STUDIES IN ORGANIC PHOTOCHEMISTRY

a thesis presented by

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ABSTRACT

Three topics are reviewed: the use of photosensitive protecting groups, the photochemistry of azides and the reactions of nitrenes formed by the decomposition of azides.

The photolysis of a suitable aryl azide is proposed as the basis for a photosensitive protecting group for carboxylic acids and alcohols. This is based on the finding that the methyl ether and benzoate ester or ortho-azido-β-phenethyl alcohol produced indole and, in the latter case, benzoic acid on photolysis. The photolysis of this and related systems was investigated.

A better yield of benzoic acid (65-70%) was obtained by irradiating 5-azido-4-benzoyloxymethyl-1-methoxynaphthalene. This result led to the attempt to prepare 4-azido-5-benzoyloxyphenanthrene, which was expected to give benzoic acid quantitatively on photolysis. Attempts to prepare this via a 4-carbonylnitrene-5-hydroxymethylphenanthrene intermediate failed. A novel Schmidt reaction for a lactone and a new reaction of N-tosyloxyimides with sodium borohydride are described in this section.

The nitrite ester of 4-hydroxy-4-methyl-1, 2, 3, 4, 5, 6, 7, 8-octahydrophenanthrene was photolysed to give 4-hydroxy-4-methyl-5-oximino-1, 2, 3, 4, 5, 6, 7, 8-octahydrophenanthrene. The Semmler aromatisation of this and related compounds was investigated and applied to the eventual formation of 4-amino-5-methylphenanthrene. This amine could not be converted to an azide and its diazonium der-

ivative underwent a Mascarelli reaction under very mild conditions.

Some nitration reactions were investigated with a view to using them in synthesis. The stability of an aryl azide to free radicals was discovered when ortho-azidotoluene was converted to ortho-azidobenzyl bromide with N-bromosuccinimide.

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Gordon G.Weingarten
Whiffen Laboratory
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MANY HANDS MAKE LIGHT WORK

CONTENTS

REVIEW

Photosensitive Protecting Groups 8

Photolysis of Azides 11

Reactions of Nitrenes derived from Azides 22

DISCUSSION

Studies in the ortho-azidophenyl series 72

Studies in the peri-azidonaphthyl series 94

Nitration of 5-acetamido-4-acetoxymethyl-1-methoxynaphthalene 106

Studies in the phenanthrene series 116

Reactions of the lactone of 4-hydroxymethyl-phenanthrene-5-carboxylic acid 120

Reactions of the lactol of 4-formylphenanthrene-5-carboxylic acid 128

Reactions of phenanthrene-4,5-anhydride 131

Orientated nitration experiments 142

Synthesis of 4-amino-5-methylphenanthrene 150

The Semmler Aromatisation Reaction 157

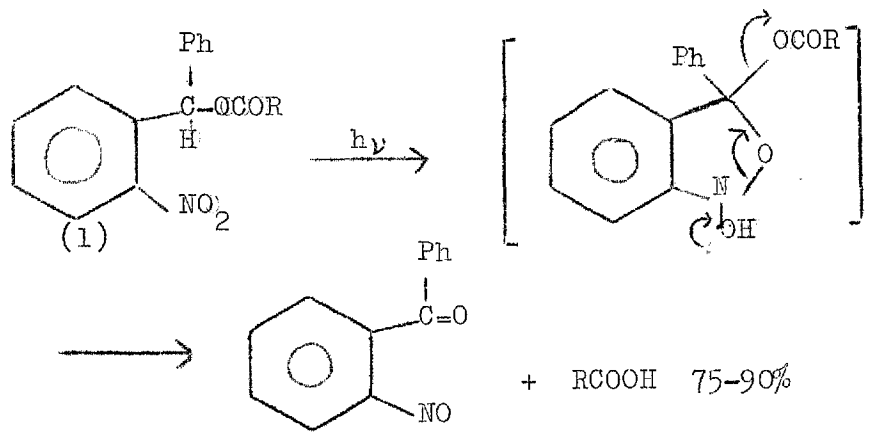
EXPERIMENTAL 174

REVIEW

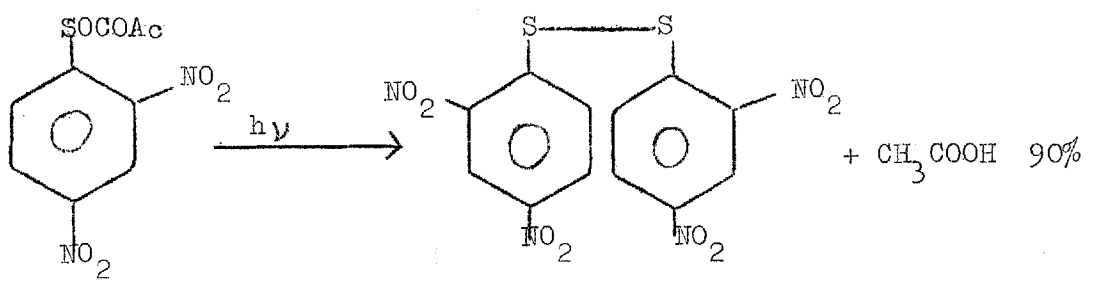
Photosensitive Protecting Groups

Organic chemists doing synthetic work have always been bedevilled by the need to protect sensitive groups during a synthesis. A large variety of protecting groups is available, but these are all subsequently removed by chemical means[1], which may sometimes be troublesome. Thus in recent years attention has been turned to the design of a protecting group which is stable to a wide range of chemical reagents but which can be removed efficiently by irradiation.

Two such photosensitive protecting groups (1)[2], (2)[3] are available for carboxylic acids.

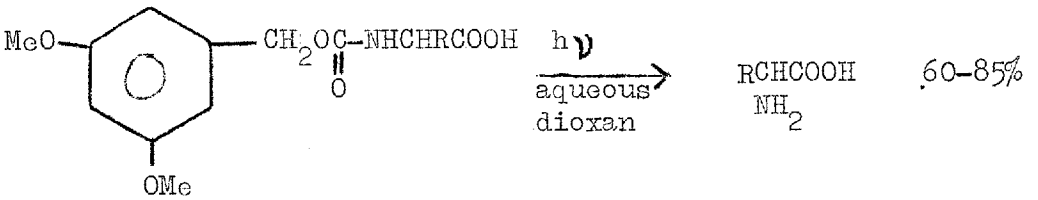


(1)



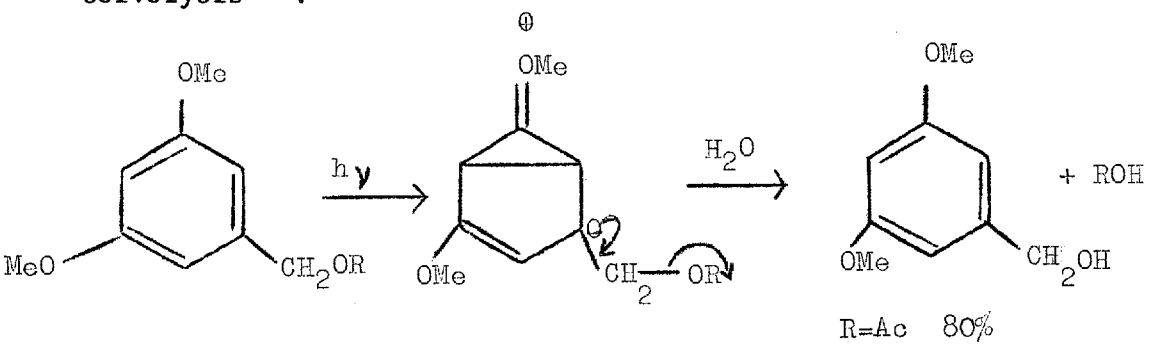
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Amino acids have been protected as the benzylurethane (3)[4].

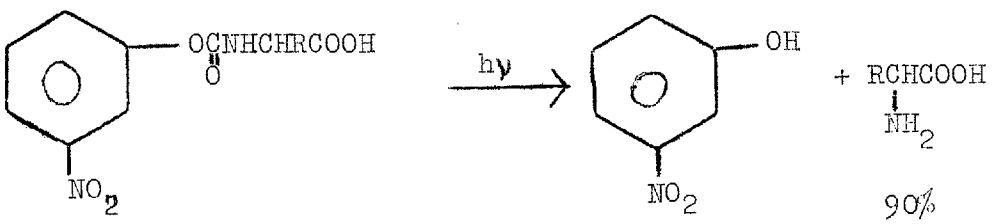


(3)

This is an application of Zimmerman's benzyl ester photo-solvolysis[5,6].

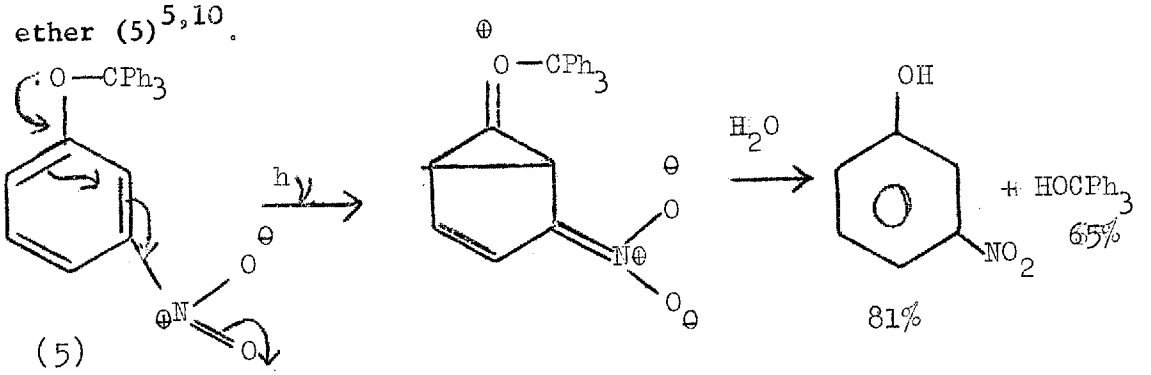


The other type of photo-solvolysis originally studied by Zimmerman has also been used as the basis of a photosensitive protecting group for amino acids (4)[7,8] and phosphates[9].



(4)

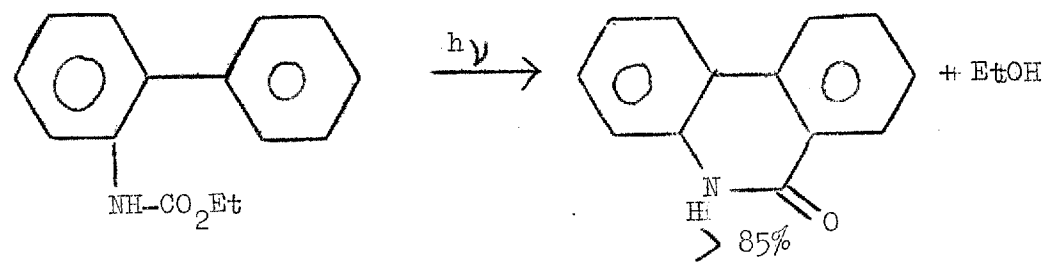
This is based on the photolysis of meta-nitrophenyltrityl ether (5)[5,10].

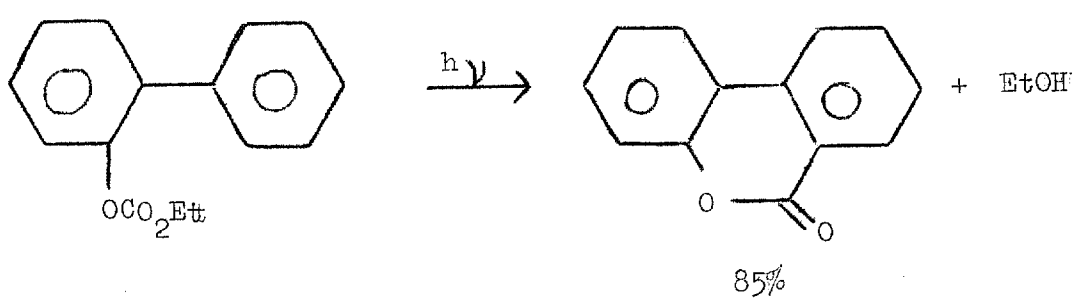


(5)

The beauty of these two protecting groups is that the substituents stabilise them to solvolysis under thermal conditions, but enhance solvolysis on irradiation. These reagents are potentially useful as general photosensitive protecting groups for acids and alcohols.

In the photochemical literature there are some photo-solvolyses [11,12] and photo-elimination reactions which could doubtless be exploited as protecting groups, for example[13]:





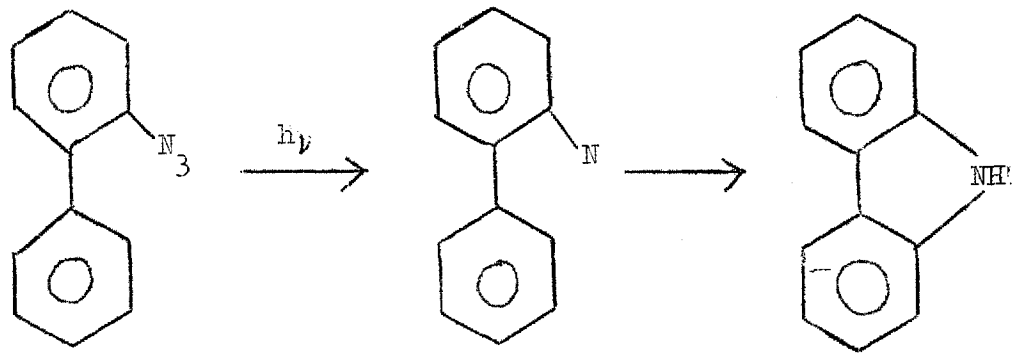
We have chosen to investigate the possibility of using an azide photolysis as the basis for a photosensitive protecting group for alcohols and acids and a review of the photochemistry of azides follows. Azides and nitrenes have been reviewed previously,[14-22] but in the light of recent work an attempt has been made here to be more definitive about the mechanisms involved and the nature of the intermediates in their reactions.

Photolysis of Azides

When azides are irradiated or pyrolysed they lose nitrogen generating nitrenes which react further. The intermediacy of nitrenes can explain the products isolated from the photolysis of azides, but this is not the only possible mechanism. Other plausible mechanisms whereby the azide reacts with a substrate and the adduct loses nitrogen have been more or less rigorously excluded in several cases. These will be dealt with in some detail later.

The formation of nitrene intermediates has been detected by various physical techniques, for example the appearance of a nitrene ultra-violet absorption spectrum, when several azides were irradiated at 77°K [23,24]. For one of these azides, 2-azidobiphenyl (6), the quantum yield for the generation of 2-nitrenobiphenyl at 77°K was the same as for the formation of carbazole at 25°C, which

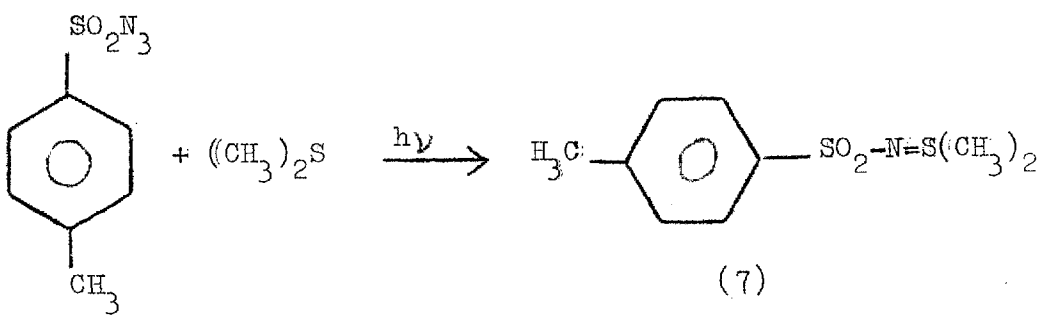
was the photo-product isolated. Hence a nitrene is indeed the intermediate in the reaction and is not confined to photolysis in a solid matrix at 77°K [23].



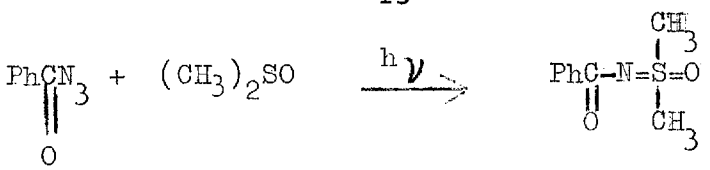
(6)

Another technique used to study the intermediate was ESR. Photolysis of alkyl[25], aryl[26-29], sulphonyl[26,27], cyanogen[30] and carboalkoxy[20] azides in a rigid matrix at 77°K gave spectra showing triplet nitrenes, confirming calculations that the triplet state is the nitrene ground state[31]. This does not, however, imply that photolysis of azides in solution at room temperature generates triplet nitrenes, indeed this would be a forbidden process.

Chemical evidence for the formation of nitrenes is the trapping of photolytically generated sulphonyl nitrenes[32] and carboxy-nitrenes[32,33] and thermally produced aryl nitrenes[34] (7), (8), (9).



(7)



(8)



(9)

The kinetics of the thermal decomposition of many azides has been studied. In agreement with the nitrene mechanism the rate of loss of azide and evolution of nitrogen has first order kinetics and is virtually independent of the nature of the solvent. The activation energy is 32-48 Kcal/mole[35-41]. In the photolytic reactions the rate depends on the light intensity and no useful investigation of the kinetics can be done. The rate is independent of concentration showing that only a single azide molecule is involved in the primary process[42].

When labelled cyanogen azide $^{15}N=N=N^{15}-C\equiv N$ was decomposed at 40°C, cyanonitrene $^{15}N=C=N^{15}$ and nitrogen N_2^{15} was produced. Loss of half the labelled nitrogen and the equal distribution of the label between the two nitrogen atoms in the symmetrical cyanonitrene was demonstrated when the nitrene was allowed to react and the products analysed[43-46]. This is excellent evidence for a nitrene and it has been argued by analogy that any other azide with the same reactions as cyanogen azide also reacts via a nitrene intermediate.

There are several other possible precursors for nitrenes eg. nitro or nitroso compounds with triethyl phosphite[46-49] or ferrous oxalate[50], N-(p-nitrobenzenesulphonyloxy)-urethanes with base[51], photolysis of nitrile oxides[52], photolysis of N-phenyl-spiro-oxaziranes[53]

Because of the similarity of the products formed from all these reactions, it has been suggested that they react via a common intermediate. Such analogies must be considered with reservation and evidence for participation of nitrenes is required in all cases. This discussion will be restricted to the generation of nitrenes by photolysis and pyrolysis of azides.

Elimination of Nitrogen from Azides [42]

This has been considered only in the case of aryl azides. The excited states of aryl azides are essentially those of the parent hydrocarbon. In addition there is a longer wavelength, lower intensity $n\pi^*$ level arising from the promotion of a non-bonding electron from a nitrogen atom. This is the lowest singlet state of the molecule. Light is absorbed by the aromatic system as a whole and the requisite energy for dissociation is localised in the N-N bond.

Three possibilities have been considered for the resulting elimination of nitrogen. It could be eliminated by the uncoupling of the spins of the electrons forming the σ bond between the first and second nitrogen atoms of the azide group. This would require an optically accessible triplet excited state of the azide ($T\sigma^*$), and hence, because of the requirement for spin conservation, triplet nitrene and triplet nitrogen to be generated. No triplet nitrogen

was found[54] and the chemistry of the nitrenes produced show that they are in the singlet state. Thus this mechanism can be rejected.

Another possibility is that the molecule is promoted to some spontaneously dissociative state. In other words, a reduction in the σ bond order between the first and second nitrogen atoms occurs on excitation. However, Huckel molecular orbital calculations show a decrease in π bond order but not σ bond order on ππ* and ππ* excitation. The dissociation energy is of the order of 17-20 Kcal/mole, so that this cannot be considered a spontaneously dissociative state.

The third mechanism postulated was that after electronic excitation, vibrational energy in excess of the bonding energy is supplied to a critical vibrational mode. The only transition releasing enough energy for bond fission is nπ* — G.S. (Fig. I). Thus absorption in the main band populates a ππ* excited singlet state followed by rapid internal conversion to the lowest excited nπ* singlet state. Further internal conversion to a vibrationally excited ground state releases enough energy to effect bond rupture.

When a monochromator was used to irradiate 1-azidonaphthalene, a quantum yield of unity was obtained when the wavelength used was such as to excite the molecule to the ^1L_a ππ* level, but somewhat less when the ππ* level was populated directly. This implies that internal conversion and dissociation are very fast processes

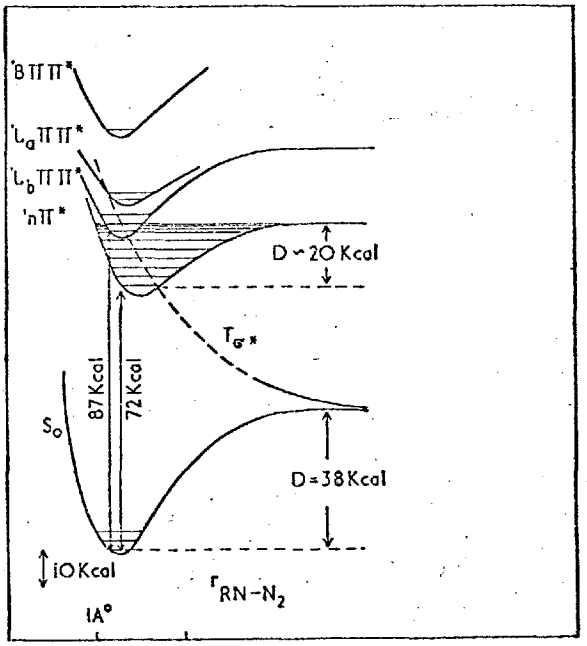
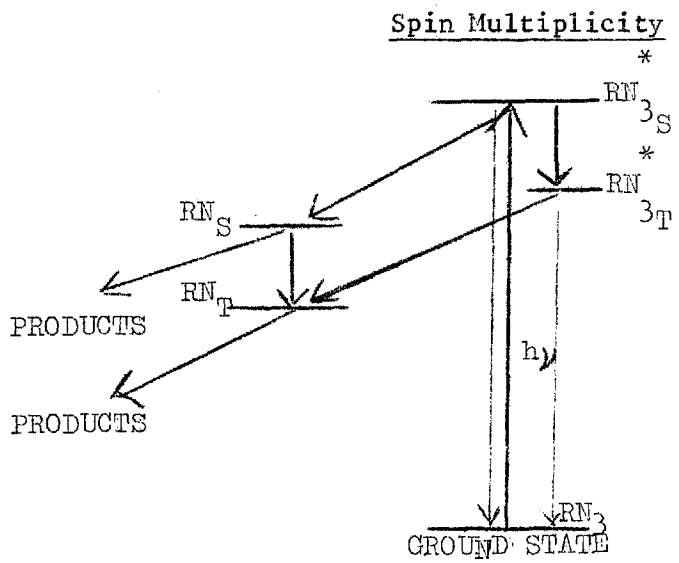


FIG. 1.—Potential energy diagram of RN—N_2 bond in 1-azidonaphthalene.

and compete with vibrational deactivation to the lowest vibrational level of the particular excited electronic state. Thus a molecule cascading from a higher excited state produces a hotter ground state molecule than an $\pi\pi^*$ excited molecule, and the loss of nitrogen is more efficient.

The efficiency of the photolytic dissociation of the azide also depends on the ease with which the vibrational energy in the aromatic nucleus is transferred to the azide side chain. This is probably the reason for the difference in quantum yield between 1-naphthyl azide or 1-anthryl azide (1.00 ± 0.02) and phenyl azide (0.53 ± 0.10). Naphthalene and anthracene are polarised in the direction of the short axis so that there is a better phase relationship between the vibrational modes of the aromatic nucleus and that of the bond to be broken than in phenyl azide.

The thermal decomposition of azides simply involves vibrational excitation of the ground state.



T = triplet state

S = singlet state

RN_3 = ground state azide

RN_3^* = excited azide

RN = nitrene

Fig. II

Figure II is a simple representation of the possible processes which can occur on photolysis of an azide. Spin conservation dictates that the ground state azide be excited to the singlet state RN_{3s}^{*}. This can lose nitrogen giving singlet nitrene RN_s which can react with suitable substrates or convert to the ground state triplet nitrene RN_T which undergoes other reactions. Alternatively, if the excited singlet azide has a sufficiently long half-life, it may undergo inter-system crossing to the triplet azide RN_{3T}^{*} which then dissociates and gives triplet nitrene RN_T and nitrogen.

The rate of collapse of a singlet nitrene to a triplet ground state nitrene is temperature dependent and has an activation energy. Since inter-system crossing is a forbidden process, the activation energy may be necessary to excite the singlet nitrene molecule to a higher vibrational level where the potential energy surfaces of the singlet and triplet nitrenes intersect, so that collapse to the triplet state is possible. If, alternatively, inter-system crossing is induced by collision with solvent molecules, the activation energy may be necessary to enable the nitrene to approach very close to a solvent molecule[55].

A singlet nitrene is best considered as sp^2 hybridised[20]. One orbital is used for the covalent bond, two others contain an electron pair and the remaining p orbital is empty. There is no net spin and it typically behaves as an electron deficient species[56]. A triplet

nitrene is sp hybridised, one orbital is used for the covalent bond and the other for an electron pair. The other two electrons have like spins and occupy separate p orbitals. It reacts as a diradical.

This simple picture will in general explain the products obtained in azide photochemistry, and is supported by some sensitiser and quencher studies which will be dealt with later[57]. For instance, it was found that all the triplet carbethoxy nitrene (NCO_2Et) came from the singlet nitrene when this was generated by α-elimination from N(p-nitrobenzenesulphonyloxy)-urethane and base[58]. On the other hand, when ethyl azido-formate was photolysed, only two thirds of the triplet nitrene originated in this way and one third came directly from the azide[59]. This 30% might well have come from the triplet excited azide.

However, the situation is not so clear and the nature of R in RN_3 may determine the course of the reaction, so that it may not be legitimate to generalise results of experiments on one class of azide to all azides. Experiments with triplet sensitisers show that the triplet energy for alkyl azides is 75-80 Kcal/mole, phenyl azide is 75 Kcal/mole and ethyl azidoformate is 79 Kcal/mole[60]. Thus quenching by piperylene with a triplet energy of 49 Kcal/mole should occur at a diffusion controlled rate. In fact, triphenyl methylazide and isobutylazide lost nitrogen at the same rate whether or not piperylene was present, and there was no isomeriation from

cis to trans piperylene[61]. This shows that no triplet azide is formed or that loss of nitrogen is faster than collision with solvent molecules. The latter is unlikely since the lifetime of the excited aryl azide is more than 10^{-6} sec.[43] (ie. a decay rate of less than 10^{6} per second) while diffusion controlled rates are generally about 10^{9} 1. $mole^{-1}sec^{-1}$.

Furthermore, the quantum yield for nitrogen evolution from alkylazides is 0.7 - 0.9 and if nitrogen is lost from an excited triplet azide, the quantum yield for inter-system crossing RN_{3s}^{*} — RN_{3T}^{*} would have to be at least 0.7 - 0.9. The energy of the lowest excited singlet state is about 100 Kcal/mole[62], so that the energy difference between the first excited singlet and triplet states is 20 - 25 Kcal/mole. Comparision with other systems with an energy difference in this range suggests that 0.7 - 0.9 is too high for the inter-system crossing[60]. Hence nitrogen must be eliminated from the lowest excited singlet azide and not the triplet.

Sensitised Photolysis[60]

When a photolysis is sensitised by a triplet sensitiser whose triplet energy exceeds that of the lowest excited triplet state of the substrate, the maximum rate of photolysis will be diffusion controlled ($k \sim 10^{9}$ 1.$mole^{-1}sec^{-1}$). If the triplet energy of the sensitiser is less than that of the substrate the rate will be much slower because the deficiency has to be made up as thermal

activation energy.

For a number of alkyl azides investigated, only with the highest energy sensitisers did nearly every molecule of azide sensitised lose nitrogen ie. sufficient energy was transferred at almost every collision. However, the low energy sensitisers were more effective than expected.

The operation of these has been explained by postulating "Phantom triplets" an energy transfer to a non-spectroscopic triplet state[63]. While the azide group in RN_3 is linear in the ground state, extended Huckel molecular orbital calculations have shown that in the first excited state, there are two energy minima, for $\theta = 140^{\circ}$ and 220°, where θ is the angle $\widehat{NNN}$. The transoid form ($\theta = 140^{\circ}$) is the more stable of the two and is more stable than the linear one ($\theta = 180^{\circ}$) by 4.8 Kcal/mole. If the low energy sensitisers give rise to this bent phantom triplet azide, this would explain why they are more efficient than anticipated assuming Franck Condon transitions. Furthermore, some ground state molecules will be in bent vibrationally excited states and another process may occur whereby these are excited to a bent triplet state, requiring even less energy. It could be that the bent configurations are non-dissociative states and an activation energy is required to give a suitable form for loss of nitrogen. On the other hand, high energy sensitisers may produce a triplet on the dissociative portion of the potential energy surface, so that only

when the highest triplet energy sensitiser (phenyl cyclopropyl ketone E_T 74.4 Kcal/mole) was used was every sensitised molecule dissociated.

Thus conclusions drawn from sensitiser experiments must be considered with reservations, because the triplets produced in a sensitised photolysis are not necessarily identical to those produced in a direct photolysis.

Reactions of Nitrenes Derived from Azides

Having discussed the operation of the primary processes which occur when an azide is irradiated, we are now in a position to consider the fate of the nitrene thus generated. The nitrene nitrogen, with six electrons, takes every opportunity of reacting with its environment to "defrustrate" itself and attain an octet structure. If the environment is inert, it merely fragments. Thus on flash photolysis of ethyl azidoformate in carbon dioxide, isocyanate radicals were formed, but in the presence of cyclohexene, addition occurred and no isocyanate radicals were detected[53,64,65].

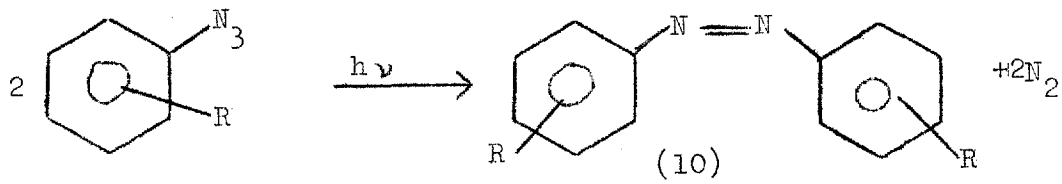
$$N_3CO_2Et \xrightarrow{h\nu} N_2 + NCO^{\cdot} + OEt^{\cdot}$$

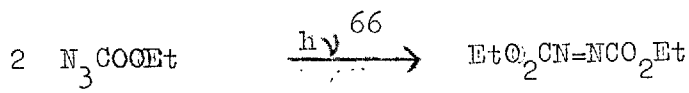
The discussion is limited to the chemistry of nitrenes derived from azides. Bearing in mind that photolytically generated nitrenes are derived from electronically excited azides, while thermally generated nitrenes are derived from vibrationally excited azides,

these two types will be dealt with together.

The objective will be to summarise the different possible reactions and the evidence that nitrenes are in fact the intermediates and to consider the evidence for the spin states of the nitrenes concerned.

Azo-compound formation



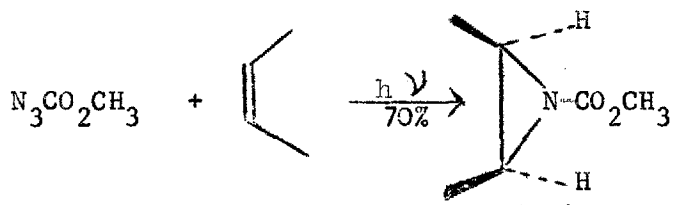


Direct irradiation of a suitably substituted aryl azide can give an azo-compound (10) usually in low or variable yield[35,67-69]. When the photolysis is sensitised, for example of 2-azidobiphenyl with acetophenone, the yield of azo-compound markedly increases, whereas in the presence of piperylene - a triplet quencher - hardly any azo-compound is obtained but carbazole is obtained in excellent yield[57]. This result indicates that this product (10) is formed by a reaction involving a triplet species, either by attack of a nitrene on a long lived triplet azide or by the combination of two triplet nitrenes originating from triplet azide molecules. Flash photolysis experiments showed that both processes can occur. At high nitrene concentrations direct dimerisation of triplet nitrenes produces the

azo-compound, while at low nitrene concentrations it is formed by reaction of a triplet nitrene and an azide[70].

Reaction with Olefins

A nitrene can add across an olefinic double bond to form an aziridine (11)[55,58,64,71-78]. This is a comparatively facile reaction and addition to the double bond in cyclohexene proceeds thirty six times as fast as insertion into the non-allylic C-H bonds in the molecule[37].



55,71

(11)

The stereochemistry of this reaction has been treated in the same way as has the addition of a carbene to an olefin[19,58]. Skell has postulated[79] that singlet carbenes add across a C=C in a single step and hence stereospecifically. Triplet carbenes first react with the olefin to form one C-C bond giving a diradical which has to undergo a spin inversion before ring closure is possible. This process allows time for rotation about the former C=C and an equilibrium is set up between the two conformers. Hence triplet carbenes give a mixture of isomeric cyclopropanes.

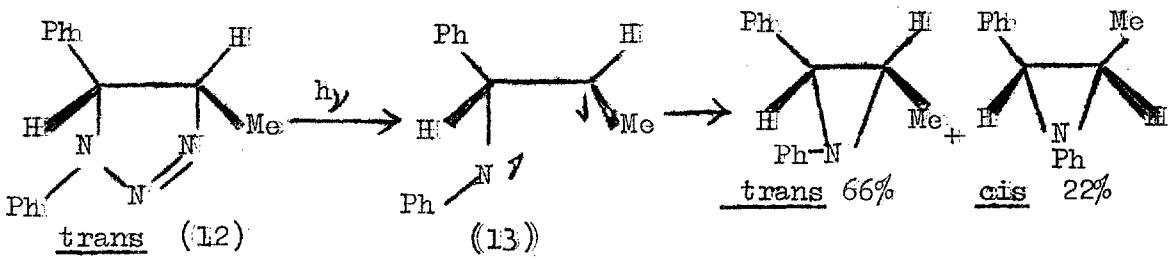
Applying the same considerations to nitrenes, it was found that photolysis of methyl azidoformate in either *cis* or *trans* but-2-ene gave the corresponding aziridine about 90% stereospecifically[71].

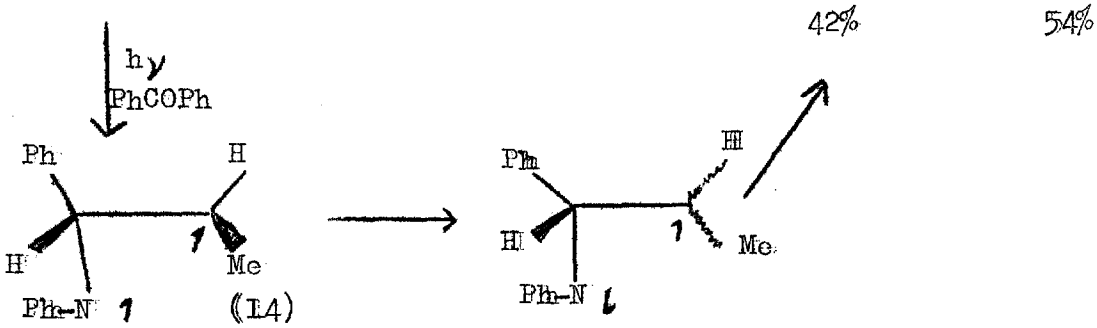
This stereospecificity shows that it is singlet nitrenes which add to olefins. However, this does not imply that triplet nitrenes cannot add to olefins. Indeed, the fact that the addition was not 100% stereospecific shows that some of the singlet nitrene had collapsed to the triplet state before reacting and this led to some non-stereospecific addition. The photolytic reaction between ethyl azidoformate and an olefin is never completely stereospecific. Even at very high olefin concentrations where collision between the singlet nitrene and a molecule of olefin is faster than inter-system crossing to a triplet nitrene, the reaction is not 100% stereospecific. This observation and some supporting kinetics show that not all the triplet nitrene is derived from singlet nitrene molecules, but about 30% is formed directly from the excited azide[59].

At low olefin concentrations, inter-system crossing by the singlet nitrene can occur before intermolecular reactions. Thus in very dilute solutions although singlet nitrenes are formed at first, it is mainly triplet nitrenes which react with the olefin. In accordance with Skell's hypothesis, it was found that the reaction was not very stereospecific in dilute solutions[55,58,59,72]. Extrapolation of these results to infinite dilution showed that in the presence of exclusively triplet nitrenes the reaction is not entirely stereorandom. This has been interpreted as showing that the rate of inter-system crossing is comparable to the rate of rotation about the C-C. Also, the nitrene reacts more rapidly with

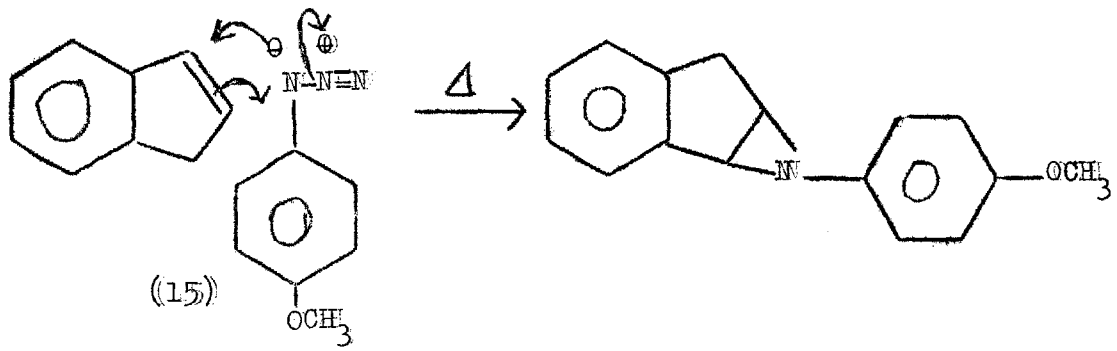
the trans olefin than with the cis isomer, because of the considerable increase in strain involved in the formation of a cis-aziridine[55].

Thus we have the two extremes of singlet nitrenes adding stereospecifically to olefins and triplet nitrenes adding without retention. Support for the validity of this analogy with carbenes comes from the generation of the postulated intermediates by photolysis of a triazole[80]. Direct photolysis of the triazole (12) gives the singlet molecule (13) which undergoes ring closure to an aziridine with reasonable retention of configuration. When benzophenone, a triplet sensitiser, was present, the intermediate is formed in the triplet state (14) and has to undergo spin inversion before rapidly coupling to give the aziridine. During the time necessary for this, rotation occurs and a mixture of cis and trans isomers results.



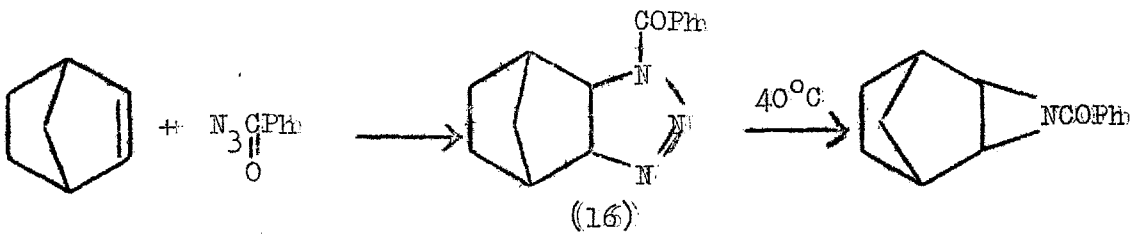


So far we have assumed that an authentic nitrene adds to the olefin and that the olefin plays no part in the dissociation of the azide. This is generally true, but there are cases where other mechanisms occur. For instance, the reduction in the activation energy and a negative activation entropy for loss of nitrogen from p-methoxy phenylazide (15) in refluxing indene compared with other solvents, indicate a concerted reaction in which nitrogen is lost and the ring is formed simultaneously[35].



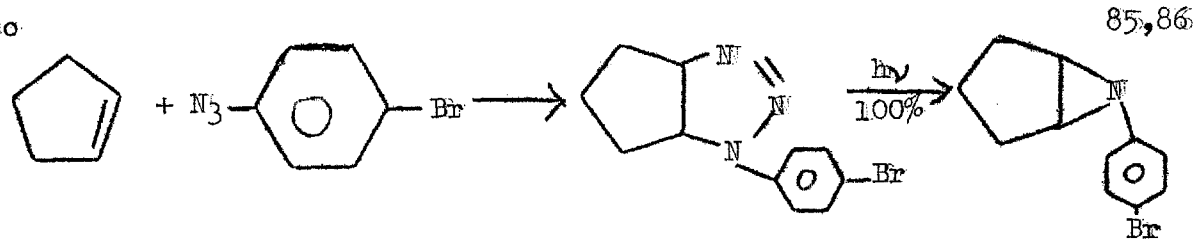
(15)

The alternative mechanism, formation of a triazoline eg (16) which loses nitrogen, has a precedent in the thermal reaction of azides with olefins, below the decomposition temperature of the azide[81-84].



(16)

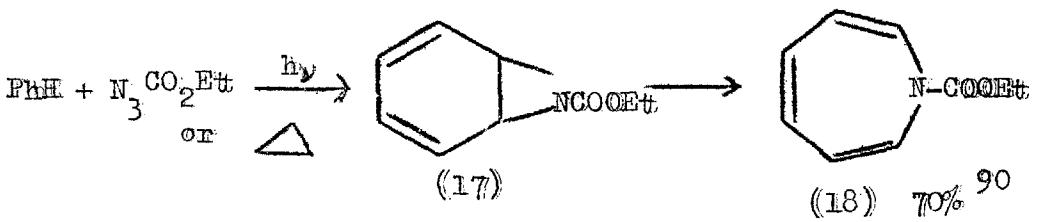
Also



85,86

It has, however, been rigorously excluded for the photolysis of ethyl azidoformate in cyclohexene where no triazole was found when the photolysis was stopped before completion. A plot of the rate of evolution of nitrogen against the intensity of the azide peak in the infra-red spectrum was a straight line up to 75% reaction, showing that a triazoline intermediate is not involved. Finally, the rate of loss of nitrogen was the same in cyclohexane and cyclohexene showing that the decomposition of the azide is independent of the solvent [64,73].

In an addition reaction the C=C can be a benzene double bond. When ethyl azidoformate is irradiated in benzene, the initially formed aziridine (17) isomerises to the N-carbethoxyazepine (18) [88-92].

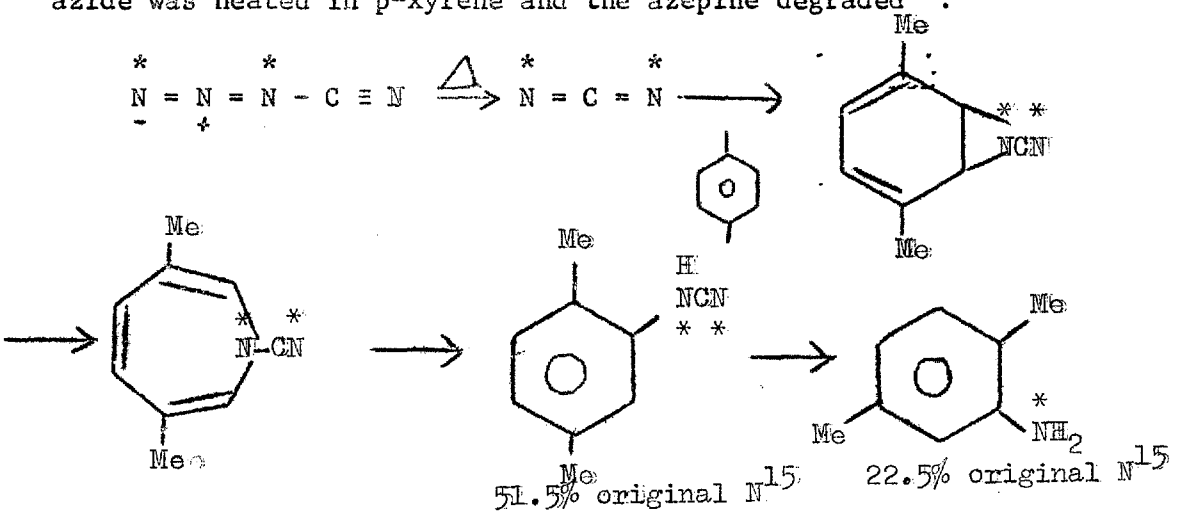


(17) (18) 70% [90]

When it was irradiated in a mixture of benzene and cyclohexene both (18) and the aziridine from cyclohexene were formed. As the dilution was increased thereby increasing the concentration of triplet nitrene, the ratio of azepine to aziridine became very small. The yield of azepine was almost 0% while that of the aziridine was a reasonable 16% when the concentration was as low as 0.1%. These

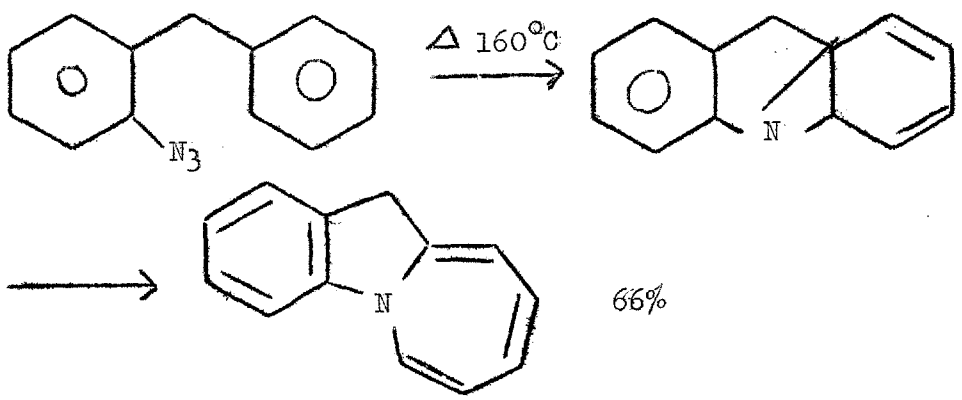
experiments show that unlike 1,2 addition to olefins only singlet nitrenes add to benzene[93].

Good evidence for a discrete nitrene intermediate is provided by the isotope distribution in the products when labelled cyanogen azide was heated in p-xylene and the azepine degraded[46].

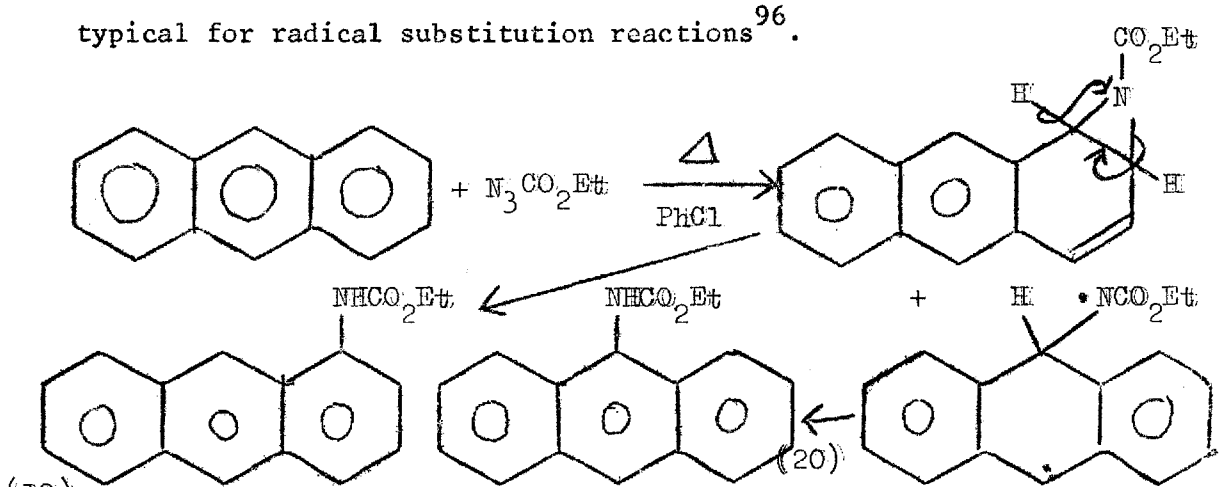


Other experiments with xylenes and durenes show that only ring expansion occurs on reaction with nitrenes and no insertion into the methyl groups takes place. Thus this reaction is more facile than C-H insertion[89,93,94].

There is only one example of an aryl nitrene reacting in this manner[95]. Indeed this is the only reported addition of an aryl nitrene across a C=C.



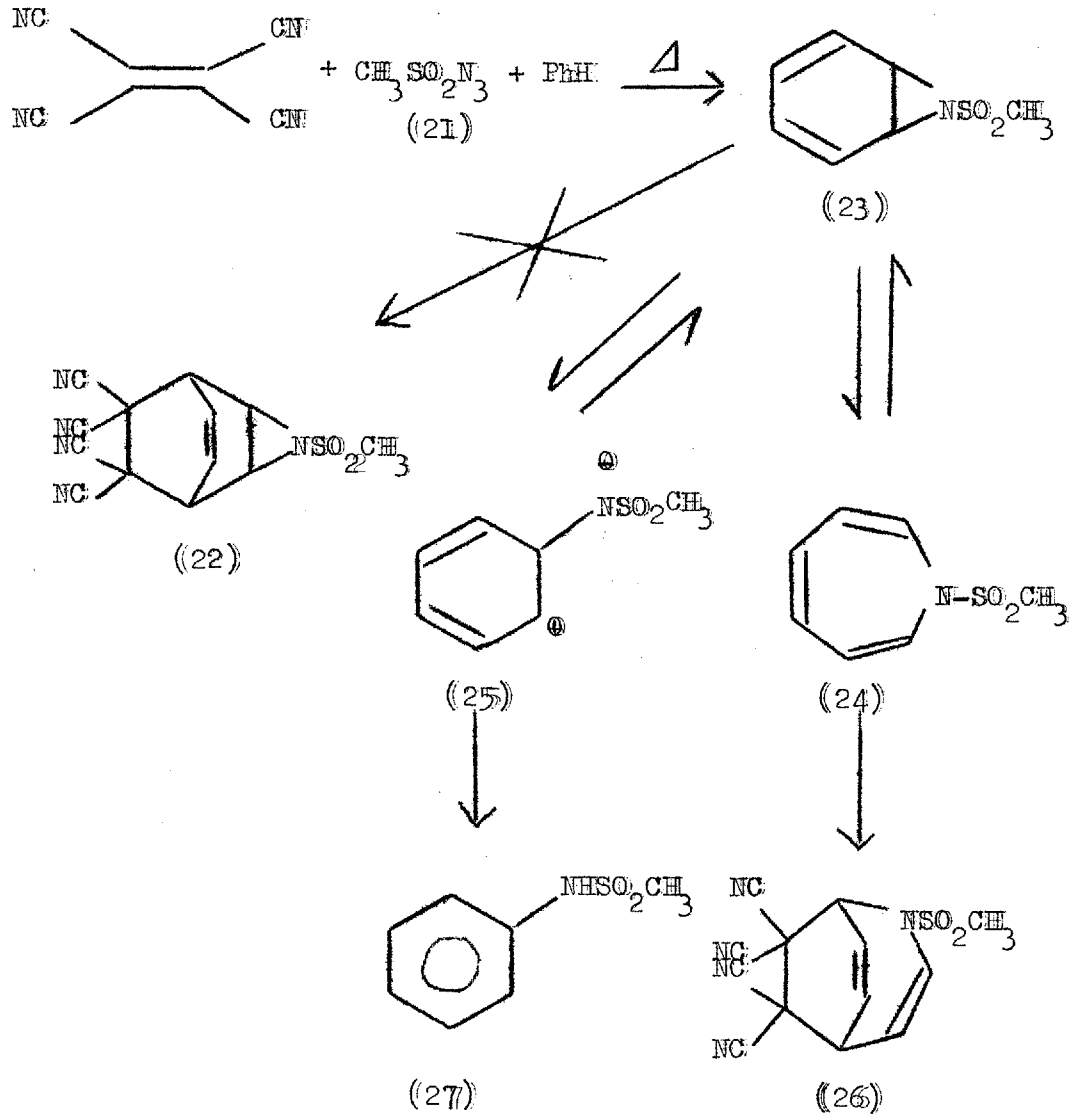
Ring expansion is not the only possible fate of the aziridine intermediate (17). Reactions such as the formation of 1-anthrylurethane (19) from ethyl azidoformate and anthracene, which appear to be insertion of a nitrene into a C-H bond proceed mainly by addition of a singlet nitrene to the aromatic C=C with most double bond character. While the 9-anthrylurethane (20) and some of (19) are formed by a two step radical addition of a triplet nitrene, it is only at high dilution that the 9:1 isomer ratio is typical for radical substitution reactions[96].



(19) (20)

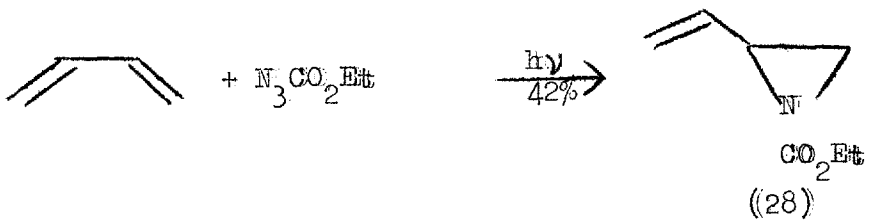
Another example of an aziridine intermediate in what appears to be an insertion reaction into an aryl C-H bond is the formation of sulphonamides (27) from sulphonyl azides eg. (21) in benzene [97-101]. An attempt to trap this intermediate (23) with tetracyanoethylene[100] did not give the anticipated adduct (22), but an adduct (26) of the ring expanded compound (24) and the yield of sulphonamide (27) was only 6%. In neat benzene, 54% (27) was obtained and no azepine (24). This means that there is an equilibrium between the aziridine (23), azepine (24) and (25).[94]

Under the reaction conditions, heating at 120°C, ((24)) is too unstable relative to ((25)) to be isolated, although it is formed more readily and can therefore be trapped by tetracyanoethylene.



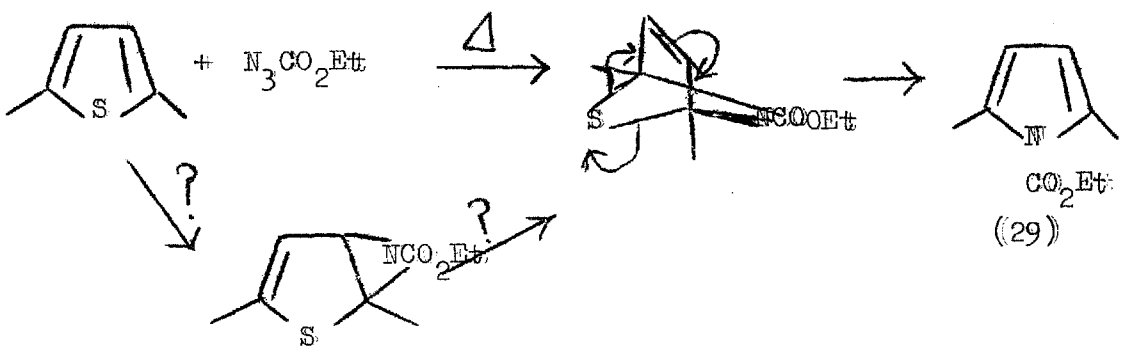
Reaction with Dienes

Photolysis of ethylazidoformate in butadiene gave only the 1,2 adduct (28) and no 1,4 adduct[71].



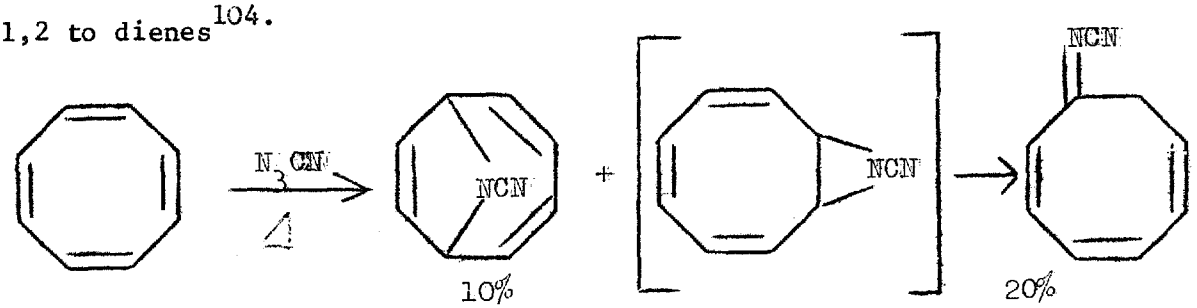
((28))

The conversion of 2,5-dimethylthiophene to N-carbethoxy-2,5-dimethylpyrrole (29) was considered to proceed via a 1,4-cyclo-addition. The alternative, a 1,2-cyclo-addition of the nitrene to 2,5-dimethylthiophene followed by isomerisation, was not rigorously disproved[102].



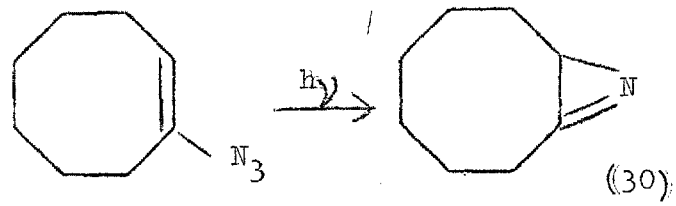
((29))

The only unambiguous case of a 1,4-addition reaction is the reaction of thermally generated cyanonitrene and cyclo-octatetraene[103]. It is suggested that this is a two step reaction of triplet cyanonitrene, but it is apparent from the photolysis of ethyl azidoformate in isoprene at high dilution, that triplet nitrenes add exclusively 1,2 to dienes[104].



Reactions of Vinyl Azides

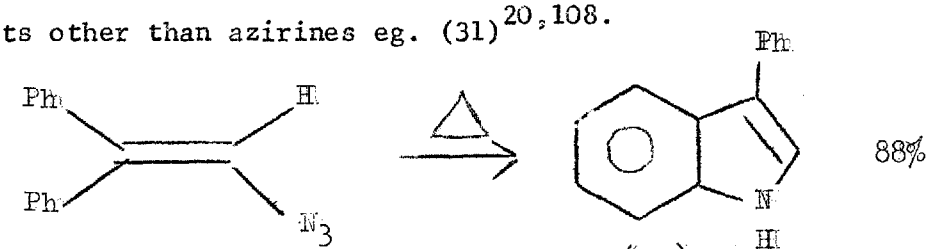
A special case of the reaction of a nitrene with a C=C is the photolysis or pyrolysis of vinyl azides. These react intramolecularly giving a 2H-azirine[20,105-114] eg. (30)[109,110].



(30)

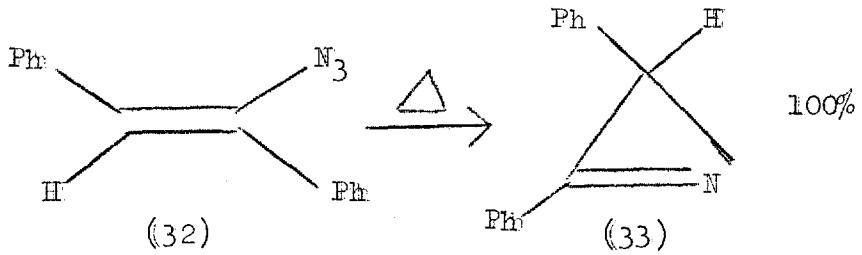
This is a very facile reaction, so much so that on vapour phase pyrolysis of o-methyl-α-azidostyrene only the azirine and no C-H insertion product was obtained[106]. This result could also be interpreted as evidence against a discrete nitrene intermediate in the formation of azirines.

Terminal vinyl nitrenes are anomalous, preferring to give products other than azirines eg. (31)[20,108].



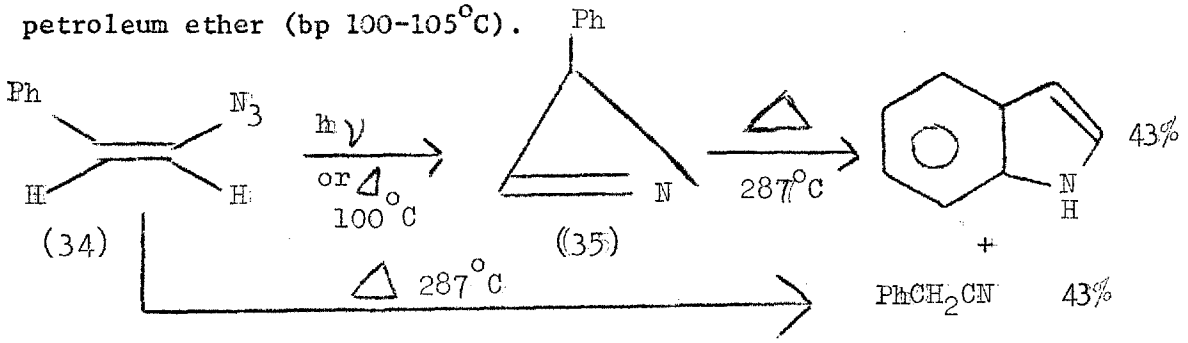
(31)

The reason for this behaviour is not known. The preference for indole formation cannot solely be due to steric factors since α-azidostilbene (32) gave the corresponding azirine (33)[20,108,115] quantitatively.



