INVESTIGATIONS OF THE SYNTHESIS OF NEW PHOTOCHROMIC OXAZINE AND OXADIAZINE DERIVATIVES

by

David Martin Rowe, B.Sc.

Thesis presented for the Degree of Doctor of Philosophy

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CONTENTS

DECLARATION

I declare that this thesis is of my own composition, that the work of which it is a record was carried out by myself and that it has not been submitted in any previous application for a Higher Degree.

This thesis describes the results of research carried out in the Department of Chemistry, The University of Edinburgh, under the supervision of Dr. G. Tennant between October 1991 and September 1994.

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POSTGRADUATE LECTURE COURSES ATTENDED

(OCTOBER 1991-SEPTEMBER 1994)

Royal Society of Chemistry - Perkin Division

Twentieth Scottish Regional Meeting (1991), Heriot-Watt University.

Twenty-first Scottish Regional Meeting (1992), The University of Edinburgh.

Twenty-second Scottish Regional Meeting (1993), University of Aberdeen.

Organic Research Group Seminars, The University of Edinburgh : 1991-92, 1992-93, 1993-94.

Organic Research Group Colloquia, The University of Edinburgh : 1991-1992, 1992-1993, 1993-1994.

"Introductory Reading Course in German" : 1992; Department of German, The University of Edinburgh.

"Topics in Medicinal Chemistry" : 1991-1992, 1992-1993, 1993-1994; various lectures from Merck, Sharp and Dohme Ltd.

"Discovery, Development and Pharmacology of Zoladex for the Treatment of Prostrate Cancer" : 1992; various lectures from ICI Pharmaceuticals Division.

"Topics in Agricultural Chemistry" : 1992; various lectures from Schering Agrochemicals Division.

"Aspects and Applications of NMR Spectroscopy" : 1992; various lectures from The University of Edinburgh.

"Mass Spectrometry in Action" : 1992; various lectures from ICI.

ABSTRACT

This thesis is concerned with the investigation of new synthetic routes to novel oxazine and oxadiazine derivatives which are of potential photochromic importance.

A general synthetic strategy for the synthesis of 2,2-disubstituted 2H-benz-1,4-oxazines based on the synthesis of 2-nitrophenoxyacetaldehydes and their reductive cyclisation *via in situ* ring-closure of intermediate 2-aminophenoxyacetaldehydes was investigated. Various attempts having failed to achieve the reductive cyclisation of the 2-nitrophenoxyacetaldehydes to the 2H-benz-1,4-oxazines, attention was turned to an alternative approach to the 2-aminophenoxyacetaldehydes involved as the incipient intermediates. This approach is based on the formation and subsequent hydrolysis of 2-formamidophenoxyacetaldehydes and successfully afforded 2,2-disubstituted 2H-benz-1,4-oxazines. The chemistry of the benz-1,4-oxazines was investigated and they were found to behave as cyclic imines. Expansion of this chemistry has led to the formation of 3-cyano-2H-benz-1,4-oxazines. The synthesis of 2,2-disubstituted 3,4-dihydro-2H-benzoxazine-3(4H)-ones as possible synthetic precursors of the 2,2-disubstituted 2H-benz-1,4-oxazines was also briefly examined.

Attempted application of the aforementioned methodologies to the synthesis of naphth-1,4-oxazine derivatives were largely unsuccessful. Alkali metal salts of 1-nitroso-2-naphthol were preformed and isolated. Reaction of these salts with 2-bromo-2,2-diphenylacetaldehyde afforded

naphthalene-1,2-dione-1-oxime diphenylformylmethyl ether. Reduction of this oxime ether with triphenylphosphine afforded 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine. Similarly 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine was prepared in a parallel synthetic sequence using 2-nitroso-1-naphthol as the key starting material. The chemical behaviour of the naphth-1,4-oxazines as cyclic amines was also investigated.

3,3-Di(4-dimethylaminophenyl)-2H-naphth[2,1-b]-1,4-oxazine was prepared by the cyclisative condensation of 1-nitroso-2-naphthol with Michler's alkene. The chemistry of Michler's alkene was investigated with a view to forming new derivatives which would react more efficiently with the nitrosonaphthol.

Work was also undertaken on various synthetic routes to disubstituted naphth-1,3-oxazines based on the oxidative manipulation of N-(diphenylmethyl)-2-hydroxy-1-naphthaldimine.

The reactivity of 2-hydroxy-1-naphthaldehyde towards various isocyanates was investigated with a view to obtaining naphthoxazinone derivatives suitable for further minipulation to the naphth-1,3-oxazines.

Investigations of synthetic routes to disubstituted naphth-1,3,4-oxadiazines were undertaken and the reactivity of nitrosonaphthols with various isocyanates was studied as a means of obtaining naphthoxadiazinone derivatives suitable for further manipulation to these naphth-1,3,4-oxadiazines.

PREFACE

The following thesis is concerned with the development of new synthetic routes to novel oxazine and oxadiazine derivatives which are of potential photochromic importance. By way of introduction, Chapter 1 provides a survey of photochromism and existing methods available for the synthesis of oxazine and oxadiazine derivatives. This is followed in Chapters 2 to 3 by an account of the results obtained in the present studies.

CHAPTER 1

A SURVEY OF PHOTOCHROMISM AND SYNTHETIC ROUTES TO POTENTIALLY PHOTOCHROMIC OXAZINE AND OXADIAZINE DERIVATIVES

1. A SURVEY OF PHOTOCHROMISM AND SYNTHETIC ROUTES TO POTENTIALLY PHOTOCHROMIC OXAZINE AND OXADIAZINE DERIVATIVES

1.1 INTRODUCTION

The following survey is concerned initially with the phenomenon of photochromism. A historical survey of the subject is taken from its initial discovery[1] through to modern day developments. A definition of the phenomenon of photochromism is given together with an account of the many reaction mechanisms responsible for photochromic behaviour. The number of photochromic compounds is now vast, so only a limited number of types of photochromic compounds will be discussed and they will be classed according to the photochromic processes they undergo. The applications[2] of photochromic materials are numerous in the different fields of science and engineering. These applications are discussed together with the specific photochromic property they utilise. Finally, a survey is presented of the known literature methods for the synthesis of potentially photochromic fused 2,2-disubstituted 1,4- and 1,3-oxazines and 1,3,4-oxadiazines.

1.2 A SURVEY OF PHOTOCHROMISM

1.2.1 Photochromism : A Historical Overview

The first report of photochromism was by Fritsche,[1] who in 1867 observed (Scheme 1) that tetracene (1), an orange solid, with air and light

formed a colourless material which regenerated tetracene (1) on heating. Shortly after, in 1876, ter Meer[3] showed that the potassium salt of dinitromethane changed colour when exposed to exciting radiation. Phipson[4] provided another early contribution to the field when he described the case of a gate post painted with a zinc pigment that was black when exposed to the sun but white at night. The paint was comparable in composition to the inorganic pigment lithopone which is a composite pigment of zinc sulphide and barium sulphate. Pigments containing zinc sulphide can produce fluorescent and phosphorescent effects which would explain the photochromic behaviour Phipson[4] observed. Marckwald[5] first recognised that photochromism was a new phenomenon when he observed (Scheme 1) that both benzo-1-naphthyridine (2) and tetrachloro-1,2-keto-naphthalenone (3) underwent colour changes on exposure to light, but reverted to their original colour in the dark. He gave the name "phototropy" to this new phenomenon which literally means turning toward light and is commonly used today to describe light-induced interactions occurring in biological systems. Therefore the phenomenon "photochromism" (literally colouration by light) was suggested by Hirshberg in 1950,[6] and is used almost exclusively today.

The first reports of photochromism stimulated the investigation of many other examples of the phenomenon. Wislicenus[7] reported the photochromic behaviour of benzalphenylhydrazone and Biltz[8] showed that benzalphenylhydrazones and certain osazones were also photochromic. Up until 1921 most photochromic studies were carried out in Italy and India.

These early investigations were confined to the synthesis of photochromic molecules, the nature of the exciting radiation, the speed of excitation, decay time and fatigue properties, but did not involve the study of the actual mechanism of the photochromic process. At the end of the decade in 1929 Chalkley[9] published a review of the subject but interest in photochromism at this time was limited. This inactivity continued into the 1930's, during which time only a few advances were made. These advances included work by Harris[10] who studied the photochromism of malachite green and Gheorghiu[11] who investigated the photochromism of semicarbazones.

Since 1940 there has been renewed interest in photochromism. Numerous organic and inorganic photochromic compounds have been prepared. Also various mechanisms have been proposed to account for the different types of photochromic processes and investigations on the structure of the products and intermediates formed and the fatigue characteristics of photochromic materials carried out. With the advent of more sophisticated investigative tools such as i.r., n.m.r., e.s.r. and x-ray spectroscopic methods, scientists such as Y. Hirshberg and his colleague E. Fischer were able to undertake far-reaching research programmes[6] on photochromic behaviour. International interest in photochromism has since grown apace with the first conference on the subject being held in the sixties. The upsurge of interest in photochromism is illustrated by the increasing number of review articles[12-16] surveying the subject.

1.2.2 The Nature of Photochromism

It has been mentioned previously that when photochromism was first observed it was associated with a reversible, light induced photochemical process that resulted in a colour change. However, it must be emphasised that similar processes are possible with all types of electromagnetic radiation, the phenomenon of photochromism being exhibited over a wider spectral range than the visible region.

In this thesis, photochromism is defined as a reversible transformation of a single chemical species induced in one or both directions by electromagnetic radiation between two states having different distinguishable absorption spectra. The inducing radiation usually has a wavelength in the ultraviolet, visible or infrared regions. Reversibility is the important criterion. Irreversible changes represent orthodox photochemical processes and are not included in the following account.

In photochromic systems (Figure 1) irradiation alters the absorption spectrum of the photochromic compound (A) to give the photochromic product (B). When the irradiation source is removed the product (B) reverts to its original state as the photochromic compound (A).

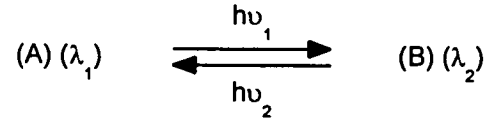


Figure 1

In some cases the reversal can be brought about by electromagnetic radiation of a different wavelength. The visible effect often involves the appearance of colour in a previously colourless material, although changes in colour, for example from red to green, are also known. The shift of an absorption spectrum towards the blue region is known as a hypsochromic shift while a shift to the red region is known as a bathochromic shift.

The typical response of a photochromic compound (A) to activating radiation is shown in Figure 2.

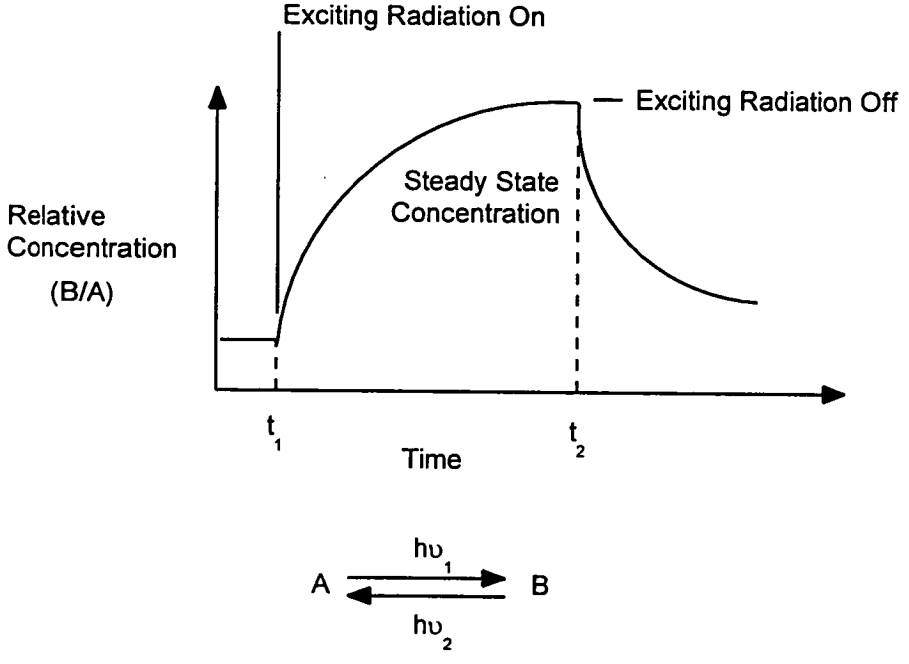
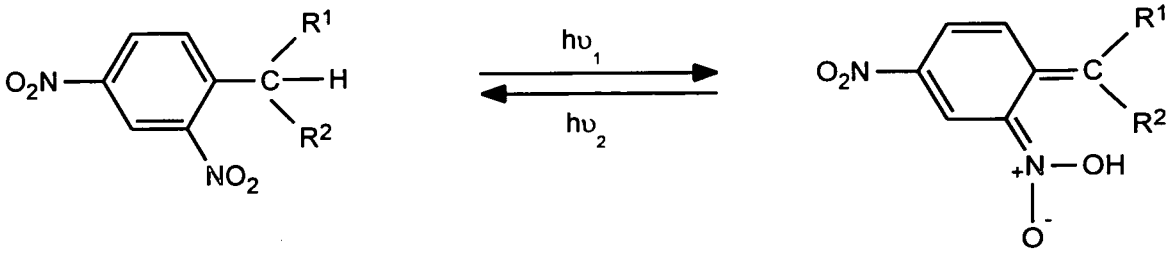


Figure 2

Initially only the (A) state of the molecule is present but when the exciting radiation ($h\upsilon$) is turned on at time (t_1) the (B) state will begin to form. The concentration of (B) builds up until the steady state concentration for the



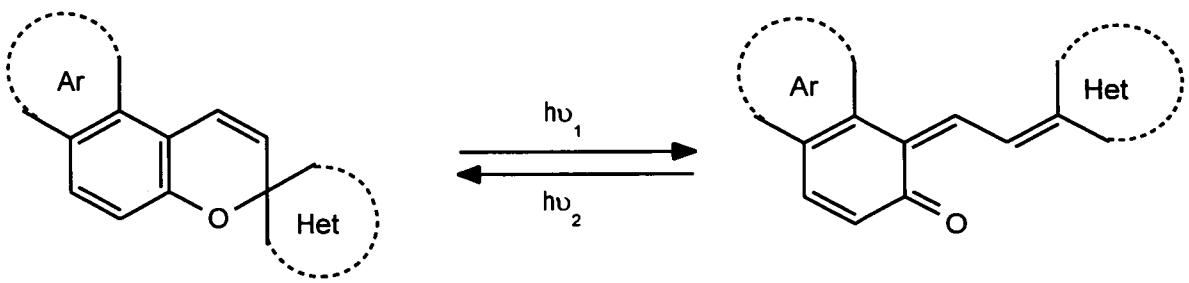
nitro form (A)

(4)

aci - nitro form (B)

(5)

(R^1 = H, Me, Ph ; R^2 = H, Br, CN)



(closed form)

(6)

(open form)

(7)

(Ar = aromatic or heteroaromatic nucleus)
(Het = heteroaromatic nucleus)

Scheme 2

equilibrium (A⇌B) is reached. When the exciting radiation is switched off the (B) form will revert to the (A) form at a rate dependent on the kinetics of the reverse reaction.

Most photochromic transformations are unimolecular processes. The photochromic entity (A) may be a single chemical species such as a molecule or an ion while the product (B) may be a single chemical species or a number of species which can recombine to give (A). For example (Scheme 2) (B) can be the aci-form (5) of an aromatic nitrocompound (4) (A). Commonly state (B) is more deeply coloured than state (A). State (B) is the thermodynamically less stable state but may not always be more coloured. For example (Scheme 2) a small number of spiropyrans are more coloured in their (A) state (6) than in their (B) state (7).

The important characteristics of a photochromic system include the absorption spectrum and extinction coefficients of both the photo-product (B) and the parent photochromic compound (A). The quantum yield of the reversible reaction is very important as is the occurrence of any photochemical side-reactions. Photochemical side-reactions are a major cause of the difficulty in the use of materials incorporating photochromic compounds. Such side-reactions are responsible for the rapid fatigue which is exhibited by most photochromic substances as they are able to undergo reversible change only a limited number of times, which ultimately leads to the loss of reversibility.

1.2.3 Photochromic Processes

There are various reaction mechanisms responsible for photochromic behaviour. The number of photochromic compounds is now vast, so only a limited number of types of photochromic compounds will be discussed and they will be classed according to the photochromic process they undergo. The main types of photochromic process are based on cis-trans isomerisation, pericyclic reactions, tautomerisation and dissociation processes.

The photoinduced cis-trans isomerisation of olefins (Figure 3) is a phenomenon that has been recognised for some time and involves a 180° rotation about a carbon-carbon double bond.

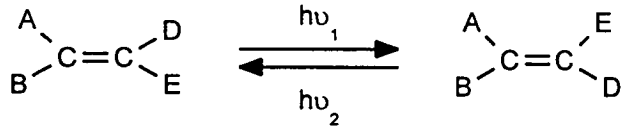
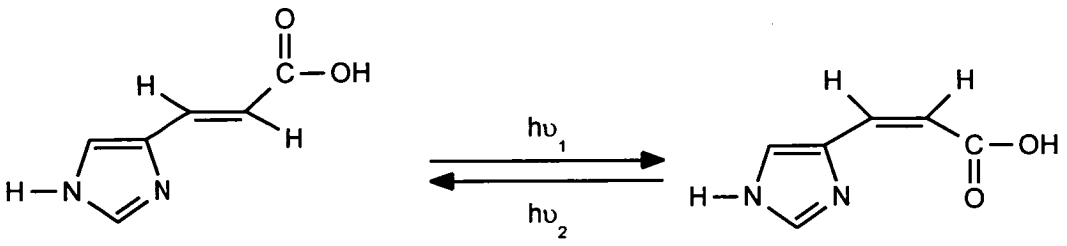


Figure 3

Depending on the olefin, reversible photoisomerisation following direct excitation can occur. Since cis and trans isomers usually have significantly different absorption spectra the reversible cis-trans isomerisation is by definition a photochromic process.

Biological molecules can undergo photochromism by cis-trans isomerisation. For example (Scheme 3) urocanic acid (8) undergoes trans to cis isomerisation in the epidermis as a photochromic process by which part of the harmful energy of ultraviolet radiation is dissipitated by the body.[17] The isomerisation of rhodopsin (10) [the Schiff base derived from 11-cis-retinal by reaction of the

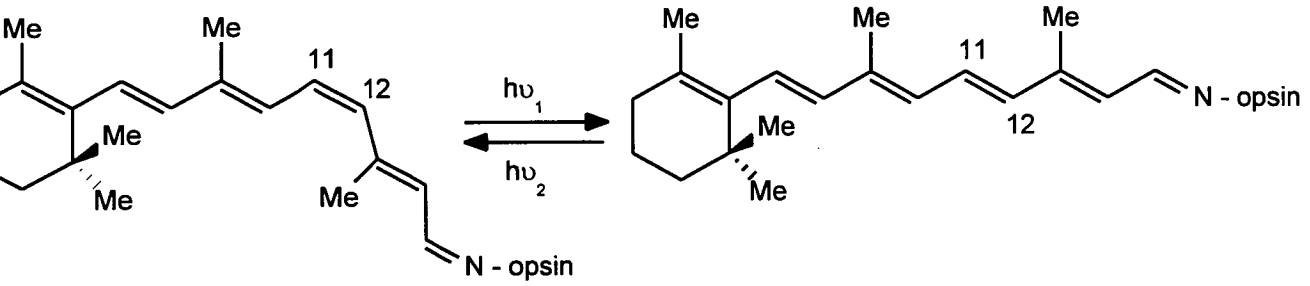


(trans)

(8)

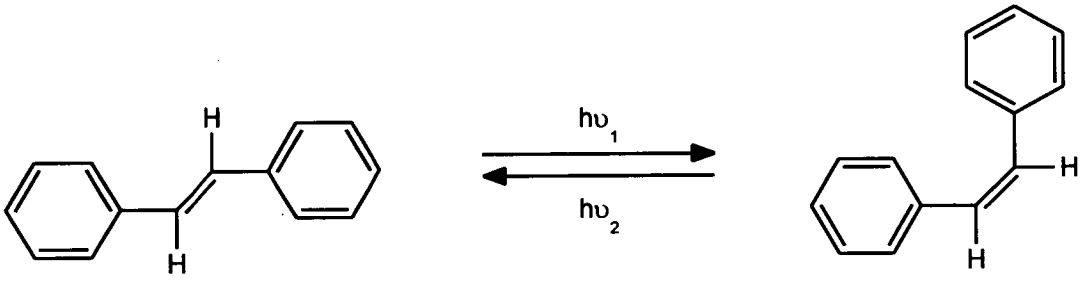
(cis)

(9)



(10)

(11)



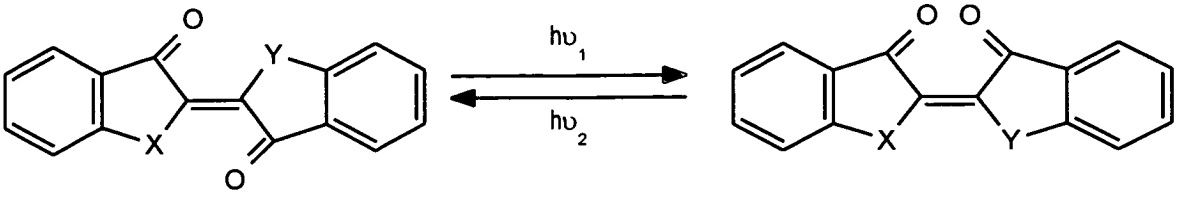
(trans)

(12)

(cis)

(13)

Scheme 3



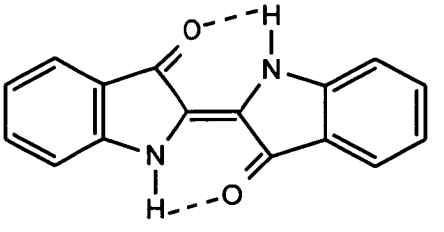
(trans)

(14)

(cis)

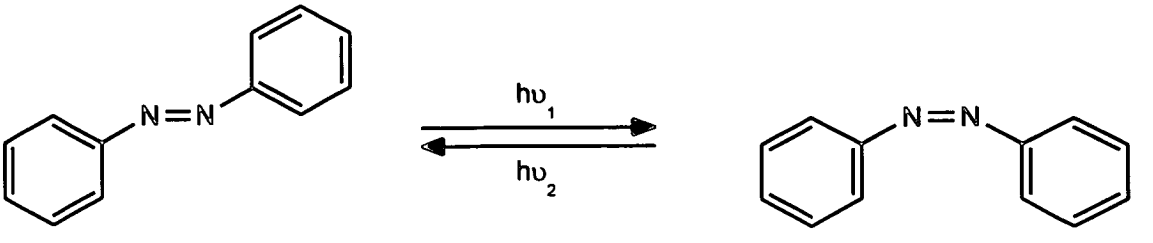
(15)

(X, Y = NR, O, S, Se)



(trans)

(16)



(*E* - isomer)

(17)

(*Z* - isomer)

(18)

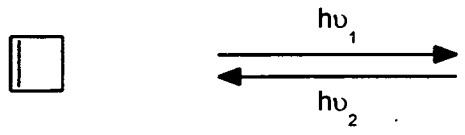
Scheme 4

aldehyde group with an amino substituent in a protein (opsin)] about the 11,12-double bond to give a derivative of all-trans-retinal (11) is the photochromic process responsible for the detection of light by the retina.[18]

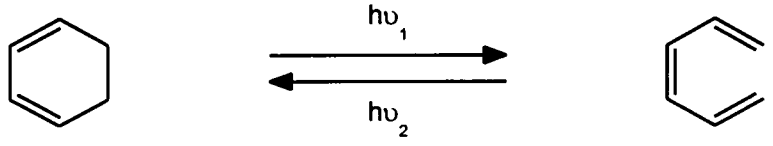
Stilbenes (Scheme 3) can also undergo reversible cis-trans isomerisation.[19,20] Generally the trans isomer (12) is thermodynamically more stable than the cis isomer (13) and as the cis and trans isomers have different absorption spectra the isomerisation is a photochromic process. Similar photochromism is exhibited by analogues of indigo as shown in general in Scheme 4. The heteroatoms X and Y can be nitrogen, oxygen, sulphur or selenium, though if either is an NH substituent photochromism is not exhibited. The lack of photochromic behaviour is suggested[21] to be due to the prevention of reversible photochemical isomerisation attributable to the preferential stabilisation of the trans configuration by hydrogen bonding between the NH and carbonyl groups as shown for indigo (16) in particular.

Aromatic azo compounds can exhibit geometric isomerisation (Scheme 4) and the *E* and *Z* forms undergo reversible photoisomerisation [(17)⇌(18)] and hence show photochromism. The photochromic and isomerisation properties of azobenzene derivatives have been reviewed in the literature.[2,22-24] Recently so-called "photoresponsive azo-bis benzocrown ethers" have been prepared whose photochromic behaviour is also based on cis-trans isomerisation.[24]

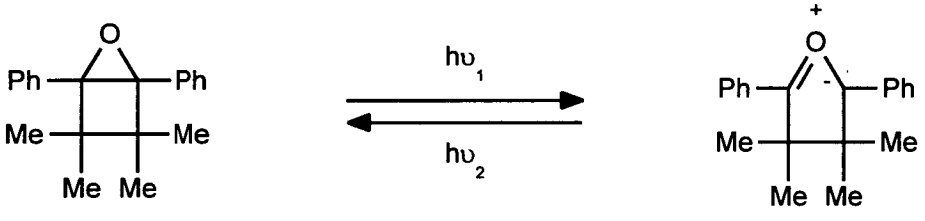
Of the different classes of pericyclic reactions, electrocyclic processes have proved to be especially suitable as a basis for photochromic systems.



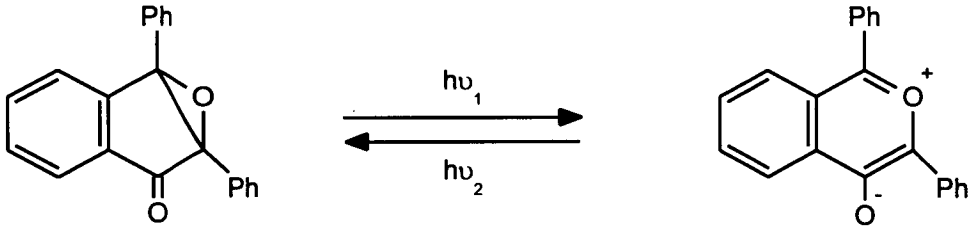
(19) (20)



(21) (22)

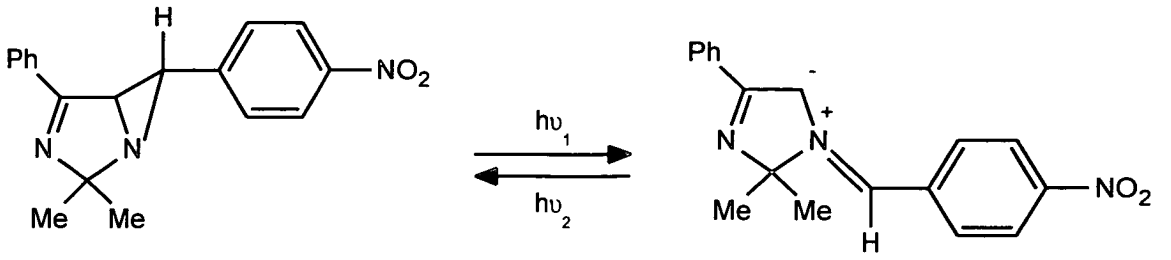


(23) (24)



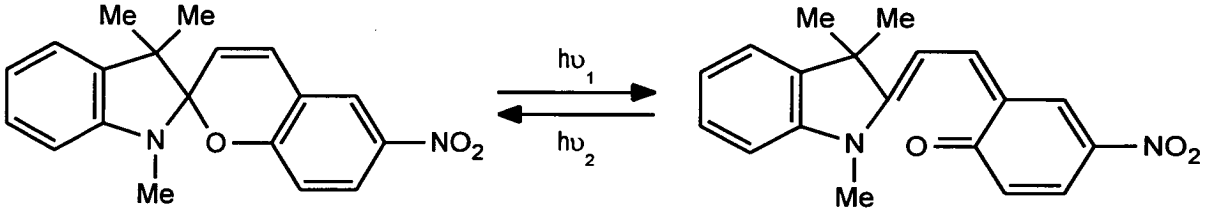
(25) (26)

Scheme 5



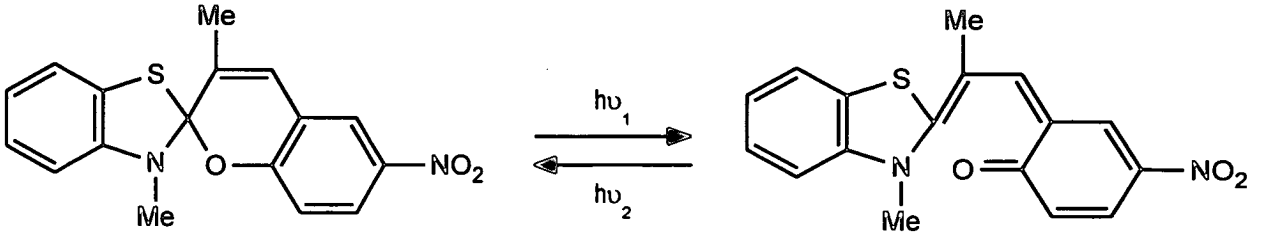
(27) (28)

Scheme 6



(closed form) (open form)

(29) (30)



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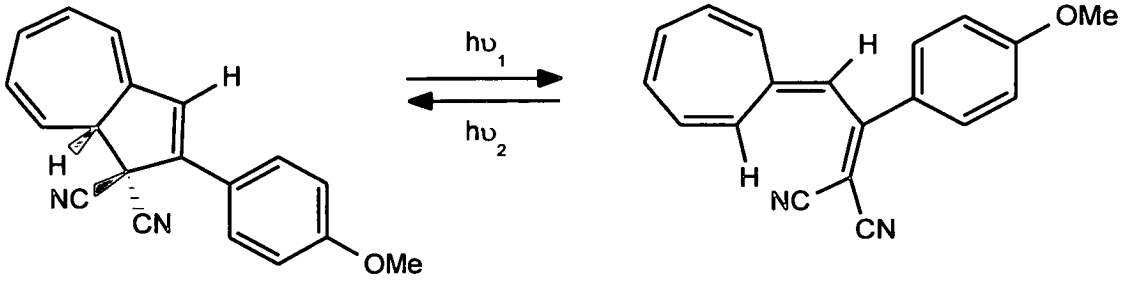
(31) (32)

Scheme 7

In electrocyclic ring-closure a new ó-bond is formed between the terminal atoms of a conjugated π-system, while electrocyclic ring-opening is the reverse of this. Simple examples (Scheme 5) of electrocyclic processes include the interconversion of cyclobutene (19) and buta-1,3-diene (20), and cyclohexa-1,3-diene (21) and hexa-1,3,5-triene (22). Since the cyclic and ring opened forms may have significantly different absorption spectra the reversible photochemical electrocyclic rearrangement is by definition a photochromic process. For example (Scheme 5) the reversible photochemical electrocyclic rearrangement of the oxirane (23) to the purple carbonyl ylide (24) is a photochromic process.[25] Similarly (Scheme 5) irradiation of 2,3-diphenylindenone oxide (25) affords the bright red diphenylbenzopyrylium oxide (26).[26] As this electrocyclic rearrangement is reversible, it too represents a photochromic process. The most important representatives of these photochromic indenone oxides have been studied in detail by Ullman.[26,27]

Interesting photochromic molecules containing an aziridine nucleus have also been described.[28,29] These molecules exhibit photochromic behaviour in the crystalline state, whereas many other systems are photochromic only in solution. An especially efficient photochromic system of this type (Scheme 6) is based on the electrocyclic ring-opening of the bicyclic aziridine (27). This undergoes the light-induced transformation[28,29] to give the imidazole derivative (28) shown in Scheme 6.

The reversible photochemical electrocyclic rearrangement (see Page 6, Scheme 2) of the spiropyrans (6) is an important photochromic process as this



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(33)

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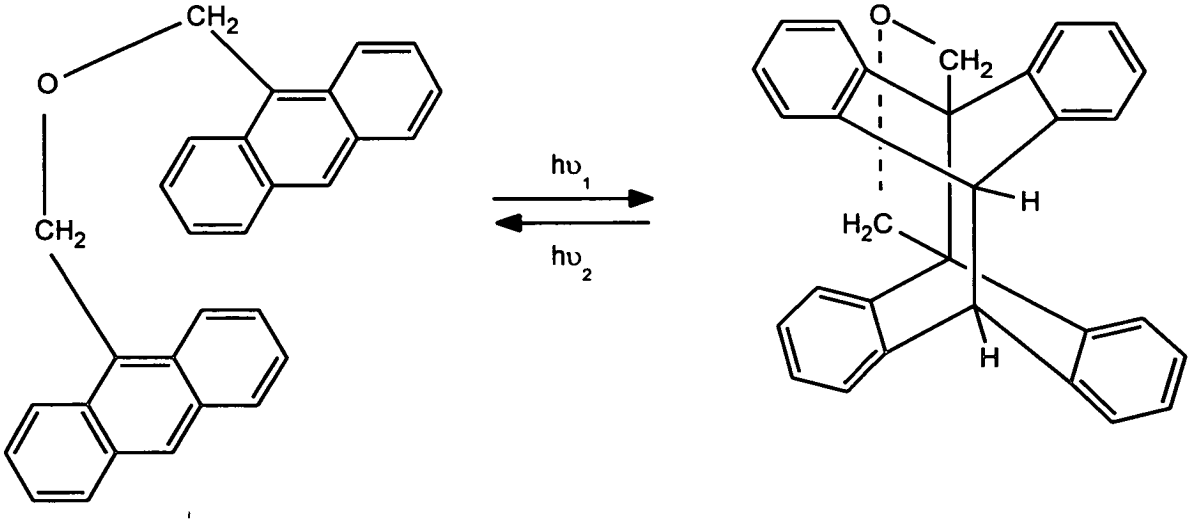
(34)



(35)

(36)

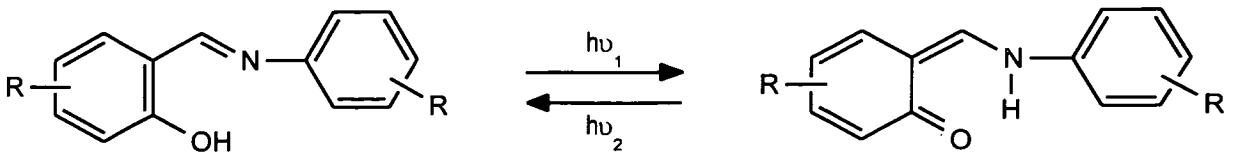
Scheme 8

system has led to quite a number of practical applications (see Page 13, Section 1.2.4). The spiropyrans are photochromic as ultraviolet irradiation of the generally colourless closed form (6) results in the reversible cleavage of the carbon-oxygen bond to afford the open chain compound (7) which usually absorbs strongly in the visible region. These highly interesting spiropyrans were first found to be photochromic by Hirshberg[30] in 1952 and have since been the subject of numerous studies.[2,31-42]

Of the many types of spiropyrans whose photochromism has been investigated, the indolobenzopyrans have been the most extensively studied.[13,14,30] A typical example (Scheme 7) is that of 6-nitro-1',3',3'-trimethylspiro-[2H-1-benzopyran-2,2'-indoline] which is stable in its closed colourless form (29). Ultraviolet irradiation of a colourless solution of (29) produces a deep purple colour due to the formation of the metastable open form (30) which absorbs intensely at 550-600 nm. The original colourless form (29) can be restored by irradiation with visible light or by heating.

As well as the abundant photochromic indolobenzopyrans, several other photochromic spiropyrans have been prepared which contain a different heterocyclic nucleus fused to the benzopyran moiety. For example (Scheme 7) the benzothiazolineospiropyran (31) which contains a benzothiazoline ring connected to a benzopyran moiety is also photochromic.[43]

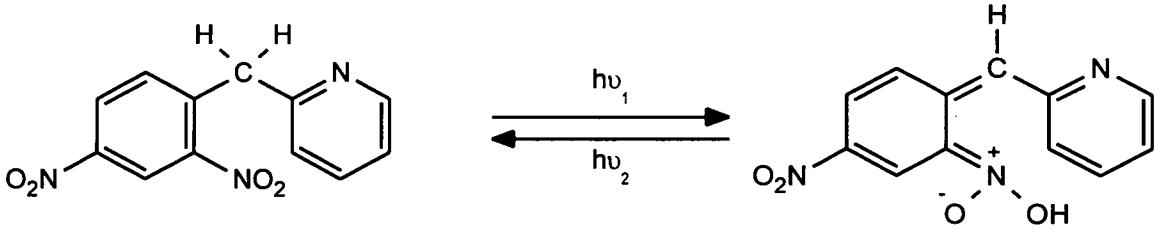
A further interesting example (Scheme 8) of photochromism based on reversible electrocyclic rearrangement is the case of the dihydroazulene (33) which on irradiation affords the dark red 8-vinylheptafulvene derivative (34).[44]



(enol)
(37)

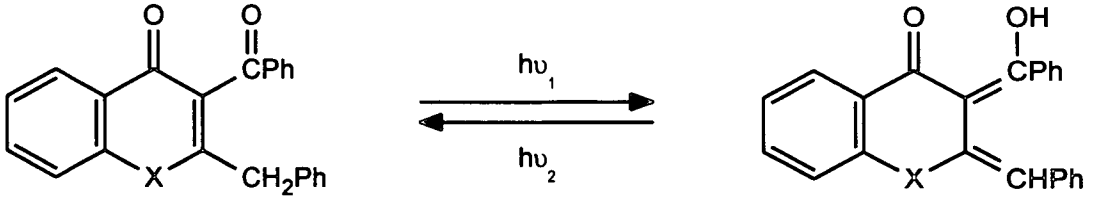
(keto)
(38)

(R = Ph, Me)



(nitro form)
(39)

(aci - nitro form)
(40)



(keto)
(41)

(enol)
(42)

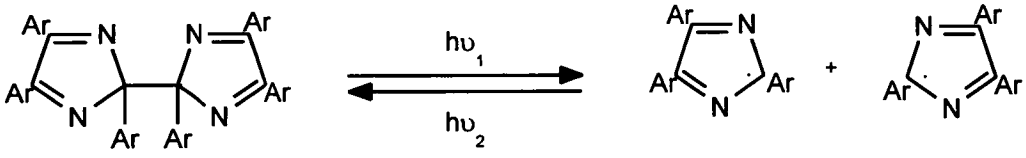
X
a; O
b; NMe

Scheme 9

Removal of the irradiation source results in the electrocyclic ring closure of the open form (34) back to the yellow dihydroazulene (33) as shown in Scheme 8.

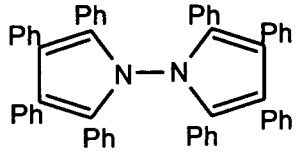
Cycloaddition reactions are another important class of pericyclic processes which provide a basis for photochromic systems. An example (Scheme 8) of a photochromic cycloaddition process is the case of the bisanthracene (35) which is able to cyclo-isomerise to the photoproduct (36) which in turn can revert to (35) by heating or irradiation processes. Since (35) and (36) have significantly different absorption spectra they provide the basis for a photochromic system.[45] The opening and closure of such systems suggest the motion of a jaw, for this reason the authors[45] amusingly proposed to call these bisanthracenes 'jaw photochromic materials'. The photochromic behaviour of various derivatives of the bisanthracene (35) have also been reported in the literature.[45-47]

Photochromism can also be associated with structures which exhibit tautomerism.[2] Photochromic tautomerism is defined as a photochemically induced shift in the equilibrium between tautomers which have significantly different absorption spectra. Photochromic tautomerism involving hydrogen transfer is observed in a number of anils of salicyclaldehyde derivatives.[48,49] For example (Scheme 9) the salicyclaldehyde anils are stable in the enol form (37). Irradiation of the enol form (37), however, produces a reversible proton transfer to afford a shift in the equilibrium in favour of the keto form (38) which has a significantly different absorption spectrum and hence the system is



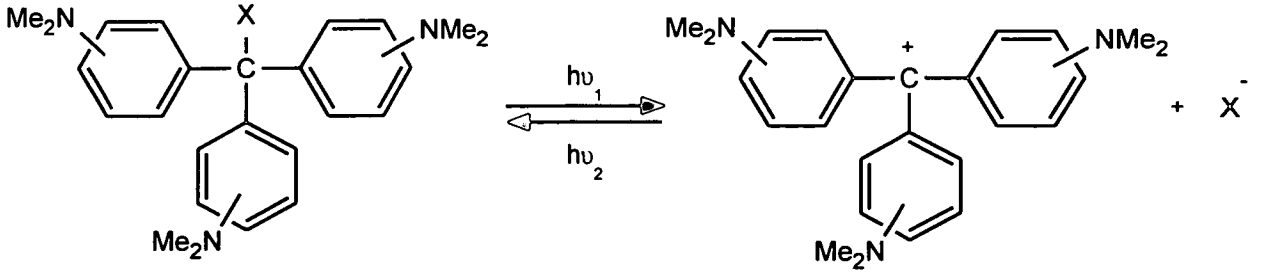
(43) (44) (45)

(Ar = aromatic or heteroaromatic nucleus)



(46)

Scheme 10

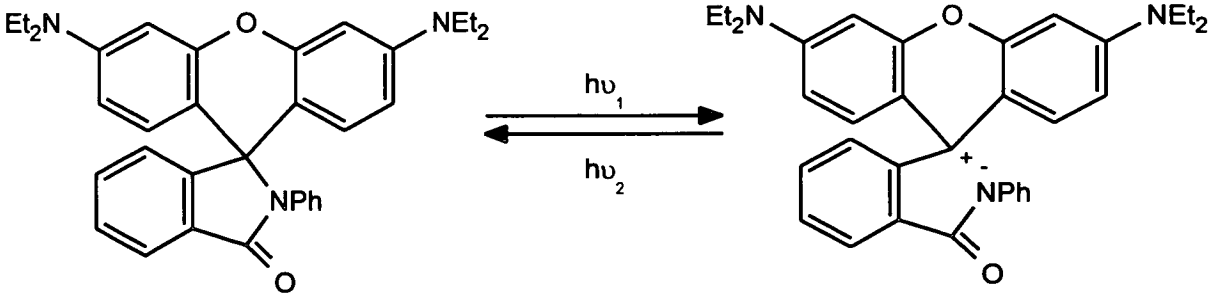


(47) (48) (49)

X

a; CN

b; SO_3H



(50) (51)

Scheme 11

photochromic.[50-53]

Photoinitiated colour changes exhibited by certain nitro compounds can also be attributed to prototropic tautomerism. For example (Scheme 9) irradiation of the colourless nitro form (39) of the dinitrobenzylpyridine results in a hydrogen transfer to afford a shift in the equilibrium in favour of the coloured aci-nitro form (40).

Further examples (Scheme 9) of compounds which exhibit photochromism due to prototropic rearrangements include 2-benzylchromone (41a) and 2-benzyl-N-methylquinolone (41b). Irradiation of the keto forms (41a and b) results in a hydrogen transfer to afford a shift in the equilibrium in favour of the enols (42a and b). These have significantly different absorption spectra in comparison with their respective keto forms (41a and b) and hence the compounds are photochromic.

Photochromism can also be associated with dissociative processes both homolytic and heterolytic. Photochromism derived by homolytic bond cleavage is due to the reversible formation of radical pairs. For example (Scheme 10) bis-2,4,5-triarylimidazoles (43) when irradiated with sunlight or ultraviolet light produce highly coloured radical pairs [(44):(45)].[54] Bis-2,3,4,5-tetraphenylpyrrole (46) behaves similarly as reported by Blinder.[55]

Photochromism associated with heterolytic bond cleavage is due to the formation of highly coloured ions. Photochromism of this type is exhibited by several triarylmethane derivatives. For example (Scheme 11) irradiation of the colourless triarylmethane derivative (47a) results in heterolytic bond cleavage

to afford the strongly coloured triarylmethyl cation (48a) and the anion (49a) which can recombine either thermally or photochemically and hence the process is photochromic. Similarly the triarylmethane derivative (47b) also exhibits photochromism associated with heterolytic bond cleavage.

Spirotriarylmethanes (Scheme 11) such as the rhodamine derivative (50) exhibit photochromism due to heterolytic bond cleavage.[41] Irradiation of the colourless rhodamine derivative (50) results in heterolytic cleavage of the carbon-nitrogen bond to afford the coloured photoproduct (51) as illustrated in Scheme 11. It should be noted (Scheme 11) that the rhodamine derivative (50) can be regarded as a triarylmethane in which the anion is retained in the photoproduct (51) in contrast to the previous examples of the triarylmethane derivatives (47a and b) where the anions (49a and b) are not retained in the photoproducts (48a and b).

1.2.4 Practical Applications of Photochromic Systems

Practical applications of photochromic systems are numerous and are of use in various fields of science and engineering.[2] Such applications are largely based on the utilisation of one or more of the important properties of photochromic materials, namely photosensitivity, colour change or spontaneous reversibility.

A number of applications exploit the photosensitive nature of photochromic compounds. Self developing photography makes use of the light sensitivity of photochromic materials. The value of such a photographic

system is not only the lower cost compared with orthodox silver based photography, but also the simpler development procedure involved (i.e. dry as opposed to wet development). It must be emphasised that in the context of photochromic systems "photography" is used in the widest context and includes the printing and display of digital and pictorial images. For these image-forming applications photochromic systems based on spiropyrans are especially promising.[56]

Photochromic materials have also found applications in dosimeters or actinometers for the measurement of the intensity and distribution of ultraviolet radiation. For example (Scheme 12) the fulgide (52) can be used as a chemical actinometer due to the ease with which it can be converted into the red anhydride (53).[57] The intensity of the radiation is then determined by measuring the increase in absorbance at λ_{max} for the anhydride (53). The photochromism of various interesting fulgides has been investigated in the literature.[58-61]

In a similar way the spiropyran [see Page 9, Scheme 7; (29)] is incorporated into dosimetric labels. Irradiation of such a label results in a colour change due to the transformation [(29)→(30)] and hence alerts the user of exposure to radiation.

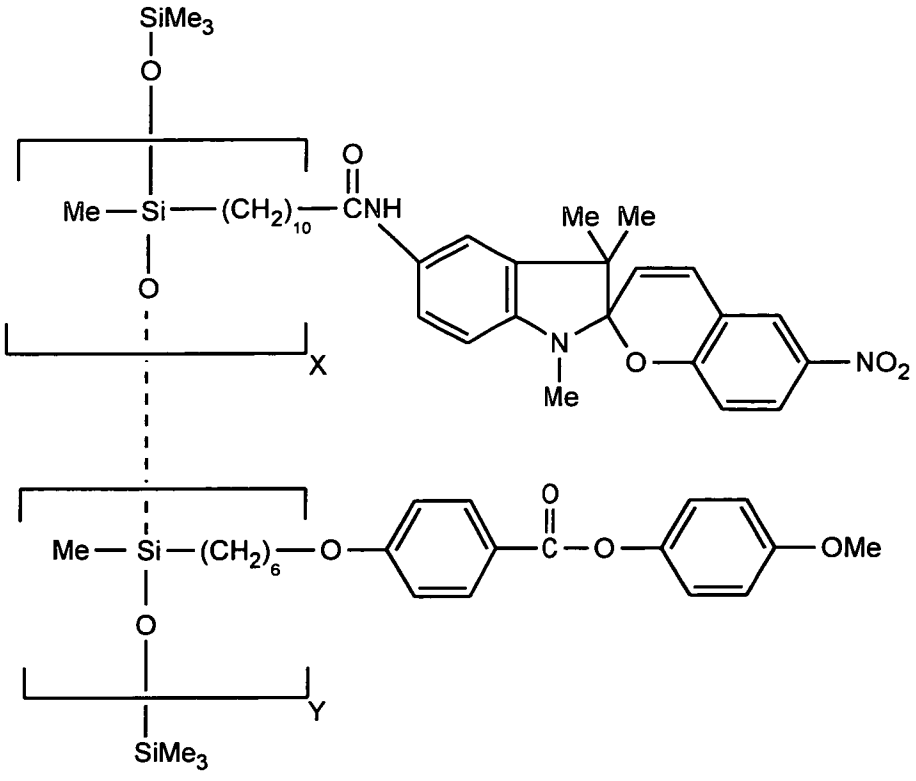
Photochromic films and glasses are potentially useful for the protection of photosensitive products. The photochromic material could be utilised as the wrapper or container and thus protect the photosensitive product from light. Photochromic materials would be useful for inclusion in the packaging of

foodstuffs and drinks, and for biological preparations such as sera and vaccines.

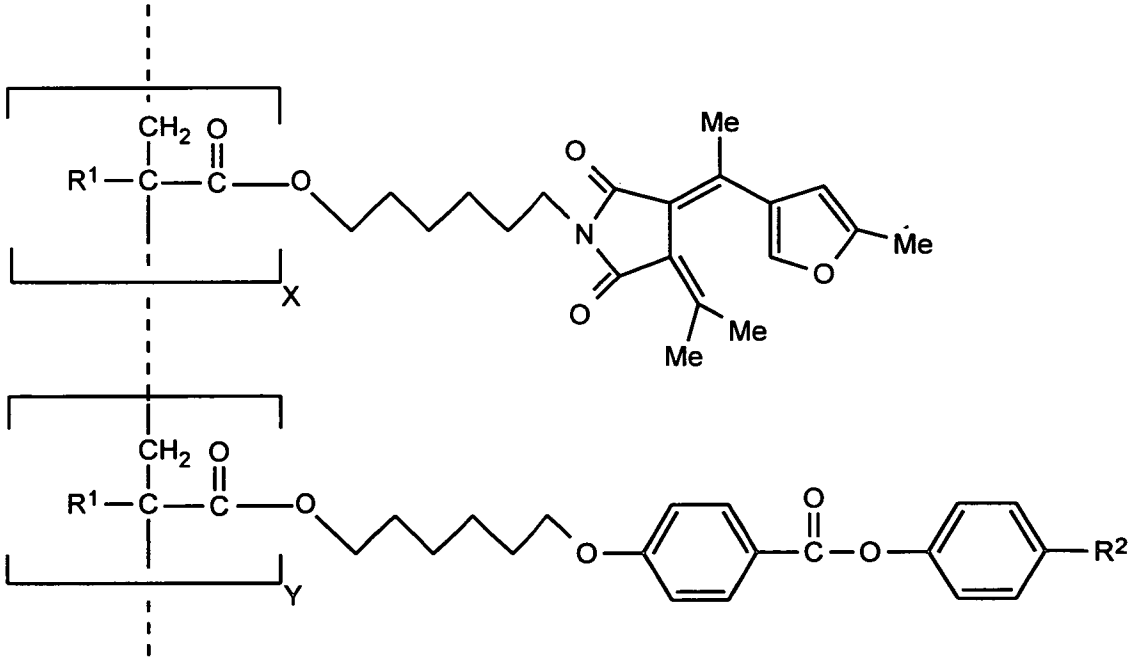
A second group of applications depend upon the specific colour change associated with photochromic materials. There is an obvious military application in the use of photochromic materials as camouflage. Photochromic paints and coatings could be used for camouflaging aircraft, land vehicles, submarines and textiles for military clothing. More frivolous applications of photochromic colour changes would be in oil paints, crayons, face powder, lipstick, toys and clothing.

The third group of applications take advantage of the spontaneous reversibility of the photochromic material to its original state and thus its reusability. The use of photochromic compounds as switches for computers is one possible application which utilises the reversible nature of the phenomenon and has been the subject of recent investigations.[62,63] Photochromic compounds could be used to coat disks or plane surfaces as a means of information storage. For example information could be written with light of wavelength λ_1, read (by reflection or transmission) with light of wavelength λ_2 and erased with light of wavelength λ_3. The major problem of the use of photochromic materials in this context is one of fatigue. If they had to undergo billions of cycles and rapid photoresponse in both directions negligible fatigue (i.e. reversible and irreversible side reactions) would be very difficult to achieve.

An alternative and more appropriate use would therefore be for



(54)



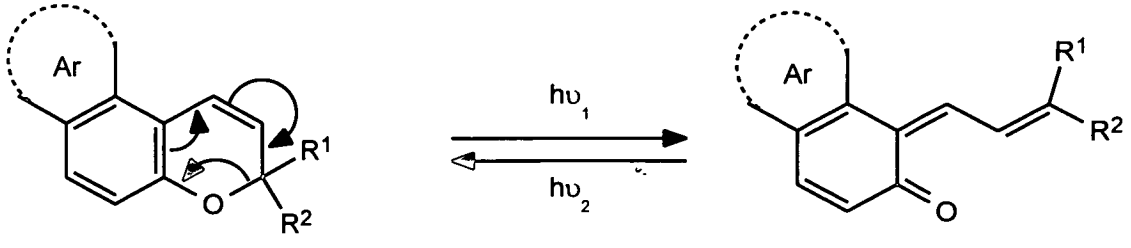
(55)

	R^1	R^2
a:	H	CN
b;	CH_3	OMe

Scheme 13

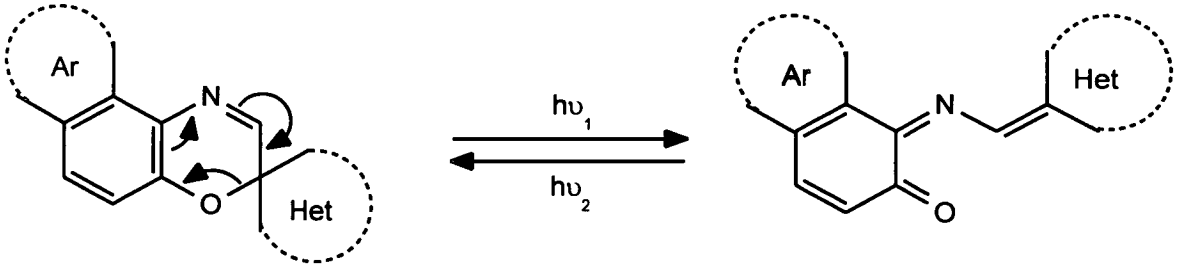
incorporation in data display devices since in this application the photochromic material would only have to switch a small number of times. Data displays based on photochromic materials would have the added advantage of high resolution due to the molecular process involved. Also the extinction coefficients of the photochromic materials are so high that they can produce very thin images free of shadow effects. For example (Scheme 13) photochromic liquid crystal polymers (54) containing spiropyran side groups have been prepared[64] with a view to tailoring these new liquid crystal polymers for applications in imaging technologies.[65] More recent developments (Scheme 13) have led to photochromic liquid crystal polymers (55a and b) containing fulgimide side groups which look very promising materials for the recording of optical information.[66]

Photochromic materials are useful as optical filters in eye protection. The human eye is injured by the ultraviolet components of sunlight with the shorter wavelength components causing conjunctivitis and the longer wavelength components causing erythema. Photochromic materials can continuously and spontaneously alter their transmittance at a rate favourable for blocking out harmful ultraviolet rays. This property finds applications where optical filters are generally used, i.e. in spectacles, optical lenses, glasses used in buildings, and windshields for automobiles and aircraft. For example photochromic silver halide spectacle lenses have traditionally been used in eye protection. Silver halide lenses, however, show fatigue effects when they have been in use for some time.[67] This has led to the development of new lenses



(closed form)
(56)

(open form)
(57)



(closed form)
(58)

(open form)
(59)

(Ar = aromatic or heteroaromatic nucleus)
(Het = heteroaromatic nucleus)

Scheme 14

which incorporate organic photochromic materials such as the spiropyran [see Page 9, Scheme 7; (29)] which has been introduced as a substance suitable for incorporation into photochromic spectacle lenses.[68] Photochromic systems showing virtually no fatigue processes have been discovered in the spirooxazines, and are being marketed by the American Optical Company and Rodenstock as materials for lenses.[69,70] Photochromic materials could also be incorporated into aircraft pilots' visors or windshields to prevent dazzling from the recently developed laser weapons. Similarly photochromic materials have been evaluated for their use in protecting the eye from nuclear flashes.[71]

The foregoing account demonstrates the substantial potential economic and commercial importance of photochromic materials. It has shown there are many possible applications for photochromic materials. Of importance in this thesis are the potentially photochromic oxazines and oxadiazines, synthetic routes to which will now be discussed.

1.3 SYNTHETIC ROUTES TO POTENTIALLY PHOTOCHROMIC OXAZINE AND OXADIAZINE DERIVATIVES

1.3.1 Introduction

The photochromism (Scheme 14) of 2,2-disubstituted 2H-benzopyrans and structurally related condensed systems (56) as well as the corresponding fused spiro-2H-benzopyrans [see Page 6, Scheme 2; (6)] has been extensively investigated and is well documented in the literature.[2] A major advantage of

2H-benzopyran structures (56) and fused spiro-2H-benzopyrans [Scheme 2; (6)] as photochromic materials is that they cover much of the visible spectrum (400-550 nm). On the other hand they have the severe disadvantage as practical photochromic agents, of poor fatigue lifetimes. In contrast replacement of the pyran ring by an oxazine ring results (Scheme 14) in fused spiro-2H-1,4-benzoxazines (58) which exhibit good fatigue lifetimes[72-74] and strong colour density as photochromics and consequently have been the subject of many investigations[72-81] since the original patent disclosure of their properties in 1970.[82]

The photochromism (Scheme 14) of spirooxazines (58) is the result of photocleavage of the spiro C-O bond induced by ultraviolet irradiation, to give an open merocyanine structure (photomerocyanine) (59) which absorbs in the visible region. The merocyanine structure (59) reverts to the original ring-closed form (58) *via* both thermal and photochemical pathways. Generally the spirooxazines (58) will not exhibit photochromism in the solid state but will show photochromism in solution or in media such as gels, films or plastic resins.

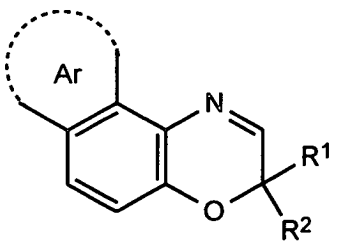
Due to their enhanced resistance to photodegradation spirooxazines (58) have several commercial applications. The majority of these applications are concerned with their use in light filters, particularly in the manufacture of ophthalmic lenses,[83] sunglasses and ski goggles[84] as well as vehicle windows.[85] The interest in organic photochromic compounds for plastic lens application has been stimulated by the commercial success of glass

photochromic lenses. At the moment approximately seventy percent of marketed lenses are plastic so a plastic photochromic lens, especially one incorporating the excellent light fatigue resistance of spirooxazines (58) is highly desirable.

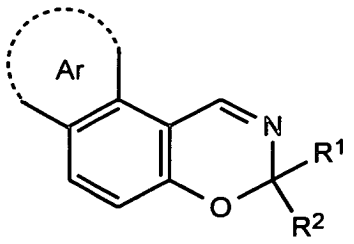
Several plastic photochromic lenses employing spirooxazine derivatives have now been introduced to the market by some of the world's leading optical companies (e.g. Rodenstock, Sola and PPG Industries). Although spirooxazine lenses have excellent light fatigue resistance they do degrade slowly on exposure to sunlight which means that they have an average life of about three years. Although there are flaws in the photochromic performance of these lenses they do represent a significant breakthrough in the photochromic applications of spirooxazines. In addition to their use in sunglass lenses spirooxazines are being evaluated for use in building and vehicle windows. However, this type of application requires a product lifetime of ten to twenty years, a durability not technically possible at present.

Spirooxazines have also found use in novelty items such as cosmetics and toys. These applications are based on the ability of the photochromic compound to undergo a specific colour change to give a desired effect. Other potential applications of spirooxazine derivatives are in the fields of data display, anti-counterfeit security systems and optical devices capable of optical recording and memory.

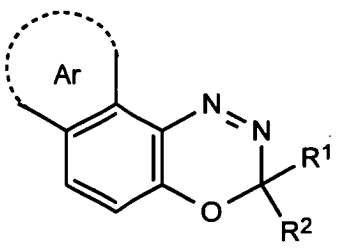
The foregoing illustrates the substantial practical potential of spirooxazine photochromism. However the practical applications of fused



(60)



(61)



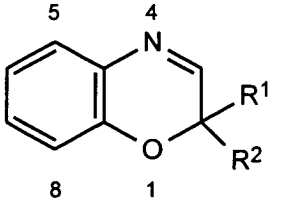
(62)

(Ar = aromatic or heteroaromatic nucleus)

Scheme 15

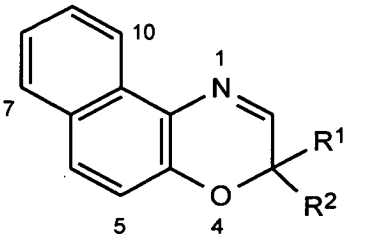
spiro-2H-1,4-oxazines [see Page 17, Scheme 14; (58)] can be restricted by their absorption characteristics which in many cases cover only a limited region of the visible spectrum (550-630 nm). There is therefore an urgent need for new classes of photochromic molecules with good fatigue lifetimes and colour density which absorb in the same region (400-500 nm) covered by the fatigue susceptible fused 2H-benzopyrans [see Page 17, Scheme 14; (56)] and fused spiro-2H-benzopyrans [see Page 6, Scheme 2; (6)]. The poor fatigue resistance of these latter photochromics can be attributed to the presence of the styryl C(3)-C(4) double bond, replacement of which by an imino (carbon-nitrogen) double bond results in the fatigue-resistant fused spiro-2H-1,4-benzoxazines [see Page 17, Scheme 14; (58)]. It follows (Scheme 15) that simple (non-spiro) fused 2,2-disubstituted 2H-1,4-oxazines (60) and 2,2-disubstituted 2H-1,3-oxazines (61) might combine the spectral features of the fused 2,2-disubstituted 2H-benzopyrans (56) with the fatigue resistance of fused spiro-2H-1,4-oxazines (58), thus providing the required new types of fatigue-resistant and spectrally appropriate photochromics. Fused 2,2-disubstituted 2H-1,3,4-oxadiazines (62) would also have potential in this context.

With the exception of a single publication in the primary literature[75] and a related patent[86] describing the photochromism of fused 2,2-disubstituted 2H-1,4-oxazine derivatives, the photochromic properties of heterocyclic structures of the types [(60)-(62)] have been unexplored to date. This lack of information on the potentially photochromic heterocyclic structures [(60)-(62)] provided the



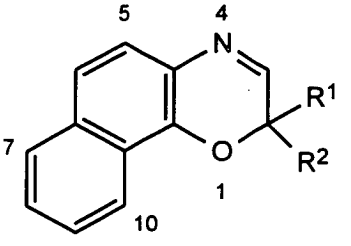
2H - Benz - 1,4 - oxazine

(63)



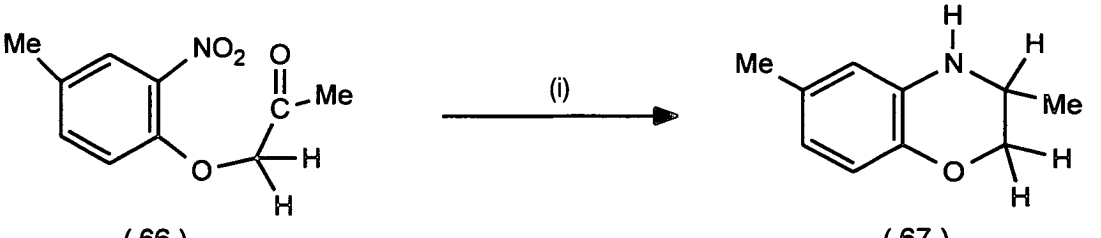
3H - Naphth [2,1 - b] - 1,4 - oxazine

(64)



2H - Naphth [1,2 - b] - 1,4 - oxazine

(65)



(66)

(67)

(i) H_2, Raney Ni, EtOH, room temp., 115 - 122 atm.

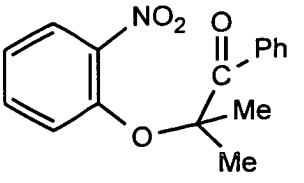
Scheme 16

stimulus for the studies described in this thesis which are largely concerned with the development of synthetic routes to fused 2,2-disubstituted 2H-1,4-oxazines (60), 2,2-disubstituted 2H-1,3-oxazines (61) and 2,2-disubstituted 2H-1,3,4-oxadiazines (62). The discussion of the results obtained in these studies are preceded by a survey of the few literature methods available for the synthesis of heterocyclic structures of the types [(60)-(62)].

1.3.2 Synthesis of Fused 2,2-Disubstituted 2H-1,4-Oxazines

The synthesis of fused 2,2-disubstituted 2H-1,4-oxazines [see Page 20, Scheme 15; (60)] has received only limited coverage in the literature and the chemistry of the fused 2,2-disubstituted 2H-1,4-oxazines [see Page 20, Scheme 15; (60)] is relatively unexplored. Of particular interest to these studies (Scheme 16) are synthetic methods pertaining to the 2,2-disubstituted 2H-benz-1,4-oxazines (63), the 3,3-disubstituted 3H-naphth[2,1-b]-1,4-oxazines (64) and the 2,2-disubstituted 2H-naphth[1,2-b]-1,4-oxazines (65).

Although the benz-1,4-oxazines (63) would not be expected to be photochromic, studies into the synthesis of such compounds would serve as a useful synthetic model for the potentially photochromic naphth-1,4-oxazines [(64) and (65)]. Derivatives of 2H-benz-1,4-oxazines (63) are available by the reduction with concurrent and spontaneous cyclisation of 2-nitrophenoxymethylketones. For example (Scheme 16) reduction of 4-methyl-2-nitrophenoxyacetone (66) with hydrogen over Raney nickel under high pressure (115-122 atm) affords 3,6-dimethyl-2H-3,4-dihydro-benz-1,4-



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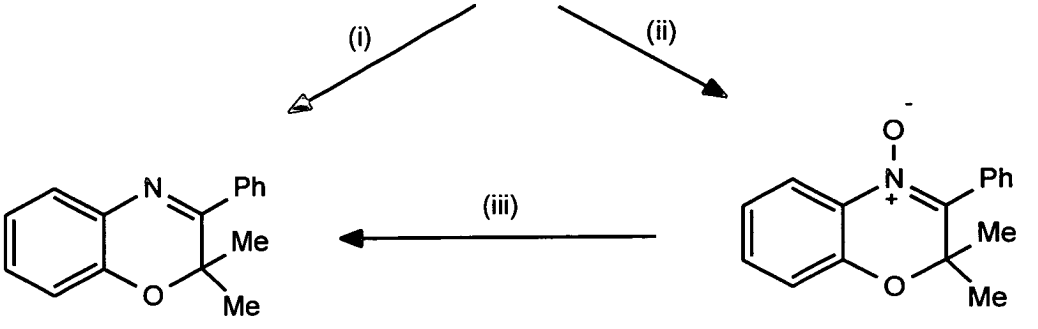
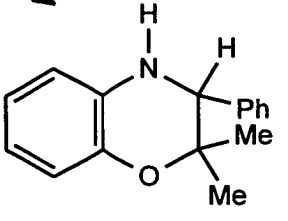


(69)

(70)



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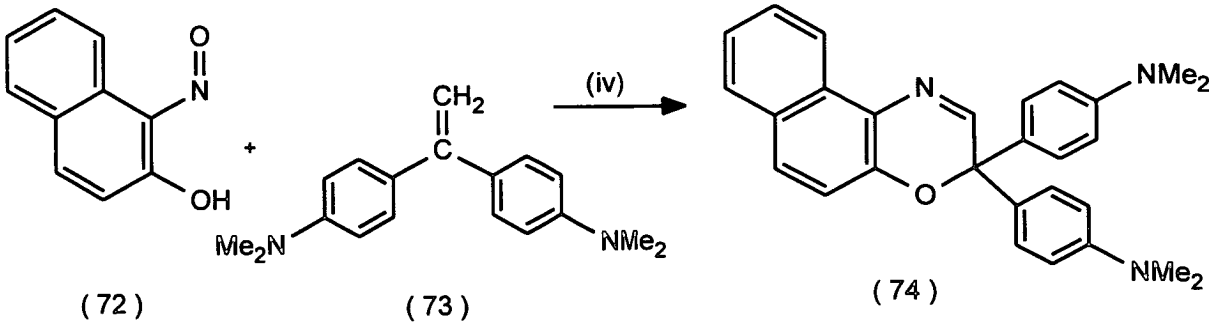


(72)

(73)

(74)

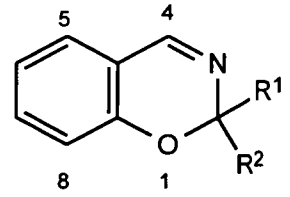
(i) NaH_2PO_2, 5% Pd - C, THF, H_2O, room temp.
(ii) Zn, NH_4Cl, EtOH, H_2O, N_2, 10°.
(iii) hυ, 1,4 - dioxane, room temp.
(iv) AcOH, EtOH, reflux.

Scheme 17

oxazine(67).[87] Similar dihydro-benz-1,4-oxazines can be prepared by the reductive cyclisation of various other 2-nitrophenoxyalkyl ketones with hydrogen over Raney nickel at lower pressures (4 atm).[88]

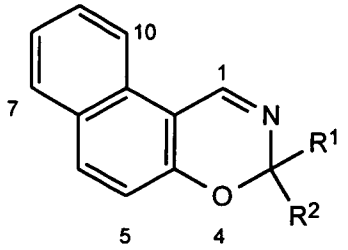
The reductive cyclisation of 2-nitrophenoxyacetophenones provides a synthetic approach to derivatives of the 2,2-disubstituted 2H-benz-1,4-oxazines [see Scheme 16; (63)]. For example (Scheme 17) reductive cyclisation of the 2-nitrophenoxyacetophenone (68) using sodium phosphinite as a hydrogen donor and 5% palladium-on-charcoal as a catalyst has afforded the 2,2-dimethyl-3-phenyl-2H-benz-1,4-oxazine (69).[89] Reduction of the 2-nitrophenoxyacetophenone (68) using excess quantities of catalyst and sodium phosphinite results in the formation of the dihydro compound (71) *via* further reduction of the benz-1,4-oxazine (69). The benz-1,4-oxazine (69) was also obtained by the irradiation (Scheme 17) of the light sensitive N-oxide (70).[90] The N-oxide (70) was readily available by the reductive cyclisation of the 2-nitrophenoxyacetophenone (68) using zinc dust and ammonium chloride. Numerous other 2H-benz-1,4-oxazine-N-oxides have been prepared[91] but the possible irradiation of these compound to afford derivatives of the 2H-benz-1,4-oxazines [see Scheme 16; (63)] has not been reported. Modification (Scheme 17) of the transformation [(68)→(69)] by replacement of the benzoyl substituent with an aldehyde group would provide a useful method for the synthesis of 2H-benz-1,4-oxazines [see Scheme 16; (63)] which to date has not been investigated.

The synthesis of derivatives of the 3,3-disubstituted 3H-naphth[2,1-b]-



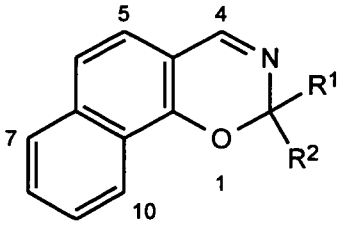
2H - Benz - 1,3 - oxazine

(75)



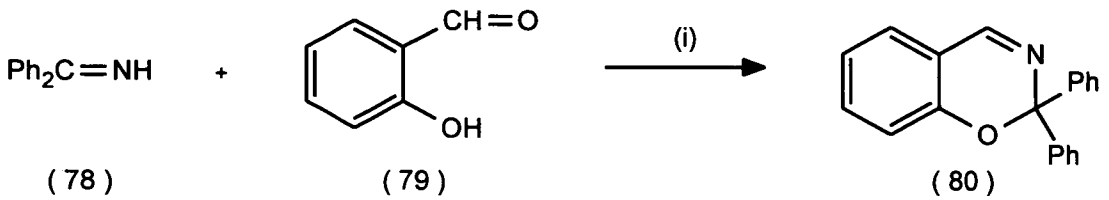
3H - Naphth [1,2 - e] - 1,3 - oxazine

(76)



2H - Naphth [2,1 - e] - 1,3 - oxazine

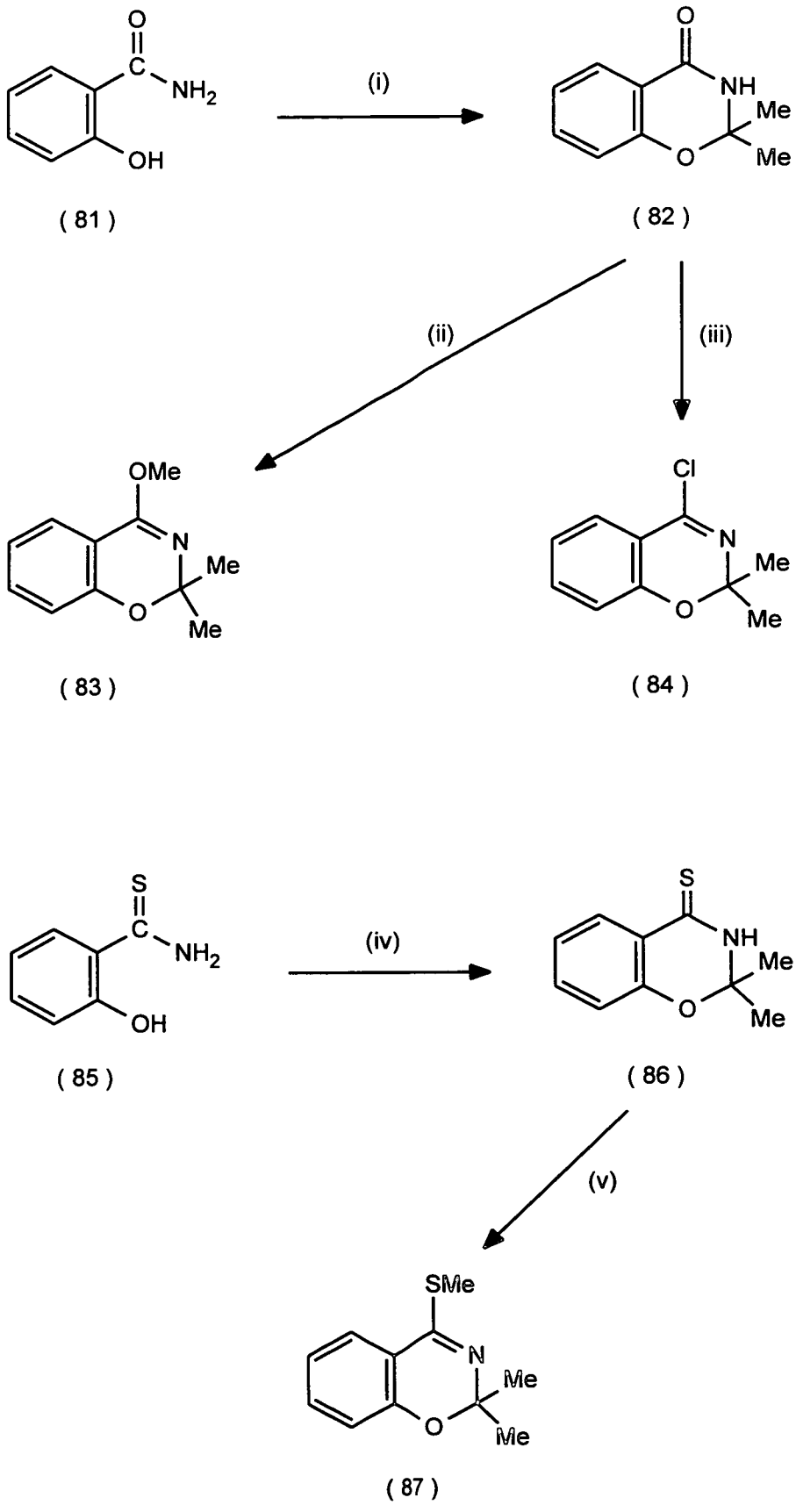
(77)



(78) (79) (80)

(i) Et_3N, benzene, reflux.

Scheme 18



(81) (82) (83) (84) (85) (86) (87)

(i) $(CH_3CO)_2O$, H_2SO_4 aqu. (conc.), acetone, 50 - 55°.
(ii) MeI, Ag_2O, 1,4 - dioxane, room temp.
(iii) PCl_3, $POCl_3$, 50°.
(iv) $(CH_3CO)_2O$, H_2SO_4 aqu. (conc.), acetone, 50 - 55°.
(v) MeI, acetone, reflux.

Scheme 19

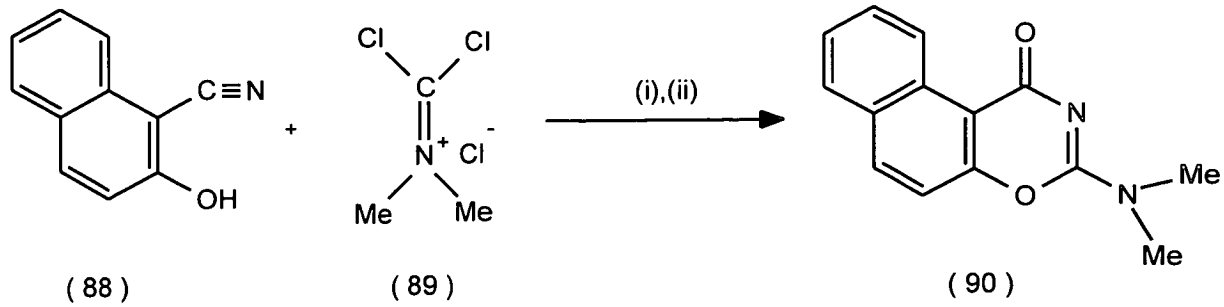
1,4-oxazine [see Page 21, Scheme 16; (64)] and the 2,2-disubstituted 2H-naphth[1,2-b]-1,4-oxazine [see Page 21, Scheme 16; (65)] has been largely unexplored. The primary literature contains only one example reported by Paetzold[75] describing the synthesis (Scheme 17) of the 3,3-disubstituted 3H-naphth-1,4-oxazine (74) by the acid catalysed reaction of 1-nitroso-2-naphthol (72) with the alkene (73). Disappointingly the details of the paper[75] are vague, no yields or quantity of reactants are given. At present, apart from this one incompletely described study, synthetic methods for the naphth-1,4-oxazines [see Page 21, Scheme 16; (64) and (65)] are unknown.

1.3.3 Synthesis of Fused 2,2-Disubstituted 2H-1,3-Oxazines

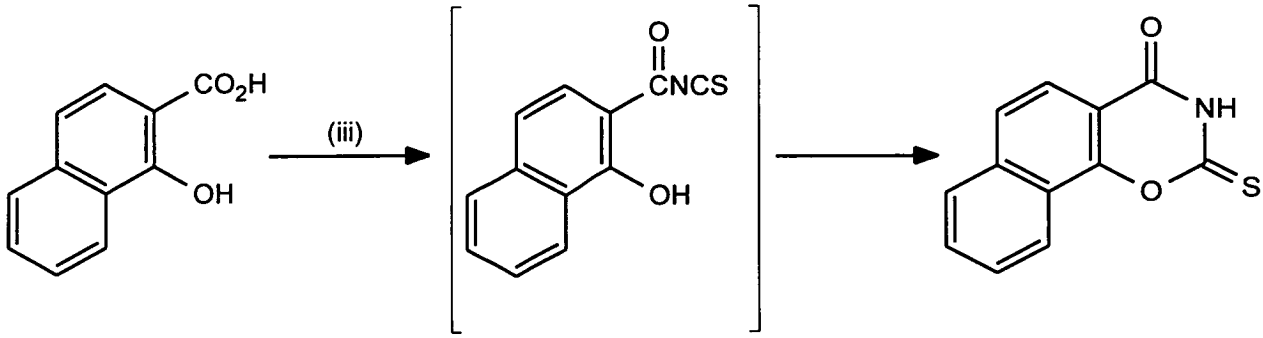
The synthesis of fused 2,2-disubstituted 2H-1,3-oxazines [see Page 20, Scheme 15; (61)] has been the subject of numerous investigations. Of interest to the present studies (Scheme 18) are synthetic routes to the 2,2-disubstituted 2H-benz-1,3-oxazines (75), the 3,3-disubstituted 3H-naphth[1,2-e]-1,3-oxazines (76) and the 2,2-disubstituted 2H-naphth[2,1-e]-1,3-oxazines (77).

The synthesis (Scheme 18) of 2,2-diphenyl-2H-benz-1,3-oxazine (80) has been achieved in good yield (70%) by the reaction of salicyclaldehyde (79) with the diphenylketimine (78) and triethylamine.[92] The usefulness of this synthetic route for the synthesis of other 2,2-disubstituted 2H-benz-1,3-oxazines (75) would depend on the availability of various ketimine derivatives and their reactivity towards salicylaldehyde (79).

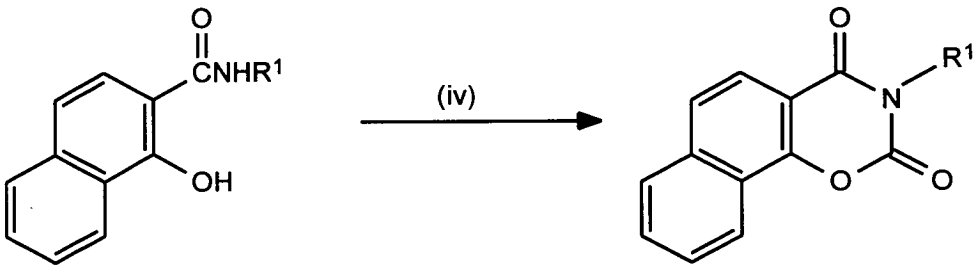
Similar (Scheme 19) to salicylaldehyde (79), salicylamide (81) is also



(88) (89) (90)



(91) (92) (93)



(94) (95)

(R^1 = H, Me, Ph ; R^2 = Me, Et)

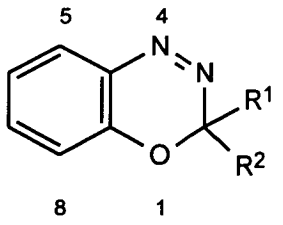
(i) $ClCH_2CH_2Cl$, reflux.
(ii) K_2CO_3, H_2O, room temp.
(iii) $Ph_3P(SCN)_2$, CH_2Cl_2, N_2, - 40°.
(iv) $ClCO_2R^2$, pyridine, 85°.

Scheme 20

useful in the synthesis of 2H-benz-1,3-oxazines [see Scheme 18; (75)]. For example (Scheme 19) salicylamide (81) condenses with a number of dialkyl ketones to afford benzoxazinones (82) which can be converted into alkoxy (83) or chloro (84) derivatives by alkylation[93] or by treatment with phosphorous oxychloride[94] respectively. A further useful reagent for the synthesis of 2H-benz-1,3-oxazines [see Scheme 18; (75)] is the thiomide (85) which reacts with acetone to afford the thioketone derivative (86).[95] The thioketone (86) can then be converted into the corresponding sulphide derivative (87) by reaction with methyl iodide.

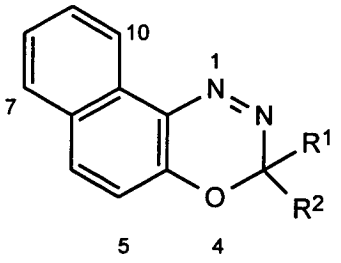
Studies concerning the synthesis of the potentially photochromic 3H-naphth[1,2-e]-1,3-oxazines [see Scheme 18; (76)] and the 2H-naphth[2,1-e]-1,3-oxazines [see Scheme 18; (77)] are largely lacking in the literature. Kokel has described[96] the synthesis (Scheme 20) of the naphth-1,3-oxazinone (90) by the reaction of 2-hydroxy-1-naphthonitrile (88) with the phosgeniminium chloride (89). Similarly (Scheme 20) the 2-thioxo-naphth[2,1-e]-1,3-oxazin-4-one (93) has also been prepared.[97] This synthesis involves the isothiocyanation of the carboxylic acid (91) to afford the acyl isothiocyanate (92) which cyclises to the 2-thioxo-naphth-1,3-oxazin-4-one (93).

The reaction (Scheme 20) of the amides (94) with various chloroformates provides a synthesis of the naphth-1,3-oxazine-2,4-dione system (95).[98,99] Unfortunately, further manipulation of the strategies (Scheme 20) employed in the synthesis of the naphth-1,3-oxazinones (90), (93) and (95) to afford synthetic routes to the naphth-1,3-oxazines [see Scheme 18; (76)-



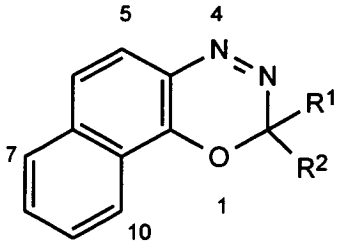
2H - Benz - 1,3,4 - oxadiazine

(96)



3H - Naphth [1,2 - e] - 1,3,4 - oxadiazine

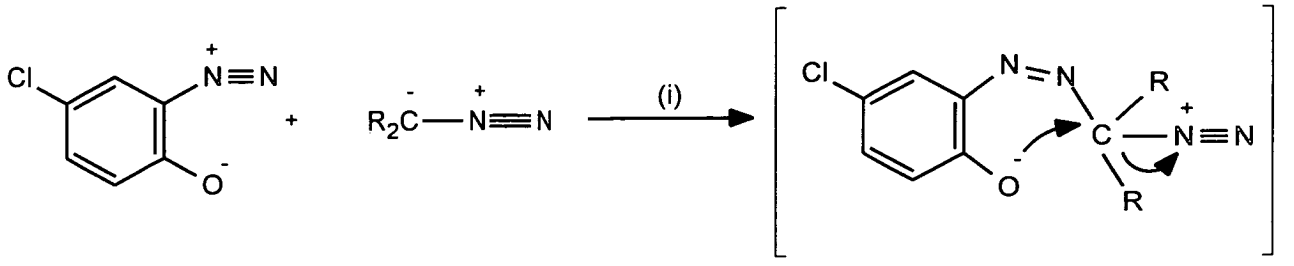
(97)



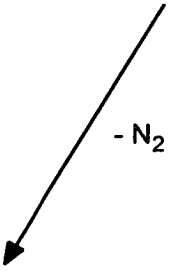
2H - Naphth [2,1 - e] - 1,3,4 - oxadiazine

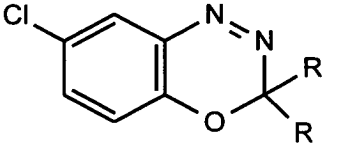
(98)

Scheme 21



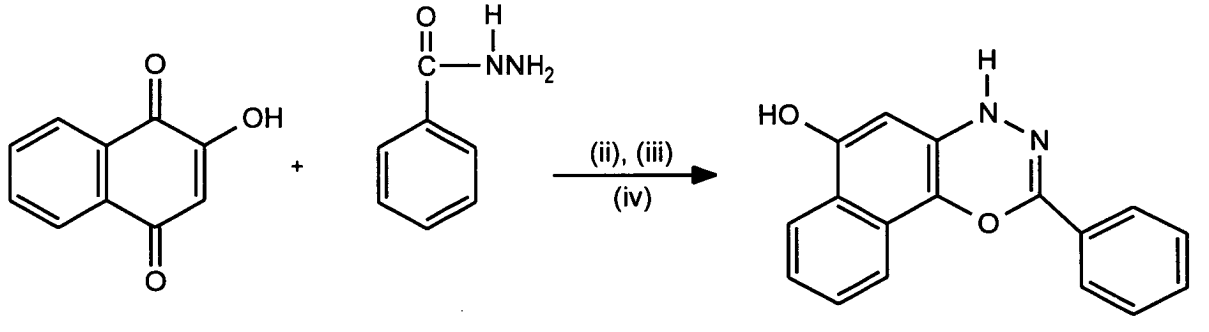
(99) (100) (101)





(102)

R
a; H
b; Ph



(103) (104) (105)

(i) THF, Ether, - 15°.
(ii) AcOH, reflux.
(iii) AcO_2, Zn, Et_3N, reflux.
(iv) 0.5% ethanolic NaOH, reflux.

Scheme 22

(77)] would not be practical. There is therefore a need for new synthetic strategies for the synthesis of naphth-1,3-oxazines of the types (76) and (77).

1.3.4 Synthesis of Fused 2,2-Disubstituted 2H-1,3,4-Oxadiazines

Fused 2,2-disubstituted 2H-1,3,4-oxadiazines [see Page 20, Scheme 15; (62)] have received only limited coverage in the literature. Of interest in the present work (Scheme 21) are synthetic routes to the 2,2-disubstituted 2H-benz-1,3,4-oxadiazines (96), the 3,3-disubstituted 3H-naphth[1,2-e]-1,3,4-oxadiazines (97) and the 2,2-disubstituted 2H-naphth[2,1-e]-1,3,4-oxadiazines (98).

It has been reported[100] that the reaction (Scheme 22) of diazomethane (100a) with the chloro-benzoquinone diazide (99) affords the diazo intermediate (101a) which cyclises with the loss of nitrogen to afford the 2H-benz-1,3,4-oxadiazine (102a). Various other derivatives of the benz-1,3,4-oxadiazine ring system of the type (102a) were also synthesised.[100] Presumably this synthetic route could be manipulated further using other diazoalkane derivatives (100) to afford a series of 2,2-disubstituted 2H-benz-1,3,4-oxadiazines (96). Huisgen[101] for example (Scheme 22) has reacted diphenyldiazomethane (100b) with the chlorobenzoquinone diazide (99) to afford the 6-chloro-2,2-diphenyl-2H-benz-1,3,4-oxadiazine (102b). Several other benz-1,3,4-oxadiazine derivatives of the type (102b) were also synthesised.[101]

The potentially photochromic naphth-1,3,4-oxadiazines [see Scheme 21;

(97) and (98)] have received only a single mention in the primary literature.[102] It was reported[102] (Scheme 22) that 2-hydroxy-1,4-naphthoquinone (103) condenses with benzhydrazide (104) to afford *via* reductive cyclisation the naphth-1,3,4-oxadiazine (105). Further manipulation of the naphth-1,3,4-oxadiazine (105) to give derivatives of the 2H-naphth[2,1-e]-1,3,4-oxadiazine ring system [see Scheme 21; (98)] would be a complicated procedure. There is therefore a need for an investigation on new synthetic methodologies for the potentially photochromic naphth-1,3,4-oxadiazines [see Scheme 21; (97)-(98)].

CHAPTER 2

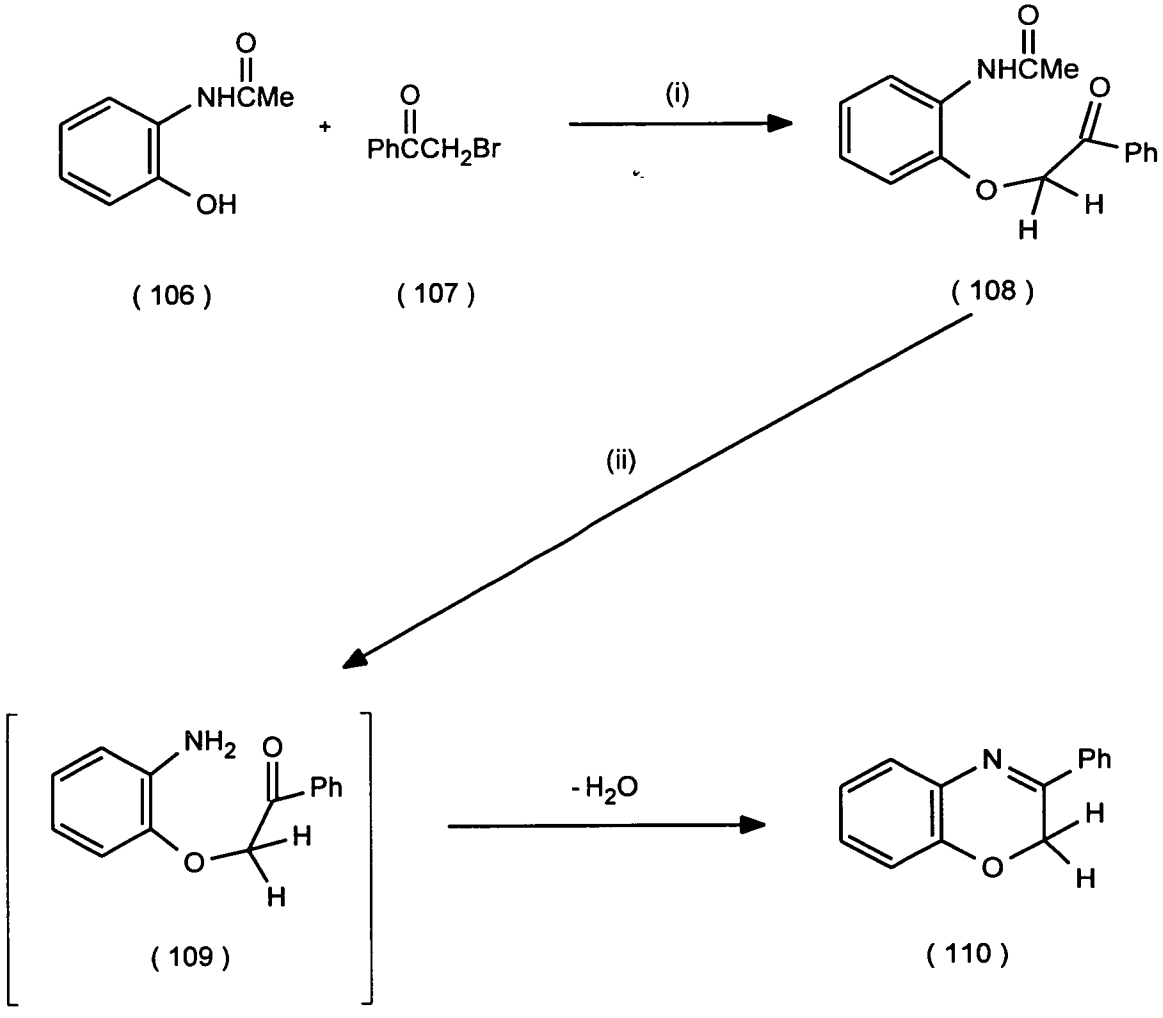
INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2H-1,4-OXAZINES AS NOVEL PHOTOCHROMIC AGENTS

2. INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2H-1,4-OXAZINES AS NOVEL PHOTOCHROMIC AGENTS

2.1 INTRODUCTION

The importance of fused 2,2-disubstituted 2H-1,4-oxazines [see Page 20, Scheme 15; (60)] as possible photochromic agents was discussed in Chapter 1 of this thesis. Due to the potential commercial applications of these fused 2,2-disubstituted 2H-1,4-oxazines [see Page 20, Scheme 15; (60)] studies (see Page 21, Scheme 16) were initiated on synthetic methods pertaining to the 2,2-disubstituted 2H-benz-1,4-oxazines (63), the 3,3-disubstituted 3H-naphth[2,1-b]-1,4-oxazines (64) and the 2,2-disubstituted 2H-naphth[1,2-b]-1,4-oxazines (65).

Few 2,2-disubstituted 2H-benz-1,4-oxazines [see Page 21, Scheme 16; (63)] have been described in the literature and their chemistry is relatively unexplored. Although benz-1,4-oxazine derivatives [see Page 21, Scheme 16; (63)] would not be expected to be photochromic, the development of synthetic routes to such compounds would serve as useful models for the synthesis of potentially photochromic naphth-1,4-oxazines [see Page 21, Scheme 16; (64) and (65)]. The most convenient method for the synthesis of 2,2-disubstituted 2H-benz-1,4-oxazines is the reduction of 2-nitrophenoxyacetophenones as illustrated in Scheme 17 (see Page 22) by the transformation [(68) → (69)].



(106) (107) (108) (109) (110)

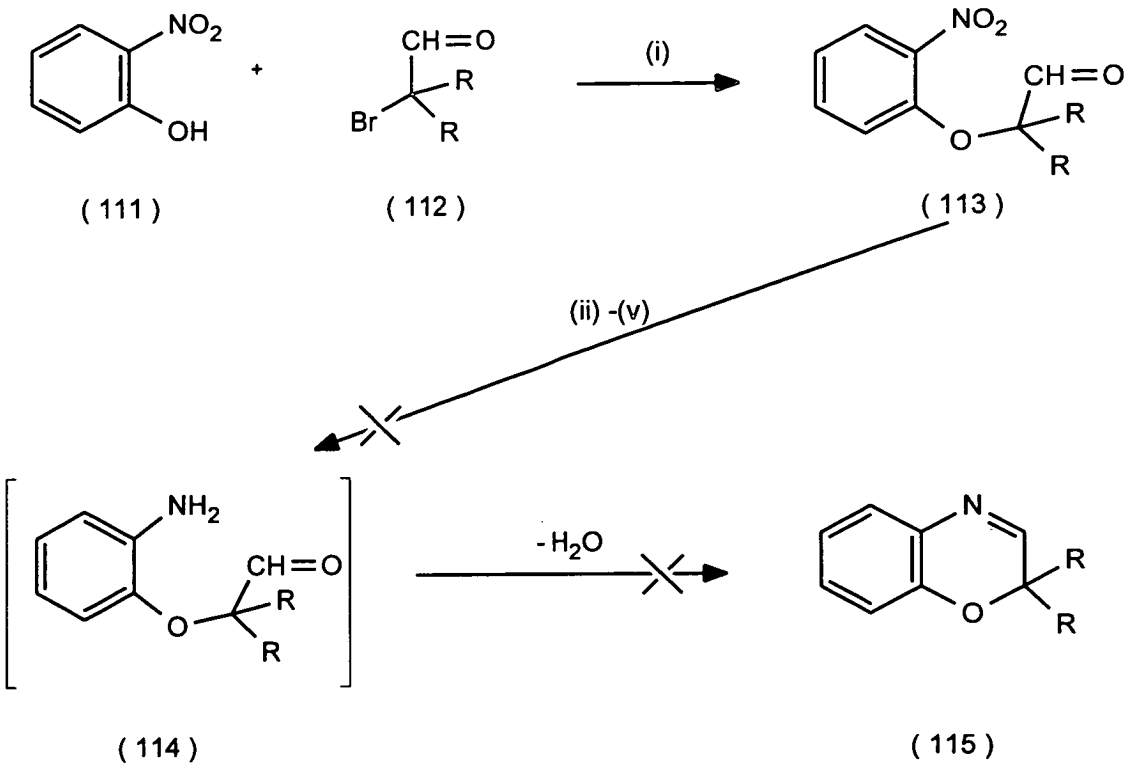
(i) KOH, EtOH, reflux.

(ii) 10% w/v ethanolic KOH, H_2O, reflux.

Scheme 23

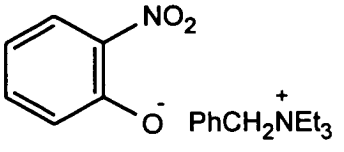
A further possible route to 2,2-disubstituted 2H-benz-1,4-oxazines involves the hydrolysis of acetamides. For example (Scheme 23) the acetamide (108) readily undergoes hydrolysis *via in situ* ring closure of the intermediate amine (109) to afford the 3-phenyl-2H-benz-1,4-oxazine (110).[103] Modification of the transformation [Scheme 23; (108) → (109) → (110)] by replacement of the benzoyl substituent with an aldehyde group would provide a useful method for the synthesis of 2H-benz-1,4-oxazines which to date has not been investigated.

