# SOME ASPECTS OF AZIDE REACTIONS

A Thesis submitted for the Degree of

Doctor of Philosophy

in the

University of Oxford

by

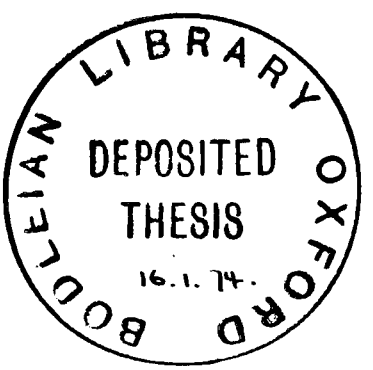
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# INTRODUCTION

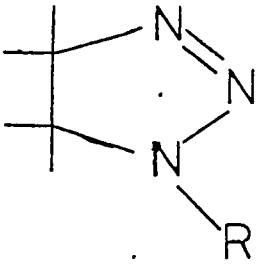
The 1,3-dipolar cycloaddition of organic azides to unsaturated compounds results in the initial formation of 1,2,3-triazole derivatives (I)[1-5]. The stabilities of these triazoles are dependent upon the nature of the group R, and in cases where R is electron-withdrawing, e.g. R = picryl[6,7], tosyl[7] or CN[8], no triazoles have been isolated. In these examples loss of nitrogen occurs readily to give aziridines (II) or imines (III). The more stable triazoles obtained when R is methyl or phenyl[4] decompose in a similar manner on heating.

Simple olefins react slowly with azides, but activated or strained olefins undergo ready reaction. The kinetics of the reactions of a wide variety of such olefins with picryl and phenyl azides have been reported[6]. Other unsaturated systems which undergo similar reactions include acetylenes, allenes, enamines, ynamines and quinones.

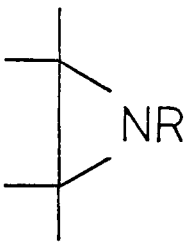
The addition of an azide to an enamine was first reported[4] following an investigation of the reaction between cyclohexene and phenyl azide. The initial product (IVa) was found to react further as its enamine tautomer (IVb) to yield the triazole (V).

Enamine systems have since been extended to include indole and its derivatives[7,9,10]. During this work the reactions of many substituted indoles with arylsulphonyl azides have been investigated, including those of 1,2,3,4-tetrahydrocarbazole and 9-methyl-1,2,3,4-tetrahydrocarbazole (VI, R = H and Me respectively).

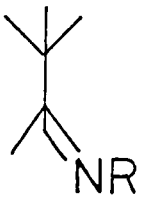
The main object of this present work was to continue the study of these reactions by investigating the effects of increasing the size of the reduced ring in cycloalkeno[b]indoles, and with a view to isolating any intermediates. Furthermore, it was hoped to study the effects of increased indole reactivity by the synthesis of pyrrolo[3,2,1-hi] indoles (VII) and the investigation of their reactions with arylsulphonyl azides.



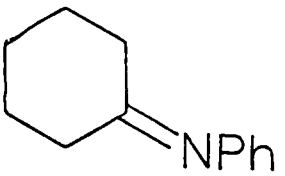

I



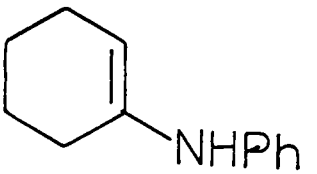

II



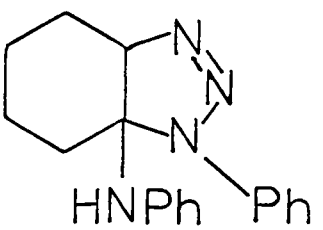

III



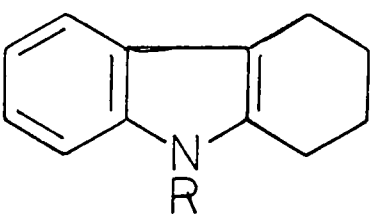

IVa



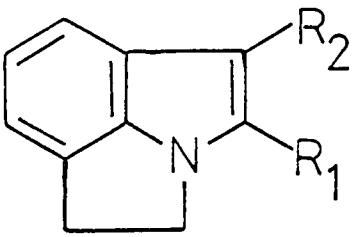

IVb




V




VI




VII

In this thesis the following abbreviations have been used

Ts = p-tolylsulphonyl-

Cbs = p-chlorobenzenesulphonyl-

Ph = phenyl-

Z = arylsulphonyl-.

N.m.r. spectra discussed in the main section were recorded in $CDCl_3$ solution unless otherwise stated. Other solvents used were dimethyl sulphoxide $_d6$ (D) and trifluoroacetic acid (TFA).

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# CHAPTER I

## General discussion

The reactions of organic azides have recently been reviewed[1,2]. Much of the literature involves investigations into the thermal or photochemical decomposition of azides to yield nitrenes, and the subsequent reactions of the latter. The nitrenes are highly reactive species which may undergo stabilisation in one of several ways. Radical dimerisation results in the formation of azo-compounds and hydrogen abstraction from solvent molecules yields amines. Rearrangements of the intermediate nitrenes are also known[3].

In reactions where the azide group is itself the reacting species electrophilic attack is found to take place at the α-nitrogen atom and nucleophilic attack at the terminal nitrogen atom[1].

## The structures of organic azides

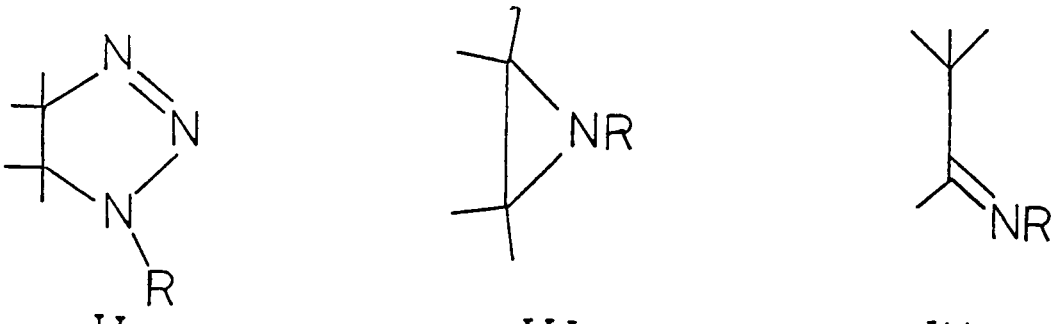
Investigations into the structures of organic azides have shown that the $N_3$ group is linear[4,5] and at an angle of approximately 120° to the C-N bond, supporting the prediction that the resonance canonicals (Ia) and (Ib) are the major contributors to the structure. However, for the cycloaddition of an azide to an olefin a bent structure is necessary[6]. Molecular orbital calculations[7] show that although the linear structure is more stable than the bent one (involving contributions from resonance canonicals bearing a lone pair of electrons on the central nitrogen atom) this difference in energy is small (5 kcal/mole). This is illustrated[8] in the case of the picryl azide - copper oxinate complex where the azide group is slightly bent.

## The addition of azides to olefins

The cycloaddition of organic azides to olefins yields 1,2,3-triazole derivatives (II)[6,9-12]. When R is an electron-withdrawing group the triazoles are unstable and decompose with loss of nitrogen



Ia Ib



II III IV

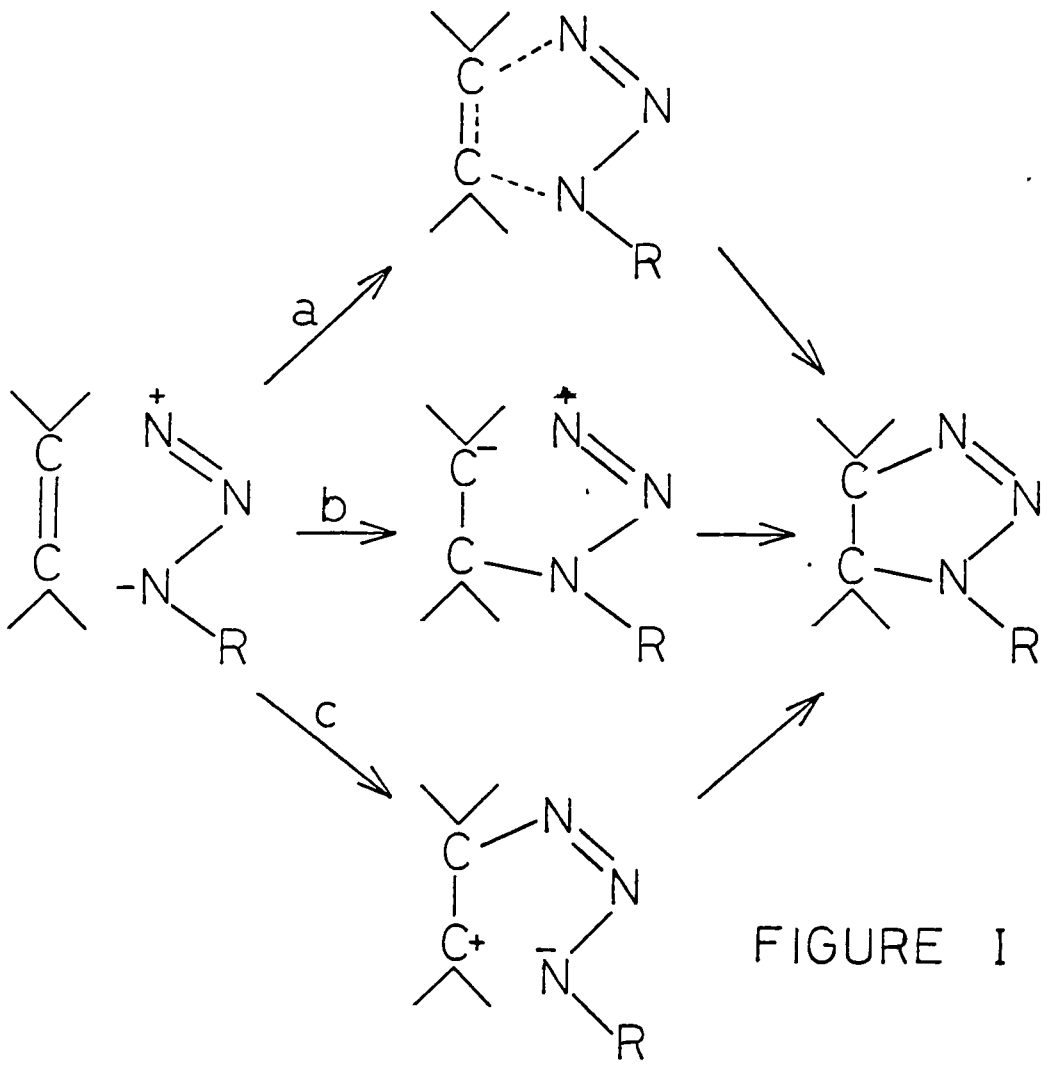


FIGURE I

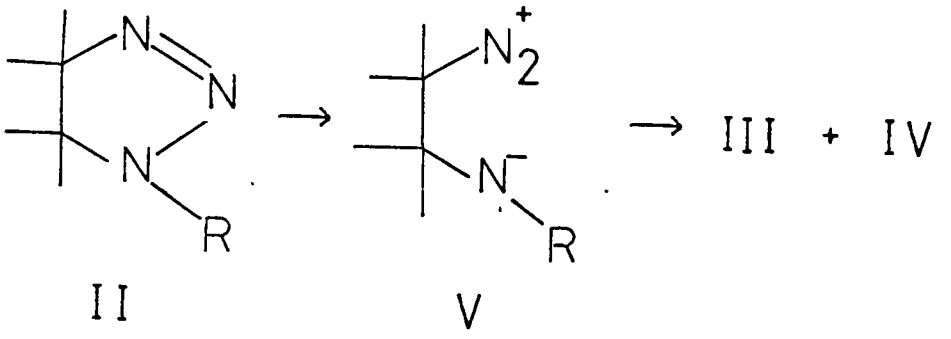
to give aziridines (III) or imines (IV). Thus no triazoles have been obtained from such reactions of arylsulphonyl[13-17] or cyanogen[18] azides. In the case of picryl azide[17,19] the same applies although one triazole has been reported[20] from the reaction of this azide with tetramethylallene.

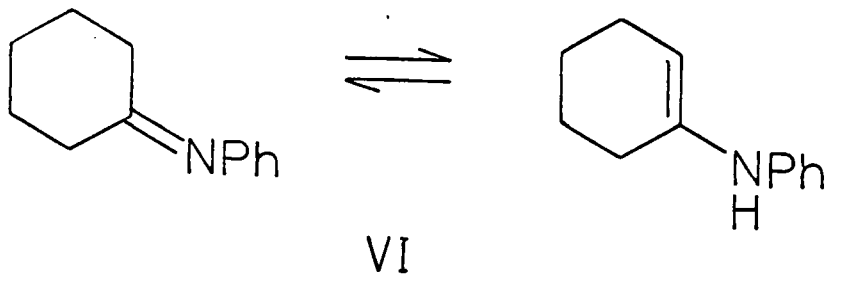
## The mechanism of cycloaddition

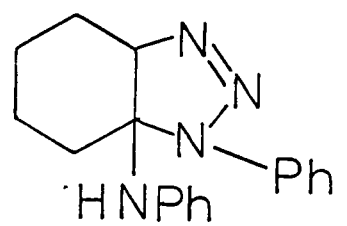
Extensive investigation[6] into the kinetics of azide cycloaddition reactions has shown that triazole formation proceeds via a concerted mechanism (route a in FIGURE I). The rate of reaction was found to be virtually independent of the polarity of the solvent, rendering unlikely mechanisms such as b or c, since both involve zwitterionic intermediates which ought to be strongly stabilised by polar solvents. In all cases studied the reactions produced only cis-addition whereas non-stereoselective addition might be expected from routes b and c in at least some cases. Moreover, the entropy of activation in these reactions is large and negative as may be expected for a concerted process. A fourth possibility, that of a 1,1-cycloaddition reaction followed by a rearrangement to the triazole is unsatisfactory since the azoaziridines which would result from such an addition are unstable and readily revert to the azide and olefin[21,22].

## The decomposition of 1,2,3-triazoles

There is some doubt as to the mechanism of the decomposition of 1,2,3-triazoles but the dipolar ion (V) has been suggested[17,18,23-25] as being a likely intermediate in many cases. Loss of nitrogen then leads to the products (III) and (IV). The ease of 1,2,3-triazole decomposition depends upon the extent to which the group R can stabilise the negative charge on the nitrogen atom in (V) and this explains the spontaneous decomposition of the triazoles where R is picryl, arylsulphonyl or CN. Moreover, the rate of decomposition is


N
N
N
R
II
N2+
N−
R
V
→ III + IV


NPh
NPh
H
VI


N
N
N
Ph
HNPh
VII

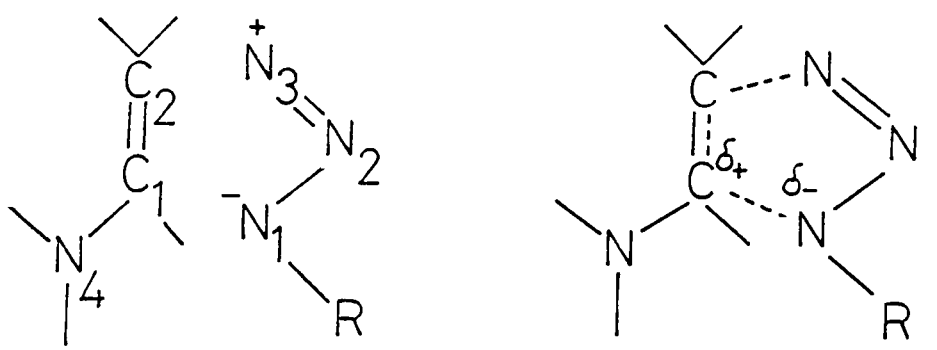

C2
C1
N4
N3+
N2
N1−
R
C
N
δ+
δ−
N
N
R

FIGURE II

enhanced in solvents of high dielectric constant[25] and this also supports the intermediacy of a charged structure such as (V).

## The reactions of azides with enamines

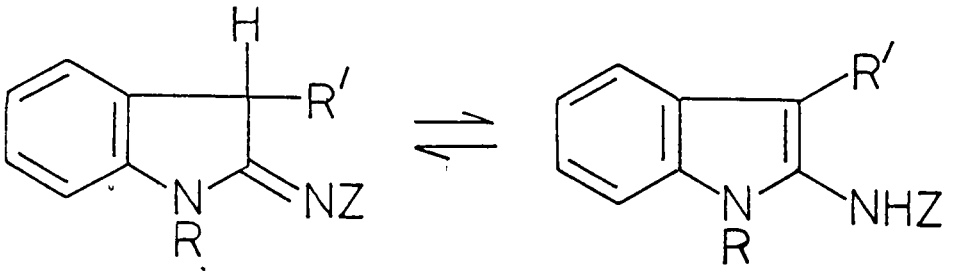
The addition of an organic azide to an enamine was first reported[12] following an investigation into the reaction between phenyl azide and cyclohexene. The initial product (VI) reacts with a second molecule of azide *via* its enamine tautomer to yield the triazole (VII). More recent studies of the addition of azides to enamines have been published[13,26-28]. These results show that the nitrogen atom of the enamine exerts a directional effect on the attacking azide group and addition takes place as in FIGURE II. The partial positive charge on $C_1$ is stabilised by the adjacent $N_4$ atom.

## The reactions of indoles with azides

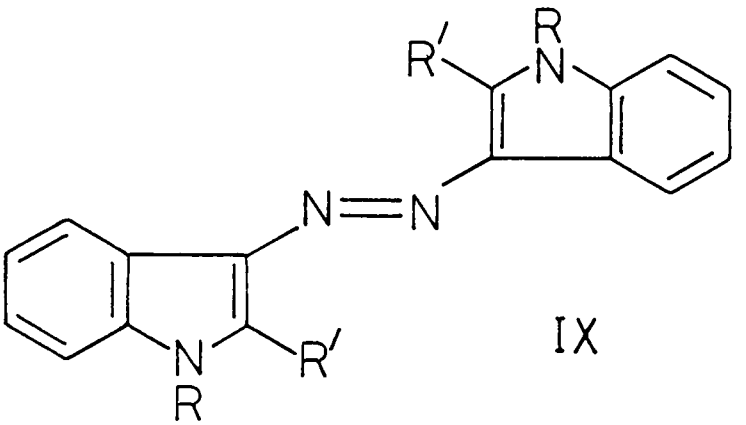
Bailey and co-workers have extended the work on enamines to include indoles. Indole, 1-methylindole and 1,3-dimethylindole react with arylsulphonyl azides to yield the tautomeric compounds (VIII, R = R' = H), (VIII, R = Me, R' = H) and (VIII, R = R' = Me) respectively[17,29-32].

2-Substituted and 1,2-disubstituted indoles react with picryl azide to yield 3,3'-azobisindoles (IX). The same indoles with arylsulphonyl azides give mixtures of the same azobisindoles and 3-arylsulphonylaminoindoles (X)[17].

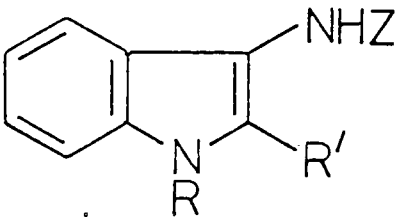
The reactions of 2,3-disubstituted and 1,2,3-trisubstituted indoles are more complex and result in several products[33]. 2,3-Disubstituted indoles react with arylsulphonyl azides *via* the intermediate (XI). When R is Me the proton is lost from the indole nitrogen atom to give the 3H-indole (XII) as the major product. When R is Et (XI) loses a proton from the ethyl methylene group yielding (XIII). This reacts further with azide to give the products (XIV) to



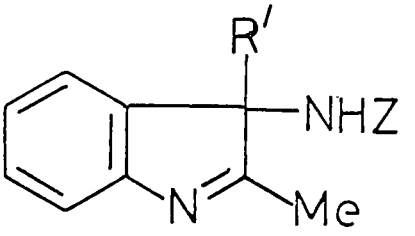
VIII



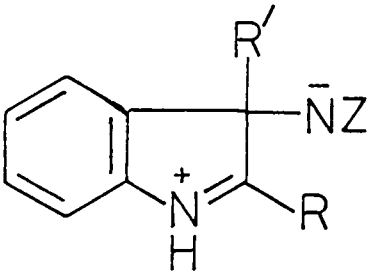
IX



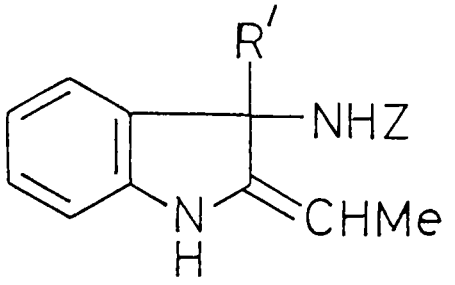
X



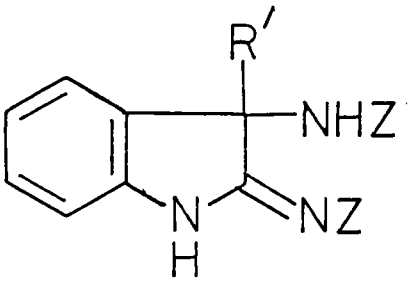
XII



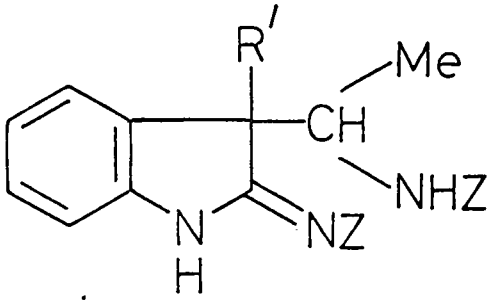
XI



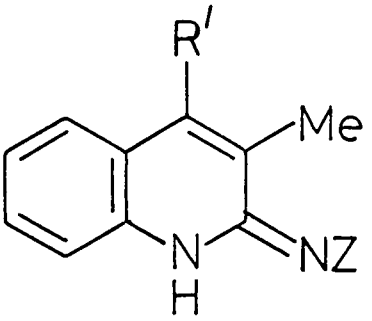

XIII



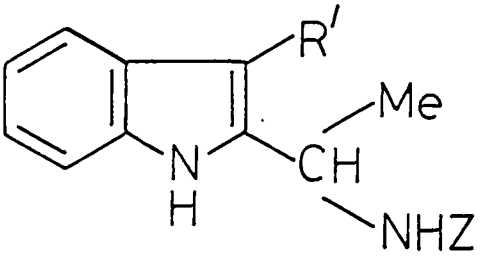

XIV




XV




XVI




XVII

(XVII). The mechanisms involved in these transformations are quite complex, as are those of 1,2,3-trisubstituted indoles. However they are very similar to the reactions of 9-methyl-1,2,3,4-tetrahydrocarbazole with arylsulphonyl azides and the latter reactions will be discussed in greater detail in Chapter II.

## Diazo-transfer reactions

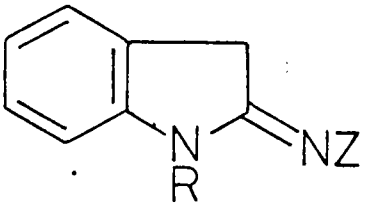
A further important aspect of azide reactions has yet to be considered. Organic azides, especially arylsulphonyl azides, may be used for the preparation of diazo-compounds[34,35]. In such reactions the two protons of an active methylene group are replaced by the terminal two nitrogen atoms of the azide group while the azide is itself converted to the corresponding sulphonamide. The reaction is carried out in the presence of a base since the anion of the active methylene compound is the actual reacting species.

It was found that the initial product from the reaction of indole or 1-methylindole with an arylsulphonyl azide (XVIII, R = H or Me) reacted further with the azide in the presence of pyridine to yield (XIX, R = H or Me)[32], by an analogous process. The reactions of these diazoindolines have since been reported[36].

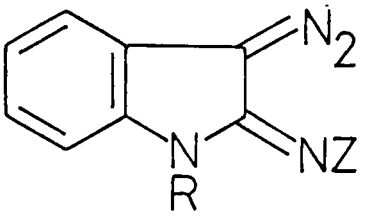
Buckley[37] extended this work to oxindole and 1-methyloxindole which are isoelectronic with (XVIII). In this case no diazo-compounds were isolated, the products of the reaction being isoindigo and 1,1'-dimethylisoindigo (XX, R = H) and (XX, R = Me) respectively. It is likely, however, that these compounds resulted from an intermediate diazooxindole since the pyrolysis of the latter is known[38] to give isoindigo derivatives.

Of particular interest to the present work is the formation of 1,2,3-thiadiazoles from diazo-transfer reactions[34]. The intermediate diazo-compound (XXII) formed from the acylthioacetamide (XXI) undergoes a cyclisation to give the thiadiazole (XXIII). Diazo-transfer

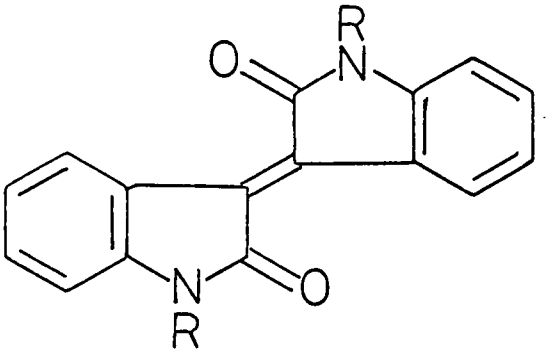
reactions such as these will be discussed further in Chapter IV.



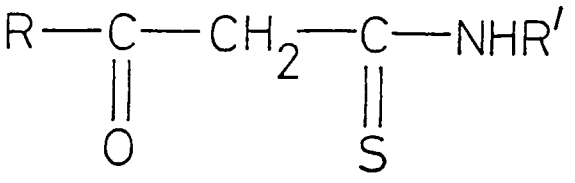
XVIII



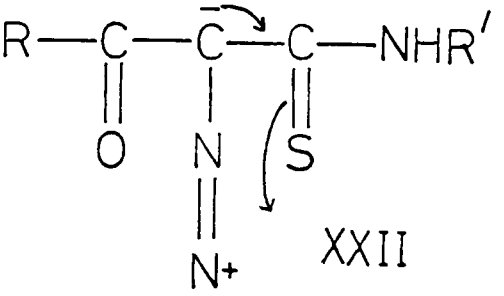
XIX



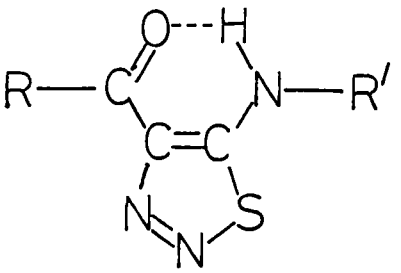
XX



XXI



XXII



XXIII

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# CHAPTER II

## The reactions of cycloalkeno [b] indoles with arylsulphonyl azides

From the reaction of 9-methyl-1,2,3,4-tetrahydrocarbazole with tosyl azide[1-3] five products have been isolated (I - V). The formation of these products has been explained by the reaction scheme shown in FIGURE I. The initially produced triazole breaks down to the dipolar ion (VI) then loss of nitrogen and rearrangement via an aziridine intermediate yields (VII). C-migration results in the formation of (I). (VII) may also lose a proton from $C_1$ to produce the olefin (VIII) which can rearrange by a 1,3-shift to the indole (II). Alternatively, attack of azide on (VIII) gives (IX) which on loss of nitrogen and rearrangement affords (IV). Elimination of toluene-p-sulphonamide from (IV) gives (V). The indole (II) may also be attacked by azide giving (X) and in turn (III) by loss of nitrogen and C-migration.

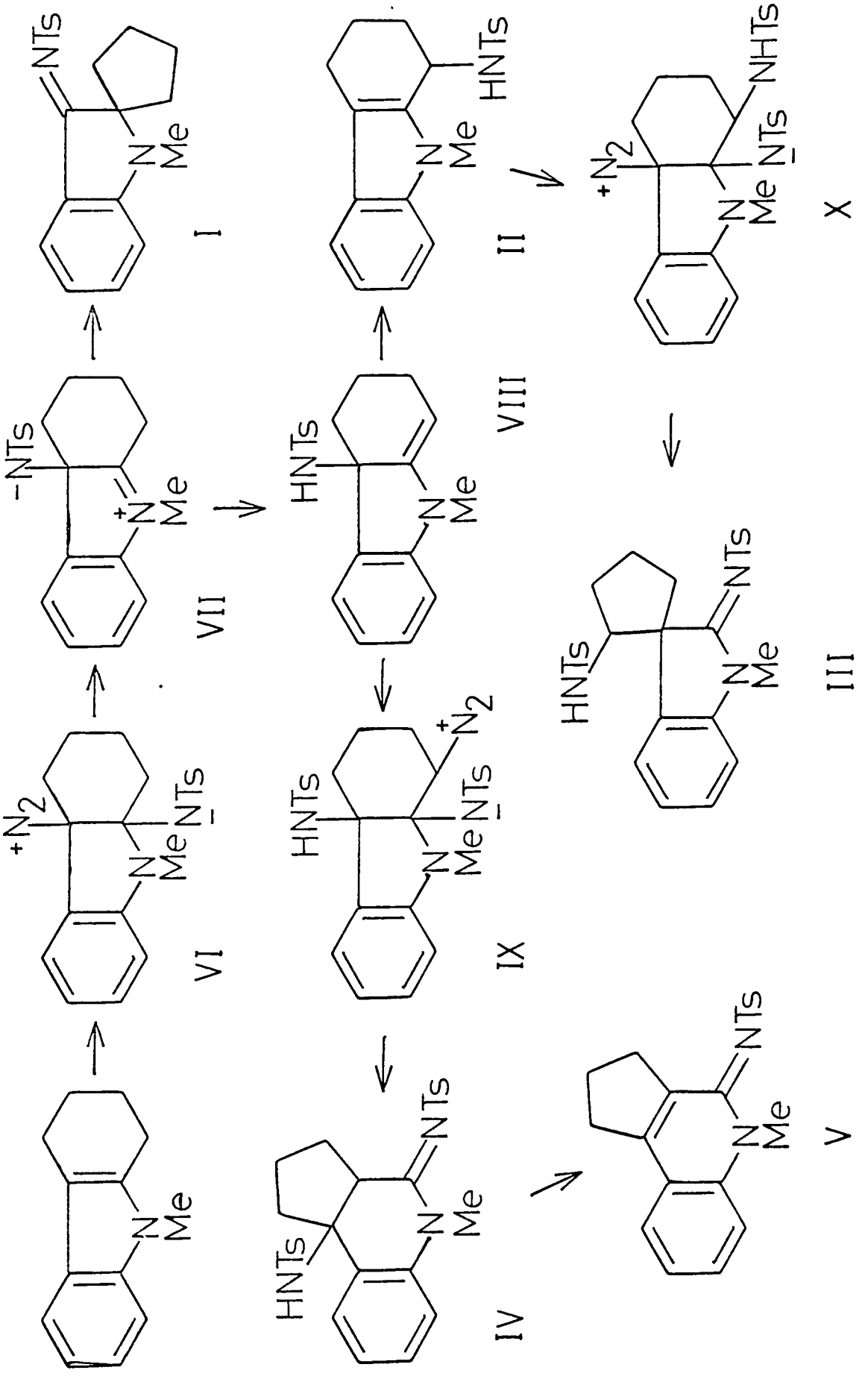
Many examples of the transformations (VII) - (I) are known in the hydroxytetrahydrocarbazole series[4]. Likewise there are parallels[5-8] for the 1,3-shift encountered in the step (VIII) - (II).

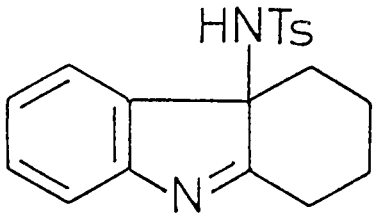
Tosyl azide added to 1,2,3,4-tetrahydrocarbazole forming (XI)[1,2], the process being analogous to the reaction of the 9-methyl compound as far as (VII) when a proton is lost from the nitrogen atom instead of $C_1$.

An important intermediate in this reaction scheme is the 2-methyleneindoline (VIII). The intermediacy of this structure is supported by the reactions of tosyl azide with 1,3,3-trimethyl-2-methyleneindoline[1,9] and 1,3,3-trimethyl-2-isopropylideneindoline[10]. The preparation of this intermediate has recently been achieved[11,12] and it was of interest to investigate its reactions with arylsulphonyl azides with a view to confirming its place in the proposed reaction scheme.

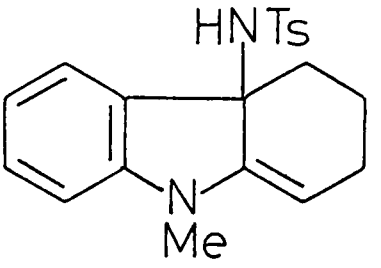
On dissolving the orange-coloured compound (I) in trifluoroacetic acid (TFA) a colourless water-soluble salt was obtained to which the

FIGURE I

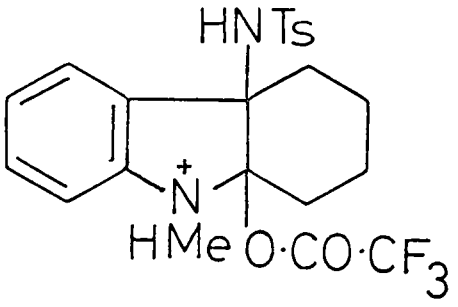

NTs
Me
N
I
HNTs
II
NHTs
$^{+}N_2$
$^{-}$NTs
X
$^{-}$NTs
$^{+}$N
VII
VIII
HNTs
HNTs
HNTs
$^{+}N_2$
$^{-}$NTs
VI
IX
HNTs
HNTs
NTs
III
HNTs
NTs
IV
V



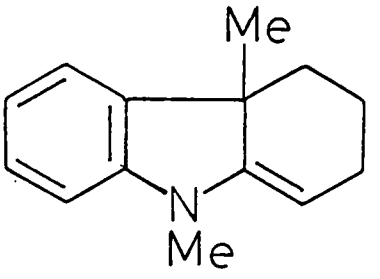

XI



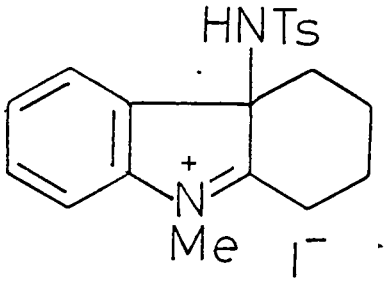

VIII



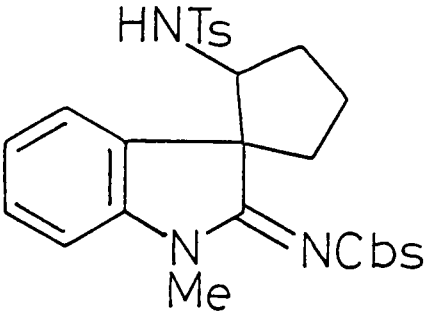

XII



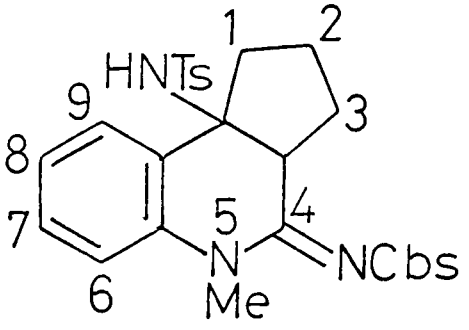

XIII



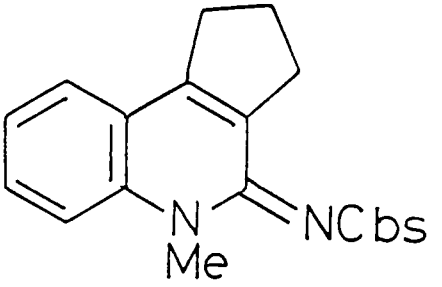

XIV




XV




XVI




XVII

structure (XII) was assigned and which on treatment with base yielded compound (II)[1,3]. When sodium carbonate was added to an ice-cold solution of this salt in water an unstable product was obtained. This product was not (II) but all attempts to purify it resulted in the formation of (II). The u.v. spectrum of this compound was very similar to those reported[13-15] for 2-methyleneindolines and likewise its n.m.r. spectrum closely resembled that of 4a,9-dimethyl-2,3,4,4a-tetrahydrocarbazole (XIII)[1].

This evidence suggested that the compound was the intermediate (VIII). It was never obtained pure, attempted recrystallisation leading to (II). The n.m.r. spectrum of (VIII) showed the presence of a small amount (15%) of (II) and after one hour the signals due to (VIII) had almost disappeared[11,12]. These observations indicated that the transformation (VIII) - (II) is rapid and in order to study further the reactions of (VIII) it was decided to carry out preparations of (VIII) in the presence of arylsulphonyl azides and to investigate the products of the ensuing reactions.

The salt (XII) had originally been prepared[1,3] by dissolving (I) in TFA. The overall yield for this preparation from 1,2,3,4-tetrahydrocarbazole was in the region of 20% and in fact slightly better yields (30% overall) were achieved by the following route. The indolenine (XI) on boiling with methyl iodide in benzene and acetonitrile gave the methiodide (XIV)[1,2]. Boiling this salt with TFA then afforded (XII) in good yield. The methiodide (XIV) was unsuitable for our purposes since it was insoluble in water.

A sample of (XII) was treated with carbonate at $0^{\circ}$ and the product was immediately extracted into chloroform containing tosyl azide. From the chloroform solution were isolated tosyl azide and compound (II), identical to an authentic sample. Nothing crystalline could be isolated from the oily residue which was then dissolved in TFA. From this acid solution was isolated compound (V), again identical to an

authentic sample[1,3]. The acid catalysed elimination of toluene-p-sulphonamide from structures such as (IV) will be discussed in greater detail later in this chapter.

This series of reactions was repeated using p-chlorobenzene-sulphonyl azide instead of tosyl azide in the chloroform solution. From this solution were isolated unreacted azide, compound (II) and the compounds (XV), (XVI) and (XVII). (XV) was a known compound[1,3], being the product from the reaction of (II) with p-chlorobenzene-sulphonyl azide, and compound (XVII) was identical to an authentic sample[11,16] prepared by a different route.

The i.r. spectrum of (XVI) showed the presence of C=N and N-H bonds (1542 and 3245 $cm^{-1}$ respectively) and the u.v. spectrum was very similar to that of (IV). The n.m.r. spectrum (D) showed the following signals:-

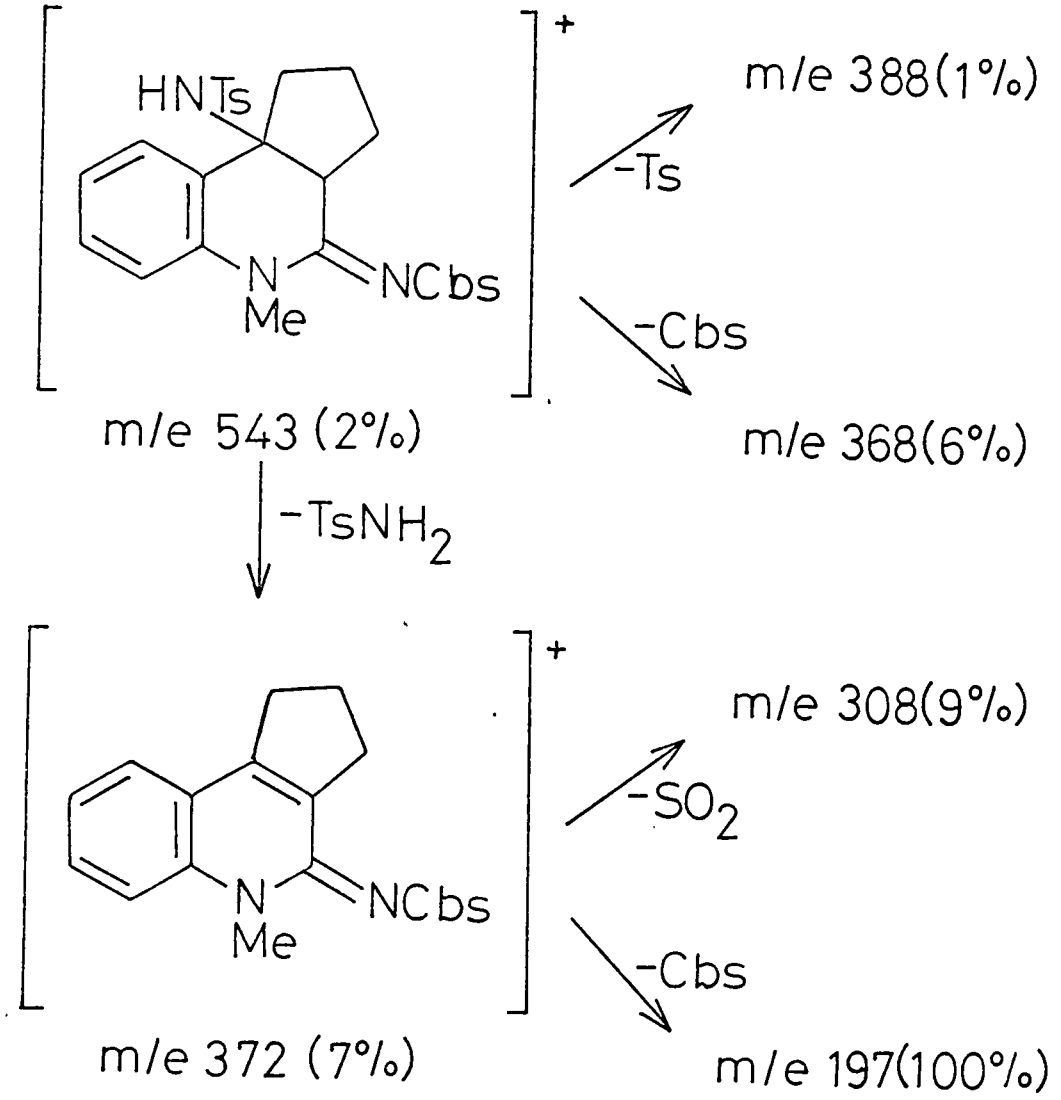
2.02τ(2H, d, J8Hz, low field half of Cbs signal), 2.34(2H, d, J8Hz, high field half of Cbs signal), 2.79(1H, s, exchanged $D_2O$, NH), 2.8-3.4(8H, m, aromatic), 5.77(1H, t, J9Hz, $C_{3a}H$), 6.64(3H, s, NMe), 7.73(3H, s, tosyl Me) and 7.4-9.2(6H, m, 3 x $CH_2$).

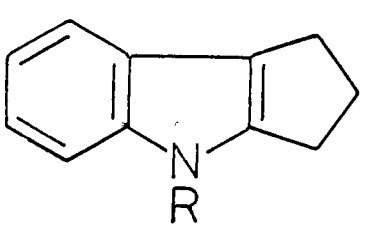
The structure of (XVI) was finally confirmed by its mass spectrum which showed the following important peaks (see FIGURE II). There was no signal corresponding to M - $CbsNH_2$ (m/e 352).

These results show that the second molecule of azide involved in the reaction of 9-methyl-1,2,3,4-tetrahydrocarbazole becomes attached to the 2-position of the quinoline ring and fully supports the reaction scheme proposed in FIGURE I.

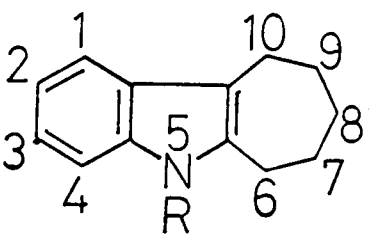
For several reasons it was of interest to extend the investigation of cycloalkeno[b]indoles to those with larger rings. It had been shown[17] that the rates of addition of azides to simple cycloalkenes varied appreciably with the size of the ring, and that cyclopentene, -heptene and -octene reacted approximately 100 times faster than

FIGURE II




XVIII




XIX

cyclohexene. By extending these findings to indole structures it was expected that the cyclohept- and cyclooct-compounds would be very much more reactive than tetrahydrocarbazole. The very high reactivities of 1,2,3,4-tetrahydrocyclopent[b]indole (XVIII, R = H) and its N-methyl derivative (XVIII, R = Me) towards arylsulphonyl azides have already been reported[2,3,10].

Secondly, Witkop[18] has demonstrated the effects of differing ring size on the oxidations of cycloalkeno[b]indoles and has shown that the products of oxidation and subsequent reactions vary considerably with difference in ring size.

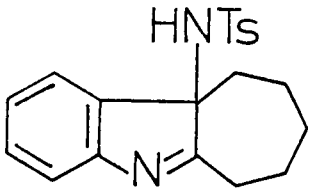
With these considerations in mind the reactions of 5,6,7,8,9,10-hexahydrocyclohept[b]indole (XIX, R = H) and its N-methyl derivative (XIX, R = Me) with tosyl azide were studied.

The reaction of (XIX, R = H) with tosyl azide proved difficult in practice because the reaction mixtures tended to form intractable tars from which no crystalline material could be isolated. Furthermore, t.l.c. of these mixtures showed the presence of a very large number of components. The reactions were carried out under varying conditions, in a variety of solvents, and at a number of temperatures, in an attempt to optimise the conditions, but in most cases the same tarry mixtures were obtained.

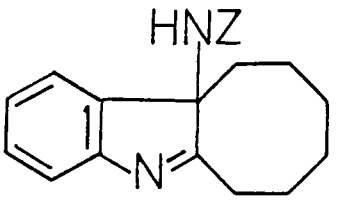
It was found that the best approach to this problem was to dissolve the indole in an excess of the azide at room temperature. By this procedure a low yield of a compound, assigned the structure (XX), was obtained. The i.r. spectrum of this compound showed a broad band at 3080 $cm^{-1}$ (N-H) and its u.v. spectrum was very similar to that of compound (XI)[1]. The u.v. spectra of these two compounds and those of the analogous compounds (LVI) obtained from hexahydrocyclooct[b]indole (see later) are shown in FIGURE III.

The n.m.r. spectrum of (XX) showed the following signals:-

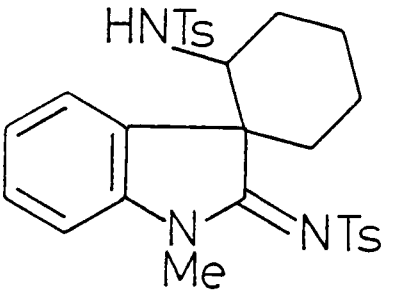
2.6-3.2$\tau$(6H, m, aromatic), 3.34(1H, t, J7Hz, aromatic), 3.53(1H,




XX

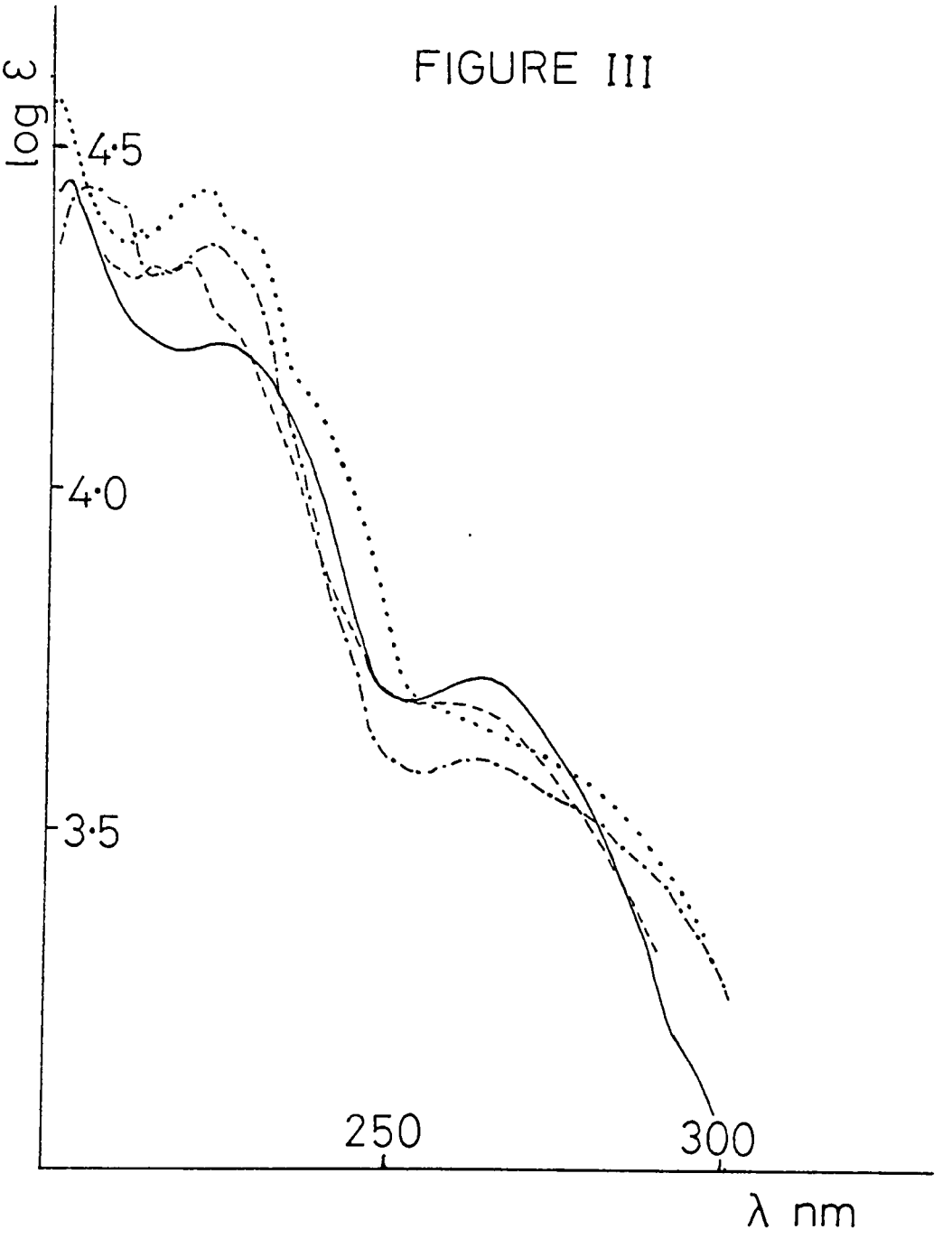



LVI




XXI

FIGURE III




——— XX

------ XI

-·-·-·- LVI, Z = Ts

·····. LVI, Z = Cbs

d, J7Hz, aromatic), 4.02(1H, s, exchanged $D_2O$, NH), 6.7-7.2(2H, m), 7.67(3H, s, tosyl Me) and 7.6-8.9(8H, m).

It had been hoped to study further the chemistry of (XX) but owing to the difficulties encountered in its preparation no such work was attempted.

5,6,7,8,9,10-Hexahydro-5-methylcyclohept[b]indole (XIX, R = Me) reacted very rapidly with tosyl azide, so much so that mixing the neat reactants resulted in explosions. The reactions were carried out in a variety of solvents and four products were obtained, the respective yields depending on the solvent in question.

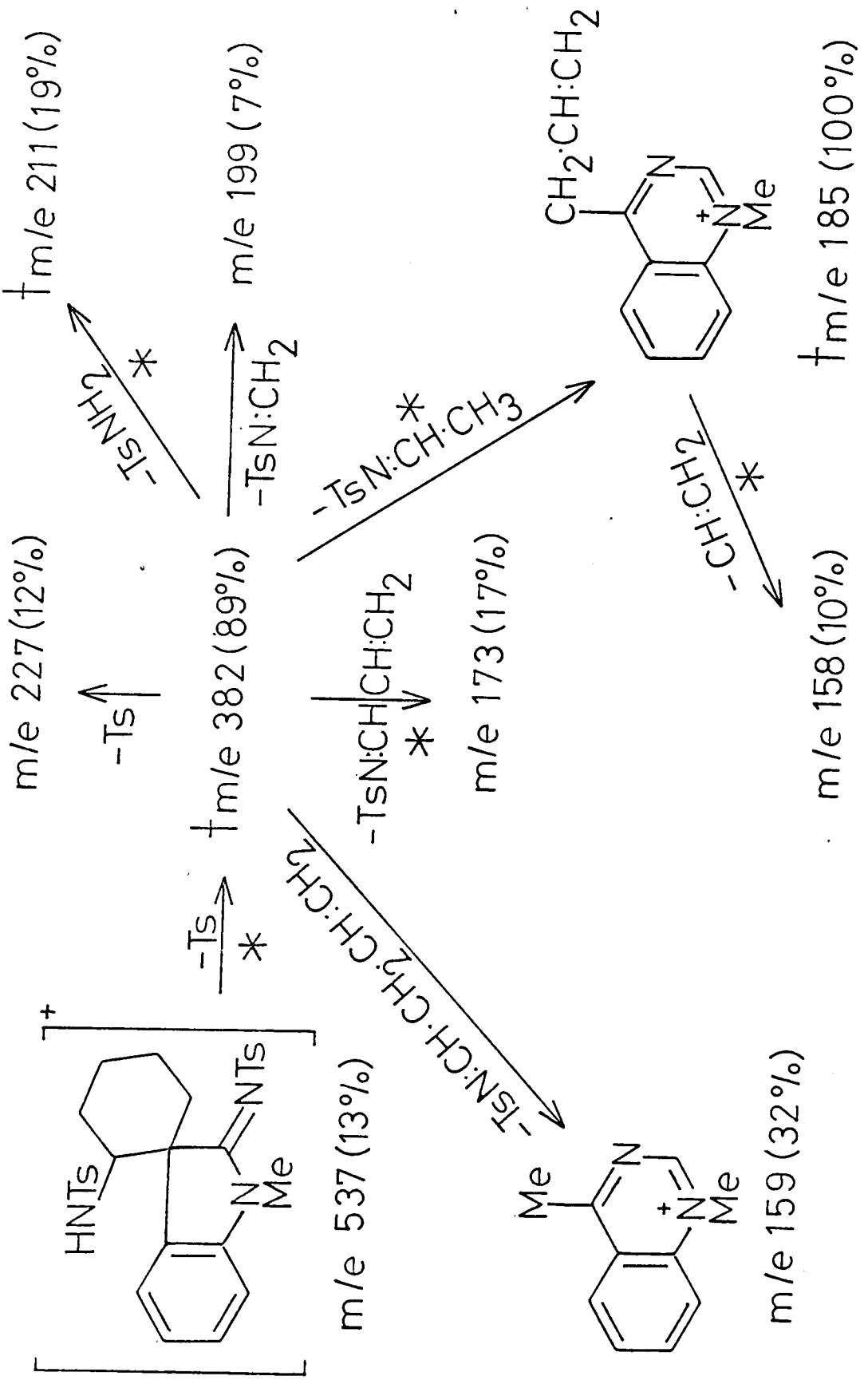
Compound A, the major product from the reaction in methanol, (49%), was also formed in 11% yield when the reactants were dissolved in pyridine. The compound had a molecular weight of 537 and analysis indicated the formula $C_{28}H_{31}N_3O_4S_2$. The i.r. spectrum contained bands at 1585 (C=N) and 3250 (N-H) $cm^{-1}$ and the u.v. spectrum was very similar to those of the amidines (III) and (IV). The n.m.r. spectrum (D) showed the following signals:-

2.04τ(2H, d, J8Hz, low field half of tosyl signal), 2.38(2H, d, J8Hz, low field half of tosyl signal), 2.4-3.0(8H, m, aromatic), 3.25(1H, d, J9Hz, exchanged $D_2O$, NH), 5.55(1H, m), 6.63(3H, s, NMe), 7.60(3H, s, tosyl Me), 7.66(3H, s, tosyl Me) and 8.1-9.0(8H, m).