(32) (33)

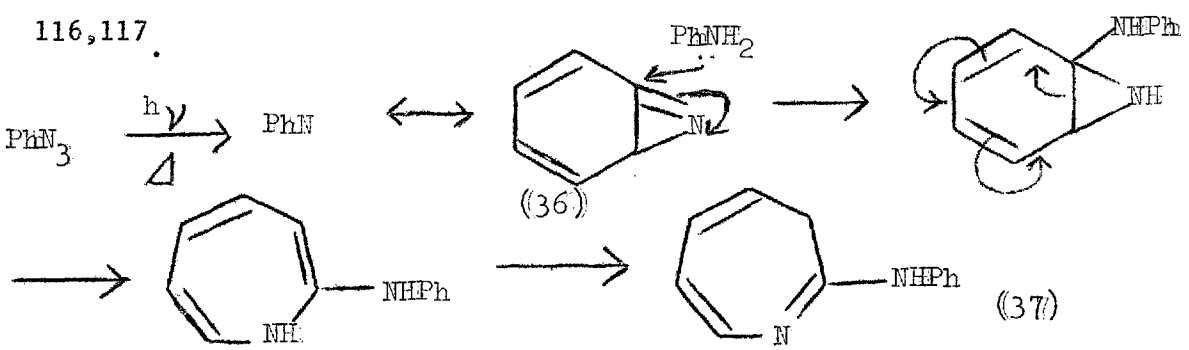
In the case of β-azidostyrene (34), indole and phenylacetonitrile are formed on heating in n-hexadecane (b.p 287°C), but phenylazirine (35) is formed on photolysis[114] or heating in petroleum ether (bp 100-105°C).



(34) (35)

When (35) was heated in n-hexadecane, indole and phenylacetonitrile were produced in exactly the same proportions and yield as when (34) was treated in the same way. Evidently the azirine is the intermediate in the formation of indole and the azide is not behaving anomalously[113].

An interesting example is the photolysis or pyrolysis of phenyl azide. Phenyl nitrene is clearly a vinyl nitrene, and the azirine (36) has been trapped by base and 3H-azepine (37) isolated[53,68,91, 116,117].



(36) (37)

A suggestion that the absence of hydrogen abstraction products might be due to a synchronous loss of nitrogen and ring formation was refuted by showing that meta substituents had no effect on the activation energy for loss of nitrogen. A substituent meta to the azide group is ortho or para to the site of cyclisation and were there a concerted process the presence of an electron withdrawing or donating substituent would be reflected in the relative ease of loss of nitrogen[118]. Photolysis of phenyl azide has once been reported to yield benzotriazole[35] and it is conceivable that this rather than phenylnitrene might be an intermediate in the formation of the azirine. There has been no investigation of this point.

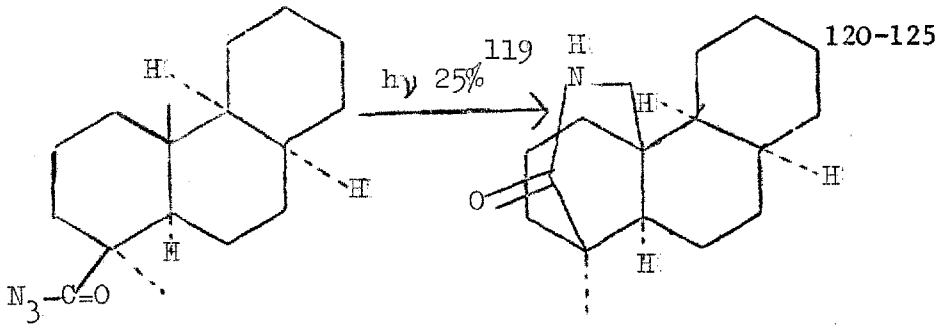
Insertion Reactions

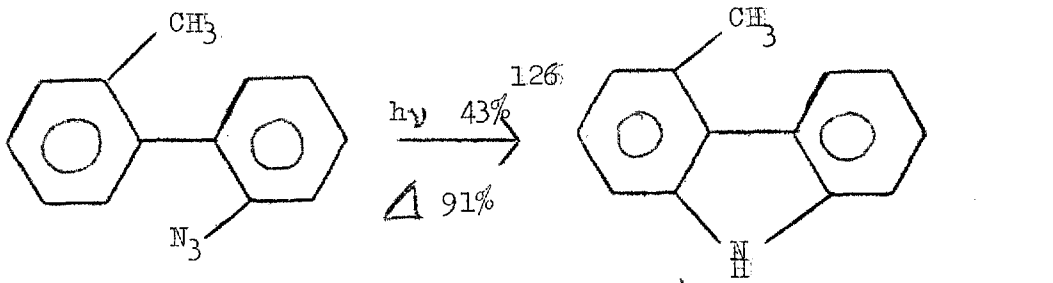
A nitrene can insert into a suitably situated C-H bond. Some illustrative examples are shown overleaf.

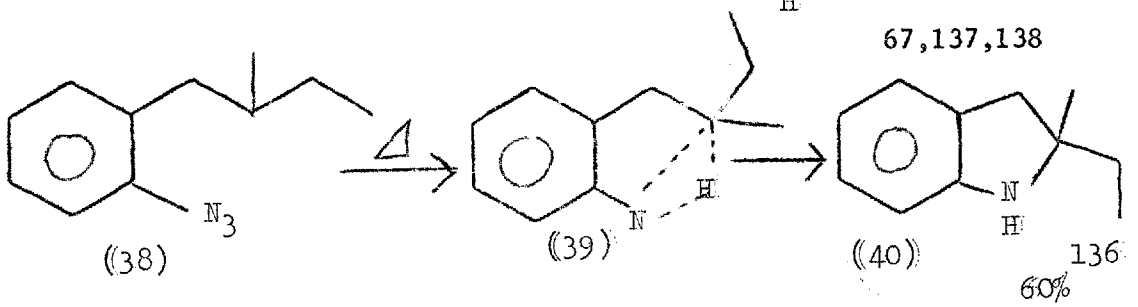
To date there has been no report of a photochemical equivalent of the thermal conversion of (38) to (40), where an aryl nitrene (39) inserts into an alkyl side chain, whereas examples are known for carboalkoxynitrenes[144]. Phenyl nitrene has little tendency to undergo intermolecular C-H insertion reactions. It has been tentatively suggested that this difference in behaviour may be due to delocalisation of electron deficiency in singlet phenyl nitrene which is not possible in cyanonitrene and carbethoxynitrene because these two have electron-withdrawing substituents. Extended Hückel calculations show an

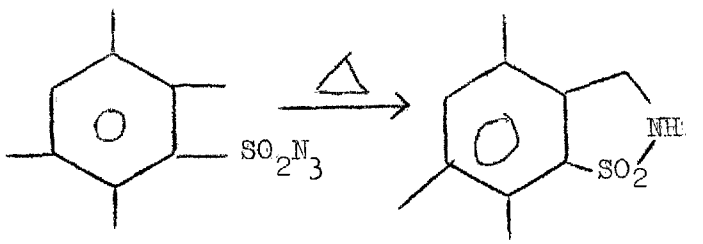
appreciable negative charge on the nitrogen atom of singlet phenyl nitrene making it less electrophilic than the other nitrenes[56].

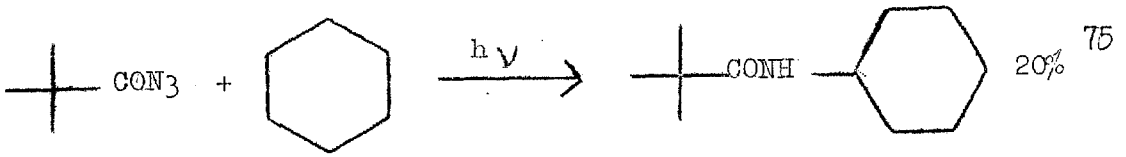
Other examples



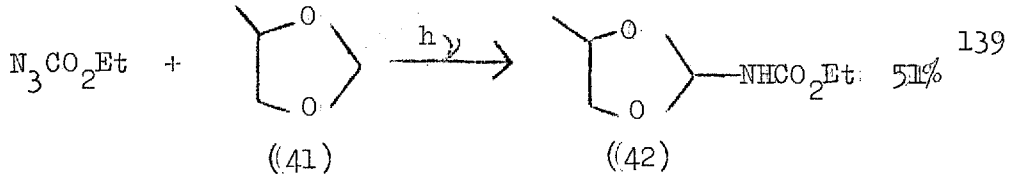






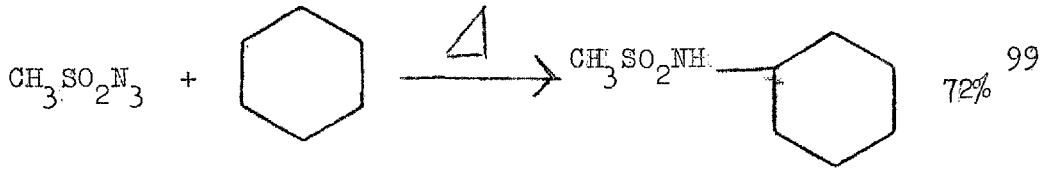


39,40,64,73,74,101,
139-144



((41)) ((42))

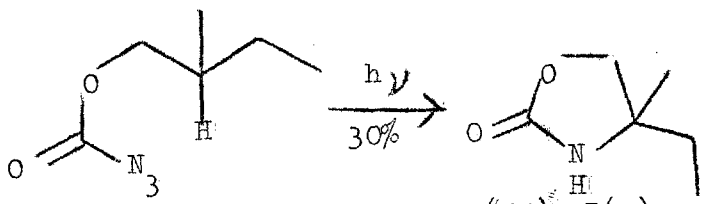
101,119,135,145



The pyrolytic insertion reaction (38) ⟶ (40) is stereospecific, proceeding with total retention of configuration. Thus it is inferred that insertion is a single step reaction of a singlet nitrene and also that the geometry of the intermediate (39) favours insertion into a C-H bond where C is five atoms away from N. A triplet nitrene would involve a diradical intermediate in a two step reaction and this would only be stereospecific if spin inversion and radical coupling were faster than isomerisation at the carbon atom[136].

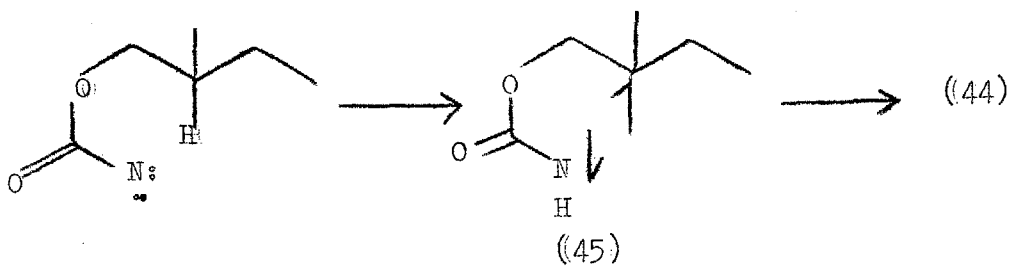
However, insertion reactions are not always completely stereospecific. Indeed (40) is only formed with complete retention when the azide (38) is pyrolysed in the vapour phase; in boiling diphenyl ether the reaction is only 60% stereospecific[20,101,136].

On the other hand the insertion reaction of 2-methylbutyl azidoformate (43) proceeds with 90% retention of configuration in boiling diphenylether and only 21% in the vapour phase[20,143,144]. On photolysis in carbon tetrachloride (44) was obtained 100% stereospecifically[144].



((43)) S (+) ((44)) R(+)

To explain these results it is necessary to refine the concept of the single step reaction via intermediate (39). It is better to consider this as a two step process in which the singlet nitrene abstracts a hydrogen atom producing a diradical intermediate (45) in which the spins are paired. Bond formation to give the cyclic product (44) then occurs very rapidly so that, unlike a triplet diradical in which time is required for spin inversion to obtain (45), no rotation is possible and the reaction proceeds with retention of configuration.



((45))

In the vapour phase, a vibrationally excited nitrene is obtained where the vibrations prevent rapid ring closure. This allows time for inversion to occur and hence a reduction in stereospecificity. In solution, however, solvent molecules make the vibrationally excited nitrenes rapidly cascade to the lowest vibrational level of the excited state where coupling of the diradical is rapid and hence stereospecific. The reduction in stereospecificity cannot be explained by assuming that some singlet nitrene molecules collapse to the triplet state and these, like triplet cyanonitrene[44,45] insert in a stereo-random manner, since it has been shown that the same species of carbethoxynitrene inserts into cyclohexane as adds to benzene; ie. only singlet and not triplet carbethoxynitrenes undergo insertion reactions[93]. There is no evidence for a similar limitation on arylnitrenes and singlet arylnitrenes are more easily converted to the triplet state than are singlet carbethoxynitrenes[41]. Thus the reduction in stereospecificity observed when (38) is pyrolysed in solution may be due to the fact that both singlet and triplet nitrenes insert.

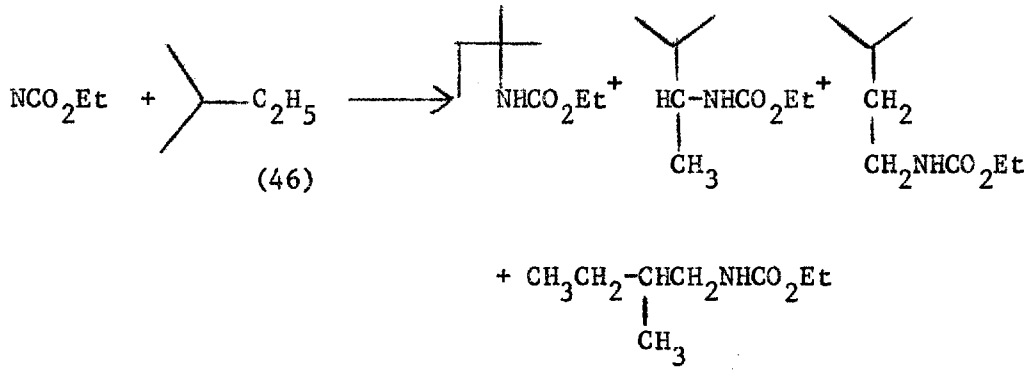
There are other examples of this difference between arylnitrenes and carboalkoxynitrenes. Pyrolysis of azidoformate in cyclohexane gave increased insertion and reduced hydrogen abstraction (see page 47) in the presence of meta-dinitrobenzene, a radical trap. This can be explained by assuming that insertion is a reaction of singlet nitrenes and abstraction is a reaction of triplet nitrenes. It could be that the imine radical ROCONH$^{\cdot}$ first produced catalyses singlet

to triplet inter-system crossing, but in the presence of a radical trap, this is captured and more singlet nitrene product is obtained [40,142]. The converse was found on sensitising the photolysis of ethyl azidoformate in dioxan. The yield of the abstraction product was increased at the expense of the insertion reaction, showing that singlet carbethoxynitrenes insert in direct photolysis[139]. However, by showing that the abstraction:insertion ratio was constant in various solvents for a wide range of concentrations it was deduced that both aniline (the hydrogen abstraction product) and the insertion products obtained on pyrolysis of phenyl azide in a hydrocarbon came from triplet phenyl nitrene. Were the insertion product to come from a singlet nitrene, very little would be found at low concentrations and there would be much more aniline than in concentrated solutions. When the hydrocarbon was 2-phenylbutane it was partially racemised[146].

Carbonyl nitrenes behave like carbethoxynitrenes only inserting in the singlet state; on sensitisation of the photolysis of hexanoyl azide only abstraction products were obtained[147].

The evidence for nitrene intermediates in insertion reactions is based mainly on analogies. All potential nitrene precursors undergo insertion reactions and this has often been used as a diagnostic test for a nitrene intermediate. Quantitative comparison of the relative reactivities of nitrenes derived from pyrolysis and photolysis of ethyl azidoformate and α elimination by base in N-(p-nitrobenz-

enesulphonyloxy) urethane with tertiary, secondary and primary C-H bonds in 2-methylbutane (46) shows good agreement ($1^{o}:2^{o}:3^{o}$ 1:10:32). This is consistent with a common nitrene intermediate for all three[87,101].



A clear proof of the existence of a nitrene intermediate is the finding of the correct isotope distribution in the products when labelled cyanogen azide $\overset{*}{\underset{-}{N}}=N=\overset{*}{\underset{+}{N}}-C\equiv N$ was heated in cyclohexane giving the symmetrical cyanonitrene $\overset{*}{N}=C=\overset{*}{N}$ which inserted in the available C-H bonds. The insertion into the tertiary C-H bonds in both <u>cis</u> and <u>trans</u> 1,2-dimethylcyclohexane was stereospecific (>98%). Thus it can be argued by analogy that all stereospecific insertion reactions of decomposed azides proceed via a singlet nitrene intermediate[43,45].

The retention of configuration was partly lost when dichloromethane was used as solvent, and completely lost in dibromomethane. The presence of a heavy atom enhanced the efficiency of inter-system crossing and triplet nitrenes inserted in a two step process. The more stable triplet nitrene has a greater affinity for tertiary C-H

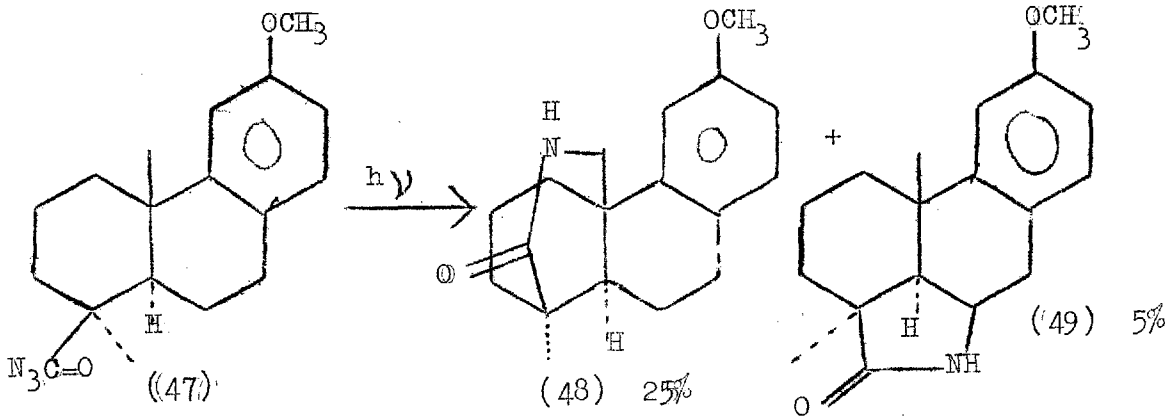
bonds and the yield of insertion product increased from 51% in neat hydrocarbon to 69% in dibromomethane[44,45].

The relative rates of insertion into primary, secondary and tertiary C-H bonds have been investigated to learn something about the size and nature of the charge distribution in the transition state. The relative reactivities are $1^{\circ}:2^{\circ}:3^{\circ}$ 1:10:32 for both photolytically and pyrolytically generated carbethoxynitrenes[40,101,148]. This trend is compatible both with a positive charge and a radical character of the carbon atom involved. In three strained hydrocarbons investigated, adamantane, bicyclo (2.2.2.) octane and norbornane, the $3^{\circ}/2^{\circ}$ reactivity ratio decreased with increasing ring strain. While there was little difference between the reactivities of the secondary positions, the relative bridgehead reactivities were adamantane 1, bicyclo (2.2.2.) octane 0.3 and norbornane 0.07. These data could indicate either a carbonium ion or a radical reaction, but exclude neither. Comparison of the relative reactivities for these compounds with their relative carbonium ion reactivities gives a correlation coefficient of 0.884; comparison likewise with a radical process gives a coefficient of 0.978. However, all that may legitimately be deduced from this work is that the singlet nitrene insertion reaction is subject to similar structural effects as a free radical reaction[148].

Hence the relative reactivity ratios are of limited use as the environment of the C-H bond is important in considering the likelihood

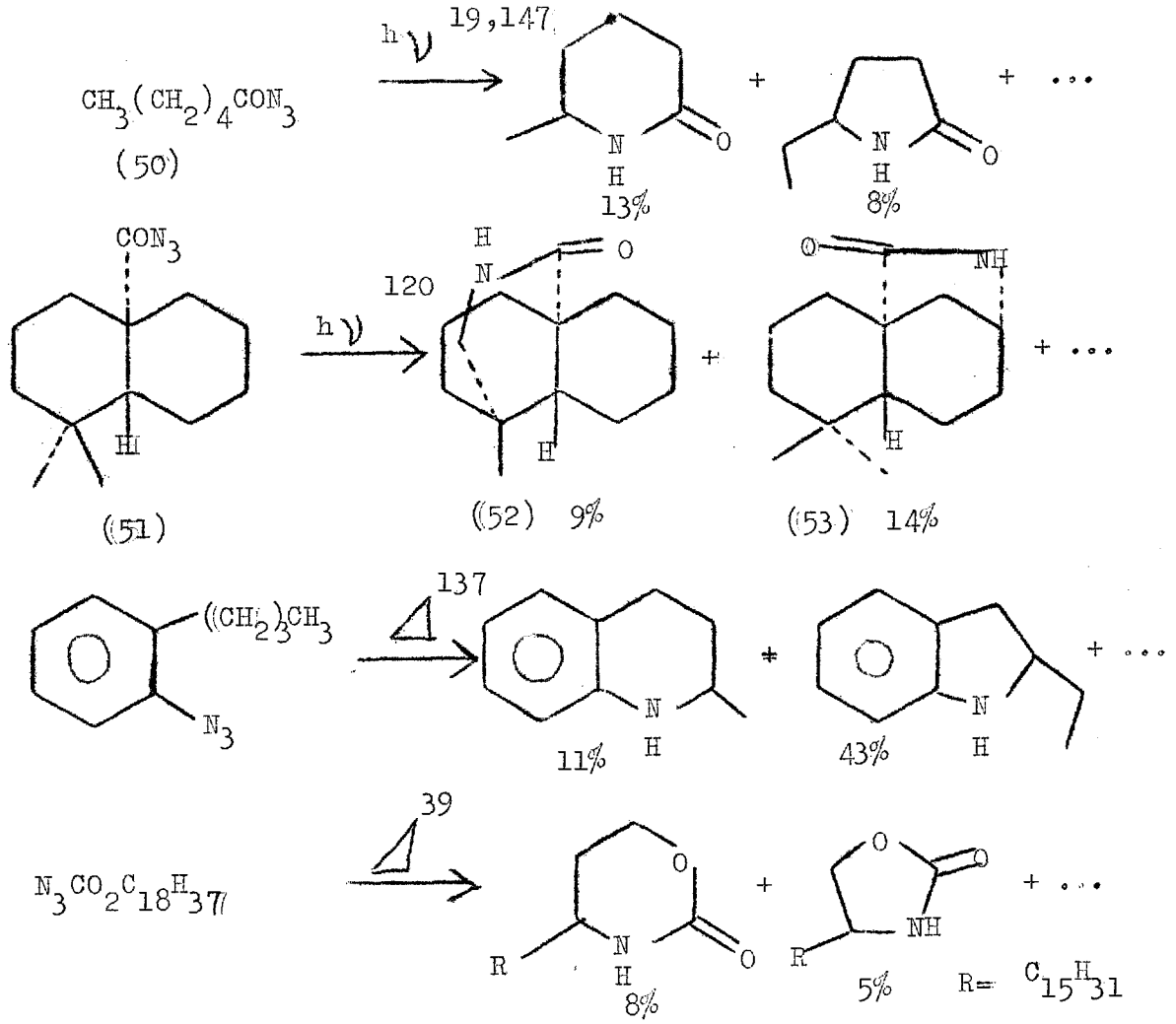
of insertion and the nature of the photoproducts. Thus, for example, carbethoxy nitrene inserts exclusively into the methylene group between the two oxygen atoms in (41) rather than into the tertiary C-H bond available in the molecule[139].

The preference for insertion into a secondary C-H bond rather than a primary one may be reversed if the geometry of the molecule demands it. For example, the photolysis of the O-methyl podocarpic acid derivative (47) gave a 25% yield of δ-lactam (48) by insertion into a primary C-H bond and only 5% of γ-lactam (49) - by insertion into a secondary C-H bond[119]. Because of the rigidity of the molecule, the γ-hydrogens are not as accessible to the nitrene as are the δ ones.[120,147]



This example shows that contrary to the earlier generalisation that insertion reactions give mainly five membered heterocycles, the site of attack depends on the geometry of the intermediate. Some other examples are given below. It is not even valid to generalise from (47) or (50) that carbonyl nitrenes give δ-lactams because when the geometry permits as in (51), insertion into a secondary position

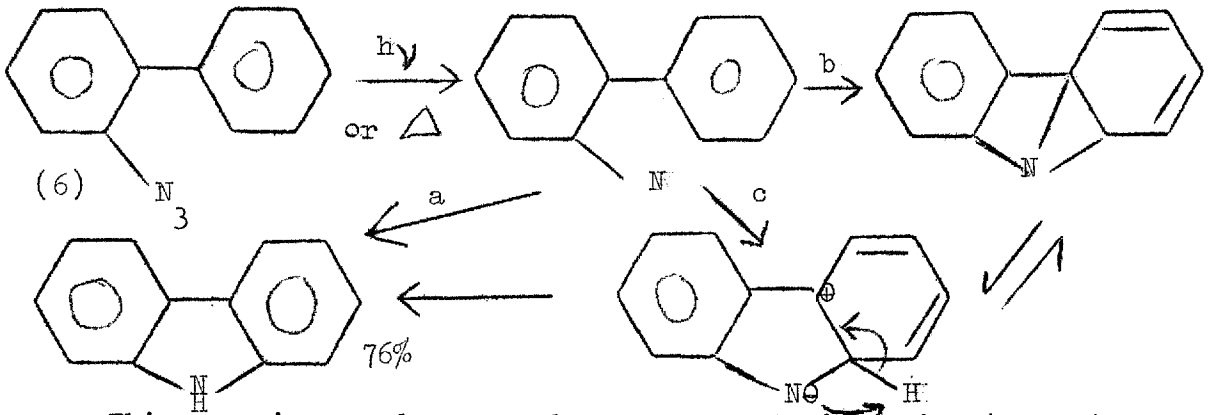
predominates and more δ-lactam (53) is produced than γ-lactam (52).



The nature of the nitrene is also important in determining its reactivity towards primary, secondary and tertiary C-H bonds. Phenyl nitrenes[149] are more selective than carboalkoxynitrenes, and sulphonyl nitrenes are less selective[101].

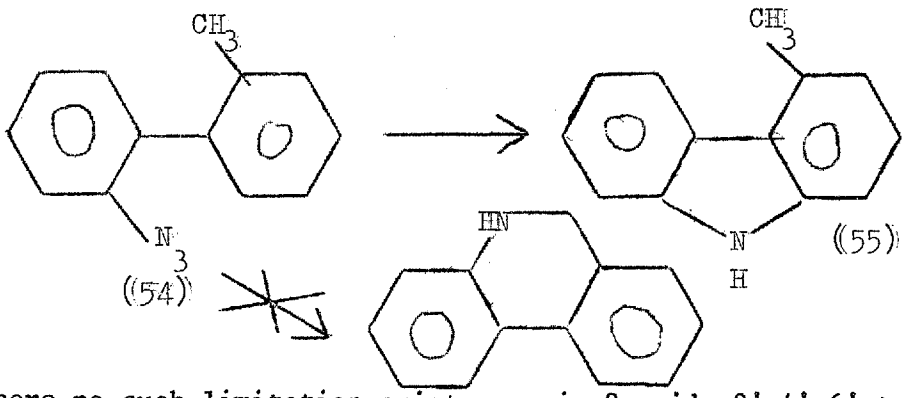
A reaction which is often superficially considered to be a nitrene insertion reaction is the formation of carbazole from 2-azido-biphenyl (6). Triplet sensitiser and quencher investigations suggest that this is a reaction of singlet nitrene[57]. Although triplet 2-nitrenobiph-

enyl generated at 77°K (observed spectroscopically) gave carbazole quantitatively on warming to room temperature[23], this result does not necessarily contradict the previous one. Indeed, it tells nothing about the course of the reaction at room temperature, merely that the triplet nitrene can cyclise to give the same product as the singlet nitrene.

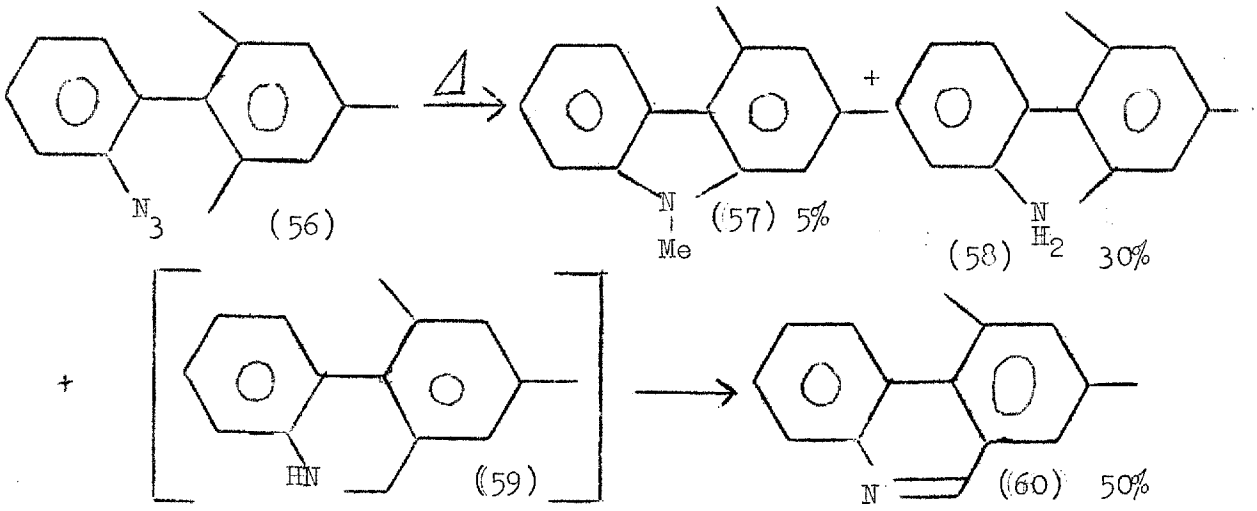


This reaction may be a standard one step CH insertion (path a). Alternatively it may be another example of aziridine formation (path b) or perhaps an aromatic nucleophilic substitution reaction (path c).

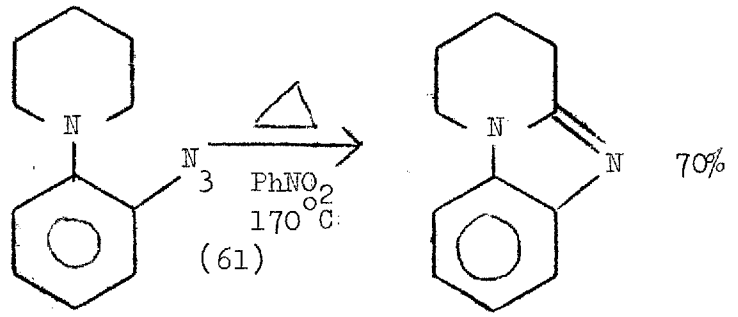
It is not clear whether this insertion process is more or less facile than authentic insertion into an alkyl C-H bond. Although 4-methylcarbazole (55) was the sole product when 2-azido-2'-methylbiphenyl (54) was decomposed[89,126], steric factors are probably responsible for the lack of a reaction of the nitrene with the methyl group. Similarly the formation of 4-azidocarbazole and not the azo-compound benzo (c)cinnoline on photolysis of 2,2'-diazidobiphenyl is doubtless due to the azide groups being on opposite sides of the molecule[133].



Where no such limitation exists, as in 2-azido-2',4',6'-trimethylbiphenyl (56), the pyrolysis in hexadecane gave only 5% carbazole (57) compared to 50% of the insertion product (60)[127,128]. Clearly this may be a special case because it involves a methyl shift instead of a hydrogen shift.



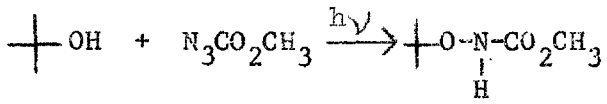
The oxidation <u>in situ</u> of the dihydrophenanthrene (59) is interesting. Perhaps this process provides the hydrogen for the formation of amine (58). Other examples have been reported where the hydrogen abstracted is α to nitrogen eg. (61)[150,151].



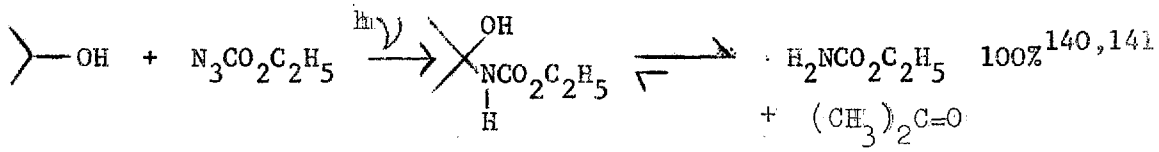
Reaction with Alcohols

There are two types of reaction of nitrenes with alcohols, insertion into the OH bond[140,152,153] and insertion into the CH bond next to the oxygen atom. The latter, obviously inapplicable to tertiary alcohols, results in the oxidation of primary and secondary alcohols[140,141,154,155].

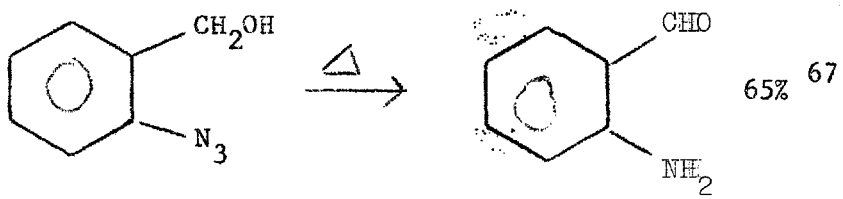
$$MeOH + PhSO_2N_3 \xrightarrow{h\nu} PhSO_2NHOCH_3 \quad 15\%\ ^{153}$$



$$+ N_3CO_2CH_3 \xrightarrow{h\nu} \text{(O-N-CO}_2\text{CH}_3\text{, H)} \quad 55\%\ ^{141}$$

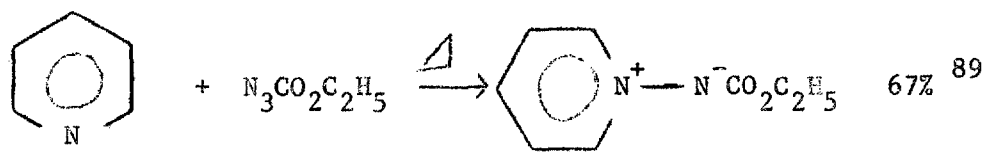


$$+ N_3CO_2C_2H_5 \xrightarrow{h\nu} \text{(OH, NCO}_2\text{C}_2\text{H}_5\text{, H)} \longrightarrow H_2NCO_2C_2H_5 + (CH_3)_2C{=}O \quad 100\%\ ^{140,141}$$



65% [67]

The OH insertion reaction could be viewed as a nucleophilic reaction like, for example, the reaction with pyridines[130,134,154,156].

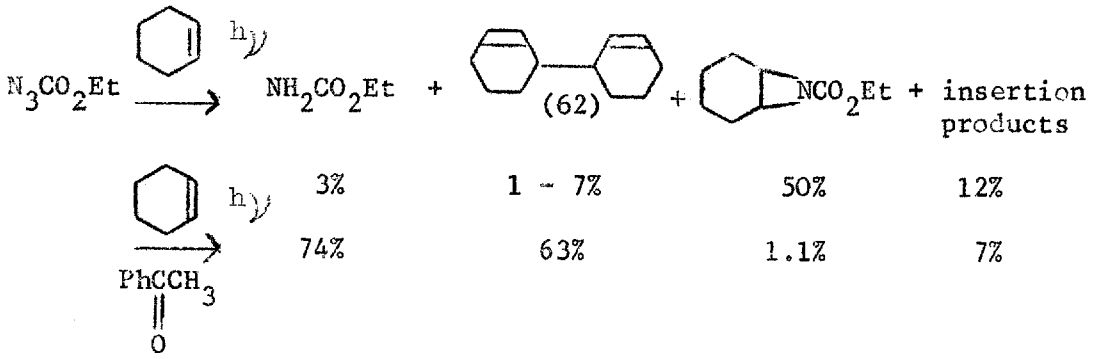


$$+ N_3CO_2C_2H_5 \xrightarrow{\Delta} \text{(N}^+\text{—N}^-\text{CO}_2\text{C}_2\text{H}_5\text{)} \quad 67\%\ ^{89}$$

Hydrogen Abstraction

Nitrenes frequently abstract hydrogen from the solvent, aryl azides giving anilines[35,36,94,95,130,135], azidoformates giving urethanes

[59,64,142], carbonylazides giving amides[147] and sulphonyl azides giving sulphonamides[22,99]. When the azide is decomposed in cyclohexene in these reactions bicyclohexene(62)[41,64] is found and in cyclohexane, cyclohexene and bicyclohexane are found[40,147], showing the origin of the abstracted hydrogen atoms.



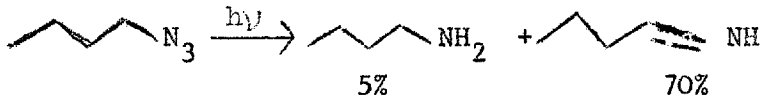
There is evidence that this abstraction reaction is a reaction of triplet nitrenes. In the sensitised photolysis of ethylazidoformate in cyclohexene the abstraction product is the major one and the yield of bicyclohexene is very much higher than in the direct photolysis[59, 64,139,147]. In another example, radical traps eg. meta-dinitrobenzene reduced the yield of urethane and increased the yield of insertion product[40,142]. Free radical sources, and thiols, by contrast, enhanced the production of anilines from aryl azides[157]. These results can be readily interpreted to show that triplet and not singlet nitrenes abstract hydrogen.

The relative tendency to undergo this reaction on direct photolysis or pyrolysis : aryl azides > formyl azides > sulphonyl azides, reflects the relative stabilities of their respective singlet nitrenes : aryl

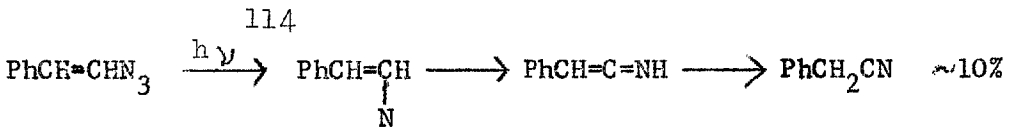
nitrene < formyl nitrene < sulphonyl nitrene[41].

1,2-Migrations

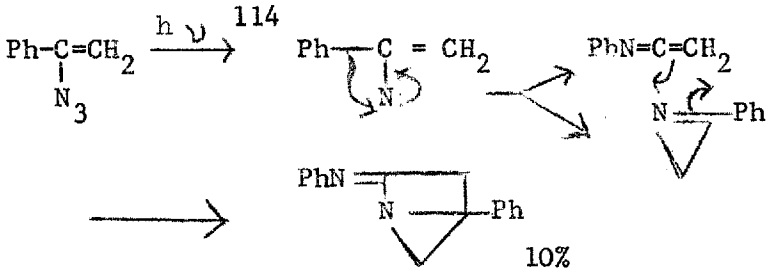
Photolysis of alkyl azides gives imines, where a hydrogen on the carbon atom bearing nitrogen migrates to the nitrene[158-162].

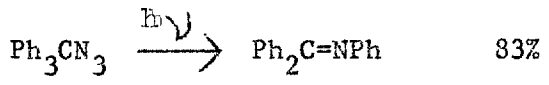


Another example is the photolysis of vinyl azides where a minor product is usually derived from a ketenimine[20,106,112,114,108,163].



Phenyl migration is often observed, and in di-and triarylmethyl azides it is the major reaction pathway[61,158,164-168].





In substituted compounds Ar' Ar'' Ar''' CN_3, the migrating aptitudes of the aryl groups are unaffected by the nature of the substituents.

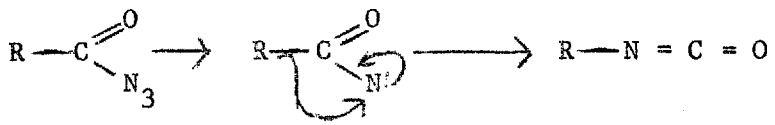
In the corresponding thermal reaction, however, electron repelling substituents in the para position increased the migrating aptitude relative to an unsubstitued phenyl group and electron withdrawing substituents reduced it. This indicates that while in the thermal reaction phenyl migration participates in the elimination of nitrogen [169], in the photochemical reaction, a discrete nitrene intermediate is formed and migration occurs subsequently[20,61,167]. The small entropy of activation in the thermal reaction is consistent with an anchimetrically assisted process[169].

The evidence for the electronic nature of the nitrene in the photochemical rearrangement is confused. The reaction is sensitised by triplet sensitisers giving the same products and the same migrating aptitudes as in a direct irradiation[167]. This suggests that the singlet excited azide undergoes inter-system crossing to the triplet excited azide which in turn loses nitrogen resulting in a triplet nitrene which rearranges. However, piperylene, which should be an efficient triplet quencher in this reaction, had no effect, indicating that no triplet excited azide is formed in the direct photolysis. A more detailed investigation of the sensitised photolyses showed that none of the sensitisers used had a high enough triplet energy for this to be a true triplet sensitised reaction. As was discussed earlier, "Phantom triplets" were invoked to explain the nature of this reaction. There is no reason to suppose that a non-spectroscopic triplet azide must give a triplet nitrene, or that the sensitised photolysis reproduces

conditions extant in a direct photolysis. In an attempt to trap the triplet nitrene with n-butyl tin hydride and sec. butyl thiol, only a few per cent of trityl amine was obtained. Thus the rearrangement of the singlet nitrene was calculated to be about twenty times faster than inter-system crossing and trapping the triplet thus produced[61]. There is ESR evidence that triplet nitrenes do not rearrange and it was deduced from other experiments with diazidodiphenyl methane that probably only singletnitrenes are involved in this rearrangement[96,170].

The quantum yield for the photolysis of trityl azide is initially 0.8 (for other simple azides it is 0.7-0.9), but drops to about 0.01. This is due to a secondary process, dissociation of the molecule to give an azide radical and a triphenylmethyl radical which acts as a strongly absorbing filter. These fragments recombine subsequently and scrambling of the N^{15} label in terminally labelled trityl azide showed that this process occurs to an extent of 15-20%[168].

The Curtius rearrangement of carbonylazides could be visualised as a 1,2-migration.

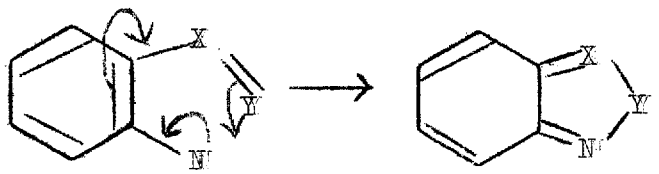


Since in thermal reactions only the isocyanate and no unrearranged nitrene products (insertion products etc.) are obtained,[19] migration of R must occur simultaneously with the loss of nitrogen, so that there is no discrete nitrene intermediate.

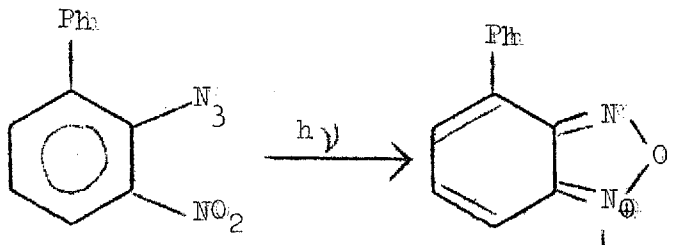
However, photolysis of pivaloyl azide (R = tBu) in a variety of solvents always gave 39 - 42% t-butyl isocyanate as well as unrearranged nitrene products. This was true whether the solvent provided opportunities for addition or insertion in primary, secondary or tertiary C-H bonds (the reactivity ratio is 1:9:160 $1^{o}:2^{o}:3^{o}$), and must imply that the isocyanate is not derived from pivaloyl nitrene. Thus the photo-Curtius reaction, like the thermal reaction, is not a 1,2-shift onto a nitrene, but a concerted process[75,171].

Reaction with ortho-X=Y

An aryl nitrene generated thermally or photolytically reacts readily with an ortho substituent if this is αβ unsaturated.



Some examples of this reaction giving useful heterocyclic products are given below.

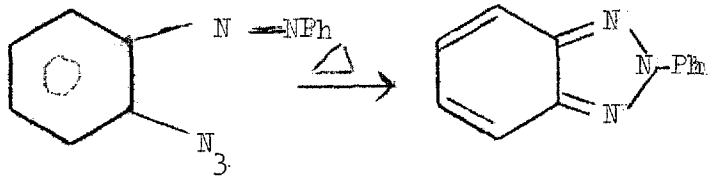


83.172-174

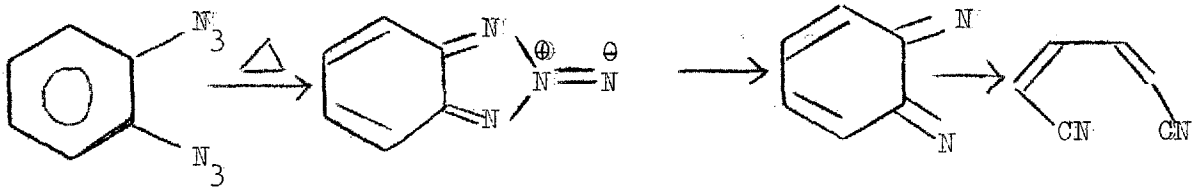


175

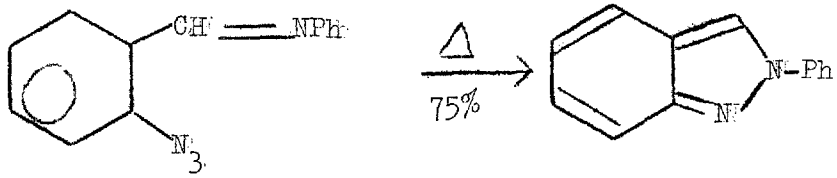
176



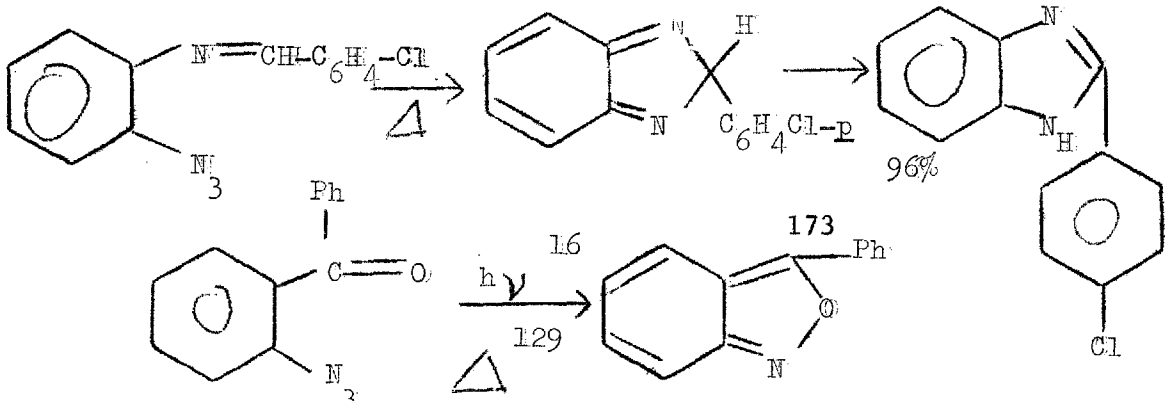
177



175,178

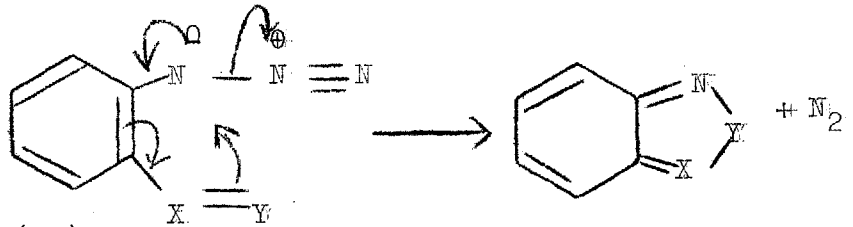


175,179,180



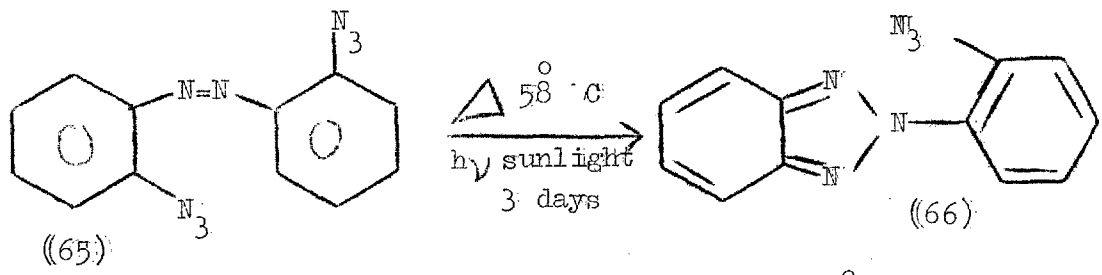
Studies of the kinetics of some of the thermal reactions show that this is not a genuine nitrene reaction but that ring formation is

simultaneous with loss of nitrogen[169,174]. Thus whereas the enthalpy of activation for loss of nitrogen from aryl azides without anchimetric assistance is 32.5 - 40.6 Kcal/mole, for o-nitrophenylazide, o-azido-azobenzene, and o-acetylphenylazide it is 22.4 - 27.2 Kcal /mole. The negative entropy of activation also supports this mechanism (64)[38,172].



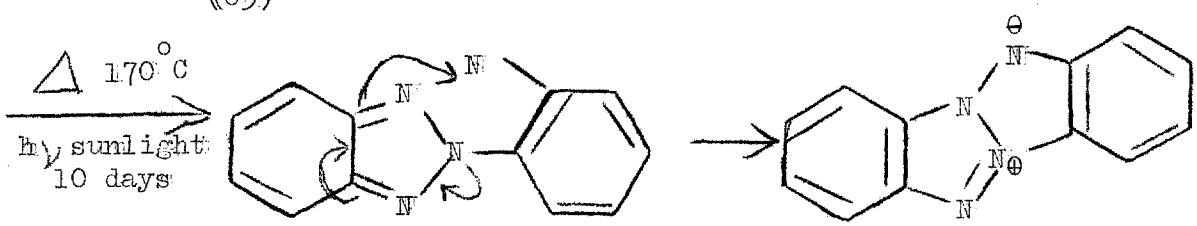
(64)

A good indication of the anchimetric assistance is found in the thermolysis of o,o'-diazido-azobenzene (65) which loses nitrogen in two distinct stages. The first molecule of nitrogen is lost with the help of the ortho-N=N at 58°C giving (66), and this only eliminates nitrogen on heating to 170°C giving (68) via an authentic nitrene (67) [176,181].



(65)

(66)

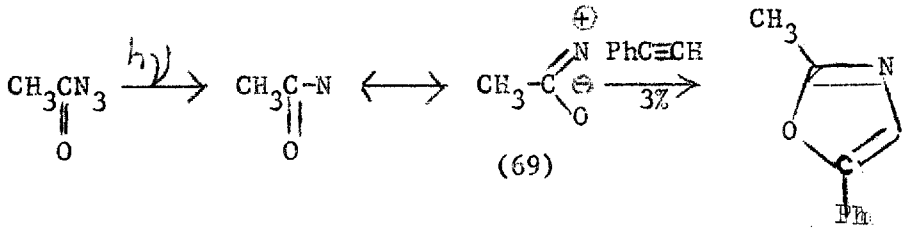


(67)

(68)

1,3-dipolar Cyclo-additions

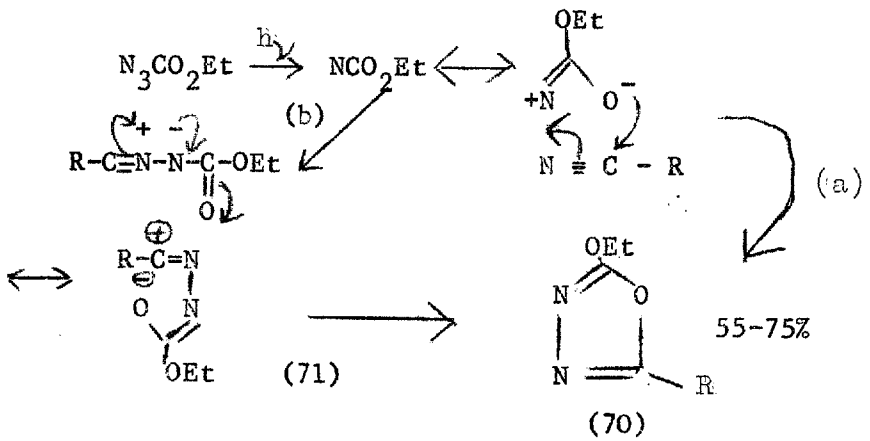
There are a few instances where carbonylnitrenes react formally in a dipolar form (69) with triple bonds[141,182-185].



(69)

This reaction is not an addition of the azide to the acetylene giving a triazole which then loses nitrogen, as when the triazole was prepared it was found to be stable to light. 1,2-cycloaddition of the nitrene to the triple bond is improbable, because this would give a 1-H azirine which is anti-aromatic[186].

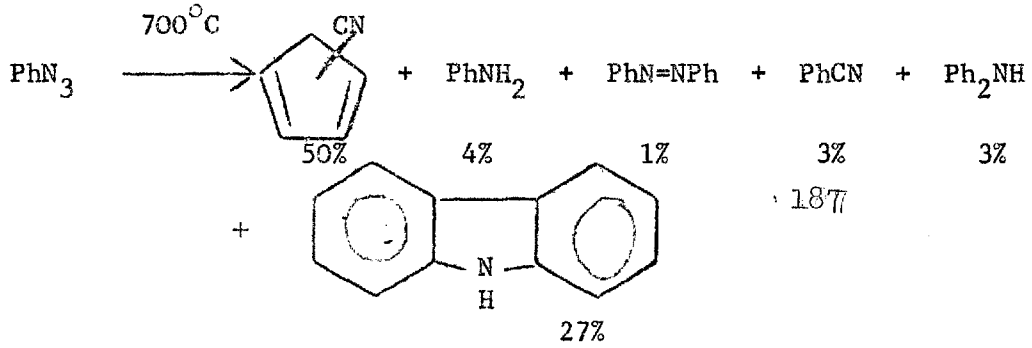
The other type of 1,3-dipolar cyclo-addition reported involves addition of a nitrene to a nitrile giving (70)[141,183-185]. This is either an authentic cycloaddition (path a) or a nucleophilic reaction giving a nitrilimine (71) which then cyclises (path b).



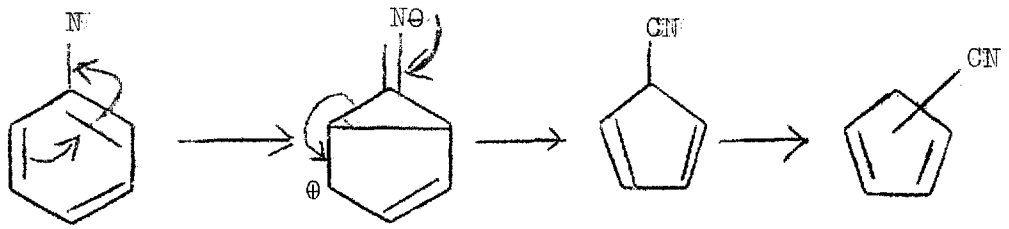
(71) (70)

High Temperature Reactions

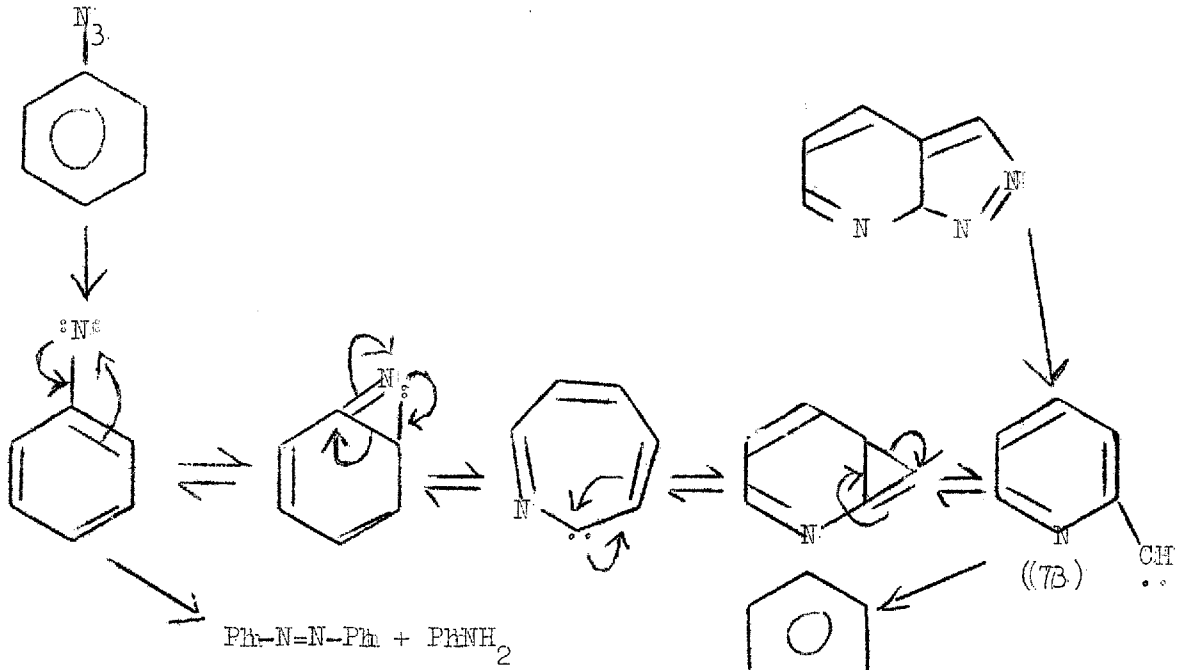
When aryl azides are pyrolysed at 500-700°C complex mixtures are obtained which include cyanocyclopentadienes[187-189].



This is considered to be a reaction of hot singlet nitrene

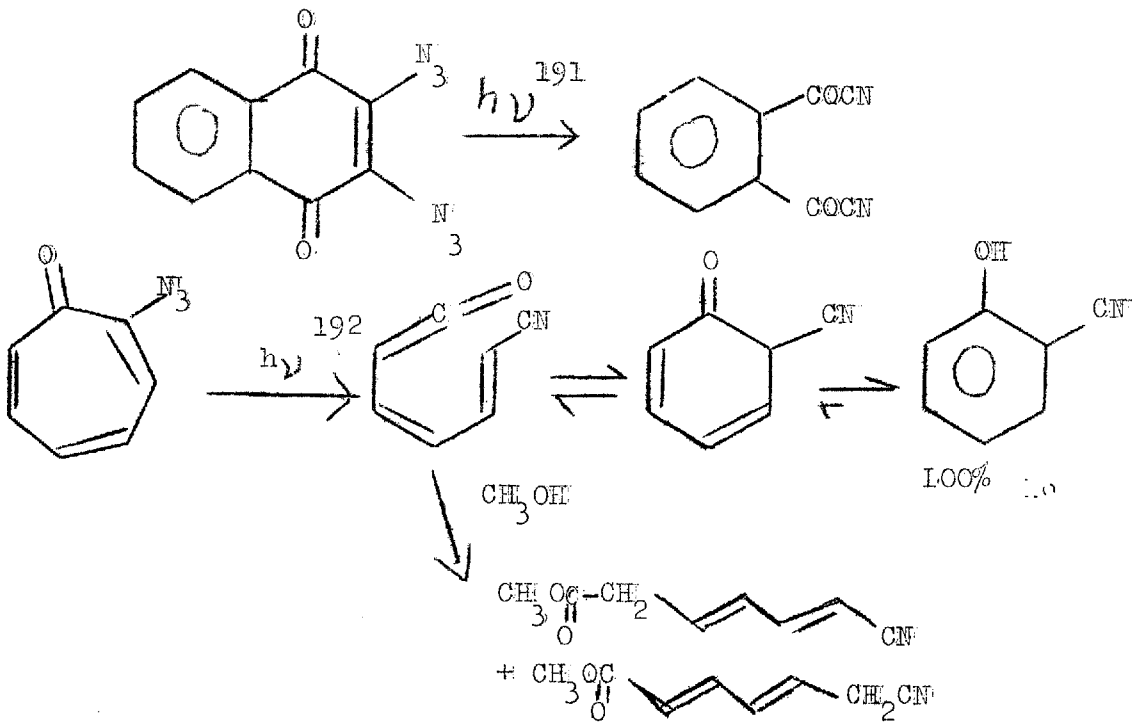


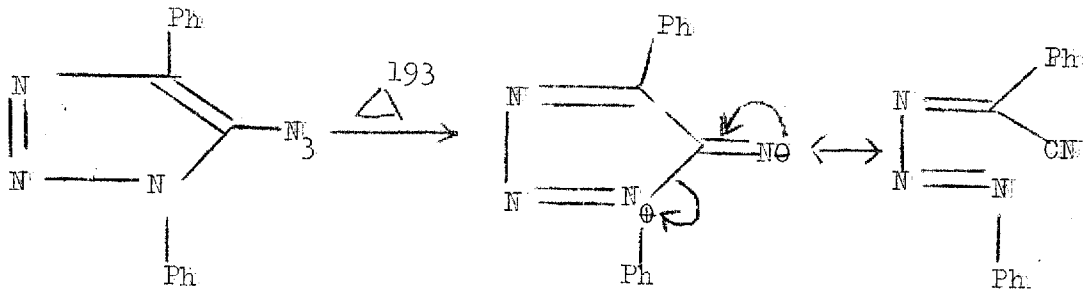
Under these conditions pyridines are also formed. This must involve N-insertion, C-extrusion and loss of carbon. Since the same products are obtained from phenyl azide and triazole (72) at 500°C and 0.04 mm it is reasonable to consider an equilibrium between phenyl nitrene and 2-pyridyl carbene (73)[190].