The synthesis of 3,3-disubstituted 3H-naphth[2,1-b]-1,4-oxazines [see Page 21, Scheme 16; (64)] and the 2,2-disubstituted 2H-naphth[1,2-b]-1,4-oxazines [see Page 21, Scheme 16; (65)] has received only limited coverage in the literature. The primary literature contains only one example, describing the synthesis of the 3,3-disubstituted 3H-naphth-1,4-oxazine (74) as illustrated in Scheme 17 (see Page 22) by the acid catalysed reaction of 1-nitroso-2-naphthol (72) with the alkene (73).[75] At present, apart from this one study, synthetic methods for the naphth-1,4-oxazines [see Page 21, Scheme 16; (64) and (65)] are unknown. There is therefore a need for investigations on the synthesis of appropriately functionalised 3,3-disubstituted 3H-naphth[2,1-b]-1,4-oxazines and 2,2-disubstituted 2H-naphth[1,2-b]-1,4-oxazines as potential photochromic agents. The present chapter initially describes the investigations into the synthesis of the benz-1,4-oxazines [see Scheme 16; (63)] and then leads into an investigation concerning the development of synthetic routes to the potentially photochromic naphth-1,4-oxazines [see Scheme 16; (64)-(65)].



(111) (112) (113)

(114) (115)



(116)

R

a; Ph
b; Me

(i) NaH, DMF, room temp. or 100°.

(ii) H_2, 10% Pd - C, EtOH or AcOH, room temp., atmos. press.

(iii) $Na_2S_2O_4$, EtOH, H_2O, reflux.

(iv) $SnCl_2$, EtOH, N_2, 70°.

(v) $TiCl_3$, THF, N_2, room temp.

Scheme 24

2.2 INVESTIGATIONS OF SYNTHETIC ROUTES TO NOVEL 2,2-DISUBSTITUTED 2H-BENZ-1,4-OXAZINE DERIVATIVES

Initial studies under this heading centred on a general synthetic strategy (Scheme 24) for the 2,2-disubstituted 2H-benz-1,4-oxazines (115a and b) based on the synthesis of the 2-nitrophenoxyacetaldehyde derivatives (113a and b) and their reductive cyclisation *via in situ* ring-closure of the intermediate amines (114a and b). This strategy is based on a modification (see Page 22, Scheme 17) of the transformation [(68) → (69)] involving replacement of the benzoyl group with an aldehyde group. Application of this strategy to the synthesis of the 2,2-diphenyl compound (115a) depended on the synthesis of the key starting material 2-bromo-2,2-diphenylacetaldehyde (112a).

The precursor of this compound was the commercially available 2,2-diphenylacetaldehyde which was brominated using one equivalent of bromine in carbon disulphide as described in the literature[104] to give 2-bromo-2,2-diphenylacetaldehyde (112a) in good yield (93%). Bromination of diphenylacetaldehyde using 1.5 equivalents of bromine in ether as solvent (instead of the more obnoxious carbon disulphide) also afforded a high yield (99%) of 2-bromo-2,2-diphenylacetaldehyde (112a). However, this compound was found to be most conveniently prepared in essentially quantitative yield by brominating diphenylacetaldehyde with 1.5 equivalents of bromine in dichloromethane.

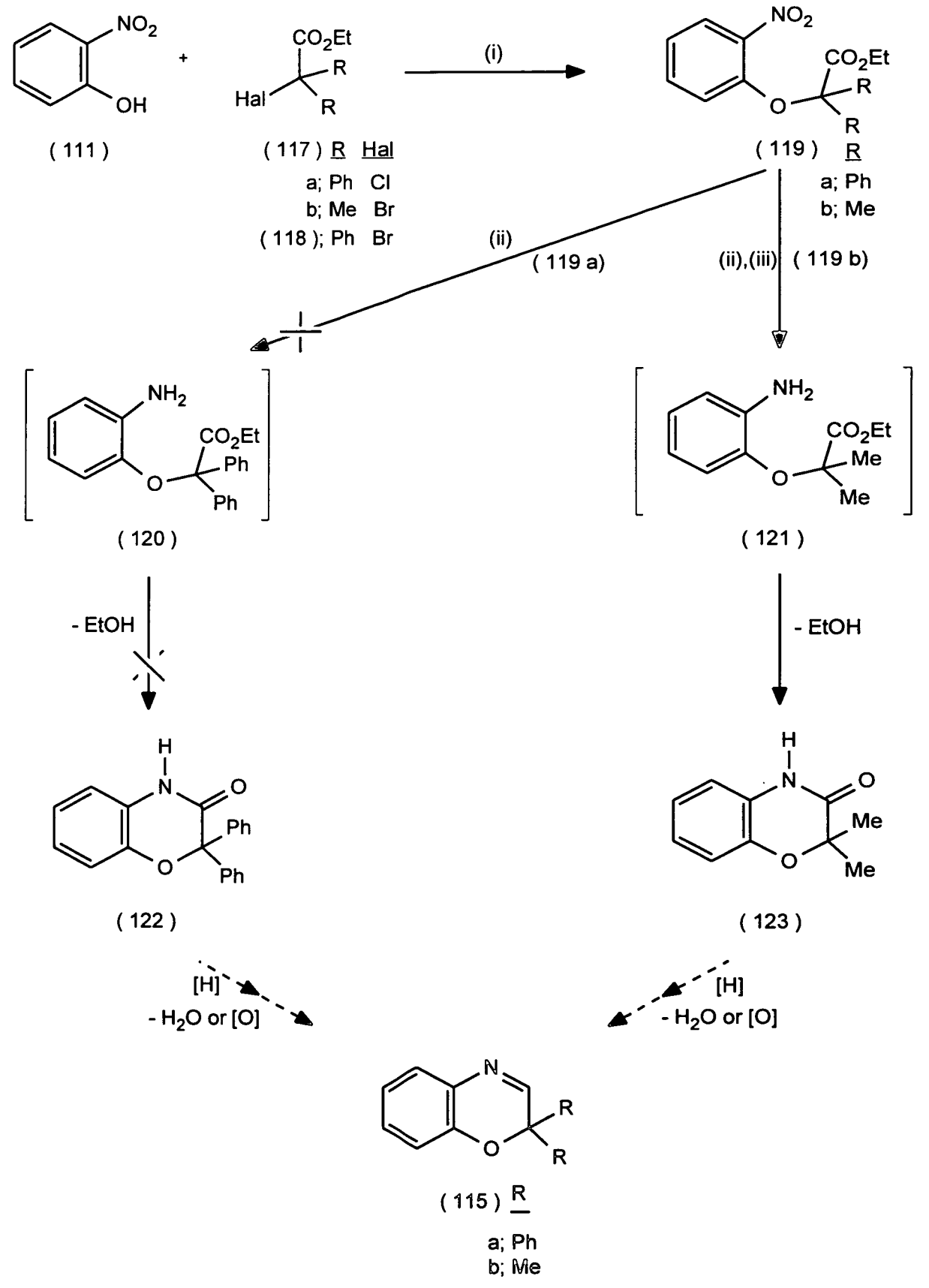
Condensation (Scheme 24) of the sodium salt of 2-nitrophenol (111) [prepared *in situ* by reaction of 2-nitrophenol (111) with sodium hydride] with

2-bromo-2,2-diphenylacetaldehyde (112a) in dimethylformamide at 100° afforded the required nitrophenoxyacetaldehyde (113a) in good yield (69%). An attempt was made to improve the yield of the aldehyde (113a) by reaction (Scheme 24) of the phase transfer salt (116) [readily obtained by reaction of the sodium salt of 2-nitrophenol (111) with the commercially available benzyltriethylammonium chloride] with the bromo-aldehyde (112a) in dichloromethane under reflux. However, under these conditions the nitrophenoxyacetaldehyde (113a) was formed only in low yield (49%).

With the nitrophenoxyacetaldehyde (113a) to hand attention was next turned to its conversion by reduction and *in situ* cyclisation of the resulting amine (114a) into the required benz-1,4-oxazine (115a). However, attempted reductive cyclisation (Scheme 24) of the nitrophenoxyacetaldehyde (113a) using hydrogen over 10% palladium-on-charcoal in ethanol gave only a high recovery (88%) of the unreacted starting-material (113a). Repetition of this reaction using acetic acid as the solvent was no more successful and again resulted only in the isolation of the unchanged starting material (113a) in high yield (100%). In contrast, the attempted reduction of the nitrophenoxyacetaldehyde (113a) using hydrogen over 10% palladium-on-charcoal in ethanol in the presence of concentrated hydrochloric acid gave a complex mixture which yielded no identifiable product. Complex mixtures also resulted when the reductive cyclisation of the nitrophenoxyacetaldehyde (113a) was attempted using sodium dithionite in aqueous ethanol under reflux. The attempted reductive cyclisation (Scheme 24) of the nitrophenoxyacetaldehyde

(113a) using stannous chloride also gave a multicomponent mixture from which no identifiable material was obtained. Correspondingly a multicomponent mixture was also the result of the attempted reductive cyclisation of the nitrophenoxyacetaldehyde (113a) using 15% w/v aqueous titanium trichloride solution in tetrahydrofuran under nitrogen at room temperature. The failure of the nitrophenoxyacetaldehyde (113a) to undergo reductive cyclisation into the required benz-1,4-oxazine (115a) is possibly due to side reactions such as co-reduction of the aldehyde group.

Initial attempts having failed to achieve the reductive cyclisation of the nitrophenoxyacetaldehyde (113a) to the required benz-1,4-oxazine (115a), attention was next focused on the analogous synthesis (Scheme 24) of the corresponding dimethyl derivative (115b). Investigations into the synthesis of the dimethyl derivative (115b) would serve as a useful contrast to the synthesis of the diphenyl derivative (115a) and be of interest to see if the synthesis of the dimethyl derivative (115b) would be more successful. To this end 2-methylpropionaldehyde was brominated as described in the literature[105] to afford the known[105] bromo-aldehyde (112b) in excellent yield (94%). In an initial attempt to obtain the 2-nitrophenoxypropionaldehyde derivative (113b) required for reductive cyclisation *via* the amine (114b) to the benz-1,4-oxazine (115b), the sodium salt of 2-nitrophenol (111) [prepared *in situ* by reaction of 2-nitrophenol (111) with sodium hydride] was reacted with the bromo-aldehyde (112b) in dimethylformamide at 100°. These conditions gave 2-methyl-2-(2-nitrophenoxypropionaldehyde (113b) as a yellow oil in low yield (26%).



(i) NaH, DMF, 100° or reflux.
(ii) H_2, 10% Pd - C, EtOH, room temp., atmos. press.
(iii) $Na_2S_2O_4$, EtOH, H_2O, reflux.

Scheme 25

Since the low yield of the product (113b) could be attributed to loss of the relatively volatile bromo-aldehyde starting material (112b) the conditions of its reaction with the sodium salt of 2-nitrophenol (111) [prepared *in situ* by reaction of 2-nitrophenol (111) with sodium hydride] were changed from a reaction temperature of 100° for 1 h to room temperature for 24 h. These conditions gave a much improved yield (57%) of the 2-nitrophenoxypropionaldehyde derivative (113b). However, when the reaction time at room temperature was extended still further to 48 h, the yield dropped to 41%.

With the 2-nitrophenoxypropionaldehyde derivative (113b) readily available attention was next turned (Scheme 24) to its conversion by reduction and *in situ* cyclisation of the resulting amine (114b) into the required benz-1,4-oxazine (115b). However, attempted reductive cyclisation of the nitro-aldehyde (113b) using hydrogen over 10% palladium-on-charcoal in ethanol gave only a complex mixture. Complex mixtures were also obtained when reduction of the nitro-aldehyde (113b) was attempted using either stannous chloride in anhydrous ethanol under nitrogen at 70° or 15% w/v aqueous titanium trichloride solution in ethanol under nitrogen at room temperature.

With various attempts to achieve the reductive cyclisation of the nitro-aldehydes (113a and b) to the required benz-1,4-oxazines (115a and b) having been unsuccessful it was decided to pursue an alternative synthetic route (Scheme 25) based on the formation of the 2,2-disubstituted 2H-benz-1,4-oxazin-3(4H)-ones [(122) and (123)]. It was anticipated that these latter

molecules could be further manipulated through either reduction followed by dehydration or reduction followed by oxidation to afford the benz-1,4-oxazines (115a and b).

It was first decided to attempt the synthesis of the key ester starting material (119a) with the intention of carrying out its reductive cyclisation *via* the amine (120) to the 2,2-diphenyl-2H-benz-1,4-oxazinone (122). However, this synthetic approach was temporarily thwarted by difficulties encountered in the synthesis of ethyl 2-bromo-2,2-diphenylacetate (118) required as a possible partner for condensation with 2-nitrophenol (111) as its sodium salt. The intention was to obtain the required bromo-ester (118) by ethanolysis of the commercially available 2-bromo-2,2-diphenylacetyl bromide. However, two batches of this chemical purchased in succession from Aldrich[106] proved to be too impure for use so it was decided to use the also commercially available 2-chloro-2,2-diphenylacetyl chloride as the starting material. The reaction of this compound with ethanol at room temperature afforded ethyl 2-chloro-2,2-diphenylacetate (117a) in good yield (90%). The reaction of the chloro-ester (117a) with the sodium salt of 2-nitrophenol (111) [prepared *in situ* by reaction of 2-nitrophenol (111) with sodium hydride] in dimethylformamide at 100° for 1 h gave the expected ester (119a) only in low yield (11%). When the time of this reaction was extended to 17 h the ester (119a) was obtained in a moderate yield (39%). In a further attempt to improve the yield of the ester (119a) ethyl 2-chloro-2,2-diphenylacetate (117a) was reacted with the sodium salt of 2-nitrophenol (111) in dimethylformamide under reflux for 17 h.

However, these conditions gave only a low yield (18%) of the ester (119a).

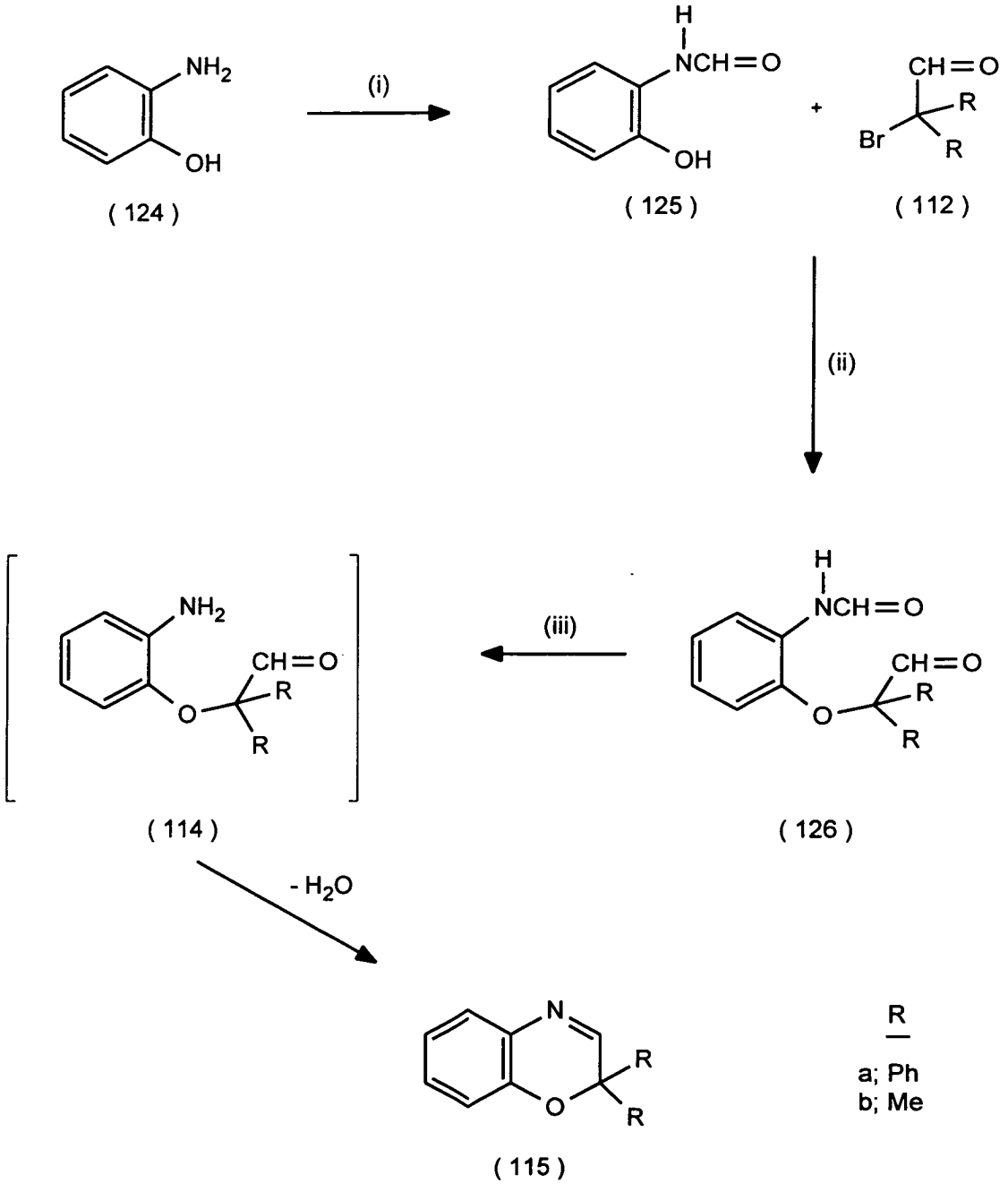
In an initial attempt to reduce the ester (119a) *via in situ* ring closure of the amine (120) to the 2,2-diphenyl-2H-benz-1,4-oxazinone (122) the ester (119a) was reduced using hydrogen over 10% palladium-on-charcoal in ethanol. Disappointingly these conditions afforded only a complex mixture which yielded no identifiable product.

More success was achieved in the synthesis (Scheme 25) of the 2,2-dimethyl-2H-benz-1,4-oxazinone derivative (123). Thus the *in situ* reaction of the sodium salt of 2-nitrophenol (111) with the commercially available ethyl 2-bromo-2-methylpropionate (117b) was attempted in the expectation of obtaining the key ester starting-material (119b). When this reaction was carried out in dimethylformamide at 100° for 1 h unreacted 2-nitrophenol (111) was recovered in high yield (60%) together with a low yield (13%) of the ester product (119b) as a yellow oil. Extension of the time of this reaction to 15 h raised the yield of the ester (119b) to only 16%. Reaction of two equivalents of the bromo-ester (117b) with the sodium salt of 2-nitrophenol (111) in dimethylformamide at 100° for 15 h resulted in a marked increase in the yield (33%) of the ester derivative (119b). In a further attempt to improve the yield of the ester (119b) the sodium salt of 2-nitrophenol (111) was reacted with the bromo-ester (117b) in 1,2-dimethoxyethane under reflux for 1 h. However, these conditions gave only unreacted 2-nitrophenol (111) in high yield (100%) together with a moderate recovery (51%) of the bromo-ester (117b). Extension of the time of this reaction to 18 h also gave only a quantitative yield of

unreacted 2-nitrophenol (111) together with a lower recovery (19%) of the bromo-ester (117b). In a final attempt to improve the yield of the ester (119b), the sodium salt of 2-nitrophenol (111) was reacted with the bromo-ester (117b) in dimethylformamide under reflux for 1 h. Once again, however, this reaction gave only a high recovery (75%) of unreacted 2-nitrophenol (111). The inefficiency of the reactions of the sodium salt of 2-nitrophenol (111) with the bromo-ester (117b) can be attributed to steric hindrance to nucleophilic displacement of the bromine atom in the latter molecule.

Despite the relative inaccessibility of the ester (119b) the study (Scheme 25) of its reductive cyclisation to the benz-1,4-oxazinone (123) was carried out. In an initial attempt to achieve the transformation [(119b) $\rightarrow$ (123)] the ester (119b) was reduced using hydrogen over 10% palladium-on-charcoal in ethanol. These conditions gave the benzoxazinone (123) in high yield (73%) as an off-white solid. This product gave analytical and mass spectral data consistent with this structure (123) and was further identified by its ^{1}H n.m.r. spectrum, which shows in addition to signals due to the benzene ring, a singlet at δ_H 8.27 (which disappears on shaking with deuterium oxide) assignable to the NH group and two sharp three-proton singlets at δ_H 1.63 and 1.24 attributable to the two methyl groups of (123). The i.r. spectrum shows a band at 1680 cm^{-1} attributable to the carbonyl absorption of a lactam and hence further supports the benzoxazinone structure (123).

Reductive cyclisation of the ester (119b) was also achieved by heating under reflux with sodium dithionite in aqueous ethanol. These conditions gave



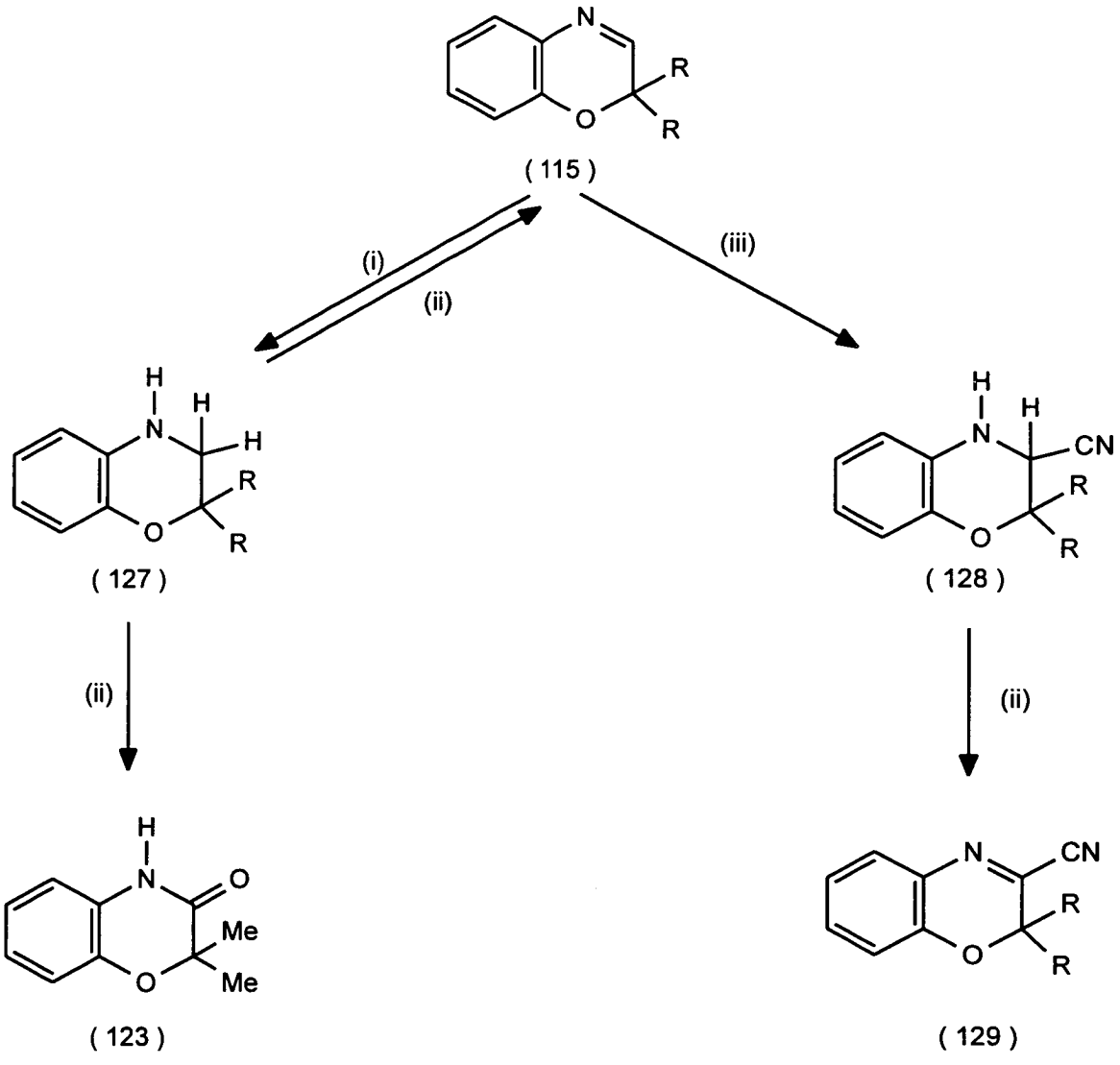
(i) HCO_2H, reflux.
(ii) NaH, DMF, room temp. or 100°.
(iii) 2M NaOH aqu., EtOH, reflux.

Scheme 26

an essentially quantitative yield of the 2,2-dimethyl-2H-benz-1,4-oxazinone (123).

In a parallel investigation (Scheme 26) to the benzoxazinone approach a more direct route to the benz-1,4-oxazines (115a and b) was investigated. This approach is based on the formation and subsequent hydrolysis of the formamide derivatives (126a and b) to afford the amine intermediates (114a and b) required for spontaneous cyclisation to the benz-1,4-oxazines (115a and b). It was anticipated that the previously undescribed formamide derivatives (126a and b) would be readily obtained by reaction of the sodium salt of the known[107] 2-formamidophenol (125) with the bromo-aldehydes (112a and b). The formamidophenol (125) was readily obtained in good yield (78%) by briefly heating 2-aminophenol (124) with formic acid under reflux. The reaction of the sodium salt of 2-formamidophenol (125) [generated *in situ* by reaction of 2-formamidophenol (125) with sodium hydride in dimethylformamide] with the bromo-aldehyde (112a) afforded the formamido-derivative (126a) in good yield (78%). The orange product (126a) gave satisfactory analytical and mass spectral data and its structure was confirmed by its i.r. and ^{1}H n.m.r. spectrum. Thus the i.r. spectrum shows bands assignable to NH and carbonyl groups, while its ^{1}H n.m.r. spectrum, shows in addition to signals due to aromatic protons, a one-proton singlet at δ_H 8.70 due to the proton of the aldehyde group and a two-proton multiplet at δ_H 7.71-7.59 arising from the formamide group present in the structure (126a).

An attempt to obtain the amine intermediate (114a) [and hence the



R

a; Ph
b; Me

(i) $NaBH_4$, MeOH, H_2O, room temp.
(ii) MnO_2, MeCN, room temp.
(iii) KCN, AcOH, room temp.

Scheme 27

benz-1,4-oxazine (115a)] involved base hydrolysis of the formamido-derivative (126a) by heating under reflux with 2 M aqueous sodium hydroxide in ethanol. This reaction gave a pale brown solid in good yield (79%) which gave analytical and mass spectral data fully in accord with its formulation as the 2,2-diphenyl-2H-benz-1,4-oxazine (115a). The benz-1,4-oxazine (115a) was further identified by its ^{1}H n.m.r. spectrum which exhibits a one-proton singlet at δ_H 7.99, arising from the methine proton of the imine group and a fourteen-proton multiplet at δ_H 7.51-6.82 arising from the aromatic protons. The i.r. spectrum further supports the benz-1,4-oxazine structure (115a) as it shows the expected imine (C=N) absorption band (υ_{max} 1616 cm^{-1}).

In view of the fact that the previously undescribed benzoxazine (115a) is a cyclic imine it was decided to investigate (Scheme 27) its chemical behaviour in this context. Initially the behaviour of the benzoxazine derivative (115a) towards hydride reduction was studied. Thus treatment of the benzoxazine (115a) with sodium borohydride in aqueous methanol at room temperature afforded an excellent yield (96%) of the expected dihydro derivative (127a). This product gave satisfactory analytical and mass spectral data, its i.r. spectrum shows the expected NH absorption band (υ_{max} 3383 cm^{-1}) and its ^{1}H n.m.r. spectrum also exhibits a broad one-proton singlet at δ_H 3.75, which can be assigned to the NH group. The remainder of the ^{1}H n.m.r. spectrum shows a fourteen-proton multiplet at δ_H 7.53-6.51 arising from the aromatic protons present in the structure (127a), together with a two-proton singlet at δ_H 3.86 due to the methylene group. In further support of its

structure oxidation of the dihydro derivative (127a) with manganese dioxide in acetonitrile at room temperature regenerated the benzoxazine (115a) albeit in only moderate yield (32%).

The benzoxazine (115a) also exhibited (Scheme 27) imine behaviour in its reactivity towards nucleophilic addition of hydrogen cyanide. Thus, treatment of the benzoxazine (115a) with potassium cyanide in glacial acetic acid at room temperature afforded a good yield (74%) of the hydrogen cyanide adduct (128a). The colourless product (128a) gave a satisfactory mass spectrum and its structure was confirmed by its i.r. and ^{1}H n.m.r. spectrum. Thus the i.r. spectrum shows bands assignable to the NH and C≡N groups, while its ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a sharp one-proton singlet at δ_H 5.20 due to the methine group. A one-proton singlet at δ_H 4.37 which is completely removed on addition of deuterium oxide is attributable to the NH group.

In further support of this structure oxidation of the hydrogen cyanide adduct (128a) with manganese dioxide in acetonitrile at room temperature afforded the cyanobenzoxazine derivative (129a) in good yield (71%). This yellow product (129a) analysed correctly and gave mass spectral data fully in accord with its formulation as the cyanobenzoxazine (129a). The cyanobenzoxazine (129a) was further identified by its i.r. spectrum which shows the C≡N absorption band (υ_{max} 2222 cm^{-1}) and its ^{1}H n.m.r. spectrum which shows only a fourteen-proton multiplet attributable to the aromatic protons.

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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λnm	211.4	271.6	286.2							
ABS	1.856	0.204	0.199							

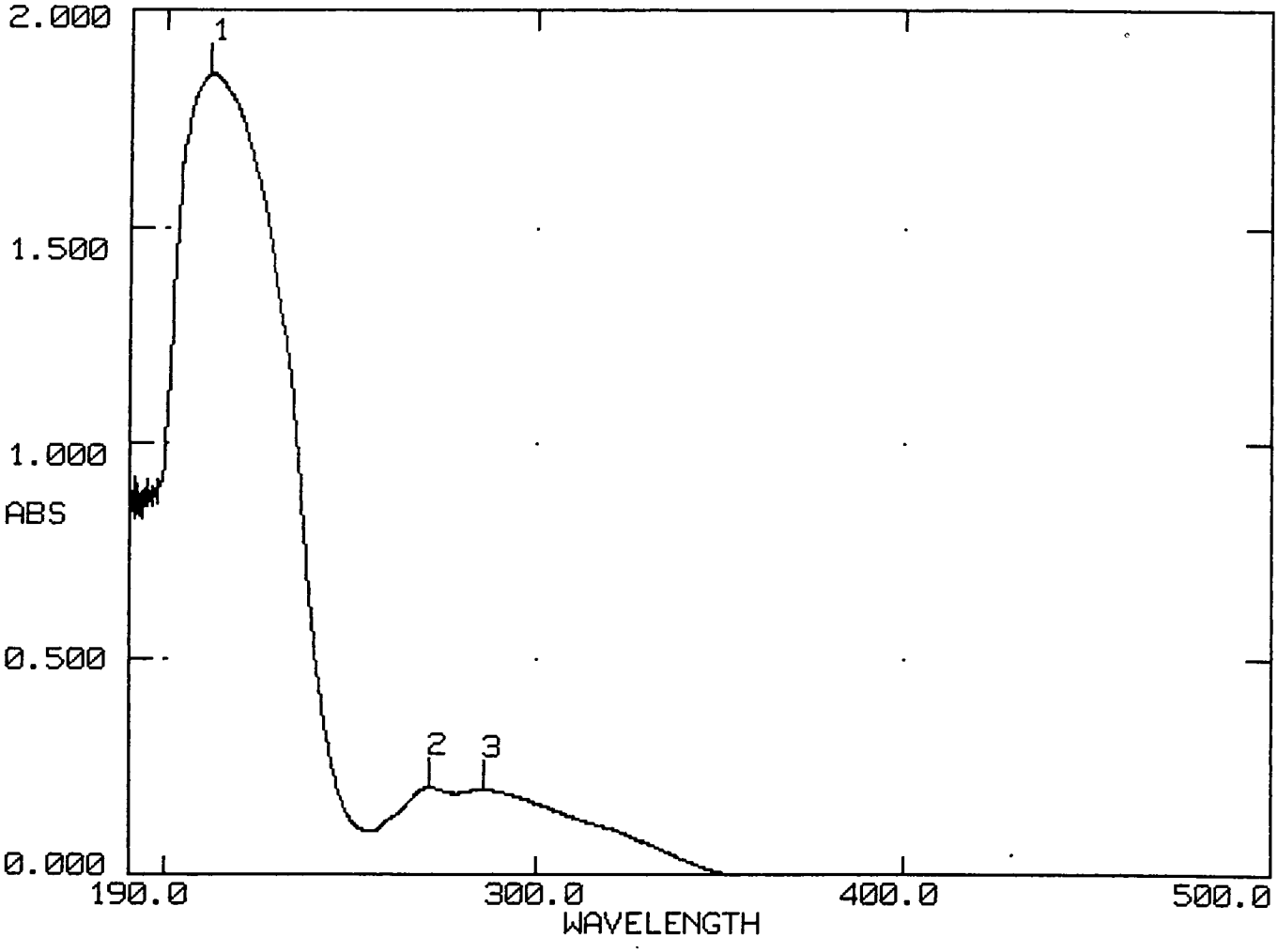

Figure 4

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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λnm	215.4	247.4	303.0							
ABS	2.896	0.934	0.585							

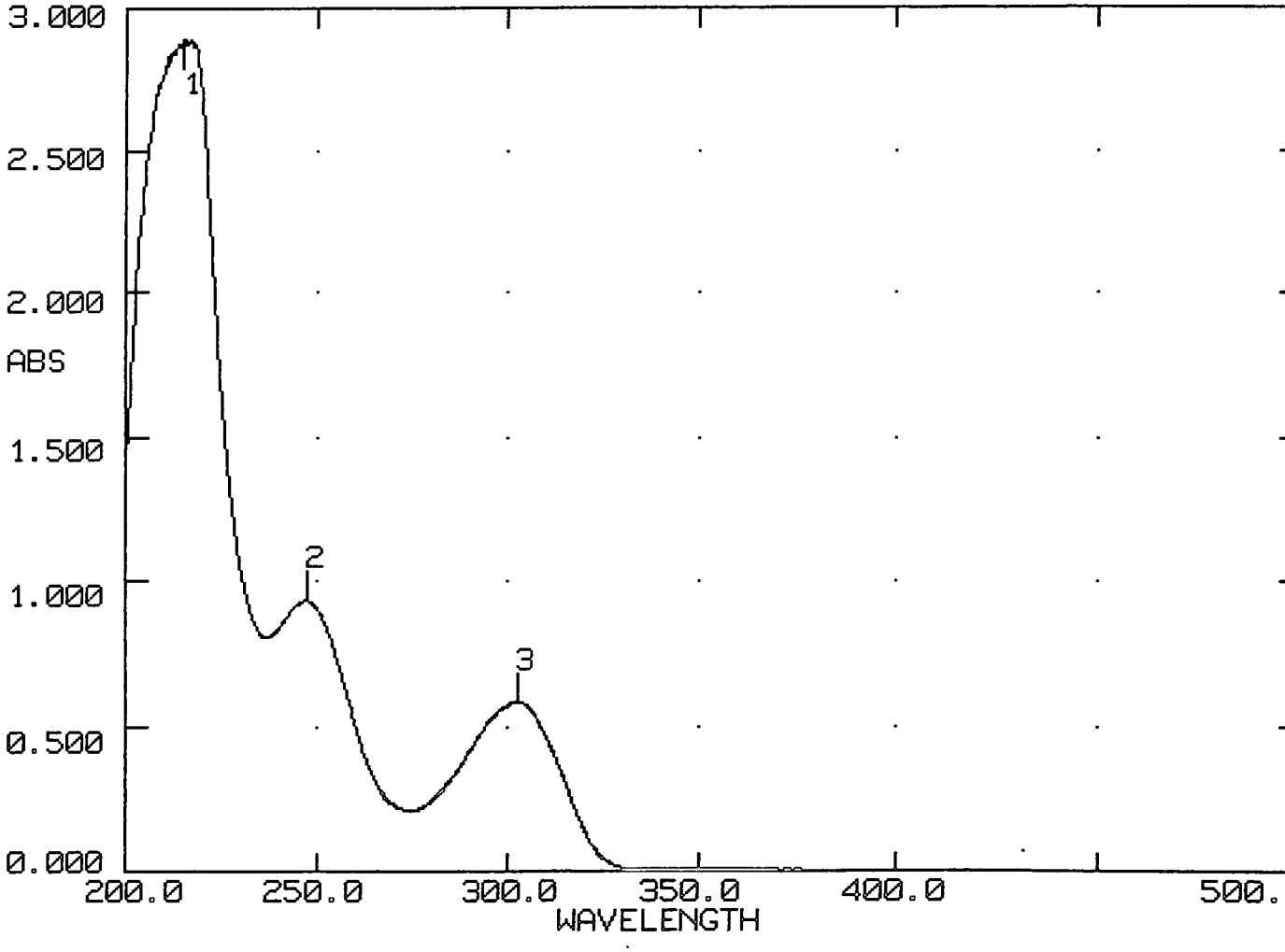

Figure 5

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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PEAKS

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λnm	207.4	292.8								
ABS	2.359	0.154								

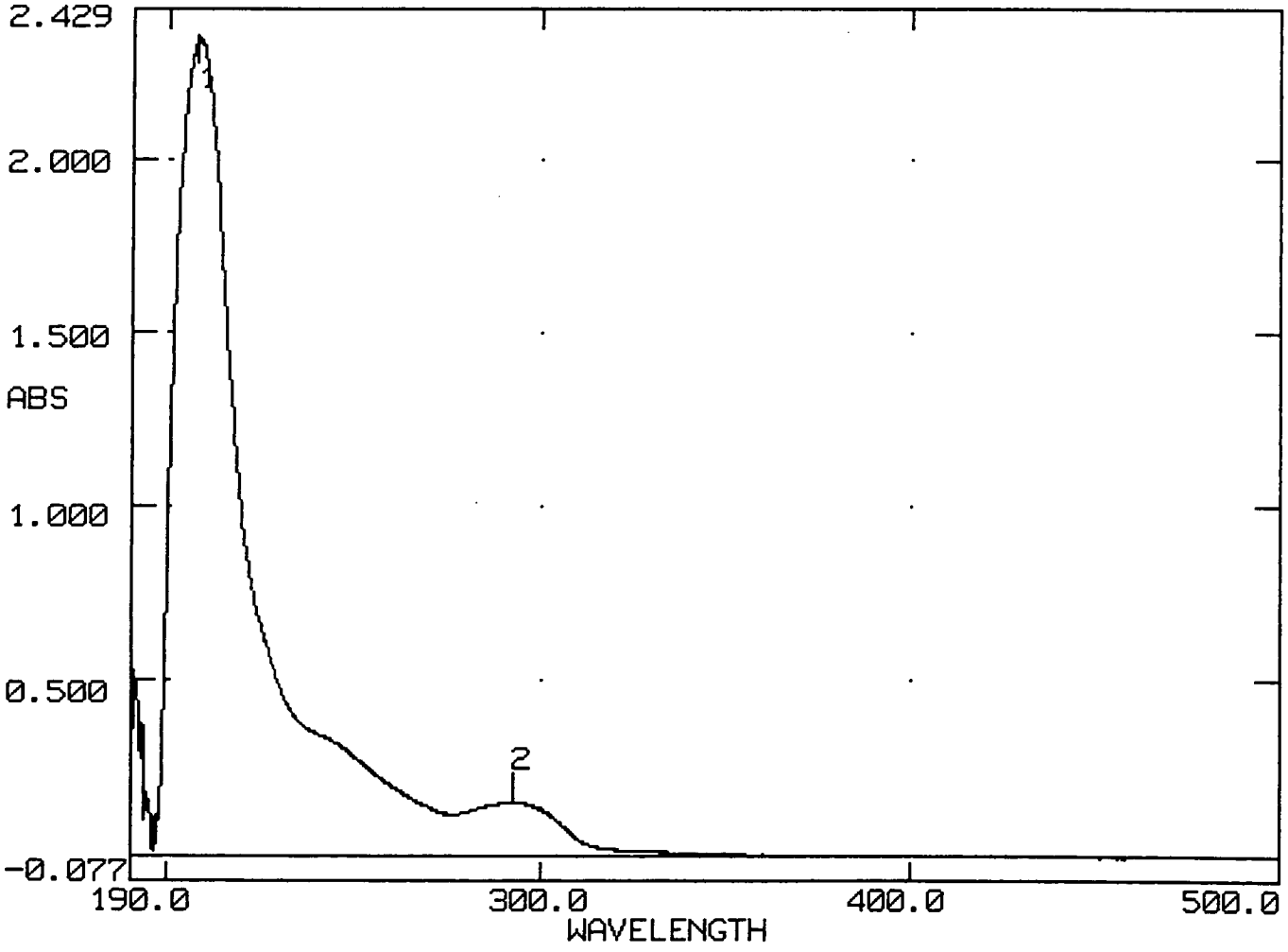

Figure 6

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

	1	2	3	4	5	6	7	8	9	10
λnm	220.6	242.6	296.8	323.6						
ABS	0.232	0.524	0.405	0.245						

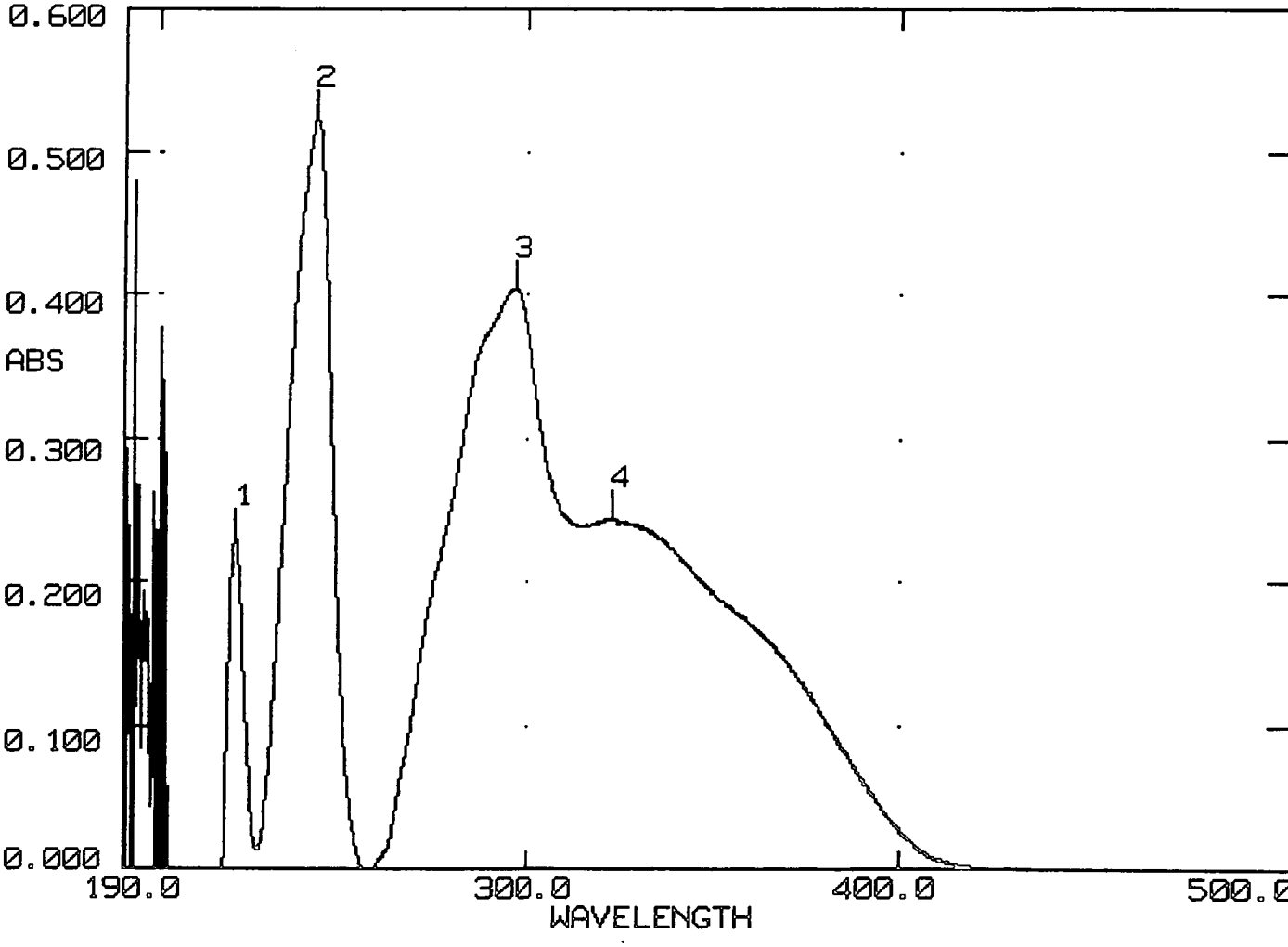

Figure 7

In view of the fact that the benzoxazine (115a) was potentially photochromic as discussed earlier (see Page 20, Section 1.3.1) a small sample of this compound (115a) was sent to Pilkington to test for its photochromic behaviour. Initial tests carried out at Pilkington indicate that the benzoxazine (115a) was not photochromic. With the subsequent closure of the labs at Pilkington a sample of the benzoxazine (115a) was sent to Gentex and is currently being investigated for photochromic behaviour.

The ultraviolet spectrum (Figure 4) of the benzoxazine (115a) was also investigated to determine if it had any absorption bands in the visible region which could possibly give rise to photochromism. The ultraviolet spectra of the dihydro derivative (127a) (Figure 5), the hydrogen cyanide adduct (128a) (Figure 6) and the cyanobenzoxazine (129a) (Figure 7) were also measured for comparison purposes. The ultraviolet spectrum (Figure 4) of the benzoxazine (115a) has a maximum absorption at 211 nm and also has weaker bands at 272 and 286 nm. The presence of the bands at 272 and 286 nm with relatively small extinction coefficients is typical of benzenoid structures. Similarly the band at 211 nm possibly represents the presence of a heterocyclic system. It is also noteworthy that the benzoxazine (115a) is transparent (*i.e.* lacks absorption bands) in the visible region (400-750 nm). Not surprisingly in view of its less conjugated structure the dihydro compound (127a) also lacked absorption in the visible region and contained an absorption maximum at 215 nm which represents a small bathochromic shift (shift to longer wavelength) of 4 nm compared with the corresponding band (λ_{max}

211 nm) in the benz-1,4-oxazine (115a). Interestingly the band at 286 nm in the u.v. spectrum (Figure 4) of the benz-1,4-oxazine (115a) also undergoes a bathochromic shift to 303 nm (Figure 5) in the dihydro compound (127a) whereas the band at 272 nm in the benz-1,4-oxazine (115a) undergoes a hypsochromic shift (shift to shorter wavelength) to 247 nm in the dihydro compound (127a).

The ultraviolet spectrum (Figure 7) of the cyanobenzoxazine (129a) is significantly different to the spectrum (Figure 4)of the benz-1,4-oxazine (115a). For example four absorption bands are present and there is a small amount of absorption in the violet region of the visible spectrum ($\lambda_{max} \cong 400$ nm) which gives rise to the pale yellow colour of the cyanobenzoxazine (129a). Comparison of the spectrum (Figure 7) of the cyanobenzoxazine (129a) with the spectrum (Figure 4) of the benzoxazine (115a) illustrates that the presence of the cyano group has induced a considerable bathochromic shift of the bands in the benzoxazine (115a). Not surprisingly in view of its less conjugated structure the cyano adduct (128a) is transparent in the visible region and its u.v. spectrum (Figure 6) is less complicated than the spectrum (Figure 7) of the cyanobenzoxazine (129a). These u.v. studies show that the benzoxazine (115a) is transparent in the visible region and increasing the conjugation in the benzoxazine system (115a) induces a bathochromic shift on the absorption.

In parallel with the investigations of synthetic approaches to the 2,2-diphenyl-2H-benz-1,4-oxazine (115a), studies were also undertaken (see Page 36, Scheme 26) on the synthesis of the corresponding dimethyl derivative

(115b), based on the formation and subsequent hydrolysis of the formamido derivative (126b). The reaction of the sodium salt of 2-formamidophenol (125) [generated *in situ* by reaction of 2-formamidophenol (125) with sodium hydride in dimethylformamide] with 2-bromo-2-methylpropionaldehyde (112b) in dimethylformamide at room temperature for 24 h afforded the formamido derivative (126b) in good yield (64%). Attempts to form the amine intermediate (114b) [and hence the benz-1,4-oxazine (115b)] involved base-catalysed hydrolysis of the formamido derivative (126b) using 2 M aqueous sodium hydroxide in ethanol under reflux. This reaction afforded a light brown oil in almost quantitative yield which gave mass spectral data and showed spectroscopic properties which confirmed its identity as the desired benz-1,4-oxazine derivative (115b). Thus the i.r. spectrum shows the expected imine (C=N) absorption band (υ_{max} 1596 cm^{-1}) while its ^1H n.m.r. spectrum shows a five-proton multiplet at δ_H 7.43-6.78 attributable to the methine and aromatic protons and a six-proton singlet at δ_H 1.44 assignable to the two methyl groups.

Further evidence for the structure of the benzoxazine (115b) was then sought. Reduction (see Page 37, Scheme 27) of the imine double bond in the benzoxazine derivative (115b) would be expected to yield the dihydro derivative (127b). In practice the benzoxazine (115b) was smoothly reduced by sodium borohydride in aqueous methanol to afford the dihydro derivative (127b) as a brown oil in moderate yield (55%). This product gave satisfactory analytical and mass spectral data and showed spectroscopic properties which

confirmed its identity as the dihydro derivative (127b). Thus the i.r. spectrum shows the expected NH absorption band (υ_{max} 3387 cm^{-1}) and its ^1H n.m.r. spectrum correctly exhibits signals due to the NH, methylene, methyl and aromatic groups. In an attempt to further verify the structure of the dihydro compound (127b) it was oxidised with activated manganese dioxide in acetonitrile at room temperature. However, in contrast to the corresponding diphenyl derivative (127a) (see before) these conditions converted the dimethyl derivative (127b) not into the benzoxazine (115b) but rather into the benzoxazinone (123) identical to the product of the reductive cyclisation of the ester (119b) (see Page 32, Scheme 25 before). The formation of the benzoxazinone (123) was presumably due to oxygen insertion occurring at one of the protons of the methylene group in the structure (127b). Subsequent dehydrogenation of the intermediate alcohol would afford the benzoxazinone (123). The origin of the oxygen in this insertion may be atmospheric or may come from the manganese dioxide.

Nucleophilic addition of hydrogen cyanide (Scheme 27) across the imine double bond in the benzoxazine (115b) was also investigated. Thus the benzoxazine (115b) reacted with potassium cyanide in glacial acetic acid to give the hydrogen cyanide adduct (128b) in excellent yield (98%). The brown product (128b) gave a satisfactory mass spectrum and its structure was confirmed by its i.r. and n.m.r. spectrum. Thus the i.r. spectrum shows bands assignable to NH and C≡N groups, while its ^1H n.m.r. spectrum shows in addition to signals due to the aromatic and methyl protons, a broad one-proton

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ABS	2.794	1.381	0.878							

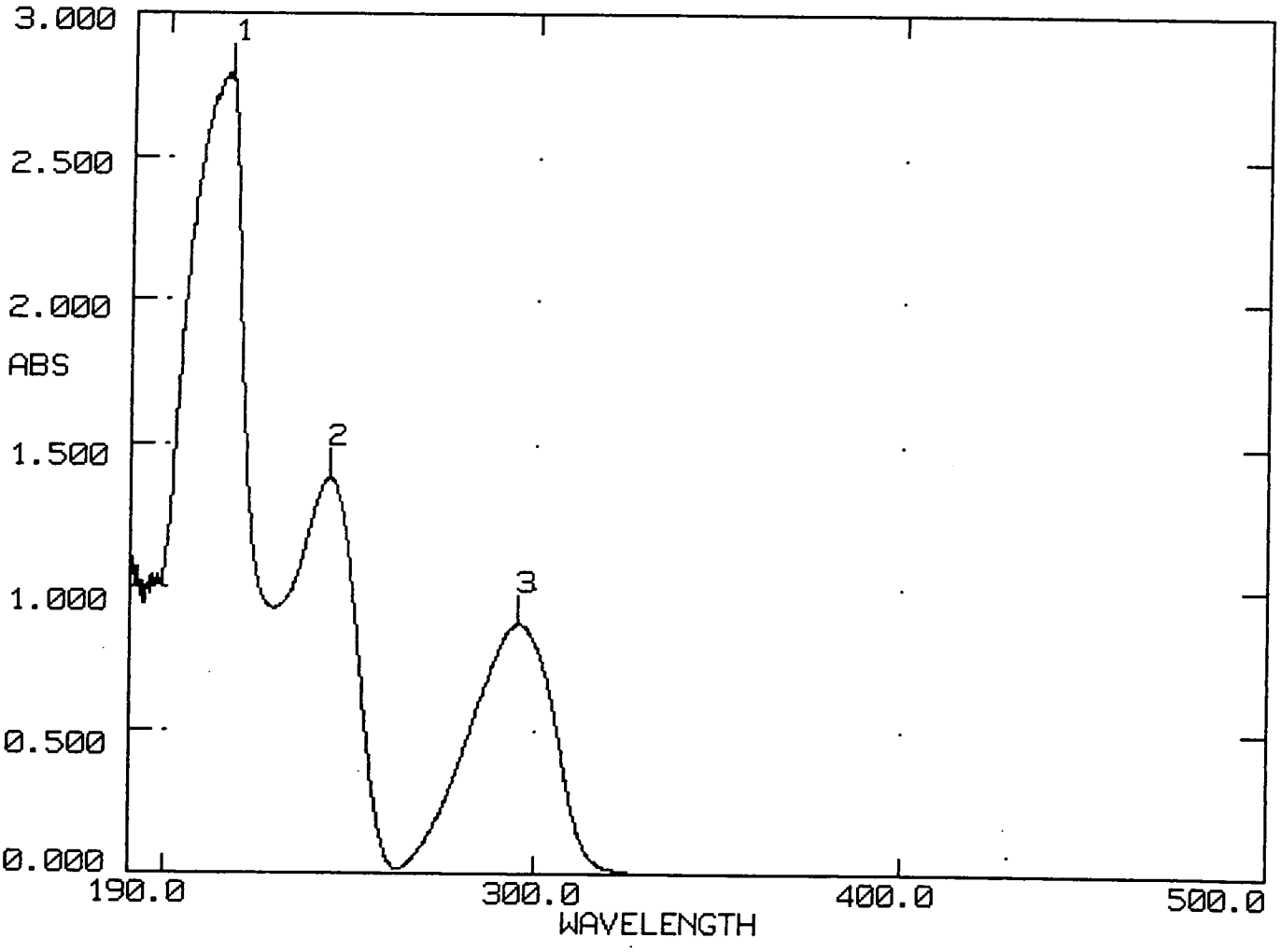
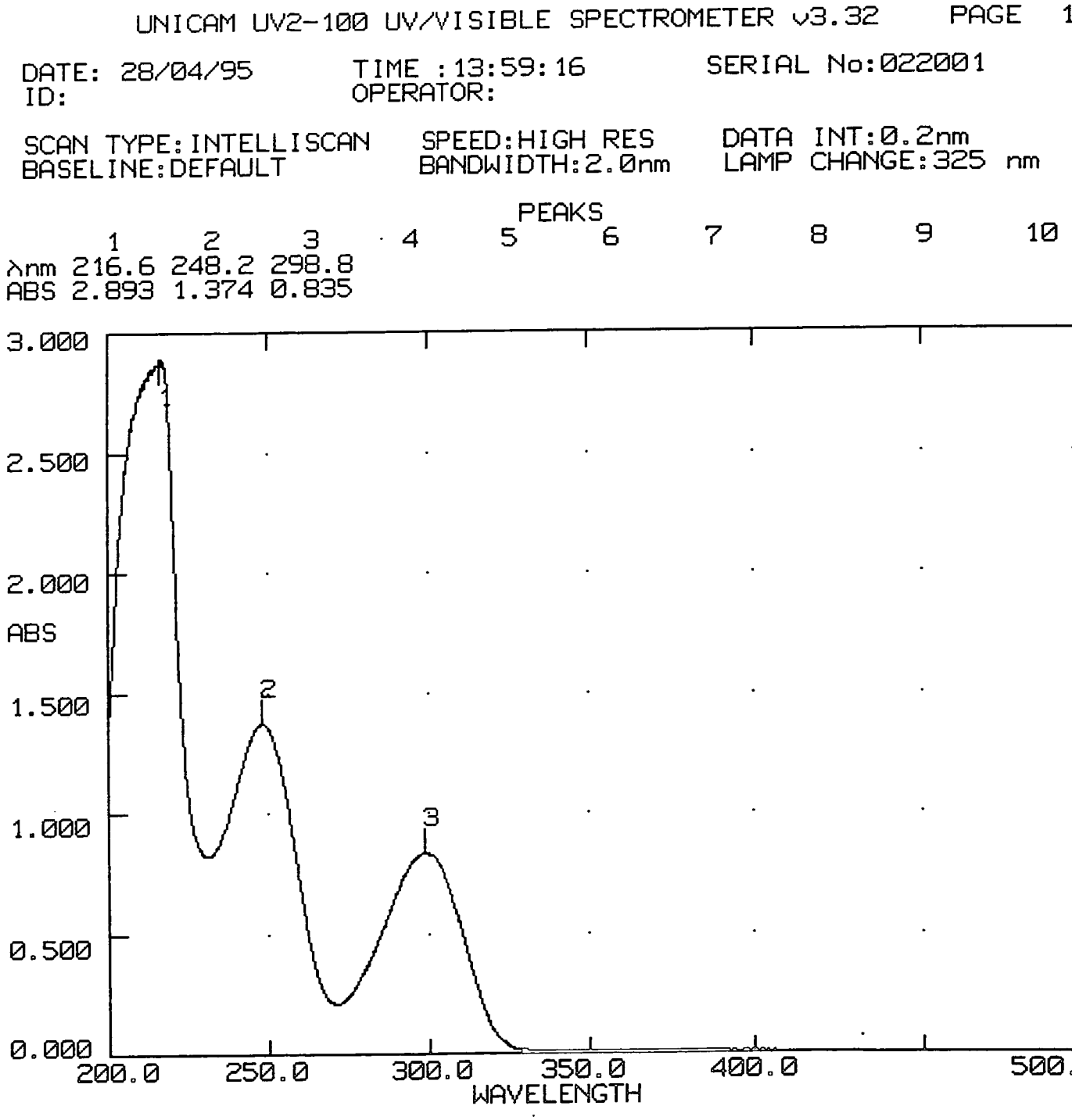


Figure 8


UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1
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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm
PEAKS
1 2 3 4 5 6 7 8 9 10
λnm 216.6 248.2 298.8
ABS 2.893 1.374 0.835
3.000
2.500
2.000
ABS
1.500
1.000
0.500
0.000
200.0 250.0 300.0 350.0 400.0 500.
WAVELENGTH
2
3

Figure 9

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

DATE: 29/04/95 TIME :10:35:00 SERIAL No:022002
ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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λnm	209.4	242.4	291.6							
ABS	2.848	0.654	0.363							

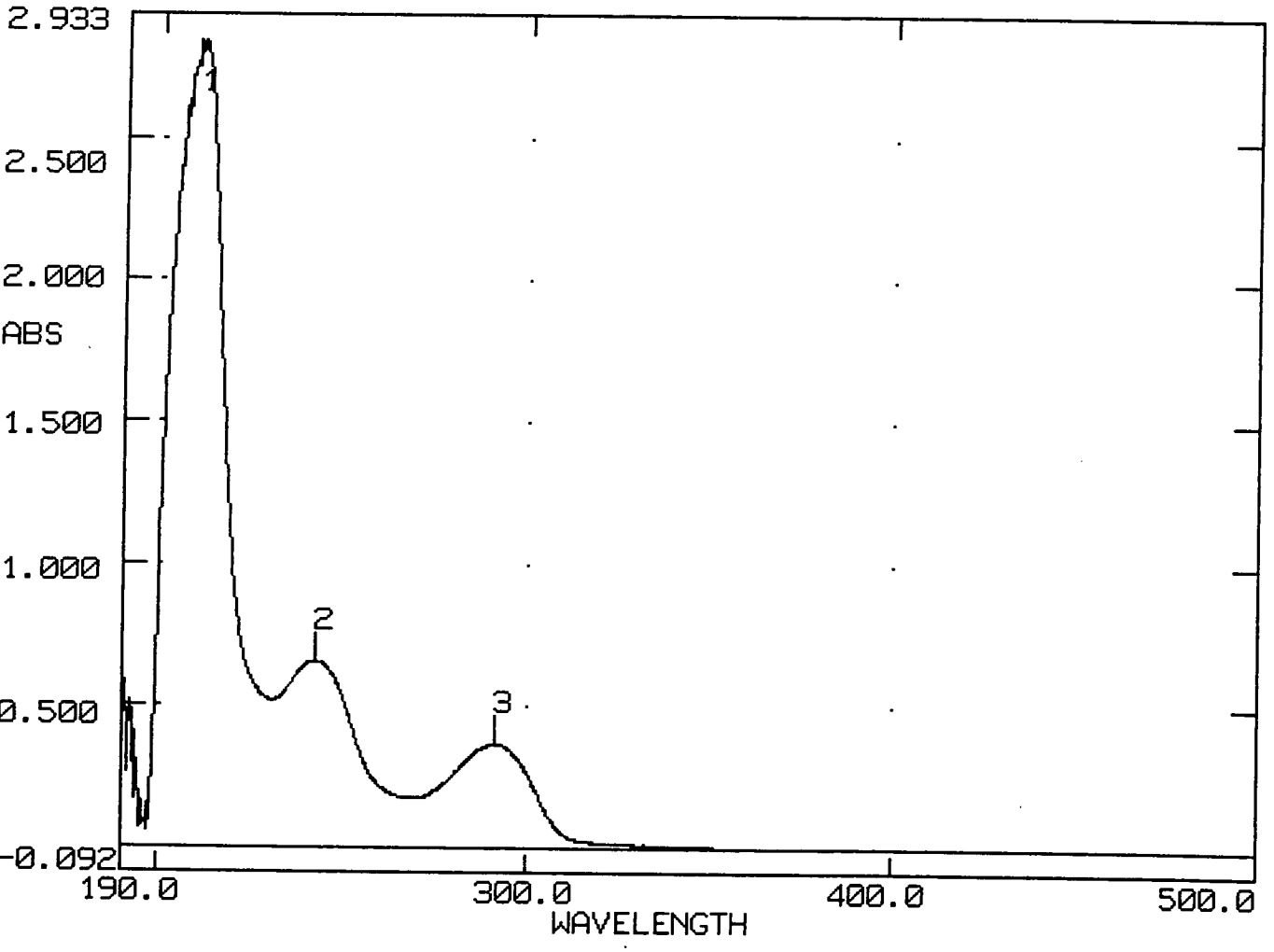

Figure 10

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

DATE: 28/04/95 TIME :14:11:36 SERIAL No:022001
ID: OPERATOR:

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TRACK

	1	2	3	4	5	6	7	8	9	10
λnm	202.4	212.0	240.8	290.0	354.8					
ABS	1.153	0.995	1.313	0.777	0.358					

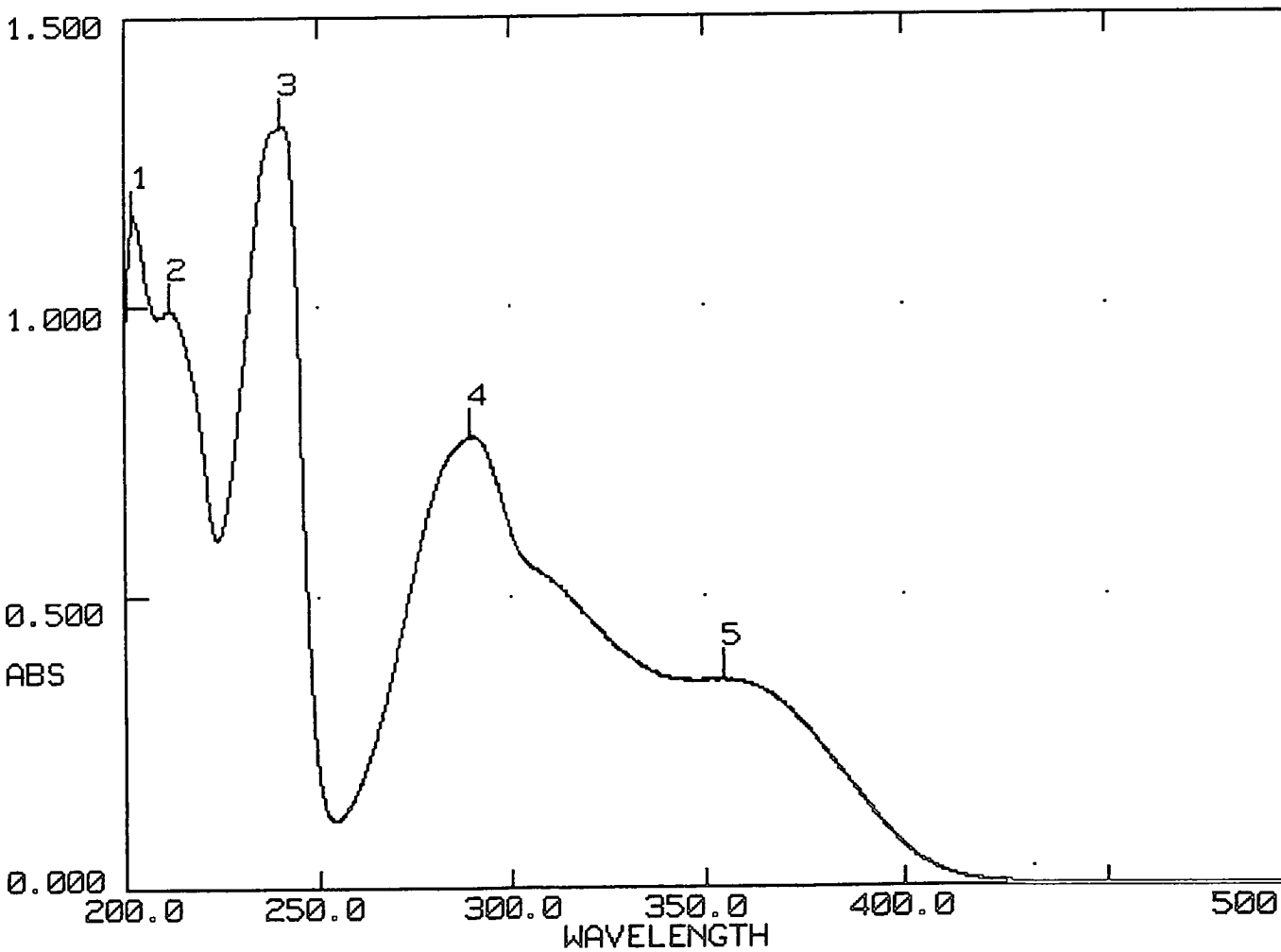


Figure 11

singlet at δ_H 4.27 due to the NH group which is completely removed on addition of deuterium oxide. A one-proton doublet at δ_H 4.01 collapses to a singlet on shaking with deuterium oxide and is attributable to the methine group of the hydrogen cyanide adduct (128b). Subsequent oxidation of the hydrogen cyanide adduct (128b) with manganese dioxide in acetonitrile afforded the expected cyanobenzoxazine derivative (129b) in moderate yield (51%). This yellow product (129b) analysed correctly, gave a satisfactory mass spectrum and its structure was supported by its i.r. spectrum which shows the C≡N absorption band (υ_{max} 2222 cm^{-1}).

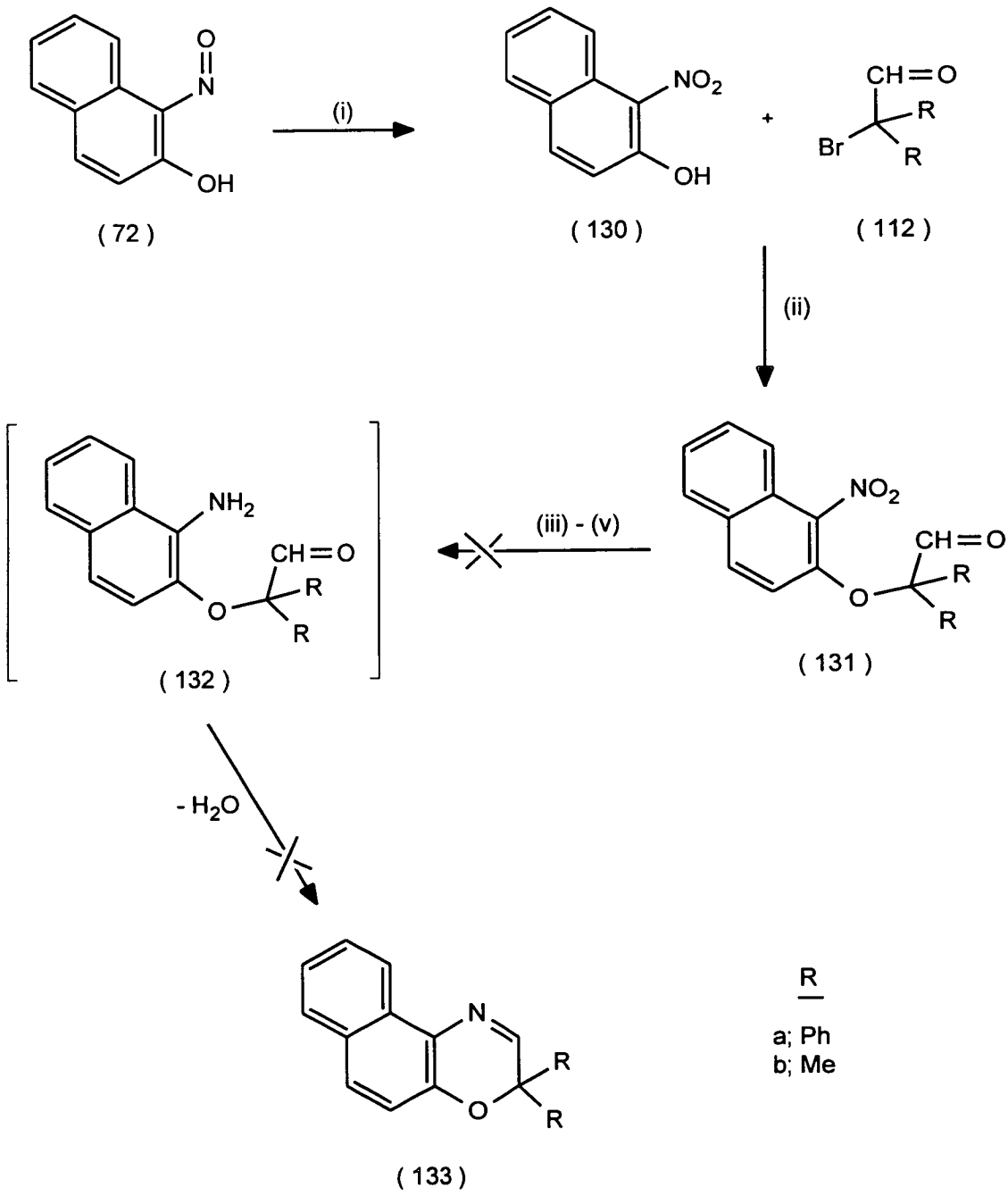
The benzoxazine (115b) as described earlier (see Page 20, Section 1.3.1) is potentially photochromic. However, initial tests carried out at Pilkington indicated that the benzoxazine (115b) was not photochromic. The benzoxazine (115b) is currently undergoing further tests into its photochromic behaviour at Gentex.

An investigation of the u.v. spectrum of the benzoxazine (115b) and its derivatives [(127b), (128b) and (129b)] was also initiated. This provided useful information on the absorption bands of these compounds and illustrated the effect of change in structure on absorption. Thus the u.v. spectrum (Figure 8) of the benzoxazine (115b) has an absorption maximum at 216 nm and also weaker bands at 244 and 295 nm. The bands at 244 and 295 nm are typical of benzenoid structures. It is also noteworthy that the benzoxazine (115b) is like its diphenyl analogue (115a) in that it is transparent (*i.e.* lacks absorption bands) in the visible region (400-750 nm). Not surprisingly, in view of its less

conjugated structure, the dihydro compound (127b) (Figure 9) also lacked absorption in the visible region and contained an absorption maximum at 217 nm and also weaker bands at 248 and 299 nm which represents a small bathochromic shift (shift to longer wavelength) throughout the spectrum, compared with the corresponding bands (λ_{max}, 216, 244 and 295 nm) in the benz-1,4-oxazine (115b). In marked contrast to the u.v. spectrum (Figure 8) of the benzoxazine (115b), the spectrum (Figure 11) of the cyanobenzoxazine (129b) is significantly different. For example, the benzoxazine (115b) as discussed earlier is transparent in the visible region, while the spectrum (Figure 11) of the cyanobenzoxazine (129b) shows a small amount of absorption in the violet region ($\lambda_{max} \simeq 400$ nm) of the visible spectrum which gives rise to the yellow colour of the cyanobenzoxazine (129b). The cyanobenzoxazine (129b) (Figure 11) contained an absorption maximum at 241 nm and also weaker bands at 202, 212, 290 and 355 nm. The bands at 241, 290 and 355 nm in the spectrum (Figure 11) of the cyanobenzoxazine (129b) represent a considerable bathochromic shift, compared with the corresponding bands (λ_{max} 216, 244 and 295 nm) in the spectrum (Figure 8) of the benz-1,4-oxazine (115b). Not surprisingly in view of its less conjugated structure the dihydro compound (128b) (Figure 10) lacked absorption in the visible region and its spectrum contained only three absorption bands, in contrast to the u.v. spectrum (Figure 11) of the more conjugated cyanobenzoxazine (129b) which contained five absorption bands.

Having successfully developed a viable synthetic route to the non-

photochromic 2,2-disubstituted 2H-benz-1,4-oxazine derivatives (115a and b), attention was next turned to the development of equally practical routes to potentially more photochromic naphth-1,4-oxazine derivatives [see Page 21, Scheme 16; (64) and (65)].



(i) 30% H_2O_2, HNO_3 aqu.(conc.), AcOH, 70°.
(ii) NaH, DMF, room temp. or 100°.
(iii) H_2, 10% Pd - C, EtOH, room temp., atmos. press.
(iv) H_2, Raney Ni, AcOH, room temp., atmos. press.
(v) $Na_2S_2O_4$, EtOH, H_2O, reflux.

Scheme 28

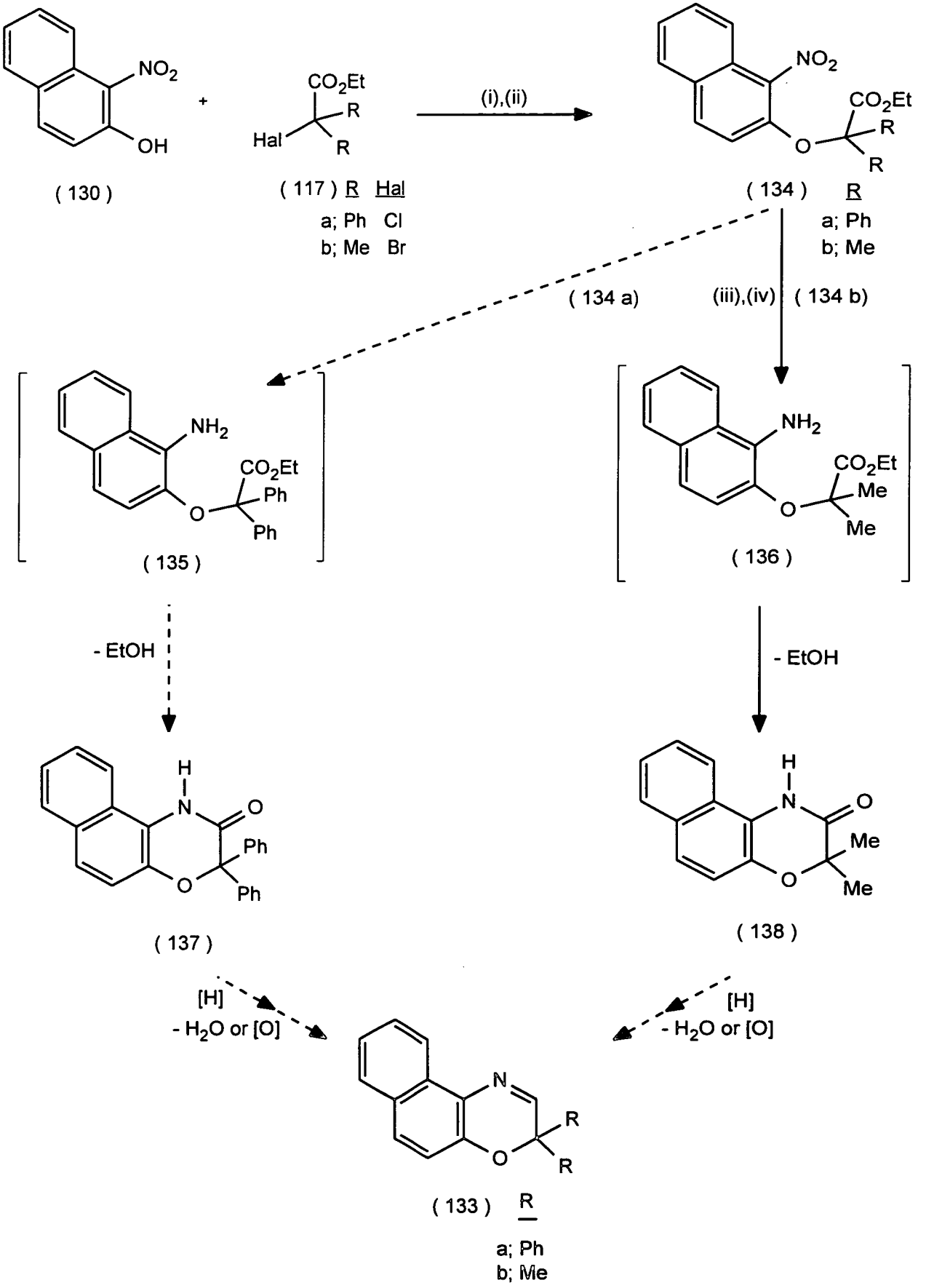
2.3 INVESTIGATIONS OF SYNTHETIC ROUTES TO NOVEL 3,3-DISUBSTITUTED 3H-NAPHTH[2,1-b]-1,4-OXAZINE DERIVATIVES

Studies under this heading were initially centred on the synthesis (Scheme 28) of the 3,3-disubstituted 3H-naphth[2,1-b]-1,4-oxazines (133a and b) based on 1-nitro-2-naphthol (130) as the key starting material. It was hoped that this compound would condense as the sodium salt with the bromo-aldehydes (112a and b) to give the ethers (131a and b) of appropriate structure for reductive cyclisation, *via* the amine intermediates (132a and b), to the respective 3,3-disubstituted naphth-1,4-oxazines (133a and b).

1-Nitro-2-naphthol (130) was obtained in moderate yield (48%) by the oxidation of the commercially available 1-nitroso-2-naphthol (72) with hydrogen peroxide in a mixture of nitric and acetic acids using the method employed for the synthesis of 2-nitroso-1-naphthol as described in the literature.[108] An initial attempt (Scheme 28) to condense the nitronaphthol (130) by heating its sodium salt [generated *in situ* by reaction of 1-nitro-2-naphthol (130) with sodium hydride in dimethylformamide] with 2-bromo-2,2-diphenylacetaldehyde (112a) in dimethylformamide at 100° for 1 h gave the ether (131a) in only low yield (16%) together with a moderate recovery (21%) of unreacted nitronaphthol (130). The structure of the ether (131a) was confirmed by its i.r. and ^{1}H n.m.r. spectra. Thus the i.r. spectrum of this material shows a carbonyl band at 1736 cm^{-1} and bands due to the nitro group at 1524 and 1350 cm^{-1}, while its ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H 10.03 assignable to the aldehyde group.

An attempt to improve the yield of the ether (131a) by extending the time of the reaction of the sodium salt of 1-nitro-2-naphthol (130) with 2-bromo-2,2-diphenylacetaldehyde (112a) to 17 h resulted in a decrease in the yield of the ether (131a) to 7% and an increase in the recovery of unreacted nitronaphthol (130) to 49%. The inefficiency of the reaction of the salt of 1-nitro-2-naphthol (130) with the bromo-aldehyde (112a) may be due to steric hindrance to nucleophilic displacement of the bromine atom in the latter molecule.

Due to the ether (131a) being available in only low yields, attention was next focused on the analogous synthesis (Scheme 28) of the 3,3-dimethyl-3H-naphth[2,1-b]-1,4-oxazine (133b). Investigation into the synthesis of the dimethyl derivative (133b) would serve as a useful contrast to the synthesis of the diphenyl derivative (133a). With 1-nitro-2-naphthol (130) readily available, attention was therefore turned to its conversion into the ether (131b). Hence the sodium salt of 1-nitro-2-naphthol (130) [generated *in situ* by reaction of 1-nitro-2-naphthol (130) with sodium hydride in dimethylformamide] was reacted with a two-fold excess of 2-bromo-2-methylpropionaldehyde (112b) in dimethylformamide at room temperature for 24 h. This reaction gave the desired ether (131b) in moderate yield (45%) together with a significant amount (53%) of unreacted 1-nitro-2-naphthol (130). A similar yield (41%) of the ether (131b) was obtained by reacting the sodium salt of 1-nitro-2-naphthol (130) with a four-fold excess of 2-bromo-2-methylpropionaldehyde (112b) in dimethylformamide at room temperature for 24 h. Unreacted starting material (130) was also recovered in moderate yield (56%) from this reaction. A vastly



(i) NaH, DMF, 100°.
(ii) KI, NaH, DMF, 100°.
(iii) H_2, 10% Pd - C, EtOH, room temp., atmos. press.
(iv) $Na_2S_2O_4$, EtOH, H_2O, reflux.

Scheme 29

improved yield (73%) of the ether (131b) was obtained by reacting the sodium salt of 1-nitro-2-naphthol (130) with a four-fold excess of 2-bromo-2-methylpropionaldehyde (112b) in dimethylformamide at room temperature for 48 h. Unreacted 1-nitro-2-naphthol (130) was recovered in moderate yield (27%) from this reaction.

With the ether (131b) readily available, attention was next turned (Scheme 28) to its conversion by reduction and *in situ* cyclisation of the resulting amine (132b) into the required naphth-1,4-oxazine (133b). However, attempted reduction of the ether (131b) using hydrogen over 10% palladium-on-charcoal in ethanol gave only a quantitative recovery (98%) of the unreacted ether (131b). Attempted reduction of the ether (131b) using hydrogen over Raney nickel in glacial acetic acid gave a complex mixture from which no identifiable material was obtained. In a final attempt to reduce the ether (131b) it was heated under reflux with sodium dithionite in aqueous ethanol. This reaction, however, gave after flash-chromatography only an unidentified brown oily product. The failure of the ether (131b) to undergo reductive cyclisation into the required naphthoxazine (133b) is possibly due to side reactions such as co-reduction of the aldehyde group.

Due to the unsuccessful attempts to reductively cyclise the ether (131b) and the poor yields of the ether (131a) attention was next directed (Scheme 29) to the synthesis of the 3,3-disubstituted 3H-naphth[2,1-b]-1,4-oxazin-2(1H)-ones [(137) and (138)]. It was anticipated that these molecules might be useful precursors to the potentially photochromic 3H-naphth[2,1-b]-1,4-oxazines

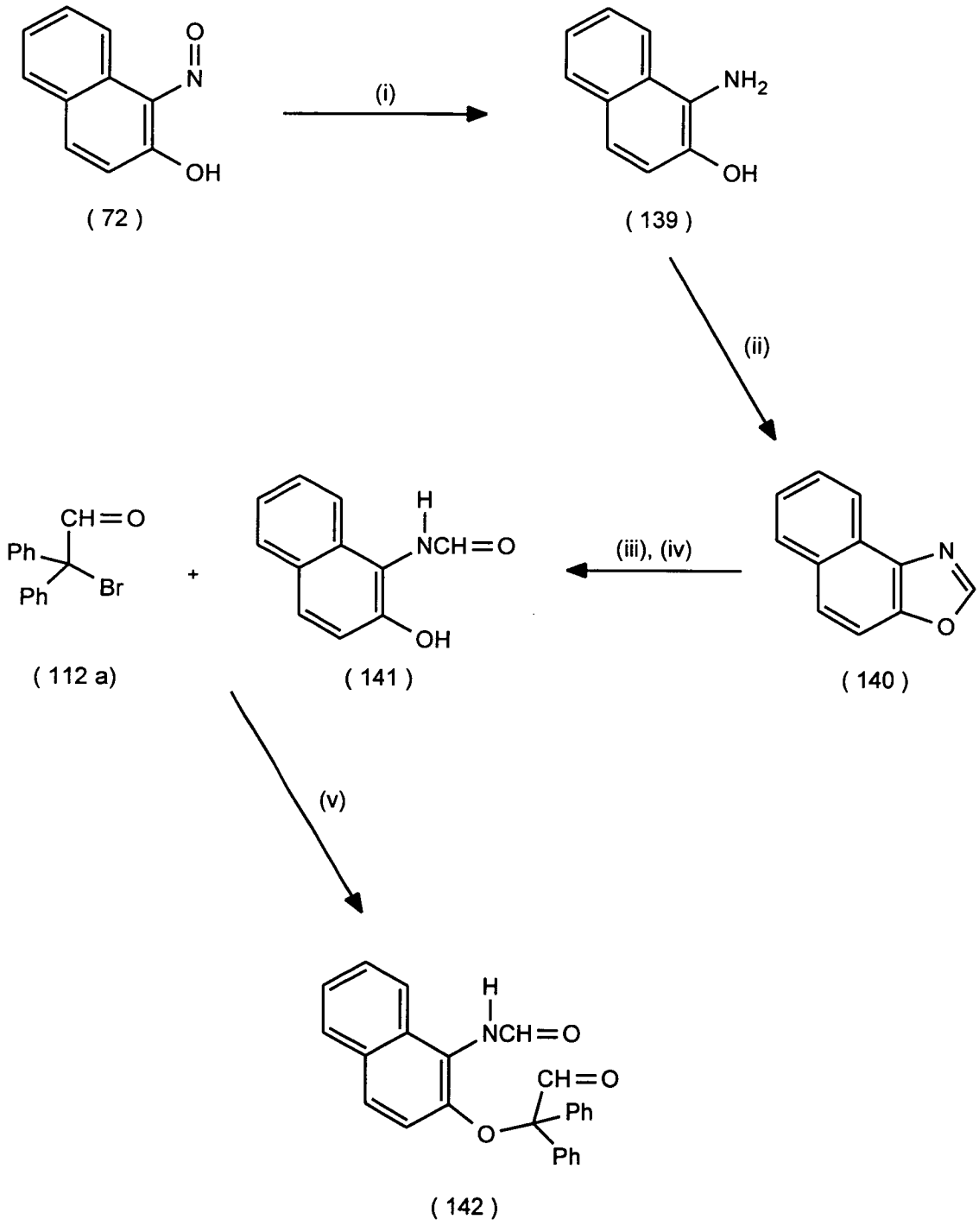
(133a and b).

It was first decided to attempt the synthesis (Scheme 29) of the key ether starting material (134a) with the intention of carrying out its reductive cyclisation *via* the amine (135) to the naphth-1,4-oxazinone (137). The reaction of the sodium salt of 1-nitro-2-naphthol (130) [generated *in situ* by reaction of 1-nitro-2-naphthol (130) with sodium hydride in dimethylformamide] with ethyl 2-chloro-2,2-diphenylacetate (117a) in dimethylformamide at 100° for 17 h, afforded the desired ether (134a) but only in low yield (12%). Unreacted ethyl 2-chloro-2,2-diphenylacetate (117a) (recovery 50%) and unreacted naphthol (130) (recovery 40%) were also isolated from this reaction. When this reaction was repeated with a small amount of potassium iodide present to catalyse the reaction only a slight increase in the yield (17%) of the desired ether (134a) was obtained. The inefficiency of the reactions of the sodium salt of 1-nitro-2-naphthol (130) with ethyl 2-chloro-2,2-diphenylacetate (117a) can be attributable to possible steric hindrance to nucleophilic displacement of the chlorine atom in the latter molecule.

Due to the poor yield of the ether (134a) studies were switched to the projected synthesis (Scheme 29) of the 3,3-dimethylnaphthoxazinone (138). Thus the reaction of the sodium salt of 1-nitro-2-naphthol (130) [again generated *in situ* by reaction of 1-nitro-2-naphthol (130) with sodium hydride in dimethylformamide] with the commercially available ethyl 2-bromo-2-methylpropionate (117b) was undertaken in the expectation of obtaining the key ether starting material (134b). When this reaction was carried out at 100°

for 1 h, unreacted 1-nitro-2-naphthol (130) was recovered in high yield (69%) together with a moderate yield (31%) of the desired ether (134b). The ether (134b) gave analytical, ^{1}H n.m.r. and mass spectral data consistent with this structure and was further identified by its i.r. spectrum which shows a band at 1740 cm^{-1} attributable to the carbonyl absorption of the ester group and a further two bands at 1532 and 1358 cm^{-1} attributable to the nitro group. Extension of the time of the reaction of the sodium salt of 1-nitro-2-naphthol (130) with ethyl 2-bromo-2-methylpropionate (117b) to 17 h gave an improved yield (55%) of the ether (134b) and a moderate recovery (44%) of unreacted 1-nitro-2-naphthol (130). In a final attempt to improve the yield of the ether (134b), the sodium salt of 1-nitro-2-naphthol (130) was reacted with a two-fold excess of ethyl 2-bromo-2-methylpropionate (117b) in dimethylformamide at 100° for 17 h. This reaction, however, gave only a low yield (33%) of the desired ether (134b) and a moderate recovery (56%) of unreacted 1-nitro-2-naphthol (130).

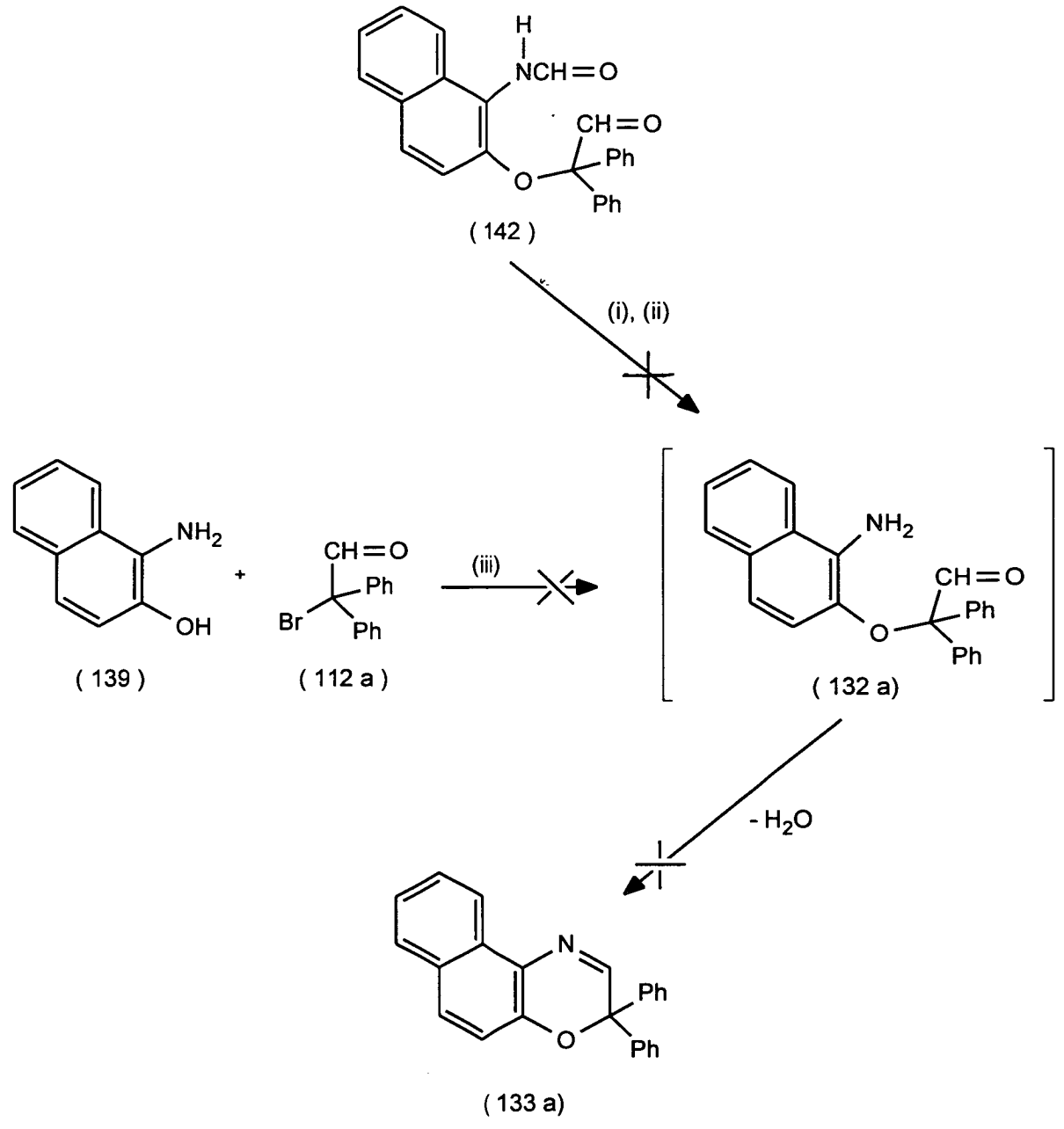
With the ether (134b) now available, studies of its reductive cyclisation to the naphth-1,4-oxazinone (138) were carried out. In an initial attempt to achieve the transformation [(134b)→(138)] the ether (134b) was reduced using hydrogen over 10% palladium-on-charcoal in ethanol. This reaction, however, afforded only a quantitative recovery (97%) of unreacted ether (134b). In contrast, reduction of the ether (134b) by heating under reflux with sodium dithionite in aqueous ethanol gave the expected naphth-1,4-oxazinone (138) in excellent yield (88%). This colourless product (138) gave analytical and



(72) (139) (140) (112 a) (141) (142)

(i) H_2, 10% Pd - C, EtOAc, room temp., atmos. press.
(ii) HCO_2H, reflux.
(iii) solvent, H_2O, reflux.
(iv) 2M HCl aqu., 1,4 - dioxane, reflux.
(v) NaH, DMF, room temp. or 100°.

Scheme 30



(i) 2M NaOH aqu., EtOH, room temp. or reflux.

(ii) 2M HCl aqu., EtOH, reflux.

(iii) NaH, DMF, 100°.

Scheme 31

mass spectral data consistent with its structure and was further identified by its i.r. and ^{1}H n.m.r. spectra. Thus the i.r. spectrum shows a band assignable to the carbonyl group, while its ^{1}H n.m.r. spectrum, shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H 9.39 which is completely removed on addition of deuterium oxide, assignable to the NH group. There are also three-proton singlets at δ_H 2.16 and at δ_H 1.60 due to the two methyl groups. Due to a lack of time and material, the conversion of the naphth-1,4-oxazinone (138) into the naphth-1,4-oxazine (133b) was not investigated.

Various attempts having failed to achieve reasonable yields of both the nitronaphthoxyacetaldehyde derivative [see Page 46, Scheme 28; (131a)] and the ether (134a) it was decided to investigate an alternative synthetic approach (Schemes 30 and 31). This approach was based on the formation and subsequent hydrolysis of the formamido derivative (142), by analogy with the strategy (see Page 36, Scheme 26) which had proved successful for the synthesis of the 2,2-disubstituted benz-1,4-oxazines (115a and b). Hence 1-nitroso-2-naphthol (72) was readily reduced using hydrogen over 10% palladium-on-charcoal in ethyl acetate to give the amine (139) as a purple solid in excellent yield (100%).

Heating 1-amino-2-naphthol (139) with 98% formic acid for 1 h under reflux with a view to obtaining the formamide (141) as described in the literature[109] gave the oxazole (140) as a dark solid in moderate yield (56%) and a low yield (20%) of the required formamide (141). Extension of the time of

this reaction to 3 h gave a quantitative yield of the oxazole (140). Attempted hydrolysis of the oxazole (140) by heating in water under reflux gave unreacted oxazole (140) (44%) and only a moderate yield (31%) of the required formamide (141). In an attempt to improve the yield of the formamide (141), the oxazole (140) was heated under reflux in aqueous 1,4-dioxane for 4 h. It was anticipated that the oxazole (140) would hydrolyse more readily with a co-solvent present, but these conditions also gave only a moderate yield (34%) of the formamide (141) and a substantial recovery (56%) of the unreacted oxazole (140). However, extending the time of the hydrolysis of the oxazole (140) in refluxing aqueous 1,4-dioxane to 17 h was more successful and afforded a much improved yield (59%) of the formamide (141), together with a moderate recovery (39%) of unreacted oxazole (140). Surprisingly, further extension of the time of the hydrolysis of the oxazole (140) to 41 h in refluxing aqueous 1,4-dioxane resulted in a substantial drop in the yield (16%) of the formamide (141) and a substantial recovery (83%) of the unreacted oxazole (140). The alternative hydrolysis of the oxazole (140) by heating under reflux in aqueous diglyme also resulted only in a low yield (7%) of the formamide (141) and a substantial recovery (91%) of the unreacted oxazole (140). The oxazole (140) was then heated in 50% v/v aqueous dimethylformamide under reflux, but under these conditions the oxazole (140) was substantially unchanged (91%) and the formamide (141) was isolated only in low yield (4%). Hydrolysis of the oxazole (140) by heating under reflux in 50% v/v aqueous glacial acetic acid, utilising the glacial acetic acid as both solvent and catalyst,

afforded the formamide (141) in moderate yield (32%). In a final attempt to improve the yield of the formamide (141), the oxazole (140) was heated under reflux in a mixture of 2 M aqueous hydrochloric acid and 1,4-dioxane. These conditions, however, gave only intractable mixtures from which no identifiable material was obtained.