The multiplet at 5.55 simplified somewhat on $D_2O$ exchange and must therefore have been coupled to the NH proton. These observations indicated that the structure (XXI) was correct for compound A, and this assignment was proved conclusively by interpretation of the mass spectrum.

Indolines bearing a spirocycloalkane ring in the 3-position, e.g. (III) and (XV), undergo an interesting fragmentation in which the 2'-tosyl group is lost attached to varying lengths of the spiroalkane ring[1]. Compound A underwent a similar fragmentation, and details of

FIGURE IV


m/e 227 (12%)
-Ts
†m/e 382 (89%)
-Ts
*
†m/e 211 (19%)
-TsNH2
*
m/e 199 (7%)
-TsN:CH2
-TsN:CH:CH2
*
m/e 173 (17%)
-TsN:CH:CH2:CH2
m/e 537 (13%)
-TsN:CH:CH:CH3
*
CH2:CH:CH2
-CH:CH2
*
m/e 158 (10%)
†m/e 185 (100%)
m/e 159 (32%)

its mass spectrum are shown in FIGURE IV. In this figure fragmentations accompanied by metastable signals are marked* and structures verified by high resolution mass spectroscopy are marked†.

This compares favourably with the fragmentation pattern of compound (XV)[1] and although there are some major differences these may be explained by the fact that in the case of A we have a cyclohexane ring which may be more stable to fragmentation than the cyclopentane ring of (XV). Thus, whereas in compound (XV) the fragmentation of the spiro-ring occurs before loss of Cbs, in the case of compound A the reverse is mainly true and spiro-ring fragmentation occurs after the loss of Ts from the $C_2$-nitrogen, although there are very weak signals at m/e 301, 313, 327 and 339 suggesting that a small amount of spiro-ring fragmentation of the molecular ion occurs.

The second compound, B, was isolated as bright yellow crystals from the reactions in methanol, pyridine and acetic acid, and yields were approximately the same in each of these solvents (15%). Analysis showed that B was isomeric with (XXI) and likewise the i.r. spectrum contained bands due to N-H and C=N stretch. The relatively high value of the C=N band (1600 $cm^{-1}$) suggested that this bond was non-conjugated. The u.v. spectrum was unusual in that it comprised a number of peaks of gradually falling intensity between 200 and 350 nm, and the mass spectrum was uninformative, the highest signal occurring at m/e 171, possibly due to toluene-p-sulphonamide. The n.m.r. spectrum contained the following signals:-

2.13τ(2H, d, J8Hz, low field half of tosyl signal), 2.60(2H, d, J8Hz, high field half of tosyl signal),2.7-3.1(5H, m, aromatic), 3.40(1H, s, exchanged $D_2O$, NH), 3.44(1H, d, J7Hz, aromatic), 3.87(1H, td, J7,1Hz, aromatic), 4.19(1H, dd, J7,1Hz, aromatic), 5.50(1H, d, J7Hz), 6.63(1H,m), 7.20(3H, s, NMe), 7.50(3H, s, tosyl Me), 7.63(3H, s, tosyl Me) and 7.7-8.6 (7H,m).

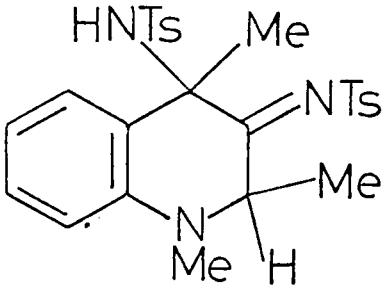
From the reaction between tosyl azide and 1,3-dimethyl-

2-ethylindole[2,10] had been isolated a very small quantity (2%) of a similar yellow compound which had been given the structure (XXII). The spectral data of B and (XXII) were very similar. For example, the mass spectrum of (XXII) at 200° was that of toluene-p-sulphonamide and in the i.r. spectrum the C=N stretch occurred at high frequency. The n.m.r. spectrum of (XXII) was similar to that of B, showing aromatic signals at high field (3.3-3.6τ) and an NMe signal at 7.11τ.

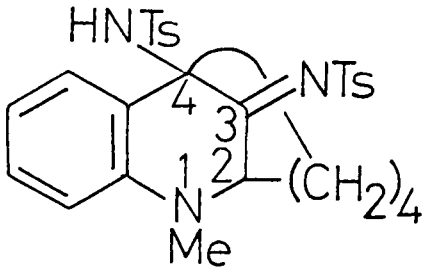
The very close similarities between B and (XXII) suggest that B has the structure (XXIII). It had been hoped to verify this structure by means of X-ray crystallography but for technical reasons this proved impossible. A crystal structure determination has, however, been carried out on (XXII)[19] and this has proved beyond doubt that (XXII) is correct. An interesting feature of this structure is that the methyl groups at $C_2$ and $C_4$ of the tetrahydroquinoline system in (XXII) are cis to each other; this is essential if the structure (XXIII) is correct.

Given the structure (XXIII) for compound B, several aspects of the n.m.r. spectrum can now be explained. The high τ-value of the NMe signal is consistent with that of a tertiary aromatic amine, as are the high positions of the aromatic protons. The multiplet centred on 6.63τ is probably one of the aliphatic ring protons affected by the proximity of an adjacent sulphonyl group. Particularly interesting is the doublet at 5.50τ which we have assigned to the proton at $C_2$. Inspection of Dreiding models of the preferred conformation of (XXIII) show that the dihedral angle between this proton and one of those on the adjacent ring carbon atom is very close to 90°. The coupling constant between these protons should therefore be small and a doublet is the overall coupling pattern (see FIGURE V).

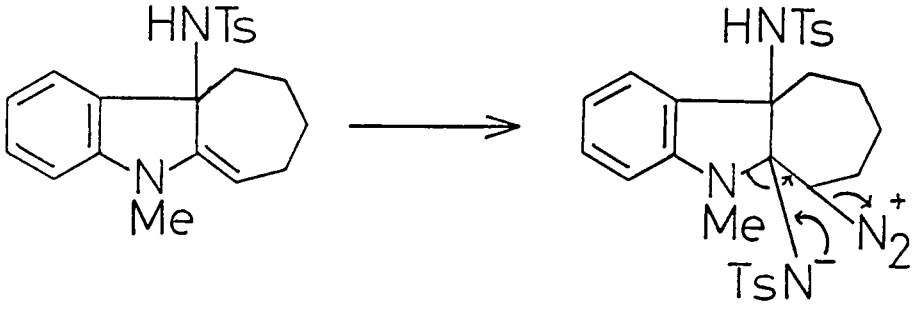
The mechanism for the formation of (XXIII) is probably as follows. Tosyl azide adds to the double bond of (XXIV) [c.f. compound (VIII)] to give the dipolar ion (XXV). Rearrangement as shown leads directly



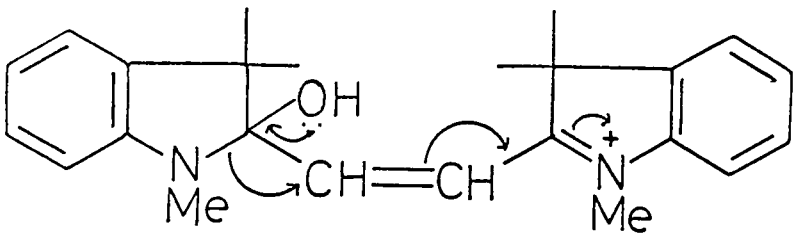

XXII



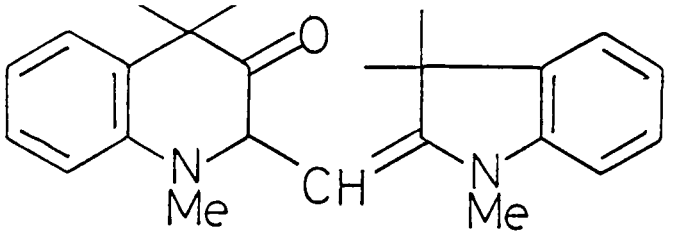

XXIII




XXIV XXV

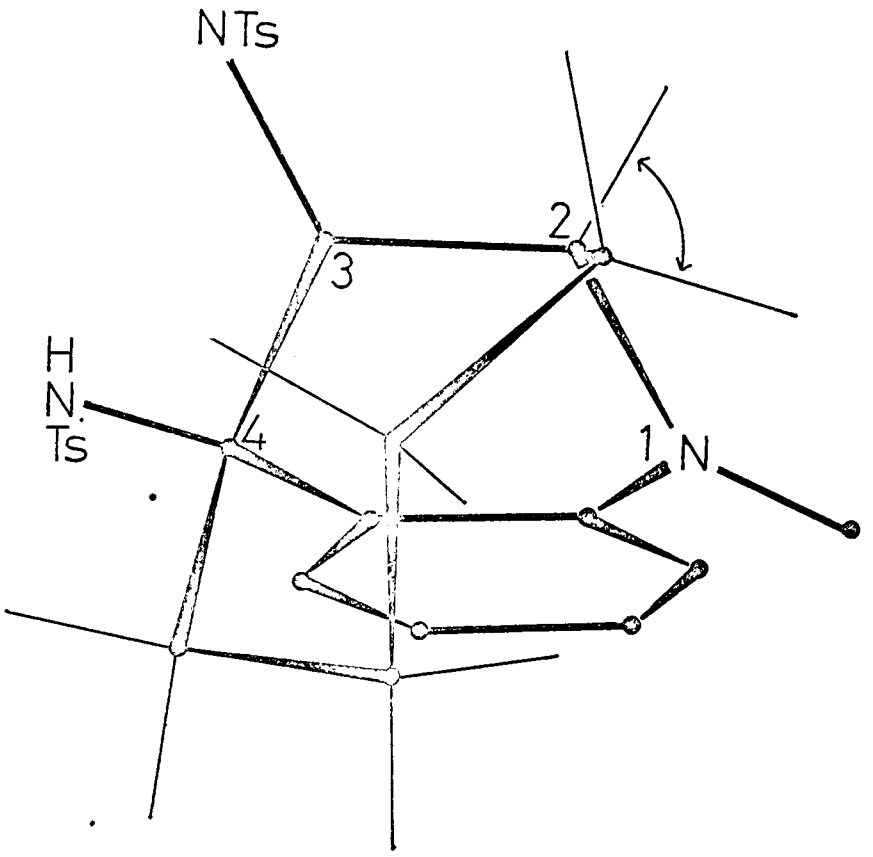


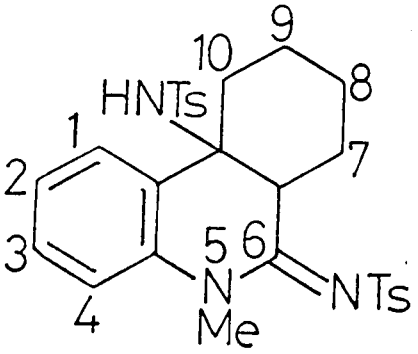

XXVI



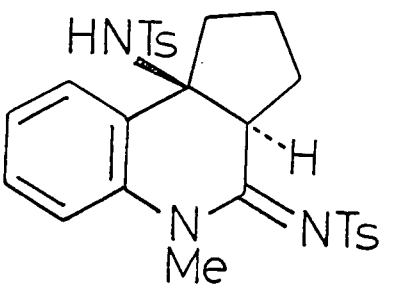

XXVII

FIGURE V




XXVIII




IV

to (XXIII). A similar type of rearrangement has recently been reported[20] to explain the formation of (XXVII) from (XXVI).

The third product, C, also isomeric with (XXI), was isolated in low yield from the reaction in methanol, but in higher yields in more acidic or basic solvents. C was the only product obtained from a reaction carried out in pyridine and aqueous caustic soda. Its spectral properties agreed with the structure (XXVIII) and the mechanism of its formation was assumed to be analogous to that of (IV) from 9-methyltetrahydocarbazole. The n.m.r. spectrum (D) contained the following signals:-

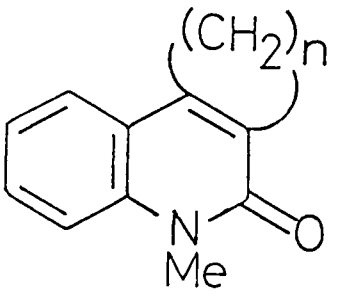
2.18τ(2H, d, J8Hz, low field half of tosyl signal), 2.37(1H, s, exchanged $D_2O$, NH), 2.5-3.2(10H, m, aromatic), 6.03(1H, m), 7.03(3H, s, NMe), 7.61(3H, s, tosyl Me), 7.70(3H, s, tosyl Me) and 7.9-9.4(8H, m).

On treatment of (IV) with base[1,3] the compound (XXIX, n = 3) was obtained. Similar treatment of C should have led to (XXIX, n = 4) and therefore should have been a useful confirmatory test. Accordingly, C was heated under reflux with caustic soda in aqueous ethanol for 24 hours. The product, however, was not the expected 2-quinolone but a compound in which one of the two tosyl groups remained.

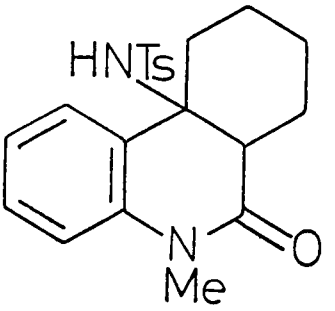
The i.r. spectrum of the product contained bands due to C=O (1650 $cm^{-1}$) and N-H (3065 $cm^{-1}$) and the mass spectrum and analysis indicated a molecular formula of $C_{21}H_{24}N_2O_3S$. It would appear that if (XXVIII) were the correct structure for C then hydrolysis of the tosylimino group had taken place but had not been accompanied by elimination of the tosylamino group as in (IV). The n.m.r. spectrum supported this, showing signals at

2.43τ(1H, m, aromatic), 2.7-3.2(6H, m, aromatic), 3.54(1H, m, aromatic), 4.70(1H, s, exchanged $D_2O$, NH), 6.72(1H, m), 7.09(3H, s, NMe), 7.39(1H, m), 7.70(3H, s, tosyl Me) and 8.0-9.1(7H, m).

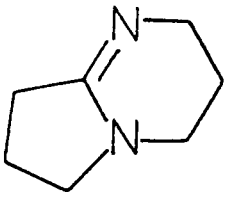
This evidence supports the structure (XXX) for the hydrolysis



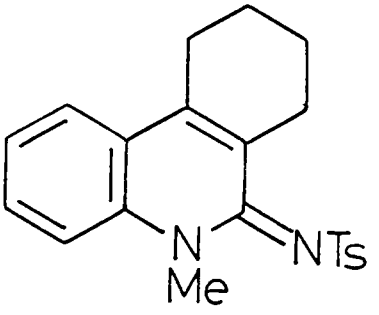

XXIX



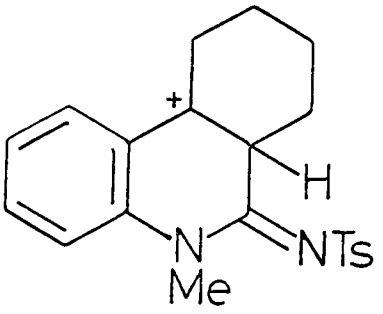

XXX



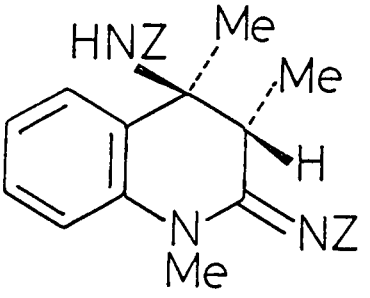

XXXI




XXXII

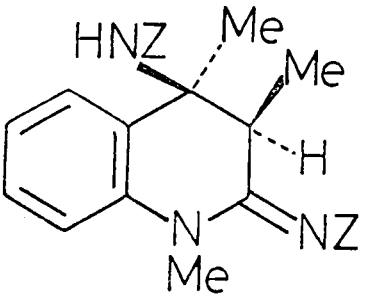



XXXIII

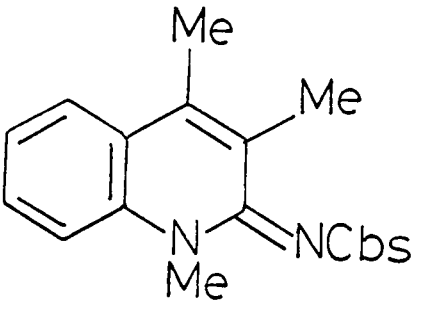



XXXIV

↓TFA




XXXVI




XXXV

product. If this is true then it must mean that the tolylsulphonylamino group and the $C_{6a}$ proton are cis to each other, contrary to the situation in (IV)[1].

The smooth elimination of toluene-p-sulphonamide from (IV) has also been achieved by the use of 1,5-diazabicyclo [4.3.0] non-5-ene (XXXI)[1,3], the product being (V). This reagent has the advantage of leaving the imino group intact. Compound C, however, was recovered unchanged after 24 hours from a refluxing solution of (XXXI) in ethanol. Even under more vigorous conditions (refluxing 2-methoxyethanol) no elimination was achieved. These observations again support a cis ring junction.

Elimination of toluene-p-sulphonamide from C was finally achieved in two ways. Sublimation gave a product whose analysis and spectral data indicated the structure (XXXII). The i.r. spectrum contained a band at 1490cm$^{-1}$ (C=N) and the n.m.r. spectrum showed the following signals:-

2.13$\tau$(2H, d, J8Hz, low field half of tosyl signal), 2.2-2.8(6H, m, aromatic), 5.89(3H, s, NMe), 6.9-7.3(4H, m), 7.60(3H, s, tosyl Me), and 8.0-8.4(4H, m).

This spectrum was very similar to that of (V).

The same product was also formed by the action of trifluoroacetic acid on C. In this case the mechanism is probably a protonation followed by elimination of toluene-p-sulphonamide to yield the ion (XXXIII). Loss of the proton from $C_{6a}$ would then give (XXXII). Since this involves a two-step elimination, the stereochemistry about the ring junction is unimportant. This was confirmed by the action of TFA on the trans compound (IV)[1,3] and the cis compound (XXXIV, Z = Cbs)[2,10] to yield the respective products (V) and (XXXV). The latter compound (XXXV) had not previously been obtained pure. Boiling (XXXIV, Z = Cbs) with (XXXI) in ethanol for 20 hours resulted in some elimination; the product was a mixture of starting material

(33%) and (XXXV) (66%)[2,10]. This is another illustration of the vigorous conditions required to achieve the base-catalysed elimination of sulphonamide from this type of compound.

The spectroscopic data for (XXXV) fit the suggested structure, the i.r. spectrum containing a band at 1503 $cm^{-1}$ (C=N) and the n.m.r. spectrum showing the following signals:-

2.03τ(1H, d, J8Hz, aromatic), 2.09(2H, d, J8Hz, low field half of Cbs signal), 2.2-2.8(5H, m, aromatic), 5.86(3H, s, NMe), 7.40(3H, s, CMe) and 7.60(3H, s, CMe).

Final proof of the structure of C was obtained by degradation to (XXIX, n = 4). This was achieved in several ways, viz.,

i. Sublimation of (XXX)

ii. Base-catalysed hydrolysis of compound (XXXII)

iii. Direct degradation of compound C under vigorous conditions.

Loss of both tosyl groups was achieved by refluxing C with potassium hydroxide in ethylene glycol.

The product from each of these reactions was very similar to (XXIX, n = 3). The u.v. spectrum was that of a 2-quinolone and the C=O absorption (1640 $cm^{-1}$) was within the range quoted[21] for 2-quinolones. The n.m.r. spectrum showed the following signals:-

2.3-2.9τ(4H, m, aromatic), 6.28(3H, s, NMe), 7.0-7.5(4H, m) and 8.0-8.3(4H, m).

The structure (XXIX, n = 4) was finally confirmed by synthesis from the known compound 7,8,9,10-tetrahydrophenanthridinone[22]. Methylation following the procedure of Scheuer and Werny[23] gave a product identical in all respects to the final degradation product.

Thus the structure of C was confirmed as (XXVIII), the ring junction being cis. An interesting property of this type of compound is manifested in the n.m.r. spectrum. It would seem that in most cases the position of the NMe signal parallels the cis or trans character of the substituents at $C_3$ and $C_4$ of the quinoline ring

system and may be illustrated by the following examples.

| Compound | | N-methyl signal τ. |
|---|---|---|
| (IV)[1,3] | (trans) | 6.74 (a) |
| (XXXVI, Z = Ts)[2,10] | (trans) | 6.56 (a), 6.59 (b) |
| (XXXVI, Z = Cbs)[2,10] | (trans) | 6.59 (b) |
| (XXXIV, Z = Ts)[2,10] | (cis) | 7.18 (a) |
| (XXXIV, Z = Cbs)[2,10] | (cis) | 6.97 (b) |
| (XXVIII) | (cis) | 7.03 (b) |

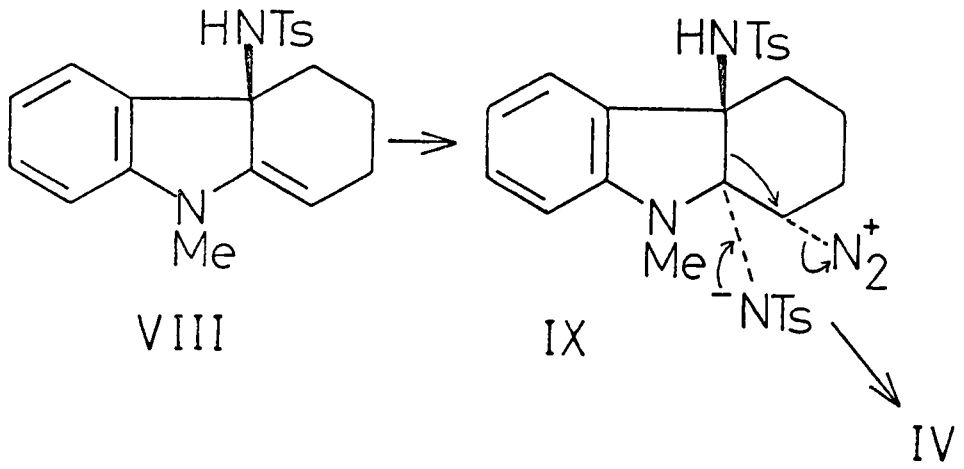
Solvents: (a) $CDCl_3$ (b) DMSO $_{d6}$

This table shows that the NMe signals of the trans isomers occur at appreciably lower fields than those of the cis isomers, although exceptions to this general rule do occur (see later). The position of the NMe signal of C, however, is further evidence for a cis ring junction in (XXVIII).

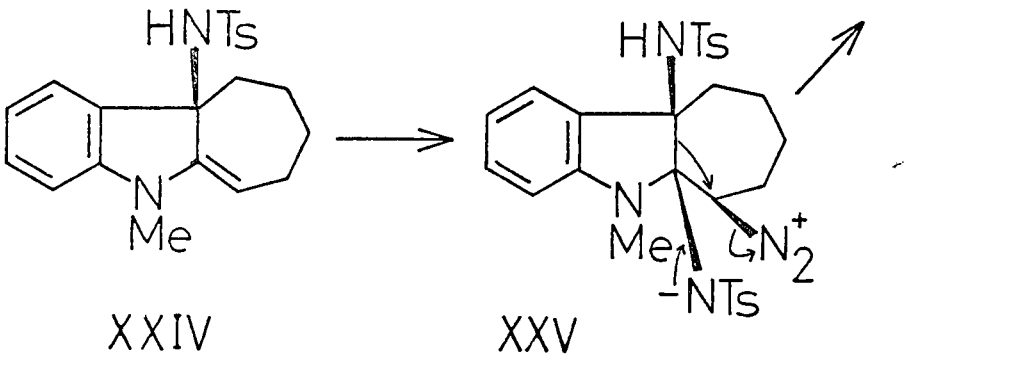
This difference in stereochemistry between the compounds (IV) and (XXVIII) can be explained as follows. In the case of (IV) attack of azide on the intermediate (VIII) takes place from the opposite side of the molecule to the tosylamino group already present[1]. Rearrangement of the intermediate (IX) as shown gives (IV). In the case of the cycloheptindole attack of azide on (XXIV) must take place from the same side as the tosylamino group to give (XXV) followed by rearrangement to (XXVIII). It should be noted that (XXV) is also the precursor of (XXIII). Use of Dreiding models shows that the formation of (XXIII) is sterically impossible if attack of azide on (XXIV) were to take place from the opposite side of the molecule as the tosylamino group, since the conformation necessary for a concerted elimination of nitrogen and rearrangement to (XXIII) cannot in this case be achieved.

Effect of solvent on the reaction products

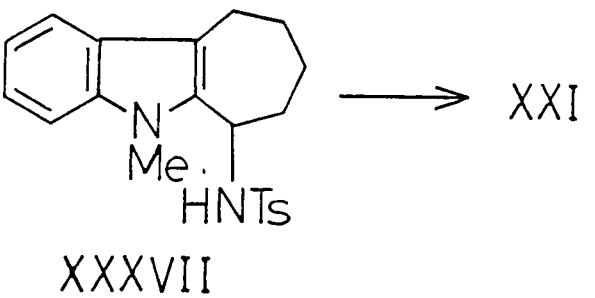
The percentage yields of the three major products from these




VIII IX IV




XXIV XXV




XXXVII

reactions in the different solvent systems used are summarised below.

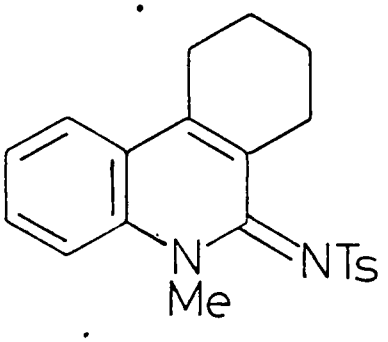
| Compound | Methanol | Pyridine | Pyridine/sodium hydroxide | Acetic acid |
|---|---|---|---|---|
| (XXI) | 49 | 11 | - | - |
| (XXIII) | 12 | 14 | - | 15 |
| (XXVIII) | 10 | 15 | 64 | 35 |

The main trend observed is the increase in the yield of (XXVIII) and corresponding decrease in that of (XXI) in basic or acidic solvents. These observations may be explained by two competing reactions of the intermediate (XXIV). Thus tosyl azide can attack (XXIV) leading to (XXV) and (XXVIII). Conversely (XXIV) can undergo a 1,3-shift to (XXXVII) with subsequent formation of (XXI). The former reaction results in a charged species which in the highly polar basic or acidic solvents is stabilised by solvation. The 1,3-shift on the other hand will be virtually independent of solvent effects. Thus in the more polar solvents attack of azide on (XXIV) predominates over the 1,3-shift, resulting in the observed proportion of products. Similar solvent effects on the addition of 1,3-dipoles have been reported[16,24].

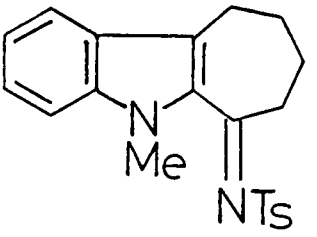
The fourth product, D, was obtained in very small yield (4%) from the reaction in acetic acid. The mass spectrum and analysis suggested the molecular formula $C_{21}H_{22}N_2O_2S$ and the i.r. spectrum contained a band at 1512 $cm^{-1}$ (C=N) but no band due to N-H. The n.m.r. spectrum showed the following signals:-

1.85$\tau$(1H, d, J8Hz, aromatic), 2.02(2H, d, J8Hz, low field half of tosyl signal), 2.6-3.0(5H, m, aromatic), 6.31(3H, s, NMe), 6.58(2H, t, J6Hz), 7.03(2H, t, J6Hz), 7.58(3H, s, tosyl Me) and 8.0-8.2(4H, m).

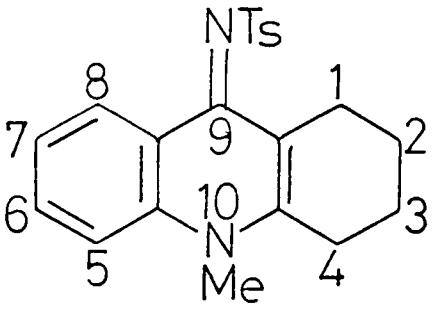
These data indicated that D had one of the four structures (XXXII), (XXXVIII), (XXXIX) or (XL). The formation of (XXXII) from (XXVIII) was evidence against this structure for D since the two compounds were different, although it did not definitely exclude the



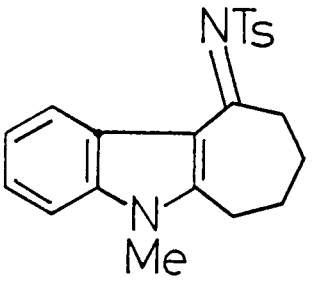

XXXII



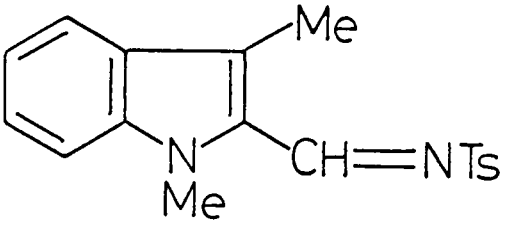

XXXVIII




XXXIX




XL




XLI

possibility of syn and anti isomerism about the C=N bond. Because of the very low yields of D it was decided to attempt to identify the compound by synthesis. The use of N-sulphinyltoluene-p-sulphonamide for the synthesis of sulphonylimino compounds from aromatic aldehydes is known[25,26], although this reagent does not seem to have been used with other carbonyl compounds. An attempted preparation of (XXXII) from (XXIX, n = 4) failed. Since it appeared unlikely that D could be synthesised by this route, attention was turned to other means of identification.

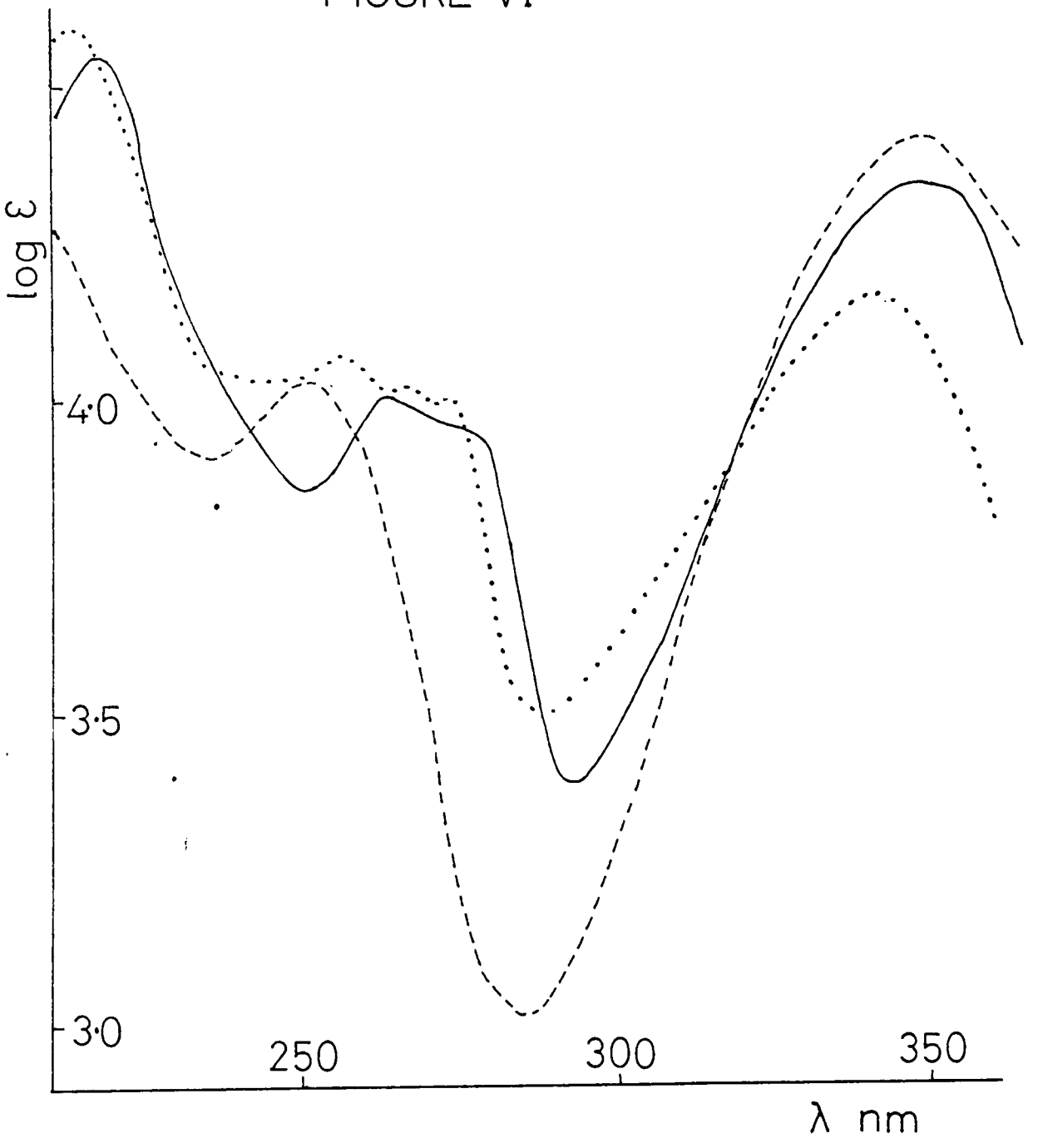
Base-catalysed hydrolysis gave a compound, E, in which the imino group had been replaced by a carbonyl group (absorption at 1628 $cm^{-1}$). The n.m.r. spectrum showed the following signals:-

1.51τ(1H, m, aromatic), 2.6-2.8(3H, m, aromatic), 6.37(3H, s, NMe), 6.99(2H, t, J6Hz), 7.22(2H, t, J6Hz) and 7.9-8.3(4H, m).

The very small amount of E available (14 mg) necessitated its identification by synthesis. The hydrolysis product was in fact different from (XXIX, n = 4) and thus the structure (XXXII) was incorrect for D. Attention was then turned to the other three possibilities. Compound (XLI) had been prepared[1,2] from tosyl azide and 1,3,3-trimethylindole and its u.v. spectrum was very similar to that of D (see FIGURE VI). We had at the time no available data for the chromophores of (XXXIX) and (XL). There were slight differences between the u.v. of D and (XLI) but these may have been due to the effects of the seven membered ring preventing coplanarity of the conjugated system. Such effects have been reported[27] for cycloalkan[b]indolones.

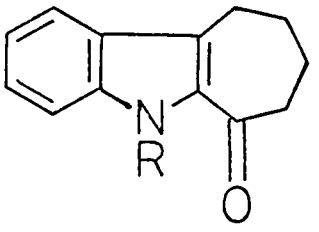
The compounds (XLII, R = H) and (XLII, R = Me) are known[28] and it was decided to carry out syntheses and to compare the products with E. Rather than use the method reported[28] it was decided to attempt the oxidation of 5,6,7,8,9,10-hexahydrocyclohept[b]indole with periodic acid. This method has been used with success for the preparation of

FIGURE VI

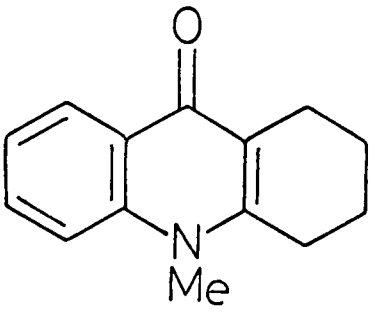



_____ Compound D  ------- XLI

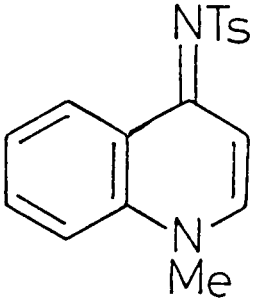
..... LXXXII (see later)



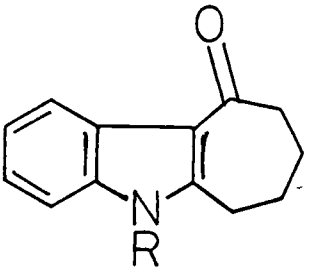

XLII



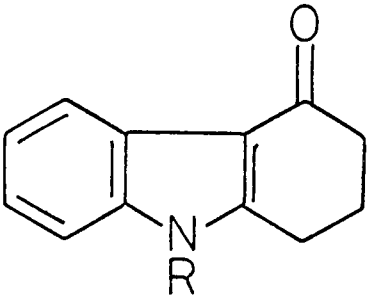

XLIII




XLIV




XLV




XLVI

1-oxo-1,2,3,4-tetrahydrocarbazole[29,30]. Oxidation of the indole in this way gave a product whose spectral data and melting point agreed with those reported[28] for (XLII, R = H). Methylation of this product gave (XLII, R = Me) which was different from E, thus eliminating the possibility that (XXXVIII) was the structure of D.

The next possibility considered was that of (XXXIX). This was perhaps more likely, since the n.m.r. spectrum of D showed an aromatic signal at very low field (1.85τ) which may have been due to the sulphonylimino group in the 9-position affecting the proton at $C_8$. A similar effect has been observed in compound (I)[1,3]. Although no structures of the type (XXXIX) had yet been isolated from the reactions of indoles and azides, Witkop[18] had prepared a related 4-quinolone from the oxidation of tetrahydrocarbazole. Synthesis of the known compound (XLIII)[31] from cyclohexanone and N-methylanthranilic acid was carried out but the product again proved different from E. During the course of this later work we had received a sample of the compound (XLIV) kindly provided by Prof. J. Renault (Faculté de Pharmacie, Université de Paris); the u.v. spectrum showed a chromophore different to that of D. These observations eliminate the structure (XXXIX) for D and we were left with the remaining structure (XL). The corresponding structure for E was (XLV, R = Me).

This compound (XLV, R = Me) was unknown, although the corresponding N-H compound and the homologues (XLVI, R = H or Me) have been prepared.

The preparation of (XLVI, R = Me) was carried out by the action of sulphuric acid on cyclohexane-1,3-dione-monophenylhydrazone[32] and subsequent methylation[33] of the product. The spectral properties of (XLVI, R = Me) were very similar to those of E. Of particular interest were signals at 1.74τ(1H, aromatic) and 6.36τ(3H, NMe) in the n.m.r. spectrum. These values compared closely with those given by E (1.51 and 6.37τ).

These observations indicated that (XLV, R = Me) was the correct

structure for E, and the synthesis of this compound was attempted in order to gain definite confirmation of this.

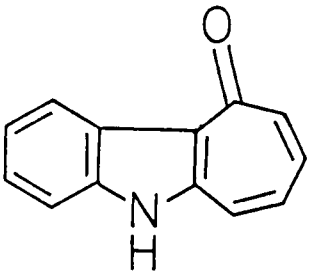
The compound (XLV, R = H) has been prepared[34] by irradiation of acridine-10-oxide to give (XLVII) followed by catalytic hydrogenation. Because of the relatively low yields and tedious separation procedures reported[35] in the preparation of acridine-10-oxide it was decided to attempt a different synthesis, starting from 5-acetylvaleric acid[36]. Condensation of this acid with phenylhydrazine followed by a Fischer synthesis should yield 5-(indol-2-yl)valeric acid (XLVIII, R = H) and/or 4-(2-methylindol-3-yl)butyric acid (XLIX, R = H). It was then hoped to cyclise the former to give (XLV, R = H).

The effect of the acid catalyst on the Fischer indole synthesis using unsymmetrical ketones has been studied[37], and it has been shown that a mixture of sulphuric acid (70% w/w) in aqueous ethanol gave the 2-substituted indole, e.g. (XLVIII) as the major product. This procedure was carried out on 5-acetylvaleric acid and three products were obtained. The properties of the first of these agreed with the structure (XLVIII, R = Et). The u.v. spectrum was that of an indole and the i.r. spectrum showed bands at 1728(C=O) and 3360(N-H) $cm^{-1}$. The n.m.r. spectrum showed signals at

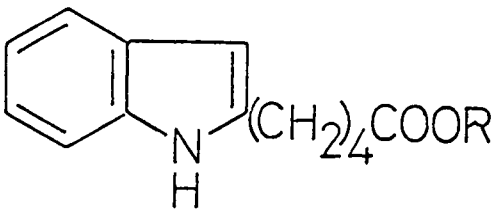
2.02τ(1H, br, exchanged $D_2O$, NH), 2.47(1H, m, aromatic), 2.6-3.0 (3H, m, aromatic), 3.76(1H, s, $C_3$,H), 5.87(2H, q, J7Hz, $CH_3\underline{CH_2}$), 7.25 (2H, t, J7Hz), 7.66(2H, t, J7Hz), 8.1-8.5(4H, m) and 8.76(3H, t, J7Hz, $\underline{CH_3}CH_2$).

The second compound was also an ester and its properties agreed with the structure (XLIX, R = Et). The n.m.r. spectrum showed the following signals:-

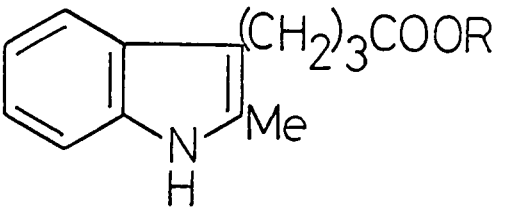
2.27τ(1H, br, exchanged $D_2O$, NH), 2.52(1H, m, aromatic), 2.7-3.0 (3H, m, aromatic), 5.89(2H, q, J7Hz, $CH_3\underline{CH_2}$), 7.25(2H, t, J7Hz), 7.65 (3H, s, $C_2$,Me), 7.66(2H, t, J7Hz), 8.03(2H, quintuplet, J7Hz, $C_3\underline{H_2}$) and 8.77(3H, t, J7Hz, $\underline{CH_3}CH_2$).



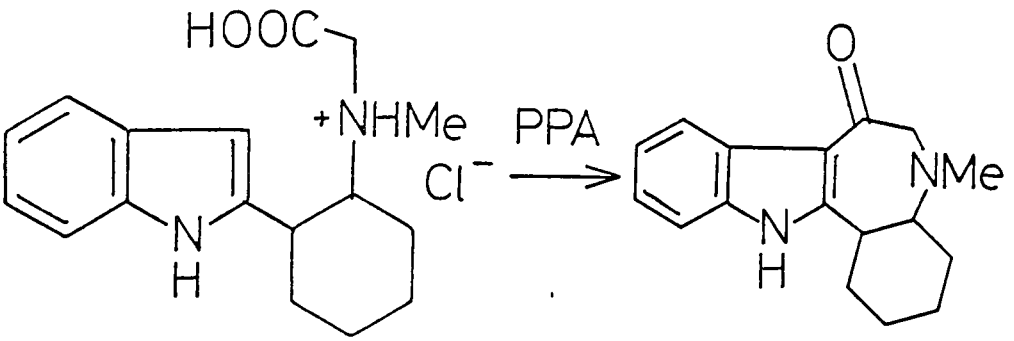
XLVII



XLVIII



XLIX



L LI

The third product obtained from this reaction was the required acid (XLVIII, R = H) and this was also obtained by hydrolysis of the corresponding ethyl ester (XLVIII, R = Et). The spectral properties of this compound agreed with the structural assignment, the u.v. spectrum being that of an indole and the i.r. spectrum showing bands at 1714 $cm^{-1}$ (C=O) and 3390 $cm^{-1}$ (N-H). There was also a very broad band in the region 2700-3300 $cm^{-1}$ characteristic of a carboxylic acid. The n.m.r. spectrum (D) showed signals at

-0.86$\tau$(1H, s, exchanged $D_2O$, NH), 2.5-2.8(2H, m, aromatic), 2.9-3.2(2H, m, aromatic), 3.85(1H,s, $C_3$,H), 7.28(2H, t, J7Hz). 7.74 (2H, t, J7Hz) and 8.1-8.7(4H, m).

The signal for the acidic proton was not observed.

Having obtained (XLVIII, R = H) all that was required was to cyclise to (XLV, R = H). Of the various cyclisation catalysts available the most commonly used was polyphosphoric acid (PPA)[28,38] and a cyclisation similar to that required for our purposes had been carried out using this reagent to convert (L) to (LI)[39].

Several attempts were made to carry out a similar cyclisation on (XLVIII, R = H) but these met with no success. The products were very high-melting solids and t.l.c. showed the presence of many components in the mixtures. These compounds may have arisen <u>via</u> intermolecular Friedal-Crafts type reactions.

The required cyclisation was finally achieved by carrying out the reaction in phosphorus oxychloride at 100°. The product was a nicely crystalline solid whose melting point agreed with that reported[34] for (XLV, R = H) and whose spectral data (i.r., u.v., n.m.r.) were identical to those of (XLV, R = H), kindly provided by Professor Kaneko.

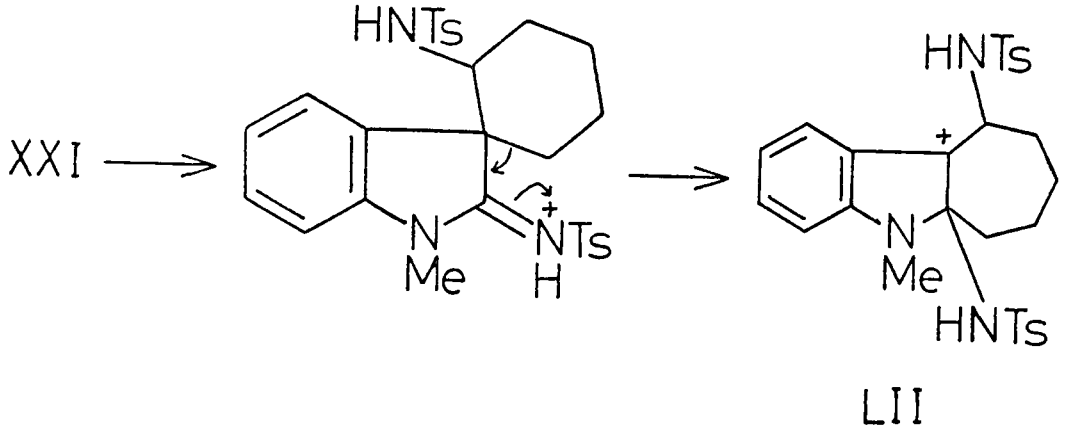
Finally, methylation of (XLV, R = H) using dimethyl sulphate/ alkali yielded (XLV, R = Me) identical in all respects to the hydrolysis product E. This evidence proves that the stucture of compound D is (XL).

The mechanism for the formation of D was difficult to visualise as taking place from any intermediate of the type found in FIGURE I, but the fact that D was produced from a reaction in acetic acid suggested that its formation was acid catalysed. A possible mechanism from (XXI) is shown. Protonation and rearrangement lead to (LII) followed by further rearrangement to (LIII). Elimination of toluene-p-sulphonamide from (LIII) leads to (XL).

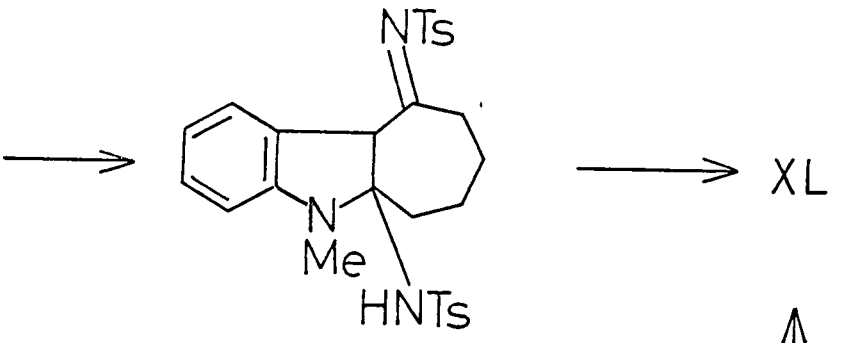
Attempts were made to verify this mechanism by treatment of (XXI) with both trifluoroacetic and hydrochloric acids. Even after prolonged boiling, (XXI) was recovered unchanged. A thermal rearrangement of (XXI) was also precluded. Sublimation of (XXI) led to tarry mixtures of several components, but t.l.c. of these mixtures showed the absence of any compound corresponding to (XL).

A second possible mechanism is one involving compound (XXIII). Protonation and rearrangement as shown leads to (LIV) when loss of toluene-p-sulphonamide gives (XL). No work was done to verify this hypothesis, but subsequent events showed that this mechanism is probably correct (see later).

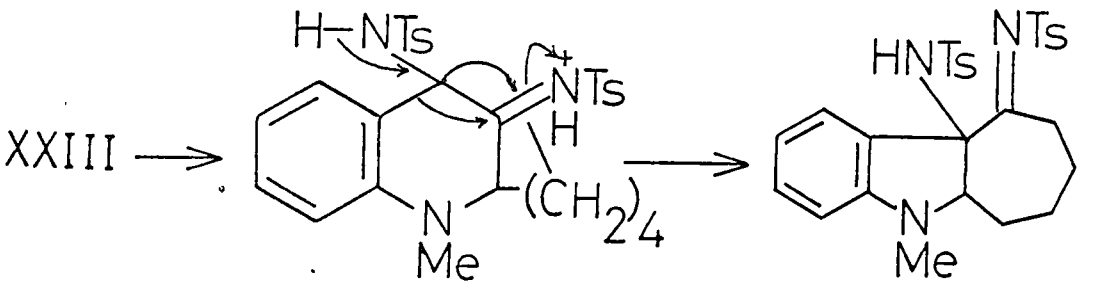
An interesting aspect of the work on 5-methyl-5,6,7,8,9,10-hexahydrocyclohept[b]indole is the failure to isolate any mono-adducts [c.f. (I) and (II) from 9-methyltetrahydrocarbazole]. An attempt was made to achieve this by carrying out a reaction using an excess of indole and adding the azide in small portions to a solution of the indole. The only products obtained, however, were the four already described and these were accompanied by a high recovery of indole. It would seem that the intermediates involved are highly reactive, and that there is no tendency for the reaction to stop at any intermediate stage.


XXI
HNTs
NTs
N
Me
H
HNTs
HNTs
N
Me

LII


NTs
N
Me
HNTs
XL

LIII


XXIII
H-NTs
NTs
H
N
Me
(CH2)4
HNTs
NTs
N
Me

LIV

The work on cycloalkeno[b]indoles was continued by an investigation into the reactions of 6,7,8,9,10,11-hexahydro-5H-cyclooct[b]indole (LV, R = H) and its N-methyl derivative (LV, R = Me) with arylsulphonyl azides.

(LV, R = H) reacted with tosyl azide to give a product which was assigned the structure (LVI, Z = Ts). An analogous product (LVI, Z = Cbs) was obtained when (LV, R = H) was treated with p-chlorobenzenesulphonyl azide. These products were very similar in properties to the corresponding compound (XX) from 5,6,7,8,9,10-hexahydrocyclohept[b]indole, and identification therefore did not prove difficult. In contrast to the preparation of (XX) the formation of (LVI) proceeded very smoothly and yields were good.

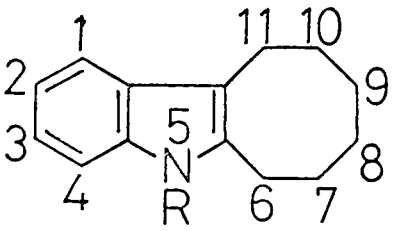
The n.m.r. spectra of the two compounds (LVI) are compared below.

| Compound | NH | Aromatic Protons | TsMe | Aliphatic protons |
|---|---|---|---|---|
| (LVI, Z = Ts) | 4.08 | 2.5-3.1(6H, m) | 7.68 | 6.8-7.4(2H, m) |
| | | 3.29(1H, t, J8Hz) | | 7.6-9.4(10H, m) |
| | | 3.46(1H, d, J8Hz) | | |
| (LVI, Z = Cbs)(D) | 1.44 | 2.6-3.0(6H, m) | - | 7.0-7.6(2H, m) |
| | | 3.32(1H, t, J8Hz) | | 7.6-9.6(10H, m) |
| | | 3.48(1H, d, J8Hz) | | |

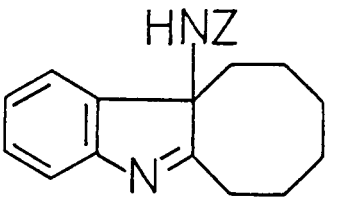
The u.v. spectra have already been shown in FIGURE III.

Buckley[16,11] had investigated the effects of basic solvents on the products of the reactions of 1,2,3,4-tetrahydrocarbazole with azides and had isolated compounds (LVII, Z = Ts) and (LVII, Z = Cbs) from the reactions with tosyl and p-chlorobenzenesulphonyl azides respectively. These products are formed by a similar process to that which leads to (V) (FIGURE I).

