Summary of a Thesis

entitled

A NOVEL ELIMINATION REACTION

by

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Submitted to the University of Glasgow for the degree of Doctor of Philosophy

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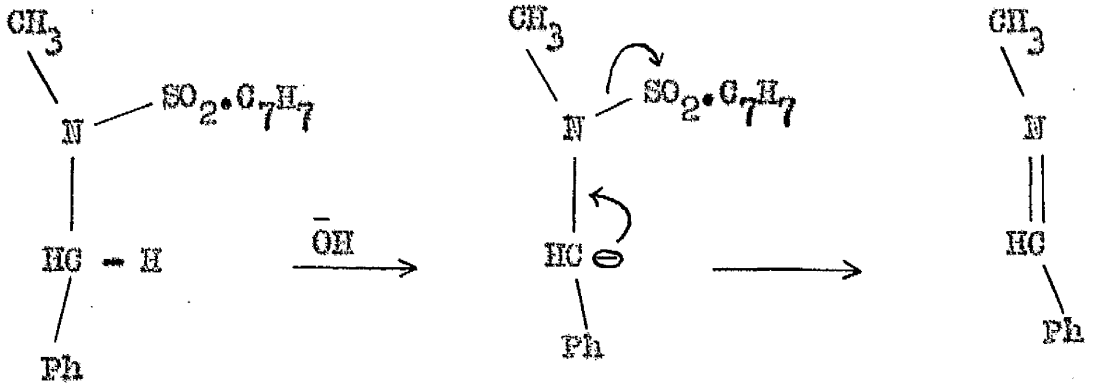
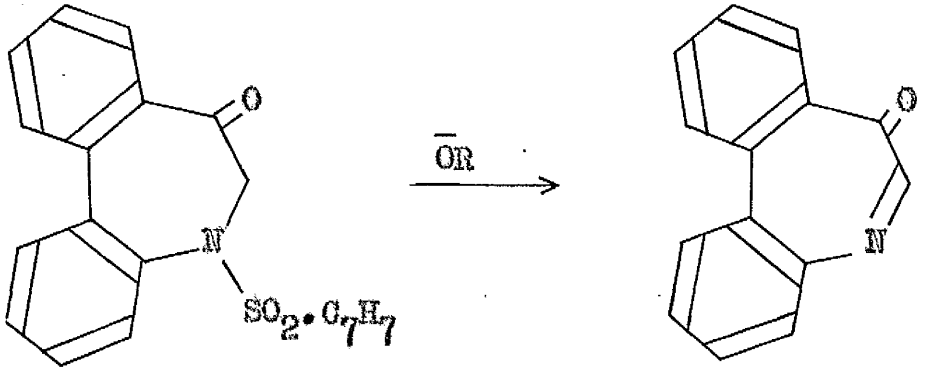
An elimination reaction leading to imines was reported in 1926, by Holmes and Ingold[1], who isolated benzylidene methylimine (II) after fusing the sulphonamide (I) with moist potassium hydroxide:

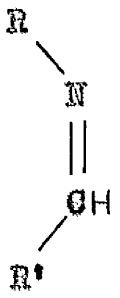


(I) (II)

One became interested in the reaction as a means of introducing carbon-nitrogen double bonds into heterocyclic rings[2]:-



A study of the literature[3-5] suggested that a successful elimination reaction leading to anils would require mild basic conditions, and the presence of electron-withdrawing groups on the carbon atom adjacent to the nitrogen atom. A preliminary investigation[6] proved the validity of this forecast: anils (III: R = Ph; R' = $C_6H_4.NO_2$-p or CO.Ph) were obtained in high yield, on treating sulphonamides (IV : R = Ph; R' = $C_6H_4.NO_2$-p or CO.Ph) with sodium methoxide in toluene at room temperature;



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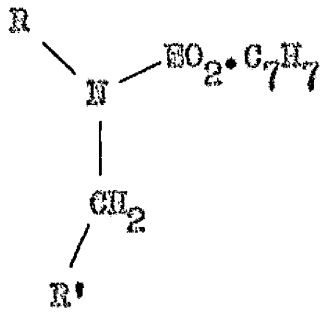
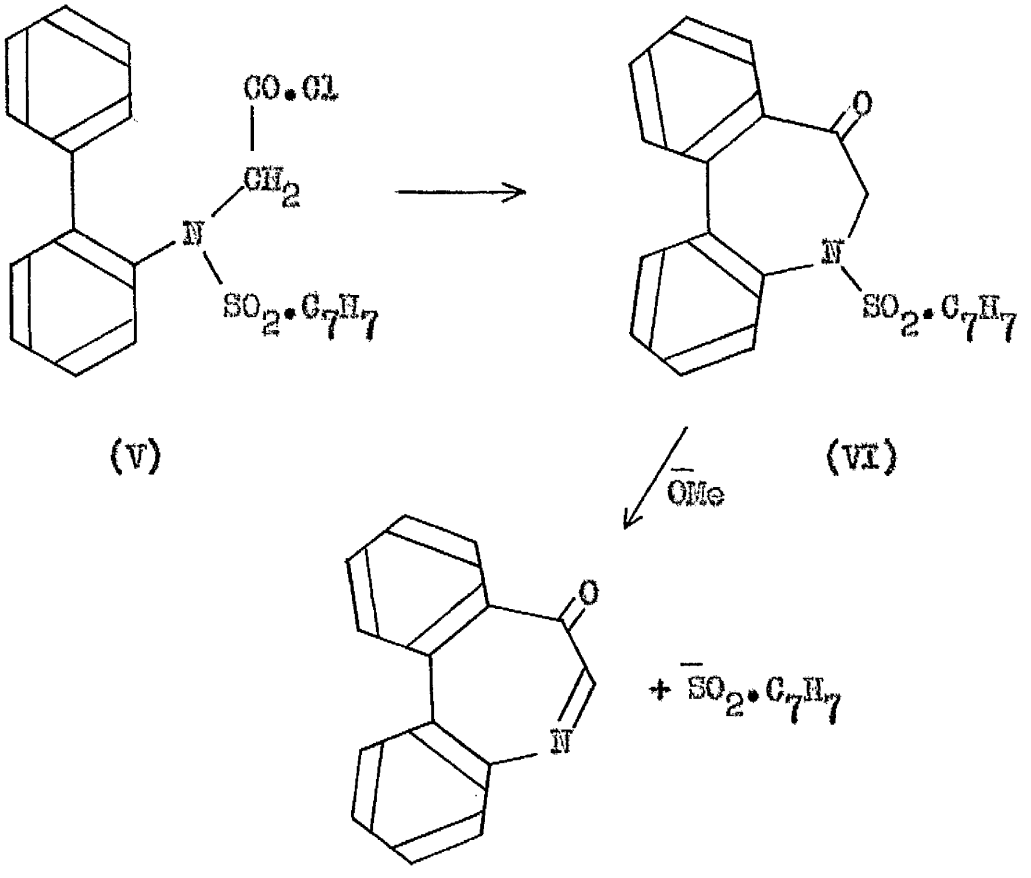


(IV)

sulphonamides such as (IV : R = Ph ; R' = CH_3. or Ph.) failed to react, even with very strong bases. It remained to demonstrate the utility of the reaction in the synthesis of certain novel heterocyclic systems:

1. The synthesis of an azatropone[7]

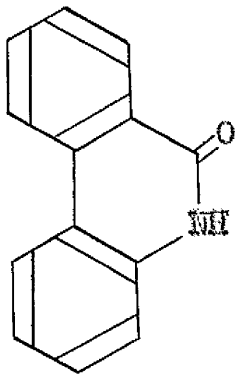
When treated with aluminium chloride in chloroform at -70°, the acid-chloride (V) underwent a Friedel-Crafts intramolecular cyclisation to give the ketone (VI). Treatment of the latter with sodium methoxide in toluene under nitrogen, gave the azatropone (VII) in 60% yield. The bi-products were phenanthridone (VIII)



(V) (VI)

(VII)

and a compound (IX), which was also obtained from (VII) on treatment with zinc dust and dilute acetic acid. Heating the azatropone (VII), either alone or with lithium aluminium hydride



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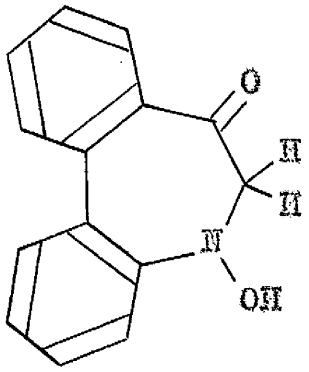

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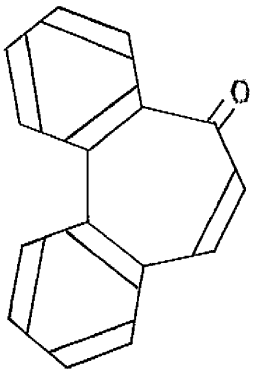

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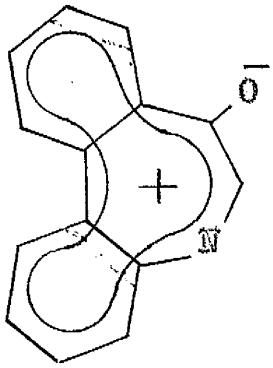


(XI)

in tetrahydrofuran gave phenanthridone (VIII); the latter was also obtained when (IX) was treated with palladised charcoal

in boiling trichlorobenzene[8].

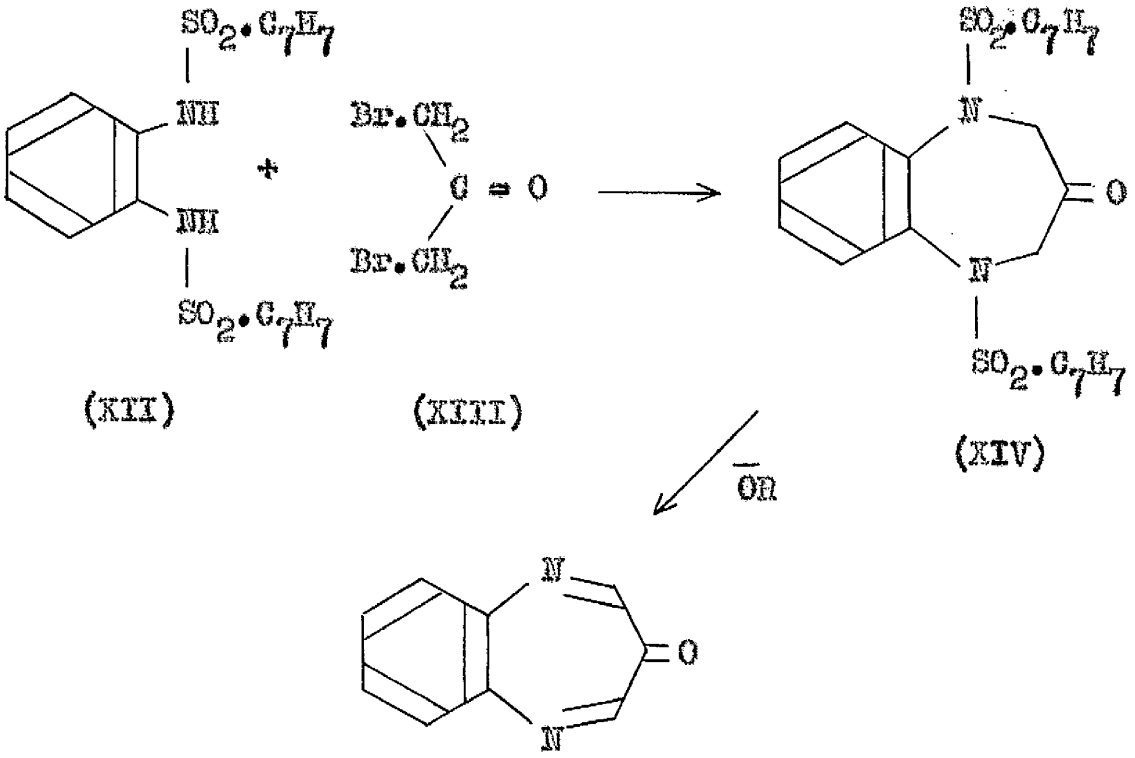
Properties of compounds (X) and (VII)

Compound (X)	Compound (VII)
m.p. 94°	m.p. 265°
Very pale yellow	Deep red. Hydrochloride, violet
Soluble in organic solvents	Poorly soluble in organic solvents
ν_{max} 1645 cm^{-1} (in K.Br.)	ν_{max} 1590; 1620 cm^{-1} (in KCl)
2,4-Dinitrophenylhydrazone m.p. 231°[9]	No 2,4-Dinitrophenylhydrazone

The above comparison shows the azatropone (VII) to be more polar than the dibenzotropone (X). Moreover, like tropolone[10], the azatropone (VII) was remarkably resistant to catalytic reduction. One proposed, therefore, that structures such as (XI) may more accurately account for some of the properties of the azatropone.

2. Attempted synthesis of a diazabenzotropone

The proposed route to (XV) was as follows:-



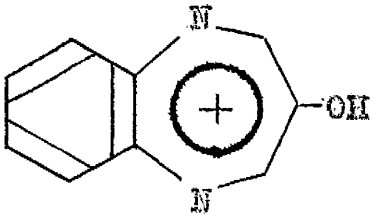
(XII) (XIII) (XIV)

(XV)

Condensation of either the free base (XII) or its potassium salt with 1,3-dibromoacetone (XIII), gave the ketone (XIV).

Treatment of (XIV) with sodium methoxide in toluene under nitrogen failed to give (XV), but a highly polar red compound (m.p. $> 360^{\circ}$)

was obtained: analytical and spectroscopic data suggested the structure (XVI). Furthermore, treatment of (XVIII) with toluene-p-sulphonyl chloride gave a similar red compound believed to be (XVII). The compounds (XVI) and (XVII) appear to be the



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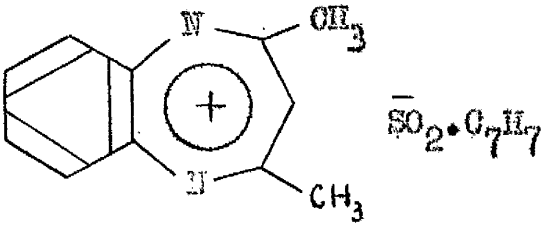
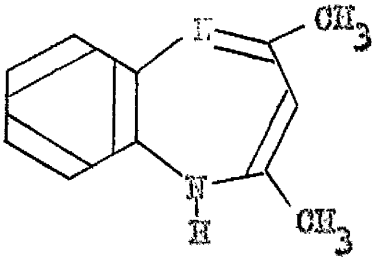


(XVII)

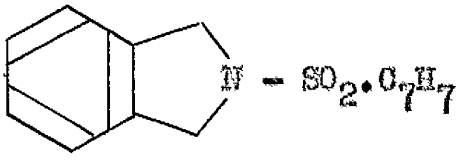


(XVIII)

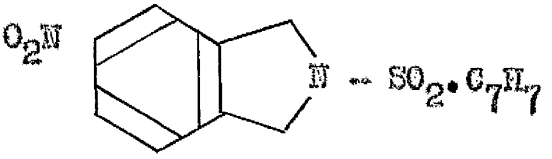
first reported diazabenzotropylium salts.

3. Attempted synthesis of 5-nitropseudoisoindole

A study of conditions favouring the elimination reaction suggested that whilst (XIX) should be resistant to basic attack, (XX) would react with mild bases to give 5-nitropseudoisoindole (XXI).



(XIX)



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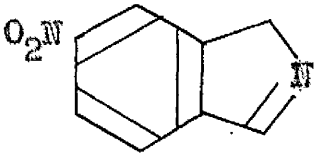
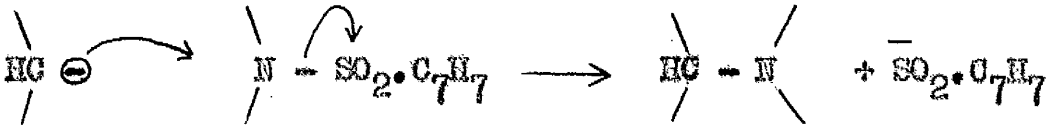


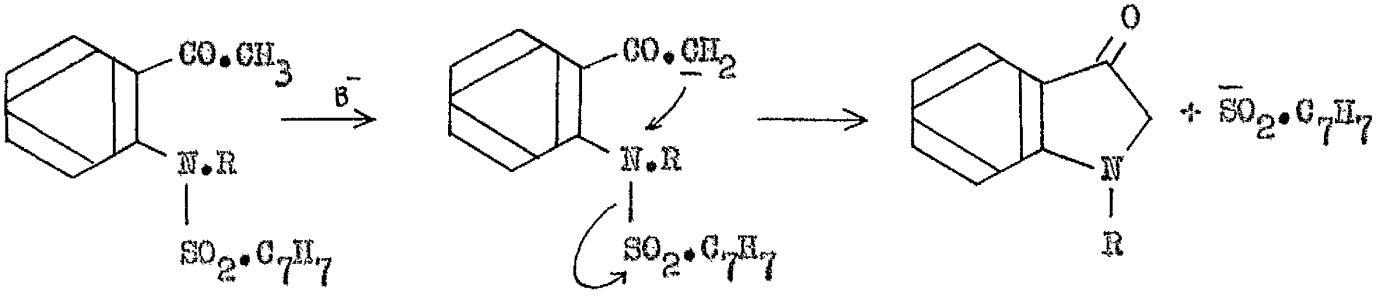
(XXI)

As expected, (XIX) was unaffected by sodium methoxide in toluene, but (XX) reacted with the base to give a deep-blue pigment (m.p. $>360^{\circ}$). This was too insoluble in most organic solvents to obtain molecular weight or nuclear magnetic resonance data, but the elementary analyses showed the pigment to contain sulphur. A structure for the blue pigment would not be deduced but, apparently, the compound did not arise from an elimination reaction.

In addition to providing carbon-nitrogen double bonds, the elimination reaction is theoretically applicable to the formation of new carbon-nitrogen single bonds:



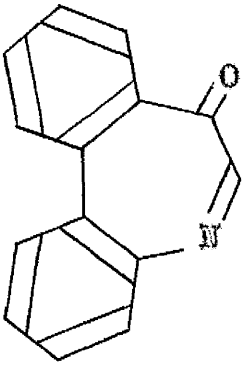
Sulphonamides such as (XV: R = CH_3 or Ph; R' = H or CH_3) failed, however, to react with anion forming compounds - e.g. diethylmalonate - in the presence of a variety of bases. Moreover, o-aminoacetophenone derivatives (XXIV : R = H, CH_3 or CH_2·Ph) failed to react intramolecularly, as follows:-



(XXIV)

The anils of phenylglyoxal[11]

Condonsation of phenylglyoxal with aniline in acetic acid solution[12] gave an anil (m.p. 145°) of phenylglyoxal. The formal similarity between the azatropone (VII) and phenylglyoxal cis-anil (XXV) aroused an interest in the anil.



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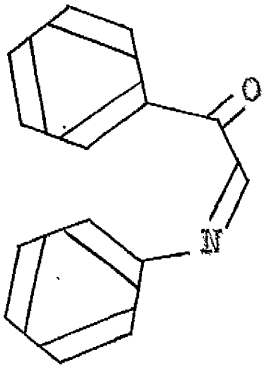

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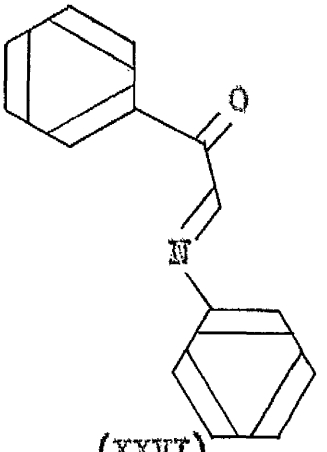
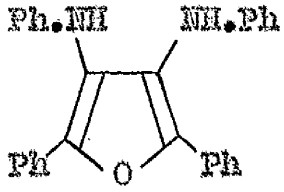


(XXVI)

N-(toluene-p-sulphonyl) phenacylaniline (IV ; R = Ph; R' = CO.Ph.) underwent a mild base-catalysed elimination to give the cis-anil (m.p. 210°) of phenylglyoxal, which was converted on a palladium catalyst into the trans-anil (XXVI; m.p. 145°). The stereochemistry of these compounds was assigned from their ultra-violet spectra. Compared with the cis-anil, the trans-anil shows a bathochromic shift (10 mμ) of the longer wave absorption band.

When treated with hydrogen on a palladium catalyst, both anils underwent an interesting reductive self-condensation to give a tetrasubstituted furan [e.g., (XXVII)] of which there are several positional isomers.



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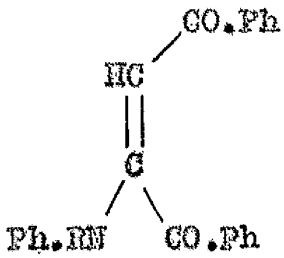

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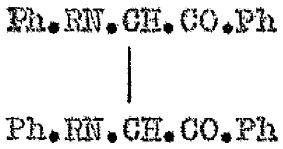

(XXIX)

Derivatives of diaminofurans are not well known and preliminary investigations of an alternative route to the isomer (XXVII) were not encouraging; when dibromobenzoylethane was allowed to react with aniline or substituted anilines, one obtained the substituted ethylene (XXVIII; R = H, CH_3 or $SO_2.C_6H_4.Me$-p) rather than the desired intermediates for furan synthesis (XXIX; R = $SO_2.C_6H_4.Me.p.$). Furthermore, (XXIX; R = H) could not be prepared from dianilinosuccinic acid.

References

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A NOVEL

ELIMINATION REACTION

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Thesis submitted to the University of Glasgow for the degree of Doctor of Philosophy.

October, 1964.

ACKNOWLEDGEMENTS

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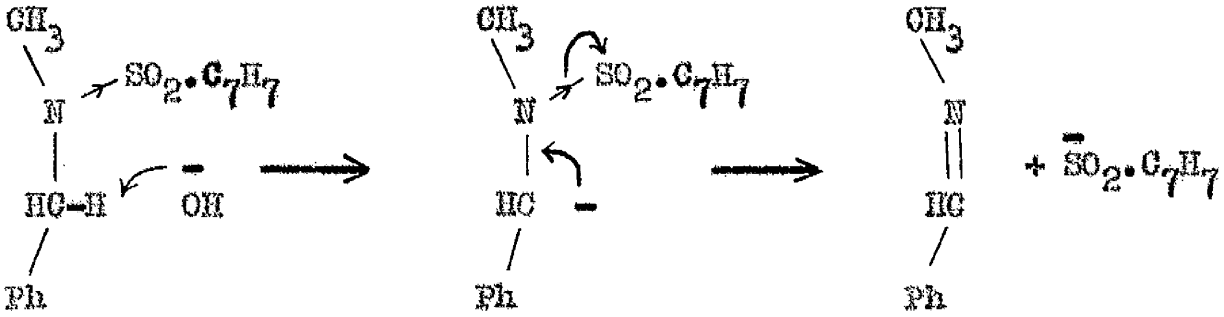
CONTENTS

I N T R O D U C T I O N

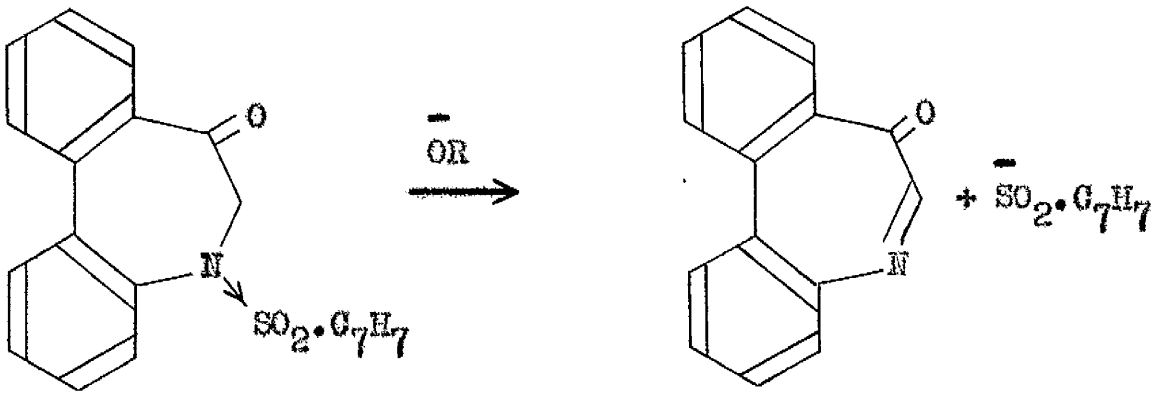
In 1926, Holmes and Ingold[1] isolated benzylidene methylimine (II) after fusing the toluene-p-sulphonamide (I) with moist potassium hydroxide:



(I) (II)

One became interested in this reaction as a means of introducing carbon-nitrogen double bonds into heterocylic rings[2]:

e.g.



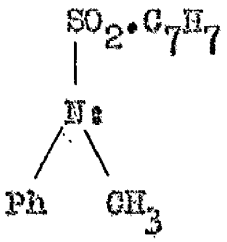
A study of the literature[3-5] suggested that a successful elimination reaction leading to anils would require mild basic conditions, and the presence of electron-withdrawing groups on the carbon atom adjacent to the nitrogen atom. It was proposed to test the validity of this forecast.

D I S C U S S I O N

PRELIMINARY INVESTIGATION OF THE

ELIMINATION REACTION

Sulphonamides (III - VIII) were prepared, and



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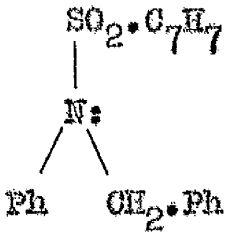

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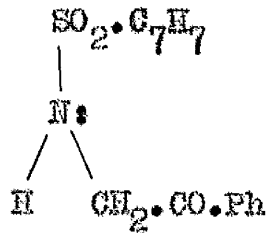

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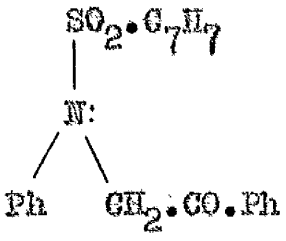

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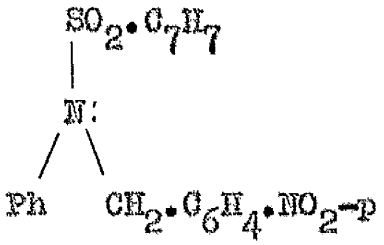

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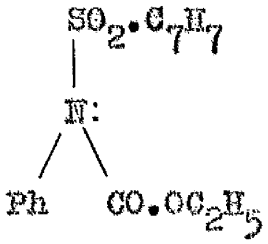


(VIII)

treated with bases under a variety of conditions[6]. The results

were as follows:-

1. N-(Toluene-p-sulphonyl) Methylaniline (III)

This compound was extremely resistant to basic attack; it was unaffected by sodium methoxide in toluene, and by freshly sublimed potassium tertiary butoxide in dimethylsulphoxide[7].