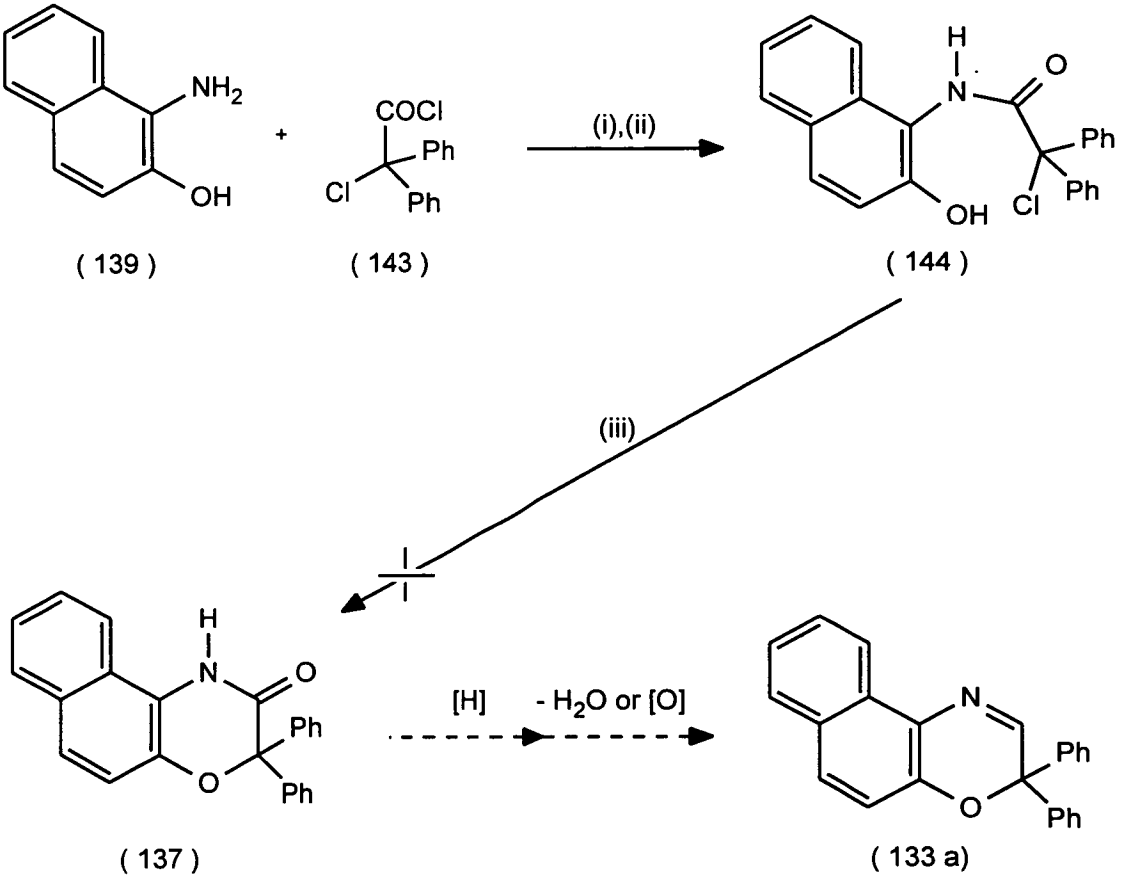
With the formamide (141) readily available using the hydrolytic methods described before, its reaction (Scheme 30) as the sodium salt [generated *in situ* by reaction of 1-formamido-2-naphthol (141) with sodium hydride in dimethylformamide] with the bromo-aldehyde (112a) with a view to obtaining the formamido-aldehyde (142), was investigated. In practice when this reaction was carried out at 100° with equivalent amounts of formamidonaphthol (141) and bromo-aldehyde (112a), a brown foam was obtained in moderate yield (39%). Attempts to crystallise this foam to provide a sample for combustion analysis proved difficult with the material remaining ill-defined. However, the foam gave i.r. and mass spectral data consistent with its formulation as the formamido derivative (142). When the reaction of the sodium salt of the formamide (141) with the bromo-aldehyde (112a) was carried out using two equivalents of the latter in dimethylformamide at 100° an increased yield (47%) of the formamido-derivative (142) was obtained. Unfortunately when the reaction of the sodium salt of the formamide (141) with the bromo-aldehyde (112a) was carried out using two equivalents of the latter in dimethylformamide at room temperature for 17 h only complex mixtures were obtained.

The presumed formamido-derivative (142), was then subjected (Scheme 31) to base-catalysed hydrolysis, in an attempt to obtain the amine intermediate (132a) [and hence the naphth-1,4-oxazine (133a)]. Hence the formamido-derivative (142) was heated under reflux in ethanol with 2 M aqueous sodium hydroxide. These conditions resulted in the recovery (18%) of the formamido-derivative (142) and the isolation of a brown oil in moderate yield (47%). This oil was identified as benzophenone by its mass spectrum and by comparison [i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica] with an authentic sample. Also by formation of the correct 2,4-dinitrophenylhydrazone derivative. The origin of the benzophenone in this transformation is unknown at the present time but whatever its mode of formation it cannot be the result of simple hydrolysis.

Base-catalysed hydrolysis of the formamido-derivative (142) by reaction with 2 M aqueous sodium hydroxide in ethanol at room temperature gave a moderate recovery (33%) of the formamido-derivative (142) and a moderate yield (55%) of benzophenone. Disappointingly this reaction afforded no evidence for the formation of the naphthoxazine (133a).

The formamido-derivative (142) was also subjected to acid-catalysed hydrolysis (Scheme 31) by reaction with 2 M aqueous hydrochloric acid in ethanol under reflux. This reaction gave unreacted formamido-derivative (142) (28%) and benzophenone (30%) was also isolated. There was again no evidence for the formation of the naphthoxazine (133a).

Due to the complications encountered in the approach starting from the



(139) (143) (144)

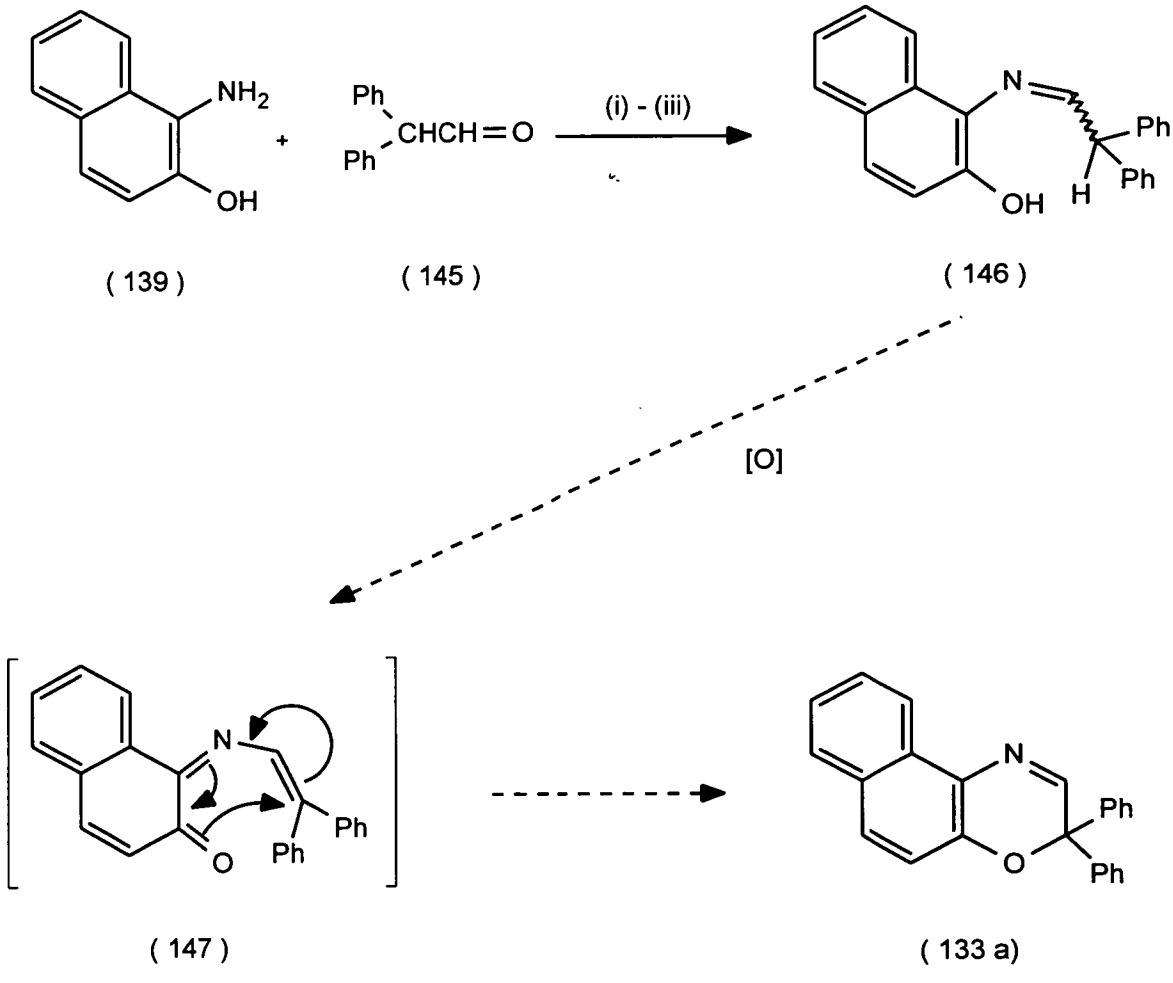
(137) (133 a)

(i) 1,4 - dioxane, reflux.
(ii) NaOAc, AcOH, room temp.
(iii) 2M NaOH aqu., EtOH, reflux.

Scheme 32

formamide (142) a more direct approach (Scheme 31) to the naphth-1,4-oxazine derivative (133a) was next investigated. It was hoped that the sodium salt of 1-amino-2-naphthol (139) [generated *in situ* by reaction of 1-amino-2-naphthol (139) with sodium hydride in dimethylformamide] would react with the bromo-aldehyde (112a) to give the amine (132a) directly. Spontaneous ring-closure of the amine (132a) would then afford the naphth-1,4-oxazine (133a). However, in practice the reaction of the sodium salt of 1-amino-2-naphthol (139) with the bromo-aldehyde (112a) in dimethylformamide at 100° gave only a complex mixture.

An alternative approach (Scheme 32) to the naphth-1,4-oxazine (133a) was then investigated. This approach involved the attempted formation of the naphthoxazinone (137) with a view to its further manipulation to give the target naphth-1,4-oxazine (133a). It was anticipated that the naphthoxazinone (137) would be readily available from the base-catalysed cyclisation of the amide (144). In practice the amide (144) was obtained as a lilac solid in moderate yield (45%) by the reaction of 1-amino-2-naphthol (139) with the commercially available 2-chloro-2,2-diphenylacetyl chloride (143) in anhydrous 1,4-dioxane under reflux. The lilac product was identified by its elemental analysis and mass spectrum which are fully consistent with its assignment as the amide (144). This structure (144) was also confirmed by the i.r. spectrum of the compound, which shows a band at 3323 cm^{-1} due to the NH group, a band at 3201 cm^{-1} consistent with the presence of an OH group and a band at 1660 cm^{-1} assigned to the amide C=O stretch. The ^1H n.m.r. spectrum of this



(139) (145) (146)

(147) (133 a)

(i) tosic acid, benzene, reflux.
(ii) 4Å mol. sieves, ether, room temp.
(iii) 4Å mol. sieves, DME, room temp., or reflux.

Scheme 33

derivative (144) shows a one-proton singlet at δ_H 9.24 due to the hydroxyl proton and a one-proton singlet at δ_H 8.24 which is completely removed on addition of deuterium oxide, attributable to the NH group. There is also a sixteen-proton multiplet in the aromatic region (δ_H 7.84-7.25), assigned to the naphthalene and phenyl groups of the structure (144).

The amide (144) was also obtained, though in lower yield (31%) by the sodium acetate catalysed reaction of 1-amino-2-naphthol (139) with 2-chloro-2,2-diphenylacetyl chloride (143) in glacial acetic acid at room temperature. This low yield of the amide (144) was a disappointment as it was hoped the sodium acetate would both catalyse the reaction and scavenge any hydrochloric acid formed, hence driving the reaction to completion.

With the amide (144) readily available, attention was focused on its base-catalysed cyclisation to the naphthoxazinone (137). Unfortunately, the reaction of the amide (144) with 2 M aqueous sodium hydroxide in ethanol under reflux gave only a multicomponent mixture. Due to a lack of material and a shortage of time, further studies into the base catalysed cyclisation of the amide (144) were not undertaken.

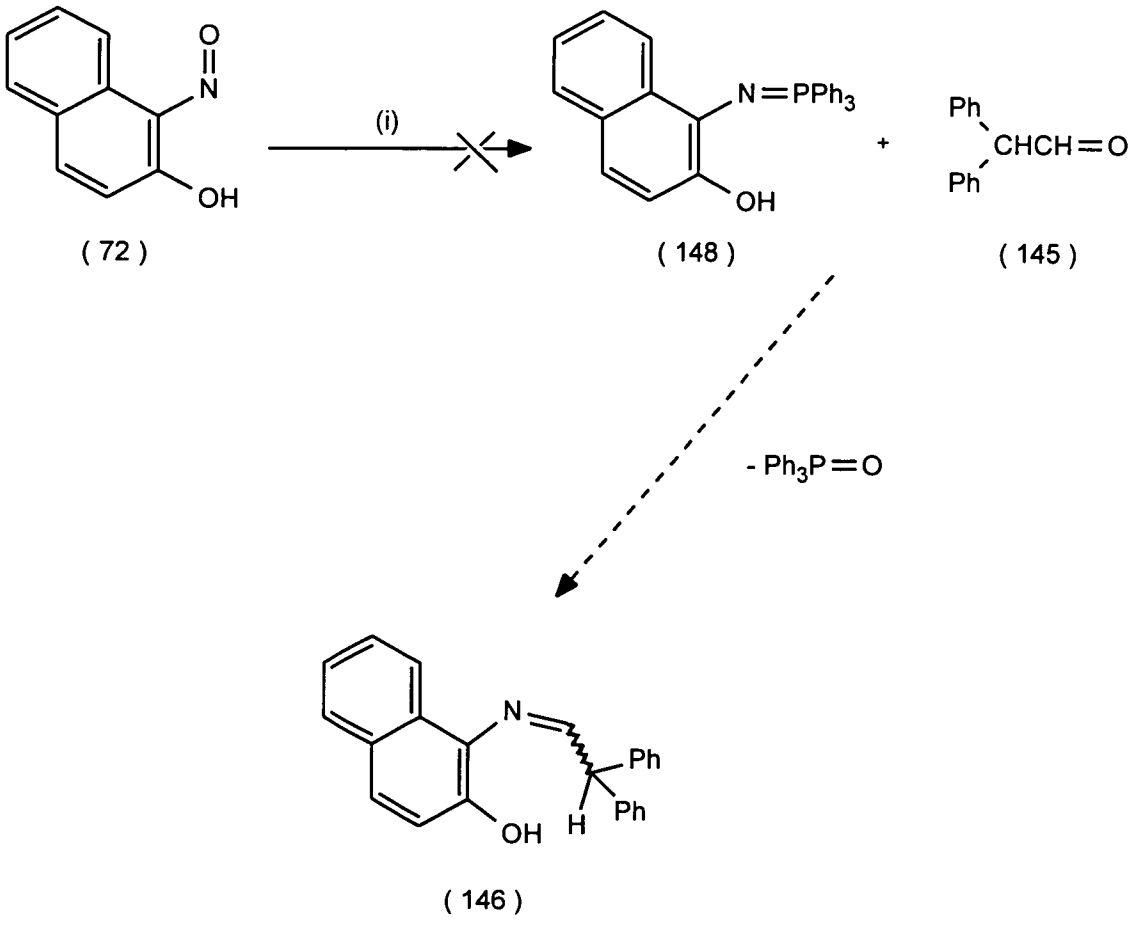
Studies were next directed to the investigation of the alternative approach (Scheme 33) to the naphth-1,4-oxazine (133a) based on the formation of the imine (146). It was hoped that oxidation of the latter would afford the quinoneimine (147) which would spontaneously cyclise to the naphthoxazine (133a). It was anticipated that 1-amino-2-naphthol (139) would condense with 2,2-diphenylacetaldehyde (145) to give the imine (146) and

further that this condensation would be reversible. Therefore the condensation would have to be driven in the direction of the imine product (146) by removal of water formed either by azeotropic distillation or by the presence of molecular sieves.

An initial attempt to form the imine (146) by the acid-catalysed reaction of 1-amino-2-naphthol (139) with the aldehyde (145) in benzene under reflux and azeotropic distillation of the water formed (Dean and Stark apparatus) gave a colourless solid in low yield (12%) whose spectroscopic properties are consistent with it being the imine (146).

Due to the poor yield of the imine (146) obtained by the previous method, alternative conditions (Scheme 33) using molecular sieves were also investigated. Hence 1-amino-2-naphthol (139) was reacted with 2,2-diphenylacetaldehyde (145) in ether, containing molecular sieves, at room temperature. This reaction gave only a high yield (77%) of unreacted diphenylacetaldehyde (145). In a further attempt to obtain the imine (146), 1-amino-2-naphthol (139) was reacted with diphenylacetaldehyde (145) in 1,2-dimethoxyethane containing molecular sieves at room temperature for 23 h. From this reaction benzophenone was obtained in high yield (73%) together with a complex mixture which yielded no other identifiable material. Repetition of this reaction, but in 1,2-dimethoxyethane under reflux gave only a high recovery of the unreacted diphenylacetaldehyde (145) (100%) and 1-amino-2-naphthol (139) (66%) starting materials.

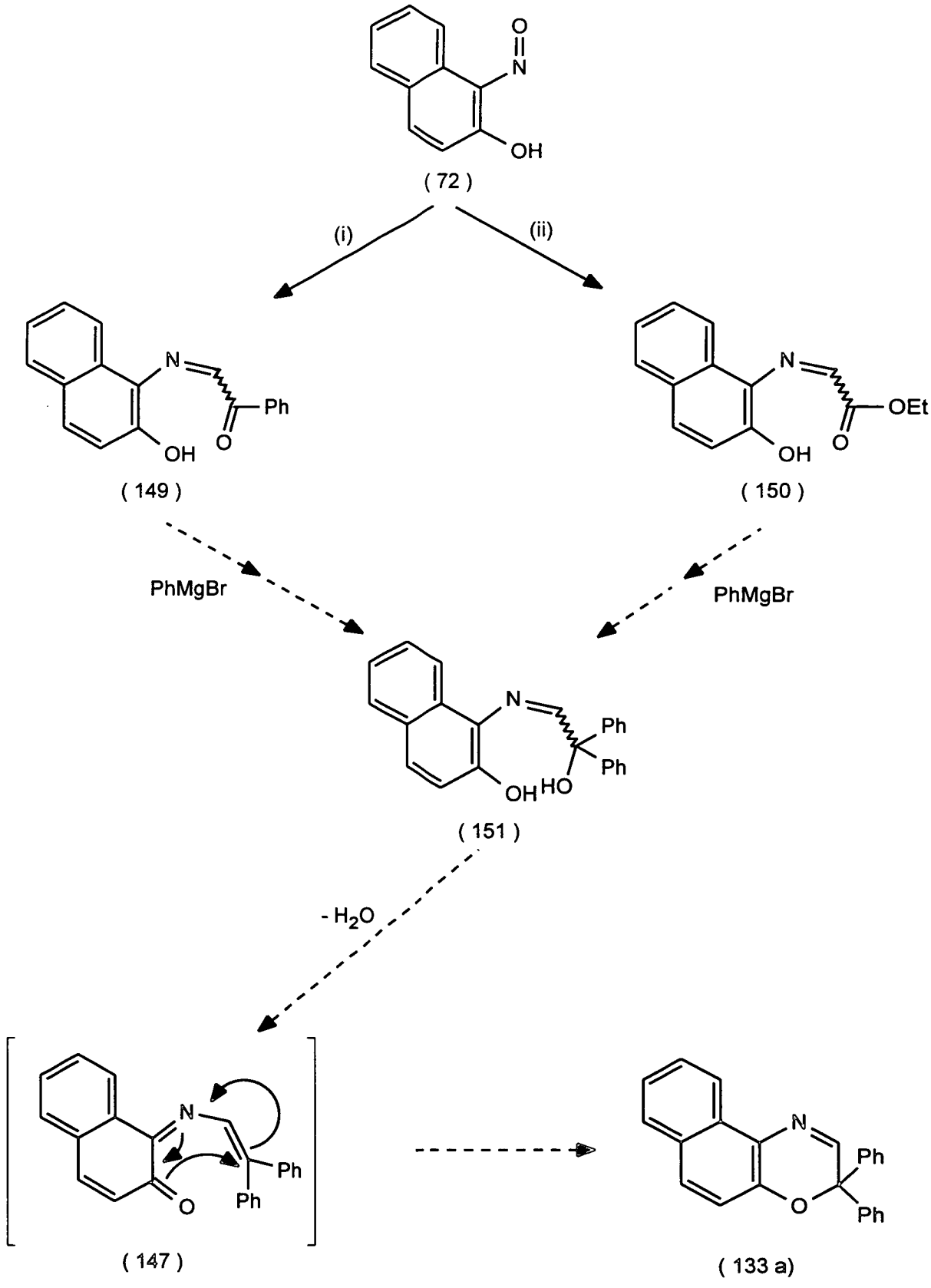
In a further attempt to devise a practical synthetic method for the imine



(72) (148) (145) (146)

(i) Ph_3P, benzene, room temp.

Scheme 34



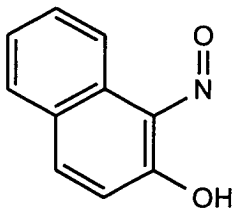
(i) $PhC(=O)CH{=}PPh_3$, solvent, reflux.

(ii) $EtO_2CCH{=}PPh_3$, benzene, reflux.

Scheme 35

(146) a new approach was evaluated (Scheme 34) which involved the formation of the known[110] phosphinimine (148) and its aza-Wittig reaction with diphenylacetaldehyde (145) to give the imine (146). The reaction of 1-nitroso-2-naphthol (72) with triphenylphosphine to give the phosphinimine (148) has been reported in the literature.[110] However, in the present studies, the reaction of 1-nitroso-2-naphthol (72) with triphenylphosphine in benzene at room temperature as described in the literature[110] gave none of the phosphinimine (148). Instead the products isolated were 1-amino-2-naphthol (139) (55%) and triphenylphosphine oxide (83%).

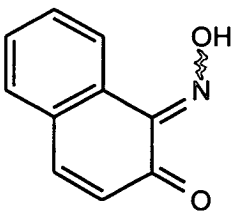
Due to the difficulties encountered in the orthodox synthetic approaches to the naphthoxazine derivative (133a), it was decided to embark on a more unorthodox synthetic strategy (Scheme 35) for this compound. This strategy again involved the synthesis and hopefully spontaneous electrocyclisation of the quinoneimine intermediate (147), the latter in this case being derived by dehydration of the dihydroxy compound (151). It was envisaged that the latter compound might be accessible (in conjunction with protection-deprotection of the phenolic hydroxy group) by the Grignard reactions of the ketone (149) or the ester (150) with phenylmagnesium bromide. The imines (149) and (150) have both been reported in the literature[111] as products of the reaction of 1-nitroso-2-naphthol (72) with the readily accessible benzoylmethylenetriphenylphosphorane and ethoxycarbonylmethylenetriphenyl-phosphorane respectively. Both of these phosphoranes were readily synthesised in high yield and their reactions with 1-nitroso-2-naphthol (72) to



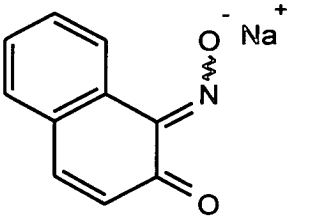
(72)

(153)

(i)

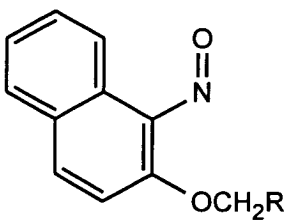


(152)



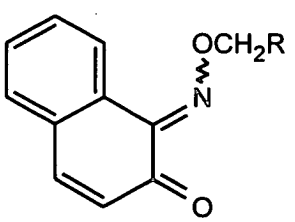
(154)

(ii) - (iv)



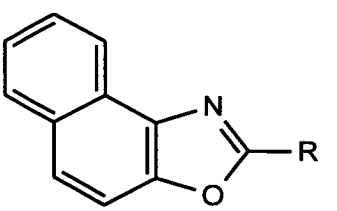
(155) R
a; H
b; Ph

or



(156) R
a; H
b; Ph

+



R
(140); H
(157); Ph

(i) NaH, DME, room temp.
(ii) Me_2SO_4, DMSO, 90°.
(iii) $PhCH_2Br$, DMSO, 90°.
(iv) $PhCH_2Br$, MeCN, reflux.

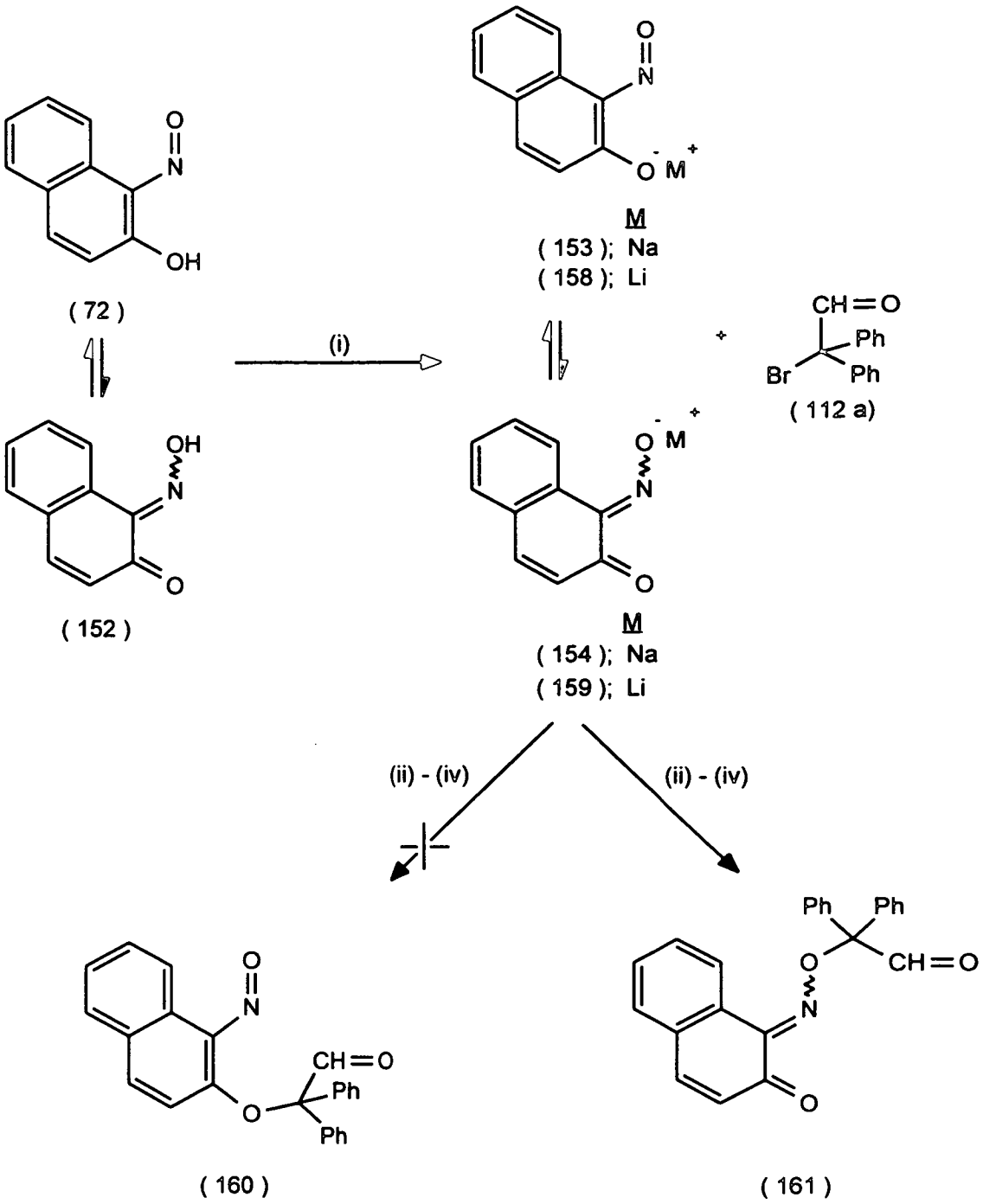
Scheme 36

give the required imines (149) and (150) as described in the literature,[111] investigated. However, reaction of the nitrosonaphthol (72) with benzoylmethylenetriphenylphosphorane in refluxing toluene gave a complex mixture rather than a good yield of the imine (149) as described in the literature.[111] Repetition of this reaction in refluxing benzene gave a green product in low yield (24%). The product gave mass spectral data consistent with the imine structure (149) and was further identified by its i.r. and ^{1}H n.m.r. spectra. Thus the i.r. spectrum shows a band at 3400 cm^{-1} attributable to the phenolic hydroxy group and a band at 1651 cm^{-1} due to the carbonyl absorption of the imine (149). The ^{1}H n.m.r. spectrum shows in addition to signals due to the methine and aromatic protons, a one-proton singlet at δ_H 7.25 assignable to the phenolic hydroxy group of the imine (149).

Reaction of ethoxycarbonylmethylenetriphenylphosphorane with 1-nitroso-2-naphthol (72) in refluxing benzene gave a high yield (89%) of triphenylphosphine oxide and a moderate yield (48%) of a pink solid. This pink solid gave spectroscopic data which fully supported its formulation as the imine (150). Disappointingly due to a lack of time and materials the possible further transformation of the imines (149) and (150) into the dihydroxy compound (151) and hence the naphthoxazine (133a) could not be investigated.

Concurrently with the foregoing investigations of synthetic routes to the naphthoxazine (133a) attention was turned to a new strategy (Scheme 36) for the synthesis of the latter molecule. It was reported in the literature[112] that 1-nitroso-2-naphthol (72) forms stable metal salts with various alkali metals. It

was therefore decided to attempt to exploit such salts in synthetic routes to the naphth-1,4-oxazine (133a). One difficulty which may arise in this approach is the existence of tautomerism between 1-nitroso-2-naphthol (72) and the oxime (152). During these studies (Scheme 36) a stable green solid was prepared and isolated in quantitative yield by treatment of 1-nitroso-2-naphthol (72) with sodium hydride in 1,2-dimethoxyethane at room temperature. This green solid analysed correctly as either of the sodium salts (153) or (154) and was tentatively assigned the structure of the sodium salt of the nitroso form (153) due to its green colour which is typical of nitroso-compounds. With the sodium salt (153) readily available, the exploitation of this reagent in synthetic routes to the naphth-1,4-oxazine (133a) was investigated. To evaluate the reactivity of the sodium salt of 1-nitroso-2-naphthol (153) towards alkylation it was methylated (Scheme 36) using dimethyl sulphate in dimethylsulphoxide at 90°. This reaction gave the naphthoxazole (140) in low yield (33%) together with a low yield (17%) of a brown solid which showed spectroscopic properties consistent with it being either the nitroso compound (155a) or the oxime compound (156a). The brown solid was tentatively assigned the nitroso structure (155a), as the formation of the naphthoxazole (140) is presumably due to cyclodehydration of the former compound. The sodium salt (153) also readily reacted with benzyl bromide in dimethylsulphoxide at 90° to give a moderate yield (42%) of a colourless solid which gave spectroscopic properties consistent with it being the naphthoxazole (157). This reaction also gave a low yield (22%) of a brown solid which gave combustion analysis and



(i) NaH or LiH, DME, room temp.
(ii) MeCN, or DME, reflux.
(iii) DMSO, 90°.
(iv) acetone, room temp.

Scheme 37

spectroscopic properties consistent with either the nitroso structure (155b) or the isomeric oxime (156b). The brown solid was tentatively assigned the nitroso structure (155b), as the formation of the naphthoxazole (157) is presumably due to cyclodehydration of the former compound. Repetition of the reaction of the sodium salt (153) with benzyl bromide in refluxing acetonitrile again gave the napthoxazole (157) in low yield (30%), together with a low recovery (17%) of unreacted 1-nitroso-2-naphthol (72).

Having shown that the sodium salt of 1-nitroso-2-naphthol (153) readily undergoes alkylation it was decided to exploit this reagent in synthetic routes to the naphth-1,4-oxazine (133a). In one such approach (Scheme 37), it was anticipated that the sodium salt (153) would react with the bromo-aldehyde (112a) to give the ether (160) which was expected could be reduced to the amine [see Page 51, Scheme 31; (132a)]. Spontaneous cyclisation of the latter compound would then afford the naphthoxazine (133a). One complication anticipated in this approach was the possibility of the salt (153) reacting as an ambident anion [(153)↔(154)] with the bromo-aldehyde (112a) to give the ether (160) and/or the oxime (161). The sodium salt (153) was therefore reacted with the bromo-aldehyde (112a) in acetonitrile under reflux. However, this reaction gave only a moderate recovery (36%) of the unreacted bromo-aldehyde (112a), together with a series of multicomponent gums. Since the sodium salt (153) was largely insoluble in acetonitrile the reaction was repeated in the more polar solvent dimethylsulphoxide at 90°. Under these conditions a readily separated mixture of a minor orange solid product (29%)

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

DATE: 09/06/95 TIME :13:33:38 SERIAL No:022001
ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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λnm	222.6	260.4	354.8							
ABS	2.152	2.026	0.803							

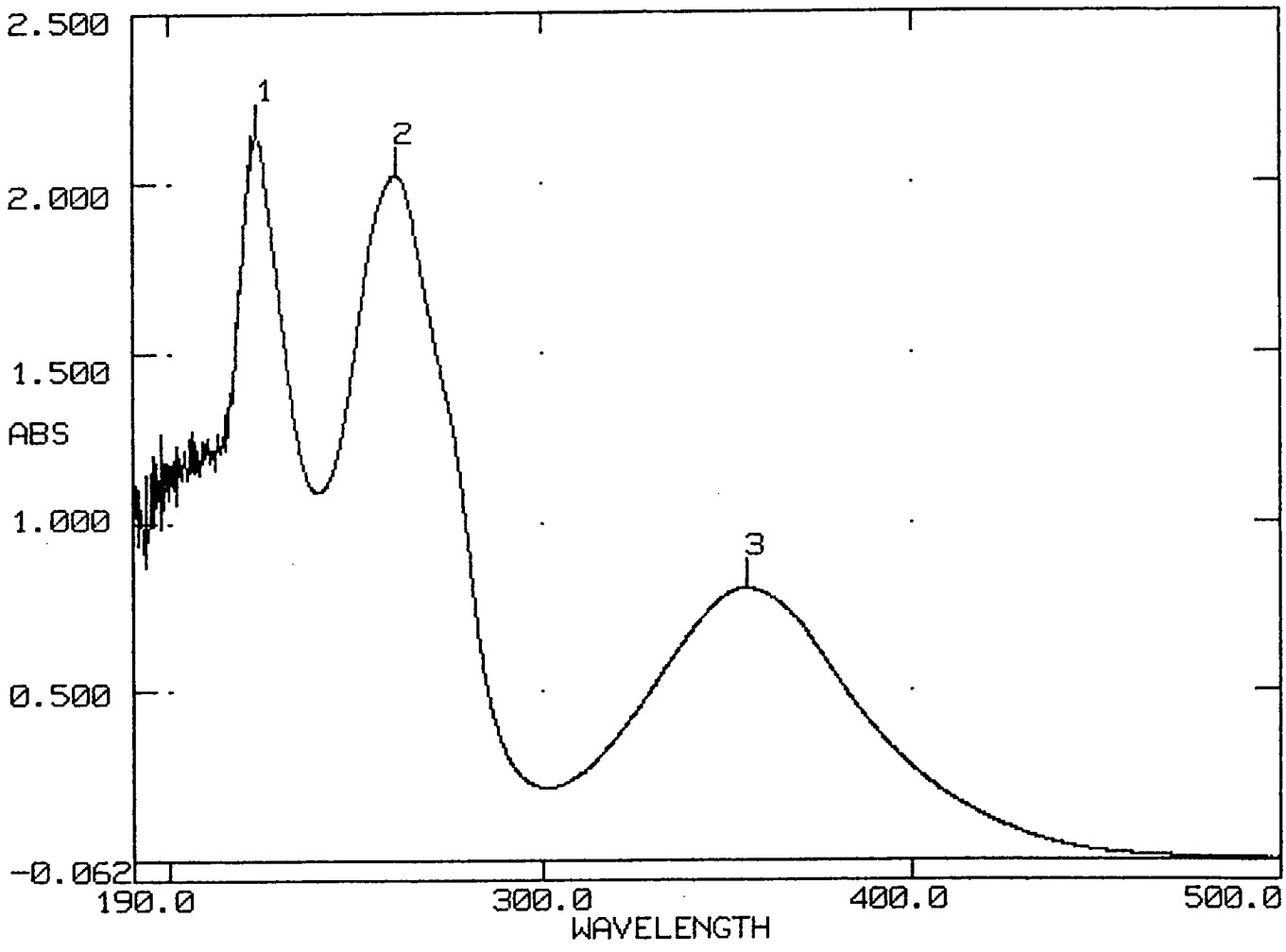
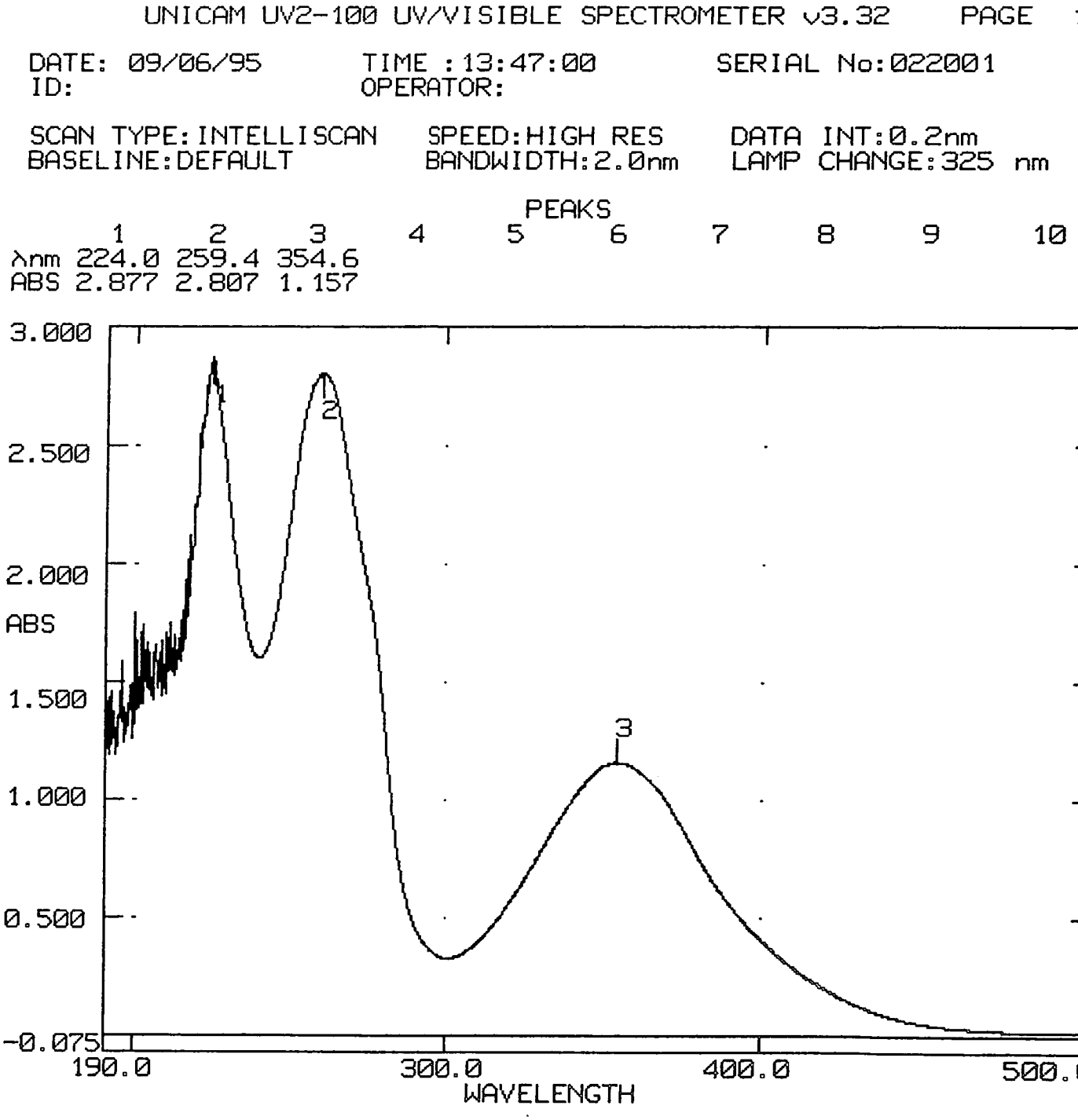


Figure 12


UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE
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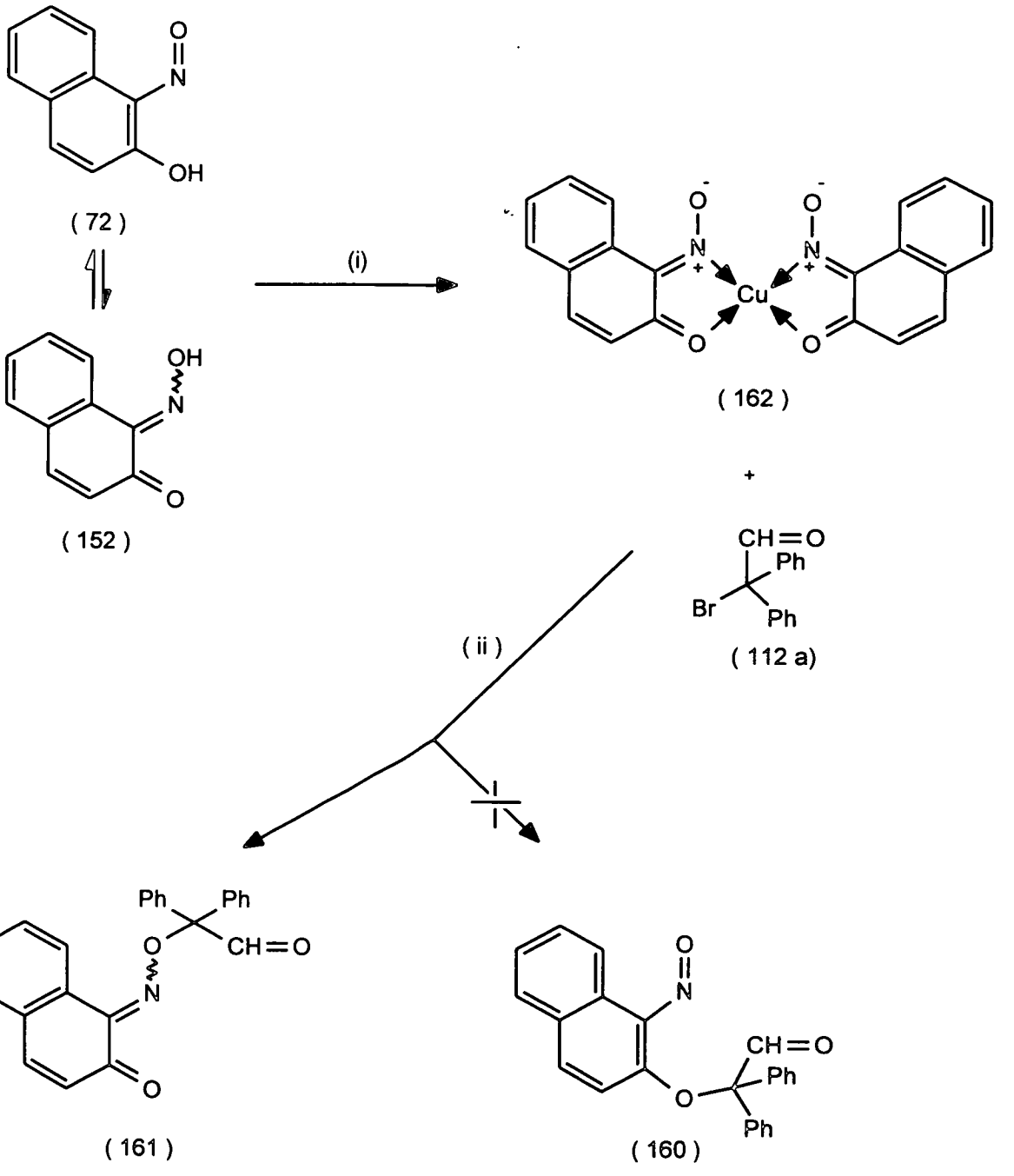
BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm
PEAKS
1 2 3 4 5 6 7 8 9 10
λnm 224.0 259.4 354.6
ABS 2.877 2.807 1.157
3.000
2.500
2.000
ABS
1.500
1.000
0.500
-0.075
190.0
300.0
400.0
500.
WAVELENGTH
1
2
3

Figure 13

and a major yellow solid product (50%) was obtained. Both products analysed correctly and gave mass, i.r. and ^{1}H n.m.r. spectral properties which tentatively supported the nitroso structure (160). Interestingly, although both products had the correct parent ion peak, the fragmentation patterns of their respective mass spectrums differed slightly. The ^{1}H n.m.r. spectrum of the minor orange solid product (160) correctly shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H9.96 due to the aldehyde proton. The ^{1}H n.m.r. spectrum of the major yellow solid product (160) also correctly shows signals due to the aromatic and aldehyde protons, but its spectrum is slightly different to the ^{1}H n.m.r. spectrum of the orange solid product (160). For example, the pattern of the signals in the aromatic region is different and the signal due to the aldehyde proton is now at δ_H10.05 in the spectrum of the yellow product (160). Similarly, small differences were also observed in the i.r. spectra of the orange and yellow products (160). For example, the fingerprint region of the two spectra show subtle differences and the carbonyl absorption band of the aldehyde group is at 1731 cm^{-1} in the i.r. spectrum of the orange product (160), while the same band appears at 1739 cm^{-1} in the i.r. spectrum of the yellow product (160). The u.v. spectrum (Figure 12) of the minor orange solid product (160) is virtually identical to the u.v. spectrum (Figure 13) of the major yellow solid product which would suggest they have the same structure. Initially it was thought the orange and yellow products were different crystalline modifications. For clarity the minor orange product was termed form A and the major yellow product was termed form B of the nitroso compound (160).



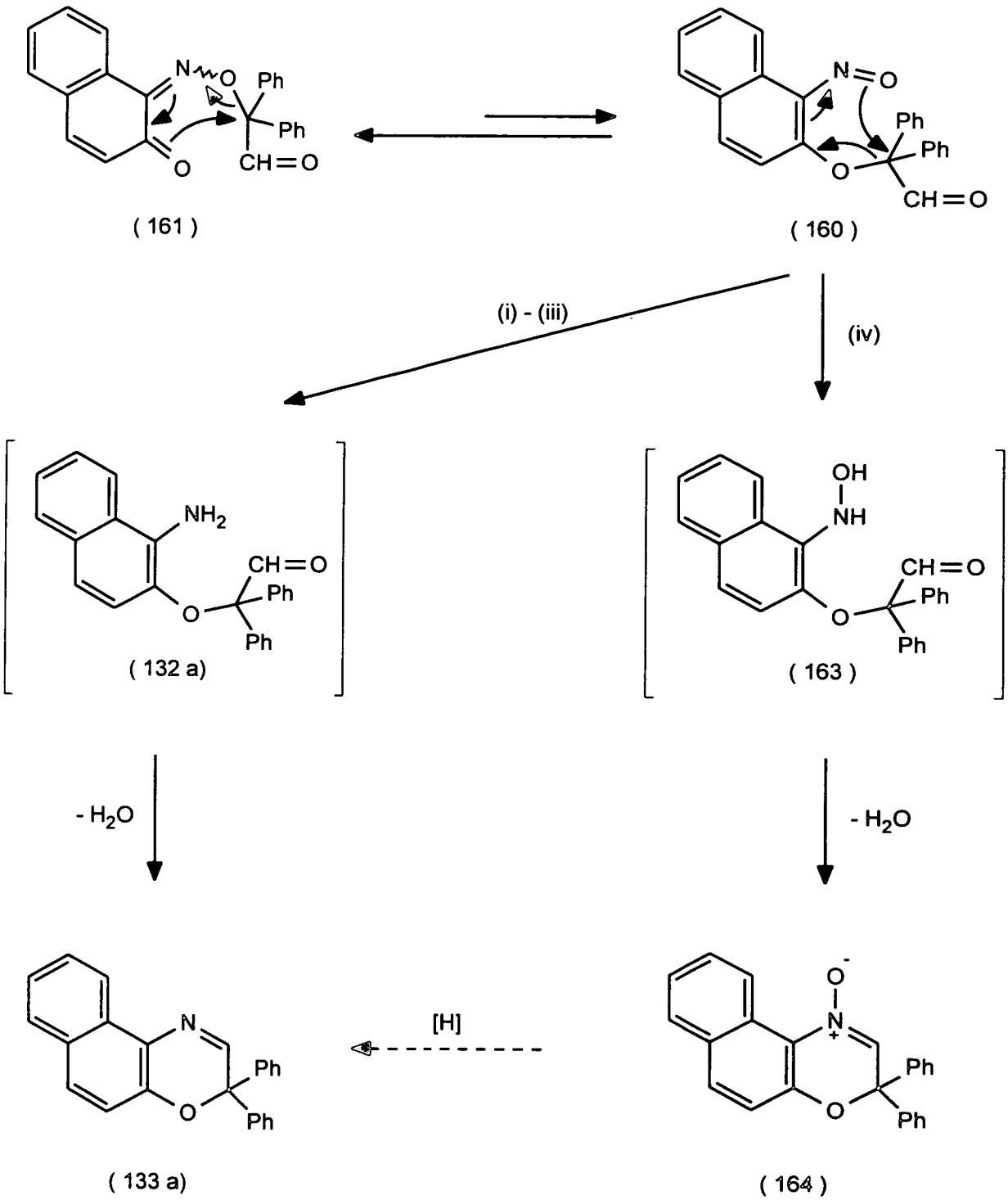
(i) $CuSO_4$, AcOH, H_2O, room temp.
(ii) DMSO, 90°.

Scheme 38

Subsequent X-ray studies (see Page 71) later revealed that these products were in fact the syn and anti forms of the oxime (161).

Analogous to the sodium salt (153) (Scheme 37) it was anticipated that the known[112] lithium salt of 1-nitroso-2-naphthol (158) could also be preformed and would hopefully be more soluble in organic solvents than the rather insoluble sodium salt (153), thus facilitating its reaction with the bromo-aldehyde (112a) to give the nitroso-aldehyde (160). In practice the lithium salt (158) was readily prepared in good yield (95%) as a stable green solid by reaction of the nitrosonaphthol (72) with lithium hydride in 1,2-dimethoxyethane at room temperature. As the lithium salt (158) was green it was tentatively assigned the nitroso structure (158) and not the oxime structure (159) on the basis that most nitroso compounds are green. Initially an attempt (Scheme 37) was made to react the lithium salt (158) with the bromo-aldehyde (112a) in 1,2-dimethoxyethane under reflux. These conditions successfully gave forms A and B of the proposed nitroso compound (160) (see Page 71) in a total yield of 62%, together with a moderate recovery (27%) of the unreacted bromo-aldehyde (112a). In a further reaction the lithium salt (158) was reacted with the bromo-aldehyde (112a) in dimethylsulphoxide at 90° to give forms A and B of the proposed nitroso compound (160) in a total yield of 43%. Finally the lithium salt (158) was reacted with the bromo-aldehyde (112a) in acetone at room temperature. This reaction again gave the combined forms of the nitroso compound (160) but in a total yield of 57%.

In a different approach (Scheme 38) to the nitroso compound (160), it



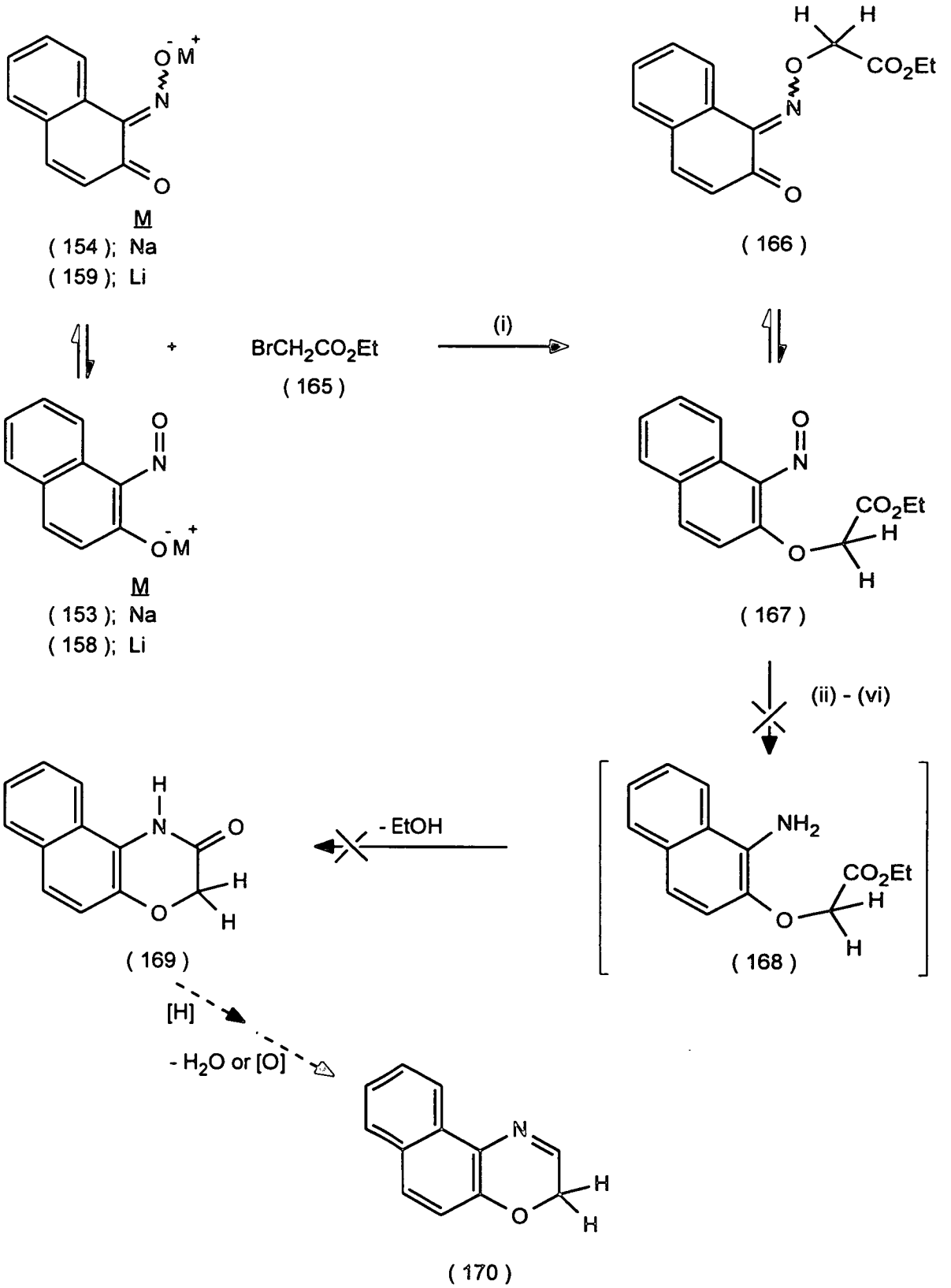
(i) H_2, 10% Pd - C, EtOH, room temp., atmos. press.
(ii) $Na_2S_2O_4$, AcOH, H_2O, room temp.
(iii) Ph_3P, DME, reflux.
(iv) PhNHNHPh, benzene, room temp.

Scheme 39

was anticipated that the known[113] copper complex (162) would also react with the bromo-aldehyde (112a) to give the nitroso-aldehyde (160). The reaction of 1-nitroso-2-naphthol (72) with copper sulphate by the procedure described in the literature[113] gave the copper(II) complex (162) monohydrate as a brown solid in moderate yield (59%) together with a moderate recovery (37%) of unreacted 1-nitroso-2-naphthol (72). The reaction of the copper complex (162) with the bromo-aldehyde (112a) in dimethylsulphoxide at 90° gave a low recovery (26%) of the copper complex (162) along with only a moderate yield (45%) of form A of the proposed nitroso-aldehyde (160) (see Page 71). Benzophenone (33%) was also isolated from this reaction.

With the two possible forms of the nitroso-aldehyde (160) (see Page 71) readily available, attention was next turned (Scheme 39) to their conversion by reduction and *in situ* cyclisation of the resulting amine (132a), into the required naphth-1,4-oxazine (133a). However, the attempted reduction of form A of the nitroso-aldehyde (160) using hydrogen over 10% palladium-on-charcoal in ethanol gave only a moderate recovery (43%) of the unreacted starting material (160) together with a low yield (27%) of benzophenone.

The attempted catalytic reduction of form B of the nitroso-aldehyde (160) also gave only a moderate recovery (45%) of the starting material (160) together with a moderate yield (55%) of benzophenone. An attempt was then made to reduce form B of the nitroso-aldehyde (160) using sodium dithionite in aqueous acetic acid at room temperature. However, this reaction gave only an intractable brown gum from which no identifiable material was obtained.

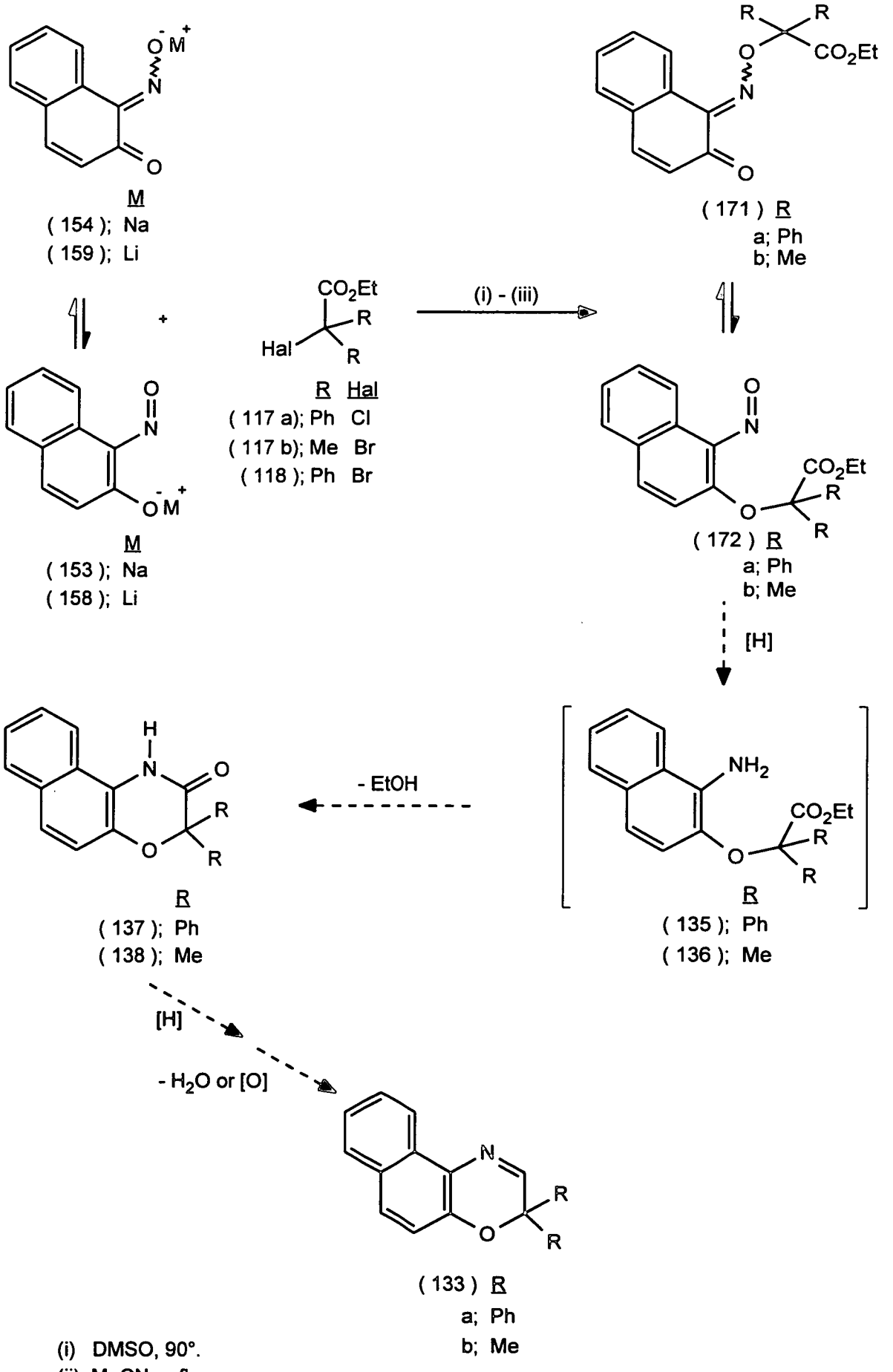


(i) MeCN, reflux.
(ii) H_2, 10% Pd - C, EtOH, room temp., atmos. press.
(iii) $Na_2S_2O_4$, EtOH, H_2O, room temp. or reflux.
(iv) $NaBH_4$, MeOH, H_2O, room temp.
(v) PhNHNHPh, benzene, room temp.
(vi) Ph_3P, DME, reflux.

Scheme 40

Studies into the reduction of the nitroso-aldehyde (160) were temporarily halted at this time.

Concurrently with the previously described investigations of the synthesis of the naphth-1,4-oxazine (133a), attempts (Scheme 40) were made to react the sodium salt of 1-nitroso-2-naphthol (153) with ethyl bromoacetate (165) with a view to obtaining the simple nitroso-ester (167) and hence by reductive cyclisation the naphthoxazinone (169). Further manipulation of the naphthoxazinone (169) as shown (Scheme 40) would afford the naphthoxazine (170). It was anticipated that the salt (153) could react as an ambident anion [(153)↔(154)] with ethyl bromoacetate (165) to give the nitroso-ester (167) and/or the oxime (166). Initially, formation of the nitroso-ester (167) by reaction of the sodium salt of 1-nitroso-2-naphthol (153) with ethyl bromoacetate (165) in acetonitrile under reflux was investigated. This reaction gave a good yield (69%) of a product which analysed correctly and had mass, i.r. and ^{1}H n.m.r. spectral properties consistent with the expected nitroso-ester (167). Hence the i.r. spectrum of this product shows the expected ester carbonyl absorption at 1742 cm^{-1} and its ^{1}H n.m.r. spectrum shows in addition to an aromatic multiplet at δ_H7.50-7.25 a two-proton singlet at δ_H5.08 due to the methylene protons. The ^{1}H n.m.r. spectrum also shows a two-proton quartet at δ_H4.25 and a three-proton triplet at δ_H1.28 attributable to the protons of the ethyl group of the nitroso-ester (167). In an attempt to improve the yield of the nitroso-ester (167), the lithium salt of 1-nitroso-2-naphthol (158) was also reacted with ethyl bromoacetate (165) in acetonitrile under reflux. However,



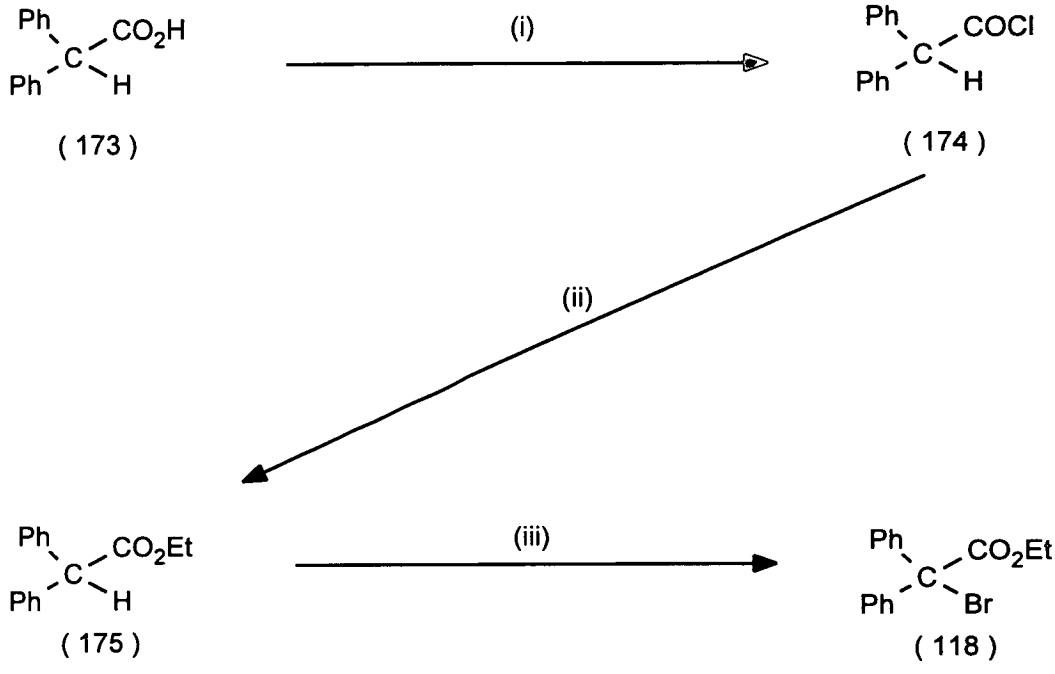
(i) DMSO, 90°.
(ii) MeCN, reflux.
(iii) acetone, reflux.

Scheme 41

these conditions gave a somewhat lower yield (64%) of the nitroso ester (167).

With the nitroso-ester (167) available, attention was next turned to its reductive cyclisation to the naphthoxazinone derivative (169). However, attempted catalytic hydrogenation of the nitroso-ester (167) gave only a multicomponent gum from which no identifiable material was obtained. Attempted reduction of the nitroso-ester (167) with sodium dithionite in aqueous ethanol at reflux afforded a complex mixture, while repetition of this reaction at room temperature gave only a good yield (72%) of 1-amino-2-naphthol (139). Correspondingly the attempted reductive cyclisation of the nitroso-ester (167) using sodium borohydride in aqueous methanol at room temperature also gave an intractable mixture which yielded no identifiable material. Attempts to effect the conversion of the nitroso-ester (167) into the naphthoxazinone (169) were temporarily halted at this point.

In a further approach (Scheme 41) to the naphthoxazine derivatives (133a and b) an attempt was made to synthesise the nitroso-esters (172a and b) with the intention of carrying out their reductive cyclisation *via* the amines [(135) and (136)] to the naphth-1,4-oxazinones [(137) and (138)]. It was anticipated that the naphthoxazinone derivative [(137) and (138)] could be further manipulated *via* reduction followed by oxidation or dehydration to afford the naphthoxazine derivatives (133a and b). As was discussed earlier (see Page 48, Scheme 29) the naphthoxazinone (138) was previously synthesised by reduction of the nitro-ester [see Page 48, Scheme 29; (134b)]. In this new approach it was anticipated that the nitroso-esters (172a and b) would reduce



(173) (174) (175) (118)

(i) $SOCl_2$, reflux.
(ii) EtOH, room temp.
(iii) NBS, $(PhCO)_2O_2$, $CHCl_3$, reflux.

Scheme 42

more readily than their nitro-ester counter-parts [see Page 48, Scheme 29; (134a and b)], thus facilitating the formation of the naphthoxazinones [(137) and (138)].

In an initial attempt to obtain the nitroso-ester (172a), the reaction of the sodium salt (153) with the chloro-ester (117a) in dimethylsulphoxide at 90° was investigated. This reaction gave a low yield (32%) of a yellow solid which analysed correctly and had mass, i.r. and ^{1}H n.m.r. spectral properties consistent with the expected nitroso-ester (172a). Hence the i.r. spectrum shows the expected C=O stretch at 1732 cm^{-1} due to the ester moiety in the nitroso-ester (172a). It was anticipated that the sodium salt (153) could react as an ambient anion [(153)↔(154)] with the chloro-ester (117a) to form the nitroso-ester (172a) and/or the oxime (171a). However the lack of a second carbonyl band in the i.r. spectrum of the nitroso-ester (172a) suggests the sodium salt (153) was reacting as the nitroso form (153). The ^{1}H n.m.r. spectrum of the yellow solid supports the nitroso-ester (172a) and shows in addition to signals due to the aromatic protons, a two-proton quartet at δ_H4.28 and a three-proton triplet at δ_H1.19 attributable to the ethyl group.

In a further attempt (Scheme 41) to obtain the nitroso-ester (172a) the key starting material ethyl 2-bromo-2,2-diphenylacetate (118) was synthesised. As described in Section 2.2 (see Page 33) difficulty had initially been encountered in attempts to synthesise this compound (118). However these difficulties have now been overcome in a three step synthesis from the commercially available diphenylacetic acid [Scheme 42;

(173)→(174)→(175)→(118)]. Thus, diphenylacetic acid (173) reacted smoothly with refluxing thionyl chloride to afford a quantitative yield of the acyl halide (174). Treatment of the latter with ethanol afforded the ester (175) in good yield (94%). Subsequent bromination of the ester (175) using N-bromosuccinimide afforded the bromo-ester (118) in quantitative yield.

With the bromo-ester (118) readily available attention was then turned to its reaction (Scheme 41) with the lithium salt of 1-nitroso-2-naphthol (158) in order to obtain the key nitroso-ester intermediate (172a). Reaction of the lithium salt (158) with the bromo-ester (118) in refluxing acetonitrile gave only an intractable mixture. Repetition of this reaction, but in dimethylsulphoxide at 90° also gave an intractable mixture and a low recovery of unreacted bromo-ester (118). In a final attempt to obtain a good yield of the nitroso-ester (172a) the lithium salt (158) was reacted with the chloro-ester (117a) in refluxing acetone to give only a high recovery (83%) of unreacted lithium salt (158). The inefficiency of the reactions of the salts of 1-nitroso-2-naphthol [(153) and (158)] with the halo-esters [(117a) and (118)] can be attributed to possible steric hindrance to nucleophilic displacement of the halogen atom in the latter molecules.

Due to the low yield of the nitroso-ester (172a) attention was turned to the further synthesis (Scheme 41) of the dimethylnaphthoxazinone (138). Further manipulation of this latter compound would afford the potentially photochromic naphthoxazine (133b). Initially formation of the nitroso-ester (172b) by reaction of the sodium salt of 1-nitroso-2-naphthol (153) with the

commercially available ethyl 2-bromo-2-methylpropionate (117b) in acetonitrile under reflux was investigated. Disappointingly, this reaction gave only an intractable mixture and due to a lack of time further investigations into the formation of the nitroso-ester (172b) were not initiated.

With various routes to the naphth-1,4-oxazines (133a and b) having failed, attention was once again turned (see Page 64, Scheme 39) to the reductive conversion of the nitroso-aldehyde (160) (see Page 71) into the naphthoxazine (133a). In the hope that hydrazobenzene might act as a reducing agent for the nitroso group in the nitroso-aldehyde (160), the form B of the latter was treated with this reducing agent in benzene at room temperature. This reaction gave a moderate yield (43%) of a light brown solid product which gave analytical, mass and ^{1}H n.m.r. spectral data consistent with its formulation as the naphthoxazine N-oxide (164). Thus the ^{1}H n.m.r. spectrum shows a sixteen-proton multiplet at δ_H8.53-7.19 assignable to the aromatic protons and a one-proton singlet at δ_H4.60 due to the methine proton. The naphthoxazine N-oxide (164) was also formed though in only low yield (17%) together with 1-amino-2-naphthol (139) (13%) when form A of the nitroso-aldehyde (160) was reduced with hydrazobenzene in benzene at room temperature. The formation of the N-oxide (164) in these reactions suggests the nitroso-aldehyde (160) was reduced to the hydroxylamine (163) and the latter compound then undergoes *in situ* ring closure to afford the N-oxide (164). Due to the low yields of the N-oxide (164) and a lack of time the further reduction of this compound to the naphth-1,4-oxazine (133a) was not attempted.

As was discussed earlier (see Page 58) triphenylphosphine reduces 1-nitroso-2-naphthol (72) to 1-amino-2-naphthol (139). It was therefore decided to investigate (Scheme 39) triphenylphosphine as a suitable reagent for the reductive conversion of the nitroso-aldehyde (160) into the naphthoxazine (133a). The form B of the nitroso-aldehyde (160) was therefore heated under reflux with triphenylphosphine in 1,2-dimethoxyethane to give in addition to triphenylphosphine oxide (88%) a moderate yield (66%) of a yellow solid product. This yellow solid product analysed correctly and gave correct mass, i.r. and ^{1}H n.m.r. spectral data consistent with its formulation as the desired naphthoxazine derivative (133a). Thus the i.r. spectrum shows the expected imine (C=N) absorption band (υ_{max} 1592 cm^{-1}) and the ^{1}H n.m.r. spectrum correctly shows the expected signals due to the methine and aromatic protons. The naphthoxazine (133a) was also obtained in good yield (78%) by the reaction of form A of the nitroso-aldehyde (160) with triphenylphosphine in refluxing 1,2-dimethoxyethane. This reaction also gave a high yield (98%) of triphenylphosphine oxide. Reacting a mixture of the yellow form B and the orange form A of the nitroso-aldehyde (160) with triphenylphosphine in refluxing 1,2-dimethoxyethane also gave a good yield (79%) of the naphthoxazine (133a) and a high yield (84%) of triphenylphosphine oxide.

Due to the initial difficulties encountered in the reduction reactions (see Page 64, Scheme 39) of the nitroso-aldehyde (160) to the naphthoxazine (133a), the exact nature of the orange form A and yellow form B of the nitroso-aldehyde (160) was investigated. Surprisingly, when the orange form A was

X-Ray Diffraction Data for form A of Naphthalene-1,2-dione 1-Oxime Diphenylformylmethyl Ether (161)

Table 1 : Bond Lengths (Angstroms) with Standard Deviations

C(1)-N(1)	1.302(2)	C(1)-C(8A)	1.478(2)
C(1)-C(2)	1.513(2)	C(2)-O(2)	1.220(2)
C(2)-C(3)	1.445(2)	C(3)-C(4)	1.331(2)
C(4)-C(4A)	1.451(2)	C(4A)-C(5)	1.397(2)
C(4A)-C(8A)	1.409(2)	C(5)-C(6)	1.373(3)
C(6)-C(7)	1.386(3)	C(7)-C(8)	1.383(2)
C(8)-C(8A)	1.396(2)	N(1)-O(9)	1.380(2)
O(9)-C(9)	1.458(2)	C(9)-C(1")	1.521(2)
C(9)-C(10)	1.524(2)	C(9)-C(1')	1.535(2)
C(10)-O(10)	1.199(2)	C(1')-C(6')	1.384(2)
C(1')-C(2')	1.395(2)	C(2')-C(3')	1.383(2)
C(3')-C(4')	1.383(3)	C(4')-C(5')	1.376(3)
C(5')-C(6')	1.394(2)	C(1")-C(6")	1.393(2)
C(1")-C(2")	1.397(2)	C(2")-C(3")	1.387(2)
C(3")-C(4")	1.389(3)	C(4")-C(5")	1.381(2)
C(5")-C(6")	1.387(2)		

Table 2 : Bond Angles (Degrees) with Standard Deviations

N(1)-C(1)-C(8A)	114.84(14)	N(1)-C(1)-C(2)	125.93(14)
C(8A)-C(1)-C(2)	119.19(13)	O(2)-C(2)-C(3)	121.3(2)
O(2)-C(2)-C(1)	122.23(14)	C(3)-C(2)-C(1)	116.46(14)
C(4)-C(3)-C(2)	122.0(2)	C(3)-C(4)-C(4A)	123.1(2)
C(5)-C(4A)-C(8A)	119.2(2)	C(5)-C(4A)-C(4)	120.5(2)
C(8A)-C(4A)-C(4)	120.3(2)	C(6)-C(5)-C(4A)	121.1(2)
C(5)-C(6)-C(7)	119.6(2)	C(8)-C(7)-C(6)	120.5(2)
C(7)-C(8)-C(8A)	120.4(2)	C(8)-C(8A)-C(4A)	119.1(2)
C(8)-C(8A)-C(1)	122.5(2)	C(4A)-C(8A)-C(1)	118.43(14)
C(1)-N(1)-O(9)	113.21(13)	N(1)-O(9)-C(9)	109.02(11)
O(9)-C(9)-C(1")	109.62(12)	O(9)-C(9)-C(10)	108.57(12)
C(1")-C(9)-C(10)	114.19(13)	O(9)-C(9)-C(1')	104.08(12)
C(1")-C(9)-C(1')	113.69(12)	C(10)-C(9)-C(1')	106.08(13)
O(10)-C(10)-C(9)	124.5(2)	C(6')-C(1')-C(2')	119.0(2)
C(6')-C(1')-C(9)	121.85(14)	C(2')-C(1')-C(9)	119.14(14)
C(3')-C(2')-C(1')	120.2(2)	C(2')-C(3')-C(4')	120.4(2)
C(5')-C(4')-C(3')	119.8(2)	C(4')-C(5')-C(6')	120.2(2)
C(1')-C(6')-C(5')	120.4(2)	C(6")-C(1")-C(2")	118.8(2)
C(6")-C(1")-C(9)	119.86(14)	C(2")-C(1")-C(9)	121.15(14)
C(3")-C(2")-C(1")	119.9(2)	C(2")-C(3")-C(4")	120.8(2)
C(5")-C(4")-C(3")	119.4(2)	C(4")-C(5")-C(6")	120.2(2)
C(5")-C(6")-C(1")	120.8(2)		

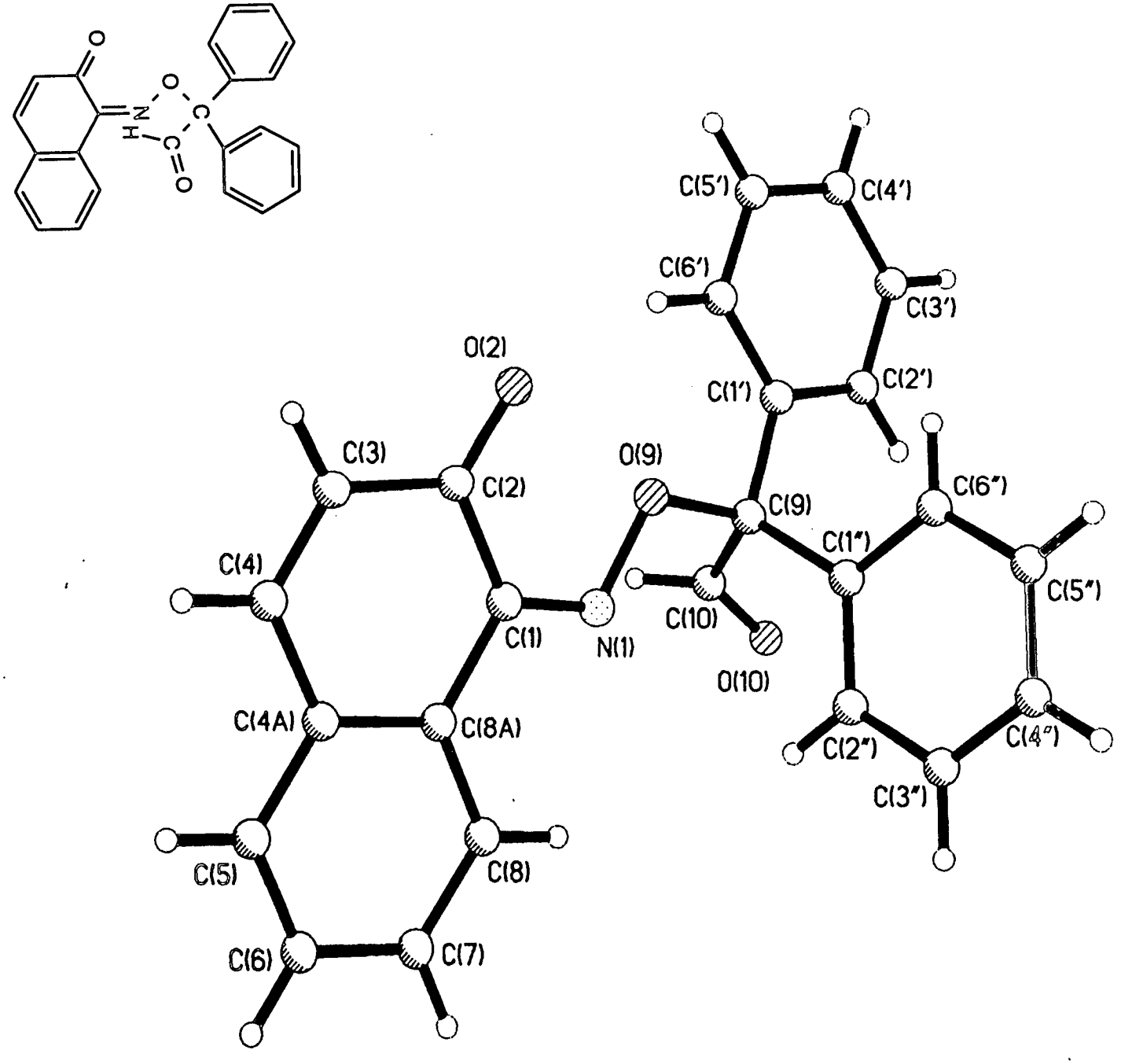
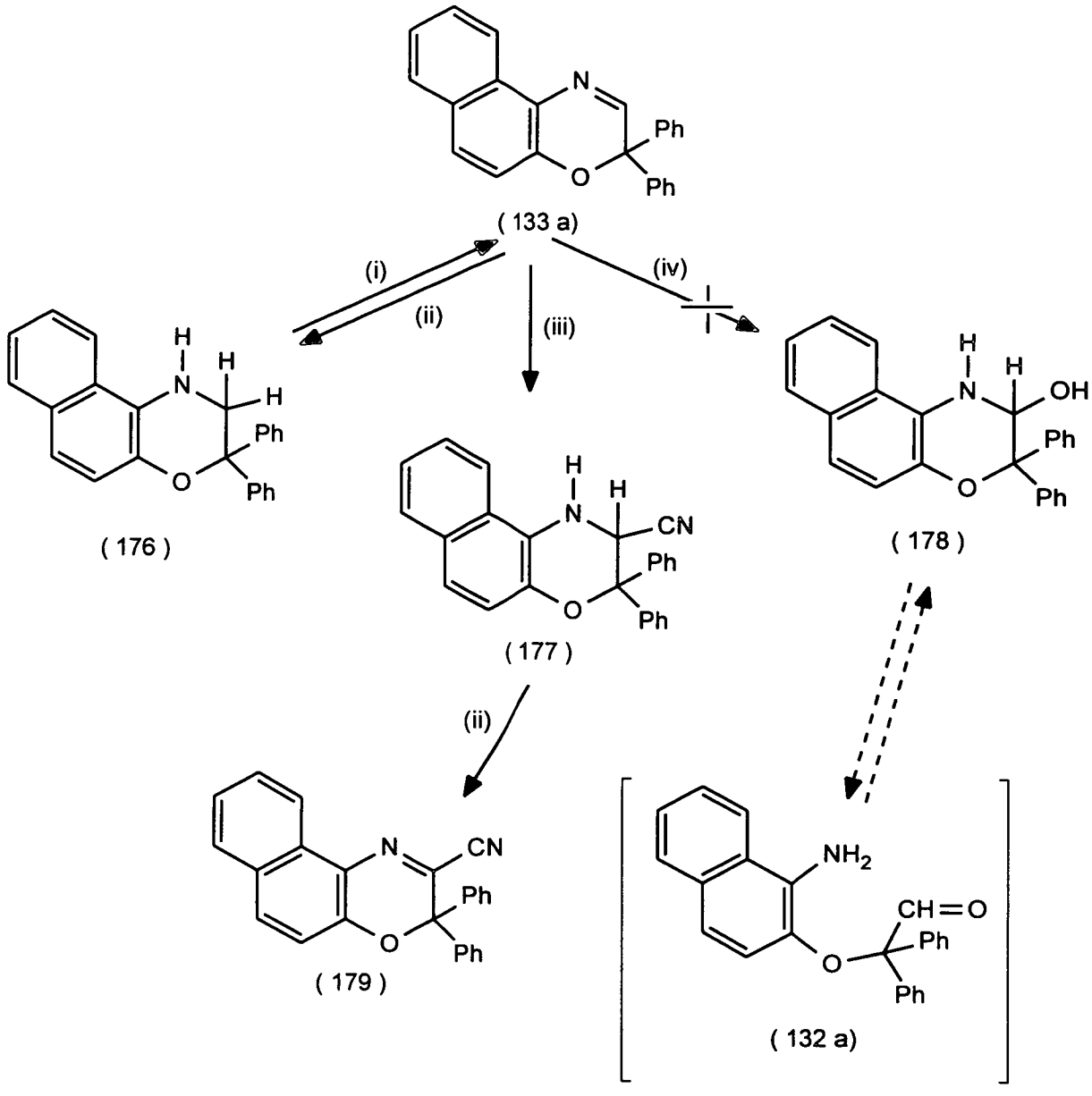

O
O
N
H
C
C
O
C(5')
C(4')
C(6')
C(3')
O(2)
C(1')
C(2')
C(3)
O(9)
C(6")
C(2)
C(9)
C(1")
C(4)
C(5")
C(10)
C(1)
N(1)
O(10)
C(4A)
C(8A)
C(2")
C(4")
C(3")
C(5)
C(8)
C(6)
C(7)

Figure 14

sent for X-ray diffraction analysis (see Figure 14; Tables 1 and 2) its structure was unequivocally established as the syn form of the oxime (161) with respect to the quinone oxygen. X-ray diffraction analysis (see Figure 15; Tables 3 and 4) of the yellow form B showed its structure was the anti form of the oxime (161) with respect to the quinone oxygen. Closer inspection of the i.r. spectrum of the orange form A (161) shows a band at 1648 cm^{-1} which may be attributed to the quinone carbonyl absorption of the oxime (161). Similarly the yellow form B (161) shows a band at 1664 cm^{-1} which may also be attributed to the quinone carbonyl absorption. Previously it was thought these absorptions were simply due to overtone/combination bands of the C=C stretch. Inspection of the ^{13}C n.m.r. spectra of the orange form A and yellow form B of the oxime (161) shows that both spectra support the oxime structure (161), but there are small differences between the two spectra. For example the ^{13}C n.m.r. spectrum of the orange form A (161) shows a signal at δ_C196.6 attributable to the aldehyde group, while the same signal appears at δ_C195.7 in the ^{13}C n.m.r. spectrum of the yellow form B (161).

The formation of the oxime (161) suggests that both the sodium salt of 1-nitoso-2-naphthol [see Page 61, Scheme 37; (153)] and the lithium salt of 1-nitroso-2-naphthol [see Page 61, Scheme 37; (158)] are reacting as their respective oxime forms [see Page 61, Scheme 37; (154) and (159)] with the bromoaldehyde (112a). The subsequent reductive conversions (see Page 64, Scheme 39) of the oxime (161) into both the naphthoxazine N-oxide (164) and the naphth-1,4-oxazine (133a), implies the oxime (161) rearranges in these



(i) $NaBH_4$, DME, H_2O, room temp.
(ii) MnO_2, MeCN, room temp. or reflux.
(iii) KCN, AcOH, room temp. or 100°.
(iv) 2M HCl aqu., EtOH, room temp. or reflux.

Scheme 43

reactions to the nitroso-aldehyde (160). The latter compound must then undergo reduction, *via in situ* ring closure of the intermediate amine (132a) or the hydroxylamine (163) to the respective naphthoxazine (133a) and naphthoxazine N-oxide (164) products.

As the previously undescribed naphthoxazine derivative (133a) is a cyclic imine it was decided to investigate (Scheme 43) its chemical behaviour in this context. Initially the behaviour of the naphthoxazine derivative (133a) towards hydride reduction was studied. Thus treatment of the naphthoxazine (133a) with sodium borohydride in aqueous 1,2-dimethoxyethane at room temperature afforded an essentially quantitative yield of a cream solid product. This product gave analytical, mass, i.r. and ^{1}H n.m.r. spectral properties which fully support its formulation as the expected dihydro derivative (176). Thus the i.r. spectrum shows the expected NH absorption band (υ_{max} 3401 cm^{-1}) and its ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a two-proton singlet at δ_H3.98 due to the methylene group and a one-proton singlet at δ_H2.16 due to the NH group. Oxidation of the dihydro derivative (176) using manganese dioxide in acetonitrile at room temperature regenerated the naphthoxazine (133a) in low yield (25%) and gave a recovery (47%) of the unreacted dihydro derivative (176). Repetition of this oxidation, but with heating under reflux in acetonitrile, again gave the naphthoxazine (133a) in only low yield (27%). Intractable mixtures were also isolated from this reaction which suggests that either the dihydro derivative (176) and/or the naphthoxazine (133a) were reacting further with the manganese dioxide to

afford a number of products. Therefore in a blank experiment the naphthoxazine derivative (133a) was reacted with manganese dioxide in acetonitrile under reflux. This reaction gave a quantitative yield of unreacted naphthoxazine (133a) which suggests it was the dihydro derivative (176) that was undergoing further reaction with manganese dioxide.

The reactivity of the naphthoxazine derivative (133a) towards nucleophilic addition of hydrogen cyanide across the imine bond was also investigated (Scheme 43). Thus treatment of the naphthoxazine derivative (133a) with potassium cyanide in glacial acetic acid at room temperature afforded only a quantitative recovery of the unreacted naphthoxazine derivative (133a). Repetition of the reaction of the naphthoxazine derivative (133a) with potassium cyanide in glacial acetic acid, but at 100° was more successful and gave a quantitative yield of a colourless solid which gave mass, i.r. and ^{1}H n.m.r. spectral properties fully in accords with its formulation as the hydrogen cyanide adduct (177). Thus the i.r. spectrum shows bands assignable to the NH and C≡N groups, while the ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a one-proton doublet at δ_H 5.40 which collapses to a singlet on shaking with deuterium oxide assignable to the methine group and a one-proton doublet at δ_H4.65 which is completely removed on addition of deuterium oxide attributable to the NH group.

In further support of this structure oxidation of the hydrogen cyanide adduct (177) with manganese dioxide in acetonitrile at reflux afforded the cyanonaphthoxazine derivative (179) in good yield (69%). The

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

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λnm	204.2	225.6	253.2	310.4	324.0	349.8				
ABS	1.842	1.554	0.775	0.159	0.203	0.081				

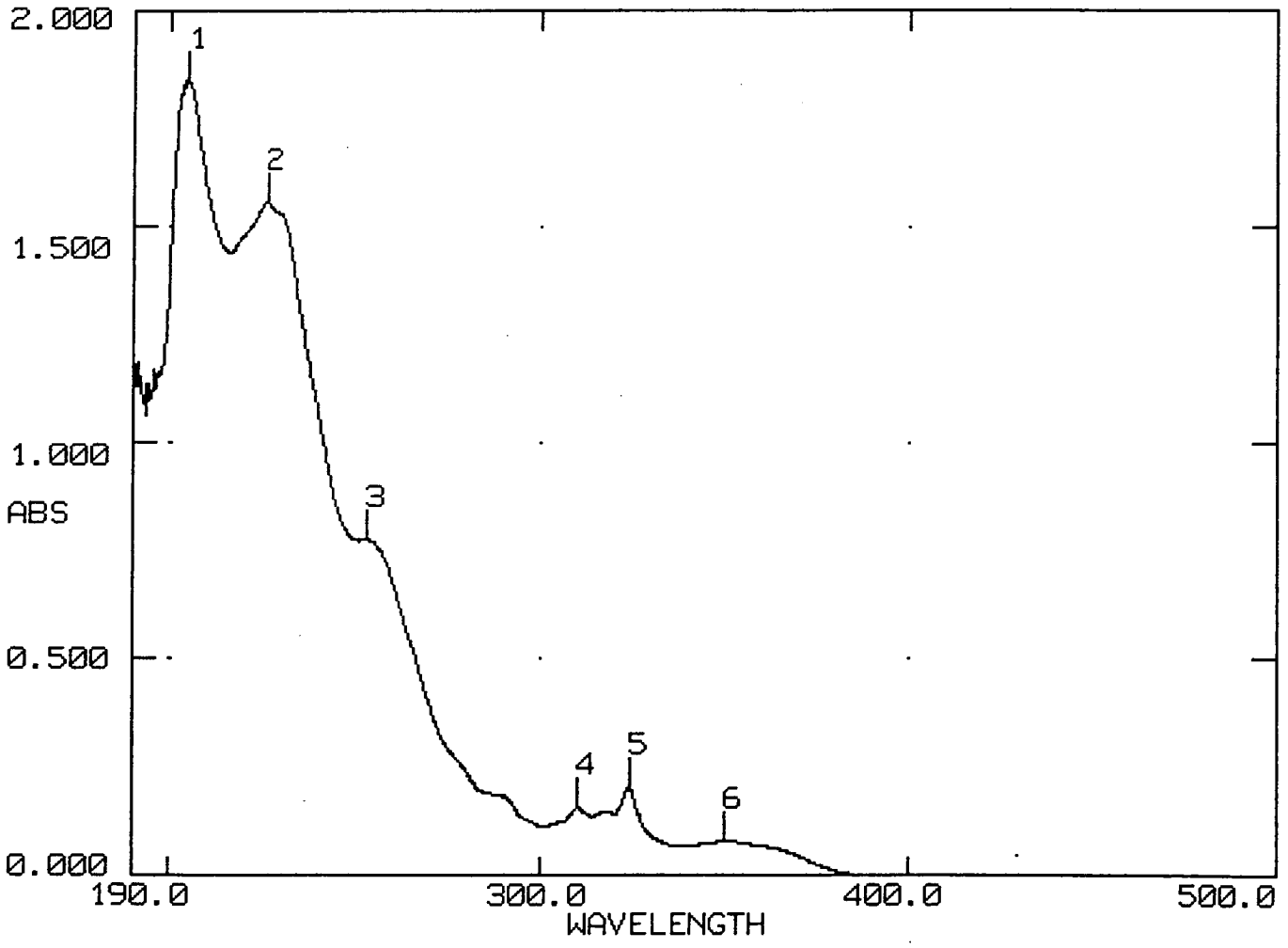

Figure 16

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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λnm	220.6	254.2	349.8							
ABS	2.428	2.142	0.345							

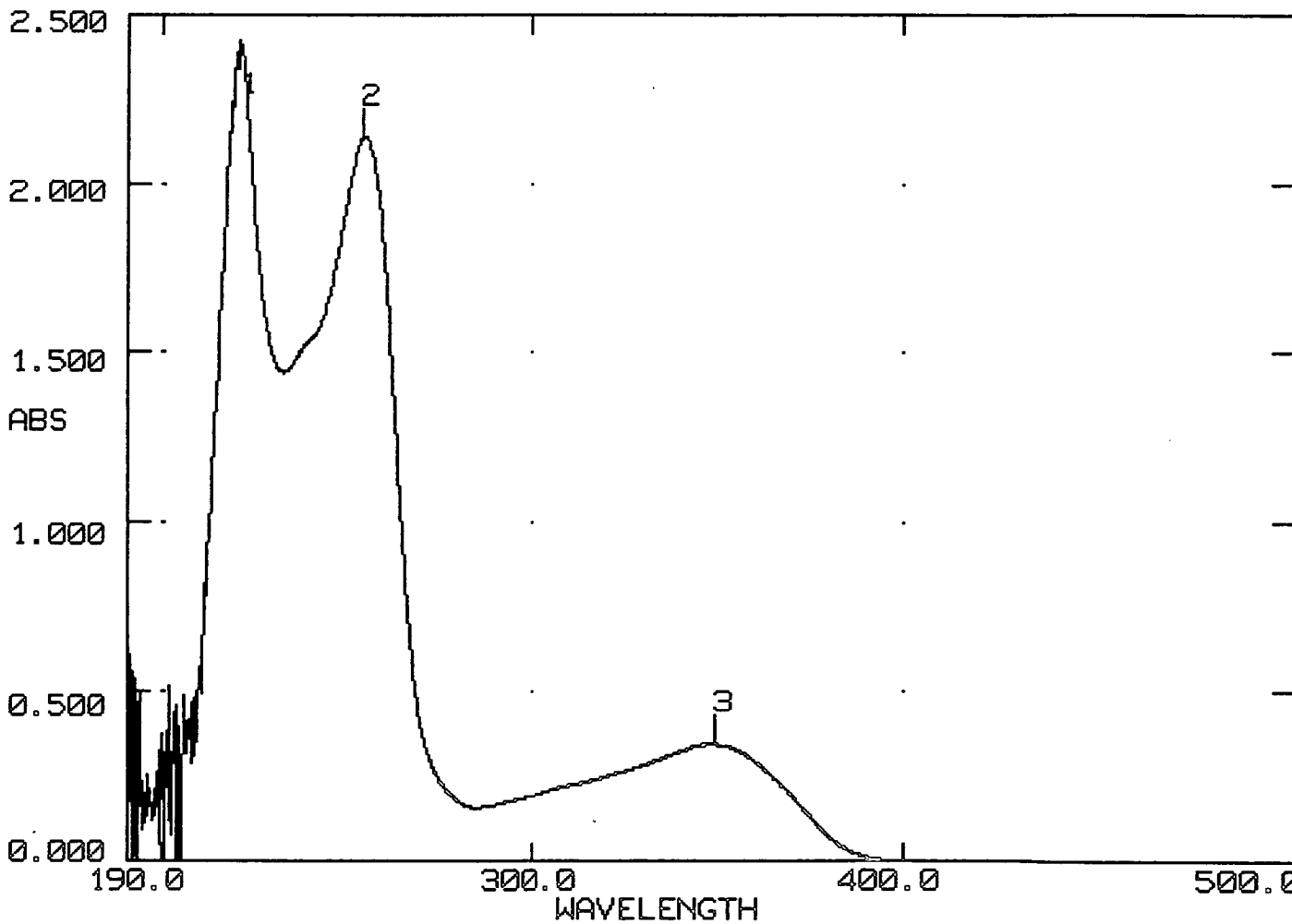

Figure 17

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

SCAN TYPE:INTELLISCAN SPEED:HIGH RES DATA INT:0.2nm
BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

TRACK

	1	2	3	4	5	6	7	8	9	10
λnm	211.8	220.2	231.0	264.6	282.6	359.4	403.8			
ABS	0.733	0.719	0.747	0.106	0.099	0.105	0.127			

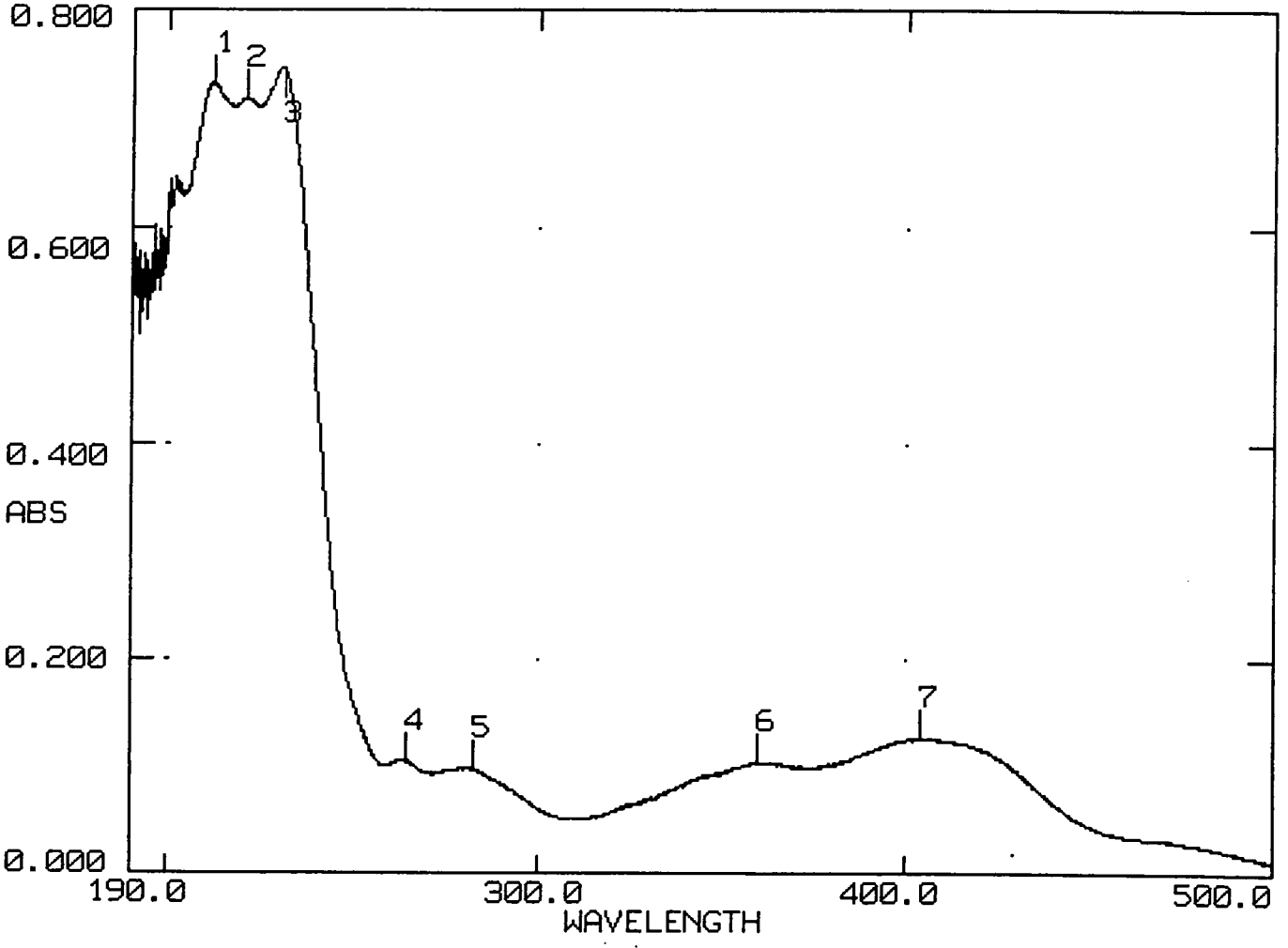

Figure 18

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

SCAN TYPE:INTELLISCAN SPEED:HIGH RES DATA INT:0.2nm
BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

TRACK

	1	2	3	4	5	6	7	8	9	10
λnm	207.0	235.8	249.0	315.0	341.4					
ABS	2.318	1.091	1.161	0.126	0.159					

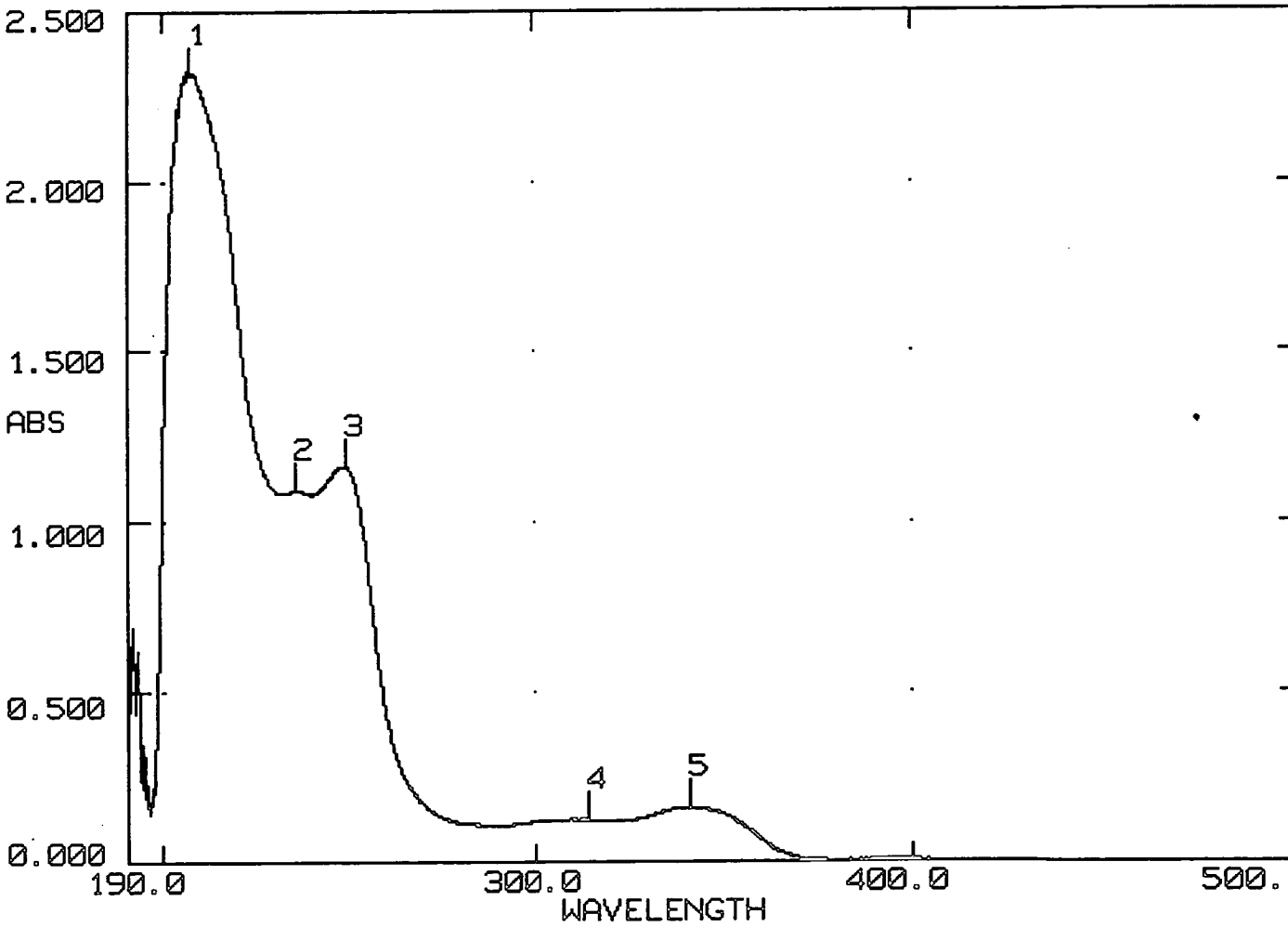


Figure 19

cyanonaphthoxazine (179) gave correct mass spectrum data and its structure was further supported by i.r. and ^{1}H n.m.r. spectral properties. Thus the i.r. spectrum shows the C≡N absorption band (υ_{max} 2214 cm^{-1}) and the ^{1}H n.m.r. spectrum shows signals only due to the protons of the phenyl and naphthalene groups.

