THE CHEMISTRY OF 4a*H*-CARBAZOLES

A thesis submitted by

JANUSZ JOZEF KULAGOWSKI

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Hofmann Laboratory,
Department of Chemistry,
Imperial College of Science and Technology,
London, SW7 2AY.

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To my parents, with love.

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J.J. Kulagowski

1983

ABBREVIATIONS

AIBN	2,2'-Azobis(2-methylpropionitrile)
BSA	Benzeneseleninic anhydride
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethylsulphoxide
$Eu(fod)_3$	Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium
FVP	Flash vacuum pyrolysis
g.l.c.	Gas liquid chromatography
HMPA	Hexamethylphosphoramide
h.p.l.c.	High pressure liquid chromatography
i.r.	Infra red
LDA	Lithium diisopropylamide
mCPBA	*meta*-Chloroperbenzoic acid
MTPI	Methyltriphenoxyphosphonium iodide
NBS	*N*-Bromosuccinimide
n.m.r.	Nuclear magnetic resonance
p.l.c.	Preparative liquid chromatography
PTAD	4-Phenyl-1,2,4-triazoline-3,5-dione
THF	Tetrahydrofuran
t.l.c.	Thin layer chromatography
u.v.	Ultraviolet

ABSTRACT

The intermediacy of heterocyclic 3a*H*-indene analogues in various cyclisation reactions is reviewed, and their ultimate fate discussed where appropriate.

Several 1-arylbenzotriazoles have been prepared, in which both *ortho* positions of the 1-aryl group are substituted. On thermolysis and photolysis these give carbazoles and cyclopentaquinolines respectively. Both types of products are consistent with the intermediacy of 4a*H*-carbazoles, the former arising by sigmatropic migrations of the 4a*H*-carbazole bridgehead substituent, whilst formation of the latter is believed to involve an aza-di-π-methane rearrangement. Although simple 4a*H*-carbazoles cannot be intercepted under these conditions, a stable benzo-fused derivative was isolated on photolysis of 1-(2-methylnaphthyl)benzotriazole. In addition to giving the 4a*H*-carbazole, this benzotriazole also underwent a novel six to eight ring expansion to afford a cycloocta[*def*]carbazole.

The enhancement of stability in these species by benzannelation is further demonstrated by the independent synthesis of two benzo-fused 4a*H*-carbazoles. Both are readily isolable and undergo analogous reactions on photolysis and thermolysis to the proposed intermediates in the decomposition of benzotriazoles.

A number of synthetic approaches directed at simple 4a*H*-carbazoles are described, and although none of these were ultimately successful, evidence exists for the generation of a 4a*H*-carbazole derivative in solution as an enolate ion.

The behaviour of 4a*H*-carbazoles is compared to that of their carbocyclic counterparts, 4a*H*-fluorenes. The validity of the di-π-methane mechanism in the photochemical rearrangement of these species is discussed. Model experiments designed to test this mechanism gave inconclusive results, and such a process remains supported only by circumstantial evidence.

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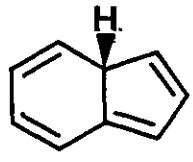
PART I. INTRODUCTION

1. HETEROCYCLIC 3a*H*-INDENE ANALOGUES.

Carbocyclic and heterocyclic derivatives of 3a*H*-indene (1) have both appeared in the literature many times in recent years but the majority of reports deal only with the transient existence of these species as reactive intermediates. Several carbocyclic examples of



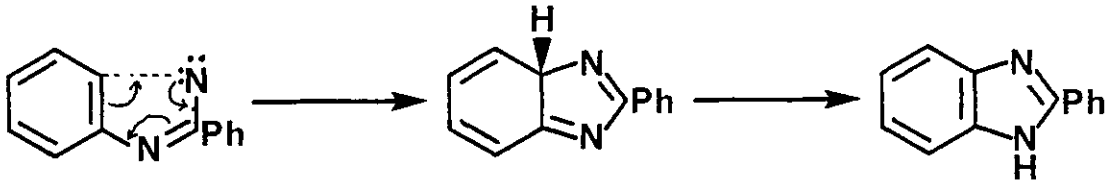
(1)

such systems have been extensively studied and, in general, their properties were found to parallel closely those of heterocyclic analogues, with which this Introduction will be concerned.

The reactions in which heterocyclic 3a*H*-indenes have been proposed as intermediates or, in a few cases, from which they can be isolated, may be considered in three categories: those involving nitrenes, those involving carbenes, and various miscellaneous reactions.

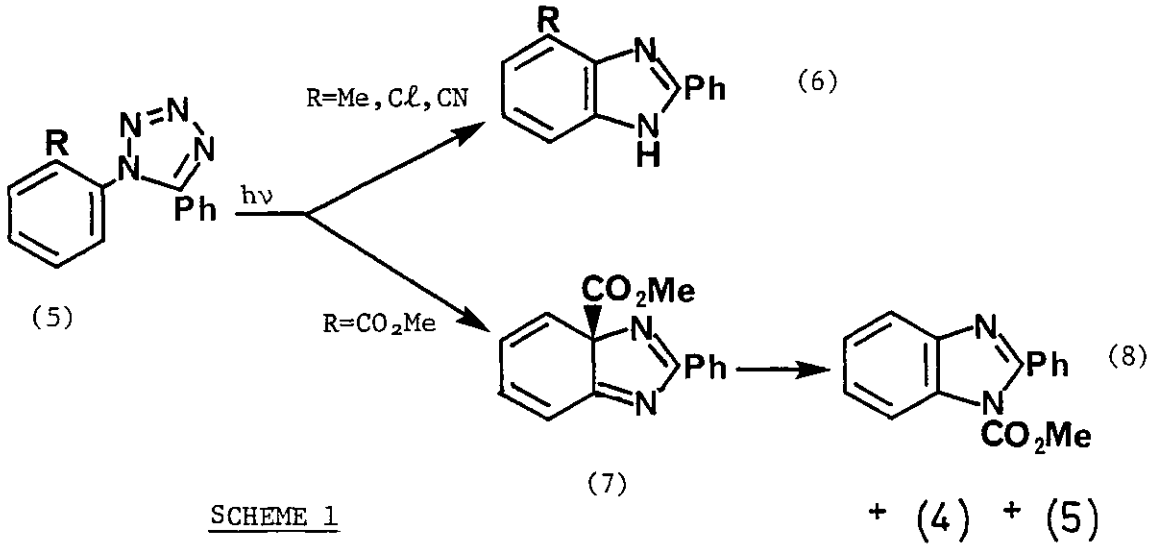
1.1. From Nitrenes.

The generation of imidoyl nitrene (2) by a variety of methods has been found to give the benzimidazole (4).[1-7] The reaction is believed to proceed *via* an electrocyclic ring closure of the nitrene to give a 3a*H*-benzimidazole (3), which then undergoes a [1,5] bridgehead hydrogen migration, affording the observed product.[1]



(2) (3) (4)

Where one of the *ortho* positions of the *N*-aryl group is substituted by a methyl, chloro, or cyano group, cyclisation occurs exclusively to the other, unoccupied *ortho* position.[2,8] However, when the substituent is an ester group, cyclisation occurs at both positions to the same extent (Scheme 1).[8] The isolation of 1-methoxycarbonyl-2-phenylbenzimidazole (8) is consistent with collapse of the nitrene, formed by



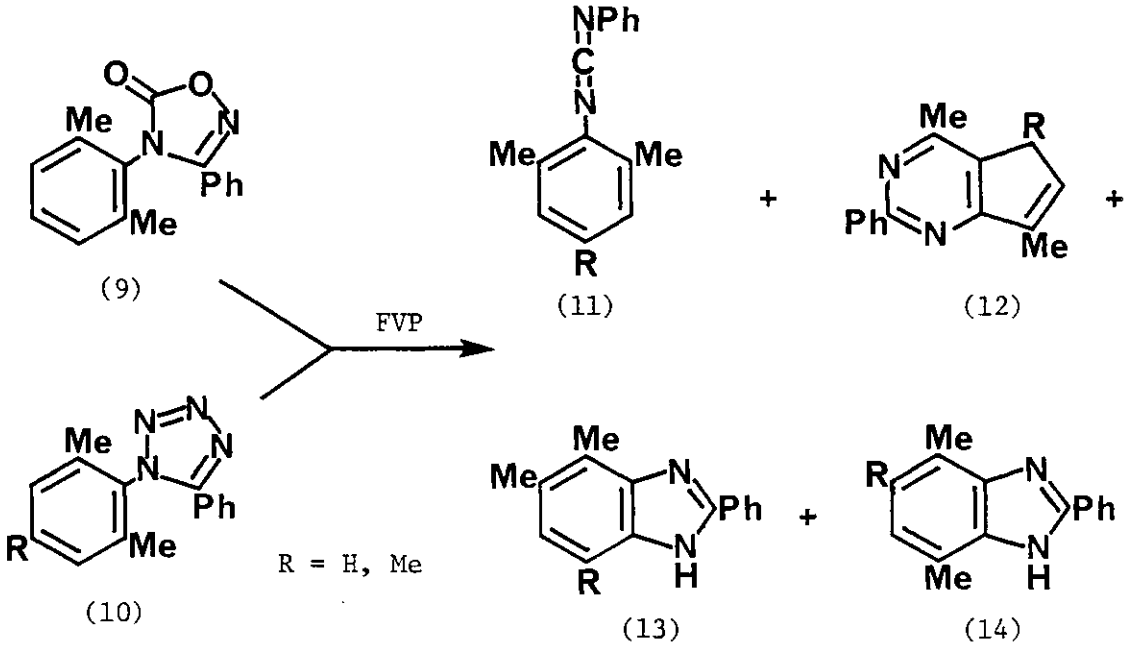
(5) (6) (7) (8)

SCHEME 1

photolysis of the tetrazole (5; R = CO_2Me), onto the substituted position, followed by a [1,5] migration of the bridgehead substituent in the

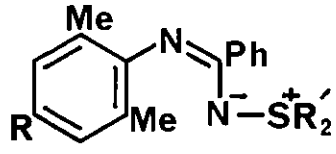
resulting 3a*H*-benzimidazole (7). Ester groups are known to have a high migratory aptitude,[9] and it is therefore not surprising that the intermediate (7) could not be isolated. The presence of benzimidazole (4) as a reaction product was attributed to loss of the substituent from (8) by hydrolysis on work up. The origin of this curious directing effect of the ester group is unclear and a satisfactory explanation has yet to be provided.

In an attempt to gain more evidence for the intermediacy of 3a*H*-benzimidazoles in this reaction, Rees and co-workers subjected the oxadiazolone (9) and the tetrazoles (10), in which both *ortho* positions carry alkyl substituents, to FVP.[10] The products isolated included the carbodiimides (11), the cyclopentapyrimidines (12), and the two benzimidazoles (13) and (14) (Scheme 2). The carbodiimides (11) and the



SCHEME 2

pyrimidines (12) were also obtained on photolysis of the tetrazoles (10) and the sulphimides (15).



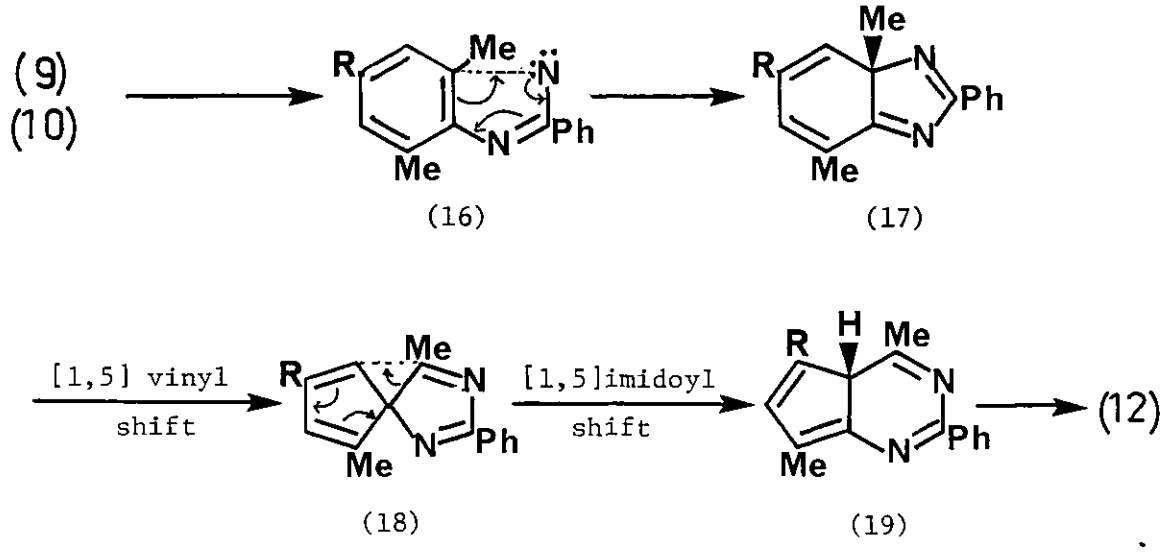
R = H, Me

R'= Me, Ph

(15)

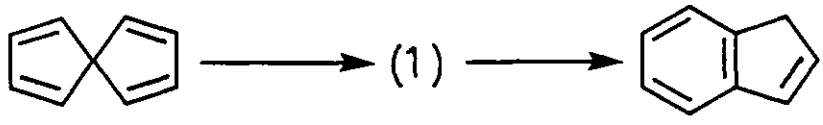
The presence of carbodiimides was expected by analogy to the behaviour of diaryl tetrazoles lacking *ortho* substituents under similar conditions. These give carbodiimides as major products on thermolysis.[4,11]

The authors suggest that formation of the other products could be rationalised by the involvement of a 3a*H*-benzimidazole (17) produced by cyclisation of the nitrene (16). The spiro intermediate (18), readily available by a [1,5] vinyl bond migration in the 3a*H*-benzimidazole (17), can itself undergo an imidoyl bond migration to give an isomeric 3a*H*-



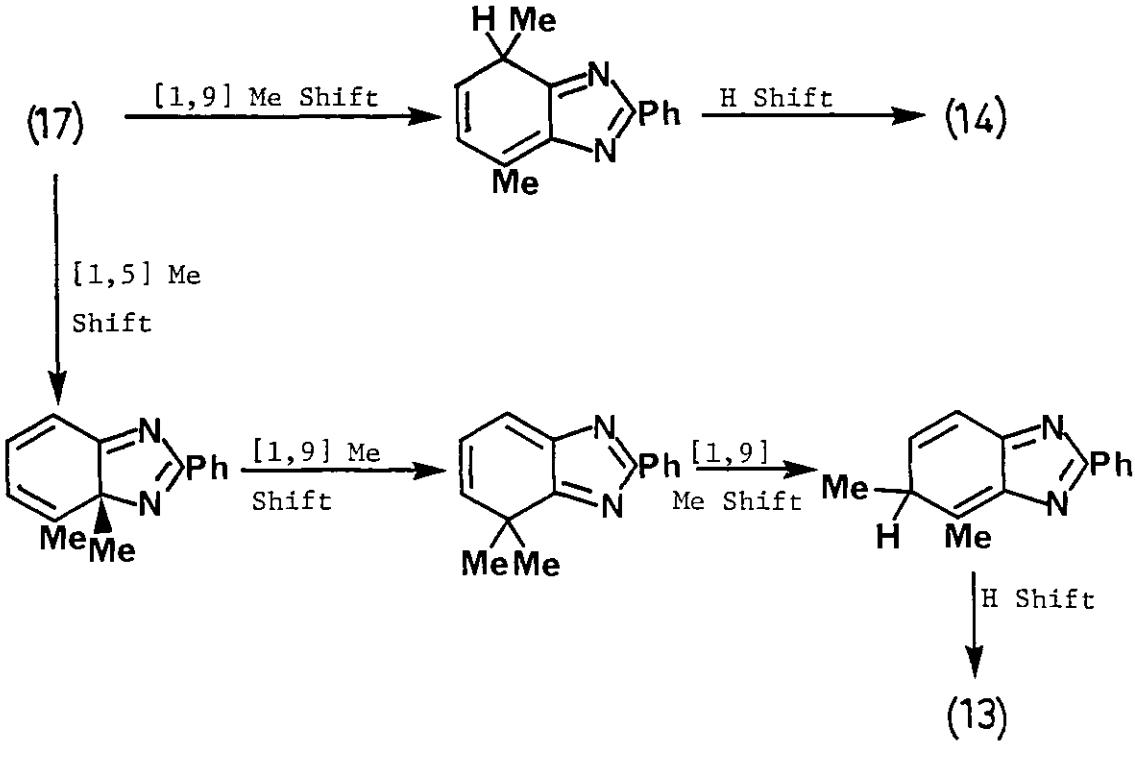
SCHEME 3

indene analogue (19). Rapid aromatisation by hydrogen migration would then afford the observed pyrimidines (12) (Scheme 3). Good precedent for such a mechanism can be found in the rearrangement of spirononatetraene (20) to 3a*H*-indene (1), a process for which the activation energy is reported to be particularly low.[12]



(20)

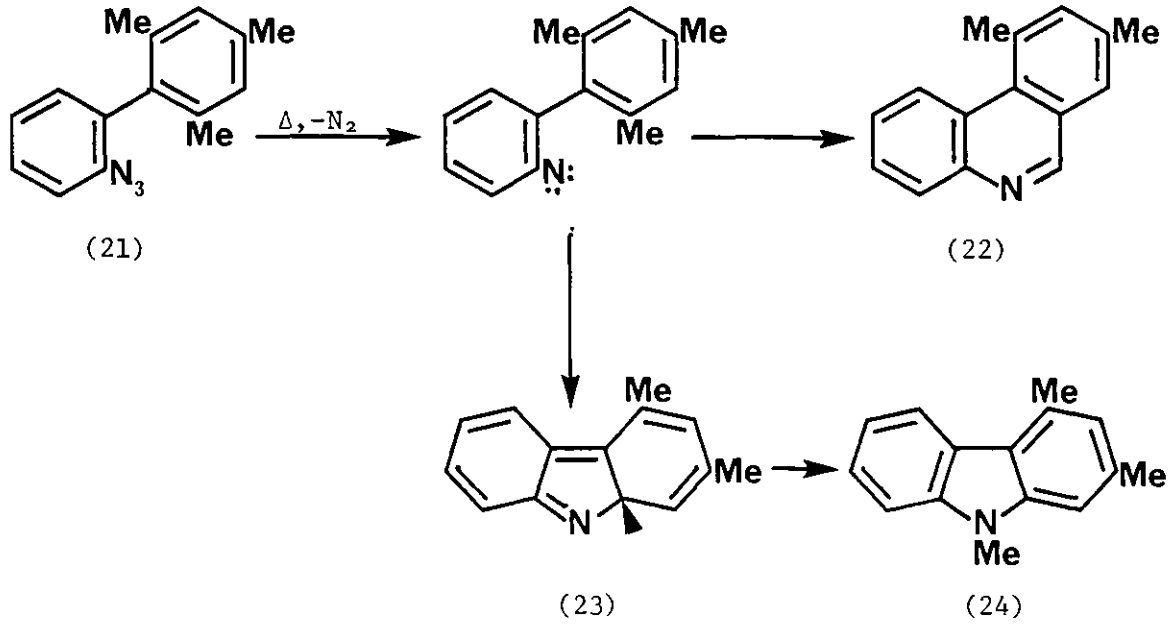
A similar sequence of sigmatropic migrations of the bridgehead methyl group was postulated to account for the formation of the benzimidazoles (13) and (14) (Scheme 4).



SCHEME 4

Although vinyl shifts are known to occur with greater facility than the corresponding alkyl migrations,[9] the presence of products derived from both pathways is thought to be attributable to a minimisation of the difference in rate of the two processes. It is also interesting to note that the benzimidazoles (13) and (14) were not obtained from any of the photolyses, implying that their formation is a purely thermal process (Scheme 4).

Cyclisation onto substituted positions has also been observed for nitrenes derived from azides. Thus, thermolysis of 2-azido-2',4',6'-trimethylbiphenyl (21) was shown by Smolinsky [13] to afford small quantities of the carbazole (24), accompanied by the nitrene insertion product, 8,10-dimethylphenanthridine (22) (Scheme 5).

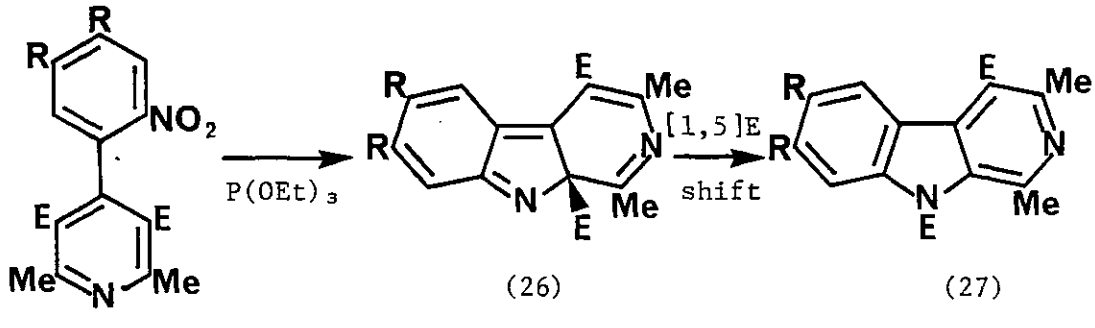


(21) (22) (23) (24)

SCHEME 5

The former product is believed to arise by a [1,5] methyl migration onto nitrogen in the intermediate 8a*H*-carbazole (23). This contrasts the behaviour of the benzimidazole (17), from which no product derived by migration of a methyl group onto nitrogen could be detected. The cyclisation of biphenyl nitrenes has been extensively studied by a number of groups,[14] in order to elucidate the mechanism involved. Meth-Cohn and co-workers[15] have recently concluded that a triplet nitrene is responsible for the products due to insertion, *e.g.*, (22), whereas cyclisation to the 8a*H*-carbazole, *e.g.*, (23) involves a singlet species.

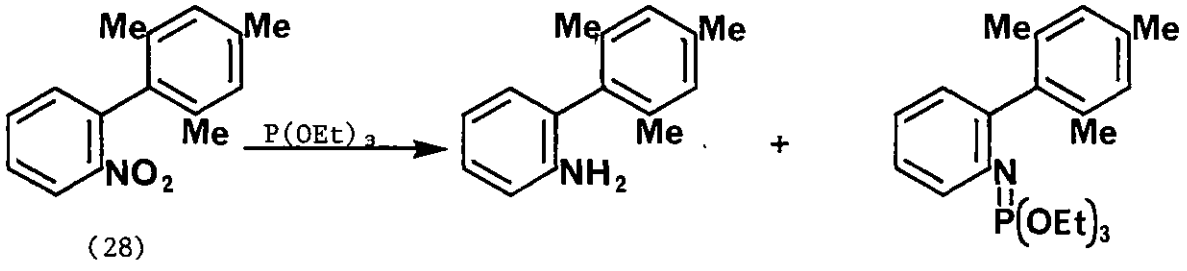
The nitrene-like species derived from nitro compounds on reduction with tervalent phosphorus reagents have been reported to behave similarly. Hence treatment of the biaryl (25) with triethyl phosphite gave the carboline (27), *via* an analogous cyclisation of the reactive species, with subsequent migration in the resultant 8a*H*-carboline (26).[16]



(25) (26) (27)

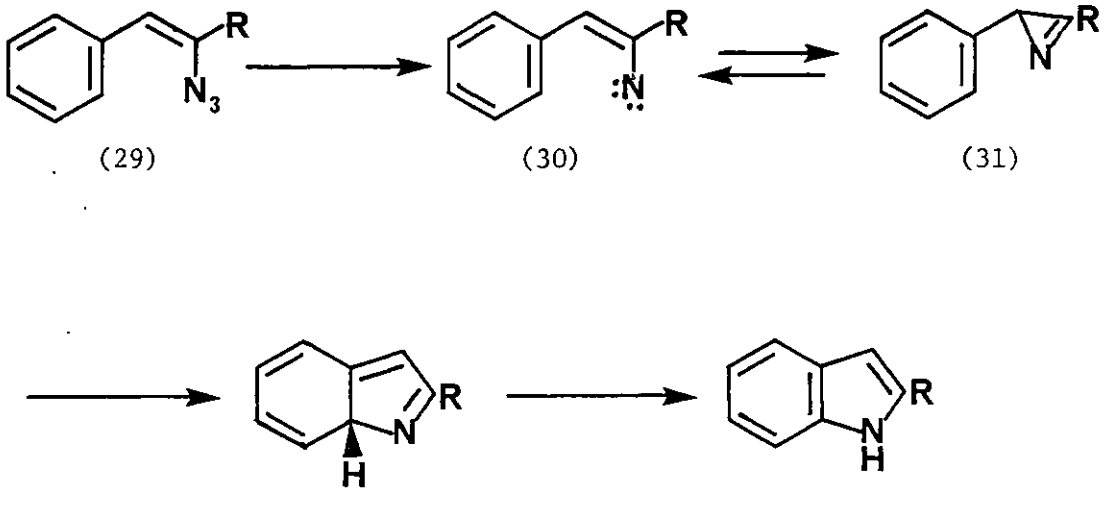
E = CO_2Me

It is interesting to compare this result with Cadogan's observation that similar treatment of an alkyl substituted nitrobiphenyl (28) does not lead to any cyclisation products.[17] The former case may be another example of the previously encountered directing effect of *ortho* ester groups in nitrene cyclisations (Scheme 1).



(28)

The formation of azirines in the thermal or photochemical decomposition of vinyl azides is a well known process.[18] In the case of styryl azides (29), thermolysis has been reported to give indoles by cyclisation of the nitrene (30), which exists in equilibrium with the phenyl azirine (31).[19] Rapid aromatisation of the initially formed 7a*H*-indole (32) leads to the observed product.



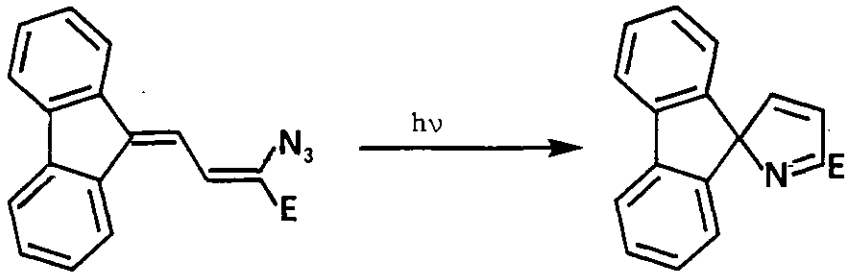
(29) (30) (31)

(32)

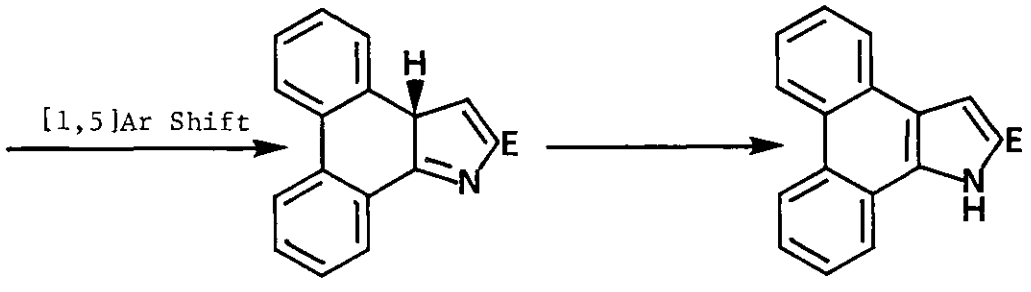
R = Me, Ph, CO_2Et

Unfortunately, this reaction is not amenable to investigation using 'blocking' groups in the *ortho* positions. In the presence of *ortho* alkyl groups the reaction is diverted, giving only dihydroisoquinolines; the products of nitrene insertion.[20]

Photolysis of conjugated dienyl azides gives 2*H*-pyrroles, which usually isomerise to the 1*H* derivatives under the conditions employed. However, the highly substituted 2*H*-pyrrole (34) is readily isolable from low temperature photolysis of the fluorene (33).[21] On heating, a [1,5] phenyl shift affords the benzo fused 3a*H*-indole (35), which is not isolable and rapidly aromatises.



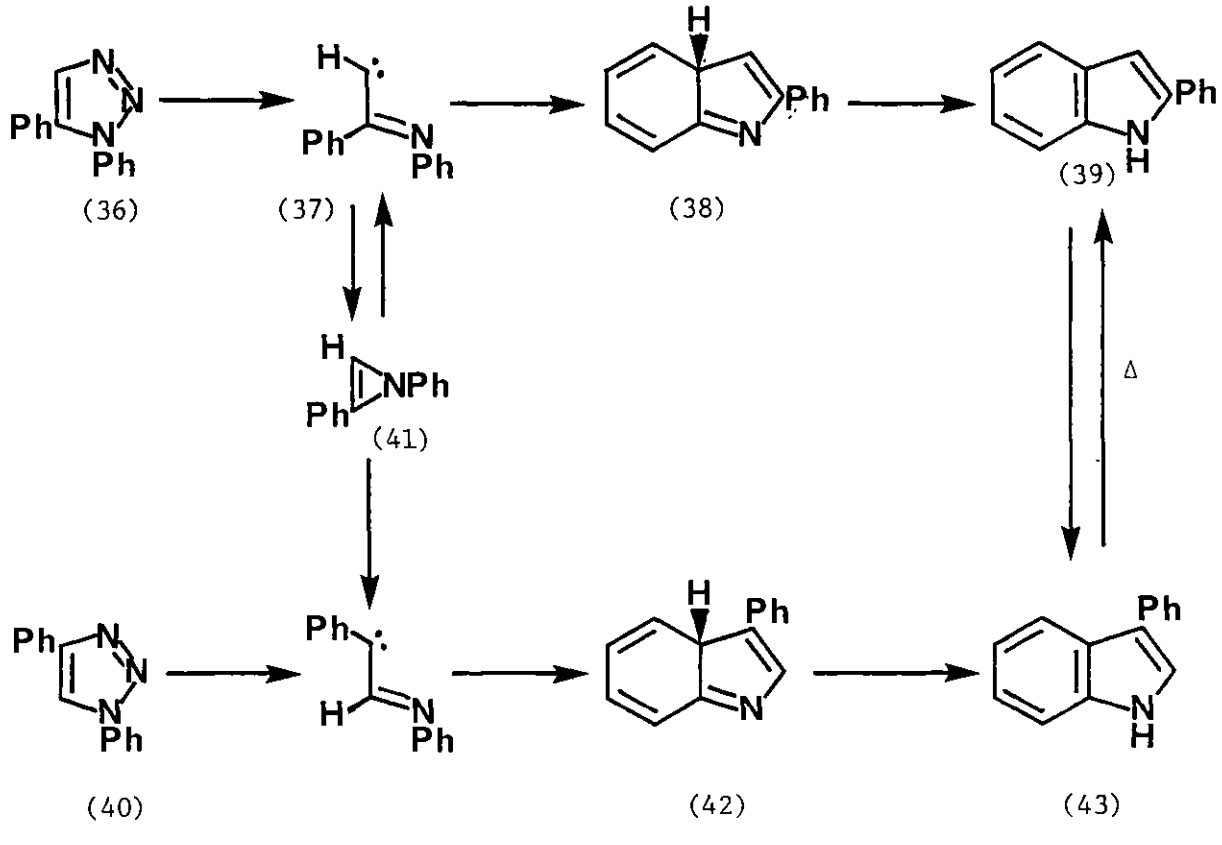
(33) (34)



(35)

1.2. From Carbenes.

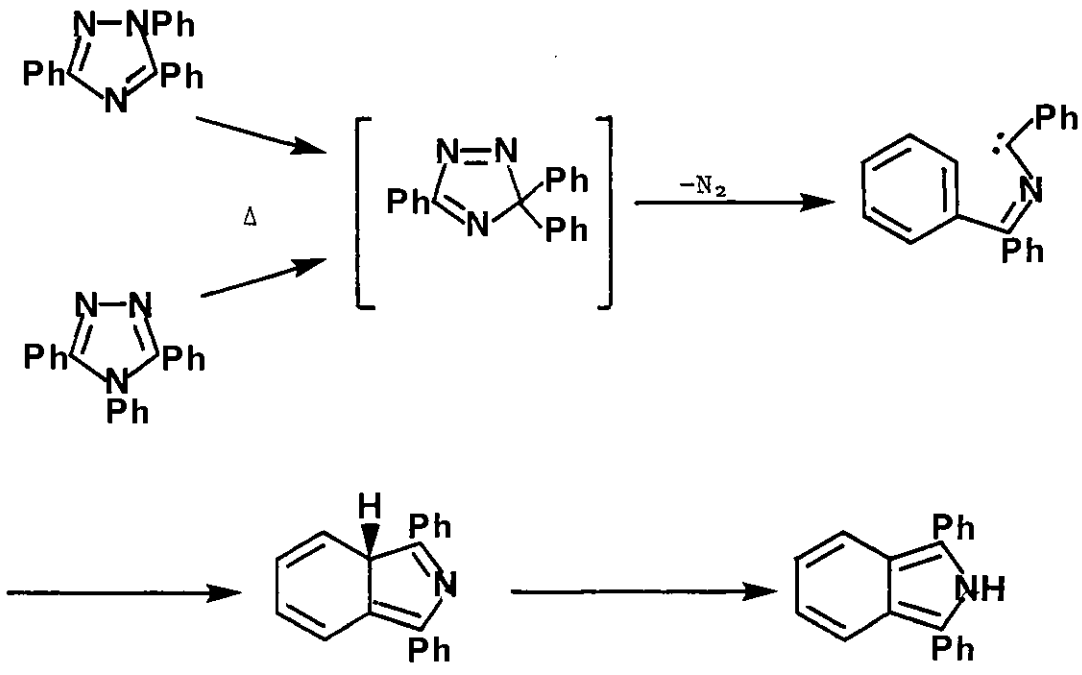
The reactions, as well as the methods of generation of many carbenes, closely resemble those of the corresponding nitrenes. Thus, thermal extrusion of nitrogen from the triazole (36) leads to the generation of the imidoyl carbene (37), a species analogous to the imidoyl nitrene (2). Cyclisation of the carbene gives 2-phenylindole (39), corresponding to the benzimidazole (3), together with 3-phenylindole (43). The same products are obtained by thermolysis of the isomeric 1,4-diphenyl-1,2,3-triazole (40).[22] The intermediacy of the azirine (41) is believed to be responsible for scrambling of the phenyl substituents, although the two indoles (39) and (43) have been shown to be thermally interconvertible; 3a*H*-indene analogues (38) and (42) are probable intermediates (Scheme 6).



SCHEME 6

Photolytic fragmentation of diaryl triazoles likewise gives similar results.[23]

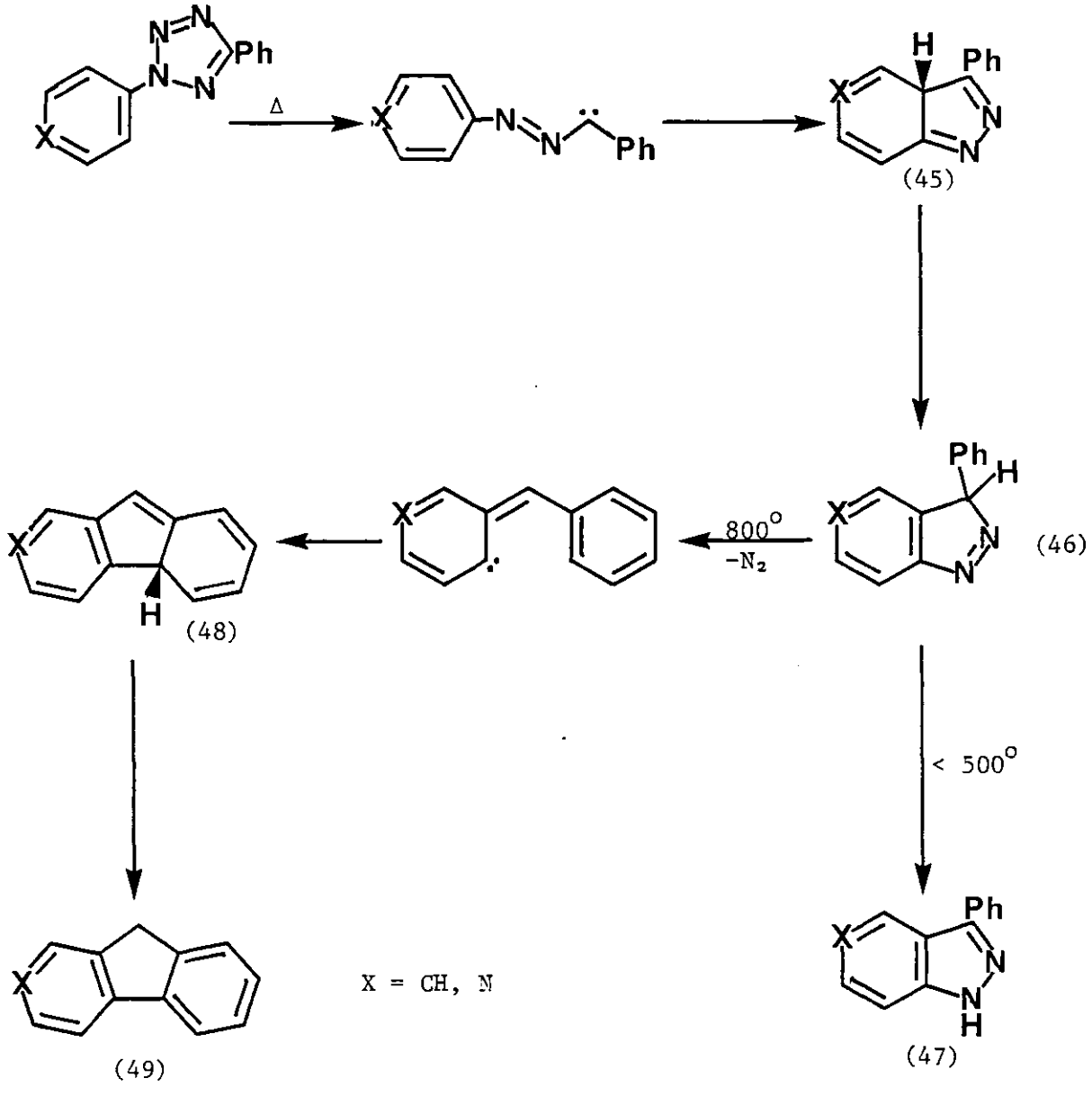
An analogous extrusion reaction involving 3a*H*-isoindoles (44) as likely intermediates has also been reported (Scheme 7).[24]



(44)

SCHEME 7

A synthetically useful route to 3-arylindazoles (47) also proceeds by carbene cyclisation (Scheme 8).[25] Evidence in support of the 3*H*-indazole (46) and hence indirectly of the 3a*H*-indazole (45) is provided by the fact that fluorene (49) is obtained if the pyrolysis is performed at elevated temperatures. Loss of nitrogen from the 3*H*-isomer affords a second carbene which also cyclises to a 3a*H*-indene analogue (48).

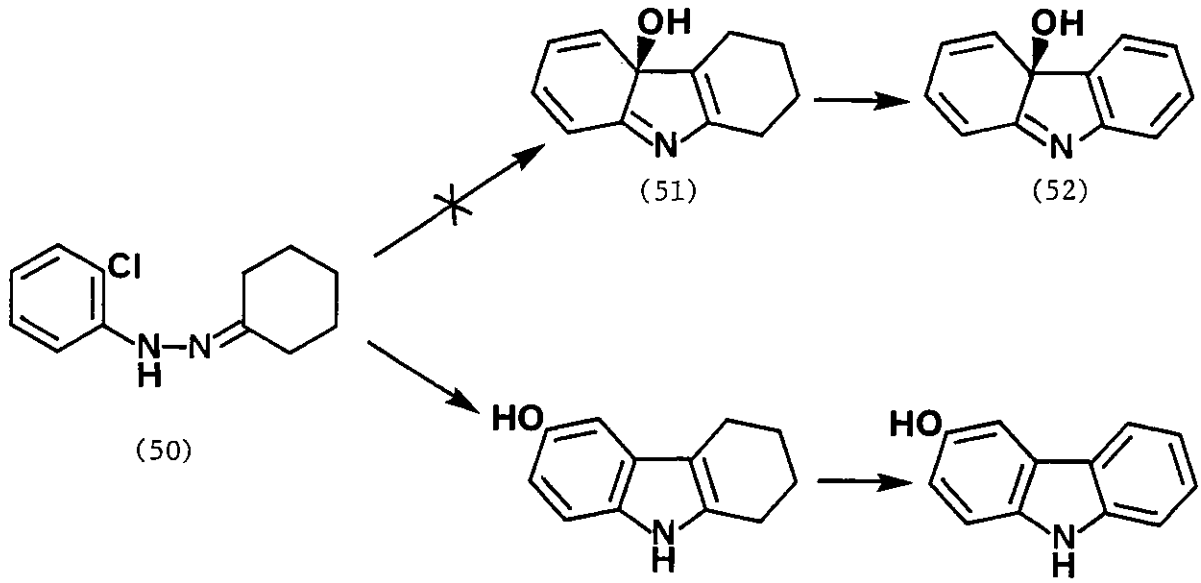


SCHEME 8

The Graebe-Ullmann synthesis of carbazoles by decomposition of 1-arylbenzotriazoles probably also proceeds through an analogous 4a*H*-carbazole. This reaction will be considered in greater detail in the Discussion.

1.3. From Miscellaneous Reactions.

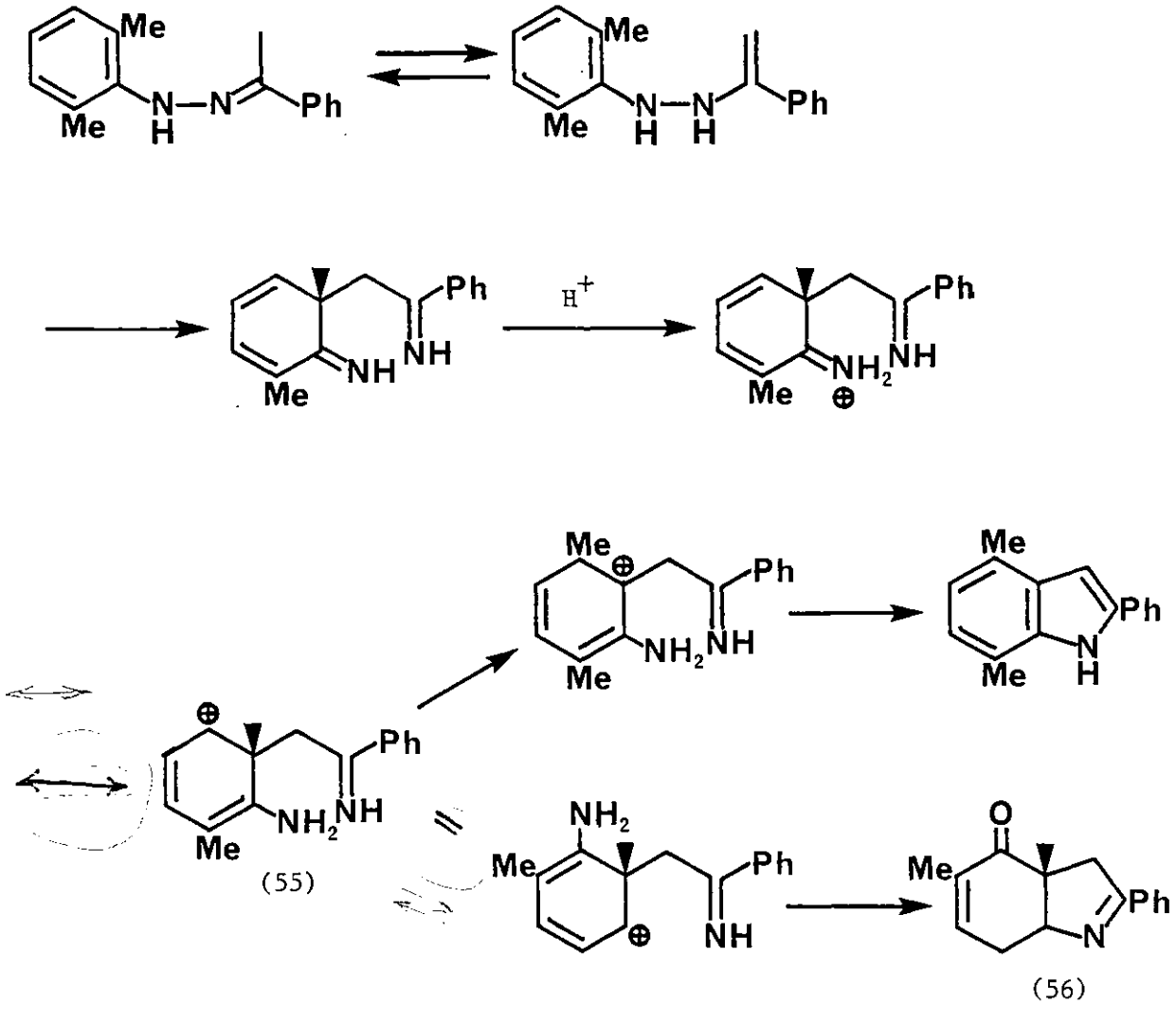
The compound (51) obtained by Robinson and Pausacker[26,27] from a Fischer indole reaction of an *ortho* substituted phenylhydrazone (50), and its subsequent dehydrogenation product (52) would be of great interest as the first examples of 3a*H*-indene analogues to appear in the literature.



(50) (51) (52) (53) (54)

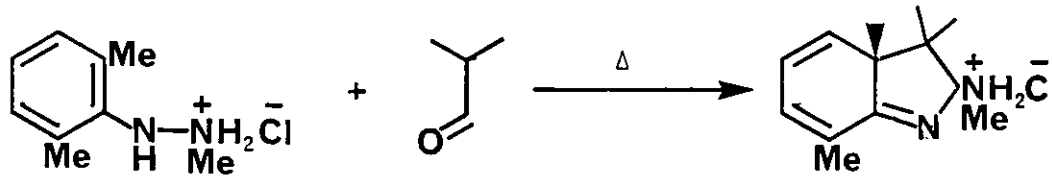
However, these products were incorrectly assigned, and were later shown to be the indole (53), in which the substituent originally in the *ortho* position had undergone hydrolysis and migration, and its dehydrogenation product, the corresponding carbazole (54).[28] Phenylhydrazones having methyl[29] and methoxy[30] groups in the *ortho* positions have also been shown to undergo substituent migrations on similar cyclisation. These migrations differ from those of substituents in 3a*H*-indene systems previously described, in that they involve carbonium ions and are believed to proceed *via* a series of [1,2] shifts.[31] The isolation of the enone

(56), probably formed through the carbonium ion (55), from one such reaction (Scheme 8)[32] has led to the suggestion that migration occurs prior to cyclisation,[33] thereby precluding the need to postulate 3a*H*-indoles as intermediates. However, products obtained from Fischer



SCHEME 8

cyclisation of some highly substituted phenylhydrazones can only be satisfactorily explained by the involvement of 3a*H*-indoles.[34] Furthermore, the diene imine (57), in which cyclisation had obviously occurred without substituent migration has been isolated from the reaction shown.[35]

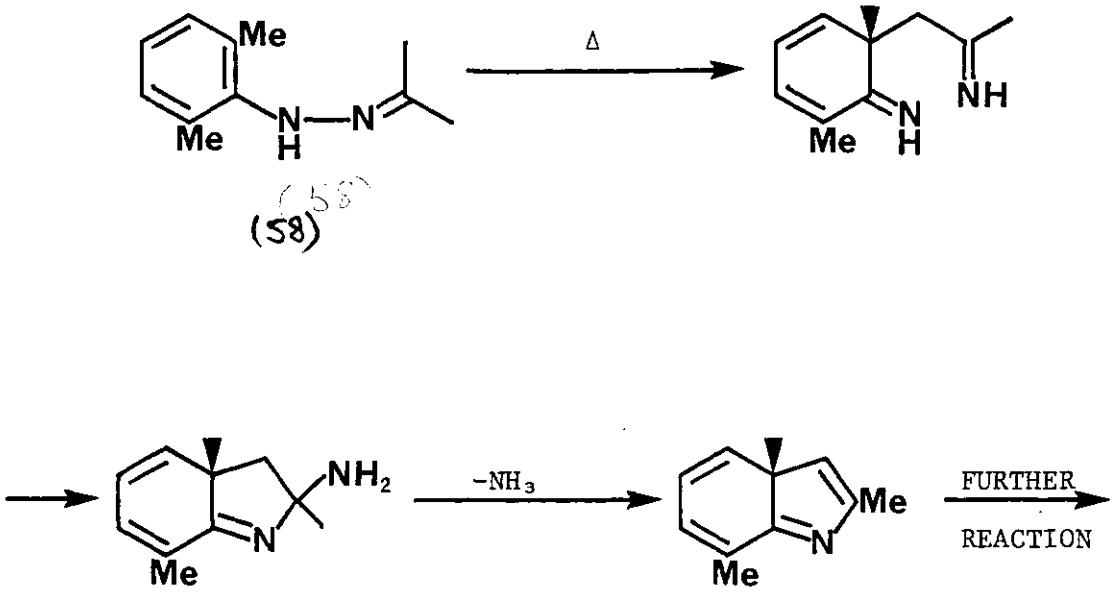


(57)

From the information available, it therefore seems that the involvement of 3a*H*-indoles in the Fischer reaction of '*ortho*-blocked' phenylhydrazones may be dependent on the structure of the substrate and perhaps also on the reaction conditions.

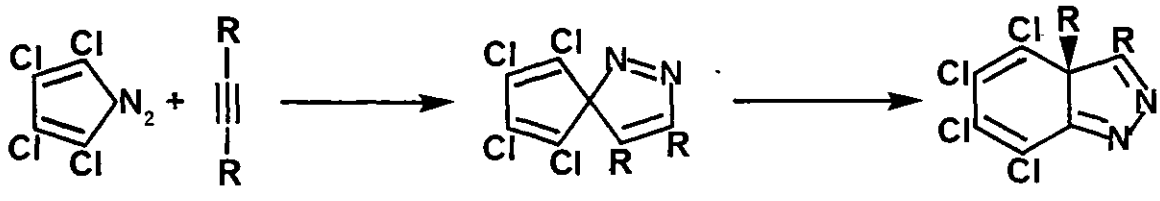
An intriguing possibility, hitherto unreported, exists of performing a thermally-induced cyclisation of an *ortho* substituted phenylhydrazone, *e.g.*, (58). Although acid catalysts do facilitate the Fischer reaction, their presence is not necessary,[33,36] and absence of acid in the purely thermal reaction would suppress carbonium ion induced migrations. If 3a*H*-indoles do participate in the reaction, the products obtained may be anticipated to be those resulting from thermally allowed [1,5] or higher migrations of the bridgehead substitutent (Scheme 9).

An example of an isolable 3a*H*-indene analogue is provided by the highly substituted indazole (61). Addition of an acetylene to tetrachlorodiazocyclopentadiene (59) affords a spiro intermediate (60) which



SCHEME 9

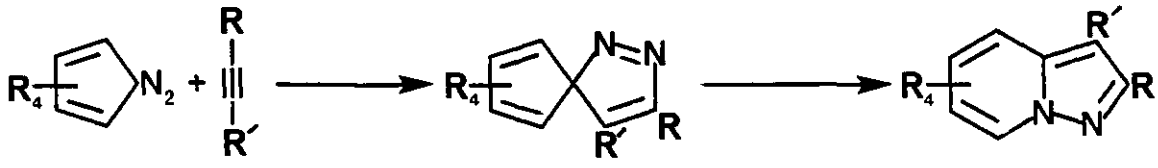
spontaneously rearranges to the indazole (61).[37,38] In view of the propensity of ester groups to migrate, the stability of the indazole



(59) (60) (61)

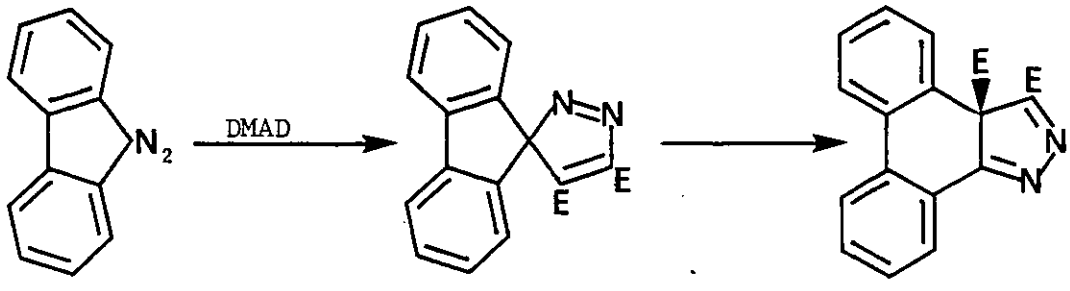
R = CO_2Me, COPh

(61) is somewhat surprising. The substituents on the cyclopentadiene (59) appear to play an important part in determining the course of reaction; where these are other than chloro, addition of various acetylenes results in the isolation of indolizines (62).[37]

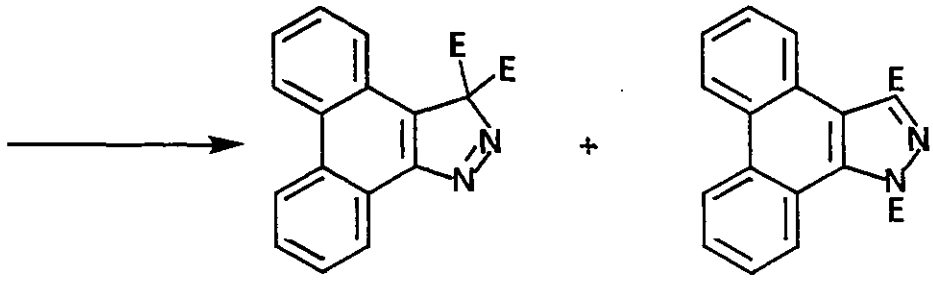


(62)

In the case of diazofluorene (63), the spiro pyrazole (64) obtained on addition of dimethyl acetylenedicarboxylate is isolable.[39] On heating in polar solvents, this rearranges *via* a 3a*H*-indazole (65) to two isomeric indazoles (66) and (67).

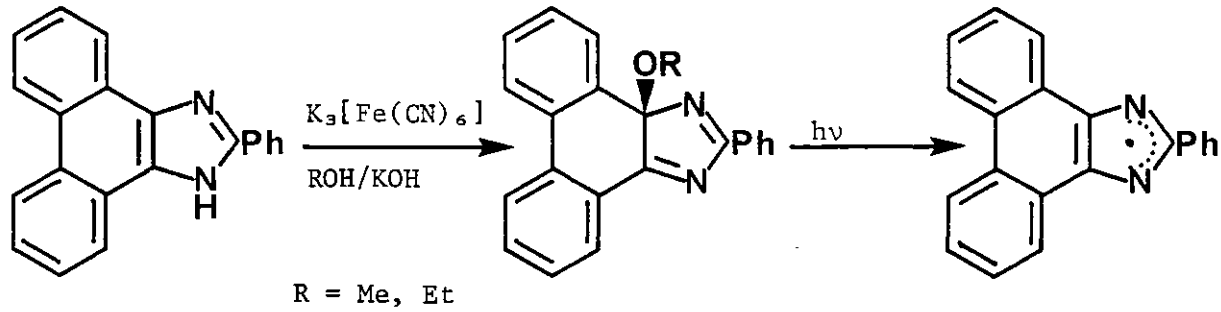


(63) (64) (65)



(66) (67)

Although the 3a*H*-indazole (65) could not be isolated, the effect on stability of benzannelation is demonstrated by the 3a*H*-benzimidazole (69). This unusual compound, which exhibits photochromic properties, is readily obtainable by ferricyanide oxidation of an alcoholic solution of the imidazole (68). On irradiation, the bridgehead substituent does not undergo sigmatropic migration, as might be expected, but is lost as the corresponding aldehyde.[40] The resultant radical (70) is believed to be the species responsible for the observed photochromism.