Reactions Producing Nitriles

Some compounds produce nitriles from the nitrene intermediate. This is the case for vinyl azides (see page 33), and some other cases are shown below.




Ph
N
N
N
N
Ph
193
Ph
N
N
N
NΘ
Θ
Ph
Ph
N
N
N
CN
Ph

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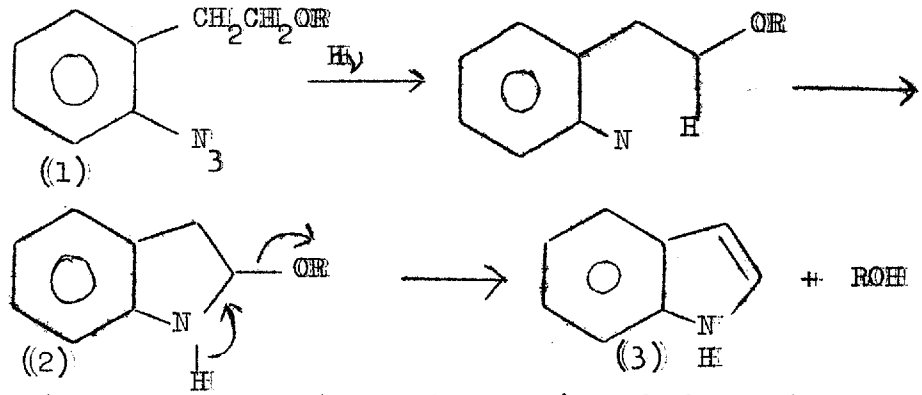
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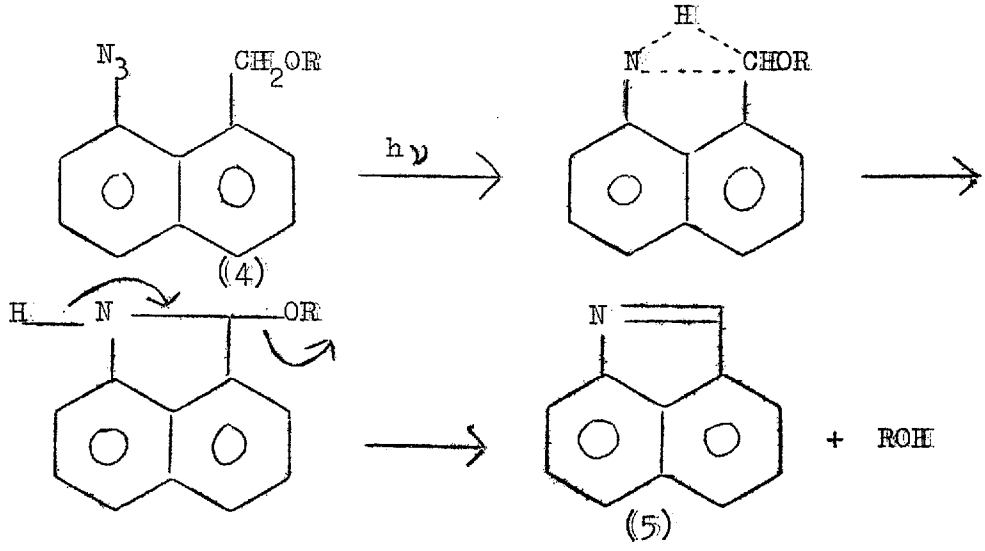
DISCUSSION

Introduction

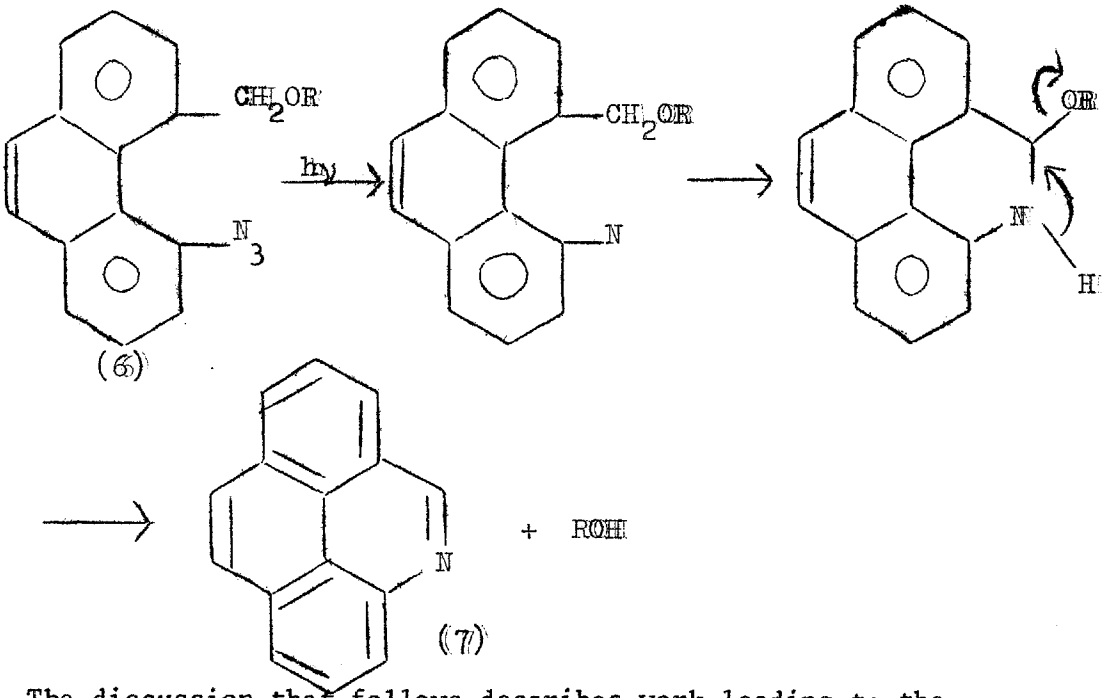
In the present design of a photosensitive protecting group for alcohols and carboxylic acids, the photolysis envisaged was that of an o-azido-β-phenethyl ether or ester (1). Insertion of the nitrene into the C-H bond adjacent to the oxygen atom should occur readily, giving a carbinolamine derivative (2) which would eliminate the acid or alcohol ROH and leave indole (3).



As an improvement on this model we envisaged the need to impose some rigidity on the system and bring the important C-H bond closer to the nitrene. Thus we planned to prepare and photolyse the peri-naphthyl azide (4).



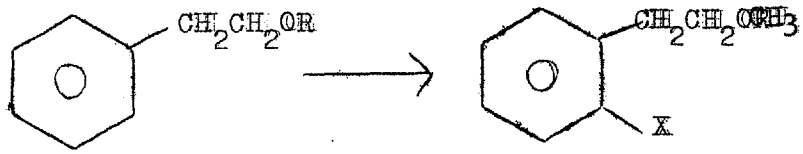
The photoproduct benz(cd)indole (5) is not completely aromatic, so its formation provides no great driving force for the elimination of ROH. Thus the 4,5-disubstituted phenanthrene(6) would probably be an even better system. The reactive centres are even closer together than in the peri-naphthyl azide and the final product 1-azapyrene (7) is fully aromatic.



The discussion that follows describes work leading to the synthesis of these compounds and the photolysis of them and related systems.

Synthesis of o-azido-β-phenethyl methyl ether (12)

The methyl ether of the first model system considered (12) was synthesised to test whether the proposed photolysis would in fact work giving indole (3) as predicted.



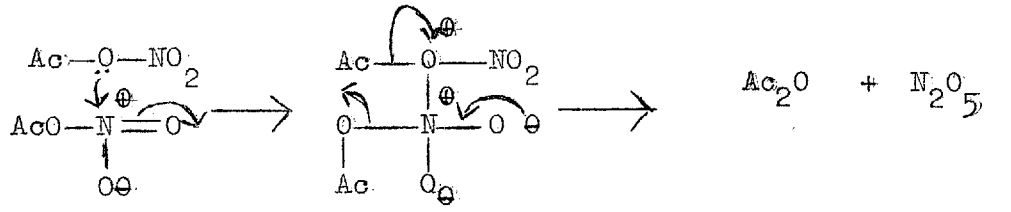
(8) R = H
(9) R = CH_3

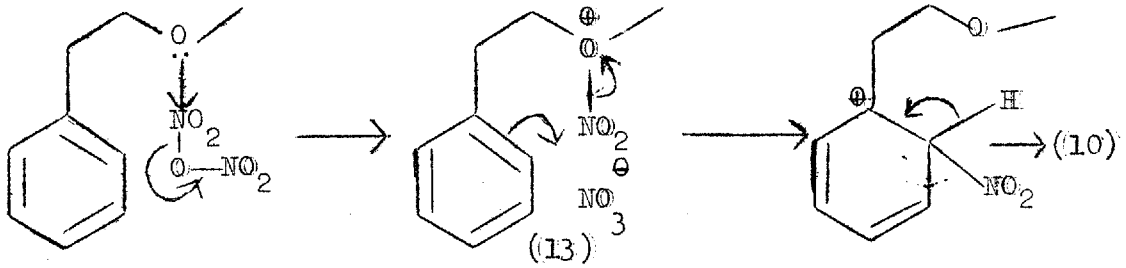
(10) X = NO_2
(11) X = NH_2
(12) X = N_3

β-phenethylalcohol (8) was methylated with dimethyl sulphate and base.[1] Nitration of the methyl ether (9) gave a mixture of ortho and para nitro isomers which were separated by column chromatography. The oily ortho isomer (10) was eluted first and the crystalline para isomer in later fractions[2,3]. The purity of (10) was established by thin layer chromatography (TLC) and gas-liquid chromatography. Confirmation of the structure was obtained from the splitting pattern of the aromatic protons in the nuclear magnetic resonance spectrum (NMR), which was identical to that of o-nitrotoluene.

Nitration of (9) with a mixture of conc. nitric acid and conc. sulphuric acid is reported to give 31.6% ortho, 9.4% meta and 59.0% para substitution. Using acetic anhydride and fuming nitric acid (acetyl nitrate), the isomer ratios were 63.3% ortho, 3.7% meta, 34.0% para,[4] and this was the nitrating agent used in the present work. The

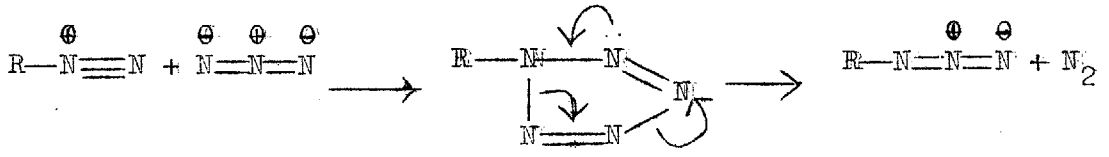
nitrating species is considered to be N_2O_5 which adds to the ethereal oxygen in the side chain and is thus held in a suitable position (13) for selective nucleophilic nitration ortho to the side chain.





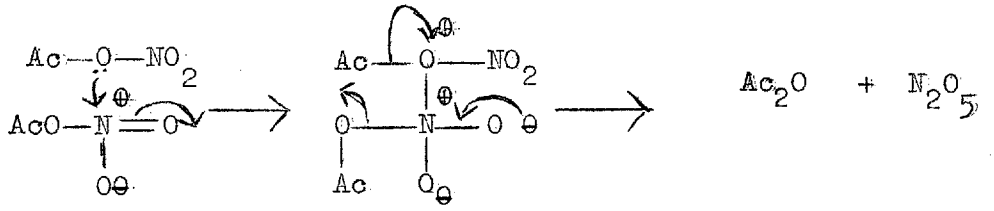
(13)

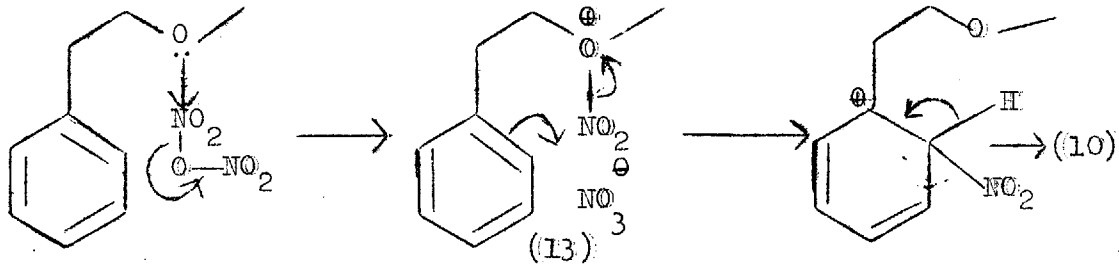
Reduction of (10) to amine (11) was accomplished with stannous chloride in hydrochloric acid in 82% yield. This was converted to the azide (12) in 77% yield by the standard procedure of diazotisation in acid solution with sodium nitrite and subsequent addition of sodium azide[5,6]. The azide (12) had a characteristic absorption at 2140 cm^{-1} in the infra-red spectrum (IR). The reaction of a diazonium compound with an azide anion has been shown to proceed via a pentazole intermediate (14)[7].



(14)

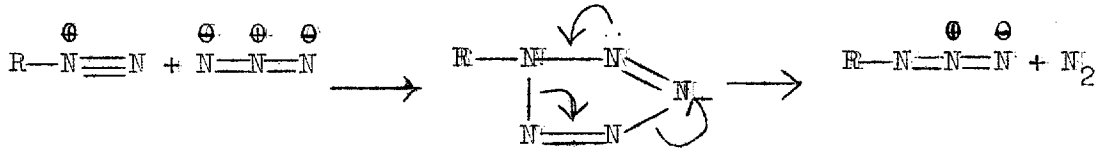
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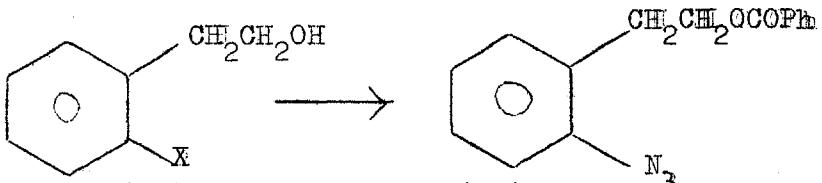
Photolysis of o-azido-β-phenethyl methyl ether

A benzene solution of azide (12) was irradiated in a pyrex flask with a medium pressure mercury vapour lamp. The course of the photolysis was followed by observing the reduction in intensity of the azide peak at 2150 cm^{-1} in the IR spectrum. After eighteen hours the photolysis was worked up and indole was isolated in 43% yield. It had the same R_f, IR spectrum and picrate as an authentic sample. Of the other photoproducts only o-aminophenethyl methyl ether (11) was identified.

This result showed that in principle the reaction under consideration was feasible as the basis for a photosensitive protecting group.

Synthesis of o-azido-β-phenethyl benzoate

Ortho-azido-β-phenethyl benzoate (18) was prepared and irradiated to test the potential of this system as a protecting group for acids and to examine some of the side products in greater detail.



(8) X = H (15) X = NO_2 (18)

(16) X = NH_2 (17) X = N_3

The azido benzoate (18) was prepared in much the same way as was the corresponding methyl ether (12). Nitration of β-phenethyl alcohol (8) with acetic anhydride and fuming nitric acid at 0° C and hydrolysis of the crude nitro acetate with methonolic HCl gave a mixture of ortho and para nitro isomers in 95% yield[8]. A crude separation by pouring the mixture onto ice gave a solid from which pure para-nitro-β-phenethyl alcohol could be obtained on recrystallisation from carbon tetrachloride and an oil from which pure ortho-nitro-β-phenethyl alcohol (15) was isolated by column chromatography.

Reduction with stannous chloride in concentrated hydrochloric acid at room temperature gave the amine (16) as a yellow oil in 77% yield. Reduction with ammonia and hydrogen sulphide gave only

a 51% yield of (16). Ortho-amino-β-phenethyl alcohol was identified by the characteristic amine absorptions at 3450, 3400 and 1630 cm^{-1} in the IR. Diazotisation and treatment with sodium azide[5,6] converted this to o-azido-β-phenethyl alcohol (17) in 80% yield which had a hydroxyl peak at 3400 cm^{-1} and an azide peak at 2150 cm^{-1} in the IR. The benzoate (18) was prepared by reaction with benzoyl chloride in pyridine in 86% yield. In the IR spectrum it had a carbonyl peak at 1720 cm^{-1} and an azide peak at 2150 cm^{-1}.

Photolysis of ortho-azido-β-phenethylbenzoate

The usual irradiation procedure employed was to irradiate a solution of about 200 mg. of the azide in about 30 ml. dry solvent. The products isolated from photolyses carried out under various conditions are summarised in Table I.

In all experiments, the major product was a brown polar benzoate of unknown structure. Polymeric products often arise on photolysing aryl azides by a process such as[9]

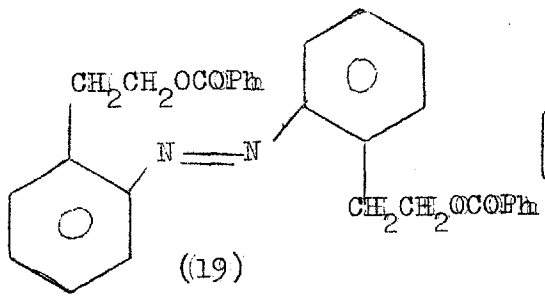
$$ArN_3 \longrightarrow Ar\,N \longrightarrow Ar - NH - AR\,N_3 \longrightarrow \ldots$$

The anticipated insertion reaction occurred only to a small extent; the yield of benzoic acid isolated was only 5 - 12%.

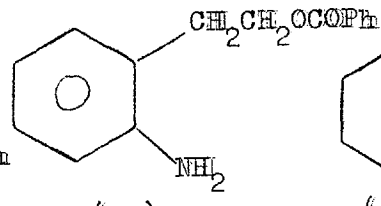
TABLE I Photolysis of ortho-azido-β-phenethyl benzoate

SOLVENT	REACTOR	LAMP	TIME	PRODUCTS
1 THF	Silica	Low Pressure	30 mins.	Benzoic acid 12% (19) 16%
2 Benzene	Silica	Low Pressure	3 hrs. 40 mins.	Benzoic acid 5% (19) 35%
3 Benzene	Flow*	Germicidal 15w.	2 passes approx. 11 mins.	Benzoic acid 6% (19) 19%
4 Benzene	Pyrex	Medium Pressure	9½ hours	Benzoic acid 7% (19) 13% Indole 8% (20) 11% (21) 5½%
5 Ether	Pyrex	Medium Pressure	12 hours No further loss. of azide after 9 hrs.	Benzoic acid 9% (19) 2% (20) 5% (21) trace indole 2%
6 Piperylene	Pyrex	Medium Pressure	9 hours	Benzoic acid 8% (23)* 8% (19) 0%
7 Piperylene 35% Benzene 65%	Silica	Low Pressure	3½ hours	Benzoic acid 11% (19) 16%
8 Piperylene 40% THF 60%	Pyrex	Medium Pressure	12 hours	Benzoic acid 21% (19) <1% Indole, (23) 4%

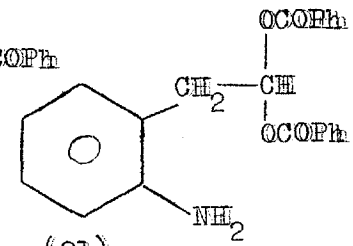
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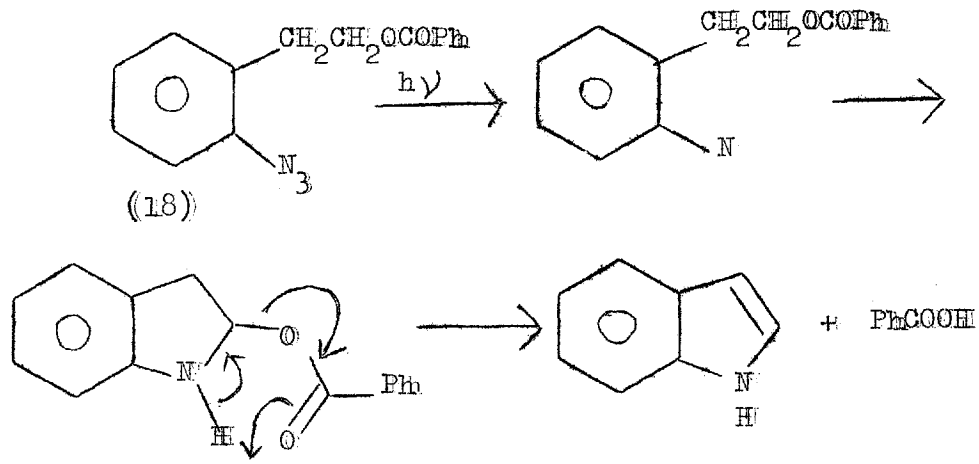
(19)



(20)



(21)

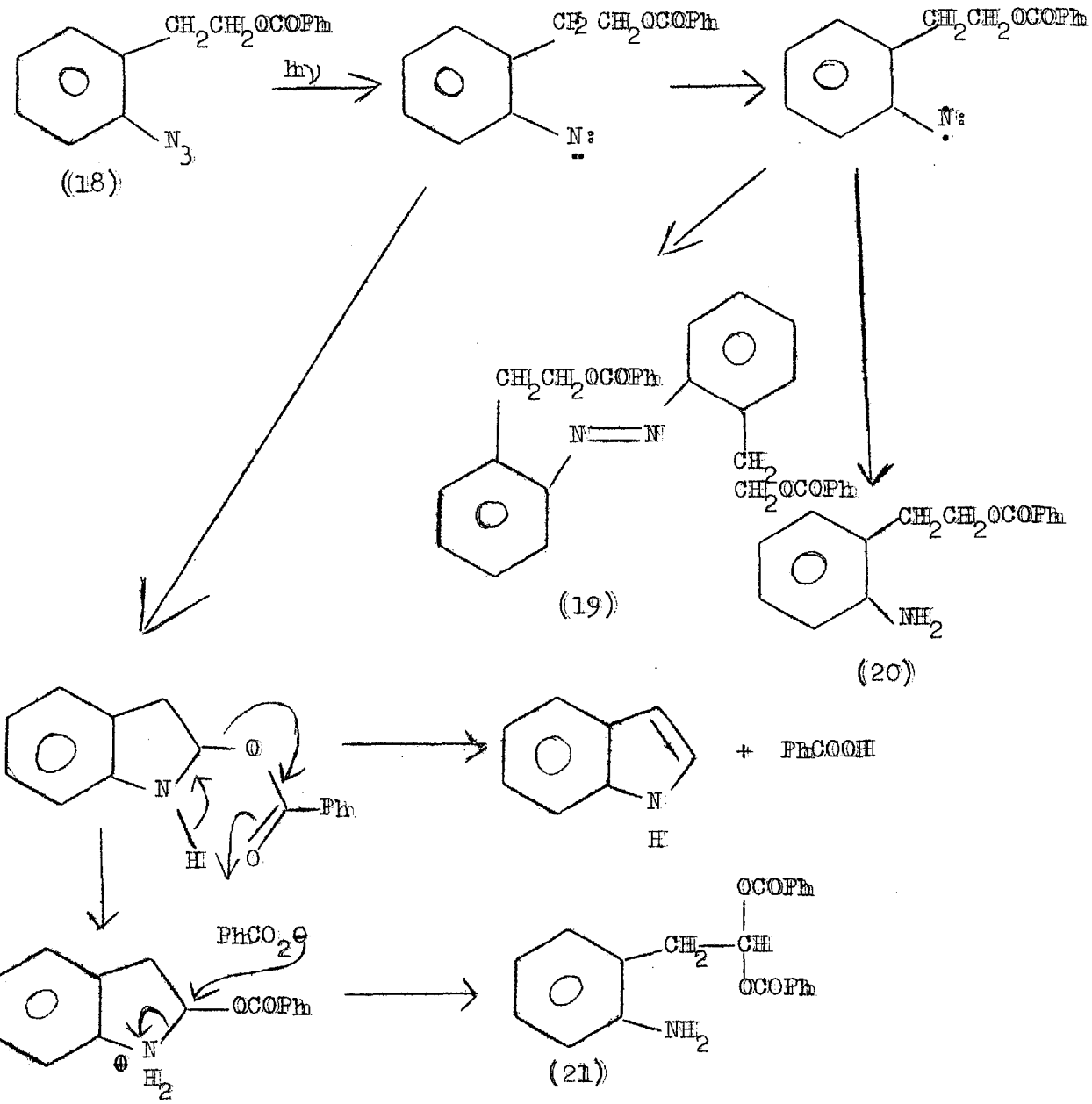


The other product, indole, was also obtained in low yield but none was found when a silica photolysis flask was used. Either a different process occurs to generate benzoic acid when light below 300 mμ is used or perhaps indole is sensitive to this irradiation. The yield of indole was often lower than that of benzoic acid, probably because indole polymerises in the presence of acid[10].

Among the other products isolated were the azo compound (19) which was formed in fair yield in all direct photolyses, ortho-amino-β-phenethylbenzoate (20) which had IR peaks at 3490, 3410, 1715 cm^{-1} and two protons at 6.2 τ in the NMR which were exchanged by D_2O, and 2-(ortho-anilino)-1,1-dibenzoylethane (21). The structure of (21) is based on the following spectral data. It analysed for $C_{22}H_{19}NO_4$. The infra-red spectrum with peaks at 3490, 3400, 1740, 1710, 1630 cm^{-1} indicated that it was a primary amine with two carbonyl groups. From the NMR spectrum it was clear that the molecule contained one methylene group which absorbed at 6.85 τ as a doublet (J = 5.5 cps) coupled to a methine proton at about

3.0 τ. The presence of two benzoate groups was evident from the aromatic portion of the NMR where there were four low field protons at 2.30τ (the protons ortho to the carboxy groups) and ten other aromatic protons at 2.5 - 3.5 τ. The amine signal at 6.5 τ disappeared when the solution was shaken with D_2O.

These products can be accounted for as follows:

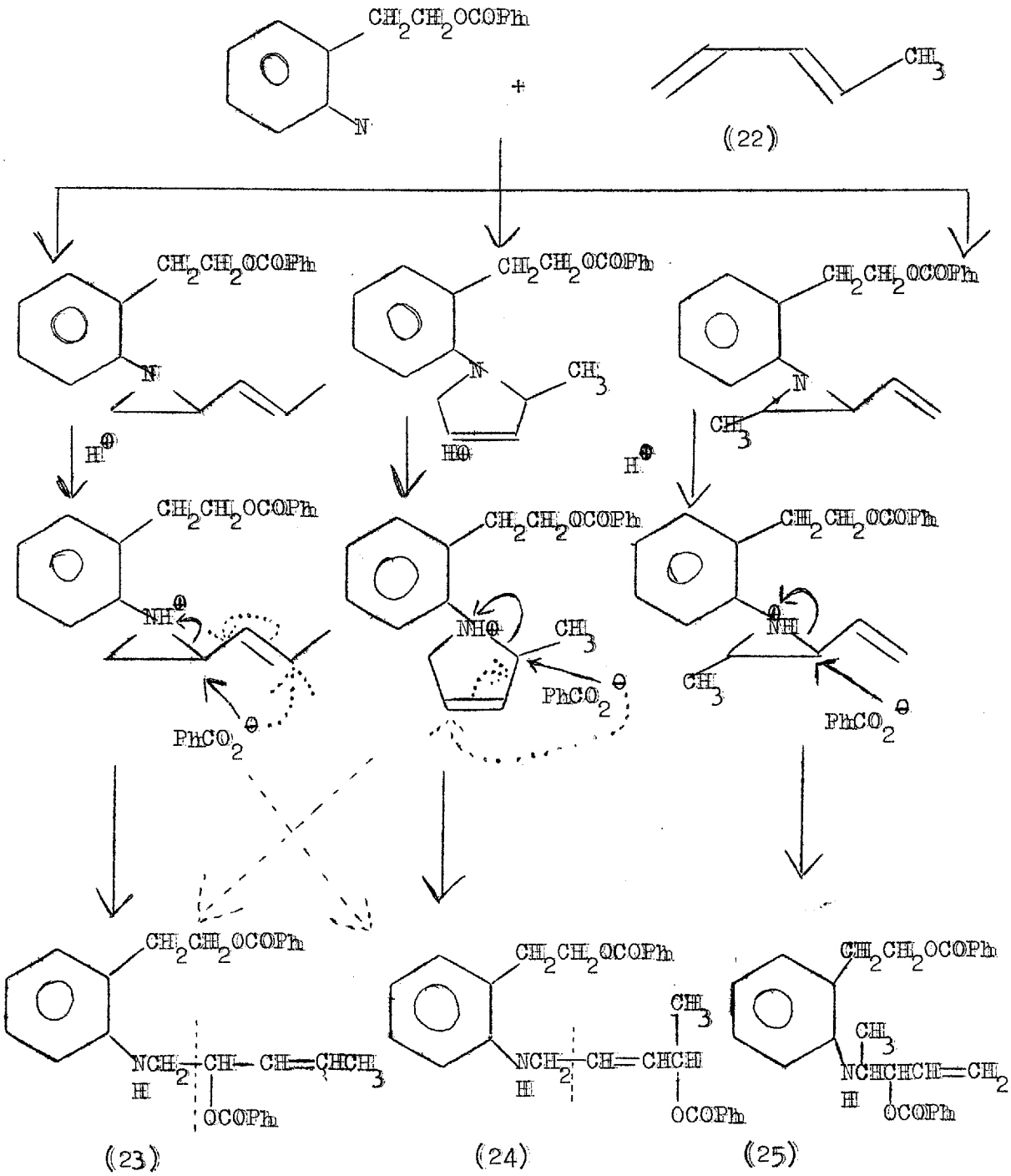


The photolysis was also carried out in the presence of a large excess of piperylene (22), a triplet quencher. In this way it was hoped that any triplet azide that might be formed would cascade to the ground state and be available for re-excitation to a singlet excited state. We would thus eliminate side products arising from triplet azide and reduce the yield of products arising from triplet nitrene, as these would no longer be formed by loss of nitrogen from triplet excited azide molecules, but only from singlet nitrene molecules by inter-system crossing.

It was found that indeed the formation of the azo compound (19) was suppressed under these conditions and the yield of benzoic acid was significantly increased. A reasonable inference from these results is that azo compound (19) is formed from a triplet species and insertion is a reaction of singlet nitrene. Thus for our purposes the photolysis should be carried out under conditions favouring the formation of a singlet nitrene.

A new product was isolated from these quenching experiments and was assigned the structure (23). It was a fairly polar oil and the infra-red spectrum showed the presence of a secondary amine (3420, 1605 cm^{-1}) and two carbonyl groups (1720, 1710 cm^{-1}). Mass measurement of the molecular ion in the mass spectrum gave the molecular formula as $C_{27}H_{27}NO_4$. The NMR spectrum would fit structures (23) and (24) but not the other structure considered (25). The ethyl side chain methylene groups appeared as triplets J = 8 cps.

at 5.72 τ and 7.18 τ respectively. The other methylene group was a multiplet at 6.55 τ. The methyl signal at 8.27 τ was complex



and the possibility of the presence of cis and trans isomers is not excluded. There were four aromatic protons at 1.9 - 2.3 τ and ten at 2.5 - 3.6 τ indicating the presence of two benzoate groups. A broad signal at 5.2 τ was the amine proton and the remaining three protons gave a complex pattern at 4.0 - 4.5 τ. Thus it was futile to attempt to decouple the methyl signal in order to distinguish between (23) and (24).

In the mass spectrum there was a fragmentation of 175 mass units from the parent ion (M/e 254, metastable peak at M/e 150). This corresponds to the loss of C_4H_6OCOPh and would be more likely from (23) than (24) (shown as a dotted line). This fragmentation rules out structures arising from addition of the nitrene to the methyl substituted double bond of (22) eg. (25) as well as structures derived from attack of the benzoate anion at non-allylic or non-vinylic positions.

An unusual fragmentation in this spectrum is the loss of C_3H_3 after loss of benzoic acid from the molecular ion (or perhaps loss of $C_3H_4OCOC_6H_5$ from the molecular ion). This fragmentation is observed in allylic esters, but the allylic benzoate (25) has already been excluded. It can be more easily accounted for by structure (23) than (24) and thus this is the preferred structure.

Ozonolysis of the compound followed by work up with zinc dust in acetic acid and subsequent addition of 2,4-dinitrophenylhydrazine did not unequivocably give acetaldehyde-2,4-dinitrophenylhydrazone.

The mechanism of this reaction is not immediately obvious. Benzoic acid probably exists as an intimate ion pair in the solvents used (neat piperylene and a piperylene-tetrahydrofuran mixture) so that attack by the benzoate anion occurs before a delocalised allylic carbonium ion has formed. In such a situation the product must arise from the aziridine intermediate and not the pyrrole. Thus the nitrene adds 1,2 to the diene and is probably in the singlet state since a triplet nitrene would have to undergo a slow spin inversion after the formation of the first C-N bond allowing time for alignment of the atoms to give the less strained five membered ring by a 1,4-cycloaddition rather than the three membered aziridine[11], (but see page 32).

Clearly this is a tennuous picture of the mechanism based on several speculative assumptions. It would be interesting to show that it is a triplet nitrene which reacts with piperylene. In contrast to a triplet excited azide where quenching by piperylene gives a ground state azide, triplet nitrene has no analogous process since this is the ground state of the nitrene. The quenching operation may, therefore, involve reaction of the triplet nitrene with the quencher. The absence of triplet nitrene products (amines and the azo compound) in the quenching experiment may indicate that this is the case (right half of Fig. III). If, on the other hand, a singlet nitrene is responsible for the adduct formation, this merely shows that it reacts faster than undergoing inter-system crossing to the triplet state (left half of Fig. III).

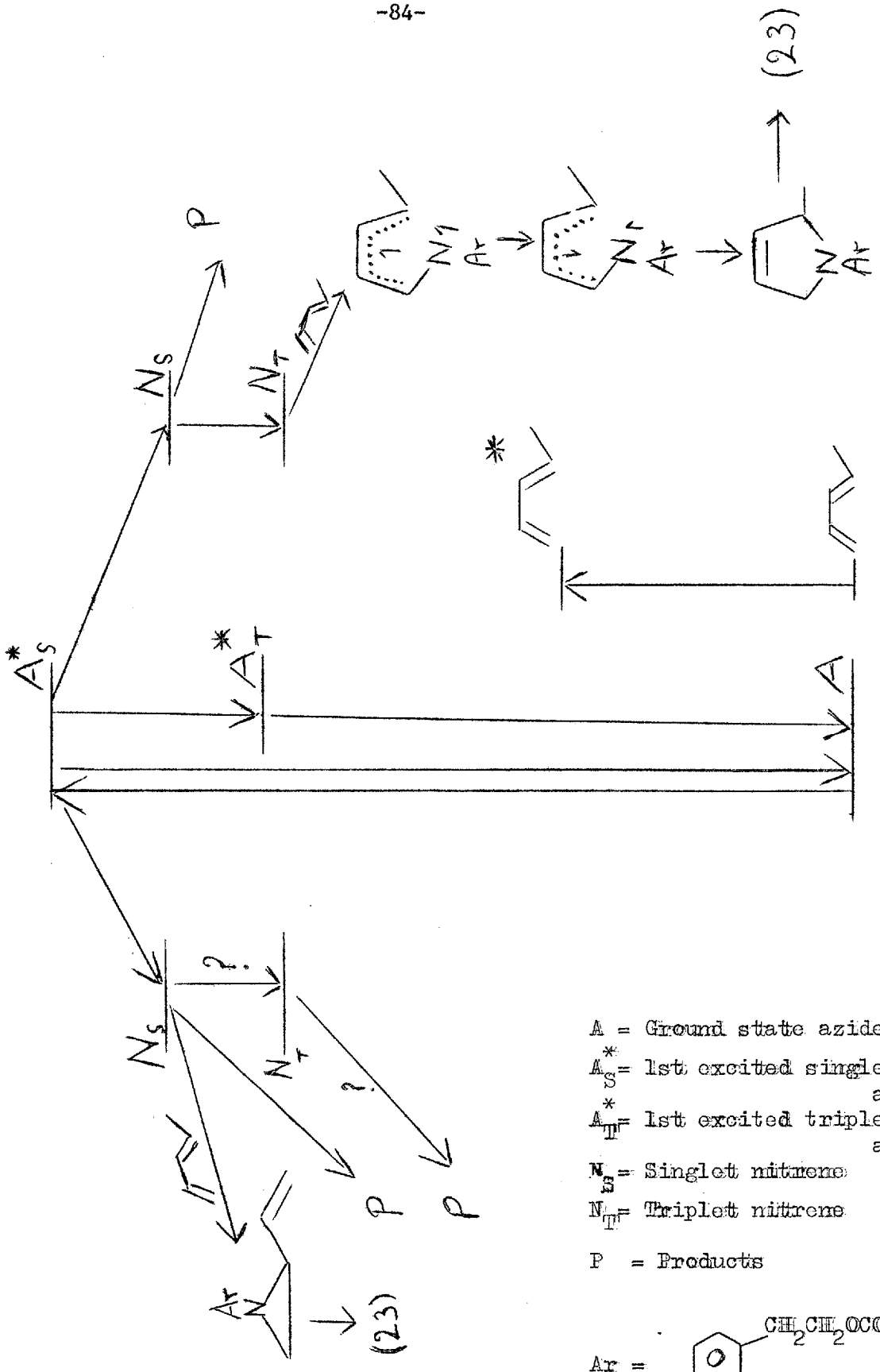


FIG. III

A = Ground state azide

A^*_S = lst excited singlet state azide

A^*_T = lst excited triplet state azide

N_S = Singlet nitrene

N_T = Triplet nitrene

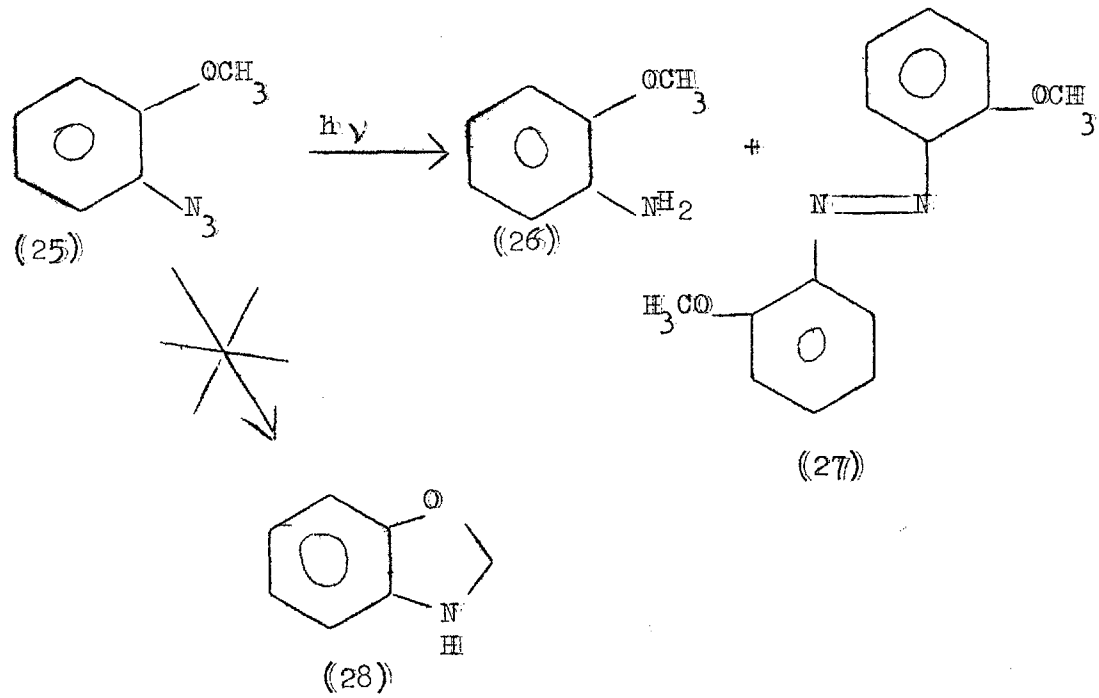
P = Products

Ar =

Photolysis of Some Related Molecules

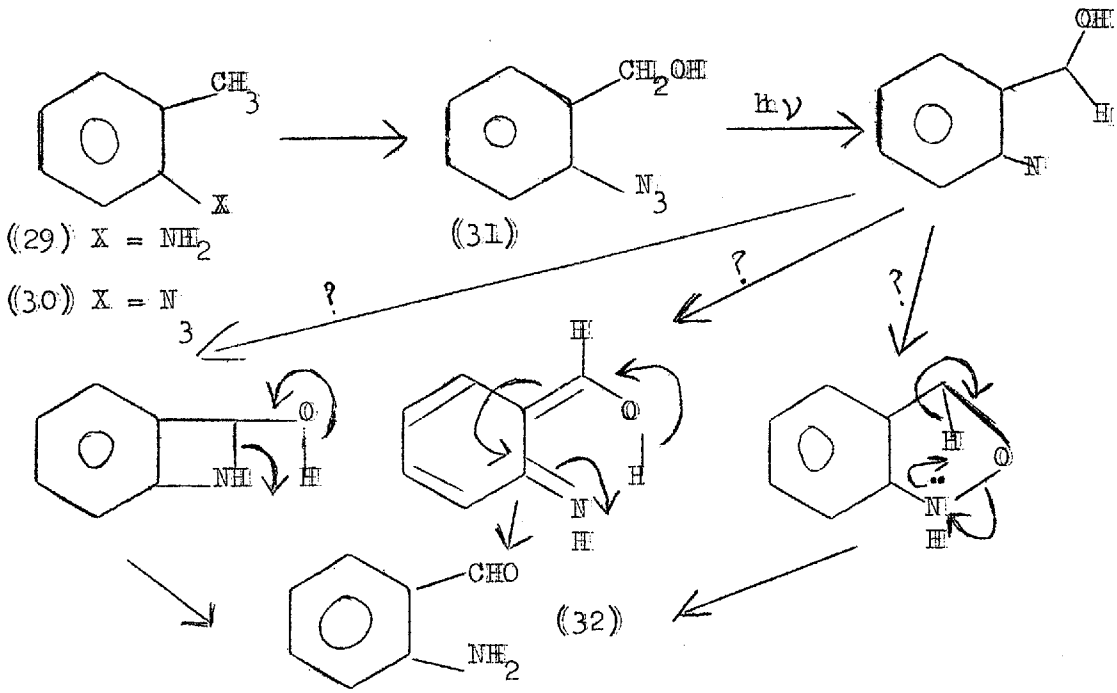
It was decided to investigate the photolysis of some azides related to the ortho-phenethyl azides where the nitrene might also insert into a C-H bond next to an oxygen atom.

The first compound considered was ortho-azidoanisole (25), which was irradiated in dimethyl sulphoxide and benzene. The major products were ortho-anisidine (26) and ortho-azo-anisole (27). There was no evidence in the NMR spectrum of the basic products of the anticipated insertion reaction products (28). The broad spread of the aromatic protons in the NMR of (27) indicated that the trans isomer was formed.



Ortho-azidobenzyl alcohol and ortho-azidobenzyl benzoate

Ortho-azidotoluene (30) was prepared from ortho-toluidine (29) in the usual way[5,6] and was then reacted with N-bromosuccinimide and benzoyl peroxide in refluxing carbon tetrachloride. Moisture was not excluded and ortho-azidobenzyl alcohol (31), was formed in 51% yield. The presence of an azide group was evident from the strong peak at 2150 cm^{-1} and the hydroxyl group from a peak at 3300 cm^{-1}. The methylene group appeared as a singlet at 5.48 τ in the NMR.

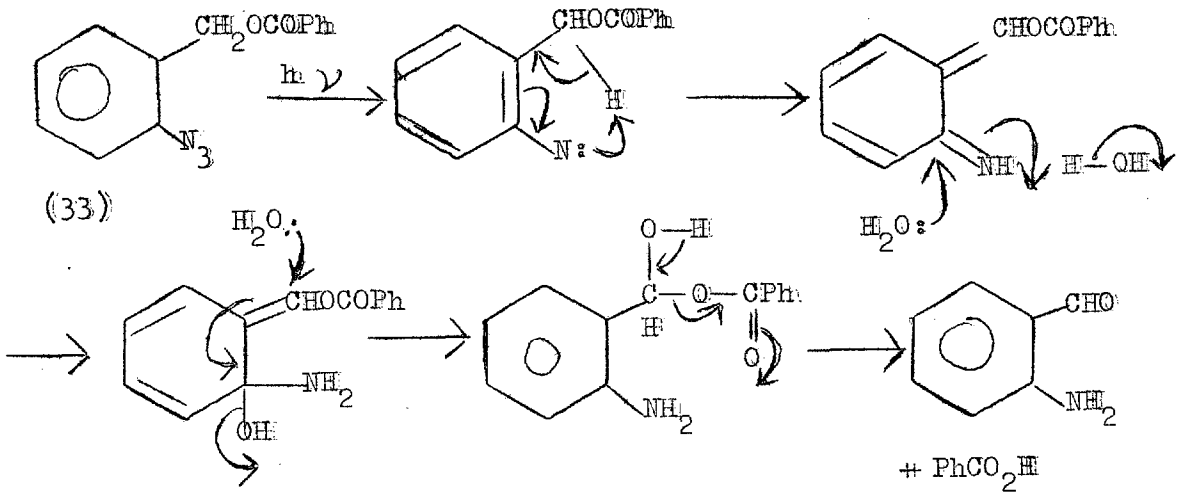


Photolysis of this azide in dry hexane gave ortho-amino-benzaldehyde (32) as the sole product as well as a tar which presumably consisted of condensation and polymeric products of this unstable compound. It was identified by the amine peaks in

the IR at 3380 cm^{-1} and at 4.4 τ in the NMR, the carbonyl absorption at 1665 cm^{-1} and the low field formyl proton at 0.2 τ. It was characterised as the phenylhydrazone derivative which had the same physical properties as is reported[12].

The same product was formed on vapour phase pyrolysis of ortho-azidobenzyl alcohol[12]. Some possible mechanisms are indicated above.

This result suggests that irradiation of ortho-azidobenzyl benzoate (33) in the presence of a nucleophile such as water might be a good way of eliminating benzoic acid in high yield.



NBS bromination of (30) in dry benzene gave o-azidobenzyl bromide in 60-75% yield which had a methylene singlet at 5.63 τ in the NMR. Heating this with sodium benzoate in N,N-dimethylacetamide furnished the benzoate (33) in 83% yield (33) had an azide absorption at 2150 cm^{-1} and a carbonyl absorption at 1715 cm^{-1} in the IR. In the NMR there were two methylene protons at 4.69 τ, two aromatic

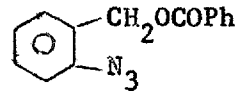
protons at 1.87 - 2.07 τ and seven aromatic protons at 2.5 - 2.9 τ. This benzoate was formed as a minor product (7%) in the radical bromination reaction. An attempt to prepare it by reacting ortho-azidotoluene with benzoyl peroxide failed.

The solvent used for the NBS bromination was dry benzene. Benzene was chosen in preference to the customary carbon tetrachloride because at the time the first reaction of azides with free radicals had just been reported[13]. Phenyl azide reacted with a trichloromethyl radical generated from carbon tetrachloride by a process initiated by the thermal decomposition of benzoyl peroxide.

$$PhN_3 + (PhCO_2)_2 + CCl_4 \longrightarrow \text{Cl}\langle\bigcirc\rangle\text{—N} = CCl_2$$

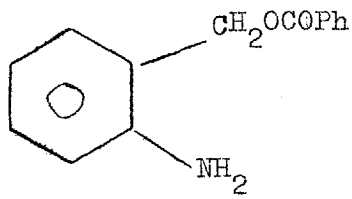
The benzoate (33) was photolysed under several conditions as summarised in Table II. Irradiation with a low pressure lamp in a Silica flask was complete in about 45 minutes, but when a medium pressure mercury lamp and a pyrex flask were used about half the original azide was recovered after a much longer period. In one case (experiment 8), following the progress of the photolysis by observing the reduction in intensity of the azide peak in the IR showed that after eighteen hours no more azide decomposed. In the extended photolyses a film was deposited on the walls of the flask obscuring the incident irradiation.

In general low yields of benzoic acid were obtained and the major product (about 60 - 70%) was a brown polar material which IR

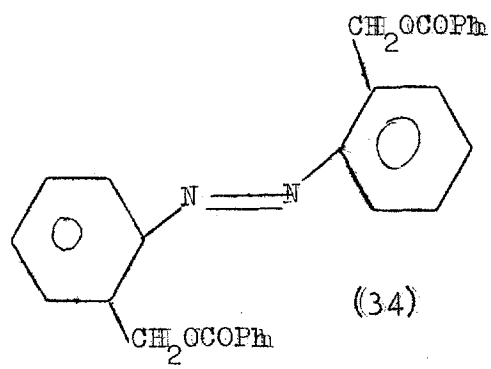
TABLE II Photolysis of 

SOLVENT	REACTOR	LAMP	TIME	PRODUCTS
1 Hexane, water	Flow[a]	Germicidal	1 pass 20 mins	Benzoic acid 14%
2 Hexane, water	Silica	Low Pressure	175 mins	Benzoic acid 12% Azo compound(34) 6%
3 THF, water	Silica	Low Pressure	45 mins	Benzoic acid 2% Azo compound(34) 7%
4 Acetone	Silica	Low Pressure	240 mins	Benzoic acid 0% Azo compound(34)16%
5 Methanol	Silica	Low Pressure	45 mins	Benzoic acid 32% Azo compound(34) 8%
6 Methanol	Flow[a]	Germicidal	1 pass 6 mins	Benzoic acid 17% Azo compound(34) 9%
7 THF, water	Pyrex	Medium Pressure	25½ hours	Benzoic acid 18% Azo compound(34) 0% Recovered azide 45% Amine(35) 31%
8 Acetone	Pyrex	Medium Pressure	37½ hours[b]	Recovered azide 43% Azo compound(34) 22% Benzoic acid 0%

a see text
b no further loss of azide after 18 hours

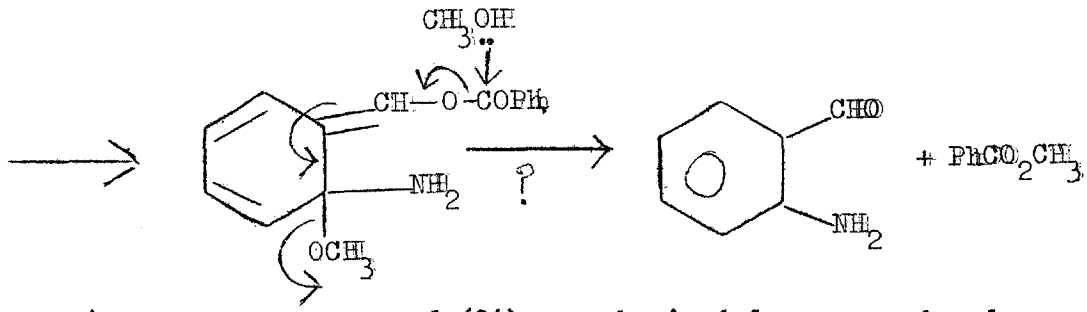


(35)



(34)

showed to retain the benzoate group. No benzoic acid was obtained in experiment 4 where no water was present, and although benzoic acid was found in experiments 5 and 6 where methanol was the nucleophile, there was no evidence for the formation the anticipated methyl benzoate.



An orange azo compound (34) was obtained from most photolyses. The increased yield of this in experiment 8 suggests that acetone is acting as a triplet sensitiser and that it is a triplet product in the direct photolyses.

These results are disappointing in that so much intractable material was formed at the expense of the desired reaction. Ortho-aminobenzaldehyde (32) was never isolated from among the products. Either it decomposed during the work up, or it was never formed and benzoic acid was produced by a photolytic hydrolysis reaction.

Flowing Film Photolysis Apparatus

Conventional photolysis equipment consists of a flask with a pyrex or silica well which contains an ultra-violet lamp or alternatively the reactor has an external light source as in the Rayonet Photochemical Reactor.

There are several drawbacks to these reactors. Over-photolysis or photolytic decomposition of the photoproducts may occur and often gives rise to polymeric coatings on the glass walls of the vessel, cutting off the radiation from the solution. Furthermore, the incident light is completely absorbed within a few millimetres of the solution from the flask walls, and hence efficient stirring is necessary. Thirdly, the mercury vapour lamps emit heat and a cooling system may be required.

Two similar falling film reactors have recently been reported[14,15] in which these problems have been overcome. A simple glass reactor based on these designs has been constructed and used in some of the azide photolyses (Fig. IV).

The apparatus is basically a long glass cylinder "turned over" at the top so as to form a reservoir into which the solution is fed. It leaves this reservoir through a narrow gap and the flow rate is adjusted so that a thin film flows down the walls of the tube and is exposed to the ultra-violet light. The irradiated solution collects in another reservoir at the bottom from where it flows out through an exit tube and can be recycled if necessary. Nitrogen can conveniently

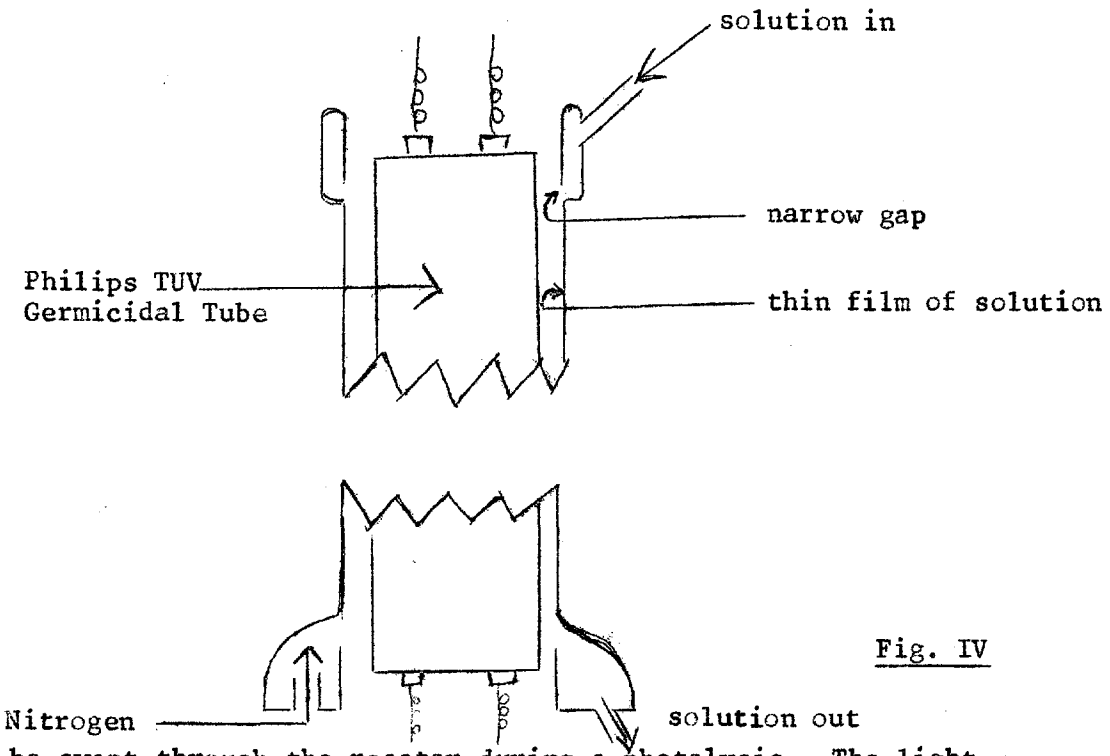


Fig. IV

be swept through the reactor during a photolysis. The light source used is a Philips 15 w. Germicidal lamp for irradiation at 2537 A^{o}, or one of the other Philips fluorescent tubes for other wavelengths.

The solution is thus irradiated directly without the intervention of expensive silica. If any solid products or films are formed, they are deposited on the glass surface and do not interfere with the transmission of the light to the solution. Over-photolysis can be avoided because the solution is not exposed to the irradiation for too long and is effectively being rapidly stirred. This apparatus could conveniently be used for large volumes of solution and if one pass is not enough, the solution can be recycled.

It is evident from the data given above for the photolysis of (18) and (33) that using this apparatus, azides are photolysed

much more quickly and efficiently than with the conventional equipment.

Based on another design in the same papers[14,15], a rotating film reactor has been constructed and used for the photolysis of a naphthyl azide (see page 104) (Fig. V).

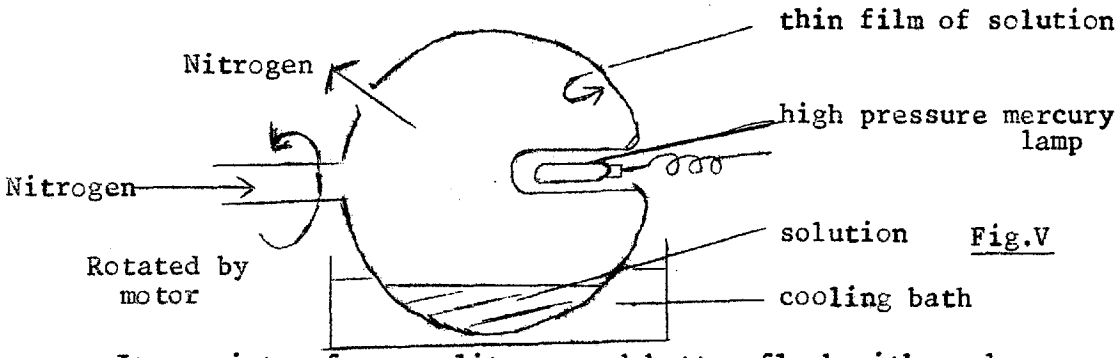
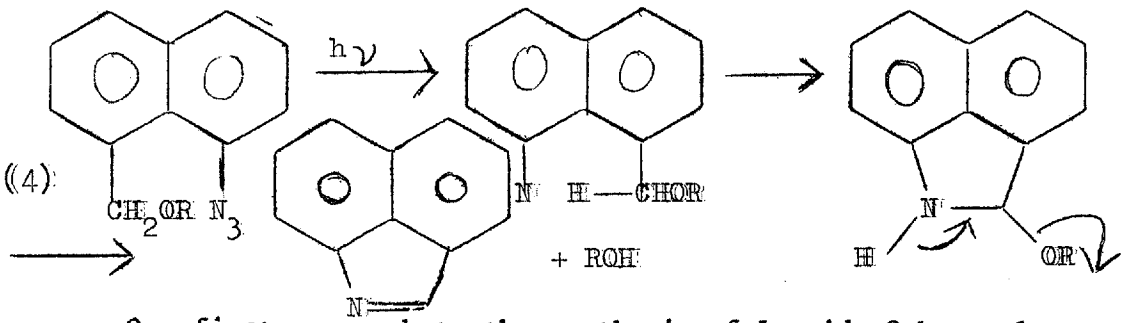


Fig.V

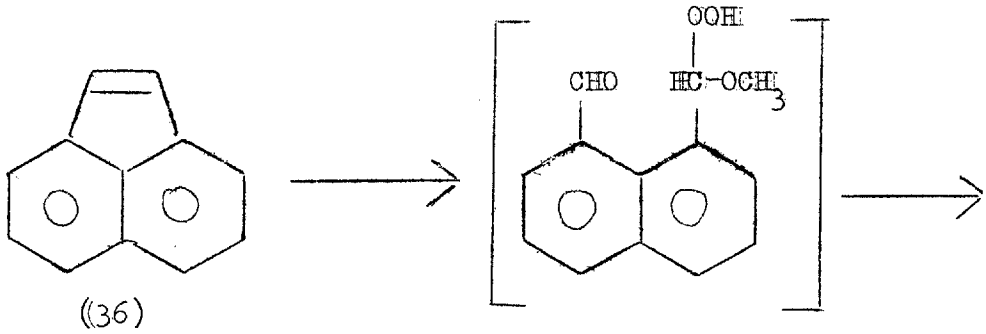
It consists of a one litre round-bottom flask with a glass thimble sealed into the bottom to contain a mercury vapour lamp. The flask is kept horizontal and rotated by means of a motor attached to the neck. A pool of solution collects at the bottom, and as the flask rotates, a thin film of solution forms on the walls and is irradiated. Since the lamp generates heat, the rotating flask is partly immersed in a cooling bath of cardice and acetone or methanol. This apparatus is also more efficient than the conventional reactor. Since the solution does not come into contact with the thimble housing the lamp, any films formed during a photolysis form on the glass surface remote from the solution and do not interrupt the light path.

Attempted synthesis of 1-azido-8 benzoyloxymethylnaphthalene

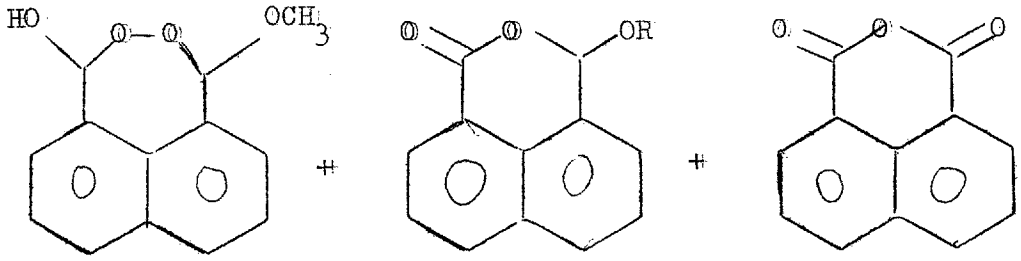
It was thought that by bringing the azide close in space to the methylene group into which nitrene insertion was to occur and by imposing some rigidity onto the molecule, the yield of the desired reaction product would be increased over what had been obtained thus far. The first model system chosen to test this hypothesis was the peri-naphthylazide (4), because it is well known that peri-substituents in naphthalene have a strong tendency to cyclise[16].