2. N-(Toluene-p-sulphonyl) Benzylaniline (IV)

The sulphonamide was recovered unchanged after treatment with sodium methoxide in toluene, under reflux. Stronger bases also failed to give an elimination reaction.

3. N-(Toluene-p-sulphonyl)-ω-Aminoacetophenone (V)

The above compound was recovered after treatment with each of the following bases:

(a) sodium methoxide in toluene

(b) sodium ethoxide in toluene

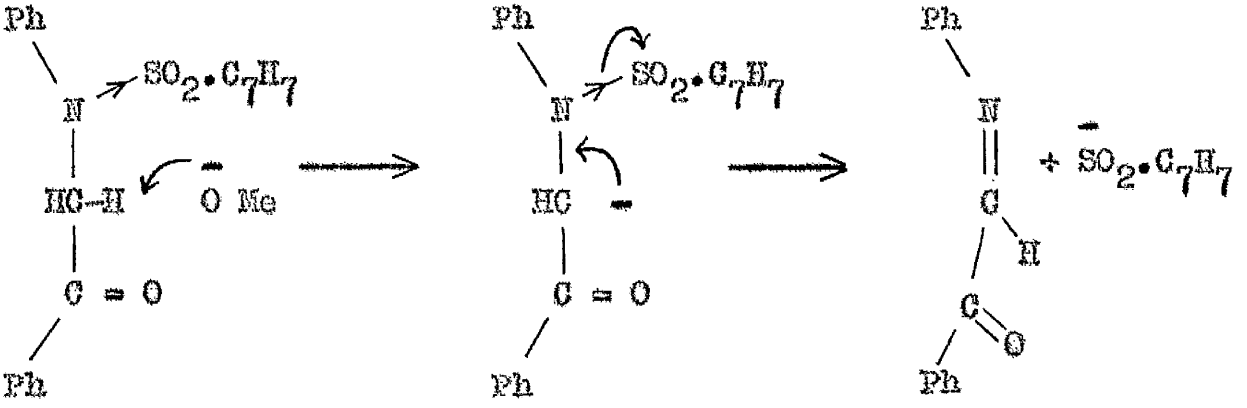
(c) potassium tertiary butoxide in dimethylsulphoxide

The sulphonamide reacted with the bases to give salts in which the negatively charged nitrogen atom shields the adjacent carbon-hydrogen linkage from basic attack[8].

4. N-(Toluene-p-sulphonyl) Phenacylaniline (VI)

Treatment of this compound with sodium methoxide in toluene at room temperature, gave phenylglyoxal mono-anil (IX) in

95% yield. The structure of the product was confirmed by elementary analysis and examination of the infra-red spectrum.



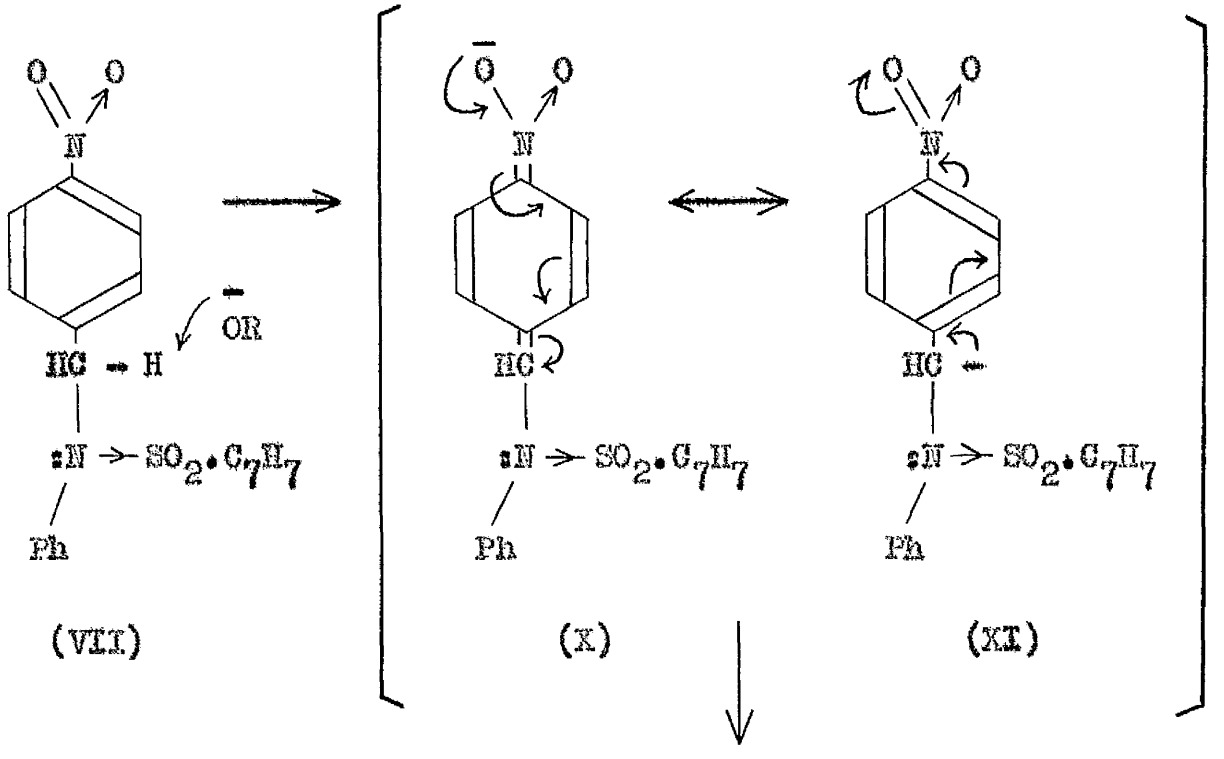
(VI) (IX)

Toluene-p-sulphinic acid was isolated from the alkaline washings.

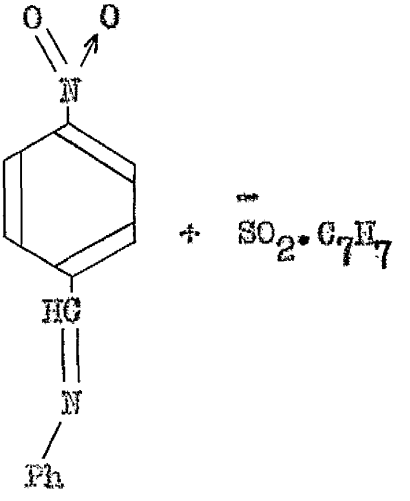
5. N-(Toluene-p-sulphonyl)-p-Nitrobenzylaniline (VII)

With sodium methoxide in toluene at room temperature, this sulphonamide gave an 84% yield of p-nitrobenzalanil (XII) which was identical with synthetic material. Evidently, the nitro group possesses sufficient electron-withdrawing power to activate the carbon-hydrogen linkage towards basic attack. Moreover, the nitro group might confer some stability on the intermediate anion by making possible resonating forms (X)

and (XI)



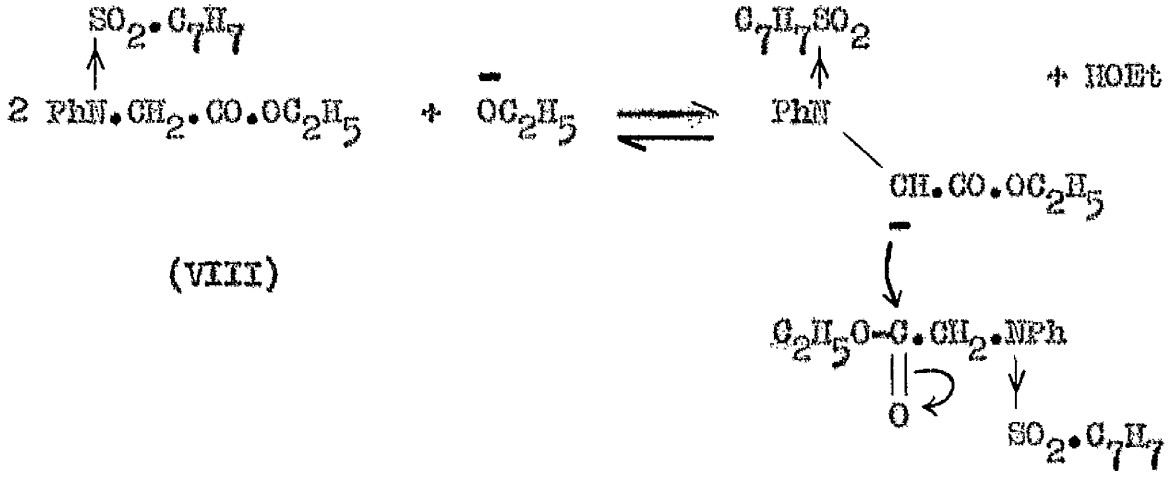
(VII) (X) (XI)



(XII)

6. N-(Toluene-p-sulphonyl) Glycine Ethyl Ester (VIII)

Treatment of the ester (under nitrogen) with sodium ethoxide in toluene gave a neutral oil (b.p. 180°/3 mm) which gave a negative colour reaction for sulphur[9], and toluene-p-sulphinic acid was isolated from the alkaline washings. Analyses and molecular weight determinations suggested a molecular formula $C_{18}H_{16}N_2O_3$. The infra-red spectrum revealed ester and carbonyl groups, and a peak at 1620 cm^{-1} which may be due to -C=N- stretching[10]. The structure (XIII) is tentatively ascribed to the product, which may have arisen from a self-condensation of (VIII), followed by elimination of toluene-p-sulphinic acid:



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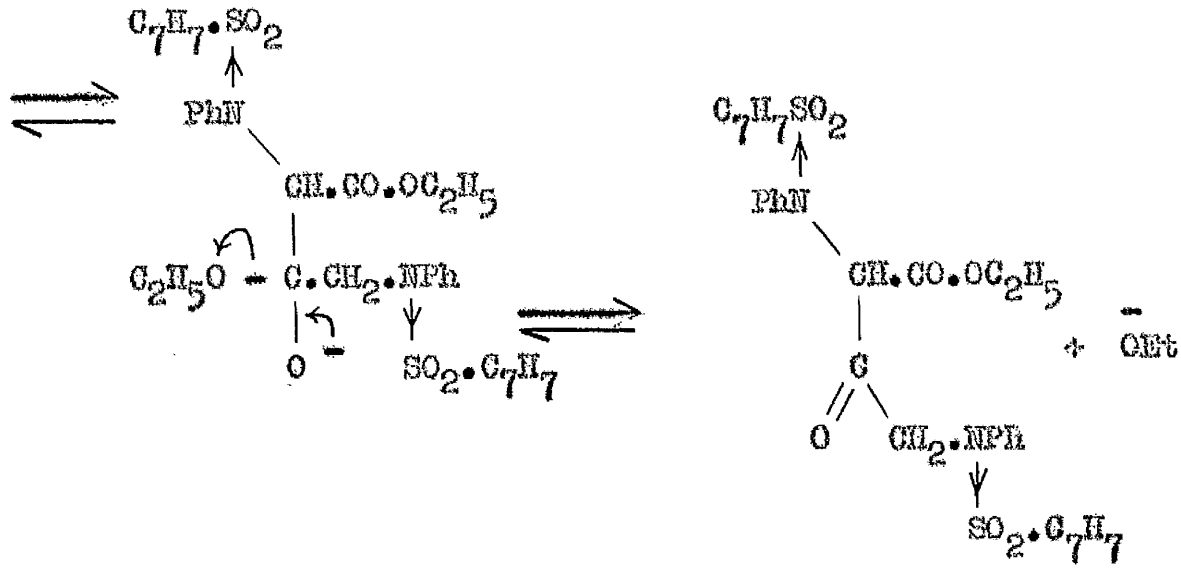

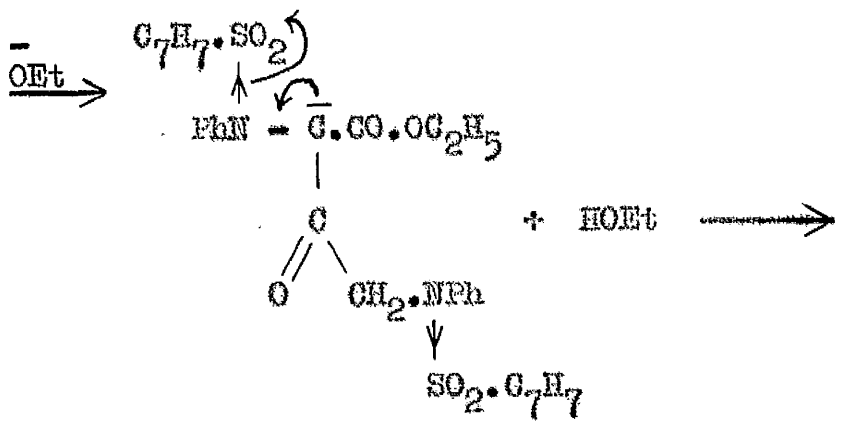

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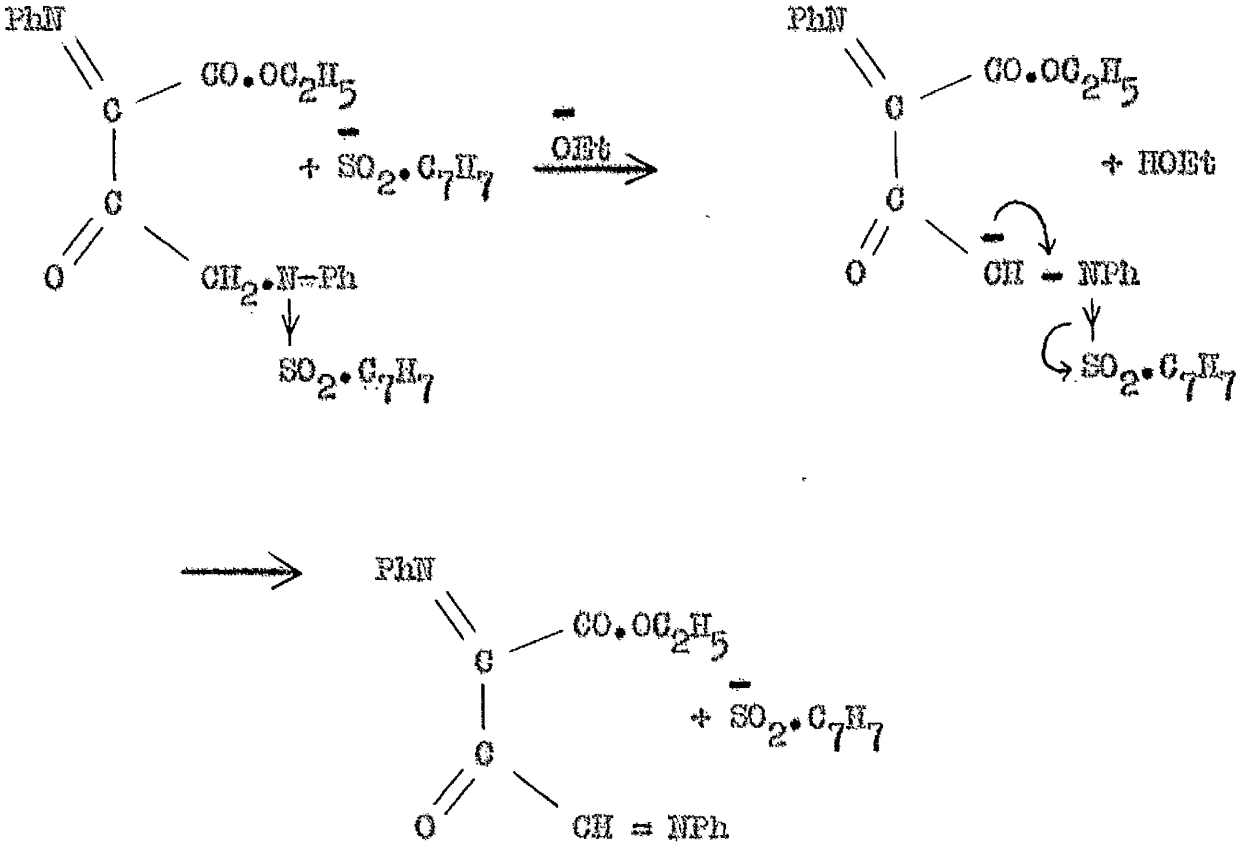
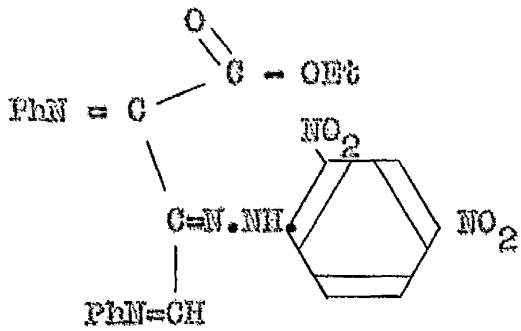


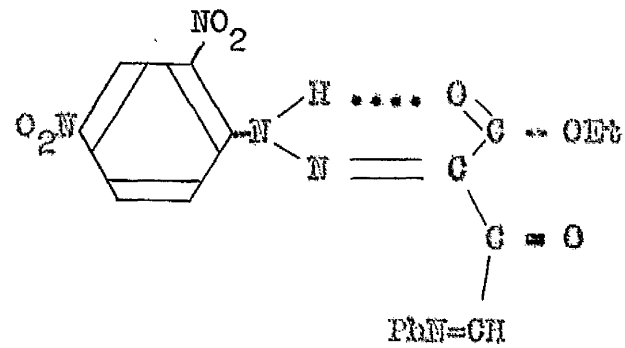
(XIII)

Treatment of (XIII) with 2,4-dinitrophenylhydrazine hydrochloride in ethanol failed to give (XIV), but a compound $C_{18}H_{15}N_5O_7$ was obtained. The infra-red spectrum revealed a carbonyl group (at 1667 cm^{-1}) and absorption bands at 3279, 1621 and 1582 cm^{-1}, but no absorption band for the ester carbonyl group in the 'normal' region (1730-1717 cm^{-1})[11].

This suggests by analogy with the spectra of α-amino-α,β-unsaturated



(XIV)



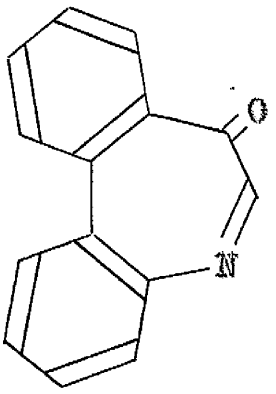
(XV)

carbonyl compounds[12], a resonance stabilised structure such as (XV).

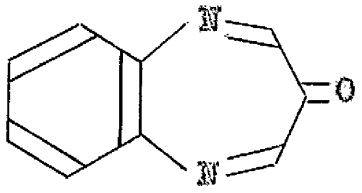
The above results suggested that the elimination reaction may be employed to introduce carbon-nitrogen double bonds into heterocyclic rings, provided one started with a toluene-p-sulphonamide containing an electron withdrawing group on the carbon atom adjacent to the nitrogen atom. It was proposed to investigate the utility of the reaction in the syntheses of

some novel heterocyclic systems:-

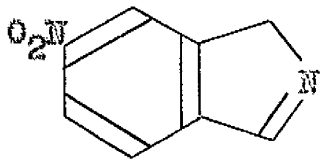
i.e.,



(XVI)



(XVII)

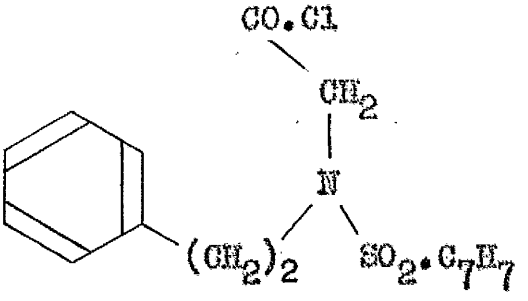


(XVIII)

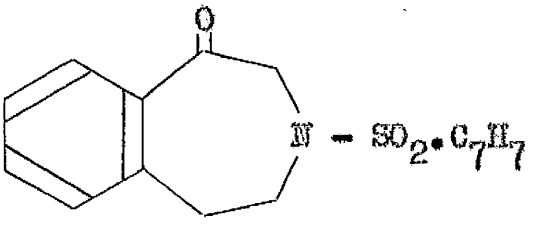
SYNTHESES INVOLVING THE ELIMINATION REACTION

1. The Synthesis of an Azatropone

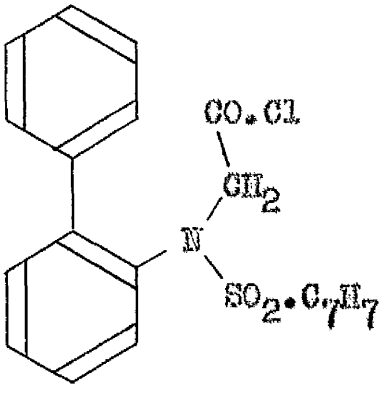
Previous work[13] has shown that Friedel-Crafts cyclisation of arylamino-acids could not be used to afford cyclic 7-membered amino-ketones, except in the case of the acid chloride (XIX) which gave the ketone (XX) - in low yield - along with an isoquinoline derivative[14]. Tertiary acid chlorides are frequently decarbonylated by treatment with aluminium chloride



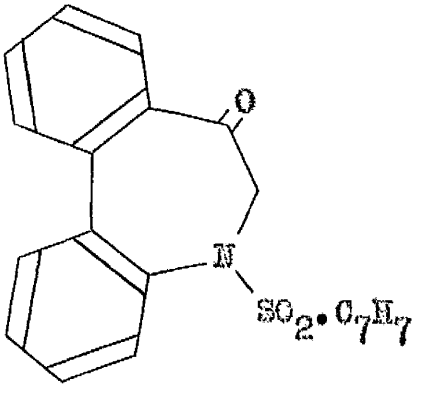
(XIX)



(XX)

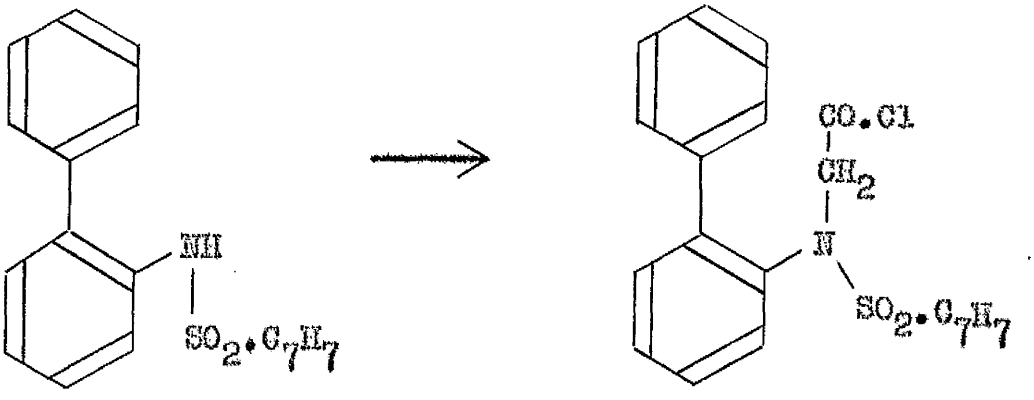


(XXI)



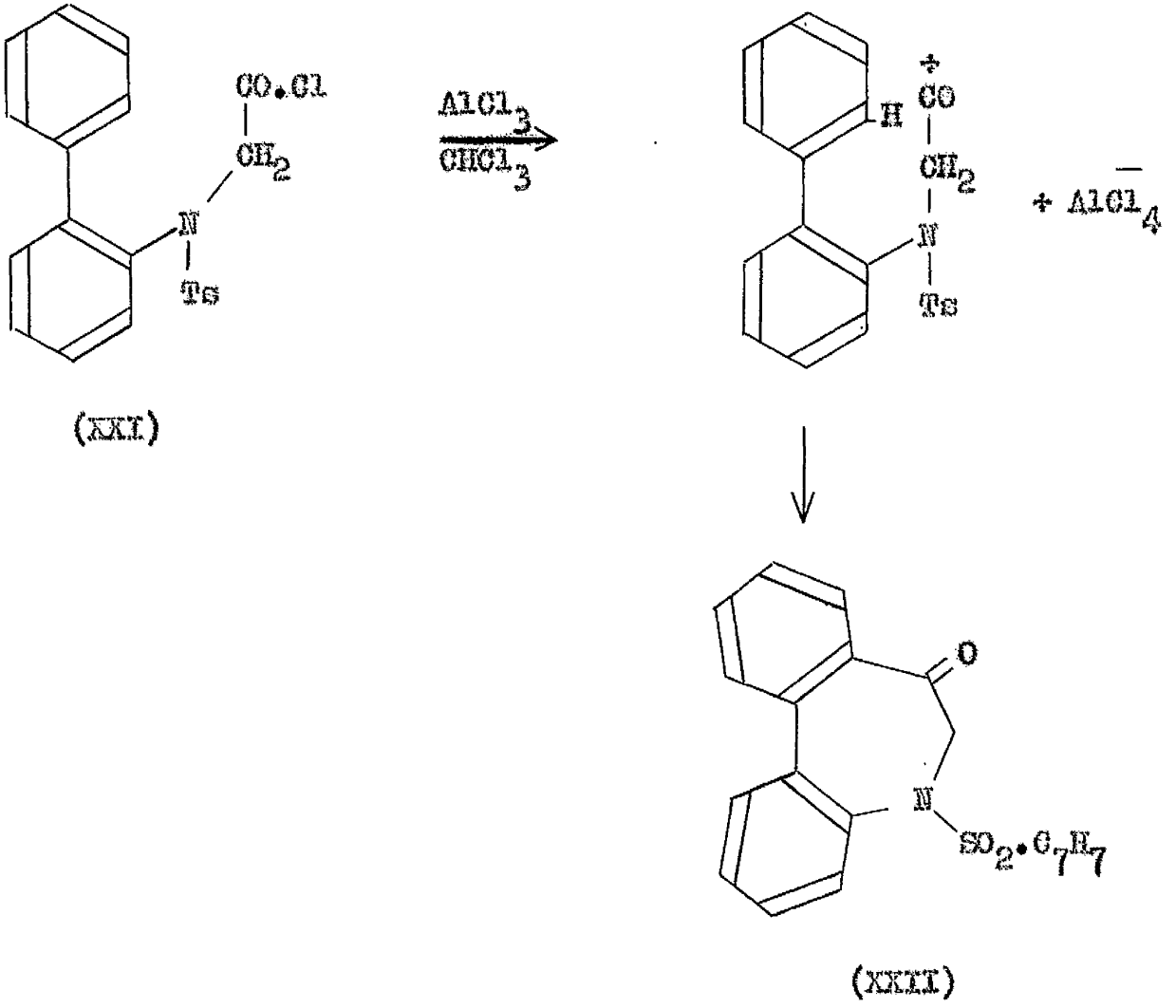
(XXII)

