired aromatic aldehyde Subsequent acid hydrolysis gave the corresponding arylidenecyclopentanone (439) Heating the ketone (439) under reflux with hydroxylamine hydrochloride and

pyridine in ethanol formed the corresponding oxime (440), which was reacted with acetyl chloride in pyridine to yield the oxime O-acetate (441) (scheme 17)

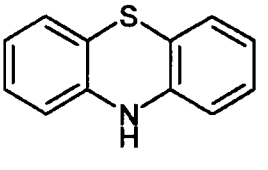


Scheme 17

Achievement of the desired aryl substitution pattern requires access to the appropriate aryl aldehyde The preparation of 1-formylphenothiazine, 3-t-butylbenzaldehyde, 3-(dimethylamino)benzaldehyde and 3-methoxy-4-methyl-benzaldehyde, which were not available commercially, is described in the following pages

3 4 1 Synthesis of 1-Formylphenothiazine (443)

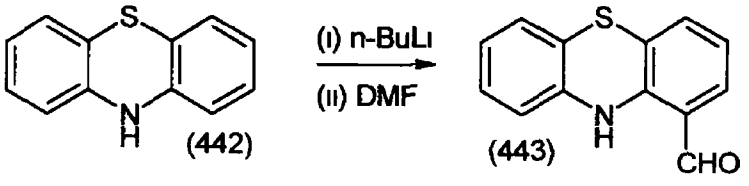
Phenothiazine (442) and its derivatives are used in the treatment of both malaria[284] and tuberculosis,[285 286] and have also been used as antipsychotic and neuroleptic agents and as antihistamines [287 288] Multidrug resistance is a serious problem in cancer chemotherapy Phenothiazine and structurally related compounds are among studied multidrug resistance modulators [289] Phenothiazine



(442)

derivatives also inhibit production of prions, the disease-causing agent of Creutzfeldt-Jacob disease [290] A synthesis of a new phenothiazine derivative has been carried out using the photocyclisation process

For the synthesis of 2-(10H-phenothiazin-1-ylmethylene)cyclopentanone oxime O-acetate, 1-formylphenothiazine (469) is required and synthesised by treatment of phenothiazine with n-buthyllithium followed by reaction with N,N-dimethylformamide as used by Hallberg and Martin [291] The structure was verified



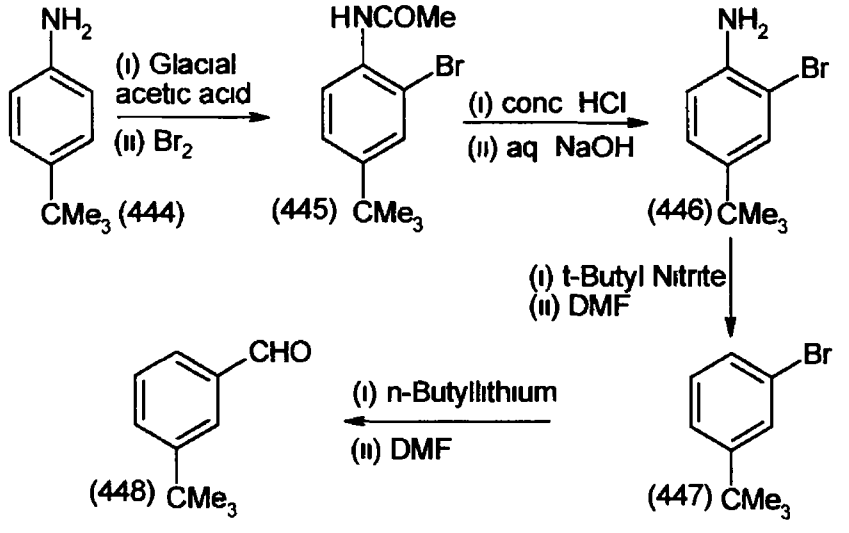
by the presence of the relevant peaks in both the IR and NMR spectra, specifically the presence of the carbonyl peak in the IR and ^{13}C-NMR spectra

3 4 2 Synthesis of 3-t-Butylbenzaldehyde (448)

For the synthesis of 2-(3-t-butylbenzylidene)cyclopentanone oxime O-acetate, 3-t-butylbenzaldehyde (448) is required The synthesis of 3-t-butylbenzaldehyde is based on Vogel's synthesis of 3-bromotoluene [292] 4-t-Butylaniline (444) was first converted into the corresponding acetamide (445) Synthesis of compound (445) was verified by the presence of a carbonyl group in the IR spectrum and the relevant peaks in the NMR Bromination, followed by removal of the acetyl group led to 4-t-butyl-2-bromoaniline (446) The absence of the carbonyl peak in the IR spectrum and the presence of the relevant peaks in the NMR confirmed its synthesis

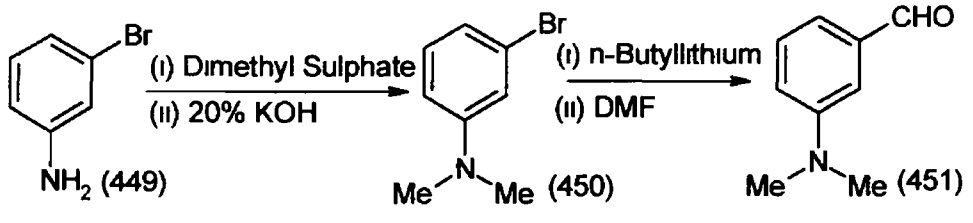
Vogel's deamination method involved a cumbersome steam distillation, which led to poor yields, so an alternative method was used Removal of the amino group was carried out by the synthetic method of Doyle and co-workers for the reductive deamination of arylamines by alkyl nitrites in DMF [293] The structure of 3-t-butylbromobenzene (447) was confirmed by IR and NMR data, specifically the

absence of the amino group The bromobenzene (447) was then converted to 3-t-butylbenzaldehyde (448) by the method used by Mallory and co-workers [137] The structure was verified by the presence of the relevant peaks in both the IR and NMR spectra, specifically the presence of the carbonyl peak in the IR and ^{13}C-NMR spectra



3 4 3 Synthesis 3-Dimethylaminobenzaldehyde (451)

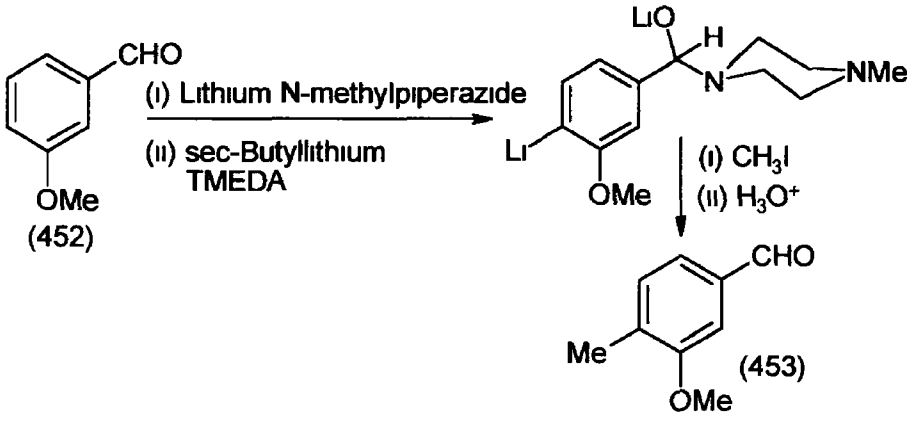
For the synthesis of 2-(3-dimethylaminobenzylidene)cyclopentanone oxime O-acetate, 3-dimethylaminobenzaldehyde (451) is required 3-Bromoaniline (449) was converted to 3-dimethylaminobromobenzene (450) by the method of Nair and co-workers [294] The presence of a singlet peak at δ 2 80ppm in the ^1H-NMR showed that (450) had been synthesised successfully The bromobenzene (450) was then converted to 3-dimethylaminobenzaldehyde (451) by the method used by Mallory and co-workers [137] Both the IR and the NMR spectra confirmed the structure of



(466), specifically the presence of the carbonyl peak in the IR spectrum and the ^{13}C-NMR spectra

3 4 4 Synthesis of 3-Methoxy-4-Methylbenzaldehyde (453)

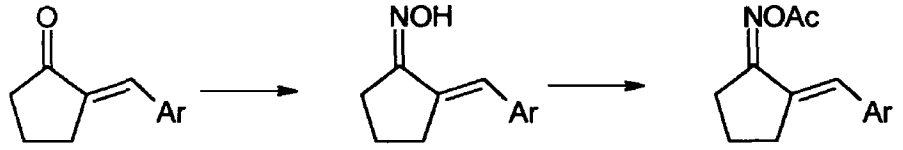
For the synthesis of 2-(3-methoxy-4-methylbenzylidene)cyclopentanone oxime O-acetate, 3-methoxy-4-methylbenzaldehyde (453) is required The synthesis of 3-methoxy-4-methylbenzaldehyde (453) was carried out following the method used by Comins and Brown for the metalation of amino alkoxides [295] N-Methylpiperazine was first reacted with N-butyllithium to form lithium N-methylpiperazide On cooling, 3-methoxybenzaldehyde (452) was added, followed by sec-butyllithium and N,N,N',N'-tetramethylethylenediamine After methylation and workup, 3-methoxy-4-methylbenzaldehyde (453) was isolated A peak at δ 2 13ppm in the ^{1}H-NMR spectrum and an extra peak at δ 17ppm in the ^{13}C-NMR spectrum shows the presence of the methyl group



3 5 Synthesis of Arylidenecyclopentanone Oxime O-Acetates

The photocyclisation has previously been investigated for aryl groups containing both electron-withdrawing and electron-donating substituents [282 283] Cyclisation had only been found with electron-donating methyl and methoxy substituents The scope of the reaction has now been extended to include other aryl groups including 4-hydroxy-, 4-acetoxy-, 4-amino-, 4-dimethylamino- and 2,5-

dimethoxyphenyl in addition to 3-substituted phenyls, designed to explore the regioselectivity of the cyclisation

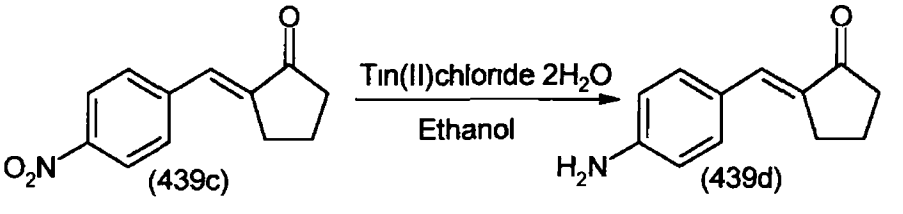


(439) (440) (441)

(439a-441a)	Ar = 4-C_6H_4OH	(441b)	Ar = 4-C_6H_4OAc
(439c)	Ar = 4-$C_6H_4NO_2$	(439d), (440d)	Ar = 4-$C_6H_4NH_2$
(439e-441e)	Ar = 4-$C_6H_4NMe_2$	(439f-441f)	Ar = 2,5-$C_6H_3(OMe)_2$
(439g-441g)	Ar = 1-Phenothiazinyl	(439h-441h)	Ar = Ph-CH=CH
(439i-441i)	Ar = 3-C_6H_4-t-Bu	(439j-441j)	Ar = 3-C_6H_4OH
(441k)	Ar = 3-C_6H_4OAc	(439l)	Ar = 3-$C_6H_4NO_2$
(439m), (440m)	Ar = 3-$C_6H_4NH_2$	(439n-441n)	Ar = 3-$C_6H_4NMe_2$
(439o-441o)	Ar = 3,4-$C_6H_3(OMe)_2$	(439p-441p)	Ar = 3-MeO-4-MeC_6H_3
(439q-441q)	Ar = 3,4-$C_6H_3Me_2$	(439r-441r)	Ar = 4-MeO-3-MeC_6H_3

The benzylidene cyclopentanones (439a,c,e-j,l,n-r) were synthesised from their corresponding aldehydes following the general method shown in scheme 17 The structures of the cyclopentanones were verified by the presence of the relevant peaks in both the IR and NMR spectra, specifically the presence of the carbonyl peak in both the IR and ^{13}C-NMR spectra

Using the method for the reduction of nitro compounds to amines developed by Bellamy and Ou,[296] the 4-nitro compound (439c) was reduced by tin chloride dihydrate to the amino compound (439d) confirmed by absorptions at 3448 and

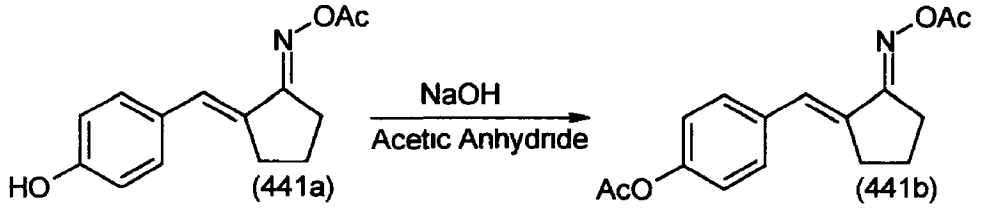


3350 cm^{-1} in the IR spectrum and the presence of the amino protons at δ 3 91 ppm in the ^{1}H-NMR spectrum 2-(3-Aminobenzylidene)cyclopentanone (439m) was synthesised by a similar method

All benzylidene cyclopentanones oximes (440a,d-j,m-r) were synthesised from their corresponding benzylidene cyclopentanones following the general method shown in scheme 17 The structures of the cyclopentanones were verified by the presence of the relevant peaks in both the IR and NMR spectra, specifically the presence of the broad NOH peak in the IR spectrum and the absence of the carbonyl peak in the ^{13}C-NMR spectrum

All benzylidene cyclopentanones oxime O-acetates (441a,d-j,m-r) were synthesised from their corresponding benzylidene cyclopentanones oximes (440a,d-j,m-r) following the general method shown in scheme 17 The structures of the cyclopentanone oxime O-acetates were verified by the presence of the relevant peaks in both the IR and NMR spectra, specifically the presence of the carbonyl peak in both the IR and ^{13}C-NMR spectra

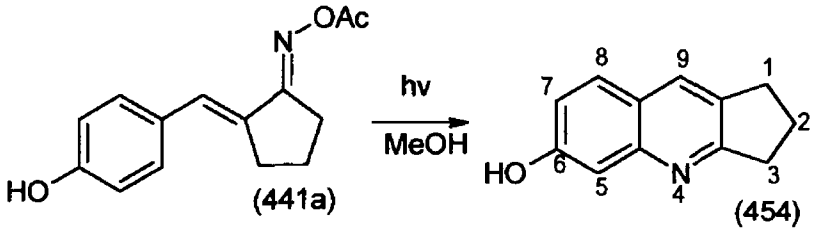
2-(4-Acetoxybenzylidene)cyclopentanone oxime O-acetate (441b) was synthesised by acetylation of (441a) by the synthetic method for the conversion of phenols to acetates shown in Vogel [292] The ^{1}H-NMR spectrum of the isolated product (441b) shows the presence of two acetyl groups The 3-acetoxy compound (441k) was synthesised from (441j) by a similar method



3 6 Photochemistry of 2-(4-Hydroxybenzylidene)cyclopentanone Oxime O-Acetate (441a)

On photolysis of (441a) in methanol for a short period, a number of new spots appeared on TLC An investigation by Austin[282] into the photoisomerisation of 2-benzylidenecyclopentanone oxime O-allyl ether (416) on irradiation in ethyl

acetate, resulted in a photostationary state of four geometrical isomers on prolonged irradiation The allyl group remained intact throughout (scheme 15) Isolation and charactensation by NOE techniques revealed the four different isomers The new spots on the TLC were therefore believed to be the various geometrical isomers of (441a) and isolation of each isomer was not carried out On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted



Isolation and charactensation of the sole photoproduct showed it to be the previously unreported heterocycle, 6-hydroxy-2,3-dihydro-1H-cyclopenta[b]-quinoline (454)

The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (454), with three signals in the range δ 28-40ppm corresponding to the three-methylene carbons C-1, C-2 and C-3 The nine signals appearing in the range δ 115-173ppm correspond to the nine aromatic carbons present

The ^{1}H-NMR spectrum of the photoproduct is also consistent with the proposed structure (454) It shows two signals in the range δ 2 09-3 01ppm, a two-hydrogen multiplet at δ 2 09ppm corresponding to the central methylene group at C-2 and a four-hydrogen multiplet at δ 2 93-3 01ppm corresponding to the methylene groups at C-1 and C-3 Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton A doublet of doublets, at δ 7 00ppm (J_1=8 8 Hz, ortho coupled, J_2=2 2 Hz, meta coupled), corresponds to the proton at C-7 A doublet at δ 7 24ppm (J=2 2 Hz, meta coupled) corresponds to the proton at C-5 A doublet at δ 7 50ppm (J=8 8 Hz, ortho coupled)

may be assigned to the proton at C-8 A singlet at δ 7 73ppm corresponds to the proton at C-9 A broad signal appeared at δ 9 65ppm, and integrated for one proton, corresponding to the hydroxy group

The COSY spectrum of the photoproduct is also consistent with the proposed structure (454) The proton at C-7 is coupled to the protons at C-5 and C-8 The proton at C-5 is coupled to the proton at C-7 as is the proton at C-8 The proton at C-9 shows no coupling interaction

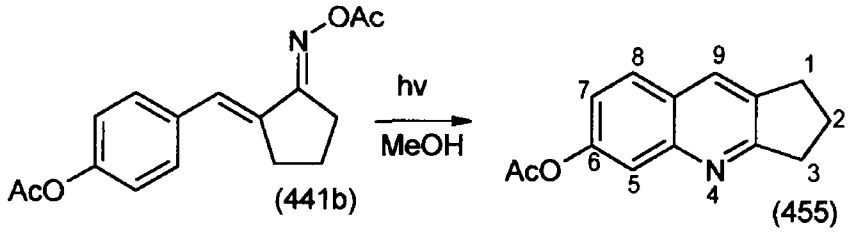
As there is only one possible photocyclisation position on the aromatic ring of (470) in the above reaction, it is clear from the spectra that the structure of the isolated product is the quinoline (454)

3 7 Photochemistry of 2-(4-Acetoxybenzylidene)cyclopentanone Oxime O-Acetate (441b)

On photolysis of (441b) in methanol for a short period, a number of new spots appeared on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted

Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 6-acetoxy-2,3-dihydro-1H-cyclopenta[b]-quinoline (455)

The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (455), with four signals in the range δ 21-35ppm corresponding to the three methylene carbons C-1, C-2, C-3 and the acetyl carbon Nine signals appear in the range δ 120-169ppm corresponding to the nine aromatic carbons present A signal at 170ppm corresponds to the carbonyl carbon



(441b) (455)

As required for the photoproduct the ^{1}H-NMR spectrum shows four signals in the range δ 2 13-3 08ppm A two-hydrogen multiplet at δ 2 13ppm corresponding to the central methylene group at C-2 a three-hydrogen singlet at δ 2 28ppm corresponding to the methyl of the acetate group and a two-hydrogen triplet at 2 93pm and a two-hydrogen triplet at δ 3 08ppm corresponding to the methylene groups at C-1 and C-3 respectively Three signals appeared in the aromatic region of the spectrum A doublet of doublets, at δ 7 00ppm (J_1=8 8 Hz, ortho coupled, J_2=2 4 Hz, meta coupled), corresponds to the proton at C-7 Multiplets at δ 7 64-7 66ppm corresponds to the protons at C-5 and C-8 and a singlet at δ 7 81ppm corresponds to the proton at C-9

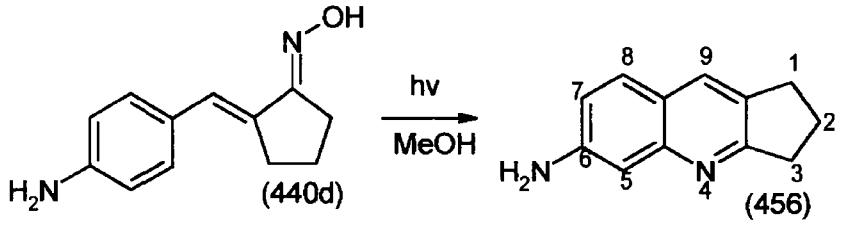
The COSY spectrum of the photoproduct is also consistent with the proposed structure (455) The proton at C-7 is coupled to the protons at C-5 and C-8 The proton at C-5 is coupled to the proton at C-7, as is the proton at C-8 The proton at C-9 shows no coupling interaction

As there is only one possible photocyclisation position on the aromatic ring of (441b) in the above reaction, it is clear from the spectra that the structure of the isolated product is the quinoline (455)

3 8 Photochemistry of 2-(4-Aminobenzylidene)cyclopentanone Oxime (440d)

Another electron-donating substituent, which could facilitate the reaction, is the amino group Conversion to the oxime O-acetate proved unsuccessful, with acetylation occurring preferentially at the amino group Olsen had previously reported[237,238] the photocyclisation of oximes to quinolines and therefore photocyclisation of the 2-(4-aminobenzylidene)cyclopentanone oxime (440d) was attempted

On photolysis of (440d) in methanol for a short period, a number of new spots appeared on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted



Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 6-amino-2,3-dihydro-1H-cyclopenta[b]quinoline (456)

The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (456), with three signals in the range δ 23-32ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Nine signals appear in the range δ 100-153ppm corresponding to the nine aromatic carbons present

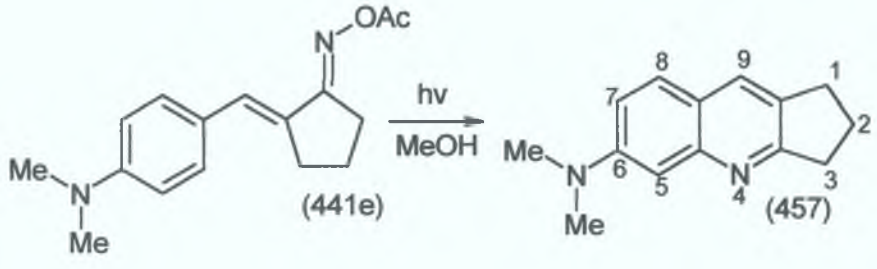
As required for the photoproduct the ^{1}H-NMR spectrum shows three signals in the range δ 2 11-3 28ppm A two-hydrogen multiplet at δ 2 15ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 3 02 and 3 26ppm correspond to the methylene groups at C-1 and C-3 and a broad signal, appearing at δ 4 18ppm and integrating for two protons, corresponds to the amino group Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton A doublet of doublets, at δ 6 89ppm (J_1=8 5 Hz, ortho coupled, J_2=2 3 Hz, meta coupled), corresponds to the proton at C-7 A singlet at δ 7 36ppm, corresponds to the proton at C-9 A doublet at δ 7 50ppm (J=8 5 Hz, ortho coupled) corresponds to the proton at C-8 and a doublet at δ 7 80ppm (J=2 3 Hz, meta coupled) may be assigned to the proton at C-5

The COSY spectrum of the photoproduct is consistent with the proposed structure (456) The proton at C-7 is coupled to the protons at C-5 and C-8 The protons at C-5 and C-8 are coupled to the proton at C-7 and the proton at C-9 shows no coupling interaction

As there is only one possible photocyclisation position on the aromatic ring of (440d) in the above reaction, it is clear from the spectra that the structure of the isolated product is the quinoline (456)

3.9 Photochemistry of 2-(4-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441e)

The dimethylamino group is also strongly electron-donating and was therefore investigated. On photolysis of (441e) in methanol for a short period, three new spots appeared on TLC. On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed. When TLC showed no further change the reaction was halted. Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 6-dimethylamino-2,3-dihydro-1H-cyclopenta[b]quinoline (457).



The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (457), with three signals in the range δ 22-34ppm corresponding to the three methylene carbons C-1, C-2 and C-3. One signal at δ 39.60ppm corresponds to the carbon of the dimethylamino group and nine signals appearing in the range δ 106-167ppm correspond to the nine aromatic carbons present.

As required for the photoproduct the ^{1}H-NMR spectrum shows four signals in the range δ 2.09-3.04ppm. A two-hydrogen multiplet at δ 2.09ppm corresponds to the central methylene group at C-2. A two-hydrogen triplet at δ 2.94ppm corresponds to one of the methylene groups at either C-1 or C-3, and an eight-hydrogen multiplet in the range 2.99-3.04ppm corresponds to the other methylene group and the dimethylamino group. Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton. A doublet of doublets, at δ 7.01ppm (J_1=9.2 Hz, ortho coupled; J_2=2.6 Hz, meta coupled), corresponds to the proton at C-7. A singlet at δ 7.07ppm (J=2.6 Hz, meta coupled),

corresponds to the proton at C-5 A doublet at δ 7 49ppm (J=9 2 Hz, ortho coupled) corresponds to the proton at C-8 and a singlet at δ 7 65ppm corresponds to the proton at C-9

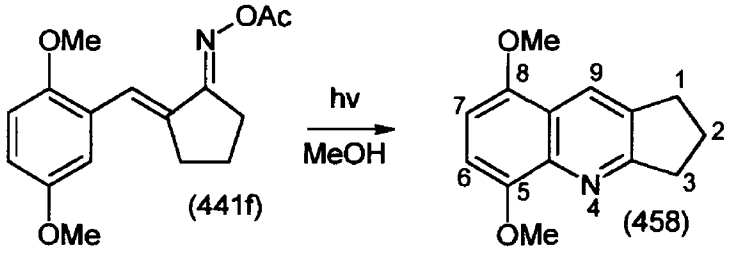
The COSY spectrum of the photoproduct is also consistent with the proposed structure (457) The proton at C-7 is coupled to the protons at C-5 and C-8 The proton at C-5 is coupled to the proton at C-7 as is the proton at C-8 The proton at C-9 shows no coupling interaction

As there is only one possible photocyclisation position on the aromatic ring of (441e) in the above reaction, it is clear from the spectra that the structure of the isolated product is the quinoline (457)

3 10 Photochemistry of 2-(2,5-Dimethoxybenzylidene)cyclopentanone Oxime O-Acetate (441f)

So far only monosubstituted aryl compounds have been investigated It was therefore of interest to extend the scope of the reaction by investigating a number of disubstituted aryl compounds The first to be investigated was 2-(2,5-dimethoxybenzylidene)cyclopentanone oxime O-acetate (441f)

On photolysis of (441f) in methanol for a short period, a number of new spots appeared on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation and characterisation of the sole photoproduct showed it to be the previously reported[297] heterocycle, 5,8-dimethoxy-2,3-dihydro-1H-cyclopenta[b]quinoline (458)



The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (458), with three signals in the range δ 22-34ppm corresponding to the three methylene carbons C-1, C-2 and C-3. Two signals at δ 54.76ppm and 54.89ppm corresponding to the carbons of the methoxy groups and nine signals appear in the range δ 101-167ppm corresponding to the nine aromatic carbons present.

As required for the photoproduct the ^{1}H-NMR spectrum shows five signals in the range δ 2.11-3.94ppm. A two-hydrogen multiplet at δ 2.11ppm corresponds to the central methylene group at C-2. Two-hydrogen triplets at δ 3.00 and 3.13ppm correspond to the methylene groups at C-1 and C-3, and two three-hydrogen singlets at δ 3.86 and 3.94ppm correspond to the two methoxy groups. Three well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton. Two doublets, one at δ 6.61ppm (J=8.8 Hz, ortho coupled) and the other at δ 6.77ppm (J=8.8 Hz, ortho coupled), corresponds to the hydrogens at C-6 and C-7. A singlet at δ 8.22ppm correspond to the proton at C-9.

The COSY spectrum for the photoproduct shows a coupling interaction for the protons at C-6 and C-7, while there was no coupling interaction for the proton at C-9.

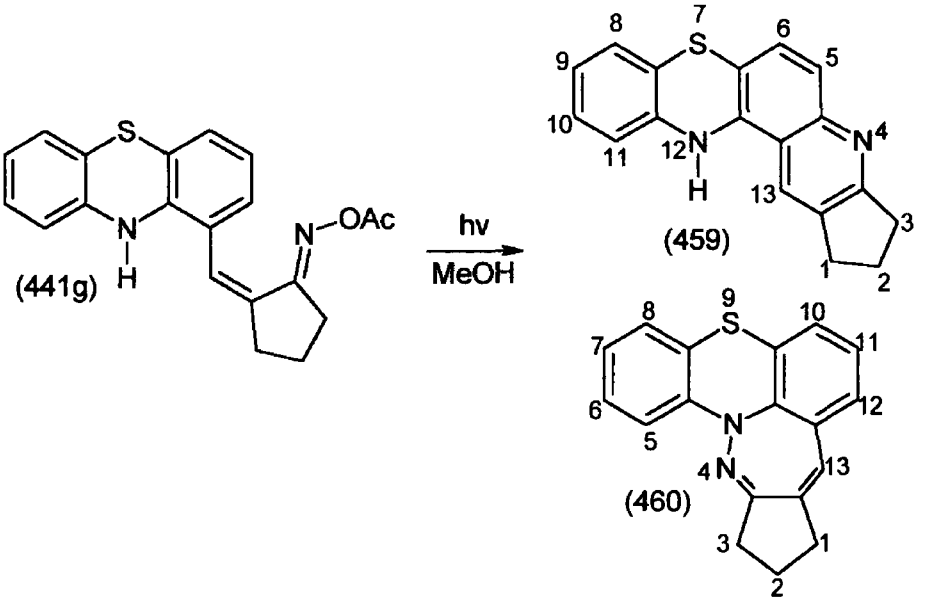
As there is only one possible photocyclisation position on the aromatic ring of (441f) in the above reaction, it is clear from the spectra that the structure of the isolated product is the quinoline (458).

3.11 Photochemistry of 2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone Oxime O-Acetate (441g)

Phenothiazine and its derivatives are widely used in the treatment of disease and it was therefore of interest to synthesise a quinoline derivative. On photolysis of (441g) in methanol for a short period, a number of new spots appeared on TLC. On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed. When TLC showed no further change the reaction was halted. Isolation

and charactensation of the sole photoproduct showed it to be the previously unreported heterocycle, 1,2,3,12-tetrahydrocyclopenta[5,6]pyrido[3,2-a]-phenothiazine (459)

The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (459), with three signals in the range δ 15-29ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Fifteen signals appearing in the range δ 106-137ppm correspond to the fifteen aromatic carbons present



As required for the photoproduct the ^{1}H-NMR spectrum shows three signals in the range δ 2 07-3 22ppm A two-hydrogen multiplet at δ 2 07ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 37 and 3 22ppm correspond to the methylene groups at C-1 and C-3 Five signals appear in the aromatic region of the spectrum, integrating for eight protons overall A singlet at δ 6 31ppm, which integrates for one proton, can be assigned to the proton attached to the nitrogen of the phenothiazine nng A doublet of doublets at δ 6 62ppm (J_1=7 2 Hz, ortho coupled, J_2=0 8 Hz, meta coupled), which integrates for one proton, corresponds to either the proton at C-8 or C-11 Two multiplets in the range δ 6 85-6 91 and 7 00-7 05ppm integrate for two and three protons

respectively A one proton doublet at δ 7 24ppm (J=8 8 Hz, ortho coupled), can be assigned to either the proton at C-5 or C-6

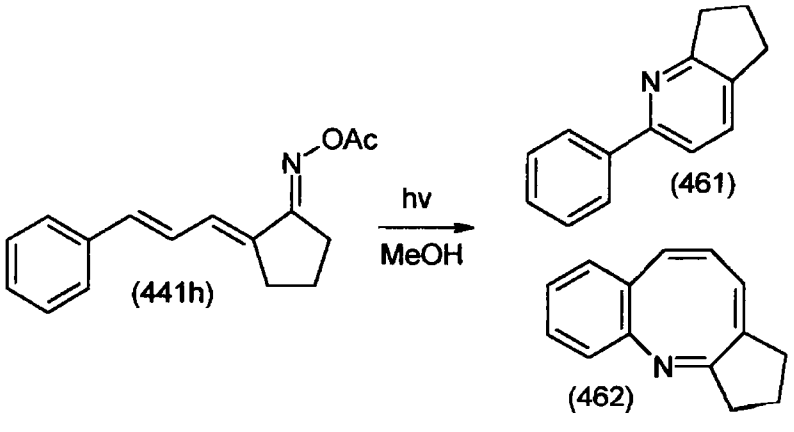
The IR spectrum shows an absorption at 3453 cm^{-1} which corresponds to the NH of the phenothiazine system

That the structure of the isolated quinoline is not (460) is evident from this information Compound (460) would be expected to display a different pattern in the ^{1}H-NMR spectrum, specifically an aliphatic CH_2 being split by a vinylic proton Also the IR spectrum shows the presence of a NH stretch with eliminates the possibility of the photoproduct being (460)

3 12 Photochemistry 2-(3-Phenylallylidene)cyclopentanone Oxime O-Acetate (441h)

Extending the scope of the cyclisation reaction 2-(3-phenylallylidene)-cyclopentanone oxime O-acetate (441h) was investigated Compound (441h) contains an additional double bond in the side chain and in principle either 6π or 8π cyclisation can occur to yield the pyndine (461) or the benzo[b]cyclopenta-[g]azocine (462) respectively

On photolysis of (441h) in methanol for a short period, a number of new spots appeared on TLC On further irradiation one product was formed in excess of the others When TLC showed no further change the reaction was halted Isolation and charactensation of this photoproduct showed it to be the previously reported[298] heterocycle, 2-phenyl-6,7-dihydro-5H-cyclopenta[b]pyndine (461)



The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (461), with three signals in the range δ 23-35ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Nine signals appearing in the range δ 118-166ppm correspond to the eleven aromatic carbons present

As required for the photoproduct the ^{1}H-NMR spectrum shows three signals in the range δ 2 10-3 02ppm A two-hydrogen multiplet at δ 2 10ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 89 and 3 02ppm correspond to the methylene groups at C-1 and C-3 As required for the photoproduct there are seven protons in the aromatic region A multiplet at δ 7 30-7 32 integrated for one proton A multiplet between δ 7 36-7 39 integrated for three protons A doublet at δ 7 48ppm (J=7 6 Hz, ortho coupled), integrated for one proton, and a multiplet between δ 7 86-7 88 integrated for two protons

The ^{13}C-NMR spectrum of (462) would in contrast also be expected to show a total of eleven aromatic and vinylic signals and therefore the presence of (462) can be eliminated In addition comparison of the previously reported[298] NMR data and a comparison of the melting point of the photoproduct with that for (461), synthesised by a different route, confirms the structural assignment