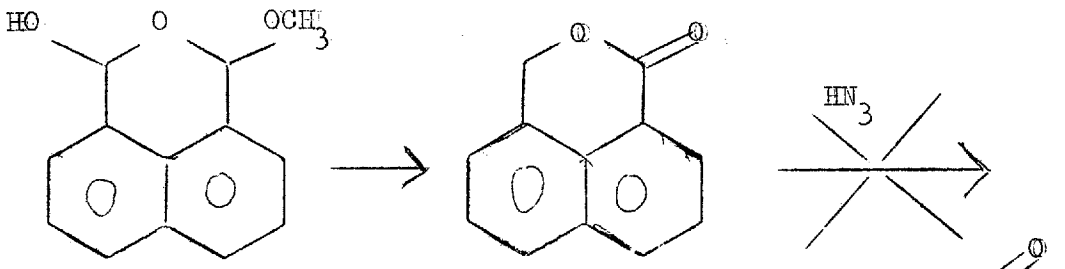
Our first approach to the synthesis of 1-azido-8-benzoyloxymethylnaphthalene (4) involved the preparation of 1,8-naphthalide (42) by ozonolysis of acenaphthalene (36) and treatment of this with hydrazoic acid. Schmidt reactions are not known for lactones[17], indeed phthalide has been reported to be inert to Schmidt conditions. Nevertheless, as no mechanistic objection to the desired reaction could be found it was decided to attempt it. The product 1-amino-8-hydroxymethylnaphthalene (43) could then be converted to (4) in two simple steps.



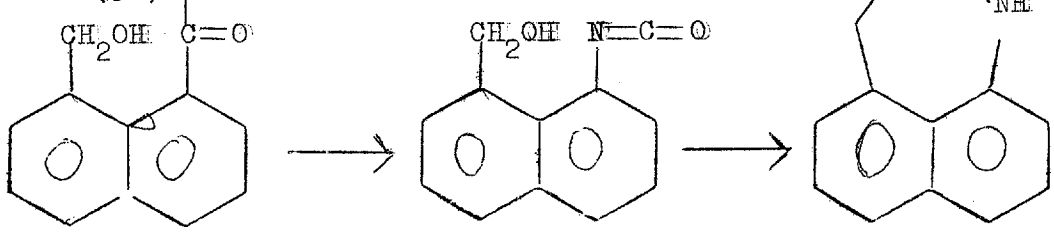
((36))

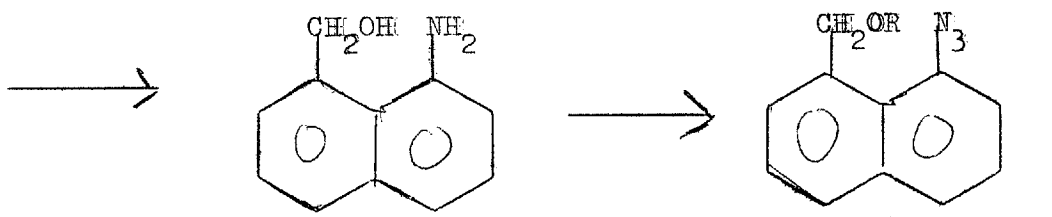


((37)) + ((39)) R = H, ((40)) R = CH_3 + ((41))



((38)) ((42))





((43)) ((4))

The ozonolysis of acenaphthalene in methanol has been reported in the literature[18,19]. 3-hydroxy-7-methoxy-4,5,6-(1,8-naphtho)-1,2-dioxacycloheptane (37) was precipitated during the ozonolysis in 18% yield. A new work up procedure, treatment with dimethyl sulphide, was employed to convert this to (38) in 88% yield. It was apparent from the methyl singlet at 6.33 τ in the NMR that we had obtained (38) and not 1,8-naphthalene-dialdehyde dihydrate which was obtained by the hydrolytic workup reported. However, on recrystallisation from hot water (38) demethylated giving the dihydrate. On stirring in aqueous sodium hydroxide (38) was converted to 1,8-naphthalide (42) in 72% yield by an intramolecular Cannizzaro reaction. In the NMR there was a methylene singlet at 5.01 τ and the carbonyl absorption in the IR came at 1710 cm^{-1}.

The filtrate obtained on filtering the ozonolysis solution contained the aldehydo acids (39) and (40) and naphthalene-1,8-anhydride (41). An intermolecular Cannizzaro reaction with potassium hydroxide and formalin reduced the aldehydo acids to 1,8-naphthalide (42) in 48% yield.

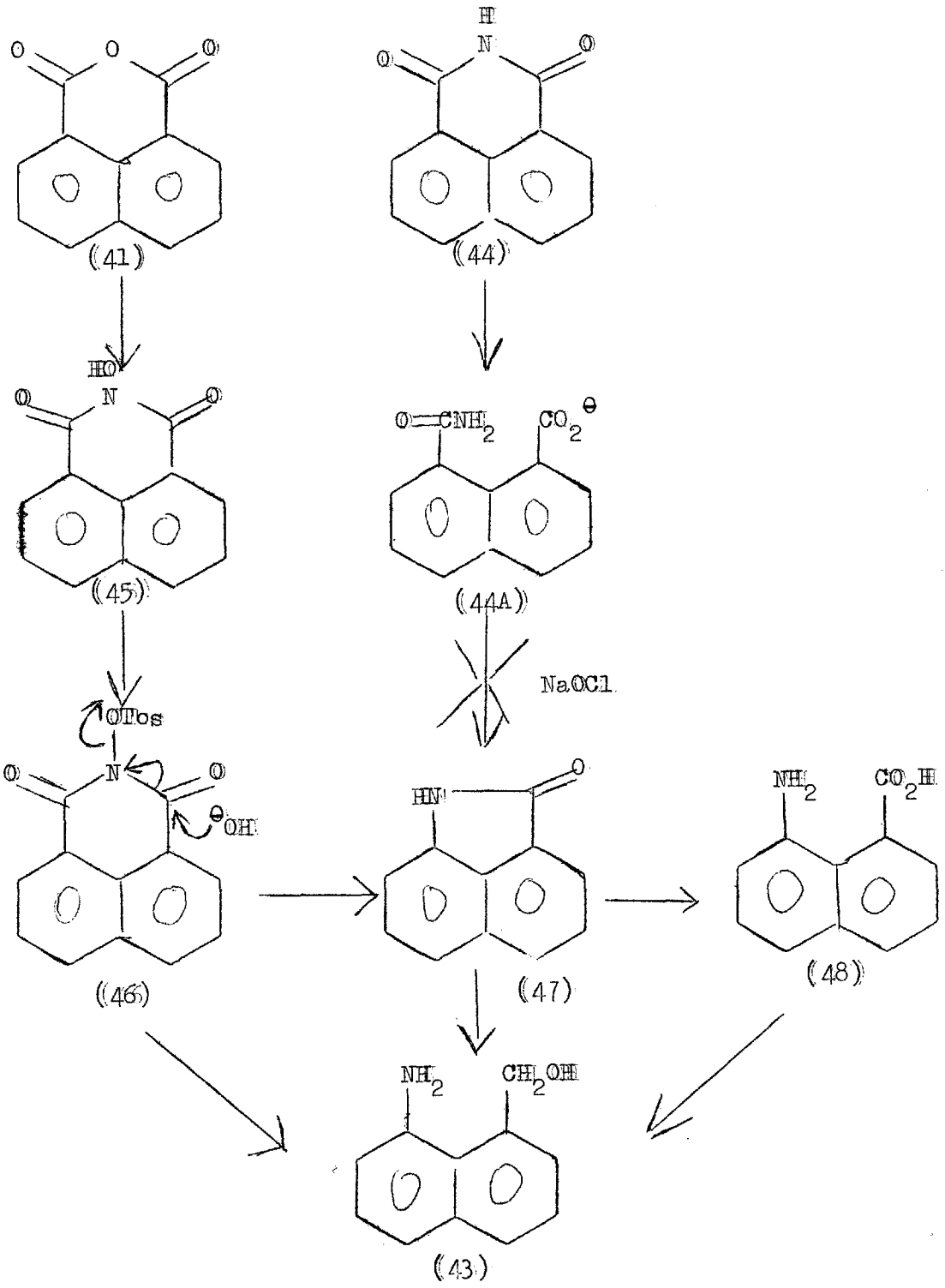
This synthetic approach was abandoned when it was found that naphthalide did not react with sodium azide in conc. sulphuric acid under various conditions.

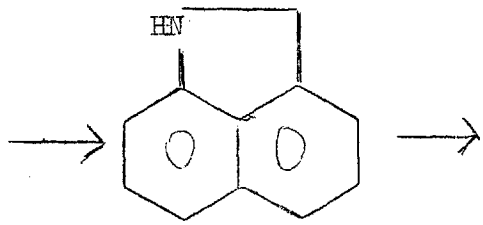
The second approach to the synthesis of (4) was the reduction of naphthostyril (47) or 1-amino-8-naphthalene carboxylic acid (48). Literature procedures for preparing naphthostyril by a Hoffman reaction

with naphthalimide (44) could not be repeated[20-23], so a new synthesis was devised.

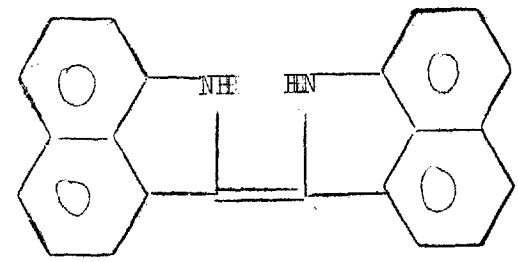
Naphthalic anhydride (41) was converted to the hydroxamic acid (45) by hydroxylamine hydrochloride in base[24] in 65% yield. Reaction of (45) with para-toluenesulphonyl chloride in pyridine gave the tosylate (46) quantitatively; (46) had bands at 1340 and 1190 cm^{-1} in the IR. Naphthostyril (47) was obtained in 60% yield when the tosylate was left standing in methanolic potassium hydroxide[25]. The lactam ring was opened by base giving (48).

Reduction of naphthostyril, the amino acid (48) and the tosylate (46) with lithium aluminium hydride all gave complex mixtures. The major component of these mixtures turned blue on exposure to air. A blue compound obtained when naphthostyril was reduced with lithium aluminium hydride in ethylmorpholine was thought to be (50) an oxidation product of benz(cd)indoline (49) which is formed initially[26].


(41)
(44)
(45)
(44A)
NaOCl
(46)
(47)
(48)
(43)



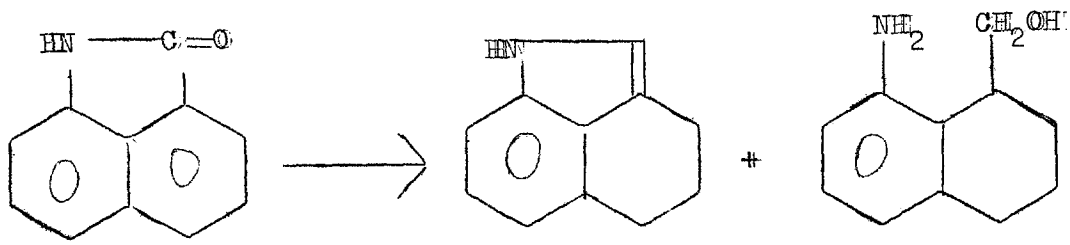
(49)



(50)

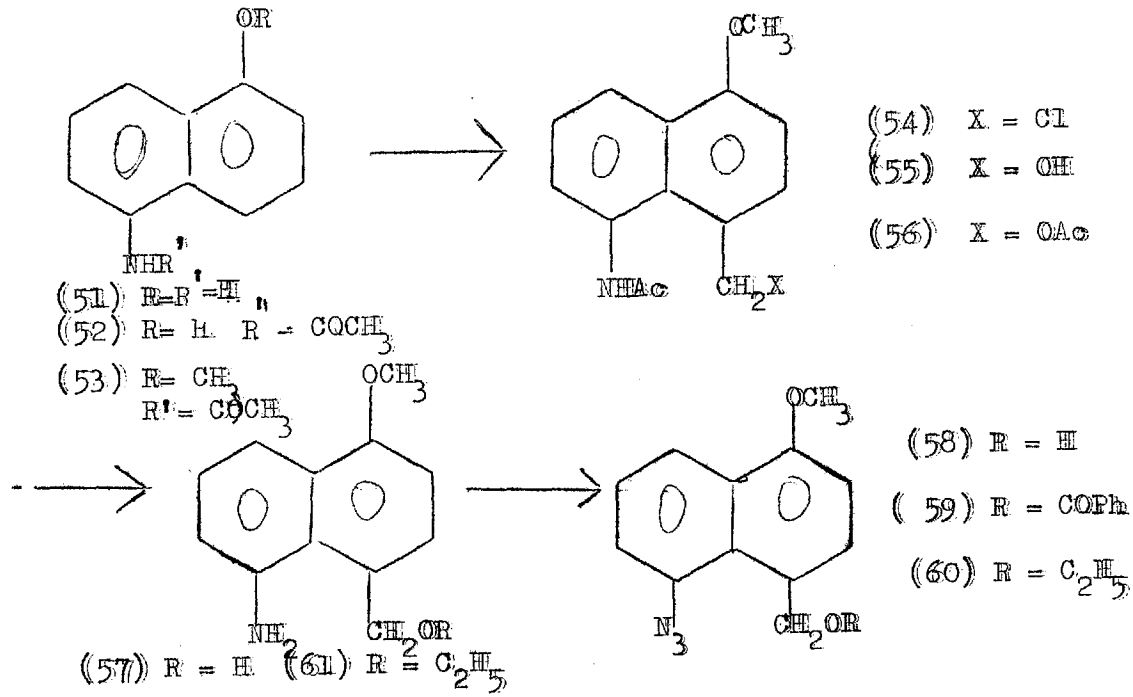
Evidently, 1-amino-8-hydroxymethylnaphthalene (43) that we had hoped to prepare is unstable and readily dehydrates to give the benz(cd)indoline (49).

Another reducing agent, sodium in butanol, is reported to partially reduce the aromatic system of naphthostyril[27,28].



Synthesis of 5-azido-4-benzoyloxymethyl-1-methoxynaphthalene

1-methoxy-4-hydroxymethyl-5-aminonaphthalene (57) is a stable compound reported in the literature[29] and it was prepared in much the same way as the literature procedure describes. 1-amino-5-hydroxynaphthalene (51) was acetylated and methylated to produce (53). Methylation of naphthol (52) with methyl iodide and potassium carbonate in refluxing dry acetone gave yields of 70 - 80% compared to 51% when the literature method was repeated using dimethyl sulphate and sodium hydroxide. Chloroformylation introduced a CH_2Cl group in excellent yield at the desired position, but hydrolysis of the crude chloro-compound (54) with potassium bicarbonate in acetone did not work well. TLC showed several products from which some (55), a pink compound MP 203-206° C, could sometimes be isolated.



The synthesis was, therefore, modified slightly, the crude chloro compound being converted to the diacetate (56) with sodium acetate in glacial acetic acid and a little acetic anhydride. The NMR (56) showed three methyl singlets at 7.94, 7.80, 6.27 τ and a methylene singlet at 4.62 τ. Base hydrolysis removed the acetate groups almost quantitatively giving the amino alcohol (57) which had IR peaks at 3320, 3200, 3080 cm^{-1} and three protons which were exchanged by D_2O in the NMR.

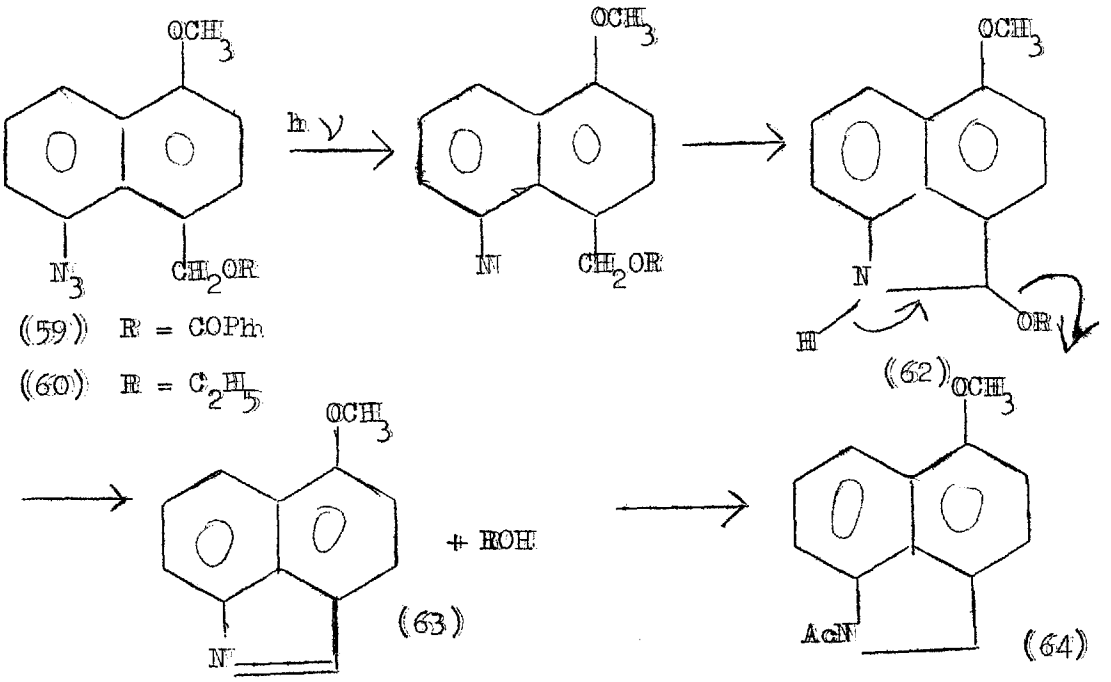
When the amine was diazotised with sodium nitrite in conc. sulphuric acid or a mixture of sulphuric acid and acetic acid and then sodium azide was added, an azide was produced, but the IR showed that the hydroxyl group had been destroyed. By consulting the relevant literature it was learnt that mineral acid is not required for diazotisation of amines. The reactive species is $N\equiv O^{+}$ and is formed from sodium nitrite in any acidic medium. Carboxylic acids[30] and even acetic anhydride[31] have been used for diazotisation reactions, and once it had been established that (57) was stable to glacial acetic acid, it was decided to use this as the reaction medium.

The azido alcohol (58) was thus produced in excellent yield and had bands at 3300 and 2150 cm^{-1} in the IR. Benzoylation with benzoyl chloride in pyridine furnished a 72% yield of (59) which had an azide stretch at 2170 cm^{-1} and a carbonyl stretch at 1703 cm^{-1} in the IR. The ethyl ether of 5-azido-4-hydroxymethyl-1-methoxy-naphthalene (60) was prepared in 90% yield by stirring the alcohol

in ethanol and a drop of conc. hydrochloric acid. In the NMR the ethyl group was evident as a triplet at 8.70 τ and a quartet at 6.35 τ J = 8 cps. This reaction showed that the benzylic carbonium ion was stable. Azide (60) was also prepared by making the amino ether (61) and converting that to an azide.

Thus both a peri-naphthyl azido ester and an ether were available for photolysis.

Photolysis of the benzoate and ethyl ether of 5-azido-4-hydroxymethyl-1-methoxynaphthalene



The azido ether (60) was irradiated in ether in a pyrex vessel with a medium pressure mercury vapour lamp. TLC showed one major product, but on attempting to isolate it by preparative scale TLC, a complex mixture was obtained due to aerial oxidation. Presumably 4-methoxybenz(cd)indole (63) is formed, but is too unstable to be isolated. Benz(cd)indoles are known to be easily oxidised by air and only one or two examples are known[32,33]. Thus as soon as the photolysis was completed excess lithium aluminium hydride was added and the crude benz(cd)indoline thus formed was acetylated with acetic anhydride giving (64) in 39% yield overall. N-acetyl-4-methoxybenz(cd)-indoline (64) had a carbonyl peak at 1655 cm^{-1} in the IR and in the NMR

there were two methyl singlets at 7.72 τ and 6.05 τ and a methylene singlet at 4.95 τ. It was identical to a sample prepared by treatment of 5-acetamido-4-chloromethyl-1-methoxynaphthalene (54) with sodium hydroxide in aqueous acetone.

Ethanol eliminated in the photolysis was characterised as the 3,5-dinitrobenzoate ester MP 87-90° C which was identical to an authentic sample.

This proved that the desired reaction had occurred but gave no information about the yield.

When the benzoate (59) was photolysed in ether, again there was only one major product. In the IR of the crude photolysate there were peaks at 3420 and 1695 cm^{-1} which may indicate that the product is (62 R = COPh), but it could not be isolated for further characterisation. Base extraction of the irradiated solution gave benzoic acid in 65-70% yield, which was identical to an authentic sample. When the residue was hydrolysed with sodium ethoxide in refluxing ethanol a further 25% benzoic acid was obtained. Thus all the benzoate was accounted for.

Using the rotating film apparatus described on page 93 , the photolysis was much faster than in a conventional flask. The photolysis was faster in ether than in benzene and was very slow in a mixture of ether and piperylene. The yield of benzoic acid in the presence of the triplet quencher was no higher than without; indeed because of

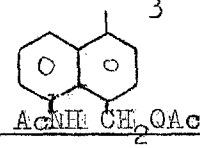
the formation of polymeric material it was somewhat lower at 51%. This result indicates that in the direct photolysis both the singlet and triplet nitrenes form the carbinolamine benzoate (62 R = COPh). No amine or azo compound was found which would be the expected alternative triplet nitrene products.

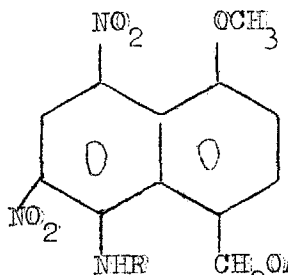
Nitration of 5-acetamido-4-acetoxymethyl-1-methoxynaphthalene

It was decided to try to prepare a nitrated derivative of the naphthalene azide (58) which would have enhanced ultra-violet absorption. Furthermore, great difficulty had been experienced in trying to convert (58) to an ether such as R = cholesteryl which was attributed to the labilising effect of the para methoxy group. As a meta nitro group could offset this effect it was hoped to nitrate at position 2. The only undesirable position for nitration is 6, because the nitrene at position 5 could then react with an ortho nitro group in a competing reaction to the desired insertion. The diacetate 5-acetamido-4-acetoxymethyl-1-methoxynaphthalene (56) was chosen for the nitration experiments because it was considered to be the least sensitive of the azide precursors. A variety of nitrating conditions was attempted giving several different products which are summarised in Table III. No attempt was made to optimise the yields.

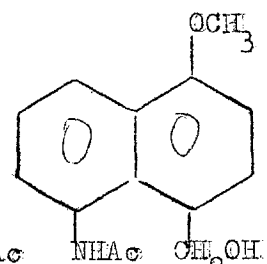
Nitration with 2 N nitric acid for twenty-two hours or briefly in 2 N nitric acid and glacial acetic acid produced a dinitro amino acetate (70). It analysed for $C_{14}H_{13}N_3O_7$ and had peaks in the IR, showing a primary amine at 3420, 3310 cm^{-1}, an acetate at 1730 cm^{-1} and a nitro group at 1550, 1370 and 850 cm^{-1}. In the NMR there was an acetate singlet at 7.83 τ, a methoxyl singlet at 6.08 τ, a methylene singlet at 4.46 τ, an AB quartet at 2.78 τ and 2.27 τ (2H J = 8 cps) and a one proton singlet at 1.72 τ.

TABLE III

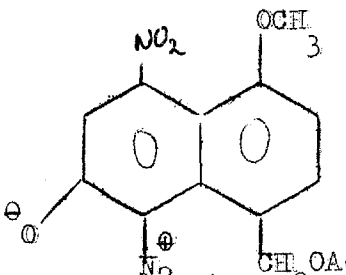
Conditions for the nitration of (56) 	(70)	(55)	(72)	(73)	(74)
Conc.HNO_3 + conc.H_2SO_4, 0° C. 30 mins.		NO PRODUCTS ISOLATED			
Conc.HNO_3, 0° C. 18 hours		NO PRODUCTS ISOLATED			
2N HNO_3, RT, 22 hours	✓ 70%		✓		
2N HNO_3/HOAc, RT, 30 mins	✓ 80%				
Conc.HNO_3/Ac_2O, 4 days	✓				
HOAc/Ac_2O/2N HNO_3 (2 equivs) 30 mins		✓			
HOAc, 3.6 equivs. 2N HNO_3 added portionwise over 1½ hours		✓ 49%			
HOAc/conc. HNO_3, 18 hours			✓		
HOAc/2N HNO_3, 20 hours			✓ 15%		
Ac_2O/2N HNO_3	✓ 5%		✓ 18%		✓
HOAc/Ac_2O/conc.HNO_3, 30 mins				✓	
HNO_3/HOAc		NO REACTION			
$Cu(NO_3)_2.H_2O$/Ac_2O 1 hr. RT				✓ 20%	✓ (major)
$Cu(NO_2)_2.H_2O$/Ac_2O RT 18 hrs	✓ 2%		✓ 7%	✓ 14%	
HOAc/Ac_2O/conc.HNO_3 (3 drop) /$NaNO_2$ 0° C. 1 hour				✓ OR	✓ 10%
HOAc/Ac_2O/2N HNO_3/$NaNO_2$ 0° C. 4 hours	✓ 12%				



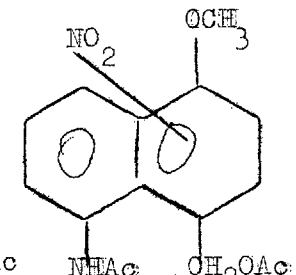
(70) R = H (73) R = Ac



(55)



(72)



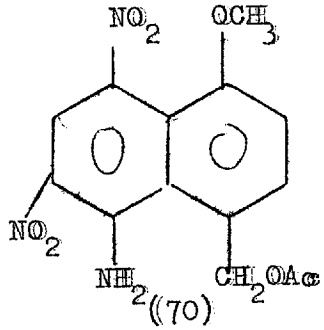
(74)

There are seven possible structures for this dinitro amine in which one aromatic hydrogen is not coupled and the two others are ortho to one another.

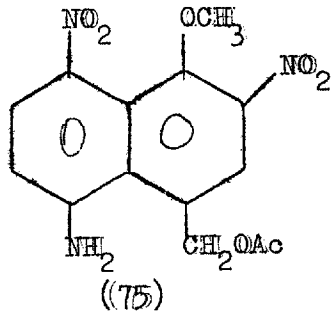
The NMR spectrum was analysed carefully comparing it with the spectra of other compounds in this series and calculating the shifts of the aromatic protons due to the nitro substituents. Data for nitro shifts due to free and some hindered nitro groups in nitronaphthalenes has been published[34] and these figures were used as far as possible. Insufficient information was available for precise calculations and estimates had to be made where necessary. For instance, the proton shifts quoted due to hindered nitro groups were calculated from spectra of nitromethylnaphthalenes. These figures were used in the present case for a nitro group hindered by an adjacent methoxyl, acetoxymethyl or amino group. No information is available about shifts due to a nitro group hindered by a peri substituent because the spectrum of 1-nitro-8-methylnaphthalene was not analysed in detail. Anisotropy of the nitro group would presumably have to be taken into consideration. Finally, the solvent used for the NMR spectra from which these shifts were calculated was N,N-dimethyl acetamide while our spectra were run in deuterochloroform.

Nevertheless, bearing these limitations in mind, the chemical shifts of the three aromatic protons in the spectrum of each of the seven possible isomers was calculated and compared with the spectrum

obtained for the nitro compound isolated. In this way, the number of possibilities was reduced to two (70) and (75).



((70)



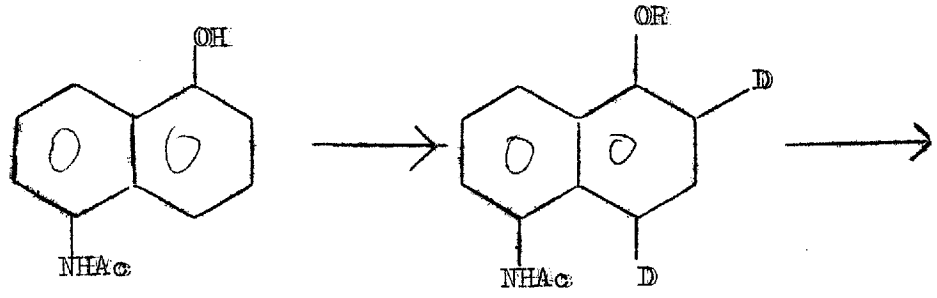
((75)

In the spectra of all the unnitrated compounds prepared, the methoxyl group singlet appears at 6.06 ±0.02 γ. In the spectrum of the dinitro amine, it appears at 6.05 γ. It is reported that the methyl shift relative to 1-methylnaphthalene in 1-methyl-2-nitronaphthalene and 1-methyl-3-nitronaphthalene is -0.16 γ and -0.14 γ respectively. However, in 1-methyl-8-nitronaphthalene the shift is + 0.15 γ owing to the anisotropy of the nitro group which is twisted so that its plane is perpendicular to the plane of the ring because of the steric compression in the peri positions. This suggests that the downfield shift of the methoxyl signal due to one nitro group in our compound is offset by the upfield shift due to a nitro group at position 8.

Attempts to distinguish between (70) and (75) chemically by reduction with zinc dust in acetic acid and treatment of the resulting triamine with benzil[35] and by diazotisation and treatment with sodium azide in order to photolyse the azide, gave no useful

information. It was therefore decided to repeat the synthesis with a deuterium label at position 2. If this is lost in the nitro derivative then it may be inferred that (75) is the correct structure; if it is retained (70) is the correct structure.

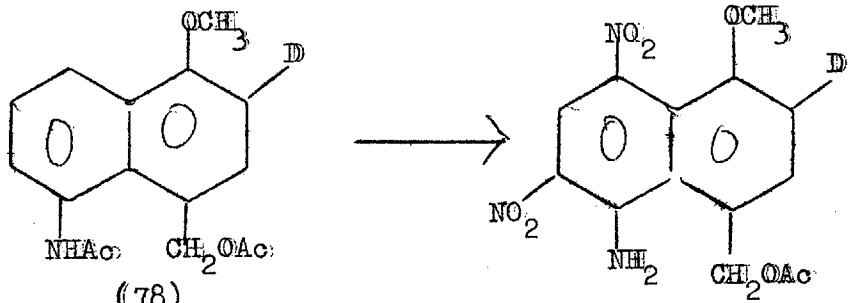
5-acetamido-1-naphthol (52) was deuterated by heating with D_2O and triethylamine in refluxing N,N-dimethylformamide. In the NMR of the product, (76), H_3 appeared as a singlet at 2.80 τ and there was a small doublet, half of an AB quartet, at 3.18 τ due to some mono-deuterated material. The parent ion in the mass spectrum at M/e 203 confirmed that the major product was the di-deuterated compound. The ratio of peak heights at M/e 201 : 202 : 203 : 204 was 1:8:23:3.6.



(52)

(76) R = H

(77) R = CH_3



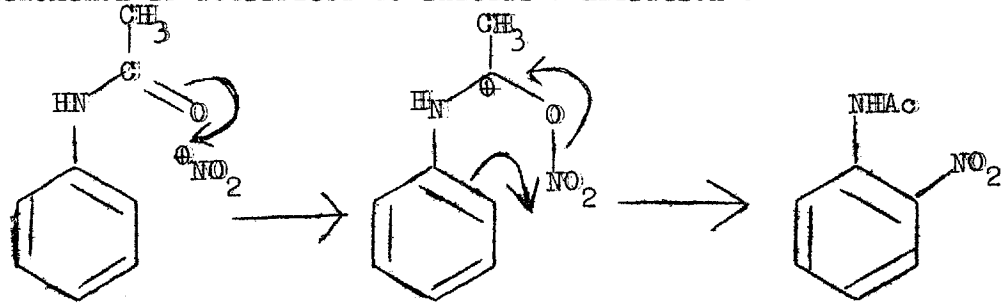
(78)

(79)

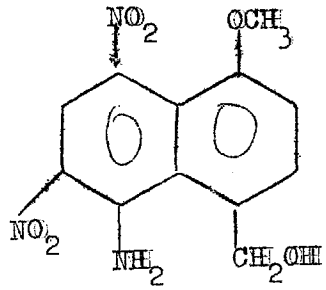
Since methylation as carried out previously with methyl iodide and potassium carbonate would probably result in loss of the label at position 2, the naphthol (76) was converted to (77) with diazomethane in 92% yield. The integration of the NMR spectrum showed four aromatic protons with a singlet at 2.57τ and a trace of doublet due to mono-deuterated (77). The most intense molecular ion peak in the mass spectrum was at M/e 217 corresponding to (77). The ratio of peak heights at M/e 215: 216 : 217 : 218 was 1:10:37: 5.9

Chloroformylation followed by acetylation as before gave the diacetate (78), but the NMR showed considerably more hydrogen at position 2 than in (77). The ratio of the peak heights for the undeuterated and mono-deuterated molecular ions was 1:1.53. Nitration of (78) with 2 N nitric acid in glacial acetic acid gave the dinitroamine (79) with the same melting point 198-9° C as (70). In the aromatic portion of the NMR there were singlets at 1.76τ (integrated for one proton) and 2.31 τ and a quartet at 2.29 and 2.68 τ J = 8 cps. Clearly this arises from a mixture of deuterated (79) and undeuterated (70) nitro amines. If the 2,8-dinitro isomer (75) had been formed, a singlet and a simple AB quartet identical to that obtained in the non-deuterated series would be seen. In the mass spectrum the major parent ion was at M/e 336 and the ratio of peak heights for M/e 335 : 336 was 1:1.59. Thus it was proved that the correct structure for the dinitro derivative was that of the 6,8-dinitro isomer (70). This is of no use for our purposes.

Relevant to this reaction is the observation that nitration of acetanilide occurs preferrentially in the ortho position. This phenomenon is attributed to initial O nitration[4].



When (70) was chromatographed on Grade 3 Alumina it deacetylated giving (71) which had no carbonyl absorption in the infra-red and had absorptions due to the amine and hydroxyl groups at 3500, 3360, 3280 cm^{-1}.



(71)

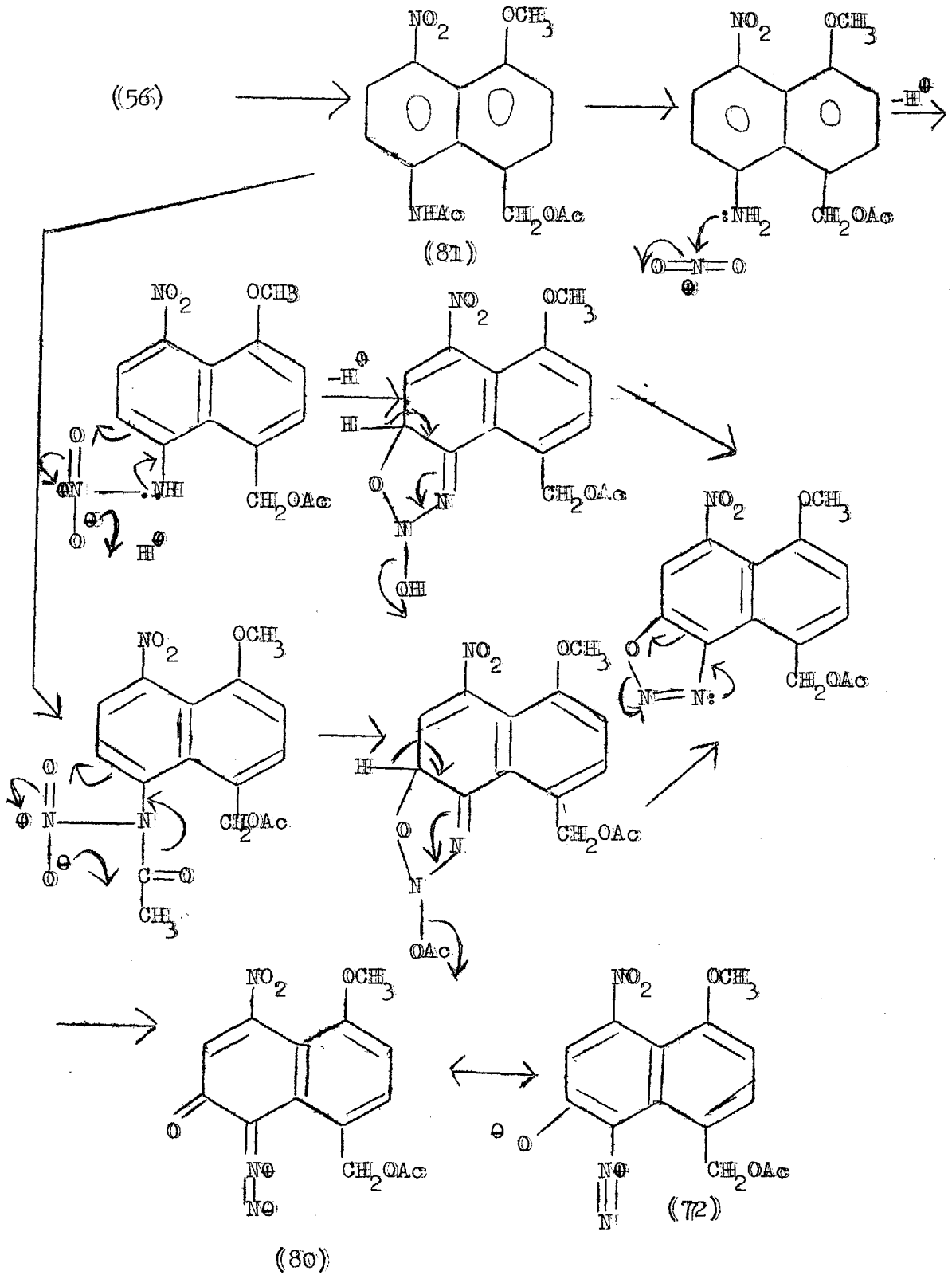
Nitration of (56) in glacial acetic acid and two equivalents of 2 N nitric acid merely hydrolysed it to 1-methoxy-4-hydroxymethyl -5-acetamidonaphthalene (55). This compound had previously been obtained in poor yield by mild alkaline hydrolysis of the corresponding chloro compound (54). It had an acetate methyl singlet at 7.82 τ

a methoxyl singlet at 6.05 τ and a methylene doublet at 5.15 τ (J = 5 cps) which appeared as a singlet after shaking the solution with D_2O. The NH and OH groups appeared at 3.8 τ and 0.8 τ in the NMR and at 3380 and 3420 cm^{-1} in the IR.

Nitration for an extended period with conc. or dilute nitric acid in glacial acetic acid gave a mono-nitro derivative which had an unexpected peak at 2150 cm^{-1} in the IR. Other peaks in the IR showed that it had a nitro group (1555, 855 cm^{-1}) and an acetate (1735 cm^{-1}), but no NH or OH. The NMR spectrum had absorptions due to the acetate at 7.91 τ, the methoxyl at 6.16 τ, the methylene at 4.75 τ, a one proton singlet at 3.34 τ and a two proton quartet (J = 8 cps) at 3.25 τ and 2.43 τ. The upfield shift of 0.1 τ relative to the methoxyl signal in the starting material suggests the presence of a peri nitro substituent. This compound analysed for $C_{14}H_{11}N_3O_6$ and on the basis of these data it was assigned structure (72) or the corresponding diazoketone (80). Two possible mechanisms for its formation are suggested.

Because (72) was formed under conditions which differred only from those used to prepare the dinitroamine (70) in that a much longer reaction time elapsed, it was thought that (70) might be an intermediate. However, when treated under these conditions (70) gave no (72) but was merely hydrolysed to the dinitro amino alcohol (71).

Nitration with cupric nitrate in acetic anhydride for one hour[36] produced a mixture from which the major product was isolated as usual.


(56)
(81)
(80)
(72)

IR showed this to contain acetate, amide and nitro groups, but the NMR showed that this was a mixture of mono- and di-nitro compounds (73) and (74). There were two methoxyl and two methylene peaks in approximately equal proportions. The fact that one of the two methoxyl peaks is at 5.97 τ, approximately 0.1 τ lower than in the unnitrated compound, indicates that in the mono-nitro compound (74) the nitro group is not at position 8 but perhaps at position 2 or 6. The mixture could not be separated chromatographically, but a sample recrystallised several times from benzene had an analysis close to that of (74).

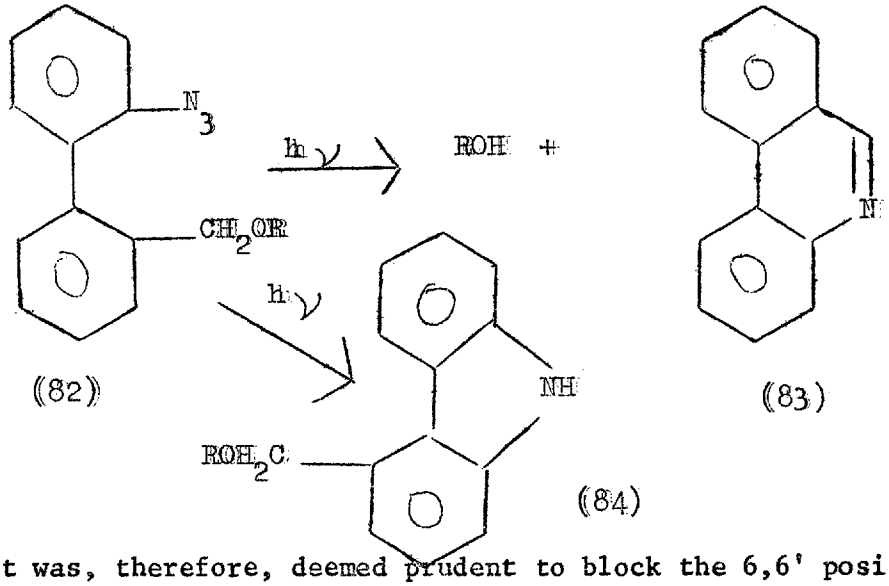
Only the dinitro compound (73) and (72) and none of the mononitro compound (74) were obtained when this reagent was used for sixteen hours. The substitution pattern in (73) was deduced from the aromatic protons in the NMR spectrum which appeared at 1.99 τ (a one proton singlet) and 2.22, 2.85 τ (an AB quartet J = 8 cps, two protons).

The mechanism of the copper nitrate nitration is thought to be nitrosation followed by cupric ion oxidation of the nitroso group to a nitro group. Since the nitrosyl cation is a weaker electrophile than is the nitronium cation, it was hoped that the reaction might stop at the mono-nitro stage. However, when the nitrosyl cation was generated from sodium nitrite in acid (70) and (73) or (74) was obtained.

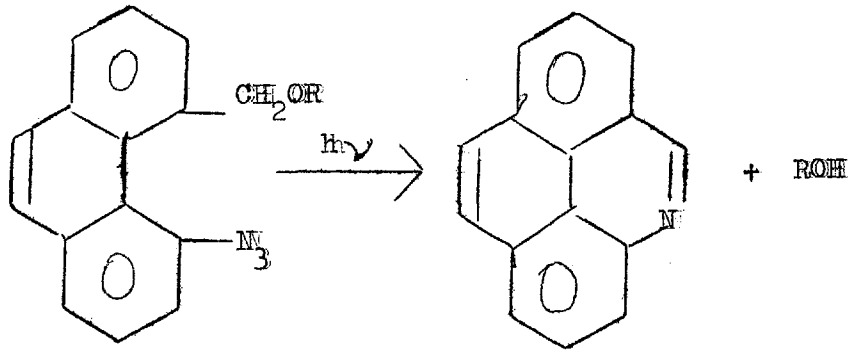
No useful nitro compound was obtained from these experiments and the quest for one was abandoned.

Approaches to the Synthesis of a Suitable Phenanthyl Azide

It was proposed to improve on the results of the naphthyl azide photolysis by preparing a 2-azido-2'-alkoxymethyl biphenyl (82) which would, in principle, eliminate ROH with the formation of a pyridine ring (83) on photolysis. A major uncertainty considered before embarking on the synthesis was the possibility of carbazole formation (84).



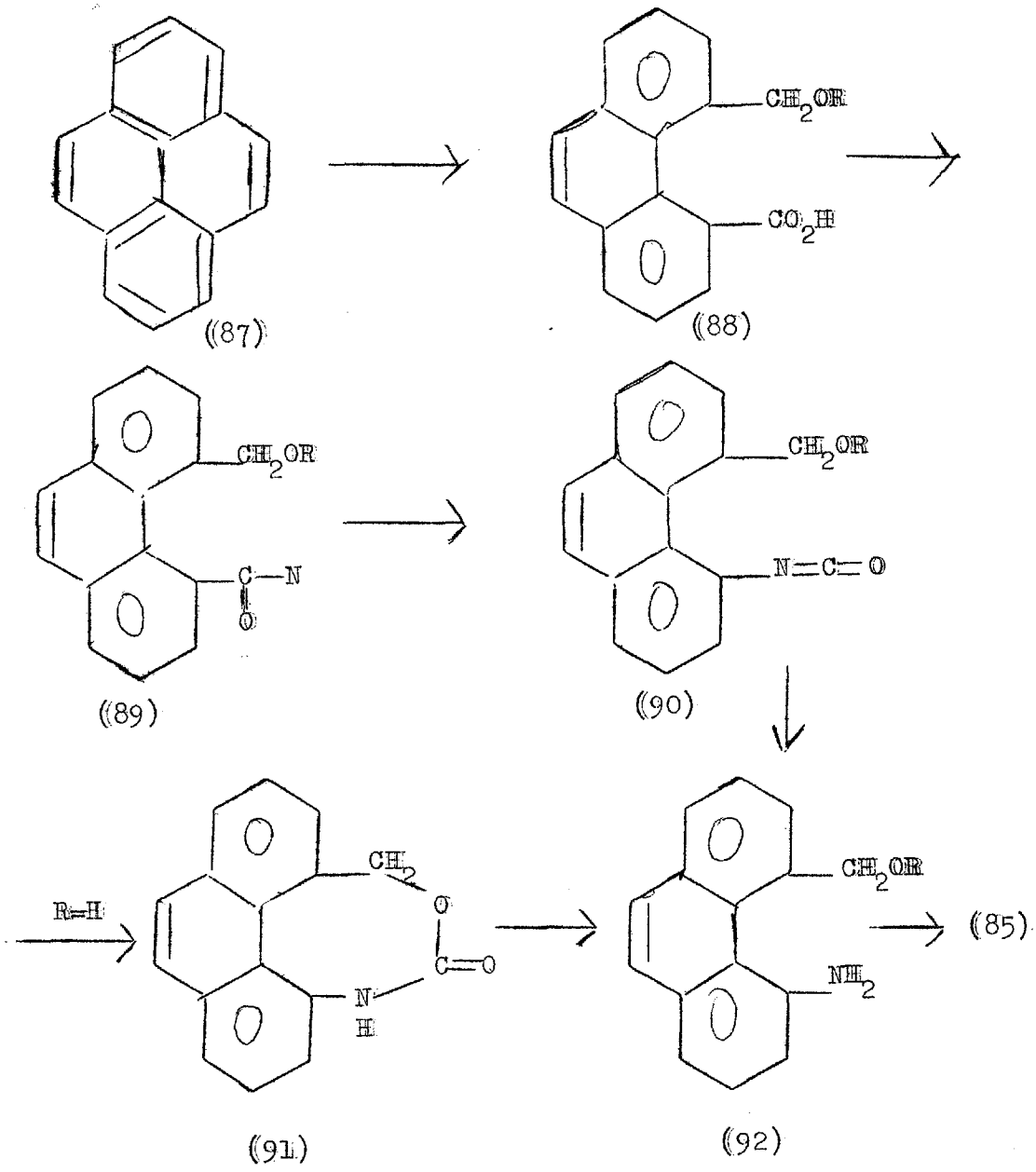
It was, therefore, deemed prudent to block the 6,6' positions with a bridging heteroatom or a C=C to prevent this happening. Thus it was decided to synthesise the phenanthryl azide(85) which on photolysis would give ROH and the fully aromatic 1-azapyrene (86)[37].



(85) (86)

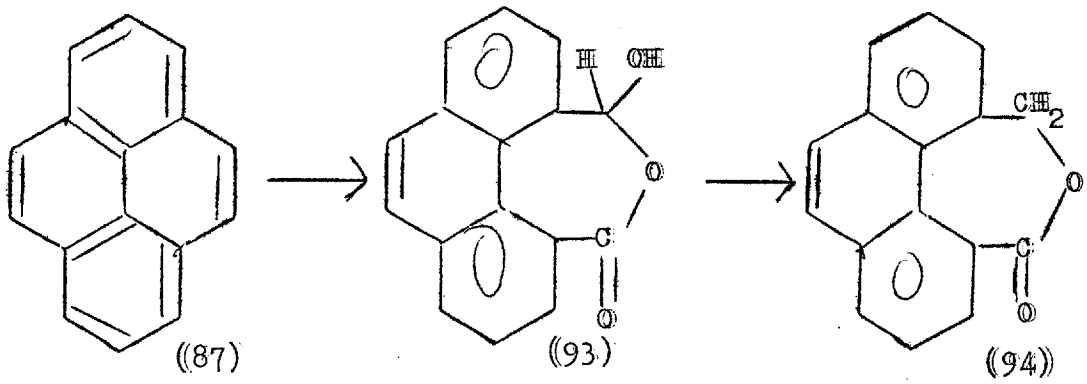
The 4 and 5 positions in phenanthrene are about 1.45 Å apart, much closer than are the corresponding peri positions in naphthalene which are about 2.4 Å apart[38]. Hence the nitrene formed from (85) should insert into the methylene group much more readily than was found hitherto. The formation of a fully aromatic molecule (86) provides another driving force for the reaction which was not present in the naphthalene case. Thus it was hoped that ROH would be eliminated quantitatively on photolysis of (85) so that this reaction could be used as the basis of a photosensitive protecting group for carboxylic acids and alcohols.

Pyrene (87) is a potentially convenient starting material. Ozonolysis followed by some suitable redox work up would give a compound at the oxidation level of (88). Treatment of this acid with a suitable reagent would give the acyl nitrene (89) which would rearrange and eventually give the amine (92) by means of a Schmidt, Lossen, Curtius etc. reaction. This is readily converted to the desired azide (85).



(87) (88) (89) (90) (91) (92)

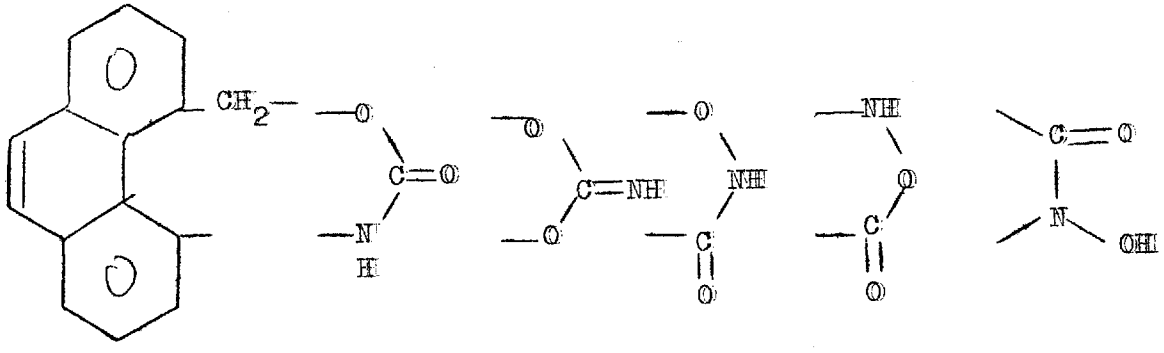
Ozonolysis of pyrene gave the cyclised 5-formylphenanthrene-4-carboxylic acid (93). There are many different procedures described in the literature for this reaction,[39-44, 50] but a better yield (56%) than any so far reported was obtained by ozonising pyrene in carbon tetrachloride in the presence of a few drops of pyridine[45].



Reduction of the lactol (93) to the lactone (94) has previously been carried out in two stages in 40% yield[44]. It was, however, cleanly reduced in 89% yield by a Cannizzaro reaction with excess formalin.

Schmidt Reaction

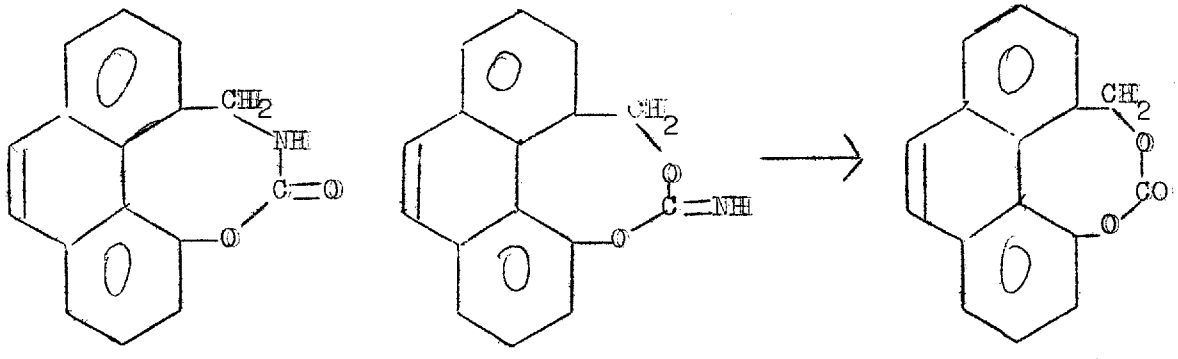
Lactone (94) is clearly at the required oxidation level (88) for the proposed synthesis, and despite earlier misgivings about Schmidt reactions with lactones, it was dissolved in conc. sulphuric acid and sodium azide was added. Nothing happened at room temperature, but on warming to 80° C nitrogen evolution was observed. A yellow product was isolated in 36% yield. Samples recrystallised from various solvents did not give consistent analyses, but a sublimed sample analysed correctly for $C_{16}H_{11}NO_2$. This formula was confirmed by the molecular ion in the mass spectrum appearing at M/e 249. In the IR there were significant peaks at 3390, 1690, 1634 cm^{-1}. The NMR showed a methylene triplet at 4.74 τ (J = 2 cps), a broad absorption at about 5.8 τ which disappeared on shaking the solution with D_2O, and eight aromatic protons at 1.6 - 3.03τ. These data suggest partial structures as shown below and would indeed fit for the desired urethane (91).



It ought to be possible to hydrolyse (91) with base to give the amino alcohol (92 R=H). Hydrolysis in refluxing aqueous methanolic potassium hydroxide or in cold 4 N aqueous sodium hydroxide and THF

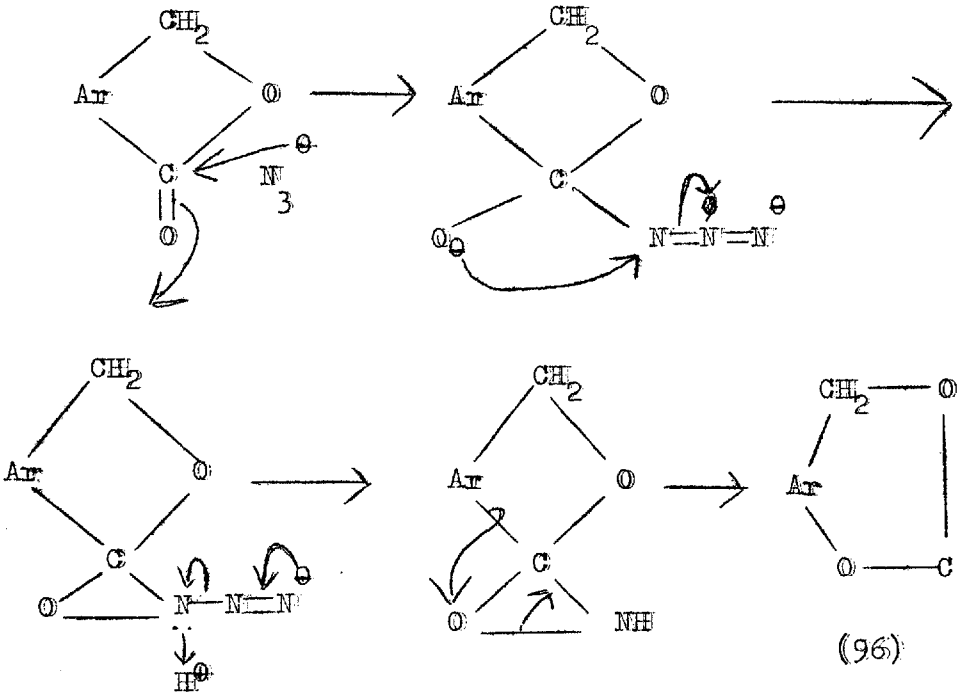
gave a complex mixture which contained some unreacted Schmidt product. Under milder conditions the compound was inert.

Hydrolysis in warm acid gave a product in moderate yield which contained no nitrogen. It analysed for $C_{16}H_{10}O_3$ and had a corresponding molecular ion at M/e 250. The IR showed the presence of a carbonyl which absorbed at 1680 cm^{-1}, but no OH or NH. In the NMR the methylene peak appeared at 4.74γ. This compound was the cyclic carbonate (95) and could not arise from urethane (91). Two possible structures for the Schmidt product are (96) and (97). The iminocarbonate (96) is preferred because the chemical shift of the methylene group in the Schmidt product is virtually the same as in the carbonate (95) and lactone (94), indicating that the methylene is probably adjacent to an oxygen atom.



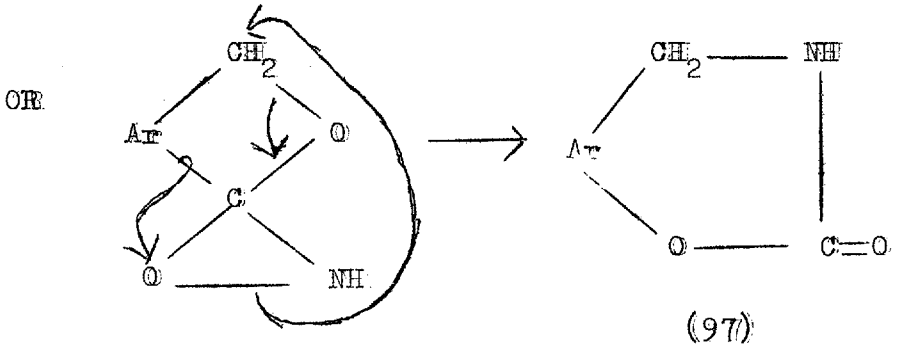
(97) (96) (95)

This reaction can be rationalised as follows:



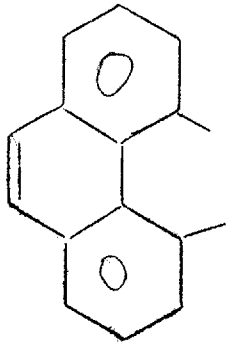
(96)

OR

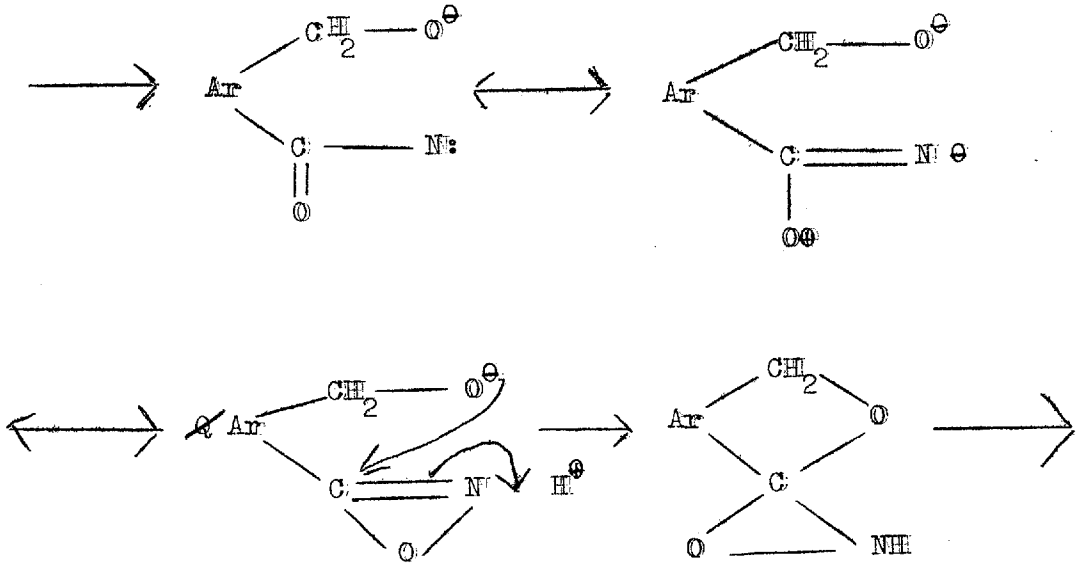


(97)

Ar =

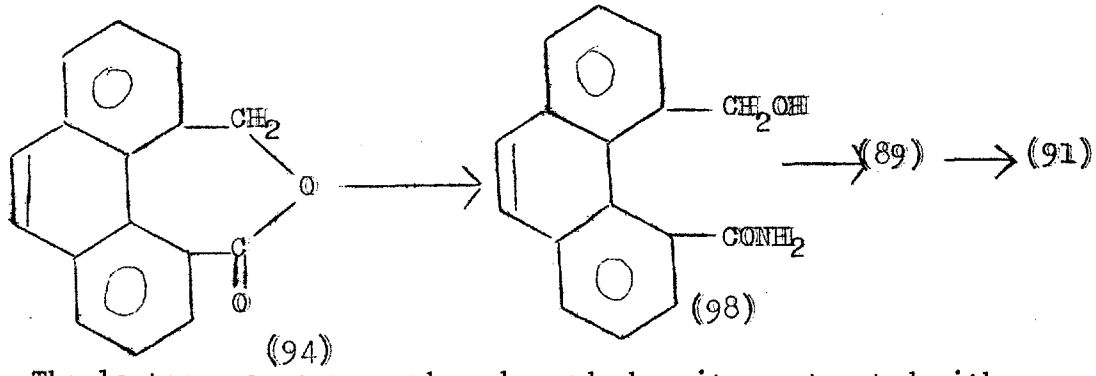


Alternatively, this may be one of the first examples of reaction at electron deficient oxygen (c.f. ref. 46).