($R.R'.R''.C.\overset{+}{C}O. \longrightarrow R.R'.R''.C^{+} + CO.$) and it has been demonstrated that the break-down of the intermediate carbonium ion is facilitated by electron release from the substituent alkyl groups[15]. Proctor and Thomson[13] postulated an analogous mechanism for their amino-acid reaction; in this case, decarbonylation was initiated by electron release from the adjacent nitrogen atom, although one might have expected the electron-withdrawing effect of the tosyl group to have opposed it. A study of the conditions which favoured decarbonylation in these examples suggested that it may be minimised by working at low temperatures and that a ketone might be obtained as the major product in a sterically more favourable case. The acid chloride (XXI) was obtained from 2-toluene-p-sulphonamidobiphenyl by standard synthetic methods, and it gave



(XXI)

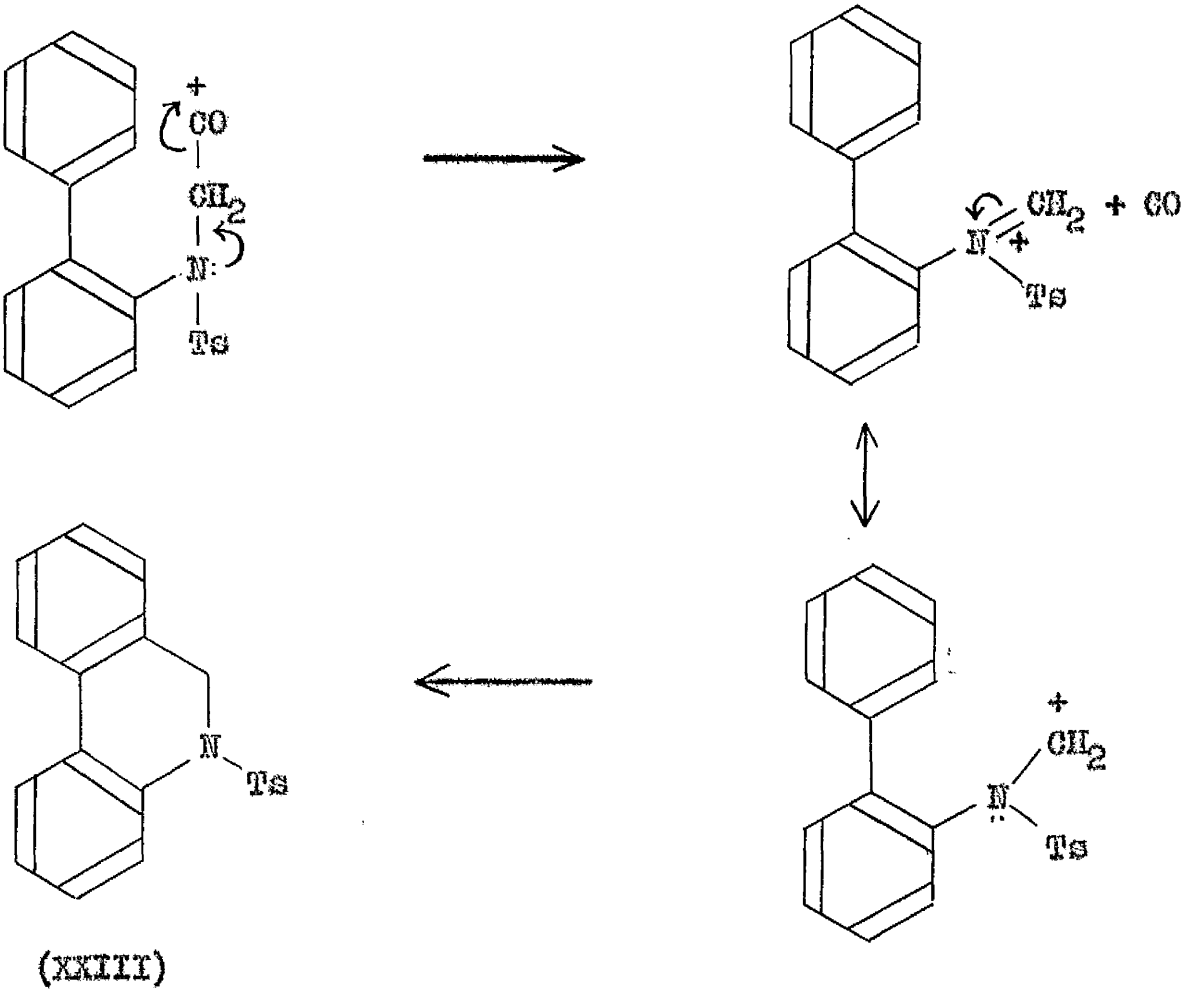
5,6-dihydro-7-oxo-5-toluene-p-sulphonyl dibenz [b.d] azepine (XXII) in almost quantitative yield when treated with aluminium chloride in chloroform at -70° to -30°[2]. The use of carbon



(XXI)

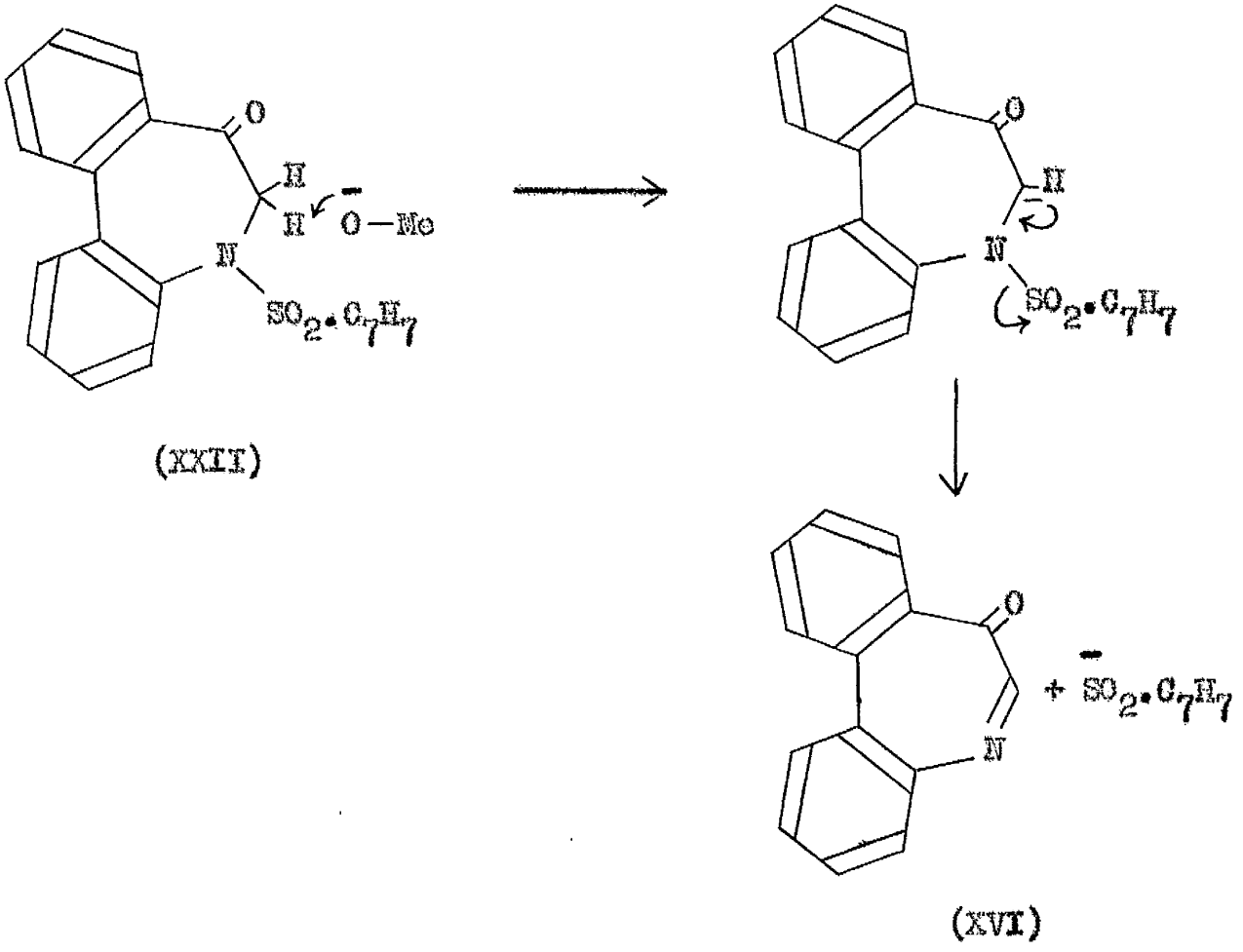
(XXII)

disulphide as solvent in this reaction gave less successful results; decarbonylation took place to some extent and a mixture of 9,10-dihydro-N-toluene-p-sulphonyl phenanthridine (XXIII) and the ketone (XXII) was obtained, the former predominating.



(XXIII)

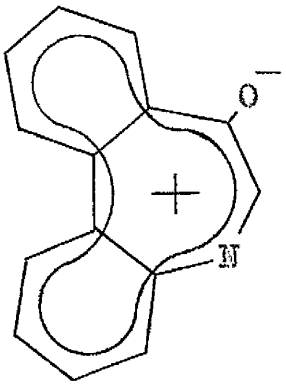
The next step in the synthesis of the azadibenzotropone (XVI)[16] was to eliminate toluene-p-sulphinic acid from the sulphonamide (XXII). This was accomplished by treatment of (XXII) - under nitrogen - with sodium methoxide in toluene, and (XVI) was obtained in 60% yield. The by-products were phenanthridone (XXIX) and a substance $C_{14}H_{11}NO_2$ of m.p. 230°.



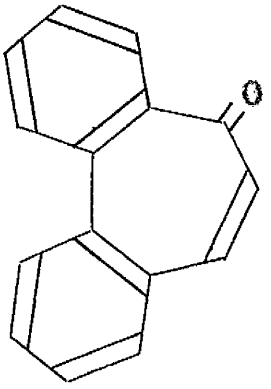
(XXII)

(XVI)

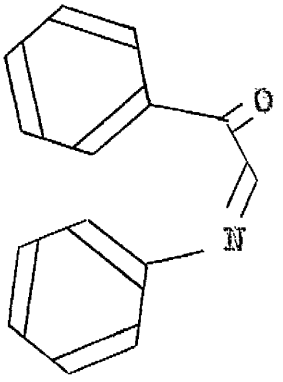
It is apparently essential that gaseous nitrogen be used in this reaction; when oxygen was bubbled through the reaction mixture, the latter compounds became major products. The structure (XVI) was assigned to the azadibenzotropone on the basis of analytical and molecular weight determinations [the molecular weight by mass-spectroscopy was 207; $C_{14}H_9NO$ requires 207]. A comparison (see Table 1) between the dibenzotropone (XXV)[17], the cis-anil of phenylglyoxal (XXVI) and the azadibenzotropone (XVI), indicates that the latter is the most polar, and in respect



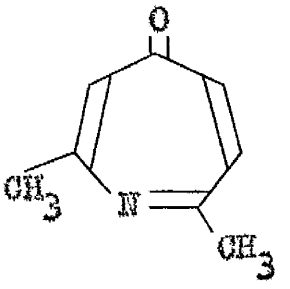
(XXIV)



(XXV)



(XXVI)



(XXVII)

of its inability to react with "carbonyl reagents" (e.g. 2,4-dinitrophenylhydrazine), more akin to tropolones[18]. It is, therefore, deduced that structures such as (XXIV) may more accurately account for some of the properties of this compound. In particular, the appearance of an infra-red carbonyl absorption band at either 1613 cm^{-1} or 1590 cm^{-1} (it is not possible to allocate the carbonyl stretching frequency with certainty) is reminiscent of tropolones[20]. A similar effect was observed recently in the case of the monocyclic azatropone (XXVII)[21], which showed an infra-red carbonyl absorption band at 1613 cm^{-1}. Unfortunately, the behaviour of the latter compound towards "carbonyl reagents" was not reported.

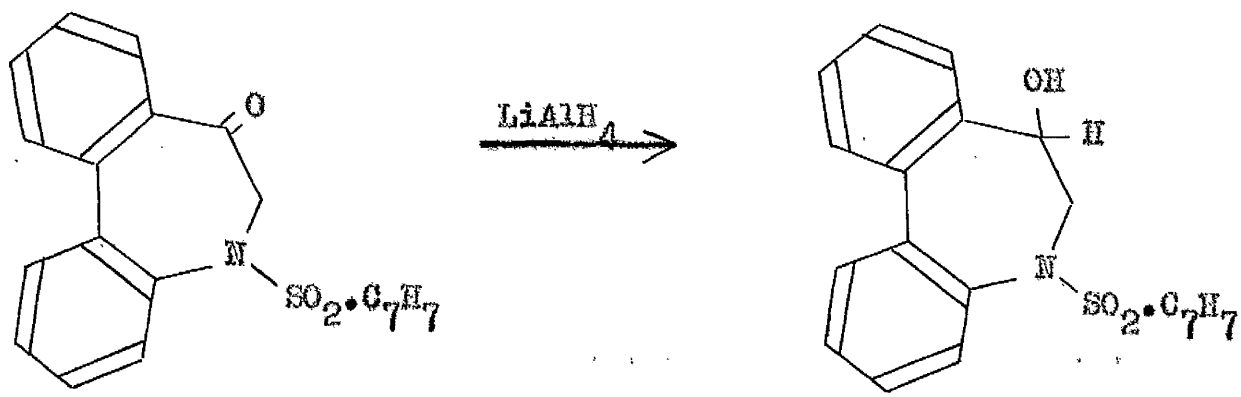
TABLE 1

Properties of Compounds (XVI), (XXV) and (XXVI)

Compound (XVI)	Compound (XXV)	Compound (XXVI)
m.p. 265°	m.p. 84°	m.p. 210°
colour: deep red (hydrochloride, violet)	colour: pale yellow	colour: yellow
ν_{max} (KCl) 1590; 1613 cm^{-1}.	ν_{max} (KBr) 1645 cm^{-1}.	ν_{max} (Nujol) 1667 cm^{-1}.
No 2,4-Dinitrophenyl-hydrazone	2,4-Dinitrophenyl-hydrazone m.p. 231°[19]	2,4-Dinitrophenyl-hydrazone m.p. 235°
Poorly soluble in organic solvents	Soluble in organic solvents	Soluble in organic solvents

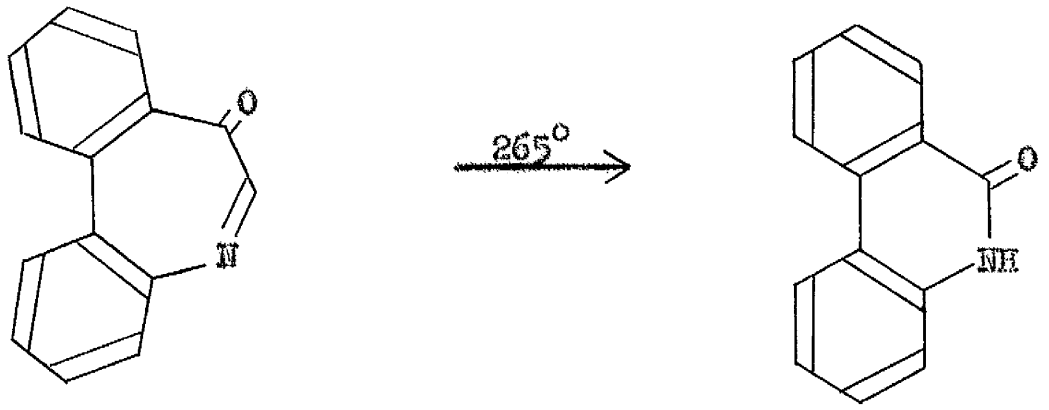
The azadibenzotropone (XVI) - like tropolone[22] - was resistant to catalytic hydrogenation at atmospheric pressure, and it was unaffected by lithium in diethylamine[23]. Moreover, whereas the ketone (XXII) was reduced to the corresponding alcohol (XXVIII) by heating with lithium aluminium hydride,

(XVI) provided phenanthridone (XXIX) by contraction of the seven-membered ring. The latter was also obtained by heating (XVI) alone, but it was impossible to demonstrate



(XXII) (XXVIII)

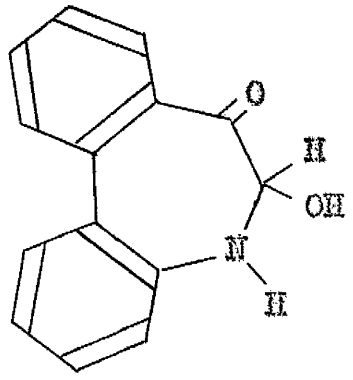
whether the reaction was monomolecular or involved a disproportionation.



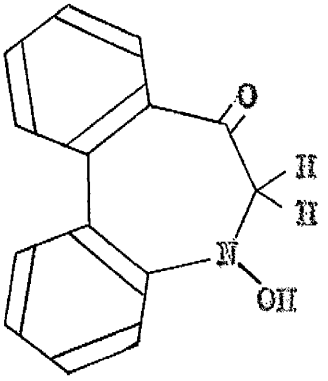
(XVI) (XXIX)

Phenanthridone (XXIX) was the only product isolated when (XVI) was treated with zinc dust and 'Analar' glacial acetic acid, but when dilute acetic acid was employed, the product was a substance $C_{14}H_{11}NO_2$ of m.p. 230°. This was identical with a compound obtained by treating the ketone (XXII) with sodium methoxide. In a recent report[2], the structure (XXX) was assigned to the product, but structure (XXXI) is now preferred. The compound did not react with acetic anhydride, sodium borohydride or toluene-p-sulphonyl chloride but gave phenanthridone (XXIX) when heated

with palladised-charcoal in boiling trichlorobenzene[24].



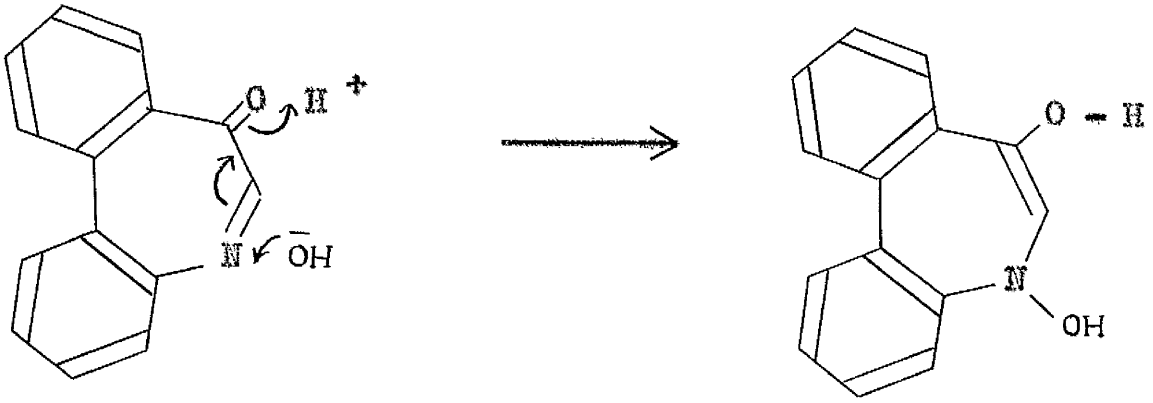
(XXX)



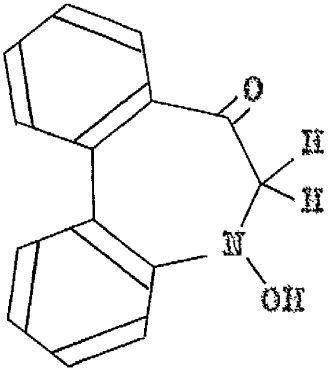
(XXXI)

The infra-red spectrum was consistent with structure (XXXI); although little information is available on substituted hydroxylamines, the peaks at 3220 cm^{-1}, 1484 cm^{-1} and 1136 cm^{-1} correspond with those reported for an isopropylhydroxylamine[25]. Moreover, a positive ferrous hydroxide colour test for hydroxylamines[26] was obtained, and the nuclear magnetic resonance spectrum showed 8 aromatic protons ($\tau = 2.17 - 3.08$), one hydroxyl proton ($\tau = 5.35$) and 2 methylene protons (singlet: $\tau = 6.99$). Usually, acid hydrolysis of Schiff's Bases proceeds by proton

attack on the nitrogen atom[27]; in this case proton attack must have taken place on the negative oxygen atom of the carbonyl



(XVI)

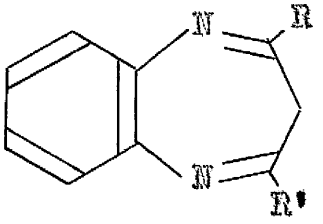


(XXXI)

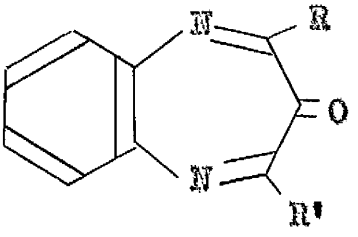
function - as one would expect if structure (XXIV) is important.

2. Attempted Synthesis of a Diazabenzotropone

Although many benzo [b]-1,5-diazepines (e.g. XXXII) are known,[28-34] the 3-oxo derivatives have never been reported. Oxidation of the methylene group at position 3 of benzo-[b]-1,5-diazepines (e.g. XXXII; R = R' = CH_3) would appear to be the most direct route to diazabenzotropones such as (XXXIII). This approach has, however, proved unsuccessful[35].



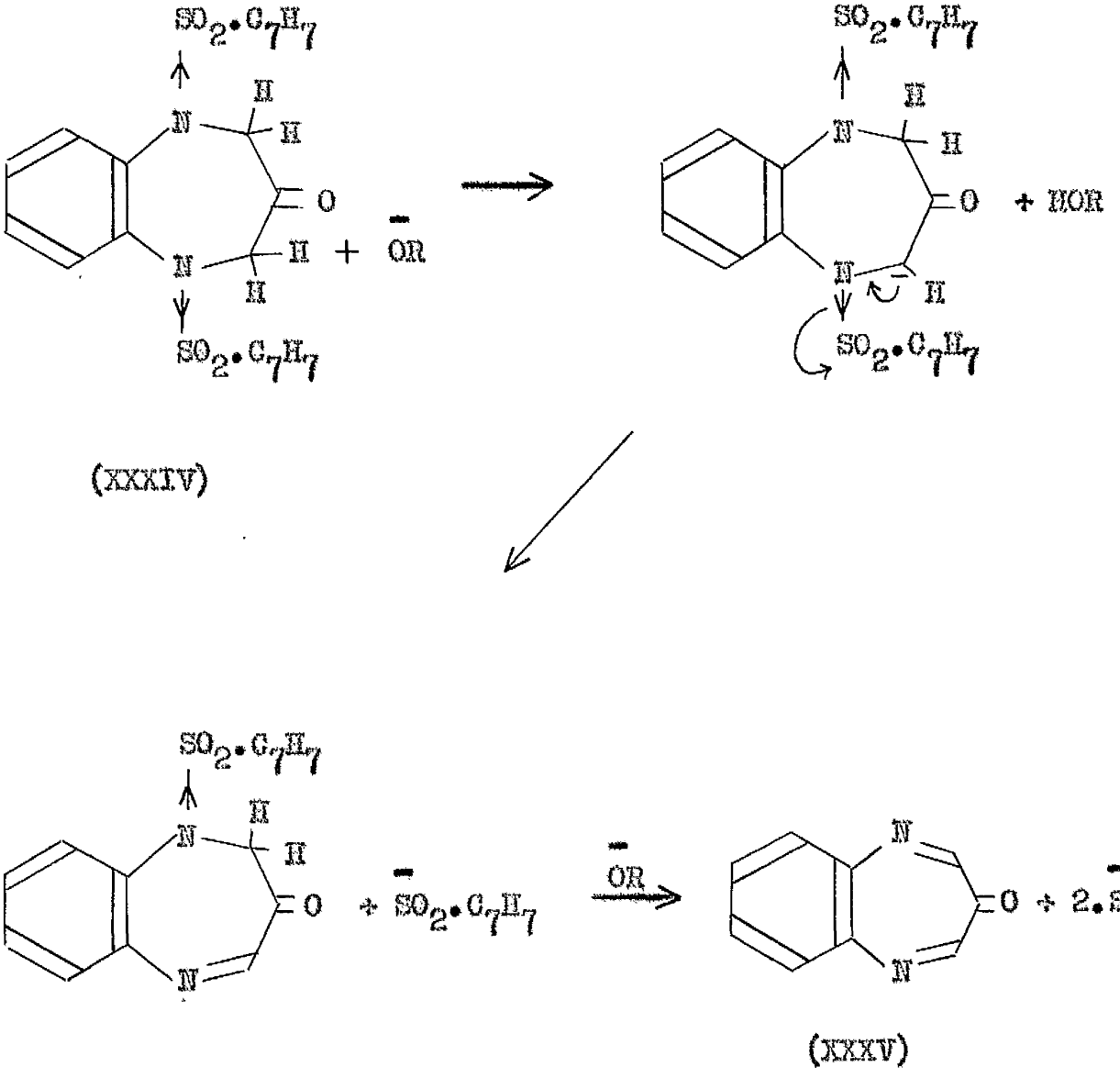
(XXXII)



(XXXIII)

The preliminary studies (vide supra) suggested that the ketone (XXXIV) might undergo a mild base-catalysed elimination

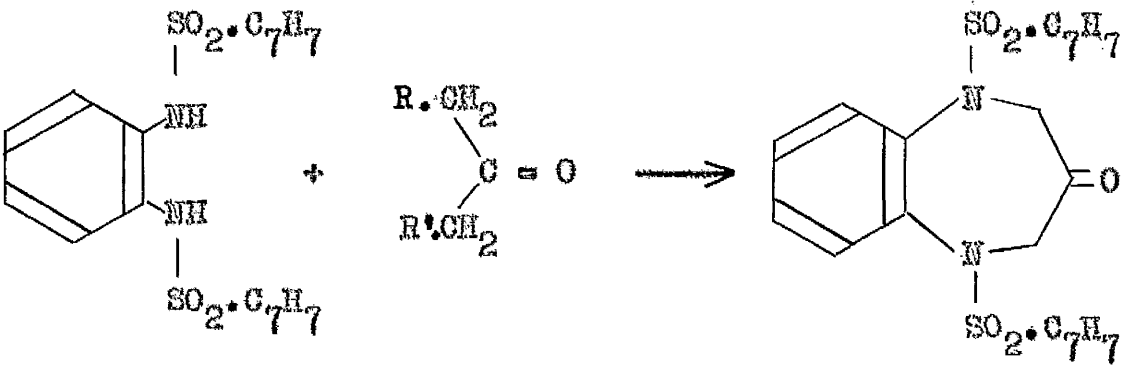
to give the diazabenzotropone (XXXV) as follows:-



(XXXIV)

(XXXV)

1,3-Dibromoacetone (XXXVII; R= R'= Br) reacted with the potassium salt of N,N'-(ditoluene-p-sulphonyl)-o-phenylene diamine (XXXVI) in benzene, to give the ketone (XXXIV) in good yield. The structure (XXXIV) was confirmed by the analysis and the infra-red spectrum. Moreover, the compound formed a 2,4-dinitrophenylhydrazone whose analysis was correct.