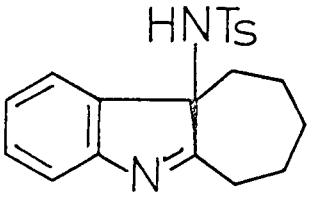
A similar investigation was carried out on cyclooctindole, with a view to obtaining structures of the type (LVIII). With tosyl azide in pyridine the product was (LVI, Z = Ts). A similar result was



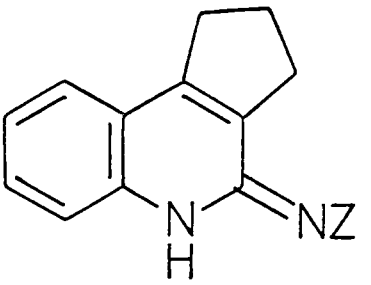

LV



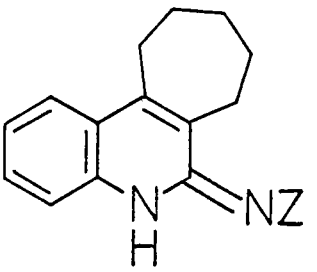

LVI




XX




LVII




LVIII

obtained using p-chlorobenzenesulphonyl azide. An attempt to use more forcing conditions in the latter case by conducting the reaction in pyridine and aqueous caustic soda resulted in the formation of large amounts of chlorobenzene-p-sulphonamide (as the sodium salt) but the residue was a very dark tarry material and t.l.c. showed the presence of many components. This line of investigation was pursued no further.

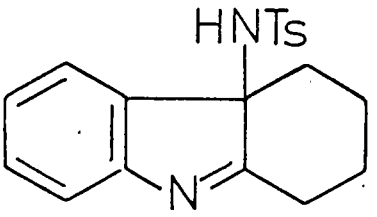
Buckley[16,11] had also investigated the action of heat on compound (XI) and had isolated the products (LIX) - (LXI). It was of interest to carry out a similar investigation on (LVI). Accordingly a sample of (LVI, Z = Ts) was heated above its melting point for 5 minutes. The dark melt yielded a product whose mass spectrum and analysis indicated the formula $C_{14}H_{15}N$ and whose n.m.r. spectrum contained the following signals:-

2.4-2.6$\tau$(2H, m, aromatic CH and NH), 2.7-3.0(3H, m, aromatic), 3.64(1H, d, J11Hz), 4.15(1H, dt, J11,8Hz), 6.9-7.2(2H, m), 7.5-7.8 (2H,m) and 7.9-8.6(4H, m).

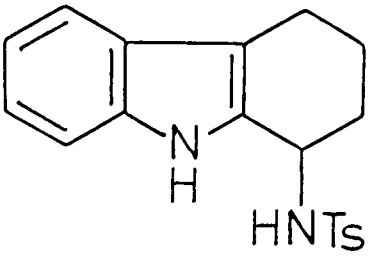
These results suggest one of two structures for the product, (LXII) or (LXIII). Of these two (LXII) is the more likely for the following reasons. The u.v. spectrum of the compound was very similar to those reported[40,41] for 2-vinylindoles, and quite different from those of 3-vinylindoles[42,43]. Moreover, 3-vinylindoles are reported[43] as being rather unstable. For these reasons we prefer the structure (LXII). This structure is also more likely on mechanistic grounds (see later).

Other products isolated from this reaction were toluene-p-sulphonamide (quantitative yield) and a very small amount of a highly insoluble, amorphous material, melting above 300°. This product was not investigated but may have been similar in structure to (LX).

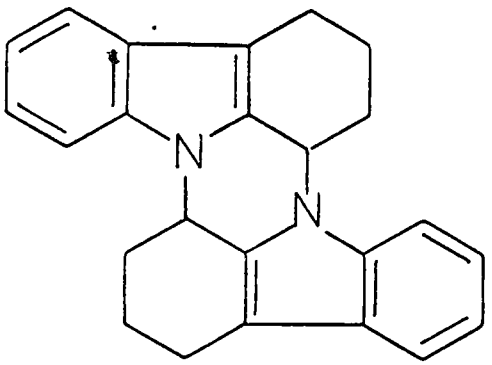
This experiment was repeated under milder conditions by boiling (LVI, Z = Ts) in propanol. The first product was assigned the



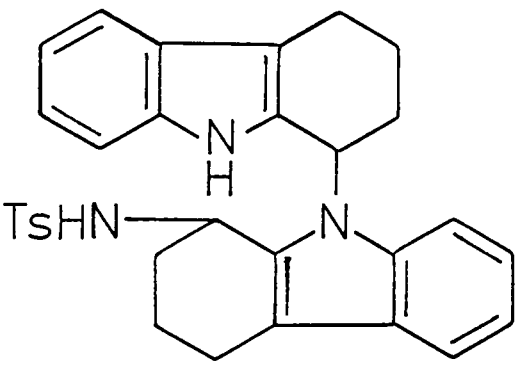

XI



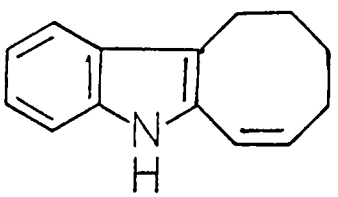

LIX



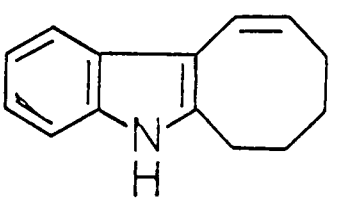

LX




LXI




LXII




LXIII

structure (LXIV). The u.v. spectrum was that of an indole, and there were bands in the i.r. spectrum at 3250 and 3380 $cm^{-1}$, corresponding to N-H stretch. The n.m.r. spectrum contained the following signals:-

1.62τ(1H, s, exchanged $D_2O$, indole NH), 2.24(2H, d, J8Hz, low field half of tosyl signal), 2.52(1H, m, aromatic), 2.7-3.0(5H, m, aromatic), 4.52(1H, d, J8Hz, exchanged $D_2O$, tosyl NH), 5.15(1H,m), 6.9-7.6(2H, m), 7.66(3H, s, tosyl Me), and 8.0-9.0(8H, m).

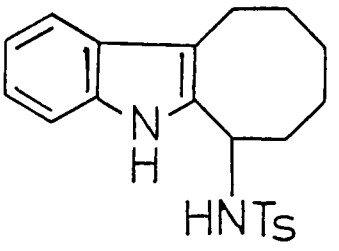
This spectrum was very similar to that of (LIX)[16,11] which showed signals at

1.64τ(1H, exchanged $D_2O$, indole NH), 2.22(2H, d, J8Hz, low field half of tosyl signal), 2.3-3.0(6H, m, aromatic), 5.15(1H, d, exchanged $D_2O$, tosyl NH), 5.49(1H, m), 7.2-8.8(6H, m) and 7.55(3H, s, tosyl Me).

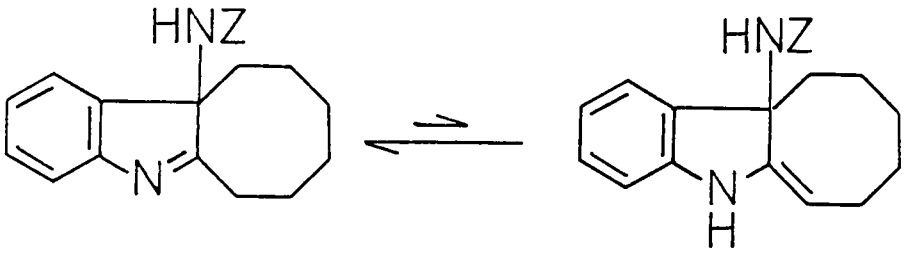
The close similarities between the properties of the two compounds left no doubt that structure (LXIV) was correct. Further investigation into the products from this reaction led to the isolation of compound (LXII) and toluene-p-sulphonamide. A small amount of a high-melting solid, presumably the same as that obtained above, was also isolated.

The mechanism for these transformations is as follows. (LVI) must exist in equilibrium with its tautomer (LXV) although the latter cannot be detected spectroscopically. Similar equilibria have been reported in the hydroxytetrahydrocarbazole series[8]. On heating, (LXV) undergoes a 1,3-shift similar to those reported above with the formation of (LXIV), and elimination of toluene-p-sulphonamide from (LXIV) leads directly to (LXII).

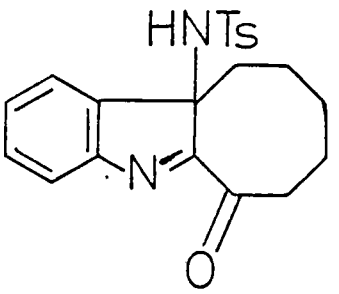
When (LV, R = H) was treated with tosyl azide in acetic acid, a product was obtained which was not (LVI, Z = Ts). The mass spectrum and analysis indicated the formula $C_{21}H_{22}N_2O_3S$ [(LVI, Z = Ts) has the formula $C_{21}H_{24}N_2O_2S$], and the i.r. spectrum contained bands at 1692 (C=O) and 3225 (N-H) $cm^{-1}$. These observations suggested that an oxidation had occurred, possibly of a methylene group to a carbonyl



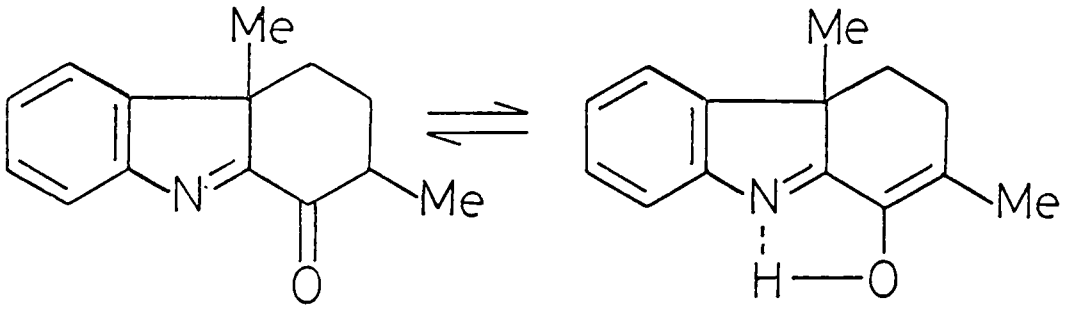

LXIV




LVI LXV




LXVI




LXVIIa LXVIIb

group. The n.m.r. spectrum (D) showed signals at

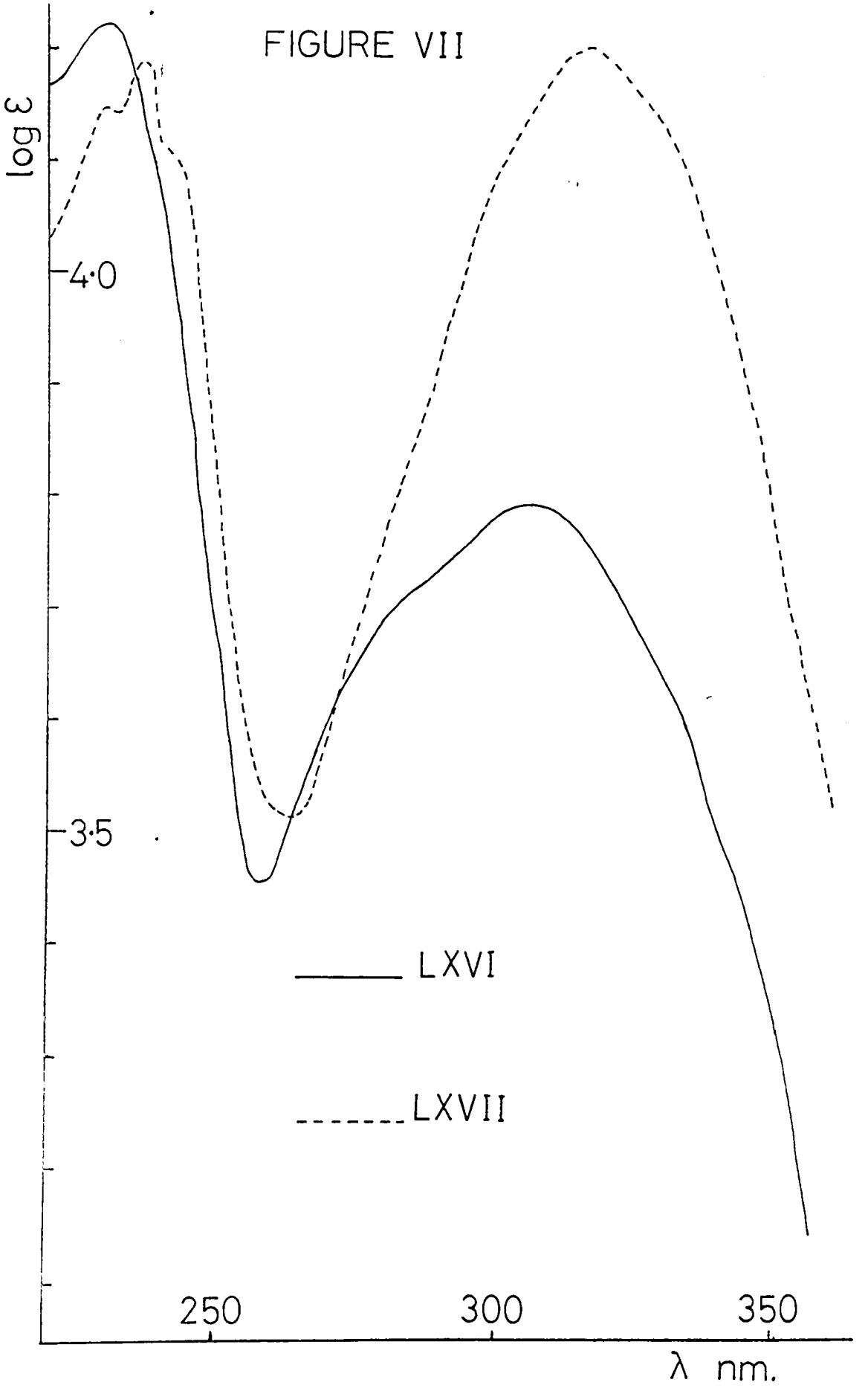
1.2τ(1H, very broad, exchanged $D_2O$, NH), 2.41(1H, d, J8Hz, aromatic), 2.76(1H, t, J8Hz, aromatic), 2.9-3.1(4H, m, aromatic), 3.18(1H, t, J8Hz, aromatic), 3.46(1H, d, J8Hz, aromatic), 6.0-6.5(1H, m), 7.73(3H, s, tosyl Me) and 7.3-9.2(9H, m).

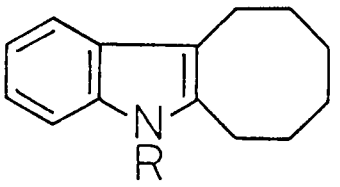
An interesting feature of this spectrum is the coincidence of the signals of all four tosyl aromatic protons.

The u.v. spectrum was totally different from that of (LVI, Z = Ts) suggesting that the conjugated system had been extended in some way, and the structure (LXVI) was proposed. The u.v. spectrum supported this structure since chromophores of this type are known[44,45]. The u.v. spectrum of our product and that of the compound (LXVII)[44] are shown in FIGURE VII. There are differences, but these may be explained by the equilibrium (LXVIIa) $\rightleftharpoons$ (LXVIIb), since it is reported[44] that the i.r. spectrum of (LXVII) contains a broad band due to O-H absorption. In our compound the i.r. spectrum did not show O-H stretch, possibly due to the conformational properties of the eight-membered ring. Nevertheless, the spectra shown in FIGURE VII do have certain similarities.

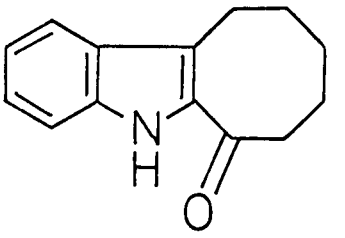
Also in favour of structure (LXVI) are the known oxidations of 2,3-dialkylindoles to 2-acyl-3-alkylindoles[8, 18, 46], especially the oxidation of (LV, R = H) to (LXVIII)[18]. It was possible that oxidation to (LXVIII) was taking place followed by attack of azide in the usual manner. In a separate experiment, however, we have shown that 9-methyl-1-oxo-1,2,3,4-tetrahydrocarbazole does not react with tosyl azide even under forcing conditions and also (LV, R = H) was recovered unchanged from a solution in acetic acid. This is of course evidence against such a mechanism.

The second possibility was that (LXVI) was formed directly by oxidation of (LVI, Z = Ts). Indeed, a solution of (LVI, Z = Ts) in acetic acid at room temperature gradually deposited (LXVI) in good

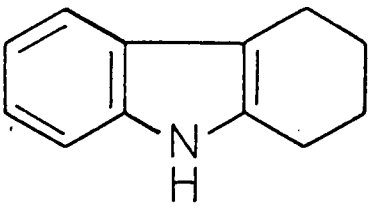

FIGURE VII
log ε
4·0
3·5
LXVI
LXVII
250
300
350
λ nm.



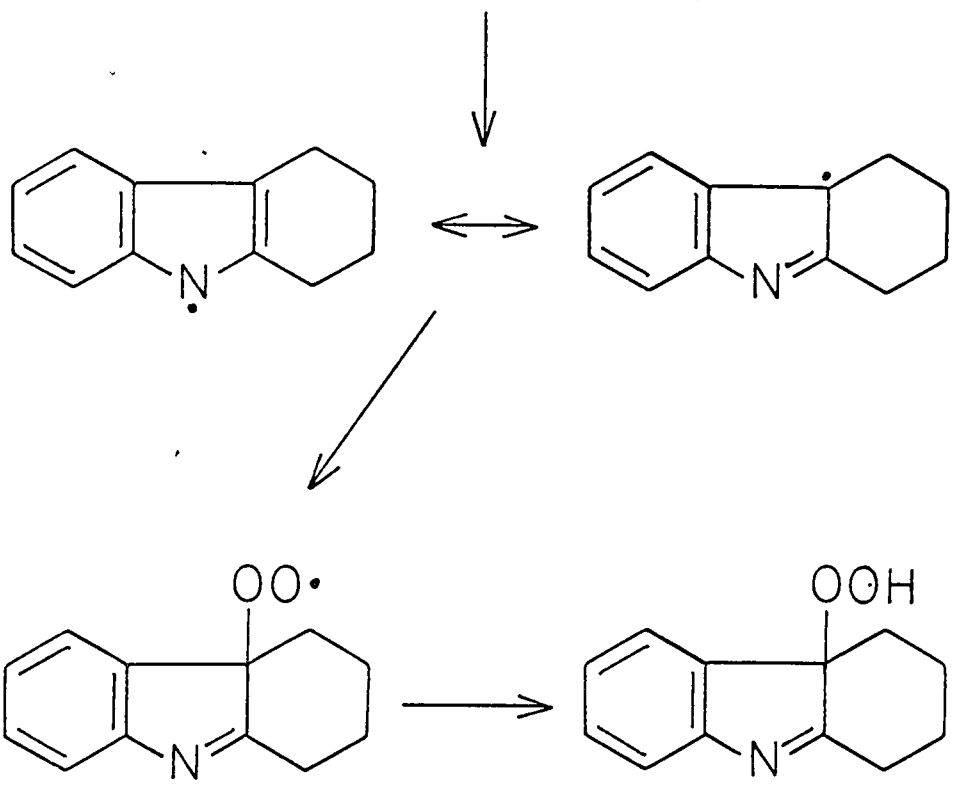

LV




LXVIII




LXIX



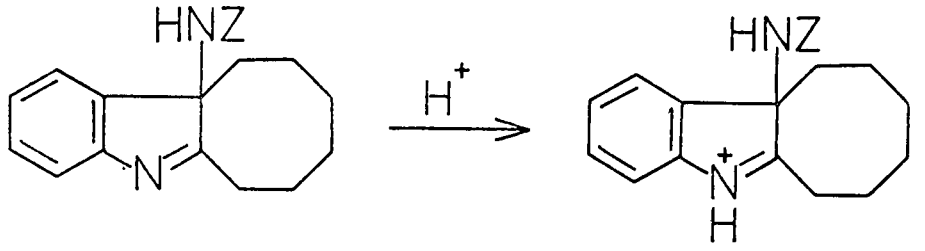

LXX

yield. Having established this, we were now in a position to propose a mechanism.

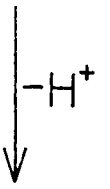
Oxidation of an indole usually occurs via initial peroxidation at the 3-position[5,8,18,47], e.g. the oxidation of (LXIX) to (LXX)[5b]. In the case of (LVI) this position is blocked by the sulphonylamino group, but a similar reaction sequence is possible. The action of the acidic solvent may be to catalyse the transformation (LVI) - (LXV). The process from here is entirely analogous to that resulting in peroxidation at the 3-position. Loss of water from (LXXI, Z = Ts) then gives (LXVI).

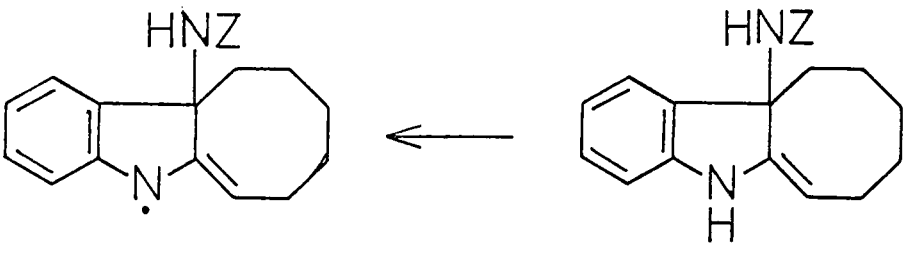
The preparation of (LXVI) by the methods so far described was slow and it was desirable to accelerate this in some way. A somewhat faster preparation was achieved by shaking a solution of (LVI, Z = Ts) in acetic acid in air with the addition of a little platinum black. This catalyst had been used[18] in the preparation of (LXVIII). However, the fastest preparation achieved was to pass a stream of air through an acetic acid solution of (LVI, Z = Ts) in the presence of a catalytic amount of cupric acetate. Reaction under these conditions was complete in 15 hours.

One of the problems encountered with (LXVI) was its low solubility in most solvents and recrystallisation was achieved with difficulty. An attempt was made to recrystallise the crude product from one of the platinum-catalysed oxidations from 2-methoxyethanol. The recovery was zero and from the solution was isolated a compound different from, but isomeric with (LXVI). The i.r. spectrum contained absorptions due to C=N (1610 $cm^{-1}$), C=O (1703 $cm^{-1}$)and N-H (3270 $cm^{-1}$). The slightly higher frequency of the C=O absorption compared to that of (LXVI) suggested that conjugation had been lost. The n.m.r. spectrum showed the following signals:-



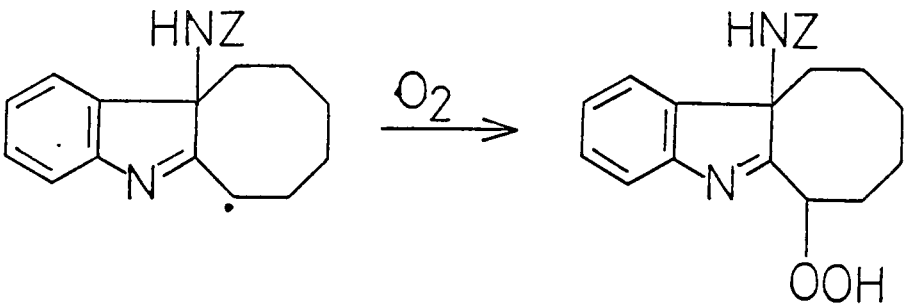

LVI




LXV






LXXI

| | | |
|---|---|---|
| 0.00τ | (0.04) | 1H, s, exchanged $D_2O$, NH |
| 2.18 | (2.13) | 2H, d, J8Hz, low field half of tosyl signal |
| 2.6-3.1 | (2.4-3.1) | 6H, m, aromatic |
| 6.8-7.1 | | 1H, m |
| 7.1-7.5 | | 1H, m |
| 7.60 | | 3H, s, tosyl Me |
| 7.6-8.4 | | 8H, m |

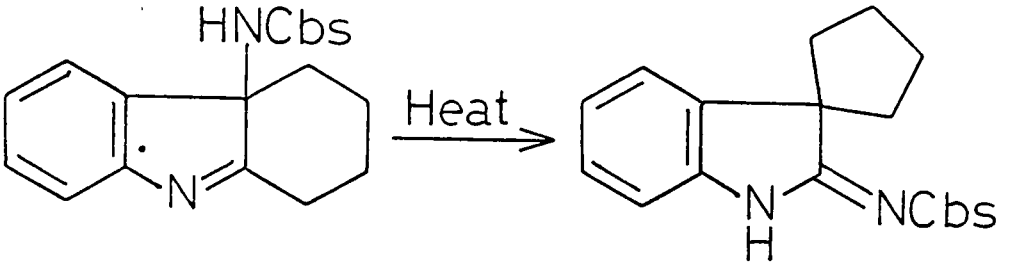
This spectrum was very similar to that of the compound (LXXIII)[11,16], formed by the action of heat on (LXXII), and for this reason the structure (LXXIV) was proposed. The corresponding τ values for (LXXIII) are shown in parentheses in the table above. The formation of (LXXIV) can be envisaged as the migration of the tosylamino group to $C_{5a}$ *via* an aziridine intermediate followed by C-migration to form the spirocycloheptanone ring. Apart from the above example, cases of similar migrations have been reported[48-50].

Compound (LXVI) was appreciably soluble in dilute alkali. On heating such a solution a product was slowly deposited. This compound had the formula $C_{21}H_{24}N_2O_4S$ and spectral data were consistent with the structure (LXXV). The i.r. spectrum showed a carbonyl absorption at 1707 $cm^{-1}$, again suggestive of loss of conjugation. The n.m.r. spectrum (D) contained the following signals:-

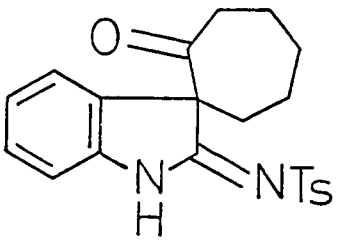
0.10τ(1H, s, exchanged $D_2O$), 2.71(1H, dd, J8,2Hz, aromatic), 2.8-3.2(6H, m, aromatic), 3.64(1H, s, exchanged $D_2O$), 3.68(1H, dd, J8,2Hz, aromatic), 4.69(1H, s, exchanged $D_2O$), 7.0-7.3(1H, m), 7.71 (3H, s, tosyl Me) and 7.8-9.2(9H, m).

This addition of water across the C=N bond of the indolenine is similar to that observed in the compounds (LXXVI)[2,3,10].

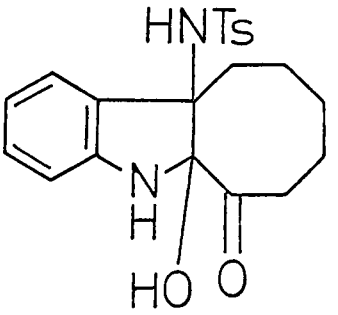
The final investigations of cycloalkeno[b]indoles were carried out on 6,7,8,9,10,11-hexahydro-5-methyl-5H-cyclooct[b]indole (LV, R = Me). This compound reacted with tosyl azide in diethyl ether to give four products, F,G,H, and J.



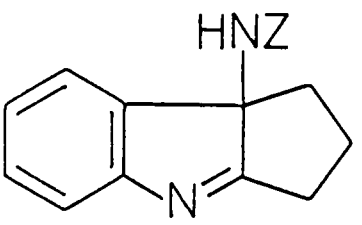

LXXII LXXIII




LXXIV




LXXV




LXXVI

The major product, F, $C_{29}H_{33}N_3O_4S_2$, was also obtained from reactions in ethanol and acetic acid and was very similar in properties to compound (IV)[1,3], having a similar u.v. spectrum and absorptions due to N-H and C=N in the i.r. spectrum. The n.m.r. spectrum showed the following signals:-

2.11τ(2H, d, J8Hz, low field half of tosyl signal), 2.44(1H, m, aromatic), 2.6-2.9(4H, m, aromatic), 3.0-3.4(5H, m, aromatic), 4.00 1H, s, exchanged $D_2O$, NH), 6.5-6.9(1H, m), 7.0-7.4(2H, m), 7.23(3H, s, NMe), 7.56(3H, s, tosyl Me), 7.76(3H, s, tosyl Me) and 6.7-9.2(8H, m).

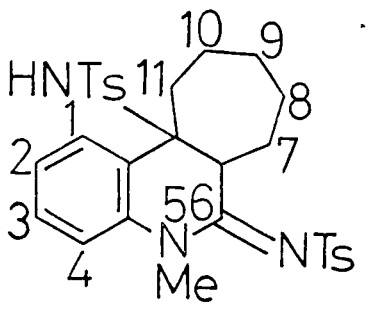
This spectroscopic evidence suggested that F had the structure (LXXVII). The mass spectrum did not contain a molecular ion (m/e 551), the highest signal occurring at m/e 380 and suggesting easy loss of toluene-p-sulphonamide. A sample of F was heated to its melting point and from the melt was isolated a compound which was assigned the structure (LXXVIII). The u.v. and i.r. spectra were in good agreement with this structure and the n.m.r. spectrum had signals at

1.9-3.1τ(8H, m, aromatic), 5.83(3H, s, NMe), 6.7-7.0(4H, m), 7.63(3H, s, tosyl Me) and 8.0-8.9(6H, m).

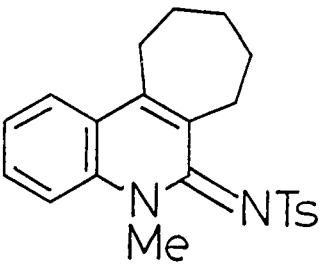
(LXXVIII) was obtained from F by two further methods. Treatment of F with 1,5-diazabicyclo[4.3.0]non-5-ene in refluxing ethanol resulted in very smooth elimination of sulphonamide, reaction being complete in five minutes. Treatment with aqueous caustic soda under the same conditions gave (LXXVIII) together with some (LXXIX). The u.v. and i.r. spectral properties of this compound were very similar to those of the 2-quinolones already described and the n.m.r. spectrum contained the following signals:-

2.0-3.0τ(4H, m, aromatic), 6.27(3H, s, NMe), 6.8-7.1(4H, m) and 7.8-8.8(6H, m).

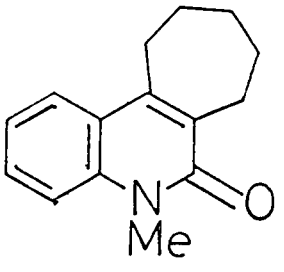
These experiments prove beyond doubt that structure (LXXVII) is correct for F. The very facile elimination of sulphonamide from F must mean that the $C_{6a}$ - $C_{11a}$ ring junction has the <u>trans</u> configuration



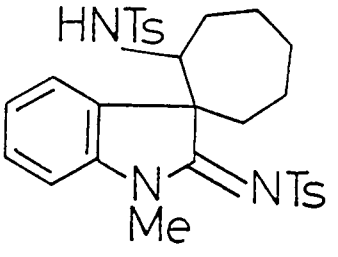

LXXVII




LXXVIII




LXXIX




LXXX

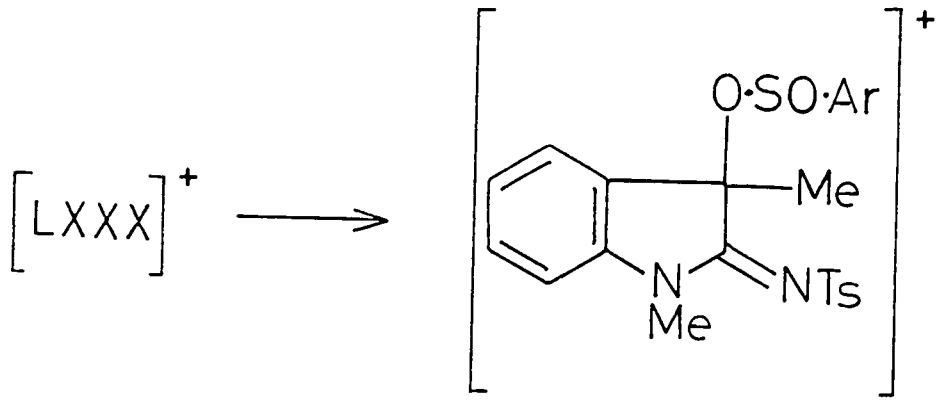
(see earlier). Indeed, this loss of sulphonamide was more facile than in any of the compounds studied thus far. As in the other examples so far reported, one reaction was carried out using pyridine as solvent. In this case the major product was the compound (LXXVIII), no (LXXVII) being isolated. This is yet another illustration of this very easy elimination.

It is interesting to note the position of the NMe signal in the n.m.r. spectrum of F. This occurs at 7.23$\tau$ and is at higher field than in any of the similar structures investigated. As has already been shown, the position of the NMe signal has been of value in assigning cis or trans geometry to the ring junction (see earlier). The high position of this signal in the present case might therefore suggest cis geometry. There is so much chemical evidence to the contrary, however, that the position of the NMe signal must be an exception to this so far general rule.

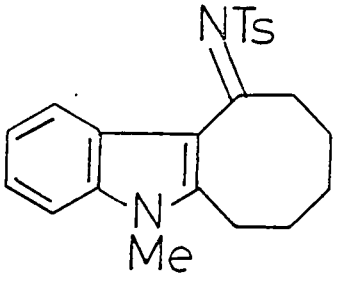
The second product, G, was isomeric with F and was assigned the structure (LXXX). The i.r. and u.v. spectra were consistent with this and the n.m.r. spectrum was similar to those of related spiro-compounds, containing signals at

2.04$\tau$(2H, d, J8Hz, low field half of tosyl signal), 2.54(1H, exchanged $D_2O$, NH), 2.6-3.3(10H, m, aromatic), 4.1-4.6(1H, m), 5.0-5.3(2H, m), 6.92(3H, s, NMe), 7.57(3H, s, tosyl Me), 7.67(3H, s, tosyl Me) and 7.1-9.6(8H, m).

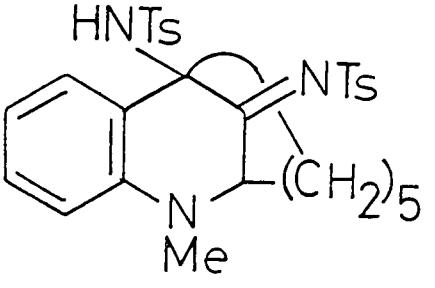
The mass spectrum showed a small molecular ion peak (9%). There were signals due to loss of Ts (m/e 396) and the characteristic fragmentations of the spirocycloheptane ring [see the fragmentation of compound (XXI), FIGURE IV], although these were for the most part very weak. An important and unusual fragmentation was the loss of 83 from the molecular ion. This was assigned to the formation of the ion (LXXXI). Similar fragmentations have been reported[51] for N-p-tolylsulphonyl-N'-acylhydrazines.




LXXXI




LXXXII




LXXXIII

The third product, H, obtained from these reactions had the molecular formula $C_{22}H_{24}N_2O_2S$ and its n.m.r. spectrum showed the following signals:-

1.77τ(1H, d, J8Hz, aromatic), 2.05(2H, d, J8Hz, low field half of tosyl signal), 2.6-3.0(5H, m, aromatic), 6.32(3H, s, NMe), 6.49(2H, t, J7Hz), 6.81(2H, t, J7Hz), 7.56(3H, s, tosyl Me) and 7.8-8.7(6H, m).

This spectrum was very similar to that of (XL) especially with regard to the very low field aromatic proton and the NMe signal. These signals were found at 1.85 and 6.31τ respectively in (XL). The structure (LXXXII) was therefore proposed for H. The i.r. and u.v. spectra were consistent with this assignment, the u.v. spectrum being shown along with that of (XL) in FIGURE VI.

J, the fourth product from this series of reactions was isolated in approximately the same yield (5%) from the reactions in ether, ethanol and acetic acid. The compound formed bright yellow prisms and analysis indicated the formula $C_{29}H_{33}N_3O_4S_2$. The i.r. spectrum contained C=N and N-H absorptions (1608 and 3245 $cm^{-1}$ respectively) and the n.m.r. spectrum showed signals at

2.06τ(2H, d, J8Hz, low field half of tosyl signal), 2.61(2H, d, J8Hz, high field half of tosyl signal), 2.9-3.3(5H, m, aromatic), 3.5-3.9(3H, m, aromatic), 4.22(1H, s, exchanged $D_2O$, NH), 6.2-6.5(2H, m), 6.8-7.2(1H,m), 7.30(3H,s, NMe), 7.49(3H, s, tosyl Me), 7.69(3H, s, tosyl Me) and 7.7-9.0(8H, m).

Of particular interest were the high τ values of the NMe signal and also the three high-field aromatic protons. These are characteristic of a tertiary aromatic amine. By analogy with the corresponding product (XXIII) from N-methylcyclohept[b]indole J was assigned the structure (LXXXIII).

It was observed that different samples of J had quite widely differing melting points and melting usually occurred over a more or less wide temperature range depending on the rate of heating. T.l.c.

of the melts showed the presence of a second component in addition to J. This effect was therefore investigated. Only one product was isolated (62%) and this proved identical in all respects to the compound (LXXXII). This transformation is strong evidence in favour of the mechanism proposed earlier for the formation of (XL) from (XXIII). Other interesting rearrangements of this type of structure will be discussed in Chapter III.

The yields obtained from this series of reactions were low, due mainly to the difficulties encountered in separating the products. No attempt has therefore been made to explain the ratios of the products on the basis of solvent effects.

# CHAPTER II

## Experimental

Melting points were determined on a Kofler block and are uncorrected.

Infrared spectra were recorded as nujol mulls on either a Unicam SP 1000 or a Perkin-Elmer 257 spectrometer.

Ultraviolet spectra were recorded on ethanol solutions unless otherwise stated, using a Cary 14M spectrometer.

The following abbreviations have been used to describe spectral bands:

br = broad, sh = shoulder

Nuclear magnetic resonance spectra (described in the Main Section) were recorded on Perkin-Elmer R10, R14 and R32 spectrometers (60, 100 and 90 MHz) by Mrs E. E. Richards.

Mass spectra were recorded on either a Varian MAT CH7 (low resolution) or an A.E.I. MS9 (high resolution) instrument under the supervision of Dr. R. T. Aplin.

Microanalyses were carried out under the supervision of Dr. F. B. Strauss.

Thin layer chromatography (t.l.c.) was carried out using Kieselgel HF 254/366 plates, eluting with benzene/ethyl acetate 9:1.

1. 2,3,4,4a-Tetrahydro-4a-p-tolylsulphonylamino-1H-carbazole (XI):-

A mixture of 1,2,3,4-tetrahydrocarbazole (14.0 g, 1 mol) and tosyl azide (16.0 g, 1 mol) was heated at 50° (oil bath) for 3 days. Methanol (10 ml) was added and the solid was collected. Recrystallisation from propanol gave colourless needles, m.p. 204-206° (lit.[1] 203-206°). (Yield 12.5 g, 45%).

2. Methiodide of 2,3,4,4a-tetrahydro-4a-p-tolylsulphonylamino-1H-carbazole (XIV):-

2,3,4,4a-Tetrahydro-4a-p-tolylsulphonylamino-1H-carbazole (5 g, 1 mol) and methyl iodide (21 g, 10 mol) were heated under reflux for 5 hours in benzene (75 ml) and acetonitrile (75 ml). The methiodide, m.p. 200-203° (lit.[1] 200-215°), separated on cooling. (Yield 5.25 g, 74%).

3. 1,2,3,4,4a,9a-Hexahydro-9-methyl-4a-p-tolylsulphonylamino-9a-trifluoroacetoxycarbazolium trifluoroacetate (XII):-

The methiodide (XIV) (200 mg) was boiled under reflux in trifluoroacetic acid (5 ml) for 3 hours. The solvent was removed and the residue triturated with methanol to give a crystalline solid, recrystallised from ethyl acetate as colourless plates, identical (i.r.) to an authentic sample, m.p. 118-121° (lit.[1] 120-124°). (Yield 200 mg, 83%).

4. Preparation of 9-methyl-2,3,4,4a-tetrahydro-4a-p-tolylsulphonylaminocarbazole (VIII) and its reaction with tosyl azide:-

A solution of the trifluoroacetate salt (XII) (2 g) in water (80 ml) was added to a solution of tosyl azide (0.72 g) in chloroform (40 ml). The mixture was stirred vigorously at 0° while aqueous sodium carbonate solution (0.36 g in 20 ml) was added dropwise. The mixture was stirred for 10 minutes, the organic phase separated and

the aqueous phase extracted with chloroform (2 x 10 ml). The combined extracts were dried (magnesium sulphate) and filtered. After 18 hours the solvent was removed and the residue triturated with methanol. The solid was collected and recrystallised from methanol as colourless prisms, m.p. 194-195°, identical (t.l.c., m.p., i.r.) to an authentic sample of 9-methyl-1,2,3,4-tetrahydro-1-p-tolyl-sulphonylaminocarbazole (II). (Yield 225 mg).

The mother liquors were evaporated and the residue chromatographed on silica, eluting with benzene/ethyl acetate mixtures. The following were obtained in order of elution: tosyl azide (510 mg), compound (II) (190 mg, total yield 34%) and an oil which would not crystallise. This was dissolved in TFA (10 ml). After 3 days the solution was poured into water, the acid neutralised (sodium carbonate) and the mixture extracted with chloroform. The extracts were dried (magnesium sulphate) and the solvent was removed *in vacuo*. The residue was filtered through silica gel in benzene/ethyl acetate (9:1). The solvent was removed and the residue recrystallised from acetonitrile as fine needles, m.p. 212-213°.(Yield 60 mg, 5%).

The product was identical (t.l.c., m.p., i.r.) to an authentic sample of 5-methyl-2,3,4,5-tetrahydro-4-p-tolylsulphonylimino-1*H*-cyclopenta[*c*]quinoline (V).

5. *Preparation of 9-methyl-2,3,4,4a-tetrahydro-4a-p-tolylsulphonyl-aminocarbazole (VIII) and its reaction with p-chlorobenzenesulphonyl azide*:-

Experiment 4 was repeated, substituting p-chlorobenzenesulphonyl azide (0.8 g) for the tosyl azide. The chloroform extracts were evaporated after standing for 20 hours and the residue was triturated with methanol. The insoluble material was separated into its two components by preparative t.l.c. (silica gel, benzene/ethyl acetate 9:1).

The fore-running component formed colourless prisms (from ethanol), m.p. 209-210°, and was identical (m.p., i.r.) to an authentic sample of 2-p-chlorobenzenesulphonylimino-1-methyl-2'-p-tolylsulphonylamino-indoline-3-spirocyclopentane (XV). (Yield 30 mg, 2%).

The slow moving component was recrystallised from ethanol as colourless prisms, m.p. 222-225° and was identified as 4-p-chloro-benzenesulphonylimino-2,3,3a,4,5,9b-hexahydro-5-methyl-9b-p-tolyl-sulphonylamino-1H-cyclopenta[c]quinoline (XVI). (Yield 50 mg).

Found: C, 57.2; H, 4.8; N, 7.5; S, 12.1%

$C_{26}H_{26}ClN_3O_4S_2$ requires C, 57.4; H, 4.8; N, 7.7; S, 11.8%

$\lambda_{max.}$: 224 and 228 nm (ε 36,500 and 24,800)

$\nu_{max.}$: 1542 (C=N) and 3245 (N-H) $cm^{-1}$.

m/e: 543 (M, 2%), 479 (M - $SO_2$, 1%; m* 422.5), 388 (M - Ts, 1%), 372 (M - $TsNH_2$, 6%; m* 254.9), 368 (M - Cbs, 6%; m* 249.4), 308 (372 - $SO_2$, 9%; m* 255.0), 307 (308 - H, 12%; m* 306.0) and 197 (368 - $TsNH_2$, 100%; m* 105.5).

The mother liquors were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The following were obtained in order of elution: p-chlorobenzenesulphonyl azide (460 mg), compound (II) (140 mg, 11%), 4-p-chlorobenzenesulphonylimino-5-methyl-2,3,4,5-tetrahydro-1H-cyclopenta[c]quinoline (XVII) (250 mg, 20%), identical to an authentic sample and compound (XVI), identical to the sample obtained by preparative t.l.c. above. (Total yield 250 mg, 13%).

6. 6,7,8,9,10,10a-Hexahydro-10a-p-tolylsulphonylaminocyclohept-[b]indole (XX):-

A mixture of 5,6,7,8,9,10-hexahydrocyclohept[b]indole (5 g, 1 mol) and tosyl azide (10.5 g, 2 mol) was allowed to stand at room temperature for 2 weeks. Benzene (5 ml) and cyclohexane (5 ml) were added to the mixture, which was then allowed to stand for a further 10 days. The solid was collected and washed with benzene.

Recrystallisation from benzene gave pale yellow needles, m.p. 147-149°. (Yield 2.8 g, 33%).

Found: C, 67.7; H, 6.3; N, 8.1; S, 8.9%

$C_{20}H_{22}N_2O_2S$ requires C, 67.8; H, 6.2; N, 7.9; S, 9.0%

$\lambda_{max.}$: 202, 224 and 263 nm (ε 28,000, 16,300 and 5,250)

$\nu_{max.}$: 3080br (N-H) $cm^{-1}$

m/e: 354 (M, 9%), 199 (M - Ts, 100%), 182 (199 - $NH_3$, 21%; $m^*$ 166.5), 158 ( 199 - MeCN, 10%; $m^*$ 125.4) and 91 (Ts - $SO_2$; 36%).

7. 1-Methyl-2'-p-tolylsulphonylamino-2-p-tolylsulphonyliminoindoline-3-spirocyclohexane (XXI):-

a. 5,6,7,8,9,10-Hexahydro-5-methylcyclohept[b]indole (2 g, 1 mol) was added to a solution of tosyl azide (4 g, 2.02 mol) in methanol (6 ml). The solid was collected after 24 hours at room temperature and recrystallised from acetonitrile as colourless prisms, m.p. 236-239°. Evaporation of the recrystallisation liquors followed by recrystallisation from acetonitrile gave a mixture of colourless and yellow prisms which were separated manually. The colourless compound was identical (t.l.c., m.p., i.r.) to that obtained above. (Yield 2.65 g, 49%).

b. Tosyl azide (2 g, 2.02 mol) was added to a solution of 5,6,7,8,9,10-hexahydro-5-methylcyclohept[b]indole (1 g, 1 mol) in pyridine (5 ml). After 4 days at room temperature the solvent was removed *in vacuo* and the residue triturated with methanol. The solid was collected and recrystallised from acetonitrile as colourless prisms, m.p. 235-239° (Yield 300 mg, 11%).

c. Tosyl azide (1.98 g, 1 mol) in methanol (10 ml) was added to a solution of 5,6,7,8,9,10-hexahydro-5-methylcyclohept[b]indole (2 g, 1 mol) in the minimum of methanol, addition being carried out in four equal portions at three-hourly intervals. The mixture was allowed to stand overnight at room temperature, then the solid was collected and

recrystallised from acetonitrile as colourless prisms, m.p. 234-237°. (Yield 330 mg, 6%).

Found: C, 62.9; H, 5.8; N, 7.9; S, 11.9%

$C_{28}H_{31}N_3O_4S_2$ requires C, 62.6; H, 5.8; N, 7.8; S, 11.9%

$\lambda_{max.}$: 200, 224, 283 and 296sh nm (ε 43,400, 34,300, 16,300 and 12,200)

$\nu_{max.}$: 1585 (C=N) and 3250 (N-H) $cm^{-1}$.

m/e: see main section.

8. 2,4-Butano-1-methyl-1,2,3,4-tetrahydro-4-p-tolylsulphonylamino-3-p-tolylsulphonyliminoquinoline (XXIII):-

a. The yellow crystals obtained in experiment 7a were further recrystallised from acetonitrile as yellow prisms, m.p. 163-165°. (Yield 650 mg, 12%).

b. Chromatography of the mother liquors from experiment 7b on silica gel, eluting with benzene/ethyl acetate mixtures, afforded the compound as pale yellow prisms (from acetonitrile), m.p. 164-165°. (Yield 390 mg, 14%).

c. A solution of 5,6,7,8,9,10-hexahydro-5-methylcyclohept[b]-indole (1 g, 1 mol) and tosyl azide (2 g, 2.02 mol) in acetic acid (5 ml) was left at room temperature for 10 days. The solid was collected and recrystallised from chloroform/methanol as yellow prisms, m.p. 163-165°. (Yield 400 mg, 15%).

d. Chromatography of the mother liquors from experiment 7c (silica; benzene/ethyl acetate mixtures), gave the compound as yellow prisms (from acetonitrile), m.p. 162-164°.(Yield 50 mg, 1%).

Found: C, 63.0; H, 5.7; N, 8.0; S, 12.2%

$C_{28}H_{31}N_3O_4S_2$ requires C, 62.6; H, 5.8; N, 7.8; S, 11.9%

$\lambda_{max.}$: 202, 231 and 305 nm (ε 47,600, 31,300 and 1,600)

$\nu_{max.}$: 1600 (C=N) and 3295 (N-H) $cm^{-1}$.

m/e: no peaks above m/e 171.

9. 5-Methyl-5,6,6a,7,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-6-p-tolylsulphonyliminophenanthridine (XXVIII):-

a. Chromatography of the mother liquors from experiment 7a on silica gel, eluting with benzene/ethyl acetate mixtures, gave the compound as colourless prisms, m.p. 232-235° (from acetonitrile). (Yield 525 mg, 10%).

b. The mother liquors from experiment 7b were chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was obtained as colourless prisms, m.p. 230-233° (from acetonitrile). (Yield 400 mg, 15%).

c. The mother liquors from experiment 8c were evaporated and the residue recrystallised from acetonitrile as colourless prisms, m.p. 233-235°. (Yield 960 mg, 35%).

d. A solution of 5,6,7,8,9,10-hexahydro-5-methylcyclohept[b]-indole (1 g, 1 mol) and tosyl azide (2 g, 2.02 mol) in pyridine (5 ml) and 2N aqueous sodium hydroxide (1 ml) was left to stand at room temperature for 2 days. The precipitate was collected and recrystallised from ethanol as colourless prisms, m.p. 233-235°. (Yield 950 mg).

Chromatography of the liquors on silica gel, eluting with benzene/ethyl acetate mixtures, gave a further 780 mg of the product. (Total yield 1.73 g, 64%). No other products were obtained from this reaction.

Found: C, 62.6; H, 5.8; N, 7.9; S, 12.1%

$C_{28}H_{31}N_3S_2O_4$ requires C, 62.6; H, 5.8; N, 7.8; S, 11.9%

$\lambda_{max.}$: 201, 223, 282 and 292sh nm (ε 36,200, 31,100, 19,600 and 18,100)

$\nu_{max.}$: 1534 (C=N) and 3305(N-H) $cm^{-1}$.

m/e: 537 (M, 3%), 382 (M - Ts, 2%), 367 (M - TsNH, 8%), 211 (367 - H - Ts, 38%) and 91 (Ts - $SO_2$, 100%).

10. 6a,7,8,9,10,10a-Hexahydro-5-methyl-10a-p-tolylsulphonylamino-phenanthridinone (XXX):-

A solution of 5-methyl-5,6,6a,7,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-6-p-tolylsulphonyliminophenanthridine (300 mg) and potassium hydroxide (1 g) in ethanol (20 ml) and water (5 ml) was heated under reflux for 24 hours. The solution was cooled, poured into water (50 ml) and neutralised with acetic acid. The precipitate was collected, washed with water, dried and recrystallised from ethanol as colourless prisms, m.p. 250-253°. (Yield 160 mg, 75%).

Found: C, 65.3; H, 6.3; N, 7.3; S, 8.4%

$C_{21}H_{24}N_2O_3S$ requires C, 65.6; H, 6.3; N, 7.3; S, 8.3%

$\lambda_{max.}$: 205, 234, 253 and 282sh nm (ε 49,200, 12,300, 9,830 and 2,130)

$\nu_{max.}$: 1650 (C=O) and 3065 (N-H) $cm^{-1}$.

m/e: 384 (M, 23%), 229 (M - Ts, 15%), 214 (M - TsNH, 100%; $m^*$ 119.3), 213 (214 - H, 22%), 199 (214 - Me, 6%), 198 (213 - Me, 8%) and 187 (214 - HCN, 22%).

11. Reaction of 5-methyl-5,6,6a,7,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-6-p-tolylsulphonyliminophenanthridine with 1,5-diazabicyclo[4.3.0]non-5-ene:-

a. A solution of the compound (200 mg) and 1,5-diazabicyclo-[4.3.0.]non-5-ene (50 mg) in ethanol (20 ml) was heated under reflux for 24 hours. The solvent was removed *in vacuo* and the residue recrystallised from ethanol as colourless prisms identical (t.l.c., m.p., i.r.) to the starting material. (Recovery 155 mg, 78%).

T.l.c. of the liquors showed the presence of no compounds other than the starting materials.

b. A solution of the compound (200 mg) and 1,5-diazabicyclo-[4.3.0]non-5-ene (100 mg) in 2-methoxyethanol (20 ml) was heated under reflux for 24 hours. The solution was cooled and poured into water

(50 ml). The solid was collected, washed with water, dried and recrystallised from ethanol as colourless prisms, identical (t.l.c., m.p., i.r.) to the starting material. (Recovery 150 mg, 75%).

12. 5,6,7,8,9,10-Hexahydro-5-methyl-6-p-tolylsulphonylimino-phenanthridine (XXXII):-

a. 5-Methyl-5,6,6a,7,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-6-p-tolylsulphonyliminophenanthridine (130 mg) was heated at 230° and 0.01 mm Hg for 10 hours. The sublimate was dissolved in chloroform (10 ml) and the solution filtered. The solvent was removed in vacuo and the residue separated into its two components by preparative t.l.c. (silica gel, benzene/ethyl acetate 9:1, 3 elutions). The fore-running compound formed colourless prisms (from ethanol) identical (t.l.c., m.p., i.r.) to the starting material.