Other Reactions of the Lactone of 4-hydroxymethyl-5-phenanthrene carboxylic acid

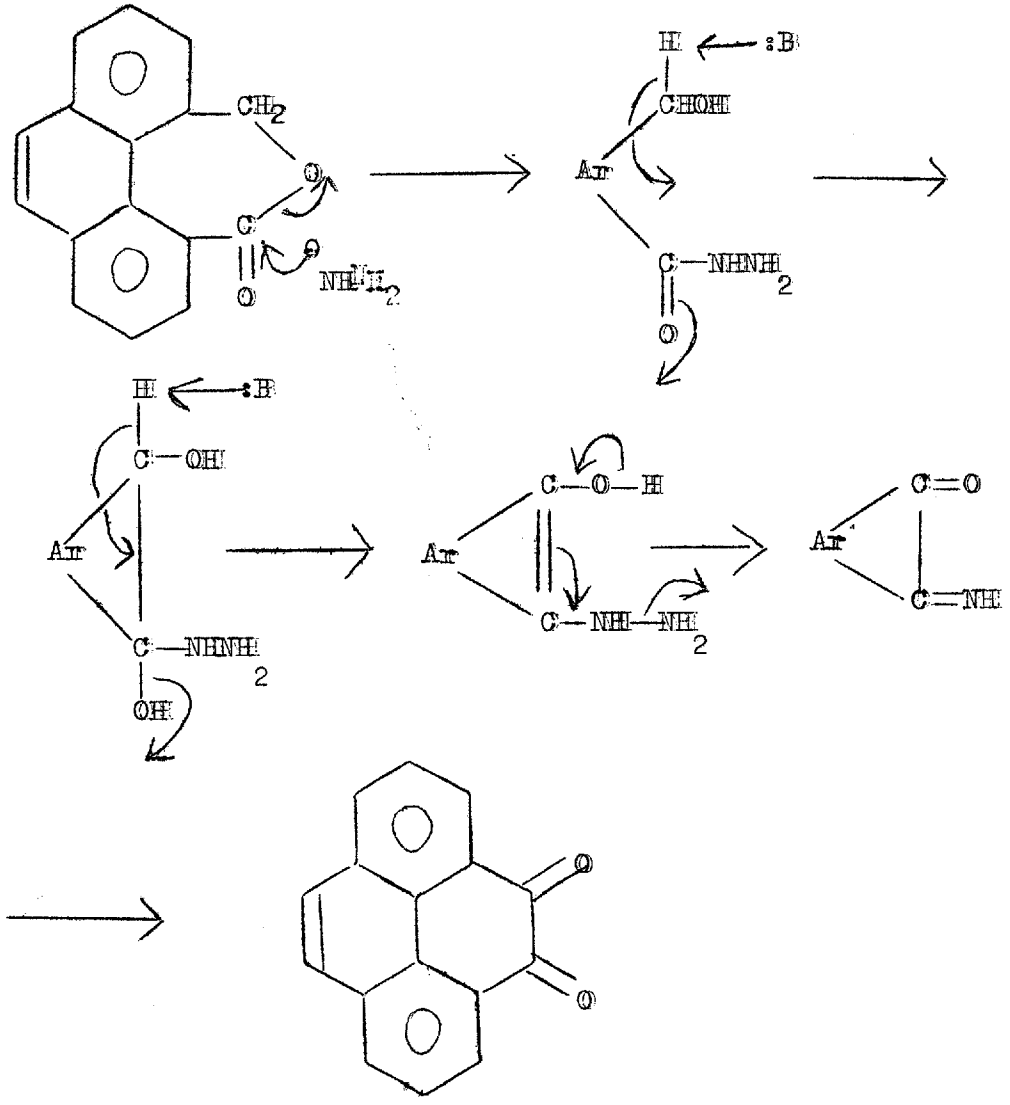
It was proposed to convert the lactone (94) to amide (98) by reaction with ammonia, in a similar reaction to that reported for phthalide.[47] The amide could then be rearranged to urethane (91) via the carbonylnitrene intermediate (89) generated by Beckwith reaction with lead tetraacetate[48].



The lactone was recovered unchanged when it was treated with 0.880 ammonia, gaseous ammonia, liquid ammonia, sodamide, hydroxylamine, hydrazine and methylamine under a variety of conditions and in several different solvents.

The lactone did, however, react with anhydrous hydrazine and sodium hydride in refluxing tetrahydrofuran and a high melting red solid was obtained in good yield. NMR showed that the methylene group was no longer present as there were only aromatic protons. The IR showed a carbonyl absorption at 1670 cm^{-1} and a mass measurement of the molecular ion showed the molecular formula to be $C_{16}H_8O_2$ which was consistent with the analysis. Important fragmentations were loss of 28 and 56 mass units. These spectral properties fit the

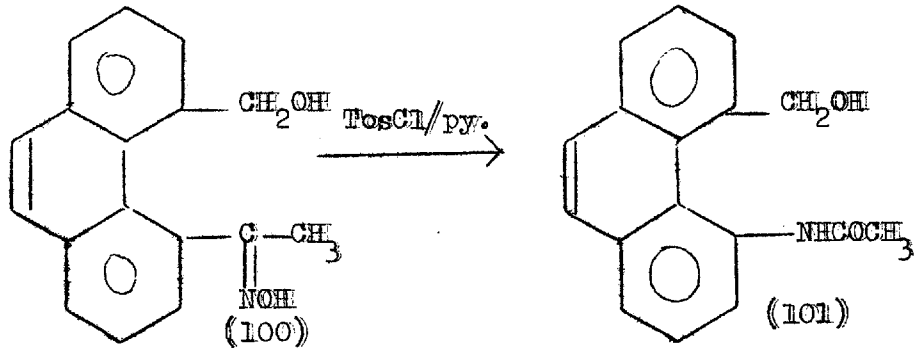
structure of the known phenanthrene-4,5-quinone (99)[49,50] and a possible mechanism for this reaction is shown below.



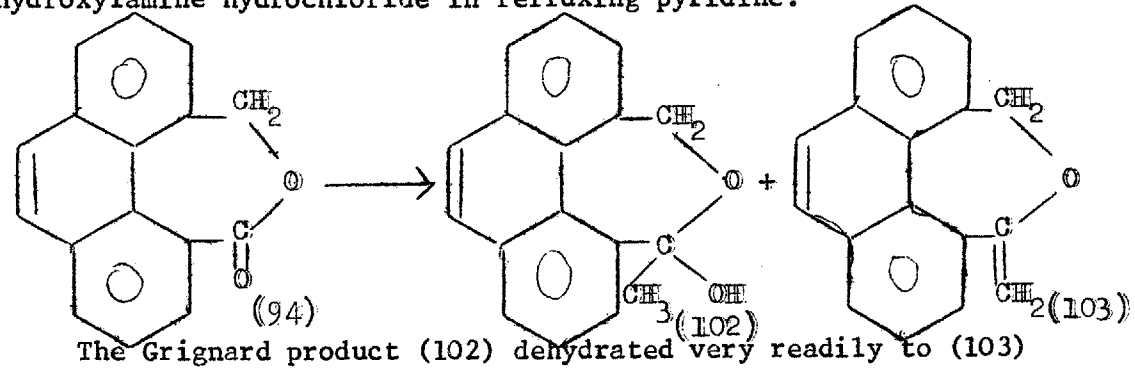
(99)

The Beckmann Rearrangement Approach

It was considered likely that oxime (100) would give the amide (101) under Beckmann rearrangement conditions. The amide is very closely related to our synthetic objective.

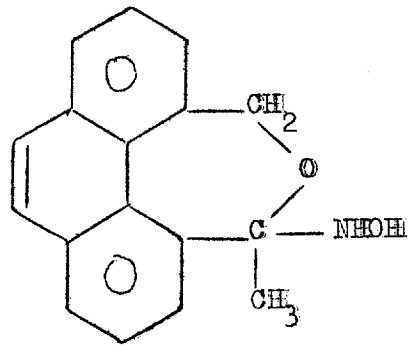


To obtain this oxime, lactone (94) was treated with methyl magnesium iodide and either product (102) or (103) oximinated with hydroxylamine hydrochloride in refluxing pyridine.



The Grignard product (102) dehydrated very readily to (103) and in several runs the relative yields of the two products varied. (102) was easily identified by the hydroxyl absorption in the IR at 3440 cm^{-1} and the methyl singlet at 8.54 τ and the methylene quartet at 4.87 τ (J = 13 cps) in the NMR. The anhydro compound (103) had neither a methyl peak in the NMR nor a hydroxyl in the IR. The two methylene groups appeared at 4.78 and 5.16 τ in the NMR.

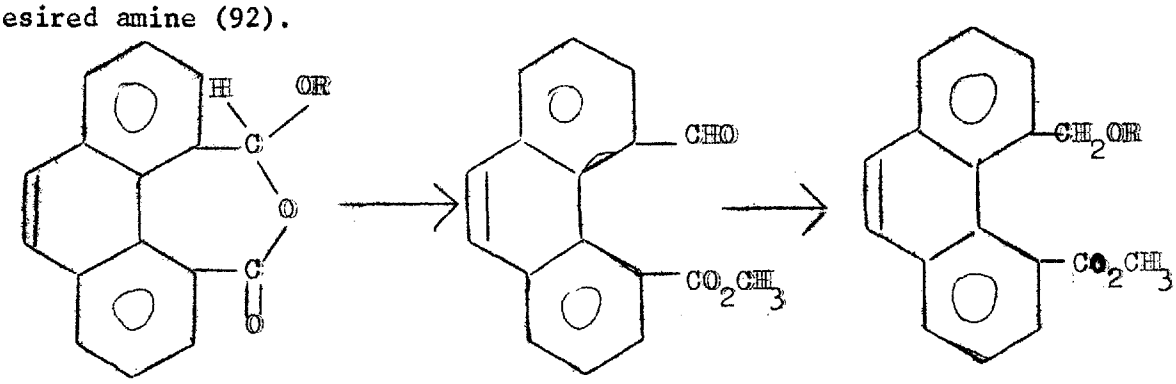
The oxime could not be crystallised and was readily hydrolysed to (102) e.g. on chromatography on Silica Gel plates. The reaction with tosyl chloride in pyridine did not give (101), but a mixture of (102) and (103). These properties would appear to indicate that the oxime is not in the open form (100) but in the cyclic form (104).



(104)

Reactions of 4-formylphenanthrene-5-carboxylic acid lactol

Having failed to open the lactone ring in (94) it was decided to open the lactol ring in (93) with diazomethane to obtain the aldehyde methyl ester (105)[43,49]. Selective reduction of the formyl group should give the methyl ester (106 R = H) which after masking the alcohol could undergo a Schmidt reaction to form the desired amine (92).



(93) R = H
(107) R = CH_3

(105)

(106)

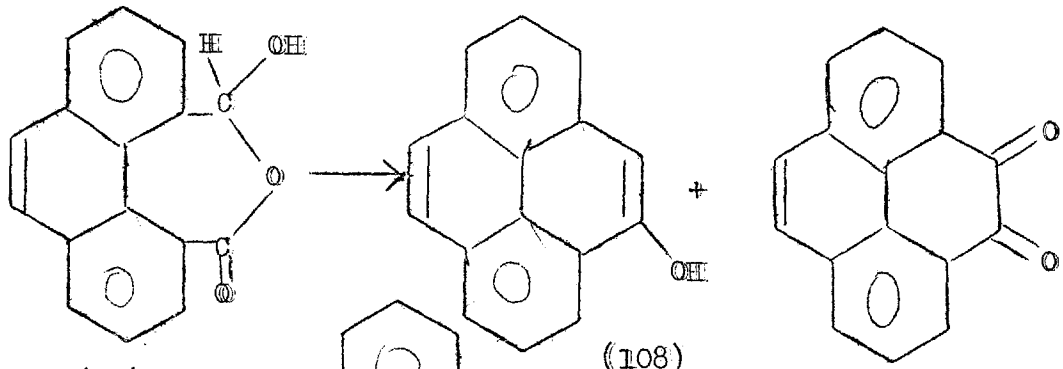
Methylation of (93) to give (105) proceeded in excellent yield (92%) but when an unwashed solution of diazomethane (i.e. a slightly alkaline solution) was used an equally excellent yield of the pseudo-methyl ester (107)[43] was obtained (c.f. ref. 51). It had a methine singlet at 3.72 τ and only one carbonyl absorption which appeared at 1700 cm^{-1} in the IR.

Reduction of (105) with sodium borohydride or with zinc borohydride (which has the advantage of being neutral in solution) or by catalytic hydrogenation in ethyl acetate gave lactone (94) as the sole product. Even an attempt at a reductive acetylation by

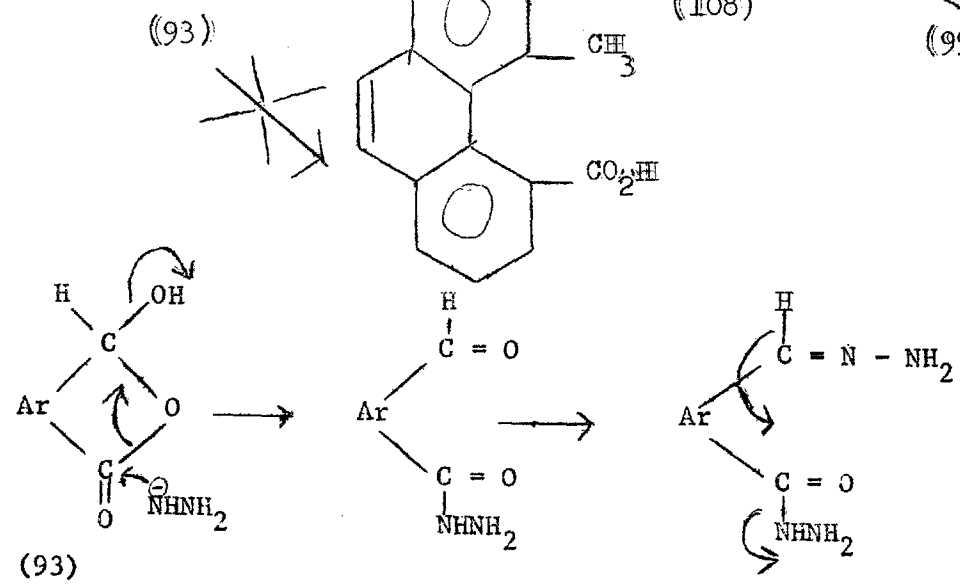
hydrogenating (105) over platinum in a mixture of acetic anhydride and glacial acetic acid, gave only the lactone (94) instead of stabilising (106 R = H) by acetylating it to (106 R = Ac). Reduction with zinc dust in hydrochloric acid, hydrochloric acid and acetic anhydride and glacial acetic acid gave tars which the NMR showed to have no methyl group.

Wolff Kishner reduction of the formyl group in lactol (93) should give 4-methylphenanthrene-5-carboxylic acid. This could be converted to 4-methyl-5-aminophenanthrene via a carbonylnitrene intermediate and a subsequent radical bromination reaction would functionalise the methyl group eventually leading to (92). This approach to the synthesis would permit operation on the substituent at position 5 without interference from the substituent at position 4.

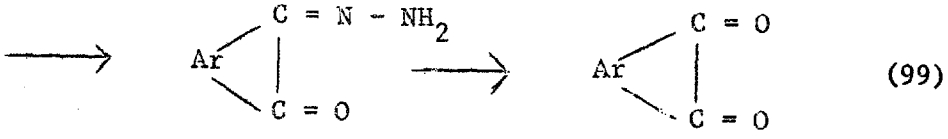
In the event, treatment of (93) with sodium hydrazide in diethylene glycol at 180° C gave two products. The minor one was immediately recognised as phenanthrene-4,5-quinone (99). The major product, isolated in 48% yield, had no carbonyl absorption in the IR, but had a hydroxyl peak at 3320 cm^{-1}. In the NMR there were eight aromatic protons at 1.37 - 2.27 and a singlet at 2.67τ. This identified the product as the known 1-pyrenol (108)[50], thus ruling out this approach to the synthesis.



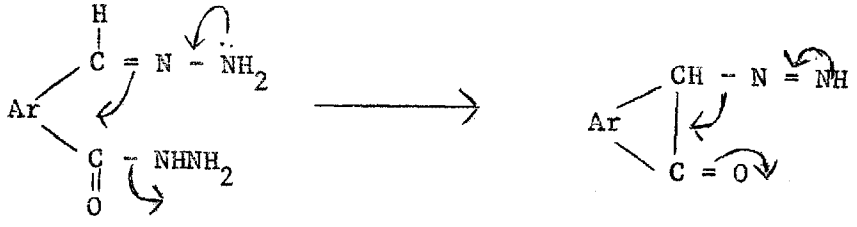
(93) (108) (99)



(93)

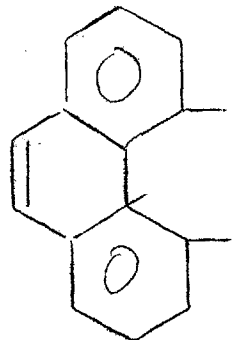


(99)



(108)

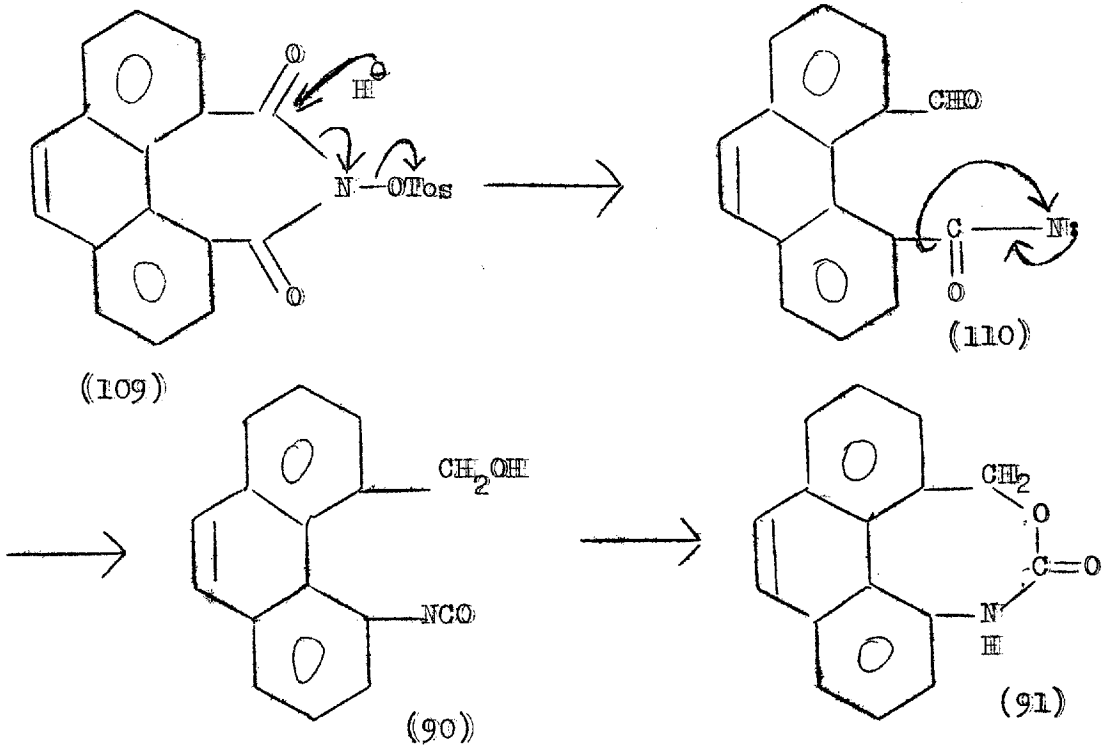
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Reactions of Phenanthrene-4,5-Anhydride

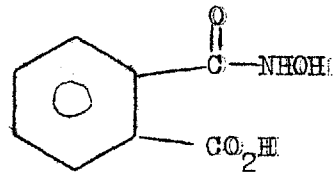
Reaction of Phenanthrene-4,5-(N-tosyloxy)-imide with Sodium Borohydride

Because of our failures with compounds at the correct oxidation level, it was decided to attempt a novel approach to the synthesis. It was predicted that by reacting phenanthrene-4,5-(N-tosyloxy)-imide (109) with sodium borohydride, the carbonyl at position 4 would be reduced simultaneously with the formation of a carbonyl-nitrene at position 5. In this reaction sodium borohydride is serving both as a nucleophile and a reducing agent. Rearrangement of (110) and subsequent cyclisation of (90) would furnish the urethane (91) which is a suitable precursor for the required azide. In effect this reaction produces the anticipated Schmidt reaction intermediates which we failed to obtain previously.

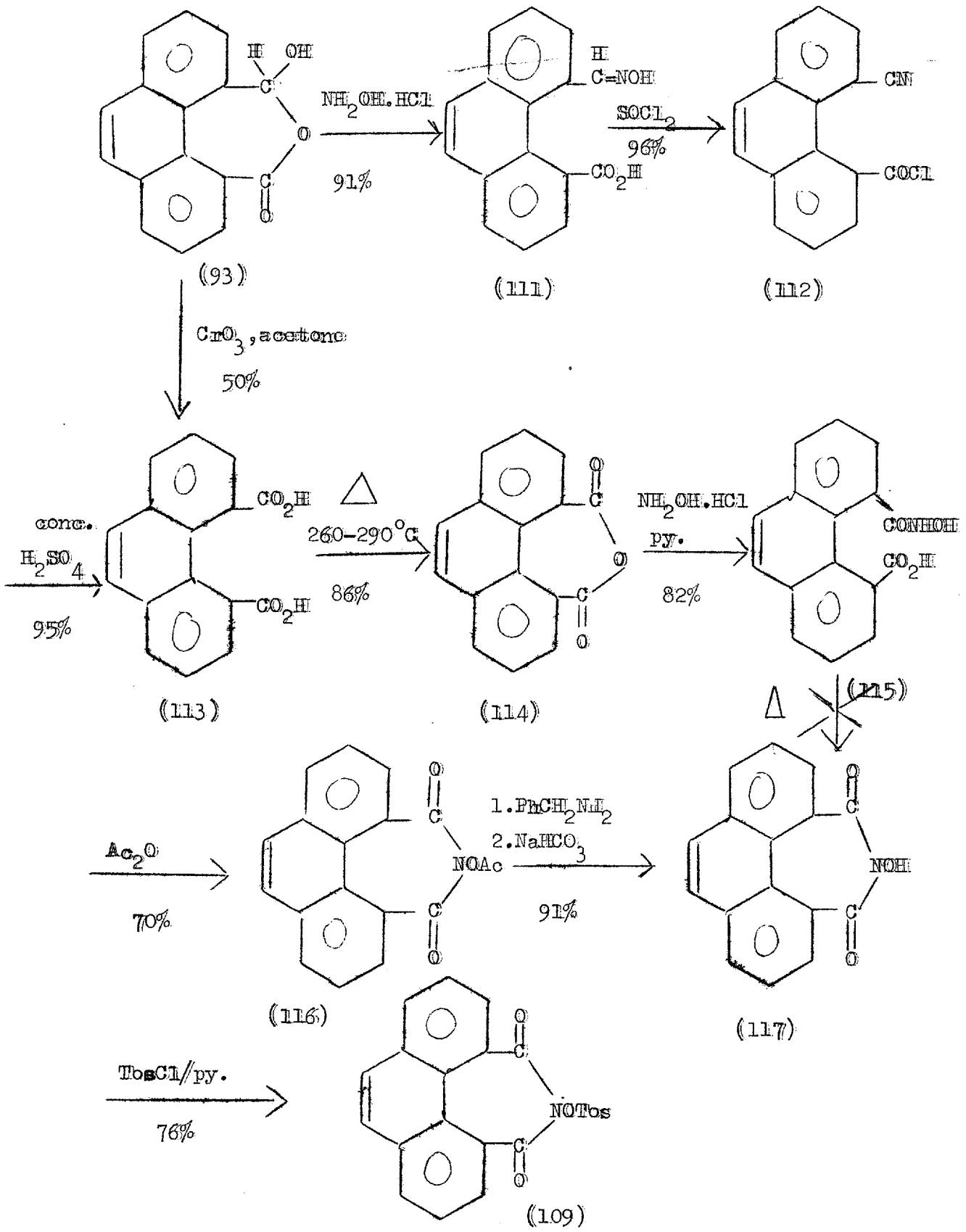


The key compound (109) was prepared by a number of straightforward reactions from phenanthrene-4,5-anhydride (114). It was not found possible to prepare phenanthrene-4,5-dicarboxylic acid (113) by ozonolysis of pyrene as reported in the literature[38,41]; under these conditions the aldehydo acid lactol (93) was invariably obtained. Conditions were, however, found for preparing it by a Jones oxidation of (93) without oxidising the 9,10 double bond or getting phenanthrene-4,5-quinone (99)[52]. It was most conveniently prepared by converting (93) to the oximino acid (111) (the same product was obtained when the pseudo-methyl ester (107) was reacted with hydroxylamine), treating the latter with thionyl chloride and hydrolysing the resulting (112). Phenanthrene-4,5-anhydride (114) was obtained by subliming the dicarboxylic acid (113)[52].

Oximination of the anhydride (114) gave the carboxylic acid hydroxamic acid (115), but not the cyclic N-hydroxyimide (117) as was anticipated by analogy with the oximination of phthalic anhydride[24,53,54]. The compound analysed correctly for $C_{16}H_{11}O_4N$ and had a very similar IR to that of the corresponding phthalic carboxylic acid hydroxamic acid (118)[54] absorbing at 3270, 2700, 1665, 1625, 1600 cm^{-1}.

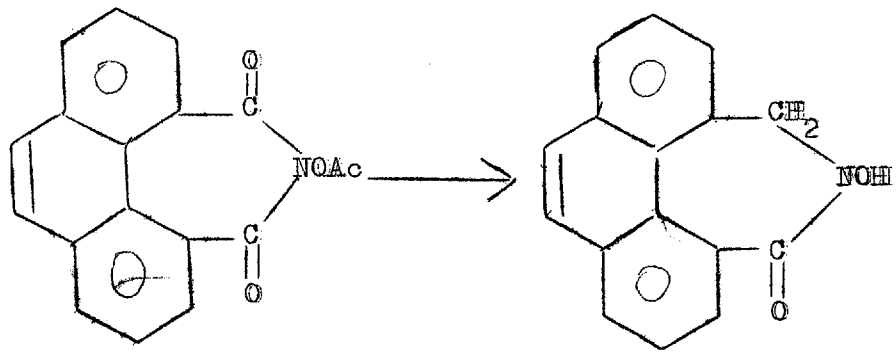


(118)


H
OH
C
O
C
O
NH2OH.HCl
91%
H
C=NOH
CO2H
SOCl2
96%
CN
COCl
(93)
(111)
(112)
CrO3, acetone
50%
conc.
H2SO4
95%
CO2H
CO2H
(113)
Δ
260-290°C
86%
C
O
O
C
O
(114)
NH2OH.HCl
py.
82%
CONHOH
CO2H
(115)
Δ
Ac2O
70%
NOAc
(116)
1. PhCH2NH2
2. NaHCO3
91%
NOH
(117)
TosCl//py.
76%
NOTos
(109)

Whereas (118) is reported to cyclise to N-hydroxyphthalimide on heating[54], (115) sublimed unchanged on heating in vacuo at 210°C. It was cyclised by heating in acetic anhydride just below reflux temperature giving (116) in 70% yield. The acetate methyl group appeared at 7.53 τ in the NMR and there were three carbonyl absorptions at 1795, 1690, 1665 cm^{-1} in the IR. N-acetoxyimide (116) was deacetylated with benzylamine and phenanthrene-4,5-(N-hydroxy)-imide (117) was obtained in excellent yield. Its structure was confirmed by infra-red absorptions at 3300, 1670 and 1625 cm^{-1}. Finally the sodium salt of (117) was converted to the desired tosylate (109) by reaction with para-toluene sulphonyl chloride (TosCl) in pyridine. In the NMR spectrum of (109) there were twelve aromatic protons at 1.5 - 2.8 τ and a methyl singlet at 7.57 τ.

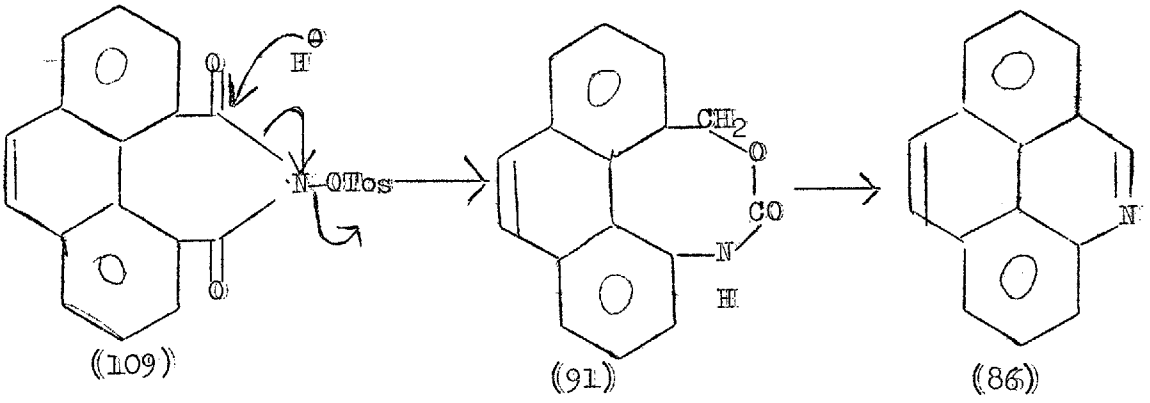
Before reacting (109) with sodium borohydride, the reaction was tried with the acetate (116). The product, obtained in about 50% yield, was a hydroxamic acid (119) which gave a positive ferric chloride test.



(116) (119)

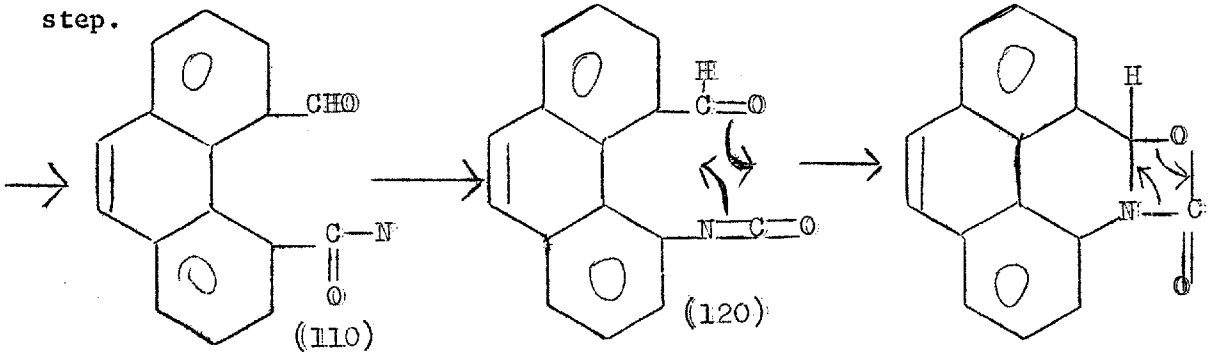
The IR showed a carbonyl absorption at 1625 cm^{-1} and a broad hydroxyl at 3100 - 2700 cm^{-1}. In the NMR there was a methylene singlet at 5.15 τ and a broad absorption at 6.5 τ which disappeared on shaking the solution with D_2O. Shortly after this surprising result was obtained, a reaction appeared in the literature in which a similar compound was reacted with sodium borohydride and there too only one carbonyl group was reduced[55].

When the tosylate (109) was treated with sodium borohydride in ethanol or t-butanol primarily one product was formed at first, but this gave way to a fluorescent compound on prolonged reaction. No spot on TLC corresponded to the Schmidt product (96). In the NMR of the crude initial product there was a methylene singlet at 5.21 τ and in the IR an absorption at 3420 cm^{-1} indicated an N-H group and at 1680 cm^{-1} a carbonyl group. This compound was never obtained pure because on chromatography or mild hydrolysis with sodium bicarbonate in aqueous acetone it was converted to the fluorescent product. The initial product is probably the cyclic urethane (91), but on hydrolysis it does not give the amino alcohol (92 R=H) but 1-azapyrene (86). This fluorescent compound melted at the reported temperature[37] and analysed for $C_{15}H_9N$. It had eight aromatic protons at 1.3 - 2 τ and a low field one at 0.45 τ in the NMR. There was no carbonyl, hydroxyl or amino peaks in the IR. The best yield of 1-azapyrene was 72%, obtained when the reaction was carried out in t-butanol and hydrolysed under mild conditions.



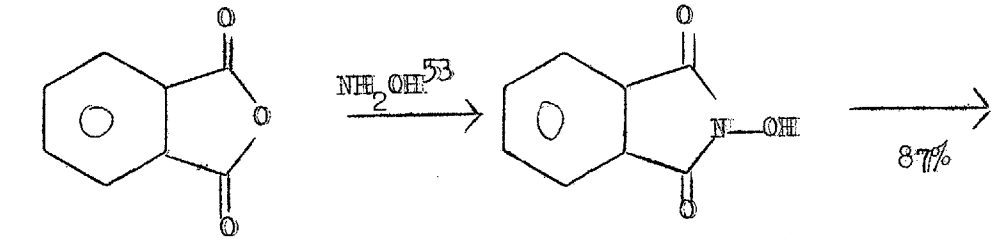
((109)) ((91)) ((86))

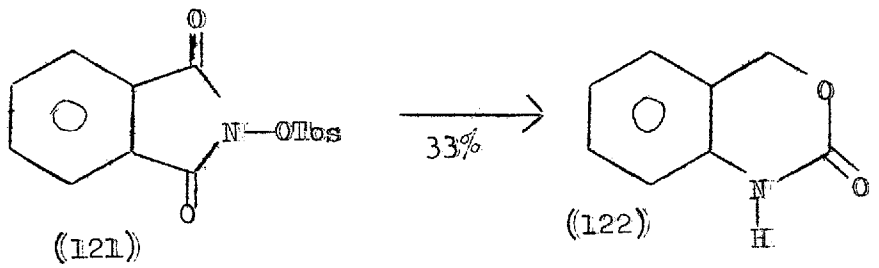
Clearly ring contraction by decarboxylation of (91) and subsequent oxidation of 1,2-dihydroazapyrene is a very facile process. The spectral data for the initial product precludes the alternative mechanism via intermediate (120) which does not require an oxidative step.



((110)) (120)

To clarify the mechanism, N-tosyloxyphthalimide (121) was prepared and reacted with sodium borohydride in ethanol.



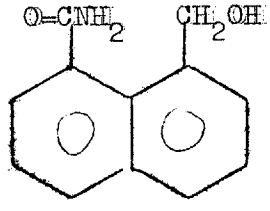


((121)) ((122))

The product was the urethane (122). In the NMR it had a methylene singlet at 4.71 τ, four aromatic protons at 2.6 - 3.3 τ and a broad exchangeable one proton peak at 0.67 τ. It analysed for $C_8H_7NO_2$ and had a carbonyl peak at 1725 cm^{-1} and an N-H stretch at 3250 cm^{-1} in the IR. This result supports the postulated intermediacy of (91) in the phenanthrene series.

The naphthalene analogue of these tosylates was available, but when this (46) was treated with sodium borohydride in ethanol the major products were naphthostyril (57%) and naphthalimide (20%). This was doubtless due to the presence of base in the solution.

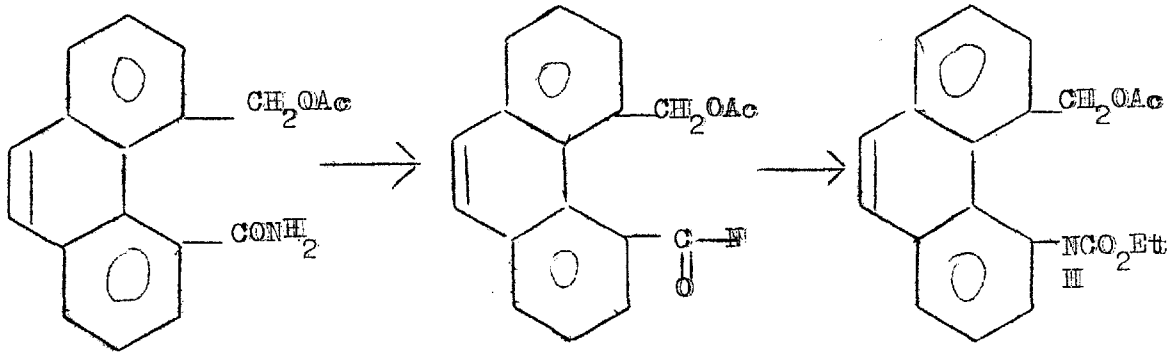
On repeating this reaction in t-butanol, decomposition of the tosylate was much slower but no naphthostyril was formed. TLC showed a large number of products including one which turned blue, suggesting the formation of the unstable benz(cd)indoline (49). One of the products obtained in both reactions was a solid which had IR peaks at 3200 - 3100 (broad) and 1680 cm^{-1} and NMR peaks at 4.96 τ, a two proton doublet with J = 4.5 cps, 3.42 τ, a broad exchangeable peak integrating for one proton, a six proton multiplet at 1.25 - 2.6 τ, and at -0.9 τ a broad peak integrating for about two protons. No more data is available, but this would satisfy structure (123).



(123)

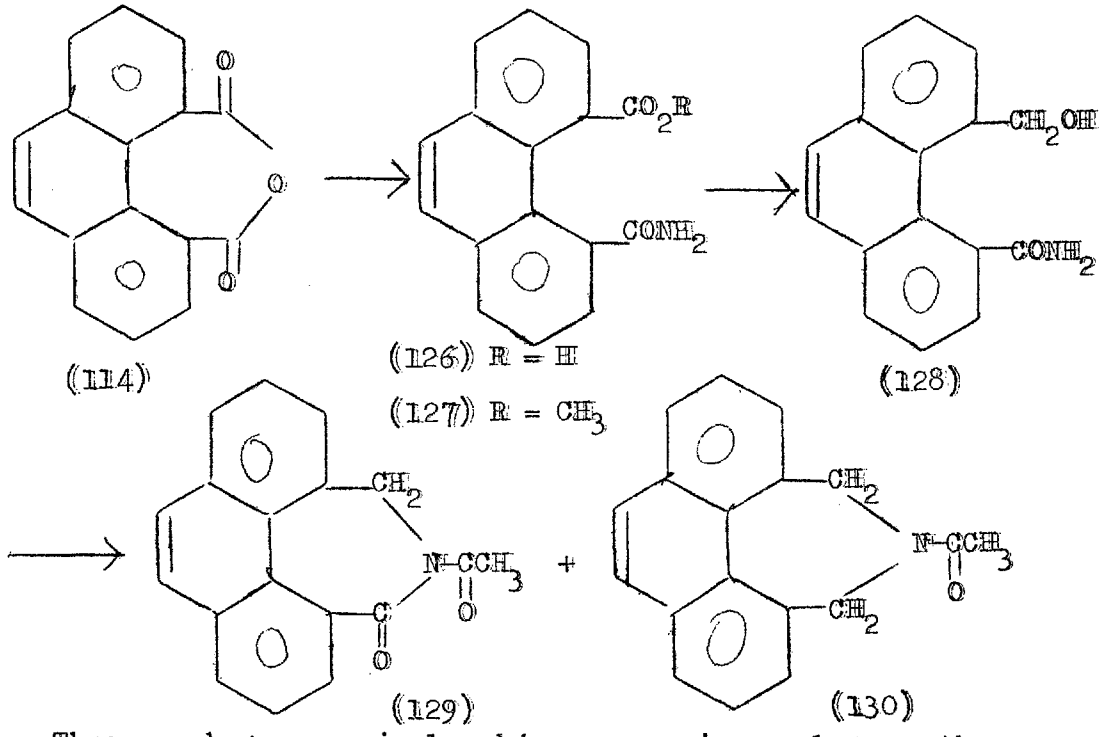
The Beckwith Reaction Approach

The sodium borohydride work showed that generating intermediate (90 R = H) leads to an intra-molecular reaction between the isocyanate and carbinol groups. The resulting urethane (91) was of no use as far as our synthetic objective was concerned. It was, therefore, decided to prevent cyclisation by a reaction involving intermediate (90 R = Ac). A suitable precursor that we proposed to prepare was the amido acetate (124). A Beckwith reaction with lead-tetra acetate in ethanol[48] should convert this to (90 R = Ac) which would rearrange to give (125) which is very closely related to the compound desired.



(124) (90) R = Ac (125)

Phenanthrene-4,5-anhydride (114) was converted to the amide acid (126) with ammonia in 51% yield[52] and this was esterified with diazomethane in 91% yield. The amido ester (127) was reduced with lithium borohydride in diglyme in 72% yield, but a peak at 2400 cm^{-1} in the IR implied that the product was a borohydride complex. After mild hydrolysis (128) was obtained and the crude material was acetylated with acetic anhydride in pyridine.

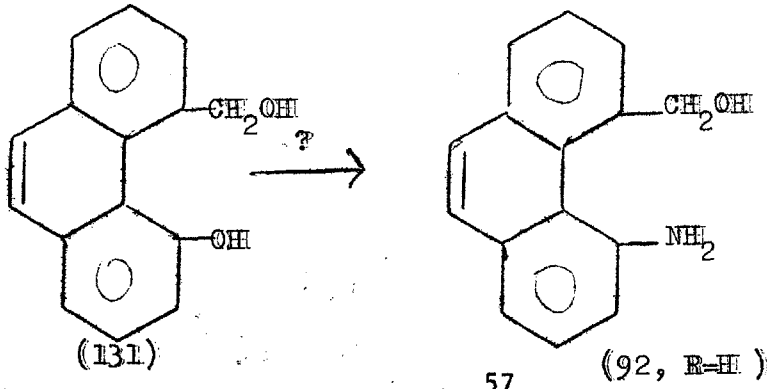


(114) (126) R = H (127) R = CH_3 (128) (129) (130)

Three products were isolated by preparative scale TLC. About 10% starting material (128) was recovered and identified by IR peaks at 3320 and 1630 cm^{-1} and a methylene doublet at 5.62 τ in the NMR which appeared as a singlet after shaking the solution with D_2O. One of the two acetates found was (129) (25% yield) which had two carbonyl groups indicated by absorptions at 1690 and 1660 cm^{-1} in the IR and a methylene singlet at 7.44 τ and a methylene singlet at 4.90 τ in the NMR. The other acetate was (130) (21% yield) which had a carbonyl absorption at 1650 cm^{-1}. In the NMR there were two methylene singlets at 5.41 τ and 5.24 τ and a methyl singlet at 7.70 τ.

These products show that lithium borohydride is not as selective a reducing agent as was thought[56] and that once again our synthetic plans were frustrated by interaction between substituents at positions 4 and 5.

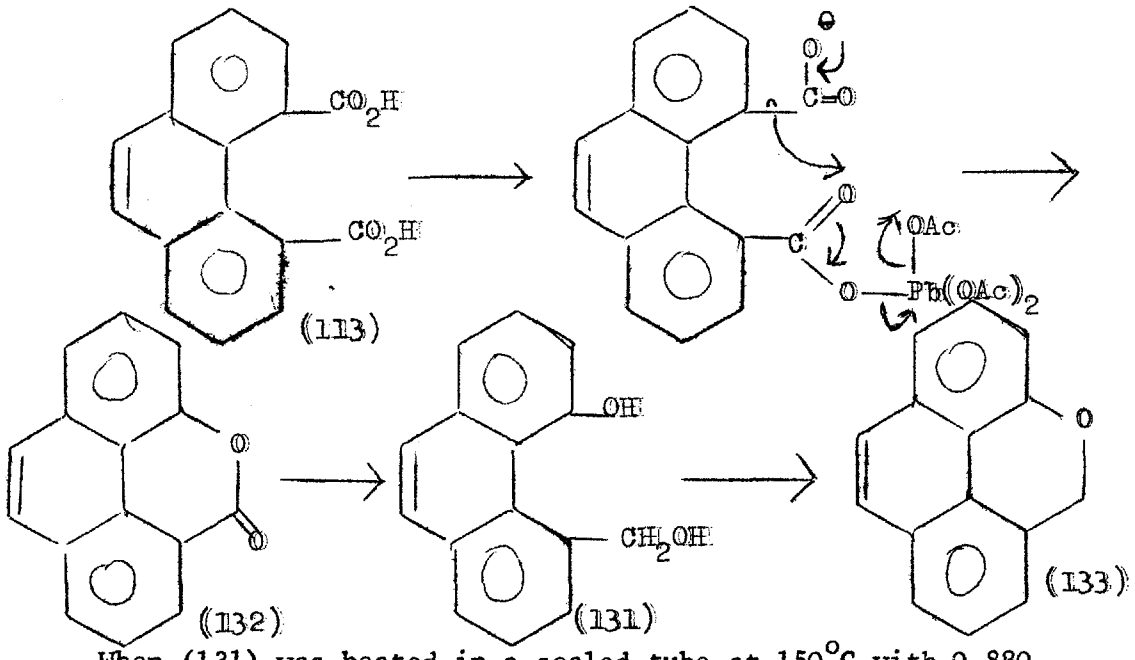
The Bucherer Reaction Approach



(131) (92, R=H)

It was hoped that a Bucherer reaction[57] would convert 4-hydroxymethyl-5-hydroxyphenanthrene (131) to amine (92).

The diol (131) seemed to be readily prepared from phenanthrene-4,5-dicarboxylic acid (113) as biphenyl-2,2'-dicarboxylic acid is reported to be cyclised to 3,4-benzocoumarin by reaction with lead tetraacetate in pyridine and acetonitrile.[58] Under similar conditions (113) was converted to the lactone (132) in 36% yield. Reduction of the lactone with lithium aluminium hydride gave a polar foam and a non-polar crystalline compound. The foam (53%) was identified as diol (131) with two hydroxyl absorptions in the IR at 3500 and 3250 cm^{-1}. The other product (17%) was the dehydration product of (131), the cyclic ether (133) which had a methylene singlet at 4.49 τ and no exchangeable protons in the NMR.

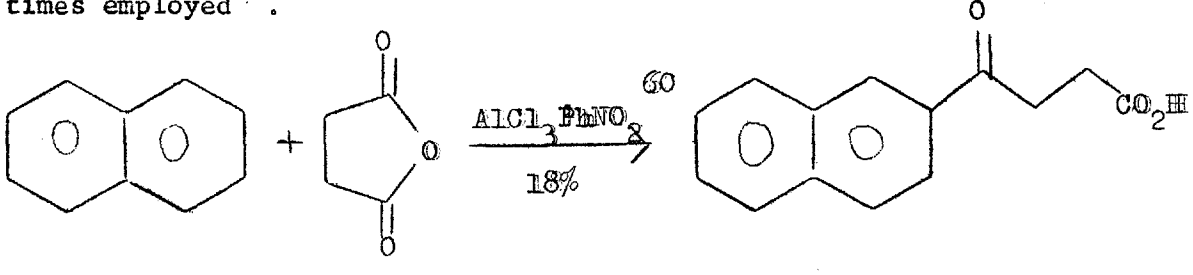


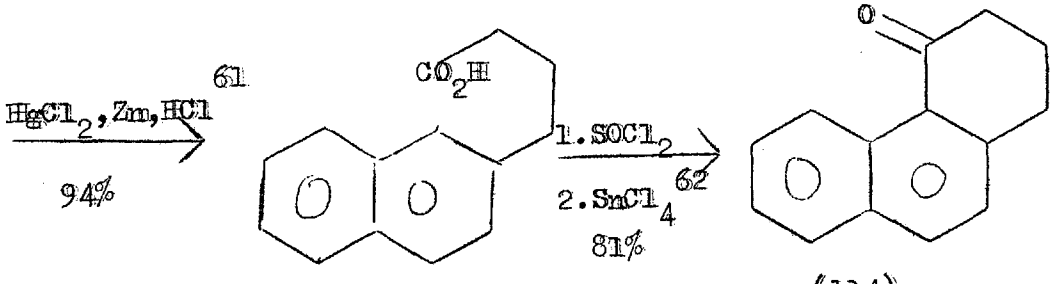
When (131) was heated in a sealed tube at 150°C with 0.880 ammonia and sulphur dioxide[59] there was a negligible amount of acid extractable product and a mixture of (131) and (133) was recovered.

Orientated Nitration Experiments

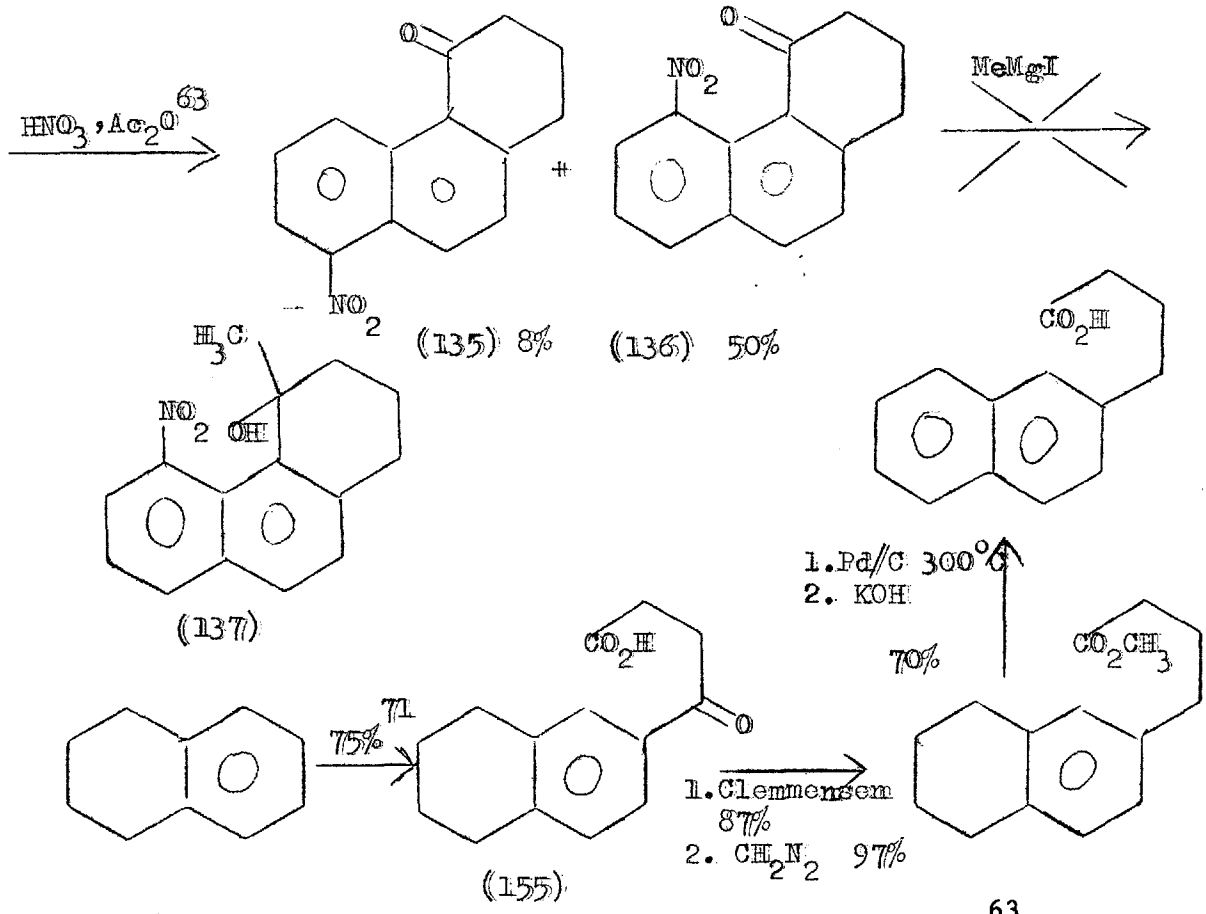
At this point experiments on compounds derived from pyrene were abandoned and work was initiated on a new approach to the synthesis. Starting with naphthalene it was proposed to construct the third ring in such a way that there would eventually be a substituent at the 4 position of the phenanthrene molecule which could be manipulated so as to become an alkoxymethyl group. It would also be suitable to assist in the introduction of a nitrogen function at position 5 by means of some preferrential orientation effect in a nitration reaction.

The first attempt at such a synthesis was taken essentially from published work. Naphthalene was converted to 4-keto-1,2,3,4-tetrahydrophenanthrene (134) in three classical steps. Another route to γ-2-naphthylbutyric acid starting with tetralin was sometimes employed[71].





(134)



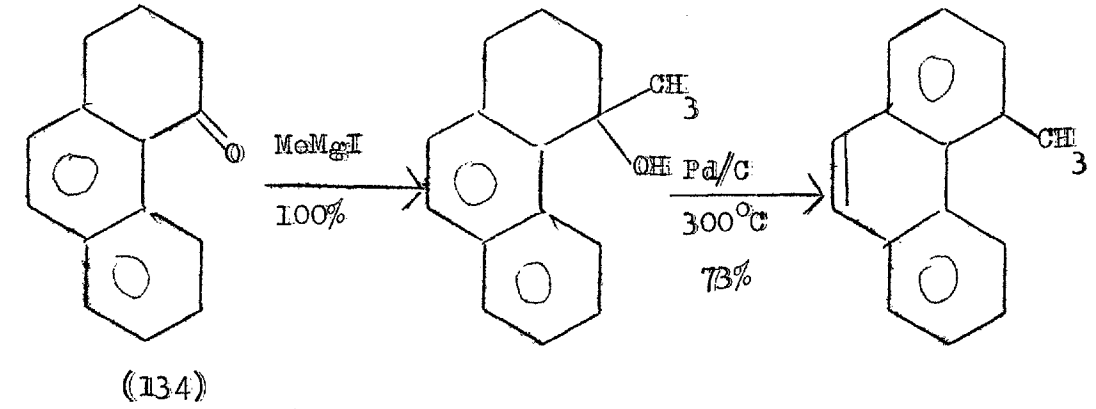
Nitration with fuming nitric acid in acetic anhydride[63] precipitated the nitroketone (136) from solution. It was easily identified as the 4-keto-5-nitro isomer by the absence of the low field aromatic proton which appeared at 0.55 τ in the NMR of (134). The position of nitration is doubtless due to an initial interaction between the carbonyl group and the nitrating species, which holds the nitronium ion in the correct position for aromatic nucleophilic substitution at position 5. A minor product (8%) was isomer (135). It had a low field proton at 0.45 τ and a pair of doublets J = 8 cps at 1.55 τ and 2.52 τ corresponding to H_9 and H_{10} respectively.

The next logical step in the synthesis is the introduction of a methyl group at position 4 by a Grignard reaction. Aromatisation of the anticipated product (137) would give 4-methyl-5-nitrophenanthrene which would require reduction of the nitro group to an amine and conversion of that to an azide, followed by funtionalisation of the methyl group with N-bromosuccinimide. Unfortunately only tars and multi-component mixtures were obtained from (136) under various conditions with methyl magnesium iodide and methyl lithium. A model reaction on the other isomer (135) showed that this failure was not due to the proximity of the ketone and the nitro group, but occurred because nitro groups are sensitive to Grignard reagents[64].

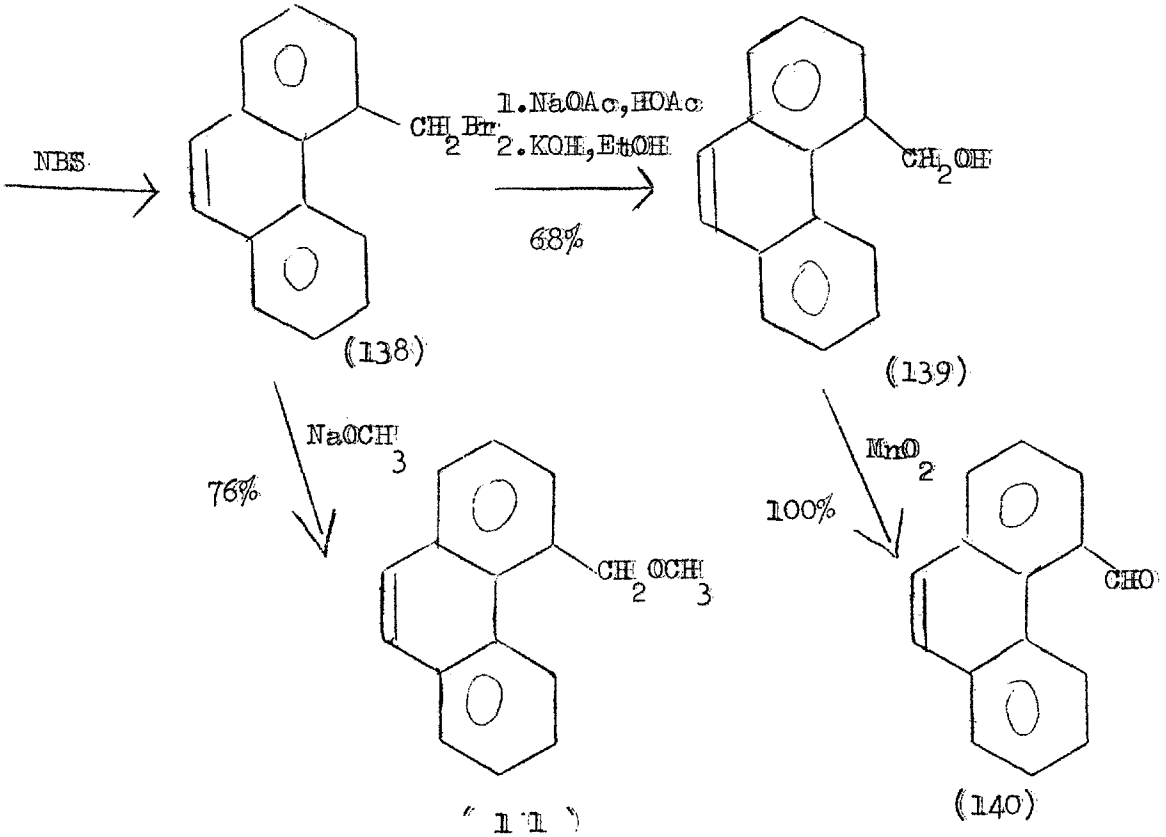
An attempt to introduce carbon at position 4 by making the cyanohydrin of (136) failed. Because of the nearness of the other substituent, the keto group in (136) does not give the common carbonyl derivatives[63].

The next logical approach is to introduce a carbon function at position 4 before the selective introduction of a nitro group at position 5. However, it has been shown that the least favourable site for nitration in phenanthrene is at position 4. For instance at 25° C the isomer distribution was 26% at C_1, 6.8% at C_2, 21.8% at C_3, 5.6% at C_4, 36.1% at C_9[65]. Thus our objective is intrinsically a difficult one. Nevertheless, it was decided to try to exploit the same orientating effect as was utilised in the phenethyl series to overcome these problems.

It was predicted that on nitration of 4-methoxymethylphenanthrene (141) initial O-nitration would enhance the yield of the 5-nitro isomer. Likewise it was thought that 4-formylphenanthrene (140) would exhibit the same orientating effect as was found for 4-keto-1,2,3,4-tetrahydrophenanthrene (134) giving the 4-formyl-5-nitro isomer.



(134)



(138)

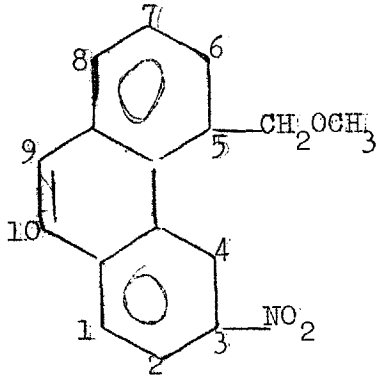
(139)

(141)

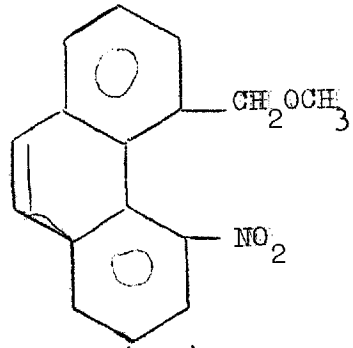
(140)

The synthesis of 4-bromomethylphenanthrene (138) from (134) is described in the literature[66]. The bromo compound (138) was converted to the required methyl ether (141) in 76% yield by refluxing with methanolic sodium methoxide. The NMR showed a methyl singlet at 6.48 τ and a methylene singlet at 4.97τ. The bromo compound (138) was also hydrolysed to 4-hydroxymethylphenanthrene (139)[66], which was oxidised quantitatively to 4-formylphenanthrene (140) with manganese dioxide. The carbonyl group in (140) absorbed at 1680 cm^{-1} in the IR and the formyl proton came at -0,60τ in the NMR.

4-methoxymethylphenanthrene (141) was nitrated with a 50% excess of silver nitrate and acetyl chloride in acetonitrile at 0° C. TLC showed two yellow spots. When these were isolated it was found that the less polar one consisted of at least four isomers as there were four methylene peaks and three methyl peaks in the NMR, and the more polar one consisted of two isomers. Both mixtures were separated carefully by multiple elution on 1 mm. Silica Gel plates. The less polar mixture was separated into two mixtures of two isomers, none of which looked like the required one (143). From the other mixture, 3-nitro-5-methoxymethylphenanthrene (142) was isolated pure.