(XXXVI) (XXXVII) (XXXIV)

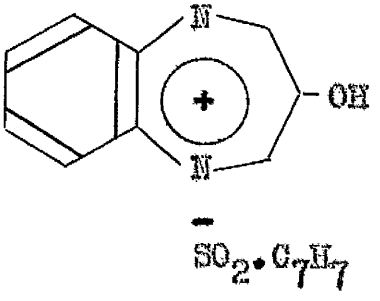
Treatment of the ketone (XXXIV) with sodium methoxide in toluene under nitrogen gave a deep red compound $C_{16}H_{14}N_2O_3S$ (of m.p. 242°). This was also obtained by heating the ketone

(XXXIV) with anhydrous sodium carbonate in toluene, and by reacting 1,3-dibromoacetone with the toluene-p-sulphonamide (XXXVI) in the presence of anhydrous sodium carbonate. The red compound was recovered after treatment with concentrated hydrochloric acid, and it was unaffected by potassium tertiary butoxide in dimethylsulphoxide[7]. The infra-red spectrum revealed a hydroxyl group and toluene-p-sulphonyl function, but no carbonyl group. The nuclear magnetic resonance spectrum revealed 10 aromatic protons (τ = 1.5 - 3.6) and 3 methyl protons (singlet τ = 7.65).

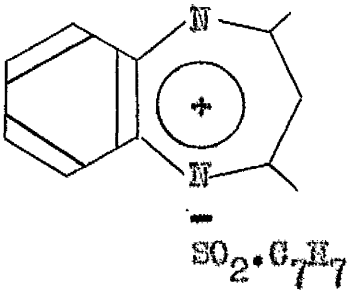
Treatment of 2,4-dimethyl-benzo [b]-1,5-diazepine (XXXII; R = R' = CH_3) with toluene-p-sulphonyl chloride in pyridine gave a similar red compound (of m.p. > 360°), which was too poorly soluble in organic solvent to obtain a nuclear magnetic resonance spectrum. The physical properties of the two compounds are compared in Table 2.

TABLE 2

Compound m.p. 242°	Compound m.p. > 360°
Colour: deep red	Colour: deep red
Poorly soluble in organic solvents	Insoluble in most organic solvents
Elutes from an alumina column in chloroform/methanol (99 : 1)	Elutes from an alumina column in chloroform/methanol (99 : 1)
ν_{max} (in nujol) 3390, 1608, 1370, 1156 cm^{-1}	ν_{max} (in nujol) 1600, 1379, 1160 cm^{-1}



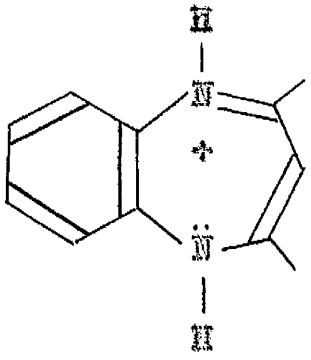
(XXXVIII)



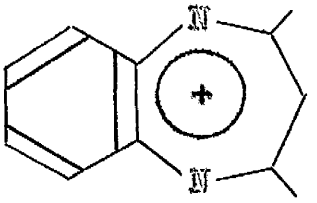
(XXXIX)

The polar nature of the compounds suggest that they may be diazabenzotropylium salts (XXXVIII) and (XXXIX).

Previous attempts[36] to prepare diazabenzotropylium salts led to violet or deep-red compounds believed to be diazepinium salts (e.g. XL). Similarly, treatment of the diazepine



X^-



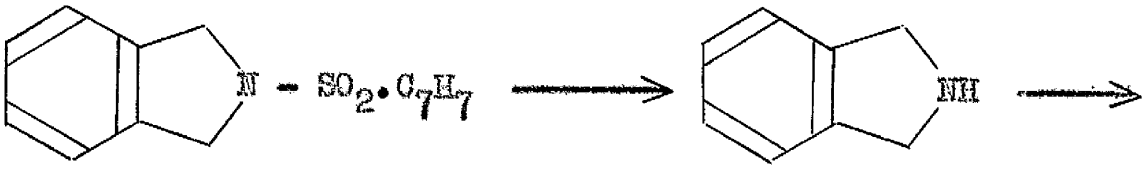
ClO_4^-

(XL) (XLI)

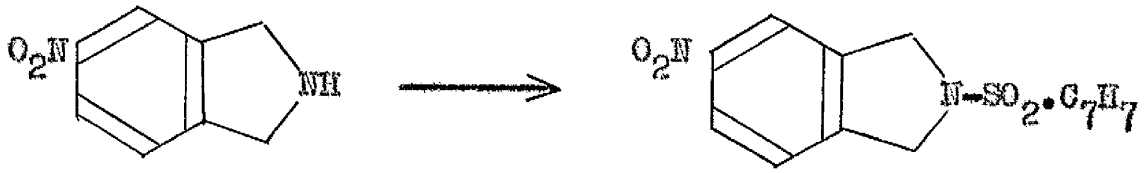
(XXXII; $R = R' = CH_3$) with triphenylmethyl perchlorate in methylene chloride[37] gave a violet perchlorate. Conclusive spectral evidence for either of the structures (XL; $X = Cl.O_4$) or (XLI) could not be obtained because the violet compound was a hydrate and too poorly soluble in organic solvents.

3. Attempted Synthesis of 5-Nitropseudoisoindole

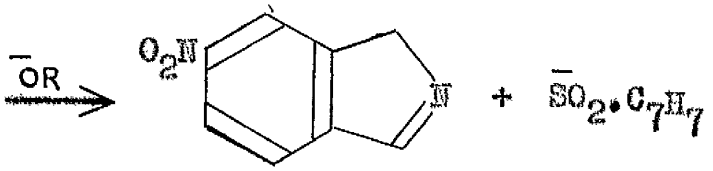
Attempted Synthesis of 5-ously related thet, whilst N-(toluene-p-sulphonyl) benzyl aniline (IV) was unaffected by treatment with bases under mild conditions, N-(toluene-p-sulphonyl)-p-nitro benzyl aniline (VII) gave the anil (XII) in high yield. This suggested, by analogy, the following route to 5-nitropseudoisoindole (XLVI):-



(XLII) (XLIII)



(XLIV) (XLV)



(XLVI)

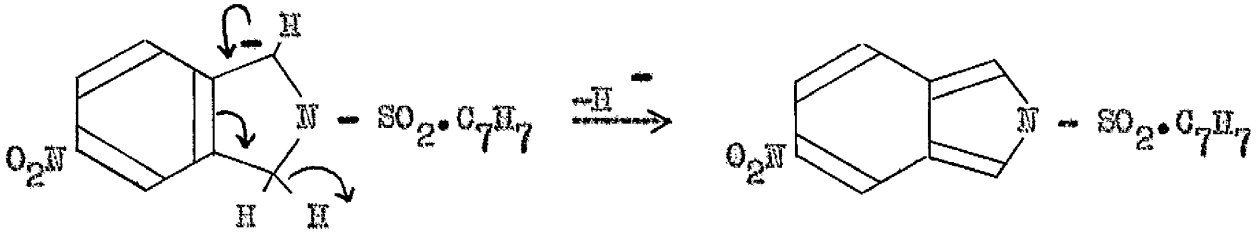
N-(toluene-p-sulphonyl) dihydroisoindole (XLII) was prepared by a literature method[38]. This compound, as expected, was unaffected by potassium tertiary butoxide in toluene. When, however, it was shaken with the base in dimethyl sulphoxide, the solution turned an inky blue colour. Chromatography of the product on alumina gave, in addition to the starting material, a small amount of a deep-blue solid (m.p. 285 - 295°) which was extremely insoluble in organic solvents. The infra-red spectrum suggested that the pigment was a sulphonamide and the elemental analyses confirmed the presence of sulphur and nitrogen.

Acid hydrolysis of the sulphonamide (XLII) gave dihydroisoindole (XLIII) which was nitrated according to a literature method[39] to give 5-nitro-dihydroisoindole (XLIV). Tosylation of the latter gave (XLV) in good yield.

Treatment of (XLV) with sodium methoxide in toluene gave a deep-blue pigment (m.p. > 360°) which was too poorly soluble in most solvents to be purified by crystallisation. Molecular weight and nuclear magnetic resonance data could not be obtained, but the elementary analyses showed the material to contain both nitrogen and sulphur. The infra-red spectrum revealed

an absorption band at 3390 cm^{-1} - of similar shape to the N-H band in the spectrum of (XLIII) - and peaks at 1348 and 1149 cm^{-1} which are characteristic of sulphonamides[40].

Although (XLV) reacts more readily than (XLII) with bases, it appears that the elimination reaction did not take place. This may be explained should the anion (XLVII) re-arrange with extrusion of a hydride ion and formation of an unstable N-substituted isoindole (XLVIII):-

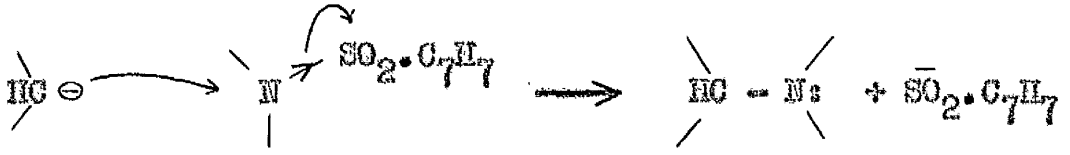


(XLVII) (XLVIII)

Since Wittig and Ludwig[41] also obtained blue substances when they attempted to prepare N-substituted isoindoles, further work to elucidate the structures of the pigments would be of interest.

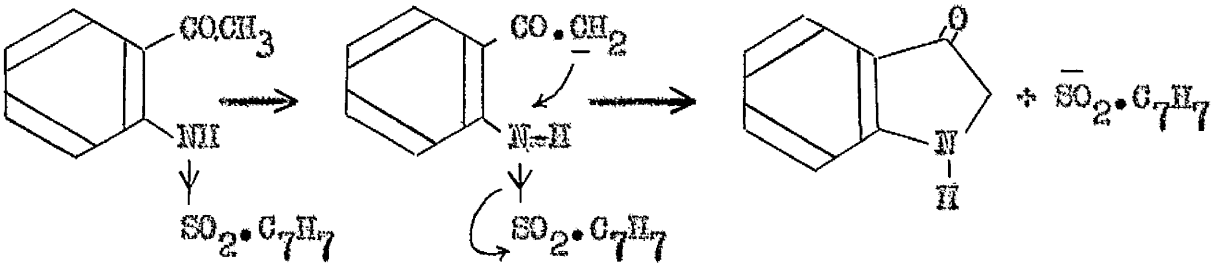
INVESTIGATION OF THE ELIMINATION REACTION AS A MEANS OF FORMING NEW CARBON-NITROGEN SINGLE BONDS

In addition to providing carbon-nitrogen double bonds, the base-catalysed elimination reaction is theoretically applicable to the formation of carbon-nitrogen single bonds:



The reaction may proceed intermolecularly as shown above, or intramolecularly to give heterocyclic compounds:

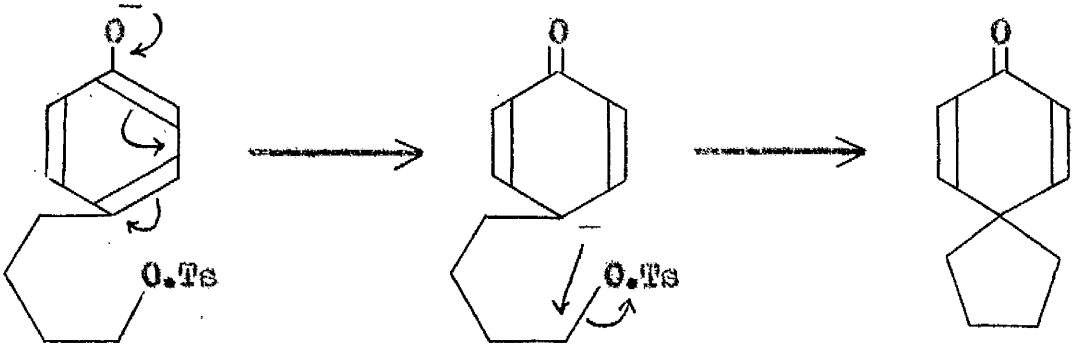
e.g.,



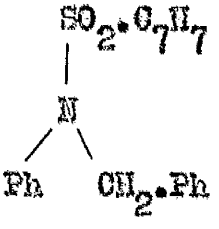
(XLIX) (L)

Carboxylic compounds have been obtained by a similar process which introduced new carbon-carbon single bonds:[42, 43]

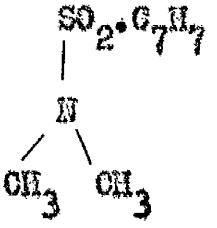
e.g.,



A preliminary investigation of the intermolecular reaction was unpromising: the sulphonamides (IV) and (LI) were recovered after treatment with anion-forming compounds (i.e., cyclohexanone and diethylmalonate) in the presence of a variety of bases. Hence, it was decided to investigate the intra-



(IV)



(LI)

molecular reaction, which may be favoured by steric factors. The results were as follows:-

1. N-(Toluene-p-sulphonyl)-o-Aminoacetophenone (XLIX)

The following conditions had no effect on (XLIX):-

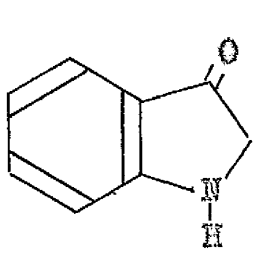
(a) Treatment with sodium methoxide in toluene at 20°.

(b) Heating with potassium tertiary butoxide in toluene, under reflux.

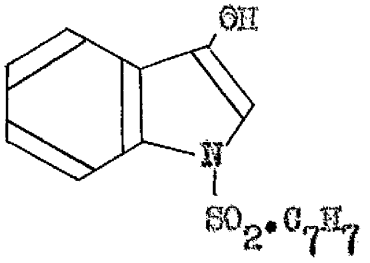
(c) Treatment with potassium tertiary butoxide in dimethylsulphoxide.

Heating (XLIX) with sodium hydroxide in ethylene glycol under reflux also failed to bring about an intramolecular reaction, but gave a compound $C_{15}H_{15}NO_2S$ (of m.p. 127°). This was soluble in dilute aqueous sodium hydroxide, but failed to give a colour reaction with ferric chloride[44]. Moreover, it was unaffected by acetic anhydride in pyridine. The infra-red spectrum revealed an olefinic function and an amino group, but no carbonyl group. The evidence excludes such structures as (L) and (LII), but suggested a structure (LIII). The nuclear

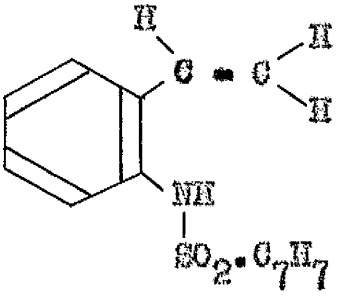
magnetic resonance spectrum revealed 8 aromatic protons



(L)



(LII)

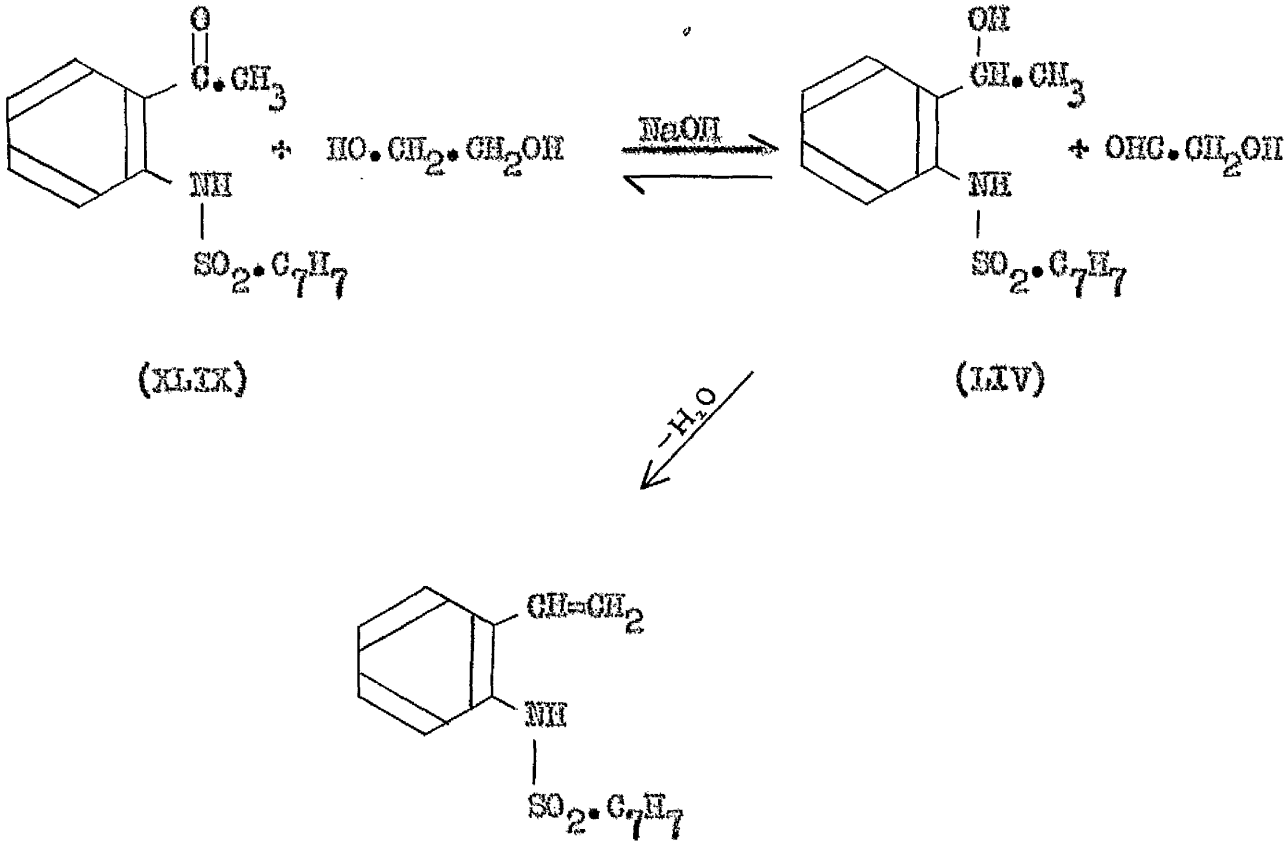


(LIII)

(τ = 2.25 - 2.8), 3 methyl protons (singlet τ = 7.64) and 3 vinyl protons. The latter gave a spectrum similar to styrene[45], with three symmetrically split quartets centred at values of τ = 3.49, 4.5 and 4.82, and with approximate splittings of 18, 12 and 3 c.p.s., corresponding to trans, cis and geminal couplings respectively, within the vinyl function. The sulphonamido hydrogen atom was not evident from the spectrum, but it may give a peak at a τ value less than zero.

The compound (LIII) may have arisen from a Meerwein-Pondorf type reduction[46], followed by dehydration of the resultant

alcohol (LIV) during the work-up:

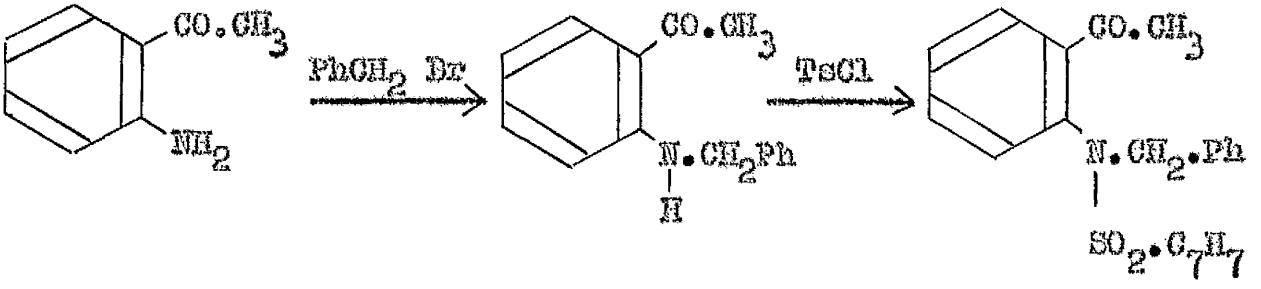


(XLIX) (LIV)

(LIII)

2. N-(Toluene-p-sulphonyl)-o-Benzylaminoacetophenone (LVII)

The above compound was prepared by standard procedures, as shown overleaf:



(LV) (LVI) (LVII)

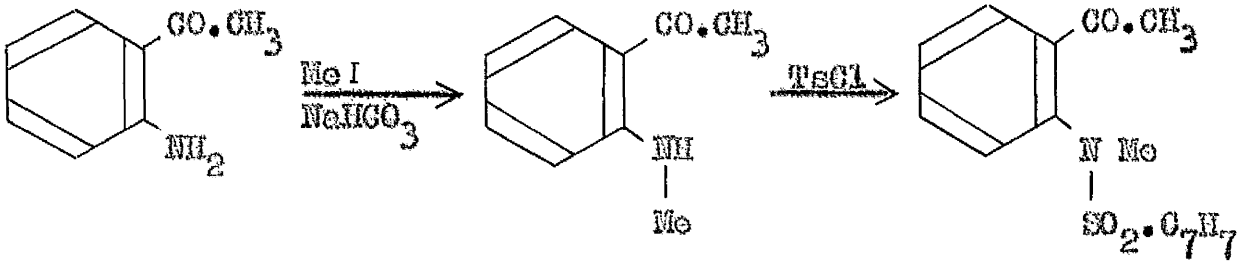
The structure (LVII) was confirmed by the elemental analysis and the infra-red spectrum. The sulphonamide was recovered after treatment with the following bases:-

1. Sodium methoxide in toluene.
2. Potassium tertiary butoxide in dimethylsulphoxide.
3. Sodium hydroxide in ethylene glycol, under reflux.

3. N-(Toluene-p-sulphonyl)-o-Methylaminoacetophenone (LIX)

Although the compound (LIX) was obtained as shown overleaf the yield was too low to permit a study of the intramolecular reaction. This led to an investigation of an alternative

route to (LIX).



(LV) (LVIII) (LIX)

An interesting method of alkylating phenols has recently been reported[47]; it involves absorption of the phenol on to a basic ion-exchange resin, followed by addition of excess alkyl bromide or iodide. An analogous reaction was envisaged for alkylating toluene-p-sulphonamides, and it was proposed to carry out some model experiments with N-(toluene-p-sulphonyl) aniline. The latter compound failed to react with ethyl bromide, bromoacetal and mono-bromoacetone, but when methyl iodide was employed the reaction reached completion after one week, and N-(toluene-p-sulphonyl) methyl aniline was obtained in almost quantitative yield - this is presumably due to the lower energy required to activate the process R.I $\longrightarrow$ R^+

$+ I^-$ compared with HBr $\longrightarrow$ $R^+ + Br^-$. Treatment of N-(toluene-p-sulphonyl)-o-aminoacetophenone (XLIX) on the resin with methyl iodide, gave N-(toluene-p-sulphonyl)-o-methylaminoacetophenone (LIX) in 90% yield.

The toluene-p-sulphonamide (LIX) was recovered after treatment with the following bases:-

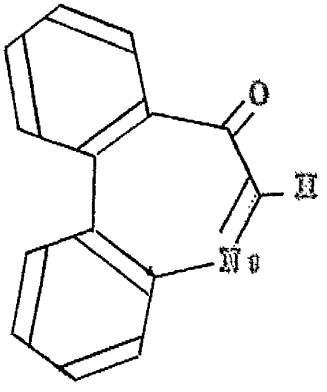
1. Sodium methoxide in toluene.