3 13 Regioselective Considerations

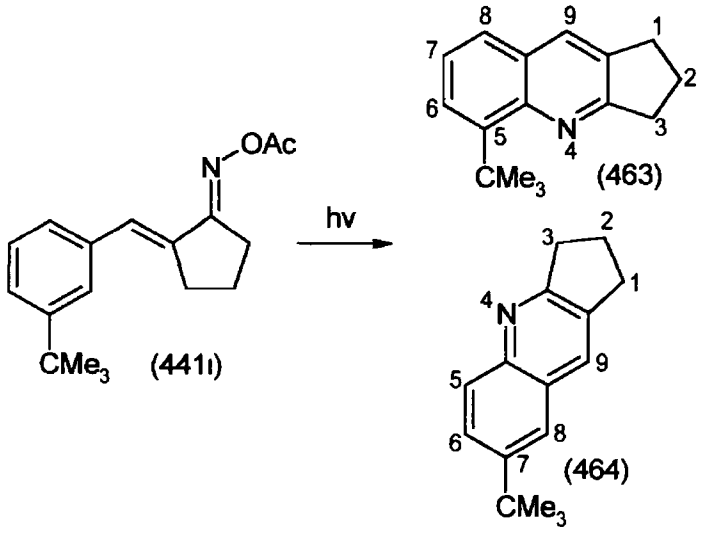
Some initial investigations into the regioselectivity of these cyclisation reactions were carried out by Egan,[283] who showed that substitution at the 3-position of the aromatic ring leads to highly regioselective outcomes The range of the regioselective reaction has been extended by substitution in the aryl 3-position with a number of electron-donating groups including substitution by t-butyl, hydroxy, acetoxy, amino and dimethylamino groups The regioselectivity of the cyclisation reaction has also been investigated with a number of disubstituted aryl groups

3 13 1 Photochemistry of 2-(3-t-Butylbenzylidene)cyclopentanone Oxime O-Acetate (441i)

An investigation into the effect of replacing the 3-methyl group of (431a) with the bulkier t-butyl group and its steric effect on the photocyclisation has been carried out On irradiation the O-acetate (441i) could possibly yield two products, (463) or (464), depending on whether cyclisation occurs at the 2- or 6-positions on the aromatic ring

Photolysis of (441i) in methanol for a short period led to four new spots appeanng on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 5-t-butyl-2,3-dihydro-1H-cyclopenta[b]quinoline (463)

The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the structures (463) or (464), with five signals in the range δ 22-34ppm corresponding to the three methylene carbons C-1, C-2 and C-3, the quaternary carbon of the t-butyl group and the three equivalent methyl groups Nine signals appear in the range δ 123-164ppm corresponding to the nine aromatic carbons present



The ^{1}H-NMR spectrum shows five signals in the range δ 1 53-2 96ppm A nine-hydrogen singlet at δ 1 53ppm corresponds to the t-butyl group A two-hydrogen multiplet at δ 2 03ppm corresponds to the central methylene group at C-2 A four-hydrogen multiplet at δ 2 89-2 96ppm corresponds to the methylene groups at C-1 and C-3 Four well-resolved signals appear in the aromatic region of the spectrum, each of which integrates for one proton Analysis of the aromatic patterns allowed a distinction between (463) and (464) A triplet at δ 7 22 (J=7 6 Hz, ortho coupled) corresponds to the proton at C-7 in (463) Two doublets of doublets at 7 43 (J_1=7 6 Hz, ortho coupled, J_2=1 3 Hz, meta coupled) and 7 50 (J_1=7 6 Hz, ortho coupled, J_2=1 3 Hz, meta coupled) correspond to the protons at C-6 and C-8 in (463) and a singlet at 7 80ppm corresponds to the proton at C-9

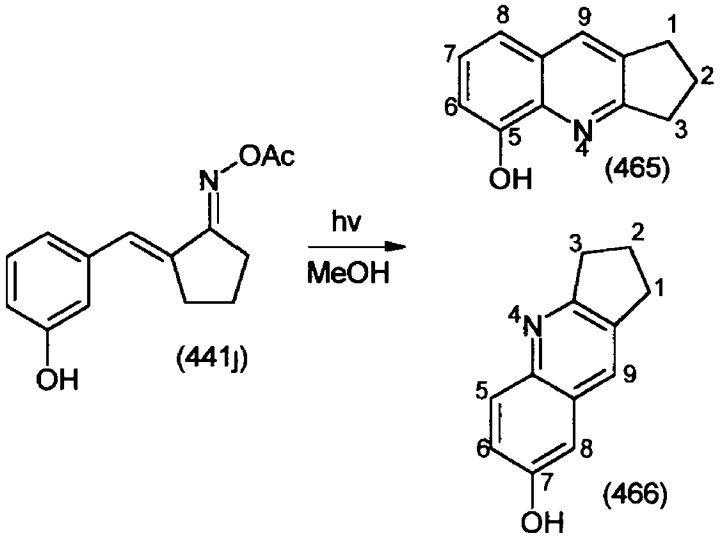
That the structure of the isolated photoproduct is not (464) is evident from this information Compound (464) would be expected to display a different pattern in the aromatic region of the proton spectrum, specifically a one proton doublet (ortho coupled) corresponding to the proton at C-5, a one proton doublet of doublets (ortho and meta coupled) corresponding to the proton at C-6, also a one proton doublet (meta coupled) and a one proton singlet corresponding to the protons at C-8 and C-9, respectively The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present and that the photoproduct is (463) rather than (464)

The COSY spectrum of the photoproduct is also consistent with the proposed structure for (463) The proton at C-7 is coupled to the protons at C-6 and C-8 The protons at C-6 and C-8 are also coupled to one another as well as the proton at C-7 The proton at C-9 shows no coupling interaction

3 13 2 Photochemistry of 2-(3-Hydroxybenzylidene)cyclopentanone Oxime O-Acetate (441j)

Continuing the investigation of the regioselectivity of the photocyclisation reaction, 2-(3-hydroxybenzylidene)cyclopentanone oxime O-acetate (441j) was synthesised On irradiation, the O-acetate (441j) could possibly yield two products (465) or (466)

On photolysis of (441j) in methanol for a short period, a number of new spots appeared on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 7-hydroxy-2,3-dihydro-1H-cyclopenta[b]quinoline (466)



The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the structures (465) or (466), with three signals in the range δ 23-34ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Nine signals appearing in the range δ 108-165ppm correspond to the nine aromatic carbons present

The ^{1}H-NMR spectrum shows three signals in the range δ 2 13-3 06ppm A two-hydrogen multiplet at δ 2 13ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 99 and 3 06ppm correspond to the methylene groups at C-1 and C-3 Four well-resolved signals appear in the aromatic region of the spectrum, each of which integrated for one proton Analysis of the aromatic patterns allowed a distinction between (465) and (466) A doublet at δ 6 99 (J=2 8 Hz, meta coupled) corresponds to the proton at C-8 of (466) A doublet of doublets at δ 7 15 (J_1=9 0 Hz, ortho coupled, J_2=2 8 Hz, meta coupled) corresponds to the

proton at C-6 of (466) A singlet at δ 7 69 corresponds to the proton at C-9 of (466) and a doublet at δ 7 83ppm (J=9 0 Hz, ortho coupled) corresponds to the proton at C-5 of (466) A broad signal appeared at δ 9 35ppm, which integrated for one proton and corresponds to the hydroxy group

That the structure of the isolated photoproduct is not (465) is clear from this information Compound (465) would be expected to display a different pattern in the aromatic region of the proton spectrum, specifically a one proton triplet (ortho coupled) corresponding to the proton at C-7, two one-proton doublet of doublets (ortho and meta coupled) corresponding to the protons at C-5 and C-8 and a one proton singlet corresponding to the proton at C-9 The aromatic signals for the photoproduct are well resolved and it is clearly evident that such a pattern is not present and that the photoproduct is (466) rather than (465)

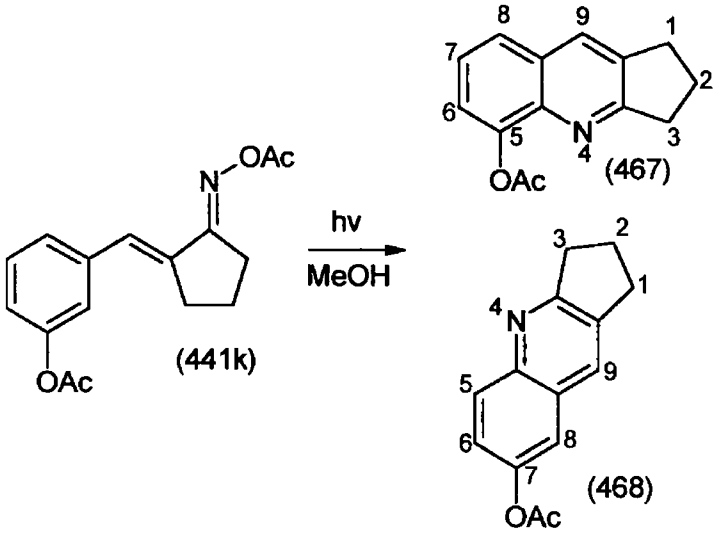
The COSY spectrum of the photoproduct is also consistent with the proposed structure (466) The proton at C-6 is coupled to the protons at C-5 and C-8 The proton at C-5 is coupled to the proton at C-6 as is the proton at C-8 The proton at C-9 shows no coupling interaction

3 13 3 Photochemistry of 2-(3-Acetoxybenzylidene)cyclopentanone Oxime O-Acetate (441k)

The regioselectivity of the acetoxy group was investigated next By replacing the hydroxy group of (441j) by an acetate group (441k) it was hoped that the electron donating potential of the hydroxy oxygen would be reduced so as to allow the photocyclisation to occur at the 2-position of the aryl system similar to the 3-methyl (431a) and 3-t-butyl aryl systems (441i) previously investigated On irradiation, the O-acetate (441k) could possibly yield two products (467) or (468)

Irradiation of (441k) in methanol for a short period, led to a number of new spots appearing on TLC On further irradiation, two of these became the major components of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation and charactensation of the first photoproduct showed it to be the

previously unreported heterocycle, 7-acetoxy-2,3-dihydro-1H-cyclopenta[b]-quinoline (468)



The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the proposed structures (467) or (468), with four signals in the range δ 20-34ppm corresponding to the three methylene carbons C-1, C-2, C-3 and the methyl carbon of the acetate group Nine signals appear in the range δ 117-167ppm corresponding to the nine aromatic carbons present A signal appears at 168ppm which corresponds to the carbonyl carbon of the acetate

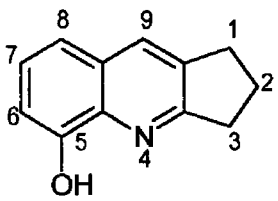
The ^{1}H-NMR spectrum shows four signals in the range δ 2 13-3 09ppm A two-hydrogen multiplet at δ 2 13ppm corresponds to the central methylene group at C-2 A three-hydrogen singlet at δ 2 27ppm corresponds to the methyl of the acetate group Two two-hydrogen triplets at δ 2 99ppm and δ 3 08ppm correspond to the methylene groups at C-1 and C-3 Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton Analysis of the aromatic patterns allowed a distinction between (467) and (468) A doublet of doublets at δ 7 27 (J_1=8 9 Hz, ortho coupled, J_2=2 5 Hz, meta coupled) corresponds to the proton at C-6 in (468) A doublet at δ 7 39 (J=2 5 Hz, meta coupled) corresponds to the proton at C-8 in (468) A singlet at δ 7 76 corresponds

to the proton at C-9 in (468) and a doublet at δ 7 94ppm (J=8 9 Hz, ortho coupled) corresponds to the proton at C-5 in (468)

That the structure of the isolated photoproduct is not (467) is evident from this information Compound (467) would be expected to display a different pattern in the aromatic region, specifically a one-proton triplet corresponding to the proton at C-7, two one-proton doublet of doublets corresponding to the protons at C-6 and C-8 and a one-proton singlet corresponding to the proton at C-9 The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present and that the photoproduct is (468) rather than (467)

The COSY spectrum of the photoproduct is consistent with the proposed structure (468) The proton at C-6 is coupled to the protons at C-5 and C-8 The proton at C-5 is coupled to the proton at C-6 as is the proton at C-8 The proton at C-9 shows no coupling interaction

Isolation and charactensation of the second photoproduct showed it to be the previously unreported heterocycle 5-hydroxy-2,3-dihydro-1H-cyclopenta[b]quinoline (465)



(465)

The IR spectrum of the photoproduct showed a broad OH signal at 3450 cm^{-1}

The ^{13}C-NMR spectrum of the photoproduct is consistent with the proposed structure (465), with three signals in the range δ 22-34ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Nine signals appear in the range δ 108-165ppm corresponding to the nine aromatic carbons present

The photoproduct the ^{1}H-NMR spectrum shows two signals in the range δ 2 12-3 05ppm A two-hydrogen multiplet at δ 2 12ppm corresponds to the central methylene group at C-2 A four-hydrogen multiplet in the range δ 2 73-3 05ppm

corresponds to the methylene groups at C-1 and C-3 Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton Two doublet of doublets at δ 7 01 (J_1=7 7 Hz, ortho coupled, J_2=1 1 Hz, meta coupled) and δ 7 15 (J_1=7 7 Hz, ortho coupled, J_2=1 1 Hz, meta coupled) correspond to the protons at C-6 and C-8 A triplet at δ 7 26 (J=7 7 Hz, ortho coupled) and a singlet at δ 7 77ppm correspond to the protons at C-7 and C-9 respectively

The COSY spectrum of the photoproduct is consistent with the proposed structure (465) The proton at C-7 is coupled to the protons at C-6 and C-8 The proton at C-6 is coupled to the protons at C-7 and C-8 The proton at C-8 is coupled to the proton at C-6 and C-7 The proton at C-9 shows no coupling interaction

The melting point of the photoproduct (465) was found to be 74-75 °C while those of the previously obtained 6- (454) and 7-hydroxyquinolines (466) were found to be 168-169 °C and 142-143 °C respectively That the structure of the isolated photoproduct is the 5-hydroxyquinoline (465) is evident from this information

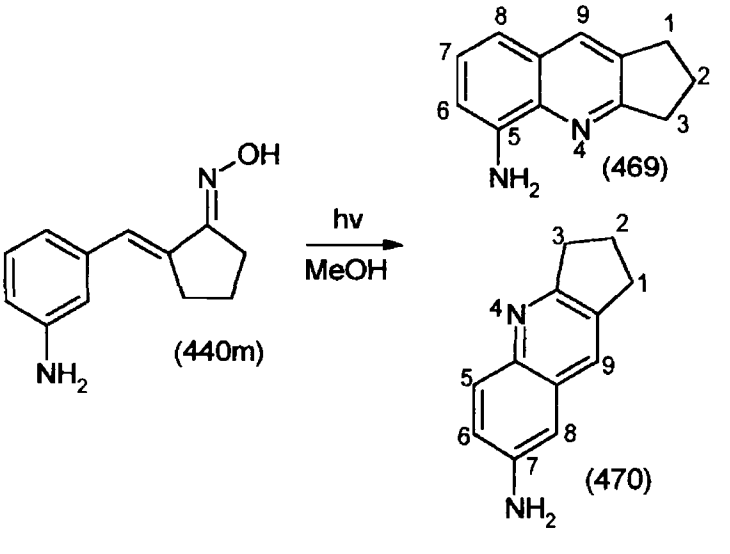
The photocyclisation of the acetoxy compound (441k) thus produced an interesting result, with two photoproducts being isolated, the acetoxy quinoline (468) and the hydroxy quinoline (465) The acetoxy quinoline (468) was formed on photocyclisation of the acetoxy compound (441k) at the 6-position of the aryl ring while the hydroxy quinoline (465) was formed on photocyclisation at the 2-position of the aryl system For the hydroxy quinoline (465) to be formed deacetylation must occur either before or after the cyclisation reaction Deacetylation prior to photocyclisation would yield the 3-hydroxy compound (441j) which cyclised at the 6-position of the aryl system Therefore for the hydroxy quinoline (465) to be formed, cyclisation must occur from the 3-acetoxy compound (441k) in the 2-position of the aryl system prior to elimination of the acetate group, aided by its proximity to the nitrogen Therefore the acetoxy group leads to reaction in both the 2- and 6-positions of the aryl system

3 13 4 Photochemistry of 2-(3-Aminobenzylidene)cyclopentanone Oxime (440m)

The regioselectivity of the amino group was also investigated As for the 4-amino compound, conversion of the oxime to the oxime O-acetate proved unsuccessful with acetylation occurring at the amino group Therefore photocyclisation of the 2-(4-aminobenzylidene)cyclopentanone oxime (440m) itself was attempted On irradiation, the oxime (440m) could possibly yield two photoproducts, (469) or (470)

Irradiation of (440m) in methanol for a short penod, led to four new spots appeanng on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 7-amino-2,3-dihydro-1H-cyclopenta[b]quinoline (470)

The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the proposed structures (469) or (470), with three signals in the range δ 24-34ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Nine signals appeanng in the range δ 108-164ppm correspond to the nine aromatic carbons present



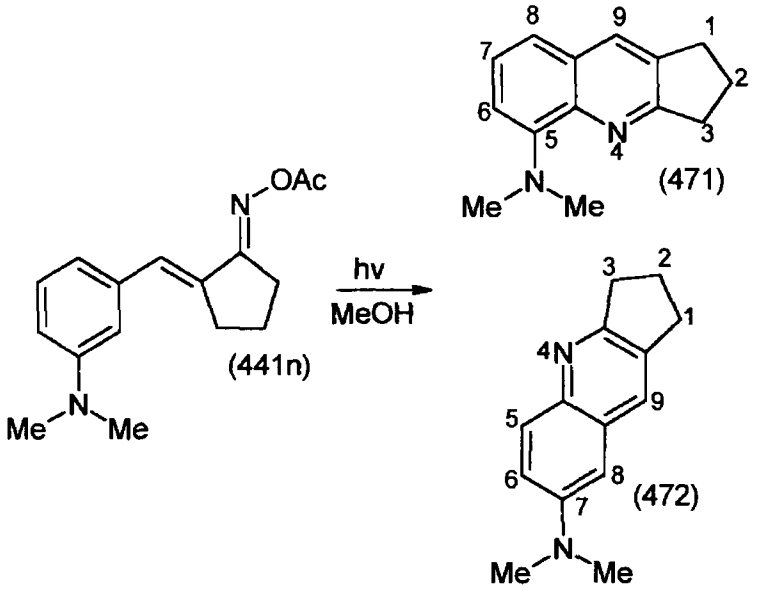
The ^{1}H-NMR spectrum shows three signals in the range δ 2 00-3 00ppm A two-hydrogen multiplet at δ 2 04ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 89 and 2 98ppm correspond to the methylene groups at C-1 and C-3 A broad signal appeared at δ 3 84ppm and corresponds to the amino group Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton and analysis of the aromatic patterns allowed a distinction between (469) and (470) A doublet at δ 6 71 (J=2 4 Hz, meta coupled) corresponds to the proton at C-8 in (470) A doublet of doublets at δ 6 93 (J_1=8 8 Hz, ortho coupled, J_2=2 4 Hz, meta coupled) corresponds to the proton at C-6 in (470) A singlet at δ 7 51 and a doublet at δ 7 80ppm (J=8 8 Hz, ortho coupled) correspond to the protons at C-9 and C-5 in (470) respectively

That the structure of the isolated photoproduct is not (469) is evident from this information as it would be expected to display a different pattern in the aromatic region, specifically a one proton triplet (ortho coupled) corresponding to the proton at C-7, two one-proton doublet of doublets (ortho and meta coupled) corresponding to the protons at C-6 and C-8 and a one proton singlet corresponding to the proton at C-9 The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present and that the photoproduct is (470) rather than (469)

The COSY spectrum of the photoproduct is consistent with the proposed structure (470) The proton at C-6 is coupled to the protons at C-5 and C-8 The proton at C-5 is coupled to the proton at C-6 The proton at C-8 is also coupled to the proton at C-6 The proton at C-9 shows no coupling interaction

3 13 5 Photochemistry of 2-(3-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441n)

The next substituent to be investigated was the dimethylamino group As the 4-dimethylamino compound (441e) had cyclised it was of interest to study the regioselectivity of the group On irradiation the O-acetate (441n) could possibly yield two products, (471) or (472)



On photolysis of (441n) in methanol for a short penod, four new spots appeared on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation and characterisation of the sole photoproduct showed it to be the previously unreported heterocycle, 7-dimethylamino-2,3-dihydro-1H-cyclopenta[b]quinoline (472)

The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the structures (471) or (472), with three signals in the range δ 24-35ppm corresponding to the three methylene carbons C-1, C-2 and C-3 One signal at δ 41 31ppm corresponds to the carbon of the dimethyl amino group and nine signals appear in the range δ 106-164ppm corresponding to the nine aromatic carbons present

The ^{1}H-NMR spectrum shows two multiplets in the range δ 2 10-3 05ppm A two-hydrogen multiplet at δ 2 10ppm corresponds to the central methylene group of (472) at C-2 A ten hydrogen multiplet at δ 2 94-3 05 corresponds to the methylene groups at C-1 and C-3, and the dimethylamino group Analysis of the aromatic patterns allowed a distinction between (471) and (472) Four well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton A doublet at δ 6 71ppm (J=2 6 Hz, meta coupled) corresponds to the proton

at C-8 in (472). A doublet of doublets at δ 7.21ppm (J_1=9.4 Hz, ortho coupled; J_2=2.6 Hz, meta coupled) corresponds to the proton at C-6 in (472). A singlet at δ 7.65ppm, corresponds to the proton at C-9 in (472) and a doublet at δ 7.80ppm (J=9.4 Hz, ortho coupled) may be assigned to the proton at C-5 in (472).

That the structure of the isolated photoproduct is not (471) is evident from this information. Compound (471) would be expected to display a different pattern in the aromatic region, specifically two one-proton doublet of doublets (ortho and meta coupled) corresponding to the protons at C-6 and C-8, a one proton triplet (ortho coupling) and a one proton singlet peak corresponding to the protons at C-7 and C-9 respectively. The aromatic signals for the photoproduct are well resolved and it is clear that the structure of the isolated quinoline is (472) rather than (471).

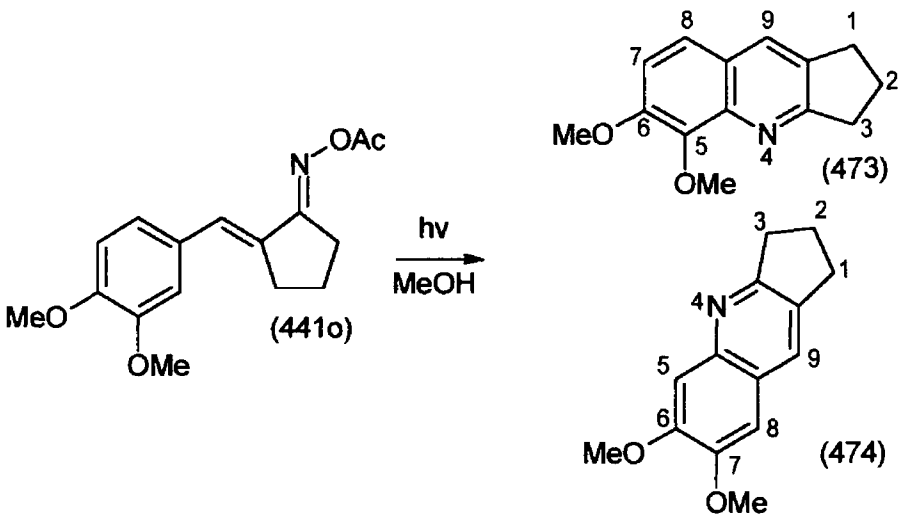
The COSY spectrum of the photoproduct is consistent with the proposed structure (472). The proton at C-6 is coupled to the protons at C-5 and C-8. The proton at C-5 is coupled to the proton at C-6. The proton at C-8 is also coupled to the proton at C-6. The proton at C-9 shows no coupling interaction.

3.13.6 Photochemistry of 2-(3,4-Dimethoxybenzylidene)cyclopentanone Oxime O-Acetate (441o)

Extending the scope of the regioselectivity investigations a number of disubstituted aryl systems that included a substituent in the 3-position were explored, the aim being to see whether the presence of an additional substituent at the 4-position might influence the directive effect of a single sustituent at the 3-position. The first compound examined was 2-(3,4-dimethoxybenzylidene)-cyclopentanone oxime O-acetate (441o). Egan's work[283] had shown that the monosubstituted 3-methoxy substituted aryl system (431b) cyclised para to the methoxy group and it was therefore of interest to see if the disubstituted system (441o) behaved similarly. The O-acetate (441o) could possibly yield two photocyclisation products, (473) or (474).

On photolysis of (441o) in methanol for a short period, four new spots appeared on TLC. On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products

formed When TLC showed no further change the reaction was halted Isolation and characterisation of the sole photoproduct showed it to be the previously reported[299] heterocycle, 6,7-dimethoxy-2,3-dihydro-1H-cyclopenta[b]quinoline (474)



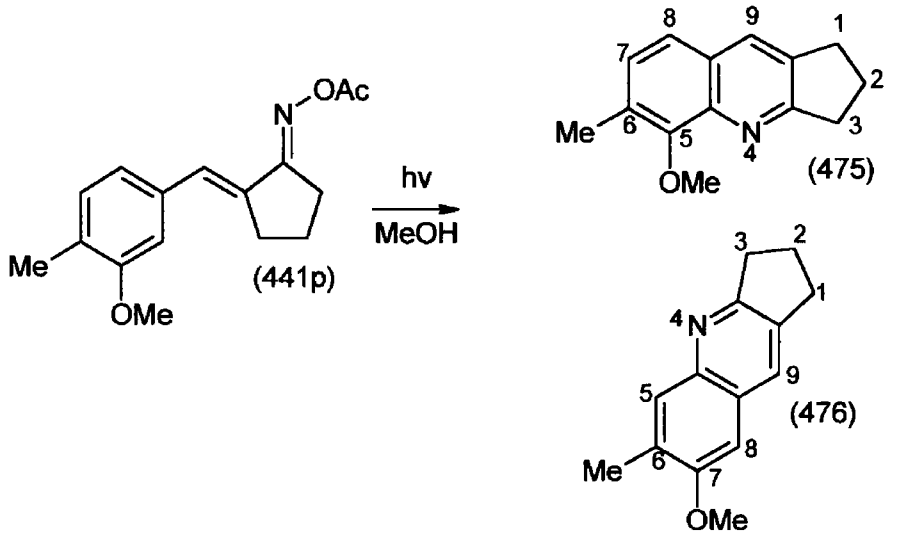
The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the structures (473) or (474), with three signals in the range δ 24-35ppm corresponding to the three methylene carbons C-1, C-2 and C-3 Two signals at δ 56 35ppm and 56 39ppm correspond to the carbons of the methoxy groups and nine signals appearing in the range δ 105-166ppm correspond to the nine aromatic carbons present

The ^{1}H-NMR spectrum shows three signals in the range δ 2 12-3 04ppm A two-hydrogen multiplet at δ 2 12ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 98 and 3 04ppm correspond to the methylene groups at C-1 and C-3 Two three-hydrogen singlets at δ 3 92 and 3 94ppm correspond to the two methoxy groups Analysis of the aromatic patterns allowed a distinction between (473) and (474) Three well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton Three singlet peaks at δ 6 92, 7 31 and 7 68ppm respectively correspond to the three protons at C-5, C-8 and C-9 in (474)

That the structure of the isolated photoproduct is not (473) is evident from this information Compound (473) would be expected to display a different pattern in the aromatic region, specifically two one-proton doublets, each showing ortho coupling and a singlet one proton peak The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present

3 13 7 Photochemistry of 2-(3-Methoxy-4-Methylbenzylidene)cyclopentanone Oxime O-Acetate (441p)

The next compound investigated was 2-(3-methoxy-4-methylbenzylidene)-cyclopentanone oxime O-acetate (441p) This system contains both methyl and methoxy groups and the effect of a 4-methyl group on the directive effect of a 3-methoxy group was examined The O-acetate (441p) could possibly yield two regioisomeric products, (475) or (476)



Initially, four new spots appeared on TLC, one of which became the sole component on prolonged irradiation When TLC showed no further change the reaction was halted Isolation by column chromatography and charactensation showed it to be the previously unreported heterocycle 7-methoxy-6-methyl-2,3-dihydro-1H-cyclopenta[b]quinoline (476)

The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the structures, (475) or (476) A signal at δ 17 47ppm corresponds to the methyl group, three signals in the range δ 24-35ppm correspond to the three methylene carbons C-1, C-2 and C-3 and a signal at δ 55 80ppm corresponds to the methoxy group Nine signals appear in the range δ 104-165ppm corresponding to the nine aromatic carbons present

The ^{1}H-NMR spectrum shows five signals in the range δ 2 10-3 84ppm A two-hydrogen multiplet at δ 2 10ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 3 00 and 3 03ppm correspond to the methylene groups at C-1 and C-3 and two three-hydrogen singlets at δ 2 31 and 3 84ppm correspond to the methyl and the methoxy groups Analysis of the aromatic pattern allowed a distinction between (475) and (476) Two well-resolved signals appeared in the aromatic region A singlet that integrated for one proton at δ 6 85ppm and a singlet that integrated for two protons at δ 7 68ppm correspond to the protons in (476) In DMSO as solvent three well-resolved signals appeared in the aromatic region of the spectrum each integrating for one proton These three singlets at δ 7 03, 7 55 and 7 74ppm, correspond to the protons at C-5, C-8 and C-9 of (476)

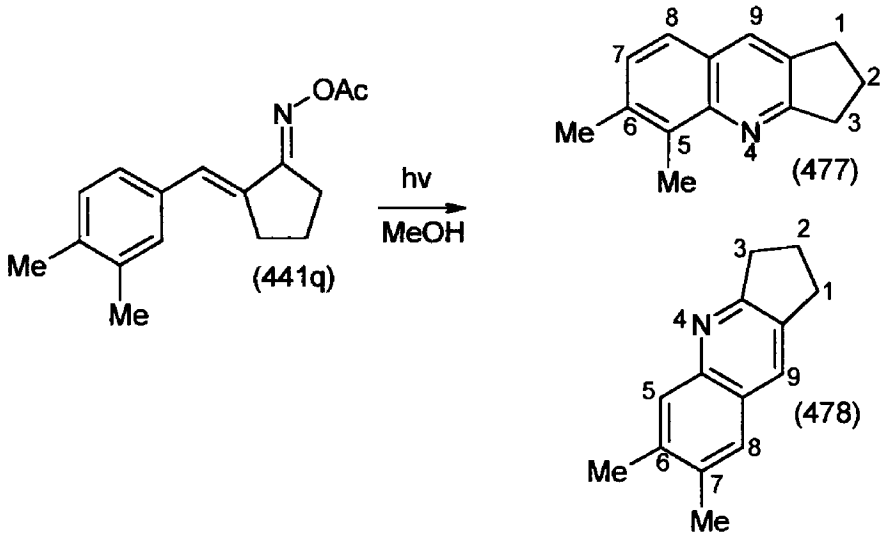
That the structure of the isolated photoproduct is not (475) is evident from this information as it would be expected to display a different pattern in the aromatic region, specifically two one proton doublets, with ortho coupling, and a one proton singlet The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present and that the photoproduct is (476) rather than (475)

3 13 8 Photochemistry of 2-(3,4-Dimethylbenzylidene)cyclopentanone Oxime O-Acetate (441q)

On cyclisation the monosubstituted 3-methyl substituted aryl system (431a), cyclised ortho to the methyl group and it was therefore of interest to see whether the presence of a 4-methyl group, as in (441q), would influence the directive effect

of the 3-methyl group The O-acetate (441q) could possibly undergo photocyclisation to yield two products, (477) or (478)

On photolysis of (441q) in methanol for a short period, four new spots appeared on TLC On further irradiation, one of these became the sole component of the mixture at the expense of the starting material and the other products formed When TLC showed no further change the reaction was halted Isolation by column chromatography and characterisation showed it to be the previously unreported heterocycle 5,6-dimethyl-2,3-dihydro-1H-cyclopenta[b]quinoline (477)



The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the proposed structures (477) or (478) Two signals, at δ 12 48 and 19 64ppm correspond to the two methyl groups Three signals in the range δ 22-34ppm correspond to the three methylene carbons C-1, C-2 and C-3 and nine signals appearing in the range δ 123-166ppm correspond to the nine aromatic carbons present

The ^{1}H-NMR spectrum shows five signals in the range δ 2 10-3 09ppm A two-hydrogen multiplet at δ 2 10ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 97 and 3 09ppm correspond to the methylene groups at C-1 and C-3, and two three-hydrogen singlets at δ 2 40 and 2 67ppm correspond to the two methyl groups Analysis of the aromatic patterns allowed a

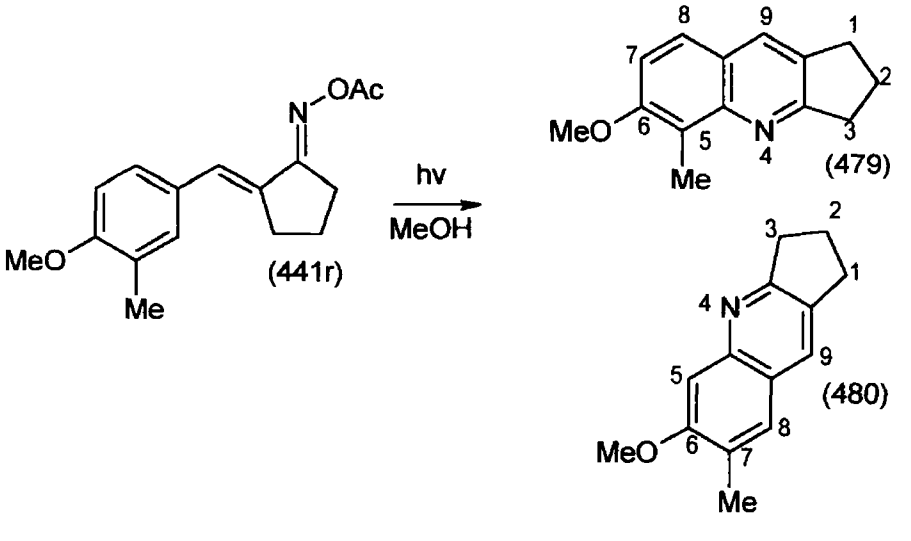
distinction between (477) and (478) Three well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton Two doublets, one at δ 7 17ppm (J=8 2 Hz, ortho coupled) and the other at δ 7 38ppm (J=8 2 Hz, ortho coupled), correspond to the hydrogens at C-7 and C-8 in (477) A singlet at δ 7 71ppm corresponds to the proton at C-9 in (477)

That the structure of the isolated quinoline is not (478) is evident from this information Compound (478) would be expected to display a different pattern in the aromatic region, specifically three one proton singlets The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present and that the photoproduct is (477) rather than (478)

The COSY spectrum shows a coupling reaction between the proton at C-7 and the proton at C-8 There is nothing coupled to the proton at C-9

3 13 9 Photochemistry of 2-(4-Methoxy-3-Methylbenzylidene)cyclopentanone Oxime O-Acetate (441r)

2-(4-Methoxy-3-methylbenzylidene)cyclopentanone oxime O-acetate (441r) was the next compound studied The presence of a 4-methoxy group on the directive effect of a 3-methyl group was examined On irradiation of the O-acetate (441r) two regioisomeric products were possible, (479) or (480)



Initially, three new spots appeared on TLC, one of which became the sole component on prolonged irradiation Isolation by column chromatography and characterisation showed it to be the previously unreported heterocycle 6-methoxy-5-methyl-2,3-dihydro-1H-cyclopenta[b]quinoline (479)

The ^{13}C-NMR spectrum of the photoproduct is consistent with either of the proposed structures (479) or (480) Five signals in the range δ 10-57ppm correspond to the three methylene carbons C-1, C-2 and C-3, and the methyl and methoxy groups Nine signals appear in the range δ 112-168ppm corresponding to the nine aromatic carbons present

The ^{1}H-NMR spectrum shows five signals in the range δ 2 12-3 90ppm A two-hydrogen multiplet at δ 2 12ppm corresponds to the central methylene group at C-2 Two-hydrogen triplets at δ 2 98 and 3 10ppm correspond to the methylene groups at C-1 and C-3, and two three-hydrogen singlets at δ 2 62 and 3 90ppm correspond to the methyl and the methoxy groups respectively Analysis of the aromatic patterns allowed a distinction between (479) and (480) Three well-resolved signals appeared in the aromatic region of the spectrum, each of which integrated for one proton Two doublets at δ 7 15 (J=9 0 Hz, ortho coupled) and 7 50 (J=9 0 Hz, ortho coupled) correspond to the protons at C-7 and C-8 in (479), and a singlet peak at 7 73ppm corresponds to the proton at C-9 in (479)

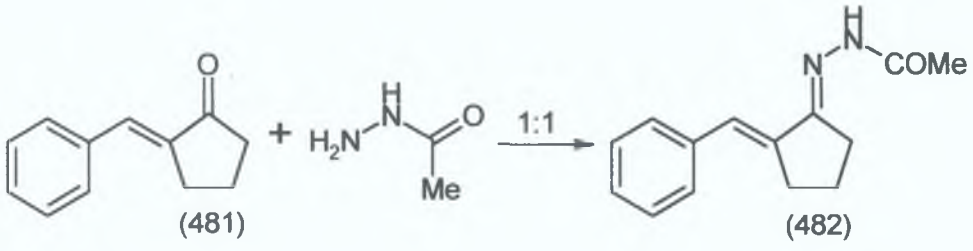
That the structure of the isolated quinoline is not (480) is evident from this information Compound (480) would be expected to display a different pattern in the aromatic region, specifically three singlets The aromatic signals for the photoproduct are well resolved and it is clear that such a pattern is not present and that the photoproduct is (479) rather than (480)

The COSY spectrum for (479) shows a coupling reaction between the protons at C-7 and C-8, while there is no coupling reaction for the proton at C-9

3 14 Nitrogen Based Leaving Groups

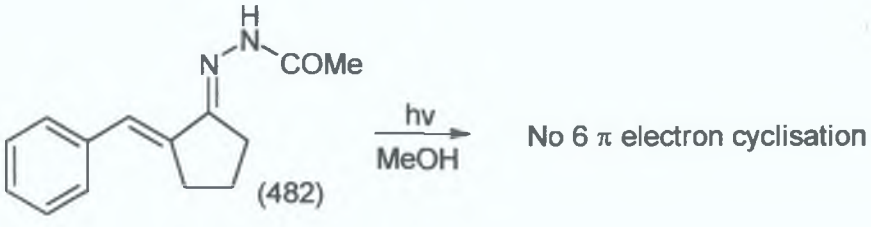
A brief investigation of an acetyl hydrazone and an azine was carried out to see whether there might be any analogy with the corresponding oxime derivatives already investigated 2-Benzylidenecyclopentanone acetylhydrazone (482) was

synthesised by the reaction of 2-benzylidenecyclopentanone (481) with one equivalent of acetyl hydrazide.