(142)



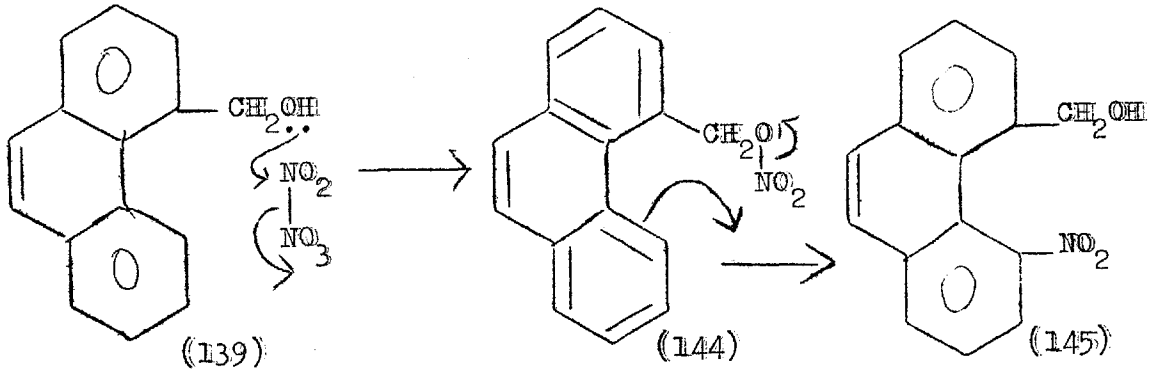
(143)

In the NMR (142) had a low field doublet at 0.18 τ J = 2.2 cps (H_4) which was coupled to a quartet at 1.68 τ J = 8.5, 2.2 cps (H_2). All the other aromatic protons appeared at 2.0 - 2.5 τ. The methyl singlet was at 6.32 τ and the methylene singlet at 5.10 τ.

The other component of this mixture was probably the 4-nitro-5-methoxymethyl isomer (143), but it could not be isolated free from (142). It was assigned the structure (143) because in the NMR of the mixture the H_5 peak at 1.25 τ in 4-methoxymethylphenanthrene (141) was missing, and the only low field protons were those due to H_2 and H_4 in (142) and a quartet at 1.85 τ due to H_3 in (143). The methyl and methylene signals at 6.93 τ and 5.38 τ respectively were shifted significantly from their positions in the spectrum of the unnitrated compound (141) where they came at 6.48 τ and 4.97 τ respectively and from their positions in the other nitro isomers where they came at 6.50 - 6.61 τ and 4.92 - 5.12 τ respectively. This is consistent with the nitro group lying in close proximity to the methoxymethyl group. However, the selectivity of nitration was not good enough and the difficulty of separating the isomers precluded this from being a viable synthetic route.

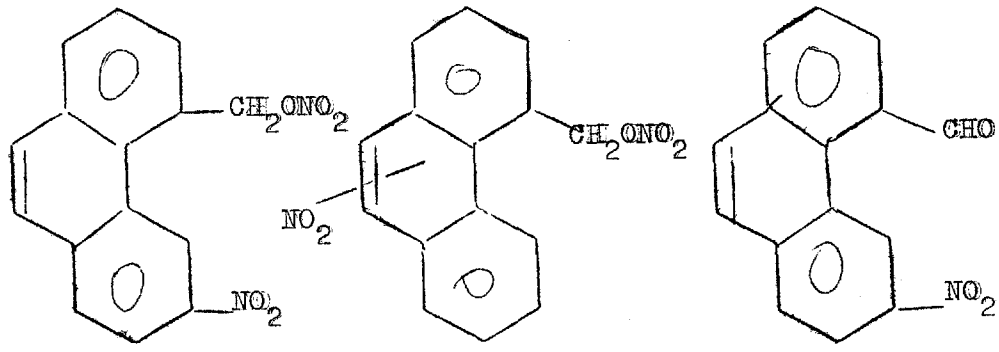
It was considered that nitration of 4-hydroxymethylphenanthrene (139) under the same conditions might *O*-nitrate giving nitrate (144) which would then be converted to (145). The reaction was rapid and the product isolated in 88% yield was indeed (144). It was identical

to the nitrate obtained on reacting the bromo compound (138) with silver nitrate in acetonitrile. The low field proton in the NMR came at 1.75 τ and the other aromatic protons were at 2.0 - 2.6 τ. Characteristic peaks in the IR were observed at 1625, 1295, 870 cm^{-1}.



(139) (144) (145)

(144) Could not be converted to (145) with boron trifluoride etherate. Nor did nitration with a large excess of nitrating agent for a longer reaction time furnish (145). Two major products were isolated and both had bands in the IR characteristic of a nitrate at 1650, 1290, 870 cm^{-1} and an aryl nitro compound at 1545 and 1350 cm^{-1}. The NMR of the minor product had a low field proton at 0.54 τ which appeared as a doublet coupled to a quartet at 1.6 τ. It was, therefore, designated as the 3-nitro isomer (146). The other product was probably (147), either the 9 or 10 nitro isomer.



(146) (147) (148)

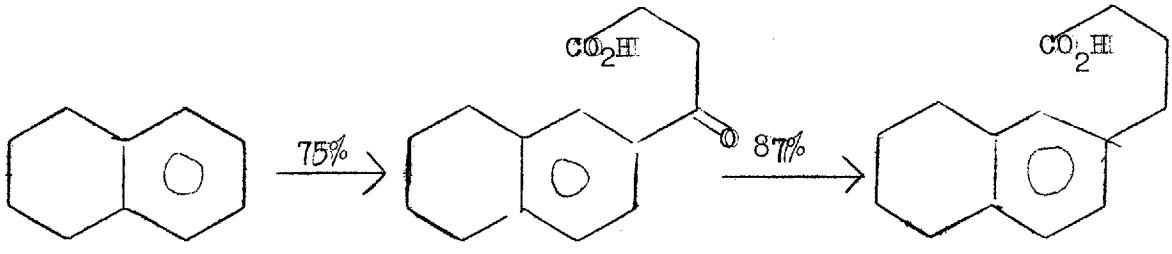
Nitration of the third compound in this series, 4-formylphenanthrene (140) also gave a mixture of isomers. Separation by multiple elution on 1 mm. Silica Gel plates gave three pure isomers, none of which looked like the desired one. Only one, the 3-nitro-5-formylphenanthrene (148) was readily identified from its NMR spectrum. The formyl proton in the NMR came at -0.64 τ, H_4 was a doublet at 0.95 τ and H_2 a quartet at 1.60 τ The other protons appeared as a complex pattern at 1.8 - 2.3 τ.

Thus these orientated nitration experiments failed to provide a satisfactory route to the 4,5-disubstituted phenanthrene we require. Precisely why we failed to get significant quantities of the predicted preferrential isomer is not too clear. Perhaps the invariable formation of the 3-nitro isomer indicates that the oxygen atom in the substituent at position 5 holds the nitronium ion over position 3 rather than position 4. Thus the orientating effect is operating in such a way as to afford the 3-nitro isomer.

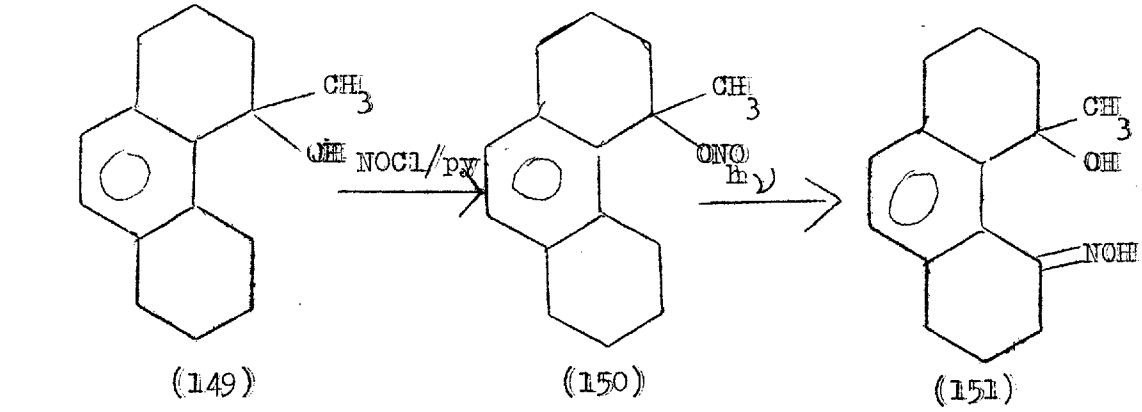
Synthesis of 4-amino-5-methylphenanthrene

Because the orientated nitration experiments failed to achieve the required selectivity, other methods of selectively introducing a nitrogen function onto a phenanthrene skeleton were considered. The Barton nitrite photolysis[67] is one such reaction and a suitable precursor for this reaction (149) is readily prepared from the known 4-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene (156). Nitrite (150) is correctly set up for the selective transfer of a nitrosyl radical to position 5. In the product (151) the ring containing the newly formed oxime group is at the required oxidation level and presumably, like 4-oximino-1,2,3,4-tetrahydrophenanthrene, it could be converted to the corresponding aryl amine by means of a Semmler reaction[68,69,70]. The product in the present case would be the amino-dihydrophenanthrene (152). As has been discovered earlier, an aryl azide is inert to radical bromination conditions, so that the amino group can be converted to an azide before functionalising the methyl group.

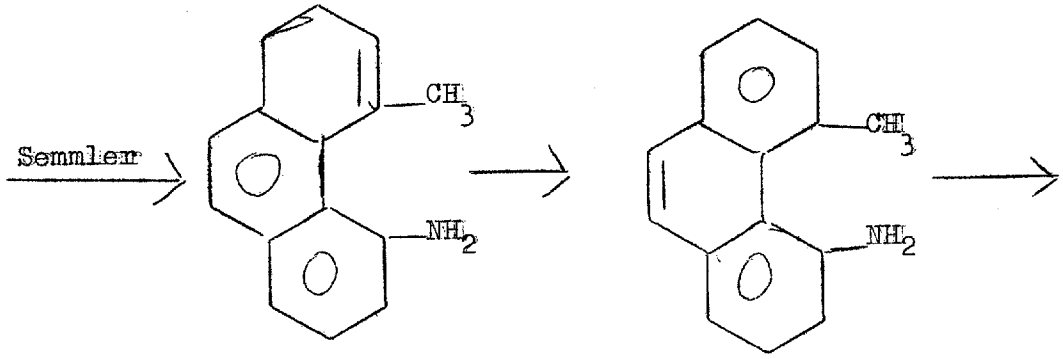
Tetralin was the starting material for this synthesis. It was converted to γ-(2-tetralyl)-butyric acid (155) by a Friedel Crafts reaction with succinic anhydride followed by Clemmensen reduction[61,71].



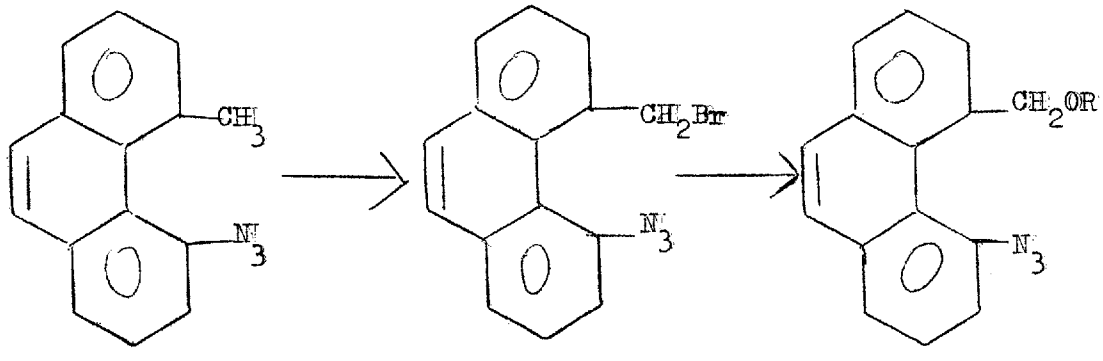
(155)



(149) (150) (151)

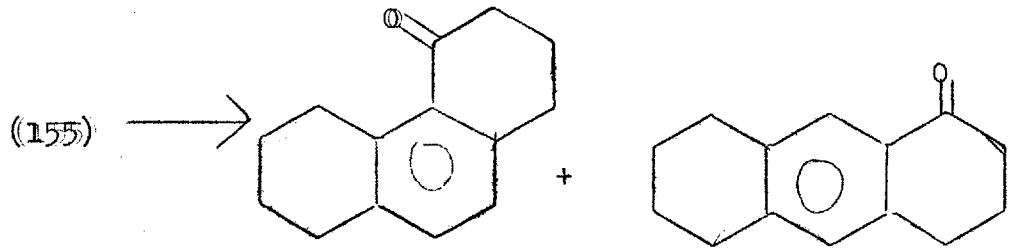


(152) (153)



(154) (85)

It was not possible to repeat any of the reported selective cyclisations of (155) to 4-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene (156)[72]. Very little of this was obtained, the major product being the linear isomer 1-keto-1,2,3,4,5,6,7,8-octahydroanthracene (157).

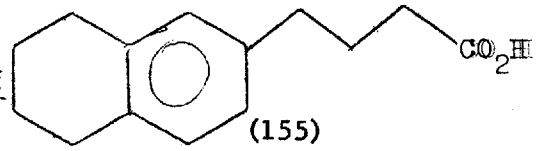


(155) (156) (157)

These two compounds were separated chromatographically and were easily differentiated. Octahydrophenanthrone (156) melted at 40 - 40.5° C and had an AB quartet at 2.95 τ J = 8 cps in the NMR while octahydroanthrone (157) melted at 47 - 47.5° C and had the two aromatic protons as singlets at 2.30 τ and 3.10 τ. Table IV shows the yields of the two isomers obtained under various conditions.

The published work implied that (157) might be converted to (156) by heating it in conc. sulphuric acid[72], but when this was tried octahydroanthrone (157) was recovered unchanged. A reasonable yield of the required octahydrophenanthrone (156) was produced by converting the acid (155) to the acid chloride with phosphorus pentachloride and distilling a mixture of ketones (156) and (157)

Table IV

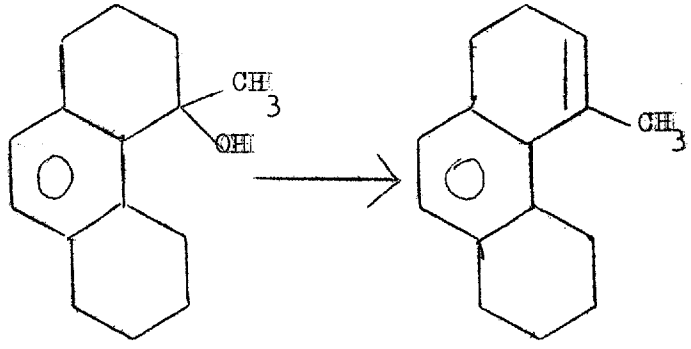
Cyclisation of  (155)

Reagent and Conditions	Yield		Literature Yield	
	(157)	(156)	(157)	(156)
PCl_5, $AlCl_3$, 120°C	91%	trace	2%	58%
Conc.H_2SO_4, 100°C, 4 hours[72]	68%	-	2%	20%
Conc.H_2SO_4, 20°C, 2 hours[72]	43%	1.8%	50%	5%
$SOCl_2$, $SnCl_4$, 0°C[72]	93%	2%	45%	22%
Polyphosphoric acid, 70°C[73]	23%	5%	47%	28%
PCl_5, distillation at 250°C, 2mm[74]	28%	25%	1 : 1	

at 250°C and 2 mm pressure. In this reaction phosphorus oxychloride is generated in making the acid chloride and then acts as a Friedel Crafts catalyst for the cyclisation when the mixture is warmed. When the procedure was repeated substituting thionyl chloride for phosphorus pentachloride, the acid chloride was obtained on distillation. When the mixture of ketones was chromatographed on a Grade 3 Alumina column, octahydrophenanthrone (156) was eluted first in 25% yield.

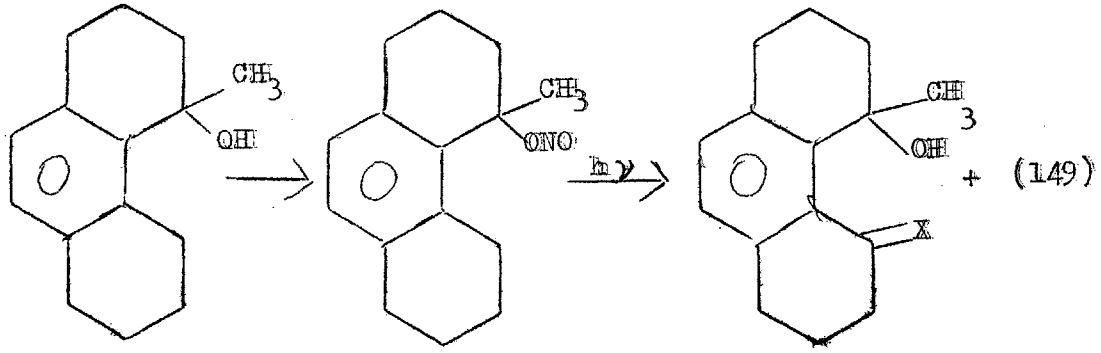
A Grignard reaction with methyl magnesium iodide followed by a careful work up with ammonium chloride converts (156) to the carbinol (149) in excellent yield. If the work up solution is

allowed to get warm dehydration takes place and some (158) is produced. This had no hydroxyl at 3320 cm^{-1} in the IR and the methyl signal at 8.43 τ in the NMR of (149) shifted to 7.83 τ and appeared as a doublet (J = 1 cps). The vinyl proton signal was a triplet (J = 5 cps) at 4.02 τ.



(149) (158)

Nitrosation of carbinol (149) with nitrosyl chloride in pyridine at -30°C gave the nitrite (150) quantitatively. It was identified by IR peaks at 1625 and 780 cm^{-1}. Without purification a benzene solution of (150) was irradiated in a pyrex flask using a medium pressure mercury vapour lamp. A drop of pyridine was always added to neutralise any acid that might be formed. The products, separated on a Grade 5 Alumina column, were carbinol (149) obtained in 44% yield, 4-hydroxy-4-methyl-5-oximino-1,2,3,4,5,6,7,8-octahydrophenanthrene (151) obtained in 35% yield, and the corresponding ketone (158) obtained in 5.5% yield.

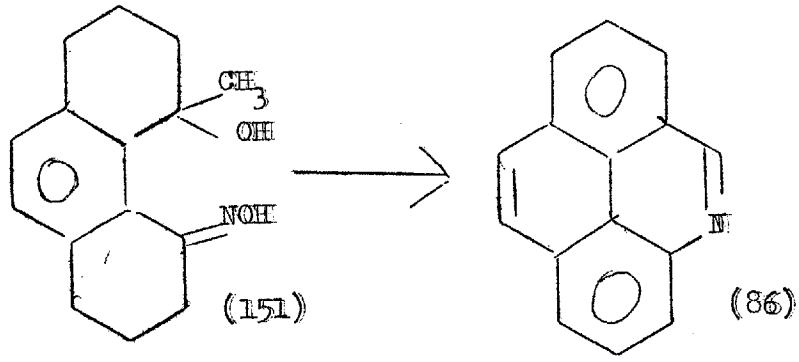


(149) (150) (151) X = NOH

(158) X = O

The relative yields of carbinol (149) and oxime (151) varied with different batches of benzene used as the solvent. In all experiments Analar benzene was dried over sodium and distilled from sodium so the hydrogen abstracted from the reaction medium probably does not come from moisture but from toluene, xylenes etc. present as impurities. With the best batch of benzene used, the photolysis was so clean that the oxime (151) was crystallised pure in 69% yield from the crude photoproduct. The worst batch of benzene, in which more than half distilled above 81° C, gave only about 20% of oxime (151) and 40-50% of carbinol (149). When the photolysis was carried out in Arcton 113 (CF_2ClCCl_2F) the oxime was obtained in 46% yield and the carbinol in 16% yield.

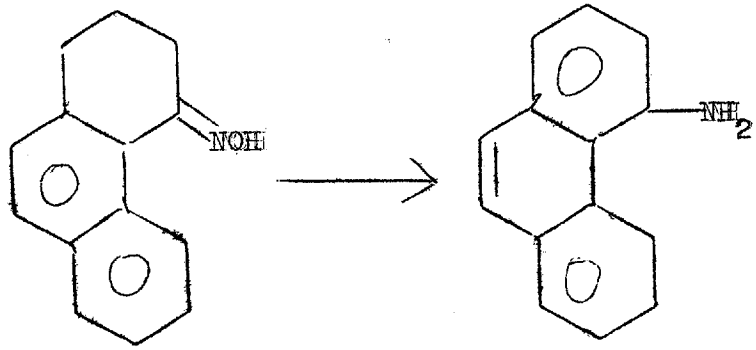
The oxime was identified by its IR spectrum which had hydroxyl absorptions at 3375 and 3160 cm^{-1} and a weak C=N peak at 1645 cm^{-1}. The position of the oximino group on the phenanthrene skeleton was confirmed by the formation of 1-azapyrene (86) when (151) was oxidised with 10% Pd/C at 300 - 320° C.



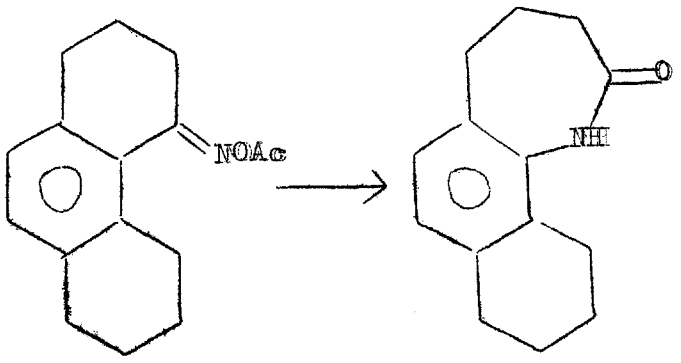
(151) (86)

The Semmler Aromatisation Reaction

The oxime of an αβ-unsaturated cyclohexenone can be converted to an aniline by passing HCl through a warm solution of the oxime in acetic anhydride and glacial acetic acid, although the yield is often not high.[69,70,74-83] An obvious competitive reaction is the Beckmann rearrangement which would give a seven membered ring lactam. For instance, whereas 4-oximino-1,2,3,4-tetrahydrophenanthrene (159) undergoes a Semmler aromatisation,[68,69,70], 4-oximino-1,2,3,4,5,6,7,8-octahydrophenanthrene (160) undergoes rearrangement[70].

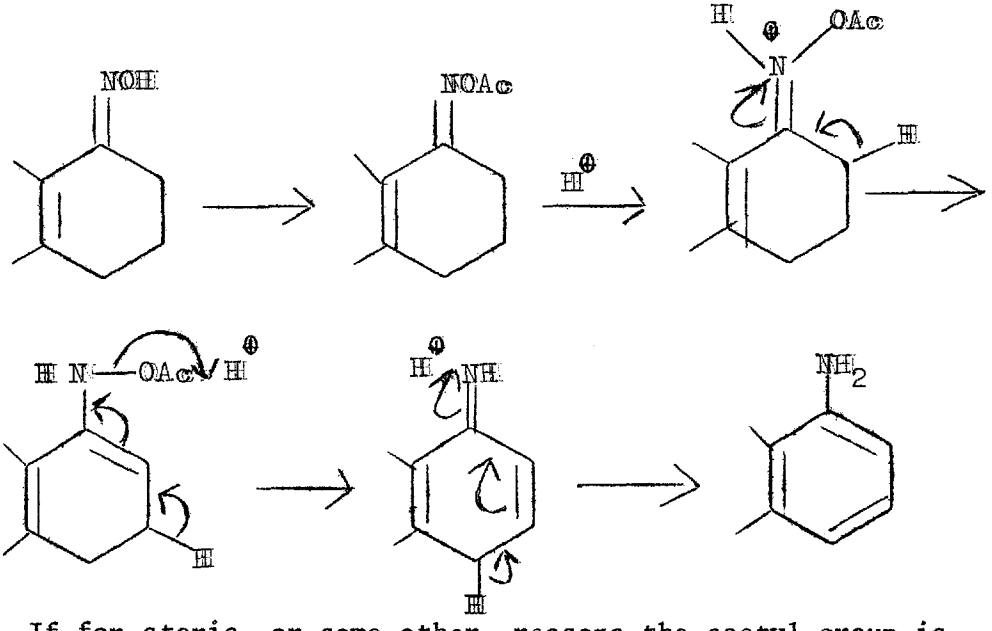


(159)

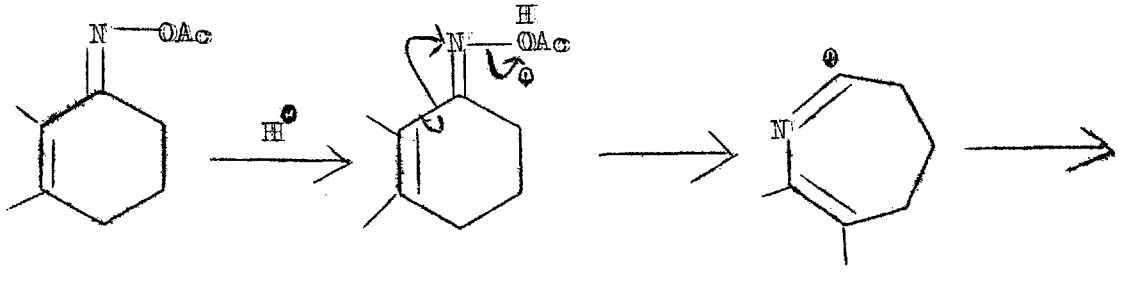


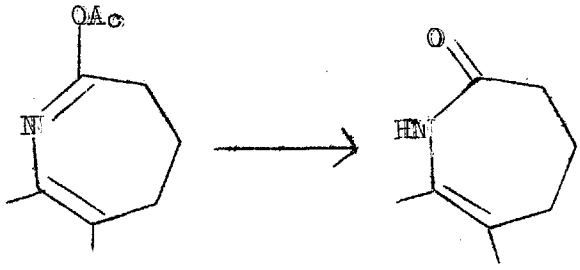
((160))

A feasible mechanism for the Semmler aromatisation is:

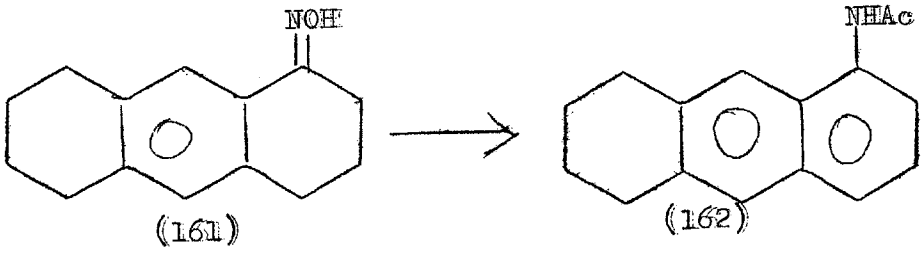


If for steric, or some other, reasons the acetyl group is protonated in preference to the nitrogen atom in the first step, and hence acetic acid lost, then a Beckmann rearrangement ensues in place of the Semmler aromatisation.



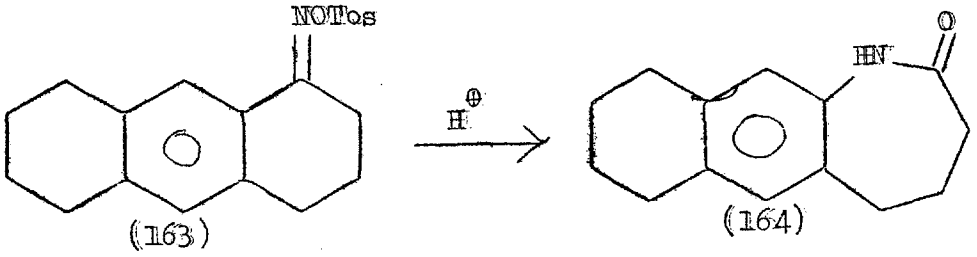


Using the oxime of octahydroanthrone (161) as a model compound in an exploratory reaction, aromatisation under Semmler conditions gave the naphthyl amide (162) in 53% yield.



(161) (162)

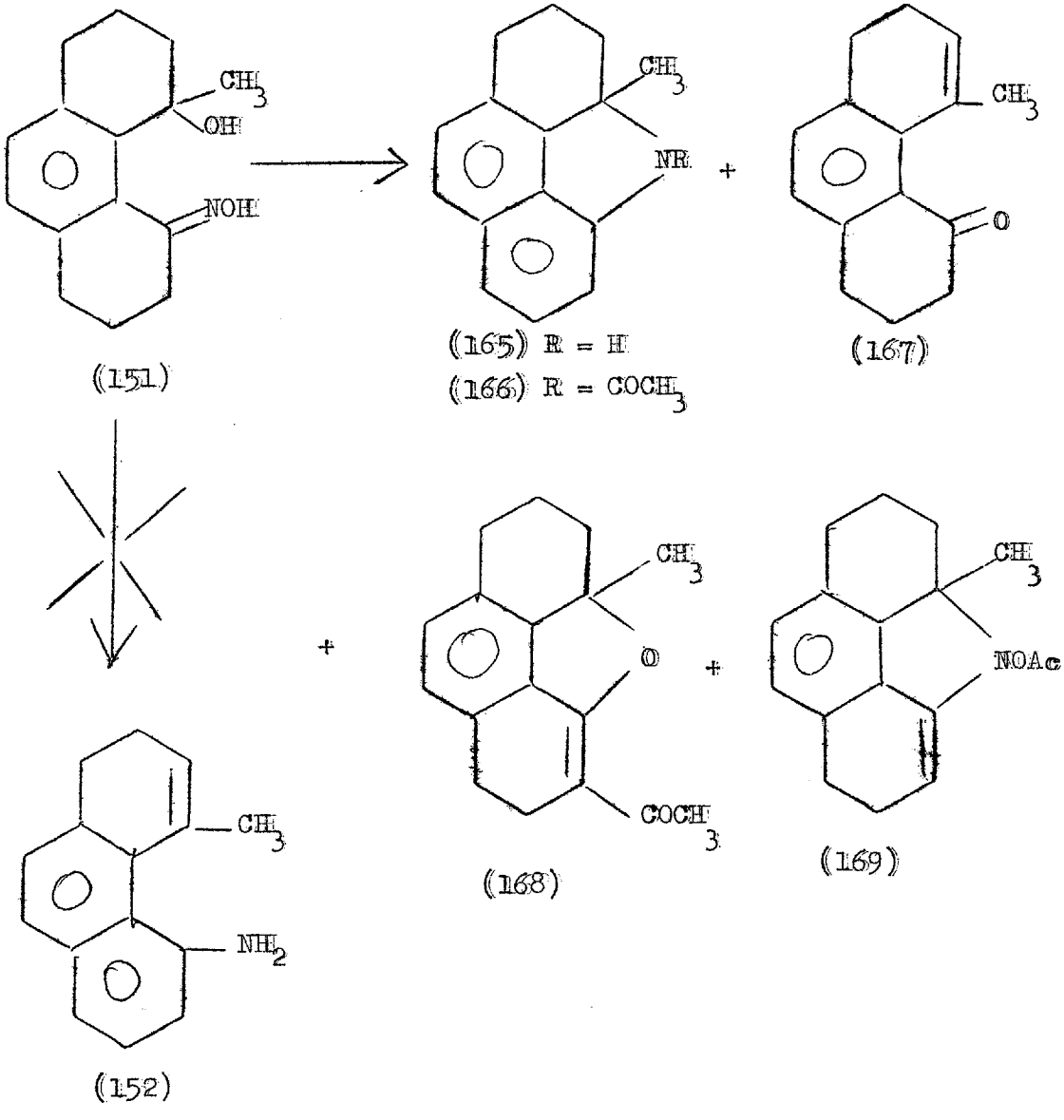
The oximino tosylate (163) on the other hand, did not aromatise on treatment with dry HCl but underwent a Beckmann rearrangement.

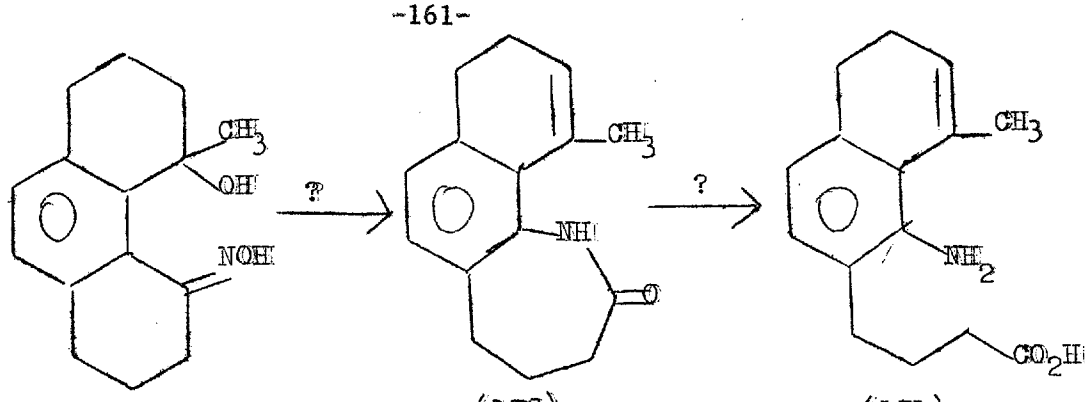


(163) (164)

Oximino tosylates invariably prefer to undergo a Beckmann rearrangement rather than a Semmler aromatisation[74,80] doubtless because protonation of the tosylate group is preferred to protonation at the nitrogen atom.

When dry HCl was bubbled through a warm solution of the oxime photoproduct (151) in acetic acid and acetic anhydride neither the anticipated dihydrophenanthrylamine (152) nor a ring expanded lactam (170) was found. Five products were isolated by preparative scale TLC, but they only accounted for about half of the starting oxime. In the aqueous extract there may have been some amino acid (171), the hydrolysed Beckmann product.

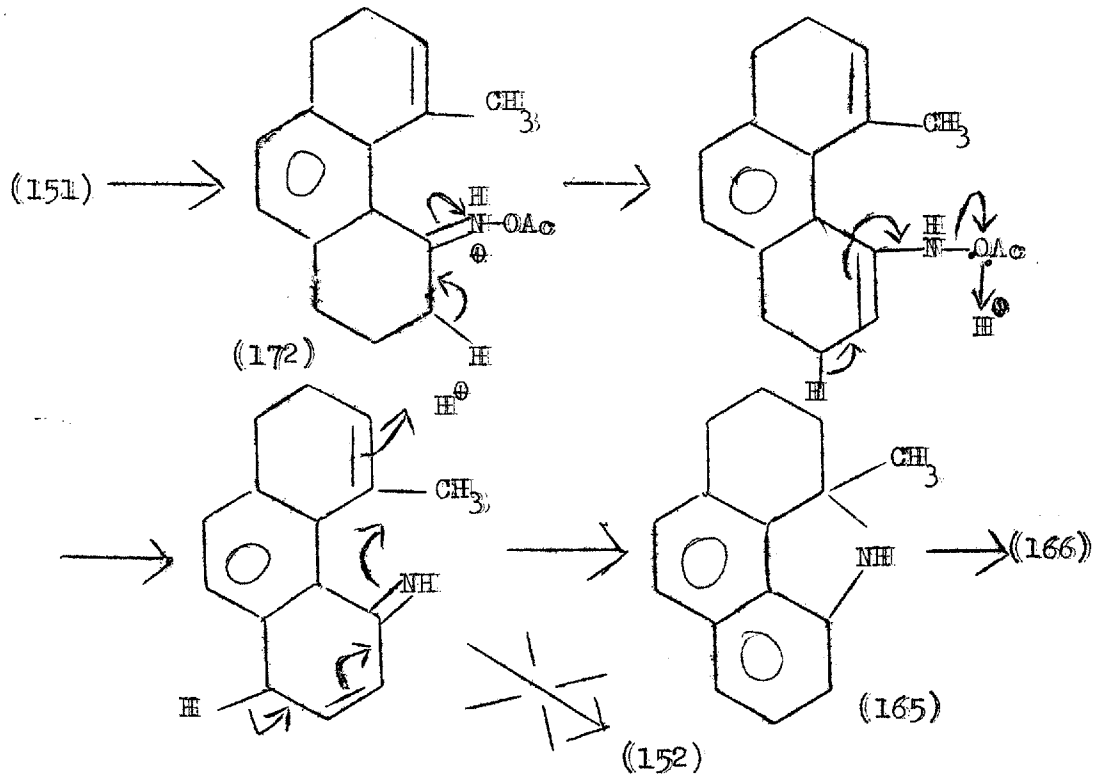




(151) (170) (171)

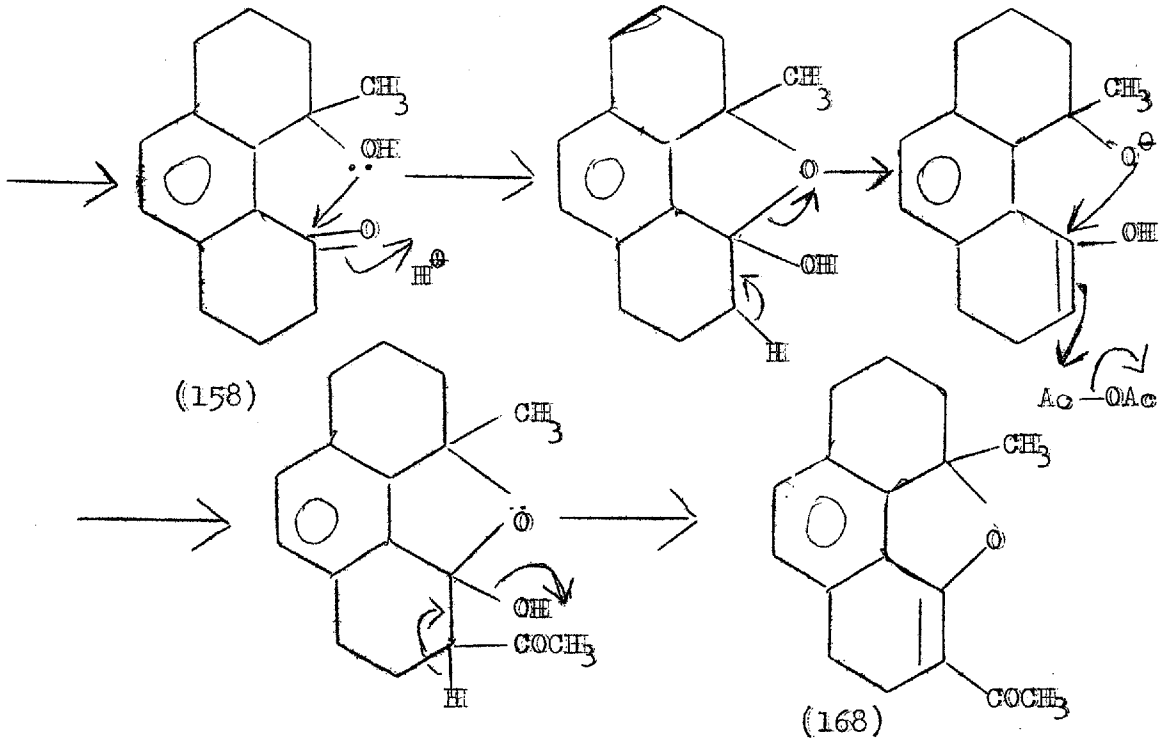
Only two of the products were naphthalene derivatives; these were (165) and (166) obtained in 19% and 2% yield respectively. Amine (165) had a single peak at 3400 cm^{-1}, which established it as a secondary amine, and no carbonyl absorption in the IR. It analysed for $C_{15}H_{15}N$ and had a corresponding molecular ion at M/e 209 in the mass spectrum. In the NMR there were four aromatic protons at 2.5 - 3.0 τ and another, H_6, which appeared as a quartet at 3.59 τ (J = 7,2 cps). The amine proton at 5.80 τ was exchanged on shaking the solution with D_2O and there were six methylene protons at 7 - 7.3 τ and 7.7 - 8.2 τ and a methyl singlet at 8.50 τ.

The other aromatised product (166) was the acetate of (165) and was prepared in excellent yield when (165) was heated in refluxing acetic anhydride. The carbonyl group absorbed at 1660 cm^{-1} in the IR and the two methyl singlets in the NMR came at 7.59 τ and 8.32 τ. In subsequent work it was found preferable to work with amide (166) rather than (165) and the conditions of the Semmler reaction were adjusted so that it produced (166) in 20 - 25% yield. The formation of the cyclic amine rather than the anticipated dihydrophenanthrylamine (152) can be rationalised as shown below.

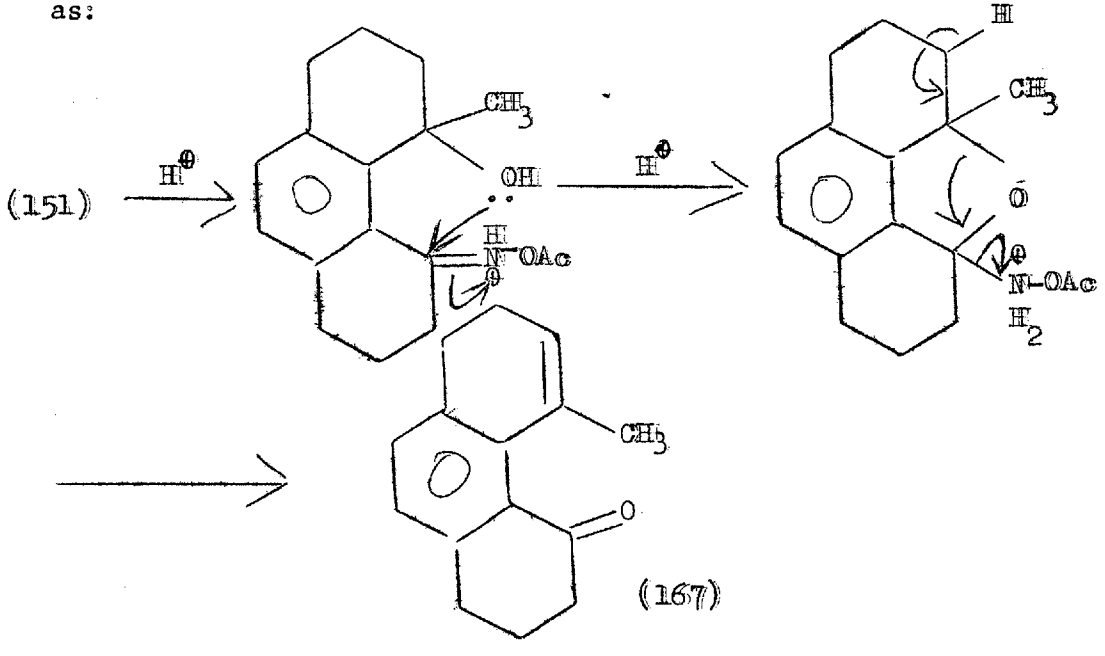


Amine (165) is an oil which can be distilled, but darkens on standing. The fact that it is a stable benz(cd)indoline lends support to the suggested explanation for the ease of oxidation of other benz(cd)indolines mentioned earlier, where there is an unsubstituted methylene group next to nitrogen which can be oxidised.

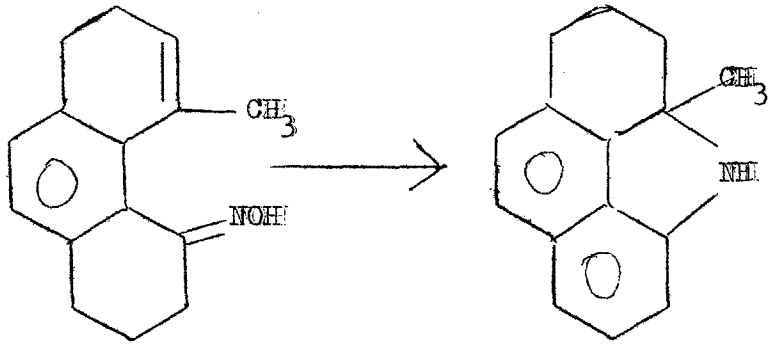
The only crystalline product isolated was (168) which was obtained in 3% yield. It analysed for $C_{17}H_{18}O_2$ and had a corresponding molecular ion at M/e 254 in the mass spectrum. It fragmented to lose 15 mass units (CH_3) and 43 mass units (CH_3CO). In the IR there was a carbonyl peak at 1675 cm^{-1} but no hydroxyl peak. In the NMR there were two methyl peaks at 7.64 γ and 7.93 γ. The two aromatic protons appeared as a quartet (J = 9 cps) at 2.91 γ and there were ten methylene protons. A possible mechanism for the formation of (168) is suggested below.



The anhydro ketone (167) was obtained in 10% yield. The keto group absorbed at 1680 cm^{-1} in the IR. In the NMR the methyl group appeared at 8.10 τ and the vinylic proton was a triplet at 3.83 τ. (167) was formed either by hydrolysis of the oxime to (158) followed by acid catalysed dehydration or by a process such as:

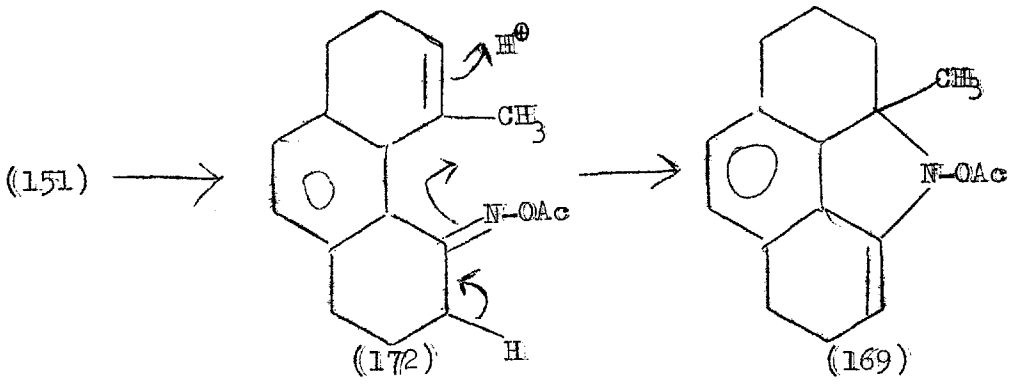


The anhydro ketone was later oximinated to (173), and under Semmler conditions this oxime also gave amine (165), thereby lending a little support to our proposed Semmler mechanism.

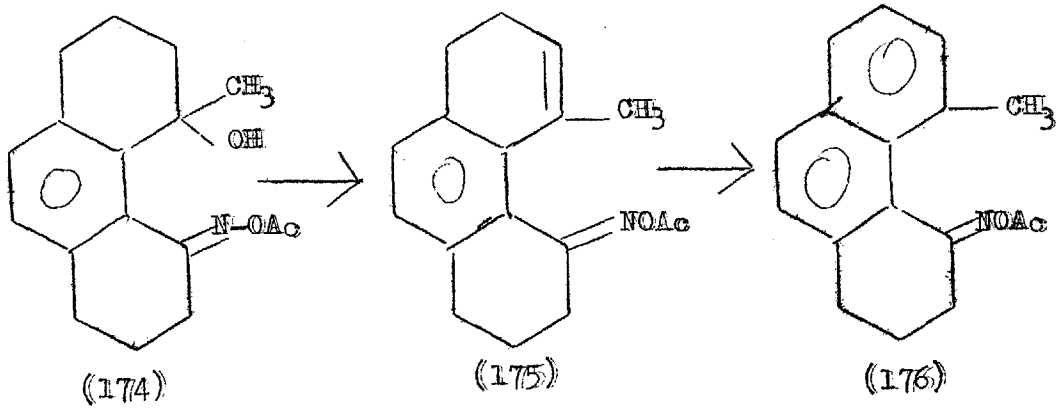


(173) (165)

The final product isolated was assigned the structure (169). On this occasion a 10% yield was obtained, although in other runs more was often produced. It is a polar compound which turned green on Silica Gel plates and was very difficult to crystallise. The compound analysed for $C_{17}H_{17}NO_2$ and had a molecular ion at M/e 269. In the IR the carbonyl stretch came at 1730 cm^{-1}. In the NMR the two methyl groups appeared as singlets at 7.80 τ and 8.58 τ and the vinylic proton was a quartet at 3.88 τ. The spectra were not identical to those of the isomeric anhydro oximino acetate (172) which was prepared independently.



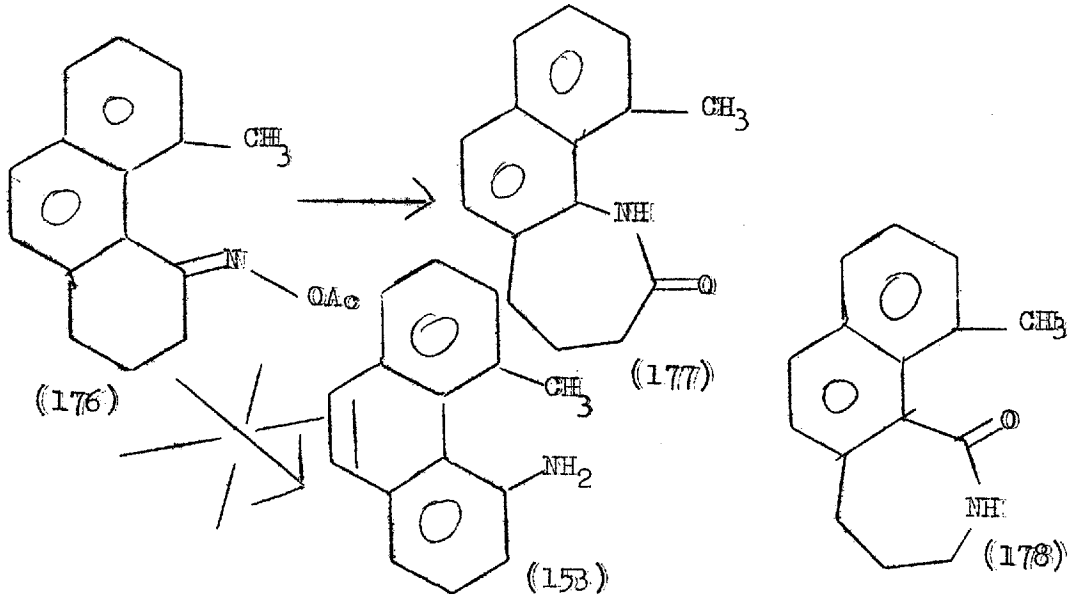
Cyclisation giving a benz(cd)indoline instead of the formation of an amino-dihydrophenanthrene (152) could clearly be avoided if the ring containing the methyl substituent in the oxime (151) is dehydrated and aromatised before carrying out the Semmler reaction.



The oxime (151) was acetylated to give (174) which had a carbonyl absorption at 1765 cm^{-1} in the IR. Attempted dehydration of (174) by treatment with acid-hydrochloric, tosyl and formic acids were tried - under anhydrous conditions was unsuccessful giving a multi-component mixture. Aqueous sulphuric acid merely hydrolysed (174) to the anhydro ketone (167). The dehydration was accomplished by reaction with phosphorus oxychloride in pyridine, but the yield of (175) was

only about 20%. In the IR spectrum the carbonyl peak at 1765 cm^{-1} remained but there was no hydroxyl peak at 3400 cm^{-1}. In the NMR spectrum the methyl singlet which appeared at 8.54 τ in the spectrum of (174) was shifted downfield to 8.10 τ and appeared as a doublet J = 1 cps coupled to the vinylic multiplet at 4.1 τ. Oxidation of (175) with dichlorodicycanobenzoquinone (DDQ) in refluxing benzene gave (176) in 45% yield. In the NMR the aromatic protons appeared as a complex multiplet at 2.1 - 2.9 τ and the methyl signal was shifted downfield from its position in the spectrum of (175) to 7.47 τ. In the spectra of all three compounds in this series the acetyl methyl signal came at 7.8 τ.

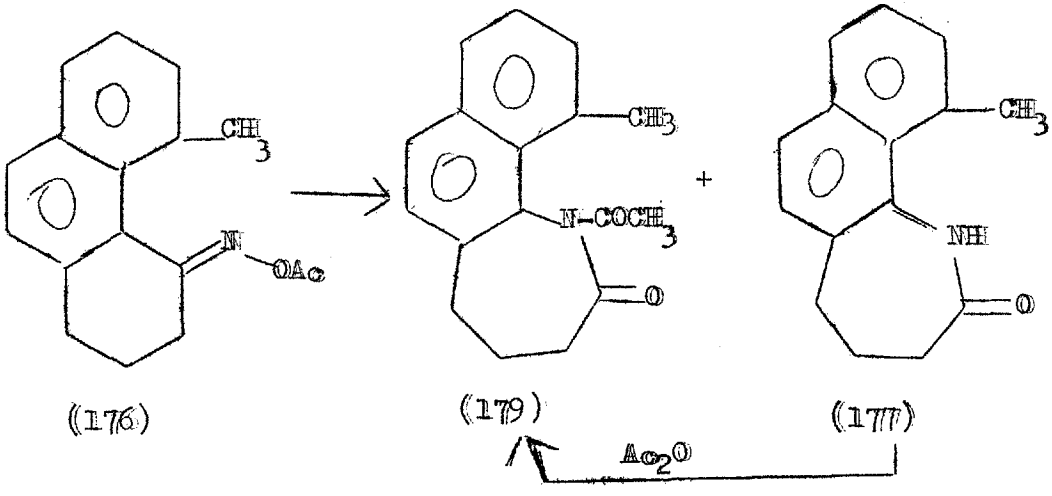
When this naphthyl oximino acetate (176) was subjected to Semmler reaction conditions a clean reaction ensued and a crystalline product was produced in 80% yield. It was not the anticipated Semmler product (153), but lactam (177), a Beckmann rearrangement product. The same compound was the sole product when (176) was heated in polyphosphoric acid at 130° C.



In the NMR spectrum there was only one methyl signal which came at 7.08 τ and there were both methylene and aromatic protons in the ratio of 6:5. In the IR spectrum there was an N-H stretch at 3200 cm^{-1} and a carbonyl stretch at 1660 cm^{-1}. The similarity of the IR to that of the related amide in the anthracene series (164) indicated that (177) is the correct structure rather than (178). The molecular ion at M/e 225 and a fragmentation where 55 mass units are lost giving an ion at M/e 170 ($M^+ - C_3H_3O$) lends support to this structure. It is quite important to establish the structure because there has been one report of a reaction where treatment of an oxime with polyphosphoric acid gave the anticipated Beckmann product, but under Semmler reaction conditions the other isomer was obtained in addition to an aryl amine[83]. It was thought that acid catalysed syn-anti isomerisation of the oxime group occurred under Semmler conditions and the anti isomer aromatised faster than the competing Beckmann reaction. The syn isomer, on the other hand, underwent ring expansion giving the isomeric lactam to that produced using Beckmann procedures when an anti oxime rearranges. The stereochemistry of our system (176) probably restricts isomerisation of the oxime, so that with the geometry as illustrated, both the Beckmann and the Semmler reactions would be expected to give (177) and not (178).

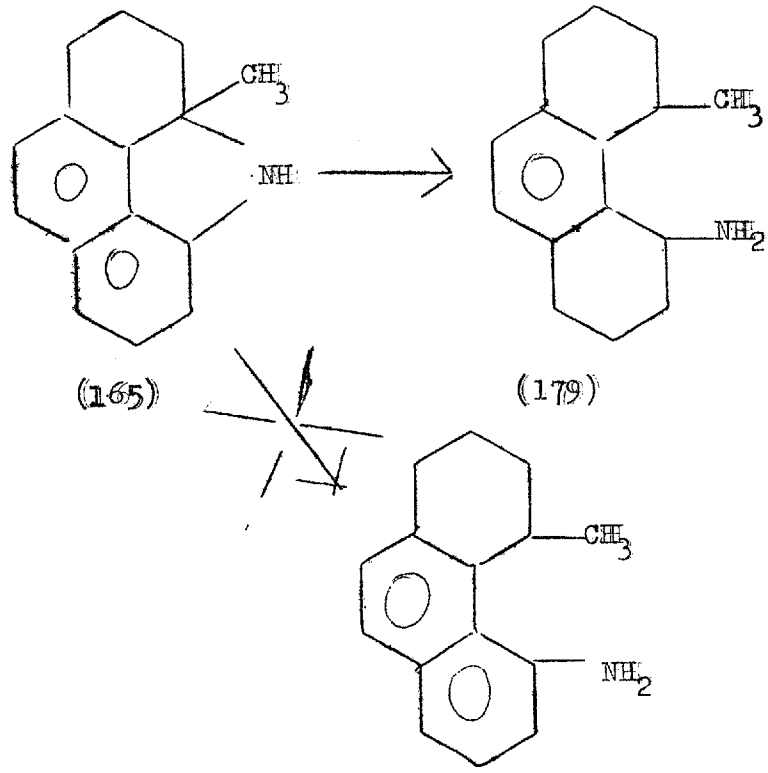
A modification of the Semmler aromatisation which has been used to aromatise a steroidal ring A was attempted. The naphthyl oximino

acetate (176) was heated in refluxing acetyl bromide with a drop of ethanol. TLC showed five products of which only two were identified as amides by their IR specta. One was the regular Beckmann product (177), and the other, the major product which was isolated in 25% yield, was the acetylated lactam (179).



(179) was also obtained when lactam (177) was acetylated with acetic anhydride under reflux. In the IR the carbonyl absorption was at 1700 cm^{-1} and the molecular ion in the mass spectrum was at M/e 267.

Attention was turned again to the Semmler product benz(cd)indoline (165). It was thought that the heterocyclic ring could be opened by hydrogenolysis in an acidic medium.



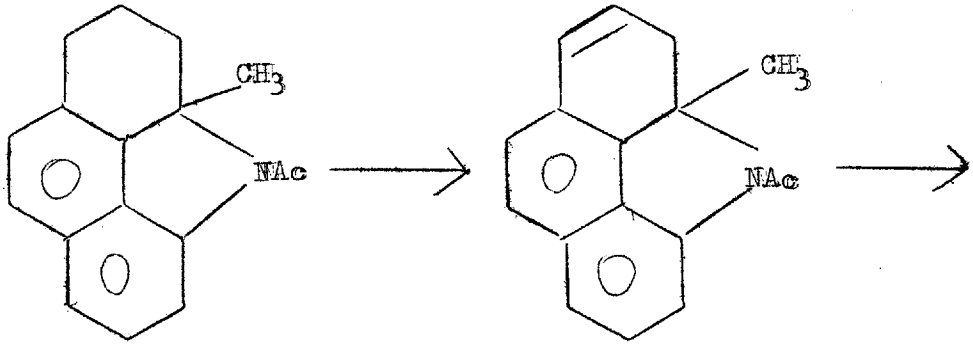
(165) (179)

(180)

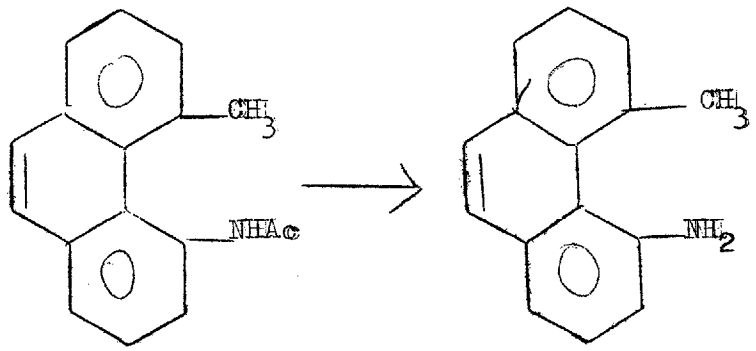
On hydrogenolysis in glacial acetic acid solution over a 5% Pd/C catalyst well over one mole equivalent of hydrogen was taken up. Thus it was no surprise to find that the product, obtained in 50% yield, was not (180) but had an NMR spectrum in which there were only two aromatic protons absorbing as a singlet at 3.10 τ. Clearly some nuclear hydrogenation had occurred and the product was assigned structure (179). The presence of an amino group was evident from the IR spectrum which had peaks at 3350, 3250, 1615 cm^{-1} and the NMR spectrum which had a two proton peak at 6.27 τ which exchanged on shaking with D_2O. (179) was purified as the hydrochloride salt.

Finally another method was used to open the heterocyclic ring in (165). The acetylated benz(cd)indoline (166) was oxidised to (181) with DDQ in refluxing benzene. The reaction was slow and could not be catalysed by benzoic acid or <u>para</u>-toluene sulphonic acid[84]. It could not be followed by TLC because (165) and (181) have the same R_f, but maxima in the ultra-violet spectrum of (166) at 237 and 307 mμ diminished as the reaction proceeded and peaks at 263, 276 and 335 mμ appeared.

(181) was isomerised to the phenanthrene amide (182) by heating it briefly with t-butanol with potassium . t-butoxide. The white crystalline amide had peaks in the IR spectrum at 3400, 1680, 1540 cm^{-1} confirming that it was a secondary amide. There were no methylene peaks in the NMR spectrum and the two methyl groups absorbed at 7.82 and 7.42τ. There were eight aromatic protons at 2.3-2.6 τ and a broad N-H signal at 1.5 τ.



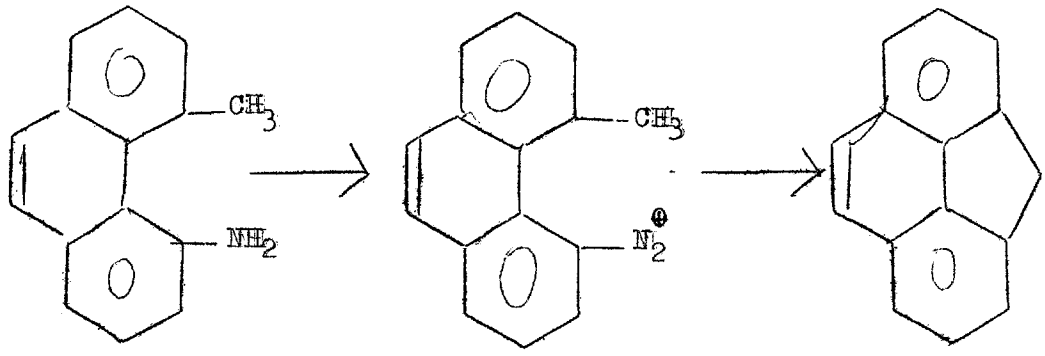
(166) (181)



(182) (153)

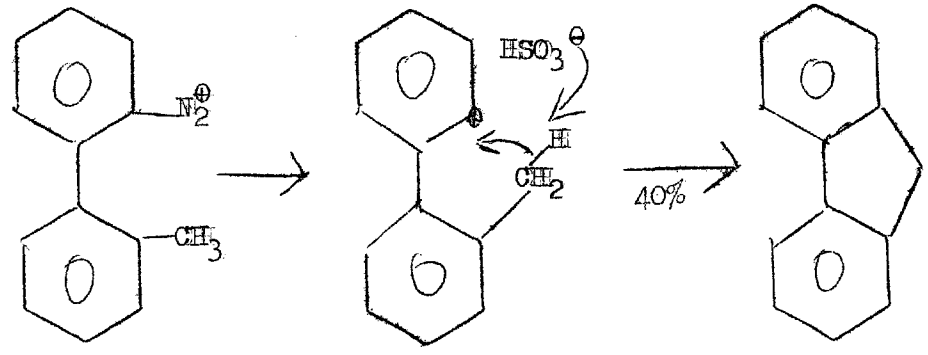
Hydrolysis of the amide (182) to 4-amino-5-methylphenanthrene (153) was carried out in excellent yield in refluxing methanolic HCl. The amine was identified by characteristic peaks at 3450, 3370 and 1615 cm^{-1} in the IR.