2. Potassium tertiary butoxide in dimethylsulphoxide.

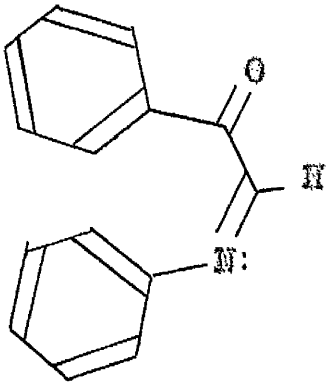
When (LIX) was heated with sodium hydroxide in ethylene glycol, it was recovered in 35% yield, but no compound analogous to (LIII) was obtained.

THE ANILS OF PHENYL GLYOXAL

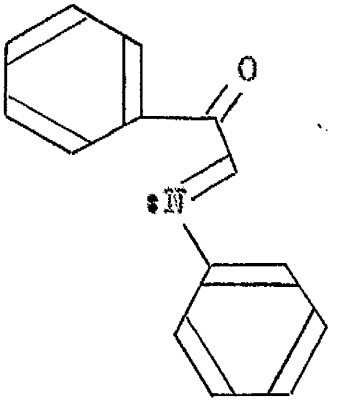
Base-catalysed elimination of toluene-p-sulphinic acid from N-(toluene-p-sulphonyl) phenacyl aniline (VI) gave an anil (m.p. 210°) of phenyl glyoxal. The formal similarity between the azatropone (XVI) and the cis-anil (LX) of phenyl glyoxal, led to a stereochemical study of the anil[48].



(XVI)



(LX)



(LXI)

There is only one reference in the literature to the anil of phenyl glyoxal[49]; but condensation of phenyl glyoxal with aniline in glacial acetic acid was found to give very erratic results; thin layer chromatography[50] showed the presence of at least five yellow products, two of which were isolated.

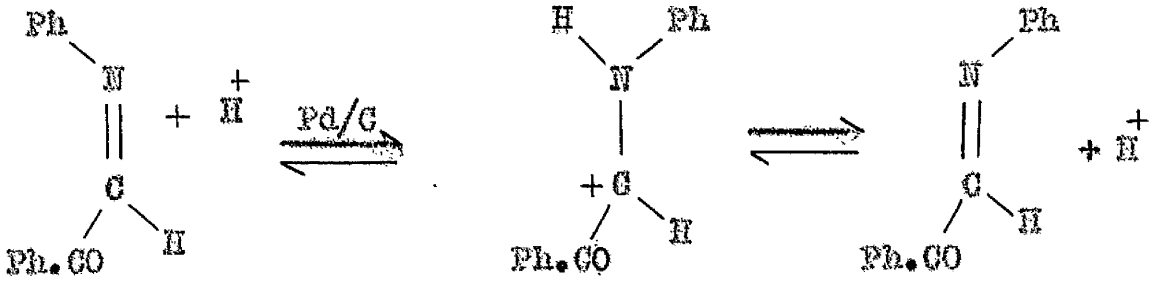
The analysis, molecular weight and infra-red spectrum of one of these (m.p. 70°) suggests that it is a dimer of the anil. The other (m.p. 145°) appears to be isomeric with the anil from the elimination reaction; Yates[49] gives its m.p. as 164°. A comparison of the anils is as follows:-

Anil from the elimination reaction	Anil from the condensation reaction
m.p. 210°	m.p. 145°
ν_{max} 1666, 1600 cm^{-1}	ν_{max} 1666, 1590 cm^{-1}
λ_{max} 207, 250 m μ	λ_{max} 207, 260 m μ
(ε: 13,920; 13,800)	(ε: 22,360; 13,800)

Since the conformation of N-(toluene-p-sulphonyl) phenacyl aniline (VI) was uncertain, it was impossible to predict whether the anil from the elimination reaction would be the cis or the trans isomer[51]. It was possible, nevertheless, to assign configurations to the anils by comparing their ultra-violet spectra[52]; although the spectra are similar in shape and general regions of absorption, the trans-anil

(m.p. 145°) shows a bathochromic shift (10 mμ) of the longer wavelength absorption band.

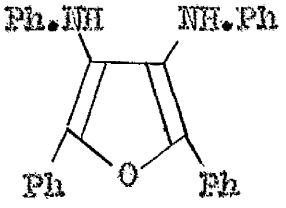
The cis-anil (m.p. 210°) was converted quantitatively into the trans-anil by treatment with an acid-washed palladium catalyst[53]:



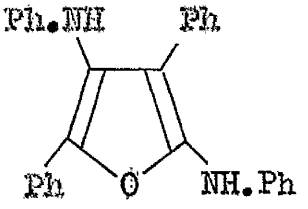
Other attempts to isomerise the anils failed: both were unaffected by ultra-violet irradiation; the trans-anil decomposed when it was heated above 145°.

Attempts to confirm the structures of the anils by reduction to phenacyl aniline proved unsuccessful: both zinc in dilute acetic acid and hydrogen on a palladium catalyst gave a compound (m.p. 187°) whose infra-red spectrum showed an amino group and an ether linkage, but neither carbonyl nor hydroxyl functions. This compound was originally thought

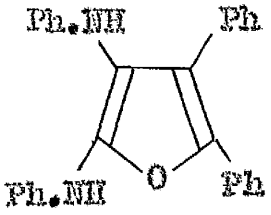
to be a 1,4-oxazine (LXV)[54], but is now considered to be a tetrasubstituted furan - the evidence is insufficient to differentiate between the positional isomers (LXII), (LXIII) and (LXIV) - for the following reasons: analytical and mass spectroscopic data gave a molecular formula $C_{28}H_{22}N_2O$; the nuclear magnetic resonance spectrum revealed twenty aromatic protons (τ = 2-3.2) and two amino protons (singlet τ = 5.65). The compound (m.p. 187°) was remarkably stable to acid



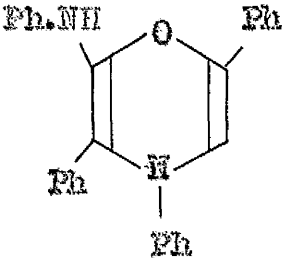
(LXII)



(LXIII)



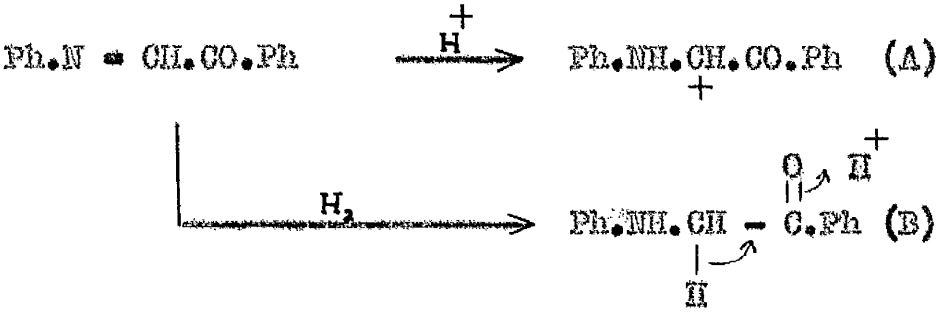
(LXIV)



(LXV)

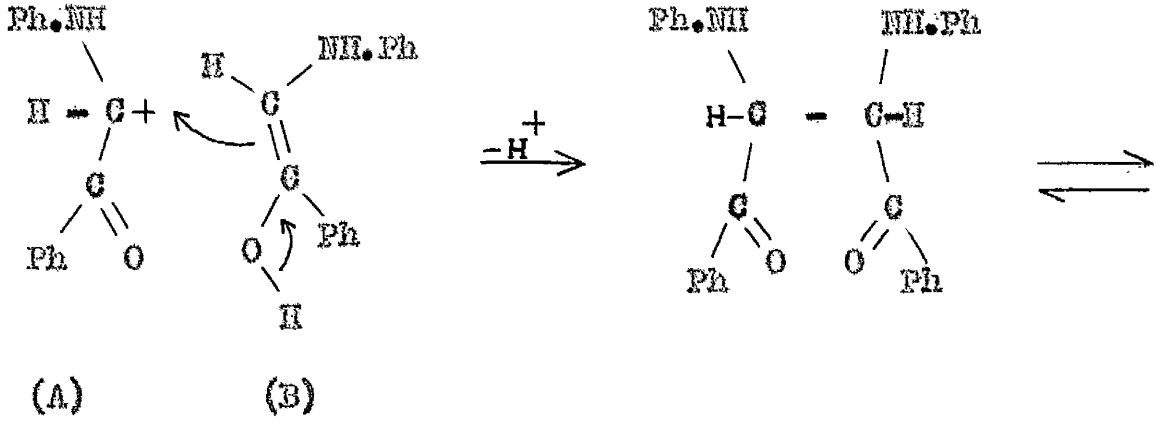
and alkalis, and it was unaffected by heating with alcoholic ammonia at 140°. Moreover, it failed to react with toluene-p-sulphonyl chloride, methyl iodide or acetic anhydride - possibly because of steric factors.

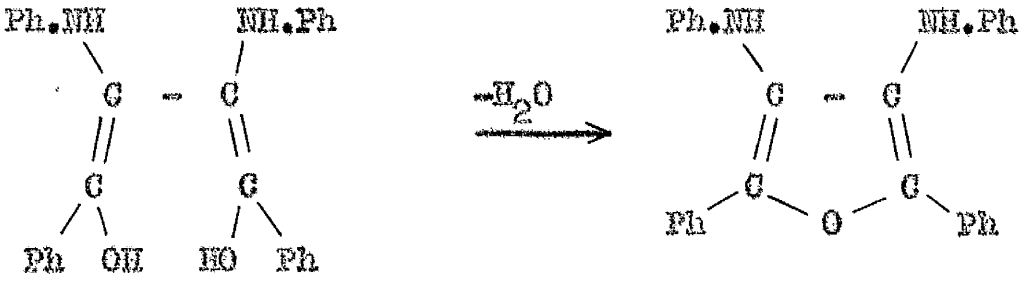
Reductive self-condensation of the anils of phenyl glyoxal may give tetrasubstituted furans, as follows:-



The carbonium ion (A) may then add to either end of the double bond in (B) as follows:

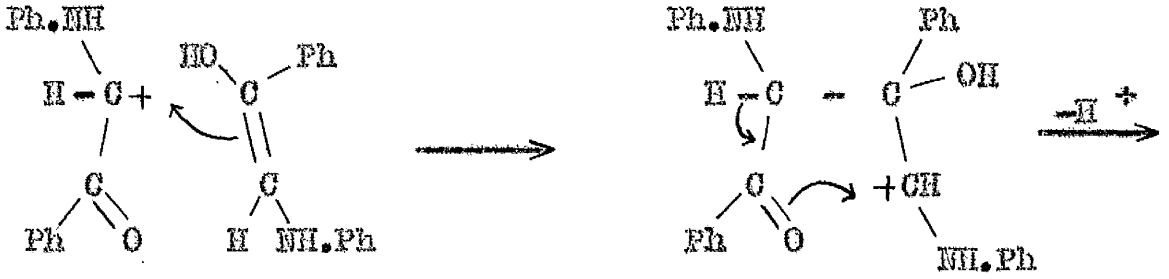
(1)



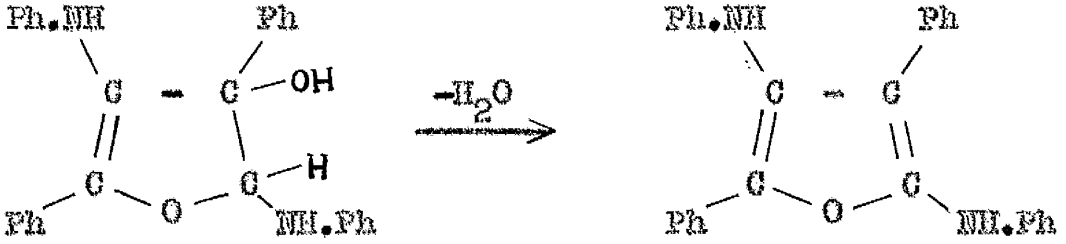


(LXII)

(2)



(A) (B)

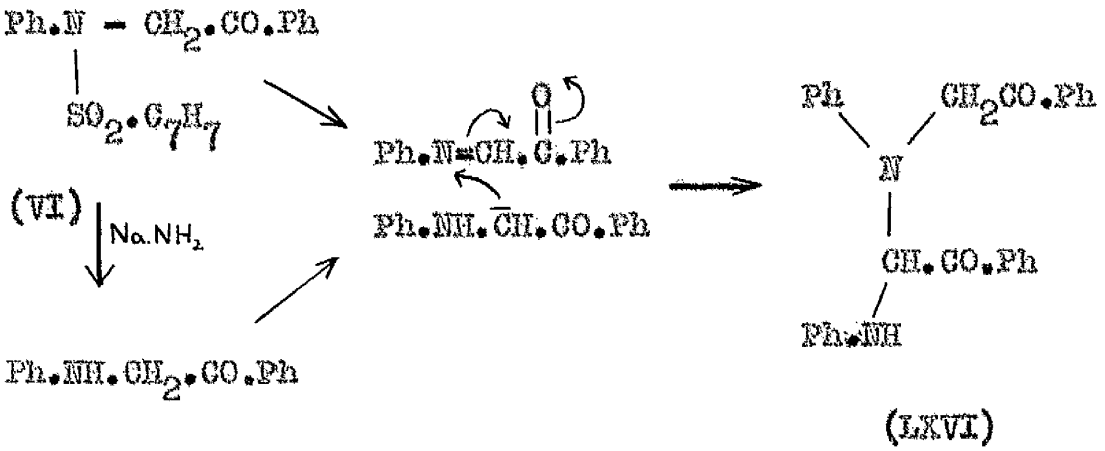


(LXIII)

Analogous mechanisms leading to (LXIV) cannot be formulated.

The existence of phenacyl aniline (B) as an intermediate in the above reaction, could not be proved; it failed to react with the anil when they were shaken together in ethanol with dilute acids; treatment of phenacyl aniline with a palladium-carbon catalyst in ethanol gave an amino-ketone (m.p. 187°) which could not be converted into the furan.

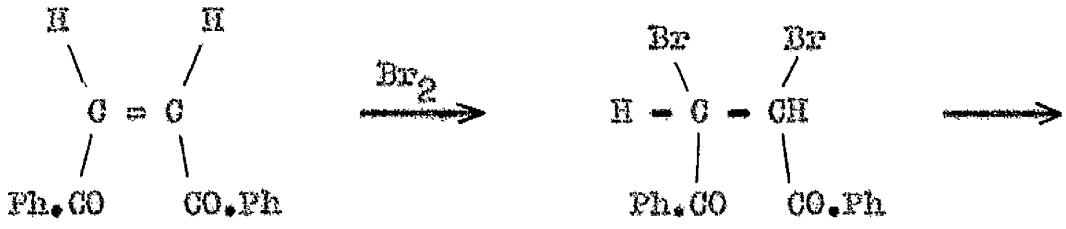
The amino-ketone (m.p. 187°) also arose when N-(toluene-p-sulphonyl) phenacyl aniline (VI) was treated with sodamide in toluene, and when solutions of phenacyl aniline were aerated. Yates[49] reported this compound as the anil, but consideration of its analysis, molecular weight and infra-red spectrum suggests a structure such as (LXVI). Mass spectroscopy gave both the expected molecular weight and a number of fragments consistent with the structure (LXVI), but the compound was too insoluble in most solvents to obtain a nuclear magnetic resonance spectrum. It is possible that the following reaction mechanism may explain the facts:-



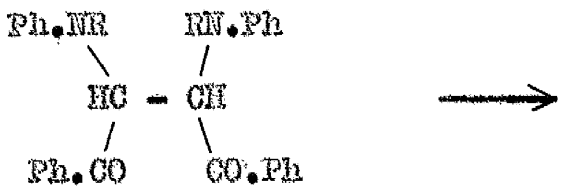
(LXVI)

Oxidation of phenacyl aniline may also give the anil of phenyl glyoxal, and a similar Michael-type reaction might occur.

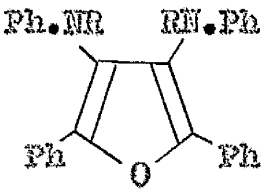
It was decided to synthesise one of the furan isomers (LXII) as follows:-



(LXVII) (LXVIII)

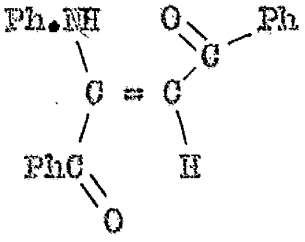


(LXIX)

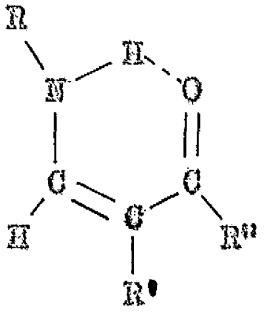


(LXII)

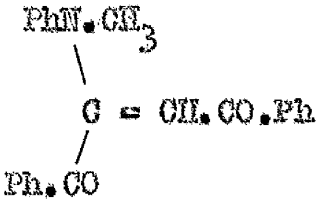
Dibenzoylethylene dibromide (LXVIII) was prepared from (LXVII) by a literature method[55]. Condensation of (LXVIII) with aniline did not give (LXIX; R=H), but gave the enamine (LXX). The infra-red spectrum of the latter revealed a hydrogen bonded structure analogous to that found in (LXXI)[56]. The nuclear magnetic resonance spectrum confirmed the presence



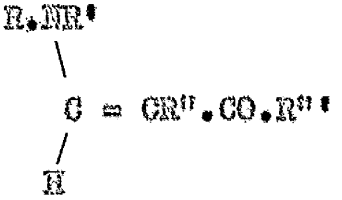
(LXX)



(LXXI)



(LXXII)



(LXXIII)

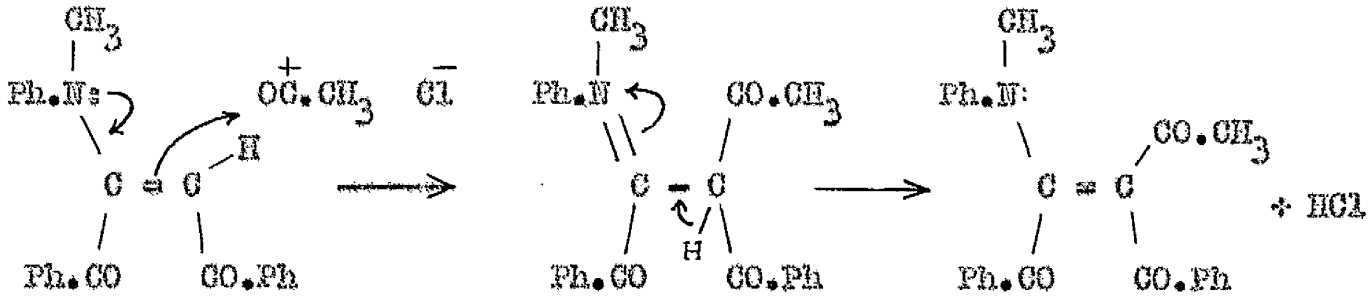
of fifteen aromatic protons (τ = 1.75-3.15) and one vinyl proton (singlet τ= 3.84), but no signal due to N-H was evident. This may be explained by the existence of resonance stabilised structures - as in (LXXI) - with a shift of the signal well out to low field - between τ = 0 and τ -10[57].

The reaction between (LXVIII), and methylaniline proceeded in an analogous fashion to the previous reaction, and gave 1,2-dibenzoyl-1-methylanilinoethylene (LXXII). The infra-red spectrum revealed an α,β unsaturated carbonyl group, and peaks at 1625, 1608 and 1587 cm^{-1} which are characteristic of eneamines such as (LXXIII)[56]. The nuclear magnetic resonance spectrum showed fifteen aromatic protons (τ = 1.75-2.9), one vinyl proton (singlet τ = 3.9) and three methyl protons (singlet τ= 6.67). On treatment with acetic anhydride and acetyl chloride, the eneamine gave (in low yield) what is believed to be (LXXIV). This is supported by:

(a) Infra-red (characteristic peaks at 1653, 1603 and 1587 cm^{-1})[56].

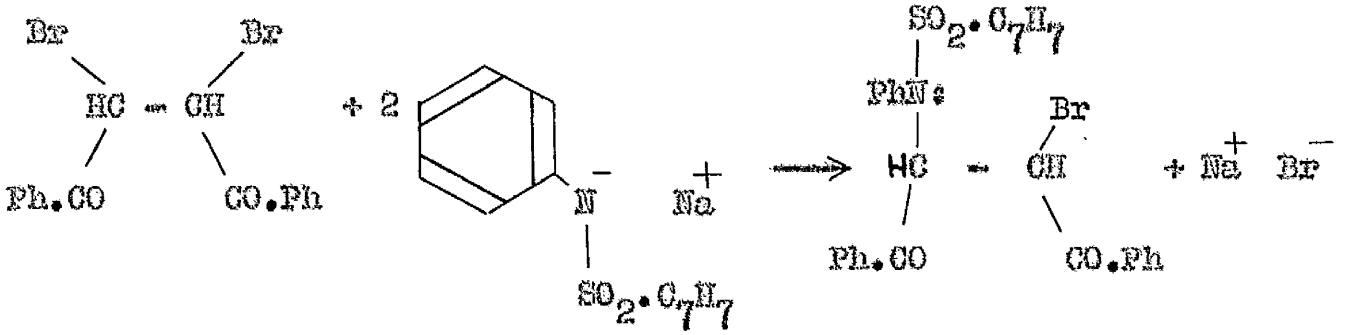
(b) Elementary analysis.

(c) Known behaviour of eneamines towards acetyl chloride[58].

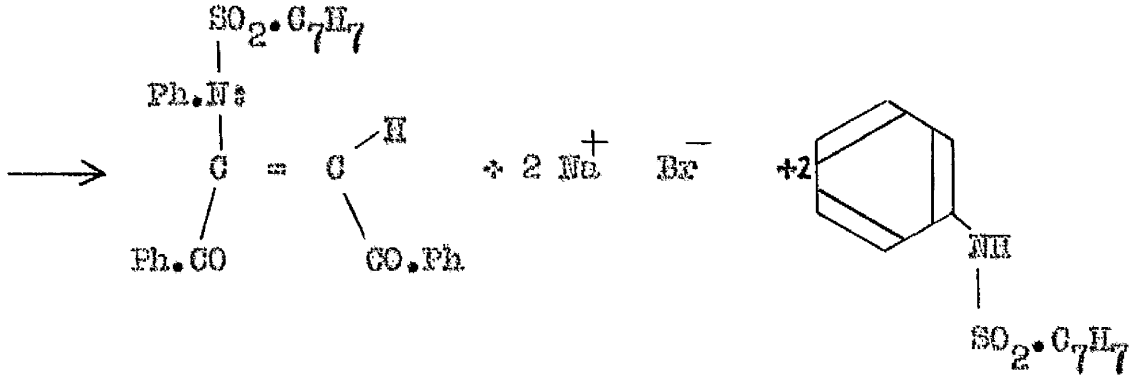


(LXXII) (LXXIV)

Treatment of the dibromide (LXVIII) with the sodium salt of N-(toluene-p-sulphonyl) aniline (LXXV) did not give (LXIX: R = toluene-p-sulphonyl) but gave (LXXVI). The latter was also obtained (in small yield) by heating the free sulphonamide with (LXVIII) and anhydrous sodium carbonate in either toluene or decalin. The structure (LXXVI) was supported by the analysis, molecular weight and infra-red spectrum. The nuclear magnetic resonance spectrum revealed nineteen aromatic protons (τ = 1.7-3.0), one vinyl proton (singlet τ = 3.36) and three methyl protons (singlet τ = 7.52).