(481) (482)

On irradiation of (482) in methanol for a short period, three new spots appeared on TLC. On further irradiation, the number of spots remained the same with no product being formed in excess. The reaction was halted and on removal of the solvent a *light brown* powder was obtained. Characterisation of the powder by NMR, IR and melting point showed it to be starting material. No photocyclisation had taken place.



(482)

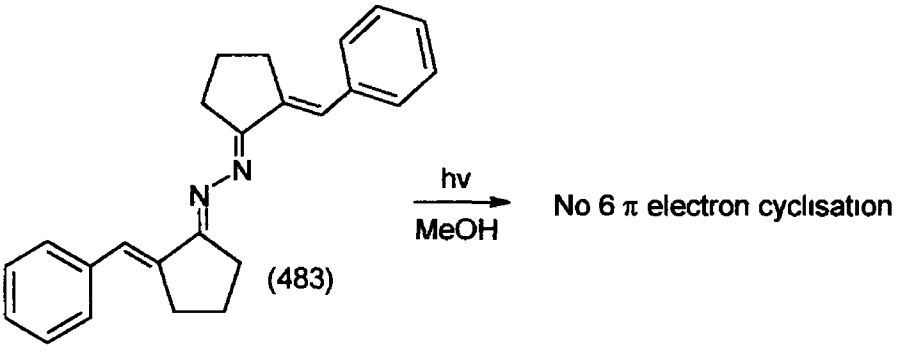
The three new spots, which appeared on TLC, are believed to be the three other geometric isomers of (482). While removing the solvent by rotary evaporation the solution was heated to ~80 °C. At this temperature the less stable geometric isomers may have thermally reverted to the most thermodynamically favoured isomer (482).

N,N'-Bis-(2-benzylidenecyclopentylidene)hydrazine (483) was synthesised from 2-benzylidenecyclopentanone (481) on reaction with hydrazine hydrate in a 2:1 ratio of ketone to hydrazine.

On irradiation of (483) in methanol for a short period, a number of new spots appeared on TLC. On further irradiation, the number of spots remained the same

with no product being formed in excess The reaction was halted and on removal of the solvent a light brown powder was obtained Characterisation of the powder by NMR, IR and melting point showed it to be starting material No photocyclisation had taken place

Again the new spots, which appeared on TLC, are believed to be geometric isomers of (483) On removing the solvent by rotary evaporation the solution was heated and the geometric isomers may have thermally reverted to the most thermodynamically favoured isomer (483)

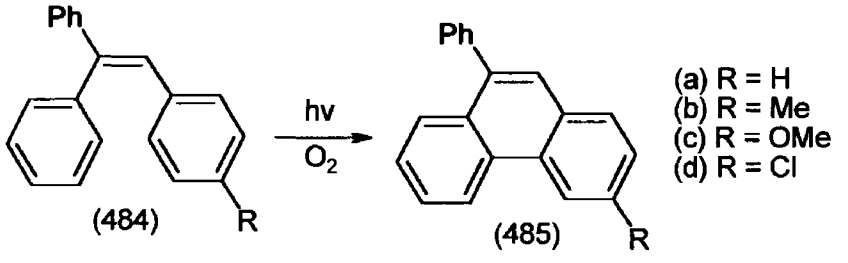


(483)

4. The Regiospecificity of the Photocyclisation Reaction

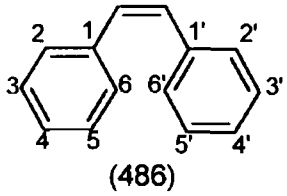
4 1 The Regiospecificity of the Photocyclisation Reaction

It has been previously reported that the efficiency and regiospecificity of photocyclisation reactions is often dependent on the substituents present on the cyclised species On irradiation of different substituted stilbenes (484a-d), Mallory and Mallory found that the quantum efficiency of cyclisation to the corresponding phenanthrenes (485a-d) was dependent on the substituent present [9] The formation of the chloro-substituted phenanthrene (485d) was the most inefficient of the reactions observed



The presence of the methyl and methoxy groups enhanced the reactivity The substituents which enhance photocyclisation are electron donating such as methyl and methoxy groups whereas electron withdrawing groups such as chlorine inhibit the reaction

In a publication by Muszkat and co-workers, electronic population analysis was applied to the photocyclisation reactions of substituted stilbenes [300] A series of stilbenes having different substituents was synthesised and irradiated in an attempt to correlate the experimental photocyclisation quantum yield with the theoretical excited state electronic overlap population for the atom pair forming

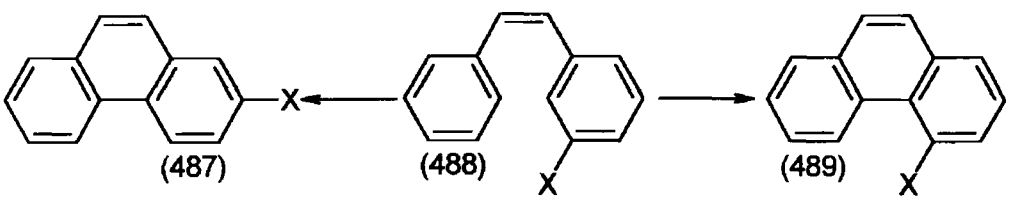


(486)

the new bond, $n^*_{6\,6'}$ in (486) The molecular geometries were theoretically derived using an energy minimalisation computer program (CONFI) The new bond forms between C centres 6 and 6'

The following conclusions were reached Both strong electron donating and attracting groups attached to the 4 (para) position in (486) significantly reduce the cyclisation quantum yield Strong electron attracting substituents such as nitro and acetyl groups in this position show the most prominent effects Substituents attached to the 3 and 5 (meta) positions produce twofold effects The strongly attracting nitro group stops the cyclisation altogether and a cyano group lowers the cyclisation yield, while a methoxy group in the 3 or 5 positions enhances the overall cyclisation yield by a factor of ~4 The expenmental results obtained correlated strongly with the theoretical results

The cyclisation of the meta substituted stilbenes (488a,b) were also investigated [300] The cyclisation of (488a) yielded the two phenanthrenes (487a) and (489a) in a 55 45 ratio The cyclisation of (488b) led to (487b) as the sole photoproduct

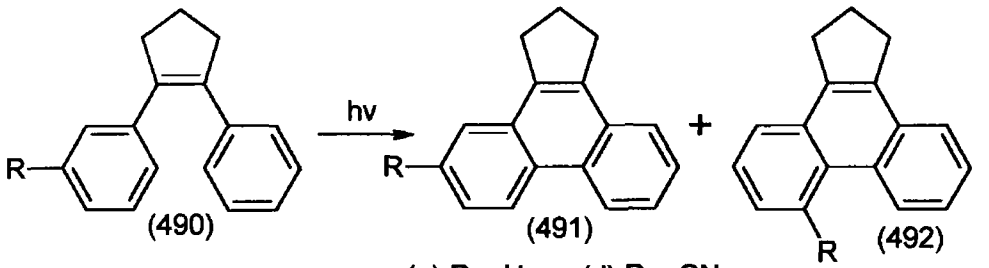


(487) (488) (489)

(a) X = OMe (b) X = CN
(c) X = Me (d) X = Cl
(e) X = CF_3

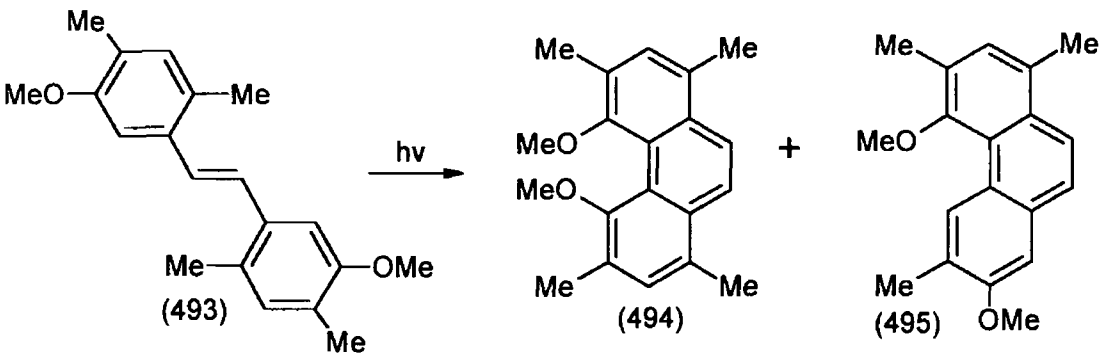
Mallory and co-workers investigated the isomer ratio of 2- and 4-substituted phenanthrenes produced by the photocyclisation of a series of meta-substituted stilbenes (488c-e) to assess the importance of steric effects on these photoreactions [9] In each case the less crowded 2-substituted product (487c-e), rather than the more crowded 4-substituted product (489c-e), was formed in excess

The influence of both meta and para substituents on the photocyclisation of 1,2-diphenylcyclopentenes (490a-f) in methanol has been investigated by Somers and Laarhoven [301 302] In almost all the cyclisation reactions the yield of (491) exceeded the yield of (492)

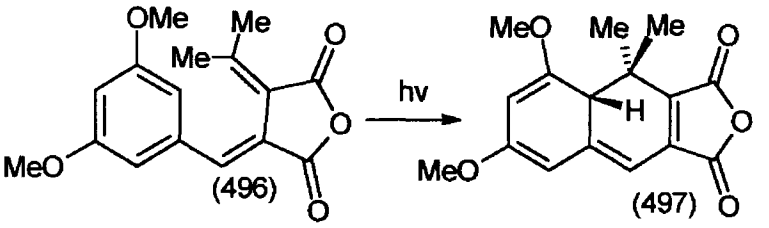


(a) R = H (d) R = CN
(b) R = Cl (e) R = Br
(c) R = Me (f) R = OMe

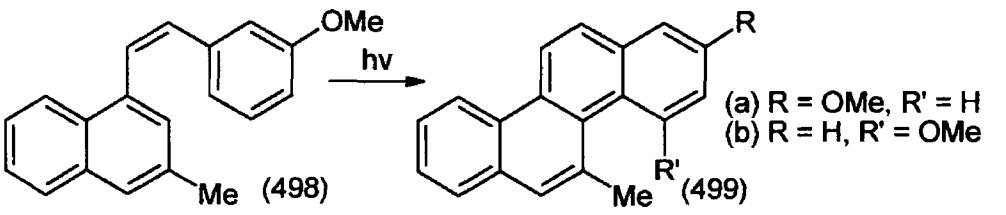
Newman and Chung have reported the synthesis of dimethoxytetramethylstilbene [62] 5,5'-Dimethoxy-2,2',4,4'-tetramethylstilbene (493) was irradiated in cyclohexane in the hope of obtaining the phenanthrene (494) Although (494) was formed in small amounts, the phenanthrene (495) was the main product of the reaction, formed by loss of the elements of methane rather than hydrogen The authors concluded that the low yield of (494) was due to the fact that on cyclisation two methoxy groups would be sited at the 4 and 5 positions of (494), each also being buttressed by the adjacent methyl groups resulting in considerable steric crowding Cyclisation to yield (495) however would involve far less unfavourable steric interactions



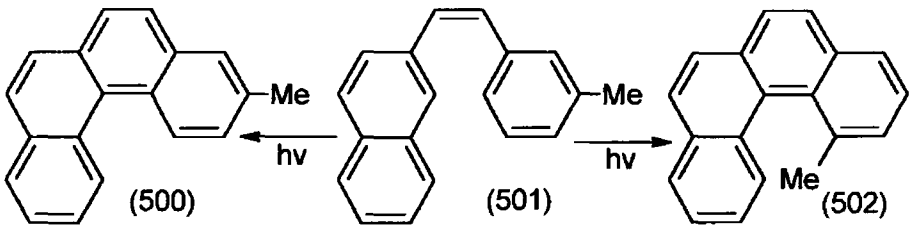
(E)-Aralkylidene(alkylidene)succinic anhydndes (496) (fulgides) with electron donating groups on the aryl ring undergo photochemically allowed 6π-electron ring closure to give highly coloured tricyclic dihydronaphthalene denvatives (497) [303] The presence of the electron donating methoxy group is believed to reduce the energy barrier to ring closure with simple fulgides



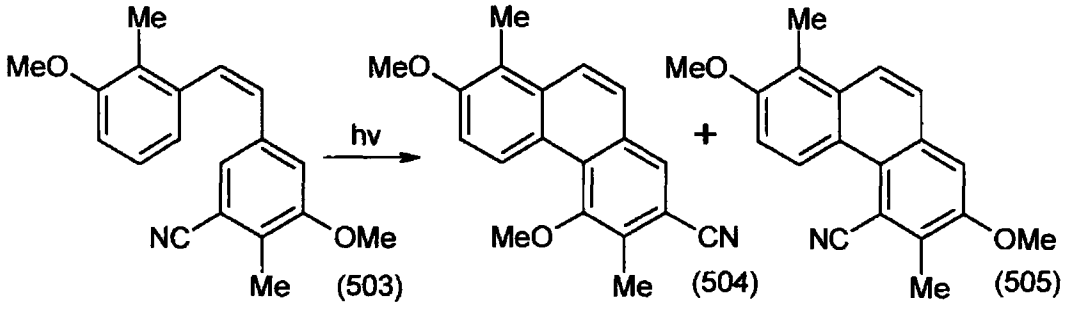
Photolysis of (498) could lead to two products, 2-methoxy-5-methylchrysene (499a) and 4-methoxy-5-methyl-chrysene (499b) [104] The photocyclisation of (498) yielded only one photoproduct (499a) with no (499b) present The authors suggested steric factors for this selective photocyclisation



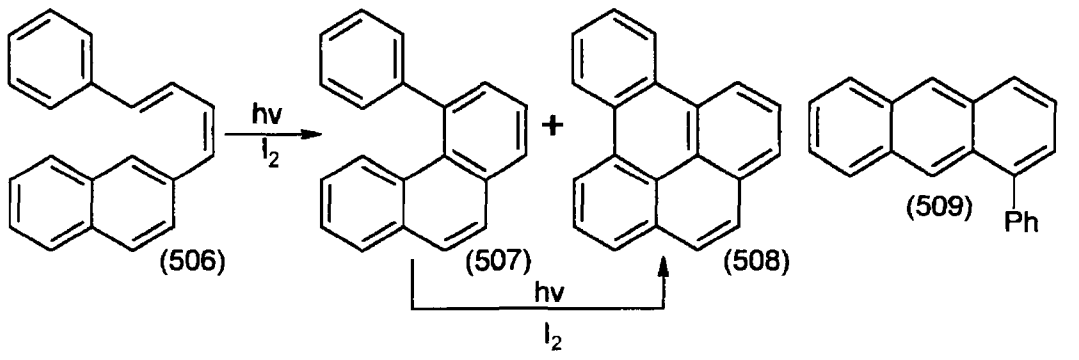
Mallory and co-workers studied the photocyclisation of cis-2-(m-methylstyryl)naphthalene (501) [9] On photocyclisation the product ratio of (500) to (502) was 61/39



The photocyclisation of the cyanostilbene (503) in benzene yielded two regioisomeric phenanthrenes (504) and (505) in a 7 1 ratio [32] The 7 1 ratio of photocyclisation isomers (504) and (505) from the cyanostilbene (503) was unexpected Studies have shown that the isomer ratios from meta-substituted stilbenes are usually of the order 1 1 to 2 1, and are relatively insensitive to the electron donor or acceptor properties of the substituent(s) [9]



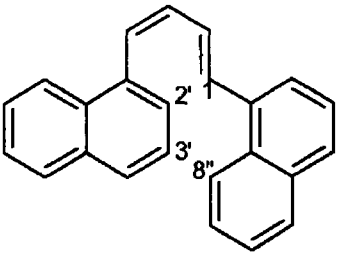
The photocyclisation of 1-(β-naphthyl)-4-phenyl-1,3-butadiene (506) has also been reported [141] When irradiated in benzene a mixture of products was obtained, 4-phenylphenanthrene (507) and 1,2-benzopyrene (508) The benzopyrene arose from a subsequent photochemical reaction of the first formed phenylphenanthrene The other possible monomeric cyclisation product



1-phenylanthracene (509) was not obtained from the irradiation The authors suggested[141] that the photocyclisation of (506) occurs to the 1-position of the naphthalene nucleus to give (507), rather than to the 3-position to give (509), as

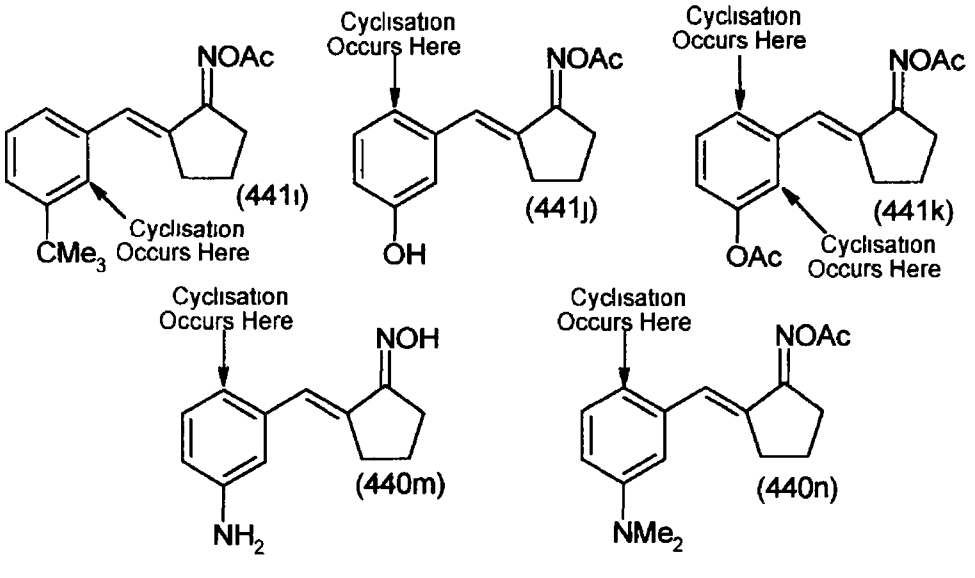
the free valence index at the 1-position of naphthalene was greater than that at the 3-position

Leznoff and co-workers have also looked at the photocyclisation of various dinaphthyl-1,3-butadienes [142] The cyclisation of 1,4-di-(α-naphthyl)-1,3-butadiene (510) led to photocyclisation at the 1,2' positions where the sum of the free valence indices was greater than unity Cyclisation does not occur at the 3',8" positions where the free valence indices was less than unity

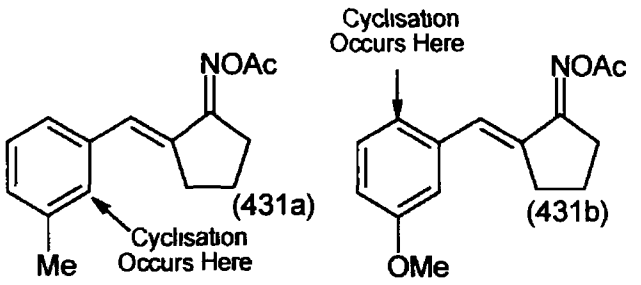


(510)

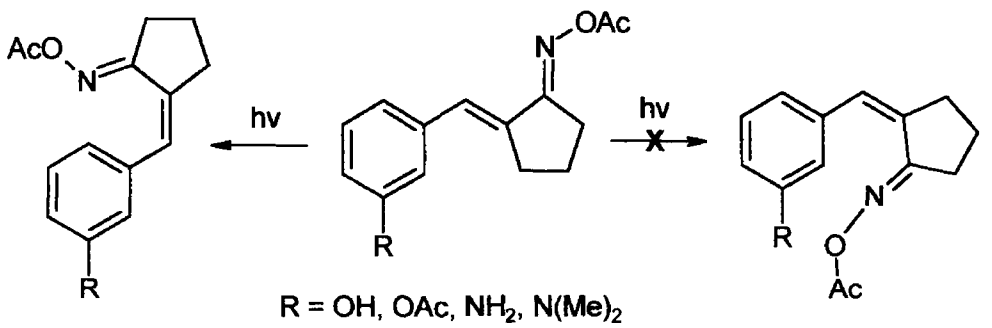
On examination of the photoproducts formed from the irradiation of the oxime acetates shown below, it is observed that the cyclisations are regiospecific, except for the 3-acetoxy derivative where both cyclisation modes were observed



Egan[283] had previously shown that the 3-methylphenyl oxime O-acetate (431a) cyclised in the ortho position while the 3-methoxyphenyl oxime O-acetate (431b) cyclised in the para position These results are in agreement with the results obtained above

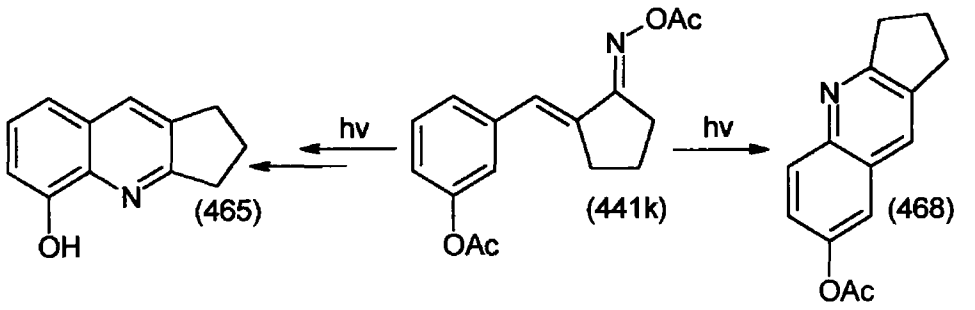


One possible reason for the difference in cyclisation regiochemistry may be due to the relative thermodynamic stabilities of the initial geometrical isomers formed on irradiation Repulsion between the lone pairs on the heteroatom of the oxime O-acetates below and the oxime O-acetate lone pairs may prevent the molecule from maintaining this configuration long enough, if at all for cyclisation to occur ortho to the heteroatom

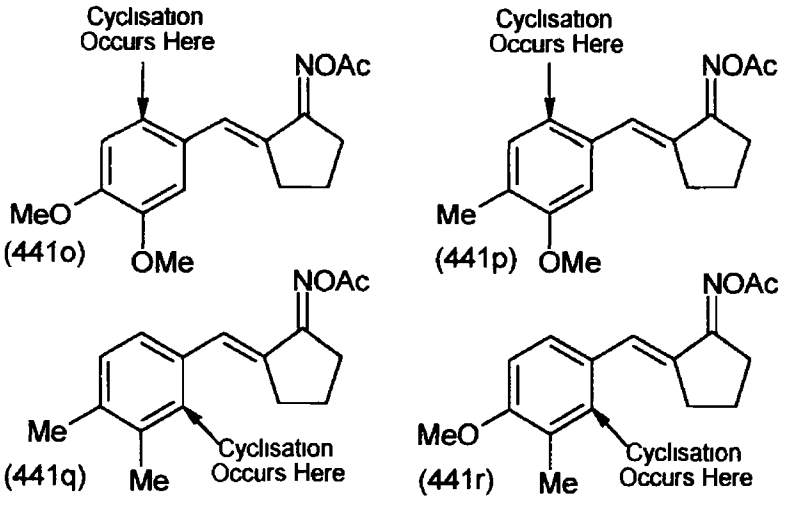


On irradiation of the 3-acetoxyphenyl oxime O-acetate (441k) it was believed that the presence of the acetyl group would reduce the effect of the lone pair on the phenoxy oxygen and therefore lead to cyclisation in the ortho position Although (441k) cyclised in the para position, a second compound, 2,3-dihydro-1H-cyclopenta[b]quinolin-5-ol (465), was also formed on irradiation The formation of the hydroxyquinoline (465) as co-product suggests that cyclisation of

(441k) takes place at both the para and ortho positions Cyclisation to yield the hydroxyquinoline (465), is probably the result of photocleavage of the acetate group from the acetoxy derivative of (465) On prolonged irradiation of a mixture of the hydroxyquinoline (465) and the acetoxyquinoline (468) the yield of the hydroxyquinoline (465) is reduced considerably while the yield of the acetoxyquinoline (468) remains constant



On examination of the photoproducts formed from the irradiation of the disubstituted oxime O-acetates it was observed that the cyclisations are regiospecific The reactions are summarised below These results parallel those reported by Egan[283] for the methoxy and methyl meta-substituted oxime O-acetates as discussed above Unfortunately an oxime O-acetate where the methyl and methoxy groups were in competition can not be synthesised



From Mallory and Mallory's work[9] and other photochemical reactions discussed in this chapter[300-302], photocyclisation of 3-substituted phenyl systems, where two sites for cyclisation occur, generally led to photocyclisation at both sites in a 1 1 ratio, the only exception being compound (498) which only gave one product on irradiation, though steric factors were given as the reason for this anomalous result [104] These results are in stark contrast to the results obtained by Egan[283] and myself where selective photocyclisation occurred in every cyclisation apart from the acetoxy group

An investigation into the photocyclisation of the 3- and 4-dimethylamino substituted oxime O-acetates in the present of trifluroacetic acid was carried out It was believed that in the presence of trifluroacetic acid the dimethylamino group would become protonated and would no longer act as an electron-donating group reducing the efficiency of the photocyclisation reaction In fact the yield for photocyclisation reaction was improved as was the efficiency of the reaction with irradiation times being reduced dramatically Only a molar equivalent of the trifluroacetic acid was added and was probably not enough for protonation of the dimethylamino group to occur

Comparison of the yields for the photocyclisation of the 3-methyl oxime O-acetate (431a) and the bulkier 3-t-butyl oxime O-acetate (441i) shows a significant decrease in the yield of cyclised product The yield of cyclisation products from the quinolines (431a) and (441i) were 32% and 13% respectively

5. Computational Chemistry

5.1 Computational Analysis

The advent of digital computers has led to vast improvements and wide usage of computational chemistry, alternatively sometimes called theoretical chemistry or molecular modelling. The computer being the instrument of the computational chemist, workers in the field have taken advantage of the advances made with computers to develop and apply new theoretical methodologies at a similarly astonishing rate. Because of the broad array of theoretical tools now available, it is a rare problem of interest that does not occupy the attention of both experimental and theoretical chemists. Indeed, the synergy between theory and experiment has vastly accelerated progress in any number of areas.

The term *ab initio* is Latin for "from the beginning". This name is given to computations which are derived directly from theoretical principles, with no inclusion of experimental data. Most of the time this refers to an approximate quantum mechanical calculation. The approximations made are usually mathematical approximations, such as using a simpler form for a function or getting an approximate solution to a differential equation.

The most common type of ab initio calculation is called a Hartree Fock calculation, in which the primary approximation is called the central field approximation. This means that the Coulombic electron-electron repulsion is not specifically taken into account. However, its net effect is included in the calculation. This is a variational calculation, meaning that the approximate energies calculated are all equal to or greater than the exact energy. Because of the central field approximation, the energies from Hartree Fock calculations are always greater than the exact energy and tend to a limiting value called the Hartree Fock limit.

The second approximation in Hartree Fock calculations is that the wave function must be described by some functional form, which is only known exactly for a few one electron systems. The plus side of ab initio methods is that they converge to the exact solution, once all of the approximations are made sufficiently small in magnitude. Sometimes, the smallest calculation gives the

best result for a given property. The downside of ab initio methods is that they are expensive. These methods often take enormous amounts of computer CPU time, memory and disk space.

In general, ab initio calculations give very good qualitative results and can give increasingly accurate quantitative results as the molecules in question become smaller.

Semiempirical calculations are set up with the same general structure as a Hartree Fock calculation. Within this framework, certain pieces of information, such as two electron integrals, are approximated or completely omitted. In order to correct for the errors introduced by omitting part of the calculation, the method is parameterised, by curve fitting in a few parameters or numbers, in order to give the best possible agreement with experimental data.

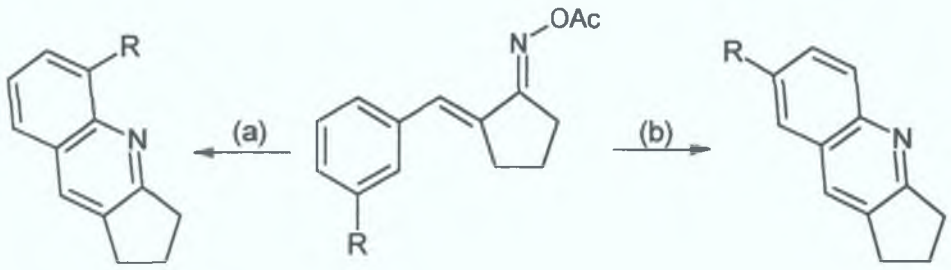
The plus side of semiempirical calculations is that they are much faster than the ab initio calculations. The downside of semiempirical calculations is that the results can be erratic. If the molecule being computed is similar to molecules in the data base used to parameterise the method, then the results may be very good. If the molecule being computed is significantly different from anything in the parameterization set, the answers may be very poor.

Semiempirical calculations have been very successful in the description of organic chemistry, where there are only a few elements used extensively and the molecules are of moderate size.

The two semiempirical models used with the present work are AM1 and PM3. AM1 or Austin Model 1 was devised in 1985, by Dewar et al.,[304] for the elements C, H, O and N. The AM1 model is based on the framework of the NDDO, or neglect of diatomic differential overlap. The NDDO method relaxes the constraints on two-centre two-electron integrals. One critical flaw in this method is that it performs very poorly in the prediction of hydrogen bonding geometries and energies. The primary error is one involving bond lengths. A key modification to the NDDO framework was to the nuclear repulsion term leading to the AM1 model. PM3 or Parameterised Model 3 was developed by Stewart.[305] Stewart, one of the authors on the original AM1 paper, had a more mathematical

philosophy, and felt that a more sophisticated search of parameter space using more complex optimisation algorithms might be more successful in producing a best possible parameter set within the Dewar-specific NDDO framework.

The cyclisation of 3-aryl-substituted cyclopentanone oxime O-acetates proceeds via a regioselective pathway. With methyl and t-butyl aryl substituents the cyclisation occurs ortho to the substituent (route a), while methoxy, amino and dimethylamino substituents cyclise para to the substituent (route b). The cyclisation reaction does not proceed in the presence of halogens, cyano and nitro groups. The reaction was analysed by semiempirical AM1 and PM3 methods of calculation.



5.2 Calculations

Calculations were carried out using HyperChem version 5.11. The compounds were first modelled with the MM+ method using the Polak-Ribiere algorithm. Hyperchem's molecular mechanics force field MM+ is based on Allinger's MM2 force field for hydrocarbons.[306] Molecular mechanics force fields were developed to describe mathematically molecular structures and properties in as practical a manner a possible. Then the MM+ models were re-evaluated using both PM3 and AM1 semi-empirical calculations, again using the Polak-Ribiere algorithm.

5.3 Results

The three-dimensional orientations of the lowest energy conformer for each of the geometrical isomers of 3-methylbenzylidenecyclopentanone oxime O-acetate were established using the molecular mechanics method MM+ and re-

evaluated using both AM1 and PM3 semi-empirical calculations. The calculations used the planar conformers (fig. 1) as the starting reference conformers in which the aryl and cyclopentano rings are coplanar. This assumption regarding a conformation with skeletal planarity is reasonable given sp^2 hybridisation of carbons 1 and 2 and the exocyclic atoms attached to them (benzylidene carbon and oximino nitrogen).