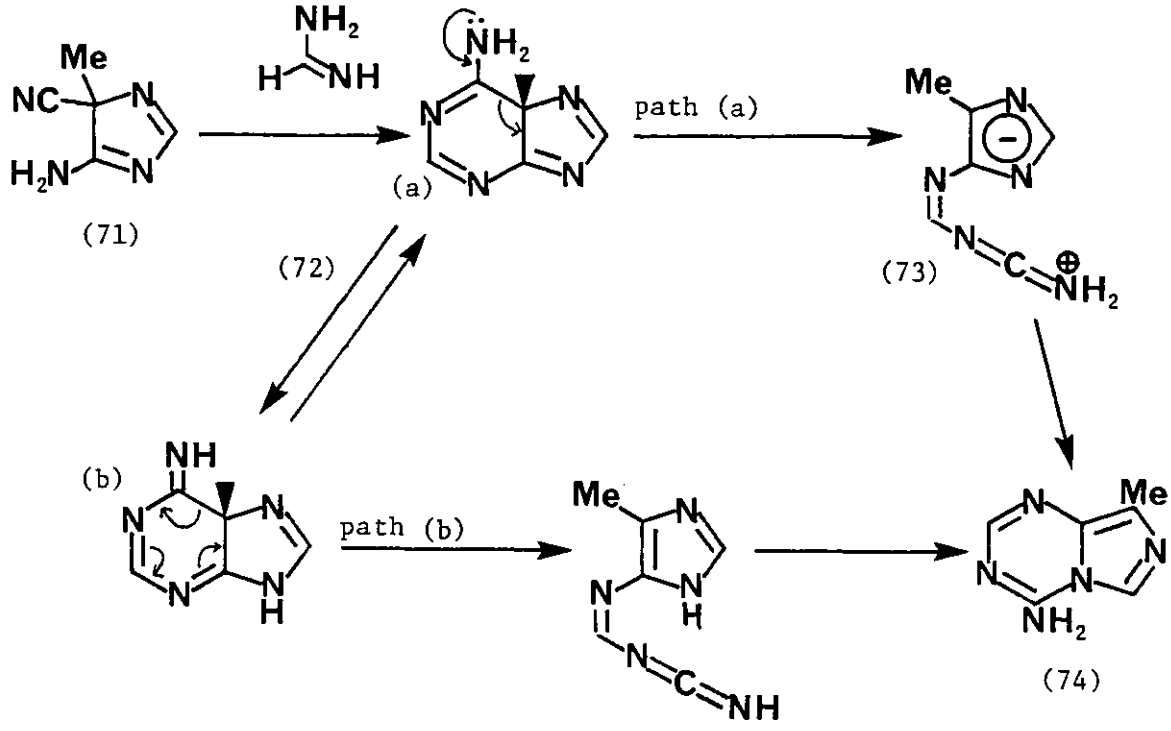


R = Me, Et

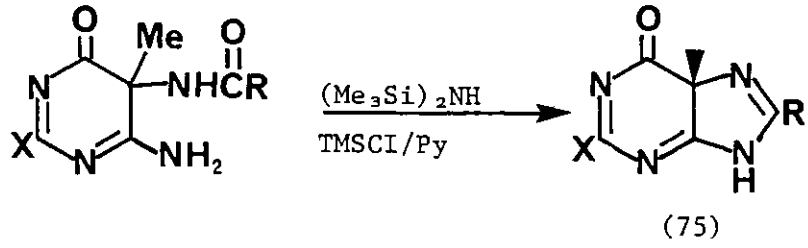
(68) (69) (70)

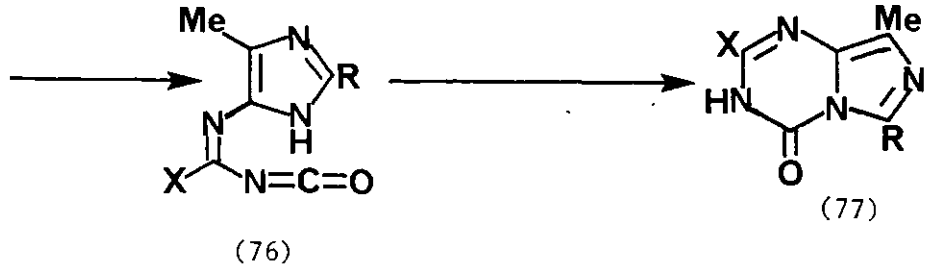
+ HCHO (R = Me)
CH_3CHO (R = Et)

An interesting attempt to synthesise a 5a*H*-adenine (72a) has recently been reported by Leonard's group.[41] Thus, treatment of the 4*H*-imidazole (71) with formamidine resulted in the azaindolizine (74) as the sole product. The authors suggest that this is derived from the desired 5a*H*-adenine (72a) and mechanistic possibilities for its formation are presented (Scheme 10). One involves an ionic intermediate (path a), whilst the other proceeds *via* an electrocyclic ring opening of the imine tautomer of the 5a*H*-adenine (72b) (path b). A mechanism similar to the latter was proposed by the same group in earlier studies on the purine (75), from which an analogous indolizine (77) was isolated.[42]



SCHEME 10

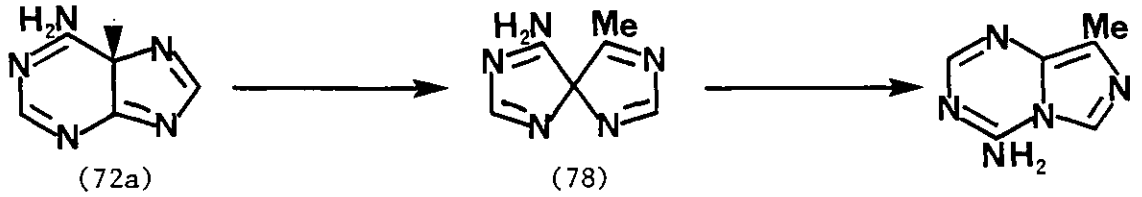




X = NH_2, SH, $N(Me)_2$

R = H, Me

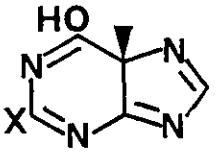
Although the validity of both mechanisms could possibly be tested by interception of the carbodiimide (73) or the isocyanate (76) with suitable nucleophiles, an alternative mechanism with good precedent in the reactions of 3a*H*-indene analogues may be proposed (Scheme 11). A [1,5] imidoyl bond migration would give the spiro intermediate (78), which may then undergo a further imidoyl migration onto nitrogen to afford the observed product (74). It is also reasonable to assume that under the



(72a) (78) (74)

SCHEME 11

reaction conditions the purine (75) would exist in equilibrium with a small amount of its enol tautomer (79), which is capable of undergoing an analogous sequence of imidoyl bond migrations.



(79)

1.4. Conclusion

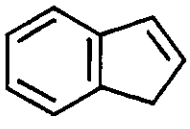
The chemistry of heterocyclic 3a*H*-indene analogues appears to be highly dependent on the nature of the bridgehead substituent. Where this is hydrogen, as in the majority of examples described, aromatisation by hydrogen migration is the exclusive process undergone by these species. In such cases the lifetimes of the intermediates are too short to allow any useful information to be gained about them. However, where the bridgehead substituent is an alkyl group, skeletal rearrangements involving vinyl bond migrations may supervene. In some cases both pathways may operate in parallel, and products arising from bridgehead substituent migrations and skeletal rearrangements can be observed.

The ultimate fate of these intermediates may also be governed by the conditions under which they are generated, but the diversity of isolated examples hinders any attempts at interpreting the factors involved. Thus, a systematic study of several, carefully chosen representatives is required in order to achieve an understanding of the general properties of these interesting species.

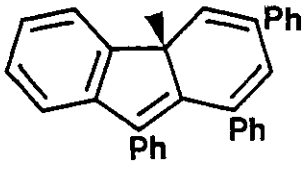
PART II. RESULTS AND DISCUSSION

2. THE GENERATION AND PROPERTIES OF 4a*H*-CARBAZOLES.

Recent theoretical studies of simple 3a*H*-indenes have disclosed a number of features which are believed to be responsible for the observed reactivity and instability of such species.[43] Calculations based on the MNDO method indicate that the ground state energy of 3a*H*-indene (1) is the highest of all the possible indene isomers, being some 27 kcal mol^{-1} higher than the aromatic 1*H* isomer (80). A computer drawn representation shows that the sp^3 bridgehead carbon atom is not significantly distorted from the usual tetrahedral configuration (Fig. 1). Consequently, the peripheral conjugated π system is prevented from assuming the planar alignment which would lead to maximum orbital overlap.



(80)



(81)

This deviation from planarity is well illustrated by an X-ray diagram of the stable, highly substituted 4a*H*-fluorene derivative (81) (Fig. 2).[44]

In simple 3a*H*-indenes, the strain imposed on the sp^3 carbon atom would be most readily relieved by [1,5] sigmatropic migration of the bridgehead substituent onto an adjacent position. Such a process has been experimentally demonstrated for the methoxy derivative (82).[45]

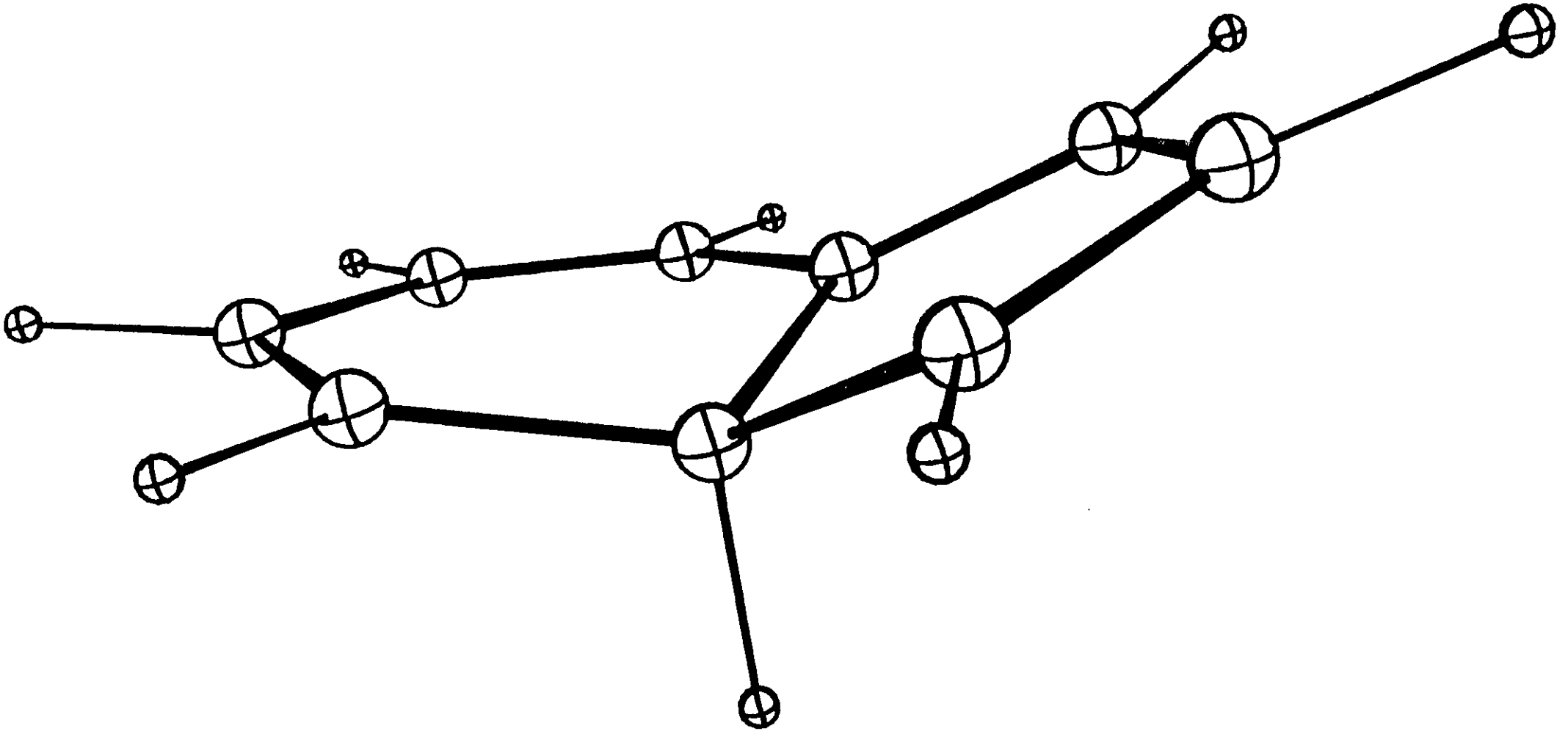


Figure 1. Computer Drawn Representation of 3a*H*-Indene

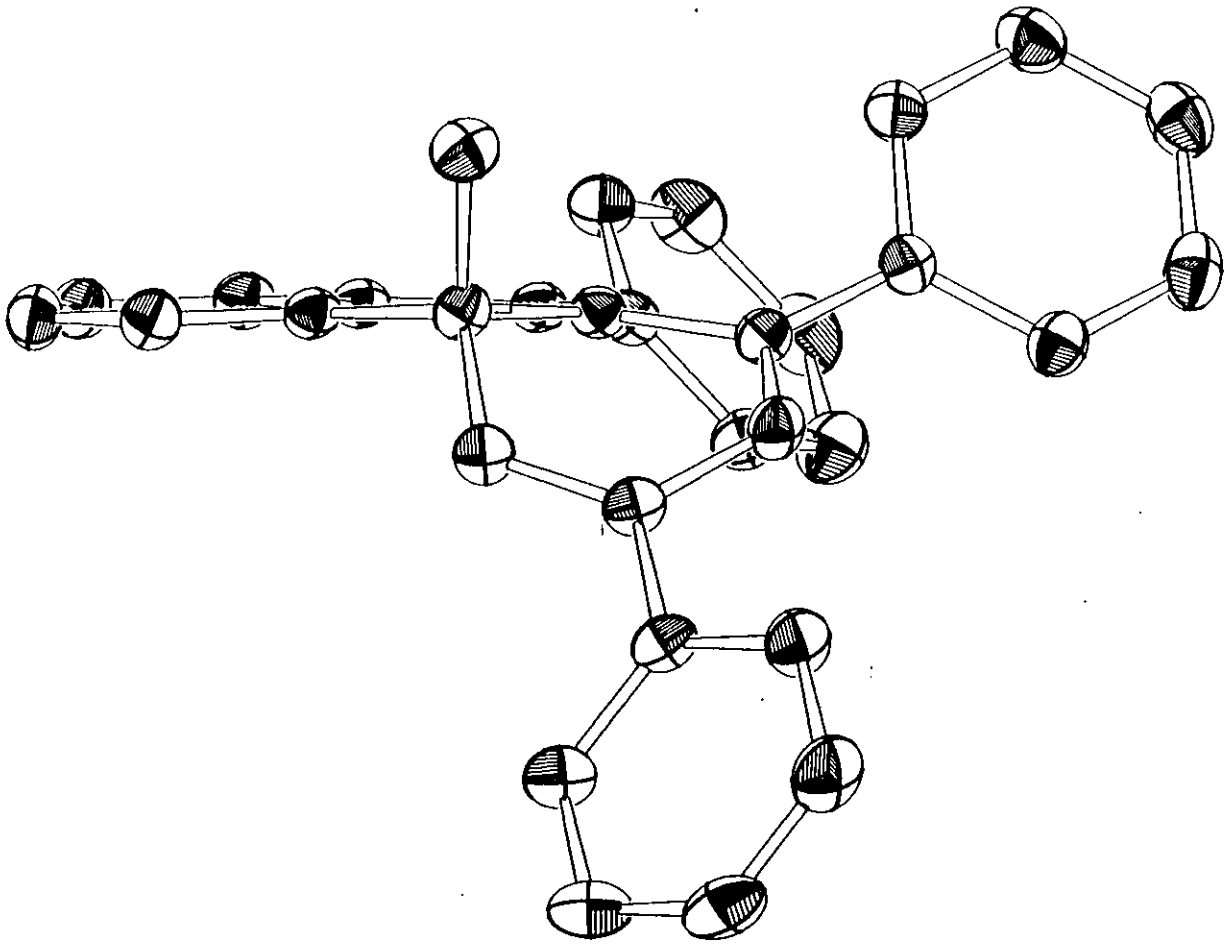
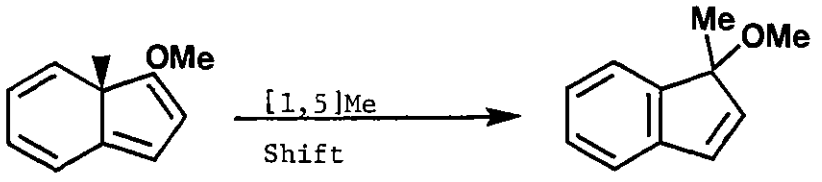
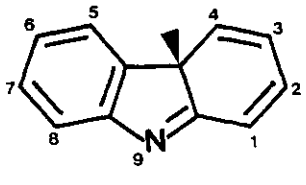


Figure 2. X-Ray Structure of (81)

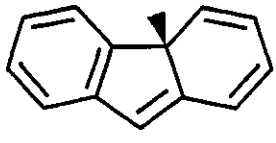


(82)

The few isolated 3a*H*-indene derivatives and analogues indicate that stability is enhanced by perturbation of the peripheral electronic system. This may be achieved by the presence of electron withdrawing substituents (*cf.* 57), or by benzannelation (*cf.* 66). Partially as a result of these considerations, the 4a*H*-carbazole system (83) was chosen as a particularly interesting example of a 3a*H*-indene analogue to investigate. It was hoped that benzannelation would confer sufficient stability to enable the system to be isolated and its properties thoroughly studied. Furthermore, the effect of introducing a heteroatom into the 3a*H*-indene periphery could be assessed by a direct comparison with the related, carbocyclic 4a*H*-fluorene system (84), the synthesis of which was in progress at the start of this work.[46]



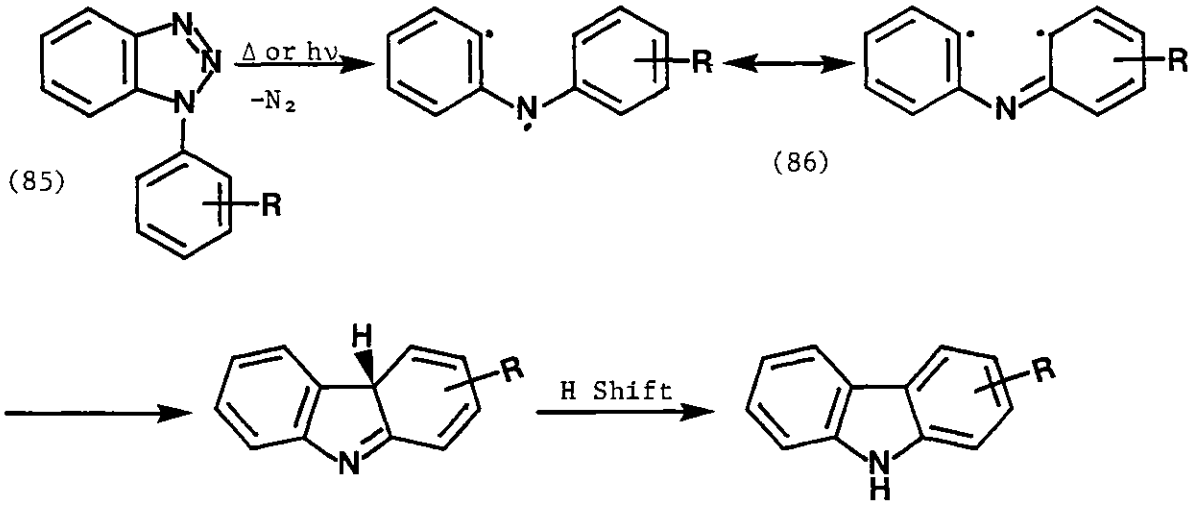
(83)



(84)

The purpose of this project, therefore, was to prepare and study the properties of derivatives of 4a*H*-carbazole (83), and compare these to related species containing the 3a*H*-indene system.

The well-known Graebe-Ullmann synthesis of carbazoles (88) by thermal[47] or photochemical[48] extrusion of nitrogen from 1-aryl benzotriazoles (85) is believed to involve cyclisation of the diradical (86) to a 4a*H*-carbazole (87) (Scheme 12). By using suitable substituents in

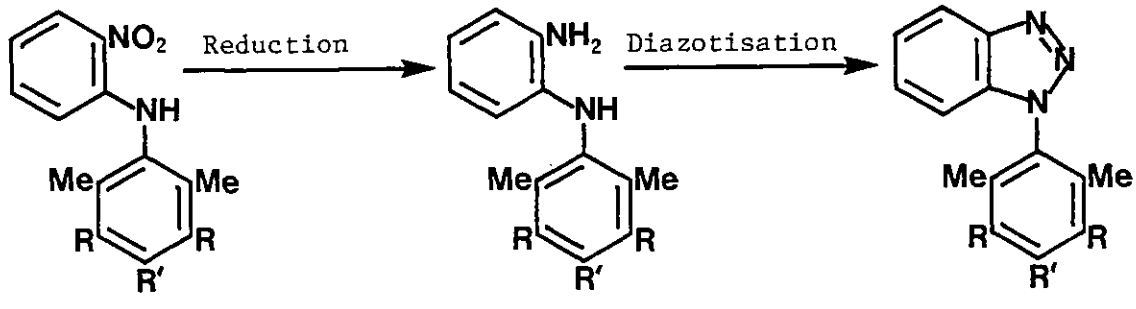


SCHEME 12

both *ortho* positions of the 1-aryl group, it was hoped that the final isomerisation to the aromatic species (88) could be suppressed. If the 4a*H*-carbazoles proved not to be isolable under the conditions employed, it was anticipated that their subsequent reactions would provide an interesting comparison with those of 3a*H*-benzimidazoles, generated from tetrazoles in an analogous manner (*cf.* Scheme 3).[10]

2.1. Preparation of Benzotriazoles.

The route employed for the preparation of the desired benzotriazoles (91) was based on literature procedures (Scheme 13).



(89) (90) (91)

a) R = R' = H
b) R = H, R' = Me
c) R = R' = Me

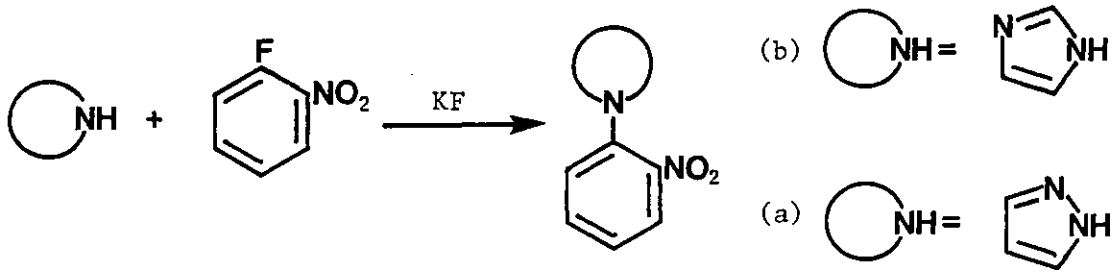
SCHEME 13

2.1.1. Preparation of 2-Nitrodiphenylamines.

Although two of the required nitrodiphenylamines, (89a) and (89b), had been previously prepared, the yields obtained were very poor. Thus, condensation of 2-chloronitrobenzene with 2,4,6-trimethylaniline at 200° in the presence of sodium acetate or bicarbonate, resulted in 7% yield of the corresponding diphenylamine (89b).[49] Substituting 2-fluoronitrobenzene in place of the chloro compound for the preparation of 2-nitro-2',6'-dimethyldiphenylamine (89a) with potassium acetate as the base afforded only a slight improvement.[50]

Potassium fluoride has been reported to be a particularly efficient base for reactions in which hydrogen fluoride is generated, due to the formation of the very stable hydrofluoride ion (HF_2^-).[51] The anticipation that improved yields of nitrodiphenylamines could be obtained by reaction of the appropriate aniline with 2-fluoronitrobenzene in the presence of

potassium fluoride was further encouraged by the results of Meth-Cohn and co-workers[15] with a related reaction. They reported that excellent yields of 2-nitrophenylimidazoles (92a) and pyrazoles (92b) are obtained on reaction of the heterocyclic compound with fluoronitrobenzene using potassium fluoride as base. The application of similar conditions to the reaction of anilines with 2-fluoronitrobenzene did indeed result



(92)

in considerably improved yields of product over those previously reported in the literature. The results obtained with a variety of anilines are summarised (Table 1). Typically, these reactions were performed in the absence of solvent, using a slight molar excess of anhydrous potassium fluoride. Two equivalents of aniline were used in order to facilitate separation of the product from unreacted 2-fluoronitrobenzene, although in later experiments with less readily available amines, the use of one equivalent did not appear to have a significantly detrimental effect on the yields obtained.

Further demonstration of the advantage offered by the fluoronitrobenzene/potassium fluoride combination is provided by control experiments in which 2,4,6-trimethylaniline was treated under identical conditions with 2-chloronitrobenzene and 2-fluoronitrobenzene, both in the presence and absence of potassium fluoride (Table 2).

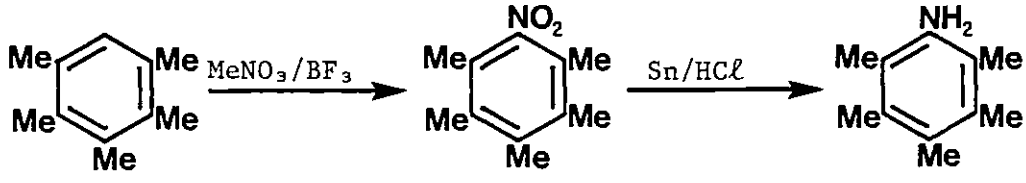
TABLE 1. Reaction of aromatic amines with 2-fluoronitrobenzene in the presence of potassium fluoride.

Amine	Equivalents of amine	Temperature (°C)	Time of reaction (h)	Yield (%)
2,4-Dimethylphenyl	2	140	20	31
2,4-Dimethylphenyl	2	160	48	72
2,4,6-Trimethylphenyl	2	160	96	63
2,4,6-Trimethylphenyl	2	180	48	62
2,4,6-Trimethylphenyl	2	150	48	40
2,6-Dimethylphenyl	2	195	24	35
2,6-Dimethylphenyl	2	190	46	65
2-Biphenyl	2	195	24	59
2-Chlorophenyl	2	180	46	48
3-Chlorophenyl	2	180	46	74
4-Chlorophenyl	2	180	46	71
4-Nitrophenyl	2	180	40	4
Pentamethylphenyl	1	185	45	51
2-Methylnaphthyl	1	180	63	52

TABLE 2. Reaction of aromatic halides with 2,4,6-trimethylaniline at 190° for 42 h.

Nitro Compound	Presence of Potassium Fluoride	Yield of Diphenylamine (%)
2-Chloronitrobenzene	-	-
2-Chloronitrobenzene	+	4
2-Fluoronitrobenzene	-	6
2-Fluoronitrobenzene	+	45

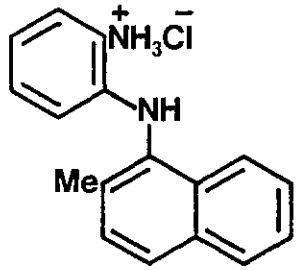
The aniline (95) required for the preparation of 2-nitro-2',3',4',5',6'-pentamethyldiphenylamine (89c) was conveniently obtained from pentamethylbenzene (93) in two steps. Nitration of the hydrocarbon under mild conditions with methyl nitrate in the presence of boron trifluoride[52] afforded the nuclearly substituted product (94), which was found to be resistant to catalytic hydrogenation over palladium, but could be smoothly reduced by the action of tin in hydrochloric acid.



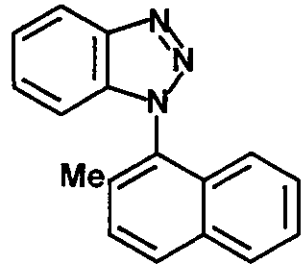
(93) (94) (95)

2.1.2. Preparation of Benzotriazoles from Nitrodiphenylamines.

Catalytic hydrogenation at atmospheric pressure of the now readily available nitrodiphenylamines (89) furnished the corresponding diamines (90) in excellent yield. However, the free amines rapidly deteriorated to dark red or purple gums on exposure to air and light, and so were immediately converted into their stable hydrochlorides. These could be handled conveniently, and gave high yields of the corresponding benzotriazoles (91) on diazotisation in aqueous media.[53] The low solubility of the naphthyl derivative (96) under these conditions, even in the presence of co-solvents, led to irreproducible yields, and the isolated product was frequently contaminated with unreacted starting material, from which it was not readily separable. Although the yield of benzo-



(96)



(97)

triazole (97) was somewhat diminished, these problems could be overcome by diazotisation of the freshly prepared free amine under aprotic conditions with pentyl nitrite in refluxing benzene.[54]

2.2. FVP of Benzotriazoles.

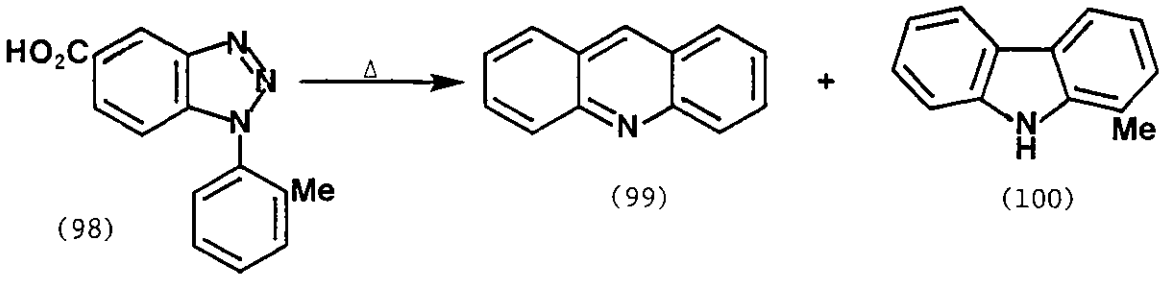
FVP of 1-(2,6-dimethylphenyl)benzotriazole (91a) at 640° and 3×10^{-2} mmHg gave 1,9-dimethyl (106a) and 1-methyl carbazole (107a) as the major products. Both were obtained in similar yields, but the latter was isolated in admixture with several other components, one of which could be partially separated by careful chromatography. From its physical properties, this component was tentatively identified as being 1,8-dimethylcarbazole (108). Since such a product was unexpected, and in view of the large variation in melting point quoted for this compound in the literature† further evidence of its identity was sought. Comparison of the pyrolysis product with independently synthesised 1,8-dimethylcarbazole (see Chapter 6) confirmed the original assignment.

---

†1,8-Dimethylcarbazole has been reported to melt at 48-50° [55a] and 176-177°,[55b] as well as being described as an "oily solid".[55c] We find m.p. 177—178°.

The remaining mixture was subjected to analytical h.p.l.c., which indicated the presence of a third component in addition to 1-methylcarbazole (107a) and some residual 1,8-dimethylcarbazole (108). Unfortunately, this component could not be isolated or identified, but was shown to be a carbazole by the use of stopped-flow scanning. In this technique, the flow of eluting solvent through the h.p.l.c. column is stopped as each fraction passes through the detector. By arranging the h.p.l.c. detector cell to double as the sample cell of a u.v. spectrometer, the u.v./visible spectrum of the fraction may be recorded.

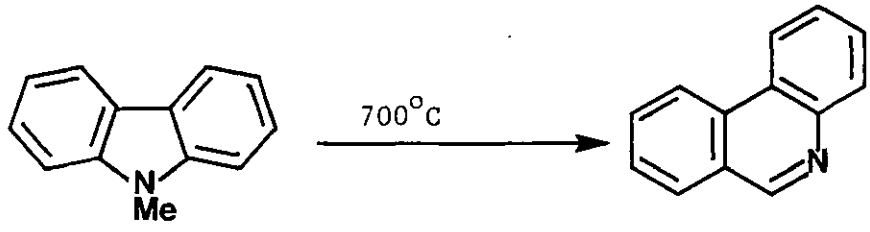
Further analysis of the crude pyrolysate revealed the presence of two minor products, together with a small amount of unchanged starting material. The two products were both aromatic, and were clearly related to each other, but were not carbazoles. They exhibited a strong fluorescence on t.l.c. under u.v. light, and one was shown by n.m.r. to have a methyl substituent, whilst the other was unsubstituted. On the basis of their spectral properties, especially the appearance of a low field one proton singlet at δ 8.7 in the n.m.r., these compounds were thought to be acridines or phenanthridines. Both are possible products in the pyrolysis of "*ortho*-blocked" benzotriazoles; acridine (99) itself is reportedly formed in addition to the expected carbazole (100) on pyrolysis of the benzotriazole (98),[56] which has only one *ortho* position substituted.



(98) (99) (100)

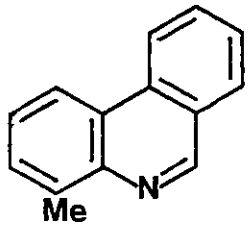
Formation of the acridine presumably occurs by insertion of the diradical generated on extrusion of nitrogen (*cf.* Scheme 1) into the methyl substituent, followed by aerial oxidation of the resulting acridan.

Phenanthridine (102) has been isolated as a product from the pyrolysis of *N*-methylcarbazole (101) at 700°.[75] An analogous reaction

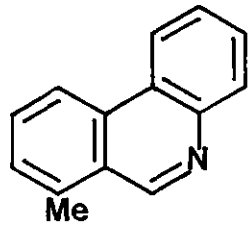


(101) (102)

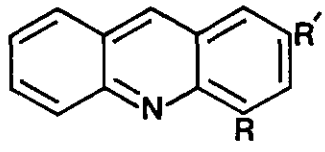
undergone by 1,9-dimethylcarbazole (106a), could give rise to two isomeric monosubstituted phenanthridines, (103) and (104). Thus, the minor, substituted product from the pyrolysis of the benzotriazole (91a) could be



(103)



(104)



(105)

a) R = Me, R' = H
b) R = R' = H
c) R = R' = Me
d) R = H, R' = Me

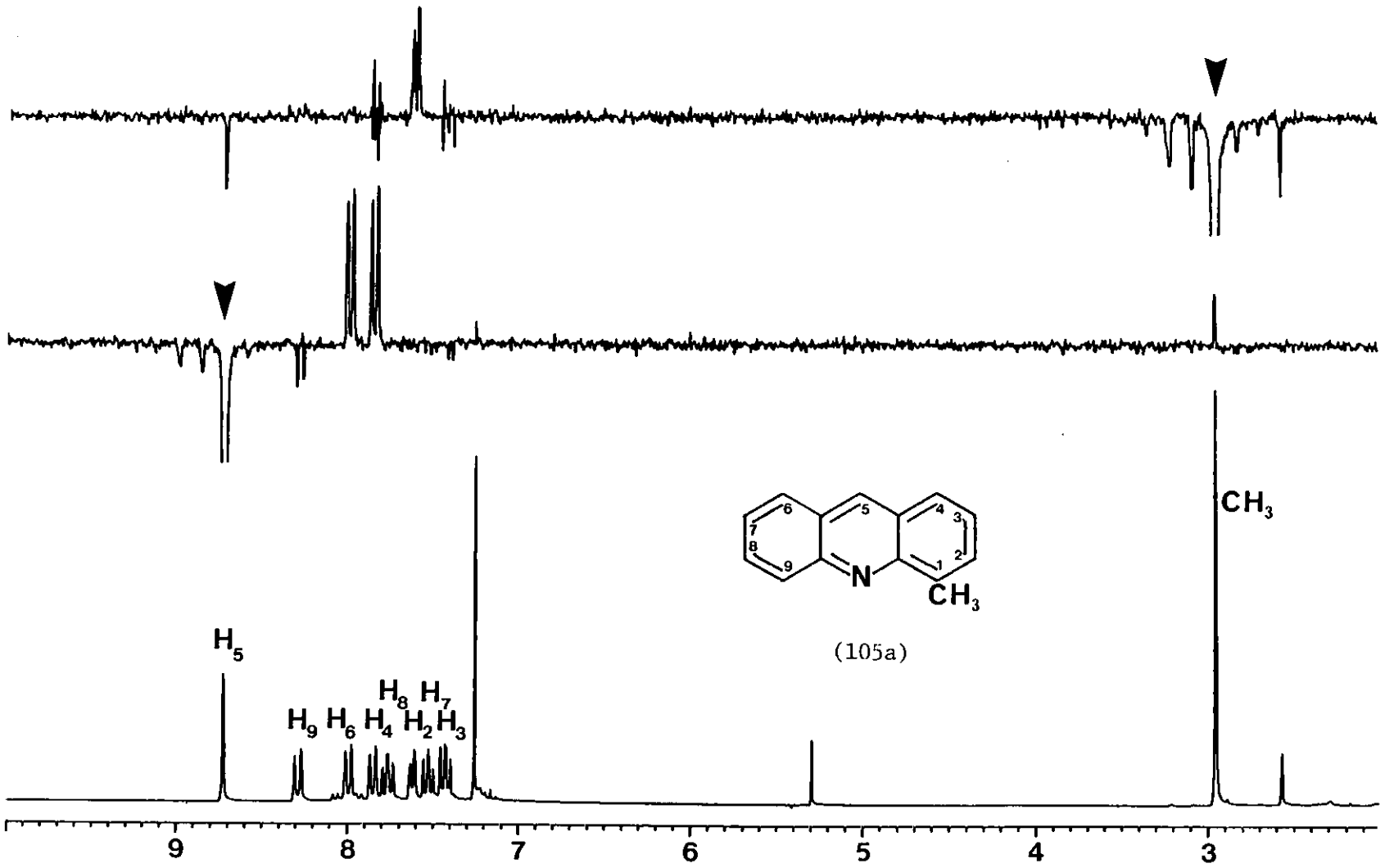
either of the phenanthridines (103) and (104), or the acridine (105a), with the unsubstituted product being the parent heterocycle, (102) or

(105b) respectively. The small quantities of these products available, and an inability to isolate them in a sufficiently pure state prevented an unequivocal differentiation between the possibilities, although the appearance of their ultraviolet spectra favoured the acridines (105a) and (105b).

The problem was finally resolved by performing an n.O.e. difference experiment (Fig. 3), which enabled the structure of the methyl substituted product to be determined. Hence, irradiation of the methyl group causes enhancement of an adjacent proton, which appears as a doublet. The phenanthridine (104) can immediately be discounted on the basis of this result, since irradiation of the methyl group would cause enhancement not only of the 8 proton, but also that at the 6-position, which would appear as a singlet. The fact that two protons are enhanced on irradiation of the low field proton singlet likewise eliminates the isomeric phenanthridine (103) since only one proton would be expected to be enhanced in that case. These results are entirely consistent with one of the minor products being 1-methylacridine (105a), which suggests that the other is acridine itself (105b).

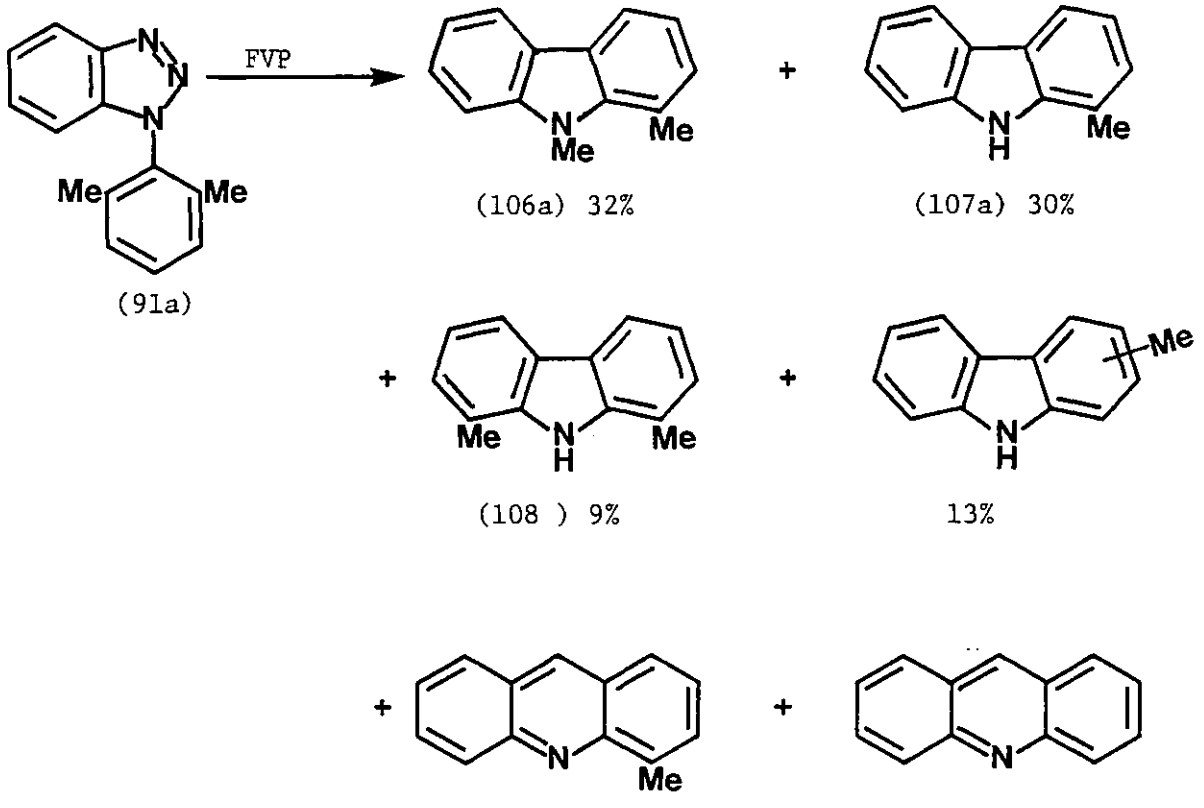
The results obtained on FVP of the dimethylphenyl benzotriazole (91a) can thus be summarised in Scheme 14.

Pyrolysis of 1-(2,4,6-trimethylphenyl)benzotriazole (91b) under identical conditions produced similar results. The isolation of 1,3,9-trimethylcarbazole (106b) was confirmed by comparison with an authentic sample. H.p.l.c. revealed that once again the demethylated carbazole (107b) was obtained in admixture with other *N*-unsubstituted carbazoles. Each of the three products detected was very minor, and none could be identified. Two further minor products were tentatively assigned



(105a)

Figure 3. N.O.e. Difference Spectra of (105a) in $CDC\ell_3$ at 250 MHz.



SCHEME 14

as 1,3-dimethylacridine (105c) and 3-methylacridine (105d) by analogy with the previously described acridines, (105a) and (105b), which they closely resembled.

Repeating the pyrolysis at various temperatures indicated that the relative proportion of *N*-methyl (106b) to *N*-unsubstituted carbazoles was approximately constant; the only major difference between the pyrolyses being higher conversion of starting material at higher temperatures (Table 3).

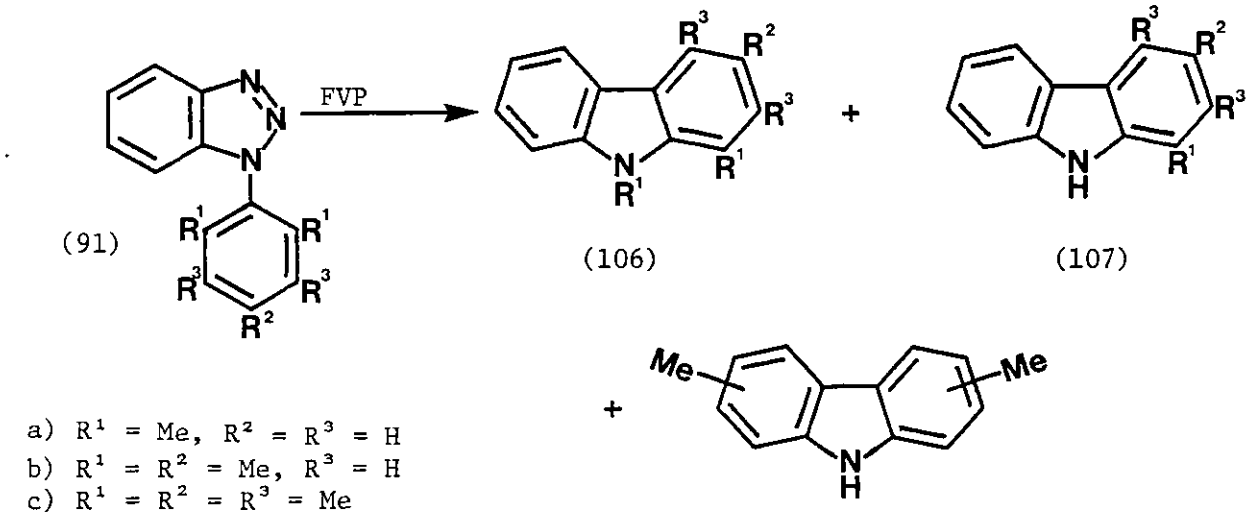
Pyrolysis of 1-(2,3,4,5,6-pentamethylphenyl)benzotriazole (91c) at 640^{o} afforded a more complex pyrolysate than in the previous examples, from which the two carbazoles (106c) and (107b) could be isolated.

TABLE 3. FVP of 1-(2,4,6-trimethylphenyl)benzotriazole (91b).

Pyrolysis Temperature °C	% Conversion	N-Me Carbazole (107b) (%)	N-H Carbazoles (%)
400	0	-	-
490	43	19	40
640	81	16	40
700	98	15	50

Spectroscopic identification of both products was supported by comparison with authentic specimens (see Chapter 6). In this case, the demethylated carbazole (107c) was accompanied by four minor, unidentified carbazoles. No acridines could be isolated.

The results obtained on FVP of all three benzotriazoles (Scheme 15) are summarised in Table 4.



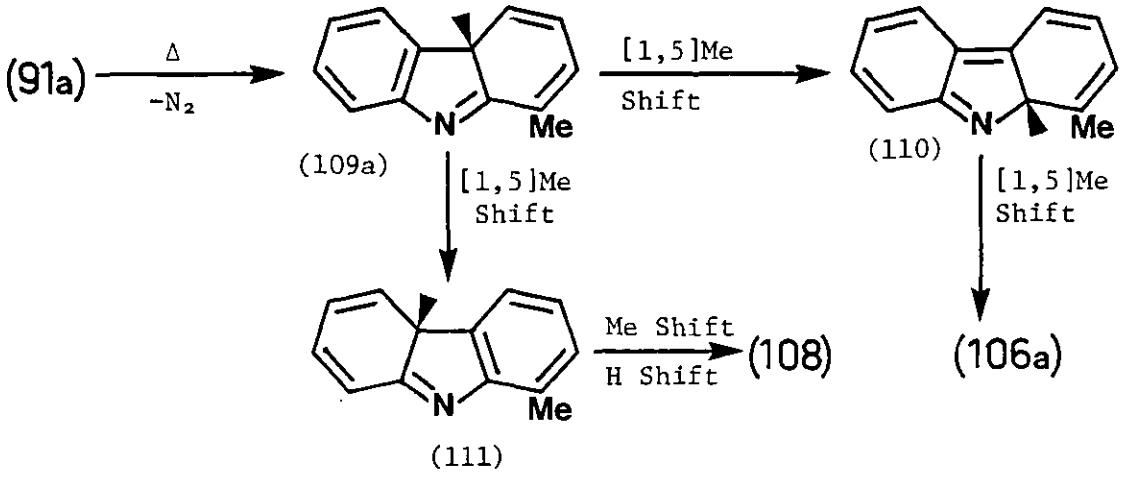
a) R^1 = Me, R^2 = R^3 = H
b) R^1 = R^2 = Me, R^3 = H
c) R^1 = R^2 = R^3 = Me

SCHEME 15

TABLE 4. FVP of benzotriazoles at 640°.

Benzotriazole	Conversion (%)	Carbazole (106) (%)	Carbazole (107) (%)	Other Carbazoles (%) (No.)
91a	96	32	30	22 (2)
91b	81	16	36	4 (3)
91c	92	23	37	10 (4)

The formation of all the identified products from these pyrolyses, with the exception of acridines, is consistent with the intermediacy of 4a*H*-carbazoles. The proposed mechanism is shown for the dimethyl compound (109a) for clarity (Scheme 16).



SCHEME 16

A [1,5]sigmatropic migration of the bridgehead substituent in the 4a*H*-carbazole (109), formed as indicated previously (Scheme 12), could give rise to an 8a*H*-carbazole (110), in which a further [1,5] methyl

migration would afford the *N*-methylated carbazole, (106a; *cf.* 24 in Scheme 5), or an isomeric 4a*H*-carbazole (111). Further [1,5] or higher order migrations of the methyl group in this intermediate, with subsequent hydrogen shifts would provide the symmetrically substituted carbazole (108). Loss of the bridgehead methyl group to give the demethylated carbazole (107a) may occur during the migrations or from any of the intermediates. It is considered unlikely that this loss occurs from nitrogen in the *N*-substituted carbazoles (106). A control experiment performed on 1,3,9-trimethylcarbazole (106b) indicated that such a loss required much higher temperatures than those used for the decomposition of benzotriazoles (91). Thus, only unchanged starting material was recovered on FVP at 650°, and although some demethylation was observed at 800°, the extent was small. It was only at 950° that this process could be completed.

The formation of acridines has been discussed previously and does not involve a 4a*H*-carbazole intermediate. The origin of the demethylated acridines, (105b) and (105d) remains obscure.

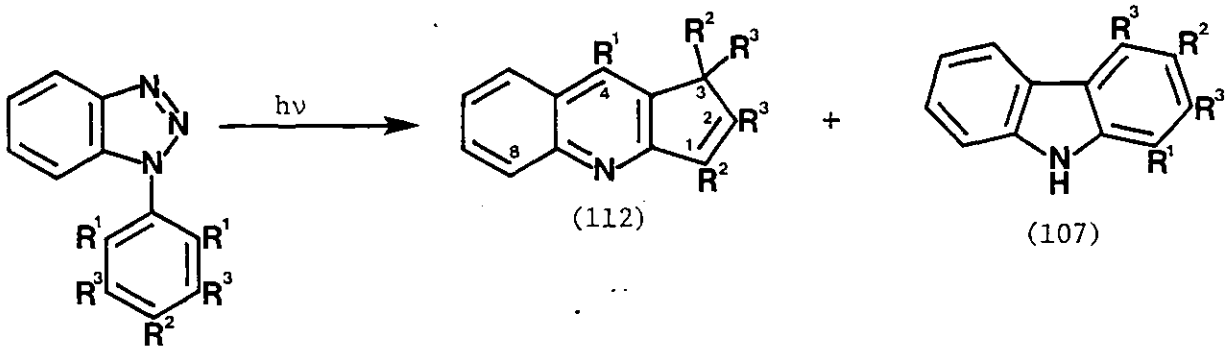
2.3. Photolysis of Benzotriazoles.

In contrast with its thermolysis, photolysis of 1-(2,6—dimethylphenyl)-benzotriazole (91a) afforded only one product, which was not a carbazole. Spectral data suggested it to be the cyclopentaquinoline (112a), the position of the five-membered ring methyl group being determined with the aid of $En(fod)_3$ chemical shift reagent (Table 5). Conclusive proof of the structure was finally provided by independent synthesis of quinoline (112a).

TABLE 5. Change in chemical shifts (ppm) of selected signals in (112a) on addition of $Eu(fod)_3$.

Signal / $Eu(fod)_3$ (mg)	1-Methyl	2-H	3-H	4-Me	8-H
1	0.09	0.03	0.03	0.02	0.14
5	0.35	0.12	0.11	0.07	0.44

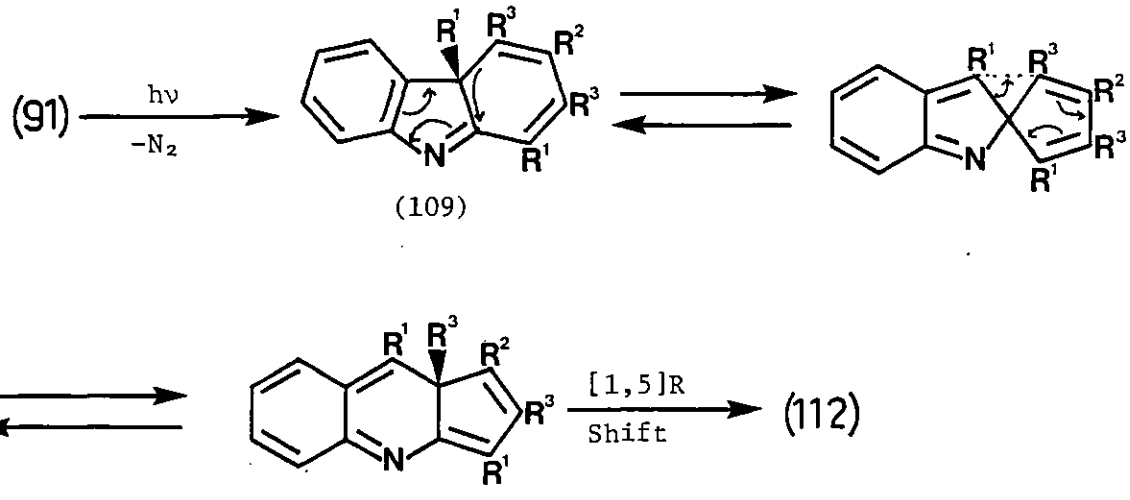
An analogous trimethylcyclopentaquinoline (112b) was obtained on photolysis of 1-mesitylbenzotriazole (91b). However, in this case, a small quantity of 1,3-dimethylcarbazole (107b) was also isolated. As with its thermolysis the pentamethyl derivative (91c) gave a much more complex mixture of products, from which could be separated the corresponding quinoline (112c) and tetramethyl carbazole (107c), in approximately equal yields.



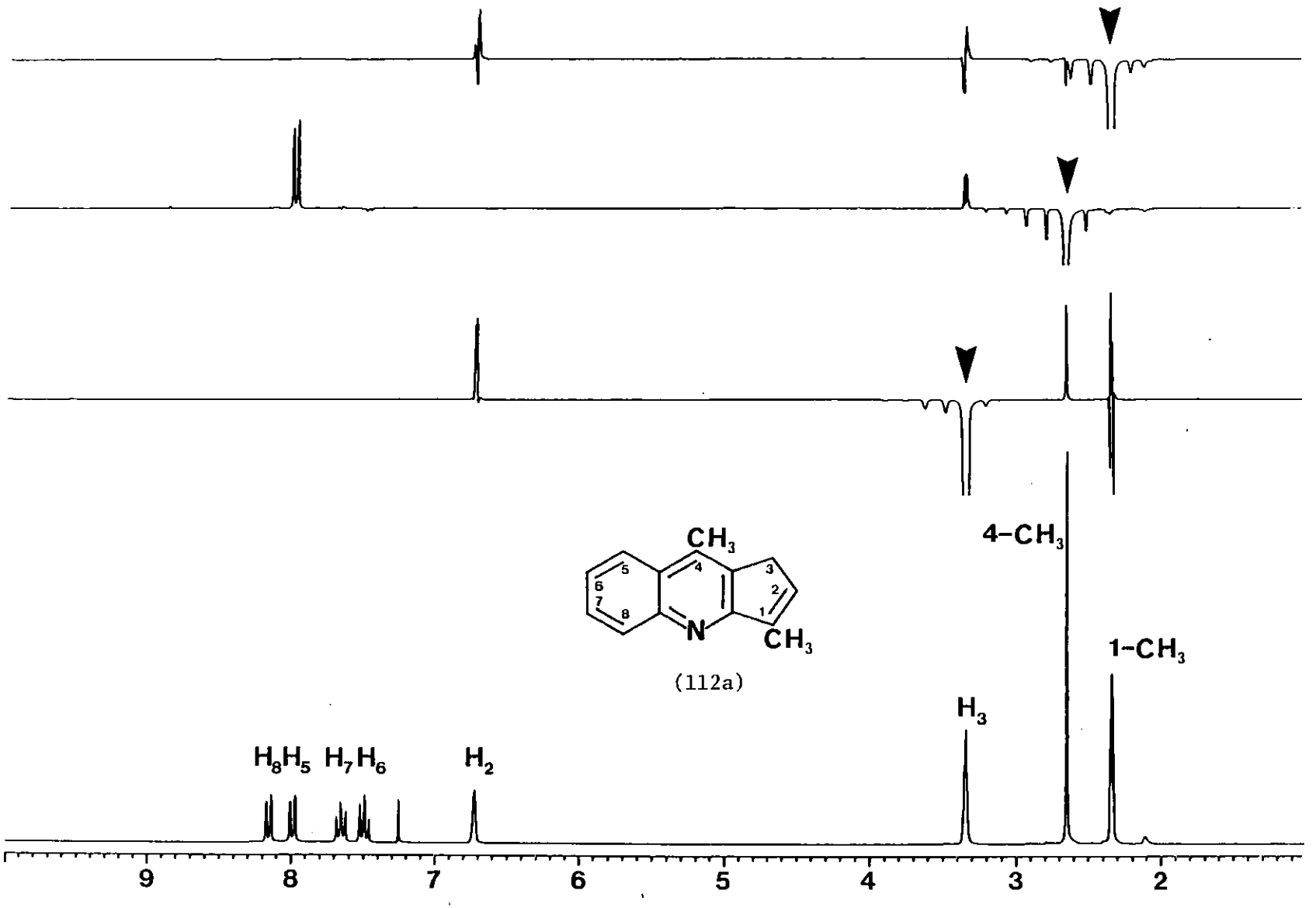
a) R^1 = Me, R^2 = R^3 = H	46%	0%
b) R^1 = R^2 = Me, R^3 = H	64%	6%
c) R^1 = R^2 = R^3 = Me	20%	18%

The structures of all three cyclopentaquinolines were determined by n.O.e. experiments (Figs. 4 to 6).

These cyclopentaquinolines are clearly analogous to the cyclopentapyrimidines (12) obtained on photolysis or thermolysis of diaryl oxadiazolones (9) or tetrazoles (10) (Scheme 2).[10] A similar mechanism to that proposed to account for the pyrimidines (12) but involving 4a*H*-carbazoles as intermediates rather than 3a*H*-benzimidazoles (17) may be written (*cf.* Scheme 3).

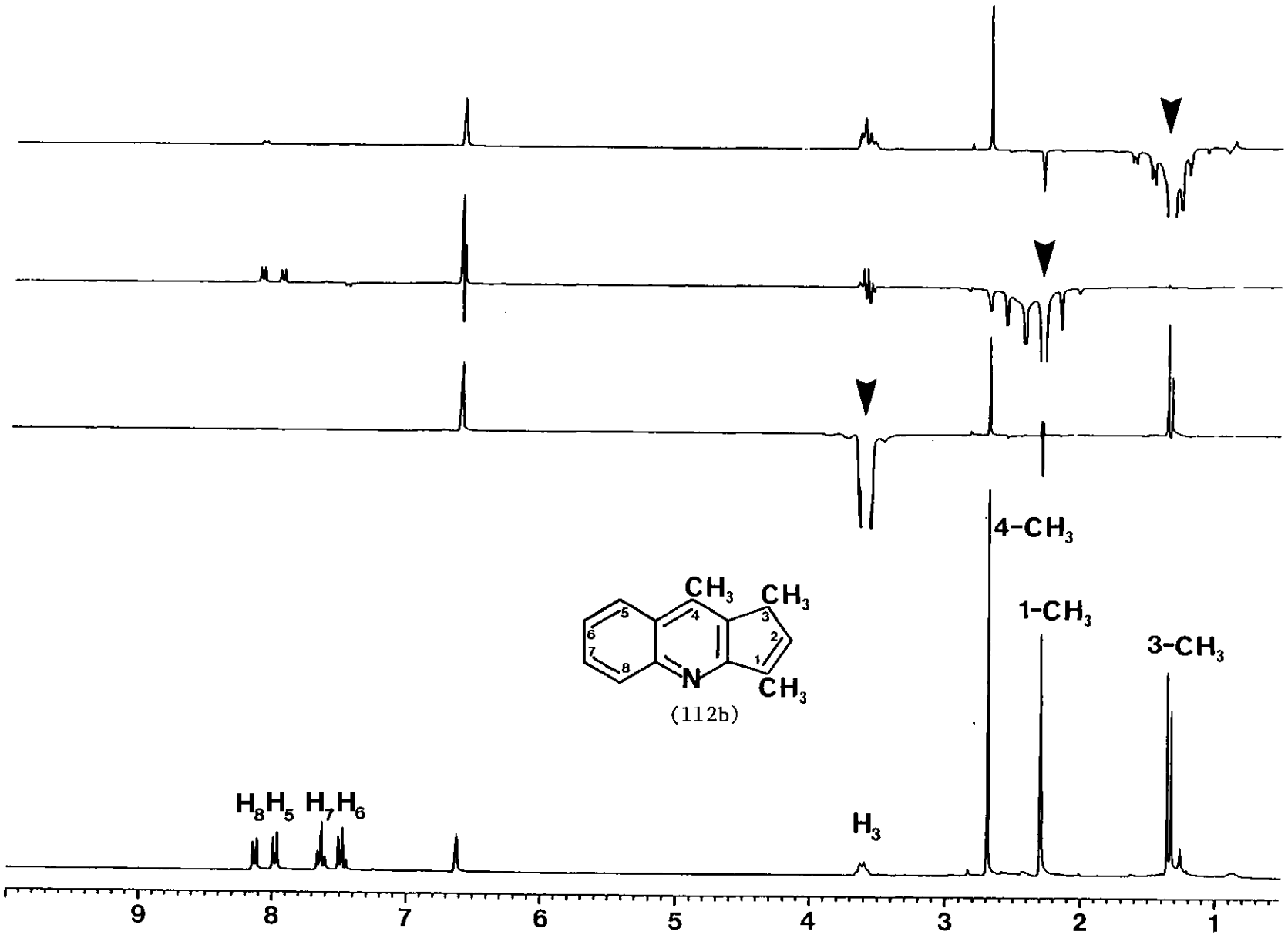


However, such a mechanism involves only thermally-allowed sigmatropic processes, and is considered inadequate in view of the total absence of cyclopentaquinolines (112) observed in the pyrolyses of the benzotriazoles (91). An alternative mechanism based on an aza-di-π-methane[58] rearrangement of the intermediary 4a*H*-carbazole (109) is proposed (Scheme 17). The viability of such a mechanism is discussed in greater detail in Chapter Five.