The usual procedure for converting an amine to an azide was carried out with (153). When (153) was diazotised in glacial acetic acid the reaction could not be performed at 0° C because the acetic acid froze. After addition of sodium azide in the normal manner the crude reaction product was isolated but surprisingly had a very weak azide peak at 2150 cm^{-1} in the IR although on TLC it appeared to be quite pure. The reaction was repeated in a mixture of acetic acid and sulphuric acid which could be kept at 0° C. The major product was the non-polar crystalline hydrocarbon (184) and was obtained in 50% yield.



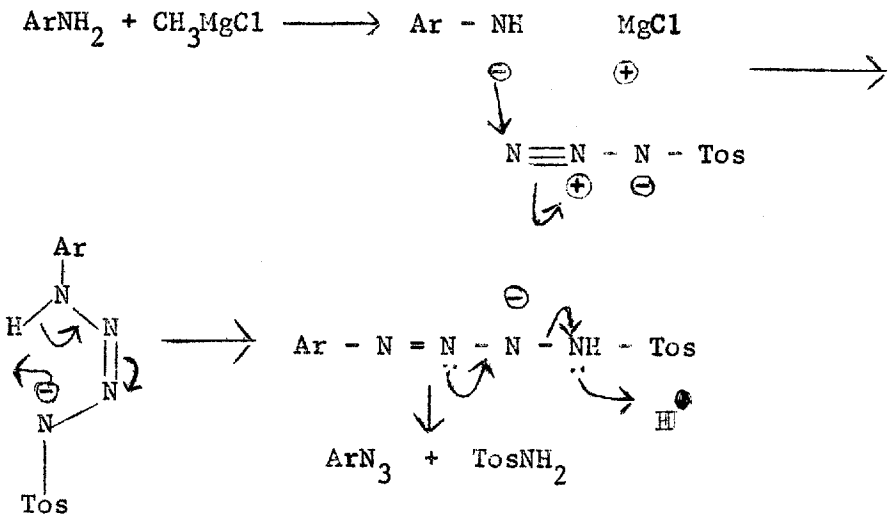
(153) (183) (184)

Phenanthrene-4,5-methane (184) had eight aromatic protons in the NMR spectrum at 2.1 - 2.4 τ and a methylene singlet at 5.71τ. It had the same melting point as reported in the literature[52]. It was formed by a Mascarelli reaction which has been reported to occur when 2-amino-2'-methylbiphenyl is diazotised and then heated in acid[85]. Steric compression in (183) makes elimination of nitrogen much easier than in (185) and hence in our case the Mascarelli reaction occured at 0° C.

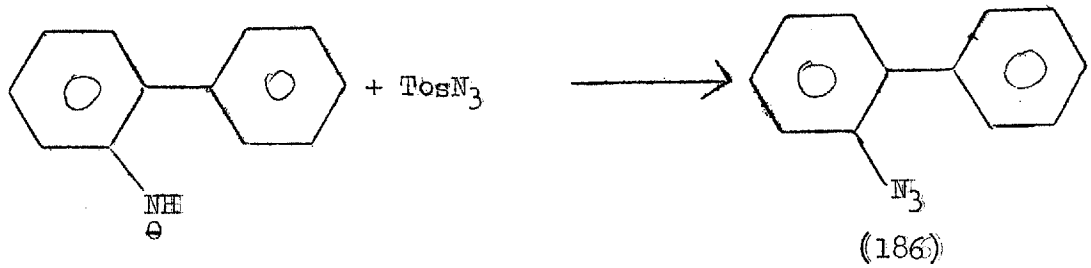


(185)

Another method was attempted for the conversion of amine (153) to 4-azido-5-methylphenanthrene(154). Tosyl azide reacts with the anion of an aryl amine to give an aryl azide and <u>para</u>-toluene sulphonamide by a diazo transfer reaction[86].



In an exploratory reaction, this conversion was tried out with 2-aminobiphenyl to find out the effect of a large substitutent in the vicinity of the amino group. Whereas the reaction of simple <u>para</u> substituted anilines with a Grignard reagent is reported to be complete in five minutes, after three and a half hours TLC still showed unreacted 2-aminobiphenyl. Reaction of the anion with tosyl azide was very rapid and clean and 2-azidobiphenyl (186) was isolated in 63% yield.



(186)

When the same reaction was attempted with 4-amino-5-methyl-phenanthrene (153), attack by the Grignard reagent appeared to be even slower. Excess methyl magnesium iodide was added but even after twenty hours TLC showed some amine. When tosyl azide was added no new products appeared on TLC indicating that no amine anion had been formed, and indeed the amine was recovered unchanged. Clearly the amino group in (153) is inaccessible to the Grignard reagent, a possibility that seemed likely when we observed how slow the reaction of 2-aminobiphenyl with methyl magnesium iodide was, compared to the unhindered anilines reported in the literature.

EXPERIMENTAL

Unless otherwise stated, the following information applies to all the experiments described.

Melting points (M.P.) were measured on a Kofler block and are uncorrected. Infra-red spectra (I.R.) were measured on a Unicam SP 200 or a Perkin-Elmer 257 Spectrometer. Nujol mulls were used for solids, otherwise the spectra were measured as smears on sodium chloride plates or in chloroform or carbon tetrachloride solution in sodium chloride cells of 0.5 mm thickness. Ultra-violet spectra (U.V.) were measured as solutions in absolute ethanol on a Unicam SP 800 B Spectrometer using 1 cm. cells. Nuclear Magnetic Resonance Spectra (NMR) were measured on a Varian A 60 Spectrometer by Mrs. I. Boston or on a Varian HA 100 100 Mc/s Spectrometer by Mr. Peter Jenkins. The spectra were measured in deuterochloroform or carbon tetrachloride solution. The symbols s, d, t, qu, m, br, exch., refer to NMR signals appearing as a singlet, doublet, triplet, quartet, multiplet, a broad band and a signal which disappears on shaking the solution with D_2O respectively. Mass spectra were measured on an AE1 MS9 Spectrometer by Mr. P.R.Boshoff or Mr. John Bilton or on a Perkin-Elmer 270 low-resolution spectrometer by Mrs. Lee. Micro-analyses were performed by Mr. K.I.Jones.

For thin-layer chromatography (TLC) 20 x 5 cm. Merk. GF 254 Silica Gel plates were used and for preparative TLC 60 x 20 x 0.1 cm. plates were used. The plates were generally run in benzene/acetone

or benzene/petroleum ether (b.p. 40 - 60°C) and were inspected under ultra-violet light and developed in iodine vapour or sprayed with concentrated sulphuric acid and heated.

Ether, dichloromethane etc. extracts were dried over sodium sulphate or magnesium sulphate before removing the solvent under vacuum on a water pump. Final traces of solvent were removed on a high vacuum oil pump. Petrol refers to petroleum ether b.p. 40 - 60°C when used for chromatography and petroleum ether b.p. 60 - 80°C when used for crystallisation. Dry benzene and ether refers to sodium dried solvents.

In photolytic experiments the following ultra-violet light sources were used: Philips High Pressure Mercury Vapour Lamp HPK 125 watt, 57203 B/00, Philips Medium Pressure Mercury Vapour Lamp MBW/V 125 watt, with the ultra-violet screening bulb removed. Hanovia U-shaped Low Pressure cold cathode Mercury Lamp 15 watt type 766/63 or AT/E 121.

Methyl-β-phenethyl ether (9)

β-phenethyl alcohol was methylated with dimethyl sulphate.[1] Yield 60%, $bp_{15-20\ mm}$ 90-93°C; IR 1120 cm^{-1}.

Ortho-nitrophenethyl methyl ether (10)

Methyl phenethyl ether (9) was nitrated with acetic anhydride and fuming nitric acid.[3,4] The isomers were separated by chromatography on Grade 3 Alumina eluting with benzene/petrol 1:1. The required ortho isomer was eluted first as an oil, followed by the

para isomer M.P. 60 - 62°C (petrol).

IR 1530, 1350, 1120 cm^{-1} NMR (CCl_4) 6.63 τ 3Hs; 6.85 τ 2Ht J = 7 cps; 6.40 τ 2H t J = 7 cps; 2.43 - 2.85 τ 3H m; 2.12 τ 1Hm.

Ortho-amino-β-phenethyl methyl ether (11)

Para-nitrophenethyl methyl ether was reduced with stannous chloride by a literature procedure[3] and the IR (3450, 3350 cm^{-1}) showed that all the nitro-compound had been converted to an amine. The same method was used to reduce (10) to (11) in 83% yield. IR 3450, 3350, 1625 cm^{-1}. The amine was purified as the hydrochloride prepared by adding the crude amine to ethereal HCl. M.P. 112-114°C (ethanol). IR 2550, 1110 cm^{-1}. NMR (CCl_4) 6.68 τ 3Hs; 6.87 τ 2Ht J = 7 cps; 6.35 τ 2Ht J = 7 cps; 2.5 - 2.75 τ 3Hbr.; 2.05 τ 1Hm.

Analysis: C 57.36% H 7.42% N 7.27% Cl 19.31%

$C_9H_{14}NOCl$ requires C 57.46% H 7.45% N 7.45% Cl 19.0%

Ortho-azido-β-phenethyl methyl ether (12)

Ortho-amino-β-phenethyl methyl ether hydrochloride (11) was diazotised and treated with sodium azide according to Method B of Smith and Brown[5] using the Smolinsky modification[6] of the work up. The azide was extracted into ether instead of petrol and was prepared in 77% yield. IR 2140, 1120 cm^{-1}. NMR (CCl_4) 6.73 τ 3Hs; 7.24 τ 2Ht J = 7 cps; 6.55 τ 2Ht J = 7 cps; 2.92 τ 4Hm.

Photolysis of ortho-azido-β-phenethyl methyl ether (12)

The azide (203 mg) in redistilled dry benzene (25 ml) was irradiated in a pyrex flask with a medium pressure lamp; dry nitrogen

was bubbled through the solution via a sintered glass disc at the bottom of the flask. The solution soon darkened and after eighteen hours IR showed that all the azide (ν_{max} 2150 cm^{-1}) had reacted. The solvent was distilled off and the crude product separated by TLC eluting with benzene. Indole (33.2 mg) was isolated, but as indole is a volatile compound a correction factor was determined by dissolving a known weight of indole in a similar volume of benzene and isolating it in the same way. A corrected yield of 41.5 mg (43%) was thereby obtained. Indole was identical in Rf and IR to an authentic sample and gave an identical picrate m.p. 146 - 148·5°C (ethanol) to that obtained from an authentic sample. Another product isolated by TLC had an identical R_f and IR to those of ortho-amino-β-phenethyl methyl ether (11).

Ortho-nitro-β-phenethyl alcohol (15)

β-phenethyl alcohol was nitrated as described in the literature[8] in 95% yield. A crude separation of the isomers was achieved by pouring the oily mixture onto ice and filtering the solid para isomer (purified by crystallisation from CCl_4) from a mixture of ortho and para isomers. Chromatography on Grade 3 Alumina eluting with benzene/acetone 5% gave pure (15). NMR (CCl_4) 7.1 τ 1H br; 6.97 τ 2Ht J = 6 cps; 6.25 τ 2Ht J = 6 cps; 2.69 τ 3Hm; 2.23 τ 1Hm.

Ortho-amino-β-phenethyl alcohol (16)

The nitro alcohol (15) (3.76 g) was stirred at room temperature for fifteen hours with stannous chloride (23 g) in conc. HCl (50 ml). 4N sodium hydroxide was carefully added till all the white tin complex

had dissolved and the amino alcohol (16) was extracted with ether (5x). After washing with water (2x) and drying over sodium sulphate the solvent was removed in vacuo giving 2.37 g 77% of the yellow oily amine.

When the nitro compound (15) (0.67 g) was reduced in 0.880 ammonia (3 ml) and water (3 ml) saturated with H_2S for 18 hours at room temperature and then heated on a steam bath for 30 minutes, 281 mg 51% of the amine was obtained after filtering off sulphur and ether extraction as described above.

IR 3450, 3400, 3300, 1630 cm^{-1}

Ortho-azido-β-phenethyl alcohol (17)

The amine (16) was converted to (17) in sulphuric acid by the standard procedure[5,6]. Yield 83%. IR 3400, 2150 cm^{-1}.

Analysis: C 58.89% H 5.56% N 25.75%

$C_8H_9N_3O$ requires C 58.80% H 5.62% N 25.67%

Ortho-azido-β-phenethyl benzoate (18)

The azido alcohol (17) (2.25 g) was benzoylated with freshly distilled benzoyl chloride (10 g) in dry pyridine (50 ml., dried over KOH). The solution was stirred at room temperature for 6 hours in the dark. It was then poured onto a mixture of ice, 6N sulphuric acid and ether. The ether layer was separated and washed with sulphuric acid, water, sodium hydroxide and water and then dried over sodium sulphate. Ether was removed in vacuo and the product purified by chromatography on a Grade 3 Alumina column

eluting with benzene/petrol 2:1. The yield of the oily benzoate was 3.18 g 86% IR 2150, 1720, 1390 cm^{-1}. NMR (CCl_4) 6.99τ 2Ht J=7 cps; 5.54τ 2Ht J=7 cps; 2.5-3.0τ 7Hm; 2.10τ 2Hm. UV λ_{max}^{EtOH} 207 mμ (ϵ 20,900), 231 mμ (ϵ 15,600), 250 mμ infl. (ϵ 10,600), 278 mμ infl. (ϵ 2,990), 287 mμ infl. (ϵ 1,960), above 300 mμ tailing ϵ 130.

Analysis (sample distilled at 0.05 mm 90°C) C 67.27% H 5.01% N 15.52%

$C_{15}H_{13}N_3O_2$ requires C 67.41% H 4.90% N 15.72%

Photolysis of ortho-azido-β-phenethyl benzoate (19)

The solvents and lamps used for this photolysis are listed in Table I (page 77). The usual procedure used was to irradiate a solution of about 200 mg. of the azide in about 30 ml. of dry solvent. The solution was stirred and dry nitrogen was bubbled through it. The progress of the photolysis was followed by taking out samples at intervals and examining the TLC and the azide peak in the IR.

When IR showed that the photolysis was complete, the solution was extracted with saturated aqueous sodium bicarbonate (twice). The basic solution was washed with ether, acidified with dilute sulphuric acid and extracted twice with ether. The ether solution was washed with water, dried over sodium sulphate and evaporated to dryness to give benzoic acid. Benzoic acid isolated in this way had the same M.p. 122°C and IR 2680, 2570, 1690 cm^{-1} as an authentic specimen.

The remainder of the photo-product was separated on Silica Gel plates eluting with benzene/petrol 10%. Four bands were isolated.i The most polar was a brown material and was rejected, IR 3400, 1720 cm^{-1}, NMR 1.9 - 2.9 τ, 5.4 τ , 7 τ br. The next band was separated into the two amino-benzoates (20) and (21) by TLC eluting with benzene/acetone 10%. The next band was the orange azo compound (19) and the least polar was separated into indole and unchanged azide by TLC eluting with benzene/acetone 10%.

Ortho-azo-β-phenethyl benzoate (19). Mp 126-7°C (orange needles from ether). IR 1710 cm^{-1}. UV λ_{max}^{EtOH} 207 mμ (ϵ 35,800), 231 mμ (ϵ 47,200), 275 mμsh (ϵ 7,280), 283 mμ sh. (ϵ 8,470), 332 mμ (ϵ 25,000).

Analysis C 75.20% H 5.43% N 5.85%

$C_{30}H_{26}N_2O_4$ requires C 75.29% H 5.48% N 5.85%

Ortho-amino-β-phenethyl benzoate (20). Ir 3490, 3410, 1715 cm^{-1} NMR 7.08 τ 2Ht J=7 cps; 6.2 τ 2Hbr; 5.57 τ 2Ht J=7 cps; 2.5-3.5 τ 7Hm; 2.1 τ 2Hm.

Analysis C 72.15% H 6.97% N 5.24%

$C_{15}H_{15}NO_2$ requires C 74.67% H 6.27% N 5.80%

2-(Ortho-aminophenyl)-1,1-dibenzoylethane (21) M.P. 168-9°C (benzene/petrol) IR 3490, 3400, 1740, 1710, 1630 cm^{-1}. NMR (100 Mc/S) (CCl_4) 6.85 τ 2Hd J=5½ cps coupled to a proton at approximately 3.0 τ; 6.5 τ 2H exch; 3.5, 2.5-3.2 τ 11 Hm; 2.03 τ 4H qu.

Analysis C 73.02% H 5.15% N 3.74%

$C_{22}H_{19}NO_4$ requires C 73.12% H 5.30% N 3.88%

When the photolysis was carried out in cis, trans-piperylene another polar product (23) was isolated by preparative TLC. IR 3420, 1720, 1710, 1605, 1590, 1280, 1120 cm^{-1}. NMR (CCl_4) 8.27 τ 3Hm; 7.18 τ 2Ht J=8 cps; 5.74 τ 2Ht J=8 cps; 6.55 τ 2Hm; 4-4.5 τ 3Hm; 5.2 τ 1Hbr; 2.5-3.6 τ 10 Hm; 1.9-2.3 τ 4Hm. Mass Spectrum: Molecular ion M/e 429.1932 c.f. $C_{27}H_{27}NO_4$ 429.193996; other peaks at M/e 307, 268, 255, 254, 186, 146. UV λ_{max}^{EtOH} 209, 230, 251 infl. 274, 282, 295 mμ.

The compound (23) (7 mg) dissolved in glacial acetic acid (5 ml) was ozonised at room temperature for two minutes. Zinc dust was added and the reaction left for two hours. It was filtered and a solution of 2,4-dinitrophenylhydrazine in conc. H_2SO_4 and ethanol was added to the filtrate. No precipitate formed, so the solution was basified with saturated sodium bicarbonate solution and extracted with ether. A yellow compound was isolated by preparative TLC (Silica Gel, benzene/petrol 10%) which had the same R_f and IR (3300, 1620, 1530, 1340 cm^{-1}) as an authentic sample of acetaldehyde-2,4-dinitrophenylhydrazone MP 146°C (ethyl acetate). It did not have the correct melting point, melting at 105-120°C.

Ortho-azidoanisole (25)

Ortho-anisidine was converted to the azide (25) by procedure A of Smith and Brown[5,6] and was obtained as a yellow liquid in 86% yield. IR 2140, 1305, 1250, 1100 cm^{-1}. NMR (CCl_4) 6.19 τ 3Hs, 3.13 τ 4Hm.

Photolysis of ortho-azidoanisole (25)

The azide (1.49 g) was photolysed in dry benzene (200 ml) in a

water cooled quartz cell with a high pressure mercury lamp. Nitrogen was bubbled through the solution. The photolysis was almost complete after 30 minutes. In another experiment, the solvent used was dimethylsulphoxide (250 ml) and irradiation was stopped after one hour. Using this solvent had the advantage that no insoluble film was formed on the quartz finger cutting out the light.

Basic photo-products were extracted with 3N HCl, which solution was washed with chloroform, neutralised with sodium bicarbonate and extracted twice with chloroform. The product was impure o-anisidine (10%). IR 3450, 3380, 1615, 1225 cm^{-1}. NMR 6.15 τ 5Hs--reduced to 3Hs after D_2O shake- 3.3 τ 4Hs. The neutral compounds were chromatographed on Grade 3 Alumina. The first compound eluted (180 mg 30%) was o-azoanisole (27) MP 153-5°C (petrol). NMR 6.00 τ 3Hs 2.3-3.2 τ 8Hm.

Analysis	C 69.23%	H 5.63%	N 11.44%
$C_{14}H_{14}N_2O_2$ requires	C 69.41%	H 5.82%	N 11.56%

Ortho-azidotoluene (30)

Ortho-azidotoluene (30) was prepared by standard procedures[5,6] from ortho-toluidine in 65% yield. IR 2150, 1600, 1500 cm^{-1}.

Ortho-azidobenzyl alcohol (31)

Ortho-azidotoluene (1.3 g), N-bromosuccinimide (1.8 g, purified by recrystallisation from hot water) and benzoyl peroxide (0.3 g, purified by recrystallisation from chloroform/methanol) were heated together in refluxing carbon tetrachloride (10 ml) in the absence of

light. No new products appeared on TLC after two hours and another 0.3 g benzoyl peroxide was added and the reaction left for three days. During this period about 10 ml of water had leaked into the solution and after separating this aqueous layer, TLC showed the presence of unreacted starting material (330 mg) and a more polar product (574 mg 51%) The two were separated by column chromatography M.P. 50-52°C (Lit[12] 52-3°C), sublimed at 0.3 mm at about 90°C. IR 3300, 2150, 1050, 1020 cm^{-1}. UV λ_{max}^{EtOH} 209 mμ (ε 18,200), 252 mμ (ε 10,200), 277 mμ sh.(ε 2,730), 286 mμ sh.(ε 1,920). NMR (CCl_4) 7.24 τ 1Hs; 5.48 τ 2Hs; 2.5-3.2 τ 4Hm.

Ortho-azidobenzyl bromide

Ortho-azidotoluene (30) (3.9 g), N-bromosuccinimide (5.5 g) and benzoyl peroxide (3.4 g) were heated in the dark under nitrogen in refluxing dry benzene (30 ml.) TLC (Silica Gel, benzene/petrol 10%) showed the reaction was complete after 4½ hours. The reaction mixture was poured into water and ether and the ether layer separated and dried over sodium sulphate. The two products were separated on a Grade 3 Alumina column eluting with benzene /petrol 1:1. The first product eluted (4.7 g, 76%) was ortho-azidobenzyl bromide M.P. 71-2°C (petrol). IR 2150 cm^{-1}. NMR (CCl_4) 5.63 τ 2Hs; 2.6-3.1 τ 4Hm. UV λ_{max}^{EtOH} 207 mμ (ε 15,800), 226 mμ infl. (ε 12,600), 255 mμ (ε 10,100).

Analysis	C 39.77%	H 3.08%	N 19.71%	Br 37.96%
$C_7H_6N_3Br$ requires	C 39.67%	H 2.85%	N 19.82%	Br 37.69%

The other product was ortho-azidobenzylbenzoate (33). Yield 7%.

Ortho-azidobenzyl benzoate (33)

Ortho-azidobenzyl bromide (866 mg) and sodium benzoate (1.46 g) were heated together in N,N-dimethylacetamide solution (20 ml) on a steam bath under nitrogen for 2½ hours. This was then poured into water and ether and the aqueous layer separated and extracted with ether. The combined ether fractions were washed with water (3x), dried, concentrated and purified on a Grade 3 Alumina column eluting with benzene/petrol 1:1. 57 mg of the bromide was recovered unchanged and the benzoate (806 mg 83%) was the next compound to be eluted. MP 63-4°C (petrol). IR 2150, 1715, 1280 cm^{-1}. UV λ_{max}^{EtOH} 205 mμ (ϵ 19,400), 230 mμ (t 13,250), 251 mμ infl. (ϵ 8,900), 281 mμ (ϵ 2000). NMR 4.69 τ 2Hs; 2.5-2.9 τ 7Hm; 1.87-2.07 τ 2Hm.

Analysis	C 66.29%	H 4.49%	N 16.45%
$C_{14}H_{11}N_3O_2$ requries	C 66.40%	H 4.38%	N 16.59%

When this reaction was carried out in dimethyl formamide it was slower and the yield was lower (76%).

Photolysis of ortho-azidobenzyl alcohol (31)

Freshly sublimed azide (338 mg) in dry benzene (200 ml) was irradiated under nitrogen in a Silica reactor with a low pressure mercury lamp. The photolysis was followed by IR and TLC. The azide peak at 2150 cm^{-1} diminished as a peak at 1680 cm^{-1} developed. The photolysis became very slow as a film formed on the reactor walls and after 44 hours, the solution was concentrated and separated on Silica

Gel plates eluting with benzene/acetone 10%. The yield of recovered azide was 77.3 mg 23% and of ortho-aminobenzaldehyde (32) was 49.6 mg 24%. IR 3380, 1665 cm^{-1}. NMR 4.4 τ 2H exch.; 2.5 τ m; 0.2 τ 1H. The phenylhydrazine derivative of (32) melted at 222-3°C (ethanol), lit.[12] 223-4°C.

Photolysis of ortho-azidobenzylbenzoate (33)

A solution of 100 - 150 mg of the azide in about 100 ml. of solvent when a silica vessel was used or 25 ml. solvent when a pyrex vessel was used, was irradiated under various conditions as summarised in Table II (page 89). The photolyses were carried out under nitrogen and the solutions were stirred. No external cooling was used so that irradiations with a medium pressure lamp were carried out under reflux. The progress of the photolyses was followed by IR and TLC. Benzoic acid was extracted as described on page 180 and the other products were isolated chromatographically.

Ortho-aminobenzylbenzoate (35) IR 3500, 3400, 1720, 1630 cm^{-1}. NMR (CCl_4) 5.47 τ 2H exch; 4.71 τ 2Hs; 1.9-3.5 τ 9Hm.

Ortho-azobenzylbenzoate (34) M.P. 113-4°C (petrol) IR 1710, 1280 cm^{-1}. UV λ_{max}^{EtOH} 205 mμ (ϵ 25,400), 230 mμ (ϵ 32,000), 273 mμ sh. (ϵ 5,500), 282 mμ sh. (ϵ 6,500), 324 mμ (ϵ 14,250).

NMR 4.00 τ 4Hs; 1.8-2.8 τ 18 Hm.

Analysis:	C 74.65%	H 5.09%	N 6.08%
$C_{28}H_{22}N_2O_4$ requires	C 74.65%	H 4.92%	N 6.22%

Ozonolysis of Acenaphthalene[18,19]

Acenaphthalene (10 g) in methanol (200 ml) was ozonised at -30°C for 40 hours till the yellow colour of the solution had almost disappeared. The precipitated hemiperacetal (37) (1.1 g) was left standing in excess dimethyl sulphide for 24 hours. The product (38) was filtered (884.5 mg 88%). M.P. 106-7°C was the same as reported for one form of the dialdehyde hydrate. NMR 6.33 τ 3Hs; 6.13 τ 1Hs; 3.7-4.15 τ 2H qu; 2.1-2.8 τ 6Hm.

On recrystallisation several times from hot water TLC (Silica Gel Benzene/Methanol 20%) showed that (38) was converted to the dihydrate. M.P. 133-5°C. IR 3330, 3200 cm^{-1}. NMR 3.72 τ 1Hd J=6 cps, collapses to singlet on shaking with D_2O; 3.44 τ 1Hd J=6 cps, collapses to singlet on shaking with D_2O; 3.5-4.0 τ 2H br.exch; 2.1-2.6 τ 6Hm. Analysis after one crystallisation: C 71.33%, H 5.45%, after three crystallisations: C 70.71%. H 4.79%. $C_{12}H_{10}O_3$ requires C 71.29%, H 4.95%, $C_{13}H_{12}O_3$ requires C 72.22% H 5.55%.

The dialdehyde (38) (550 mg) was left at room temperature with 10% aqueous sodium hydroxide (20 ml) for four days. It was filtered and acidified with conc. HCl (6 ml); the solution was heated and methanol added to dissolve the precipitated product. Naphthalide (42) crystallised out on cooling the solution (376 mg 72%) M.P. 153-4°C IR 1710 cm^{-1}, NMR 5.01 τ 2Hs; 2.3-3.5 τ 6Hm.

The pale yellow filtrate obtained after the ozonolysis was converted to naphthalide by a published method[19]. The product (4.55 g 48%) was contaminated by naphthalic anhydride (41) IR 1770, 1720 cm^{-1}

and was purified on an Alumina column eluting with benzene/acetone 10% to give material which melted at 156-7°C.

Naphthostyril (47)

Several literature preparations[20-23] were repeated without success. The sodium hypochlorite solution used contained 10% active chlorine and was much more concentrated than that used in the reported Hoffman procedures. The amido acid salt (44A) was precipitated on addition of sodium hypochlorite to naphthalimide and failed to react further. IR 3400, 1635, 1550 cm^{-1}. This salt was not the N-chloroamido acid salt, as reported[23], because when the procedure for converting this to naphthostyril was attempted[23], naphthalimide was obtained.

N-hydroxynaphthalimide (45)

This was prepared in 67% yield from naphthalic anhydride (20 g)[24]. M.P. 276-7°C (ethanol) IR 3150, 1700, 1660 cm^{-1}.

N-tosyloxynaphthalimide (46)

The hydroxamic acid (45) (5 g) in dry pyridine (50 ml) was stirred overnight at room temperature with tosyl chloride (5.5 g, recrystallised from petrol). The yellow tosylate (46) was filtered (7.7 g) and recrystallised from benzene (5.4 g). A further quantity (2.8 g) was obtained by adding water to the pyridine mother liquor, filtering and recrystallising from benzene. Yield 89%. M.P. 228-9°C. IR 1715, 1705, 1330, 1180, 1230, 1020 cm^{-1}.

Analysis:	C 62.30%	H 3.69%	B 3.67%	S 8.46%
$C_{19}H_{13}NSO_4$ requires	C 62.13%	H 3.57%	N 3.81%	S 8.71%

Naphthostyril (47)

The tosylate (5.4 g) (46) and potassium hydroxide (5.7 g) were dissolved in methanol (300 ml). The solution turned orange and on standing overnight a white precipitate formed. The solvent was removed in vacuo and the residue digested with chloroform. Insoluble inorganic matter was filtered off and the yellow naphthostyril (47) (1.4 g) 60% isolated from the three other products by column chromatography on Grade 3 Alumina. M.P. 180.5-182°C (benzene) Ir 3180, 1695, 1640 cm^{-1}.

1-amino-8-naphthalene carboxylic acid (48)

This was prepared quantitatively from naphthostyril by the method of Bamberger and Philip[87].

Reduction of the tosylate (46)

The tosylate (46) (400 mg) was reduced with lithium aluminium hydride (400 mg) in refluxing dry ether (100 ml) under nitrogen for two hours. Wet ether was added and the ether layer separated. The aqueous layer was extracted with ether (2x). The combined ether extracts were dried and evaporated to dryness giving an oil (120 mg) which was separated into several components on TLC.

Reduction of the amino acid (48)

The amino acid (200 mg) (48) and lithium aluminium hydride (300 mg) were stirred in dry ether (150 ml) under nitrogen at room temperature overnight. Water was added carefully and the pink ether solution filtered and separated. On evaporation a dark greenish blue

solid was obtained. This solid residue was acid soluble and on extraction with ether gave a blue solution.

5-acetamido-1-naphthol (52)

5-amino-1-naphthol was acetylated with acetic anhydride[88]. Yield 79%. M.P. 176°C (chloroform). IR 3290, 1630, 1530 cm^{-1}.

5-acetamido-1-methoxynaphthalene (53)

When the literature procedure was used[88], a yield of 51% was obtained.

5-acetamido-1-naphthol (52) (41 g), methyl iodide (90 g) and potassium carbonate (30 g) were heated in dry acetone (600 ml) under reflux for 5½ hours. The reaction mixture was well stirred and after allowing it to cool to room temperature, it was poured into water (3 l.) and the white product was filtered and vacuum dried. The compound was TLC pure and obtained in 82% yield (35.8 g). M.P. 188-9°C. IR 3250, 1650, 1540, 1040 cm^{-1}.

1-methoxy-5-acetamido-4-chloromethylnaphthalene (54)

Chloroformylation of (53) was carried out following the published procedure[29]. Yield 77%. M.P. 155-165°C. IR 3250, 1640, 1530 cm^{-1}.

1-methoxy-5-acetamido-4-hydroxymethylnaphthalene (55)

The literature procedure for hydrolysis of (54)[29] gave a mixture of several products from which (55) was isolated by TLC.

5-acetamido-4-acetoxymethyl-1-methoxynaphthalene (56)

Freshly prepared (54) obtained from the chloroformylation of 35.8 g (53), was dissolved in hot glacial acetic acid (2200 ml) and

sodium acetate (38 g) and acetic anhydride (5 ml) was added portion-wise. The solution was kept at 60°C under nitrogen for one hour. The precipitated sodium chloride was filtered and acetic anhydride (75 g) was added to the filtrate which was left standing overnight. After addition of water and extraction into chloroform, the solvent was removed in vacuo and the crude diacetate (56) crystallised from alcohol. Yield 27 g (56%). M.P. 149-150°C.
IR 3250, 1730, 1645 cm^{-1}. NMR 7.94 τ 3Hs; 7.80 τ 3Hs; 6.27 τ 3Hs; 4.62 τ 2Hs; 1.55 τ 1H; 3.33 τ H_2d; 2.45-2.70 τqu H_3 and H_7, decoupling shows H_3 at 2.63 τ; 2.20 τ H_8 d; 1.78 τ H_6 d.

5-amino-4-hydroxymethyl-1-methoxynaphthalene (57)

The diacetate (56) (27 g) and sodium (7 g) were dissolved in dry ethanol (1250 ml) and heated under reflux for five hours under nitrogen. The hydrolysis was followed by TLC and when it was completed the solvent was evaporated off. The solid residue was partitioned between ether and 6N HCl. The acid layer was separated and basified with solid sodium bicarbonate. The precipitated amine (57) was filtered, washed and dried and crystallised from alcohol. Yield 14.8 g 78%. M.P. 121.5-122.5°C. IR 3320, 3200, 3080, 1600 cm^{-1}. NMR 6.07 τ 3Hs; 5.05 τ 2Hs; 2.1-3.5 τ 5Hm; broad NH_2 and OH peaks were exchanged on shaking with D_2O.

5-amino-4-ethoxymethyl-1-methoxynaphthalene (61)

This was prepared from (57) by the literature method[29]. M.P. 76-7°C. IR 3410, 3320 cm^{-1}. NMR 8.77 τ 3Ht J=7 cps; 6.42 τ 2H qu J=7 cps. 6.08 τ 3Hs; 5.12 τ 2Hs; 4.68 τ 2H br. s; 3.39 τ H_2 d J=7.5 cps; 3.20 τ qu 2.88 τ qu J= 8, 2 cps H_6 and H_7; 2.72 τ d J=7.5 cps

H_3; 2.22 τ qu J=8.5, 1.5 τ H_8.

5-azido-4-hydroxymethyl-1-methoxynaphthalene (58)

The method B of Smith and Brown[5,6] gave a product with an N_3 peak in the IR, but no OH. When this was modified by using glacial acetic acid as the solvent (58) was obtained in 88% yield. M.P. 142.5-144°C (ethanol). IR 2130, 3300 cm^{-1} UV λ_{max}^{EtoH} 207 mμ (ϵ 32,400), 232 mμ (ϵ 46,200), 317 mμ (ϵ 10,500). NMR 7-7.4 τ 1H br; 6.05 τ 3Hs; 4.97 τ 2Hs; 1.8-3.3 τ 5Hm.

Analysis:	C 62.64%	H 4.99%	N 18.09%
$C_{12}H_{11}N_3O_2$ requires	C 62.90%	H 4.81%	N 18.34%

5-azido-4-ethoxymethyl-1-methoxynaphthalene (60)

(58) was converted to the ethyl ether (60) in the same manner as was the corresponding amine (57) but was kept at 20°C overnight instead of refluxing. Yield 89%. M.P. 56-7°C (ethanol). IR 2120 cm^{-1}. UV λ_{max}^{EtoH} 210 mμ sh; 232 mμ (ϵ 33,000), 317 mμ (ϵ 8,000) NMR 8.71 τ 3Ht J=7 cps; 6.33 τ 2Hqu J=7 cps; 6.06 τ 3Hs; 4.92 τ 2Hs; 1.9-3.3 τ 5Hm.

Analysis	C 65.43%	H 5.87%	N 16.19%
$C_{14}H_{15}N_3O_2$ requires	C 65.37%	H 5.84%	N 16.34%

(60) was also prepared from the amino ether (61) by the standard procedure[5,6] in glacial acetic acid.

5-azido-4-benzoyloxymethyl-1-methoxynaphthalene (60)

The azido alcohol (58) (2 g) and redistilled benzoyl chloride (10 g) were stirred in dry pyridine (100 ml) under nitrogen in the absence of light for one hour. The solution was poured into ice

water, 6N HCl and ether and the ether layer was separated. It was washed with 6N HCl, water, 4N NaOH and water and dried. It was evaporated to dryness and benzoic anhydride removed by washing the oil with petrol. The resulting solid benzoate (60) was crystallised from petrol. Yield 2.1 g 72%. M.P. 111-112°C. IR 2150, 1703 cm^{-1}. UV λ_{max}^{EtoH} 232 mμ (ε 63,340), 319 mμ (ε 12,800). NMR 6.04 τ 3Hs; 4.07 τ 2Hs; 1.7-3.4 τ 10 Hm.

Analysis: C 68.57% H 4.50% N 12.53%

$C_{19}H_{15}N_3O_3$ requires C 68.46% H 4.54% N 12.61%

Photolysis of 5-azido-4-hydroxymethyl-1-methoxynaphthalene (58)

(58) (10 mg) in dry benzene (20 ml) was irradiated in a pyrex cell under nitrogen with a medium pressure lamp. TLC and IR showed that the photolysis was complete after 24 minutes, and there was only one photo-product on TLC. In dry ether (25 ml) the photolysis took 5 minutes. On attempting to isolate the product by preparative TLC on Silica Gel (Benzene/acetone 10%), it decomposed to several coloured products.

The photolysis was repeated with 62.5 mg (58) in dry ether (25 ml). When all the azide had disappeared after 35 minutes, lithium aluminium hydride (100 mg) was added and the solution was heated under reflux for 1½ hours under nitrogen. Wet ether and water were then added and the ether layer separated and dried under nitrogen. The dry ether solution was filtered from the sodium

sulphate under nitrogen into acetic anhydride (5 ml) and the ether was then removed in vacuo. It was left standing overnight and then acetic anhydride was removed by azeotroping it with toluene, in vacuo. The crude product, N-acetyl-4-methoxybenz(cd)indoline (64) was purified by TLC and was obtained in 35% yield (20 mg). It was identical to an authentic specimen prepared according to the literature method[29]. M.P. 146°C (ethanol). IR 1655 cm^{-1}. UV λ_{max}^{EtoH} 231 mμ(ε 45,400), 317 mμ(ε 13,700), 336 mμ(ε 13,000). NMR 7.72 τ 3Hs; 6.05 τ 3Hs; 4.95 τ 2Hs; 2-3.3 τ 5Hm.

Photolysis of 5-azido-4-ethoxymethyl-1-methoxynaphthalene (60)

(60) was photolysed (80 mg) in dry ether (25 ml) for 25 minutes exactly as described for (58). The yield of (64) was 27.5 mg 39%.

In another run the solvent was distilled off and pyridine and a benzene solution of 3,5-dinitrobenzoyl chloride added to the distillate. 3,5-dinitrobenzoyl chloride was prepared by heating 3,5-dinotrobenzoic acid (2 g) with PCl_5 (2 4 g) in refluxing carbon tetrachloride for two hours. On cooling and filtering the crude acid chloride was obtained and it was recrystallised from petrol; M.P. 71°C.

The benzoylation reaction proceeded for 15 minutes under reflux The solution was washed with 2 N, HCl, 2N NaOH and water and dried. The organic layer was evaporated to dryness giving ethyl-3,5-dinitrobenzoate (4 mg) M.P. 87-90°C, which was identical to an authentic sample.

Photolysis of 5-azido-4-benzoyloxymethyl-1-methoxynaphthalene (59)

(59) (120 mg) was irradiated in the same manner as was described above for 25 minutes. The solution was extracted with 4 N NaOH and water and the alkaline solution subsequently acidified with conc. HCl. This solution was extracted with chloroform and on careful evaporation benzoic acid (27 mg 65%) was obtained. It was purified by sublimation and was identical to an authentic specimen.

The photolysis of the azide (59) (666 mg) in dry ether (300 ml) using a high pressure lamp took 40 minutes (interrupted every 10 minutes for examination of the progress of the reaction). Extraction (4x with NaOH) as before gave benzoic acid (153 mg 64½%). The neutral products were refluxed with sodium in ethanol for two hours. The solvent was then removed in vacuo and the residue partitioned between water and dichloromethane. The aqueous fraction was acidified and benzoic acid (60 mg 24½%) extracted into dichloromethane.

Photolysis of the benzoate (59) (333 mg) in dry ether (50 ml) using the new rotary photolysis apparatus and a high pressure lamp took ten minutes. The yield of benzoic acid was 65 mg 58%.

There was no dark reaction.

Nitration of 5-acetamido-4-acetoxymethyl-1-methoxynaphthalene (56)

The nitration reactions described below were generally worked up by pouring the acidic solution into a mixture of saturated sodium bicarboante and ether or dichloromethane, separating the organic layer, washing with water, drying and stripping the solvent. The

products were separated by preparative TLC on Silica Gel plates eluting with benzene/acetone 10%.

A Nitration of the diacetate (56) (100 mg) with a mixture of conc. HNO_3 and conc. H_2SO_4 at 0°C gave a yellow product with no carbonyl absorption in the IR, which did not run on TLC.

B Nitration of (56) (100 mg) with conc. nitric acid (2 ml) at 0°C for 18 hours gave a yellow product which did not run on TLC.

C Nitration of (56) (100 mg) with 2 N nitric acid (5 ml) for 22 hours at room temperature gave a yellow crystalline compound (70) (70 mg) which was filtered and washed with water. It was separated by TLC from a small amount of (72) also produced. When (70) was purified by chromatography on Grade III Alumina it was converted to the dinitro amino alcohol (71).

D Nitration of the diacetate (56) (1 g) in glacial acetic acid (35 ml) and 2 N nitric acid (20 ml) at room temperature for two hours gave the dinitro amino acetate (70) (799 mg 80%).

E Nitration of the diacetate (100 mg) with acetic anhydride (2 ml) and conc. nitric acid (1 ml) for 4 days at room temperature gave a mixture of several products including the dinitro amino acetate (70).

F The diacetate (56) (143 mg) was dissolved in glacial acetic acid (5 ml) acetic anhydride (1 ml) and 2 N nitric acid (0.5 ml 2 equivalents) at room temperature for 30 minutes. Many products

were obtained of which only the unnitrated amidoalcohol (55) was identified.

G The diacetate (100 mg) in glacial acetic acid (5 ml) was nitrated by the addition of 2 N nitric acid in 0.05 ml portions every five minutes over a period of 1½ hours. After about ten minutes the amido alcohol (55) was seen on TLC and about ten minutes after that a yellow product was seen on TLC. Of the many products eventually found the unnitrated amido alcohol (55) was the major one (37 g 49%).

H The diacetate (100 mg) in glacial acetic acid (7 ml) was nitrated with conc. nitric acid (1 ml) for 18 hours at room temperature. The major product was the diazoketone (72).

I The diacetate (100 mg) in glacial acetic acid (10 ml) was stirred with 2 N nitric acid for 20 hours at room temperature. Some unchanged starting material was isolated (11.2 mg) as well as the diazo ketone (72) (16.3 mg 15%).

J To a solution of the diacetate (100 mg) in acetic anhydride (2 ml) 2 N nitric acid (1 ml) was added. Initially nothing happened, but on stirring the layers mixed and a vigorous reaction ensued as the anhydride was hydrolysed and became hot. The dinitro amino acetate (70) (7 mg 5%), the diazoketone (72) (20 mg 18%) and some mono-nitro diacetate (74) were isolated.

K The dinitro amino acetate (70) (8 mg) was stirred in glacial acetic acid (4 ml) and 2 N nitric acid (1 ml) overnight at room

temperature. No diazoketone (72) was formed and only dinitro amino alcohol (71) was isolated.

L Extended nitration of (56) (100 mg) with acetic anhydride (2 ml) and conc. nitric acid (1 ml) for four days at room temperature gave a multi-component mixture from which the dinitro amino acetate (70) was isolated.

M When the diacetate was nitrated with conc. nitric acid in glacial acetic acid and acetic anhydride one of the products was the dinitrodiacetate (74).

N 2N nitric acid (5 ml) and water (25 ml) merely hydrolysed the diacetate (108 mg) in three days to 5-amino-4-hydroxymethyl-1-methoxynaphthalene.

O The diacetate (143 mg) in glacial acetic acid (5 ml) was treated with potassium nitrate (150 mg). No reaction was observed as the salt was insoluble. A few drops of water were added, but after 30 minutes only starting material was seen on TLC. One drop of 6N H_2SO_4 was added, but after 30 minutes no reaction was observed.

P The diacetate (150 mg) was added to cupric nitrate monohydrate (210 mg) in acetic anhydride (10 ml) and the mixture stirred for one hour. The product (98.6 mg) was separated on an Alumina plate eluting with benzene/acetone 20% or chloroform/carbon tetrachloride 1:1. A mixture of mono and dinitro amido acetates was obtained (20%). (73,74).

Q The diacetate (509 mg) was treated with copper nitrate (763 mg) in acetic anhydride (40 ml) at room temperature overnight. Chromatography on Silica Gel gave dinitro amino acetate (70) (9 mg, 2%) diazo ketone (72) (40 mg 7%), dinitro acetamido acetate (73) (90 mg 14%).

R The diacetate (101 mg) in a mixture of acetic anhydride (1 ml) and glacial acetic acid (3 ml) was treated with sodium nitrite (30 mg) and conc. nitric acid (3 drops). This mixture was stirred at 0°C for two hours. The product contained starting material and mono- or di- nitro acetamido acetate (73) or (74) (13 mg 10%).

S The diacetate (108 mg) was stirred at 0°C for 4 hours in glacial acetic acid (3 ml) acetic anhydride (2 ml), 2N nitric acid (3 ml) and sodium nitrite (30 mg). The major product was the dinitro amino acetate (70) (15 mg 12%).

5-amino-4-acetoxymethyl-6,7-dinitro-1-methoxynaphthalene (70)

M.P. 207-8°C (ethyl acetate) IR 3420, 3310, 1730, 1550, 1370, 850 cm^{-1}. UV λ_{max}^{EtoH} 212 mμ (ε 17,300), 273 mμ (ε 15,200), 334 mμ (ε 5,150), 435 mμ (ε 8,050). NMR ($CDCl_3$ + DMSO d_6) 7.83 τ 3Hs; 6.08 τ 3Hs; 4.46 τ 2Hs; 2.78 τ 1Hd J=8 cps; 2.27 τ 1 Hd J=8 cps; 1.72 τ 1Hs H_7.

Analysis: C 50.31% H 3.83% N 12.38% Calculated for $C_{14}H_{13}N_3O_7$: C 50.15% H 3.91% N 12.53%

5-amino-4-hydroxymethyl-6,8-dinitro-1-methoxynaphthalene (71)

M.P. 221-2°C (benzene) IR 3500, 3360, 3280, 1550, 845 cm^{-1}

Analysis C 49.03% H 3.93% N 14.04%

$C_{12}H_{11}N_3O_6$ requires C 49.15% H 3.78% N 14.33%

5-acetamido-4-hydroxymethyl-1-methoxynaphthalene (55)

M.P. 203-6°C (ethanol). IR 3380, 3240, 1660 cm^{-1}. NMR (DMSO d_6) 7.82 τ 3Hs; 6.05 τ 3Hs; 5.15 τ 2Hd J=5 cps becomes a singlet after shaking with D_2O; 3.8 τ 1H br. exch; 3.3 τ 2.55 τ AB qu. J=8 cps H_2 and H_3; 2.8 τ 2Hm H_6 and H_7; 1.97 τ H_8 qu. J=8,2 cps 0.8 τ 1H br. exch.

5-acetoxymethyl-4-diazo-3-keto-8-methoxy-1-nitronaphthalene (72)

M.P. 155-6°C (benzene). IR 2150, 1735, 1625, 1555, 855 cm^{-1}.
UV λ_{max}^{EtoH} 208 mμ (ϵ 28,900) 240 mμ (ϵ 35,500), 267 mμ sh., 377 mμ (ϵ 6,460), 408 mμ (ϵ 5,960), 428 mμ sh. NMR 7.81 τ 3Hs; 6.16 τ 3Hs; 4.75 τ 2Hs; 3.34 τ H_2s; 3.25 τ 2.43 τ AB qu. J=8 cps H_6 and H_7.

Analysis C 53.27% H 3.52% N 13.31%

$C_{14}H_{11}N_3O_6$ requires C 53.02% H 3.47% N 13.27%

5-acetamido-4-acetoxymethyl-6,8-dinitro-1-methoxynaphthalene (73)

M.P. 187-8°C (benzene/petrol). IR 3230, 1740, 1670, 1540, 1240, 850 cm^{-1}. NMR 7.94 τ 3Hs; 7.82 τ 3Hs, 6.05 τ 3Hs, 4.36 τ 2Hs, 2.85 τ and 2.22 τ AB qu J=8 cps H_2 and H_3; 1.99 τ 1Hs H_7; -0.08 τ 1 Hbr.

Analysis: C 51.21% H 3.99% N 10.96%

$C_{16}H_{15}N_3O_8$ requires C 50.93% H 4.01% N 11.14%

5-acetamido-4-acetoxymethyl-2 or 6-nitro-1-methoxynaphthalene (74)

IR 3220, 1730, 1660, 1550, 1370, 845 cm^{-1}. NMR (by subtraction of the spectrum of (73) from that of a mixture) 7.93 τ 3Hs; 7.80 τ 3Hs; 5.97 τ 3Hs; 4.46 τ 2Hs, 1.6-3.1 τ 4Hm; 0.8 τ 1Hbr.

Analysis: C 56.13% H 4.57% N 8.09%

$C_{16}H_{16}N_2O_6$ requires C 57.83% H 4.85% N 8.43%

5-acetamido-2,4-dideutero-1-hydroxynaphthalene (76)

5-acetamido-1-naphthol (62) (1. 85 g) was heated under reflux for five hours in a nitrogen atmosphere with triethylamine (1.10 g), deuterium oxide (3 g) and dimethyl formamide (12 ml). The solution was cooled and acidified with 6 N hydrochloric acid. Water was added and the solution extracted with ether five times. The ether solutions were dried and evaporated (100 %). The product was crystallised from chloroform.

M.P. 176-7°C. IR 3280, 1620, 1540 cm^{-1}. NMR (DMSO d_6) 2.80 γ H_3s; 2.75 γ 2.45 γ qu H_6H_7; 1.9 2 γ H_8 d J=8 cps; 7.84 γ 3Hs; 0.76 1 Hbr exch; 0.50 γ 1 H exch. Mass spectrum M^+ M/e 203.

5-acetamido-2,4-dideutero-1-methoxynaphthalene (77)

The naphthol (76) (1.2 g) dissolved in methanol was treated with excess diazomethane in ether[89]. After six hours at room temperature the solvents were stripped giving the ether (77) (1.18 g 92%) which was crystallised from ethanol.

M.P. 186-7°C. NMR (DMSO d_6) 7.82 γ 3Hs; 6.05 γ 3Hs; 2.57 γ H_3s; 2.43 γ 2.24 γ AB qu J=6 cps H_6, H_7; 1.92 γ H_8 d J=8 cps; 0.17 γ 1H br. Mass spectrum M^+ M/e 217.

5-acetamido-4-acetoxymethyl-2-deutero-1-methoxynaphthalene (78)

This was prepared in 30% yield as before.

M.P. 150-151°C. IR 3250, 1730, 1650 cm^{-1}. NMR 7.99 γ 3Hs; 7.84 γ 3Hs; 6.06 γ 3Hs; 4.57 γ 2Hs; 2.62 γ H_3s; 2.6 γ 2.3 γ H_6 H_7 m; 1.85 γ H_8 d J=8 cps; 3.36 γ d J=8 cps, H_2 in some undeuterated; 1.5 γ 1H br. Mass spectrum M^+ M/e 288, other peaks 287 (65% of M^+), 229 (base peak).

5-amino-4-acetoxymethyl-2-deutero-6,8-dinitro-1-methoxynaphthalene (79)

The diacetate (78) (285 mg) was stirred in glacial acetic acid (10 ml) and 2N nitric acid (6 ml) at room temperature for one hour. The product (167 mg) was filtered, washed with water, dried and recrystallised from ethyl acetate. M.P. 198-9°C.

NMR ($CDCl_3$ + DMSO - d_6) 7.87 γ 3Hs; 6.10 γ 3Hs; 4.50 γ 2Hs; 2.68, 2.29 γ AB qu J=8 cps H_2H_3; 2.29 γ H_3s; 1.76 γ H_7s. Mass spectrum M^+ M/e 336, 335 (63% of M^+).

Ozonolysis of Pyrene

When pyrene was ozonised according to the method of Vollmann[39, 40,43,44,50] using a sodium hypochlorite workup, 47% pyrene (87) was recovered and 4-formyl-5-phenanthrene carboxylic acid)93) was obtained in 40% yield after recrystallisation from acetone.

When the ozonolysis was carried out in the presence of 1% pyridine[45] 55% pyrene was recovered and (93) was obtained on crystallisation of the crude ozonolysis product in 56% yield.

M.P. 265-6°C. IR 3200, 1680 cm^{-1}. NMR (DMSO-d_6) 3.36 γ 1Hs; 1.7-2.4 γ 8Hm; 3 γ 1H br exch.

Lactone of 4-hydroxymethylphenanthrene-5-carboxylic acid (94)

The lactol (93) (2.3 g) and KOH (50 g) were dissolved in methanol (50 ml) and water (50 ml) and 40% aqueous formalin (10 ml) was added. The solution was heated under reflux for three hours when TLC showed that there was no starting material left. Methanol was evaporated off in vacuo and the aqueous solution acidified with 6N HCl. The

precipitated lactone was extracted with dichloromethane (twice), washed with water, dried over sodium sulphate and evaporated to dryness. The product (94) was recrystallised from ethanol giving 1.91 g (89%).

M.P. 177-8°C. IR 1700 cm^{-1}. NMR 4.68 τ 2Hs; 1.6-2.8 τ 8Hm.

Analysis C 81.91% H 4.32%

$C_{16}H_{10}O_2$ requires C 82.04% H 4.30%

UV λ_{max}^{EtoH} 217 mμ (ϵ 31,800), 254 mμ (ϵ 31,020), 259 mμ (ϵ 30,700), 262 mμ (ϵ 30,700), 276 mμ (ϵ 28,400), 297 inf. mμ (ϵ 9,050), 328 mμ infl.(ϵ 725), 346 mμ (ϵ 1,050), 363 mμ (ϵ 1,070).

Schmidt Reaction

No reaction was observed when the lactone was dissolved in conc. sulphuric acid and sodium azide was added at room temperature. The lactone was recovered unchanged.

The lactone (94) (714 mg) in conc. sulphuric acid (10 ml) was heated on a steam bath at 80°C while sodium azide (4.5 g) was added in portions over two hours. The solution was allowed to cool and then basified with sodium bicarbonate and extracted with dichloromethane (5x). It was washed with water and dried over sodium sulphate and concentrated. The product (96) was isolated by preparative TLC (Silica Gel, benzene/acetone 20%) and purified by crystallisation from benzene/petrol or carbon tetrachloride. Yield 374 mg, 49%. An analytical sample was sublimed at 150-165°C at 10^{-4} mm.

(96) sublimed at ~85°C, melted at 215-220°C.

Analysis: C 76.85% H 4.57% N 5.57%

$C_{16}H_{11}NO_2$ requires C 77.10% H 4.45% N 5.62%

IR 3390, 1690, 1634 cm^{-1}. Mass spectrum M/e 249, 221, 220, 218, 205, 204. NMR 5.8 τ 1H br exch; 4.74 τ 2H t J=3 cps; 1.6-3.03 τ 8Hm. UV λ_{max}^{EtoH} 215 mμ (ϵ 28,800), 236 mμ (ϵ 23,500), 256 mμ (ϵ 20,000), 283 mμ (ϵ 12,800), 338 mμ (ϵ 3,760).

Acid hydrolysis of Schmidt Product (96)

The Schmidt product (80 mg) was heated on a steam bath at 80°C in conc. hydrochloric acid (5 ml) for 1½ hours. Bubbles were formed as a product was precipitated. The solution was cooled and the product filtered and washed with water (39.2 g). Most of the solid was soluble in chloroform and was purified on Silica Gel plates eluting with benzene/acetone 10%. Yield 17.2 mg 22% of carbonate (95).

The same product was obtained on refluxing (96) in tetrahydrofuran and 6 N hydrochloric acid overnight and on hydrolysis in 6 N sulphuric acid on a steam bath for one hour and crystallising the product out at 0°C.

M.P. 231-233°C (benzene). IR 1680, 1630 cm^{-1}. NMR ($CDCl_3$+DMSO-d_6) 4.74 τ 2Hs; 1.26-2.88 τ 8Hm. Mass spectrum M/e 250, 234, 222, 221, 205, 194, 193, 177, 176.

Analysis	C 76.79%	H 4.32% N 0%
$C_{16}H_{10}O_3$ requires	C 76.79%	H 4.03%

Reaction of (94) with ammonia

The lactone (94) was recovered unchanged after treatment with ammonia under the following conditions.

a) The lactone (99 mg), 0.880 ammonia (5 ml), ethanol (10 ml) and benzene (3 ml) were stirred at room temperature for 20 hours.

b) The lactone (106 mg) 0.880 ammonia (10 ml) and ethanol (10 ml) were stirred and heated under reflux for 22 hours.

c) The lactone (100 mg) was dissolved in warm ethanol (25 ml) and gaseous ammonia was bubbled through for 16 hours.

d) The lactone (112 mg) was stirred in ethanol (50 ml) and liquid ammonia (10 ml) for 22 hours.

e) The lactone (100 mg) and sodamide (100 mg) were dissolved in benzene (25 ml) and heated under reflux for 4 hours.

f) The lactone (70 mg) and sodamide (large excess) were dissolved in aqueous dioxan and heated under reflux for 3 hours.

Reaction of (94) with hydroxylamine hydrochloride

The lactone was recovered unchanged when treated with hydroxylamine hydrochloride under the following conditions.

a) The lactone (100 mg) was dissolved in hot 4 N sodium hydroxide (5 ml), water (5 ml) and ethanol, and hydroxylamine hydrochloride (120 mg) in water was added. The solution was heated on a steam bath for one hour, cooled and acidified with 6 N HCl. The white solid product was filtered and washed and found to be the lactone (94).

b) Procedure a) was repeated in methanolic solution.

c) The lactone (201 mg), hydroxylamine hydrochloride (348.3mg) and sodium acetate (410.2 mg) were dissolved in dimethyl formamide and stirred at room temperature overnight.

d) The lactone (101.4 mg) and hydroxylamine hydrochloride (170 mg) were heated in refluxing pyridine (10 ml) for one hour. The solution was poured into dilute hydrochloric acid, cooled and the product (88 mg) filtered.

Reaction of lactone (94) with hydrazine

Anhydrous hydrazine was prepared by heating 64% hydrazine hydrate (10 g) with sodium hydroxide (10 g) for three hours at $113 \pm 2^{o}C$. The temperature was raised and anhydrous hydrazine distilled.

To the lactone (92 mg) in dry tetrahydrofuran (dried over potassium carbonate and distilled from LAH), anhydrous hydrazine (0.5 g) was added. The solution was heated under reflux under nitrogen, but TLC showed no new products. Sodium hydride (0.75 g) was then added and the refluxing continued under nitrogen for a further six hours. Methanol was added to the dark red solution to decompose any excess sodium hydride. Water was added and the solution concentrated in vacuo. The product was extracted into dichloromethane and after washing and drying the solvent was stripped. The crude product showed mainly one spot on TLC and was crystallised as a red solid from petrol and recrystallised from ethanol. It was identified as phenanthrene-4,5-quinone (99).

M.P. $274\text{-}6^{o}C$. IR 1670, 1620 cm^{-1}. NMR 1.6 - 2.53 τ m.

Analysis C 81.71% H 3.65% N 0%

$C_{16}H_{18}O_2$ requires C 82.75% H 3.47% Mass spectrum M^+ M/e 232.052426

$C_{16}H_{18}O_2$ requires 232.05325869. M/e 204,176.

Reaction of lactone (94) with a Grignard Reagent

To the lactone (117 mg) in dry ether (200 ml), methyl magnesium

iodide (1 equivalent) in dry ether was added and the reaction stirred under nitrogen at room temperature for one hour. No reaction was observed. After adding another equivalent of Grignard and waiting another hour, a large excess (approx. 50 equivalents) of Grignard was added and allowed to react for five hours. The solution was poured into water, dried over sodium sulphate and concentrated to small volume. It was separated on Silica Gel plates eluting with benzene/acetone 10%. Although, when following the reaction by TLC only one product was observed, on workup some of the ketol (102) dehydrated. Some lactone (32.5 g 27%) was recovered and the ketol (102) was obtained in 60% yield (75 mg). It dehydrated on recrystallisation from alcohol.

In another run using 500 mg of lactone (94), there was a 16% (80 mg) recovery, and 15% (80 mg) of ketol (102) and 60% (300 mg) of the anhydro-ketol (103).