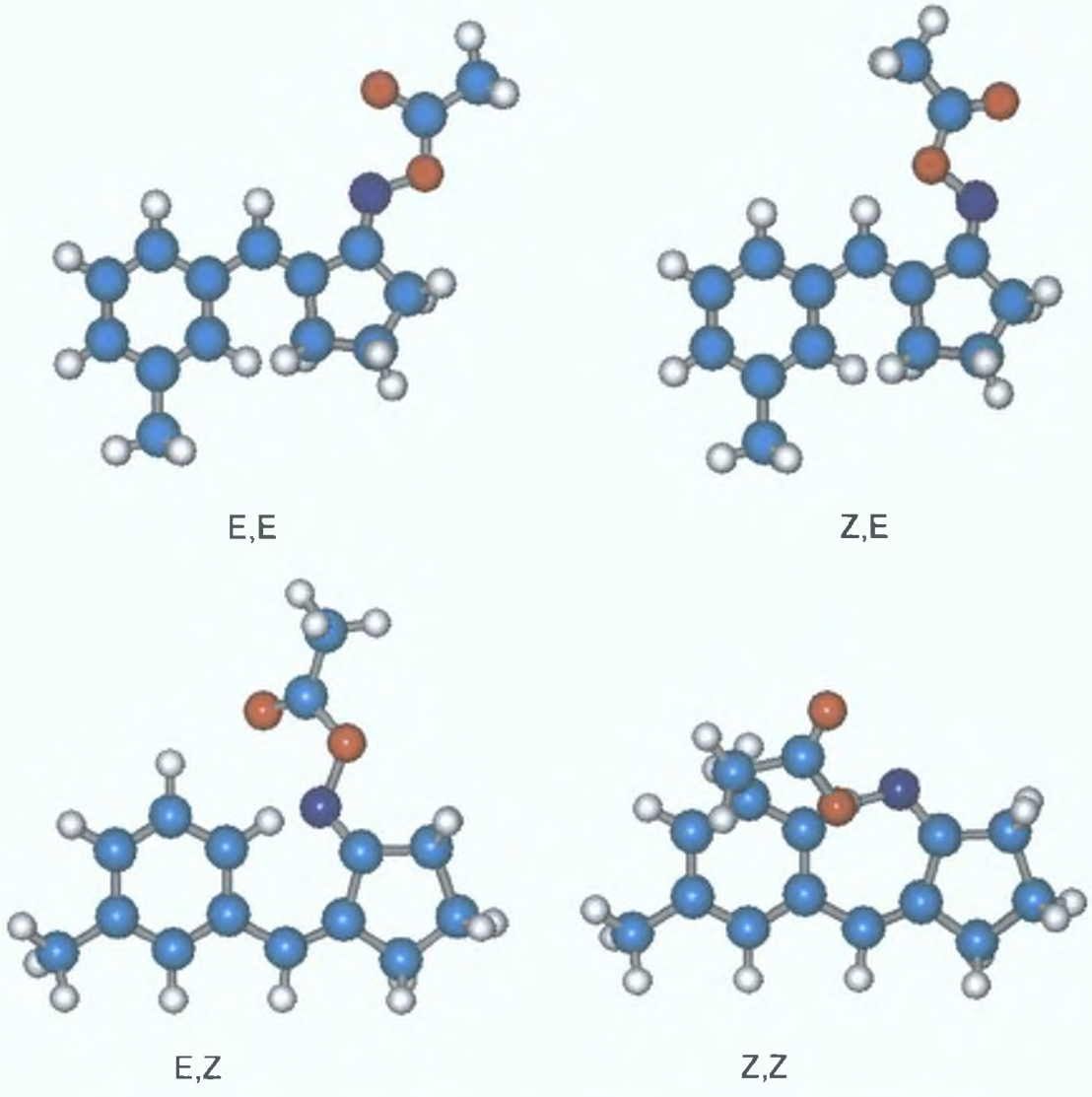


Fig. 1 *HyperChem representation of the four geometrical isomers of 2-(3-methylbenzylidene)cyclopentanone oxime O-acetate.*

Austin[282] had previously isolated and characterised the four geometrical isomers formed by photoequilibration of 2-benzylidene-cyclopentanone oxime O-

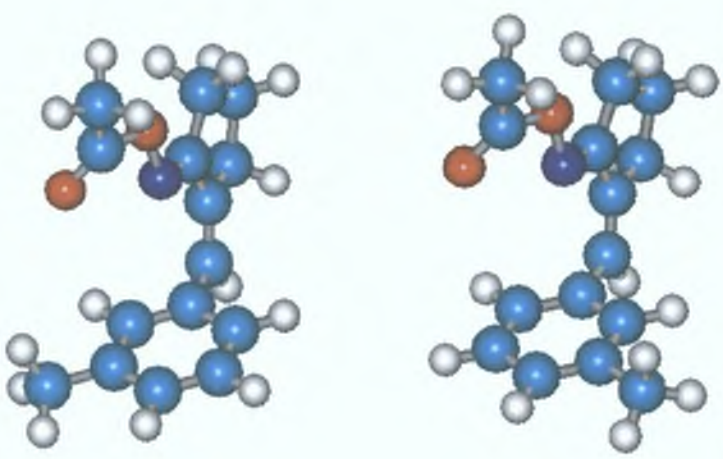
methyl ether, confirming the thermal stability of the individual geometrical isomers.

The lowest energy conformations of the other 3-substituted benzylidene-cyclopentanone oxime O-acetate derivatives were similarly drawn and modelled using the MM+ force field and re-evaluated using semi-empirical calculations. The heat of formation, the heat evolved or absorbed during the formation of one mole of a substance from its component elements, for each of the energy optimised geometrical isomers is shown below (table 1). In each case the E,E isomer has the lowest energy, while the Z,Z isomer is the least favoured which is what one would expect, as it is the most sterically hindered.

Isomer	Heat of Formation (kJ/mol)						
	Methyl	Methoxy	t-Butyl	Amino	DMA	Hydroxy	Acetoxy
E,E	-56.9	-176.3	-118.3	-25.8	-32.7	-206.3	-348.6
Z,E	-44.8	-166.0	-104.3	-15.6	-22.1	-196.0	-337.9
E,Z	-41.7	-161.5	-99.3	-10.0	-16.5	-191.0	-344.6
Z,Z	-31.4	-144.1	-87.7	-0.1	-6.9	-174.1	-325.0

*DMA = Dimethylamino

Table 1. *The heat of formation for the various geometrical isomers with each of the substituents.*



(a) (b)

Fig. 2 *HyperChem representation of E,Z-2-(3-methylbenzylidene)cyclopentanone oxime O-acetate showing the two lowest energy conformers.*

For the photocyclisation process to occur, involving nitrogen to aryl-carbon bond formation, the oxime acetate derivatives must be in either the E,Z or Z,Z configuration. The energy optimised models of the E,Z and Z,Z isomers for each of the 3-substituted oxime O-acetate derivatives were calculated using semi-empirical calculations with the planar models (fig. 1) as the starting reference conformation. The calculation for E,Z-2-(3-methylbenzylidene)cyclopentanone oxime O-acetate revealed two conformers (fig. 2) having the lowest energies, obtained by free rotation of the aryl system around the carbon/aryl bond.

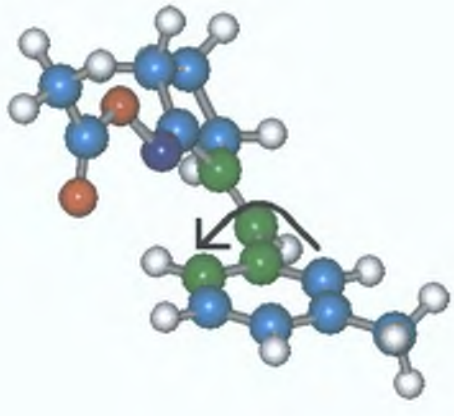


Fig. 3 *HyperChem representation of E,Z-2-(3-methylbenzylidene)cyclopentanone oxime O-acetate with a torsion angle of 45°. Free rotation, in an anti-clockwise motion, of the aryl-carbon bond was achieved by varying the torsion angle of the four highlighted carbons.*

Further investigation of the change in conformational energy as free rotation around the carbon-aryl bond occurs was carried out. A graph of torsion angle, obtained by rotation of the phenyl ring about the carbon/aryl bond in increments of 15° for both the 3-methyl- and 3-methoxy oxime O-acetate derivatives (fig. 3) versus heat of formation, calculated after each rotation, was drawn (fig. 4). The graph revealed two broad energy minimums in each case.

The torsion angles for the lowest energy conformers in each case are shown below (table 2). The torsion angles for the methyl oxime O-acetate

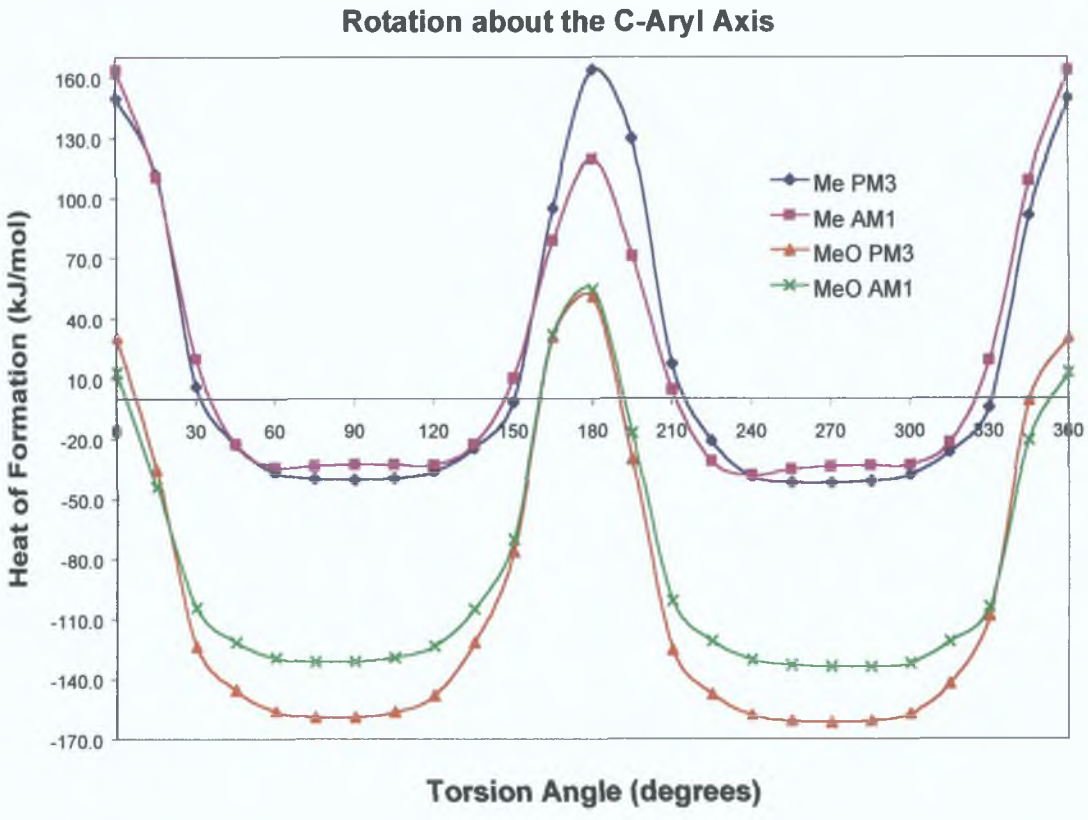


Fig. 4 *Graph showing the results for the E,Z isomers of the 3-methyl and 3-methoxy oxime O-acetate derivatives with rotation about the carbon/aryl bond.*

Substituent	Torsion Angle (degrees) (a)	Torsion Angle (degrees) (b)
Methyl	88	264
Methoxy	95	271
t-Butyl	87	274
Amino	91	274
Dimethylamino	101	277
Hydroxy	91	267
Acetoxy	95	267

Table 2*. The torsion angle for each of the 3-substituted oxime O-acetate derivatives in their lowest energy conformers. (a) and (b) refer to the two lowest energy conformers, analogous to those shown for E,Z-2-(3-methylbenzylidene)-cyclopentanone oxime O-acetate in fig 2.*

derivatives, (a) and (b) in fig. 2, are 265 and 86°. These compare very favourably to the graph (fig 4) which shows two broad energy minimums, one in the range 60-120° and the other in the range 240-300°. Therefore it can be assumed that the models in fig. 2 are in fact the lowest energy conformers.

In these conformations the benzene ring is essentially perpendicular to the cyclopentane ring. Although the models in fig. 2 show the lowest energy conformations for the E,Z isomer it can be concluded that there is no absolutely unique lowest energy conformation as the torsion angle oscillates over a broad range (60-120° and 240-300°). Across both energy minimums the heat of formation varies by only ~2/3 kJ/mol. The two peaks in fig. 4 correspond to the sterically hindered planar conformations, similar to the E,Z isomer in fig. 1.

As photocyclisation can potentially also occur from the Z,Z isomer it was also investigated. A comparison of the E,Z and Z,Z conformers of the 3-methoxy oxime O-acetate derivative are shown below (fig 5). The Z,Z isomer, as anticipated is more sterically hindered with the acetate "arm" twisting the phenyl ring. A graph of torsion angle versus heat of formation, obtained by rotation of the phenyl ring about the carbon/aryl bond, in a similar manner to that which was carried out on the E,Z isomer (fig. 3), was drawn for the 3-methyl and 3-methoxy oxime O-acetate derivatives (fig. 6).

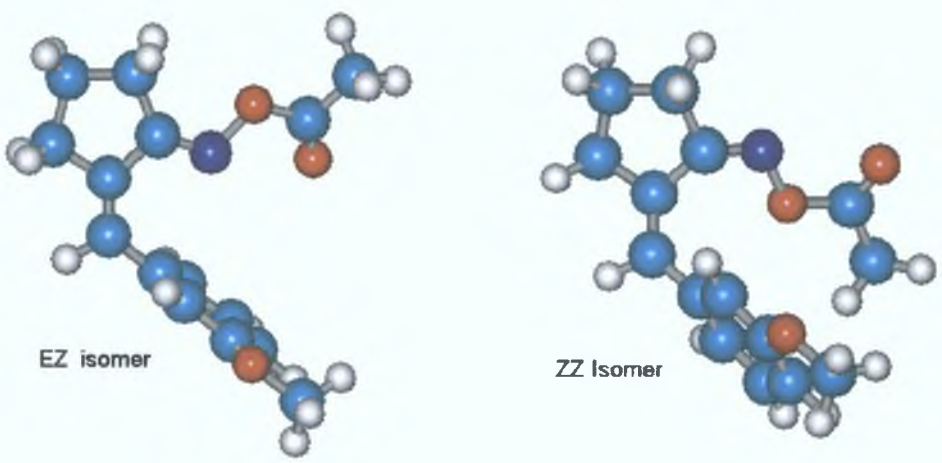


Fig. 5 *HyperChem representation of the lowest energy conformers of E,Z and Z,Z isomers of 2-(3-methoxybenzylidene)cyclopentanone oxime O-acetate.*

Both the 3-methyl and 3-methoxy oxime O-acetate derivatives showed two broad energy minimums in the range 105-150° and 285-330° (fig. 6). The two large peaks in fig. 6 correspond to planar conformations where either a hydrogen or in the case of the larger peak, the methyl or methoxy group, is overlapping with the acetate "arm". Where the methyl group is overlapping with the acetate "arm" the energy difference is very large compared to the methoxy derivative due to the greater steric bulk of the methyl group.

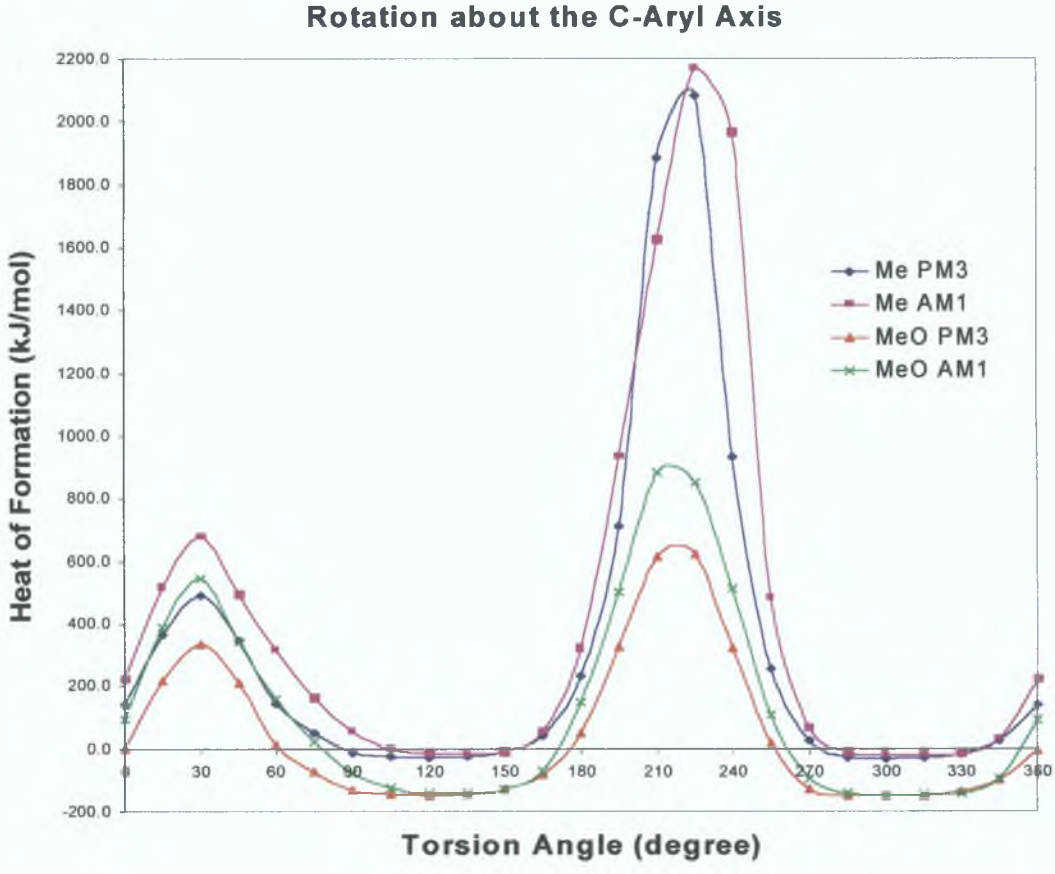


Fig. 6 *Graph showing the results for the Z,Z isomers of 3-methyl and 3-methoxy oxime O-acetate derivatives with rotation about the carbon/aryl bond.*

The torsion angles for the various Z,Z-oxime O-acetate derivatives are given in table 3. The torsion angles of 123° and 296° for the 3-methyl oxime O-acetate and 121° and 299° for the 3-methoxy oxime O-acetate compare very favourably to those shown in fig. 6. Again there are very broad energy minimums and it can be concluded that there is no absolutely unique lowest energy

conformation, the torsion angle oscillating over a broad range (105-150° and 285-330°) Across both energy minimums the heat of formation varies by only ~2/3 kJ/mol

Substituent	Torsion Angle (degrees)	Torsion Angle (degrees)
Methyl	123	296
Methoxy	121	299
t-Butyl	118	301
Amino	120	303
Dimethylamino	120	299
Hydroxy	118	300
Acetoxy	115	297

Table 3 *The torsion angles for each of the Z,Z-3-substituted oxime O-acetate derivatives in their lowest energy conformers*

PM3 Calculations			
Substituent	Hf E,Z isomer (kJ/mol)	Hf Z,Z isomer (kJ/mol)	Diff in Hf (kJ/mol)
Methyl	-41 7	-31 4	-10 3
Methoxy	-161 5	-144 1	-17 4
t-Butyl	-99 3	-87 7	-10 5
Amino	-10 0	-0 1	-10 0
Dimethylamino	-16 5	-6 9	-9 2
Hydroxy	-191 0	-174 1	-16 9
Acetoxy	-344 6	-325 0	-19 6
AM1 Calculations			
Methyl	-38 3	-21 2	-17 1
Methoxy	-162 5	-145 8	-16 7
t-Butyl	-79 0	-66 7	-12 3
Amino	-8 7	4 7	-13 4
Dimethylamino	35 3	47 3	12 0
Hydroxy	-186 9	-174 2	-12 7
Acetoxy	-314 4	-298 4	-16 0

Table 4 *Comparison of the heats of formation of the E,Z and Z,Z isomers of the 3-substituted benzylidenecyclopentanone oxime O-acetates*

The photocyclisation reaction must proceed via either the E,Z or the Z,Z isomer to permit C-N bond formation. A comparison of the heats of formation for both the E,Z and Z,Z isomers showed that the E,Z isomer was more stable, as expected, than its Z,Z counterpart (table 4). This does not rule out cyclisation from the Z,Z isomer but it is more likely to occur predominantly from the less sterically hindered E,Z isomer.

There are two carbons on the aryl system to which the nitrogen of the oxime acetate can potentially form a bond during photocyclisation. Fig 7 shows the two carbons (highlighted in green) at which this reaction can occur.

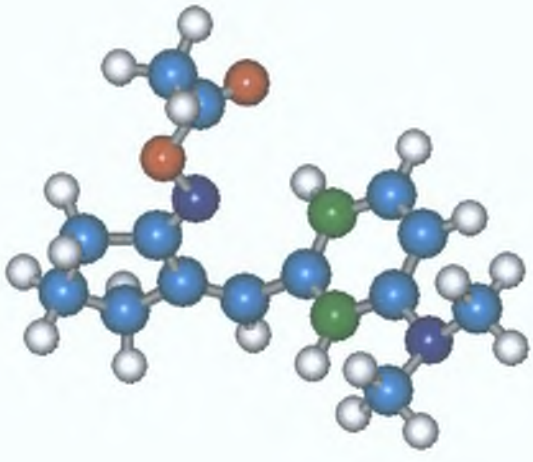


Fig. 7 *HyperChem representation of 2-(3-dimethylaminobenzylidene)cyclo-pentanone oxime O-acetate showing the two possible carbons where photocyclisation can occur.*

As determined experimentally the photocyclisation reaction occurs at the carbon ortho to a methyl or t-butyl group whereas it occurs at the carbon para to a methoxy, amino, dimethylamino, hydroxy or acetoxy group. From the graph in fig. 4 it can be concluded that there is no absolutely unique lowest energy conformation as the torsion angle oscillates over a broad range (60-120° and 240-300°).

To explore whether the regioselective photoreaction might be conformationally controlled, the distances between the nitrogen and the reactive and unreactive carbons were calculated over the range 60-120°. The results for the range 240-300° were found to be very similar.

Both PM3 and AM1 calculations show that the reactive carbon for each E,Z isomer in the lowest energy conformer, as calculated using semi-empirical methods, is in fact closer to the oximino nitrogen than is the unreactive carbon (table 5), the only exception being in the 3-t-butylphenyl derivative. When the torsion angle was set to 60° the reactive carbon in both the methyl and t-butyl derivatives was found to be closer to the oximino nitrogen whereas the

PM3	60 deg.		Min. Energy		120 deg.	
Substrate	Rxn	No-Rxn	Rxn	No-Rxn	Rxn	No-Rxn
Methyl	2.87	4.04	3.36	3.65	3.92	3.03
Methoxy	3.96	2.95	3.42	3.57	2.93	3.97
t-Butyl	2.96	3.97	3.64	3.37	3.99	2.94
Amino	3.95	2.98	3.35	3.65	2.92	4.00
DMA*	3.98	2.98	3.32	3.71	2.96	4.01
Hydroxy	3.96	2.95	3.48	3.51	2.92	3.98
Acetate	3.96	2.89	3.38	3.56	2.93	3.93
AM1	60 deg.		Min. Energy		120 deg.	
Substrate	Rxn	No-Rxn	Rxn	No-Rxn	Rxn	No-Rxn
Methyl	2.97	4.06	2.95	4.07	3.98	3.03
Methoxy	4.02	2.98	3.01	4.02	3.01	4.02
t-Butyl	2.91	3.94	3.76	3.15	3.95	2.91
Amino	4.01	2.88	3.08	3.88	3.01	3.94
DMA*	4.00	2.96	3.03	3.97	2.99	4.00
Hydroxy	3.97	2.86	3.40	3.52	2.96	3.90
Acetate	3.98	2.97	2.99	3.98	2.96	4.01

*DMA = Dimethylamino

Table 5. *Distances from the nitrogen of the oxime O-acetate to both the reacting and the unreacting carbon in the* E,Z *isomers.*

unreactive carbon was found to be closer to the oximino nitrogen in the other substituted derivatives. When the torsion angle was set to 120° the above

situation was reversed with the unreactive carbon in the methyl and t-butyl derivatives found to be closer to the oximino nitrogen while the reactive carbon in the other substituted derivatives was found to be closer to the oximino nitrogen

This strongly suggests that the photocyclisation reaction is conformationally controlled Where the aryl substituent contains a heteroatom attached directly to the ring, repulsion between the lone pair electrons on this heteroatom and the oxime O-acetate group lone pairs may reduce the probability of the torsion angle of the molecule being at the 60° end of the range, thereby preventing cyclisation from this conformation

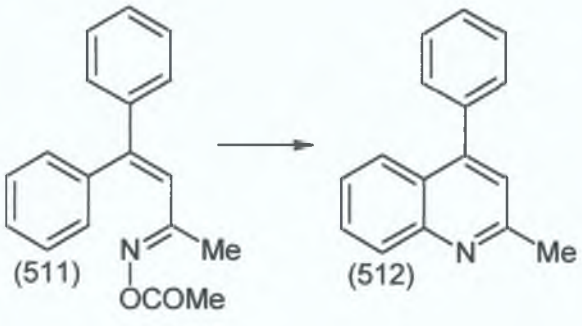
A brief investigation of electronic effects was also carried out Both PM3 and AM1 semi-empirical calculations were used to determine the partial charges of the carbons where cyclisation could occur (table 6) The carbon which led to

Substituent	Partial Charge at Rxn C	Partial Charge at Non-Rxn C	Difference in Partial Charge
PM3 Calculations			
Methyl	-0 073	-0 099	0 026
Methoxy	-0 112	-0 129	0 017
t-Butyl	-0 098	-0 075	-0 023
Amino	-0 102	-0 135	0 033
Dimethylamino	-0 099	-0 141	0 042
Hydroxy	-0 124	-0 125	0 001
Acetoxy	-0 091	-0 101	0 010
t-Butyl (Z,Z)	-0 094	-0 096	0 002
AM1 Calculations			
Methyl	-0 084	-0 125	0 041
Methoxy	-0 117	-0 146	0 029
t-Butyl	-0 115	-0 094	-0 021
Amino	-0 125	-0 178	0 053
Dimethylamino	-0 123	-0 172	0 049
Hydroxy	-0 142	-0 137	-0 005
Acetoxy	-0 090	-0 124	0 034
t-Butyl (Z,Z)	-0 108	-0 126	0 018

Table 6. *Comparison of the calculated partial charges on both the reacting and non-reacting carbon centres of the* E,Z *and Z,Z-oxime O-acetate derivatives*

the observed photoproduct had a smaller partial charge in all cases, with the exception of the t-butyl derivative. Interestingly however the carbon that led to the correct photoproduct on cyclisation of the t-butyl derivative was found to have a smaller partial charge in the *Z,Z* isomer.

Suwiński and Mohamed[307] reported the thermal cyclisation of 4,4-diphenyl-3-buten-2-one oxime acetate (511) to 2-methyl-4-phenylquinoline (512). They used semiempirical AM1 and PM3 calculations to investigate the reaction mechanism by calculating the heat of formation and the enthalpy for each step in



the cyclisation. Calculations of heats of formation of the dihydroaromatic intermediate were made for my own systems. Unfortunately HyperChem is

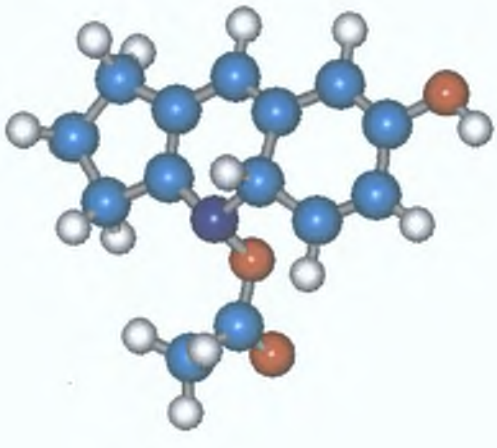


Fig. 8 *Dihydroquinoline photoproduct for 2-(3-hydroxybenzylidene)-cyclopentanone oxime O-acetate.*

unable to calculate enthalpy at the semi-empirical level and this therefore could not be investigated

The reaction consists of two steps, a concerted conrotatory photocyclisation of the starting oxime O-acetate leading to a dihydroquinoline derivative (fig 8) followed by thermal elimination of acetic acid from the photoproduct to give the quinoline derivative

A comparison of the heats of formation for the intermediates leading to the observed and non-observed photoproducts, shows that the one leading to the observed photoproduct has the lower heat of formation in all cases, except for the t-butyl intermediate (table 7) The E,Z isomer for the t-butyl intermediate is lower in energy than the more sterically hindered *Z,Z* isomer, although previous results suggest that the cyclisation reaction for the t-butyl oxime O-acetate derivative may take place from the *Z,Z* isomer

Substituent	Hf (kJ/mol) Observed	Hf (kJ/mol) Unobserved	Difference Hf (kJ/mol)
Methyl	-11 8	0 3	-12 1
Methoxy	-139 6	-120 0	-19 6
t-Butyl	-55 1	-56 9	1 8
Amino	8 7	23 8	-15 2
Dimethylamino	3 1	31 5	-28 4
Hydroxy	-169 2	-153 1	-16 1
Acetate	-323 5	-296 9	-26 5
t-Butyl (Z,Z)	-40 2	-54 9	14 7

Table 7. *A comparison of the heat of formation for the intermediates leading to the observed and unobserved photoproducts from the* E,Z *isomers The Z,Z isomer also included for the t-butyl substituent*

HyperChem can be used to plot the LUMO orbitals on each of the 3-substituted oxime O-acetate derivatives and these can then be used to calculate the coefficients on the frontier orbitals that play an important part in pericyclic reactions, particularly influencing the regioselectivity of cycloaddition reactions The PM3 derived frontier orbitals of the various oxime O-acetates are shown

below (fig 9 and 10). These are calculated by simply using the orbital function in HyperChem and using the Gouraud shaded surface rendering. The green and purple shapes in fig. 9 and 10 represent the plus and minus lobes respectively of the various orbitals associated with the first LUMO level of the various 3-substituted oxime O-acetate derivatives.

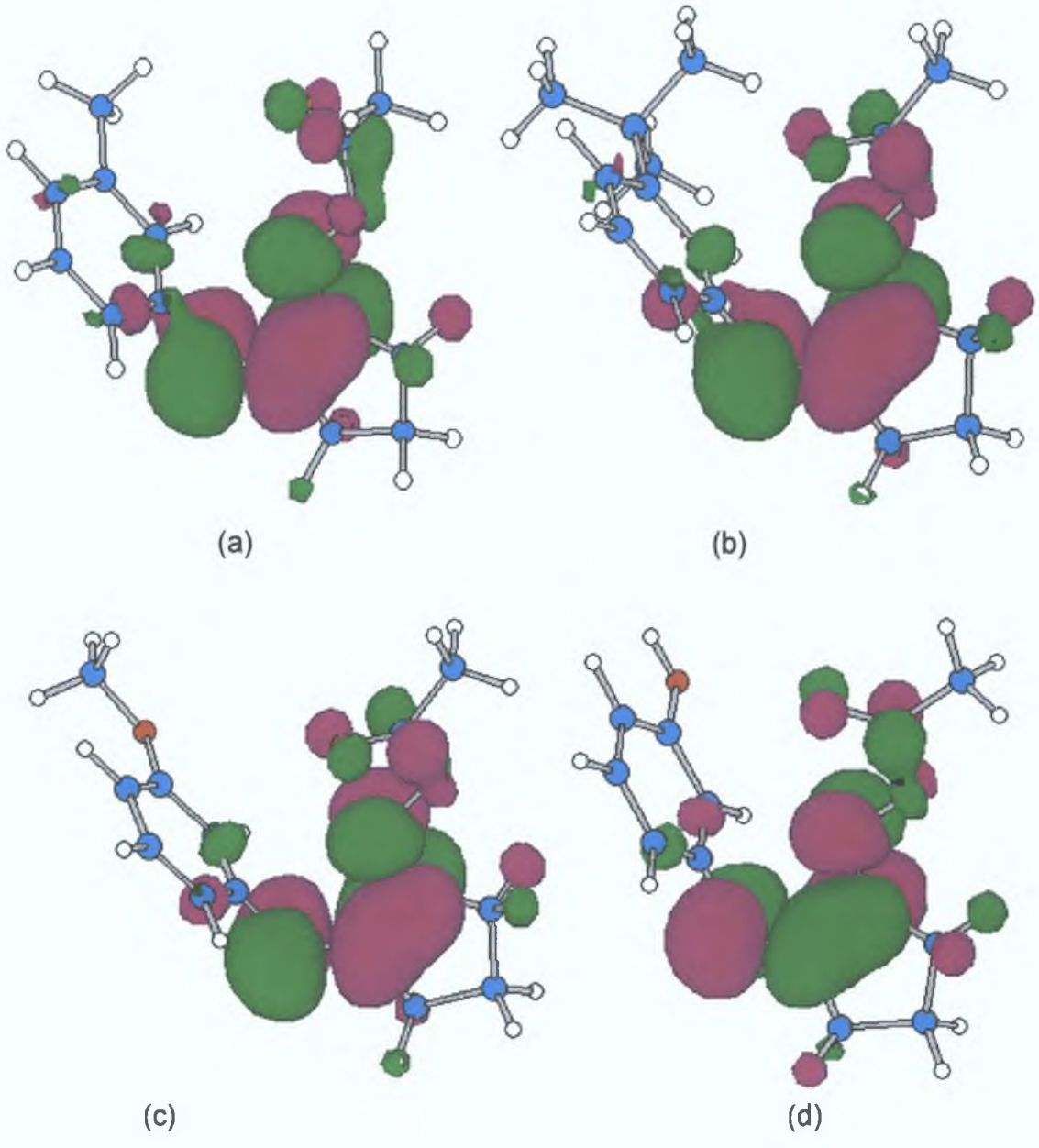


***Fig. 9**. HyperChem PM3 representation of the frontier orbitals of the first LUMO level for (a) the 3-methyl-, (b) 3-t-butyl-, (c) 3-methoxy- and (d) 3-hydroxy-substituted oxime O-acetates.*

The corresponding frontier orbital coefficients were then calculated using Hyperchem, the results for which can be seen below (table 8). The frontier orbital coefficients are the sum of the contributions from all the s and p orbitals associated with each individual atom.