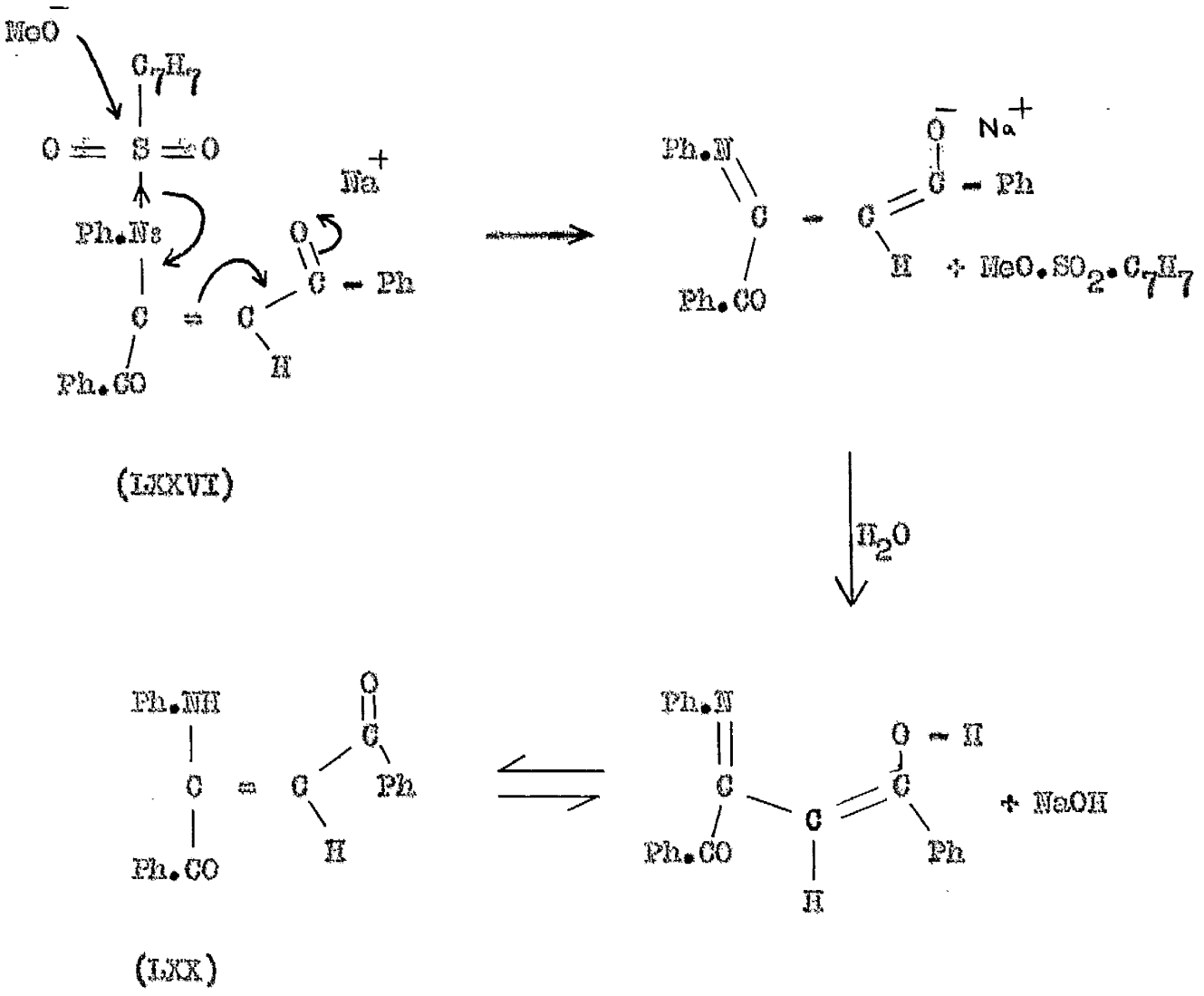
(LXVIII) (LXXV)



(LXXVI)

Treatment of (LXXVI) with sodium methoxide in benzene gave the eneamine (LXX) by cleavage of the nitrogen-sulphur bond[8]. Basic attack at the sulphur atom is presumably facilitated by the electron withdrawing groups adjacent

to the nitrogen atom. This being the case, the reaction may proceed as follows:-

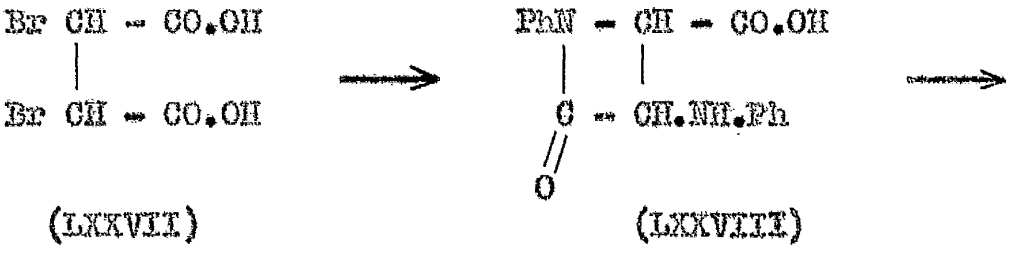


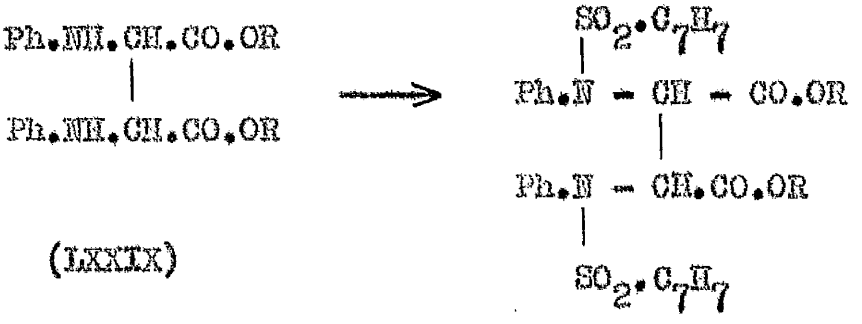
(LXXVI)

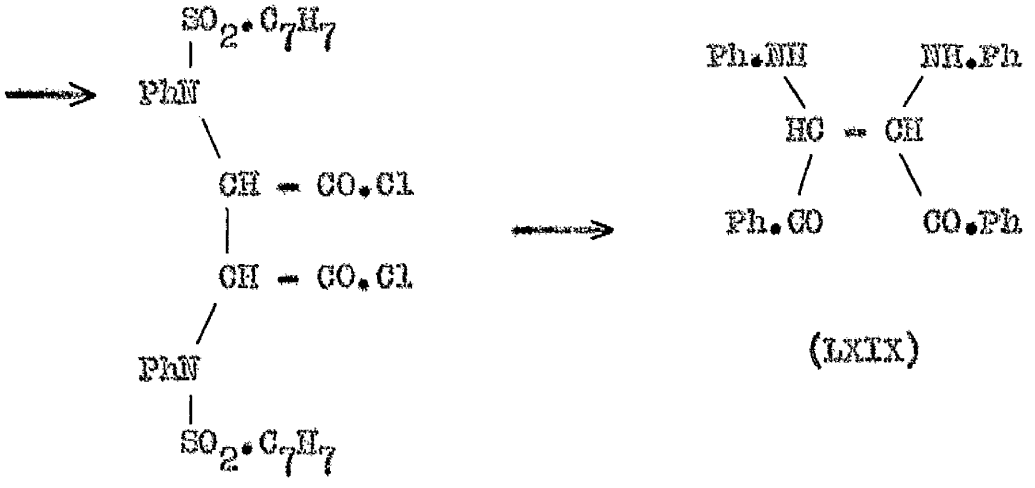
(LXX)

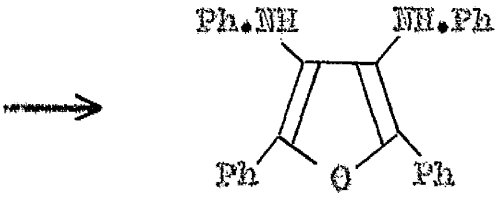
As it is known that the dibromide (LXVIII) may react with bases with elimination of HBr[59], it was interesting to

examine the diiodide. The latter could not, however, be prepared from the dibromide using standard procedures[60]. Another approach to (LXII) which avoids basic conditions is as follows:-









(LXXI)

Dibromosuccinic acid (LXXVII) was prepared by a literature method[61]. Condensation of (LXXVII) with aniline gave (LXXVIII) which was hydrolysed to the diacid (LXXIX: R = H). Since the final stage in the synthesis of the diketone would involve a Friedel-Crafts reaction, it was essential that the nitrogen atom be protected. It proved impossible, however, to tosylate either the amino-acid (LXXIX: R = H) or its ester (LXXIX: R = C_2H_5) and the work was abandoned at this stage.

EXPERIMENTAL

Melting points are uncorrected. Infra-red spectra (in Nujol) measured on the Grubb-Parsons S4 spectrophotometer and ultra-violet spectra on the Unicam S.P. 500.

Reactions of N-(Toluene-p-sulphonyl) Methylaniline

The above compound was recovered quantitatively after:-

1. Treatment with excess sodium methoxide in toluene at 20° for 24 hours.
2. Shaking with potassium tertiary butoxide in dry dimethylsulphoxide[7] at 20° for 24 hours.
3. Heating with excess sodium ethoxide in toluene, under reflux.
4. Heating with excess potassium hydroxide in ethylene glycol, under reflux.

Reactions of N-(Toluene-p-sulphonyl) Benzylaniline

(a) The sulphonamide (3.3 g) was recovered after treatment with sodium methoxide in toluene under nitrogen, at 20° for 24 hours.

(b) The sulphonamide (5.2 g) was recovered quantitatively after heating with sodium methoxide (3.2 g) in toluene (250 ml) at 95° for 2 hours.

(c) The sulphonamide (1.36 g) was recovered after heating with potassium tertiary butoxide (1.3 g) in toluene, under reflux.

(d) The sulphonamide was unaffected by treatment with freshly sublimed potassium tertiary butoxide in dry dimethylsulphoxide at 20° for 48 hours.

p-Nitrobenzylaniline

A mixture of p-nitrobenzylbromide (4.75 g), aniline (5 ml) and ethanol (100 ml) was heated under reflux for 3 hours, cooled and extracted with chloroform. The chloroform extract was washed with dilute hydrochloric acid and water, dried and evaporated leaving the product (3.6 g) as a red oil.

ν_{max} 3333, 1625, 1539 cm^{-1}.

N-(Toluene-p-sulphonyl)-p-Nitrobenzylaniline

Toluene-p-sulphonyl chloride (3.2 g) was added to a solution of p-nitrobenzylaniline (3.6 g) in dry pyridine (100 ml). The mixture was left at 20° for 2 hours, then poured into a mixture of ice and concentrated hydrochloric acid. The product (6.2 g) was filtered, dried and crystallised from methanol in cubes m.p. 122°. Yield 80%. FOUND: C, 62.90; H, 4.95; N, 7.30. $C_{20}H_{18}N_2O_4S$ requires C, 62.80; H, 4.70; N, 7.35%. ν_{max} 1600, 1538, 1342, 1163 cm^{-1}. λ_{max} (in ethanol) 210, 225 mμ. (ε : 25,000; 18,200).

p-Nitrobenzalanil

(a) A nitrogen saturated solution of N-(toluene-p-sulphonyl)-p-nitrobenzylaniline (1.66 g) in dry toluene (150 ml) was added to a nitrogen saturated suspension of sodium methoxide (4 g) in dry toluene (50 ml). The mixture was left at 20° for 48 hours, poured into water and the toluene layer separated. The aqueous layer was extracted with chloroform, and the combined organic extracts washed with water, dried and evaporated. The product (827 mg) crystallised from methanol in yellow plates m.p. 92°. Yield 84%. FOUND: C, 69.0; H, 4.5; N, 12.55. Calculated for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.1; N, 12.40%. ν_{max} 1575, 1504, 1327 cm^{-1}.

A solid (139 mg) was obtained from the aqueous extracts after acidification with dilute hydrochloric acid and extraction with chloroform; it crystallised from methanol in colourless cubes. The melting point and mixed melting point with toluene-p-sulphinic acid was 84°62.

(b) A mixture of p-nitrobenzaldehyde (349 mg), aniline (200 mg) and anhydrous sodium sulphate (210 mg) was heated gently at 100° for 5 minutes, then extracted with ethanol. The anil (312 mg) crystallised from ethanol in yellow plates m.p. 92°.

Treatment of the anil (450 mg) with 2,4-dinitrophenylhydrazine hydrochloride (1 g) in ethanol (20 ml) gave the 2,4-dinitrophenylhydrazone of p-nitrobenzaldehyde m.p. 312°.

Phenacylaniline[63]

Phenacyl bromide (100 g) was added to a solution of aniline (100 g) in ethanol (400 ml) and the temperature of the mixture kept below 30°. After standing for 1 hour at 0°, the crystals which had separated from the solution, were filtered and washed with ice cold ethanol. The product (83 g) crystallised from ethanol in needles m.p. 98°. FOUND: C, 80.0; H, 6.15; N, 6.6. Calculated for $C_{14}H_{13}NO$: C, 79.6; H, 6.15; N, 6.6%. ν_{max} 3342, 1695, 1605 cm^{-1}. λ_{max} (in ethanol) 208, 246, 286 mμ (ε: 17,200; 29,150; 3,870).

The 2,4-dinitrophenylhydrazone crystallised from nitrobenzene in needles m.p. 220°. FOUND: C, 61.8; H, 4.15, $C_{20}H_{17}N_5O_4$ requires C, 61.8; H, 4.3%.

N-(Toluene-p-sulphonyl) Phenacylaniline

A mixture of phenacylaniline (1.25 g), toluene-p-sulphonyl chloride (1 g) and dry pyridine (10 ml) was heated at 95° for 5 minutes, cooled and poured into ice and concentrated hydrochloric acid. The product (1.1 g) was filtered and washed, dried and crystallised from methanol in needles m.p. 130°. FOUND: C, 68.85; H, 5.30; N, 3.95. $C_{21}H_{19}NO_3S$ requires C, 69.0; H, 5.20; N, 3.85%. ν_{max} 1740, 1600, 1200, 1156, 1105 cm^{-1}. λ_{max} (in ethanol) 212, 225 mμ. (ε : 25,630; 18,720).

Phenylglyoxal Monoanil (cis-isomer)

A nitrogen saturated solution of N-(toluene-p-sulphonyl) phenacylaniline (8.4 g) in dry toluene (300 ml) was added at once to a nitrogen saturated suspension of sodium methoxide (9 g) in dry toluene (200 ml). The mixture was left at 20° for 24 hours, poured into water (500 ml) and filtered. The residue (4.6 g) crystallised from methanol in plates m.p. 210°. Yield 95%.

FOUND: C, 80.4; H, 5.3; N, 6.6. $C_{14}H_{11}NO$ requires C, 80.4; H, 5.25; N, 6.75%. (Molecular weight by isothermal distillation[64] 218; $C_{14}H_{11}NO$ requires 209.) ν_{max} 1666, 1600 cm^{-1}. λ_{max} (in ethanol) 207, 250 mμ (ε: 13,920; 13,800).

(The 2,4-dinitrophenylhydrazone crystallised from nitrobenzene in orange needles m.p. 235°. FOUND: N, 17.95. $C_{20}H_{13}N_3O_4$ requires N, 17.95%.)

The aqueous extracts from the above reaction were acidified with dilute hydrochloric acid and extracted with chloroform. Evaporation of the latter gave toluene-p-sulphinic acid (93 mg) m.p. 84°.

The Potassium Salt of Toluene-p-sulphonamide

The Potassium Salt of Toluene-p-sulphonamide) g) in aqueous ethanol (75% ethanol; 12 ml) was added to a solution of toluene-p-sulphonamide (8 g) in ethanol (16 ml) and the mixture heated under reflux for 5 minutes, then cooled. On addition of excess acetone, the potassium salt of toluene-p-sulphonamide separated in plates m.p. > 360°. Yield 75%.

N-(Toluene-p-sulphonyl)-ω-Aminoacetophenone

A mixture of the potassium salt of toluene-p-sulphonamide (7.95 g), phenacyl bromide (7.6 g) and benzene (90 ml) was

heated under reflux for 3 hours, and filtered. The filtrate was washed with dilute sulphuric acid and water, dried and evaporated, leaving a yellow oil (7.8 g) which was chromatographed on alumina. Elution of the column with petroleum ether (b.p. 60-80°) gave N-(toluene-p-sulphonyl) diphenacylamine (1.6 g) m.p. 132°. FOUND: C, 67.7%; H, 5.15%; N, 3.55. $C_{23}H_{21}NO_4S$ requires C, 67.8%; H, 5.15%; N, 3.44%. ν_{max} 1670, 1324, 1152 cm^{-1}. Elution of the column with benzene gave N-(toluene-p-sulphonyl)-ω-aminoacetophenone (3.5 g) which crystallised from ethanol in cubes m.p. 116° (lit. m.p. 116-117°[65]). FOUND: C, 62.3%; H, 4.75%; N, 4.5%. Calculated for $C_{15}H_{15}NO_3S$: C, 62.3%; H, 5.2%; N, 4.85%. ν_{max} 3333, 1681, 1342, 1170 cm^{-1}.

Reactions of N-(Toluene-p-sulphonyl)-ω-Aminoacetophenone

(a) When a mixture of the sulphonamide (763 mg), sodium methoxide (0.5 g) and dry toluene (50 ml) was left under nitrogen at 20° for 24 hours, the starting material (660 mg) was recovered.

(b) The sulphonamide (5.0 g) was recovered quantitatively after treatment with sodium methoxide in toluene at 120° for 8 hours.

(c) The sulphonamide (3.1 g) was unaffected by potassium tertiary butoxide (2.6 g) in dry dimethylsulphoxide (120 ml).

N-(Toluene-p-sulphonyl) N-Phenylglycine Ethyl Ester

A mixture of N-(toluene-p-sulphonyl) aniline (10 g), ethylbromoacetate (7 g), dry toluene (250 ml) and sodium carbonate (20 g) was heated under reflux for 70 hours, then cooled and filtered. Evaporation of the filtrate gave a solid which crystallised from ethanol in needles m.p. 110°. FOUND: C, 61.2; H, 5.55; N, 4.15. Calculated for $C_{17}H_{19}NO_4S$, C, 61.3; H, 5.72; N, 4.2%. ν_{max} 1754, 1600, 1351, 1167 cm^{-1}.

Reaction of N-(Toluene-p-sulphonyl) N-Phenylglycine Ethyl Ester

A nitrogen saturated solution of N-(toluene-p-sulphonyl) N-phenylglycine ethyl ester (2.4 g) in dry toluene (100 ml) was added to a nitrogen saturated suspension of sodium methoxide (4.25 g) in toluene (50 ml). The mixture was left at 20° for 48 hours, poured into water (200 ml) and the toluene layer separated. The aqueous layer was extracted with chloroform and the combined organic extracts washed with water, dried and evaporated leaving a yellow oil which distilled at 150°/3 mm.

FOUND: C, 70.00; H, 5.6; N, 9.2. $C_{18}H_{16}N_2O_3$ requires C, 70.13; H, 5.2; N, 9.1%. (Molecular weight by Rast determination[66] 323; $C_{18}H_{16}N_2O_3$ requires 308.) ν_{max} 1730; 1669; 1620 cm^{-1}.

Treatment of the above compound (900 mg) with 2,4-dinitrophenylhydrazine hydrochloride (500 mg) in methanol (10 ml) gave a yellow product (650 mg) which crystallised from nitrobenzene in needles m.p. 264°. FOUND: C, 52.82; H, 3.33; N, 17.25. $C_{18}H_{15}N_5O_7$ requires C, 52.3; H, 3.63; N, 16.95%. ν_{max} 3279; 1667; 1621; 1582 cm^{-1}.

Reactions of N-(toluene-p-sulphonyl) Benzylaniline

The above compound was recovered quantitatively after:-

1. Adding cyclohexanone (1 g) dropwise to a nitrogen saturated mixture of the sulphonamide (3.4 g), sodium methoxide (1.6 g) and toluene (100 ml) at 20°.
2. Heating with sodium methoxide, cyclohexanone and toluene at 100° for 4 hours.

N-(Toluene-p-sulphonyl) Dimethylamine

Dimethylamine (12 g) was added dropwise to a solution of toluene-p-sulphonyl chloride (50 g) in pyridine (100 ml) at 0°. The mixture was poured into ice and concentrated hydrochloric acid,

and the residue (15.5 g) filtered. The latter was washed with water, dried and crystallised from petroleum ether (b.p. 60-80°) in cubes m.p. 88° (lit. m.p. 86-87°)[67].

Reactions of N-(Toluene-p-sulphonyl) Dimethylamine

(a) The sulphonamide (4 g) was recovered quantitatively after treatment with diethylmalonate (3.6 g) and sodium methoxide (2 g) in toluene at 20° for 12 hours.

(b) The sulphonamide (4 g) was recovered after heating with potassium ethoxide (2.2 g) and diethylmalonate (3.6 g) in toluene under reflux, for 4 hours.

(c) Freshly sublimed potassium tertiary butoxide (2 g) was added to a nitrogen saturated solution of the sulphonamide (2 g) and diethylmalonate (1.4 g) in dimethylsulphoxide (50 ml), and the mixture left at 20° for 48 hours before adding water (200 ml). Extraction with chloroform followed by evaporation gave the starting sulphonamide (1.7 g).

(d) The sulphonamide (6 g) was recovered after treatment with diethylmalonate (4 g), sodium hydroxide and ethylene glycol, under reflux.

Reactions of N-(Toluene-p-sulphonyl) Methylaniline

1. The sulphonamide (4 g) was recovered after heating with potassium ethoxide (2.5 g) and diethylmalonate (3.7 g) in toluene (200 ml) under reflux.

2. The sulphonamide (12.6 g) was recovered quantitatively after heating with excess sodium ethoxide and diethylmalonate (8 g) in ethanol (300 ml) under reflux for 2⅔ hours.

3. A mixture of the sulphonamide (500 mg), acetophenone (500 mg), sodium hydroxide (8 g) and ethylene glycol (40 ml) was heated under reflux for 6 hours, and left at 20° for 24 hours before adding water (200 ml) and extracting with chloroform. The product (1.2 g) obtained after evaporation of the chloroform was chromatographed on an alumina column; elution with chloroform gave the starting sulphonamide (460 mg).

N-(Toluene-p-sulphonyl)-o-Aminoacetophenone[68]

The above compound was prepared by tosylating o-aminoacetophenone with toluene-p-sulphonyl chloride in pyridine; it crystallised from methanol in cubes m.p. 142°. FOUND: C, 62.1; H, 5.55;

N, 4.72. Calculated for $C_{15}H_{15}NO_3S$: C, 62.3; H, 5.2; N, 4.85%.

ν_{max} 3077, 1665, 1325, 1159 cm^{-1}.

Reactions of N-(Toluene-p-sulphonyl)-o-Aminoacetophenone

(a) The sulphonamide (1 g) was recovered unchanged after treatment with sodium methoxide (2 g) in toluene (400 ml) under nitrogen, at 20° for 24 hours.

(b) The sulphonamide (1.5 g) was recovered quantitatively after treatment with potassium tertiary butoxide (2.6 g) in toluene (200 ml) at 122° for 12 hours.

(c) The sulphonamide (1 g) was unaffected by potassium tertiary butoxide (2 g) in dimethylsulphoxide (50 ml).

(d) Potassium hydroxide (6 g) was added to a solution of the sulphonamide (1.5 g) in ethylene glycol (100 ml). The mixture was heated under reflux for 2 hours, and left at 20° for 8 hours before diluting with water and extracting with chloroform. Evaporation of the chloroform gave the starting material (700 mg).

The alkaline extracts from the reaction (d), were acidified with dilute hydrochloric acid and extracted with chloroform. Evaporation of the chloroform left an oil (254 mg) which crystallised

from petroleum ether (b.p. 100-120°) in colourless cubes m.p. 127°. FOUND: C, 65.46; H, 5.71; N, 5.36%. $C_{15}H_{15}NO_2S$ requires C, 65.95; H, 5.5; N, 5.13%. ν_{max} 3311, 1629, 1595, 1323, 1156, 985 cm^{-1}.

The product (m.p. 127°) was recovered unchanged after:-

1. Heating with polyphosphoric acid at 95°.
2. Treatment with excess acetic anhydride in pyridine at 20°.

N-(Toluene-p-sulphonyl)-o-Methylaminoacetophenone

Methyl iodide (2.1 g) was added dropwise to a stirred suspension of o-aminoacetophenone (3.47 g) in aqueous sodium bicarbonate solution (0.75%; 150 ml) at 100°. The mixture was heated, under reflux, for 6 hours before cooling and extracting with chloroform. The latter was washed with water, dried and evaporated to give an oil (3.51 g). This was treated at 20° with excess toluene-p-sulphonyl chloride (9 g) in pyridine (75 ml) and the solution poured into ice and concentrated hydrochloric acid. Filtration gave a residue which was washed, dried and chromatographed on alumina: elution of the column with benzene gave the product (300 mg) which crystallised from methanol in cubes m.p. 114°. FOUND: C, 63.40; H, 5.5; N, 4.65.

$C_{16}H_{17}NO_3S$ requires: C, 63.35; H, 5.5; N, 4.6%.

ν_{max} 1686; 1342; 1170 cm^{-1}.

Elution of the column with benzene/chloroform (99 : 1) gave N-(toluene-p-sulphonyl)-o-aminoacetophenone (2.6 g; m.p. 142°).

N-(Toluene-p-sulphonyl) Methylaniline

Amberlite resin (30 g; I.R.A. 410) was activated by treatment with sodium hydroxide solution (1 N), then washed with water until the eluate was neutral to litmus.

The resin, N-(toluene-p-sulphonyl) aniline (2.0 g) and benzene (50 ml) were shaken together with methyl iodide (6 ml) for 10 minutes and the mixture left at 20° for 48 hours before filtration. The filtrate was washed successively with dilute sodium hydroxide solution, dilute hydrochloric acid and water, dried and evaporated. The product (2.0 g) crystallised from methanol in cubes; m.p. and mixed m.p. with an authentic sample of N-(toluene-p-sulphonyl) methylaniline was 99°. Yield 98%.

N-(Toluene-p-sulphonyl)-o-Methylaminoacetophenone

Methyl iodide (12 ml) was added to a mixture of the resin (20 g dry weight), N-(toluene-p-sulphonyl)-o-aminoacetophenone

(1 g) and benzene (100 ml), which had been previously shaken at 20° for 1 hour. The mixture was left at 20° for 96 hours before filtration, and the benzene washed successively with dilute sodium hydroxide solution, dilute hydrochloric acid and water, dried and evaporated. The product (959 mg) crystallised from methanol in cubes m.p. 116°. Yield 90%.

Reactions of N-(Toluene-p-sulphonyl)-o-Methylaminoacetophenone

(a) The sulphonamide (500 mg) was recovered, in almost quantitative yield, after treatment with sodium methoxide (1 g) in toluene (150 ml) - under nitrogen - at 20° for 48 hours.

(b) A nitrogen saturated suspension of freshly sublimed potassium tertiary butoxide (2 g) in dry dimethylsulphoxide (25 ml) was added to a nitrogen saturated solution of the sulphonamide (1 g) in dimethylsulphoxide (50 ml) and the mixture left at 20° for 48 hours before adding water (200 ml) and extracting with chloroform. Evaporation of the chloroform gave an oil (900 mg) which was chromatographed on alumina: elution of the column with benzene gave the starting material (850 mg).

(c) The sulphonamide (450 mg) was recovered unchanged after heating with sodium ethoxide (1 g) in ethanol (100 ml) under reflux, for 3 hours.

(d) A mixture of the sulphonamide (850 mg), sodium hydroxide (6 g) and ethylene glycol (40 ml) was heated under reflux for 6 hours and left at 20° for 60 hours. Water (100 ml) was added, and a white precipitate (291 mg) which formed was filtered and crystallised from methanol in cubes m.p. 116° (the mixed m.p. with the starting material did not depress). The filtrate was extracted with chloroform and the alkaline layer separated. Acidification of the latter with dilute hydrochloric acid gave an insoluble inorganic solid (257 mg).

Reactions on Amberlite Resin (I.R.A. 410)

(a) N-(toluene-p-sulphonyl) aniline (2 g) was adsorbed from benzene (100 ml) on to Amberlite resin (dry weight: 20 g) which had been previously washed with concentrated sodium hydroxide solution and water. The sulphonamide remained on the resin after standing

for 48 hours in benzene with ethyl bromide (5 ml).