The back-running compound was recrystallised from ethanol as colourless needles, m.p. 181-182°. (Yield 20 mg, 23%).

b. A solution of 5-methyl-5,6,6a,7,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-6-p-tolylsulphonyliminophenanthridine (100 mg) in trifluoroacetic acid (0.5 ml) was allowed to stand at room temperature for 2 days. The solution was poured into water (10 ml), neutralised with 2N aqueous sodium carbonate and extracted with chloroform (3 x 5 ml). The extracts were washed with water and dried (magnesium sulphate). The solvent was removed in vacuo and the residue recrystallised from ethanol as colourless needles, m.p. 182-183°. (Yield 45 mg, 66%).

Found: C, 68.7; H, 6.0; N, 7.5; S, 8.9%

$C_{21}H_{22}N_2O_2S$ requires C, 68.9; H, 6.0; N, 7.7; S, 8.7%

$\lambda_{max.}$: 217, 259, 342 and 350sh nm ($\varepsilon$ 47,800, 25,200, 13,900 and 13,000)

$\nu_{max.}$: 1490 (C=N) $cm^{-1}$

m/e: 366 (M, 7%), 302 (M - $SO_2$, 17%), 301 (M - $SO_2$ - H, 36%; $m^*$ 247.5) and 211 (M - Ts, 100%).

13. Action of trifluoroacetic acid on 2,3,3a,4,5,9b-hexahydro-5-methyl-9b-p-tolylsulphonylamino-4-p-tolylsulphonylimino-1H-cyclopenta[c]quinoline (IV):-

A solution of the compound (200 mg) in trifluoroacetic acid (1 ml) was allowed to stand at room temperature for 2 days. The solution was poured into water (10 ml), neutralised with 2N aqueous sodium carbonate and extracted with chloroform (3 x 5 ml). The extracts were washed with water and dried (magnesium sulphate). The solvent was removed *in vacuo* and the residue recrystallised from acetonitrile as colourless needles, m.p. 212-213°. (Yield 80 mg, 59%).

The product was identical (m.p., i.r.) to an authentic sample of 5-methyl-4-p-tolylsulphonylimino-2,3,4,5-tetrahydro-1H-cyclopenta[c]-quinoline (V), recorded[1] m.p. 213-214°.

14. Action of trifluoroacetic acid on 4-p-chlorobenzenesulphonylamino-2-p-chlorobenzenesulphonylimino-1,2,3,4-tetrahydro-1,3,4-trimethylquinoline (XXXIV, Z = Cbs):-

A solution of the compound (200 mg) in trifluoroacetic acid (1 ml) was allowed to stand at room temperature for 2 days. Water (10 ml) was added and the solution was neutralised with 2N aqueous sodium carbonate , then extracted with chloroform (3 x 10 ml). The extracts were washed with water and dried (magnesium sulphate). The solvent was removed *in vacuo* and the residue recrystallised from acetonitrile. 2-p-Chlorobenzenesulphonylimino-1,2-dihydro-1,3,4-trimethylquinoline (XXXV) formed colourless needles, m.p. 178-179°. (Yield 107 mg, 82%).

Found: C, 59.9; H, 4.7; Cl, 9.7; N, 7.9; S, 9.3%

$C_{18}H_{17}ClN_2O_2S$ requires C, 59.9; H, 4.7; Cl, 9.9; N, 7.8; S, 8.9%

$\lambda_{max.}$: 215, 259 and 343 nm (ε 40,700, 21,700 and 9,490)

$\nu_{max.}$: 1503 (C=N) $cm^{-1}$.

m/e: 360 (M, 3%), 296(M - $SO_2$, 19%; $m^*$ 243.4), 295 (296 - H, 10%; $m^*$ 294.0), 185 (M - Cbs, 100%), 158 (185 - HCN, 9%; $m^*$ 134.9),

143 (158 - Me, 5%) and 128 (143 - Me, 5%; m* 114.6).

15. 5-Methyl-7,8,9,10-tetrahydrophenanthridinone (XXIX, n = 4):-

a. 6a,7,8,9,10,10a-Hexahydro-5-methyl-10a-p-tolylsulphonylaminophenanthridinone (200 mg) was heated at 230° and 0.01 mm Hg for 6 hours. The sublimate was dissolved in chloroform and the solution filtered. The solvent was removed in vacuo and the residue recrystallised from ethanol to give colourless prisms identical (t.l.c., m.p., i.r.) to the starting material. (Recovery 94 mg, 47%).

The liquors were evaporated to give a crystalline residue which was extracted with boiling petroleum ether (b.p. 60-80°). The petrol was removed in vacuo to give a colourless solid, recrystallised from petroleum ether (b.p. 60-80°) as colourless needles, m.p. 97-99°. (Yield 30 mg, 27%).

b. A solution of 5-methyl-5,6,6a,7,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-6-p-tolylsulphonyliminophenanthridine (1 g) and potassium hydroxide (2 g) in ethylene glycol (50 ml) and water (10 ml) was heated at 150° (oil bath) for 6 hours. The solution was cooled and poured into water (200 ml). The precipitate was collected, washed with water, dried and recrystallised from petroleum ether (b.p. 60-80°) as colourless needles, m.p. 100-101°. (Yield 240 mg, 61%).

c. A solution of 5,6,7,8,9,10-hexahydro-5-methyl-6-p-tolylsulphonyliminophenanthridine (40 mg) and potassium hydroxide (200 mg) in ethanol (4 ml) and water (1 ml) was heated under reflux for 2 hours. The solution was cooled and poured into water (10 ml). The mixture was extracted with chloroform (3 x 5 ml) then the extracts washed with water and dried (magnesium sulphate). The solvent was removed in vacuo and the residue recrystallised from petroleum ether (b.p. 60-80°) as colourless needles, m.p. 98-99°. (Yield 15 mg, 64%).

Found: C, 78.8; H, 7.2; N, 6.7%

$C_{14}H_{15}NO$ requires C, 78.9; H, 7.0; N, 6.6%

$\lambda_{max.}$: 209sh, 227, 245sh, 264sh, 272, 281, 315sh, 324 and 366sh nm

(ε 14,900, 30,000, 8,790, 4,140, 5,650, 5,050, 5,010, 6,280, and 4,260)

$\nu_{max.}$: 1640 (C=O) $cm^{-1}$

m/e: 213 (M, 100%), 212 (M - H, 73%; $m^*$ 211.0) and 198 (M - Me, 87%; $m^*$ 184.1).

16. 7,8,9,10-Tetrahydrophenanthridinone:-

A mixture of methyl cyclohexanone-2-carboxylate (6.6g, 1 mol) and aniline (4.0 g, 1 mol) was heated under reflux for 2 minutes. The mixture was cooled and poured dropwise into concentrated sulphuric acid (10 ml) with cooling and stirring. The mixture was heated (steam bath) for 15 minutes, then cooled and poured into water. The precipitate was collected. Three recrystallisations from acetic acid gave colourless needles, m.p. 268-270° (lit.[22] 267-268°). (Yield 850 mg, 10%).

17. 5-Methyl-7,8,9,10-tetrahydrophenanthridinone (XXIX, n = 4):-

7,8,9,10-Tetrahydrophenanthridinone (850 mg) was added to a solution of potassium hydroxide (400 mg) in ethanol (20 ml). The mixture was heated under reflux until the solid had dissolved, then the solvent was removed in vacuo. Dimethyl sulphate (10 ml) was added dropwise to the residue and the mixture was heated at 100° for ½ hour. 40% aqueous potassium hydroxide was added slowly until the mixture was strongly alkaline, then the precipitate was extracted into ether. The extracts were dried (magnesium sulphate) and the solvent removed in vacuo to yield a dark brown residue. This was extracted into boiling petroleum ether (b.p. 60-80°). Removal of the solvent and recrystallisation from petroleum ether (b.p. 60-80°) gave the product as colourless needles, m.p. 99-100°, identical (mixed m.p., i.r.) to that obtained in experiment 15. (Yield 585 mg, 64%).

18. 5,6,7,8,9,10-Hexahydro-5-methyl-10-p-tolylsulphonyliminocyclohept[b]indole (XL):-

a. Chromatography of the mother liquors from experiment 8c on silica gel, eluting with benzene/ethyl acetate mixtures, gave the compound as pale yellow needles, m.p. 177-179° (from ethanol). (Yield 80 mg, 4%).

b. The mother liquors from experiment 7c were evaporated and the residue chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was obtained as pale yellow needles (from ethanol), m.p. 175-178°. (Yield 30 mg, 1%).

Found: C, 68.5; H, 5.9; N, 7.6; S, 8.9%

$C_{21}H_{22}N_2O_2S$ requires C, 68.9; H, 6.0; N, 7.7; S, 8.7%

$\lambda_{max.}$: 217, 263, 272sh and 349 nm (ε 35,400, 10,200, 9,180 and 21,700)

$\nu_{max.}$: 1512 (C=N) $cm^{-1}$

m/e: 366 (M, 36%), 302 (M - $SO_2$, 37%; $m^*$ 249.2), 301 (302 - H, 22%; $m^*$ 300.0), 211 (M - Ts, 100%), 196 (211 - Me, 14%) and 169 ( 211 - MeCN - H, 90%; $m^*$ 135.4)

19. 5,6,7,8,9,10-Hexahydro-5-methyl-10-oxocyclohept[b]indole (XLV, R = Me):-

A solution of 5,6,7,8,9,10-hexahydro-5-methyl-10-p-tolylsulphonyliminocyclohept[b]indole (XL) (32 mg) and potassium hydroxide (300 mg) in ethanol (1 ml) and water (1 ml) was heated under reflux for 17 hours. The solution was cooled, poured into water and extracted with chloroform. The extracts were dried (magnesium sulphate) and the solvent removed in vacuo to give a brown crystalline residue. The crude product had m.p. 130-135°. (Yield 14 mg, 75%).

$\lambda_{max.}$: 212, 248, 263sh and 304 nm (ε 18,500, 10,700, 6,200 and 9,370)

20. 5,6,7,8,9,10-Hexahydro-6-oxocyclohept[b]indole (XLII, R = H):-

A solution of 5,6,7,8,9,10-hexahydrocyclohept[b]indole (4.5 g) in methanol (100 ml) was added dropwise to a stirred solution of periodic acid (12 g) in water (20 ml) and methanol (50 ml). The mixture was stirred for 20 minutes at 20° then poured into water and extracted with ether (2 x 100 ml). The combined extracts were washed with saturated sodium thiosulphate solution, then water, and finally dried (magnesium sulphate). Removal of the solvent *in vacuo* gave a dark brown tar. The crude product was chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The last compound to be eluted from the column was recrystallised from benzene/petroleum ether (b.p. 60-80°) as colourless plates, m.p. 147-149° (lit.[28] 144.5-147°). (Yield 680 mg, 14%).

$\nu_{max.}$: 1648 (C=O) and 3295 (N-H) $cm^{-1}$.

21. 5,6,7,8,9,10-Hexahydro-5-methyl-6-oxocyclohept[b]indole (XLII, R = Me):-

Dimethyl sulphate (1.9 ml) was added dropwise to a solution of 5,6,7,8,9,10-hexahydro-6-oxocyclohept[b]indole (630 mg) and potassium hydroxide (3 g) in acetone (2.5 ml) and water (4.5 ml), heated under reflux. After addition the solution was heated for 45 minutes, then cooled and poured into water. The resulting mixture was extracted with benzene. The extracts were washed with saturated sodium chloride solution, then water, and dried (magnesium sulphate). Removal of the solvent *in vacuo* gave a dark oil which was triturated with methanol. Removal of the methanol *in vacuo* gave a brown crystalline solid, recrystallised from methanol as colourless plates, m.p. 61-63° (lit.[28] 64.5-65.5). (Yield 310 mg, 46%).

22. 10-Methyl-1,2,3,4-tetrahydro-9-acridanone (XLIII):-

A mixture of N-methylanthranilic acid (0.8 g, 1 mol) and cyclohexanone (1 g, 1.9 mol) was heated at 220° for 3 hours. Cooling gave a brown solid residue, recrystallised from benzene as pale brown prisms, m.p. 170-173° (lit.[31] 170-172°). (Yield 650 mg, 58%).

23. 4-Oxo-1,2,3,4-tetrahydrocarbazole (XLVI, R = H):-

Acetic acid was added to a mixture of phenylhydrazine (4.8 g, 1 mol) in water (30 ml) until a clear solution was obtained. This was added rapidly to a solution of cyclohexane-1,3-dione (5 g, 1 mol) in water (50 ml), with stirring and cooling in ice. The precipitate was collected, washed with water and dried. Recrystallisation from ethanol gave cyclohexane-1,3-dione monophenylhydrazone, m.p. 179-181°. (Yield 5.5 g, 61%).

A mixture of the monophenylhydrazone (5.5 g) in water (55 ml) and concentrated sulphuric acid (21 ml) was heated at 100° for 1½ hours. The solution was decanted from some tarry material formed, then slowly diluted with water (180 ml). The precipitate was allowed to stand overnight to harden, then collected and washed with water. Drying and recrystallisation from ethanol gave pale brown prisms, m.p. 219-224°. (Yield 2.1 g, 42%).

A second recrystallisation from ethanol/decolourising charcoal gave m.p. 225-227° (lit.[32] 223°).

24. 9-Methyl-4-oxo-1,2,3,4-tetrahydrocarbazole (XLVI, R = Me):-

Dimethyl sulphate was added dropwise to a stirred, hot solution of 4-oxo-1,2,3,4-tetrahydrocarbazole (1 g) in 2N aqueous sodium hydroxide (250 ml) until precipitation was complete. The mixture was cooled and the solid collected, washed with water and dried. Recrystallisation from ethanol gave colourless plates, m.p. 199-201° (lit.[33] 198-199°). (Yield 700 mg, 65%).

25. 5-Acetylvaleric acid:-

A solution of chromium trioxide (73 g) in concentrated sulphuric acid (123 g) and water (220 ml) was added to a cooled, stirred solution of 2-methylcyclohexanol (38 g) in concentrated sulphuric acid (123 g) and water (220 ml). The rate of addition was controlled to maintain the temperature in the range 30-2°. After addition was complete stirring was continued for 1 hour, then the mixture was allowed to stand overnight at room temperature. The acid solution was extracted with ether (4 x 200 ml) and the extracts were dried (magnesium sulphate). The ether was removed *in vacuo* to yield a pale yellow oil (39.2 g). This was distilled *in vacuo* and the fraction distilling over the range 135-136°/0.05 mm Hg (lit.[36] 122-123°/1 mm) was collected as a colourless oil. (Yield 28.1 g, 59%).

26. Ethyl 5-(indol-2-yl)valerate (XLVIII, R = Et):-

A solution of ethanol (280 ml) and water (40 ml) was prepared. To this solution (240 g) was added concentrated sulphuric acid (560 g, 304 ml) with stirring and cooling.

A mixture of 5-acetylvaleric acid (15 g, 1 mol) and phenylhydrazine (11.25 g, 1 mol) was allowed to stand at room temperature for 15 minutes and then at 100° for 10 minutes. To the resulting mixture was added the above sulphuric acid/ethanol/water solution (500 ml). The mixture was heated under reflux for 30 minutes then cooled and poured into ice/water (1 litre). The mixture was extracted with ether (4 x 200 ml) and the extracts washed with sodium carbonate solution (2 x 100 ml) and dried (magnesium sulphate). The ether was removed *in vacuo* to give a crystalline solid (16.1 g). This was boiled with ethanol (15 ml) and allowed to stand overnight. The solid was collected, washed with ethanol and dried. The compound formed colourless plates, m.p. 93-95°. (Yield 4.1 g, 16%).

Found: C, 73.3; H, 7.8; N, 5.6%

$C_{15}H_{19}NO_2$ requires C, 73.5; H, 7.8; N, 5.7%

$\lambda_{max.}$: 210, 273, 278, 282 and 289 nm ($\varepsilon$ 30,100, 7,180, 7,200, 7,130 and 5,790)

$\nu_{max.}$: 1728 (C=O) and 3360 (N-H) $cm^{-1}$

m/e: 245 (M, 37%), 200 (M - OEt, 19%), 172 (M - COOEt, 4%), 157 (M - $CH_3COOEt$, 9%), 144 (M - $CH_2CH_2COOEt$, 63%; $m^*$ 84.6), 143 (144 - H, 27%; $m^*$ 142.0), 131 (M - $CH_2$:$CHCH_2COOEt$, 55%; $m^*$ 70.0) and 130 (131 - H, 100%; $m^*$ 129.0)

27. Ethyl 4-(2-methylindol-3-yl)butyrate (XLIX, R = Et):-

The ethanolic liquors from the recrystallisation of ethyl 5-(indol-2-yl)valerate (experiment 26) were evaporated and the residue left to stand overnight at 0°. The solid was collected and recrystallised from cyclohexane as colourless needles, m.p. 65-68°. (Yield 1.7 g, 7%).

Found: C, 73.5; H, 7.7; N, 5.8%

$C_{15}H_{19}NO_2$ requires C, 73.5; H, 7.8; N, 5.7%

$\lambda_{max.}$: 227, 283 and 291 nm ($\varepsilon$ 41,200, 8,800, and 7,840)

$\nu_{max.}$: 1726 (C=O) and 3370 (N-H) $cm^{-1}$

m/e: 245 (M, 21%), 200 (M - OEt, 9%), 144 (M - $CH_2CH_2COOEt$, 100%; $m^*$ 84.6) and 143 (144 - H, 10%; $m^*$ 142.0).

28. 5-(Indol-2-yl)valeric acid (XLVIII, R = H):-

a. A solution of ethyl 5-(indol-2-yl)valerate (2.5 g) in 2N aqueous sodium hydroxide (10 ml) and ethanol (10 ml) was heated for 10 minutes (steam bath). The solution was cooled and poured into water (50 ml). The resultant solution was acidified with concentrated hydrochloric acid and the precipitate was collected, washed with water and dried. Recrystallisation from benzene gave colourless plates, m.p. 147-148°. (Yield 2.0 g, 90%).

b. The carbonate washings from experiment 26 were acidified with concentrated hydrochloric acid. The solid was collected, washed with water and dried. Recrystallisation from benzene gave colourless plates, m.p. 145-147°. (Yield 1.7 g, 8%).

Found: C, 72.1; H, 7.0; N, 6.4%

$C_{13}H_{15}NO_2$ requires C, 71.9; H, 6.9; N, 6.5%

$\lambda_{max.}$: 220, 273, 278, 282 and 289 nm ($\varepsilon$ 29,800, 7,430, 7,480 7,410 and 6,050)

$\nu_{max.}$: 1714 (C=O) and 3390(N-H) $cm^{-1}$.

m/e: 217 (M, 29%), 172 (M - COOH, 1%), 158 (M - $CH_2COOH$, 2%), 144 (M - $CH_2CH_2COOH$, 19%; $m^*$ 95.6), 143 (144 - H, 13%; $m^*$ 142.0), 131 (M - $CH_2$:$CHCH_2COOH$, 45%; $m^*$ 79.1) and 130 (131 - H, 100%; $m^*$ 129.0).

29. 5,6,7,8,9,10-Hexahydro-10-oxocyclohept[b]indole (XLV, R = H):-

5-(Indol-2-yl)valeric acid (200 mg) and phosphorus oxychloride (5 ml) were heated at 100° for 5 minutes. The solution was cooled and poured carefully into water (50 ml). The mixture was extracted with chloroform (5 x 10 ml) and the extracts were washed with 2N aqueous sodium carbonate (2 x 10 ml) then dried (magnesium sulphate). Removal of the solvent *in vacuo* gave a crystalline residue, recrystallised from ethanol as colourless prisms, m.p. 224-225° (sealed capillary) (lit.[34b] 221°). (Yield 105 mg, 57%).

Found: C, 78.2; H, 6.6; N, 7.1%

Calculated for $C_{13}H_{13}NO$: C, 78.4; H, 6.5; N, 7.0%

30. 5,6,7,8,9,10-Hexahydro-5-methyl-10-oxocyclohept[b]indole (XLV, R = Me):-

A suspension of 5,6,7,8,9,10-hexahydro-10-oxocyclohept[b]indole (210 mg) in acetone (5 ml) and 50% aqueous sodium hydroxide (2 ml) was stirred while dimethyl sulphate (1 ml) was added dropwise. The

mixture was stirred for 30 minutes then poured into water (25 ml). The solid was collected, washed with water, dried and recrystallised from ethanol as colourless needles, m.p. 135-137°. (Yield 165 mg, 73%).

Found: C, 78.8; H, 7.2; N, 6.6%

$C_{14}H_{15}NO$ requires C, 78.9; H, 7.0; N, 6.6%

$\nu_{max.}$: 1628 (C=O) $cm^{-1}$

m/e: 213 (M, 100%), 185 (M - CO, 28%; $m^*$ 160.7), 184 (185 - H, 80%; $m^*$ 183.0) and 144 ($C_{10}H_{10}N$, 88%).

31. Action of acids on 1-methyl-2'-p-tolylsulphonylamino-2-p-tolylsulphonyliminoindoline-3-spirocyclohexane (XXI):-

a. A solution of the compound (100 mg) in the minimum of trifluoroacetic acid was allowed to stand at room temperature for 24 hours. The solution was poured into water and extracted with chloroform. The extracts were washed with 2N aqueous sodium carbonate, then water, and dried (magnesium sulphate). Evaporation and recrystallisation from acetonitrile resulted in the recovery of starting material.

b. A solution of the compound (100 mg) in ethanol (4 ml) and concentrated hydrochloric acid (1 ml) was heated under reflux for 2 hours. The solution was cooled and diluted with water. Work-up as above resulted in the recovery of starting material.

In neither of these experiments did t.l.c. of the liquors show any material present other than starting material.

32. Action of heat on 1-methyl-2'-p-tolylsulphonylamino-2-p-tolylsulphonyliminoindoline-3-spirocyclohexane (XXI):-

The compound (300 mg) was heated at 200° and 0.01 mm Hg for 5 hours. The sublimate was recrystallised from benzene as colourless plates, m.p. 132-134°, identical (i.r.) to toluene-p-sulphonamide.

(Yield 56 mg, 59%).

No crystalline material could be obtained from the sublimation residue, but t.l.c. showed the absence of any spot corresponding to compound (XL).

33. 7,8,9,10,11,11a-Hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (LVI, Z = Ts):-

a. A mixture of 6,7,8,9,10,11-hexahydro-5H-cyclooct[b]indole (3 g, 1 mol) and tosyl azide (6 g, 2 mol) was allowed to stand at room temperature for 5 days. Benzene (15 ml) was added to the mixture and the solid was collected. Recrystallisation from benzene gave colourless needles, m.p. 163-164°. (Yield 4.9 g, 88%).

b. A solution of 6,7,8,9,10,11-hexahydro-5H-cyclooct[b]indole (500 mg, 1 mol) and tosyl azide (1 g, 2 mol) in pyridine (5 ml) was left at room temperature for 5 days. The solvent was removed in vacuo and benzene (5 ml) was added to the residue. The solid was collected and recrystallised from benzene as colourless needles, m.p. 162-164°. (Yield 470 mg, 51%).

c. 2N Aqueous sodium hydroxide (1 ml) was added to a solution of 6,7,8,9,10,11-hexahydro-5H- cyclooct[b]indole (500 mg, 1 mol) and tosyl azide (1 g, 2 mol) in pyridine (5 ml). The mixture was left at room temperature for 3 days then the solvent was removed in vacuo and the gelatinous residue extracted several times with hot benzene. Evaporation of the extracts followed by recrystallisation from benzene gave colourless rods, m.p. 180-181°. The product was identical (t.l.c., i.r.) to that obtained in experiments a and b above. (Yield 540 mg, 58%).

Found: C, 69.0; H, 6.5; N, 7.6; S, 8.6%

$C_{21}H_{24}N_2O_2S$ requires C, 68.5; H, 6.5; N, 7.6; S, 8.7%

$\lambda_{max.}$: 204, 223 and 262 nm ($\varepsilon$ 27,300, 23,100 and 3,990)

$\nu_{max.}$: 3090 (N-H) $cm^{-1}$

m/e: 368 (M, 3%), 213 (M - Ts, 100%) and 91 (Ts - $SO_2$, 13%).

34. 11a-p-Chlorobenzenesulphonylamino-7,8,9,10,11,11a-hexahydro-6H-cyclooct[b]indole (LVI, Z = Cbs):-

A solution of 6,7,8,9,10,11-hexahydro-5H-cyclooct[b]indole (1 g, 1 mol) and p-chlorobenzenesulphonyl azide (2.3 g, 2.1 mol) in benzene (10 ml) was allowed to stand at room temperature for 7 days. The crystalline precipitate was collected. Recrystallisation from benzene gave very fine colourless needles, m.p. 169-171°. (Yield 1.56 g, 80%).

Found: C, 61.9; H, 5.7; Cl, 9.0; N, 7.3; S, 8.0%

$C_{20}H_{21}ClN_2O_2S$ requires C, 61.8; H, 5.4; Cl, 9.1; N, 7.2; S, 8.2%

$\lambda_{max.}$: 201, 223, 229sh, 283sh and 263sh nm ($\varepsilon$ 36,600, 26,900, 21,000, 13,400 and 4,450)

$\nu_{max.}$: 3245 (N-H) $cm^{-1}$

m/e: 388 (M, 1%), 213 (M - Cbs, 100%) and 111 (Cbs - $SO_2$, 6%).

35. Action of heat on 7,8,9,10,11,11a-hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (LVI, Z = Ts):-

a. 7,8,9,10,11,11a-Hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (3 g) was heated at 170° for 5 minutes. The melt was cooled and methanol (10 ml) was added. The solid was collected and recrystallised from benzene/hexane. 8,9,10,11-Tetrahydro-5H-cyclooct[b]indole (LXII) formed almost colourless plates, m.p. 122-124°. (Yield 175 mg).

Found: C, 85.2; H, 7.8; N, 7.1%

$C_{14}H_{15}N$ requires C, 85.3; H, 7.6; N, 7.1%

$\lambda_{max.}$: 207, 236 and 303 nm ($\varepsilon$ 23,500, 30,800 and 18,200)

$\nu_{max.}$: 3375 (N-H) $cm^{-1}$

m/e: 197 (M, 93%), 196 (M - H, 31%; $m^*$ 195.0) and 168 (M - $C_2H_4$ - H, 100%; $m^*$ 143.2)

The mother liquors were evaporated and benzene (10 ml) was added. The solid was collected and recrystallised from benzene as colourless plates, m.p. 136-137°. The compound was identical (m.p., t.l.c., i.r.) to toluene-p-sulphonamide. The mother liquors were again evaporated and chromatographed on silica gel, eluting firstly with benzene/hexane mixtures and then benzene/ethyl acetate mixtures. The following compounds were obtained in order of elution:

i A small amount of a highly insoluble, colourless solid, m.p. 300°.

ii 8,9,10,11-tetrahydro-5H-cyclooct[b]indole, m.p. 120-124° (from hexane). (Yield 370 mg; total yield 545 mg, 34%).

iii Toluene-p-sulphonamide (Yield 140 mg; total yield 1.38 g, 98%).

b. A solution of 7,8,9,10,11,11a-hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (3 g) in propanol (20 ml) was boiled under reflux for 24 hours. The solvent was removed in vacuo and methanol (10 ml) was added to the residue. The solid was collected and recrystallised from ethanol. 6,7,8,9,10,11-Hexahydro-6-p-tolylsulphonylamino-5H-cyclooct[b]indole (LXIV) formed colourless plates, m.p. 192-193°. (Yield 390 mg).

Found: C, 68.4; H, 6.6; N, 7.6; S, 8.6%

$C_{21}H_{24}N_2O_2S$ requires C, 68.5; H, 6.5; N, 7.6; S, 8.7%

$\lambda_{max.}$: 225, 277sh, 284 and 291sh nm ($\varepsilon$ 40,100, 6,280, 6,590 and 5,600)

$\nu_{max.}$: 3250 (N-H) and 3380 (N-H) $cm^{-1}$.

m/e: 368 (M, 74%), 213 (M - Ts, 92%), 197 (M - $TsNH_2$, 20%), 186 (213 - HCN, 53%), 170 (197 - $C_2H_2$ - H, 44%) and 130 ($C_9H_8N$, 100%).

The liquors were evaporated and benzene (10 ml) was added. The solid was collected after 24 hours and recrystallised from benzene as colourless plates, m.p. 135-137°. The compound was identical (m.p., i.r.) to toluene-p-sulphonamide. (Yield 870 mg).

The liquors were again evaporated and chromatographed on silica gel, eluting firstly with benzene/hexane mixtures and then with benzene/ethyl acetate mixtures. The following products were obtained in order of elution:

i 8,9,10,11-Tetrahydro-5H-cyclooct[b]indole as colourless prisms, m.p. 124-126° (from hexane). (Yield 505 mg, 31%).

ii 6,7,8,9,10,11-Hexahydro-6-p-tolylsulphonylamino-5H-cyclooct[b]indole, recrystallised from ethanol as colourless plates, m.p. 190-192°. (Yield 130 mg; total yield 520 mg, 17%).

iii Toluene-p-sulphonamide (Yield 130 mg; 1.0 g).

36. 7,8,9,10,11,11a-Hexahydro-6-oxo-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (LXVI):-

a. A solution of 6,7,8,9,10,11-hexahydro-5H-cyclooct[b]indole (500 mg, 1 mol) and tosyl azide (1 g, 2 mol) in acetic acid (5 ml) was left to stand at room temperature for 3 weeks. The solid was collected and recrystallised from acetonitrile as colourless needles, m.p. 204-206°. (Yield 270 mg, 28%).

b. 7,8,9,10,11,11a-Hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (1 g) was dissolved in acetic acid (20 ml) and the solution was left to stand at room temperature for 4 weeks. The solid was collected, washed with methanol and dried. The crude solid had m.p. 205-207°. (Yield 765 mg, 74%).

c. A slow stream of air was passed at room temperature through a solution of 7,8,9,10,11,11a-hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (2 g) and cupric acetate (100 mg) in acetic acid (40 ml). After 15 hours the solvent was removed in vacuo and methanol (50 ml) and 2N aqueous ammonia (100 ml) were added to the residue. After 1 hour the solid was collected. This was boiled with acetonitrile (20 ml) and the solid was again collected. Recrystallisation from pyridine/methanol gave almost colourless

needles, m.p. 197-200°. (Yield 650 mg, 31%).

d. A mixture of 7,8,9,10,11,11a-hexahydro-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (1 g) and platinum black (50 mg) in acetic acid (20 ml) was shaken in air at room temperature. After 2 weeks the solvent was removed in vacuo and the residue extracted several times with boiling chloroform. The extracts were cooled, washed with sodium carbonate solution and dried (magnesium sulphate). Removal of the chloroform in vacuo and trituration with methanol gave a brown solid which was collected and washed with methanol. The crude product had m.p. 201-204°. (Yield 820 mg, 79%).

Found: C, 66.0; H, 5.9; N, 7.3; S, 8.2%

$C_{21}H_{22}N_2O_3S$ requires C, 66.0; H, 5.8; N, 7.3; S, 8.4%

$\lambda_{max.}$: 201, 231, 287sh and 305 nm (ε 32,500, 16,600, 5,180 and 6,170).

$\nu_{max.}$: 1692 (C=O) and 3225 (N-H) $cm^{-1}$

m/e: 382 (M, 7%), 354 (M - CO, 7%; $m^*$ 328.1), 325 (M - $C_2H_5CO$, 8%), 318 (M - $SO_2$, 15%; $m^*$ 264.7), 227 (M - Ts, 100%) and 199 (227 - CO, 96%).

37. 2'-Oxo-2-p-tolylsulphonyliminoindoline-3-spirocycloheptane (LXXIV):-

Experiment 36d was repeated and the crude solid was boiled in 2-methoxyethanol. The solvent was removed in vacuo and methanol (5 ml) was added to the residue. The solid was collected and recrystallised from ethanol as pale yellow prisms, m.p. 173-174°. (Yield 333 mg, 32%).

Found: C, 66.0; H, 5.9; N, 7.3; S, 8.0%

$C_{21}H_{22}N_2O_3S$ requires C, 66.0; H, 5.8; N, 7.3; S, 8.4%

$\lambda_{max.}$: 224, 279, 291 sh and 302sh nm (ε 24,800, 15,900, 11,400 and 8,650)

$\nu_{max.}$: 1610 (C=N), 1703 (C=O) and 3270 (N-H) $cm^{-1}$

m/e: 382 (M, 22%), 354 (M - CO, 28%; $m^*$ 328.1), 325 (354 - $C_2H_5$, 28%; $m^*$ 298.4), 227 (M - Ts, 68%) and 199 (354 - Ts, 100%; $m^*$ 111.9).

38. 5a-Hydroxy-5a,6,7,8,9,10,11,11a-octahydro-6-oxo-11a-p-tolylsulphonylamino-5H-cyclooct[b]indole (LXXV):-

A suspension of 7,8,9,10,11,11a-hexahydro-6-oxo-11a-p-tolylsulphonylamino-6H-cyclooct[b]indole (500 mg) in 2N aqueous sodium hydroxide (10 ml) was heated at 100° (steam bath). A deep orange solution was formed and after 30 minutes a pale yellow precipitate began to separate. Heating was continued for a further 1½ hours then the solution was cooled and the solid collected. Recrystallisation from ethanol gave colourless needles, m.p. 240-241°. (Yield 105 mg, 20%).

Found: C, 62.5; H, 6.1; N, 7.0; S, 8.1%

$C_{21}H_{24}N_2O_4S$ requires C, 63.0; H, 6.0; N, 7.0; S, 8.0%

$\lambda_{max.}$: 233, 250, 257 and 283 nm ($\varepsilon$ 13,200, 10,300, 8,900 and 2,530)

$\nu_{max.}$: 1707 (C=O), 3275 (N-H) and 3420 (O-H) $cm^{-1}$

m/e: 400 (M, 10%), 372 (M - CO, 7%; $m^*$ 346.0), 245 (M - Ts, 100%), 228 (245 - OH, 46%; $m^*$ 212.2), 227 (228 - H, 41%) and 217 (372 - Ts, 56%; $m^*$ 126.6).

39. 5-Methyl-5,6,6a,8,9,10,11,11a-octahydro-11a-p-tolylsulphonylamino-6-p-tolylsulphonylimino-7H-cyclohepta[c]quinoline (LXXVII):-

a. A solution of 6,7,8,9,10,11-hexahydro-5-methyl-5H-cyclooct[b]indole (2 g, 1 mol) and tosyl azide (3.9 g, 2.1 mol) in diethyl ether (25 ml) was left at room temperature for 2 weeks. The solid was collected and recrystallised from propanol as colourless needles, m.p. 188-190°. (Yield 2.39 g, 46%).

b. 6,7,8,9,10,11-Hexahydro-5-methyl-5H-cyclooct[b]indole

(1 g, 1 mol) and tosyl azide (1.9 g, 2 mol) were dissolved in acetic acid (10 ml). After 4 days at room temperature the solid was collected and recrystallised from propanol as colourless needles, m.p. 188-190°. (Yield 420 mg, 16%).

c. A solution of 6,7,8,9,10,11-hexahydro-5-methyl-5H-cyclooct[b]indole (2 g, 1 mol) and tosyl azide (3.9 g, 2.1 mol) in ethanol (20 ml) was allowed to stand at room temperature for 2 days. The solid was collected and recrystallised from propanol as colourless plates, m.p. 207-209°. The compound was identical (t.l.c., i.r.) to that obtained in preparations a and b above. (Yield 2.3 g, 45%).

Found:. C, 63.4; H, 6.2; N, 7.6; S, 11.9%

$C_{29}H_{33}N_3O_4S_2$ requires C, 63.2; H, 6.0; N, 7.6; S, 11.6%

$\lambda_{max.}$: 224 and 287 nm ($\varepsilon$ 26,100 and 15,200)

$\nu_{max.}$: 1536 (C=N) and 3230 (N-H) $cm^{-1}$

m/e: 380 (M - $TsNH_2$, 5%), 316 (380 - $SO_2$, 2%; $m^*$ 262.8), 315 (316 - H, 2%), 225 (380 - Ts, 100%; $m^*$ 133.2) and 91 (Ts - $SO_2$, 24%).

40. 5,6,8,9,10,11-Hexahydro-5-methyl-6-p-tolylsulphonylimino-7H-cyclohepta[c]quinoline (LXXVIII):-

a. 5-Methyl-5,6,6a,8,9,10,11,11a-octahydro-11a-p-tolylsulphonylamino-6-p-tolylsulphonylimino-7H-cyclohepta[c]quinoline (500 mg) was heated for 5 minutes at 100° (steam bath) in ethanol (2 ml) and 2N aqueous sodium hydroxide (2 ml). The solution was cooled, diluted with water and the precipitate was extracted into chloroform (3 x 5 ml). The extracts were dried (magnesium sulphate) and the solvent was removed in vacuo to give a colourless crystalline solid. Recrystallisation from methanol gave colourless prisms, m.p. 147-148°. (Yield 96 mg, 28%).

b. 5-Methyl-5,6,6a,8,9,10,11,11a-octahydro-11a-p-tolylsulphonylamino-6-p-tolylsulphonylimino-7H-cyclohepta[c]quinoline (250 mg) and

1,5-diazabicyclo[4.3.0]non-5-ene (60 mg) were boiled under reflux for 5 minutes in ethanol (3 ml). Water (10 ml) was added and the mixture was extracted with chloroform (3 x 5 ml). The extracts were dried (magnesium sulphate) and the solvent removed *in vacuo*. Recrystallisation of the residue from methanol gave colourless prisms, m.p. 147-148°. (Yield 143 mg, 83%).

c. 5-Methyl-5,6,6a,8,9,10,11,11a-octahydro-11a-*p*-tolylsulphonylamino-6-*p*-tolylsulphonylimino-7*H*-cyclohepta[*c*]quinoline (200 mg) was heated slowly to its melting point (oil bath). The melt was allowed to cool and then dissolved in chloroform (5 ml). The solution was washed with 2N aqueous sodium hydroxide (10 ml) and dried (magnesium sulphate). Evaporation and recrystallisation from methanol gave colourless prisms, m.p. 146-147°. (Yield 96 mg, 70%).

d. A solution of 6,7,8,9,10,11-hexahydro-5-methyl-5*H*-cyclooct[*b*]indole (2 *g*, 1 mol) and tosyl azide (3.9 *g*, 2.1 mol) in pyridine (10 ml) was left to stand at room temperature for 2 days. The solvent was removed *in vacuo* and acetonitrile (10 ml) was added to the residue. The solid was collected and recrystallised from methanol as colourless prisms, m.p. 147-148°. (Yield 440 mg).

Chromatography of the liquors on silica gel, eluting with benzene/ethyl acetate mixtures gave a further 720 mg of the product as the last compound to be eluted. (Total yield 1.16 *g*, 33%).

e. The mother liquors from experiment 39b were chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The last compound to be eluted was recrystallised from methanol as colourless prisms, m.p. 148-149°. (Yield 230 mg, 13%).

f. Evaporation and chromatography (silica gel; benzene/ethyl acetate mixtures) of the mother liquors from experiment 39c gave the compound as colourless prisms, m.p. 145-147° (from methanol). (Yield 94 mg, 3%).

Found: C, 68.8; H, 6.2; N, 7.3; S, 8.6%

$C_{22}H_{24}N_2O_2S$ requires C, 69.5; H, 6.3; N, 7.4; S, 8.4%

$\lambda_{max.}$: 218, 259, 307sh, 348 and 356sh nm ($\varepsilon$ 43,300, 25,400, 6,250, 13,200 and 11,700)

$\nu_{max.}$: 1495 (C=N) $cm^{-1}$

m/e: 380 (M, 5%), 316 (M - $SO_2$, 3%; $m^*$ 262.8), 315 (316 - H, 2%), 225 (M - Ts, 100%; $m^*$ 133.2), 198 (225 - HCN, 26%) and 91 (Ts - $SO_2$, 13%).

41. 5,6,8,9,10,11-Hexahydro-5-methyl-6-oxo-7H-cyclohepta[c]quinoline (LXXIX):-

Preparative thin layer chromatography (silica, benzene/ethyl acetate 9:1) of the methanolic mother liquors from experiment 40a gave the compound as colourless prisms, m.p. 100-102° (from 50% aqueous methanol). (Yield 70 mg, 34%).

Found: C, 79.1; H, 7.5; N, 6.2%

$C_{15}H_{17}N$ O requires C, 79.3; H, 7.5; N, 6.2%

$\lambda_{max.}$: 211sh, 232, 248sh, 271sh, 278, 288, 320sh, 331 and 345 nm ($\varepsilon$ 20,600, 42,400, 8,310, 5,950, 8,120, 7,400, 6,450, 8,060 and 5,500)

$\nu_{max.}$: 1635 (C=O) $cm^{-1}$.

m/e: 227 (M, 100%), 226 (M - H, 38%; $m^*$ 225.0), 212 (M - Me, 59%; $m^*$ 198.0), 199 (M - CO, 34%) and 198 (199 - H, 88%; $m^*$ 197.0)

42. 1-Methyl-2'-p-tolylsulphonylamino-2-p-tolylsulphonylimino-indoline-3-spirocycloheptane (LXXX):-

a. The mother liquors from experiment 39a were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The product was recrystallised from ethanol as colourless needles, m.p. 168-170°. (Yield 64 mg, 1%).

b. Chromatography of the mother liquors from experiment 39c (silica, benzene/ethyl acetate) gave the compound as colourless

needles (from ethanol), m.p. 170-172°. (Yield 200 mg, 4%).

c. The mother liquors from experiment 40d were chromatographed (silica, benzene/ethyl acetate) and the product was recrystallised from ethanol as colourless needles, m.p. 168-170°. (Yield 91 mg, 2%).

Found: C, 63.0; H, 5.9; N, 7.6; S, 11.5%

$C_{29}H_{33}N_3O_4S_2$ requires C, 63.2; H, 6.0; N, 7.6; S, 11.6%

$\lambda_{max.}$: 205, 226, 281sh, 287 and 305 nm ($\varepsilon$ 31,800, 37,400, 13,900, 15,200 and 11,500)

$\nu_{max.}$: 1570 (C=N) and 3190 (N-H) $cm^{-1}$

m/e: 551 (M, 9%), 468 (M - $C_5H_9N$, 31%), 396 (M - Ts, 9%; $m^*$ 284.6), 381 (M - TsNH, 1%), 368 (M -$TsN{:}CH_2$, 1%), 314 (M - $TsN{:}CHCH_2CH_2CH{:}CH_2$, 33%; $m^*$ 178.9) and 91 (Ts - $SO_2$, 100%)

43. 6,7,8,9,10,11-Hexahydro-5-methyl-11-p-tolylsulphonylimino-5H-cyclooct[b]indole (LXXXII):-

The compound was obtained by chromatography (silica gel, benzene/ethyl acetate mixtures) of the mother liquors from experiments 39a, 39c and 40d. The results were as follows.

| Experiment | Yield | m.p. |
|---|---|---|
| 39a | 50 mg (1%) | 195-196° |
| 39c | 92 mg (3%) | 193-195° |
| 40d | 184 mg (5%) | 194-195° |

The compound formed almost colourless plates from propanol.

Found: C, 69.7; H, 6.6; N, 7.2; S, 7.9%

$C_{22}H_{24}N_2O_2S$ requires C, 69.5; H, 6.3; N, 7.4; S, 8.4%

$\lambda_{max.}$: 213, 256, 267, 274 and 342 nm ($\varepsilon$ 38,500, 11,800, 10,400, 10,100 and 14,700)

$\nu_{max.}$: 1514 (C=N) $cm^{-1}$

m/e: 380 (M, 22%), 316 (M - $SO_2$, 11%; $m^*$ 262.6), 225 (M - Ts, 100%), 210 (225 - Me, 13%) and 198 (225 - HCN, 19%; $m^*$ 174.2)

44. 1-Methyl-2,4-pentano-1,2,3,4-tetrahydro-4-p-tolylsulphonylamino-3-p-tolylsulphonyliminoquinoline (LXXXIII):-

The compound was obtained as pale yellow prisms (from methanol/chloroform) by chromatography (silica gel, benzene/ethyl acetate) of the mother liquors from experiments 39a, 39b, 39c, and 40d. The following yields and melting points were obtained.

| Experiment | Yield | m.p. |
|---|---|---|
| 39a | 240 mg (5%) | 167-172° |
| 39b | 252 mg (5%) | 168-173° |
| 39c | 205 mg (4%) | 173-175° |
| 40d | 15 mg (0.3%) | 165-169° |

In all cases the crystals darkened and became opaque at temperature higher than 130°.

Found: C, 62.9; H, 6.2; N, 7.7; S, 11.5%

$C_{29}H_{33}N_3O_4S_2$ requires C, 63.2; H, 6.0; N, 7.6; S, 11.6%

$\lambda_{max.}$: 230 and 290 nm (ε 25,900 and 2,200)

$\nu_{max.}$: 1608 (C=N) and 3245 (N-H) $cm^{-1}$

m/e: 551 (M, 0.1%), 380 (M - $TsNH_2$, 34%), 316 (380 - $SO_2$, 12%; $m^*$ 262.6), 225 (380 - Ts, 100%), 210 (225 - Me, 12%; $m^*$ 196.0) and 198 (225 - HCN, 22%; $m^*$ 174.2)

45. Action of heat on 1-methyl-2,4-pentano-1,2,3,4-tetrahydro-4-p-tolylsulphonylamino-3-p-tolylsulphonyliminoquinoline (LXXXIII):-

The compound (70 mg) was heated at 180° (oil bath) for 5 minutes. The melt was cooled and methanol (0.5 ml) was added. The solid was collected and recrystallised from propanol as pale pink plates, m.p. 194-195°. The product was identical (m.p., t.l.c., i.r.) to an authentic sample of 6,7,8,9,10,11-hexahydro-5-methyl-11-p-tolylsulphonylimino-5H-cyclooct[b]indole (LXXXII). (Yield 30 mg, 62%).

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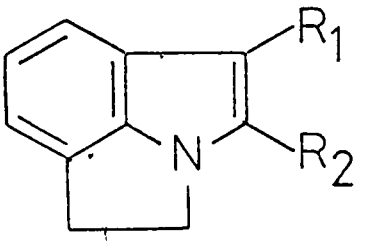
# CHAPTER III

## The reactions of arylsulphonyl azides with dihydropyrrolo[3,2,1-hi]cycloalkeno[b]indoles

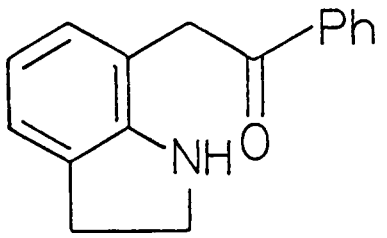
Rapoport[1,2] has described the preparation and properties of some 1,2-dihydropyrrolo[3,2,1-hi]indoles (I). These structures are highly strained, so much so that they undergo certain reactions which do not occur with simple indoles. For example, acid hydrolysis of compound (I, $R_1$ = COOEt, $R_2$ = Ph) leads to (II), the driving force being the relief of steric strain. It should be noted that indoles of the type (III) do not undergo hydrolytic ring opening, even under more forcing conditions[1]. The proposed mechanism for this cleavage is shown in FIGURE I. The step involving addition of water has an interesting parallel in indole/azide chemistry. The similarly strained molecule (IV) was found to add solvent readily with the formation of (V)[3,4], although in the case of (V, R = H) there was no tendency for ring opening.

It was of interest to study the reactions of arylsulphonyl azides with dihydropyrrolo[3,2,1-hi]indoles, since addition of azide across the indole double bond would also result in some relief of steric strain, and these indoles were therefore expected to be highly reactive towards azides. It was decided to attempt the syntheses of compounds (VI) and (VII) and to investigate their reactions with azides.

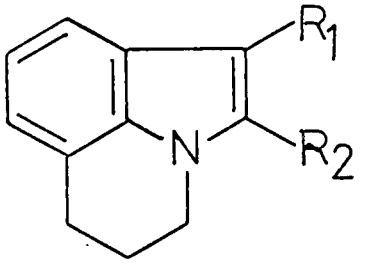
4,5,7,8,9,10-Hexahydropyrrolo[3,2,1-jk]carbazole (VI) is known[5] and was prepared in 50% yield by a Fischer synthesis involving cyclohexanone and 1-aminoindoline. (VI) reacted rapidly with tosyl azide in methanol, the major product having a molecular formula $C_{21}H_{24}N_2O_3S$ (mass spectrum and analysis). This compares with a formula of $C_{21}H_{22}N_2O_2S$ which would be expected given the usual elimination of nitrogen between one molecule each of the indole and azide, and suggested that water in the solvent had added to the molecule at some stage. The most likely mechanism for this addition is as follows. Tosyl azide adds to the double bond of the indole (VI) forming the dipolar ion (VIII) which eliminates nitrogen to give




I




II




III

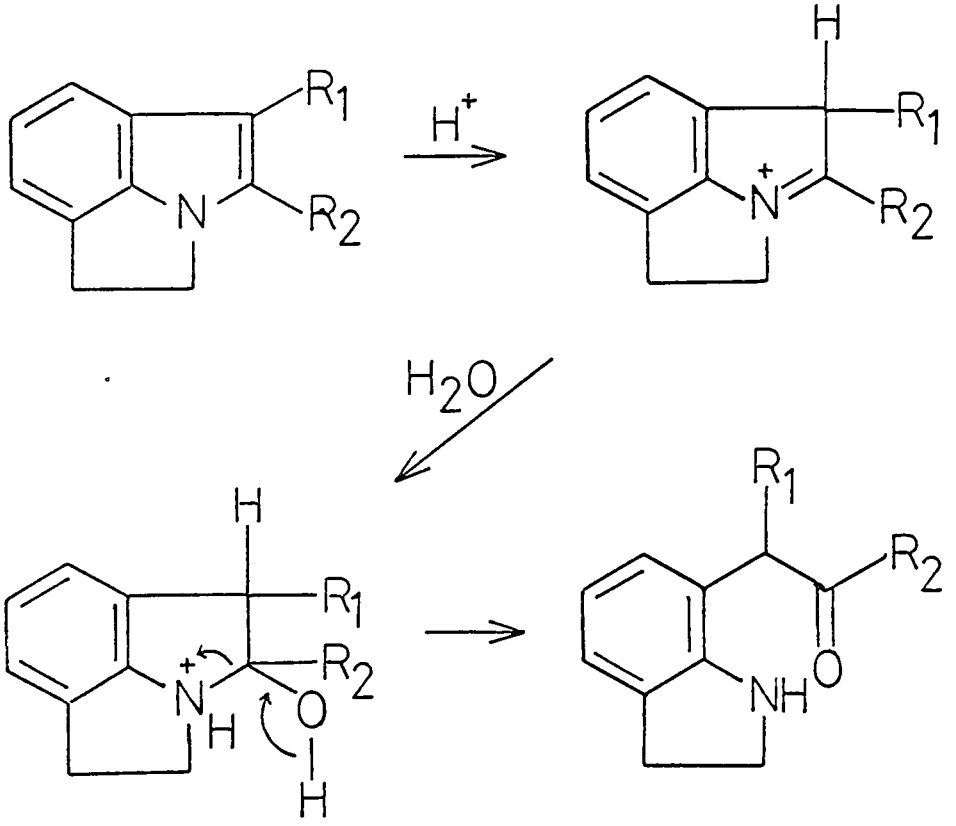
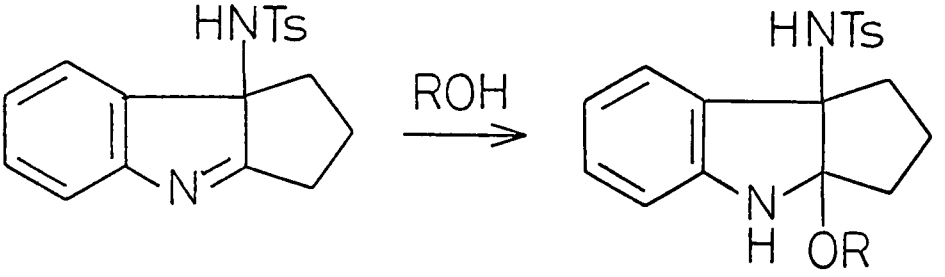
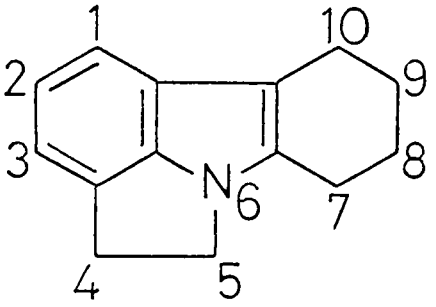


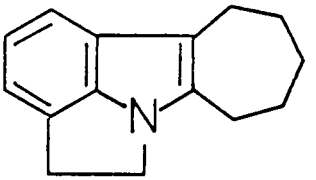

FIGURE I



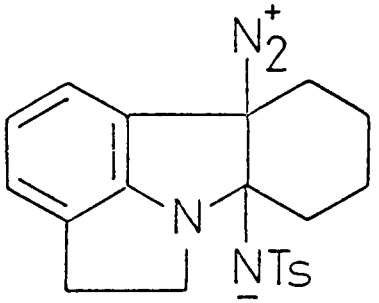

IV V



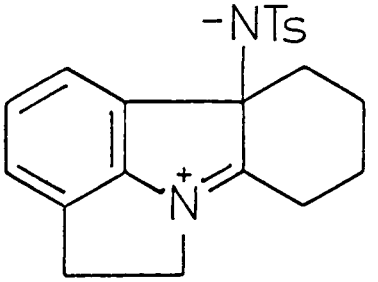

VI



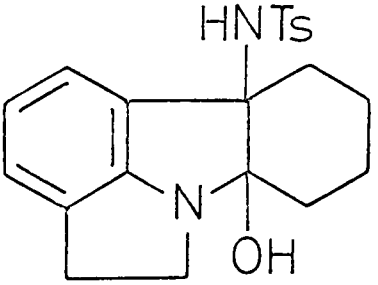

VII



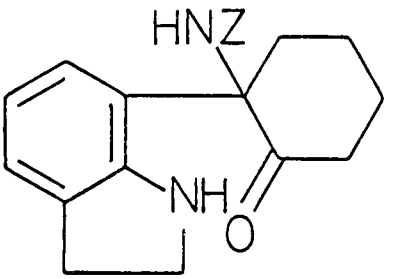

VIII




IX




X




XI

the intermediate (IX) (c.f. FIGURE I, Chapter II). Addition of water as in FIGURE I yields (X) which then undergoes ring opening. This would mean that our product had the structure (XI, Z = Ts).