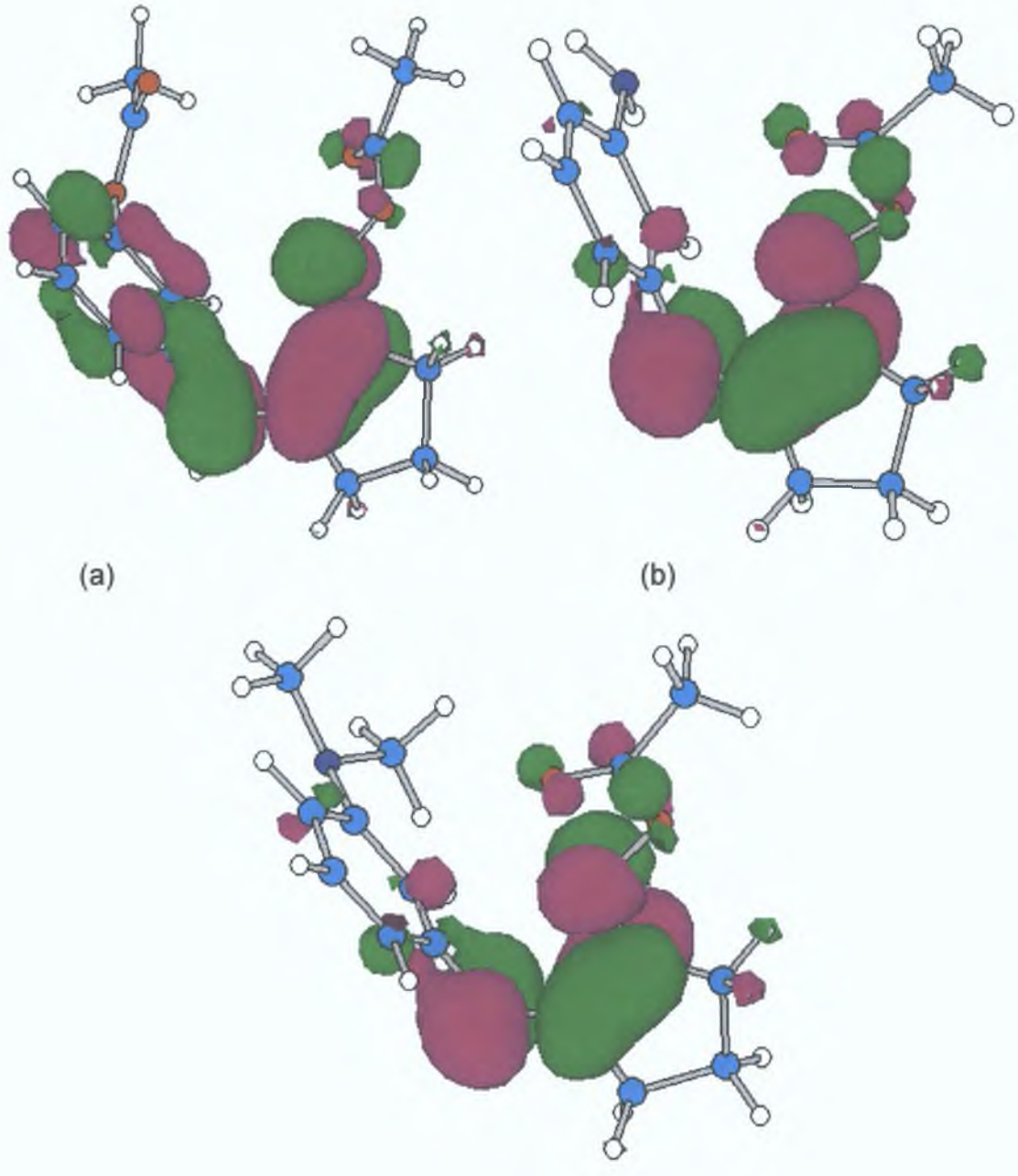


***Fig. 10**. HyperChem PM3 representation of the frontier orbitals of the first LUMO level for (a) the 3-acetoxy- (b) 3-amino-, and (c) 3-dimethylamino-substituted oxime O-acetates*

As can be seen from table 8 the coefficients on each carbon are small and there are only minor differences between the ortho and para carbons with no apparent correlation with experimental results Frontier orbital coefficient differences therefore do not explain the regioselectivity of the photocyclisation reaction of 3-substituted oxime O-acetates derivatives

Substituent	Ortho Carbon (C5)	Para Carbon (C3)
Methyl	0 008	-0 096
t-Butyl	0 158	0 051
Methoxy	0 124	0 018
Amino	-0 038	-0 177
Dimethylamino	0 073	0 213
Hydroxy	0 000	0 136
Acetate	0 060	-0 074

Table 8 *A comparison of the frontier orbital coefficients for the ortho and para carbons With the methyl and t-butyl substituent the cyclisation reaction occurs to the ortho carbon while the other substituents cyclise at the para carbon*

5 4 Conclusions

To try to explain the regioselectivity of the photocyclisation reaction of 3-aryl-substituted cyclopentanone oxime O-acetates, molecular modelling was employed Both steric and electronic factors were investigated From the results it appears that steric factors play an important role in the photocyclisation reaction Of the two isomers from which the photocyclisation reaction can take place, the E,Z and Z,Z isomers, it is likely that the reaction takes place from the E,Z isomer

Steric factors seem to account for the carbon to which the photocyclisation reaction occurs The distances between the nitrogen and both the reactive and unreactive carbons were calculated over the range 60-120° Both PM3 and AM1 calculations show that the reactive carbon for each E,Z isomer in the lowest energy conformer, is in fact closer to the oximino nitrogen than is the unreactive

carbon, the only exception being in the 3-t-butylphenyl derivative When the torsion angle was set to 60° the reactive carbon in both the methyl and t-butyl derivatives were found to be closer to the oximino nitrogen whereas the unreactive carbon was found to be closer to the oximino nitrogen in the other substituted denvatives When the torsion angle was set to 120° the above situation was reversed with the unreactive carbon in the methyl and t-butyl derivatives found to be closer to the oximino nitrogen while the reactive carbon in the other substituted denvatives was found to be closer to the oximino nitrogen This strongly suggests that the photocyclisation reaction is sterically controlled

An investigation of the partial charges of the two carbons also gave some interesting results The carbon, where photocyclisation leading to the observed photoproduct takes place, was found to have smaller partial charge than the carbon that led to the unobserved photoproduct This was found to be the case in all E,Z isomers except for that with the t-butyl substituent A look at the *Z,Z* isomer of the t-butyl denvative found that the carbon where photocyclisation takes place had the slightly smaller partial charge

An investigation of the heat of formation for the two possible photoproducts showed that the one formed which resulted in the observed photoproduct than that which would lead to the non-observed product was generally lower in energy

An investigation of the frontier orbital coefficients failed to give any evidence as to why the cyclisation reaction is regioselective

Overall steric and electronic properties seem to combine to play an important role in the photocyclisation reaction with steric properties playing a very important role

6. Experimental

6 1 Introductory remarks

Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker AC-400 instrument operating at 400M Hz for ^{1}H-NMR and 100M Hz for ^{13}C-NMR Spectra were recorded using deuterated chloroform as solvent unless otherwise stated (d = doublet, t = triplet, q = quartet, m = multiplet)

Infrared (IR) spectra were recorded on a Perkin Elmer 983G infrared spectrophotometer

Ultraviolet (UV) spectra were recorded on a Hewlett Packard 8452A diode array UV-Vis spectrophotometer

Melting ranges were recorded using a Griffin melting point apparatus and are uncorrected

The Microanalytical Laboratory of University College Dublin carried out elemental analysis

Thin layer chromatography (TLC) was carried out on silica gel TLC plates containing a fluorescent indicator (Riedel-de-Haen, DC-cards SIF, layer thickness 0 2mm)

Laboratory photochemical reactions were carried out using a water cooled immersion well containing a Photochemical Reactors 400W medium pressure mercury lamp fitted with a Pyrex filter (λ>300nm) Methanol and dichloromethane for photochemical reactions was spectophotometric grade of 99 9% purity Passing a stream of argon through the solution for 30 minutes prior to irradiation deoxygenated all solutions for photochemical reaction and an atmosphere of argon was maintained over the solutions for the duration of irradiation

Purification of crude photoproducts was carried out using column chromatography with silica gel as stationary phase unless otherwise stated

Light Petroleum of boiling point 40-60 °C was used for chromatography, while light petroleum of boiling point 60-80 °C was used for recrystallisation

All chemicals were purchased from Aldrich and were used without further purification

6 2 Preparation of 1-Formylphenothiazine (443)

A 2 5M solution of n-butyllithium in hexane (37 5 cm^3, 94 mmol) was added to anhydrous diethyl ether (200 cm^3) in a 500 cm^3 round-bottomed flask Phenothiazine (7 42 g, 37 5 mmol) was added slowly and the reaction mixture was stirred under nitrogen for 48 hours The mixture was cooled to –70 °C using a liquid nitrogen/ethyl acetate sludge and dimethylformamide (2 74 g, 37 5 mmol) was added dropwise at –70 °C The reaction temperature was raised to room temperature and the mixture stirred for 1 hour 0 5M Hydrochloric acid (100 cm^3) was added with vigorous shaking and the organic layer was separated The aqueous layer was extracted three times with diethyl ether (50 cm^3) and the combined organic layers were washed with water (100 cm^3) and dried over magnesium sulphate After removal of solvent by rotary evaporation the red residue was chromatographed using a silica gel column with mobile phase 90 10 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded bright red crystals of 1-formylphenothiazine (443) (4 1 g, 48%), melting range 81-82 °C (lit [291], 80-81 °C)

IR (KBr pellet) 3281 (NH), 3135, 2927 (aromatic CH), 2856, 2824, 2743 (both CHO), 1657 (C=O), 1594, 1563, 1500, 1479, 1440, 1400, 1303, 1243, 1202, 1128, 942, 745, 715 and 671 cm^{-1}

^{1}H-NMR δ 6 61-6 63 (m, 1H, aromatic proton), 6 79-6 88 (m, 3H, aromatic protons), 6 98-7 05 (m, 2H, aromatic proton), 9 80 (s, 1H, CHO) and 10 11 (s, 1H, NH) ppm

^{13}C-NMR δ 116 41, 117 57, 118 61, 119 73, 121 11, 124 18, 126 89, 128 11, 131 92, 133 87, 139 13, 144 87 (aromatic carbon) and 194 72 (CHO) ppm

6 3 Preparation of N-(2-Bromo-4-t-Butylphenyl)acetamide (445)

4-t-Butylaniline (25 0 g, 16 8 mmol), dissolved in glacial acetic acid (100 cm^3), was placed in a 250 cm^3 three-necked round-bottom flask, provided with a

reflux condenser and thermometer The solution was heated under reflux for 3 hours and allowed to cool to about 45 °C A dropping funnel was connected to the flask and bromine (27 2 g, 17 mmol) was added to the solution, with rapid stirring, maintaining a temperature below 55 °C Stirring was continued for 1 hour after all of the bromine was added The reaction mixture was poured in a thin stream into a well stirred solution of ice/water (100 cm^3 each) Sodium metabisulphite was added until the bromine colour no longer persisted The N-(2-bromo-4-t-butylphenyl)-acetamide was vacuum filtered and washed thoroughly with water and then light petroleum ether of b pt 40-60 °C After drying overnight the acetamide (445) was obtained as pink/white crystals (42 2 g, 93%) melting range 159-160 °C (lit [308], 159 5 °C) The acetamide (445) was used in the next step without further purification

IR 3250, 2963, 2923 (aromatic and aliphatic CH), 1659 (C=O), 1584, 1572, 1521, 1385, 1284, 1047, 874, 747 and 705 cm^{-1}

^{1}H-NMR δ 1 31 (s, 9H, CMe_3), 2 25 (s, 3H, C(O)Me) 7 35 (d of d, 1H, J_1=8 9 Hz, J_2=2 2 Hz, aromatic proton), 7 44 (d, 1H, J=8 9 Hz, aromatic proton) 7 54 (d, 1H, J=2 2 Hz, aromatic proton) and 8 20 (s, 1H, NHAc) ppm

^{13}C-NMR δ 25 18 (C(O)Me), 31 74 (CMe_3), 34 89 (CMe_3), 120 27, 122 21, 125 84, 126 20, 129 47, 133 40 (aromatic carbons), and 168 53 (C=O) ppm

6 4 Preparation of 2-Bromo-4-t-Butylaniline (446)

The dried N-(2-bromo-4-t-butylphenyl)acetamide (45 5 g 168 3 mmol) was dissolved in ethanol (50 cm^3) with gentle heating and placed in a 250 cm^3 round-bottom flask which was set up for reflux Concentrated hydrochloric acid (50 cm^3) was added slowly to the reaction through the condenser The mixture was heated under reflux for 3 hours On cooling, water (50 cm^3) was added and the flask was set up for distillation After removal of ethanol/water (75 cm^3) the mixture was allowed to cool and transferred to a 500 cm^3 conical flask A 10% sodium

hydroxide solution was added until the reaction became alkaline. At this stage most of the water was decanted off and the remaining material added to a separating funnel. The bottom layer was run off and washed twice with water (50 cm^3). The 2-bromo-4-t-butyl aniline (446) was separated as a deep red oil (31.5 g, 82%). All physical data agreed with the reported literature values.[309] The aniline was used in the next step without further purification.

IR: 3477, 3380 (NH_2), 2963, 2869 (aromatic and aliphatic CH), 1621, 1505, 1402, 1348, 1270, 1165, 1114, 1035, 876, 817 and 705 cm^{-1}.

^{1}H-NMR: δ 1.24 (s, 9H, CMe_3), 4.70 (s, 2H, NH_2), 7.24 (d, 1H, J=8.4 Hz, aromatic proton), 7.12 (d of d, 1H, J_1=8.4 Hz, J_2=2.2 Hz, aromatic proton) and 7.40 (d, 1H, J=2.2 Hz, aromatic proton) ppm.

^{13}C-NMR: δ 31.64 ($C\underline{Me}_3$), 34.46 ($\underline{C}Me_3$), 110.15, 116.51, 125.86, 129.80, 141.20 and 143.80 (aromatic carbons) ppm.

6.5 Preparation of 3-t-Butylbromobenzene (447)

t-Butyl nitrite (21.4 g, 20.7 mmol), dissolved in DMF (40 cm^3), was placed in a 100 cm^3 three-necked round-bottom flask, fitted with reflux condenser, addition funnel and gas outlet tube. The mixture was heated to 65 °C. The 2-bromo-4-t-butylphenylamine (32.1 g, 140.7 mmol), dissolved in DMF (20 cm^3), was added dropwise to the solution with rapid stirring. On complete addition of the amine the reaction mixture was allowed stir for a further 20 minutes and then added to a stirred aqueous 20% hydrochloric acid solution (150 cm^3) which was then extracted twice with diethyl ether (100 cm^3). The ether extract was washed firstly with an aqueous 10% hydrochloric acid solution (50 cm^3) and then water (50 cm^3). After drying over magnesium sulphate the ether was removed on a rotary evaporator to yield a brown oil. After purification on a silica gel column with mobile phase 99:1 light petroleum/ethyl acetate, 3-t-butylbromobenzene (447) was obtained as a yellow oil (13.5 g, 45%). All physical data agreed with the reported literature

values [310] The bromobenzene (447) was used in the next step without further purification

IR 3067, 2964, 2869 (aromatic and aliphatic CH), 1866, 1682, 1592, 1481, 1417, 1365, 1261, 1075, 996, 879, 850, 782, 745, 696 and 658 cm^{-1}

^{1}H-NMR δ 1 40 (s, 9H, CMe_3), 7 24 (t, 1H, J=8 0 Hz, aromatic proton), 7 38-7 40 (m, 2H, aromatic protons) and 7 62 (t, 1H, J=1 8 Hz, aromatic proton) ppm

^{13}C-NMR δ 31 68 ($C\underline{Me_3}$), 35 30 ($\underline{C}Me_3$), 122 92, 124 48, 129 02, 129 12, 130 15 and 154 02 (aromatic carbons) ppm

6.6 Preparation of 3-t-Butylbenzaldehyde (448)

3-t-Butylbromobenzene (3 92 g, 18 4 mmol) was added to a 250 cm^3 round-bottom flask, fitted with dropping funnel, thermometer and a nitrogen inlet Anhydrous diethyl ether (100 cm^3) was added to the reaction vessel with stirring and the solution cooled to 0 °C A 2 5M solution of n-butyl lithium in hexane (15 cm^3, 37 mmol) was added dropwise and the reaction mixture was stirred for a further 30 minutes after the last of the n-butyl lithium was added The reaction mixture was warmed to room temperature and poured into a 20% aqueous phosphoric acid solution with vigorous stirring The resulting mixture was extracted twice with diethyl ether (50 cm^3) The extract was washed with an aqueous 10% sodium bicarbonate solution (50 cm^3), then with water (50 cm^3) and dried over magnesium sulphate The ether was removed by rotary evaporation to yield a dark orange oil After purification on a silica gel column with mobile phase 90 10 light petroleum/ethyl acetate, 3-t-butylbenzaldehyde (448) was obtained as a yellow oil (2 43 g, 81%) All physical data agreed with the reported literature values [311]

IR 3380, 3065, 2964, 2869 (aromatic and aliphatic CH), 2724 (CHO), 1699 (C=O), 1600, 1481, 1366, 1290, 1196, 1089, 927, 797, 697 and 651 cm^{-1}

^{1}H-NMR δ 1 25 (s, 9H, CMe_3), 7 36 (t, 1H, J=7 6 Hz, aromatic proton), 7 58 (m, 2H, aromatic protons), 7 81 (t, 1H, J=1 8 Hz, aromatic proton) and 9 91 (s, 1H, CHO) ppm

^{13}C-NMR δ 31 58 ($C\underline{Me}_3$), 35 21 ($\underline{C}Me_3$), 126 66, 127 84, 129 19, 132 11, 136 73, 152 58 (aromatic carbons) and 193 13 (CHO) ppm

6 7 Preparation of 3-(Dimethylamino)bromobenzene (450)

3-Bromoaniline (17 2 g, 100 mmol) was added to water (18 cm^3) in a 250 cm^3 round-bottomed flask and the reaction mixture was stirred vigorously Dimethyl sulphate (9 46 cm^3, 100 mmol) was added dropwise, through a dropping funnel, over 15 minutes and the mixture stirred for a further hour, then neutralised by addition of 20% aqueous potassium hydroxide solution Additional dimethyl sulphate (9 46 cm^3, 100 mmol) was added and stirring was continued for another hour The pH was brought to pH≈8 by addition of 20% aqueous potassium hydroxide solution and further dimethyl sulphate (4 73 cm^3, 50 mmol) was added The reaction was stirred for 30 minutes and again the pH was brought to pH≈8 by addition of 20% aqueous potassium hydroxide solution The product was extracted with diethyl ether (2 x 75 cm^3) and the combined organic layers washed with water (3 x 25 cm^3) and dried over magnesium sulphate The solvent was removed by rotary evaporation to yield a dark gum which was distilled under reduced pressure yielding 3-(dimethylamino)bromobenzene (450) as a light orange oil (4 1 g, 20%) All physical data agreed with the reported literature values [294]

IR (KBr pellet) 3425, 3083, 2889, 2807 (aromatic and aliphatic CH), 1595, 1498, 1444, 1354, 1230, 1180, 1096, 1069, 983, 830, 759 and 681 cm^{-1}

^{1}H-NMR δ 2 80 (s, 6H, NMe_2), 6 49 (m 1H, aromatic proton), 6 69-6 72 (m, 2H, aromatic protons) and 6 95 (t, 1H, J_1=8 4 Hz) ppm

^{13}C-NMR δ 40 79 (NMe_2), 111 34, 115 46, 119 46, 123 83, 130 72 and 152 06 (aromatic carbons) ppm

6 8 Preparation of 3-(Dimethylamino)benzaldehyde (451)

3-(Dimethylamino)bromobenzene (4 02 g, 20 mmol) was dissolved in diethyl ether (50 cm^3) in a 100 cm^3 round-bottom flask A 2 5M solution of n-butyllithium in hexane (8 0 cm^3, 20 mmol) was added dropwise under nitrogen at 0 °C, and the mixture was stirred for 30 minutes Dimethylformamide (1 83 g, 25 mmol) was added dropwise and stirring was continued for 5 minutes The reaction mixture was allowed to reach room temperature and then was poured into a 20% aqueous phosphonic acid solution (50 cm^3) with rapid stirring It was neutralised with 10% sodium carbonate solution and extracted with diethyl ether (2 x 50 cm^3) The extract was washed with 10% sodium carbonate solution (25 cm^3), then water (25 cm^3) and finally dried over magnesium sulphate The diethyl ether was removed by rotary evaporation, yielding a dark orange oil Purification was achieved by silica gel chromatography, with a mobile phase of 25% ethyl acetate in petroleum ether, yielding 3-(dimethylamino)benzaldehyde (451) as an orange oil (2 9 g, 97%) All physical data agreed with the reported literature values [312]

IR (KBr pellet) 3374, 2918, 2851 (aromatic and aliphatic CH), 2809, 2727 (both CHO), 1698 (C=O), 1601, 1498, 1442, 1393, 1357, 1206, 1064, 999, 982, 894, 860, 780 and 683 cm^{-1}

^{1}H-NMR δ 2 87 (s, 6H, NMe_2), 6 82 (m, 1H, aromatic proton), 7 05-7 10 (m, 2H, aromatic protons), 7 26 (t, 1H, J_1=7 8 Hz) and 9 83 (s, 1H, CHO) ppm

^{13}C-NMR δ 40 50 (NMe_2), 111 94, 118 48, 118 87, 129 91, 137 58, 151 01 (aromatic carbons) and 193 39 (CHO) ppm

6.9 Preparation of 3-Methoxy-4-Methylbenzaldehyde (453)

To a solution of n-methylpiperazine (11.8 cm^3, 107 mmol) in THF (200 cm^3), cooled to –20 °C, was added a 2.5M solution of n-butyllithium in hexane (41.2 cm^3, 103 mmol) dropwise. After stirring under nitrogen for 15 minutes 3-methoxybenzaldehyde (13.6 g, 100 mmol) was added and the solution stirred for a further 15 minutes. Tetramethylethylenediamine (45.3 cm^3, 30 mmol) was added to the mixture followed by a 1.4M solution of sec-butyllithium in cyclohexane (214 cm^3, 300 mmol). The reaction was stirred for a further 10 minutes and then left in the freezer overnight. The reaction vessel was cooled to –78 °C and methyl iodide (37.3 cm^3, 600 mmol) was added slowly with stirring, following which the reaction temperature was allowed to rise to room temperature. The mixture was poured into a stirred solution of an aqueous 10% HCl solution and extracted with diethyl ether (2 X 100 cm^3), washed with brine (50 cm^3), water (2 X 50 cm^3) and dried over magnesium sulphate. Purification on a silica gel column with mobile phase 90:10 light petroleum/ethyl acetate, yielded light yellow needles of 3-methoxy-4-methylbenzaldehyde (453) (4.3 g, 29%), melting range 45-46 °C (lit.[295], 45-46 °C).

IR (KBr pellet): 2957, 2927(aromatic and aliphatic CH), 2838 (OMe), 1701 (C=O), 1606, 1501, 1467, 1394, 1260, 1149, 1038, 874, 815, 735 and 621 cm^{-1}.

^{1}H-NMR: δ 2.13 (s, 3H, Me), 3.72 (s, 3H, OMe), 7.12 (d, 1H, J_1=7.6 Hz, aromatic proton), 7.17-7.20 (m, 2H, aromatic protons) and 9.76 (s, 1H, CHO) ppm.

^{13}C-NMR: δ 17.11 (Me), 55.67 (OMe), 108.18, 124.68, 131.17, 135.05, 136.25, 158.59 (aromatic carbons) and 192.21 (C=O) ppm.

6.10 General Procedure for the Preparation of Arylidenecyclopentanones (439a,c,e-j,l,n-r)

Cyclopentanone (2.10 g, 25 mmol) and morpholine (2.18 g, 25 mmol) were placed in a 250ml round-bottom flask containing toluene (75 cm^3). The mixture was

heated under reflux with continuous azetropic removal of water using a Dean and Stark distillation apparatus until no further water collected (0 45 cm^3) The reaction mixture was allowed to cool and the desired aldehyde (25 mmol) was added The mixture was again heated under reflux with the azeotropic removal of water, until no further water collected (0 45 cm^3) The reaction mixture was allowed to cool and transferred to a 250 cm^3 conical flask A 1 1 mixture of conc HCl / water (20 cm^3) was added dropwise to the flask with stirring and the mixture was then stirred for a further 30 minutes The contents of the flask were then transferred to a 250 cm^3 separating funnel and the lower aqueous layer was removed The upper organic layer was washed first with a 10% aqueous sodium carbonate solution (40 cm^3) and then with water (2 x 30 cm^3) The organic layer was dried over anhydrous magnesium sulphate and the toluene was removed by rotary evaporation, yielding the required arylidenecyclopentanone The arylidenecyclopentanones were recrystallised from methanol unless otherwise stated

6 11 2-(4-Hydroxybenzylidene)cyclopentanone (439a)

2-(4-Hydroxybenzylidene)cyclopentanone was prepared from 4-hydroxy-benzaldehyde (12 2 g, 100 mmol) yielding sandy coloured crystals of product (10 7 g, 57%), melting range 187-188 °C (lit [313], 188-192 °C)

IR (KBr pellet) 3276 (OH), 2962, 2921 (aromatic and aliphatic CH), 1693 (C=O), 1588, 1515, 1436, 1364, 1281, 1250, 1187, 1168, 1110, 916 and 835 cm^{-1}

^{1}H-NMR δ 1 95 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 35 (t, 2H, J=7 5 Hz, CH_2-C=O), 2 88 (t of d, 2H, J_1=7 5 Hz, J_2=2 8 Hz, CH_2-C=C), 6 11 (s, 1H, OH), 6 83 (d of t, 2H, J_t=8 8 Hz, J_d=2 7 Hz, aromatic protons), 7 30 (t, 1H, J=2 7 Hz, vinylic proton) and 7 39 (d, 2H, J=8 8 Hz, aromatic protons) ppm

^{13}C-NMR (DMSO) δ 21 48, 30 48, 38 84 (cyclopentane ring saturated carbons), 116 99, 128 33, 134 08, 134 32, 134 40, 160 77 (aromatic and vinylic carbons) and 210 94 (C=O) ppm

6 12 2-(4-Nitrobenzylidene)cyclopentanone (439c)

2-(4-Nitrobenzylidene)cyclopentanone was prepared from 4-nitrobenzaldehyde (9 83 g, 65 mmol) yielding orange crystals of product (6 5 g, 46%), melting range 141-142 °C (lit [282], 145-146 °C)

IR (KBr pellet) 2942, 2917 (aromatic and aliphatic CH), 1711 (C=O), 1625, 1584, 1510, 1342 (both NO_2), 1268, 1231, 1175, 1107, 1029, 842, 749 and 689 cm^{-1}

^{1}H-NMR δ 2 11 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 48 (t, 2H, J=7 6 Hz, CH_2-C=N), 3 03 (t of d, 2H, J_1=7 6 Hz, J_2=2 8 Hz, CH_2-C=C), 7 40 (t, 1H, J=2 8 Hz, vinylic proton), 7 68 (d, 2H, J=8 8 Hz, aromatic protons) and 8 28 (d of t, 2H, J_t=8 8 Hz, J_d=2 8 Hz, aromatic protons) ppm

^{13}C-NMR δ 20 48, 29 82, 38 09 (nng saturated cyclopentane carbons), 124 28, 129 69, 131 20, 140 28, 142 33, 147 90 (aromatic and vinylic carbons) and 207 79 (C=O) ppm

6 13 Preparation of 2-(4-Aminobenzylidene)cyclopentanone (439d)

A mixture of 2-(4-nitrobenzylidene)cyclopentanone (5 86 g, 27 mmol) and tin(II)chloride dihydrate (30 5 g, 135 mmol) were dissolved in ethanol (85 cm^3) with stirring under nitrogen The mixture was heated under reflux at 70 °C for 30 minutes The reaction was then cooled and the pH brought to pH~8 using a 20% aqueous solution of sodium carbonate The reaction was extracted with ethyl acetate (2 X 50 cm^3) The organic layer was washed with brine (50 cm^3) and then dried over magnesium sulphate The ethyl acetate was removed by rotary evaporation, yielding an orange gum Recrystallisation from methanol yielded red/orange crystals of 2-(4-aminobenzylidene)cyclopentanone (2 6 g, 41%), melting range 177-179 °C (decomp)

IR (KBr pellet) 3448, 3350 (both NH_2), 3233, 2954, 2897 (aromatic and aliphatic CH), 1683 (C=O), 1573, 1515, 1441, 1301, 1174, 919 and 826 cm^{-1}

^{1}H-NMR δ 1 95 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 31 (t, 2H, J=7 6 Hz, CH_2-C=N), 3 03 (t of d, 2H, J_1=7 6 Hz, J_2=2 6 Hz, CH_2-C=C), 3 91 (s, 2H, NH_2) 6 62 (d of t, 2H, J_t=8 6 Hz, J_d=2 6 Hz, aromatic protons) 7 25 (t, 1H, J=2 6 Hz, vinylic proton) and 7 32 (d, 2H, J=8 6 Hz, aromatic protons) ppm

^{13}C-NMR δ 20 55, 29 79, 38 18 (ring saturated cyclopentane carbons), 115 18, 126 15, 132 40, 132 98, 133 38, 148 31 (aromatic and vinylic carbons) and 208 67 (C=O) ppm

Found C, 76 68, H, 6 96, N, 7 43 $C_{12}H_{13}NO$ requires C, 76 98, H, 7 00, N, 7 48%

6 14 2-(4-Dimethylaminobenzylidene)cyclopentanone (439e)

2-(4-Dimethylaminobenzylidene)cyclopentanone was prepared from 4-dimethyl-aminobenzaldehyde (14 92 g, 100 mmol) yielding orange plates of product (15 50 g, 72%), melting range 149-151 °C The reaction was analogous to the general synthesis of 2-benzylidenecyclopentanone with one minor modification

After acid hydrolysis the aqueous layer was separated and neutralised with a 10% aqueous solution of sodium hydroxide The aqueous layer was extracted with diethyl ether (2 X 50 cm^3) The organic layer was washed with water (2 X 30 cm^3) and dried over magnesium sulphate After removal of the diethyl ether, recrystallisation from methanol furnished 2-(4-dimethylaminobenzylidene)-cyclopentanone

IR (KBr pellet) 2975, 2905 (aromatic and aliphatic CH), 1687 (C=O), 1586, 1529, 1375, 1301, 1169 and 814 cm^{-1}

^{1}H-NMR δ 1 94 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 30 (t, 2H, J=7 6 Hz, CH_2-C=O), 2 88 (t of d, 2H, J_1=7 6 Hz, J_2=2 4 Hz, CH_2-C=C), 2 96 (s, 6H, NMe_2), 6 64 (d, 2H, J=8 8 Hz, aromatic protons), 7 28 (t, J=2 4 Hz, 1H, vinylic proton) and 7 40 (d, 2H, J=8 8 Hz, aromatic proton) ppm

^{13}C-NMR δ 20 57, 29 82, 38 21 (cyclopentane ring saturated carbons), 40 52 (NMe_2), 112 18, 123 67, 131 43, 132 90, 133 75, 151 32 (aromatic and vinylic carbons) and 208 62 (C=O) ppm

Found C, 77 65, H, 7 95, N, 6 46 $C_{14}H_{17}NO$ requires C, 78 10, H, 7 96, N, 6 51%

6 15 2-(2,5-Dimethoxybenzylidene)cyclopentanone (439f)

2-(2,5-Dimethoxybenzylidene)cyclopentanone was prepared from 2,5-dimethoxybenzaldehyde (4 15 g, 25 mmol) yielding yellow crystals of product (3 95 g, 68%), melting range 73-75 °C

IR (KBr pellet) 2955, 2925 (aromatic and aliphatic CH), 2834 (OMe), 1678 (C=O), 1616, 1492, 1427, 1287, 1218, 1185, 1053, 797 and 717 cm^{-1}

^{1}H-NMR δ 1 93 (m, 2H, J=7 5 Hz, CH_2-$C\underline{H}_2$-CH_2), 2 33 (t, 2H, J=7 5 Hz, CH_2-C=O), 3 29 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 72 (s, 3H, OMe), 3 75 (s, 3H, OMe), 6 77 (d, 1H, J=8 9 Hz, aromatic proton), 6 81 (d of d, 1H, J_1=8 9 Hz, J_2=3 1 Hz, aromatic proton), 6 96 (d, 1H, J=3 1 Hz, aromatic proton) and 7 69 (t, 1H, J=2 6 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 76, 29 86, 38 31 (cyclopentane ring saturated carbons), 56 18, 56 47 (both OMe), 112 12, 115 82, 125 74, 127 25, 136 72, 153 46, 153 89 (aromatic and vinylic carbons) and 208 30 (C=O) ppm

Found C, 72 36, H, 7 00 $C_{14}H_{16}O_3$ requires C, 72 39, H, 6 94%

6 16 2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone (439g)

1-Formylphenothiazine (6 00 g, 26 mmol) on reaction with the cyclopentanone enamine yielded a deep red waxy solid The waxy solid was purified on a silica gel column, mobile phase 80 20 light petroleum/ethyl acetate

yielding dark purple crystals of 2-(10H-phenothiazin-1-ylmethylene)cyclopentanone (1 32 g, 17%) melting range 171-172 °C

IR (KBr pellet) 3433, 3323 (NH), 3135, 2929 (aromatic CH), 1691 (C=O), 1593, 1545, 1476, 1401, 1267, 1200, 1123, 865, 752 and 666 cm^{-1}

^{1}H-NMR δ 1 93 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 37 (t, 2H, J=7 5 Hz, CH_2-C=O), 2 76 (d of d, 2H, J_1=7 5 Hz, J_2=2 7 Hz, CH_2-C=C), 6 29 (s, 1H, NH), 6 61 (d of d, 1H, J_1=7 8 Hz, J_2=1 0 Hz, aromatic proton), 6 72-6 79 (m, 2H, aromatic protons), 6 89-6 98 (m, 4H, aromatic proton) and 7 30 (t, 1H, J=2 7 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 83, 29 73, 38 55 (cyclopentane ring saturated carbons), 115 74, 118 86, 119 75, 120 97, 122 08, 123 58, 125 75, 127 01, 127 90, 127 99, 128 07, 139 80, 141 35, 141 44 (aromatic and vinylic carbons) and 208 07 (C=O) ppm

Found C, 73 47, H, 5 13, N, 4 65 $C_{18}H_{15}NOS$ requires C, 73 69, H, 5 15, N, 4 77%

6 17 2-(3-Phenylallylidene)cyclopentanone (439h)

2-(3-Phenylallylidene)cyclopentanone was prepared from trans-cinnamaldehyde (10 57 g, 80 mmol) yielding dark orange crystals of product (7 45 g, 47%), melting range 89-90 °C (lit [314], 87-89 °C)

IR (KBr pellet) 3029, 2956 (aromatic CH), 1707 (C=O), 1604, 1495, 1450, 1401, 1273, 1192, 1027, 972, 754 and 700 cm^{-1}

^{1}H-NMR δ 1 95 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 33 (t, 2H, J=7 6 Hz, CH_2-C=N), 2 75 (t of d, 2H, J_1=7 6 Hz, J_2=2 4 Hz, CH_2-C=C), 6 78-6 90 (m, 2H, vinylic protons), 7 02 (d of t, 1H, J_t=10 7 Hz, J_d=2 7 Hz, vinylic proton), 7 21-7 31 (m, 3H, aromatic protons) and 7 41 (d, 2H, J=7 2 Hz, aromatic protons) ppm