(112a)

Figure 4. N.O.e. Difference Spectra of (112a) in $CDC\ell_3$ at 250 MHz.



(112b)

Figure 5. N.O.e. Difference Spectra of (112b) in $CDC\ell_3$ at 250 MHz.

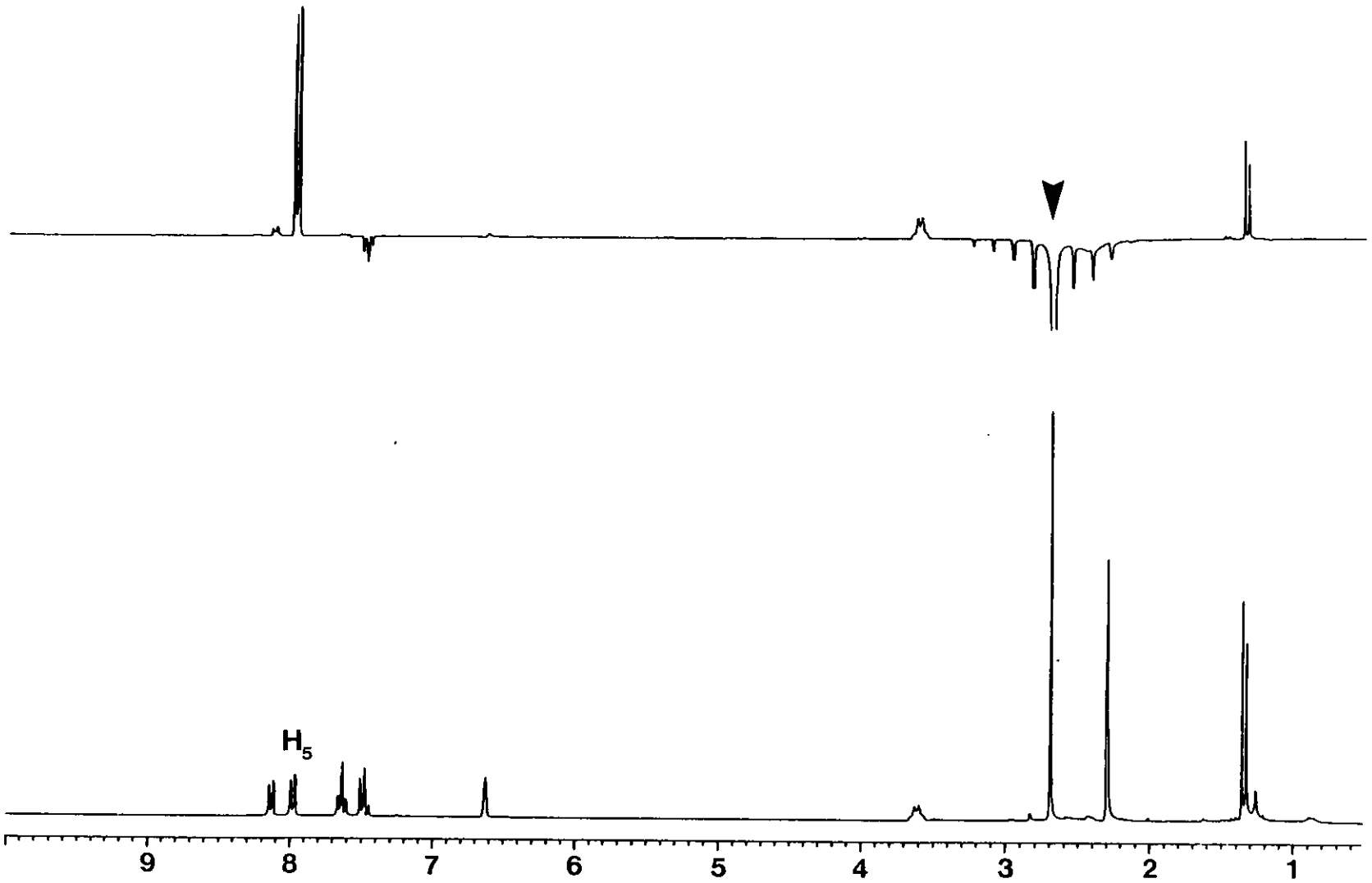
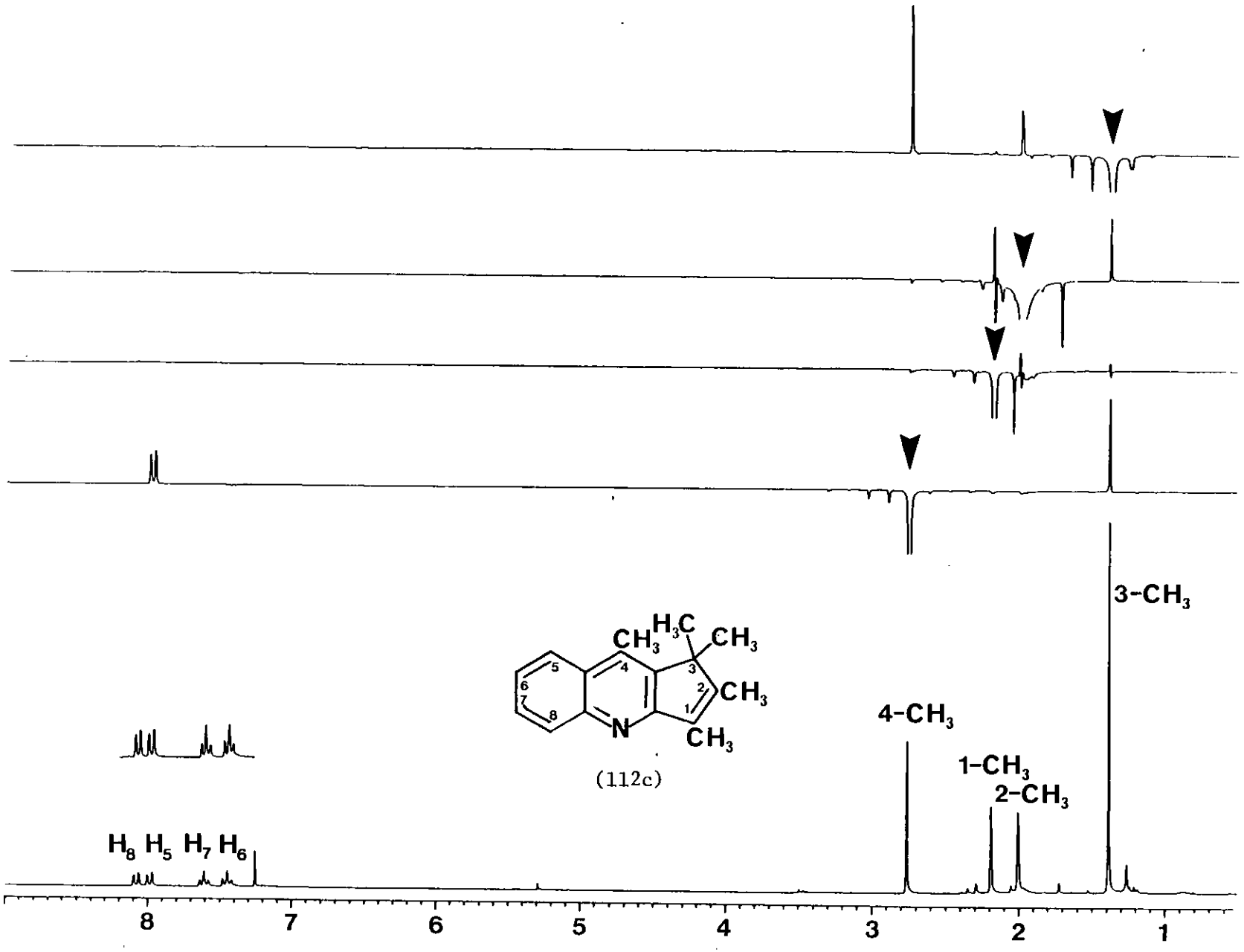
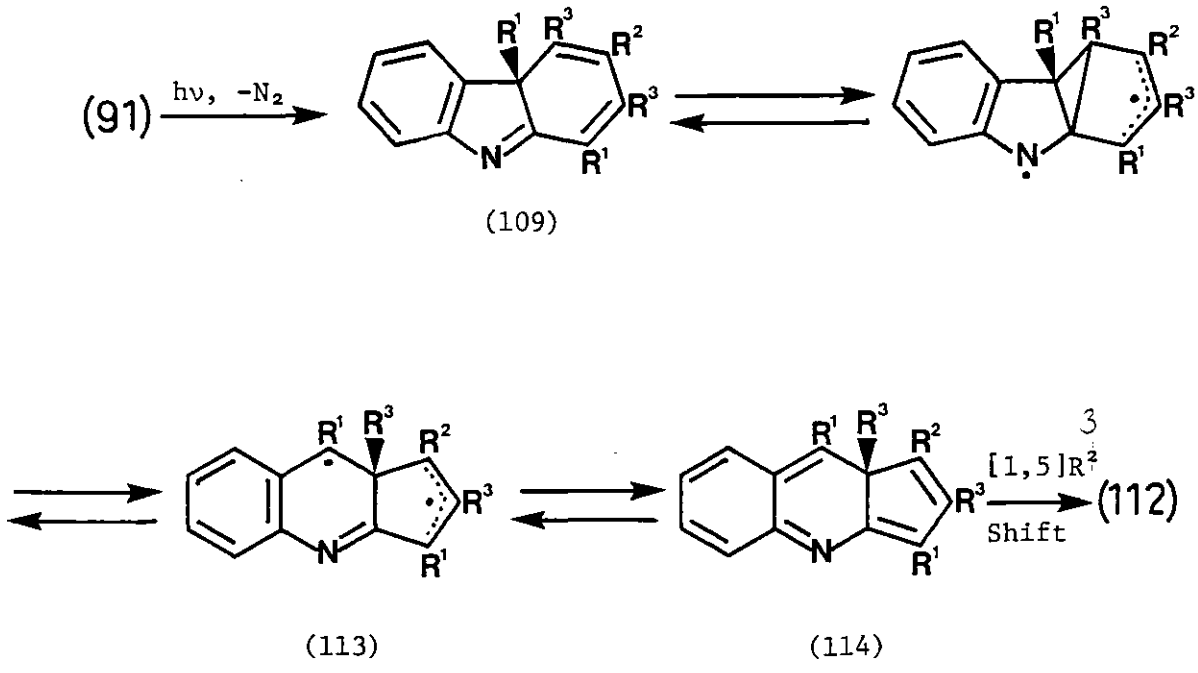


Figure 5 (continued).



(112c)

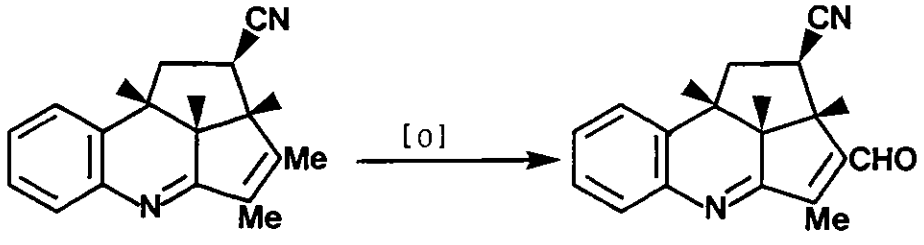
Figure 6. N.O. e. Difference Spectra of (112c) in $CDC\ell_3$ at 250 MHz



SCHEME 17

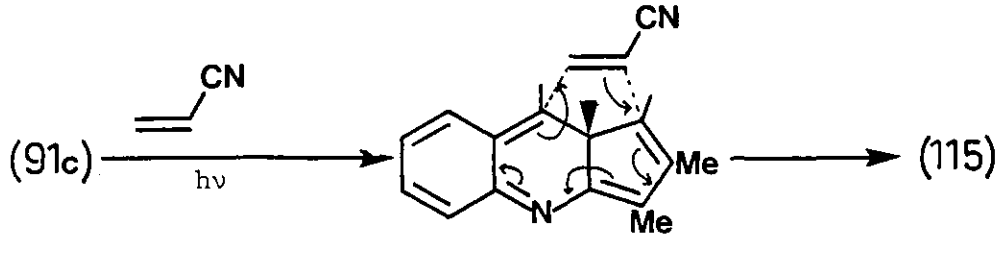
The formation of demethylated carbazoles (107b) and (107c) is believed to occur by loss of a methyl group from an energetic state of the 4a*H*-carbazoles (109b) and (109c), which is initially formed on collapse of the biradical generated on extrusion of nitrogen from the corresponding benzotriazoles. Severe steric congestion in the intermediate (114c) resulting from the presence of methyl substituents at both the bridgehead and the adjacent position to which the bridgehead substituent migrates is thought to account for the high proportion of carbazole (107c) to quinoline (112c) isolated in the photolysis of compound (91c). Furthermore, an increase in the lifetime of intermediate (114c) would also be a likely manifestation of this reluctance of the bridgehead substituent to undergo migration. In anticipation of this fact, the photolysis of 1-(2,3,4,5,6-

pentamethylphenyl)benzotriazole (91c) was repeated in the presence of acrylonitrile in an effort to trap this intermediate. No carbazoles or quinolines could be detected, the major product (45%) was found to be a 1:1 adduct of the intermediate (114c) with acrylonitrile. The structure of this adduct (115) was elucidated by X-ray crystallography (Fig. 7). Interestingly, this compound in solution underwent aerial oxidation to the aldehyde (116), which resolved spontaneously on crystallisation.



(115) (116)

Although a second adduct was detected, it was present in such minor quantities as to be insignificant. The high degree of stereo- and regio-selectivity shown in the adduct (115) suggests that addition of acrylonitrile occurs to the 3a*H*-indene type intermediate (114c), rather than to the diradical (113), in which no selectivity would be expected.



(114c)

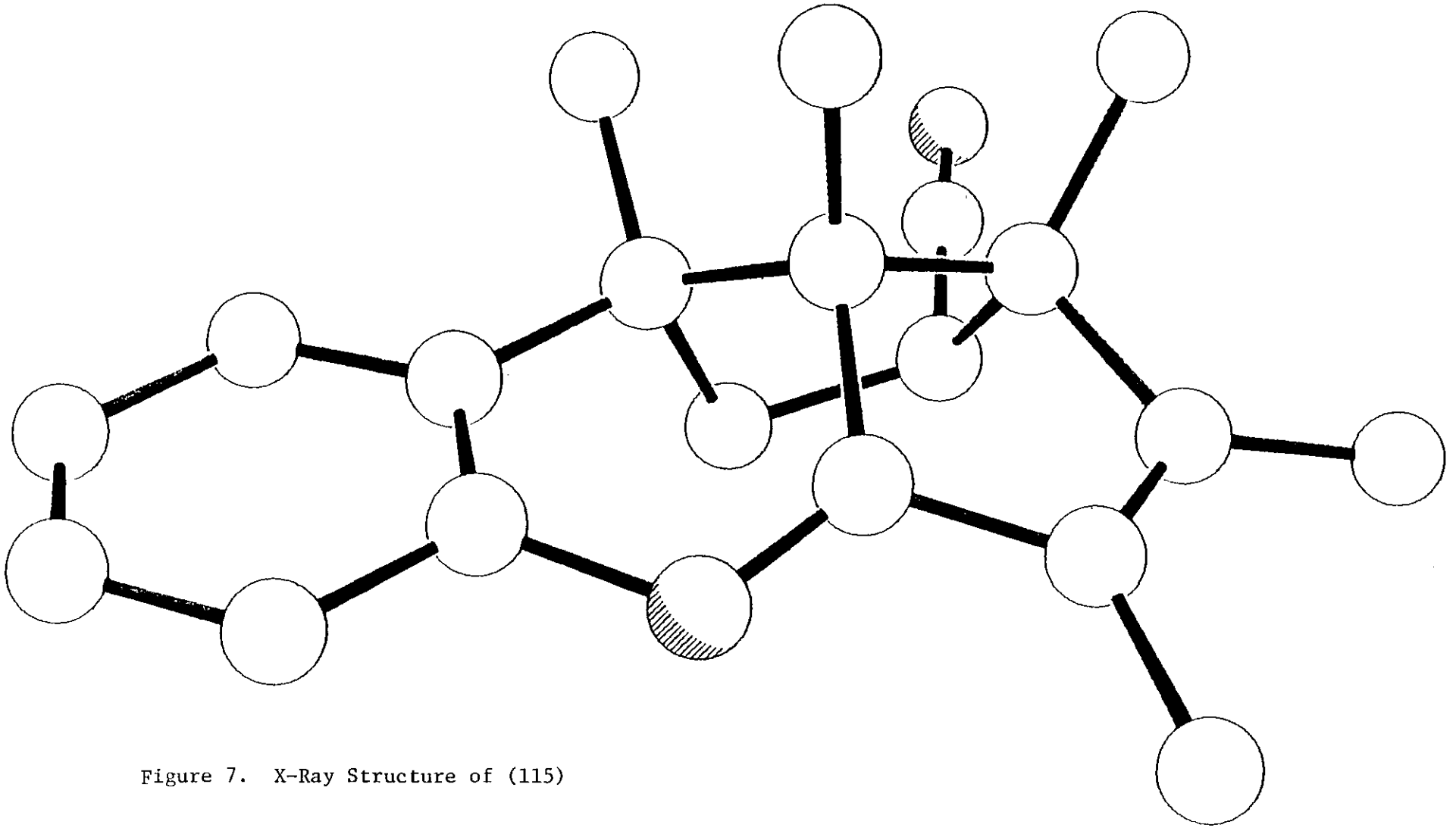
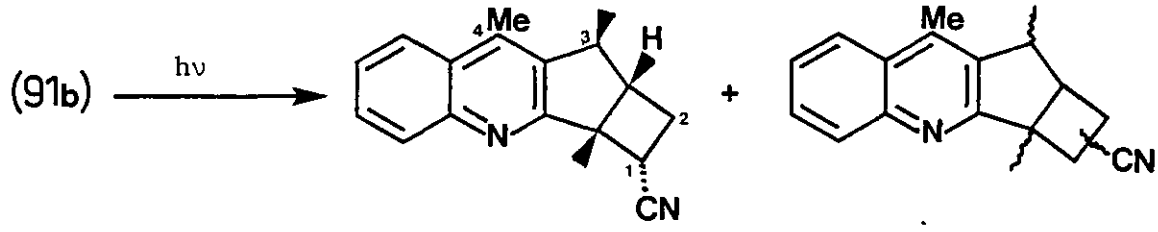


Figure 7. X-Ray Structure of (115)

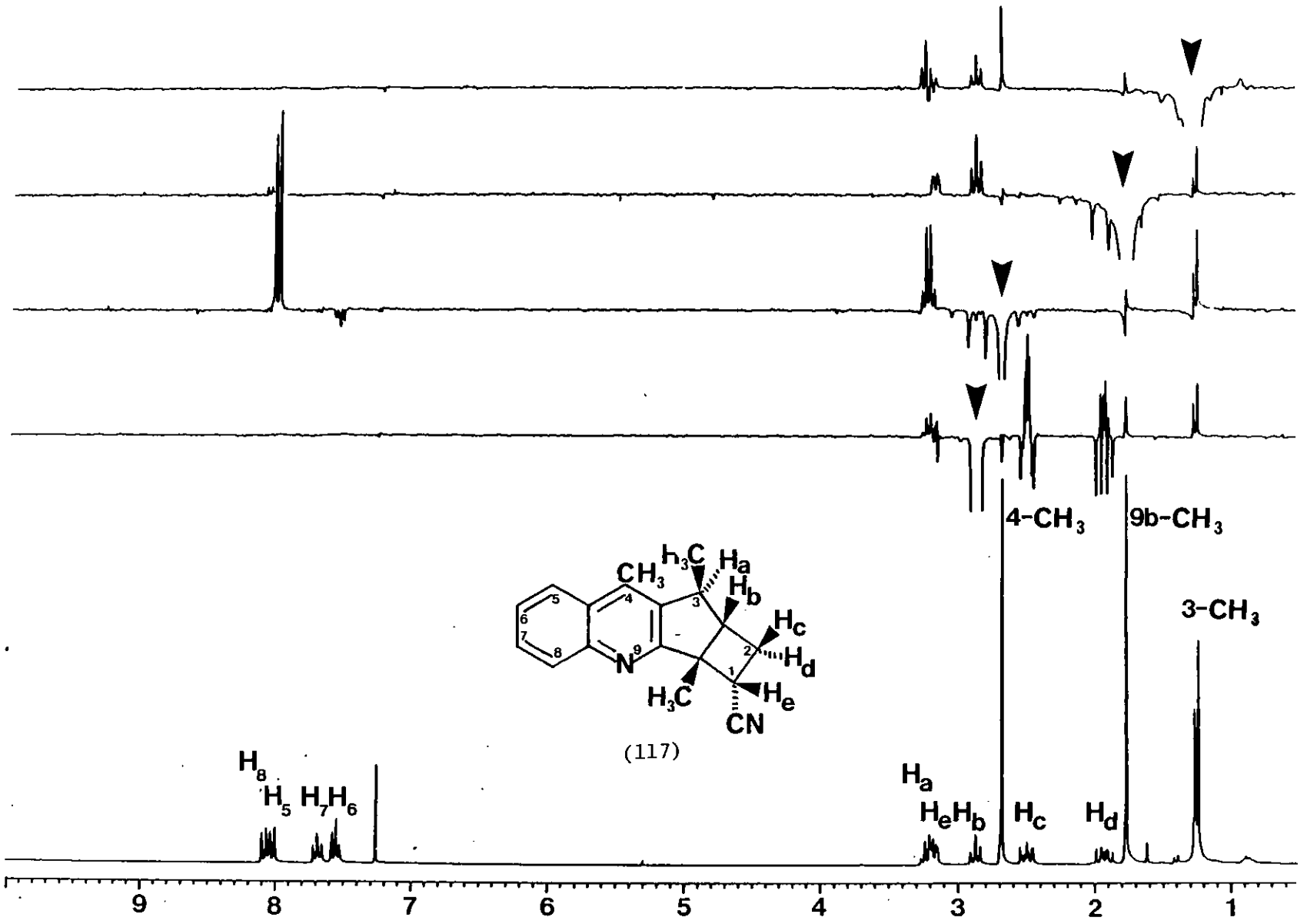
The regio-selectivity of this [8 (or 12) + 2] cyclo-addition may be rationalised on the grounds of frontier orbital coefficients. FMO calculations performed on the unsubstituted intermediate (114, R = H), predict that an interaction involving the LUMO of this with the HOMO of acrylonitrile leads to the observed regiochemistry.[59] However, the *exo* stereospecificity observed here is somewhat surprising in view of the preferred *endo* mode of addition of most dienophiles,[60] and could not be adequately rationalised by simple calculations.

In contrast, photolysis of 1-(2,4,6-trimethylphenyl)benzotriazole (91b) under the same conditions afforded none of the corresponding [8 + 2] adduct; the only products obtained being three isomeric [2 + 2] adducts. The structure of the major adduct (117), accounting for 60% of the total, was established by decoupling and n.O.e. experiments (Fig. 8). In this case,



(117)

migration of the hydrogen bridgehead substituent in intermediate (114b) occurs too fast for interception to occur, and the adducts obtained are formed subsequently to aromatisation by photochemical addition of the dienophile to cyclopentaquinoline (112b). The same three [2 + 2] adducts were obtained on irradiation of a solution of cyclopentaquinoline (112b) containing acrylonitrile. Attempts to intercept the intermediate (114b)



(117)

Figure 8. N.O.e. Difference Spectra of (117) in $CDC\ell_3$ at 250 MHz

using more reactive dienophiles such as chloroacrylonitrile or dimethyl azodicarboxylate led only to complex mixtures containing much polymeric material, from which no adducts could be isolated.

2.4. 1-(2-Methylnaphthyl)benzotriazole.

Although strong evidence exists in support of the formation of 4a*H*-carbazoles by extrusion of nitrogen from appropriate benzotriazoles, it is clear from the foregoing examples that these intermediates are not isolable under the conditions used to generate them. Stabilisation of systems related to-3a*H* indenes has been achieved by the inclusion of substituents (*cf.* 80), but in the present case, it was reasoned that stability might be most economically conferred to 4a*H*-carbazoles by further benzannelation. In order to test the validity of such reasoning, decomposition of the naphthyl benzotriazole (97), prepared as described previously, was investigated.

On subjection to FVP at 640°, the benzotriazole (97) gave rise to a very complex mixture of highly coloured components. No major products could be detected and this mode of decomposition was not further studied.

2.4.1. Photolysis of 1-(2-methylnaphthyl)benzotriazole.

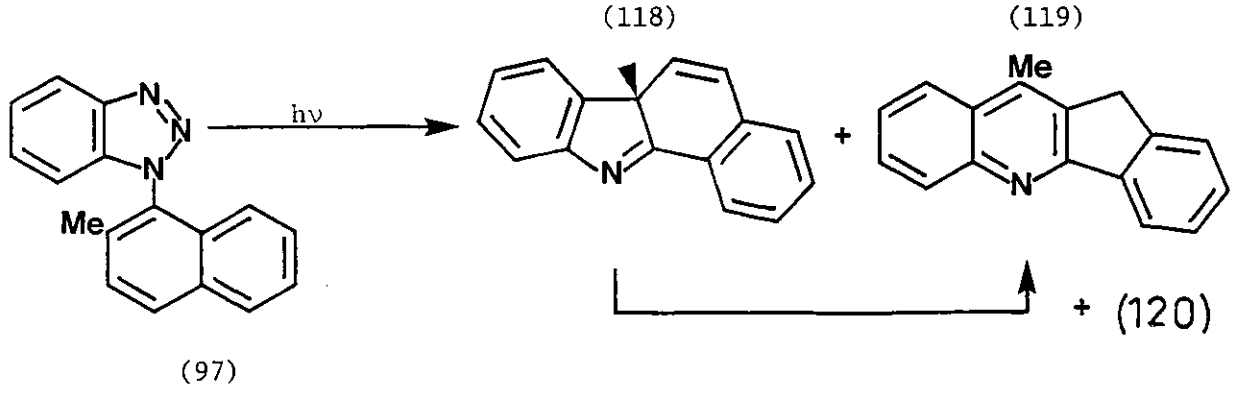
Irradiation of a solution of the benzotriazole in acetonitrile at 254 nm afforded a mixture of three products (Scheme 18).

Separation by careful chromatography enabled the first of these products to be identified as 6a-methyl-6a*H*-benzo[*a*]-carbazole (118). This exhibited an alkyl methyl group in the n.m.r. spectrum, together with a

characteristic AB quartet (J 8.6 Hz) due to the two olefinic protons. Further support for the isolation of this important product was provided by comparison with an authentic sample, previously synthesised by independent means (see next Chapter).

The second, and major component isolated exhibited only aromatic protons in the n.m.r. spectrum, with the exception of an aromatic methyl group and a two proton singlet at δ 4. From these and other spectroscopic properties, it was assigned as the indenoquinoline (119). It was established that this compound was a secondary product formed by further photochemical reaction of the 4a*H*-carbazole (118). The mechanism of this transformation and also further proof of the structure will be discussed in the next Chapter. A third product, (120), isolated as a red gum, eluded identification for some time. The properties of this compound, and the elucidation of its structure are described in the following section.

Maximum absorption by the 4a*H*-carbazole derivative (118) occurs at 250 nm, and it was anticipated that performing the photolysis of benzotriazole (97) at longer wavelength would suppress further reaction of the carbazole to the quinoline (119). This was indeed so; irradiation at 300 nm resulted in an inversion of product ratios, with the desired 4a*H*-carbazole (118), becoming the major product at the expense of the quinoline (Table 6).



(97)

SCHEME 18

TABLE 6. Photolysis of (97) for 10 h.

Wavelength (nm)	Conversion (%)	118 (%)	119 (%)	120 (%)
254	76	24	31	30
300	51	38	21	36

It is interesting to note that little change is observed in the yield of the third product (120).

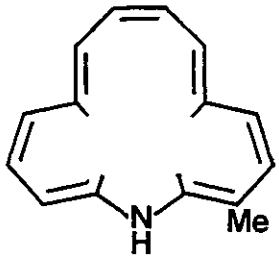
2.4.2. 1-Methylcycloocta[*def*]carbazole.

The mass spectrum of the red product (120) exhibited only a single peak which was taken to be due to the molecular ion, indicating it to be isomeric to the two other products, (118) and (119). Ionisation at higher energies lead to extensive decomposition and was of no diagnostic value.

With the exception of a one proton broad singlet, all of the remaining protons resonated above δ 7.1, which was in marked contrast with the starting material. Although not exchangeable with D_2O, the singlet was assigned as being due to an NH group, and this was supported by the i.r. spectrum. A three proton singlet at δ 2.3 suggested that the methyl group of the starting material had been retained, and was probably still attached to an aromatic nucleus. Decoupling experiments indicated that the remaining nine protons were arranged in three groups of two, three, and four protons and that each group was isolated from the others. The appearance of the four-spin system as two pairs of protons at δ 5.3 and 5.7 was strongly suggestive of the presence of an unsubstituted diene unit in the molecule. Confirmation of this was provided by the ^{13}C

spectrum, which showed only one carbon atom, taken as being that of the methyl group, to be sp^3 hybridised; the rest were all sp^2.

It is clear from the data presented that the starting material (97) had undergone a considerable transformation to give the red product (120), and that this was not related structurally to the two other products (118) and (119). The diversity of structures that could be suggested as being consistent with the data illustrated the need for further structural information, particularly regarding the periphery of the molecule. The required information was provided by two simple n.O.e. experiments. Thus, irradiation of the NH broad singlet induced enhancements of both the methyl group and one proton of the three proton group, indicating that the nitrogen is adjacent to both these groups. Irradiation of the methyl group in the reverse experiment confirmed its proximity to the nitrogen, and also established it to be flanked by the two proton group on the opposite side (Fig. 9). Assuming that each group of protons is isolated by a ring junction, the periphery of the molecule is deduced to be as shown (121). An obvious placing of the two remaining interior carbon



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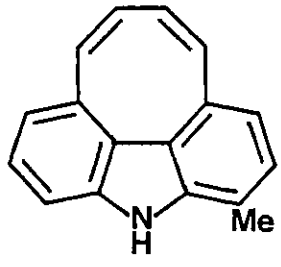


(120)

atoms would be such as to give two six membered aromatic rings, leading to 1-methylcycloocta[*def*]carbazole (120) as the third photolysis product of the benzotriazole (97).

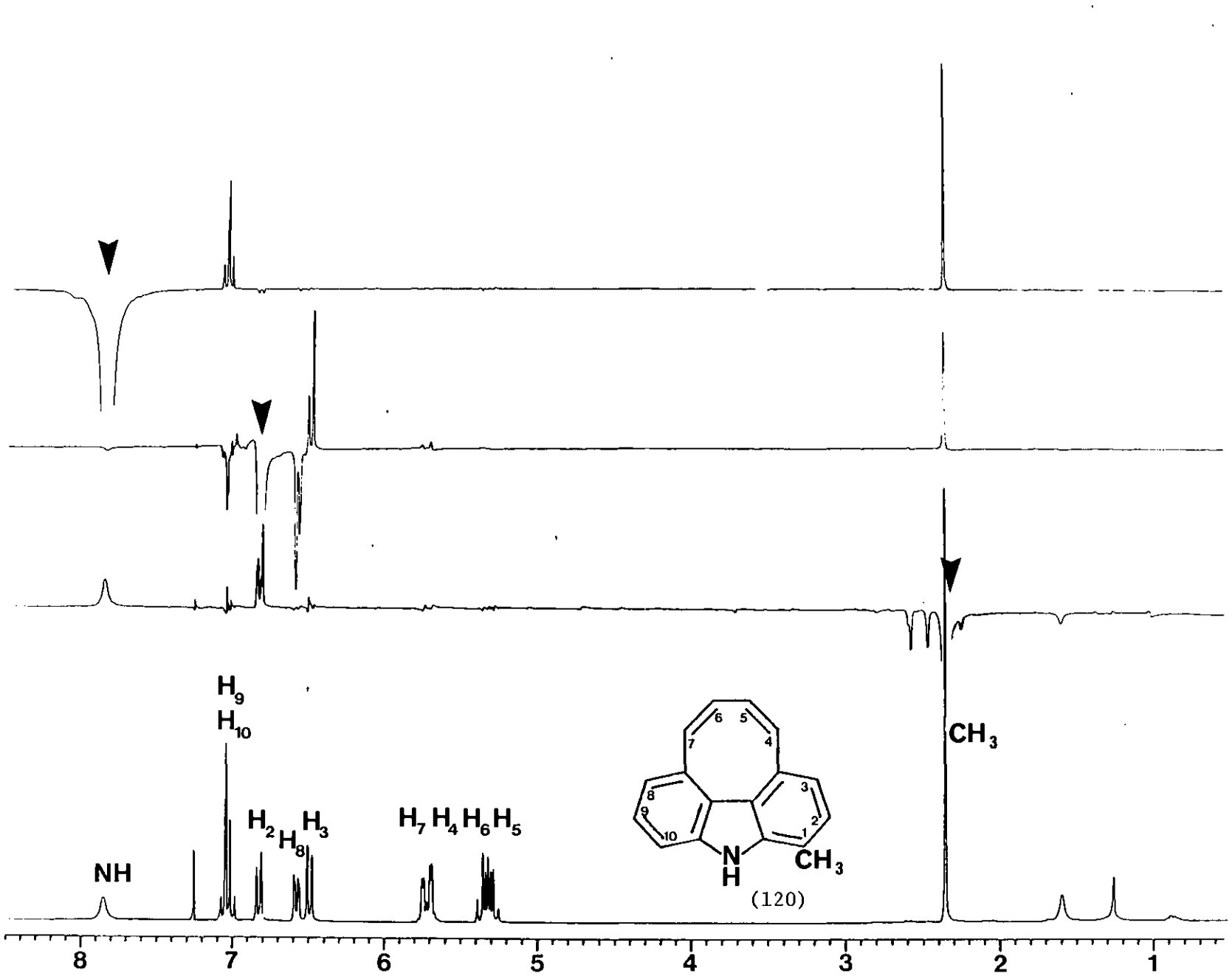
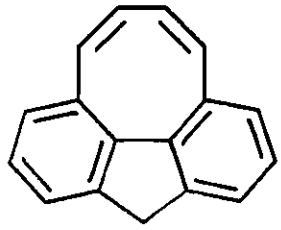
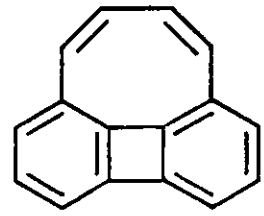


Figure 9. N.O.e. Difference Spectra of (120) in $CDC\ell_3$ at 250 MHz

Although neither the proposed product (120), nor its unsubstituted parent have been reported in the literature, the two related hydrocarbons (122)[61] and (123)[62] are known. These compounds have recently commanded



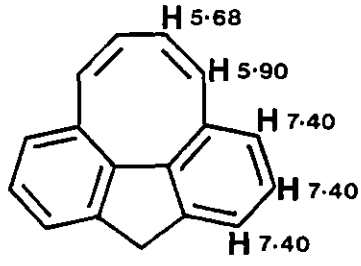
(122)



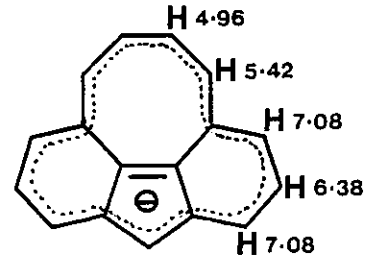
(123)

considerable theoretical interest since they are formally examples of planar cyclooctatetraenes and as such, might be expected to show antiaromatic properties. The paratropicity[63] observed in their n.m.r. spectra is claimed to be a manifestation of this proposed antiaromaticity.[61]

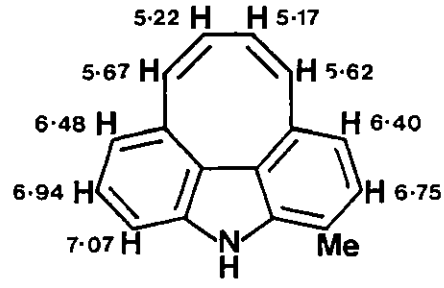
A comparison of the chemical shifts of protons in the red product with those of the fluorene (122) and its anion (124)[61] indicates that the former is intermediate between the two, with regard to its paratropic properties. The considerable upfield shift of the protons observed



(122)

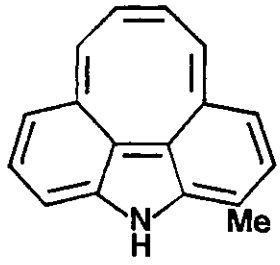


(124)

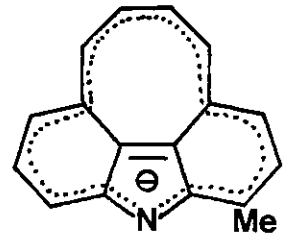


(126)

on going from the hydrocarbon (122) to the heterocycle (120) cannot be adequately explained solely in terms of electron donation by nitrogen. Simple carbazoles do not show analogous trends with their carbocyclic counterparts. Although some paratropic contribution may be provided by the peripherally delocalised 16π resonance form (120a), the extent



(120a)



(125)

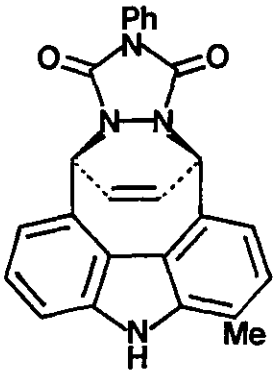
of this cannot be assessed by n.m.r. properties alone. Whilst the ring currents of monocyclic annulenes, as determined by the n.m.r. properties of peripheral substituents, may be taken as a criterion for their degree of aromaticity,[64] the same is not true for polycyclic molecules containing both $(4n + 2)\pi$ and $4n\pi$ delocalised systems. Wilcox has demonstrated[65] that in these cases the overall magnetic properties are further complicated by additional contributions from individual rings.

An attempt to investigate the effect on paratropicity of electron donation by deprotonation of the carbazole (120) to the anion (125)[61] was unsuccessful, leading only to complete destruction of the molecule.

In view of the novelty of the carbazole (120), an unequivocal structure determination by X-ray crystallography was desirable. Although initially obtained as a gum, the photolysis product (120) was induced to crystallise. Unfortunately, however, the crystals obtained were too disordered to allow

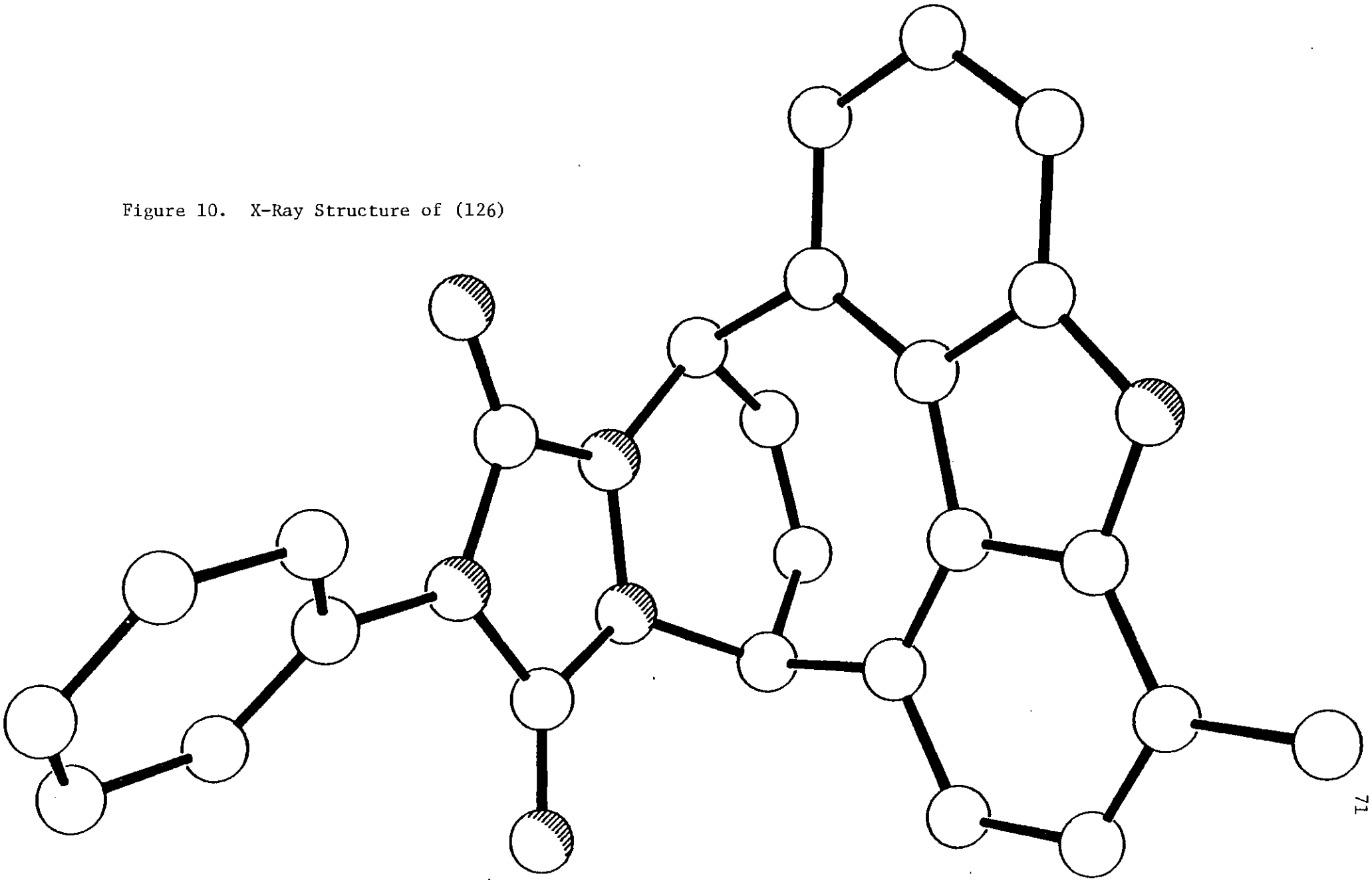
for an X-ray determination to be performed. All attempts to obtain crystalline derivatives by alkylation or acylation on nitrogen under a variety of conditions failed; either recovery of starting material or decomposition took place. Addition of bromine to the olefinic double bonds resulted in an intractable tar. However, with PTAD[66] a quantitative yield of a high melting 1:1 adduct was obtained, and assigned the structure due to [4 + 2] addition (126). Confirmation was provided by an X-ray determination (Fig. 10).

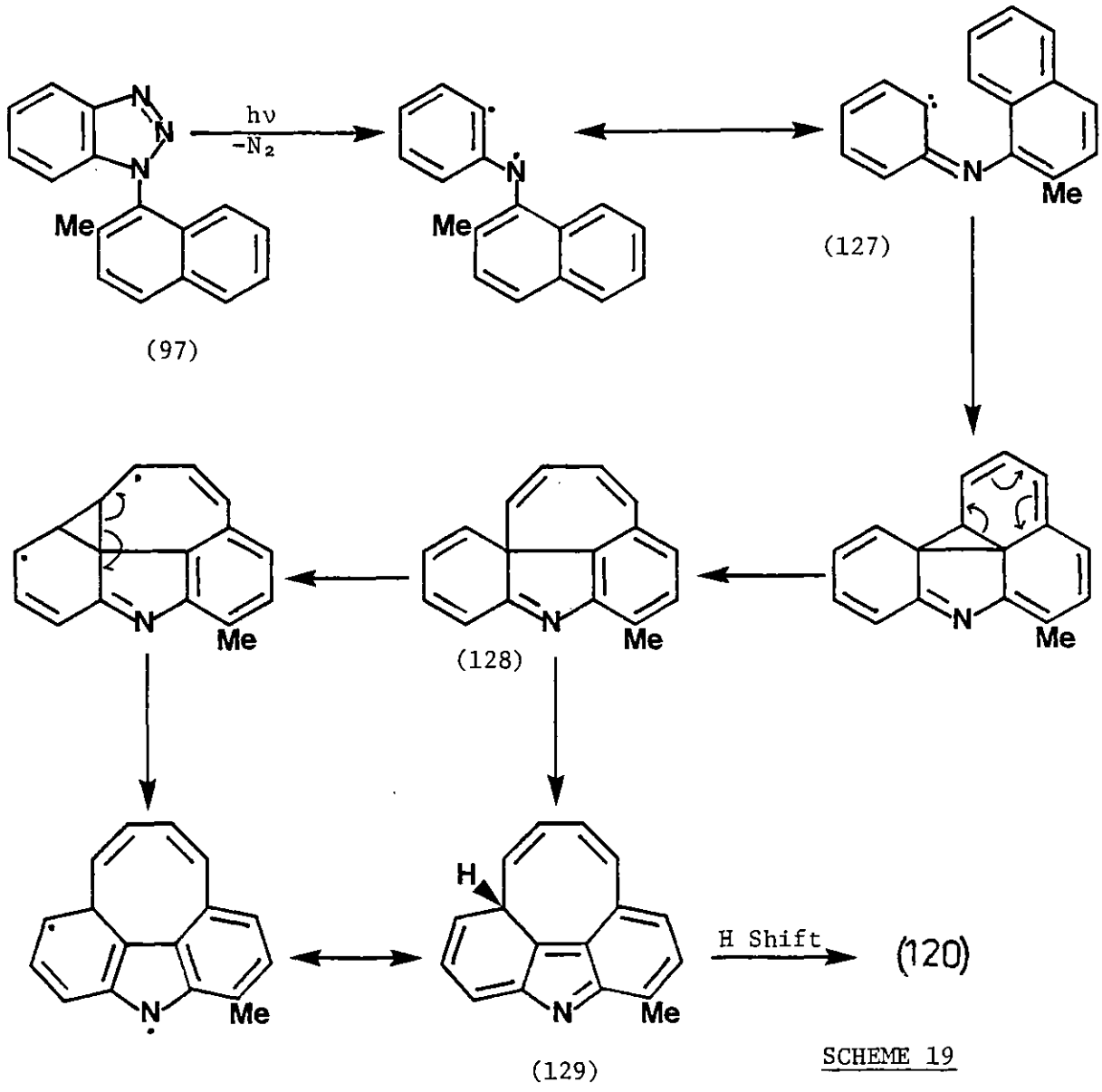
(126)



The formation of 1-methylcycloocta[*def*]carbazole (120) on photolysis of the benzotriazole (97) presents an interesting mechanistic problem. It may, for instance, involve addition of the imidoyl carbene form of the diradical (127), generated on extrusion of nitrogen, to a double bond of the naphthyl group. Concommitant ring opening of the resultant norcaradiene by Cope rearrangement leads to the seven membered ring 4a*H*-carbazole (128). Ring expansion of this intermediate to the 4*H*-carbazole (129) formally involves a [1,9] migration of a σ bond. A thermally allowed concerted process of this type is considered unfavourable and a two step di-π-methane rearrangement is presented as a more plausible alternative (Scheme 19).

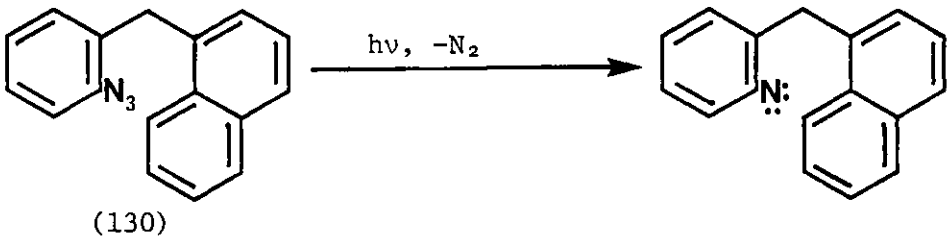
Figure 10. X-Ray Structure of (126)



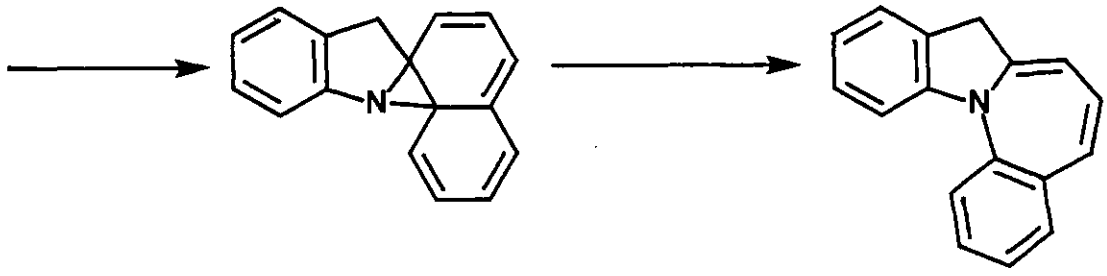


SCHEME 19

Although other mechanisms are possible, all require an electrocyclic reaction of some kind to occur at the ring junction (8a) position of the naphthyl group. Such processes appear to be exceedingly rare; only one related example could be found in the literature. Similar addition of a nitrene to a double bond in a naphthyl group, with subsequent ring expansion has been proposed by Jones, *et al.*[67] to account for the formation of the azepine (131) as a minor product on photolysis of the azide (130).

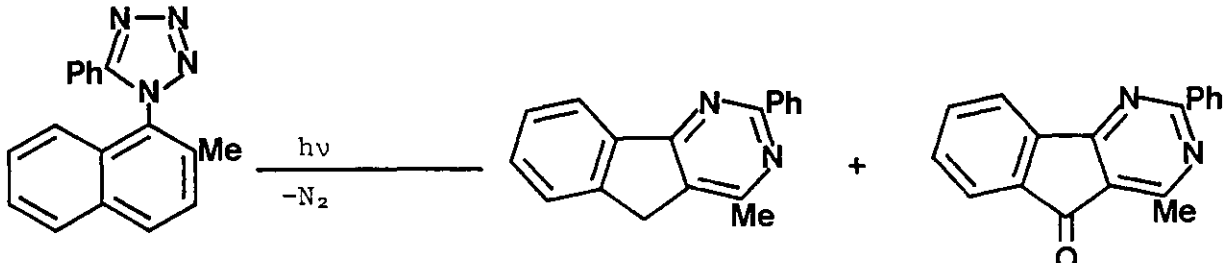


(130)

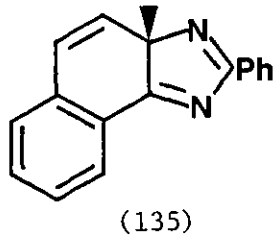


(131)

The behaviour of photolysis and thermolysis of benzotriazoles (91) bearing a mononuclear aryl substituent clearly resembles that of the corresponding tetrazoles (10). It is interesting, therefore, to contrast the properties of naphthyl benzotriazole (97) with those of the tetrazole (132). The pyrimidine (133), corresponding to the indenoquinoline (119), together with some of its oxidised derivative (134) were the only products isolated on photolysis of the latter.[10] No mention was made by the authors of the presence of the 3a*H*-benzimidazole (135), or any ring expanded products.



(132) (133) (134)



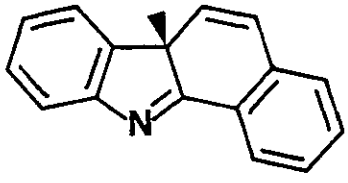
(135)

3. THE SYNTHESES AND PROPERTIES OF BENZANNELATED 4a*H*-CARBAZOLE DERIVATIVES

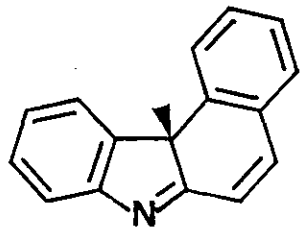
3. THE SYNTHESIS AND PROPERTIES OF BENZANNELATED 4a*H* CARBAZOLE DERIVATIVES.

The work described in this chapter was based on the assumption that the stability of 4a*H*-carbazoles could be greatly enhanced by benzannelation. At the time these investigations were in progress, this fact had not yet been demonstrated by isolation of the 4a*H*-carbazole (118) from photolysis of the benzotriazole (97) (Scheme 18).

The two isomeric benzo-fused derivatives (118) and (136) were chosen for investigation.



(118)

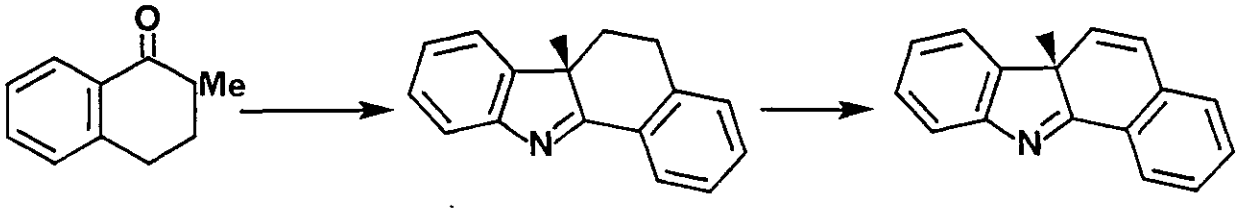


(136)

3.1. Synthesis.

3.1.1. 6a-Methyl-6a*H*-Benzo[*a*] carbazole.

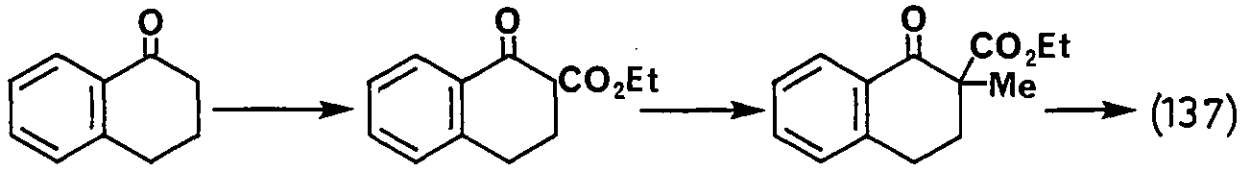
The proposed route to the benzo[*a*] derivative (118) involved introduction of a double bond into the known dihydro-compound (138),[68] readily available by Fischer cyclisation of the phenylhydrazone of 2-methyl-1-tetralone (137). It was hoped that the final transformation could be



(137) (138) (118)

effected using one of the many methods developed for functionalising benzylic positions.

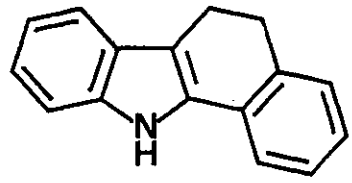
According to Temple Robinson,[69] methylation of the 2-ethoxycarbonyl derivative of tetralone (139) followed by hydrolysis and decarboxylation provided the starting material.



(139)

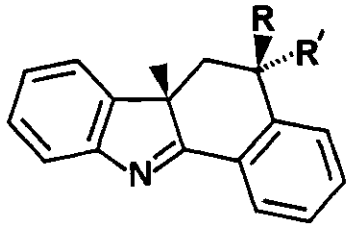
On reflux in acetic acid containing boron trifluoride etherate, the phenylhydrazone of this ketone afforded the dihydro precursor (138) in 74% yield. This method for performing the Fischer cyclisation represents a considerable improvement, both in ease of manipulation and yield of product obtained, over the literature procedure, in which polyphosphoric acid is used as the catalyst.[68]

Although it afforded a pure product, the aforementioned methylation of tetralone was discontinued on account of its length and inefficiency in favour of direct methylation. Treatment of the LDA-generated enolate of tetralone with methyl iodide in the presence of HMPA furnished a mixture predominating in the desired product (137), together with unreacted starting material. Inability to separate the two presented no difficulties; on exposure of the mixture of phenylhydrazones to Fischer reaction conditions, the required carbazolenine (138) was readily separable from the accompanying indole (140) by virtue of its greater basicity.



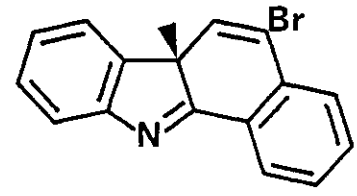
(140)

Attention was next turned to oxidation of the benzylic position in the dihydro compound (138), either to introduce functionality at this position, or to effect direct dehydrogenation. Treatment with DDQ in refluxing toluene,[70] BSA in chlorobenzene at 100°,[71] or selenium dioxide in ethyl acetate[72] lead only to recovery of starting material. Use of the latter reagent in acetic acid and anhydride resulted in a complex mixture of polar components. However, benzylic bromination was more successful. Hence, irradiation of a refluxing solution of the carbazole-nine (138) in carbon tetrachloride containing suspended NBS[73] afforded three products, together with some unchanged starting material. One of these was isolated as a crystalline solid, and identified as the β-bromide (141a) on the basis of n.m.r. coupling constants. The other two products were inseparable, but spectroscopic properties indicated them to be the isomeric α-bromide (141b), and the bromo olefin (142).



(141)

a) R = Br, R^1 = H
b) R = H, R^1 = Br
c) R = R^1 = Br



(142)

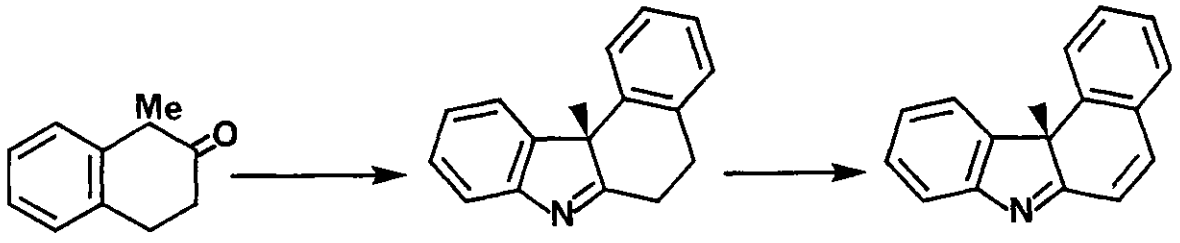
The relative yields of these products were dependent on reaction conditions, and the highest yields of monobromides (141a) and (141b) were obtainable by using 1.25 equivalents of NBS in refluxing carbon tetrachloride with irradiation in the presence of a trace of radical initiator. Under these conditions, all of the starting material was consumed to give the α-bromide (141b) as the major product. The presence of *gem*-dibromide (141c) was also detected, but its instability precluded isolation; on chromatography, rapid elimination occurred, resulting in the olefin (142).

Smooth elimination of hydrogen bromide occurred from both bromides (141a) and (141b), on treatment with DBU in refluxing benzene, furnishing the desired 4a*H*-carbazole derivative (118) in excellent yield. The product isolated from the α-bromide (141b), however, was consistently found to be contaminated by the vinyl bromide (142), from which it was inseparable. Attempted debromination of the contaminant *via* its Grignard or lithio derivatives proved unsuccessful. Partial separation was finally achieved by the use of multiple chromatography but was very time consuming and wasteful of materials.

As had been hoped, this derivative of 4a*H*-carbazole proved to be totally stable under normal conditions, and could even be purified by short path distillation at reduced pressure, to give a pale green gum which very slowly discoloured on exposure to air.