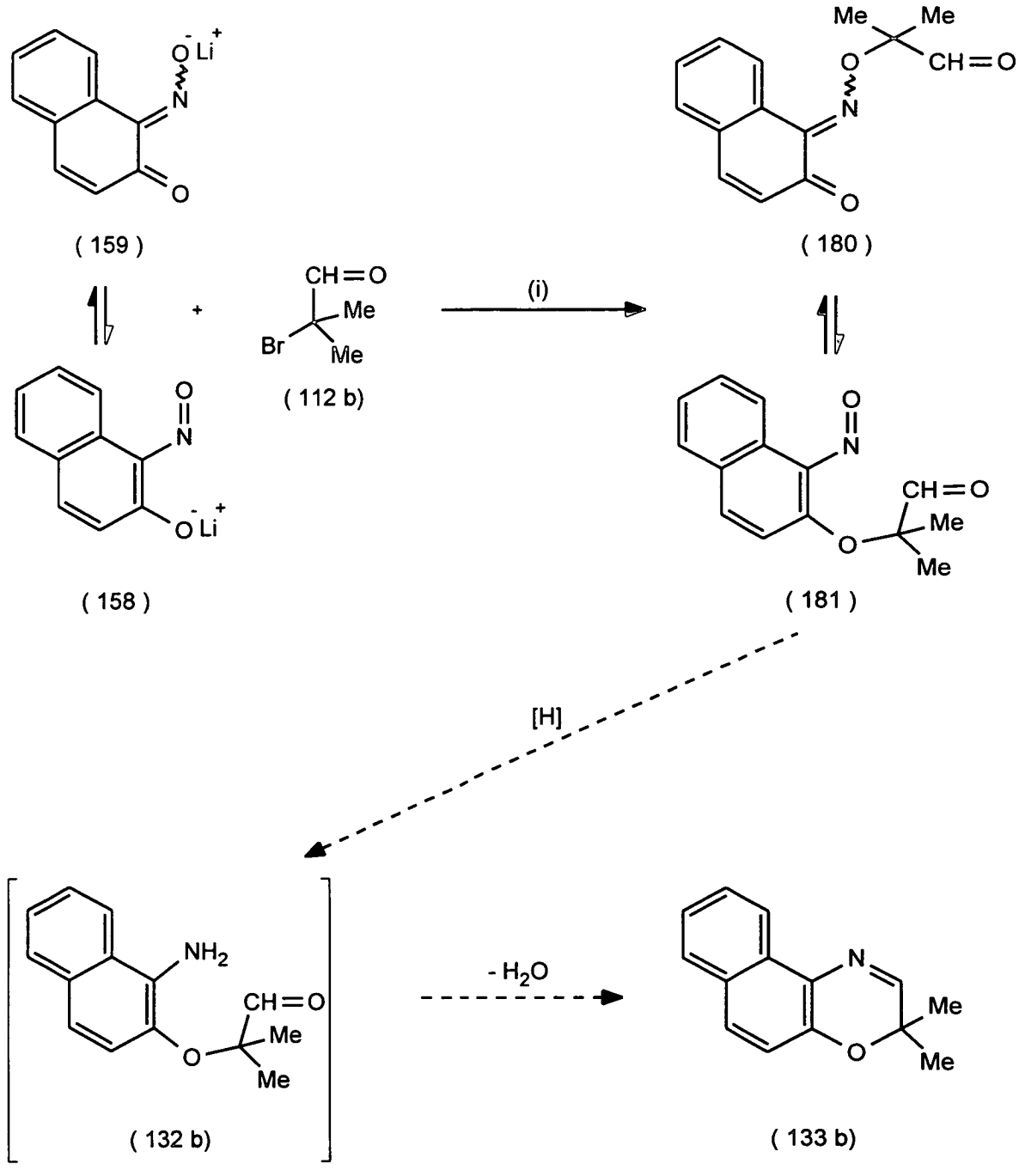
Hydrolysis (Scheme 43) of the naphthoxazine derivative (133a) would be expected to give either the amine (132a) or the alcohol (178). Therefore the naphthoxazine derivative (133a) was reacted with 2M aqueous hydrochloric acid in ethanol at room temperature to give only a high yield (81%) of unreacted naphthoxazine (133a). Repetition of this attempted hydrolysis of the naphthoxazine (133a), but with heating under reflux gave only an intractable mixture.

As the naphthoxazine (133a) is potentially photochromic (see Page 20, Section 1.3.1) a small sample was sent to Gentex and is currently undergoing investigation of its photochromic behaviour.

An investigation of the u.v. spectrum of the naphthoxazine (133a) and its derivatives [(176), (177) and (179)] was also undertaken. These u.v. spectra provided useful information on the absorption bands of these compounds and illustrated the effect of change in structure on absorption. Thus the u.v. spectrum (Figure 16) of the naphthoxazine (133a) has an absorption maximum at 204 nm and has a further band of high intensity at 226 nm. Although the naphthoxazine (133a) has a further four bands of low intensity, it is transparent (i.e. lacks absorption bands) in the visible region

(400-750 nm). Not surprisingly, in view of its less conjugated structure, the dihydro compound (176) (Figure 17) also lacked absorption in the visible region and contained an absorption maximum of 221 nm and also weaker bands at 254 and 350 nm. The u.v. spectrum (Figure 18) of the cyanonaphthoxazine (179) is significantly different to the u.v. spectrum (Figure 16) of the naphthoxazine (133a). For example, the naphthoxazine (133a) as discussed earlier, is transparent in the visible region, while the u.v. spectrum (Figure 18) of the cyanonaphthoxazine (179) shows an absorption band at 404 nm in the violet region of the visible spectrum which gives rise to its yellow colour. The presence of the cyano group has produced a considerable bathochromic shift of the bands in the u.v. spectrum (Figure 16) of the naphthoxazine (133a) to the bands in the u.v. spectrum (Figure 18) of the cyanonaphthoxazine (179). Comparison of the u.v. spectrum (Figure 18) of the cyanonaphthoxazine (179) with the u.v. spectrum (Figure 19) of the dihydro compound (177) shows the less conjugated dihydro compound (177) lacks absorption in the visible region. The u.v. spectrum (Figure 19) of the dihydro compound (177) shows the less conjugated dihydro compound (177) also contained only five absorption bands, in contrast to the u.v. spectrum (Figure 18) of the more conjugated cyanonaphthoxazine (179) which contained seven absorption bands.

Attention was next turned to the further reduction (see Page 65, Scheme 40) of the nitroso-ester (167) to the naphthoxazinone derivative (169). It was hoped that both hydrazobenzene and triphenylphosphine which had

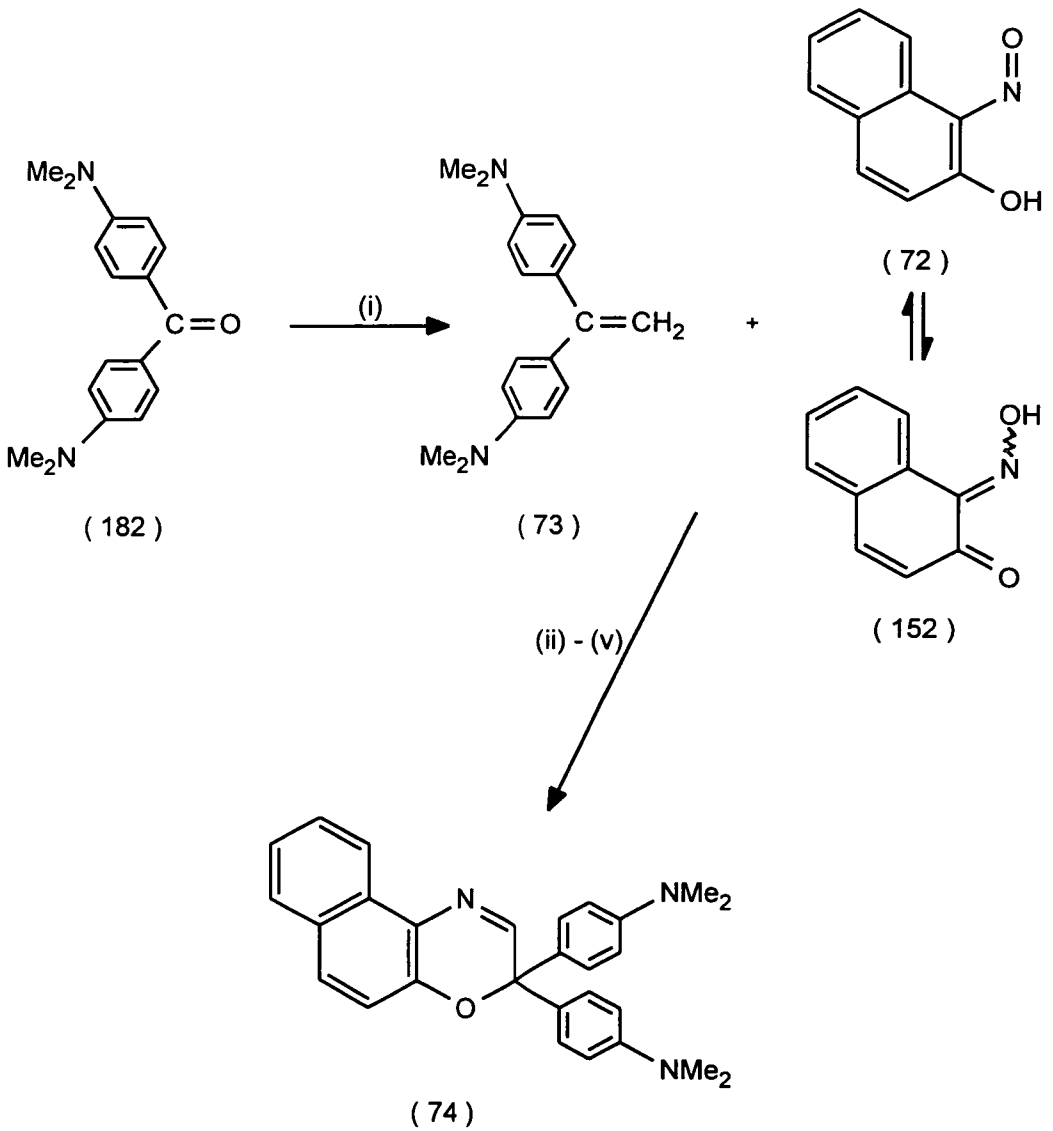


(i) acetone, room temp.

Scheme 44

successfully reduced the oxime [see Page 64, Scheme 39; (161)] would be of use in the reduction of the nitroso-ester [see Page 65, Scheme 40; (167)]. Therefore, the nitroso-ester (167) was reacted with hydrazobenzene in benzene at room temperature. This reaction gave a moderate yield (53%) of 1-amino-2-naphthol (139), together with a moderate recovery (37%) of unreacted nitroso-ester (167) and a high yield (89%) of azobenzene. Attempted reduction of the nitroso-ester (167) using triphenylphosphine in 1,2-dimethoxyethane under reflux also gave a moderate yield (47%) of 1-amino-2-naphthol (139) and a moderate yield (56%) of triphenylphosphine oxide. The formation of 1-amino-2-naphthol (139) suggests that the nitroso-ester (167) was reductively cleaved by the aforementioned reducing agents. Disappointingly due to a lack of time, the further reduction of the nitroso-ester (167) was not investigated.

Parallel to this work, investigations of methods for the synthesis of the 3,3-dimethyl-3H-naphth[2,1-b]-1,4-oxazine (133b) were continued. Attention was now focused on a route (Scheme 44) for the formation of the nitroso-aldehyde (181) which it was expected could be reduced to the amine (132b). It was anticipated that the latter compound would undergo spontaneous cyclisation to give the naphthoxazine (133b). One complication anticipated in this approach was the possibility of the salt (158) reacting as an ambident anion [(158)↔(159)] with the bromo-aldehyde (112b) to give the nitroso-aldehyde (181) and/or the oxime (180). The lithium salt (158) was therefore reacted with 2-bromo-2-methylpropionaldehyde (112b) in acetone at room



(182) (73) (72) (152) (74)

(i) MeMgI, benzene, room temp.
(ii) AcOH, solvent, reflux.
(iii) AcOH, reflux.
(iv) HCl aqu. (conc.), DME, reflux.
(v) ptsa, toluene, reflux.

Scheme 45

temperature. This reaction gave a yellow solid in low yield (26%) which analysed correctly and gave mass spectrum data which supported both the nitroso-aldehyde (181) and oxime (180) structures. The ^{1}H n.m.r. spectrum of this yellow solid also supported both structures [(180) and (181)] and shows in addition to the signals due to the aromatic protons, a one-proton singlet at δ_H9.79 due to the aldehyde group and a six-proton singlet at δ_H1.58 due to the two methyl groups. The i.r. spectrum of this product shows the carbonyl absorption band of the aldehyde group at 1733 cm^{-1} and also shows an absorption band at 1658 cm^{-1} which can be attributed to the quinone carbonyl of the oxime (180) structure. Therefore the yellow solid was tentatively assigned the oxime (180) structure on the evidence of its i.r. spectrum. Unfortunately, due to a lack of time, attempts to further identify and improve the yield of the oxime (180) with a view to its further manipulation to the naphthoxazine (133b) were not initiated.

Studies (Scheme 45) on synthetic approaches to the 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) were also initiated and initially centred on a synthetic strategy based on the synthesis of the alkene (73) and its cyclisative condensation with 1-nitroso-2-naphthol (72). This transformation was briefly reported in the literature[75] but in the view of the present author requires substantiation.

The alkene (73) was readily synthesised in high yield (96%) by the reaction of the commercially available Michler's ketone (182) with methylmagnesium iodide as described in the literature.[114] The reaction of 1-

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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ABS	1.507	1.590	1.395	0.342	0.199					

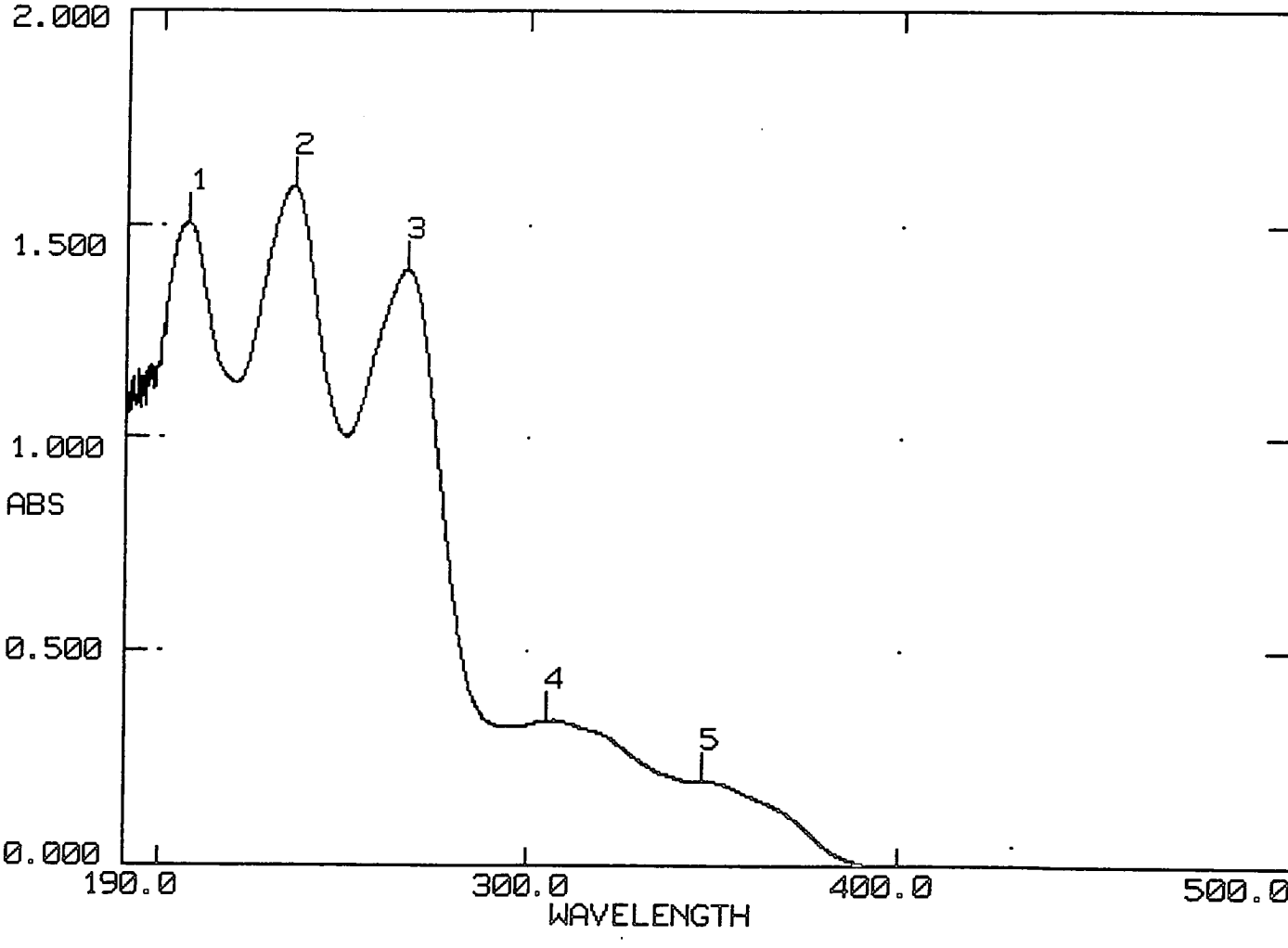
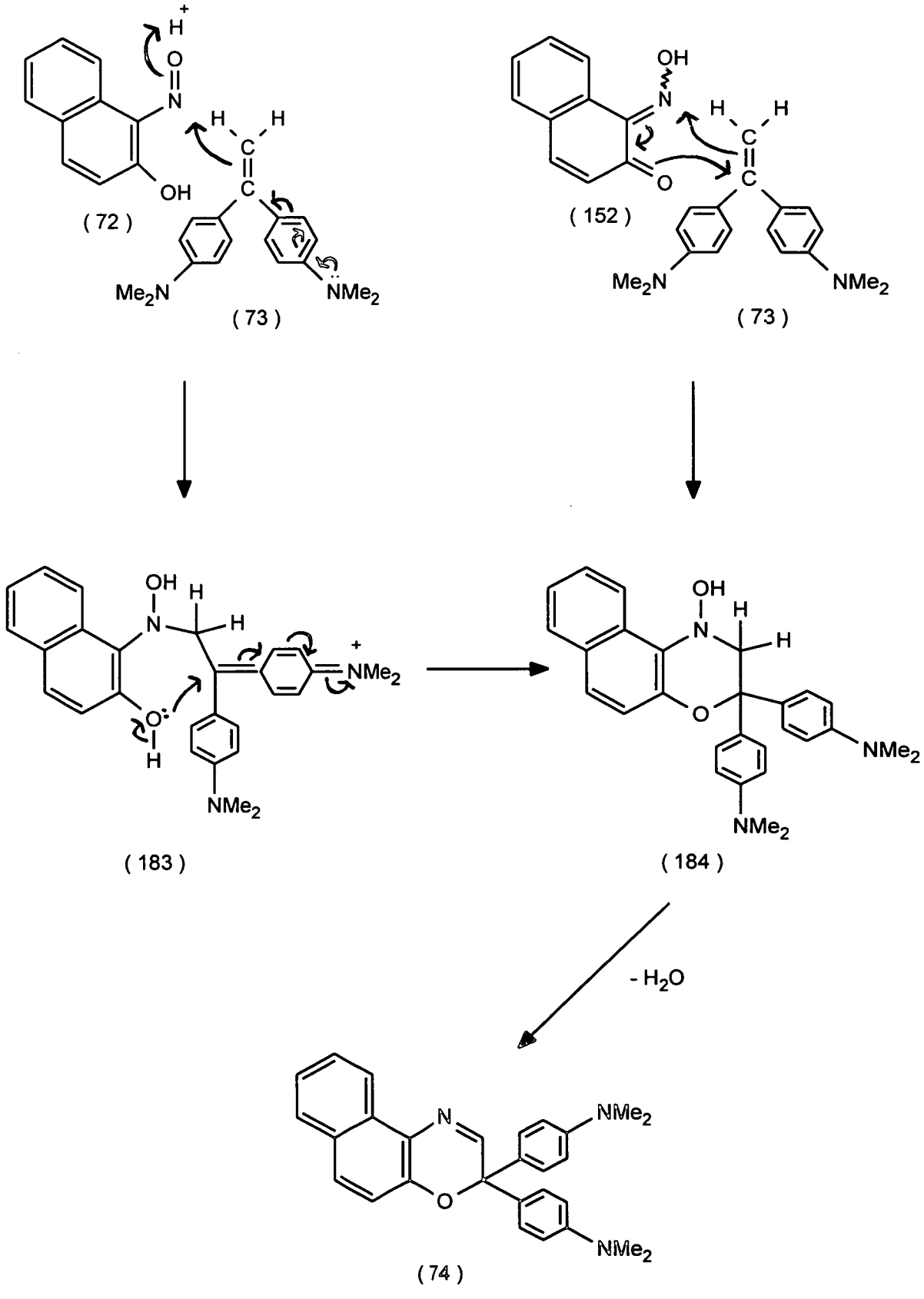


Figure 20

nitroso-2-naphthol (72) with the alkene (73) was initially carried out in ethanol containing a few drops of glacial acetic acid under reflux as described by Paetzold *et al.*[75] The resulting mixture was readily separated by flash-chromatography to give a low yield (24%) of a colourless solid product whose combustion analysis and mass spectrum data fully supported the naphthoxazine derivative (74). The i.r. and ^{1}H n.m.r. spectral data also supported the formation of the naphthoxazine derivative (74). Thus, the i.r. spectrum, shows the imine (C=N) absorption band (υ_{max} 1611 cm^{-1}) and the ^{1}H n.m.r. spectrum shows in addition to signals due to the methine and aromatic protons a twelve-proton singlet at δ_H2.92 due to the dimethylamino groups. The u.v. spectrum (Figure 20) of the naphthoxazine (74) was also recorded and shows a maximum absorption at 236 nm and also weaker bands at 207, 267, 306 and 348 nm. It is noteworthy that the naphthoxazine (74) is transparent (i.e. lacks absorption bands) in the visible region (400-750 nm). Comparison of the u.v. spectrum (Figure 20) of the naphthoxazine (74) with the u.v. spectrum (see Page 74, Figure 16) of the 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) shows the presence of the dimethylamino groups has induced considerable differences between the two u.v. spectra (see Figures 16 and 20). For example the naphthoxazine (74) (Figure 20) has an absorption maximum at 236 nm which represents a bathochromic shift of 32 nm compared with the corresponding band (λ_{max} 204 nm) in the diphenylnaphthoxazine (133a) (Figure 16). The u.v. spectrum (Figure 20) of the naphthoxazine (74) also contains only five absorption bands compared with

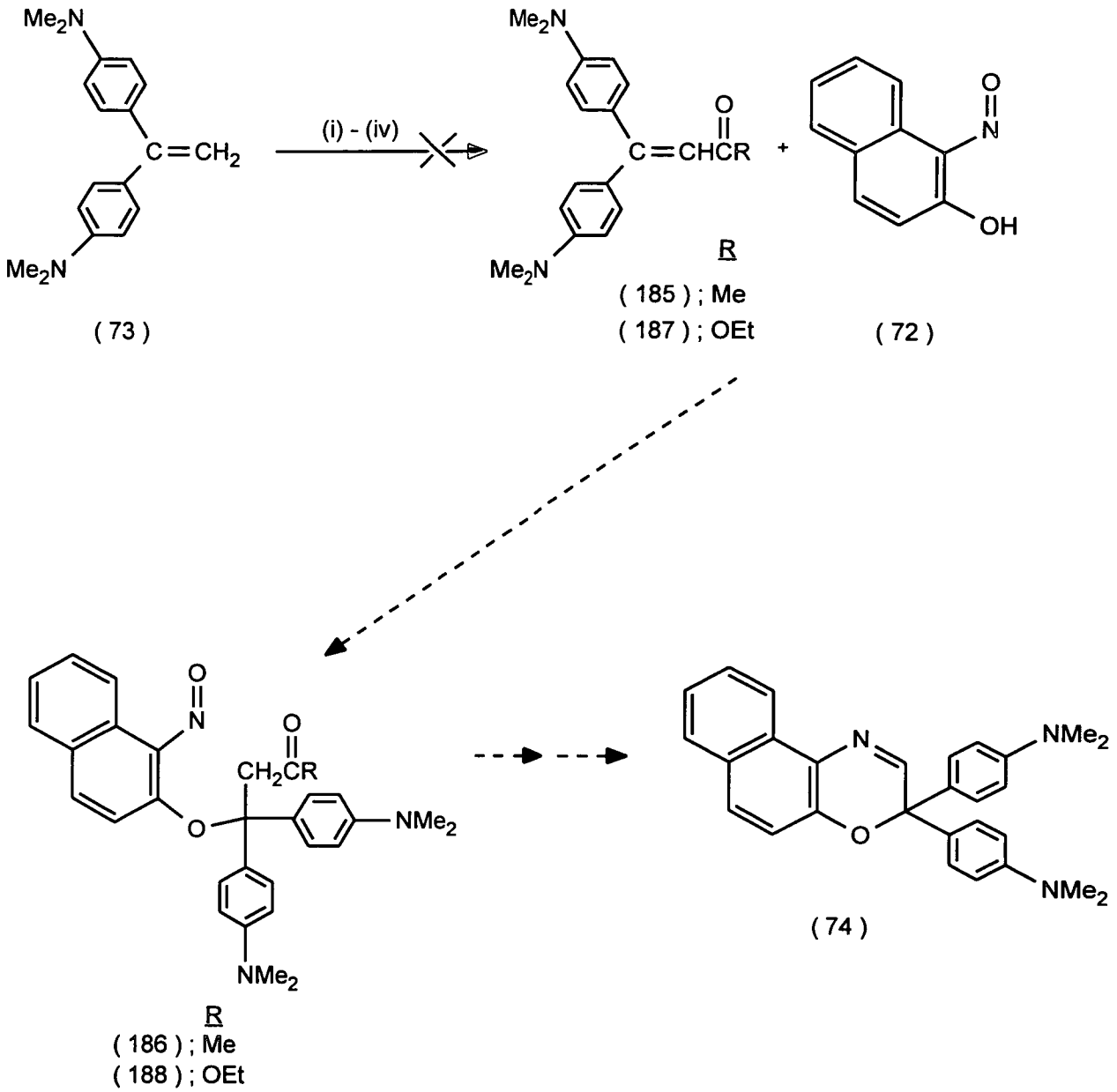


Scheme 46

the six bands observed in the u.v. spectrum (Figure 16) of the diphenylnaphthoxazine (133a).

As the naphthoxazine (74) was reported in the literature[75] to be photochromic a small sample of this compound (74) was sent to Pilkington to test for its photochromic behaviour. Initial tests carried out at Pilkington indicated that the naphthoxazine (74) was not photochromic. With the subsequent closure of the labs at Pilkington a sample of the naphthoxazine (74) was sent to Gentex and is currently being investigated for photochromic behaviour.

There are two possible mechanisms for the formation of the naphthoxazine (74), since the nitrosonaphthol (72) as shown in Scheme 45 may exist as either the nitroso form (72) or the tautomeric oxime form (152) and undergo reactions characteristic of both forms. Hence the two possible mechanisms for the formation of the naphthoxazine (74) are shown in Scheme 46. Thus the naphthol (72) may react as the nitroso form (72) with the alkene (73) in a two step acid catalysed electrophilic addition *via* the intermediate (183) to afford the alcohol (184). Subsequent dehydration of the alcohol (184) affords the naphthoxazine (74). Alternatively, the naphthol (72) may react as the oxime form (152) with the alkene (73) in a concerted 4+2 cycloaddition reaction to afford the alcohol (184). To determine the mechanism for the formation of the naphthoxazine (74), the alkene (73) was reacted with 1-nitroso-2-naphthol (72) in refluxing 1,2-dimethoxyethane. Monitoring of this reaction by t.l.c. showed that the starting materials [(73) and (72)] were not



(i) MeCOCl, DME, 0° or reflux.
(ii) MeCOCl, $AlCl_3$, CH_2Cl_2, room temp.
(iii) $ClCO_2Et$, NaOAc, AcOH, room temp. or 100°.
(iv) $ClCO_2Et$, Et_3N, 1,4 - dioxane, room temp. or reflux.

Scheme 47

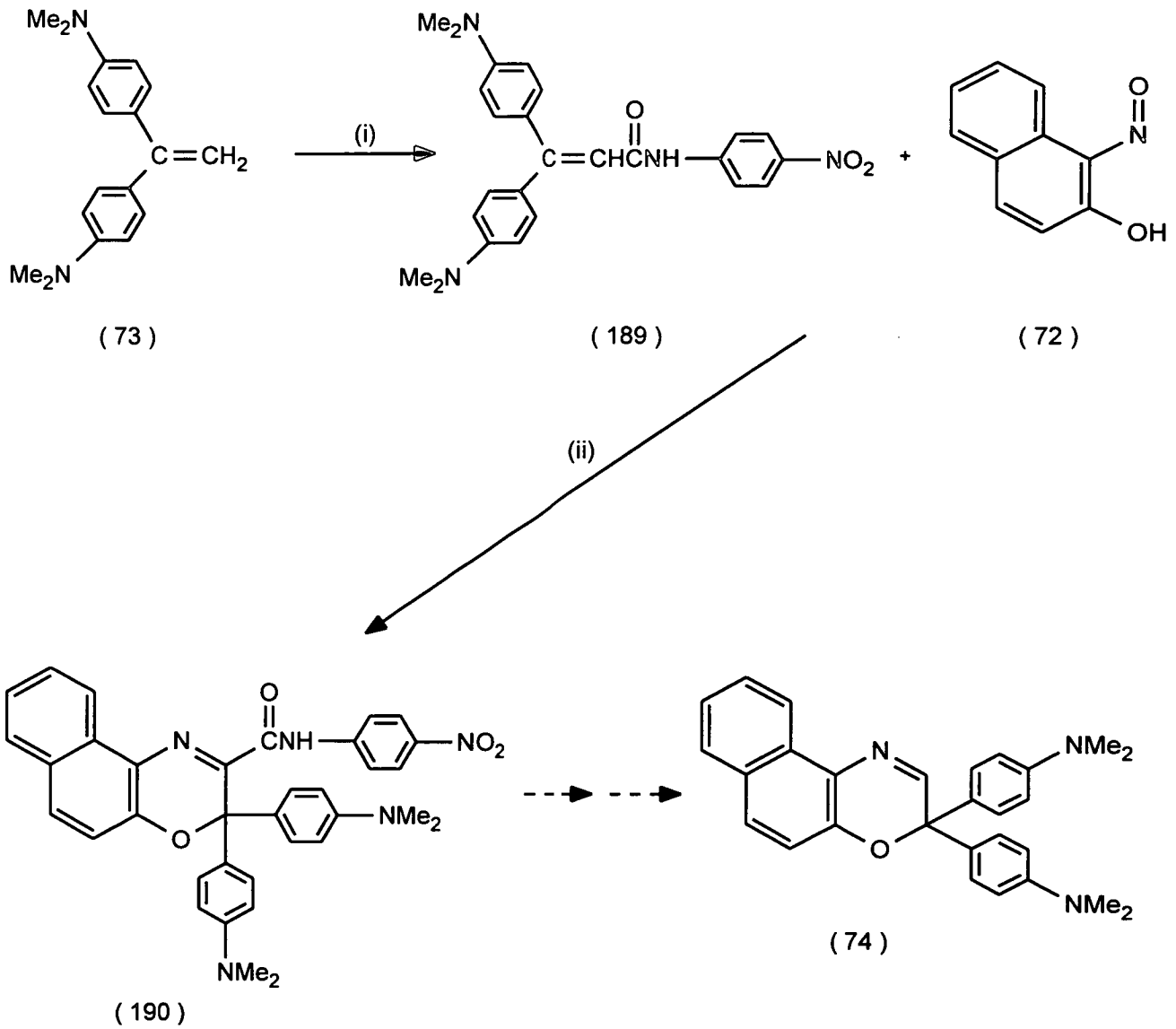
consumed even after 7 h, indicating the need for acid catalysis. Correspondingly heating the nitrosonaphthol (72) and the alkene (73) under reflux in 1,2-dimethoxyethane containing two drops of glacial acetic acid gave the naphthoxazine (74) in low yield (12%). The need for acid catalysis suggests the nitrosonaphthol (72) was reacting as the nitroso form (72) with the alkene (73) by the mechanism shown in Scheme 46.

Reaction (Scheme 45) of 1-nitroso-2-naphthol (72) with the alkene (73) in refluxing dioxane containing a catalytic amount of glacial acetic acid gave only a low yield (8%) of the naphthoxazine derivative (74). The nitrosonaphthol (72) was then heated under reflux with the alkene (73) in glacial acetic acid, utilising the glacial acetic acid as both solvent and catalyst. Unfortunately, this reaction gave only an intractable mixture. 1-Nitroso-2-naphthol (72) was then reacted with the alkene (73) in refluxing 1,2-dimethoxyethane containing concentrated hydrochloric acid as the catalyst, to give a low yield (18%) of the naphthoxazine derivative (74). Finally the nitrosonaphthol (72) was reacted with the alkene (73) in refluxing toluene, using toluene-4-sulphonic acid as the catalyst. This reaction again gave the naphthoxazine derivative (74) in low yield (15%).

Changing the acid catalyst in the reaction of the alkene (73) with the nitrosonaphthol (72) did not improve the yield of the naphthoxazine derivative (74). Therefore a different approach (Scheme 47) to the naphthoxazine (74) was investigated. Hence an attempt was made to react the alkene (73) with acetyl chloride to afford the keto derivative (185) which it was hoped would

react more efficiently with the nitroso-naphthol (72) to give an intermediate (186) more appropriate for conversion into the naphthoxazine (74). However, the reaction of the alkene (73) with acetyl chloride in 1,2-dimethoxyethane at 0° gave only a high recovery (92%) of unreacted alkene (73). Repetition of this reaction of the alkene (73) with acetyl chloride, but with heating under reflux, again gave only unreacted alkene (73) but in low yield (34%). An attempt was then made to react the alkene (73) with acetyl chloride in dichloromethane using the Lewis acid aluminium(III) chloride as catalyst. This reaction gave only a high recovery (87%) of the unreacted alkene (73).

Various attempts having failed to react acetyl chloride with the alkene (73), attention was turned to the reaction (Scheme 47) of ethyl chloroformate with the alkene (73). It was hoped that ethyl chloroformate would react with the alkene (73) to afford the ethoxycarbonyl derivative (187). This derivative (187) would hopefully react efficiently with the nitrosonaphthol (72) to give an appropriate intermediate (188) for conversion into the naphthoxazine (74). The attempted reaction of the alkene (73) with ethyl chloroformate in glacial acetic acid in the presence of fused sodium acetate at room temperature for 3 h gave only a moderate recovery (47%) of unreacted alkene (73). Correspondingly, repetition of this reaction at elevated temperature (100°) afforded only an intractable mixture. The alkene (73) was therefore reacted with ethyl chloroformate in glacial acetic acid in the presence of sodium acetate at room temperature for the longer time of 17 h. This reaction gave only a low recovery (26%) of unreacted alkene (73). The failure of the alkene (73) to



(i) 4 - $NO_2C_6H_4N=C=O$, xylene, reflux.
(ii) AcOH, xylene, reflux.

Scheme 48

X-Ray Diffraction Data for form B of Naphthalene-1,2-dione 1-Oxime Diphenylformylmethyl Ether (161)

Table 3 : Bond Lengths (Angstroms) with Standard Deviations

C(1)-N(1)	1.291(2)	C(1)-C(8A)	1.475(2)
C(1)-C(2)	1.515(2)	C(2)-O(2)	1.219(2)
C(2)-C(3)	1.454(2)	C(3)-C(4)	1.333(2)
C(4)-C(4A)	1.453(2)	C(4A)-C(5)	1.396(2)
C(4A)-C(8A)	1.413(2)	C(5)-C(6)	1.378(2)
C(6)-C(7)	1.378(2)	C(7)-C(8)	1.384(2)
C(8)-C(8A)	1.394(2)	N(1)-O(9)	1.396(2)
O(9)-C(9)	1.456(2)	C(9)-C(1C)	1.519(2)
C(9)-C(1B)	1.529(2)	C(9)-C(10)	1.541(2)
C(10)-O(10)	1.185(2)	C(1B)-C(6B)	1.391(2)
C(1B)-C(2B)	1.391(2)	C(2B)-C(3B)	1.386(2)
C(3B)-C(4B)	1.379(3)	C(4B)-C(5B)	1.382(2)
C(5B)-C(6B)	1.383(2)	C(1C)-C(6C)	1.395(2)
C(1C)-C(2C)	1.395(2)	C(2C)-C(3C)	1.387(2)
C(3C)-C(4C)	1.379(2)	C(4C)-C(5C)	1.378(2)
C(5C)-C(6C)	1.386(2)		

Table 4 : Bond Angles (Degrees) with Standard Deviations

N(1)-C(1)-C(8A)	129.53(12)	N(1)-C(1)-C(2)	110.89(12)
C(8A)-C(1)-C(2)	119.29(12)	O(2)-C(2)-C(3)	122.82(14)
O(2)-C(2)-C(1)	120.92(14)	C(3)-C(2)-C(1)	116.25(13)
C(4)-C(3)-C(2)	120.99(13)	C(3)-C(4)-C(4A)	123.26(14)
C(5)-C(4A)-C(8A)	119.35(13)	C(5)-C(4A)-C(4)	119.86(13)
C(8A)-C(4A)-C(4)	120.76(13)	C(6)-C(5)-C(4A)	121.1(2)
C(5)-C(6)-C(7)	119.31(14)	C(6)-C(7)-C(8)	121.0(2)
C(7)-C(8)-C(8A)	120.60(14)	C(8)-C(8A)-C(4A)	118.58(13)
C(8)-C(8A)-C(1)	124.55(13)	C(4A)-C(8A)-C(1)	116.87(12)
C(1)-N(1)-O(9)	114.20(11)	N(1)-O(9)-C(9)	106.50(9)
O(9)-C(9)-C(1C)	109.53(10)	O(9)-C(9)-C(1B)	105.31(10)
C(1C)-C(9)-C(1B)	114.79(11)	O(9)-C(9)-C(10)	104.74(11)
C(1C)-C(9)-C(10)	116.00(11)	C(1B)-C(9)-C(10)	105.49(11)
O(10)-C(10)-C(9)	127.03(14)	C(6B)-C(1B)-C(2B)	118.77(13)
C(6B)-C(1B)-C(9)	119.36(12)	C(2B)-C(1B)-C(9)	121.76(12)
C(3B)-C(2B)-C(1B)	120.2(14)	C(4B)-C(3B)-C(2B)	120.75(14)
C(3B)-C(4B)-C(5B)	119.61(14)	C(4B)-C(5B)-C(6B)	119.97(14)
C(5B)-C(6B)-C(1B)	120.88(13)	C(6C)-C(1C)-C(2C)	118.70(13)
C(6C)-C(1C)-C(9)	122.00(12)	C(2C)-C(1C)-C(9)	119.27(12)
C(3C)-C(2C)-C(1C)	120.4(2)	C(4C)-C(3C)-C(2C)	120.4(2)
C(5C)-C(4C)-C(3C)	119.62(14)	C(4C)-C(5C)-C(6C)	120.8(2)
C(5C)-C(6C)-C(1C)	120.13(14)		

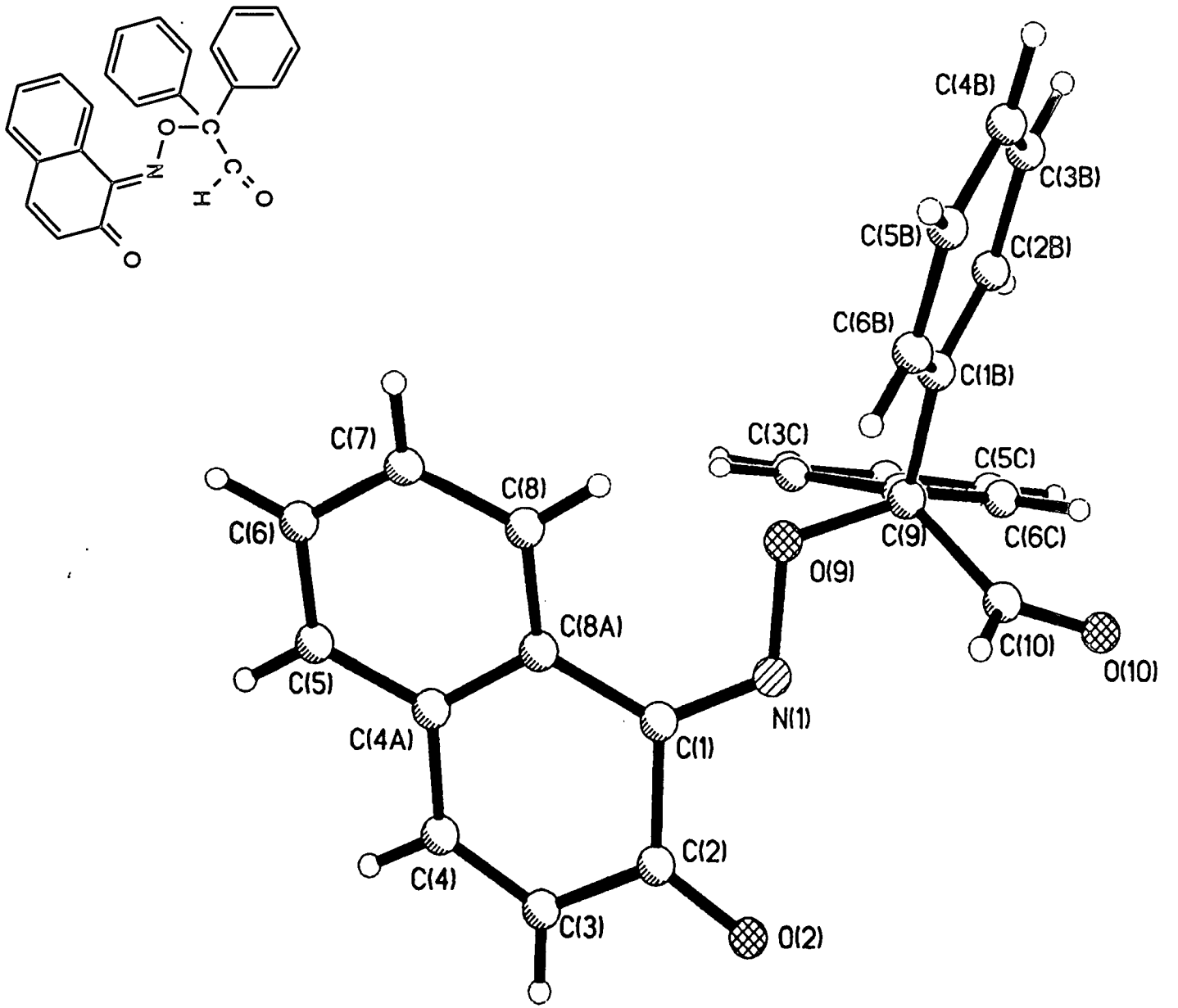
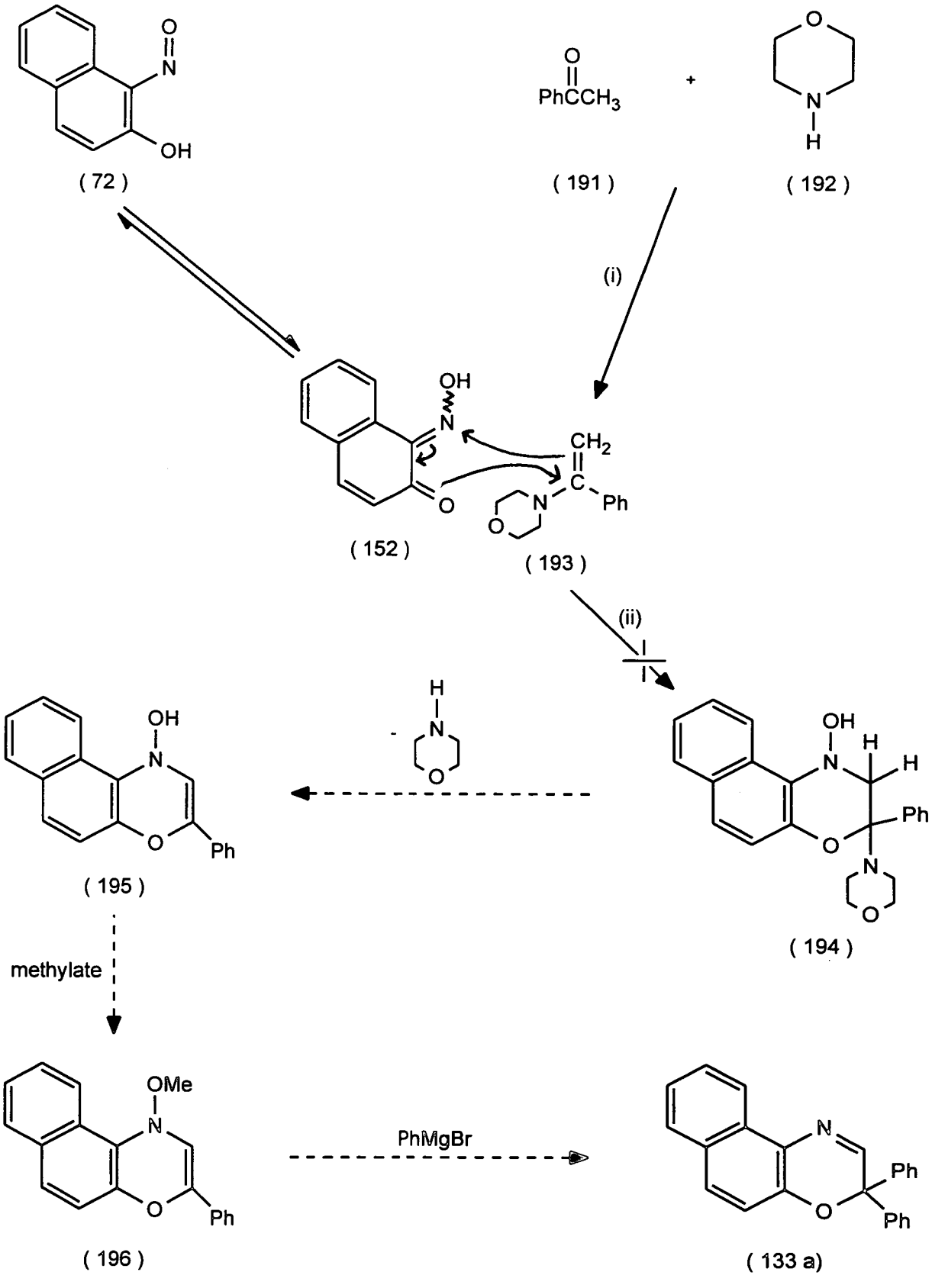

C(4B)
C(3B)
C(5B)
C(2B)
C(6B)
C(1B)
C(3C)
C(5C)
C(7)
C(8)
C(6)
C(9)
C(6C)
O(9)
C(8A)
C(10)
O(10)
C(5)
N(1)
C(4A)
C(1)
C(2)
C(4)
C(3)
O(2)

Figure 15

react with ethyl chloroformate in the presence of sodium acetate was a disappointment as it was hoped the sodium acetate would both catalyse the reaction and scavenge any hydrochloric acid formed, hence driving the reaction to completion. Changing the basic catalyst in this reaction also failed to give the ethoxycarbonyl derivative (187). Thus the attempted reaction (Scheme 47) of the alkene (73) with ethyl chloroformate in refluxing 1,4-dioxane in the presence of triethylamine gave only a high recovery (98%) of unreacted alkene (73).

In a slightly different approach (Scheme 48) to the naphthoxazine (74), the reaction of the alkene (73) with 4-nitrophenyl isocyanate was investigated as a route to the amide derivative (189). It was hoped that this compound would react more efficiently with the nitrosonaphthol (72) to give an intermediate (190) appropriate for conversion *via* hydrolysis and decarboxylation into the naphthoxazine (74). The amide (189) was readily prepared in good yield (87%) by reaction of the alkene (73) with 4-nitrophenyl isocyanate in xylene under reflux. The amide (189) was obtained as a yellow solid which gave analytical and mass spectrum data fully in accord with its assigned structure. The amide (189) was further identified by its i.r. and ^1H n.m.r. spectra. Thus, the i.r. spectrum correctly shows bands due to the NH, C=O and NO_2 groups, while the ^1H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H10.52 due to the amide proton. The ^1H n.m.r. spectrum also shows a one-proton singlet at δ_H6.29 due to the methine proton of the olefin group and two six-proton



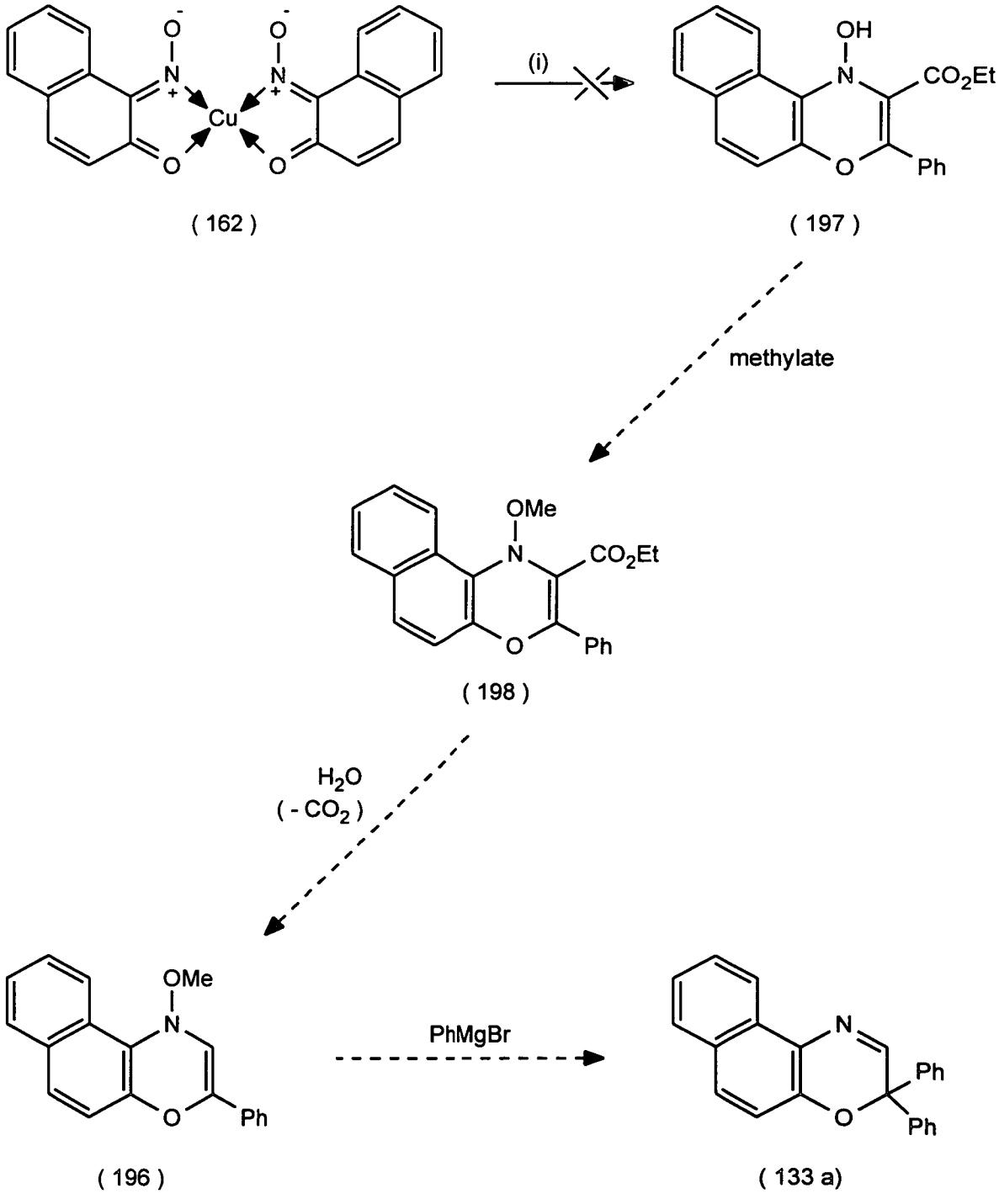
(i) ptsa, benzene, reflux.
(ii) benzene, room temp.

Scheme 49

singlets at δ_H2.94 and 2.50 due to the dimethylamino groups.

With the amide (189) readily available, attention was turned to its reaction with the nitrosonaphthol (72). In practice, reaction of the amide (189) with the nitrosonaphthol (72) in xylene under reflux in the presence of a catalytic amount of glacial acetic acid afforded a multicomponent mixture, flash-chromatography of which gave a low yield (13%) of a yellow solid. This product gave analytical, mass, i.r. and ^{1}H n.m.r. data fully consistent with its formulation as the naphthoxazine derivative (190). Thus, the i.r. spectrum shows bands due to the NH, C=O and NO_2 groups, while the ^{1}H n.m.r. spectrum shows in addition to an eighteen-proton multiplet at δ_H8.41-7.17 due to the aromatic protons, a one-proton singlet at δ_H9.96 due to the amide proton and a twelve-proton singlet at δ_H2.91 due to the dimethylamino groups. Due to the poor yield of the oxazine (190) and a lack of time, the further investigation of the conversion of this compound into the required naphthoxazine (74) was halted.

Attention was then refocussed on a further route (Scheme 49) to the naphth-1,4-oxazine (133a). This route was based on the known[115] reactions of 1-nitroso-2-naphthol (72) with enamines. Thus it was hoped that the cycloaddition reaction of the known[116] enamine (193) with 1-nitroso-2-naphthol (72) [which may react as its tautomeric oxime form (152)] would provide access to the N-hydroxyoxazine (194). Elimination of morpholine from the latter would then afford the N-hydroxy compound (195) and further with methylation the methoxy derivative (196). It was anticipated that the latter



(162)

(197)

(198)

(196)

(133 a)

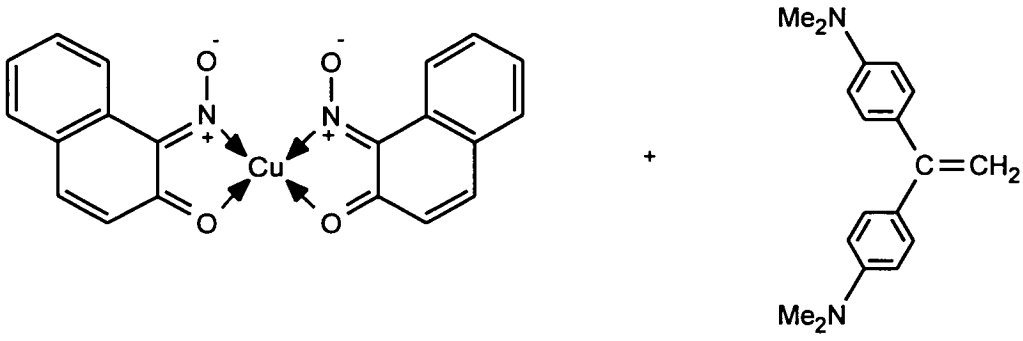
(i) $PhC \equiv CCO_2Et$, DME, H_2O, reflux.

Scheme 50

would conjugatively add phenylmagnesium bromide with the methoxy substituent acting as a leaving-group thus affording the naphthoxazine (133a). The enamine (193) was readily prepared by reaction of acetophenone (191) with morpholine (192) as described in the literature.[116] Unfortunately, however, the attempted reaction of 1-nitroso-2-naphthol (72) with the enamine (193) in benzene at room temperature gave only a complex mixture with no evidence for the formation of the oxazine derivative (194). Alternative conditions to accomplish the cycloaddition reaction of 1-nitroso-2-naphthol (72) with the enamine (193) will have to be the subject of future investigations.

A further approach (Scheme 50) to the naphthoxazine derivative (133a) was also evaluated. This entailed the synthesis of the N-hydroxy derivative (197) which it was anticipated could be further manipulated to the naphthoxazine (133a) as indicated [(197)→(198)→(196)→(133a)]. It was reported[117] that the nitrosonaphthol copper complex (162) reacts with dimethyl acetylenedicarboxylate to afford the N-hydroxynaphthoxazine derivative [(197); CO_2Me for Ph and CO_2Et] in good yield. It was therefore anticipated that the corresponding reaction of the copper complex (162) with ethyl phenylpropiolate would afford the N-hydroxynaphthoxazine (197) required for further manipulation to the naphthoxazine (133a).

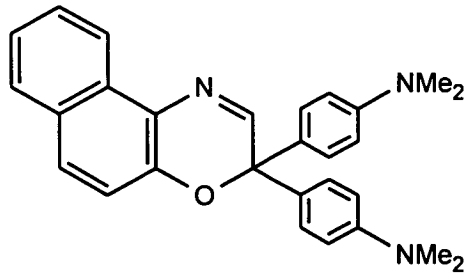
In practice, the attempted reaction of the copper complex (162) with ethyl phenylpropiolate in aqueous 1,2-dimethoxyethane under reflux gave only a low recovery (33%) of the unreacted copper complex (162), with no evidence for the formation of the desired N-hydroxynaphthoxazine (197).



(162)

(73)

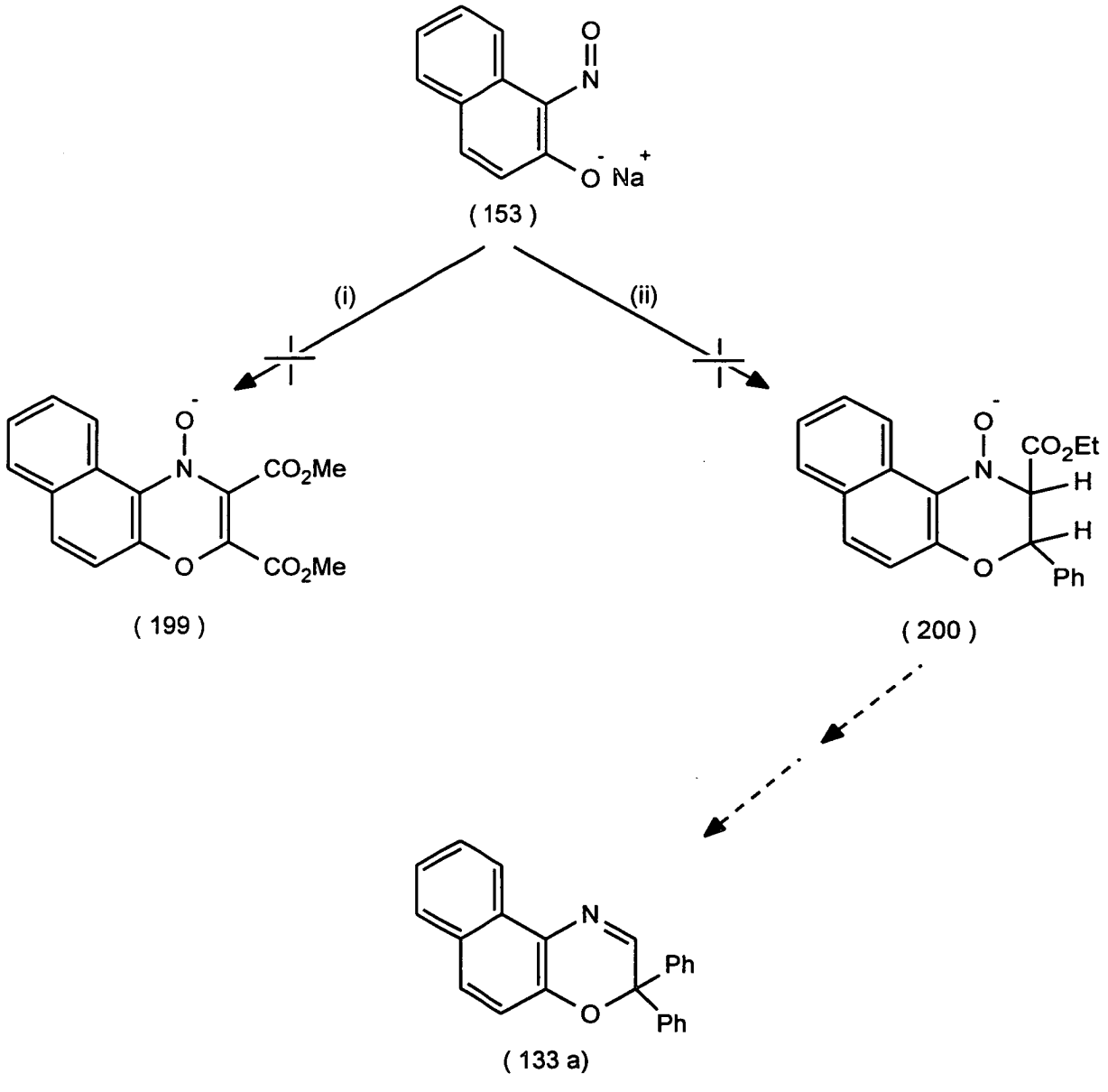
(i)



(74)

(i) DME, H_2O, reflux.

Scheme 51



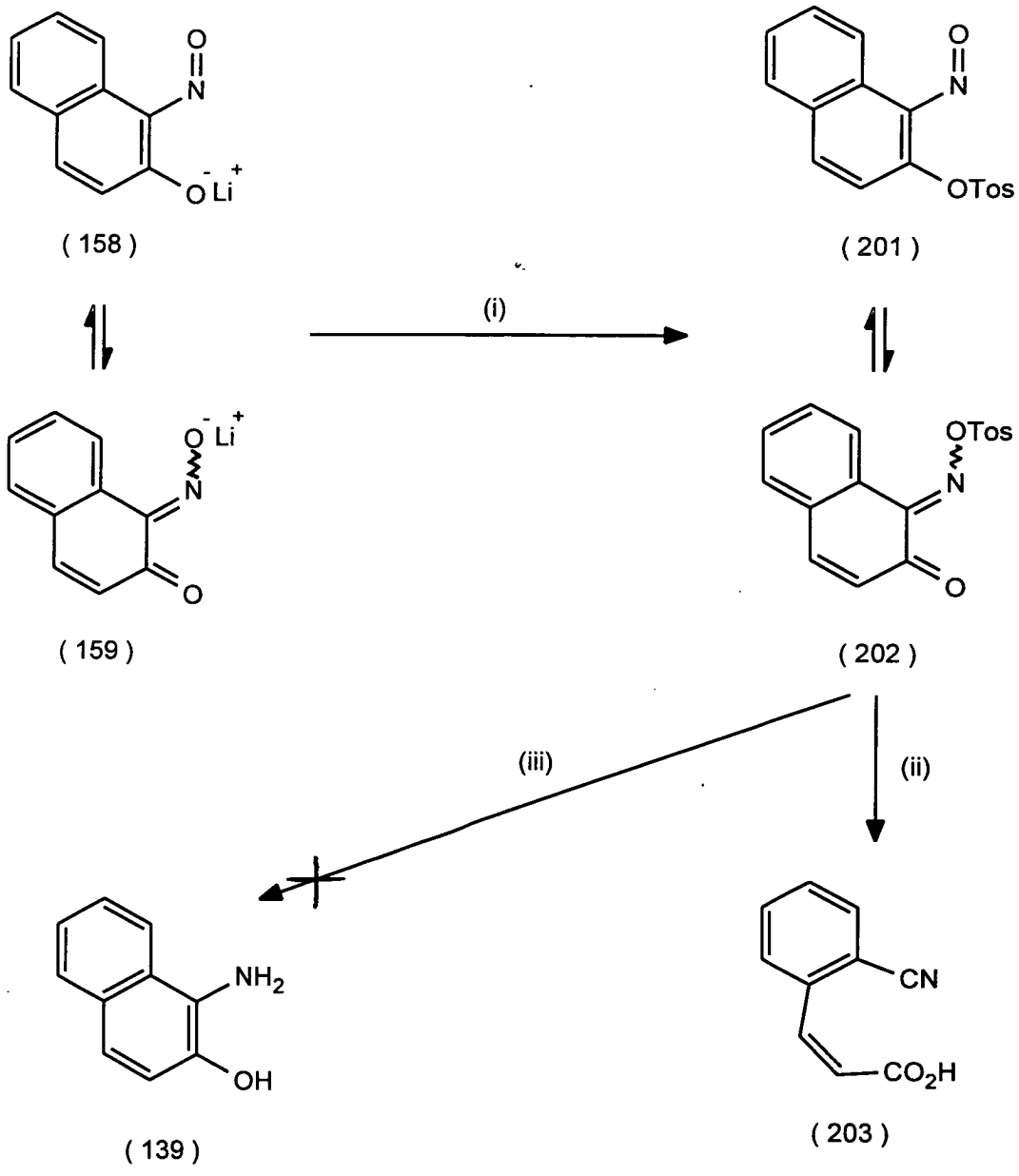
(i) $MeO_2CC{\equiv}CCO_2Me$, DMSO, 90°.
(ii) $PhCH{=}CHCO_2Et$, DMSO, 90°.

Scheme 52

The utilisation of the copper complex (162) in an alternative approach (Scheme 51) to the 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) was also evaluated. This approach involved the attempted cyclisative condensation reaction of the copper complex (162) with Michler's alkene (73). Disappointingly the attempted reaction of the copper complex (162) with Michler's alkene (73) in aqueous 1,2-dimethoxyethane under reflux gave none of the hoped for naphthoxazine (74). Instead this reaction gave only the unreacted copper complex (162) (recovery 60%) and unreacted alkene (73) (recovery 41%).

The possible cycloaddition reactions (Scheme 52) of 1-nitroso-2-naphthol sodium salt (153) with dimethyl acetylenedicarboxylate and ethyl cinnamate were also investigated in the hope of obtaining the naphthoxazine derivatives (199) and (200). It was anticipated that the latter compound (200) could be further transformed into the target naphthoxazine (133a), while the reaction of the salt (153) with dimethyl acetylenedicarboxylate would be a useful investigation of the ability of the sodium salt (153) to undergo cycloaddition reactions. In practice heating the salt (153) with dimethyl acetylenedicarboxylate in dimethylsulphoxide at 90° gave only a complex mixture from which no identifiable material was obtained. In contrast, the attempted reaction of the salt (153) with ethyl cinnamate in dimethylsulphoxide at 90° gave after workup, only the unreacted nitrosonaphthol (72) (97%) and a quantitatively recovery of ethyl cinnamate.

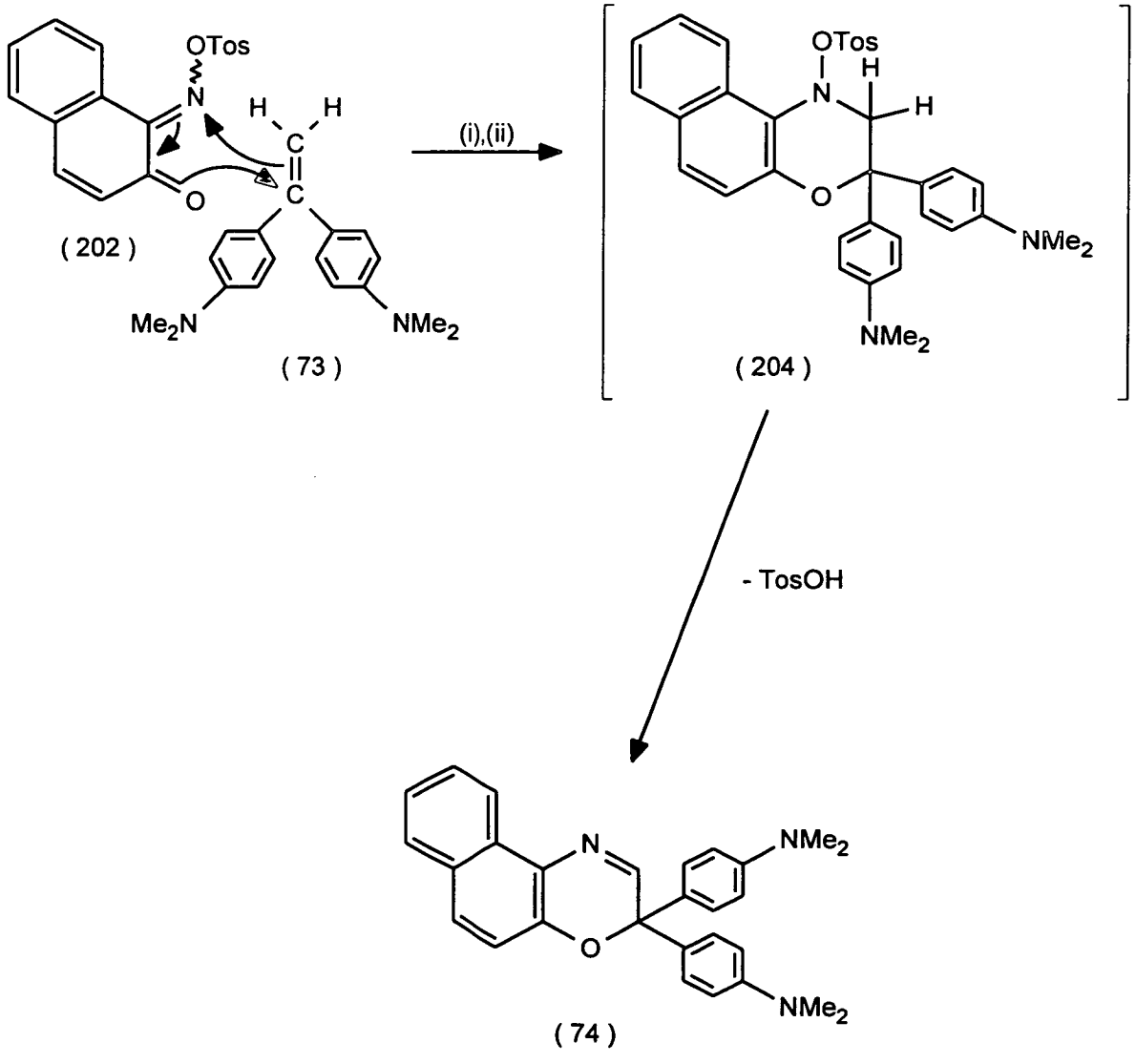
Due to the lack of success of the nitrosonaphthol (72), copper complex



(i) TosCl, acetone, room temp.
(ii) 2M NaOH aqu., 100°.
(iii) H_2, 10% Pd - C, DMF, room temp., atmos. press.

Scheme 53

(162) and the sodium salt (153) to react in various cycloaddition reactions (see Schemes 49 to 52), attention was turned (Scheme 53) to the possible synthesis of the tosyl derivatives [(201) and (202)] which would hopefully react more readily in cycloaddition reactions. As the lithium salt (158) may react as an ambident anion [(158)↔(159)] with tosyl chloride, either the nitroso derivative (201) and/or the oxime (202) may be formed. In practice the reaction of the lithium salt (158) with tosyl chloride in acetone at room temperature gave a yellow solid in excellent yield (92%). The mass and ^{1}H n.m.r. spectral data of this yellow solid supports both the nitroso (201) and oxime (202) structures. However, the i.r. spectrum of the yellow solid shows bands at 1677 and 1592 cm^{-1} which can be attributed to the quinone carbonyl and imine (C=N) absorptions respectively of the oxime (202). Further evidence for the oxime structure (202) of the yellow solid was then sought. Hence the oxime tosyl derivative (202) was briefly heated with 2 M aqueous sodium hydroxide at 100°. On acidic workup this reaction gave a high yield (90%) of cis 2-cyanocinnamic acid (203), the expected hydrolysis product of the oxime (202). The cis 2-cyanocinnamic acid (203) was obtained as a colourless solid, which analysed correctly and had mass, i.r. and ^{1}H n.m.r. spectral data fully in accord with its assigned structure. Additionally, reduction of the tosyl derivative (202) would be expected to give 1-amino-2-naphthol (139), but in practice hydrogenation of the tosyl derivative (202) over 10% palladium-on-charcoal in dimethylformamide gave only a complex mixture which afforded no identifiable material.

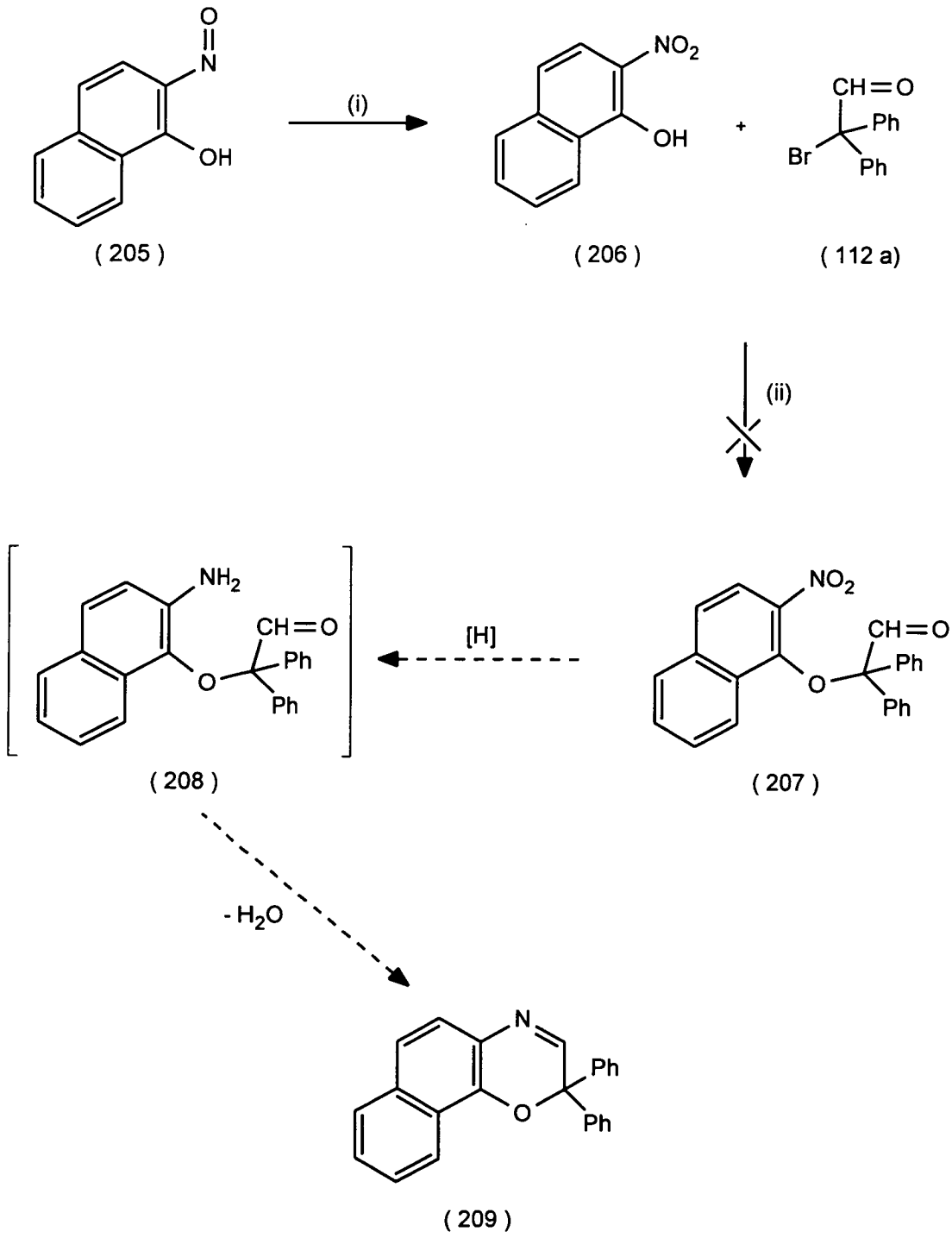


(i) toluene, reflux.

(ii) ptsa, DME, reflux.

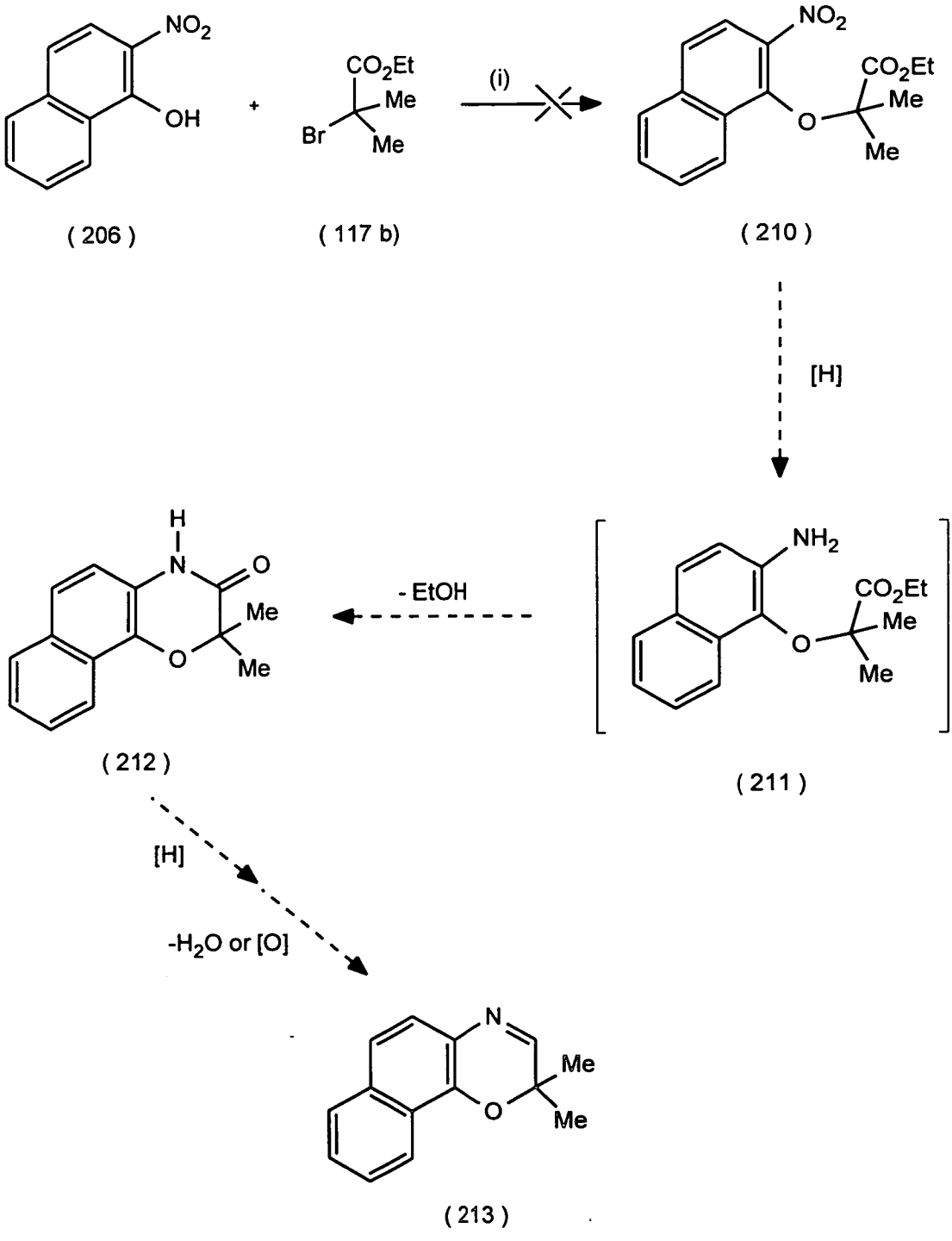
Scheme 54

With the tosyl derivative (202) available, attention was focused (Scheme 54), to its cycloaddition reaction with Michler's alkene (73) to afford *via* the tosyl intermediate (204) the naphthoxazine (74). In practice the reaction of the tosyl derivative (202) with Michler's alkene (73) in toluene under reflux gave only a low yield (10%) of the naphthoxazine (74). In a bid to improve this reaction, the reaction was repeated in refluxing 1,2-dimethoxyethane with a few crystals of toluene-4-sulphonic acid present as catalyst. Unfortunately only a complex mixture was obtained, which yielded no identifiable material. Due to a lack of time investigations into reactions of the tosyl derivative (202) with the alkene (73) were halted at this stage.



(i) 30% H_2O_2, HNO_3 aqu.(conc.), AcOH, 70°.
(ii) NaH, DMF, 100°.

Scheme 55



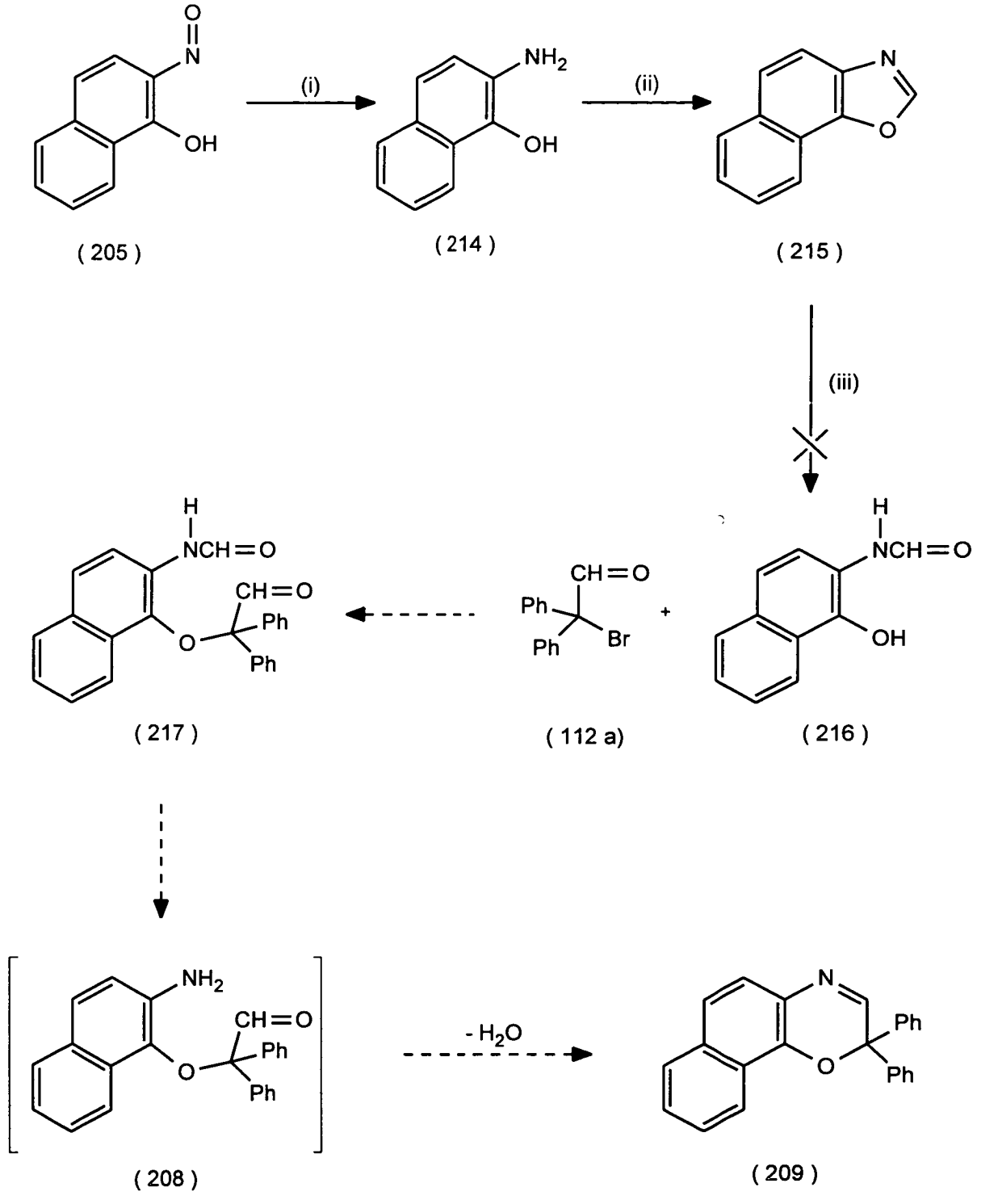
(i) NaH, DMF, 100°.

Scheme 56

2.4 INVESTIGATIONS OF SYNTHETIC ROUTES TO NOVEL 2,2-DISUBSTITUTED 2H-NAPHTH[1,2-b]-1,4-OXAZINE DERIVATIVES

Studies under this heading initially centred (Scheme 55) on the synthesis of the 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209). Here the key starting material was the known[108] 2-nitro-1-naphthol (206) which it was hoped would condense as the sodium salt with the bromo-aldehyde (112a) to give the ether (207) of appropriate structure for reductive cyclisation, *via* the amine intermediate (208) to the 2,2-diphenyl-naphth-1,4-oxazine (209). 2-Nitro-1-naphthol (206) was readily obtained, albeit in only moderate yield (40%) by the oxidation of the commercially available 2-nitroso-1-naphthol (205) with hydrogen peroxide in a mixture of nitric and acetic acids as described in the literature.[108] Disappointingly an initial attempt to convert the nitro-naphthol (206) into the ether (207) by heating its sodium salt [generated *in situ* by reaction of 2-nitro-1-naphthol (206) with sodium hydride in dimethylformamide] with 2-bromo-2,2-diphenylacetaldehyde (112a) in dimethylformamide at 100° gave only a quantitative recovery of the unreacted 2-nitro-1-naphthol (206). It was thought that the difficulty encountered in forming the ether (207) may be due to steric hindrance of approach to the 1-hydroxy group of the 2-nitro-1-naphthol (206).

In conjunction with this work, studies were also undertaken (Scheme 56) on the synthesis of the 2,2-dimethyl-2H-naphth[1,2-b]-1,4-oxazin-3(4H)-one (212). This molecule was viewed as a useful precursor to the potential photochromic 2,2-dimethyl-2H-naphth[1,2-b]-1,4-oxazine (213). It was first

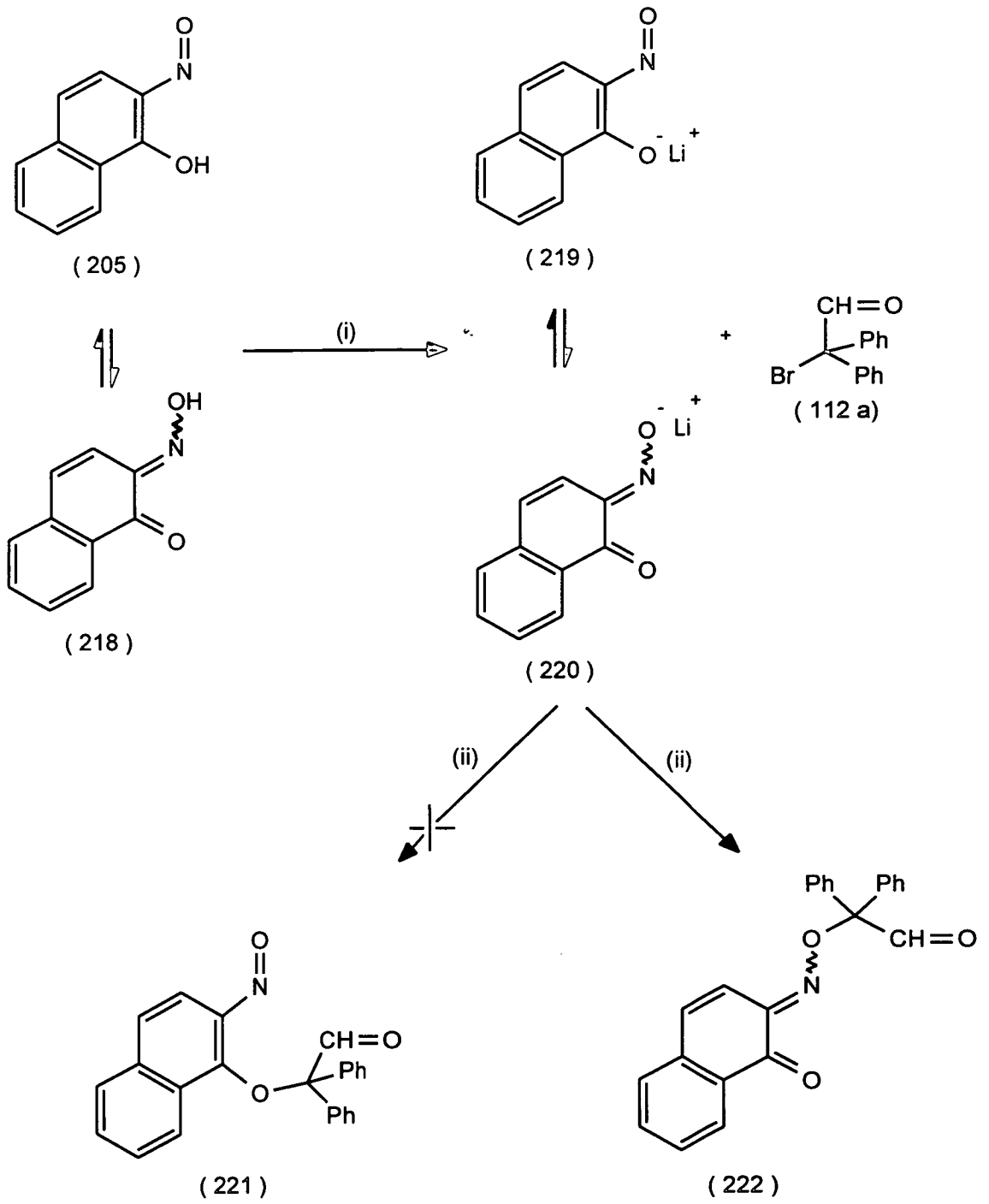


(i) H_2, 10% Pd - C, EtOAc, room temp., atmos. press.
(ii) HCO_2H, reflux.
(iii) 1,4 - dioxane, H_2O, reflux.

Scheme 57

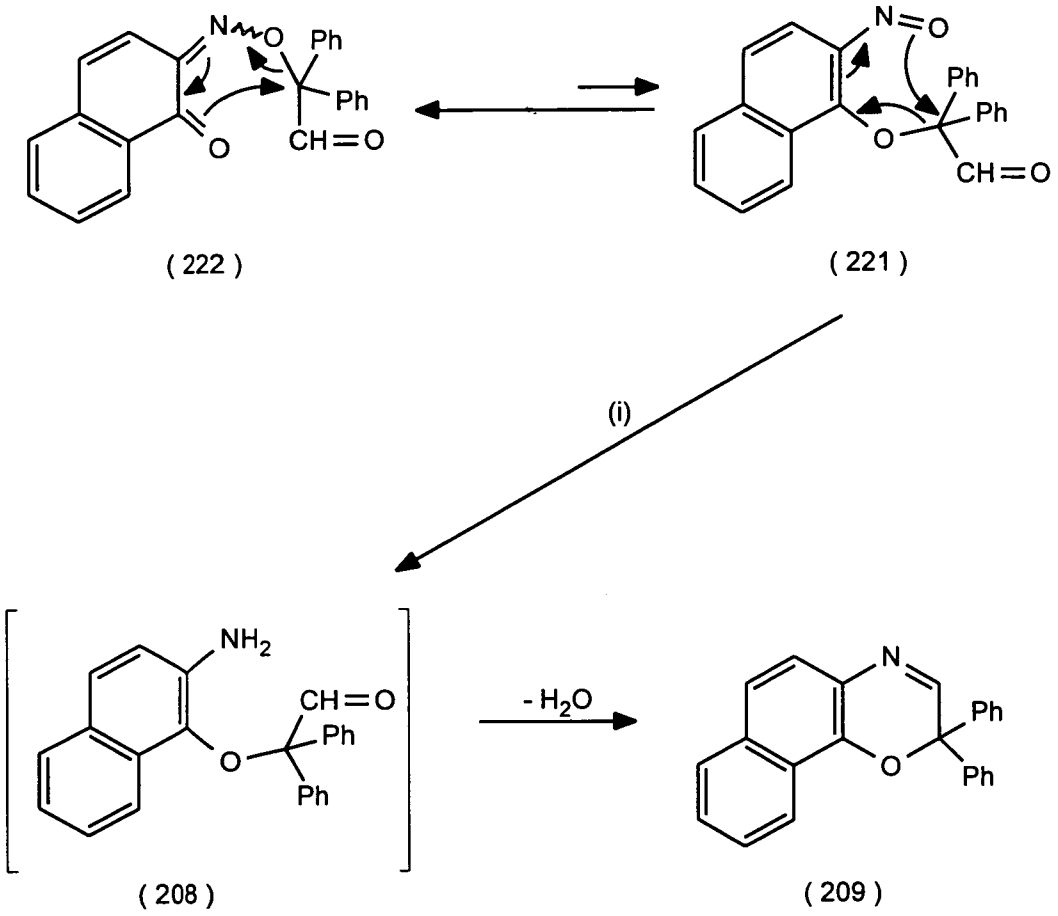
decided to attempt the synthesis of the key ether starting material (210) with the intention of carrying out its reductive cyclisation *via* the amine (211) to the naphth-1,4-oxazinone (212). It was anticipated that the commercially available ethyl 2-bromo-2-methylpropionate (117b) would be less prone to steric hindrance of approach to the 1-hydroxy group of the 2-nitro-1-naphthol (206) than the more bulky bromo-aldehyde (112a) previously discussed. In an initial attempt to form the ether (210) the sodium salt of 2-nitro-1-naphthol (206) [generated *in situ* by reaction of 2-nitro-1-naphthol (206) with sodium hydride in dimethylformamide] was reacted with ethyl 2-bromo-2-methylpropionate (117b) in dimethylformamide at 100°. This reaction however gave only a high recovery (76%) of unreacted 2-nitro-1-naphthol (206).