^{13}C-NMR δ 20 25, 27 76, 39 05 (cyclopentane ring saturated carbons), 125 09, 127 56, 129 20, 129 39, 131 93, 136 84, 137 44, 141 88 (aromatic and vinylic carbons) and 207 97 (C=O) ppm

6 18 2-(3-t-Butylbenzylidene)cyclopentanone (439i)

2-(3-t-Butylbenzylidene)cyclopentanone was prepared from 3-t-butylbenzaldehyde (3 24 g, 20 mmol), yielding pale yellow crystals of product (4 20 g, 92%), melting range 54-55 °C

IR (KBr pellet) 3031, 2963, 2903 (aromatic and aliphatic CH), 1708 (C=O), 1620, 1492, 1420, 1275, 1177, 1127, 930, 765 and 702 cm^{-1}

^{1}H-NMR δ 1 27 (s, 9H, CMe_3), 1 96 (m, 2H, J=7 6 Hz, CH_2-$C\underline{H_2}$-CH_2), 2 34 (t, 2H, J=7 6 Hz, CH_2-C=O), 2 92 (t of d, 2H, J_1=7 6 Hz, J_2=2 8 Hz, CH_2-C=C), 7 28-7 35 (m, **4H**, aromatic protons) and 7 49 (t, 1H, J=2 8 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 66, 29 83, 31 67, 35 10, 38 26 (cyclopentane ring saturated carbons, $\underline{C}Me_3$ and $C\underline{Me_3}$), 126 98, 127 84, 128 29, 128 84, 133 37, 135 59, 136 07, 151 95 (aromatic and vinylic carbons) and 208 61 (C=O) ppm

Found C, 83 76, H, 8 89 $C_{16}H_{20}O$ requires C, 84 16, H, 8 83%

6 19 2-(3-Hydroxybenzylidene)cyclopentanone (439j)

2-(3-Hydroxybenzylidene)cyclopentanone was prepared from 3-hydroxybenzaldehyde (6 1 g, 100 mmol) yielding red/brown crystals of product (6 7 g, 72%), melting range 161-162 °C

IR (KBr pellet) 3176 (OH), 3092 (vinylic CH), 2961, 2915 (aromatic and aliphatic CH), 1686 (C=O), 1604, 1575, 1479, 1406, 1357, 1314, 1254, 1197, 786 and 687 cm^{-1}

^{1}H-NMR δ 1 97 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 35 (t, 2H, J=7 6 Hz, CH_2-C=O), 2 91 (t of d, 2H, J_1=7 6 Hz, J_2=2 8 Hz, CH_2-C=C), 5 73 (s, 1H, OH), 6 81 (m, 1H, aromatic proton), 6 98 (m, 1H, aromatic proton), 7 04 (m, 1H, aromatic proton), 7 22 (t, 1H, J=8 0 Hz, aromatic proton) and 7 28 (t, 1H, J=2 8 Hz, vinylic proton) ppm

^{13}C-NMR (DMSO) δ 21 38, 30 58, 38 84 (nng saturated cyclopentane carbons), 118 00, 118 08, 123 51, 131 02, 133 84, 137 60, 138 20, 159 05 (aromatic and vinylic carbons) and 210 72 (C=O) ppm

Found C, 76 49, H, 6 48 $C_{12}H_{12}O_2$ requires C, 76 57, H, 6 43%

6 20 2-(3-Nitrobenzylidene)cyclopentanone (439l)

2-(3-Nitrobenzylidene)cyclopentanone was prepared from 3-nitrobenzaldehyde (7 56 g, 75 mmol) yielding dark brown needles of product (5 81 g, 53%), melting range 108-109 °C (lit [283], 110-111 °C)

IR (KBr pellet) 2972, 2903 (aromatic and aliphatic CH), 1716 (C=O), 1630, 1521 (NO_2), 1408, 1349 (NO_2), 1299, 1233, 1174, 1083, 914, 812, 739 and 671 cm^{-1}

^{1}H-NMR δ 2 03 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 39 (t, 2H, J=7 6 Hz, CH_2-C=O), 2 97 (t of d, 2H, J_1=7 6 Hz, J_2=2 9 Hz, C$\underline{H_2}$-C=CH), 7 32 (t, 1H, J=2 9 Hz, vinylic proton), 7 54 (t, 1H, J=8 0 Hz, aromatic proton) 7 75 (d, 1H, J=8 0 Hz, aromatic proton) 8 14 (m, 1H, aromatic proton) and 8 31 (m, 1H, aromatic proton) ppm

^{13}C-NMR δ 20 50, 29 67, 38 10 (nng saturated cyclopentane carbons), 124 00, 124 61, 129 65, 130 13, 136 59, 137 62, 139 24, 148 85 (aromatic and vinylic carbons) and 207 85 (C=O) ppm

6 21 Preparation of 2-(3-Aminobenzylidene)cyclopentanone (439m)

A mixture of 2-(3-nitrobenzylidene)cyclopentanone (5 43 g, 25 mmol) and tin(II)chloride dihydrate (28 2 g, 125 mmol) were dissolved in ethanol (75 cm^3) with stirring under nitrogen The mixture was heated under reflux at 70 °C and refluxed for 30 minutes The reaction was then cooled and the pH brought to pH~8 using a 20% aqueous solution of sodium carbonate The reaction mixture was extracted with ethyl acetate (2 X 50 cm^3) and the organic layer was washed with brine (50 cm^3) and then dried over magnesium sulphate The ethyl acetate was removed by rotary evaporation, yielding an orange gum Recrystallisation from methanol yielded yellow crystals of 2-(3-aminobenzylidene)cyclopentanone (3 2 g, 68%), melting range 119-120 °C

IR (KBr pellet) 3436, 3340 (both NH_2), 2956, 2930 (aromatic and aliphatic CH), 1696 (C=O), 1615, 1576, 1493, 1449, 1308, 1206, 1172, 925, 870, 789 and 694 cm^{-1}

^{1}H-NMR δ 1 95 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 33 (t, 2H, J=7 5 Hz, CH_2-C=O), 2 90 (t of d, 2H, J_1=7 5 Hz, J_2=2 7 Hz, CH_2-C=C), 3 67 (s, 2H, NH_2), 6 63 (m, 1H, aromatic proton), 6 77 (m, 1H, aromatic proton), 6 89 (d, 1H, J=7 9 Hz, aromatic proton), 7 13 (t, 1H, J=7 9 Hz, aromatic proton) and 7 23 (t, 1H, J=2 7 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 58, 29 83, 38 24 (ring saturated cyclopentane carbons), 116 69, 117 20, 121 28, 129 94, 133 09, 136 28, 136 88, 147 02 (aromatic and vinylic carbons) and 208 79 (C=O) ppm

Found C, 76 83, H, 6 97, N, 7 42 $C_{12}H_{13}NO$ requires C, 76 98, H, 7 00, N, 7 48%

6 22 2-(3-Dimethylaminobenzylidene)cyclopentanone (439n)

2-(3-Dimethylaminobenzylidene)cyclopentanone was prepared from 3-dimethylaminobenzaldehyde (3 1 g, 14 mmol) yielding orange plates of product

(2 15 g, 48%), melting range 92-93 °C The reaction was analogous to the general synthesis of 2-benzylidenecyclopentanone with one minor modification

After acid hydrolysis the aqueous layer was separated and neutralised with a 10% aqueous solution of sodium hydroxide The aqueous layer was extracted with diethyl ether (2 X 50 cm^3) The organic layer was washed with water (2 X 30 cm^3) and dried over magnesium sulphate After removal of the diethyl ether, recrystallisation from methanol furnished 2-(3-dimethylaminobenzylidene)-cyclopentanone

IR (KBr pellet) 2960, 2918 (aromatic and aliphatic CH), 2810, 1703 (C=O), 1618, 1597, 1501, 1449, 1358, 1236, 1182, 995, 925, 844, 773 and 686 cm^{-1}

^{1}H-NMR δ 1 95 (m, 2H, J = 7 7 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 33 (t, 2H, J = 7 7 Hz, CH_2-C=O), 2 86-2 94 (m, 8H, NMe_2 and CH_2-C=C), 6 68 (m, 1H, aromatic proton), 6 79 (m, 1H, aromatic proton), 6 85 (d, 1H, J=7 9 Hz, aromatic proton), 7 21 (t, 1H, J=7 9 Hz, aromatic proton) and 7 30 (t, 1H, J=2 8 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 63, 29 81, 38 26 (nng saturated cyclopentane carbons), 40 93 (Me_2), 114 10, 115 18, 119 03, 129 68, 133 94, 135 97, 136 54, 151 04 (aromatic and vinylic carbons) and 208 68 (C=O) ppm

Found C, 77 80, H, 7 95, N, 6 51 $C_{14}H_{17}NO$ requires C, 78 10, H, 7 96, N, 6 51%

6 23 2-(3,4-Dimethoxybenzylidene)cyclopentanone (439o)

2-(3,4-Dimethoxybenzylidene)cyclopentanone was prepared from 3,4-dimethoxybenzaldehyde (4 15 g, 25 mmol) yielding pale yellow crystals of product (4 76 g, 82%), melting range 111-112 °C (lit [315], 113-114 °C)

IR (KBr pellet) 3080, 2967 (aromatic and aliphatic CH), 2944 (OMe), 1703 (C=O), 1623, 1593, 1519, 1333, 1265, 1210, 1187, 1138, 1021, 939 and 809 cm^{-1}

^{1}H-NMR δ 1 97 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 33 (t, 2H, J=7 5 Hz, CH_2-C=O), 2 91 (t of d, 2H, J_1=7 5 Hz, J_2=2 5 Hz, CH_2-C=C), 3 84 (s, 3H, OMe), 3 85 (s, 3H, OMe), 6 84 (d, 1H, J=8 2 Hz, aromatic proton), 7 04 (d, 1H, J=1 8 Hz, aromatic proton), 7 09 (d of d, J_1=8 2 Hz, J_2=1 8 Hz, aromatic proton) and 7 27 (t, 1H, J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 53, 29 64, 38 11 (cyclopentane ring saturated carbons), 56 24 56 33 (both OMe), 111 48, 113 56, 124 78, 128 90, 132 87, 134 27, 149 24, 150 61 (aromatic and vinylic carbons) and 208 38 (C=O) ppm

6 24 2-(3-Methoxy-4-Methylbenzylidene)cyclopentanone (439p)

2-(3-Methoxy-4-methylbenzylidene)cyclopentanone was prepared from 3-methoxy-4-methylbenzaldehyde (3 75 g, 25 mmol) yielding golden plates of product (2 72 g, 50%), melting range 91-92 °C

IR (KBr pellet) 3068, 2962, 2921 (aromatic and aliphatic CH), 2839 (OMe), 1702 (C=O), 1614, 1599, 1509, 1459, 1304, 1224, 1183, 1136, 1033, 939, 887, 807 and 617 cm^{-1}

^{1}H-NMR δ 2 06 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 27 (s, 1H, Me), 2 43 (t, 2H, J=7 5 Hz, CH_2-C=O), 3 01 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 88 (s, 1H, OMe), 7 00 (s, 1H, aromatic proton), 7 10 (d, 1H, J=7 6 Hz), 7 20 (d, 1H, 7 6 Hz) and 7 39 (t, 1H, J=2 6 Hz, vinylic proton) ppm

^{13}C-NMR δ 16 72 (Me), 20 58, 29 79, 38 20 (cyclopentane ring saturated carbons), 55 64 (Me), 112 25, 123 17, 129 18, 131 17, 133 16, 134 77, 135 79, 158 13 (aromatic and vinylic carbons) and 208 54 (C=O) ppm

Found C, 77 34, H, 7 48 $C_{14}H_{16}O_2$ requires C, 77 75, H, 7 46%

6 25 2-(3,4-Dimethylbenzylidene)cyclopentanone (439q)

2-(3,4-Dimethylbenzylidene)cyclopentanone was prepared from 3,4-dimethylbenzaldehyde (3 45 g, 25 mmol) yielding off-white crystals of product (2 15 g, 43%), melting range 85-87 °C

IR (KBr pellet) 2962, 2906 (aromatic and aliphatic CH), 1702 (C=O), 1619, 1503, 1459, 1407, 1290, 1185, 1124, 1012, 927, 817 and 710 cm^{-1}

^{1}H-NMR δ 1 91 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 19 (s, 6H, Me), 2 29 (t, 2H, J=7 6 Hz, CH_2-C=O), 2 86 (t of d, 2H, J_1=7 6 Hz, J_2=2 5 Hz, CH_2-C=C), 7 07 (d, 1H, J=7 6 Hz, aromatic proton), 7 18-7 20 (m, 2H, aromatic protons) and 7 25 (t, 1H J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 22, 20 27 (both Me), 20 58, 29 80, 38 19 (cyclopentane ring saturated carbons), 128 48, 130 42, 132 35, 132 94, 133 57, 135 36, 137 33, 138 92 (aromatic and vinylic carbons) and 208 60 (C=O) ppm

Found C, 83 91, H, 7 94 $C_{14}H_{16}O$ requires C, 83 96, H, 8 05%

6 26 2-(4-Methoxy-3-Methylbenzylidene)cyclopentanone (439r)

2-(4-Methoxy-3-methylbenzylidene)cyclopentanone was prepared from 4-methoxy-3-methylbenzaldehyde (4 56 g, 30 mmol) yielding pale lemon plates of product (4 80 g, 74%), melting range 80-82 °C

IR (KBr pellet) 2963, 2928 (aromatic and aliphatic CH), 2841 (OMe), 1706 (C=O), 1625, 1599, 1505, 1460, 1440, 1265, 1240, 1190, 1136, 1025, 915, 819 and 758 cm^{-1}

^{1}H-NMR δ 1 95 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 16 (s, 3H, Me), 2 32 (t, 2H, J=7 5 Hz, CH_2-C=O), 2 89 (t of d, 2H, J_1=7 5 Hz, J_2=2 4 Hz, CH_2-C=C), 3 79 (s,

3H, OMe), 6.79 (d, 1H, J=8.4 Hz, aromatic proton) and 7.26-7.33 (m, 3H, aromatic and vinylic protons) ppm.

^{13}C-NMR: δ 15.33, 19.13, 28.30, 36.74 (cyclopentane ring saturated carbons and Me), 54.38 (OMe), 108.92, 125.99, 126.75, 129.15, 131.52, 131.96, 132.40, 157.85 (aromatic and vinylic carbons) and 207.16 (C=O) ppm.

Found: C, 77.47; H, 7.46. $C_{14}H_{16}O_2$ requires C, 77.75; H, 7.46%.

6.27 2-Benzylidenecyclopentanone (481)

2-Benzylidenecyclopentanone was prepared from benzaldehyde (10.2 g, 100 mmol) yielding light brown crystals of product (11.8 g, 69%), melting range 68-69 °C (lit.[282], 69–70 °C).

IR (KBr pellet): 3024, 2955, 2909 (aromatic and aliphatic CH), 1712 (C=O), 1619, 1572, 1490, 1401, 1322, 1276, 1173, 898, 820 and 697 cm^{-1}.

^{1}H-NMR: δ 2.06 (m, 2H, J=7.6 Hz, CH_2-CH_2-CH_2), 2.44 (t, 2H, J=7.6 Hz, CH_2-C=O), 3.01 (t of d, 2H, J_1=7.6Hz, J_2=2.0 Hz, CH_2-C=C), 7.37-7.46 (m, 4H, aromatic and vinylic protons) and 7.55-7.57 (m, 2H, aromatic protons) ppm.

^{13}C-NMR: δ 20.60, 29.76, 38.20 (ring saturated cyclopentane carbons), 129.10, 129.18, 129.72, 130.91, 131.15, 132.71, 135.93, 136.47 (aromatic and vinylic carbons) and 208.58 (C=O) ppm.

6.28 General Procedure for the Preparation of Arylidenecyclopentanone Oximes (440a,d-j,m-r)

The desired arylidenecyclopentanone (20 mmol) was added to a solution containing pyridine (2.4 g, 30 mmol) and hydroxylamine hydrochloride (2.1 g, 30 mmol) in ethanol (40 cm^3) in a 100 cm^3 round-bottom flask. The mixture was then heated under reflux for 1 hour and allowed to cool. The ethanol was removed on a

rotary evaporator and 30 cm^3 of ice / water was added The solution was allowed to stir for 1 hour and then vacuum filtered and washed with cold water yielding the crude oxime Recrystallisation was from methanol unless otherwise stated

6 29 2-(4-Hydroxybenzylidene)cyclopentanone Oxime (440a)

2-(4-Hydroxybenzylidene)cyclopentanone oxime was prepared from 2-(4-hydroxybenzylidene)cyclopentanone (3 77 g, 20 mmol) yielding orange crystals of product (2 7 g, 66%), melting range 179-181 °C (degrad)

IR (KBr pellet) 3530, 3141 (N-OH and OH), 2959, 2917 (aromatic and aliphatic CH), 1639, 1603, 1516, 1448, 1400, 1265, 1172, 1108, 1047, 930, 889, 826 and 724 cm^{-1}

^{1}H-NMR (DMSO) δ 1 76 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 44 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 67 (t of d, 2H, J_1=7 5 Hz, J_2=2 4 Hz, CH_2-C=C), 6 77 (d, 2H, J=8 6 Hz, aromatic protons), 6 96 (s, 1H, vinylic proton), 7 26 (d, 2H, J=8 6 Hz, aromatic protons), 9 62 and 10 73 (NOH and OH) ppm

^{13}C-NMR (DMSO) δ 23 75, 28 08, 32 56 (nng saturated cyclopentane carbons), 116 49, 123 73, 130 43, 132 02, 135 24, 158 38 (aromatic and vinylic carbons) and 164 77 (C=N) ppm

Found C, 70 90, H, 6 64, N, 6 53 $C_{12}H_{13}NO_2$ requires C, 70 92, H, 6 45, N, 6 89%

6 30 2-(4-Aminobenzylidene)cyclopentanone Oxime (440d)

2-(4-Aminobenzylidene)cyclopentanone oxime was prepared from 2-(4-aminobenzylidene)cyclopentanone (2 17 g, 10 mmol) yielding deep red crystals of product (1 85 g, 80%), melting range 206-207 °C (decomp)

IR (KBr pellet) 3356 (NH_2), 3298 (NOH), 2965, 2855 (aromatic and aliphatic CH), 1594, 1513, 1461, 1433, 1385, 1267, 1184, 936 and 901 cm^{-1}

^{1}H-NMR δ 1 80 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 57 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 70 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 70 (s, 2H, NH_2), 6 60 (d of t, 2H, J_t=9 0 Hz, J_d=2 2 Hz, aromatic protons), 7 02 (t, 1H, J=2 6 Hz, vinylic proton) and 7 18 (d, 2H, J=9 0 Hz, aromatic protons) ppm

^{13}C-NMR (DMSO) δ 22 47, 27 05, 31 31 (nng saturated cyclopentane carbons), 114 03, 121 75, 125 04, 130 04, 131 85, 148 60 (aromatic and vinylic carbons) and 161 46 (C=N) ppm

UV (methanol) λ_{max} 330 (ε=21941), 236 (ε=10830), 208 nm (ε=14824)

Found C, 70 96, H, 6 95, N, 13 63 $C_{12}H_{14}N_2O$ requires C, 71 26, H, 6 98, N, 13 85%

6 31 2-(4-Dimethylaminobenzylidene)cyclopentanone Oxime (440e)

2-(4-Dimethylaminobenzylidene)cyclopentanone oxime was prepared from 2-(4-dimethylaminobenzylidene)cyclopentanone (4 31 g, 20 mmol) yielding orange crystals of product (3 92 g, 85%), melting range 196-198 °C (decomp)

IR (KBr pellet) 3187 (OH), 2972, 2907 (aromatic and aliphatic CH), 1599, 1524, 1446, 1366, 1299, 1186, 933 and 809 cm^{-1}

^{1}H-NMR δ 1 80 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 58 (t, 2H, 7 6 Hz, CH_2-C=N), 2 72 (t of d, 2H, J_1=7 6 Hz, J_2=2 4 Hz, CH_2-C=C), 2 91 (s, 6H, NMe_2), 6 63 (d, 2H, J=9 0 Hz, aromatic protons), 7 04 (t, 1H, J=2 4 Hz, vinylic proton), 7 26 (d, 2H, J=9 0 Hz, aromatic protons) and 8 38 (s, 1H, NOH) ppm

^{13}C-NMR δ 22 97, 27 43, 31 82 (cyclopentane ring saturated carbons), 40 74 (NMe_2), 112 29, 112 42, 123 80, 125 86, 131 05, 132 43, 132 98, 150 04 (aromatic and vinylic carbons) and 164 81 (C=N) ppm

Found C, 72 81, H, 7 92, N, 12 16 $C_{14}H_{18}N_2O$ requires C, 73 01, H, 7 88, N, 12 16%

6 32 2-(2,5-Dimethoxybenzylidene)cyclopentanone Oxime (440f)

2-(2,5-Dimethoxybenzylidene)cyclopentanone oxime was prepared from 2-(2,5-dimethoxybenzylidene)cyclopentanone (3 48 g, 15 mmol) yielding yellow cystals of product (3 12 g, 84%), melting range 119-121 °C

IR (KBr pellet) 3206 (OH), 2972, 2930 (aromatic and aliphatic CH), 2832 (OMe), 1609, 1497, 1459, 1424, 1282, 1226, 1181, 1046, 965, 921, 804 and 693 cm^{-1}

^{1}H-NMR δ 1 77 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 58 (t, 2H, 7 5 Hz, CH_2-C=N), 2 68 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 71 (s, 3H, OMe), 3 73 (s, 3H, OMe), 6 73 (m, 2H, aromatic protons), 6 87 (d, 1H, J=2 4 Hz, aromatic proton), 7 35 (t, 1H, J=2 6 Hz, vinylic proton) and 8 02 (s, 1H, NOH) ppm

^{13}C-NMR δ 22 88, 27 45, 31 90 (cyclopentane ring saturated carbons), 56 16, 56 48 (both OMe), 111 79, 113 66, 115 90, 118 24, 127 41, 137 48, 152 58, 153 44 (aromatic and vinylic carbons) and 164 04 (C=N) ppm

Found C, 67 78, H, 7 02, N, 5 56 $C_{14}H_{17}NO_3$ requires C, 68 00, H, 6 93, N, 5 66%

6 33 2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone Oxime (440g)

2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone oxime was prepared from 2-(10H-phenothiazin-1-ylmethylene)cyclopentanone (1 15 g, 3 92 mmol) yielding bright orange crystals of product (1 12 g, 93%), melting range 129-130°C (decomp)

IR (KBr pellet) 3373 (NH), 3154 (NOH), 2961, 2925 (aromatic and aliphatic CH), 2872, 1477, 1437, 1402, 1287, 1126, 1054, 1026, 951, 920, 857 and 743 cm^{-1}

^{1}H-NMR δ 1 73 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 55 (d of d, 2H, J_1=7 4 Hz, J_2=2 4 Hz, CH_2-C=C), 2 62 (t, 2H, J=7 4 Hz, CH_2-C=N), 6 26 (s, 1H, NH), 6 58 (d of d, 1H, J_1=7 8 Hz, J_2=1 0 Hz, aromatic proton), 6 72-6 77 (m, 2H, aromatic protons), 6 84-6 91 (m, 4H, aromatic proton), 7 07 (s, 1H, vinylic proton) and 8 99 (s, 1H, N-OH) ppm

^{13}C-NMR δ 22 76, 28 02, 31 62 (cyclopentane ring saturated carbons), 115 62, 117 41, 118 91, 119 05, 122 02, 122 75, 123 21, 126 66, 126 99, 127 72, 128 03, 140 36, 140 73, 141 87 (aromatic and vinylic carbons) and 163 73 (C=N) ppm

Found C, 70 28, H, 5 60, N, 9 41 $C_{18}H_{16}N_2OS$ requires C, 70 10, H, 5 23, N, 9 08 %

6 34 2-(3-Phenylallylidene)cyclopentanone Oxime (440h)

2-(3-Phenylallylidene)cyclopentanone oxime was prepared from 2-(3-phenylallylidene)cyclopentanone (3 97 g, 20 mmol) yielding red crystals of product (3 20 g, 75%), melting range 167-168 °C

IR (KBr pellet) 3282 (OH), 3026, 2955, 2917 (aromatic and aliphatic CH), 1600, 1449, 1432, 1291, 1231, 1029, 963, 928, 754 and 692 cm^{-1}

^{1}H-NMR δ 1 82 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 59-2 65 (m, 4H, CH_2-C=N and CH_2-C=C), 6 63 (d, 1H, J=12 8 Hz, vinylic proton), 6 84-6 90 (m, 2H, vinylic protons), 7 13-7 17 (m, 1H, aromatic proton), 7 25 (t, 2H, J=7 4 Hz, aromatic proton), 7 36 (d, 2H, J=7 4 Hz, aromatic proton) and 8 29 (s, 1H, NOH) ppm

^{13}C-NMR δ 22 33, 28 40, 30 08 (cyclopentane ring saturated carbons), 123 50, 126 19, 127 00, 128 28, 129 08, 135 51, 137 68, 137 79 (aromatic and vinylic carbons) and 163 23 (C=N) ppm

Found C, 78 64, H, 7 07, N, 6 56 $C_{14}H_{15}NO$ requires C 78 84, H, 7 09, N, 6 57%

6 35 2-(3-t-Butylbenzylidene)cyclopentanone Oxime (440i)

2-(3-t-Butylbenzylidene)cyclopentanone oxime was prepared from 2-(3-t-butylbenzylidene)cyclopentanone (2 28 g, 10 mmol) yielding white plates of product (1 51 g, 62%), melting range 109-111 °C

IR (KBr pellet) 3284 (OH), 2960, 2918 (aromatic and aliphatic CH), 1596, 1416, 1362, 1277, 1195, 1047, 939, 910, 791, 730 and 699 cm^{-1}

^{1}H-NMR δ 1 16 (s, 9H, CMe_3), 1 71 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 51 (t, 2H, J=7 4Hz, CH_2-C=N), 2 65 (t of d, 2H, J_1=7 4Hz, J_2=2 3 Hz, CH_2-C=C), 7 21-7 24 (m, 4H, aromatic and vinylic protons) and 7 26 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 22 99, 27 56, 31 73, 32 00, 35 06 (cyclopentane ring saturated carbons, $\underline{C}Me_3$ and $C\underline{Me_3}$), 124 22, 124 99, 126 73, 127 06, 128 48, 136 68, 137 13, 151 51 (aromatic and vinylic carbons) and 164 23 (C=N) ppm

Found C, 78 86, H, 8 82, N, 5 48 $C_{16}H_{21}NO$ requires C, 78 97, H, 8 70, N, 5 76%

6 36 2-(3-Hydroxybenzylidene)cyclopentanone Oxime (440j)

2-(3-Hydroxybenzylidene)cyclopentanone oxime was prepared from 2-(3-hydroxybenzylidene)cyclopentanone (3 77 g, 20 mmol) yielding sandy brown coloured crystals of product (2 9 g, 71%), melting range 130-131 °C

IR (KBr pellet) 3458, 3212 (N-OH and OH), 2962, 2915 (aromatic and aliphatic CH), 1618, 1579, 1470, 1335, 1294, 1225, 1161, 968, 925, 778 and 687 cm^{-1}

^{1}H-NMR (DMSO) δ 1 79 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 58 (t, 2H, J=7 4 Hz, CH_2-C=N), 2 71 (t of d, 2H, J_1=7 4 Hz, J_2=2 6 Hz, CH_2-C=C), 6 68 (m, 1H, aromatic proton), 6 79 (s, 1H, aromatic proton), 6 89 (d, 1H, J=8 0 Hz, aromatic proton), 7 04 (t, 1H, J=2 6 Hz, vinylic proton), 7 14 (t, 1H, J=8 0 Hz, aromatic proton), 9 21 (s, 1H, OH) and 10 74 (s, 1H, NOH) ppm

^{13}C-NMR δ 22 87, 27 47, 31 90 (nng saturated cyclopentane carbons), 115 11, 116 43, 122 67, 123 49, 129 95, 137 43, 138 98, 155 95 (aromatic and vinylic carbons) and 164 57 (C=N) ppm

Found C, 70 89, H, 6 62, N, 6 66 $C_{12}H_{13}NO_2$ requires C, 70 92, H, 6 45, N, 6 89%

6 37 2-(3-Aminobenzylidene)cyclopentanone Oxime (440m)

2-(3-Aminobenzylidene)cyclopentanone oxime was prepared from 2-(3-aminobenzylidene)cyclopentanone (2 81 g, 15 mmol) yielding gold flakes of product (2 80 g, 92%), melting range 150-151 °C (decomp)

IR (KBr pellet) 3373 (NH_2), 3199 (NOH), 2926, 2857 (aromatic and aliphatic CH), 1602, 1579, 1493, 1450, 1243, 1049, 956, 826 and 762 cm^{-1}

^{1}H-NMR δ 1 80 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2) 2 58 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 73 (t of d, 2H, J_1=7 5 Hz, J_2=2 7 Hz, CH_2-C=C), 3 60 (s, broad, NH_2), 6 54 (m, 1H, aromatic proton), 6 66 (s, 1H, aromatic proton), 6 77 (d, 1H, J=7 9 Hz, aromatic proton), 7 03 (t, 1H, J=2 7 Hz, vinylic proton) and 7 08 (t, 1H, J=7 9 Hz, aromatic proton) ppm

^{13}C-NMR δ 22 93, 27 37, 31 94 (nng saturated cyclopentane carbons), 114 91, 116 29, 120 39, 123 71, 129 64, 136 99, 138 52, 146 67 (aromatic and vinylic carbons) and 164 32 (C=N) ppm

UV (methanol) λ_{max} 296 (ε=23587), 240 (ε=14630), 212 nm (ε=21431)

Found C, 71 00, H, 6 95, N, 13 59 $C_{12}H_{14}N_2O$ requires C, 71 26, H, 6 98, N, 13 85%

6 38 2-(3-Dimethylaminobenzylidene)cyclopentanone Oxime (440n)

2-(3-Dimethylaminobenzylidene)cyclopentanone oxime was prepared from 2-(3-dimethylaminobenzylidene)cyclopentanone (1 94 g, 9 mmol) yielding bright orange plates of product (1 71 g, 82%), melting range 157-158 °C

IR (KBr pellet) 3272 (NOH), 2920, 2858 (aromatic and aliphatic CH), 2808, 1606, 1588, 1566, 1493, 1433, 1351, 1304, 1240, 1203, 1154, 999, 931, 775 and 687 cm^{-1}

^{1}H-NMR δ 1 79 (m, 2H, J=7 5 Hz, CH_2-$C\underline{H_2}$-CH_2), 2 60 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 76 (d of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 2 88 (s, 6H, NMe_2), 6 61 (d of d, 1H, J_1=7 8 Hz, J_2=2 4 Hz, aromatic proton), 6 70 (s, 1H, aromatic proton), 6 75 (d, 1H, J=7 8 Hz, aromatic proton), 7 10 (t, 1H, J=2 6 Hz, vinylic proton) and 7 16 (t, 1H, J=7 8 Hz, aromatic proton)ppm

^{13}C-NMR δ 22 97, 27 50, 31 99 (nng saturated cyclopentane carbons), 41 13 (NMe_2), 112 57, 114 30, 118 35, 124 55, 129 37, 136 64, 138 16, 150 94 (aromatic and vinylic carbons) and 164 27 (C=N) ppm

Found C, 72 92, H, 7 95, N, 11 89 $C_{14}H_{18}N_2O$ requires C, 73 01, H, 7 88, N, 12 16%

6 39 2-(3,4-Dimethoxybenzylidene)cyclopentanone Oxime (440o)

2-(3,4-Dimethoxybenzylidene)cyclopentanone oxime was prepared from 2-(3,4-dimethoxybenzylidene)cyclopentanone (4 65 g, 20 mmol) yielding yellow crystals of product (3 91 g, 79%), melting range 151-153 °C (lit [316], 114-116 °C)

IR (KBr pellet) 3188 (OH), 2960, 2918 (aromatic and aliphatic CH), 2836 (OMe), 1597, 1516, 1466, 1420, 1333, 1255, 1143, 1022, 956, 923, 892, 812 and 762 cm^{-1}

^{1}H-NMR δ 1 82 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 60 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 74 (t of d, 2H, J_1=7 5 Hz, J_2=2 4 Hz, CH_2-C=C), 3 82 (s, 3H, OMe), 3 83 (s, 3H, OMe), 6 80 (d, 1H, J=8 4 Hz, aromatic proton), 6 88 (d, 1H, J=1 8 Hz, aromatic proton), 6 94 (d of d, J_1=8 4 Hz, J_2=1 8 Hz, aromatic proton) and 7 07 (t, 1H, J=2 4 Hz, vinylic proton) ppm

^{13}C-NMR δ 22 93, 27 42, 31 80 (cyclopentane ring saturated carbons), 56 24, 56 30 (OMe), 111 41, 112 82, 122 75, 123 49, 130 59, 135 06, 149 01, 149 05 (aromatic and vinylic carbons) and 164 33 (C=N) ppm

6 40 2-(3-Methoxy-4-Methylbenzylidene)cyclopentanone Oxime (440p)

2-(3-Methoxy-4-methylbenzylidene)cyclopentanone oxime was prepared from 2-(3-methxoy-4-methylbenzylidene)cyclopentanone (2 38 g, 11 mmol) yielding golden crystals of product (2 43 g, 95%), melting range 147-149 °C

IR (KBr pellet) 3215 (NOH), 2949, 2918 (aromatic and aliphatic CH), 2841 (OMe), 1615, 1561, 1507, 1460, 1413, 1270, 1239, 1156, 1133, 1035, 961, 925, 805, 744 and 703 cm^{-1}

^{1}H-NMR δ 1 91 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 25 (s, 3H, Me), 2 71 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 85 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 86 (s 3H, OMe), 6 89 (s, 1H, aromatic proton), 6 97 (m, 1H, aromatic proton), 7 14 (d, 1H, J=7 6 Hz, aromatic proton) and 7 20 (t, 1H, J=2 6 Hz, vinylic proton) ppm

^{13}C-NMR δ 16 55 (Me), 22 94, 27 51, 31 97 (cyclopentane ring saturated carbons), 55 64 (OMe), 111 35, 121 82, 123 92, 126 78, 130 86, 136 16, 136 34, 157 92 (aromatic and vinylic carbons) and 164 25 (C=N) ppm

Found C, 72 57, H, 7 47, N, 6 03 $C_{14}H_{17}NO_2$ requires C, 72 70, H, 7 41, N, 6 06%

6.41 2-(3,4-Dimethylbenzylidene)cyclopentanone Oxime (440q)

2-(3,4-Dimethylbenzylidene)cyclopentanone oxime was prepared from 2-(3,4-dimethylbenzylidene)cyclopentanone (3 23 g, 15 mmol) yielding orange crystals of product (2 81 g, 87%), melting range 157-159 °C (decomp)