The u.v. and i.r. spectra supported this suggestion, the u.v. spectrum being that of an indoline and the i.r. spectrum containing bands at 1702 (C=O), 3320 (N-H) and 3375 (N-H) $cm^{-1}$. Examples of u.v. spectra of this type of molecule are shown in FIGURE II.

The n.m.r. spectrum of (XI, Z = Ts) fully supported this structure, showing signals at

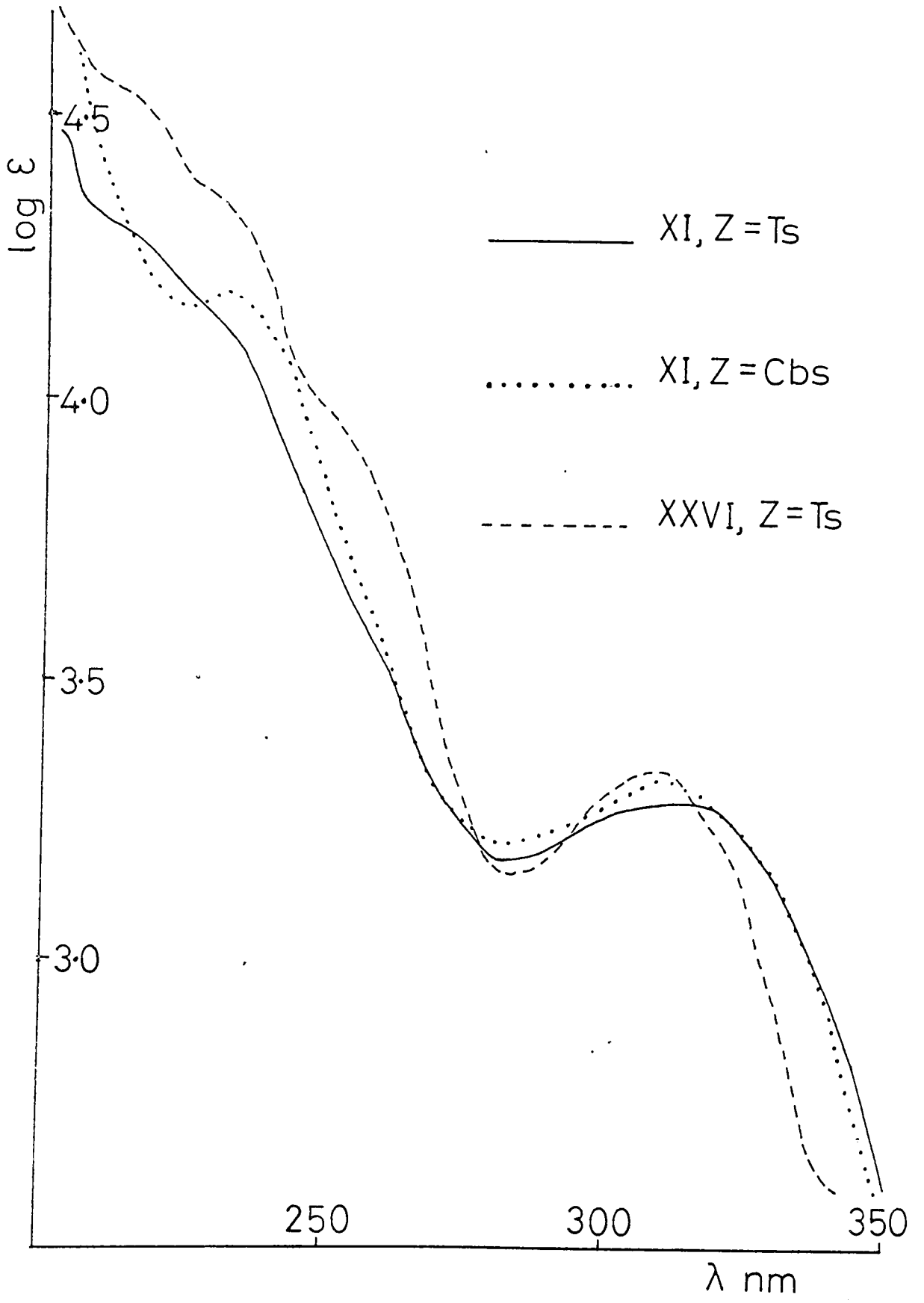
2.70τ(1H, d, J8Hz, aromatic), 2.8-3.4(6H, m, aromatic), 3.72(1H, s, exchanged $D_2O$, tosyl NH), 6.30(1H, m), 6.80(1H, m), 6.99(1H, m, exchanged $D_2O$, indoline NH), 7.74(3H, s, tosyl Me) and 7.1-8.5(10H, m).

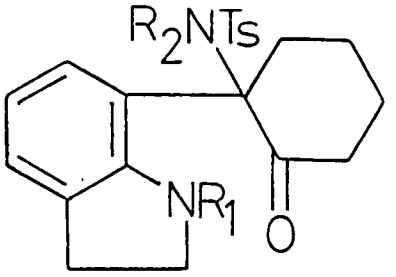
It proved possible to methylate (XI, Z = Ts) to form the three compounds (XIIa, b and c) depending on the conditions employed. Boiling with methyl iodide gave the indoline-methylated product (XIIa), while the use of dimethyl sulphate/alkali yielded (XIIb) together with a small amount of the dimethylated product. The latter was also prepared by a combination of these two methods. The spectroscopic data for the compounds (XII) agreed with the suggested structures and the main features of the n.m.r. spectra are tabulated below.

| Compound | Aromatic protons | NH | Methyl groups |
|---|---|---|---|
| (XIIa) | 2.34(1H, d, J8Hz) | 3.60 | 8.15(NMe) |
| | 2.7-3.2(6H, m) | | 7.73(TsMe) |
| (XIIb) | 2.06(2H, d, J8Hz, tosyl signal) | 4.74 | 7.57 |
| | 2.6-3.1(4H, m) | | 7.57 |
| | 3.37(1H, t, J8Hz) | | |
| (XIIc) | 2.13(2H, d, J8Hz, tosyl signal) | - | 7.38 |
| | 2.6-3.3(5H, m) | | 7.53 |
| | | | 7.60 |

The signals due to the aliphatic protons were uninformative and have been omitted from this table.

FIGURE II



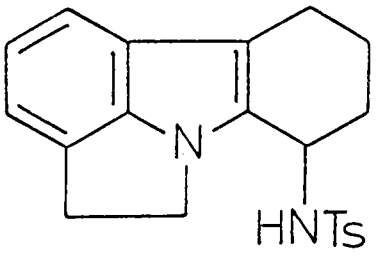



XII

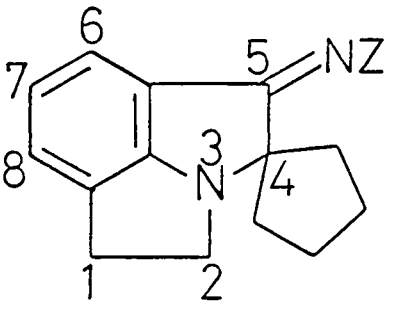
a, $R_1$=Me, $R_2$=H

b. $R_1$=H, $R_2$=Me

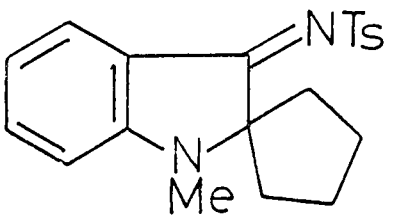
c. $R_1$=$R_2$=Me



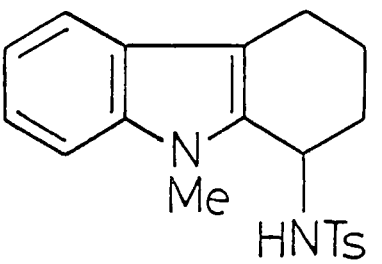

XIII




XIV




XV




XVI

It can be seen from this table that the spectrum of (XIIa) closely resembles that of (XI, Z = Ts) especially with respect to the aromatic region. In the spectra of (XIIb) and (XIIc) the low field tosyl signals occur at much lower field and the tosyl methyl signals are also at slightly lower field than those of (XI, Z = Ts) or (XIIa). This effect could be due to intramolecular hydrogen bonding, and in (XI, Z = Ts) and (XIIa) the toluene ring may be oriented over the indoline ring, producing mutual shielding. Similar upfield shifts have been reported[6]. When the sulphonylamino nitrogen is methylated the constraints imposed by hydrogen bonding are removed. In this context it is significant that (XIIc) has a melting point 20° higher than that of (XIIa); this is evidence in favour of strong intramolecular hydrogen bonding.

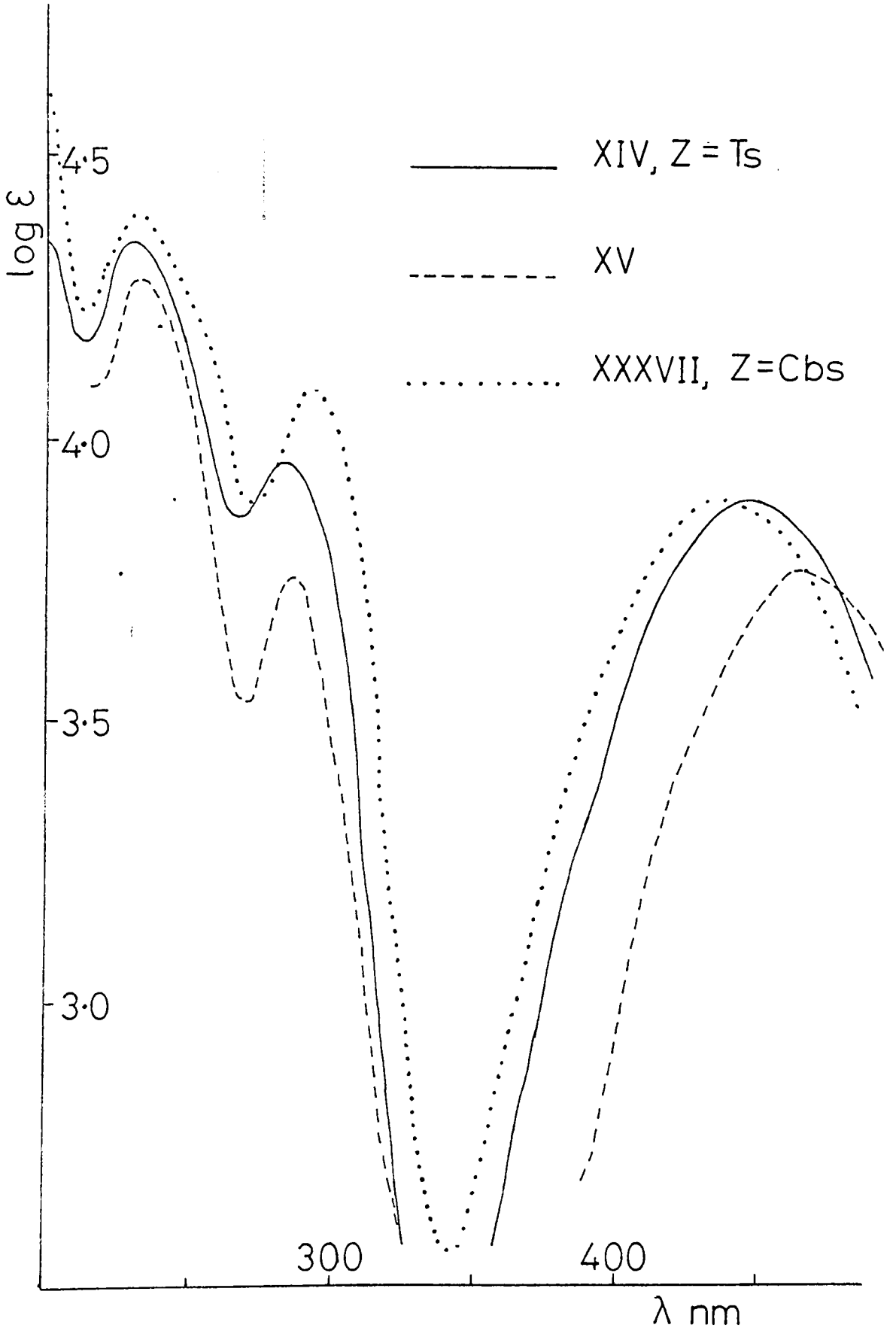
Two other products were isolated from the reaction of (VI) with tosyl azide in methanol. The first of these was the compound (XIII) obtained in very low yield (1%); this compound will be discussed later. The final product was a bright orange fluorescent material which was assigned the structure (XIV, Z = Ts). This product was very similar to the compound (XV) isolated from the reaction of tosyl azide with 9-methyl-1,2,3,4-tetrahydrocarbazole[7,8]. Analysis agreed with the proposed structure and the i.r. spectrum contained a band due to C=N stretch (1555 $cm^{-1}$). The n.m.r. spectrum showed the following signals.

2.0-2.2τ(3H, m, aromatic), 2.76(2H, d, J8Hz, high field half of tosyl signal), 2.91(1H, d, J8Hz, $C_8H$), 3.41(1H, t, J8Hz, $C_7H$), 6.35 (2H, t, J7Hz), 6.75(2H, t, J7Hz), 7.62(3H, s, tosyl Me) and 7.9-8.3 (8H, m).

The u.v. spectrum was very similar to that of (XV), showing the absorption in the visible region characteristic of this type of structure (FIGURE III).

It had been noticed that compound (XI, Z = Ts) decomposed with

FIGURE III



effervescence on heating to give a deep red melt. Moreover, the mass spectrum showed a signal at m/e 366 (M - 18). These observations suggested that (XI) could be eliminating water to give (XIV). This possibility was investigated by heating a sample of (XI, Z = Ts) to its melting point. Only one product could be isolated from the dark melt, this being a colourless compound with the molecular formula $C_{21}H_{22}N_2O_2S$, i.e. an isomer of (XIV, Z = Ts). The u.v. spectrum was that of an indole and the i.r. spectrum contained a band at 3240 $cm^{-1}$ (N-H). The n.m.r. spectrum contained signals at

| | | |
|---|---|---|
| 2.23τ | (2.20) | 2H, d, J8Hz, low field half of tosyl signal |
| 2.6-3.2 | (2.5-3.3) | 5H, m, aromatic |
| 5.33 | | 2H, s, br, NH and CH |
| 5.78 | | 2H, t, J7Hz |
| 6.42 | | 2H, t, J7Hz |
| 7.2-7.5 | (7.2-7.8) | 2H, m |
| 7.58 | (7.58) | 3H, s, tosyl Me |
| 8.1-8.6 | (8.36) | 4H, m |

The signal at 5.33τ diminished by approximately 50% on $D_2O$ exchange. The same was observed on shaking the solution with TFA, suggesting that one of the two protons contributing to this signal was the NH proton.

These data suggest the structure (XIII) for the product and were very similar to those obtained for the compound (XVI)[7,8]. The corresponding signals in the n.m.r. spectrum (D) of (XVI) are given in parentheses in the table above. The NH signal of (XVI) occurred at 2.04τ and the NMe signal at 6.50τ. Compound (XIII) was identical to that already reported as being formed in low yield from the reaction of (VI) with tosyl azide.

Although the red melt of (XI, Z = Ts) undoubtedly contained some (XIV, Z = Ts) (t.l.c.) the latter was present in much too small a quantity to permit isolation. This is perhaps not surprising, since

(XV) is known[7,8] to isomerise to (XVI) on heating. The formation of (XIII) from (XI, Z = Ts) probably occurs by a recyclisation to form (X) followed by loss of water and a 1,3-shift of the tolylsulphonylamino group from $C_{10a}$ to $C_7$.

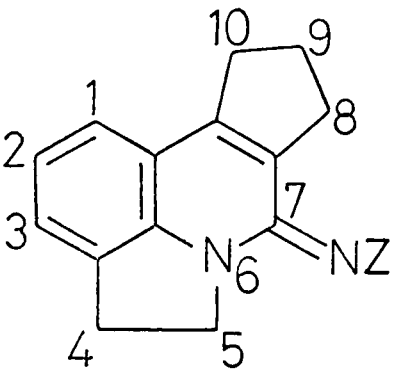
Compound (XVI) had also been prepared as the major product from the reaction of tosyl azide with N-methyltetrahydrocarbazole in acetic acid[7,8]. This suggested a possible route to (XIII) in higher yields. Accordingly a solution of (VI) and tosyl azide in acetic acid was left at room temperature for two weeks. The reaction product, however, was a black tar, from which only a very small yield (5%) of (XIII) could be isolated. It may be that in this case hydrolysis and similar reactions were competing with the azide addition.

Since compound (XI, Z = Ts) had been formed by the addition of water to an intermediate it was desirable to carry out a reaction in an anhydrous solvent and to identify the products formed under these conditions. Moreover, it was also desirable to investigate the effects of a basic solvent, an acidic solvent already having been studied. It was decided to combine these two features and the reaction was conducted using pyridine as solvent. The pyridine had previously been dried by distillation from potassium hydroxide.

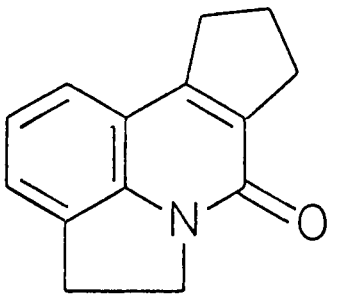
Although precautions had been taken to prevent moisture entering the system, an appreciable yield of (XI, Z = Ts) was obtained (17%). The major product from the reaction, however, was a colourless compound with a molecular formula of $C_{21}H_{20}N_2O_2S$. The i.r. spectrum contained a band at 1508 $cm^{-1}$ (C=N) and the n.m.r. spectrum showed the following signals.

2.05τ(2H, d, J8Hz, low field half of tosyl signal), 2.5-2.9(5H, m, aromatic), 5.50(2H, t, J8Hz), 6.3-6.7(4H, m), 6.88(2H, t, J8Hz), 7.61(3H, s, tosyl Me) and 7.77(2H, quintuplet, J8Hz).

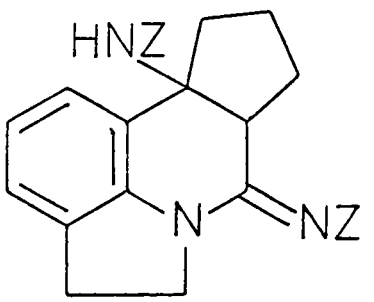
By analogy with the similar reaction of 9-methyltetrahydrocarbazole (see Chapter II) the compound was assigned the structure



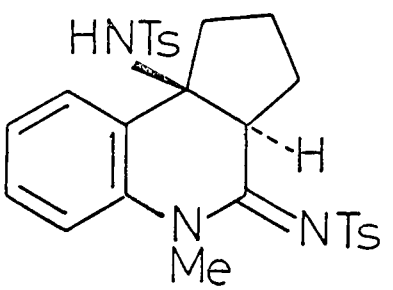

XVII




XVIII




XIX




XX

(XVII, Z = Ts). The analytical and spectroscopic data are in full agreement with this assignment. Definite proof that this structure was correct was obtained by base-catalysed hydrolysis of (XVII, Z = Ts) to the compound (XVIII). The u.v. spectrum was that of a 2-quinolone as was the carbonyl stretching frequency (1640 $cm^{-1}$). The n.m.r. spectrum showed signals at

2.6-3.1τ(3H, m, aromatic), 5.63(2H, t, J8Hz), 6.61(2H, t, J8Hz), 6.8-7.2(4H, m) and 7.82(2H, quintuplet, J8Hz), and was in complete agreement with the suggested structure.

The third and final product from the reaction of tosyl azide and (VI) in pyridine was compound (XIX, Z = Ts), the precursor of (XVII, Z = Ts). Analytical and spectroscopic data supported the structure, the n.m.r. spectrum (D) showing the following signals.

1.64τ(1H, s, br, exchanged $D_2O$, NH), 2.22(2H, d, J8Hz, low field half of tosyl signal), 2.65(2H, d, J8Hz, high field half of tosyl signal), 2.8-3.5(7H, m, aromatic). 5.73(1H, t, J9Hz), 5.9-6.3(2H, m), 6.8-7.2(2H, m), 7.65(3H, s, tosyl Me), 7.75(3H, s, tosyl Me) and 7.4-9.0(6H, m).

The i.r. spectrum contained bands due to C=N and N-H (1550 and 3250 $cm^{-1}$ respectively). All data were similar to those reported[7,8] for the compound (XX) and by analogy with (XX) the $C_{7a}$-$C_{10a}$ ring junction was assumed to have the <u>trans</u> configuration (Chapter II). The isolation of compound (XVII, Z = Ts) from the same reaction mixture was strong evidence in support of this, since (XVII) can only have been formed by elimination of sulphonamide from (XIX) and the reaction conditions were only weakly basic. This assumption was finally justified by the smooth conversion of (XIX, Z = Ts) to (XVII, Z = Ts) by treatment with 1,5-diazabicyclo[4.3.0]non-5-ene. (See Chapter II).

As an extension to the above work it was of interest to repeat these investigations with the more reactive <u>p</u>-chlorobenzenesulphonyl

and p-nitrobenzenesulphonyl azides.

The former reacted rapidly with (VI) giving as the major product (48%) compound (XI, Z = Cbs). Like that of (XI, Z = Ts), the i.r. spectrum contained bands due to carbonyl and N-H groups and the n.m.r. spectrum contained the following signals.

2.72τ(1H, d, J8Hz, aromatic), 2.8-3.4(6H, m, aromatic), 3.62(1H, s, exchanged $D_2O$, Cbs NH), 6.31(1H, m), 6.79(1H, m), 6.96(1H, m, exchanged $D_2O$, indoline NH) and 7.1-8.6(10H, m).
This spectrum was very similar to that of (XI, Z = Ts).

Three other compounds were isolated from this reaction, all being the Cbs analogues of known tosyl compounds. The first of these was the orange fluorescent spiro-compound (XIV, Z = Cbs) whose n.m.r. spectrum contained signals at

2.07τ(3H, m, aromatic), 2.57(2H, d, J8Hz, high field half of Cbs signal), 2.88(1H, d, J7Hz, $C_8H$), 3.38(1H, t, J7Hz, $C_7H$), 6.32(2H, t, J7Hz), 6.72(2H, t, J7Hz) and 7.8-8.3(8H, m).

The remaining two products were isolated in very low yields (2%) and were assigned the structures (XVII, Z = Cbs) and (XIX, Z = Cbs) respectively. The n.m.r. spectrum of the former showed the following signals:

2.02τ(2H, d, J8Hz, low field half of Cbs signal), 2.5-2.9(5H, m, aromatic), 5.50(2H, t, J8Hz), 6.4-6.7(4H, m), 6.86(2H, t, J8Hz) and 7.75(2H, quintuplet, J8Hz)

and that of (XIX,Z = Cbs) (D) had signals at

1.40τ(1H, br, exchanged $D_2O$, NH), 2.09(2H, d, J8Hz, low field half of Cbs signal), 2.45(2H, d, J8Hz, high field half of Cbs signal), 2.6-3.6(7H, m, aromatic), 5.78(1H, t, J9Hz), 5.9-6.2(2H, m), 6.91(2H, t, J8Hz) and 7.4-9.0(6H, m).

So similar were these products to their tosyl analogues that further proof of structure was not considered necessary.

One feature of the work with p-chlorobenzenesulphonyl azide was

the significant increase in yield of the spiro-compound (XIV) compared with that obtained from tosyl azide (16% as opposed to 3%).

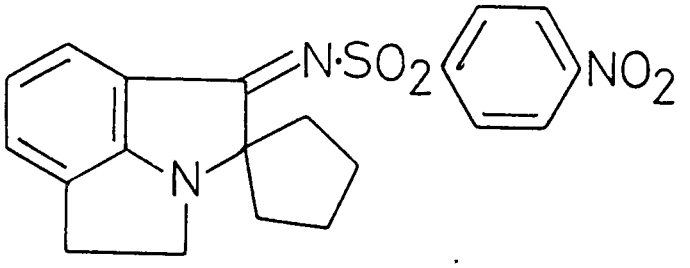
This observation led to a similar series of reactions with the still more reactive p-nitrobenzenesulphonyl azide, to see whether still higher yields of the spiro-compound could be obtained. (VI) reacted very rapidly with the nitro-azide, reaction in refluxing methanol being complete within fifteen minutes. A pale orange solid was collected. An attempt was made to recrystallise this from propanol, but the hot solution deposited a sticky red mass. T.l.c. showed the presence of two compounds in addition to the initial crude material.

Obviously, further reaction was taking place and the propanolic mixture was boiled until this was complete. It was significant that the solution was much darker in colour after this treatment than originally. Evaporation and recrystallisation yielded a bright red compound whose spectral and analytical data agreed with the structure (XXI), being very similar to those of (XIV, Z = Ts or Cbs). The n.m.r. spectrum included signals at

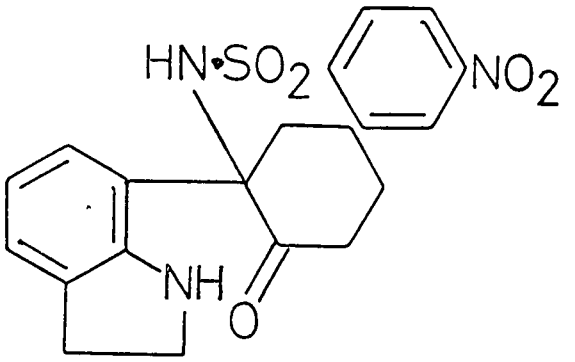
1.67τ(2H, d, J8Hz, low field half of sulphonyl signal), 1.82(2H, d, high field half of sulphonyl signal), 2.10(1H, d, J8Hz, $C_6H$), 2.85(1H, d, J8Hz, $C_8H$), 3.35(1H, t, J8Hz, $C_7H$), 6.29(2H, t, J7Hz), 6.70(2H, t, J7Hz) and 7.9-8.3(8H, m).

Besides (XXI) a second product was isolated from this series of reactions. Its i.r. spectrum contained bands due to carbonyl and N-H absorptions and analysis indicated the formula $C_{20}H_{21}N_3O_5S$. These observations indicated the structure (XXII), and this was confirmed by the n.m.r. spectrum (D).

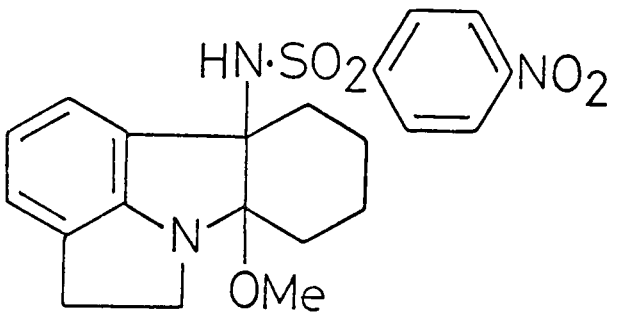
2.0-2.1τ(3H, m, sulphonyl NH and low field half of sulphonyl signal), 2.45(2H, d, J8Hz, high field half of sulphonyl signal), 2.86(1H, d, aromatic), 3.2-3.6(2H, m, aromatic), 5.6-5.8(1H, m, exchanged $D_2O$, indoline NH), 6.3-7.0(2H, m) and 7.0-8.6(10H, m).



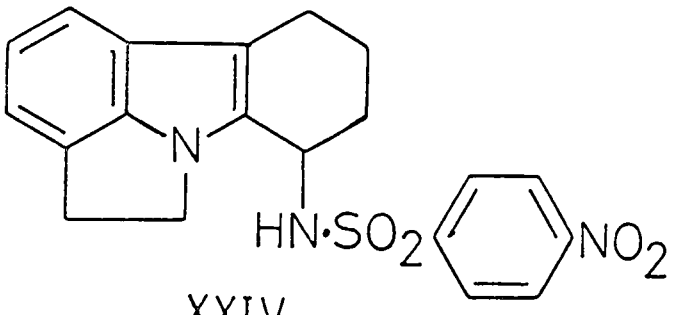

XXI




XXII




XXIII




XXIV

It was necessary to repeat the reaction of (VI) with nitro-azide in order to identify the initially formed product. This time the crude product was rapidly recrystallised from chloroform/methanol. Analysis indicated the formula $C_{21}H_{23}N_3O_5S$ which corresponded to the addition of methanol to the 1:1 adduct. The i.r. spectrum showed bands due to N-H but no carbonyl absorption and the n.m.r. spectrum contained signals at the following values.

2.06τ(2H, d, J8Hz, low field half of sulphonyl signal), 2.46(2H, d, J8Hz, high field half of sulphonyl signal), 2.98(1H, d, J8Hz, aromatic), 3.3-3.7(2H, m, aromatic), 3.45(1H, s, exchanged $D_2O$, NH), 6.52(3H, s, OMe), 6.5-7.0(2H, m), 7.1-7.3(2H, m) and 7.8-9.3(8H, m).

These observations indicated the structure (XXIII), i.e. addition of methanol had taken place rather than addition of water. With a methoxy group rather than a hydroxy group in the 6a position ring opening cannot occur.

The mass spectrum of (XXIII) showed no molecular ion (m/e 429) but there were peaks at 415 and 397 (ratio 1:3). That at m/e 415 corresponds to the structure (XXII), and may have arisen due to the presence of a small quantity of (XXII) in the product or perhaps more likely by exchange with water in the spectrometer itself. It is of interest to note that the mass spectrum of (XXII) also contains peaks at m/e 415 and 397 (ratio 10:1). This means that only a very small proportion of the 397 peak in (XXIII) is due to loss of water from (XXII) and the major contribution is the loss of methanol from (XXIII).

This would help to explain the observed effect when the compound was boiled in propanol. Ring contraction and elimination of methanol would lead to (XXI) while exchange with water present in the propanol would give the ring-opened product (XXII).

One final experiment was carried out on (XXIII). The compound was heated above its melting point when effervescence occurred and the melt turned deep red, yielding two products. The first of these was

the red spiro-compound (XXI) and the second was (XXIV) isomeric with (XXI) and very similar in properties to (XIII). The n.m.r. spectrum (D) showed the following signals:

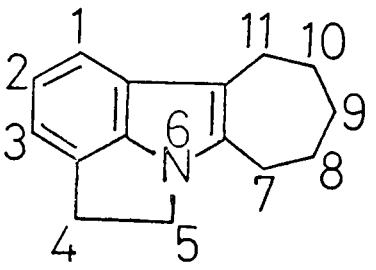
1.57τ(2H, d, J8Hz, low field half of sulphonyl signal), 1.87(2H, d, J8Hz, high field half of sulphonyl signal), 2.90(1H, t, J5Hz, aromatic), 3.1-3.2(2H, m, aromatic), 5.29(1H, m, $C_7H$), 5.79 (2H, t, J7Hz), 6.38(2H, t, J7Hz), 7.42(2H, m) and 8.0-8.5(4H, m).

The NH signal could not be seen, even by scanning down to -5τ, and may possibly have coincided with the "water peak".

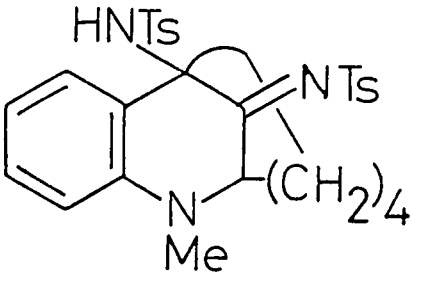
Compound (VII) was previously unknown, but was successfully prepared by condensation of cycloheptanone and 1-aminoindoline. It reacted very rapidly with tosyl azide, mixtures of the neat reactants being explosive. Reaction occurred smoothly, however, in chloroform solution at room temperature. This solvent had previously been purified by passing it through an alumina column in order to remove traces of acid and water which may have catalysed cleavage reactions. The major product from such a reaction was a bright yellow compound with the formula $C_{29}H_{31}N_3O_4S_2$. The i.r. spectrum contained bands due to N-H and C=N groups and the u.v. spectrum was similar to that of the indoline (XI) (see FIGURE II). The n.m.r. spectrum showed signals at

2.09τ(2H, d, J8Hz, low field half of tosyl signal), 2.5-3.2(7H, m, aromatic), 3.32(1H, d, J8Hz, aromatic), 3.66(1H, t, J8Hz, aromatic), 4.44(1H, s, exchanged $D_2O$, NH), 4.59(1H, dd, J8,3Hz), 6.4-6.7(2H, m), 6.8-7.1(2H, m), 7.57(3H, s, tosyl Me), 7.66(3H, s, tosyl Me) and 7.6-9.3(8H, m).

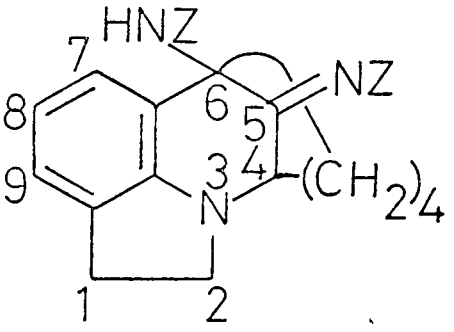
The spectral data were very similar to those of the compound (XXV) (see Chapter II) and for this reason the structure (XXVI, Z = Ts) was assigned. There was a dramatic increase in yield from 15% in the case of (XXV) to 60% for the bridged compound (XXVI, Z = Ts) and this meant that we would be able to investigate the chemistry of this type



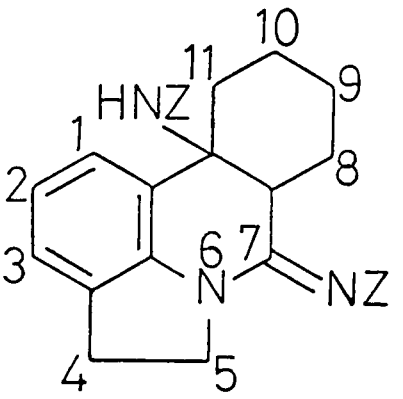

VII



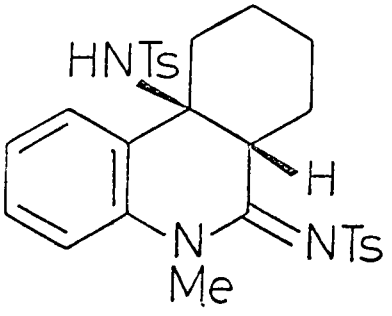

XXV



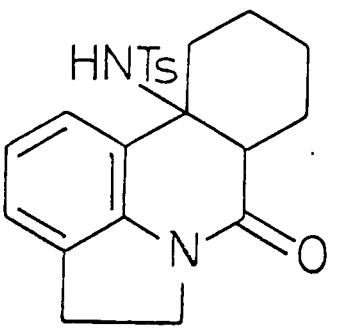

XXVI




XXVII




XXVIII




XXIX

of structure in greater detail (see later).

Two other products were isolated from the reaction of (VII) with tosyl azide in chloroform. The first of these was isolated in very low yield and was not further investigated, although the mass spectrum showed a molecular ion at m/e 563 [the normal 2:1 adduct e.g. (XXVI, Z = Ts) has molecular weight 549]. This might suggest that an oxidation had taken place at some stage in the reaction.

The third product, isomeric with (XXVI, Z = Ts), was isolated in 8% yield and was assigned the structure (XXVII, Z = Ts). Its spectral properties were in good agreement with this structure, the i.r. spectrum showing C=N and N-H absorptions and the n.m.r. spectrum containing the following signals:

2.08τ(2H, d, J8Hz, low field half of tosyl signal), 2.6-2.8(3H, m, aromatic), 2.9-3.2(6H, m, aromatic), 5.52(1H, s, exchanged $D_2O$, NH), 5.9-7.3(5H, m), 7.57(3H, s, tosyl Me), 7.70(3H, s, tosyl Me) and 7.8-9.3(8H, m).

A similar compound (XXVIII) had been obtained from the reaction of 5,6,7,8,9,10-hexahydro-5-methylcyclohept[b]indole with tosyl azide (Chapter II) and it had been shown that the $C_{6a}$-$C_{10a}$ ring junction had the cis configuration. It was expected that a similar situation might arise in this case. The mass spectrum of (XXVII, Z = Ts) supported this, showing loss of Ts and TsNH, but no loss of $TsNH_2$, and suggesting that elimination of sulphonamide was difficult.

To verify this prediction a sample of (XXVII, Z = Ts) was heated under reflux with sodium hydroxide in ethanol. A product (XXIX) was obtained in which hydrolysis of the tosylimino group had occurred, and in which the tosylamino group had been left intact. The n.m.r. spectrum of (XXIX) contained signals at

2.6-3.2τ(7H, m, aromatic), 4.38(1H, s, exchanged $D_2O$, NH), 5.8-7.5 (5H, m), 7.68(3H, s, tosyl Me) and 8.0-9.2(8H, m).

As in the case of (XXVIII) the fact that hydrolysis had occurred

without elimination proved that (XXVII, Z = Ts) had a cis ring junction.

A second reaction between (VII) and tosyl azide was carried out, this time using dry pyridine as solvent and the same two major products were obtained.

A similar investigation was conducted into the reaction of (VII) with p-chlorobenzenesulphonyl azide. From a reaction in dry chloroform, three products were obtained. The first of these (XXVI, Z = Cbs) was so similar to the tosyl analogue that identification was not difficult. The n.m.r. spectrum (D) contained the following signals.

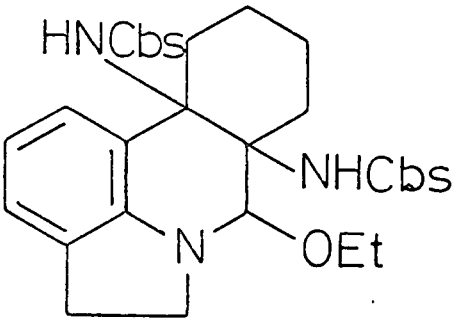
1.46τ(1H, s, exchanged $D_2O$, NH), 2.01(2H, d, J8Hz, low field half of Cbs signal), 2.29(2H, d, J8Hz, high field half of Cbs signal), 2.69 (2H, d, J8Hz, low field half of Cbs signal), 2.84(2H, d, J8Hz, high field half of Cbs signal), 3.11(1H, d, J8Hz, aromatic), 3.5-3.9(2H, m, aromatic), 4.56(1H, d, J8Hz), 6.4-6.7(2H, m), 6.8-7.1(2H, m) and 7.6-9.4(8H, m).

The second compound was again easily identified, being (XXVII, Z = Cbs). The n.m.r. spectrum (D) showed signals at

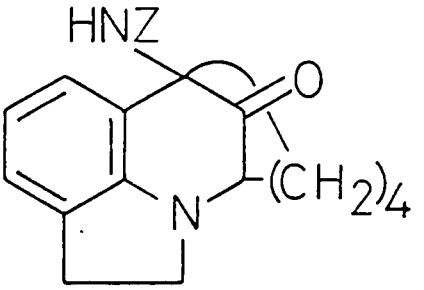
1.82τ(1H, s, exchanged $D_2O$, NH), 2.03(2H, d, J8Hz, low field half of Cbs signal), 2.37(2H, d, J8Hz, high field half of Cbs signal), 2.64 (2H, d, J8Hz, low field half of Cbs signal), 2.8-3.2(5H, m, aromatic), 5.9-7.5(5H, m) and 7.9-9.4(8H, m).

The third product was formed in low yield (2%) and was assigned the structure (XXX). Its properties and formation will be discussed later in this chapter.

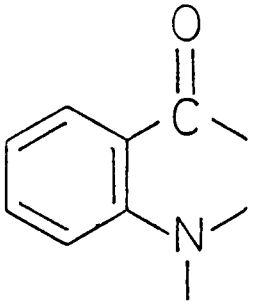
The fact that structures of the type (XXVI) could be obtained easily and in good yield meant that their chemistry could be investigated in some detail. Accordingly a sample of (XXVI, Z = Ts) was heated under reflux with caustic soda in ethanol, with a view to obtaining the ketone (XXXI, Z = Ts). From this reaction was obtained a yellow fluorescent compound with the formula $C_{15}H_{17}NO_2$ (mass spectrum



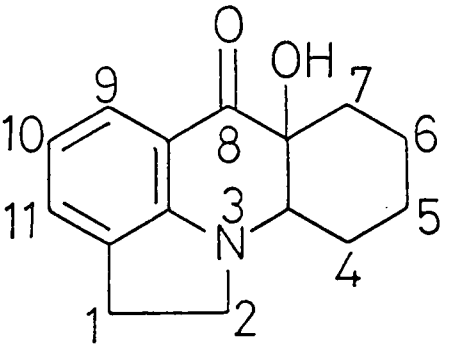

XXX



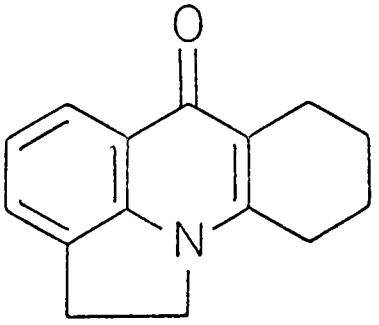

XXXI



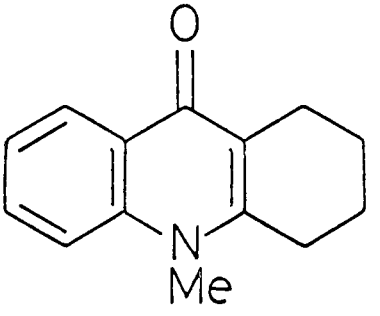

XXXII




XXXIII




XXXIV




XXXV

and analysis). The i.r. spectrum contained bands due to carbonyl and hydroxy groups (1656 and 3490 $cm^{-1}$ respectively) and the n.m.r. spectrum contained the following signals:

2.47τ(1H, d, J8Hz, aromatic), 2.78(1H, d, J8Hz, aromatic), 3.35 (1H, t, J8Hz, aromatic), 6.0-6.3(1H, m), 6.30(1H, s, exchanged $D_2O$, OH), 6.7-7.0(4H, m) and 8.0-8.9(8H, m).

The fluorescence of the material strongly suggested that its structure contained the chromophore (XXXII) since compounds containing this partial structure are known[9] to be fluorescent. These observations lead to the assignment of structure (XXXIII) for this product. Moreover the positions of the aromatic signals in the n.m.r. spectrum are within the ranges quoted[10] for 2,3-dihydroquinolin-4(1H)-ones.

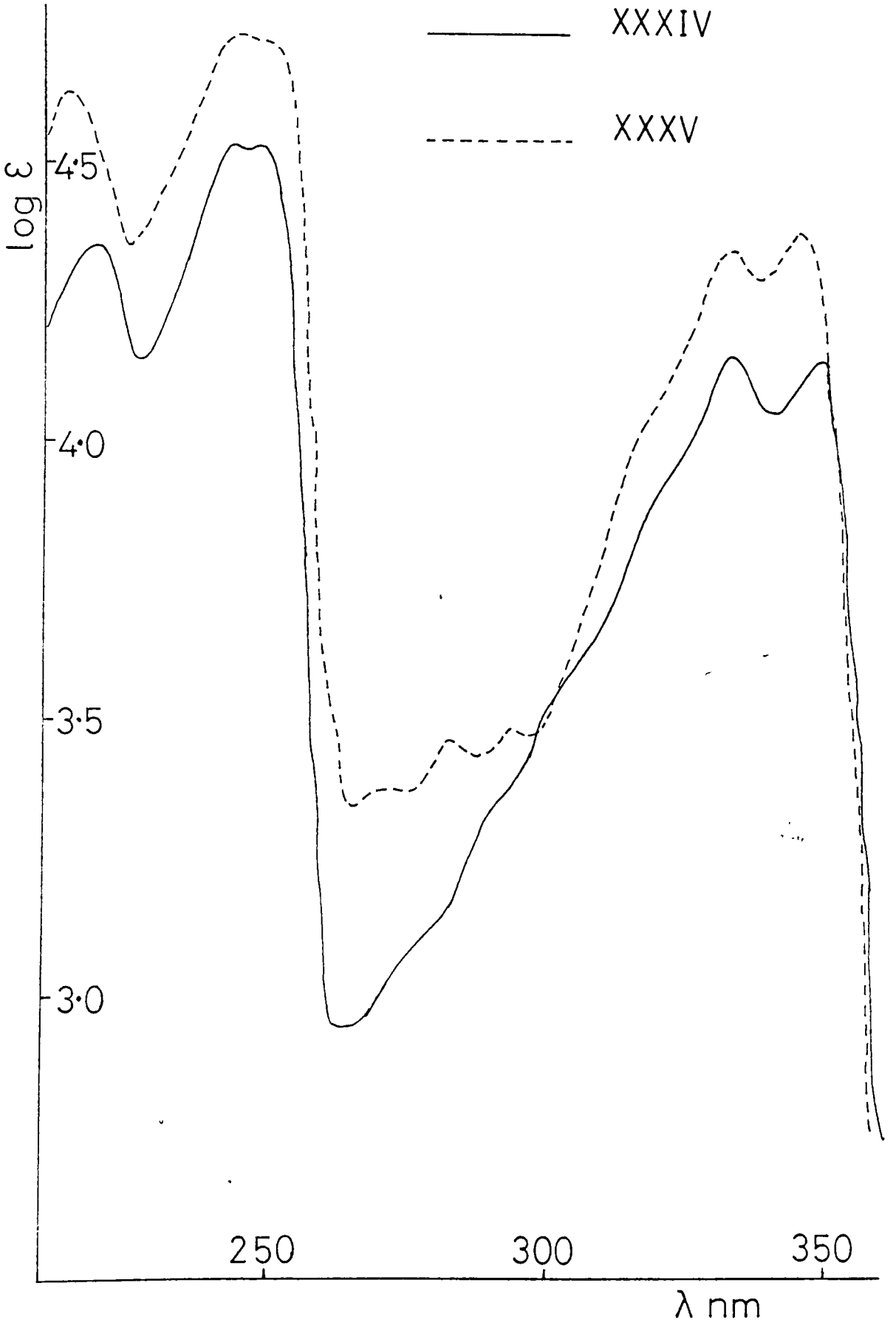
On warming the yellow compound in concentrated sulphuric acid the colour was gradually discharged. This suggested that dehydration might be taking place to yield a colourless tetrahydro-9-acridanone. This experiment was repeated using polyphosphoric acid instead of sulphuric acid in order to prevent possible sulphonation and dehydration occurred to yield compound (XXXIV). Analytical and spectral data agreed with this structure, the i.r. spectrum containing a band due to carbonyl, but not hydroxyl, absorption and the n.m.r. spectrum showed signals at

2.09τ(1H, d, J7Hz, aromatic), 2.7-3.0(2H, m, aromatic), 5.78(2H, t, J8Hz), 6.65(2H, t, J8Hz), 7.2-7.6(4H, m) and 8.0-8.4(4H, m).

The u.v. spectrum was that of a 4-quinolone and the u.v. spectra of this compound and (XXXV) (prepared during the work reported in Chapter II) are shown in FIGURE IV.

There is no doubt that structure (XXXIV) is correct and hence structure (XXXIII) for the hydrolysis product must also be the correct one. The mechanism for the formation of (XXXIII) is probably as follows. Initial hydrolysis to (XXXI, Z = Ts) occurs firstly, then

FIGURE IV



the ion (XXXVI) undergoes rearrangement as shown to yield (XXXVII, Z = Ts). A second hydrolysis then occurs with the formation of (XXXIII).

By repeating this hydrolysis at room temperature it was possible to obtain compound (XXXI) without further rearrangement. A sample of (XXVI, Z = Cbs) was treated with sodium hydroxide at room temperature in aqueous acetone and the compound (XXXI, Z = Cbs) was obtained. The i.r. spectrum contained C=O and N-H absorptions and the n.m.r. spectrum showed signals at

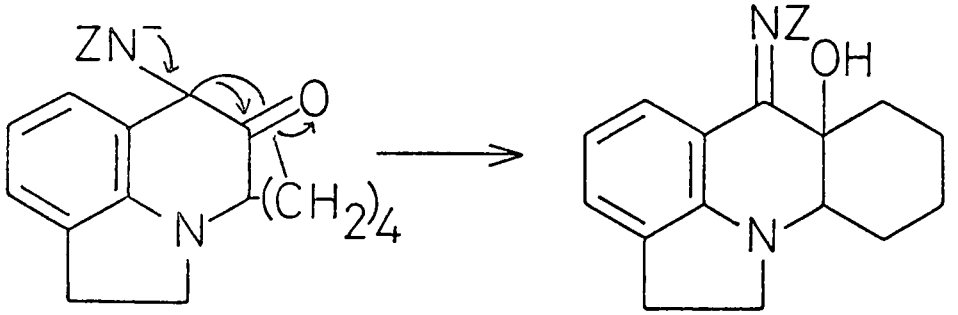
2.47$\tau$(2H, d, J8Hz, low field half of Cbs signal), 2.71(2H, d, J8Hz, high field half of Cbs signal), 2.9-3.1(2H, m, aromatic), 3.47 (1H, t, J7Hz, aromatic), 4.16(1H, s, exchanged $D_2O$, NH), 6.1-7.0(5H, m) and 7.7-9.0(8H, m).

Since treatment with base under more forcing conditions would result in the formation of (XXXIII) it was decided to study the effects of heating the compound with a view to investigating any further rearrangements. A sample of (XXXI, Z = Cbs) was therefore heated <u>in vacuo</u> and from the residue was isolated a 45% yield of a bright orange compound, assigned the structure (XXXVII, Z = Cbs). Analytical data agreed with this assignment and the n.m.r. spectrum contained the following signals:

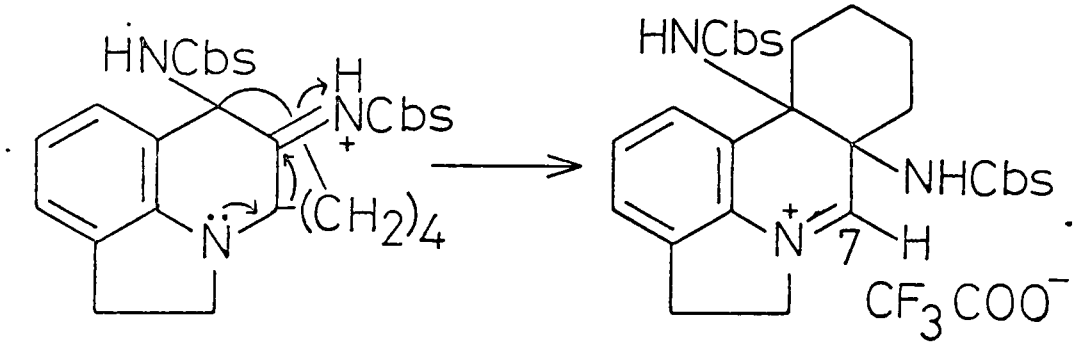
1.9-2.1$\tau$(3H, m, aromatic), 2.56(2H, d, J8Hz, high field half of Cbs signal), 2.85(1H, d, J7Hz, aromatic), 3.37(1H, t, J7Hz, aromatic), 5.84(1H, s, exchanged $D_2O$, OH), 6.0-7.0(5H, m) and 7.8-8.6(8H, m).

It should be noted that the chromophore of this compound is the same as those of the compounds (XIV) and (XV) (see FIGURE III).

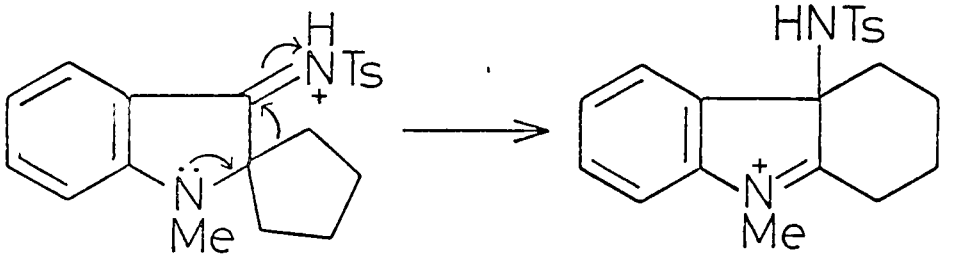
Having studied the effects of base on compound (XXVI) it was desirable to investigate the effects of acid, if any. A sample of (XXVI, Z = Cbs) was dissolved in trifluoroacetic acid and after one week the solvent was removed and the residue triturated with methanol. The colourless crystalline solid thereby obtained was recrystallised



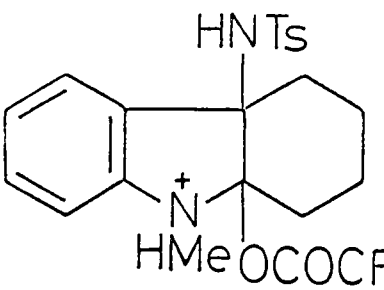

XXXVI XXXVII




XXXVIII XXXIX




XL XLI




XLII

from ethanol. The product was found to have the molecular formula $C_{29}H_{31}Cl_2N_3O_5S_2$, which corresponds to the addition of one molecule of ethanol to the normal 2:1 adduct. The ethanol was not present as solvent of crystallisation since prolonged drying in vacuo resulted in no loss of ethanol. Moreover, the mass spectrum showed a molecular ion at m/e 635 and this supports the above formula. The n.m.r. spectrum of the compound indicated the structure (XXX), containing signals at

2.19(2H, d, J8Hz, low field half of Cbs signal), 2.3-2.8(7H, m, 6 aromatic protons and NH), 3.13(1H, d, J8Hz, aromatic), 3.41(1H, d, J8Hz, aromatic), 3.65(1H, t, J8Hz, aromatic), 4.27(1H, s, exchanged $D_2O$, NH), 5.00(1H, s), 5.8-6.6(4H, m), 7.05(2H, t, J8Hz), 7.2-7.5(1H, m), 7.6-9.8(7H, m) and 8.61(3H, t, J8Hz, ethyl Me).

The u.v. spectrum was that of an indoline and the i.r. spectrum contained bands due to N-H, but not C=N, absorptions.