Due to the lack of success in the previous approaches for the synthesis of the naphth-1,4-oxazines (209) and (213), attention was turned to the alternative approach to the 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209) outlined in Scheme 57. This involved the formation and subsequent hydrolysis of the formamido derivative (217). 2-Nitroso-1-naphthol (205) was readily reduced using hydrogen over 10% palladium-on-charcoal to give the amine (214) as a deep purple solid in excellent yield (99%). Heating 2-amino-1-naphthol (214) with 98% formic acid under reflux as described in the literature[109] gave the naphthoxazole (215) in good yield (71%) as a purple solid. The attempted hydrolysis of the naphthoxazole (215) to 2-formamido-1-naphthol (216) using refluxing aqueous dioxane gave only a multicomponent dark brown gum which yielded no identifiable material.



(i) LiH, DME, room temp.
(ii) acetone, room temp.

Scheme 58



(i) Ph_3P, DME, reflux.

Scheme 59

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

TRACK

	1	2	3	4	5	6	7	8	9	10
λnm	220.2	259.8	287.4	397.8						
ABS	1.231	1.913	0.503	0.341						

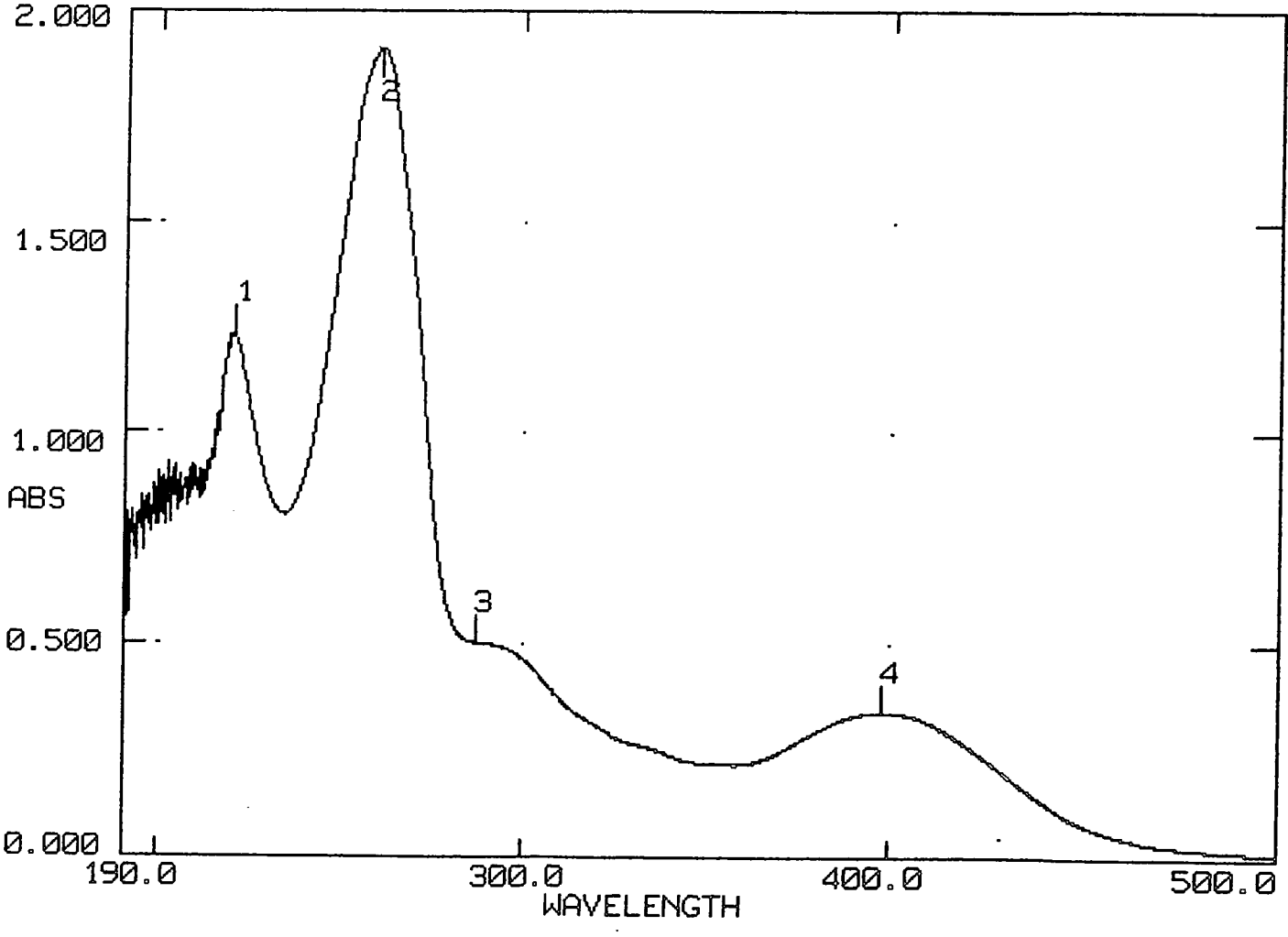


Figure 21

Attention was then focused on a new route (Schemes 58 and 59) based on the formation of the ether (221) and its subsequent reduction to the amine (208). It was anticipated that the latter compound would undergo spontaneous cyclisation to give the naphthoxazine (209). One complication anticipated in this approach was the possibility of tautomerism in the 2-nitroso-1-naphthol [(205)⇌(218)] which could on base treatment lead to an anion capable of reacting with the bromo-aldehyde (112a) to give the ether (221) and/or the oxime (222).

The key step in obtaining the ether (221), involved the formation and isolation of the 2-nitroso-1-naphthol lithium salt (219). Hence 2-nitroso-1-naphthol (205) was reacted with lithium hydride in 1,2-dimethoxyethane at room temperature. This reaction gave a good yield (77%) of a red-brown solid which was tentatively assigned the nitroso structure (219). It should be noted, the nitroso structure (219) is possibly tautomeric with the oxime (220) and hence the red-brown solid may be a mixture of both forms.

In an initial attempt to form the ether (221), the lithium salt (219) was reacted with the bromo-aldehyde (112a) in acetone at room temperature. This reaction gave a recovery (30%) of unreacted bromo-aldehyde (112a) and a moderate yield (49%) of a green solid. This green solid gave mass and ^1H n.m.r. spectral data which supported both the ether (221) and oxime (222) structures. The i.r. spectrum of the green solid shows bands at 1727 and 1681 cm^{-1} which are attributable to the aldehyde and quinone carbonyls of the oxime (222). Comparison of the u.v. spectrum (Figure 21) of the proposed

X-Ray Diffraction Data for Naphthalene-1,2-dione 2-Oxime Diphenylformylmethyl Ether (222)

Table 5 : Bond Lengths (Angstroms) with Standard Deviations

C(1)-O(9)	1.214(3)	C(1)-C(8A)	1.470(3)
C(1)-C(2)	1.499(3)	C(2)-N(10)	1.291(3)
C(2)-C(3)	1.441(3)	C(3)-C(4)	1.334(3)
C(4)-C(4A)	1.449(3)	C(4A)-C(5)	1.397(3)
C(4A)-C(8A)	1.400(3)	C(5)-C(6)	1.370(4)
C(6)-C(7)	1.372(4)	C(7)-C(8)	1.378(4)
C(8)-C(8A)	1.386(3)	N(10)-O(11)	1.396(2)
O(11)-C(12)	1.454(3)	C(12)-C(1")	1.518(3)
C(12)-C(1')	1.521(4)	C(12)-C(13)	1.526(4)
C(13)-O(14)	1.189(3)	C(1')-C(2')	1.379(4)
C(1')-C(6')	1.382(3)	C(2')-C(3')	1.378(4)
C(3')-C(4')	1.371(4)	C(4')-C(5')	1.351(4)
C(5')-C(6')	1.385(4)	C(1")-C(2")	1.382(3)
C(1")-C(6")	1.385(4)	C(2")-C(3")	1.372(4)
C(3")-C(4")	1.374(4)	C(4")-C(5")	1.369(4)
C(5")-C(6")	1.383(4)		

Table 6 : Bond Angles (Degrees) with Standard Deviations

O(9)-C(1)-C(8A)	122.1(2)	O(9)-C(1)-C(2)	120.8(2)
C(8A)-C(1)-C(2)	117.1(2)	N(10)-C(2)-C(3)	127.3(2)
N(10)-C(2)-C(1)	113.5(2)	C(3)-C(2)-C(1)	119.1(2)
C(4)-C(3)-C(2)	120.3(2)	C(3)-C(4)-C(4A)	122.9(2)
C(5)-C(4A)-C(8A)	118.1(2)	C(5)-C(4A)-C(4)	121.7(2)
C(8A)-C(4A)-C(4)	120.2(2)	C(6)-C(5)-C(4A)	120.7(2)
C(5)-C(6)-C(7)	120.7(3)	C(6)-C(7)-C(8)	120.0(3)
C(7)-C(8)-C(8A)	120.0(3)	C(8)-C(8A)-C(4A)	120.5(2)
C(8)-C(8A)-C(1)	119.9(2)	C(4A)-C(8A)-C(1)	119.6(2)
C(2)-N(10)-O(11)	112.2(2)	N(10)-O(11)-C(12)	107.4(2)
O(11)-C(12)-C(1")	105.8(2)	O(11)-C(12)-C(1')	108.7(2)
C(1")-C(12)-C(1')	113.0(2)	O(11)-C(12)-C(13)	107.5(2)
C(1")-C(12)-C(13)	105.4(2)	C(1')-C(12)-C(13)	115.9(2)
O(14)-C(13)-C(12)	125.3(3)	C(2')-C(1')-C(6')	117.6(3)
C(2')-C(1')-C(12)	117.8(2)	C(6')-C(1')-C(12)	124.5(2)
C(3')-C(2')-C(1')	121.7(3)	C(4')-C(3')-C(2')	119.5(3)
C(5')-C(4')-C(3')	119.9(3)	C(4')-C(5')-C(6')	120.9(3)
C(1')-C(6')-C(5')	120.4(3)	C(2")-C(1")-C(6")	118.3(3)
C(2")-C(1")-C(12)	119.3(2)	C(6")-C(1")-C(12)	122.2(2)
C(3")-C(2")-C(1")	121.2(3)	C(2")-C(3")-C(4")	120.0(3)
C(5")-C(4")-C(3")	119.8(3)	C(4")-C(5")-C(6")	120.3(3)
C(5")-C(6")-C(1")	120.4(3)		

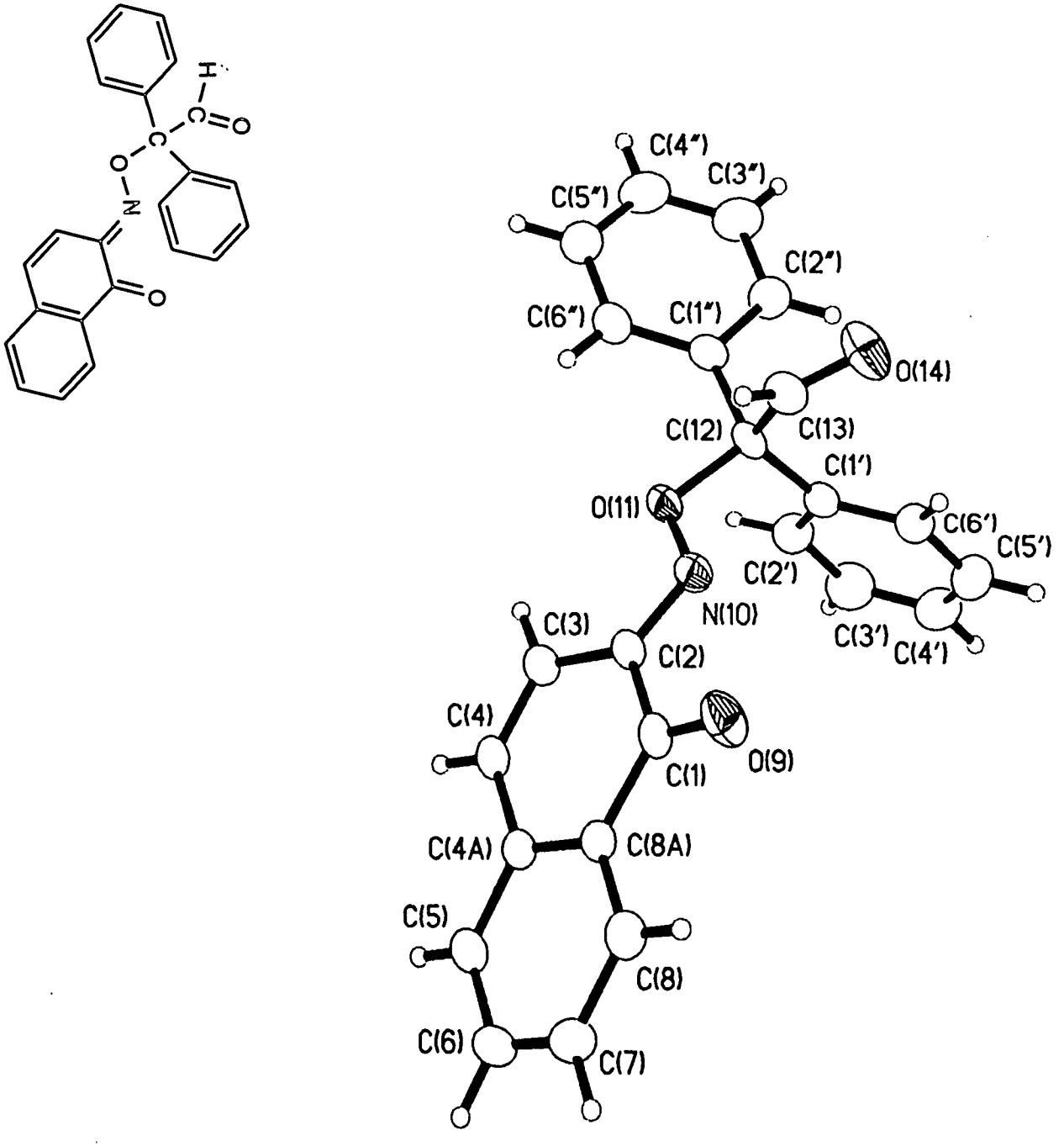
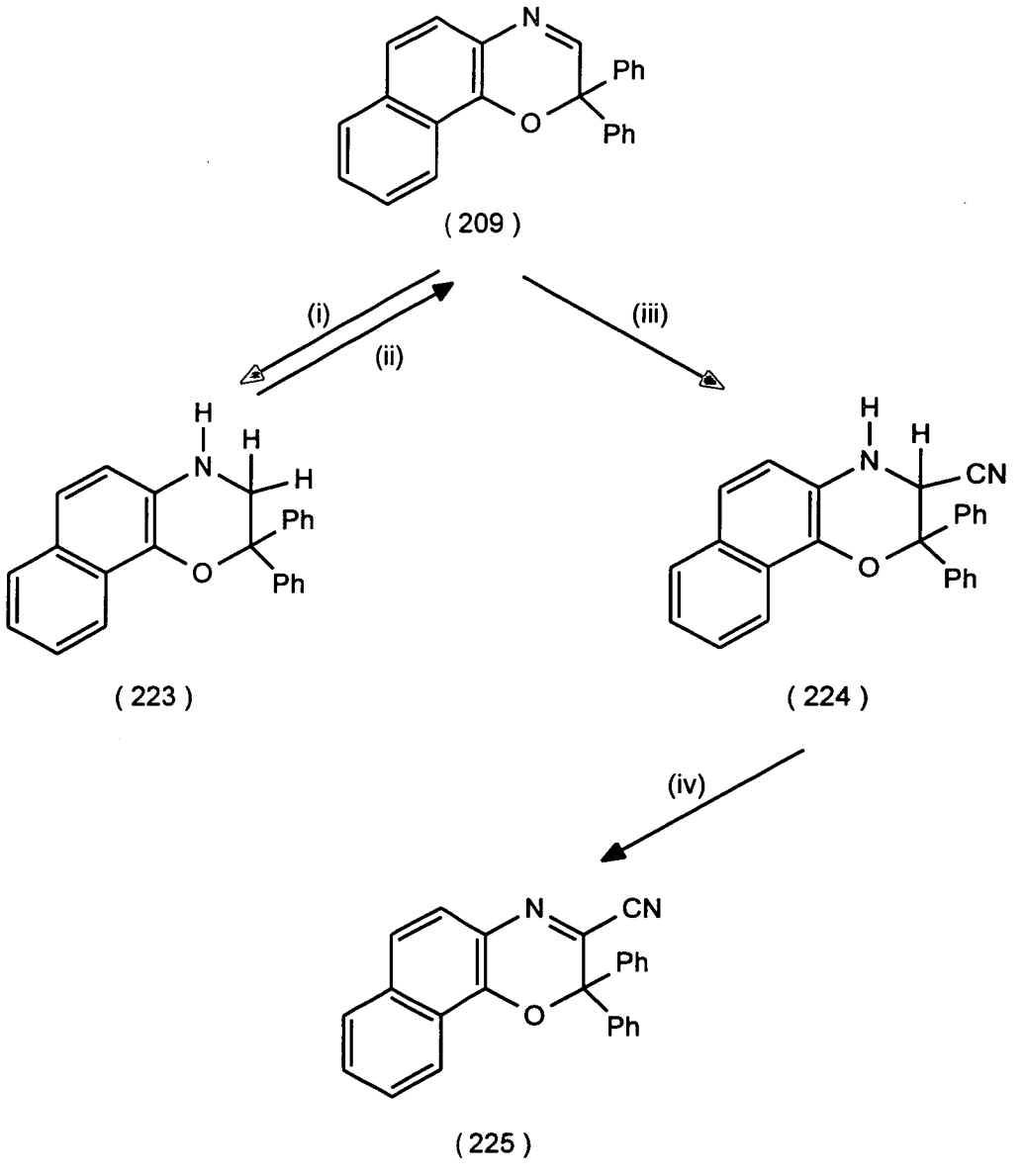

H
C=O
O
O
N
O
C(4″)
C(3″)
C(5″)
C(2″)
C(6″)
C(1″)
O(14)
C(12)
C(13)
C(1′)
O(11)
C(6′)
C(5′)
C(2′)
N(10)
C(3)
C(3′)
C(4′)
C(2)
C(4)
O(9)
C(1)
C(4A)
C(8A)
C(5)
C(8)
C(6)
C(7)

Figure 22

oxime (222) with the u.v. spectra (see Page 62, Figures 12 and 13) of the oxime [see Page 61, Scheme 37; (161)] shows the oxime (222) has a more complicated u.v. spectrum (Figure 21) with four absorption bands while the u.v. spectra (see Page 62, Figures 12 and 13) of the forms A and B of the oxime (161) have only three bands. Thus, the u.v. spectrum of the proposed oxime (222) has an absorption maximum at 260 nm and weaker bands at 220, 287 and 398 nm. There is also absorption in the visible region of the spectrum which accounts for the green colour of the oxime (222). The structure of the green solid product was finally and unequivocally established as the oxime (222) by X-ray diffraction analysis (see Figure 22; Tables 5 and 6). In an attempt to improve the yield of the oxime (222), the lithium salt (219) was reacted with the bromo-aldehyde (112a) in acetone at room temperature for the extended time of 47 h. This reaction gave an improved yield (62%) of the oxime (222) and a low recovery (8%) of 2-nitroso-1-naphthol (205).

With the oxime (222) to hand, attention was turned (Scheme 59) to its further manipulation by reaction with triphenylphosphine to the naphthoxazine (209) by analogy with the strategy (see Page 64, Scheme 39) which had proved successful for the synthesis of the 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a). Thus, the oxime (222) was heated under reflux with triphenylphosphine in 1,2-dimethoxyethane to give in addition to triphenylphosphine oxide (67%) a moderate yield (30%) of a colourless solid which gave mass spectra data fully in accord with its formulation as the 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209). The naphth-1,4-oxazine (209)



(i) $NaBH_4$, DME, H_2O, room temp.
(ii) MnO_2, MeCN, room temp.
(iii) KCN, AcOH, 100°.
(iv) MnO_2, MeCN, reflux.

Scheme 60

was further identified by its ^{1}H n.m.r. spectrum which shows signals only due to the methine and aromatic protons and the i.r. spectrum which contains no bands which can be assigned to a carbonyl group. The formation of the naphthoxazine (209) by the reaction of the oxime (222) with triphenylphosphine suggests under these conditions the oxime (222) rearranges to the ether (221) and the latter compound undergoes reduction to the naphthoxazine (209).

In an attempt to improve the yield of the naphthoxazine (209), the oxime (222) was heated under reflux with triphenylphosphine in 1,2-dimethoxyethane for the longer time of 23 h. This reaction gave an improved yield (51%) of the naphthoxazine (209) and a high yield (77%) of triphenylphosphine oxide. Unreacted triphenylphosphine (22%) was also obtained.

In view of the fact the previously undescribed naphthoxazine (209) is a cyclic imine it was decided to investigate (Scheme 60) its chemical behaviour in this context. Reduction of the imine double bond in the naphthoxazine (209) was expected to yield the dihydro derivative (223). Thus treatment of the naphthoxazine (209) with sodium borohydride in aqueous 1,2-dimethoxyethane at room temperature afforded a good yield (62%) of a colourless solid which gave mass, i.r. and ^{1}H n.m.r. spectral properties fully in accord with its formulation as the expected dihydro derivative (223). Thus the i.r. spectrum shows the expected NH absorption band (υ_{max} 3380 cm^{-1}) and the ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H4.76 which is completely removed on addition of deuterium oxide attributable to the NH group and a two-proton singlet at δ_H3.93

attributable to the methylene group. The formation of the dihydro derivative (223), in turn firmly establishes the structure of the naphthoxazine derivative (209). Oxidation of the dihydro derivative (223) with manganese dioxide in acetonitrile regenerated the naphthoxazine (209) in moderate yield (30%).

The naphthoxazine (209) also exhibited (Scheme 60) imine behaviour in its reactivity towards nucleophilic addition of hydrogen cyanide. Thus, treatment of the naphthoxazine (209) with potassium cyanide in glacial acetic acid at 100° afforded a good yield (75%) of the hydrogen cyanide adduct (224). The pink product (224) gave a satisfactory mass spectrum and the structure was confirmed by its i.r. and ^{1}H n.m.r. spectra. Thus the i.r. spectrums shows bands assignable to the NH and C≡N groups, while the ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a sharp one-proton singlet at δ_H5.32 due to the methine group and a broad one-proton singlet at δ_H4.48 which is completely removed on addition of deuterium oxide attributable to the NH group.

In further support of this structure oxidation of the hydrogen cyanide adduct (224) with manganese dioxide in acetonitrile at room temperature afforded the cyanonaphthoxazine derivative (225) in good yield (76%). This yellow product (225) analysed correctly and gave satisfactory mass, i.r. and ^{1}H n.m.r. spectral data for its assigned structure. Thus the i.r. spectrum shows the C≡N absorption band (υ_{max} 2218 cm^{-1}) and contains no band assignable to a NH group, while the ^{1}H n.m.r. spectrum shows only a sixteen-proton multiplet at δ_H8.33-7.25 attributable to the aromatic protons.

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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λnm	205.4	218.2	250.0	269.8	312.4	327.8	354.8			
ABS	1.836	1.837	1.129	0.864	0.181	0.146	0.109			

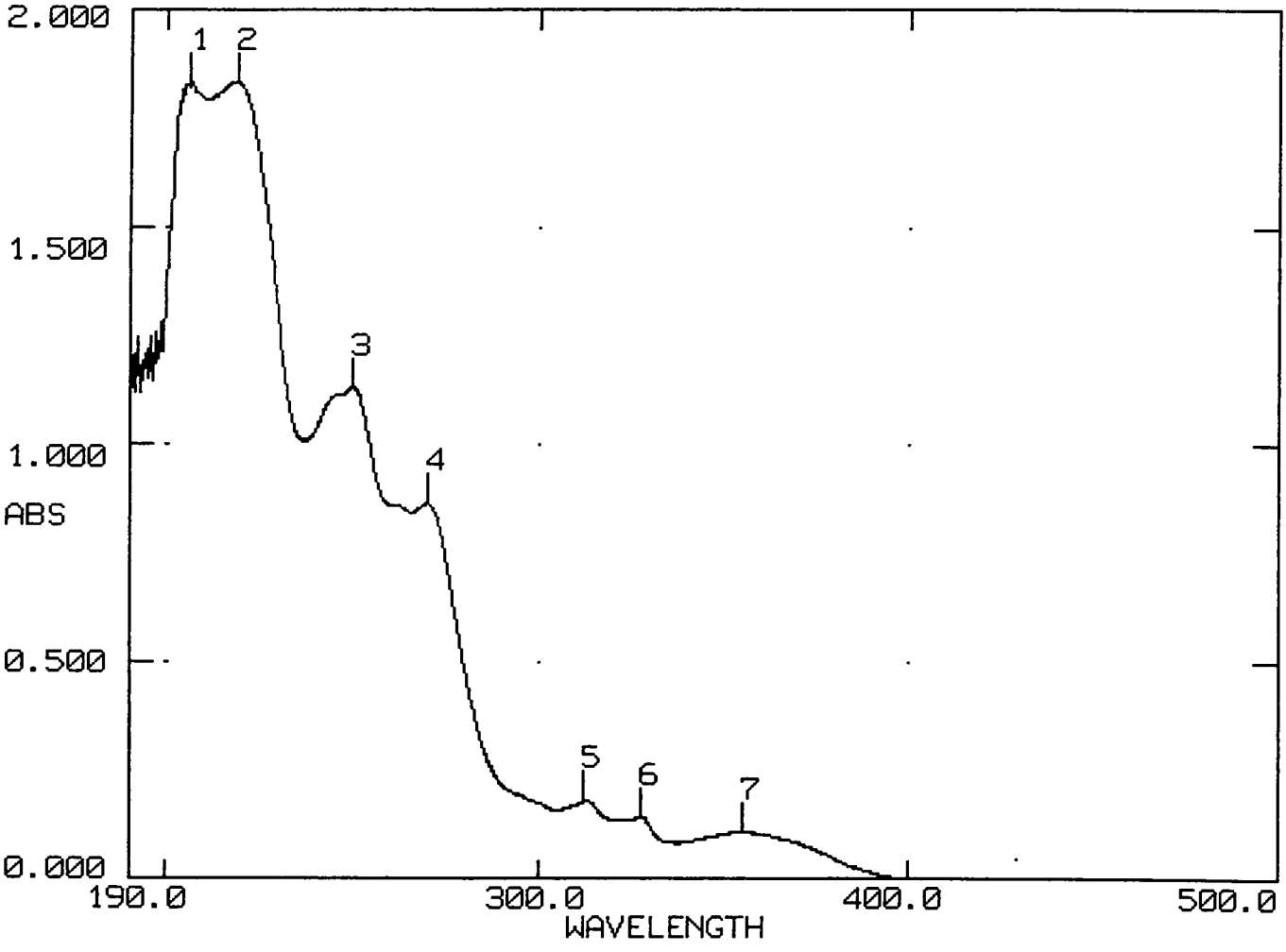

Figure 23

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

TRACK	1	2	3	4	5	6	7	8	9	10
λnm	222.6	253.8	299.4	310.2	358.2					
ABS	0.606	1.992	0.277	0.261	0.103					

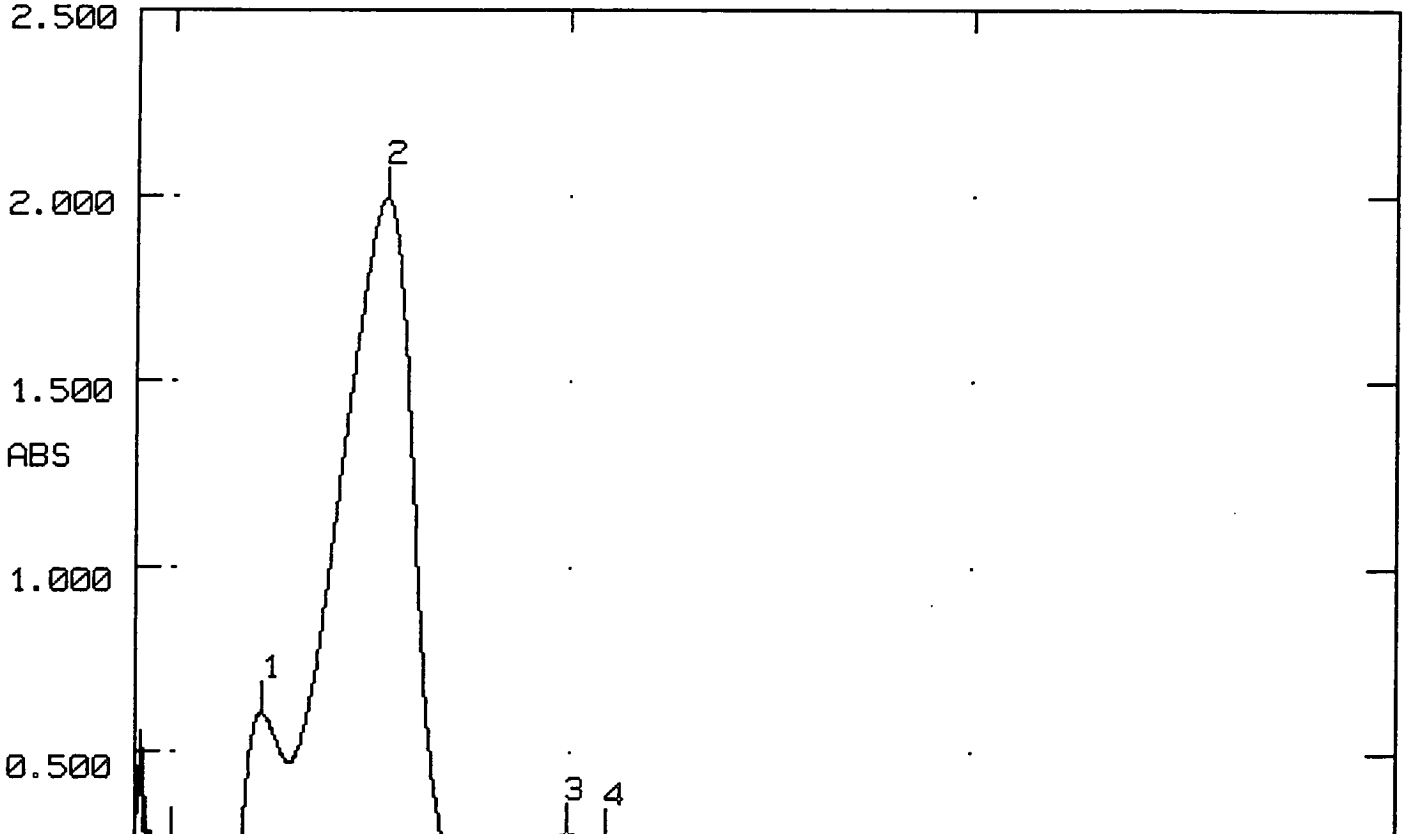

Figure 24

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

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λnm	210.6	276.8	285.2	343.4	408.2					
ABS	1.620	0.972	1.089	0.321	0.225					

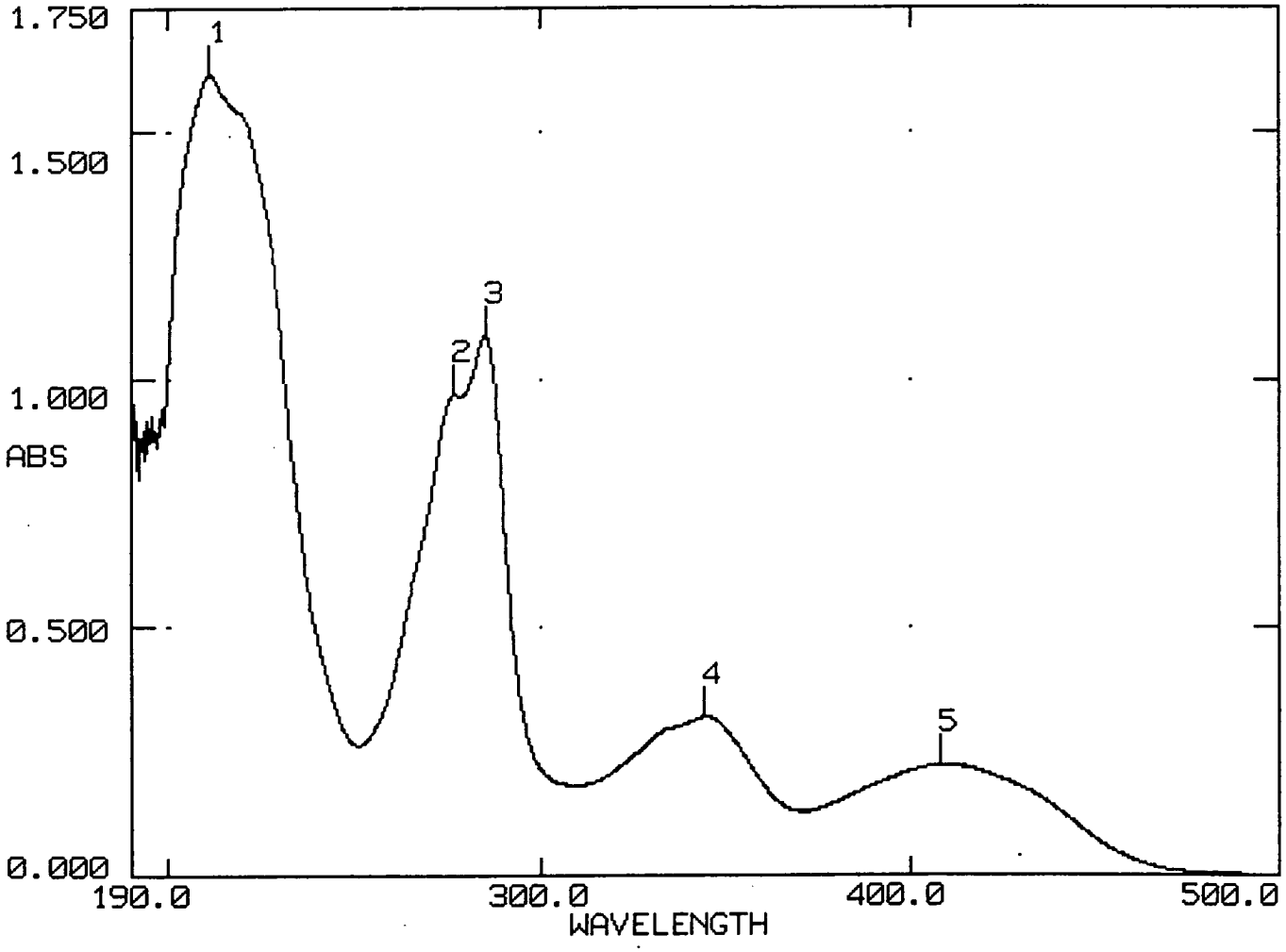

Figure 25

UNICAM UV2-100 UV/VISIBLE SPECTROMETER v3.32 PAGE 1

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ID: OPERATOR:

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BASELINE:DEFAULT BANDWIDTH:2.0nm LAMP CHANGE:325 nm

PEAKS

	1	2	3	4	5	6	7	8	9	10
λnm	208.8	249.4	283.0	292.4	304.6	343.8				
ABS	2.816	1.911	0.263	0.254	0.210	0.112				

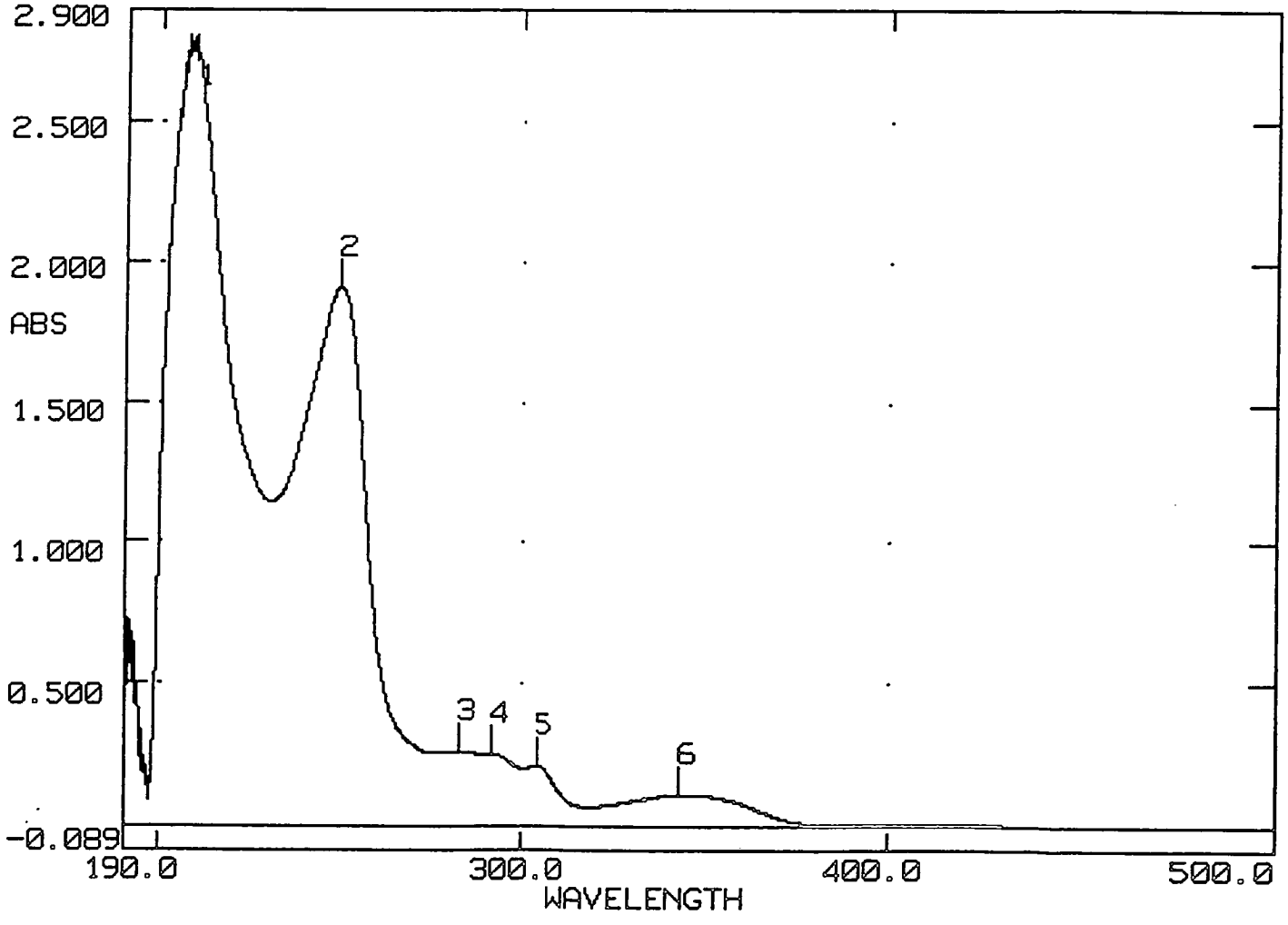
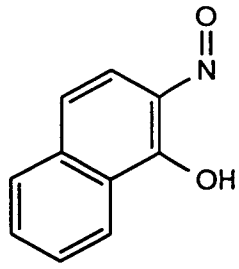


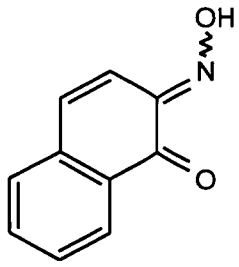
Figure 26

In view of the fact the naphthoxazine (209) was potentially photochromic as discussed earlier (see Page 20, Section 1.3.1) a small sample of this compound (209) was sent to Gentex and is currently being investigated for photochromic behaviour.

An investigation of the u.v. spectrum of the naphthoxazine (209) and its derivatives [(223), (224) and (225)] was also undertaken. These u.v. spectra provided useful information on the absorption bands of these compounds and illustrated the effect of change in structure on absorption. Thus the u.v. spectrum (Figure 23) of the naphthoxazine (209) has an absorption maximum at 218 nm, a band of almost equal intensity at 205 nm and weaker bands at 250, 270, 312, 328 and 355 nm. Comparison of this u.v. spectrum (Figure 23) with the u.v. spectrum (see Page 74, Figure 16) of the naphthoxazine [see Page 64, Scheme 39; (133a)] shows the naphthoxazine (209) has an additional band at 270 nm in its u.v. spectrum (Figure 23) and the intensity of the bands also vary between the two spectra. The naphthoxazine (209) also lacks absorption in the visible region (400-750 nm) and hence is transparent. Not surprisingly, in view of its less conjugated structure, the dihydro compound (223) (Figure 24) also lacked absorption in the visible region and contained an absorption maximum at 254 nm and also weaker bands at 223, 299, 310 and 358 nm. The u.v. spectrum (Figure 25) of the cyanonaphthoxazine (225) is significantly different to the u.v. spectrum (Figure 23) of the naphthoxazine (209). For example, the naphthoxazine (209) is transparent in the visible region while the u.v. spectrum (Figure 25) of the cyanonaphthoxazine (225)

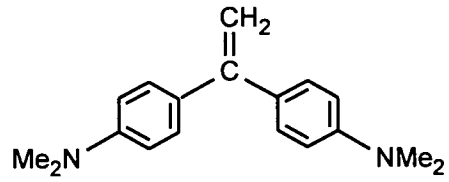


(205)



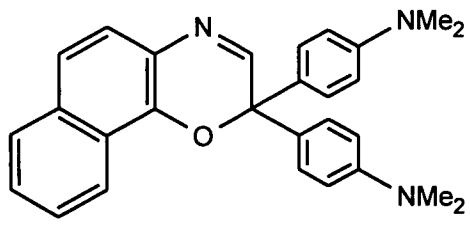
(218)

+



(73)

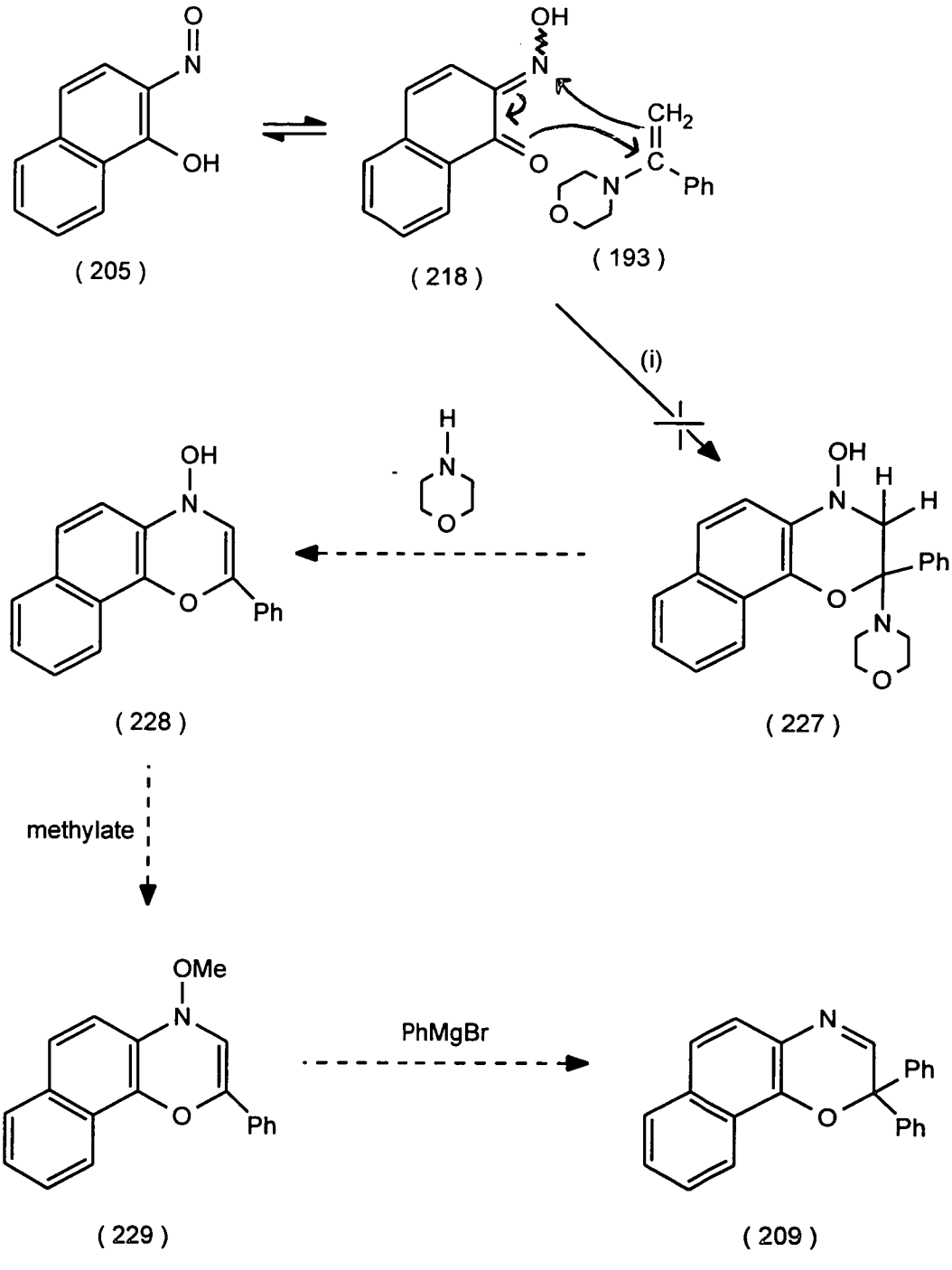
(i)



(226)

(i) ptsa, toluene, reflux.

Scheme 61



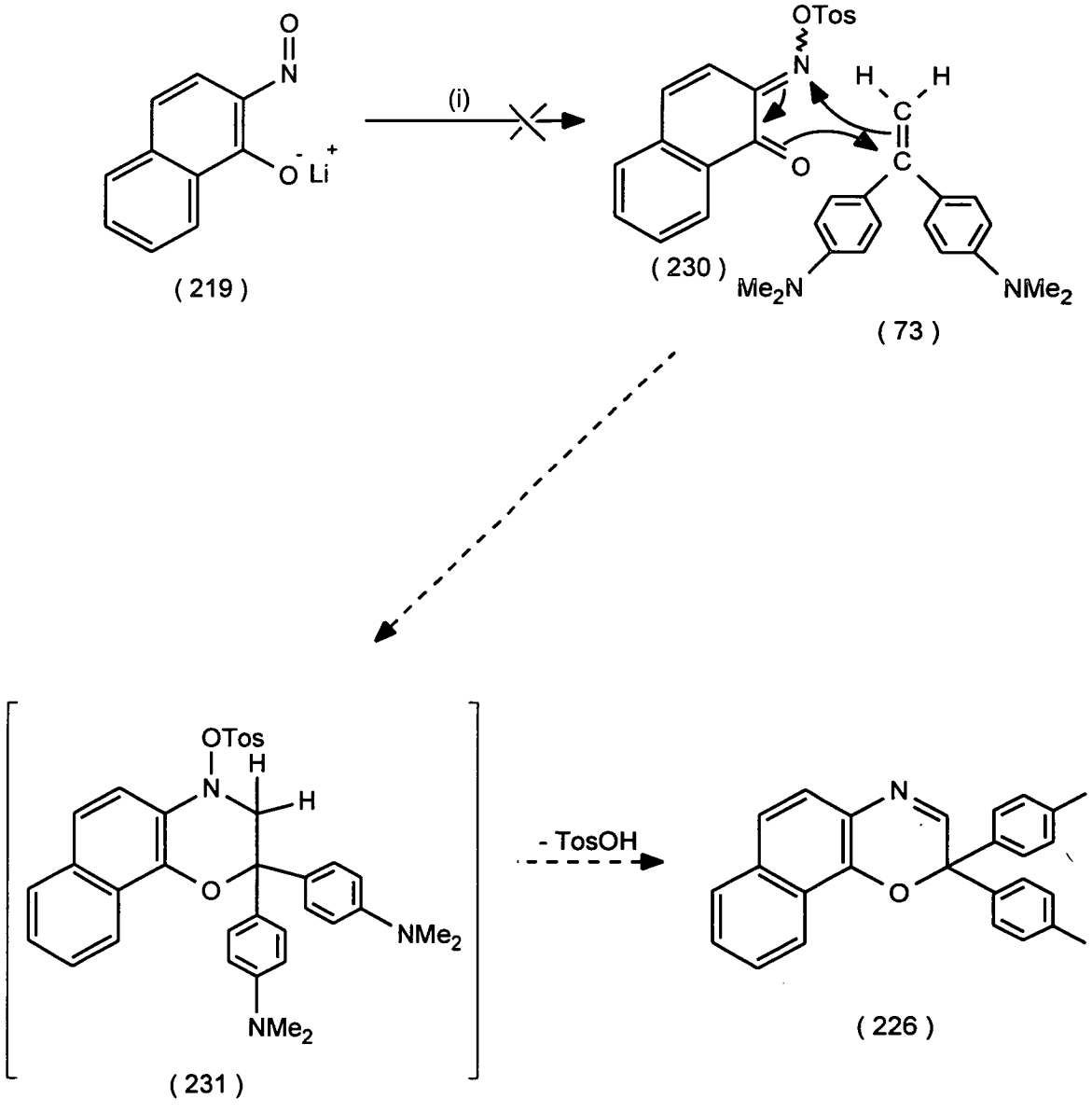
(i) benzene, room temp. or reflux.

Scheme 62

shows an absorption band at 408 nm in the violet region of the visible spectrum which gives rise to its yellow colour. The presence of the cyano group has induced a considerable bathochromic shift (shift to longer wavelength) of the bands in the u.v. spectrum (Figure 23) of the naphthoxazine (209) to the bands in the u.v. spectrum (Figure 25) of the cyanonaphthoxazine (225). Investigation of the u.v. spectrum (Figure 26) of the dihydro compound (224) shows the less conjugated dihydro compound (224) lacks absorption in the visible region.

In conjunction with the previous work, studies (Scheme 61) were also undertaken into the synthesis of the 2,2-di-(4-dimethylaminophenyl)-2H-naphth[1,2-b]-1,4-oxazine (226). Initial work centred on a synthetic strategy based on the cyclisative condensation of the alkene (73) with 2-nitroso-1-naphthol (205) by analogy with the strategy (see Page 77, Scheme 45) which had proved successful for the synthesis of the 3,3-di(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74). It should be noted that 2-nitroso-1-naphthol (205) may exist as either the nitroso form (205) or the tautomeric oxime form (218) and undergo reactions characteristic of both forms. Hence 2-nitroso-1-naphthol (205) was reacted with the alkene (73) in toluene under reflux containing a catalytic amount of toluene-4-sulphonic acid. This reaction gave only unreacted alkene (73) (31%) together with intractable mixtures.

Attention was then refocussed on a further route (Scheme 62) to the naphth-1,4-oxazine (209). This route was based on the cycloaddition reaction of the known[116] enamine (193) with 2-nitroso-1-naphthol (205) by analogy with



(219)

(230)

(73)

(231)

(226)

(i) TosCl, acetone, room temp. or reflux.

Scheme 63

the strategy (see Page 83, Scheme 49) for the cycloaddition reaction of 1-nitroso-2-naphthol (72). Thus it was hoped that the cycloaddition reaction of the known[116] enamine (193) with 2-nitroso-1-naphthol (205) [which may react as its tautomeric oxime form (218)] would provide access to the N-hydroxyoxazine (227). Elimination of morpholine from the latter would then afford the N-hydroxy compound (228) and further with methylation the methoxy derivative (229). It was anticipated that the latter would conjugatively add phenylmagnesium bromide with the methoxy substituent acting as a leaving-group thus affording the naphthoxazine (209). In practice the reaction of 2-nitroso-1-naphthol (205) with the enamine (193) in benzene at room temperature gave only a good recovery of the unreacted starting materials. Repetition of this reaction, but in refluxing benzene gave only a complex mixture which yielded no identifiable material.

Attention was then turned to a further route (Scheme 63) to the naphthoxazine derivative (226). This route was based on the formation of the tosyl derivative (230) and its reaction with Michler's alkene (73) to afford *via* the tosyl intermediate (231) the naphthoxazine (226). In practice reaction of the lithium salt (219) with tosyl chloride in acetone at room temperature followed by heating under reflux gave a multi-component mixture which yielded no identifiable material.

Due to a lack of time, investigations under all the foregoing headings were terminated at this stage.

2.5 EXPERIMENTAL

General Experimental Details

Infrared spectra were recorded using a Perkin-Elmer 298 spectrophotometer or a Bio-Rad FTS-7 Fourier-Transform spectrophotometer, and bands were strong and sharp unless specified as w (weak) or br (broad). Solids were measured as suspensions (mulls) in Nujol and liquids as thin films.

^{1}H n.m.r. spectra were measured in the stated solvent at 80 MHz using a Bruker WP-80SY instrument, at 200 MHz using a Bruker WP-200SY instrument, or at 360 MHz using a Bruker WH-360 instrument. Signals were sharp unless specified as b (broad); s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet and m = multiplet. ^{13}C n.m.r. spectra were measured in the stated solvent at 50 MHz using a Bruker 200SY instrument and were fully decoupled. Signals were sharp and quat = quaternary carbon atom. Quaternary carbon atoms and methylene groups were identified by $3\pi/4$ DEPT (Distortionless Enhancement by Polarisation Transfer) pulse sequence spectra.

Electron Impact (EI) mass spectra were recorded at 70 eV on A.I.E. MS-902 and Kratos MS-50TC instruments. Fast Atom Bombardment (FAB) mass spectra were recorded on a Kratos MS-50TC instrument for matrices in thioglycerol.

X-ray diffraction data were collected using a Stoe-Stadi four circle diffractometer on single crystals grown from the stated crystallisation solvent.

Ultraviolet spectra were recorded in 95% ethanol using a Unicam UV2-

100 UV/visible spectrometer.

Elemental analysis were determined using Carlo-Erba Strumentazione 1106 or Perkin-Elmer 2400 elemental analysers. Routine melting points (m.p.) were carried out using a Gallenkamp apparatus and are uncorrected. Melting points of analytical samples were determined using a Kofler hot-stage apparatus and are uncorrected.

All reagents were laboratory grade unless specified. Sodium hydride was an 80% or 60% dispersion in mineral oil and was washed with anhydrous ether before use. Solvents were of technical grade unless otherwise stated and light petroleum had b.p. 60-80°.

Organic extracts were dried over anhydrous magnesium sulphate prior to filtration and rotary evaporation under reduced pressure. Atmospheric moisture was excluded from reaction mixtures using a guard-tube containing self-indicating silica gel (Fisons 6-16 mesh).

Wet column flash-chromatography was carried out over silica (Fluka Kieselgel 60, 220-440 mesh) or alumina (Merck Aluminium oxide 90, 70-230 mesh). Dry column flash-chromatography was carried out over silica (Fluka Kieselgel GF_{254}). Thin layer chromatography (t.l.c.) was carried out using Polygram SIL G/UV_{254} or Polygram $ALOXN/UV_{254}$ precoated plastic sheets.

Anhydrous Solvents

Solvents were dried as described below.

1. Acetonitrile, dimethylformamide, dichloromethane, and chloroform were

distilled and stored over anhydrous 4 Å molecular sieves.

2. 1,4-Dioxane and 1,2-dimethoxyethane were distilled from calcium hydride and stored over 4 Å molecular sieves.
3. Xylene was distilled and stored over sodium wire.
4. Benzene, ether and toluene were dried with sodium wire.
5. Ethanol was distilled from magnesium and iodine and stored over 4 Å molecular sieves.

Elemental Analyses and Mass Spectroscopic Data

Elemental analyses and mass spectroscopic data are collected in Table 7; Page 243 - 245.

2-Bromo-2,2-diphenylacetaldehyde (112a)

(a) A solution of 2,2-diphenylacetaldehyde (145) (19.6 g; 0.1 mol) in carbon disulphide (450 ml) was stirred mechanically and treated dropwise at room temperature with the exclusion of atmospheric moisture with a solution of bromine (16.0 g; 0.01 mol) in carbon disulphide (50.0 ml). The resulting red solution was then stirred mechanically at room temperature with the exclusion of atmospheric moisture for a further 1 h after the addition was complete.

The red solution was treated with 1% w/v aqueous sodium thiosulphate solution (200 ml) and the carbon disulphide layer was separated and rotary evaporated to yield 2-bromo-2,2-diphenylacetaldehyde (112a) as a yellow solid (25.7 g; 93%), m.p. 53-54° (from light petroleum), υ_{max} 1725 (C=O) cm^{-1},

$\delta_H(CDCl_3)$ 9.72(1H, s, CHO) and 7.35(10H, m, ArH).

(b) A solution of 2,2-diphenylacetaldehyde (145) (7.8 g; 0.04 mol) in anhydrous ether (160 ml) was stirred mechanically and treated dropwise at room temperature with the exclusion of atmospheric moisture with a solution of bromine (6.4 g; 0.04 mol) in anhydrous ether (40.0 ml). The resulting pale yellow solution was then stirred mechanically at room temperature with the exclusion of atmospheric moisture for a further 1 h after the addition was complete.

The pale yellow solution was treated with 1% w/v aqueous sodium thiosulphate solution (80.0 ml) and extracted with ether to yield 2-bromo-2,2-diphenylacetaldehyde (112a) as a yellow oil (10.9 g; 99%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared in (a) before.

(c) A solution of 2,2-diphenylacetaldehyde (145) (19.6 g; 0.1 mol) in anhydrous dichloromethane (350 ml) was stirred mechanically and treated dropwise at room temperature with the exclusion of atmospheric moisture with a solution of bromine (24.0 g; 0.15 mol) in anhydrous dichloromethane (150 ml). The resulting red solution was then stirred mechanically at room temperature with the exclusion of atmospheric moisture for a further 1 h after the addition was complete.

The red solution was treated with 1% w/v aqueous sodium thiosulphate

solution (300 ml) and extracted with dichloromethane to yield 2-bromo-2,2-diphenylacetaldehyde (112a) as a yellow solid (27.5 g; 100%), m.p. 53-54°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Sodium 2-Nitrophenolate

A stirred suspension of sodium hydride (1.9 g; 0.08 ml) in anhydrous 1,2-dimethoxyethane (40.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (12.2 g; 0.088 mol) in anhydrous 1,2-dimethoxyethane (40.0 ml). Vigorous gas evolution occurred and the suspension became red in colour. A further quantity of anhydrous 1,2-dimethoxyethane (10.0 ml) was added to aid stirring and the red suspension was stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The red suspension was rotary evaporated to give a red solid which was washed with ether and collected to afford sodium 2-nitrophenolate as a red solid (11.7 g; 91%), m.p. >300°, υ_{max}1510 and 1335(NO_2) cm^{-1}.

Benzyltriethylammonium 2-Nitrophenolate (116)

A stirred solution of benzyltriethylammonium chloride (4.6 g; 0.02 mol) in water (10.0 ml) was treated with a solution of sodium 2-nitrophenolate (4.8 g; 0.03 mol) in water (10.0 ml) and the resulting red mixture was stirred at room temperature for 10 min.

The aqueous mixture was extracted continuously with dichloromethane

for 23 h to give benzyltriethylammonium 2-nitrophenolate (116) as a red oil (6.6 g; 100%).

The aqueous layer was acidified with 2 M aqueous hydrochloric acid (15.0 ml) and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (1.1 g; 23%), m.p. 43-45°, identical (m.p. and i.r. spectrum) to an authentic sample.

2,2-Diphenyl-2-(2-nitrophenoxy)acetaldehyde (113a)

(a) A stirred suspension of sodium hydride (0.55 g; 0.023 mol) in anhydrous dimethylformamide (10.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.02 mol) in anhydrous dimethylformamide (20.0 ml). The resulting orange suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min. A solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (5.5 g; 0.02 mol) in anhydrous dimethylformamide (10.0 ml) was added in one portion and the resulting mixture was stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with water (20.0 ml) and extracted with dichloromethane to give a brown waxy solid (6.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) afforded a yellow oil (0.62 g) which was identified as a mixture of benzophenone and 2-bromo-2,2-

diphenylacetaldehyde (112a) by comparison [t.l.c. in hexane-ether (4:1) over silica] with authentic samples.

Further elution with hexane-ether (19:1) afforded 2,2-diphenyl-2-(2-nitrophenoxy)acetaldehyde (113a) as a colourless crystalline solid (4.6 g; 69%), m.p. 77-78° (from light petroleum-toluene), υ_{max}1730(C=O) and 1525 and 1355(NO_2) cm^{-1}, δ_H($CDCl_3$) 9.93(1H, s, CHO) and 7.83-6.60(14H, m, ArH).

Further elution with hexane-ether (19:1) through to ether gave only a series of multicomponent brown oils (total 0.21 g) which were not investigated further.

Final elution with methanol gave a negligible amount of material.

(b) A stirred suspension of sodium hydride (0.77 g; 0.032 mol) in anhydrous 1,2-dimethoxyethane (16.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (4.9 g; 0.035 mol) in anhydrous 1,2-dimethoxyethane (16.0 ml) to give a red solution which quickly formed a thick semi-solid. Anhydrous 1,2-dimethoxyethane (20.0 ml) was added and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The mixture was then rotary evaporated to give the sodium phenolate as a red solid (5.2 g; 0.032 mol). This was dissolved in water (36.0 ml) and the solution was added at room temperature to a stirred solution of benzyltriethylammonium chloride (3.6 g; 0.016 mol) in water (8.0 ml). The resulting deep red mixture was stirred at room temperature for 10 min.

The mixture was extracted with dichloromethane then chloroform to give the benzyltriethylammonium phenolate (116) as a brown oil (2.3 g; 0.007 mol).

The benzyltriethylammonium phenolate (116) (1.6 g; 0.005 mol) was dissolved in dichloromethane (16.0 ml) and the solution was cooled to 0°C (ice-salt bath) and treated dropwise with stirring with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (0.69 g; 0.025 mol) in dichloromethane (4.0 ml). The resulting mixture was then stirred and heated under reflux for 1 h to give an orange solution.

The orange solution was rotary evaporated and the residue was treated with 2 M aqueous hydrochloric acid (2.5 ml); water (10.0 ml) and extracted with dichloromethane to give a brown oil (1.0 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) afforded the nitrophenoxydiphenylacetaldehyde (113a) as a yellow solid (0.41 g; 49%) , m.p. 76-78°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Further elution with hexane-ether (19:1) through to ether gave only a series of multicomponent orange oils (total 0.40 g) which were not investigated further.

Final elution with methanol gave only a negligible quantity of a brown gum.

(c) A stirred solution of benzyltriethylammonium 2-nitrophenolate (116)

(3.3 g; 0.01 mol) in dichloromethane (20.0 ml) was cooled to 0° (ice-salt bath) and treated dropwise with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (2.7 g; 0.01 mol) in dichloromethane (20.0 ml). The orange mixture was then stirred and heated under reflux for 1 h.

The mixture was allowed to cool and rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (5.0 ml) then water (20.0 ml) and extracted with dichloromethane to give a yellow waxy solid (2.9 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) afforded unreacted 2-bromo-2,2-diphenylacetaldehyde (112a) as a pale yellow oil (0.51 g; 18%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared before.

Elution with hexane-dichloromethane (3:2) afforded the nitrophenoxydiphenylacetaldehyde (113a) as a pale yellow solid (1.4 g; 42%), m.p. 68-74°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared in (a) before.

Further elution with hexane-dichloromethane (1:1) and then dichloromethane gave only a series of multicomponent solids (total 0.53 g) from which no identifiable material was obtained.

Final elution with methanol gave no further material.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave 2-nitrophenol (111) as an orange solid (0.28 g; 20%), m.p. 38-42°, identified by comparison (m.p.

and i.r. spectrum) with an authentic sample.

Attempted Reduction Reactions of 2,2-Diphenyl-2-(2-nitrophenoxy)acetaldehyde (113a)

(a) A stirred solution of the nitrophenoxydiphenylacetaldehyde (113a) (0.67 g; 0.002 mol) in ethanol (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.067 g) at room temperature and atmospheric pressure for 3 h.

The mixture was then filtered through celite and the filtrate rotary evaporated to give a brown foam which was crystallised from toluene-light petroleum to give the unreacted nitrophenoxydiphenylacetaldehyde (113a) as a brown solid (0.59 g; 88%), m.p. 77-78°, identical (m.p. and i.r. spectrum) to an authentic sample prepared before.

(b) A stirred solution of the nitrophenoxydiphenylacetaldehyde (113a) (0.67 g; 0.002 mol) in glacial acetic acid (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.067 g) at room temperature and atmospheric pressure for 6 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give the unreacted nitrophenoxydiphenylacetaldehyde (113a) as a brown solid (0.67 g; 100%), m.p. 77-78°, identical (m.p. and i.r. spectrum) to an authentic sample.

(c) A stirred solution of the nitrophenoxydiphenylacetaldehyde (113a)

(0.43 g; 0.0013 mol) in ethanol (20.0 ml) containing concentrated hydrochloric acid (0.25 ml) was hydrogenated over 10% palladium-on-charcoal (0.043 g) at room temperature and atmospheric pressure for 2.5 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a several component brown gum (0.42 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through to ether and then finally with methanol, gave only a series of complex, multicomponent oils and gums (total 0.40 g) from which no identifiable material could be identified.

(d) A pale yellow solution of the nitrophenoxydiphenylacetaldehyde (113a) (0.67 g; 0.002 mol) in 70% v/v aqueous ethanol (20.0 ml) was stirred and treated with sodium dithionite (0.67 g) and the mixture was heated under reflux for 1 h. A further portion of sodium dithionite (0.67 g) was added and the mixture was then stirred and heated under reflux for a further 1 h.

The mixture was rotary evaporated to give a yellow semisolid which was treated with water (5.0 ml) and extracted with dichloromethane to give a brown foam (0.45 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave a several component brown oil (0.14 g) which was not further investigated.

Further elution with hexane-ethyl acetate (19:1) through to ethyl acetate gave only a series of multicomponent brown solids (total 0.17 g) which were not further investigated.

Final elution with methanol gave only a multicomponent glass (0.10 g) which was not further investigated.

Rotary evaporation of the aqueous mother liquor gave a residue which was extracted with refluxing ethyl acetate to afford only a multicomponent brown gum (0.15 g) which was not further investigated.

(e) A stirred solution of the nitrophenoxydiphenylacetaldehyde (113a) (0.67 g; 0.002 mol) in anhydrous ethanol (10.0 ml) under nitrogen was treated with a single portion of tin(II) chloride dihydrate (2.3 g; 0.01 mol). The mixture was then stirred and heated at 70° (oil-bath) under nitrogen for 0.5 h.

The mixture was poured on to ice (10.0 g) and adjusted to pH≅7 by the addition of 5% w/v aqueous sodium hydrogen carbonate solution. Extraction with ethyl acetate gave a multicomponent light brown solid (0.63 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through to ether and finally methanol gave only a series of multicomponent solids and gums (total 0.46 g) from which no identifiable material was obtained.

(f) A stirred solution of the nitrophenoxydiphenylacetaldehyde (113a) (0.67 g; 0.002 mol) in tetrahydrofuran (10.0 ml) under nitrogen was treated at room temperature with a 15% w/v aqueous solution of titanium(III) chloride (20.0 ml; 0.02 mol) added in several portions. The resulting purple suspension was then stirred at room temperature under nitrogen for 26 h.

The purple suspension was concentrated by rotary evaporation to *ca* two thirds of the original volume and the residue was cooled in an ice bath and made basic by the cautious addition of 50% w/v aqueous sodium hydroxide solution (10.0 ml). The resulting suspension was then diluted with water (10.0 ml) and extracted with dichloromethane to give a multicomponent pale brown solid (0.52 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through ether to methanol gave only a series of multicomponent solids and gums (total 0.31 g) which yielded not identifiable material.

(g) Repetition of the reaction described in (f) before but at room temperature for 64 h gave a purple suspension which was concentrated by rotary evaporation to *ca* two-thirds of the original volume. The resulting aqueous residue was cooled in an ice-bath and made basic by the cautious addition of 50% w/v aqueous sodium hydroxide solution (10.0 ml). The resulting suspension was then diluted with water (10.0 ml) and extracted with dichloromethane to give a multicomponent brown gum (0.44 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol, gave only a series of complex, multicomponent oils and gums (total 0.29 g) from which no identifiable material could be obtained.

2-Bromo-2-methylpropionaldehyde (112b)

2-Bromo-2-methylpropionaldehyde (112b) was prepared by the reaction of 2-methylpropionaldehyde with bromine as described by Beckwith and Thomas,[105] as a yellow oil (yield 94%), υ_{max}1725(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 9.34(1H, s, CHO) and 1.78(6H, s, 2xCH_3).

2-Methyl-2-(2-nitrophenoxy)propionaldehyde (113b)

(a) A stirred suspension of sodium hydride (0.53 g; 0.023 mol) in anhydrous dimethylformamide (10.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.02 mol) in anhydrous dimethylformamide (10.0 ml). The resulting orange suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min. A solution of 2-bromo-2-methylpropionaldehyde (112b) (4.2 g; 0.028 mol) in anhydrous dimethylformamide (20.0 ml) was then added in one portion and the resulting mixture was stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with water (20.0 ml) and 2 M aqueous sodium hydroxide solution (10.0 ml) and extracted with dichloromethane to give a light brown oil (2.7 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave 2-methyl-2-(2-nitrophenoxy)propionaldehyde (113b) as a yellow oil (1.1 g; 26%), b.p.

70°/1 mm Hg, υ_{max}1740(C=O) and 1530 and 1355(NO_2) cm^{-1}, δ_H($CDCl_3$) 9.82(1H, s, CHO), 7.82-6.86(4H, m, ArH) and 1.48(6H, s, 2xCH_3).

Elution with hexane-ethyl acetate (4:1) through to ethyl acetate and finally methanol gave only a series of multicomponent oils and solids (total 0.45 g) from which no identifiable material could be obtained.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give 2-nitrophenol (111) as a yellow oil (1.6 g; 57%), identified by comparison [i.r. spectrum and t.l.c. in hexane dichloromethane (1:1) over silica] with an authentic sample.

(b) A stirred suspension of sodium hydride (0.53 g; 0.023 mol) in anhydrous dimethylformamide (10.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.02 mol) in anhydrous dimethylformamide (20.0 ml). The resulting orange suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min. A solution of 2-bromo-2-methylpropionaldehyde (112b) (6.0 g; 0.04 mol) in anhydrous dimethylformamide (20.0 ml) was then added in one portion and the resulting mixture was stirred at room temperature with the exclusion of atmospheric moisture for 24 h.

The resulting orange mixture was diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated and the residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give 2-methyl-2-(2-

nitrophenoxy)propionaldehyde (113b) as a yellow oil (2.4 g; 57%), $\delta_H(CDCl_3)$ 9.81(1H, s, CHO), 7.81-6.85(4H, m, ArH) and 1.47(6H, s, 2xCH_3), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (1:1) over silica] with a sample prepared in (a) before.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give 2-nitrophenol(111) as a yellow solid (1.2 g; 43%), m.p. 40-42°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(c) Repetition of the reaction described in (b) before but at room temperature for 48 h gave an orange mixture which was diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated and the residue treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give 2-methyl-2-(2-nitrophenoxy)propionaldehyde (113b) as a yellow oil (1.7 g; 41%), identical [i.r. spectrum and t.l.c. in hexane-ethylacetate (1:1) over silica] to a sample prepared in (a) before.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give 2-nitrophenol(111) as a yellow solid (1.4 g; 50%), m.p. 40-45°, identical (m.p. and i.r. spectrum) to an authentic sample.

Attempted Reduction Reactions of 2-Methyl-2-(2-nitrophenoxy)propionaldehyde (113b)

(a) A stirred solution of 2-methyl-2-(2-nitrophenoxy)propionaldehyde (113b) (0.84 g; 0.004 mol) in ethanol (30.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.084 g) at room temperature and atmospheric pressure for 7.5 h.

The mixture was then filtered through celite and rotary evaporated to give a multicomponent dark brown gum (0.79g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through to ether and then finally methanol, gave only a series of complex, multicomponent oils and gums (total 0.71 g) from which no identifiable material could be obtained.

(b) A stirred solution of 2-methyl-2-(2-nitrophenoxy)propionaldehyde (113b) (0.84 g; 0.004 mol) in anhydrous ethanol (20.0 ml) under nitrogen was treated with a single portion of tin(II) chloride dihydrate (4.6 g; 0.02 mol). The mixture was then stirred and heated at 70° (oil bath) under nitrogen for 0.5 h.

The mixture was poured on to ice (20.0 g) and adjusted to pH≅7 by the addition of 5% w/v aqueous sodium hydrogen carbonate solution. Extraction with ethyl acetate gave a multicomponent brown gum (0.61 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through to ether and then finally methanol, gave only a series of complex, multicomponent oils and gums (total

0.56 g) from which no identifiable material could be obtained.

(c) A stirred solution of 2-methyl-2-(2-nitrophenoxy)propionaldehyde (113b) (0.84 g; 0.004 mol) in tetrahydrofuran (20.0 ml) under nitrogen was treated at room temperature with a 15% w/v aqueous solution of titanium(III) chloride (40.0 ml; 0.04 mol) added in several portions. The resulting purple suspension was then stirred at room temperature under nitrogen for 48 h.

The purple suspension was concentrated by rotary evaporation to *ca* two-thirds of the original volume and the residue was cooled in an ice bath and made basic by the cautious addition of 50% w/v aqueous sodium hydroxide solution (30.0 ml). The resulting suspension was then diluted with water (20.0 ml) and extracted with dichloromethane to give a multicomponent brown gum (0.80 g) which was not investigated further.

Ethyl 2-Chloro-2,2-diphenylacetate (117a)

2-Chloro-2,2-diphenylacetyl chloride (3.6 g; 0.013 mol) was added in small portions to anhydrous ethanol (50.0 ml) and the colourless solution was stirred at room temperature with the exclusion of atmospheric moisture for 2 h. The colourless solution was rotary evaporated to give a colourless oil (3.9 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) afforded ethyl 2-chloro-2,2-diphenylacetate (117a) as a colourless solid (3.2 g; 90%), m.p. 52-54°, b.p. 150-156°/2 mm Hg, υ_{max}1730(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 7.46-7.24(10H, m, ArH),

4.30(2H, q, J7Hz, CH_2) and 1.25(3H, t, J7Hz, CH_3),

Elution with hexane-dichloromethane (7:3) through dichloromethane to methanol gave no other identifiable material.

Ethyl 2,2-Diphenyl-2-(2-nitrophenoxy)acetate (119a)

(a) A stirred suspension of sodium hydride (0.14 g; 0.0058 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 2-nitrophenol(111) (0.70 g; 0.005 mol) in anhydrous dimethylformamide (10.0 ml). The resulting orange suspension was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of the chloro ester (117a) (1.4 g; 0.005 mol) in anhydrous dimethylformamide (5.0 ml). The mixture was then stirred and heated at 100° with the exclusion of atmospheric moisture for 1 h.

The resulting dark brown mixture was allowed to cool and was diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated and the residue treated with 2 M aqueous sodium hydroxide (2.5 ml) and water (5.0 ml). Extraction with dichloromethane gave a brown gum (1.4 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) afforded unreacted chloro ester (117a) as a colourless solid (0.80 g; 57%), m.p. 49-52°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared previously.

Elution with hexane-dichloromethane (7:3) gave ethyl 2,2-diphenyl-2-(2-

nitrophenoxy)acetate (119a) as a pale yellow oil (0.21 g; 11%), b.p. 100-110°/0.2 mm Hg, υ_{max}1740 (C=O) and 1530 and 1350 (NO_2) cm^{-1}, $\delta_H(CDCl_3)$ 7.81-6.89(14H, m, ArH), 4.16(2H, q, J7Hz, CH_2) and 1.02(3H, t, J7Hz, CH_3),

Elution with hexane-dichloromethane (3:2) through dichloromethane to methanol gave only a series of intractable gums (total 0.040 g).

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (0.47 g; 67%), m.p. 40-44°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) Repetition of the reaction described in (a) but at 100° for 17 h gave a dark brown mixture which was allowed to cool, diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.5 ml) and water (5.0 ml) and extracted with dichloromethane to give a brown gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) afforded the unreacted chloro ester (117a) as a colourless solid (0.55 g; 39%), m.p. 39-43°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared previously.

Elution with hexane-dichloromethane (7:3) gave the nitrophenoxy ester (119a) as a pale yellow oil (0.75 g; 39%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared in (a) before.

Elution with hexane-dichloromethane (3:2) through to dichloromethane

gave negligible material.

Final elution with methanol gave an intractable brown gum (0.12 g).

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (0.42 g; 60%), m.p. 41-44°; identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(c) Repetition of the reaction described in (a) before but under reflux for 17 h gave a dark brown mixture which was allowed to cool, diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.5 ml) and water (5.0 ml) and extracted with dichloromethane to give a brown gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) afforded the unreacted chloro ester (117a) as a colourless solid (1.1 g; 79%), m.p. 39-43°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared before.

Elution with hexane-dichloromethane (7:3) gave the nitrophenoxy ester (119a) as a pale yellow oil (0.35 g; 18%), identical [i.r. spectrum and t.l.c. in hexane-methylene chloride (1:1) over silica] to a sample prepared in (a) before.

Elution with hexane-dichloromethane (3:2) through to dichloromethane gave negligible material.

Final elution with methanol gave an intractable brown gum (0.097 g).

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric

acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (0.51 g; 73%), m.p. 39-43°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The Attempted Reduction of Ethyl 2,2-Diphenyl-2-(2-nitrophenoxy)acetate (119a)

A stirred solution of the nitrophenoxy ester (119a) (0.38 g, 0.001 mol) in ethanol (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.038 g) at room temperature and atmospheric pressure for 4 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a dark brown oil (0.32 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave an unidentified yellow oil (0.12 g).

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of multicomponent oils and gums (total 0.15 g).

Ethyl 2-Methyl-2-(2-nitrophenoxy)propionate (119b)

(a) A stirred suspension of sodium hydride (0.53 g; 0.023 mol) in anhydrous dimethylformamide (10.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.02 mol) in anhydrous dimethylformamide (10.0 ml). The resulting orange suspension was stirred at

room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of ethyl 2-bromo-2-methylpropionate (117b) (3.9 g; 0.02 mol) in anhydrous dimethylformamide (20.0 ml). The resulting mixture was then stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool and was diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give ethyl 2-methyl-2-(2-nitrophenoxy)propionate (119b) as a yellow oil (0.66 g; 13%), b.p. 110-120°/1 mm Hg, υ_{max}1735(C=O) and 1540 and 1360(NO_2) cm^{-1}; δ_H($CDCl_3$) 7.71(1H, dd, J_{ortho} 8Hz, J_{meta} 2Hz, ArH), 7.44-7.35(1H, m, ArH), 7.25-6.91(2H, m, ArH), 4.21(2H, q, J7Hz, CH_2), 1.61(6H, s, 2xCH_3) and 1.22(3H, t, J7Hz, CH_3).

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (1.7 g; 60%), m.p. 43-45°, identical (m.p. and i.r. spectrum) to an authentic sample.

(b) Repetition of the reaction described in (a) before but at 100° for 15 h gave a mixture which was allowed to cool, diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (20.0 ml) and extracted with dichloromethane to give ethyl 2-methyl-2-(2-

nitrophenoxy)propionate (119b) as a yellow oil (0.79 g; 16%), b.p. 110-120°/1 mm Hg, identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared in (a) before.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (1.8 g; 64%), m.p. 43-45°, identical (m.p. and i.r. spectrum) to an authentic sample.

(c) A stirred suspension of sodium hydride (0.53 g; 0.023 mol) in anhydrous dimethylformamide (10.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.02 mol) in anhydrous dimethylformamide (10.0 ml). The resulting orange suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of ethyl 2-bromo-2-methylpropionate (117b) (7.8 g; 0.04 mol) in anhydrous dimethylformamide (40.0 ml). The resulting mixture was then stirred at 100° (oil-bath) with the exclusion of atmospheric moisture for 15 h.

The mixture was allowed to cool and was diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The resulting residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give a brown oil (4.3 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:2) gave a multicomponent

yellow oil (0.056 g) which was not investigated further.

Further elution with hexane-dichloromethane (1:1) gave ethyl 2-methyl-2-(2-nitrophenoxy)propionate (119b) as a yellow oil (1.7 g; 33%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared in (a) before.

Elution with hexane-dichloromethane (2:3) through dichloromethane to methanol gave only a series of multicomponent oils (total 2.5 g) from which no identifiable material was obtained.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (1.2 g; 43%), m.p. 43-45°, identical (m.p. and i.r. spectrum) to an authentic sample.

(d) A stirred suspension of sodium hydride (0.53 g; 0.023 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml). The resulting red suspension was stirred at room temperature with the exclusion of atmospheric moisture for 15 min then was treated in one portion with a solution of ethyl 2-bromo-2-methylpropionate (117b) (3.9 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (20.0 ml). The resulting mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, diluted with water (2.0 ml) and stirred

at room temperature for 15 min then rotary evaporated. The resulting residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give unreacted ethyl 2-bromo-2-methylpropionate (117b) as a yellow oil (2.0 g; 51%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to an authentic sample.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (2.8 g; 100%), m.p. 44-46°, identical (m.p. and i.r. spectrum) to an authentic sample.

(e) Repetition of the reaction described in (d) before but under reflux for 18 h gave a mixture which was allowed to cool and diluted with water (2.0 ml), stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give unreacted ethyl 2-bromo-2-methylpropionate (117b) as a yellow oil (0.73 g; 19%), identified by comparison [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to an authentic sample.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (2.8 g; 100%), m.p. 38-42°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(f) A stirred suspension of sodium hydride (0.53 g; 0.023 mol) in anhydrous dimethylformamide (10.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitrophenol (111) (2.8 g; 0.002 mol) in anhydrous dimethylformamide (10.0 ml). The resulting orange suspension was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then treated in one portion with a solution of ethyl 2-bromo-2-methylpropionate (117b) (3.9 g; 0.02 mol) in anhydrous dimethylformamide (20.0 ml). The resulting mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, diluted with water (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The resulting residue was treated with 2 M aqueous sodium hydroxide (10.0 ml) and water (10.0 ml) and extracted with dichloromethane to give an intractable yellow oil (2.9 g) which yielded no identifiable material.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitrophenol (111) as a yellow solid (2.1 g; 75%), m.p. 43-45°, identical (m.p. and i.r. spectrum) to an authentic sample.

2,2-Dimethyl-3,4-dihydro-2H-benzoxazin-3(4H)-one (123)

(a) A stirred solution of ethyl 2-methyl-2-(2-nitrophenoxy)propionate (119b) (0.51 g; 0.002 mol) in ethanol (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.051 g) at room temperature and atmospheric

pressure for 2 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a light brown solid (0.41 g) which was crystallised to afford 2,2-dimethyl-3,4-dihydro-2H-benzoxazin-3(4H)-one (123) as off-white crystals (0.26 g; 73%), m.p. 162-163° (from light petroleum), υ_{max}1680(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 8.27(1H, s, NH) (exch.), 6.96-6.69(4H, m, ArH), 1.63(3H, s, CH_3) and 1.24(3H, s, CH_3).

(b) A stirred solution of ethyl 2-methyl-2-(2-nitrophenoxy)propionate (119b) (0.51 g; 0.002 mol) in 70% v/v aqueous ethanol (10.0 ml) was treated with sodium dithionite (0.51 g) added in one portion and the mixture was stirred under reflux for 1 h. A further portion of sodium dithionite (0.51 g) was then added and the mixture was stirred under reflux for a further 1 h.

The mixture was allowed to cool, then rotary evaporated and the residue treated with water (10.0 ml) and extracted with dichloromethane to give 2,2-dimethyl-3,4-dihydro-2H-benzoxazin-3(4H)-one (123) as an off-white solid (0.33 g; 93%), m.p. 153-156°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared in (a) before.

2-Formamidophenol (125)

2-Aminophenol (124) (55.0 g; 0.5 mol) was treated with 98% formic acid (65.0 ml) and the dark mixture was mechanically stirred and heated under reflux with the exclusion of atmospheric moisture for 1.5 h.

The dark mixture was rotary evaporated to give a brown solid (79.1 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (1:1) gave 2-formamidophenol (125) as a brown solid (53.3 g, 78%), m.p. 125-129°, (lit.,[107] 129-130°).

Further elution with hexane-ethyl acetate (1:1) through ethylacetate to methanol gave only a series of dark brown intractable gums (total 5.2 g) which were not investigated further.

2,2-Diphenyl-2-(2-formamidophenoxy)acetaldehyde (126a)

A stirred suspension of sodium hydride (0.80 g; 0.033 mol) in anhydrous dimethylformamide (15.0 ml) was cooled to 10° (ice-bath) then treated dropwise with a solution of 2-formamidophenol (125) (4.2 g; 0.03 mol) in anhydrous dimethylformamide (45.0 ml). Vigorous gas evolution occurred and the mixture turned brown. The mixture was stirred at room temperature for 15 min with the exclusion of atmospheric moisture and then treated dropwise at room temperature with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (8.3 g; 0.03 mol) in anhydrous dimethylformamide (15.0 ml). The mixture was then stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, diluted with water (6.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The resulting residue was treated with 2 M aqueous sodium hydroxide (15.0 ml) and water (15.0 ml) and extracted with dichloromethane to give a brown gum (9.9 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) afforded benzophenone as a brown oil (0.71 g; 13%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica] with an authentic sample.

Elution with hexane-ethyl acetate (3:2) afforded 2,2-diphenyl-2-(2-formamidophenoxy) acetaldehyde (126a) as an orange foam (7.7 g; 78%), m.p. 59-62°, υ_{max}3400-3300(NH) and 1670-1650(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 8.70(1H, s, CHO) 7.71-7.59(2H, m, CHO and NH) and 7.48-6.97(14H, m, ArH).

Further elution with hexane-ethyl acetate (1:1) through to ethyl acetate gave negligible material.

Final elution with methanol gave only an intractable brown gum (0.40 g).

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave unreacted impure 2-formamidophenol (125) as a brown gum (0.50 g; 12%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica] with a sample prepared previously.

2,2-Diphenyl-2H-benz-1,4-oxazine (115a)

A stirred solution of 2,2-diphenyl-2-(2-formamidophenoxy)acetaldehyde (126a) (6.6 g; 0.02 mol) in ethanol (20.0 ml) was treated with 2 M aqueous sodium hydroxide solution (20.0 ml) added in one portion and the mixture was stirred under reflux for 0.5 h.

The mixture was cooled and rotary evaporated to give a brown residue which was treated with water (20.0 ml) and extracted with dichloromethane to give a brown solid. This was washed with ethanol to afford 2,2-diphenyl-2H-benz-1,4-oxazine (115a) as a light brown solid (4.5 g; 79%), m.p. 87-88° (from light petroleum), υ_{max}1616(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 7.99(1H, s, CH) and 7.51-6.82(14H, m, ArH).

Rotary evaporation of the ethanol mother liquor gave an intractable brown gum (0.69 g) which was not investigated further.

3,4-Dihydro-2,2-diphenyl-2H-benz-1,4-oxazine (127a)

A stirred solution of 2,2-diphenyl-2H-benz-1,4-oxazine (115a) (1.1 g; 0.004 mol) in methanol (20.0 ml) was treated dropwise over 15 min at room temperature with a solution of sodium borohydride (0.67 g; 0.018 mol) in water (10.0 ml). The mixture which contained a colourless precipitate was stirred at room temperature for 3 h.

The mixture was rotary evaporated and the residue was treated with water (20.0 ml) and extracted with dichloromethane to afford 3,4-dihydro-2,2-diphenyl-2H-benz-1,4-oxazine (127a) (1.1 g; 96%), which formed colourless

plates, m.p. 125-126° (from ethanol), υ_{max}3383(NH) cm^{-1}, $\delta_H(CDCl_3)$ 7.53-6.51(14H, m, ArH), 3.86(2H, s, CH_2) and 3.75(1H, bs, NH) (exch.).

The Oxidation of 3,4-Dihydro-2,2-diphenyl-2H-benz-1,4-oxazine (127a)

A stirred solution of the dihydro compound (127a) (0.57 g; 0.002 mol) in anhydrous acetonitrile (20.0 ml) was treated with activated manganese(IV) oxide (1.0 g) added in one portion. The suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a brown gum (0.57 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (7:3) gave a multicomponent grey solid (0.093 g), which was not investigated further.

Further elution with hexane-dichloromethane (2:3) gave a multicomponent brown oil (0.12 g) which was not investigated further.

Elution with hexane-dichloromethane (1:9) afforded 2,2-diphenyl-2H-benz-1,4-oxazine (115a) as a brown solid (0.18 g; 32%), m.p. 79-82°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared previously.

Further elution with hexane-dichloromethane (1:9) and then finally with methanol gave only a series of multicomponent solids and gums (total 0.17 g), which were not investigated further.

3-Cyano-3,4-dihydro-2,2-diphenyl-2H-benz-1,4-oxazine (128a)

A stirred solution of 2,2-diphenyl-2H-benz-1,4-oxazine (115a) (1.1 g; 0.004 mol) in glacial acetic acid (10.0 ml) was treated with potassium cyanide (1.3 g; 0.02 mol) added in one portion and the mixture was stirred at room temperature for 6 h.

The mixture was rotary evaporated under high vacuum and the residue was treated with water (20.0 ml) and extracted with dichloromethane. The extracts were washed with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 10.0 ml) and rotary evaporated to give an orange foam which was crystallised to give 3-cyano-3,4-dihydro-2,2-diphenyl-2H-benz-1,4-oxazine (128a) as a colourless solid (0.92 g; 74%), m.p. 164-166° (from toluene), υ_{max}3394(NH) and 2235w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 7.67-6.49(14H, m, ArH), 5.20(1H, s, CH) and 4.37(1H, s, NH) (exch.).

3-Cyano-2,2-diphenyl-2H-benz-1,4-oxazine (129a)

A stirred solution of the dihydro compound (128a) (0.31 g; 0.001 mol) in anhydrous acetonitrile (10.0 ml) was treated with activated manganese(IV) oxide (0.5 g) added in one portion and the dark suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a yellow gum (0.38 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 3-cyano-2,2-diphenyl-2H-benz-

1,4-oxazine (129a) as a pale yellow solid (0.22 g; 71%), m.p. 104-105° (from toluene-light petroleum), υ_{max}2222w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 7.48-6.88(14H, m, ArH).

Further elution with hexane-ether (1:1) gave the unreacted impure cyano compound (128a) as a yellow foam (0.089 g; 29%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with a sample prepared previously.

Elution with hexane-ether (2:3) through ether to methanol afforded no further material.

2-Formamidophenoxy-2-methylpropionaldehyde (126b)

A stirred suspension of sodium hydride (1.3 g; 0.055 mol) in anhydrous dimethylformamide (20.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-formamidophenol (125) (6.9 g; 0.05 mol) in anhydrous dimethylformamide (60.0 ml). The brown mixture was then stirred at room temperature with the exclusion of atmospheric moisture for a further 15 min and then treated in one portion with a solution of 2-bromo-2-methylpropionaldehyde (112b) (15.1 g; 0.1 mol) in anhydrous dimethylformamide (40.0 ml). The resulting mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 24 h.

The dark brown mixture was diluted with water (5.0 ml) and stirred at room temperature for 15 min, then rotary evaporated. The residue obtained was treated with 2 M aqueous sodium hydroxide (25.0 ml) and water (25.0 ml)

and extracted with a dichloromethane to give a brown gum (9.2 g) which was washed with light petroleum to give 2-formamidophenoxy-2-methylpropionaldehyde (126b) (6.6 g; 64%) as a brown solid which formed pink microcrystals, m.p. 161-163° (from toluene-ethyl acetate), υ_{max}3406(NH) and 1670(C=O) cm^{-1}; $\delta_H(CDCl_3)$ 8.96(1H, s, CHO), 8.39-8.24(2H, m, CHO and NH) 7.10-6.59(4H, m, ArH), 1.42(3H, s, CH_3) and 1.07(3H, s, CH_3).

Rotary evaporation of the light petroleum washings gave only a multicomponent brown oil (1.1 g) which was not investigated further.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave unreacted 2-formamidophenol (125) as a waxy brown solid (1.0 g; 14%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (1:1) over silica] with a sample prepared previously.

2,2-Dimethyl-2H-benz-1,4-oxazine (115b)

A stirred solution of 2-formamidophenoxy-2-methylpropionaldehyde (126b) (6.2 g; 0.03 mol) in ethanol (60.0 ml) was treated with 2 M aqueous sodium hydroxide (30.0 ml) and the solution was stirred and heated under reflux for 0.5 h.

The mixture was cooled and rotary evaporated to give a dark residue which was treated with water (40.0 ml) and extracted with dichloromethane to give 2,2-dimethyl-2H-benz-1,4-oxazine (115b) as a brown oil (4.7 g; 97%), b.p. 58-62°/0.3 mm Hg, υ_{max}1596(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 7.43-6.78(5H, m, ArH and

CH) and 1.44(6H, s, 2xCH_3).

3,4-Dihydro-2,2-dimethyl-2H-benz-1,4-oxazine (127b)

A stirred solution of 2,2-dimethyl-2H-benz-1,4-oxazine (115b) (0.64 g; 0.004 mol) in methanol (20.0 ml) was treated dropwise at room temperature over 15 min with a solution of sodium borohydride (0.67 g; 0.018 mol) in water (10.0 ml). The mixture became cloudy and gas evolution occurred. The mixture was then stirred at room temperature for 3 h.

The mixture was rotary evaporated and the residue was treated with water (20.0 ml) and extracted with dichloromethane to give a brown oil (0.63 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (1:1) gave 3,4-dihydro-2,2-dimethyl-2H-benz-1,4-oxazine (127b) as a brown oil (0.36 g; 55%), b.p. 50-58°/0.2 mm Hg, υ_{max}3387(NH) cm^{-1}, δ_H($CDCl_3$) 6.81-6.56(4H, m, ArH), 3.08-3.06(3H, s, CH_2 and NH) and 1.33(6H, s, 2xCH_3).

Elution with hexane-dichloromethane (1:9) gave unreacted 2,2-dimethyl-2H-benz-1,4-oxazine (115b) as a brown oil (0.071 g; 11%), identified by comparison [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared previously.

Further elution with hexane-dichloromethane (1:9) through dichloromethane gave no further material.

Final elution with methanol gave an intractable brown gum (0.11 g).

The Oxidation of 3,4-Dihydro-2,2-dimethyl-2H-benz-1,4-oxazine (127b)

A stirred solution of the dihydro compound (127b) (0.16 g; 0.001 mol) in anhydrous acetonitrile (10.0 ml) was treated with activated manganese(IV) oxide (0.5 g) added in one portion. The suspension was then stirred at room temperature for 17 h.

The mixture was filtered through celite and rotary evaporated to give a dark brown waxy solid (0.26 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave a several component grey solid (0.071 g) from which no identifiable material was obtained.

Elution with hexane-ethyl acetate (8:2) gave 2,2-dimethyl-3,4-dihydro-2H-benzoxazin-3(4H)-one (123) as an off-white solid (0.14 g; 79%), m.p. 162-163°, identical (m.p. and i.r. spectrum) to a sample prepared before.

Further elution with hexane-ethyl acetate (7:3) through ethyl acetate to methanol gave no further identifiable material.

3-Cyano-3,4-dihydro-2,2-dimethyl-2H-benz-1,4-oxazine (128b)

A stirred solution of 2,2-dimethyl-2H-benz-1,4-oxazine (115b) (0.33 g; 0.002 mol) in glacial acetic acid (5.0 ml) was treated with potassium cyanide (0.52 g; 0.008 mol) added in a single portion and the red-brown mixture was stirred at room temperature for 2 h.

The mixture was rotary evaporated and the residue was treated with water (10.0 ml) and extracted with dichloromethane. The dichloromethane extracts were washed with 10% w/v aqueous sodium hydrogen carbonate (2

x 5.0 ml) and rotary evaporated to give 3-cyano-3,4-dihydro-2,2-dimethyl-2H-benz-1,4-oxazine (128b) as a brown oil (0.37 g; 98%), b.p. 144-150°/0.3 mm Hg, υ_{max} 3370(NH) and 2234w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 6.88-6.58(4H, m, ArH), 4.27(1H, bs, NH) (exch.), 4.01(1H, d, J3Hz, CH) collapses to a singlet on shaking with D_2O, 1.56(3H, s, CH_3) and 1.38(3H, s, CH_3).

3-Cyano-2,2-dimethyl-2H-benz-1,4-oxazine (129b)

A stirred solution of the dihydrocompound (128b) (0.19 g; 0.001 mol) in anhydrous acetonitrile (10.0 ml) was treated with activated manganese(IV) oxide (0.5 g) added in one portion and the suspension was stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was then filtered through celite and the filtrate was rotary evaporated to give a brown oil (0.21 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave 3-cyano-2,2-dimethyl-2H-benz-1,4-oxazine (129b) as a yellow solid (0.094 g; 51%), m.p. 58-60°, υ_{max}2222w (C≡N) cm^{-1}.

Elution with hexane-ethyl acetate (9:1) through ethyl acetate to methanol gave only a series of multicomponent oils (total 0.050 g) from which no identifiable material was obtained.

1-Nitro-2-naphthol (130)

A stirred solution of 1-nitroso-2-naphthol (72) (17.3 g; 0.1 mol) in glacial

acetic acid (300 ml) was carefully treated with 30% v/v aqueous hydrogen peroxide solution (100 ml) followed by concentrated (d = 1.42) nitric acid (20.0 ml). The mixture was stirred and slowly heated to 70° (oil-bath) over 15 min then stirred at 70° for a further 15 min.

The mixture was allowed to cool and was poured on to ice (500 g) and the solid collected and washed with water to give 1-nitro-2-naphthol (130) as a brown solid (9.1 g; 48%), m.p. 95-97° (lit.,[118] 103°).

The aqueous filtrate was extracted with dichloromethane and the combined extracts were washed with saturated aqueous sodium sulphite solution (200 ml) and rotary evaporated to give only an intractable brown gum (3.1 g).

2,2-Diphenyl-2-(1-nitronaphth-2-yl)oxyacetaldehyde (131a)

(a) A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 1-nitro-2-naphthol (130) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). The resulting red solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.1 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). The resulting mixture was then stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, treated with water (1.0 ml), stirred at

room temperature for 15 min then rotary evaporated. The residue was treated with 2M aqueous sodium hydroxide (2.0 ml) and water (10.0 ml) and extracted with dichloromethane to give a brown solid (1.2 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an intractable brown gum (0.11 g).

Further elution with hexane-ether (19:1) gave 2,2-diphenyl-2-(1-nitronaphth-2-yl)oxyacetaldehyde (131a) (0.24 g; 16%) which formed colourless microcrystals, m.p.148-152° (from toluene-light petroleum), υ_{max} 1736(C=O) and 1524 and 1350(NO_2) cm^{-1}, δ_H($CDCl_3$) 10.03(1H, s, CHO) and 7.83-7.25(16H, m, ArH).

Further elution with hexane-ether (19:1) through ether to methanol gave only a series of intractable gums (total 0.33 g) from which no identifiable material was obtained.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 1-nitro-2-naphthol (130) as a brown solid (0.16 g; 21%), m.p. 94-96°, identical (m.p. and i.r. spectrum) to an authentic sample.

(b) Repetition of the reaction described in (a) before but at 100° for 17 h gave a mixture which was allowed to cool, treated with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.0 ml) and water (10.0 ml)

and extracted with dichloromethane to give a brown gum(0.96 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) gave a pale brown solid (0.30 g) which was washed with ether to give 2,2-diphenyl-2-(1-nitronaphth-2-yl)oxyacetaldehyde (131a) as a pale brown solid (0.11 g; 7%), m.p. 147-150°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared in (a) before. Rotary evaporation of the ether washings gave only an intractable brown oil (0.19 g).

Further elution with hexane-dichloromethane (4:1) also gave an intractable brown gum (0.066 g).