IR (KBr pellet) 3199 (OH), 2971, 2916 (aromatic and aliphatic CH), 1605, 1501, 1438, 1288, 1233, 1051, 945, 921, 748 and 711 cm^{-1}

^{1}H-NMR δ 1 80 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 19 (s, 6H, Me), 2 60 (t, 2H, J=7 6 Hz, CH_2-C=N), 2 73 (t of d, 2H, J_1=7 6 Hz, J_2=2 4 Hz, CH_2-C=C) and 7 04-7 11 (m, 4H, aromatic and vinylic protons) ppm

^{13}C-NMR δ 20 04, 20 29, 22 94, 27 51, 31 93 (cyclopentane ring saturated carbons and Me), 123 74, 127 17, 130 08, 131 16, 135 14, 135 91, 136 59, 136 91 (aromatic and vinylic carbons) and 164 32 (C=N) ppm

Found C, 77 80, H, 7 95, N, 6 40 $C_{14}H_{17}NO$ requires C, 78 10, H, 7 96, N, 6 51%

6 42 2-(4-Methoxy-3-Methylbenzylidene)cyclopentanone Oxime (440r)

2-(4-Methoxy-3-methylbenzylidene)cyclopentanone oxime was prepared from 2-(4-methoxy-3-methylbenzylidene)cyclopentanone (3 47 g, 15 mmol) yielding pale lemon crystals of product (3 19 g, 92%), melting range 136-138 °C

IR (KBr pellet) 3145 (OH), 2973, 2923 (aromatic and aliphatic CH), 2834 (OMe), 1594, 1505, 1462, 1454, 1258, 1136, 1025, 954, 925, 894, 804, 760 cm^{-1}

^{1}H-NMR δ 1 81 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 15 (s, 3H, Me), 2 59 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 72 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 78 (s, 3H, OMe), 6 75 (d, 1H, J=8 4 Hz, aromatic proton), 7 04 (t, 1H, J=2 6 Hz, vinylic proton) and 7 15-7 19 (m, 2H, aromatic protons) ppm

^{13}C-NMR δ 16 76 (Me), 22 95, 27 39, 31 79 (cyclopentane nng saturated carbons), 55 76 (OMe) 110 13, 123 37, 126 91, 128 61, 129 81, 132 18, 134 50, 157 65 (aromatic and vinylic carbons) and 164 54 (C=N) ppm

Found C, 72 59, H, 7 12, N, 5 96 $C_{14}H_{17}NO_2$ requires C, 72 70, H, 7 41, N, 6 06%

6 43 Irradiation of 2-(4-Aminobenzylidene)cyclopentanone Oxime (440d)

2-(4-Aminobenzylidene)cyclopentanone oxime (527 mg, 2 61 mmole) was dissolved in methanol (225 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 50 50 light petroleum/ethyl acetate After 20 minutes a number of new spots had appeared on TLC After 2 hours one of the new spots had become the sole component while the other new spots and the starting material had faded After 3 5 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 50 50 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 7-amino-2,3-dihydro-1H-cyclopenta{b}quinoline (456) (168 mg, 36%), melting range 94-96 °C

IR (KBr pellet) 3438, 3157, 2964, 2927 (aromatic and aliphatic CH), 2857, 1636, 1563, 1515, 1460, 1401, 1322, 1198, 1113 and 1046 cm^{-1}

^{1}H-NMR δ 2 15 (m, 2H, J=7 6 Hz CH_2-C<u>H</u>$_2$-CH_2), 3 02 (t, 2H, J=7 6 Hz, CH_2), 3 26 (t, 2H, J=7 6 Hz, CH_2), 6 89 (d of d, 1H, J_1=8 5 Hz, J_2=2 3 Hz, aromatic proton), 7 36 (s, 1H, aromatic proton), 7 50 (d, 1H, J=8 5 Hz) and 7 80 (d, 1H, J=2 3 Hz, aromatic protons) ppm

^{13}C-NMR δ 23 15, 30 73, 31 59 (nng saturated cyclopentane carbons), 100 25, 119 26, 122 38, 123 97, 129 47, 133 76, 142 24, 148 56 and 152 67 (aromatic carbons) ppm

UV (methanol) λ_{max} 390 (ε=4252), 300 (ε=4779), 258 (ε=18105) and 226 nm (ε=12063)

Found C, 78 11, H, 6 68, N, 15 17 $C_{12}H_{12}N_2$ requires C, 78 23, H, 6 57, N, 15 20%

6 44 Irradiation of 2-(3-Aminobenzylidene)cyclopentanone Oxime (440m)

2-(3-Aminobenzylidene)cyclopentanone oxime (626 2 mg, 3 10 mmole) was dissolved in methanol (225 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 50 50 light petroleum/ethyl acetate After 1 hour four new spots had appeared on TLC After 3 hours the starting material and three of the new spots had faded leaving one spot as the sole component After 4 hours no further change had occurred so the photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 50 50 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 7-amino-2,3-dihydro-1H-cyclopenta[b]quinoline (470) (150 mg, 26%), melting range 121-122 °C

IR (KBr pellet) 3423, 3312 (NH_2), 3138, 2953, 2936 (aromatic and aliphatic CH), 1638, 1626, 1510, 1401, 1368, 1322, 1245, 1220, 1136, 1032, 913, 821 and 747 cm^{-1}

^{1}H-NMR δ 2 04 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 89 (t, 2H, J=7 4 Hz, CH_2), 2 98 (t, 2H, J=7 4 Hz, CH_2), 3 84 (s, 2H, NH_2), 6 71 (d, 1H, J=2 4 Hz, aromatic proton), 6 93 (d of d, 1H, J_1=8 8 Hz, J_2=2 4 Hz, aromatic proton), 7 51 (s, 1H, aromatic proton) and 7 72 (d, 1H, J=8 8 Hz, aromatic protons) ppm

^{13}C-NMR δ 24 05, 30 91, 34 47 (nng saturated cyclopentane carbons), 108 45, 120 67, 128 93, 129 13, 129 70, 136 29, 142 68, 144 35 and 164 44 (aromatic carbons) ppm

UV (methanol) λ_{max} 354 (ε=4969), 248 (ε=29679) and 224 nm (ε=27141)

Found C, 77 99, H, 6 62, N, 15 11 $C_{12}H_{12}N_2$ requires C, 78 23, H, 6 57, N, 15 20%

6 45 General Procedure for the Arylidenecyclopentanone Oxime O-Acetates (441a-b,e-k,n-r)

The desired arylidenecyclopentanone oxime (15 mmol) was added to pyridine (25 cm^3) in a 100 cm^3 round-bottom flask with stirring at room temperature until the oxime was totally dissolved The resulting solution was then cooled to 5 °C in an ice bath While the solution was stirred vigorously and maintained at 5 °C, acetyl chloride (2 1 g, 20 mmol) was added dropwise When all the acetyl chloride had been added, the solution was stirred at room temperature for one hour and then crushed ice (50 g) was added with stirring When all the ice had melted, the resulting arylidenecyclopentanone oxime acetate suspension was filtered on a Buchner funnel and washed thoroughly with cold water The crude O-acetate was recrystallised from methanol unless otherwise stated

6 46 2-(4-Hydroxybenzylidene)cyclopentanone Oxime O-Acetate (441a)

2-(4-Hydroxybenzylidene)cyclopentanone oxime O-acetate was prepared from 2-(4-hydroxybenzylidene)cyclopentanone oxime (2 3 g, 10 mmol) yielding yellow/orange crystals of product (1 95 g, 80%), melting range 153-154 °C

IR (KBr pellet) 3336 (OH), 2960, 2935 (aromatic and aliphatic CH), 1752 (C=O), 1609, 1576, 1512, 1372, 1283, 1223, 1172, 1008, 956, 882 and 833 cm^{-1}

^{1}H-NMR δ 1 82 (m, 2H, J=7 5 Hz, CH_2-CH_2-CH_2), 2 16 (s 3H, MeC=O), 2 64 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 71 (t of d, 2H, J_1=7 5 Hz, J_2=2 5 Hz, CH_2-C=C), 6 81 (m, 2H, aromatic protons), 7 20 (d, 2H, J=8 4 Hz, aromatic protons) and 7 34 (t, 1H, J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 18 (Me-C=O), 22 84, 29 52, 31 58 (ring saturated cyclopentane carbons), 116 03, 127 76, 129 27, 131 88, 132 13, 156 70, 169 88 and 171 25 (aromatic carbons) ppm

UV (methanol) λ_{max} 324 (ε=22814), 230 (ε=7581), 206 nm (ε=8077)

Found C, 68 26, H, 6 41, N, 5 52 $C_{14}H_{15}NO_3$ requires C, 68 56, H, 6 16, N, 5 71%

6 47 Preparation of 2-(4-Acetoxybenzylidene)cyclopentanone Oxime O-Acetate (441b)

2-(4-Hydroxybenzylidene)cyclopentanone oxime O-acetate (0 76 g, 3 1 mmol) was dissolved in a 5M sodium hydroxide solution (10 cm^3) Ice (10 g) was added to the mixture with stirring Acetic anhydride (1 25 g, 12 2 mmol) was added quickly to the solution with vigorous stirring The mixture was stirred for an additional 10 minutes and then filtered, yielding a pink powder The product was recrystallised from methanol, yielding yellow crystals of 2-(4-acetoxybenzylidene)cyclopentanone oxime O-acetate (0 85 g, 95%), melting range 107-108 °C

IR (KBr pellet) 3444, 2967, 2885 (aromatic and aliphatic CH), 1761 (C=O), 1598, 1509, 1416, 1367, 1195, 1013, 945, 913 and 882 cm^{-1}

^{1}H-NMR δ 1 83 (m, 2H, J=7 5 Hz, CH_2-C<u>H</u>$_2$-CH_2), 2 16 (s, 3H, MeC=O), 2 24 (s, 3H, MeC=O), 2 66 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 75 (d of d, 2H, J_1=7 5 Hz, J_2=2 5 Hz, CH_2-C=C), 7 03 (d, 2H, J=8 6 Hz, aromatic protons) 7 37 (d, 2H, J=8 6 Hz, aromatic protons) and 7 44 (t, 1H, J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 13, 21 57, 22 84, 29 46, 31 61 (cyclopentane ring saturated carbons and MeC=O), 122 06, 126 67, 131 12, 134 58, 135 26, 150 66 (aromatic and vinylic carbons), 169 42, 169 83 and 170 53 (C=N and two Me<u>C</u>=O) ppm

UV (methanol) λ_{max} 306 (ε=22537), 224 (ε=10717), 208 nm (ε=14825)

Found C, 66 84, H, 5 98, N, 4 85 $C_{16}H_{17}NO_4$ requires C, 66 89, H, 5 96, N, 4 87%

6 48 2-(4-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441e)

2-(4-Dimethylaminobenzylidene)cyclopentanone oxime acetate was prepared from 2-(4-dimethylaminobenzylidene)cyclopentanone oxime (3 45 g, 15mmol) yielding orange crystals of product (3 51 g, 86%), melting range 91-92 °C

IR (KBr pellet) 2971, 2899 (aromatic and aliphatic CH), 1740 (C=O), 1615, 1577, 1528, 1451, 1369, 1275, 1238, 1221, 1188, 1010, 961, 880 and 805 cm^{-1}

^{1}H-NMR δ 1 83 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 14 (s, 3H, MeC=O), 2 63 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 75 (t of d, 2H, J_1=7 5 Hz, J_2=2 4 Hz, CH_2-C=C), 2 92 (s, 6H, NMe_2), 6 63 (d, 2H, J=8 8 Hz, aromatic protons), 7 30 (d, 2H, J=8 8 Hz, aromatic proton) and 7 39 (t, 1H, J=2 4 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 21, 22 87, 29 56, 31 71 (cyclopentane ring saturated carbons and MeC=O), 40 61 (NMe_2), 112 25, 124 97, 128 12, 129 89, 131 67, 150 49 (aromatic and vinylic carbons), 169 58 and 171 32 (C=N and C=O) ppm

UV (methanol) λ_{max} 372 (ε=24611), 250 (ε=8832), 208 nm (ε=10524)

Found C, 70 64, H, 7 50, N, 10 23 $C_{16}H_{20}N_2O_2$ requires C, 70 56, H, 7 40, N, 10 29%

6 49 2-(2,5-Dimethoxybenzylidene)cyclopentanone Oxime O-Acetate (441f)

2-(2,5-Dimethoxybenzylidene)cyclopentanone oxime acetate was prepared from 2-(2,5-dimethoxybenzylidene)cyclopentanone oxime (2 97 g, 12 mmol) yielding golden crystals of product (2 92 g, 84%), melting range 112-113 °C

IR (KBr pellet) 2997, 2962 (aromatic and aliphatic CH), 2838 (OMe), 1760 (C=O), 1602, 1491, 1427, 1290, 1221, 1203, 1124, 1052, 1024, 996, 948, 881, 808 and 713 cm^{-1}

^{1}H-NMR δ 1 79 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 16 (s, 3H, MeC=O), 2 65 (t, 2H, J=7 4 Hz, CH_2-C=N), 2 70 (t of d, 2H, J_1=7 4 Hz, J_2=2 7 Hz, CH_2-C=C), 3 71 (s, 3H, OMe), 3 73 (s, 3H, OMe), 6 76 (m 2H, aromatic protons), 6 85 (d, 1H, J=1 6 Hz, aromatic proton) and 7 66 (t, 1H, J=2 7 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 18, 22 78, 29 44, 31 79 (MeC=O and cyclopentane ring saturated carbons), 56 16, 56 36 (both OMe), 111 75, 114 41, 116 16, 122 69, 126 71, 135 65, 152 86, 153 35 (aromatic and vinylic carbons), 169 61 and 170 41 (C=N and C=O) ppm

UV (methanol) λ_{max} 348 (ε=9224), 292 (ε=15149), 212 nm (ε=16063)

Found C, 66 36, H, 6 68, N, 4 73 $C_{16}H_{19}NO_4$ requires C, 66 42, H, 6 62, N, 4 84%

6 50 2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone Oxime O-Acetate (441g)

2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone oxime O-acetate was prepared from 2-(10H-phenothiazin-1-ylmethylene)cyclopentanone oxime (0 95 g, 3 08 mmol) yielding rusty brown needles of product (0 81 g, 75%), melting range 159-160 °C

IR (KBr pellet) 3330 (NH), 2959, 2926 (aromatic and aliphatic CH), 1764, 1736 (C=O), 1598, 1479, 1439, 1370, 1292, 1241, 1198, 1124, 1045, 1009, 943, 874, 858 and 743 cm^{-1}

^{1}H-NMR δ 1 86 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 26 (s, 3H, MeC=O), 2 65 (d of t, 2H, J_t=7 4 Hz, J_d=2 3 Hz, CH_2-C=C), 2 78 (t, 2H, J=7 4 Hz, CH_2-C=N), 6 18 (s,

1H, NH), 6 66 (d of d, 1H, J_1=8 0 Hz, J_2=1 2 Hz, aromatic proton), 6 79-6 87 (m, 4H, aromatic protons) and 7 42 (t, 1H, J=2 3 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 09, 22 64, 29 80, 31 68 (cyclopentane ring saturated carbons and MeC=O), 115 61, 118 76, 119 08, 121 46, 122 02, 122 10, 123 35, 127 00, 127 17, 127 79, 128 27, 139 34, 140 37, 141 49 (aromatic and vinylic carbons), 169 19 and 169 63 (C=N and C=O) ppm

UV (methanol) λ_{max} 206 (ε=12283), 252 (ε=18319), 312 (ε=8399) and 400 nm (ε=1760)

Found C, 68 54, H, 5 29, N, 7 87 $C_{20}H_{18}N_2O_2S$ requires C, 68 55, H, 5 18, N, 7 99%

6 51 2-(3-Phenylallylidene)cyclopentanone Oxime O-Acetate (441h)

2-(3-Phenylallylidene)cyclopentanone oxime acetate was prepared from 2-(3-Phenylallylidene)cyclopentanone oxime (2 56 g, 12 mmol) yielding yellow/orange crystals of product (2 60 g, 85%), melting range 97-99 °C

IR (KBr pellet) 3029, 2958, 2922 (aromatic and aliphatic CH), 1766 (C=O), 1638, 1578, 1365, 1307, 1195, 1001, 961, 942, 882, 756, 694 cm^{-1}

^{1}H-NMR δ 1 82 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 14 (s, 3H, MeC=O), 2 65 (m, 4H, CH_2-C=N and CH_2-C=C), 6 70 (d, 1H, J=15 6 Hz, vinylic proton), 6 82 (d, 1H, J=11 6 Hz, vinylic proton) and 7 15-7 39 (m, 6H, aromatic and vinylic protons) ppm

^{13}C-NMR δ 20 17, 22 27, 29 74, 30 30 (cyclopentane ring saturated carbons and MeC=O), 125 60, 127 25, 127 43, 128 75, 129 12, 135 74, 137 28, 137 66 (aromatic and vinylic carbons), 169 39 and 169 54 (C=N and C=O) ppm

UV (methanol) λ_{max} 334 (ε=37078), 234 (ε=9684), 206 nm (ε=13729)

Found C, 75 18, H, 6 89, N, 5 47 $C_{16}H_{17}NO_2$ requires C, 75 27, H, 6 71, N, 5 49%

6 52 2-(3-t-Butylbenzylidene)cyclopentanone Oxime O-Acetate (441i)

2-(3-t-Butylbenzylidene)cyclopentanone oxime acetate was prepared from 2-(3-t-butylbenzylidene)cyclopentanone oxime (1 95 g, 8 mmol) yielding a yellow oil as product (1 55 g, 68%)

IR (KBr pellet) 3024, 2963, 2872 (aromatic and aliphatic CH), 1770 (C=O), 1652, 1599, 1482, 1438, 1366, 1297, 1259, 1206, 1001, 939, 879, 798 and 703 cm^{-1}

^{1}H-NMR δ 1 24 (s, 9H, CMe_3), 1 81 (m, 2H, J=7 4 Hz, CH_2-$C\underline{H}_2$-CH_2) 2 13 (s, 3H, MeC=O), 2 64 (t, 2H, J=7 4 Hz, CH_2-C=N), 2 76 (t of d, 2H, J_1=7 4 Hz, J_2=2 4 Hz, CH_2-C=C), 7 21-7 24 (m, 3H, aromatic protons), 7 39 (s, 1H, aromatic proton) and 7 48 (t, 1H, J=2 4 Hz, vinylic proton) ppm

^{13}C-NMR δ 18 87 (MeC=O), 21 47, 28 05, 30 25, 30 31, 33 62 (cyclopentane ring saturated carbons, $\underline{C}Me_3$ and $C\underline{Me}_3$), 124 26, 125 43, 126 23, 126 74, 127 16, 133 25, 135 02, 150 22 (aromatic and vinylic carbons), 167 89 and 169 15 (C=N and C=O) ppm

UV (methanol) λ_{max} 304 (ε=47785) and 224 nm (ε=32183)

Found C, 75 74, H, 8 35, N, 4 83 $C_{18}H_{23}NO_2$ requires C, 75 76, H, 8 12, N, 4 91%

6 53 2-(3-Hydroxybenzylidene)cyclopentanone Oxime O-Acetate (441j)

2-(3-Hydroxybenzylidene)cyclopentanone oxime O-acetate was prepared from 2-(3-hydroxybenzylidene)cyclopentanone oxime (2 5 g, 12 mmol) yielding pale pink crystals of product (2 4 g, 80%), melting range 189-190 °C

IR (KBr pellet) 3355 (OH), 2971, 2945 (aromatic and aliphatic CH), 1738 (C=O), 1597, 1578, 1490, 1367, 1288, 1259, 1214, 1159, 1008, 951, 873, 796 and 701 cm^{-1}

^{1}H-NMR (DMSO) δ 1 83 (m, 2H, J=7 5 Hz, CH_2-$C\underline{H}_2$-CH_2), 2 18 (s 3H, $\underline{Me}C$=O), 2 67 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 78 (t of d, 2H, J_1=7 5 Hz, J_2=2 7 Hz, CH_2-C=C), 6 76 (d of d, 1H, J_1=7 8 Hz, J_2=2 2 Hz, aromatic proton), 6 92 (s, 1H, vinylic proton), 6 94 (d, 1H, J=7 8 Hz, aromatic proton), 7 23 (t, 1H, J=7 8 Hz, aromatic proton) and 9 56 (s, 1H, OH) ppm

^{13}C-NMR δ 19 91 (MeC=O), 22 37, 28 96, 31 32 (ring saturated cyclopentane carbons), 115 85, 116 22, 121 04, 126 10, 129 98, 135 74, 137 47, 157 76 (aromatic and vinylic carbons), 168 63 and 170 03 (C=N and C=O) ppm

UV (methanol) λ_{max} 300 (ε=20043), 224 (ε=8322), 208 nm (ε=14753)

Found C, 68 13, H, 6 22, N, 5 61 $C_{14}H_{15}NO_3$ requires C, 68 56, H, 6 16, N, 5 71%

6 54 Preparation of 2-(3-Acetoxybenzylidene)cyclopentanone Oxime O-Acetate (441k)

2-(3-Hydroxybenzylidene)cyclopentanone oxime O-acetate (0 71 g, 2 9 mmol) was dissolved in a 5M sodium hydroxide solution (10 cm^3) Ice (10 g) was added to the mixture with stirring Acetic anhydride (1 25 g, 12 2 mmol) was added quickly to the solution with vigorous stirring The reaction was stirred for 10 minutes and then filtered, yielding a pink powder The acetoxy product was recrystallised from methanol yielding white crystals of 2-(3-acetoxybenzylidene)cyclopentanone oxime O-acetate (0 78 g, 94%), melting range 110-111 °C

IR (KBr pellet) 3365, 2965, 2900 (aromatic and aliphatic CH), 1763 (C=O), 1598, 1578, 1480, 1374, 1209, 1002, 943, 912, 885 and 694 cm^{-1}

^{1}H-NMR δ 1 92 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H}_2$-CH_2), 2 25 (s, 3H, MeC=O), 2 34 (s, 3H, MeC=O), 2 75 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 85 (d of d, 2H, J_1=7 5 Hz, J_2=2 5 Hz, CH_2-C=C), 7 05 (d of d, 1H, J_1=8 0 Hz, J_2=1 6 Hz, aromatic proton) 7 18 (s, 1H, aromatic proton) 7 31 (d, 1H, J=8 0 Hz, aromatic proton), 7 40 (t, 1H, J=8 0 Hz, aromatic proton) and 7 52 (t, 1H, J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 13, 21 60, 22 84, 29 43, 31 68 (cyclopentane ring saturated carbons and MeC=O), 121 66, 122 67, 126 60, 127 72, 129 81, 136 31, 138 32, 151 03 (aromatic and vinylic carbons), 169 37, 169 85 and 170 32 (C=N and two Me$\underline{C}$=O) ppm

UV (methanol) λ_{max} 298 (ε=23760), 224 nm (ε=15818)

Found C, 66 75, H, 5 99, N, 4 81 $C_{16}H_{17}NO_4$ requires C, 66 89, H, 5 96, N, 4 87%

6 55 2-(3-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441n)

2-(3-Dimethylaminobenzylidene)cyclopentanone oxime O-acetate was prepared from 2-(3-dimethylaminobenzylidene)cyclopentanone oxime (2 45 g, 9 mmol), yielding bright yellow crystals of product (1 71 g, 82%), melting range 96-97 °C

IR (KBr pellet) 2946, 2919 (aromatic and aliphatic CH), 2811, 1763 (C=O), 1599, 1568, 1494, 1431, 1366, 1353, 1264, 1210, 1003, 950, 908, 879, 829, 762 and 684 cm^{-1}

^{1}H-NMR δ 1 89 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H}_2$-CH_2), 2 15 (s, 3H, MeC=O), 2 65 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 79 (d of d, 2H, J_1=7 5 Hz, J_2=2 7 Hz, CH_2-C=C), 2 89 (s, 6H, NMe_2), 6 63 (d of d, 1H, J_1=8 0 Hz, J_2=2 4 Hz, aromatic proton), 6 73 (s, 1H, aromatic proton), 6 78 (d, 1H, J=8 0 Hz, aromatic proton), 7 18 (t, 1H, J=8 0 Hz, aromatic proton) and 7 45 (t, 1H, J=2 7 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 18 (MeC=O), 22 90, 29 52, 31 77 (ring saturated cyclopentane carbons), 40 98 (NMe_2), 113 02, 114 72, 118 21, 128 71, 129 45, 134 56, 137 45, 150 95 (aromatic and vinylic carbons), 169 40 and 170 71 (C=N and C=O) ppm
UV (methanol) λ_{max} 302 (ε=21204), 280 (ε=19641), 216 nm (ε=17149)

Found C, 70 76, H, 7 39, N, 10 21 $C_{16}H_{20}N_2O_2$ requires C, 70 56, H, 7 40, N, 10 29%

6 56 2-(3,4-Dimethoxybenzylidene)cyclopentanone Oxime O-Acetate (441o)

2-(3,4-Dimethoxybenzylidene)cyclopentanone oxime acetate was prepared from 2-(3,4-dimethoxybenzylidene)cyclopentanone oxime (2 47 g, 10 mmol) yielding gold crystals of product (2 31 g, 80%), melting range 122-123 °C

IR (KBr pellet) 2934 (OMe), 1759 (C=O), 1591, 1517, 1459, 1401, 1333, 1257, 1207, 1141, 1015, 946, 877, 816 and 761 cm^{-1}

1H-NMR δ 1 84 (m, 2H, J=7 5 Hz, CH_2-CH_2-CH_2), 2 14 (s, 3H MeC=O), 2 64 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 76 (t of d, 2H, J_1=7 5 Hz, J_2=2 5 Hz, CH_2-C=C), 3 81 (s, 3H, OMe), 3 83 (s, 3H, OMe), 6 81 (d, 1H, J=8 4 Hz, aromatic proton), 6 92 (d, 1H, J=1 6 Hz, aromatic proton), 6 99 (d of d, 1H, J_1=8 4 Hz, J_2=1 6 Hz, aromatic proton) and 7 41 (t, 1H, J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 10 (MeC=O), 22 83, 29 41, 31 57 (cyclopentane ring saturated carbons), 56 23, 56 29 (both OMe), 111 46, 113 27, 123 26, 127 50, 129 90, 132 91, 149 11, 149 61 (aromatic and vinylic carbons), 169 30 (C=N) and 170 65 (C=O) ppm

UV (methanol) λ_{max} 330 (ε=22023), 246 (ε=8101), 212 nm (ε=3427)

Found C, 66 62, H, 6 50, N, 4 58 $C_{16}H_{19}NO_4$ requires C, 66 42, H, 6 62, N, 4 84%

6.57 2-(3-Methoxy-4-Methylbenzylidene)cyclopentanone Oxime O-Acetate (441p)

2-(3-Methoxy-4-methylbenzylidene)cyclopentanone oxime O-acetate was prepared from 2-(3-methoxy-4-methylbenzylidene)cyclopentanone oxime (2 2 g, 9 5 mmol) yielding off-white crystals of product (2 21 g, 85%), melting range 108-109 °C

IR (KBr pellet) 3028, 2971, 2927 (aromatic and aliphatic CH), 2880 (OMe), 1761 (C=O), 1608, 1566, 1508, 1459, 1412, 1362, 1244, 1200, 1135, 1034, 1001, 945, 882, 825, 691 and 629 cm^{-1}

^{1}H-NMR δ 1 93 (m, 2H, J=7 5 Hz, CH_2-CH_2-CH_2), 2 24-2 27 (m, 6H, Me and MeC=O), 2 75 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 87 (t of d, 2H, J_1=7 5 Hz, J_2=2 6 Hz, CH_2-C=C), 3 86 (s, 3H, OMe), 6 92 (s, 1H, aromatic proton), 7 01 (d, 1H, J=7 6 Hz, aromatic proton), 7 15 (d, 1H, J=7 6 Hz, aromatic proton) and 7 54 (t, 1H, J=2 6 Hz, vinylic proton) ppm

^{13}C-NMR δ 16 57 (Me), 20 16 (Me-C=O), 22 87, 29 47, 31 72 (cyclopentane ring saturated carbons), 55 64 (OMe), 111 86, 122 04, 127 66, 127 94, 130 95, 134 12, 135 67, 157 97 (aromatic and vinylic carbons), 169 34 and 170 63 (C=N and C=O) ppm

UV (methanol) λ_{max} 310 (ε=18638), 242 (ε=8491), 208 nm (ε=17667)

Found C, 70 05, H, 7 03, N, 5 12 $C_{16}H_{19}NO_3$ requires C, 70 31, H, 7 01, N, 5 12%

6 58 2-(3,4-Dimethylbenzylidene)cyclopentanone Oxime O-Acetate (441q)

2-(3,4-Dimethylbenzylidene)cyclopentanone oxime acetate was prepared from 2-(3,4-dimethylbenzylidene)cyclopentanone oxime (2 15 g, 10 mmol) yielding pale yellow crystals of product (2 29 g, 89%), melting range 99-101 °C

IR (KBr pellet) 2963, 2920 (aromatic and aliphatic CH), 1765 (C=O), 1590, 1501, 1451 6, 1368, 1196, 999, 942, 924, 877, 811 and 709 cm^{-1}

^{1}H-NMR δ 1 91 (m, 2H, J=7 6 Hz, CH_2-$C\underline{H_2}$-CH_2), 2 24 (s, 3H, MeC=O), 2 33 (s, 6H Me), 2 74 (t, 2H, J=7 6 Hz, CH_2-C=N), 2 86 (t of d, 2H, J_1=7 6 Hz, J_2=2 4 Hz, CH_2-C=C), 7 15-7 28 (m, 3H, aromatic protons) and 7 51 (t, 1H, J=2 4 Hz, vinylic proton) ppm

^{13}C-NMR δ 20 10, 20 19, 20 32 (MeC=O and Me), 22 87, 29 49, 31 75 (cyclopentane ring saturated carbons), 127 63, 127 78, 130 19, 131 46, 133 96, 134 49, 137 06, 137 49 (aromatic and vinylic carbons), 169 45 and 170 78 (C=N and C=O) ppm

UV (methanol) λ_{max} 312 (ε=23421), 234 (ε=6326), 206 nm (ε=2026)

Found C, 74 65, H, 7 48, N, 5 38 $C_{16}H_{19}NO_2$ requires C, 74 68, H, 7 44, N, 5 44%

6 59 2-(4-Methoxy-3-Methylbenzylidene)cyclopentanone Oxime O-Acetate (441r)

2-(4-Methoxy-3-methylbenzylidene)cyclopentanone oxime acetate was prepared from 2-(4-methoxy-3-methylbenzylidene)cyclopentanone oxime (2 31 g, 10 mmol) yielding yellow crystals of product (2 10 g, 77%), melting range 77-79 °C (decomp)

IR (KBr pellet) 2963, 2915, 2848, 1761, 1591, 1507, 1473, 1365, 1252, 1205, 1133, 1019, 915, 814 and 753 cm^{-1}

^{1}H-NMR δ 1 82 (m, 2H, J=7 6 Hz, CH_2-$C\underline{H_2}$-CH_2), 2 12-2 15 (m, 6H, MeC=O and Me), 2 64 (t, 2H, J=7 6 Hz, CH_2-C=O), 2 75 (t of d, 2H, J_1=7 6 Hz, J_2=2 6 Hz, CH_2-C=C), 3 78 (s, 3H, OMe), 6 76 (d, 1H, J=8 4 Hz, aromatic proton), 7 18-7 22 (m, 2H, aromatic protons) and 7 39 (t, 1H, J=2 6 Hz, vinylic proton) ppm

^{13}C-NMR δ 16 77 (Me), 20 17 (MeC=O), 22 85, 29 48, 31 65 (cyclopentane ring saturated carbons), 55 76 (OMe) 110 19, 127 06, 127 62, 129 15, 129 36, 132 32, 132 50, 158 25 (aromatic and vinylic carbons), 169 51 and 170 96 (C=N and C=O) ppm

UV (methanol) λ_{max} 326 (ε=26380), 238 (ε=9601), 206 nm (ε=15316)

Found C, 70 31, H, 6 98, N, 5 15 $C_{16}H_{19}NO_3$ requires C, 70 31, H, 7 01, N, 5 12%

6 60 Irradiation of 2-(4-Hydroxybenzylidene)cyclopentanone Oxime O-Acetate (441a)

2-(4-Hydroxybenzylidene)cyclopentanone oxime O-acetate (610 2 mg, 2 49 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 50 50 light petroleum/ethyl acetate After 20 minutes a number of new spots had appeared on TLC After 1 hour one of the new spots had become the sole component while the other new spots and the starting material had faded After 3 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 50 50 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 6-hydroxy-2,3-dihydro-1H-cyclopenta[b]quinoline (454) (168 mg, 36%), melting range 168-169 °C

IR (KBr pellet) 3132 (OH), 2966, 2927(aromatic and aliphatic CH), 2854, 1620, 1466, 1401, 1243, 1135, 920, 860 and 816 cm^{-1}

^{1}H-NMR δ 2 09 (m, 2H, J=7 5 Hz CH_2-C$\underline{H}_2$-CH_2), 2 93-3 01 (m, 4H, C$\underline{H}_2$-C=CH and CH_2-C=N), 7 00 (1H, d of d, J_1=8 8 Hz, J_2=2 2 Hz, aromatic proton), 7 24 (1H, d, J=2 2 Hz, aromatic proton), 7 50 (d, 1H, J=8 8 Hz, aromatic proton) and 7 73 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 28 72, 35 35, 39 67 (cyclopentane ring saturated carbons), 115 38, 123 24, 126 81, 133 64, 135 51, 137 58, 154 14, 163 14 and 172 75 (aromatic carbons) ppm

UV (methanol) λ_{max} 338 (ε=4346) and 214 nm (ε=24859)

Found C, 77 89, H, 6 12, N, 7 51 $C_{12}H_{11}NO$ requires C, 77 81, H, 5 99, N, 7 56%

6 61 Irradiation of 2-(4-Acetoxybenzylidene)cyclopentanone Oxime O-Acetate (441b)

2-(4-Acetoxybenzylidene)cyclopentanone oxime O-acetate (610 2 mg, 2 49 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 50 50 light petroleum/ethyl acetate After 20 minutes a number of new spots had appeared on TLC After 1 hour one of the new spots had become the sole component while the other new spots and the starting material had faded After 3 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 50 50 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 6-acetoxy-2,3-dihydro-1H-cyclopenta[b]quinoline (455) (168 mg, 36%), melting range 96-97 °C

IR (KBr pellet) 2957, 2925 (aromatic and aliphatic CH), 1758, 1621, 1573, 1486, 1416, 1372, 1206, 1132, 1015, 972 and 926 cm^{-1}

^{1}H-NMR δ 2 13 (m, 2H, J=7 6 Hz CH_2-C<u>H_2</u>-CH_2), 2 28 (s, 3H, MeC=O), 2 93 (t, 2H, J=7 6 Hz, CH_2), 3 08 (t, 2H, J=7 6 Hz, CH_2-C=N), 7 16 (d of d, 1H, J_1=8 8 Hz, J_2=2 4 Hz, aromatic proton), 7 64-7 66 (m, 2H, aromatic protons) and 7 81 (s, 1H, aromatic protons) ppm