The formation of (XXX) can be envisaged as follows. Protonation of (XXVI, Z.= Cbs) leads to (XXXVIII) which rearranges as shown to give the salt (XXXIX). On removal of the acid and trituration with methanol the latter solvent adds across the double bond and on recrystallisation from ethanol solvent exchange takes place to give (XXX). This process is entirely analogous to that reported[7,8] for the action of TFA on the orange compound (XV). Protonation yields (XL) and rearrangement gives the ion (XLI). In this case, however, TFA itself added to the double bond giving the salt (XLII).

(XXX) was also obtained in low yield from the reaction of (VII) with p-chlorobenzenesulphonyl azide (see earlier). It is unlikely that this compound arose directly from this reaction since drying the solvent with alumina would effectively remove traces of ethanol, and a more likely explanation is that (XXX) was formed via (XXVI, Z = Cbs) at some stage in the work-up procedure.

Since it appeared that isolation of the intermediate (XXXIX) was

unlikely, it was decided to study this rearrangement as it occurred, by means of n.m.r. spectroscopy. (XXVI, Z = Cbs) was dissolved in TFA and its n.m.r. spectrum immediately recorded. This spectrum showed signals at

1.94τ(2H, d, J8Hz, low field half of Cbs signal), 2.2-3.0(9H, m, aromatic), 3.3-3.6(1H, m), 5.2-5.5(1H, m), 5.7-6.1(1H, m), 6.32(2H, t, J8Hz) and 7.1-9.3(8H, m),

and was presumably due to the protonated form of (XXVI, Z = Cbs) (see FIGURE Va). After two days the spectrum was re-recorded. Of particular interest were the following changes (FIGURE Vb). Three sharp singlets had appeared at τ0.59, 3.26 and 3.62. The aliphatic region of the spectrum had not altered considerably, and for clarity has been omitted from these figures.

After seven days the spectrum had the appearence of FIGURE Vc, showing that conversion was complete. The low field signal was assigned to the proton at $C_7$ of (XXXIX). This agrees with the value reported[11] for the similar proton at $C_2$ in the protonated form of skatole (XLIII) which occurs at a position 1.43τ downfield of the aromatic multiplet. The signals at 3.26 and 3.62τ were more intriguing. These could not be due to aromatic protons, since they were uncoupled, and it was first thought that they were arising due to secondary reactions of (XXXVIII) although this was unlikely since they each integrated to one proton.

The n.m.r. spectrum of (XXX) was recorded in TFA and proved identical to that of (XXVI, Z = Cbs) after seven days (FIGURE Vc) with the exception of signals from two different ethoxy groups. This meant that addition of ethanol across the double bond in (XXXIX) was rapid and reversible. The two different ethoxy signals are probably due to free ethanol and ethyl trifluoroacetate.

The important feature of this spectrum was again the appearence of singlets at 0.59, 3.26 and 3.62τ, each integrating to one proton.

FIGURE Va

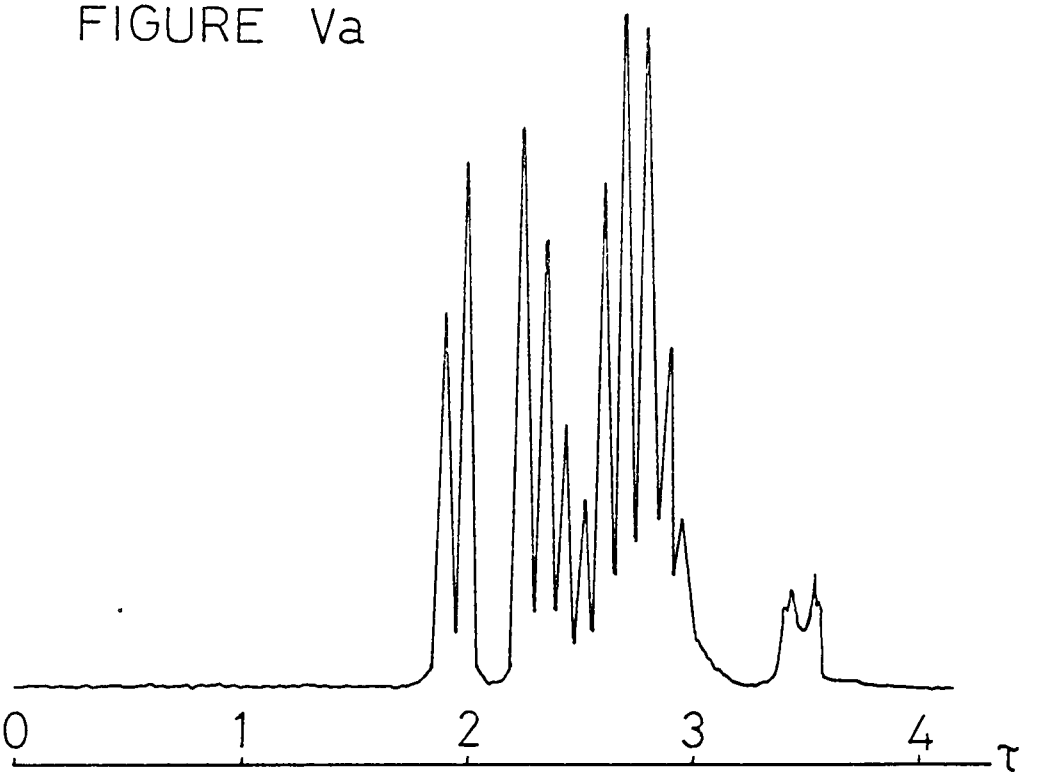



FIGURE Vb

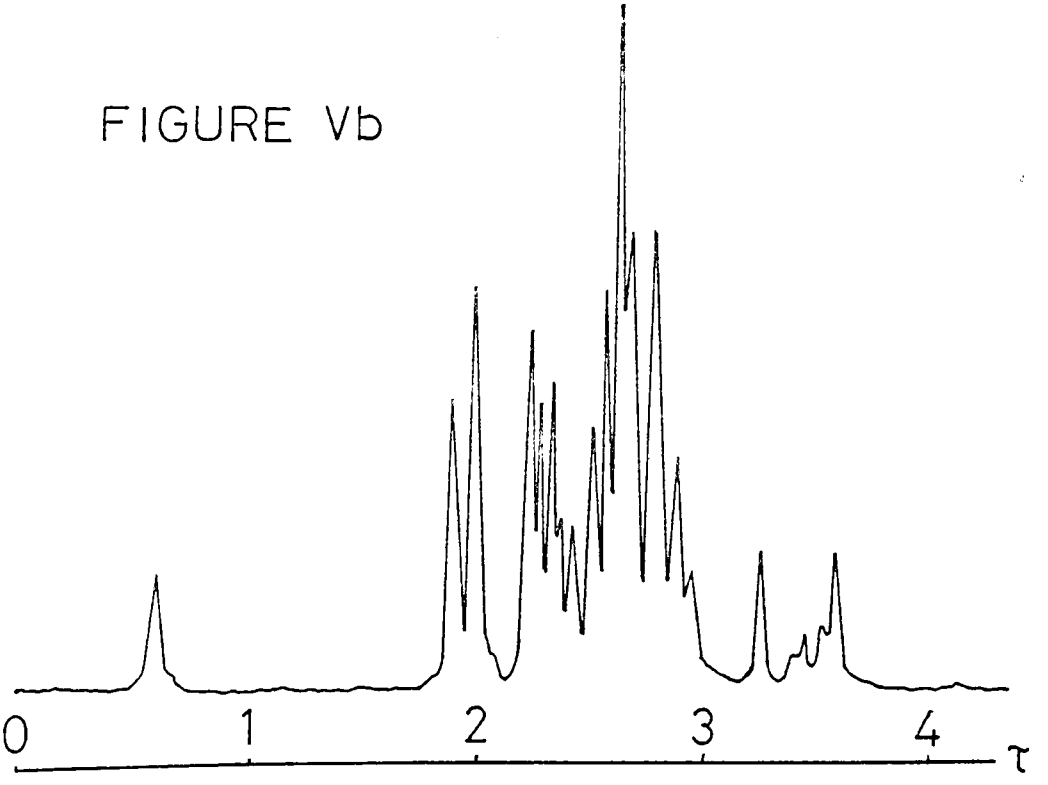


FIGURE Vc

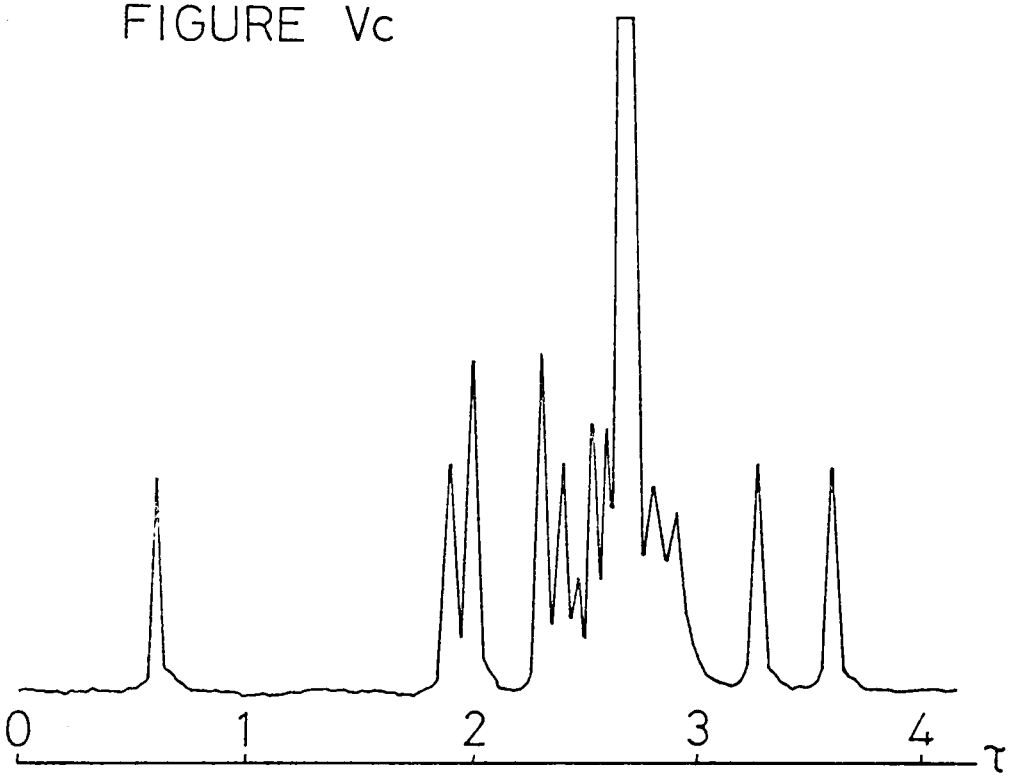
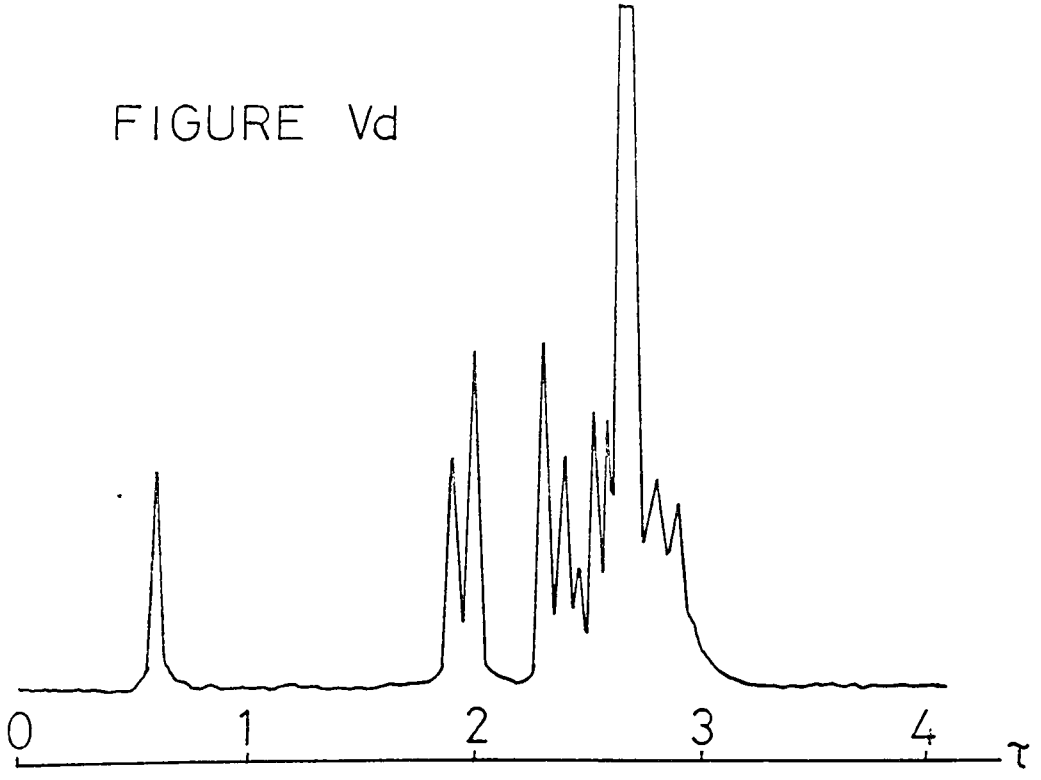
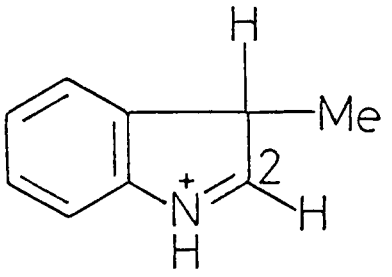
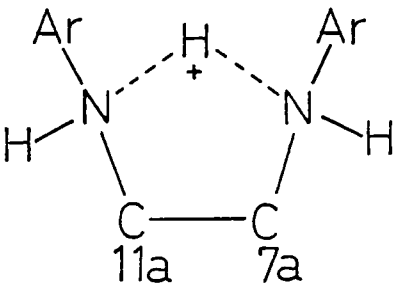



FIGURE Vd

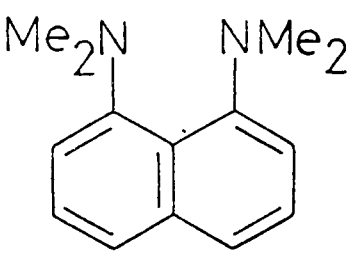




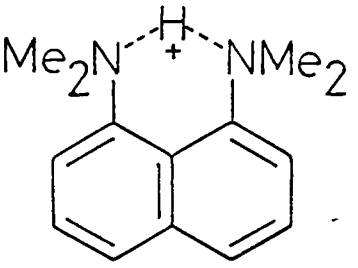

XLIII



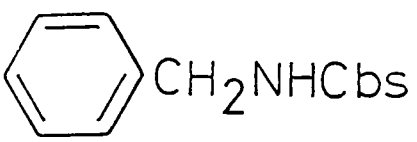

XLIV




XLV




XLVI




XLVII

There was now no alternative but to assign the signals at 3.26 and 3.62τ to the two NH protons, although in TFA exchange usually takes place so rapidly that such protons do not appear in the n.m.r. spectrum. In order to check these assignments the above work was repeated, this time using deuteriated trifluoroacetic acid (TFA-D) as solvent.

Compound (XXVI, Z = Cbs) was dissolved in TFA-D and the spectrum immediately recorded. This spectrum was identical to that shown in FIGURE Va. After 24 hours at 40° the spectrum was re-recorded and now appeared as in FIGURE Vd. The arrearance of a one-proton singlet at 0.59τ showed that conversion was complete, but in this case the two singlets at 3.26 and 3.62τ were absent. For comparison the spectrum of (XXX) was recorded in TFA-D. This spectrum again showed the absence of these two signals.

This work proves beyond doubt that these signals were due to the two NH protons and that exchange with the solvent was slow enough for these protons to register in the n.m.r. spectrum. This may be explained by the formation of the ion whose partial structure is shown as (XLIV). Because of strong intramolecular hydrogen bonding proton exchange with the solvent must be slow. A similar effect has been observed in the case of 1,8-bis(dimethylamino)naphthalene (XLV). In $CDCl_3$ solution the methyl groups appear as a singlet at 7.29τ whereas in TFA they appear as a doublet (J2Hz) at 6.79τ[12]. This coupling can only occur if proton exchange is slow and this has been explained by the formation of the ion (XLVI). Furthermore the rate of this proton exchange in (XLVI) has been estimated[13] as occurring $10^5$ times more slowly than for other amines, largely because of a strong intramolecular hydrogen bond in the protonated amine.

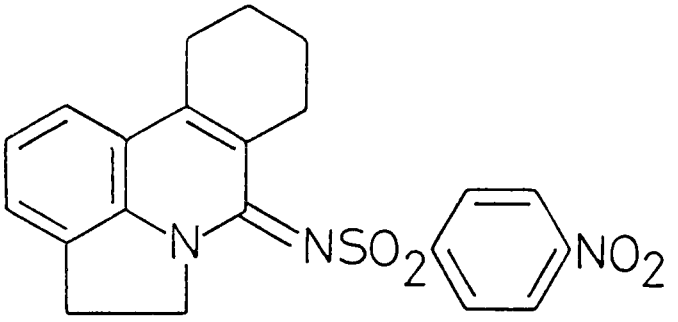
As a final experiment in this series, the n.m.r. spectrum of compound (XLVII) was recorded in TFA. The methylene signal occurred as a singlet at 5.75τ, showing no coupling to NH and demonstrating the

rapid exchange in compounds where the protonated form cannot be stabilised by hydrogen bonding.

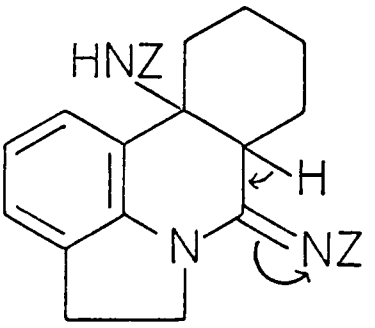
The final experiments into the reactions of (VII) with azides were carried out using p-nitrobenzenesulphonyl azide. From this reaction four products were obtained. The first of these, A, was similar in properties to the compounds (XXVII) and was assigned the structure (XXVII, Z = p-nitrobenzenesulphonyl). This compound was highly insoluble and n.m.r. spectra could not be obtained in $CDCl_3$ or $DMSO_d6$. Although the compound was soluble in TFA this solvent was avoided since the acid is known to catalyse the elimination of sulphonamide from this type of structure (see Chapter II). It was decided to attempt a hydrolysis to the p-nitrobenzenesulphonyl analogue of (XXIX) and to confirm the structure of the latter. On heating a suspension of A in aqueous ethanolic sodium hydroxide a product was obtained which was not the expected compound, but whose analytical data corresponded to elimination of nitrobenzene-p-sulphonamide. The i.r. spectrum showed an absorption due to C=N and the n.m.r. spectrum(TFA) contained signals at

1.44$\tau$(2H, d, J9Hz, low field half of sulphonyl signal), 1.74(2H, d, J9Hz, high field half of sulphonyl signal), 1.8-2.1(3H, m, aromatic), 4.52(2H, t, J7Hz), 6.14(2H, t, J7Hz), 6.56(2H, t, J7Hz), 7.40(2H, t, J7Hz) and 7.8-8.4(4H, m).

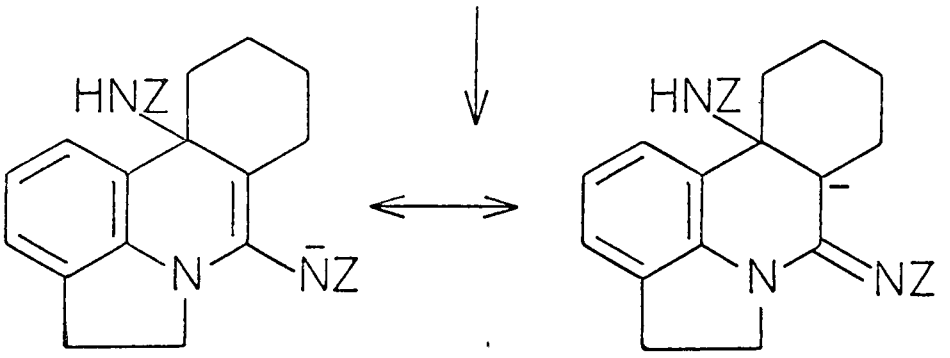
These data suggest the structure(XLVIII) for the compound, which in fact supports structure (XXVII, Z = p-nitrobenzenesulphonyl) for A. The elimination of sulphonamide, however, is contrary to the behaviour of compound (XXVII, Z = Ts) and might be taken as evidence that in this case we have a trans ring junction. It is hardly likely, however, that the stereochemical course of the indole/azide reaction would be altered by a change of azide and we prefer the alternative explanation that the strongly electron-withdrawing p-nitro group activates the hydrogen atom at $C_{7a}$ as shown to give (XLIX) and in fact



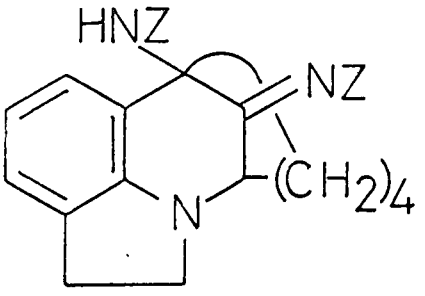

XLVIII




XXVII




XLIX




XXVI

elimination does not occur by the usual concerted process. In support of this theory it was observed that an accurate melting point of A could not be obtained. The compound melted over a wide temperature range starting about 245° then resolidified, to remelt at approximately 300° [the melting point of (XLVIII) is 312-314°]; this again suggests that elimination of sulphonamide takes place readily.

The second compound, B, was isolated as orange prisms (from acetonitrile) and was assigned the structure (XXVI, Z = p-nitrobenzenesulphonyl) by analogy with the compounds (XXVI, Z = Ts or Cbs). The n.m.r. spectrum showed the following signals:

1.59τ, 1.73, 1.97, 2.62(each 2H, d, J8Hz, p-nitrobenzenesulphonyl signals), 3.07(1H, d, J7Hz, aromatic), 3.6-4.0(2H, m, aromatic), 4.35 (1H, dd, J9,3Hz), 4.40(1H, s, exchanged $D_2O$, NH), 6.2-7.0(5H, m), 7.99 (3H, s, MeCN) and 7.5-9.3(7H, m).

This spectrum showed the presence of one molecule of acetonitrile of crystallisation in the molecule and this observation was supported by the analysis and i.r. spectrum, which showed a sharp peak at 2250 $cm^{-1}$. Prolonged drying of the compound in vacuo at 100° resulted in decomposition, and an attempt was made to recrystallise the product from propanol in order to remove the acetonitrile. On doing this, however, decomposition started to occur and boiling was continued until this was complete. The product was recrystallised from ethanol and a compound was obtained whose spectral data were very similar to those of (XXX). The n.m.r. spectrum (D) contained the following signals:

1.31-1.6τ(5H, m), 1.6-1.9(3H, m), 2.0-2.5(2H, m), 3.1-3.4(2H, m), 3.74(1H, t, J8Hz, aromatic), 4.62(1H, s), 5.9-6.6(4H, m), 7.1(2H, m), 8.74(3H, t, J7Hz, ethyl Me) and 7.4-9.6(8H, m).

On addition of $D_2O$ to the solution the compound was precipitated and no definite NH assignments can therefore be made. The structure (L) was proposed for this compound which was presumably formed by a

thermal rearrangement analogous to the acid catalysed formation of (XXX).

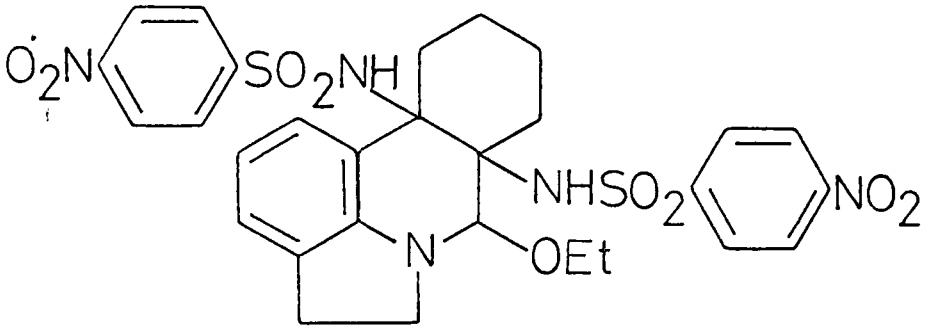
The third compound, C, was unlike any of the products obtained so far from these investigations. It was isomeric with (XLVIII), the i.r. spectrum contained a band due to C=N absorption and the n.m.r. spectrum contained signals at

1.66τ(2H, d, J8Hz, low field half of sulphonyl signal), 1.84(2H, d, J8Hz, high field half of sulphonyl signal), 2.70(1H, m, aromatic), 2.9-3.1(2H, m, aromatic), 5.63(2H, t, J7Hz), 6.3-6.6(4H, m), 6.93(2H, t, J7Hz) and 7.8-8.3(4H, m).

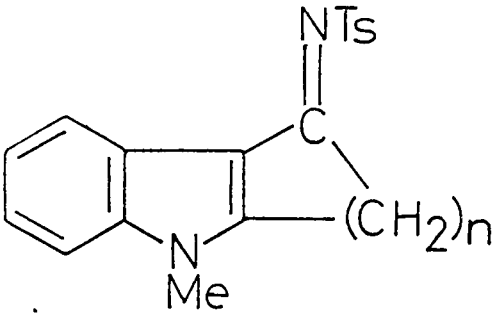
The u.v. spectrum was very similar to those of the compounds (LI, n = 4 or 5) (see Chapter II) and the structure (LII) was proposed. The other analytical and spectroscopic data are also in agreement with this structure.

The fourth product from the reaction of (VII) with p-nitrobenzenesulphonyl azide was the compound (L), identical in all respects to that obtained above from (XXVI, Z = p-nitrobenzenesulphonyl) and presumably formed in a similar manner during work-up of the reaction mixture.

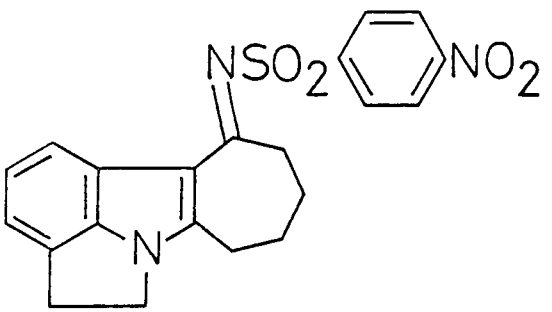
A logical continuation of this work would be a study of the reactions of the indole (LIII) with azides, bearing in mind the differences encountered between the simple and bridged cyclohept-indoles.



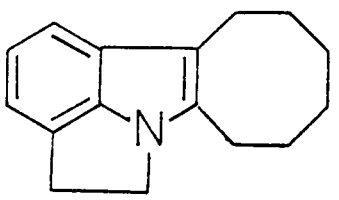

L




LI




LII




LIII

# CHAPTER III

## Experimental

1. 2-(Indolin-7-yl)-2-p-tolylsulphonylaminocyclohexanone (XI, Z = Ts):-

a. 4,5,7,8,9,10-Hexahydropyrrolo[3,2,1-jk]carbazole (2 g, 1 mol) and tosyl azide (2.1 g, 1.05 mol) were boiled under reflux in methanol (20 ml) for 3 hours. The solution was cooled and the solid collected. Recrystallisation from acetonitrile gave colourless prisms, m.p. 223-225° (decomp.). (Yield 2.11 g, 55%).

b. 4,5,7,8,9,10-Hexahydropyrrolo[3,2,1-jk]carbazole (2 g, 1 mol) and tosyl azide (4 g, 2 mol) were dissolved in pyridine (20 ml; dried by distillation from potassium hydroxide) and the solution was allowed to stand at room temperature for 3 days, then at 60° (oil bath) for 4 hours. The mixture was cooled and the solid (A) collected. The liquors were evaporated and the residue chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was obtained as colourless prisms, m.p. 222-224° (from acetonitrile). (Yield 0.67 g, 17%).

Found: C, 65.7; H, 6.3; N, 7.3; S, 8.4%

$C_{21}H_{24}N_2O_3S$ requires C, 65.6; H, 6.3; N, 7.3; S, 8.3%

$\lambda_{max.}$: 202, 212sh, 227sh and 312 nm ($\epsilon$ 29,300, 20,600, 14,800 and 1,940)

$\nu_{max.}$: 1702 (C=O), 3320 (N-H) and 3375 (N-H) $cm^{-1}$.

m/e: 384 (M, 12%), 366 (M - $H_2O$, 5%), 229 (M - Ts, 27%; $m^*$ 136.6), 213 (M - $TsNH_2$, 10%), 211 (366 - Ts, 15%) and 185 (213 - $C_2H_4$, 100%).

2. 2-(Indolin-7-yl)-2-(N-methyl-p-tolylsulphonylamino)cyclohexanone (XIIb):-

Dimethyl sulphate (2 ml) was added dropwise at room temperature to a stirred solution of 2-(indolin-7-yl)-2-p-tolylsulphonylamino-cyclohexanone (200 mg) in acetone (5 ml) and 50% aqueous potassium hydroxide (5 ml). The mixture was stirred for 1 hour after the addition and then poured into water (20 ml) and extracted with benzene

(3 x 5 ml). The extracts were dried (magnesium sulphate). Removal of the solvent *in vacuo* gave a colourless crystalline residue. T.l.c. showed the presence of two components, separated by chromatography on silica, eluting with benzene/ethyl acetate (9:1). The fore running compound formed colourless needles, m.p. 165-166° (from ethanol). (Yield 85 mg, 41%).

Found: C, 66.4; H, 6.6; N, 7.2; S, 8.3%

$C_{22}H_{26}N_2O_3S$ requires C, 66.4; H, 6.5; N, 7.0; S, 8.0%

$\lambda_{max.}$: 201, 223sh, 252sh, 305sh and 335 nm ($\varepsilon$ 26,600, 21,100 7,760, 1,640 and 3,550)

$\nu_{max.}$: 1705 (C=O) and 3380 (N-H) $cm^{-1}$

m/e: 398 (M, 5%), 380 (M - $H_2O$, 1%), 243 (M - Ts, 17%; m* 148.4), 213 (M - TsNHMe, 50%), 185 (213 - $C_2H_4$, 67%) and 91 (Ts - $SO_2$, 100%).

3. 2-(1-Methylindolin-7-yl)-2-p-tolylsulphonylaminocyclohexanone (XIIa):-

A solution of 2-(indolin-7-yl)-2-p-tolylsulphonylaminocyclohexanone (500 mg) in methyl iodide (2 ml) and acetonitrile (5 ml) was heated under reflux for 48 hours. The solvent was removed *in vacuo* and the residue dissolved in ethanol (5 ml) and water (5 ml). The solution was neutralised (2N aqueous sodium carbonate) and the precipitate extracted into chloroform (3 x 5 ml). The extracts were dried (magnesium sulphate) and the solvent was removed to give a crystalline residue. This was dissolved in benzene/ethyl acetate (9:1) and filtered through a short silica column to remove starting material. The product was recrystallised from methanol as colourless prisms, m.p. 133-134°. (Yield 210 mg, 41%).

Found: C, 66.4; H, 6.6; N, 7.2%

$C_{22}H_{26}N_2O_3S$ requires C, 66.4; H, 6.5; N, 7.0%

$\lambda_{max.}$: 219, 254sh and 292 nm ($\varepsilon$ 19,000, 4,920 and 1,850)

$\nu_{max.}$: 1710 (C=O) and 3235 (N-H) $cm^{-1}$.

m/e: 398 (M, 36%), 370 (M - $C_2H_4$, 22%; $m^*$ 344.0), 243 (M - Ts, 21%; $m^*$ 148.4), 215 (370 - Ts, 100%) and 200 (215 - Me, 100%)

4. 2-(1-Methylindolin-7-yl)-2-(N-methyl-p-tolylsulphonylamino)-cyclohexanone (XIIc):-

a. Dimethyl sulphate (2 ml) was added dropwise at room temperature to a stirred solution of 2-(indolin-7-yl)-2-p-tolylsulphonylamino-cyclohexanone (200 mg) in acetone (5 ml) and 50% aqueous potassium hydroxide (5 ml). The mixture was stirred for 1 hour then poured into water (20 ml) and extracted with benzene (3 x 5 ml). The extracts were dried (magnesium sulphate) and the solvent was removed in vacuo to give a colourless crystalline residue. This was dissolved in acetonitrile (5 ml) and methyl iodide (2 ml) and the solution was boiled under reflux for 48 hours. The solvent was removed in vacuo and the residue dissolved in ethanol (5 ml) and water (5 ml). The solution was neutralised (2N aqueous sodium carbonate) and the precipitate extracted into chloroform (3 x 5 ml). The extracts were washed with sodium thiosulphate solution, then water, and finally dried (magnesium sulphate). Evaporation gave a tarry residue, which was filtered through a short silica column, eluting with benzene/ethyl acetate (9:1). Evaporation and recrystallisation from methanol gave colourless prisms, m.p. 153-154°. (Yield 76 mg, 36%).

b. The slow moving component of the mixture obtained in experiment 2 was recrystallised from ethanol as colourless prisms, m.p. 153-154°. (Yield 46 mg, 22%).

Found: C, 66.6; H, 6.7; N, 7.0; S, 7.7%

$C_{23}H_{28}N_2O_3S$ requires C, 67.0; H, 6.8; N, 6.8; S, 7.8%

$\lambda_{max.}$: 201, 217sh and 304 nm (ε 26,300, 21,700 and 2,550)

$\nu_{max.}$: 1724 and 1738 (C=O) $cm^{-1}$

m/e: 412 (M, 16%), 384 (M - $C_2H_4$, 3%), 257 (M - Ts, 7%),

229 (384 - Ts, 90%), 228 (M - TsNMe, 20%), 227 (M - TsNHMe, 23%), 213 (228 - Me, 34%), 200 (228 - $C_2H_4$, 90%) and 91 (Ts - $SO_2$, 100%).

5. 1,2-Dihydro-5-p-tolylsulphonyliminopyrrolo[3,2,1-hi]indoline-4-spirocyclopentane (XIV, Z = Ts):-

The mother liquors from experiment 1a were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was obtained as bright orange plates, (from ethanol), m.p. 210-212°. (Yield 110 mg, 3%).

Found: C, 68.7; H, 6.0; N, 7.6; S, 9.0%

$C_{21}H_{22}N_2O_2S$ requires C, 68.9; H, 6.0; N, 7.7; S, 8.7%

$\lambda_{max.}$: 202, 230, 283 and 450 nm ($\epsilon$ 22,300, 22,200, 9,270 and 7,780)

$\nu_{max.}$: 1555 (C=N) $cm^{-1}$

m/e: 366 (M, 8%), 211 (M - Ts, 100%; $m^*$ 121.6), 209 (211 - 2H, 8%; $m^*$ 207.0), 194 (211 - $NH_3$, 6%; $m^*$ 178.4) and 183 (211 - $C_2H_4$, 16%).

6. 4,5,7,8,9,10-Hexahydro-7-p-tolylsulphonylaminopyrrolo[3,2,1-jk]-carbazole (XIII):-

a. A solution of 4,5,7,8,9,10-hexahydropyrrolo[3,2,1-jk]-carbazole (1 g, 1 mol) and tosyl azide (1.1 g, 1.1 mol) in acetic acid (10 ml) was allowed to stand at room temperature for 2 weeks. The solution was poured into water (25 ml) and the mixture was extracted with chloroform (3 x 10 ml). The extracts were washed with 2N aqueous sodium carbonate, then water, and finally dried (magnesium sulphate). Evaporation of the solvent gave a black tar. Chromatography on silica gel, eluting with benzene/ethyl acetate mixtures gave the compound as pale yellow prisms, m.p. 200-203° (from ethanol). (Yield 90 mg, 5%).

b. The mother liquors from experiment 1a were chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The

compound was obtained as colourless prisms (from ethanol), m.p. 198-204°. (Yield 30 mg, 1%).

c. 2-(Indolin-7-yl)-2-p-tolylsulphonylaminocyclohexanone (200 mg) was heated slowly to its melting point (oil bath). This temperature was maintained for 30 minutes during which the melt became bright orange and gas was evolved. The melt was cooled and triturated with methanol. The solid was collected and recrystallised from ethanol as colourless prisms, 204-205°. (Yield 85 mg, 45%).

Found: C, 68.7; H, 5.9; N, 7.4; S, 9.0%

$C_{21}H_{22}N_2O_2S$ requires C, 68.9; H, 6.0; N, 7.7; S, 8.7%

$\lambda_{max.}$: 203, 233 and 283 nm ($\varepsilon$ 23,100, 38,000 and 7,420)

$\nu_{max.}$: 3240 (N-H) $cm^{-1}$

m/e: 366 (M, 69%), 323 (M - $C_3H_7$, 16%), 211 (M - Ts, 85%; $m^*$ 121.6), 210 (211 - H, 72%; $m^*$ 209.0), 196 (M - TsNH, 100%) and 195 (196 - H, 48%; $m^*$ 194.0).

7. 4,5,7,8,9,10-Hexahydro-7-p-tolylsulphonyliminocyclopenta[c]-pyrrolo[3,2,1-ij]quinoline (XVII, Z = Ts):-

a. The solid (A) obtained from experiment 1b was recrystallised from acetonitrile as very fine colourless needles, m.p. 230-232°. (Yield 0.87 g). Chromatography of the liquors on silica gel, eluting with benzene/ethyl acetate mixtures gave a further 0.93 g of the compound. (Total yield 1.80 g, 49%).

b. The mother liquors from experiment 1a were evaporated and chromatographed on silica, eluting with benzene/ethyl acetate mixtures. Recrystallisation from acetonitrile gave the compound as colourless needles, m.p. 229-230°. (Yield 91 mg, 2%).

c. A solution of 4,5,7,7a,8,9,10,10a-octahydro-10a-p-tolylsulphonylamino-7-p-tolylsulphonyliminocyclopenta[c]pyrrolo[3,2,1-ij]-quinoline (XIX, Z = Ts) (200 mg) and 1,5-diazabicyclo[4.3.0]non-5-ene (50 mg) in ethanol (4 ml) was heated under reflux for 19 hours. The

solution was cooled and poured into water (20 ml). The mixture was made alkaline (2N aqueous sodium hydroxide) and extracted with chloroform (3 x 5 ml). The extracts were dried (magnesium sulphate) and the solvent was removed in vacuo to give a crystalline residue, recrystallised from acetonitrile as colourless needles, m.p. 230-232°. (Yield 77 mg, 5%).

Found: C, 69.5; H, 5.5; N, 7.6; S, 8.6%

$C_{21}H_{20}N_2O_2S$ requires C, 69.2; H, 5.5; N, 7.7; S, 8.8%

$\lambda_{max.}$: 220, 269, 310, 340sh and 350 nm ($\varepsilon$ 34,800, 39,300, 4,840, 9,650 and 11,900)

$\nu_{max.}$: 1508 (C=N) $cm^{-1}$

m/e: 364 (M, 6%), 299 (M - $SO_2$ - H, 5%; $m^*$ 245.6), 209 (M - Ts, 100%; $m^*$ 120.0) and 192 (209 - $NH_3$, 4%; $m^*$ 176.4).

8. 4,5,7,7a,8,9,10,10a-Octahydro-10a-p-tolylsulphonylamino-7-p-tolylsulphonyliminocyclopenta[c]pyrrolo[3,2,1-ij]quinoline (XIX, Z = Ts):-

Chromatography of the mother liquors from experiment 1b on silica gel, eluting with benzene/ethyl acetate mixtures, gave the compound as colourless prisms, m.p. 239-241° (from acetonitrile). (Yield 0.97 g, 18%).

Found: C, 62.7; H, 5.5; N, 7.9; S, 12.0%

$C_{28}H_{29}N_3O_4S_2$ requires C, 62.8; H, 5.4; N, 7.9; S, 12.0%

$\lambda_{max.}$: 223, 273, 283 and 309 nm ($\varepsilon$ 18,300, 9,930, 11,200 and 9,180)

$\nu_{max.}$: 1550(C=N) and 3250 (N-H) $cm^{-1}$

m/e: 535 (M, 4%), 380 (M - Ts, 1%), 365 (M - TsNH, 12%), 364 (365 - H, 12%), 299 (364 - $SO_2$ - H, 7%; $m^*$ 245.6), 209 (364 - Ts, 100%; $m^*$ 120.0) and 192 (209 - $NH_3$, 4%; $m^*$ 176.4).

9. 4,5,7,8,9,10-Hexahydro-7-oxocyclopenta[c]pyrrolo[3,2,1-ij]-quinoline (XVIII):-

4,5,7,8,9,10-Hexahydro-7-p-tolylsulphonyliminocyclopenta[c]-pyrrolo[3,2,1-ij]quinoline (200 mg) was heated under reflux in ethanol (5 ml) and 2N aqueous sodium hydroxide (5 ml) for 6 hours. The ethanol was removed in vacuo and water (20 ml) was added. The precipitate was extracted into chloroform (3 x 5 ml) and the extracts were dried (magnesium sulphate). The solvent was removed and the residue recrystallised from benzene as colourless needles, m.p. 171-173°. (Yield 86 mg, 74%).

Found: C, 79.7; H, 6.4; N, 6.9%

$C_{14}H_{13}NO$ requires C, 79.6; H, 6.2; N, 6.6%

$\lambda_{max.}$: 205, 220sh, 234, 251, 268, 278, 288, 316sh, 327 and 340 nm (ε 31,700, 24,100, 26,800, 18,300, 4,110, 5,020, 4,600, 3,770, 5,150 and 4,020)

$\nu_{max.}$: 1640 (C=O) $cm^{-1}$

m/e: 211 (M, 80%), 210 (M - H, 100%; $m^*$ 209.0) and 192 (210 - $H_2O$, 3%; $m^*$ 175.5).

10. Reaction of 4,5,7,8,9,10-hexahydropyrrolo[3,2,1-jk]carbazole with p-chlorobenzenesulphonyl azide:-

A solution of the indole (2 g, 1 mol) and p-chlorobenzene-sulphonyl azide (3.3 g, 1.5 mol) in methanol (20 ml) was boiled under reflux for 2 hours. The solution was cooled and the solid collected. Recrystallisation from acetonitrile gave 2-p-chlorobenzenesulphonyl-amino-2-(indolin-7-yl)cyclohexanone (XI, Z = Cbs) as pale yellow prisms, m.p. 230° (decomp; m.p. depends on rate of heating). (Yield 370 mg).

Found: C, 59.8; H, 5.5; Cl, 8.8; N, 6.9; S, 7.4%

$C_{20}H_{21}ClN_2O_3S$ requires C, 59.3; H, 5.2; Cl, 8.8; N, 6.9; S, 7.9%

$\lambda_{max.}$: 281 and 310 nm (ε 15,500 and 1,890)

$\nu_{max.}$: 1692 (C=O), 3315 (N-H) and 3355 (N-H) $cm^{-1}$

m/e: 404 (M, 23%), 386 (M - $H_2O$, 2%), 229 (M - Cbs, 67%; $m^*$ 129.8), 213 (M - $CbsNH_2$, 10%), 212 (229 - OH, 20%; $m^*$ 196.3), 211 (386 - Cbs, 16%), 201 (229 - $C_2H_4$, 19%) and 185 (213 - $C_2H_4$, 100%).

The mother liquors were evaporated and chromatographed on silica, eluting with benzene/ethyl acetate mixtures. The following compounds were obtained in order of elution:-

i. 5-p-Chlorobenzenesulphonylimino-1,2-dihydropyrrolo[3,2,1-hi]-indoline-4-spirocyclopentane (XIV, Z = Cbs) as bright orange prisms (from acetonitrile), m.p. 225-227°. (Yield 630 mg, 16%).

Found: C, 62.1; H, 4.9; Cl, 9.4; N, 7.2; S, 8.3%

$C_{20}H_{19}ClN_2O_2S$ requires C, 62.1; H, 4.9; Cl, 9.2; N, 7.2; S, 8.3%

$\lambda_{max.}$: 202, 233, 288 and 453 nm ($\varepsilon$ 27,600, 27,400, 10,100 and 8,490)

$\nu_{max.}$: 1553 (C=N) $cm^{-1}$

m/e: 386 (M, 11%), 211 (M - Cbs, 100%; $m^*$ 115.3), 209 (211 - 2H, 9%; $m^*$ 207.0), 194 (211 - $NH_3$, 5%) and 183 (211 - $C_2H_4$, 9%).

ii. Compound (XI, Z = Cbs). (Yield 1.6 g, total yield 48%).

iii. 7-p-Chlorobenzenesulphonylimino-4,5,7,8,9,10-hexahydro-cyclopenta[c]pyrrolo[3,2,1-ij]quinoline (XVII, Z = Cbs), recrystallised from acetonitrile as colourless needles, m.p. 268-271°. (Yield 71 mg, 2%).

Found: C, 62.3; H, 4.7; N, 7.4%

$C_{20}H_{17}ClN_2O_2S$ requires C, 62.4; H, 4.4; N, 7.3%

$\lambda_{max.}$: 219, 269, 310, 338sh and 350 nm ($\varepsilon$ 34,800, 35,800, 5,550, 9,780 and 12,100).

$\nu_{max.}$: 1520 (C=N) $cm^{-1}$

m/e: 384 (M, 6%), 319 (M - $SO_2$ - H, 8%) and 209 (M - Cbs, 100%).

iv. Chlorobenzene-p-sulphonamide as colourless plates (from benzene, m.p. 143-145°. (Yield 142 mg).

v. 10a-p-Chlorobenzenesulphonylamino-7-p-chlorobenzenesulphonyl-

imino-4,5,7,7a,8,9,10,10a-octahydrocyclopenta[c]pyrrolo[3,2,1-ij]-quinoline (XIX, Z = Cbs), recrystallised from acetonitrile as colourless prisms, m.p. 229-231°. (Yield 91 mg, 2%).

Found: C, 54.4; H, 4.2; Cl, 12.2; N, 7.0; S, 10.9%

$C_{26}H_{23}Cl_2N_3O_4S_2$ requires C, 54.2; H, 4.0; Cl, 12.3; N, 7.3; S, 11.1%

$\lambda_{max.}$: 227, 276sh, 283 and 310 nm (ε 37,100, 17,100, 18,900 and 17,100)

$\nu_{max.}$: 1548 (C=N) and 3235 (N-H) $cm^{-1}$

m/e: 575 (M, 9%), 400 (M - Cbs, 2%), 385 (M - CbsNH, 15%), 384 (385 - H, 11%), 319 (384 - $SO_2$ - H, 7%) and 209 (384 - Cbs, 100%).

11. 1,2-Dihydro-5-p-nitrobenzenesulphonyliminopyrrolo[3,2,1-hi]-indoline-4-spirocyclopentane (XXI):-

a. A solution of 4,5,7,8,9,10-hexahydropyrrolo[3,2,1-jk]-carbazole (700 mg, 1 mol) and p-nitrobenzenesulphonyl azide (1.20 g, 1.5 mol) in methanol (10 ml) was boiled under reflux for 15 minutes. The solution was cooled and the solid collected, then boiled in propanol (10 ml) for 3 hours. The solvent was removed in vacuo and the residue recrystallised from acetonitrile as bright red prisms, m.p. 193-194°. (Yield 184 mg, 13%).

b. The mother liquors from experiment 13 were chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The product was recrystallised from acetonitrile as red prisms, m.p. 194-195°. (Yield 67 mg, 3%).

c. The mother liquors from experiment 14 were evaporated and the residue recrystallised from acetonitrile as red prisms, m.p. 193-194°. (Yield 35 mg, 15%).

Found: C, 60.7; H, 4.9; N, 10.4; S, 8.1%

$C_{20}H_{19}N_3O_4S$ requires C, 60.5; H, 4.8; N, 10.6; S, 8.1%

$\lambda_{max.}$: 236, 289 and 456 nm (ε 26,500, 14,200 and 9,150)

$\nu_{max.}$: 1545 (C=N) $cm^{-1}$

m/e: 397 (M, 20%), 356 (M - $C_3H_5$, 3%; $m^*$ 319.2), and 211 (M - $NO_2.C_6H_4.SO_2$, 100%; $m^*$ 112.1).

12. 2-(Indolin-7-yl)-2-p-nitrobenzenesulphonylaminocyclohexanone (XXII):-

The mother liquors from experiment 11 were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was recrystallised from ethanol as orange needles, m.p. 187-189° (decomposition). (Yield 180 mg, 12%).

Found: C, 57.7; H, 5.2; N, 9.9; S, 7.5%

$C_{20}H_{21}N_3O_5S$ requires C, 57.8; H, 5.1; N,10.1; S, 7.7%

$\lambda_{max.}$: 203 and 256 nm ($\varepsilon$ 25,600 and 12,300)

$\nu_{max.}$: 1710 (C=O), 3170, 3315 and 3365 (N-H) $cm^{-1}$

m/e: 415 (M, 67%), 397 (M - $H_2O$, 7%), 229 (M - $NO_2.C_6H_4.SO_2$, 70%) and 185 (M - $NO_2.C_6H_4.SO_2NH_2$ - $C_2H_4$, 100%).

13. 6a-Methoxy-10a-p-nitrobenzenesulphonylamino-4,5,6a,7,8,9,10,10a-octahydropyrrolo[3,2,1-jk]carbazole (XXIII):-

A solution of 4,5,7,8,9,10-hexahydropyrrolo[3,2,1-jk]carbazole (1 g, 1 mol) and p-nitrobenzenesulphonyl azide (1.75 g, 1.5 mol) in methanol (15 ml) was boiled under reflux for 15 minutes. The solution was cooled and the solid collected. Recrystallisation from chloroform/methanol gave pale orange prisms, m.p. 106-110° (decomp). (Yield 1.64 g). Chromatography of the mother liquors (silica gel, benzene/ethyl acetate mixtures) gave a further 280 mg of this product. (Total yield 1.92 g, 89%).

Found: C, 58.2; H, 5.7; N, 9.8; S, 7.6%

$C_{21}H_{23}N_3O_5S$ requires C, 58.7; H, 5.4; N, 9.8; S, 7.5%

$\lambda_{max.}$: 210, 252 and 265sh nm ($\varepsilon$ 23,200, 11,700 and 10,300)

$\nu_{max.}$: 3240 and 3305 (N-H) $cm^{-1}$

m/e: 397 (M - MeOH, 39%), 356 (397 - $C_3H_5$, 3%), 211 (397 -

$NO_2.C_6H_4.SO_2$, 100%) and 194 (211 - $NH_3$, 81%).

14. 4,5,7,8,9,10-Hexahydro-7-p-nitrobenzenesulphonylaminopyrrolo-[3,2,1-jk]carbazole (XXIV):-

6a-Methoxy-10a-p-nitrobenzenesulphonylamino-4,5,6a,7,8,9,10,10a-octahydropyrrolo[3,2,1-jk]carbazole (250 mg) was heated at 110° for 15 minutes. The melt was cooled, triturated with methanol and the solid was collected. Recrystallisation from acetonitrile gave pale yellow prisms, m.p. 198-200°. (Yield 138 mg, 60%).

Found: C, 60.7; H, 4.9; N, 10.4%

$C_{20}H_{19}N_3O_4S$ requires C, 60.5; H, 4.8; N, 10.6%

$\lambda_{max.}$: 205, 232 and 280 nm (ε 29,200, 36,800 and 17,100)

$\nu_{max.}$: 3240 (N-H) $cm^{-1}$

m/e: 397 (M, 47%), 211 (M - $NO_2.C_6H_4.SO_2$, 22%; $m^*$ 112.1), 210 (211 - H, 27%), 196 (M - $NO_2.C_6H_4.SO_2NH$, 90%; $m^*$ 96.8), 195 (196 - H, 80%) and 194 (195 - H, 100%).

15. 4,6-Butano-1,2,5,6-tetrahydro-6-p-tolylsulphonylamino-5-p-tolylsulphonylimino-4H-pyrrolo[3,2,1-ij]quinoline (XXVI, Z = Ts):-

a. A solution of 4,5,8,9,10,11-hexahydro-7H-cyclohept[b]-pyrrolo[3,2,1-hi]indole (2 g, 1 mol) and tosyl azide (3.8 g, 2 mol) in chloroform (20 ml; purified over alumina) was allowed to stand at room temperature for 48 hours. The solvent was removed *in vacuo* and the residue triturated with methanol. The yellow solid was collected and recrystallised from acetonitrile as yellow prisms, m.p. 186-187°. (Yield 3.06 g, 59%).

b. A solution of 4,5,8,9,10,11-hexahydro-7H-cyclohept[b]-pyrrolo[3,2,1-hi]indole (1 g,1 mol) and tosyl azide (1.9 g, 2 mol) in dry pyridine (20 ml) was allowed to stand at room temperature for 48 hours. The solvent was removed *in vacuo* and methanol (10 ml) was added. The solid was collected and recrystallised from acetonitrile

as yellow prisms, m.p. 183-185°. (Yield 500 mg). Chromatography of the residue on silica gel, eluting with benzene/ethyl acetate mixtures, gave a further 425 mg of the compound. (Total yield 925 mg, 36%).

Found: C, 63.8; H, 5.6; N, 7.7; S, 11.7%

$C_{29}H_{31}N_3O_4S_2$ requires C, 63.4; H, 5.7; N, 7.7; S, 11.7%

$\lambda_{max.}$: 212sh, 228sh, 251sh and 310 nm ($\varepsilon$ 35,800, 24,000, 9,650 and 2,240)

$\nu_{max.}$: 1640 (C=N) and 3285 (N-H) $cm^{-1}$

m/e: 549 (M, 7%), 394 (M - Ts, 16%), 378 (M - $TsNH_2$, 5%) and 91 (Ts - $SO_2$, 100%).

16. 4,5,7a,8,9,10,11,11a-Octahydro-11a-p-tolylsulphonylamino-7-p-tolylsulphonylimino-7H-pyrrolo[3,2,1-de]phenanthridine (XXVII, Z = Ts):-

a. The mother liquors from experiment 15a were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was recrystallised from ethanol as colourless needles, m.p. 244-246°. (Yield 420 mg, 8%).

b. Chromatography of the mother liquors from experiment 15b (silica gel, benzene/ethyl acetate mixtures) gave the compound as colourless needles (from ethanol), m.p. 245-248°. (Yield 380 mg, 15%).