Elution with hexane-dichloromethane (7:3) through dichloromethane to methanol gave only a series of multicomponent gums (total 0.44 g) from which no identifiable material was obtained.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 1-nitro-2-naphthol (130) as a brown solid (0.37 g; 49%), m.p. 90-94°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

2-Methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b)

(a) A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 1-nitro-2-naphthol (130) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting red solution was

stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then treated in one portion with a solution of 2-bromo-2-methylpropionaldehyde (112b) (1.3 g; 0.008 mol) in anhydrous dimethylformamide (10.0 ml). The resulting mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 24 h.

The mixture was diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated and the residue treated with 2 M aqueous sodium hydroxide solution (2.0 ml) and water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a brown solid (0.37 g) which was acidified with 2 M aqueous hydrochloric acid to give 1-nitro-2-naphthol (130) as a brown solid (0.22 g; 29%), m.p. 99-103°, identical (m.p. and i.r. spectrum) to an authentic sample.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give 2-methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b) as a brown oil (0.47 g; 45%), b.p. 122-132°/1.5 mm Hg, υ_{max} 1736(C=O) and 1532 and 1358(NO_2) cm^{-1}, δ_H($CDCl_3$) 10.93(1H, s, CHO), 7.88(1H, d, J3Hz, ArH), 7.88(1H, d, J3Hz, ArH), 7.67-7.47(4H, m, ArH) and 1.51(6H, s, 2xCH_3).

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give a second crop of 1-nitro-2-naphthol (130) as a brown solid (0.18 g; 24%), m.p. 95-97°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) Repetition of the reaction described in (a) before but using four equivalents of 2-bromo-2-methylpropionaldehyde (112b) gave after similar work up of the mixture 2-methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b) as a brown oil (0.43 g; 41%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to an authentic sample prepared in (a) before, together with unreacted 1-nitro-2-naphthol (130) (0.43 g; 56%), m.p. 95-97°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(c) Repetition of the reaction described in (a) before but using four equivalents of 2-bromo-2-methylpropionaldehyde (112b) and an increase in the reaction time to 48 h gave, after similar workup of the mixture, 2-methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b) as a brown oil (0.76 g; 73%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to an authentic sample prepared in (a) before, together with unreacted 1-nitro-2-naphthol (130) as a brown solid (0.21 g; 27%), m.p. 96-97°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Attempted Reduction Reactions of 2-Methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b)

(a) A stirred solution of 2-methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b) (0.52 g; 0.002 mol) in ethanol (30.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.052 g) at room temperature and atmospheric pressure for 5 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give the unreacted 2-methyl-2-(1-nitronaphth-2-yl) oxypropionaldehyde (131b) as a brown oil (0.51 g; 98%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over alumina] to an authentic sample.

(b) A stirred solution of 2-methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b) (1.0 g; 0.004 mol) in glacial acetic acid (15.0 ml) was hydrogenated over raney nickel (0.20 ml; 0.10 g) at room temperature and atmospheric pressure for 5 h. A further portion of raney nickel (0.20 ml; 0.10 g) was added and the mixture was hydrogenated at room temperature and atmospheric pressure for a further 3 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a multicomponent brown solid (1.0 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) through ethyl acetate to methanol gave only a series of multicomponent gums and solids (total 0.71 g) from which no identifiable material was obtained.

(c) A stirred solution of 2-methyl-2-(1-nitronaphth-2-yl)oxypropionaldehyde (131b) (0.52 g; 0.002 mol) in 70% v/v aqueous ethanol (30.0 ml) was treated with sodium dithionite (0.52 g) and the mixture heated under reflux for 1 h. A further portion of sodium dithionite (0.52 g) was added and the mixture was then stirred and heated under reflux for a further 1 h.

The mixture was allowed to cool and was rotary evaporated to give a solid residue. The residue was treated with water (10.0 ml) and extracted with dichloromethane to give a brown oil (0.35 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an intractable brown oil (0.15 g) from which no identifiable material was obtained.

Further elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable multicomponent oils and gums (total 0.12 g) from which no identifiable material was obtained.

Ethyl 2,2-Diphenyl-2-(1-nitronaphth-2-yl)oxyethanoate (134a)

(a) A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 1-nitro-2-naphthol (130) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting red solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then treated in one portion with a solution of ethyl 2-chloro-2,2-diphenylacetate (117a) (1.1 g; 0.004 mol) in anhydrous dimethylformamide (5.0

ml). The resulting mixture was then stirred at 100° (oil-bath) with the exclusion of atmospheric moisture for 17 h.

The mixture was allowed to cool, diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide solution (2.0 ml) and water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a brown solid (0.24 g) which was acidified with 2 M aqueous hydrochloric acid to give 1-nitro-2-naphthol (130) as a brown solid (0.11 g; 14%), m.p. 94-96°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give a brown oil (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (9:1) gave unreacted ethyl 2-chloro-2,2-diphenylacetate (117a) as a yellow solid (0.55 g; 50%), m.p. 39-42°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Further elution with hexane-dichloromethane (9:1) gave a multicomponent yellow oil (0.12 g) which afforded no identifiable material.

Further elution with hexane-dichloromethane (9:1) gave a yellow solid (0.44 g) which was washed with hexane to give ethyl 2,2-diphenyl-2-(1-nitronaphth-2-yl)oxyethanoate (134a) as a pale yellow solid (0.20 g; 12%), m.p. 113-115° (from toluene-light petroleum), υ_{max} 1740(C=O) and 1520 and

1358(NO_2) cm^{-1}, δ_H($CDCl_3$) 7.73-7.24(16H, m, ArH), 4.21(2H, q, J7Hz, CH_2) and 1.08(3H, t, J7Hz, CH_3). Rotary evaporation of the hexane washings gave only an intractable yellow oil (0.21 g).

Elution with hexane-dichloromethane (4:1) through dichloromethane to methanol gave only a series of intractable brown gums (total 0.12 g) from which no identifiable material was obtained.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give a second crop of 1-nitro-2-naphthol (130) as a brown solid (0.20 g; 26%), m.p. 94-96°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 1-nitro-2-naphthol (130) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting red solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then treated in one portion with a solution of ethyl 2-chloro-2,2-diphenylacetate (117a) (1.1 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). Potassium iodide (0.020 g; 0.0012 mol) was then added in one portion and the resulting mixture was stirred at 100° (oil-bath) with the exclusion of atmospheric moisture for 17 h.

The mixture was allowed to cool, diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated and the residue treated

with 2 M aqueous sodium hydroxide solution (2.0 ml) and water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a brown solid (0.25 g) which was acidified with 2 M aqueous hydrochloric acid to give 1-nitro-2-naphthol (130) as a brown solid (0.21 g; 28%), m.p. 91-94°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give a brown oil (1.7 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (9:1) gave unreacted ethyl 2-chloro-2,2-diphenylacetate (117a) as a yellow solid (0.33 g; 30%), m.p. 39-42°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Elution with hexane-dichloromethane (4:1) gave an intractable brown oil (0.062 g) which afforded no identifiable material.

Further elution with hexane-dichloromethane (4:1) gave a brown solid (0.50 g) which was washed with hexane to give ethyl 2,2-diphenyl-2-(1-nitronaphth-2-yl)oxyethanoate (134a) as a yellow solid (0.29 g; 17%), m.p. 109-114°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before. Rotary evaporation of the hexane washings gave only an intractable yellow oil (0.14 g).

Elution with hexane-dichloromethane (7:3) through dichloromethane to methanol gave only a series of intractable brown gums (total 0.32 g) from

which no identifiable material was obtained.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give a second crop of 1-nitro-2-naphthol (130) as a brown solid (0.21 g; 28%), m.p. 94-96°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Ethyl-2-Methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b)

(a) A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 1-nitro-2-naphthol (130) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting red solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then treated in one portion with a solution of ethyl 2-bromo-2-methylpropionate (117b) (0.78 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). The resulting mixture was then stirred at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, diluted with water (1.0 ml) and stirred at room temperature for 15 min, then rotary evaporated and the residue treated with 2 M aqueous sodium hydroxide solution (2.0 ml) and water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a brown solid (0.65 g) which was acidified with 2 M aqueous hydrochloric acid to give 1-nitro-2-naphthol (130) as a brown solid (0.44 g; 58%), m.p. 96-99°, identified by comparison (m.p. and i.r. spectrum) with an

authentic sample.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give ethyl 2-methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b) as a brown oil (0.37 g; 31%), b.p. 155-164°/0.3 mm Hg, υ_{max} 1740(C=O), 1532 and 1358(NO_2) cm^{-1}, δ_H($CDCl_3$) 7.86(1H, d, J3Hz, ArH), 7.82-7.18(5H, m, ArH), 4.28(2H, q, J7Hz, CH_2), 1.64(6H, s, 2xCH_3) and 1.29(3H, t, J7Hz, CH_3).

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give a second crop of 1-nitro-2-naphthol (130) as a brown solid (0.088 g; 11%), m.p. 96-99°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) Repetition of the reaction described in (a) before but at 100° for 17 h gave, after similar workup of the mixture, ethyl 2-methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b) as a brown oil (0.67 g; 55%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to a sample prepared in (a) before, together with unreacted 1-nitro-2-naphthol (130) as a brown solid (0.33 g; 44%), m.p. 97-99°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(c) Repetition of the reaction described in (a) before but using two equivalents of ethyl 2-bromo-2-methylpropionate (117b) and an increase in the reaction time to 17 h gave, after similar workup of the mixture, ethyl 2-methyl-

2-(1-nitronaphth-2-yl)oxypropanoate (134b) as a brown oil (0.40 g; 33%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to an authentic sample prepared in (a) before, together with unreacted 1-nitro-2-naphthol (130) as a brown solid (0.43 g; 57%), m.p. 95-97°, identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reduction of Ethyl 2-Methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b)

A stirred solution of ethyl 2-methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b) (0.61 g; 0.002 mol) in ethanol (30.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.061 g) at room temperature and atmospheric pressure for 3 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give the unreacted ethyl 2-methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b) as a brown oil (0.59 g; 97%), identical [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:1) over silica] to an authentic sample.

3,3-Dimethyl-1,2-dihydro-3H-naphth[2,1-b]-1,4-oxazin-2(1H)one (138)

A stirred solution of ethyl 2-methyl-2-(1-nitronaphth-2-yl)oxypropanoate (134b) (0.61 g; 0.002 mol) in 70% v/v aqueous ethanol (30.0 ml) was treated with sodium dithionite (0.61 g) and the mixture heated under reflux 1 h. A further portion of sodium dithionite (0.61 g) was added and the mixture was then stirred and heated under reflux for a further 1 h.

The mixture was allowed to cool and was rotary evaporated to give a solid residue. The residue was treated with water (10.0 ml) and extracted with dichloromethane to give 3,3-dimethyl-1,2-dihydro-3H-naphth[2,1-b]-1,4-oxazin-2(1H)one (138) as a colourless solid (0.40 g; 88%) which formed colourless needles, m.p. 174-175° (from toluene-light petroleum), υ_{max} 1680(C=O) cm^{-1}, $\delta_H(CDCl_3)$, 9.39(1H, s, NH) (exch.), 7.94-7.16(6H, m, ArH), 2.16(3H, s, CH_3) and 1.60(3H, s, CH_3).

1-Amino-2-naphthol (139)

A stirred solution of 1-nitroso-2-naphthol (72) (26.0 g; 0.15 mol) in ethyl acetate (500 ml) was hydrogenated over 10% palladium-on-charcoal (2.6 g) at room temperature and atmospheric pressure for 1.5 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give 1-amino-2-naphthol (139) as a purple solid (23.9 g; 100%), m.p. 184-188° (lit.,[119] 175°) which was used without further purification.

The Reaction of 1-Amino-2-naphthol (139) with Formic Acid

1-Amino-2-naphthol (139) (1.6 g; 0.01 mol) was treated with 98% formic acid (10.0 ml) and the dark mixture was stirred under reflux with the exclusion of atmospheric moisture for 1 h.

The dark mixture was allowed to cool and was then rotary evaporated to give a dark brown gum (1.7 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave the naphth[1,2-d]oxazole

(140) as a brown solid (0.94 g; 56%), m.p. 63-65° (lit.,[109] 63-64°); $\delta_H(CDCl_3)$ 8.54-7.25(7H, m, ArH and CH).

Elution with hexane-ethyl acetate (1:1) gave 1-formamido-2-naphthol (141) as a grey solid (0.36 g; 20%), m.p. 213-215°, υ_{max} 3271(NH), 3234(OH) and 1658(C=O) cm-1, $\delta_H[(CD_3)_2SO]$, 9.65-9.27(2H, m, NH and CHO) (exch.) and 8.40-7.14(7H, m, ArH and OH).

Further elution with hexane-ethyl acetate (2:3) through ethyl acetate to methanol gave only a multicomponent brown solid (0.12 g) which was not further investigated.

Naphth[1,2-d]oxazole (140)

1-Amino-2-naphthol (139) (16.0 g; 0.1 mol) was treated with 98% formic acid (100 ml) and the dark mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The dark mixture was allowed to cool, then rotary evaporated to give a dark purple solid residue, which was washed with light petroleum to give a brown solid which was combined with a second crop obtained by rotary evaporation of the light petroleum mother liquor to give the naphthoxazole (140) (16.9 g; 100%), m.p. 58-60°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared previously.

1-Formamido-2-naphthol (141)

(a) The naphthoxazole (140) (1.7 g; 0.01 mol) was treated with water

(20.0 ml) and the suspension was stirred and heated under reflux for 4 h.

The mixture was allowed to cool, rotary evaporated and the residue was treated with water (10.0 ml) and extracted with dichloromethane. The insoluble solid was collected and crystallised from ethanol to give 1-formamido-2-naphthol (141) (0.59 g; 31%), m.p. 210-214°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample obtained before. Rotary evaporation of the ethanol mother liquor gave a solid which was combined with further material obtained by rotary evaporation of the dichloromethane extract to give unreacted naphthoxazole (140) (0.74 g; 44%), m.p. 58-61°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) Repetition of the reaction described in (a) before but using 50% v/v aqueous dioxane instead of water gave a mixture which was allowed to cool then rotary evaporated. The resulting dark purple residue was washed with dichloromethane to give 1-formamido-2-naphthol (141) as a grey solid (0.64 g; 34%), m.p. 202-204°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

Rotary evaporation of the dichloromethane washings gave unreacted naphthoxazole (140) as a brown solid (0.95 g; 56%), m.p. 55-60°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(c) Repetition of the reaction described in (b) before but with heating under reflux for 17 h followed by the usual workup gave 1-formamido-2-naphthol

(141) as a grey solid (1.1 g; 59%), m.p. 202-204°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample together with a dark brown gum (0.66 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to consist largely of the unreacted naphthoxazole (140).

(d) Repetition of the reaction described in (c) before but with heating under reflux for 41 h followed by the usual workup gave 1-formamido-2-naphthol (141) as a grey solid (0.30 g, 16%), m.p. 210-214°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample, together with unreacted naphthoxazole (140) (1.4 g; 83%), m.p. 59-64° identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(e) Repetition of the reaction described in (d) before but in 50% v/v aqueous dimethylformamide under reflux for 4 h followed by the usual workup gave 1-formamido-2-naphthol (141) as a grey solid (0.075 g; 4%), m.p. 205-210°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample, together with unreacted naphthoxazole (140) (1.5 g; 91%), m.p. 59-63° identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(f) Repetition of the reaction described in (e) before but in 50% v/v aqueous diglyme under reflux for 4 h followed by the usual workup gave 1-formamido-2-naphthol (141) as a grey solid (0.13 g; 7%), m.p. 214-218°, identified by comparison, m.p. and i.r. spectrum with an authentic sample,

together with unreacted naphthoxazole (140) (1.5 g; 91%), m.p. 54-58°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(g) Repetition of the reaction described in (f) before but in 50% v/v aqueous acetic acid under reflux for 4 h followed by the usual workup gave 1-formamido-2-naphthol (141) as a grey solid (0.60 g; 32%), m.p. 210-214°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample, together with a multicomponent brown gum (1.1 g) from which no identifiable material could be obtained.

The Attempted Acid Catalysed Hydrolysis of Naph[1,2-d]oxazole (140) to 1-Formamido-2-naphthol (141)

A stirred solution of the naphthoxazole (140) (0.85 g; 0.005 mol) in 1,4-dioxane (10.0 ml) was treated with 2 M aqueous hydrochloric acid (2.5 ml) and the dark brown solution was stirred and heated under reflux for 1.5 h.

The resulting suspension was filtered to give an intractable grey solid (0.11 g) from which no identifiable material was obtained.

The filtrate was rotary evaporated to give a purple solid which was treated with water (10.0 ml) and filtered to give a multicomponent purple solid (0.36 g) which yielded no identifiable material.

The aqueous washings were neutralised (pH=7) by the addition of solid sodium acetate and extracted with dichloromethane to give a multicomponent dark brown solid (0.29 g) which was not investigated further.

2-(1-Formamidonaphth-2-yl)oxy-2,2-diphenylacetaldehyde (142)

(a) A stirred suspension of sodium hydride (0.11 g; 0.0046 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 1-formamido-2-naphthol (141) (0.75 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting green mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.1 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). The resulting dark green solution was then stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The green solution was allowed to cool, diluted with water (1.0 ml), stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.0 ml) and water (10.0 ml) and extracted with dichloromethane to give a dark brown gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-ether (99:1) gave a brown oil (0.70 g) whose i.r. spectrum and t.l.c. in hexane-ether (1:1) showed it to be a mixture of benzophenone and unreacted 2-bromo-2,2-diphenylacetaldehyde (112a).

Elution with hexane-ether (1:1) gave 2-(1-formamidonaphth-2-yl)oxy-2,2-diphenylacetaldehyde (142) as a brown solid (0.60 g; 39%), m.p. 76-79°, which formed a gum on attempted crystallisation, υ_{max} 3392(NH) and 1728(C=O) cm^{-1}.

Elution with hexane-ether (2:3) through to ether gave no further material.

Final elution with methanol gave an intractable brown gum (0.18 g) which was not further investigated.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave only an intractable brown solid (0.25 g).

(b) Repetition of the reaction described in (a) before but using two equivalents of 2-bromo-2,2-diphenylacetaldehyde (112a) gave a mixture which was allowed to cool, treated with water (1.0 ml), stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.0 ml) and water (10.0 ml) and extracted with dichloromethane to give a dark brown gum (2.9 g) which was flash-chromatographed over silica.

Elution with hexane-ether (99:1) gave a brown oil (1.1 g) whose i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica showed it to be a mixture of benzophenone and unreacted 2-bromo-2,2-diphenylacetaldehyde (112a).

Elution with hexane-ether (4:1) gave the formamidonaphthoxydiphenylacetaldehyde (142) as a brown solid (0.72 g; 47%), m.p. 76-79°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Further elution with hexane-ether (7:3) through to ether gave no further material.

Final elution with methanol gave only an intractable brown oil (0.98 g)

which yielded no identifiable material.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give only an intractable brown solid (0.15 g) from which no identifiable material could be obtained.

The Attempted Base Catalysed Condensation of 1-Formamido-2-naphthol (141) with 2-Bromo-2,2-diphenylacetaldehyde (112a)

A stirred suspension of sodium hydride (0.13 g; 0.0055 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 1-formamido-2-naphthol (141) (0.94 g; 0.005 mol) in anhydrous dimethylformamide (10.0 ml). The resulting green mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (2.8 g; 0.01 mol) in anhydrous dimethylformamide (10.0 ml). The resulting dark brown mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The dark brown mixture was diluted with water (5.0 ml), stirred at room temperature for 15 min, then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.5 ml) and water (10.0 ml) and extracted with dichloromethane to give a dark brown oil (2.7 g) which was flash-chromatographed over silica.

Elution with hexane-ether (99:1) gave a brown oil (0.83 g) whose i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica showed it to be a mixture

of benzophenone and unreacted 2-bromo-2,2-diphenylacetaldehyde (112a).

Elution with hexane-ether (4:1) through ether to methanol gave only a series of multicomponent gums (total 1.5 g) which yielded no identifiable material.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give an intractable brown solid (0.41 g) which was not further investigated.

Attempted Hydrolyses of 2-(1-Formamidonaphth-2-yl)oxy-2,2-diphenylacetaldehyde (142)

(a) A stirred solution of the formamidonaphthoxydiphenylacetaldehyde (142) (0.76 g; 0.002 mol) in ethanol (10.0 ml) was treated with 2 M aqueous sodium hydroxide (2.0 ml) and the mixture was stirred and heated under reflux for 0.5 h.

The dark brown solution was allowed to cool and a solid was deposited which was collected to give the unreacted formamidonaphthyloxydiphenylacetaldehyde (142) as a brown solid (0.031 g; 4%), m.p. 72-73°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The filtrate was rotary evaporated to give a brown residue which was treated with water (10.0 ml) and extracted with dichloromethane to give a brown solid (0.56 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave benzophenone as a brown oil (0.17

g; 47%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica] with an authentic sample. A small portion (0.070 g) of the brown oil was treated with an acidic solution of 2,4-dinitrophenylhydrazone (0.2 M Brady's solution) (2.0 ml) and the mixture shaken for 2-3 mins until a solid was deposited. The mixture was filtered to afford the dinitrophenylhydrazone derivative of benzophenone as an orange solid (0.055 g), m.p. 238-239° (lit.,[120] 238-239°).

Elution with hexane-ether (4:1) gave a multicomponent brown gum (0.18 g) which was not further investigated.

Elution with hexane-ether (1:1) gave the unreacted formamidonaphthyloxydiphenylacetaldehyde (142) as a brown solid (0.14 g; 18%), m.p. 68-72°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Final elution with methanol gave only a negligible quantity of a brown gum.

(b) Repetition of the reaction described in (a) before but at room temperature for 24 h gave a brown solution which was rotary evaporated. The brown residue was treated with water (10.0 ml) and extracted with dichloromethane to give a purple gum (0.58 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (99:1) gave benzophenone as a brown oil (0.20 g; 55%), identified by comparison [i.r. spectrum and t.l.c. in hexane-

ether (3:2) over silica] with an authentic sample.

Elution with hexane-ethyl acetate (19:1) gave only a small amount of a multicomponent brown gum (0.071 g).

Further elution with hexane-ethyl acetate (1:1) gave a brown solid (0.25 g) whose i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica showed it to be mainly the unreacted formamidonaphthyloxydiphenylacetaldehyde (142).

Elution with hexane-ethyl acetate (2:3) through ethyl acetate to methanol gave only a negligible quantity of brown gum.

(c) A stirred solution of the formamidonaphthyloxydiphenylacetaldehyde (142) (0.76 g; 0.002 mol) in ethanol (10.0 ml) was treated with 2 M aqueous hydrochloric acid (2.0 ml) and the mixture was stirred and heated under reflux for 30 min.

The dark brown solution was allowed to cool and rotary evaporated to give a brown gum which was treated with water (10.0 ml). Extraction with dichloromethane gave a brown foam (0.67 g) which was flash-chromatographed over silica.

Elution with hexane-ether (99:1) gave benzophenone as a brown oil (0.11 g; 30%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica] with an authentic sample.

Further elution with hexane-ether (19:1) gave only a small amount of an intractable red gum (0.049 g).

Elution with hexane-ether (9:1) gave the unreacted

formamidonaphthyloxydiphenylacetaldehyde (142) as a brown solid (0.21 g; 28%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (3:2) over silica] with an authentic sample.

Further elution with hexane-ether (9:1) through to ether gave only negligible material.

Final elution with methanol gave only an intractable brown gum (0.22 g).

The Attempted Base Catalysed Condensation of 1-Amino-2-naphthol (139) with 2-Bromo-2,2-diphenylacetaldehyde (112a)

A stirred solution of sodium hydride (0.14 g; 0.0058 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 1-amino-2-naphthol (139) (0.80 g; 0.005 mol) in anhydrous dimethylformamide (10.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.4 g; 0.005 mol) in anhydrous dimethylformamide (10.0 ml). The resulting dark brown mixture was then stirred at 100° (oil-bath) with the exclusion of atmospheric moisture for 1h.

The mixture was allowed to cool and was treated with H_2O (2.0 ml) and stirred at room temperature for 15 min then rotary evaporated. The residue was treated with 2 M aqueous sodium hydroxide (2.5 ml) and water (10.0 ml) and extracted with dichloromethane to give a multicomponent brown gum (1.8

g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave a multicomponent green oil (0.48 g) which was not further investigated.

Further elution with hexane-ethyl acetate (19:1) through ethyl acetate to methanol gave only a series of multicomponent oils and gums (total 1.2 g) which yielded no identifiable material.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and brought to neutral pH by the addition of solid sodium acetate. Extraction with dichloromethane gave only a multicomponent dark brown gum (0.18 g) which was not further investigated.

2-Chloro-2,2-diphenyl-N-(2-hydroxynaphth-1-yl)acetamide (144)

(a) A stirred solution of 1-amino-2-naphthol (139) (0.80 g; 0.005 mol) in anhydrous 1,4-dioxane (10.0 ml) was treated with a solution of 2-chloro-2,2-diphenylacetyl chloride (143) (1.3 g; 0.005 mol) in anhydrous 1,4-dioxane (10.0 ml). The resulting dark brown solution was then stirred under reflux with the exclusion of atmospheric moisture for 30 min.

The mixture was allowed to cool and rotary evaporated to give a purple residue. The residue was treated with 10% w/v aqueous sodium hydrogen carbonate (10.0 ml) and extracted with dichloromethane to give a purple gum (1.9 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an intractable red oil (0.10 g).

Further elution with hexane-ether (9:1) gave an intractable brown gum

(0.15 g).

Elution with hexane-ether (4:1) gave 2-chloro-2,2-diphenyl-N-(2-hydroxynaphth-1-yl)acetamide (144) as a lilac solid (0.87 g; 45%), m.p. 165-168° (from hexane-toluene), υ_{max} 3323(NH), 3201(OH) and 1660(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 9.24(1H, s, ArOH), 8.24(1H, s, NH) (exch.) and 7.84-7.25(16H, m, ArH).

Further elution with hexane-ether (7:3) through to ether gave negligible material.

Final elution with methanol gave only a multicomponent purple solid (0.52 g) which yielded no identifiable material.

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and brought to neutral pH by the addition of solid sodium acetate. Extraction with dichloromethane gave only negligible material.

(b) A stirred suspension of fused sodium acetate (0.82 g; 0.01 mol) in glacial acetic acid (5.0 ml) was treated dropwise with a solution of 1-amino-2-napthol (139) (0.32 g; 0.002 ml) in glacial acetic acid (2.5 ml). The mixture was then treated with a solution of 2-chloro-2,2-diphenylacetyl chloride (143) (0.53 g; 0.002 ml) in glacial acetic acid (2.5 ml) and the resulting purple suspension was stirred at room temperature for 3 h.

The purple suspension was rotary evaporated to give a purple solid. The purple solid was treated with water (5.0 ml) and extracted with dichloromethane to give a purple gum (0.80 g) which was flash-

chromatographed over silica.

Elution with hexane-ether (19:1) gave a multicomponent brown gum (0.040 g) which was not investigated further.

Elution with hexane-ether (9:1) gave 2-chloro-2,2-diphenyl-N-(2-hydroxynaphth-1-yl)acetamide (144) as a brown solid (0.24 g; 31%), m.p. 156-163°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Elution with hexane-ether (4:1) through to ether gave negligible material.

Final elution with methanol gave a multicomponent brown foam (0.38 g) which was not investigated further.

The Attempted Base Catalysed Cyclisation of 2-Chloro-2,2-diphenyl-N-(2-hydroxynaphth-1-yl)acetamide (144)

A stirred solution of the acetamide (144) (0.097 g; 0.00025 mol) in ethanol (5.0 ml) was treated with 2 M aqueous sodium hydroxide (1.0 ml) and the brown solution was stirred under reflux for 1 h.

The brown solution was allowed to cool and rotary evaporated. The resulting brown residue was washed with water (5.0 ml) to give an intractable multicomponent brown solid (0.059 g).

The aqueous washings were extracted with dichloromethane to give an intractable multicomponent brown gum (0.010 g).

The aqueous layer was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give an intractable multicomponent

brown gum (0.012 g).

2,2-Diphenyl-N-(2-hydroxynaphth-1-yl)acetaldimine (146)

A stirred solution of 2,2-diphenylacetaldehyde (145) (0.78 g; 0.004 mol) in anhydrous benzene (25.0 ml) was mixed with a suspension of 1-amino-2-naphthol (139) (0.64 g; 0.004 mol) in anhydrous benzene (25.0 ml), then toluene-4-sulphonic acid (0.078 g) was added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 5 h.

The mixture was hot filtered to remove an intractable purple solid (0.14 g) and the filtrate was washed twice with 10% w/v aqueous sodium hydrogen carbonate solution (2 x 10.0 ml) and rotary evaporated to give a dark red gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave a multicomponent brown gum (0.90 g) which was not further investigated.

Further elution with hexane-ether (19:1) gave a red gum (0.32 g) which was washed with light petroleum to give 2,2-diphenyl-N-(2-hydroxynaphth-1-yl)acetaldemine (146) as a colourless solid (0.16 g; 12%), m.p. 116-117° (from hexane-toluene), υ_{max} 1583(C=N) cm^{-1}. Rotary evaporation of the light petroleum mother liquor gave only an intractable brown oil (0.10 g).

Elution with hexane-ether (19:1) through to ether gave negligible material.

Final elution with methanol gave a multicomponent brown gum (0.10 g)

which was not further investigated.

Attempted Reactions of 1-Amino-2-naphthol (139) with 2,2-Diphenylacetaldehyde (145)

(a) A stirred solution of 2,2-diphenylacetaldehyde (145) (0.39 g; 0.002 mol) in anhydrous ether (5.0 ml) containing freshly regenerated 4 Å molecular sieves (1.0 g) was treated at room temperature with a solution of 1-amino-2-naphthol (139) (0.32 g; 0.002 mol) in anhydrous ether (20.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The mixture was filtered to remove the sieves and the sieves were washed twice with anhydrous ether (2 x 5.0 ml). The combined ether filtrate and washings were rotary evaporated to give a brown gum (0.67 g) which was flash-chromatographed over silica.

Elution with hexane-ether (49:1) gave unreacted 2,2-diphenylacetaldehyde (145) as a light brown oil (0.30 g; 77%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Further elution with hexane-ether (49:1) through ether to methanol gave only a series of multicomponent oils and gums (total 0.29 g) from which no identifiable material was obtained.

(b) A stirred solution of 2,2-diphenylacetaldehyde (145) (0.78 g; 0.004 mol)

in anhydrous 1,2-dimethoxyethane (10.0 ml) containing freshly regenerated 4 Å molecular sieves (2.0 g), was treated with a solution of 1-amino-2-naphthol (139) (0.64 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (40.0 ml) and the suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 23 h.

The suspension was filtered to remove the sieves and the sieves washed twice with anhydrous 1,2-dimethoxyethane (2 x 10.0 ml). The combined 1,2-dimethoxyethane filtrate and washings were rotary evaporated to give a multicomponent brown gum (1.6 g) which was flash-chromatographed over silica.

Elution with light petroleum-ethyl acetate (49:1) gave benzophenone as a brown oil (0.53 g; 73%), identified by comparison [i.r. spectrum and t.l.c. in light petroleum-ethyl acetate (7:3) over silica] with an authentic sample.

Further elution with light petroleum-ethyl acetate (19:1) through ethyl acetate to methanol gave only a series of multicomponent oils and gums (total 0.54 g) from which no identifiable material was obtained.

(c) Repetition of the reaction described in (b) before but in 1,2-dimethoxyethane under reflux gave a mixture which was allowed to cool, filtered to remove the sieves and the sieves washed twice with anhydrous 1,2-dimethoxyethane (2 x 10.0 ml). The combined 1,2-dimethoxyethane filtrate and washings were rotary evaporated to give a brown gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-ether (99:1) gave unreacted 2,2-diphenylacetaldehyde (145) as a light brown oil (0.78 g; 100%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Elution with hexane-ether (1:1) gave unreacted 1-amino-2-naphthol (139) as a brown solid (0.42 g; 66%), m.p. 178-182°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Further elution with hexane-ether (1:1) through ether to methanol gave only a negligible amount of material.

The Reaction of 1-Nitroso-2-naphthol (72) with Triphenylphosphine

A stirred solution of 1-nitroso-2-naphthol (72) (1.7 g; 0.01 mol) in anhydrous benzene (25.0 ml) was treated in one portion with a solution of triphenylphosphine (5.2 g; 0.02 mol) in anhydrous benzene (25.0 ml). The dark mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The dark mixture was rotary evaporated to give a dark brown gum (6.9 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (4:1) gave 1-amino-2-naphthol (139) as a dark brown solid (0.88 g; 55%), m.p. 175-180°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Elution with hexane-ethyl acetate (1:1) followed by methanol gave triphenylphosphine oxide as a brown solid (4.6 g; 83%), m.p. 148-150°,

identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Benzoylmethyltriphenylphosphonium Bromide

A stirred solution of triphenylphosphine (13.1 g; 0.05 mol) in anhydrous chloroform (50.0 ml) was treated dropwise at room temperature over 15 min with a solution of phenacyl bromide (10.0 g; 0.05 mol) in anhydrous chloroform (50.0 ml). The pale yellow mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 30 min.

The mixture was filtered to remove some insoluble solid and the filtrate poured into anhydrous ether (1000 ml). The precipitated solid was collected and washed with ether to give benzoylmethyltriphenylphosphonium bromide as a colourless solid (12.4 g; 54%), m.p. 270-272° (lit.,[121] 269-271°).

The ether-chloroform mother liquor was rotary evaporated to give an off-white waxy solid (8.3 g) which was washed with ether to give triphenylphosphine oxide (4.5 g; 32%), m.p. 144-145°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the ethereal washings gave unreacted phenacyl bromide as an orange waxy solid (3.4 g; 34%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Benzoylmethylenetriphenylphosphorane

A suspension of benzoylmethyltriphenylphosphonium bromide (9.2 g; 0.02 mol) in 10% w/v aqueous sodium carbonate solution (100 ml) was stirred

at room temperature for 17 h.

The mixture was filtered to give a colourless solid which was extracted with boiling benzene (50.0 ml). Hot filtration of the benzene extract and dilution of the benzene filtrate with light petroleum (100 ml) precipitated benzoylmethylenetriphenylphosphorane as a colourless solid (6.3 g; 83%), m.p. 177-180° (lit.,[121] 178-180°).

Rotary evaporated of the benzene-light petroleum mother liquor gave only an intractable pale yellow solid (1.0 g), which was not further investigated.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with Benzoylmethylenetriphenylphosphorane

A stirred solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous toluene (10.0 ml) was treated with a solution of benzoylmethylenetriphenylphosphorane (1.5 g; 0.004 mol) in anhydrous toluene (10.0 ml) and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 17 h.

The mixture was allowed to cool, then rotary evaporated to give a dark brown gum (2.5 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) through ethyl acetate to methanol gave only a series of multicomponent gums (total 2.0 g) which afforded no identifiable material.

Phenylglyoxal 1-(2-Hydroxynaphth-1-yl)imine (149)

A stirred solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous benzene (10.0 ml) was treated with a solution of benzoylmethylenetriphenylphosphorane (1.5 g; 0.004 mol) in anhydrous benzene (10.0 ml) and the brown mixture was then stirred under reflux with the exclusion of atmospheric moisture for 24 h.

The brown solution was allowed to cool and filtered to remove a small amount of insoluble solid and rotary evaporated to give a dark brown gum (2.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an intractable yellow gum (0.090 g).

Further elution with hexane-ether (4:1) gave a brown gum (0.30 g) which was washed with hexane to give phenylglyoxal 1-(2-hydroxynaphth-1-yl)imine (149) (0.26 g; 24%) which formed green plates, m.p. 128-129° (from hexane-toluene) (lit.,[111] 110-112°), υ_{max} 3400(OH) and 1651(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 8.71-7.57(12H, m, ArH and CH) and 7.25(1H, s, OH). Rotary evaporation of the hexane mother liquor gave only a negligible amount of a brown gum.

Further elution with hexane-ether (1:1) through ether to methanol gave only a series of multicomponent gums (total 1.7 g) from which no identifiable material was obtained.

Ethoxycarbonylmethyltriphenylphosphonium Bromide

A stirred solution of triphenylphosphine (13.1 g; 0.05 mol) in anhydrous chloroform (50.0 ml) was treated dropwise at room temperature over 15 min with a solution of ethyl bromoacetate (8.4 g; 0.05 mol) in anhydrous chloroform (50.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 30 min.

The mixture was filtered to remove some insoluble solid and the filtrate was poured into anhydrous ether (1000 ml). The precipitated solid was collected and washed with ether to give ethoxycarbonylmethyltriphenylphosphonium bromide as a colourless solid (19.4 g; 90%), m.p. 159-161°, (lit.,[122] 163°).

Evaporation of the ether-chloroform mother liquor gave only an intractable waxy brown solid (2.2 g) which yielded no identifiable material.

Ethoxycarbonylmethylenetriphenylphosphorane

A suspension of ethoxycarbonylmethyltriphenylphosphonium bromide (8.6 g; 0.02 mol) in 10% w/v aqueous sodium carbonate (100 ml) was stirred at room temperature for 17 h.

The mixture was filtered to give a colourless solid which was extracted with boiling benzene (50.0 ml). Hot filtration of the benzene extract and dilution of the benzene filtrate with light petroleum (100 ml) precipitated ethoxycarbonylmethylenetriphenylphosphorane as a colourless solid (4.8 g; 69%), m.p. 125-127°, (lit.,[122] 126-127°).

Rotary evaporation of the benzene-light petroleum mother liquor gave only an intractable yellow solid (1.8 g), which yielded no further identifiable material.

Ethyl Glyoxylate N-(2-Hydroxynaphth-1-yl)imine (150)

A stirred solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous benzene (10.0 ml) was treated with a solution of ethoxycarbonylmethylenetriphenylphosphorane (1.4 g; 0.004 mol) in anhydrous benzene (10.0 ml) and the dark brown mixture was then stirred under reflux with the exclusion of atmospheric moisture for 4 h.

The dark brown mixture was allowed to cool and then rotary evaporated to give a reddish-brown gum (2.3 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave a multicomponent brown waxy solid (0.15 g) which was not further investigated.

Further elution with hexane-ethyl acetate (19:1) gave ethyl glyoxylate N-(2-hydroxynaphth-1-yl)imine (150) as a pink solid (0.47 g; 48%), m.p. 104-106° (from hexane-toluene), (lit.,[111] 85°), υ_{max} 3450(OH), 1735(C=O) and 1634(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 8.63(1H, d, J8Hz, ArH), 7.99-7.55(6H, m, ArH and CH), 4.59(2H, q, J7Hz, CH_2) and 1.49(3H, t, J7Hz, CH_3).

Elution with hexane-ethyl acetate (1:1) through to ethyl acetate gave only a series of multicomponent brown gums (total 0.61 g) which yielded no identifiable material.

Final elution with methanol gave triphenylphosphine oxide as a pale brown solid (1.0 g; 89%), m.p. 148-150°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Sodium Salt of 1-Nitroso-2-naphthol (153)

A stirred suspension of sodium hydride (3.6 g; 0.15 mol) in anhydrous 1,2-dimethoxyethane (75.0 ml) was cooled to 10° (ice-bath) and was treated dropwise with a solution of 1-nitroso-2-naphthol (72) (29.4 g; 0.17 mol) in anhydrous 1,2-dimethoxyethane (150 ml) and the green suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 15 min.

The green suspension was filtered to give the sodium salt of 1-nitroso-2-naphthol (153) as a green solid (27.2 g; 93%), m.p. 300-303° (from ethanol-dimethylsulphoxide), $\delta_H[(CD_3)_2SO]$ 8.74-6.52(6H, m, ArH).

Rotary evaporation of the 1,2-dimethoxyethane mother liquor gave only an intractable brown solid (6.6 g).

The Reaction of the Sodium Salt of 1-Nitroso-2-naphthol (153) with Dimethyl Sulphate

A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153) (0.78 g; 0.004 mol) in anhydrous dimethyl sulphoxide (10.0 ml) was treated with a solution of dimethyl sulphate (1.0 g; 0.008 mol) in anhydrous dimethyl sulphoxide (10.0 ml). The resulting brown solution was stirred and heated at

90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The dark purple solution was allowed to cool and rotary evaporated to give a dark purple oil. The dark purple oil was treated with water (10.0 ml) and extracted with dichloromethane to give a dark brown oil (0.76 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave a brown gum (0.25 g) which was washed with light petroleum to give naphth[1,2-d]oxazole (140) as a yellow solid (0.21 g; 28%), m.p. 59-63°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample. Rotary evaporation of the light petroleum washings gave a negligible brown gum.

Further elution with hexane-ether (4:1) gave a multicomponent brown gum (0.060 g) which was not investigated further.

Elution with hexane-ether (7:3) gave a brown gum (0.21 g) which was washed with hexane to give 2-methoxy-1-nitrosonaphthalene (155a) as a brown solid (0.13 g; 17%), m.p. 58-60° (from light petroleum-ethyl acetate), $\delta_H(CDCl_3)$ 7.95-7.25(6H, m, ArH) and 4.23(3H, s, CH_3). The hexane washings were rotary evaporated to give an intractable multicomponent brown gum (0.071 g).

Elution with hexane-ether (3:2) through to ether gave negligible material.

Final elution with methanol gave a multicomponent brown gum (0.22 g) which afforded no identifiable material.

The Reactions of the Sodium Salt of 1-Nitroso-2-naphthol (153) with Benzyl Bromide

(a) A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153) (0.78 g; 0.004 mol) in anhydrous dimethyl sulphoxide (10.0 ml) was treated with a solution of benzyl bromide (0.68 g; 0.004 mol) in anhydrous dimethyl sulphoxide (5.0 ml). The resulting green solution was stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The resulting red solution was allowed to cool and rotary evaporated to give a red gum. The red gum was treated with water (10.0 ml) and extracted with dichloromethane to give a red gum (1.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2-phenylnaphth[1,2-d]oxazole (157) (0.41 g; 42%) which formed colourless microcrystals, m.p. 135-136° (from cyclohexane-ethyl acetate), υ_{max} 1588(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 8.61-7.24(11H, m, ArH).

Further elution with hexane-ether (4:1) gave an intractable brown gum (0.13 g) which yielded no identifiable material.

Elution with ether gave a brown gum (0.34 g) which was washed with hexane to give 2-benzyloxy-1-nitrosonaphthalene (155b) as a brown solid (0.23 g; 22%), m.p. 98-99° (from hexane-ethyl acetate), $\delta_H(CDCl_3)$ 7.37(11H, m, ArH) and 5.59(2H, s, ArH). The hexane washings were rotary evaporated to give an intractable brown gum (0.051 g).

Final elution with methanol gave negligible material.

(b) Repetition of the reaction described in (a) before but in acetonitrile under reflux instead of dimethyl sulphoxide at 90° gave a mixture which was hot filtered to give a green solid (0.38 g). The green solid was acidified with 2 M aqueous hydrochloric acid to give 1-nitroso-2-naphthol (72) as a brown solid (0.12 g; 17%), m.p. 106-108°, identical (m.p. and i.r. spectrum) to an authentic sample.

The acetonitrile filtrate was allowed to cool and rotary evaporated to give a brown gum (0.80 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2-phenylnaphth[1,2-d]oxazole (157) as a colourless solid (0.29 g; 30%), m.p. 135-136°, identical (m.p. and i.r. spectrum) to an authentic sample.

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of multicomponent gums (total 0.50 g) from which no identifiable material was obtained.

The Attempted Reaction of the Sodium Salt of 1-Nitroso-2-naphthol (153) with 2-Bromo-2,2-diphenylacetaldehyde (112a)

A stirred suspension of the sodium salt of 1-nitroso-2-naphthol (153) (0.39 g; 0.002 mol) in anhydrous acetonitrile (7.5 ml) was treated with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (0.55 g; 0.002 mol) in anhydrous acetonitrile (2.5 ml). The resulting green suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 20 h.

The mixture was hot filtered to remove a negligible solid and the filtrate

was allowed to cool and rotary evaporated to give a brown gum (0.77 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted 2-bromo-2,2-diphenylacetaldehyde (112a) as a red oil (0.20 g; 36%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (7:3) over silica] with an authentic sample.

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of multicomponent gums (total 0.50 g) which were not investigated further.

Lithium Salt of 1-Nitroso-2-naphthol (158)

A stirred suspension of lithium hydride (0.80 g; 0.1 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 1-nitroso-2-naphthol (72) (19.0 g; 0.11 mol) in anhydrous 1,2-dimethoxyethane (100 ml) and the brown suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 30 min.

The green suspension was filtered to give the lithium salt of 1-nitroso-2-naphthol (158) as a green solid (17.0 g; 95%), m.p. 263-267° (from tetrahydrofuran), $\delta_H[(CD_3)_2SO]$ 8.72-6.59(6H, m, ArH).

Rotary evaporation of the 1,2-dimethoxyethane mother liquor gave only an intractable brown solid (3.0 g).

Naphthalene-1,2-dione 1-Oxime Diphenylformylmethyl Ether (161)

(a) A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153) (0.78g; 0.004 mol) in anhydrous dimethyl sulphoxide (10.0 ml) was treated with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.1g; 0.004 mol) in anhydrous dimethyl sulphoxide (5.0 ml) and the resulting green solution was stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool and rotary evaporated under high vacuum to give a brown oil. The brown oil was treated with water (10.0 ml) and extracted with dichloromethane to give a brown oil (2.3 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted 2-bromo-2,2-diphenylacetaldehyde (112a) as a brown oil (0.21 g; 19%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (3:1) over silica] with an authentic sample.

Elution with hexane-ether (4:1) gave form A of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as an orange solid (0.42 g; 29%), m.p. 154-157° (from 1,2-dimethoxyethane-ethanol), υ_{max} 1731(C=O) and 1648(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 9.96(1H,s,CHO) and 7.62-7.24(16H,m,ArH), $\delta_c(CDCl_3)$ 196.6(CHO), 178.4(quat), 144.9(quat), 143.0(CH), 137.2(quat), 130.8(quat), 130.1(CH), 129.9(CH), 129.8(CH), 128.9(CH), 128.5(CH), 128.3(CH), 127.9(CH), 124.6(CH) and 94.5(quat).

Elution with hexane-ether (1:9) gave form B of naphthalene-1,2-dione 1-

oxime diphenylformylmethyl ether (161) (0.74 g; 50%) which formed yellow microplates, m.p. 155-157° (from 1,2-dimethoxyethane-ethanol), υ_{max} 1739(C=O) and 1664(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 10.05(1H, s, CHO) and 7.62-7.25(16H, m, ArH), $\delta_c(CDCl_3)$ 195.7(CHO), 183.4(quat), 146.9(quat), 144.1(CH), 136.9(quat), 131.9(CH), 131.4(quat), 131.2(CH), 130.1(CH), 129.9(CH), 128.6(CH), 128.4(CH), 128.3(CH), 127.3(CH), 126.5(quat), 95.0(quat).

Further elution with hexane-ether (1:9) through to ether gave negligible material.

Final elution with methanol gave only an intractable brown oil (0.91 g).

(b) A stirred solution of the lithium salt of 1-nitroso-2-naphthol (158) (0.72 g; 0.004 mol) in anhydrous dimethyl sulphoxide (7.5 ml) was treated with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.1 g; 0.004 mol) in anhydrous dimethyl sulphoxide (2.5 ml). The resulting green solution was stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool and rotary evaporated under high vacuum to give a brown gum. The brown gum was treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (1.6 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave a brown gum (0.24 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to consist largely of the unreacted

2-bromo-2,2-diphenylacetaldehyde (112a).

Elution with hexane-ether (4:1) gave a brown gum (0.38 g) which was washed with ether to give form A of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as an orange solid (0.29 g; 20%), m.p. 154-157°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before. The ether washings were rotary evaporated to give a multicomponent brown gum (0.050 g) which was not further investigated.

Elution with hexane-ether (1:4) gave a brown gum (0.49 g) which was washed with ether to give form B of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as a yellow solid (0.34 g; 23%), m.p. 155-157°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before. The ether washings were rotary evaporated to give an intractable brown gum (0.099 g) which was not further investigated.

Elution with hexane-ether (1:9) through ether to methanol gave only a series of intractable multicomponent gums (total 0.48 g) which yielded no identifiable material.

(c) Repetition of the reaction described in (b) before but in anhydrous 1,2-dimethoxyethane under reflux for 1 h gave a mixture which was allowed to cool then rotary evaporated. The resulting brown gum was treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave unreacted 2-bromo-2,2-

diphenylacetaldehyde (112a) as a brown oil (0.30 g; 27%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Elution with hexane-ether (4:1) gave a brown gum (0.28 g) which was washed with ether to give form A of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as an orange solid (0.13 g; 9%), m.p. 154-157°, identical (m.p. and i.r. spectrum) to an authentic sample prepared in (a) before. The ether washings were rotary evaporated to give a multicomponent brown gum (0.12 g) which was not further investigated.

Elution with hexane-ether (3:2) gave form B of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as a yellow solid (0.78 g; 53%), m.p. 155-157°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Elution with hexane-ether (1:1) through ether to methanol gave only a series of multicomponent gums (total 0.44 g) which yielded no identifiable material.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave no further material.

(d) Repetition of the reaction described in (b) before but in anhydrous acetone at room temperature for 1 h gave a mixture which was rotary evaporated. The resulting brown gum was treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted 2-bromo-2,2-diphenylacetaldehyde (112a) as a brown oil (0.17 g, 15%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Elution with hexane-ether (4:1) gave an orange solid (0.17 g) which was washed with ethanol to give form A of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as an orange solid (0.097 g; 7%), m.p. 154-157°, identical (m.p. and i.r. spectrum) to an authentic sample prepared in (a) before. Rotary evaporation of the ethanol washings gave a multicomponent brown gum (0.051 g) which was not further investigated.

Elution with hexane-ether (3:2) gave a yellow solid (1.0 g) which was washed with ethanol to give form B of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as a yellow solid (0.73 g; 50%), m.p. 155-157°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before. Rotary evaporation of the ethanol washings gave a multicomponent brown gum (0.24 g) which was not further investigated.

Elution with hexane-ether (1:1) through ether to methanol gave only a series of multicomponent gums (total 0.16 g) which yielded no identifiable material.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave no further material.

Bis-(1,2-naphthoquinone-1-oximato)copper(II) Monohydrate (162)

Bis-(1,2-naphthoquinone-1-oximato)copper(II) monohydrate (162) was prepared by the reaction of 1-nitroso-2-naphthol (72) with copper(II) sulphate pentahydrate as described by Charalambous, Frazer and Taylor,[113] as a brown solid (yield 59%), m.p. 256° (decomp.), which was used without further purification.

The Reaction of Bis-(1,2-naphthoquinone-1-oximato)copper(II) Monohydrate (162) with 2-Bromo-2,2-diphenylacetaldehyde (112a)

A stirred solution of bis-(1,2-naphthoquinone-1-oximato)copper(II) monohydrate (162) (0.43 g; 0.001 mol) in anhydrous dimethyl sulphoxide (7.5 ml) was treated with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (0.55 g; 0.002 mol) in anhydrous dimethyl sulphoxide (2.5 ml). The resulting dark brown solution was then stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The dark brown solution was allowed to cool, then rotary evaporated to give a brown gum which was treated with water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give unreacted bis-(1,2-naphthoquinone-1-oximato)copper(II) monohydrate (162) as a brown solid (0.11 g; 26%), m.p. 222° (decomp.), identified by comparison (m.p. and i.r. spectrum) with a sample prepared before.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane, and the combined extracts rotary

evaporated to give a brown gum (0.83 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave benzophenone as a yellow oil (0.12 g; 33%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Elution with hexane-ether (4:1) gave form A of naphthalene-1,2-dione 1-oxime diphenylformylmethyl ether (161) as an orange solid (0.33 g; 45%), m.p. 155-158° identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Elution with hexane-ether (7:3) through ether to methanol gave only a series of multicomponent gums (total 0.23 g) which afforded no identifiable material.

Attempted Reduction Reactions of Naphthalene-1,2-dione 1-Oxime Diphenylformylmethyl Ether (161)

(a) A stirred solution of form A of the oxime ether (161) (0.37 g; 0.001 mol) in ethanol (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.037 g) at room temperature and atmospheric pressure for 1 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a brown gum (0.35 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave benzophenone as a brown oil (0.050 g; 27%), identified by comparison [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:3) over silica] with an authentic sample.

Further elution with hexane-ether (19:1) gave a multicomponent brown oil (0.030 g) which was not further investigated.

Elution with hexane-ether (9:1) gave a red gum (0.25 g) which was washed with ether to give unreacted form A of the oxime ether (161) as an orange solid (0.16 g; 43%), m.p. 150-155°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample. Rotary evaporation of the ether washings gave only an intractable red gum (0.070 g).

Elution with hexane-ether (4:1) through ether to methanol gave no further material.

(b) A stirred solution of form B of the oxime ether (161) (0.37 g; 0.001 mol) in ethanol (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.037 g) at room temperature and atmospheric pressure for 2 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a brown gum (0.35 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (3:7) gave benzophenone as a brown oil (0.10 g; 55%), identified by comparison [i.r. spectrum and t.l.c. in hexane-dichloromethane (1:3) over silica] with an authentic sample.

Elution with hexane-dichloromethane (1:4) gave an intractable brown gum (0.060 g).

Elution with dichloromethane gave a brown oil (0.17 g) whose t.l.c. in hexane-dichloromethane (1:3) over silica showed it to be mainly the unreacted form B of the oxime ether (161).

Final elution with methanol afforded no further material.

(c) A stirred suspension of form B of the oxime ether (161) (0.73g; 0.002 mol) in 70% v/v aqueous acetic acid (20.0 ml) was treated with sodium dithionite (0.73 g) and the mixture stirred at room temperature in a stoppered flask for 30 min.

The mixture was rotary evaporated to give a brown residue. This was treated with water (5.0 ml) and extracted with dichloromethane to give a multicomponent brown gum (0.37 g) which afforded no identifiable material.

Neutralisation of the aqueous mother liquor with 2 M aqueous sodium hydroxide and glacial acetic acid and extraction with dichloromethane gave no further material.

Ethyl 2-(1-Nitrosonaphth-2-yl)oxethanoate (167)

(a) A stirred suspension of the sodium salt of 1-nitroso-2-naphthol (153) (2.0 g; 0.01 mol) in anhydrous acetonitrile (37.5 ml) was treated with a solution of ethyl bromoacetate (165) (1.7 g; 0.01 mol) in anhydrous acetonitrile (12.5 ml) and the resulting green suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The mixture was hot filtered to remove an intractable brown solid (1.1 g) and the filtrate was allowed to cool and rotary evaporated. The residual brown gum (2.2 g) was washed with light petroleum and ether to afford ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) as a brown solid (1.8 g; 69%) m.p. 102-105°, υ_{max} 1742(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 7.50-7.25(6H, m, ArH), 5.08(2H, s, CH_2), 4.25(2H, q, J7Hz, CH_2) and 1.28(3H, t, J7Hz, CH_3).

Rotary evaporation of the light petroleum-ether washings gave only an intractable brown gum (0.25 g) which was not further investigated.

(b) A stirred suspension of the lithium salt of 1-nitroso-2-naphthol (158) (3.6 g; 0.02 mol) in anhydrous acetonitrile (87.5 ml) was treated with a solution of ethyl bromoacetate (165) (3.3 g; 0.02 mol) in anhydrous acetonitrile (12.5 ml) and the resulting green suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The mixture was hot filtered to remove an intractable brown solid (0.37 g) and the filtrate was allowed to cool and rotary evaporated. The residual brown solid obtained was treated with water (50.0 ml) and extracted with

dichloromethane to give a brown waxy solid (4.5 g) which was washed with light petroleum and ether to give ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) as a brown solid (3.3 g; 64%), m.p. 102-105°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Rotary evaporation of the light petroleum-ether washings gave only an intractable brown gum (0.95 g) which was not further investigated.

Attempted Reduction Reactions of Ethyl 2-(1-Nitrosonaphth-2-yl)oxyethanoate (167)

(a) A stirred solution of ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) (0.52 g; 0.002 mol) in ethanol (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.052 g) at room temperature and atmospheric pressure for 2 h.

The mixture was then filtered through celite and the filtrate rotary evaporated to give a brown gum (0.40 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of multicomponent gums (total 0.35 g) from which no identifiable material was obtained.

(b) A stirred solution of ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) (0.52 g; 0.002 mol) in 70% v/v aqueous ethanol (10.0 ml) was treated with sodium dithionite (0.52 g) and the mixture was heated under reflux for 1 h. A

further portion of sodium dithionite (0.52 g) was added and the mixture was then stirred and heated under reflux for a further 1 h.

The mixture was allowed to cool and rotary evaporated to give a brown residue. This was treated with water (5.0 ml) and extracted with dichloromethane to give an intractable multicomponent gum (0.22 g) from which no identifiable material was obtained.

(c) A stirred solution of ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) (0.52 g; 0.002 mol) in 70% v/v aqueous ethanol (20.0 ml) was treated with sodium dithionite (0.52 g) and the mixture stirred at room temperature for 30 min.

The mixture was rotary evaporated to give a brown residue which was treated with water (2.5 ml). The resulting suspension was filtered to give 1-amino-2-naphthol (139) as a brown solid (0.23 g; 72%), m.p. 183-186°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

The aqueous mother liquor was neutralised with 2 M aqueous sodium hydroxide and glacial acetic acid and extracted with dichloromethane to give no further material.

(d) A stirred solution of ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) (0.52 g; 0.002 mol) in methanol (10.0 ml) was treated dropwise over 15 min at room temperature with a solution of sodium borohydride (0.34 g; 0.009 mol) in water (5.0 ml) and the mixture was then stirred at room temperature for 3

h.

The mixture was rotary evaporated and the residue was treated with water (5.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to remove an intractable brown solid (0.042 g).

The aqueous-dichloromethane filtrate was separated and the aqueous layer extracted with dichloromethane. The combined extracts were rotary evaporated to give a brown gum (0.28 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable multicomponent gums (total 0.23 g) from which no identifiable material was obtained.

Ethyl 2,2-Diphenyl-2-(1-nitrosonaphth-2-yl)oxyethanoate (172a)

A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153) (2.0 g; 0.01 mol) in anhydrous dimethyl sulphoxide (25.0 ml) was treated with a solution of ethyl 2-chloro-2,2-diphenylacetate (117a) (2.7 g; 0.01 mol) in anhydrous dimethyl sulphoxide (5.0 ml) and the resulting green solution was stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool and rotary evaporated under high vacuum. The residue was treated with water (25.0 ml) and extracted with dichloromethane to give a brown gum (3.6 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave a brown oil (0.40 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to be mainly unreacted ethyl 2-chloro-2,2-diphenylacetate (117a).

Elution with hexane-ether (9:1) gave a brown gum (1.3 g) which was washed with light petroleum to give an intractable solid (1.0 g). The light petroleum washings were rotary evaporated to give a multicomponent red gum (0.18 g) from which no identifiable material was obtained.

Elution with hexane-ether (7:3) gave a brown gum (1.8 g) which was washed with pentane and hexane to give ethyl 2,2-diphenyl-2-(1-nitrosonaphth-2-yl)oxyethanoate (172a) as a yellow solid (1.3 g; 32%), m.p. 108-110° (from hexane-ethyl acetate), υ_{max} 1732(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 7.67-7.25(16H, m, ArH), 4.28(2H, q, J7Hz, CH_2) and 1.19(3H, t, J7Hz, CH_3). Rotary evaporation of the pentane-hexane washings gave only a multicomponent brown gum (0.41 g) from which no further material was obtained.

Further elution with hexane-ether (1:1) through to ether gave no further material.

Final elution with methanol gave a multicomponent brown gum (0.081 g) from which no identifiable material was obtained.

Diphenylacetyl Chloride (174)

A stirred suspension of diphenylacetic acid (173) (42.4 g; 0.2 mol) in thionyl chloride (50.0 ml) was heated under reflux with the exclusion of atmospheric moisture for 3 h.

The mixture was allowed to cool and rotary evaporated to give diphenylacetyl chloride (174) as a yellow waxy solid (46.1 g; 100%), which was used without further purification.

Ethyl 2,2-Diphenylacetate (175)

Diphenylacetyl chloride (174) (46.1 g; 0.2 mol) was added in portions to anhydrous ethanol (500 ml) and the resulting pale yellow solution was stirred at room temperature with the exclusion of atmospheric moisture for 2 h.

The mixture was rotary evaporated to give an orange oil (47.6 g) which was dissolved in ether (500 ml) and the solution washed with 10% w/v aqueous sodium hydrogen carbonate (3 x 20.0 ml) then rotary evaporated to give ethyl 2,2-diphenylacetate (175) as a pale yellow solid (45.1 g; 94%), m.p. 61-64° (lit.,[123] 56-57°), υ_{max} 1728(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 7.37-7.25(10H, m, ArH), 5.03(1H, s, CH), 4.23(2H, q, J7Hz, CH_2) and 1.25(3H, t, J7Hz, CH_3).

Ethyl 2-Bromo-2,2-diphenylacetate (118)

A stirred suspension of ethyl 2,2-diphenylacetate (175) (9.6 g; 0.04 mol) and N-bromosuccinimide (14.2 g; 0.08 mol) in anhydrous chloroform (200 ml) was treated with dibenzoyl peroxide (0.02 g). The resulting pale yellow suspension was then stirred and heated under reflux with the exclusion of atmospheric moisture for 36 h.

The mixture was allowed to cool, then rotary evaporated. The resulting yellow solid (21.3 g) was washed with light petroleum and ether to give succinimide as a pale yellow solid (6.8 g; 86%), m.p. 130-133°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the combined light petroleum-ether washings gave an orange oil (14.1 g) which was washed with light petroleum to give a second crop of succinimide as a pale yellow solid (1.1 g; 14%), m.p. 115-117°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the light petroleum washings gave ethyl 2-bromo-2,2-diphenylacetate (118) as a pale yellow oil (12.8 g; 100%), b.p. 110-115°/0.4 mm Hg, υ_{max} 1730(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 7.46-7.25(10H, m, ArH), 4.28(2H, q, J7Hz, CH_2) and 1.26(3H, t, J7Hz, CH_3).

Attempted Reactions of the Lithium Salt of 1-Nitroso-2-naphthol (158) with Ethyl 2-Bromo-2,2-diphenylacetate (118)

(a) A stirred suspension of the lithium salt of 1-nitroso-2-naphthol (158) (0.72 g; 0.004 mol) in anhydrous acetonitrile (17.5 ml) was treated with a

solution of ethyl 2-bromo-2,2-diphenylacetate (118) (1.3 g; 0.004 mol) in anhydrous acetonitrile (2.5 ml) and the resulting green suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 20 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (2.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable oils and gums (total 2.1 g) from which no identifiable material was obtained.

(b) Repetition of the reaction described in (a) before but in anhydrous dimethyl sulphoxide at 90° (oil-bath) for 1 h gave a mixture which was allowed to cool, then rotary evaporated. The residue was treated with water (10.0 ml) and extracted with dichloromethane to give a brown oil (2.0 g) which was flash-chromatographed over silica.

Elution with hexane-ether (7:3) gave unreacted ethyl 2-bromo-2,2-diphenylacetate (118) as a brown oil (0.27 g; 21%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Further elution with hexane-ether (3:2), through ether to methanol gave only intractable mixtures (total 1.5 g) from which no further identifiable material was obtained.

The Attempted Reaction of the Lithium Salt of 1-Nitroso-2-naphthol (158) with Ethyl 2-Chloro-2,2-diphenylacetate (117a)

A stirred suspension of the lithium salt of 1-nitroso-2-naphthol (158) (1.8 g; 0.01 mol) in anhydrous acetone (80.0 ml) was treated with a solution of ethyl 2-chloro-2,2-diphenylacetate (117a) (2.7 g; 0.01 mol) in anhydrous acetone (20.0 ml) and the resulting brown suspension was stirred at room temperature with the exclusion of atmospheric moisture for 6 h and then heated under reflux for a further 16 h.

The mixture was allowed to cool, then rotary evaporated and the residue treated with water (25.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give the unreacted lithium salt of 1-nitroso-2-naphthol (158) as a green solid (1.5 g; 83%), m.p. 259-263°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane. Rotary evaporation of the combined extracts gave a brown gum (3.0 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to be mainly the unreacted ester (117a).

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave 1-nitroso-2-naphthol (72) as a brown solid (0.11 g; 6%), m.p. 106-108°, identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of the Sodium Salt of 1-Nitroso-2-naphthol (153) with Ethyl 2-Bromo-2-methylpropionate (117b)

A stirred suspension of the sodium salt of 1-nitroso-2-naphthol (153) (0.39 g; 0.002 mol) in anhydrous acetonitrile (7.5 ml) was treated with a solution of ethyl 2-bromo-2-methylpropionate (117b) (0.39 g; 0.002 mol) in anhydrous acetonitrile (2.5 ml) and the resulting green suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 24 h.

The mixture was allowed to cool, then rotary evaporated and the residue was treated with water (5.0 ml) and extracted with dichloromethane to give a brown gum (0.52 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through ether to methanol gave only a series of intractable gums (total 0.49 g) from which no identifiable material was obtained.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave no further identifiable material.

3,3-Diphenyl-3H-naphth[2,1-b]-1,4-oxazine 1-N-Oxide (164)

(a) A stirred solution of hydrazobenzene (0.44 g; 0.0024 mol) in anhydrous benzene (5.0 ml) was treated with a solution of form B of the oxime ether (161) (0.73 g; 0.002 mol) in anhydrous benzene (5.0 ml) and the resulting brown solution was stirred at room temperature in a stoppered flask for 2 h.

The mixture was filtered to remove an intractable colourless solid (0.17 g) and the benzene filtrate was rotary evaporated to give a brown gum (1.1 g)

which was washed with warm hexane (3 x 10.0 ml) to give 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine 1-N-oxide (164) as a pale brown solid (0.30 g; 43%), m.p. 162-164° (from hexane-toluene), $\delta_H(CDCl_3)$ 8.53-7.19(16H, m, ArH) and 4.60(1H, s, CH) (exch.).

Rotary evaporation of the hexane washings gave an orange waxy solid (0.61 g) whose t.l.c. in hexane-dichloromethane (1:1) over silica showed it to be mainly a mixture of benzophenone and azobenzene.

(b) Repetition of the reaction described in (a) before but using form A of the oxime ether (161) gave a mixture which was filtered to afford 1-amino-2-naphthol (139) as a colourless solid (0.042 g; 13%), m.p. 184-188°, identical (m.p. and i.r. spectrum) to an authentic sample prepared before.

The benzene filtrate was rotary evaporated to give an orange gum (1.2 g) which was washed with warm hexane (3 x 10.0 ml) to give 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine 1-N-oxide (164) as a pale yellow solid (0.12 g; 17%), m.p. 162-164°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Rotary evaporation of the hexane washings gave an orange waxy solid (1.0 g) whose t.l.c. in hexane-ether (7:3) over silica showed it to be mainly a mixture of benzophenone and azobenzene.

3,3-Diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a)

(a) A stirred solution of form B of the oxime ether (161) (0.73 g; 0.002 mol)

in anhydrous 1,2-dimethoxyethane (10.0 ml) was treated with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the resulting yellow solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 20 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.8 g) which was washed with ether to afford triphenylphosphine oxide as a grey solid (0.84 g; 76%), m.p. 152-155°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the ether washings gave a brown gum (1.0 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave a brown gum (0.80 g) which was washed with light petroleum to yield 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a yellow solid (0.44 g; 66%) which formed yellow irregular microcrystals, m.p. 124-125° (from hexane-ethyl acetate), υ_{max} 1592(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 8.49-7.17(17H, m, ArH and CH). Rotary evaporation of the light petroleum washings gave a multicomponent brown oil (0.36 g) which afforded no further identifiable material.

Further elution with hexane-ether (4:1) through to hexane-ether (1:9) gave no further material.

Elution with ether gave a second crop of triphenylphosphine oxide (0.14 g; 12%), m.p. 151-154°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Final elution with methanol gave no further material.

(b) Repetition of the reaction described in (a) before but using form A of the oxime ether (161) gave a mixture which was allowed to cool, then rotary evaporated to give a brown semisolid (1.7 g). This was washed with ether to give triphenylphosphine oxide as a grey solid (0.74 g; 67%), m.p. 152-155°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the ether washings gave a brown gum (1.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an intractable brown gum (0.090 g) which was not further investigated.

Further elution with hexane-ether (19:1) gave 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a yellow solid (0.52 g; 78%), m.p. 120-124°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared in (a) before.

Further elution with hexane-ether (9:1) through to hexane-ether (1:9) then ether gave no identifiable material.

Final elution with methanol gave a second crop of triphenylphosphine oxide (0.35 g; 31%), m.p. 150-152°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(c) Repetition of the reaction described in (a) before but using a mixture of the yellow B form and the orange A form of the oxime ether (161) gave a mixture which was allowed to cool, then rotary evaporated. The resulting brown solid (1.7 g) was washed with ether to give triphenylphosphine oxide as a pink solid (0.80 g; 72%), m.p. 152-154°, identified by comparison (m.p. and

i.r. spectrum) with an authentic sample.

Rotary evaporation of the ether washings gave a brown semisolid (0.90 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an intractable brown gum (0.064 g) which was not further investigated.

Further elution with hexane-ether (19:1) gave 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a yellow solid (0.53 g; 79%), m.p. 120-123°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before.

Elution with hexane-ether (9:1) through to hexane-ether (1:9) and ether gave no further identifiable material.

Final elution with methanol gave a second crop of triphenylphosphine oxide as a brown solid (0.13 g; 12%), m.p. 150-152°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

1,2-Dihydro-3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (176)

A stirred solution of 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) (0.67 g; 0.002 mol) in 1,2-dimethoxyethane (10.0 ml) was treated dropwise over 15 min at room temperature with a solution of sodium borohydride (0.34 g; 0.009 mol) in water (5.0 ml). The mixture which contained a pink precipitate was then stirred at room temperature for 5 h.

The mixture was rotary evaporated and the residue was treated with water (10.0 ml) and extracted with dichloromethane to afford 1,2-dihydro-3,3-

diphenyl-3H-naphth[2,1-b]-1,4-oxazine (176) as a cream solid (0.67 g; 99%), m.p. 159-162° (from ethyl acetate-hexane), υ_{max} 3401(NH) cm^{-1}, $\delta_H(CDCl_3)$ 7.74-7.19(16H, m, ArH), 3.98(2H, s, CH_2) and 2.16(1H, s, NH).

Oxidation Reactions of 1,2-Dihydro-3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (176)

(a) A stirred solution of the dihydro compound (176) (0.34 g; 0.001 mol) in anhydrous acetonitrile (10.0 ml) was treated with activated manganese(IV) oxide (0.50 g) added in one portion and the suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 18 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a brown gum (0.34 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a brown solid (0.085 g; 25%), m.p. 119-123°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

Elution with hexane-ether (4:1) gave unreacted dihydro compound (176) as a yellow solid (0.16 g; 47%), m.p. 141-148°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Further elution with hexane-ether (4:1) through to ether then methanol gave no further identifiable material.

(b) Repetition of the reaction described in (a) before but with heating under

reflux for 2 h gave a mixture which was allowed to cool, then filtered through celite. The filtrate was rotary evaporated to give a brown gum (0.34 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave an orange gum (0.11 g) which was washed with light petroleum to afford 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a yellow solid (0.090 g; 27%), m.p. 124-125°, identical (m.p. and i.r. spectrum) to an authentic sample prepared before. Rotary evaporation of the light petroleum washings gave no other material.

Further elution with hexane-ether (19:1) through ether to methanol gave no further identifiable material.

The Attempted Reaction of 3,3-Diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) with Manganese(IV) Oxide

A stirred solution of 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) (0.34 g; 0.001 mol) in anhydrous acetonitrile (5.0 ml) was treated with activated manganese(IV) oxide (0.5 g) added in one portion. The suspension was then stirred and heated under reflux with the exclusion of atmospheric moisture for 5 h.

The mixture was allowed to cool, then filtered through celite. The filtrate was rotary evaporated to afford a brown semisolid (0.39 g) which was washed with hexane to give unreacted 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a yellow solid (0.34 g; 100%), m.p. 124-125°, identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of 3,3-Diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) with Potassium Cyanide

A stirred solution of 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) (0.67 g; 0.002 mol) in glacial acetic acid (5.0 ml) was treated with potassium cyanide (0.65 g; 0.01 mol) added in one portion and the brown mixture was stirred at room temperature for 6 h.

The mixture was rotary evaporated and the residue washed with water (2 x 10.0 ml) to give unreacted 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a pink solid (0.67 g; 100%), m.p. 124-125°, identical (m.p. and i.r. spectrum) to an authentic sample prepared before.

2-Cyano-1,2-dihydro-3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (177)

A stirred solution of 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) (0.67 g; 0.002 mol) in glacial acetic acid (5.0 ml) was treated with potassium cyanide (0.65 g; 0.01 mol) added in one portion and the mixture was stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 6 h.

The mixture was allowed to cool, then rotary evaporated to give a yellow solid which was washed with water (2 x 10.0 ml) to afford 2-cyano-1,2-dihydro-3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (177) (0.73 g; 100%) which formed colourless irregular microcrystals, m.p. 229-233° (from ethyl acetate-hexane), υ_{max} 3380(NH) and 2234w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 7.77-7.13(16H, m, ArH), 5.40(1H, d, J5Hz, CH; collapses to a singlet on shaking with D_2O), and

4.65(1H, d, J5Hz, NH) (exch.).

The Attempted Oxidation of 2-Cyano-1,2-dihydro-3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (177)

A stirred solution of the dihydro compound (177) (0.54 g; 0.0015 mol) in anhydrous acetonitrile (15.0 ml) was treated with activated manganese(IV) oxide (0.75 g) added in one portion and the dark suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 18 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a brown gum (0.55 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable multicomponent gums (total 0.54 g) which yielded no identifiable material.

2-Cyano-3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (179)

A stirred solution of the dihydro compound (177) (0.72 g; 0.002 mol) in anhydrous acetonitrile (20.0 ml) was treated with activated manganese(IV) oxide (1.0 g) added in one portion and the dark suspension was stirred and heated under reflux with the exclusion of atmospheric moisture for 5 h.

The hot mixture was filtered through celite and the filtrate was rotary evaporated to give a brown gum (0.72 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave 2-cyano-3,3-diphenyl-3H-naph[2,1-b]-1,4-oxazine (179) as a yellow solid (0.50 g; 69%), m.p. 147-150° (from ethyl acetate-hexane), υ_{max} 2214w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 8.45(1H, d, J8Hz, ArH) and 7.83-7.05(15H, m, ArH).

Elution with hexane-ether (9:1) through ether to methanol gave only a series of multicomponent gums (total 0.18 g) from which no identifiable material was obtained.

The Attempted Acid Catalysed Hydrolysis of 3,3-Diphenyl-3H-naphth[2,1-b]1-4-oxazine (133a)

(a) A stirred solution of 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) (0.67 g; 0.002 mol) in ethanol (10.0 ml) was treated with 2 M aqueous hydrochloric acid (2.5 ml) and the mixture was stirred at room temperature for 1 h.

The mixture was filtered to give unreacted 3,3-diphenyl-3H-naphth[2,1-b]-1,4-oxazine (133a) as a brown solid (0.54 g; 81%), m.p. 124-125°, identical (m.p. and i.r. spectrum) to an authentic sample.

The aqueous ethanol filtrate was rotary evaporated to give an intractable brown semisolid (0.14 g) which yielded no identifiable material.

(b) Repetition of the reaction described in (a) before but with heating under reflux for 1 h gave a mixture which was hot filtered to give an intractable multicomponent brown solid (0.57 g).

The filtrate was allowed to cool, then rotary evaporated to give a multicomponent brown solid (0.089 g) which was not further investigated.

The Attempted Reduction of Ethyl 2-(1-Nitrosonaphth-2-yl)oxyethanoate (167) with Hydrazobenzene

A stirred solution of hydrazobenzene (0.44 g; 0.0024 mol) in anhydrous benzene (5.0 ml) was treated with a solution of ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) (0.52 g; 0.002 mol) in anhydrous benzene (5.0 m) and the resulting brown solution was stirred at room temperature in a stoppered flask for 30 min.

The mixture was then filtered to give 1-amino-2-naphthol (139) as a brown solid (0.17 g; 53%), m.p. 186-194°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the benzene filtrate gave a brown gum (0.68 g) which was washed with ether and hexane to give unreacted ethyl 2-(1-nitrosanaphth-2-yl)oxyethanoate (167) as a brown solid (0.19 g; 37%), m.p. 104-107°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The combined hexane and ether washings were rotary evaporated to give azobenzene as an orange solid (0.39 g; 89%), m.p. 68-70°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The Attempted Reduction of Ethyl 2-(1-Nitrosonaphth-2-yl)oxyethanoate (167) with Triphenylphosphine

A stirred solution of ethyl 2-(1-nitrosonaphth-2-yl)oxyethanoate (167) (0.52 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was treated with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the resulting brown solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 22 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave a multicomponent brown gum (0.41 g) from which no identifiable material was obtained.

Further elution with hexane-ether (4:1) gave an intractable multicomponent brown gum (0.22 g).

Elution with hexane-ether (1:1) gave 1-amino-2-naphthol (139) as a brown solid (0.15 g; 47%), m.p. 185-188°, identical (m.p. and i.r. spectrum) with an authentic sample prepared before.

Elution with hexane-ether (2:3) through to ether gave no further material.

Elution with methanol gave a brown gum (0.83 g) which was washed with ether to give triphenylphosphine oxide as a brown solid (0.62 g; 56%), m.p. 145-151°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the ether washings gave only an intractable brown gum (0.11 g).

Naphthalene-1,2-dione 1-Oxime 1-Formyl-2-propyl Ether (180)

A stirred solution of the lithium salt of 1-nitroso-2-naphthol (158) (0.72 g; 0.004 mol) in anhydrous acetone (35.0 ml) was treated with a solution of 2-bromo-2-methylpropionaldehyde (112b) (0.60 g; 0.004 mol) in anhydrous acetone (5.0 ml) and the resulting green suspension was stirred at room temperature with the exclusion of atmospheric moisture for 7 h. A further portion of 2-bromo-2-methylpropionaldehyde (112b) (0.60 g; 0.004 mol) in anhydrous acetone (5.0 ml) was then added and the green suspension stirred at room temperature with the exclusion of atmospheric moisture for a further 17 h. A further portion of 2-bromo-2-methylpropionaldehyde (112b) (0.60 g; 0.004 mol) in anhydrous acetone (5.0 ml) was then added and the mixture stirred at room temperature with the exclusion of atmospheric moisture for a further 7 h.

Rotary evaporation of the mixture gave a brown residue which was treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (1.3 g). This was flash-chromatographed over silica.

Elution with hexane-ether (3:2) gave an intractable multicomponent brown oil (0.31 g).

Elution with hexane-ether (2:3) gave a brown gum (0.51 g) which was washed with ether to afford naphthalene-1,2-dione 1-oxime 1-formyl-2-propyl ether (180) (0.25 g; 26%) which forms yellow irregular microcrystals, m.p. 110-112° (from ethyl acetate-hexane), υ_{max} 1733(C=O) and 1658(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 9.79(1H, s, CHO), 8.70(1H, d, J8Hz, ArH), 7.52-7.25(4H, m, ArH),

6.37(1H, d, J8Hz, ArH) and 1.58(6H, s, 2xCH_3). Rotary evaporation of the ether washings gave an intractable brown gum (0.22 g).

Elution with hexane-ether (3:7) through to ether then methanol gave no further identifiable material.

1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73)

A stirred suspension of magnesium turnings (9.6 g; 0.4 mol) in anhydrous ether (40.0 ml) was treated with a crystal of iodine and the mixture heated at 45° (water-bath) for 5 min during which time an exothermic reaction occurred. The water-bath was then removed and gentle reflux was maintained by the dropwise addition of a solution of methyl iodide (56.8 g; 0.04 mol) in anhydrous ether (160 ml). The mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture for 30 min.

The resulting solution of methylmagnesium iodide in ether was stirred under nitrogen and treated dropwise with a solution of 4,4'-bis(dimethylamino)benzophenone (182) (21.4 g; 0.08 mol) in anhydrous benzene (600 ml). The resulting brown turbid solution was stirred at room temperature under nitrogen for 24 h.

The mixture was treated dropwise with water until the vigorous reaction subsided, then treated with water (600 ml), glacial acetic acid (40.0 ml) and ammonium chloride (70.0 g). The resulting mixture was stirred at room temperature for 3 h.

The combined benzene-ether layer was separated and the aqueous layer

extracted further with benzene. The combined extracts were rotary evaporated to give 1,1-bis-(4-dimethylaminophenyl)ethene (Michler's alkene) (73) as a pale green solid (20.4 g; 96%), m.p. 124-128° (lit.,[114] 123-124°), $\delta_H(CDCl_3)$ 7.31-6.66(8H, dd, J9Hz,J2Hz, ArH), 5.20(2H, s, CH_2) and 2.97(12H, s, 4xCH_3), $\delta_c(CDCl_3)$ 149.9(quat), 149.4(quat), 130.1(quat), 129.0(CH), 111.8(CH), 108.9(CH_2) and 40.5(CH_3).

3,3-Di-(4-dimethylaminopheny)-3H-naphth[2,1-b]-1,4-oxazine (74)

(a) A stirred solution of the alkene (73) (1.1 g; 0.004 mol) in anhydrous ethanol (20.0 ml) was treated with a solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous ethanol (10.0 ml). Glacial acetic acid (2 drops) was added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 7 h.

The mixture was allowed to cool, then rotary evaporated to give a brown solid (1.6 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) as a colourless solid (0.40 g; 24%), m.p. 184-185° (from hexane-toluene), υ_{max} 1611(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 8.49-6.63(15H, m, ArH and CH) and 2.92(12H, s, 4xCH_3).

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of intractable multicomponent gums (total 0.82 g) from which no further identifiable material was obtained.

(b) A stirred solution of the alkene (73) (0.53 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was treated with a solution of 1-nitroso-2-naphthol (72) (0.35 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 7 h. Glacial acetic acid (2 drops) was added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for a further 16 h.

The mixture was then hot filtered to remove an intractable grey solid (0.11 g).

Rotary evaporation of the 1,2-dimethoxyethane mother liquor gave a dark brown solid (0.76 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) as a colourless solid (0.10 g; 12%), m.p. 175-178°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared in (a) before.

Elution with hexane-ether (7:3) through ether to methanol gave only a series of intractable gums and solids (total 0.65 g) from which no further identifiable material was obtained.

(c) Repetition of the reaction described in (a) before but in anhydrous 1,4-dioxane under reflux for 23 h gave a mixture which was allowed to cool, then rotary evaporated to give a brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave an intractable multicomponent brown gum (0.18 g) from which no identifiable material was obtained.

Elution with hexane-ether (4:1) gave 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) as a brown solid (0.14 g; 8%), m.p. 182-185°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before.

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of multicomponent gums and solids (total 1.4 g) from which no further identifiable material was obtained.

(d) A stirred solution of the alkene (73) (0.53 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was treated with a solution of 1-nitroso-2-naphthol (72) (0.35 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml). Concentrated hydrochloric acid (1 drop) was added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 23 h.

The mixture was allowed to cool, then rotary evaporated to give a dark brown gum (0.91 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave a multicomponent green gum (0.080 g) from which no identifiable material was obtained.

Elution with hexane-ether (4:1) gave 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) as a brown solid (0.15 g; 18%), m.p. 178-181°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before.

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of intractable multicomponent gums and solids (total 0.63 g) from which no further identifiable material was obtained.

(e) A stirred solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous toluene (20.0 ml) was treated with a solution of the alkene (73) (1.1 g; 0.004 mol) in anhydrous toluene (20.0 ml). Toluene-4-sulphonic acid (0.069 g) was added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 6 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave an intractable multicomponent brown gum (0.16 g).

Further elution with hexane-ether (4:1) gave a brown gum (0.43 g) which was washed with hexane to afford 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) as a brown solid (0.26 g; 15%), m.p. 175-180°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before. Rotary evaporation of the hexane washings gave an intractable brown gum (0.12 g).

Elution with hexane-ether (1:1) through ether to methanol gave only a series of multicomponent gums (total 0.91 g) from which no further identifiable material was obtained.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with 1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73)

A stirred solution of the alkene (73) (0.53 g; 0.002 mol) in glacial acetic acid (5.0 ml) was treated with a solution of 1-nitroso-2-naphthol (72) (0.35 g; 0.002 mol) in glacial acetic acid (5.0 ml). The resulting green solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The mixture was allowed to cool, then rotary evaporated to give a black gum which was washed with 10% w/v aqueous sodium hydrogen carbonate and extracted with dichloromethane to give an intractable multicomponent black solid (0.98 g).

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave no further material.

Attempted Reactions of 1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73) with Acetyl Chloride

(a) A stirred solution of the alkene (73) (0.53 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was cooled to 0° (ice-salt bath) and treated dropwise with a solution of acetyl chloride (0.16 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) at such a rate that the reaction temperature remained at 0°. The mixture was then stirred at 0° (ice-salt bath) with the exclusion of atmospheric moisture for 30 min.

The mixture was filtered to remove some insoluble solid and the filtrate

was rotary evaporated to give the unreacted alkene (73) as a green solid (0.49 g; 92%), m.p. 125-127°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

(b) A stirred solution of the alkene (73) (0.53 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was treated dropwise at room temperature with a solution of acetyl chloride (0.16 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml).

The resulting green suspension was then stirred and heated under reflux with the exclusion of atmospheric moisture for 22 h.

The mixture was hot filtered to afford an intractable grey solid (0.35 g).

Rotary evaporation of the 1,2-dimethoxyethane mother liquor gave the unreacted alkene (73) as a green solid (0.18 g, 34%), m.p. 123-126°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

(c) A stirred suspension of aluminium(III) chloride (0.27 g; 0.002 mol) in anhydrous dichloromethane (5.0 ml) was cooled to 0° (ice-salt bath), then treated dropwise with a solution of acetyl chloride (0.16 g; 0.002 mol) in anhydrous dichloromethane (5.0 ml) at such a rate that the reaction temperature remained at 0°. The mixture was stirred at 0° (ice-salt bath) for 10 min, then treated dropwise with a solution of the alkene (73) (0.53 g; 0.002 mol) in anhydrous dichloromethane (10.0 ml) at such a rate that the reaction

temperature was 0°. The resulting blue solution was then stirred in the melting ice-salt bath, with the exclusion of atmospheric moisture for 4 h.

The mixture was poured into 10% w/v aqueous sodium hydrogen carbonate solution (20.0 ml), stirred at room temperature for 15 min, then filtered to remove the aluminium residues which were washed with dichloromethane (2 x 5.0 ml). The combined aqueous dichloromethane filtrate and washings were separated and the aqueous layer further extracted with dichloromethane. The combined dichloromethane extracts were rotary evaporated to give a green solid (0.49 g) which was crystallised from ethanol to afford the unreacted alkene (73) as a green solid (0.46 g; 87%), m.p. 125-127°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared before.

Attempted Reactions of 1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73) with Ethyl Chloroformate

(a) A stirred suspension of fused sodium acetate (0.82 g; 0.01 mol) in glacial acetic acid (5.0 ml) was treated dropwise with a solution of the alkene (73) (0.53 g; 0.002 mol) in glacial acetic acid (2.5 ml). The mixture was then stirred and treated dropwise with a solution of ethyl chloroformate (0.22 g; 0.002 mol) in glacial acetic acid (2.5 ml) and the resulting blue suspension stirred at room temperature for 3 h.

The mixture was rotary evaporated and the residue was treated with water (5.0 ml) and extracted with dichloromethane to give a green gum (0.71

g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave the unreacted alkene (73) as a cream solid (0.25 g; 47%), m.p. 115-120°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Further elution with hexane-ethyl acetate (4:1) through ethyl acetate to methanol gave only a series of intractable gums and solids (total 0.43 g) which yielded no further identifiable material.

(b) Repetition of the reaction described in (a) before but at 100° for 1 h gave a mixture which was allowed to cool, then rotary evaporated. The residue was treated with water (5.0 ml) and extracted with dichloromethane to give only an intractable multicomponent dark brown gum (0.75 g) which was not further investigated.

(c) Repetition of the reaction described in (a) before but at room temperature for 17 h gave a mixture which was rotary evaporated. The residue was treated with water (5.0 ml) and extracted with dichloromethane to give a green gum (0.75 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave the unreacted alkene (73) as a cream solid (0.14 g; 26%), m.p. 118-120°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Further elution with hexane-ethyl acetate (4:1) through ethyl acetate to methanol gave no further identifiable material.

(d) A stirred solution of the alkene (73) (0.53 g; 0.002 mol) in anhydrous 1,4-dioxane (5.0 ml) was treated dropwise with a solution of triethylamine (0.30 g; 0.003 mol) in anhydrous 1,4-dioxane (2.5 ml). The resulting green solution was cooled to 10° (ice-bath) and treated dropwise with a solution of ethyl chloroformate (0.22 g; 0.002 mol) in anhydrous 1,4-dioxane (2.5 ml). The mixture was allowed to come to room temperature in the melting ice-bath, then stirred at room temperature for 48 h, then stirred and heated under reflux for a further 22 h.

The mixture was hot filtered to remove some insoluble solid and the filtrate was rotary evaporated to give a green solid (0.58 g) which was crystallised from hexane-toluene to afford the unreacted alkene (73) as a green solid (0.52 g; 98%), m.p. 122-126°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

N-(4-nitrophenyl)-2,2-bis-(4-dimethylaminophenyl)acrylamide (189)

A stirred solution of the alkene (73) (1.1 g; 0.004 mol) in anhydrous xylene (10.0 ml) was treated with a solution of 4-nitrophenyl isocyanate (0.66 g; 0.004 mol) in anhydrous xylene (10.0 ml) and the green solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 18 h.

The mixture was allowed to cool and the precipitated solid was collected to afford N-(4-nitrophenyl)-2,2-bis-(4-dimethylaminophenyl)acrylamide (189) as a yellow solid (1.5 g; 87%), m.p. 243-244° (from xylene) (lit.,[124] 222-224°), υ_{max} 3354(NH), 1665(C=O) and 1527 and 1321(NO_2) cm^{-1}, δ_H[$(CD_3)_2SO$] 10.52(1H,

s, NH), 8.19-6.65(12H, m, ArH), 6.29(1H, s, CH), 2.94(6H, s, 2xCH_3) and 2.50(6H, s, 2xCH_3).

The xylene mother liquor was rotary evaporated to give a multicomponent brown glass (0.28 g) which was not further investigated.

3,3-Di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine-2-(4-nitrophenyl)carboxamide (190)

A stirred solution of the amide (189) (0.86 g; 0.002 mol) in anhydrous xylene (20.0 ml) was treated with a solution of 1-nitroso-2-naphthol (72) (0.35 g; 0.002 mol) in anhydrous xylene (10.0 ml) and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 2 h. Glacial acetic acid (2 drops) was then added and the mixture was stirred and heated under reflux for a further 2 h.

The mixture was allowed to cool, then filtered to remove an intractable multicomponent brown solid (0.51 g). The xylene mother liquor was rotary evaporated to give a brown gum (1.0 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave an intractable multicomponent brown gum (0.11 g) which was not further investigated.

Elution with hexane-ether (7:3) gave a brown gum (0.24 g) which was washed with light petroleum, then ether to afford 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine-2-(4-nitrophenyl)carboxamide (190) as a yellow solid (0.15 g; 13%), m.p. 250-252°

(from hexane-toluene), υ_{max} 3342(NH), 1693(C=O) and 1523 and 1336(NO_2) cm^{-1}, $\delta_H(CDCl_3)$ 9.96(1H, s, NH), 8.41-7.17(18H, m, ArH) and 2.91(12H, s, 4xCH_3). Rotary evaporation of the combined light petroleum and ether washings gave only an intractable brown gum (0.030 g).

Elution with hexane-ether (3:2) through ether to methanol gave only a series of multicomponent gums and solids (total 0.41 g) from which no further identifiable material was obtained.

1-(Morpholin-4-yl)-1-phenylethene (193)

A stirred solution of acetophenone (191) (37.5 g; 0.31 mol) in anhydrous benzene (60.0 ml) was treated with a solution of morpholine (192) (40.5 g; 0.47 mol) in anhydrous benzene (60.0 ml), toluene-4-sulphonic acid (0.10 g; 0.005 mol) was added and the light brown solution was stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic removal of the water formed (Dean and Stark apparatus) for 184 h.

The mixture was allowed to cool, treated with solid sodium ethoxide (0.20 g; 0.003 mol) and rotary evaporated to give a brown oil (67.0 g) which was distilled under reduced pressure.

A forerun of a colourless oil (2.9 g), b.p. 30-110°/35 mm Hg was collected whose i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica showed it to be a mixture of unreacted morpholine (192) and acetophenone (191).

A second fraction was collected to give 1-(morpholin-4-yl)-1-phenylethene (193) as a pale yellow oil (45.2 g; 77%), b.p. 100-108°/0.8 mm Hg, (lit.,[116] 85-

90°/0.3 mm Hg), $\delta_H(CDCl_3)$ 7.95-7.25(5H, m, ArH), 4.29(1H, s, CH), 4.16(1H, s, CH), 3.75-3.63(4H, m, 2xCH_2) and 2.89-2.77(4H, m, 2xCH_2).

The distillation residue was an intractable brown gum (6.3 g).

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with 1-(Morpholin-4-yl)-1-phenylethene (193)

A stirred suspension of 1-nitroso-2-naphthol (72) (0.87 g; 0.005 mol) in anhydrous benzene (10.0 ml) was cooled to 0° (ice-salt bath), then treated dropwise with a solution of 1-(morpholin-4-yl)-1-phenylethene (193) (0.95 g; 0.005 mol) in anhydrous benzene (10.0 ml) at such a rate that the reaction temperature was 0-5°. The brown suspension was stirred at 0-5° for 30 min then allowed to come to room temperature, stirred at room temperature with the exclusion of atmospheric moisture for 4 h and then heated under reflux for 16 h.

The dark brown mixture was allowed to cool, then rotary evaporated to give a multicomponent brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave the unreacted enamine (193) as a brown oil (0.16 g; 17%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (7:3) over silica] with an authentic sample.

Further elution with hexane-ether (9:1) through ether to methanol gave only a series of multicomponent gums and solids (total 1.4 g) from which no identifiable material was obtained.

The Attempted Reaction of Bis-(1,2-naphthoquinone-1-oximato)copper(II) Monohydrate (162) with Ethyl Phenylpropiolate

A stirred suspension of the copper complex (162) (1.7 g; 0.004 mol) in 1,2-dimethoxyethane (120 ml) and water (16.0 ml) was treated with a solution of ethyl phenylpropiolate (1.4 g; 0.008 mol) in 1,2-dimethoxyethane (8.0 ml) and the mixture was stirred and heated under reflux for 5 h.

The brown mixture was allowed to cool and the solid collected to give the unreacted copper complex (162) as a brown solid (0.51 g; 30%), m.p. 256° (decomp.), identical (m.p. and i.r. spectrum) to an authentic sample.

Rotary evaporation of the aqueous-1,2-dimethoxyethane mother liquor gave a brown residue which was treated with water (20.0 ml) and extracted with dichloromethane. The resulting three-phase mixture was filtered to give a second crop of the copper complex (162) as a brown solid (0.045 g; 3%), m.p. 256° (decomp.), identical (m.p. and i.r. spectrum) to an authentic sample prepared before.

The aqueous-dichloromethane filtrate was separated, the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give an intractable multicomponent brown gum (2.3 g) which was not further investigated.

The Attempted Reaction of Bis-(1,2-naphthoquinone-1-oximato)copper(II) Monohydrate (162) with 1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73)

A stirred suspension of the copper complex (162) (1.7 g; 0.004 mol) in 1,2-dimethoxyethane (120 ml) and water (16.0 ml) was treated with a solution of the alkene (73) (2.1 g; 0.008 mol) in 1,2-dimethoxyethane (8.0 ml) and the mixture was stirred and heated under reflux for 3 h.

The brown mixture was allowed to cool and the solid collected to give the unreacted copper complex (162) as a brown solid (0.87 g; 51%), m.p. 256° (decomp.), identical (m.p. and i.r. spectrum) to an authentic sample prepared before.

Rotary evaporation of the aqueous-1,2-dimethoxyethane mother liquor gave a brown residue which was treated with water (20.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a second crop of the copper complex (162) (0.16 g; 9%), m.p. 256° (decomp.) identical (m.p. and i.r. spectrum) to a sample prepared before.

The aqueous-dichloromethane filtrate was separated, the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give a brown gum (3.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave the unreacted alkene (73) as a colourless solid (0.86 g; 41%), m.p. 124-127°, identical (m.p. and i.r. spectrum) to an authentic sample.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of multicomponent gums and solids (total 1.6 g) from which no further identifiable material was obtained.

The Attempted Reaction of the Sodium Salt of 1-Nitroso-2-naphthol (153) with Dimethyl Acetylenedicarboxylate

A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153) (0.78 g; 0.004 mol) in anhydrous dimethyl sulphoxide (10.0 ml) was treated with a solution of dimethyl acetylenedicarboxylate (0.57 g; 0.004 mol) in anhydrous dimethyl sulphoxide (5.0 ml) and the mixture was stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The brown mixture was allowed to cool, then rotary evaporated under high vacuum to give a brown oil. This was treated with water (10.0 ml) and extracted with dichloromethane to give a brown oil (0.95 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of multicomponent oils and gums (total 0.95 g) from which no identifiable material was obtained.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave only a multicomponent brown gum (0.39 g) which was not further investigated.

The Attempted Reaction of the Sodium Salt of 1-Nitroso-2-naphthol (153) with Ethyl Cinnamate

A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153) (0.78 g; 0.004 mol) in anhydrous dimethyl sulphoxide (10.0 ml) was treated with a solution of ethyl cinnamate (0.70 g; 0.004 mol) in anhydrous dimethyl sulphoxide (5.0 ml) and the mixture was stirred and heated at 90° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, then rotary evaporated under high vacuum to give a green solid which was treated with water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give the unreacted sodium salt of 1-nitroso-2-naphthol (153) as a green solid (0.45 g; 58%), m.p. 295-296°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The aqueous-dichloromethane filtrate was separated, the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give unreacted ethyl cinnamate as a brown oil (0.70 g; 100%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (3:2) over silica] with an authentic sample.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave 1-nitroso-2-naphthol (72) as a brown solid (0.27 g; 39%), m.p. 106-108°, identical (m.p. and i.r. spectrum) to an authentic sample.

Naphthalene-1,2-dione 1-Oxime Tosylate (202)

A stirred suspension of the lithium salt of 1-nitroso-2-naphthol (158) (0.72 g; 0.004 mol) in anhydrous acetone (35.0 ml) was treated dropwise with a solution of toluene-4-sulphonyl chloride (0.76 g; 0.004 mol) in anhydrous acetone (5.0 ml) and the resulting mixture was stirred at room temperature with the exclusion of atmospheric moisture for 1 h.

The mixture was rotary evaporated to give a brown solid (1.5 g) which was washed with dichloromethane to give an intractable brown solid (0.19 g).