^{13}C-NMR δ 21 62, 24 01, 30 85, 35 00 (cyclopentane ring saturated carbons and COMe), 120 07, 121 12, 125 83, 128 77, 130 58, 136 05, 148 34, 150 89, 169 20 and 169 84(aromatic carbons and C=O) ppm

UV (methanol) λ_{max} 322 (ε=5468), 236 (ε=19548) and 212 nm (ε=30496)

Found C, 73 95, H, 5 85, N, 6 24 $C_{14}H_{13}NO_2$ requires C, 73 99, H, 5 77, N, 6 16%

6 62 Irradiation of 2-(4-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441e)

2-(4-Dimethylaminobenzylidene)cyclopentanone oxime O-acetate (638 mg, 2 34 mmole) was dissolved in methanol (300 cm^3) and irradiated under standard conditions, the reaction being monitored by TLC with mobile phase of ethanol After irradiation for 15 minutes three new spots had appeared on TLC After 2 hours two of the new spots had become the sole component while the other new spot and the starting material had faded After 7 hours one spot remained the sole component The photolysis was halted and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 95 5 ethyl acetate /light petroleum Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off orange crystals of 6-dimethylamino-2,3-dihydro-1H-cyclopenta[b]quinoline (457) (131 mg, 26%), melting range 104-106 °C

IR (KBr pellet) 2962, 2929 (aromatic and aliphatic CH), 1624, 1515 (C=C and C=N), 1450, 1417, 1383, 1368, 1306, 1262, 1163, 1141, 974, 915, 928 and 801 cm^{-1}

^{1}H-NMR δ 2 09 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H}_2$-CH_2), 2 94 (t, 2H, J=7 5 Hz, CH_2), 2 99-3 04 (m, 8H, CH_2 and NMe_2), 7 01 (d of d, 1H, J_1=9 2 Hz, J_2=2 6 Hz, aromatic proton), 7 08 (d, 1H, J=2 6 Hz, aromatic proton), 7 49 (d, 1H, J=9 2, aromatic proton) and 7 65 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 22 60, 29 33, 33 70 (cyclopentane ring saturated carbons), 39 60 (NMe_2), 106 11, 114 15, 118 93, 126 86, 129 08, 130 41, 148 20, 149 67 and 166 77 (aromatic carbons) ppm

UV (methanol) λ_{max} 378 (ε=4581), 292 (ε=4733), 258 (ε=18878) and 216 nm (ε=21212)

Found C, 79 42, H, 7 63, N, 13 32 $C_{14}H_{16}N_2$ requires C, 79 21, H, 7 60, N, 13 20%

6 63 Irradiation of 2-(4-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441e) in the presence of Trifluroacetic Acid

2-(4-Dimethylaminobenzylidene)cyclopentanone oxime O-acetate (225 2 mg, 0 83 mmole) was dissolved in methanol (225 cm^3) Trifluroacetic acid (0 10 g, 0 90 mmole) was added and the mixture was irradiated under standard conditions The reaction was monitored by TLC with mobile phase of 5 95 light petroleum/ethyl acetate, the samples being first neutralised with an aqueous 10% sodium carbonate solution After irradiation for 15 minutes three new spots had appeared on TLC After 2 hours two of the new spots had become the sole component while the other new spot and the starting material had faded After 4 hours one spot remained the sole component The photolysis was halted and the pH adjusted to pH~8 by addition of an aqueous 10% sodium carbonate solution The solution was then extracted twice with diethyl ether (100 cm^3) The extract was dried with magnesium sulphate and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 95 5 ethyl acetate/light petroleum Recrystallisation from a mixture of light petroleum/ethyl acetate yielded orange crystals of 6-dimethylamino-2,3-dihydro-1H-cyclopenta[b]quinoline (457) (43 mg, 24%), melting range 104-106 °C

6 64 Irradiation of 2-(2,5-Dimethoxybenzylidene)cyclopentanone Oxime O-Acetate (441f)

2-(2,5-Dimethoxybenzylidene)cyclopentanone oxime O-acetate (495 mg 1 71 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 50 50 light petroleum/ethyl acetate After 10 minutes a number of new spots had appeared on TLC After 2 hours two of the new spots had become the sole component while the other new spot and the starting material had faded After 4 hours one spot remained the sole component The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 90 10 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 5,8-dimethoxy-2,3-dihydro-1H-cyclopenta[b]-quinoline (458) (32 mg, 8%), melting range 104-105 °C (lit [297], 98-100 °C)

IR (KBr pellet) 3370, 2994, 2952, 2937 (aromatic and aliphatic CH), 2839, 1614, 1486 (C=C and C=N), 1460, 1378, 1327, 1279, 1264, 1211, 1143, 1094, 1068, 977, 911, 814, 793 and 724 cm^{-1}

^{1}H-NMR δ 2 11 (m, 2H, J=7 5 Hz CH_2-C$\underline{H_2}$-CH_2), 3 00 (t, 2H, J=7 5 Hz, CH_2), 3 13 (t, 2H, J=7 5 Hz, CH_2), 3 86, 3 94 (both OMe), 6 61 (d, 1H, J=8 8 Hz, aromatic proton), 6 77 (d, 1H, J=8 8 Hz, aromatic proton) and 8 22 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 22 62, 29 64, 33 86 (cyclopentane ring saturated carbons), 54 76, 54 89 (both OMe), 101 89, 104 76, 119 58, 124 20, 134 44, 138 64, 147 73, 148 24 and 166 25 (aromatic carbons) ppm

UV (methanol) λ_{max} 336 (ε=2261), 260 (ε=31005) and 208 nm (ε=18626)

Found C, 72 84, H, 6 53, N, 6 01 $C_{14}H_{15}NO_2$ requires C, 73 34, H, 6 59, N, 6 11%

6.65 Irradiation of 2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone Oxime O-Acetate (441g)

2-(10H-Phenothiazin-1-ylmethylene)cyclopentanone oxime O-acetate (425 mg, 1 21 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being monitored by TLC with mobile phase of ethanol After irradiation for 15 minutes a number of new spots had appeared on TLC After 2 hours two of the new spots had become the sole component while the other new spot and the starting material had faded After 5 hours one spot remained the sole component The photolysis was halted and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 95 5 ethyl acetate /light petroleum Recrystallisation from a mixture of light petroleum/ethyl acetate yielded orange crystals of 1,2,3,12-tetrahydrocyclopenta[5,6]pyrido[3,2-a]phenothiazine (459) (43 mg, 12%), melting range 67-68 °C

IR (KBr pellet) 3453 (NH) 2962, 2926 (aromatic and aliphatic CH), 1650, 1475, 1426, 1384, 1262, 1095, 1024, 868, 802 and 738 cm^{-1}

^{1}H-NMR δ 2 07 (m, 2H, J=7 2 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 37 (t, 2H, J=7 2 Hz, C$\underline{H_2}$-C=CH), 3 22 (t, 2H, J=7 2 Hz, CH_2-C=N), 6 31 (s, 1H, NH), 6 62 (d of d, 1H, J_1=7 2 Hz, J_2=0 8 Hz, aromatic proton), 6 85-6 91 (m, 2H, aromatic protons), 7 00-7 05 (m, 3H, aromatic protons) and 7 24 (d, 1H, J=8 8 Hz, aromatic proton) ppm

^{13}C-NMR δ 15 59, 23 46, 28 68 (cyclopentane ring saturated carbons), 106 54, 115 24, 115 36, 115 64, 116 09, 118 08, 121 92, 122 67, 123 64, 125 42, 126 46, 127 15, 134 98, 135 08 and 136 46 (aromatic carbons) ppm

UV (methanol) λ_{max} 206 (ε=12009), 232 (ε=10229), 252 (ε=9318) and 324 nm (ε=2435)

Found C, 74 41, H, 4 56, N, 9 73 $C_{18}H_{14}N_2S$ requires C, 74 45, H, 4 86, N, 9 65%

6 66 Irradiation of 2-(3-Phenylallylidene)cyclopentanone Oxime O-Acetate (441h)

2-(3-Phenylallylidene)cyclopentanone oxime O-acetate (496 mg, 1 94 mmole) was dissolved in methanol (250 cm^3), and the solution was irradiated under the standard conditions, the reaction being monitored by TLC with mobile phase 90 10 light petroleum/ethyl acetate After irradiation for 20 minutes, a number of new spots were observed on TLC After a further hour the number of spots had increased After 4 hours, there was no further change to the TLC The photolysis was halted and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 90 10 ethyl acetate /light petroleum Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 2-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine (461) (38 mg, 10%), melting range 79-80 °C (lit [298], 81-82 °C)

IR (KBr pellet) 2960, 2960, 2927(aromatic and aliphatic CH), 2857, 1656, 1544, 1441, 1401, 1263, 842, 772, 734 and 695 cm^{-1}

^{1}H-NMR δ 2 10 (m, 2H, J=7 6 Hz CH_2-C$\underline{H_2}$-CH_2), 2 90 (t, 2H, J=7 6 Hz, C$\underline{H_2}$-C=CH), 3 02 (t, 2H, J=7 6 Hz, CH_2-C=N), 7 28-7 32 (m, 1H, aromatic proton), 7 36-7 39 (m, 3H, aromatic protons), 7 48 (d, 1H, J=7 6 Hz, aromatic proton) and 7 86-7 88 (m, 2H, aromatic protons) ppm

^{13}C-NMR δ 23 66, 30 91, 34 84 (cyclopentane ring saturated carbons), 118 68, 127 32, 128 75, 129 04, 132 99, 135 84, 140 42, 156 30 and 166 26 (aromatic protons) ppm

UV (methanol) λ_{max} 206 (ε=17715), 248 (ε=11918) and 292 nm (ε=11433)

6 67 Irradiation of 2-(3-t-Butylbenzylidene)cyclopentanone Oxime O-Acetate (441i)

2-(3-t-Butylbenzylidene)cyclopentanone oxime O-acetate (500 mg, 1 75 mmole) was dissolved in methanol (350 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 95 5 light petroleum/ethyl acetate After 20 minutes four new spots had appeared on TLC After 1 hour one of the new spots had become the sole component while the other new spots and the starting material had faded After 4 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown tar The photoproduct was separated using a silica gel column with mobile phase 90 10 light petroleum/ethyl acetate Recrystallisation from light petroleum yielded light yellow crystals 5-t-butyl-2,3-dihydro-1H-cyclopenta[b]quinoline (463) (52mg, 13%) melting range 62-64 °C

IR (KBr pellet) 3048, 2957, 2925 (aromatic and aliphatic CH), 2855, 1630, 1607, 1488, 1466, 1411, 1353, 1265, 1148, 1097, 1082, 1026, 891, 800 and 763 cm^{-1}

^{1}H-NMR (d_6-acetone) δ 1 53 (s, 9H, CMe_3), 2 03 (m, 2H, J=7 4 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 89-2 96 (m 4H, C$\underline{H_2}$-C=CH and CH_2-C=N), 7 22 (t, 1H, J=7 6 Hz, aromatic proton), 7 43 (d of d, 1H, J_1=7 6 Hz, J_2=1 3 Hz, aromatic proton), 7 50 (d of d, 1H, J_1=7 6 Hz, J_2=1 3 Hz, aromatic proton) and 7 80 (s, 1H, vinylic proton) ppm

^{13}C-NMR δ 22 61, 28 68, 29 39, 30 03, 33 82 (cyclopentane ring saturated carbons, $\underline{C}Me_3$ and $C\underline{Me_3}$), 123 73, 123 78, 125 35, 127 04, 129 50, 132 94, 145 59, 146 31 and 163 70 (aromatic carbons) ppm

UV (methanol) λ_{max} 320 (ε=3172), 238 (ε=20631) and 212 nm (ε=24863)

Found C, 85 15, H, 8 62, N, 6 48 $C_{16}H_{19}N$ requires C, 85 29, H, 8 50, N, 6 22%

6.68 Irradiation of 2-(3-Hydroxybenzylidene)cyclopentanone Oxime O-Acetate (441)

2-(3-Hydroxybenzylidene)cyclopentanone oxime O-acetate (601 4 mg, 2 45 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 85 15 light petroleum/ethyl acetate After 20 minutes a number of new spots had appeared on TLC After 1 hour one of the new spots had become the sole component while the other new spots and the starting material had faded After 2 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 50 50 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 7-hydroxy-2,3-dihydro-1H-cyclopenta{b}quinoline (466) (134 mg, 30%), melting range 142-143 °C

IR (KBr pellet) 3450 (OH), 3154, 2955, 2956 (aromatic and aliphatic CH), 2855, 1655, 1619, 1461, 1399, 1276, 1235, 1127, 907 and 827 cm^{-1}

^{1}H-NMR δ 2 13 (m, 2H, J=7 3 Hz CH_2-C$\underline{H}_2$-CH_2), 2 99 (t, 2H, J=7 3 Hz, CH_2), 3 06 (t, 2H, J=7 3 Hz, CH_2), 6 99 (d, 1H, J=2 8 Hz, aromatic proton), 7 15 (d of d, 1H, J_1=9 0 Hz, J_2=2 8 Hz, aromatic proton), 7 69 (s, 1H, aromatic proton), 7 83 (d, 1H, J=9 0 Hz, aromatic protons) and 9 35 (s, 1H, OH) ppm

^{13}C-NMR δ 23 59, 30 40, 34 08 (cyclopentane ring saturated carbons), 108 85, 120 49, 128 54, 128 88, 129 31, 135 62, 142 39, 154 84 and 164 42 (aromatic carbons) ppm

UV (methanol) λ_{max} 336 (ε=4475), 284 (ε=2877) and 218 nm (ε=24752)

Found C, 77 75, H, 5 84, N, 7 72 $C_{12}H_{11}NO$ requires C, 77 81, H, 5 99, N, 7 56%

6.69 Irradiation of 2-(3-Acetoxybenzylidene)cyclopentanone Oxime O-Acetate (441k)

2-(3-Acetoxybenzylidene)cyclopentanone oxime O-acetate (506.8 mg, 1.76 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 90:10 light petroleum/ethyl acetate. After 20 minutes a number of new spots had appeared on TLC. After 3 hours two of the new spots had become the major components while the other spots and the starting material had faded. After 4 hours two of the spots remained. The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum. The photoproducts were separated using a silica gel column with mobile phase 10:90 light petroleum/ethyl acetate. The first photoproduct isolated was recrystallised from a mixture of light petroleum/ethyl acetate yielding off-white crystals of 7-acetoxy-2,3-dihydro-1H-cyclopenta[b]-quinoline (468) (78 mg, 20%), melting range 118-119 °C.

The second photoproduct isolated was recrystallised from a mixture of light petroleum/ethyl acetate yielding white crystals of 5-hydroxy-2,3-dihydro-1H-cyclopenta[b]quinoline (465) (56 mg, 17%), melting range 74-75 °C.

7-Acetoxy-2,3-dihydro-1H-cyclopenta[b]quinoline (468):

IR (KBr pellet): 2957, 2925 (aromatic and aliphatic CH), 2853, 1765 (C=O), 1620, 1498, 1462, 1431, 1371, 1192, 1145, 1014, 966, 922, 878, 836 and 744 cm^{-1}.

^{1}H-NMR: δ 2.13 (m, 2H, J=7.5 Hz CH_2-CH_2-CH_2), 2.27 (s, 3H, MeC=O, 2.99 (t, 2H, J=7.5 Hz, CH_2), 3.07 (t, 2H, J=7.5 Hz, CH_2), 7.27 (d of d, 1H, J_1=8.9 Hz, J_2=2.5 Hz, aromatic proton), 7.39 (d, 1H, J=2.5 Hz, aromatic proton), 7.76 (s, 1H, aromatic proton) and 7.95 (d, 1H, J=8.9 Hz, aromatic proton) ppm.

^{13}C-NMR: δ 20.17, 22.59, 29.49, 33.45 (cyclopentane ring saturated carbons and MeC=O), 117.21, 122.27, 126.62, 128.84, 129.05, 135.35, 144.38, 146.81 (aromatic carbons), 166.94 and 168.53 (C=O and aromatic carbon) ppm.

UV (methanol) λ_{max} 332 (ε=6079), 282 (ε=5703), 234 (ε=23357) and 214 nm (ε=34206)

Found C, 74 25, H, 5 83, N, 5 79 $C_{14}H_{13}NO_2$ requires C, 73 99, H, 5 77, N, 6 16%

5-Hydroxy-2,3-dihydro-1H-cyclopenta[b]quinoline (465)

IR (KBr pellet) 3450 (OH), 2958, 2925 (aromatic and aliphatic CH), 2854, 1498, 1462, 1379, 1331, 1237, 1210, 1129, 964, 916, 870 and 755 cm^{-1}

^{1}H-NMR δ 2 12 (m, 2H, J=7 5 Hz CH_2-$C\underline{H}_2$-CH_2), 2 97-3 05 (m, 4H, $C\underline{H}_2$-C=CH and CH_2-C=N), 7 01 (d of d, 1H, J_1=7 7 Hz, J_2=1 1 Hz, aromatic proton), 7 15 (d of d, 1H, J_1=7 7 Hz, J_2=1 1 Hz, aromatic proton), 7 26 (t, 1H, J=7 7 Hz, aromatic proton) and 7 77 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 22 65, 29 47, 33 11 (cyclopentane ring saturated carbons), 108 15, 116 65, 125 39, 126 53, 129 35, 135 60, 136 35, 150 49 and 164 70 (aromatic carbons) ppm

UV (methanol) λ_{max} 210 (ε=13450), 248 (ε=23041) and 310 nm (ε=2157)

Found C, 77 56, H, 5 84, N, 7 59 $C_{12}H_{11}NO$ requires C, 77 81, H, 5 99, N, 7 56 %

6 70 Irradiation of 2-(3-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441n)

2-(3-Dimethylaminobenzylidene)cyclopentanone oxime O-acetate (503 1 mg, 1 85 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being monitored by TLC with mobile phase of ethanol After irradiation for 15 minutes four new spots had appeared on TLC After 2 hours two of the new spots had become the sole component while the other new spot and the starting material had faded After 5 hours one spot remained as the

sole component The photolysis was halted and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 95 5 ethyl acetate /light petroleum Recrystallisation from a mixture of light petroleum/ethyl acetate yielded orange crystals of 7-dimethylamino-2,3-dihydro-1H-cyclopenta[b]quinoline (472) (23mg, 6%), melting range 122-123 °C

IR (KBr pellet) 3164, 2955, 2927 (aromatic and aliphatic CH), 2858, 1619, 1513, 1400, 1363, 1142, 968, 906 and 815 cm^{-1}

^{1}H-NMR δ 2 10 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H}_2$-CH_2), 2 94-3 05 (m, 10H, C$\underline{H}_2$-C=CH, CH_2-C=N and NMe_2), 6 71 (d, 1H, J=2 6 Hz, aromatic proton), 7 21 (d of d, 1H, J_1=9 4 Hz, J_2=2 6 Hz, aromatic proton), 7 65 (s, 1H, aromatic proton) and 7 80 (d, 1H, J=9 4 Hz, aromatic proton) ppm

^{13}C-NMR δ 23 91, 31 00, 34 57 (cyclopentane ring saturated carbons), 41 31 (NMe_2), 106 18, 118 70, 129 13, 129 26, 129 30, 129 33, 136 18, 148 61 and 163 99 (aromatic carbons) ppm

UV (methanol) λ_{max} 374 (ε=3597), 260 (ε=24681) and 216 nm (ε=17695)

Found C, 79 27, H, 7 63, N, 13 41 $C_{14}H_{16}N_2$ requires C, 79 21, H, 7 60, N, 13 20%

6 71 Irradiation of 2-(3-Dimethylaminobenzylidene)cyclopentanone Oxime O-Acetate (441n) in the presence of Trifluroacetic Acid

2-(3-Dimethylaminobenzylidene)cyclopentanone oxime O-acetate (150 5 mg, 0 55 mmole) was dissolved in methanol (225 cm^3) Trifluroacetic acid (0 07 g, 0 60 mmole) was added and the mixture was irradiated under standard conditions The reaction was monitored by TLC with mobile phase of 5 95 light petroleum/ethyl acetate, the samples being first neutralised with an aqueous 10% sodium

carbonate solution After irradiation for 15 minutes four new spots had appeared on TLC After 2 hours two of the new spots had become the sole component while the other new spot and the starting material had faded After 3 hours one spot remained the sole component The photolysis was halted and pH was to pH~8 by addition of aqueous 10% sodium carbonate solution The solution was then extracted twice with diethyl ether (100 cm3) The extract was dried with magnesium sulphate and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 95 5 ethyl acetate/light petroleum Recrystallisation from a mixture of light petroleum/ethyl acetate yielded orange crystals of 7-dimethylamino-2,3-dihydro-1H-cyclopenta[b]quinoline (472) (41mg, 35%), melting range 122-123 °C

6 72 Irradiation of 2-(3,4-Dimethoxybenzylidene)cyclopentanone Oxime O-Acetate (441o)

2-(3,4-Dimethoxybenzylidene)cyclopentanone oxime O-acetate (500mg, 1 77 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being monitored by TLC with mobile phase of 50 50 light petroleum/ethyl acetate After irradiation for 15 minutes four new spots had appeared on TLC The irradiation was continued and after a further 90 minutes one of the new spots had become the sole component of the mixture After 3 hours, all starting material had disappeared and only one component remained The photolysis was halted and the solvent removed by rotary evaporation, yielding an orange gum The photoproduct was separated using a silica gel column with mobile phase 80 20 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 6,7-dimethoxy-2,3-dihydro-1H-cyclopenta[b]quinoline (474) (86 mg, 21%), melting range 99-100 °C (lit [299], 112-113 °C)

IR (KBr pellet) 3000, 2958, 2834 (aromatic and aliphatic CH), 1619, 1505 (C=C and C=N ring stretching), 1456, 1421, 1384, 1284, 1243, 1150, 1011, 910, 884 and 748 cm^{-1}

^{1}H-NMR δ 2 12 (m, 2H, J=7 6 Hz, CH_2-C$\underline{H_2}$-CH_2), 2 98 (t, 2H, J=7 6 Hz, CH_2), 3 04 (t, 2H, J=7 6 Hz, CH_2), 3 92 (s, 3H, OMe), 3 94 (s, 3H, OMe), 6 92 (s, 1H, aromatic proton), 7 31 (s, 1H, aromatic proton) and 7 68 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 24 04, 30 91, 34 79 (cyclopentane ring saturated carbons), 56 35, 56 39 (both OMe), 105 66, 107 94, 122 89, 129 55, 134 14, 144 44, 149 27, 151 79 and 165 69 (aromatic carbons) ppm

UV (methanol) λ_{max} 336 (ε=14280), 324 (ε=10455) and 222 nm (ε=36394)

Found C, 73 39, H, 6 46, N, 5 84 $C_{14}H_{15}NO_2$ requires C, 73 34, H, 6 59, N, 6 11%

6 73 Irradiation of 2-(3-Methoxy-4-Methylbenzylidene)cyclopentanone Oxime O-Acetate (441p)

2-(3-Methoxy-4-methylbenzylidene)cyclopentanone oxime O-acetate (502 3 mg, 1 84 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 85 15 light petroleum/ethyl acetate After 20 minutes four new spots had appeared on TLC After 1 hour one of the new spots had become the sole component while the other new spots and the starting material had faded After 2 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 85 15 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 7-methoxy-6-methyl-2,3-dihydro-1H-cyclopenta[b]quinoline (476) (223 mg, 57%), melting range 129-130 °C

IR (KBr pellet) 2954, 2927 (aromatic and aliphatic CH), 2855 (OMe), 1628, 1498 (C=C and C=N), 1461, 1426, 1383, 1370, 1232, 1136, 1100, 1026, 923, 884 and 832 cm^{-1}

^{1}H-NMR δ 2 10 (m, 2H, J=7 4 Hz CH_2-C$\underline{H}_2$-CH_2), 2 31 (s, 3H, Me), 3 00 (t, 2H, J=7 4 Hz, CH_2), 3 03 (t, 2H, J=7 4 Hz, CH_2), 3 84 (s, 3H, Me), 6 85 (s, 1H, aromatic proton) and 7 68 (m, 2H, aromatic protons) ppm

^{1}H-NMR (DMSO) δ 2 01 (m, 2H, J=7 6 Hz CH_2-C$\underline{H}_2$-CH_2), 2 21 (s, 3H, Me), 2 84-2 92 (m, 4H, C$\underline{H}_2$-C=CH and CH_2-C=N), 3 80 (s, 3H, Me), 7 03 (s, 1H, aromatic proton) 7 55 (s, 1H, aromatic proton) and 7 74 (s, 1H, aromatic protons) ppm

^{13}C-NMR δ 17 47 (Me), 24 08, 30 95, 34 70 (cyclopentane ring saturated carbons), 55 80 (OMe), 104 18, 127 21, 129 51, 129 66, 131 39, 135 30, 143 53, 156 67 and 165 29 (aromatic carbons) ppm

UV (methanol) λ_{max} 336 (ε=8273), 322 (ε=6713), 246 (ε=15494) and 224 nm (ε=33990)

Found C, 78 59, H, 7 26, N, 6 54 $C_{14}H_{15}NO$ requires C, 78 84, H, 7 09, N, 6 57%

6 74 Irradiation of 2-(3,4-Dimethylbenzylidene)cyclopentanone Oxime O-Acetate (441q)

2-(3,4-Dimethylbenzylidene)cyclopentanone oxime O-acetate (501 mg, 1 95 mmole) was dissolved in methanol (250 cm^3) and irradiated under standard conditions, the reaction being monitored by TLC for its duration with mobile phase 90 10 light petroleum/ethyl acetate After 20 minutes four new spots had appeared on TLC After an hour one of the new spots had become the sole component while the other spots and the starting material had faded After 2 hours only one spot remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 90 10 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded white crystals of 5,6-dimethyl-2,3-dihydro-1H-cyclopenta[b]quinoline (477) (67 mg, 17%), melting range 90-91 °C

IR (KBr pellet) 2954, 2843 (aromatic and aliphatic CH), 1625, 1509 (C=C and C=N), 1474, 1434, 1358, 1247, 1212, 1160, 1063, 1016 and 850 cm^{-1}

^{1}H-NMR δ 2 10 (m, 2H, J=7 5 Hz, CH_2-$C\underline{H_2}$-CH_2), 2 40 (s, 3H, Me), 2 67 (s, 3H, Me), 2 97 (t, J=7 5 Hz, CH_2), 3 09 (t, J=7 5 Hz, CH_2), 7 18 (d, J=8 2, 1H, aromatic proton), 7 39 (d, J=8 2 Hz, 1H, aromatic proton) and 7 71 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 12 48, 19 64 (both Me), 22 75, 29 33, 33 88 (cyclopentane ring saturated carbons), 123 45, 124 55, 127 17, 129 46, 132 49, 132 97, 134 91, 145 53 and 165 75 (aromatic carbons) ppm

UV (methanol) λ_{max} 326 (ε=3664), 314 (ε=3442), 242 (ε=23997) and 210 nm (ε=26082)

Found C, 85 54, H, 7 95, N, 6 79 $C_{14}H_{15}N$ requires C, 85 24, H, 7 66, N, 7 10%

6 75 Irradiation of 2-(4-Methoxy-3-Methylbenzylidene)cyclopentanone Oxime O-Acetate (441r)

2-(4-Methoxy-3-methylbenzylidene)cyclopentanone oxime O-acetate (522 mg 1 91 mmole) was dissolved in methanol (300 cm^3) and irradiated under standard conditions, the reaction being followed by TLC for its duration with mobile phase 80 20 light petroleum/ethyl acetate After 10 minutes three new spots had appeared on TLC After 1 hour one of the new spots had become the sole component while the other new spots and the starting material had faded After 2 hours only one of the spots remained The photolysis was stopped and the solvent removed by rotary evaporation, yielding a brown gum The photoproduct was separated using a silica gel column with mobile phase 95 5 light petroleum/ethyl acetate Recrystallisation from a mixture of light petroleum/ethyl acetate yielded off-white crystals of 7-methoxy-8-methyl-2,3-dihydro-1H-cyclopenta[*b*]quinoline (479) (62 mg, 15%), melting range 89-91 °C

IR (KBr pellet) 2961, 2926, 2854 (aromatic and aliphatic CH), 1738, 1613, 1503 (C=C and C=N), 1461, 1407, 1344, 1255, 1171, 1105, 1030, 803 and 783 cm^{-1}

^{1}H-NMR δ 2 12 (m, 2H, J=7 5 Hz CH_2-$C\underline{H}_2$-CH_2), 2 62 (s, 3H, Me), 2 98 (t, 2H, J=7 5 Hz, CH_2), 3 10 (t, 2H, J=7 5 Hz, CH_2), 3 90 (s, 3H, OMe), 7 15 (d, 1H, J=9 0 Hz, aromatic proton), 7 50 (d, 1H, J=9 0 Hz, aromatic proton) and 7 73 (s, 1H, aromatic proton) ppm

^{13}C-NMR δ 8 94 (Me), 22 78, 29 29, 34 00 (cyclopentane ring saturated carbons), 55 41 (OMe), 111 25, 120 54, 121 46, 124 56, 129 47, 131 81, 146 15, 155 58 and 166 65 (aromatic carbons) ppm

UV (methanol) λ_{max} 334 (ε=5466), 244 (ε=23025) and 212 nm (ε=21695)

Found C, 78 69, H, 6 98, N, 6 59 $C_{14}H_{15}NO$ requires C, 78 84, H, 7 09, N, 6 57%

6 76 Preparation of Acetyl(2-Benzylidenecyclopentylidene)hydrazide (482)

2-Benzylidenecyclopentanone (1 72 g, 10 mmol) and acetyl hydrazide (0 82 g, 11 mmol) were dissolved in toluene (40 cm^3) in a 100 cm^3 round-bottom flask The mixture was heated under reflux with continuous azetropic removal of water using a Dean and Stark distillation apparatus until no more water collected (0 18 cm^3) On cooling the yellow precipitate was vacuum filtered and washed with cold petroleum ether Recrystallisation from dichloromethane yielded yellow crystals of acetyl(2-benzylidenecyclopentylidene)hydrazide (482) (1 92 g, 84%), melting range 211-212 °C

IR (KBr pellet) 3167, 3081, 3055 (NH stretch), 2954, 2910 (aromatic and aliphatic CH), 1700 (C=O), 1646, 1589, 1473, 1376, 1340, 1257, 1137, 1021, 921, 749 and 693 cm^{-1}

^{1}H-NMR δ 1 90 (m, 2H, J=7 3 Hz, CH_2-C$\underline{H}_2$-CH_2), 2 32-2 38 (m, 5H, CH_2-C=N and MeC=O), 2 77 (d of t, 2H, J_t=7 3 Hz, J_d=2 4 Hz, CH_2-C=C), 7 19-7 38 (m, 6H aromatic and vinylic protons) and 8 57 (s, 1H, =N-N$\underline{H}$-Ac) ppm

^{13}C-NMR δ 20 88 (MeC=O), 22 99, 27 46, 31 38 (cyclopentane ring saturated carbons), 123 76, 127 92, 128 84, 129 75, 137 42, 138 29 (aromatic and vinylic carbons), 156 93 (C=N) and 173 91 (C=O) ppm

UV (methanol) λ_{max} 318 (ε=22689) and 236 nm (ε=8363)

Found C, 73 69, H, 7 11, N, 12 61 $C_{14}H_{16}N_2O$ requires C, 73 66, H, 7 06, N, 12 27%

6 77 Preparation of N,N'-Bis-(2-Benzylidenecyclopentylidene)hydrazine (483)

2-Benzylidenecyclopentanone (2 1 g, 12 mmol), hydrazine hydrate (1 61g, 25 mmol) and 3 drops of concentrated hydrochloric acid were dissolved in methanol (40 cm^3) in a 100 cm^3 round-bottom flask The solution was stirred vigorously for 1 hour The yellow precipitate was vacuum filtrated and washed with cold methanol Recrystallisation from dichloromethane yielded pale yellow crystals of N,N'-bis-(2-benzylidenecyclopenthylidene)hydrazine (483) (0 45 g, 22%), melting range 191-192 °C

IR (KBr pellet) 3051 (NH), 2959, 2913 (aromatic and aliphatic CH), 1600, 1489, 1445, 1252, 1193, 924, 749, 695 and 516 cm^{-1}

^{1}H-NMR δ 1 85 (m, 2H, J=7 5 Hz, CH_2-C$\underline{H}_2$-CH_2), 2 69 (t, 2H, J=7 5 Hz, CH_2-C=N), 2 81 (d of t, 2H, J_t=7 5 Hz, J_d=2 5 Hz, CH_2-C=N), 7 21 (t, 1H, J=7 5 Hz, aromatic proton), 7 32 (t, 2H, J=7 5 Hz, aromatic protons), 7 43 (d, 2H, J=7 5 Hz, aromatic proton) and 7 48 (t, 1H, J=2 5 Hz, vinylic proton) ppm

^{13}C-NMR δ 23 12, 30 10, 31 67 (cyclopentane ring saturated carbons), 125 33, 127 92, 128 80, 129 99, 137 69, 139 23 (aromatic and vinylic carbons) and 170 55 (C=N) ppm

UV (methanol) λ_{max} 352 (ε=26752) and 238 nm (ε=14082)

Found C, 84 86, H, 6 98, N, 7 98 $C_{24}H_{24}N_2$ requires C, 84 67, H, 7 11, N, 8 23%

6 78 Irradiation of Acetyl(2-Benzylidenecyclopentylidene)hydrazide (482)

Acetyl(2-benzylidenecyclopentylidene)hydrazide (482) was dissolved in a 90 10 mix of methanol/dichloromethane (350 cm^3), and the solution was irradiated under the standard conditions, the reaction being monitored by TLC with mobile phase ethyl acetate/petroleum ether 95 5 After 20 minutes three new spots were noticed by TLC After a further 4 hours none of the products was observed in excess to the others and the reaction was halted and the solvent removed by rotary evaporation, yielding a light brown powder Recrystallisation from dichloromethane yielded off-white crystals yielded, on comparison of IR, 1H- and ^{13}C-NMR spectra and melting point, starting material (482)

6 79 Irradiation of N,N'-Bis-(2-Benzylidenecyclopentylidene)hydrazine (483)

N,N'-Bis-(2-benzylidenecyclopentylidene)hydrazine (483) was dissolved in a 50 50 mix of methanol/dichloromethane (350 cm^3), and the solution was irradiated under the standard conditions, the reaction being monitored by TLC with mobile phase ethyl acetate/light petroleum 95 5 After 20 minutes three new spots were noticed by TLC After a further 4 hours none of the products was observed in excess to the others and the reaction was halted and the solvent removed by rotary evaporation, yielding a light brown gum The residue was triturated using dichloromethane, and the resulting off-white solid recrystallised from dichloromethane On comparison of IR, 1H- and ^{13}C-NMR spectra and melting point it was found to be starting material (483)

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