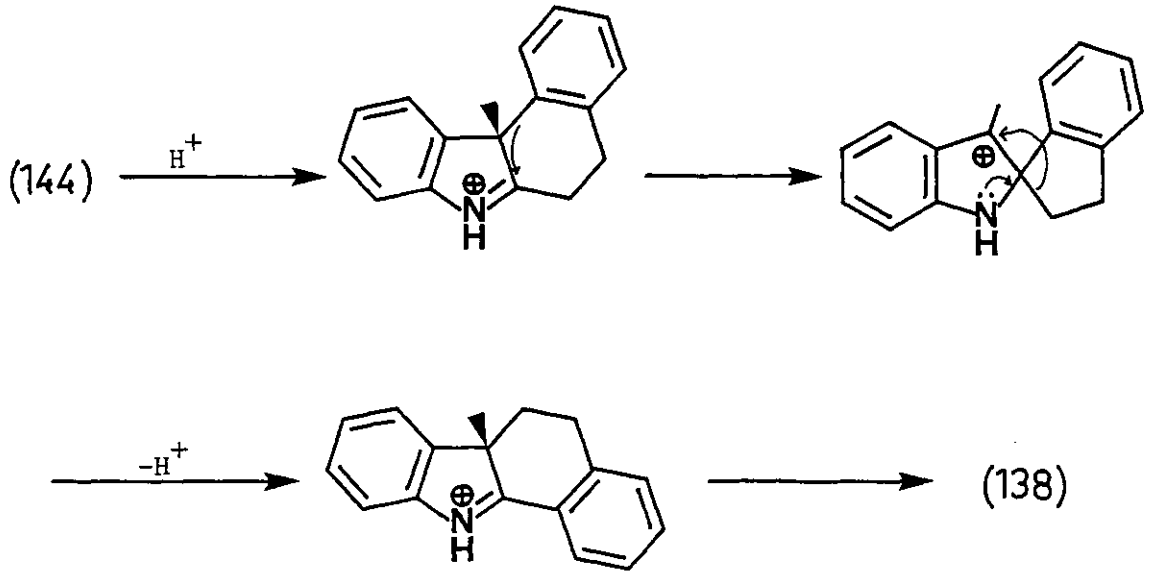
3.1.2. 11b-Methyl-11b*H*-Benzo[*c*]carbazole.

An analogous strategy to that described for the benzo[*a*]isomer (118) was adopted for this derivative.



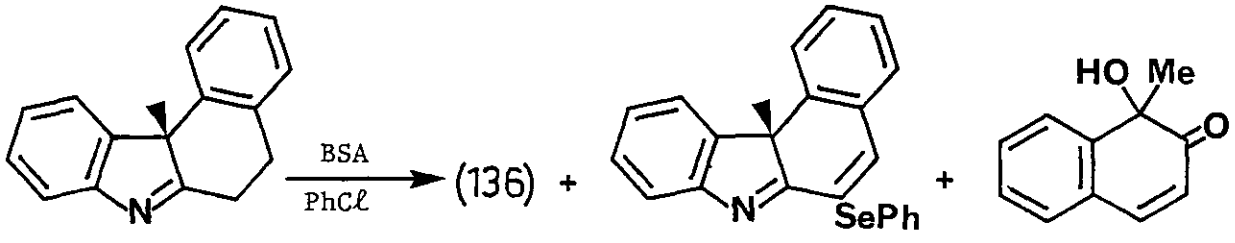
(143) (144) (136)

Excellent and reproducible yields of starting material (143) were provided by methylation of 2-tetralone *via* its pyrrolidine enamine.[74] On reflux in acetic acid, the phenylhydrazone of 1-methyl-2-tetralone afforded a carbazolenine which, on isolation, was unexpectedly found to be identical to that derived from the isomeric ketone (138). In retrospect, this result is not entirely surprising; similar examples of "Plancher rearrangements" have been reported by Nakazaki[68] and are believed to involve successive Wagner-Meerwein shifts. These rearrangements



could be suppressed by using less vigorous conditions for the cyclisation. With cold, ethanolic hydrogen chloride,[68] the only isolable product proved to be the desired carbazolenine (144); the literature yield[68] could be substantially improved upon by simply prolonging the time of reaction.

Oxidation of this isomer was expected to be easier than the benzo[*a*]-carbazolenine (138) due to the extra activation provided by the presence of the imino group. Although DDQ in toluene afforded a complex mixture, smooth dehydrogenation occurred with BSA in chlorobenzene, providing 11b-methyl-11b*H*-benzo[*c*]carbazole (136) in yields of 50%. In addition to the desired olefin (136), substantial quantities of a selenated product, identified as the 6-phenylseleno derivative (145) were obtained, and in one case, a trace of the hydroxy enone (146) was found (Scheme 20).



(144) (145) (146)

SCHEME 20

Analogous formation of vinyl selenides corresponding to (145) has been observed in the dehydrogenation of steroidal ketones with BSA,[75] and is thought to involve low valent selenium species, formed on reduction of the anhydride, as the selenating agents. A solution to the problem recently developed by Barton and his co-workers makes use of a co-oxidant which keeps these selenium species at as high an oxidation level as possible.[75] The use of such oxidants as iodoxybenzene, which has been found particularly effective, is beneficial both in suppressing undesirable side reactions, and also by allowing catalytic quantities of BSA to be used.

Application of these conditions to the oxidation of the carbazolenine (144) resulted in a slight increase in yield of the 4a*H*-carbazole derivative (136), at the expense of vinyl selenide (145) formation. A small quantity of a second, previously undetected selenium containing species was also observed, but this compound was not identified.

As with the benzo[*a*] isomer (118), 11b-methyl-11b*H*-benzo[*c*]carbazole (136) possessed considerable thermal stability and on distillation was obtained as a gum which later solidified m.p.90-92°.

3.2. Photolysis of Benzannelated 4a*H*-Carbazole Derivatives.

Irradiation of an acetonitrile solution of 6a-methyl-6a*H*-benzo[*a*]-carbazole (118) at 254 nm for seven hours resulted in the formation of two products, together with an amorphous solid which appeared to be polymeric and was not further investigated. The minor of the products was shown by comparison with an authentic sample to be benzo[*a*]carbazole (147). The other product was found to be identical to that obtained on photolysis of 1-(2-methylnaphthyl)benzotriazole (97), (Scheme 18), and its identification as the indenoquinoline (119) was supported by an n.O.e. experiment (Fig. 11), which established that the methyl and methylene groups were proximate to one another. Unequivocal confirmation of the structure was further provided by independent synthesis (Chapter 6).

In contrast, the benzo[*c*] derivative (136) proved photochemically inert; irradiation in acetonitrile solution at 254 nm for forty four hours resulted in 78% recovery of starting material, the remainder having decomposed to base line material.

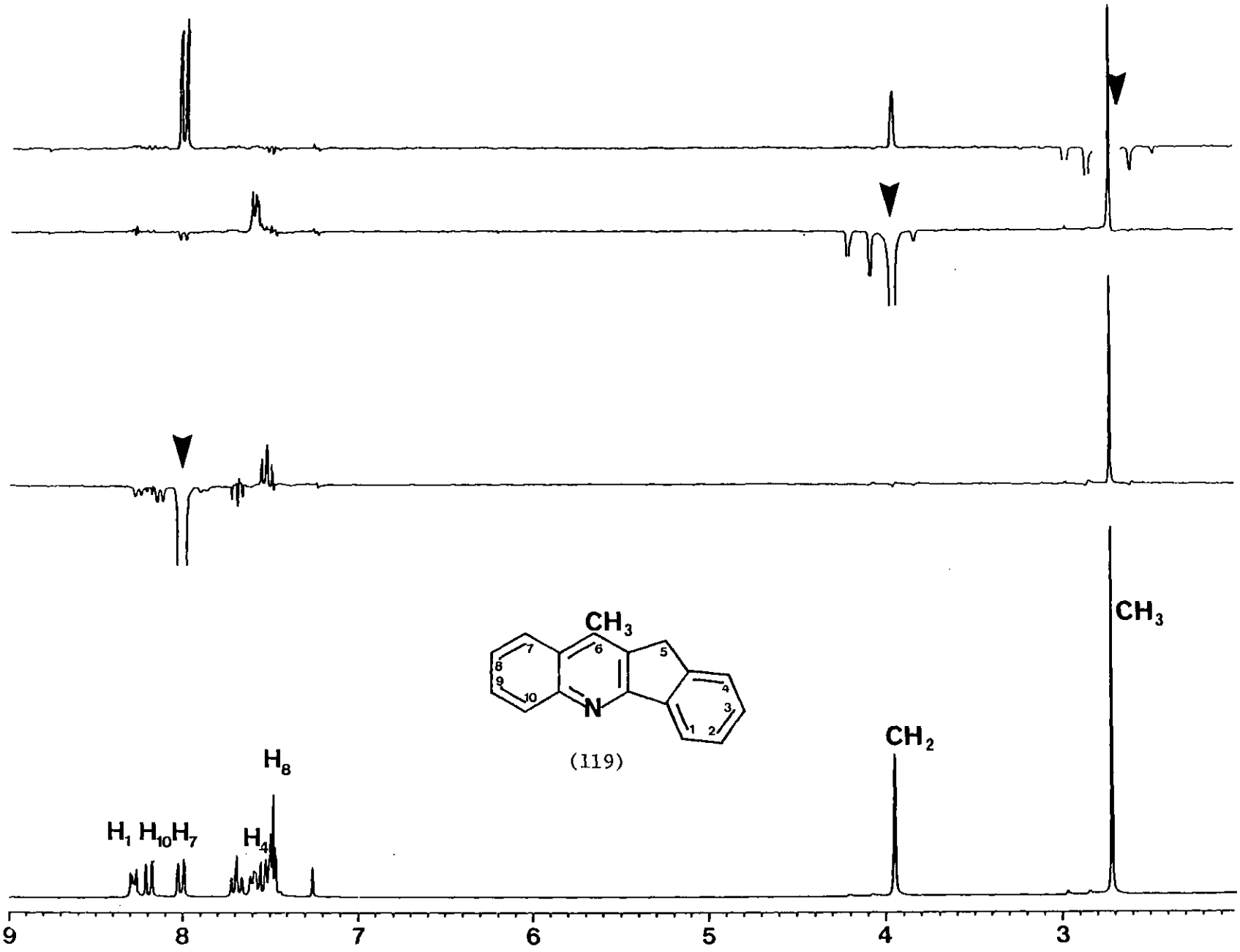
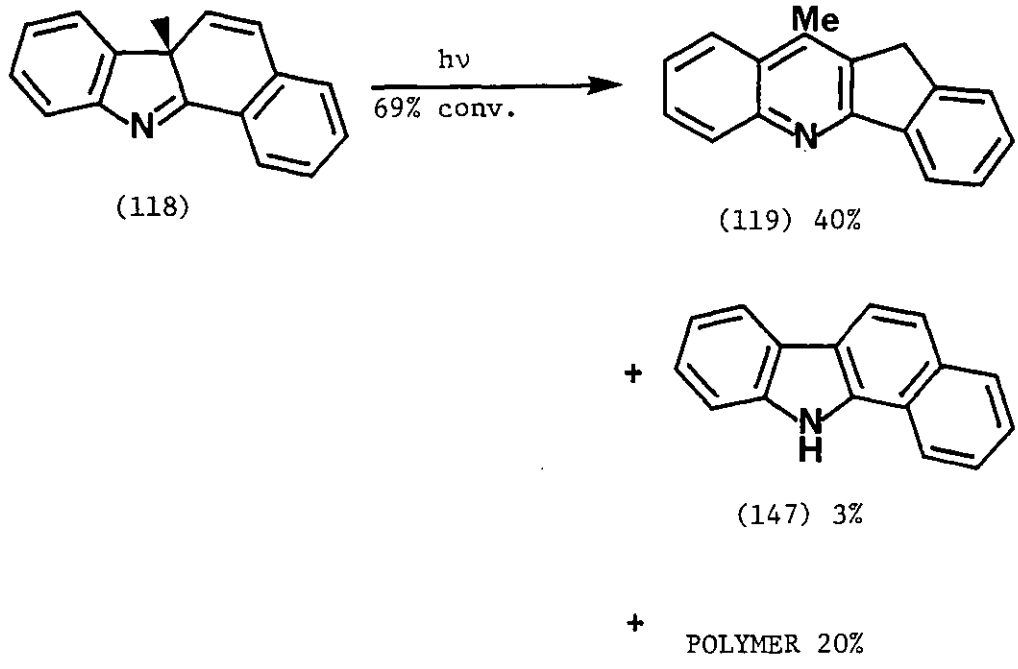


Figure 11. N.O.e. Difference Spectra of (119) in $CDC\ell_3$ at 250 MHz



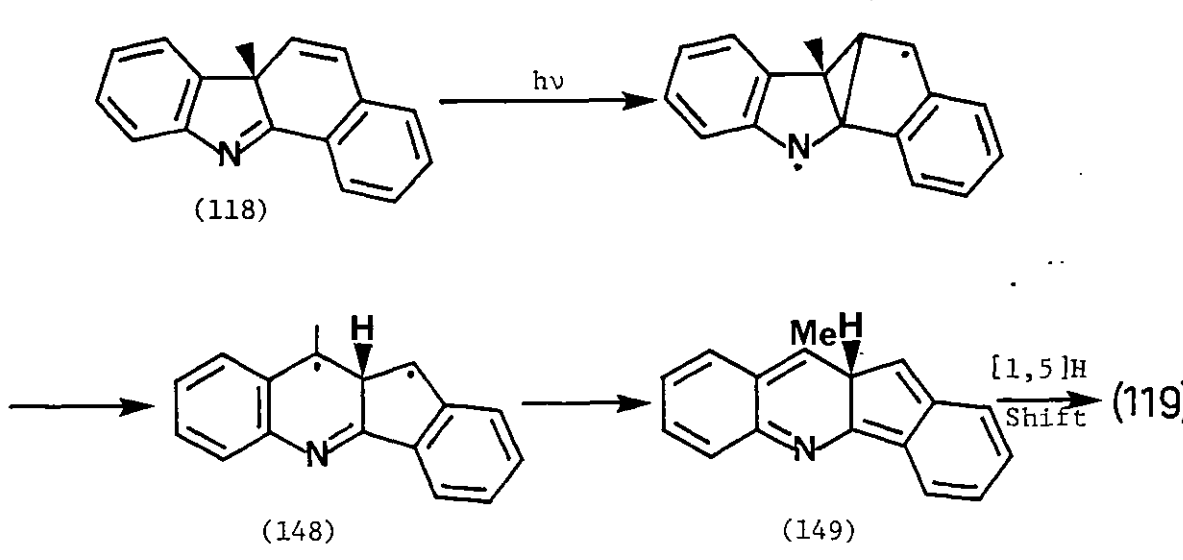
(118)

(119) 40%

(147) 3%

+ POLYMER 20%

The indenoquinoline (119) clearly resembles the cyclopentaquinolines (112) obtained on photolysis of benzotriazoles (91), and an analogous mechanism may be proposed for its formation (Scheme 21; *cf.* Scheme 17). In this case, however, aromatisation may occur directly from the diradical (148) by a simple[1,2] hydrogen migration, thereby circumventing the need



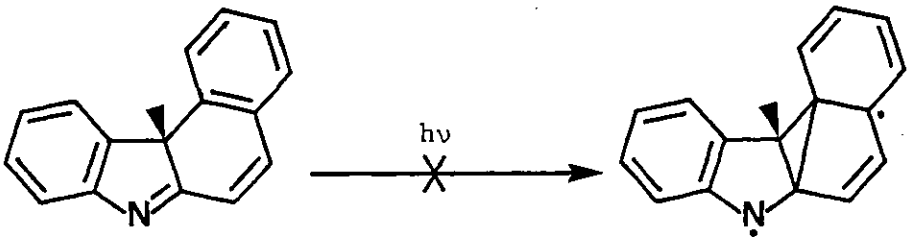
(118)

(148)

(149)

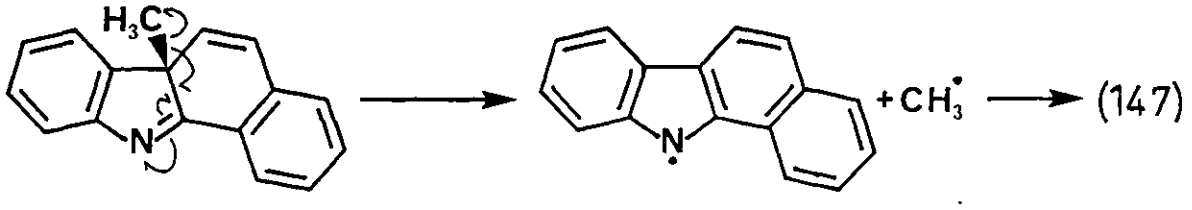
SCHEME 21

propose a high energy, bis-σ-quinoidal intermediate (149). The stability of 11b-methyl-11b*H*-benzo[*c*]carbazole (136) under these conditions, lends further support for such a mechanism. Presumably in this case the first step of the aza-di-π-methane rearrangement is a highly unfavourable process due to the disruption of aromaticity in one ring.



(136)

The loss of a methyl group observed on photolysis of some benzotriazoles (Section 2.3) was proposed to occur from a highly energetic state of the corresponding 4a*H*-carbazole derivative produced on collapse of the di-radical generated on extrusion of nitrogen from the triazole. Such a rationale is not possible for the benzannelated derivative (118) which was not generated *in situ*. A possible mechanism to account for the formation of benzo[*a*]carbazole (147) involves homolytic cleavage of the bridgehead methyl group to give a stabilised carbazolyl radical (150) which may then abstract hydrogen from the solvent.

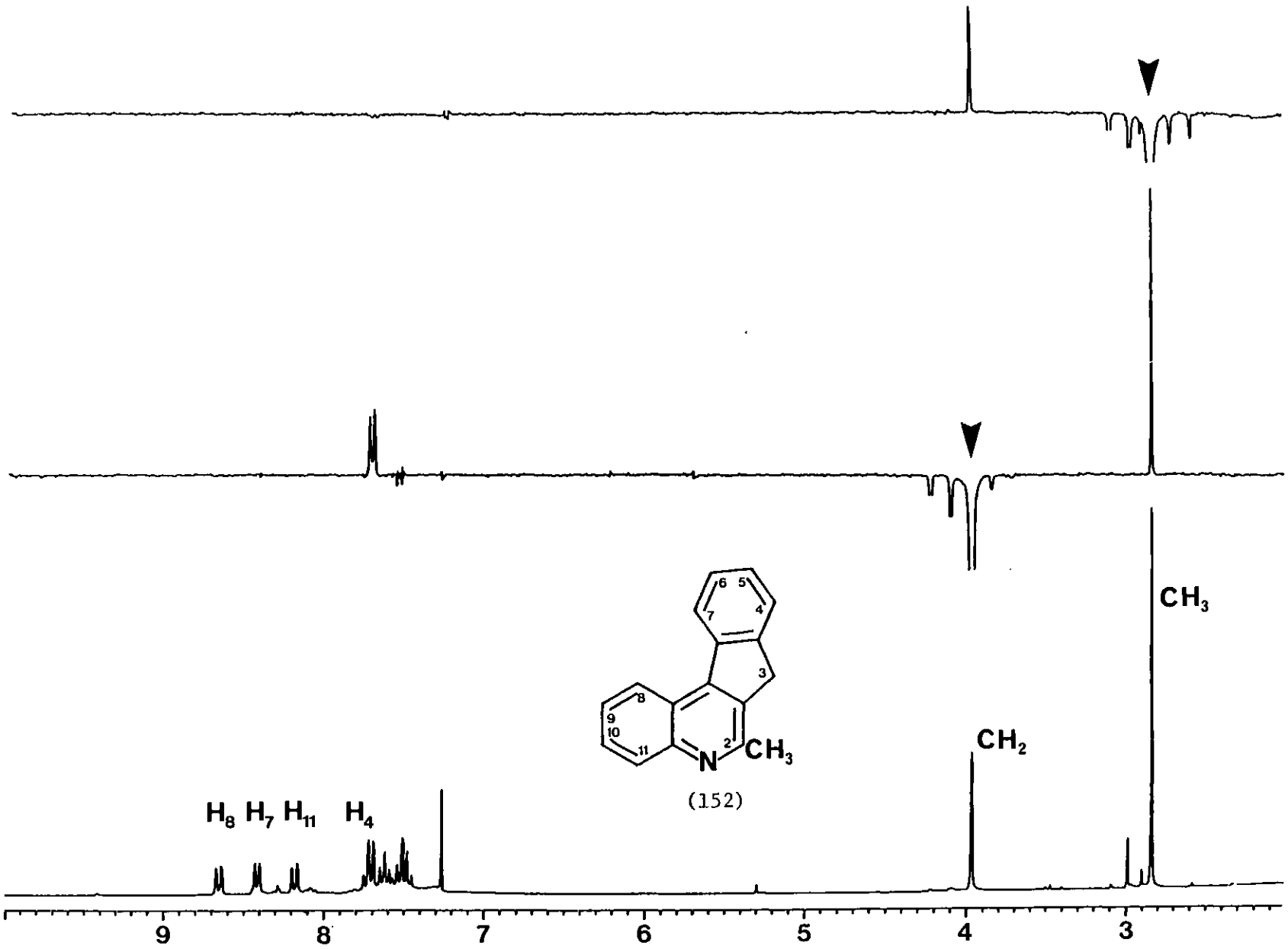


(150)

3.3. FVP of Benzannelated 4a*H*-Carbazole Derivatives.

FVP at 640° and 3 x 10^{-2} mm Hg of 6a-methyl-6a*H*-benzo[*a*]carbazole (118) resulted in the isolation of three products, the major of which was benzo[*a*]carbazole (147). A methyl singlet at δ 4 in the n.m.r. spectrum of the second product was suggestive of 11-methylbenzo[*a*]carbazole (151), and this was confirmed by other spectral data and comparison with an independently synthesised sample. The spectral characteristics of the third product bore very close resemblance to those of the indenoquinoline (119), but the two were shown not to be the same by their properties on t.l.c.; the pyrolysis product being much more polar than that from photolysis. The enhancement of the methyl group on irradiation of the methylene singlet in an n.O.e. experiment (Fig. 12) indicated that the two were close to each other (*cf.* Fig. 11). However, the reverse experiment, although showing the expected enhancement of the methylene group, did not lead to any enhancement of aromatic protons, suggesting that the methyl group is adjacent to the quinoline nitrogen. Confirmation of this was obtained on addition of Eu(Fod)$_3$ shift reagent, which was expected to complex with the basic nitrogen and hence exert considerable effect on the adjacent methyl group. The results obtained on gradual addition of the lanthanide reagent are presented in Table 7 and show that maximum change in chemical shift occurred for the methyl group and also one of the low-field protons, identified as being that at the 8-position of the quinoline.

These results, combined with the presence of two low field protons suggest that the third pyrolysis product is the angular indenoquinoline (152); the two low field protons being those in the " bay region" .

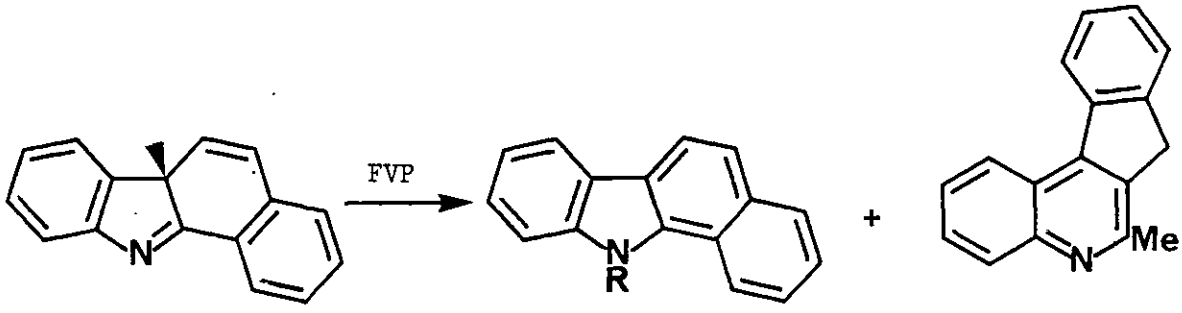


(152)

Figure 12. N.O.e. Difference Spectra of (152) in $CDC\ell_3$ at 250 MHz.

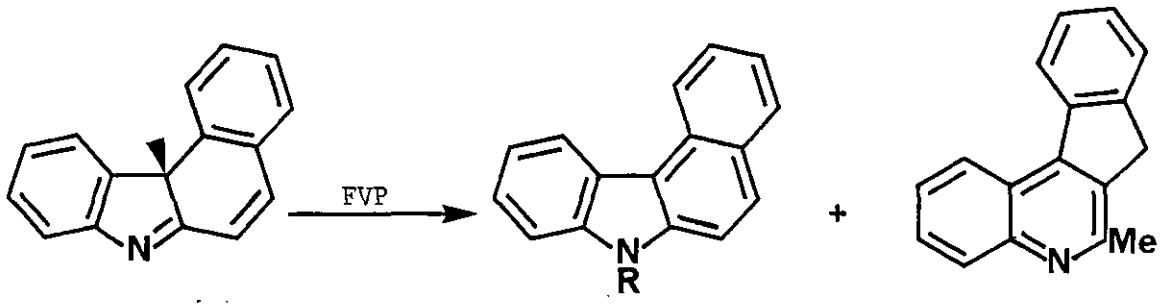
TABLE 7. Change in chemical shift of selected n.m.r. signals in (152) on addition of $Eu(fod)_3$.

Signal / $Eu(fod)_3$ (mg)	Me group	$-CH_2-$ group	Proton at δ 8.17	Proton at δ 8.40	Proton at δ 8.63
0.5	0.03	0	0.05	0	0
1.5	0.10	0.01	0.14	0	0.01
3.0	0.15	0.04	0.20	0	0.02



(118) (147) R = H (151) R = Me (152)

Under identical FVP conditions, the isomeric benzannelated 4a*H*-carbazole (136) similarly afforded the corresponding unsubstituted benzocarbazole (153), together with its *N*-methyl derivative (154) and also, rather surprisingly, the same angular indenoquinoline (152) as obtained from the benzo[*a*] isomer. The results of both pyrolyses are compared (Table 8).

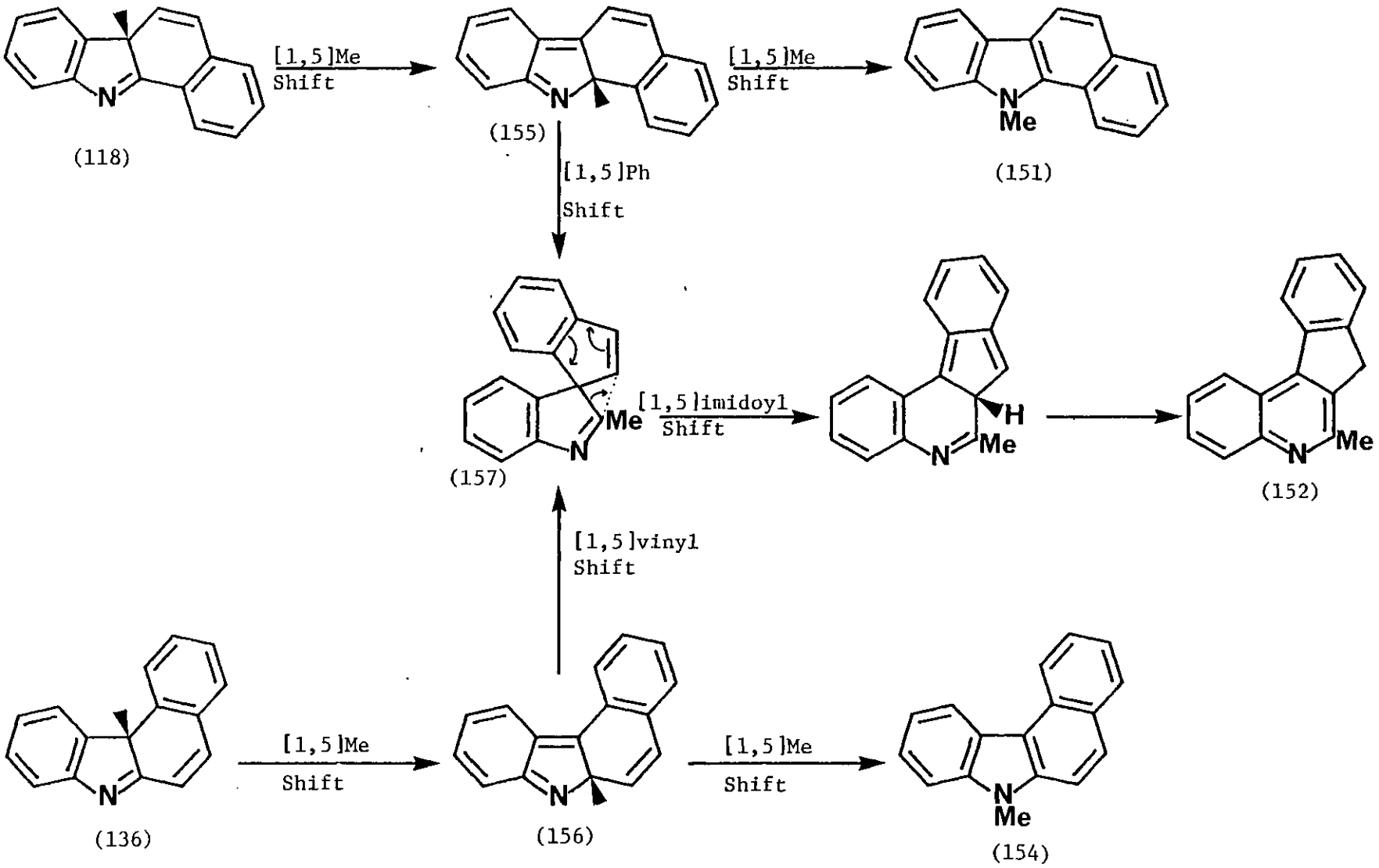


(136) (153) R = H (154) R = Me (152)

TABLE 8. FVP of benzannelated 4a*H*-carbazole derivatives at 640°.

4a*H*-Carbazole Derivative	Conversion (%)	Yield of N-Me Carbazole (%)	Yield of N-H Carbazole (%)	Yield of Indeno-quinoline (152) (%)
118	93	24	32	23
136	88	12	19	47

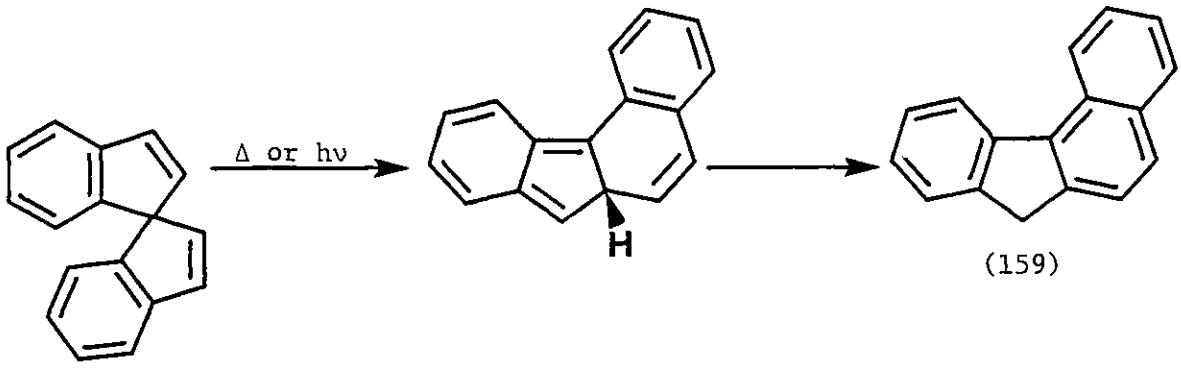
Both *N*-methylated carbazoles (151) and (154) are most probably formed by two subsequent [1,5] methyl migrations of the bridgehead substituent in the corresponding 4a*H*-carbazole derivatives, (118) and (136) respectively. Loss of the methyl group to give the two demethylated products (147) and (153), is most likely to occur in the course of these migrations, rather than from nitrogen in the final product, since pyrolysis of the substituted carbazole (154) at 640° afforded no demethylated product. The isolation of indenoquinoline (152) on pyrolysis of both benzo fused derivatives, (118) and (136) suggests that a common intermediate is involved in its formation. A spiro intermediate of the type shown (157) may be involved (Scheme 22).


[1,5]Me Shift
[1,5]Me Shift
(118)
(155)
(151)
[1,5]Ph Shift
Me
N
[1,5]imidoyl Shift
H
Me
N
(157)
(152)
[1,5]vinyl Shift
[1,5]Me Shift
[1,5]Me Shift
(136)
(156)
(154)

SCHEME 22

The 8a*H*-carbazole intermediate (155) has a choice of undergoing a competing [1,5] methyl or [1,5] aryl migration to give the *N*-methylated carbazole (151) or the spiro intermediate (157) respectively. Its benzo[*c*] counterpart (156) has an analogous choice of a methyl or vinyl migration, and the much greater proportion of indenoquinoline (152) obtained on pyrolysis of this benzo-fused isomer (136) may reflect the greater facility of vinyl migrations over the corresponding aryl cases.[9]

Further rearrangements of the spiro intermediate (157) are expected to be particularly facile by analogy to those of the related carbocycle: 1,1'-spirobiindene (158). The ready isomerisation of this compound to the benzofluorene (159) is attributed to destabilisation of the indene (158) by spiroconjugation.[76]

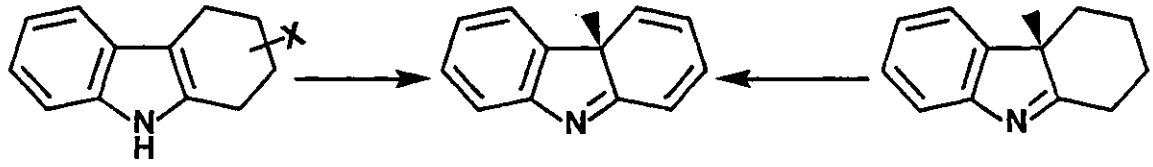


(158) (159)

4. SYNTHETIC APPROACHES TO 4a-METHYL 4a*H*-CARBAZOLE

4. SYNTHETIC APPROACHES TO 4a-METHYL-4a*H*-CARBAZOLE.

In considering synthetic approaches to 4a-methyl-4a*H*-carbazole (83) or its simple derivatives, precursors of the type shown (160) and (161) appear particularly attractive. Both functionalised tetrahydrocarbazoles



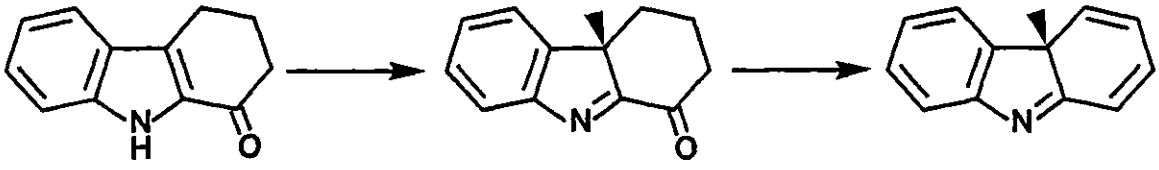
(160) (83) (161)

(160) and the carbazolenine (161) present a facile entry to the desired tricyclic skeleton. Methylation at the 4a position with subsequent manipulation of the functionality X in the former case (160), or double dehydrogenation of the 3*H*-indole derivative (161) would then afford the 4a*H*-carbazole.

4.1. From Tetrahydrocarbazole Derivatives.

The necessity to use indolyl Grignard derivatives to favour electrophilic substitution at the 3-position in indoles [or 4a in the tetrahydrocarbazole (160)], rather than on nitrogen,[77] imposes severe limitations on the nature of the functionality X. This, therefore, has to be compatible with organometallic reagents of this type, and must also be readily convertible to a diene.

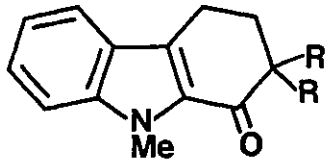
The carbonyl group in 1-oxo-1,2,3,4,9-tetrahydrocarbazole (162) was considered to satisfy these requirements as it had previously been shown to be inert towards Grignard reagents,[78] and several methods could be envisaged for its elaboration to a diene in the methylated derivative (163).



(162) (163) (83)

The ketone (162) was readily prepared using the literature procedure,[78] and afforded the required Grignard derivative on reaction with methylmagnesium iodide. However, this failed to give any of the 4a-alkylated derivative (163) on treatment with methyl iodide or benzyl bromide in either ether or THF, and only starting material could be isolated. Although alkali metal derivatives of indoles usually undergo substitution exclusively at nitrogen with electrophiles[79] it was hoped that in the case of the tetrahydrocarbazole (162) some degree of chelation may occur between the oxygen of the carbonyl group and the cation, thereby "masking" the nitrogen and favouring alkylation on carbon. Unfortunately, this proved not to be the case; treatment with potassium hydride followed by an excess of methyl iodide gave the *N*-methylated compound (164a), together with a small quantity of a trimethyl derivative tenatively assigned as (164b). With *n*-butyl lithium in place of the hydride a complex mixture

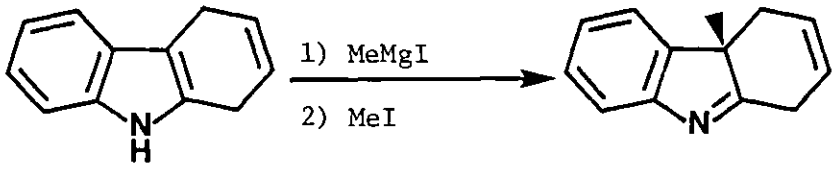
of products resulted, some of which appeared to have incorporated a butyl group.



a) R = H
b) R = Me

(164)

An alternative approach, which was very appealing in principle, involved similar methylation of 1,4-dihydrocarbazole (165). The starting



(165)

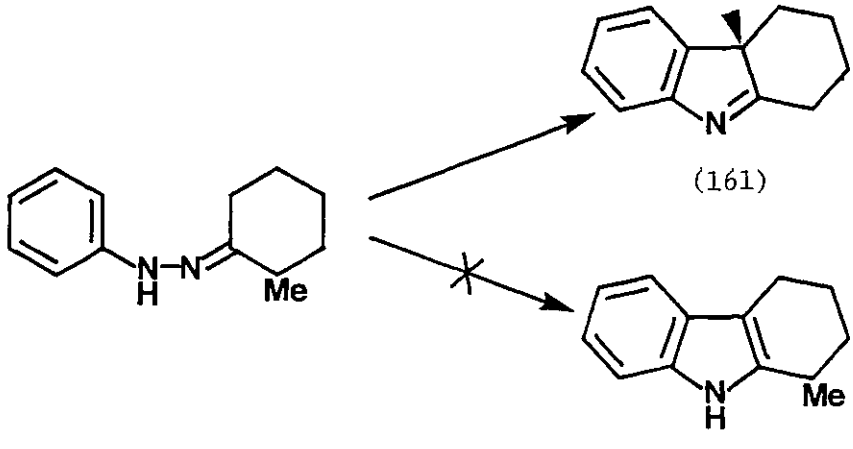
material (165) was readily obtained by Birch reduction of carbazole with lithium in ammonia, in the presence of propan-2-ol,[80] but gave only intractable tars on treatment with methylmagnesium iodide. Attempts to protect the isolated double bond by addition of bromine or cyclopentadiene were unsuccessful.

In retrospect, the lack of success encountered in these reactions is not wholly surprising. The 3-alkylation of Grignard derivatives of 2,3-disubstituted indoles to afford non-aromatic indolenines is much less satisfactory than the corresponding reaction with 3-unsubstituted indoles.

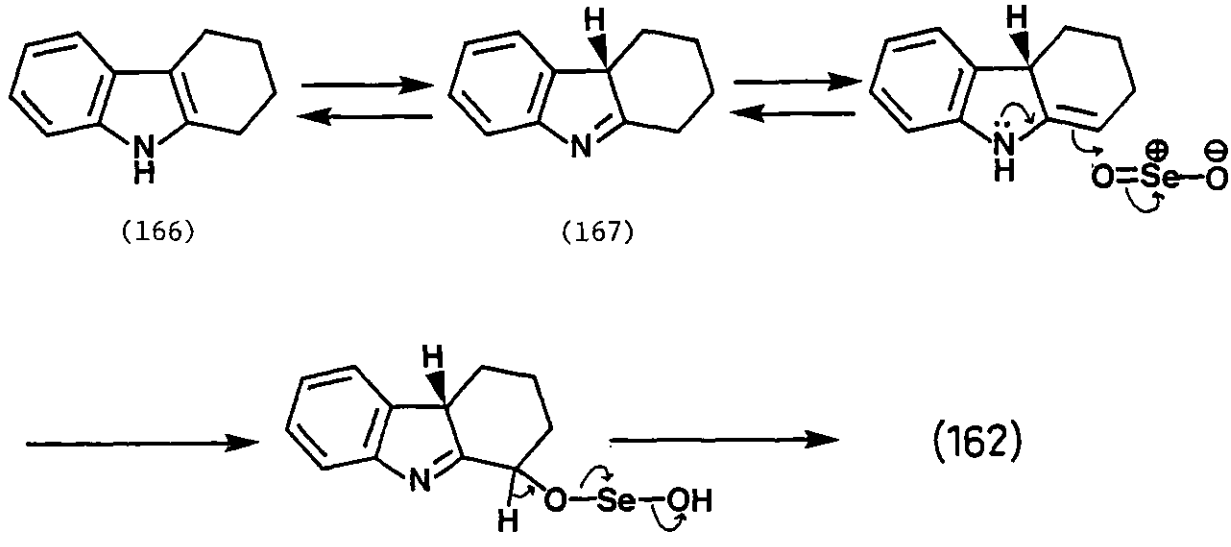
At best, only modest yields of 3*H*-indoles are usually obtained, and the success of the reaction has been observed to be highly dependent on the conditions employed.[81] These problems appear to be exacerbated when the substituents are other than simple alkyl groups, and so this approach was abandoned in favour of those involving less functionalised precursors already containing the bridgehead methyl group.

4.2. From 4a-Methyl-1,2,3,4,4a-Tetrahydrocarbazole.

4a-Methyl-1,2,3,4,4a-tetrahydrocarbazole (161) is readily available by Fischer cyclisation of the phenylhydrazone of 2-methylcyclohexanone in acetic acid. Cyclisation occurs almost exclusively to the substituted position under these conditions,[82] and yields of up to 73% of the carbazolenine (161) could be routinely achieved.



The oxidation of tetrahydrocarbazole (166) to the ketone (162) with selenium dioxide, has been proposed to involve the carbazolenine (167).[83]

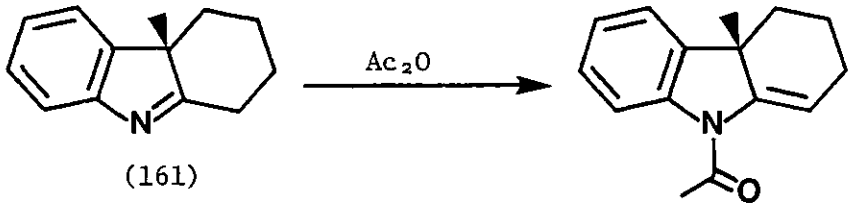


(166) (167)

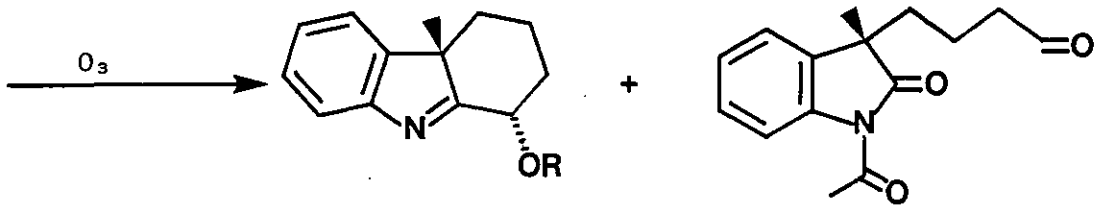
(162)

Application of the same conditions to the methyl carbazolenine (161) in an attempt to functionalise it to the ketone (163) resulted only in complete destruction of starting material. Using periodic acid as the oxidant[84] lead to the same result.

The introduction of functionality at the 1-position was finally achieved by employing a novel oxidative rearrangement originally described by McLean and his co-workers.[85] Treatment of the amide (168), available by acetylation of the carbazolenine (161),[86] with ozone, followed by reductive work-up afforded the acetate (169a) together with a small quantity of a product assigned as the aldehyde (170). This unusual reaction is believed to proceed by initial electrophilic attack of the enamide (168) by ozone, followed by loss of oxygen with concomittant transfer of the acetyl group. The stereochemistry of the product (169a) was assigned on the appearance in the n.m.r. spectrum of the proton to the acetoxy group as a double doublet with coupling constants of 6 and 11.5 Hz. These



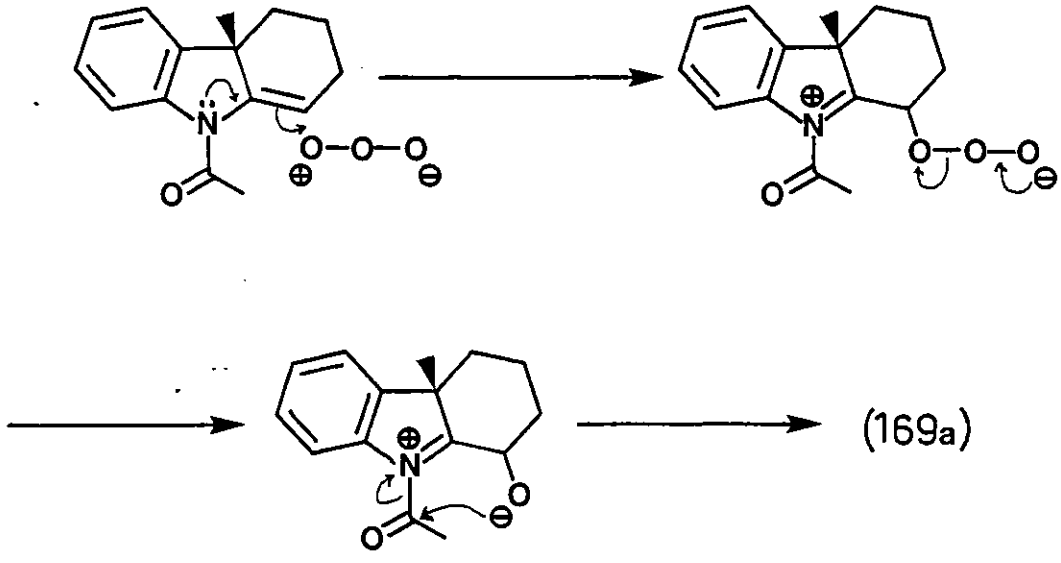
(161) (168)



(169) a) R = Ac
b) R = H

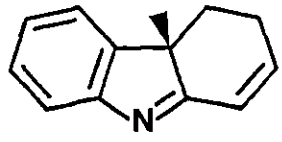
(170)

values are consistent with one coupling being axial-equatorial and the other axial-axial, hence indicating the α proton to be axial.



Treatment of the enamide (168) with mCPBA in the hope of effecting oxidative rearrangement *via* the epoxide,[87] thereby suppressing the formation of the aldehyde (170), the product of ozonolysis, failed to give any reaction.

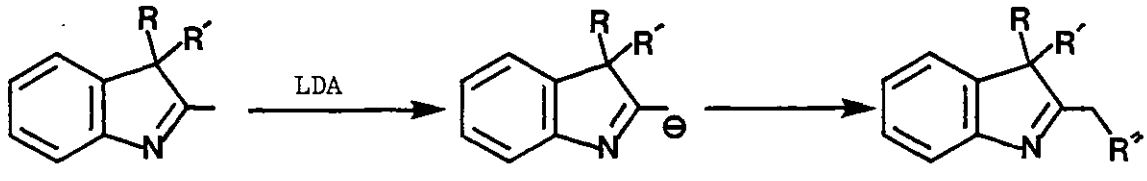
Hydrolysis of the acetate (169a) provided the corresponding alcohol (169b) which was found to be exceedingly sensitive to air, and considerable decomposition occurred even on work up. This unfortunate property had been previously observed in related compounds,[85] and precluded any attempt at oxidation of the alcohol to the ketone (163) or dehydration to the olefin (171). Attempts to eliminate acetic acid directly from the ester



(171)

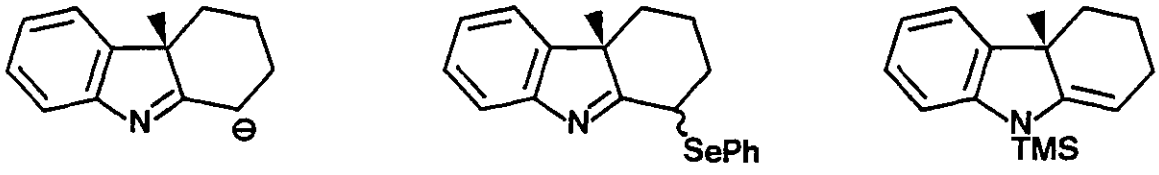
(169a), thus circumventing the need for the alcohol (169b), were unsuccessful. The acetate proved inert to DBU in refluxing toluene, whilst pyrolytic *cis*-elimination[88] lead only to complex mixtures of unidentified products.

In the light of these disappointing results, the possibility of introducing non-oxygenated functions at the 1-position of the carbazolenine (161) was considered. Dmitrienko *et al.*[89] have recently reported that indolenines bearing a methyl group at the 2-position (172) may be deprotonated with LDA and the anion thus formed (173) alkylated or acylated on carbon. Extending this reaction to the 1-phenylselenation of the carbazolenine (161) by quenching its LDA-generated anion (174) with phenylselenium



(172) (173)

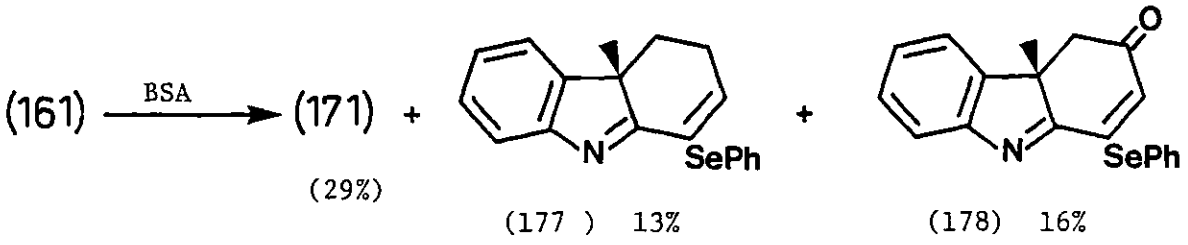
bromide[90] lead to none of the desired selenide (175), and only starting material and diphenyl diselenide could be isolated form the reaction



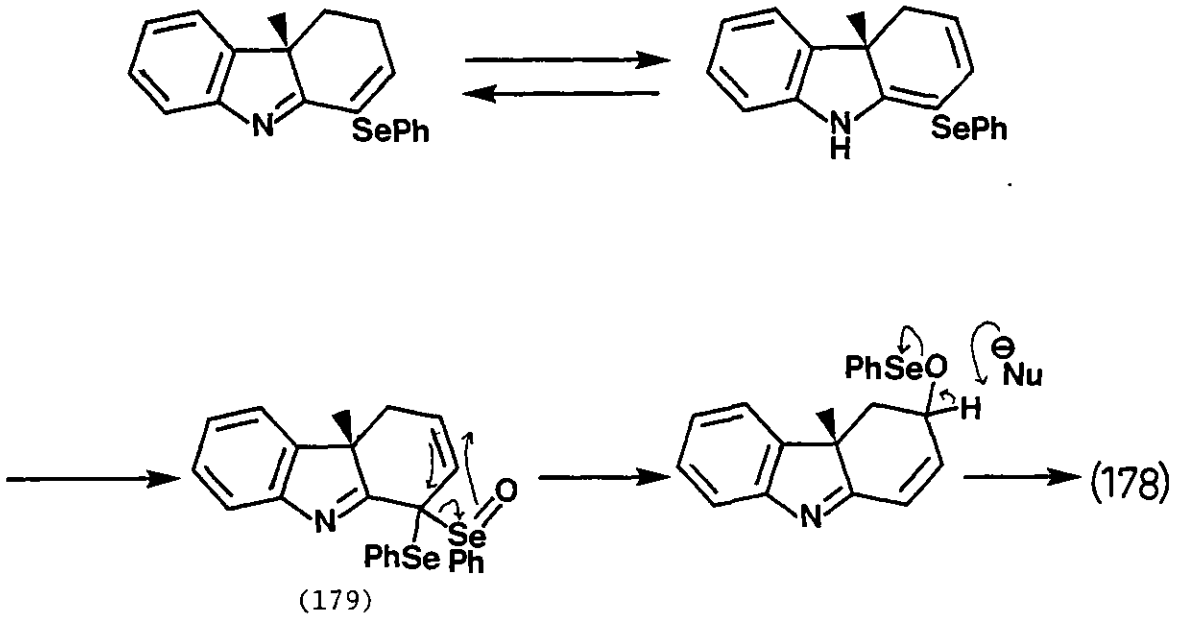
(174) (175) (176)

mixture. *In situ* selenation of the *N*-trimethylsilyl derivative (176), formed by quenching the anion (174) with trimethylsilylchloride[91] provided two unstable products whose n.m.r. spectra suggested that they may be the two diastereomeric selenides (175). However, oxidation with hydrogen peroxide resulted only in rapid deterioration to give a complex mixture of polar components, in which none of the desired olefin (171) could be detected.

The successful use of BSA in the synthesis of the benzo-fused 4a*H*-carbazole derivative (136; Scheme 20) suggested that a similar reaction may be fruitful in the present case. The carbazolenine (161) reacted rapidly with one equivalent of BSA in chlorobenzene at 100° to give three

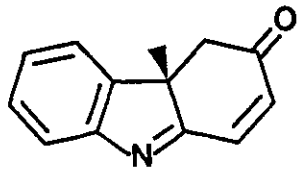


products, the major of which was the olefin (171). Another product was the vinyl selenide (177), corresponding to the selenated by-product isolated from analogous dehydrogenation of the benzo derivative (145). Spectroscopy indicated that the third product had incorporated oxygen, and was consequently assigned as the enone (178). It is believed that this product arises by allylic oxygenation of the vinyl selenide (177), and a possible mechanism involves [2,3] migration of an intermediate selenoxide (179). Similar oxygenation at allylic positions has been previously observed in BSA dehydrogenations.[92]



(179)

Attempts to increase the yield of olefin (171) at the expense of the vinyl selenide (177) by using catalytic quantities of BSA with iodoxybenzene as co-oxidant were not successful. The only product to be isolated from these reactions was the unsubstituted enone (180), itself a useful precursor to 4a*H*-carbazoles. However, the irreproducible but invariably low yields obtained lead to the development of an alternative route to this compound, which is described later.

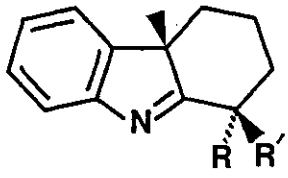


(180)

On attempted distillation at reduced pressure, the olefin (171) was observed to decompose to a complex, dark mixture, and was totally destroyed at 145°C. This thermal sensitivity may account for the low yield obtained under the vigorous conditions of the BSA dehydrogenation, and, together with the necessity to use stoichiometric quantities of the expensive oxidant, lead to further investigation into alternative sources of the olefin.

Treatment of the carbazolenine (161) with a variety of electrophilic brominating agents failed to introduce bromine at the 1-position. Only tar was produced with copper(II) bromide,[93] whereas pyridinium hydrobromide perbromide,[94] bromine in acetic acid,[95] or NBS in ethanol gave varying amounts of an unidentified product that had incorporated bromine but was not the desired 1-bromide. However, bromination at this position did occur when NBS was used as a source of radical bromine.[96]

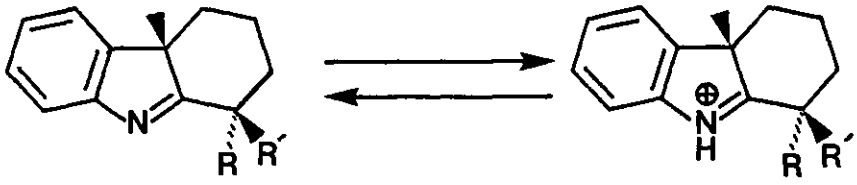
Thus, with one equivalent of NBS in refluxing carbon tetrachloride, a mixture of diastereomeric monobromides, (181a) and (181b) was obtained, together with a small quantity of the *gem* dibromide (181c) and a little unreacted starting material. As in the case of benzylic bromination of



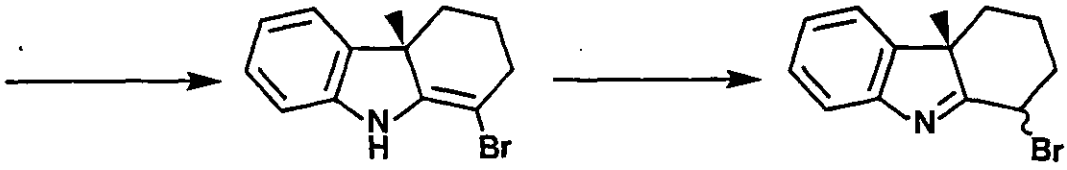
a) R = H, R^1 = Br
b) R = Br, R^1 = H
c) R = R^1 = Br

(181)

the benzocarbazolenine (138, p. 77), the product distribution was dependent on reaction conditions. Conversion of starting material could be maximised by using a slight excess of NBS in the presence of a radical initiator, usually AIBN, which appeared to accelerate the reaction. Reflux was routinely maintained for several hours, until all of the brominating agent had been observed to be consumed. Irradiation with a tungsten lamp did not appear to offer any advantage. Under these conditions, the major product was rather surprisingly always found to be the axial bromide (181a)[97] as determined by n.m.r. However, the relative yields of both monobromides (181a) and (181b), could not be accurately determined since the two were not separable by chromatography, and contact with silica gel resulted in equilibration of the two isomers. In one experiment, n.m.r. analysis of the crude reaction mixture after bromination indicated the axial epimer (181a) to be the only monobromide present, but on silica gel chromatography a mixture of axial and equatorial (181b) monobromides was isolated in a ratio of 2:1. This epimerisation presumably occurs *via* the enamine (182) produced on acid catalysed " enolisation" of the basic carbazolenine.