Rotary evaporation of the dichloromethane washings gave naphthalene-1,2-dione 1-oxime tosylate (202) as a yellow solid (1.2 g; 92%) which formed yellow microneedles, m.p. 109-114° (from dimethylformamide), υ_{max} 1677(C=O) and 1592(C=N) cm^{-1}, $\delta_H[(CD_3)_2SO]$ 7.88-7.11(9H, m, ArH), 6.24(1H, d, J12Hz, ArH) and 2.29(3H, s, CH_3).

Cis 2-Cyanocinnamic Acid (203)

The oxime tosylate (202) (0.65 g; 0.002 mol) was treated with 2 M aqueous sodium hydroxide solution (2.5 ml) and the mixture was heated in a boiling water-bath until a yellow solution was formed, then stirred in the boiling water bath for a further 5 min.

The mixture was cooled (ice-bath) and acidified by the dropwise addition of concentrated hydrochloric acid. The precipitated solid was collected to give cis 2-cyanocinnamic acid (203) (0.31 g; 90%) which formed colourless microneedles, m.p. 130-140° (from water) (lit.,[125] 137-138°), υ_{max} 3500 br(OH),

2250(C≡N) and 1699(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 9.88(1H, bs, COOH), 7.68-7.37(4H, m, ArH), 7.28(1H, s, CH) and 6.20(1H, s, CH).

The Attempted Reduction of Naphthalene-1,2-dione 1-Oxime Tosylate (202)

A stirred solution of the oxime tosylate (202) (0.65 g; 0.002 mol) in dimethylformamide (10.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.065 g) at room temperature and atmospheric pressure for 2.5 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a brown gum (0.69 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) through ethyl acetate to methanol gave only a series of multicomponent gums (total 0.65 g) from which no identifiable material was obtained.

Reactions of Naphthalene-1,2-dione 1-Oxime Tosylate (202) with 1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73)

(a) A stirred solution of the alkene (73) (0.27 g; 0.001 mol) in anhydrous toluene (5.0 ml) was treated with a solution of the oxime tosylate (202) (0.33 g; 0.001 mol) in anhydrous toluene (5.0 ml) and the resulting brown solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 17 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (0.62 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave an intractable brown gum (0.090 g) which was not further investigated.

Elution with hexane-ether (4:1) gave 3,3-di-(4-dimethylaminophenyl)-3H-naphth[2,1-b]-1,4-oxazine (74) as a brown solid (0.040 g; 10%), m.p. 178-182°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

Elution with hexane-ether (7:3) through ether to methanol gave only a series of multicomponent gums (total 0.42 g) from which no further identifiable material was obtained.

(b) A stirred solution of the alkene (73) (0.27 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was treated with a solution of the oxime tosylate (202) (0.33 g; 0.001 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the resulting mixture was stirred and heated at 50° (oil-bath) for 2 h. Toluene-4-sulphonic acid (3 crystals) was added and the mixture was stirred and heated at 50° with the exclusion of atmospheric moisture for a further 17 h.

The mixture was allowed to cool, then rotary evaporated to give a multicomponent brown gum (0.61 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of multicomponent gums (total 0.61 g) from which no identifiable material was obtained.

2-Nitro-1-naphthol (206)

A stirred solution of 2-nitroso-1-naphthol (205) (8.7 g; 0.05 mol) in glacial acetic acid (450 ml) was carefully treated with 30% v/v aqueous hydrogen peroxide solution (150 ml) followed by concentrated (d = 1.42) nitric acid (10.0 ml). The mixture was stirred and slowly heated to 70° (oil-bath) over 15 min then stirred at 70° for a further 15 min.

The mixture was allowed to cool, then poured on to ice (750 g). The precipitated solid was collected and washed with water to give a brown solid (5.9 g) which was crystallised from ethanol to give 2-nitro-1-naphthol (206) as a yellow solid (3.8 g; 40%), m.p. 118-121° (lit.,[108] 128-129°).

Rotary evaporation of the ethanol mother liquor gave only an intractable orange gum (1.6 g).

The Attempted Base Catalysed Condensation of 2-Nitro-1-naphthol (206) with 2-Bromo-2,2-diphenylacetaldehyde (112a)

A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitro-1-naphthol (206) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). The resulting red solution was stirred at room temperature with the exclusion of atmospheric moisture for 15 min and then was treated in one portion with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.1 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting mixture was then stirred and heated at 100° (oil-bath) with the

exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, treated with water (1.0 ml), stirred at room temperature for 15 min then rotary evaporated under high vacuum. The residue was treated with 2 M aqueous sodium hydroxide solution (2.0 ml) and water (5.0 ml) and extracted with dichloromethane to give an intractable brown gum (1.1 g) which yielded no identifiable material.

The aqueous mother liquor was acidified with 2 M aqueous hydrochloric acid and extracted with dichloromethane to give unreacted 2-nitro-1-naphthol (206) as a light brown solid (0.76 g; 100%), m.p. 105-110°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

The Attempted Base Catalysed Condensation of 2-Nitro-1-naphthol (206) with Ethyl 2-Bromo-2-methylpropionate (117b)

A stirred suspension of sodium hydride (0.10 g; 0.0042 mol) in anhydrous dimethylformamide (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitro-1-naphthol (206) (0.76 g; 0.004 mol) in anhydrous dimethylformamide (5.0 ml). The mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min then treated in one portion with a solution of ethyl 2-bromo-2-methylpropionate (117b) (0.78 g; 0.004 mol) in anhydrous dimethylformamide (10.0 ml). The resulting mixture was then stirred and heated at 100° (oil-bath) with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, diluted with water (1.0 ml) and stirred

at room temperature for 15 min, then rotary evaporated under high vacuum and the residue treated with 2 M aqueous sodium hydroxide solution (2.0 ml) and water (5.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a red solid (0.12 g) which was acidified with 2 M aqueous hydrochloric acid to give 2-nitro-1-naphthol (206) as an orange solid (0.10 g; 13%), m.p. 115-116°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The aqueous-dichloromethane filtrate was separated, the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give a multicomponent brown oil (0.18 g) from which no identifiable material was obtained.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave a second crop of unreacted 2-nitro-1-naphthol (206) as an orange solid (0.48 g; 63%), m.p. 115-116°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

2-Amino-1-naphthol (214)

A stirred solution of 2-nitroso-1-naphthol (205) (8.7 g; 0.05 mol) in ethanol (500 ml) was hydrogenated over 10% palladium-on-charcoal (0.87 g) at room temperature and atmospheric pressure for 30 min.

The mixture was filtered through celite and the filtrate rotary evaporated to give 2-amino-1-naphthol (214) as a purple solid (7.9 g; 99%), m.p. 183-185°

(lit.,[126] 150°) which was used without further purification.

Naphth[2,1-d]oxazole (215)

2-Amino-1-naphthol (214) (3.2 g; 0.02 mol) was treated with 98% formic acid (25.0 ml) and the dark mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The dark mixture was allowed to cool, then rotary evaporated to give a purple gum which was treated with 10% w/v aqueous sodium hydrogen carbonate (20.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to remove an intractable black solid (0.26 g).

The aqueous-dichloromethane filtrate was separated, the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give the naphth[2,1-d]oxazole (215) as a purple solid (2.4 g; 71%), m.p. 80-83° (lit.,[109] 79°) which was used without further purification.

The Attempted Hydrolysis of Naphth[2,1-d]oxazole (215) to 2-Formamido-1-naphthol (216)

A stirred solution of the naphthoxazole (215) (0.85 g; 0.005 mol) in 50% v/v aqueous dioxane (10.0 ml) was heated under reflux for 17 h.

The mixture was allowed to cool and rotary evaporated to give a gummy residue. This was dissolved in dichloromethane and the solution dried ($MgSO_4$) and rotary evaporated to give a multicomponent dark brown gum(1.2 g) which yielded no identifiable material.

The Lithium Salt of 2-Nitroso-1-naphthol (219)

A stirred suspension of lithium hydride (0.80 g; 0.1 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 2-nitroso-1-naphthol (205) (19.0 g; 0.11 mol) in anhydrous 1,2-dimethoxyethane (250 ml) and the brown suspension was stirred at room temperature with the exclusion of atmospheric moisture for 30 min.

The mixture was filtered to remove some insoluble solid and the filtrate was rotary evaporated to give a brown solid (19.4 g) which was washed with boiling ethyl acetate to afford the lithium salt of 2-nitroso-1-naphthol (219) as a brown solid (13.8 g; 77%), m.p. 205-209° (from 1,2-dimethoxyethane-tetrahydrofuran), $\delta_H[(CD_3)_2SO]$ 8.41-6.33(6H, m, ArH).

Rotary evaporation of the ethyl acetate washings gave only an intractable brown solid (4.4 g) from which no further identifiable material was obtained.

Naphthalene-1,2-dione 2-Oxime Diphenylformylmethyl Ether (222)

(a) A stirred solution of the lithium salt of 2-nitroso-1-naphthol (219) (0.90 g; 0.005 mol) in anhydrous acetone (40.0 ml) was treated with a solution of 2-bromo-2,2-diphenylacetaldehyde (112a) (1.4 g; 0.005 mol) in anhydrous acetone (10.0 ml) and the mixture was stirred at room temperature with the exclusion of atmospheric moisture for 23 h.

The mixture was rotary evaporated, the residue treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (2.1 g) which was

flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted 2-bromo-2,2-diphenylacetaldehyde (112a) as a brown oil (0.42 g; 30%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ethyl acetate (7:3) over silica] with an authentic sample prepared before.

Elution with hexane-ether (4:1) gave a brown solid (1.6 g) which was crystallised to give naphthalene-1,2-dione 2-oxime diphenylformylmethyl ether (222) as a green-yellow solid (0.90 g; 49%), m.p. 170-173° (from 1,2-dimethoxyethane-ethanol), υ_{max} 1727(C=O) and 1681(C=O) cm^{-1}, δ_H[$(CD_3)_2SO$] 10.06(1H, s, CHO) and 7.98-7.23(16H, m, ArH). Rotary evaporation of the ethanolic mother liquors gave a multicomponent brown gum (0.38 g) from which no further identifiable material was obtained.

Elution with hexane-ether (1:1) through ether to methanol gave no other identifiable material.

(b) Repetition of the reaction described in (a) before but at room temperature for the longer time of 47 h gave a mixture which was filtered to afford the oxime ether (222) as a yellow solid (0.40 g; 22%), m.p. 170-173°, identical (m.p. and i.r. spectrum) to an authentic sample prepared in (a) before.

The acetone mother liquor was rotary evaporated, the residue treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (1.6 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave a brown oil (0.12 g) whose

t.l.c. in hexane-ethyl acetate (7:3) over silica showed it to be a mixture of benzophenone and unreacted 2-bromo-2,2-diphenylacetaldehyde (112a).

Elution with hexane-ethyl acetate (9:1) gave an orange gum (0.14 g) which was washed with ethyl acetate to give 2-nitroso-1-naphthol (205) as a yellow solid (0.069 g; 8%), m.p. 156-158° (decomp.), identical (m.p. and i.r. spectrum) to an authentic sample. Rotary evaporation of the ethyl acetate washings gave only an intractable brown gum (0.056 g) which was not further investigated.

Elution with hexane-ethyl acetate (1:1) gave a brown solid (1.0 g) which was washed with ethyl acetate to afford a second crop of naphthalene-1,2-dione 2-oxime diphenylformylmethyl ether (222) as a yellow solid (0.73 g; 40%), m.p. 168-172°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample. Rotary evaporation of the ethyl acetate washings gave only an intractable brown gum (0.24 g) from which no further identifiable material was obtained.

Elution with hexane-ethyl acetate (2:3) through to ethyl acetate then methanol gave no further identifiable material.

2,2-Diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209)

(a) A stirred solution of the oxime ether (222) (0.65 g; 0.0018 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was treated with a solution of triphenylphosphine (0.94 g; 0.0036 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the resulting brown solution was then stirred and heated under

reflux with the exclusion of atmospheric moisture for 23 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted triphenylphosphine as a brown solid (0.21 g; 22%), m.p. 79-81°, identical (m.p. and i.r. spectrum) to an authentic sample.

Further elution with hexane-ether (19:1) gave an intractable brown gum (0.10 g) from which no identifiable material was obtained.

Elution with hexane-ether (9:1) gave 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209) (0.34 g; 51%) which formed colourless microneedles, m.p. 115-124° (from hexane-ethyl acetate), υ_{max} 1571(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 8.35-7.03(17H, m, ArH and CH).

Further elution with hexane-ether (7:3) through to ether gave no other identifiable material.

Final elution with methanol gave triphenylphosphine oxide as a brown solid (0.77 g; 77%), m.p. 151-153° identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) Repetition of the reaction described in (a) before but under reflux for 17 h gave a mixture which was allowed to cool, then rotary evaporated to afford a brown gum (1.7 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted triphenylphosphine as a brown solid (0.23 g; 24%), m.p. 65-69°, identified by comparison (m.p. and

i.r. spectrum) with an authentic sample.

Further elution with hexane-ether (19:1) gave only an intractable brown oil (0.028 g) from which no further identifiable material was obtained.

Elution with hexane-ether (9:1) gave a brown solid (0.26 g) which was washed with hexane to give 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209) as a brown solid (0.19 g; 30%), m.p 110-115°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before. Rotary evaporation of the hexane washings gave only an intractable brown gum (0.062 g) from which no further identifiable material was obtained.

Further elution with hexane-ether (7:3) through to ether gave only a series of multicomponent gums (total 0.46 g) from which no further identifiable material was obtained.

Elution with methanol gave triphenylphosphine oxide as a brown solid (0.67 g; 67%), m.p. 149-151°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

3,4-Dihydro-2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (223)

A stirred solution of 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209) (0.34 g; 0.001 mol) in 1,2-dimethoxyethane (10.0 ml) was treated dropwise over 15 min at room temperature with a solution of sodium borohydride (0.17 g; 0.0045 mol) in water (2.0 ml) and the mixture was stirred at room temperature for 2 h.

The mixture was rotary evaporated and the residue treated with water

(5.0 ml) and extracted with dichloromethane to give a green gum (0.35 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave only a multicomponent green gum (0.040 g) which yielded no identifiable material.

Elution with hexane-ether (4:1) gave a purple gum (0.28 g) which was washed with hexane to afford 3,4-dihydro-2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (223) as a colourless solid (0.21 g; 62%), m.p. 136-138° (from hexane-ethyl acetate), υ_{max} 3380(NH), $\delta_H(CDCl_3)$ 8.37(1H, d, J8Hz, ArH), 7.71-7.19(14H, m, ArH), 6.81(1H, d, J8Hz, ArH), 4.76(1H, s, NH) (exch.) and 3.93(2H, s, CH_2). Rotary evaporation of the hexane washings gave only an intractable purple gum (0.070 g) from which no further identifiable material was obtained.

Elution with hexane-ether (1:1) through ether to methanol gave no further material.

The Oxidation of 3,4-Dihydro-2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (223)

A stirred solution of the dihydro compound (223) (0.20 g; 0.006 mol) in anhydrous acetonitrile (10.0 ml) was treated with activated manganese(IV) oxide (0.3 g) added in one portion. The suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 18 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give a brown gum (0.22 g) which was flash-chromatographed

over silica.

Elution with hexane-ether (4:1) gave an unidentified yellow solid (0.048 g).

Elution with hexane-ether (7:3) gave a brown gum (0.070 g) which was washed with hexane to yield 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209) as a brown solid (0.061 g; 30%), m.p. 118-124°, identical (m.p. and i.r. spectrum) to an authentic sample prepared before. Rotary evaporation of the hexane washings gave no material.

Further elution with hexane-ether (3:2) through ether to methanol gave no other identifiable material.

3-Cyano-3,4-dihydro-2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (224)

A stirred solution of 2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (209) (0.34 g; 0.001 mol) in glacial acetic acid (5.0 ml) was treated with potassium cyanide (0.33 g; 0.005 mol) added in one portion and the mixture was stirred and heated at 100° (oil-bath) for 6 h.

The mixture was allowed to cool, then rotary evaporated to give a brown solid. This was washed with water (5.0 ml) to give a brown solid (0.38 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave a multicomponent brown gum (0.090 g) which yielded no identifiable material.

Elution with hexane-ether (1:1) gave 3-cyano-3,4-dihydro-2,2-diphenyl-2H-naphth[1,2-b]-1,4 oxazine (224) (0.27 g; 75%) which formed pink

microcrystals, m.p. 219-221° (from hexane-ethyl acetate), υ_{max} 3379(NH) and 2236w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 8.44(1H, d, J8Hz, ArH), 7.75-7.04(14H, m, ArH), 6.77(1H, d, J8Hz, ArH), 5.32(1H, s, CH) and 4.48(1H, bs, NH) (Exch.).

Further elution with hexane-ether (2:3) through ether to methanol gave no further material.

3-Cyano-2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (225)

A stirred solution of the dihydro compound (224) (0.24 g; 0.00066 mol) in anhydrous acetonitrile (10.0 ml) was treated with activated manganese(IV) oxide (0.33 g) added in one portion and the dark suspension was then stirred and heated under reflux with the exclusion of atmospheric moisture for 2 h.

The mixture was allowed to cool, filtered through celite and the filtrate rotary evaporated to give a yellow solid (0.24 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave 3-cyano-2,2-diphenyl-2H-naphth[1,2-b]-1,4-oxazine (225) (0.18 g; 76%) which formed yellow irregular microcrystals, m.p. 167-169° (from hexane-ethyl acetate), υ_{max} 2218w (C≡N) cm^{-1}, $\delta_H(CDCl_3)$ 8.33-7.25(16H, m, ArH).

Elution with hexane-ether (4:1) through ether to methanol gave no further identifiable material.

The Attempted Reaction of 2-Nitroso-1-naphthol (205) with 1,1-Bis-(4-dimethylaminophenyl)ethene (Michler's Alkene) (73)

A stirred suspension of 2-nitroso-1-naphthol (205) (0.69 g; 0.004 mol) in anhydrous toluene (20.0 ml) was treated with a solution of the alkene (73) (1.1 g; 0.004 mol) in anhydrous toluene (20.0 ml). Toluene-4-sulphonic acid (0.069 g) was added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture and azeotropic distillation of the water formed (Dean and Stark apparatus) for 22 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.9 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave the unreacted alkene (73) as a purple solid (0.34 g; 31%), m.p. 121-125° identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of intractable multicomponent gums and solids (total 1.5 g) which yielded no further identifiable material.

The Attempted Reactions of 2-Nitroso-1-naphthol (205) with 1-(Morpholin-4-yl)-1-phenylethene (193)

(a) A stirred suspension of 2-nitroso-1-naphthol (205) (0.87 g; 0.005 mol) in anhydrous benzene (10.0 ml) was cooled to 0° (ice-salt bath), then treated dropwise with a solution of 1-(morpholin-4-yl)-1-phenylethene (193) (0.95 g; 0.005 mol) in anhydrous benzene (10.0 ml) at such a rate that the reaction

temperature was 0-5°. The brown suspension was stirred at 0-5° for 30 min then allowed to come to room temperature and stirred at room temperature with the exclusion of atmospheric moisture for 4 h.

The mixture was filtered to give unreacted 2-nitroso-1-naphthol (205) as a brown solid (0.45 g; 52%), m.p. 156-159° (decomp.) identical (m.p. and i.r. spectrum) to an authentic sample.

Rotary evaporation of the benzene mother liquor gave a brown gum (1.3 g) whose t.l.c. in hexane-ethyl acetate (7:3) over silica showed it to be a mixture of unreacted 2-nitroso-1-naphthol (205) and 1-(morpholin-4-yl)-1-phenylethene (193).

(b) Repetition of the reaction described in (a) before but with heating under reflux for 30 min gave a mixture which was allowed to cool, then rotary evaporated to give an intractable multicomponent brown gum (1.8 g) which yielded no identifiable material.

The Attempted Reaction of the Lithium Salt of 2-Nitroso-1-naphthol (219) with Toluene-4-sulphonyl Chloride

A stirred solution of the lithium salt of 2-nitroso-1-naphthol (219) (1.8 g; 0.01 mol) in anhydrous acetone (80.0 ml) was treated dropwise with a solution of toluene-4-sulphonyl chloride (1.9 g; 0.01 mol) in anhydrous acetone (20.0 ml) and the resulting mixture was stirred at room temperature with the exclusion of atmospheric moisture for 6 h, then heated under reflux for a

further 18 h.

The mixture was allowed to cool then filtered to give an intractable brown solid (0.59 g) which yielded no identifiable material.

Rotary evaporation of the acetone mother liquor gave a brown gum (3.8 g) which was washed with dichloromethane to give an intractable multicomponent brown solid (0.93 g) which yielded no identifiable material.

Rotary evaporation of the dichloromethane washings gave a multicomponent brown gum (2.8 g) from which no identifiable material was obtained.

Table 7: Elemental Analysis and Mass Spectroscopic Data

Compound	Found				Required			
	C%	H%	N%	M^+, $(M+H)^{+}$ [a]	C%	H%	N%	M, $(M+H)^{+}$ [a]
(74) ($C_{28}H_{27}N_3O$)	79.5	6.6	10.0	421	79.8	6.4	10.0	421
(112a) ($C_{14}H_{11}BrO$)	60.3	4.7	0.0	276,274	61.1	4.0	0.0	276,274
(113a) ($C_{20}H_{15}NO_4$)				(334.10766)				(334.10793)
(113b) ($C_{10}H_{11}NO_4$)				(210.07713)				(210.07663)
(115a) ($C_{20}H_{15}NO$)	83.9	5.6	4.8	285	84.2	5.3	4.9	285
(115b) ($C_{10}H_{11}NO$)				(162.09155)				(162.09189)
(117a) ($C_{16}H_{15}ClO_2$)	69.9	5.5	0	276,274	69.9	5.5	0	276,274
(119a) ($C_{22}H_{19}NO_5$)	70.3	5.2	3.8	377	70.0	5.0	3.7	377
(119b) ($C_{12}H_{15}NO_{5)}$	57.2	6.2	5.8	(254)	56.9	5.9	5.5	253
(123) ($C_{10}H_{11}NO_2$)	67.7	6.4	7.8	177	67.8	6.2	7.9	177
(126a) ($C_{21}H_{17}NO_3$)	75.4	5.4	3.9	331	76.1	5.1	4.2	331
(126b) ($C_{11}H_{13}NO_3$)	63.9	6.4	6.7	207	63.8	6.3	6.8	207
(127a) ($C_{20}H_{17}NO$)	83.6	5.9	5.0	287	83.7	6.0	4.9	287
(127b) ($C_{10}H_{13}NO$)	73.7	8.1	8.5	163	73.7	8.0	8.6	163
(128a) ($C_{21}H_{16}N_2O$)	80.5	5.6	9.0	312	80.8	5.1	9.0	312
(128b) ($C_{11}H_{12}N_2O$)	70.4	6.5	14.6	188	70.2	6.4	14.9	188
(129a) ($C_{21}H_{14}N_2O$)	81.1	4.5	8.8	310	81.3	4.5	9.0	310
(129b) ($C_{11}H_{10}N_2O$)	70.9	5.4	15.0	186	71.0	5.4	15.0	186
(131a) ($C_{24}H_{17}NO_4$)	75.4	4.5	3.7	383	75.2	4.4	3.7	383
(131b) ($C_{14}H_{13}NO_4$)				(260.09337)				(260.09228)

a; Molecular ions detected by Electron Impact Mass Spectrometry or, for values in parentheses, molecular ions detected by Fast Atom Bombardment Mass Spectroscopy.

Table 7: Elemental Analysis and Mass Spectroscopic Data (cont.)

Compound	Found				Required			
	C%	H%	N%	M^+, $(M+H)^{+}$ [a]	C%	H%	N%	M, $(M+H)^{+}$ [a]
(133a) ($C_{24}H_{17}NO$)	85.9	4.9	4.2	335	86.0	5.0	4.2	335
(134a) ($C_{26}H_{21}NO_5$)	73.1	5.2	3.3	427	73.1	4.9	3.3	427
(134b) ($C_{16}H_{17}NO_5$)	63.7	5.8	4.6	303	63.4	5.6	4.6	303
(138) ($C_{14}H_{13}NO_2$)	73.8	5.9	6.3	227	74.0	5.7	6.2	227
(140) ($C_{11}H_7NO$)	78.1	4.2	8.3	169	78.1	4.1	8.3	169
(141) ($C_{11}H_9NO_{2)}$	70.5	4.8	7.5	187	70.6	4.8	7.5	187
(142) ($C_{25}H_{19}NO_3$)				(382.14606)				(382.14432)
(144) ($C_{24}H_{18}ClNO_2$)	74.3	4.7	3.6	389,387	74.3	4.7	3.6	389,387
(146) ($C_{24}H_{19}NO$)				(338.15487)				(338.15449)
(149) ($C_{18}H_{13}NO_2$)				(276.10229)				(276.10245)
(150) ($C_{14}H_{13}NO_3$)				(244.09835)				(244.09737)
(153) ($C_{10}H_6NNaO_2$)	61.3	2.9	7.1	(196.03853)	61.5	3.1	7.2	(196.03748)
(155a) ($C_{11}H_9NO_2$)				(188.07209)				(188.07115)
(155b) ($C_{17}H_{13}NO_2$)	77.5	5.0	5.1	263	77.6	4.9	5.3	263
(157) ($C_{17}H_{11}NO$)	82.9	4.8	5.8	245	83.3	4.5	5.7	245
(161) ($C_{24}H_{17}NO_3$)	78.6	4.8	3.8	(368)	78.5	4.6	3.8	367
(164) ($C_{24}H_{17}NO_{2)}$	81.8	4.8	3.8	351	82.0	4.8	4.0	351
(167) ($C_{14}H_{13}NO_4$)	64.8	5.1	5.4	(260)	64.9	5.0	5.4	259
(172) ($C_{26}H_{21}NO_4$)	76.2	5.1	3.3	(412)	75.9	5.1	3.4	411
(176) ($C_{24}H_{19}NO$)	85.6	5.9	4.1	337	85.5	5.6	4.1	337

a; Molecular ions detected by Electron Impact Mass Spectrometry or, for values in parentheses, molecular ions detected by Fast Atom Bombardment Mass Spectroscopy.

Table 7: Elemental Analysis and Mass Spectroscopic Data (cont.)

Compound	Found				Required			
	C%	H%	N%	M^+, $(M+H)^{+}$ [a]	C%	H%	N%	M, $(M+H)^{+}$ [a]
(177) ($C_{25}H_{18}N_2O$)				(363.14879)				(363.14974)
(179) ($C_{25}H_{16}N_2O$)				(361.13290)				(361.13409)
(180) ($C_{14}H_{13}NO_3$)	69.4	5.5	5.7	(244)	69.1	5.3	5.8	243
(189) ($C_{25}H_{26}N_4O_3$)	69.6	5.9	12.8	430	69.8	6.0	13.0	430
(190) ($C_{35}H_{31}N_5O_4$)	72.1	5.3	11.9	(586)	71.8	5.3	12.0	585
(202) ($C_{17}H_{13}NO_4S$)				(328.06472)				(328.06436)
(203) ($C_{10}H_7NO_2$)	69.5	4.1	8.0	173	69.4	4.0	8.1	173
(209) ($C_{24}H_{17}NO$)				(336.13983)				(336.13884)
(219) ($C_{10}H_6NO_2Li$)				(179.06289)				(179.06280)
(222) ($C_{24}H_{17}NO_3$)	78.9	4.6	3.8	(368)	78.5	4.6	3.8	367
(223) ($C_{24}H_{19}NO$)				(338.15561)				(338.15449)
(224) ($C_{25}H_{18}N_2O$)				(363.15252)				(363.14974)
(225) ($C_{25}H_{16}N_2O$)	83.0	4.5	7.7	360	83.3	4.4	7.8	360

a; Molecular ions detected by Electron Impact Mass Spectrometry or, for values in parentheses, molecular ions detected by Fast Atom Bombardment Mass Spectroscopy.

CHAPTER 3

INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2H-1,3-OXAZINES AND 2,2-DISUBSTITUTED 2H-1,3,4-OXADIAZINES AS NOVEL PHOTOCHROMIC AGENTS

3. INVESTIGATIONS OF SYNTHETIC ROUTES TO FUSED 2,2-DISUBSTITUTED 2H-1,3-OXAZINES AND 2,2-DISUBSTITUTED 2H-1,3,4-OXADIAZINES AS NOVEL PHOTOCHROMIC AGENTS

3.1 INTRODUCTION

Fused 2,2-disubstituted 2H-1,3-oxazines [see Page 20, Scheme 15; (61)] and 2,2-disubstituted 2H-1,3,4-oxadiazines [see Page 20, Scheme 15; (62)] as discussed in Chapter 1 have potential as possible photochromic agents. At present these compounds have attracted only limited attention in the literature regarding their properties and reactivity.

Of particular interest in the present studies are synthetic methods pertaining to the fused 2,2-disubstituted 2H-1,3-oxazines [see Page 20, Scheme 15; (61)], especially the 2,2-disubstituted 2H-benz-1,3-oxazines [see Page 23, Scheme 18; (75)], the 3,3-disubstituted 3H-naphth[1,2-e]-1,3-oxazines [see Page 23, Scheme 18; (76)] and the 2,2-disubstituted 2H-naphth[2,1-e]-1,3-oxazines [see Page 23, Scheme 18; (77)]. Although the benz-1,3-oxazines [see Page 23, Scheme 18; (75)] would not be expected to be photochromic, studies into the synthesis of such compounds would serve as a useful synthetic model for the potentially photochromic naphth-1,3-oxazines [see Page 23, Scheme 18; (76) and (77)].

As previously mentioned in Chapter 1 the synthesis of 2,2-diphenyl-2H-

benz-1,3-oxazine [see Page 23, Scheme 18; (80)] is described in the literature.[92] The synthesis of this compound involves the reaction of the diphenylketimine [see Page 23, Scheme 18; (78)] with 2-hydroxybenzaldehyde (79). The extension of this reaction to the synthesis of other 2,2-disubstituted 2H-benz-1,3-oxazines [see Page 23, Scheme 18; (75)] would depend on the availability of various ketimine derivatives and their reactivity towards 2-hydroxybenzaldehyde [see Page 23, Scheme 18; (79)].

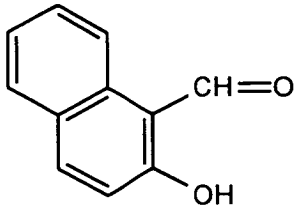
A further possible route (Scheme 64) to the 2,2-diphenyl-2H-benz-1,3-oxazine (80) could involve the formation of the benz-1,3-oxazinone (233) as precursor. It was reported[127] that the benz-1,3-oxazinone (233) is readily available by the reaction of 2-hydroxybenzaldehyde (79) with chlorosulphonyl isocyanate (232). Subsequent reaction of the benz-1,3-oxazinone (233) with phenylmagnesium bromide would then provide a potential route to the 2,2-diphenyl-2H-benz-1,3-oxazine (80). Replacement of phenylmagnesium bromide with other Grignard reagents in this synthetic approach would also afford a possible route to various 2,2-disubstituted 2H-benz-1,3-oxazines [see Page 23, Scheme 18; (75)].

As described in Chapter 1 synthetic routes to the naphth-1,3-oxazines [see Page 23, Scheme 18; (76) and (77)] are largely lacking in the primary literature. Replacement of 2-hydroxybenzaldehyde (79) in Scheme 18 (see Page 23) and Scheme 64 with 2-hydroxy-1-naphthaldehyde would therefore provide possible synthetic routes to the 3,3-disubstituted 3H-naphth[1,2-e]-1,3-oxazines [see Page 23, Scheme 18; (76)]. Unfortunately, 1-hydroxy-2-

naphthaldehyde is not readily available and new synthetic strategies are therefore required for the synthesis of the 2,2-disubstituted 2H-naphth[2,1-e]-1,3-oxazines [see Page 23, Scheme 18; (77)].

Fused 2,2-disubstituted 2H-1,3,4-oxadiazines [see Page 20, Scheme 15; (62)] have also received limited attention in the literature. Only one method for the synthesis of 2,2-disubstituted 2H-benz-1,3,4-oxadiazines [see Page 25; Scheme 21; (96)] was found. This method (see Page 25, Scheme 22) involved the reaction of various diazoalkanes (100) with the benzoquinone diazide (99). Replacement of the benzene ring in the benzoquinone diazide [see Page 25, Scheme 22; (99)] with a naphthalene ring would therefore afford a potential route to various disubstituted naphth-1,3,4-oxadiazines [see Page 25, Scheme 21; (97) and (98)] which have not been synthesised.

The present Chapter describes investigations of various synthetic routes to potentially photochromic fused 2,2-disubstituted 2H-1,3-oxazines [see Page 20, Scheme 15; (61)] and 2,2-disubstituted 2H-1,3,4-oxadiazines [see Page 20, Scheme 15; (62)].



(234)

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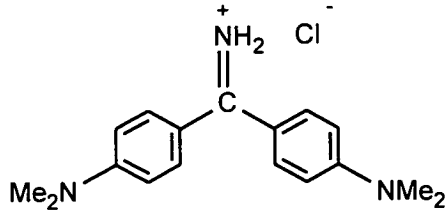

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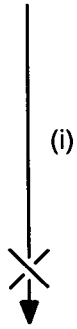
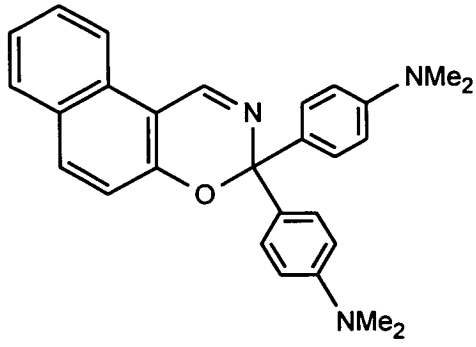
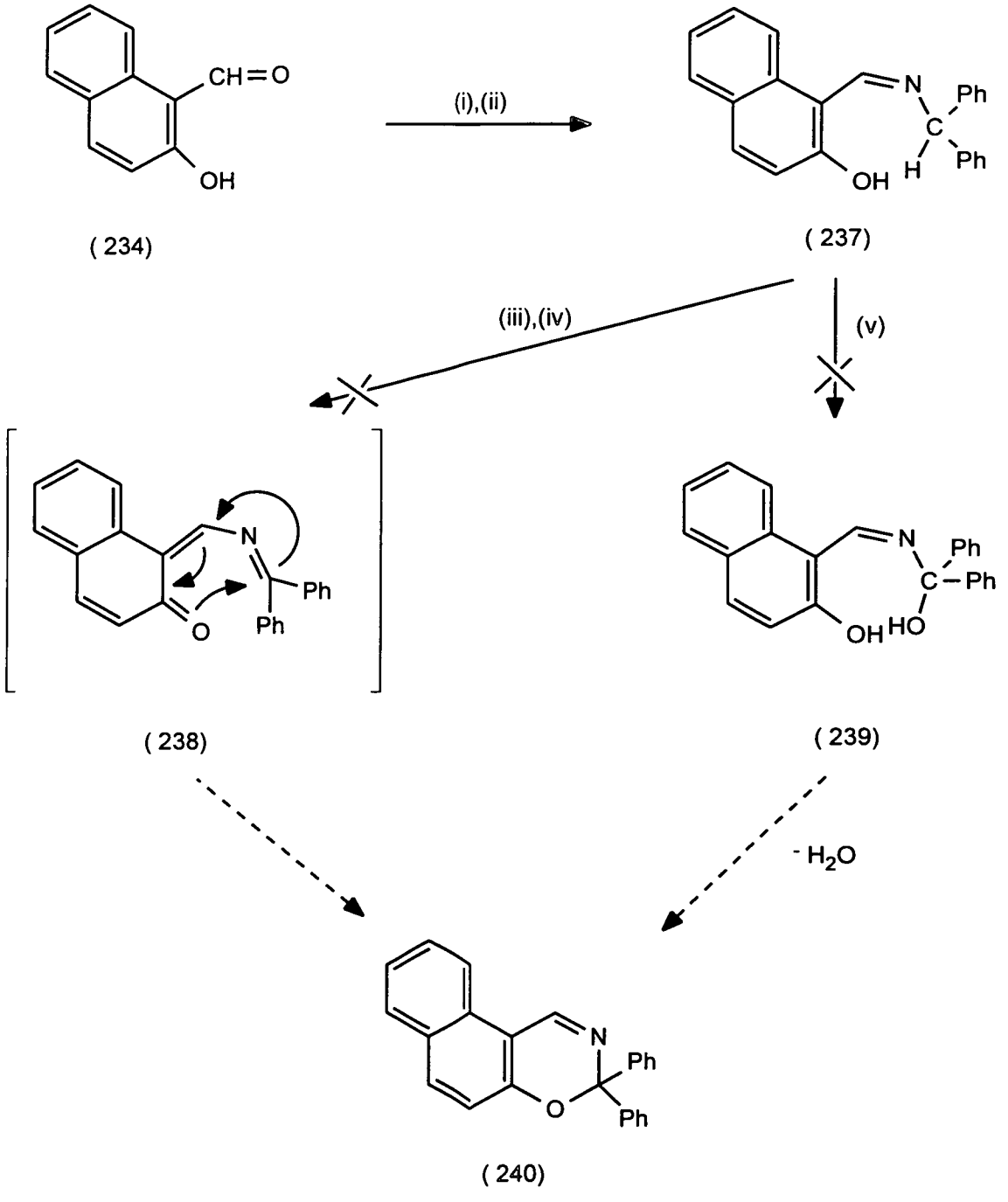




(236)

(i) EtOH, reflux.

Scheme 65



(234)

(237)

(238)

(239)

(240)

(i) $PH_2CHN{=}PPH_3$, DME, reflux.
(ii) PH_2CHNH_2, 4Å mol. sieves, DME, room temp.
(iii) MnO_2, MeCN, room temp.
(iv) 30% H_2O_2, 1M NaOH aqu., room temp.
(v) $(NH_4)_2Ce(NO_3)_6$, H_2O, AcOH, or THF, room temp.

Scheme 66

3.2 INVESTIGATIONS OF SYNTHETIC ROUTES TO NOVEL FUSED 2,2-DISUBSTITUTED 2H-1,3-OXAZINE DERIVATIVES

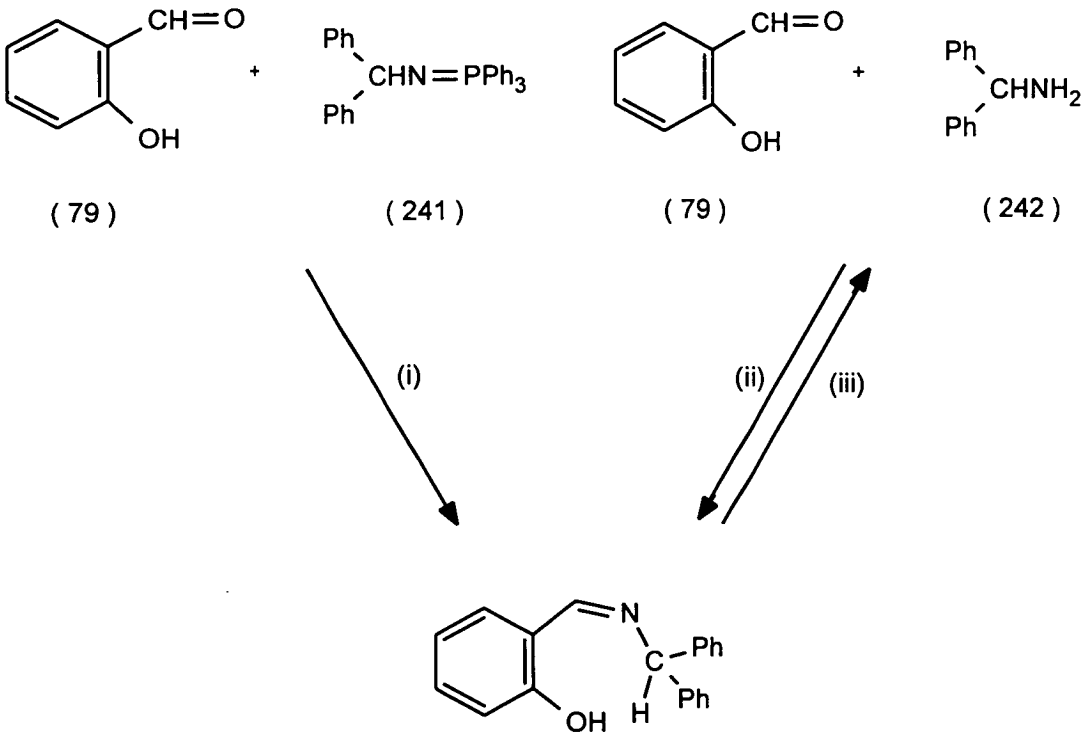
Initial studies under this heading were centred on the synthesis (Scheme 65) of the 3,3-di-(4-dimethylaminophenyl)-3H-naphth[1,2-e]-1,3-oxazine (236). This synthetic approach was based on the condensation of 2-hydroxy-1-naphthaldehyde (234) with the hydrochloride (235). However, the attempted reaction of the hydroxy-aldehyde (234) with the hydrochloride (235) in ethanol under reflux gave only quantitative recoveries of the unreacted starting materials.

In conjunction with this work studies were also initiated on a synthetic route (Scheme 66) for the synthesis of the 3,3-diphenyl-3H-naphth[1,2-e]-1,3-oxazine (240). This synthetic route was based on the formation of the imine (237) and its direct oxidative conversion into the naphth-1,3-oxazine [(237)→(238)→(240)] or its oxidative transformation into the dihydroxy intermediate (239) followed by cyclodehydration of the latter. In an initial attempt to form the imine (237), the reaction of 2-hydroxy-1-naphthaldehyde (234) with N-(diphenylmethyl)triphenylphosphinimine was investigated. N-(Diphenylmethyl)triphenylphosphinimine was readily prepared in quantitative yield by the reaction of triphenylphosphine with diphenylmethyl azide accessible from diphenylmethyl bromide and sodium azide. Reaction of 2-hydroxy-1-naphthaldehyde (234) with N-(diphenylmethyl)triphenylphosphinimine in refluxing 1,2-dimethoxyethane gave a yellow solid product in excellent yield (92%). This analysed correctly and gave mass, i.r. and ^{1}H n.m.r. spectral data

which fully support its formulation as the required imine (237). Thus, the i.r. spectrum shows the OH stretch at 3432 cm^{-1} and the imine C=N stretch at 1625 cm^{-1}, while the ^1H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H15.44 due to the OH group, and one-proton singlets at δ_H9.54 and 6.15 due to the two methine groups. Triphenylphosphine oxide was also obtained in high yield (85%) from this reaction. The imine (237) was also synthesised by the reaction of the commercially available diphenylmethylamine with 2-hydroxy-1-naphthaldehyde (234) in 1,2-dimethoxyethane containing molecular sieves. This reaction gave the imine (237) in quantitative yield and had the advantages of a simpler work-up and the commercial availability of both starting materials.

With the imine (237) readily available, investigations (Scheme 66) into its further manipulation to the naphthoxazine (240) were undertaken. Thus, in an initial attempt to obtain the naphthoxazine (240) *via in situ* ring closure of the quinone intermediate (238), the imine (237) was reacted with manganese dioxide in acetonitrile at room temperature. Unfortunately, this reaction gave only a high recovery (93%) of unreacted imine (237). A high recovery (97%) of the unreacted imine (237) was also obtained when the imine (237) was treated with a mixture of hydrogen peroxide and sodium hydroxide at room temperature.

A new method (Scheme 66) for the conversion of the imine (237) into the naphthoxazine (240) was sought, due to the initial difficulties encountered in the attempted oxidation of the former to the naphthoxazine (240). This new

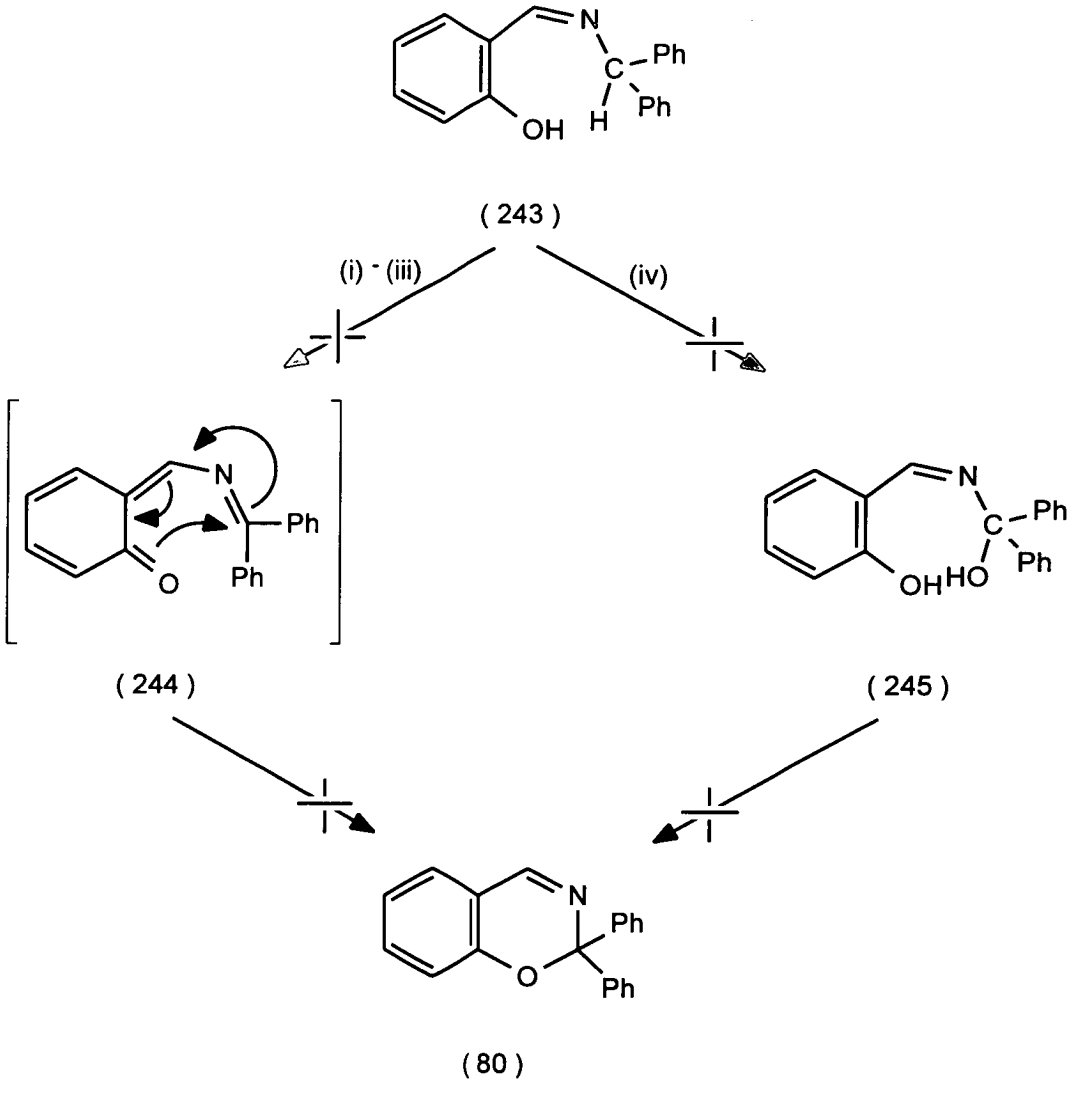


(79) (241) (79) (242)

(243)

(i) benzene, reflux.
(ii) 4Å mol. sieves, ether, room temp.
(iii) 2M HCl aqu., EtOH, reflux.

Scheme 67



(i) MnO_2, MeCN, room temp.
(ii) NBS, $(PhCO)_2O_2$, CCl_4, reflux.
(iii) 30% H_2O_2, 1M NaOH aqu., room temp.
(iv) $(NH_4)_2Ce(NO_3)_6$, MeCN, H_2O.

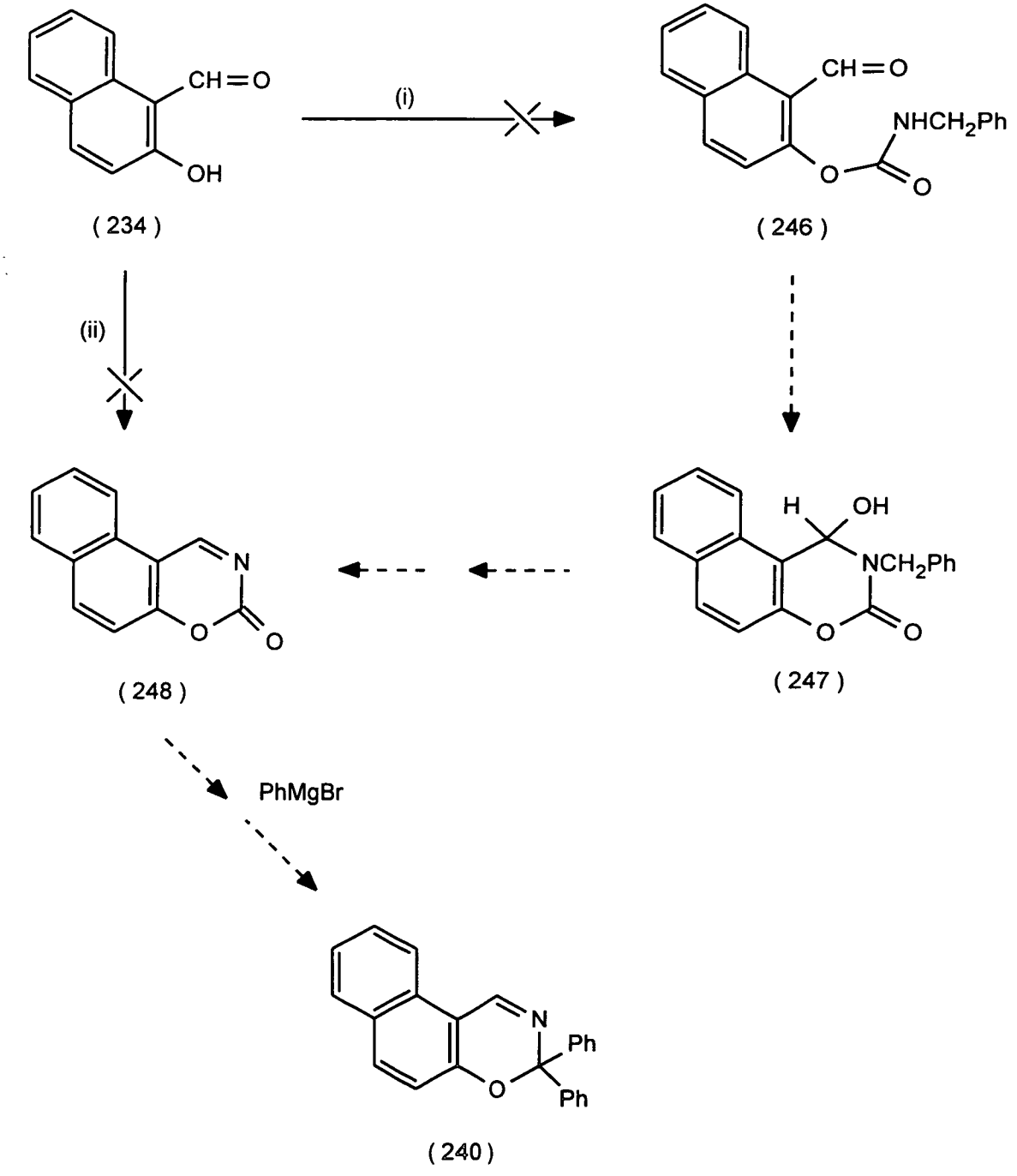
Scheme 68

method involved the oxidative transformation of the imine (237) into the dihydroxy intermediate (239), followed by cyclodehydration of the latter to afford the naphthoxazine (240). The imine (237) was reacted with ammonium cerium(IV) nitrate in aqueous acetic acid at room temperature. Unfortunately this reaction did not afford any of the desired dihydroxy derivative (239), but instead gave only intractable mixtures. Repetition of this reaction in aqueous tetrahydrofuran gave a low yield of 2-hydroxy-1-naphthaldehyde (234) which suggests that cleavage of the imine (carbon-nitrogen) double bond of the imine (237) had occurred.

Due to the lack of success in the attempted synthesis of the naphth-1,3-oxazine (240), attention was next focused on the analogous synthesis (Schemes 67 and 68) of the 2,2-diphenyl-2H-benz-1,3-oxazine (80). Investigations into the synthesis of the benz-1,3-oxazine (80) would serve as a useful contrast to the synthesis of the naphth-1,3-oxazine (240). In an initial attempt to obtain the imine (243), 2-hydroxybenzaldehyde (79) was heated under reflux with the phosphinimine (241) in benzene. This reaction gave a yellow solid product in moderate yield (54%) which analysed correctly and gave mass, i.r. and ^{1}H n.m.r. spectral data which fully support its formulation as the required imine (243). Thus the i.r. spectrum shows the imine C=N band at 1622 cm^{-1}, while the ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons, a one-proton singlet at δ_H13.55 due to the OH group, and one-proton singlets at δ_H8.49 and 5.65 due to the two methine groups. Unreacted 2-hydroxybenzaldehyde (79) (41%) and a moderate yield (57%) of

triphenylphosphine oxide were also obtained from this reaction. Further proof of the imine (243) structure was then sought. The behaviour of the imine (243) towards hydrolysis was studied. Thus, treatment of the imine (243) with 2 M aqueous hydrochloric acid in ethanol under reflux gave the expected hydrolysis products 2-hydroxybenzaldehyde (79) in moderate yield (53%) and diphenylmethylamine (242) in high yield (79%). The imine (243) was also synthesised by the reaction of 2-hydroxybenzaldehyde (79) with diphenylmethylamine (242) in ether containing molecular sieves. This reaction gave the imine (243) in quantitative yield and had the added advantage of a simpler work-up and commercial availability of both starting materials.

With the imine (243) readily available, investigations (Scheme 68) into its further manipulation to the benzoxazine (80) were undertaken. Thus, in an initial attempt to obtain the benzoxazine (80) *via in situ* ring closure of the quinone intermediate (244), the imine (243) was reacted with manganese dioxide in acetonitrile at room temperature. Unfortunately, this reaction gave only a quantitative recovery of unreacted imine (243). Reaction of the imine (243) with N-bromosuccinimide in refluxing carbon tetrachloride containing a catalytic amount of dibenzoylperoxide also failed to oxidise the imine (243) and instead resulted in bromination to afford N-(diphenylmethyl)-3,5-dibromo-2-hydroxybenzaldimine in high yield (68%). The imine (243) was then reacted with a mixture of hydrogen peroxide and sodium hydroxide in the hope of obtaining the benzoxazine (80). However this reaction gave only unreacted imine (243) in high yield (98%).



(234)

(246)

(248)

(247)

(240)

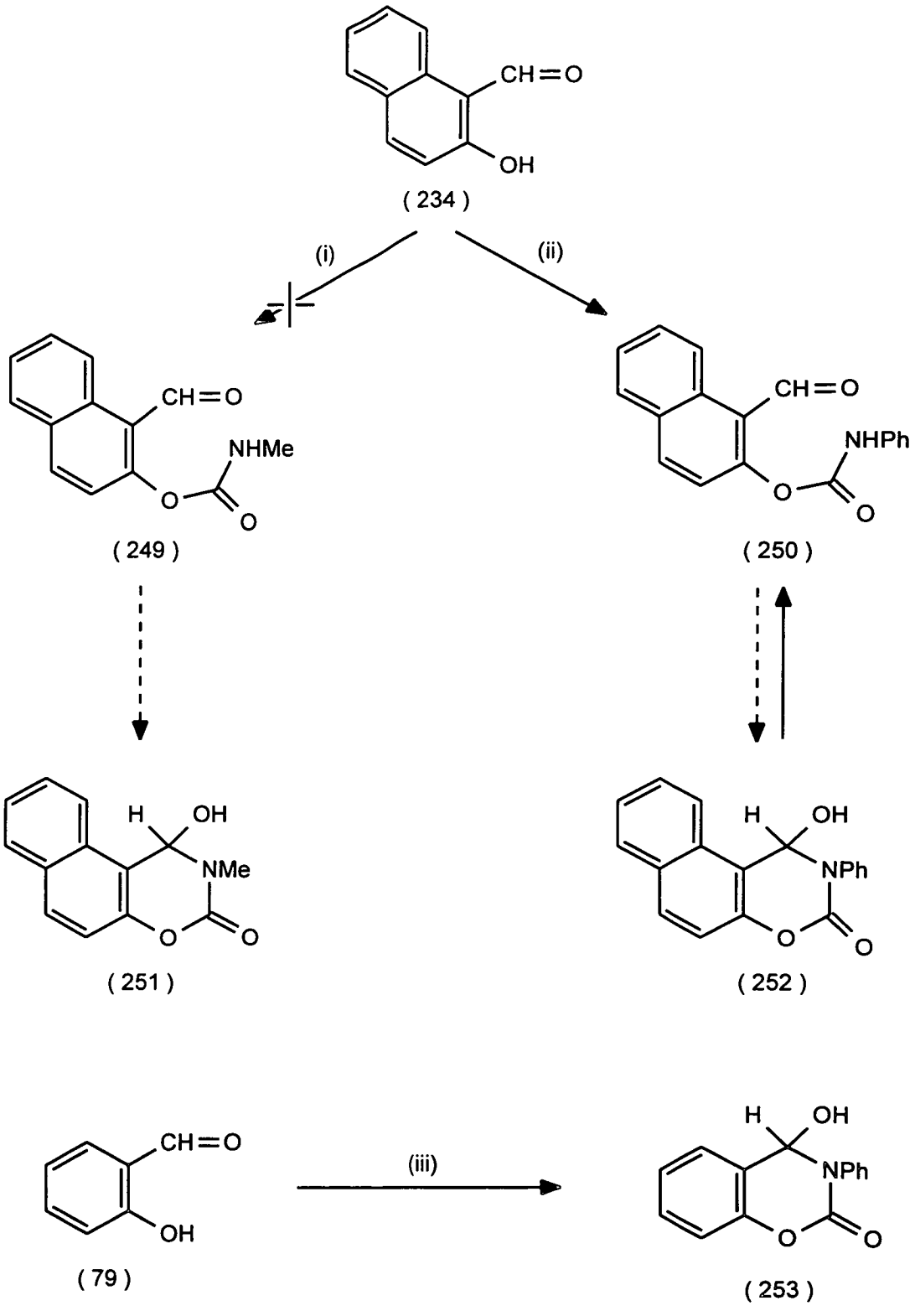
(i) $PhCH_2N{=}C{=}O$, DME, room temp. or reflux.
(ii) $ClSO_2N{=}C{=}O$, DME, room temp.

Scheme 69

With various attempts to oxidise the imine (243) to the benzoxazine (80) having failed a new approach (Scheme 68) was investigated. This approach involved the oxidative transformation of the imine (243) into the dihydroxy intermediate (245), followed by cyclodehydration of the latter to afford the benzoxazine (80). Thus, the imine (243) was reacted with ammonium cerium(IV) nitrate in aqueous acetonitrile at room temperature to give only intractable mixtures. The failure of the imine (243) to undergo oxidation to the benzoxazine (80), mirrors the problems encountered in the analogous approach (see Page 249, Scheme 66) to the naphthoxazine (240). Unfortunately due to a lack of time, investigations into the manipulation of the imines (237) and (243) were halted at this stage.

Attention was then turned to a further approach (Scheme 69) for the synthesis of the potentially photochromic naphth-1,3-oxazine (240). This approach was based on the formation of the naphth-1,3-oxazinone (248) and it subsequent reaction with phenylmagnesium bromide to afford the naphth-1,3-oxazine (240). It was hoped the naphth-1,3-oxazinone (248) would be readily available from the further manipulation of the urethane derivative (246). Thus, in an attempt to obtain the urethane derivative (246), 2-hydroxy-1-naphthaldehyde (234) was reacted with benzyl isocyanate in 1,2-dimethoxyethane at room temperature and then at reflux. This reaction however gave only quantitative recoveries of the unreacted 2-hydroxy-1-naphthaldehyde (234) and benzyl isocyanate starting materials.

A more direct approach (Scheme 69) to the naphth-1,3-oxazinone (248)



(i) MeN=C=O, DME, room temp.
(ii) PhN=C=O, DME, or dioxane, room temp. or reflux.
(iii) PhN=C=O, DME, room temp.

Scheme 70

and hence by further manipulation the naphth-1,3-oxazine (240) was evaluated. This approach was based on the reaction of 2-hydroxy-1-naphthaldehyde (234) with chlorosulphonyl isocyanate to afford the naphth-1,3-oxazinone (248), by analogy with the strategy (see Page 247, Scheme 64) for the synthesis of the benz-1,3-oxazine (80). Thus, 2-hydroxy-1-naphthaldehyde (234) was reacted with chlorosulphonyl isocyanate in 1,2-dimethoxyethane at room temperature. This reaction gave only a moderate recovery (59%) of unreacted aldehyde (234) with no evidence for the formation of the naphth-1,3-oxazinone (248).

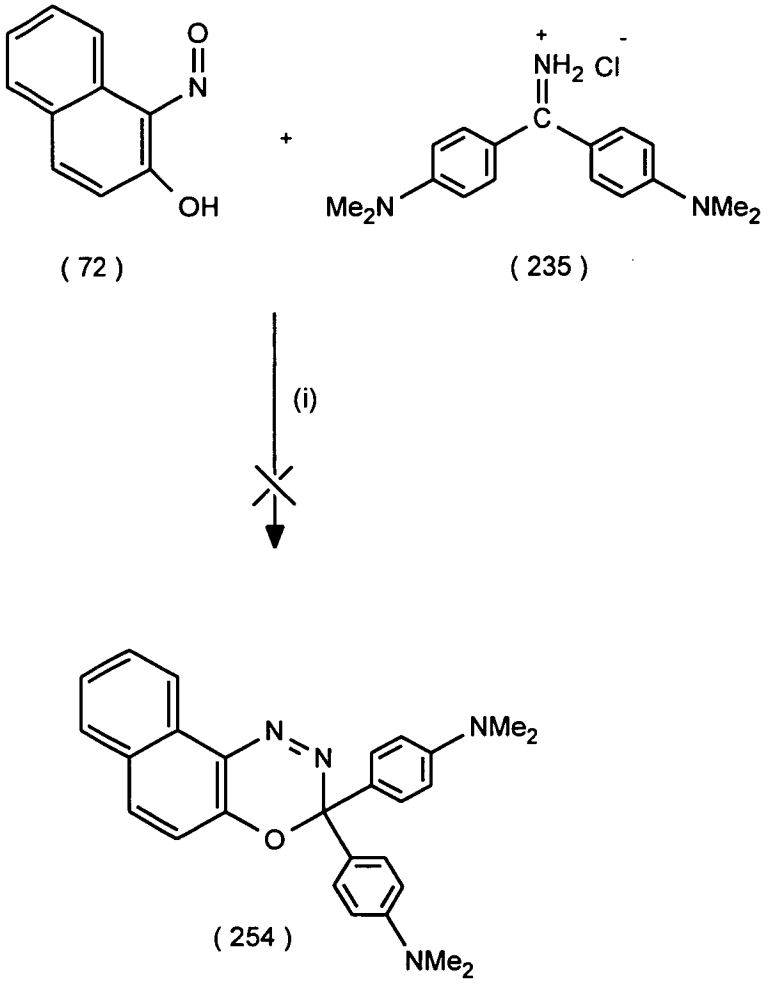
Concurrently with the previous studies of the reactions of 2-hydroxy-1-naphthaldehyde (234) with chlorosulphonyl isocyanate and benzyl isocyanate, the reactivity (Scheme 70) of 2-hydroxy-1-naphthaldehyde (234) towards other isocyanates was also investigated as this would prove useful for comparison purposes. The reaction of 2-hydroxy-1-naphthaldehyde (234) with methyl isocyanate in 1,2-dimethoxyethane gave only a quantitative recovery of unreacted 2-hydroxy-1-naphthaldehyde (234). Reaction of 2-hydroxy-1-naphthaldehyde (234) with phenyl isocyanate in 1,2-dimethoxyethane under reflux, gave in addition to a high recovery (72%) of unreacted 2-hydroxy-1-naphthaldehyde (234), a low yield (27%) of a colourless solid product. This colourless product analysed correctly and gave mass spectral data in accord with either the open-chain urethane structure (250) or the hydroxynaphthoxazinone structure (252). The infrared spectrum shows bands at 3329 (NH) and 1754 and 1668 (C=O) cm^{-1} which supports the colourless

product having the open-chain urethane structure (250). The urethane structure (250) was further supported by the ^{1}H n.m.r. spectrum which shows signals due to the aldehyde and urethane NH groups. Reaction of 2-hydroxy-1-naphthaldehyde (234) with two equivalents of phenyl isocyanate in the higher boiling 1,4-dioxane under reflux gave an even lower yield (22%) of the urethane (250). Repetition of this reaction, but in 1,2-dimethoxyethane at room temperature, gave in addition to unreacted 2-hydroxy-1-naphthaldehyde (234) (49%), a much improved yield (50%) of the urethane (250). Elevation of the temperature in the reaction of 2-hydroxy-1-naphthaldehyde (234) with phenyl isocyanate was detrimental to the efficiency of the reaction.

By way of comparison of the reaction (Scheme 70) of 2-hydroxy-1-naphthaldehyde (234) with phenyl isocyanate, 2-hydroxybenzaldehyde (79) was also reacted with phenyl isocyanate in 1,2-dimethoxyethane at room temperature to afford a high yield (79%) of a colourless solid product. The spectroscopic data of this colourless product fully supports the benzoxazinone structure (253) as opposed to the open chain urethane structure reported in the literature.[128] The i.r. spectrum shows bands at 3376 (OH) and 1706 (C=O) cm^{-1}, while the ^{1}H n.m.r. spectrum shows in addition to signals due to the aromatic protons a one-proton doublet at δ_H5.97 which collapses to a singlet on shaking with deuterium oxide attributable to the CH group and a one-proton doublet at δ_H3.78 which is completely removed on addition of deuterium oxide attributable to the OH group of the benzoxazinone (253).

Unfortunately due to a lack of time, investigations of synthetic routes to

novel fused 2,2-disubstituted 2H-1,3-oxazine derivatives were halted at this stage.

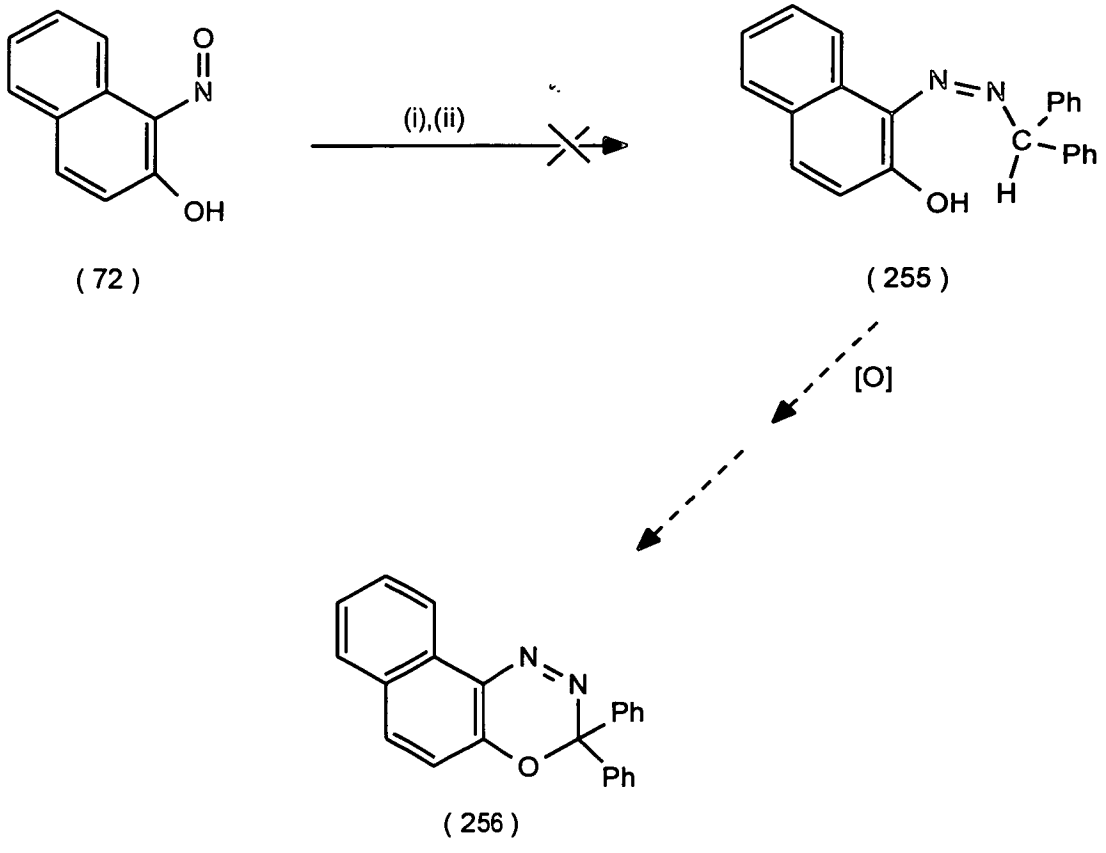


(72) (235)

(254)

(i) EtOH, reflux.

Scheme 71



(72)

(255)

(256)

(i) $Ph_2CHN{=}PPh_3$, benzene, reflux.

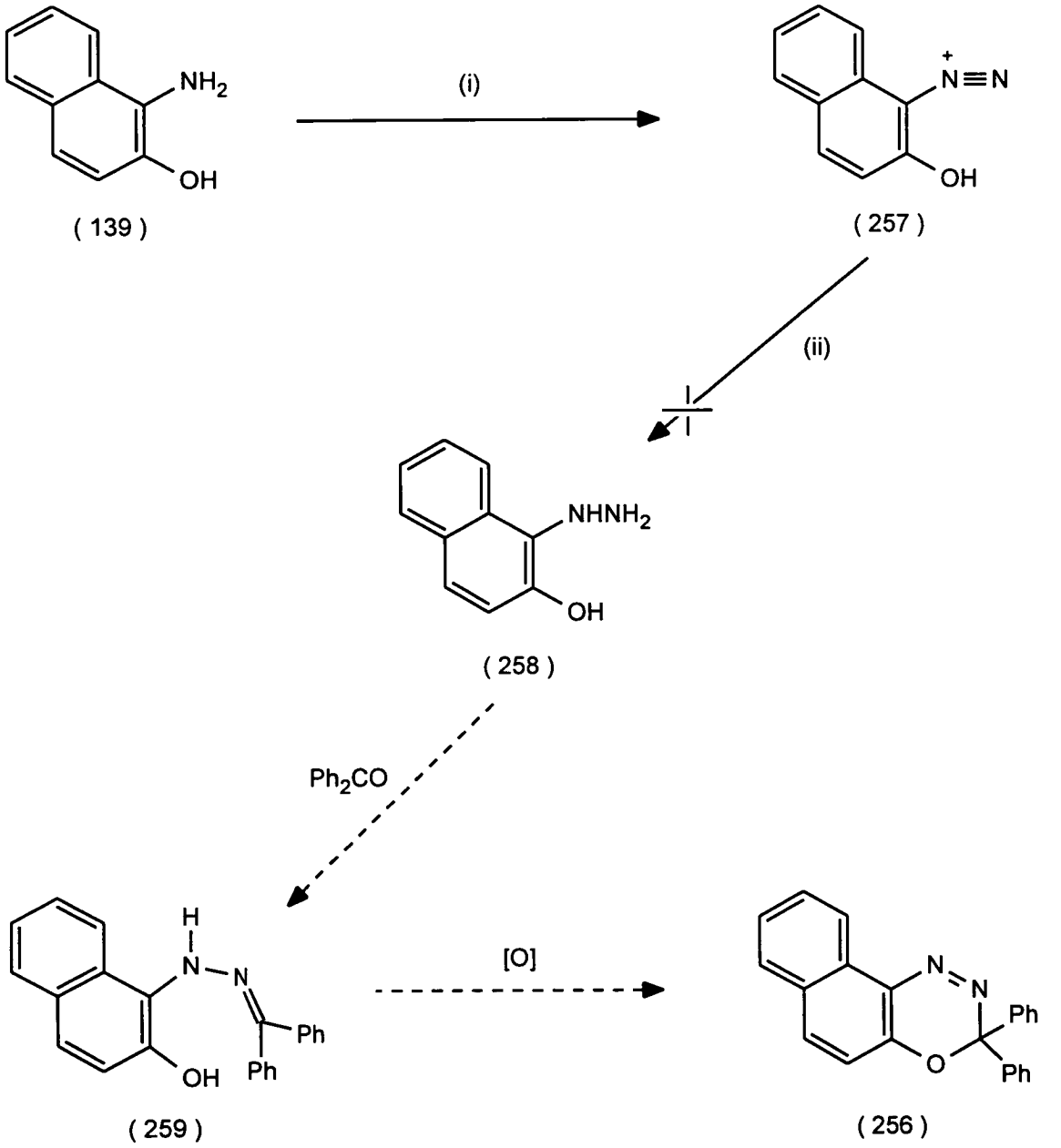
(ii) Ph_2CHNH_2, toluene, room temperature or reflux.

Scheme 72

3.3 INVESTIGATIONS OF SYNTHETIC ROUTES TO NOVEL FUSED 2,2-DISUBSTITUTED 2H-1,3,4-OXADIAZINE DERIVATIVES

Initial studies under this heading were centred on a potential synthetic route (Scheme 71) to the 3,3-di-(4-dimethylaminophenyl)-3H-naphth[1,2-e]-1,3,4-oxadiazine (254) based on the cyclisative condensation of 1-nitroso-2-naphthol (72) with the hydrochloride (235). However, the reaction of the nitrosonaphthol (72) with the hydrochloride (235) in ethanol under reflux gave only high yields (99-100%) of the unreacted starting materials. Reaction of the nitrosonaphthol sodium salt (153) with the hydrochloride (235) in dimethylsulphoxide at 90° also failed to give the naphthoxadiazine (254) and gave only a low yield (15%) of 4,4'-bis(dimethylamino)benzophenone. The exact origin of the 4,4'-bis(dimethylamino)benzophenone in this transformation is unknown at the present time.

In conjunction with the previous work studies were also undertaken on the synthesis (Scheme 72) of the 3,3-diphenyl-3H-naphth[1,2-e]-1,3,4-oxadiazine (256). Attention was focused on the synthesis of the azo-naphthol (255) as a potential precursor (through oxidation) to the target naphthoxadiazine (256). Thus, in an attempt to obtain the azo-naphthol (255), N-(diphenylmethyl)triphenylphosphinimine was reacted with 1-nitroso-2-naphthol (72) in refluxing benzene. It was hoped the phosphinimine would react with the nitrosonaphthol (72) in an aza-Wittig reaction to obtain the azo-naphthol (255), but this reaction disappointingly gave only a complex mixture which yielded no identifiable material. In a further attempt to obtain the azo-



(139)

(257)

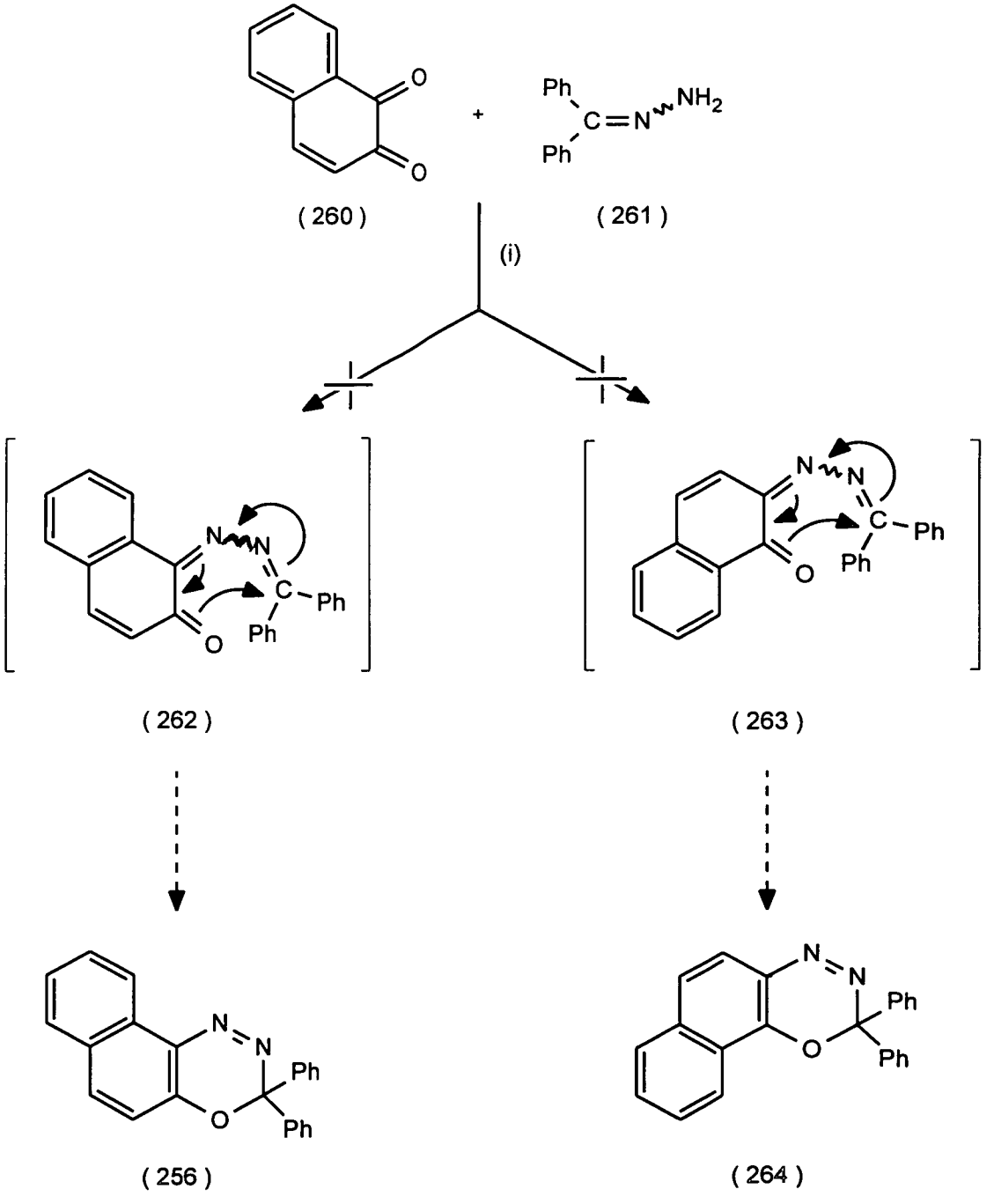
(258)

(259)

(256)

(i) $NaNO_2$, HCl aqu. (conc.), AcOH, H_2O, 0 - 5°.
(ii) $SnCl_2$, HCl aqu. (conc.), 0 - 5°.

Scheme 73



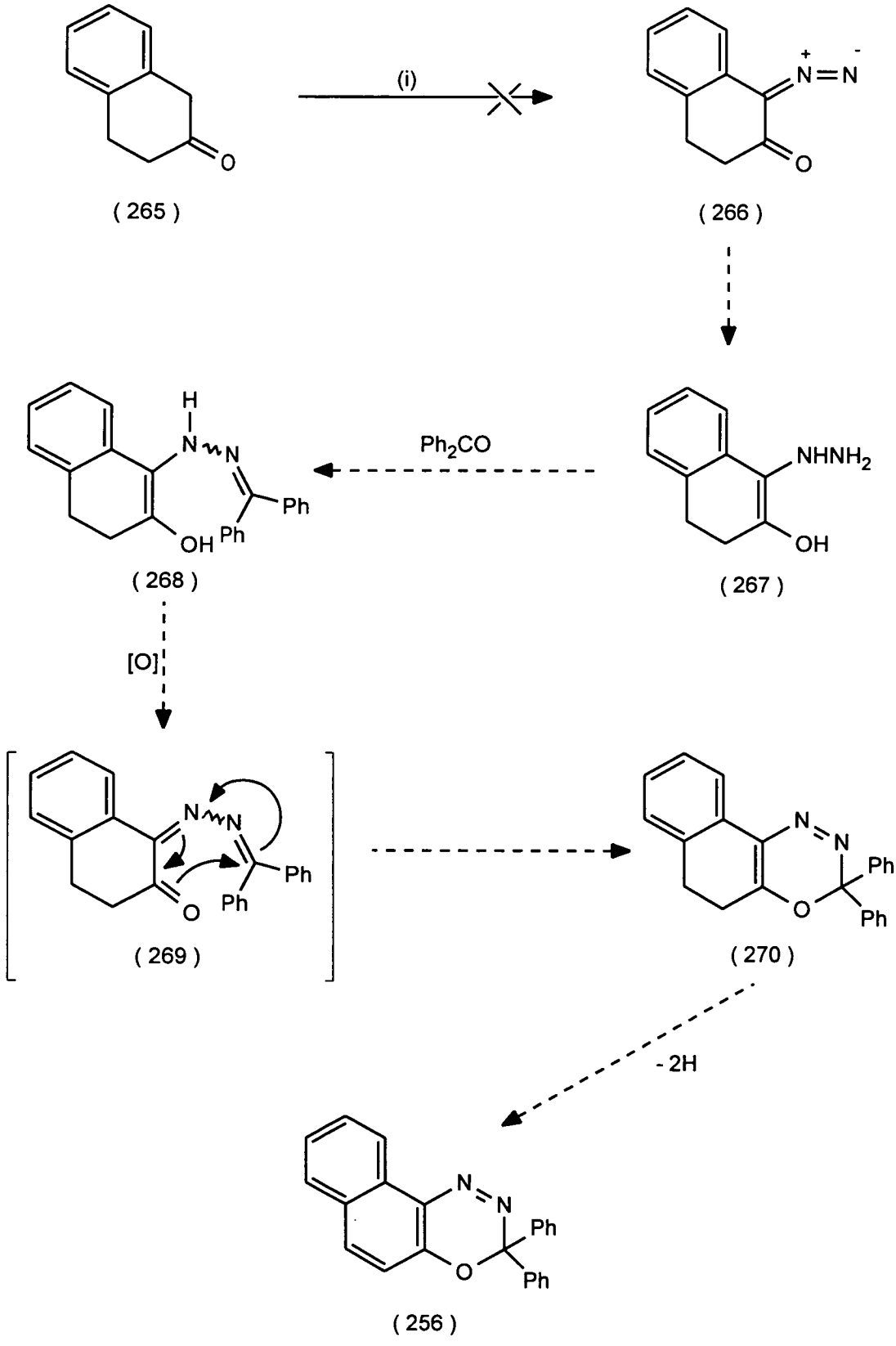
(i) 4Å mol. sieves, DME, reflux.

Scheme 74

naphthol (255), an attempt was made to condense 1-nitroso-2-naphthol (72) with diphenylmethylamine in toluene, initially at room temperature and then with heating under reflux. However, these conditions gave only a complex mixture which afforded no identifiable material.

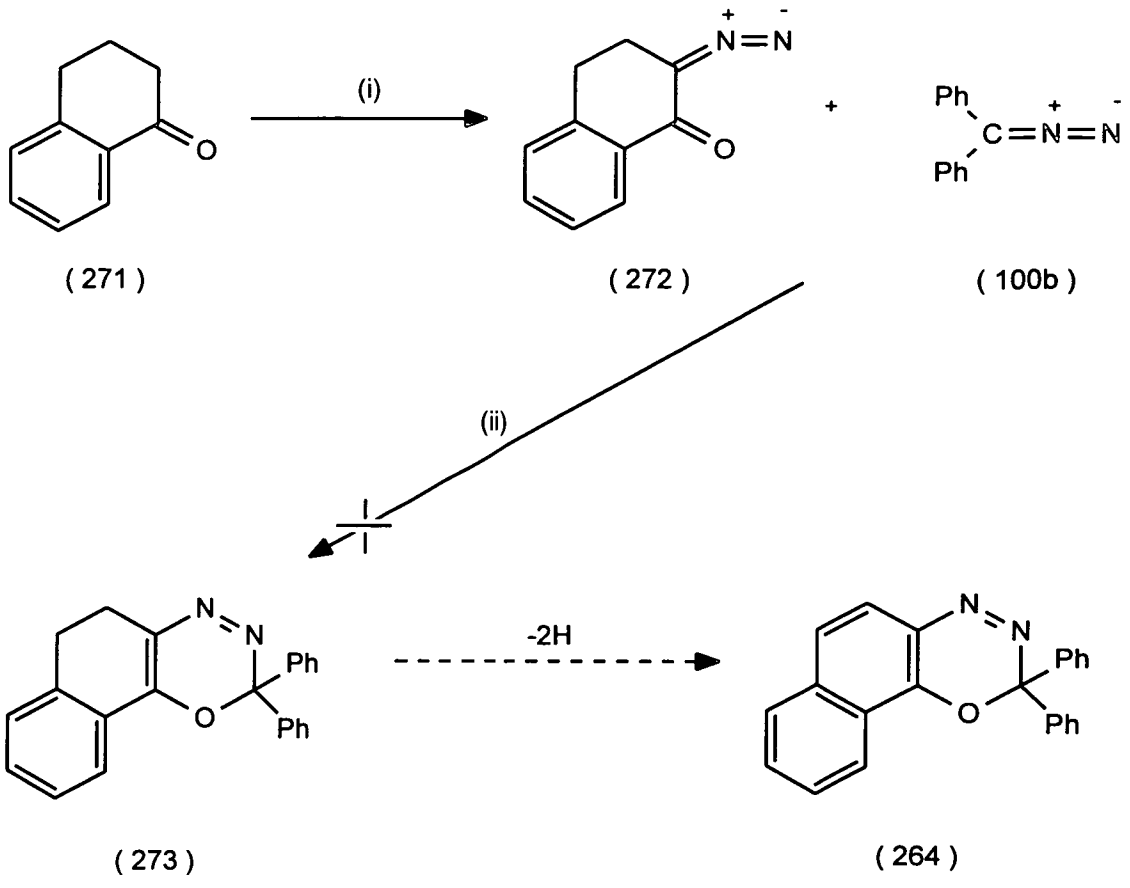
Due to the difficulties encountered in the synthesis of the azo-naphthol (255), attention was turned to an alternative approach (Scheme 73) for the synthesis of the naphth-1,3,4-oxadiazine (256) product. This approach centred on the synthesis of the hydrazine (258) and its subsequent condensation reaction with benzophenone to generate the hydrazone (259). It was then hoped that oxidation of the latter would afford the naphth-1,3,4-oxadiazine (256). Therefore in an attempt to obtain the hydrazine (258), 1-amino-2-naphthol (139) was diazotised using sodium nitrite in a mixture of concentrated hydrochloric and glacial acetic acids and the resulting diazonium salt (257) was reduced *in situ* with tin(II) chloride dihydrate. This reaction however gave only a complex mixture from which no identifiable material was obtained.

An alternative approach to the naphth-1,3,4-oxadiazine (256) was then investigated. This approach involved the synthesis (Scheme 74) and hopefully spontaneous electrocyclisation of the quinone intermediate (262) to afford the naphth-1,3,4-oxadiazine (256). It was anticipated the quinone (262) would be available from the reaction of the hydrazone (261) with 1,2-naphthoquinone (260). One complication anticipated in this approach was the possibility of the hydrazone (261) reacting with the naphthoquinone (260) to afford the alternative quinone intermediate (263) and hence the naphth[2,1-e]-1,3,4-



(i) $TosN_3$, NaH, DME, room temp.

Scheme 75



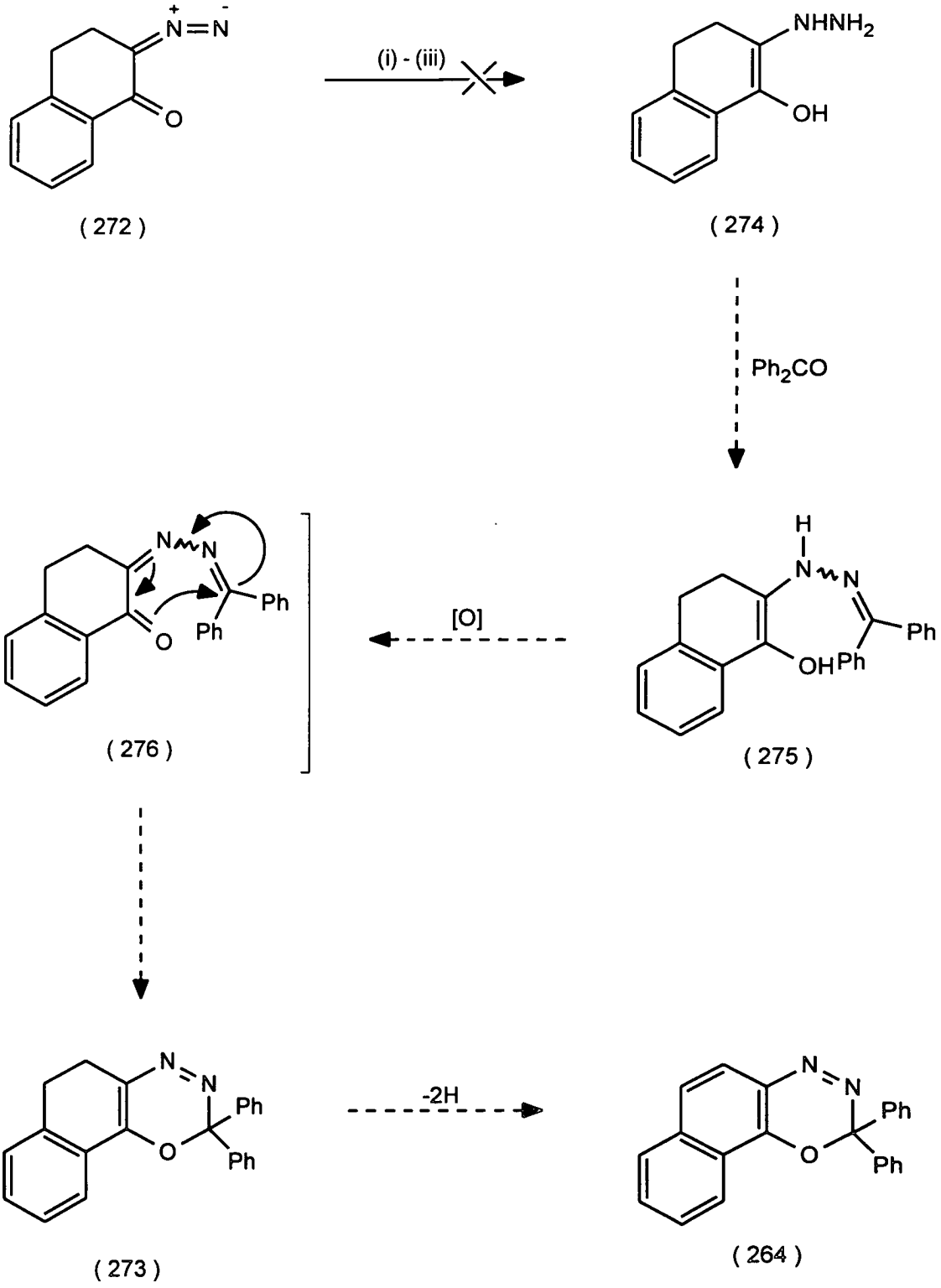
(i) $TosN_3$, NaH, DME, room temp.
(ii) DME, reflux.

Scheme 76

oxadiazine (264). Thus the reaction of benzophenone with hydrazine in n-butanol gave the hydrazone (261) in good yield (74%). Subsequent reaction of the hydrazone (261) with 1,2-naphthoquinone (260) in refluxing 1,2-dimethoxyethane containing molecular sieves gave only a complex mixture from which no identifiable material was obtained.

A further approach (Scheme 75) to the target naphthoxadiazine (256) was then evaluated. This approach involved the synthesis of the diazoketone (266) and its subsequent conversion into the hydrazine (267). The hydrazine (267) on reaction with benzophenone would afford the hydrazone derivative (268), capable of being oxidised to the quinone intermediate (269). Spontaneous electrocyclisation of the latter would afford the dihydronaphthoxadiazine (270), which on dehydrogenation would afford the desired naphthoxadiazine (256). Therefore in an attempt to obtain the key diazoketone (266), 3,4-dihydro-2(1H)-naphthalenone (265) was reacted with sodium hydride and toluene-4-sulphonyl azide in 1,2-dimethoxyethane. This reaction gave only an intractable mixture from which no identifiable material was obtained. The toluene-4-sulphonyl azide required for this reaction was readily available from reaction of toluene-4-sulphonyl chloride and sodium azide. Unfortunately due to a lack of time investigations into the synthesis of the diazoketone (266) were halted at this stage.

In conjunction with the previous work, investigations into the synthesis (Scheme 76) of the 2,2-diphenyl-2H-naphth[2,1-e]-1,3,4-oxadiazine (264) were also undertaken. Initial work was centred on the synthesis of the



(i) $NaBH_4$, DME, H_2O, room temp.

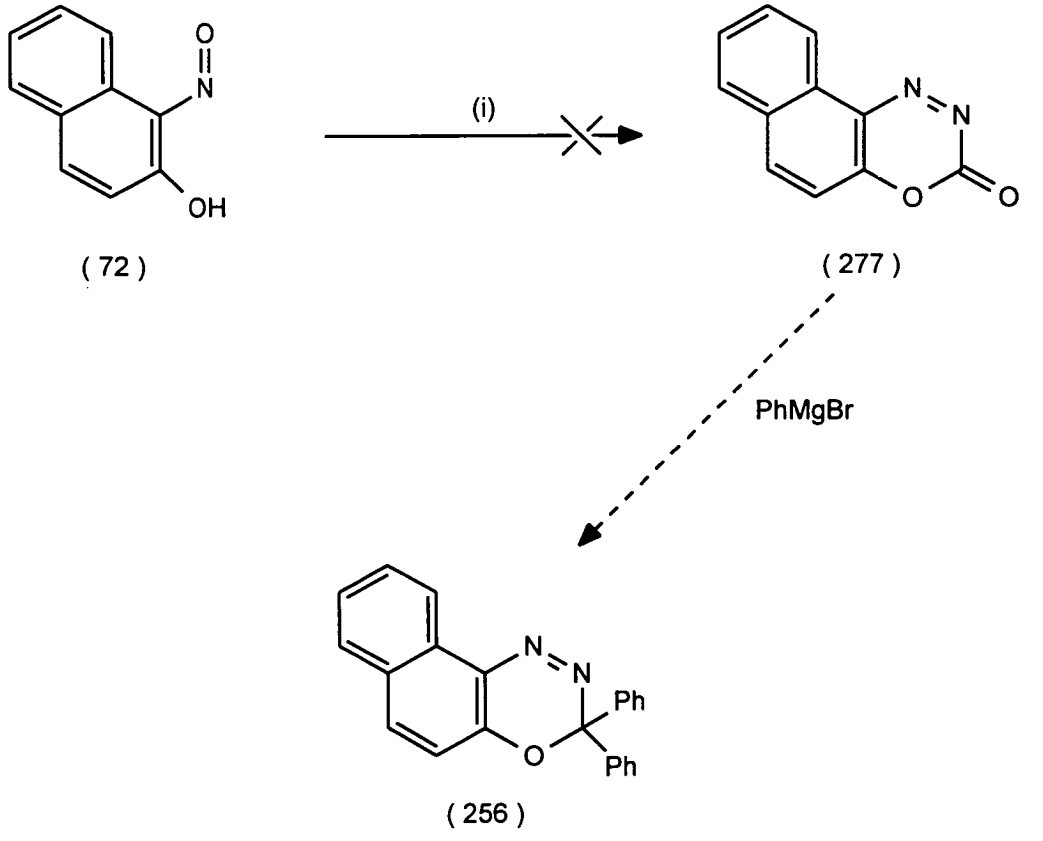
(ii) H_2, 10% Pd - C, EtOH, room temp., atmos. press.

(iii) $SnCl_2$, 2M HCl aqu., THF, reflux.

Scheme 77

dihydronaphthoxadiazine (273) as a potential precursor to the naphthoxadiazine (264). It was anticipated the dihydronaphthoxadiazine (273) would be available from the reaction of the diazoketone (272) with diazodiphenylmethane (100b), the latter compound readily available from the oxidation of benzophenone hydrazone. Therefore in an attempt to obtain the diazoketone (272), 3,4-dihydro-1(2H)-naphthalenone (271) underwent a sodium hydride catalysed reaction with toluene-4-sulphonyl azide in 1,2-dimethoxyethane at room temperature. This reaction afforded the diazoketone (272), albeit in low yield (27%) and also a low recovery (24%) of unreacted 3,4-dihydro-1(2H)-naphthalenone (271). The melting point of the red diazoketone (272) agreed with the literature value of this compound prepared by a more involved route.[129] Reaction of the diazoketone (272) with diazodiphenylmethane (100b) in refluxing 1,2-dimethoxyethane failed to give the dihydronaphthoxadiazine (273) and gave only a quantitative recovery of the diazoketone (272).

Due to the lack of success in the previous approach, a further route (Scheme 77) to the naphth-1,3,4-oxadiazine (264) involving the conversion of the diazoketone (272) into the hydrazine (274) was investigated. Further manipulation of the hydrazine (274) as shown [Scheme 77; (274)→(275)→(276)→(273)→(264)] would provide a synthetic route to the naphth-1,3,4-oxadiazine (264). Disappointingly attempted reduction of the diazoketone (272) using sodium borohydride in 1,2-dimethoxyethane gave none of the desired hydrazine (274) but only a complex mixture from which no identifiable



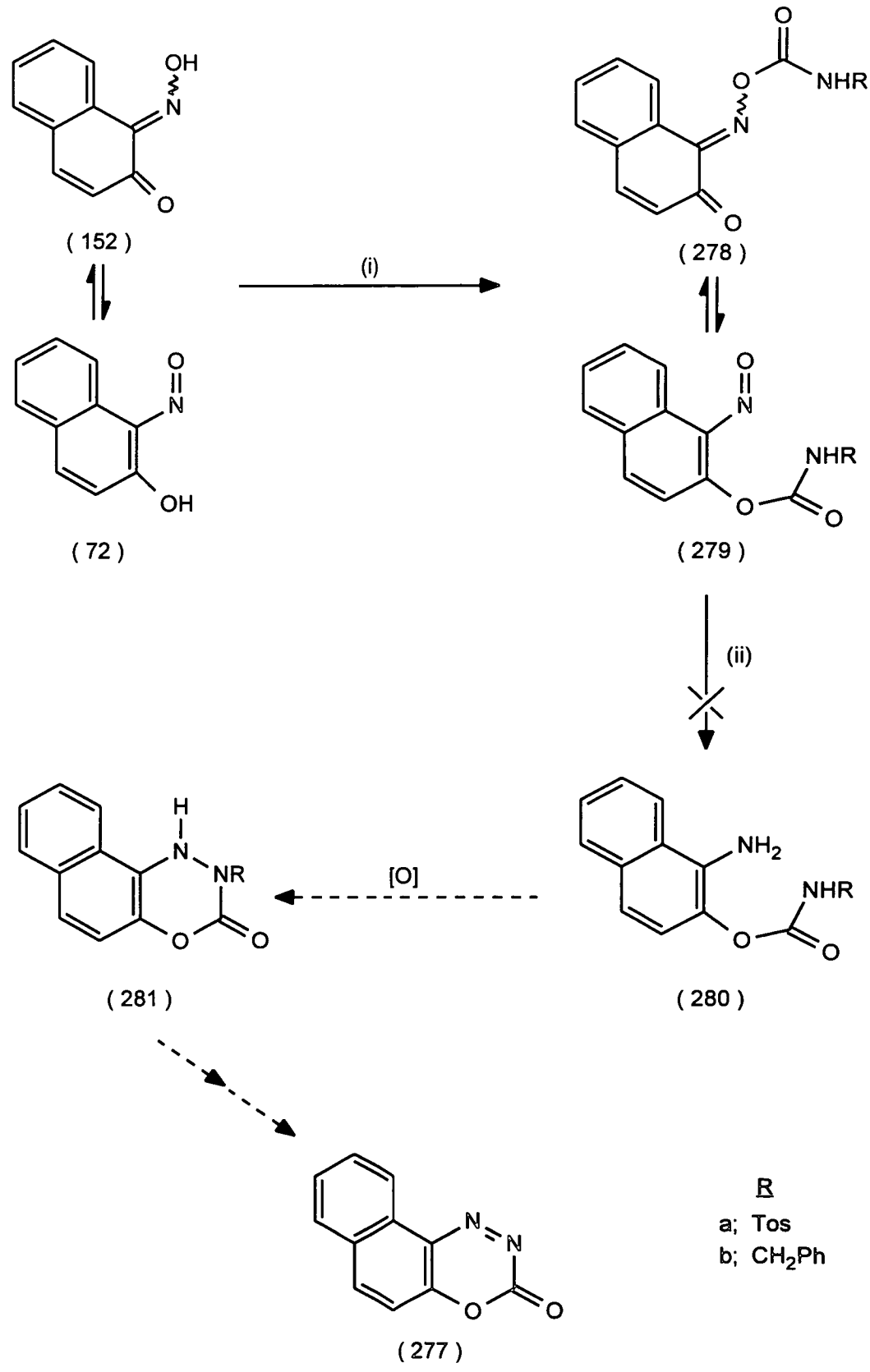
(72)

(277)

(256)

(i) $ClSO_2N=C=O$, CH_2Cl_2, room temp.