(b) N-(toluene-p-sulphonyl) aniline (2 g) was adsorbed from benzene (100 ml) on to the resin (dry weight: 20 g) which had been previously washed with concentrated sodium hydroxide solution and water. The sulphonamide remained on the resin after standing at 20° for 48 hours in benzene with bromoacetal (5 ml).

(c) N-(toluene-p-sulphonyl) aniline (2 g) was adsorbed from benzene (100 ml) on to the basic resin (dry weight: 20 g). The sulphonamide remained on the resin after standing at 20° for 24 hours in benzene with monobromoacetone (5 ml).

(d) N,N'-(Ditoluene-p-sulphonyl)-o-phenylenediamine (2 g) was adsorbed from benzene (200 ml) on to the resin (dry weight: 30 g) as above. 1,3-Dibromoacetone (4.3 g) was added and the mixture left at 20° for 48 hours before filtration. The starting sulphonamide (700 mg) was recovered on evaporation of the benzene.

N-(Toluene-p-sulphonyl)-o-Benzylaminoacetophenone

Benzyl chloride (1.6 g) was added dropwise over 2 hours to a stirred mixture of o-aminoacetophenone (6.46 g), sodium bicarbonate (3.0 g) and water (20 ml) at 95°. The mixture was heated under reflux for 1 hour and left at 20° for 12 hours. The brown oil, which separated from the aqueous layer, was dissolved in chloroform; the solution was washed with saturated aqueous sodium chloride solution and extracted with dilute hydrochloric acid. The latter was basified by addition of ammonium hydroxide and extracted with chloroform. The red oil (4.5 g) obtained by evaporation of the chloroform, was separated into its components by fractional distillation; this gave o-aminoacetophenone (b.p. 95-100°; 0.2 mm) and o-benzylaminoacetophenone (725 mg; b.p. 120-125°/0.2 mm). ν_{max} 3333, 1653 cm^{-1}.

Toluene-p-sulphonyl chloride (0.96 g) was added to a solution of o-benzylaminoacetophenone (725 mg) in dry pyridine (100 ml). The mixture was left at 95° for 1 hour, cooled and poured into ice and concentrated hydrochloric acid. The residue (650 mg), obtained on filtration, crystallised from ethanol in

cubes m.p. 130°. FOUND: C, 69.0; H, 6.1; $C_{22}H_{21}NO_3S$ requires C, 69.65; H, 5.55%.

ν_{max} 1675; 1357; 1163 cm^{-1}.

Reactions of N-(Toluene-p-sulphonyl)-o-Benzylaminoacetophenone

(a) The sulphonamide (1 mole) was recovered unchanged after treatment - under nitrogen - with sodium methoxide (2 mole) in dry toluene for 4 hours at 90°.

(b) The sulphonamide was unaffected by heating with sodium methoxide in toluene - under reflux - for 4 hours.

(c) The sulphonamide (350 mg) was recoverable after shaking at 20° with potassium tertiary butoxide (1.4 g) in dimethylsulphoxide (120 ml).

(d) A mixture of the sulphonamide (273 mg), sodium hydroxide (6 g) and ethylene glycol (40 ml) was heated under reflux for 6 hours and left at 20° for 24 hours. Water (100 ml) was added and the solution extracted with chloroform. Evaporation of the latter gave the starting material (165 mg).

2-Toluene-p-sulphonamidobiphenyl

Toluene-p-sulphonyl chloride (60 g) was added to a solution of 2-aminobiphenyl (50 g) in dry pyridine (30 ml) at 0°. The mixture was left at room temperature for 5 hours, poured into ice and concentrated hydrochloric acid and the product (73 g) collected by filtration. The residue was washed with dilute hydrochloric acid and water, dried and crystallised from methanol in prisms m.p. 99°. Yield 76%. FOUND: C, 70.1; H, 5.2; N, 4.3. $C_{19}H_{17}NO_2S$ requires C, 70.7; H, 5.3; N, 4.3%. ν_{max} 3178; 1309; 1145 cm^{-1}. λ_{max} (in ethanol) 210 m μ (ε 27,000).

N-2-Biphenylyl-N-toluene-p-sulphonylglycine Methyl Ester

A mixture of 2-toluene-p-sulphonamidobiphenyl (70 g), dry toluene (300 ml), methyl bromoacetate (41 g) and anhydrous sodium carbonate (70 g) was heated under reflux for 4 days. The mixture was filtered and extracted with chloroform. A neutral solid (69 g) was obtained from the filtrate on evaporation; it crystallised from methanol in prisms m.p. 117°. Yield 80%. FOUND: C, 66.7; H, 5.1; N, 3.5. $C_{22}H_{21}NO_4S$ requires C, 66.8; H, 5.3; N, 3.5%. ν_{max} 1739; 1376;

1333; 1141 cm^{-1}. λ_{max} (in ethanol) 208; 230 m μ (ε : 35,000; 23,800).

N-2-Biphenylyl-N-toluene-p-sulphonylglycine

N-2-biphenylyl-N-toluene-p-sulphonylglycine methyl ester (65 g) and a 15% aqueous solution of sodium hydroxide (55 ml) were heated together at 50° for 1 hour. The solution was cooled, diluted with water and acidified with dilute hydrochloric acid. The product (60 g) was collected, dried and crystallised from toluene in needles m.p. 195°. Yield 96%. FOUND: C, 66.4; H, 5.2; N, 3.6. $C_{21}H_{19}NO_4S$ requires C, 66.2; H, 5.0; N, 3.7%. ν_{max} 3122; 1739; 1724; 1316; 1130 cm^{-1}. λ_{max} (in ethanol) 210; 230 m μ (ε : 30,000; 18,600).

N-(Toluene-p-sulphonyl)-2-Biphenylamino-Acetyl Chloride

N-2-biphenylyl-N-toluene-p-sulphonylglycine (10.5 g) was dissolved in thionyl chloride (60 ml) and the solution refluxed for 1 hour. The excess thionyl chloride was distilled off leaving the product (11 g). Yield 100%.

5,6-Dihydro-7-oxo-5-toluene-p-sulphonyldibenz [b.d] azepine

N-(toluene-p-sulphonyl)-2-biphenylamino-acetyl chloride (11 g) was dissolved with mechanical stirring in dry chloroform (75 ml) and the temperature of the solution lowered to -70°.

Anhydrous aluminium chloride (15 g) was slowly added, the mixture stirred at -10° for 3 hours and left at 20° for 12 hours. The mixture was poured into iced water and stirred. The chloroform was washed with ice cold sodium hydroxide solution (3%), dilute hydrochloric acid and water, dried and evaporated leaving a gum (9.5 g) which crystallised from methanol in prisms m.p. 137°. Yield 90%. FOUND: C, 69.1; H, 4.9; N, 3.8%. $C_{21}H_{17}NO_3S$ requires C, 69.4; H, 4.7; N, 3.8%. ν_{max} 1685; 1590; 1325; 1140 cm^{-1}. λ_{max} (in ethanol) 207, 232 mμ (ε : 36,000; 32,200). The ketone formed a 2,4-dinitrophenyl-hydrazone derivative m.p. 212°.

9, 10-Dihydro-N-toluene-p-sulphonylphenanthridine

Anhydrous aluminium chloride (10 g) was added to a solution of N-(toluene-p-sulphonyl)-2-biphenylamino-acetyl chloride (9 g) in carbon disulphide (500 ml) at -70° — CO_2/acetone . The cooling bath was removed and the mixture was stirred so that it rapidly attained room temperature. After 12 hours chloroform was added and the organic extract washed with aqueous ammonia, dilute hydrochloric acid and water, dried and evaporated leaving a tar (6.2 g) which was chromatographed on deactivated alumina.

The product (2.3 g) eluted from the column in benzene and crystallised from methanol in cubes m.p. 102°. Yield 20%. FOUND: C, 71.4; H, 5.2; N, 4.4. $C_{20}H_{17}NO_2S$ requires C, 71.6; H, 5.1; N, 4.2%. ν_{max} 1590; 1326; 1140 cm^{-1}. λ_{max} (in ethanol) 215; 242; 252 m μ (ε : 24,200; 21,900; 13,000). Elution of the column with benzene-light petroleum (2 : 1) gave 5,6-dihydro-7-oxo-5-toluene-p-sulphonyldibenz [b.d.] azepine (1.5 g).

7-Oxodibenz [b.d.] azepine

A solution of 5,6-dihydro-7-oxo-5-toluene-p-sulphonyl-dibenz [b.d.] azepine (2 g) in dry toluene (80 ml) was added to a suspension of sodium methoxide (2 g) in dry toluene (150 ml). Both were previously saturated with nitrogen. The mixture was left at 20° for 12 hours then poured into water (300 ml). A purple solid (611 mg), which separated from the toluene layer, crystallised from tetralin in needles m.p. 267°. Yield 60%. FOUND: C, 81.0; H, 4.5; N, 7.0. $C_{14}H_9NO$ requires C, 81.1; H, 4.3; N, 6.8%. (Molecular weight by mass spectroscopy 207; $C_{14}H_9NO$ requires 207.)

ν_{max} 1613; 1591; 1575 cm^{-1}. λ_{max} (in chloroform) 226, 246; 350; 520 mμ (ε : 5,000; 17,000; 4,990; 2,920).

Phenanthridone was obtained from the aqueous layer in 13% yield.

5,6-Dihydro-7-hydroxy-5-toluene-p-sulphonyldibenz [b.d.] azepine

A mixture of 5,6-dihydro-7-oxo-5-toluene-p-sulphonyldibenz [b.d.] azepine (1.9 g), excess lithium aluminium hydride and tetrahydrofuran (250 ml) was heated under reflux for 17 hours. The tetrahydrofuran was evaporated and water cautiously added to the residue. The precipitate was filtered, dried and extracted with chloroform, from which a neutral oil (1.32 g) was obtained. The product crystallised from methanol in prisms m.p. 140°. Yield 70%. FOUND: C, 68.8; H, 5.3; N, 3.9. $C_{21}H_{19}NO_3S$ requires C, 69.0; H, 5.2; N, 3.9%. ν_{max} 3390; 1325; 1148 cm^{-1}. λ_{max} (in ethanol) 218; 238 mμ (ε : 23,550; 25,620).

Phenanthridone

(a) 7-oxodibenz [b.d.] azepine (77 mg) was heated for 6 days in a soda glass tube at 190° and atmospheric pressure. White crystals (36 mg) sublimed into the cold part of the tube and crystallised from methanol in needles m.p. 293°. Yield 43%. FOUND: C, 80.1; H, 4.3; N, 7.4. Calculated for $C_{13}H_9NO$: C, 80.0;

H, 4.6; N, 7.2%. ν_{max} 3,000; 1640; 1580 cm^{-1}. λ_{max} (in ethanol) 242; 250; 260; 310; 322 mμ (ε : 23,200; 17,600; 19,700; 8,310; 10,800).

(b) A mixture of 7-oxodibenz [b.d.] azepine (1.23 g), dry tetrahydrofuran (250 ml) and excess lithium aluminium hydride was refluxed for 40 hours, cooled and poured into a mixture of ice and concentrated hydrochloric acid. The chloroform extract was washed with dilute hydrochloric acid and water, dried and evaporated. The product (1.1 g) was chromatographed on an alumina column; elution with benzene/chloroform (1 : 1) gave a solid (350 mg) which crystallised from methanol in prisms m.p. 293°. Yield 30%. The mixed m.p. with an authentic sample of phenanthridone was 293°.

(c) A mixture of sodium methoxide (4.5 g), 5,6-dihydro-7-oxo-5-toluene-p-sulphonyldibenz [b.d.] azepine (1.9 g) and dry toluene (250 ml) was saturated with oxygen and left at 20° for 3 hours. Water (300 ml) was added, the aqueous layer separated, acidified

with dilute hydrochloric acid and extracted with chloroform. This was washed with water, dried and evaporated to give an oil (300 mg) which crystallised from methanol in needles m.p. 293°.

(d) 5,6-dihydro-5-hydroxy-7-oxodibenz [b.d.] azepine (130 mg), 20% palladised-charcoal (542 mg) and trichlorobenzene were heated together under reflux for 5 hours, cooled and filtered. The organic layer was washed successively with dilute alkali, acid and water. After drying and evaporating the solvent, a colourless solid (70 mg) - indistinguishable from phenanthridone - was obtained.

(e) 7-oxodibenz [b.d.] azepine (58 mg), glacial acetic acid (25 ml) and zinc dust (2 g) were left at 20° for 48 hours before filtration. Removal of the solvent, chromatography on alumina, and elution with 99 : 1 chloroform-methanol gave phenanthridone (12 mg).

Reactions of 7-oxodibenz [b.d.] azepine

(a) The azepine was recovered unchanged after being shaken for 24 hours at 1 atmosphere with hydrogen and the following catalysts: palladium-carbon,

palladium-calcium carbonate, reduced platinum oxide-carbon. Both dioxan and ethanol were used as solvents.

(b) The azepine was recovered after treatment in tetrahydrofuran for 24 hours with an excess of lithium in diethylamine at 20°.

7-Oxodibenz [b.d.] azepine Hydrochloride

(a) When 7-oxodibenz [b.d.] azepine (108 mg) in dioxan was saturated with dry hydrogen chloride, a violet hydrochloride (100 mg) separated. This crystallised from ether in needles m.p. 249°. FOUND: C, 68.5; H, 4.5; Cl; 14.7. $C_{14}H_{10}ClNO$ requires C, 69.0; H, 4.1; Cl; 14.6%. ν_{max} 3200; 1675 cm^{-1}. λ_{max} (in ethanol) 202; 211; 238; 530 mμ (ε : 22,100; 20,000; 17,250; 2,625).

(b) 70% Perchloric acid (1 ml) was added to 7-oxodibenz [b.d.] azepine (188 mg) in dioxan (100 ml). The solution was extracted with chloroform which was washed with water, dried and evaporated, leaving a purple solid (260 mg) m.p. 135-140°.

Crystallisation from ether yielded the hydrochloride (180 mg) m.p. 249°.

5,6-Dihydro-5-hydroxy-7-oxodibenz [b.d.] azepine

(a) In the preparation of 7-oxodibenz [b.d.] azepine above, a product (m.p. 201-225°) was obtained from the organic extract on evaporation; it crystallised from methanol in needles m.p. 230°. FOUND: C, 74.6; H, 5.0; N, 6.3. $C_{14}H_{11}NO_2$ requires C, 74.6; H, 4.9; N, 6.3% - molecular weight (cryoscopic) 233; $C_{14}H_{11}NO_2$ requires 225. ν_{max} 3225; 1680 cm^{-1}. λ_{max} (in ethanol) 209, 232, 250 mμ (ε : 27,600; 42,700; 12,600). A reaction, positive for hydroxylamines, was obtained with ferrous hydroxide[26]. A negative result was found for phenanthridone and 5,6-dihydro-7-oxo-5-toluene-p-sulphonyldibenz [b.d.] azepine.

(b) Treatment of 5,6-dihydro-7-oxo-5-toluene-p-sulphonyl-dibenz [b.d.] azepine (2 g) in dry toluene (250 ml) with sodium methoxide (4.5 g) and oxygen at room temperature gave a neutral oil (250 g) which crystallised from methanol in needles m.p. 230°.

(c) A mixture of 7-oxodibenz [b.d.] azepine (64 mg), glacial acetic acid (30 ml), water and zinc dust (2 g) was left at 80° for 6 hours before filtration. The filtrate was diluted with water and extracted with chloroform. The product (40 mg) crystallised from methanol in needles m.p. 230°.

Reactions of 5,6-Dihydro-5-hydroxy-7-oxodibenz [b.d.] azepine

1. A mixture of the azepine (32 mg), pyridine (10 ml) and acetic anhydride (2 ml) was left at room temperature for 48 hours, poured into a mixture of ice and concentrated hydrochloric acid and extracted with chloroform. The starting material was recovered quantitatively.

2. The azepine (130 mg) glacial acetic acid (25 ml) and concentrated hydrochloric acid (25 ml) were refluxed together for 1 hour, poured into water and extracted with chloroform. On removal of the solvent, the azepine was recovered in 50% yield.

3. The azepine (30 mg) in an excess of dry pyridine was treated with toluene-p-sulphonyl chloride (25 mg) at room temperature overnight, but the starting

material (24 mg) was recovered.

4. The azepine was recovered unchanged after heating for 2 hours in polyphosphoric acid at 100°.

The Dipotassium Salt of N,N'-(Ditoluene-p-sulphonyl)-o-Phenylenediamine

A solution of potassium hydroxide (2.1 g) in aqueous ethanol (10%; 5 ml) was added to a hot solution of N,N'-(ditoluene-p-sulphonyl)-o-phenylenediamine (7.04 g) in ethanol (200 ml) and the mixture cooled to 20°. Addition of excess acetone gave the dipotassium salt (4.8 g) as a flocculent precipitate. This was filtered and sucked dry, m.p. > 300°. FOUND: C, 47.36; H, 3.8. $C_{20}H_{18}N_2O_4S_2K_2$ requires: C, 48.77; H, 3.66%. ν_{max} 1608; 1307; 1183 cm^{-1}.

Attempted condensation of N,N'-(Ditoluene-p-sulphonyl)-o-Phenylenediamine with 1,3-Dichloroacetone

(a) The disulphonamide (9.7 g), 1,3-dichloroacetone (3.1 g), anhydrous sodium carbonate (25 g) and dry toluene (500 ml) were heated together, under reflux, for 50 hours, cooled and left at 20° for 70 hours, before filtration. The disulphonamide (9.1 g) was recovered on evaporation of the toluene.

(b) The disulphonamide (2.2 g) was recovered unchanged after heating with 1,3-dichloroacetone (655 mg) in pyridine (50 ml) for 1 hour at 95°.

(c) The dipotassium salt (474 mg) of the above sulphonamide, was heated in benzene, under reflux, with 1,3-dichloroacetone (124 mg) for 3 hours. After washing with dilute hydrochloric acid and water, evaporation of the benzene gave the disulphonamide (326 mg).

(d) Heating the dipotassium salt (1.01 g) with 1,3-dichloroacetone (234 mg) in water (100 ml), under reflux for 3 hours, gave the starting disulphonamide (0.65 g).

1,3-Dibromoacetone[70]

Bromine (650 ml) was added, dropwise to a stirred mixture of acetone (500 ml), water (1,600 ml) and glacial acetic acid (375 ml) at 70°. The solution was cooled, water (800 ml) was added and the mixture left at 20° for 2 hours before decantation. The oil (546 g) which remained, was separated into its components by fractional distillation through a packed

column: 1,3-dibromoacetone (b.p. 95-98°/20 mm; lit. b.p. 97-98°/21-22 mm) formed colourless crystals m.p. 20° on standing. Yield 33%. FOUND: Br, 71.5. Calculated for $C_3H_4Br_2O$: Br, 72%.

The other products were monobromoacetone (b.p. 43-44°/20 mm) and 1,1-dibromoacetone (b.p. 66-70°/20 mm).

N,N'-(Ditoluene-p-sulphonyl)-1, 2, 3, 4-Tetrahydro-3-oxo-benzo [b] -1,5-diazepine

1. A mixture of the dipotassium salt of N,N'-(ditoluene-p-sulphonyl)-o-phenylenediamine (1.75 g), 1,3-dibromoacetone (700 mg) and dry benzene (50 ml) was heated under reflux for 2 hours before filtration. The gum (1.5 g) obtained on evaporation of the filtrate was chromatographed on neutralised alumina: elution of the column with benzene gave the product (250 mg) which crystallised from methanol in colourless cubes m.p. 182°. FOUND: C, 58.95; H, 4.8; N, 6.1. Molecular weight by isothermal distillation 458. $C_{23}H_{22}N_2O_5S_2$ requires: C, 58.8; H, 4.7; N, 5.95%. Molecular weight 470. ν_{max} 1762; 1352; 1224 cm^{-1}.

Elution of the above column with chloroform afforded N,N'-(ditoluene-p-sulphonyl)-o-phenylenediamine (865 mg).

2. A mixture of the potassium salt (1.8 g), 1,3-dibromoacetone (700 mg) and water (80 ml) was heated at 80° for 3 hours and filtered. The dried residue was chromatographed on alumina: elution with benzene gave the product (216 mg); m.p. and mixed m.p. with the diazepine from above, was 182°.

Elution of the column with chloroform gave N,N'-(ditoluene-p-sulphonyl)-o-phenylenediamine (820 mg) as before.

3. A mixture of N,N'-(ditoluene-p-sulphonyl)-o-phenylenediamine (6.9 g), 1,3-dibromoacetone (3.75 g), anhydrous sodium carbonate (20 g) and dry toluene (1 litre) was heated under reflux for 24 hours. The wine coloured solution was filtered and the residue extracted with chloroform. Evaporation of the organic extracts gave a gum (8.05 g) which was chromatographed on neutralised alumina: elution of the column with benzene gave the

product (2.4 g) which crystallised from methanol in cubes. The m.p. and mixed m.p. with the product from (1) was 182°. The 2,4-dinitrophenylhydrazone crystallised from nitrobenzene in yellow needles m.p. 208°. FOUND: C, 53.95; H, 4.0; N, 12.75. $C_{29}H_{26}N_6O_8S_2$ requires C, 53.55; H, 4.0; N, 12.9%. ν_{max} 3333; 1626; 1600; 1511 cm^{-1}.

Elution of the afore-mentioned column with chloroform gave the starting disulphonamide (4.3 g).

Reactions of N,N'-(Ditoluene-p-sulphonyl)-1, 2, 3, 4-Tetrahydro-3-oxo-benzo [b] -1,5-diazepine

(a) A nitrogen saturated solution of the diazepine (1 g) in dry toluene (180 ml) was added to a nitrogen saturated suspension of sodium methoxide (2 g) in dry toluene (50 ml). The mixture was left at 20° for 48 hours, poured into water (200 ml) and the toluene layer separated. Evaporation of the toluene gave a red solid (550 mg) which crystallised from ethanol in plates m.p. 242°. FOUND: C, 61.54; H, 4.2; N, 8.37. $C_{16}H_{14}N_2O_3S$ requires C, 61.15; H, 4.45;

N, 8.92%. (Molecular weight by isothermal distillation; 350. $C_{16}H_{14}N_2O_3S$ requires 314.) ν_{max} 3390; 1608; 1170; 1156 cm^{-1}. Nuclear magnetic resonance peaks at ~ 1.5-3.6τ; 7.65τ(area ratio 10 : 3).

(b) When the above reaction was repeated using potassium tertiary butoxide, the red compound (m.p. 242°) was obtained in 70% yield.

(c) Freshly sublimed potassium tertiary butoxide (1.3 g) was added to a nitrogen saturated solution of the diazepine (800 mg) in dry dimethylsulphoxide (10 ml). The mixture was left at 20° for 24 hours, poured into water (100 ml) and extracted with chloroform.
A red compound (700 mg) was obtained on evaporation of the chloroform; it crystallised from ethanol in deep-red plates m.p. 242° (mixed m.p. with compound from (a); 242°).

(d) The diazepine (5.1 g), anhydrous sodium carbonate (22 g) and toluene (200 ml), were heated together under reflux for 48 hours and filtered. The filtrate was washed with water, dried and evaporated, leaving a red solid

(2.2 g) which crystallised from ethanol in deep-red plates. The m.p. and mixed m.p. with the product from (a) was 242°.

Reactions of the compound $C_{16}H_{14}N_2O_3S$ (m.p. 242°)

1. Potassium hydroxide (2 g) was added to a solution of the red compound (250 mg; m.p. 242°) in ethanol (150 ml) and the mixture heated under reflux for 5 hours, then cooled and poured into water. Filtration gave the starting material (220 mg).

2. A mixture of the red compound (m.p. 242°; 268 mg), concentrated hydrochloric acid (5 ml), glacial acetic acid (5 ml) and water (12 ml), was heated under reflux for 5 hours, before adding water (100 ml) and extracting with chloroform. Evaporation of the latter left the starting compound (221 mg).

2,4-Dimethyl-benzo [b] -1,5-diazepine[28] sublimed at 90° (0.5 mm) and crystallised from benzene in colourless cubes m.p. 130° (lit. m.p. 131-133°). FOUND: C, 76.75; H, 6.95. Calculated for $C_{11}H_{12}N_2$: C, 76.8; H, 7.0. ν_{max}: 1639 cm^{-1}.

Reactions of 2,4-Dimethyl-benzo [b] -1,5-diazepine

(a) Perchloric acid (5 ml; 70%) was added to a solution of the diazepine (1 g) in glacial acetic acid (20 ml). The purple crystals which separated were filtered, dried and crystallised from water in needles m.p. 185°. FOUND: C, 45.10; H, 4.95; N, 9.65. $C_{11}H_{13}ClN_2O_4H_2O$ requires C, 45.43; H, 5.16; N, 9.64%. ν_{max} 3333; 3226; 3175; 1639; 1600; 1064 cm^{-1}.

The perchlorate (3.1 g) in water (200 ml) was shaken with dilute potassium hydroxide solution and the mixture extracted with chloroform. The latter was washed with water, dried and evaporated leaving 2,4-dimethyl-benzo [b] -1,5-diazepine (2.3 g).

(b) Triphenylmethylperchlorate (1.6 g) was added to a solution of the diazepine (1.3 g) in dry methylene chloride (20 ml). The solution was left at 20° for 24 hours, excess petroleum ether (b.p. 60-80°) was added and the precipitate filtered. The residue (1.05 g) crystallised from methylene chloride in purple needles. The m.p. and mixed m.p. with the

perchlorate obtained from (a) was 185°.

Evaporation of the filtrate gave triphenylmethane (234 mg) m.p. 92° (lit. m.p. 94°)[71].

(c) Toluene-p-sulphonyl chloride (5.9 g) was added to a solution of the diazepine (6.1 g) in dry pyridine (100 ml). The mixture was left at 20° for 24 hours, poured into excess ice and concentrated hydrochloric acid and filtered. The dried residue (4 g) was chromatographed on alumina: elution of the column with chloroform-methanol (99 : 1) gave a compound (2.8 g) which separated from methanol-methylene chloride as a deep red amorphous solid m.p. > 360°.

FOUND: C, 66.6; H, 5.75; N, 8.5; S, 9.1.

$C_{18}H_{18}N_2O_2S$ requires C, 66.25; H, 5.5; N, 8.6; S, 9.81%; ν_{max} 1600; 1379; 1160 cm^{-1}.