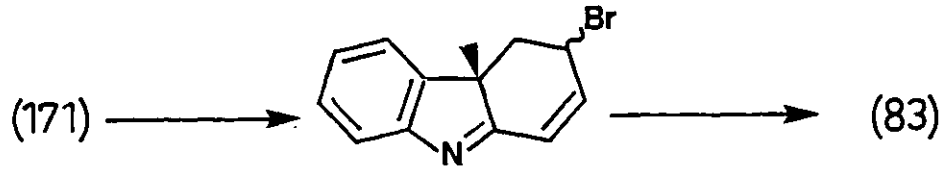
(181a,b)



(182) (181a,b)

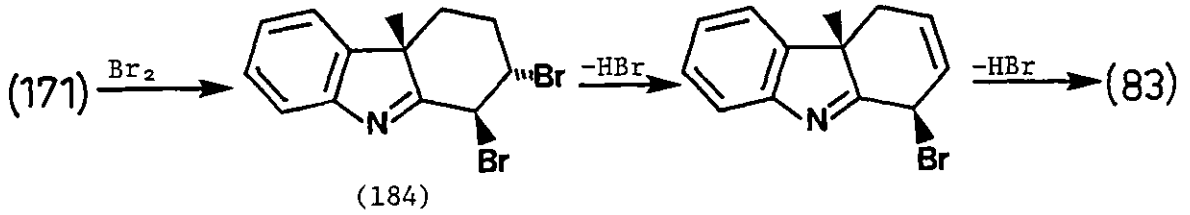
Both monobromides were rather unstable, and so were immediately subjected to the action of DBU in warm benzene, which effected smooth elimination of the axial bromide (181a), but not of the equatorial (181b). The lack of a favourable *trans* diaxial relationship between the bromine atom and a β-hydrogen is thought to account for this observation. Although n.m.r. analysis of the crude reaction mixture indicated the presence of only the olefin (171) and unreacted equatorial bromide (181b), equilibration again occurred on chromatography, and the latter was isolated as a 1:1 mixture with its epimer (181a).

Since the product was expected to be rather delicate, mild conditions were sought for the conversion of olefin (171) to the desired 4a*H*-carbazole (83). Allylic bromination to the bromide (183) followed by elimination appeared promising, but exposure of the olefin (171) to the same conditions used to brominate the carbazolenine (161) lead only to the formation of a complex mixture in which significant amounts of allylic bromide could not



(183)

be detected. Irradiation of a solution of the olefin containing NBS and a trace of AIBN failed to give any reaction and resulted only in the gradual deterioration of starting material. It was also hoped that double dehydrohalogenation of the dibromide (184) formed by addition of bromine to the olefin (171) could also serve as a source of 4a*H*-carbazole.



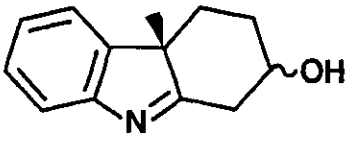
(184)

Unfortunately, addition of bromine to a solution of the olefin at 0° again succeeded only in converting it to base line material.

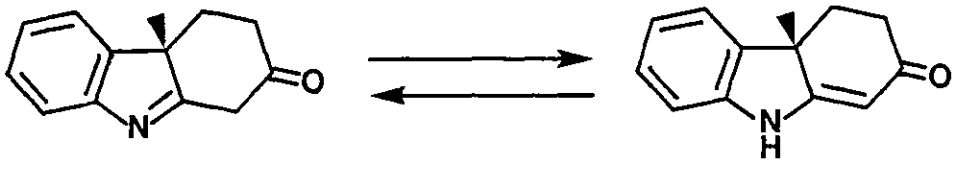
4.3. From 3-Hydroxy-4a-Methyl-1,2, 3,4,4a-Tetrahydrocarbazole.

The foregoing examples illustrate some of the problems associated with synthetic routes involving carbazolenines functionalised at the 1-position. The intermediates are usually unstable and are themselves provided by

reactions that often give rise to mixtures of products. A possible solution to these difficulties lies in the use of remotely functionalised carbazolenines, in which interference from the imine bond could be expected to be minimised. For the purpose of developing unsaturation in the non-aromatic six ring, an oxygen containing function appears particularly desirable. An alcohol, for example, could be dehydrated to an olefin, or oxidised to a ketone, from which further unsaturation could be readily introduced. Furthermore, the placing of such functionality at the 3-position rather than at any other would offer the greatest versatility for subsequent elaboration. Dehydration of the 2-hydroxy compound (185) would probably give rise to the conjugated olefin (171) which had already proven resistant to further manipulation. Complications also arise with the ketone (186a)



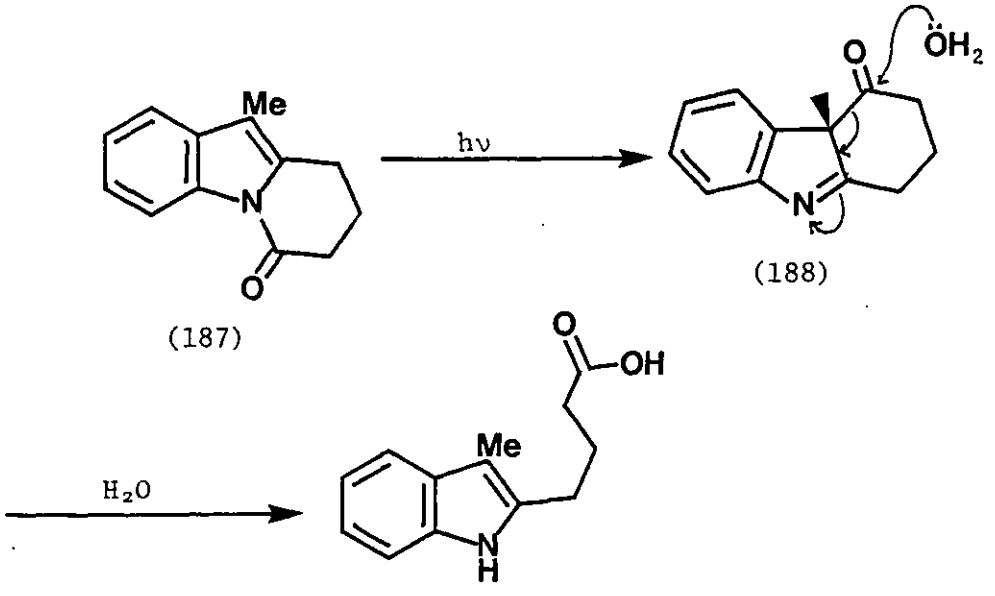
(185)



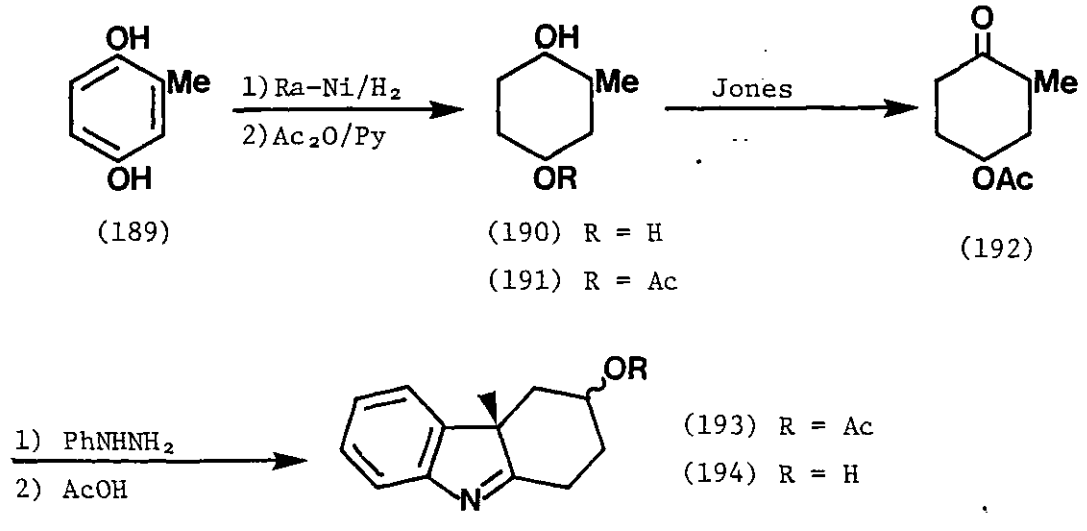
(a) (186) (b)

which has been shown to exist predominantly as the enamine tautomer (186b) in closely related systems.[98] Although the 4-keto derivative (188) has been prepared previously by a photo-Fries rearrangement of the indole (187)

the low yield obtained and the sensitivity of the product to hydrolysis make it unsuitable as a synthetic precursor to 4a*H*-carbazoles.[99]

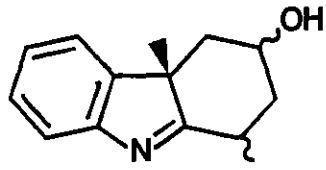


Since the 3-position in carbazolenines is unactivated, any synthesis of such functionalised derivatives clearly requires the desired functionality to be present at the outset. Thus, the route chosen to 3-hydroxy-4a-methyl-1,2,3,4,4a-tetrahydrocarbazole (194) involved the acetoxy ketone (192), and is shown in Scheme 22. An analogous approach has been described by Teuber



SCHEME 22

and Cornelius for the preparation of the related, dimethyl compound (195).[98] Although straightforward in principle, this route was found

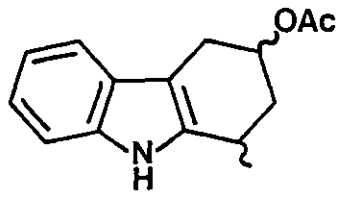


(195)

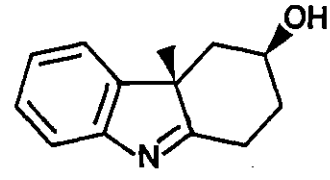
in practice to be plagued by a number of minor, but nonetheless frustrating complications. The ketone (192) had been prepared previously by the same method as that shown, but little consolation was offered by the absence of experimental details.[100] Also, the purity of both precursors (190) and (191), as well as the ketone itself, could not be determined by either spectroscopic methods or g.l.c.

High temperature and pressure hydrogenation of methylhydroquinone (189) over Raney nickel[101] provided the diol (190) as a mixture of diastereomers. These were isolated together with varying quantities of unchanged starting material, from which they were only partially separable by distillation. Attempts to extract the phenolic contaminant by the use of aqueous alkali lead to considerable losses due to the substantial solubility of the diol (190). Acetylation with one equivalent of acetic anhydride in the presence of pyridine occurred predominantly at the less hindered hydroxyl group[102] to afford the monoacetate (191), which was oxidised to the ketone (192) with Jones' reagent. This, on heating with phenylhydrazine furnished the corresponding phenylhydrazone which was subjected directly to Fischer cyclisation, since attempted purification by distillation resulted only in decomposition.

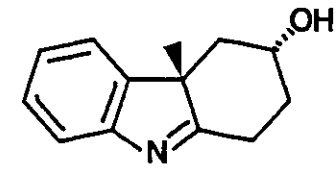
Cyclisation with acetic acid at 100° gave the acetoxy carbazolenine (193) as a 1:1 mixture of both diastereomers in 40% yield. This could not be improved upon by performing the cyclisation with a saturated solution of hydrogen chloride in propan-2-ol[82] or by treating the ketone (192) with phenylhydrazine hydrochloride in refluxing pyridine.[103] Evidence for some cyclisation occurring at the unsubstituted position of the ketone was provided by the isolation of a gum whose spectral properties indicated it to be a mixture of diastereomers of the 9*H*-tetrahydrocarbazole (196). In one case, a particularly low yield of the acetate (193) was



(196)



(194a)

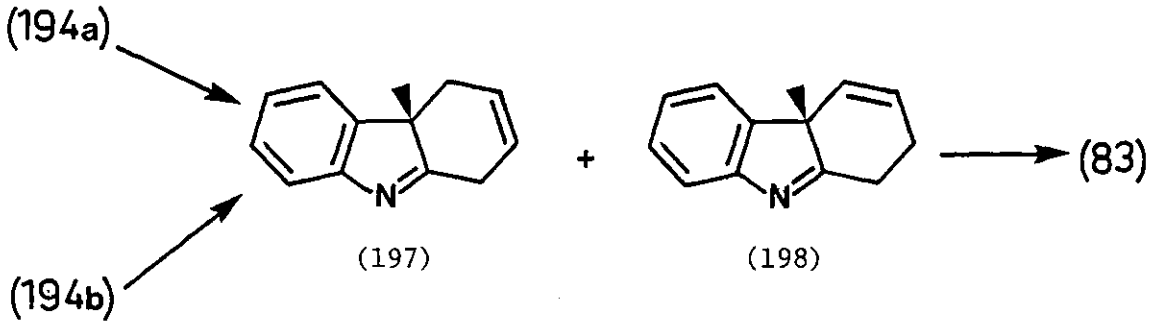


(194b)

accompanied by the isolation of the two diastereomeric alcohols (194a) and (194b), which are believed to have arisen by hydrazinolysis of the ester (192) during phenylhydrazone formation.[104] Hydrolysis of the acetates (193) with sodium hydroxide was found to be a more convenient source of the two alcohols, which could be chromatographically separated into individual diastereomers more readily than the ester (193). A convenient but less efficient means of separating the two isomers relied on the lower solubility of the axial alcohol (194a) in carbon tetrachloride, from which it could be isolated as a colourless crystalline solid. The equatorial alcohol (194b) could not be induced to solidify and was always obtained as a brown gum. In marked contrast to the 1-hydroxy isomer (169b), both

of the carbazolenines (194a) and (194b) could be kept exposed to the atmosphere for prolonged periods of time with no significant deterioration.

Although elimination of the acetates (193) either pyrolytically[88] or by the action of sodamide in liquid ammonia[105] met with little success, greater optimism was reserved for dehydration of the two alcohols (194a) and (194b). Most of the large number of methods available to effect this transformation were expected to provide a mixture of both possible olefins (197) and (198). This was not considered a disadvantage, however, since conversion to 4a*H*-carbazole (83) could be accomplished by the same reactions in either case.



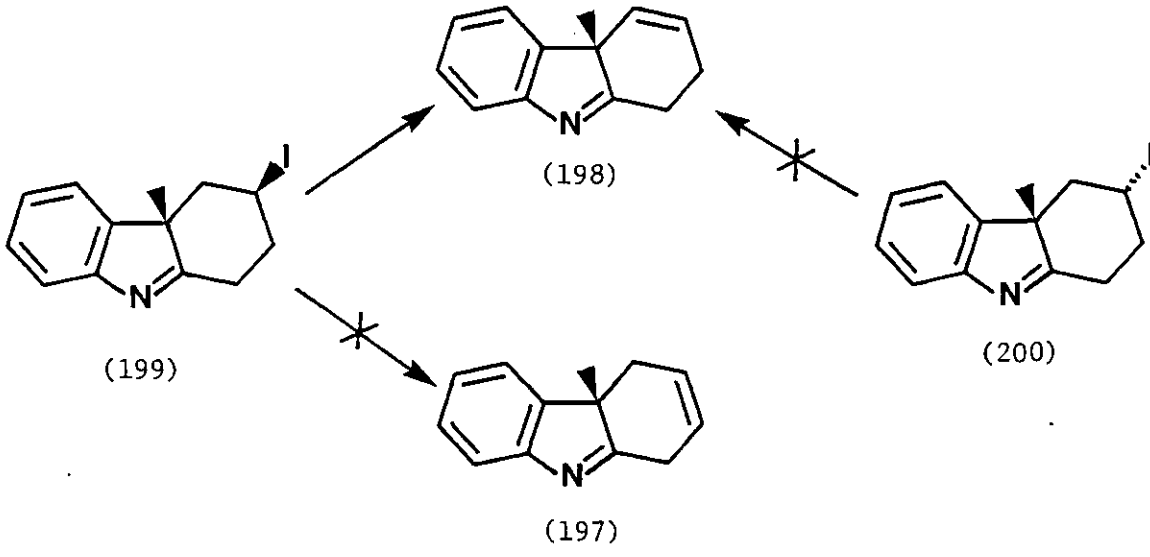
(197) (198)

Addition of thionyl chloride to a cold solution of the alcohols in pyridine[106] resulted in the immediate precipitation of a dark, amorphous solid, which indicated only base-line components on t.l.c. Complex mixtures resulted with methyl(carboxysulphamoyl)triethylammonium hydroxide inner salt (Burgess' salt),[107] in which none of the desired olefins could be detected. MTPI,[108] a reagent which has previously been used to good effect with sensitive alcohols, gave similar results. A modification in its

use has been recently developed and involves initial treatment of the alcohol with the phosphorus reagent, followed by addition of the reaction mixture to aqueous hydroxide. This not only results in elimination of the intermediate iodide but also serves to hydrolyse phosphorus containing by-products to water soluble species, allowing for easier isolation of product.[109] Adoption of this technique offered no improvement, but in one case, addition of the MTPI mixture, in which all of the starting material had been consumed, to the aqueous hydroxide was observed to result in regeneration of the alcohol, presumably by displacement of an intermediate iodide. Attempts to isolate the iodide or to eliminate it *in situ* with DBU rather than hydroxide also failed.

Equally unsuccessful were attempts to convert either of the alcohols to a selenide using o-nitrophenylselenocyanate in the presence of tributylphosphine,[110] or to a halide with phosphorus tribromide[111] or carbon tetrachloride and triphenylphosphine.[112] However, the equatorial alcohol (194b) could be converted to the epimeric iodide (199), albeit in very poor yield, by the action of triphenylphosphine, dimethyl azodicarboxylate, and methyl iodide.[113] Although relatively unstable, the halide could be smoothly eliminated with DBU to give a good yield of a single product. Surprisingly, n.m.r. revealed this to be the Δ^3 olefin (198) and no trace of its isomer (197) could be detected. This result was unexpected in view of predictions previously made with the help of models. These suggested that the axial proton in the 2-position was marginally less sterically hindered than that in the 4-position for the iodide (199). Also little thermodynamic distinction could be observed between the two olefins; neither had an exclusively favourable conformation, and at best, a 1:1 mixture of both olefins was expected on elmination of the iodide. Analogous treatment of the axial alcohol (194a) afforded the equatorial iodide (200) in low yield, together with an equal quantity of the olefin (198), from

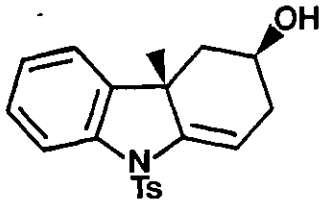
which it was inseparable. Formation of the latter is attributed to elimination of an intermediate in the iodination reaction, rather than from the iodide (200), since treatment of the mixture with DBU failed to eliminate the iodide, resulting only in its gradual decomposition.



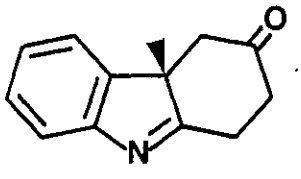
The low yield of axial iodide (199) obtained was attributed to steric hindrance of the approach of iodide ion by a 1,3-diaxial interaction with the angular methyl group. Further complications arising from irreversible reaction of methyl iodide with the basic nitrogen of the carbazolenine[114] were also envisaged. The former difficulty could be overcome by using a smaller halide, whereas the latter requires the use of a less electrophilic source of halide ions. Alkali metal azides have been used in conjunction with triphenylphosphine and the azo ester to convert alcohols to azides,[115] but attempted bromination of the alcohol (194b) under the same conditions using lithium bromide as the halide source did not afford any of the desired bromo carbazolenine. An attempt to prepare

the tosylate of the axial alcohol (194a) as an alternative to the iodide (199) was unsuccessful; treatment of the alcohol with tosyl chloride in the presence of pyridine gave only the *N*-tosyl derivative (201).

The small quantity of olefin (198) available prevented extensive investigation of its conversion into the 4a*H*-carbazole (83). Most of the sample prepared was used in model studies related to the di-π-methane rearrangement (see next Chapter) when it became apparent that this isomer suffered from similar drawbacks to those associated with the conjugated olefin (171). Addition of bromine to the Δ^3 olefin (198), for example, also resulted in complete destruction of starting material. Further studies relating to dehydration of the alcohols (194a) and (194b) were discontinued in favour of their oxidation to the corresponding ketone (202).



(201)



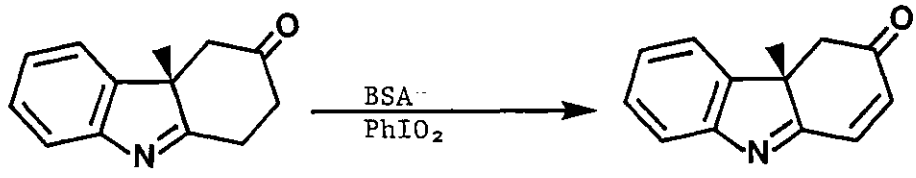
(202)

4.4. From 4a-Methyl-3-Oxo-1,2,3,4,4a-Tetrahydrocarbazole.

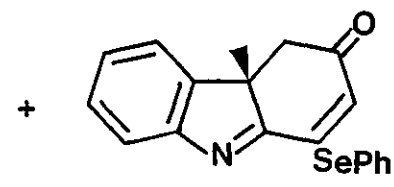
Oxidation of the hydroxy carbazolenine (195) had been achieved by Teuber and Cornelius by using an unusual combination of Raney nickel and cyclohexanone,[98] presumably as a modification of the better known Oppenauer method utilising acetone with aluminium isopropoxide.[116] However, the reaction proceeded in poor yield, and an improvement was sought for the conversion of the alcohols (194a) and (194b) to the ketone (202). All

of the pyridine-chromium trioxide reagents tried were uniformly unsuccessful. Thus pyridinium chlorochromate,[117] fluorochromate, both alone[118] and buffered with sodium acetate,[119] and dichromate[120] resulted in the recovery of starting material contaminated with polar material, although the oxidant was observed to be reduced in each case. A trace of the ketone (202) was observed with NBS in aqueous DME,[121] but the action of this reagent was so slow as to make the reaction synthetically impractical. Double oxidation of the alcohols directly to the enone (180) with BSA resulted in only 2% yield of product. Further investigation revealed the reagent of choice for the oxidation of the alcohol (194) to ketone to be DMSO activated with oxalyl chloride according to the method of Swern.[122] Using this combination, yields of up to 89% of the sensitive ketone (202) could be achieved.

Dehydrogenation of the ketone (202) to the enone (180) with catalytic quantities of BSA in the presence of iodoxybenzene proceeded cleanly to give a readily separable mixture of the desired product with the selenide (178). The yield of enone (180) was dependent on the reaction conditions and the results are summarised in Table 9.



(202) (180)



(178)

TABLE 9. Reaction of ketone (202) with BSA (0.2 eq.) and $PhIO_2$ (3 eq.).

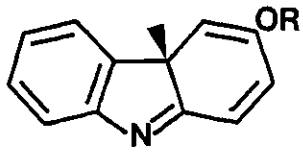
Solvent	Temp. (°C)	Time (h)	Yield of enone (180) (%)	Yield of selenide (178)(%)
Benzene	80	2	41	16
Toluene	111	1	50	17
Toluene	111	0.6	58	18
Chlorobenzene	120	0.3	41	16

In contrast to the enone (180), which rapidly discoloured on exposure to ambient conditions, the selenide (178) was found to be air stable and did not require to be stored at low temperatures. The greater sensitivity of the enone is believed to be responsible for the variation in the yield obtained of this compound. Decomposition takes place at higher temperatures or with prolonged reaction times, thereby decreasing the yield. The selenide (178), on the other hand, is stable to the reaction conditions and consequently the yield does not vary.

Other methods of dehydrogenating the ketone (202) were investigated, including α-bromination with pyridinium hydrobromide perbromide or selenation of the ketone enolate, but neither offered any advantage over BSA oxidation. In both cases, spontaneous elmination of the substituent occurred, giving complex mixtures containing the enone (180).

The enol form of the enone (180), is, of course, a 4a*H*-carbazole derivative (203), and several related, carbocyclic 3a*H*-indene derivatives have been prepared by trapping the enolates of highly conjugated ketones with suitable electrophiles.[123] One such method utilises potassium hydride in the presence of 18-crown-6 to generate the enolate ion, with subsequent

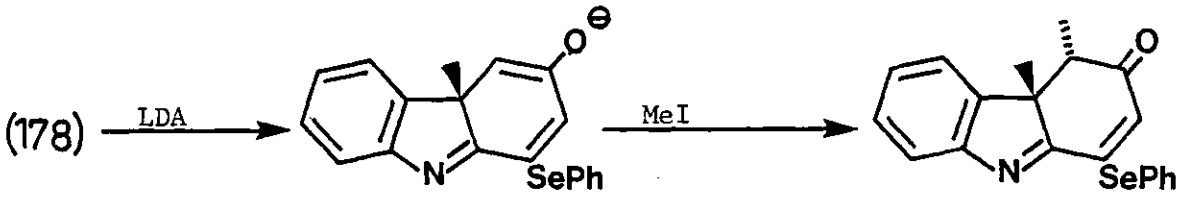
methylation on oxygen using methyl fluorosulphonate.[124] Application of these conditions to the attempted preparation of 3-methoxy-4a*H*-carbazole



(203) R = H
(204) R = Me
(205) R = $SiMe_3$

(205) was unsuccessful, however, and lead instead to the immediate decomposition of enone (180) on contact with the hydride/crown ether mixture. Trapping the enolate as its trimethylsilyl enol ether (205) with trimethylsilyltrifluoromethyl sulphonate in the presence of triethylamine[125] failed similarly.

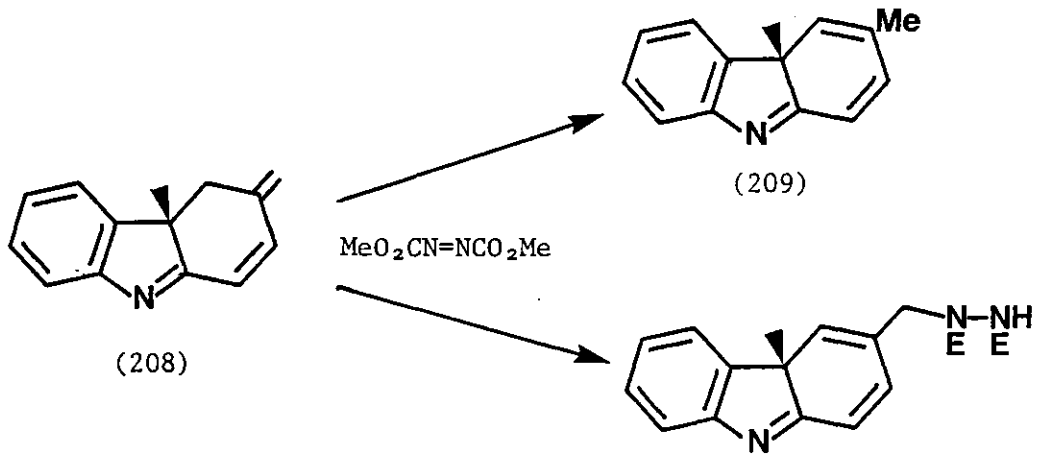
Addition of LDA to a solution of the selenide (178) produced an immediate deep red colouration which persisted indefinitely at low temperatures and was attributed to the enolate (206). However, this also resisted all attempts at trapping; no discernable product could be isolated on adding methyl fluorosulphonate, while substituting trimethylsilyl chloride for the methylating agent with subsequent addition of PTAD to intercept any 4a*H*-carbazole present lead only to partial recovery of starting material. Doubts about the presence of enolate ion (206), were, however, dispelled when a good yield of the 4-methyl derivative (207) was isolated after reaction with methyl iodide. The stereochemistry of the methyl group was assigned on the expectation that approach of the electrophile occurs from the less hindered face of the intermediate (206). Although its intermediacy was conclusively proven, further exploitation of the enolate (206) as a source of 4a*H*-carbazole derivatives was prevented by lack of time.



(206) (207)

Other intermediates that showed promise as 4a*H*-carbazole precursors, but investigation of which was similarly curtailed, included the *exo*-methylene derivative of the enone (208). Prepared in modest yield by Wittig reaction of the enone (180) with triphenylmethylene phosphorane, it was hoped that isomerisation of the exocyclic double bond would provide the methyl substituted 4a*H*-carbazole (209). A number of methods were considered, including rhodium-catalysed isomerisation,[126] treatment with strong bases,[127] or complexation with iron carbonyls,[128] but the mildest was thought to be an ene reaction with a suitable enophile. Unfortunately, however, none of the expected ene product (210) could be detected in the complex mixture resulting from reaction of the diene (208) with dimethyl azodicarboxylate.[129]

The enone (180) also provides an entry to the unsubstituted 4a*H*-carbazole (83) by base induced fragmentation of its arenesulphonyl hydrazones.[130] Preliminary experiments aimed at preparing the triisopropyl-benzenesulphonyl (trisyl) hydrazone, reported to be superior to the tosyl derivative,[131] were met with little success. The enone (180) failed to react at all with the appropriate hydrazide when Amberlite IR 120 ion



exchange resin was used as acid catalyst,[132] whereas boron trifluoride[133] resulted in slow decomposition of starting material and reagent to base line material. Similar results were obtained with the more stable tosyl-hydrazide, although again, as in previous examples, lack of time prevented anything more than a superficial investigation.

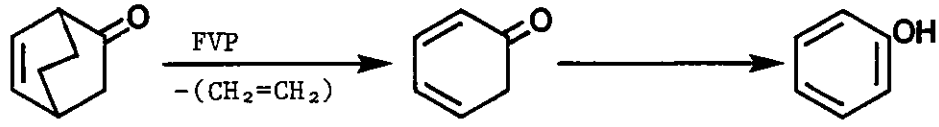
4.5. From Bicyclo[2.2.2.]octenone Derivatives.

This route, although not extensively investigated, merits brief discussion since it is conceptually different from the previous approaches described in this Chapter.

The most obvious source of 4a-methyl-4a*H*-carbazole (83), on paper at least, is the Fischer reaction of 6-methylphenone (211) with phenyl-hydrazine. Such a reaction as it stands is of course impossible since the ketone (211) exists exclusively in its enol form as 2-methylphenol.

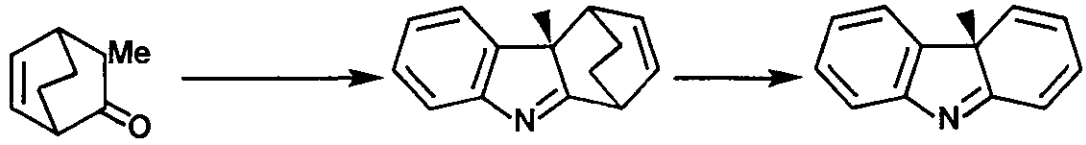
(211) (83)

However, a recent publication describes the transient isolation and detection of phenone (213) as a product on FVP of bicyclo[2.2.2.]oct-2-en-5-one (212).[134] The use of methylated bicyclooctenone (214) as a



(212) (213)

masked form of the phenone (211) amenable to Fischer cyclisation is immediately apparent (Scheme 23).



(214) (215) (83)

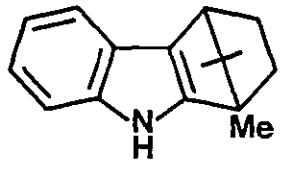
SCHEME 23

The preparation of bicyclo[2.2.2.]octenone (212) by Diels-Alder cycloaddition of a suitable ketene equivalent to cyclohexadiene has been the subject of many publications in the last few decades, but on repeating some of these, the yields of ketone (212) obtained were found to fall considerably short of those quoted in the literature. Contrary to a previous report,[135] the reaction of chloroacrylonitrile with cyclohexadiene proved to be the most efficient source of a cycloadduct (216) that could be readily converted to the ketone (212). Performing the reaction in refluxing xylene afforded the chloronitrile (216) in 45% yield, and was superior to a two step procedure involving chlorination of a cyclohexadiene-acrylonitrile adduct.[136] Of the methods available for the hydrolysis of the adduct to the ketone (212), that described by Brown *et al.*[137] and involving ethanolic sodium hydroxide containing DMSO proved most effective.

(217)

Methylation of the bicyclic ketone (212) could not be achieved *via* its enamine,[74] α-hydroxymethylene,[138] or alkoxy carbonyl derivatives, preparation of the latter being attempted with both diethylcarbonate and base, and by reaction with methylmagnesium carbonate.[139] Although the *gem*-

dimethyl derivative was the major product on treatment of the lithium hexamethyldisilazide-generated enolate with methyl iodide,[140] a good yield of the desired monomethyl ketone (214) was finally obtained by using LDA as base and adding methyl iodide in the presence of HMPA.[141] Further elaboration of the ketone (214) to the carbazolenine (215) was prevented by the reluctance of its phenylhydrazone to cyclise under a variety of conditions. The unsubstituted ketone (212) behaved similarly. This failure to undergo cyclisation is perhaps not too surprising in view of the observations made previously with other bicyclic ketones; thus the Fischer product of camphor phenylhydrazone (217) still remains unknown despite considerable efforts towards its preparation.[142]



(217)

These setbacks, coupled with doubt about whether the 4a*H* carbazole (83) would be isolable under the conditions required for the *retro* Diels-Alder reaction of (215), lead to the eventual discontinuation of this approach.

5. MECHANISTIC INVESTIGATIONS

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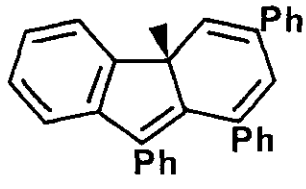
5.1. Comparison of 4a*H*-Carbazoles with 4a*H*-Fluorenes.

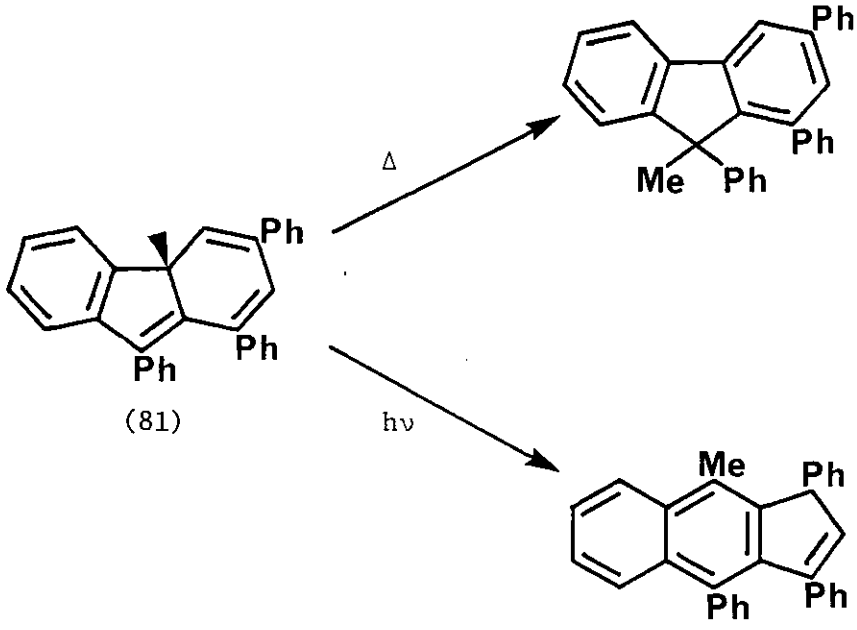
It is probable that 4a*H*-carbazoles generated *in situ* from benzotriazoles react through an initially formed, excited, or at least, highly energetic form. Thus, it cannot be assumed that the molecules in their ground states would undergo the same reactions under similar conditions. For comparative purposes, therefore, a study of the thermal and photochemical properties of isolated, simple (*i.e.*, not benzo-fused) 4a*H*-carbazoles was considered to be of value. Since no isolated 4a*H*-carbazoles of this type were available, the 4a*H*-fluorene derivative (81) was chosen as a suitable alternative.



(81)

This compound is obtained by polyphosphoric acid catalysed self condensation of acetophenone,[143] and was available from earlier studies relating to 3a*H*-indenes.[144] Although its chemical properties had been extensively studied,[145] no reports of its thermolysis or photolysis could be found.

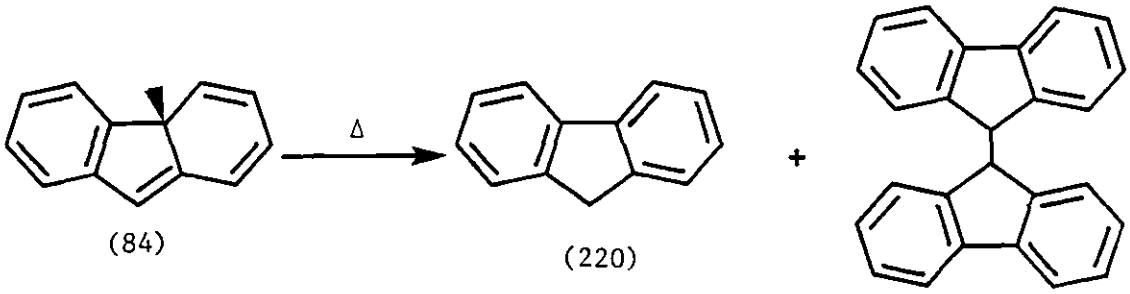
FVP of 4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (81) at 540°C afforded a mixture of products of which one was by far the major. On isolation and purification, this product was identified as being 9-methyl-1,3,9-triphenylfluorene (218). Confirmation of the assigment was provided by comparison of the melting point and chemical shift of the methyl signal in the n.m.r. spectrum with the values quoted by Snyder for independently synthesised 9-methyl-1,3,9-triphenylfluorene.[146]



Irradiation of the 4a*H*-fluorene (81) in acetonitrile at 254 nm again gave rise to one major product which was readily isolated on account of its low solubility in most organic solvents. From its properties it was identified as 9-methyl-1,3,4-triphenyl-1*H*-cyclopenta[*b*]naphthalene (219), the position of the double bond in the 5-ring with respect to the methyl group being confirmed by n.O.e. experiments.[147]

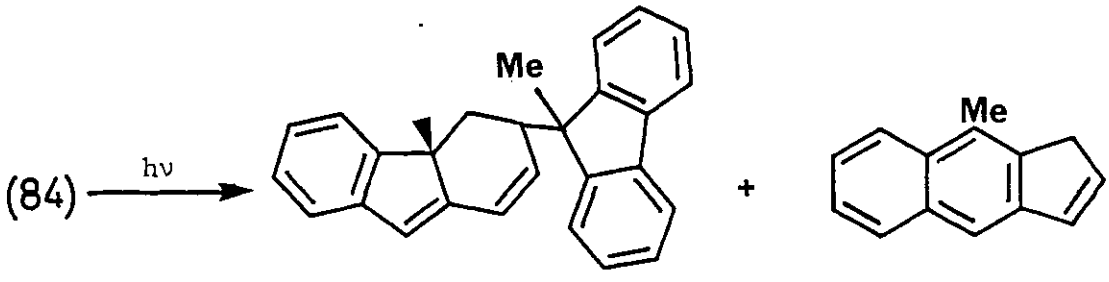
Both of these results are clearly consistent with those obtained with 4a*H*-carbazoles (Chapter 2); the fluorene (218) corresponding to *N*-methylated carbazoles (106), whilst the naphthalene (219) is analogous to the cyclopentaquinolines (112).

In both reactions products arising from loss of a methyl group were neither sought nor detected. However, demethylation has been shown to occur on thermolysis of less highly substituted 4a*H*-fluorenes. Thus, 4a-methyl-4a*H*-fluorene (84) provides 9-methylfluorene (220) as the major product on FVP at 650°C, together with a significant quantity of the bifluorenyl (221).[147]



(84) (220) (221)

In contrast, photolysis afforded the dimer (222) as the major (31%) product, together with the expected cyclopentanaphthalene (223) (20%).[147]



(222) (223)

From the limited data available, therefore, it would appear that in general 4a*H*-fluorenes behave analogously to *in situ* generated 4a*H*-carbazoles with respect to their thermal and photochemical properties.

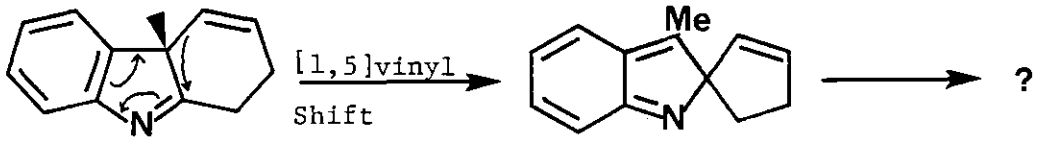
5.2. Studies Relating to the Aza-Di-π-Methane Rearrangement.

The mechanism by which formation of cyclopentapyrimidines (12) from 3a*H*-benzimidazoles (17) was rationalised consisted solely of thermally allowed migrations (Scheme 3). This suggests that in photolysis, the role of light is only to effect extrusion of nitrogen from the starting

tetrazoles (10). Such a process may be true in this particular case, where ring permuted products are also obtained on pyrolysis, but not in the case of 4a*H*-carbazoles, in which cyclopentaquinolines were observed only on photolysis. The isolation of ring-permuted products from photolysis of the 4a*H*-fluorene (81) or the benzo-fused 4a*H*-carbazole (118), neither of which were generated *in situ*, suggests that light plays a more important role in the rearrangement than merely to effect decomposition of a precursor. The invocation of a di-π-methane mechanism for these rearrangements (Scheme 17) is based largely on circumstantial evidence and there is no firm proof of its operation. Since ring permutative rearrangements seemingly occur in many 3a*H*-indene derivatives and analogues it was considered desirable to test the validity of such a mechanism by using suitable models.

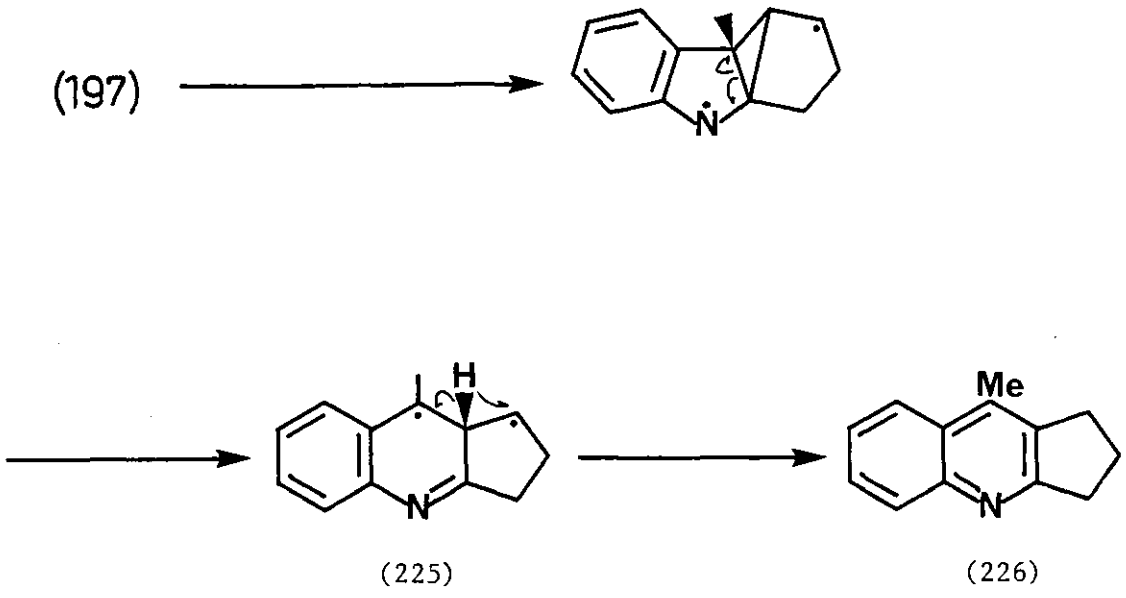
5.2.1. 1,2-Dihydro-4a-Methyl-4a*H*-Carbazole.

The previously mentioned olefin (197) appeared a particularly attractive model for the aza-di-π-methane rearrangement. Since the double bond in the non-aromatic 6-ring is not conjugated, an electrocyclic ring permutation *via* a spiro intermediate (224), in the manner proposed earlier (*cf.* Scheme 3) is not possible. However, the same olefin is able to undergo a di-π-



(197) (224)

methane rearrangement very similar to that proposed for fully unsaturated 4a*H*-carbazoles (Scheme 17), the only difference being that aromatisation of the intermediate (226) would have to occur by homolytic cleavage of the

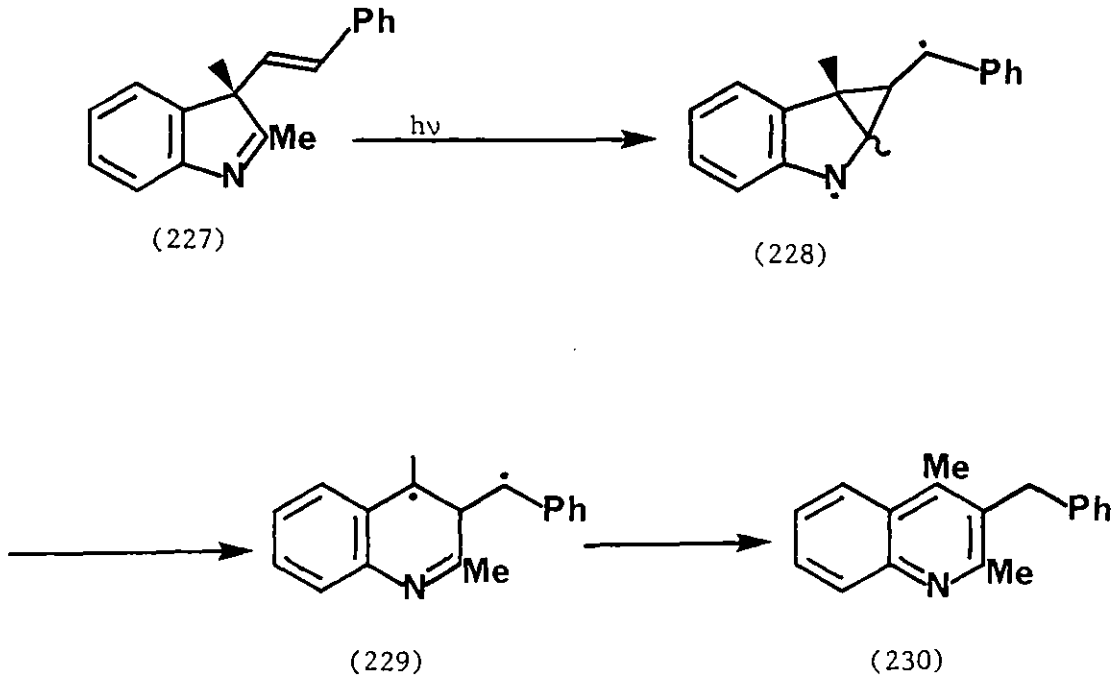


(225) (226)

bridgehead substituent. In the analogous fully unsaturated intermediate (114), aromatisation can occur by sigmatropic migration of this substituent (Scheme 17).

Thus, photolysis of the olefin (197) was expected to afford the quinoline (226). Unfortunately, however, on irradiation at 254 nm, a solution of the olefin rapidly discoloured, and after 1 h only starting material could be partially recovered. The remainder had been converted into polar material, and no trace of the desired quinoline (226), or any other product, could be detected.

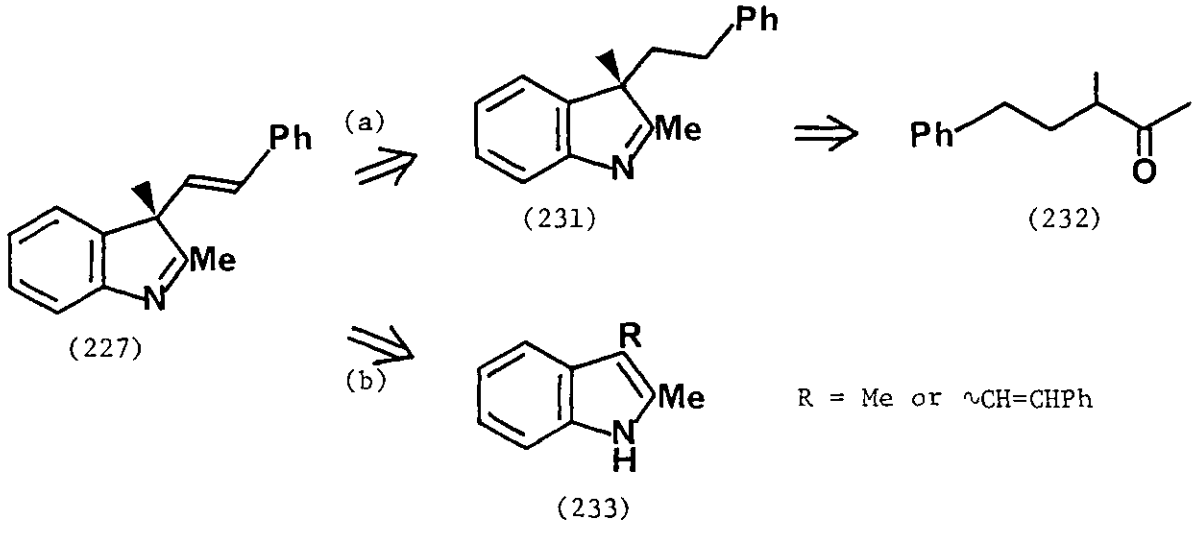
This disappointing result prompted a synthesis of the styryl indolenine (227), photolysis of which was expected to afford the benzylquinoline (230). It was hoped that this model would undergo the desired photo-rearrangement more readily, since both of the proposed diradical intermediates, (228) and (229), would be stabilised by being doubly benzylic.



(227) (228) (229) (230)

5.2.2. 2,3-Dimethyl-3-(2-Phenylethenyl)-3*H*-Indole.

A retrosynthetic analysis of the molecule (227) disclosed two possible approaches; one involving dehydrogenation of the saturated phenethyl indolenine (231), itself available through Fischer reaction of the ketone (232) (Scheme 24a), with the other relying on alkylation of a suitable indole precursor (233) (Scheme 24b).

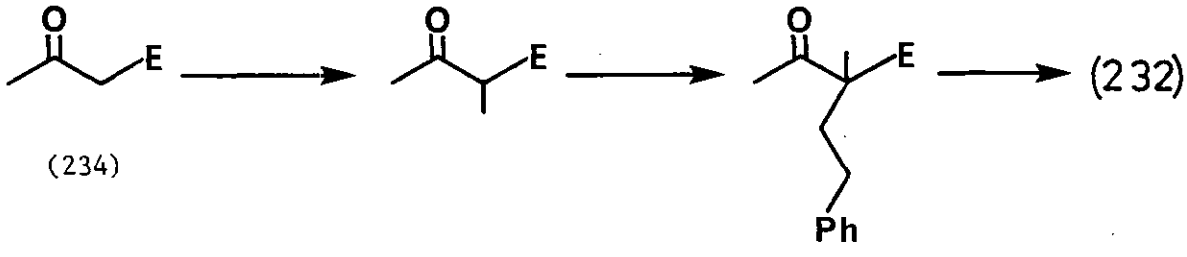


(227) (231) (232) (233)

SCHEME 24

5.2.2.1. From 2,3-Dimethyl-3-(2-Phenylethyl)-3*H*-Indole.

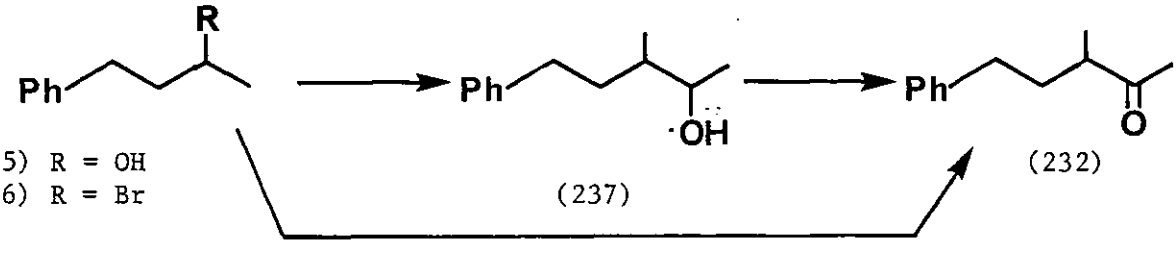
The ketone (232) required for the synthesis of the indolenine (231) had been prepared previously by alkylation of acetoacetic ester (234), with subsequent hydrolysis and decarboxylation.[148] However, in practice



(234)

this route was found to be cumbersome, and difficulties were experienced in the separation of products from by-products or unchanged starting material, and an alternative was sought.

The bromide (236), obtained in excellent yield by treatment of the alcohol (235) with phosphorus tribromide,[149] was converted into its Grignard derivative. On reaction of this with acetyl chloride in the presence of a trace of ferric chloride,[150] a low yield of the desired ketone (232) was obtained. Using acetonitrile[151] in place of the acyl chloride gave no identifiable product. A two step procedure was next attempted, in which



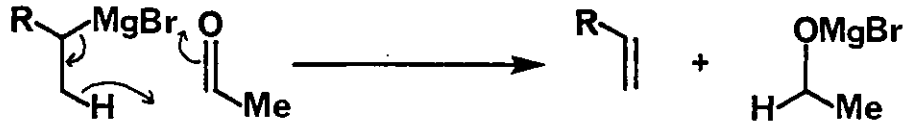
(235) R = OH
(236) R = Br

(237)

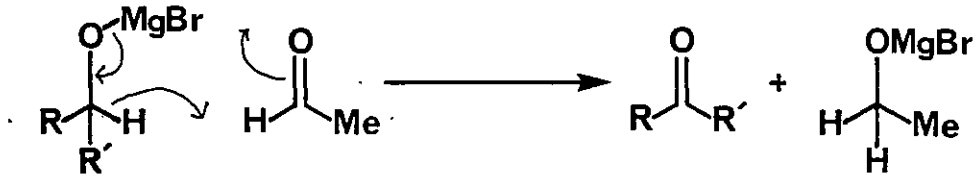
(232)

the intermediate alcohol (237) could be oxidised to the ketone. Addition of acetaldehyde to the Grignard derivative unexpectedly resulted in the

isolation of a number of products of which the major (50%) was a hydrocarbon. Further investigation showed that this fraction consisted of an inseparable mixture of 1-phenylbutane together with phenylbutene. A second product was readily identified as being the desired alcohol (237), whilst the third surprisingly proved identical to the ketone (232) obtained previously. The alkane is thought to originate by quenching of the Grignard reagent with residual water remaining in the acetaldehyde after drying, or by deprotonation of the aldehyde to give the enolate, or possibly both. Reduction of the aldehyde by the Grignard derivative[152] could account for the presence of the olefin. Oxidation of the initially formed alcohol



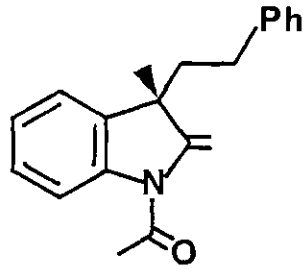
(237) to the ketone (232) may proceed by an Oppenauer-type process.



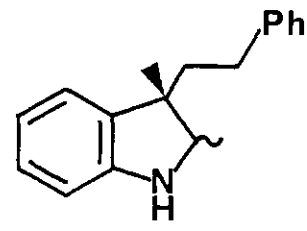
Pyridinium chlorochromate[117] oxidation of the alcohol (237) afforded an excellent yield of the ketone (232), the phenylhydrazone of which smoothly underwent Fischer cyclisation to the indolenine (231). It was anticipated that dehydrogenation *via* initial bromination of this to the

olefin (228) could be achieved using NBS under radical conditions. Although some attack at the 2-methyl group was expected by analogy with the carbazolenine (160), it was hoped that benzylic bromination would occur more readily and hence predominate. Once formed, the benzylic bromide would probably eliminate hydrogen bromide *in situ*.

However, reaction of the indolenine (232) with NBS under similar conditions to those described previously (p. 77) resulted in complex mixtures of unstable products, in which the 2-methyl group had been attacked almost exclusively. No trace of benzylically-brominated, or eliminated products could be detected. An attempt to suppress acid-catalysed 'enolisation' of the imine in (232), and hence electrophilic attack at the 2-position by addition of calcium carbonate[153] was unsuccessful. Similarly, acetylation to the enamide (238) or reduction to the indoline (239) failed to induce benzylic bromination. The 2-position was again attacked in the former case, whereas nuclear substitution of the indoline aromatic ring appeared to occur in the latter. Subsequent efforts towards the synthesis of the styryl indolenine (227) were directed at approaches involving elaboration of indoles (Scheme 24b).



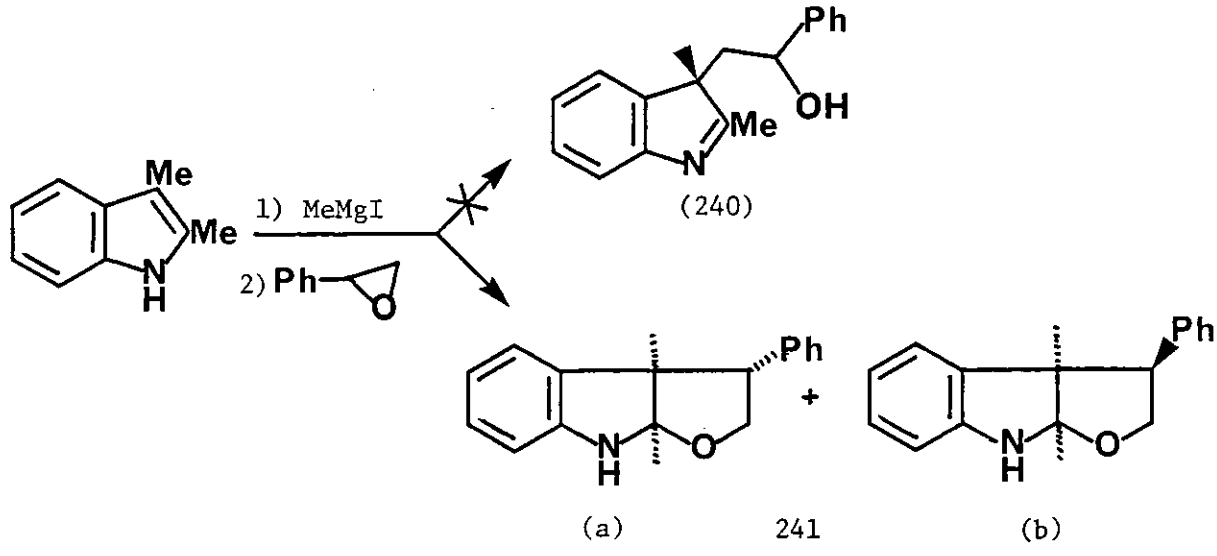
(238)



(239)

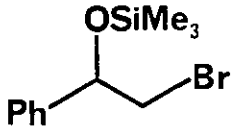
5.2.2.2. From Indoles.

One possible approach to the indolenine (227) involves alkylation of 2,3-dimethylindole at the 3-position with a suitable styrene derivative in which the desired unsaturation could be introduced subsequently. One such derivative considered was the oxide, which on reaction with the Grignard derivative of 2,3-dimethylindole was expected to afford the alcohol (240), dehydration of which would lead to the desired olefin. In practice, however, treatment of the appropriate indolyl Grignard reagent with styrene oxide lead to the isolation of two acid-soluble products in low yield both of which were isomeric with the desired alcohol (240). Spectral properties suggested these to be the two diastereomeric tetrahydrofuranoindolines, (241a) and (241b). Similar products have been isolated from the 3-alkylation of tryptophol.[154] The regio- and stereo-

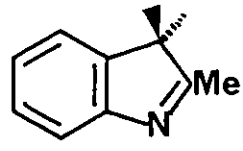


chemistry of both products was tentatively assigned on the basis of their n.m.r. spectra. Attack of the indole at the more hindered α position in the epoxide was not as expected, and suggests some degree of S_N1 type displacement.