Scheme 78



(i) RN=C=O, DME, room temp.

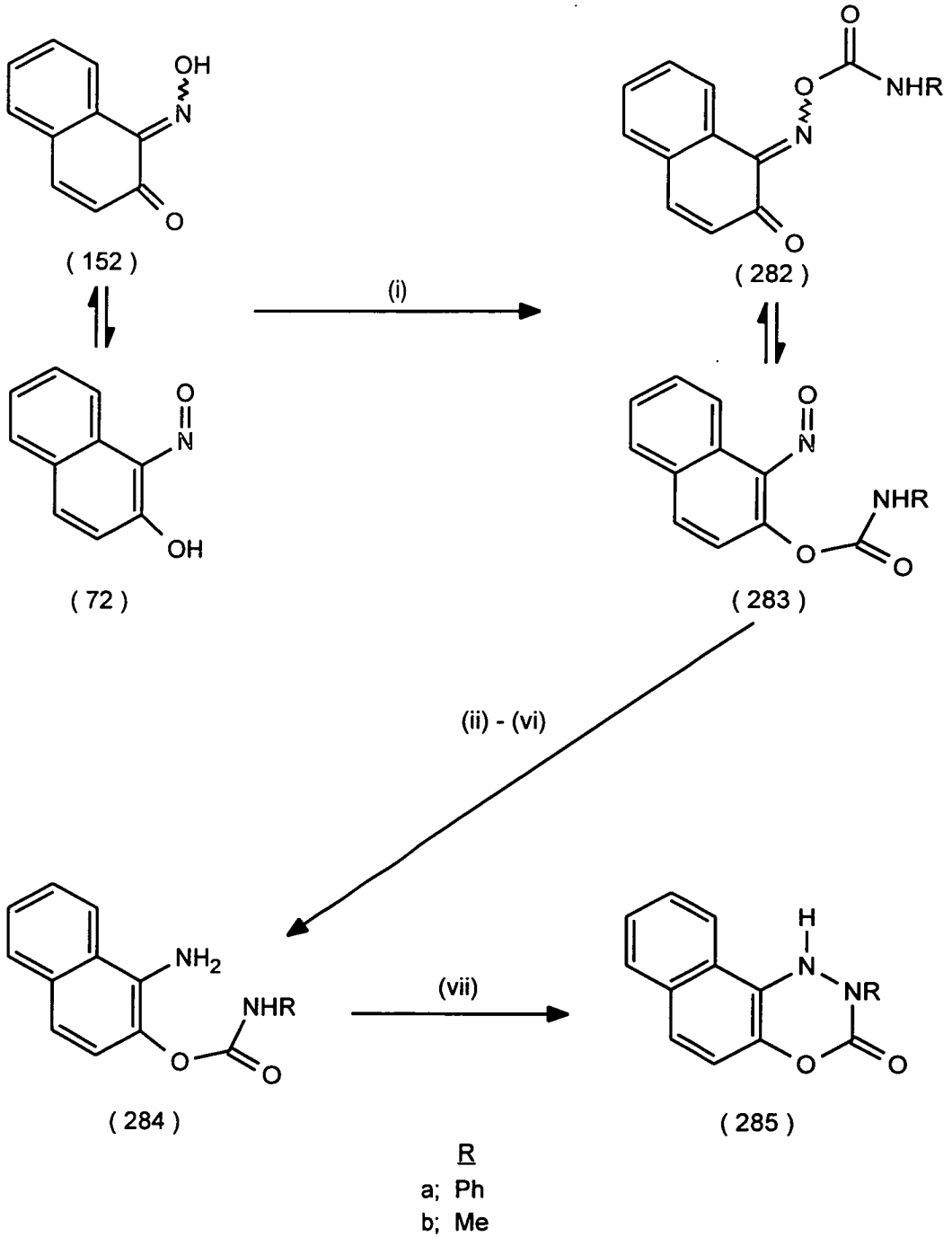
(ii) H_2, 10% Pd - C, DME, room temp., atmos. press.

Scheme 79

material was obtained. Reduction of the diazoketone (272) with hydrogen over 10% palladium-on-charcoal also afforded only complex mixtures. In a final attempt to obtain the hydrazine (274), the diazoketone (272) was reacted under reflux with tin(II) chloride dihydrate in a mixture of 2 M aqueous hydrochloric acid and tetrahydrofuran. Disappointingly this reaction also gave only an intractable mixture.

Due to the initial difficulties encountered in attempts to synthesise the naphth-1,3,4-oxadiazines (256) and (264), attention was turned to new strategies for the synthesis of these compounds, involving naphth-1,3,4-oxadiazinones as the key intermediates. Thus in one such approach (Scheme 78) it was hoped that 1-nitroso-2-naphthol (72) would react with chlorosulphonyl isocyanate to afford the naphthoxadiazinone (277) capable of conversion into the naphthoxadiazine (256). In practice, reaction of 1-nitroso-2-naphthol (72) with chlorosulphonyl isocyanate in dichloromethane gave only a low recovery (35%) of unreacted 1-nitroso-2-naphthol (72).

An alternative approach (Scheme 79) to the naphthoxadiazinone (277) was investigated. This approach was based on the reactions of 1-nitroso-2-naphthol (72) with toluene-4-sulphonyl isocyanate and benzyl isocyanate to afford the urethane adducts (279a and b) respectively, which could be elaborated through the amines (280a and b) and the dihydronaphthoxadiazinones (281a and b), *via* detosylation or debenzylation to afford the required naphthoxadiazinone (277). One complication anticipated in this approach was the possibility of tautomerism in 1-nitroso-2-naphthol



R

a; Ph

b; Me

(i) RN=C=O, DME, room temp.

(ii) H_2, 10% Pd - C, solvent, room temp., atmos. press.

(iii) $NaBH_4$, solvent, H_2O, room temp.

(iv) $Na_2S_2O_4$, EtOH, H_2O, room temp.

(v) PhNHNHPh, benzene, room remp.

(vi) Ph_3P, DME, room temp.

(vii) MnO_2, DME, room temp.

Scheme 80

[(72)⇌(152)] which could on reaction with the isocyanates afford the oximes (278a and b) and/or the urethanes (279a and b). In practice, 1-nitroso-2-naphthol (72) failed to react with toluene-4-sulphonyl isocyanate in 1,2-dimethoxyethane at room temperature. Benzyl isocyanate on the other hand reacted smoothly with 1-nitroso-2-naphthol (72) in 1,2-dimethoxyethane at room temperature to give a brown solid product in high yield (92%). This product gave mass and ^{1}H n.m.r. data consistent with both the oxime (278b) and urethane (279b) structures. The i.r. spectrum shows a band at 3305 cm^{-1} due to the NH group and bands at 1740 and 1665 cm^{-1} which are assignable to the urethane and quinone carbonyls of the oxime (278b). In further support of the oxime (278b) structure, reduction of the brown solid product using catalytic hydrogenation afforded a high yield (98%) of 1-amino-2-naphthol (139), the expected reductive cleavage product of the oxime (278b). Due to a lack of time, studies into the conversion of the oxime (278b) to the naphthoxadiazinone (277) were not undertaken.

The reactivity (Scheme 80) of 1-nitroso-2-naphthol (72) towards other isocyanates was also investigated. These studies provided a useful comparison with the previous attempted synthesis (Scheme 79) of the naphthoxadiazinone (277). Thus 1-nitroso-2-naphthol (72) reacted smoothly (Scheme 80) with methyl isocyanate in 1,2-dimethoxyethane at room temperature to give a yellow solid product in high yield (98%). This yellow solid product analysed correctly and gave correct mass and ^{1}H n.m.r. data to support both the oxime (282b) and the urethane (283b) structures. The i.r.

spectrum shows a band at 3295 cm^{-1} due to the NH group and bands at 1753 and 1666 cm^{-1} which are assignable to the urethane and quinone carbonyls of the oxime (282b). In further support of the proposed oxime (282b), reduction of the yellow solid product using catalytic hydrogenation afforded a high yield (94%) of 1-amino-2-naphthol (139). Similarly, reduction of the yellow solid product using sodium borohydride in aqueous dimethylformamide at room temperature also gave a high yield (75%) of 1-amino-2-naphthol (139), the expected reductive cleavage product of the oxime (282b). The formation of the oxime (282b) indicates 1-nitroso-2-naphthol (72) reacted predominantly as the tautomeric oxime form (152) with methyl isocyanate.

The reactivity (Scheme 80) of 1-nitroso-2-naphthol (72) towards phenyl isocyanate was also investigated. Thus, the reaction of 1-nitroso-2-naphthol (72) with phenyl isocyanate in 1,2-dimethoxyethane at room temperature gave a high yield (94%) of a yellow solid product. This product gave correct analytical, mass and ^1H n.m.r. data to support both the oxime (282a) and the urethane (283a) structures. The i.r. spectrum shows a band at 3261 cm^{-1} due to the NH group and bands at 1731 and 1666 cm^{-1} which are assignable to the urethane and quinone carbonyls of the oxime (282a). Further evidence for the oxime structure (282a) was then sought. Hydrolysis of the oxime (282a) would afford 1-nitroso-2-naphthol (72). Thus, the proposed oxime (282a) was heated under reflux in ethanol with 2 M aqueous hydrochloric acid to give only an intractable mixture. In contrast, basic hydrolysis of the oxime (282a) using 2 M aqueous sodium hydroxide at room temperature gave a high yield (87%) of 1-

nitroso-2-naphthol (72), the expected hydrolysis product of the oxime (282a). In a further reaction the oxime (282a) was heated with acetic anhydride at 100°, but this reaction gave only intractable mixtures.

The behaviour of the oxime (282a) towards reduction was also investigated (Scheme 80). Thus, the oxime (282a) was reacted with sodium borohydride in 1,2-dimethoxyethane at room temperature to give a high yield (97%) of 1-amino-2-naphthol (139), the expected reductive cleavage product of the oxime (282a). Reduction of the oxime (282a) with sodium dithionite in aqueous ethanol also gave 1-amino-2-naphthol (139) but only in low yield (22%). The formation of 1-amino-2-naphthol (139) further establishes the oxime structure (282a) of the yellow solid product and indicated 1-nitroso-2-naphthol (72) reacted as the tautomeric oxime form (152) with phenyl isocyanate.

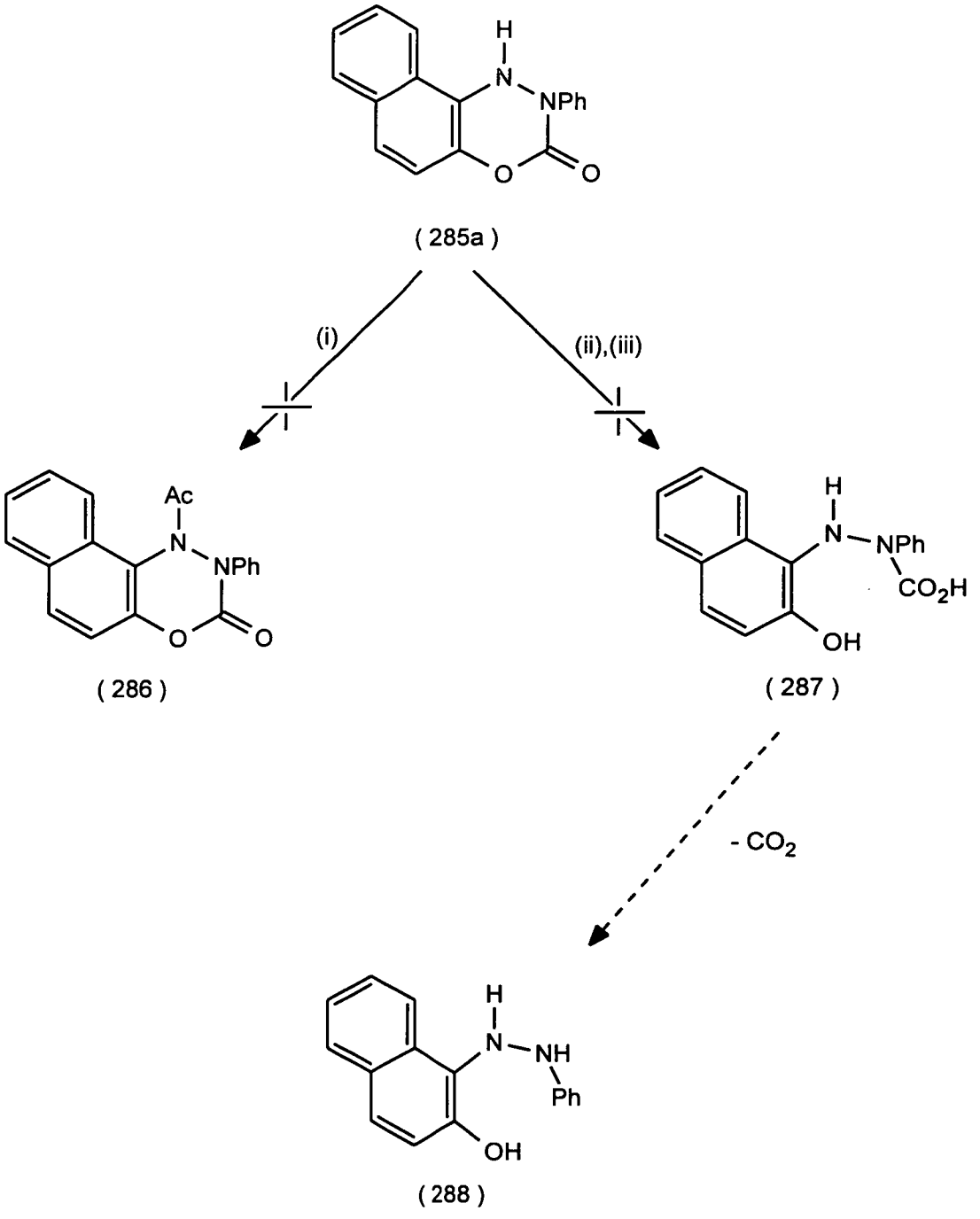
Interestingly, reduction of the oxime (282a) in ethyl acetate using catalytic hydrogenation did not give 1-amino-2-naphthol (139). This reaction gave a good yield (61%) of a colourless solid product. This colourless product gave mass spectrum data which supported the amine (284a). The i.r. spectrum shows a broad absorption 3320-3240 cm^{-1} which may be attributed to the NH stretch of the amine and urethane groups of the amine (284a). There is also an absorption band at 1611 cm^{-1} which may be attributed to the carbonyl absorption of the urethane group in the amine (284a). The unusual low absorption frequency of the carbonyl group in the amine (284a) may be due to intramolecular hydrogen bonding between the amine and carbonyl

groups which results in a lowering of the absorption frequency. The formation of the amine (284a) suggests the oxime (282a) has rearranged to the urethane (283a) under catalytic hydrogenation and the latter compound was reduced.

Further proof of the amine structure (284a) was then sought. Thus, reaction of the amine (284a) with acetic anhydride was expected to give an amide derivative. However reaction of the amine (284a) with refluxing acetic anhydride gave only an intractable mixture. The reactivity of the amine (284a) towards acid and basic hydrolysis was also investigated. The amine (284a) was heated under reflux in ethanol with 2 M aqueous hydrochloric acid to give only a quantitative recovery of unreacted amine (284a). Reaction of the amine (284a) with 2 M aqueous sodium hydroxide in ethanol at room temperature gave only a low recovery (36%) of unreacted amine (284a). Repetition of this reaction in refluxing 2 M aqueous sodium hydroxide gave only an intractable mixture.

As previously mentioned (see Page 264), reaction of the oxime (282a) with sodium borohydride gave a high yield (97%) of 1-amino-2-naphthol (139). In a blank experiment the amine (284a) was also reacted with sodium borohydride in 1,2-dimethoxyethane at room temperature. This reaction gave a high recovery (93%) of unreacted amine (284a) which suggests the oxime (282a) on reaction with sodium borohydride undergoes reductive cleavage to 1-amino-2-naphthol (139) rather than forming the amine (284a) and the latter cleaving.

An attempt was then made to improve the yield of the amine (284a)



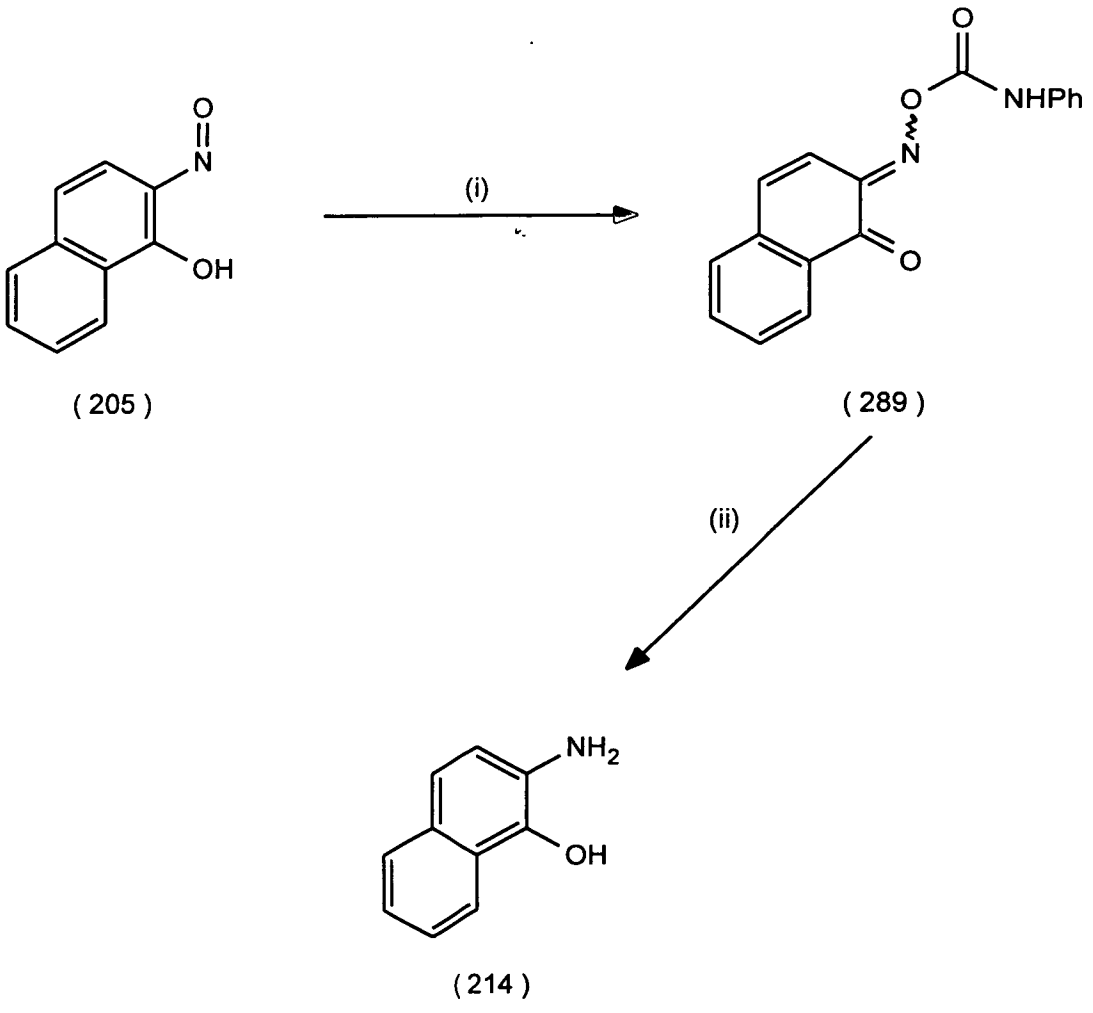
(i) Ac_2O, reflux.
(ii) 2M HCl aqu., EtOH, reflux.
(iii) 2M NaOH aqu., EtOH, reflux.

Scheme 81

using a different solvent in the catalytic hydrogenation of the oxime (282a). Hence the oxime (282a) was hydrogenated over 10% palladium-on-charcoal in 1,2-dimethoxyethane rather than ethyl acetate to give the amine (284a) in only a slightly better yield (65%). The amine (284a) was also obtained from the reaction of the oxime (282a) with hydrazobenzene in benzene at room temperature. This reaction gave a moderate yield (47%) of the amine (284a) and a high yield (100%) of azobenzene. The oxime (282a) also reacted with triphenylphosphine in 1,2-dimethoxyethane at room temperature to give a low yield (32%) of the amine (284a), a low recovery (27%) of triphenylphosphine and a high yield (72%) of triphenylphosphine oxide.

With the proposed amine (284a) available, investigations (Scheme 80) into its possible oxidative cyclisation to the naphthoxadiazinone derivative (285a) were undertaken. Reaction of the amine (284a) with activated manganese dioxide in 1,2-dimethoxyethane gave a good yield (65%) of a brown solid product which gave the correct parent ion in its mass spectrum and had i.r. spectral properties which supported the naphthoxadiazinone derivative (285a). Thus, the i.r. spectrum shows an absorption at 3289 cm^{-1} due to the NH group and a band at 1720 cm^{-1} attributable to the carbonyl absorption of the naphthoxadiazinone derivative (285a). The formation of the naphthoxadiazinone (285a) is in turn further proof of the existence of the amine (284a).

With the naphthoxadiazinone (285a) to hand, investigation (Scheme 81) of its chemical behaviour towards acetic anhydride was undertaken. Reaction



(205)

(289)

(214)

(i) PhN=C=O, DMF, room temp.
(ii) H_2, 10% Pd - C, DME, room temp., atmos. press.

Scheme 82

of the naphthoxadiazinone (285a) with acetic anhydride was expected to afford the acylated product (286). In practice, reaction of the naphthoxadiazinone (285a) with refluxing acetic anhydride gave only a complex mixture.

The behaviour (Scheme 81) of the naphthoxadiazinone (285a) towards acid and basic hydrolysis was also investigated. The reaction of the naphthoxadiazinone (285a) with 2 M aqueous hydrochloric acid in refluxing ethanol gave only a moderate recovery (50%) of unreacted naphthoxadiazinone (285a) with no evidence for the formation of the possible hydrolysis products (287) or (288). Repetition of this hydrolysis but using 2 M aqueous sodium hydroxide gave a complex mixture which yielded no identifiable material. Due to a lack of time studies into the reactions of 1-nitroso-2-naphthol (72) with isocyanates and the manipulation of the products obtained were halted at this stage.

Investigations of the reactivity (Scheme 82) of 2-nitroso-1-naphthol (205) with phenyl isocyanate were also undertaken. Reaction of 2-nitroso-1-naphthol (205) with phenyl isocyanate in dimethylformamide at room temperature gave an orange solid product in high yield (96%). This product analysed correctly and gave mass, i.r. and ^{1}H n.m.r. data that supported the oxime (289) structure. Thus, the i.r. spectrum shows a band at 3310 cm^{-1} due to the NH group and bands at 1771 and 1667 cm^{-1} due to the carbonyl absorptions of the urethane and quinone groups. In further support of the oxime (289), catalytic hydrogenation of the orange product gave a moderate yield (46%) of 2-amino-1-naphthol (214), the expected reductive cleavage product of the oxime (289).

3.4 EXPERIMENTAL

General Experimental Details

For general experimental details see Chapter 2, Section 2.5, pages 97-99.

Elemental Analyses and Mass Spectroscopic Data

Elemental analyses and mass spectroscopic data are collected in Table 8, page 312.

The Attempted Reaction of 2-Hydroxy-1-naphthaldehyde (234) with 4,4'-Carbonimidoyl-bis(N,N-dimethylamino)benzene Hydrochloride (235)

A stirred suspension of 4,4'-carbonimidoyl-bis(N,N-dimethylamino)benzene hydrochloride (235) (1.2 g; 0.004 mol) in anhydrous ethanol (20.0 ml) was mixed with a solution of 2-hydroxy-1-naphthaldehyde (234) (0.69 g; 0.004 mol) in anhydrous ethanol (10.0 ml) and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 4 h.

The mixture was allowed to cool, then rotary evaporated to give a brown solid (2.0 g) which was washed with boiling ethyl acetate (25.0 ml) to give the unreacted hydrochloride (235) as a yellow solid (1.2 g; 100%), identical [i.r. spectrum and t.l.c. in hexane-ethyl acetate (7:3) over silica] to an authentic sample.

The ethyl acetate washings were rotary evaporated to afford unreacted 2-hydroxy-1-naphthaldehyde (234) as a brown solid (0.69 g; 100%), m.p. 80-

83°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Diphenylmethyl Azide

A stirred solution of diphenylmethyl bromide (9.9 g; 0.04 mol) in anhydrous dimethylformamide (16.0 ml) was treated with sodium azide (2.6 g; 0.04 mol) added in one portion and the suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 24 h.

The mixture was diluted with water (160 ml) and extracted with ether. The combined extracts were washed three times with water (3 x 40.0 ml), then rotary evaporated to afford diphenylmethyl azide as a yellow oil (8.4 g; 100%), υ_{max} 2140(N_3) cm^{-1} which was used without further purification.

***N*-(Diphenylmethyl)triphenylphosphinimine (241)**

A stirred solution of diphenylmethyl azide (2.1 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) was treated with a solution of triphenylphosphine (2.6 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) and the resulting pale brown solution was stirred at room temperature for 17 h, then at 60° (water-bath) for a further 8 h.

The mixture was allowed to cool, then rotary evaporated to give *N*-diphenylmethyltriphenylphosinimine (241) as an off-white solid (4.4 g; 99%), m.p. 138-139° (lit.,[130] 129-131°), $\delta_H(CDCl_3)$ 7.68-7.08(25H, m, ArH) and 6.06(1H, s, CH).

***N*-(Diphenylmethyl-2-hydroxy-1-naphthaldimine (237)**

(a) A stirred solution of 2-hydroxy-1-naphthaldehyde (234) (0.34 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was treated with a solution of *N*-(diphenylmethyl)triphenylphoshinimine (241) (0.89 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) and the resulting brown solution was then stirred and heated under reflux with the exclusion of atmospheric moisture for 17 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.3 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave only an intractable yellow solid (0.11 g).

Elution with hexane-ether (9:1) gave *N*-(diphenylmethyl)-2-hydroxy-1-naphthaldimine (237) as a yellow solid (0.62 g; 92%), m.p. 166-167° (from ethanol), υ_{max} 3432(OH) and 1625(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 15.44(1H, s, OH), 9.54(1H, s, CH), 8.23-6.89(16H, m, ArH) and 6.15(1H, s, CH).

Final elution with methanol gave triphenylphosphine oxide as a light brown solid (0.47 g; 85%), m.p. 153-155° identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) A stirred solution of 2-hydroxy-1-naphthaldehyde (234) (3.4 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) containing freshly regenerated 4 Å molecular sieves (10.0 g) was treated with a solution of diphenylmethylamine (242) (3.7 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) and the

mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The mixture was filtered to remove the sieves and the sieves were washed twice with anhydrous 1,2-dimethoxyethane (2 x 50.0 ml). The combined 1,2-dimethoxyethane filtrate and washings were rotary evaporated to give the imine (237) as a yellow solid (6.8 g; 100%), m.p. 166-167°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

Attempted Oxidation Reactions of *N*-(Diphenylmethyl)-2-hydroxy-1-naphthaldimine (237)

(a) A stirred solution of the imine (237) (0.67 g; 0.002 mol) in anhydrous acetonitrile (50.0 ml) was treated with activated manganese(IV) oxide (1.0 g) added in one portion and the suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give the unreacted imine (237) as a yellow solid (0.62 g; 93%), m.p. 160-164°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

(b) A stirred solution of the imine (237) (0.67 g; 0.002 mol) in glacial acetic acid (20.0 ml) was treated dropwise over 1 h with a suspension of ammonium cerium(IV) nitrate (2.2 g; 0.004 mol) in 50% v/v aqueous acetic acid (10.0 ml) and the mixture was then stirred at room temperature for 17 h.

The mixture was concentrated by rotary evaporation to *ca.* one quarter of the original volume, treated with 10% w/v aqueous sodium hydrogen carbonate solution (10.0 ml) and extracted with dichloromethane to give a brown gum (0.67 g) which was flash-chromatographed over silica.

Elution with light petroleum-ether (19:1) through ether to methanol gave only a series of intractable multicomponent gums (total 0.60 g) from which no identifiable material was obtained.

(c) A stirred solution of the imine (237) (0.67 g; 0.002 mol) in 75% v/v aqueous tetrahydrofuran (40.0 ml) was treated with ammonium cerium(IV) nitrate (2.2 g; 0.004 mol) added in one portion and the mixture was stirred at room temperature for 5 h.

The mixture was concentrated by rotary evaporation to *ca.* one quarter of the original volume, treated with water (10.0 ml) and extracted with dichloromethane to give a brown gum (0.67 g) which was flash-chromatographed over silica.

Elution with hexane-ether (99:1) gave an orange oil (0.070 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to be mainly 2-hydroxy-1-naphthaldehyde (234).

Further elution with hexane-ether (4:1) through ether to methanol gave only a series of multicomponent gums (total 0.43 g) from which no further identifiable material was obtained.

(d) A stirred suspension of the imine (237) (0.67 g; 0.002 mol) in 1 M aqueous sodium hydroxide solution (5.0 ml) was treated with 30% w/v aqueous hydrogen peroxide (1.0 ml) and the yellow suspension was stirred at room temperature for 17 h.

The mixture was filtered to give the unreacted imine (237) as a yellow solid (0.65 g; 97%), m.p. 165-167°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared before.

***N*-Diphenylmethyl)-2-hydroxybenzaldimine (243)**

(a) A stirred solution of 2-hydroxybenzaldehyde (79) (0.24 g; 0.002 mol) in anhydrous benzene (5.0 ml) was treated with a solution of *N*-(diphenylmethyl)triphenylphosphinimine (241) (0.89 g; 0.002 mol) in anhydrous benzene (5.0 ml) and the resulting yellow solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 3 h.

The mixture was allowed to cool, then rotary evaporated to give a yellow semisolid (1.2 g) which was flash-chromatographed over silica.

Elution with hexane-ether (24:1) gave a yellow solid (0.57 g) which was washed with light petroleum to afford *N*-(diphenylmethyl)-2-hydroxybenzaldimine (243) as a yellow solid (0.31 g; 54%), m.p. 130-133° (from hexane-toluene), υ_{max} 1622(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 13.55(1H, s, OH), 8.49(1H, s, CH), 7.50-6.87(14H, m, ArH) and 5.65(1H, s, CH). Rotary evaporation of the light petroleum washings gave unreacted 2-hydroxybenzaldehyde (79) as a yellow oil (0.10 g; 41%), identical [i.r. spectrum

and t.l.c. in hexane-ether (3:2) over silica] to an authentic sample.

Elution with methanol gave a green gum (0.64 g) which was washed with ether to afford triphenylphosphine oxide as a light brown solid (0.32 g; 57%), m.p. 155-159°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample. Rotary evaporation of the ether washings gave only a multicomponent brown gum (0.17 g) from which no further identifiable material was obtained.

(b) A stirred solution of 2-hydroxybenzaldehyde (79) (2.4 g; 0.02 mol) in anhydrous ether (50.0 ml) containing freshly regenerated 4 Å molecular sieves (10.0 g) was treated with a solution of diphenylamine (242) (3.7 g; 0.02 mol) in anhydrous ether (50.0 ml) and the mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The mixture was filtered to remove the sieves and the sieves were washed twice with anhydrous ether (2 x 50.0 ml). The combined ether filtrate and washings were rotary evaporated to give *N*-(diphenylmethyl)-2-hydroxybenzaldimine (243) as a yellow solid (5.7 g; 99%), m.p. 130-133°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

The Acid Catalysed Hydrolysis of *N*-(Diphenylmethyl)-2-hydroxybenzaldimine (243)

A stirred solution of the imine (243) (0.57 g; 0.002 mol) in ethanol (10.0 ml) was treated with 2 M aqueous hydrochloric acid (2.5 ml) and the

mixture was stirred and heated under reflux for 1 h.

The mixture was allowed to cool, then rotary evaporated. The residue was treated with water (10.0 ml) and extracted with dichloromethane to give 2-hydroxybenzaldehyde (79) as a yellow oil (0.13 g; 53%), identical [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] to an authentic sample.

The aqueous mother liquor was made basic by the addition of 2 M aqueous sodium hydroxide solution and extracted with dichloromethane to give diphenylmethylamine (242) as a light brown oil (0.29 g; 79%), identical [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] to an authentic sample.

Attempted Oxidation Reactions of *N*-(Diphenylmethyl)-2-hydroxybenzaldimine (243)

(a) A stirred solution of the imine (243) (0.57 g; 0.002 mol) in anhydrous acetonitrile (20.0 ml) was treated with activated manganese(IV) oxide (1.0 g) added in one portion. The dark suspension was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give the unreacted imine (243) as a yellow solid (0.57 g; 100%), m.p. 124-127°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared before.

(b) A stirred solution of the imine (243) (0.57 g; 0.002 mol) in 75% v/v aqueous acetonitrile (40.0 ml) was treated with ammonium cerium(IV) nitrate

(2.2 g; 0.004 mol) added in one portion and the mixture was stirred at room temperature for 23 h.

The mixture was filtered to remove some insoluble material and the filtrate was concentrated by rotary evaporation to *ca.* one quarter of the original volume, then treated with water (10.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to remove an intractable unidentified yellow solid (0.27 g).

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane and the combined extracts rotary evaporated to give an intractable multicomponent red solid (0.16 g) from which no identifiable material was obtained.

(c) A stirred suspension of the imine (243) (0.57 g; 0.002 mol) in 1 M aqueous sodium hydroxide solution (5.0 ml) was treated with 30% w/v aqueous hydrogen peroxide (1.0 ml) and the yellow suspension was stirred at room temperature for 17 h.

The mixture was filtered to give a yellow solid which was washed twice with water (2 x 5.0 ml) to give the unreacted imine (243) as a yellow solid (0.56 g; 98%), m.p. 129-132°, identical (m.p. and i.r. spectrum) to a sample prepared previously.

Bromination of *N*-(Diphenylmethyl)-2-hydroxybenzaldimine (243)

A stirred solution of the imine (243) (0.57 g; 0.002 mol) in anhydrous

carbon tetrachloride (5.0 ml) was mixed with a suspension of *N*-bromosuccinimide (0.71 g; 0.004 mol) in anhydrous carbon tetrachloride (5.0 ml). Dibenzoyl peroxide (0.001 g) was then added and the mixture was stirred and heated under reflux with the exclusion of atmospheric moisture for 21 h.

The mixture was hot filtered to afford succinimide as a colourless solid (0.36 g; 91%), m.p. 123-125°, identical (m.p. and i.r. spectrum) to an authentic sample.

The carbon tetrachloride mother-liquor was allowed to cool and the precipitated solid collected to afford a second crop of succinimide as a colourless solid (0.031 g; 8%), m.p. 123-125°, identical (m.p. and i.r. spectrum) to an authentic sample.

Rotary evaporation of the carbon tetrachloride filtrate gave a brown solid (0.96 g) which was flash-chromatographed over silica.

Elution with hexane-dichloromethane (4:1) gave a product tentatively identified as *N*-(diphenylmethyl)-3,5-dibromo-2-hydroxybenzaldimine which formed yellow needles (0.46 g; 52%), m.p. 146-148° (from hexane-toluene), υ_{max} 1626(C=N) cm^{-1}, $\delta_H(CDCl_3)$ 14.61(1H, s, OH), 8.32(1H, s, CH), 7.70(1H, d, J_{meta} 2Hz, ArH), 7.31-7.22(11H, m, ArH) and 5.69(1H, s, CH).

Found: C, 54.1; H, 3.6; N, 3.2; M^+, 447, 445, 443

$C_{20}H_{15}Br_2NO$: C, 53.9; H, 3.4; N, 3.2; M^+, 447, 445, 443

Elution with hexane-dichloromethane (1:1) gave an orange semisolid (0.27 g) which was washed with hexane to afford a second crop of *N*-(diphenylmethyl)-3,5-dibromo-2-hydroxybenzaldimine as a yellow solid (0.14

g; 16%), m.p. 136-141°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared previously.

Further elution with hexane-dichloromethane (1:1) through dichloromethane to methanol gave no further material.

Attempted Reactions of 2-Hydroxy-1-naphthaldehyde (234) with Isocyanates

A stirred solution of 2-hydroxy-1-naphthaldehyde (234) (0.69 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was treated with a solution of the isocyanate (0.004 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) and the resulting solution was stirred with the exclusion of atmospheric moisture at the temperature and for the time indicated then worked up as described for the individual reactions below.

(a) Chlorosulphonyl isocyanate

Stirring was continued at room temperature for 23 h. The solution was then rotary evaporated to give a brown gum (1.2 g) which was washed with hexane to afford unreacted 2-hydroxy-1-naphthaldehyde (234) as a brown solid (0.41 g; 59%), m.p. 82-85°, identical (m.p. and i.r. spectrum) to an authentic sample.

Rotary evaporation of the hexane washings gave only an intractable brown gum (0.65 g) from which no further identifiable material was obtained.

(b) Benzyl isocyanate

Stirring was continued at room temperature for 24 h and the mixture was stirred and heated under reflux for a further 23 h. The solution was allowed to cool, then rotary evaporated to give a brown gum (1.3 g) which was washed with hexane to afford unreacted 2-hydroxy-1-naphthaldehyde (234) as a brown solid (0.69 g; 100%), m.p. 82-85°, identical (m.p. and i.r. spectrum) to an authentic sample.

Rotary evaporation of the hexane washings gave unreacted benzyl isocyanate as a yellow oil (0.52 g; 98%), identical [i.r. spectrum and t.l.c. in hexane-ethyl acetate (7:3) over silica] to an authentic sample.

(c) Methyl isocyanate

Stirring was continued at room temperature for 2 h. A further portion of methyl isocyanate (0.68 g; 0.012 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was then added and the solution stirred at room temperature for a further 21 h. The solution was rotary evaporated to afford unreacted 2-hydroxy-1-naphthaldehyde (234) as a brown solid (0.69 g; 100%), m.p. 82-84°, identical (m.p. and i.r. spectrum) to an authentic sample.

2-(*N*-Phenylcarbanoyl)oxy-1-naphthaldehyde (250)

(a) A stirred solution of 2-hydroxy-1-naphthaldehyde (234) (0.69 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was treated with a solution of phenyl isocyanate (0.48 g; 0.004 mol) in anhydrous 1,2-

dimethoxyethane (5.0 ml) and the resulting brown solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 23 h.

The mixture was allowed to cool, then rotary evaporated to give a brown semisolid (1.2 g) which was washed with ether to afford 2-(*N*-phenylcarbanoyl)oxy-1-naphthaldehyde (250) (0.31 g; 27%) which formed colourless microcrystals, m.p. 145-149° (from ethyl acetate-ethanol), υ_{max} 3329(NH) and 1754 and 1668(C=O) cm^{-1}, $\delta_H[(CD_3)_2SO)]$8.09-7.04(12H, m, ArH and NH) and 6.56(1H, s, CHO).

Rotary evaporation of the ether washings gave a brown gum (0.80 g) which was washed with hexane to afford unreacted 2-hydroxy-1-naphthaldehyde (234) as an orange solid (0.50 g; 72%), m.p. 75-80° identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the hexane washings gave no further material.

(b) Repetition of the reaction described in (a) before but in 1,4-dioxane and using two equivalents of phenyl isocyanate gave after similar workup of the mixture, 2-(*N*-phenylcarbanoyl)oxy-1-naphthaldehyde (250) as a pale brown solid (0.26 g; 22%), m.p. 140-144°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before, together with a brown gum (1.0 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to be a mixture of 2-hydroxy-1-naphthaldehyde (234) and phenyl isocyanate.

(c) Repetition of the reaction described in (a) before but at room

temperature for 24 h gave after similar workup of the mixture 2-(*N*-phenylcarbanoyl)oxy-1-naphthaldehyde (250) as a pale brown solid (0.58 g; 50%), m.p. 145-149°, identical (m.p. and i.r. spectrum) to an authentic sample prepared in (a) before, together with unreacted 2-hydroxy-1-naphthaldehyde (234) as a brown solid (0.34 g; 49%), m.p. 83-85°, identical (m.p. and i.r. spectrum) to an authentic sample.

4-Hydroxy-3-phenyl-3,4-dihydro-2H-benzoxazin-2-one (253)

A stirred solution of salicylaldehyde (79) (0.49 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was treated with a solution of phenyl isocyanate (0.48 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) and the resulting solution was then stirred at room temperature with the exclusion of atmospheric moisture for 20 h.

The mixture was rotary evaporated to give a yellow solid (0.96 g) which was crystallised to afford 4-hydroxy-3-phenyl-3,4-dihydro-2H-benzoxazin-2-one (253) (0.76 g; 79%) as colourless needles, m.p. 118-121° (from benzene), υ_{max} 3376(OH) and 1706(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 7.60-7.10(9H, m, ArH), 5.97(1H, d, J8Hz, CH, collapses to a singlet on shaking with D_2O), and 3.78(1H, d, J8Hz, OH) (exch.).

Rotary evaporation of the benzene mother liquor gave only a multicomponent orange gum (0.18 g) from which no further identifiable material was obtained.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with 4,4'-Carbonimidoylbis(N,N-dimethylamino)benzene Hydrochloride (235)

A stirred suspension of 4,4'-carbonimidoylbis(N,N-dimethylamino)benzene hydrochloride (235) (1.2 g; 0.004 mol) in anhydrous ethanol (20.0 ml) was treated with a solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous ethanol (10.0 ml) and the mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture for 18 h.

The mixture was allowed to cool, then rotary evaporated to give a brown solid (1.9 g) which was washed with boiling ethyl acetate (25.0 ml) to afford unreacted 4,4'-carbonimidoylbis(N,N-dimethylamino)benzene hydrochloride (235) as a yellow solid (1.2 g; 100%), identical [i.r. spectrum and t.l.c. in hexane-ethyl acetate (7:3) over silica] to an authentic sample.

The ethyl acetate washings were allowed to cool, then rotary evaporated to give unreacted 1-nitroso-2-naphthol (72) as a brown solid (0.68 g; 99%), m.p. 106-107°, identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of the Sodium Salt of 1-Nitroso-2-naphthol (153) with 4,4'-Carbonimidoylbis(N,N-dimethylamino)benzene Hydrochloride (235)

A stirred solution of the sodium salt of 1-nitroso-2-naphthol (153)

(0.39 g; 0.002 mol) in anhydrous dimethyl sulphoxide (5.0 ml) was treated with a solution of the hydrochloride (235) (0.61 g; 0.002 mol) in anhydrous dimethyl sulphoxide (5.0 ml) and the resulting green solution was stirred and heated at 90° with the exclusion of atmospheric moisture for 1 h.

The mixture was allowed to cool, then rotary evaporated. The residue was treated with water (5.0 ml) and extracted with dichloromethane to give a brown gum (1.0 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave a multicomponent brown gum (0.092 g) from which no identifiable material was obtained.

Further elution with hexane-ether (3:2) gave 4,4'-bis(dimethylamino)benzophenone (182) as a brown solid (0.081 g; 15%), m.p. 173-175°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Elution with hexane-ether (1:1) through ether to methanol gave only a series of multicomponent gums (total 0.61 g) from which no further identifiable material was obtained.

Acidification of the aqueous mother liquor with 2 M aqueous hydrochloric acid and extraction with dichloromethane gave only a small amount of an intractable brown oil (0.079 g) which was not further investigated.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with *N*-(Diphenylmethyl)triphenylphosphinimine (241)

A stirred solution of 1-nitroso-2-naphthol (72) (0.35 g; 0.002 mol) in

anhydrous benzene (5.0 ml) was treated with a solution of *N*-(diphenylmethyl)triphenylphosinimine (241) (0.89 g; 0.002 mol) in anhydrous benzene (5.0 ml) and the resulting brown solution was stirred and heated under reflux with the exclusion of atmospheric moisture for 1.5 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (1.4 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through ether to methanol gave only a series of intractable multicomponent oils and gums (total 1.0 g) from which no identifiable material was obtained.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with Diphenylmethylamine (242)

A stirred solution of 1-nitroso-2-naphthol (72) (0.87 g; 0.005 mol) in anhydrous toluene (10.0 ml) was treated with a solution of diphenylmethylamine (242) (0.92 g; 0.005 mol) in anhydrous toluene (10.0 ml). The resulting brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 2 h and then stirred and heated under reflux with azeotropic distillation of the water formed (Dean and Stark apparatus) for 1 h.

The mixture was allowed to cool, then rotary evaporated to give a dark brown gum (1.8 g) which was flash-chromatographed over silica.

Elution with hexane-ether (49:1) through ether to methanol gave only a series of intractable multicomponent gums and solids (total 1.7 g) from which

no identifiable material was obtained.

The Attempted Conversion of 1-Amino-2-naphthol (139) into *N*-(2-Hydroxy-1-naphthylhydrazine (258)

A stirred solution of 1-amino-2-naphthol (139) (1.6 g; 0.01 mol) in glacial acetic acid (50.0 ml) was treated with concentrated hydrochloric acid (4.0 ml) and the mixture was cooled to 0° (ice-salt bath) and treated dropwise with a solution of sodium nitrite (0.76 g; 0.011 mol) in water (4.0 ml) at such a rate that the reaction temperature was 0-5°. The resulting mixture was stirred at 0-5° for 30 min and then was treated dropwise with a solution of tin(II) chloride dihydrate (4.5 g; 0.02 mol) in concentrated hydrochloric acid (5.0 ml) at such a rate that the reaction temperature was 0-5°. The mixture was then stirred in the melting ice-bath for 21 h.

The mixture was rotary evaporated to *ca.* one-third of the original volume, treated with a few drops of concentrated hydrochloric acid, then slowly added in portions to a cooled solution (ice-bath) of 40% w/v aqueous sodium hydroxide (5.0 ml) at such a rate that the reaction temperature was 10°. The mixture was stirred at 10° (ice-bath) for 30 min, then extracted with dichloromethane. The resulting three phase mixture was filtered to give a multicomponent dark brown solid (0.90 g) which yielded no identifiable material.

The aqueous-dichloromethane filtrate was separated and the aqueous layer further extracted with dichloromethane. Rotary evaporation of the

combined extracts gave only a multicomponent brown gum (0.041 g) which was not further investigated.

Benzophenone Hydrazone (261)

A stirred solution of benzophenone (9.1 g; 0.05 mol) in 1-butanol (25.0 ml) was treated with 98% hydrazine monohydrate (10.0 ml) and the resulting colourless solution was stirred and heated under reflux for 3 h.

The mixture was allowed to cool to room temperature and methanol was added dropwise to maintain a homogeneous solution. The resulting colourless solution was storred in a stoppered flask in a refrigerator for 17 h and the precipitated solid collected to afford benzophenone hydrazone (261) as a colourless solid (7.3 g; 74%), m.p. 95-97°, (lit.,[131] 98°) which was used without further purification.

The Attempted Reaction of 1,2-Naphthoquinone (260) with Benzophenone Hydrazone (261)

A stirred solution of the hydrazone (261) (0.78 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) containing freshly regenerated 4 Å molecular sieves (2.0 g), was treated with a solution of 1,2-naphthoquinone (260) (0.63 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the mixture was then stirred and heated under reflux with the exclusion of atmospheric moisture for 1 h.

The suspension was hot filtered to remove the sieves and the sieves

washed twice with anhydrous 1,2-dimethoxyethane (2 x 10.0 ml). The combined 1,2-dimethoxyethane filtrate and washings were rotary evaporated to give a red gum (1.3 g) which was flash-chromatographed over silica.

Elution with light petroleum (99:1) through ether to methanol gave only a series of intractable multicomponent gums (total 1.3 g) from which no identifiable material was obtained.

Toluene-4-sulphonyl Azide

A stirred solution of toluene-4-sulphonyl chloride (34.0 g; 0.18 mol) in ethanol (400 ml) was treated dropwise with a solution of sodium azide (14.0 g; 0.22 mol) in water (40.0 ml) and the resulting suspension was stirred at room temperature for 1 h.

The mixture was poured into water (1500 ml) and extracted with dichloromethane to afford toluene-4-sulphonyl azide as a pale yellow oil (30.2 g; 85%), υ_{max} 2126(N_3) cm^{-1} which was used without further purification.

The Attempted Reaction of 3,4-Dihydro-2(1H)-napthalenone (265) with Toluene-4-sulphonyl Azide

A stirred suspension of sodium hydride (0.26 g; 0.011 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 3,4-dihydro-2(1H)-naphthalenone (265) (1.5 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml). The mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min to

ensure salt formation and then was treated in one portion with a solution of toluene-4-sulphonyl azide (2.0 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml). The mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was diluted with water (1.0 ml), stirred at room temperature for 15 min to destroy any unreacted sodium hydride, then rotary evaporated. The residue was treated with water (10.0 ml) and extracted with dichloromethane to give a purple gum (1.5 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) through ether to methanol gave only a series of multicomponent gums and solids (total 1.5 g) from which no identifiable material was obtained.

2-Diazo-3,4-dihydro-1(2H)-naphthalenone (272)

(a) A stirred suspension of sodium hydride (0.26 g; 0.011 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 3,4-dihydro-1(2H)-naphthalenone (271) (1.5 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml). The mixture was stirred at room temperature with the exclusion of atmospheric moisture for 15 min, then treated in one portion with a solution of toluene-4-sulphonyl azide (2.0 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml). The resulting mixture was stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was diluted with water (1.0 ml) and stirred at room temperature for 15 min then rotary evaporated and the residue was treated with water (10.0 ml) and extracted with dichloromethane to give a red gum (2.1 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted 3,4-dihydro-1(2H)-naphthalenone (271) as a red oil (0.36 g; 24%), identical [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] to an authentic sample.

Elution with hexane-ether (4:1) gave a red gum (0.63 g) which was washed with light petroleum to afford 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) as a red solid (0.47 g; 27%), m.p. 58-59° (lit.,[129] 52°). Rotary evaporation of the light petroleum washings gave only an intractable purple oil (0.12 g) which yielded no further identifiable material.

Further elution with hexane-ether (1:1) through ether to methanol gave only intractable gums (total 0.78 g) from which no further identifiable material was obtained.

(b) A stirred suspension of sodium hydride (2.4 g; 0.099 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of 3,4-dihydro-1(2H)-naphthalenone (271) (13.1 g; 0.09 mol) in anhydrous 1,2-dimethoxyethane (100 ml). The mixture was stirred at room temperature with the exclusion of atmospheric moisture for 30 min to ensure salt formation and then treated in one portion with a solution of toluene-4-sulphonyl azide (17.7 g; 0.09 mol) in anhydrous 1,2-dimethoxyethane

(50.0 ml). The resulting mixture was then stirred at room temperature with the exclusion of atmospheric moisture for 17 h.

The mixture was diluted with water (10.0 ml) and stirred at room temperature for 15 min to destroy any unreacted sodium hydride, then rotary evaporated. The residue was treated with water (100 ml) and extracted with dichloromethane to give a purple gum (16.3 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted 3,4-dihydro-1(2H)-naphthalenone (271) as a red oil (4.0 g; 30%), identical [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] to an authentic sample.

Elution with hexane-ether (4:1) gave a red gum (6.3 g) which was washed with light petroleum to afford 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) as a red solid (4.2 g; 27%), m.p. 55-58°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample prepared in (a) before. Rotary evaporated of the light petroleum washings gave an intractable red gum (1.7 g) which yielded no further identifiable material.

Further elution with hexane-ether (1:1) through ether to methanol gave only intractable gums (total 4.2 g) from which no further identifiable material was obtained.

Diazodiphenylmethane (100b)

A stirred solution of the hydrazone (261) (2.0 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (40.0 ml) was treated with activated manganese(IV) oxide

(5.0 g) added in one portion and the resulting suspension was stirred at room temperature with the exclusion of atmospheric moisture for 1.5 h.

The mixture was filtered through celite and the filtrate was rotary evaporated to give diazodiphenylmethane (100b) as a purple solid (1.9 g; 98%), m.p. 32-33° (lit.,[131] 29-30°), which was used without further purification.

The Attempted Reaction of 2-Diazo-3,4-dihydro-1(2H)-naphthalenone (272) with Diazodiphenylmethane (100b)

A stirred solution of 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) (0.34 g; 0.002 mol) in anhydrous 1,2- dimethoxyethane (5.0 ml) was cooled to 10° (ice-bath) and treated dropwise with a solution of diazodiphenylmethane (100b) (0.39 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (5.0 ml). The resulting red solution was stirred at room temperature with the exclusion of atmospheric moisture for 17 h and then heated under reflux for a further 2 h.

The mixture was allowed to cool, then rotary evaporated to give a red oil (0.80 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave only an intractable red gum (0.38 g) from which no identifiable material was obtained.

Elution with hexane-ether (1:1) gave impure unreacted 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) as a brown gum (0.34 g; 100%), identified by comparison [i.r. spectrum and t.l.c. in hexane-ether (1:1) over silica] with an authentic sample.

Further elution with hexane-ether (1:1) through to ether gave negligible material.

Elution with methanol gave only an intractable brown gum (0.030 g) which was not further investigated.

Attempted Reduction Reactions of 2-Diazo-3,4-dihydro-1(2H)-naphthalenone (272)

(a) A stirred solution of 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) (0.34 g; 0.002 mol) in 1,2-dimethoxyethane (10.0 ml) was treated with a solution of sodium borohydride (0.30 g; 0.008 mol) in water (5.0 ml). The mixture became cloudy and gas evolution occurred and was then stirred at room temperature for 3 h.

The mixture was rotary evaporated, and the residue treated with water (10.0 ml). The resulting solution was acidified dropwise with glacial acetic acid and brought to neutral pH by the addition of solid sodium acetate. Extraction with dichloromethane gave only a multicomponent brown gum (0.14 g) which yielded no identifiable material.

(b) A stirred solution of 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) (0.34 g; 0.002 mol) in anhydrous ethanol (30.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.034 g) at room temperature and atmospheric

pressure for 3 h. A second portion of palladium-on-charcoal (0.034 g) was then added and hydrogenation continued at room temperature and atmospheric pressure for a further 5 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a brown gum (0.35 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable multicomponent oils and gums (total 0.30 g) from which no identifiable material was obtained.

(c) A stirred solution of 2-diazo-3,4-dihydro-1(2H)-naphthalenone (272) (0.34 g; 0.002 mol) in tetrahydrofuran (20.0 ml) was treated with a solution of tin(II) chloride dihydrate (2.0 g; 0.009 mol) in 2 M aqueous hydrochloric acid (20.0 ml) and the mixture was then stirred and heated under reflux for 1 h.

The mixture was cooled in an ice-bath, stirred and slowly treated with 30% w/v aqueous sodium hydroxide (16.0 ml). The mixture was then stirred in the melting ice-bath for 15 min, treated with a further portion of 30% w/v aqueous sodium hydroxide (4.0 ml) and rotary evaporated to *ca.* two-thirds of the original volume. Extraction with ether gave a three phase mixture which was filtered to afford an intractable red solid (0.22 g) which yielded no identifiable material.

The aqueous-ether filtrate was separated and the aqueous layer further extracted with ether, and the combined extracts rotary evaporated to give only a multicomponent brown oil (0.22 g) which yielded no identifiable material.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with Chlorosulphonyl Isocyanate

A stirred solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous dichloromethane (15.0 ml) was treated with a solution of chlorosulphonyl isocyanate (0.57 g; 0.004 mol) in anhydrous dichloromethane (5.0 ml) and the resulting brown mixture was stirred at room temperature with the exclusion of atmospheric moisture for 7 h. A further portion of chlorosulphonyl isocyanate (0.57 g; 0.004 mol) in anhydrous dichloromethane (5.0 ml) was then added and the mixture stirred at room temperature with the exclusion of atmospheric moisture for a further 17 h.

The mixture was filtered to give a brown solid (0.36 g) which was washed with water to afford unreacted 1-nitroso-2-naphthol (72) as a brown solid (0.24 g; 35%), m.p. 106-108°, identical (m.p. and i.r. spectrum) to an authentic sample.

Rotary evaporation of the dichlormethane mother liquor gave only an intractable multicomponent brown gum (1.4 g) which yielded no further identifiable material.

The Attempted Reaction of 1-Nitroso-2-naphthol (72) with Toluene-4-sulphonyl Isocyanate

A stirred solution of 1-nitroso-2-naphthol (72) (0.69 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (15.0 ml) was treated with a solution of toluene-4-sulphonyl isocyanate (0.79 g; 0.004 mol) in anhydrous 1,2-

dimethoxyethane (5.0 ml). The resulting brown solution was then stirred at room temperature with the exclusion of atmospheric moisture for 3 h.

The mixture was rotary evaporated to give a brown gum (1.4 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) gave unreacted 1-nitroso-2-naphthol (72) as a brown solid (0.46 g; 67%), m.p. 106-108°, identical (m.p. and i.r. spectrum) to an authentic sample.

Further elution with hexane-ether (4:1) gave a brown solid (0.55 g) whose t.l.c. in hexane-ether (1:1) over silica showed it to contain two components, one of which corresponded to 1-nitroso-2-naphthol (72) and the other to toluene-4-sulphonamide.

Elution with hexane-ether (1:1) through to ether gave negligible material.

Final elution with methanol gave only an intractable brown semi-solid (0.12 g) which yielded no further identifiable material.

1-(N-Benzylcarbamoyloxy)imino-2-naphthalenone (278b)

A stirred solution of 1-nitroso-2-naphthol (72) (3.5 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (75.0 ml) was treated with a solution of benzyl isocyanate (2.7 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) and the resulting brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 30 min.

The mixture was then rotary evaporated to give a brown gum (6.4 g) which was washed with ether to afford 1-(*N*-benzylcarbanoyloxy)imino-2-

naphthalenone (278b) as a brown solid (5.6 g; 92%), m.p. 98-100° (from hexane-ethyl acetate), υ_{max} 3305(NH), 1740 and 1665(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 8.82(1H, t, J5Hz, NH), 7.54-7.25(10H, m, ArH), 6.34(1H, d, J10Hz, ArH) and 4.55(2H, d, J6Hz, CH_2).

Rotary evaporation of the ether mother liquor gave only an intractable brown gum (0.60 g) which yielded no further identifiable material.

The Reduction of 1-(*N*-Benzylcarbamoyloxy)imino-2-naphthalenone (278b)

A stirred solution of the oxime (278b) (0.61 g; 0.002 mol) in 1,2-dimethoxyethane (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.061 g) at room temperature and atmospheric pressure for 3 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a dark brown solid (0.61 g) which was washed with hexane and ether to afford 1-amino-2-naphthol (139) as a brown solid (0.31 g; 98%), m.p. 184-187°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the combined hexane-ether washings gave only a multicomponent brown gum (0.23 g) which yielded no further identifiable material.

1-(N-Methylcarbamoyloxy)imino-2-naphthalenone (282b)

A stirred solution of 1-nitroso-2-naphthol (72) (3.5 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (75.0 ml) was treated with a solution of methyl

isocyanate (2.3 g; 0.04 mol) in anhydrous 1,2-dimethoxyethane (25.0 ml) and the resulting brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 24 h.

The mixture was filtered to give a yellow solid, which was combined with a second crop, obtained by rotary evaporation of the filtrate and washing the residue with ether to afford 1-(*N*-methylcarbamoyloxy)imino-2-naphthalenone (282b) as yellow irregular crystals (4.5 g; 98%), m.p. 121-124° (from 1,2-dimethoxyethane-ethanol), υ_{max} 3295(NH) and 1753 and 1666(C=O) cm^{-1}, $\delta_H[(CD_3)_2SO]$ 8.66(1H, d, J7Hz, ArH), 7.95(1H, q, J5Hz, NH), 7.75-7.52(4H, m, ArH), 6.39(1H, d, J10Hz, ArH) and 2.76(3H, d, J5Hz, CH_3).

Rotary evaporation of the ether washings gave only an intractable multicomponent brown gum (0.70 g) which yielded no further identifiable material.

Reduction Reactions of 1-(*N*-methylcarbamoyloxy)imino-2-naphthalenone (282b)

(a) A stirred solution of 1-(*N*-methylcarbamoyloxy)imino-2-naphthalenone (282b) (0.46 g; 0.002 mol) in 1,2-dimethoxyethane (20.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.046 g) at room temperature and atmospheric pressure for 1 h.

The mixture was then filtered through celite and the filtrate rotary evaporated to give a brown gum (0.46 g) which was washed with hexane then ether to afford 1-amino-2-naphthol (139) as a brown solid (0.30 g; 94%), m.p.

175-180°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the combined hexane-ether washings gave only a multicomponent brown gum (0.11 g) which yielded no further identifiable material.

(b) A stirred solution of 1-(*N*-methylcarbamoyloxy)imino-2-naphthalenone (282b) (0.92 g; 0.004 mol) in dimethylformamide (10.0 ml) was treated with a solution of sodium borohydride (0.61 g; 0.016 mol) in water (5.0 ml) and the mixture was stirred at room temperature for 3 h.

The mixture was rotary evaporated and the residue was treated with water (20.0 ml) and extracted with dichloromethane. The resulting three phase mixture was filtered to give a brown solid (1.1 g) which was treated with water (10.0 ml) and the solution neutralised with 2 M aqueous hydrochloric acid and solid sodium acetate. Extraction with dichloromethane gave 1-amino-2-naphthol (139) as a brown solid (0.48 g; 75%), m.p. 184-188°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The aqueous-dichloromethane filtrate was separated, the aqueous layer further extracted with dichloromethane, and the combined extracts rotary evaporated to give only a multicomponent brown gum (0.29 g) which yielded no further identifiable material.

Neutralisation of the aqueous mother liquor with 2 M aqueous hydrochloric acid then solid sodium acetate gave no further material.

1-(*N*-Phenylcarbamoyloxy)imino-2-naphthalenone (282a)

A stirred solution of 1-nitroso-2-naphthol (72) (3.5 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (80.0 ml) was treated with a solution of phenyl isocyanate (2.4 g; 0.02 mol) in anhydrous 1,2-dimethoxyethane (20.0 ml) and the resulting brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 1.5 h.

The mixture was filtered to give a yellow solid, which was combined with a second crop, obtained by rotary evaporation of the filtrate and washing the residue with ether to afford 1-(*N*-phenylcarbamoyloxy)imino-2-naphthalenone (282a) (5.5 g; 94%) which formed yellow needles, m.p. 124-127° (from hexane-ethyl acetate), υ_{max} 3261(NH) and 1731 and 1666(C=O) cm^{-1}, $\delta_H(CDCl_3)$ 13.00(1H, s, NH) (exch.) and 7.72-7.04(11H, m, ArH).

Rotary evaporation of the ether washings gave only an intractable brown gum (0.46 g) which yielded no further identifiable material.

The Attempted Acid Catalysed Hydrolysis of 1-(*N*-Phenylcarbamoyloxy)imino-2-naphthalenone (282a)

A stirred solution of the oxime (282a) (0.58 g; 0.002 mol) in ethanol (10.0 ml) was treated with 2 M aqueous hydrochloric acid (5.0 ml) and the resulting orange solution was stirred and heated under reflux for 1 h.

The mixture was allowed to cool and rotary evaporated to give a brown residue which was treated with water (10.0 ml) and the solution extracted with dichloromethane to give a brown gum (0.66 g) which was flash-

chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) through ethyl acetate to methanol gave only a series of intractable multicomponent gums and solids (total 0.65 g) which yielded no identifiable material.

The Base Catalysed Hydrolysis of 1-(*N*-Phenylcarbamoyloxy)imino-2-naphthalenone (282a)

The oxime (282a) (0.58 g; 0.002 mol) was treated with 2 M aqueous sodium hydroxide (5.0 ml) and the resulting green suspension was stirred at room temperature for 30 min.

The mixture was filtered to give a green solid (0.36 g) which was acidified with 2 M aqueous hydrochloric acid to give 1-nitroso-2-naphthol (72) as a brown solid (0.30 g; 87%), m.p. 106-108°, identical (m.p. and i.r. spectrum) to an authentic sample.

Neutralisation of the aqueous mother liquor with 2 M aqueous hydrochloric acid then solid sodium acetate and extraction with dichloromethane gave no further identifiable material.

The Attempted Reaction of 1-(*N*-Phenylcarbamoyloxy)imino-2-naphthalenone (282a) with Acetic Anhydride

The oxime (282a) (0.29 g; 0.001 mol) was treated with acetic anhydride (2.0 ml) and the mixture gently warmed (water-bath). A further portion of acetic anhydride (3.0 ml) was added and the resulting brown melt was stirred

and heated at 90° for 10 min. The mixture was then allowed to stand at room temperature for 10 min to afford a brown gum which was washed with ether to afford only an intractable multicomponent brown solid (0.15 g) which yielded no identifiable material.

Rotary evaporation of the ether washings gave only an intractable multicomponent brown gum (0.20 g) which yielded no identifiable material.

Reduction Reactions of 1-(*N*-Phenylcarbamoyloxy)imino-2-naphthalenone (282a)

(a) A stirred solution of the oxime (282a) (0.58 g; 0.002 mol) in 1,2-dimethoxyethane (10.0 ml) was treated with a solution of sodium borohydride (0.30 g; 0.008 mol) in water (5.0 ml) and the brown solution was stirred at room temperature for 3 h.

The mixture was rotary evaporated and the residue was treated with water (10.0 ml) to give a brown solid (0.42 g) which was washed with hexane to afford 1-amino-2-naphthol (139) as a brown solid (0.31 g; 97%), m.p. 184-188° identified by (m.p. and i.r. spectrum) with an authentic sample.

(b) A stirred solution of the oxime (282a) (0.58 g; 0.002 mol) in 70% v/v aqueous ethanol (10.0 ml) was treated with sodium dithionite (0.58 g) added in one portion and the resulting green mixture was stirred at room temperature in a stoppered flask for 30 min.

The mixture was rotary evaporated to give a brown residue. This was

washed with water (2.5 ml) to give a grey solid (0.40 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) gave only an intractable brown solid (0.17 g) which yielded no identifiable material.

Elution with hexane-ether (1:1) gave 1-amino-2-naphthol (139) as a brown solid (0.070 g; 22%), m.p. 180-184°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Elution with hexane-ether (1:1) through ether to methanol gave no further material.

Neutralisation of the aqueous mother liquor with 2 M aqueous sodium hydroxide and glacial acetic acid and extraction with dichloromethane gave no further material.

1-Amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a)

(a) A stirred solution of the oxime (282a) (0.58 g; 0.002 mol) in ethyl acetate (40.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.058 g) at room temperature and atmospheric pressure for 1.5 h.

The mixture was warmed and hot filtered through celite and the filtrate rotary evaporated to give a brown solid (0.55 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through to ether gave only a series of intractable multicomponent solids (total 0.20 g) which yielded no identifiable material.

Further elution with ether followed by methanol gave 1-amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a), (0.34 g; 61%) which formed colourless needles, m.p. 203-205° (from 1,2-dimethoxyethane-ethanol), υ_{max} 3320-3240 br(NH) and 1611(C=O) cm^{-1}.

(b) Repetition of the reaction described in (a) before but in 1,2-dimethoxyethane gave a mixture which was filtered through celite and the filtrate rotary evaporated to give a brown solid (0.56 g) which was flash-chromatographed over silica.

Elution with hexane-ether (4:1) through to hexane-ether (1:9) gave only a series of intractable multicomponent solids (total 0.13 g) from which no identifiable material was obtained.

Elution with ether followed by methanol gave 1-amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a) as a brown solid (0.36 g; 65%), m.p. 203-205°, identical (m.p. and i.r. spectrum) to a sample prepared in (a) before.

(c) A stirred solution of hydrazobenzene (0.44 g; 0.0024 mol) in anhydrous benzene (5.0 ml) was treated with a solution of the oxime (282a) (0.58 g; 0.002 mol) in anhydrous benzene (15.0 ml) and the resulting brown solution was stirred at room temperature in a stoppered flask for 17 h.

The mixture was then filtered to give 1-amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a) as a light brown solid (0.26 g; 47%), m.p. 202-203°, identified by comparison (m.p. and i.r. spectrum) with an

authentic sample prepared in (a) before.

Rotary evaporation of the benzene mother liquor gave a brown solid (0.83 g) which was washed with warm hexane then ether to leave an intractable multicomponent brown solid (0.11 g) which yielded no identifiable material.

Rotary evaporation of the hexane washings gave azobenzene as a brown solid (0.44 g; 100%), m.p. 68-69°, identical (m.p. and i.r. spectrum) to an authentic sample.

(d) A stirred solution of the oxime (282a) (0.58 g; 0.002 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) was treated with a solution of triphenylphosphine (1.0 g; 0.004 mol) in anhydrous 1,2-dimethoxyethane (10.0 ml) and the resulting brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 18 h.

The mixture was rotary evaporated to give a brown gum (1.7 g) which was flash-chromatographed over silica.

Elution with hexane-ether (19:1) gave unreacted triphenylphosphine as a brown solid (0.27 g; 27%), m.p. 79-81°, identical (m.p. and i.r. spectrum) to an authentic sample.

Elution with hexane-ether (4:1) gave an intractable multicomponent brown solid (0.15 g) which yielded no further identifiable material.

Further elution with hexane-ether (4:1) through to hexane-ether (1:9) gave no further material.

Elution with ether gave 1-amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a) as a brown solid (0.18 g; 32%), m.p. 200-203°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared in (a) before.

Elution with methanol gave a brown solid (1.1 g) which was washed with ether to give triphenylphosphine oxide as a light brown solid (0.80 g; 72%), m.p. 140-146°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

The Attempted Reaction of 1-Amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a) with Acetic Anhydride

A stirred solution of the amine (284a) (0.56 g; 0.002 mol) in acetic anhydride (10.0 ml) was heated under reflux for 1 h.

The mixture was allowed to cool, then rotary evaporated to give a purple gum (0.85 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) through ethyl acetate to methanol gave only a series of intractable multicomponent oils, gums and solids (total 0.73 g) which yielded no identifiable material.

The Attempted Acid Catalysed Hydrolysis of 1-Amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a)

A stirred solution of the amine (284a) (0.56 g; 0.002 mol) in ethanol (20.0 ml) was treated with 2 M aqueous hydrochloric acid (5.0 ml) and the resulting brown solution was stirred and heated under reflux for 1 h.

The mixture was allowed to cool, then rotary evaporated to give a violet residue which was washed with water (10.0 ml) to give the unreacted amine (284a) as a brown solid (0.56 g; 100%), m.p. 195-200°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Attempted Base Catalysed Hydrolysis Reactions of 1-Amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a)

(a) The amine (284a) (0.28 g; 0.001 mol) was treated with 2 M aqueous sodium hydroxide (2.5 ml) and the resulting brown suspension was stirred at room temperature for 30 min.

The mixture was filtered to remove some insoluble solid and the aqueous filtrate was acidified with 2 M aqueous hydrochloric acid to precipitate a brown solid (0.21 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (1:1) gave the unreacted amine (284a) as a brown solid (0.10 g; 36%), m.p. 197-200°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Further elution with hexane-ethyl acetate (1:1) through ethyl acetate to methanol gave only a series of intractable gums and solids (total 0.077 g) which were not further investigated.

Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with dichloromethane gave no further material.

(b) Repetition of the reaction described in (a) before but with heating under

reflux for 10 min gave a mixture which was allowed to cool then extracted with ether. The resulting three phase mixture was filtered to give only a multicomponent brown solid (0.081 g) which was not further investigated.

The aqueous-ether filtrate was separated and the aqueous layer further extracted with ether, and the combined extracts rotary evaporated to give only an intractable multicomponent brown gum (0.029 g) which yielded no identifiable material.

Neutralisation of the aqueous layer with 2 M aqueous hydrochloric acid and solid sodium acetate and extraction with ether gave only a multicomponent brown solid (0.089 g) which yielded no identifiable material.

The Attempted Reaction of 1-Amino-2-(*N*-phenylcarbamoyl)oxynaphthalene (284a) with Sodium Borohydride

A stirred solution of the amine (284a) (0.56 g; 0.002 mol) in 1,2-dimethoxyethane (10.0 ml) was treated with a solution of sodium borohydride (0.30 g; 0.008 mol) in water (5.0 ml) and the resulting brown mixture was stirred at room temperature for 3 h.

The mixture was rotary evaporated and the residue treated with water (10.0 ml) and extracted with dichloromethane to give the unreacted amine (284a) as a brown solid (0.52 g; 93%), m.p. 196-200°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

2-Phenyl-1,2-dihydro-3H-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a)

A stirred solution of the amine (284a) (2.8 g; 0.01 mol) in anhydrous 1,2-dimethoxyethane (50.0 ml) was treated with activated manganese(IV) oxide (5.0 g) and the suspension was stirred at room temperature with the exclusion of atmospheric moisture for 7 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a brown gum (2.9 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (9:1) gave only an intractable brown solid (0.090 g) which yielded no identifiable material.

Elution with hexane-ethyl acetate (3:2) gave a brown solid (2.8 g) which was crystallised to yield 2-phenyl-1,2-dihydro-3H-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a) as a brown solid (1.8 g; 65%), m.p. 162-165° (from toluene), υ_{max} 3289(NH) and 1720(C=O) cm^{-1}.

Rotary evaporation of the toluene mother liquor gave a multicomponent brown gum (0.61 g) which yielded no further identifiable material.

Further elution with hexane-ethyl acetate (3:2) through ethyl acetate to methanol gave no further material.

The Attempted Reaction of 2-Phenyl-1,2-dihydro-3*H*-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a) with Acetic Anhydride

A stirred solution of 2-phenyl-1,2-dihydro-3H-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a) (0.28 g; 0.001 mol) in acetic anhydride (5.0 ml) was

heated under reflux for 1 h.

The mixture was allowed to cool, then rotary evaporated to give a brown gum (0.29 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (3:2) through ethyl acetate to methanol gave only a series of intractable multicomponent gums and solids (total 0.23 g) which yielded no identifiable material.

Attempted Hydrolysis Reactions of 2-Phenyl-1,2-dihydro-3H-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a)

(a) A stirred solution of 2-phenyl-1,2-dihydro-3H-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a) (0.28 g; 0.001 mol) in ethanol (5.0 ml) was treated with 2 M aqueous hydrochloric acid (2.5 ml) and the resulting brown solution was stirred and heated under reflux for 1 h.

The mixture was allowed to cool, then rotary evaporated and the residue treated with water (5.0 ml) and extracted with dichloromethane to give a brown gum (0.23 g). This was washed with ether to afford unreacted 2-phenyl-1,2-dihydro-3H-naphth[1,2-e]-1,3,4-oxadiazin-3-one (285a) as a brown solid (0.14 g; 50%), m.p. 141-151°, identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Rotary evaporation of the ether washings gave only a multicomponent brown gum (0.070 g) which yielded no identifiable material.

Neutralisation of the aqueous mother liquor with 2 M aqueous sodium hydroxide then glacial acetic acid and extraction with dichloromethane gave no

further material.

(b) Repetition of the reaction described in (a) before but using 2 M aqueous sodium hydroxide gave a mixture which was allowed to cool then rotary evaporated. The residue was then treated with water (5.0 ml) and filtered to give only an intractable multicomponent brown solid (0.049 g) which yielded no identifiable material.

Neutralisation of the aqueous mother liquor with 2 M aqueous hydrochloric acid and solid sodium acetate and extraction with dichloromethane gave a brown solid (0.23 g) which was flash-chromatographed over silica.

Elution with hexane-ether (9:1) through ether to methanol gave only a series of intractable multicomponent solids (total 0.20 g) which yielded no identifiable material.

2-(*N*-Phenylcarbamoyloxy)imino-1-naphthalenone (289)

A stirred solution of 2-nitroso-1-naphthol (205) (1.7 g; 0.01 mol) in anhydrous dimethylformamide (20.0 ml) was treated with a solution of phenyl isocyanate (1.2 g; 0.01 mol) in anhydrous dimethylformamide (5.0 ml) and the resulting brown solution was stirred at room temperature with the exclusion of atmospheric moisture for 1.5 h.

The mixture was rotary evaporated to give a brown solid (2.9 g) which was washed with ether to afford 2-(*N*-phenylcarbamoyloxy)imino-1-naphthalenone (289) as an orange solid (2.8 g; 96%), m.p. 144-146° (from 1,2-

dimethoxyethane-ethanol), υ_{max} 3310(NH) and 1771 and 1667(C=O) cm^{-1}, $\delta_H[(CD_3)_2SO]$ 8.04-6.45(12H, m, ArH and NH).

Rotary evaporation of the ether washings gave no further identifiable material.

The Reduction of 2-(*N*-Phenylcarabamoyloxy)imino-1-naphthalenone (289)

A stirred solution of 2-(*N*-phenylcarbamoyloxy)imino-1-naphthalenone (289) (1.2 g; 0.004 mol) in 1,2-dimethoxyethane (40.0 ml) was hydrogenated over 10% palladium-on-charcoal (0.12 g) at room temperature and atmospheric pressure for 1 h.

The mixture was filtered through celite and the filtrate rotary evaporated to give a brown gum (1.1 g) which was flash-chromatographed over silica.

Elution with hexane-ethyl acetate (19:1) gave 2-amino-1-naphthol (214) as a brown solid (0.29 g; 46%), m.p. 184-187°, identified by comparison (m.p. and i.r. spectrum) with a sample prepared before.

Elution with hexane-ethyl acetate (9:1) through ethyl acetate to methanol gave only a series of multicomponent gums (total 0.63 g) which yielded no identifiable material.

Table 8: Elemental Analysis and Mass Spectroscopic Data

Compound	Found				Required			
	C%	H%	N%	M^+, $(M+H)^{+\ a}$	C%	H%	N%	M, $(M+H)^a$
(237) ($C_{24}H_{19}NO$)	85.3	5.5	4.1	337	85.5	5.6	4.1	337
(243) ($C_{20}H_{17}NO$)	83.7	5.9	4.8	(288)	83.6	5.9	4.9	287
(250) ($C_{18}H_{13}NO_3$)	74.2	4.5	4.9	(292)	74.2	4.5	4.8	291
(253) ($C_{14}H_{11}NO_3$)	70.0	4.5	5.8	(242)	69.7	4.6	5.8	241
(278b) ($C_{18}H_{14}N_2O_3$)				(307.10764)				(307.10827)
(282a) ($C_{17}H_{12}N_2O_3$)	69.8	4.4	9.7	(293)	69.9	4.1	9.6	292
(282b) ($C_{12}H_{10}N_2O_3$)	62.9	4.5	12.2	(231)	62.6	4.3	12.2	230
(284a) ($C_{17}H_{14}N_2O_2$)	73.0	5.1	10.2	278	73.4	5.0	10.1	278
(285a) ($C_{17}H_{12}N_2O_2$)				(277.09770)				(277.09770)
(289) ($C_{17}H_{12}N_2O_3$)	69.6	4.3	9.4	(293)	69.9	4.1	9.6	292

a; Molecular ions detected by Electron Impact Mass Spectroscopy or for values in parentheses, molecular ions detected by Fast Atom Bombardment Mass Spectroscopy.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. M. Fritsche, *Comp.Rend.*, 1867, **69**, 1035.
2. "Photochromism", ed. G.H. Brown, Vol. 3 of "Techniques of Chemistry", Wiley-Interscience, New York, 1971.
3. E. ter Meer, *Ann.Chem.*, 1876, **181**, 1.
4. T.L. Phipson, *Chem.News*, 1881, **43**, 283.
5. W. Marckwald, *Z.Phys.Chem.*, 1899, **30**, 140.
6. Y. Hirshberg, *Compt.Rend.*, 1950, **231**, 903.
7. W. Wislicenus, *Ann.Chem.*, 1893, **277**, 366.
8. H. Biltz, *Ann.Chem.*, 1899, **305**, 170; H. Biltz, *Z.Phys.Chem.*, 1899, **30**, 527; H. Biltz and A. Wienands, *Ann.Chem., 1899,* **308**, 1.
9. L. Chalkley, *Chem.Rev.*, 1929, **6**, 217.
10. L. Harris, J. Kaminsky and R.G. Simard, *J.Am.Chem.Soc.*, 1935, **57**, 1151.
11. C.V. Gheorghiu and V. Matei, *Bull.Soc.Chim.,* 1939, **6**, 1324; C.V. Gheorghiu and B. Arrventieu, *Bull.Soc.Chim.*, 1930, **47**, 195; C.V. Gheorghiu, *Bull.Soc.Chim.*, 1934, **1**, 97.
12. G.H. Brown and W.G. Shaw, *Rev.Pure Appl.Chem.,* 1961, **11**, 2.
13. W. Luck and H. Sand, *Angew.Chem., Int.Ed.Engl.,* 1964, **3**, 570.
14. R. Exelby and R. Grinter, *Chem.Rev.*, 1965, **65**, 247.
15. E. Fischer, *Chem.Unserer Zeit*, 1975, **9**, 85.
16. H. Duerr, *Prax.Naturwiss.Chem.*, 1991, **40**, 22.
17. H. Morrison and R.M. Deibel, *Photochem.Photobiol.*, 1986, **43**, 663.

18. R.R. Birge, *Ann.Rev.Biophys.Bioeng.*, 1981, **10**, 315.

19. D. Gegiou, K.A. Muszkat and E. Fischer, *J.Am.Chem.Soc.,* 1968, **90**, 3907.

20. F.B. Mallory, C.W. Mallory and S.E. Sen Loeb, *Tetrahedron Lett.*, 1985, **26**, 3773.

21. W.R. Brode, E.G. Pearson and G.M. Wyman, *J.Am.Chem.Soc.*, 1954, **76**, 1034.

22. G. Wyman, *Chem.Rev.*, 1955, **55**, 625.

23. H. Rau, *Angew.Chem., Int.Ed.Engl.*, 1973, **12**, 224.

24. S. Shinkai, T. Okawa, Y. Kusano, O. Manabe, K. Kikukawa, T. Goto and T. Matsuda, *J.Am.Chem.Soc.*, 1982, **104**, 1960.

25. D.R. Arnold and L.A. Karnischky, *J.Am.Chem.Soc.,* 1970, **92**, 1404.

26. E.F. Ullman and W.A. Henderson, Jr., *J.Am.Chem.Soc.,* 1966, **88**, 4942; E.F. Ullman and W.A. Henderson, Jr., *J.Am.Chem.Soc.*, 1967, **89**, 4390.

27. E.F. Ullman and J.E. Milks, *J.Am.Chem.Soc.,* 1962, **84**, 1315.

28. A.M. Trozzollo, W. Yager, G. Griffin, H. Kristinsson and I. Sarker, *J.Am.Chem.Soc.*, 1967, **89**, 3357; T. Do Minh and A.M. Trozzolo, *J.Am.Chem.Soc.*, 1972, **94**, 4046.

29. A.M. Trozzolo, T.M. Leslie, A.S. Sarpotdar, R.D. Small, G.J. Ferraudi, T. Do Minh and R.L. Hartless, *Pure Appl.Chem.*, 1979, **51**, 1261.

30. E. Fischer and Y. Hirshberg, *J.Chem.Soc.*, 1952, 4522.

31. Y. Hirshberg and E. Fischer, *J.Chem.Soc.*, 1954, 297; Y. Hirshberg and E. Fischer, *J.Chem.Soc.,* 1954, 3129.

32. A. Mustafa, *Chem.Rev.*, 1948, **43**, 509.

33. J.H. Day, *Chem.Rev.*, 1963, **63**, 65.

34. L.D. Weis, T.R. Evans and P.H. Leermaker, *J.Am.Chem.Soc.*, 1968, **90**, 6115.

35. J. Peyches, *Chim.Ind.*, 1970, **103**, 2611.

36. E. Berman, R.E. Fox and F.D. Thomson, *J.Am.Chem.Soc.*, 1959, **81**, 5605.

37. V.A. Krongauz and A.A. Parshutkin, *Photochem.Photobiol.*, 1972, **15**, 503.

38. P. de Mayo, A. Safarzadeh-Amiri and S. King Wong, *Can.J.Chem.*, 1984, **62**, 1001.

39. K. Kimura, T. Yanashita and M. Yokoyama, *J.Chem.Soc., Perkin Trans. 2*, 1992, 613.

40. A. Samat, R. Gugliemetti and J. Metzger, *Helv.Chim.Acta*, 1972, **55**, 1782.

41. K.H. Knauer and R. Gleiter, *Angew.Chem., Int.Ed.Engl.*, 1977, **16**, 113.

42. M. Gehrtz, C. Bräuchle and J. Voitländer, *J.Am.Chem.Soc.*, 1982, **104**, 2094.

43. P.H. Vandewyer, J. Hoefnagels and G. Smets, *Tetrahedron*, 1969, **25**, 3251.

44. J. Daub, T. Knöchel and A. Mannschreck, *Angew.Chem., Int.Ed.Engl.*, 1984, **23**, 960.

45. A. Castellan, J.M. Lacoste and H. Bouas-Laurent, *J.Chem.Soc., Perkin*

Trans.2, 1979, 411.

46. A. Castellan, J.P. Desvergne and H. Bouas-Laurent, *Nouv.J.Chem.3*, 1979, 231.

47. H.D. Becker, K. Sandross and K. Anderson, *Chem.Phys.Lett.*, 1981, **77**, 246.

48. M.D. Cohen, Y. Hirshberg and G.M.J. Schmidt, *J.Chem.Soc.*, 1964, 2051.

49. M.D. Cohen and S. Flavian, *J.Chem.Soc.B*, 1967, 334.

50. V. de Gaouck and R.J.W. Le Févre, *J.Chem.Soc.*, 1939, 1457.

51. E. Hadjoudis and E. Hayon, *J.Phys.Chem.*, 1970, **74**, 3184.

52. J.W. Lewis and J.W. Sandorfy, *Can.J.Chem.*, 1982, **60**, 1738.

53. R.S. Becker, C. Lenoble and A. Zein, *J.Phys.Chem.*, 1987, **91**, 3509, R.S. Becker, C. Lenoble and A. Zein, *J.Phys.Chem.*, 1987, **91**, 3517.

54. T. Hayashi and K. Maeda, *Bull.Chem.Soc.Jap.*, 1963, **36**, 1052.

55. S.M. Blinder, M.L. Peller, N.W. Lord, L.C. Aamodt and J. Iuanchukov, *J.Chem.Phys.*, 1962, **36**, 540.

56. J. Metzger in "Non-Silver Photogr. Processes", Proc.Symp., Ed. R.J. Cox, Academic, London, England, 1975 (*Chem.Abstr.*, 1978, **88**, 14284); J.J. Robillard in "Non-Silver Photogr. Processes", Proc.Symp., Ed. R.J. Cox, Academic, London, England, 1975 (*Chem.Abstr.*, 1978, **88**, 14283); M. Tanaka, A. Miyazaki and T. Kitao, Jap.Pat., 03,137,634 (*Chem.Abstr.*, 1992, **116**, 72370); A.S. Dvornikov, J. Malkin and P.M. Rentzepis, Proc. SPIE-Int.Soc.Opt.Eng. 1993, 1852, 243 (*Chem.Abstr.*,

1993, **119**, 149320); Y. Fujimori, N. Kitamura, Jap.Pat., 05,42,766 (*Chem.Abstr.*, 1993, **119**, 82994).

57. H.G. Heller and J.R. Langan, *J.Chem.Soc., Perkin Trans.2*, 1981, 341.

58. R.J. Hart and H.G. Heller, *J.Chem.Soc., Perkin Trans.1,* 1972, 1321; H.G. Heller and M. Szewczyk, *J.Chem.Soc., Perkin Trans. 1*, 1974, 1487.

59. P.J. Darcy, R.J. Hart and H.G. Heller, *J.Chem.Soc., Perkin Trans.1*, 1978, 571; C. Oscar, H.G. Heller and S. Patharakorn, *J.Chem.Soc., Perkin Trans. 1*, 1986, 1599; P.J. Darcy, H.G. Heller, S. Patharakorn, R.D. Piggott and J. Whittal, *J.Chem.Soc., Perkin Trans.1*, 1986, 315.

60. P.J. Darcy, H.G. Heller, P.J. Strydom and J. Whittal, *J.Chem.Soc., Perkin Trans.1*, 1981, 202.

61. A.P. Glaze, S.A. Harris, H.G. Heller, W. Johncock, S.N. Oliver, P.J. Strydom and J. Whittal, *J.Chem.Soc., Perkin Trans.1*, 1985, 957; C. Lenoble and R.S. Becker, *J.Phys.Chem.,* 1986, **90**, 2651.

62. J. Daub, C. Fischer, S. Gierisch and J. Sixt, *Mol.Cryst.Liq.Cryst.Sci.Technol.*, Sect. A, 1992, **217**, 177.

63. S. Nespurek, *Int.J.Electron*, 1992, **73**, 1059.

64. I. Cabrera, V. Krongauz and H. Ringsdorf, *Angew.Chem., Int.Ed.Engl.*, 1987, **26**, 1178.

65. G. Attard and G. Williams, *Nature*, 1987, **326**, 544.

66. I. Cabrera, A. Dittrich and H. Ringsdorf, *Angew.Chem., Int.Ed.Engl.*, 1991, **30**, 76.

67. G. Gliemeroth and K.H. Mader, *Angew.Chem., Int.Ed.Engl.*, 1970, **9**, 434.

68. S. Seikosha Co., Jap.Pat. 59,78,272 (*Chem.Abstr.*, 1984, **101**, 173188).

69. R.J. Hovey, C.H. Fuchsman, N.Y.C. Chu and P.G. Piusz, Ger.Pat.2,936,255 (*Chem.Abstr.*, 1980, **93**, 73788).

70. M. Melzig, G. Martinuzzi and E. Effer, Ger.Pat. 3,516,568 (*Chem.Abstr.*, 1986, **104**, 188338).

71. A. Harrah, Report 1976, SAND-75-0402,29. Avail.NTIS.From Nucl.Sci.Abstr. 1976, 33(12), Abstr. No. 29059 (*Chem.Abstr.*, 1976, **85**, 169657).

72. N.Y.C. Chu, *Can.J.Chem.*, 1983, **61**, 300.

73. S. Kawanchi, H. Yoshida, N. Yamashina, M. Ohiva, S. Saeda and M. Irie, *Bull.Chem.Soc.Jpn.*, 1990, **63**, 267.

74. D. Eloy, P. Escaffre, R. Gautron, E. Pottier, P. Tardieu and R. Gugliemetti, *Bull.Soc.Chim.Belg.*, 1991, **100**, 315.

75. U.W. Grummt, M. Reichenbacher and R. Paetzold, *Tetrahedron Lett.*, 1981, **22**, 3945.

76. S. Aramaki and G.H. Atkinson, *Chem.Phys.Lett.*, 1990, **170**, 181.

77. E. Pottier, A. Samat, R. Guglielmetti, D. Siri and G. Pepe, *Bull.Soc.Chim.Belg.*, 1992, **101**, 207.

78. C. Bohne, M.G. Fan, Z.J. Li, J. Lusztyk and J.C. Scaiano, *J.Chem.Soc., Chem.Commun.*, 1990, 571.

79. F. Wilkinson, J. Hobley and M. Naftaly, *J.Chem.Soc., Faradon Trans.*,

1992, **88**, 1511.

80 D. Eloy, P. Escaffre, R. Gautron and P. Jardon, *Bull.Soc.Chim.Belg.*, 1992, **101**, 779.

81. G. Arnold and G. Paal, *Tetrahedron*, 1971, **27**, 1699.

82. Fuji Photo Film Co., Brit.Pat.1,186,987 (*Chem.Abstr.*, 1970, **73**, 16317).

83. M. Rickwood, Ger Offen. DE 31739,415 (*Chem.Abstr.*, 1988, **109**, 129032); K. Iwamoto, T. Tanaka, S. Imura, S. Okazaki and S. Tanaka, Eur.Pat.Appl.Ep. 449,669 (*Chem.Abstr.*, 1992, **116**, 21065); Y. Nishira, Jap.Pat. 04,208,919 (*Chem.Abstr.*, 1992, **117**, 220162).

84. N.Y.C. Chu, Eur.Pat.Appl. E.P. 134,633 (*Chem.Abstr.*, 1985, **102**, 212747); P.L. Kwiatkowski and W.S. Kwak, U.S. Pat. 4,931,219 (*Chem.Abstr.*, 1990, **113**, 201444).

85. M. Rickwood and J.D. Hepworth, Eur.Pat.Appl. E.P. 245,020 (*Chem.Abstr.*, 1988, **109**, 14836).

86. M. Reichenbacher, U.W. Grummt, R. Paetzold and J. Epperlein, Ger.Pat. DD 156,372 (*Chem.Abstr.*, 1983, **98**, 135279).

87. M.A. Weaver, D.J. Wallace and J.M. Straley, U.S.Pat. 3,453,270 (*Chem.Abstr.*)., 1969, **71**, 92661.

88. S.P. Gupta, S.S. Chatterjee, P.C. Jain and N. Anand, *Synthesis*, 1974, 660.

89. P. Battistoni, P. Bruni and G. Fava, *Synthesis*, 1979, 220.

90. P. Battistoni, P. Bruni, G. Fava and G. Tosi,, *J.Heterocycl.Chem.*, 1983, **20**, 451.

91. P. Battistoni, P. Bruni and G. Fava, *Tetrahedron*, 1979, **35**, 1771.

92. H. Böhme amd A. Ingendoh, *Annalen.*, 1978, 1928.

93. H.O.L. Fischer, G. Dangschat and H. Stettiner, *Chem.Ber.*, 1932, **65**, 1032.

94. K. Wachi and A. Terada, *Chem.Pharm.Bull.*, 1980, **28**, 465.

95. S. Leistner, W. Sachse, J. Preussler and G. Wagner, *Pharmazie*, 1977, **32**, 325 (*Chem.Abstr.*, 1977, **87**, 201436).

96. B. Kokel, G. Menichi and M. Hubert-Habart, *Tetrahedron Lett.*, 1984, **25**, 3837.

97. Y. Tamura, T. Kawasaki, M. Tanio and Y. Kita, *Chem. and Ind.*, 1978, 806.

98. G. Wagner, J. Kamecki and S. Leistner, *Pharmazie*, 1976, **31**, 704 (*Chem.Abstr.*, 1977, **86**, 139964).

99. B.S. Joshi, R. Srinivason, R.V. Talavdekar and K. Venkataraman, *Tetrahedron*, 1960, **11**, 133.

100 W. Ried and E. Kahr, *Chem.Ber.*, 1970, **103**, 331.

101. R. Huisgen and R. Fleischmann, *Annalen.*, 1959, **623**, 47.

102. R.A. Kumar, C.K. Kokate, M.S. Rao and T.V.P. Rao, *Org.Prep.Proced.Int.*, 1989, **21**, 380 (*Chem.Abstr.*, 1990, **112**, 216884).

103. F. Chioccara, E. Ponsiglione, G. Proto and R. Thomson, *Tetrahedron*, 1976, **32**, 2033.

104 . A. Padwa and D. Dehm, *J.Org.Chem.*, 1975, **40**, 3139.

105. A.L.J. Beckwith and C.B. Thomas, *J.Chem.Soc., Perkin Trans.2*, 1973,

861.

106. Aldrich, **16**, 446-1.

107. E. Bamberger, *Chem.Ber.*, 1903, **36** 2042.

108. R.T. Coutts and M. Wohllebe, *Can.J.Chem.*, 1974, **52**, 3432.

109. O. Fischer and F. Romer, *J.Prakt.Chem.*, 1906, **73**, 404.

110. M.M. Sidky, F.M. Soliman and R. Shabana., *Egypt.J.Chem.*, 1978, **21**, 29 (*Chem.Abstr.*, 1980, **93**, 204759).

111. M.R. Mahran, W.M. Abdou and N.A.F. Ganoub, *Phosphorus and Sulphur*, 1988, **39**, 51.

112. A.K. Banerjee, A.J. Layton, R.S. Nyholm and M.R. Truter, *J.Chem.Soc.A.*, 1969, 2536; A.K. Banarjee, A.J. Layton, R.S. Nyholm and M.R. Truter, *J.Chem.Soc.A.*, 1970, 292.

113. J. Charalambous, M.J. Frazer and F.B. Taylor, *J.Chem.Soc.A*, 1969, 2787.

114. R. Wizinger and R. Gross, *Helv.Chim.Acta*, 1952, **35**, 411.

115. J.W. Lewis, P.L. Myers and J.A. Ormerod, *J.Chem.Soc., Perkin Trans.1*, 1973, 1129.

116. R. Noyori, K. Yokoyama and Y. Hayakawa, *Org.Synth.*, 1978, **58**, 56.

117. A. McKillop and T.S.B. Sayer, *J.Org.Chem.*, 1976, **41**, 1079.

118 H.M. Chowla and R.S. Mittal, *Synthesis*, 1985, 70.

119. P. Ruggli and A. Courtin, *Helv.Chim.Acta.*, 1932, **15**, 96.

120. "Dictionary of Organic Compounds", 4th ed, Vol 1, Pg 348, ed. I. Heilbron, Eyre & Spottiswoode, London, 1965.

121 F. Ramirez and S. Dershowitz, *J.Org.Chem.,* 1957, **22**, 41.

122. O. Isler, H. Gutmann, M. Montavon, R. Ruegg, G. Ryser and P. Zeller, *Helv. Chim. Acta,* 1957, **40**, 1242.

123. E.L. Eliel, C. Herrmann and J.T. Traxler, *J.Am.Chem.Soc.*, 1956, **78**, 1193.

124 M. Coenen, *Chem.Ber.*, 1947, **80**, 546.

125. E. Gellert and O.C. Wong, *Aust.J.Chem.*, 1984, **37**, 1931.

126. R.D. Desai, R.F. Hunter and A.R.K. Khalidi, *J.Chem.Soc.*, 1938, 321.

127. A. Kamal and P.B. Sattur, *Synth.Commun.*, 1982, **12**, 157 (*Chem.Abstr.*, 1982, **96**, 162618).

128. O.L. Brady and F.P. Dunn, *J.Chem.Soc.,* 1916, **109**, 675.

129. L. Horner, W. Kirmse and K. Muth, *Chem.Ber.,* 1958, **91**, 430.

130 K.Y. Lee and L.A. Singer, *J.Org.Chem.,* 1974, **39**, 3780.

131. L.I. Smith and K.L. Howard, *Org.Synth.*, Coll.Vol. III,. 351.