Found: C, 62.9; H, 5.7; N, 7.9; S, 11.9%

$C_{29}H_{31}N_3O_4S_2$ requires C, 63.4; H, 5.7; N, 7.7; S, 11.7%

$\lambda_{max.}$: 225, 273, 283 and 313 nm ($\varepsilon$ 31,900, 15,000, 16,700 and 18,200)

$\nu_{max.}$: 1555 (C=N) and 3335 (N-H) $cm^{-1}$

m/e: 549 (M, 35%), 394 (M - Ts, 8%), 379 (M - TsNH, 45%), 239 (394 - Ts, 12%), 224 (379 - Ts, 45%) and 223 (224 - H, 100%).

17. 4,5,7a,8,9,10,11,11a-Octahydro-7-oxo-11a-p-tolylsulphonylamino-7H-pyrrolo[3,2,1-de]phenanthridine (XXIX):-

A solution of 4,5,7a,8,9,10,11,11a-octahydro-11a-p-tolylsulphonyl-

amino-7-p-tolylsulphonylimino-7H-pyrrolo[3,2,1-de]phenanthridine (250 mg) and sodium hydroxide (300 mg) in ethanol (5 ml) and water (2 ml) was heated under reflux for 2 hours. The solution was neutralised with concentrated hydrochloric acid and the solid was collected. Recrystallisation from ethanol gave colourless prisms, m.p. 241-242°. (Yield 139 mg, 77%).

Found: C, 66.3; H, 6.2; N, 6.9; S, 7.9%

$C_{22}H_{24}N_2O_3S$ requires C, 66.7; H, 6.1; N, 7.1; S, 8.1%

$\lambda_{max.}$: 215, 233sh, 255 and 295 nm (ε 26,200, 12,600, 11,000 and 4,210)

$\nu_{max.}$: 1682 (C=O) and 3100br (N-H) $cm^{-1}$

m/e: 396 (M, 25%), 241 (M - Ts, 10%) and 226 (M - TsNH, 100%; $m^*$ 129.0).

18. Reaction of 4,5,8,9,10,11-hexahydro-7H-cyclohept[b]pyrrolo-[3,2,1-hi]indole with p-chlorobenzenesulphonyl azide:-

A solution of the indole (2 g, 1 mol) and the azide (4.2 g, 2 mol) in chloroform (20 ml; purified over alumina) was allowed to stand at room temperature for 2 days. The solvent was removed in vacuo and methanol (10 ml) was added. The solid was collected and recrystallised from acetonitrile. 4,6-Butano-6-p-chlorobenzenesulphonylamino-5-p-chlorobenzenesulphonylimino-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]-quinoline (XXVI, Z = Cbs) formed bright yellow prisms, m.p. 183-185° (decomp.). (Yield 2.32 g).

Found: C, 55.4; H, 4.5; Cl, 12.3; N, 7.3; S, 10.8%

$C_{27}H_{25}Cl_2N_3O_4S_2$ requires C, 54.9; H, 4.2; Cl, 12.0; N, 7.1; S, 10.9%

$\lambda_{max.}$: 213sh, 233 and 309 nm (ε 37,600, 33,500 and 2,990)

$\nu_{max.}$: 1637 (C=N) and 3275 (N-H) $cm^{-1}$

The mother liquors were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures, and the following compounds were obtained in order of elution.

i. Compound (XXVI, Z = Cbs). (Yield 1.0 g; Total yield 3.32 g, 59%).

ii. 7a,11a-Di(p-chlorobenzenesulphonylamino)-7-ethoxy-4,5,7a,-8,9,10,11,11a-octahydro-7H-pyrrolo[3,2,1-de]phenanthridine (XXX), recrystallised from ethanol as colourless prisms, m.p. 155-158°. (Yield 105 mg, 2%).

Found: C, 54.7; H, 5.0; Cl, 11.0; N, 6.6; S, 10.3%

$C_{29}H_{31}Cl_2N_3O_5S_2$ requires C, 54.7; H, 4.9; Cl, 11.2; N, 6.6; S, 10.1%

$\lambda_{max.}$: 233 and 310 nm ($\varepsilon$ 34,500 and 3,760)

$\nu_{max.}$: 3195 and 3275 (N-H) $cm^{-1}$

m/e: 635 (M, 2%), 589 (M - EtOH, 6%), 414 (589 - Cbs, 100%) and 223 (414 - $CbsNH_2$, 50%).

iii. 11a-p-Chlorobenzenesulphonylamino-7-p-chlorobenzene-sulphonylimino-4,5,7a,8,9,10,11,11a-octahydro-7H-pyrrolo[3,2,1-de]-phenanthridine (XXVII, Z = Cbs) as colourless prisms, (from ethanol), m.p. 203-205°. (Yield 195 mg, 3%).

Found: C, 54.7; H, 4.4; Cl, 12.1; N, 7.2; S, 10.9%

$C_{27}H_{25}Cl_2N_3O_4S_2$ requires C, 54.9; H, 4.2; Cl, 12.0; N, 7.1; S, 10.9%

$\lambda_{max.}$: 227, 274, 284 and 313 nm ($\varepsilon$ 37,100, 14,900, 16,200 and 19,100)

$\nu_{max.}$: 1555 (C=N) and 3200 (N-H) $cm^{-1}$

m/e: 589 (M, 24%), 414 (M - Cbs, 6%), 399 (M - CbsNH, 52%; $m^*$ 270.3), 333 (399 - 2H - $SO_2$, 11%; $m^*$ 277.9), 239 (414 - Cbs, 13%), 224 (399 - Cbs, 60%; $m^*$ 125.8) and 223 (224 - H, 100%).

19. 7a-Hydroxy-1,2,4,5,6,7,7a,8-octahydro-8-oxo-3aH-pyrrolo[3,2,1-de]-acridine (XXXIII):-

4,6-Butano-1,2,5,6-tetrahydro-6-p-tolylsulphonylamino-5-p-tolylsulphonylimino-4H-pyrrolo[3,2,1-ij]quinoline (500 mg) was heated under reflux for 4 hours in ethanol (10 ml) and 2N aqueous sodium hydroxide (10 ml). The solution was cooled and poured into water

(50 ml). The mixture was extracted with chloroform (3 x 10 ml) and the extracts dried (magnesium sulphate). Evaporation gave a pale yellow solid, recrystallised from ethanol as yellow fluorescent prisms, m.p. 180-181°. (Yield 175 mg, 79%).

Found: C, 74.1; H, 7.0; N, 5.8%

$C_{15}H_{17}NO_2$ requires C, 74.1; H, 7.0; N, 5.8%

$\lambda_{max.}$: 238, 257sh and 385 nm (ε 23,100, 8,110 and 4,860)

$\nu_{max.}$: 1656 (C=O) and 3490 (O-H) $cm^{-1}$

20. 1,2,4,5,6,7-Hexahydro-8-oxo-8H-pyrrolo[3,2,1-de]acridine (XXXIV):-

7a-Hydroxy-1,2,4,5,6,7,7a,8-octahydro-8-oxo-3aH-pyrrolo[3,2,1-de]-acridine (150 mg) in polyphosphoric acid (2.5 g) was heated at 120° for 15 minutes. The mixture was cooled and water (5 ml) was added. The solution was neutralised with 2N aqueous caustic soda and the solid extracted into chloroform (3 x 10 ml). The extracts were dried (magnesium sulphate) and the solvent removed *in vacuo*. The residue was recrystallised from benzene as colourless needles, m.p. 230-232°. (Yield 79 mg, 57%).

Found: C, 79.9; H, 6.7; N, 6.2%

$C_{15}H_{15}NO$ requires C, 80.0; H, 6.7; N, 6.2%

$\lambda_{max.}$: 220, 243, 249, 278sh, 293sh, 305sh, 322sh, 333 and 349 nm (ε 22,100, 33,700, 33,400, 1,280, 2,320, 4,050, 8,790, 14,100 and 14,000)

$\nu_{max.}$: 1630 (C=O) $cm^{-1}$

21. 4,6-butano-6-p-chlorobenzenesulphonylamino-5-oxo-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinoline (XXXI, Z = Cbs):-

A solution of sodium hydroxide (500 mg) in water (2 ml) was added dropwise at room temperature to a stirred suspension of 4,6-butano-6-p-chlorobenzenesulphonylamino-5-p-chlorobenzenesulphonylimino-

1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinoline (500 mg) in acetone (10 ml). The mixture was stirred for 15 minutes after addition, then poured into water (50 ml). The solution was neutralised with concentrated hydrochloric acid and the solid was collected, dried and recrystallised from ethanol as colourless prisms, m.p. 192-200° (decomp). (Yield 293 mg, 83%).

Found: C, 60.5; H, 5.1; Cl, 8.3; N, 6.7; S, 7.5%

$C_{21}H_{21}ClN_2O_3S$ requires C, 60.5; H, 5.0; Cl, 8.5; N, 6.7; S, 7.7%

$\lambda_{max.}$: 202, 228sh, 254sh and 308 nm ($\varepsilon$ 48,600, 21,000, 8,720 and 2,400)

$\nu_{max.}$: 1723 (C=O) and 3250 (N-H) $cm^{-1}$

m/e: 416 (M, 18%), 241 (M - Cbs, 100%; $m^*$ 139.6) and 224 (241 - OH, 27%; $m^*$ 208.2).

22. 8-p-Chlorobenzenesulphonylimino-7a-hydroxy-1,2,4,5,6,7,7a,8-octahydro-3aH-pyrrolo[3,2,1-de]acridine (XXXVII, Z = Cbs):-

4,6-butano-6-p-chlorobenzenesulphonylamino-5-oxo-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinoline (200 mg) was heated at 180° and 0.1 mm Hg for 1½ hours. The residue contained two components, separated by preparative t.l.c. (benzene/ethyl acetate 9:1). The slow moving component was recrystallised from ethanol as colourless prisms, m.p. 185-190° (decomp.), and was identical (t.l.c., i.r. spectrum) to the starting material. (Recovery 50 mg, 25%).

The fore-running component was recrystallised from ethanol as bright orange prisms, m.p. 145-146°. (Yield 89 mg, 45%).

Found: C, 60.5; H, 5.2; N, 6.7%

$C_{21}H_{21}ClN_2O_3S$ requires C, 60.5; H, 5.0; N, 6.7%

$\lambda_{max.}$: 231, 293 and 438 nm ($\varepsilon$ 24,800, 12,300 and 7,810)

$\nu_{max.}$: 1573 (C=N) and 3410 (O-H) $cm^{-1}$

m/e: 416 (M, 15%), 241 (M - Cbs, 100%; $m^*$ 139.6), and 224 (241 - OH, 38%; $m^*$ 208.2).

23. 7a,11a-Di(p-chlorobenzenesulphonylamino)-7-ethoxy-4,5,7a,8,-9,10,11,11a-octahydro-7H-pyrrolo[3,2,1-de]phenanthridine (XXX):-

A solution of 4,6-butano-6-p-chlorobenzenesulphonylamino-5-p-chlorobenzenesulphonylimino-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]-quinoline (400 mg) in trifluoroacetic acid (4 ml) was allowed to stand at room temperature for 7 days. The solvent was removed in vacuo and methanol (5 ml) was added to the residue. The solid was collected and recrystallised from ethanol as colourless prisms, m.p. 159-162°. (Yield 304 mg, 70%).

The compound was identical (t.l.c., i.r. spectrum) to that obtained in experiment 18.

24. Reaction of 4,5,8,9,10,11-hexahydro-7H-cyclohept[b]pyrrolo-[3,2,1-hi]indole with p-nitrobenzenesulphonyl azide:-

A solution of the indole (2 g, 1 mol) and the azide (4.4 g, 2 mol) in chloroform (25 ml; purified over alumina) was allowed to stand at room temperature for 24 hours. The solvent was removed and acetonitrile (10 ml) was added to the residue. The solid was collected and recrystallised from acetonitrile. 11a-p-nitrobenzene-sulphonylamino-7-p-nitrobenzenesulphonylimino-4,5,7a,8,9,10,11,11a-octahydro-7H-pyrrolo[3,2,1-de]phenanthridine (XXVII, Z = p-nitro-benzenesulphonyl) formed colourless prisms, m.p. 245° (resolidifies then remelts at 300°). (Yield 1.14 g).

Found: C, 53.4; H, 4.1; N, 11.8%

$C_{27}H_{25}N_5S_2O_8$ requires C, 53.0; H, 4.1; N, 11.5%

$\lambda_{max.}(CHCl_3)$: 272, 305 and 322 nm ($\epsilon$ 26,900, 18,100 and 14,200)

$\nu_{max.}$: 1564 (C=N) and 3280 (N-H) $cm^{-1}$

m/e: 409 ($M - NO_2.C_6H_4.SO_2NH_2$, 7%), 344 (409 - $SO_2$ - H, 14%), 328 (344 - O, 7%) and 223 (409 - $NO_2.C_6H_4.SO_2$, 100%).

The mother liquors were evaporated and acetonitrile (10 ml) was added to the residue. The solid was collected and recrystallised

from acetonitrile as orange prisms. 4,6-Butano-6-p-nitrobenzenesulphonylamino-5-p-nitrobenzenesulphonylimino-1,2,5,6-tetrahydro-4H pyrrolo[3,2,1-ij]quinoline (XXVI, Z = p-nitrobenzenesulphonyl) had m.p. 129-137° (decomp.). (Yield 1.45 g).

Found: C, 53.7; H, 4.8; N, 13.6; S, 10.3%

$C_{27}H_{25}N_5O_8S_2$.MeCN requires C, 53.4; H, 4.3; N, 12.9; S, 9.8%

$C_{27}H_{25}N_5O_8S_2$ requires C, 53.0; H, 4.1; N, 11.5; S, 10.5%

$\lambda_{max.}$: 256 nm ($\varepsilon$ 27,600)

$\nu_{max.}$: 1632 (C=N), 2250 (MeCN) and 3220 (N-H) $cm^{-1}$.

The mother liquors were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures, and the following compounds were obtained.

i. 4,5,8,9,10,11-Hexahydro-11-p-nitrobenzenesulphonylimino-7H-cyclohept[b]pyrrolo[3,2,1-hi]indole (LII), recrystallised from ethanol as yellow needles, m.p. 189-191°. (Yield 190 mg, 5%).

Found: C, 61.6; H, 5.0; N, 9.9; S, 7.8%

$C_{21}H_{19}N_3O_4S$ requires C, 61.6; H, 4.7; N, 10.3; S, 7.8%

$\lambda_{max.}$: 210, 257 and 360 nm ($\varepsilon$ 33,900, 24,000 and 31,000)

$\nu_{max.}$: 1531 (C=N) $cm^{-1}$

m/e: 409 (M, 82%), 345 (M - $SO_2$, 100%) and 223 (M - $NO_2.C_6H_4.SO_2$, 94%).

ii. Compound (XXVII, Z = p-nitrobenzenesulphonyl). (Yield 120 mg; total yield 1.26g, 21%).

iii. Compound (XXVI, Z = p-nitrobenzenesulphonyl). (Yield 30 mg; total yield 1.48 g, 26%).

iv. 7a,11a-Di(p-nitrobenzenesulphonylamino)-7-ethoxy-4,5,7a,8,-9,10,11,11a-octahydro-7H-pyrrolo[3,2,1-de]phenanthridine (L), recrystallised from ethanol as orange prisms, m.p. 158-160°. (Yield 170 mg, 3%).

Found: C, 53.4; H, 4.8; N, 10.9; S, 9.9%

$C_{29}H_{31}N_5O_9S_2$ requires C, 53.0; H, 4.7; N, 10.7; S, 9.7%

$\lambda_{max.}$: 258 nm (ε 25,200)

$\nu_{max.}$: 3265br (N-H) $cm^{-1}$.

25. 4,5,8,9,10,11-Hexahydro-7-p-nitrobenzenesulphonylimino-7H-pyrrolo[3,2,1-de]phenanthridine (XLVIII):-

A suspension of 11a-p-nitrobenzenesulphonylamino-7-p-nitrobenzenesulphonylimino-4,5,7a,8,9,10,11,11a-octahydro-7H-pyrrolo-[3,2,1-de]phenanthridine (250 mg) and sodium hydroxide (300 mg) in ethanol (5 ml) and water (5 ml) was heated under reflux for 30 minutes. The mixture was cooled and poured into water (25 ml) and the solid was collected. Recrystallisation from chloroform/methanol gave pale yellow needles, m.p. 312-314° (decomp.). (Yield 156 mg, 93%).

Found: C, 62.2; H, 4.8; N, 10.0; S, 7.9%

$C_{21}H_{19}N_3O_4S$ requires C, 61.6; H, 4.7; N. 10.3; S, 7.8%

$\lambda_{max.}(CHCl_3)$: 268, 329sh, 342 and 357 nm (ε 40,300, 11,900, 17,600 and 15,600)

$\nu_{max.}$: 1500 (C=N) $cm^{-1}$

m/e: 409 (M, 3%), 344 (M - $SO_2$ - H, 5%), 328 (344 - O, 2%) and 223 (M - $NO_2.C_6H_4.SO_2$, 100%).

26. 7a,11a-Di(p-nitrobenzenesulphonylamino)-7-ethoxy-4,5,7a,8,9,10,-11,11a-octahydro-7H-pyrrolo[3,2,1-de]phenanthridine (L):-

A solution of 4,6-butano-6-p-nitrobenzenesulphonylamino-5-p-nitrobenzenesulphonylimino-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]-quinoline (200 mg) in propanol (10 ml) was boiled under reflux for 1 hour. The solution was cooled and the solvent removed in vacuo. T.l.c. of the residue showed two components, separated by chromatography (silica gel, benzene/ethyl acetate mixtures). The fore-running compound amounted to only 4 mg and was discarded. The slow moving component was recrystallised from ethanol as yellow prisms, m.p. 159-161°. (Yield 137 mg, 64%).

The compound was identical (t.l.c., i.r. spectrum) to that obtained in experiment 24.

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13. F.Hibbert, Chem.Comm., 1973, 463.

# CHAPTER IV

## The reactions of arylsulphonyl azides with 2-alkylthioindoles and 2-indolinethiones

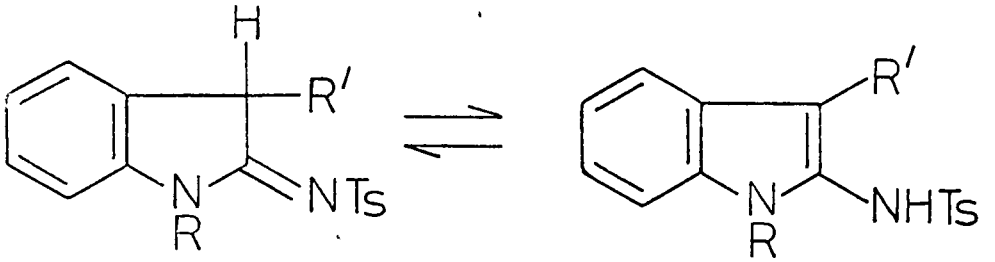
Indole, 1-methylindole and 1,3-dimethylindole react with tosyl azide to yield the tautomeric compounds (I, R = R' = H), (I, R = Me, R' = H) and (I, R = R' = Me) respectively[1-5]. The mechanism proposed for the formation of these compounds is as follows. The intermediate (II) undergoes rearrangement as shown, leading to (Ia). This mechanism involves a hydride ion shift from $C_2$ to $C_3$.

Merer[1,6] investigated the reactions of 2-substituted and 1,2-disubstituted indoles with a view to observing similar alkyl shifts. Treatment of 2-methylindole with tosyl azide gave two products, (III) and (IV). The formation of these products was explained by the reaction sequence shown in FIGURE I. The intermediate (V) can couple with a second molecule of the indole to give (VI) when loss of sulphonamide as shown yields (III). Rearrangement of (V) *via* an aziridine intermediate (VII) leads to (IV). An alternative mechanism for the formation of (III) *via* the diazonium ion (VIII) was unlikely since it has been shown[7] that 3-diazo-1,2-diphenylindole does not couple with 1,2-diphenylindole.

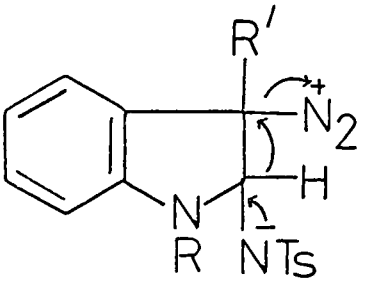
During the course of this work no examples of methyl group migration were observed.

Rashid[8] extended this work to an investigation of the reactions of 2-alkylthioindoles (IX), since a transfer of the alkylthio group may have been likely due to the nucleophilic sulphur atom. Owing to the unfortunate loss of samples and spectroscopic data, however, much of this work has had to be repeated.

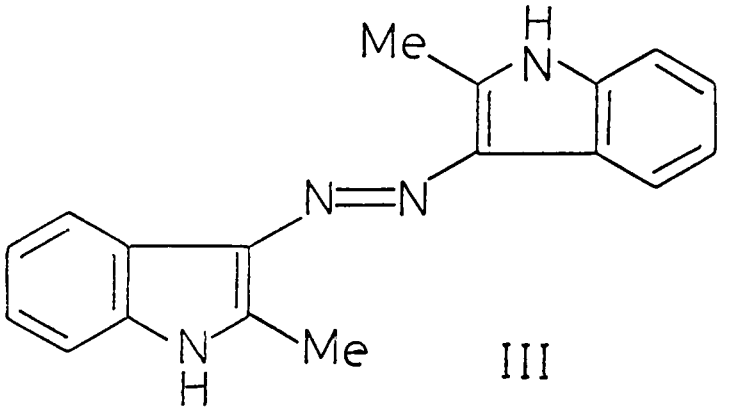
Only one product could be isolated from the reaction of 2-methylthioindole (IX, R = H, R' = Me) with tosyl azide. This compound had the molecular formula $C_{18}H_{16}N_4S_2$ and the u.v. spectrum was very similar to that of the azo-compound (III). For this reason the structure (X, R = H, R' = Me) was proposed. The same compound was also formed when 2-methylthioindole was treated with *p*-chlorobenzene-



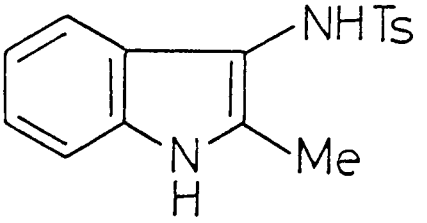

Ia Ib




II

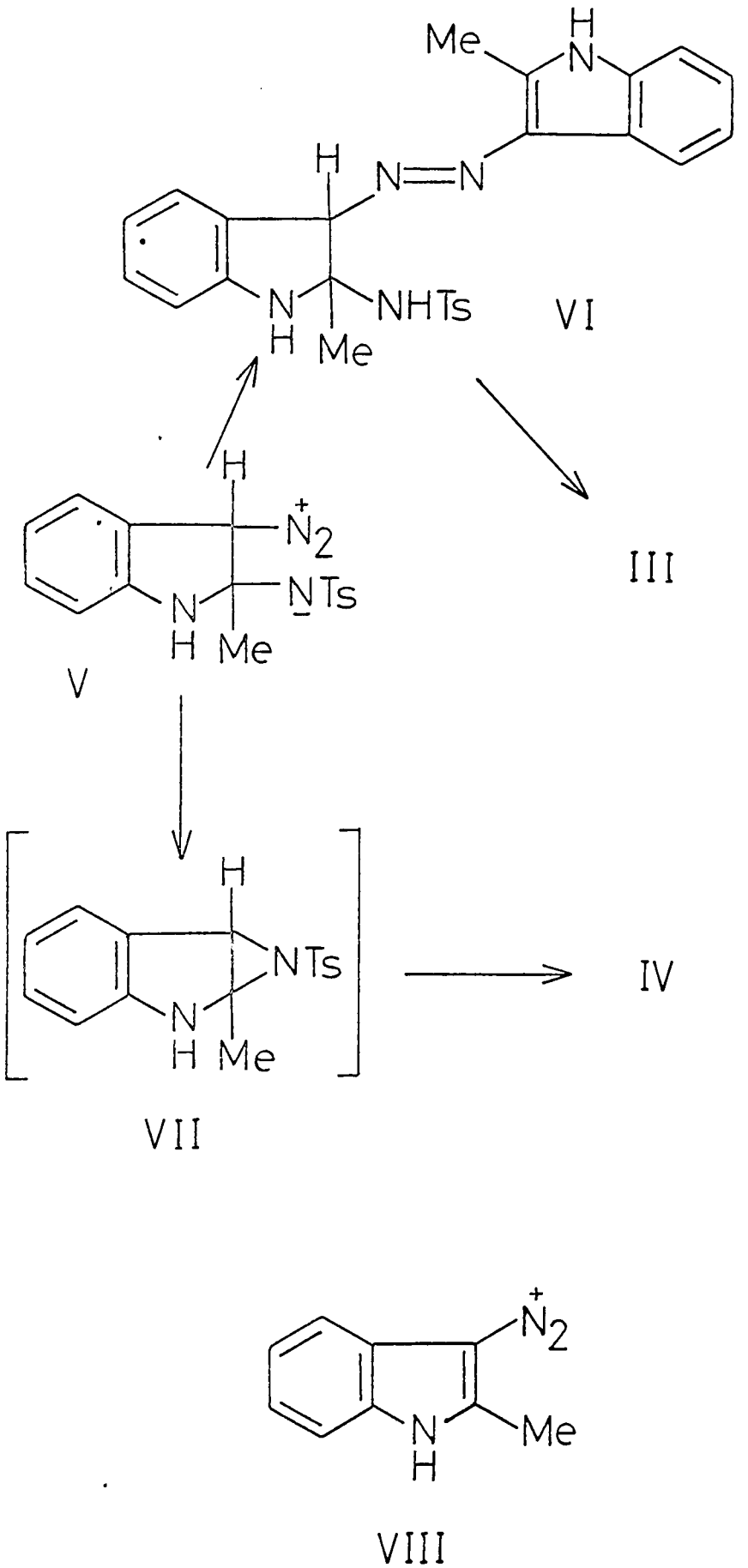


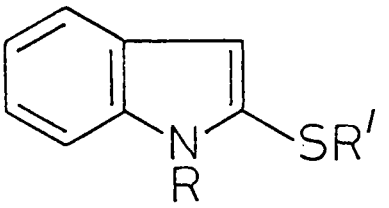

III



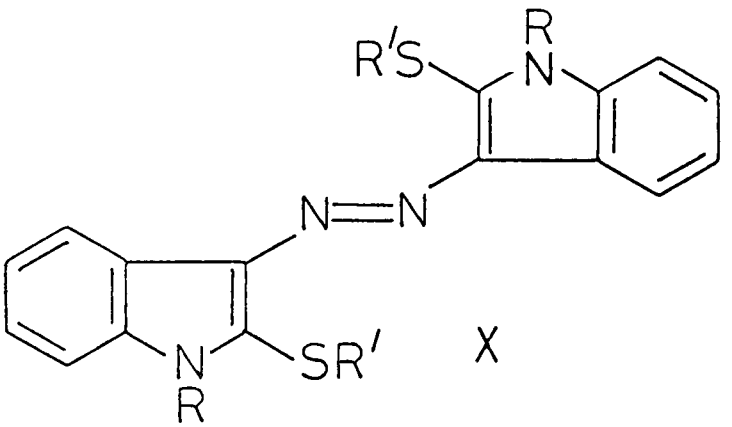

IV

FIGURE I

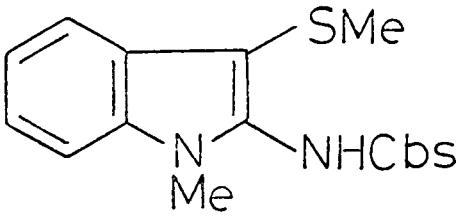

Me
H
N
H
N=N
N
NHTs
H
Me
VI
III
H
N2
NTs
N
H
Me
V
H
NTs
N
H
Me
VII
IV
N2
N
H
Me
VIII



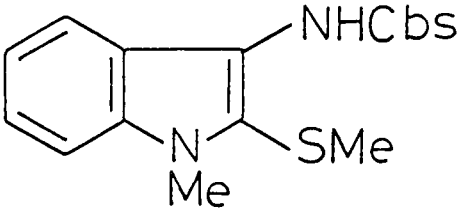

IX



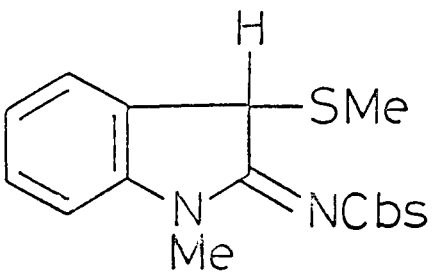

X



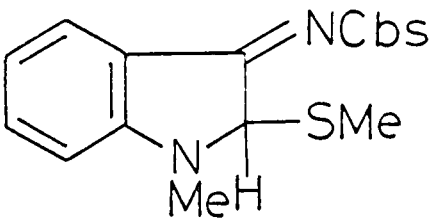

XI




XII




XIII




XIV

sulphonyl azide. Although the yields of this compound were only 50%, no other products, apart from toluene-p-sulphonamide and chlorobenzene-p-sulphonamide, could be isolated from the dark tarry residue.

A similar treatment of 2-ethylthioindole gave compound (X, R = H, R' = Et) as the only isolable product. The n.m.r. spectra (D) of the two azo-compounds are tabulated below.

| Compound | NH | Aromatic protons | S-alkyl group |
|---|---|---|---|
| (X, R = H, R' = Me) | -1.73(2H) | 1.60(2H, m) | 7.23(6H, s) |
| | | 2.5-2.9(6H, m) | |
| (X, R = H, R' = Et) | -1.78(2H) | 1.52(2H, m) | 6.77(4H, q, J7Hz) |
| | | 2.5-3.0(6H, m) | 8.67(6H, t, J7Hz) |

From the reaction of 1-methyl-2-methylthioindole (IX, R = R' = Me) with p-chlorobenzenesulphonyl azide were isolated two products. The first of these was the azo-compound (X, R = R' = Me). Analytical and spectroscopic data agreed with the assignment, the n.m.r. spectrum showing signals at

1.38τ(2H, dd, J7, 2Hz, aromatic), 2.3-2.8(6H, m, aromatic), 6.07 (6H, s, NMe) and 7.37(6H, s, SMe).

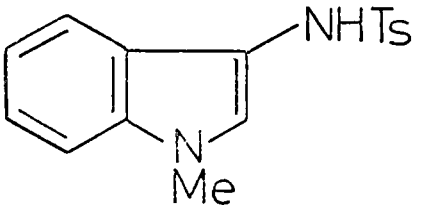
The second compound had the molecular formula $C_{16}H_{15}ClN_2O_2S_2$ and the i.r. spectrum contained a band due to N-H absorption (3225 $cm^{-1}$). The n.m.r. spectrum (D) showed the following signals.

-0.60τ(1H, br, exchanged $D_2O$, NH), 2.2-3.0(8H, m, aromatic), 6.37 (3H, s, NMe) and 8.09(3H, s, SMe).

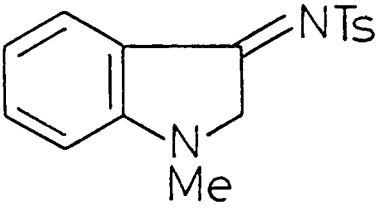
These observations indicated one of the two structures (XI) or (XII) for the product. The n.m.r. spectrum was re-recorded in $CDCl_3$ solution and showed the presence of two tautomers, containing signals at

2.05τ(d, J8Hz, low field half of Cbs-N=C signal), 2.3-2.9(m, aromatic), 3.05(exchanged $D_2O$, NH), 4.53(s, CH.SMe), 6.17(s, indole NMe), 6.71(s, indoline NMe), 8.10(s, =CSMe) and 8.46(s, CH.SMe).

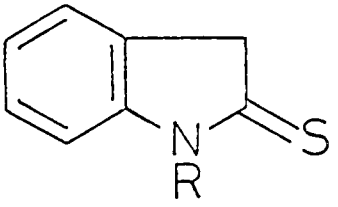
We have assigned the structure (XIII) or (XIV) to the second



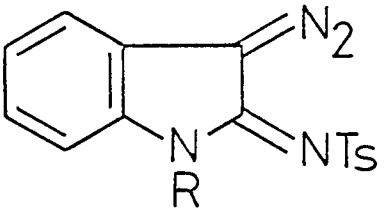

XV



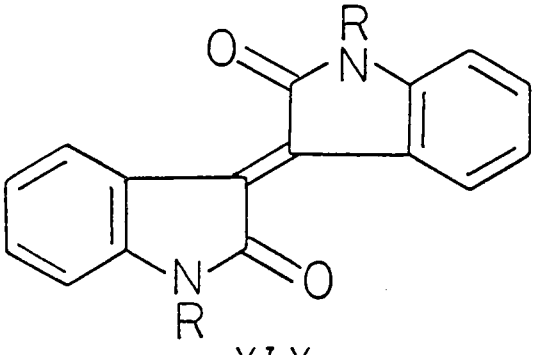

XVI




XVII




XVIII




XIX

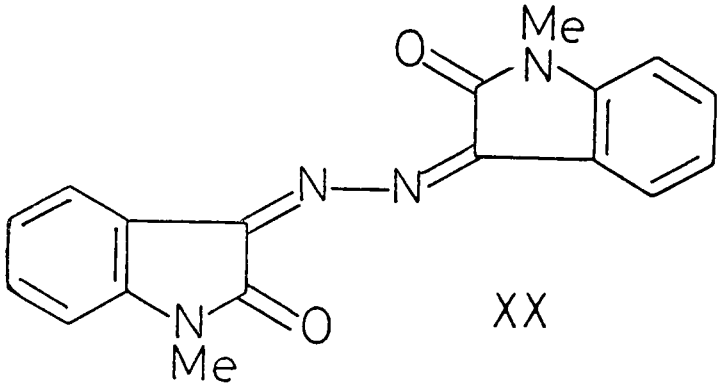
(indoline) tautomer [c.f. the tautomerism of (I)]. The ratio of indole:indoline was approximately 2:1. This tautomerism enabled a definite assignment of structure (XI)⇌(XIII) for our product since the chloroform solution was colourless, and compounds of the type (XIV) are known[9] to be bright orange in colour. Furthermore, the spectral data of compound (XV)[5] indicate the absence of any detectable quantity of the indoline tautomer (XVI).

This means that the formation of (XI) must involve a shift of the -SMe group from $C_2$ to $C_3$ in preference to the alternative formation of an aziridine [leading to (XII)], and reflects the nucleophilicity of the sulphur atom.

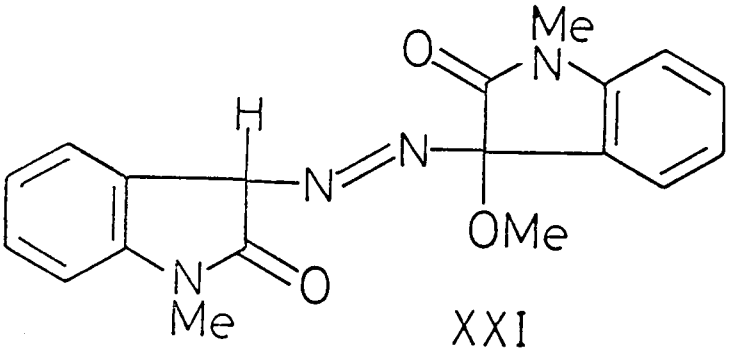
The compounds (IX) used in these investigations had been prepared by alkylation of the 2-indolinethiones (XVII). It was of interest to examine the reactions of the latter compounds with arylsulphonyl azides for the following reasons.

It was found that the initial product from the reaction of indole or 1-methylindole with tosyl azide (I, R = H or Me, R' = H) reacted further with the azide in pyridine as solvent to yield the stable diazo-compound (XVIII)[5]. The reactions of these diazoindolines have since been reported[10]. The base catalysed formation of diazo-compounds from arylsulphonyl azides and compounds containing active methylene groups is well established[11,12].

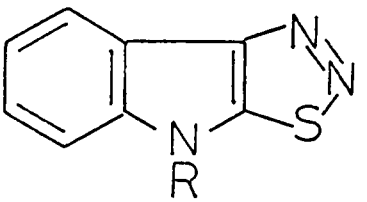
Buckley[13] has extended this work to oxindole and 1-methyloxindole. In this case, however, no diazo-compounds were isolated, the products being isoindigo and 1,1'-dimethylisoindigo (XIX, R = H) and (XIX, R = Me) respectively. It was likely, however, that these products were derived from an intermediate diazooxindole since pyrolysis of the latter is known to give isoindigo derivatives[14,15]. When milder conditions were used in the case of 1-methyloxindole the compound (XX) was obtained, almost certainly produced <u>via</u> 1-methyldiazooxindole, and on boiling with methanol (XX) gave (XXI).



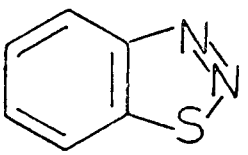
XX



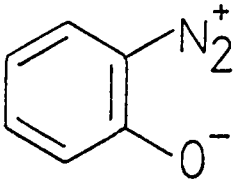
XXI



XXII



XXIII



XXIV

Since (XVII) is similar in structure to oxindole and the compounds (I, R' = H), it too should readily undergo reaction with azide to form similar diazo-compounds.

Compound (XVII, R = H) reacted rapidly with tosyl azide in pyridine solution to give as major product (60%) a compound with the molecular formula $C_8H_5N_3S$. The u.v. spectrum was unlike any previously obtained in these investigations (see FIGURE II) and the n.m.r. spectrum (D) contained signals at

1.85τ(1H, dd, J8,1Hz, aromatic), 2.32(1H, dd, J8,1Hz, aromatic), 2.4-2.8(2H, m, aromatic) and 4.6-6.0(1H, very broad, exchanged $D_2O$, NH).

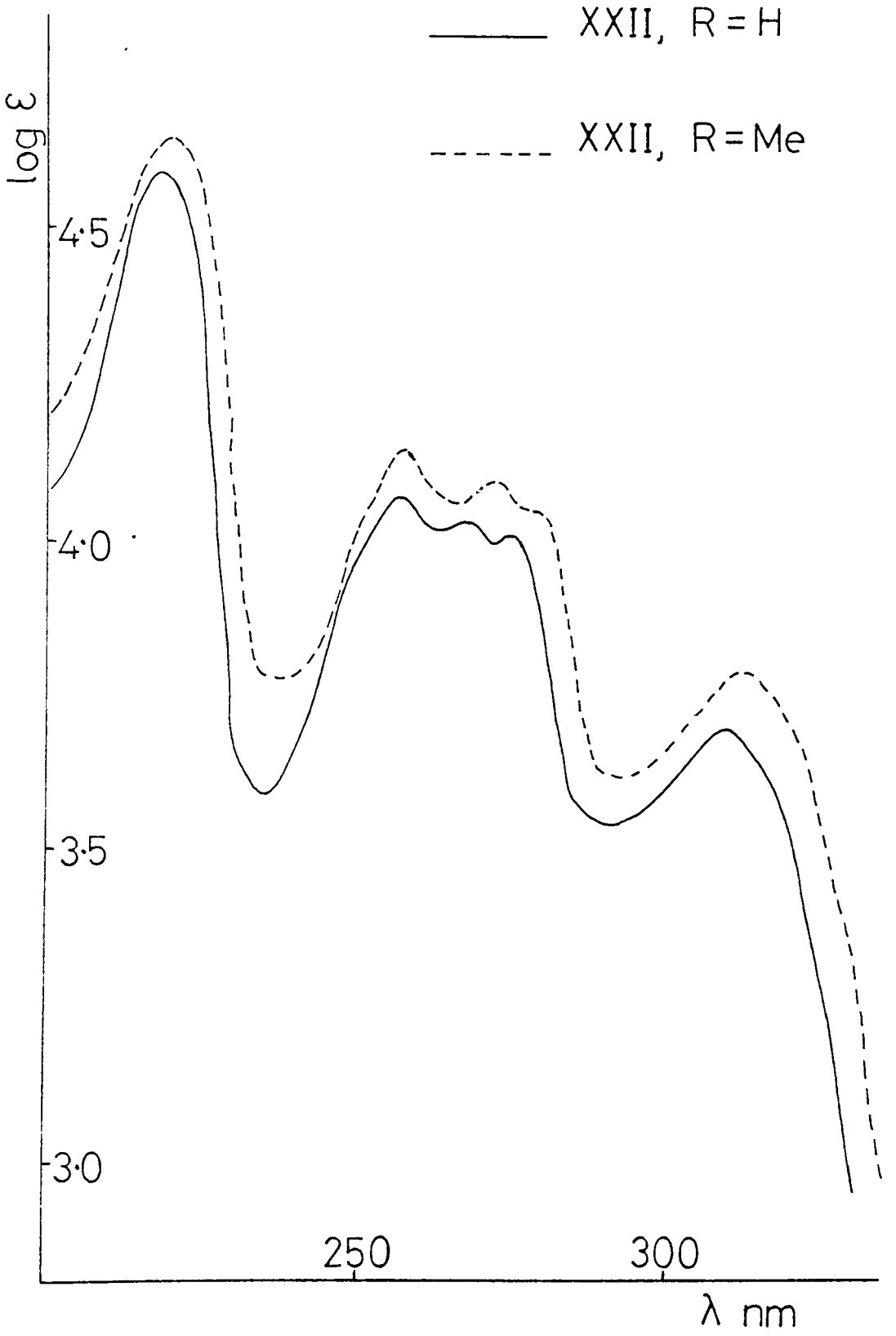
The same compound was obtained from a reaction of (XVII, R = H) with p-chlorobenzenesulphonyl azide and it was assigned the structure (XXII, R = H). The preparation of 1,2,3-thiadiazoles by treatment of acylthioacetamides with tosyl azide has been reported[11a]. A second product, compound A, was also formed in low yield from these reactions and will be discussed later.

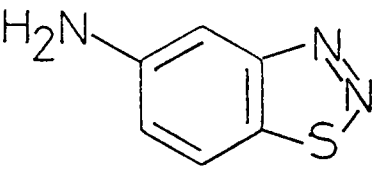
When 1-methyl-2-indolinethione (XVII, R = Me) was treated with tosyl azide the thiadiazole (XXII, R = Me) was obtained, though in this instance the yield was low. The n.m.r. spectrum contained the following signals.

1.89τ(1H, m, aromatic), 2.5-2.8(3H, m, aromatic) and 6.14(3H, s, NMe).

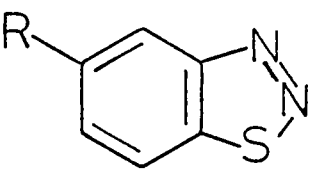
The failure to isolate analogous "oxadiazoles" from oxindole is an illustration of the nucleophilicity of the sulphur atom relative to oxygen. It has been reported[16,17] that benzothiadiazole (XXIII) is colourless whereas the corresponding oxygen compound (XXIV) is brightly coloured[17,18], existing in the dipolar, ring opened form. The great stability of the thiadiazole grouping has also been illustrated by the fact that diazotisation of (XXV) followed by a Sandmeyer reaction yields (XXVI)[19] (R = halogen) and not the dihalogenated compound (XXVII) that might be expected if there were

FIGURE II

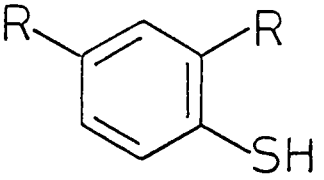




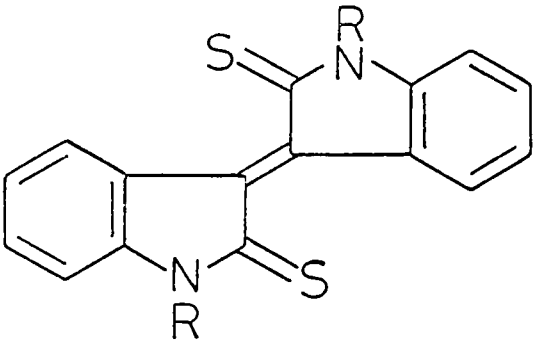
XXV



XXVI



XXVII



XXVIII

any tendency for (XXV) to exist to even a small extent in the ring opened form.

The major product from the reaction of (XVII, R = Me) with tosyl azide, compound B, was not obtained pure. Moreover, the compound was very insoluble and an n.m.r. spectrum could not be obtained. Analysis of the impure compound suggested that B might possibly have the formula $C_{18}H_{14}N_2S_2$. The highest major peak in the mass spectrum occurred at m/e 322 (47%), also supporting this formula. Other major peaks were m/e 307 (322 - Me, 8%), 290 (322 - S, 100%), 275 (290 - Me, 74%) and 260 (275 - Me, 28%). This spectrum also showed small peaks at m/e 386 and 419.

On this limited evidence the structure (XXVIII, R = Me) was proposed.

1,1'-Dimethylisoindigo (XIX, R = Me) had been prepared from 1-methyloxindole by a variety of methods and it was decided to carry out similar reactions with (XVII, R = Me) in the hope of preparing (XXVIII, R = Me). Two methods were adopted. Boiling (XVII, R = Me) with p-nitrosodimethylaniline in acetic acid according to Stollé et al[20] gave a red-brown product, also obtained by oxidation of (XVII, R = Me) with potassium ferricyanide, adapting the method of Harley-Mason and Ingleby[21].

The melting points of this compound and that of B were very close to each other, and the t.l.c. and i.r. spectra were identical, showing that the structure assigned to B was probably correct.

A low yield of a compound, A, had been isolated from the reaction of (XVII, R = H) with tosyl azide. This compound had originally been recrystallised from dioxan and the n.m.r. spectrum (D) showed the presence of an appreciable amount of this solvent. Otherwise the spectrum was uninformative, showing signals at

-2.14$\tau$(s, exchanged $D_2O$), -1.94(s, exchanged $D_2O$), -1.40 (s, exchanged $D_2O$), 1.54(m, aromatic) and 2.4-3.2(m, aromatic).

The presence of three labile protons suggested tautomerism, as did the low field aromatic proton which integrated to less than 1H. The compound was recrystallised a second time from acetonitrile; the n.m.r. spectrum was unchanged apart from signals due to acetonitrile and dioxan.

On carrying out the reaction of (XVII, R = H) with p-chloro-benzenesulphonyl azide a small amount of a product, assumed to be A, was obtained. The i.r. spectrum was different to that of A, but this may have been due to the above solvents of crystallisation. This time the compound was recrystallised from acetonitrile. The n.m.r. spectrum was identical to that of A, allowing for these solvents, as were the u.v. spectrum and t.l.c.

Analysis was close enough to suggest the formula $C_{16}H_{10}N_2S_2$ and the mass spectrum showed peaks at m/e 294 (possibly $C_{16}H_{10}N_2S_2$, 79%), 262(294 - S, 100%) and 235 (262 - HCN). Like that of B, the mass spectrum showed signals at higher m/e (345, 358, 377 and 407). The u.v. spectrum of A was similar in shape to that of B and by analogy with B the compound was assigned the structure (XXVIII, R = H).

It must be emphasised that the assignments for A and B are based upon very limited information, and further work is obviously needed in order to verify or disprove them.

# CHAPTER IV

## Experimental

1. 3,3'-Azobis-(2-methylthioindole) (X, R = H, R' = Me):-

a. 2-Methylthioindole (1 g, 1 mol) and tosyl azide (3.7 g, 3 mol) were heated at 60° for 24 hours. Methanol (10 ml) was added to the mixture and the solid was collected. Recrystallisation from acetonitrile gave the product as yellow-brown prisms. Drying *in vacuo* at 100° gave a brown amorphous solid, m.p. 226-228° (decomp.). (Yield 497 mg, 46%).

b. 2-Methylthioindole (1.35 g, 1 mol) and p-chlorobenzenesulphonyl azide (4.9 g, 2.7 mol) were heated at 60° for 18 hours. Methanol (5 ml) was added to the mixture and the solid was collected and recrystallised from acetonitrile as yellow-brown prisms (drying gave brown solid), m.p. 226-227°. (Yield 715 mg, 49%).

Found: C, 61.2; H, 4.5; N, 16.0; S, 17.5%

$C_{18}H_{16}N_4S_2$ requires C, 61.4; H, 4.6; N, 15.9; S, 18.2%

$\lambda_{max.}$: 205, 246, 288, 400, 427sh and 440 nm ($\varepsilon$ 26,400, 16,900, 16,000, 16,000, 17,200 and 17,800)

$\nu_{max.}$: 3385 (N-H) $cm^{-1}$

m/e: 352(M, 100%), 337 (M - Me, 5%; $m^*$ 322.6), 294 (M - $N_2$ - 2Me, 26%), 293 (294 - H, 22%; $m^*$ 292.0), 262 (294 - S, 63%) and 261 (262 - H, 25%; $m^*$ 260.0).

2. 3,3'-Azobis-(2-ethylthioindole) (X, R = H, R' = Et):-

2-Ethylthioindole (750 mg, 1 mol) and tosyl azide (2.5 g, 3 mol) were heated at 60° for 24 hours. Methanol (5 ml) was added to the mixture. Next day the solid was collected and recrystallised from 2-methoxyethanol as orange prisms, m.p. 264-266° (decomp.). (Yield 220 mg, 27%).

Found: C, 63.0; H, 5.4; N, 14.4; S, 17.0%

$C_{20}H_{20}N_4S_2$ requires C, 63.2; H, 5.3; N, 14.7; S, 16.8%

$\lambda_{max.}$: 203, 239sh, 287, 402 and 432 nm ($\varepsilon$ 35,200, 20,700, 19,800, 22,500 and 21,300)

$\nu_{max.}$: 3275br (N-H) $cm^{-1}$

m/e: 380 (M, 100%), 351 (M - Et, 13%), 294 (M - $N_2$ - 2Et, 50%), 293 (294 - H, 35%), 262 (294 - S, 90%) and 261 (262 - H, 37%).

3. Reaction of 1-methyl-2-methylthioindole with p-chlorobenzenesulphonyl azide:-

1-Methyl-2-methylthioindole (1.88 g, 1 mol) and p-chlorobenzenesulphonyl azide (4.5 g, 2 mol) were heated at 45° for 24 hours. Methanol (30 ml) was added and the mixture was boiled and filtered hot. The insoluble fraction (240 mg) was recrystallised from dioxan/ethanol yielding 3,3'-azobis-(1-methyl-2-methylthioindole) (X, R = R' = Me) as orange plates, m.p. 228-231°. (Yield 130 mg, 6%). A second recrystallisation from 2-methoxyethanol gave m.p. 230-232°.

Found: C, 62.9; H, 5.2; N, 14.6; S, 16.6%

$C_{20}H_{20}N_4S_2$ requires C, 63.2; H, 5.3; N, 14.7; S, 16.8%

$\lambda_{max.}$: 242, 285, 300sh, 410 and 447 nm ($\varepsilon$ 20,700, 18,800, 15,300, 23,500 and 22,200)

$\nu_{max.}$: nothing informative above 1400 $cm^{-1}$

m/e: 380 (M, 100%), 365 (M - Me, 17%; $m^*$ 350.6), 322 (M - $N_2$ - 2Me, 31%), 321 (322 - H, 14%), 290 (322 - S, 87%) and 275 (290 - Me, 51%; $m^*$ 260.8).

The methanolic mother liquors were evaporated to 10 ml. Next day the solid (1.72 g) was collected. Recrystallisation from propanol gave a mixture of prisms and needles with the same t.l.c. (probably polymorphic). The product was recrystallised from benzene/petroleum ether (b.p. 60-80°) as colourless prisms. 2-p-Chlorobenzenesulphonylamino-1-methyl-3-methylthioindole (XI) had m.p. 155-157°. (Yield 1.1 g, 28%).

Found: C, 52.4; H, 4.0; Cl, 9.8; N, 7.7; S, 17.4%

$C_{16}H_{15}ClN_2O_2S_2$ requires C, 52.4; H, 4.1; Cl, 9.7; N, 7.6; S, 17.5%

$\lambda_{max.}$: 203, 226 and 288 nm ($\varepsilon$ 27,500, 43,800 and 10,000)

$\nu_{max.}$: 3225 (N-H) $cm^{-1}$

m/e: 366 (M, 9%), 191 (M - Cbs, 100%; $m^*$ 99.7) and 159 (191 - S, 8%).

4. Reaction of 2-indolinethione with arylsulphonyl azides:-

a. Tosyl azide (3.2 g, 1.2 mol) was added to a solution of 2-indolinethione (2 g, 1 mol) in pyridine (20 ml). A vigorous exothermic reaction took place and after 1 hour the solvent was removed in vacuo and methanol (10 ml) was added to the residue. The solid (1.15 g) was collected and recrystallised from ethanol (decolourising charcoal) as grey needles. [1,2,3]Thiadiazolo[5,4-b]-indole (XXII, R = H) had m.p. 180° (decomp.). (Yield 800 mg).

Found: C, 55.0; H, 3.0; N, 24.2; S, 18.0%

$C_8H_5N_3S$ requires C, 54.9; H, 2.9; N, 24.0; S, 18.3%

$\lambda_{max.}$: 218, 256, 267, 274 and 310 nm ($\epsilon$ 39,800, 11,600, 10,900, 10,300 and 4,910)

$\nu_{max.}$: 3100-3400 (N-H) $cm^{-1}$

m/e: 175 (M, 34%), 147 (M - $N_2$, 71%; $m^*$ 123.5), 146 (147 - H, 53%; $m^*$ 145.0), 120 (147 - HCN, 100%; $m^*$ 98.0) and 103 (147 - CS, 32%).

The liquors were evaporated and benzene (10 ml) was added to the residue. Next day the solid was collected and recrystallised from benzene as colourless plates, m.p. 136-137°. The product was identical (m.p., i.r. spectrum) to toluene-p-sulphonamide. (Yield 1.46 g).