By using a suitably protected bromohydrin, it was reasoned that the problem of addition of alkoxide ion, formed on opening the epoxide, to the C=N in the indolenine may be circumvented. The derivative chosen was the trimethylsilyl ether of styrene bromohydrin (242), readily prepared by silylation of styrene bromohydrin[155] in the presence of triethylamine. Reaction with the indolyl Grignard reagent at elevated temperature in anisole solution resulted in a very complex mixture, from which the only acid soluble product to be isolated was identified as being 2,3,3-trimethyl-3*H*-indole (243). This is believed to have arisen



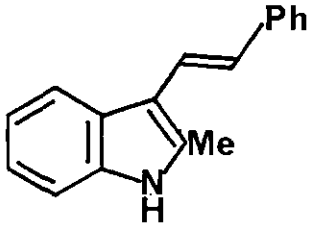
(242)



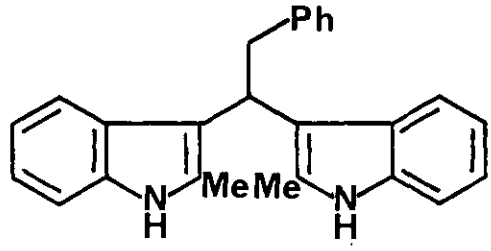
(243)

by reaction of residual methyl iodide remaining after formation of methylmagnesium iodide, with the subsequently introduced dimethylindole.

The alternative approach depicted in path b of Scheme 24 was also investigated, and proved ultimately successful, although a number of frustrating problems needed to be overcome in the process. The preparation of a key intermediate, 2-methyl-3-styrylindole (244) had been previously reported, and involved addition of phenylacetaldehyde to the Grignard derivative of 2-methylindole, with subsequent *in situ* elimination of the resultant alkoxide by addition of ethyl formate.[156] Repeating the reaction under the conditions described afforded a product with a similar melting point to that quoted by the authors, but with spectral properties wholly inconsistent with it having the proposed structure.



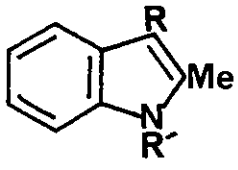
(244)



(245)

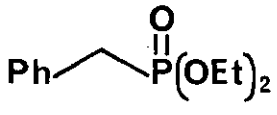
The only spectral data provided in the original paper consisted of a single peak in the i.r. at 970-950 cm^{-1}, which was taken to be indicative of a *trans* olefin. However, no such peak could be detected in the i.r. spectrum of the product obtained, which furthermore exhibited no signals due to olefinic protons in the n.m.r. spectrum. Instead, this showed signals due to thirteen protons in the aromatic region, a two- and six-proton singlet at δ 10.5 and 2.1 respectively, and a two-proton doublet at δ 3.65, coupled to a one-proton triplet at δ 4.5. These, and other spectral data suggested the product to be the diindolyl methane (245). Similar double addition of indolyl Grignard reagents to carbonyl compounds has been observed previously.[157] Variation of reaction conditions offered no improvement, and a multi-step preparation of the desired olefin (244) was subsequently adopted. Thus Vilsmeier-Haack reaction[158] of 2-methyl indole afforded the corresponding 3-formyl derivative (246) in excellent yield. Contrary to a previous report,[159] direct Wittig olefination of the *N*-unprotected indole was unsuccessful, and lead only to recovery of starting material, presumably due to deprotonation of the

activated indole by the ylide. Protection of the indole by tosylation proved troublesome; thus deprotonation of the formyl derivative (246) with sodium hydride in DMF, followed by treatment with tosyl chloride resulted in the formation of an amorphous yellow solid which appeared to be polymeric. Using dimethoxyethane as solvent[160] afforded the desired tosylate (247) in only 20% yield. With potassium



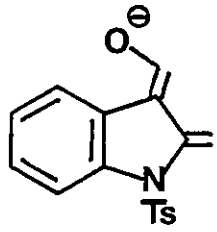
(246) R = CHO, R^1 = H
(247) R = CHO, R^1 = Ts
(248) R = $-CH_2$=CHPh, R^1 = Ts

carbonate as base, in acetone or butanone yields were found to be variable, the optimum yield (55%) being obtained with butanone as solvent with relatively short reaction times. Prolonging the time of reaction decreased the yield of product, and in all cases the crude reaction mixtures were observed to contain considerable quantities of dark, polar material. Conversion of the aldehyde (247) to the olefin (248) was effected by Wittig reaction with the ylide derived from benzyltriphenylphosphonium bromide on deprotonation with dimsyl sodium in DMSO.[162] A cleaner reaction resulting in superior yields could be achieved using *n*-butyllithium in THF as base.[163] Attempts to facilitate work-up by employing the Wadsworth-Emmons-Horner reaction failed with the phosphonate (249). Hydrolysis of the tosylate (248) to the *N*-unsubstituted indole (244) proceeded smoothly with sodium hydroxide in aqueous methanol.

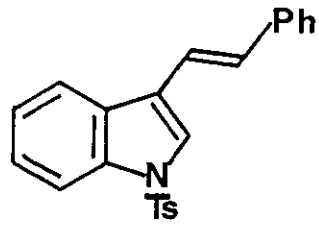


(249)

In a recent paper,[160] Gallagher and Magnus also report experiencing difficulties in the preparation of *N*-arenesulphonyl derivatives of 3-formylindoles bearing a 2-methyl group. The increase in acidity of the 2-methyl group on tosylation facilitates deprotonation at this site, giving an anion which is capable of existing in the *o*-quinoidal enolate form (250). It is this presumably reactive species which is thought responsible for various undesirable side-reactions leading to a decrease in yield of product. It was reasoned that such a problem could be



(250)



(251)

obviated by introduction of the 2-methyl group at a later stage, and with this in mind, the styryl indole (251) was prepared. Tosylation of 3-formylindole under identical conditions to those used for the 2-methyl derivative (246) resulted in 87% yield of the corresponding *N*-tosyl derivative, which required no further purification. Wittig olefination again proceeded in good yield to afford an inseparable 1:1 mixture of geometric isomers (251). However, deprotonation at the 2-position using *n*-butyllithium, with subsequent methylation[165] afforded only modest yields of the methyl derivative (248) which could not be separated from unreacted starting material, and hence the original procedure, starting from 2-methylindole was retained.

By analogy with the enolates of α,β-unsaturated ketones, methylation of the Grignard derivative of styryl indole (244) was expected to occur at the 3-position, rather than at the conjugated benzylic position of the side-chain. This proved to be correct, but the reaction could not be induced to proceed in greater than 11% yield. Performing the reaction at elevated temperatures offered no improvement in yield, and only lead instead to diminished recovery of starting material.

Frustratingly, irradiation of the indolenine (227) in acetonitrile at 300 nm gave no reaction, while at 254 nm extensive decomposition occurred. Several very minor products were isolated but could not be identified, although all were shown not to be the desired quinoline (231) by comparison with an authentic specimen.

6. INDEPENDENT SYNTHESES OF REACTION PRODUCTS.

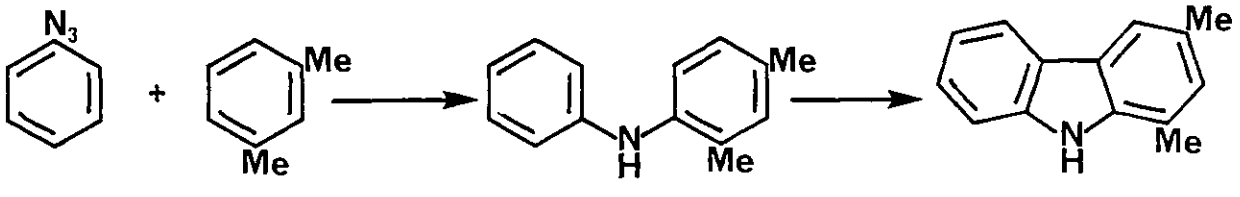
6) INDEPENDENT SYNTHESES OF REACTION PRODUCTS.

During the course of the work described in Chapters 2 and 3, it became necessary to prepare a number of the proposed products obtained from photolyses and thermolyses. Many of these products were difficult to purify, especially polymethylated carbazoles, and consequently accurate melting points could not be determined. Some were unknown, while for others, values quoted for their physical properties in the literature were often variable. Furthermore, the substitution pattern of many carbazoles could not be determined spectroscopically and it was therefore considered that comparison of these products with compounds synthesised by independent and unambiguous routes was the only way to ensure unequivocal identification.

6.1. Carbazoles.

6.1.1. Di- and Trimethylcarbazoles.

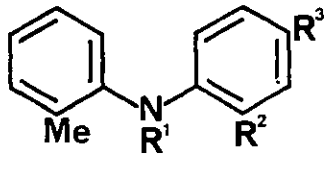
Although some of the steps proceeded in poor yield, an approach involving photocyclisation of diphenylamines to carbazoles was adopted as being the shortest and most economical entry to these heterocycles. The preparation of 1,3-dimethylcarbazole (107b) is outlined. Reaction of



(252) (107b)

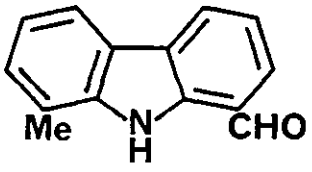
meta-xylene with phenyl azide in trifluoroacetic acid[166] provided the diphenylamine (252) in 53% yield. Irradiation of a solution of this amine in petrol at 300 nm, in the presence of air,[167,55a] afforded a 26% yield of 1,3-dimethylcarbazole (107b). Methylation of this to 1,3,9-trimethylcarbazole (106b) could be accomplished smoothly by the action of sodium hydride in DMF followed by methyl iodide.[168]

An analogous procedure was used to prepare 1,8-dimethylcarbazole (108), although the diphenylamine (255) was prepared by an alternative method, since it was expected that toluene would not be sufficiently activated to undergo electrophilic attack by 2-methylphenylazide. A mixture of isomers with 2,4'-dimethyldiphenylamine (253) predominating could also be anticipated if reaction did indeed occur.



(253) $R^1 = R^2 = H$, $R^3 = Me$
(254) $R^1 = Ac$, $R^2 = Me$, $R^3 = H$
(255) $R^1 = R^3 = H$, $R^2 = Me$

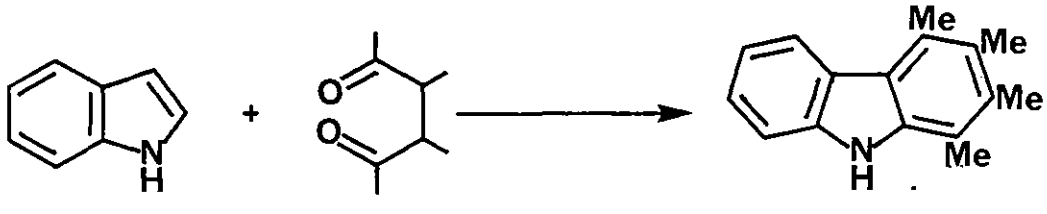
Thus, condensation of 2-methylacetanilide with 2-bromotoluene in the presence of copper(I) iodide and potassium carbonate[169] afforded the acetyldiphenylamine (254) in 36% yield. No hydrolysis took place when this was treated with refluxing ethanolic potassium hydroxide, but with ethylene glycol as solvent an excellent yield of the free amine (255) resulted. Irradiation of an aerated solution of this in petrol using a medium pressure immersion lamp gave rise to two products, of which the major was identified as the desired 1,8-dimethylcarbazole (108). The second product had incorporated oxygen, and was suggested by spectroscopic properties to be the aldehyde (256).



(256)

6.1.2. 1,2,3,4,9-Pentamethylcarbazole.

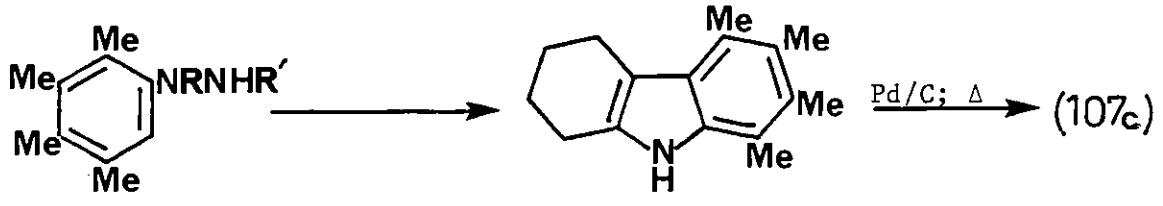
An attempt to prepare 1,2,3,4-tetramethylcarbazole (107c) by photocyclisation of the appropriate diphenylamine was unsuccessful. Although the amine was readily available from reaction of phenyl azide with tetramethylbenzene, irradiation afforded only a negligable quantity of the desired carbazole, and lead instead to decomposition of the rather sensitive starting material. An alternative method for its preparation was thus sought. A previous synthesis involving condensation of indole with 3,4-dimethylhexa-2,5-dione[170] was considered unsatisfactory due to the very low yield of product obtained.



(107c)

For these reasons, a synthesis based on the Fischer reaction was adopted. The required phenylhydrazine (258) was prepared by hydrolysis of the corresponding carbazate (257), itself prepared by reaction of

tetramethylbenzene with dimethyl azodicarboxylate in the presence of boron trifluoride.[171] The phenylhydrazine (258) was found to be sensitive to air and light, and so was converted into its stable hydrochloride (259). This salt was used directly in the Fischer reaction[172] with cyclohexanone to give the unstable tetrahydrocarbazole (260), which was immediately dehydrogenated with palladium on charcoal to the desired carbazole (107c). A moderate yield of the pentamethylcarbazole (106c) was provided by *N*-methylation as described previously.



(260)

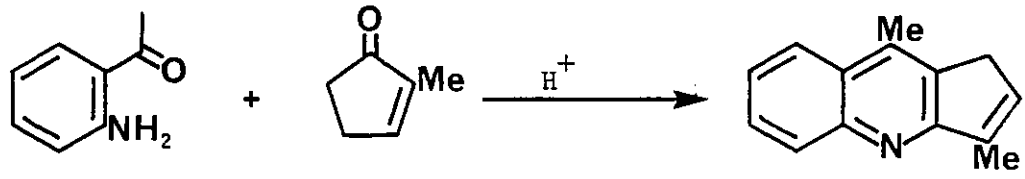
(258) R = R^1 = CO_2Me
(259) R = R^1 = H
(260) R = H, R^1 = $H_2^+C\ell_2^-$

6.1.3. Benzo-Fused Carbazoles.

Both of the benzocarbazoles (147) and (153) were prepared by standard methods. Thus Fischer reaction of the appropriate tetralone gave the corresponding dihydrobenzocarbazole, which was readily dehydrogenated with palladium on charcoal to afford the fully aromatic carbazoles. Methylation on nitrogen was accomplished in good yield as before, using sodium hydride and methyl iodide.

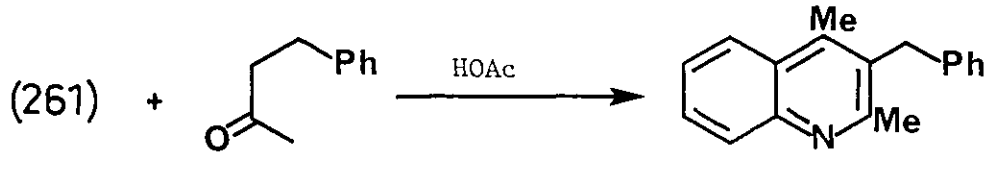
6.2. Quinolines.

All of the required quinolines were available by using the Friedlander synthesis, in which 2-aminoacetophenone (201) was condensed with the appropriate ketone under acidic conditions. In this way, a low yield of 1,4-dimethylcyclopenta[*b*]quinoline (112a) was obtained using 2-methyl cyclopentenone (262) as the ketone.



(261) (262) (112a)

Repeating the reaction with 1-indanone as the ketone afforded a modest yield of the indenoquinoline (119). However, no reaction was observed with 4-phenylbutan-2-one (203) using hydrochloric acid in aqueous ethanol as the acidic medium, as in the previous two cases. The problem was eventually resolved by performing the reaction in acetic acid,[174] which furnished a moderate yield of the benzylquinoline (230).



(263) (230)

6.3. Conclusions.

The products obtained on thermolysis and photolysis of benzotriazoles bearing "*ortho*-blocked" 1-aryl substituents are derived from intermediate 4a*H*-carbazoles. Confirmation of this fact is provided by the photolysis of a naphthyl benzotriazole, in which benzannelation confers sufficient stability to allow for isolation of the initially-formed 4a*H*-carbazole. Simpler 4a*H*-carbazoles are not isolable under the conditions employed for their generation, and rearrange further to aromatic carbazoles in the case of thermolysis, or cyclopentaquinolines in photolyses. Each type of product is exclusive to the mode of decomposition of benzotriazoles employed and it is presumed that they arise by different pathways; the carbazoles being formed by thermally-allowed migration of the 4a*H*-carbazole bridgehead substituent, whilst formation of quinolines is believed to proceed *via* an aza-di-π-methane rearrangement. The proposal of such a rearrangement differs considerably from a mechanism involving thermally, but not photochemically, allowed vinyl bond migration and spiro-intermediates, previously proposed to account for the formation of ring-permuted products, analogous to cyclopentaquinolines, from 3a*H*-benzimidazoles. Although supported only by circumstantial evidence, the photochemical mechanism is nonetheless considered to be a more satisfactory rationalisation for the formation of quinolines from 4a*H*-carbazoles. The formation of a ring-permuted product, differing from that obtained on photolysis, on thermolysis of both isomeric benzo-fused 4a*H*-carbazoles is thought to be the only genuine example of the operation of a mechanism involving spiro-intermediates and vinyl-bond migration.

In contrast to the benzannelated 4a*H*-carbazoles mentioned previously which are readily prepared and stable, simple examples of this ring system have eluded all attempts at their isolation, although good evidence exists

for the generation of a tricyclic 4a*H*-carbazole in solution as an enolate ion. However, it is believed that several of the species investigated do show future promise as 4a*H*-carbazole precursors.

The generality of photochemical rearrangement to ring-permuted products or aromatisation by thermal migration of the bridgehead substituent in species bearing the 3a*H*-indene system is further illustrated by the reactions of 4a*H*-fluorenes.

PART III. EXPERIMENTAL

7.1. GENERAL INFORMATION

Petrol refers to that fraction of b.p. 60-80°C, and was distilled prior to use. Ether and benzene were dried by standing over sodium wire, and were stored in darkened bottles. THF and dimethoxyethane (DME) were distilled from potassium and benzophenone ketal, and stored under dry nitrogen. Anisole and chlorobenzene were dried by distillation from calcium hydride. DMF, DMSO, and HMPA were distilled from calcium hydride at reduced pressure and stored under nitrogen over 4A molecular sieves. Pyridine was distilled from potassium hydroxide and stored under nitrogen over potassium hydroxide pellets. Carbon tetrachloride and dichloromethane were purified by distillation. Acetonitrile for photolyses was distilled from phosphorus pentoxide.

Potassium fluoride for fluoronitrobenzene condensations was dried immediately prior to use by heating to dull red heat for *ca.* 10 min, and then rapidly pulverised.

Chromatography refers to medium pressure column chromatography performed at 5-10 $lbin^{-2}$ and employing Merck Kieselgel 60 H silica gel. Samples were usually applied as a dry, pre-absorbed mixture with a small amount of absorbant. Reactions were monitored by t.l.c. using Merck Kieselgel 60 F_{254} aluminium backed silica gel plates cut to the appropriate size. Plates were visualised under u.v. light at 254 and 306 nm, or by the use of iodine vapour for compounds lacking a suitable chromaphore. P.l.c. employed glass plates (20 x 20 or 2 x 40 cm) coated to a thickness of 2 mm with Merck Kieselgel Type 60 GF_{254}. A Perkin Elmer Sigma 3 gas chromatograph with nitrogen as the carrier gas was used for all g.l.c. determinations. H.p.l.c. utilised an Altex 110A pump and a 4.6 x 250 mm Ultrasphere ODS 5 μ reverse-phase column, in

conjunction with a Cecil Instruments CE 515 Double Beam Scanning Monitor. Stopped-flow scans were recorded on a Cecil Instruments CE 500 Control-Record Module.

I.r. spectra were recorded in the range 4000-600 cm^{-1} using a Perkin Elmer 257 grating spectrophotometer. Samples were run as Nujol mulls or in solution for solids, and as thin films for liquids. U.v. spectra were recorded on a Pye-Unicam SP 800 recording spectrophotometer in the range 200-450 nm, and points of inflexion are abbreviated (sh). Proton n.m.r. spectra were determined using a Perkin Elmer R32 instrument operating at 90 MHz or a Bruker WM 250 spectrometer operating at 250 MHz. All spectra included tetramethylsilane (TMS) as an internal standard; most of those run at 90 MHz employed a heteronuclear lock (TMS), while all of those recorded at 250 MHz employed a homonuclear lock (deuterium of the solvent). Other spectrometers used were Varian EM 360 and T60 instruments, operating at 60 MHz. Signals are described as singlets (s), doublets (d), triplets (t), quartets (q), multiplets (m), broad (br.), double doublets (dd), etc. Broad band decoupled ^{13}C n.m.r. spectra were recorded using a Bruker WM 250 spectrometer operating at 62.9 MHz. Mass spectra were recorded at low resolution using A.E.I. MS 12 and VG Micromass 7070 B instruments, the latter being used also for high resolution determinations. Samples were mostly recorded at 70 eV using a direct insertion probe.

Photolyses were performed in a Rayonet photochemical reactor using lamps of 254 or 300 nm. Solutions were contained in quartz vessels and were purged with nitrogen for at least 0.5 h prior to irradiation. A thin stream of nitrogen was passed through the solutions for the duration of the photolysis.

Melting points were determined on a Kofler hot stage apparatus and are corrected.

7.2. EXPERIMENTAL FOR CHAPTER 2.

General Procedure for the Preparation of 2-Nitrodiphenylamines - A mixture of the appropriate amine (2 eq.), 2-fluoronitrobenzene (1 eq.), and anhydrous potassium fluoride (1.2 eq.) was heated with stirring under the conditions indicated in Table 1 (p. 41). On cooling, the mixture was extracted with chloroform (150-200 ml) and water (150 ml), the layers separated and the lower washed with water (100 ml), dried ($MgSO_4$) and evaporated to leave a black gum. On chromatography (petrol or 19:1 petrol-dichloromethane) this afforded the corresponding nitrodiphenylamine. The following compounds were prepared in this way:

2,4-*Dimethyl*-2'-*nitrodiphenylamine* - red prisms, m.p., 62-63°C (from petrol-dichloromethane) (Found: C, 69.6; H, 5.85; N, 11.6. $C_{14}H_{14}N_2O_2$ requires C, 69.4; H, 5.8; N, 11.6%); ν_{max} ($CC\ell_4$) 3350, 1615, and 1610 cm^{-1}; δ ($CDC\ell_3$) 2.20 (3H, s, 2-Me), 2.35 (3H, s, 4-Me), 6.50-7.50 (6 H, m, ArH), 8.25 (1H, m, ArH), and 9.33 (1H, br.s, N*H*); *m/e* 242 (M^+; base), 208, 194 and 180.

2,6-Dimethyl-2'-nitrodiphenylamine (89a) - yellow plates, m.p., 108.5-109.5° (from ethanol) (lit.,[50] 106-107°C).

2-Nitro-2',4',6'-trimethyldiphenylamine (89b) - orange needles, m.p., 142-142.5°C (from ethanol) (lit.,[49] 138.5-139.5°C); ν_{max} ($CC\ell_4$) 3360, 2930, 1610, 1570, 1490, 1450, 1410, and 1270 cm^{-1}; δ ($CC\ell_4$) 2.22 (6 H, s, 2',6'-Me), 2.37 (3H, s, 4'-Me), 6.45 (1 H, dd, *J* 7 Hz, 6-H), 6.60-7.60 (5 H, m, ArH), 8.25 (1H, dd, *J* 7 Hz, 3-H), and 9.10 (1 H, br.s, N*H*); *m/e* 256 (M^+; base), 222, 208 and 194.

2-Chloro-2'-nitrodiphenylamine - orange needles, m.p., 116-117°C (from ethanol) (lit.,[175] 115-116°C).

3-*Chloro*-2'-*nitrodiphenylamine* - orange needles, m.p., 88°C (from ethanol) (Found: C, 57.8; H, 3.6; N, 11.1. $C_{12}H_9C\ell N_2O_2$ requires C, 58.0; H, 3.65; N, 11.3%); ν_{max} ($CC\ell_4$) 3350, 1615, 1570, 1490, and 1260 cm^{-1}; δ ($CC\ell_4$) 6.60-7.55 (6 H, m, ArH), 8.15 (1 H, m, ArH), and 9.35 (1H, br.s, N*H*); *m/e* 250, 248 (M^+; base), 214, 203, 201, and 167.

4-Chloro-2'-nitrodiphenylamine - red needles, m.p., 145.5°C (from ethanol) (lit.,[176] 145-146°C).

2-*Nitro*-2'-*phenyldiphenylamine* - red needles, m.p., 64-66°C (from petrol-dichloromethane) (Found: C, 74.3; H, 4.9; N, 9.6. $C_{18}H_{14}N_2O_2$ requires C, 74.5; H, 4.9; N, 9.65%); ν_{max} ($CC\ell_4$) 3350, 3060, 1610, 1565, 1490, 1340, 1270, and 695 cm^{-1}; δ ($CC\ell_4$) 6.35-8.20 (13 H, m, ArH) and 9.33 (1 H, br.s, N*H*); *m/e* 290 (M^+; base), 255, 243, 242, and 241.

2-*Nitro*-2',3',4',5',6'-*pentamethyldiphenylamine* (89c) - orange rods, m.p., 153°C (from ethanol) (Found: C, 71.6; H, 7.1; N, 9.8. $C_{17}H_{20}N_2O_2$ requires C, 71.8; H, 7.1; N, 9.85%); ν ($CC\ell_4$), 3350, 2910, 1605, 1560, 1485, 1250 and 1140 cm^{-1}; δ ($CC\ell_4$) 2.11 (6 H, s, 3',5'-Me), 2.23 (9 H, s, 2',4',6'-Me), 6.30 (1 H, dd, *J* 9, 1 Hz, 6-H), 6.65 (1 H, m, 4-H), 7.22 (1 H, m, 5-H), 8.16 (1 H, dd, *J* 8, 2 Hz, 3-H), and 9.12 (1 H, br.s, N*H*); *m/e* 285, 284 (M^+; base), 237, 236, 235, 222, and 221.

2-*Methyl*-N-(2-*nitrophenyl*)-1-*naphthylamine* - yellow prisms, m.p., 142-144°C (from ethanol-benzene) (Found: C, 73.2; H, 5.05; N, 10.0. $C_{17}H_{14}N_2O_2$ requires C, 73.4; H, 5.1; N, 10.1%); ν_{max} ($CC\ell_4$) 3360, 1620, 1500 and 1275 cm^{-1}; δ ($CC\ell_4$) 2.42 (3 H, s, Me), 6.20-8.35 (10 H, m, ArH), and 9.43 (1 H, br.s, N*H*); *m/e* 278 (M^+; base), 231, 230, and 217.

2,3,4,5,6-Pentamethylnitrobenzene (94) - Prepared in 71% yield from pentamethylbenzene according to the method of Olah,[52] m.p., 152-156°C (from ethanol) (lit.,[177] 154°C).

2,3,4,5,6-Pentamethylaminobenzene (95) - Granulated tin (15.9 g, 0.13 mol) was added to a solution of pentamethylnitrobenzene (13.0 g, 67 mmol) in hot acetic acid (150 ml), followed by concentrated hydrochloric acid (50 ml). After refluxing for 2.5 h, a portion of the solvent (ca. 100 ml) was removed by distillation, and the mixture cautiously added to sodium hydroxide (210 g), in water (350 ml) on cooling. Steam distillation of the resultant mixture afforded 2000 ml of distillate which was saturated with sodium chloride, cooled, and extracted with ether (4 x 150 ml). The combined extracts were dried ($MgSO_4$) and evaporated to give the product as a pale yellow powder (6.35 g, 58%), m.p., 140-143°C (lit.,[178] 151°C). The product was used without further purification.

Reduction of 2-Nitrodiphenylamines - A suspension of the nitro compound in degassed ethanol containing palladium on charcoal (10%; 10% of the weight of nitro compound) was stirred under hydrogen at atmospheric pressure until uptake of gas had ceased. The resulting suspension was filtered through Celite and the filtrate reduced to ca. 10 ml. Conversion of the amine to its hydrochloride was achieved by addition of an excess of concentrated hydrochloric acid, followed by evaporation to dryness. Where necessary, black, tarry contaminants were removed by trituration with benzene. The purified salts were recrystallised from aqueous ethanol containing a trace of hydrochloric acid.

The pentamethyl compound (90c) was converted to its hydrochloride under anhydrous conditions by treatment with an ethereal solution of hydrogen chloride.

2-Amino-2'6'-dimethyldiphenylamine Hydrochloride (90a.HCℓ) - grey needles (88%), m.p., 185°C (dec.) (Found: C, 67.6; H, 7.0; N, 11.3. $C_{14}H_{17}C\ell N_2$ requires C, 67.3; H, 7.3; N, 11.2%); ν_{max} (Nujol) 3320, 2960-2840, 2585,

1625, 1510, 1300, 770, and 745 cm^{-1}; δ (d_6-DMSO) 2.17 (6 H, s, 2',6'-Me), 6.15 (1 H, dd, *J* 7 Hz, 6-H), 6.65-7.65 (9 H, m, ArH, and $NH_3C\ell$), and 8.05 (1 H, br.s, N*H*); *m/e* 212 (M^+ - HCℓ; base), 197, 195, 194, and 180.

2-*Amino*-2',4',6'-*trimethyldiphenylamine Hydrochloride* (90b. HCℓ) - amorphous pink solid (93%), m.p., 172-175°C (dec.) (Found: C, 68.5; H, 7.35; N, 10.6. $C_{15}H_{19}C\ell N_2$ requires C, 68.6; H, 7.3; N, 10.7%); ν_{max} (Nujol) 3410, 3350, 1640, 1505, 1380, and 1325 cm^{-1}; δ (d_6-DMSO) 2.00 (6 H, s, 2',6'-Me), 2.18 (3 H, s, 4'-Me), 6.05 (1 H, dd, *J* 7, 1 Hz, 6-H), and 6.50-7.50 (6 H, m, ArH, and N*H*); *m/e* 227, 226 (M^+ - HCℓ; base), 211 and 208.

2-*Amino*-2',3',4',5',6'-*pentamethyldiphenylamine Hydrochloride* (90c. HCℓ) - white microneedles (92%) m.p., 175-176°C (dec.) (Found: C, 70.45; H, 8.0; N, 9.6. $C_{17}H_{23}C\ell N_2$ requires C, 70.2; H, 8.0; N, 9.6%); ν_{max} (Nujol) 3310, 2550, 1620, 1505, and 740 cm^{-1}; δ (d_6-DMSO) 2.05 (6 H, s, 3',5'-Me), 2.19 (9 H, s, 2',4',6'-Me), 2.85-3.90 (3 H, br, $NH_3C\ell$), 6.00 (1 H, d, *J* 8 Hz, 6-H), and 6.40-7.45 (4 H, m, ArH and N*H*); *m/e* 255, 254 (M^+ - HCℓ; base), 239, 224 and 222.

1-(2-*Aminophenyl*)-2-*methyl*-1-*naphthylamine Hydrochloride* (96) - grey, amorphous solid (88%), m.p., 192-194°C (dec.) (Found: C, 71.8; H, 6.0; N, 9.8. $C_{17}H_{17}C\ell N_2$ requires C, 71.8; H, 6.0; N, 9.8%); ν_{max} (Nujol) 3290, 2560, 1615, 1505, 805, and 735 cm^{-1}; *m/e* 249, 248 (M^+ - HCℓ; base), 247, 232, and 230.

1-(2,6-Dimethylphenyl)benzotriazole (91a) - 2-Amino-2',6'-dimethyldiphenylamine hydrochloride (3.72 g, 15 mmol) was dissolved in hot hydrochloric acid (1 M; 180 ml) containing ethanol (45 ml), and the solution rapidly cooled to 0°C with vigorous stirring. The resultant suspension was maintained at 0-5°C during dropwise addition of a solution of sodium

nitrite (1.36 g, 20 mmol) in water (10 ml), after which it was allowed to warm to room temperature and stirred for a further 4 h. Addition of an equal volume of brine was followed by filtration, the brown solid collected being washed well with water and dried. Sublimation at 70°C and 2 x 10^{-2} mmHg with subsequent recrystallisation from petrol gave 1-(2,6-*dimethylphenyl*)*benzotriazole* as large, square plates (2.61 g, 78%), m.p., 68-70°C. (Found: C, 75.55; H, 6.0; N, 19.0. $C_{14}H_{13}N_3$ requires C, 75.3; H, 5.9; N, 18.8%); ν_{max} ($CC\ell_4$), 3060, 2970, 2910, 1610, 1490, 1470, 1270, 1180, 1060 and 1030 cm^{-1}; λ_{max} (EtOH) 210 (log, ε 4.26), 256 (3.94), 261 sh (3.92), 272 sh (3.72) and 283 nm (3.69); δ ($CC\ell_4$) 1.79 (6 H, s, 2,6-Me), 6.96-7.37 (6 H, m, ArH), and 8.03 (1 H, m, ArH); *m/e* 223 (M^+), 195, 194 (base), and 180.

Similarly prepared were:

1-(2,4,6-*Trimethylphenyl*)*benzotriazole* (91b) - colourless prisms (96%), m.p., 120-121°C (from petrol) (Found: C, 76.0; H, 6.4; N, 17.8. $C_{15}H_{15}N_3$ requires C, 75.9; H, 6.4; N, 17.7%); ν_{max} ($CC\ell_4$) 2930, 1615, 1500, 1455, 1385, 1280, and 1070 cm^{-1}; λ_{max} (EtOH) 208 (log ε 4.26), 254 (3.82), and 279 sh nm (3.57); δ ($CC\ell_4$) 1.85 (6 H, s, 2,6-Me), 2.40 (3 H, s, 4-Me), and 6.90-8.30 (6 H, m, ArH); *m/e* 237 (M^+), 209, 208, and 194 (base).

1-(2,3,4,5,6-*Pentamethylphenyl*)*benzotriazole* (91c) - amber prisms (86%) m.p., 211-213°C (from petrol-chloroform) (Found: C, 76.7; H, 7.2; N, 15.8. $C_{17}H_{19}N_3$ requires C, 76.95; H, 7.2; N, 15.8%); ν_{max} ($CC\ell_4$) 3010, 2940, 1615, 1450, 1275 and 1065 cm^{-1}; λ_{max} (EtOH) 208 (log ε 4.56), 222 sh (4.17), 256 (3.95), and 276 sh nm (3.80); δ ($CC\ell_4$) 1.72 (6 H, s, 2,6-Me), 2.31 (6 H, s, 3,5-Me), 2.37 (3 H, s, 4-Me), 7.05-7.65 (3 H, m, ArH), and 8.15 (1 H, m, ArH); *m/e* 265 (M^+), 237, 236, 222 (base), and 207.

1-(2-*Methylnaphthyl)benzotriazole* (97) - needles (75%), m.p., 135-137°C (from petrol-dichloromethane) (Found: C, 78.4; H, 5.0; N, 16.15. $C_{17}H_{13}N_3$ requires C, 78.7; H, 5.05; N, 16.2%); ν_{max} ($CC\ell_4$) 3060, 1490, 1450, 1410, 1280, and 1060 cm^{-1}; λ_{max} (EtOH) 214 sh (log ε 4.72), 225 (4.90), 259 sh (4.08), 263 (4.10), 276 sh (4.12), 285 (4.10), 306 sh (3.64), and 321 nm (3.21); δ ($CC\ell_4$) 2.12 (3 H, s, Me), 6.80-7.15 (2 H, m, ArH), 7.21-7.60 (5 H, m, ArH), 7.76-8.05 (2 H, m, ArH), and 8.18 (1 H, m, ArH); *m/e* 259 (M^+), 231, 230 (base), 217, 216, and 115.

1-(2-Methylnaphthyl)benzotriazole (97) - Method B - A suspension of 2-methyl-*N*-(2-nitrophenyl)-1-naphthylamine (2.78 g, 10 mmol) and palladium on charcoal (5%; 638 mg) in methanol (50 ml) was stirred vigorously under hydrogen until uptake of gas had ceased (observed uptake 745 ml; calculated 721 ml). The mixture was filtered through Celite, the filtrate evaporated and the residual green gum dissolved in benzene (40 ml). Addition of amyl nitrite (1.75 g, 15 mmol; 2 ml) was followed by reflux for 4 h, after which the solvent was removed and the residue chromatographed (6:4 petrol-ether) to give a red gum. Trituration with cold ether and subsequent recrystallisation of the solid produced, from petrol-chloroform afforded the *benzotriazole* (97) as pink needles (1.30 g, 50%).

FVP of 1-(2,6-Dimethylphenyl)benzotriazole (91a) - Distillation of the benzotriazole (237 mg) at 110-115°C and 3 x 10^{-2} mmHg into a quartz tube maintained at 640°C gave a brown gum (207 mg). On subjection to p.l.c. (13:6:1 petrol-dichloromethane-ether), this afforded the following fractions: i) 1,9-Dimethylcarbazole (106a) as a buff solid (63 mg, 32%), R_F 0.67; m.p., 113-116°C (from petrol) (lit.,[179] 117°C); δ ($CC\ell_4$) 2.20 (3 H, s, 1-Me), 3.91 (3 H, s, 9-Me), 6.95-7.45 (5 H, m, ArH), and 7.80-8.05 (2 H, m, ArH).

ii) Brown gum (111 mg), R_F 0.52. Chromatography (9:1 petrol-dichloromethane) afforded 1,8-dimethylcarbazole (108) (9.6 mg, 5%), m.p., 176-178°C (from petrol) (lit.,[55b] 178-180°C), undepressed when mixed with an authentic specimen; ν_{max} ($CC\ell_4$) 3475 cm^{-1}; δ ($CC\ell_4$) 2.54 (6 H, s, 1,8-Me), and 7.00-7.95 (7 H, m, ArH and NH); *m/e* 195 (M^+; base), 194, 180, 97.5 and 96.5. Further elution afforded a mixture of carbazoles as a brown semi-solid (87 mg), which h.p.l.c. (7:3 methanol-water) indicated to consist of 1-methylcarbazole (107a) (62%; retention time 6.0 min); λ_{max} 225 sh, 237, 247 sh, 257, 292, 325, and 338 nm, 1,8-dimethylcarbazole (108) (9%; retention time 8.4 min); λ_{max} 221, 238, 245 sh, 256 sh, 291, 325 sh, and 335 nm, and an unidentified carbazole (29% ; retention time 9.1 min); λ_{max} 225 sh, 238, 247sh, 259, 293, 330, and 342 nm.

iii) Yellow oil (14 mg), R_F 0.36 - purified further by p.l.c. (1 x 3:1 petrol-dichloromethane, then 2 x 13:6:1 petrol-dichloromethane-ether) to give 1-methylacridine (105a) as a yellow oil (6.2 mg, 3%); λ_{max} (EtOH), 212, 246 sh, 252, 285 sh, 293, 328 sh, 335 sh, 342, 349, 360 and 381 sh nm; δ ($CDC\ell_3$) 2.95 (3 H, s, Me), 7.42 (1 H, dd, *J* 8, 6.5 Hz, 3-H), 7.52 (1 H, m, 7-H), 7.62 (1 H, dd, *J* 6, 2.5 Hz, 2-H), 7.76 (1 H, ddd, *J* 9, 7, 2 Hz, 8-H), 7.85 (1 H, d, *J* 8 Hz, 4-H), 7.98 (1 H, d, *J* 8.5 Hz, 6-H), 8.28 (1 H, d, *J* 9 Hz, 9-H), and 8.72 (1 H, s, 5-H); *m/e* 193 (M^+; base), 192, 181, and 180.

(iv) Unchanged starting material as a brown gum (10 mg, 4% recovery, R_F 0.24.

v) Acridine (105b) as a brown gum (17.4 mg, 9%), R_F 0.09; λ_{max} (EtOH) 217, 244 sh, 250, 262 sh, 291 sh, 313, 322 sh, 328, 344, 359 and 376 sh nm; δ ($CC\ell_4$) 7.48 (2 H, ddd, 3,7-H), 7.73 (2 H, ddd, 2,8-H), 7.92 (2 H, dd, 4,6-H), 8.25 (2 H, dd, 1,9-H), and 8.67 (1 H, s, 5-H); *m/e* 179 (M^+), 86, 84 (base), 71 and 57.

FVP of 1-(2,4,6-Trimethylphenyl)benzotriazole (91b) - The benzotriazole (155 mg) was sublimed at 100°C and 7.5 x 10^{-2} mmHg into a quartz tube maintained at 700°C. The resultant pyrolysate (136 mg) was subjected to chromatography (7:3 petrol-dichloromethane initially, then with addition of ether in 1% increments up to 5%) to afford:

i) 1,3,9-*Trimethylcarbazole* (106b) as a white solid (20.4 mg, 15%), m.p., 99.5-100.5°C (from petrol-chloroform), undepressed when mixed with an authentic specimen.

ii) Yellow solid (63.1 mg, 50%), which spectroscopy indicated to consist mainly of 1,3-dimethylcarbazole (107b); ν_{max} ($CC\ell_4$) 3480 cm^{-1}.

iii) 1,3-Dimethylacridine (105c) as a dark yellow oil (7.2 mg, 5%); ν_{max} ($CC\ell_4$) 3050, 2910, 1610, 1445, and 905 cm^{-1}; λ_{max} (cyclohexane) 215 (log ε 4.32), 252 (5.04), 285 sh (3.78), 293 (3.82), 332 sh (3.70), 341 (3.80) 356 (3.82), and 378 nm (3.47); δ ($CC\ell_4$) 2.83 (6 H, s, 1,3-Me), 6.88-8.08 (6 H, m, ArH), and 8.35 (1 H, s, 5-H); *m/e* 208,207 (M^+; base), 206, 193 and 192.

iv) Unchanged starting material as a yellow film (2.2 mg, 1.6% recovery).

v) 3-Methylacridine (105d) as a pale yellow gum (7.4 mg, 5%); ν_{max} ($CC\ell_4$) 3060, 2815, 1620, and 1445 cm^{-1}; λ_{max} (EtOH) 212 (log ε 3.25), 245 sh (4.85), 252 (5.18), 296 (2.46), 343 (2.76), 349 (2.81), 358 (2.86), and 375 sh nm (2.40); δ ($CC\ell_4$) 2.56 (3 H, s, Me), 7.20-8.23 (7 H, m, ArH), and 8.50 (1 H, s, 5-H); *m/e* 194, 193 (M^+; base), and 192.

In a subsequent pyrolysis, performed at 640°C, the second fraction was subjected to h.p.l.c. (7:3 methanol-water), which indicated it to consist of 1,3-dimethylcarbazole (106b) (79%; retention time 9.4 min); λ_{max} 223 sh, 238, 247 sh, 260, 295, 330 and 343 nm, and three unidentified carbazoles which had characterstics as follows: (3%; retention time 12.3 min); λ_{max} 222 sh, 238, 248 sh, 260, 295, and 330 nm; (10%; retention time 13.5 min); λ_{max} 220, 240, 249 sh, 258 sh, 292, 328, and 340 nm; and (8%; retention time 14.6 min); λ_{max} 210 sh, 228 sh, 235, 248 sh, 262, 297, 338, and 348 nm.

FVP of 1-(2,3,4,5,6-Pentamethylphenyl)benzotriazole (91c) - Sublimation of the benzotriazole (228 mg) at 120-150°C and 4 x 10^{-2} mmHg into a quartz tube at 640°C afforded a pyrolysate (196 mg), which on chromatography (petrol, then petrol-dichloromethane up to 7:3, and finally with addition of 5% ether) gave:

i) 1,2,3,4,9-*Pentamethylcarbazole* (106c) as a pale brown solid (43 mg, 23%), m.p., 149-152°C (from ethanol), undepressed on admixture with an independently synthesised specimen.

ii) Pale brown solid (83 mg) which h.p.l.c. (7:3 methanol-water) indicated to consist of 1,2,3,4-tetramethylcarbazole (107c) (75%; retention time 22.3 min), and four unidentified carbazoles of retention times 24.1, 29.3, 30.7, and 34.5 min (4, 4.5, 3.5, and 13% respectively).

iii) Starting material as a colourless solid (18 mg, 8% recovery), m.p., 210-212°C.

Photolysis of 1-(2,6-Dimethylphenyl)benzotriazole (91a) - A solution of the benzotriazole (225 mg) in acetonitrile (150 ml) was irradiated at 254 nm for 6.25 h. The gum remaining on removal of solvent was subjected to chromatography (4:1 petrol-ether) to afford unchanged starting material as a colourless gum (90.6 mg, 40% recovery) and 1,4-*dimethyl*-3H-*cyclopenta*[b]-*quinoline* (112a) as white needles (53 mg, 46% based on conversion m.p., 106-108°C (from petrol), undepressed when mixed with an authentic specimen.

Photolysis of 1-(2,4,6-Trimethylphenyl)benzotriazole (91b) - Irradiation of a solution of the benzotriazole (310 mg) in acetonitrile (180 ml) at 254 nm for 22 h afforded a brown solution which was evaporated and the residue chromatographed (1:1 petrol-dichloromethane) to give:

i) 1,3-Dimethylcarbazole (12.4 mg, 6% based on conversion), m.p., 99-100°C (from petrol), undepressed on admixture with an authentic sample.

ii) Unchanged starting material as a yellow solid (28.2 mg, 9% recovery) m.p., 118-120°C.

iii) A green oil (173.3 mg) which n.m.r. indicated to consist of starting material (18%) and 1,3,4-*trimethyl*-3H-*cyclopenta*[b]*quinoline* (112b) (82%). The *quinoline* could be separated by extraction into acid with subsequent basification to give an *oil* b.p., 85-90°C (Kugelrohr) at 0.35 mmHg; ν_{max} ($CC\ell_4$) 3060, 2970, 2920, 2870, 1625, 1440, and 1375 cm^{-1}; λ_{max} (EtOH) 211 (log ε 4.42), 225 (4.52), 249 (4.64), 289 (3.98), 293 (3.99), 297 sh (3.97), 306 (3.96), 313 sh (3.81), 320 (4.00), 328 (3.71), and 335 nm (4.08); δ ($CDC\ell_3$) 1.34 (3 H, d, *J* 7 Hz, 3-Me), 2.29 (3 H, t, *J* 2 Hz, 1-Me),

2.69 (3 H, s, 4-Me), 3.61 (1 H, m, 3-H), 6.62 (1 H, m, 2-H), 7.48 (1 H, ddd, 6-H), 7.63 (1 H, ddd, 7-H), 7.98 (1 H, dd, *J* 8, 1 Hz, 5-H), and 8.13 (1 H, dd, *J* 8, 1 Hz, 8-H); *m/e* 209 (M^+), 194 (base), 180, 167, 152, 139, 115, 89 and 77.

A *picrate* was prepared; yellow needles, m.p., 184-185°C (dec.) (from ethanol) (Found: C, 57.55; H, 4.1; N, 12.7. $C_{21}H_{18}N_4O_7$ requires C, 57.5; H, 4.1; N, 12.8%).

Photolysis of 1-(2,3,4,5,6-Pentamethylphenyl)benzotriazole (91c) - The benzotriazole (122 mg) in acetonitrile (100 ml) was irradiated at 254 nm for 14.5 h, after which the solvent was removed and the residue subjected to p.l.c. (3:1 petrol-ether) to give:

i) A pale yellow solid (16.5 mg, 18% based on conversion), R_F 0.63, which had spectral properties identical to those of 1,2,3,4-tetramethylcarbazole (107c).

ii) A yellow gum (30.6 mg), R_F 0.50, which n.m.r. indicated to consist of unchanged starting material (34%) and 1,2,3,3,4-*pentamethyl*-3H-*cyclopenta*-[b]-*quinoline* (112c) (66%). The *quinoline* was separated by extraction into acid, followed by basification and solvent extraction to give an *oil;* b.p., 120°C (Kugelrohr) at 2 x 10^{-2} mmHg; ν_{max} ($CC\ell_4$) 3070, 2965, 2920, 2860, 1610, 1460, 1440, 1400, and 1375 cm^{-1}; λ_{max} (EtOH) 209 sh (log ε 4.05), 215 sh (4.11), 226 (4.20), 258 (4.30), 283 sh (3.81), 312 (3.71), 320 sh (3.61), 326 (3.84), 335 (3.63), and 342 nm (3.92); δ ($CDC\ell_3$) 1.38 (6 H, s, 3,3-Me), 2.00 (3 H, s, 2-Me), 2.19 (3 H, s, 1-Me), 2.76 (3 H, s, 4-Me), 7.44 (1 H, m, 6-H), 7.61 (1 H, m, 7-H), 7.99 (1 H, d, 5-H), and 8.08 (1 H, d, 8-H); *m/e* 237 (M^+), 222 (base), 167, 123, 114, and 87.

A *picrate* was prepared; yellow plates, m.p., 212-215°C (dec.) (from ethanol) (Found: C, 59.1; H, 4.7; N, 11.9. $C_{23}H_{22}N_4O_7$ requires C, 59.2; H, 4.75; N, 12.0%).

Photolysis of 1-(2,3,4,5,6-Pentamethylphenyl)benzotriazole (91c) in the Presence of Acrylonitrile - A solution of the benzotriazole (100 mg) in a mixture of acetonitrile and acrylonitrile (9:1; 100 ml) was irradiated at 254 nm for 6 h. The resultant turbid suspension was filtered through Celite to remove photopolymer, the filtrate evaporated and the residue subjected to p.l.c. (3:1 petrol-ether) to give:

i) Unreacted starting material (10 mg, 10% recovery), R_F 0.35.

ii) An unidentified *adduct* (4.3 mg, 4%), R_F 0.22; δ ($CC\ell_4$) 0.60 (3 H, s), 1.40 (6 H, s), 1.67-2.43 (2 H, m), 2.00 (3 H, s), 2.12 (3 H, s), 2.74 (1 H, m), and 7.05-7.50 (4 H, m); *m/e* 291, 290 (M^+; base), 238, 237, 236, and 222.

iii) The [*8 + 2*]*adduct* (115) as colourless prisms (44.3 mg, 45% based on conversion), m.p., 169-170°C (dec.) (from petrol-ether)(Found: C, 82.6; H, 7.7 ; N, 9.6 . $C_{20}H_{22}N_2$ requires C, 82.7; H, 7.6 ; N,9.65%); ν_{max} ($CC\ell_4$) 2975, 2865, 2230, 1620, 1590, 1445, 1375, and 1115 cm^{-1}; λ_{max} (EtOH) 205 (log ε 3.99), 228 sh (3.97), 238 (4.09), 241 (4.05), 283 (4.00), and 303 nm (3.92); δ_H ($CDC\ell_3$) 0.69 (3 H, s, Me), 1.53 (3 H, s, Me), 1.63 (3 H, s, Me), 1.83 (1 H, dd, *J* 13.8, 9.6 Hz, α 4-H), 1.94 (6 H, s, 2 x Me), 1.96 (1 H, dd, *J* 13.8, 1.3 Hz, β 4-H), 2.64 (1 H, dd, *J* 9.6, 1.3 Hz, 3-H), 7.19 (1 H, dt, *J* 7.5, 1.6 Hz, ArH), 7.31 (1 H, dt, *J* 7.5, 1.6 Hz, ArH), 7.40 (1 H, dd, *J* 7.5, 1.6 Hz, ArH), and 7.43 (1 H, dd, *J* 7.5, 1.6 Hz, ArH); δ_C ($CDC\ell_3$) 9.3, 11.9, 12.4, 19.6, 20.2, 33.0, 41.1, 45.7, 52.5, 58.7, 121.9

125.7, 126.3, 127.4, 127.9, 132.0, 134.7, 142.7, 158.6, and 181.3; *m/e* 290 (M^+), 275, 237 and 222 (base).

On standing in solution, the adduct (115) was oxidised to the *aldehyde* (116); yellow prisms, m.p., 260-262°C (dec.) (from methanol-dioxan)(Found: C, 78.75; H, 6.6; N, 9.1. $C_{20}H_{20}N_2O$ requires C, 78.9; H, 6.6; N, 9.2%); ν_{max} ($CH_2C\ell_2$) 2920, 2850, 2765, 2735, 1660, 1620, and 1380 cm^{-1}; λ_{max} (EtOH) 209 (log ε 4.03), 237 sh (3.85), 247 (3.95), 255 (4.02), 309 (3.99), and 341 sh nm (3.86); δ ($CDC\ell_3$) 0.70 (3 H, s, Me), 1.65 (3 H, s, Me), 1.71 (3 H, s, Me), 1.81 (1 H, dd, *J* 14, 9.8 Hz, α 4-H), 1.98 (1 H, dd, *J* 14, 1 Hz, β 4-H), 2.39 (3 H, s, Me), 2.88 (1 H, dd, *J* 9.8, 1 Hz, 3-H), 7.28 (1 H, dt, *J* 6.9, 1.9 Hz, ArH), 7.36 (1 H, dt, *J* 6.9, 1.9 Hz, ArH), 7.43 (1 H, dd, *J* 6.9, 1.9 Hz, ArH), 7.49 (1 H, dd, *J* 6.9, 1.9 Hz, ArH), and 10.47 (1 H, s, *CH*O); *m/e* 305, 304 (M^+; base), 251, 236, 222, and 208.

Photolysis of 1-(2,4,6-Trimethylphenyl)benzotriazole (91b) in the Presence of Acrylonitrile - A solution of the benzotriazole (212 mg) in a mixture of acetonitrile and acrylonitrile (9:1 ; 100 ml) was irradiated at 254 nm for 7 h. Most of the solvent was removed, and the remaining solution filtered through Celite and the filtrate evaporated to dryness. The brown gum so produced was subjected to p.l.c. (2 x 1:1 petrol-ether) to give:

i) Unchanged starting material (53 mg, 25% recovery), R_F 0.79.

ii) The [2 + 2] *adduct* (117) as a pale green solid (56 mg, 32%), R_F 0.59, which afforded a white solid on trituration with petrol, m.p., 183-185°C (from petrol-ether, after sublimation at 145°C and 7.5 x 10^{-2} mmHg)(Found: C, 82.6; H, 7.0; N, 10.7. $C_{18}H_{18}N_2$ requires C, 82.4; H, 6.9; N, 10.7%); ν_{max} ($CC\ell_4$) 3060, 2950, 2860, 2225, 1600, 1575, 1500, 1440, and 1395 cm^{-1}; λ_{max} (EtOH) 212 (log ε 4.39), 232 (4.53), 238 (4.53), 289 (3.58), 296 (3.61), 302 (3.53), 309 (3.68), 316 (3.51), and 322 nm (3.80); δ ($CDC\ell_3$) 1.25 (3 H,

d, *J* 7.5 Hz, 3-Me), 1.77 (3 H, s, 9b-Me), 1.93 (1 H, m, α 2-H), 2.48 (1 H, ddd, β 2-H), 2.69 (3 H, s, 4-Me), 2.86 (1 H, m, 2a-H), 3.15 (1 H, m, 1-H), 3.22 (1 H, q, 3-H), 7.54 (1 H, ddd, *J* 8, 6.7, 1.4 Hz, 6-H), 7.67 (1 H, ddd, *J* 8, 6.7, 1.4 Hz, 7-H), 8.02 (1 H, dd, *J* 8, 1.4 Hz, 5-H), and 8.08 (1 H, dd, *J* 8, 1.4 Hz, 8-H); *m/e* 262 (M^+), 210, 209 (base), 208, 194, and 182.

A *picrate* was prepared; yellow microcrystalline solid, m.p., 229-230°C (dec.)(from acetonitrile) (Found: C, 58.8; H, 4.3; N, 14.2. $C_{24}H_{21}N_5O_7$ requires C, 58.65; H, 4.3; N, 14.25%).

iii) An unidentified [*2 + 2*]*adduct* as a green gum (29.3 mg, 17%), R_F 0.24; λ_{max} (EtOH) 212 (log ε 4.43), 232 (4.55), 238 (4.54), 283 (3.56), 295 (3.59), 303 sh (3.53), 309 (3.65), 317 (3.46), and 323 nm (3.76); δ ($CC\ell_4$) 1.15 (3 H, d, *J* 7.5, Me), 1.60 (3 H, s, Me), 1.65-1.95 (1 H, m), 2.19-2.55 (2 H, m), 2.63 (3 H, s, ArMe), 2.95-3.30 (2 H, m), 7.45 (1 H, ddd, 6-H), 7.61 (1 H, ddd, 7-H), 7.92 (1 H, dd, 5-H), and 8.17 (1 H, dd, 8-H); *m/e* 263,262 (M^+), 210, 209 (base), 208, 195, 194, and 193.

iv) Another [*2 + 2*]*adduct* as a green gum (7.5 mg, 4%), R_F 0.15; δ ($CC\ell_4$) 1.18 (3 H, d, *J* 8 Hz), 1.65 (3 H, s, Me), 1.78-3.48 (5 H, m), 2.67 (3 H, s, ArMe), and 7.38-8.25 (4 H, m, ArH); *m/e* 262 (M^+), 210, 209 (base), 208, and 195.

Photolysis of 1,3,4-Trimethyl-3*H*-cyclopenta[*b*]quinoline (112b) in the Presence of Acrylonitrile - A solution of the quinoline (45 mg) in a mixture of acetonitrile and acrylonitrile (9:1; 50 ml) was irradiated at 254 nm for 2 h, after which period the solvent was removed and the residue redissolved

in THF (3 ml). Addition of methanol (30 ml) precipitated photo polymer, which was removed by filtration through Celite, and the filtrate evaporated to leave a green oil. P.l.c. (2 x dichloromethane, then 13:7 petrol-ether) of this gave:

i) The 2 + 2 adduct (117) as a white solid (22 mg, 39%), R_F 0.72, m.p., 175-179°C (from petrol-ether, and sublimation), undepressed on admixture with an authentic specimen.

ii) A colourless oil (11.2 mg, 20%), R_F 0.22, which n.m.r. indicated to be a 1:1 mixture of the two minor adducts obtained from the previous photolysis (δ Me 1.77 and 1.71 respectively).