Ketol (102) IR 3440 cm^{-1}. NMR ($CDCl_3$+DMSO-d_6) 8.54 τ 3Hs; 4.87 τ 2H qu J=13 cps; 3.60 τ 1Hs exch; 1.6-2.5 τ 8Hm.

Anhydroketol (103) M.P. 136-8°C (ethanol). IR 1630 cm^{-1}. NMR (pyridine-d_5) 5.16 τ d, 4.78 τ d 4H; 2-2.6 τ 8Hm. UV λ_{max}^{EtoH} 213 mμ (ϵ 27,700), 252 mμ (ϵ 36,200), 303 mμ inf. (ϵ 12,300).

Analysis C 85.85% H 5.2%

$C_{17}H_{12}O$ requires C 87.9% H 5.2%

Attempted Beckmann Rearrangement

Both (102) and (103) were oximinated with hydroxylamine hydrochloride

in pyridine or aqueous ethanol and sodium acetate as described above. TLC showed several products with a polar product as the major component. It could not be crystallised and was hydrolysed on preparative TLC to the Grignard product (102). IR 3580, 1610, 1000 cm^{-1}.

The crude product obtained from 103 mg (102) was treated with tosylchloride (222 mg) in pyridine for 18 hours at room temperature. In another run, (102) (175 mg) was oximinated (0.5 g) in refluxing pyridine (15 ml) and after 1½ hours the solution was cooled and tosyl chloride (1 g) was added. It was left at room temperature overnight and then refluxed for five hours. All experiments gave the Grignard product (102) on workup.

4-formylphenanthrene-5-carboxylic acid methyl ester (105)

4-formylphenanthrene-5-carboxylic acid was treated with diazomethane[43,49] to give (105) in 92% yield. M.P. 112-3°C (methanol) IR 1714, 1680 cm^{-1}.

4-formylphenanthrene-5-carboxylic acid pseudo methyl ester (107)

When the lactol (1.44 g) (93) suspended in acetone (25 ml) was treated with excess ethereal diazomethane which had not been washed free of base, the reaction was complete in 20 minutes. The solvents were evaporated and the product crystallised from methanol giving (107) (1.4 g 92%). M.P. 179-180°C. IR 1700 cm^{-1}. NMR (DMSO-d_6) 6.45 τ 3Hs; 3.72 τ 1Hs; 1.7-2.6 τ 8Hm.

Reduction of 4-formylphenanthrene-5-carboxylic acid methyl ester (105) with sodium borohydride

A methanolic solution (40 ml) of the aldehydo ester (105) (265 mg) and sodium borohydride (41 mg) was stirred at room temperature for four hours. It was acidified to pH 5 with dilute HCl, methanol was stripped in vacuo and the resulting aqueous solution was extracted with dichloromethane. After washing and drying, the solvent was removed in vacuo and the product (202 mg 81%) was found to have the same M.P., IR. Rf and NMR as lactone (94).

When this reduction was repeated in the presence of a pH 7 buffer (200 mg each of KH_2PO_4 and Na_2HPO_4), the reaction was over in twenty seconds. The product was lactone (94) (79% yield).

Reduction of (105) with zinc borohydride

Sodium borohydride (761 mg) was stirred with an ethereal solution (500 ml) of zinc chloride (1.42 g) for four days. The ether was distilled off and the residue extracted with dry ether. This solution was added to an ethereal solution of (105) (109 mg) and stirred at room temperature for 30 minutes. The solvent was removed in vacuo and the residue extracted with chloroform. The sole product was lactone (94).

Catalytic reduction of (105)

A solution of (105) (53 mg) in ethyl acetate (10 ml) was hydrogenated over a Pt catalyst (21 mg PtO_2) at 1 atmosphere pressure and room temperature. One equivalent of hydrogen (4.3 ml) was taken up

but on stripping the solvent only lactone (94) was found.

Reduction of (105) with zinc and acid

The aldehydo-ester (105) (50.6 mg) was dissolved in a minimum of glacial acetic acid or methanol and 6 N HCl and zinc dust was added. It was stirred for one hour and the inorganic salts filtered off. The filtrate was extracted with chloroform, washed with water, sodium bicarbonate and water. It was dried over sodium sulphate and evaporated to dryness. Two products were visible on TLC, one with the same R_f as lactone (94); but it appeared that the other decomposed on the plate. The NMR had fewer than three methyl protons and IR 3580, 3280, 1712, 1678 cm^{-1}.

Reductive Acetylation of (105)

Conc. HCl at 0°C was added to acetic anhydride at 0°C. The mixture was then added to (105) (26.4 mg) and zinc dust at 0°C. It was slowly warmed up to room temperature and after 30 mins. it was extracted with dichloromethane. After washing and drying, TLC showed the same product as was obtained in the zinc dust/acetic acid reduction.

Catalytic reductive acetylation of (105)

The aldehydo ester (105) (49.4 mg) in acetic acid (7 ml) and acetic anhydride (3 ml) was hydrogenated over Pt (20 mg PtO_2) at atmospheric pressure and room temperature for 22 hours. Somewhat less than one equivalent of hydrogen was taken up (3.28 ml) but on workup TLC showed only starting material and lactone (94).

Catalytic hydrogenation of the pseudo methyl ester (107)

(107) (58.6 mg) in ethyl acetate (10 ml) took up no hydrogen on attempted hydrogenation over Pt (22 mg Pt O_2).

Attempted Wolff-Kishner Reduction of 4-formylphenanthrene-5-carboxylic acid (93)

Sodium (1 g) was dissolved in diethylene glycol (redistilled, 30 ml) and the solution was heated to 180°C. Anhydrous hydrazine (from 10 g hydrazine hydrate) was distilled into this and after cooling the mixture to room temperature, the lactol (93) (0.5 g) was added. Heating at 180°C was continued overnight and then some hydrazine was distilled out so that refluxing could be continued at 210°C. After 7 hours the solution was poured into water and extracted twice with ether. After washing with water (4x) and drying over sodium sulphate, the solution was reduced to small bulk and the two products 1-pyrenol (108) (233 mg 48%) and the minor product phenanthrene-4,5-quinone (99) were separated by preparative TLC eluting with benzene. 1-pyrenol had M.P. 190-192°C (petrol bp 80-100°C) and had an intense green fluorescence in conc. sulphuric acid. IR 3350, 1635, 1605, 1595, 1270 cm^{-1}. NMR 1.37-2.2γ 8Hm, 2.67γ 1Hs.

Oxime of 4-formylphenanthrene-5-carboxylic acid (111)

(93) (4 g) was oximinated in 91% yield (3.85 g) according to the literature procedure[52]. The pseudo methyl ester (107), when oximinated in the same way also gave (111). IR 3430, 3250, 2600, 1685, 1675 cm^{-1}. NMR (DMSO-d_6) 1.75-2.53γ 8Hm; 1.52γ 1Hs; -1.10 γ 1Hbr; -2.3 γ 1H very broad.

4-cyanophenanthrene-5-carboxylic acid chloride (112)

The dehydration of (111) was carried out according to the literature procedure[52] in 96% yield. A sample was recrystallised from dioxan. IR 2250, 1735 cm^{-1}.

Phenanthrene-4,5-dicarboxylic acid (113)

Hydrolysis of (112) was carried out according to the reported procedure[52] in 91% yield. IR 2650, 1690 cm^{-1}. NMR (DMSO-d_6) 1.8-2.6 γ m.

When pyrene was ozonised following the procedures reported in the literature[38,41], only 4-formylphenanthrene-5-carboxylic acid (93) was obtained.

The aldehydo acid (93) (0.5 g) in acetone (600 ml) was oxidised with chromic acid (2.678 g chromium trioxide in conc. sulphuric acid (2.3 ml) made up to 100 ml with distilled water), at room temperature for one week. It was then diluted with water and the product extracted with ether. The yield of phenanthrene-4,5-dicarboxylic acid was 0.25 g 50%.

Phenanthrene-4,5-anhydride (114)

Sublimation of (113) at 260-290°C at atmospheric pressure gave (114) in 86% yield[52]. M.P. 257-8°C (dioxan). IR 1750, 1720 cm^{-1}.

Analysis C 77.60% H 3.38%

$C_{16}H_8O_3$ requires C 77.4% H 3.25%

Phenanthrene-4-carboxyhydroxamic acid-5-carboxylic acid (115)

Phenanthrene-4,5-anhydride (114) (201 mg) was dissolved in hot 4N sodium hydroxide and excess hydroxylamine hydrochloride was added. After heating on a steam bath for 30 minutes, the solution was cooled and acidified with 6 N HCl and the product filtered. It was found to be phenanthrene-4,5-dicarboxylic acid (113).

The anhydride (238 mg) was added to hydroxylamine hydrochloride (140 mg) and sodium carbonate (214 mg) in water (5 ml) and the solution heated on a steam bath for one hour. The solution was cooled and filtered and the filtrate acidified with 6 N HCl. The product was filtered and found to be phenanthrene-4,5-dicarboxylic acid (113).

The anhydride (114) (2.8 g) was treated with hydroxylamine hydrochloride (4.2 g) in refluxing dry pyridine (70 ml) for one hour. The solution was poured into ice and 6N HCl and after 30 minutes the product (115) was filtered (2.60 g, 82%).

M.P. 202-3°C (ethanol or ethyl acetate). IR. 3270, 2700, 1665, 1625 cm^{-1}.

Analysis	C 71.94%	H 3.85%	N 5.13%
$C_{16}H_{11}NO_4$ requires	C 68.33%	H 3.94%	N 4.98%

N-acetoxyphenanthrene-4,5-imide (116)

The carboxylic acid hydroxamic acid (115) sublimed unchanged

when heated at 210°C at 10^{-4} mm pressure for one hour.

The compound (115) (2.6 g) in acetic anhydride was heated just below reflux temperature for one hour. Toluene was added and the acetic anhydride azeotroped off. The product (116) was recrystallised from ethanol (2.18 g, 78%). M.P. 179-181°C. IR 1795,1690,1665 cm^{-1}. NMR 7.53 τ 3Hs; 1.5-2.5 τ 8Hm.

Analysis C 70.98% H 3.64% N 4.50% Required for $C_{18}H_{11}NO_4$ C 70.82% H 3.63% N 4.59%

N-hydroxyphenanthrene-4,5-imide (117)

The acetate (116) (1.08 g) and benzylamine (0.45 g) in dry chloroform was left at room temperature for three days. (In other experiments it was found satisfactory to work up the reaction after 17 hours). The solution was shaken with aqueous sodium bicarbonate and the yellow sodium salt of (117) was precipiated. It was filtered and washed with chloroform and water and dried (0.92 g, 91%). On acidification of a small portion a white solid (117) was obtained which gave a violet colouration with ferric chloride. M.P. 196-7°C (ethanol). IR 3300, 1670, 1625 cm^{-1}.

Analysis C 72.75% H 3.56% N 5.05%

$C_{16}H_9NO_3$ requires C 73.00% H 3.45% N 5.32%

N-tosyloxyphenanthrene-4,5-imide (109)

The sodium salt of (117) (886 mg) was suspended in pyridine and recrystallised tosyl chloride (730 mg) was added. A clear

solution was soon formed and after one hour this was poured onto ice and the resulting white solid filtered (1.04 g 76%). The tosylate (109) was recrystallised from ethanol M.P. 200-201°C. IR 1730, 1690 cm^{-1}. NMR 7.57τ 3Hs; 1.5-2.8τ 12 Hm.

Analysis: C 65.98% H 3.53% N 3.23% S 7.67%

$C_{23}H_{15}NSO_5$ requires C 66.19% H 3.62% N 3.36% S 7.39%

Reaction of N-acetoxyphenanthrene-4,5-imide with sodium borohydride

The acetoxy imide (116) (103 mg) was reduced with excess sodium borohydride in ethanol and N,N-dimethylformamide at room temperature for 20 hours. It was diluted with water and the ethanol boiled off in vacuo. The solution was extracted with chloroform (3x) and DMF washed out with water (6x). On evaporating to dryness 54.6 mg of a polar product was obtained which on crystallisation from ethanol gave pink crystals of (119) (24 mg) which melted at 222-4°C. (119) gave a dark colouration with ferric chloride.

NMR ($CDCl_3$+DMSO-d_6) 6.5τ 1 Hbr.exch; 5.15τ 2Hs; 1.7-2.4τ 8Hm.

Analysis: C 76.85% H 4.55% N 5.37%

$C_{16}H_{11}NO_2$ requires C 77.10% H 4.45% N 5.62%

IR 3100-2700, 1635, 1275 cm^{-1}.

Reaction of N-tosyloxyphenanthrene-4,5imide with sodium borohydride

The tosylate (109) (151 mg) and sodium borohydride (29 mg) were reacted in ethanol (200 ml). On stirring, some (109) crystallised out but after ten minutes the solution was clear. After 1¼ hours the

solution was evaporated to dryness and the solid thus obtained was partitioned between water and ether. The ether layer contained two products, the major one of which (37 mg 47%) was 1-azapyrene (86). M.P. 158-160°C (sublimed at 10^{-4} mm. recrystallised from toluene). IR 1690 wk, 1630, 1600, 1585, 1260, 1170, 1110, 1090 cm^{-1}.

NMR 0.45γ 1Hs; 1.3-2.8γ 8Hm.

Analysis: C 88.8% H 4.63% N 6.61%

$C_{15}H_9N$ requires C 88.64% H 4.46% N 6.89%

The tosylate (109) (102 mg) in t-butanol (90 ml) was reduced with sodium borohydride (100 mg) at room temperature for one hour. The solvent was removed in vacuo keeping the temperature below 40°C. The solid residue was partitioned between water and ether. The ether was stripped in vacuo at room temperature. The crude product contained the same two products as found previously and the spectra indicated that it was a mixture of 1-azapyrene (86) and (91). NMR ($CDCl_3$+DMSO-d_6) 0.6γ s; 1.5-2.8γ m; 5.21γ s; IR 3420, 1680, 1630, 1595, 1290 cm^{-1}.

The crude mixture was hydrolysed by stirring it with sodium bicarbonate in aqueous acetone under nitrogen for three hours at room temperature. 1-azapyrene (86) (72%) was extracted with ether.

N-hydroxyphthalimide

N-hydroxyphthalimide was prepared from phthalic anhydride[53]. IR 3200, 1850, 1785, 1740, 1710 cm^{-1}.

N-tosyloxyphthalimide

N-hydroxyphthalimide (3.5 g) was dissolved in pyridine (30 ml) and tosyl chloride (4.2 g) was added. The initial yellow colour was discharged after one hour and after 1½ hours the solution was poured into water and the precipitated tosylate (121) filtered, washed and crystallised from ethanol in 87% yield (5.9 g). M.P. 161½-162½°C. IR 1860, 1795, 1745 cm^{-1}. NMR 7.50 τ 3Hs; 2-2.7 τ 8Hm.

Analysis:	C 56.79%	H 3.49%	N 4.41%	S 10.09%
$C_{15}H_{11}NO_5S$ requires	C 56.76%	H 3.53%	N 4.38%	S 10.41%

Reaction of N-tosyloxyphthalimide (121) with sodium borohydride

The tosylate (121) (501 mg) in dry pyridine (20 ml) was reduced with sodium borohydride (976 mg). As the reaction became hot on mixing the reagents, it was cooled to 20°C and stirred at that temperature for 1½ hours. The solution was then poured into water and extracted twice with ether. A liquid product (202 mg) was obtained on removing the solvent in vacuo. This was distilled at 85-95°C 0.2 mm and found to be pyridine borane, identical to that formed by reacting pyridinium hydrochloride with sodium borohydride. IR 3100, 2420-2350, 1620, 1490, 1465, 1175, 1095 cm^{-1}. NMR 1.47τ 2Hd J=5 cps; 2.12 τ 1H qu; 2.53 τ 2Ht; 4.5-9 τ 3H very broad. UV λ_{max}^{EtoH} 206, 250, 257, 263, 270 mμ.

The reduction was performed on the same scale in ethanol (150 ml).

After one hour TLC showed no starting material and two products. Ethanol was boiled off in vacuo and the product partitioned between water and chloroform. The organic layer was concentrated and separated on Alumina plates eluting with benzene/acetone 10%. The less polar product was (122) (78.5 mg 34%); the product at the origin was an oil (52 mg) and as it had no aromatic protons in the NMR it was discarded. M.P. 119-120°C (petrol)[92]. IR 3250, 3180, 3120, 1725 cm^{-1}. NMR 0.67 τ 1H exch; 4.71 τ 2Hs; 2.6-3.3 τ 4Hm.

Analysis: C 64.31% H 4.61% N 9.27%

$C_8H_7NO_2$ requires C 64.42% H 4.73% N 9.37%

The same yield was obtained when the solvent used was t-butanol or diglyme.

Reaction of N-tosyloxynaphthalimide (46) with sodium borohydride

The tosylate (1 g) was added over 30 minutes to sodium borohydride (1 g) in ethanol (400 ml). After stirring at room temperature for another 30 mins, it was clear from TLC that the reaction was over. The solution was evaporated to dryness and water and ether added to the solid residue. The ether layer was separated and dried and evaporated to dryness. A rather insoluble compound was filtered and crystallised from benzene. It was found to be naphthalimide (100 mg 20%). IR 3150, 3050, 1690, 1680, 1585 cm^{-1}. NMR (pyridine-d_5) 1.30 τ 2H; 1.84 τ 1H; 2.38 τ 2H; 2.80 τ 1H; 5.16 τ 1H exch.

Analysis: C 72.24% H 3.45% N 7.23%

$C_{12}H_7NO_2$ requires C 73.09% H 3.58% N 7.10%

The remainder of the crude product was chromatographed on Grade 3 Alumina eluting with benzene/acetone 2-5%. Naphthostyril (263 g 57%) was the only product eluted; the other product remained on the column. M.P. 179-180°C (benzene). IR 3230, 1725, 1665, 1650 cm^{-1}.

The tosylate (0.5 g) and sodium borohydride (0.5 g) were reacted in t-butanol (300 ml). After five hours TLC showed that the reaction was not completed and it was left for 24 hours and worked up as before. The crude product (200 mg) was separated on Silica Gel plates eluting with benzene/acetone 10%. TLC showed a multicomponent mixture from which naphthalimide (26 mg) was isolated and another product (123) which had also been formed in ethanolic solution (35.3 mg) and was crystallised from benzene. IR 3200-3100 br, 1680 cm^{-1}.
NMR 4.96 τ 2Hd J=4.5 cps; 3.42 τ 1Hd exch. J=4.5 cps; 1.25-2.6 τ 6Hm; -0.9 τ br. exch.

Phenanthrene-4-carboxylic acid-5-carboxyamide (126)

Phenanthrene-4,5-anhydride (114) was converted to (126) according to the published procedure[52]. IR 3520, 3320, 3180, 2600 br, 1690, 1650, 1270 cm^{-1}.

Phenanthrene-4-(carboxylic acid methyl ester)-5-carboxyamide (127)

The amido acid (126) (454 mg) was methylated with excess diazomethane in ether at room temperature overnight. The white product was filtered and crystallised from ethyl acetate. Yield 442 mg 91%. M.P. 234-5°C. IR 3420, 3250, 1715, 1650, 1530, 1270 cm^{-1}. NMR ($CDCl_3$+DMSO-d_6) 6.16 τ 3Hs; 3.2-2.7 τ 2H exch; 2-2.5 τ 8Hm.

Analysis: C 73.11% H 4.69% N 5.01%

$C_{17}H_{13}NO_3$ requires C 73.11% H 4.73% N 4.88%

Reduction of (127) with lithium borohydride

Sodium borohydride (933mg) and lithium bromide (2.145 g) in diglyme (40 ml) was stirred at room temperature for 30 minutes. The amido ester (127) (327 mg) was added and after 16 hours the reaction mixture was poured onto ice and 2N HCl and left for 2 hours. The white amido alcohol (128) (206 mg 72%) was filtered, washed and dried in vacuo.

Acetylation of (128)

The crude amido alcohol(128) (206 mg) was reacted with acetic anhydride (5 ml) in dry pyridine (5 ml) at room temperature for 3 days. The reaction mixture was poured into water and left standing for one hour. The product was extracted with ether (3 x), pyridine was washed out with water (2x) and after drying and evaporation the products were separated by preparative TLC on Silica Gel plates eluting with benzene/acetone 10%. Unchanged amido alcohol (21.5 g 10%) was isolated. M.P. 248-250°C (ethyl acetate). IR 3320, 1630 cm^{-1}. NMR ($CDCl_3$+ DMSO-d_6) 5.62 τ 2Hd J=7 cps colapsed to singlet after D_2O shake; 1.5-2.5 τ 8Hm. Another product was amide (130) (47.5 mg 21%). M.P. 112-114°C (petrol). IR 1650 cm^{-1}. NMR 7.70 τ 3Hs; 5.41 τ 2Hs; 5.24 τ 2Hs; 2-2.7 τ 8Hm. UV λ_{max}^{EtoH} 207 mμ (ϵ 24,700), 258 mμ (ϵ 48,900), 280 mμ (ϵ 10,400), 290 mμ (ϵ 8,940), 303 mμ (ϵ 9,540).

Analysis C 82.65% H 5.65% N 5.24%

$C_{18}H_{15}NO$ requires C 82.73% H 5.79% N 5.36%

The third product was imide (129) (56 mg, 25%). M.P. 150-152°C (petrol). IR 1690, 1660 cm^{-1}. UV λ_{max}^{EtoH} 221 mμ (ε 31,500), 253 mμ (ε 24,800), 273 mμ (ε 25,200). NMR 7.44 τ 3Hs; 4.90 τ 2Hs; 1.5-2.4 τ 8Hm.

Analysis C 77.75% H 4.71% N 4.84%

$C_{18}H_{13}NO_2$ requires C 78.53% H 4.76% N 5.09%

Phenanthrene-4,5-lactone (132)

Lead tetraacetate (683 mg), washed with petrol and dried over KOH in vacuo, was heated in refluxing acetonitrile (20 ml) with phenanthrene-4,5-dicarboxylic acid (113) (267 mg) and pyridine (1 ml) for 45 minutes. The mixture was cooled and diluted with benzene (70 ml). It was filtered and the residue washed with benzene (50 ml). The combined benzene solutions were washed with 2N HCl and water and dried over sodium sulphate. The solvent was removed in vacuo and the crude product was dissolved in hot 4N NaOH and charcoaled. The lactone (132) (81 mg 37%) was obtained on acidification and filtration. M.P. 135-6°C (petrol). IR, 1735, 1238 cm^{-1}.

Analysis: C 81.63% H 3.76%

$C_{15}H_8O_2$ requires C 81.81% H 3.66%

4-hydroxymethyl-5-hydroxyphenanthrene (131)

The lactone (132) (226 mg) was reduced with lithium aluminium hydride (1 g) in refluxing dry ether. After 2 hours, wet ether was added followed by dilute hydrochloric acid. The ether layer was separated, washed, dried and concentrated. The two products

were separated on Silica Gel plates eluting with benzene/acetone 10%. The major product (122 mg, 53%) was a polar foam and was identified as diol (131). IR 3500, 3250, 1240 cm^{-1}. NMR 5.05 τ 4Hs, after shaking with D_2O 2H; 2.2-2.8 τ 8Hm. The other product (36 mg, 17%) was the crystalline ether (133). M.P. 80-82°C (petrol). IR 1240 cm^{-1}. NMR 4.49 τ 2Hs; 2.2-3.1 τ 8Hm.

A sample was sublimed for analysis at 75-85°C 0.07 mm. M.P. 91-93°C.

Analysis	C 85.83%	H 4.80%
$C_{15}H_{10}O$ requires	C 87.35%	H 4.89%

Attempted Bucherer Reaction

The diol (131) (100 mg) was heated in a Carius tube with 0.880 ammonia (5 ml) which had been saturated with SO_2 and 0.880 ammonia (2 ml). After 5 hours the temperature of the furnace reached 150°C and it was kept at 150°C for another 8 hours. The tube was cooled water was added and the solution was extracted with chloroform. TLC showed diol (131) and ether (133). A negligible quantity of material was extractable into acid.

2-β-naphtho ylpropionic acid

The acid was prepared from naphthalene and succinic anhydride according to the literature method[60] in 18% yield. M.P. 172-4°C. IR 2700-2600 br, 1705, 1678 cm^{-1}. NMR ($CDCl_3$,DMSO-d_6) 7.22 τ 2Ht J=6.5 cps; 6.59 τ 2Ht J=6.5 cps; 1.9-2.6 τ 6Hm; 1.52 τ H_1s; 0 τ 1 Hbr. exch.

2-β-naphthylbutyric acid

2-β-naphthoylpropionic acid was reduced by Martins's Clemmensen reduction procedure[61] in 94% yield. M.P. 95-6°C. IR 2700-2600 br, 1690 cm^{-1}.

4-keto-1,2,3,4-tetrahydrophenanthrene (134)

The Friedel-Crafts cyclisation was carried out in dichloromethane instead of benzene[62] and was worked up 90 seconds after the addition of stannic chloric. Yield 85%. The product was distilled and crystallised from alcohol. M.P. 65-67°C. IR 1657 cm^{-1}. NMR[90] 7.83τ H_2m; 7.26τ H_3 t J=6 cps; 6.94τ H_1 t J=6 cps; 2.77τ H_{10} d J=8 cps; 2.4τ $H_{6,7,8}$ m; 2.12τ H_9 d J=8 cps; 0.55τ H_5m.

4-keto-5-nitro-1,2,3,4-tetrahydrophenanthrene (136)

On nitration of (134) in fuming nitric acid and acetic anhydride[63] (136) precipitated from solution in 45% yield. M.P. 162°C (ethanol). IR 1665, 1530, 1350, 840 cm^{-1}. UV λ_{max}^{EtoH} 207 mμ (ϵ 18,760), 234 mμ (ϵ 30,400), 298 mμ (ϵ 6,420). NMR 7.80τ 2Hm; 7.26 τ 2Ht J=6 cps; 6.96 τ 2Ht J=6 cps; 2.58 τ 2Ht J=8 cps; 2.09 τ 3Hm. The acid solution was poured into water and extracted with ether. This ether extract was washed with sodium hydroxide and water and chromatographed on Grade 3 Alumina. Another 6% of (136) was obtained and 8% of 4-keto-8-nitro-1,2,3,4-tetrahydrophenanthrene (135). M.P. 117-119°C (ether). IR 1665, 1530, 1360, 820 cm^{-1}. NMR 7.81τ H_2m; 7.23 τ H_3 t J=6 cps; 6.88 τ H_1 t J=6 cps; 2.52τ H_{10} d J=8 cps; 2.43τ H_6 t J=8 cps;

1.92 τ H_7 qu J=8,1 cps; 1.55 τ H_9 d J=8 cps; 0.45 τ H_5 d J=8 cps.

UV λ_{max}^{EtoH} 208 mμ (ϵ 24,600), 237 mμ (ϵ 26,100), 317 mμ (ϵ 6,860).

Analysis:	C 69.44%	H 4.50%	N 5.75%
$C_{14}H_{11}NO_3$ requires	C 69.70%	H 4.60%	N 5.81%

2-β-tetralylpropionic acid

The acid was prepared by the literature method[71] in 75% yield. IR 3300 br, 2750, 2650, 1710, 1690 cm^{-1}.

γ-2-tetralylbutyric acid (155)

The keto acid was reduced in 87% yield by the literature method[61]. IR 2700, 2600, 1690 cm^{-1}. M.P. 47-9°C. B.P. 195-200°C 4.5-5 mm.

γ-2-tetralylbutyric acid methyl ester

γ-2-tetralylbutyric acid was methylated with excess diazomethane in ether for 2 hours at 0°C in 97% yield. IR 1735,1220 cm^{-1}.

γ-2-naphthylbutyric acid

The methyl ester of γ-2-tetralylbutyric acid was aromatised at 300°C with 10% Pd/C[71], and hydrolysed with ethanolic KOH. M.P. 97-99°C (toluene). Yield 70%. IR 1688 cm^{-1}.

4-hydroxy-4-methyl-1,2,3,4-tetrahydrophenanthrene

The Grignard reaction with 4-keto-1,2,3,4-tetrahydrophenanthrene (134)[60,62,66] was quantitative. It was worked up with ammonium chloride at 0°C. IR 3350 cm^{-1}. NMR 8.13 τ 3Hs; 8.10 τ 4Hm; 7.10 τ 2Hm; 2.3-3.0 τ 5Hm; 1.32 τ 1Hm.

4-methylphenanthrene

The carbinol was aromatised with 10% Pd/C at 300°C as reported in the literature[66] in 73% yield. M.P. 47-48°C (ethanol). NMR 6.73 τ 3Hs; 2.1-2.5 τ 8Hm; 1.0 τ 1Hm.

4-bromomethylphenanthrene (138)

The NBS bromination of 4-methylphenanthrene was carried out as reported[66].

4-hydroxymethylphenanthrene (139)

The crude bromo-compound was hydrolysed according to the reported procedure[66]. Overall yield 68%. M.P. 145½-147°C (benzene/petrol). IR 3320, 1025 cm^{-1}.

4-formylphenanthrene (140)

4-hydroxymethylphenanthrene (1.04 g) was oxidised with active manganese dioxide (15 g) in Analar chloroform (60 ml) at room temperature for 24 hours. The reagent was filtered off through Kieselguhr and on evaporating the chloroform (140) was obtained pure quantitatively. M.P. 84°C (ether). IR $^{2710}_{wk}$, 1680 cm^{-1}. NMR -0.60 τ 1H; 1.9-2.52 τ 9Hm.

Analysis: C 87.20% H 5.06%

$C_{15}H_{10}O$ requires C 87.35% H 4.89%

4-methoxymethylphenanthrene (141)

The crude bromo compound (138) was refluxed with sodium in methanol overnight. The methanol was distilled off in vacuo and the

solid remaining was partitioned between water and chloroform. The chloroform solution was washed with 6N HCl (2x) and water (2x) and dried over sodium sulphate. It was evaporated to dryness and chromatographed on Grade 3 Alumina. The methyl ether (141) was obtained in 76% yield as an oil. IR 1090 cm^{-1}. NMR 6.48 τ 3Hs; 4.97 τ 2Hs; 2.1-2.5 τ 8Hm, 1.25τ 1Hm.

Nitration of 4-methoxymethylphenanthrene (141)

4-methoxymethylphenanthrene (141) (204 mg) and silver nitrate (257 mg) were dissolved in dry acetonitrile (7 ml). The acetonitrile was dried over Linde 4A molecular sieve and then over calcium hydride and then distilled. The solution was cooled to 0°C and acetyl chloride (131 mg) in dry acetonitrile (2 ml) was added over 15 minutes. It was stirred for 7 hours till TLC showed no trace of starting material. It was poured into water and extracted twice with ether. This was separated by multiple elution on Silica Gel plates eluting with benzene/petrol 1:1. 3-nitro-5-methoxymethylphenanthrene (142) melted at 135-136°C (petrol).

Analysis: C 71.83% H 5.00% N 5.24%

$C_{16}H_{13}NO_3$ requires C 71.90% H 4.90% N 5.14%

NMR 6.32 τ 3Hs; 5.10 τ 2Hs, 2.0-2.5τ 6Hm; 1.68 τ 1H qu J=8.5, 2.2 cps; 0.18 τ 1Hd J=2.2 cps.

Nitration of 4-hydroxymethylphenanthrene (139)

4-hydroxymethylphenanthrene (139) (50 mg) and silver nitrate (70 mg) were dissolved in acetonitrile (3 ml) at 0°C and acetyl chloride (36 mg) in acetonitrile (1 ml) was added. A rapid reaction ensued and after one hour silver chloride was filtered off, the filtrate diluted with ether and washed with water, sodium bicarbonate and water and dried and evaporated to dryness. The product (54 mg, 88%) was the nitrate (144). M.P. 98-100°C (petrol). IR 1625, 1295, 870 cm^{-1}. NMR 3.94 τ 2Hs, 2-2.6 τ 1.75 τ 9Hm. UV λ_{max}^{EtoH} 213 mμ (ϵ 29,220) 252 mμ (ϵ 50,100), 277 mμ infl. (ϵ 9,720), 286 mμ infl. (ϵ 7,790), 298 mμ (ϵ 7,400), 336 mμ (ϵ 490), 352 mμ (ϵ 506).

Analysis:	C 71.17%	H 4.68%	N 5.35%
$C_{15}H_{11}NO_3$ requires	C 71.14%	H 4.38%	N 5.53%

The carbinol (139) (51.7 mg) and silver nitrate (251 mg) were dissolved in acetonitrile (10 ml) and acetyl chloride (124 mg) in acetonitrile (2 ml) was added at 0°C over 15 minutes. 15 minutes later TLC showed complete conversion to the nitrate (144). 1½ hours later a more polar spot was observed on TLC and the reaction was left for 15 hours at 0°C and then 24 hours at room temperature. It was worked up as in the previous experiment. 3-nitro-5-hydroxymethyl-phenanthrene nitrate ester (146) was one product isolated. IR 1640, 1545, 1520, 1350, 1290 cm^{-1}. NMR 3.88 τ 2Hs; 1.9-2.3 τ 6Hm, 1.6 τ

1 H qu; 0.54 γ 1Hd.

Analysis: C 59.79% H 3.37% N 9.20%

$C_{15}H_{10}N_2O_4$ requires C 60.41% H 3.38% N 9.39%

Nitrate ester of 4-hydroxymethylphenanthrene (144)

4-methylphenanthrene (300 mg) was converted to 4-bromomethylphenanthrene (138) in the usual way and the crude product was reacted with silver nitrate (592 mg) in acetonitrile (15 ml) at room temperature for 3 days. The silver bromide was filtered off and the filtrate concentrated and separated by preparative TLC. The nitrate (144) was obtained in 34% yield (132 mg).

When the nitrate (144) was reacted with boron trifluoride etherate in refluxing dry ether, a mess was obtained.

Nitration of 4-formylphenanthrene (140)

4-formylphenanthrene (140) (105 mg) was dissolved in dry acetonitrile (10 ml) and silver nitrate (129 mg) and acetyl chloride (63 mg) were added. After 24 hours at 0°C TLC showed that very little reaction had occurred. More silver nitrate (252 mg) and acetyl chloride (146 mg) were added and after six hours the reaction was worked up as before. Multiple elution gave six yellow bands. They all had nitrate bands in the IR at 1520, 1350 cm^{-1} and a carbonyl at 1680 cm^{-1}. One band had NMR -0.51γ -0.5γ (mixture of two aldehydes); 1.34γ d, 1.49γ t 2H; 1.7-2.3γ m. Another band had -0.62 γ ; 1.95-2.6γ m. Another band which was probably 3-nitro-5-

formylphenanthrene M.P. 140-145°C had -0.64τ; 0.95τ d; 1.60τ qu; 1.8-2.3τ m.

Analysis C 71.69% H 3.44% N 5.52%

$C_{15}H_9NO_3$ requires C 71.7% H 3.61% N 5.57%

Friedel-Crafts Cyclisation of γ-2-tetralylbutyric acid (155)

The following literature procedures were followed:

A) The acid (155) was converted to the acid chloride with PCl_5 and cyclised with $AlCl_3$[72]. 1-keto-1,2,3,4,5,6,7,8-octa-hydro-anthracene (157) was formed in 91% yield.

B) The acid (155) was heated with conc.sulphuric acid for four hours.[72] Anthrone (157) was formed in 68% yield.

C) The acid (155) was stirred with conc. sulphuric acid for two hours at room temperature[72]. Anthrone (157) was formed in 43% yield and phenanthrone (156) in 20% yield.

D) The acid (155) was converted to the acid chloride with thionyl chloride and a drop of pyridine in ether and the acid chloride cyclised with stannic chloride in methylene dichloride[72]. Yield of anthrone 93%, phenanthrone 2%.

E) The acid was heated with polyphosphoric acid[73] giving the anthrone (22%) and phenanthrone (5%).

(F) The acid was converted to the acid chloride with PCl_5, it was warmed and $POCl_3$ distilled off. A mixture of ketones was distilled at 15 mm pressure and about 200°C.[74] It was separated

by column chromatography on Grade 3 Alumina eluting with benzene/petrol 1:1. 4-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene (156) was eluted first (25%) followed by anthrone (157) (28%).

When the acid chloride was prepared using thionyl chloride and pyridine, the acid chloride distilled without cyclising.

4-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene (156) M.P. 40-40.5°C IR 1672 cm^{-1}. NMR 6.7-8.4 τ 14 Hm; 2.95 τ 2H ABqu J=8 cps. 1-keto-1,2,3,4,5,6,7,8-octahydroanthracene (157) M.P. 47-47.5°C. Semicarbazone M.P. 250-252°C. IR 1680 cm^{-1}. NMR 7-8.4 τ 14Hm; 3.10 τ 1Hs, 2.28 τ 1Hs.

4-hydroxy-4-methyl-1,2,3,4,5,6,7,8-octahydrophenanthrene (149)

The phenanthrone (156) (15 g) in dry ether (250 ml) was added slowly to a Grignard reagent prepared from magnesium (19 g) and methyl iodide (120 g) in dry ether (200ml). The reaction was carried out under nitrogen at 0°C for six hours. The solution was then poured onto ice and ammonium chloride. The aqueous layer was separated and extracted with ether (3x). After washing with water and drying over magnesium sulphate, the ether was removed in vacuo and the alcohol (149) crystallised from ethyl acetate (13 g, 80%).
M.P. 118-120°C. IR 3320, 1174, 1115 cm^{-1}. NMR 8.43 τ 3Hs; 8.35 τ t J=4 cps, 8.19 τ t J=4 cps, 6.5-7.5 τ m 14H; 6 τ br 1H exch; 3.19 τ 2Hs.
UV λ_{max}^{EtoH} 209 mμ (ϵ 19,650), 231 mμ infl. (ϵ 9,790), 270 mμ sh (ϵ 617 mμ), 273 mμ (ϵ 644), 277 mμ sh (ϵ 554), 283 mμ sh (ϵ 503).

Analysis: C 83.18% H 9.28%

$C_{15}H_{20}O$ requires C 83.29% H 9.32%

A small amount (5%) of 4-methyl-1,2,5,6,7,8-hexahydrophenanthrene (158) was isolated by chromatography of the mother liquors. M.P. 65-6°C (ethanol). NMR 7.9-8.4 τ m, 7-7.6 τ m 12H; 7.83 τ 3Hd J=1 cps; 4.02 τ 1Ht J=5 cps; 3.11 τ 2Hs. UV λ_{max}^{EtOH} 223 mμ (ε 21,700), 264 mμ (ε 7,860), 300 mμ infl. (ε 830).

Analysis C 91.04% H 9.27%

$C_{15}H_{18}$ requires C 90.85% H 9.15%

4-methyl-4-nitrito-1,2,3,4,5,6,7,8-octahydrophenanthrene (150)

The carbinol (149) (1.14 g) was dissolved in dry pyridine (40 ml) at -30°C and nitrosyl chloride was bubbled through the solution for 1-2 minutes. It was poured onto ice and extracted with ether (3x). The ether extract was washed with water (6x) and dried over sodium sulphate before the solvent was removed in vacuo without external heating. TLC showed a single non-polar spot which after a brief exposure to iodine vapour and spraying with sulphuric acid coloured up blue on warming. IR 1625, 780 cm^{-1}.

4-hydroxy-4-methyl-5-oximino-1,2,3,4,5,6,7,8-octahydrophenanthrene (151)

The oily nitrite (150) was dissolved in dry benzene (30 ml) and a drop of pyridine was added. The stirred solution was irradiated in a pyrex vessle under nitrogen with a medium pressure lamp. After two

hours TLC showed that the photolysis was essentially completed and the solution was concentrated and separated on Grade 5 Alumina eluting first with benzene/petrol 20%. Some nitrite (80.3 mg) was recovered in the early fractions. Carbinol (149) (470 mg 44%) was obtained next, followed by 4-hydroxy-4-methyl-5-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene (158) (63 mg 5½%) IR 3400, 1668 cm^{-1}. UV λ_{max}^{EtoH} 218 mμ (ϵ 12,500), 262 mμ (ϵ 7,840), 311 mμ (ϵ 2,370). NMR 8.62 τ 3Hs; 7.9-8.5 τ, 7.0-7.4 τ 12 Hm; 3.40 τ 1H exch; 2.92 τ 2Hd (qu?) J=5 cps.

Analysis C 78.38% H 8.17%

$C_{15}H_{18}O_2$ requires C 78.23% H 7.88%

Some unidentified minor products were then eluted and after a yellow band had been eluted, the eluent was changed to benzene/ether 2:1 and the crystalline oxime (151) was obtained (420 mg, 35%). M.P. 229-230°C (ethyl acetate). IR 3375, 3160, 1645 wk, 1276, 1185, 1105, 1085, 1052, 1000, 960 cm^{-1}. UV λ_{max}^{EtoH} 216 mμ (ϵ 21,700), 254 mμ (ϵ 9,040), 291 mμ sh(ϵ 2,180). NMR 0.48 τ 3Hs; 7.7-8.3, 6.8-7.5 τ 12Hm; 2.99 τ 2Hs.

Analysis: C 73.27% H 7.66% N 5.60%

$C_{15}H_{19}NO_2$ requires C 73.44% H 7.81% N 5.71%

Photolysis of the nitrite prepared from 515 mg of carbinol (149) in Areton 113 gave only 16% (84 mg) of carbinol (149) and 46% (270 mg) oxime (151).

Photolysis of the nitrite prepared from 2.5 g carbinol (140) in dry benzene (300 ml) under nitrogen and cooled to room temperature by a water bath took 4 hours. The oxime (1.69 g 65%) was obtained pure by one recrystallisation of the crude photoproduct from ethyl acetate (70 ml).

The same photolysis carried out without a cooling bath took 1 hour 10 mins. and the yield was 69%.

Use of a high pressure mercury lamp halved the irradiation time but had no effect on the yield.

From one photolysis a small amount of isomeric 4-hydroxy-4-methyl-1-oximino-1,2,3,4,5,6,7,8-octahydrophenanthrene was isolated by preparative TLC. M.P. 184-5°C (ethyl acetate). IR 3400, 3300, 1650 cm^{-1}. NMR 8.62 τ 3Hd J=2 cps, 8.1-8.7, 7.1-7.3 τ 12Hm, 3.82 τ 1Hs; 4.03 τ 1Hs; 3.11 τ 2Hd J=5 cps.

Analysis: C 73.58% H 7.76% N 5.02%

$C_{15}H_{19}NO_2$ requires C 73.44% H 7.81% N 5.71%

Oxidation of the oxime (151)

The oxime (21 mg) was heated with 10% Pd/C (7.5 mg) at 300-320°C for 15 minutes under nitrogen. After cooling, the product was dissolved in dichloromethane and the catalyst filtered off. Basic products were extracted into dilute sulphuric acid. The acid solution was basified with sodium bicarbonate and extracted with ether. The major product isolted by preparative TLC was 1-aza-pyrene (86).

1-oximino-1,2,3,4,5,6,7,8-octahydroanthracene (161)

Octahydroanthrone (157) (4.9 g) in ethanol (25 ml) was reacted with hydroxylamine hydrochloride (3.5 g) and sodium acetate (6 g) in alcohol (350 ml) and water (50 ml) under reflux for one hour. It was cooled and diluted with water and the oxime (161) filtered and crystallised from ethanol (4.8 g 93%). M.P. 146°C. IR 3200, 1645 cm^{-1}. NMR 8.0-8.4τ 6Hm; 7.1-7.4τ 8Hm; 3.18τ 1Hs; 2.43τ 1Hs, approx 1τ 1H exch.

8-acetamido-1,2,3,4-tetrahydroanthracene (162)

The oxime (161) (106.2 mg) was dissolved in glacial acetic acid (5 ml) and acetic anhydride (2 ml) and the solution saturated with HCl gas. It was left at 40°C for 24 hours, poured into water, make alkaline with sodium bicarbonate and extracted with ether. Preparative TLC gave amide (162) (61.2 mg 53%) as the major product. M.P. 192-3°C (ethyl acetate). Ir 3240, 1650, 1550 cm^{-1}. NMR 8.3-7.7τ 7Hm; 7.3-7.0τ 4Hm; 2.9-2.3τ 6Hm.

Analysis:	C 80.32%	H 7.20%	N 5.76%
$C_{16}H_{17}NO$ requires	C 80.30%	H 7.16%	N 5.85%

1-oximinotosylate-1,2,3,4,5,6,7,8-octahydroanthracene (163)

The oxime (161) (502 mg) was reacted with tosyl chloride (547 mg) in dry pyridine (10 ml) for 5½ hours at -20 to -30°C. It was poured onto ice and extracted with ether (3x). The ether solution was washed

with water (6x), dried over sodium sulphate and concentrated. The product was purified by column chromatography on Grade 3 Alumina (80 g) eluting with benzene/petrol 10% and was obtained in 65% yield (559 mg). M.P. 151-3°C (ethyl acetate). IR 1600, 1380, 1190, 1170 cm^{-1}. NMR 8.4-8.1 τ 6Hm, 7.60 τ 3Hs, 7.5-7.1 τ 3Hm, 3.21 τ 1Hs, 2.73 τ 2Hd J=9 cps, 2.47 τ 1Hs, 2.10 τ 2Hd J=9 cps.

Analysis: C 68.22% H 6.32% N 3.65% S 8.58%

$C_{21}H_{23}NSO_3$ requires C 68.28% H 6.28% N 3.79% S 8.66%

Reaction of (163) with acid

The tosylate (163) (137 mg) was dissolved in chloroform (5 ml) and dry HCl passed through the solution for five minutes. Very little change occurred during 2 hours at room temperature, so the reaction was continued at reflux temperature for 24 hours, resaturating the solution with dry HCl every two hours. The solution was then allowed to cool and was washed with sodium bicarbonate and water and separated by preparative TLC on Silica Gel plates eluting with benzene/acetone 10%. Four products were isolated: unreacted tosylate (163) (19 mg 12%), octahydroanthrone (157) (14 mg 20%), the lactam of 3-amino-2-γ-tetralylbutyric acid (164) (15 mg 17.5%). M.P. 191°C (ether). IR 3180, 1660, 1570 cm^{-1}.

Analysis: C 77.93% H 7.37% N 6.34%

$C_{14}H_{19}NO$ requires C 78.10% H 7.96% N 6.51%; and an unidentified amide (7.5 mg 8%). M.P. 192-4°C (ether). IR 3180, 1665, 1570 cm^{-1}.

Semmler Aromatisation of Oxime (151)

The oxime (151) (495 mg) dissolved in glacial acetic acid (20 ml) and acetic anhydride (5 ml) was heated on a steam bath for 1½ hours while dry HCl gas was bubbled through. The solution was poured onto ice and made alkaline with sodium bicarbonate. It was extracted with ether (4x) and washed with water (2x) before being separated on Silica Gel plates eluting first with benzene/petrol 10% and then benzene/acetone 10%. The least polar compound was 4,5-amino-4-methyl-1,2,3,4,-tetrahydrophenanthrene (165), an oil which darkened on standing but distilled under high vaccuum (85.1 mg, 19%). IR 3400, 1615, 1600, 1315 cm^{-1}. Mass spectrum M/e 209, 194, 181. NMR 8.50 τ 3Hs, 7.7-8.2 τ 4Hm; 7.2 τ 2Hm; 5.80 τ 1 H exch, 3.50 τ 1 H qu J=7, 2 cps; 2.5-3.0 τ 4Hm.

Analysis:	C 85.97%	H 8.97%	N 6.37%
$C_{15}H_{15}N$ requires	C 86.08%	H 7.22%	N 6.67%

The next product gave a fluorescent band on TLC and was identified as 4-methyl-5-keto-1,2,5,6,7,8-hexahydrophenanthrene (167) (45.2 mg 10½%). IR 1680 cm^{-1}. NMR 8.10 τ 3Hs, 7.7-8.1 τ 7.0-7.5 τ 10 Hm; 3.33 τ 1 H, tr; 3.00 2H AB qu J=8 cps. Distilled for analysis at 60 °C. 10^{-4} mm. giving a solid M.P. 42-44°C. Analysis C 84.60% H 7.48% $C_{15}H_{18}O$ requires C 84.87% H 7.60%. The next product was the amide (166), (6.5 mg 2%). The physical data are given below. The next

product was 6-acetyl-4-methyl-4,5-oxy-1,2,3,4,7,8-hexahydrophenanthrene (168) (13 mg 3%). M.P. 119.5-120.5°C (ether). IR 1675, 1550, 1250 cm^{-1}. Mass spectrum M/e 254, 239, 211. NMR 7.93 τ 3Ht J=7 cps, 7.64 τ 3Hs, 7.8-8.0 τ 7.1 7.6 τ 10 Hm, 2.91 τ 2H qu J=9 cps.

Analysis: C 80.30% H 7.29%

$C_{17}H_{18}O_2$ requires C 80.28% H 7.13%

The final product isolated was a very polar band which turned green but could be crystallised with difficulty from ether or petrol (52.5 mg 10%), N-acetoxy-4,5-amino-4-methyl-1,2,3,4,7,8-hexahydrophenanthrene (169). M.P. 98-100°C. IR 1730, 1640 wk, 1230, 1075, 1055, cm^{-1}. NMR 8.58 τ 3Hs, 7.80 τ 3Hs, 7.0-8.1 τ 10Hm, 3.88 τ 1Hqu, 3.03 τ 2Hs. Mass spectrum M/e 269, 226.

Analysis: C 75.67% H 7.15% N 5.09%

$C_{17}H_{19}NO_2$ requires C 75.81% H 7.11% N 5.20%

The oxime (151) (2 g) was dissolved in warm glacial acetic acid (40 ml) and acetic anhydride (8 ml) and dry HCl bubbled slowly through the heated solution for 2 hours. It was worked up as before giving amine (165) (34 mg 2%) and N-acetyl-4,5-amino-4-methyl-1,2,3,4-tetrahydrophenanthrene (166) (834 mg 22%). This was identical to the compound obtained by refluxing amine (165) in acetic anhydride over night. IR 1660 cm^{-1}. Nmr 8.32 τ 3Hs, 7.59 τ 3Hs, 6.8-8.2 τ 6Hm, 2.2-3.2 τ 5Hm. $UV\lambda_{max}^{EtOH}$ 237, 307 mμ.

4-hydroxy-4-methyl-5-oximinoacetate-1,2,3,4,5,6,7,8-octahydrophenanthrene (174)

The oxime (151) (1 g) was dissolved in dry pyridine (30 ml) and acetic anhydride (10 ml) and the solution stirred at room temperature for 15 hours. The solution was poured into water, extracted with ether and the ethereal solution was washed with water (6x). It was dried over sodium sulphate and evaporated to dryness and the acetate (174) (1.08 g) was recrystallised from ether. M.P. 106-7°C NMR 8.54 τ 3Hs; 7.79 τ 3Hs, 7-8.6 τ 18Hm; 3.81 τ 1H br exch, 2.98 τ 2Hd J=3 cps (qu?). IR 3400, 1765, 1615, 1200 cm^{-1}.

Analysis	C 70.94%	H 7.25%	N 4.90%
$C_{17}H_{21}NO_3$ requires	C 71.06%	H 7.37%	N 4.87%

4-methyl-5-oximinoacetate-1,2,5,6,7,8-hexahydrophenanthrene (175)

The oximino acetate (174) (1.1 g) was dissolved in dry pyridine (40 ml) and phosphorus oxychloride (10 ml) was added. The solution was stirred under nitrogen at room temperature for 5½ hours when TLC showed no more (174). It was poured into ice-water and extracted with ether (3x). The ether solution was washed with water (6x) and dried over sodium sulphate. 602 mg was obtained from which 197.5 mg (18%) (175) was isolated by preparative TLC on Silica Gel plates eluting first with benzene and then with benzene/acetone 2%. IR 1760, 1605, 1200 cm^{-1}. NMR 8.10 τ 3Hd J=1 cps; 7.87 τ 3Hs; 7-7.5 τ 10Hm; 4.10 τ 1Hm; 3.13 τ 2H d (qu?) J= 4 cps

5-methyl-4-oximinoacetate-1,2,3,4-tetrahydrophenanthrene (176)

The anhydro compound (175) (198 mg) and DDQ (200 mg) were heated in refluxing dry benzene (8 ml) under nitrogen and in the dark for 5½ hours. Chromatography on Silica Gel plates eluting with benzene/acetone 5% gave pure (176) (85 mg, 45%). M.P. 137-140°C (ethyl acetate). IR 1760, 1610, 1600, 1200 cm^{-1}. UV λ_{max}^{EtoH} 206 mμ (ϵ15,100), 217 mμ sh (ϵ19,600), 227 mμ (ϵ21,600), 243 mμ (ϵ18,500), 312 mμ (ϵ4,600), 336 mμ sh(ϵ2,700), NMR 7.79 τ 3Hs, 7.47 τ 3Hs, 7.6-8.2 τ 6.8-7.3 τ 6Hm; 2.12-2.85 τ 5Hm.

Analysis:	C 76.61%	H 6.26%	N 5.07%
$C_{18}H_{17}NO_2$ requires	C 76.38%	H 6.41%	N 5.24%

Semmler Reaction with (176)

The oximino acetate (176) (25 mg)in acetic anhydride (1 ml) and glacial acetic acid (3 ml) was heated on a steam bath for 30 minutes with dry HCl bub bling through the solution. It was poured into ether and made basic with sodium bicarbonate and the ether layer separated, washed and dried over sodium sulphate. The ether was removed in vacuo and the product (177) crystallised from ether in 80% yield (20 mg). M.P. 198-9°C. IR 3200, 1660, 1570 cm^{-1}. NMR 7.0-8.5 τ 6Hm; 7.08 τ 3Hs, 2.2-2.8 τ 5Hm. UV λ_{max}^{EtoH} 208 mμ sh(ϵ14,800), 233 mμ (ϵ39,600), 287 mμ sh(ϵ4,000), 298 mμ (ϵ4,560), 327 mμ (ϵ913). Mass spec. M/e 225, 170, 155, 154, 141.

Analysis:	C 79.78%	H 6.53%	N 6.22%
$C_{15}H_{15}O$ requires	C 79.97%	H 6.71%	N 6.22%

Beckmann Reaction with (176)

The oximino acetate (176) (12.7 mg) was stirred in polyphosphoric acid (2 ml) at 130°C for 10 minutes. It was poured into water and extracted with chloroform. The organic layer was separated, washed with sodium bicarbonate and water, and evaporated to dryness. The product was identical to lactam (177) in its MP, R_f, IR, UV. A minor product was an acetyl derivative of (177). IR 3200, 1670, 1570 cm^{-1}. M.P. 250°C. Mass spectrum 267, 252, 212.

Reaction of (176) with acetyl bromide

The oximino acetate (176) (29 mg) was refluxed in acetyl bromide (2 ml) and a drop of ethanol for 2½ hours. The solution was poured into water, extracted with ether, washed, dried and chromatographed. A small amount of lactam (177) was isolated. The major product (8.4 mg) (179) was identical to the compound obtained when lactam (177) was acetylated in refluxing acetic anhydride. M.P. 96-8°C (petrol). IR 1700, 1220 cm^{-1}. Mass spectrum 267, 249, 225, 180, 170 (base peak).

4-methyl-5-oximino-1,2,5,6,7,8-hexahydrophenanthrene (173)

The anhydro ketone (167) (49 mg) was oximinated with excess hydroxylamine hydrochloride in refluxing dry pyridine for three hours. It was poured into water and ether, washed with water (2x), dilute sulphuric acid, water (4x) and dried. The product (173) (16 mg) was crystallised from ethyl acetate. M.P. 205-7°C. IR 3250, 1630 wk. cm^{-1}.

Analysis: C 79.4% H 7.51% N 6.13%

$C_{15}H_{16}NO$ requires C 79.26% H 7.54% N 6.16%

Semmler Reaction with (173)

The oxime (173) (19 mg) in glacial acetic acid (3 ml) and acetic anhydride (1 ml) was heated on a steam bath for 30 minutes with dry HCl bubbling through the solution. This reaction was worked up in the usual way and the major product isolated by TLC was benz(cd)indoline (165).

Hydrogenolysis of 4-methyl-4,5-amino-1,2,3,4,-tetrahydrophenanthrene (165)

The amine (165) (60 mg) was hydrogenated in glacial acetic acid (10 ml) over 5% Pd/C (60 mg) at room temperature and atmospheric pressure. 1.7 mole equivalents (10.4 ml) of hydrogen was taken up. The catalyst was filtered off and the solution diluted with water and made basic with sodium bicarbonate. It was extracted with ether (2x) and the ether extract was washed with water, dried and evaporated. The polar product (30.3 mg) was purified by preparative TLC on Silica Gel eluting with benzene/acetone 5% and was identified as 4-methyl-5-amino-1,2,3,4,5,6,7,8-octahydrophenanthrene (179). IR 3350, 3250, 1615 cm^{-1}. NMR 8.48 γ 3Hs; 7-8.5 γ m; 6.27 γ 2H exch; 5.65 γ 1Hm, 3.10 γ 2Hs. It was converted to the crystalline amine hydrochloride M.P. 213-215°C (acetone) with ethereal HCl.

4,5-acetamido-4-methyl-3,4-dihydrophenanthrene (181)

4,5-acetamido-4-methyl-,2,3,4-tetrahydrophenanthrene (166) (720 mg) and DDQ (2.17 g) in dry benzene (200 ml) was refluxed under nitrogen in the absence of light for 28 hours. The solution was cooled and diluted with ether (approx 1 l.) and the solution was washed with aqueous sodium dithionite (3x), dilute sodium hydroxide (3x), water (5x). It was dried over sodium sulphate and evaporated to dryness giving 401 mg (56%) (181). The reaction could not be followed by TLC because both product and starting material have the same R_f even on silver nitrate impregnated plates. In the UV the product (181) has peaks at 263, 271, 335 mμ and the UV of the reaction product isolated showed that the oxidation was incomplete. Neither benzoic acid nor tosyl acid catalysed the reaction. A longer reaction time gave a lower yield, presumably due to decomposition. IR 1660, 1575, 1085 cm^{-1}. NMR 8.30 γ CH_3s, 7.52 γ CH_3s, 7.9γ CH_2m; 3-3.5 γ olefinic protons; 2.3-2.8γ aromatic protons.

4-methyl-5-acetamido-phenanthrene (182)

The crude dihydrophenanthrene (181) (400 mg) in t-butanol (50 ml) was stirred with potassium t-butoxide (1.5 g) under nitrogen at room temperature for 24 hours. In refluxing t-butanol the reaction was completed within half an hour. The solvent was evaporated in vacuo and ether and water added. The ether layer was washed, dried and concentrated and the product (182) (118 mg, 30%) isolated by

preparative TLC on Silica Gel eluting with benzene/acetone 10%. M.P. 189-191°C (carbon tetrachloride or diisopropyl ether). IR 3280, 1660, 1540 cm^{-1}. NMR 7.82γ 3Hs; 7.42γ 3Hs, 2.3-2.6γ 8Hm; 1.5γ 1H br. UV λ_{max}^{EtOH} 220 mμ (ε 30,000), 263 mμ (ε 32,200), 284 mμ (ε 18,000), 303 mμ sh(ε 9,300), 313 mμ sh(ε 8,200) Mass spectrum M/e 249, 206.

Analysis:	C 82.10%	H 6.02%	N 5.54%
$C_{17}H_{15}NO$ requires	C 81.90%	H 6.06%	N 5.62%

A less polar product was isolated (19 mg) which had IR 3400, 1620, 1600 cm^{-1} and may be 4,5-amino-4-methyl-3,4-dihydrophenanthrene.

4-methyl-5-amino-phenanthrene (153)

The amide (182) (118 mg) was refluxed in dry methanolic HCl for 20 hours. Methanol was evaporated in vacuo and ether and aqueous sodium bicarbonate were added. The ether solution was separated and washed with water and dried. The ether was stripped giving the solid amine (153) (77 mg, 79%) which was crystallised from petrol. IR 3450, 3370, 1615 cm^{-1}. M.P. 107-9°C. An analytical sample was sublimed at 90°C 0.1 mm. C 87.3% H 6.4% N 6.3% $C_{15}H_{13}N$ requires C 86.92% H 6.32% N 6.76%.

Attempted conversion of (153) to 4-methyl-5-azidophenanthrene (154)

To the amine (75 mg) in glacial acetic acid (4 ml) and conc. sulphuric acid (1 ml), sodium nitrite (34 mg) was added and the solution stirred at 0°C for 15 minutes. Urea was added and after ten minutes excess sodium azide was also added. After two hours at

0°C ether and water were added, the ether layer was separated and washed with sodium bicarbonate(3x) and water (3x). It was dried and concentrated and separated on Silica Gel plates eluting with benzene/petrol 1:1. No azide was present in the mixture. The major product (34 mg, 50%) was phenanthrene-4,5-methane (134) which was recrystallised from ethanol M.P. 115-117°C. NMR 5.71 τ 2Hs, 2.1-2.4 τ 8Hm.

2-azidobiphenyl (126)

Tosyl azide was prepared in 65% yield by the reported procedure[91].

2-aminobiphenyl (1.715 g) was added to one equivalent of methyl magnesium iodide (prepared from 245 mg Mg and 1.53 g MeI) in dry ether (50 ml) and stirred at 0°C under nitrogen for 3½ hours. TLC showed that not all the amine had reacted yet. Tosyl azide (1.893 g) was added and the precipitate that had formed rapidly dissolved. After thirty minutes, the ether solution was washed with water, 2N sulphuric acid and water, dried and concentrated. The mixture was separated on a Grade 3 Alumina column (200 g) eluting with benzene/petrol 1:2. Tosyl azide was recovered (0.613 g) and 2-azidobiphenyl was isolated (0.56 g 41%). IR 2150 cm^{-1}.

Attempted diazo-transfer to 4-methyl-5-aminophenanthrene (153)

The amine (11 mg) and one equivalent of methyl magnesium iodide were stirred in dry ether (10 ml) at room temperature under nitrogen. After 3 hours TLC showed no change and a large excess of Grignard reagent was added. After 20 hours TLC still showed that there was

unreacted amine (153). Tosyl azide was added but after one hour TLC (Silica Gel plates eluted with benzene/petrol 1:1) showed only tosyl azide and amine (153) and no new products.

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