(Molecular weight by isothermal distillation 346; $C_{18}H_{18}N_2O_2S$ requires 326.) The product was unaffected by heating with dilute hydrochloric acid and by heating with excess concentrated sodium hydroxide solution, under reflux.

N-(Toluene-p-sulphonyl) dihydroisoindole[38] was obtained in 55% yield by heating ω,ω'-dibromo-o-xylene (26 g) and p-toluenesulphonamide (17 g) together with anhydrous sodium carbonate (10 g), sodium ethoxide (6 g) and ethanol (250 ml) under reflux for 3 hours. The product (14 g) crystallised from ethanol in colourless needles m.p. 176°.

FOUND: C, 65.8; H, 5.4; N, 5.6. Calculated for $C_{15}H_{15}NO_2S$: C, 65.95; H, 5.5; N, 5.13%.

ν_{max} 1600; 1342; 1163 cm^{-1}.

Reactions of N-(Toluene-p-sulphonyl) dihydroisoindole

1. A solution of the sulphonamide (2.0 g) in dry toluene (80 ml) was added to a suspension of sodium methoxide (2 g) in dry toluene (150 ml) - both were previously saturated with nitrogen. The mixture was left at 20° for 12 hours, poured into water (200 ml) and extracted with chloroform. The starting material (1.9 g) was recovered from the chloroform extract on evaporation.

2. The sulphonamide (2.0 g) was recovered quantitatively after treatment - under nitrogen - with potassium tertiary butoxide (2.2 g) in dry toluene (100 ml)

at 20° for 48 hours.

3. Freshly sublimed potassium tertiary butoxide (2.0 g) was added to a solution of N-(toluene-p-sulphonyl) dihydroisoindole (2.0 g) in dry distilled dimethylsulphoxide (100 ml). The blue coloured solution was shaken at 20° for 24 hours, poured into water (100 ml) and extracted with chloroform. The chloroform extract was washed with dilute sodium hydroxide solution and water, dried and evaporated leaving a blue solid (1.69 g). The product was chromatographed on neutralised alumina: elution with chloroform gave the starting material (1.5 g). Elution of the column with chloroform-methanol (99 : 1) gave a deep purple solid (20 mg) m.p. 281-286°. (This compound was extremely insoluble in organic solvents and could not be purified; it gave a positive sodium nitroprussido colour reaction for sulphur[9].) ν_{max} 3333; 1709; 1613 cm^{-1}.

Dihydroisoindole

N-(toluene-p-sulphonyl) dihydroisoindole (40 g), glacial acetic acid (250 ml) and concentrated hydrochloric acid (50 ml)

were heated together with zinc chloride (40 g.) under reflux. Concentrated hydrochloric acid was added portionwise (25 ml) every 2 hours for a period of 80 hours. The mixture was cooled and diluted with water (500 ml), neutralised with dilute sodium carbonate solution, and extracted with chloroform. The latter was washed with water, dried and evaporated leaving a basic oil (12.7 g). Pure dihydroisoindole (7.5 g) - b.p. 100°/20 mm[72] was obtained by fractional distillation; it formed colourless needles m.p. 20°. FOUND: C, 80.48; H, 7.76; N, 11.5. Calculated for C_8H_9N: C, 80.63; H, 7.61; N, 11.76%.

ν_{max} (liquid film) 3333; 1600 cm^{-1}.

5-Nitrodihydroisoindole[39]

Dihydroisoindole (3.3 g) was added dropwise to ice cold concentrated sulphuric acid (14 ml) and the solution heated at 95° for 5 minutes, then cooled. Analytically pure nitric acid (1.9 ml: 1.425 g) was added dropwise to the solution at 0°, and the mixture allowed to attain room temperature slowly. The solution was neutralised with ammonium hydroxide, saturated with sodium chloride and extracted with chloroform. The chloroform extract was washed with water, dried and evaporated

leaving 5-nitrodihydroisoindole as a brown oil (3.5 g). Colourless crystals (m.p. 247°; lit. m.p.[39] 240-260°) of the mono-acid salt separated from a solution of the product in concentrated sulphuric acid.

N-(Toluene-p-sulphonyl)-5-nitrodihydroisoindole

Toluene-p-sulphonyl chloride (3.2 g) was added to a solution of 5-nitrodihydroisoindole (3.0 g) in dry pyridine (50 ml) at 0°. The mixture was left at 20° for 2 hours, poured into ice and concentrated hydrochloric acid, and the product (3.1 g) collected by filtration. This was washed with dilute hydrochloric acid and water, dried and crystallised from methanol in colourless plates m.p. 165°. Yield 60%. FOUND: C, 56.3; H, 4.0; N, 8.6. $C_{15}H_{14}N_2O_4S$ requires C, 56.65; H, 4.4; N, 8.8%. ν_{max} 1600; 1527; 1379; 1348; 1149 cm^{-1}.

Reactions of N-(Toluene-p-sulphonyl)-5-nitrodihydroisoindole

(a) A nitrogen saturated solution of N-(toluene-p-sulphonyl)-5-nitrodihydroisoindole (1.1 g) in dry toluene (50 ml) was added to a nitrogen saturated suspension of sodium methoxide (1.5 g) in dry toluene (50 ml). The mixture was left at 20° for 48 hours, poured into water (200 ml) and filtered. Evaporation of the toluene gave the starting material (10%). The residue (450 mg;

m.p. 360°) was a deep blue amorphous powder; it was slightly soluble in acetone, methanol and methylene chloride. The product was extracted with the latter solvent and adsorbed onto the top of an alumina column: elution with chloroform-methanol (99 : 1) gave a solid (95 mg) which crystallised from acetone/methanol in purple needles m.p. > 360°. FOUND: C, 58.62; H, 4.25; N, 6.13%. ν_{max} 3390; 1600; 1527; 1379; 1348; 1149; 836 cm^{-1}.

The pigment was insoluble in dilute hydrochloric acid and dilute aqueous sodium hydroxide solution; it dissolved in concentrated perchloric acid giving an inky blue solution.

(b) The sulphonamide (842 mg), sodium ethoxide (1 g) and ethanol (100 ml) were heated together under reflux for 1 hour, cooled and filtered. Extraction of the residue with methylene chloride followed by evaporation gave an insoluble blue-black amorphous powder (222 mg; m.p. > 360°). (The infra-red spectrum was identical with the product obtained from (a).)

(c) Potassium tertiary butoxide (1.5 g) was added to a solution of the sulphonamide (1.65 g) in dry dimethylsulphoxide (200 ml) and the mixture left under nitrogen at 20° for 48 hours, before pouring into water and filtering. The residue (1.1 g) was identical with the purple compound obtained from (a) above. It gave a positive sodium nitroprusside colour reaction for sulphur[9].

Phenylglyoxal Monoanil (Trans-isomer)

(a) A mixture of phenylglyoxal hydrate[49] (7.95 g), aniline (4.6 ml), glacial acetic acid (10 ml) and ethanol (50 ml) was heated on the steam bath for 30 minutes. After addition of water (12 ml) and cooling, a yellow oil separated - thin layer and paper chromatography showed this to contain at least five products. The mixture was adsorbed on to the top of an alumina column from benzene; elution with benzene/light petroleum (9 : 1) gave a dimer of phenylglyoxal anil which crystallised from petroleum ether (b.p. 60-80°) in yellow needles m.p. 76°. Yield 32%. FOUND: C, 80.3; H, 5.25; N, 7.2. Molecular weight (Rast) 408.

$C_{28}H_{22}N_2O_2$ requires: C, 80.4; H, 5.25; N, 6.75%. Molecular weight 418. ν_{max} 1666; 1589 cm^{-1}. λ_{max} (in ethanol): 205; 247; 337 m μ. (ε : 44,640; 33,640; 10,051.)

Elution of the column with chloroform gave the trans-anil (m.p. 145°) which crystallised from ethanol in yellow plates. Yield 10.5%. FOUND: C, 80.6; H, 4.8; N, 7.05. Molecular weight (by isothermal) distillation) 214. $C_{14}H_{11}NO$ requires C, 80.4; H, 5.25; N, 6.75%. Molecular weight 209. ν_{max} 1666; 1599 cm^{-1}. λ_{max} (in ethanol) 207; 260 m μ. (ε : 22,360; 13,800.) Treatment of the anil with 2,4-dinitrophenylhydrazine hydrochloride in ethanol, gave a red oil which could not be crystallised.

(b) The cis-isomer (88 mg; m.p. 210°) was shaken with a palladised-carbon catalyst (100 mg; 5%) in ethanol (100 ml) at 20° for 16 hours. The product (75 mg) which was obtained on evaporating the filtrate, crystallised from ethanol in yellow plates m.p. 145°. The mixed m.p. with the trans-anil was undepressed.

Attempted Isomerisation of the Anils of Phenylglyoxal[53]

1. The cis-isomer (160 mg; m.p. 210°) was shaken in ethanol (100 ml) with excess palladium-barium carbonate catalyst at 20° for 24 hours. After filtration, the ethanol was evaporated to give the starting material (106 mg; m.p. 210°).

2. The cis-isomer (176 mg) was unaffected by shaking in dilute aqueous-ethanolic hydrochloric acid (100 ml) for 1 week at room temperature.

3. When the trans-isomer (m.p. 145°) was heated above its melting point it decomposed to give a black tar.

4. A solution of the cis-isomer (76 mg) in dry distilled dioxan was saturated with nitrogen and irradiated with ultra-violet light for 2 hours. Evaporation of the dioxan gave the starting material quantitatively.

5. The trans-isomer (70 mg) was recovered unchanged after irradiation in dioxan (50 ml) with ultra-violet light for 2 hours.

Reduction of the Anils of Phenylglyoxal1

(a) A solution of phenylglyoxal mono-anil (cis-isomer; 76 mg) in ethanol (100 ml) was shaken at 20° for

24 hours with hydrogen gas and palladised charcoal (100 mg; 5%). Evaporation of the filtrate gave a product (63 mg) which crystallised from methanol in colourless cubes m.p. 188°. FOUND: C, 83.6; H, 5.5; N, 7.3%. Molecular weight (mass spectroscopy) 402. $C_{28}H_{22}N_2O$ requires C, 83.6; H, 5.5; N, 7.0%; M, 402. ν_{max} 3310; 1575; 1235 cm^{-1}. λ_{max} (in ethanol) 210; 242; 286; 337 m μ. (ε: 26,500; 28,600; 24,400; 18,600.)

(b) As in (a) with palladised barium carbonate catalyst. The yield of material m.p. and mixed m.p. 188° was 20%. The remainder was the starting material.

(c) Phenylglyoxal cis-anil (314 mg), glacial acetic acid (150 ml) and water (10 ml) were heated together on the steam bath for 1 hour with zinc dust (6 g). After filtration, the reaction mixture was diluted with water (200 ml) and extracted with chloroform. This was washed with dilute ammonium hydroxide and water, dried and evaporated to give an oil (217 mg) which was chromatographed on alumina. Elution of the

column with benzene gave the product (210 mg) which crystallised from methanol in colourless cubes: m.p. and mixed m.p. with the compound from (a) was 188°.

Reactions of the Furan Derivative (i.e. LXII, LXIII, or LXIV)

(a) The above compound (m.p. 188°) was recovered unchanged after heating with excess liquid ammonia in a sealed tube at 140° for 40 hours.

(b) The compound (m.p. 188°) was recovered quantitatively after treatment with excess toluene-p-sulphonyl chloride in dry pyridine at 20° for 1 week.

(c) The compound was unaffected by acetic anhydride in dry pyridine at 20° for 24 hours.

(d) The compound (120 mg; m.p. 188°) was recovered unchanged after heating in ethanol (50 ml) with concentrated hydrochloric acid (10 N; 10 ml) for 2½ hours.

Amino-Ketone (LXVI) from Phenacylaniline

(a) Phenacylaniline (1.2 g) and ethanol (150 ml) were shaken at 20° for 16 hours with palladised charcoal

(100 mg; 5%). The product crystallised from ethyl acetate in yellow needles m.p. 187°. Yield 90%. FOUND: C, 79.6; H, 5.9; N, 6.5. Molecular weight (by mass spectroscopy) 420. $C_{28}H_{24}N_2O_2$ requires: C, 79.95; H, 5.75; N, 6.65%. Molecular weight 420. ν_{max} 3330; 1668; 1600 cm^{-1}. λ_{max} (in chloroform) 249; 283 mμ. (ε : 38,360; 6,613.)

(b) A nitrogen saturated solution of N-(toluene-p-sulphonyl) phenacylaniline (1.2 g) in dry toluene (200 ml) was added to a nitrogen saturated suspension of sodamide (1 g) in dry toluene (100 ml). After 14 days at 20°, the reaction mixture was poured into water (200 ml) and extracted with chloroform. The product (600 mg) crystallised as before m.p. and mixed m.p. 187°.

(c) When phenacylaniline in ethanol was agitated in a stream of oxygen for 6 days the product was obtained identical with that in (a) and (b). Yield 2%. The mass spectrum of (LXVI) showed the following peaks: 420, 327, 315, 222, 210, 116 and 79.

The 2,4-dinitrophenylhydrazone crystallised from glacial acetic acid m.p. 272°. FOUND: N, 17.9. $C_{40}H_{32}N_{10}O_8$ requires N, 18.0%.

Reactions of the Amino-Ketone (LXVI)

1. The amino-ketone was recovered unchanged after heating with excess toluene-p-sulphonyl chloride in pyridine at 95° for 1 hour.

2. The compound (LXVI) was recovered quantitatively after heating with a mixture of ethanol (150 ml) and concentrated hydrochloric acid (10 ml) for 3 hours under reflux.

3. The amino-ketone (275 mg) was shaken in ethanol (200 ml), with palladised charcoal (500 mg; 5%) at 20° for 5 days. The product (150 mg) separated from chloroform as a white amorphous solid (m.p. > 360°). FOUND: C, 46.69; H, 5.1%. ν_{max} 1600; 1380 cm^{-1}. The Lassaigne test for nitrogen was negative.

4. The amino-ketone (234 mg) in dioxan (50 ml) was shaken at 20° for 24 hours with hydrogen on a palladium-carbon catalyst. The product (230 mg) separated as in (3)

m.p. > 360°. The same product was obtained when the dimer of phenylglyoxal mono-anil (m.p. 76°) was shaken in ethanol with hydrogen on a palladised charcoal catalyst.

1,2-Dibromodibenzoylethane

Bromine (1 ml) was added, in one lot, to a suspension of 1,2-dibenzoylethylene[55] (4.2 g) in water (10 ml) at 95°, and the mixture stirred under reflux for 10 minutes before filtration. The residue (6.6 g) crystallised from ethanol in colourless cubes m.p. 190°. Yield 96%. FOUND: C, 48.21; H, 2.96; Br, 39.98. Calculated for $C_{16}H_{12}Br_2O_2$: C, 48.49; H, 3.03; Br, 40.4%. ν_{max} 1684; 1600 cm^{-1}.

Attempts to prepare 1,2-Diiododibenzoylethane

1. 1,2-Dibromodibenzoylethane (0.93 g), sodium iodide (1.5 g) and acetone (150 ml) were heated together under reflux for 2 hours[60]. Aqueous sodium thiosulphate solution (10%) was added to the cooled solution, until the iodine colour was completely discharged, and the mixture poured into water (250 ml). After filtration, the residue was dried and

crystallised from methanol in yellow needles. The m.p. and mixed m.p. with 1,2-dibenzoylethylene did not depress. Yield 95%.

2. 1,2-Dibenzoylethylene (1 g), iodine (1 g) and water (100 ml) were heated together under reflux for 1 hour before adding excess sodium thiosulphate solution and extracting with chloroform. The product (1.52 g) was a black tar which could not be purified.

1-Anilino-1,2-dibenzoylethylene

(a) 1,2-Dibromodibenzoylethane (1.3 g), aniline (1.4 ml) and ethanol (50 ml) were heated together, under reflux, for 5 hours and left at 20° for 12 hours before filtration. The residue (200 mg; m.p. 190°) was identical with the starting material. The filtrate was evaporated to dryness, excess water was added and the mixture extracted with chloroform. Evaporation of the chloroform gave an oil (650 mg) which was chromatographed on alumina: elution of the column with benzene gave the product (400 mg); it crystallised from methanol in yellow plates m.p. 129°.

Yield 44%. FOUND: C, 81.19; H, 5.12; N, 4.35. $C_{22}H_{17}NO_2$ requires C, 80.74; H, 5.2; N, 4.28%. ν_{max} 3067; 1667; 1626; 1572 cm^{-1}. λ_{max} (in ethanol) 256, 374 mμ. (ε: 18,485; 15,895) The nuclear magnetic resonance spectrum showed peaks at 1.75-3.15 τ and 3.84 τ; their respective areas were in the ratio 15 : 1.

Elution of the column with chloroform-methanol (99 : 1) gave a red tar (255 mg) which could not be purified.

(b) 1,2-Dibromodibenzoylethane (1.9 g), aniline (2 ml) and water (100 ml) were heated together on the steam bath for ½ hour, cooled and extracted with chloroform. Evaporation of the chloroform gave a red tar (2.2 g) from which the starting material (710 mg) was recovered - by crystallisation from ethylacetate. Evaporation of the mother liquors gave an oil which was chromatographed on an alumina column: elution with benzene gave the product (690 mg); it crystallised from methanol in plates m.p. 129°. Yield 70%.

Reduction of the product (600 mg) with hydrogen gas and a palladium-carbon catalyst (500 mg; 5%) in ethanol (300 ml) at 20° for 24 hours gave a tar (430 mg) which chromatography on alumina showed to be a complex mixture: elution of the column with petroleum ether (b.p. 60-80°) gave an oil (50 mg) which crystallised, with difficulty, from methanol in yellow cubes m.p. 144°. ν_{max} 1681; 1639; 1597 cm^{-1}.

Further elution of the column with chloroform gave tars which could not be purified.

1,2-Dibenzoyl-1-methylanilinoethylene

1,2-Dibromodibenzoylethene (6.6 g), methylaniline (2 g) and ethanol (150 ml) were heated together under reflux for 8 hours. The solution was cooled, poured into water (200 ml) and extracted with chloroform. The chloroform extract was washed with dilute hydrochloric acid and water, dried and evaporated. The product (5.6 g) crystallised from methanol in yellow needles m.p. 142°. Yield 98%. FOUND: C, 81.15; H, 5.93; N, 3.98. $C_{23}H_{19}NO_2$ requires C, 80.95; H, 5.6; N, 4.10%. ν_{max} 1666; 1625; 1608; 1587; 1567 cm^{-1}. λ_{max} (in ethanol) 256; 341 mμ.

(ε : 20,797; 18,300.) The nuclear magnetic resonance spectrum showed peaks 1.75-2.9, 3.9 and 6.67 τ; their areas were in respective ratio 15 : 1 : 3.

Acetylation of 1,2-dibenzoyl-1-methylanilinoethylene

The enaamine (1.95 g), acetyl chloride (6 ml), acetic anhydride (10 ml) and concentrated sulphuric acid (2 ml) were heated together at 50° for 5 minutes, cooled and left at 20° for 15 minutes before pouring into water (200 ml) and extracting with chloroform. The latter was washed with water, dried and evaporated to give an oil (2.1 g) which was chromatographed on alumina: elution with petroleum ether (b.p. 60-80°) gave a yellow oil (200 mg) which crystallised from light petroleum in cubes m.p. 122°. FOUND: C, 77.75; H, 5.26; N, 3.82. $C_{25}H_{21}NO_3$ requires C, 77.85; H, 5.48; N, 3.66%. ν_{max} 1653; 1603; 1587; 1565 cm^{-1}.

The Sodium Salt of N-(Toluene-p-sulphonyl) Aniline

A solution of sodium hydroxide (1 mole) in ethanol (5 ml) was added to a hot solution of N-(toluene-p-sulphonyl) aniline (2 g) in ethanol (5 ml). The solution was cooled and diluted with acetone (200 ml). The product (2.1 g) was obtained on filtration.

1,2-Dibenzoyl-1-(N-toluene-p-sulphonanilino) ethylene

(a) 1,2-Dibromodibenzoylethane (6.5 g), the sodium salt of N-(toluene-p-sulphonyl) aniline (9 g) and benzene (200 ml) were heated together, under reflux, for 7 hours, cooled and filtered. The filtrate was washed with dilute aqueous sodium hydroxide solution, dilute sulphuric acid and water, dried and evaporated. The yellow oil (6.45 g) thus obtained, was chromatographed on an alumina column; elution with light petroleum-benzene (9:1) gave the product (6.2 g); it crystallised from ethanol in colourless needles m.p. 172°. Yield 82.5%. FOUND: C, 72.38; H, 4.45; N, 2.83. $C_{29}H_{23}NO_4S$ requires: C, 72.36; H, 4.78; N, 2.91%. ν_{max} 3067; 1684; 1658; 1600; 1361; 1176 cm^{-1}. The nuclear magnetic resonance spectrum showed peaks at 1.7-3.0, 3.36 and 7.52τ their respective areas were in the ratio 19 : 1 : 3.

(b) N-(toluene-p-sulphonyl) aniline (800 mg), 1,2-dibromo-dibenzoylethane (626 mg), anhydrous sodium carbonate (2 g) and toluene (100 ml) were heated together under

reflux for 30 hours before filtration. Evaporation of the toluene gave an oil (1.4 g) from which N-(toluene-p-sulphonyl) aniline (253 mg) and 1,2-dibromo-dibenzoylethane (73 mg) were obtained by fractional crystallisation from methanol. Evaporation of the mother liquors gave the product (80 mg) which crystallised from methanol in needles m.p. and mixed m.p. 172°.

(c) N-(toluene-p-sulphonyl) aniline (5.8 g), 1,2-dibromo-dibenzoylethane (5.5 g), anhyrous sodium carbonate (20 g) and decalin (150 ml) were heated together under reflux for 5 minutes, stirred at 180° for 2 hours and left at 20° for 12 hours before filtration.
The filtrate was cooled to 0° and the decalin decanted off leaving a red tar. The latter was washed thoroughly with petroleum ether (b.p. 60-80°) and chromatographed on an alumina column. Elution with benzene/light petroleum (1 : 1) gave an oil (586 mg) which distilled at 160° (0.5 mm) and crystallised from methanol in needles m.p. 170-171°.

Reactions of 1,2-dibenzoyl-1-(N-toluene-p-sulphonanilino) ethylene

1. A solution of the sulphonamide (2.6 g) in benzene (150 ml) was saturated with nitrogen and added to a suspension of sodium methoxide (2.2 g) in benzene (150 ml). The mixture was left - under nitrogen - at 20° for 12 hours, then poured into water (300 ml) and the benzene layer separated. The aqueous layer was extracted with chloroform, and the combined organic extracts washed with water, dried and evaporated. The product (1.1 g) crystallised from ethanol in yellow needles m.p. and mixed m.p. with 1-anilino-1,2-dibenzoyl-ethylene was 129°.

2. The sulphonamide (900 mg), acetic anhydride (5 ml), acetyl chloride (3 ml) and concentrated sulphuric acid (6 drops) were heated together at 50° for 1 minute, cooled and left at 20° for 15 minutes before pouring into water and extracting with chloroform. Evaporation gave an oil (1 g) which crystallised from ethanol in needles m.p. and mixed m.p. with the starting material was 172°. (80% recovery).

Evaporation of the mother liquors gave an oil (124 mg) which was chromatographed on an alumina column: elution with benzene gave an oil (15 mg) which could not be crystallised. ν_{max} 1656; 1608; 1587; 1567; 1351 cm^{-1}. λ_{max} (in ethanol) 209; 241; 322 m μ. ($E^{1\%}_{1\ cm}$ 6,794; 4,348; 4,348.)

1,2-Dianilinosuccinic acid

Aniline (170 g) was added to a hot solution of 1,2-dibromosuccinic acid (85 g) in water (800 ml). The solution was heated, under reflux, for 1 hour, cooled and filtered. The residue (59 g) crystallised from benzene in yellow needles m.p. 174° (lit. m.p.[73] for LXXVIII; 175°). ν_{max} 1690; 1666 cm^{-1}. The residue was heated under reflux for 3 hours with aqueous sodium hydroxide solution (500 ml; 10%), then the solution was cooled and acidified with a mixture of hydrochloric acid ($\bar{N}$) and glacial acetic acid (1:1). The product (30 g) was filtered from the solution, then washed with water and dried; it crystallised (m.p. 210-215°) from toluene. FOUND: C, 63.83; H, 5.12; N, 9.03. Calculated for $C_{16}H_{16}N_2O_4$: C, 64.0; H, 5.33; N, 9.33%.

Attempted Tosylation of 1,2-dianilinosuccinic acid

1. Toluene-p-sulphonyl chloride (4 g) in ether (50 ml) was added to a solution of the diacid (3.0 g) in N-sodium hydroxide (20 ml) and the mixture shaken for 3 hours at 20°74. The aqueous layer was separated, acidified to "Congo Red" with dilute hydrochloric acid and filtered. The residue (2.96 g) crystallised from toluene in colourless needles; m.p. and mixed m.p. with the starting material 210°.

2. Toluene-p-sulphonyl chloride (0.82 g) was added to a solution of the diacid (796 mg) in dry pyridine (10 ml) and the mixture left at 20° for 60 hours before pouring into ice and concentrated hydrochloric acid. The diacid (0.76 g) was recovered by filtration.

1,2-Dianilino-diethylsuccinate

1,2-Dianilino-diethylsuccinate 1,2-Dianilinosuccinic acid (3 g), ethanol (15.5 ml), benzene (24 ml) and concentrated sulphuric acid (2 ml) were heated together under reflux for 8 hours, then poured into water (200 ml). The benzene layer was separated, washed with dilute sodium bicarbonate solution and water, dried and evaporated. The product (1.45 g)

crystallised from petroleum ether (b.p. 60-80°) in colourless needles m.p. 148° (lit.[75] m.p. 149°). FOUND: C, 68.10; H, 6.68. Calculated for $C_{20}H_{24}N_2O_4$: C, 67.45; H, 6.74%. ν_{max} 1757 cm^{-1}. The diester (947 mg) was recovered unchanged after treatment with toluene-p-sulphonyl chloride (1 g) in pyridine (20 ml) at 20° for 24 hours.

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