Photolysis of 1-(2-Methylnaphthyl)benzotriazole (97) - Irradiation of a solution of the benzotriazole (253 mg) in acetonitrile (200 ml) at 254 nm for 10 h, with subsequent removal of solvent afforded a brown gum which on chromatography (petrol, then petrol-dichloromethane up to 6:4 in 2-5% increments) gave 1-*methylcycloocta*[def]*carbazole* (120) as a red gum (52 mg, 30% based on conversion), which solidified on standing, m.p., 69-72°C (from petrol) (Found: C, 88.5; H, 5.6; N, 6.1. $C_{17}H_{13}N$ requires C, 88.3; H, 5.7; N, 6.1%); ν_{max} ($CC\ell_4$) 3470, 3035, 3010, 2910, 2870, 1600, 1590, 1415, 1400 1380, 1370, 1310, 1155, and 1030 cm^{-1}; λ_{max} (cyclohexane) 212 (log ε 4.46), 242 sh (4.61), 245 sh (4.66), 247 (4.69), 267 (4.26), 274 (4.31), 282 (4.24), 332 sh (3.68), 339 (3.79), 356 (3.79), 382 sh (3.56), 394 (3.65), 408 sh (3.53), and 418 nm (3.52); δ_H (d_4-THF) 2.36 (3 H, s, Me), 5.17 (1 H, m, 5-H), 5.22 (1 H, m, 6-H), 5.62 (1 H, m, 4-H), 5.67 (1 H, m, 7-H), 6.40 (1 H, d, *J* 7.5 Hz, 3-H), 6.48 (1 H, d, *J* 6.9 Hz, 8-H), 6.75 (1 H, dd, *J* 7.5,

1 Hz, 2-H), 6.94 (1 H, t, 7.5 Hz, 9-H), 7.07 (1 H, dd, *J* 7.5, 1.25 Hz, 10-H), and 10.17 (1 H, br.s, NH); δ_C ($CDC\ell_3$) (quaternary) 120.2, 121.2, 122.1, 130.9, 133.2, 139.5, and 139.9; (non-quaternary) 16.5, 113.0, 124.4, 125.5, 126.6, 127.2, 128.0, 128.3, 133.1, and 133.6; *m/e* 232, 231 (M^+; base), and 205.

Picrate; dark brown needles, m.p., 175-177°C (dec.) (from ethanol) (Found: C, 60.2; H, 3.6; N, 12.15. $C_{23}H_{16}N_4O_7$ requires C, 60.0; H, 3.5; N, 12.2%).

Further elution afforded a green gum (157 mg) which n.m.r. indicated to consist of unchanged starting material (39%; δ Me 2.12), 6a-*methyl*-6aH-*benzo*[a]*carbazole* (118) (27%; δ Me 1.45), and 6-*methylindeno*[1,2-b]*quinoline* (119) (34.5%, δ Me 2.65 and δ CH_2 3.84). In a subsequent experiment, the identity of these products was verified by isolation using repeated p.l.c. and acid extraction.

Reaction of 1-Methylcycloocta[*def*]carbazole (120) with PTAD - Addition of PTAD[180] (17.5 mg, 1 x 10^{-4} mol) in dichloromethane (0.5 ml) to a solution of the carbazole (23 mg, 1 x 10^{-4} mol) in dichloromethane (0.5 ml) at 0°C gave a dark coloured solution which decolourised within a few seconds. Evaporation of the resultant colourless solution gave a quantitative yield of the *adduct* (126) as a colourless solid, m.p., 273-275°C (from nitromethane) (Found: C, 73.6; H, 4.3; N, 13.75. $C_{25}H_{18}N_4O_2$ requires C, 73.9; H, 4.5; N, 13.8%); δ ($CDC\ell_3$) 2.43 (3 H, s, Me), 5.97 (2 H, m), 6.26 (2 H, m), 7.05-7.48 (10 H, m, ArH), and 8.81 (1 H, br.s, NH); *m/e* 407, 406 (M^+), 245, 244, 231, 230, 218 (base), and 217.

7.3. EXPERIMENTAL FOR CHAPTER 3.

2-Ethoxycarbonyl-2-Methyl-1-Tetralone - Prepared in 45% from 1-tetralone by the method of Temple Robinson;[69] viscous oil, b.p., 120-130°C at 1 mmHg (lit.,[181] b.p. 183-84°C at 18 mmHg); ν_{max} (film) 2935, 1725, 1685, and 1600 cm^{-1}; δ ($CC\ell_4$) 1.11 (3 H, t, *J* 7 Hz, - CH_2CH_3), 1.40 (3 H, s, Me), 1.70-3.10 (4 H, m, $-CH_2-CH_2-$), 4.08 (2 H, q, *J* 7 Hz, $-CH_2CH_3$), 7.05-7.50 (3 H, m, ArH), and 7.97 (1 H, m, ArH).

2-Methyl-1-Tetralone (137) - (a)[69] A mixture of 2-ethoxycarbonyl-2-methyl-1-tetralone (10 g, 43 mmol), acetic acid (35 ml), concentrated hydrochloric acid (25 ml), and water (10 ml) was refluxed for 6 h. On cooling, aqueous sodium hydroxide (20%; 175 ml) was added and the mixture extracted with ether (3 x 50 ml), the extracts washed with water (75 ml), dried ($MgSO_4$) and evaporated to afford a brown oil. Distillation gave the product as a colourless oil (5.1 g, 80%), b.p., 142-147°C at 20 mmHg (lit.,[182] b.p., 127-131°C at 12 mmHg).

(b) *n*-Butyllithium in hexane (1.5 M; 75 ml, 0.11 mol) was added to a solution of diisopropylamine (10.12 g, 0.10 mol) in THF (100 ml) at 0°C. After stirring for 0.25 h, the solution was cooled to -78°C and 1-tetralone (14.6 g, 0.10 mol) in THF (100 ml) added, followed after 0.5 h by a mixture of methyl iodide (15.7 g, 0.11 mol) and HMPA (21.5 g, 0.12 mol). After 3 h at -78°C, the mixture was allowed to warm to room temperature and stirred overnight before adding saturated ammonium chloride solution (100 ml). The organic layer was separated and washed with water (100 ml) and the combined aqueous layers extracted with ether (100 ml). After

drying ($MgSO_4$), the combined organic layers were evaporated to leave a purple oil. Distillation at 122-130°C and 10 mmHg gave a colourless oil (14.83 g) which was shown by g.l.c. (10% OV-17 on 80/100 mesh Chromosorb WAW DMCS; 1/8" x 2 m; 100°C) to consist of unreacted starting material (30%; retention time 5.9 min) and the product (70%; retention time 7.4 min).

5,6-Dihydro-6a-Methyl-6a*H*-Benzo[*a*]carbazole (138) - A mixture of 1-tetralone and 2-methyl-1-tetralone (3:7; 6.2 g) was heated with phenylhydrazine (4.32 g, 40 mmol) at 105°C under reduced pressure for 1.25 h. The resulting orange gum was dissolved in acetic acid (25 ml) and boron trifluoride etherate (5.7 g, 40 mmol) and the solution refluxed for 3 h, after which it was allowed to cool and ammonia solution (*ca.* 15%; 50 ml) added. Extraction with ether (1 x 50 ml; 2 x 25 ml) was followed by washing of the combined extracts with hydrochloric acid (2 M; 4 x 25 ml) and drying ($MgSO_4$). The orange solid obtained on evaporation of solvent was recrystallised from methanol to give 5,6-dihydro-11*H*-benzo[*a*]carbazole (140) as a colourless solid (1.30 g, 42%), m.p., 163-164°C (lit.,[183] 163-164°C). The acid washings were cooled to 0°C, basified with ammonia solution, and extracted with dichloromethane (4 x 25 ml). After drying ($MgSO_4$), the extracts were evaporated to leave a brown oil which was distilled at 122°C (Kugelrohr) and 2 x 10^{-2} mmHg to afford 5,6-dihydro-6a-methyl-6a*H*-benzo[*a*]carbazole (138) as a viscous, pale green gum (3.60 g, 60%), which solidified on standing, m.p., 95-98°C (from petrol-chloroform) (lit.,[68] 98-98.5°C); ν_{max} (film) 2920, 1605, 1570, 1550, 1460, 1200, 775, 750 and 735 cm^{-1}; δ ($CC\ell_4$) 1.20 (3 H, s, Me), 1.62 (1 H, m, 6-H), 2.26 (1 H, m, 6-H), 2.70-3.45 (2 H, m, 5-H), 7.00-7.45 (6 H, m, ArH), 7.59 (1 H, m, 7-H), and 8.10 (1 H, m, 1-H); *m/e* 233 (M^+; base), 232, 218, and 217.

Repeating the reaction with pure 2-methyl-1-tetralone afforded the carbazolenine (138) in 76% yield.

Benzeneselenimic Anhydride (BSA)[184] - Nitric acid (10 ml) was cautiously added to a stirred suspension of diphenyl diselenide (10 g) in water (10 ml) at 60-65°C. After 0.3 h, the resulting solution was filtered and cooled to 2°C. The crystals thus produced were collected and heated at 120°C and 3 mmHg for 3.5 days to give the product as an amorphous white solid (7 g, 61%), m.p., 165-169°C (lit.,[184] m.p., 170-173°C).

Attempted Oxidation of the Carbazolenine (138) with BSA - BSA (360 mg, 1 mmol) was added to a solution of the carbazolenine (233 mg, 1 mmol) in chlorobenzene (6 ml) maintained at 95-100°C. After 7.5 h, the red solution was allowed to cool, dichloromethane (10 ml) added and the mixture washed with saturated sodium bicarbonate solution (10 ml), dried ($MgSO_4$), evaporated and the residue chromatographed (petrol-ether) to give crude diphenyl diselenide as an orange oil (240 mg, 77%) and the starting carbazolenine as a pale yellow oil (198 mg, 85% recovery).

Bromination of the Carbazolenine (138) - A mixture of the carbazolenine (1.186 g, 5.1 mmol), NBS (1.13 g, 6.35 mmol) and AIBN (20 mg) in carbon tetrachloride (25 ml) was irradiated (100W tungsten lamp) with reflux for 0.5 h, during which all of the suspended solid was observed to float near the surface. The hot suspension was filtered and the filtrate evaporated to leave an orange syrup, which n.m.r. indicated to consist of the α- and β-*bromides* (141b) and (141a), and the gem-*dibromide* (141c), with no trace of the *vinyl bromide* (142). Chromatography (9:1 petrol-ether) gave:

i) A brown gum (55 mg) consisting of the gem-*dibromide* (141c) (40%; 1% overall yield); δ ($CC\ell_4$) 1.51 (3 H, s, Me), 3.04 (1 H, d, *J* 15 Hz, 6-H), 3.87 (1 H, d, *J* 15 Hz, 6-H), and 7.10-8.30 (8 H, m, ArH), and the *vinyl bromide* (142) (60%); δ ($CC\ell_4$) 1.40 (3 H, s, Me), 6.94 (1 H, s, 6-H), and 7.10-8.30 (8 H, m, ArH); *m/e* 311 and 309 (M^+), 296, 294,and 230 (base).

ii) A pale yellow gum (738 mg) consisting of the vinyl bromide (30%; 16% overall yield) and 5α-*bromo*-5,6-*dihydro*-6a-*methyl*-6aH-*benzo*[a]-*carbazole* (141b) (70%; 32% overall yield); δ ($CC\ell_4$) 1.18 (3 H, s, Me), 2.18 (1 H, dd, *J* 13, 11 Hz, 6-H), 3.02 (1 H, dd, *J* 13, 7 Hz, 6-H), 5.72 (1 H, dd, *J* 11, 7 Hz, 5-H), and 7.05-8.20 (8 H, m, ArH); *m/e* 313 and 311 (M^+), 233, 232 (base), 231, 230, 217 and 216.

iii) A sticky brown solid (532 mg) which on trituration with hot petrol afforded 5β-*bromo*-5,6-*dihydro*-6a-*methyl*-6aH-*benzo*[a]*carbazole* (141a) as a buff solid (413 mg, 26%), m.p., 140-141°C (from petrol-dichloromethane) (Found: C, 65.4; H, 4.4; N, 4.6. $C_{17}H_{14}BrN$ requires C, 65.4; H, 4.5; N, 4.5%); δ ($CC\ell_4$-$CDC\ell_3$) 1.62 (3 H, s, Me), 2.25 (1 H, dd, *J* 15, 6 Hz, 6β-H), 2.96 (1 H, d, *J* 15 Hz, 6α-H), 5.76 (1 H, d, *J* 6 Hz, 5-H), 7.10-7.80 (7 H, m, ArH), and 8.08 (1 H, m, ArH); *m/e* 313 and 311 (M^+), 233, 232 (base), 231, 230, 217 and 216.

6a-Methyl-6a*H*-Benzo[*a*]carbazole (118) - A solution of the β-bromide (141a) (312 mg, 1 mmol) and DBU (168 mg, 1.1 mmol) in benzene (10 ml) was refluxed for 1 h, allowed to cool, filtered, and the filtrate evaporated. Distillation of the residue at 132°C (Kugelrohr) and 7 x 10^{-2} mmHg gave 6a-*methyl*-6aH-*benzo*[a]*carbazole* as a pale green gum (220 mg, 95%); ν_{max} (film) 3060, 3040, 2980, 2915, 1565, 1555, 1455, 1445, 790, 775 and 755 cm^{-1};

λ_{max} (EtOH) 209 (log ε 4.15), 243 (4.49), 249 (4.49), and 326 nm (3.88); δ_H ($CDC\ell_3$) 1.45 (3 H, s, Me), 6.43 (1 H, d, *J* 8.6 Hz, 6-H), 6.52 (1 H, d, *J* 8.6 Hz, 5-H), 7.22 (2 H, m, ArH), 7.30-7.47 (4 H, m, ArH), 7.68 (1 H, d, *J* 7.5 Hz, 7-H), and 8.01 (1 H, dd, *J* 6.5, 1.5 Hz, 1-H); δ_C ($CDC\ell_3$) (quaternary) 57.1, 129.2, 136.6, 142.0, 154.7, and 185.4, (non quaternary) 28.1, 121.4, 121.5, 125.3, 125.6, 126.8, 127.5, 128.1, 128.4, 131.6, and 134.0; *m/e* 232, 231 (M^+; base), 230, 216, 115,and 108.

Picrate, yellow needles, m.p., 163-164°C (dec.) (from ethanol) (Found: C, 59.8; H, 3.45; N, 12.1. $C_{23}H_{16}N_4O_7$ requires C, 60.0; H, 3.5; N, 12.2%).

Similar results were obtained by using the α-bromide (141b), although in this case the product had to be separated from the vinyl bromide (142) by a combination of fractional distillation and careful chromatography.

1-Methyl-2-Tetralone (143) - Prepared in 80% yield by the method of Stork *et al.*[74] b.p., 130-140°C at 13 mmHg (lit.,[74] b.p., 138-142°C at 20 mmHg).

Attempted Preparation of 5,6-Dihydro-11b-Methyl-11b*H*-Benzo[*c*]carbazole (144) - 1-Methyl-2-tetralone (150 mg, 0.94 mmol) was heated at 95°C with phenylhydrazine (120 mg, 1.1 mmol) for 10 min, benzene (5 ml) was added, and the solution evaporated. The residual gum was dissolved in acetic acid (2 ml) containing boron trifluoride etherate (140 mg, 1 mmol) and the solution refluxed for 2.5 h. On cooling, ammonia solution (*ca.* 15%; 10 ml) was added and the suspension extracted with ether (2 x 10 ml) and the combined extracts washed with hydrochloric acid (2 M; 1 x 10 ml; 2 x 5 ml). Basification of the washings with ammonia solution, followed by extraction with dichloromethane (1 x 5 ml; 1 x 10 ml), drying ($MgSO_4$) and evaporation

afforded a brown oil which was distilled at 150-180°C (Kugelrohr) and 0.5 mmHg to give a pale green gum (134 mg, 61%) which proved identical to the carbazolenine (138).

5,6-Dihydro-11b-Methyl-11b*H*-Benzo[*c*]carbazole (144) - A solution of 1-methyl-2-tetralone (1.60 g, 10 mmol) and phenylhydrazine (1.19 g, 11 mmol) in benzene (10 ml) was refluxed in a Dean and Stark trap for 0.75 h, after which the solvent was replaced by ethanol (15 ml), the solution cooled to 0°C and saturated with hydrogen chloride. After standing for 3 days at 2°C, the dark mixture was poured into water (75 ml), the resulting suspension basified with ammonia solution, and extracted with ether (3 x 25 ml). The combined extracts were washed with hydrochloric acid (2 M; 3 x 25 ml), the washings basified with ammonia solution, and extracted with dichloromethane (4 x 25 ml). The gum remaining after drying ($MgSO_4$) and evaporating the extracts was distilled to give the carbazolenine as an orange gum (1.55 g, 66%), b.p., 130°C (Kugelrohr) at 6×10^{-2} mmHg (lit.[68] b.p., 159-163°C at 1 mmHg); ν_{max} (film) 3060, 2975, 2920, 1615, 1590, 1480, 1455, 1445, 770, 760, and 745 cm^{-1}; δ ($CC\ell_4$) 1.55 (3 H, s, Me), 2.99-3.47 (4 H, m, $-CH_2-CH_2-$), and 7.00-7.75 (8 H, m, ArH).

Oxidation of the Carbazolenine (144) with BSA - (a) BSA (1.80 g, 5 mmol) was added to a solution of the carbazolenine (1.09 g, 4.7 mmol) in chlorobenzene (25 ml) at 100°C. After 2 min, the red solution was cooled, chloroform (25 ml) added and the mixture washed with aqueous potassium hydroxide (10%, 2 x 25 ml), dried ($MgSO_4$) and evaporated. The red gum so obtained was subjected to chromatography (19:1 petrol-ether, then 7:3) to give:

i) Diphenyl diselenide as an orange solid (400 mg), m.p., 53-60°C (lit.,[90] m.p., 60-62°C).

ii) 11b-*Methyl*-6-*phenylseleno*-11bH-*benzo*[c]*carbazole* (145) as an orange gum (518 mg, 29%); ν_{max} (film) 3060, 1550, 1475, 1440, 750, 740, and 690 cm^{-1}; λ_{max} (EtOH) 207 (log ε 4.48), 253 (4.44), 284 sh (3.79), 328 (3.76), and 380 nm (3.75); δ ($CC\ell_4$) 1.52 (3 H, s, Me), 6.60 (1 H, s, 5-H), and 6.90-7.84 (13 H, m, ArH); *m/e* 387 (M^+; base), 385, 372, 307, 291, 230, and 145.

Picrate, scarlet prisms, m.p., 149-151°C (from ethanol) (Found: C, 56.8; H, 3.2; N, 9.1. $C_{29}H_{18}N_4O_7Se$ requires C, 56.6; H, 3.3; N, 9.1%).

iii) 11b-*Methyl*-11bH-*benzo*[c]*carbazole* (136) as an orange gum (529 mg, 49%), b.p. 130°C (Kugelrohr) at 5 x 10^{-2} mmHg, which solidified on standing, m.p., 90-92°C (from petrol)(Found: C, 88.1; H, 5.7; N, 6.05. $C_{17}H_{13}N$ requires C, 88.3; H, 5.7; N, 6.1%); ν_{max} ($CC\ell_4$) 3070, 2980, 2920, 2860, 1590, 1445, 1195, 670, and 635 cm^{-1}; λ_{max} (EtOH) 209 (log ε 4.18), 245 (4.31), 330 sh (3.76), 354 (3.86), and 391 sh nm (3.40); δ_H ($CDC\ell_3$) 1.55 (3 H, s, Me), 6.79 (1 H, d, *J* 10 Hz, 6-H), 7.05 (1 H, d, *J* 10 Hz, 5-H), 7.19-7.44 (5 H, m, ArH), 7.68 (1 H, dd, *J* 6, 1 Hz, ArH), 7.73 (1 H, m, ArH), and 7.82 (1 H, d, *J* 7.5 Hz, ArH); δ_C ($CDC\ell_3$) (quaternary) 58.3, 132.0, 141.1, 143.0, 155.2, and 184.9, (non quaternary), 33.2, 121.4, 121.8, 123.5, 124.6, 127.0, 128.2, 128.5, 130.1, and 139.1; *m/e* 232, 231 (M^+; base), 230, 216, 214, 190, and 189.

Picrate, yellow prisms, m.p., 200-202°C (dec.) (from ethanol)(Found: C, 60.3; H, 3.5; N, 12.2. $C_{23}H_{16}N_4O_7$ requires C, 60.0; H, 3.5; N, 12.2%).

In a subsequent experiment, 1-hydroxy-1-methyl-2(1*H*)-naphthalenone (146) separated on distillation as colourless prisms (1.6%), m.p., 89-90°C

(lit.,[185] m.p., 87-89°C); δ ($CDC\ell_3$) 1.55 (3 H, s, Me), 3.70 (1 H, s, -O*H*), 6.22 (1 H, d, *J* 10 Hz, 3-H), 7.30-7.50 (4 H, m, ArH, and 4-H), and 7.72 (1 H, d, *J* 7.5 Hz, ArH); *m/e* 174 (M^+), 146 (base), 145, 131, 103, and 73.

(b) Refluxing the carbazolenine (144) (176 mg, 0.75 mmol) with a suspension of BSA (67.5 mg, 0.19 mmol) and iodoxybenzene (226 mg, 1.13 mmol) in benzene (8 ml) for 1.75 h afforded a dark mixture which was filtered, evaporated and chromatographed (7:3 petrol ether) to give:

i) Diphenyl diselenide as an orange oil (26 mg).

ii) An orange gum (53.6 mg) which n.m.r. indicated to consist of the selenide (145) (44%; 8% overall yield), and an unidentified component (56%); δ ($CC\ell_4$) 1.18 (3 H, s, Me), 3.15 (1 H, d, *J* 17 Hz), 3.75 (1 H, d, *J* 17 Hz), and 6.80-7.95 (ArH).

iii) The olefin (136) as a red gum (111 mg, 64%).

Photolysis of 6a-Methyl-6a*H*-Benzo[*a*]carbazole (118) - A solution of the olefin (226 mg) in acetonitrile (110 ml) was irradiated at 254 nm for 7 h. The brown gum remaining on removal of solvent was chromatographed (6:4 petrol-dichloromethane, then dichloromethane only) to give:

i) 11*H*-Benzo[*a*]carbazole (147) as a white solid (4.7 mg, 3% based on conversion), m.p., 219-222°C, undepressed when mixed with an authentic sample.

ii) Starting material as a colourless gum (70.2 mg, 31% recovery).

iii) The *indenoquinoline* (119) as white needles (62.5 mg, 40% based on conversion), m.p., 116-118°C (from petrol), undepressed on admixture with independently synthesised material.

iv) An unidentified, amorphous tan solid (32 mg, 20%).

Photolysis of 11b-Methyl-11b*H*-Benzo[*c*]carbazole (136) - The olefin (73 mg) in acetonitrile (50 ml) was irradiated at 254 nm for 44 h, after which evaporation of the solution left a brown oil. Chromatography (petrol-ether) afforded unchanged starting material as a yellow gum (57 mg, 78% recovery). No products could be detected.

FVP of 6a-Methyl-6a*H*-Benzo[*a*]carbazole (118) - The olefin (145 mg) was distilled at 90°C and 3 x 10^{-2} mmHg into a quartz tube at 640°C to afford a brown gum (140 mg). A portion (106 mg) of this was subjected to p.l.c. (2 x 3:1 petrol-ether) to give:

i) 11-*Methyl*-11H-*benzo*[a]*carbazole* (151) as a buff solid (23.8 mg, 24% based on conversion), R_F 0.75, m.p., 165-167°C (from petrol-ether), undepressed on admixture with an authentic sample.

ii) 11*H*-Benzo[*a*]carbazole (147) as a buff solid (29.4 mg, 32% based on conversion), R_F 0.50, identical to an authentic specimen.

iii) Unchanged starting material as a yellow gum (7.7 mg, 7% recovery), R_F 0.42.

iv) 2-*Methylindeno*[2,1-c]*quinoline* (152) as a pale yellow gummy solid (23.1 mg, 23% based on conversion), R_F 0.09, which resisted further purification (Found: M^+ 231.1046. $C_{17}H_{13}N$ requires M^+ 231.1048); λ_{max} (EtOH) 214 sh, 224, 228 sh, 237, 245, 274 sh, 282, 312 sh, 316, and 330 nm; δ ($CDC\ell_3$) 2.83 (3 H, s, Me), 3.97 (2 H, s, $-CH_2-$), 7.42-7.76 (5 H, m, ArH), 8.17 (1 H, d, *J* 7 Hz, 11-H), 8.42 (1 H, d, *J* 7 Hz, 7-H), and 8.64 (1 H, d, *J* 8.5 Hz, 8-H); *M/e* 232, 231 (M^+; base), 230, 216, and 189.

Picrate, yellow microcrystalline powder, m.p., 243-245°C (dec.) (from acetonitrile) (Found: C, 60.3; H, 3.45; N, 12.1. $C_{23}H_{16}N_4O_7$ requires C, 60.0; H, 3.5; N, 12.2%).

FVP of 11b-Methyl-11b*H*-Benzo[*c*]carbazole (136) - Distillation of the olefin (114 mg) at 100°C and 3 x 10^{-2} mmHg into a quartz tube maintained at 640°C afforded a brown gum (104 mg) which was subjected to p.l.c. (3 x 3:1 petrol-ether) to give:

i) 7-Methyl-7*H*-benzo[*c*]carbazole (154) as a buff solid (11.4 mg, 12% based on conversion), R_F 0.70, m.p., 105-108°C, undepressed on admixture with authentic material.

ii) 7*H*-Benzo[*c*]carbazole (153) as a buff solid (16.4 mg, 19% base on conversion), R_F 0.41, identical to an authentic sample.

iii) Unchanged starting material as a colourless gum (12.2 mg, 12% recovery), R_F 0.24.

iv) 2-Methylindeno[2,1-*c*]quinoline (152) as a yellow solid (43.4 mg, 47% based on conversion), R_F 0.09.

7.4. EXPERIMENTAL FOR CHAPTER 4.

Cyclohexa-1,2-dione Monophenylhydrazone - Prepared as red plates (28%) by the method of Anderson and Campbell,[78] m.p., 182-184°C (from ethanol) (lit.,[78] m.p., 183-185°C).

1-Oxo-1,2,3,4,9-Tetrahydro-9*H*-Carbazole (162) - Cyclisation of the above phenylhydrazone with a mixture of acetic and hydrochloric acid[78] gave the product as pale yellow plates (48%), m.p., 169-171°C (from ethanol) (lit.,[78] m.p., 170°C).

Attempted 4a-Methylation of (162). (a) A solution of the ketone (0.50 g, 2.7 mmol) in ether (10 ml) and THF (4 ml) was added to a solution of methylmagnesium iodide, prepared from magnesium (0.10 g, 4 mmol) and methyl iodide (0.3 ml), in ether (4 ml). Effervescence was accompanied by the formation of an orange precipitate, and the resulting suspension stirred for 10 min before adding methyl iodide (0.5 ml), and stirring for a further 0.5 h. The reaction mixture was then added to aqueous acetic acid (10%; 20 ml), the aqueous layer extracted with ether (15 ml), the combined etheral layers dried ($MgSO_4$), evaporated, and the residue recrystallised from ethanol to give unchanged starting material as pale yellow needles (0.24 g, 48% recovery), m.p., 168°C.

(b) A dispersion of potassium hydride in mineral oil (25%; 0.4 g, 2.5 mmol) was suspended in ether (3 ml), and a solution of the ketone (0.35 g, 2 mmol) in THF (5 ml) and ether (5 ml) added. The brown solution so formed was stirred for 0.5 h, methyl iodide (0.5 ml) added, and stirring continued for 3 h. Addition of the mixture to aqueous acetic acid (20%; 10 ml) was

followed by separation of the layers, the organic being dried ($MgSO_4$), evaporated, and the residue chromatographed (petrol-ether) to give 1-*oxo*-1,2,3,4,9-*tetrahydro*-2,2,9-*trimethylcarbazole* (164b) as a colourless oil (105 mg, 56%); ν_{max} (film) 2910, 1650, 1605, 1460, 1215, 960, and 735 cm^{-1}; λ_{max} (EtOH) 212 (log ε 4.07), 239 (4.18), 311 (4.22), 332 sh (3.81), and 346 sh nm (3.68); δ ($CC\ell_4$) 1.18 (3 H, s, 2-Me), 1.25 (3 H, s, 2-Me), 1.70-3.05 (4 H, m, $-CH_2-CH_2-$), 4.03 (3 H, s, 9-Me), and 6.92-7.60 (4 H, m, ArH); *m/e* 227 (M^+), 213, 184, and 143 (base), and 9-methyl-1-oxo-1,2,3,4,9-tetrahydrocarbazole (164a) as a pale yellow solid (224 mg, 56%), m.p., 95-100°C (lit.,[83] m.p., 100-100.5°C); δ ($CC\ell_4$) 2.14 (2 H, m, $-CH_2-$), 2.50 (2 H, m, $-CH_2-$), 2.91 (2 H, m, 2-H), 3.91 (3 H, s, Me), 6.92-7.42 (3 H, m, ArH), and 7.53 (1 H, m, 5-H); *m/e* 199 (M^+; base), 170, and 143.

4a-Methyl-1,2,3,4,4a-Tetrahydrocarbazole (161) - 2-Methylcyclohexanone (11.2 g, 0.10 mol) was refluxed with phenylhydrazine (10.8 g, 0.10 mol) in acetic acid (50 ml) for 2 h, and the cool solution added to ice-water (250 ml), followed by aqueous sodium hydroxide solution (20%; *ca.* 180 ml). The resulting suspension was extracted with ether (4 x 75 ml), the combined extracts washed with sodium hydroxide solution (1 M; 100 ml) and hydrochloric acid (2 M; 3 x 75 ml), the acid washings cooled in ice and basified with sodium hydroxide (4 M). Extraction of the oily suspension with dichloromethane (3 x 75 ml), drying ($MgSO_4$) of the extracts and evaporation gave a brown oil which was distilled at 112-118°C and 2 mmHg to give the product as an oil which solidified on standing. Recrystallisation from petrol afforded orange prisms (13.6 g, 73%), m.p., 65-66°C (lit.,[82] m.p., 71°C).

9-Acetyl-4a-Methyl-2,3,4,4a,9-Tetrahydrocarbazole (168) - Prepared in 81% yield using the procedure described by McLean,[85] m.p., 102-103°C (from petrol-chloroform) (lit.,[86] m.p., 101-102°C).

Reaction of the Amide (168) with Ozone - Oxygen containing ozone (*ca.* 5%) was passed through a stirred suspension of the amide (3.42, 15 mmol) in methanol (250 ml) at -78°C, until the appearance of a persistent blue colour (*ca.* 0.5 h). After removing excess ozone by purging the mixture with ozone-free oxygen the process was repeated, and a solution of potassium iodide (20 g) in aqueous acetic acid (1:1, 50 ml) added to the cold suspension. After allowing the mixture to warm to room temperature over 5 h, it was decolourised by the addition of aqueous sodium thiosulphate (20%; 10 ml) and evaporated to *ca.* 100 ml. Addition of water (100 ml) was followed by extraction with chloroform (3 x 50 ml), the extracts washed with saturated sodium bicarbonate solution (25 ml), dried ($MgSO_4$) and evaporated to leave a yellow oil (3.94 g) which was chromatographed (7:3 petrol-ether) to give:

i) Unreacted starting material as white needles (626 mg, 18% recovery), m.p., 101-102°C (from petrol).

ii) A turbid, pale yellow oil (293 mg) which was distilled at 150°C (Kugelrohr) and 5 x 10^{-2} mmHg to afford 4-(1-*acetyl*-3-*methyloxindol*-3-*yl*)-*butanal* (170) as a colourless oil (100 mg, 3%); ν_{max} (film) 2930, 2710, 1750, 1710 (br), 1660, 1600, 1475, 1460, 1365, 1335, 1270, 1160, 1010, and 760 cm^{-1}; δ ($CC\ell_4$) 1.25 (2 H, m, $-CH_2-$), 1.37 (3 H, s, 3-Me), 1.81 (2 H, m, $-CH_2-$), 2.24 (2 H, m, $-CH_2CHO$), 2.59 (3 H, s, $-COMe$), 7.20 (3 H, m, ArH), 8.19 (1 H, m, 4-H), and 9.52 (1 H, t, J 1.5 Hz, $-CHO$); *m/e* 259 (M^+), 217, 179, 147 (base), and 146.

A 2,4-*dinitrophenylhydrazone* was prepared, but did not give a satisfactory microanalysis; yellow needles, m.p., 165-166°C (from ethanol) (Found: C, 57.2; H, 4.7; N, 17.5. $C_{21}H_{21}N_5O_6$ requires C, 57.4; H, 4.8; N, 15.9%).

iii) 1α-*Acetoxy*-4a-*methyl*-1,2,3,4,4a-*tetrahydrocarbazole* (169a) as a pale yellow solid (1.81 g, 61%), m.p., 111-114°C. An analytical sample was obtained as large, colourless prisms, m.p., 113.5-115°C (from petrol-ether)(Found: C, 74.05; H, 7.1; N, 5.8. $C_{15}H_{17}NO_2$ requires C, 74.05; H, 7.0; N, 5.8%); ν_{max} ($CC\ell_4$) 2940, 1740, 1615, 1585, 1450, 1370, 1220, 1060 and 1040 cm^{-1}; δ ($CC\ell_4$) 1.14-2.48 (6 H, m, aliphatic H), 1.31 (3 H, s, 4a-Me), 2.17 (3 H, s, acetate Me), 5.57 (1 H, dd, *J* 12, 6 Hz, 1-H), 7.03-7.35 (3 H, m, ArH), and 7.54 (1 H, m, 5-H); *m/e* 243 (M^+), 201, 200, 186 (base), 172, and 144.

Selenation of the Carbazolenine (161) - *n*-Butyllithium in hexane (1.5 M; 1 ml, 1.5 mmol) was added to a solution of diisopropylamine (111 mg, 1.1 mmol, 0.15 ml) in THF (5 ml) at 0°C, and the mixture stirred for 0.25 h before cooling to -78°C and adding the carbazolenine (185 mg, 1 mmol) in THF (1 ml). After warming to room temperature over 0.5 h, the solution was re-cooled to -78°C, and trimethylsilyl chloride (125 μℓ) in THF (1 ml) added, followed by stirring at room temperature for 0.25 h and addition of phenylselenyl bromide, prepared from diphenyl diselenide (156 mg, 0.5 mmol) and bromine (26 μℓ; 0.5 mmol) in THF (5 ml) at -78°C. The mixture was stirred overnight at room temperature, water (30 ml) and ether (10 ml) added, the organic layer washed with water (10 ml), saturated sodium bicarbonate solution (10 ml), and water (10 ml), dried ($MgSO_4$) and evaporated. The resulting orange oil was chromatographed (1:1 petrol-ether) to give:

i) Diphenyl diselenide as a yellow oil (18 mg).

ii) A yellow gum (38 mg, 15% based on conversion), identified as 4a-*methyl*-1α-*phenylseleno*-1,2,3,4,4a-*tetrahydrocarbazole* (175); δ ($CC\ell_4$) 1.45-2.48 (6 H, m, aliphatic H), 1.30 (3 H, s, Me), 4.22 (1 H, dd, *J* 11, 6 Hz, 1-H), and 7.05-7.80 (9 H, m, ArH).

iii) 4a-*Methyl*-1β-*phenylseleno*-1,2,3,4,4a-*tetrahydrocarbazole* (175) as an orange gum (177 mg, 70% based on conversion); δ ($CC\ell_4$) 1.10-2.50 (6 H, m, aliphatic H), 1.52 (3 H, s, Me), 4.74 (1 H, dd, *J* 3, 1 Hz, 1-H), and 7.05-7.75 (9 H, m, ArH).

iv) Unreacted starting material as an orange oil (47 mg, 25% recovery).

Attempted Oxidation of Selenide (175) to Selenoxide - Repeating the above experiment on five times the scale afforded a mixture of both selenides as a brown oil (1.15 g, 67%), which was dissolved in THF (20 ml), the solution cooled to 0°C and aqueous hydrogen peroxide (30%; 1.7 ml, 3 eq.) added dropwise. The resulting black solution was shown by t.l.c. to be a complex mixture and was discarded without further investigation.

Reaction of the Carbazolenine (161) with BSA - BSA (360 mg, 1 mmol) was added to a solution of the carbazolenine (185 mg, 1 mmol) in chlorobenzene (6 ml) at 90°C. After 10 min, the solvent was removed, the residue dissolved in ether, the solution filtered, washed with saturated sodium bicarbonate solution (10 ml), dried ($MgSO_4$) and evaporated. The resulting red gum was chromatographed (petrol-ether) to afford:

i) Diphenyl diselenide as a dark orange oil (197 mg), solidifying to an orange solid, m.p., 54-58°C (lit.,[90] m.p., 60-62°C).

ii) 3,4-*Dihydro*-4a-*methyl*-1-*phenylseleno*-4aH-*carbazole* (177) as an orange gum (44 mg, 13%); λ_{max} (EtOH) 212 (log ε 4.18), 226 sh (4.10), 234 (4.12), 242 (4.09), and 280 nm (4.03); δ ($CC\ell_4$) 1.21 (3 H, s, Me), 1.55 (1 H, m, 4-H), 2.03-2.64 (3 H, m, 2 x 3-H, 1 x 4-H), 6.02 (1 H, dd, *J* 5.5, 4 Hz, 2-H), and 7.08-7.76 (9 H, m, ArH); *m/e* 339 (M^+), 337, 314, 312, 258, 221, 220 (base), 167, and 157.

iii) 3,4-*Dihydro*-4a-*methyl*-3-*oxo*-1-*phenylseleno*-4aH-*carbazole* (178) as a yellow gum (57 mg, 16%), solidifying to yellow prisms, m.p., 166-168.5°C (from petrol-ether) (Found: C, 64.85; H, 4.2; N, 3.95. $C_{19}H_{15}NOSe$ requires C, 64.8; H, 4.3; N, 4.0%); ν_{max} ($CC\ell_4$), 3060, 2970, 1640, 1450, 1440, 1227, 935, 900, and 875 cm^{-1}; λ_{max} (EtOH) 210 (log ε 4.25), 247 (4.12), 265 sh (3.91), and 336 nm (4.14); δ ($CC\ell_4$) 1.40 (3 H, s, Me), 2.27 (1 H, d, sl.br., *J* 15.5 Hz, 4β-H), 2.89 (1 H, d, *J* 15.5 Hz, 4α-H), 5.84 (1 H, s, 2-H), and 7.11-7.87 (9 H, m, ArH); *m/e* 353 (M^+), 351, 221, 220 (base), 158, 157 and 115.

iv) 3,4-*Dihydro*-4a-*methyl*-4aH-*carbazole* (171) as an unstable brown gum (53 mg, 29%) (Found: M^+ 183.1046. $C_{13}H_{13}N$ requires M^+ 183.1048); ν_{max} (film) 2960, 2920, 1615, 1597, 1540, 1450, 1190, 785, 770, 750, 645, and 620 cm^{-1}; λ_{max} (EtOH) 214 (log ε 3.86), 219 (3.84), 227 (3.90), 234 (3.93), 240 sh (3.88), and 297 nm (3.81); δ ($CC\ell_4$) 1.24 (3 H, s, Me), 1.67 (1 H, m, 4-H), 2.10-2.64 (3 H, m, 2 x 3-H, 1 x 4-H), 6.38 (1 H, m, 2-H), 6.58 (1 H, ddd, *J* 10, 2.5, 1.5 Hz, 1-H), and 7.03-7.57 (4 H, m, ArH); *m/e* 183 (M^+; base), 182, 168, 167, 115 and 77.

Iodoxybenzene - Prepared in 70% yield as described by Sharefkin and Saltzman[186] m.p., 226-229°C (dec.) [lit.,[186] m.p., 230°C (dec.)].

Reaction of the Carbazolenine (161) with BSA in the Presence of Iodoxybenzene. - Addition of a solution of the carbazolenine (3.70 mg, 2 mmol) in chlorobenzene (5 ml) to a suspension of BSA (144 mg, 0.4 mmol) and iodoxybenzene (1.56 g, 6.6 mmol) in refluxing chlorobenzene (25 ml) gave an immediate orange colouration. The mixture was refluxed for a further 0.25 h, after which it was cooled, carbon tetrachloride (20 ml) added, and the suspension filtered. The filtrate was washed with saturated sodium bicarbonate solution (25 ml), dried ($MgSO_4$) and evaporated to leave a dark gum which on chromatography (petrol-ether) gave the *enone* (180) as a brown gum (77 mg, 19%), which had properties identical to those of the compound obtained on dehydrogenation of the ketone (202).

Bromination of the Carbazolenine (161) - A mixture of the carbazolenine (925 mg, 5 mmol), NBS (1.34 g, 7.5 mmol) and AIBN (10 mg) in carbon tetrachloride (25 ml) was refluxed for 9 h, adding more AIBN (10 mg) after 5 h. On cooling, the suspension was filtered and the filtrate evaporated to give a brown gum and solid which on chromatography afforded:

i) 1,1-*Dibromo*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* (181c) as an unstable white solid (248 mg, 14%), m.p., 128-130°C (from petrol-ether) (Found: C, 45.6; H 3.8 ; N, 4.05. $C_{13}H_{13}Br_2N$ requires C, 45.5; H, 3.8; N, 4.1%); δ ($CDC\ell_3$) 1.63 (3 H, s, Me), 1.68-2.74 (5 H, m, aliphatic H), 3.16 (1 H, m, aliphatic H), 7.10-7.45 (3 H, m, ArH), and 7.68 (1 H, m, ArH); *m/e* 345, 343 (M^+), 341, 265, 264, 263, 262, 250, 248, 184, 183, 182, 169, 168, 167 (base), 166, 156, 154, and 152.

ii) An unstable orange gum (1.15 g, 87%) which partially crystallised on standing. N.m.r. indicated it to consist of equal quantities of 1β-*bromo*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* (181a); δ ($CDC\ell_3$)

1.62 (3 H, s, Me), 1.72-2.83 (aliphatic H), 5.35 (1 H, m, 1-H) and 7.15-7.80 (ArH), and 1α-*bromo*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* (181b); δ ($CDC\ell_3$) 1.31 (3 H, s, Me), 1.72-2.83 (aliphatic H), 4.98 (1 H, dd, *J* 12,6 Hz, 1-H), and 7.15-7.80 (ArH); *m/e* 265, 263 (M^+), 185, 184 (base), 109, and 107 (Found: M^+ 263.0304. $C_{13}H_{14}BrN$ requires M^+ 263.0310).

Elimination of Hydrogen Bromide from the Bromide (181) - A mixture of axial and equatorial bromides, (181a) and (181b) (1:1, 767 mg, 2.9 mmol) was stirred at 75°C with DBU (660 mg, 4.3 mmol) in benzene (7 ml) for 1 h, after which the cool mixture was filtered, the filtrate evaporated and the residue chromatographed (4:1 petrol-ether) to afford:

i) An equlibrated mixture of starting bromides (*ca.* 1:1) as a dark gum (274 mg, 36% recovery).

ii) The olefin (171) as a pale brown gum (230 mg, 67% based on recovered starting material).

2-Methylcyclohexa-1,4-diol (190)[101] - 2-Methylhydroquinone (50 g, 0.40 mol) in methanol (70 ml) was hydrogenated at 150 atm. and 150°C for 24 h over Raney nickel[187] (*ca.* 10 g). After filtration through Celite, the filtrate was evaporated to give a dark brown resin which on distillation afforded the diol, contaminated with a little of the starting phenol, as a viscous, colourless syrup (34.8 g, 67%), b.p., 131-140°C at 12 mmHg (lit.,[101] b.p., 114-125°C at 0.5 mmHg).

4-Acetoxy-2-Methylcyclohexanol (191) - Acetic anhydride (30.6 g, 0.30 ml) in chloroform (50 ml) was added dropwise to a cold (3°C) solution of the diol (190) (36.3 g, 0.28 mol) in chloroform (75 ml) containing pyridine

(35 ml). After stirring at room temperature for 2 days, the solution was washed with hydrochloric acid (2 M; 2 x 50 ml) and water (50 ml), dried ($MgSO_4$) and evaporated. The remaining pale yellow oil was distilled to give the product as a colourless, slightly viscous oil (35.5 g, 70%), b.p., 149-153°C at 28 mmHg (lit.,[100] b.p., 140-142°C at 30 mmHg); ν_{max} (film) 3480 (br.) and 1715 cm^{-1}.

4-Acetoxy-2-Methylcyclohexanone (192) - Jones' reagent[188] (4 M; 15 ml) was added dropwise to a solution of the alcohol (191) (8.50 g, 50 mmol) in acetone (20 ml), with cooling. After 10 min, water (15 ml) was added and the dark mixture stirred overnight at room temperature before adding more water (25 ml) and extracting with chloroform (3 x 25 ml). The extracts were washed with water (25 ml), dried ($MgSO_4$) and evaporated to give a yellow oil from which the product was obtained as a pale yellow oil (6.46 g, 76%) by distillation at 125-135°C and 20 mmHg (lit.,[100] m.p., 58-59°C).

3-Acetoxy-4a-Methyl-1,2,3,4,4a-Tetrahydro-4a*H*-Carbazole (193) (a) 4-Acetoxy-2-methylcyclohexanone (1.70 g, 10 mmol) was heated at 95°C with phenylhydrazine (1.08 g, 10 mmol) for 2 h, and the water produced removed under reduced pressure. On cooling, the resulting orange gum was dissolved in acetic acid (8 ml) and the solution stirred at 95°C for 1 h, after which it was added to water (50 ml) and extracted with ether (4 x 25 ml). The combined extracts were washed with hydrochloric acid (2 M; 4 x 25 ml), the washings cooled in ice, basified with ammonia soltuion and extracted with chloroform (3 x 25 ml). The extracts were dried ($MgSO_4$) and evaporated to leave a red oil which was chromatographed (6:4 petrol-ethyl acetate) to afford a 1:1 mixture of the diasteromeric *acetates* (193)

as a red gum (1.0 g, 41%), b.p., 135°C (Kugelrohr) at 0.2 mmHg; ν_{max} (film) 2960, 2930, 1725, 1580, 1375, 1250, 1235, 1215, 1025, 785, 770,and 760 cm^{-1}; *m/e* 243 (M^+), 183 (base), 182, 168, and 134. A sample of the mixture was subjected to p.l.c. (2 x 1:1 petrol ether, then 4 x 1:2 petrol-ether) to give 3α-*acetoxy*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* as a colourless gum, R_F 0.50; δ ($CC\ell_4$) 1.38 (3 H, s, 4a-Me), 1.35-2.95 (6 H, m, aliphatic H), 1.98 (3 H, s, acetate Me), 5.26 (1 H, tt, *J* 12, 4.5 Hz, 3-H), 7.03-7.41 (3 H, m, ArH), and 7.45 (1 H, m, 5-H).

Picrate, yellow crystals, m.p., 160-162°C (dec.) (from acetonitrile) (Found: C, 53.5; H, 4.25; N, 11.7. $C_{21}H_{20}N_4O_9$ requires C, 53.4; H, 4.3; N, 11.9%), and 3β-*acetoxy*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* as a colourless gum, R_F 0.44 ; δ ($CC\ell_4$) 1.40 (3 H, s, 4a-Me), 1.40-2.97 (6 H, m, aliphatic H), 2.11 (3 H, s, acetate Me), 5.12 (1 H, m, 3-H) 7.10-7.40 (3 H, m, ArH), and 7.55 (1 H, m, 5-H).

Picrate, yellow prisms, m.p., 163-165°C (dec.) (from acetonitrile) (Found: C, 53.3; H, 4.35; N, 11.65. $C_{21}H_{20}N_4O_9$ requires C, 53.4; H, 4.3; N, 11.9%).

In a subsequent experiment, the crude reaction mixture was not extracted with acid as before, but subjected directly to chromatography (4:1 petrol-ethylacetate) to afford 3-*acetoxy*-1-*methyl*-1,2,3,4,9-*tetrahydrocarbazole* (196) as a mixture of two diastereomers which were not separated. Distillation gave an orange glass (16%), b.p., 160°C (Kugelrohr) at 5 x 10^{-2} mmHg; ν_{max} ($CH_2C\ell_2$) 3460, 2920, 1715, 1365, and 1030 cm^{-1}; λ_{max} (EtOH) 230, 260 sh, 278 sh, 283,and 292 nm; δ ($CC\ell_4$) 0.95 and 1.04 (d, *J* 6 Hz, 1-Me), 1.90-3.25 (m, aliphatic H), 1.95 and 2.01 (s, acetate Me), 4.91 and 5.22 (m, 3-H), 6.87-7.41 (m, ArH), and 7.62 (br.s., N*H*); *m/e* 243 (M^+), 183, and 168 (base).

(b) The ketone (192) (1.70 g, 10 mmol) was refluxed with phenylhydrazine hydrochloride (1.45 g, 10 mmol) in pyridine (3 ml) for 2 h, and the dark mixture added to water (30 ml) on cooling. The resulting suspension was extracted with ether (3 x 15 ml), the extracts washed with hydrochloric acid (2 M; 5 x 15 ml), the cooled ($0^{\circ}C$) washings basified with ammonia solution, and extracted with chloroform (3 x 25 ml). After drying ($MgSO_4$), the solvent was removed to leave a dark oil which on distillation at $145^{\circ}C$ (Kugelrohr) and 0.2 mmHg afforded a 1:1 mixture of the two diastereomeric acetates (193) as a viscous, yellow gum (770 mg, 32%).

Hydrolysis of the Acetate (193) - A solution of the acetate (1:1 diastereomer ratio; 1.01g,4 mmol) in methanol (12 ml) containing aqueous potassium hydroxide (1 M; 12 ml) was stirred overnight, after which the solution was evaporated until turbidity was observed. Addition of water (10 ml) was followed by extraction with chloroform (3 x 20 ml), the extracts washed with water (15 ml), dried ($MgSO_4$) and evaporated to give a 1:1 diastereomeric mixture of the *alcohols* (194a) and (194b) as a brown gum (720 mg, 90%). The mixture could be resolved into individual isomers by careful chromatography (petrol, then petrol-ether mixtures up to 1:1) to give 3β-*hydroxy*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* (194a) as colourless plates, m.p., 168-170°C (from aqueous ethanol) (Found: C, 77.4; H, 7.7; N, 6.9. $C_{13}H_{15}NO$ requires C, 77.6; H, 7.5; N, 7.0%); ν_{max} (Nujol) 3230 (br), 1575, 965, 870, 845, and 840 cm^{-1}; δ ($CDC\ell_3$) 1.42 (1 H, dd, *J* 14, 3 Hz, 4-H), 1.56 (3 H, s, Me), 1.64-3.30 (5 H, m, aliphatic H), 2.27 (1 H, br.s , O*H*), 4.24 (1 H, m, 3-H), 7.14-7.35 (3 H, m, ArH), and 7.60 (1 H, m, 5-H); *m/e* 201 (M^+), 182, 168, 167 (base), 146, and 145, and

3α-*hydroxy*-4a-*methyl*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* (194b) as a brown gum; ν_{max} (film) 3600 (br.), 2960, 2915, 2860, 1610, 1580, 1450, 1040, 770, 750, and 740 cm^{-1}; δ ($CC\ell_4$) 0.90-1.80 (2 H, m, aliphatic H), 1.24 (3 H, s, Me), 1.87-2.97 (4 H, m, aliphatic H), 3.28 (1 H, br.s, O*H*), 4.17 (1 H, m, 3-H), 7.03-7.34 (3 H, m, ArH), and 7.48 (1 H, m, 5-H); *m/e* 201 (M^+), 182, 168 (base), 167, and 145.

Picrate, yellow prisms, m.p., 166-168°C (from ethanol)(Found: C, 53.2; H, 4.2; N, 12.9. $C_{19}H_{18}N_4O_8$ requires C, 53.0; H, 4.2; N, 13.0%).

3β-Iodo-4a-Methyl-1,2,3,4,4a-Tetrahydro-4aH-Carbazole (199) - A solution of dimethyl azodicarboxylate (470 mg, 2.7 mmol) in benzene (5 ml) was added to a solution of the equatorial alcohol (194b) (490 mg, 2.4 mmol) and triphenylphosphine (710 mg, 2.7 mmol) in benzene (13 ml). After *ca.* 5 min, methyl iodide (0.38 g, 2.7 mmol; 0.17 ml) in benzene (5 ml) was added, and the mixture stirred for 24 h, adding more methyl iodide (0.1 ml) after 3 h. Filtration followed by evaporation of the filtrate afforded a brown gum which was chromatographed (4:1 petrol-ether) to give the *iodide* (199) as an unstable brown oil (121 mg, 16%). (Found: M^+ 311.0177. $C_{13}H_{14}I^{127}N$ requires 311.0173); δ ($CC\ell_4$) 1.15-2.05 (2 H, m, aliphatic H), 1.68 (3 H, s, Me), 2.48-3.37 (4 H, m, aliphatic H), 4.70 (1 H, m, 3-H), 7.12-7.45 (3 H, m, ArH), and 7.59 (1 H, m, 5-H); *m/e* 311 (M^+), 200, 184, 144, 85, and 83 (base).

Elimination of Hydrogen Iodide from the Iodide (199) - The iodide (120 mg, 0.38 mmol) was stirred with DBU (76 mg, 0.5 mmol) in benzene (2 ml) at 60°C for 1 h, and then at room temperature overnight. Filtration of the dark mixture, followed by evaporation of the filtrate gave a black gum

which on subjection to p.l.c. (2 x 1:1 petrol-ether) gave 1,2-*dihydro*-4a-*methyl*-4aH-*carbazole* (198) as a brown gum (54.5 mg, 78%) (Found: M^+ 183.1048. $C_{13}H_{13}N$ requires M^+ 183.1048); δ ($CDC\ell_3$) 1.41 (3 H, s, Me), 2.46 (1 H, m, 2-H), 2.73 (1 H, m, 2-H), 2.95 (2 H, m, 1-H), 5.64 (1 H, ddd, *J* 9.2, 4.2, 2.5 Hz, 3-H), 5.92 (1 H, ddd, *J* 9.2, 2.6, 1.6 Hz, 4-H), 7.15-7.40 (3 H, m, ArH), and 7.58 (1 H, m, 5-H); *m/e* 183 (M^+), 182 (base), 168, and 167.

3α-Iodo-4a-Methyl-1,2,3,4,4a-Tetrahydro-4a*H*-Carbazole (200) - A solution of dimethyl azodicarboxylate (336 mg, 2.3 mmol) in benzene (2 ml) was added to a solution of the axial alcohol (194a) (417 mg, 2.07 mmol) and triphenyl phosphine (603 mg, 2.3 mmol) in benzene (10 ml) and THF (5 ml). After stirring for 5 min, methyl iodide (355 mg, 2.5 mmol; 156 μℓ) in benzene (2 ml) as added and stirring continued overnight before filtering and evaporating the filtrate. The residue was chromatographed (7:3 petrol-ether) to give an inseparable mixture of the *iodide* (200) (Found: M^+ 311.0171. $C_{13}H_{14}I^{127}N$ requires M^+ 311.0173); δ ($CC\ell_4$) 1.30 (3 H, s, Me), 1.59-2.98 (6 H, m, aliphatic H), 4.63 (1 H, tt, *J* 12, 3.5 Hz, 3-H), 7.02-7.42 (3 H, m, ArH), and 7.55 (1 H, m, 5-H); *m/e* 312, 311 (M^+; base), 184, and 170 and the olefin (198) (121 mg, 25% yield of each based on conversion) and a brown gum from which the starting alcohol (220 mg, 53% recovery) was recovered by acid extraction.

Tosylation of the Axial Alcohol (194a) - Tosyl chloride (310 mg, 1.6 mmol) was added to the alcohol (325 mg, 1.6 mmol) in pyridine (5 ml) and the resulting solution stirred overnight, after which water (30 ml) was added and the mixture extracted with ether (2 x 25 ml; 1 x 15 ml). The extracts

were washed wtih water (3 x 20 ml), dried (Na_2SO_4), evaporated, and the residue chromatographed (petrol, then petrol-ether up to 1:1) to give 3β-*hydroxy*-4a-*methyl*-9-(4-*methylphenylsulphonyl*)-2,3,4,4a,9-*tetrahydro*-4aH-*carbazole* (201) as white needles (372 mg, 66%), m.p., 131-133°C (from petrol-dichloromethane)(Found: C,67.4; H,6.9; N,3.9; S,9.15. $C_{20}H_{21}N_2S$ requires C,67.6; H,6.0; N,3.9; S,9.0%); ν_{max} ($CHC\ell_2$) 3415, 2910, 1595, 1455, 1355, and 1155 cm^{-1}; λ_{max} (EtOH) 211 (log ε 4.14), 222 (4.08), 242 sh (3.84); 270 (3.73), and 288 sh nm (3.64); δ ($CDC\ell_3$) 0.66 (3 H, s, 4a-Me), 1.60-2.95 (4 H, m, aliphatic H), 2.30 (3 H, s, tosyl Me), 4.13 (1 H, m, 3-H), 6.00 (1 H, dd, *J* 9, 3 Hz, 1-H), 6.92-7.34 (3 H, m, ArH), 7.17 (2 H, d, *J* 8 Hz, tosyl 3,5-H), 7.62 (2 H, d, *J* 8 Hz, tosyl 2,6-H), and 7.78 (1 H, m, 5-H); *m/e* 355 (M^+), 340, 311, 200 (base), 157, and 156.

Oxidation of the Alcohol (194) - A solution of DMSO (1.1 ml, 14.1 mmol) in dichloromethane (3 ml) was added to oxalyl chloride (0.7 ml, 7.7 mmol) in dichloromethane (15 ml) at -78°C. After 5 min, a solution of the alcohol (1:1 diastereomer ratio; 1.28 g, 6.4 mmol) in dichloromethane (15 ml) and DMSO (1 ml) was added, the mixture stirred for 0.3 h, triethylamine (4.5 ml, 32 mmol) added and stirring at -78°C continued for a further 5 min before allowing to warm to room temperature and stirring for 2 h. Addition of water (25 ml) was followed by separation of layers, the organic being washed with brine (25 ml), saturated sodium bicarbonate solution (25 ml) and water (25 ml), dried ($MgSO_4$) and evaporated. The remaining brown solid was chromatographed (7:3 petrol-ether) to give 4a-*methyl*-3-*oxo*-1,2,3,4,4a-*tetrahydro*-4aH-*carbazole* (202) as an unstable pale yellow solid (1.14 g, 89%), m.p., 102-106°C (Found: M^+ 199.0992. $C_{13}H_{13}NO$ requires M^+ 199.0997); ν_{max} ($CC\ell_4$) 2970, 1720, 1585, 1445, 1435, and 1145 cm^{-1}; λ_{max} (EtOH) 208 sh (log ε 4.11), 213 (4.17), 219 (4.20), 223 sh (4.13)

260 (3.65), and 329 nm (2.55); δ ($CDC\ell_3$) 1.34 (3 H, s, Me), 2.32 (1 H, d, *J* 14 Hz, 4-H), 2.59-3.32 (5 H, m, aliphatic H), 7.21-7.52 (3 H, m, ArH), and 7.67 (1 H, m, 5-H); *m/e* 199 (M^+; base), 184, 170, 157, 156, 145,and 144.