The liquors were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The following compounds were obtained in order of elution.

i. Tosyl azide. (Recovery 530 mg)

ii. Compound A, recrystallised from dioxan as yellow prisms, m.p. 248-250°. (Yield 250 mg).

iii. Compound (XXII, R = H) as grey needles (from ethanol). (Yield 620 mg; total yield 1.42 g, 60%).

iv. Toluene-p-sulphonamide. (Yield 690 mg; total yield 2.15 g, 93%).

b. p-Chlorobenzenesulphonyl azide (1.5 g, 1.05 mol) was added gradually over 15 minutes to a solution of 2-indolinethione (1 g, 1 mol) in pyridine (10 ml). The solution was left to stand for 1 hour then work-up as in a above gave the following products.

i. Compound (XXII, R = H) as grey needles (from ethanol), m.p. 177° (decomp.). (Yield 730 mg, 62%).

ii. Chlorobenzene-p-sulphonamide, recrystallised from benzene as colourless plates, m.p. 142-144°. (Yield 820 mg, 64%).

iii. Compound A, recrystallised from acetonitrile as yellow-brown prisms, m.p. 243-246°. (Yield 220 mg).

Found: C, 65.5; H, 3.9; N, 9.5; S, 21.0%

$C_{16}H_{10}N_2S_2$ requires C, 65.3; H, 3.4; N, 9.5; S, 21.8%

$\lambda_{max.}$: 224, 289 and 336sh nm.

$\nu_{max.}$: 3350, 3370 and 3410 $cm^{-1}$

m/e: see Main Section.

5. Reaction of 1-methyl-2-indolinethione with tosyl azide:-

1-Methyl-2-indolinethione (2 g, 1 mol) was added portionwise to a solution of tosyl azide (2.42 g, 1 mol) in pyridine (20 ml). After addition the solution was left to stand for 1 hour, then the solvent was removed in vacuo. The residue was warmed with methanol (10 ml) and the mixture was allowed to cool. The solid was collected and recrystallised from pyridine/methanol. Compound B formed orange prisms, m.p. 209-210°. (Yield 1.0 g). A second recrystallisation from chloroform/ethanol gave a red-brown amorphous solid, m.p. 213-215°.

Found: C, 67.9; H, 4.5; N, 8.9; S, 18.7%

$C_{18}H_{14}N_2S_2$ requires C, 67.1; H, 4.4; N, 8.7; S, 19.9%

$\lambda_{max.}(CHCl_3)$: 290, 316 and 328sh nm

$\nu_{max.}$: nothing informative above 1400 $cm^{-1}$

m/e: see Main Section.

The mother liquors were evaporated and benzene (10 ml) was added. Next day the solid was collected and recrystallised from benzene as colourless plates, m.p. 135-136°, identical (m.p., i.r. spectrum) to toluene-p-sulphonamide. (Yield 1.82 g, 87%).

The mother liquors were evaporated and the residue chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The following compounds were obtained.

i. Compound B. (Yield 750 mg, total yield 1.75 g).

ii. 4-Methyl[1,2,3]thiadiazolo[5,4-b]indole (XXII, R = Me) as dark grey needles (from ethanol), m.p. 91-92°. (Yield 105 mg, 5%).

Found: C, 57.3; H, 4.1; N, 22.2; S, 16.9%

$C_9H_7N_3S$ requires C, 57.1; H, 3.7; N, 22.2; S, 16.9%

$\lambda_{max.}$: 220, 257, 272, 277sh and 313 nm (ε 44,400, 13,800, 12,300, 11,800 and 6,040)

$\nu_{max.}$: nothing informative above 1400 $cm^{-1}$

m/e: 189 (M, 89%), 161 (M - $N_2$, 55%), 160 (161 - H, 43%), 146 (161 - Me, 59%), 120 (161 - MeCN, 37%) and 117 (161 - CS, 100%).

6. 1,1'-Dimethyl[$\Delta^{3,3'}$-biindoline]-2,2'-dithione (XXVIII, R = Me):-

a. 1-Methyl-2-indolinethione (500 mg) and p-nitrosodimethylaniline (250 mg) were boiled for 15 minutes in acetic acid (5 ml). The solution was cooled and the dark red solid was collected and dried in vacuo, m.p. 210-213°. (Yield 390 mg, 80%).

b. A solution of potassium ferricyanide (500 mg) and sodium hydroxide (100 mg) in water (10 ml) was added dropwise at room temperature to a stirred solution of 1-methyl-2-indolinethione (250 mg)

in carbon tetrachloride (10 ml). Stirring was continued for 30 minutes, then the organic layer was separated. The aqueous layer was extracted with carbon tetrachloride (10 ml) and the combined extracts were dried (magnesium sulphate). The solvent was removed *in vacuo* and the residue dissolved in boiling 2-methoxyethanol. The product was slowly deposited as a red-brown solid, m.p. 213-217°. (Yield 36 mg, 15%).

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# CHAPTER V

## Further investigations into the reaction between tosyl azide and 1,2,3,4-tetrahydro-2,5-dimethyl-5*H*-pyrido[4,3-*b*]indole

As a further extension to the work on tetrahydrocarbazoles the reactions of 1,2,3,4-tetrahydro-2,5-dimethyl-5H-pyrido[4,3-b]indole (I) with azides have been examined[1,2] to determine the effect of introducing a heteroatom into the reduced ring.

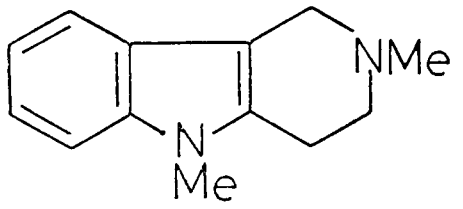
Only one product was isolated from the reaction with tosyl azide[2] and this did not correspond to any of the products obtained from the analogous reaction of 9-methyl-1,2,3,4-tetrahydrocarbazole (see Chapter II, FIGURE I). This product (50% yield) was assigned the structure (II) and this has been confirmed by degradation[1,2]. The mother liquors from the isolation of (II) had not been investigated, however, and this work was therefore repeated with a view to identifying any further products.

When compound (I) was heated with tosyl azide a 54% yield of (II) was obtained. Chromatography of the residue gave a small quantity (2%) of a second product. This latter product was obtained in higher yield (9%) from a reaction carried out in boiling propanol. The compound had a molecular formula $C_{26}H_{29}N_3O_4S_2$ (high resolution mass spectroscopy) and the u.v. spectrum was that of an indole. The i.r. spectrum contained a band at 3260 $cm^{-1}$ (N-H) but no absorption due to a C=N group. The n.m.r. spectrum showed the following signals:

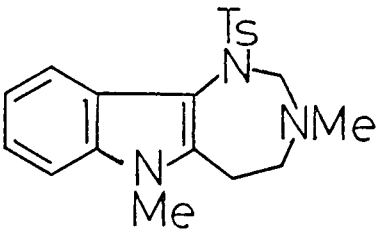
2.3-2.5τ(4H, m, aromatic), 2.6-3.1(6H, m, aromatic), 3.25(1H, t, J8Hz, aromatic), 3.52(1H, d, J8Hz, aromatic), 3.75(1H, s, exchanged $D_2O$, NH), 6.25(3H, s, indole NMe), 6.5-7.1(4H, m), 7.23(3H, s, NMe), 7.63(3H, s, tosyl Me) and 7.66(3H, s, tosyl Me).

This spectrum showed the presence of high field aromatic signals. This effect has also been observed in the n.m.r. spectrum of compound (III), a degradation product of (II)[2], and is probably due to mutual shielding between the toluene and indole rings.

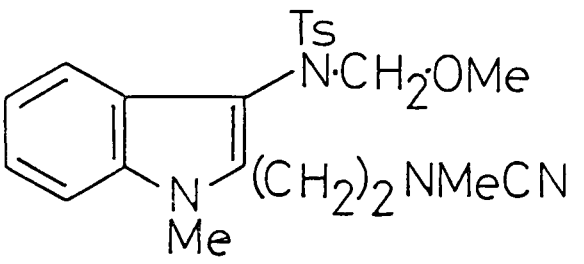
This evidence indicated that the product had the structure (IV, R = Ts). Also in favour of this assignment was the bright red stain



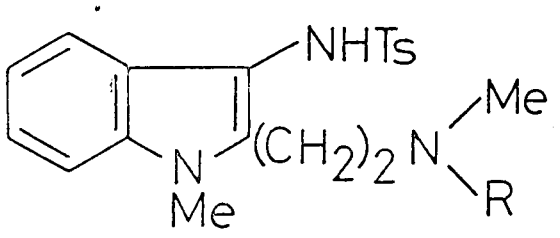

I



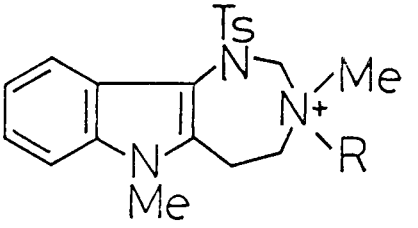

II



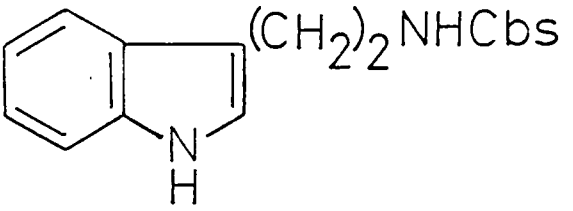

III




IV




V




VI

produced by iodine on t.l.c. spots of the compound, this effect being characteristic of 3-arylsulphonylaminoindoles[3].

Compound (IV, R = Ts) was also obtained (13% yield) by prolonged boiling of a solution of (II) with tosyl azide in propanol. This observation suggests that (IV, R = Ts) was being formed from (II) *via* the ion (V, R = Ts) (c.f. the reactions of tosyl azide with aniline and pyridine[4]). A similar type of reaction has been reported[3] in which *p*-chlorobenzenesulphonyl azide reacts with tryptamine to give the compound (VI), no addition to the indole double bond occurring. Attack of water on (V, R = Ts) and loss of formaldehyde would then lead directly to (IV, R = Ts).

In order to support this hypothesis it was decided to attempt an acetylation of (II). The compound reacted smoothly with acetic anhydride at room temperature to give a product to which we assigned the structure (IV, R = Ac), presumably formed *via* the ion (V, R = Ac). Reports of similar acetylations accompanied by ring opening have been published[5-8]. The spectral properties were in good agreement with the proposed structure, the u.v. spectrum being that of an indole and the i.r. spectrum containing a band due to C=O (1615 $cm^{-1}$). The n.m.r. spectrum showed the following signals:

2.38τ(2H, d, J8Hz, low field half of tosyl signal), 2.7-3.1(4H, m, aromatic), 3.23(1H, t, J8Hz, aromatic), 3.41(1H, s, exchanged $D_2O$, NH), 3.48(1H, d, J8Hz, aromatic), 6.23(3H, s, indole NMe), 6.3-7.1 (4H, m), 6.92(3H, s, NMe), 7.63(3H, s, tosyl Me), 7.91(s, acetyl Me) and 8.16(s, acetyl Me).

Of particular interest in this spectrum are the high field aromatic protons and the two singlets at 7.91 and 8.16τ (ratio 2:1) for the acetyl signals. On adding a drop of trifluoroacetic acid to the solution these signals moved to 7.69 and 8.01τ (ratio 2:1). In pyridine, however, these signals appeared at 7.94 and 8.05τ (ratio 1:2). The effect of aromatic solvents such as pyridine upon the

chemical shifts of protons in systems possessing internal hindered rotation has been reported[9].

Holton[2] had treated compound (II) with dilute methanolic hydrochloric acid and had obtained a product which was assumed to be the hydrochloride of (II). In the light of the above observations, however, it was possible that hydrolysis had taken place and the product was in fact the hydrochloride of (IV, R = H). Moreover, analytical data were in closer agreement with the latter structure than the former.

A sample of the hydrochloride was treated with base and a low-melting solid was obtained. A suitable solvent for recrystallisation could not be found, but the compound was homogeneous on t.l.c. Its spectral properties were in good agreement with the proposed structure (IV, R = H), the n.m.r. spectrum containing the following signals:

2.39$\tau$(2H, d, J8Hz, low field half of tosyl signal), 2.6-3.2(6H, m, aromatic), 5.63(2H, br, exchanged $D_2O$, 2 x NH), 6.40(3H, s, indole NMe), 7.30(4H, m), 7.60(3H, s, NMe) and 7.63(3H, s, tosyl Me).

As a final experiment compound (II) was heated with Brady's reagent, yielding formaldehyde 2,4-dinitrophenylhydrazone, and supplying proof of the proposed hydrolysis.

There were important differences in the mass spectra of the compounds (IV, R = Ts) and (IV, R = Ac) (see FIGURES I and II). In the former case the base peak is the fragment $CH_2{=}\overset{+}{N}TsMe$ (m/e 198) whereas in the latter case the corresponding peak (m/e 86) is very small. The mass spectrum of (IV, R = H) is shown for comparison in FIGURE III.

FIGURE I

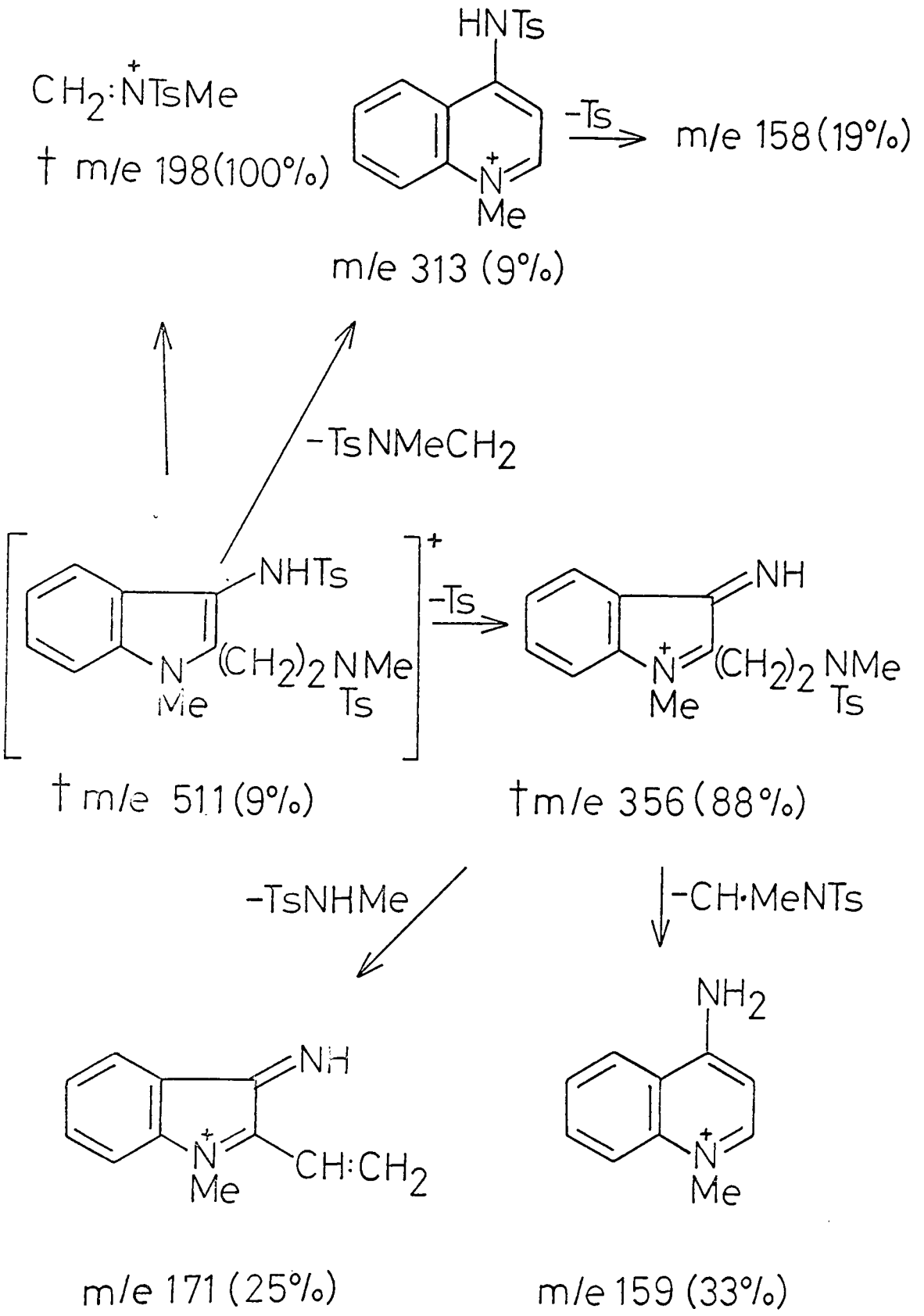

HNTs
CH2:NTsMe
† m/e 198(100%)
-Ts
m/e 158(19%)
Me
m/e 313 (9%)
-TsNMeCH2
NHTs
(CH2)2 NMe
Me
Ts
-Ts
NH
† m/e 511(9%)
† m/e 356(88%)
-TsNHMe
-CH·MeNTs
CH:CH2
NH2
m/e 171 (25%)
m/e 159 (33%)

FIGURE II

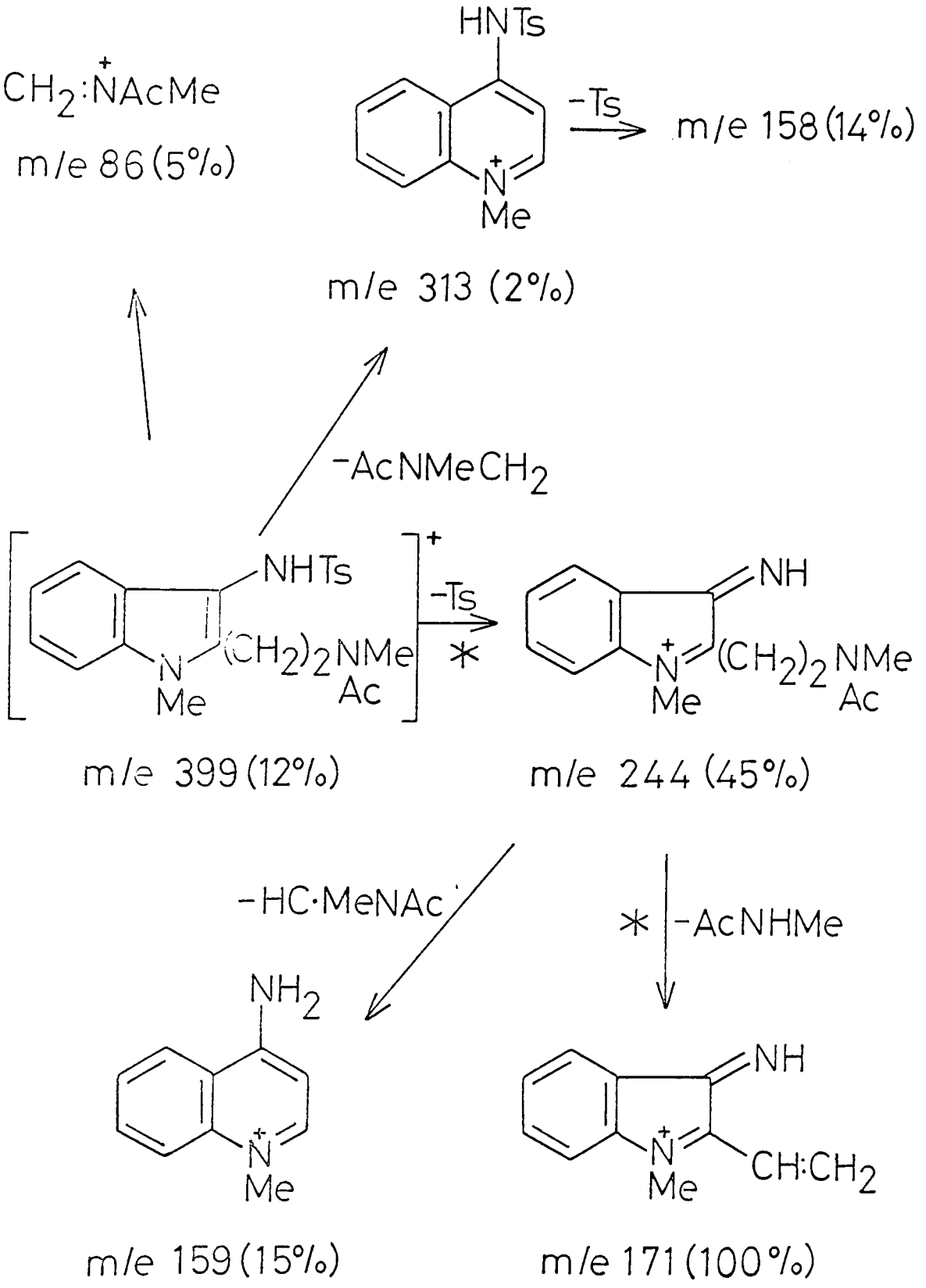
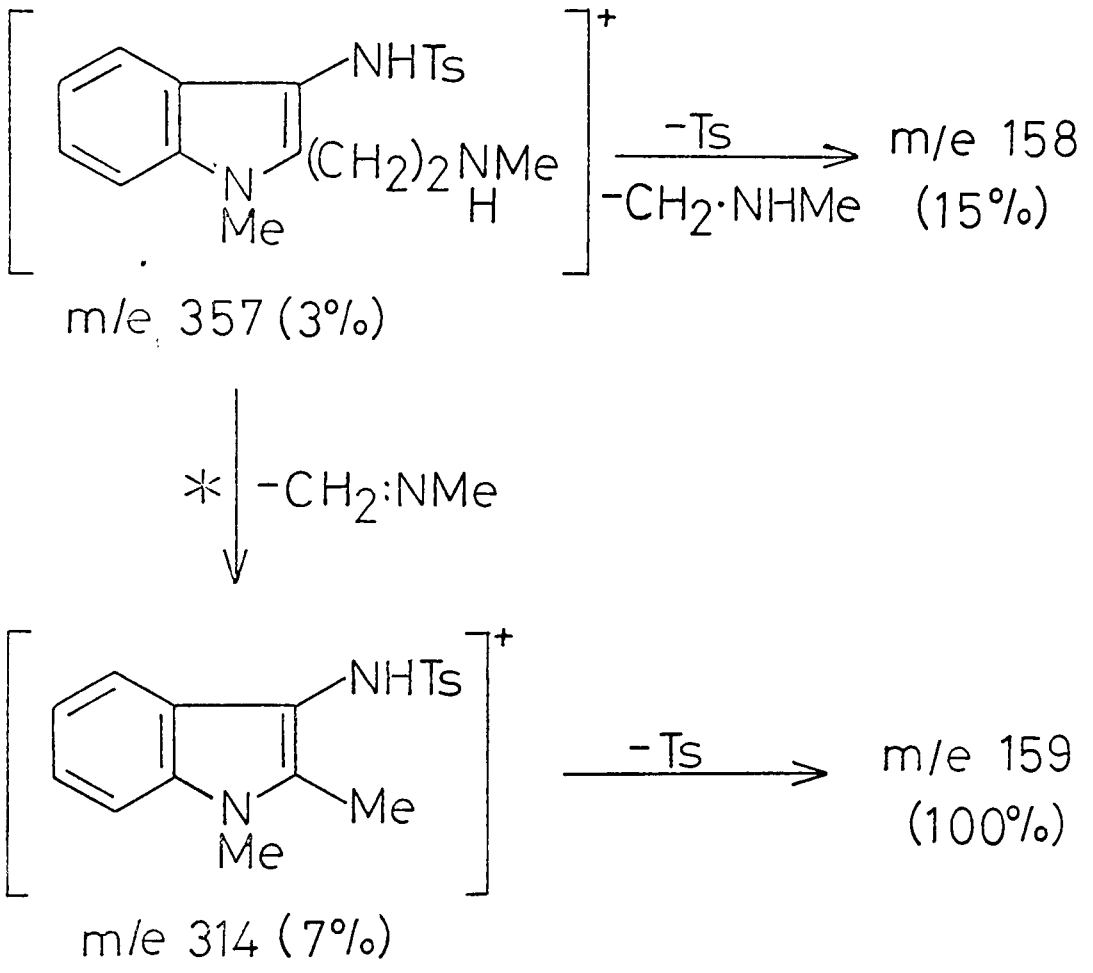

CH2:N+AcMe
m/e 86 (5%)
HNTs
-Ts
m/e 158 (14%)
N+
Me
m/e 313 (2%)
-AcNMeCH2
NHTs
(CH2)2NMe
Ac
N
Me
-Ts
*
NH
(CH2)2NMe
Ac
m/e 399 (12%)
m/e 244 (45%)
-HC·MeNAc
*
-AcNHMe
NH2
NH
CH:CH2
m/e 159 (15%)
m/e 171 (100%)

FIGURE III


NHTs
(CH2)2NMe
H
N
Me
+
-Ts
-CH2·NHMe
m/e 158
(15%)
m/e 357 (3%)
*
-CH2:NMe
NHTs
N
Me
Me
+
-Ts
m/e 159
(100%)
m/e 314 (7%)

# CHAPTER V

## Experimental

1. 1,2,3,4,5,6-Hexahydro-3,6-dimethyl-1-p-tolylsulphonyl[1,3]-diazacino[5,4-b]indole (II):-

a. 2,5-Dimethyl-1,2,3,4-tetrahydro-5H-pyrido[4,3-b]indole (500 mg, 1 mol) and tosyl azide (880 mg, 1.8 mol) were heated together at 50° (oil bath) for 2 days. A little methanol was added and the solid was collected. Recrystallisation from ethanol gave colourless prisms, m.p. 185-188° (lit.[1,2] m.p. 188-189°). (Yield 500 mg, 54%).

b. 2,5-Dimethyl-1,2,3,4-tetrahydro-5H-pyrido[4,3-b]indole (500 mg, 1 mol) and tosyl azide (880 mg, 1.8 mol) in propanol (4 ml) were heated at 100° for 24 hours. The solution was cooled and the solid collected, m.p. 187-188° (lit.[1,2] 188-189°). (Yield 325 mg, 35%).

2. 1-Methyl-2-[2-(N-methyl-p-tolylsulphonylamino)ethyl]-3-p-tolylsulphonylaminoindole (IV, R = Ts):-

a. The methanolic mother liquors from experiment 1a were evaporated and the residue was chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. The compound was obtained as colourless plates, m.p. 161-164° (from methanol). (Yield 30 mg, 2%).

b. The mother liquors from experiment 1b were evaporated and chromatographed on silica gel, eluting with benzene/ethyl acetate mixtures. Recrystallisation of the product from methanol gave colourless plates, m.p. 170-171°. (Yield 120 mg, 9%).

c. A solution of 1,2,3,4,5,6-hexahydro-3,6-dimethyl-1-p-tolylsulphonyl[1,3]-diazacino[5,4-b]indole (500 mg) and tosyl azide (300 mg) was boiled under reflux in propanol (25 ml) for 7 days. The solvent was removed in vacuo and the residue filtered through silica gel in benzene/ethyl acetate (9:1). The solvent was removed and the residue recrystallised from benzene, yielding toluene-p-sulphonamide (150 mg). The residue from this recrystallisation was recrystallised from methanol as colourless plates, m.p. 169-171°. (Yield 90 mg, 13%).

Found: M 511.1599

$C_{26}H_{29}N_3O_4S_2$ requires M 511.1587

$\lambda_{max.}$: 202, 224, 277sh, 283 and 290sh nm ($\varepsilon$ 41,700, 43,600 8,040, 8,410 and 7,350)

$\nu_{max.}$: 3260 (N-H) $cm^{-1}$

m/e: 511 (M, 9%), 356 (M - Ts, 88%), 313 (M - TsNMe.$CH_2$, 9%), 198 ($CH_2$:$\overset{+}{N}$TsMe, 100%), 171 (356 - TsNHMe, 25%) and 159 (356 - TsNMe.CH, 33%).

3. 1-Methyl-2-[2-(N-methylacetamido)ethyl]-3-p-tolylsulphonylaminoindole (IV, R = Ac):-

1,2,3,4,5,6-Hexahydro-3,6-dimethyl-1-p-tolylsulphonyl[1,3]-diazacino[5,4-b]indole (1 g) was dissolved in the minimum of chloroform and acetic anhydride (3 ml) was added. The solution was allowed to stand at room temperature for 24 hours then the solvent was removed in vacuo. Methanol (10 ml) was added, the mixture was left for 1 hour and the solvent was removed. This process was repeated until the excess acetic anhydride had been destroyed. The residue was triturated with petroleum ether (b.p. 60-80°) and then recrystallised from methanol as colourless prisms, m.p. 195-197°. (Yield 790 mg, 73%).

Found: C, 62.5; H, 6.4; N, 10.3; S, 8.3%

$C_{21}H_{25}N_3O_3S$ requires C, 63.2; H, 6.3; N, 10.5; S, 8.0%

$\lambda_{max.}$: 223, 277sh, 283 and 292 nm ($\varepsilon$ 49,800, 9,790, 10,500 and 9,250)

$\nu_{max.}$: 1615 (C=O) $cm^{-1}$

m/e: 399 (M, 12%), 313 (M - $CH_2$:$\overset{+}{N}$AcMe, 2%), 244 (M - Ts, 45%; $m^*$ 149.2), 171 (244 - NHMeAc, 100%; $m^*$ 119.8), 159 (244 - CH.NAcMe, 15%) and 86 ($CH_2$:$\overset{+}{N}$AcMe, 5%).

4. 1-Methyl-2-(2-methylaminoethyl)-3-p-tolylsulphonylaminoindole (IV, R = H):-

1-Methyl-2-(2-methylaminoethyl)-3-p-tolylsulphonylaminoindole hydrochloride (115 mg) was dissolved in the minimum of water and 2N aqueous sodium carbonate was added dropwise until the mixture was alkaline . The precipitate was allowed to harden, then collected and dried in vacuo at 50°. The product had m.p. 63-71°. (Yield 90 mg, 86%).

A suitable solvent for recrystallisation could not be found but the compound gave only one spot on t.l.c.

m/e: 357 (M, 3%), 314 (M - $CH_2$:NMe, 7%; $m^*$ 276.2) and 159 (314 - Ts, 100%).

5. Hydrolysis of 1,2,3,4,5,6-hexahydro-3,6-dimethyl-1-p-tolylsulphonyl[1,3]-diazacino[5,4-b]indole (II):-

The indole (10 mg) was boiled for 2 minutes with aqueous 2,4-dinitrophenylhydrazine hydrochloride (Brady's reagent). A yellow solid separated; this was washed several times with boiling 2N hydrochloric acid and recrystallised from methanol, yielding formaldehyde dinitrophenylhydrazone, identical (t.l.c. and u.v. spectrum) to an authentic sample.

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# CHAPTER VI

## Preparation of starting materials

Arylsulphonyl azides

The arylsulphonyl azides used in these investigations were prepared from commercial samples of the appropriate arylsulphonyl chloride and sodium azide using aqueous acetone as solvent. It was advantageous to use an excess of azide since equimolar proportions of the reactants tended to result in impure samples of azide and these impurities interfered with subsequent reactions. A convenient test for the purity of the azide was to heat it with 1,2,3,4-tetrahydrocarbazole, when an intense purple colour developed in the presence of these impurities.

Two distinct methods were used to prepare the azides.

i. Tosyl azide: A solution of sodium azide (1.1 mol) in water was added dropwise to a stirred, cooled solution of tosyl chloride (1 mol) in acetone, addition being controlled so as to maintain the temperature in the range 0-5°. After addition the mixture was stirred for 2 hours, then poured into ice/water. The mixture was extracted with ether, then the extracts were washed with copious amounts of water and dried (magnesium sulphate). The solvent was removed *in vacuo* to give a pale yellow oil which crystallised on standing, m.p. 21° (lit.[1] 21-22°). (Yield 95%).

ii. p-Nitrobenzenesulphonyl azide:- A solution of p-nitrobenzenesulphonyl chloride (1 mol) in acetone was added dropwise to a stirred solution of sodium azide (1.1 mol) in acetone and water (2:1), cooled to 0°. The mixture was stirred at 0° for 2 hours, then poured into ice/water. The solid was collected and recrystallised from ethanol as colourless needles, m.p. 104-105° (lit.[2] 101.5-102°). (Yield 93%).

Indoles

1,2,3,4,-Tetrahydrocarbazole and 5,6,7,8,9,10-hexahydrocyclohept-[b]indole were prepared by condensation of cyclohexanone and cyclo-

heptanone respectively with phenyl hydrazine. The resulting phenylhydrazones were heated with sulphuric acid and the indoles were collected and recrystallised. This method gave 1,2,3,4-tetrahydrocarbazole as colourless plates (from aqueous methanol), m.p. 118-119° (lit.[3] 119°) (yield 90%) 5,6,7,8,9,10-hexahydrocyclohept[b]indole as colourless plates (from ethanol), m.p. 144-145° (lit.[4] 144°) (yield 84%).

6,7,8,9,10,11-Hexahydro-5H-cyclooct[b]indole was prepared by a different method. Phenylhydrazine was added dropwise to a refluxing solution of cyclooctanone in acetic acid. The product separated on cooling, and was recrystallised from methanol as colourless needles, m.p. 75-76° (lit.[5] 72-74°). (Yield 53%).

The above indoles were methylated by the method of Potts and Saxton[6], using sodamide and methyl iodide in liquid ammonia. 5,6,7,8,9,10-Hexahydro-5-methylcyclohept[b]indole was obtained as colourless needles (from ethanol), m.p. 53-54° (lit[7] 50°). (Yield 80%). 6,7,8,9,10,11-Hexahydro-5-methyl-5H-cyclooct[b]indole was obtained as a pale yellow oil, b.p. 122-124°/0.03 mm (lit.[8] 212-213°/17 mm). (Yield 62%).

Bridged indoles

The bridged indoles investigated in Chapter III were prepared by condensation of cyclohexanone and cycloheptanone with 1-aminoindoline. The following series of reactions was used.

1-Nitrosoindoline was prepared by the method of Kost et al[9]. An aqueous solution of sodium nitrite was added dropwise to a stirred, cooled solution of indoline in 20% sulphuric acid, at such a rate to maintain the temperature in the range -2 to 0°. The precipitated 1-nitrosoindoline was collected and washed with copious amounts of water, then dried in vacuo, m.p. 82-83° (lit.[10] 83-84°)

1-Aminoindoline was prepared by lithium aluminium hydride reduction of 1-nitrosoindoline. The method of Rapoport et al[11] was

originally attempted in which ethereal lithium aluminium hydride was added to a stirred, cooled solution of 1-nitrosoindoline under nitrogen. Our final product, however, always contained a high proportion of the nitroso-compound. Better results were obtained using the method of Ames and Kucharska[12]. In this preparation the nitroso-compound in benzene was added to a stirred suspension of lithium aluminium hydride in ether, followed by boiling under reflux. By varying the conditions to use ether instead of benzene as solvent for the nitroso-compound we were able to avoid the induction periods reported[12]. 1-Aminoindoline was obtained as a pale yellow oil, b.p. 60-62°/0.05.mm (lit.[12] 62-64°/0.1 mm). (Yield 80%).

The 1-aminoindoline thus obtained was immediately condensed with cyclohexanone by heating at 100° for 30 minutes[9], and the resulting hydrazone was cyclised using sulphuric acid as catalyst. Contrary to the results of Kost et al[9] the use of 20% sulphuric acid resulted in charring but we were able to carry out a successful cyclisation by reducing the acid concentration to 4% (v/v). Recrystallisation of the product from ethanol gave colourless plates, m.p. 157-158° (lit.[9] 169.5-170°). (Yield 50%).

Similar treatment of cycloheptanone gave the seven-membered homologue.

1-Aminoindoline (5.3 g, 1 mol) and cycloheptanone (4.4 g, 1 mol) were heated at 100° for 1 hour. 5% Sulphuric acid (50 ml) was added and the mixture was heated at 100° for a further hour. The mixture was cooled and the solid collected, washed with water and dried in vacuo. Recrystallisation from ethanol gave colourless needles, m.p. 129-131°. (Yield 5.1 g, 61%).

Found: C, 85.6; H, 7.9; N, 6.8%

$C_{15}H_{17}N$ requires C, 85.3; H, 8.1; N, 6.6%

$\lambda_{max.}$: 212, 234 and 293 nm ($\varepsilon$ 20,000, 30,400 and 7,700)

$\nu_{max.}$: nothing informative above 1400 $cm^{-1}$

$\tau(CDCl_3)$: 2.85(1H, d, J8Hz, aromatic), 3.0-3.3(2H, m, aromatic), 5.67(2H, t, J7Hz), 6.32(2H, t, J7Hz), 7.1-7.3(4H, m) and 8.0-8.5(6H, m).

2-Indolinethiones

2-Indolinethione and 1-methyl-2-indolinethione were prepared from oxindole and 1-methyloxindole respectively by treatment with phosphorus pentasulphide as reported[13]. 2-Indolinethione was recrystallised from methanol as yellow prisms, m.p. 145-148° (lit.[13] 147-149°). (Yield 42%). 1-Methyl-2-indolinethione formed pale yellow plates (from benzene/hexane), m.p. 108-110° (lit.[13] 108-110°). (Yield 59%).

2-Alkylthioindoles

2-Methylthioindole was prepared by methylation of 2-indolinethione at room temperature by means of methyl iodide/potassium carbonate. Purification by chromatography (silica, benzene/hexane 1:1) gave the compound as a colourless crystalline solid, m.p. 46-48° (lit.[13] 48-49°). (Yield 94%).

Similar treatment of 2-indolinethione with ethyl iodide and potassium carbonate gave 2-ethylthioindole as a pale yellow oil which crystallised on standing, m.p. 33-35° (lit.[14] 36-37.5°). (Yield 84%).

Samples of 1-methyl-2-methylthioindole were prepared by a previous worker.

The 1,2,3,4-tetrahydro-2,5-dimethyl-5H-pyrido[4,3-b]indole used in the investigations reported in Chapter V was prepared by a previous worker.

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# ABSTRACT

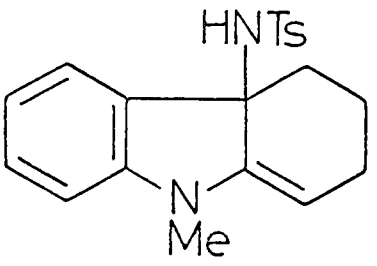
The reported work on the reactions between indoles and arylsulphonyl azides[1-4] was extended with a view to identifying any intermediates involved and establishing the relationships between the products formed. The effect of varying the structures of the indoles on these products has also been investigated.

Compounds of type (I) appear to be key intermediates in the reactions of alkyl indoles with azides. Compound (I) has recently been prepared[5]. The suggested[2a] intermediacy of this compound in the reaction between tosyl azide and 9-methyltetrahydrocarbazole was proved, the reaction of (I) with p-chlorobenzenesulphonyl azide yielding (II).

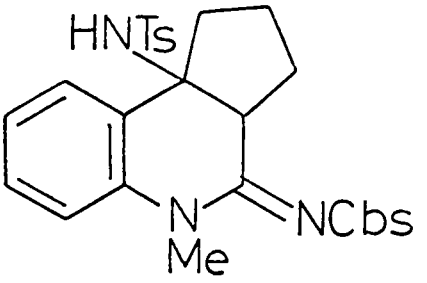
As an extension of the work on tetrahydrocarbazoles[2a], the reactions of 5,6,7,8,9,10-hexahydrocyclohept[b]indole, 6,7,8,9,10,11-hexahydro-5H-cyclooct[b]indole and their N-methyl derivatives have been examined. From the reactions of the N-H compounds have been isolated the products (III, n = 5, Z = Ts), (III, n = 6, Z = Ts) and (III, n = 6, Z = Cbs).

The action of heat on (III, n = 6, Z = Ts) has been investigated and the products (IV) and (V) isolated. In acetic acid solution (III, n = 6, Z = Ts) was oxidised to (VI); a plausible mechanism for this oxidation was proposed. On heating, (VI) isomerised to (VII), and on treatment with base (VI) added water, giving (VIII).

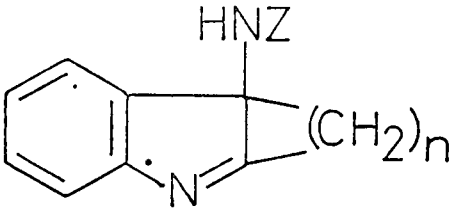
5,6,7,8,9,10-Hexahydro-5-methylcyclohept[b]indole gave four products on treatment with tosyl azide, (IX - XII, n = 4). The structures of the latter two products were proved by degradation to the compounds (XIII) and (XIV), and synthesis of these degradation products. The homologous compounds (IX - XII, n = 5) were obtained when 6,7,8,9,10,11-hexahydro-5-methyl-5H-cyclooct[b]indole was treated with tosyl azide. The stereochemistry of the compounds (XI, n = 4)



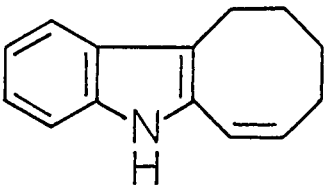

I



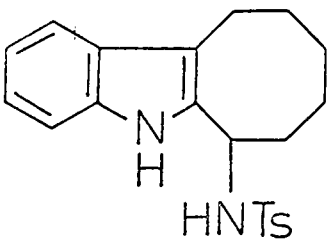

II



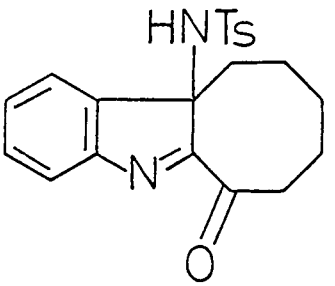

III



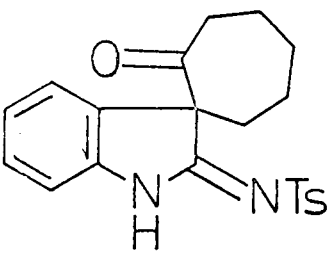

IV



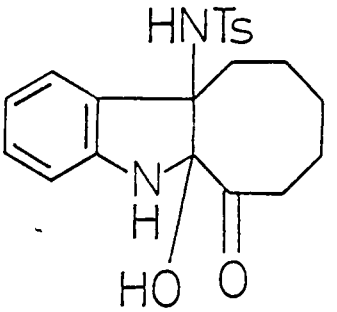

V



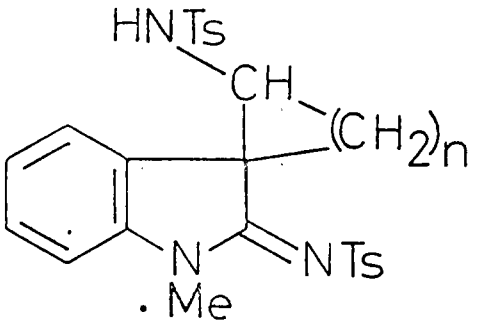

VI



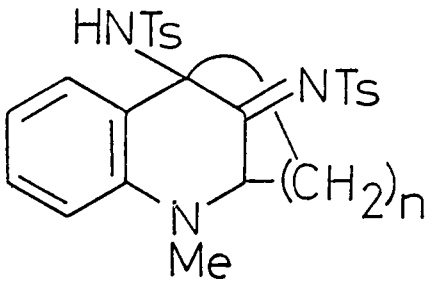

VII



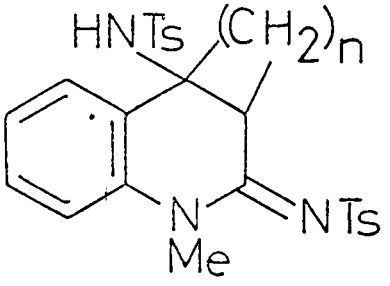

VIII



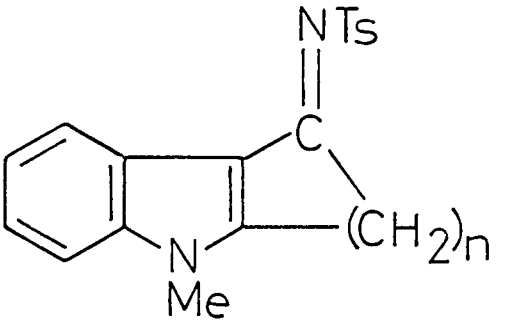

IX



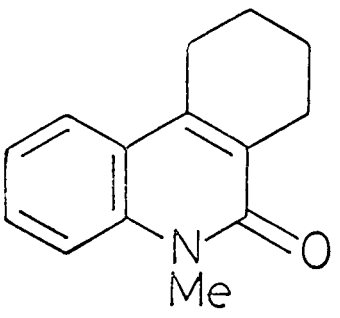

X



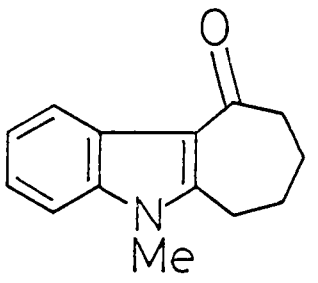

XI



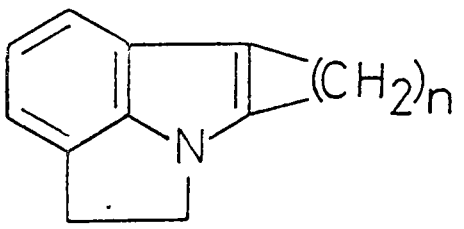

XII



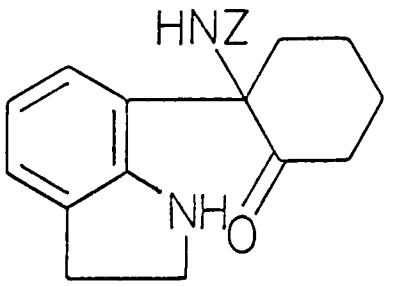

XIII




XIV




XV




XVI

and (XI, n = 5) has been determined and the transformation of (X, n = 5) into (XII, n = 5) on heating was demonstrated.

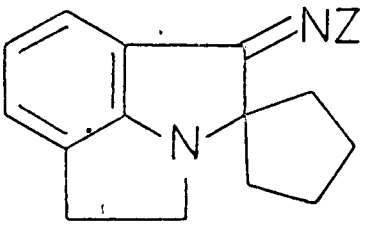
Rapoport[6] has reported the high reactivity of indoles with structures of the type (XV), this reactivity being due to a high degree of strain in the molecule. It was of interest, therefore, to extend the present work by synthesising the compounds (XV, n = 4) and (XV, n = 5) and investigating their reactions with arylsulphonyl azides.

The former yielded the products (XVI), (XVII), (XVIII, n = 3) and (XIX), depending on the conditions used. From the reaction of p-nitrobenzenesulphonyl azide in methanol a further product (XX) was obtained. The effect of heat on the compounds (XVI) and (XX) has been examined, both yielding (XXI).

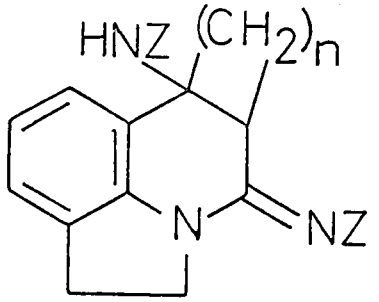
(XV, n = 5) reacted with azides to give the compounds (XXII) as major product. Also obtained were compounds (XVIII, n = 4) and from the reaction with p-nitrobenzenesulphonyl azide (XXIII) was also isolated. Since this was the first time that compounds of the type of structure (XXII) had been obtained in good yield, the chemistry of these products was studied in some detail. A number of interesting rearrangements were observed. Treatment with base gave the compounds (XXIV, R = NZ) and (XXIV, R = O), while the effect of acid was to produce the ion (XXV). This was not isolated, products resulting from the addition of hydroxylic solvents to the molecule being the only compounds obtained. A similar rearrangement occurred on heating (XXII) in hydroxylic solvents. The rearrangement in acidic solvent was studied by means of n.m.r. spectroscopy.

The reactions of 2-alkylthioindoles with azides were investigated, the major products being the azobisindoles (XXVI). From the reaction of 1-methyl-2-methylthioindole compound (XXVII) was also obtained; the formation of this compound involves a 1,2-shift of the alkylthio group.

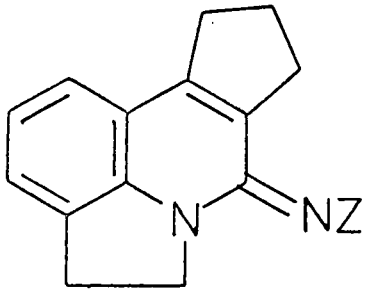
2-Indolinethiones gave two products on treatment with aryl-



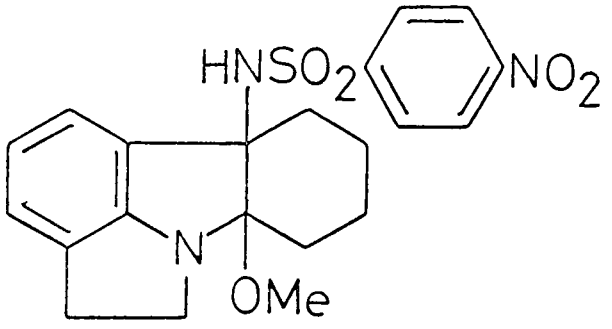

XVII



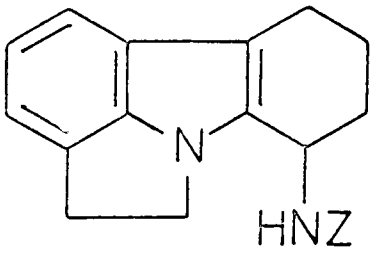

XVIII



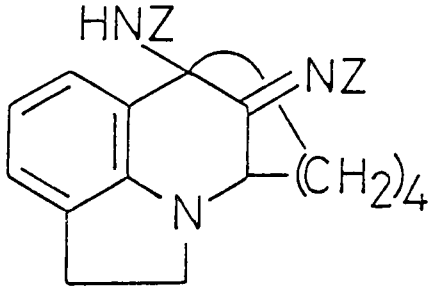

XIX



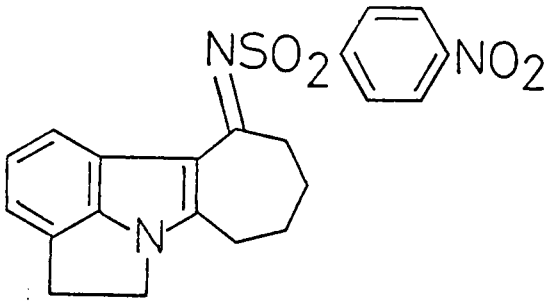

XX



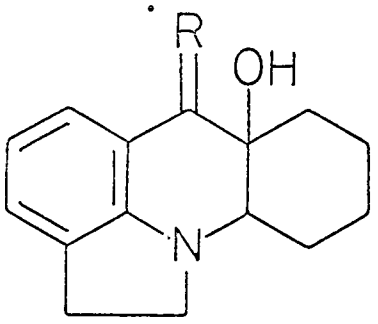

XXI



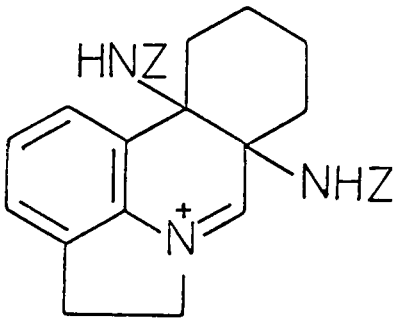

XXII



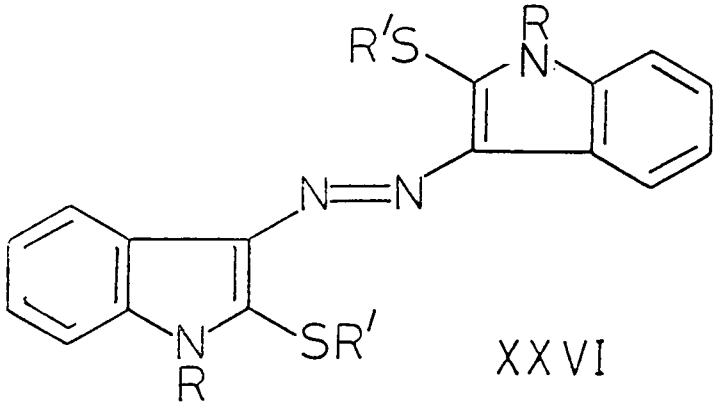

XXIII



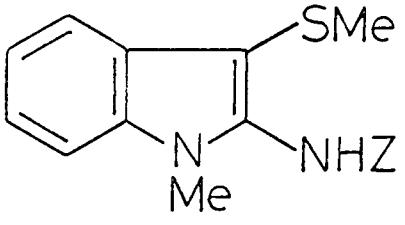

XXIV




XXV




XXVI



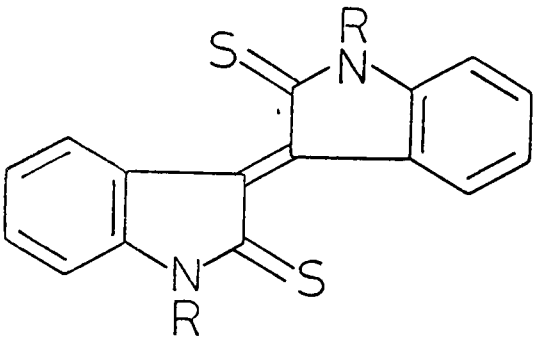

XXVII

sulphonyl azides, compounds (XXVIII) and the 1,2,3-thiadiazoles (XXIX).

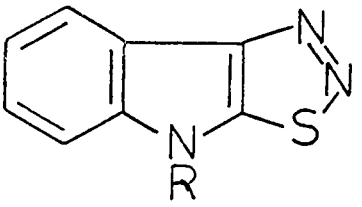
Finally, the reported[7] work on 1,2,3,4-tetrahydro-2,5-dimethyl-5*H*-pyrido[4,3-*b*]indole was repeated and a further product (XXX) was obtained.

## References

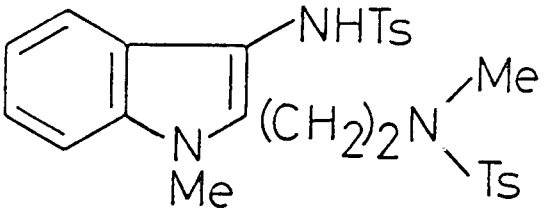

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XXVIII



XXIX



XXX