Reaction of the Ketone (202) with BSA - The ketone was heated with BSA and iodoxybenzene under the conditions given in Table 8 (p. 88). After allowing the mixture to cool, chloroform (20-30 ml) was added and the suspension filtered, the filtrate evaporated and the residue chromatographed (4:1, petrol-ether) to afford the *selenide* (178), m.p., 168-170°C, undepressed when mixed with a sample obtained from reaction of the carbazolenine (161) with BSA, and 3,4-*dihydro*-4a-*methyl*-3-*oxo*-4aH-*carbazole* (180) as an unstable brown oil which solidified on standing, m.p., 54-57°C (Found: M^+ 197.0837. $C_{13}H_{11}NO$ requires M^+ 197.0841); ν_{max} ($CC\ell_4$) 1680 cm^{-1}; λ_{max} (EtOH) 211 (log ε 4.05), 228 sh (3.96), 233 (3.97), 238 sh (3.96), and 333 nm (3.92); δ ($CC\ell_4$) 1.38 (3 H, s, Me), 2.36 (1 H, d, *J* 15 Hz, 4α-H), 3.00 (1 H, dd, *J* 15, 1 Hz, 4β-H), 6.46 (1 H, dd, *J* 10, 1 Hz, 2-H), 7.14-7.52 (3 H, m, ArH), 7.48 (1 H, d, *J* 10 Hz, 1-H), and 7.74 (1 H, m, 5-H); *m/e* 197 (M^+; base), 196, 182, 168, and ,154.

Methylation of the Selenide (178) - *n*-Butyllithium in hexane (1.5 M, 0.2 ml, 0.3 mmol) was added to a solution of diisopropylamine (35 mg, 0.35 mmol, 49 μℓ) in THF (1 ml) at -78°C, followed after 0.25 h by a

solution of the enone (178) (106 mg, 0.3 mmol) in THF (1 ml). The resulting bright red solution was stirred for 0.5 h, methyl iodide (47 mg, 0.3 mmol, 19 μℓ) added, and the now yellow solution stirred for a further 1.5 h, during which it was warmed to room temperature. Addition of saturated ammonium chloride solution (5 ml) was followed by extraction with ether (2 x 5 ml), the extracts washed with water (2 x 5 ml) dried, ($MgSO_4$), evaporated and chromatographed (9:1 petrol-ether) to afford 3,4-*dihydro*-4,4a-*dimethyl*-3-*oxo*-1-*phenylseleno*-4aH-*carbazole* (207) as a yellow gum (60 mg, 55%), which solidified on standing, m.p., 128-130°C (from petrol-ether)(Found: 65.7; H, 4.5; N, 3.9. $C_{20}H_{17}NOSe$ requires C, 65.6; H, 4.7; N, 3.8%); δ ($CC\ell_4$) 0.53 (3 H, d, *J* 8 Hz, 4-Me), 1.37 (3 H, s, 4a-Me), 2.93 (1 H, q, *J* 8 Hz, 4-H), 5.77 (1 H, s, 2-H), and 7.12-7.94 (9 H, m, ArH); *m/e* 367 (M^+), 365, 352, 264, 252, and 234 (base).

3,4-Dihydro-4a-Methyl-3-Methylene-4a*H*-Carbazole (208) - *n*-Butyllithium in hexane (1.5 M; 0.7 ml, 1 mmol) was added to a suspension of methyltriphenylphosphonium bromide (357 mg, 1 mmol) in THF (5 ml), maintained at -78°C. After warming to room temperature, the mixture was stirred for 1.5 h, re-cooled to -23°C, and the enone (180) (60 mg, 0.3 mmol) in THF (1 ml) added. Stirring at room temperature for 2 h was followed by addition of water (15 ml), extraction with ether (3 x 10 ml), the extracts washed with water (2 x 10 ml), dried (Na_2SO_4), evaporated and the residue chromatographed (6:4 petrol-ether) to give the *olefin* (208) as a pale brown gum (25 mg, 43%); δ ($CC\ell_4$) 1.18 (3 H, s, Me), 2.27 (1 H, m, 4β-H), 2.84 (1 H, d, *J* 13.5 Hz, 4α-H), 5.30 (2 H, m, $=CH_2$), 6.58 (1 H, d, *J* 10 Hz, 2-H), 6.75 (1 H, d, *J* 10 Hz, 1-H), 7.08-7.43 (3 H, m, ArH), and 7.56 (1 H, m, 5-H).

1,3-Cyclohexadiene - Prepared in 87% yield by the procedure of Schaefer and Endres.[189]

5-Chloro-5-Cyanobicyclo[2.2.2]oct-2-ene (216)[190] - A mixture of cyclohexadiene (4 g, 50 mmol), 2-chloroacrylonitrile (5 g, 57 mmol), and hydroquinone (0.1 g) was refluxed in xylene (15 ml) for 43 h. On cooling, the mixture was diluted with methanol (125 ml) the precipitated polymer removed by filtration through Celite, and the filtrate evaporated. Distillation of the residual gum gave the product as a waxy semi-solid (3.9 g, 45%), b.p., 100°C at 7 x 10^{-2} mmHg (lit.,[191] b.p., 95-98°C at 0.1 mmHg); ν_{max} (film) 2970, 2940, 2870, 2230, and 715 cm^{-1}; *m/e* 167 (M^+), 116, 104, 80 (base), 79, and 77.

Bicyclo[2.2.2]oct-2-en-5-one (212) - A solution of the chloronitrile (216) (10 g, 60 mmol) in ethanol (35 ml) was added to a refluxing solution of sodium hydroxide (6 g, 0.15 mol) in DMSO (30 ml) and ethanol (85 ml). After refluxing for 14 h, the mixture was allowed to cool and added to water (250 ml), extracted with ether (4 x 100 ml), the extracts washed with water (4 x 100 ml), dried (Na_2SO_4), and evaporated to leave a brown oil. Distillation at 140°C and 40 mmHg afforded the ketone as a soft, waxy solid, (4 g, 55%); ν_{max} (film) 2940, 2905, 2870, 1720, 1115, 1080, and 700 cm^{-1}; δ ($CDC\ell_3$) 1.45-1.95 (4 H, m, 7,8-H), 2.03 (2 H, m, 6-H), 3.00 (1 H, m, 1-H), 3.15 (1 H, m, 4-H), 6.21 (1 H, ddd, *J* 6.25, 6.25, 1.5 Hz, olefinic H), and 6.48 (1 H, ddd, *J* 6.25, 6.25, 1.5 Hz, olefinic H); *m/e* 122 (M^+), 91, 81, 80 (base), 79, 78, and 77.

Methylation of the Ketone (212) - A solution of the ketone (0.61, 5 mmol) in THF (5 ml) was added to a solution of LDA (5 mmol) in THF (5 ml) at -78°C, followed after 0.5 h by a mixture of methyl iodide (0.78 g, 5.5 mmol) and HMPA (1 ml, *ca.* 6 mmol). The resulting solution was allowed to warm to room temperature over 1 h before adding saturated ammonium chloride solution (10 ml) and water (10 ml), and extracting with dichloromethane (3 x 10 ml). The extracts were washed with water (3 x 10 ml), dried ($MgSO_4$), and evaporated to leave a brown oil which on chromatography (6:4 petrol-dichloromethane) gave:

i) 6-Methylbicyclo[2.2.2]oct-2-en-5-one (214) as a pale yellow oil (150 mg); δ ($CC\ell_4$) 0.96 (3 H, d, *J* 7 Hz, Me), 1.35-2.05 (5 H, m, aliphatic H), 2.75 (1 H, m, 1-H), 3.00 (1 H, m, 4-H), 6.07-6.52 (2 H, m, 2,3-H); *m/e* 136 (M^+), 80 (base), and 79.

ii) A yellow oil (164 mg) which g.l.c. (7% OV-17 on Chromosorb WAW DMCS; 1/8" x 4'; 100°C) indicated to consist of the methylated ketone (66% ; retention time 1.75 min) and starting material (33%; retention time 2.25 min).

iii) A pale yellow semi-solid (103 mg) consisting of the product (12%) and starting material (88%).

The total yield of methylated product was 40%.

7.5. EXPERIMENTAL FOR CHAPTER 5.

FVP of 4a-Methyl-1,3,9-Triphenyl-4a*H*-Fluorene (81). - The fluorene (113 mg) was distilled at 320°C and 3 x 10^{-2} mmHg into a quartz tube at 540°C and the resulting pyrolysate (100 mg) subjected to p.l.c. (4:1 petrol-dichloromethane). The major band was isolated to afford crude 9-methyl-1,3,9-triphenylfluorene (218) as a colourless semisolid (71 mg, 63%), R_F 0.8. Recrystallisation from petrol-ether afforded the pure product as large colourless prisms, m.p., 170-171°C (lit.,[146] m.p., 171-172°C); δ ($CC\ell_4$) 1.55 (3 H, s, Me), and 6.55-8.00 (21 H, m, ArH).

Photolysis of 4a-Methyl-1,3,9-Triphenyl-4a*H*-Fluorene (81) - A solution of the fluorene (370 mg) in acetonitrile (100 ml) was irradiated at 254 nm for 17 h, during which period the colour of the solution was observed to fade from yellow to almost colourless. The precipitated solid was collected, and thoroughly washed with acetone. Recrystallisation from ethanol-benzene gave 4-*methyl*-1,3,9-*triphenyl*-3H-*cyclopenta*[b]*naphthalene* (219) as white needles (162 mg, 59%), m.p., 227-229°C (Found: C, 94.3; H, 6.0. $C_{32}H_{24}$ requires C, 94.1; H, 5.9%); ν_{max} ($CC\ell_4$) 3050, 3020, 2920, 1595, 1485, 1435, and 690 cm^{-1}; λ_{max} (cyclohexane) 210 (log ε 4.57), 226 (4.59), 247 (4.62), 261 sh (4.47), 275 (4.34), 293 sh (4.12), 303 (4.23), 315 (4.21), 333 sh (3.39), and 349 sh nm (3.09); δ ($CC\ell_4$) 2.48 (3 H, s, Me), 4.95 (1 H, d, *J* 2.5 Hz, 3-H), 6.47 (1 H, d, *J* 2.5 Hz, 2-H), and 6.70-8.15 (19 H, m, ArH); *m/e* 408 (M^+; base), 393, 334, 315,and 252.

2-Bromo-4-Phenylbutane (236) - Prepared in 95% yield according to Sneedon and Zeiss,[149] b.p., 110-115°C at 10 mmHg (lit.,[149] b.p., 60-65°C at 0.2 mmHg).

3-Methyl-5-Phenylpentan-2-one (232) - (a) A solution of 4-phenyl-2-butylmagnesium bromide, prepared from magnesium (0.48 g, 20 mmol) and 4-phenyl-2-butyl bromide (4.26 g, 20 mmol) in ether (25 ml), was added dropwise over 0.5 h to a suspension of acetyl chloride (4.71 g, 60 mmol) in ether (20 ml) and benzene (20 ml), containing anhydrous ferric chloride (33 mg, 0.2 mmol), at -78°C. After stirring at -78°C for a further 0.5 h the mixture was stirred overnight at room temperature. Addition to ice-water (100 ml) was followed by separation of layers, the aqueuos being extracted with ether (2 x 25 ml), the combined organic layers washed with potassium hydroxide solution (1 M; 2 x 25 ml) and water (25 ml), dried ($MgSO_4$) and evaporated. The residual brown oil was distilled to afford the product as a pale yellow oil (1.25 g, 36%), b.p., 120°C at 15 mmHg (lit.,[148] b.p., 130°C at 15 mmHg); ν_{max} (film) 3015, 2960, 2930, 1705, 1600, 750, and 700 cm^{-1}; δ ($CC\ell_4$) 1.07 (3 H, d, *J* 7 Hz, 3-Me), 1.40-2.08 (2 H, m, aliphatic H), 2.03 (3 H, s, -CO*Me*), 2.25-2.70 (3 H, m, aliphatic H), and 7.17 (5 H, m, ArH); *m/e* 176 (M^+), 104, 91, 85, 83, and 72 (base). (b) A solution of 2-bromo-4-phenylbutane (7.2 g, 34 mmol) in ether (25 ml) was added to magnesium (0.81 g, 34 mmol) in ether (5 ml), the resulting solution refluxed for 1 h, then cooled to 0°C and acetaldehyde (1.98 g, 45 mmol) in ether (20 ml) added dropwise. Reflux for 3.5 h was followed on cooling by the addition of ammonium chloride solution (10%; 50 ml), the layers separated and the aqueous extracted with ether (3 x 25 ml). The combined ethereal layers were washed with water (50 ml), dried ($MgSO_4$), evaporated and the residue chromatographed (24:1 petrol-ether) to give:

i) An inseparable mixture of 1-phenylbutane and phenylbutene as a colourless oil (2.30 g, 50%); ν_{max} (film), 3020, 2960, 2920, 2850, 1600, 1490, 1450, 1260, 740,and 700 cm^{-1}; *m/e* 134 (M^+, alkane), 132 (M^+, alkene), 117, 92 and 91 (base).

ii) The ketone (232) as a colourless oil (1.32 g, 22%).

iii) 3-*Methyl*-5-*phenylpentan*-2-*ol* (237) as a viscous colourless oil (1.70 g, 28%), b.p., 95°C (Kugelrohr) at 0.2 mmHg, a satisfactory analysis was not obtained (Found: C, 80.1; H, 10.3. $C_{12}H_{18}O$ requires C, 80.85; H, 10.2%); ν_{max} (film) 3360 (br.), 3020, 2970, 2920, 2870, 1600, 1490, 1450, 750,and 700 cm^{-1}; δ ($CC\ell_4$) 0.89 (3 H, d, *J* 7 Hz, 3-Me), 1.07 (3 H, d, *J* 7 Hz, -CHOHC*H*$_3$), 1.20-2.02 (4 H, m, aliphatic H and OH), 2.30-2.85 (2 H, m, aliphatic H), 3.61 (1 H, m, 2-H), and 7.15 (5 H, m, ArH); *m/e* 178 (M^+), 160, 145, 131, 117, 104 (base), and 91.

(c) A solution of the alcohol (237) (0.91 g, 5.1 mmol) in dichloromethane (5 ml) was added to a stirred suspension of pyridinium chlorochromate (1.5 g, 7 mmol) in dichloromethane (10 ml), and the mixture stirred for 2 h before adding ether (50 ml). After filtering through Celite, the filtrate was evaporated and the residue distilled at 145°C (Kugelrohr) and 20 mmHg to afford the ketone (232) as a colourless oil (0.48 g, 96%).

2,3-Dimethyl-3-(2-Phenylethyl)-3*H*-Indole (231) - 3-Methyl-5-phenylpentan-2-one (1.20 g, 6.8 mmol) was heated with phenylhydrazine (0.74 g, 6.8 mmol) at 100°C for 2 h, after which the water produced was removed by azeotroping with benzene. The residual orange gum was dissolved in acetic acid (10 ml) and the solution stirred at 105°C for 3 h, added to ice-water (60 ml), and extracted with ether (3 x 25 ml). The combined extracts were washed with hydrochloric acid (2 M; 3 x 25 ml), the washings cooled, basified with ammonia solution, and extracted with chloroform (3 x 25 ml). After

drying ($MgSO_4$) and evaporating the extracts, the crude product was distilled to give 2,3-*dimethyl*-3-(2-*phenylethyl*)-3H-*indole* as a viscous, pale green gum (1.26 g, 74%), b.p., 130°C (Kugelrohr) at 0.1 mmHg; ν_{max} (film), 3015, 2960, 2915, 1600, 1575, 1450, 775, 755, and 705 cm^{-1}; λ_{max} (EtOH) 220 and 257 nm; δ ($CC\ell_4$) 1.23 (3 H, s, 3-Me), 1.92 (4 H, m, $-CH_2CH_2Ph$), 2.17 (3 H, s, 2-Me), 6.85-7.37 (8 H, m, ArH), and 7.52 (1 H, m, 4-H), *m/e* 249 (M^+), 234, 158 (base), 145, 115, 105, and 91.

Picrate, yellow needles, m.p., 158.5-160°C (from ethanol) (Found: C, 60.55; H, 4.6; N, 11.65. $C_{24}H_{22}N_4O_7$ requires C, 60.25; H, 4.6; N, 11.7%).

Acetylation of the Indolenine (231) - A solution of the indolenine (430 mg, 1.43 mmol) in acetic anhydride (2 ml) was stirred at 120°C for 2 h, allowed to cool, and added to water. Extraction with ether (2 x 10 ml), washing of the extracts with saturated sodium bicarbonate solution (5 x 10 ml), drying (K_2CO_3),and removal of solvent afforded an orange gum which on distillation gave 1-*acetyl*-1,2-*dihydro*-3-*methyl*-2-*methylene*-3-(2-*phenylethyl*)-3H-*indole* (238) as a pale green gum (470 mg, 94%), b.p., 180°C (Kugelrohr) at 0.1 mmHg (Found: M^+ 291.1627. $C_{20}H_{21}NO$ requires M^+ 291.1623); ν_{max} (film) 3020, 2915, 1670, 1600, 1480, 1365, 1340, 755, and 700 cm^{-1}; λ_{max} (EtOH) 218, 252, 280 sh, and 288 sh nm; δ ($CC\ell_4$) 1.42 (3 H, s, 3-Me), 1.82-2.43 (4 H, m, $-CH_2CH_2Ph$), 2.46 (3 H, s, $-COMe$), 4.76 (1 H, d, *J* 4 Hz, $=CH_2$), 5.22 (1 H, d, *J* 4 Hz, $=CH_2$), 6.90-7.38 (8 H, m, ArH), and 7.99 (1 H, m, 7-H); *m/e* 291 (M^+), 249, 234, 187, 158, 150, 145 (base), and 144.

Reduction of the Indolenine (231) - The indolenine (461 mg, 1.85 mmol) in ethanol (5 ml) was added dropwise to a solution of sodium borohydride (210 mg, 5.5 mmol) in ethanol (5 ml) and the mixture stirred for 1 h before adding concentrated hydrochloric acid (1 drop). After a further 2 h, more hydrochloric acid (2 M; 0.25 ml) was added and the mixture stirred overnight before adding ether (30 ml), filtering and evaporating the filtrate to dryness. The green oil so obtained was chromatographed (3:1 petrol-ether) to afford 1,2-*dihydro*-2,3-*dimethyl*-3-(2-*phenylethyl*)-3H-*indole* (239) as a green gum (277 mg, 60%)(Found: M^+ 251.1679. $C_{18}H_{21}N$ requires M^+ 251.1674); ν_{max} (film) 3370, 3030, 2960, 2930, 1605, 1480, 1460, 745,and 700 cm^{-1}; δ ($CC\ell_4$) 1.22 (3 H, d, *J* 7 Hz, 2-Me), 1.28 (3 H, s, 3-Me), 1.40-2.04 (2 H, m, $-CH_2CH_2-$), 2.17-2.81 (2 H, m, $-CH_2CH_2-$), 3.48 (1 H, br.s, exch. D_2O, N*H*), 3.57 (1 H, m, 2-H), and 6.43-7.28 (9 H, m, ArH); *m/e* 251 (M^+), 160, 147, 146 (base), 144, 130,and 129.

2,3-Dimethylindole (233; R = Me) - Prepared in 71% yield using the method of Ockenden and Schofield,[192] m.p., 99-104°C (from petrol) (lit.,[172] m.p., 106-107°C).

Alkylation of 2,3-Dimethylindole with Styrene Oxide - A solution of methyl iodide (7.2 g, 51 mmol) in ether (50 ml) was added to magnesium (1.21 g, 50 mmol) in ether (5 ml), the resulting solution cooled to 0°C and 2,3-dimethylindole (7.25 g, 50 mmol) in ether (75 ml) added. After refluxing the mixture for 0.5 h, styrene oxide (7.2 g, 60 mmol) in ether (50 ml) was added and reflux continued for 17 h. On cooling, saturated ammonium chloride solution (50 ml) was added, the aqueous layer extracted with ether (50 ml), and the combined ethereal layers washed with hydrochloric acid (2 M; 4 x 25 ml). The washings were basified with

ammonia solution, extracted with dichloromethane (3 x 25 ml), the extracts dried ($MgSO_4$), and evaporated. The residue was chromatographed (9:1 petrol-ether, then up to 1:1 petrol-ether) to afford 3aα,8aα-*dimethyl*-3α-*phenyl*-*tetrahydrofurano*[5,4-b]*indole* (241a) as a pale brown solid (1.10 g, 8.3%). An analytical sample was recrystallised from petrol-dichloromethane to give colourless prisms, m.p., 130°C (Found: C, 81.5; H, 7.3; N, 5.25. $C_{18}H_{19}NO$ requires C, 81.5; H, 7.2; N, 5.3%); ν_{max} ($CC\ell_4$) 3430, 3340, 3060, 2980, 2940, 2870, 1605, 1480, 1465, 1380, 1320, 1150, 1095, 1035, 1020, and 700 cm^{-1}; λ_{max} (EtOH) 218, 243, and 307 nm; δ_H ($CDC\ell_3$) 0.92 (3 H, s, 3a-Me), 1.44 (3 H, s, 8a-Me), 3.39 (1 H, dd, *J* 5.8, 2 Hz, 3-H), 3.94 (1 H, dd, *J* 9.2, 5.8 Hz, 2β-H), 4.08 (1 H, dd, *J* 9.2, 2 Hz, 2α-H), 4.52 (1 H, br.s, N*H*), 6.52 (1 H, d, *J* 7.5 Hz, 4-H), 6.75 (1 H, dt, *J* 7.5, 0.8 Hz, 5-H), and 6.98-7.39 (7 H, m, ArH); δ_C ($CDC\ell_3$) 20.3, 23.2, 57.5, 57.9, 70.9, 103.8, 107.8, 118.6, 123.0, 126.6, 128.0, 128.2(2), 128.6(2), 135.9, 141.3, and 147.7; *m/e* 266, 265 (M^+; base), 161, 158, 146, 145, and 144, and 3aα,8aα-*dimethyl*-3β-*phenyltetrahydrofurano*[4,5-b]*indole* (241b) as a pink solid (1.20 g, 9%), m.p., 110-111°C (from petrol-dichloromethane) (Found: C, 81.4; H, 7.2; N, 5.2. $C_{18}H_{19}NO$ requires C, 81.5; H, 7.2; N, 5.3%); ν_{max} ($CC\ell_4$) 3430, 3340, 3040, 2970, 2940, 2880, 1605, 1460, 1380, 1320, 1040, and 700 cm^{-1}; λ_{max} (EtOH) 219, 242, and 303 nm; δ_H ($CDC\ell_3$) 1.38 (3 H, s, 3a-Me), 1.57 (3 H, s, 8a-Me), 3.33 (1 H, dd, *J* 11.7, 6.7 Hz, 3-H), 3.86 (1 H, dd, *J* 11.7, 8.3 Hz, 2α-H), 4.00 (1 H, dd, *J* 8.3, 6.7 Hz, 2β-H), 4.48 (1 H, br.s , N*H*), 5.76 (1 H, dd, *J* 7.5, 1 Hz, 4-H), 6.33 (1 H, dt, *J* 6.3, 1 Hz, 5-H), 6.48 (1 H, d, *J* 7.5 Hz, 3Ph *o*-H), 6.85-6.98 (3 H, m, ArH), and 7.20 (3 H, m, ArH); δ_C ($CDC\ell_3$) 22.7, 23.3, 57.3, 57.8, 68.2, 104.3, 107.3, 117.3, 125.9, 127.0, 127.7(2), 127.8, 129.2(2), 129.9, 136.6, and 148.5; *m/e* 266, 265 (M^+; base), 161, 158, 146, 145,and 144.

2-Bromo-1-Phenylethanol - Prepared from styrene using aqueous NBS as described by Buckles and Maurer[155] in 75% yield, b.p., 100-105°C at 1 mmHg (lit.,[155] b.p., 96-97°C at 1 mmHg).

2-Bromo-1-Phenyl-1-Trimethylsilyloxyethane (242) - Trimethylsilyl chloride (3.53 g, 32.4 mmol, 4.13 ml) was added to a cold (0°C) solution of styrene bromohydrin (4.34 g, 21.6 mmol) in THF (25 ml), followed by triethylamine (3.72 g, 32.4 mmol; 4.5 ml), and the resulting white suspension stirred overnight at room temperature. Addition of water (100 ml) was followed by extraction with ether (4 x 25 ml), the extracts washed with water (2 x 25 ml), dried ($MgSO_4$), evaporated, and the residue distilled at 136°C (Kugelrohr) and 12 mmHg to give the *bromide* (242) as a colourless oil (5.0 g, 85%); ν_{max} (film) 2950, 1245, 840, and 700 cm^{-1}; δ ($CC\ell_4$) 0.13 (9 H, s, -OTMS), 3.44 (2 H, m, $-CH_2Br$), 4.89 (1 H, m, O-$CH<$), and 7.36 (5 H, m, ArH); *m/e* 259 (M^+ - 15), 257, 180, 179 (base), 177, 138, 136, 106, and 73.

Attempted Alkylation of 2,3-Dimethylindole - An ethereal solution of methylmagnesium iodide was prepared by adding methyl iodide (1.42 g, 10 mmol; 0.65 ml) in ether (15 ml) to magnesium (0.24 g, 10 mmol) in ether (5 ml). After dissolution of the metal was complete, anisole (15 ml) was added and the ether removed by distillation at 70°C. The remaining solution was cooled to 0°C, 2,3-dimethylindole (1.45 g, 10 mmol) in anisole (15 ml) added, and the mixture stirred at 90°C for 0.25 h before adding the bromide (242) (2.72 g, 10 mmol) in anisole (10 ml). Stirring at 95°C was continued for 20 h, after which the mixture was allowed to cool and saturated ammonium chloride solution (5 ml) added. The organic layer was washed with a solution of hydrochloric acid (2 M) and potassium fluoride (2%) (4 x 25 ml), the washings extracted with ether (50 ml), cooled, and basified with ammonia solution. Extraction with chloroform (4 x 25 ml),

followed by drying ($MgSO_4$) and evaporation of the extracts afforded 2,3,3-trimethyl-3*H*-indole (243) as a red gum (200 mg); δ ($CC\ell_4$) 1.24 (6 H, s,3,3-Me), 2.21 (3 H, s, 2-Me), and 6.95-7.67 (4 H, m, ArH) as the only acid-soluble product.

Attempted Preparation of 2-Methyl-3*Z*-Styrylindole (244)[156] - A solution of 2-methylindole (3.93 g, 30 mmol) in ether (15 ml) was added to methylmagnesium iodide, prepared from magnesium (0.72 g, 30 mmol) and methyl iodide (4.36 g, 30 mmol; 1.9 ml) in ether (15 ml). After refluxing for 0.25 h, the mixture was cooled to 0°C and a solution of phenylacetaldehyde (3.6 g, 30 mmol; 3.5 ml) in ether (10 ml) added. Reflux for 2.5 h was followed by addition of ethyl formate (2.22 g, 30 mmol; 2.42 ml) and the resulting suspension stirred at 30°C overnight before adding hydrochloric acid (2 M; 25 ml), and ether (25 ml). The organic layer was washed with water (25 ml), saturated sodium bicarbonate solution (25 ml),and filtered to afford crude 1,1-*bis*-(2-*methyl*-1H-*indol*-3-*yl*)-2-*phenylethane* (245) as an unstable white solid (3.70 g, 68%), m.p., 175-183°C (dec.). A sample recrystallised from nitromethane had m.p. 255-257°C (dec.). (Found: M^+ 364.1932. $C_{26}H_{24}N_2$ requires M^+ 364.1939); ν_{max} (Nujol) 3405, 1455, 760, 730 and 700 cm^{-1}; λ_{max} (EtOH) 212 sh (log ε 3.92), 230 (4.15), 278 sh (3.74), 285 (3.78), and 293 nm (3.77); δ (d_6-DMSO) 2.10 (6 H, s, indole Me), 3.64 (2 H, d, *J* 9 Hz, 2-H), 4.52 (1 H, t, *J* 9 Hz, 1-H), 6.75-7.21 (1 H, m, ArH), 7.50 (2 H, d, *J* 7.5 Hz, ArH), and 10.52 (2 H, br.s, N*H*); *m/e* 364 (M^+), 274, 273 (base), 257, 223, 218, 217, 131, and 130.

2-Methylindole-3-Aldehyde (246) - Prepared in 98% yield by the method of James and Snyder,[158] m.p., 193-196°C (lit.,[193] 198°C).

Tosylation of 2-Methylindole-3-Aldehyde - The indole (3.18 g, 20 mmol) was refluxed with tosyl chloride (7.71 g, 40 mmol) and anhydrous potassium carbonate (11.05 g, 80 mmol) in butanone (80 ml) for 3.25 h. The dark suspension was filtered and the filtrate evaporated to leave a brown gum which on chromatography (3:1 petrol-dichloromethane) gave *2-methyl-1-(4-methylphenylsulphonyl)indole-3-aldehyde* (247) as a pink solid (3.50 g, 55%), m.p., 148-150°C (from petrol-ethyl acetate) (Found: C, 65.0; H, 4.8; N, 4.5. $C_{17}H_{15}NO_3S$ requires C, 65.2; H, 4.8; N, 4.5%); ν_{max} (Nujol) 1665, 1365, 1190, 1180, 990, 760, 745, 670, and 655 cm^{-1}; δ ($CC\ell_4$) 2.32 (3 H, s, 2-Me), 2.84 (3 H, s, tosyl Me), 6.95-7.60 (5 H, m, ArH), 7.68 (2 H, d, *J* 8 Hz, tosyl 2,6-H), 8.15 (2 H, m, ArH), and 10.20 (1 H, s, C*H*O); *m/e* 313 (M^+), 158, 155, 130, 111, and 91 (base).

2-Methyl-3-Styryl-1-Tosylindole (248) - (a) A suspension of sodium hydride (50% dispersion in mineral oil; 0.48 g, 10 mmol) in DMSO (10 ml) was stirred for 1 h at 70°C, until no further effervescence could be observed. The resulting solution was cooled to 0°C, benzyltriphenylphosphonium bromide (4.33 g, 10 mmol) in DMSO (25 ml) added, followed, after stirring for 0.5 h at room temperature, by a solution of the aldehyde (247) (3.16 g, 10 mmol) in DMSO (20 ml). After stirring for 22 h, the dark mixture was added to ice-water (150 ml) and extracted with ether (4 x 50 ml). The extracts were washed with water (4 x 50 ml), dried ($MgSO_4$) and evaporated to give a brown gum which on chromatography (9:1 petrol-dichloromethane) afforded a 3:2 mixture of *E* and *Z* isomers of the *styrylindole* (248) as a pale brown gum (2.44 g, 63%). Further chromatography (49:1 petrol-ether) gave *2-methyl-1-(4-methylphenylsulphonyl)-3Z-(2-phenylethenyl)-1H-indole* as a

gum: δ ($CDC\ell_3$) 2.30 (3 H, d, *J* 0.8 Hz, 2-Me), 2.32 (3 H, s, tosyl Me), 6.42 (1 H, dd, *J* 11, 0.8 Hz, -C*H*=CHPh), 6.74 (1 H, d, *J* 11 Hz, -CH=C*H*Ph), 6.97-7.34 (10 H, m, ArH), 7.61 (2 H, d, *J* 7.5 Hz, tosyl 2,6-H), and 8.21 (1 H, d, *J* 7.5 Hz, 4-H); *m/e* 387 (M^+), 233, 232, 217, 121, 119, and 117 (base), and *2-methyl-1-(4-methylphenylsulphonyl)-3E-(2-phenylethenyl)-1H-indole* as a gum; δ($CDC\ell_3$) 2.28 (3 H, s, 2-Me), 2.69 (3 H, s, tosyl Me), 7.06-7.84 (14 H, m, olefinic and ArH), and 8.27 (1 H, m, ArH); *m/e* 388, 387 (M^+), 298, 294, 293, 233, 232 (base), 231, 217, and 189.

(b) *n*-Butyllithium in hexane (1.5 M; 4.3 ml, 6.5 mmol) was added to a suspension of benzyltriphenylphosphonium bromide (2.82 g, 6.5 mmol) in THF (20 ml) at -78°C. After allowing to warm to room temperature and stirring for 1.5 h, the red solution was cooled to 0°C and a solution of the aldehyde (247) (1.70 g, 5.4 mmol) in THF (10 ml) added. Stirring overnight at room temperature was followed by addition of the mixture to water (100 ml) and extraction with ether (1 x 15 ml; 3 x 25 ml). The combined extracts were washed with water (2 x 25 ml), dried (Na_2SO_4) and evaporated. The residual gum was triturated with cold ether to partially remove triphenylphosphine oxide, the mixture filtered and the filtrate evaporated and chromatographed (97:3 petrol-ether) to afford a mixture of *Z* and *E* isomers (ratio 44:56 respectively, by n.m.r.) of the *olefin* (248) as a brown gum (1.85 g, 88%).

Hydrolysis of the Tosyl Indole (248) - The tosyl indole (1.77 g, 4.6 mmol) as a mixutre of *Z* and *E* isomers (ratio 44:56) was refluxed in dioxan (11 ml) and methanol (3 ml) with aqueous sodium hydroxide (2 M; 4 ml, 8 mmol) for 16 h, after which the solution was reduced to *ca.* 5 ml. Addition of water (20 ml) was followed by extraction with dichloromethane (3 x 15 ml), the extracts washed with water (2 x 10 ml), dried ($MgSO_4$),

and evaporated. Chromatography (9:1 petrol-ether) of the residue gave recovered starting material (0.48 g, 27% recovery; *Z/E* ratio 3:1), and 2-*methyl*-3E—(2-*phenylethenyl*)-1H-*indole* (233, R = CH=CHPh) as a buff solid (0.64 g, 83% based on conversion), m.p., 113-115°C (from petrol-ether) (Found: 87.0; H, 6.6; N, 5.9. $C_{17}H_{15}N$ requires C, 87.5; H, 6.5; N, 6.0%); ν_{max} ($CC\ell_4$) 3480, 1630, 1460, 953, and 680 cm^{-1}; λ_{max} (EtOH) 210 (log ε 4.19), 238 (4.35), 291 (4.11), and 340 nm (4.39); δ ($CC\ell_4$) 2.50 (3 H, s, Me), 7.02-7.55,(11 H, m, olefinic and ArH, N*H*), and 7.86 (1 H, m, 4-H); *m/e* 234, 233 (M^+; base), 232, 218, and 217.

Diethyl Benzylphosphonate (249) - Benzyl bromide (29.5 g, 0.17 mmol) was refluxed with triethyl phosphite (28.6 g, 0.17 mol) for 4 h, and the resulting mixture distilled to give the phosphonate as a colourless oil (31 g, 80%), b.p., 112-114°C at 1 mmHg (lit.,[194] b.p., 155°C at 14 mmHg).

Indole-3-Aldehyde - Prepared as for the 2-methyl derivative (246) in 95% yield, m.p., 195°C (lit.,[158] m.p., 196-197°C).

1-Tosylindole-3-Aldehyde[161] - A mixture of indole-3-aldehyde (10.15 g, 0.07 mol), tosyl chloride (19.06 g, 0.1 mol), and anhydrous potassium carbonate (27.64 g, 0.2 mol) was refluxed in acetone (150 ml) for 4.5 h. Dilution of the reaction mixture with hot acetone and filtration through Celite was followed by trituration of the residue remaining on removal of solvent with cold ether, to give the product as a pale yellow powder (18.21 g, 87%), m.p., 147-149°C (lit.,[161] m.p., 148-150°C).

3-Styryl-1-Tosylindole (251) - *n*-Butyllithium in hexane (1.5 M; 4 ml, 6 mmol) was added to a suspension of benzyltriphenylphosphonium bromide (2.13 g, 5 mmol) in ether (20 ml) at -78°C and the mixture stirred at room temperature

for 1.5 h before adding a solution of 1-tosylindole-3-aldehyde (1.50 g, 5 mmol) in ether (10 ml) and THF (15 ml). After stirring for 3 h, the mixture was filtered, the filtrate washed with water (2 x 25 ml), dried ($MgSO_4$), evaporated, and the residue chromatographed (9:1 petrol-ether) to give the *product* as a pale yellow gum (1.30 g, 70%). N.m.r. indicated a 1:1 mixture of isomers: δ ($CC\ell_4$) 2.26 and 2.30 (tosyl Me), and 7.03-8.10 (ArH). The *Z* isomer had in addition two doublets at δ 6.54 and 6.75 (*J* 11 Hz); *m/e* 373 (M^+), 218 (base), 217, 183, and 165.

2,3-Dimethyl-3*E*-(2-Phenylethenyl)-3*H*-indole (227) - A solution of methyl bromide in THF (2.85 M, 0.42 ml, 1.2 mmol) was added to magnesium (28 mg, 1.17 mmol) in THF (2.5 ml). After complete dissolution of the metal, a solution of 2-methyl-3*E*-(2-phenylethyenyl)-1*H*-indole (273 mg, 1.16 mmol) in THF (3 ml) was added and stirring continued for 0.35 h, after which no more effervescence could be observed, before adding methyl iodide (199 mg, 1.4 mmol; 90 μℓ) and stirring overnight. The resulting mixture was added to water (20 ml), extracted with ether (2 x 10 ml), the extracts washed with water (10 ml), dried ($MgSO_4$) and evaporated to give a brown gum. On chromatography (4:1 petrol-ether), this afforded the starting indole (191 mg, 70% recovery) and the *product* as a green gum, (9.6 mg, 11% based on conversion) (Found: M^+ 247.1358. $C_{18}H_{17}N$ requires M^+ 247.1361); ν_{max} ($CC\ell_4$) 3030, 2960, 2920, 1575, 965, and 690 cm^{-1}; λ_{max} (EtOH) 213 (log ε 3.90), 219 (3.91), 250 (3.92), 284 sh (3.65), and 292 sh nm (3.56); δ ($CC\ell_4$) 1.43 (3 H, s, 3-Me), 2.20 (3 H, s, 2-Me), 5.94 (1 H, d, *J* 16 Hz, -C*H*=CHPh), 6.46 (1 H, d, *J* 16 Hz, -CH=C*H*Ph), 7.02-7.40 (8 H, m, ArH), and 7.50 (1 H, m, 4-H); *m/e* 247 (M^+, base), 246, 223, and 217.

7.6. EXPERIMENTAL FOR CHAPTER 6.

Phenyl Azide - Obtained as a yellow oil, in 69% yield,[195a] b.p., 32°C at 4 mmHg (lit.,[195b] b.p., 49-50°C at 5 mmHg).

2,4-Dimethyldiphenylamine (252)[166] - A solution of phenylazide (6.0 g, 50 mmol) and trifluoroacetic acid (16 ml) in *m*-xylene (200 ml) was stirred at 100°C for 26 h. On cooling, ether (200 ml) was added, the mixture washed with water (250 ml), saturated sodium bicarbonate solution (250 ml) and water (2 x 250 ml), dried ($MgSO_4$) and evaporated. The residual purple solid was treated with sodium hydroxide solution (10%; 100 ml) and the mixture extracted with ether (3 x 250 ml), the combined extracts washed with water (3 x 250 ml), dried ($MgSO_4$), evaporated, and the gum obtained distilled to give the diphenylamine (252) as a viscous golden oil (5.20 g, 53%), b.p., 110-115°C at 0.1 mmHg (lit.,[196] m.p., 43°C).

1,3-Dimethylcarbazole (107b)[167] - A solution of the diphenylamine (252) (900 mg) in petrol (700 ml) was irradiated at 300 nm for 30 h, and the residue remaining on removal of solvent chromatographed (petrol-dichloromethane) to give 1,3-dimethylcarbazole as white needles (230 mg, 26%) m.p., 100°C (from 80-100°C petrol)(lit.,[56] m.p. 95°C).A picrate was prepared; red flocculent solid, m.p., 192-193°C (from benzene) (lit.,[56] m.p., 188.5°C)

1,3,9-Trimethylcarbazole (106b) - Sodium hydride (50% dispension in mineral oil; 60 mg, 1.25 mmol) was washed free of oil with petrol (4 ml), dried and suspended in DMF (4 ml),and the mixture cooled to 0°C. Addition of 1,3-dimethylcarbazole (193 mg, 1 mmol) in DMF (1 ml) was followed by

stirring at room temperature for 1.5 h, after which methyl iodide (250 mg, 1.8 mmol) in DMF (1 ml) was added. The reaction was quenched after 3 h by the addition of water (25 ml), the precipitate formed was collected, washed, dried, and recrystallised from petrol to afford 1,3,9-*trimethylcarbazole* as white needles (146 mg, 70%), m.p., 100-101°C (Found: C, 86.1; H, 7.2; N, 6.7. $C_{15}H_{15}N$ requires C, 86.1; H, 7.2; N, 6.7%); δ ($CC\ell_4$) 2.42 (3 H, s, 3-Me), 2.76 (3 H, s, 1-Me), 4.04 (3 H, s, 9-Me), 6.98 (1 H, d, *J* 1 Hz, 2-H), 7.02-7.33 (3 H, m, ArH), 7.61 (1 H, d, *J* 1 Hz, 4-H), and 7.88 (1 H, dd, *J* 7, 1 Hz, 5-H); *m/e* 210, 209 (M^+; base), 208, 194, 191, and 135.

Picrate, red needles, m.p., 173°C (from ethanol).

2-Methylacetanilide - Prepared in 60% yield by standard procedure,[197] m.p., 107-109°C (from ethanol) (lit.,[197] m.p., 112°C).

N-Acetyl-2,2'-Dimethyldiphenylamine (254)[169] - 2-Methylacetanilide (7.45 g, 50 mmol) was refluxed in 2-bromotoluene (8.55 g, 50 mmol) in the presence of copper(I) iodide (0.9 g) and anhydrous potassium carbonate (5 g) for 19 h. On cooling, the mixture was suspended in ether (150 ml), washed with water (2 x 150 ml), dried ($MgSO_4$) and evaporated to give a black gum which on chromatography (7:3 petrol-ether) and subsequent recrystallisation from petrol-dichloromethane gave the product as large, colourless prisms (4.33 g, 36%), m.p., 89-90°C (lit.,[198] m.p., 82-83°C) (Found: C, 80.5; H, 7.2; N, 5.9. $C_{16}H_{17}NO$ requires C, 80.3; H, 7.2; N, 5.85%); ν_{max} (Nujol) 1670, 770, 755, and 725 cm^{-1}; δ ($CC\ell_4$) 1.91 (3 H, s, -CO*Me*), 2.27 (6 H, s, 2,2'-Me), and 6.70-7.30 (8 H, m, ArH); *m/e* 239 (M^+), 197 (base), 182, 180, and 132.

2,2'-Dimethyldiphenylamine (255) - A solution of *N*-acetyl-2,2'-dimethyldiphenylamine (2.4 g, 10 mmol) in ethylene glycol (40 ml) containing potassium hydroxide (3.3 g, 60 mmol) was refluxed for 24 h after which the cooled mixture was added to water (100 ml) and extracted with ether (3 x 50 ml). The combined extracts were washed with water (3 x 50 ml), dried (Na_2SO_4) and evaporated to leave a green oil which was distilled at 140°C (Kugelrohr) and 3 mmHg to give the diphenylamine as a yellow oil (1.73 g, 88%) which crystallised on standing, m.p., 46-49°C (lit.,[199] m.p., 48.5-49.5°C).

1,8-Dimethylcarbazole (108) - An aerated solution of the diphenylamine (255) (985 mg) in petrol (1000 ml) was irradiated with a medium pressure immersion lamp for 24 h. The residue remaining on removal of solvent was chromatographed (4:1 petrol-dichloromethane) to give:

i) Unreacted starting material as a green oil (346 mg, 35% recovery) which solidified on standing, m.p., 45-49°C.

ii) 1,8-Dimethylcarbazole as a white solid (125 mg, 20%), m.p., 177.5-178.5°C (from petrol-dichloromethane) (lit.,[55b] m.p., 176-177°C).

iii) 1-*Formyl*-8-*methylcarbazole* (256) as a buff solid (30 mg, 4.5%), m.p., 152.5-153.5°C (from petrol-chloroform)(Found: M^+ 209.0845. $C_{14}H_{14}NO$ requires M^+ 209.0841); ν_{max} ($CC\ell_4$) 3440, 3060, 2830, 2805, 2715, 1665, 1600, and 1585 cm^{-1}; λ_{max} (EtOH) 205 sh (log ε 4.20), 224 (4.68), 226 sh (4.67), 255 (4.09), 260 (4.12), 285 sh (4.08), 291 (4.20), 320 (3.58), and 378 nm (3.84); δ ($CDC\ell_3$) 2.63 (3 H, s, 8-Me), 7.20-7.38 (3 H, m, ArH), 7.83 (1 H, d, *J* 7 Hz, 5-H), 7.96 (1 H, d, *J* 7 Hz, 4-H), 8.32 (1 H, d, *J* 7 Hz, 2-H), 10.10 (1 H, br.s, N*H*), and 10.19 (1 H, s, -C*H*O); *m/e* 210, 209 (M^+; base), 208, 194, 181, 180, 178, 153, and 152.

2,3,4,5-Tetramethyldiphenylamine - Phenyl azide (1.80 g, 15 mmol) was heated at 80°C for 18 h in 1,2,3,4 -tetramethylbenzene (50 ml) containing trifluoroacetic acid (6 ml). The cool solution was washed with water (20 ml) and saturated sodium bicarbonate solution (20 ml), dried ($MgSO_4$) and evaporated to leave a purple oil. Distillation at 130°C (Kugelrohr) and 3 x 10^{-2} mmHg gave 2,3,4,5-*tetramethyldiphenylamine* as a yellow oil (2.76 g, 82%) which solidified on standing, m.p., 77.5-78.5°C (from petrol), (Found: C, 85.1; H, 8.5; N, 6.2. $C_{16}H_{19}N$ requires C, 85.3; H, 8.5; N, 6.2%); ν_{max} (film) 3350, 3010, 2940, 2920, 1600, 1495, 750, 740, and 690 cm^{-1}; λ_{max} (EtOH) 222 and 282 nm; δ ($CC\ell_4$) 2.07 (3 H, s, 2-Me), 2.12 (3 H, s, 4-Me), 2.17 (6 H, s, 3,5-Me), 5.03 (1 H, br.s, N*H*), 6.45-6.83 (4 H, m, ArH), and 6.93-7.18 (2 H, m, ArH); *m/e* 226, 225 (M^+; base), 224, 210, 208, and 194.

Dimethyl Azodicarboxylate - Prepared as an orange oil in 62% yield by literature procedure,[200] b.p., 81-82.5°C at 8 mmHg (lit.,[200] b.p., 90-91°C at 15 mmHg).

Dimethyl-1-(2,3,4,5-Tetramethylphenyl)hydrazine-1,2-Dicarboxylate (257)[171] - Dimethyl azodicarboxylate (2.92 g, 20 mmol) was added to a vigorously stirred, cooled solution of 1,2,3,4-tetramethylbenzene (3.35 g, 25 mmol) in boron trifluoride etherate (4 ml). After 1 h, ether (5 ml) was added, the precipitated solid collected, washed with ice-cold ether (3 x 5 ml) and recrystallised from methanol to give the *diester* (258) as white prisms (4.23 g, 76%), m.p., 173-174°C (Found: C, 60.0; H, 7.2; N, 9.95. $C_{14}H_{20}N_2O_4$ requires C, 60.0; H, 7.2; N, 10.0%); ν_{max} (Nujol) 3290, 1755, and 1695 cm^{-1}; δ ($CDC\ell_3$) 2.18 (6 H, s,) 2.20 (3 H, s, Me), 2.25 (3 H, s, Me), 3.73 (6 H, s, 2 x CO_2Me), 7.09 (1 H, s, 6-H), and 7.22 (1 H, br.s, N*H*); *m/e* 280 (M^+) 206, 205 (base), 190, 189, 174, 173, 162, 161, 160, 147, 146, and 133.

2,3,4,5-Tetramethylphenylhydrazine Hydrochloride (259) - The diester (257) (2.00 g, 7.1 mmol) was refluxed for 24 h with potassium hydroxide (2 g) in ethanol (10 ml). On cooling, water (20 ml) was added and the mixture evaporated until the residual liquid became turbid. The resulting suspension was extracted with ether (2 x 20 ml), the extracts washed with brine (20 ml), dried (K_2CO_3) and evaporated. The brown gum remaining was dissolved in ether (10 ml) and the solution cooled in ice whilst a saturated solution of hydrogen chloride in ether (15 ml) was slowly added. The precipitated *hydrochloride* was collected as a beige powder (0.86 g, 60%), m.p., 195.5-196.5°C (dec.)(Found: C, 60.2; H, 8.6; N, 13.6. $C_{10}H_{17}C\ell N_2$ requries C, 59.8; H, 8.5; N, 14.0%); ν_{max} (Nujol) 3340 and 3080-2500 cm^{-1}; δ (d_6-DMSO) 2.11 (6 H, s, 2 x Me), 2.17 (3 H, s, Me), 2.24 (3 H, s, Me), and 6.78 (1 H, s, 6-H); *m/e* 165 (M^+ - HCℓ) 149, 148, 134, 133, 120, 119 (base), and 91.

1,2,3,4-Tetramethylcarbazole (107c) - 2,3,4,5-Tetramethylphenylhydrazine hydrochloride (400 mg, 2 mmol) was refluxed with cyclohexanone (290 mg, 3 mmol) in acetic acid (3 ml) for 0.35 h, after which the mixture was allowed to cool, filtered and the filtrate evaporated. The residue was dissolved in ether (5 ml), washed with water (10 ml) and saturated sodium bicarbonate solution (10 ml), dried ($MgSO_4$), and evaporated to give a brown solid (360 mg). This was intimately mixed with palladium on charcoal (10%; 125 mg), the mixture heated at 220°C for 0.5 h, and extracted with chloroform (30 ml). The residue remaining on removal of solvent was chromatographed (24:1 petrol-ether) and subsequently recrystallised from petrol-ether to give the carbazole as colourless prisms (178 mg, 39%), m.p., 135-137°C (lit.,[170] m.p., 144°C).

Picrate, dark brown needles, m.p., 208-210°C (dec.)(from ethanol) (Found: C, 58.8; H, 4.5; N, 12.1. $C_{22}H_{20}N_4O_7$ requires C, 58.4; H, 4.5; N, 12.4%).

1,2,3,4,9-Pentamethylcarbazole (106c) - Sodium hydride (50% dispersion in mineral oil; 30 mg, 0.63 mmol) was washed with petrol, dried, suspended in cold (0°C) DMF (0.5 ml), and a solution of the tetramethylcarbazole (90 mg, 0.4 mmol) added. Stirring at room temperature for 0.75 h was followed by cooling to 0°C and addition of methyl iodide (0.25 ml) in DMF (0.25 ml). After stirring for 0.5 h, the solution was added to water (10 ml) and extracted with chloroform (3 x 10 ml), the extracts washed with water (3 x 10 ml), dried ($MgSO_4$), evaporated and the residue chromatographed (petrol-ether). Recrystallisation of the product from petrol gave 1,2,3,4,9-*pentamethylcarbazole* as colourless prisms (53 mg, 56%), m.p., 155-157°C (Found: C, 85.9; H, 8.3; N, 6.1. $C_{17}H_{19}N$ requires C, 86.0; H, 8.1; N, 5.9%); δ ($CC\ell_4$) 2.30 (6 H, s, 2 x Me), 2.60 (3 H, s, Me), 2.74 (3 H, s, Me), 3.90 (3 H, s, 9-Me), 6.98-7.42 (3 H, m, ArH), and 8.08 (1 H, m, 5-H); *m/e* 237 (M^+; base), 231, 222, and 216.

Picrate, dark brown needles, m.p., 178°C (from ethanol) (Found: C, 59.4; H, 4.7; N, 11.8. $C_{23}H_{22}N_4O_7$ requires C, 59.2; H, 4.75; N, 12.0%).

5,6-Dihydro-11*H*-Benzo[*a*]carbazole (140) - Prepared as described by Nakazaki[183] in 43% yield, m.p., 163-164.5°C (from methanol) (lit.,[183] m.p., 164-164°C).

11*H*-Benzo[*a*]carbazole (147) - An intimate mixture of the dihydrocarbazole (140) (1.30 g, 6 mmol) and palladium on charcoal (10%; 237 mg), was heated at 215°C for 0.5 h, and on cooling extracted with boiling chloroform (30 ml). The extract was filtered through Celite, evaporated, and the residue recrystallised from benzene to afford the carbazole as colourless prisms (0.83 g, 64%), m.p., 224.5-225.5°C (sealed capillary) (lit.,[183] m.p., 227-229°C.

11-Methyl-11*H*-Benzo[*a*]carbazole (151) - The carbazole (147) was methylated with sodium hydride and methyl iodide in DMF as described previously, to give 11-*methyl*-11H-*benzo*[a]*carbazole* (151) as prisms (69%), m.p., 172.5-173.5°C (from petrol-chloroform) (Found: C, 88.3; H, 5.7; N, 6.1. $C_{17}H_{13}N$ requires C, 88.3; H, 5.7; N, 6.1%); δ 4.26 (3 H, s, Me), 7.04-7.54 (6 H, m, ArH), 7.78-8.04 (3 H, m, ArH), and 8.49 (1 H, m, ArH); *m/e* 231 (M^+; base), 230, 216, and 202.

A *picrate* was prepared, red needles, m.p., 163-165°C (dec.) (from ethanol), but did not give a satisfactory microanalysis (Found: C, 60.5; H, 3.65; N, 12.2. $C_{23}H_{16}N_4O_7$ requires C, 60.0; H, 3.5; N, 12.2%).

7*H*-Benzo[*c*]carbazole (153) - Prepared in 50% yield from 2-tetralone, as described for the benzo[*a*] isomer, m.p., 136-138°C (from 80-100°C petrol-benzene)(lit.,[183] m.p., 135-136°C).

7-Methyl-7*H*-Benzo[*c*]carbazole (154) - Methylation of the carbazole (153) with sodium hydride and methyl iodide in DMF afforded the *N*-methyl derivative as colourless prisms (72%), m.p., 117-118°C (from 80-100°C petrol)(lit.,[201] m.p., 117-118°C).

2-Methylcyclopent-2-enone (262) - Obtained as a yellow oil in 15% yield by the method of Herloff Inhoffen and Kramer,[202] b.p., 100-110°C (Kugelrohr) at 50 mmHg (lit.,[203] b.p., 78°C at 17 mmHg).

1,4-Dimethyl-3*H*-Cyclopenta[*b*]quinoline (112a) - 2-methylcyclopent-2-enone (0.24 g, 2.5 mmol) was refluxed for 19 h with 2-aminoacetophenone hydrochloride (0.43 g, 2.5 mmol) in aqueous ethanol (50%; 1.5 ml) and concentrated hydrochloric acid (0.5 ml). On cooling, the solution was basified

by the addition of ammonia solution (35%; 5 ml), extracted with dichloromethane (3 x 10 ml), the extracts washed with water (10 ml), dried (Na_2SO_4), and evaporated. Chromatography (petrol-ether) of the residue afforded 1,4-*dimethyl*-3H-*cyclopenta*[b]*quinoline* as buff needles (105 mg, 21%), m.p., 105-107°C (from petrol) (Found: C, 85.7; H, 6.7; N, 7.1. $C_{14}H_{13}N$ requires C, 86.1; H, 6.7; N, 7.2%); λ_{max} (EtOH) 214 sh (log ε 4.26), 224 (4.33), 250 (4.50), 293 (3.88), 299 sh (3.86), 306 (3.88), 312 sh (3.76), 320 (3.92), 327 (3.65),and 335 nm (4.01); δ ($CDC\ell_3$) 2.35 (3 H, q, *J* 1.5 Hz, 1-Me), 2.69 (3 H, s, 4-Me), 3.39 (2 H, t, *J* 1.5 Hz, 3-H), 6.76 (1 H, m, 2-H), 7.52 (1 H, ddd, 6-H), 7.67 (1 H, ddd, 7-H), 8.02 (1 H, m, 5-H), and 8.16 (1 H, m, 8-H);*m/e* 196, 195 (M^+; base), 194, 180, and 152.

Picrate, yellow prisms, m.p., 222-224°C (dec.) (from ethanol) (Found: C, 56.7; H, 3.8; N, 13.2. $C_{20}H_{16}N_4O_7$ requires C, 56.6; H, 3.8; N, 13.2%).

6-Methylindeno[1,2-*b*]quinoline (119) - Repeating the above reaction with 1-indanone gave the *quinoline* as white needles (23%), m.p., 118-120°C (from petrol) (Found: C, 88.4; H, 5.7; N, 6.1. $C_{17}H_{13}N$ requires C, 88.3; H, 5.7; N, 6.1%); λ_{max} (EtOH) 212 (log ε 4.52), 224 (4.43) 256 sh, (4.53), 262 (4.66), 288 (3.74), 296 sh (3.80), 304 sh (3.90), 309 sh (3.98), 314 (4.09), 321 (4.08), 328 (4.31), 337 (4.13), and 344 nm (4.48); δ ($CC\ell_4$) 2.60 (3 H, s, Me), 3.80 (2 H, s, $-CH_2-$), and 7.30-8.30 (8 H, m, ArH); *m/e* 231 (M^+; base), 230 and 216.

Picrate, yellow prisms, m.p., 250°C (dec.) (from acetonitrile)(Found: C, 60.4; H, 3.5; N, 12.1. $C_{23}H_{16}N_4O_7$ requires C, 60.0; H, 3.5; N, 12.1%).

4-Phenylbutan-2-One (263) - DMSO (3.4 ml, 44 mmol) in dichloromethane (7 ml) was added to oxalyl chloride (2 ml, 22 mmol) in dichloromethane (40 ml) at -78°C and the mixture stirred for 5 min before adding 4-phenylbutan-2-ol (3.0 g, 20 mmol) in dichloromethane (15 ml). After 0.5 h, triethylamine (14 ml) was added and the mixture allowed to warm to room temperature and stirred for a further 1 h. Addition of water (70 ml) was followed by separation of the layers and washing the organic with brine (50 ml), hydrochloric acid (2 M; 2 x 50 ml), water (50 ml), saturated sodium bicarbonate solution (50 ml), and water (50 ml), dried ($MgSO_4$) and evaporated. The residual yellow oil was distilled to afford the ketone as a colourless oil (2.51 g, 85%), b.p., 115-117°C (Kugelrohr) at 13 mmHg (lit.,[203] b.p., 115°C at 15 mmHg).

2,4-Dimethyl-3-Benzylquinoline (230) - 4-Phenylbutan-2-one (0.74 g, 5 mmol) was refluxed for 12 h with 2-aminoacetophenone (0.68 g, 5 mmol) in acetic acid (7 ml) containing concentrated sulphuric acid (4 drops). On cooling the mixture was added to a mixture of dilute ammonia solution and ice, extracted with dichloromethane (1 x 50 ml; 1 x 25 ml), the extracts washed with water (50 ml), dried ($MgSO_4$) and evaporated. Chromatography (4:1 petrol-ether) of the residue gave 2,4-*dimethyl*-3-*benzylquinoline* (230) as needles (522 mg, 42%), m.p., 135-136°C (from petrol-chloroform)(Found: C, 87.5; H, 7.0; N, 5.7. $C_{18}H_{17}N$ requires C, 87.4; H, 6.9; N, 5.7%); λ_{max} (EtOH) 217 sh (log ε 4.57), 229 (4.68), 262 sh (3.38), 266 (3.41) 270 (3.45), 278 (3.44), 282 (3.42), 288 sh (3.41), 294 (3.45), 301 (3.38), 308 (3.54), 315 (3.36), and 322 nm (3.67); δ ($CC\ell_4$) 2.54 (3 H, s, 2-Me), 2.57 (3 H, s, 4-Me), 4.16 (2 H, s, $-CH_2-$), 6.74-7.53 (7 H, m, ArH), and 7.76 (2 H, m, ArH); *m/e* 248, 247 (M^+; base), 246, and 232.

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